KU LEUVEN

ARENBERG DOCTORAL SCHOOL
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Rhodium(III)-catalyzed annulation for the construction of indolizinone and quinolizinone scaffolds through C(sp^2)-H activation

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Summary

This thesis focuses on several explorations of the construction of indolizinone and quinolizinone scaffolds through rhodium(III)-catalyzed C(sp^2)-H activation followed by annulation with alkynes. Based on the understanding of transition metal-catalyzed C-H activation, as well as knowing the significance of indolizinone and quinolizinone scaffolds, the possibility of combining them is investigated. By different designs of substrate structures, indolizinone and quinolizinone scaffolds could be synthesized in different ways.

Chapter 1 gives a general introduction to rhodium(III)-catalyzed cascade annulations *via* C-H activation, and describes the synthesis of rosettacin and tetrahydropalmatine, as well as late-stage peptide modification. Related pioneering work is briefly described. The goals of the present research are outlined in this chapter.

Chapter 2 presents an intramolecular annulation of alkyne-tethered benzamides through rhodium(III)-catalyzed C-H activation for the synthesis of indolizinone and quinolizinone scaffolds, providing a flexible and efficient synthesis of rosettacin and tetrahydropalmatine.

Chapter 3 depicts a chemoselective rhodium(III)-catalyzed cascade annulation for the construction of indolizinone and quinolizinone scaffolds. Diversification of peptidomimetics and oligopeptides is achieved in a rapid and step-economical manner through the combination of Ugi reaction and microwave-assisted rhodium(III)-catalyzed intramolecular annulation *via* C(sp^2)-H activation.

Chapter 4 introduces an intramolecular cascade annulation of *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the construction of indolizinone scaffolds without adding an external oxidant. Through rhodium(III)-catalyzed sequential C(sp^2)-H activation and C(sp^3)-H amination, diverse indolizinones are obtained under mild conditions by using an internal oxidant.

Chapter 5 shows an intermolecular cascade annulation of 2-acetylenic aldehydes or ketones with *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the formation of isoquinolone and indolizinone scaffolds employing an internal oxidant. The rhodium(III)-catalyzed intermolecular annulation avoids the employment of a stoichiometric external oxidant, harsh conditions and lengthy synthetic operations.

Finally, **General conclusions and perspectives** are highlighted.

Samenvatting

Deze thesis legt de focus op verschillende exploraties van de constructie van indolizinon- en quinolizinon-skeletten door rhodium(III)-gekatalyseerde C(sp^2)-H activatie, gevolgd door annulatie met alkynen. De mogelijkheid tot het combineren van de transitiemetaal gekatalyseerde C-H activatie, en het belang van indolizinon- en quinolizinon-skeletten werd onderzocht. Door het differentiëren van de substraten kunnen de indolizinon- en quinolizinon-skeletten worden gesynthetiseerd op verschillende manieren.

Hoofdstuk 1 geeft een algemene introductie tot rhodium(III)-gekatalyseerde cascade-annulatie door middel van C-H activatie, en beschrijft de synthese van rosettacin en tetrahydropalmatine, inclusief peptide modificaties op een laat stadium. Gerelateerd baanbrekend onderzoek wordt kort beschreven. De doelen van het onderzoek worden in dit hoofdstuk overlopen.

Hoofdstuk 2 bespreekt een intramoleculaire annulatie van benzamiden gekoppeld met een alkyn, door rhodium(III)-gekatalyseerde C-H activatie voor de synthese van indolizinon- en quinolizinon-skeletten. Dit levert een flexibele en efficiënte synthese van rosettacine en tetrahydropalmatine op.

Hoofdstuk 3 geeft een chemoselectieve rhodium(III)-gekatalyseerde cascade annulatie voor de constructie van indolizinon- en quinolizinon-skeletten. Diversificatie van peptidomimetica en oligopeptides werd in een snelle en stap-economische manier bekomen door de combinatie van de Ugi-reactie met een microgolf-geassisteerde rhodium(III)-gekatalyseerde intramoleculaire annulatie via C(sp^2)-H activatie.

Hoofdstuk 4 introduceert een intramoleculaire cascade annulatie van O-gesubstitueerde N-hydroxybenzamides voor de constructie van indolizinon-

skeletten, zonder een extern oxidans toe te voegen. Door rhodium(III)-gekatalyseerde sequentiële C(sp^2)-H activatie en C(sp^3)-H aminatie werden diverse indolizinonen bekomen onder milde omstandigheden door middel van een intern oxidans.

Hoofdstuk 5 toont een intermoleculaire cascade annulatie van 2-acetylenische aldehyden of ketonen met *O*-gesubstitueerde *N*-hydroxybenzamides of *N*-hydroxyacrylamides voor het vormen van isoquinolon- en indolizinone-skeletten, gebruik makend van een intern oxidans. De rhodium(III)-gekatalyseerde intermoleculaire annulatie vermijdt het gebruik van een stoichiometrische hoeveelheid extern oxidans, harde reactieomstandigheden en lange synthesesequenties.

Tot slot worden **algemene conclusies en perspectieven** besproken.

List of abbreviations

Ac	acetyl
ADM	adamantyl
AIBN	2,2'-azobis(2-methylpropionitrile)
Ar	aryl
Boc	*tert*-butyloxycarbonyl
Bn	benzyl
Cp*	pentamethylcyclopentadiene
Cp	cyclopentadiene
Cy	cyclohexyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
DG	directing group
DIAD	diisopropyl azodicarboxylate
DMAP	4-(dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide
DPPA	diphenyl phosphoryl azide
EA	ethyl acetate
Equiv	equivalent
Et	ethyl
iBu	isobutyl
Me	methyl
MIDA	*N*-methyliminodiacetic acid
MW	microwave
NEM	*N*-ethylmorpholine
NMO	*N*-methyl morpholine-*N*-oxide
OMe	methoxyl
PCC	pyridinium chlorochromate
p-cymene	4-isopropyltoluene

Ph	phenyl
Piv	trimethylacetyl
PTSA	*p*-toluenesulfonic acid
r.t.	room temperature
t-AmOH	*tert*-amyl alcohol
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl
*t*Bu	*tert*-butyl
TEA	triethylamine
Tf	tifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFE	trifluoroethanol
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin-layer chromatography
TMB	1,1,3,3-tetramethylbutyl
TMS	trimethylsilyl
TPAP	*tetra*-*n*-propyl ammonium perruthenate

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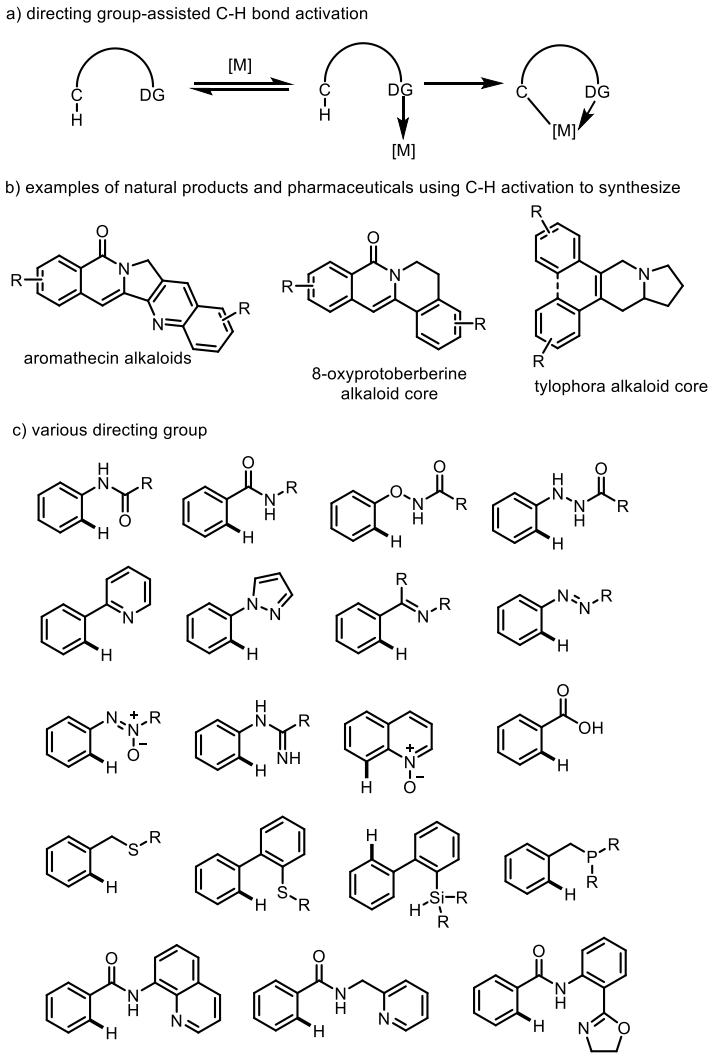
Chapter 1

1. Introduction

1.1. Rhodium-catalyzed cascade annulation *via* C-H activation

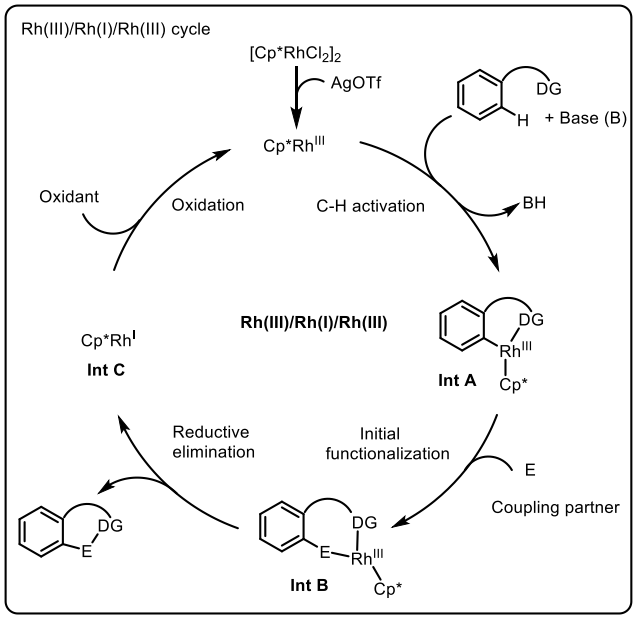
In the past decade, transition metal-catalyzed C-H bond activation has played an important role in synthetic organic chemistry (Scheme 1a).[1] Moreover, this approach has been widely used in the synthesis of natural products and pharmaceuticals (Scheme 1b). Compared to traditional methods, C-H activation does not require preactivated substrates, which typically avoid lengthy synthetic procedures and the generation of lots of waste. Although employing C-H bond as starting points for organic synthesis has been popular, there are still two main problems: cleaving the strong C-H bond and controlling the positional selectivity. To overcome the difficulties, directing group-assisted C-H bond activation has been investigated. Site selectivity could be achieved by the coordination of heteroatoms with transition metal catalysts to improve the necessary substrate-catalyst interactions, resulting in easier cleavage of the C-H bond adjacent to the reactive metal centre. Therefore, the coordination of directing groups with transition metal catalysts is usually treated as the key step during the whole C-H bond functionalization processes. Various monodentate and bidentate directing groups have been developed, such as functional groups involving nitrogen, oxygen, sulfur, phosphorus and silicon (Scheme 1c). By using different transition metal catalysts together with different directing groups, diverse reactions are realized, such as Pd(II)-catalyzed olefination, arylation, carboxylation, acylation, amination, alkoxylation, halogenation and trifluoromethylation, Ru(II)-catalyzed olefination, arylation, hydroxylation and oxidative annulations, and Rh(III)-catlyzed olefination, arylation, alkynylation, acetoxylation, amination, hydroxyamination and oxidative annulation.



Scheme 1 Transition metal-catalyzed C-H bond activation.

$[Cp^*RhCl_2]_2$ was synthesized by Maitlis in 1968.[2] Then it was firstly used in catalytic C-H bond activation reactions by Miura and Satoh,[3] and got lots of important developments by other groups.[4-10] The Cp-derived Rh(III)-complexes have been well-developed to realize a number of catalytic reactions, because of their high reactivity, selectivity, functional-group tolerance and mild reaction conditions.[11] The initial steps of the reaction mechanism are mostly similar (Scheme 2). Firstly, the unreactive 18-electron complex dimer is activated by

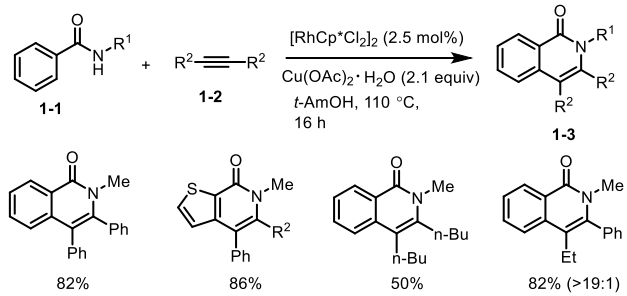
interaction with chloride acceptors like Ag(I)-salts, NaOAc and CsOAc. Then through AMLA (ambiphilic metal-ligand assistance)/CMD (concerted metalation-deprotonation), that is, coordination to a directing group (Lewis base), metalation is achieved under base activation, directing the metal center to a specific C-H bond. Considering the reaction conditions and coupling partners, Rh(III)-catalyzed annulations are performed under redox-neutral conditions or by using stoichiometric external or internal oxidants. Generally, after the formation of a metallacycle (**Int A**) and following functionalization of the coupling partner, the Rh(III)-species (**Int B**) suffers from reductive elimination, leading to the formation of the corresponding new bond and the Rh(I) (**Int C**). The Rh(III) catalyst is regenerated from the Rh(I)-intermidiate by the oxidant. A general Rh(III)/Rh(I)/Rh(III) cycle is involved in most transformations.



Scheme 2 General mechanism of Rh(III)-catalyzed annulations.

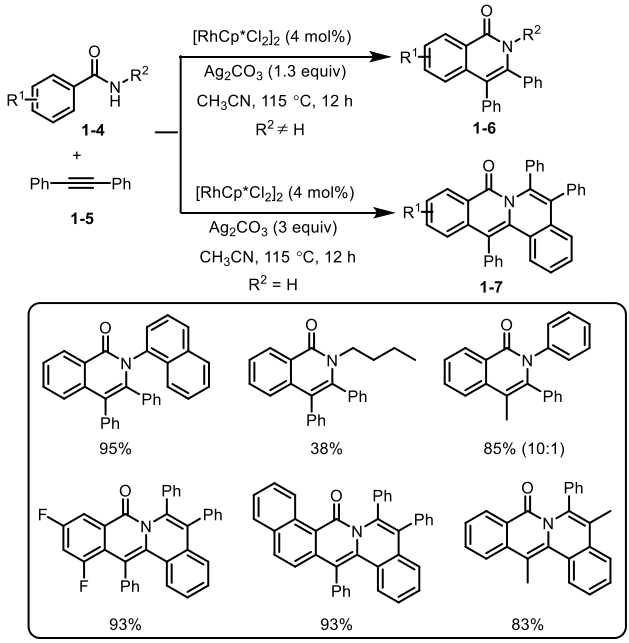
In 2010, Rovis' group reported the oxidative cycloaddition of benzamides **1-1** and alkynes **1-2** to synthesize isoquinolones **1-3** (Scheme 3).[12] This approach showed broad substrate scope and excellent functional-group tolerance by using Rh(III)-catalyzed *ortho* C-H activation employing Cu(II) oxidants, including heteroaryl carboxamides. Unsymmetrical alkynes were also tolerated with

excellent regioselectivity.



Scheme 3 Rh(III)-catalyzed *ortho* C-H activation employing Cu(II) oxidants.

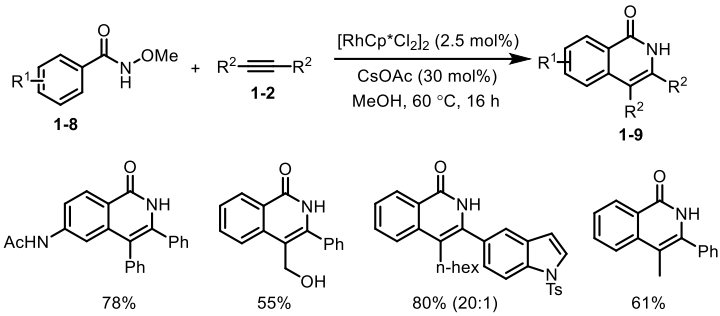
In the same year, Li's group developed a Rh(III)-catalyzed oxidative coupling of secondary benzamides and alkynes for the synthesis of isoquinolones **1-6** through *ortho* C-H activation using Ag(I)-oxidants (Scheme 4).[13] When primary benzamides were utilized, two alkyne units were involved in cascade annulation to give tricyclic products **1-7**.



Scheme 4 Rh(III)-catalyzed annulation for the synthesis of isoquinolones and tricyclic products.

Redox neutral Rh(III)-catalyzed annulation of benzhydroxamic esters

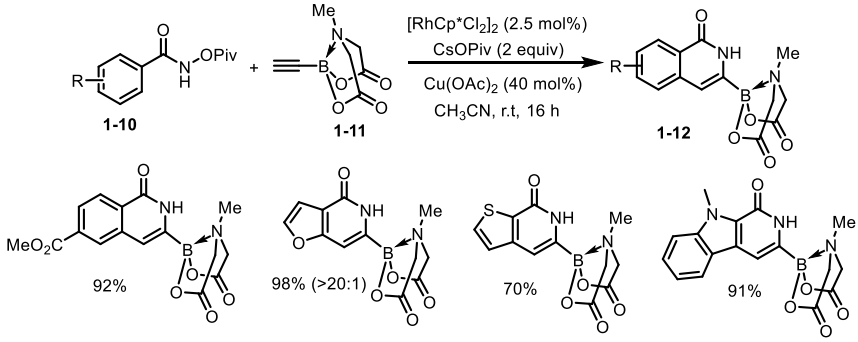
1-8 and alkynes through C-H activation was found by Fagnou's group in 2010 (Scheme 5).[14] Various isoquinolone **1-9** were obtained under mild conditions without adding an external oxidant.



Scheme 5 Rh(III)-catalyzed annulation without adding external oxidant.

Since the finding that the N-O bond cleavage could act as an internal oxidant for transition metal-catalyzed annulation, many new redox-neutral reactions have been developed by using N-O bond cleavage as an internal oxidant.

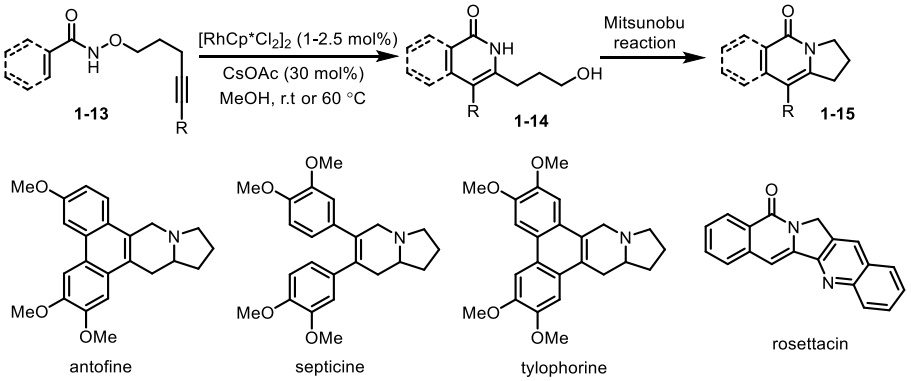
In 2012, Glorius' group reported a redox neutral Rh(III)-catalyzed annulation of benzhydroxamic esters **1-10** and ethynyl MIDA boronates **1-11** to synthesize bench-stable 3-isoquinolone MIDA boronates **1-12** (Scheme 6).[15] This approach featured an internal oxidant, mild conditions and high efficiency. The boron substituted products could serve as useful intermediates for further transformations.



Scheme 6 Rh(III)-catalyzed annulation of benzhydroxamic esters and ethynyl MIDA boronates.

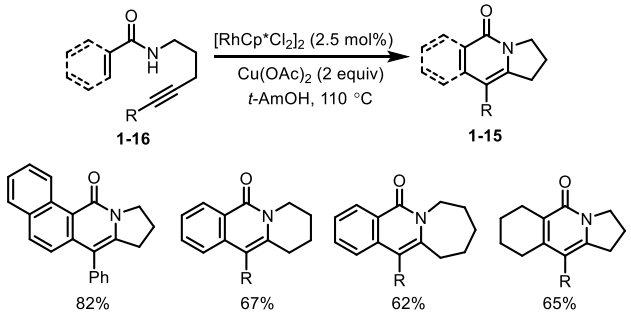
A redox neutral intramolecular annulation of alkyne-tethered hydroxamic esters **1-13** triggered by a Rh(III)-catalyzed C-H activation

for the synthesis of 3-hydroxyalkyl isoquinolones and 6-hydroxyalkyl-2-pyridones **1-14** was developed by the Park group in 2012 (Scheme 7).[16] This method showed high reverse regioselectivity, mild reaction conditions, low catalyst loading and an internal oxidant. Moreover this strategy could be used for the efficient total synthesis of antofine, septicine, tylophorine and rosettacin.



Scheme 7 Rh(III)-catalyzed intramolecular annulation of alkyne-tethered hydroxamic esters.

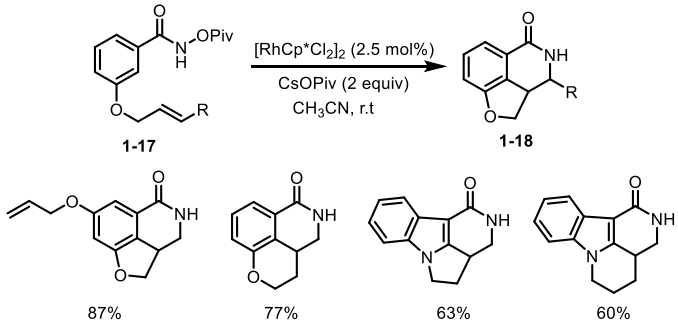
In 2013, Gulías' group reported a Rh(III)-catalyzed intramolecular annulation of alkyne-tethered benzamides or acrylamides **1-16** for the synthesis of polycyclic isoquinolones or indolizinones **1-15** in a straightforward manner (Scheme 8).[17]



Scheme 8 Rh(III)-catalyzed intramolecular annulation of alkyne-tethered benzamides.

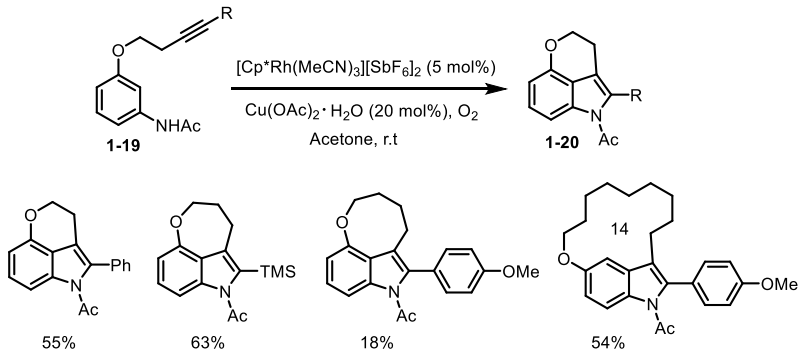
In 2014, Glorius' group developed a redox neutral intramolecular annulation of alkene-tethered benzhydroxamic esters **1-17** through

Rh(III)-catalyzed C-H activation for the synthesis of fused oligocyclic lactam skeletons **1-18** (Scheme 9).[18] This reaction featured oligocyclic systems with high selectivity and a directing group as an internal oxidant.



Scheme 9 Rh(III)-catalyzed intramolecular annulation for the synthesis of fused oligocyclic lactam skeletons.

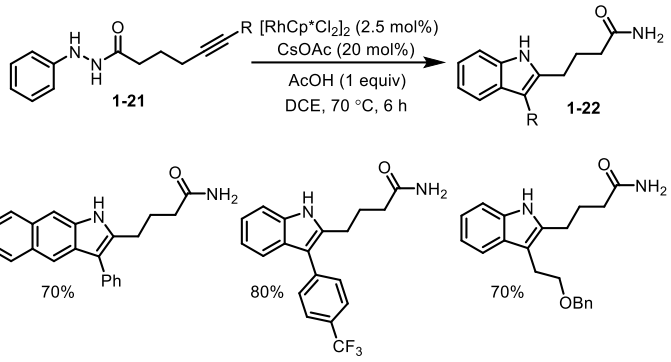
The Rh(III)-catalyzed intramolecular annulation of alkyne-tethered acetanilides **1-19** through C-H activation for the synthesis of fused tricyclic indole scaffolds **1-20** was reported by Jia's group in 2014 (Scheme 10).[19] This method was performed under mild reaction conditions and employed molecular oxygen as the stoichiometric external oxidant.



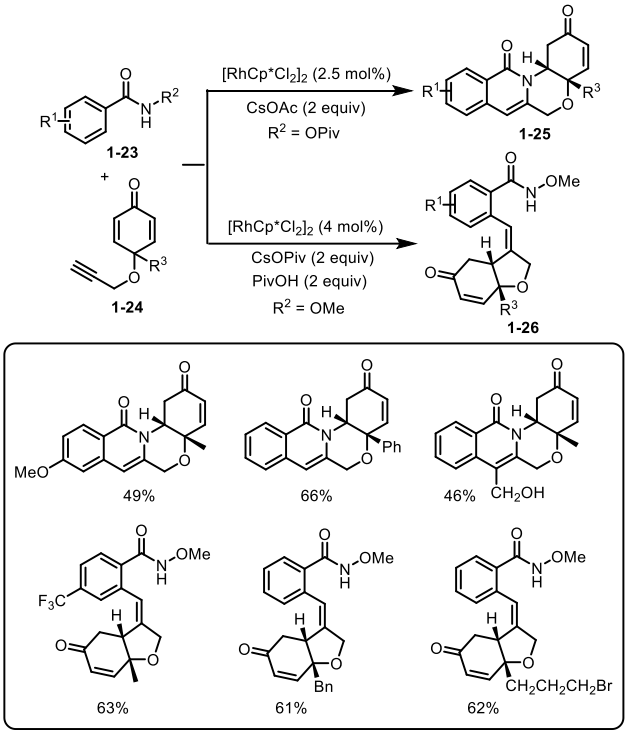
Scheme 10 Rh(III)-catalyzed intramolecular annulation of alkyne-tethered acetanilides.

In the same year, the Li group developed a Rh(III)-catalyzed intramolecular redox neutral annulation of alkyne-tethered arylhydrazines **1-21** for the synthesis of 2-amidoalkyl indoles **1-22** *via* C-H activation (Scheme 11).[20] This reaction did not need external

oxidant and gave the products with high reverse regioselectivity. Moreover this strategy could be utilized for the formal total synthesis of goniomitine.



Scheme 11 Rh(III)-catalyzed intramolecular redox neutral annulation of alkyne-tethered arylhydrazines.

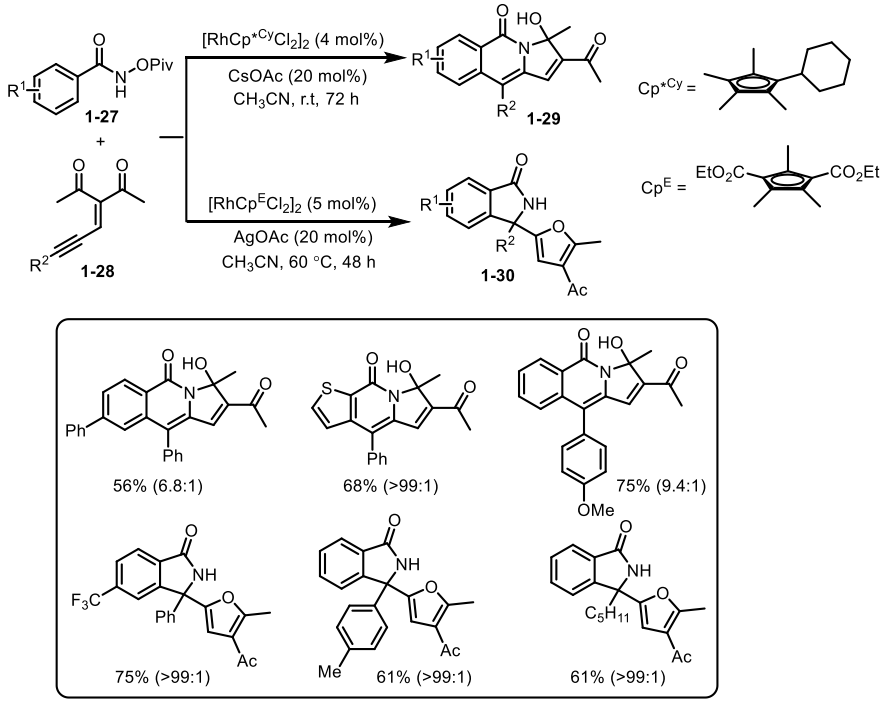


Scheme 12 Rh(III)-catalyzed tunable arylative cyclizations of benzhydroxamic esters and cyclohexadienone-containing 1,6-enynes.

In 2014, Lin's group reported two tunable arylative cyclizations of

benzhydroxamic esters **1-23** and cyclohexadienone-containing 1,6-enynes **1-24** triggered by Rh(III)-catalyzed C-H activation (Scheme 12).[21] Based on the selection of different *O*-substitutions, tetracyclic products **1-25** and *cis*-hydrobenzofuran frameworks **1-26** were yielded through Michael addition process.

In 2017, the Chang group developed a switch between [4+2] and [4+1] annulation by tuning the Cp-ligand of a Rh(III)-catalyzed annulation of benzhydroxamic esters **1-27** and conjugated enynones **1-28** (Scheme 13).[22] When electron-rich Cp-ligands were used, tricyclic isoquinolinones **1-29** were delivered by [4+2] annulation. [4+1] Cyclization products **1-30** were formed using electron-withdrawing Cp-ligands *via* formal carbene transfer.

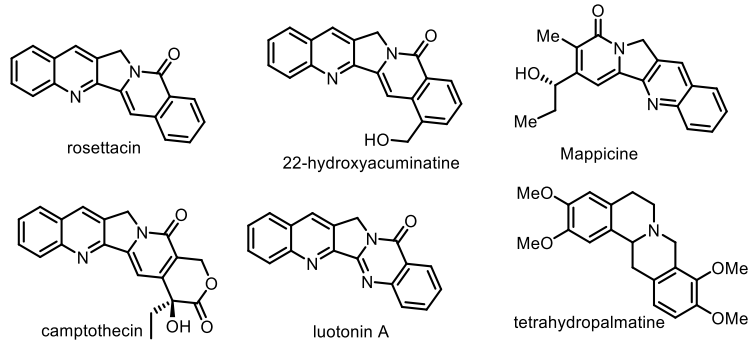


Scheme 13 Rh(III)-catalyzed a switch between [4+2] and [4+1] annulation.

1.2. Synthesis of rosettacin and tetrahydropalmatine

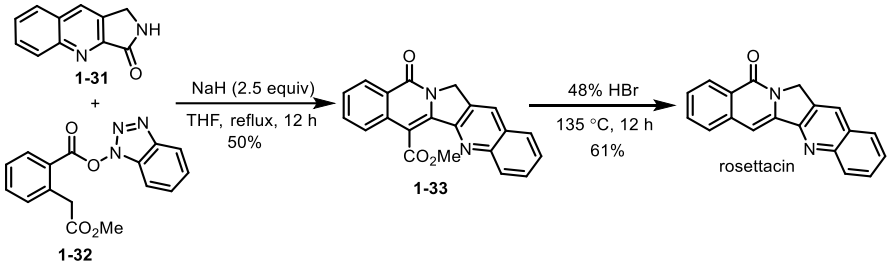
Rosettacin and its analogues, such as 22-hydroxyacuminatine, mappicine, camptothecin and luotonin A, are an important kind of

aromathecin alkaloids,[23-29] which exert a remarkable and modular degree of inhibitory effects on tumor growth by binding to the binary complex formed transiently between DNA and topoisomerase I, preventing DNA relaxation (Scheme 14). So far, several methods have been reported for the total synthesis of rosettacin.[16, 30-37]

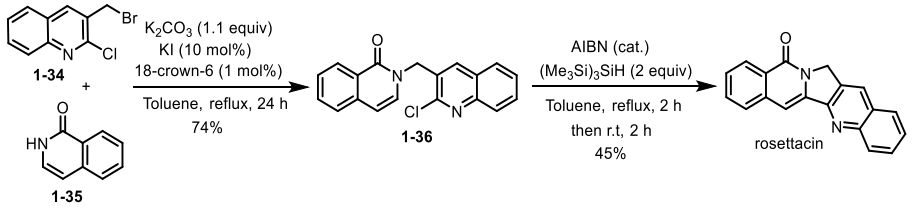


Scheme 14 Rosettacin and its analogues.

In 2008, the Daïch group developed a domino *N*-amidoacylation/aldol-type condensation to synthesize poly-*N*-heterocycle **1-33**, which underwent the removal of the aromatic methoxycarbonyl group to provide rosettacin (Scheme 15).[30]



Scheme 15 Domino *N*-amidoacylation/aldol-type condensation to synthesize rosettacin.

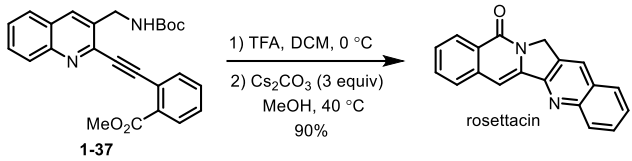


Scheme 16 Radical cyclization to synthesize rosettacin.

Then the same group in 2015 reported an alternative pathway to

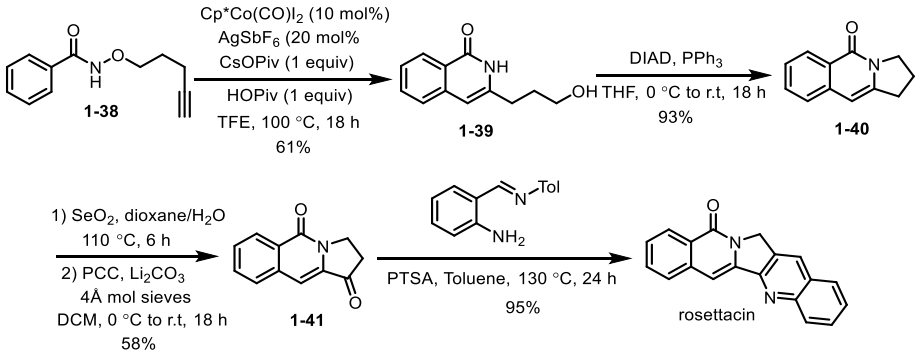
synthesize rosettacin, involving *N*-alkylation of isoquinolin-1(2*H*)-one **1-35** and radical cyclization (Scheme 16).[31]

A flexible strategy for the construction of rosettacin under extremely mild conditions without adding transition metals was developed by Gao's group in 2016 (Scheme 17).[32] This cascade intramolecular cyclization involved a cascade *exo*-type hydroamination followed by spontaneous lactamization with good regioselectivity.



Scheme 17 Cascade hydroamination and lactamization to synthesize rosettacin.

In 2017, Glorius' group reported a Cp*Co^{III}-catalyzed intramolecular C-H activation approach for the synthesis of isoquinolone **1-39** (Scheme 18).[33] Then the product underwent Mitsunobu reaction, sequential oxidation and cyclization to deliver rosettacin.

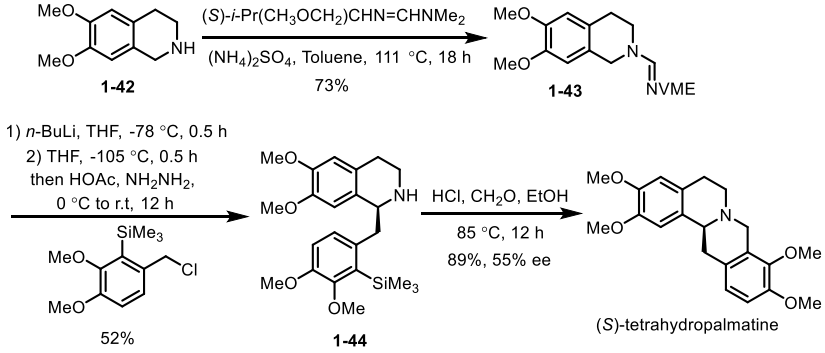


Scheme 18 Cp*Co^{III}-catalyzed intramolecular C-H activation approach for the synthesis of rosettacin.

Corydalis yanhusuo W.T. Wang is a well known Chinese herbal medicine. It has been employed to improve blood circulation, to enhance vital energy and to alleviate pain.[38] From its active components, *dl*-tetrahydropalmatine (*dl*-THP) was isolated as one of the isoquinoline alkaloid family (Scheme 14). Pharmacologically, *dl*-THP shows notable

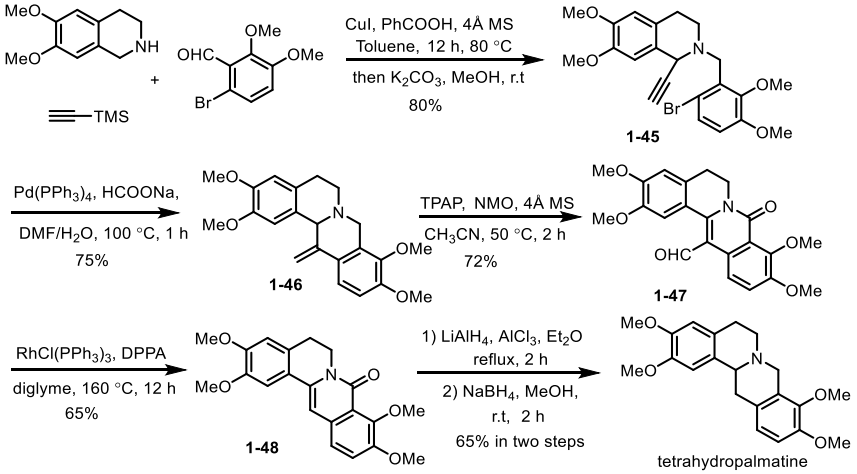
anxiolytic and analgesic effects.[39] To date, the total synthesis of *dl*-THP has been accomplished by several groups.[40-47]

In 2002, the Schore group reported an enantioenriched synthesis of (*S*)-tetrahydropalmatine, involving Meyers' formamidine valinol methyl ether chiral auxiliary assistance, enantioselective alkylation and silyl-directed Pictet-Spengler cyclization (Scheme 19).[44]



Scheme 19 Enantioenriched synthesis of (*S*)-tetrahydropalmatine.

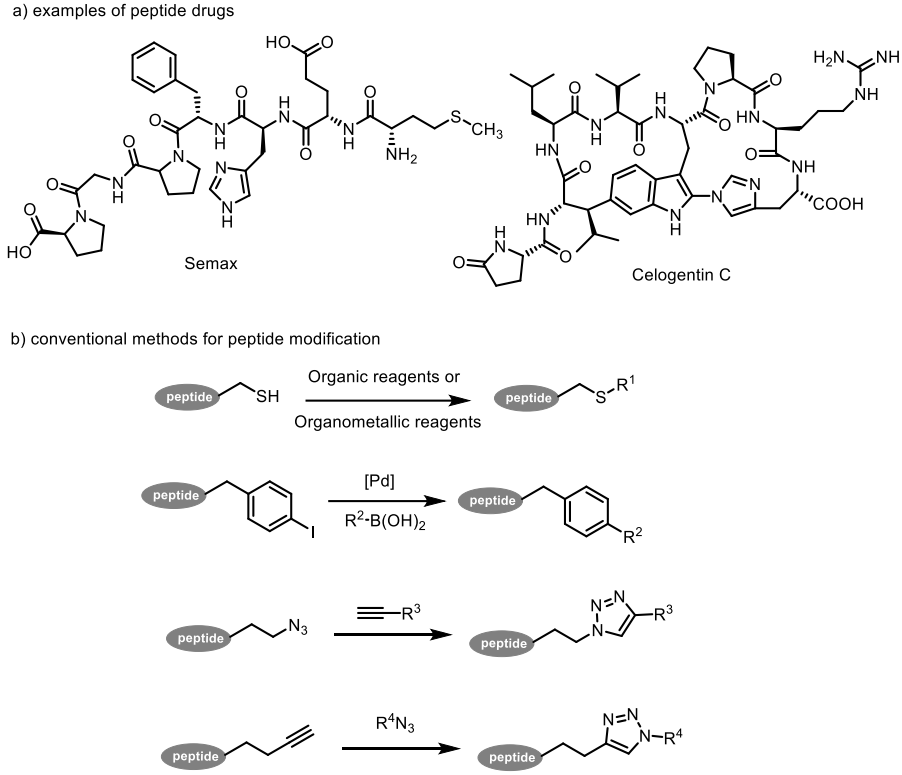
In 2016, Tong's group developed a catalytic and general strategy for the total synthesis of tetrahydropalmatine, involving a CuI-catalyzed redox-A^3 reaction, Pd-catalyzed reductive carbocyclization, TPAP/NMO oxidation, Rh-catlyzed reductive decarbonylation, $LiAlH_4$ reduction and $NaBH_4$ reduction (Scheme 20).[45]



Scheme 20 A catalytic and general strategy for the total synthesis of tetrahydropalmatine.

1.3. Overview of late-stage peptide modification

Peptide therapy has recently received widespread attention in the pharmaceutical industry because of its specificity for targets compared to small molecules.[48] In the past decade, more and more peptide drugs have been approved for clinical use (Scheme 21a). Therefore, postsynthetic modification of peptides has become much necessary in synthetic organic chemistry,[49] especially specific site modification of peptides, which is essential for many biological and therapeutic applications.[50]



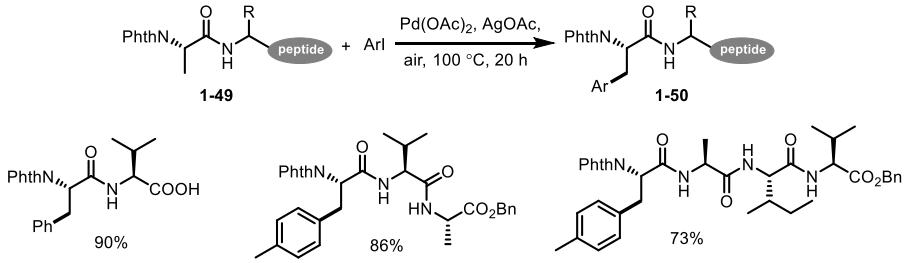
Scheme 21 Peptide drugs and classical reactions for peptide modifications.

So far, peptide modifications largely rely on classical reactions (Scheme 21b).[51] Significant improvements have been achieved by using palladium-catalyzed cross-coupling reactions for peptide modifications.[52] However, despite undisputed achievements, these

methods continue to be compromised by their restriction to the synthesis and use of preactivated substrates, which results in lengthy synthetic procedures and undesired byproducts.

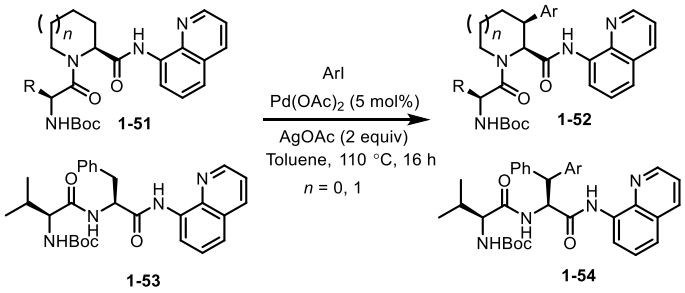
Considering above situations, direct peptide diversification has been designed to specifically modify ubiquitous C-H bonds in a chemo- and site-selective manner through transition metal-catalyzed C-H bond activation.[53-54] Recently, transition metal-catalyzed C-H activation has emerged as an increasingly powerful tool for direct peptide modification.[55-61]

In 2014, Yu's group reported site-selective inert C(sp^3)-H bond functionalization of di-, tri-, and tetra-peptides **1-49** at the N-terminus without installing a directing group (Scheme 22).[55b] The amino acid moiety of peptide is utilized as directing group to accelerate the C-H activation.



Scheme 22 Site-selective inert C(sp^3)-H bond functionalization.

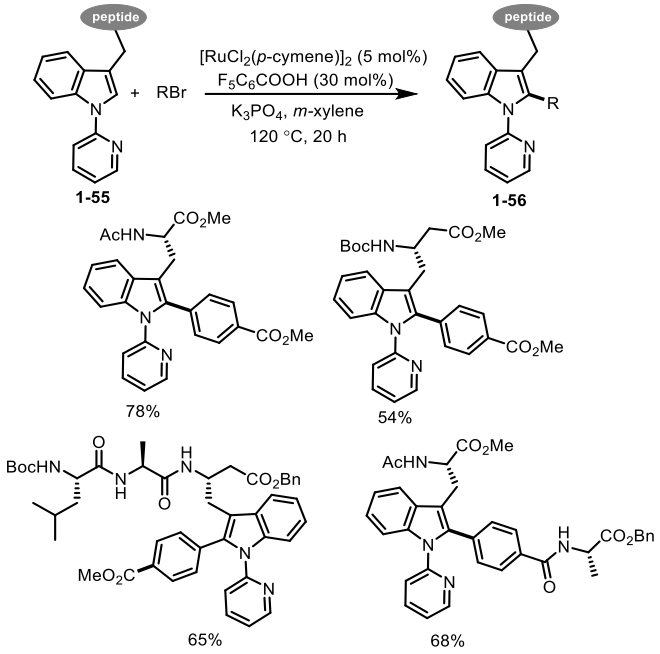
Stereoselective peptide modification *via* palladium-catalyzed β-C(sp^3)-H arylations was achieved by Kazmaier's group in 2016 (Scheme 23).[61b] For the substrate scope, phenylalanine, proline- and pipecolinic acid-containing peptides were evaluated.



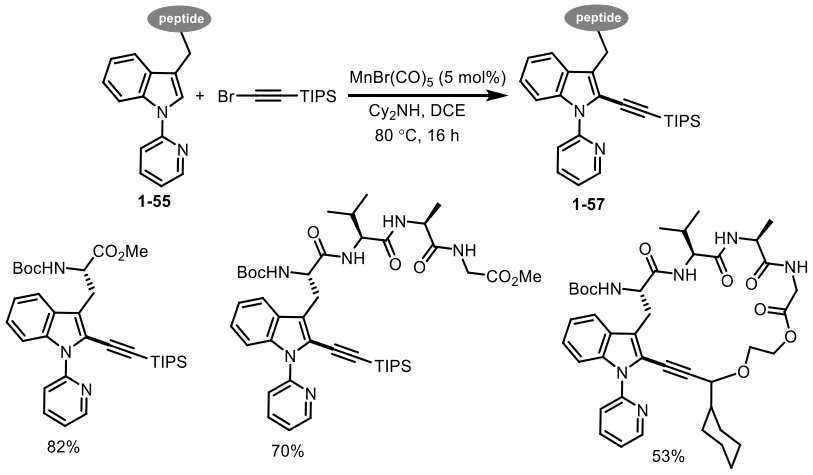
Scheme 23 Palladium-catalyzed β-C(sp^3)-H arylations.

In 2017, Ackermann's group reported a ruthenium(II)-catalyzed late-

stage diversification of α and β-amino acids, as well as peptides **1-55** in a chemoselective manner (Scheme 24).[60a] This strategy featured water-tolerance and peptide ligation in a bioorthogonal fashion.



Scheme 24 Ruthenium(II)-catalyzed diversification of amino acids and peptides.

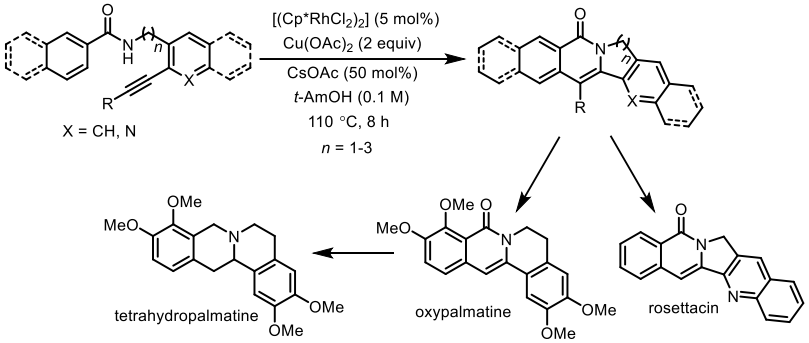


Scheme 25 Manganese-catalyzed peptide modification through C-H alkynylation.

In the same year, Ackermann's group developed a manganese-catalyzed peptide modification through C-H alkynylation (Scheme 25).[60b] This approach could also be used for the synthesis of cyclic peptides.
Despite major advances, there are still some limitations: 1) Late-stage peptide diversification based on C-H activation frequently focuses on the synthesis of non-natural peptides or fluorescence peptide labelling; drugs labeled with peptides which could be used for Antibody-Drug Conjugates (ADCs), are less investigated.[49-51] 2) As the approaches are mostly limited to one-step coupling through C-H activation, it is necessary to explore new cascade annulation reactions for the labelling of peptides with polycycles; these could be employed for new fluorescence peptide labelling.[49-51] 3) External monodentate or bidentate auxiliary assistance for C-H activation is mostly required, causing the need to introduce and remove a directing group. The development of efficient peptide diversification methods employing the internal peptide amide groups as directing group is still required.

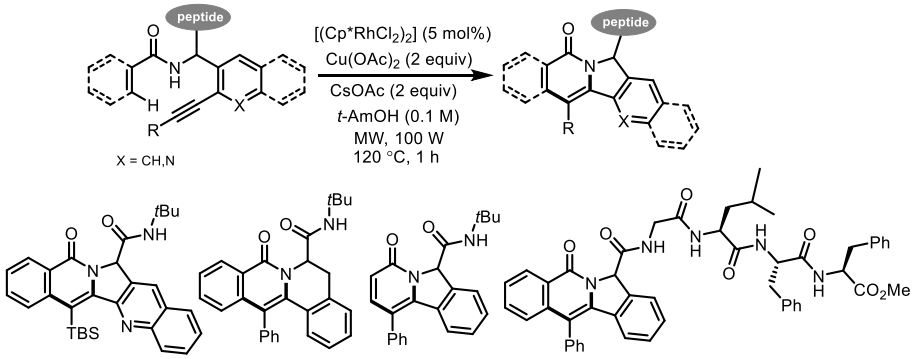
1.4. Goals of this work

Considering the advantages of transition metal-catalyzed C-H activation and the importance of rosettacin and tetrahydropalmatine, we aimed to develop an intramolecular annulation of alkyne-tethered benzamides through rhodium(III)-catalyzed C-H activation for the synthesis of indolizinone and quinolizinone scaffolds, providing a flexible and efficient synthesis of rosettacin and tetrahydropalmatine (Scheme 26).



Scheme 26 Intramolecular annulation for the synthesis of indolizinone and quinolizinone scaffolds.

Based on the advantages of transition metal-catalyzed C-H activation and the significance of late-stage peptide diversification, we aimed to develop a chemoselective rhodium(III)-catalyzed cascade annulation for the construction of indolizinone and quinolizinone scaffolds. Diversification of peptidomimetics and oligopeptides could be achieved in a rapid and step-economical manner through the combination of Ugi reaction and microwave-assisted rhodium(III)-catalyzed intramolecular annulation *via* C(sp^2)-H activation (Scheme 27).



Scheme 27 Chemoselective rhodium(III)-catalyzed cascade annulation for diversification of peptidomimetics and oligopeptides.

Chapter 2

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[Rhodium(III)-catalyzed intramolecular annulation through C-H activation: concise synthesis of rosettacin and oxypalmatine, Liangliang Song, Guilong Tian, Yi He and Erik V. Van der Eycken, *Chemical Communications*, **2017**, *53*, 12394-12397] Copyright © 2017, The Royal Society of Chemistry.

L. Song, G. Tian and E. V. Van der Eycken designed the project and wrote the manuscript. L. Song and Y. He carried out the experiments. E. V. Van der Eycken organized the research. All authors analysed the data, discussed the results and commented on the manuscript.

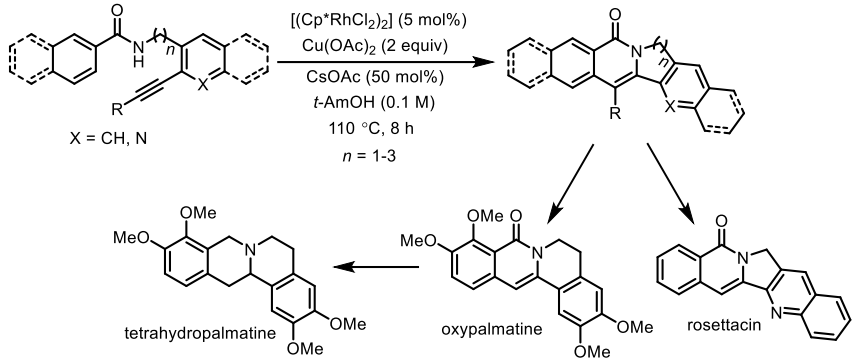
2. Rhodium(III)-catalyzed intramolecular annulation through C-H activation: concise synthesis of rosettacin and oxypalmatine

2.1. Introduction

Indolizinone and quinolizinone frameworks form the core of lots of natural products with pharmacological relevance, such as rosettacin,[30-37] camptothecin,[25] oxypalmatime and tetrahydropalmatine.[40-47] Although several methods for synthesizing these scaffolds have been reported, most of them need harsh conditions or many steps. Thus developing easy synthetic approaches still has significant value.

In recent years, transition-metal catalyzed C-H bond activation and functionalization have played an important role in synthetic organic chemistry.[1] One of the challenges is the control of position selectivity. When a weakly coordinating directing group is used for medicinally important heterocyclic substrates, the heteroatoms can strongly coordinate with the transition-metal catalyst, leading to either poisoning of the catalyst or undesired selectivity. Therefore, new methods should be explored to overcome these problems.

During the last decade, rhodium(III)-catalyzed C-H activation has received great attention because of its high efficiency, selectivity and functional-group tolerance.[4-10] Many reports show that rhodium(III)-catalyzed C-H activation is a powerful strategy to achieve intermolecular annulation of alkynes with aryl or alkenyl amides with different directing groups. However, most of the intermolecular annulations result in the formation of a single ring and few cascade reactions to build multiple rings are reported. When unsymmetrical alkynes are utilized, the regioselectivity depends on the difference between both substituents on the alkynes, often leading to poor regioselectivity. Obviously, intramolecular annulation of alkynes with aryl or alkenyl amides can overcome these limitations and can also allow the construction of multiple rings existing in more complex scaffolds. Considering the advantages, we planned to design an intramolecular annulation of alkyne-tethered benzamides through rhodium(III)-catalyzed C-H activation for the synthesis of indolizinone and quinolizinone scaffolds, providing a flexible and efficient synthesis of rosettacin and tetrahydropalmatine (Scheme 28).



Scheme 28 Intramolecular annulation for the synthesis of indolizinone and quinolizinone scaffolds.

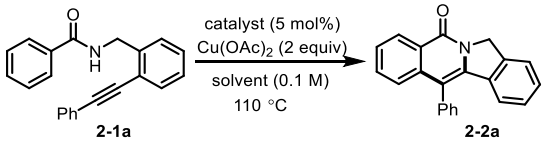
2.2. Results and discussion

We selected *N*-alkynylbenzamide **2-1a** as our model substrate. As revealed by the results in Table 1, $[RhCp^*Cl_2]_2$ could easily perform the construction of indolizinone **2-2a**. We found that treatment of **2-1a** with $[RhCp^*Cl_2]_2$ (5 mol%) and $Cu(OAc)_2$ (2 equiv) in *t*-AmOH at 110 °C gave **2-2a** in 98% yield in 12 h (Table 1, entry 1). Screening of various solvents, such as 1,4-dioxane, DMF and toluene, assured that *t*-AmOH was the most efficient one (Table 1, entries 2-4). We also evaluated the performance of other metals, confirming $[RhCp^*Cl_2]_2$ as the best choice. $Pd(OAc)_2$ and $Ni(OAc)_2{\cdot}4H_2O$ did not work, while with $[Ru(p\text{-cymene})Cl_2]_2$, 83% yield was obtained (Table 1, entries 5-7). Further investigation showed that a lower temperature was deleterious for the reaction, leading to a very poor conversion (Table 1, entry 8). We also tested $[RhCp^*Cl_2]_2$ in combination with CsOAc, resulting in an acceleration of the reaction, yielding **2-2a** in 99% yield in 8 h when 50 mol% CsOAc was added (Table 1, entry 9).

With the optimized reaction conditions in hand, we next examined various substrates to evaluate the scope of the protocol. The annulation reactions proceeded smoothly to afford indolizinones and quinolizinones in good to excellent yields (Table 2). Substrates with electron-donating or electron-withdrawing groups at the *para* position of the aryl moiety of benzamide performed well under the reaction conditions (**2-2b~2-2e**). The *meta*-methyl benzamide was totally selective to give the corresponding indolizinone **2-2f** in good yield. We

also tested the reactions with substrates containing a methyl or fluoro group in the *ortho* position of the benzamide. Both gave the corresponding products **2-2g** and **2-2h** in excellent yields. Naphthylbenzamide was an acceptable substrate, leading to the cycloadduct **2-2i** in excellent yield. The annulation reaction also tolerated electron-donating and electron-withdrawing groups in the phenyl substituent of the alkyne, like methyl and trifluoromethyl groups (**2-2j** and **2-2k**). When we replaced the aryl groups of the alkyne by a cyclohexyl, cyclopropyl or a *tert*-butyldimethylsiyl (TBS) group, the reaction smoothly proceeded to give the cycloadducts **2-2m**, **2-2n** and **2-2l**. Finally we tested substrates containing electron-donating or electron-withdrawing groups in the phenyl substituent of the benzylamine. Both gave the corresponding products **2-2o** and **2-2p** in excellent yields.

Table 1 Optimization of the reaction conditions[a]



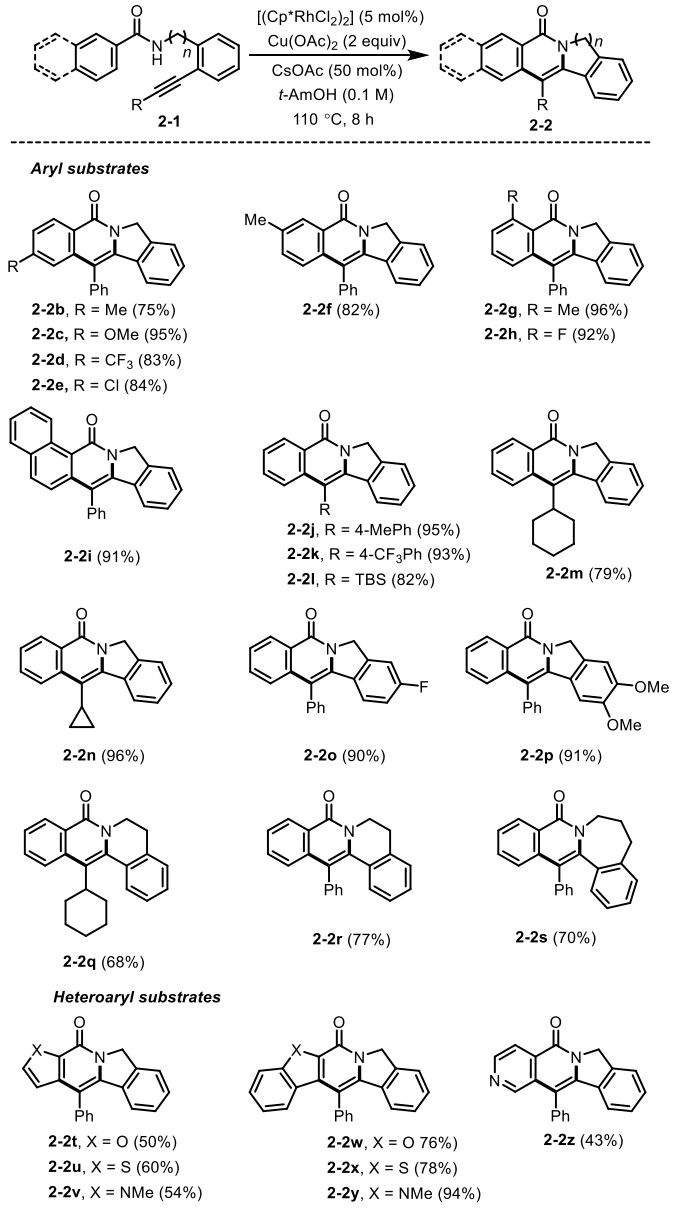
Entry	Solvent	Catalyst	*t* (h)	Yield (%)[b]
1	*t*-AmOH	$[RhCp^*Cl_2]_2$	12	98
2	1,4-Dioxane	$[RhCp^*Cl_2]_2$	12	87
3	DMF	$[RhCp^*Cl_2]_2$	12	<5
4	Toluene	$[RhCp^*Cl_2]_2$	12	<5
5	*t*-AmOH	$Pd(OAc)_2$	12	0
6	*t*-AmOH	$[Ru(p\text{-cymene})Cl_2]_2$	12	83
7	*t*-AmOH	$Ni(OAc)_2{\cdot}4H_2O$	12	0
8[c]	*t*-AmOH	$[RhCp^*Cl_2]_2$	12	<5
9[d]	***t*-AmOH**	**$[RhCp^*Cl_2]_2$**	**8**	**99(93)**[e]

[a] Condition: **2-1a** (0.3 mmol), catalyst (0.015 mmol), $Cu(OAc)_2$ (0.6 mmol), solvent (3.0 mL). [b] Determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard. [c] 90 °C. [d] CsOAc (50 mol%) were added. [e] Isolated yield.

Interestingly, we found that the cycloaddition worked with substrates bearing a longer carbon chain between the benzamide and the alkyne, leading to interesting products containing either a six- (**2-2q~2-2r**) or

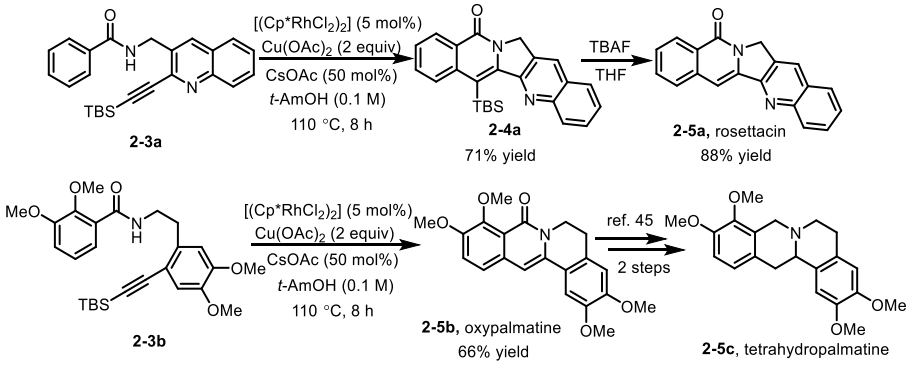
seven-membered ring (**2-2s**) in good yields. We extended the cycloaddi-

Table 2 Scope for aryl and heteroaryl substrates[ab]

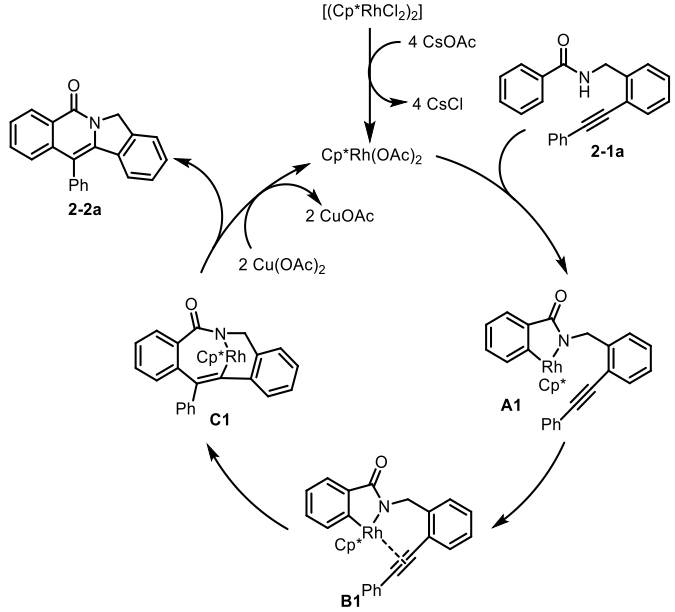


[a] Condition: **2-1** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), $Cu(OAc)_2$ (0.6 mmol), *t*-AmOH (3.0 mL), CsOAc (0.15 mmol). [b] Isolated yield.

tion to heteroaryl carboxamides, such as furan, thiophene, pyrrole, benzofuran, benzothiophene and indole. They all smoothly afforded the corresponding cycloadducts in moderate to excellent yields (**2-2t~2-2y**). Even an isonicotinamide substrate delivered the cycloadduct in moderate yield (**2-2z**).



Scheme 29 Synthesis of rosettacin (**2-5a**) and tetrahydropalmatine (**2-5c**).



Scheme 30 Plausible mechanism.

To further demonstrate the synthetic utility, we used this intramolecular

annulation as a key ring-forming step for the concise synthesis of rosettacin (**2-5a**) and tetrahydropalmatine (**2-5c**) (Scheme 29). Cycloadduct **2-4a** could be obtained from benzamide **2-3a** using the optimized conditions in 71% yield. Removal of the TBS-group afforded rosettacin (**2-5a**) in good overall yield. To our surprise, under the standard condition, benzamide **2-3b** could directly give oxypalmatine (**2-5b**) in 66% yield through one step, which is a key intermediate for the synthesis of tetrahydropalmatine[45] (**2-5c**).

Based on the above results, we proposed a possible mechanism (Scheme 30). First, an irreversible C-H bond cleavage occurs to afford a five-membered rhodacycle intermediate **A1** with simultaneous loss of acetic acid. Next, coordination of the alkyne furnishes intermediate **B1**, which undergoes insertion into the Rh-C bond to produce seven-membered rhodacycle **C1**. Subsequent reductive elimination gives the desired product, followed by reoxidation of Rh(I) by $Cu(OAc)_2$ to regenerate the catalyst.

2.3. Conclusions

In summary, we have developed an efficient rhodium(III)-catalyzed intramolecular annulation of benzamides bearing *N*-tethered alkynes for the synthesis of indolizinones and quinolizinones. This reaction features a broad substrate scope and excellent functional-group tolerance. Substrates bearing a longer carbon chain between the benzamide and the alkyne performed well. Different heterocyclic substrates performed smoothly, such as furan, thiophene, pyrrole, benzofuran, benzothiophene, indole and isonicotinamide substrates. This method also provides a reliable and highly efficient approach for the synthesis of rosettacin, oxypalmatine and tetrahydropalmatine.

Chapter 3

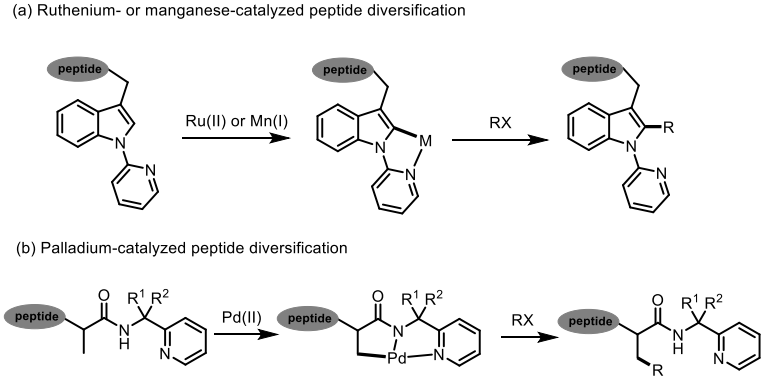
Unpublished work

3. Diversification of peptidomimetics and oligopeptides through microwave-assisted rhodium(III)-catalyzed intramolecular annulation

3.1. Introduction

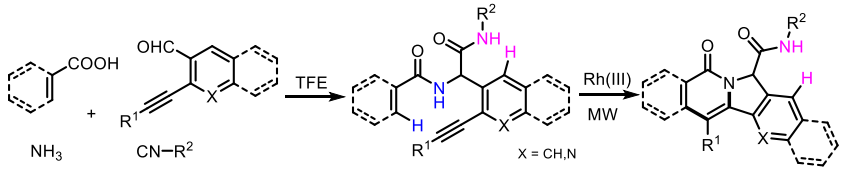
Site specific modification of peptides is necessary for many biological and therapeutic applications.[48-50] Peptides from nonproteinogenic amino acids are required for medicinal and pharmaceutical chemistry, since they show improved pharmacokinetics and bioactivity in comparison with their natural versions. For instance, peptides labeled with fluorescent groups could be used for realtime tracking of biomolecules, metabolites and cells under physiological conditions. In addition, peptides labeled with drugs have been designed for selectively targeting tumor cells. However, contemporary labelling strategies are mainly limited to classical reactions and transition metal-catalyzed cross-coupling reactions, largely relying on prefunctionalizations, often leading to the formation of undesired byproducts and lengthy synthetic procedures.[51-52]

Recently, transition metal-catalyzed C-H activation has emerged as an increasingly powerful strategy for direct peptide modification.[55-61] Despite major advances, late-stage peptide diversification frequently focuses on the synthesis of non-natural peptides or fluorescence peptide labelling through one-step coupling, and mostly requires external monodentate or bidentate auxiliary assistance, causing the need to introduce and remove a directing group (Scheme 31).



Scheme 31 Late-stage peptide diversification through external monodentate or bidentate auxiliary assistance.

Based on the above mentioned work (Chapter 2) and the significance of late-stage peptide diversification, we aimed to develop a chemoselective rhodium(III)-catalyzed cascade annulation for the construction of indolizinone and quinolizinone scaffolds. Diversification of peptidomimetics and oligopeptides could be achieved in a rapid and step-economical manner through the combination of Ugi reaction and microwave-assisted rhodium(III)-catalyzed intramolecular annulation *via* C(sp^2)-H activation (Scheme 32).



Scheme 32 Chemoselective rhodium(III)-catalyzed cascade annulation for diversification of peptidomimetics and oligopeptides.

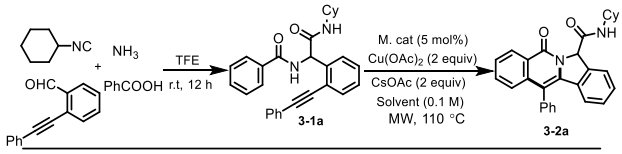
3.2. Results and discussion

We commenced our exploration with optimization studies on the annulation of peptidomimetic **3-1a**, which was readily constructed through Ugi-4CR. When the reaction was performed with $[RhCp^*Cl_2]_2$ (5 mol%), $Cu(OAc)_2$ (2 equiv) and CsOAc (2 equiv) in *t*-AmOH at 110 °C for 1 h with 300 W maximum power, the indolizinone **3-2a** was obtained in 90% yield (Table 3, entry 1). Then various solvents were screened, showing that *t*-AmOH was the best one (Table 3, entries 2-7). When $[Ru(p\text{-cymene})Cl_2]_2$ was used, a lower conversion was observed (Table 3, entry 8). Extension of the reaction time to 2 h resulted in the formation of **3-2a** in 99% yield (Table 3, entry 9). Decreasing the maximum power to 100 W for 1 h, yielded **3-2a** in 92% (Table 3, entry 10). A higher temperature of 120 °C for 1 h (100 W), delivered **3-2a** in 99% yield (Table 3, entry 11). Only 36% yield of **3-2a** was observed when the reaction was performed under conventional heating for 1 h at 120 °C in *t*-AmOH (Table 3, entry 12).

With the optimal conditions in hand, we next evaluated the scope of the protocol (Table 4). Peptidomimetics bearing various secondary amide groups derived from the corresponding isocyanides, yielded the corresponding indolizinones **3-2b~3-2d** in 87-92%. The reaction was also applicable to *para*-Me and -CF_3 substrates, giving the

indolizinones **3-2e** (93%) and **3-2f** (79%). The reactions with *meta*- or *ortho*-Me substrates smoothly afforded the corresponding indolizinones in 86% (**3-2g**) and 74% (**3-2h**) yield respectively. The phenyl substituent of the alkyne could be replaced by a cyclopropyl, cyclohexyl or TBS group, yielding the indolizinones **3-2i~3-2k** in 58-82%. However, the terminal alkyne substrate failed to give the corresponding indolizinone **3-2l**. The substrate with a fluoro or dimethoxy group in the phenyl substituent derived from the benzaldehyde, turned out to be compatible, offering the indolizinones **3-2m** (95%) and **3-2n** (93%). The 2-ethynylquinoline substrate smoothly reacted to yield the corresponding indolizinone **3-2o** (78%), which has the same skeleton as the natural product rosettacin. The annulation worked well with substrates bearing a longer carbon chain between the benzamide and the phenylalkyne, leading to the corresponding quinolizinones **3-2p** (89%) and **3-2q** (73%), having the same scaffold as the natural product oxypalmatine.

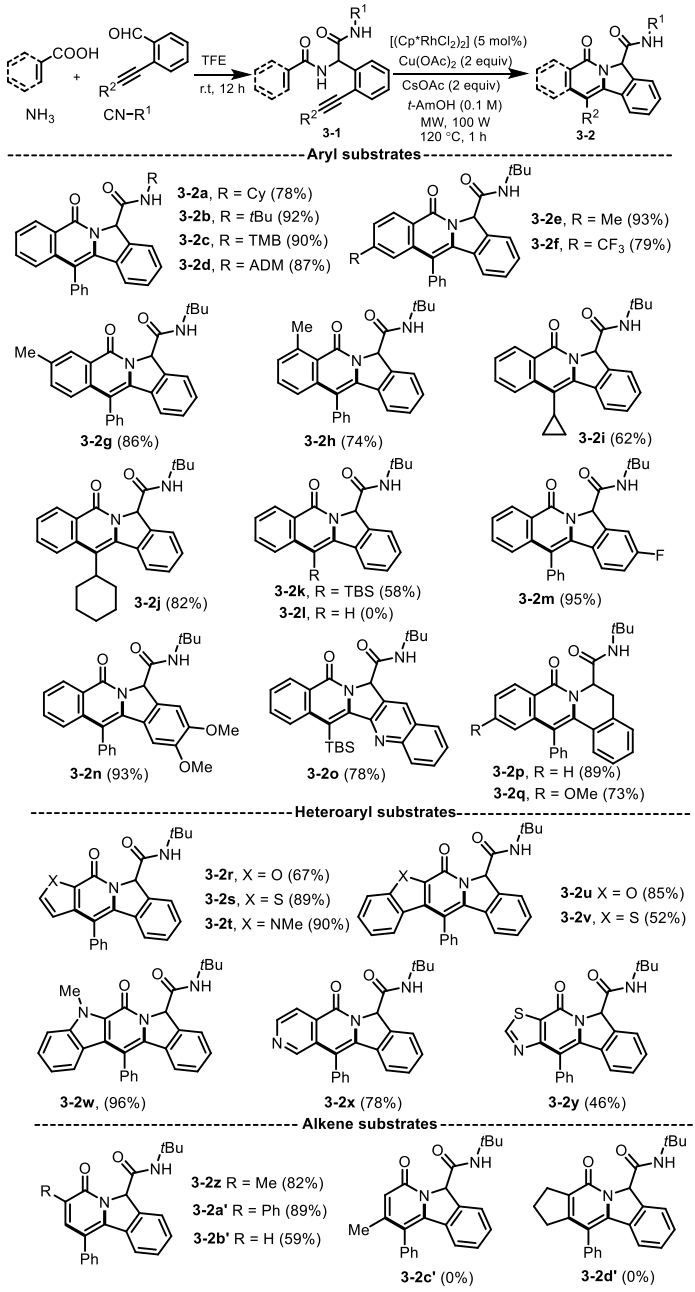
Table 3 Optimization of the reaction conditions[a]



Entry	Solvent	M. cat	Power (W)	t (h)	Yield[b] (%)
1	*t*-AmOH	$[RhCp^*Cl_2]_2$	300	1	90
2	1,4-Dioxane	$[RhCp^*Cl_2]_2$	300	1	79
3	Toluene	$[RhCp^*Cl_2]_2$	300	1	67
4	DMF	$[RhCp^*Cl_2]_2$	300	1	22
5	CH_3CN	$[RhCp^*Cl_2]_2$	300	1	46
6	THF	$[RhCp^*Cl_2]_2$	300	1	78
7	DCE	$[RhCp^*Cl_2]_2$	300	1	73
8	*t*-AmOH	$[Ru(p\text{-cymene})Cl_2]_2$	300	1	39
9	*t*-AmOH	$[RhCp^*Cl_2]_2$	300	2	99
10	*t*-AmOH	$[RhCp^*Cl_2]_2$	100	1	92
11[c]	***t*-AmOH**	**$[RhCp^*Cl_2]_2$**	**100**	**1**	**99 (78)[d]**
12[e]	*t*-AmOH	$[RhCp^*Cl_2]_2$	—	1	36

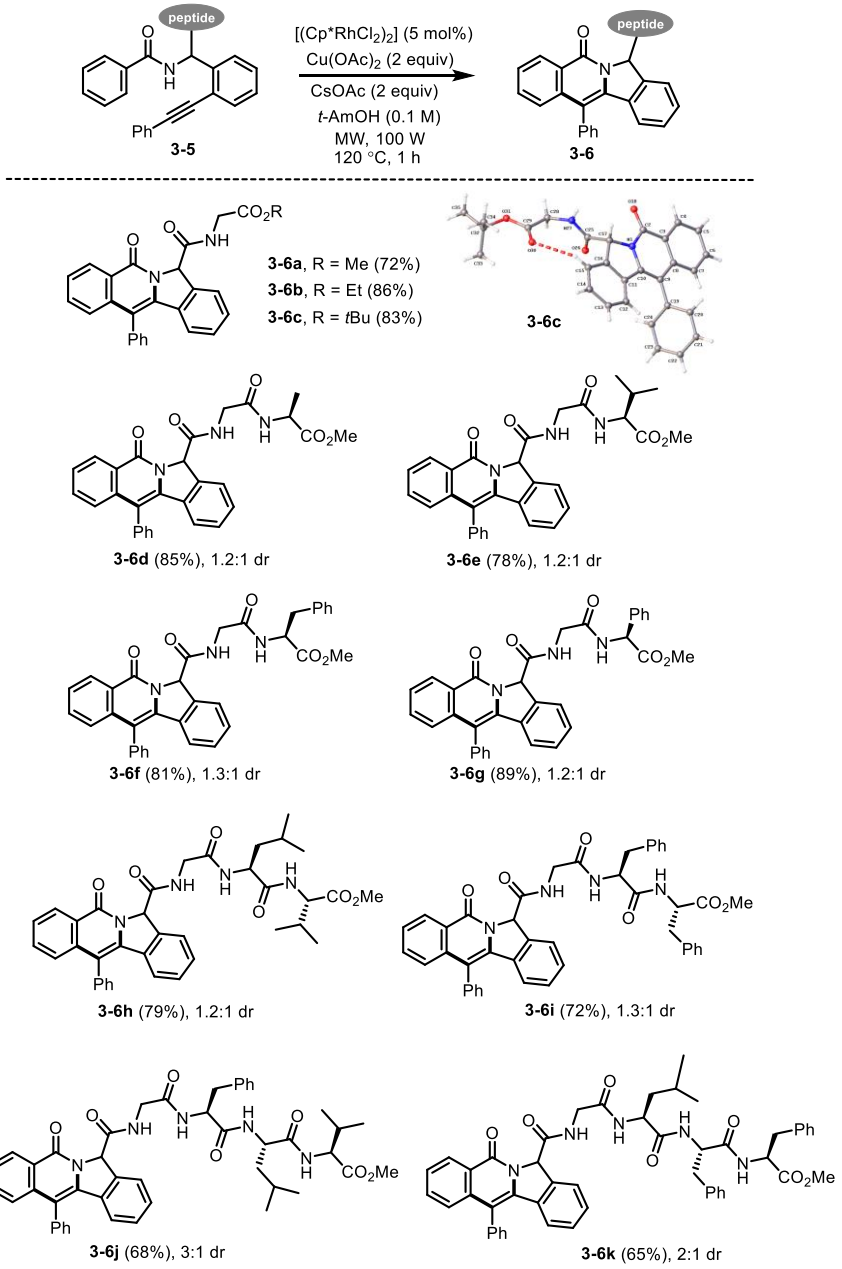
[a] Conditions: **3-1a** (0.3 mmol), catalyst (0.015 mmol), $Cu(OAc)_2$ (0.6 mmol), CsOAc (0.6 mmol), solvent (3.0 mL). [b] Determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard. [c] 120 °C. [d] Isolated yield. [e] Reaction was performed conventionally at 120 °C in *t*-AmOH.

Table 4 Rhodium(III)-catalyzed annulation of peptidomimetics[ab]



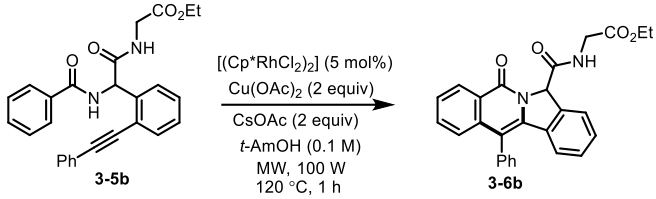
[a] Conditions: **3-1** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), $Cu(OAc)_2$ (0.6 mmol), CsOAc (0.6 mmol), *t*-AmOH (3.0 mL). [b] Isolated yield.

Table 5 Rhodium(III)-catalyzed annulation of oligopeptides[ab]



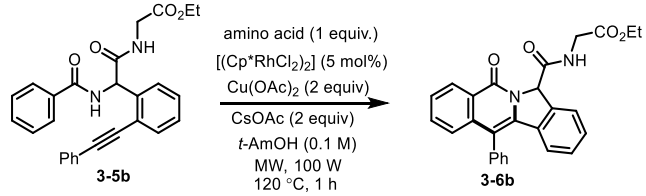
[a] Conditions: **3-5** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), $Cu(OAc)_2$ (0.6 mmol), CsOAc (0.6 mmol), *t*-AmOH (3.0 mL). [b] Isolated yield.

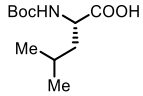
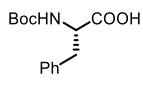
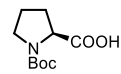
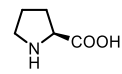
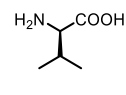
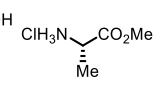
We extended the reaction scope to heteroaryl peptidomimetics, containing a furan, a thiophene, a pyrrole, a benzofuran, a benzothiophene and an indole moiety. They all smoothly afforded the corresponding indolizinones **3-2r~3-2w** in 52-96% yield. Even isonicotinamide and thiazole-5-carboxamide substrates delivered the corresponding indolizinones **3-2x** (78%) and **3-2y** (46%). It was also observed that the benzamide substrates could be replaced by α-substituted acrylamide substrates, resulting in the corresponding indolizinones **3-2z~3-2b'** in 59-89% yield. However, β-substituted or α, β-disubstituted acrylamide substrates **3-1c'** and **3-1d'** did not undergo the reaction.



standard conditions	86% **3-6b**
t-AmOH/H_2O (1:1)	54% **3-6b**
H_2O	41% **3-6b**

Scheme 33 Rhodium(III)-catalyzed annulation with H_2O.



					
Boc-Leu-OH	Boc-Phe-OH	Boc-Pro-OH	H-L-Pro-OH	H-D-Val-OH	H-Ala-OMe·HCl
72% **3-6b**	78% **3-6b**	82% **3-6b**	14% **3-6b**	12% **3-6b**	23% **3-6b**

Scheme 34 Chemoselectivity screen with amino acids.

Subsequently, we evaluated our procedure for oligopeptides (Table 5). Dipeptides **3-5a~3-5c** were well tolerated, affording the corresponding indolizinones **3-6a~3-6c** in 72-86%. Compound **3-6c** was unambiguously characterized by X-ray crystallography. Diverse tri-,

tetra- and pentapeptides were compatible with this approach, delivering the corresponding indolizinones **3-6d~3-6k** with excellent levels of chemoselectivity control.

The compatiblity on Rh^{III}-catalyzed intramolecular annulation protocol for diversification of peptides was evaluated by using water as solvent (Scheme 33). Employing *t*-AmOH/H_2O (1:1) could not give complete conversion, delivering **3-6b** in 54% yield. Using solely H_2O gave **3-6b** in 41% yield. In addition, the excellent robustness of the Rh^{III}-catalyzed intramolecular annulation was proven by a chemoselectivity screen in the presence of specifically added *O*-unprotected amino acids (Scheme 34). *N*-unprotected amino acids seem to have a detrimental effect on the reaction.

3.3. Conclusions

In conclusion, we have developed a chemoselective rhodium(III)-catalyzed intramolecular annulation protocol for the construction of indolizinone and quinolizinone scaffolds. Ugi reaction and microwave-assisted C(sp^2)-H activation set the stage for the diversification of various peptidomimetics and oligopeptides in a rapid and step-economical manner. The 2-ethynylquinoline substrate smoothly reacted to give the rosettacin analogue. Substrates bearing a longer carbon chain between the benzamide and the phenylalkyne, smoothly afforded oxypalmatine analogues. Heteroaryl substrates worked well, containing furan, thiophene, pyrrole, benzofuran, benzothiophene, indole, isonicotinamide and thiazole-5-carboxamide substrates. α-Substituted acrylamide substrates were acceptable for the reaction. Oligopeptides including di-, tri-, tetra- and pentapeptides were well tolerated. Notably, this approach was compatible with water.

Chapter 4

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[Intramolecular cascade annulation triggered by C-H activation via rhodium hydride intermediate, Liangliang Song, Xiaoyong Zhang, Guilong Tian, Koen Robeyns, Luc Van Meervelt, Jeremy N. Harvey and Erik V. Van der Eycken, *Molecular Catalysis*, **2019**, *463*, 30-36] Copyright © 2018, Elsevier.

L. Song, X. Zhang, G. Tian, J. N. Harvey and E. V. Van der Eycken designed the project and wrote the manuscript. L. Song carried out the experiments. X. Zhang performed DFT calculations. K. Robeyns and L. Van Meervelt collected X-ray intensity data and did the X-ray crystallographic analysis. E. V. Van der Eycken organized the research. All authors analysed the data, discussed the results and commented on the manuscript.

[Intramolecular cascade annulation triggered by rhodium(III)-catalyzed sequential C(sp^2)-H activation and C(sp^3)-H amination, Liangliang Song, Guilong Tian, Johan Van der Eycken and Erik V. Van der Eycken, *Beilstein Journal of Organic Chemistry*, **2019**, *15*, 571-576] Copyright © 2019, Beilstein-Institut.

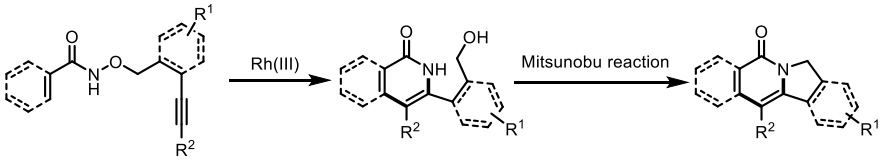
L. Song and E. V. Van der Eycken designed the project and wrote the manuscript. L. Song and G. Tian carried out the experiments. J. Van der Eycken collected the HRMS sample data. E. V. Van der Eycken organized the research. All authors analysed the data, discussed the results and commented on the manuscript.

4. Intramolecular cascade annulation triggered by C-H activation *via* rhodium hydride intermediate

4.1. Introduction

Transition-metal-catalyzed C-H activation and functionalization has played a prominent role in synthetic organic chemistry in the last decade.[1] Especially rhodium(III)-catalyzed C-H activation followed by annulation with 2π components (such as alkenes, alkynes) has received signifcant interest for constructing N-heterocycles and carbocycles because of its high efciency, selectivity and functional-group tolerance.[4-10] For intermolecular annulation reactions, most of them result in the formation of a single ring, suffering from uncontrolled regioselectivity, which inevitably leads to mixtures of positional isomers, especially when unsymmetrical alkynes are employed. When sequential twofold C-H activation and couplings or combination of C-H activation/coupling and further interactions with a proximal group is accessed, polycycles can be built, providing an effcient strategy for the construction of important complicated scaffolds. However, intramolecular annulations can make it much easier to achieve high regioselectivity and to form the polycycles common in complex molecules. Compared to aromatic C(sp^2)-H bonds, studies on activation of vinylic C(sp^2)-H bonds have been less explored, due to an intrinsic inactivity, tended to undergo polymerization, prone to go through conjugate additions. Moreover, the cyclometalation intermediates are unstable, and the β-substitution or α,β-disubstitution of acrylate sterically prevents the cyclometalation.

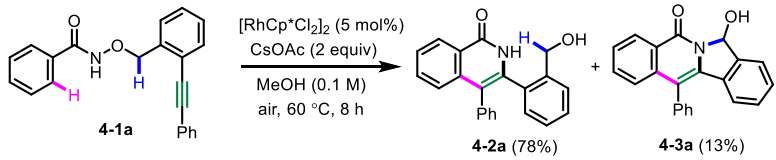
Based on the above mentioned works (Chapter 2 and 3), we aimed to develop an intramolecular cascade annulation of *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the synthesis of 3-hydroxyalkyl isoquinolones or 6-hydroxyalkyl-2-pyridones without adding a stoichiometric external oxidant, which could undergo Mitsunobu reaction to form indolizinones (Scheme 35).



Scheme 35 Designed pathway to synthesize indolizinones

4.2. Results and discussion

Our initial attempt began with the reaction of hydroxamic ester **4-1a** using 5 mol% $[RhCp^*Cl_2]_2$ as the catalyst and CsOAc (2 equiv) as the base. When the reaction was conducted in MeOH at 60 ^oC for 8 h, the envisaged isoquinolone **4-2a** was obtained in 78% yield. Unexpectedly, indolizinone **4-3a** was also observed in 13% yield, and structurally characterized by X-ray crystallography (Scheme 36).



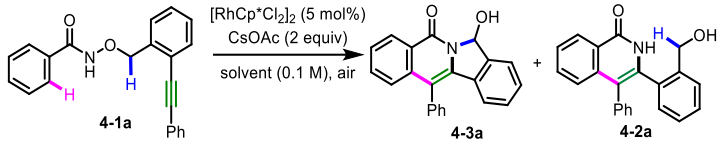
Scheme 36 Initial attempt to synthesize indolizinone.

Considering that the formation of indolizinone **4-3a** directly from hydroxamic ester **4-1a** was more interesting, we began to optimize the reaction conditions of forming **4-3a** (Table 6). Solvent screening with 1,4-dioxane, DMF, toluene, DCE, THF, CH_3CN and acetone, identified 1,4-dioxane as the preferred medium for reaction, giving **4-3a** in 52% yield, together with **4-2a** in 35 % yield (Table 6, entries 2-8). The alternative catalyst $[Ru(p\text{-cymene})Cl_2]_2$, gave a very poor conversion of **4-3a** (Table 6, entry 9). Increased or decreased temperature did not improve the yield of **4-3a** (Table 6, entries 10-11). The employment of a longer reaction time gave **4-3a** in 49% yield (Table 6, entry 12). Increasing the catalyst loading to 10 mol%, delivered **4-3a** in 55% yield (Table 6, entry 13). Decreasing the catalyst loading to 2.5 mol%, afforded **4-3a** in 31% yield (Table 6, entry 14). Without CsOAc, the reaction worked very slowly (Table 6, entry 15). Further, when the reaction was performed for only 30 min under optimized conditions, the products **4-3a** and **4-2a** were obtained in 12% and 16% yields, respectively (Table 6, entry 16). This indicated that **4-3a** was formed from the beginning.

Next, various substrates were studied to evaluate the scope of the protocol under the optimized reaction conditions (Table 7). The reaction was applicable to hydroxamic esters with various electron-donating or electron-withdrawing groups at the *para* position of the benzamide moiety. The corresponding products **4-3b~4-3g** were obtained in 49-67%

yield. Reaction with *ortho* or *meta*-methyl benzamide also smoothly proceeded to give the corresponding indolizinone in the yields of 52%

Table 6 Optimization of the reaction conditions[a]



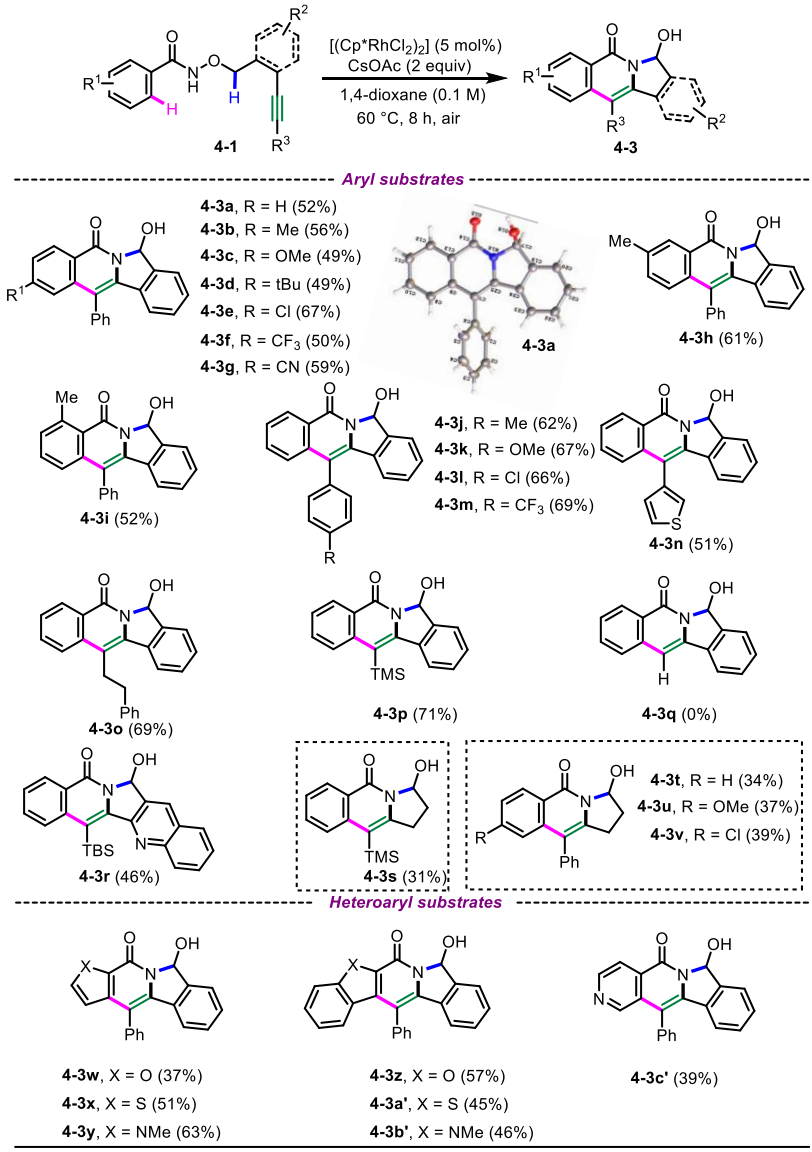
Entry	Solvent	T (ºC)	T (h)	Yield(4-3a, 4-2a)[b]
1	MeOH	60	8	(13%, 78%)
2	**1,4-Dioxane**	**60**	**8**	**(52%, 35%)**
3	DMF	60	8	(10%, 46%)
4	Toluene	60	8	(21%, 51%)
5	DCE	60	8	(15%, 62%)
6	THF	60	8	(41%, 45%)
7	CH_3CN	60	8	(26%, 58%)
8	Acetone	60	8	(31%, 47%)
9[c]	1,4-Dioxane	60	8	(<5%, 62%)
10	1,4-Dioxane	40	8	(42%, 37%)
11	1,4-Dioxane	80	8	(41%, 51%)
12	1,4-Dioxane	60	16	(49%, 32%)
13[d]	1,4-Dioxane	60	8	(55%, 28%)
14[e]	1,4-Dioxane	60	8	(31%, 51%)
15[f]	1,4-Dioxane	60	8	(9%, 21%)
16	1,4-Dioxane	60	0.5	(12%, 16%)

[a] Conditions: **4-1a** (0.3 mmol), catalyst (0.015 mmol), CsOAc (0.6 mmol), solvent (3.0 mL). [b] Isolated yield. [c] [Ru(*p*-cymene)Cl_2]$_2$ (5 mol%) was used instead of [RhCp*Cl_2]$_2$. [d] [RhCp*Cl_2]$_2$ (10 mol%) was used. [e] [RhCp*Cl_2]$_2$ (2.5 mol%) was used. [f] Without CsOAc.

(**4-3i**) and 61% (**4-3h**) respectively. The electronic nature of the phenyl substituent of the alkyne appeared to have limited effects on the reaction outcome, and the corresponding products **4-3j~4-3m** were observed in 62-69% yield. Additionally, the phenyl group could be replaced by a heteroaryl group, an aliphatic group and a TMS group without a significant impact on the results for the corresponding indolizinones **4-**

3n~4-3p. However, the terminal alkyne substrate could not yield the corresponding product **4-3q**. 2-Ethynylquinoline substrate worked well, yielding the corresponding indolizinone **4-3r** (46%). Furthermore, sub-

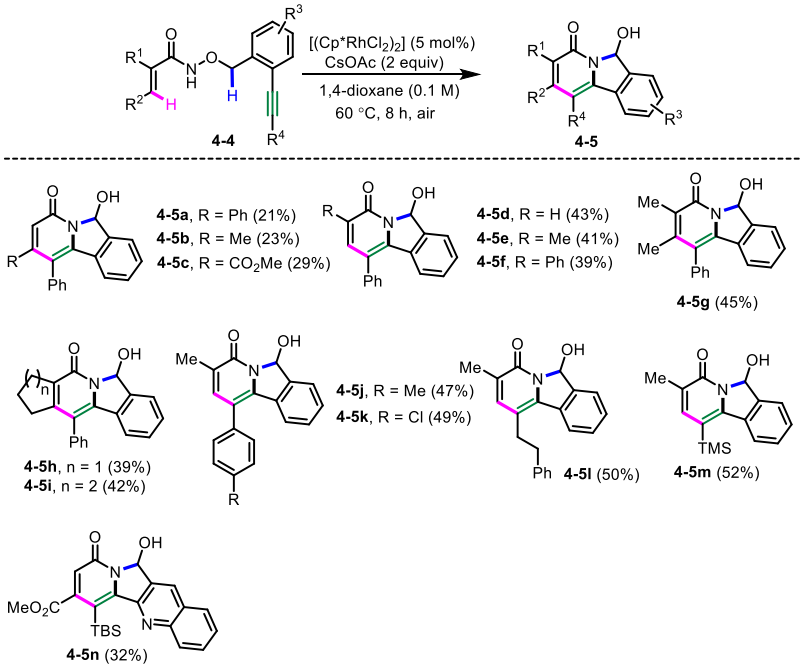
Table 7 Scope for aryl and heteroaryl substrates[ab]



[a] Conditions: **4-1** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), 1,4-dioxane (3.0 mL). [b] Isolated yield.

strates with flexible tethers bearing different substituents were well tolerated, leading to the corresponding indolizinones **4-3s~4-3v** in 31-39% yield. Next, we extended the reaction scope to heteroaryl carboxamides, such as furan, thiophene, pyrrole, benzofuran, benzothiophene and indole. They all smoothly furnished the corresponding products **4-3w~4-3b'** in 37-63% yield. Even isonicotinamide substrate could deliver the corresponding indolizinone **4-3c'** in 39% yield.

Table 8 Scope for alkene substrates[ab]

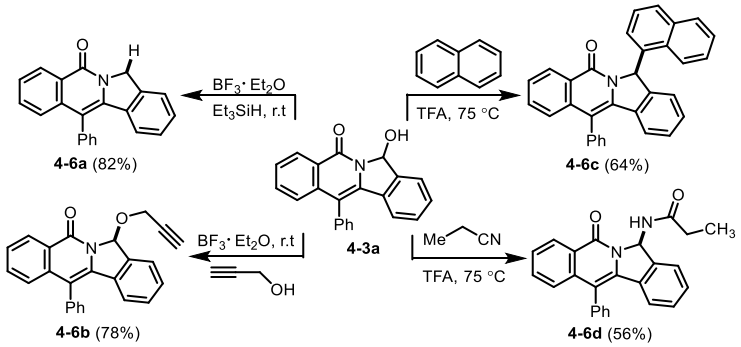


[a] Conditions: **4-4** (0.3 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), 1,4-dioxane (3.0 mL). [b] Isolated yield.

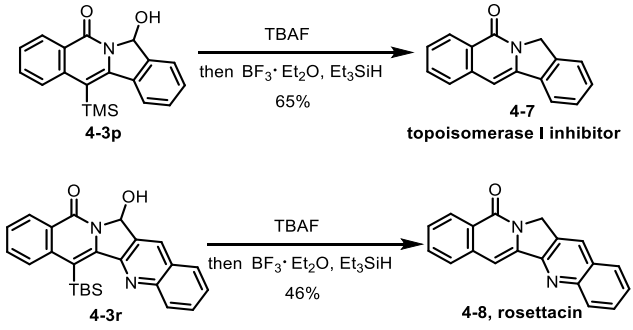
It follows that the benzamide substrates could be extended to acrylamides, resulting in the corresponding indolizinones (Table 8). Substituents at the α or β positions of the acrylamide were tolerated well. Substrates having an α-substituent facilitated the reaction with higher yield as compared to β-substituent under the same conditions (**4-5a~4-5f**). It should be pointed out that α, β-disubstituted acrylamides were also suitable substrates for this transformation, and the corresponding

products **4-5g~4-5i** were obtained in 39-45% yield. Substrates with different substituents on the alkyne, including 4-methylphenyl, 4-chlorophenyl, phenethyl and TMS group, could deliver the corresponding indolizinones **4-5j~4-5m** in 47-52% yield. 2-Ethynylquinoline substrate worked well, yielding the corresponding indolizinone **4-5n** (32%).

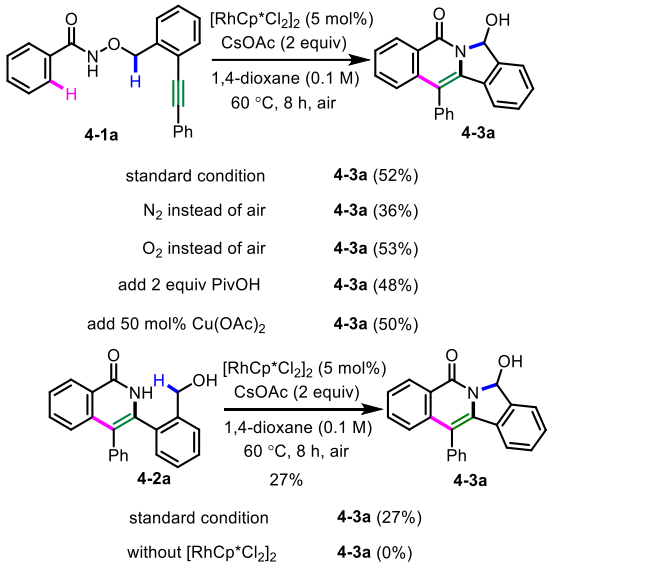
Next various transformations of **4-3a** were employed (Scheme 37). Under the conditions of $BF_3{\cdot}Et_2O/Et_3SiH$, **4-3a** was reduced to give **4-6a** in 82% yield. Similarly, **4-6b** was obtained in 78% yield through C-O bond formation from the reaction between **4-3a** and propargyl alcohol. Moreover, the reaction of **4-3a** with naphthalene in the presence of TFA was performed to afford **4-6c** in 64% yield *via* C-C bond formation. Likewise, **4-6d** was given in 56% yield through C-N bond formation by the reaction of **4-3a** with propionitrile. Additionally, the indolizinone **4-3p** could be transformed into the topoisomerase I inhibitor (**4-7**) in 65% yield by one pot. Similarly, indolizinone **4-3r** could deliver rosettacin (**4-8**) in 46% yield by one pot (Scheme 38).



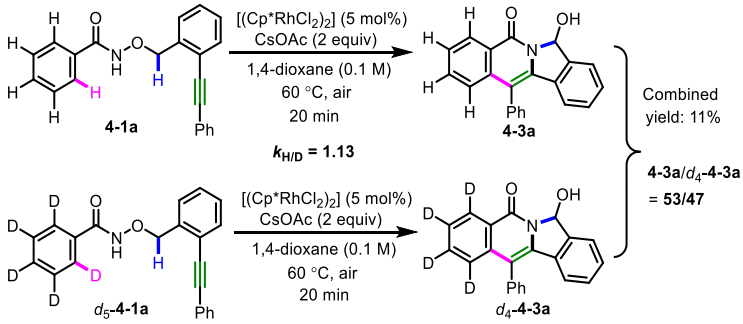
Scheme 37 Transformations of indolizinone **4-3a**.



Scheme 38 Synthesis of topoisomerase I inhibitor and rosettacin.



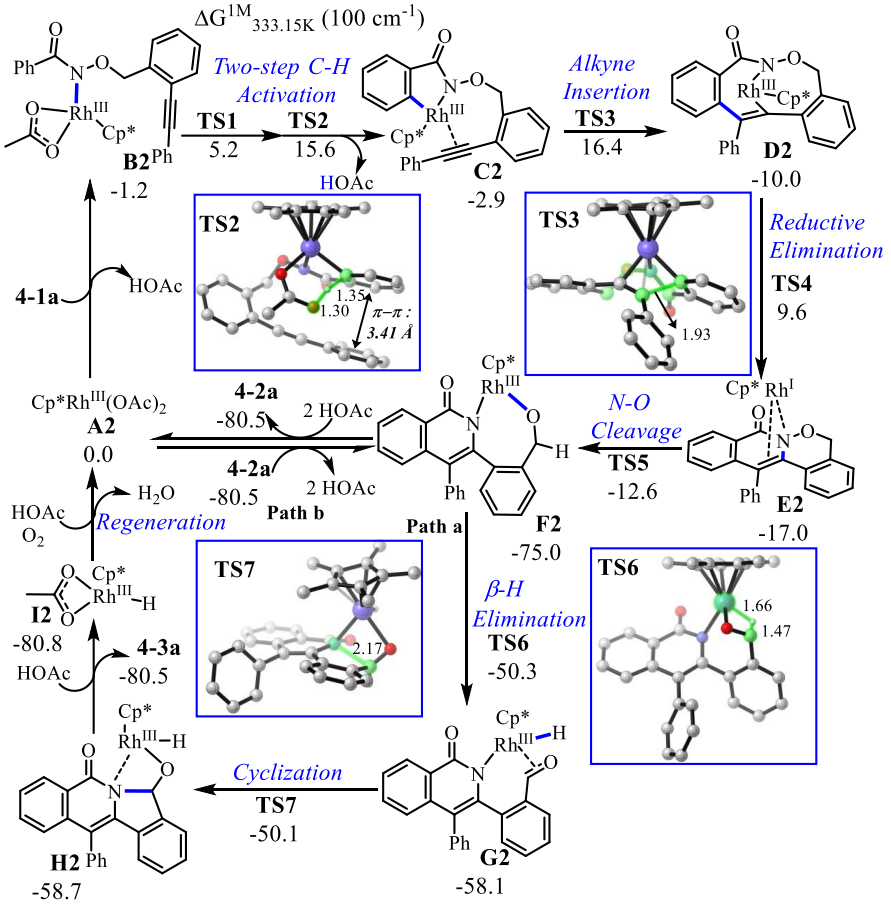
Scheme 39 Control experiments.



Scheme 40 Study of the kinetic isotope effect.

To explore the mechanism of this annulation reaction, a series of experiments were performed (Scheme 39). When the reaction of **4-1a** was conducted under N_2, **4-3a** was obtained in a lower yield (36%). Using O_2 instead of air, the yield of **4-3a** was improved a little. These results suggest that O_2 is not essential for the reaction and air is enough to accelerate the formation of **4-3a**. When $Cu(OAc)_2$ as oxidant was added under N_2, no significant change was observed. With PivOH under air, the yield of **4-3a** decreased. Moreover, under standard conditions, **4-3a** could be formed from **4-2a** in 27% yield (just almost half of 52% yield), there was no **4-3a** formed from **4-2a** without adding

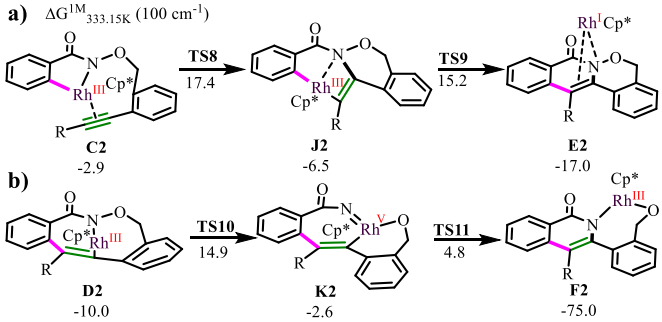
$[RhCp^*Cl_2]_2$. This suggests that two pathways are involved in the construction of **4-3a** and **4-2a** is only an intermediate of minor pathway, the main pathway is leading directly to **4-3a** from **4-1a**, consistent with the above result (Table 6, entry 16). In addition, a modest kinetic isotope effect (KIE) of k_H/k_D = 1.13 was observed using a 1:1 ratio of **4-1a**/d_5-**4-1a** in two parallel reactions, indicating that the C-H bond cleavage process is likely not involved in the rate-limiting step (Scheme 40).



Scheme 41 Plausible pathway of Rh^{III}-catalyzed annulation to afford **4-2a** and **4-3a**.

To better understand the Rh-catalyzed intramolecular annulation reaction and explore the transformation from **4-1a** to **4-3a**, the underlying mechanistic profile was constructed based on density

functional theory calculation (B3LYP-D3) results focusing on **4-1a** as the substrate (Scheme 41). A plausible mechanism for formation of **4-2a** was identified, involving fairly standard C-H bond activation followed by the hypothesized Rh^{III}-Rh^{I}-Rh^{III} tandem reductive elimination and N-O oxidative addition to yield intermediate **F2**, which can undergo ready acetolysis to reversibly form **4-2a**. Direct formation of **4-3a** from **4-1a** (path a) and subsequent transformation from **4-2a** to **4-3a** (path b) were also identified. The proposed mechanism starts with substrate coordination to $Cp^*Rh(OAc)_2$, which itself is known to be readily obtained from $[Cp^*RhCl_2]_2$ in presence of acetate. Then, C-H activation takes place through an AMLA (ambiphilic metal-ligand assistance)/CMD (concerted metalation-deprotonation) process to yield **C2**. Alkyne insertion into the Rh-C bond *via* **TS3** (16.4 kcal/mol) provides intermediate **D2**, which can undergo a reductive elimination over the quite demanding **TS4** (19.6 kcal/mol above **D2**). The Rh^{I} intermediate **E2** is able to insert into the N-O bond in a low-barrier step that is notably exothermic and should thus be irreversible. Two successive and facile protonation steps from **F2** then lead to product **4-2a** and regeneration of catalyst. Two alternative mechanisms for the key bond formation and breaking steps were explored (Scheme 42). Insertion of the alkyne into the Rh-N bond is less facile than into the Rh-C bond, while N-O bond cleavage prior to C-N bond formation requires a Rh^{V}-nitrene intermediate **K2** and was also found to be less favorable.



Scheme 42 Energetic profile (kcal/mol) of a) pathway involving alkyne insertion into the Rh-N bond followed by reductive elimination, and b) pathway comprised of the N-O cleavage prior to the C-N bond formation.

Additional reaction steps (β-H elimination, tandem cyclization and regeneration of catalyst) from intermediate **F2** are required to form **4-3a**. Both β-H elimination to **G2** and tandem cyclization to **H2** were calculated to be energetically demanding. The tandem cyclization (**TS7**) is predicted to be overall rate-limiting, consistent with the very small kinetic isotope effect (Scheme 40), though **TS6** has a very similar calculated free energy. **TS7** lies 24.9 kcal/mol above intermediate **F2** and 30.4 kcal/mol above **4-2a**. While this barrier may seem high, kinetic modelling shows that it is fully consistent with the observed reactivity. After the formation and dissociation of **4-3a**, the resulting Rh-H intermediate **I2** can be easily transformed to the catalyst *via* AcOH assisted H_2-formation pathway or AcOH-O_2 assisted H_2O-formation pathway.

4.3. Conclusions

In conclusion, we have developed a novel intramolecular cascade annulation of *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the synthesis of indolizinones *via* rhodium(III)-catalyzed sequential C(sp^2)-H activation and C(sp^3)-H amination. This method shows broad substrate scope and excellent functional-group tolerance, including annulation of various heterocyclic substrates, such as furan, thiophene, pyrrole, benzofuran, benzothiophene, indole and isonicotinamide. Substrates with flexible tethers bearing different substituents were well tolerated. 2-Ethynylquinoline benzamide or acrylamide substrate worked well, giving rosettacin analogue or mappicine analogue. The synthetic utility of this strategy is successfully illustrated by the further derivatization of indolizinone products with aminal functionality. This method also provides an efficient approach for the total synthesis of a topoisomerase I inhibitor and rosettacin. Mechanistic studies and DFT calculations suggest that C-H bond cleavage is likely not involved in the rate-limiting step and that tandem cyclization is probably the rate-limiting step in the formation of indolizinones, in which two pathways are involved through a rhodium hydride intermediate.

Chapter 5

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[Rhodium(III)-catalyzed intermolecular cascade annulation through C-H activation: concise synthesis of rosettacin, Liangliang Song, Guilong Tian and Erik V. Van der Eycken, *Molecular Catalysis*, **2018**, *459*, 129-134] Copyright © 2018, Elsevier.

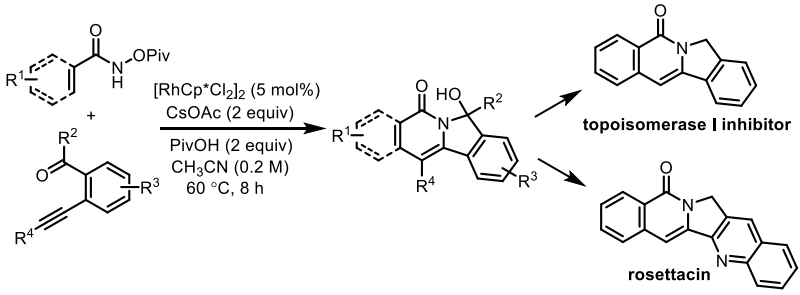
L. Song and E. V. Van der Eycken designed the project and wrote the manuscript. L. Song and G. Tian carried out the experiments. E. V. Van der Eycken organized the research. All authors analysed the data, discussed the results and commented on the manuscript.

5. Rhodium(III)-catalyzed intermolecular cascade annulation through C-H activation: concise synthesis of rosettacin

5.1. Introduction

Tetracyclic heteroring scaffolds are extensively presenting as the core of many natural products and medicines candidates, such as rosettacin,[30-37] oxypalmatine[40-47] and camptothecin,[25] which have been widely investigated for their variety of interesting biological activities such as antifungal, antitumor and antimicrobial properties. Although several approaches for the synthesis of tetracyclic heterorings have been reported, most of them comprise a multistep reaction sequence or harsh conditions. Therefore, developing a concise and novel synthetic methodology is still of great value.

Recently rhodium(III)-catalyzed C-H activation followed by annulation with alkynes has received significant interest for the construction of N-heterocycles and carbocycles owing to efficient metal-substrate interactions.[4-10] Although great progress has been achieved for intermolecular annulation reactions, most of them lead to the formation of a single ring and inevitably go through uncontrolled regioselectivity, resulting in the mixtures of positional isomers, which are mostly difficult to be isolated by flash column. Especially when unbiased unsymmetrical alkynes are employed, the regioselectivity depends on the distinction between both substituents of alkynes.



Scheme 43 Rhodium(III)-catalyzed intermolecular annulation for the synthesis of indolizinones

Based on the above mentioned works (Chapter 2, 3 and 4), we aimed to develop an intermolecular cascade annulation of 2-acetylenic aldehydes

or ketones with *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the synthesis of indolizinones with an internal oxidant. The rhodium(III)-catalyzed intermolecular annulation could avoid the employment of a stoichiometric external oxidant, harsh conditions and lengthy synthetic operations (Scheme 43).

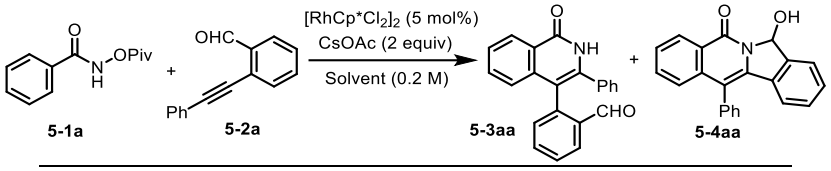
5.2. Results and discussion

We selected *O*-substituted *N*-hydroxybenzamide **5-1a** and ethynylbenzaldehyde **5-2a** as our model substrates (Table 9). When the reaction was performed in MeOH with $[RhCp^*Cl_2]_2$ (5 mol%) and CsOAc (2 equiv) at 60 ℃ for 8 h, the isoquinolone **5-3aa** was obtained in 48 % yield, together with indolizinone **5-4aa** in 17 % yield (Table 9, entry 1). On the base of these promising results, a set of various solvents were screened, such as 1,4-dioxane, DMF, toluene, DCE, THF and CH_3CN, showing that CH_3CN was the best one, which yielded **5-3aa** in 47% and **5-4aa** in 33% (Table 9, entries 2-7). Application of $[Ru(p\text{-cymene})Cl_2]_2$ resulted in a lower yield of **5-3aa** and almost no conversion into **5-4aa** (Table 9, entry 8). Further investigation showed that a lower or higher temperature could not improve the reaction (Table 9, entries 9-10). We also tested PivOH (2 equiv) as additive, resulting in a little improvement of the reaction, yielding **5-3aa** in 48% and **5-4aa** in 39% (Table 9, entry 11).

With the optimal reaction conditions in hand, we examined the scope with respect to the *N*-hydroxybenzamide substrates (Table 10). Introduction of various electron-donating or electron-withdrawing groups to the *para* position of the benzamide is well tolerated, and the isoquinolones were isolated in 42-53% yield (**5-3ba~5-3ga**), while the indolizinones were obtained in 33-40% yield (**5-4ba~5-4ga**). The *meta*-methyl benzamide substrate smoothly reacted to give isoquinolone **5-3ha** in 61% yield, and the indolizinone **5-4ha** in 31% yield. However, the *ortho*-methyl benzamide substrate did not afford the desired products. We next focused on a diverse array of heteroaryl carboxamides, such as furan, thiophene, benzofuran, benzothiophene and indole. All of them successfully proceeded to provide the corresponding. isoquinolones in 32-60% yield (**5-3ja~5-3na**), and the indolizinones in 20-32% yield (**5-4ja~5-4na**). Also, the

isonicotinamide substrate was well tolerated, forming the isoquinolone **3oa** in 39% yield and the indolizinone **5-4oa** in 23% yield. We next inv-

Table 9 Optimization of the reaction conditions[a]

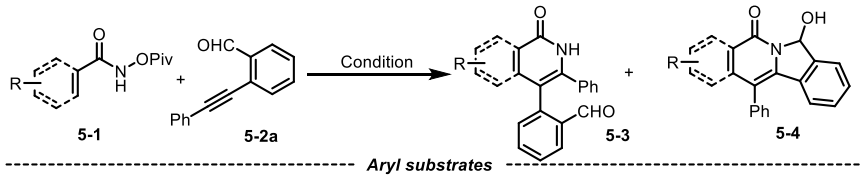


Entry	Solvent	T (°C)	t (h)	Yield (5-3aa, 5-4aa)[b]
1	MeOH	60	8	(48%, 17%)
2	1,4-Dioxane	60	8	(<5%, <5%)
3	DMF	60	8	(<5%, <5%)
4	Toluene	60	8	(52%, 23%)
5	DCE	60	8	(51%, 25%)
6	THF	60	8	(<5%, <5%)
7	CH_3CN	60	8	(47%, 33%)
8[c]	CH_3CN	60	8	(39%, <5%)
9	CH_3CN	40	8	(38%, 27%)
10	CH_3CN	80	8	(44%, 32%)
11[d]	**CH_3CN**	**60**	**8**	**(48%, 39%)**

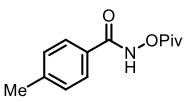
[a] Conditions: **5-1a** (0.3 mmol), **5-2a** (0.45 mmol), catalyst (0.015 mmol), CsOAc (0.6 mmol), solvent (1.5 mL). [b] Isolated yields. [c] [Ru(*p*-

cymene)Cl_2]$_2$ (5 mol%) was used instead of [RhCp*Cl_2]$_2$. [d] PivOH (2 equiv) was added.

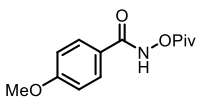
Table 10 Substrate scope for benzamides[ab]



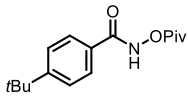
Aryl substrates



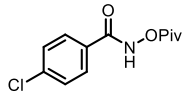
5-3ba (42%)
5-4ba (40%)



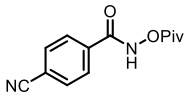
5-3ca (46%)
5-4ca (33%)



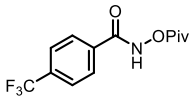
5-3da (51%)
5-4da (34%)



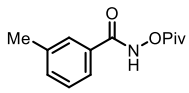
5-3ea (49%)
5-4ea (38%)



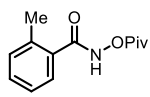
5-3fa (43%)
5-4fa (38%)



5-3ga (53%)
5-4ga (36%)

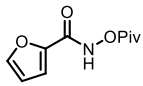


5-3ha (61%)
5-4ha (31%)

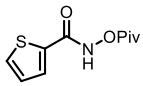


5-3ia (0%)
5-4ia (0%)

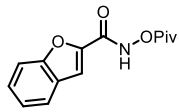
Heteroaryl substrates



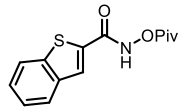
5-3ja (32%)
5-4ja (20%)



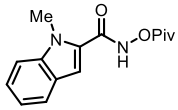
5-3ka (51%)
5-4ka (31%)



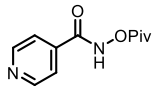
5-3la (36%)
5-4la (21%)



5-3ma (60%)
5-4ma (25%)

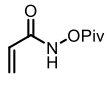


5-3na (46%)
5-4na (32%)

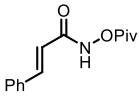


5-3oa (39%)
5-4oa (23%)

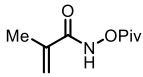
Alkene substrates



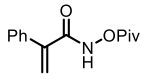
5-3pa (0%)
5-4pa (20%)



5-3qa (0%)
5-4qa (0%)



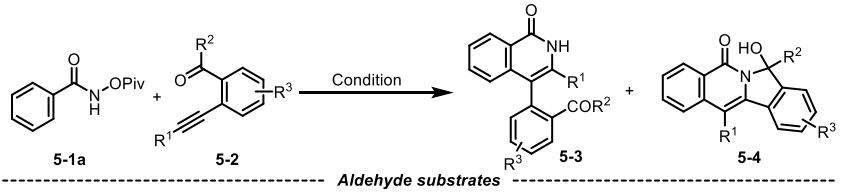
5-3ra (23%)
5-4ra (39%)



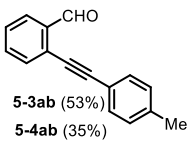
5-3sa (0%)
5-4sa (45%)

[a] Conditions: **5-1** (0.3 mmol), **5-2a** (0.45 mmol), [RhCp*Cl_2]$_2$ (0.015 mmol), CsOAc (0.6 mmol), CH_3CN (1.5 mL), PivOH (0.6 mmol), 60 ^oC, 8 h. [b] Isolated yield.

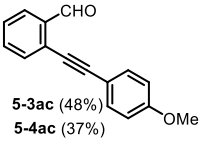
Table 11 Substrate scope for aldehydes and ketones[ab]



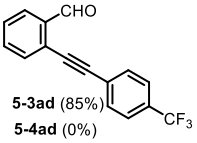
Aldehyde substrates



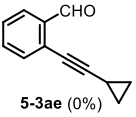
5-3ab (53%)
5-4ab (35%)



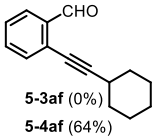
5-3ac (48%)
5-4ac (37%)



5-3ad (85%)
5-4ad (0%)

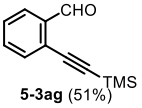


5-3ae (0%)
5-4ae (72%)

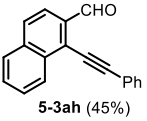


5-3af (0%)
5-4af (64%)

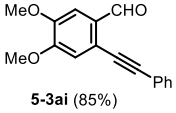
5-3ag (0%)
5-4ag (42%)



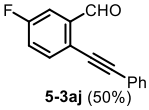
5-3ag (51%)
5-4ag (30%)



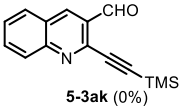
5-3ah (45%)
5-4ah (0%)



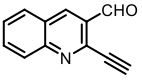
5-3ai (85%)
5-4ai (0%)



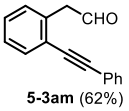
5-3aj (50%)
5-4aj (43%)



5-3ak (0%)
5-4ak (65%)

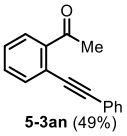


5-3al (0%)
5-4al (46%)

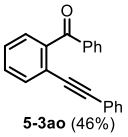


5-3am (62%)
5-4am (0%)

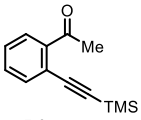
Ketone substrates



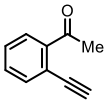
5-3an (49%)
5-4an (31%)



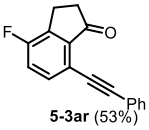
5-3ao (46%)
5-4ao (37%)



5-3ap (33%)
5-4ap (0%)



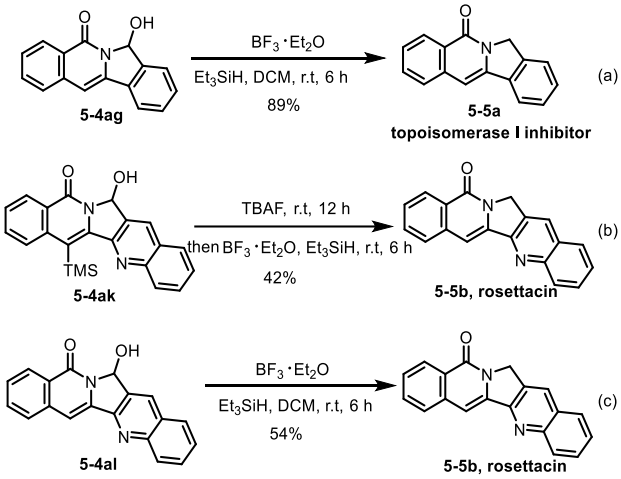
5-3aq (0%)
5-4aq (39%)



5-3ar (53%)
5-4ar (0%)

[a] Conditions: **5-1a** (0.3 mmol), **5-2** (0.45 mmol), $[RhCp^*Cl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), CH_3CN (1.5 mL), PivOH (0.6 mmol), 60 °C, 8 h. [b] Isolated yield.

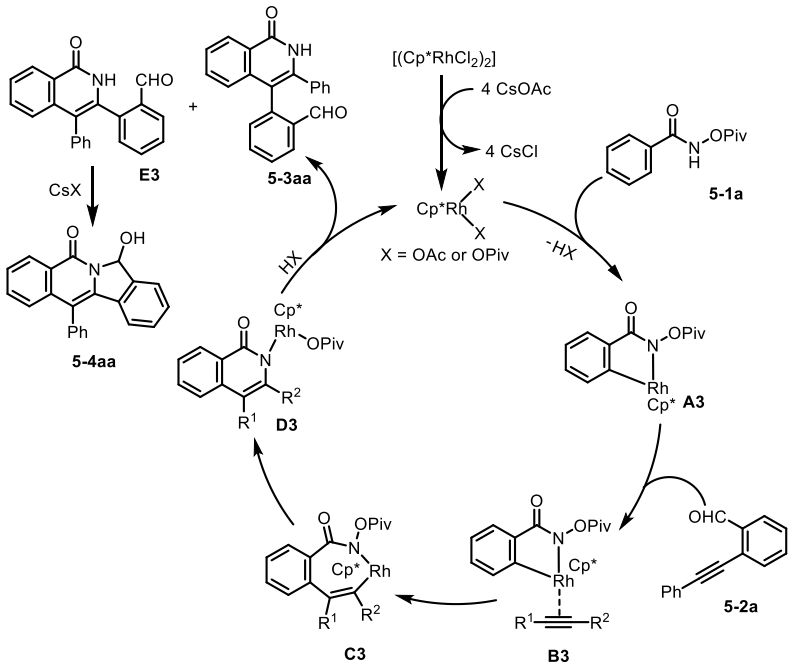
estigated the reactivity of acrylamide substrates. Acrylamide itself only yielded the indolizinone **5-4pa** (20%). While methacrylamide afforded the corresponding isoquinolone **5-3ra** in 23% yield, and the indolizinone **5-4ra** in 39% yield. Only the indolizinone **5-4sa** was obtained in 45% yield from 2-phenylacrylamide. However, the cinnamamide substrate did not give the desired products.



Scheme 44 Synthesis of topoisomerase I inhibitor and rosettacin.

We next focused on the scope varying the ethynylbenzaldehyde (Table 11). When substrates with a *para*-methyl or *para*-methoxy group in the phenyl substituent of the alkyne were utilized, the corresponding isoquinolones (**5-3ab** and **5-3ac**) and indolizinones (**5-4ab** and **5-4ac**) were smoothly formed. For the substrate bearing a *para*-trifluoromethyl group, only the corresponding isoquinolone **5-3ad** was observed (85%). When we replaced the aryl groups of the alkyne by a cyclopropyl or cyclohexyl group, both of them only yielded the corresponding indolizinone **5-4ae** (72%) and **5-4af** (64%). Also a terminal alkyne substrate was tolerated, only giving the indolizinone **5-4ag** (42%). The TMS-protected alkyne substrate provided the isoquinolone **5-3ag** without TMS group in 51% yield and the indolizinone **5-4ag** without TMS group in 30% yield. Naphthaldehyde and dimethoxybenzaldehyde substrates turned out to be compatible, only offering the corresponding

isoquinolone **5-3ah** (45%) and **5-3ai** (85%). The fluorobenzaldehyde substrate smoothly reacted to yield the corresponding isoquinolone **5-3aj** (50%) and indolizinone **5-4aj** (43%). The reaction also tolerated the 2-ethynylquinoline-3-carbaldehyde and the TMS-protected derivative, resulting in the sole formation of indolizinone **5-4ak** (65%) and **5-4al** (46%). Interestingly, the phenylacetaldehyde substrate worked well, only yielding the corresponding isoquinolone **5-3am** (62%).
Then we extended the reaction to ketone substrates. Acetophenone and benzophenone derivatives were both acceptable, giving the corresponding isoquinolones (**5-3an** and **5-3ao**) and indolizinones (**5-4an** and **5-4ao**). The terminal alkyne ketone only afforded the indolizinone **5-4aq** in 39% yield. But only the isoquinolone **5-3ap** was obtained from the TMS-protected analogue. Also the cycloketone substrate was proved to be suitable, leading to only the isoquinolone **5-3ar** in 53% yield.



Scheme 45. Proposed mechanism.

We next investigated the synthetic utility of the reaction. Upon treatment with $BF_3 \cdot Et_2O/Et_3SiH$, indolizinone **5-4ag** could be transformed into the topoisomerase I inhibitor (**5-5a**) in 89% yield in

one step (Scheme 44a). Similarly, indolizinone **5-4ak** underwent TMS-removal with TBAF, followed by treatment with $BF_3 \cdot Et_2O/Et_3SiH$, delivering rosettacin (**5-5b**) in 42% yield in a one pot protocol (Scheme 44b). This compound could also be obtained from indolizinone **5-4al** in 54% yield under treatment with $BF_3 \cdot Et_2O/Et_3SiH$ (Scheme 44c).
On the basis of our experimental results, a plausible mechanism is proposed (Scheme 45). First, a rhodium-catalyzed C-H bond activation occurs to form the five-membered rhodacycle intermediate **A3**. Subsequent intermolecular coordination of the alkyne of **5-2a** produces intermediate **B3**, which undergoes insertion into the Rh-C bond to afford seven-membered rhodacycle **C3**. Reductive elimination followed by oxidative addition into the N-O bond furnishes intermediate **D3**, which undergoes protonation by acetic/pivalic acid to give product **5-3aa**, intermediate **E3** and regenerate the catalyst. Finally, tandem cyclization under CsOAc/CsOPiv leads to the formation of the product **5-4aa**.

5.3. Conclusions

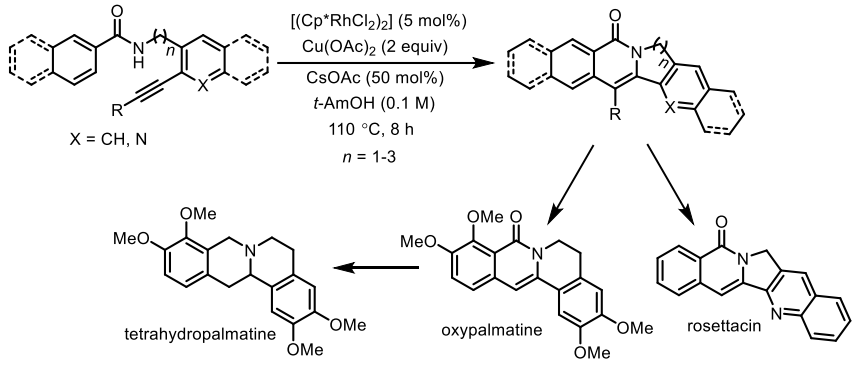
In summary, we have developed an intermolecular annulation of 2-acetylenic aldehydes or ketones with *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides through rhodium(III)-catalyzed C-H activation for the synthesis of isoquinolones and indolizinones. This reaction shows excellent functional-group tolerance and broad substrate scope, including annulation of various heterocyclic substrates, such as furan, thiophene, benzofuran, benzothiophene, indole and isonicotinamide. And cycloketone substrate was proved to be suitable for the reaction. Notably, terminal alkyne substrates and aliphatic substituted alkyne substrates only gave indolizinones. This method also furnishes an efficient approach for the total synthesis of rosettacin and a topoisomerase I inhibitor.

General conclusions and perspectives

General Conlusions

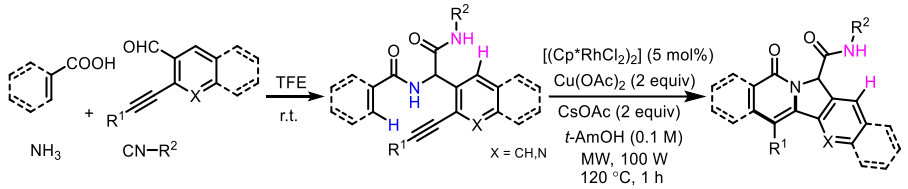
In this thesis, several methods have been developed for the construction of indolizinone and quinolizinone scaffolds through rhodium(III)-catalyzed cascade annulations triggered by C(sp^2)-H activation. These novel and efficient strategies extend the existing methodologies, providing more mild and concise pathways to synthesize indolizinone and quinolizinone scaffolds.

In **Chapter 2**, an efficient rhodium(III)-catalyzed intramolecular annulation of benzamides bearing *N*-tethered alkynes for the synthesis of indolizinones and quinolizinones is developed. This reaction features a broad substrate scope and excellent functional-group tolerance, including substrates bearing a longer carbon chain between the benzamide and the alkyne, as well as different heterocyclic substrates, such as furan, thiophene, pyrrole, benzofuran, benzothiophene, indole and isonicotinamide substrates. This method also provides a reliable and highly efficient approach for the synthesis of rosettacin, oxypalmatine and tetrahydropalmatine.

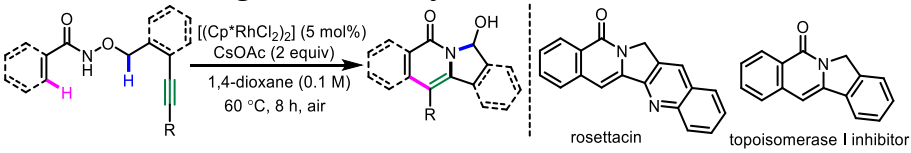


In **Chapter 3**, a chemoselective rhodium(III)-catalyzed intramolecular annulation protocol for the construction of the indolizinone and

quinolizinone scaffold is developed. Ugi reaction and microwave-assisted C(sp^2)-H activation set the stage for the diversification of various peptidomimetics and oligopeptides in a rapid and step-economical manner, including heteroaryl peptidomimetics, such as furan, thiophene, pyrrole, benzofuran, benzothiophene, indole, isonicotinamide and thiazole-5-carboxamide peptidomimetics, as well as di-, tri-, tetra- and pentapeptides. Notably, this approach is compatible with water.

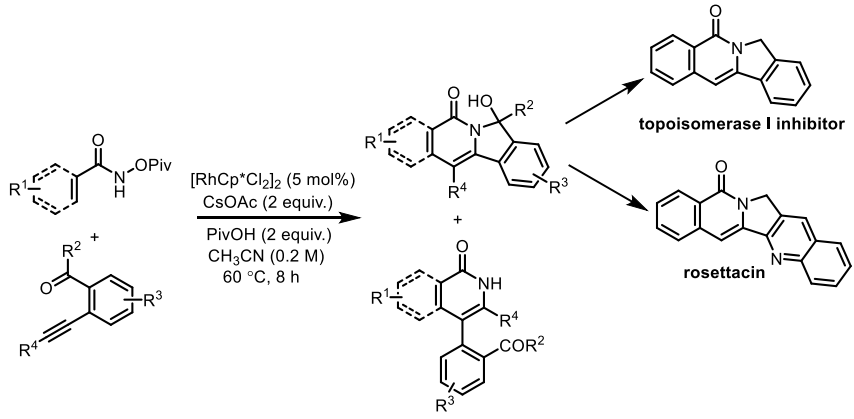


In **Chapter 4**, a novel intramolecular cascade annulation of *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides for the synthesis of indolizinones *via* a rhodium(III)-catalyzed sequential C(sp^2)-H activation and C(sp^3)-H amination is developed. This method shows broad substrate scope and excellent functional-group tolerance, including substrates with flexible tethers bearing different substituents, as well as heterocyclic substrates, such as furan, thiophene, pyrrole, benzofuran, benzothiophene, indole and isonicotinamide substrates. The synthetic utility of this strategy is successfully illustrated by the further derivatization of indolizinone products with aminal functionality. This method also provides an efficient approach for the total synthesis of a topoisomerase I inhibitor and rosettacin. Mechanistic studies and DFT calculations suggest that C-H bond cleavage is likely not involved in the rate-limiting step and that tandem cyclization is probably the rate-limiting step in the formation of indolizinones, in which two pathways are involved through a rhodium hydride intermediate.



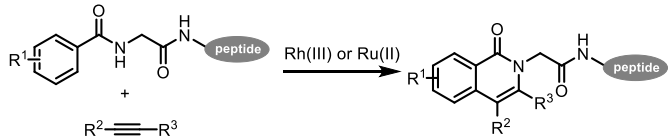
In **Chapter 5**, an intermolecular annulation of 2-acetylenic aldehydes or ketones with *O*-substituted *N*-hydroxybenzamides or *N*-hydroxyacrylamides through rhodium(III)-catalyzed C-H activation for the synthesis of isoquinolones and indolizinones is developed. This

reaction shows excellent functional-group tolerance and broad substrate scope, including heterocyclic substrates, such as furan, thiophene, benzofuran, benzothiophene, indole and isonicotinamide substrates, as well as cycloketone substrate. Notably, terminal alkyne substrates and aliphatic substituted alkyne substrates only gave indolizinones. This method also furnishes an efficient and concise approach for the total synthesis of rosettacin and a topoisomerase I inhibitor.



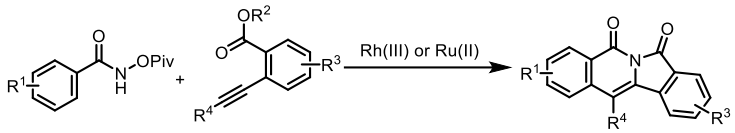
Perspectives

Following the direction of **Chapter 3**, transition metal-catalyzed intermolecular annulation of peptides with alkynes could be tried in the further work. In this case, diverse peptides could be labelled by various isoquinolone scaffolds without diastereoselectivity problem (Scheme 46).



Scheme 46 Transition metal-catalyzed intermolecular annulation of peptides with alkynes.

Following the direction of **Chapter 5**, transition metal-catalyzed intermolecular annulation of 2-acetylenic esters with *O*-substituted *N*-hydroxybenzamides could be attempted in the further work. In this case, various isoindolo[2,1-*b*]isoquinoline-5,7-dione scaffolds could be synthesized in a concise manner (Scheme 47).



Scheme 47 Transition metal-catalyzed intermolecular annulation of 2-acetylenic esters with *O*-substituted *N*-hydroxybenzamides.

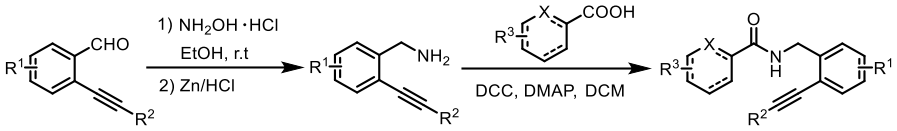
Experimental part

General information

Commercially available reagents were used without additional purification. Column chromatography was performed with silica gel (70-230 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance (300 or 400 or 600 MHz) spectrometer at ambient temperature using $CDCl_3$ or DMSO-d_6 as solvent. HRMS (ESI) spectrometry data were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer [Synapt G2 high definition mass spectrometer (HDMS), Waters, Milford, MA]. Samples were infused at 3 μL min^{-1}, and spectra were obtained in the positive ionization mode with a resolution of 15000 [full width at half maximum (FWHM)] with leucine encephalin as lock mass. Melting points were recorded on a Reichert Thermovar apparatus and are uncorrected. The microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus, operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300 W. The reactions were carried out in 10 mL glass tubes, sealed with Teflon septum and placed in the microwave cavity. The reactions were irradiated at the required set temperature and power for the stipulated time and then cooled to ambient temperature with air jet cooling.

Chapter 2

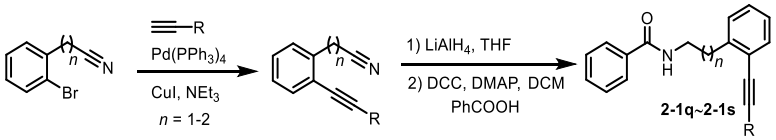
Synthesis of the substrates



General Procedure A

A solution of corresponding 2-alkynylbenzaldehyde (4 mmol, 1 equiv.) and hydroxyl-ammonium chloride (4.8 mmol, 1.2 equiv.) in ethanol (2.5 mL) was stirred for 60 min. Subsequently, hydrochloric acid (12 M, 1.34 mL, 4 equiv.) and zinc dust (10 mmol, 2.5 equiv.) were slowly added to the solution and the mixture was stirred at room temperature for 30 min. A solution of ammonia (30%, 1.4 mL) and sodium hydroxide (6 M, 3mL) was added dropwise to the resulting slurry, and the mixture was stirred at room temperature for 30 min. Then, the resultant solution was extracted with DCM, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The resulting crude primary amine was used in the subsequent step without further purification[62].

Under the protection of argon[63], a solution of the crude primary amine and the corresponding aryl acid (4.4 mmol, 1.1 equiv.) in DCM (2 mL) was cooled to 0 °C. Then, DMAP (0.4 mmol, 0.1 equiv.) and DCC (4.4 mmol, 1.1 equiv.) in DCM (4 mL) were added dropwise. The mixture was then stirred at room temperature until full consumption of the starting material as monitored by TLC. The crude mixture was filtered and washed with DCM. The filtrate was concentrated and the residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-1a~2-1p**, **2-1t~2-1z**.



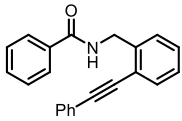
General Procedure B

To a solution of corresponding 2-bromophenylacetonitrile (5.0 mmol, 1 equiv.) and corresponding ethyne (6.0 mmol, 1.2 equiv.) in Et_3N (20 mL) were added $Pd(PPh_3)_4$ (0.25 mmol, 5 mol%) and CuI (0.15 mmol, 3 mol%) at room temperature under argon. Then the reaction mixture was

gradually warmed up to 85 ℃ and stirred at the same temperature for 30 h. After cooling down to room temperature, the crude mixture was filtered and extracted with ethyl acetate. The combined organic extracts were washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford corresponding 2-ethynylphenylacetonitrile[64].

The 2-ethynylphenylacetonitrile, and distilled THF (20 mL) were mixed together, then $LiAlH_4$ (25 mmol, 5 equiv.) was added portion-wise to the solution at 0 °C. The mixture was left under stirring for 24 h at room temperature, then it was hydrolyzed at 0 °C with water to neutralize excess $LiAlH_4$ and extracted with DCM. The combined organic phases were washed with brine, dried over Na_2SO_4 and the solvent was removed under vacuum. The residue was used in the subsequent step without further purification[65].

Under the protection of argon[63], a solution of the crude primary amine and benzoic acid (5.5 mmol, 1.1 equiv.) in DCM (2.5 mL) was cooled to 0 °C. Then, DMAP (0.5 mmol, 0.1 equiv.) and DCC (5.5 mmol, 1.1 equiv.) in DCM (5 mL) were added dropwise. The mixture was then stirred at room temperature until full consumption of the starting material as monitored by TLC. The crude mixture was filtered and washed with DCM. The filtrate was concentrated and the residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-1q~2-1s**.



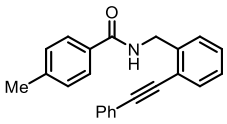
2-1a

Following **General Procedure A**, **2-1a** was obtained as a white solid (64%, three steps). Melting point 100-102 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.74 (2H, m), 7.56 (1H, dd, J = 7.3, 1.7 Hz), 7.54-7.50 (2H, m), 7.46-7.42 (2H, m), 7.40-7.32 (5H, m), 7.32-7.24 (2H, m), 6.78 (1H, s), 4.87 (2H, d, J = 5.8 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 139.7, 134.4, 132.4, 131.5, 131.4, 128.8, 128.64, 128.58, 128.5, 128.4, 127.6, 126.9, 122.8, 122.4, 94.3, 87.1, 43.0.

HRMS (ESI, m/z) calcd for $C_{22}H_{18}NO$ $(M+H)^+$: 312.1383, found: 312.1383.



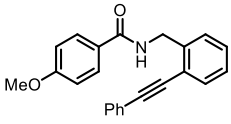
2-1b

Following **General Procedure A**, **2-1b** was obtained as a white solid (56%, three steps). Melting point 126-128 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (2H, d, J = 8.1 Hz), 7.56-7.48 (3H, m), 7.42-7.38 (1H, m), 7.35-7.30 (3H, m), 7.29-7.22 (2H, m), 7.14 (2H, d, J = 8.0 Hz), 6.85 (1H, s), 4.84 (2H, d, J = 5.8 Hz), 2.33 (3H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 141.8, 139.8, 132.3, 131.48, 131.45, 129.1, 128.7, 128.5, 128.38, 128.36, 127.4, 126.9, 122.8, 122.3, 94.3, 87.1, 42.8, 21.3.

HRMS (ESI, m/z) calcd for $C_{23}H_{19}NONa$ $(M+Na)^+$: 348.1359, found: 348.1354.



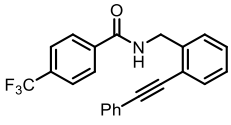
2-1c

Following **General Procedure A**, **2-1c** was obtained as a yellow solid (62%, three steps). Melting point 143-145 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (2H, d, J = 8.8 Hz), 7.58-7.50 (3H, m), 7.44 (1H, d, J = 7.2 Hz), 7.37-7.33 (3H, m), 7.33-7.25 (2H, m), 6.87 (2H, d, J = 8.8 Hz), 6.66 (1H, s), 4.85 (2H, d, J = 5.8 Hz), 3.81 (3H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 162.1, 140.0, 132.4, 131.5, 128.8, 128.72, 128.65, 128.6, 128.4, 127.5, 126.7, 122.8, 122.4, 113.7, 94.3, 87.1, 55.3, 42.9.

HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_2$ $(M+H)^+$: 342.1488, found: 342.1481.

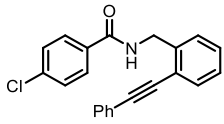


2-1d

Following **General Procedure A**, **2-1d** was obtained as a white solid (61%, three steps). Melting point 134-136 ℃.

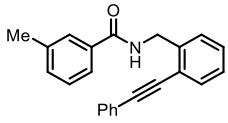
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (2H, d, J = 8.1 Hz), 7.62 (2H, d, J = 8.2 Hz), 7.59-7.55 (1H, m), 7.53-7.49 (2H, m), 7.42 (1H, dd, J = 5.8, 3.2 Hz), 7.37-7.29 (5H, m), 6.86 (1H, s), 4.86 (2H, d, J = 5.8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 139.3, 137.7, 133.3, 132.9, 132.5, 131.5, 128.9, 128.7, 128.5, 127.8, 127.4, 125.6 (d, J = 3.7 Hz), 122.6, 122.5, 121.8, 94.5, 87.0, 43.1.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.97.
HRMS (ESI, m/z) calcd for $C_{23}H_{16}F_3NONa$ $(M+Na)^+$: 402.1076, found: 402.1078.



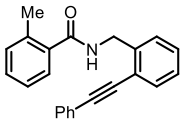
2-1e

Following **General Procedure A**, **2-1e** was obtained as a red solid (57%, three steps). Melting point 130-132 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.67 (2H, m), 7.56 (1H, dd, J = 7.1, 1.8 Hz), 7.53-7.49 (2H, m), 7.44-7.40 (1H, m), 7.36-7.29 (7H, m), 6.74 (1H, s), 4.84 (2H, d, J = 5.8 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 139.5, 137.7, 132.8, 132.5, 131.5, 128.83, 128.76, 128.72, 128.67, 128.5, 128.4, 127.7, 122.7, 122.5, 94.4, 87.0, 43.1.
HRMS (ESI, m/z) calcd for $C_{22}H_{16}ClNONa$ $(M+Na)^+$: 368.0813, found: 368.0810.



2-1f

Following **General Procedure A**, **2-1f** was obtained as a white solid (60%, three steps). Melting point 96-98 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (1H, s), 7.52 (4H, m), 7.40 (1H, d, J = 7.1 Hz), 7.35-7.30 (3H, m), 7.30-7.22 (4H, m), 6.87 (1H, s), 4.84 (2H, d, J = 5.8 Hz), 2.29 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 139.8, 138.2, 134.3, 132.3, 132.1, 131.5, 128.7, 128.5, 128.4, 128.3, 127.6, 127.4, 123.9, 122.7, 122.2, 94.3, 87.1, 42.8, 21.2.
HRMS (ESI, m/z) calcd for $C_{23}H_{19}NONa$ $(M+Na)^+$: 348.1359, found: 348.1352.



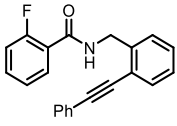
2-1g

Following **General Procedure A**, **2-1g** was obtained as a yellow solid (54%, three steps). Melting point 128-130 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.48 (3H, m), 7.44 (1H, d, J = 7.1 Hz), 7.36-7.23 (7H, m), 7.18-7.09 (2H, m), 6.31 (1H, s), 4.82 (2H, d, J = 5.7 Hz), 2.40 (3H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 139.6, 136.2, 136.1, 132.4, 131.5, 130.9, 129.8, 128.8, 128.6, 128.5, 128.4, 127.6, 126.7, 125.6, 122.7, 122.4, 94.3, 87.0, 42.7, 19.7.

HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO$ $(M+H)^+$: 326.1539, found: 326.1537.



2-1h

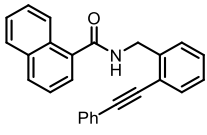
Following **General Procedure A**, **2-1h** was obtained as a yellow solid (62%, three steps). Melting point 84-86 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (1H, td, J = 7.9, 1.2 Hz), 7.59-7.53 (3H, m), 7.46 (2H, dd, J = 13.4, 7.4 Hz), 7.35 (4H, dd, J = 6.9, 4.8 Hz), 7.23 (2H, dd, J = 14.7, 7.2 Hz), 7.11-7.06 (1H, m), 4.90 (2H, d, J = 5.8 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1 (d, J = 3.2 Hz), 161.9, 159.4, 139.6, 133.3 (d, J = 9.7 Hz), 132.4, 132.1 (d, J = 2.1 Hz), 131.6, 128.8, 128.5 (d, J = 3.0 Hz), 128.4, 127.6, 124.8 (d, J = 3.3 Hz), 122.9, 122.5, 120.9 (d, J = 11.4 Hz), 116.0 (d, J = 24.8 Hz), 94.4, 86.9, 42.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -113.34.

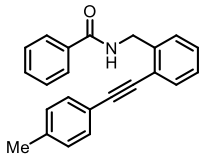
HRMS (ESI, m/z) calcd for $C_{22}H_{17}FNO$ $(M+H)^+$: 330.1289, found: 330.1288.



2-1i

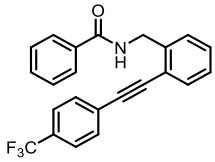
Following **General Procedure A**, **2-1i** was obtained as a red solid (59%, three steps). Melting point 128-130 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (1H, d, J = 8.2 Hz), 7.80 (3H, dd, J = 12.5, 8.3 Hz), 7.55 (2H, d, J = 6.9 Hz), 7.50 (2H, dd, J = 6.4, 2.8 Hz), 7.47-7.42 (3H, m), 7.30 (5H, dd, J = 6.5, 4.3 Hz), 6.56 (1H, s), 4.90 (2H, d, J = 5.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 139.5, 134.2, 133.5, 132.4, 131.5, 130.5, 130.1, 128.7, 128.6, 128.5, 128.4, 128.1, 127.6, 127.0, 126.3, 125.4, 124.9, 124.6, 122.7, 122.5, 94.4, 87.0, 43.0.
HRMS (ESI, m/z) calcd for $C_{26}H_{19}NONa$ $(M+Na)^+$: 384.1359, found: 384.1361.



2-1j

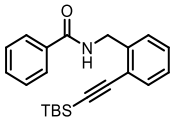
Following **General Procedure A**, **2-1j** was obtained as a yellow solid (57%, three steps). Melting point 126-128 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.74 (2H, m), 7.57-7.52 (1H, m), 7.46-7.39 (5H, m), 7.37 (1H, t, J = 1.6 Hz), 7.31-7.26 (2H, m), 7.15 (2H, dd, J = 8.4, 0.6 Hz), 6.78 (1H, s), 4.86 (2H, d, J = 5.8 Hz), 2.36 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 139.6, 138.8, 134.4, 132.3, 131.4, 129.2, 128.6, 128.5, 127.6, 126.9, 122.6, 119.6, 94.6, 86.5, 43.0, 21.5.
HRMS (ESI, m/z) calcd for $C_{23}H_{19}NONa$ $(M+Na)^+$: 348.1359, found: 348.1356.



2-1k

Following **General Procedure A**, **2-1k** was obtained as a white solid (60%, three steps). Melting point 149-151 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.74 (2H, m), 7.65-7.57 (5H, m), 7.50-7.44 (2H, m), 7.43-7.39 (2H, m), 7.38-7.31 (2H, m), 6.61 (1H, s), 4.88 (2H, d, J = 5.7 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 139.9, 134.3, 132.7, 131.8, 131.6, 129.4, 128.7, 128.6, 127.7, 126.9, 125.3 (d, J = 3.8 Hz), 121.8, 92.9, 89.3, 42.9.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.81.

HRMS (ESI, m/z) calcd for $C_{23}H_{16}F_3NONa$ $(M+Na)^+$: 402.1076, found: 402.1074.



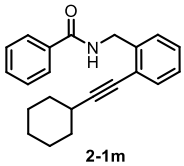
2-1l

Following **General Procedure A**, **2-1l** was obtained as a white solid (48%, three steps). Melting point 77-79 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83-7.76 (2H, m), 7.47 (5H, m), 7.32-7.22 (2H, m), 6.89 (1H, s), 4.79 (2H, d, J = 6.0 Hz), 1.01 (9H, s), 0.21 (6H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 140.3, 134.4, 132.8, 131.4, 129.0, 128.7, 128.5, 127.4, 126.9, 122.3, 103.7, 97.9, 42.9, 26.1, 16.6, -4.6.

HRMS (ESI, m/z) calcd for $C_{22}H_{27}NOSiNa$ $(M+Na)^+$: 372.1754, found: 372.1749.



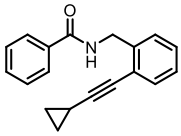
2-1m

Following **General Procedure A**, **2-1m** was obtained as a yellow solid (50%, three steps). Melting point 82-84 ℃.

^{1}H NMR (400 MHz, CDCl3) δ 7.80-7.75 (2H, m), 7.51-7.45 (1H, m), 7.45-7.36 (4H, m), 7.27-7.20 (2H, m), 6.74 (1H, s), 4.76 (2H, d, J = 5.8 Hz), 2.64 (1H, ddd, J = 12.7, 8.8, 3.7 Hz), 1.87 (2H, dd, J = 9.7, 3.6 Hz), 1.79-1.66 (2H, m), 1.53 (3H, m), 1.34 (3H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 139.5, 134.5, 132.3, 131.4, 128.6, 128.5, 128.0, 127.4, 126.9, 123.3, 99.7, 78.4, 43.1, 32.7, 29.8, 25.8, 24.8.

HRMS (ESI, m/z) calcd for $C_{22}H_{23}NONa$ $(M+Na)^+$: 340.1672, found: 340.1671.

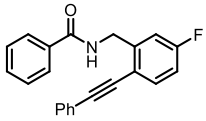


2-1n

Following **General Procedure A**, **2-1n** was obtained as a yellow solid (46%, three steps). Melting point 96-98 ℃.

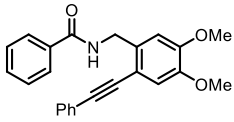
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.75 (2H, m), 7.53-7.43 (2H, m), 7.41 (2H, dd, J = 8.5, 1.9 Hz), 7.38-7.34 (1H, m), 7.27-7.20 (2H, m),

6.70 (1H, s), 4.73 (2H, d, J = 5.8 Hz), 1.48 (1H, tt, J = 8.2, 5.1 Hz), 0.93-0.84 (2H, m), 0.79 (2H, m).
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 139.6, 134.5, 132.4, 131.4, 128.5, 127.9, 127.4, 126.9, 123.1, 98.7, 73.6, 43.0, 8.8, 0.2.
HRMS (ESI, m/z) calcd for $C_{19}H_{17}NONa$ $(M+Na)^+$: 298.1203, found: 298.1196.



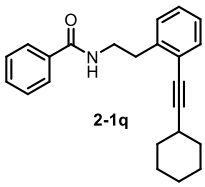
2-1o

Following **General Procedure A**, **2-1o** was obtained as a yellow solid (61%, three steps). Melting point 144-146 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.75 (2H, m), 7.55-7.44 (5H, m), 7.39 (1H, d, J = 1.5 Hz), 7.37-7.33 (3H, m), 7.15 (1H, dd, J = 9.2, 2.6 Hz), 6.97 (1H, td, J = 8.4, 2.7 Hz), 6.85 (1H, s), 4.85 (2H, d, J = 6.0 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 167.5, 164.2, 160.9, 142.5 (d, J = 7.6 Hz), 134.1 (d, J = 10.8 Hz), 133.6, 131.6 (d, J = 13.0 Hz), 130.1, 128.5 (dd, J = 14.0, 3.8 Hz), 127.0, 122.6, 118.2 (d, J = 3.4 Hz), 115.5 (d, J = 22.9 Hz), 114.7 (d, J = 22.0 Hz), 94.0, 86.1, 42.5.
^{19}F NMR (377 MHz, $CDCl_3$) δ -109.78.
HRMS (ESI, m/z) calcd for $C_{22}H_{16}FNONa$ $(M+Na)^+$: 352.1108, found: 352.1105.



2-1p

Following **General Procedure A**, **2-1p** was obtained as a yellow solid (64%, three steps). Melting point 168-170 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.73 (2H, m), 7.52-7.43 (3H, m), 7.41-7.32 (5H, m), 7.04 (1H, s), 6.98 (1H, s), 6.73 (1H, d, J = 7.0 Hz), 4.81 (2H, d, J = 5.8 Hz), 3.90 (3H, s), 3.89 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 149.6, 148.1, 134.4, 133.4, 131.4, 131.4, 128.5, 128.4, 128.4, 126.9, 122.9, 114.5, 114.4, 112.1, 92.7, 87.3, 56.0, 42.8, 30.9.
HRMS (ESI, m/z) calcd for $C_{24}H_{21}NO_3Na$ $(M+Na)^+$: 394.1414, found: 394.1409.



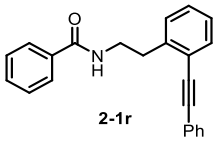
2-1q

Following **General Procedure B**, **2-1q** was obtained as a white solid (49%, three steps). Melting point 100-102 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74-7.67 (2H, m), 7.50-7.38 (4H, m), 7.25-7.14 (3H, m), 6.31 (1H, s), 3.85-3.70 (2H, m), 3.18-3.06 (2H, m), 2.66-2.51 (1H, m), 1.83 (2H, dd, J = 9.5, 3.4 Hz), 1.72 (2H, dd, J = 9.0, 3.6 Hz), 1.57-1.42 (3H, m), 1.36-1.25 (3H, m).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 140.7, 134.6, 132.4, 131.3, 129.3, 128.4, 128.0, 126.9, 126.5, 123.7, 98.8, 79.1, 40.8, 33.8, 32.6, 29.7, 25.8, 24.8.

HRMS (ESI, m/z) calcd for $C_{23}H_{25}NONa$ $(M+Na)^+$: 354.1829, found: 354.1829.



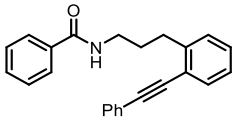
2-1r

Following **General Procedure B**, **2-1r** was obtained as a yellow solid (55%, three steps). Melting point 103-105 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70-7.64 (2H, m), 7.58-7.48 (3H, m), 7.40 (1H, dt, J = 2.6, 1.8 Hz), 7.34-7.22 (8H, m), 6.40 (1H, s), 3.89-3.77 (2H, m), 3.20 (2H, t, J = 6.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 141.0, 138.3, 134.5, 132.4, 131.5, 131.2, 129.5, 128.8, 128.43, 128.37, 126.8, 126.6, 122.90, 122.88, 93.4, 87.9, 40.9, 34.0.

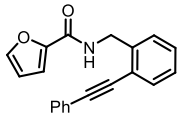
HRMS (ESI, m/z) calcd for $C_{23}H_{19}NONa$ $(M+Na)^+$: 348.1359, found: 348.1360.



2-1s

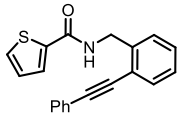
Following **General Procedure B**, **2-1s** was obtained as a red solid (50%, three steps). Melting point 63-65 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.60 (2H, m), 7.53-7.40 (4H, m), 7.32-7.21 (8H, m), 6.38 (1H, s), 3.51 (2H, dd, J = 12.7, 6.7 Hz), 2.97 (2H, t, J = 7.5 Hz), 2.11-1.96 (2H, m).
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 143.3, 134.4, 132.3, 131.4, 131.2, 128.9, 128.7, 128.4, 128.34, 128.29, 126.8, 126.1, 123.1, 122.5, 93.0, 88.0, 39.5, 31.9, 30.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{21}NONa$ $(M+Na)^+$: 362.1516, found: 362.1511.



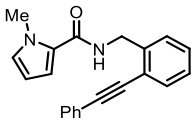
2-1t

Following **General Procedure A**, **2-1t** was obtained as a red solid (50%, three steps). Melting point 76-78 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (3H, dd, J = 6.2, 3.6 Hz), 7.46-7.40 (1H, m), 7.38-7.32 (4H, m), 7.32-7.24 (2H, m), 7.11 (1H, d, J = 3.4 Hz), 6.94 (1H, s), 6.46 (1H, dd, J = 3.5, 1.7 Hz), 4.84 (2H, d, J = 6.1 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 147.9, 143.8, 139.5, 132.3, 131.5, 128.7, 128.5, 128.4, 127.5, 122.8, 122.4, 114.3, 112.1, 94.4, 86.9, 41.9.
HRMS (ESI, m/z) calcd for $C_{20}H_{16}NO_2$ $(M+H)^+$: 302.1175, found: 302.1174.



2-1u

Following **General Procedure A**, **2-1u** was obtained as a red solid (52%, three steps). Melting point 64-66 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.46 (4H, m), 7.41-7.36 (2H, m), 7.35-7.30 (3H, m), 7.28-7.21 (2H, m), 6.97 (1H, dd, J = 4.8, 3.9 Hz), 6.85 (1H, s), 4.80 (2H, d, J = 5.9 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 139.6, 138.7, 132.2, 131.5, 129.9, 128.7, 128.5, 128.4, 128.3, 128.1, 127.5, 127.4, 122.7, 122.2, 94.4, 87.0, 42.6.
HRMS (ESI, m/z) calcd for $C_{20}H_{15}NOSNa$ $(M+Na)^+$: 340.0767, found: 340.0769.



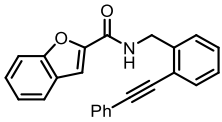
2-1v

Following **General Procedure A**, **2-1v** was obtained as a red oil (56%, three steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (3H, m), 7.40 (1H, d, J = 7.3 Hz), 7.33 (3H, dd, J = 4.9, 1.8 Hz), 7.26 (2H, m), 6.69-6.64 (1H, m), 6.52 (2H, dd, J = 4.0, 1.7 Hz), 6.02 (1H, dd, J = 3.9, 2.6 Hz), 4.77 (2H, d, J = 6.0 Hz), 3.90 (3H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 140.2, 132.2, 131.5, 128.7, 128.5, 128.3, 128.1, 127.8, 127.3, 125.5, 122.8, 122.2, 111.5, 107.1, 94.2, 87.1, 41.9, 36.6.

HRMS (ESI, m/z) calcd for $C_{21}H_{18}N_2ONa$ $(M+Na)^+$: 337.1312, found: 337.1313.



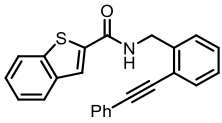
2-1w

Following **General Procedure A**, **2-1w** was obtained as a red solid (58%, three steps). Melting point 107-109 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, d, J = 7.8 Hz), 7.61-7.55 (3H, m), 7.46 (2H, d, J = 8.3 Hz), 7.35 (5H, m), 7.33-7.28 (3H, m), 7.26-7.23 (1H, m), 4.89 (2H, d, J = 6.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 154.6, 148.6, 139.3, 132.4, 131.6, 128.8, 128.63, 128.58, 128.4, 127.7, 127.5, 126.8, 123.6, 122.8, 122.6, 122.5, 111.6, 110.5, 94.5, 87.0, 42.2.

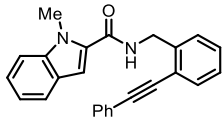
HRMS (ESI, m/z) calcd for $C_{24}H_{17}NO_2Na$ $(M+Na)^+$: 374.1152, found: 374.1147.



2-1x

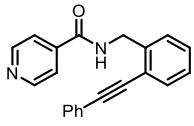
Following **General Procedure A**, **2-1x** was obtained as a white solid (55%, three steps). Melting point 174-176 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (1H, d, J = 7.9 Hz), 7.73 (2H, d, J = 11.2 Hz), 7.56 (3H, m), 7.45 (1H, d, J = 7.0 Hz), 7.40-7.33 (5H, m), 7.33-7.28 (2H, m), 6.78 (1H, d, J = 5.2 Hz), 4.87 (2H, d, J = 5.9 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 140.8, 139.4, 139.0, 138.3, 132.5, 131.6, 128.9, 128.7, 128.6, 128.5, 127.7, 126.3, 125.3, 125.0, 124.8, 122.7, 122.6, 122.5, 94.5, 87.0, 43.0.
HRMS (ESI, m/z) calcd for $C_{24}H_{17}NOSNa$ $(M+Na)^+$: 390.0923, found: 390.0918.



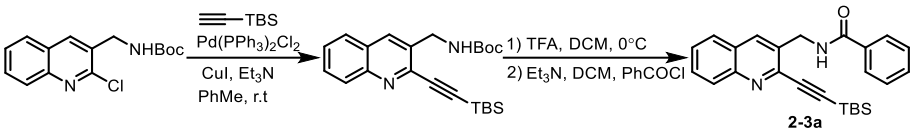
2-1y

Following **General Procedure A**, **2-1y** was obtained as a red solid (59%, three steps). Melting point 137-139 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (4H, m), 7.47-7.42 (1H, m), 7.36-7.28 (7H, m), 7.13-7.08 (1H, m), 6.81 (1H, s), 6.77 (1H, t, J = 5.2 Hz), 4.85 (2H, d, J = 5.9 Hz), 4.03 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 139.7, 139.0, 132.5, 131.8, 131.6, 128.8, 128.6, 128.5, 128.5, 127.6, 126.0, 124.0, 122.8, 122.4, 121.7, 120.4, 110.1, 103.8, 94.4, 87.1, 42.5, 31.5.
HRMS (ESI, m/z) calcd for $C_{25}H_{21}N_2O$ $(M+H)^+$: 365.1648, found: 365.1647.



2-1z

Following **General Procedure A**, **2-1z** was obtained as a white solid (55%, three steps). Melting point 122-124 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (2H, d, J = 4.6 Hz), 7.59-7.53 (3H, m), 7.50 (2H, dd, J = 6.6, 3.0 Hz), 7.39 (1H, d, J = 6.4 Hz), 7.36-7.32 (3H, m), 7.32-7.27 (2H, m), 7.11 (1H, s), 4.84 (2H, d, J = 5.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 150.4, 141.4, 139.0, 132.5, 131.5, 128.8, 128.7, 128.5, 127.8, 122.6, 122.5, 120.8, 94.5, 86.9, 43.1.
HRMS (ESI, m/z) calcd for $C_{21}H_{16}N_2ONa$ $(M+Na)^+$: 335.1155, found: 335.1151.



To a round-bottom flask equipped with 2-chloroquinoline (5 mmol, 1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (0.25 mmol, 0.05 equiv.) and CuI (0.25 mmol, 0.05 equiv.) was added degassed PhMe (25 mL) under nitrogen. The mixture was added Et_3N (20 mmol, 4.0 equiv.) and (*tert*-butyldimethylsilyl)acetylene (7.5 mmol, 1.5 equiv.). The mixture was stirred at 25 ℃ for 12 h, filtered through a pad of celite, concentrated, and purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the 2-ethynylquinoline[32].

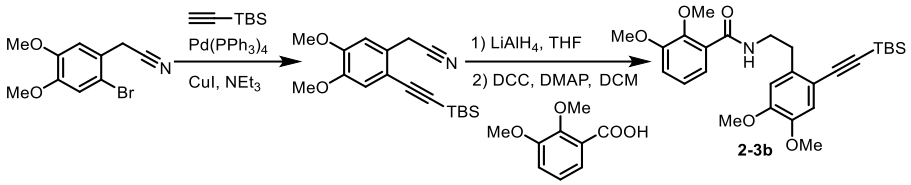
To a solution of 2-ethynylquinoline in DCM (25 mL) was added TFA (5 mL) at 0 ℃. The mixture was stirred at 25 ℃ for 12 h. Then extracted with DCM, the combined organic phases were washed with saturated solution of Na_2CO_3, dried over Na_2SO_4 and the solvent was removed under vacuum. The residue was used in the subsequent step without further purification[32].

To a solution of the crude primary amine in DCM (10 mL) was added Et_3N (2 mL) and benzoyl chloride (5.5 mmol, 1.1 equiv.) at 0 ℃. The mixture was stirred at 25 ℃ for 12 h, then quenched with saturated solution of NH_4Cl. Extracted with DCM, the combined organic phases dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-3a** as a yellow solid (50%, three steps)[66]. Melting point 140-142 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (1H, s), 8.08 (1H, d, J = 8.4 Hz), 7.83-7.77 (2H, m), 7.76-7.65 (2H, m), 7.55-7.46 (2H, m), 7.46-7.38 (2H, m), 7.07 (1H, t, J = 6.0 Hz), 4.92 (2H, d, J = 6.1 Hz), 1.03 (9H, s), 0.26 (6H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 147.2, 142.6, 135.4, 134.0, 132.6, 131.7, 129.9, 128.9, 128.6, 127.6, 127.5, 127.2, 126.9, 103.0, 98.7, 41.8, 26.2, 16.6, -4.7, -4.7.

HRMS (ESI, m/z) calcd for $C_{25}H_{29}N_2OSi$ $(M+H)^+$: 401.2044, found: 401.2040.



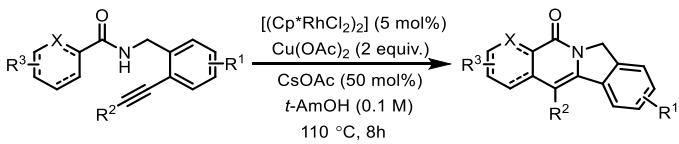
Following **General Procedure B**, **2-3b** was obtained as a yellow oil (54%, three steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (1H, s), 7.71 (1H, d, J = 7.9 Hz), 7.13 (1H, t, J = 8.0 Hz), 7.02 (1H, d, J = 8.0 Hz), 6.97 (1H, s), 6.76 (1H, s), 3.87 (6H, s), 3.82 (3H, s), 3.78 (2H, dd, J = 12.9, 6.6 Hz), 3.70 (3H, s), 3.09 (2H, t, J = 6.9 Hz), 1.00 (9H, s), 0.19 (6H, s).

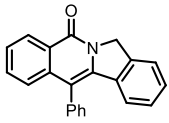
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 152.4, 149.4, 147.4, 147.0, 134.9, 126.5, 124.1, 122.6, 115.2, 114.9, 114.5, 112.2, 104.2, 94.8, 60.9, 55.9, 55.9, 55.8, 39.9, 33.8, 26.0, 16.5, -4.6.

HRMS (ESI, m/z) calcd for $C_{27}H_{38}NO_5Si$ $(M+H)^+$: 484.2514, found: 484.2515.

Rhodium(III)-catalyzed intramolecular annulations



To a Schlenk flask equipped with a stir bar were added **2-1** (0.3 mmol), $[Cp^*RhCl_2]_2$ (9.3 mg, 5 mol%), $Cu(OAc)_2$ (109 mg, 2 equiv.), CsOAc (28.8 mg, 50 mol%) and *t*-AmOH (3.0 mL) without any particular precautions to extrude oxygen or moisture. The reaction was stirred for 8 h at 110°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-2**.

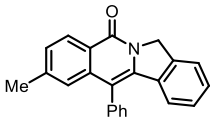


2-2a

2-2a was obtained as a red solid (93%).

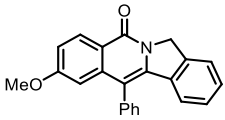
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, dd, J = 8.0, 0.9 Hz), 7.57 (4H, m), 7.54-7.46 (2H, m), 7.43-7.37 (2H, m), 7.35 (1H, t, J = 7.5 Hz), 7.23

(1H, d, *J* = 8.0 Hz), 7.10 (1H, t, *J* = 7.7 Hz), 6.44 (1H, d, *J* = 8.0 Hz), 5.24 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 138.7, 138.4, 138.0, 135.2, 134.3, 131.9, 131.0, 129.4, 129.2, 128.4, 127.8, 127.2, 126.2, 125.1, 124.1, 124.0, 123.0, 114.4, 51.8.
Spectral data was consistent with that previously reported[67].



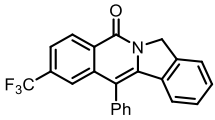
2-2b

2-2b was obtained as a yellow solid (75%). Melting point 271-273 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (1H, d, *J* = 8.2 Hz), 7.62-7.56 (3H, m), 7.49 (1H, s), 7.42-7.37 (2H, m), 7.35-7.28 (2H, m), 7.08 (1H, s), 6.99 (1H, s), 6.39 (1H, d, *J* = 8.0 Hz), 5.20 (2H, s), 2.36 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 142.4, 138.8, 138.4, 138.0, 135.3, 134.4, 131.0, 129.3, 129.0, 128.3, 127.81, 127.76, 127.2, 124.8, 123.9, 122.9, 122.0, 114.3, 51.6, 21.9.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO$ $(M+H)^+$: 324.1383, found: 324.1382.



2-2c

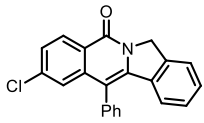
2-2c was obtained as a yellow solid (95%). Melting point 258-260 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (1H, d, *J* = 8.9 Hz), 7.63-7.50 (4H, m), 7.43-7.32 (3H, m), 7.13-7.04 (2H, m), 6.58 (1H, d, *J* = 2.5 Hz), 6.42 (1H, d, *J* = 8.0 Hz), 5.23 (2H, s), 3.73 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 160.4, 140.9, 139.0, 138.3, 135.3, 134.4, 131.0, 129.5, 129.3, 129.2, 128.4, 127.8, 124.0, 123.0, 118.2, 115.0, 114.1, 106.9, 55.2, 51.6.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1332.



2-2d

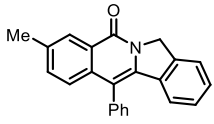
2-2d was obtained as a yellow solid (83%). Melting point 275-277℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (1H, d, J = 8.4 Hz), 7.66-7.60 (4H, m), 7.56-7.47 (2H, m), 7.39 (3H, m), 7.13 (1H, t, J = 7.7 Hz), 6.44 (1H, d, J = 8.0 Hz), 5.22 (2H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 139.9, 138.7, 138.1, 134.1, 133.84, 133.79, 133.4, 130.9, 129.7, 128.9, 128.3, 128.0, 125.9, 125.5, 124.3, 123.1, 122.3 (d, J = 4.1 Hz), 122.0, 114.0, 51.9.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.85.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO$ $(M+H)^+$: 378.1100, found: 378.1096.



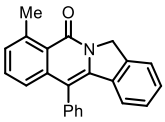
2-2e

2-2e was obtained as a red solid (84%). Melting point 283-285 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (1H, d, J = 8.6 Hz), 7.64-7.57 (3H, m), 7.52 (1H, d, J = 7.6 Hz), 7.41-7.34 (4H, m), 7.18 (1H, d, J = 1.7 Hz), 7.11 (1H, t, J = 7.7 Hz), 6.42 (1H, d, J = 8.0 Hz), 5.21 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 140.1, 139.7, 138.7, 138.2, 134.4, 134.0, 131.0, 129.6, 129.5, 129.0, 128.7, 128.0, 126.6, 124.4, 124.2, 123.0, 122.4, 113.4, 51.8.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}ClNO$ $(M+H)^+$: 344.0837, found: 344.0826.



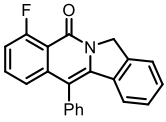
2-2f

2-2f was obtained as a yellow solid (82%). Melting point 274-276 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (1H, s), 7.59-7.54 (3H, m), 7.49 (1H, d, J = 7.7 Hz), 7.38 (3H, m), 7.30 (1H, d, J = 7.7 Hz), 7.13 (1H, d, J = 8.3 Hz), 7.08 (1H, t, J = 7.7 Hz), 6.43 (1H, d, J = 8.0 Hz), 5.20 (2H, s), 2.47 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 137.9, 137.4, 136.4, 136.3, 135.3, 134.4, 133.4, 131.0, 129.3, 128.9, 128.3, 127.7, 126.7, 125.1, 124.0, 123.7, 122.9, 114.4, 51.7, 21.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{17}NONa$ $(M+Na)^+$: 346.1203, found: 346.1200.



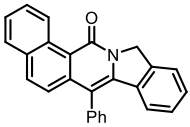
2-2g

2-2g was obtained as a yellow solid (96%). Melting point 305-307 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (3H, m), 7.53 (1H, d, J = 7.6 Hz), 7.38 (3H, m), 7.34 (1H, d, J = 7.5 Hz), 7.25 (1H, s), 7.10-7.05 (2H, m), 6.36 (1H, d, J = 8.0 Hz), 5.20 (2H, s), 3.06 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 141.6, 140.5, 138.2, 138.2, 135.9, 134.5, 131.2, 131.1, 129.5, 129.4, 129.1, 128.3, 127.8, 124.0, 123.6, 123.0, 122.6, 114.4, 51.9, 24.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{17}NONa$ $(M+Na)^+$: 346.1203, found: 346.1211.



2-2h

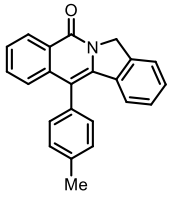
2-2h was obtained as a yellow solid (92%). Melting point 269-271 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.57 (3H, m), 7.54 (1H, d, J = 7.6 Hz), 7.47 (1H, td, J = 8.1, 5.1 Hz), 7.38 (3H, t, J = 7.7 Hz), 7.12 (2H, dd, J = 13.2, 6.6 Hz), 6.99 (1H, d, J = 8.2 Hz), 6.39 (1H, d, J = 8.0 Hz), 5.23 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 161.4, 158.1 (d, J = 4.0 Hz), 141.8, 139.5, 138.3, 135.1, 134.1, 132.6 (d, J = 10.1 Hz), 131.1, 129.6, 128.6, 127.9, 124.2, 123.1, 121.1 (d, J = 4.4 Hz), 113.5 (d, J = 2.8 Hz), 113.3 (d, J = 5.7 Hz), 113.0 (d, J = 21.6 Hz), 51.9.
^{19}F NMR (377 MHz, $CDCl_3$) δ -111.38.
HRMS (ESI, m/z) calcd for $C_{22}H_{14}FNONa$ $(M+Na)^+$: 350.0952, found: 350.0952.



2-2i

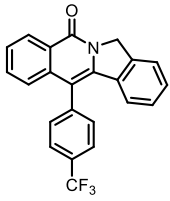
2-2i was obtained as a yellow solid (91%). Melting point 236-238 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (1H, d, J = 8.7 Hz), 7.83 (1H, d, J = 9.0 Hz), 7.80 (1H, d, J = 7.9 Hz), 7.72-7.69 (1H, m), 7.58 (3H, m),

7.48 (1H, d, *J* = 7.6 Hz), 7.40 (2H, m), 7.29 (3H, m), 7.07 (1H, t, *J* = 7.6 Hz), 6.39 (1H, d, *J* = 7.9 Hz), 5.23 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 139.8, 139.7, 138.3, 135.7, 134.3, 133.0, 131.9, 131.8, 131.2, 129.4, 129.2, 128.4, 128.2, 127.9, 127.8, 127.4, 126.1, 123.9, 123.1, 122.9, 117.1, 114.6, 52.5.
HRMS (ESI, m/z) calcd for $C_{26}H_{18}NO$ $(M+H)^+$: 360.1383, found: 360.1370.



2-2j

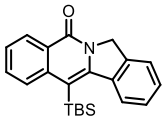
2-2j was obtained as a yellow solid (95%). Melting point 253-255 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (1H, dd, *J* = 7.9, 1.1 Hz), 7.56-7.45 (3H, m), 7.36 (3H, m), 7.26 (3H, m), 7.11 (1H, t, *J* = 7.6 Hz), 6.52 (1H, d, *J* = 8.0 Hz), 5.24 (2H, s), 2.52 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 138.9, 138.3, 138.1, 138.0, 134.4, 132.0, 131.9, 130.8, 130.1, 129.1, 127.8, 127.2, 126.1, 125.2, 124.0, 123.0, 114.5, 51.8, 21.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO$ $(M+H)^+$: 324.1383, found: 324.1377.



2-2k

2-2k was obtained as a red solid (93%). Melting point 254-256 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (1H, dd, *J* = 7.9, 1.0 Hz), 7.88 (2H, d, *J* = 8.0 Hz), 7.61-7.52 (4H, m), 7.51-7.45 (1H, m), 7.40 (1H, dd, *J* = 10.9, 4.1 Hz), 7.14 (2H, dd, *J* = 13.0, 7.8 Hz), 6.43 (1H, d, *J* = 8.0 Hz), 5.22 (2H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.6, 139.3, 138.5, 138.2, 138.1, 133.9, 132.2, 131.8, 130.9, 130.5, 129.6, 128.0, 127.4, 126.4 (d, *J* = 3.7 Hz), 124.7, 124.1, 123.7, 123.2, 122.3, 112.7, 51.8.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.37.

HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO$ $(M+H)^+$: 378.1100, found: 378.1105.



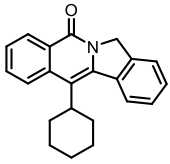
2-2l

2-2l was obtained as a red oil (82%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (1H, dd, J = 8.0, 1.5 Hz), 8.15 (1H, d, J = 7.2 Hz), 7.96 (1H, d, J = 8.4 Hz), 7.62 (2H, m), 7.47 (3H, m), 5.21 (2H, s), 1.32 (9H, s), 0.39 (6H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 149.3, 142.2, 139.1, 135.1, 130.6, 129.7, 129.6, 127.1, 126.5, 126.3, 125.7, 124.5, 123.1, 108.3, 51.9, 29.7, 19.4, 2.1.

HRMS (ESI, m/z) calcd for $C_{22}H_{26}NOSi$ $(M+H)^+$: 348.1778, found: 348.1774.



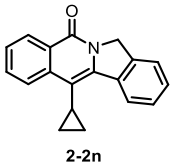
2-2m

2-2m was obtained as a red solid (79%). Melting point 151-153 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, dd, J = 8.0, 1.2 Hz), 8.24 (1H, d, J = 8.4 Hz), 8.03 (1H, d, J = 7.4 Hz), 7.71-7.63 (1H, m), 7.60 (1H, d, J = 6.8 Hz), 7.53-7.44 (3H, m), 5.18 (2H, s), 3.81 (1H, tt, J = 12.6, 3.3 Hz), 2.43-2.29 (2H, m), 2.01 (2H, d, J = 13.0 Hz), 1.90 (3H, d, J = 12.0 Hz), 1.60-1.44 (3H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 138.6, 138.1, 137.6, 135.1, 130.8, 128.9, 128.2, 127.8, 125.8, 125.1, 124.5, 123.5, 118.7, 51.7, 39.0, 31.2, 27.5, 26.1.

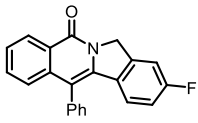
HRMS (ESI, m/z) calcd for $C_{22}H_{22}NO$ $(M+H)^+$: 316.1696, found: 316.1692.



2-2n

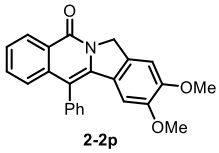
2-2n was obtained as a yellow solid (96%). Melting point 196-198 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (1 H, dd, J = 8.0, 1.1 Hz), 8.39-8.32 (1 H, m), 8.28 (1 H, d, J = 8.3 Hz), 7.72-7.64 (1 H, m), 7.55-7.42 (4 H, m), 5.12 (2 H, s), 2.12-1.97 (1 H, m), 1.36-1.28 (2 H, m), 0.70-0.60 (2 H, m).
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 141.0, 139.2, 138.2, 134.3, 131.4, 129.0, 127.6, 127.2, 125.8, 125.7, 124.8, 124.2, 122.8, 113.4, 51.7, 10.7, 7.9.
HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO$ $(M+H)^+$: 274.1226, found: 274.1231.



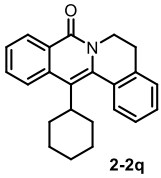
2-2o

2-2o was obtained as a yellow solid (90%). Melting point 188-190 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (1H, dd, J = 7.9, 1.5 Hz), 7.61-7.48 (5H, m), 7.41-7.37 (2H, m), 7.22 (2H, d, J = 7.6 Hz), 6.81 (1H, td, J = 8.8, 2.2 Hz), 6.38 (1H, dd, J = 8.8, 5.0 Hz), 5.22 (2H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 161.6, 160.6, 140.2 (d, J = 9.4 Hz), 138.7, 137.5, 135.0, 132.1, 131.0, 130.5 (d, J = 2.6 Hz), 129.5, 128.5, 126.7 (d, J = 73.3 Hz), 125.7 (d, J = 9.0 Hz), 125.1, 123.9, 115.6 (d, J = 22.9 Hz), 114.0, 110.4 (d, J = 24.0 Hz), 51.5.
^{19}F NMR (377 MHz, $CDCl_3$) δ -110.32.
HRMS (ESI, m/z) calcd for $C_{22}H_{14}FNONa$ $(M+Na)^+$: 350.0952, found: 350.0937.



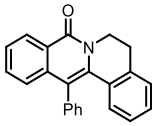
2-2p

2-2p was obtained as a yellow solid (91%). Melting point 202-204 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (1H, dd, J = 8.0, 1.0 Hz), 7.63-7.52 (4H, m), 7.45 (3H, m), 7.27-7.23 (1H, m), 6.98 (1H, s), 5.88 (1H, s), 5.14 (2H, s), 3.91 (3H, s), 3.41 (3H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 150.6, 148.8, 138.8, 138.7, 135.3, 131.9, 131.6, 131.1, 129.2, 128.2, 127.2, 126.5, 125.7, 124.7, 123.5, 112.6, 106.0, 105.1, 56.1, 55.2, 51.6.
HRMS (ESI, m/z) calcd for $C_{24}H_{20}NO_3$ $(M+H)^+$: 370.1438, found: 370.1432.



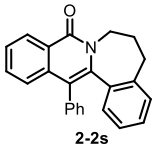
2-2q

2-2q was obtained as a yellow solid (68%). Melting point 118-120 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (1H, dd, J = 8.0, 1.4 Hz), 8.29 (1H, d, J = 8.4 Hz), 7.65 (1H, ddd, J = 8.5, 7.1, 1.6 Hz), 7.58-7.53 (1H, m), 7.50-7.44 (1H, m), 7.38-7.29 (3H, m), 4.23 (2H, s), 3.48-3.32 (1H, m), 2.90 (2H, t, J = 5.8 Hz), 2.37 (2H, dd, J = 23.2, 11.3 Hz), 1.86 (4H, d, J = 11.1 Hz), 1.39-1.22 (4H, m).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 139.3, 136.4, 135.6, 131.5, 130.9, 129.4, 128.9, 128.5, 127.1, 126.1, 125.9, 125.74, 125.65, 120.3, 42.0, 41.8, 32.4, 29.7, 27.1, 26.1.
HRMS (ESI, m/z) calcd for $C_{23}H_{24}NO$ $(M+H)^+$: 330.1852, found: 330.1850.



2-2r

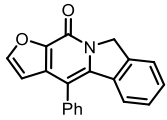
2-2r was obtained as a yellow solid (77%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62-8.46 (1H, m), 7.54-7.37 (5H, m), 7.35-7.30 (1H, m), 7.27-7.11 (4H, m), 6.81 (2H, m), 4.51-4.19 (2H, m), 3.04-2.88 (2H, m).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 138.3, 137.7, 137.3, 134.6, 131.9, 131.0, 130.4, 128.9, 128.3, 127.7, 127.5, 126.9, 126.6, 125.5, 124.8, 117.8, 41.5, 29.6.
Spectral data was consistent with that previously reported[10].



2-2s

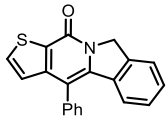
2-2s was obtained as a yellow solid (70%). Melting point 245-247 ℃.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63-8.52 (1H, m), 7.58-7.39 (4H, m), 7.38-7.31 (1H, m), 7.26-7.13 (3H, m), 7.10-7.01 (1H, m), 6.92-6.80 (2H, m), 6.60 (1H, d, J = 7.6 Hz), 5.19 (1H, dd, J = 13.5, 5.2 Hz), 3.08 (1H, td, J = 13.2, 4.9 Hz), 2.85-2.64 (2H, m), 2.40 (1H, tdd, J = 16.0, 5.9, 2.7 Hz), 1.93-1.77 (1H, m).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 140.8, 138.7, 137.1, 136.7, 133.9, 132.3, 131.9, 131.1, 128.9, 128.7, 128.0, 127.5, 126.9, 126.5, 125.7, 125.3, 124.7, 118.1, 41.5, 29.8, 28.6.
HRMS (ESI, m/z) calcd for $C_{24}H_{19}NONa$ $(M+Na)^+$: 360.1359, found: 360.1356.



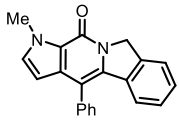
2-2t

2-2t was obtained as a red solid (50%). Melting point 190-192℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (1H, d, J = 1.9 Hz), 7.55 (4H, m), 7.48 (2H, m), 7.37 (1H, t, J = 7.4 Hz), 7.15 (1H, t, J = 7.7 Hz), 6.91 (1H, d, J = 8.0 Hz), 6.47 (1H, d, J = 1.9 Hz), 5.25 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 137.8, 135.8, 135.1, 134.9, 134.4, 131.4, 130.3, 128.9, 127.9, 127.9, 127.6, 123.0, 122.7, 121.5, 112.5, 101.9, 51.2.
HRMS (ESI, m/z) calcd for $C_{20}H_{13}NO_2Na$ $(M+Na)^+$: 322.0839, found: 322.0840.



2-2u

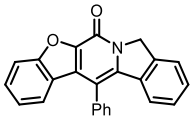
2-2u was obtained as a yellow solid (60%). Melting point 259-261 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, d, J = 5.1 Hz), 7.55 (4H, m), 7.45 (2H, d, J = 7.4 Hz), 7.37 (1H, t, J = 7.5 Hz), 7.13 (1H, t, J = 7.6 Hz), 6.92 (1H, d, J = 5.2 Hz), 6.71 (1H, d, J = 7.9 Hz), 5.25 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 147.8, 140.1, 138.1, 135.4, 134.1, 132.8, 130.4, 129.24, 129.15, 128.5, 127.9, 127.3, 124.3, 123.5, 123.1, 113.6, 51.7.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NOS$ $(M+H)^+$: 316.0791, found: 316.0786.



2-2v

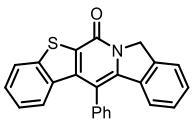
2-2v was obtained as a yellow solid (54%). Melting point 282-284 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (6H, m), 7.29 (1H, t, J = 7.4 Hz), 7.10 (1H, t, J = 7.6 Hz), 6.99 (1H, d, J = 2.8 Hz), 6.81 (1H, d, J = 8.0 Hz), 6.03 (1H, d, J = 2.8 Hz), 5.17 (2H, s), 4.26 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 137.8, 135.8, 135.1, 134.9, 134.4, 131.4, 130.3, 128.9, 127.93, 127.88, 127.6, 123.0, 122.7, 121.5, 112.5, 101.9, 51.2, 35.8.
HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_2O$ (M+H) $^+$: 313.1335, found: 313.1335.



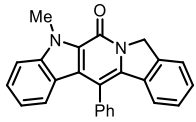
2-2w

2-2w was obtained as a red solid (76%). Melting point 358-360 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.64 (3H, m), 7.60-7.54 (4H, m), 7.47 (1H, d, J = 8.0 Hz), 7.38 (1H, t, J = 7.5 Hz), 7.16-7.08 (2H, m), 6.83 (1H, d, J = 7.9 Hz), 6.73 (1H, d, J = 8.0 Hz), 5.31 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 152.4, 142.0, 139.5, 138.3, 134.5, 134.0, 130.3, 129.9, 129.6, 129.0, 128.5, 128.0, 123.5, 123.3, 123.2, 123.2, 122.8, 112.8, 112.7, 111.4, 52.2.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_2$ (M+H) $^+$: 350.1175, found: 350.1173.



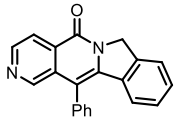
2-2x

2-2x was obtained as a green solid (78%). Melting point 306-308 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1H, d, J = 8.1 Hz), 7.66 (3H, d, J = 6.2 Hz), 7.58-7.50 (3H, m), 7.38 (2H, dd, J = 14.9, 7.5 Hz), 7.13-7.06 (2H, m), 6.81 (1H, d, J = 8.4 Hz), 6.40 (1H, d, J = 8.0 Hz), 5.27 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 142.6, 141.2, 141.0, 138.0, 135.8, 135.5, 134.4, 130.7, 129.9, 129.1, 129.1, 128.0, 127.9, 127.2, 125.6, 124.3, 123.7, 123.4, 123.1, 114.3, 51.8.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NOS$ (M+H) $^+$: 366.0947, found: 366.0953.



2-2y

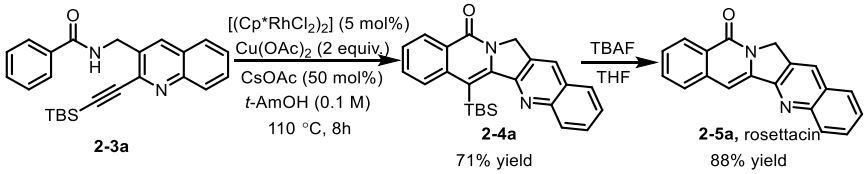
2-2y was obtained as a yellow solid (94%). Melting point 304-306 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (3H, m), 7.53 (2H, dd, J = 6.5, 3.0 Hz), 7.48 (1H, d, J = 7.6 Hz), 7.40 (2H, d, J = 5.0 Hz), 7.26 (1H, dd, J = 13.6, 6.1 Hz), 7.09 (1H, t, J = 7.6 Hz), 6.94 (1H, ddd, J = 8.0, 5.4, 2.6 Hz), 6.79 (1H, d, J = 8.1 Hz), 6.57 (1H, d, J = 7.9 Hz), 5.16 (2H, s), 4.34 (3H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 141.2, 137.4, 136.0, 134.9, 134.8, 130.4, 129.4, 128.5, 127.8, 127.7, 126.3, 125.8, 125.3, 123.0, 122.7, 122.5, 121.8, 119.7, 113.4, 109.8, 51.6, 31.2.
HRMS (ESI, m/z) calcd for $C_{25}H_{19}N_2O$ $(M+H)^+$: 363.1492, found: 363.1484.



2-2z

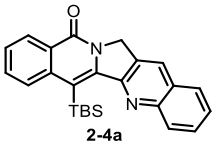
2-2z was obtained as a yellow solid (43%). Melting point 236-238 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (2H, d, J = 5.7 Hz), 8.29 (1H, d, J = 5.2 Hz), 7.65-7.60 (3H, m), 7.56 (1H, d, J = 7.6 Hz), 7.47-7.38 (3H, m), 7.15 (1H, t, J = 7.7 Hz), 6.54 (1H, d, J = 8.0 Hz), 5.27 (2H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 149.1, 145.6, 140.1, 137.9, 133.8, 133.4, 132.9, 130.9, 129.8, 129.6, 128.9, 128.5, 128.2, 124.3, 123.1, 119.3, 112.7, 52.0.
HRMS (ESI, m/z) calcd for $C_{21}H_{15}N_2O$ $(M+H)^+$: 311.1179, found: 311.1181.

Synthesis of Rosettacin and Oxypalmatime



To a Schlenk flask equipped with a stir bar were added **2-3a** (0.6 mmol), $[Cp^*RhCl_2]_2$ (18.6 mg, 5 mol%), $Cu(OAc)_2$ (218 mg, 2 equiv.), CsOAc

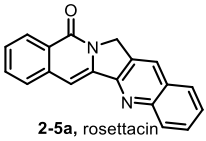
(57.6 mg, 50 mol%) and *t*-AmOH (6.0 mL) without any particular precautions to extrude oxygen or moisture. The reaction was stirred for 8 h at 110°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-4a** as a yellow solid (71%). Melting point 212-214 °C.



2-4a

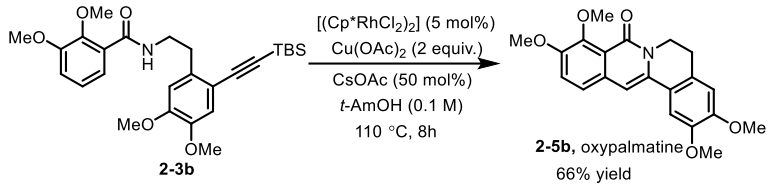
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (1H, dd, J = 8.0, 1.2 Hz), 8.26 (2H, d, J = 8.6 Hz), 8.14 (1H, d, J = 8.4 Hz), 7.86 (1H, d, J = 8.3 Hz), 7.80-7.66 (2H, m), 7.62-7.50 (2H, m), 5.32 (2H, s), 1.35 (9H, d, J = 1.9 Hz), 0.52 (6H, d, J = 2.0 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 154.2, 147.6, 146.1, 141.9, 130.8, 130.3, 129.8, 129.61, 129.57, 129.2, 129.0, 127.8, 127.3, 127.2, 126.5, 125.6, 112.3, 49.1, 29.4, 19.2, 2.8, 2.7.
HRMS (ESI, m/z) calcd for $C_{25}H_{27}N_2OSi$ $(M+H)^+$: 399.1887, found: 399.1888.

A 25 mL round-bottomed flask equipped with a stirring bar is charged with **2-4a** (0.4 mmol), *tetra*-*n*-butylammonium fluoride (TBAF, 1 M in THF, 0.8 mL, 0.8 mmol) and 2 mL of anhydrous THF. Then allowed to stir at 60°C for 12 h. The solvent was removed and the residue purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-5a** as a yellow solid (88%)[16].



2-5a, rosettacin

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (1H, d, J = 8.0 Hz), 8.26 (1H, s), 8.18 (1H, d, J = 8.5 Hz), 7.85 (1H, d, J = 8.2 Hz), 7.78-7.69 (3H, m), 7.61 (1H, s), 7.55 (2H, ddd, J = 8.2, 5.0, 1.5 Hz), 5.32 (2H, d, J = 0.8 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 153.6, 148.8, 139.9, 137.5, 132.4, 130.7, 130.2, 129.4, 128.8, 128.0, 128.0, 127.5, 127.3, 126.0, 101.1, 49.4.
Spectral data was consistent with that previously reported[32].



To a Schlenk flask equipped with a stir bar were added **2-3b** (0.6 mmol), $[Cp^*RhCl_2]_2$ (18.6 mg, 5 mol%), $Cu(OAc)_2$ (218 mg, 2 equiv.), CsOAc (57.6 mg, 50 mol%) and *t*-AmOH (6.0 mL) without any particular precautions to extrude oxygen or moisture. The reaction was stirred for 8 h at 110°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **2-5b** as a yellow solid (66%).

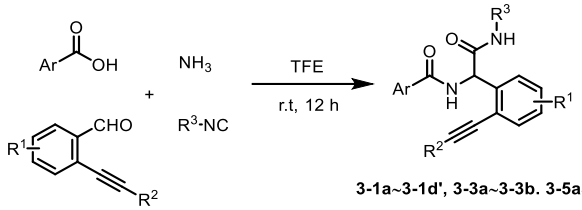
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (2H, d, J = 3.1 Hz), 7.23 (1H, s), 6.74 (2H, d, J = 9.2 Hz), 4.31 (2H, s), 4.02 (3H, s), 3.98 (3H, s), 3.94 (6H, d, J = 4.3 Hz), 2.92 (2H, t, J = 5.6 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 151.2, 150.0, 149.4, 148.3, 135.5, 132.3, 128.4, 122.2, 122.1, 119.2, 118.9, 110.4, 107.4, 100.8, 61.5, 56.7, 56.1, 55.9, 39.3, 28.1.

Spectral data was consistent with that previously reported[32].

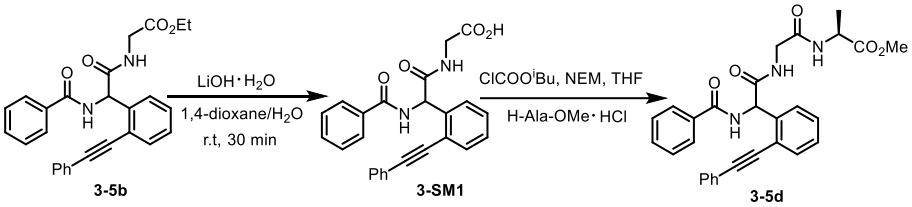
Chapter 3

Synthesis of the substrates



3-1a~3-1d', 3-3a~3-3b. 3-5a~3-5c

To a solution of aldehyde (1.2 mmol) in TFE (2, 2, 2-trifluoroethanol, 3 mL) were added successively ammonia solution (7 N in methanol, 0.172 mL), acid (1 mmol) and isonitrile (1.2 mmol) in a screw capped vial equipped with a magnetic stir bar.[68] The reaction mixture was stirred at room temperature for 12 h in a closed vial. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **3-1a~3-1d'**, **3-3a~3-3b**, **3-5a~3-5c**.

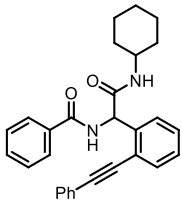


3-5b **3-SM1** **3-5d**

To a solution of **3-5b** (0.3 mmol) in 1,4-dioxane (1 mL) was added $LiOH \cdot H_2O$ (0.45 mmol) dissolved in water (1 mL) and the mixture was stirred at room temperature for 30 min.[69] The resulting solution was acidified with 1 M HCl to pH = 2 and extracted with DCM. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to give the crude acid **3-SM1**, which was used in next step without further purification.

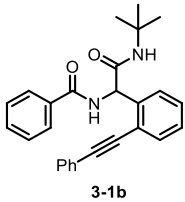
To an ice-cooled solution of **3-SM1** and *N*-ethylmorpholine (0.75 mmol) in THF (2 mL), isobutylchloroformate (0.33 mmol) was added dropwise and stirred under ice water bath for 1h.[69] Then H-Ala-OMe·HCl (0.39 mmol) was added and the solution left to warn to room temperature and stirred overnight. The resulting mixture was concentrated in *vacuo*. The residue was purified by a silica gel column

chromatography (*n*-heptane/ethyl acetate) to afford the product **3-5d~3-5k**.



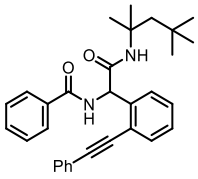
3-1a

3-1a was obtained as a white solid (68%). Melting point 169-171 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 6.1 Hz, 1H), 7.90-7.84 (m, 2H), 7.61 (dt, *J* = 5.0, 2.8 Hz, 3H), 7.51-7.43 (m, 3H), 7.40 (m, 4H), 7.35-7.29 (m, 2H), 6.30 (d, *J* = 7.9 Hz, 1H), 6.08 (d, *J* = 6.0 Hz, 1H), 3.82-3.65 (m, 1H), 1.86 (d, *J* = 8.4 Hz, 1H), 1.56 (m, 4H), 1.35-1.22 (m, 2H), 1.14-0.93 (m, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5, 166.2, 140.5, 133.9, 132.9, 131.7, 131.6, 129.3, 129.0, 128.6, 128.5, 128.0, 127.2, 126.5, 122.3, 121.4, 95.4, 87.7, 55.8, 48.6, 32.6, 32.3, 25.3, 24.3, 24.2.
HRMS (ESI, m/z) calcd for $C_{29}H_{29}N_2O_2$ $(M+H)^+$: 437.2223, found: 437.2220.



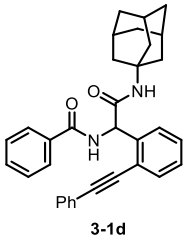
3-1b

3-1b was obtained as a white solid (20%). Melting point 148-150 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 4.3 Hz, 1H), 7.91-7.83 (m, 2H), 7.64-7.57 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.42-7.35 (m, 5H), 7.31 (dd, *J* = 16.8, 7.6 Hz, 2H), 6.28 (s, 1H), 6.03 (d, *J* = 6.0 Hz, 1H), 1.23 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 166.0, 140.6, 133.9, 132.9, 131.6, 131.6, 129.3, 128.9, 128.6, 128.5, 127.9, 127.2, 126.4, 122.3, 121.3, 95.4, 87.6, 56.1, 51.8, 28.5.
HRMS (ESI, m/z) calcd for $C_{27}H_{27}N_2O_2$ $(M+H)^+$: 411.2067, found: 411.2061.



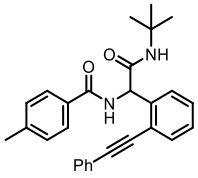
3-1c

3-1c was obtained as a white solid (33%). Melting point 75-77 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 5.6 Hz, 1H), 7.88 (d, *J* = 7.3 Hz, 2H), 7.66-7.57 (m, 3H), 7.47 (t, *J* = 8.0 Hz, 2H), 7.43-7.36 (m, 5H), 7.34-7.26 (m, 2H), 6.20 (s, 1H), 6.01 (d, *J* = 5.7 Hz, 1H), 1.69 (d, *J* = 15.0 Hz, 1H), 1.53 (d, *J* = 14.9 Hz, 1H), 1.33 (s, 3H), 1.27 (s, 3H), 0.74 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.7, 165.9, 140.3, 133.8, 132.8, 131.5, 129.2, 128.8, 128.4, 128.4, 127.8, 127.1, 126.5, 122.2, 121.4, 95.3, 87.6, 56.1, 55.6, 51.5, 31.2, 30.9, 29.0, 28.8.
HRMS (ESI, m/z) calcd for $C_{31}H_{35}N_2O_2$ $(M+H)^+$: 467.2693, found: 467.2689.



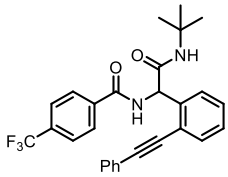
3-1d

3-1d was obtained as a light brown solid (70%). Melting point 83-85 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 5.8 Hz, 1H), 7.91-7.85 (m, 2H), 7.65-7.58 (m, 3H), 7.50-7.46 (m, 1H), 7.45-7.38 (m, 6H), 7.32 (m, 2H), 6.14 (s, 1H), 6.01 (d, *J* = 5.9 Hz, 1H), 1.99 (s, 3H), 1.88 (t, *J* = 7.7 Hz, 6H), 1.60 (s, 6H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 166.0, 140.8, 133.9, 132.9, 131.6, 131.6, 129.3, 128.9, 128.6, 128.5, 127.9, 127.2, 126.3, 122.4, 121.4, 95.4, 87.7, 56.0, 52.5, 41.3, 36.1, 29.3.
HRMS (ESI, m/z) calcd for $C_{33}H_{33}N_2O_2$ $(M+H)^+$: 489.2536, found: 489.2533.



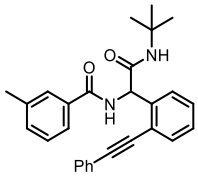
3-1e

3-1e was obtained as a light brown solid (52%). Melting point 153-155 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 5.9 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.60 (td, *J* = 7.1, 2.5 Hz, 3H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.41-7.36 (m, 3H), 7.31 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.28 (s, 1H), 6.01 (d, *J* = 6.0 Hz, 1H), 2.37 (s, 3H), 1.23 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 166.0, 142.0, 140.7, 132.8, 131.5, 131.0, 129.2, 129.1, 128.9, 128.5, 127.8, 127.1, 126.4, 122.3, 121.3, 95.3, 87.6, 56.0, 51.7, 28.5, 21.4.
HRMS (ESI, m/z) calcd for $C_{28}H_{29}N_2O_2$ $(M+H)^+$: 425.2223, found: 425.2222.



3-1f

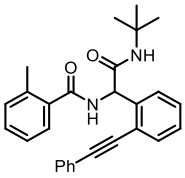
3-1f was obtained as a light brown solid (65%). Melting point 77-79 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 5.8 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.61 (dd, *J* = 6.5, 1.7 Hz, 3H), 7.48-7.44 (m, 1H), 7.42-7.38 (m, 3H), 7.37-7.29 (m, 2H), 6.20 (s, 1H), 5.99 (d, *J* = 5.9 Hz, 1H), 1.24 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 164.7, 140.2, 137.1, 133.3 (d, *J* = 32.7 Hz), 133.0, 131.5, 129.3, 129.0, 128.6, 128.1, 127.6, 126.5, 125.7-125.4 (m), 125.0, 122.2, 121.4, 95.5, 87.4, 56.2, 51.9, 28.5.
HRMS (ESI, m/z) calcd for $C_{28}H_{26}F_3N_2O_2$ $(M+H)^+$: 479.1941, found: 479.1931.



3-1g

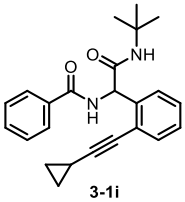
3-1g was obtained as a beige solid (70%). Melting point 120-122 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 5.7 Hz, 1H), 7.67 (s, 2H), 7.61 (td, *J* = 7.4, 2.5 Hz, 3H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.42-7.37 (m, 3H), 7.36-7.28 (m, 4H), 6.24 (s, 1H), 5.99 (d, *J* = 6.0 Hz, 1H), 2.35 (s, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 166.2, 140.7, 138.3, 133.8, 132.9, 132.4, 131.6, 129.3, 128.9, 128.6, 128.4, 127.9, 127.7, 126.6, 124.3, 122.4, 121.3, 95.4, 87.7, 56.1, 51.8, 28.6, 21.3.
HRMS (ESI, m/z) calcd for $C_{28}H_{29}N_2O_2$ (M+H) $^+$: 425.2223, found: 425.2220.



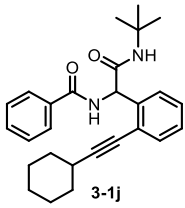
3-1h

3-1h was obtained as a white solid (54%). Melting point 130-132 °C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (m, 3H), 7.55 (dd, *J* = 18.3, 7.4 Hz, 3H), 7.42-7.38 (m, 4H), 7.36-7.30 (m, 2H), 7.21 (dd, *J* = 13.8, 7.3 Hz, 2H), 6.27 (s, 1H), 6.06 (d, *J* = 6.4 Hz, 1H), 2.47 (s, 3H), 1.27 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.8, 168.5, 140.4, 136.6, 135.4, 133.0, 131.5, 131.0, 130.0, 129.2, 128.9, 128.5, 127.9, 127.2, 126.5, 125.6, 122.3, 121.5, 95.4, 87.5, 56.1, 51.7, 28.5, 20.0.
HRMS (ESI, m/z) calcd for $C_{28}H_{29}N_2O_2$ (M+H) $^+$: 425.2223, found: 425.2219.



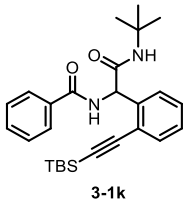
3-1i

3-1i was obtained as a beige solid (40%). Melting point 124-126 °C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96-7.89 (m, 3H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 3H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.29-7.26 (m, 1H), 7.23 (td, *J* = 7.5, 1.1 Hz, 1H), 6.40 (s, 1H), 5.95 (d, *J* = 6.1 Hz, 1H), 1.57 (m, 1H), 1.32 (s, 9H), 1.00-0.89 (m, 4H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7, 166.0, 140.6, 133.9, 133.4, 132.9, 131.6, 128.5, 127.6, 127.2, 125.8, 121.9, 99.7, 74.5, 55.7, 51.7, 28.6, 8.8, 8.7, 0.3.
HRMS (ESI, m/z) calcd for $C_{24}H_{27}N_2O_2$ (M+H) $^+$: 375.2067, found: 375.2068.



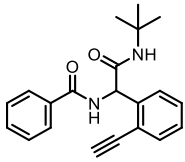
3-1j

3-1j was obtained as a light yellow solid (44%). Melting point 55-57 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.85 (m, 3H), 7.54-7.40 (m, 4H), 7.39-7.34 (m, 1H), 7.26-7.18 (m, 2H), 6.32 (s, 1H), 5.98 (d, *J* = 6.1 Hz, 1H), 2.76-2.63 (m, 1H), 1.95 (s, 2H), 1.85-1.73 (m, 2H), 1.61 (dd, *J* = 11.8, 7.6 Hz, 3H), 1.39 (dd, *J* = 17.6, 8.3 Hz, 3H), 1.28 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.8, 166.0, 140.5, 134.0, 132.9, 131.6, 128.5, 128.5, 127.6, 127.2, 125.7, 122.1, 100.6, 79.1, 55.6, 51.8, 32.7, 30.0, 28.6, 25.8, 25.0.
HRMS (ESI, m/z) calcd for $C_{27}H_{33}N_2O_2$ $(M+H)^+$: 417.2536, found: 417.2528.



3-1k

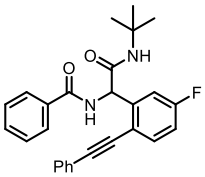
3-1k was obtained as rufous oil (67%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.93-7.86 (m, 2H), 7.58-7.29 (m, 7H), 6.33 (s, 1H), 6.01 (d, *J* = 5.8 Hz, 1H), 1.30 (d, *J* = 1.8 Hz, 9H), 1.06 (d, *J* = 2.0 Hz, 9H), 0.27 (d, *J* = 0.8 Hz, 6H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5, 165.8, 141.3, 134.0, 133.5, 131.6, 129.5, 128.5, 127.6, 127.2, 125.7, 121.3, 104.2, 99.1, 55.6, 51.9, 28.6, 26.2, 16.7, -4.5, -4.6.
HRMS (ESI, m/z) calcd for $C_{27}H_{37}N_2O_2Si$ $(M+H)^+$: 449.2619, found: 449.2623.



3-1l

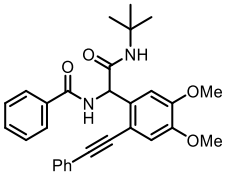
3-1l was obtained as a light brown solid (53%). Melting point 146-148 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (t, *J* = 7.3 Hz, 3H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.48-7.43 (m, 3H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 6.23 (s, 1H), 6.00 (d, *J* = 5.9 Hz, 1H), 3.56 (s, 1H), 1.31 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 166.0, 141.5, 133.8, 133.5, 131.7, 129.9, 128.5, 127.8, 127.2, 125.9, 120.1, 83.2, 82.4, 55.6, 52.0, 28.5.
HRMS (ESI, m/z) calcd for $C_{21}H_{22}N_2O_2$ $(M+H)^+$: 335.1754, found: 335.1757.



3-1m

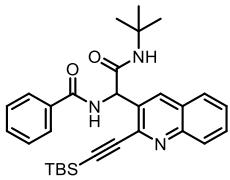
3-1m was obtained as a white solid (61%). Melting point 155-157 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 5.4 Hz, 1H), 7.89 (d, *J* = 7.4 Hz, 2H), 7.59 (td, *J* = 5.4, 2.2 Hz, 3H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.47-7.37 (m, 5H), 7.17 (dd, *J* = 9.4, 2.5 Hz, 1H), 7.00 (td, *J* = 8.3, 2.6 Hz, 1H), 6.39 (s, 1H), 5.99 (d, *J* = 5.6 Hz, 1H), 1.24 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 166.1, 163.0 (d, *J* = 251.6 Hz), 143.6 (d, *J* = 7.4 Hz), 134.7 (d, *J* = 8.5 Hz), 133.6, 131.8, 131.5, 129.1, 128.6 (d, *J* = 2.7 Hz), 127.2, 122.1, 117.3 (d, *J* = 3.5 Hz), 115.4 (d, *J* = 22.2 Hz), 113.5 (d, *J* = 23.6 Hz), 95.2, 86.8, 55.8, 51.9, 28.5.
HRMS (ESI, m/z) calcd for $C_{27}H_{26}FN_2O_2$ $(M+H)^+$: 429.1973, found: 429.1971.



3-1n

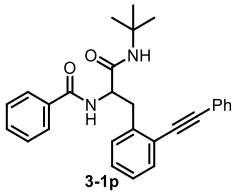
3-1n was obtained as a white solid (60%). Melting point 169-171 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 16.0, 6.5 Hz, 3H), 7.59 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.40 (m, 5H), 7.07 (s, 1H), 6.91 (s, 1H), 6.24 (s, 1H), 5.93 (d, *J* = 5.7 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 1.25 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 166.1, 150.1, 148.3, 134.3, 133.9, 131.6, 131.4, 128.6, 128.5, 127.1, 122.6, 114.9, 113.3, 109.1, 94.0, 87.7, 56.0, 56.0, 55.9, 51.7, 28.6.

HRMS (ESI, m/z) calcd for $C_{29}H_{31}N_2O_4$ $(M+H)^+$: 471.2278, found: 471.2277.



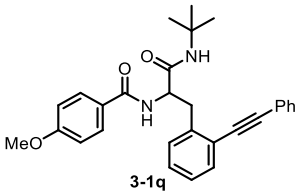
3-1o

3-1o was obtained as a white solid (69%). Melting point 99-101 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 5.6 Hz, 1H), 7.94-7.87 (m, 2H), 7.78-7.68 (m, 2H), 7.56-7.42 (m, 4H), 6.36 (s, 1H), 6.14 (d, *J* = 5.7 Hz, 1H), 1.28 (s, 9H), 1.09 (s, 9H), 0.34 (s, 3H), 0.31 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.9, 165.9, 147.6, 141.4, 133.9, 133.6, 131.8, 130.3, 129.1, 128.6, 127.8, 127.7, 127.3, 127.2, 103.7, 99.5, 54.8, 52.2, 28.6, 26.3, 16.8, -4.6, -4.6.
HRMS (ESI, m/z) calcd for $C_{30}H_{38}N_3O_2Si$ $(M+H)^+$: 500.2728, found: 500.2726.



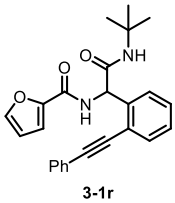
3-1p

3-1p was obtained as a yellow solid (75%). Melting point 137-139 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.73 (m, 2H), 7.64-7.58 (m, 2H), 7.55 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.45 (dt, *J* = 2.6, 1.8 Hz, 1H), 7.40-7.33 (m, 6H), 7.29-7.26 (m, 1H), 7.25-7.14 (m, 2H), 5.64 (s, 1H), 4.87 (q, *J* = 7.5 Hz, 1H), 3.51 (dd, *J* = 13.5, 7.8 Hz, 1H), 3.31 (dd, *J* = 13.5, 7.1 Hz, 1H), 1.21 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 167.1, 139.2, 133.9, 132.4, 131.7, 131.6, 130.1, 128.8, 128.6, 128.5, 127.1, 127.0, 123.3, 122.8, 94.0, 87.9, 55.3, 51.3, 37.2, 28.5.
HRMS (ESI, m/z) calcd for $C_{28}H_{29}N_2O_2$ $(M+H)^+$: 425.2223, found: 425.2227.



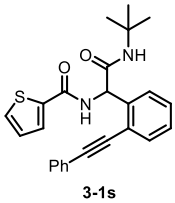
3-1q

3-1q was obtained as a yellow solid (56%). Melting point 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78-7.70 (m, 2H), 7.62-7.57 (m, 2H), 7.55-7.50 (m, 1H), 7.40-7.31 (m, 4H), 7.28-7.20 (m, 3H), 6.85-6.77 (m, 2H), 5.92 (s, 1H), 4.90 (dd, *J* = 14.6, 7.7 Hz, 1H), 3.80 (s, 3H), 3.48 (dd, *J* = 13.6, 8.1 Hz, 1H), 3.33 (dd, *J* = 13.6, 6.7 Hz, 1H), 1.22 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 166.6, 162.2, 139.3, 132.3, 131.6, 130.1, 128.9, 128.7, 128.5, 128.4, 126.9, 126.1, 123.3, 122.8, 113.5, 93.9, 88.0, 55.3, 55.3, 51.2, 37.1, 28.5.
HRMS (ESI, m/z) calcd for $C_{29}H_{31}N_2O_3$ $(M+H)^+$: 455.2329, found: 455.2334.



3-1r

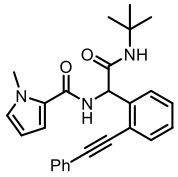
3-1r was obtained as a yellow solid (52%). Melting point 149-151 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 6.3 Hz, 1H), 7.60 (m, 3H), 7.46 (dd, *J* = 7.6, 1.3 Hz, 2H), 7.41-7.37 (m, 3H), 7.36-7.29 (m, 2H), 7.08 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.48 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.22 (s, 1H), 5.99 (d, *J* = 6.5 Hz, 1H), 1.23 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 157.4, 147.8, 144.1, 140.4, 132.8, 131.6, 129.3, 128.9, 128.5, 127.9, 126.5, 122.3, 121.3, 114.5, 112.0, 95.4, 87.5, 55.4, 51.7, 28.5.
HRMS (ESI, m/z) calcd for $C_{25}H_{25}N_2O_3$ $(M+H)^+$: 401.1860, found: 401.1859.



3-1s

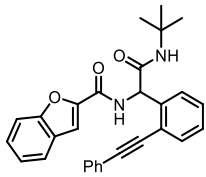
3-1s was obtained as a light yellow solid (56%). Melting point 169-171 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 5.8 Hz, 1H), 7.63-7.57 (m, 4H), 7.46 (dd, *J* = 4.6, 3.7 Hz, 2H), 7.39 (dd, *J* = 6.4, 3.9 Hz, 3H), 7.35 (td, *J* = 7.6, 1.3 Hz, 1H), 7.30 (td, *J* = 7.5, 1.2 Hz, 1H), 7.07 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.22 (s, 1H), 5.97 (d, *J* = 5.9 Hz, 1H), 1.23 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 160.8, 140.5, 138.6, 132.9, 131.6, 130.3, 129.3, 129.0, 128.6, 128.4, 128.0, 127.6, 126.5, 122.3, 121.3, 95.4, 87.5, 56.0, 51.8, 28.5.
HRMS (ESI, m/z) calcd for $C_{25}H_{25}N_2O_2S$ $(M+H)^+$: 417.1631, found: 417.1626.



3-1t

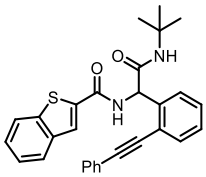
3-1t was obtained as a beige solid (65%). Melting point 127-129 °C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (m, 4H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.41-7.37 (m, 3H), 7.36-7.32 (m, 1H), 7.31-7.27 (m, 1H), 6.78 (dd, *J* = 3.9, 1.6 Hz, 1H), 6.69 (s, 1H), 6.33 (s, 1H), 6.09 (dd, *J* = 3.9, 2.6 Hz, 1H), 5.93 (d, *J* = 6.1 Hz, 1H), 3.87 (s, 3H), 1.23 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 160.8, 141.1, 132.9, 131.6, 129.3, 128.9, 128.6, 128.1, 127.8, 126.4, 125.2, 122.4, 121.1, 112.5, 107.3, 95.4, 87.8, 55.6, 51.7, 36.8, 28.6.
HRMS (ESI, m/z) calcd for $C_{26}H_{28}N_3O_2$ $(M+H)^+$: 414.2176, found: 414.2174.



3-1u

3-1u was obtained as a beige solid (55%). Melting point 140-142 °C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (m, 3H), 7.55 (dd, *J* = 18.3, 7.4 Hz, 3H), 7.42-7.38 (m, 4H), 7.36-7.30 (m, 2H), 7.21 (dd, *J* = 13.8, 7.3 Hz, 2H), 6.27 (s, 1H), 6.06 (d, *J* = 6.4 Hz, 1H), 1.27 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 157.8, 154.8, 148.4, 140.1, 132.8, 131.5, 129.3, 128.9, 128.5, 127.9, 127.4, 126.8, 126.5, 123.5, 122.5, 122.2, 121.3, 111.8, 110.5, 95.5, 87.4, 55.5, 51.7, 28.4.

HRMS (ESI, m/z) calcd for $C_{29}H_{27}N_2O_3$ (M+H) $^+$: 451.2016, found: 451.2014.



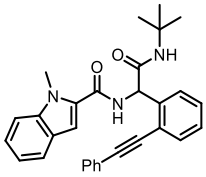
3-1v

3-1v was obtained as a light brown solid (60%). Melting point 105-107 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 5.8 Hz, 1H), 7.86-7.78 (m, 3H), 7.61 (td, *J* = 6.9, 2.4 Hz, 3H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.45-7.37 (m, 5H), 7.33 (m, 2H), 6.24 (s, 1H), 6.00 (d, *J* = 5.9 Hz, 1H), 1.25 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.2, 161.2, 141.1, 140.3, 139.1, 138.2, 132.9, 131.6, 129.4, 129.0, 128.6, 128.0, 126.5, 126.3, 125.4, 125.1, 124.8, 122.7, 122.3, 121.3, 95.5, 87.5, 56.1, 51.8, 28.5.

HRMS (ESI, m/z) calcd for $C_{29}H_{27}N_2O_2S$ (M+H) $^+$: 467.1788, found: 467.1782.



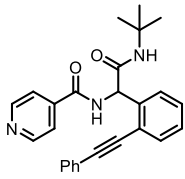
3-1w

3-1w was obtained as a light brown solid (53%). Melting point 165-167 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 5.9 Hz, 1H), 7.65-7.57 (m, 4H), 7.53-7.46 (m, 1H), 7.40-7.27 (m, 7H), 7.17-7.12 (m, 1H), 7.09 (s, 1H), 6.30 (s, 1H), 5.99 (d, *J* = 6.0 Hz, 1H), 3.99 (s, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 161.4, 140.6, 139.0, 132.9, 131.5, 131.2, 129.3, 128.9, 128.5, 127.9, 126.3, 126.0, 124.1, 122.2, 121.9, 121.2, 120.4, 110.0, 104.7, 95.5, 87.6, 55.8, 51.7, 31.5, 28.5.

HRMS (ESI, m/z) calcd for $C_{30}H_{30}N_3O_2$ (M+H) $^+$: 464.2332, found: 464.2332.



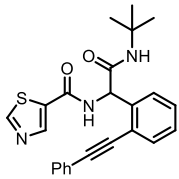
3-1x

3-1x was obtained as a light yellow solid (52%). Melting point 156-158 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76-8.72 (m, 2H), 8.08 (d, *J* = 5.6 Hz, 1H), 7.71 (dd, *J* = 4.6, 1.4 Hz, 2H), 7.63 (dd, *J* = 5.6, 4.1 Hz, 3H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.44-7.41 (m, 3H), 7.36 (m, 2H), 6.19 (s, 1H), 5.98 (d, *J* = 5.9 Hz, 1H), 1.27 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.18, 164.1, 150.6, 140.9, 139.9, 133.0, 131.5, 129.4, 129.1, 128.6, 128.2, 126.5, 122.2, 121.4, 121.0, 95.6, 87.3, 56.1, 51.9, 28.5.

HRMS (ESI, m/z) calcd for $C_{26}H_{26}N_3O_2$ $(M+H)^+$: 412.2019, found: 412.2021.



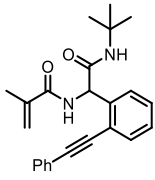
3-1y

3-1y was obtained as a light yellow solid (59%). Melting point 84-86 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.35 (s, 1H), 7.85 (s, 1H), 7.60 (d, *J* = 1.7 Hz, 3H), 7.49-7.30 (m, 6H), 6.16 (s, 1H), 5.96 (d, *J* = 4.6 Hz, 1H), 1.24 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 159.3, 156.4, 144.1, 139.9, 134.4, 133.0, 131.5, 129.3, 129.0, 128.6, 128.2, 126.6, 122.2, 121.4, 95.6, 87.2, 56.1, 51.9, 28.5.

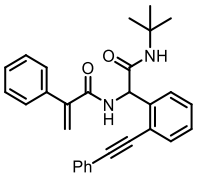
HRMS (ESI, m/z) calcd for $C_{24}H_{24}N_3O_2S$ $(M+H)^+$: 418.1584, found: 418.1589.



3-1z

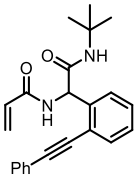
3-1z was obtained as a white solid (62%). Melting point 119-121 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (m, 4H), 7.38 (m, 4H), 7.36-7.28 (m, 2H), 6.15 (s, 1H), 5.84 (dd, *J* = 3.5, 2.5 Hz, 2H), 5.39-5.34 (m, 1H), 1.99 (d, *J* = 1.0 Hz, 3H), 1.22 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 167.1, 140.6, 139.3, 132.9, 131.5, 129.3, 128.9, 128.5, 127.9, 126.6, 122.3, 121.3, 120.5, 95.3, 87.5, 55.9, 51.7, 28.5, 18.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{27}N_2O_2$ (M+H) $^{+}$: 375.2067, found: 375.2064.



3-1a'

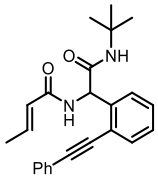
3-1a' was obtained as a light yellow solid (54%). Melting point 130-132 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.54 (m, 1H), 7.50 (dd, *J* = 7.0, 2.7 Hz, 2H), 7.43-7.24 (m, 12H), 6.18 (s, 1H), 5.93 (s, 1H), 5.86 (d, *J* = 6.4 Hz, 1H), 5.61 (s, 1H), 1.19 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.2, 166.2, 144.4, 140.2, 136.8, 132.9, 131.6, 129.1, 128.8, 128.6, 128.4, 128.4, 128.1, 128.0, 127.4, 122.8, 122.3, 121.5, 95.3, 87.2, 56.6, 51.6, 28.5.
HRMS (ESI, m/z) calcd for $C_{29}H_{29}N_2O_2$ (M+H) $^{+}$: 437.2223, found: 437.2225.



3-1b'

3-1b' was obtained as a light yellow solid (63%). Melting point 132-134 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.55 (m, 3H), 7.43-7.28 (m, 7H), 6.28-6.26 (m, 1H), 6.23 (s, 1H), 5.93 (d, *J* = 6.3 Hz, 1H), 5.65 (dd, *J* = 9.0, 2.8 Hz, 1H), 1.21 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 164.4, 140.4, 132.8, 131.5, 130.5, 129.3, 128.9, 128.5, 127.8, 126.9, 126.3, 122.3, 121.3, 95.3, 87.5, 55.6, 51.7, 28.5.

HRMS (ESI, m/z) calcd for $C_{23}H_{25}N_2O_2$ (M+H) $^+$: 361.1910, found: 361.1915.



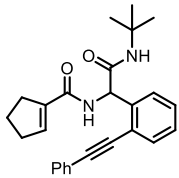
3-1c'

3-1c' was obtained as a light yellow solid (66%). Melting point 111-113 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63-7.57 (m, 3H), 7.41 (dd, *J* = 7.2, 3.6 Hz, 4H), 7.35 (td, *J* = 7.6, 1.1 Hz, 1H), 7.31 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.14 (d, *J* = 6.0 Hz, 1H), 6.86 (dq, *J* = 13.7, 6.8 Hz, 1H), 6.25 (s, 1H), 5.98-5.91 (m, 2H), 1.86 (dd, *J* = 6.9, 1.5 Hz, 3H), 1.23 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 164.9, 140.7, 140.5, 132.8, 131.6, 129.3, 128.9, 128.5, 127.8, 126.3, 124.7, 122.4, 121.3, 95.3, 87.6, 55.6, 51.7, 28.5, 17.7.

HRMS (ESI, m/z) calcd for $C_{24}H_{26}N_2O_2$ (M+H) $^+$: 375.2067, found: 375.2054.



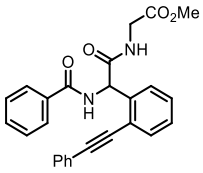
3-1d'

3-1d' was obtained as a light yellow solid (55%). Melting point 148-150 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.55 (m, 3H), 7.43-7.27 (m, 7H), 6.61 (p, *J* = 2.4 Hz, 1H), 6.17 (s, 1H), 5.88 (d, *J* = 6.3 Hz, 1H), 2.67-2.55 (m, 2H), 2.47 (dtd, *J* = 10.5, 5.1, 2.6 Hz, 2H), 1.97 (p, *J* = 7.6 Hz, 2H), 1.21 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 164.4, 140.7, 138.9, 138.9, 132.8, 131.5, 129.2, 128.8, 128.5, 127.8, 126.7, 122.3, 121.3, 95.2, 87.5, 55.6, 51.6, 33.1, 31.3, 28.5, 23.3.

HRMS (ESI, m/z) calcd for $C_{26}H_{29}N_2O_2$ (M+H) $^+$: 401.2223, found: 401.2233.



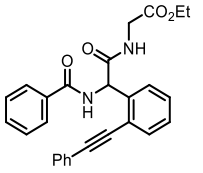
3-5a

3-5a was obtained as a light yellow solid (47%). Melting point 110-112 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.78 (m, 3H), 7.64 (ddt, *J* = 7.3, 4.7, 3.1 Hz, 3H), 7.54-7.46 (m, 2H), 7.41 (dd, *J* = 6.3, 1.4 Hz, 2H), 7.39-7.32 (m, 5H), 6.79 (t, *J* = 5.0 Hz, 1H), 6.22 (d, *J* = 6.2 Hz, 1H), 4.19-4.08 (m, 1H), 3.95 (dd, *J* = 18.3, 4.8 Hz, 1H), 3.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 169.4, 166.3, 139.5, 133.7, 133.0, 131.7, 129.2, 128.9, 128.5, 128.5, 128.3, 127.2, 127.1, 122.3, 121.9, 95.6, 87.0, 55.9, 52.4, 41.7.

HRMS (ESI, m/z) calcd for $C_{26}H_{23}N_2O_4$ $(M+H)^+$: 427.1652, found: 427.1657.



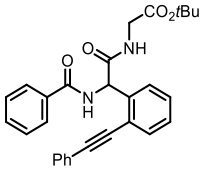
3-5b

3-5b was obtained as a white solid (52%). Melting point 132-134 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.79 (m, 3H), 7.68-7.59 (m, 3H), 7.53-7.45 (m, 2H), 7.44-7.39 (m, 2H), 7.39-7.31 (m, 5H), 6.78 (t, *J* = 5.0 Hz, 1H), 6.22 (d, *J* = 6.2 Hz, 1H), 4.17-4.05 (m, 3H), 3.95 (dd, *J* = 18.3, 4.9 Hz, 1H), 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8, 168.9, 166.3, 139.5, 133.7, 133.0, 131.8, 131.7, 129.2, 128.9, 128.5, 128.5, 128.3, 127.2, 127.1, 122.4, 122.0, 95.6, 87.0, 61.6, 55.9, 41.9, 14.0.

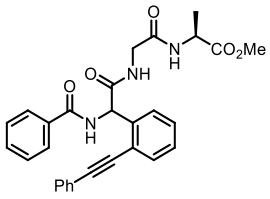
HRMS (ESI, m/z) calcd for $C_{27}H_{25}N_2O_4$ $(M+H)^+$: 441.1809, found: 441.1810.



3-5c

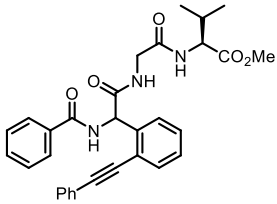
3-5c was obtained as light yellow oil (42%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 3.6, 2.5 Hz, 3H), 7.69-7.58 (m, 3H), 7.48 (ddd, *J* = 8.6, 4.6, 1.6 Hz, 2H), 7.43-7.31 (m, 7H), 6.72 (t, *J* = 4.8 Hz, 1H), 6.19 (d, *J* = 6.1 Hz, 1H), 4.03 (dd, *J* = 18.2, 5.4 Hz, 1H), 3.84 (dd, *J* = 18.2, 4.5 Hz, 1H), 1.39 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 168.0, 166.3, 139.6, 133.8, 133.1, 131.8, 131.7, 129.2, 128.8, 128.5, 128.4, 128.2, 127.2, 127.2, 122.4, 122.0, 95.6, 87.0, 82.5, 56.0, 42.6, 27.9.
HRMS (ESI, m/z) calcd for $C_{29}H_{29}N_2O_4$ (M+H) $^{+}$: 469.2122, found: 469.2132.



3-5d

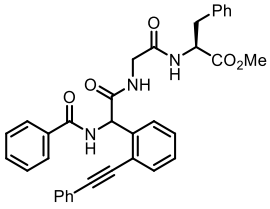
3-5d was obtained as a light yellow solid (86%, last step), 1.1:1 dr. Melting point 127-129 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 2H), 7.70 (dd, *J* = 26.4, 6.1 Hz, 1H), 7.60 (d, *J* = 5.5 Hz, 3H), 7.56-7.44 (m, 2H), 7.41-7.29 (m, 7H), 6.92 (t, *J* = 5.0 Hz, 1H), 6.75 (dd, *J* = 41.2, 7.2 Hz, 1H), 6.18-6.08 (m, 1H), 4.55-4.40 (m, 1H), 4.08-3.86 (m, 2H), 3.67 (d, *J* = 4.7 Hz, 3H), 1.31 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 173.0, 173.0, 170.1, 170.1, 167.8, 167.8, 166.8, 166.8, 138.9, 138.6, 133.6, 133.5, 133.2, 133.1, 131.8, 131.7, 131.7, 129.2, 128.9, 128.9, 128.5, 128.5, 127.9, 127.6, 127.2, 127.2, 122.3, 122.2, 122.1, 95.6, 95.6, 86.8, 86.7, 56.7, 56.5, 52.4, 48.0, 48.0, 43.3, 43.3, 17.9.
HRMS (ESI, m/z) calcd for $C_{29}H_{28}N_3O_5$ (M+H) $^{+}$: 498.2023, found: 498.2033.



3-5e

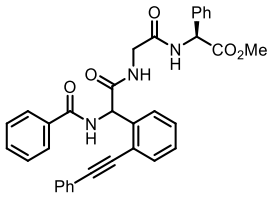
3-5e was obtained as a light yellow solid (79%, last step), 1.1:1 dr. Melting point 135-137 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.7 Hz, 2H), 7.76 (dd, *J* = 22.6, 6.3 Hz, 1H), 7.65-7.57 (m, 3H), 7.55-7.43 (m, 2H), 7.41-7.29 (m, 7H), 7.00 (s, 1H), 6.64 (dd, *J* = 25.1, 8.6 Hz, 1H), 6.23-6.14 (m, 1H), 4.46 (dt, *J* = 8.5, 5.8 Hz, 1H), 4.13-3.93 (m, 2H), 3.66 (d, *J* = 7.2 Hz, 3H), 1.30-1.22 (m, 1H), 0.88-0.76 (m, 6H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.0, 172.0, 170.2, 170.1, 168.1, 168.0, 166.6, 139.1, 138.9, 133.6, 133.6, 133.2, 133.1, 131.7, 131.7, 129.2, 128.8, 128.5, 128.5, 128.5, 128.4, 128.4, 127.5, 127.4, 127.2, 127.2, 122.3, 122.3, 122.1, 122.1, 95.6, 95.6, 86.8, 86.8, 57.3, 57.2, 56.3, 56.3, 52.1, 52.1, 43.6, 43.4, 31.1, 31.0, 18.8, 18.8, 17.8, 17.7.
HRMS (ESI, m/z) calcd for $C_{31}H_{32}N_3O_5$ $(M+H)^+$: 526.2336, found: 526.2341.



3-5f

3-5f was obtained as a light yellow solid (89%, last step), 1.1:1 dr. Melting point 110-112 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.5, 3.4 Hz, 2H), 7.72 (t, *J* = 6.2 Hz, 1H), 7.60 (d, *J* = 5.3 Hz, 3H), 7.49 (dd, *J* = 15.2, 7.6 Hz, 2H), 7.41-7.30 (m, 7H), 7.23-7.15 (m, 3H), 7.08-6.97 (m, 2H), 6.86 (t, *J* = 5.0 Hz, 1H), 6.55 (t, *J* = 6.8 Hz, 1H), 6.13 (d, *J* = 5.9 Hz, 1H), 4.78 (q, *J* = 6.6 Hz, 1H), 4.07-3.75 (m, 2H), 3.64 (d, *J* = 4.2 Hz, 3H), 3.13-2.93 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6, 170.0, 170.0, 167.7, 166.6, 166.6, 139.0, 138.9, 135.7, 135.6, 133.6, 133.6, 133.1, 131.8, 131.7, 129.2, 129.1, 129.1, 128.9, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 127.6, 127.5, 127.2, 127.2, 127.1, 127.1, 122.3, 122.3, 122.1, 95.6, 95.6, 86.8, 86.8, 56.4, 53.3, 53.2, 52.3, 43.3, 37.7, 37.7.
HRMS (ESI, m/z) calcd for $C_{35}H_{32}N_3O_5$ $(M+H)^+$: 574.2336, found: 574.2339.



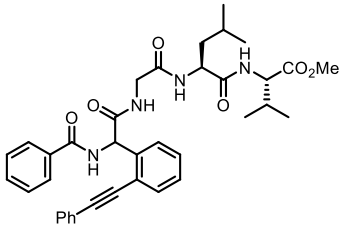
3-5g

3-5g was obtained as a light yellow solid (71%, last step), 1.1:1 dr. Melting point 100-102 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.73 (m, 3H), 7.63-7.54 (m, 3H), 7.52-7.41 (m, 2H), 7.39-7.26 (m, 12H), 7.22 (s, 1H), 7.02-6.87 (m, 1H), 6.17 (t, *J* = 7.1 Hz, 1H), 5.50 (t, *J* = 7.2 Hz, 1H), 4.15-3.90 (m, 2H), 3.63 (d, *J* = 7.9 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9, 170.9, 170.2, 170.1, 167.5, 167.4, 166.6, 166.5, 139.2, 139.0, 135.9, 133.7, 133.6, 133.2, 133.1, 131.8, 131.8, 131.7, 131.7, 129.2, 129.2, 128.9, 128.9, 128.8, 128.8, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 127.6, 127.3, 127.3, 127.2, 127.2, 122.3, 122.3, 122.1, 122.0, 95.6, 95.6, 86.8, 86.8, 56.4, 56.4, 56.3, 56.2, 52.8, 43.4, 43.4.

HRMS (ESI, m/z) calcd for $C_{34}H_{30}N_3O_5$ $(M+H)^+$: 560.2180, found: 560.2175.



3-5h

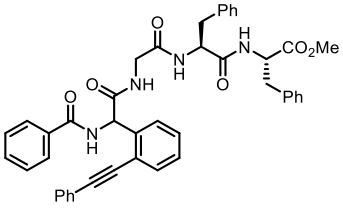
3-5h was obtained as a light yellow solid (81%, last step), 1.2:1 dr. Melting point 102-104 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.78 (m, 2H), 7.68 (d, *J* = 5.9 Hz, 1H), 7.64-7.52 (m, 4H), 7.51-7.42 (m, 1H), 7.42-7.28 (m, 7H), 7.23-7.11 (m, 1H), 7.04 (dd, *J* = 8.0, 4.3 Hz, 1H), 6.85 (t, *J* = 9.1 Hz, 1H), 6.17 (dd, *J* = 26.7, 6.1 Hz, 1H), 4.59-4.34 (m, 2H), 4.14-3.81 (m, 2H), 3.67 (d, *J* = 5.8 Hz, 3H), 2.17-2.04 (m, 1H), 1.71-1.44 (m, 3H), 0.92-0.74 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 172.1, 171.8, 170.3, 170.2, 168.5, 168.2, 167.0, 166.9, 138.7, 138.2, 133.4, 133.3, 133.1, 131.9, 131.8, 131.7, 131.7, 129.2, 128.8, 128.5, 128.4, 127.6, 127.5, 127.3, 127.2,

122.5, 122.3, 122.3, 122.3, 95.4, 86.8, 86.6, 57.2, 57.1, 56.8, 56.4, 52.1, 52.0, 52.0, 51.9, 43.5, 43.4, 40.8, 40.6, 31.0, 30.9, 24.6, 22.8, 22.7, 21.9, 21.9, 18.8, 18.8, 17.7, 17.7.

HRMS (ESI, m/z) calcd for $C_{37}H_{43}N_4O_6$ $(M+H)^+$: 639.3177, found: 639.3172.



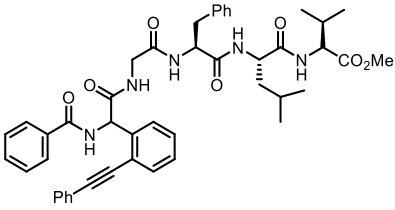
3-5i

3-5i was obtained as a light yellow solid (92%, last step), 1.2:1 dr. Melting point 116-118 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00-7.77 (m, 3H), 7.65-7.43 (m, 5H), 7.39-7.25 (m, 7H), 7.19-6.85 (m, 13H), 6.22 (dd, *J* = 23.3, 6.4 Hz, 1H), 4.78-4.56 (m, 2H), 3.96-3.79 (m, 1H), 3.78-3.64 (m, 1H), 3.59 (d, *J* = 5.1 Hz, 3H), 3.07-2.79 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 171.4, 170.4, 170.3, 170.3, 170.0, 168.2, 167.8, 167.0, 166.8, 139.1, 138.6, 136.5, 136.4, 135.8, 135.7, 133.5, 133.5, 133.1, 131.7, 129.1, 129.1, 129.1, 128.8, 128.7, 128.5, 128.4, 128.4, 127.7, 127.6, 127.3, 127.3, 126.9, 126.9, 126.8, 126.7, 122.4, 122.3, 122.3, 95.5, 95.3, 86.9, 86.8, 56.6, 56.2, 54.6, 54.2, 53.5, 53.3, 52.2, 52.2, 43.4, 43.3, 38.1, 37.8.

HRMS (ESI, m/z) calcd for $C_{44}H_{41}N_4O_6$ $(M+H)^+$: 721.3020, found: 721.3015.

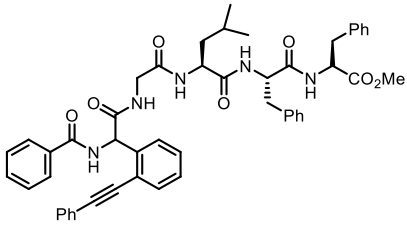


3-5j

3-5j was obtained as a light yellow solid (73%, last step), 1.3:1 dr. Melting point 131-133 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 6.8 Hz, 1H), 7.88 (dd, *J* = 11.7, 7.1 Hz, 3H), 7.68-7.53 (m, 4H), 7.50-7.42 (m, 2H), 7.39-7.25 (m, 8H), 7.20-7.00 (m, 6H), 6.34 (t, *J* = 5.8 Hz, 1H), 4.79 (d, *J* = 29.3 Hz, 2H), 4.43 (dd, *J* = 15.6, 7.1 Hz, 1H), 4.02-3.86 (m, 1H), 3.78-3.71 (m,

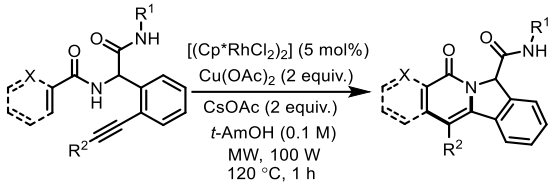
1H), 3.60 (d, *J* = 2.9 Hz, 3H), 2.91 (d, *J* = 5.4 Hz, 2H), 2.42 (dd, *J* = 14.5, 7.1 Hz, 1H), 1.54-1.42 (m, 2H), 1.26 (s, 1H), 0.84 (dt, *J* = 11.9, 4.6 Hz, 6H), 0.76-0.63 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 172.0, 172.0, 170.7, 170.6, 170.5, 170.3, 168.0, 167.7, 167.1, 166.8, 138.9, 136.6, 136.3, 133.7, 133.5, 133.3, 133.0, 131.8, 131.8, 131.7, 129.3, 129.2, 129.0, 128.7, 128.4, 128.4, 128.3, 128.2, 127.5, 127.5, 127.3, 126.8, 126.8, 122.8, 122.5, 122.2, 95.4, 95.2, 87.1, 86.7, 57.4, 56.3, 54.6, 54.4, 53.3, 52.7, 51.9, 51.6, 43.6, 41.6, 38.8, 31.0, 24.5, 24.5, 22.6, 22.6, 22.2, 21.9, 18.9, 18.9, 18.0, 18.0.
HRMS (ESI, m/z) calcd for $C_{46}H_{52}N_5O_7$ $(M+H)^+$: 786.3861, found: 786.3852.



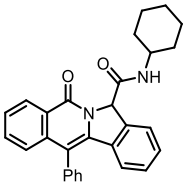
3-5k

3-5k was obtained as a light yellow solid (76%, last step), 1.3:1 dr. Melting point 149-151 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (t, *J* = 21.7 Hz, 3H), 7.66-25 (m, 15H), 7.03 (dd, *J* = 31.1, 10.1 Hz, 11H), 6.28 (s, 1H), 4.70 (t, *J* = 57.4 Hz, 3H), 3.81 (dd, *J* = 38.2, 13.5 Hz, 2H), 3.54 (s, 3H), 3.04-2.76 (m, 4H), 2.43 (d, *J* = 14.0 Hz, 1H), 1.47 (s, 2H), 0.90-0.77 (m, 6H).
^{13}C NMR (151 MHz, DMSO) δ 172.1, 172.1, 172.0, 172.0, 171.5, 171.4, 170.8, 170.6, 169.0, 168.9, 167.2, 167.0, 140.0, 139.7, 138.1, 138.0, 137.4, 134.3, 134.3, 131.9, 131.9, 129.7, 129.6, 129.5, 129.3, 129.1, 129.0, 129.0, 128.7, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 127.0, 126.7, 123.6, 123.5, 122.8, 122.7, 94.4, 87.7, 56.9, 56.7, 54.1, 54.0, 52.3, 52.3, 51.4, 42.9, 42.9, 41.3, 41.2, 37.9, 37.1, 24.5, 24.4, 23.5, 23.5, 22.1, 22.0.
HRMS (ESI, m/z) calcd for $C_{50}H_{52}N_5O_7$ $(M+H)^+$: 834.3861, found: 834.3863.

Rhodium(III)-catalyzed intramolecular annulations

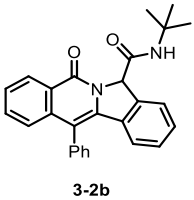


To a 10 mL glass tube equipped with a stir bar were added **3-1**, **3-3** or **3-5** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), $Cu(OAc)_2$ (0.6 mmpl) and *t*-AmOH (3 mL) without any particular precautions to extrude oxygen or moisture. The reaction mixture was irradiated under MW at 120 °C with maximum power of 100 W for 1 h, then cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **3-2**, **3-4** or **3-6**.



3-2a

3-2a was obtained as a brown solid (78%). Melting point 189-191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 7.8 Hz, 1H), 7.65-7.56 (m, 5H), 7.53-7.48 (m, 2H), 7.36-7.30 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 6.9 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 1H), 3.89-3.72 (m, 1H), 1.94 (dd, *J* = 26.8, 11.7 Hz, 2H), 1.74-1.52 (m, 4H), 1.31 (dd, *J* = 19.8, 7.4 Hz, 2H), 1.22-1.13 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 160.9, 139.0, 138.3, 137.9, 134.9, 134.0, 132.4, 131.3, 130.8, 129.5, 129.4, 128.5, 127.6, 126.5, 125.4, 124.5, 124.0, 123.1, 114.9, 66.4, 48.9, 32.9, 32.6, 29.7, 25.5, 24.7. HRMS (ESI, m/z) calcd for $C_{29}H_{27}N_2O_2$ $(M+H)^+$: 435.2067, found: 435.2066.



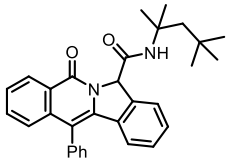
3-2b

3-2b was obtained as a light yellow solid (92%). Melting point 264-266 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59-8.49 (m, 1H), 7.63-7.45 (m, 7H), 7.26 (m, 4H), 7.08 (t, *J* = 7.7 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 1H), 6.03 (s, 1H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 160.7, 139.0, 138.3, 138.2, 134.9, 134.1, 132.3, 131.3, 130.7, 129.4, 129.3, 128.4, 127.4, 126.3, 125.3, 124.5, 124.0, 122.7, 114.7, 66.8, 51.9, 28.7.

HRMS (ESI, m/z) calcd for $C_{27}H_{25}N_2O_2$ $(M+H)^+$: 409.1910, found: 409.1906.



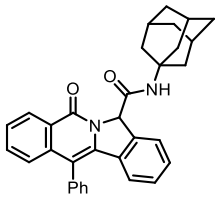
3-2c

3-2c was obtained as a brown solid (90%). Melting point 214-216 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.65-7.56 (m, 5H), 7.52 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.49-7.46 (m, 1H), 7.36-7.32 (m, 2H), 7.24-7.20 (m, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.52 (s, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.91 (s, 1H), 1.66 (d, *J* = 8.3 Hz, 2H), 1.43 (d, *J* = 1.4 Hz, 6H), 0.90 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6, 160.9, 138.8, 138.1, 137.9, 134.9, 133.8, 132.4, 131.2, 130.8, 129.5, 129.4, 128.5, 127.6, 126.5, 125.4, 124.6, 123.9, 123.5, 114.9, 67.1, 55.9, 52.6, 31.5, 31.4, 28.8, 28.5.

HRMS (ESI, m/z) calcd for $C_{31}H_{33}N_2O_2$ $(M+H)^+$: 465.2536, found: 465.2531.

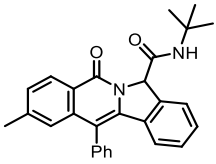


3-2d

3-2d was obtained as a brown solid (87%). Melting point 173-175 °C.

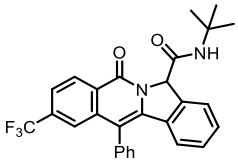
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.62-7.54 (m, 5H), 7.50 (m, 2H), 7.35-7.29 (m, 2H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 6.39 (d, *J* = 8.0 Hz, 1H), 6.00 (s, 1H), 2.07 (s, 9H), 1.65 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 160.8, 139.0, 138.3, 138.2, 134.9, 134.1, 132.3, 131.3, 130.8, 129.5, 129.3, 128.4, 127.5, 126.4, 125.3, 124.5, 124.0, 122.8, 114.7, 66.9, 52.6, 41.4, 36.3, 29.4.
HRMS (ESI, m/z) calcd for $C_{33}H_{31}N_2O_2$ $(M+H)^+$: 487.2380, found: 487.2372.



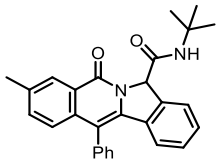
3-2e

3-2e was obtained as a white solid (93%). Melting point 237-239 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.2 Hz, 1H), 7.64-7.54 (m, 4H), 7.53-7.46 (m, 1H), 7.35-7.30 (m, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.77 (s, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 2.38 (s, 3H), 1.39 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 160.8, 143.0, 139.1, 138.3, 138.0, 135.1, 134.2, 131.3, 130.8, 129.5, 129.3, 128.6, 128.1, 127.6, 125.1, 124.0, 123.1, 122.4, 114.7, 66.8, 51.9, 28.7, 22.0.
HRMS (ESI, m/z) calcd for $C_{28}H_{27}N_2O_2$ $(M+H)^+$: 423.2067, found: 423.2064.



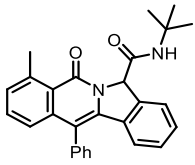
3-2f

3-2f was obtained as a white solid (79%). Melting point 219-221°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.3 Hz, 1H), 7.69 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.64-7.56 (m, 4H), 7.52-7.47 (m, 2H), 7.41-7.32 (m, 2H), 7.14 (t, *J* = 7.7 Hz, 1H), 6.54 (s, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.88 (s, 1H), 1.41 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 160.0, 139.8, 139.1, 138.1, 133.8 (d, *J* = 2.6 Hz), 131.2, 130.7, 130.0, 129.8, 129.7, 129.0 (d, *J* = 5.4 Hz), 128.7, 126.5, 124.4, 122.8, 122.4, 114.4, 67.1, 52.2, 28.7.
HRMS (ESI, m/z) calcd for $C_{28}H_{24}F_3N_2O_2$ $(M+H)^+$: 477.1784, found: 477.1776.



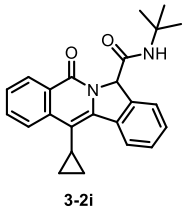
3-2g

3-2g was obtained as a brown solid (86%). Melting point 159-161 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.56 (m, 4H), 7.50-7.45 (m, 1H), 7.41-7.36 (m, 1H), 7.32-7.28 (m, 2H), 7.13-7.04 (m, 3H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.96 (s, 1H), 2.49 (s, 3H), 1.39 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 160.7, 138.0, 137.4, 136.7, 136.5, 135.0, 134.2, 133.7, 131.2, 130.7, 129.3, 129.1, 128.3, 127.1, 125.3, 124.4, 123.7, 122.8, 114.7, 66.8, 51.8, 28.7, 21.3.
HRMS (ESI, m/z) calcd for $C_{28}H_{27}N_2O_2$ $(M+H)^+$: 423.2067, found: 423.2065.



3-2h

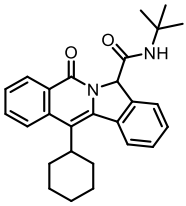
3-2h was obtained as a light yellow solid (74%). Melting point 233-235 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60-7.54 (m, 4H), 7.49-7.44 (m, 1H), 7.43-7.33 (m, 2H), 7.30 (m, 2H), 7.07 (dd, *J* = 15.1, 7.8 Hz, 2H), 6.83 (s, 1H), 6.32 (d, *J* = 7.9 Hz, 1H), 5.93 (s, 1H), 3.05 (s, 3H), 1.41 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 161.7, 141.8, 140.7, 138.1, 135.6, 134.2, 131.5, 131.4, 130.8, 129.7, 129.5, 129.4, 129.3, 128.6, 128.4, 124.0, 123.8, 122.8, 114.7, 67.0, 51.9, 28.7, 24.1.
HRMS (ESI, m/z) calcd for $C_{28}H_{27}N_2O_2$ $(M+H)^+$: 423.2067, found: 423.2064.



3-2i

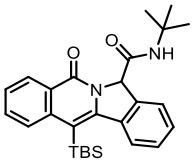
3-2i was obtained as a brown solid (62%). Melting point 138-140 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.0 Hz, 1H), 8.34 (dd, *J* = 13.6, 7.6 Hz, 2H), 7.75-7.69 (m, 1H), 7.63 (d, *J* = 7.0 Hz, 1H), 7.49 (m, 3H), 6.71 (s, 1H), 5.84 (s, 1H), 2.12-2.04 (m, 1H), 1.36 (s, 9H), 1.27 (d, *J* = 8.1 Hz, 2H), 0.77 (dd, *J* = 9.0, 5.3 Hz, 1H), 0.69 (dd, *J* = 8.8, 5.2 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 160.7, 141.0, 139.6, 138.3, 134.2, 132.0, 129.3, 128.5, 127.6, 126.2, 125.8, 125.0, 124.7, 122.9, 114.0, 67.0, 51.9, 28.7, 10.8, 10.6, 8.0.
HRMS (ESI, m/z) calcd for $C_{24}H_{24}N_2O_2$ $(M+H)^+$: 373.1910, found: 373.1902.



3-2j

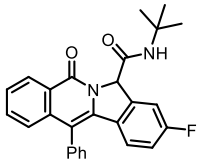
3-2j was obtained as a yellow solid (82%). Melting point 256-258 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.67 (m, 2H), 7.52-7.39 (m, 3H), 6.97 (s, 1H), 5.90 (s, 1H), 3.78 (t, *J* = 12.6 Hz, 1H), 2.41-2.22 (m, 2H), 1.93 (m, 5H), 1.60-1.46 (m, 3H), 1.37 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.5, 160.4, 138.5, 138.0, 137.9, 134.9, 131.2, 129.1, 129.0, 128.1, 126.0, 125.4, 124.5, 123.3, 119.1, 66.7, 51.8, 39.0, 31.8, 28.7, 27.6, 27.4, 26.1, 22.7.
HRMS (ESI, m/z) calcd for $C_{27}H_{31}N_2O_2$ $(M+H)^+$: 415.2380, found: 415.2375.



3-2k

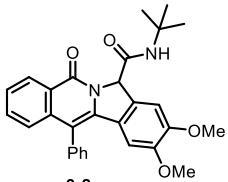
3-2k was obtained as a rufous solid (58%). Melting point 94-96 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, *J* = 6.7 Hz, 1H), 8.11 (dd, *J* = 6.0, 2.9 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.68-7.60 (m, 2H), 7.46 (dd, *J* = 9.2, 5.6 Hz, 3H), 6.53 (s, 1H), 5.81 (s, 1H), 1.38 (s, 9H), 1.30 (s, 9H), 0.41 (s, 3H), 0.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 161.1, 149.0, 142.3, 139.1, 134.9, 130.9, 129.9, 129.8, 127.3, 127.3, 126.2, 125.9, 124.8, 122.7, 109.1, 67.0, 51.9, 29.7, 28.7, 19.4, 2.1, 2.0.
HRMS (ESI, m/z) calcd for $C_{27}H_{35}N_2O_2Si$ $(M+H)^+$: 447.2462, found: 447.2459.



3-2m

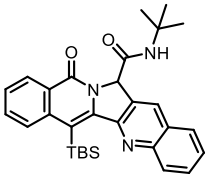
3-2m was obtained as a pale yellow solid (95%). Melting point 235-237 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.62-7.46 (m, 6H), 7.32-7.25 (m, 3H), 7.21 (d, *J* = 7.7 Hz, 1H), 6.79 (td, *J* = 8.8, 2.4 Hz, 1H), 6.34 (dd, *J* = 8.8, 5.0 Hz, 1H), 6.02 (s, 1H), 1.41 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 163.2 (d, *J* = 250.7 Hz), 160.8, 140.4 (d, *J* = 9.3 Hz), 138.9, 137.4, 134.6, 132.5, 131.0 (d, *J* = 86.6 Hz), 130.2 (d, *J* = 2.5 Hz), 129.5 (d, *J* = 20.3 Hz), 128.6, 127.4, 126.5, 125.6 (d, *J* = 8.7 Hz), 125.3, 124.3, 116.3 (d, *J* = 23.0 Hz), 114.4, 110.3 (d, *J* = 24.3 Hz), 66.6, 52.0, 28.7.
HRMS (ESI, m/z) calcd for $C_{27}H_{24}FN_2O_2$ $(M+H)^+$: 427.1816, found: 427.1811.



3-2n

3-2n was obtained as a light brown solid (93%). Melting point 153-155 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.60-7.49 (m, 5H), 7.48-7.42 (m, 1H), 7.34 (dd, *J* = 5.1, 3.9 Hz, 1H), 7.27-7.19 (m, 2H), 7.05 (s, 1H), 5.93 (s, 1H), 5.82 (s, 1H), 3.87 (s, 3H), 3.37 (s, 3H), 1.41 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 160.7, 150.7, 149.4, 138.9, 138.8, 134.9, 132.2, 131.7, 131.2, 129.2, 128.3, 127.3, 126.2, 125.8, 124.9, 123.9, 112.9, 106.0, 105.0, 66.6, 56.0, 55.2, 51.7, 28.7.

HRMS (ESI, m/z) calcd for $C_{29}H_{29}N_2O_4$ $(M+H)^+$: 469.2122, found: 469.2121.



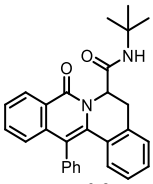
3-2o

3-2o was obtained as a light yellow solid (78%). Melting point 259-261 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.0 Hz, 1H), 8.36 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.82-7.67 (m, 2H), 7.57 (dt, *J* = 14.2, 7.1 Hz, 2H), 6.97 (s, 1H), 6.07 (s, 1H), 1.39 (s, 9H), 1.33 (s, 9H), 0.56 (s, 3H), 0.51 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 161.4, 153.6, 148.1, 146.0, 142.1, 131.4, 130.5, 130.1, 130.1, 129.6, 129.0, 128.3, 127.5, 127.4, 126.8, 125.9, 113.4, 64.4, 52.1, 29.4, 28.7, 19.3, 2.8, 2.8.

HRMS (ESI, m/z) calcd for $C_{30}H_{36}N_3O_2Si$ $(M+H)^+$: 498.2571, found: 498.2579.



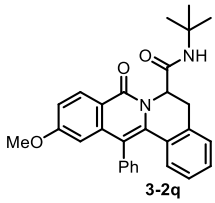
3-2p

3-2p was obtained as a yellow solid (89%). Melting point 209-211 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62-8.50 (m, 1H), 7.65-7.51 (m, 4H), 7.44-7.35 (m, 2H), 7.27 (dd, *J* = 10.4, 2.8 Hz, 2H), 7.18-7.09 (m, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 3.8 Hz, 2H), 6.04 (s, 1H), 5.86 (dd, *J* = 5.0, 2.3 Hz, 1H), 3.53 (dd, *J* = 15.0, 2.3 Hz, 1H), 3.11 (dd, *J* = 14.9, 5.0 Hz, 1H), 1.04 (s, 9H).

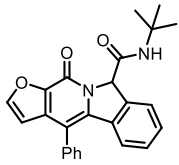
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 162.3, 137.5, 137.1, 136.0, 134.0, 132.6, 132.4, 131.4, 130.2, 129.7, 129.6, 128.7, 128.3, 128.2, 128.0, 127.7, 127.1, 125.8, 125.7, 124.6, 118.6, 55.0, 51.1, 32.0, 28.2.

HRMS (ESI, m/z) calcd for $C_{28}H_{27}N_2O_2$ $(M+H)^+$: 423.2067, found: 423.2069.



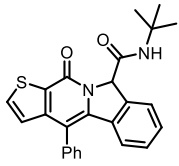
3-2q

3-2q was obtained as a yellow solid (73%). Melting point 275-277 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.9 Hz, 1H), 7.63 (t, *J* = 4.5 Hz, 1H), 7.56 (dd, *J* = 8.7, 7.7 Hz, 1H), 7.39 (ddd, *J* = 14.1, 4.7, 1.9 Hz, 2H), 7.24 (s, 1H), 7.16-7.09 (m, 2H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.79-6.74 (m, 2H), 6.73 (d, *J* = 2.5 Hz, 1H), 6.05 (s, 1H), 5.84 (dd, *J* = 5.0, 2.3 Hz, 1H), 3.74 (s, 3H), 3.52 (dd, *J* = 15.0, 2.3 Hz, 1H), 3.10 (dd, *J* = 14.9, 5.1 Hz, 1H), 1.04 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 163.0, 162.0, 139.7, 137.2, 136.2, 134.7, 132.2, 131.5, 130.2, 130.2, 129.7, 128.7, 128.3, 128.2, 127.8, 125.6, 118.5, 118.3, 115.9, 113.6, 107.7, 55.3, 54.8, 51.0, 31.9, 28.3.
HRMS (ESI, m/z) calcd for $C_{29}H_{29}N_2O_3$ $(M+H)^+$: 453.2173, found: 453.2183.



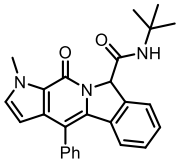
3-2r

3-2r was obtained as a brown solid (67%). Melting point 253-255 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 2.0 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.58-7.50 (m, 4H), 7.41 (dd, *J* = 5.8, 2.7 Hz, 1H), 7.33 (td, *J* = 7.6, 0.9 Hz, 1H), 7.18-7.07 (m, 2H), 6.86 (d, *J* = 7.9 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 6.01 (s, 1H), 1.38 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 151.7, 148.6, 141.5, 139.3, 138.5, 136.6, 134.4, 133.8, 130.4, 129.8, 129.2, 129.1, 128.5, 123.2, 123.0, 111.2, 107.3, 66.8, 52.1, 28.6.
HRMS (ESI, m/z) calcd for $C_{25}H_{23}N_2O_3$ $(M+H)^+$: 399.1703, found: 399.1696.



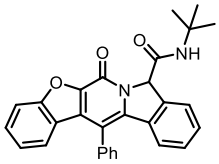
3-2s

3-2s was obtained as a pale brown solid (89%). Melting point 152-154 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 5.2 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.57-7.50 (m, 4H), 7.36 (m, 2H), 7.18 (s, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 5.2 Hz, 1H), 6.66 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 1H), 1.40 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 156.9, 148.2, 140.2, 138.2, 135.1, 133.9, 133.2, 130.6, 130.1, 129.3, 129.2, 128.6, 127.7, 124.4, 123.5, 123.0, 113.8, 66.7, 52.0, 28.7.
HRMS (ESI, m/z) calcd for $C_{25}H_{22}N_2O_2S$ $(M+H)^+$: 415.1475, found: 415.1475.



3-2t

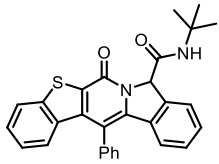
3-2t was obtained as a pale brown solid (90%). Melting point 223-225 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57-7.45 (m, 5H), 7.42-7.36 (m, 1H), 7.23 (m, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.00 (d, *J* = 2.8 Hz, 1H), 5.97 (s, 1H), 4.24 (s, 3H), 1.42 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 153.9, 137.8, 135.5, 135.1, 134.8, 134.6, 131.6, 130.5, 129.9, 128.9, 128.3, 127.9, 122.6, 122.4, 121.6, 112.8, 102.2, 66.2, 51.7, 35.8, 28.7.
HRMS (ESI, m/z) calcd for $C_{26}H_{25}N_3O_2$ $(M+H)^+$: 412.2019, found: 412.2014.



3-2u

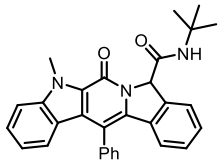
3-2u was obtained as a brown solid (85%). Melting point 264-266 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69-7.59 (m, 6H), 7.47 (m, 2H), 7.35 (td, *J* = 7.6, 0.9 Hz, 1H), 7.12 (m, 2H), 6.98 (s, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 6.02 (s, 1H), 1.40 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 157.3, 152.5, 142.2, 139.7, 138.4, 134.1, 133.8, 131.0, 130.5, 130.0, 129.6, 129.5, 129.2, 129.0, 128.8, 128.7, 123.4, 123.2, 122.9, 112.7, 111.7, 67.2, 52.2, 28.6.
HRMS (ESI, m/z) calcd for $C_{29}H_{25}N_2O_3$ (M+H) $^+$: 449.1860, found: 449.1856.



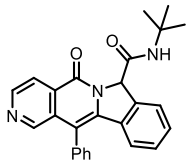
3-2v

3-2v was obtained as a yellow solid (52%). Melting point 253-255 °C.
^{1}H NMR (300 MHz, DMSO-d_6) δ 8.63 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 5.7 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 3.8 Hz, 1H), 7.56-7.44 (m, 4H), 7.21 (dd, *J* = 14.0, 6.6 Hz, 2H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.27 (d, *J* = 7.9 Hz, 1H), 6.09 (s, 1H), 1.32 (s, 9H).
^{13}C NMR (151 MHz, DMSO-d_6) δ 165.2, 156.0, 142.1, 141.7, 141.0, 139.3, 135.8, 135.4, 134.2, 130.8, 130.6, 130.2, 129.9, 129.1, 128.2, 127.9, 125.3, 125.2, 124.5, 123.4, 123.2, 113.3, 55.4, 51.3, 28.9.
HRMS (ESI, m/z) calcd for $C_{29}H_{25}N_2O_2S$ (M+H) $^+$: 465.1631, found: 465.1631.



3-2w

3-2w was obtained as a white solid (96%). Melting point 267-269 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (m, 5H), 7.44 (m, 3H), 7.30-7.26 (m, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.94 (m, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.66 (s, 1H), 6.54 (d, *J* = 7.9 Hz, 1H), 5.91 (s, 1H), 4.39 (s, 3H), 1.41 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.5, 154.5, 141.4, 137.4, 135.6, 135.0, 134.6, 130.6, 130.2, 129.5, 129.4, 128.6, 128.1, 126.6, 126.2, 125.6, 122.7, 122.7, 122.6, 121.9, 120.0, 113.7, 109.8, 66.8, 51.9, 31.4, 28.7.
HRMS (ESI, m/z) calcd for $C_{30}H_{28}N_3O_2$ (M+H) $^+$: 462.2176, found: 462.2167.



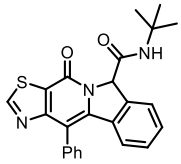
3-2x

3-2x was obtained as a pale yellow solid (78%). Melting point 261-263 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.29 (s, 1H), 7.66-7.51 (m, 5H), 7.37 (dd, *J* = 10.8, 4.3 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 5.88 (s, 1H), 1.42 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 159.6, 149.1, 145.9, 139.9, 137.9, 133.8, 133.1, 131.2, 130.7, 130.0, 129.7, 129.6, 129.0, 124.4, 122.6, 113.0, 67.1, 52.3, 28.7.

HRMS (ESI, m/z) calcd for $C_{26}H_{23}N_3O_2$ $(M+H)^+$: 410.1863, found: 410.1862.



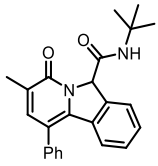
3-2y

3-2y was obtained as a rufous solid (46%). Melting point 177-179 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.58 (dt, *J* = 5.8, 3.0 Hz, 5H), 7.46 (d, *J* = 7.0 Hz, 1H), 7.39 (d, *J* = 3.3 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 6.58 (s, 1H), 5.86 (s, 1H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 161.0, 159.8, 142.6, 138.1, 133.7, 133.6, 130.8, 130.4, 130.0, 129.2, 129.1, 128.9, 128.8, 124.2, 122.7, 113.8, 67.0, 52.3, 28.7.

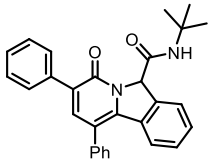
HRMS (ESI, m/z) calcd for $C_{24}H_{22}N_3O_2S$ $(M+H)^+$: 416.1427, found: 416.1432.



3-2z

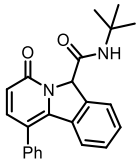
3-2z was obtained as a brown solid (82%). Melting point 254-256°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.45 (s, 4H), 7.40-7.29 (m, 3H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.03 (s, 1H), 2.28 (d, *J* = 0.9 Hz, 3H), 1.41 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 161.1, 141.7, 141.4, 138.6, 137.0, 134.0, 129.5, 128.8, 128.4, 128.0, 126.6, 123.3, 122.7, 116.9, 67.3, 51.8, 28.7, 16.5.
HRMS (ESI, m/z) calcd for $C_{24}H_{25}N_2O_2$ (M+H) $^{+}$: 373.1910, found: 373.1906.



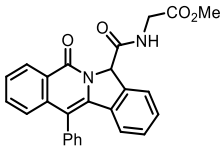
3-2a'

3-2a' was obtained as a rufous solid (89%). Melting point 260-262 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84-7.78 (m, 3H), 7.63 (s, 1H), 7.48-7.26 (m, 10H), 7.18-7.09 (m, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.10 (s, 1H), 1.41 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 159.5, 143.4, 141.9, 139.3, 136.8, 136.3, 133.8, 129.9, 128.9, 128.8, 128.5, 128.2, 128.0, 127.7, 123.5, 122.4, 117.5, 67.8, 51.9, 28.7.
HRMS (ESI, m/z) calcd for $C_{29}H_{27}N_2O_2$ (M+H) $^{+}$: 435.2067, found: 435.2076.



3-2b'

3-2b' was obtained as a rufous solid (59%). Melting point 200-202 °C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.51-7.37 (m, 7H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.08 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 9.2 Hz, 1H), 5.89 (s, 1H), 1.37 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 161.2, 144.1, 143.9, 138.5, 136.6, 133.6, 130.1, 129.0, 128.6, 128.3, 123.7, 123.3, 117.6, 117.4, 67.5, 52.0, 28.6.
HRMS (ESI, m/z) calcd for $C_{23}H_{23}N_2O_2$ (M+H) $^{+}$: 359.1754, found: 359.1760.



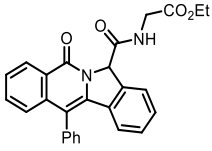
3-6a

3-6a was obtained as a light yellow solid (72%). Melting point 214-216 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.60 (tdd, *J* = 7.3, 5.3, 1.9 Hz, 4H), 7.54-7.47 (m, 2H), 7.40-7.32 (m, 2H), 7.26-7.22 (m, 2H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 6.08 (s, 1H), 4.23 (dd, *J* = 18.3, 5.8 Hz, 1H), 4.06 (dd, *J* = 18.3, 4.7 Hz, 1H), 3.73 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 167.3, 160.9, 139.0, 138.0, 137.2, 134.7, 134.0, 132.6, 131.2, 130.8, 129.6, 129.5, 129.4, 129.0, 128.6, 127.6, 126.7, 125.5, 124.4, 124.0, 123.5, 115.2, 65.9, 52.4, 41.5.

HRMS (ESI, m/z) calcd for $C_{26}H_{21}N_2O_4$ $(M+H)^+$: 425.1496, found: 425.1498.



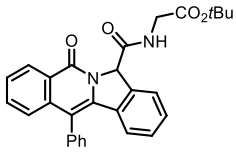
3-6b

3-6b was obtained as a light red solid (86%). Melting point 228-230 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 5.3 Hz, 1H), 7.64-7.54 (m, 4H), 7.52-7.45 (m, 2H), 7.38-7.31 (m, 2H), 7.25-7.20 (m, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.15 (s, 1H), 4.25 (dd, *J* = 18.2, 6.0 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.02 (dd, *J* = 18.2, 4.6 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 169.6, 167.4, 160.8, 139.0, 138.1, 137.4, 134.8, 134.0, 132.4, 131.2, 130.8, 129.5, 129.5, 129.4, 128.9, 128.5, 127.5, 126.5, 125.4, 124.4, 123.9, 123.4, 115.1, 65.9, 61.4, 41.6, 14.0.

HRMS (ESI, m/z) calcd for $C_{27}H_{23}N_2O_4$ $(M+H)^+$: 439.1652, found: 439.1655.



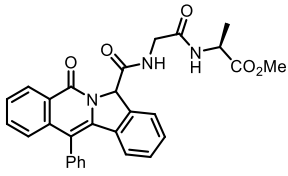
3-6c

3-6c was obtained as a light yellow solid (83%). Melting point 131-133 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.65-7.55 (m, 4H), 7.54-7.46 (m, 2H), 7.40-7.31 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 2H), 6.41 (d, *J* = 7.9 Hz, 1H), 6.07 (s, 1H), 4.03 (ddd, *J* = 22.8, 18.4, 5.0 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 167.0, 160.9, 139.0, 138.0, 137.3, 134.8, 134.0, 132.5, 131.2, 130.8, 129.5, 129.5, 129.4, 128.9, 128.5, 127.6, 126.6, 125.4, 124.5, 124.0, 123.4, 115.1, 82.4, 66.0, 42.4, 28.0.

HRMS (ESI, m/z) calcd for $C_{29}H_{27}N_2O_4$ $(M+H)^+$: 467.1965, found: 467.1962.



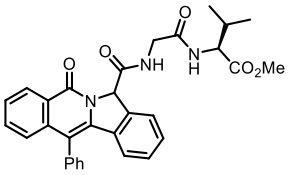
3-6d

3-6d was obtained as a light yellow solid (85%, 1.2:1 dr). Melting point 132-134 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 49.5, 7.1 Hz, 1H), 8.07 (d, *J* = 48.4 Hz, 1H), 7.83-7.66 (m, 1H), 7.58 (dd, *J* = 7.6, 4.9 Hz, 4H), 7.51-7.29 (m, 4H), 7.28-7.19 (m, 2H), 7.11 (td, *J* = 7.7, 3.4 Hz, 1H), 6.40 (t, *J* = 7.2 Hz, 1H), 6.06 (s, 1H), 4.61 (s, 1H), 4.27 (s, 1H), 4.06 (t, *J* = 6.7 Hz, 1H), 3.70 (d, *J* = 37.1 Hz, 3H), 1.64-1.52 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.0, 173.4, 169.0, 168.8, 167.9, 167.4, 161.2, 160.8, 139.0, 139.0, 138.1, 137.8, 137.2, 136.7, 134.5, 134.4, 134.2, 133.7, 132.8, 132.5, 131.1, 131.0, 130.7, 129.8, 129.7, 129.5, 129.3, 129.1, 128.9, 128.7, 128.6, 127.4, 127.0, 126.8, 126.5, 125.6, 125.5, 124.2, 124.1, 124.1, 124.0, 123.0, 122.7, 115.7, 115.2, 66.4, 66.2, 52.4, 52.2, 48.3, 48.2, 43.3, 43.0, 17.4, 17.4.

HRMS (ESI, m/z) calcd for $C_{29}H_{26}N_3O_5$ $(M+H)^+$: 496.1867, found: 496.1875.



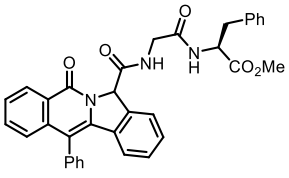
3-6e

3-6e was obtained as a light red solid (78%, 1.2:1 dr). Melting point 125-127 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 85.9, 7.8 Hz, 1H), 8.12-7.70 (m, 1H), 7.69-7.53 (m, 5H), 7.52-7.43 (m, 2H), 7.39-7.30 (m, 2H), 7.26-7.06 (m, 3H), 6.38 (dd, *J* = 13.2, 7.9 Hz, 1H), 6.08 (d, *J* = 14.4 Hz, 1H), 4.56-4.44 (m, 1H), 4.28 (dd, *J* = 17.1, 6.5 Hz, 1H), 4.10-3.99 (m, 1H), 3.71 (d, *J* = 27.0 Hz, 3H), 2.32 (dt, *J* = 19.9, 6.7 Hz, 1H), 0.96 (ddd, *J* = 14.1, 10.3, 5.5 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.1, 172.3, 169.2, 169.0, 167.9, 167.4, 161.1, 160.6, 139.0, 139.0, 138.0, 137.7, 137.3, 136.8, 134.6, 134.5, 134.2, 133.7, 132.7, 132.4, 131.1, 131.0, 130.7, 130.7, 129.8, 129.6, 129.5, 129.5, 129.3, 129.1, 128.9, 128.7, 128.5, 127.6, 127.1, 126.7, 126.4, 125.5, 125.4, 124.3, 124.1, 124.0, 124.0, 123.1, 122.7, 115.5, 115.0, 66.2, 66.1, 58.0, 57.9, 52.1, 51.9, 43.5, 43.2, 30.7, 30.7, 19.1, 19.1, 18.6, 18.3.

HRMS (ESI, m/z) calcd for $C_{31}H_{30}N_3O_5$ $(M+H)^+$: 524.2180, found: 524.2189.



3-6f

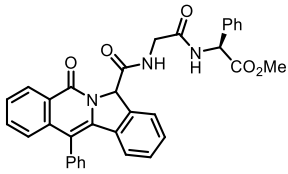
3-6f was obtained as a light yellow solid (81%, 1.3:1 dr). Melting point 139-141 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 53.0, 7.7 Hz, 1H), 7.83-7.47 (m, 8H), 7.37-7.12 (m, 10H), 6.41 (t, *J* = 7.6 Hz, 1H), 6.05 (d, *J* = 13.8 Hz, 1H), 4.83 (ddd, *J* = 21.9, 14.5, 7.5 Hz, 1H), 4.20 (ddd, *J* = 17.1, 6.8, 3.9 Hz, 1H), 4.11-3.87 (m, 1H), 3.64 (d, *J* = 24.1 Hz, 3H), 3.23 (ddd, *J* = 21.4, 13.1, 7.4 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.6, 172.1, 168.8, 168.7, 167.6, 167.1, 161.2, 160.9, 139.1, 138.0, 137.8, 137.1, 136.7, 136.6, 136.5, 134.5, 134.5, 134.2, 133.7, 132.8, 132.6, 131.1, 131.0, 130.7, 129.9, 129.7,

129.6, 129.5, 129.4, 129.3, 129.2, 129.0, 128.7, 128.6, 128.5, 128.4, 127.6, 127.2, 126.9, 126.8, 126.7, 125.6, 125.5, 124.3, 124.1, 124.1, 124.1, 123.1, 122.8, 115.7, 115.4, 66.4, 66.3, 54.1, 54.0, 52.3, 52.2, 43.3, 42.9, 37.8, 37.6.

HRMS (ESI, m/z) calcd for $C_{35}H_{30}N_3O_5$ $(M+H)^+$: 572.2180, found: 572.2187.



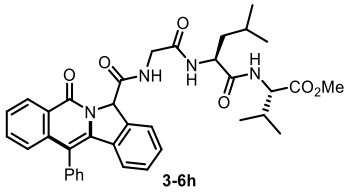
3-6g

3-6g was obtained as a light red solid (89%, 1.2:1 dr). Melting point 134-136 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 44.1, 7.5 Hz, 1H), 8.06-7.82 (m, 2H), 7.69-7.53 (m, 5H), 7.51-7.39 (m, 4H), 7.34-7.26 (m, 5H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.10 (td, *J* = 7.6, 3.6 Hz, 1H), 6.38 (dd, *J* = 7.8, 4.6 Hz, 1H), 6.03 (d, *J* = 15.0 Hz, 1H), 5.64 (dd, *J* = 13.3, 7.2 Hz, 1H), 4.32-4.00 (m, 2H), 3.66 (d, *J* = 22.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.5, 171.1, 168.9, 168.7, 167.8, 167.5, 160.9, 160.7, 139.0, 138.9, 137.9, 137.8, 137.1, 136.9, 135.8, 135.8, 134.6, 134.5, 134.1, 133.8, 132.6, 132.4, 131.1, 131.1, 130.7, 129.7, 129.6, 129.5, 129.4, 129.3, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 127.9, 127.7, 127.6, 127.5, 126.6, 126.3, 125.4, 125.3, 124.3, 124.1, 124.0, 124.0, 123.1, 122.9, 115.3, 115.2, 66.1, 66.1, 56.7, 56.7, 52.7, 52.6, 43.3, 43.2.

HRMS (ESI, m/z) calcd for $C_{34}H_{28}N_3O_5$ $(M+H)^+$: 558.2023, found: 558.2017.



3-6h

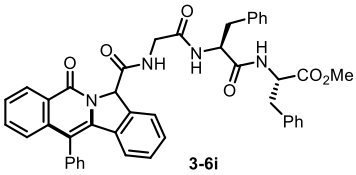
3-6h was obtained as a light yellow solid (79%, 1.2:1 dr). Melting point 120-122 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 45.0, 8.0 Hz, 1H), 7.85 (dd, *J* = 22.1, 8.0 Hz, 1H), 7.62 (dd, *J* = 15.8, 7.9 Hz, 5H), 7.55-7.27 (m, 6H), 7.24 (s, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.58 (dd, *J* = 117.7, 8.2 Hz,

1H), 6.03 (d, *J* = 17.1 Hz, 1H), 4.50 (dddd, *J* = 36.7, 25.1, 16.4, 8.4 Hz, 2H), 4.33-4.02 (m, 2H), 3.70 (d, *J* = 48.8 Hz, 3H), 1.78 (s, 2H), 1.26 (s, 2H), 1.17-0.76 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 172.9, 172.4, 172.0, 169.3, 168.8, 168.2, 167.9, 161.2, 160.9, 139.2, 139.0, 138.0, 137.8, 136.8, 136.6, 134.4, 134.3, 134.2, 134.1, 132.9, 132.8, 131.0, 131.0, 130.9, 130.8, 130.7, 130.7, 129.9, 129.6, 129.5, 129.2, 129.2, 128.8, 128.7, 128.7, 128.5, 128.3, 127.5, 127.0, 126.7, 125.7, 125.5, 124.2, 122.9, 122.7, 115.7, 115.7, 66.5, 66.3, 57.1, 52.2, 51.9, 43.7, 40.2, 39.8, 30.9, 29.7, 24.9, 24.8, 23.3, 22.9, 21.8, 21.6, 19.1, 18.5, 17.9, 17.5.

HRMS (ESI, m/z) calcd for $C_{37}H_{41}N_4O_6$ $(M+H)^+$: 637.3020, found: 637.3011.



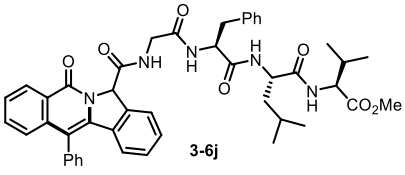
3-6i

3-6i was obtained as a light yellow solid (72%, 1.3:1 dr). Melting point 120-122 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52-8.24 (m, 2H), 8.03 (s, 1H), 7.60-7.51 (m, 5H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.31 (dd, *J* = 13.0, 7.2 Hz, 4H), 7.21 (dd, *J* = 8.3, 2.6 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 7H), 7.00 (d, *J* = 7.0 Hz, 2H), 6.75-6.66 (m, 1H), 6.38 (dt, *J* = 8.4, 4.3 Hz, 1H), 6.09 (d, *J* = 24.2 Hz, 1H), 4.94-4.62 (m, 2H), 3.99-3.70 (m, 2H), 3.51 (d, *J* = 52.1 Hz, 3H), 3.21-2.64 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 171.6, 171.5, 171.2, 169.4, 169.0, 168.9, 168.0, 160.9, 160.6, 139.0, 138.0, 138.0, 137.9, 137.1, 136.9, 136.0, 136.0, 134.4, 134.2, 134.1, 134.0, 132.7, 132.5, 131.0, 130.9, 130.6, 130.5, 129.8, 129.7, 129.4, 129.3, 129.2, 129.1, 128.9, 128.5, 128.3, 128.0, 127.3, 127.0, 127.0, 126.7, 126.6, 126.5, 126.4, 126.4, 125.6, 125.4, 124.0, 123.9, 122.8, 122.7, 115.3, 115.3, 66.2, 66.0, 55.6, 55.0, 53.8, 53.6, 52.18, 51.8, 43.7, 43.5, 37.7, 37.6, 37.5, 36.9.

HRMS (ESI, m/z) calcd for $C_{44}H_{39}N_4O_6$ $(M+H)^+$: 719.2864, found: 719.2864.



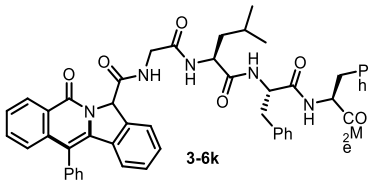
3-6j

3-6j was obtained as a light red solid (68%, 3:1 dr). Melting point 123-125 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 7.9 Hz, 1H), 8.19 (d, *J* = 6.9 Hz, 2H), 7.63 (dd, *J* = 16.2, 4.7 Hz, 5H), 7.58-7.51 (m, 4H), 7.43-7.36 (m, 3H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.17-7.12 (m, 2H), 6.96 (dd, *J* = 17.2, 8.1 Hz, 2H), 6.46 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 1H), 4.74-4.63 (m, 1H), 4.38-4.16 (m, 3H), 4.05 (dd, *J* = 13.8, 6.3 Hz, 1H), 3.61 (s, 3H), 3.56-3.51 (m, 2H), 1.80 (s, 2H), 1.00-0.78 (m, 14H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 172.1, 171.8, 169.7, 160.8, 139.2, 138.4, 138.0, 136.5, 134.4, 134.3, 132.8, 130.9, 130.8, 129.9, 129.6, 129.5, 129.3, 128.8, 128.5, 127.1, 127.0, 126.6, 125.8, 124.3, 124.0, 122.6, 115.5, 66.1, 64.4, 57.6, 56.8, 52.0, 51.9, 44.2, 39.7, 36.2, 30.9, 29.7, 24.5, 22.6, 20.6, 18.9, 18.1.

HRMS (ESI, m/z) calcd for $C_{46}H_{50}N_5O_7$ $(M+H)^+$: 784.3704, found: 784.3700.



3-6k

3-6k was obtained as a light red solid (65%, 2:1 dr). Melting point 127-129 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 76.5, 7.9 Hz, 1H), 8.14-7.80 (m, 2H), 7.73-7.31 (m, 10H), 7.24-6.84 (m, 11H), 6.75 (dd, *J* = 13.4, 5.6 Hz, 2H), 6.49 (dd, *J* = 20.6, 8.0 Hz, 1H), 5.98 (s, 1H), 5.18-4.88 (m, 1H), 4.77-4.29 (m, 3H), 4.14-3.99 (m, 1H), 3.71 (d, *J* = 90.0 Hz, 3H), 3.23-2.77 (m, 4H), 1.26 (s, 1H), 1.06-0.65 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 172.4, 172.4, 171.7, 171.5, 170.6, 169.4, 168.3, 168.1, 161.1, 160.9, 139.3, 139.1, 138.1, 137.2, 136.9, 136.8, 136.3, 135.7, 134.2, 133.1, 133.0, 131.1, 130.9, 130.6, 130.5, 130.0, 129.8, 129.6, 129.5, 129.3, 129.3, 129.2, 129.0, 128.9, 128.5, 128.4, 128.0, 127.9, 127.5, 127.2, 126.9, 126.8, 126.7, 126.5, 126.0, 125.8, 124.3, 124.2, 124.1, 123.6, 122.8, 122.2, 116.2, 115.8, 66.3, 66.1, 53.4, 52.2, 43.8, 41.0, 37.6, 37.3, 37.0, 30.9, 29.7, 24.8, 24.5, 23.0, 22.3, 22.2, 21.7.

HRMS (ESI, m/z) calcd for $C_{50}H_{50}N_5O_7$ $(M+H)^+$: 832.3704, found: 832.3699.

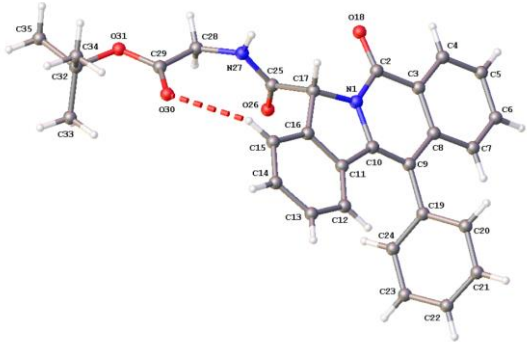
Additional experiments

To a 10 mL glass tube equipped with a stir bar were added **3-5b** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), $Cu(OAc)_2$ (0.6 mmpl), *t*-AmOH (1.5 mL) and H_2O (1.5 mL) without any particular precautions to extrude oxygen or moisture. The reaction mixture was irradiated under MW at 120 °C with maximum power of 100 W for 1 h, then cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **3-6b** (54%).
To a 10 mL glass tube equipped with a stir bar were added **3-5b** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), $Cu(OAc)_2$ (0.6 mmpl) and H_2O (3 mL) without any particular precautions to extrude oxygen or moisture. The reaction mixture was irradiated under MW at 120 °C with maximum power of 100 W for 1 h, then cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **3-6b** (41%).
To a 10 mL glass tube equipped with a stir bar were added **3-5b** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), $Cu(OAc)_2$ (0.6 mmpl), amino acid (0.3 mmol) and *t*-AmOH (3 mL) without any particular precautions to extrude oxygen or moisture. The reaction mixture was irradiated under MW at 120 °C with maximum power of 100 W for 1 h, then cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **3-6b**.

Single crystal X-ray diffraction

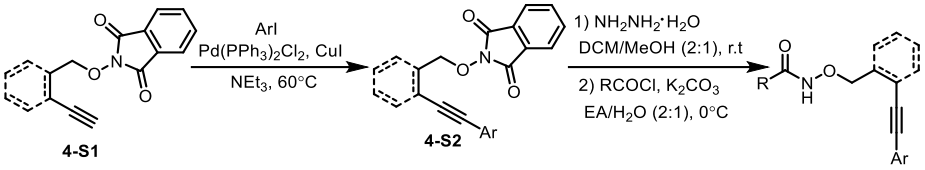
Crystal of **3-6c** was obtained by slow diffusion from a solution of the compound in $CHCl_3$ layered with heptane at room temperature for several days. X-ray intensity data were collected at 293.9(3) K on an Agilent SuperNova diffractometer with Eos CCD detector using Mo-Kα radiation (λ = 0.71073 Å). The images were interpreted and integrated with CrysAlisPRO and the implemented absorption correction was applied. The structures were solved using Olex2 with

the ShelXS structure solution program by Direct Methods and refined with the ShelXL refinement package using full-matrix least-squares minimization on F^2. Non-hydrogen atoms were refined anisotropically and hydrogen atoms in the riding mode with isotropic temperature factors fixed at 1.2 times U_{eq} of the parent atoms (1.5 times U_{eq} for methyl groups). Crystallographic data for **3-6c** has been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 1885561.



Chapter 4

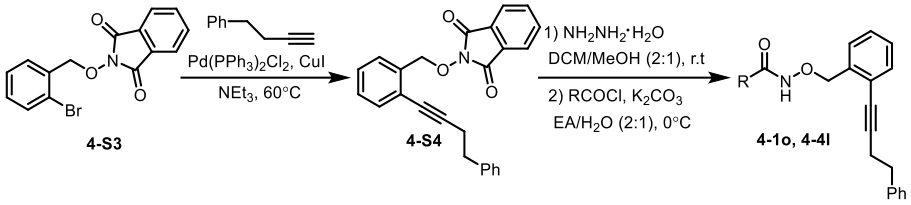
Synthesis of the substrates



General Procedure A

To a 100 mL round-bottom flask,[16] under N_2, was added **4-S1** (5.0 mmol), $PdCl_2(PPh_3)_2$ (0.25 mmol), CuI (0.25 mmol) and anhydrous TEA (20 mL). The mixture was stirred at room temperature for 1 min and then ArI (6.0 mmol) was added. The flask was placed in a preheated oil bath (60°C). The reaction was stirred overnight and then cooled to room temperature and checked by TLC. The reaction was filtered over celite, washing with dichloromethane. The solvent was removed and the residue purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to afford **4-S2**.

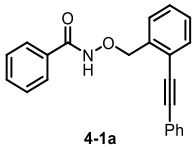
In a 100 mL round-bottom flask was charged **4-S2** (3.0 mmol),[16] solvent 15 mL [MeOH/DCM (1:2)], and then slowly added hydrazine monohydrate (3.3 mmol), then stirred at room temperature for 4h. Upon completion (indicated by TLC), the solvent was then removed under reduce pressure. The residue was washed with DCM and filtered, collected the DCM part and removed the solvent to give the crude *O*-alkoxylamine, which was used in next step without further purification. The crude *O*-alkoxylamine which was obtained in the previous step was added to a biphasic mixture of K_2CO_3 (3.6 mmol) in solvent 15 mL [EA/H_2O (2:1)].[16] The resulting solution was cooled to 0°C followed by dropwise addition of the acid chloride (3.3 mmol) dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at same temperature for 6h. Upon completion (indicated by TLC), the phases were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to give the product **4-1a~4-1n**, **4-1q**, **4-1w~4-1c'**, **4-4a~4-4k, 4-4m**.



General Procedure B

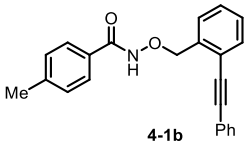
To a 100 mL round-bottom flask, under N_2,[16] was added **4-S3** (5.0 mmol), $PdCl_2(PPh_3)_2$ (0.25 mmol), CuI (0.25 mmol) and anhydrous TEA (20 mL). The mixture was stirred at room temperature for 1 min and then alkyne (6.0 mmol) was added. The flask was placed in a pre-heated oil bath (60°C). The reaction was stirred overnight and then cooled to room temperature and checked by TLC. The reaction was filtered over celite, washing with dichloromethane. The solvent was removed and the residue purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to afford **4-S4**.

In a 100 mL round-bottom flask was charged **4-S4** (3.0 mmol), solvent 15 mL [MeOH/DCM (1:2)],[16] and then slowly added hydrazine monohydrate (3.3 mmol), then stirred at room temperature for 4h. Upon completion (indicated by TLC), the solvent was then removed under reduce pressure. The residue was washed with DCM and filtered, collected the DCM part and removed the solvent to give the crude *O*-alkoxylamine, which was used in next step without further purification. The crude *O*-alkoxylamine which was obtained in the previous step was added to a biphasic mixture of K_2CO_3 (3.6 mmol) in solvent 15 mL [EA/H_2O (2:1)].[16] The resulting solution was cooled to 0°C followed by dropwise addition of the acid chloride (3.3 mmol) dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at same temperature for 6h. Upon completion (indicated by TLC), the phases were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to give the product **4-1o**, **4-4l**.



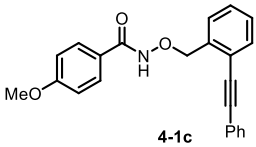
4-1a

Following **General Procedure A**, **4-1a** was obtained as a yellow solid (42%, three steps). Melting point 112-114°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (1 H, s), 7.65-7.56 (4 H, m), 7.53-7.46 (3 H, m), 7.40-7.31 (7 H, m), 5.33 (2 H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 136.9, 132.2, 131.8, 131.5, 129.9, 128.5, 128.4, 128.3, 127.1, 123.5, 122.7, 93.9, 86.8, 76.3.
HRMS (ESI, m/z) calcd for $C_{22}H_{18}NO_2$ $(M+H)^+$: 328.1332, found: 328.1342.



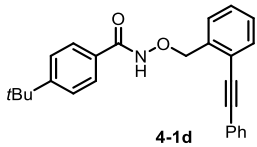
4-1b

Following **General Procedure A**, **4-1b** was obtained as a yellow solid (34%, three steps). Melting point 127-129°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (4 H, m), 7.52-7.48 (2 H, m), 7.36-7.29 (5 H, m), 7.12 (2 H, d, J = 7.8 Hz), 5.30 (2 H, s), 2.33 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 142.3, 137.1, 132.3, 131.6, 129.9, 129.2, 128.9, 128.5, 128.5, 128.3, 127.0, 123.5, 122.8, 94.0, 86.9, 76.3, 21.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_2$ $(M+H)^+$: 342.1489, found: 342.1495.



4-1c

Following **General Procedure A**, **4-1c** was obtained as a yellow solid (43%, three steps). Melting point 118-120°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (1 H, s), 7.65-7.53 (4 H, m), 7.52-7.46 (2 H, m), 7.40-7.28 (5 H, m), 6.86-6.77 (2 H, m), 5.29 (2 H, s), 3.79 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 162.5, 137.0, 132.3, 131.6, 130.0, 128.9, 128.6, 128.6, 128.5, 128.3, 124.1, 123.7, 122.8, 113.8, 94.0, 86.9, 76.5, 55.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_3$ $(M+H)^+$: 358.1438, found: 358.1439.



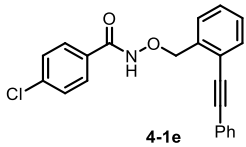
4-1d

Following **General Procedure A**, **4-1d** was obtained as a yellow solid (45%, three steps). Melting point 130-132°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.48 (6 H, m), 7.38-7.30 (7 H, m), 5.32 (2 H, s), 1.29 (9 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 137.1, 132.4, 131.6, 130.0, 128.6, 128.6, 128.5, 128.3, 126.9, 125.5, 123.7, 122.8, 94.0, 86.9, 76.4, 31.9, 31.1.

HRMS (ESI, m/z) calcd for $C_{26}H_{26}NO_2$ $(M+H)^+$: 384.1958, found: 384.1962.



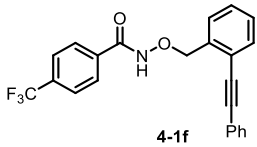
4-1e

Following **General Procedure A**, **4-1e** was obtained as a yellow solid (39%, three steps). Melting point 128-130°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (1 H, s), 7.56 (4 H, m), 7.50-7.46 (2 H, m), 7.38-7.34 (2 H, m), 7.33-7.27 (5 H, m), 5.28 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 138.2, 136.7, 132.4, 131.6, 130.2, 130.1, 128.82, 128.78, 128.6, 128.6, 128.5, 128.4, 123.8, 122.7, 94.0, 86.9, 76.5.

HRMS (ESI, m/z) calcd for $C_{22}H_{17}ClNO_2$ $(M+H)^+$: 362.0942, found: 362.0947.



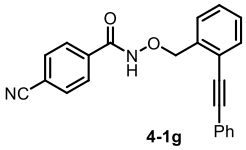
4-1f

Following **General Procedure A**, **4-1f** was obtained as a yellow solid (41%, three steps). Melting point 126-128°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (1 H, s), 7.71 (2 H, d, J = 7.9 Hz), 7.59-7.50 (4 H, m), 7.49-7.44 (2 H, m), 7.36 (2 H, dd, J = 5.2, 3.7 Hz), 7.31 (3 H, d, J = 5.9 Hz), 5.30 (2 H, s).

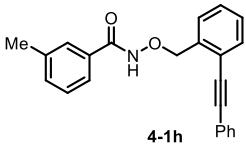
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 136.5, 135.2, 132.4, 131.5, 130.2, 128.9, 128.6 (d, J = 4.6 Hz), 128.4, 127.6, 125.5, 123.9, 122.6, 94.1, 86.9, 76.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -63.12.
HRMS (ESI, m/z) calcd for $C_{23}H_{17}F_3NO_2$ (M+H) $^+$: 396.1206, found: 396.1215.



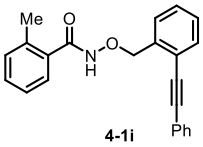
4-1g

Following **General Procedure A**, **4-1g** was obtained as a yellow solid (42%, three steps). Melting point 109-111°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (2 H, d, J = 8.4 Hz), 7.57 (3 H, dd, J = 9.2, 2.6 Hz), 7.53-7.44 (3 H, m), 7.39-7.29 (5 H, m), 5.31 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 135.5, 132.4, 132.2, 131.5, 130.0, 128.8, 128.6, 128.4, 127.5, 123.7, 122.7, 117.9, 115.0, 94.0, 86.9, 76.2.
HRMS (ESI, m/z) calcd for $C_{23}H_{17}N_2O_2$ (M+H) $^+$: 353.1285, found: 353.1286.



4-1h

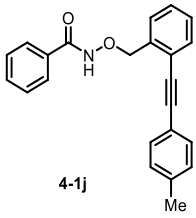
Following **General Procedure A**, **4-1h** was obtained as a yellow oil (36%, three steps).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (1 H, s), 7.57 (2 H, m), 7.51 (2 H, dd, J = 6.6, 3.0 Hz), 7.47 (1 H, s), 7.42-7.35 (3 H, m), 7.34-7.30 (3 H, m), 7.23 (2 H, dd, J = 15.6, 8.1 Hz), 5.31 (2 H, s), 2.30 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 138.5, 136.9, 132.7, 132.4, 131.9, 131.6, 130.1, 128.7, 128.6, 128.5, 128.4, 128.3, 127.8, 123.9, 123.7, 122.8, 76.5, 21.2.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_2$ (M+H) $^+$: 342.1489, found: 342.1488.



4-1i

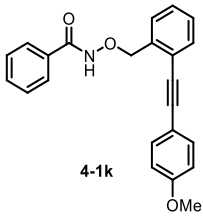
Following **General Procedure A**, **4-1i** was obtained as a yellow solid (38%, three steps). Melting point 90-92°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (1 H, s), 7.63-7.48 (4 H, m), 7.38-7.24 (7 H, m), 7.18 (1 H, d, J = 7.6 Hz), 7.11 (1 H, t, J = 7.5 Hz), 5.33 (2 H, s), 2.40 (3 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 136.9, 136.8, 132.7, 132.4, 131.6, 131.0, 130.5, 129.9, 128.7, 128.6, 128.6, 128.4, 127.1, 125.6, 123.7, 122.8, 94.1, 86.8, 76.5, 19.5.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_2$ (M+H) $^+$: 342.1489, found: 342.1491.



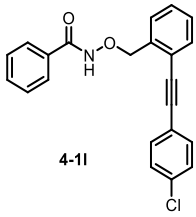
4-1j

Following **General Procedure A**, **4-1j** was obtained as a yellow solid (35%, three steps). Melting point 98-100°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (1 H, s), 7.63 (2 H, d, J = 7.4 Hz), 7.58-7.51 (2 H, m), 7.45 (1 H, t, J = 7.4 Hz), 7.39 (2 H, d, J = 8.0 Hz), 7.36-7.30 (4 H, m), 7.11 (2 H, d, J = 7.9 Hz), 5.29 (2 H, s), 2.35 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 138.7, 136.8, 132.2, 131.9, 131.9, 131.5, 130.0, 129.1, 128.6, 128.5, 128.4, 127.1, 123.9, 119.7, 94.3, 86.3, 76.5, 21.5.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_2$ (M+H) $^+$: 342.1489, found: 342.1495.



4-1k

Following **General Procedure A**, **4-1k** was obtained as a yellow solid (46%, three steps). Melting point 135-137°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (1 H, s), 7.63 (2 H, d, J = 7.3 Hz), 7.57-7.51 (2 H, m), 7.44 (3 H, dd, J = 9.2, 2.4 Hz), 7.33 (4 H, m), 6.86-6.83 (1 H, m), 6.83-6.80 (1 H, m), 5.30 (2 H, s), 3.80 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 138.1, 136.7, 133.1, 132.1, 132.0, 131.9, 130.0, 128.6, 128.5, 128.2, 127.1, 124.1, 114.9, 114.0, 94.1, 85.6, 76.5, 55.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{20}NO_3$ (M+H) $^+$: 358.1438, found: 358.1430.



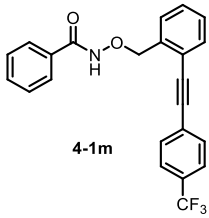
4-1l

Following **General Procedure A**, **4-1l** was obtained as a yellow solid (48%, three steps). Melting point 103-105°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.89 (1 H, s), 7.67-7.61 (2 H, m), 7.54 (2 H, td, J = 5.3, 1.7 Hz), 7.46-7.38 (3 H, m), 7.37-7.30 (4 H, m), 7.28-7.24 (2 H, m), 5.28 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 137.0, 134.4, 132.8, 132.3, 131.8, 130. 0, 128.7, 128.6, 128.5, 127.0, 123.3, 121.3, 92.8, 87.8, 76.1.

HRMS (ESI, m/z) calcd for $C_{22}H_{17}ClNO_2$ $(M+H)^+$: 362.0942, found: 362.0945.



4-1m

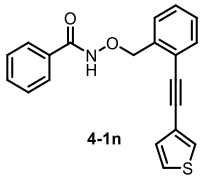
Following **General Procedure A**, **4-1m** was obtained as a yellow solid (37%, three steps). Melting point 112-114°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (1 H, s), 7.66-7.61 (2 H, m), 7.60-7.51 (6 H, m), 7.47-7.40 (1 H, m), 7.39-7.29 (4 H, m), 5.29 (2 H, s).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 137.2, 132.5, 132.0, 131.8 (d, J = 5.4 Hz), 130.2, 129.1, 128.7, 128.5, 127.1, 125.2 (q, J = 3.5 Hz), 123.0, 92.4, 89.2, 76.2.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.79.

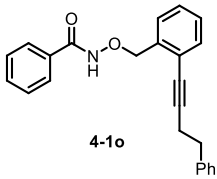
HRMS (ESI, m/z) calcd for $C_{23}H_{17}F_3NO_2$ $(M+H)^+$: 396.1206, found: 396.1211.



4-1n

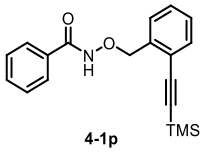
Following **General Procedure A**, **4-1n** was obtained as a yellow oil (32%, three steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.62 (2 H, m), 7.55-7.49 (2 H, m), 7.47 (1 H, dd, J = 2.9, 0.9 Hz), 7.40 (1 H, t, J = 7.4 Hz), 7.29 (4 H, dd, J = 9.0, 6.0 Hz), 7.22 (1 H, dd, J = 4.9, 3.0 Hz), 7.13 (1 H, dd, J = 5.0, 0.9 Hz), 5.26 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 137.0, 132.0, 131.8, 131.7, 129.7, 129.7, 129.0, 128.4, 128.4, 127.0, 125.3, 123.4, 121.8, 89.0, 86.4, 76.1.
HRMS (ESI, m/z) calcd for $C_{20}H_{16}NO_2S$ $(M+H)^+$: 334.0896, found: 334.0896.



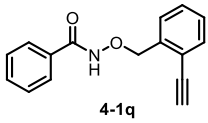
4-1o

Following **General Procedure B**, **4-1o** was obtained as a yellow oil (33%, three steps).
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.19 (1 H, s), 7.65 (2 H, d, J = 7.4 Hz), 7.46-7.39 (2 H, m), 7.37-7.34 (1 H, m), 7.30 (2 H, t, J = 7.7 Hz), 7.25-7.19 (4 H, m), 7.18 (2 H, d, J = 7.3 Hz), 7.13 (1 H, t, J = 7.3 Hz), 5.08 (2 H, s), 2.81 (2 H, t, J = 7.4 Hz), 2.61 (2 H, t, J = 7.4 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 140.4, 136.7, 132.1, 131.8, 131.7, 129.4, 128.3, 128.3, 128.2, 128.2, 127.7, 127.1, 126.1, 123.8, 94.2, 78.8, 76.0, 34.7, 21.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{22}NO_2$ $(M+H)^+$: 356.1645, found: 356.1641.



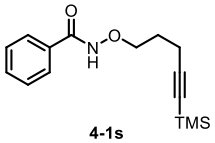
4-1p

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (2 H, d, J = 7.4 Hz), 7.55-7.48 (3 H, m), 7.42-7.38 (2 H, m), 7.35 (1 H, td, J = 7.5, 1.4 Hz), 7.31 (1 H, td, J = 7.5, 1.2 Hz), 5.24 (2 H, s), 0.22 (9 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 137.3, 132.6, 131.9, 130.0, 129.6, 128.7, 128.5, 128.4, 127.1, 123.3, 102.4, 99.3, 76.1, -0.2.
Spectral data was consistent with that previously reported.[16]



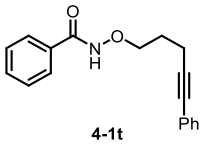
4-1q

Following **General Procedure A**, **4-1q** was obtained as a white solid (75%, two steps). Melting point 120-122°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (1 H, s), 7.68 (2 H, d, J = 7.4 Hz), 7.50 (3 H, m), 7.38-7.28 (4 H, m), 5.21 (2 H, s), 3.25 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 137.5, 132.8, 131.9, 131.9, 129.7, 129.0, 128.5, 128.4, 127.1, 122.2, 81.9, 81.1, 76.1.
HRMS (ESI, m/z) calcd for $C_{16}H_{14}NO_2$ $(M+H)^+$: 252.1019, found: 252.1018.



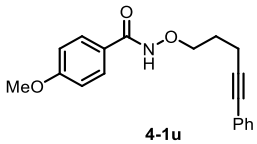
4-1s

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.09 (1 H, s), 7.74 (2 H, d, J = 7.2 Hz), 7.52 (1 H, t, J = 7.3 Hz), 7.42 (2 H, t, J = 7.4 Hz), 4.11 (2 H, t, J = 6.2 Hz), 2.40 (2 H, t, J = 6.9 Hz), 1.92 (2 H, p, J = 6.6 Hz), 0.14 (9 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.7, 132.0, 131.9, 128.6, 127.1, 106.4, 85.2, 75.4, 27.1, 16.6, 0.1.
Spectral data was consistent with that previously reported.[16]



4-1t

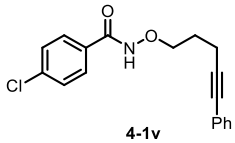
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.20 (1 H, s), 7.75 (2 H, d, J = 7.9 Hz), 7.54-7.50 (1 H, m), 7.41 (4 H, dd, J = 9.2, 5.7 Hz), 7.30-7.28 (3 H, m), 4.20 (2 H, t, J = 6.2 Hz), 2.61 (2 H, t, J = 6.9 Hz), 2.02 (2 H, p, J = 6.6 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.7, 132.0, 131.9, 131.5, 128.6, 128.2, 127.7, 127.1, 123.6, 89.1, 81.2, 75.4, 27.2, 16.1.
Spectral data was consistent with that previously reported.[16]



4-1u

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (1 H, s), 7.73-7.67 (2 H, m), 7.42-7.36 (2 H, m), 7.29-7.26 (3 H, m), 6.92- 6.86 (2 H, m), 4.17 (2 H, t, J = 6.2 Hz), 3.83 (3 H, s), 2.60 (2 H, t, J = 6.9 Hz), 2.05-1.96 (2 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.6, 131.6, 128.9, 128.2, 127.7, 124.1, 123.7, 113.9, 89.2, 81.2, 75.5, 55.4, 27.3, 16.1.

Spectral data was consistent with that previously reported.[16]

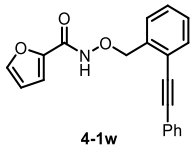


4-1v

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.42 (1 H, s), 7.70-7.64 (2 H, m), 7.39-7.32 (4 H, m), 7.27 (3 H, dt, J = 3.5, 3.0 Hz), 4.16 (2 H, t, J = 6.2 Hz), 2.57 (2 H, t, J = 6.9 Hz), 2.04-1.92 (2 H, m).

^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 131.5, 130.2, 128.8, 128.6, 128.2, 127.7, 123.6, 89.0, 81.2, 75.4, 27.2, 16.1.

Spectral data was consistent with that previously reported.[16]



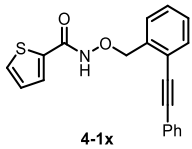
4-1w

Following **General Procedure A**, **4-1w** was obtained as a yellow oil (33%, three steps).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (1 H, s), 7.61-7.49 (4 H, m), 7.39-7.31 (6 H, m), 7.13 (1 H, dd, J = 3.5, 0.7 Hz), 6.44 (1 H, dd, J = 3.5, 1.8 Hz), 5.30 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 145.7, 144.3, 136.7, 132.3, 131.6, 129.9, 128.7, 128.6, 128.5, 128.3, 123.6, 122.8, 115.6, 111.9, 94.0, 86.7, 77.0.

HRMS (ESI, m/z) calcd for $C_{20}H_{16}NO_3$ $(M+H)^+$: 318.1125, found: 318.1134.



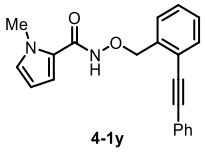
4-1x

Following **General Procedure A**, **4-1x** was obtained as a yellow oil (36%, three steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (1 H, s), 7.61-7.51 (3 H, m), 7.50-7.44 (3 H, m), 7.37-7.33 (2 H, m), 7.31 (3 H, dd, J = 4.3, 2.3 Hz), 7.00 (1 H, dd, J = 4.8, 3.9 Hz), 5.27 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 136.5, 132.3, 131.6, 129.9, 128.7, 128.6, 128.5, 128.3, 127.4, 123.6, 122.8, 94.1, 86.8, 76.9.

HRMS (ESI, m/z) calcd for $C_{20}H_{16}NO_2S$ $(M+H)^+$: 334.0896, found: 334.0892.



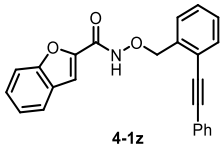
4-1y

Following **General Procedure A**, **4-1y** was obtained as a yellow solid (39%, three steps). Melting point 76-78°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (1 H, s), 7.59-7.53 (2 H, m), 7.52-7.46 (2 H, m), 7.36-7.29 (5 H, m), 6.73-6.65 (1 H, m), 6.46 (1 H, dd, J = 3.9, 1.6 Hz), 6.00 (1 H, dd, J = 3.9, 2.6 Hz), 5.26 (2 H, s), 3.86 (3 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 137.1, 132.2, 131.6, 129.8, 128.6, 128.5, 128.4, 128.4, 128.3, 123.5, 122.9, 122.3, 112.5, 107.4, 93.9, 86.9, 76.5, 36.4.

HRMS (ESI, m/z) calcd for $C_{21}H_{19}N_2O_2$ $(M+H)^+$: 331.1441, found: 331.1439.



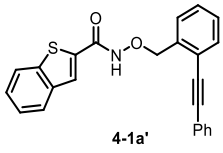
4-1z

Following **General Procedure A**, **4-1z** was obtained as a yellow solid (32%, three steps). Melting point 105-107°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (1 H, s), 7.64-7.56 (3 H, m), 7.51 (2 H, dt, J = 5.5, 2.1 Hz), 7.46 (1 H, s), 7.43-7.35 (4 H, m), 7.33-7.26 (4 H, m), 5.36 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 154.7, 146.6, 136.6, 132.4, 131.6, 130.1, 128.8, 128.6, 128.5, 128.3, 127.2, 127.1, 123.8, 123.8, 122.8, 122.7, 111.8, 111.8, 94.1, 86.8, 77.1.

HRMS (ESI, m/z) calcd for $C_{24}H_{18}NO_3$ $(M+H)^+$: 368.1281, found: 368.1275.

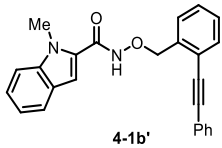


4-1a'

Following **General Procedure A**, **4-1a'** was obtained as a yellow solid (42%, three steps). Melting point 127-129°C.

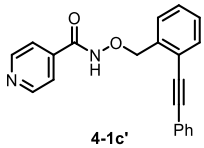
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (1 H, s), 7.75 (3 H, dd, J = 23.0, 7.8 Hz), 7.55 (2 H, dd, J = 9.9, 6.4 Hz), 7.47 (2 H, d, J = 6.6 Hz), 7.36 (4 H, dd, J = 13.5, 6.7 Hz), 7.29 -7.24 (3 H, m), 5.31 (2 H, s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 161.8, 156.4, 141.0, 138.6, 136.6, 134.5, 132.1, 131.5, 129.8, 128.4, 128.3, 128.2, 126.3, 125.1, 124.6, 123.3, 122.6, 122.3, 94.0, 86.8, 69.9.
HRMS (ESI, m/z) calcd for $C_{24}H_{18}NO_2S$ (M+H) $^+$: 384.1053, found: 384.1042.



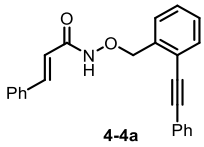
4-1b'

Following **General Procedure A**, **4-1b'** was obtained as a yellow solid (45%, three steps). Melting point 99-101°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (1 H, s), 7.59-7.46 (5 H, m), 7.37-7.33 (2 H, m), 7.31-7.25 (5 H, m), 7.10 (1 H, m), 6.69 (1 H, s), 5.31 (2 H, s), 3.91 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 139.1, 136.8, 132.4, 131.6, 130.1, 128.7, 128.6, 128.5, 128.5, 128.3, 125.9, 124.4, 123.8, 122.8, 122.0, 120.6, 110.1, 104.7, 94.0, 86.9, 77.3, 31.3.
HRMS (ESI, m/z) calcd for $C_{25}H_{21}N_2O_2$ (M+H) $^+$: 381.1598, found: 381.1601.



4-1c'

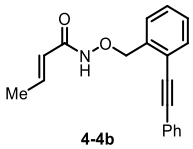
Following **General Procedure A**, **4-1c'** was obtained as a yellow solid (29%, three steps). Melting point 127-129°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (1 H, s), 7.59-7.36 (7 H, m), 7.34-7.25 (6 H, m), 5.30 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.8, 132.3, 132.1, 132.0, 131.9, 131.5, 130.2, 128.6, 128.5, 128.4, 123.8, 122.7, 94.0, 86.9, 76.2.
HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_2O_2$ (M+H) $^+$: 329.1285, found: 329.1291.



4-4a

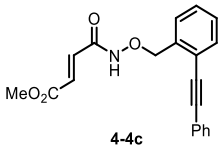
Following **General Procedure A**, **4-4a** was obtained as a yellow solid (33%, three steps). Melting point 82-84°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (1 H, d, J = 15.8 Hz), 7.49 (4 H, d, J = 2.9 Hz), 7.36 (2 H, s), 7.24 (9 H, d, J = 2.7 Hz), 5.23 (2 H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 156.5, 134.5, 132.1, 131.5, 129.6, 128.5, 128.4, 128.2, 127.8, 122.6, 94.0, 86.7, 69.7.
HRMS (ESI, m/z) calcd for $C_{24}H_{20}NO_2$ (M+H) $^{+}$: 354.1489, found: 354.1490.



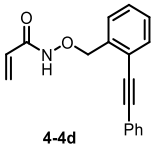
4-4b

Following **General Procedure A**, **4-4b** was obtained as a yellow solid (31%, three steps). Melting point 109-111°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (1 H, s), 7.60-7.51 (3 H, m), 7.48 (1 H, d, J = 4.4 Hz), 7.40-7.30 (5 H, m), 6.91 (1 H, dd, J = 14.4, 6.9 Hz), 5.18 (2 H, s), 1.76 (3 H, dd, J = 6.9, 1.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 132.4, 131.6, 129.9, 128.7, 128.5, 128.3, 123.7, 122.8, 94.0, 86.8, 77.2, 18.0.
HRMS (ESI, m/z) calcd for $C_{19}H_{18}NO_2$ (M+H) $^{+}$: 292.1332, found: 292.1326.



4-4c

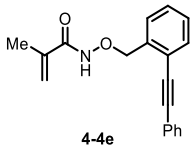
Following **General Procedure A**, **4-4c** was obtained as a yellow solid (27%, three steps). Melting point 87-89°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.42 (4 H, m), 7.30 (5 H, s), 6.79 (2 H, dd, J = 37.2, 14.2 Hz), 5.24 (2 H, s), 3.64 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9, 161.6, 136.6, 133.2, 132.1, 131.5, 130.2, 129.8, 128.4, 128.2, 123.4, 122.7, 94.0, 86.7, 76.0, 52.0.
HRMS (ESI, m/z) calcd for $C_{20}H_{18}NO_4$ (M+H) $^{+}$: 336.1230, found: 336.1236.



4-4d

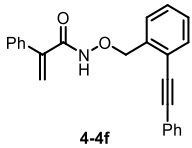
Following **General Procedure A**, **4-4d** was obtained as a yellow solid (37%, three steps). Melting point 81-83°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (1 H, s), 7.59-7.47 (4 H, m), 7.35 (5 H, dd, J = 6.3, 3.0 Hz), 6.34 (1 H, d, J = 17.1 Hz), 5.96 (1 H, s), 5.62 (1 H, d, J = 11.6 Hz), 5.20 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 136.8, 132.3, 131.6, 129.8, 128.5, 128.3, 127.0, 123.5, 122.8, 94.0, 86.7, 76.2.
HRMS (ESI, m/z) calcd for $C_{18}H_{16}NO_2$ (M+H) $^+$: 278.1176, found: 278.1181.



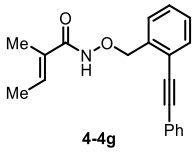
4-4e

Following **General Procedure A**, **4-4e** was obtained as a yellow oil (35%, three steps).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (1 H, s), 7.58-7.51 (4 H, m), 7.37-7.32 (5 H, m), 5.56 (1 H, s), 5.28-5.25 (1 H, m), 5.23 (2 H, s), 1.87 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 137.7, 136.8, 132.3, 131.6, 130.0, 128.6, 128.5, 128.3, 123.7, 122.8, 120.4, 93.9, 86.8, 76.1, 18.4.
HRMS (ESI, m/z) calcd for $C_{19}H_{18}NO_2$ (M+H) $^+$: 292.1332, found: 292.1327.



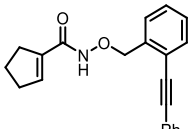
4-4f

Following **General Procedure A**, **4-4f** was obtained as a yellow solid (41%, three steps). Melting point 88-90°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (1 H, d, J = 10.5 Hz), 7.59-7.49 (4 H, m), 7.35-7.26 (10 H, m), 5.98 (1 H, s), 5.59 (1 H, s), 5.27 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 142.1, 136.7, 135.8, 132.3, 131.6, 130.0, 128.7, 128.6, 128.6, 128.5, 128.3, 127.6, 123.7, 122.8, 122.2, 94.1, 86.8, 76.2.
HRMS (ESI, m/z) calcd for $C_{24}H_{20}NO_2$ (M+H) $^+$: 354.1489, found: 354.1490.



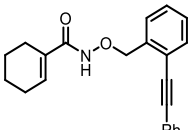
4-4g

Following **General Procedure A**, **4-4g** was obtained as a yellow oil (39%, three steps).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.49 (4 H, m), 7.39-7.31 (5 H, m), 6.29 (1 H, qd, J = 6.9, 1.3 Hz), 5.22 (2 H, s), 1.74 (3 H, s), 1.64 (3 H, dd, J = 6.9, 0.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 132.2, 131.6, 129.9, 128.5, 128.5, 128.3, 123.5, 122.8, 93.9, 86.9, 76.0, 13.7, 12.0.
HRMS (ESI, m/z) calcd for $C_{20}H_{20}NO_2$ $(M+H)^+$: 306.1489, found: 306.1489.



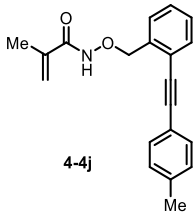
4-4h

Following **General Procedure A**, **4-4h** was obtained as a yellow solid (36%, three steps). Melting point 83-85°C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (1 H, s), 7.60 (1 H, dd, J = 7.1, 1.8 Hz), 7.57-7.53 (3 H, m), 7.39-7.35 (5 H, m), 6.50 (1 H, s), 5.25 (2 H, s), 2.48-2.42 (2 H, m), 2.41-2.36 (2 H, m), 1.92-1.86 (2 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 139.7, 137.0, 136.1, 132.3, 131.6, 130.0, 128.6, 128.5, 128.5, 128.3, 123.6, 122.8, 93.9, 86.9, 76.4, 33.0, 31.2, 23.0.
HRMS (ESI, m/z) calcd for $C_{21}H_{20}NO_2$ $(M+H)^+$: 318.1489, found: 318.1487.



4-4i

Following **General Procedure A**, **4-4i** was obtained as a yellow solid (42%, three steps). Melting point 91-93°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (1 H, s), 7.58-7.48 (4 H, m), 7.37-7.30 (5 H, m), 6.53-6.44 (1 H, m), 5.20 (2 H, s), 2.11 (2 H, d, J = 1.4 Hz), 2.01 (2 H, d, J = 2.8 Hz), 1.52 (4 H, m).
^{13}C NMR (101 MHz, CDCl3) δ 167.3, 137.1, 134.5, 132.1, 131.5, 130.9, 129.7, 128.4, 128.3, 128.2, 123.3, 122.8, 93.8, 86.8, 76.0, 25.1, 23.7, 21.7, 21.2.
HRMS (ESI, m/z) calcd for $C_{22}H_{22}NO_2$ $(M+H)^+$: 332.1645, found: 332.1640.

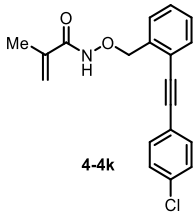


Following **General Procedure A**, **4-4j** was obtained as a yellow oil (36%, three steps).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (1 H, s), 7.52-7.47 (2 H, m), 7.40 (2 H, d, J = 8.1 Hz), 7.29-7.24 (2 H, m), 7.09 (2 H, d, J = 7.9 Hz), 5.58 (1 H, s), 5.22-5.19 (1 H, m), 5.18 (2 H, s), 2.30 (3 H, s), 1.82 (3 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 138.3, 137.3, 136.7, 131.8, 131.2, 129.4, 128.8, 128.1, 128.0, 123.1, 120.3, 119.6, 93.9, 86.0, 75.7, 21.2, 18.1.

HRMS (ESI, m/z) calcd for $C_{20}H_{20}NO_2$ $(M+H)^+$: 306.1489, found: 306.1489.

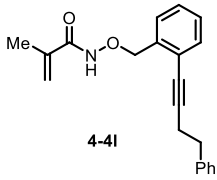


Following **General Procedure A**, **4-4k** was obtained as a yellow oil (32%, three steps).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (1 H, s), 7.55-7.48 (2 H, m), 7.46-7.42 (2 H, m), 7.34-7.30 (2 H, m), 7.29-7.26 (2 H, m), 5.57 (1 H, s), 5.24 (1 H, d, J = 1.2 Hz), 5.18 (2 H, s), 1.84 (3 H, s).

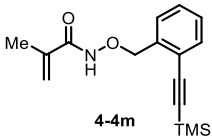
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 137.5, 136.9, 134.3, 132.7, 132.1, 129.8, 128.6, 128.5, 128.4, 123.1, 121.2, 120.4, 92.6, 87.7, 75.7, 18.2.

HRMS (ESI, m/z) calcd for $C_{19}H_{17}ClNO_2$ $(M+H)^+$: 326.0942, found: 326.0943.



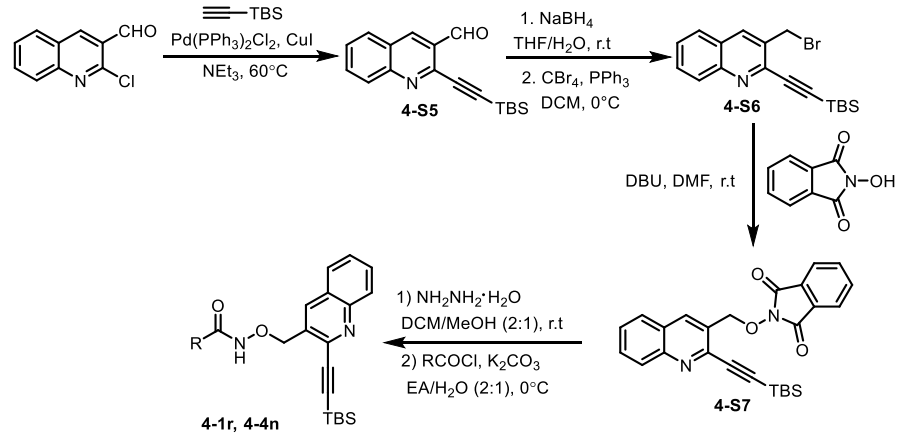
Following **General Procedure B**, **4-4l** was obtained as a yellow oil (29%, three steps).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (1 H, s), 7.45-7.43 (1 H, m), 7.37 (1 H, dd, J = 7.4, 1.5 Hz), 7.28 (2 H, t, J = 7.5 Hz), 7.24-7.22 (3 H, m), 7.21-7.17 (2 H, m), 5.56 (1 H, s), 5.25-5.23 (1 H, m), 5.02 (2 H, s), 2.88 (2 H, t, J = 7.4 Hz), 2.69 (2 H, t, J = 7.4 Hz), 1.86 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.7, 140.4, 137.5, 136.7, 132.0, 129.3, 128.3, 128.2, 128.1, 127.7, 126.1, 123.7, 120.2, 94.1, 78.7, 75.7, 34.7, 21.4, 18.2.
HRMS (ESI, m/z) calcd for $C_{21}H_{22}NO_2$ $(M+H)^+$: 320.1645, found: 320.1651.



4-4m

Following **General Procedure A**, **4-4m** was obtained as a yellow solid (33%, three steps). Melting point 76-78°C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (2 H, dt, J = 14.8, 7.4 Hz), 7.36 (1 H, dd, J = 7.5, 6.6 Hz), 7.33-7.29 (1 H, m), 5.61 (1 H, s), 5.33 (1 H, s), 5.17 (2 H, s), 1.93 (3 H, s), 0.27 (9 H, d, J = 0.5 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 137.3, 132.6, 129.7, 128.7, 128.4, 123.4, 120.2, 102.4, 99.3, 76.0, 18.4, -0.1.
HRMS (ESI, m/z) calcd for $C_{16}H_{22}NO_2Si$ $(M+H)^+$: 288.1414, found: 288.1414.



To a 100 mL round-bottom flask,[16] under N_2, was added 2-chloro-3-quinolinecarboxaldehyde (5.0 mmol), $PdCl_2(PPh_3)_2$ (0.25 mmol), CuI (0.25 mmol) and anhydrous TEA (20 mL). The mixture was stirred at room temperature for 1 min and then (tert-butyldimethylsilyl)acetylene (6.0 mmol) was added. The flask was placed in a preheated oil bath

(60°C). The reaction was stirred overnight and then cooled to room temperature and checked by TLC. The reaction was filtered over celite, washing with dichloromethane. The solvent was removed and the residue purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to afford **4-S5**.

A solution of **4-S5** (4.0 mmol) in THF (10 mL) and water (1 mL) was cooled to 0°C, $NaBH_4$ (4.8 mmol) was then added.[16] After stirring for a further period of 1 h, the reaction was completed as indicated by TLC. The reaction mixture was extracted twice with DCM. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure, affording the crude product, which was used in next step without further purification.

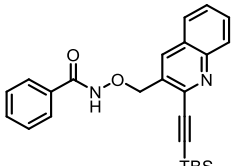
To a stirring solution of CBr_4 (7.2 mmol) in DCM (12 mL), a solution of crude product from the previous step in DCM was added to the resulting mixture at 0°C.[70] After stirring for another 5 minutes, a solution of PPh_3 (8.0 mmol) in DCM was added dropwise at 0°C. The reaction media was then stirred at 0°C for 1 h (judging by TLC analysis). The solution was concentrated in *vacuo*. The obtained crude product was purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to give the desired product **4-S6**.

To a stirred mixture of *N*-hydroxyphthalimide (3.0 mmol) and **4-S6** (3.3 mmol) in DMF (6 mL) was added DBU (3.6 mmol) slowly at ambient temperature.[71] After completion of the addition, water (20 mL) was added, and the precipitate was filtered off and washed with water to afford **4-S7**, which was used in next step without further purification.

In a 100 mL round-bottom flask was charged **4-S7** (3.0 mmol),[16] solvent 15 mL [MeOH/DCM (1:2)], and then slowly added hydrazine monohydrate (3.3 mmol), then stirred at room temperature for 4h. Upon completion (indicated by TLC), the solvent was then removed under reduce pressure. The residue was washed with DCM and filtered, collected the DCM part and removed the solvent to give the crude *O*-alkoxylamine, which was used in next step without further purification.

The crude *O*-alkoxylamine which was obtained in the previous step was added to a biphasic mixture of K_2CO_3 (3.6 mmol) in solvent 15 mL [EA/H_2O (2:1)].[16] The resulting solution was cooled to 0°C followed by dropwise addition of the acid chloride (3.3 mmol) dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at same temperature for 6h. Upon completion (indicated by TLC), the phases

were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to give the product **4-1r**, **4-4n**.



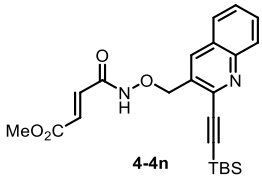
4-1r

4-1r was obtained as a yellow solid (72%, last two steps). Melting point 192-194°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (1 H, s), 8.31 (1 H, s), 8.08 (1 H, d, J = 8.5 Hz), 7.77 (1 H, d, J = 8.1 Hz), 7.71 (3 H, m), 7.57-7.47 (2 H, m), 7.42-7.36 (2 H, m), 5.41 (2 H, s), 1.02 (9H, s), 0.22 (6 H, s).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8, 147.7, 142.8, 136.8, 132.2, 131.7, 130.4, 130.1, 129.0, 128.7, 127.7, 127.6, 127.0, 102.4, 98.8, 75.3, 26.2, 16.7, -4.8.

HRMS (ESI, m/z) calcd for $C_{25}H_{29}N_2O_2Si$ $(M+H)^+$: 417.1993, found: 417.1995.



4-4n

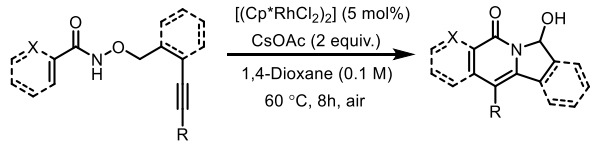
4-4n was obtained as a yellow oil (79%, last two steps).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (1 H, s), 8.04 (1 H, d, J = 8.3 Hz), 7.69 (2 H, dd, J = 13.2, 5.0 Hz), 7.51 (1 H, t, J = 7.4 Hz), 6.89 (1 H, d, J = 16.5 Hz), 6.72 (1 H, d, J = 15.5 Hz), 5.36 (2 H, s), 3.76 (3 H, s), 1.02 (9 H, s), 0.23 (6 H, s).

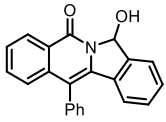
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 158.4, 147.5, 142.6, 136.4, 133.2, 130.4, 128.9, 127.6, 127.6, 126.9, 102.1, 99.2, 74.4, 52.1, 26.1, 16.7, -4.8.

HRMS (ESI, m/z) calcd for $C_{23}H_{29}N_2O_4Si$ $(M+H)^+$: 425.1891, found: 425.1891.

Rhodium(III)-catalyzed intramolecular annulations

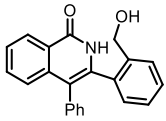


To a Schlenk flask equipped with a stir bar were added **4-1** or **4-4** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under air. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3** or **4-5**.



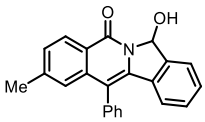
4-3a

4-3a was obtained as a yellow solid (52%). Melting point 193-195°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50-8.40 (1 H, m), 7.68-7.63 (1 H, m), 7.62-7.54 (4 H, m), 7.52-7.45 (1 H, m), 7.43-7.35 (3 H, m), 7.22-7.12 (2 H, m), 7.03 (1 H, s), 6.39 (1 H, d, J = 7.9 Hz), 5.72 (1 H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 139.1, 138.9, 136.1, 134.6, 133.2, 132.6, 130.8, 129.8, 129.7, 129.5, 129.4, 128.5, 126.7, 125.6, 125.0, 124.3, 123.8, 115.2, 84.1.
HRMS (ESI, m/z) calcd for $C_{22}H_{16}NO_2$ $(M+H)^+$: 326.1176, found: 326.1183.



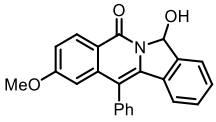
4-2a

4-2a was obtained as a yellow solid (78%). Melting point 213-215°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (1 H, s), 8.26 (1 H, d, J = 7.9 Hz), 7.63-7.53 (2 H, m), 7.46 (1 H, t, J = 7.4 Hz), 7.35-7.18 (6 H, m), 7.08-6.99 (2 H, m), 6.91 (1 H, s), 4.61 (3 H, d, J = 56.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 139.8, 138.5, 136.9, 135.4, 133.3, 132.8, 131.2, 129.8, 129.3, 127.3, 127.2, 127.2, 126.7, 125.5, 124.7, 119.2, 62.5.
HRMS (ESI, m/z) calcd for $C_{22}H_{18}NO_2$ $(M+H)^+$: 328.1332, found: 328.1340.



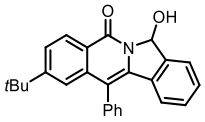
4-3b

4-3b was obtained as a yellow solid (56%). Melting point 218-220°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (1 H, d, J = 8.1 Hz), 7.68-7.55 (4 H, m), 7.42-7.31 (4 H, m), 7.14 (1 H, dd, J = 11.4, 4.0 Hz), 7.01 (1 H, s), 6.96 (1 H, s), 6.34 (1 H, d, J = 7.9 Hz), 5.58 (1 H, s), 2.37 (3 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 143.3, 139.3, 138.8, 134.8, 133.3, 130.8, 129.8, 129.6, 129.5, 129.4, 128.5, 128.4, 127.2, 125.4, 124.3, 123.8, 122.8, 115.2, 84.0, 22.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1335.



4-3c

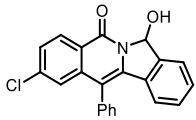
4-3c was obtained as a yellow solid (49%). Melting point 168-170°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1 H, d, J = 8.9 Hz), 7.64 (1 H, d, J = 7.6 Hz), 7.62-7.54 (3 H, m), 7.43-7.34 (3 H, m), 7.14 (1 H, t, J = 7.7 Hz), 7.06 (1 H, dd, J = 8.9, 2.5 Hz), 7.00 (1 H, s), 6.55 (1 H, d, J = 2.4 Hz), 6.36 (1 H, d, J = 7.9 Hz), 5.69 (1 H, s), 3.72 (3 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 161.6, 141.4, 139.1, 136.7, 134.7, 133.2, 130.8, 129.7, 129.5, 129.4, 129.3, 128.6, 124.3, 123.8, 118.9, 115.2, 114.9, 107.7, 84.0, 55.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1295.



4-3d

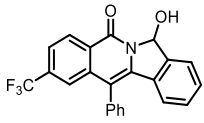
4-3d was obtained as a yellow solid (49%). Melting point 221-223°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (1 H, d, J = 8.5 Hz), 7.67-7.54 (5 H, m), 7.45-7.33 (3 H, m), 7.19-7.11 (2 H, m), 7.02 (1 H, s), 6.39 (1 H, d, J = 7.9 Hz), 5.66 (1 H, s), 1.24 (9 H, s). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.8, 156.1, 139.1, 138.9, 136.0, 134.8, 133.4, 130.8, 129.7, 129.5, 129.3, 128.5, 126.9, 124.9, 124.3, 123.7, 122.8, 121.6, 115.6, 84.0, 35.2, 30.9.

HRMS (ESI, m/z) calcd for $C_{26}H_{24}NO_2$ $(M+H)^+$: 382.1802, found: 382.1806.



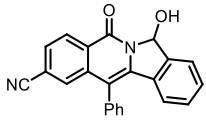
4-3e

4-3e was obtained as a yellow solid (67%). Melting point 189-191°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1 H, d, J = 8.5 Hz), 7.66 (1 H, d, J = 7.6 Hz), 7.63-7.57 (3 H, m), 7.44-7.34 (4 H, m), 7.16 (2 H, dd, J = 7.5, 4.8 Hz), 7.01 (1 H, s), 6.36 (1 H, d, J = 7.9 Hz), 5.56 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 140.6, 139.4, 139.0, 133.9, 132.9, 130.8, 130.8, 130.1, 129.9, 129.7, 129.6, 129.0, 128.9, 127.2, 124.9, 124.4, 124.0, 114.3, 84.2.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}ClNO_2$ $(M+H)^+$: 360.0786, found: 360.0802.



4-3f

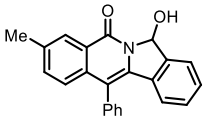
4-3f was obtained as a yellow solid (50%). Melting point 193-195°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1 H, d, J = 8.3 Hz), 7.68-7.61 (4 H, m), 7.44 (1 H, s), 7.41 (1 H, dd, J = 5.0, 2.3 Hz), 7.35 (2 H, m), 7.29 (1 H, s), 7.20-7.15 (1 H, m), 7.04 (1 H, d, J = 2.7 Hz), 6.38 (1 H, d, J = 7.9 Hz), 5.83 (1 H, d, J = 2.8 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 139.3, 139.0, 137.6, 134.3 (q, J = 32.5 Hz), 133.6, 132.7, 130.7 (d, J = 7.1 Hz), 130.3, 130.0, 129.8 (d, J = 8.0 Hz), 129.1, 128.4, 127.0, 124.5, 124.1, 122.8-122.5 (m), 114.9, 84.3.
^{19}F NMR (377 MHz, $CDCl_3$) δ -63.01.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO_2$ $(M+H)^+$: 394.1049, found: 394.1050.



4-3g

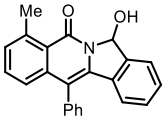
4-3g was obtained as a yellow solid (59%). Melting point 201-203°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (1 H, d, J = 8.2 Hz), 7.70-7.61 (5 H, m), 7.52 (1 H, d, J = 1.3 Hz), 7.47-7.34 (3 H, m), 7.19 (1 H, t, J = 7.4 Hz), 7.03 (1 H, s), 6.42 (1 H, d, J = 7.9 Hz), 5.53 (1 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 139.4, 139.0, 138.1, 133.2, 132.5, 130.7, 130.7, 130.5, 130.3, 130.1, 129.9, 129.3, 128.3, 127.3, 124.5, 124.2, 118.2, 116.2, 114.0, 84.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}N_2O_2$ $(M+H)^+$: 351.1128, found: 351.1142.



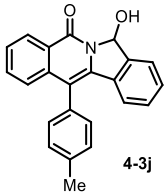
4-3h

4-3h was obtained as a yellow solid (61%). Melting point 190-192°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (1 H, s), 7.64 (1 H, d, J = 7.5 Hz), 7.59-7.54 (3 H, m), 7.41-7.34 (4 H, m), 7.12 (2 H, dd, J = 15.3, 8.1 Hz), 7.02 (1 H, s), 6.37 (1 H, d, J = 7.9 Hz), 5.75 (1 H, s), 2.48 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 138.8, 137.0, 136.8, 135.2, 134.8, 134.0, 133.3, 130.8, 130.8, 129.7, 129.4, 129.3, 128.4, 126.8, 125.5, 124.3, 123.6, 115.2, 84.0, 21.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1339.



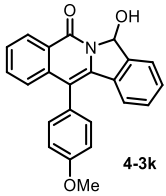
4-3i

4-3i was obtained as a yellow solid (52%). Melting point 209-211°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1 H, d, J = 7.6 Hz), 7.60-7.54 (3 H, m), 7.41-7.32 (4 H, m), 7.19-7.10 (2 H, m), 7.03 (1 H, d, J = 8.1 Hz), 6.97 (1 H, d, J = 3.0 Hz), 6.30 (1 H, d, J = 7.9 Hz), 5.51 (1 H, d, J = 3.1 Hz), 3.02 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 141.8, 140.9, 138.9, 135.3, 133.1, 131.7, 130.9, 130.9, 130.0, 129.7, 129.6, 129.5, 129.4, 128.4, 124.2, 124.0, 123.7, 115.2, 84.3, 23.7.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1332.



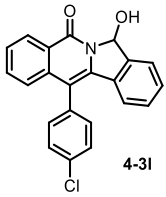
4-3j

4-3j was obtained as a yellow solid (62%). Melting point 197-199°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1 H, dd, J = 7.9, 0.8 Hz), 7.65 (1 H, d, J = 7.6 Hz), 7.59-7.54 (1 H, m), 7.52-7.46 (1 H, m), 7.42-7.35 (3 H, m), 7.29 (1 H, dd, J = 6.2, 3.3 Hz), 7.24 (2 H, dd, J = 8.3, 5.8 Hz), 7.17 (1 H, t, J = 7.6 Hz), 7.03 (1 H, d, J = 2.7 Hz), 6.47 (1 H, d, J = 7.9 Hz), 5.60 (1 H, dd, J = 12.1, 5.3 Hz), 2.52 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 139.4, 138.8, 138.3, 136.1, 133.4, 132.5, 131.5, 130.7, 130.2, 129.8, 129.6, 127.2, 126.7, 125.7, 125.1, 124.3, 123.9, 115.3, 84.1, 21.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1339.



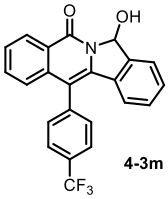
4-3k

4-3k was obtained as a yellow solid (67%). Melting point 198-200°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (1 H, dd, J = 7.8, 1.1 Hz), 7.65 (1 H, d, J = 7.4 Hz), 7.62-7.45 (2 H, m), 7.38 (1 H, td, J = 7.5, 0.8 Hz), 7.35-7.25 (3 H, m), 7.24-7.18 (1 H, m), 7.17-7.09 (2 H, m), 7.02 (1 H, d, J = 3.1 Hz), 6.50 (1 H, d, J = 7.9 Hz), 5.58 (1 H, d, J = 3.2 Hz), 3.95 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 159.7, 139.5, 138.8, 136.3, 133.4, 132.5, 131.9, 129.8, 129.6, 127.2, 126.7, 126.6, 125.6, 125.0, 124.3, 123.9, 114.9, 114.8, 84.1, 55.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1297.



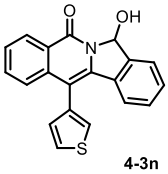
4-3l

4-3l was obtained as a yellow solid (66%). Melting point 219-221°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.43 (1 H, m), 7.67 (1 H, d, J = 7.6 Hz), 7.58 (3 H, m), 7.49 (1 H, dd, J = 11.1, 3.9 Hz), 7.42-7.31 (3 H, m), 7.23-7.14 (2 H, m), 7.02 (1 H, d, J = 3.1 Hz), 6.47 (1 H, d, J = 7.9 Hz), 5.76 (1 H, d, J = 3.3 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 139.0, 138.9, 136.3, 134.7, 133.2, 132.9, 132.7, 132.3, 129.9, 129.8, 129.8, 127.3, 126.9, 125.2, 125.1, 124.5, 123.6, 113.8, 84.1.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}ClNO_2$ $(M+H)^+$: 360.0786, found: 360.0795.



4-3m

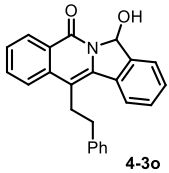
4-3m was obtained as a yellow solid (69%). Melting point 189-191°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (1 H, dd, J = 7.9, 1.3 Hz), 7.93-7.83 (2 H, m), 7.68 (1 H, d, J = 7.6 Hz), 7.63-7.49 (4 H, m), 7.42 (1 H, td, J = 7.5, 0.8 Hz), 7.20 (1 H, t, J = 7.7 Hz), 7.10 (1 H, d, J = 7.8 Hz), 7.04 (1 H, d, J = 3.1 Hz), 6.37 (1 H, d, J = 7.9 Hz), 5.58 (1 H, d, J = 3.3 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 139.1, 138.8, 138.6, 136.3, 132.8 (d, J = 7.0 Hz), 131.6 (d, J = 6.7 Hz), 130.1 (d, J = 12.3 Hz), 127.4, 127.1, 126.6-126.4 (m), 125.1 (d, J = 7.5 Hz), 124.6, 123.5, 113.6, 84.2.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.44.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO_2$ $(M+H)^+$: 394.1049, found: 394.1059.



4-3n

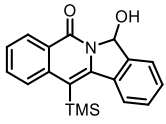
4-3n was obtained as a yellow solid (51%). Melting point 202-204°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1 H, d, J = 7.3 Hz), 7.67-7.59 (3 H, m), 7.50 (1 H, dd, J = 11.0, 4.0 Hz), 7.39 (2 H, m), 7.30 (1 H, d, J = 8.1 Hz), 7.26-7.22 (1 H, m), 7.16-7.08 (1 H, m), 7.00 (1 H, d, J = 2.5 Hz), 6.54 (1 H, dd, J = 7.9, 3.0 Hz), 5.39 (1 H, d, J = 8.8 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 139.3, 138.8, 136.8, 134.3, 133.2, 132.7, 130.0, 129.9, 129.7, 129.5, 127.2, 126.8, 125.6, 125.5, 125.0, 124.3, 123.7, 109.8, 84.2.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_2S$ (M+H) $^+$: 332.0740, found: 332.0749.



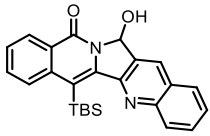
4-3o

4-3o was obtained as a yellow solid (69%). Melting point 211-213°C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (1 H, d, J = 7.9 Hz), 7.96 (1 H, d, J = 7.8 Hz), 7.89 (1 H, d, J = 8.2 Hz), 7.78 (2 H, dd, J = 9.0, 7.9 Hz), 7.57 (3 H, m), 7.40-7.39 (3 H, m), 7.33-7.27 (2 H, m), 7.00 (1 H, d, J = 2.3 Hz), 5.46 (1 H, d, J = 2.9 Hz), 3.53-3.46 (2 H, m), 3.05 (2 H, t, J = 8.6 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.8, 141.0, 139.0, 138.2, 136.1, 133.5, 132.9, 130.5, 129.6, 128.8, 128.2, 127.7, 126.8, 126.5, 125.5, 124.9, 123.7, 123.1, 113.3, 83.9, 35.2, 27.8.
HRMS (ESI, m/z) calcd for $C_{24}H_{20}NO_2$ (M+H) $^+$: 354.1489, found: 354.1487.



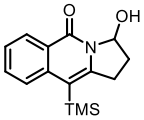
4-3p

4-3p was obtained as a yellow solid (71%). Melting point 134-136°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1 H, dd, J = 8.0, 1.2 Hz), 7.86 (2 H, dd, J = 8.5, 2.5 Hz), 7.72-7.67 (1 H, m), 7.66-7.60 (1 H, m), 7.52-7.44 (3 H, m), 6.95 (1 H, d, J = 3.0 Hz), 5.64 (1 H, d, J = 2.9 Hz), 0.55 (9 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 146.1, 142.2, 139.9, 134.2, 131.5, 130.0, 128.9, 128.5, 127.1, 126.2, 126.2, 125.2, 124.4, 110.1, 83.9, 3.2.
HRMS (ESI, m/z) calcd for $C_{19}H_{20}NO_2Si$ (M+H) $^+$: 322.1258, found: 322.1266.



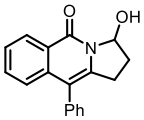
4-3r

4-3r was obtained as a yellow solid (46%). Melting point 125-127°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (1 H, dd, J = 8.0, 1.4 Hz), 8.43 (1 H, s), 8.25 (1 H, d, J = 8.5 Hz), 8.12 (1 H, d, J = 8.3 Hz), 7.93 (1 H, d, J = 7.4 Hz), 7.81 (1 H, m), 7.75-7.67 (1 H, m), 7.65-7.52 (2 H, m), 7.15 (1 H, d, J = 2.3 Hz), 5.75 (1 H, d, J = 3.0 Hz), 1.33 (9 H, s), 0.53 (6 H, d, J = 3.3 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 153.1, 148.7, 144.2, 142.3, 131.8, 131.5, 130.7, 130.5, 130.4, 129.2, 128.5, 127.5, 127.5, 127.2, 127.0, 126.3, 113.4, 81.9, 29.3, 19.3, 2.7, 2.6.
HRMS (ESI, m/z) calcd for $C_{25}H_{27}N_2O_2Si$ $(M+H)^+$: 415.1836, found: 415.1835.



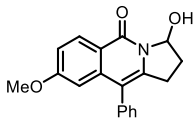
4-3s

4-3s was obtained as a yellow solid (31%). Melting point 135-137°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (1 H, dd, J = 8.0, 1.3 Hz), 7.81 (1 H, d, J = 8.2 Hz), 7.62 (1 H, m), 7.43 (1 H, dd, J = 11.1, 4.0 Hz), 6.30 (1 H, dt, J = 6.5, 2.6 Hz), 5.02 (1 H, d, J = 1.9 Hz), 3.44-3.29 (1 H, m), 3.10 (1 H, m), 2.36 (1 H, dt, J = 15.2, 8.5 Hz), 2.16 (1 H, m), 0.45 (9 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.6, 147.9, 141.7, 131.9, 127.6, 126.8, 125.4, 125.1, 106.4, 83.8, 30.7, 29.0, 2.4.
HRMS (ESI, m/z) calcd for $C_{15}H_{20}NO_2Si$ $(M+H)^+$: 274.1258, found: 274.1264.



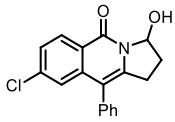
4-3t

4-3t was obtained as a yellow solid (34%). Melting point 149-151°C.
^{1}H NMR (300 MHz, CDCl3) δ 8.46 (1 H, dd, J = 8.0, 1.0 Hz), 7.59-7.52 (1 H, m), 7.51-7.41 (4 H, m), 7.36-7.26 (3 H, m), 6.42 (1 H, d, J = 4.2 Hz), 5.19 (1 H, s), 3.25-3.07 (1 H, m), 2.79 (1 H, m), 2.38 (1 H, m), 2.15 (1 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 140.2, 138.7, 135.8, 132.4, 130.6, 128.9, 127.7, 127.3, 125.8, 124.9, 124.5, 114.1, 84.9, 29.3, 27.9.
HRMS (ESI, m/z) calcd for $C_{18}H_{16}NO_2$ $(M+H)^+$: 278.1176, found: 278.1185.



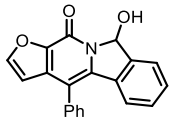
4-3u

4-3u was obtained as a yellow solid (37%). Melting point 170-172°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (1 H, d, J = 8.9 Hz), 7.52-7.40 (3 H, m), 7.31 (2 H, t, J = 8.2 Hz), 7.02 (1 H, dd, J = 8.9, 2.5 Hz), 6.63 (1 H, d, J = 2.5 Hz), 6.41-6.34 (1 H, m), 4.97 (1 H, s), 3.73 (3 H, s), 3.19-3.05 (1 H, m), 2.76 (1 H, m), 2.38 (1 H, dt, J = 16.0, 7.6 Hz), 2.17-2.07 (1 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 161.7, 140.9, 135.9, 130.6, 130.3, 129.3, 128.9, 127.7, 118.9, 114.7, 113.6, 106.3, 84.9, 55.3, 29.2, 27.9.
HRMS (ESI, m/z) calcd for $C_{19}H_{18}NO_3$ $(M+H)^+$: 308.1281, found: 308.1284.



4-3v

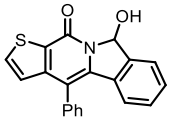
4-3v was obtained as a yellow solid (39%). Melting point 136-138°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (1 H, d, J = 8.6 Hz), 7.55-7.43 (3 H, m), 7.38 (1 H, dd, J = 8.6, 2.0 Hz), 7.32-7.26 (2 H, m), 7.23 (1 H, d, J = 1.9 Hz), 6.39 (1 H, d, J = 4.2 Hz), 5.10 (1 H, s), 3.23-3.07 (1 H, m), 2.78 (1 H, m), 2.38 (1 H, dt, J = 15.7, 8.1 Hz), 2.17-2.09 (1 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3, 141.8, 140.0, 139.2, 135.0, 130.5, 129.1, 128.9, 128.0, 126.4, 123.9, 123.3, 113.2, 85.0, 29.3, 28.1.
HRMS (ESI, m/z) calcd for $C_{18}H_{15}ClNO_2$ $(M+H)^+$: 312.0786, found: 312.0796.



4-3w

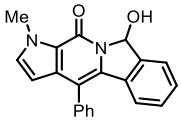
4-3w was obtained as a yellow solid (37%). Melting point 185-187°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (1 H, d, J = 2.0 Hz), 7.65 (1 H, d, J = 7.7 Hz), 7.59-7.51 (3 H, m), 7.50-7.42 (2 H, m), 7.38 (1 H, td, J = 7.5, 0.9 Hz), 7.22-7.13 (1 H, m), 6.99 (1 H, s), 6.83 (1 H, d, J = 7.9 Hz), 6.45 (1 H, d, J = 2.0 Hz), 5.50 (1 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 148.8, 141.8, 139.2, 137.0, 134.1, 132.8, 129.9, 129.9, 129.8, 129.5, 129.3, 128.7, 124.4, 123.1, 111.7, 107.4, 84.3.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_3$ $(M+H)^+$: 316.0968, found: 316.0981.



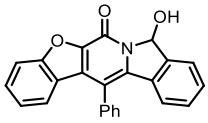
4-3x

4-3x was obtained as a yellow solid (51%). Melting point 204-206°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (2 H, d, J = 5.3 Hz), 7.56 (3 H, m), 7.48-7.35 (3 H, m), 7.16 (1 H, dd, J = 11.3, 4.0 Hz), 6.99 (1 H, s), 6.90 (1 H, d, J = 5.2 Hz), 6.64 (1 H, d, J = 7.9 Hz), 5.54 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 148.6, 138.9, 137.9, 134.9, 133.4, 133.0, 130.2, 129.8, 129.7, 129.3, 129.2, 128.6, 124.6, 124.4, 123.4, 114.2, 84.2.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_2S$ $(M+H)^+$: 332.0740, found: 332.0740.



4-3y

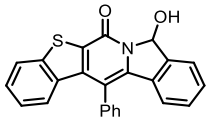
4-3y was obtained as a yellow solid (63%). Melting point 223-225°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (1 H, d, J = 7.6 Hz), 7.49 (5 H, m), 7.31 (1 H, t, J = 7.1 Hz), 7.14 (1 H, t, J = 7.7 Hz), 6.98 (1 H, d, J = 2.8 Hz), 6.95 (1 H, d, J = 2.2 Hz), 6.73 (1 H, d, J = 7.9 Hz), 6.01 (1 H, d, J = 2.8 Hz), 5.39 (1 H, d, J = 2.8 Hz), 4.22 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.5, 138.6, 135.2, 133.7, 133.0, 131.9, 130.1, 130.1, 129.6, 129.0, 128.5, 128.1, 124.2, 122.6, 121.8, 113.5, 102.7, 83.9, 35.8.
HRMS (ESI, m/z) calcd for $C_{21}H_{17}N_2O_2$ $(M+H)^+$: 329.1285, found: 329.1279.



4-3z

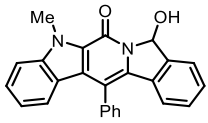
4-3z was obtained as a yellow solid (57%). Melting point 332-334°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.62 (5 H, m), 7.57-7.36 (4 H, m), 7.14 (2 H, m), 7.04 (1 H, s), 6.79 (1 H, d, J = 8.0 Hz), 6.64 (1 H, d, J = 7.9 Hz), 5.45 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 153.6, 142.6, 139.1, 137.4, 133.9, 132.9, 131.4, 130.1, 130.0, 129.7, 129.6, 129.1, 128.8, 124.5, 123.5, 123.3, 123.2, 122.9, 112.8, 112.2, 84.7.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_3$ $(M+H)^+$: 366.1125, found: 366.1131.



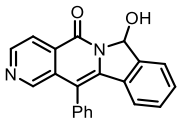
4-3a'

4-3a' was obtained as a yellow solid (45%). Melting point 259-261°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1 H, d, J = 8.1 Hz), 7.73-7.60 (4 H, m), 7.51 (2 H, m), 7.40 (2 H, m), 7.18-7.07 (2 H, m), 7.01 (1 H, s), 6.79 (1 H, d, J = 8.3 Hz), 6.32 (1 H, d, J = 7.9 Hz), 5.49 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 142.8, 142.1, 138.7, 135.7, 135.0, 133.2, 130.5, 130.4, 130.0, 129.9, 129.7, 129.2, 129.0, 127.5, 125.7, 124.5, 124.4, 123.6, 123.5, 115.0, 84.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_2S$ $(M+H)^+$: 382.0896, found: 382.0893.



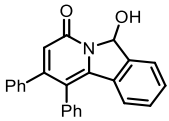
4-3b'

4-3b' was obtained as a yellow solid (46%). Melting point 264-266°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.59 (4 H, m), 7.58-7.47 (2 H, m), 7.47-7.40 (2 H, m), 7.31 (1 H, td, J = 7.5, 1.0 Hz), 7.14 (1 H, t, J = 7.2 Hz), 7.02 (1 H, d, J = 2.6 Hz), 6.95 (1 H, m), 6.76 (1 H, d, J = 8.1 Hz), 6.50 (1 H, d, J = 7.9 Hz), 5.45 (1 H, d, J = 3.0 Hz), 4.39 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 141.5, 138.3, 135.5, 133.8, 133.0, 130.2, 129.8, 129.5, 128.7, 128.4, 126.7, 126.6, 126.0, 124.2, 122.8, 122.5, 122.0, 120.2, 114.3, 110.0, 84.4, 31.4.
HRMS (ESI, m/z) calcd for $C_{25}H_{19}N_2O_2$ $(M+H)^+$: 379.1441, found: 379.1447.



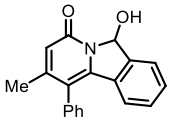
4-3c'

4-3c' was obtained as a yellow solid (39%). Melting point 246-248°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (1 H, d, J = 4.5 Hz), 8.43 (1 H, s), 8.17 (1 H, d, J = 5.1 Hz), 7.67 (2 H, dd, J = 6.1, 3.0 Hz), 7.63 (1 H, d, J = 7.6 Hz), 7.54 (1 H, dd, J = 6.7, 1.3 Hz), 7.50-7.43 (3 H, m), 7.26-7.21 (2 H, m), 6.88 (1 H, d, J = 7.5 Hz), 6.31 (1 H, d, J = 7.9 Hz). ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.7, 158.7, 148.1, 146.2, 141.1, 137.8, 134.3, 133.9, 133.0, 131.7, 130.7, 129.9, 129.8, 127.8, 123.0, 119.1, 113.6, 111.6, 83.4.
HRMS (ESI, m/z) calcd for $C_{21}H_{15}N_2O_2$ $(M+H)^+$: 327.1128, found: 327.1130.



4-5a

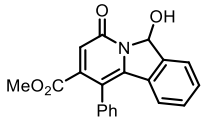
4-5a was obtained as a yellow solid (21%). Melting point 253-255°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (1 H, d, J = 7.6 Hz), 7.41 (1 H, t, J = 7.5 Hz), 7.35-7.30 (3 H, m), 7.21-7.12 (6 H, m), 7.07 (2 H, dd, J = 7.8, 1.6 Hz), 6.91 (1 H, s), 6.58 (1 H, s), 6.44 (1 H, d, J = 8.0 Hz), 5.56 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 156.5, 142.3, 139.4, 138.0, 134.8, 132.9, 131.0, 131.0, 130.3, 129.9, 128.7, 128.1, 127.9, 127.8, 124.3, 124.2, 118.7, 117.5, 84.6.
HRMS (ESI, m/z) calcd for $C_{24}H_{18}NO_2$ $(M+H)^+$: 352.1332, found: 352.1343.



4-5b

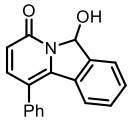
4-5b was obtained as a yellow solid (23%). Melting point 217-219°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (1 H, d, J = 7.6 Hz), 7.56-7.49 (3 H, m), 7.38 (1 H, td, J = 7.6, 0.8 Hz), 7.31-7.25 (2 H, m), 7.12 (1 H, t, J = 7.7 Hz), 6.84 (1 H, s), 6.46 (1 H, s), 6.28 (1 H, d, J = 7.9 Hz), 5.66 (1 H, s), 1.99 (3 H, d, J = 0.8 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 153.4, 141.4, 139.4, 135.2, 132.8, 130.1, 130.0, 129.8, 129.4, 128.4, 124.3, 123.8, 118.5, 117.9, 84.4, 20.8.
HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO_2$ $(M+H)^+$: 290.1176, found: 290.1178.



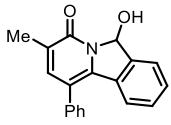
4-5c

4-5c was obtained as a yellow solid (29%). Melting point 129-131°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (1 H, d, J = 7.7 Hz), 7.52-7.47 (3 H, m), 7.43 (1 H, t, J = 7.5 Hz), 7.33 (2 H, dd, J = 9.2, 5.1 Hz), 7.17 (1 H, t, J = 7.7 Hz), 6.87 (1 H, s), 6.85 (1 H, s), 6.39 (1 H, d, J = 7.9 Hz), 3.60 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 161.6, 146.1, 143.5, 139.2, 134.3, 132.3, 130.7, 130.1, 130.0, 129.9, 128.9, 128.9, 128.6, 124.3, 119.0, 84.9, 52.5.
HRMS (ESI, m/z) calcd for $C_{20}H_{16}NO_4$ $(M+H)^+$: 334.1074, found: 334.1076.



4-5d

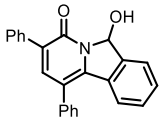
4-5d was obtained as a yellow solid (43%). Melting point 183-185°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (1 H, d, J = 7.6 Hz), 7.50 (3 H, tt, J = 8.4, 4.1 Hz), 7.43 (4 H, dd, J = 12.0, 5.0 Hz), 7.21 (1 H, t, J = 7.5 Hz), 6.94 (1 H, d, J = 7.9 Hz), 6.87 (1 H, s), 6.57 (1 H, d, J = 9.2 Hz), 5.68 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 144.6, 141.7, 139.1, 136.4, 132.5, 130.4, 129.8, 129.4, 129.0, 128.4, 124.4, 123.6, 118.6, 117.7, 84.9.
HRMS (ESI, m/z) calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 276.1019, found: 276.1020.



4-5e

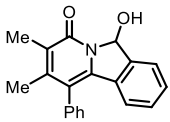
4-5e was obtained as a dark solid (41%). Melting point 185-187°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (1 H, d, J = 7.6 Hz), 7.52-7.45 (3 H, m), 7.44-7.36 (3 H, m), 7.29 (1 H, d, J = 1.0 Hz), 7.19 (1 H, t, J = 7.7 Hz), 6.94 (1 H, d, J = 7.9 Hz), 6.87 (1 H, s), 5.73 (1 H, s), 2.25 (3 H, d, J = 0.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 142.0, 139.2, 138.9, 136.7, 132.8, 129.9, 129.7, 129.4, 128.9, 128.2, 128.0, 124.3, 123.2, 117.4, 84.8, 16.0.
HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO_2$ $(M+H)^+$: 290.1176, found: 290.1178.



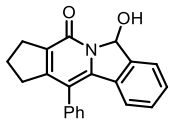
4-5f

4-5f was obtained as a yellow solid (39%). Melting point 116-118°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84-7.74 (2 H, m), 7.68 (1 H, d, J = 7.6 Hz), 7.61 (1 H, s), 7.53-7.32 (9 H, m), 7.22 (1 H, d, J = 7.2 Hz), 6.99 (1 H, d, J = 7.9 Hz), 6.93 (1 H, s), 5.67 (1 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 142.4, 140.7, 139.3, 136.5, 135.6, 132.5, 130.3, 129.9, 129.6, 129.5, 129.0, 128.6, 128.4, 128.3, 128.0, 124.4, 123.5, 117.8, 85.3.
HRMS (ESI, m/z) calcd for $C_{24}H_{18}NO_2$ $(M+H)^+$: 352.1332, found: 352.1346.



4-5g

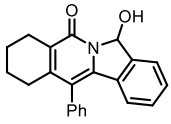
4-5g was obtained as a yellow solid (45%). Melting point 234-236°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (1 H, d, J = 7.4 Hz), 7.57-7.47 (3 H, m), 7.37-7.22 (3 H, m), 7.13-7.05 (1 H, m), 6.86 (1 H, d, J = 1.8 Hz), 6.19 (1 H, d, J = 7.9 Hz), 5.81 (1 H, d, J = 2.7 Hz), 2.23 (3 H, d, J = 0.5 Hz), 1.95 (3 H, d, J = 0.5 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 148.2, 138.9, 138.3, 136.2, 133.2, 130.2, 129.7, 129.5, 129.3, 128.3, 125.1, 124.2, 123.5, 118.7, 84.8, 17.6, 12.4.
HRMS (ESI, m/z) calcd for $C_{20}H_{18}NO_2$ $(M+H)^+$: 304.1332, found: 304.1331.



4-5h

4-5h was obtained as a yellow solid (39%). Melting point 201-203°C. ^{1}H NMR (300 MHz, CDCl3) δ 7.63 (1 H, d, J = 7.5 Hz), 7.54-7.45 (3 H, m), 7.39-7.28 (3 H, m), 7.15 (1 H, dd, J = 11.9, 4.2 Hz), 6.85 (1 H, d, J = 2.5 Hz), 6.57 (1 H, d, J = 7.9 Hz), 5.59 (1 H, d, J = 2.8 Hz), 2.96 (2 H, t, J = 7.5 Hz), 2.63 (2 H, t, J = 7.4 Hz), 2.07 (2 H, p, J = 7.8 Hz). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.5, 157.9, 140.7, 139.3, 135.3, 132.9, 130.9, 129.7, 129.6, 129.1, 129.1, 128.3, 124.3, 123.4, 116.0, 84.4, 33.5, 29.7, 23.5.

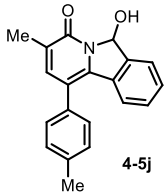
HRMS (ESI, m/z) calcd for $C_{21}H_{18}NO_2$ $(M+H)^+$: 316.1332, found: 316.1340.



4-5i

4-5i was obtained as a yellow solid (42%). Melting point 182-184°C. ^{1}H NMR (400 MHz, CDCl3) δ 7.61 (1 H, d, J = 7.6 Hz), 7.55-7.48 (3 H, m), 7.33 (1 H, t, J = 7.5 Hz), 7.30-7.27 (1 H, m), 7.24 (1 H, s), 7.09 (1 H, t, J = 7.7 Hz), 6.85 (1 H, s), 6.21 (1 H, d, J = 7.9 Hz), 5.78 (1 H, s), 2.68 (2 H, t, J = 5.9 Hz), 2.23 (2 H, t, J = 5.3 Hz), 1.75 (2 H, dt, J = 6.1, 4.3 Hz), 1.67 (2 H, dd, J = 12.0, 6.0 Hz). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 148.9, 138.8, 137.9, 135.4, 133.2, 130.1, 129.6, 129.4, 129.2, 128.2, 126.5, 124.2, 123.4, 118.1, 84.5, 28.3, 23.5, 22.1, 21.7.

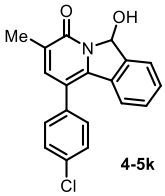
HRMS (ESI, m/z) calcd for $C_{22}H_{20}NO_2$ $(M+H)^+$: 330.1489, found: 330.1499.



4-5j

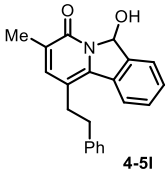
4-5j was obtained as a white solid (47%). Melting point 223-225°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (1 H, d, J = 7.6 Hz), 7.39 (1 H, t, J = 7.5 Hz), 7.31-7.26 (5 H, m), 7.20 (1 H, t, J = 7.6 Hz), 6.99 (1 H, d, J

= 7.9 Hz), 6.86 (1 H, d, *J* = 2.6 Hz), 5.63 (1 H, d, *J* = 2.9 Hz), 2.46 (3 H, s), 2.24 (3 H, d, *J* = 0.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 142.2, 139.1, 138.8, 138.0, 133.7, 132.9, 129.8, 129.7, 129.6, 129.2, 127.9, 124.3, 123.3, 117.4, 84.9, 21.3, 16.0.
HRMS (ESI, m/z) calcd for $C_{20}H_{18}NO_2$ $(M+H)^+$: 304.1332, found: 304.1334.



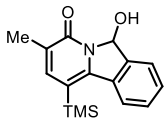
4-5k

4-5k was obtained as a yellow solid (49%). Melting point 209-211°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (1 H, d, *J* = 7.6 Hz), 7.48 (2 H, d, *J* = 8.6 Hz), 7.42 (1 H, t, *J* = 7.5 Hz), 7.35 (2 H, d, *J* = 7.9 Hz), 7.26 (1 H, s), 7.24 (1 H, s), 6.96 (1 H, d, *J* = 7.9 Hz), 6.85 (1 H, d, *J* = 2.5 Hz), 5.52 (1 H, d, *J* = 2.8 Hz), 2.24 (3 H, d, *J* = 0.8 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 141.6, 139.3, 138.9, 135.2, 134.3, 132.6, 130.8, 130.1, 129.9, 129.2, 128.3, 124.5, 123.1, 116.0, 84.9, 16.0.
HRMS (ESI, m/z) calcd for $C_{19}H_{15}ClNO_2$ $(M+H)^+$: 324.0786, found: 324.0801.



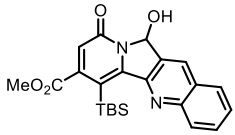
4-5l

4-5l was obtained as a yellow solid (50%). Melting point 179-181°C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (1 H, d, *J* = 7.6 Hz), 7.73 (1 H, d, *J* = 7.2 Hz), 7.52 (2 H, dt, *J* = 19.0, 7.4 Hz), 7.35 (2 H, t, *J* = 7.6 Hz), 7.26 (3 H, t, *J* = 7.1 Hz), 7.14 (1 H, s), 6.84 (1 H, d, *J* = 2.3 Hz), 5.70 (1 H, d, *J* = 2.8 Hz), 3.13-3.06 (2 H, m), 2.96 (2 H, t, *J* = 8.1 Hz), 2.20 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 142.4, 140.6, 139.2, 138.9, 133.1, 130.3, 129.5, 128.6, 128.3, 128.2, 126.4, 124.7, 122.9, 115.8, 84.7, 36.1, 32.4, 15.9.
HRMS (ESI, m/z) calcd for $C_{21}H_{20}NO_2$ $(M+H)^+$: 318.1489, found: 318.1483.



4-5m

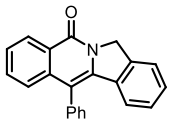
4-5m was obtained as a yellow solid (52%). Melting point 186-188°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (1 H, m), 7.73-7.67 (1 H, m), 7.54-7.46 (2 H, m), 7.44 (1 H, d, J = 0.9 Hz), 6.80 (1 H, d, J = 2.6 Hz), 5.76 (1 H, d, J = 2.6 Hz), 2.21 (3 H, d, J = 0.8 Hz), 0.44 (9 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 148.0, 144.2, 139.5, 133.9, 129.8, 129.6, 127.1, 124.6, 124.0, 110.0, 84.6, 16.0, -0.1.
HRMS (ESI, m/z) calcd for $C_{16}H_{20}NO_2Si$ $(M+H)^+$: 286.1258, found: 286.1252.



4-5n

4-5n was obtained as a yellow solid (32%). Melting point 238-240°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (1 H, s), 8.29 (1 H, d, J = 8.5 Hz), 7.96 (1 H, d, J = 8.2 Hz), 7.84 (1 H, m), 7.67 (1 H, m), 7.00 (1 H, s), 6.85 (1 H, s), 5.64 (1 H, d, J = 2.6 Hz), 3.94 (3 H, s), 1.26 (9 H, s), 0.34 (6 H, d, J = 1.7 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 169.0, 161.7, 152.7, 152.3, 150.3, 148.8, 132.2, 130.9, 130.1, 129.3, 128.6, 128.2, 127.7, 121.1, 111.9, 82.6, 52.9, 29.4, 17.9, 0.7, 0.7.
HRMS (ESI, m/z) calcd for $C_{23}H_{27}N_2O_4Si$ $(M+H)^+$: 423.1735, found: 423.1728.

Transformations of annulation products



4-6a

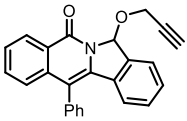
To the solution of **4-3a** (0.2 mmol) in DCM (2 mL) was added $BF_3{\cdot}Et_2O$ (0.2 mmol) at 0 ℃ and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.6 mmol) dissolved in DCM (1 mL) was added dropwise for 5 min at 0 ℃ and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with

saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-6a** as a yellow solid (82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, dd, J = 8.0, 0.9 Hz), 7.57 (4H, m), 7.54-7.46 (2H, m), 7.43-7.37 (2H, m), 7.35 (1H, t, J = 7.5 Hz), 7.23 (1H, d, J = 8.0 Hz), 7.10 (1H, t, J = 7.7 Hz), 6.44 (1H, d, J = 8.0 Hz), 5.24 (2H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 138.7, 138.4, 138.0, 135.2, 134.3, 131.9, 131.0, 129.4, 129.2, 128.4, 127.8, 127.2, 126.2, 125.1, 124.1, 124.0, 123.0, 114.4, 51.8.

Spectral data was consistent with that previously reported.[67]



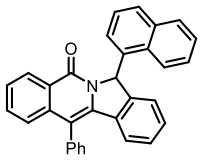
4-6b

To the solution of **4-3a** (0.2 mmol) in DCM (2 mL) was added $BF_3{\cdot}Et_2O$ (0.2 mmol) at 0 °C and stirred for 5 minutes.[72] To the resulting solution, propargyl alcohol (0.6 mmol) dissolved in DCM (1 mL) was added dropwise for 5 min at 0 °C and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-6b** as a yellow solid (78%). Melting point 117-119°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (1 H, dd, J = 7.8, 1.5 Hz), 7.69 (1 H, d, J = 7.6 Hz), 7.64-7.54 (4 H, m), 7.54-7.48 (1 H, m), 7.46-7.42 (1 H, m), 7.34 (2 H, dt, J = 7.8, 4.9 Hz), 7.13 (2 H, dd, J = 15.4, 7.9 Hz), 6.91 (1 H, s), 6.31 (1 H, d, J = 7.9 Hz), 5.22 (1 H, dd, J = 16.0, 2.4 Hz), 4.63 (1 H, dd, J = 16.0, 2.4 Hz), 2.61 (1 H, t, J = 2.4 Hz).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.7, 138.9, 138.3, 136.3, 134.8, 132.9, 132.5, 131.0, 130.7, 129.8, 129.6, 129.4, 128.5, 127.6, 126.8, 125.5, 124.9, 123.6, 115.5, 88.9, 80.8, 75.2, 59.4.

HRMS (ESI, m/z) calcd for $C_{25}H_{18}NO_2$ $(M+H)^+$: 364.1332, found: 364.1326.



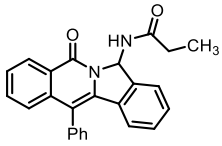
4-6c

To a suspension of **4-3a** (0.2 mmol) in DCE (1 mL) at room temperature was added naphthalene (2 mmol) and stirred for 10 min.[73] To this suspension, TFA (2.2 mmol) was added. The reaction mixture was heated to 75 °C and maintained for 16h (monitored by TLC). It was then cooled to room temperature, diluted with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-6c** as a yellow solid (64%). Melting point 253-255°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (1 H, d, J = 8.6 Hz), 8.42 (1 H, d, J = 7.1 Hz), 7.91 (1 H, d, J = 8.1 Hz), 7.73 (1 H, d, J = 8.0 Hz), 7.65-7.54 (6 H, m), 7.51 (1 H, s), 7.47-7.40 (2 H, m), 7.30-7.26 (1 H, m), 7.25-7.21 (3 H, m), 7.12 (1 H, t, J = 7.0 Hz), 7.03 (1 H, t, J = 7.4 Hz), 6.88 (1 H, d, J = 6.7 Hz), 6.47 (1 H, d, J = 7.8 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 143.9, 138.9, 138.7, 135.2, 135.2, 134.2, 132.7, 132.1, 131.3, 131.1, 129.5, 129.5, 129.1, 128.5, 128.2, 128.1, 127.6, 126.6, 126.3, 125.8, 125.6, 125.3, 125.1, 124.1, 123.1, 123.0, 121.7, 114.4, 62.1.

HRMS (ESI, m/z) calcd for $C_{32}H_{22}NO$ $(M+H)^+$: 436.1696, found: 436.1693.



4-6d

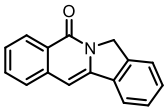
To a suspension of **4-3a** (0.2 mmol) in DCE (1 mL) at room temperature was added propionitrile (2.5 mmol) and stirred for 10 min.[73] To this suspension, TFA (2.2 mmol) was added. The reaction mixture was heated to 75 °C and maintained for 16h (monitored by TLC). It was then cooled to room temperature, diluted with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*.

The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-6d** as a yellow solid (56%). Melting point 165-167°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (1 H, d, J = 7.6 Hz), 7.60-7.49 (5 H, m), 7.42 (2 H, t, J = 7.0 Hz), 7.36-7.29 (2 H, m), 7.18-7.06 (3 H m), 6.75 (1 H, d, J = 7.7 Hz), 6.33 (1 H, d, J = 7.9 Hz), 2.44-2.17 (2 H, m), 1.14 (3 H, t, J = 7.5 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 160.6, 139.5, 138.8, 137.0, 134.8, 133.1, 132.3, 131.0, 130.8, 129.6, 129.4, 129.0, 128.5, 127.3, 126.5, 125.3, 123.6, 123.4, 114.8, 67.5, 29.4, 9.3.

HRMS (ESI, m/z) calcd for $C_{25}H_{21}N_2O_2$ $(M+H)^+$: 381.1598, found: 381.1605.



4-7

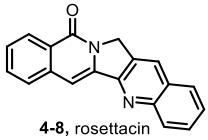
A 25 mL round-bottomed flask equipped with a stirring bar is charged with **4-3p** (0.2 mmol), *tetra*-*n*-butylammonium fluoride (TBAF, 1 M in THF, 0.4 mL, 0.4 mmol) and 2 mL of anhydrous THF.[16] Then allowed to stir at room temperature for 12 h. The solvent was removed and the residue was used in next step without further purification.

To the solution of above residue in DCM (2 mL) was added $BF_3{\cdot}Et_2O$ (0.2 mmol) at 0 ℃ and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.6 mmol) dissolved in DCM (1 mL) was added dropwise for 5 min at 0 ℃ and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-7** as a yellow solid (65%)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (1 H, d, J = 7.7 Hz), 7.81 (1 H, dd, J = 5.2, 3.5 Hz), 7.71-7.62 (2 H, m), 7.58 (1 H, dd, J = 5.6, 3.2 Hz), 7.52-7.44 (3 H, m), 7.04 (1 H, s), 5.20 (2 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 142.2, 137.9, 137.6, 134.1, 132.2, 129.8, 128.3, 127.4, 126.4, 126.2, 124.7, 123.5, 121.0, 98.0, 52.0.

Spectral data was consistent with that previously reported.[72]



4-8, rosettacin

A 25 mL round-bottomed flask equipped with a stirring bar is charged with **4-3r** (0.2 mmol), *tetra*-*n*-butylammonium fluoride (TBAF, 1 M in THF, 0.4 mL, 0.4 mmol) and 2 mL of anhydrous THF.[16] Then allowed to stir at room temperature for 12 h. The solvent was removed and the residue was used in next step without further purification.

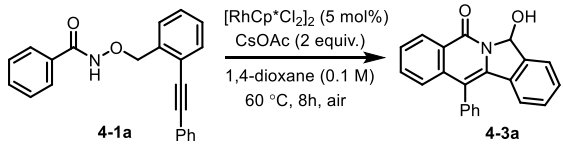
To the solution of above residue in DCM (2 mL) was added $BF_3 \cdot Et_2O$ (0.2 mmol) at 0 °C and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.6 mmol) dissolved in DCM (1 mL) was added dropwise for 5 min at 0 °C and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **4-8** as a yellow solid (46%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (1 H, d, J = 8.0 Hz), 8.26 (1 H, s), 8.18 (1 H, d, J = 8.5 Hz), 7.85 (1 H, d, J = 8.2 Hz), 7.78-7.69 (3 H, m), 7.61 (1 H, s), 7.55 (2 H, m), 5.32 (2 H, d, J = 0.8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 153.6, 148.8, 139.9, 137.5, 132.4, 130.7, 130.2, 129.4, 128.8, 128.0, 128.0, 127.5, 127.3, 126.0, 101.1, 49.4.

Spectral data was consistent with that previously reported.[32]

Control experiments and mechanistic studies



4-1a **4-3a**

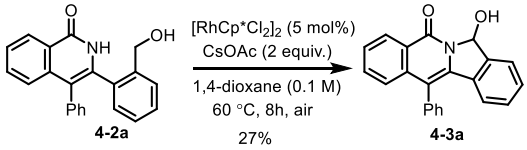
standard condition	**4-3a** (52%)
under N_2	**4-3a** (36%)
under O_2	**4-3a** (53%)
add 2 equiv. PivOH	**4-3a** (48%)
add 50 mol% $Cu(OAc)_2$	**4-3a** (50%)

To a Schlenk flask equipped with a stir bar were added **4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under N_2. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3a** (36%).

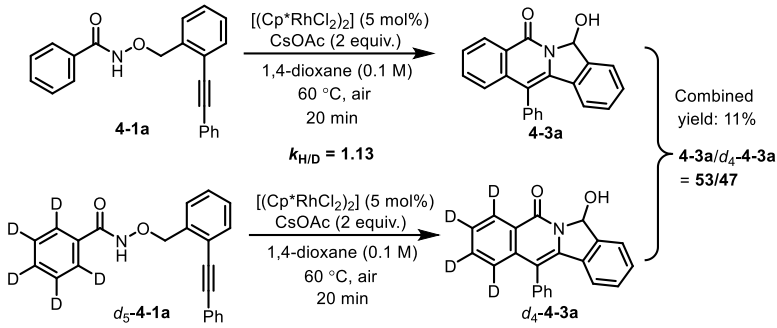
To a Schlenk flask equipped with a stir bar were added **4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under O_2. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3a** (53%).

To a Schlenk flask equipped with a stir bar were added **4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), PivOH (0.6 mmol) and 1,4-dioxane (3.0 mL) under air. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3a** (48%).

To a Schlenk flask equipped with a stir bar were added **4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), $Cu(OAc)_2$ (0.15 mmol)and 1,4-dioxane (3.0 mL) under N_2. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3a** (50%).



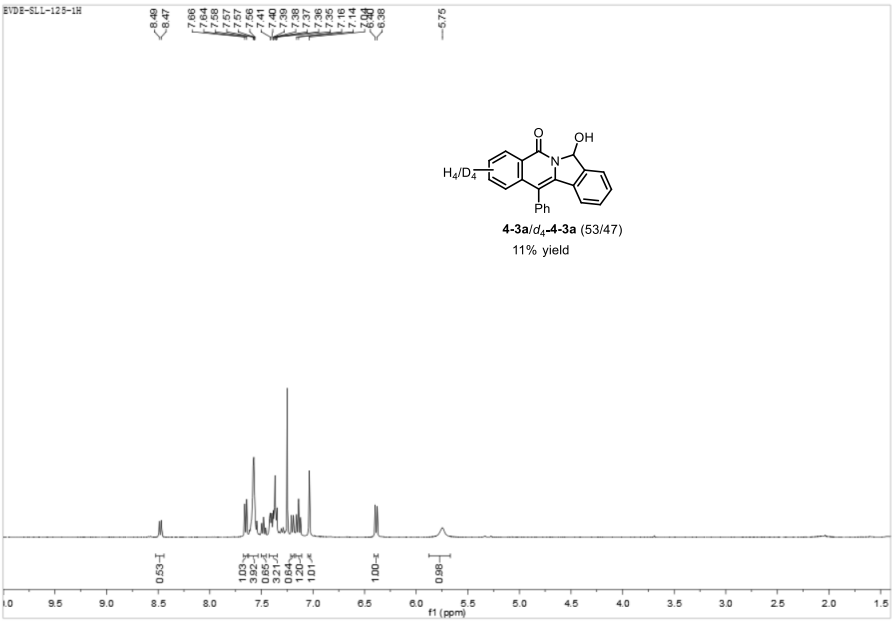
To a Schlenk flask equipped with a stir bar were added **4-2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under air. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **4-3a** (27%).



To one Schlenk flask equipped with a stir bar were added **4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under air. The reaction was stirred for 20 min at 60°C, cooled to room temperature.

To another Schlenk flask equipped with a stir bar were added d_5-**4-1a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol) and 1,4-dioxane (3.0 mL) under air. The reaction was stirred for 20 min at 60°C, cooled to room temperature.

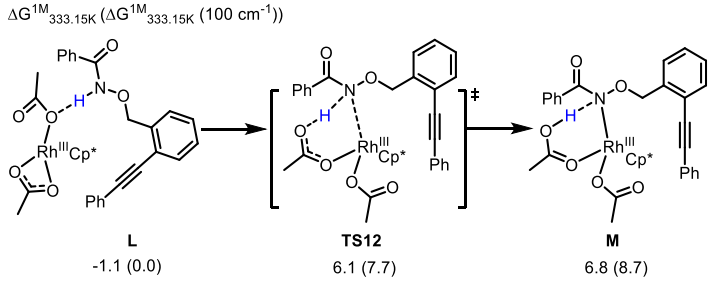
Then these two reaction mixture were combined and the solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the desired product (11%). The ratio of **4-3a** and d_4-**4-3a** was determined by ^{1}H NMR to be 0.53:0.47 (see below).



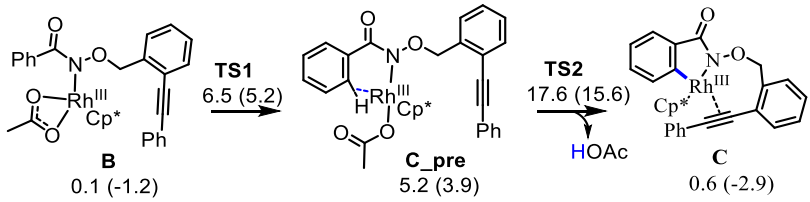
DFT calculations

All the density functional theory (DFT) calculations were performed using Gaussian 16 software. Geometries were optimized in the gas phase using the dispersion (D3) corrected B3LYP functional and 6-31G(d) basis set for light elements (H, C, N, O), and SDD basis set and its effective core potential for Rh element. This basis set combination was labeled as **SB**. The stable nature of each structure along the reaction pathway was examined by harmonic vibrational frequency analysis. Reactants and intermediates were verified to be minimum structures without any imaginary frequencies, while transition states were found to have only one imaginary frequency. To obtain reliable energetic data, a larger basis set def2-TZVPP (labeled as **LB**) was used in the single point energy calculation. The solvation energy in 1,4-dioxane was calculated using the continuum solvation SMD model at the B3LYP-D3/**SB** level. The energetic values listed in the context were obtained at the B3LYP-D3/**LB**//B3LYP-D3/**SB**+SMD level with thermodynamic values corrected at 333.15 K and the solute standard state 1 M, labeled as $G_{1M}^{333.15K}$. In the current molecular system, there are several low frequency vibrations (lower than 100 cm^{-1}), and many researchers have

questioned the validity of harmonic oscillator model in the free energy calculation of such low-frequency modes. To evaluate the potential error, the thermodynamic calculations were repeated with the frequencies lower than 100 cm^{-1} raised to 100 cm^{-1} ($G^{1M}_{333.15K}$ (100 cm^{-1})). Both the $G^{1M}_{333.15K}$ and $G^{1M}_{333.15K}$(100 cm^{-1}) values are provided in this SI; all energies in the main text related to $G^{1M}_{333.15K}$(100 cm^{-1}). In general, the differences between $G^{1M}_{333.15K}$ and $G^{1M}_{333.15K}$(100 cm^{-1}) results are relatively modest, within the expected error range of the methodology.



Scheme S1. Energetic profile (kcal/mol) of N-H deprotonation process. As shown, the barrier of N-H deprotonation is predicted to be 7.2 kcal/mol, implying a rapid process. Notably, the resulting intermediate **M** has a higher free-energy than the transition state **TS12**, but the electronic energy of **M** is 0.5 kcal/mol lower than that of **TS12** .



Scheme S2. Energetic profile (kcal/mol) of the two step C-H activation process.

C-H activation takes place through a two-step AMLA (ambiphilic metal-ligand assistance)/CMD (concerted metalation–deprotonation) processes and the rhodacycle intermediate **C** (0.6 kcal/mol) is given from an agostic intermediate **C_pre** (5.2 kcal/mol). The CMD step (**TS2**,17.6 kcal/mol) has a higher energy barrier than the AMLA step (**TS1**, 6.5 kcal/mol).

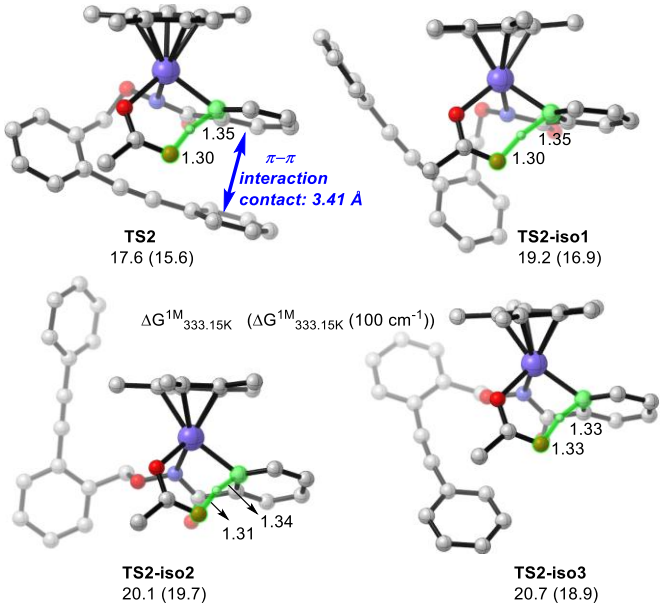


Figure S1. Geometries (Å) and Energies (kcal/mol) of transition states of different conformations in the CMD C-H activation step.

Four isomers of CMD C-H activation transition states were found with energies between 17.6 and 20.7 kcal/mol. The lowest-lying **TS2** isomer presents π-π stacking interactions between the phenyl groups, and such interaction is absent in other high-energy isomers.

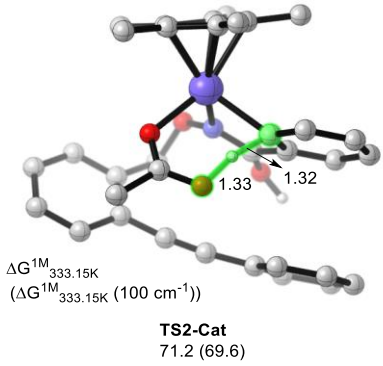


Figure S2 Geometry (Å) of transition state in CMD C-H activation step using the cationic Cp*RhOAc$^+$ catalyst.

The CMD transition state is chosen to examine the reactivity of cationic Cp*RhOAc$^+$ catalyst. Calculation predicted a highly unfavorable

transition state **TS2-Cat** with an overall free-energy barrier of around 70 kcal/mol, and thus the reactivity of cationic catalyst can be excluded in the reaction.

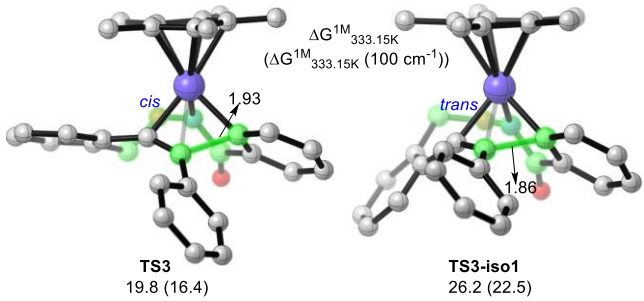
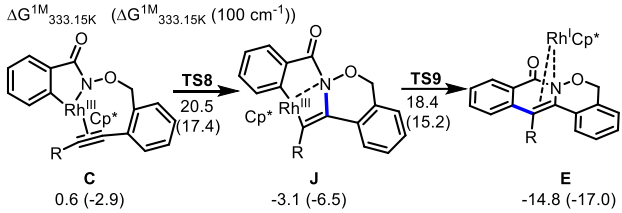


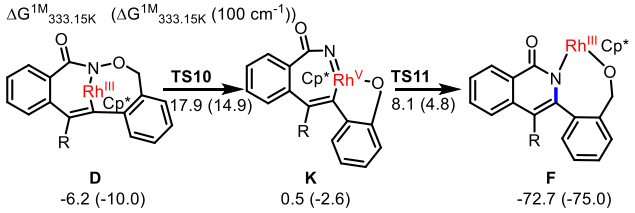
Figure S3. Geometries (Å) and Energies (kcal/mol) of transition states of alkyne-insertion into the Rh-C bond.

Two conformers of transition state in the alkyne-insertion step were found, and their difference lies in the relative orientation of the functional groups linked to the N-O bond. The *cis* conformer **TS3** is determined to be 6.4 kcal/mol lower in energy than the *trans* isomer.



Scheme S3. Energetic profile (kcal/mol) of pathway involving alkyne insertion into the Rh-N bond followed by reductive elimination.

The pathway with alkyne insertion into the Rh-N bond *via* **TS8** shows a slightly higher barrier (by 0.7-1.0 kcal/mol) than that of insertion into the Rh-C bond (**TS3**). In addition, the subsequent reductive elimination transition state **TS9** is higher in energy by ca. 6 kcal/mol than **TS4**. Therefore, insertion of alkyne into the Rh-C bond should be preferred.



Scheme S4. Energetic profile (kcal/mol) of pathway comprised of the N-O cleavage prior to the C-N bond formation.

After the insertion of alkyne into the Rh-C bond, the pathway of N-O cleavage prior to the C-N bond formation is energetically inferior and **TS10** is higher in energy by 5.6 kcal/mol than **TS4**. In addition, the Rh^{V} intermediate **K** is quite unstable with respect to the Rh^{I} intermediate **E**. Therefore, the reaction would prefer the formation of C-N bond prior to the cleavage of N-O bond, and involves Rh^{I} intermediate.

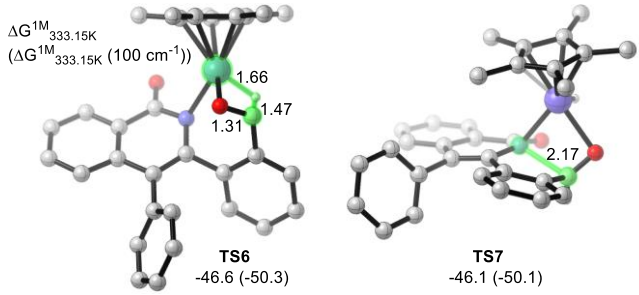


Figure S4. Geometries (Å) and Energies (kcal/mol) of the transition states for β-H elimination and tandem cyclization step.

Table S1. Free energy difference ($\triangle\triangle G^{1M}_{333.15K}$, kcal/mol) between **TS6** and **TS7** obtained using different DFT functionals in the single point energy calculation.

DFT	B3LYP-D3	M06	PBE0-D3	ωB97XD	TPSSh-D3
$\triangle\triangle G^{1M}_{333.15K}$	0.5	1.4	3.3	0.4	3.0

Given the small free energy difference between **TS6** and **TS7** obtained with our favored methodology, test calculations with different DFT methods were carried out (**Table** S1). The β-H elimination transition state **TS6** is found to be lower in free energy (by 0.4-3.3 kcal/mol)

compared to the tandem cyclization transition state **TS7** with all the functionals tested. Thus, tandem cyclization is proposed as the rate determining step to yield **4-3a**.

Catalyst + **4-2a** ⇌**F** + 2**AcOH** ΔG° = 4.7 kcal/mol

Initial (mol·L^{-1} 0.01 0.1

Equilibrium (mol·L^{-1}) 0.01-x 0.1-x x 2x

Since $\Delta G^\circ = -RTln\mathrm{K}^\circ$

$$\mathrm{K}^\circ = \frac{4x^3}{(0.01-x)\times(0.1-x)}\ ; x \ll 0.1$$

Then $\mathrm{K}^\circ = 8.1\times10^{-4}$; $x = 4.7\times10^{-3}$

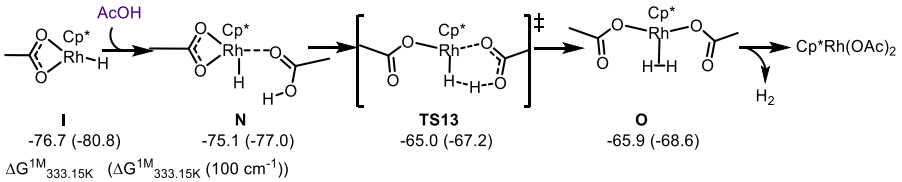
$$\mathrm{K_{app}} = \frac{[\mathrm{F}]}{[\mathrm{Catalyst}]} = \frac{x}{0.01\text{-}x} = 0.9$$

Then $\Delta G_{app} = -RTln\mathrm{K_{app}}$ = 0.1 kcal/mol

Scheme S5. Chemical equilibrium principle in the process from **4-2a** to intermediate **F**. Catalyst: Cp*Rh(OAc)$_2$.

As mentioned in the text, the free energy difference between catalysts + **4-2a** and **TS7** initially seemed too high to be consistent with experiment. Accordingly, a kinetic model (Scheme **S5**) was developed to test the consistency of the predicted model. In this model, the overall free energy change from **4-2a** + catalyst to **TS7** was broken down into two parts: △G(**4-2a**-**F**) and △G(**F**-**TS**). The TS and intermediate **F** have the same chemical composition so this second component of the free energy should not depend on the experimental conditions. However, the step **4-2a** → **F** involves two reactants, and leads to formation of two acetic acid molecules as well as **F**. The different species will be present with concentrations very different from 1 M, so that using △G calculated for this standard state will be misleading. Considering the experimental conditions, and assuming that **4-2a** is in equilibrium with **F**, an 'apparent' $\triangle G_{app}$ can be considered. The derivation is shown in **Scheme S5**, with $\triangle G_{app}$ being just 0.1 kcal/mol, compared to the standard-state value of 4.7 kcal/mol ($\triangle G^{1M}_{333.15K}$). This leads to a net free energy of activation of 26.7 kcal/mol, corresponding to an apparent rate constant k_{app} = 2 × 10^{-5} s^{-1} for conversion of **4-2a**. This would correspond to a reaction half-life of *ca.* 15 h, which is indeed of the

same order of magnitude as the observed reaction time. In terms of the free energy change obtained by $G^{1M}_{333.15K}$, the activation barrier of **TS7** reduces from 30.4 to 25.3 kcal/mol.



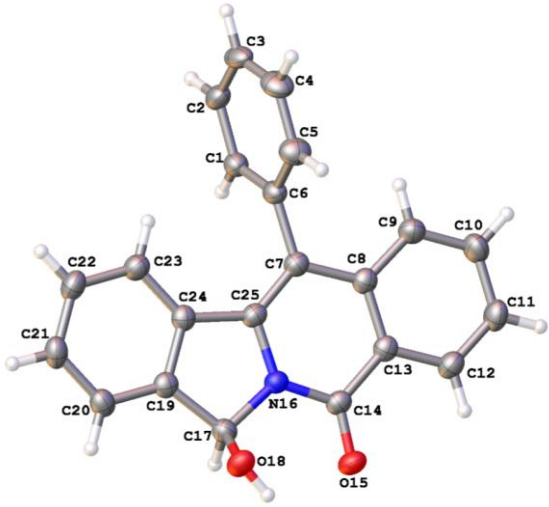
Scheme S6. Pathway of catalyst regeneration from the Rh-hydride complex mediated by the acetic acid.

Considering the reaction goes smoothly in the O_2-free environment (e.g., N_2), an acid assisted H_2-formation pathway was proposed to regenerate the catalyst. The regeneration of Rh-hydride complex **I** occurs through coordination of acetic acid, formation of Rh-dihydrogen σ-complex **N** and release of H_2. This H_2-formation process is found to involve a concerted six-membered transition state **TS13** (-65.0 kcal/mol), in which the distance of the two hydrogen atoms is 0.86 Å. Further dissociation of H_2 would regenerate the catalyst. Note that the current results could not exclude other mechanistic possibilities for the catalyst regeneration, but the moderate barrier (<13 kcal/mol) of the proposed H_2-forming pathway already reflects that the regeneration step should not play a dominant role.

Single crystal X-ray diffraction

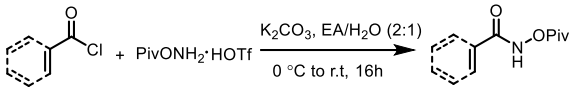
Crystal of **4-3a** was obtained by slow diffusion from a solution of the compound in DCM layered with heptane at room temperature for several days. X-ray intensity data were collected at 150K on a Rigaku Ultra 18S generator (Xenocs mirrors, Mo-Kα radiation, λ = 0.71073 Å) using a MAR345 image plate. The images were interpreted and integrated with CrysAlisPRO and the implemented absorption correction was applied. The structures were solved using Olex2 with the ShelXS structure solution program by Direct Methods and refined with the ShelXL refinement package using full-matrix least-squares minimization on F^2. Non-hydrogen atoms were refined anisotropically and hydrogen atoms in the riding mode with isotropic temperature factors fixed at 1.2 times U_{eq} of the parent atoms (1.5 for -OH and methyl groups). Crystallographic data for **4-3a** has been deposited with

the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1844890.



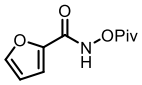
Chapter 5

Synthesis of the substrates



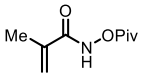
5-1j, **5-1r**, **5-1s**

In a 100 mL round-bottom flask,[74] *O*-pivaloylhydroxamine triflic acid (3.6 mmol) and K_2CO_3 (6.0 mmol) were combined in a 2:1 mixture of EtOAc (20 mL) and H_2O (10 mL). The flask was capped and the mixture was cooled in an ice bath. No special precautions were taken to exclude moisture or oxygen. The acid chloride (3.0 mmol) was added dropwise and the mixture was stirred to r.t over 16 h. The reaction mixture was then diluted with EtOAc and washed twice with sat. $NaHCO_3$ and brine. The organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (*n*-heptane/ethyl acetate) to give the products **5-1j**, **5-1r** and **5-1s**.



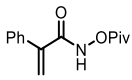
5-1j

5-1j was obtained as a yellow solid (49%). Melting point 97-99°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.47 (1 H, m), 7.25-7.20 (1 H, m), 6.53 (1 H, dd, J = 3.5, 1.8 Hz), 1.35 (9 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 156.9, 145.0, 145.0, 116.6, 112.1, 38.4, 27.0.
HRMS (ESI, m/z) calcd for $C_{10}H_{14}NO_4$ $(M+H)^+$: 212.0917, found: 212.0926.



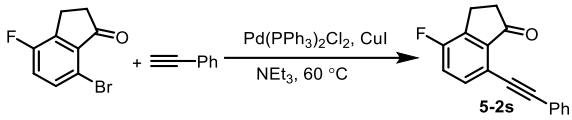
5-1r

5-1r was obtained as a colorless oil (73%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (1 H, s), 5.83 (1 H, s), 5.47 (1 H, d, J = 0.7 Hz), 1.98 (3 H, s), 1.32 (9 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 167.2, 136.8, 121.8, 38.3, 26.9, 18.2.
HRMS (ESI, m/z) calcd for $C_9H_{16}NO_3$ $(M+H)^+$: 186.1125, found: 186.1129.



5-1s

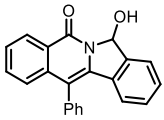
5-1s was obtained as a yellow oil (64%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (1 H, s), 7.50-7.43 (2 H, m), 7.40-7.34 (3 H, m), 6.14 (1 H, s), 5.75 (1 H, s), 1.32 (9 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 165.9, 141.5, 135.6, 128.9, 128.8, 127.8, 123.4, 38.3, 26.9.
HRMS (ESI, m/z) calcd for $C_{14}H_{18}NO_3$ $(M+H)^+$: 248.1281, found: 248.1280.



To a solution of corresponding 2-bromoketone (5.0 mmol) and ethynylbenzene (6.0 mmol) in Et_3N (20 mL) were added $Pd(PPh_3)_2Cl_2$ (0.25 mmol) and CuI (0.15 mmol) at room temperature under argon.[16] Then the reaction mixture was gradually warmed up to 60 ℃ and stirred at the same temperature for 16h. After cooling down to room temperature, the crude mixture was filtered and extracted with ethyl acetate. The combined organic extracts were washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **5-2s** as a yellow solid (72%). Melting point 106-108°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.60 (2 H, m), 7.49 (1 H, dd, J = 8.3, 4.5 Hz), 7.40-7.32 (3 H, m), 7.26 (1 H, d, J = 2.5 Hz), 3.17-3.07 (2 H, m), 2.81-2.73 (2 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.3, 160.8, 158.3, 141.5 (d, J = 20.5 Hz), 139.0 (d, J = 5.0 Hz), 133.6 (d, J = 6.4 Hz), 132.0, 128.5 (d, J = 37.1 Hz), 123.0, 120.2 (d, J = 21.1 Hz), 116.4 (d, J = 4.1 Hz), 95.0, 85.6, 36.2, 31.9.
^{19}F NMR (377 MHz, $CDCl_3$) δ -117.8.
HRMS (ESI, m/z) calcd for $C_{17}H_{12}FO$ $(M+H)^+$: 251.0867, found: 251.0879.

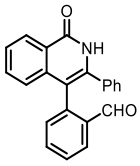
Rhodium(III)-catalyzed intermolecular annulations

To a Schlenk flask equipped with a stir bar were added **5-1** (0.3 mmol), **5-2** (0.45 mmol), $[Cp^*RhCl_2]_2$ (0.015 mmol), CsOAc (0.6 mmol), PivOH (0.6 mmpl) and CH_3CN (1.5 mL) without any particular precautions to extrude oxygen or moisture. The reaction was stirred for 8 h at 60°C, cooled to room temperature. The solvent was removed in *vacuo* and the remaining residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford the product **5-3** and **5-4**.



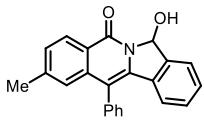
5-4aa

5-4aa was obtained as a yellow solid (39%). Melting point 193-195°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50-8.40 (1 H, m), 7.68-7.63 (1 H, m), 7.62-7.54 (4 H, m), 7.52-7.45 (1 H, m), 7.43-7.35 (3 H, m), 7.22-7.12 (2 H, m), 7.03 (1 H, s), 6.39 (1 H, d, *J* = 7.9 Hz), 5.72 (1 H, s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 139.1, 138.9, 136.1, 134.6, 133.2, 132.6, 130.8, 129.8, 129.7, 129.5, 129.4, 128.5, 126.7, 125.6, 125.0, 124.3, 123.8, 115.2, 84.1.
HRMS (ESI, m/z) calcd for $C_{22}H_{16}NO_2$ $(M+H)^+$: 326.1176, found: 326.1183.



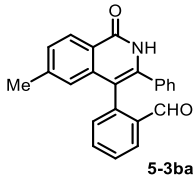
5-3aa

5-3aa was obtained as a yellow solid (48%). Melting point 204-206°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.88 (1 H, s), 9.85 (1 H, s), 8.41 (1 H, d, *J* = 7.9 Hz), 7.92 (1 H, d, *J* = 7.7 Hz), 7.62-7.54 (2 H, m), 7.48 (2 H, dd, *J* = 17.4, 7.9 Hz), 7.32 (1 H, d, *J* = 7.5 Hz), 7.27-7.21 (5 H, m), 7.12 (1 H, d, *J* = 8.1 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 163.3, 139.3, 138.9, 138.6, 135.5, 134.0, 133.9, 133.5, 133.1, 129.2, 129.0, 128.4, 128.4, 128.0, 127.6, 126.9, 125.2, 124.8, 112.4.
HRMS (ESI, m/z) calcd for $C_{22}H_{16}NO_2$ $(M+H)^+$: 326.1176, found: 326.1181.



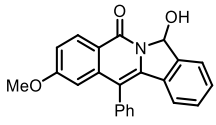
5-4ba

5-4ba was obtained as a yellow solid (40%). Melting point 218-220°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (1 H, d, J = 8.1 Hz), 7.68-7.55 (4 H, m), 7.42-7.31 (4 H, m), 7.14 (1 H, dd, J = 11.4, 4.0 Hz), 7.01 (1 H, s), 6.96 (1 H, s), 6.34 (1 H, d, J = 7.9 Hz), 5.58 (1 H, s), 2.37 (3 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 143.3, 139.3, 138.8, 134.8, 133.3, 130.8, 129.8, 129.6, 129.5, 129.4, 128.5, 128.4, 127.2, 125.4, 124.3, 123.8, 122.8, 115.2, 84.0, 22.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1335.



5-3ba

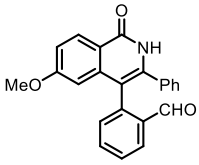
5-3ba was obtained as a yellow solid (42%). Melting point 264-266°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.57 (1 H, s), 9.85 (1 H, s), 8.32 (1 H, d, J = 8.2 Hz), 7.92 (1 H, dd, J = 7.8, 1.2 Hz), 7.59 (1 H, td, J = 7.5, 1.4 Hz), 7.47 (1 H, t, J = 7.6 Hz), 7.35-7.30 (2 H, m), 7.26-7.18 (5 H, m), 6.87 (1 H, s), 2.34 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 163.1, 143.9, 139.5, 139.0, 138.8, 135.5, 134.1, 133.9, 133.6, 129.2, 128.9, 128.5, 128.4, 127.8, 127.6, 125.0, 122.7, 112.2, 22.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1345.



5-4ca

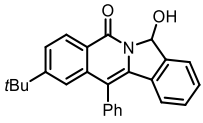
5-4ca was obtained as a yellow solid (33%). Melting point 168-170°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1 H, d, J = 8.9 Hz), 7.64 (1 H, d, J = 7.6 Hz), 7.62-7.54 (3 H, m), 7.43-7.34 (3 H, m), 7.14 (1 H, t, J = 7.7 Hz), 7.06 (1 H, dd, J = 8.9, 2.5 Hz), 7.00 (1 H, s), 6.55 (1 H, d, J = 2.4 Hz), 6.36 (1 H, d, J = 7.9 Hz), 5.69 (1 H, s), 3.72 (3 H, s).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 161.6, 141.4, 139.1, 136.7, 134.7, 133.2, 130.8, 129.7, 129.5, 129.4, 129.3, 128.6, 124.3, 123.8, 118.9, 115.2, 114.9, 107.7, 84.0, 55.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1295.



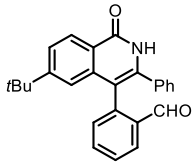
5-3ca

5-3ca was obtained as a yellow solid (46%). Melting point 206-208°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.37 (1 H, s), 9.87 (1 H, d, J = 0.6 Hz), 8.36 (1 H, d, J = 8.9 Hz), 7.92 (1 H, dd, J = 7.8, 1.3 Hz), 7.58 (1 H, td, J = 7.5, 1.5 Hz), 7.46 (1 H, t, J = 7.5 Hz), 7.32 (1 H, dd, J = 7.6, 0.9 Hz), 7.26-7.17 (5 H, m), 7.07 (1 H, dd, J = 8.9, 2.4 Hz), 6.46 (1 H, d, J = 2.4 Hz), 3.70 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0, 164.0, 163.2, 141.4, 140.1, 140.0, 136.1, 134.8, 134.6, 134.1, 130.5, 129.6, 129.1, 128.5, 119.3, 116.0, 112.7, 108.1, 55.9.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1298.



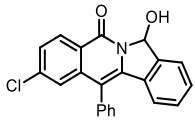
5-4da

5-4da was obtained as a yellow solid (34%). Melting point 221-223°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (1 H, d, J = 8.5 Hz), 7.67-7.54 (5 H, m), 7.45-7.33 (3 H, m), 7.19-7.11 (2 H, m), 7.02 (1 H, s), 6.39 (1 H, d, J = 7.9 Hz), 5.66 (1 H, s), 1.24 (9 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.8, 156.1, 139.1, 138.9, 136.0, 134.8, 133.4, 130.8, 129.7, 129.5, 129.3, 128.5, 126.9, 124.9, 124.3, 123.7, 122.8, 121.6, 115.6, 84.0, 35.2, 30.9.
HRMS (ESI, m/z) calcd for $C_{26}H_{24}NO_2$ $(M+H)^+$: 382.1802, found: 382.1806.



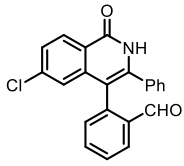
5-3da

5-3da was obtained as a dark solid (51%). Melting point 246-248°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.17 (1 H, s), 9.86 (1 H, d, J = 0.7 Hz), 8.39 (1 H, d, J = 8.5 Hz), 7.94 (1 H, dd, J = 7.7, 1.2 Hz), 7.59 (2 H, ddd, J = 7.0, 3.7, 1.3 Hz), 7.47 (1 H, t, J = 7.5 Hz), 7.32 (1 H, dd, J = 7.6, 0.9 Hz), 7.27-7.18 (5 H, m), 7.09 (1 H, d, J = 1.7 Hz), 1.21 (9 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 162.7, 156.9, 139.4, 138.6, 138.5, 135.6, 134.4, 133.9, 133.5, 129.1, 129.0, 128.6, 128.5, 127.8, 127.5, 125.2, 122.7, 121.4, 112.7, 35.3, 30.9.
HRMS (ESI, m/z) calcd for $C_{26}H_{24}NO_2$ $(M+H)^+$: 382.1802, found: 382.1808.



5-4ea

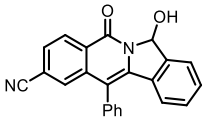
5-4ea was obtained as a yellow solid (38%). Melting point 189-191°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1 H, d, J = 8.5 Hz), 7.66 (1 H, d, J = 7.6 Hz), 7.63-7.57 (3 H, m), 7.44-7.34 (4 H, m), 7.16 (2 H, dd, J = 7.5, 4.8 Hz), 7.01 (1 H, s), 6.36 (1 H, d, J = 7.9 Hz), 5.56 (1 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 140.6, 139.4, 139.0, 133.9, 132.9, 130.8, 130.8, 130.1, 129.9, 129.7, 129.6, 129.0, 128.9, 127.2, 124.9, 124.4, 124.0, 114.3, 84.2.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}ClNO_2$ $(M+H)^+$: 360.0786, found: 360.0802.



5-3ea

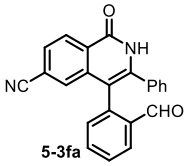
5-3ea was obtained as a yellow solid (49%). Melting point 260-262°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.63 (1 H, s), 9.84 (1 H, s), 8.34 (1 H, d, J = 8.6 Hz), 7.91 (1 H, dd, J = 7.8, 1.2 Hz), 7.62 (1 H, td, J = 7.5, 1.4 Hz), 7.50 (1 H, t, J = 7.5 Hz), 7.44 (1 H, dd, J = 8.6, 2.0 Hz), 7.32 (1 H,

dd, *J* = 7.5, 0.6 Hz), 7.26-7.21 (3 H, m), 7.18 (2 H, dd, *J* = 8.1, 1.5 Hz), 7.06 (1 H, d, *J* = 1.9 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 162.6, 140.2, 140.0, 139.9, 138.2, 135.4, 134.1, 133.7, 133.5, 129.5, 129.3, 129.1, 128.8, 128.8, 128.5, 127.5, 124.6, 123.2, 111.9.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}ClNO_2$ $(M+H)^+$: 360.0786, found: 360.0802.



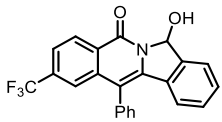
5-4fa

5-4fa was obtained as a yellow solid (38%). Melting point 201-203°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (1 H, d, *J* = 8.2 Hz), 7.70-7.61 (5 H, m), 7.52 (1 H, d, *J* = 1.3 Hz), 7.47-7.34 (3 H, m), 7.19 (1 H, t, *J* = 7.4 Hz), 7.03 (1 H, s), 6.42 (1 H, d, *J* = 7.9 Hz), 5.53 (1 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 139.4, 139.0, 138.1, 133.2, 132.5, 130.7, 130.7, 130.5, 130.3, 130.1, 129.9, 129.3, 128.3, 127.3, 124.5, 124.2, 118.2, 116.2, 114.0, 84.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}N_2O_2$ $(M+H)^+$: 351.1128, found: 351.1142.



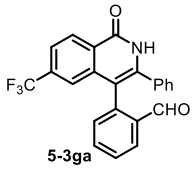
5-3fa

5-3fa was obtained as a yellow solid (43%). Melting point 252-254°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.84 (1 H, s), 9.35 (1 H, s), 8.58 (1 H, d, *J* = 8.3 Hz), 7.96-7.89 (1 H, m), 7.73-7.65 (2 H, m), 7.55 (2 H, dd, *J* = 15.7, 8.1 Hz), 7.41 (1 H, d, *J* = 1.0 Hz), 7.30 (3 H, dd, *J* = 9.9, 3.9 Hz), 7.16 (2 H, dd, *J* = 8.1, 1.6 Hz).
^{13}C NMR (151 MHz, $CDCl_3$) δ 190.7, 161.4, 140.1, 138.8, 136.8, 135.5, 134.3, 133.6, 133.5, 130.3, 129.9, 129.7, 129.3, 129.0, 128.9, 128.7, 128.7, 127.4, 118.0, 116.8, 112.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}N_2O_2$ $(M+H)^+$: 351.1128, found: 351.1133.



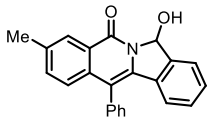
5-4ga

5-4ga was obtained as a yellow solid (36%). Melting point 193-195°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (1 H, d, J = 8.3 Hz), 7.72-7.59 (5 H, m), 7.46 (1 H, s), 7.44-7.34 (3 H, m), 7.17 (1 H, t, J = 7.5 Hz), 7.05 (1 H, s), 6.38 (1 H, d, J = 7.9 Hz), 5.86 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 139.3, 139.0, 137.6, 134.3 (q, J = 32.5 Hz), 133.6, 132.7, 130.7 (d, J = 7.1 Hz), 130.3, 130.0, 129.8 (d, J = 8.0 Hz), 129.1, 128.4, 127.0, 124.5, 124.1, 122.8-122.5 (m), 114.9, 84.3.
^{19}F NMR (377 MHz, $CDCl_3$) δ -63.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO_2$ $(M+H)^+$: 394.1049, found: 394.1050.



5-3ga

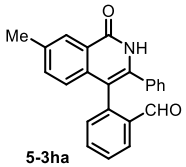
5-3ga was obtained as a yellow solid (53%). Melting point 226-228°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.50 (1 H, s), 9.83 (1 H, s), 8.58 (1 H, d, J = 8.4 Hz), 7.92 (1 H, dd, J = 7.8, 1.2 Hz), 7.72 (1 H, dd, J = 8.4, 1.2 Hz), 7.65 (1 H, td, J = 7.5, 1.3 Hz), 7.53 (1 H, t, J = 7.5 Hz), 7.38-7.34 (2 H, m), 7.24 (3 H, dt, J = 3.6, 2.2 Hz), 7.20-7.17 (2 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 162.4, 140.1, 138.7, 137.6, 135.5, 134.9, 134.6, 134.2, 133.6, 133.5, 129.4 (d, J = 5.2 Hz), 129.0 (t, J = 6.7 Hz), 128.6, 127.5, 127.4, 127.0, 123.0, 122.3, 112.8.
^{19}F NMR (377 MHz, $CDCl_3$) δ -63.1.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO_2$ $(M+H)^+$: 394.1049, found: 394.1057.



5-4ha

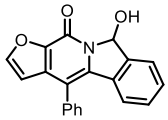
5-4ha was obtained as a yellow solid (31%). Melting point 190-192°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (1 H, s), 7.64 (1 H, d, J = 7.6 Hz), 7.61-7.55 (3 H, m), 7.42-7.34 (4 H, m), 7.13 (2 H, dd, J = 15.6, 8.1 Hz), 7.02 (1 H, s), 6.38 (1 H, d, J = 7.9 Hz), 5.69 (1 H, s), 2.49 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 138.7, 137.0, 136.9, 135.2, 134.8, 134.1, 133.3, 130.8, 129.7, 129.4, 129.3, 128.5, 126.8, 125.6, 124.9, 124.3, 123.6, 115.4, 84.1, 21.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1339.



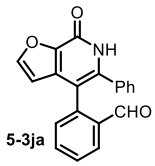
5-3ha

5-3ha was obtained as a yellow solid (61%). Melting point 257-259°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (1 H, s), 9.84 (1 H, s), 8.28 (1 H, s), 7.92 (1 H, dd, J = 7.8, 1.1 Hz), 7.58 (1 H, td, J = 7.5, 1.4 Hz), 7.48-7.40 (2 H, m), 7.30 (1 H, d, J = 7.6 Hz), 7.23 (5 H, m), 7.02 (1 H, d, J = 8.3 Hz), 2.49 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 162.9, 139.4, 137.7, 137.3, 136.4, 135.6, 134.6, 134.2, 133.9, 133.5, 129.0, 129.0, 128.5, 128.4, 127.9, 127.3, 125.3, 124.8, 112.5, 21.3.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1340.



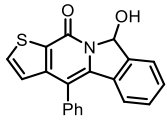
5-4ja

5-4ja was obtained as a yellow solid (20%). Melting point 185-187°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (1 H, d, J = 2.0 Hz), 7.65 (1 H, d, J = 7.7 Hz), 7.59-7.51 (3 H, m), 7.50-7.42 (2 H, m), 7.38 (1 H, td, J = 7.5, 0.9 Hz), 7.22-7.13 (1 H, m), 6.99 (1 H, s), 6.83 (1 H, d, J = 7.9 Hz), 6.45 (1 H, d, J = 2.0 Hz), 5.50 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 148.8, 141.8, 139.2, 137.0, 134.1, 132.8, 129.9, 129.9, 129.8, 129.5, 129.3, 128.7, 124.4, 123.1, 111.7, 107.4, 84.3.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_3$ $(M+H)^+$: 316.0968, found: 316.0981.



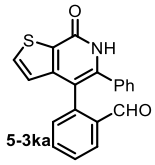
5-3ja

5-3ja was obtained as a yellow solid (32%). Melting point 84-86°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (1 H, s), 9.88 (1 H, s), 7.89 (1 H, dd, J = 7.8, 1.2 Hz), 7.77 (1 H, d, J = 1.9 Hz), 7.58 (1 H, td, J = 7.5, 1.4 Hz), 7.46 (2 H, t, J = 7.5 Hz), 7.32-7.29 (1 H, m), 7.26 (1 H, s), 7.19 (2 H, dd, J = 7.8, 1.4 Hz), 7.14-7.09 (1 H, m), 6.39 (1 H, d, J = 2.0 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 160.2, 153.6, 149.1, 144.3, 141.8, 136.3, 134.3, 134.0, 133.0, 132.3, 129.4, 128.7, 128.5, 115.1, 112.2, 109.3, 107.2.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_3$ $(M+H)^+$: 316.0968, found: 316.0969.



5-4ka

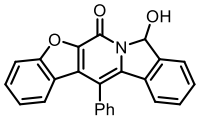
5-4ka was obtained as a yellow solid (31%). Melting point 204-206°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (2 H, d, J = 5.3 Hz), 7.56 (3 H, m), 7.48-7.35 (3 H, m), 7.16 (1 H, dd, J = 11.3, 4.0 Hz), 6.99 (1 H, s), 6.90 (1 H, d, J = 5.2 Hz), 6.64 (1 H, d, J = 7.9 Hz), 5.54 (1 H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 148.6, 138.9, 137.9, 134.9, 133.4, 133.0, 130.2, 129.8, 129.7, 129.3, 129.2, 128.6, 124.6, 124.4, 123.4, 114.2, 84.2.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_2S$ $(M+H)^+$: 332.0740, found: 332.0740.



5-3ka

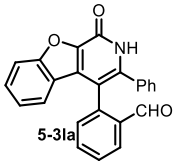
5-3ka was obtained as a yellow solid (51%). Melting point 205-207°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (1 H, s), 9.87 (1 H, d, J = 0.5 Hz), 7.90 (1 H, dd, J = 7.8, 1.3 Hz), 7.71 (1 H, d, J = 5.2 Hz), 7.62-7.43 (3 H, m), 7.33 (1 H, dd, J = 7.6, 1.0 Hz), 7.30-7.27 (1 H, m), 7.24 (1 H, d, J = 5.4 Hz), 7.20 (2 H, dd, J = 7.9, 1.8 Hz), 6.85 (1 H, d, J = 5.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 191.1, 159.2, 147.7, 140.3, 139.5, 134.7, 134.4, 133.3, 132.7, 129.2, 128.7, 128.5, 128.2, 127.8, 124.5, 111.6.
HRMS (ESI, m/z) calcd for $C_{20}H_{14}NO_2S$ (M+H) $^+$: 332.0740, found: 332.0748.



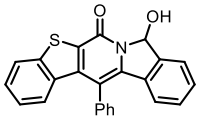
5-4la

5-4la was obtained as a yellow solid (21%). Melting point 332-334°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.62 (5 H, m), 7.57-7.36 (4 H, m), 7.14 (2 H, m), 7.04 (1 H, s), 6.79 (1 H, d, J = 8.0 Hz), 6.64 (1 H, d, J = 7.9 Hz), 5.45 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 153.6, 142.6, 139.1, 137.4, 133.9, 132.9, 131.4, 130.1, 130.0, 129.7, 129.6, 129.1, 128.8, 124.5, 123.5, 123.3, 123.2, 122.9, 112.8, 112.2, 84.7.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_3$ (M+H) $^+$: 366.1125, found: 366.1131.



5-3la

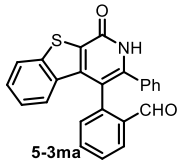
5-3la was obtained as a yellow solid (36%). Melting point 242-244°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.36 (1 H, s), 9.94 (1 H, s), 7.98 (1 H, dd, J = 7.7, 1.2 Hz), 7.68-7.63 (2 H, m), 7.58 (1 H, t, J = 7.4 Hz), 7.50-7.42 (2 H, m), 7.28-7.26 (5 H, m), 7.09 (1 H, t, J = 7.6 Hz), 6.67 (1 H, d, J = 7.9 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 157.2, 154.7, 142.7, 139.9, 138.2, 134.9, 134.1, 132.9, 132.9, 130.6, 129.3, 129.3, 129.1, 129.0, 128.6, 123.6, 122.9, 122.4, 112.9, 110.1.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_3$ (M+H) $^+$: 366.1125, found: 366.1135.



5-4ma

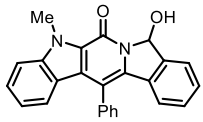
5-4ma was obtained as a yellow solid (25%). Melting point 259-261°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1 H, d, J = 8.1 Hz), 7.73-7.60 (4 H, m), 7.51 (2 H, m), 7.40 (2 H, m), 7.18-7.07 (2 H, m), 7.01 (1 H, s), 6.79 (1 H, d, J = 8.3 Hz), 6.32 (1 H, d, J = 7.9 Hz), 5.49 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 142.8, 142.1, 138.7, 135.7, 135.0, 133.2, 130.5, 130.4, 130.0, 129.9, 129.7, 129.2, 129.0, 127.5, 125.7, 124.5, 124.4, 123.6, 123.5, 115.0, 84.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_2S$ $(M+H)^+$: 382.0896, found: 382.0893.



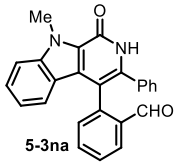
5-3ma

5-3ma was obtained as a yellow solid (60%). Melting point 275-277°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.90 (1 H, s), 9.91 (1 H, s), 7.98-7.90 (2 H, m), 7.84-7.80 (3 H, m), 7.65-7.59 (1 H, m), 7.43-7.38 (4 H, m), 7.20 (1 H, d, J = 1.6 Hz), 7.09-7.03 (1 H, m), 6.56 (1 H, d, J = 8.4 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0, 164.4, 159.6, 142.9, 141.4, 141.3, 140.9, 139.0, 137.4, 135.3, 134.2, 133.3, 129.3, 128.5, 126.4, 125.2, 124.6, 123.6, 122.7, 112.4.
HRMS (ESI, m/z) calcd for $C_{24}H_{16}NO_2S$ $(M+H)^+$: 382.0896, found: 382.0894.



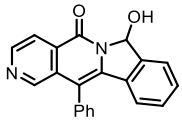
5-4na

5-4na was obtained as a yellow solid (32%). Melting point 264-266°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.59 (4 H, m), 7.58-7.47 (2 H, m), 7.47-7.40 (2 H, m), 7.31 (1 H, td, J = 7.5, 1.0 Hz), 7.14 (1 H, t, J = 7.2 Hz), 7.02 (1 H, d, J = 2.6 Hz), 6.95 (1 H, m), 6.76 (1 H, d, J = 8.1 Hz), 6.50 (1 H, d, J = 7.9 Hz), 5.45 (1 H, d, J = 3.0 Hz), 4.39 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 141.5, 138.3, 135.5, 133.8, 133.0, 130.2, 129.8, 129.5, 128.7, 128.4, 126.7, 126.6, 126.0, 124.2, 122.8, 122.5, 122.0, 120.2, 114.3, 110.0, 84.4, 31.4.
HRMS (ESI, m/z) calcd for $C_{25}H_{19}N_2O_2$ $(M+H)^+$: 379.1441, found: 379.1447.



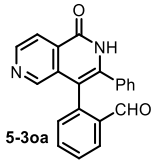
5-3na

5-3na was obtained as a yellow solid (46%). Melting point 280-282°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.04 (1 H, s), 9.92 (1 H, s), 7.98 (1 H, dd, J = 7.7, 1.3 Hz), 7.65 (1 H, td, J = 7.4, 1.5 Hz), 7.55 (1 H, t, J = 7.4 Hz), 7.49-7.42 (3 H, m), 7.25 (5 H, d, J = 4.1 Hz), 6.92 (1 H, m), 6.61 (1 H, d, J = 8.2 Hz), 4.30 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 191.4, 157.0, 141.4, 140.1, 135.2, 135.0, 134.0, 133.9, 133.1, 129.5, 128.7, 128.5, 128.4, 127.8, 126.8, 125.9, 125.7, 122.3, 121.6, 120.3, 111.3, 110.1, 31.2.
HRMS (ESI, m/z) calcd for $C_{25}H_{19}N_2O_2$ $(M+H)^+$: 379.1441, found: 379.1445.



5-4oa

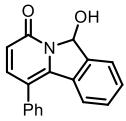
5-4oa was obtained as a yellow solid (23%). Melting point 246-248°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (1 H, d, J = 4.5 Hz), 8.43 (1 H, s), 8.17 (1 H, d, J = 5.1 Hz), 7.67 (2 H, dd, J = 6.1, 3.0 Hz), 7.63 (1 H, d, J = 7.6 Hz), 7.54 (1 H, dd, J = 6.7, 1.3 Hz), 7.50-7.43 (3 H, m), 7.26-7.21 (2 H, m), 6.88 (1 H, d, J = 7.5 Hz), 6.31 (1 H, d, J = 7.9 Hz).
^{13}C NMR (151 MHz, DMSO-d_6) δ 160.7, 158.7, 148.1, 146.2, 141.1, 137.8, 134.3, 133.9, 133.0, 131.7, 130.7, 129.9, 129.8, 127.8, 123.0, 119.1, 113.6, 111.6, 83.4.
HRMS (ESI, m/z) calcd for $C_{21}H_{15}N_2O_2$ $(M+H)^+$: 327.1128, found: 327.1130.



5-3oa

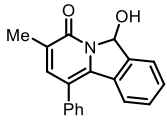
5-3oa was obtained as a yellow solid (39%). Melting point 248-250°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (1 H, s), 9.81 (1 H, s), 8.73 (1 H, d, J = 5.1 Hz), 8.54 (1 H, d, J = 7.2 Hz), 8.22 (1 H, d, J = 5.2 Hz), 7.92 (1 H, dd, J = 7.7, 1.2 Hz), 7.69-7.65 (1 H, m), 7.63 (1 H, dd, J = 7.5, 1.4

Hz), 7.56-7.52 (1 H, m), 7.50-7.44 (1 H, m), 7.38-7.35 (1 H, m), 7.30 (1 H, d, *J* = 3.0 Hz), 7.18 (2 H, dd, *J* = 8.1, 1.4 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 161.6, 148.8, 146.6, 139.9, 136.7, 135.5, 134.1, 133.5, 133.5, 132.1, 129.8, 129.7, 129.6, 129.1, 128.9, 128.8, 119.6, 111.2.
HRMS (ESI, m/z) calcd for $C_{21}H_{15}N_2O_2$ $(M+H)^+$: 327.1128, found: 327.1130.



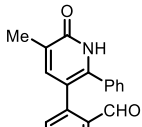
5-4pa

5-4pa was obtained as a yellow solid (20%). Melting point 183-185°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (1 H, d, *J* = 7.6 Hz), 7.50 (3 H, tt, *J* = 8.4, 4.1 Hz), 7.43 (4 H, dd, *J* = 12.0, 5.0 Hz), 7.21 (1 H, t, *J* = 7.5 Hz), 6.94 (1 H, d, *J* = 7.9 Hz), 6.87 (1 H, s), 6.57 (1 H, d, *J* = 9.2 Hz), 5.68 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 144.6, 141.7, 139.1, 136.4, 132.5, 130.4, 129.8, 129.4, 129.0, 128.4, 124.4, 123.6, 118.6, 117.7, 84.9.
HRMS (ESI, m/z) calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 276.1019, found: 276.1020.



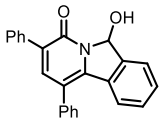
5-4ra

5-4ra was obtained as a dark solid (39%). Melting point 185-187°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (1 H, d, *J* = 7.6 Hz), 7.52-7.45 (3 H, m), 7.44-7.36 (3 H, m), 7.29 (1 H, d, *J* = 1.0 Hz), 7.19 (1 H, t, *J* = 7.7 Hz), 6.94 (1 H, d, *J* = 7.9 Hz), 6.87 (1 H, s), 5.73 (1 H, s), 2.25 (3 H, d, *J* = 0.7 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 142.0, 139.2, 138.9, 136.7, 132.8, 129.9, 129.7, 129.4, 128.9, 128.2, 128.0, 124.3, 123.2, 117.4, 84.8, 16.0.
HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO_2$ $(M+H)^+$: 290.1176, found: 290.1178.



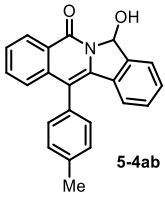
5-3ra

5-3ra was obtained as a dark solid (23%). Melting point 164-166°C.
^{1}H NMR (300 MHz, DMSO-d_6) δ 11.87 (1 H, s), 9.80 (1 H, d, J = 0.5 Hz), 7.66 (1 H, dd, J = 7.7, 1.2 Hz), 7.59 (1 H, td, J = 7.5, 1.5 Hz), 7.45-7.39 (2 H, m), 7.29 (1 H, dd, J = 7.7, 0.8 Hz), 7.25-7.17 (3 H, m), 7.11 (2 H, dd, J = 7.9, 1.7 Hz), 2.08 (3 H, d, J = 0.9 Hz).
^{13}C NMR (151 MHz, DMSO-d_6) δ 191.7, 163.3, 142.0, 141.2, 134.3, 134.0, 132.7, 130.2, 129.2, 128.5, 128.3, 128.0, 16.5.
HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO_2$ (M+H) $^{+}$: 290.1176, found: 290.1181.



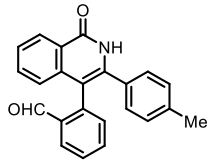
5-4sa

5-4sa was obtained as a yellow solid (45%). Melting point 116-118°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84-7.74 (2 H, m), 7.68 (1 H, d, J = 7.6 Hz), 7.61 (1 H, s), 7.53-7.32 (9 H, m), 7.22 (1 H, d, J = 7.2 Hz), 6.99 (1 H, d, J = 7.9 Hz), 6.93 (1 H, s), 5.67 (1 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 142.4, 140.7, 139.3, 136.5, 135.6, 132.5, 130.3, 129.9, 129.6, 129.5, 129.0, 128.6, 128.4, 128.3, 128.0, 124.4, 123.5, 117.8, 85.3.
HRMS (ESI, m/z) calcd for $C_{24}H_{18}NO_2$ (M+H) $^{+}$: 352.1332, found: 352.1346.



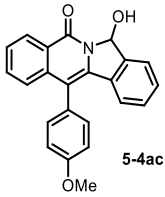
5-4ab

5-4ab was obtained as a yellow solid (35%). Melting point 197-199°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1 H, dd, J = 7.9, 0.8 Hz), 7.65 (1 H, d, J = 7.6 Hz), 7.59-7.54 (1 H, m), 7.52-7.46 (1 H, m), 7.42-7.35 (3 H, m), 7.29 (1 H, dd, J = 6.2, 3.3 Hz), 7.24 (2 H, dd, J = 8.3, 5.8 Hz), 7.17 (1 H, t, J = 7.6 Hz), 7.03 (1 H, d, J = 2.7 Hz), 6.47 (1 H, d, J = 7.9 Hz), 5.60 (1 H, dd, J = 12.1, 5.3 Hz), 2.52 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 139.4, 138.8, 138.3, 136.1, 133.3, 132.6, 131.5, 130.7, 130.2, 129.8, 129.6, 127.2, 126.7, 125.7, 125.0, 124.3, 123.9, 115.4, 84.1, 21.5.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ (M+H) $^{+}$: 340.1332, found: 340.1339.



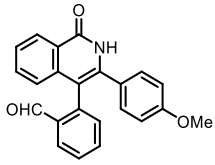
5-3ab

5-3ab was obtained as a yellow solid (53%). Melting point 240-242°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (1 H, d, J = 37.8 Hz), 9.85 (1 H, d, J = 0.5 Hz), 8.47 (1 H, d, J = 7.9 Hz), 7.93 (1 H, dd, J = 7.8, 1.2 Hz), 7.59 (2 H, m), 7.50 (2 H, m), 7.33 (1 H, dd, J = 7.6, 0.7 Hz), 7.12-7.01 (5 H, m), 2.28 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 162.9, 139.5, 139.2, 138.7, 135.5, 134.0, 133.5, 133.1, 131.2, 129.3, 128.8, 128.4, 128.0, 127.7, 126.9, 125.2, 124.8, 112.2, 21.2.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1340.



5-4ac

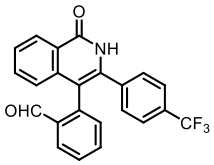
5-4ac was obtained as a yellow solid (37%). Melting point 198-200°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (1 H, dd, J = 7.8, 1.1 Hz), 7.65 (1 H, d, J = 7.4 Hz), 7.62-7.45 (2 H, m), 7.38 (1 H, td, J = 7.5, 0.8 Hz), 7.35-7.25 (3 H, m), 7.24-7.18 (1 H, m), 7.17-7.09 (2 H, m), 7.02 (1 H, d, J = 3.1 Hz), 6.50 (1 H, d, J = 7.9 Hz), 5.58 (1 H, d, J = 3.2 Hz), 3.95 (3 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.9, 159.7, 139.5, 138.8, 136.3, 133.4, 132.5, 131.9, 129.8, 129.6, 127.2, 126.7, 126.6, 125.6, 125.0, 124.3, 123.9, 114.9, 114.8, 84.1, 55.4.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1297.



5-3ac

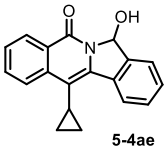
5-3ac was obtained as a yellow solid (48%). Melting point 244-246°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (1 H, s), 9.41 (1 H, s), 8.49 (1 H, d, *J* = 7.1 Hz), 7.94 (1 H, dd, *J* = 7.8, 1.1 Hz), 7.85-7.77 (1 H, m), 7.64-7.56 (2 H, m), 7.54-7.44 (3 H, m), 7.33 (1 H, d, *J* = 7.4 Hz), 7.09 (2 H, d, *J* = 8.8 Hz), 6.74 (1 H, d, *J* = 8.8 Hz), 3.75 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 162.8, 160.0, 139.5, 138.8, 138.3, 135.5, 134.0, 133.5, 133.2, 130.2, 128.6, 128.5, 128.1, 127.7, 127.3, 126.9, 125.2, 124.8, 114.1, 55.2.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_3$ $(M+H)^+$: 356.1281, found: 356.1296.



5-3ad

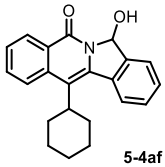
5-3ad was obtained as a yellow solid (85%). Melting point 234-236°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.43 (1 H, s), 9.86 (1 H, s), 8.44-8.35 (1 H, m), 7.95 (1 H, dd, *J* = 7.7, 1.0 Hz), 7.61 (2 H, t, *J* = 7.5 Hz), 7.57-7.50 (4 H, m), 7.39 (2 H, d, *J* = 8.2 Hz), 7.33-7.28 (1 H, m), 7.12 (1 H, d, *J* = 8.0 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 163.6, 138.4 (d, *J* = 1.2 Hz), 137.5, 137.3, 135.7, 134.2, 133.4 (d, *J* = 7.3 Hz), 129.9, 128.8 (d, *J* = 11.8 Hz), 127.6 (d, *J* = 13.7 Hz), 125.4 (dd, *J* = 7.2, 3.4 Hz), 124.9, 113.8.
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.9.
HRMS (ESI, m/z) calcd for $C_{23}H_{15}F_3NO_2$ $(M+H)^+$: 394.1049, found: 394.1062.



5-4ae

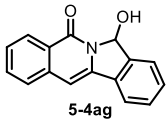
5-4ae was obtained as a yellow solid (72%). Melting point 205-207°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (1 H, dd, *J* = 8.0, 1.0 Hz), 8.32 (2 H, dd, *J* = 7.8, 4.9 Hz), 7.74 (2 H, m), 7.60-7.48 (3 H, m), 6.94 (1 H, s), 5.37 (1 H, d, *J* = 2.1 Hz), 2.07 (1 H, tt, *J* = 8.1, 5.4 Hz), 1.35 (2 H, m), 0.71 (2 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 139.8, 139.0, 138.8, 133.3, 132.3, 129.8, 129.6, 127.2, 126.6, 125.7, 125.3, 125.2, 124.3, 114.5, 84.1, 10.6, 10.5, 7.9.

HRMS (ESI, m/z) calcd for $C_{19}H_{16}NO_2$ $(M+H)^+$: 290.1176, found: 290.1172.



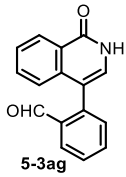
5-4af

5-4af was obtained as a yellow solid (64%). Melting point 192-194°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (1 H, dd, J = 8.0, 1.3 Hz), 8.21 (1 H, d, J = 8.4 Hz), 7.94 (1 H, d, J = 7.8 Hz), 7.75-7.62 (2 H, m), 7.57-7.46 (3 H, m), 6.93 (1 H, s), 5.77 (1 H, s), 3.74 (1 H, tt, J = 12.6, 3.3 Hz), 2.31 (2 H, qd, J = 12.7, 3.2 Hz), 1.94 (5 H, m), 1.61-1.42 (3 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 139.3, 138.0, 135.8, 133.9, 131.5, 130.2, 129.4, 127.7, 126.4, 126.2, 125.9, 124.9, 124.2, 119.7, 83.5, 38.9, 31.0, 27.5, 26.0.
HRMS (ESI, m/z) calcd for $C_{22}H_{22}NO_2$ $(M+H)^+$: 332.1645, found: 332.1650.



5-4ag

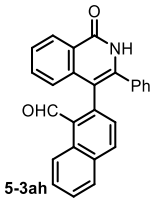
5-4ag was obtained as a yellow solid (42%, 30%). Melting point 153-155°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (1 H, d, J = 8.0 Hz), 7.72 (1 H, dd, J = 6.1, 2.1 Hz), 7.69-7.63 (2 H, m), 7.60 (1 H, d, J = 7.3 Hz), 7.52-7.48 (2 H, m), 7.46 (1 H, dd, J = 7.0, 1.2 Hz), 6.95 (1 H, s), 6.94 (1 H, s), 5.36 (1 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 139.8, 138.5, 138.2, 132.9, 132.8, 130.3, 130.2, 127.4, 126.8, 126.8, 125.5, 124.6, 120.9, 99.0, 84.6.
HRMS (ESI, m/z) calcd for $C_{16}H_{12}NO_2$ $(M+H)^+$: 250.0863, found: 250.0871.



5-3ag

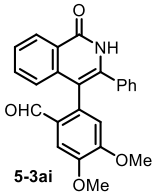
5-3ag was obtained as a colorless oil (51%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (1 H, s), 9.67 (1 H, d, J = 5.6 Hz), 8.03-7.98 (1 H, m), 7.87 (1 H, d, J = 7.6 Hz), 7.68-7.63 (1 H, m), 7.60-

7.55 (2 H, m), 7.45 (1 H, t, *J* = 7.5 Hz), 7.34-7.29 (1 H, m), 7.02-6.97 (2 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 168.7, 137.7, 136.4, 135.2, 134.4, 134.0, 132.0, 131.5, 131.4, 130.1, 129.8, 128.6, 123.6, 123.1, 108.1.
HRMS (ESI, m/z) calcd for $C_{16}H_{12}NO_2$ $(M+H)^+$: 250.0863, found: 250.0869.



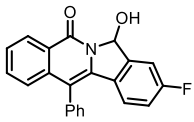
5-3ah

5-3ah was obtained as a yellow solid (45%). Melting point 209-211°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (1 H, s), 9.97 (1 H, s), 8.51 (1 H, dd, *J* = 7.8, 1.4 Hz), 7.92 (2 H, s), 7.79 (1 H, d, *J* = 8.4 Hz), 7.65-7.60 (1 H, m), 7.54-7.44 (4 H, m), 7.16 (1 H, dd, *J* = 8.7, 4.4 Hz), 7.09 (4 H, t, *J* = 4.2 Hz), 6.85-6.77 (1 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 163.3, 139.8, 139.7, 138.9, 137.4, 136.1, 134.0, 133.7, 133.4, 132.8, 129.3, 129.2, 129.0, 128.7, 128.5, 128.0, 127.7, 127.6, 127.2, 127.1, 125.9, 122.6, 109.8.
HRMS (ESI, m/z) calcd for $C_{26}H_{18}NO_2$ $(M+H)^+$: 376.1332, found: 376.1346.



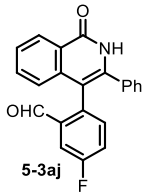
5-3ai

5-3ai was obtained as a yellow solid (85%). Melting point 208-210°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.48 (1 H, s), 9.71 (1 H, s), 8.47 (1 H, dd, *J* = 7.9, 1.2 Hz), 7.65-7.59 (1 H, m), 7.56-7.49 (2 H, m), 7.43 (1 H, s), 7.30 (1 H, dd, *J* = 4.4, 2.2 Hz), 7.25 (2 H, d, *J* = 5.0 Hz), 7.23-7.17 (2 H, m), 6.71 (1 H, s), 3.95 (3 H, s), 3.81 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.1, 163.0, 153.9, 149.1, 138.9, 134.3, 133.2, 129.1, 129.0, 128.8, 128.7, 128.5, 127.7, 127.3, 127.0, 125.3, 124.8, 114.9, 112.2, 108.6, 56.2, 56.0.
HRMS (ESI, m/z) calcd for $C_{24}H_{20}NO_4$ $(M+H)^+$: 386.1387, found: 386.1386.



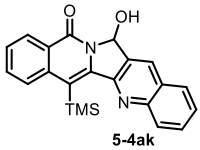
5-4aj

5-4aj was obtained as a yellow solid (43%). Melting point 112-114°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (1 H, dd, J = 7.9, 1.2 Hz), 7.64-7.55 (4 H, m), 7.54-7.47 (1 H, m), 7.43-7.33 (3 H, m), 7.20 (1 H, dd, J = 8.1, 0.7 Hz), 7.01 (1 H, s), 6.85 (1 H, td, J = 8.8, 2.5 Hz), 6.33 (1 H, dd, J = 8.7, 4.9 Hz).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 162.3, 161.9, 141.3 (d, J = 8.9 Hz), 139.1, 135.3, 134.4, 132.8, 130.8 (d, J = 7.6 Hz), 129.6 (d, J = 7.6 Hz), 129.2 (d, J = 2.7 Hz), 128.7, 127.3, 126.8, 125.5 (d, J = 7.4 Hz), 124.7, 117.4 (d, J = 23.0 Hz), 115.0 (d, J = 1.8 Hz), 111.8 (d, J = 24.0 Hz), 83.6 (d, J = 2.7 Hz).
^{19}F NMR (377 MHz, $CDCl_3$) δ -109.5.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}FNO_2$ $(M+H)^+$: 344.1081, found: 344.1075.



5-3aj

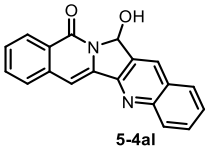
5-3aj was obtained as a yellow solid (50%). Melting point 189-191°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.34 (1 H, s), 9.78 (1 H, d, J = 3.1 Hz), 8.45 (1 H, dd, J = 7.9, 1.1 Hz), 7.65-7.50 (3 H, m), 7.34-7.26 (5 H, m), 7.22-7.16 (2 H, m), 7.13-7.08 (1 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0 (d, J = 1.6 Hz), 163.7, 163.1, 161.2, 139.3, 138.6, 137.3 (d, J = 6.4 Hz), 135.4 (d, J = 7.2 Hz), 135.2 (d, J = 3.4 Hz), 133.9, 133.3, 129.2, 129.1, 128.7, 127.8, 127.2, 125.0 (d, J = 16.2 Hz), 121.3 (d, J = 22.0 Hz), 114.2 (d, J = 22.3 Hz), 111.4.
^{19}F NMR (377 MHz, $CDCl_3$) δ -111.3.
HRMS (ESI, m/z) calcd for $C_{22}H_{15}FNO_2$ $(M+H)^+$: 344.1081, found: 344.1074.



5-4ak

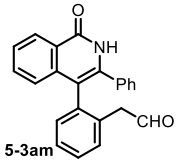
5-4ak was obtained as a yellow solid (65%). Melting point 243-245°C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (1 H, dd, J = 7.9, 1.2 Hz), 8.44 (1 H, s), 8.21 (1 H, d, J = 8.3 Hz), 8.17 (1 H, d, J = 8.4 Hz), 7.94 (1 H, d, J = 8.0 Hz), 7.81 (1 H, dd, J = 11.2, 4.1 Hz), 7.73-7.69 (1 H, m), 7.63 (1 H, t, J = 7.4 Hz), 7.56 (1 H, t, J = 7.4 Hz), 7.15 (1 H, s), 5.54 (1 H, s), 0.67 (9 H, s).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4, 153.4, 148.9, 143.4, 142.1, 132.0, 131.9, 130.6, 130.2, 129.5, 129.2, 128.5, 127.6, 127.4, 127.4, 127.1, 126.3, 114.2, 82.2, 4.0.
HRMS (ESI, m/z) calcd for $C_{22}H_{21}N_2O_2Si$ $(M+H)^+$: 373.1367, found: 373.1379.



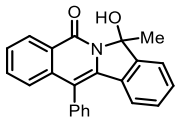
5-4al

5-4al was obtained as a yellow solid (46%).
^{1}H NMR (600 MHz, DMSO-d_6) δ 8.67 (1 H, s), 8.34 (1 H, d, J = 7.8 Hz), 8.18-8.14 (2 H, m), 7.95 (1 H, d, J = 7.9 Hz), 7.87 (2 H, dd, J = 5.8, 2.7 Hz), 7.82-7.79 (1 H, m), 7.61 (1 H, dd, J = 11.1, 4.0 Hz), 7.59 (1 H, s), 7.45 (1 H, t, J = 7.6 Hz), 7.04 (1 H, d, J = 7.9 Hz).
^{13}C NMR (151 MHz, DMSO-d_6) δ 160.1, 152.0, 148.9, 138.6, 137.4, 132.8, 132.7, 131.2, 130.7, 129.0, 128.9, 128.2, 128.0, 127.6, 127.4, 127.3, 126.9, 99.7, 81.8.
Spectral data was consistent with that previously reported.[72]



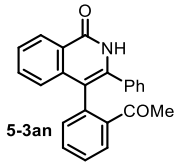
5-3am

5-3am was obtained as a yellow solid (62%). Melting point 127-129°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.41 (1 H, s), 9.06 (1 H, t, J = 2.1 Hz), 8.45-8.39 (1 H, m), 7.60-7.53 (1 H, m), 7.51-7.45 (1 H, m), 7.38-7.34 (3 H, m), 7.26 (5 H, d, J = 2.1 Hz), 7.19-7.15 (1 H, m), 7.12-7.08 (1 H, m), 3.39-3.21 (2 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 199.0, 163.2, 138.6, 137.7, 135.7, 134.3, 133.5, 132.9, 132.5, 130.8, 129.1, 129.0, 128.4, 128.4, 127.6, 127.5, 126.8, 125.3, 125.1, 114.8, 47.6.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1326.



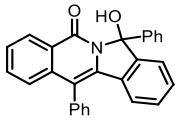
5-4an

5-4an was obtained as a yellow solid (31%). Melting point 145-147°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (1 H, dd, J = 7.9, 1.0 Hz), 7.60-7.54 (5 H, m), 7.52-7.47 (1 H, m), 7.45-7.41 (1 H, m), 7.37 (2 H, dd, J = 7.9, 7.3 Hz), 7.18 (1 H, d, J = 8.1 Hz), 7.14-7.08 (1 H, m), 6.32 (1 H, d, J = 7.9 Hz), 5.83 (1 H, s), 2.24 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 143.8, 138.9, 135.8, 134.8, 132.5, 131.6, 130.9, 130.8, 129.9, 129.6, 129.4, 128.6, 127.1, 126.7, 125.5, 123.8, 122.5, 115.2, 94.4, 27.0.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1338.



5-3an

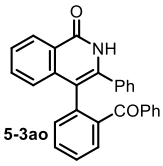
5-3an was obtained as a yellow solid (49%). Melting point 229-231°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (1 H, s), 8.45 (1 H, dd, J = 7.9, 0.9 Hz), 7.63 (1 H, dd, J = 7.7, 1.0 Hz), 7.60-7.54 (1 H, m), 7.48 (2 H, t, J = 7.5 Hz), 7.40 (1 H, td, J = 7.6, 1.2 Hz), 7.30 (1 H, d, J = 7.7 Hz), 7.28-7.18 (6 H, m), 2.09 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 162.9, 141.0, 138.4, 136.7, 134.8, 134.6, 133.8, 132.8, 131.3, 129.1, 128.8, 128.8, 128.3, 127.9, 127.7, 126.6, 125.1, 125.0, 116.1, 28.7.
HRMS (ESI, m/z) calcd for $C_{23}H_{18}NO_2$ $(M+H)^+$: 340.1332, found: 340.1337.



5-4ao

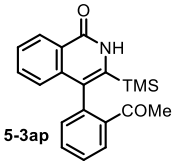
5-4ao was obtained as a dark solid (37%). Melting point 156-158°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (1 H, dd, J = 7.9, 1.2 Hz), 7.67-7.57 (4 H, m), 7.56-7.40 (6 H, m), 7.36-7.25 (5 H, m), 7.09-7.01 (1 H, m), 6.37 (1 H, d, J = 7.9 Hz).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6, 144.1, 141.6, 139.1, 136.7, 134.7, 132.7, 131.1, 130.8, 130.1, 129.6, 129.5, 129.4, 128.8, 128.7, 128.3, 127.4, 126.8, 125.6, 124.5, 123.9, 123.6, 115.2, 95.9.
HRMS (ESI, m/z) calcd for $C_{28}H_{20}NO_2$ $(M+H)^+$: 402.1489, found: 402.1483.



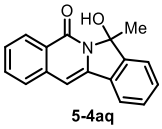
5-3ao

5-3ao was obtained as a yellow solid (46%). Melting point 241-243°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.09 (1 H, s), 8.36 (1 H, dd, *J* = 8.0, 1.1 Hz), 7.63-7.53 (3 H, m), 7.48-7.32 (5 H, m), 7.25-7.05 (9 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 162.7, 140.3, 138.7, 136.9, 136.7, 135.8, 134.6, 134.0, 132.5, 132.3, 130.4, 130.1, 129.3, 129.2, 128.8, 128.4, 127.8, 127.4, 127.2, 126.5, 125.7, 124.8, 115.5.
HRMS (ESI, m/z) calcd for $C_{28}H_{20}NO_2$ $(M+H)^+$: 402.1489, found: 402.1482.



5-3ap

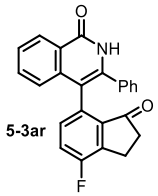
5-3ap was obtained as a yellow solid (33%). Melting point 203-205°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1 H, dd, *J* = 7.7, 1.1 Hz), 7.81 (1 H, d, *J* = 7.6 Hz), 7.60-7.57 (2 H, m), 7.51 (1 H, td, J = 7.6, 1.3 Hz), 7.35 (1 H, t, *J* = 7.5 Hz), 7.16 (2 H, dd, *J* = 11.3, 4.1 Hz), 5.99 (1 H, d, *J* = 7.9 Hz), 2.48 (3 H, s), 0.25 (9 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 168.1, 141.3, 136.7, 136.4, 132.6, 131.8, 131.1, 130.1, 129.9, 129.7, 128.7, 127.7, 127.0, 123.4, 123.2, 28.7, -0.6.
HRMS (ESI, m/z) calcd for $C_{20}H_{22}NO_2Si$ $(M+H)^+$: 336.1414, found: 336.1413.



5-4aq

5-4aq was obtained as a yellow solid (39%). Melting point 142-144°C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (1 H, d, *J* = 8.0 Hz), 7.73-7.70 (1 H, m), 7.68-7.64 (1 H, m), 7.60 (2 H, dd, *J* = 8.4, 3.2 Hz), 7.55 (1 H, d,

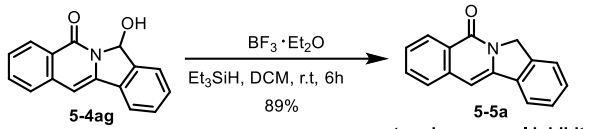
J = 1.9 Hz), 7.51-7.48 (2 H, m), 6.93 (1 H, s), 5.50 (1 H, s), 2.20 (3 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 143.3, 139.6, 137.9, 132.7, 131.1, 130.5, 130.0, 127.8, 127.3, 126.7, 126.6, 122.8, 120.8, 98.7, 94.9, 26.0.
HRMS (ESI, m/z) calcd for $C_{17}H_{14}NO_2$ $(M+H)^+$: 264.1019, found: 264.1014.



5-3ar

5-3ar was obtained as a yellow solid (53%). Melting point 264-266°C.
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.32 (1 H, s), 8.52-8.41 (1 H, m), 7.57-7.40 (3 H, m), 7.24-7.14 (6 H, m), 7.02-6.96 (1 H, m), 3.15-2.98 (2 H, m), 2.53 (2 H, m).
^{13}C NMR (151 MHz, $CDCl_3$) δ 203.7, 162.9, 159.5 (d, *J* = 251.0 Hz), 141.5 (d, *J* = 19.9 Hz), 138.5 (d, *J* = 4.8 Hz), 138.0 (d, *J* = 102.7 Hz), 134.9, 133.7 (d, *J* = 6.0 Hz), 132.6, 130.1 (d, *J* = 4.3 Hz), 129.1, 128.7, 128.6, 128.2, 127.5 (d, *J* = 47.7 Hz), 126.5, 125.0, 124.5, 120.1 (d, *J* = 20.1 Hz), 112.7, 36.1, 21.0.
^{19}F NMR (377 MHz, $CDCl_3$) δ -119.9.
HRMS (ESI, m/z) calcd for $C_{24}H_{17}FNO_2$ $(M+H)^+$: 370.1238, found: 370.1248.

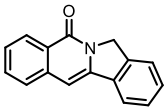
Transformations of annulation products



5-4ag
5-5a
topoisomerase I inhibitor

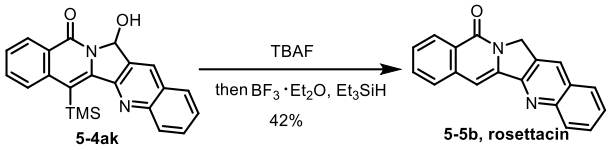
To the solution of **5-4ag** (0.2 mmol) in DCM (2 mL) was added $BF_3{\cdot}Et_2O$ (0.2 mmol) at 0 °C and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.6 mmol) dissolved in DCM (1 mL) was added dropwise for 5 min at 0 °C and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was

purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **5-5a** as a yellow solid (89%).

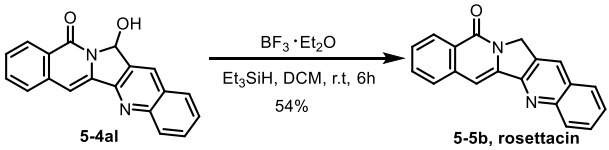


5-5a

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (1 H, d, J = 7.7 Hz), 7.81 (1 H, dd, J = 5.2, 3.5 Hz), 7.71-7.62 (2 H, m), 7.58 (1 H, dd, J = 5.6, 3.2 Hz), 7.52-7.44 (3 H, m), 7.04 (1 H, s), 5.20 (2 H, s).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 142.2, 137.9, 137.6, 134.1, 132.2, 129.8, 128.3, 127.4, 126.4, 126.2, 124.7, 123.5, 121.0, 98.0, 52.0.
Spectral data was consistent with that previously reported.[72]

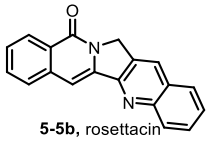


A 25 mL round-bottomed flask equipped with a stirring bar is charged with **5-4ak** (0.3 mmol), *tetra*-*n*-butylammonium fluoride (TBAF, 1 M in THF, 0.6 mL, 0.6 mmol) and 2 mL of anhydrous THF.[16] Then allowed to stir at room temperature for 12 h. The solvent was removed and the residue was used in next step without further purification.
To the solution of above residue in DCM (3 mL) was added $BF_3{\cdot}Et_2O$ (0.3 mmol) at 0 ℃ and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.9 mmol) dissolved in DCM (1.5 mL) was added dropwise for 5 min at 0 ℃ and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **5-5b** as a yellow solid (42%, two steps).



To the solution of **5-4al** (0.2 mmol) in DCM (2 mL) was added $BF_3{\cdot}Et_2O$ (0.2 mmol) at 0 ℃ and stirred for 5 minutes.[72] To the resulting solution, Et_3SiH (0.6 mmol) dissolved in DCM (1 mL) was added

dropwise for 5 min at 0 °C and stirred at room temperature for 6 h. After completion of the reaction (monitored by TLC), the mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by a silica gel column chromatography (*n*-heptane/ethyl acetate) to afford **5-5b** as a yellow solid (54%).



5-5b, rosettacin

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (1 H, d, J = 8.0 Hz), 8.26 (1 H, s), 8.18 (1 H, d, J = 8.5 Hz), 7.85 (1 H, d, J = 8.2 Hz), 7.78-7.69 (3 H, m), 7.61 (1 H, s), 7.55 (2 H, m), 5.32 (2 H, d, J = 0.8 Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 153.6, 148.8, 139.9, 137.5, 132.4, 130.7, 130.2, 129.4, 128.8, 128.0, 128.0, 127.5, 127.3, 126.0, 101.1, 49.4.
Spectral data was consistent with that previously reported.[32]

Safety aspects

This part involves some guidelines for safely handling with chemicals, when repeating the experiments shown in this thesis.
Firstly, before starting any experiments, it is highly necessary to know the properties of all used chemicals from the MSDS. KU Leuven Database of Hazardous Products is another source to prepare yourself for the risk assessments. In this thesis, a lot of commercially available aryl acids, acid chlorides, aldehydes, ketones, alkynes, isocyanides, strong inorganic acids and bases, and metal salts are used as starting materials. Most of them are involved in the KU Leuven Database of Hazardous Products.
It should also be noted that improper operations of common solvents and materials may bring certain danger because of bulk quantities used. For example, chronic exposure to DCM is presumably carcinogenic. Long-term exposure to silica gel may result in chronic silicosis.
Isocyanides are very smelly and toxic, resulting in allergies after skin contact. Therefore they should only be handled in fumehood. All disposable syringes, glass and gloves exposed to isocyanides should be washed in the fumehood and all wastes should be treated with water before throwing away. When removing the solvents of reaction mixtures involving isocyanides, rotary evaporators in closed fumehood should be used.

List of publications

1. Asymmetric synthesis of hydrocarbazoles catalyzed by an octahedral chiral-at-rhodium lewis acid, Yong Huang, **Liangliang Song**, Lei Gong*, Eric Meggers*, *Chem. Asian J.* **2015**, *10*, 2738-2743.

2. Asymmetric dual catalysis via fragmentation of a single rhodium precursor complex, **Liangliang Song**, Lei Gong*, Eric Meggers*, *Chem. Commun.* **2016**, *52*, 7699-7702.

3. Gold-catalyzed diastereoselective domino dearomatization/ipso-cyclization/aza-Michael sequence: a facile access to diverse fused azaspiro tetracyclic scaffolds, Yi He, Zhenghua Li*, Guilong Tian, **Liangliang Song**, Luc Van Meervelt, Erik V. Van der Eycken*, *Chem. Commun.* **2017**, *53*, 6413-6416.

4. Rhodium(III)-catalyzed intramolecular annulation through C–H activation: concise synthesis of rosettacin and oxypalmatime, **Liangliang Song**, Guilong Tian*, Yi He, Erik V. Van der Eycken*, *Chem. Commun.* **2017**, *53*, 12394-12397.

5. Cationic gold(I)-catalyzed cascade bicyclizations for divergent synthesis of (spiro)polyheterocycles, Zhenghua Li†, **Liangliang Song**†(equal contribution), Luc Van Meervelt, Guilong Tian*, Erik V. Van der Eycken*, *ACS Catal.* **2018**, *8*, 6388-6393.

6. Rhodium(III)-catalyzed intermolecular cascade annulation through C-H activation: Concise synthesis of rosettacin, **Liangliang Song**, Guilong Tian, Erik V. Van der Eycken*, *Mol. Catal.* **2018**, *459*, 129-134.

7. Intramolecular cascade annulation triggered by C-H activation via rhodium hydride intermediate, **Liangliang Song**, Xiaoyong Zhang, Guilong Tian*, Koen Robeyns, Luc Van Meervelt, Jeremy N. Harvey*, Erik V. Van der Eycken*, *Mol. Catal.* **2019**, *463*, 30-36.

8. Intramolecular cascade annulation triggered by rhodium(III)-catalyzed sequential C(sp^2)-H activation and C(sp^3)-H amination, **Liangliang Song**, Guilong Tian, Johan Van der Eycken, Erik V. Van der Eycken*, *Beilstein J. Org. Chem.* **2019**, *15*, 571-576.

9. Chemo- and regioselective catalyst-controlled carbocyclization of alkynyl ketones: rapid synthesis of 1-indanones and 1-naphthols, **Liangliang Song**, Guilong Tian, Erik V. Van der Eycken*, *Chem. Eur. J.* **2019**, 25, 7645-7648.

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