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Annulations involving 1-indanones to access fused- and spiro frameworks

Suven Das *[a] and Arpita Dutta[b]

Indanones are prominent motifs found in number of natural products and pharmaceuticals. Particularly, 1-indanones occupy important niche in chemical landscape due to their easy accessibility and versatile reactivity. In the past few years, significant advancement has been achieved regarding cyclization of 1-indanone core. The present review focuses on recent (2016–2022) annulations involving 1-indanones for the construction of fused- and spirocyclic frameworks. In this context, new strategies for synthesis of various carbocyclic as well as heterocyclic skeletons are demonstrated. Mechanistic aspects of representative reactions are illustrated for better understanding of reaction pathways. A large number of transformations described in this review offer stereoselective formation of desired polycyclic compounds. Importantly, several reactions provide biologically relevant compounds and natural products, such as, plecarpenene/plecarpenone, swinhoeisterol A, cephanolides A–D, diptoindonesin G and atlanticone C.

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1. Introduction

Indanones are privileged structural motifs frequently found in numerous natural products and synthetically bioactive molecules.[1–6] In particular, annulated indanone scaffolds constitute key structural components of many bioactive natural products (Fig. 1). For example, jatropholone A and B isolated from the roots of *Jatropha integerrima*, exhibit antiplasmodial and cytotoxic activities.[7,8] Coleophomone A extracted from a fungus *Coleophoma* sp. displays bacterial transglycosylase activity,[9] whereas coleophomone D isolated from *Stachybotrys cylindrospora* reveal antifungal activity.[10] Fredericamycin A obtained from *Streptomyces griseus* displays antitumor/anticancer activity.[11,12] Euplectin (and coneuplectin), derived from the Lichen *Flavoparmelia euplecta* was found to exhibit promising cytotoxic and other biological activities.[13] Likewise, several spirobenzylisoquinoline alkaloids containing indanone motif, *viz.* sibiricine, corydaine, raddeanine and yenhusomidine are well known for their potent pharmacological relevance.[14,15]

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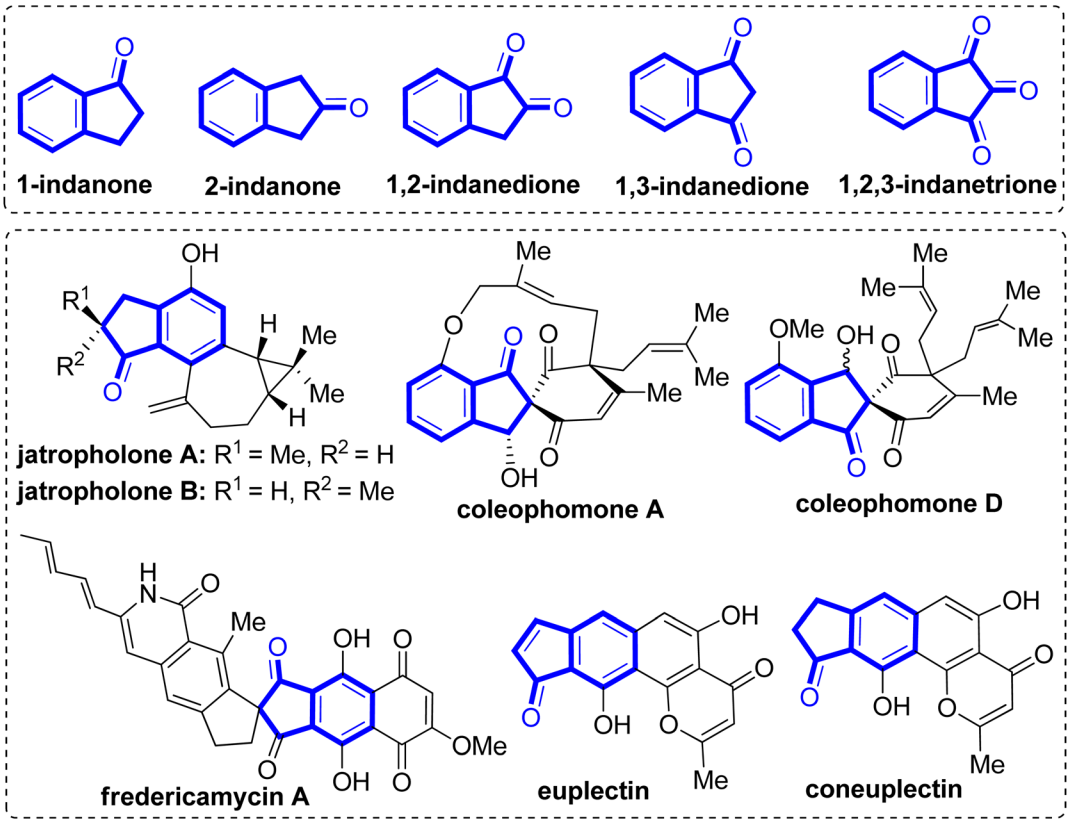


Fig. 1 Examples of various indanones and bioactive natural products containing indanone motif.

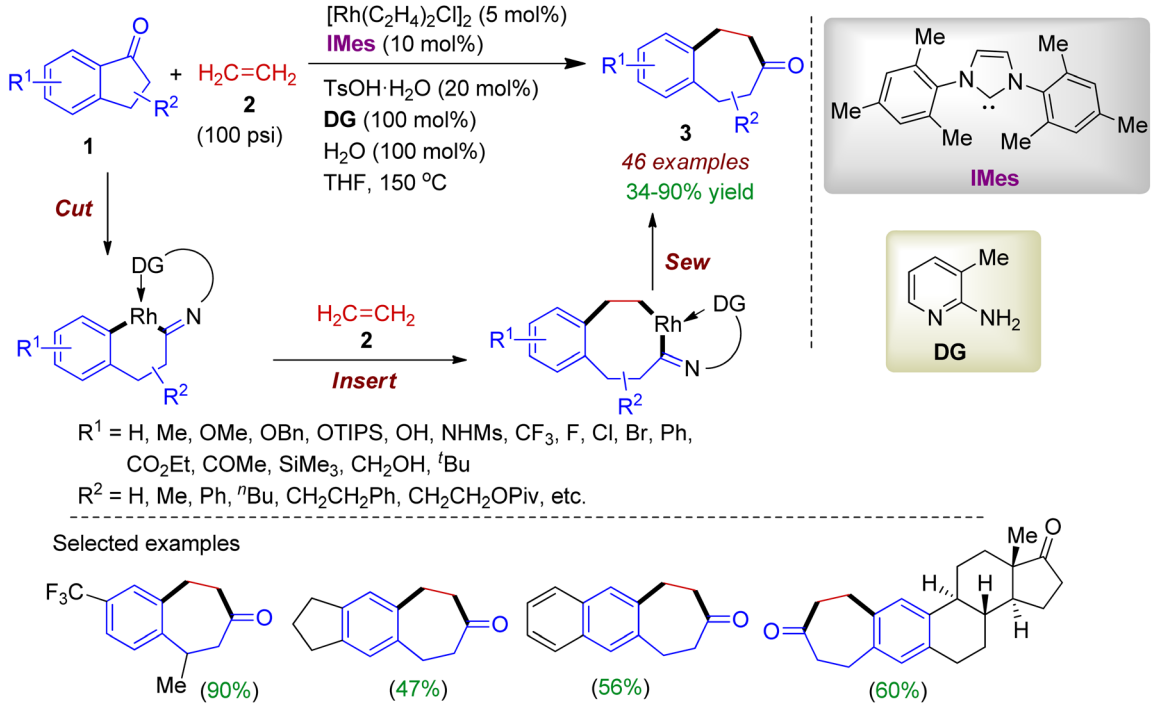
In addition to their profound biological profile, indanones have played significant role in the development of catalytic asymmetric synthesis.[16–18] Moreover, indanone derivatives are largely employed as organic functional materials,[19–21] OLEDs,[22] dyes and fluorophores.[23–27] Due to their ample appliances in different fields, various metal-catalyzed or metal-free methodologies have been adopted to develop 1-indanone core.[28,29] Previously, Chanda and Singh published a review article on synthesis and application of 3-hydroxyindanone scaffolds covering the literature until 2015.[30] However, the last few years have witnessed the emergence of efficient protocols for the target-oriented synthesis of novel annulation products involving 1-indanone moieties. This review emphasizes recent (2016–2022) applications of 1-indanones in cyclization to build up various fused- and spiro carbo-/heterocyclic compounds.

2. Synthesis of fused scaffolds

2.1. Fused carbocycles

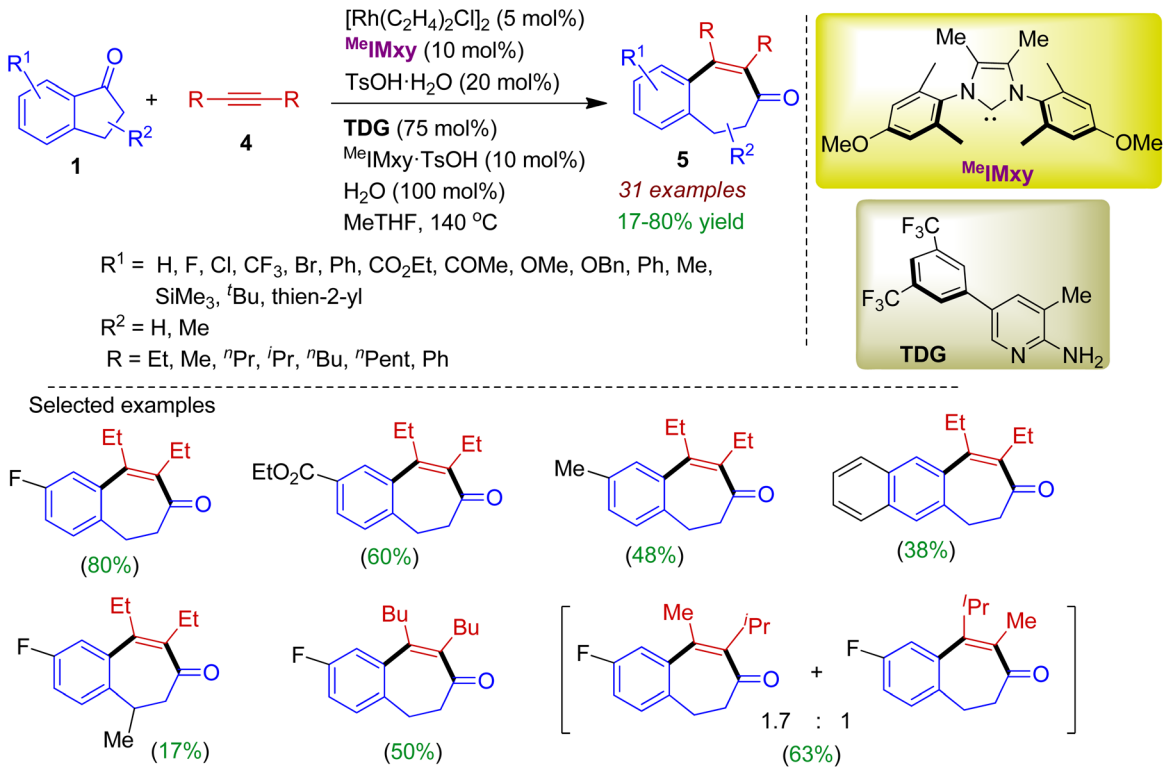
2.1.1. Benzannulated carbocycles *via* ring expansion. Ring expansion reactions of carbonyl compounds are frequently employed in organic transformations for the construction of complex molecular scaffolds. In this regard, 1-indanone **1** could serve as an effective cyclic substrate for various two-carbon ring expansion reactions. In 2019, Dong group carried out a rhodium-catalyzed direct insertion of ethylene **2** into relatively unstrained C–C bonds in 1-indanones **1** to form benzocycloheptenone skeleton **3**.[31] The reaction occurred in the presence of 5 mol% of catalyst $[Rh(C_2H_4)_2Cl]_2$, 10 mol% 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene (IMes, ligand), 20 mol% *p*-toluenesulfonic acid monohydrate ($TsOH\cdot H_2O$), 100 mol% 2-amino-3-picoline (donor group) and 100 mol% H_2O in THF to afford the desired compound. Substituted 1-indanones bearing electron-donating or -withdrawing substituents smoothly reacted with ethylene gas (100 psi) resulting benzannulated carbocycles in good yields (up to 90%). This two carbon ring-expansion reaction proceeded through "cut-insert-sew" fashion involving ethylene as a 2π unit (Scheme 1). The reaction is scalable, and also applied to natural product-derived or tethered indanones. Overall, the transition-metal catalyzed transformation is chemoselective, byproduct-free, redox-neutral, and applicable for straightforward synthesis of fused medium ring systems which are valuable synthetic intermediates for bioactive compounds.

In 2021, the same author synthesized similar type of ring expansion products employing internal alkynes as the reaction partner.[32] In fact, alkynes have better affinity with transition metals compared to alkenes due to smaller HOMO/LUMO gap, thereby facilitating the 2π-insertion process. The intermolecular [5+2] cycloaddition reaction between indanones **1** and internal alkynes **4** proceeded *via* the Rh-catalyzed C–C activation resulting richly decorated benzocycloheptenones **5** in moderate to good yields. The reaction was enabled by a strongly σ-donating NHC ligand (^{Me}IMxy) in the presence of a temporary



Scheme 1 Ring expansion of 1-indanones *via* insertion of ethylene to access fused seven-membered carbocycles.

directing group (TDG) containing an electron-deficient 3,5-ditrifluoromethylphenyl moiety as depicted in Scheme 2. As expected, 1-indanones bearing halogen, ester, ketone, trimethylsilyl, methoxy, phenyl, thienyl functionalities were compatible with this protocol. The reaction worked well for alkynes with different alkyl substituents, however, diaryl-substituted alkynes and terminal alkynes failed to provide desired carbocycles.

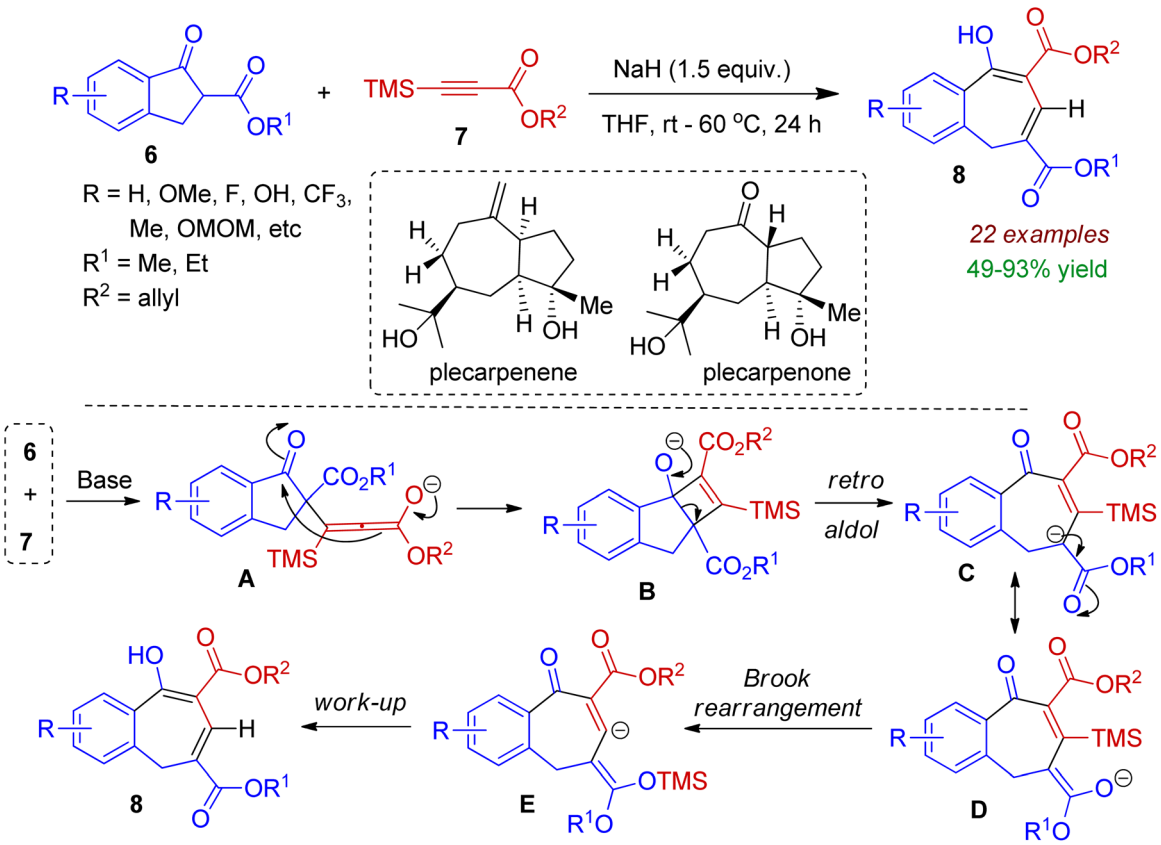


Scheme 2 Ring expansion of 1-indanones *via* insertion of alkynes to form fused seven-membered carbocycles.

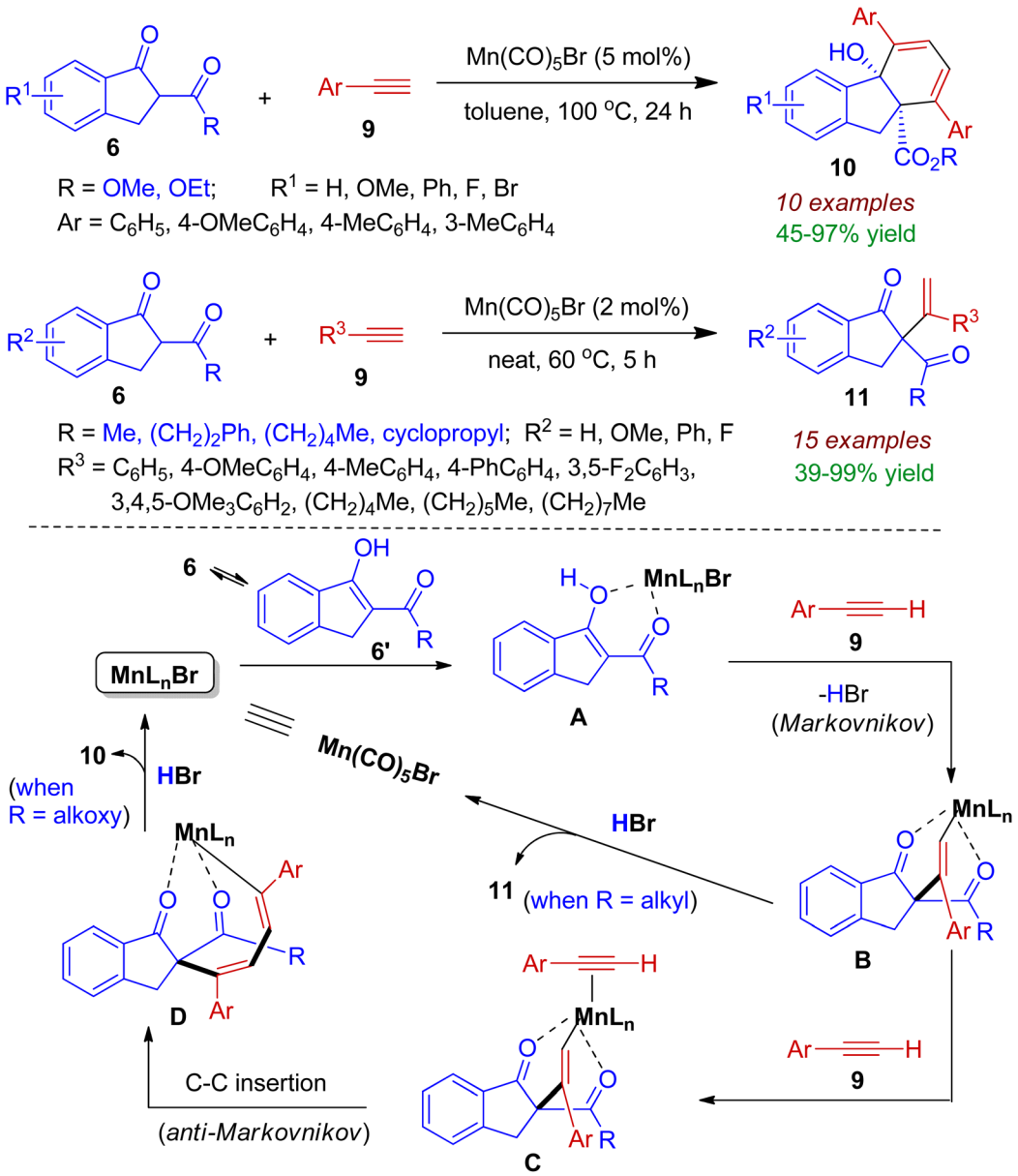
Very recently, Xie, Wang and co-workers devised a base-promoted ring expansion strategy to prepare benzocycloheptene systems from 2-substituted 1-indanone **6**.[33] In this reaction tetramethylsilyl (TMS)-substituted alkyne **7** was chosen to mimic the terminal alkyne. Among various organic and inorganic bases (such as DABCO, Na_2CO_3, K_2CO_3, NaOH, NaH *etc.*) NaH was found to offer best result in THF medium. A plausible mechanism is outlined in Scheme 3. In the presence of base, nucleophilic attack of carbanion (generated from indanone **6**) to alkyne **7** produced intermediate **A**, which underwent intramolecular nucleophilic addition to form intermediate **B**. Retro-aldol reaction led to intermediate **C**, which remained in equilibrium with tautomer **D**. Subsequently the C–Si bond of the intermediate **D** was broken *via* 1,4-Brook rearrangement to afford intermediate **E**, which could be transformed to the desired product **8** during work-up process. Notably, the authors also synthesized two sesquiterpenoid natural products plecarpenene and plecarpenone on the basis of this protocol.

2.1.2. Indeno-fused carbocycles. Indanone derivatives acting as β-ketoester are good synthons for indeno-fused carbocycles. Maji *et al.* realized regioselective addition of indanone derivatives to terminal alkynes with the aid of $Mn(CO)_5Br$ catalyst.[34] The indanones **6** (R = OMe, OEt) efficiently combined with aryl acetylene **9** *via* domino Markovnikov–anti-Markovnikov fashion to afford fused tricyclic scaffold **10** containing two all-carbon quaternary centers (Scheme 4). However, reaction of 2-carbonyl-1-indanones (**6**, R = alkyl) with alkyl/aryl acetylene **9** led to the formation of Markovnikov addition product **11**. The proposed mechanism for the regioselective reaction is shown in Scheme 4. In the presence of Mn-catalyst, the keto–enol tautomerization (**6**→**6′**) forms an enolate **A**, which subsequently reacts with alkyne **9** to generate Markovnikov adduct **B**. For 1,3-diketone (**6**, R = alkyl), protonation of **B** delivered the desired product **11** along with regeneration of catalyst. In case of β-ketoester (**6**, R = OMe, OEt), complex **B** get further stabilized by stronger coordination with another equivalent of alkyne to form intermediate **C**. Next, alkyne insertion in an anti-Markovnikov manner affords intermediate **D**. Intramolecular cyclization of **D** by nucleophilic attack at the more electrophilic carbonyl carbon and protonation produces fused tricyclic compound **10** with regeneration of the catalyst. This regio-/stereoselective transformation is highly atom-economic and environmentally benign.

During the course of their study, Ramasastry and co-workers synthesized chiral indanone scaffolds **13** from symmetrical enone compounds **12**.[35] This diastereoselective transformation was facilitated by the Corey–Chaykovsky reagent, namely dimethyloxosulfonium methylide (DOSM) through initial Michael addition followed by aldol-type reaction. The indanone containing allylic-benzylic tertiary alcohol moiety **13** could be converted to fluorenone **14** in excellent yields with catalytic amount of *p*-TSA. Aromatic moieties possessing electron-donating and -withdrawing groups smoothly underwent this



Scheme 3 Ring expansion of 1-indanones *via* reaction of alkynes towards fused seven-membered carbocycles.

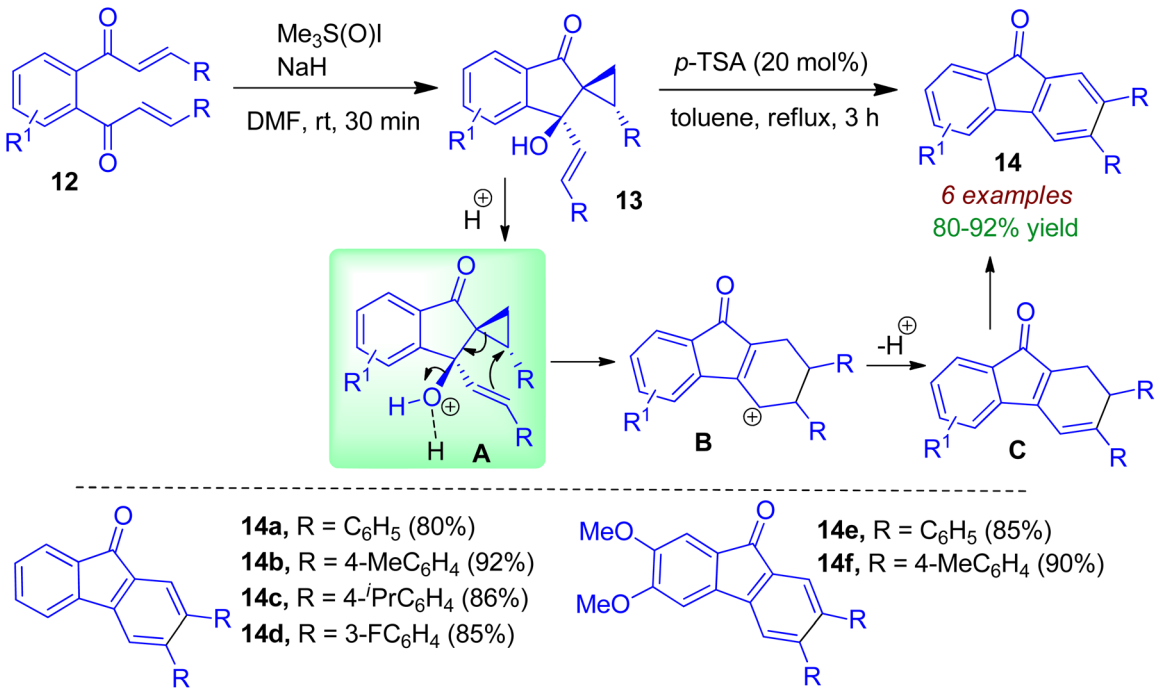


Scheme 4 Regio-/stereoselective reaction of 2-carbonyl-1-indanones with terminal alkynes to afford fused carbocycles.

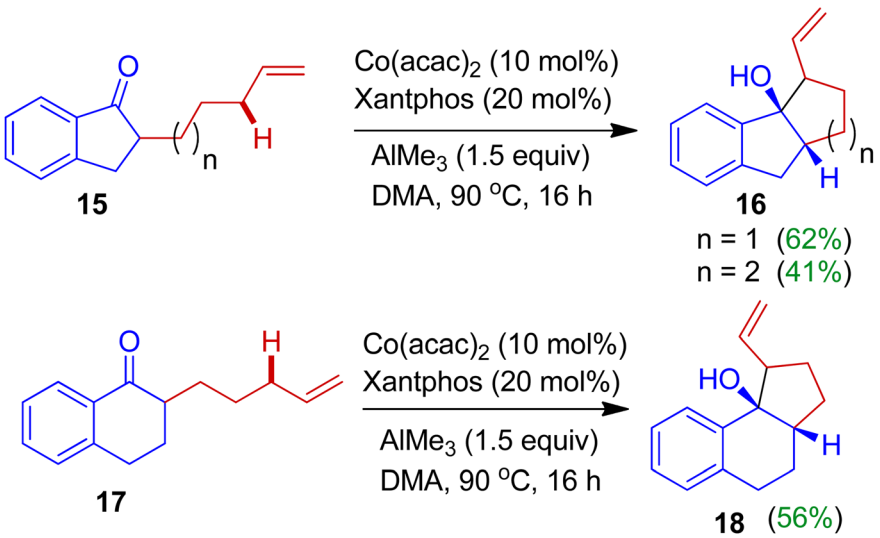
rearrangement. As shown in Scheme 5, a formal homo-Nazarov-type cyclization of vinyl-cyclopropyl cationic system (*via* intermediate **A**) leads to the formation of tetrahydrofluorenyl cation **B**. Intermediate **B** then undergoes deprotonation to form intermediate **C**, which is followed by aromatization to form fluorenone **14**.

A fascinating cobalt-catalyzed intramolecular cyclization of alkylated indanones was investigated by Mita, Uchiyama and Sato.[36] The authors found that alkylated indanones **15** in the presence of cobalt(II)acetylacetone/Xantphos combined catalyst system and trimethylaluminium ($AlMe_3$) afforded fused carbocyclic compounds **16** with good regio- and stereoselectivity (Scheme 6). The reaction of was triggered by allylic C(sp^3)–H bond activation. Under similar reaction conditions, cyclohexanone derivatives **17** delivered corresponding annulated product **18** as single diastereoisomer. Importantly, this strategy offers efficient approach of the synthesis of bi- and tricarbocyclic derivatives initiated by C(sp^3)–H activation without a *gem*-disubstituent on the tethered carbon atoms (without the Thorpe–Ingold effect).[37]

Photodimerization of 3-arylindenone derivatives in both solution and in the solid state was examined by Sakamoto and co-workers.[38] The photoreaction of 3-arylindenones **19** using 365 nm line in benzene solution led to efficient dimerization, resulting in *anti*-HH dimers **20** as the exclusive stereoisomer (Scheme 7). In contrast to the solution photochemistry, the solid-state photoreaction furnished *syn*-HH cyclobutane dimers **21** in moderate yields. The latter is formed probably by the influence of molecular rearrangement, which was affected by π–π-stacking in the crystal lattices. Various *para* substituted 3-



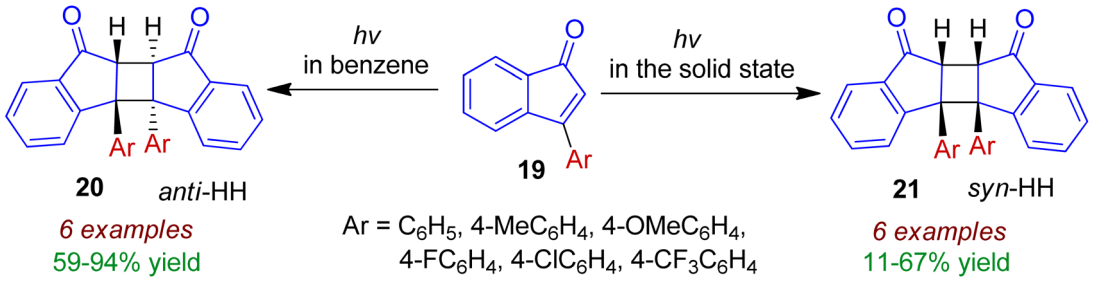
Scheme 5 Synthesis of chiral indanones and acid-catalyzed transformations to fluorenones.



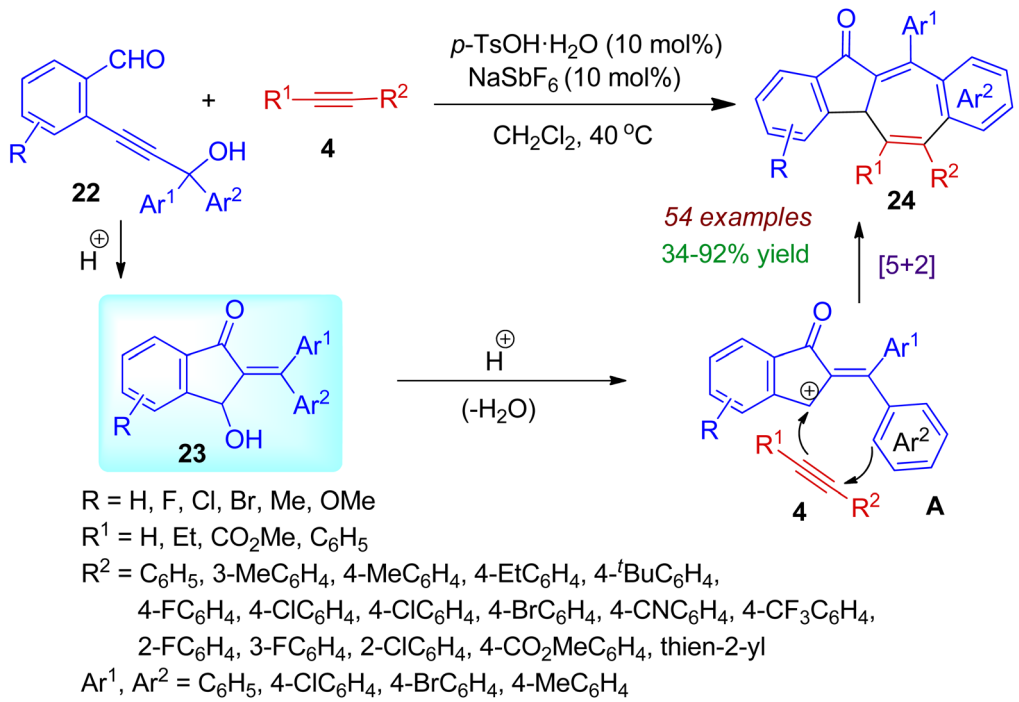
Scheme 6 Cobalt-catalyzed intramolecular cyclization of alkylated indanones towards fused tricarbocycles.

arylindenones (Ar = 4-MeC_6H_4, 4-$OMeC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-$CF_3C_6H_4$) were well tolerated for these transformations.

Fused azulenone architectures are important structural motifs often found in bioactive natural products. In 2020, Zhou *et al.* successfully designed and synthesized dibenzo[*a*,*f*] azulene-12-one derivatives **24** from readily available *o*-propargyl alcohol benzaldehydes **22** and alkynes **4** with the help of *p*-TsOH catalyst (Scheme 8).[39] Various tertiary/secondary aryl propargyl alcohols participated in the annulation process. The cycloaddition reaction was relevant for both terminal as well as internal alkynes with a variety of substituents such as alkyl, eater, aryl, heteroaryl, *etc.* Under the acidic conditions, 3-hydroxy-1-indanones **23** are formed through intramolecular cyclization of aldehydes **22**. The *in situ* generated indanone **23** then undergoes acid-catalyzed dehydration to form cationic intermediate **A**. Then formal [5+2] cycloaddition with alkyne yields final polycarbocyclic scaffolds **24**. The reaction is regioselective and applicable for wide range of substrates (54 examples). Significantly, this annulation strategy comprised high atom-economy, resulting three C–C and one C=O bonds under mild conditions.



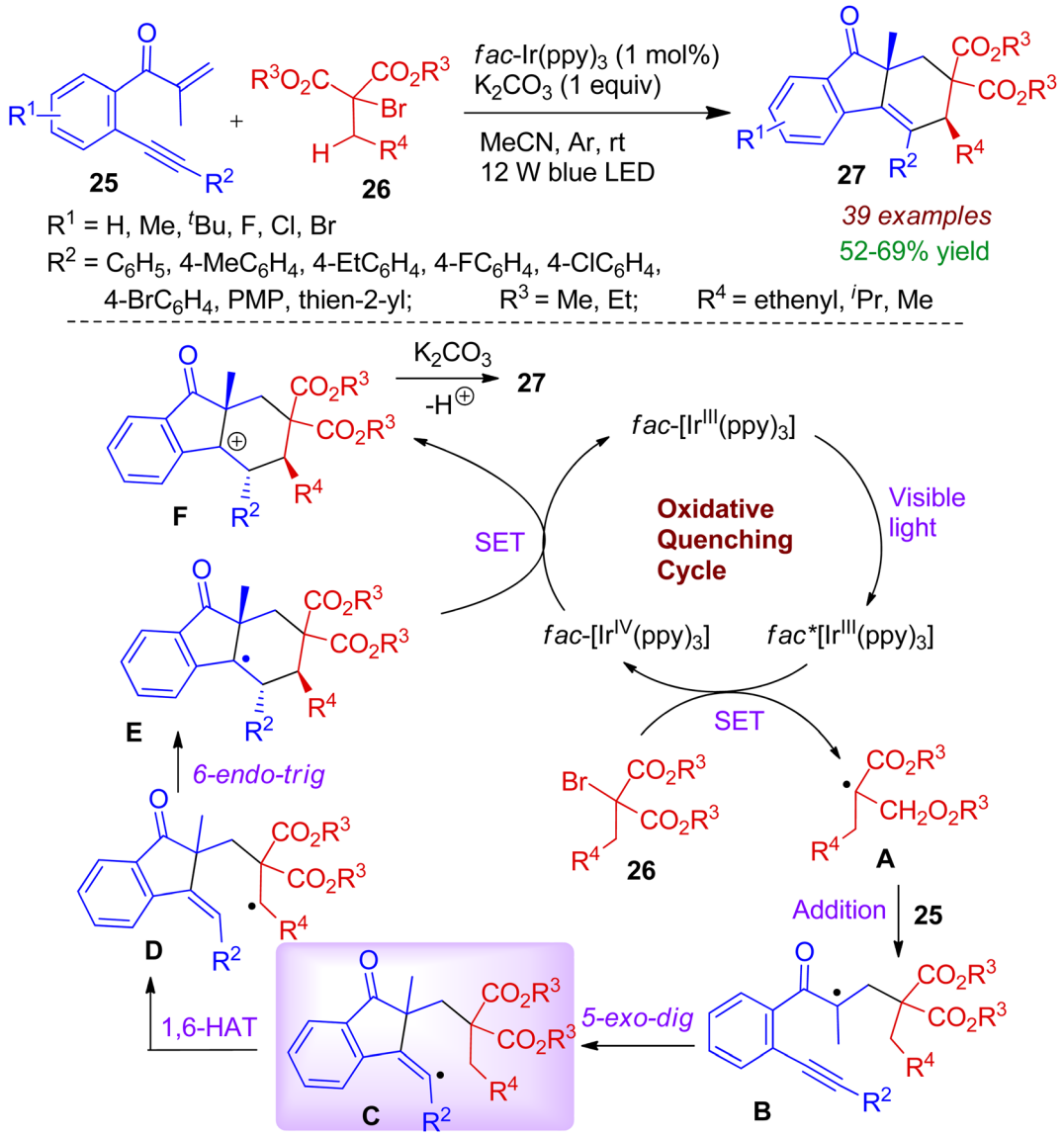
Scheme 7 Photodimerization of 3-arylindenone derivatives in solution and in the solid state.



Scheme 8 Acid-catalyzed cyclization of *o*-propargyl alcohol benzaldehydes and alkynes resulting dibenzo[*a*,*f*]azulene-12-ones.

Starting from β-alkynylpropanones **25** and α-bromomalonates **26**, an interesting visible-light photocatalytic conversion was realized by Jiang and co-workers.[40] This photocatalytic approach accommodates high diastereoselectivity with broad substrate scope resulting substituted *syn*-fluoren-9-ones **27** in the presence of iridium-photocatalyst. The startegy comprises formation of two new rings *via* radical-induced C(sp^3)–H bond cleavage. The reaction takes place through single electron transfer (SET) process (Scheme 9). Initially, visible light triggers [*fac*-^{III}Ir(ppy)$_3$] photocatalyst to the excited state [*fac*-^{III}Ir(ppy)$_3$]*, which reduces α-bromomalonate **26** to form a C-centered radical **A** along with [*fac*-^{IV}Ir(ppy)$_3$] *via* SET process. The radical addition of intermediate **A** to C=C of β-alkynylpropanones **25** affords quaternary carbon radical **B**. Intermediate **B** then experiences 5-*exo*-*dig* cyclization (intermediate **C**) and 1,6-hydrogen atom transfer (HAT) to generate intermediate **D**, which subsequently undergoes *6-endo-trig* cyclization leading to *trans*-intermediate **E**. Meanwhile, a crucial oxidation (SET) step between **E** and [*fac*-^{IV}Ir(ppy)$_3$] occurs, regenerating the photocatalyst and the cationic intermediate **F**. Finally, deprotonation delivers desired *syn*-products **27**.

Zhu group exploited donor–acceptor cyclopropanes as efficient 1,3-dipoles to trap the *in situ* generated electron deficient indenones through [3+2] cycloaddition reaction for synthesizing indanone fused scaffolds.[41] The assembly of enynals **28** and donor–acceptor cyclopropanes **29** in the presence of Zn-catalyst successfully generated indanone fused cyclopentanes **30**. Cycloprapanes bearing vinyl and aromatic moieties responded the reaction well, however, the reaction failed for heteroaromatic cyclopropanes. A plausible mechanism for cascade cyclization is depicted in Scheme 10. At first, activation of alkyne moiety through a [Zn]-π complex **A** generates the 5-*exo*-*dig* intermediate **B**. Hydrolysis of **B** produces keto ester **C** in the presence of catalytic amount of water. Keto–enol tautomerism/Knoevenagel condensation sequence affords key intermediate **E** (*via* intermediate **D**) and water is liberated for the next catalytic cycle. In the mean time, the 1,3-dipole **29′** is formed *in situ via* ring opening of the cyclopropane **29** with the

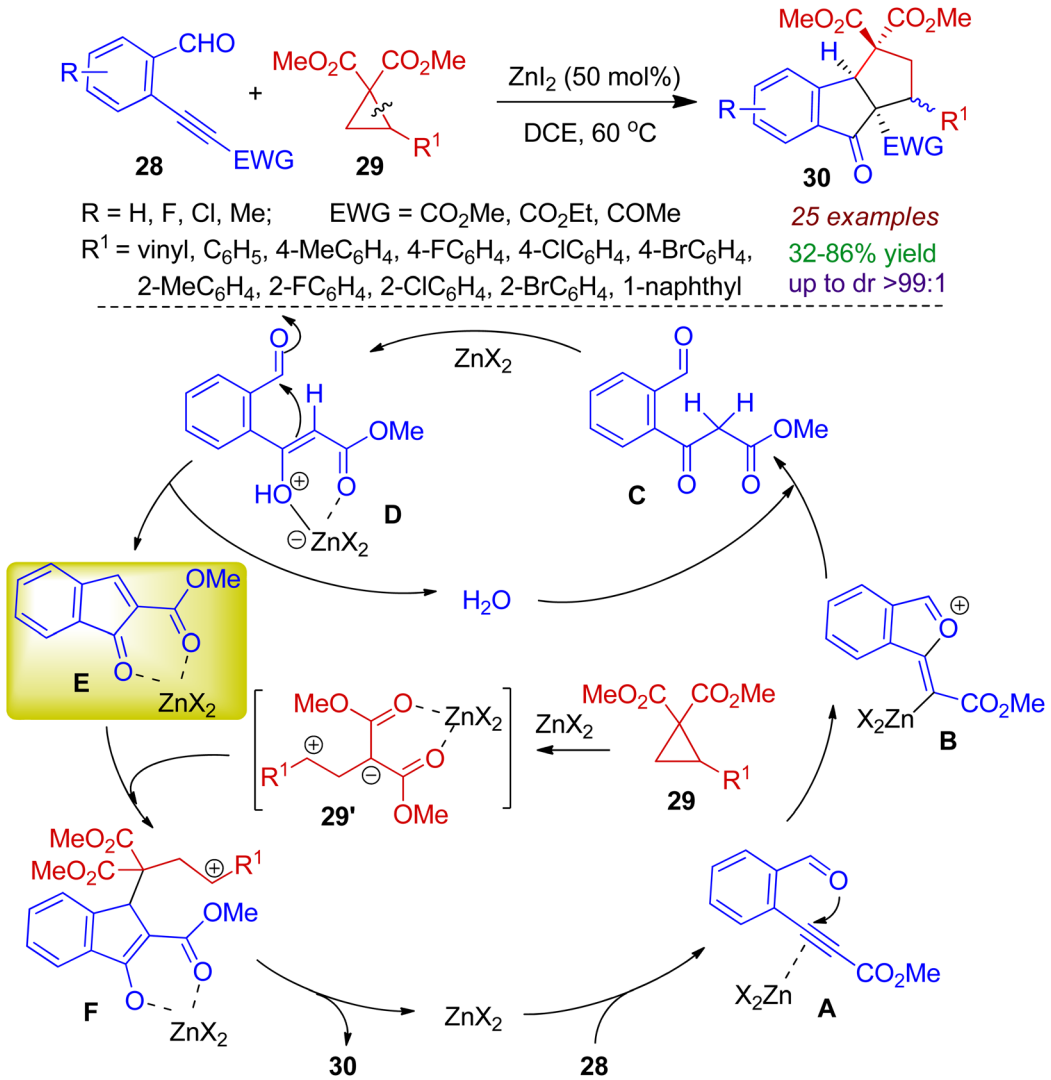


Scheme 9 Visible-light photocatalytic cyclization between β-alkynylpropenones and α-bromomalonates towards *syn*-fluoren-9-ones.

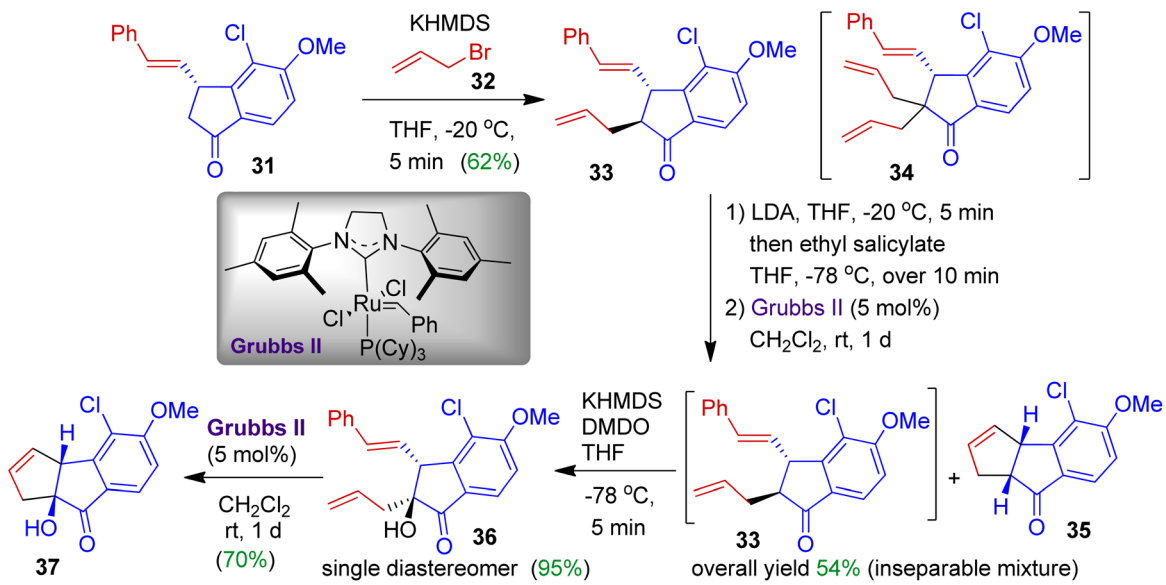
aid of Zn-salt. Next, [3+2] cycloaddition reaction between the indenone **E** and 1,3-dipole **29′** accomplishes final product **30.**

Benzo-dihydropentalenes are unique structural motifs usually found in many naturally occurring compounds. As part of their total synthesis programme, Koert *et al.* constructed cyclopentane fused indanone skeleton *via* a multistep approach (Scheme 11).[42] The authors employed styryl substituted indanone **31** and installed an allyl substitution at α-position using allyl bromide **32** to obtain *trans*-indanone **33.** At this stage, doubly allylated compound **34** was formed as a side product. The *trans*-indanone **33,** after ring closing metathesis (RCM) with Grubbs II catalyst gives inseparable mixture of tricyclic compounds **35** and **33.** The introduction of the hydroxyl group at C9 position of compound **33** could be achieved by treatment of potassium enolate with dimethyldioxirane (DMDO). This strategy offered alcohol **36** as a single diastereoisomer in 95% yield. In the next step, ring closing metathesis successfully yielded hydroxylated tricycle **37** (70% yield).

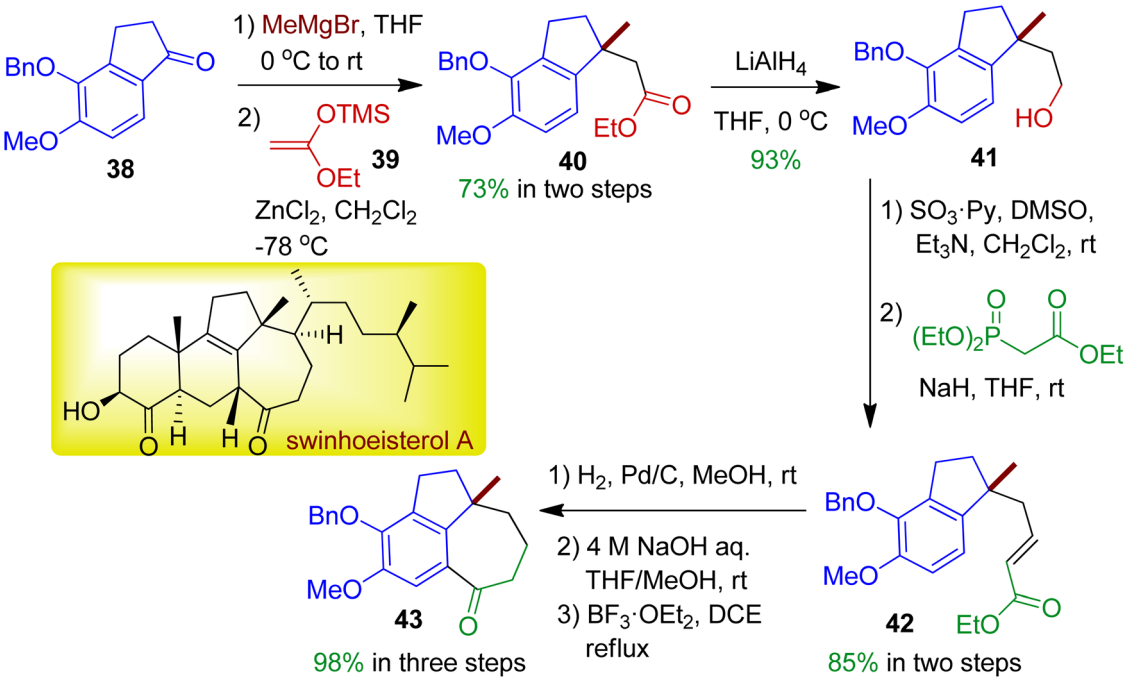
In 2019, Kigoshi's group employed indanone derivative **38** towards novel fused tricyclic compound **43** which has core structural similarity with natural product swinhoeisterol A.[43] The reaction sequence is outlined in Scheme 12. Initially, methylation of indanone **38** by MeMgBr and substitution of the resultant benzylic tertiary alcohol with ketene silyl acetal **39** afforded ester **40** (73% in two steps). Reduction of the ester with $LiAlH_4$ resulted corresponding alcohol **41.** Subsequent oxidation followed by Horner–Wadsworth–Emmons reaction accomplished unsaturated ester **42,** which could be converted into desired tricyclic scaffold **43** with 6/5/7 ring *via* three step reaction sequence (98% in three steps). The relative configuration of the target compound was determined by NOE experiments.



Scheme 10 Reaction of donor–acceptor cyclopropanes and enynals to obtain indanone fused cyclopentanes.



Scheme 11 Multistep synthesis of cyclopentane fused indanone from indanone motif.

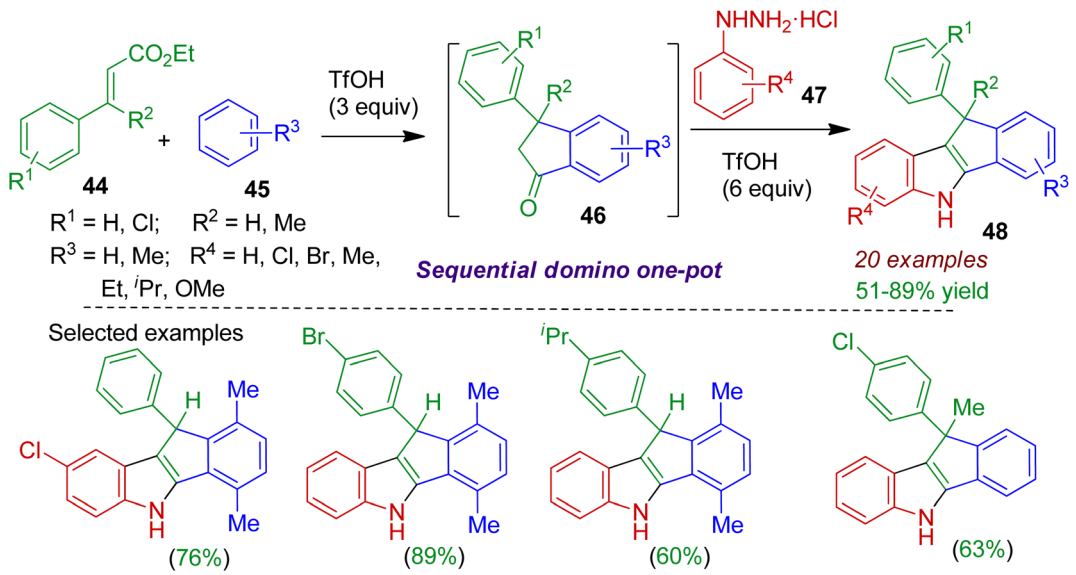


Scheme 12 Multistep synthesis of novel fused tricyclic skeleton (6/5/7) starting from indanone derivative.

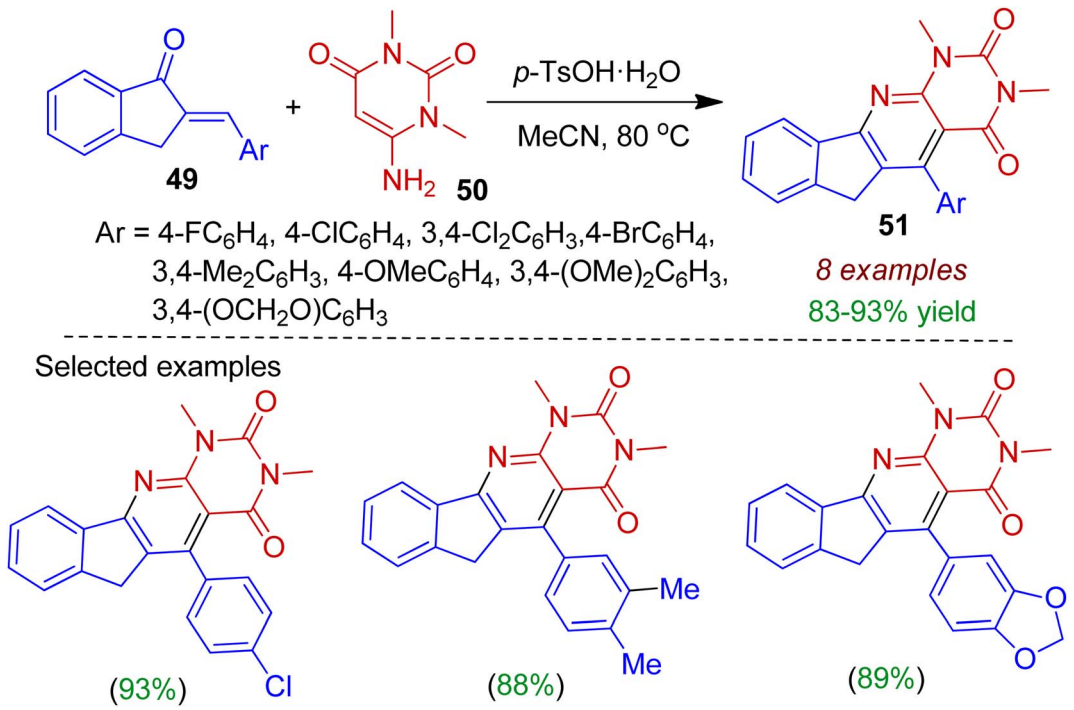
2.2. Fused heterocycles

2.2.1. N-Containing fused heterocycles. Nitrogenous heterocycles fused with indane substructure are commonly encountered in alkaloids and several useful pharmaceuticals.[44] An efficient sequential domino one-pot protocol to build fused tetracyclic indole skeleton was realized by Reddy and Satyanarayana.[45] The reaction between ethyl cinnamates **44** and arenes **45** in the presence of superacidic triflic acid (TfOH) afforded indanone derivative **46,** which after reaction with aryl hydrazines **47** led to indenoindoles **48** in good yields (Scheme 13). The reaction proceeded *via* a domino intermolecular Friedel–Crafts alkylation and intramolecular acylation of ethyl cinnamates to form indanones **46,** followed by the Fischer indole reaction under acidic conditions. The conversion was enabled for large number of substrates and comprised formation of three C–C and one C–N bonds. Significantly, synthesis of dihydroindeno[1,2-*b*]indoles containing quaternary carbon at 10 position could also be achieved using this methodology.

Rong *et al.* carried out the one-step synthesis of indeno-fused pyridopyrimidine scaffolds **51** involving readily accessible 2-arylidene 1-indanone system under mild reaction conditions.[46] The authors employed 6-amino-1,3-dimethylpyrimidine **50** as



Scheme 13 TfOH-promoted sequential domino one-pot synthesis of indenoindoles from ethyl cinnamate, arene and aryl hydrazine.

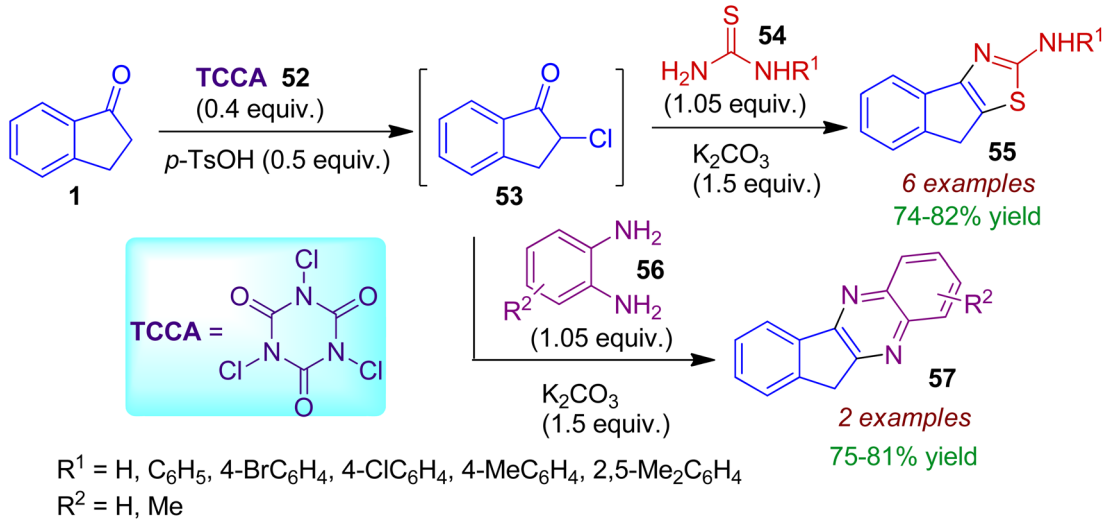


Scheme 14 Synthesis of indeno-fused pyridopyrimidine scaffolds from 2-arylidedene indanones and 6-aminopyrimidine.

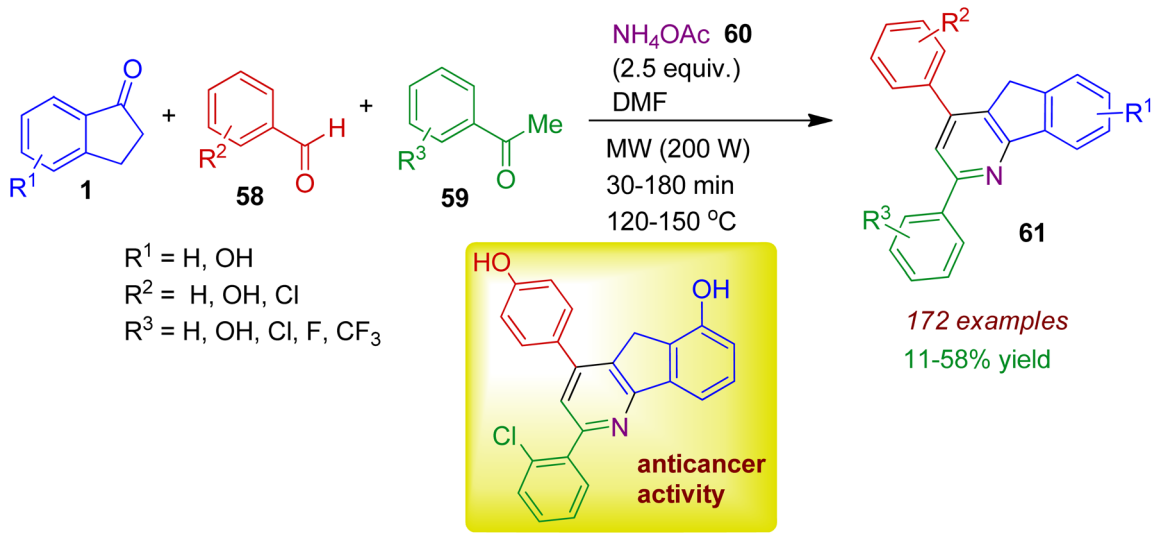
the annulation partner to react with 2-arylidene 1-indanone **49** in the presence of catalytic amount of *p*-TsOH in refluxing acetonitrile resulting polyheterocyclic compounds **51** in excellent yields (Scheme 14). The reaction was also applicable for 2-arylidene dihydronaphthalenone systems.

α-Chlorination reaction of indanone **1** with trichloroisocyanuric acid (TCCA) **52** under mechanochemical ball-milling condition may be applied for synthesis of fused heterocycles.[47] The intermediary α-chloroindanone **53** formed in this process was directly subjected to base-mediated condensation with thiourea/*N*-arylthiourea **54** resulting 2-indenothiazoles **55** in 74–82% yields (Scheme 15). In the similar sequential manner, *o*-phenylenediamines **56** could be treated with α-chloroketone **53** to accomplish corresponding indenoquinoxaline derivatives **57**. This strategy is environmentally benign, comprising one-pot sequential acid- and base-mediated reactions in the solid state resulting biologically relevant heterocycles.

Starting from readily available substrates Kwon, Lee and co-workers synthesized indeno pyridine derivatives under microwave irradiation.[48] This multicomponent strategy involved the assembly of 1-indanones **1**, aromatic aldehydes **58**,



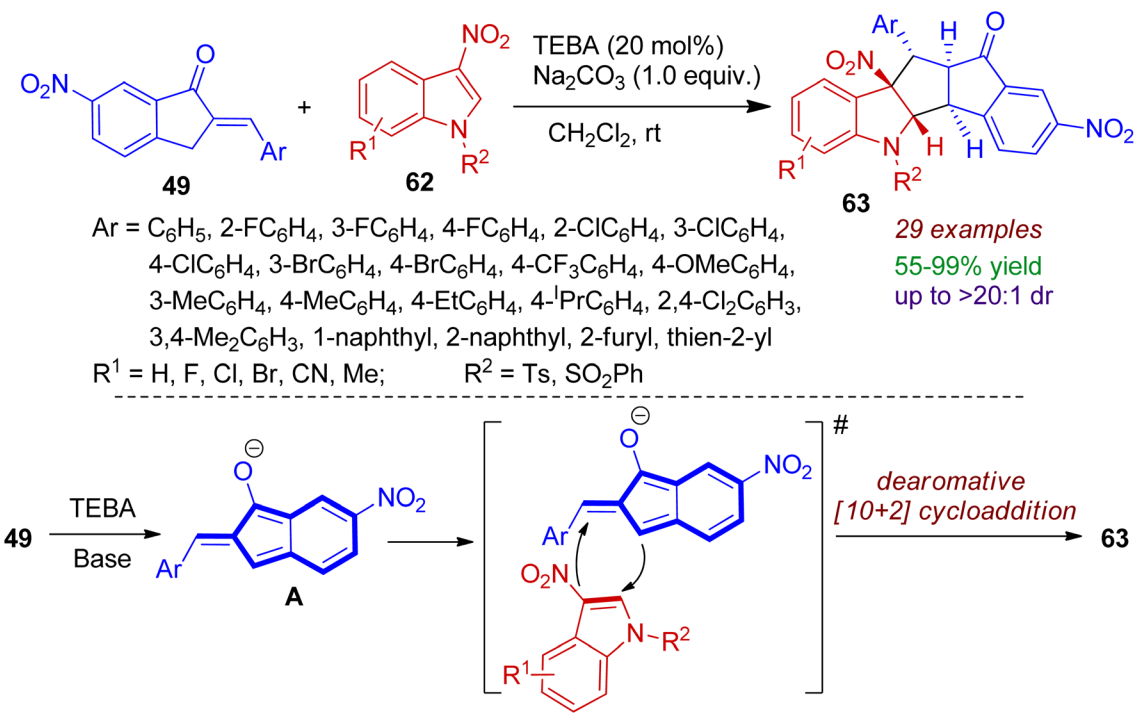
Scheme 15 Solid-state synthesis of 2-indenothiazoles and indenoquinoxalines exploiting α-chloroindanone.



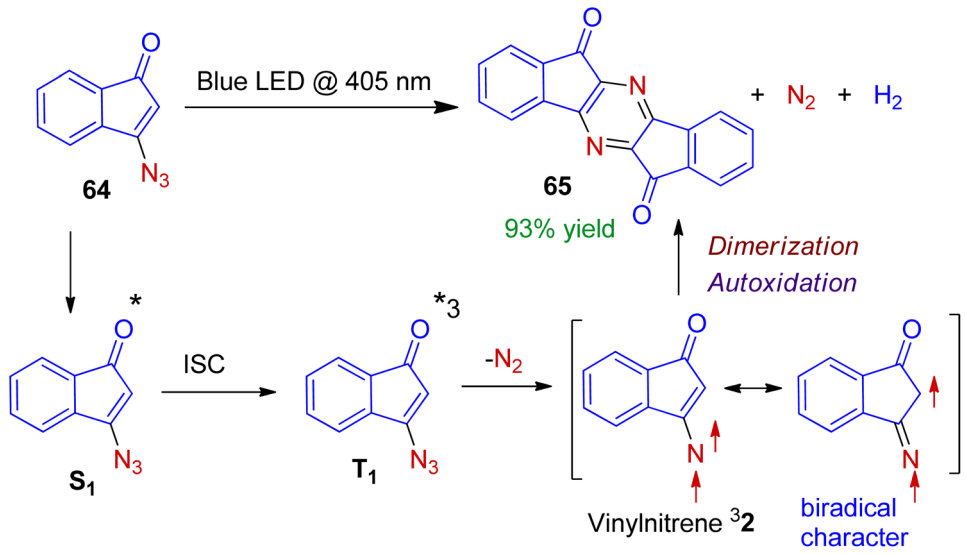
Scheme 16 MW-assisted multicomponent synthesis of indeno pyridines from 1-indanones, aromatic aldehydes, acetophenones and NH_4OAc.

acetophenones **59,** and NH_4OAc **60** to obtain a library of hydroxy- and halogenated 2,4-diphenylindeno[1,2-*b*]pyridinols **61** in acceptable yields (Scheme 16). The authors fruitfully investigated structure–activity relationships of the synthesized compounds. It has been found that the majority of compounds with chlorophenyl group at 2-position and phenol moiety at the 4-position of the indeno[1,2-*b*]pyridinols revealed potent anti-proliferative activity and topoisomerase IIα-selective inhibition against human breast cancer cell lines.

Higher order cycloaddition strategy is an important tool for constructing polycyclic architectures in a single step. Very recently, dearomative [10+2] cycloaddition of 2-arylidene-1-indanones **49** and 3-nitroindoles **62** at ambient temperature was developed.[49] This transformation was attained using triethyl benzyl ammonium chloride (TEBA) as phase transfer catalyst under basic conditions (Na_2CO_3) to afford wide range of polycyclic cyclopenta[*b*]indolines **63** in excellent yields and diastereoselectivity (up to 99% yield and >20 : 1 dr). 3-Nitroindoles bearing electron-withdrawing and donating substituents (F, Cl, Br, CN, Me) were well tolerated with the catalytic system. A plausible mechanism is illustrated in Scheme 17. In the presence of TEBA and base, 2-arylidene-1-indanone **49** is



Scheme 17 Higher-order [10+2] cycloaddition of 2-arylidene-1-indanones and 3-nitroindoles to access polycyclic cyclopenta[*b*]indolines.

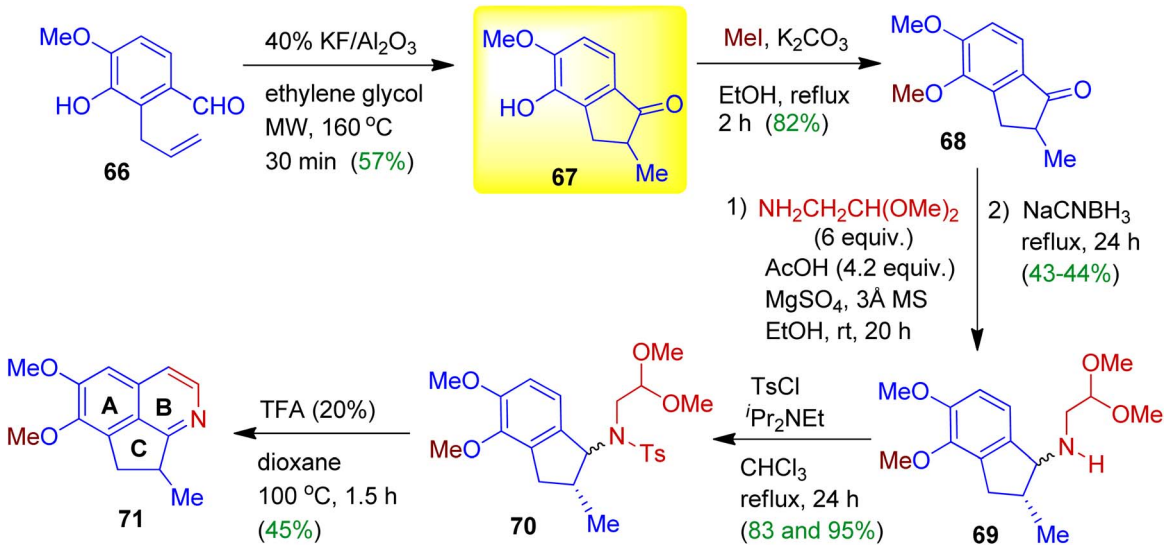


Scheme 18 Photodimerization of 3-azido-1-indenone to form N-heterocyclic dimer.

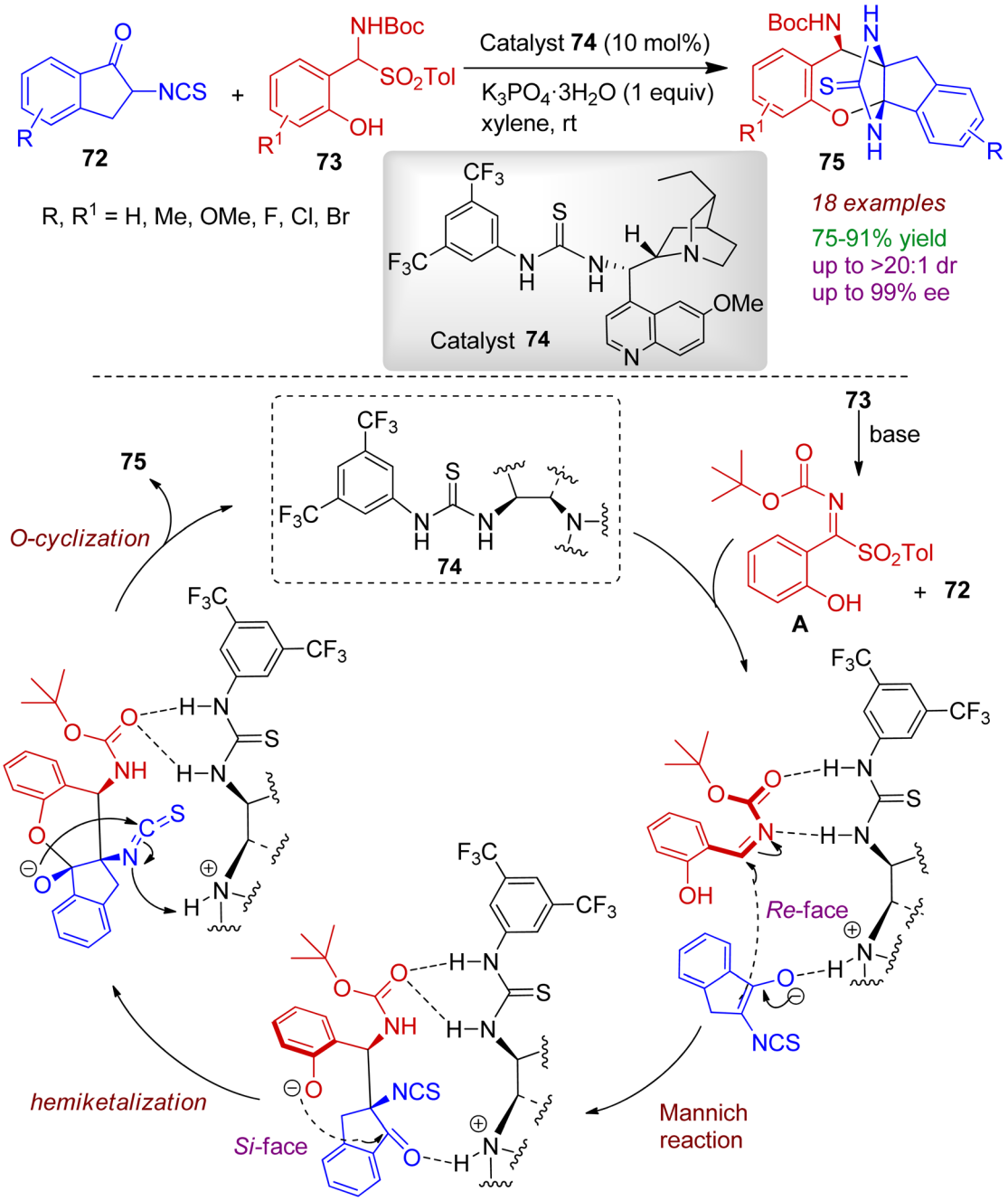
first converted to 1-hydroxyl isobenzofulvene anion intermediates **A**, which is highly nucleophilic in nature. After that, higher order [10+2] cycloaddition takes place between *in situ* generated intermediate **A** and 3-nitroindoles **62** to accomplish dearomatized annulation products **63**. Notably, the reaction is amenable for gram-scale synthesis of desired products.

The mission for sustainable chemistry using sunlight or low energy light-emitting diodes (LED) has sparked interest in the recent synthetic research. Gudmundsdottir *et al.* realized photolysis of 3-azido-1-indenone **64** with light-emitting diode (LED, $\lambda = 405$ nm) or mercury arc lamp to access heterocyclic dimer **65** in excellent yield.[50] Mechanistically it is conceivable that (Scheme 18), the irradiation of azido-1-indenone **64** forms its first singlet excited state S_1. Intersystem crossing leads to the triplet configuration T_1, which is followed by extrusion of an N_2 molecule to generate vinylnitrene ^{3}**2**. The vinylnitrene ^{3}**2** is sufficiently stable to dimerize (not decayed by intramolecular rearrangement) to produce N-heterocyclic dimer **65**. Importantly, due to the significant 1,3-biradical character of vinylnitrene ^{3}**2** (which is confirmed by ESR spectroscopy), it dimerizes to form C–N bond, rather than N–N bond. In this methodology, the molecular architecture is finely tuned to control the reactivity of triplet vinylnitrene.

During their synthetic programme, Vargas, Larghi and Kaufman derived cyclopenta[*ij*]isoquinoline **71** starting from readily accessible 2-allylbenzaldehyde 66 (Scheme 19).[51] When compound **66** was exposed to 40% w/w KF/Al_2O_3 in ethylene glycol under microwave irradiation, 5-*exo-trig* cyclised product, *viz.* indanone **67** obtained in 57% yield. Then alkylation of the phenolic moiety was carried out using MeI/K_2CO_3 in ethanol (**68**, yield 82%). The indanone **68** was subjected to a reductive amination with aminoacetaldehyde dimethyl acetal in the



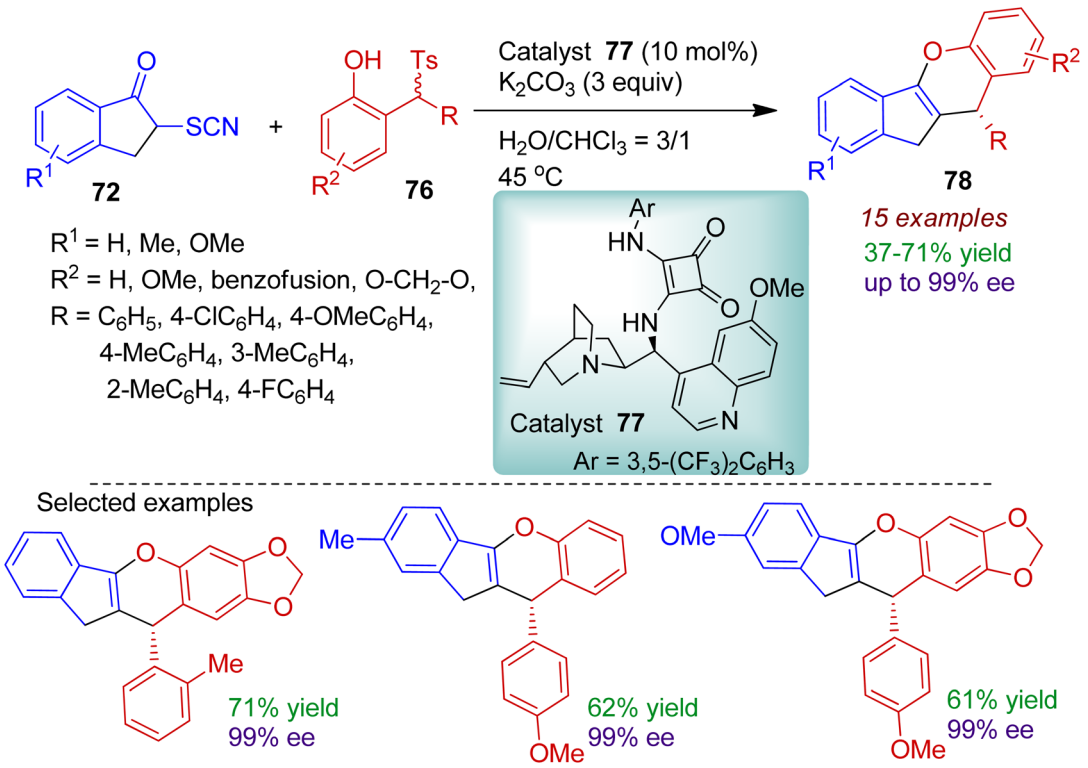
Scheme 19 Sequential synthesis of cyclopenta[*ij*]isoquinoline involving 1-indanone scaffold.



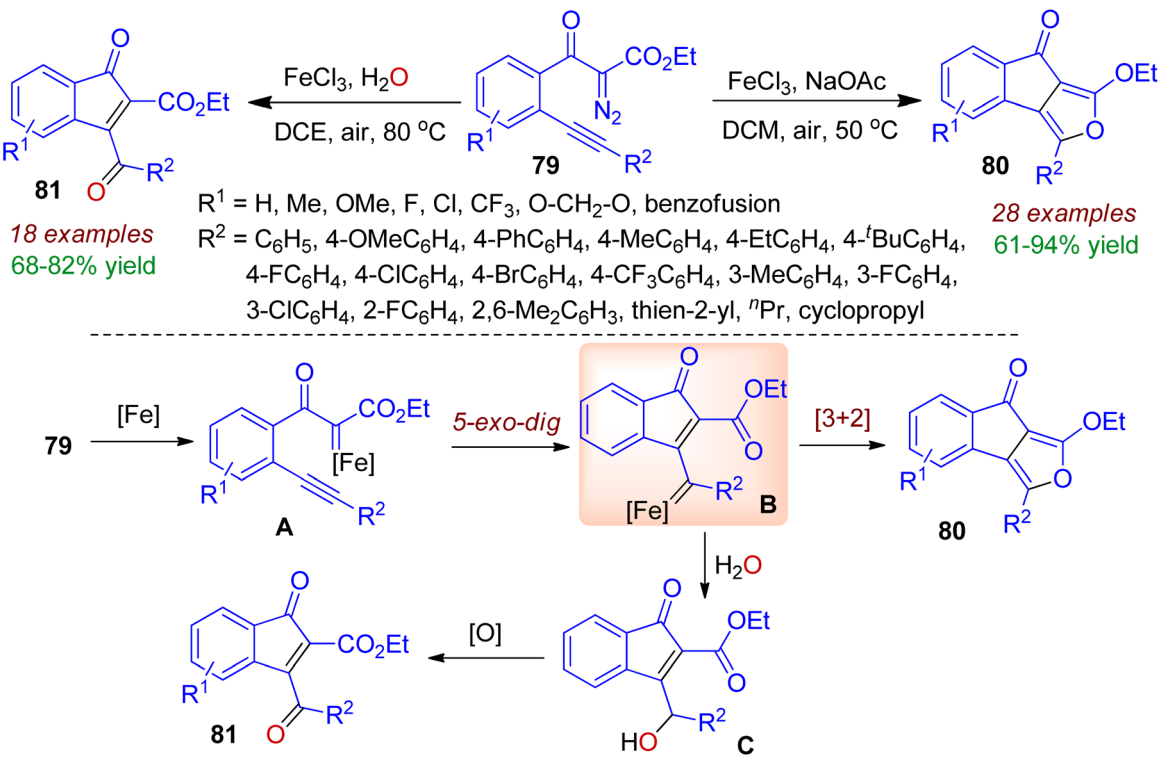
Scheme 20 Stereoselective construction of bridged fused heterocycles from 2-isothiocyanato-1-indanones and 2-hydroxyaryl-α-amido sulfones.

presence of anhydrous $MgSO_4$ and 3 Å MS. To promote condensation of the intermediate imine and further iminium ion formation AcOH might be added. After reduction with $NaCNBH_3$ in refluxing EtOH, the expected amine **69** was produced as diastereomers in good yields. The amines **69** then allowed to react with tosyl chloride to give corresponding tosylated diastereomers **70.** Treatment with 20% trifluoroacetic acid (TFA) in refluxing dioxane delivered cyclopenta[*ij*]isoquinoline **71** in 45% yield (Pomeranz–Fritsch cyclization). It should be mentioned that ABC-ring system of this type are ubiquitous in alkaloids, such as, azafluoranthene, tropoisoquinoline and proaporphine.

2.2.2. O-Containing fused heterocycles. Isothiocyanato-1-indanones can be employed as building blocks in the hetero-annulation reactions. In 2021, Du *et al.* developed a one-pot asymmetric domino annulation of 2-isothiocyanato-1-indanones **72** with 2-hydroxyaryl-substituted α-amido sulfones **73** using thiourea derived tertiary amine organocatalyst **74.**[52] This reaction prescribes an efficient protocol for preparing fused ring heterocycles **75** with three adjacent stereogenic



Scheme 21 Water-triggered formation of oxygen-containing fused polycyclic compounds from α-thiocyanato indanone and 2-(tosylmethyl) phenols.

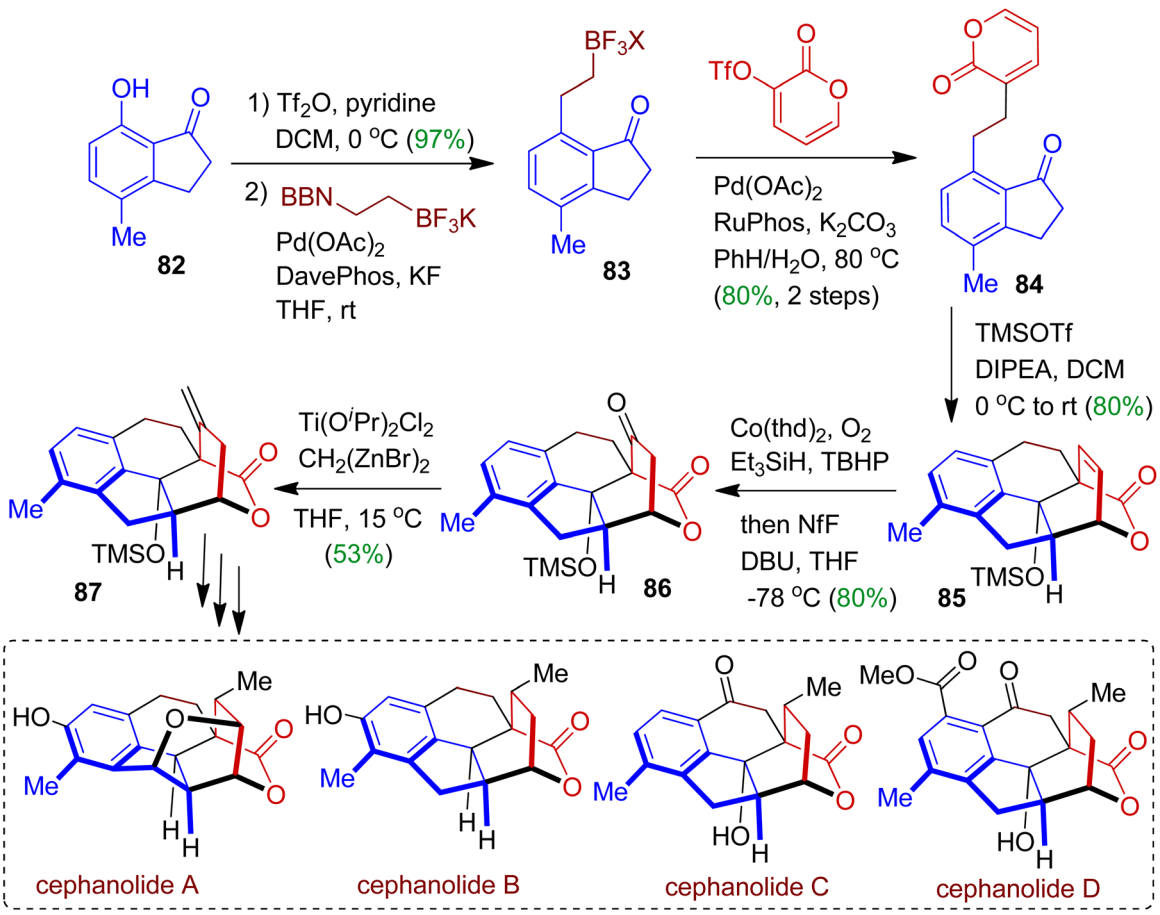


Scheme 22 $FeCl_3$-catalyzed carbene/alkyne metathesis reaction of *o*-alkynylbenzoyl diazoacetates to obtain indeno[1,2-*c*]furans.

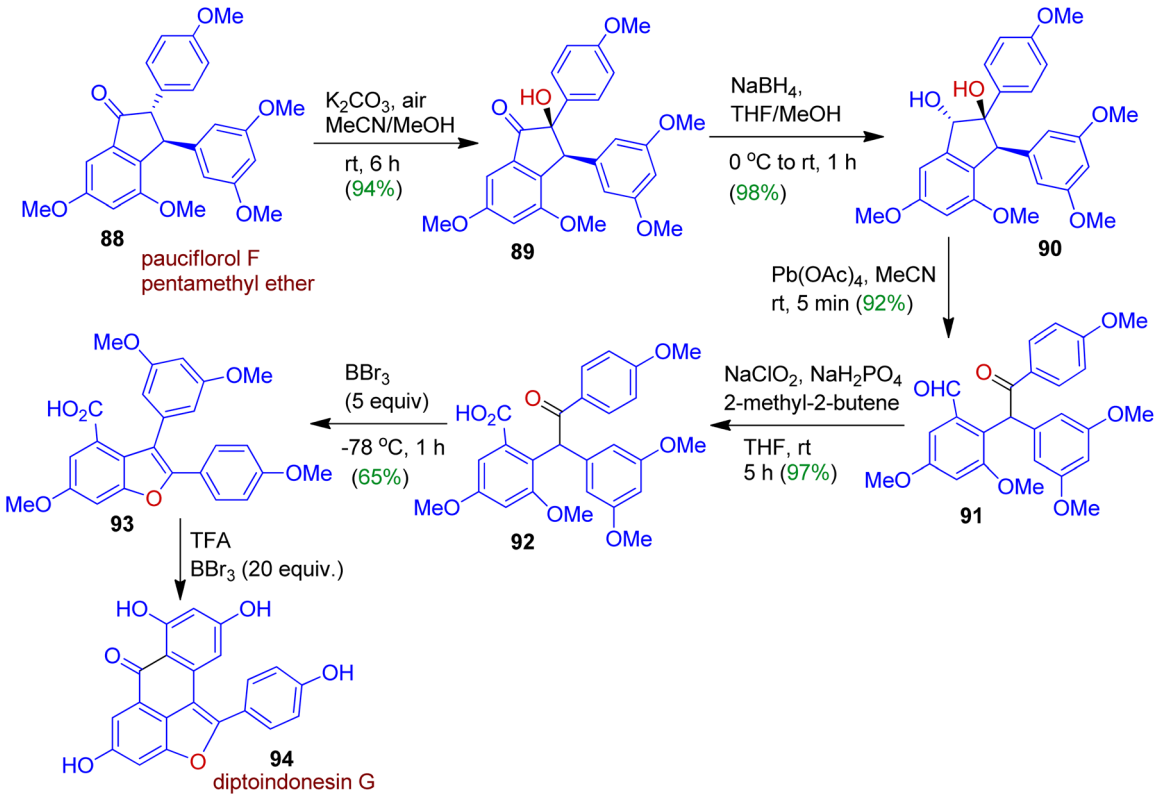
centers in good yields (up to 91%) with excellent stereoselectivities (up to 99% ee and >20 : 1 dr). A plausible reaction mechanism is illustrated in Scheme 20. Firstly, the salicyl *N*-carbamoyl imine intermediate **A** is generated from **73** in the presence of a base. In the mean time, nitrogen atom of quinine in organocatalyst **74** promotes the enolization of indanone moiety. The imine is activated by double hydrogen bonding between the thiourea moiety, and carbonyl oxygen and the nitrogen atom form the *N*-Boc protected imine. Subsequently, the enolate of indanone attacks imine moiety from the *Re*-face (Mannich addition), and the phenoxide ion (generated by deprotonation of hydroxyl group) attacks the carbonyl of indanone from *Si*-face (hemiketalization step). The bridged fused heterocyclic product **75** is formed *via* intramolecular *O*-cyclization reaction with regeneration of the organocatalyst. The reaction is a rare example of asymmetric catalytic hemiketalization reaction involving indanone system.

An interesting water-triggered chemodivergent stereoselective cyclization of α-thiocyanato indanone was investigated by Li's group.[53] The reaction of α-thiocyanato indanone **72** with 2-(tosylmethyl)phenols **76** catalyzed by quinine-derived squaramide catalyst **77** in H_2O : $CHCl_3$ (3 : 1) system conveniently delivered dihydroindeno[1,2-*b*]chromene compound **78** (Scheme 21). The products were formed with excellent enantioselectivity (up to 99% ee) and the absolute configuration was determined with the help of X-ray crystallographic study. The α-thiocyanato indanone **72** containing methyl and methoxy substituents were amenable for the catalytic process. Notably, 2-(tosylmethyl)-sesamols bearing different aryl substituents smoothly afforded corresponding cascade products in acceptable yields with excellent chemo- and enantioselectivity.

o-Alkynylaryl α-diazoester may be used in metal-catalyzed carbonylation reaction for building indanone skeleton. In 2021, Li, Fan and co-workers reported the $FeCl_3$-catalyzed carbene/alkyne metathesis (CAM) reaction of *o*-alkynylbenzoyl diazoacetates **79** for the synthesis of indeno[1,2-*c*]furan core **80**.[54] The reaction readily occurred in dichloromethane with NaOAc and air at 50 °C. However, the presence of water in the reaction medium resulted in 3-benzoylindenone derivatives **81**. The different types of product formation could be realized by mechanism (Scheme 22). Initially, iron-catalyzed dinitrogen elimination from *o*-alkynylbenzoyl diazoacetates **79** afforded iron carbene intermediate **A**. Next, 5-*exo*-*dig* carbocyclization process produced vinyl iron carbene **B** which might be the key intermediate. Subsequently intramolecular [3+2] cycloaddition directed the formation of fused indenofuran core **80**. On the other hand, in the presence of H_2O, **B** is terminated with O–H insertion to give intermediate **C**, which underwent aerial oxidation resulting indenone motif **81**.

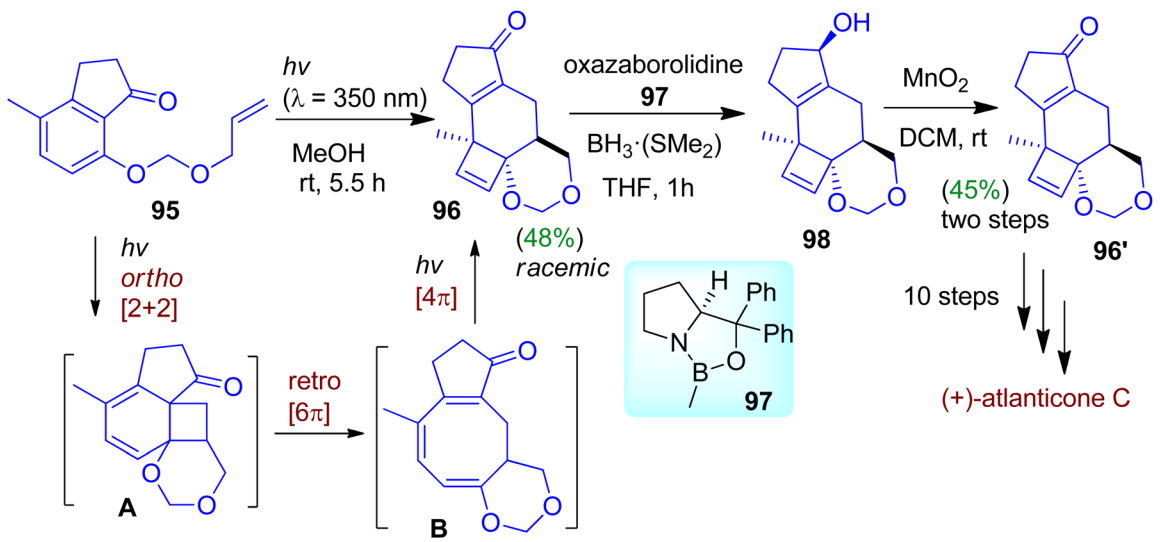


Scheme 23 Multistep synthesis of cephanolides A–D starting from 7-hydroxy-4-methylindanone.



Scheme 24 Synthesis of diptoindonesin G strating from pauciflorol F pentamethyl ether *via* skeletal reorganization.

Sarpong *et al.* employed commercially available 7-hydroxy-4-methylindanone **82** and assembled successfully to synthesize naturally occurring cephanolides A–D *via* multistep approach.[55] At the outset, the triflation product of indanone **82** was subjected to react with BF_3K-ethylene-9BBN to obtain boron compound **83.** Iterative sp^3–sp^3 Suzuki cross-coupling with pyrone triflate accomplished indanone derivative **84** (80% yield). In the next step, [4+2] cycloaddition reaction was performed by using TMSOTf/DIPEA to afford corresponding cycloadduct **85** as sole diastereoisomer. The cycloadduct **85** was then converted to ketone **86** in one-pot *via* hydrocobaltation process. Olefination of **86** using $Ti(O^iPr)_2Cl_2$ led to *exo*-methylene product **87** (53% yield) which is the key synthon for cephanolide core. This reaction was generally performed on a 500 mg scale. Compound **87** could be transformed into cephanolides A–D through multistep synthesis and structural diversification (Scheme 23).



Scheme 25 Construction of complex polycyclic skeleton *via* photochemical reaction cascade of 1-indanone derivative.

Singh and Kim devised a novel synthetic approach towards diptoindonesin G, a potent anticancer natural product starting from readily accessible pauciflorol F pentamethyl ether **88.** The transformation could be achieved through skeletal reconstruction adapting oxidative ring-opening and sequential ring closure strategy (Scheme 24).[56] As expected, the α-hydroxylation of indanone **88** in the presence of K_2CO_3 and air at room temperature afforded hydroxy keto compound **89** (94% yield), which was then reduced with sodium borohydride for the diastereoselective formation of *trans*-diol dreivative **90.** The conversion of *trans*-diol **90** into ketoaldehyde **91** was carried out with $Pb(OAc)_4$. Subsequently, Pinnick–Kraus oxidation of **91** with $NaClO_2/NaH_2PO_4$ gave corresponding acid **92** in 97% yield. Exposure of acid **92** to BBr_3 led to 65% of benzofuran **93** which was finally converted to target tetracyclic skeleton **94** (diptoindonesin G) using TFA/BBr_3 system.

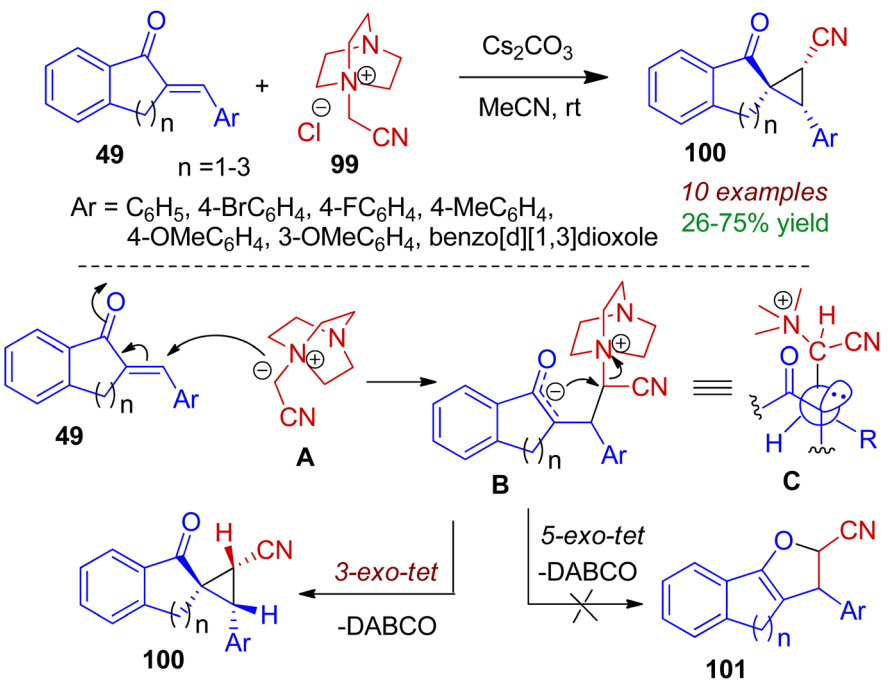
Recently, Bach's group designed and synthesized strained polycyclic frameworks based on photochemical reaction cascade exploiting an indanone precursor.[57] The photochemical reaction cascade was started with *ortho*-photocycloaddition of the indanone substrate **95.** The strained diene intermediate **A** formed by this process then underwent thermal disrotatory ring opening to give triene intermediate **B** (Scheme 25). Further irradiation of triene **B** afforded [4π]-photocyclized product **96** possessing three stereogenic centers as racemic mixtures (in 48% yield). The authors tactfully carried out the resolution employing Corey–Bakshi–Shibata (CBS) reduction process. Enantioselective CBS reduction of the racemic photoproduct (*i.e.* catalytic chiral resolution using oxazaborolidine **97** and $BH_3 \cdot SMe_2$) led to the formation of enantiopure alcohol **98.** Subsequent oxidation accomplished enantiopure ketone **96′.** The enantiomerically enriched product could be transformed into naturally occurring (+)-atlanticone C after 10 steps.

3. Synthesis of spiro scaffolds

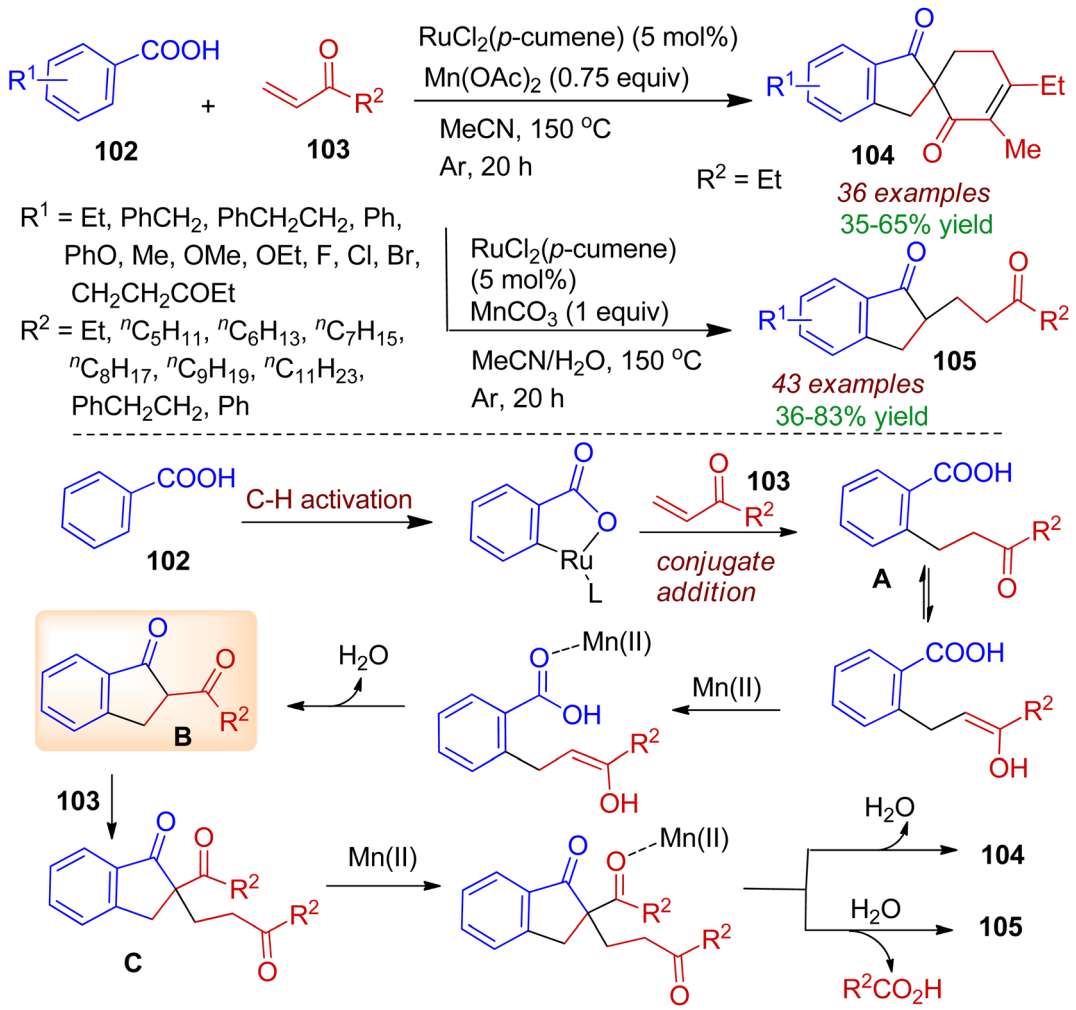
3.1. Spiro carbocycles

Spirocyclic compounds play an important role in drug development due to their three dimensionality and structural novelty. Particularly, spiroindanones are special class of compounds found in many natural products and pharmaceuticals. This type of molecules could be accomplished through cyclopropanation strategy. In 2017, Namboothiri *et al.* devised a new route towards spirocyclopropanes **100** *via* addition of 2-arylidene indanones **49** to DABCO derivative **99** at ambient temperature (Scheme 26).[58] The reaction holds good for tetralone ($n = 2$) and benzosuberone ($n = 3$) system resulting corresponding spirocyclic analogues in moderate to good yields (up to 75%). Interestingly, in all the cases single diastereoisomers were obtained. According to the mechanism, initially ylide **A** is generated from **99** in the presence of base Cs_2CO_3. Michael type addition of intermediate **A** towards chalcone **49** gives enolate **B** which is stabilized in a conformation **B** (where the carbonyl and the R groups are *anti* to each other *i.e.*, conformation **C**). Finally cyclization in 3-*exo-tet* fashion selectively produces spiroindeno cyclopropane **100** instead of fused product **101.**

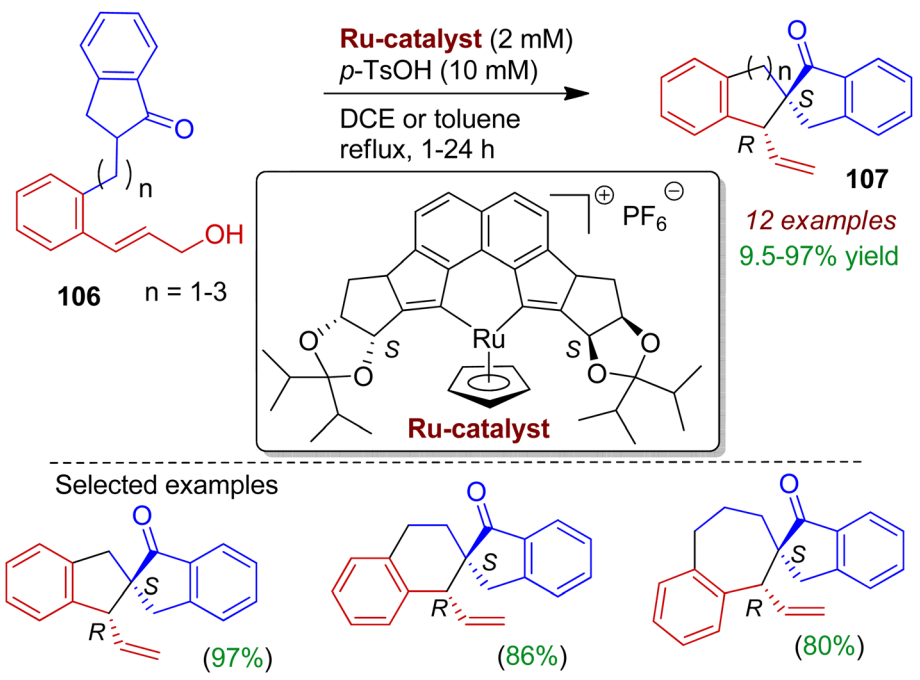
Starting from commercially available aromatic acids **102** and α,β-unsaturated ketones **103** Shi's group developed a ruthenium-catalyzed tandem coupling and cyclization reaction to obtain structurally diverse 1-indanone derivatives.[59] In this case, switchable access to wide range of spiroindanones **104** and 2-substituted indanones **105** could be tuned by Mn(II) additive and water. A probable mechanism is illustrated in Scheme 27. Initially, a ruthenium-catalyzed and carboxyl group directed conjugate addition of C–H bond to the α,β-unsaturated ketones **103** gave *ortho* alkylated benzoic acid intermediate **A.**



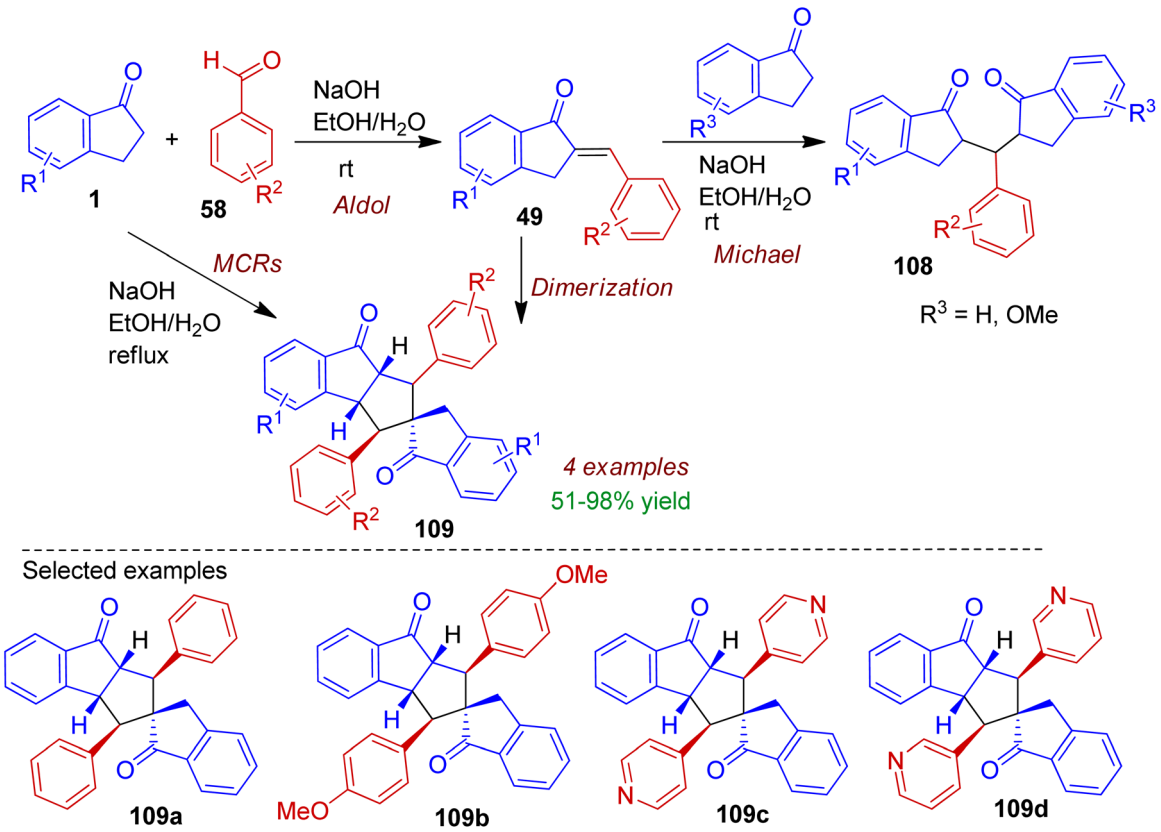
Scheme 26 Base-promoted synthesis of spiroindeno cyclopropanes from arylidene indanones and DABCO-derived N-ylides.



Scheme 27 Ru-catalyzed annulation of aromatic acids and α,β-unsaturated ketones to form spiroindanones.



Scheme 28 Synthesis of enantiopure spiroindanone-carbocycles *via* intramolecular Tsuji–Trost strategy.



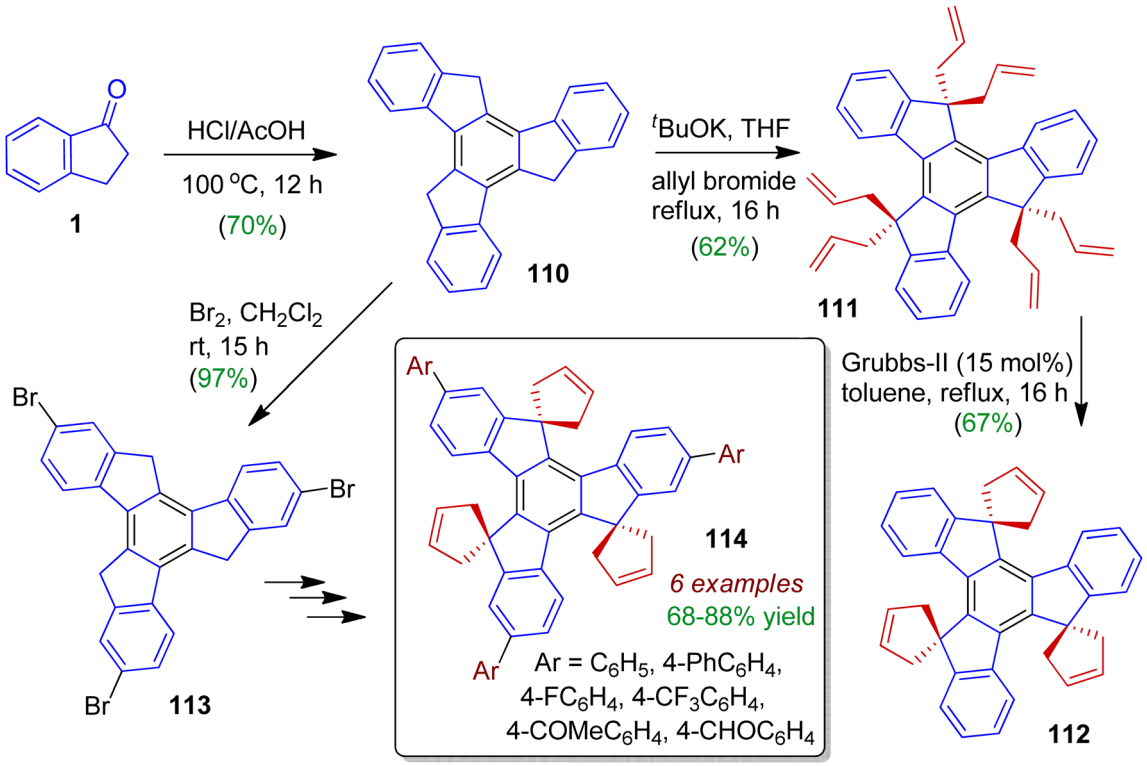
Scheme 29 Multicomponent synthesis of spirocarbocycles from 1-indanones and aryl aldehydes.

Subsequently, intermediate **A** underwent Dieckmann condensation reaction through enol attacking Mn(II)-activated carbonyl to form 2-acyl-1-indanone **B**. Michael addition of the intermediate **B** to the second α,β-unsaturated ketone resulted intermediate **C**. Finally, the intermediate **C** could proceed by two pathways depending upon chelation interactions of Mn(II) and oxygen atom. The intramolecular Aldol condensation directly furnished spiroindanone **104**. Notably, presence of trace amount of water caused hydrolysis to give 2-substituted-1-indanones **105**.

Synthesis of enantiopure spirocycles is important for medicinal chemistry research. Kitamura's group realized stereoselective construction of spiroindanone-carbocycles *via* an intramolecular Tsuji–Trost strategy.[60] The authors applied [Ru(II)Cp((*S*,*S*)-Naph-diPIM-dioxo-^{i}Pr)]PF_6 and sulfonic acid combined catalyst system for the first time to facilitate dehydrative one-pot access to spirocarbocycles from simple racemic ketone-containing allylic alcohols **106** without strochiometric activation of both the C=O and OH group (Scheme 28). This enantio- and diastereoselective protocol simultaneously installs the spiro-all-carbon quaternary center at C=O β position, resulting corresponding *trans* isomer **107** among four possible stereoisomers. The selection of sulfonic acid and an *E*-configured cinnamyl alcohol-type substrate is crucial for high selectivity and reactivity. A double hydrogen bond between OH and SO_3H might be important for the activation of allylic alcohol moiety. Notably, synthesis of spiroindanones bearing five-, six-, or seven-membered cyclic systems is possible applying this methodology.

During their research with indanone analogues, Lantano and co-workers studied the influence of reaction temperature and electronic nature of aldehydes under classical Claisen–Schmidt condensation conditions.[61] The reaction of 2-arylidene-1-indanones **49** with 1-indanones (R = H, OMe) at room temperature in the presence of aqueous ethanolic NaOH resulted Michael addition product bis-indane-1,5-diketones **108** (Scheme 29). On the other hand, multicomponent reaction between 1-indanone **1** (2 equiv.) and benzaldehydes **58** (2 equiv.) under refluxing conditions accomplished spirocarbocyclic compounds **109a-b** in good yields. It is worth mentioned that reaction with 3- and 4-pyridine aldehydes occurred at room temperature affording spiro-products **109c-d** in excellent yields (up to 98%). The dimerization of 2-arylidene-1-indanones **49** could also generate corresponding spiro compounds **109**.

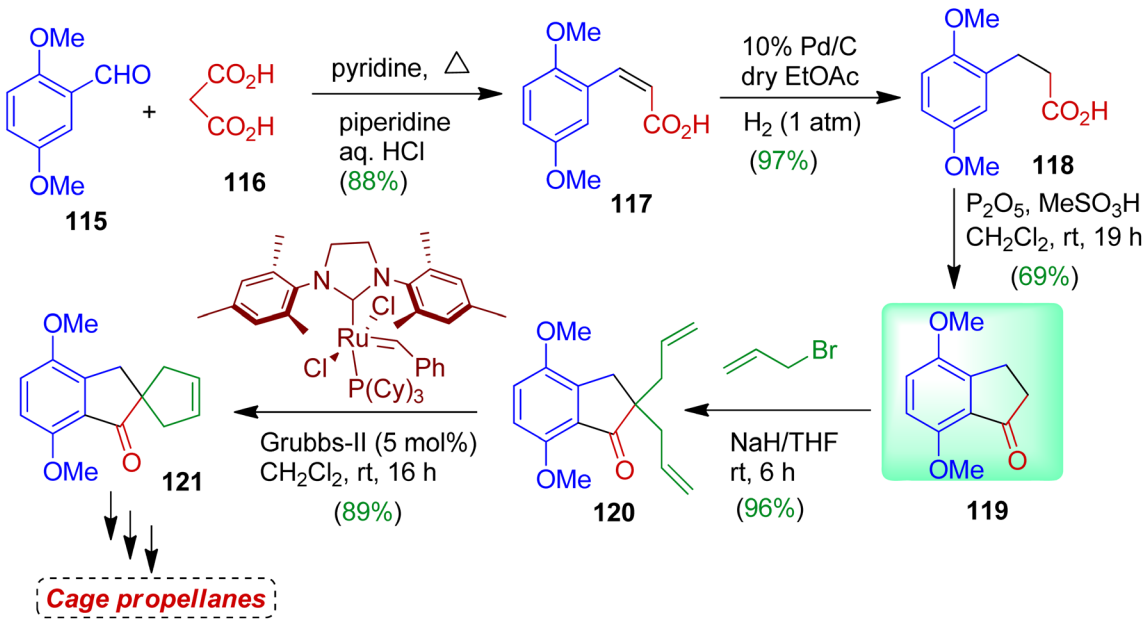
Synthesis as well as investigation of photophysical properties of indanone derived spirotruxenes was carried out by Kotha's group.[62] Firstly, cyclotrimerization of 1-indanone **1** was achieved with HCl/AcOH to generate truxene **110** (in 70% yield). Then treatment of ^{t}BuOK/allyl bromide in refluxing THF furnished hexallyl derivative **111** in 62% yield (Scheme 30). Subsequently, three-fold ring-closing metathesis (RCM) of **111** was attempted with Grubbs' second-generation catalyst to furnish desired compound **112** (67%). Bromination of truxene **110** may be performed using bromine in dichloromethane to



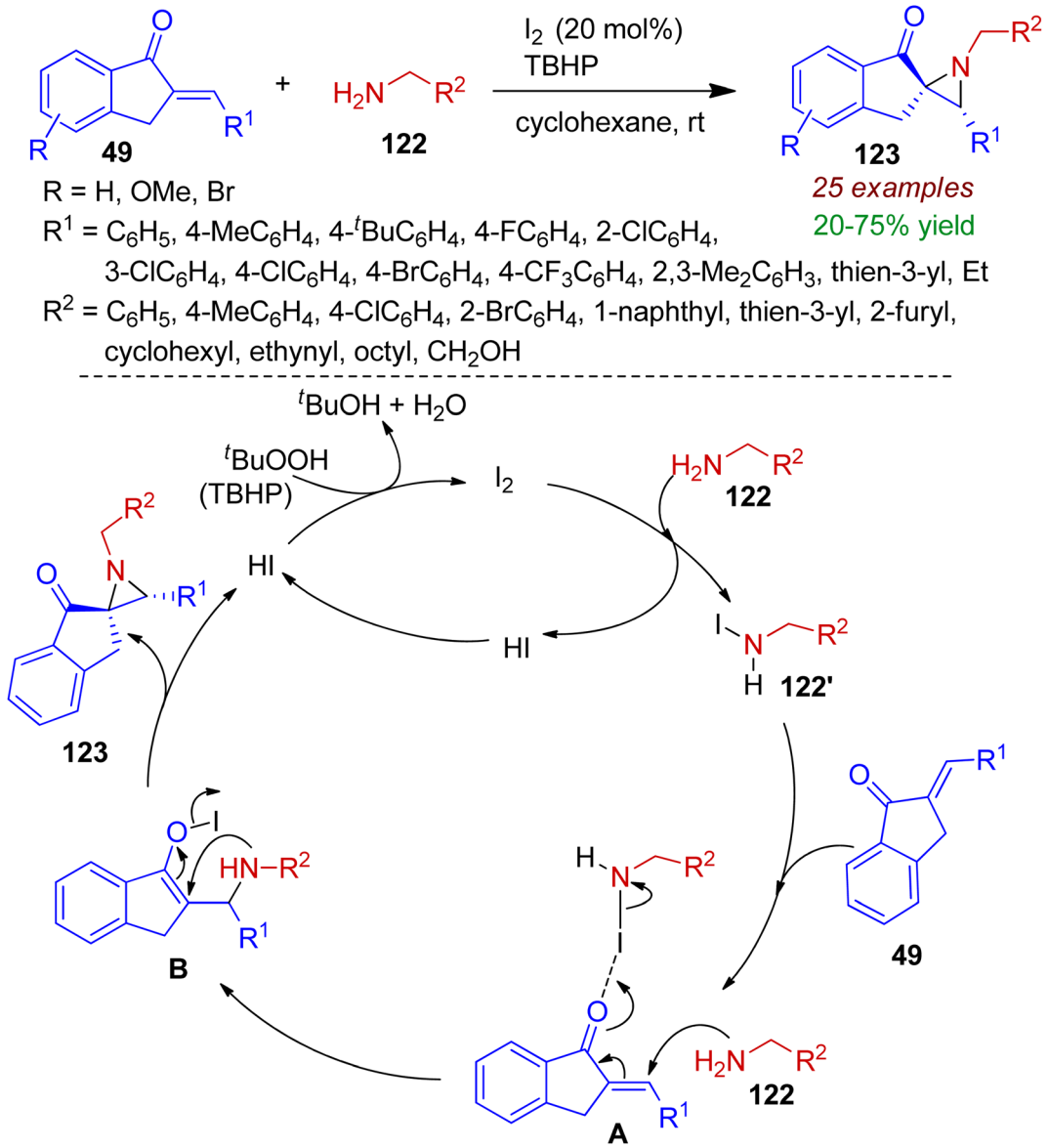
Scheme 30 Synthesis of various spirotruxenes from 1-indanone *via* RCM strategy.

offer 2,7,12-tribromotruxene **113**, which was followed by successive steps to deliver various arylated spirotruxenes **114**. These arylated substances exhibit fascinating photophysical properties with strong quantum yields (due to enhanced conjugation), and might be considered as C_3-symmetric 'blue-green-light-emitting materials'.

The authors also prepared 1-indanone compound **119** and used as the building block for synthesizing spirocarbocycle as well as cage propellanes.[63] The sequence of reactions is outlined in Scheme 31. In the first step, readily available 2,5-dimethoxybenzaldehyde **115** was subjected to react with malonic acid **116** to obtain unsaturated acid derivative **117** (Knoevenagel product) in 88% yield. Then hydrogenation with 10% Pd/C afforded



Scheme 31 Synthesis and application of 1-indanone derivative to access spiro carbocycles.

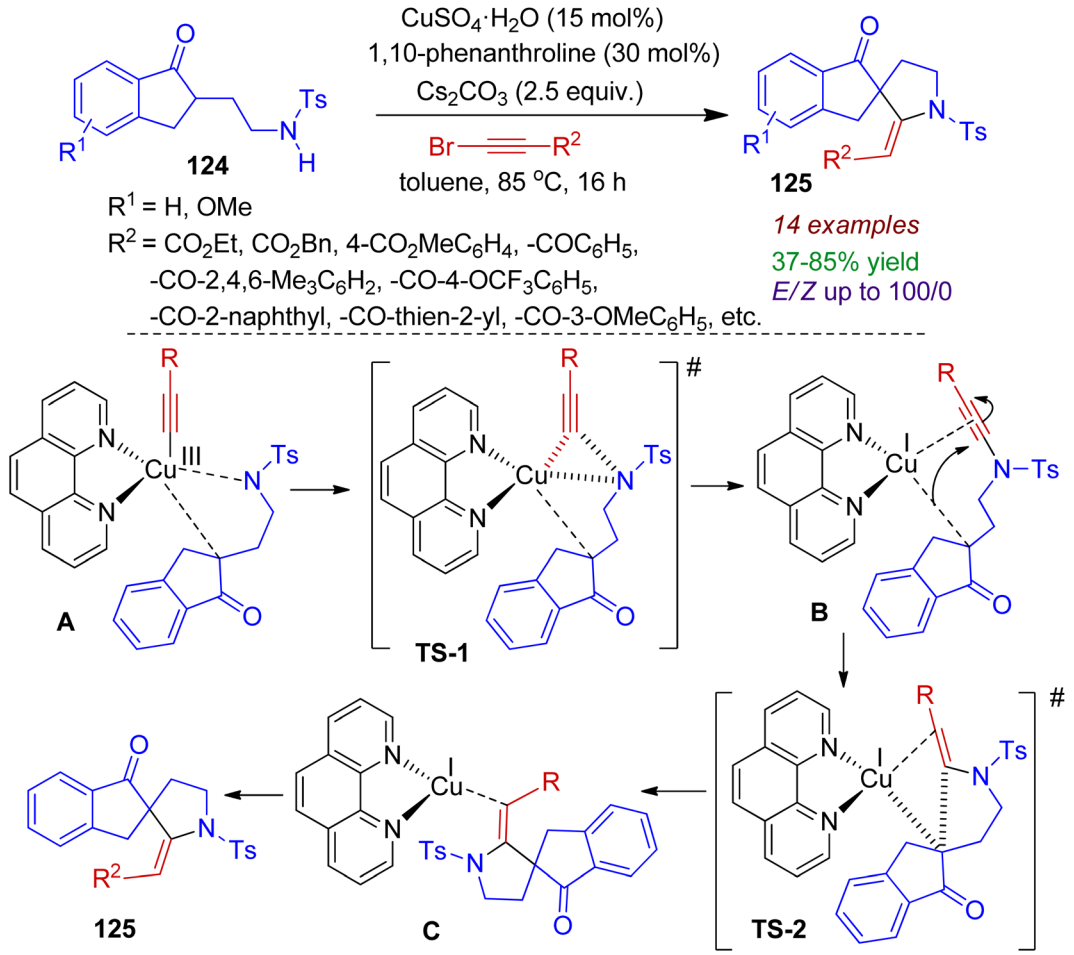


Scheme 32 I_2/TBHP mediated diastereoselective synthesis of *N*-alkylspiroaziridines from primary amines and 2-arylated-1-indanones.

corresponding saturated compound **118** (97% yield). Treatment of **118** with P_2O_5 and $MeSO_3H$ gave 1-indanone derivative **119** which was considered as the key building block for spiro products. Indanone **119** was then treated with allyl bromide in the presence of NaH in THF to furnish diallyl indanone compound **120** (96%). Finally the diallyl derivative **120** was subjected to RCM with Grubbs second generation catalyst resulting ring closure product spiro[4,4]nonane **121** (89%). Compound **121** could be employed as precursor for several cage propellanes and bioactive compounds.[64]

3.2. Spiro heterocycles

3.2.1. N-containing spiro-heterocycles. Spiro heterocycles are valuable structural motifs for synthetic transformations and considered as emerging drug candidates. Particularly, the synthetic utility of three-membered nitrogen heterocycles (aziridines) can be extended *via* ring opening reactions due to inherent ring strain.[65] Recently, Somappa *et al.* developed a I_2/TBHP mediated method for diastereoselective construction of *N*-alkylspiroaziridines **123** from primary amines **122** and easily accessible 2-arylated-1-indanones **49**.[66] Among various types of oxidants TBHP was found to provide the best result in the presence of catalytic amount of I_2. Benzyl amines and primary amines bearing aliphatic and heterocyclic core (thiophene, furan) were well tolerated under standard conditions. The proposed mechanism is demonstrated in Scheme 32. Initially primary amine **122** reacted with I_2 to generate *N*-iodoamine species **122′**. Afterwards, coordination with *N*-iodoamine with carbonyl group of indanone **49** assisted the Aza-Michael addition with another amine molecule resulting intermediate **A**. Intramolecular cyclization of intermediate **A** delivered the spiroannulated product **123** with regeneration of HI, which is

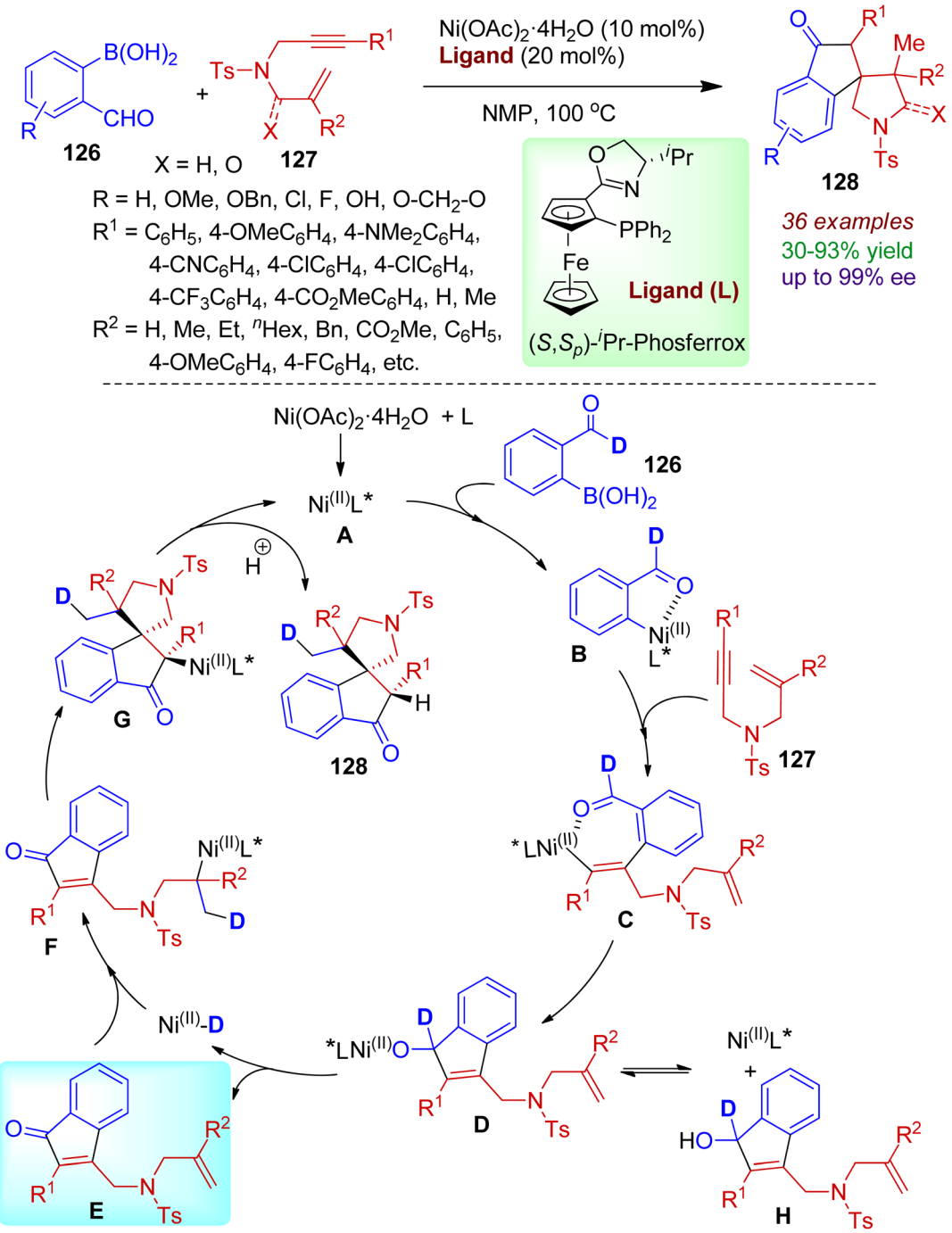


Scheme 33 Cu-catalyzed reaction of keto-sulfonamides with alkynyl bromide to result azaspiroindanone compounds.

oxidized to I_2 by TBHP for next catalytic cycle. Significantly, this transformation involves unprotected primary amines as the nitrogen source.

In 2017, spirocyclization of keto-sulfonamides was reported by Miesch and co-workers.[67] The copper-catalyzed reaction of keto-sulfonamides **124** with alkynyl bromide could be proceeded in the presence of base Cs_2CO_3 and ligand 1,10-phenanthroline affording spiroindeno-pyrrolidine compounds **125** in acceptable yields (Scheme 33). The protocol was found to be general for electron-withdrawing groups as substituents affording desired products with *E*-selectivity (up to *E*/*Z* ratio 100/0). Mechanistically, it is conceivable that oxidative addition of *in situ* formed copper species to the alkynyl bromide generates a Cu(III) alkynylcopper species. The excess base might lead to double deprotonation of the keto sulphonamide which interacts with Cu(III) complex, producing intermediate **A**. Subsequent reductive elimination (C–N bond formation, intermediate **B**) and 1,4-addition of the resulting Cu(I) enolate to the alkynoate produces alkenylcopper(I) intermediate **C** (C–C bond formation). Finally, protonation provides azaspiro compounds **125**. The synthesized azaspiro compounds can serve as building blocks for several indole alkaloids.

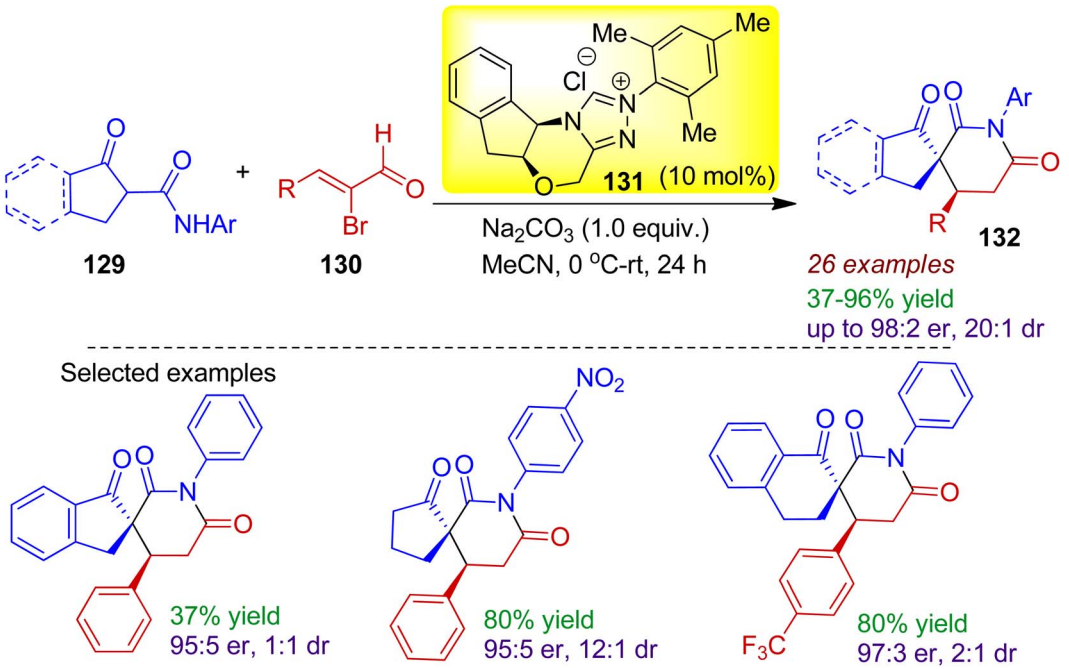
A nickel-catalyzed redox-neutral protocol for one-pot synthesis of spiroindanones from readily accessible *o*-formylarylboronic acids **126** and 1,6-enynes **127** was reported by Kong's group.[68] The reaction comprised *in situ* formation of indanone species furnishing a library of enantioenriched spiroindanones **128** in good yields with high enantio- and diastereoselectivity (up to 99% ee and >20 : 1 dr). Phos-type ligands such as, (S,S_p)-^{i}Pr-Phosferrox was found to be most effective, and aryl boronic acids containing electron-donating groups (methoxy or benzyloxy) and electron-withdrawing groups (Cl, F) were amenable in this process. Even heteroaromatic boronic acids responded the reaction satisfactorily. However, the reaction failed for substrates containing vinyl moieties instead of aldehydes. The practicality of the Ni-catalyzed asymmetric process was certified by gram-scale synthesis of the desired products. A plausible mechanism of the catalytic conversion is outlined in Scheme 34. Initially, transmetallation of *o*-formylarylboronic acids **126** with chiral nickel complex **A** delivered aryl nickel complex **B**, which possibly be stabilized by coordination between the aldehyde group and the nickel center. In the next step, the seven-membered nickel species **C** was generated *via* migratory insertion of the alkyne into the aryl–nickel bond. Intramolecular nucleophilic addition led to alkoxynickel



Scheme 34 Nickel-catalyzed synthesis of spiroindanones from *o*-formylarylboronic acids and 1,6-enynes.

intermediate **D**. During the process, formation of an appreciable quantity of indenol intermediate **H** was observed. Subsequent β-H elimination resulted enone **E** and key Ni(II)–**D** species. Regioselective 1,2-addition of Ni(II)–D species to the unactivated alkene (intermediate **F**), followed by spirocyclization gave C(sp^3)–nickel intermediate **G**. Hydrolysis furnished spiroindanone product **128** with regeneration of the nickel catalyst.

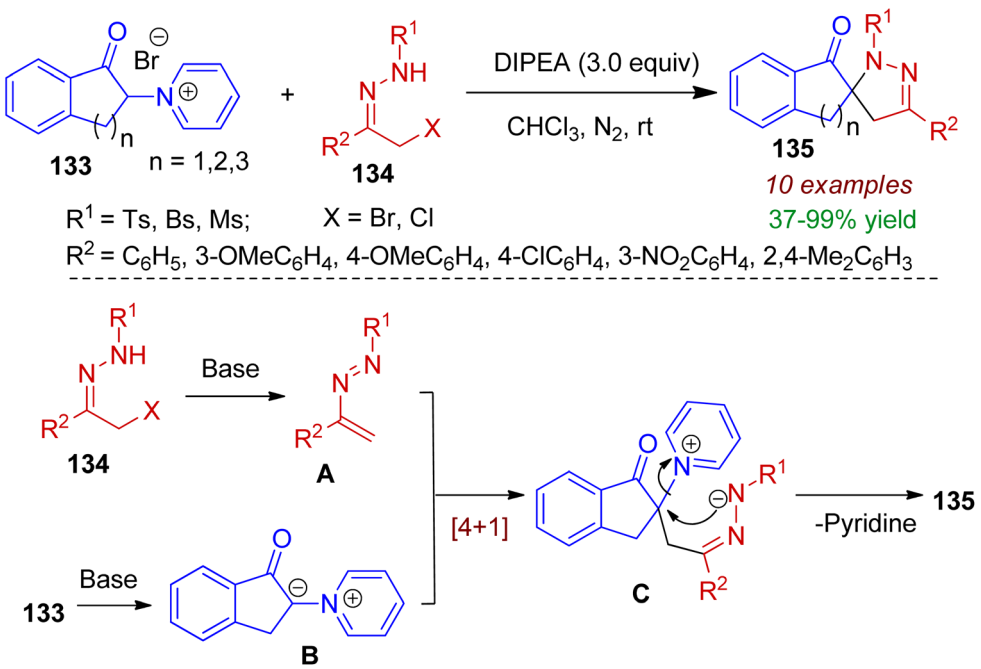
In 2018, Biju's group devised an organocatalytic stereoselective [3+3] spiro-annulation strategy to obtain spiro-glutarimide derivatives **132** containing two contiguous stereocenters including one all-carbon quaternary spirocenter.[69] The reaction of cyclic β-ketoamides **129** with enal compounds **130** catalyzed by 10 mol% N-heterocyclic carbene catalyst **131** in acetonitrile solvent efficiently produced spiro-glutarimides **132** (Scheme 35). In addition to indanone derived β-ketoamides, various cyclopentanone and α-tetralone derived β-ketoamides underwent smooth annulation resulting desired compounds with acceptable enantio- and diastereoselectivity. The assembly of the ketoamides with catalytically generated chiral α,β-



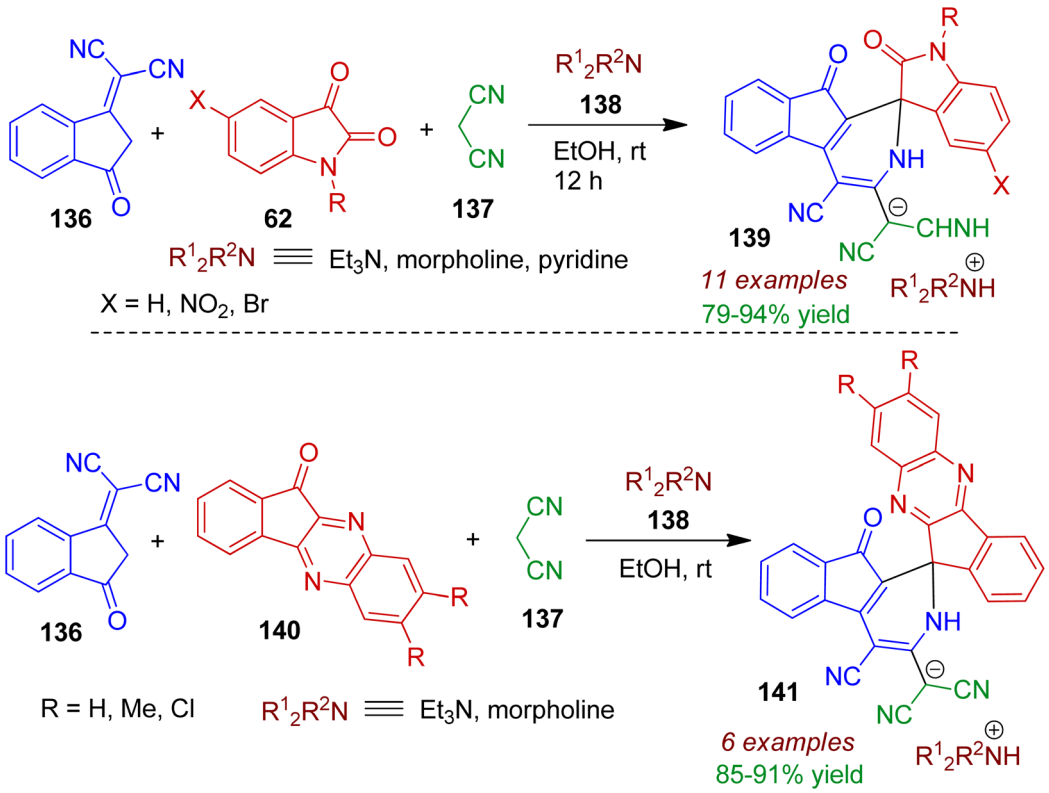
Scheme 35 Organocatalytic stereoselective synthesis of spiro-glutarimides from cyclic β-ketoamides and enal compounds.

unsaturated acylazoliums proceeded in a Michael addition-proton transfer-cyclization sequence.

Cyclic pyridinium ylides may also be used as new synthon for spiro-heterocyclic compounds. In 2020, Yuan's group designed indanone-3-pyridinium salts **133** and allowed them to react with α-halo hydrazones **134** for the construction of spiropyrazoline indanones **135** (yield up to 99%) *via* [4+1] annulation strategy.[70] DIPEA was found to be most effective base and chloroform as solvent. Notably, indanone-3-pyridinium ylides acted as C1 synthons in this reaction. Analysis of the X-ray crystallographic data of a single crystal unambiguously confirmed its structure. The probable mechanism is depicted in Scheme 36. The α-halo hydrazone **134** upon base-catalyzed elimination forms azoalkene **A** which is the key intermediate. Meanwhile, the deprotonation of indanone-3-pyridinium salts furnishes ylide **B**. Afterwards, conjugate addition of ylide **B** to intermediate **A**



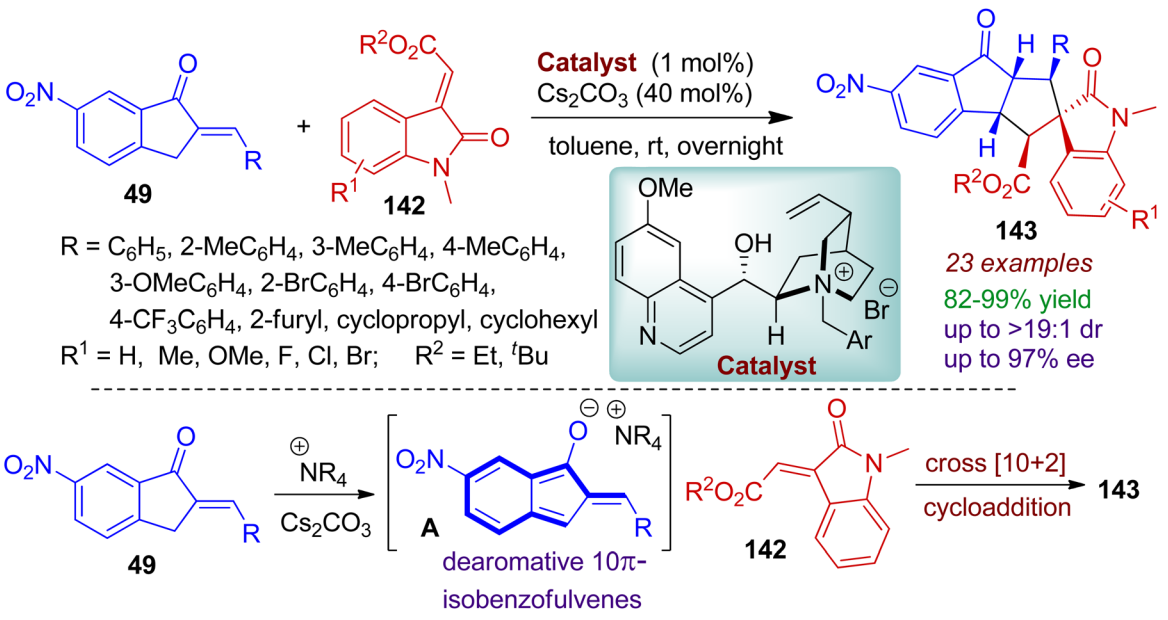
Scheme 36 Construction of spiropyrazoline indanones *via* the reaction of indanone-3-pyridinium ylides and α-halo hydrazones.



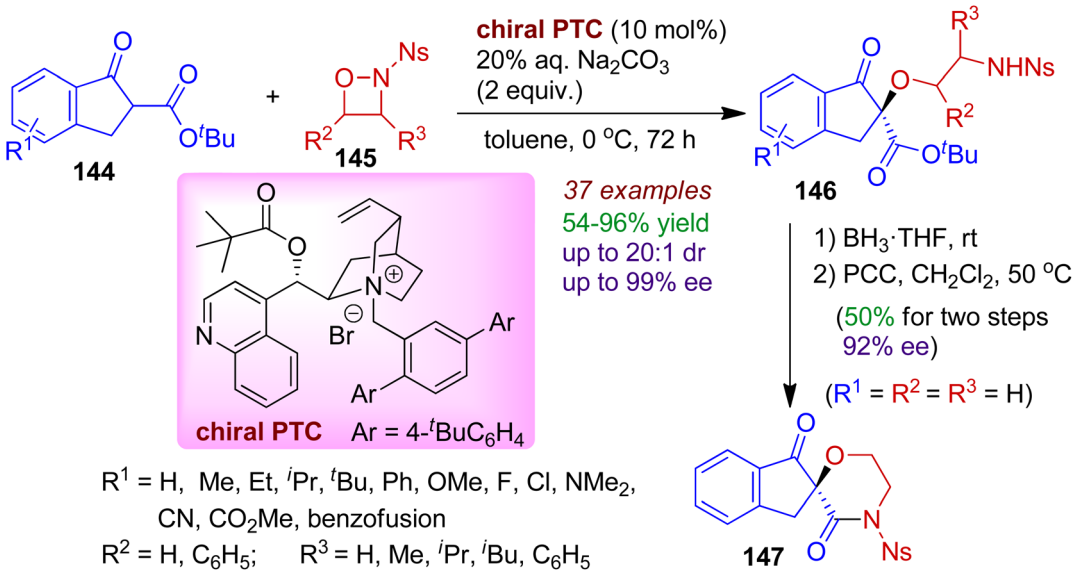
Scheme 37 Multicomponent synthesis of spiroindenopyridine-oxindoles and spiroindenopyridine-indenoquinoxalines.

generates intermediate **C**. Finally, intramolecular cyclization leads to the formation of spiro-annulated product **135** with elimination of pyridine to complete the [4+1] annulation process.

A facile metal-free, green approach towards indenopyridine-spirocyclic systems *via* multicomponent reaction (MCR) was reported by Shakibaei and Bazgir.[71] The four-component reaction of 1,1-dicyanomethylene-3-indanone **136**, isatins **62** and malononitrile **137** and amines (morpholine, triethylamine or pyridine) **138** in ethanol regioselectively delivered spiroindenopyridine–oxindole framework **139** at ambient temperature (Scheme 37). The reaction was believed to proceed *via*



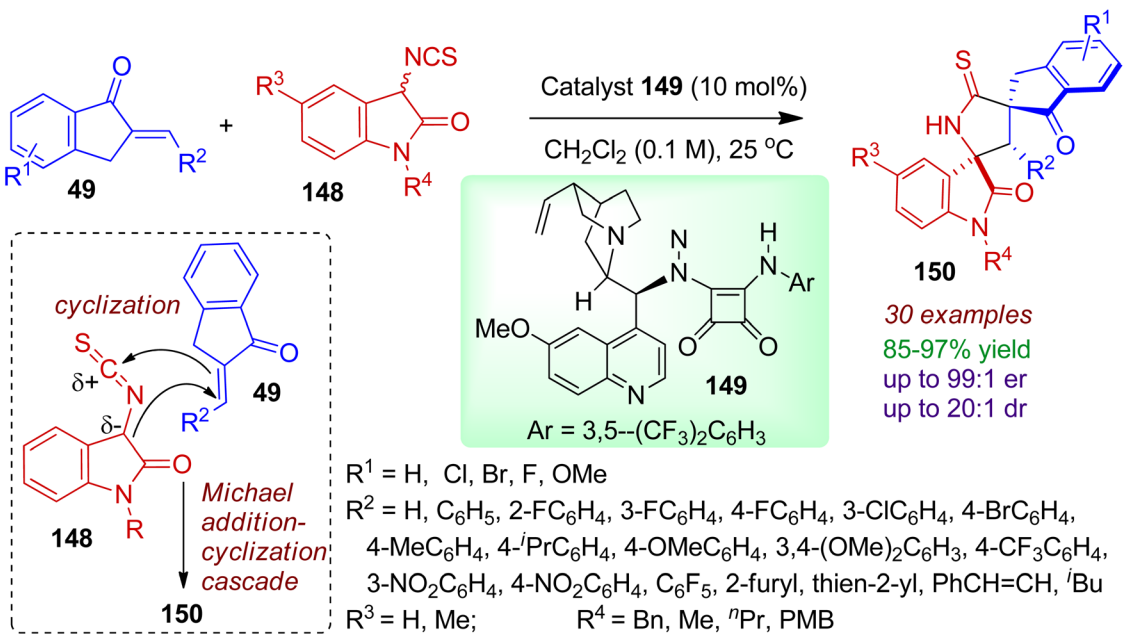
Scheme 38 Cross formal [10+2] cycloaddition of 1-hydroxyl isobenzofulvene species with electron-deficient alkenes to form spiro-cyclopentaindeno-indolines.



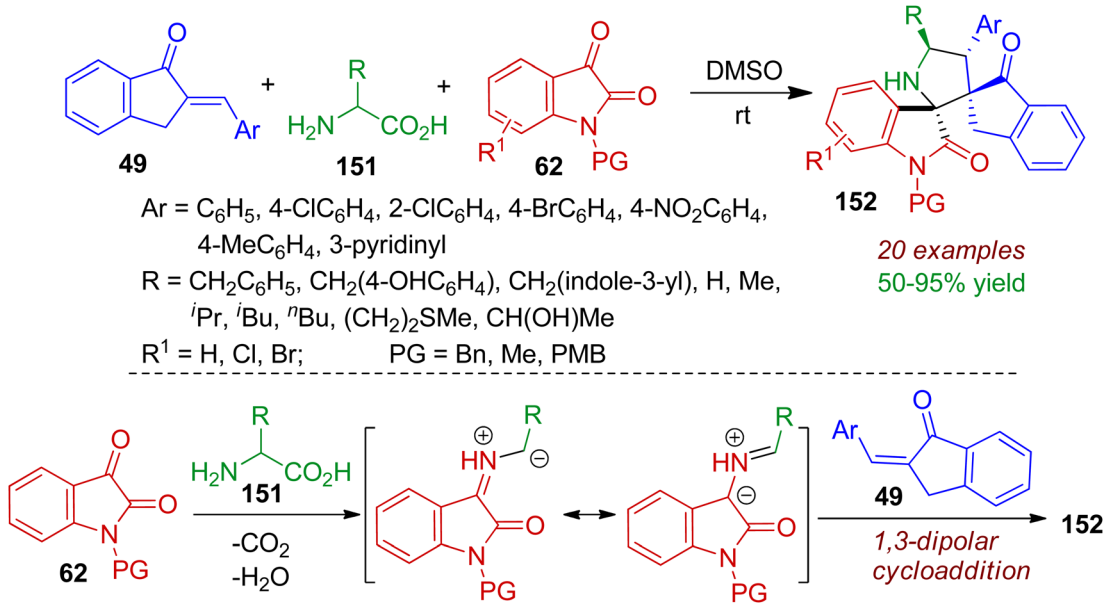
Scheme 39 Asymmetric synthesis of spiroindeno-morpholines *via* the reaction of 1,2-oxazetidines and indanone carboxylates.

tandem knoevenagel/Michael/elimination/[5+1] annulation sequence. The pure products could be isolated simply by evaporation of solvent and washing by cold diethyl ether. As expected, the assembly of indanone **136**, malononitrile **137**, indenoquinoxalines **140** in the presence of amines **138** under same reaction condition led to the formation of spiroindenopyridine-indenoquinoxaline derivatives **141** in good yields (up to 91%).

2-Arylidene-1-indanones compounds could be converted to dearomative 1-hydroxyl isobenzofulvene-type species for chemoselective cross formal [10+2] cycloaddition reaction with electron-deficient alkenes **142**.[72] Excellent diastereo- and enantioselectivity were maintained by employing a novel bulky cinchona-based ammonium salt as catalyst (1 mol%) to afford richly decorated spiro-cyclopentaindeno-indolines **143** (Scheme 38). Significantly, the 2-arylidene-1-indanones **49** possessing aryl groups, cyclopropyl, cyclohexyl, furyl moieties were well tolerated by this process. Considering the acceptor system **142**, ethyl as well as sterically hindered *tert* butyl ester group offered good yields and selectivity. Mechanistically, it is conceivable that under the basic conditions, dearomative 1-hydroxyl isobenzofulvene anion intermediate **A** was generated from 2-



Scheme 40 Catalytic enantioselective cyclization of 3-isothiocyanato oxindoles and 2-arylidene-indanones towards 3,2′-pyrrolidinyl bispirooxindoles.

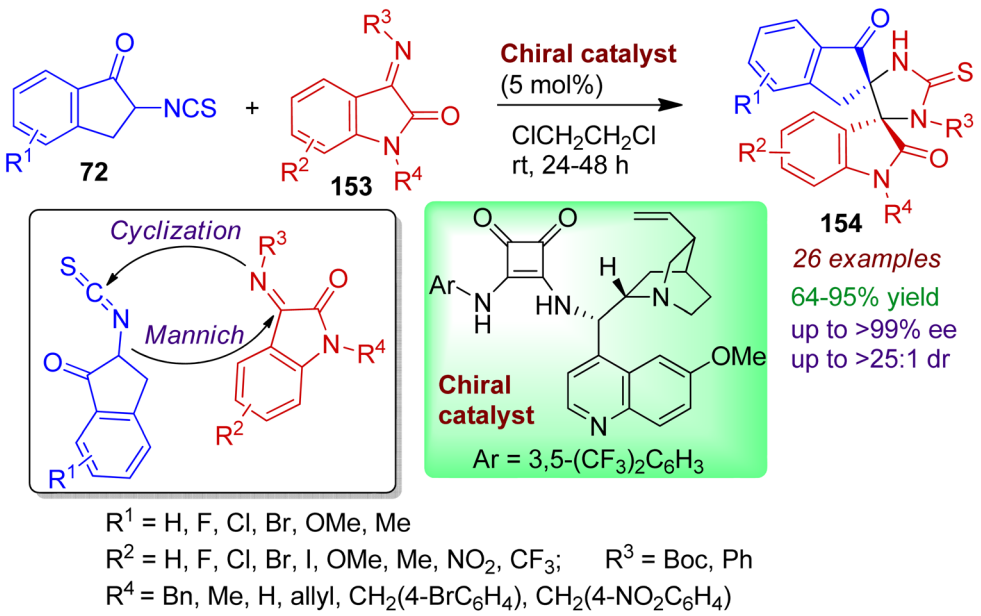


Scheme 41 Formation of bispiro compounds *via* three-component reaction between 2-arylidene-indanones, isatins and primary amino acids.

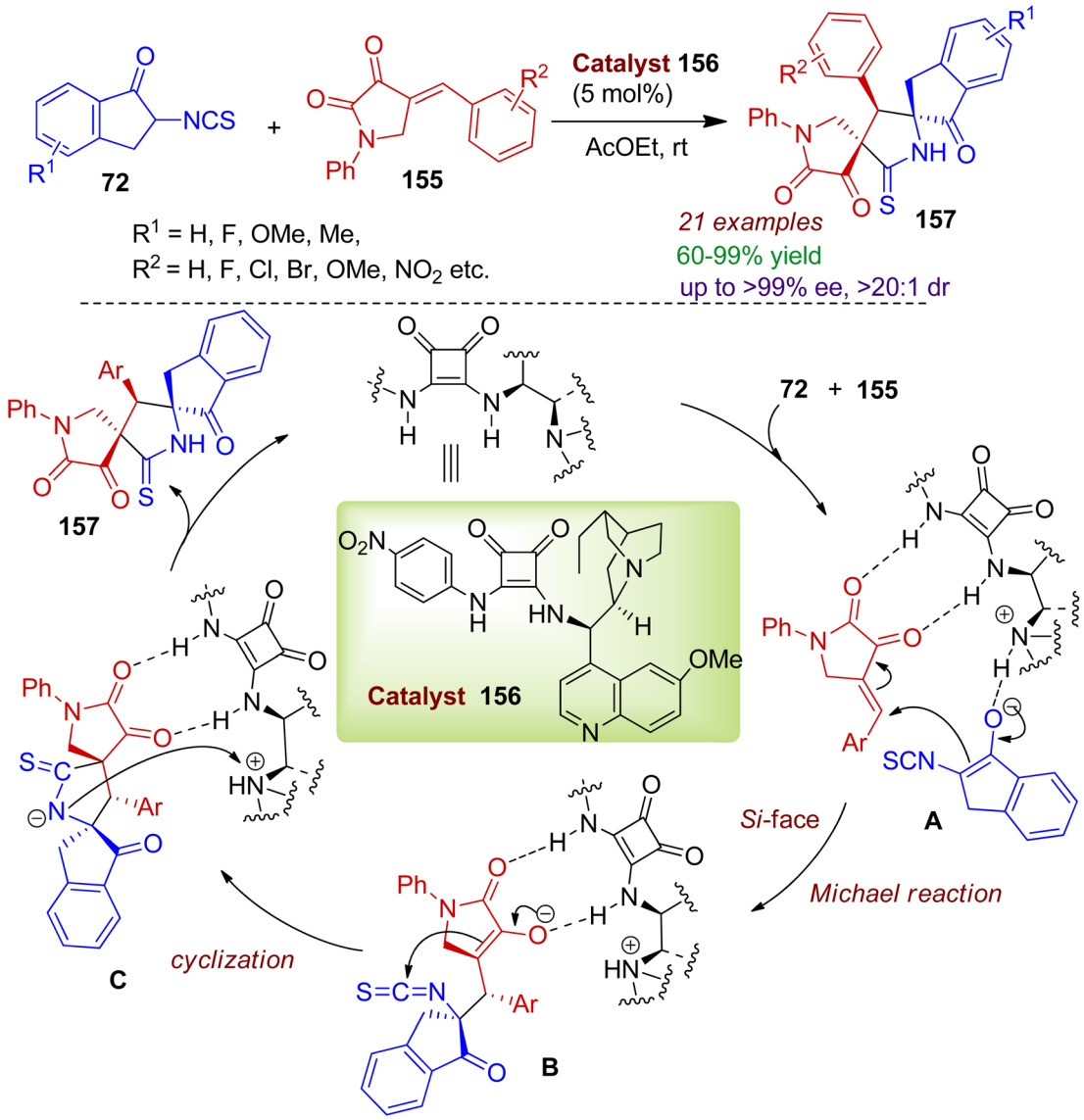
arylidene-1-indanones **49** in the presence of cinchona-derived catalyst. The *in situ* formed intermediate **A**, effectively acted as 10π electron system and underwent cross formal [10+2] cycloaddition reaction with electron-deficient alkenes **142** thereby forming the spiro- compound **143** with stereoselectivity.

A highly enantio- and diastereoselective ring opening reaction of 1,2-oxazetidines **145** with indanone carboxylates **144** in the presence of a chiral phase transfer catalyst (PTC) was reported by Hu's group.[73] Exploiting the unique electrophilic oxygen reactivity of highly functionalized *N*-nosyl 1,2-oxazetidines, a library of *N,O*-containing chiral ether **146** bearing a quaternary carbon center was obtained in good yields and stereoselectivities (up to 97% ee and 20 : 1 dr) under mild conditions. This is an interesting example of catalytic asymmetric umpolung reaction involving indanone system. Significantly, the products could be effectively converted into biologically important spiroindeno-morpholine derivatives **147** *via* two steps (Scheme 39).

3.2.2. N-Containing bispiro-heterocycles. Synthesis of bispiro skeleton with stereochemical diversity is a challenging task in organic chemistry. Kayal and Mukherjee synthesized enantioenriched 3,2′-pyrrolidinyl bispirooxindole derivatives **150** from readily available 3-isothiocyanato oxindoles **148** and 2-arylidene-indanones **49** catalyzed by a quinine-derived tertiary



Scheme 42 Access to bispiro indanone-thioimidazolidine-oxindoles from 2-isothiocyanato-1-indanones and isatinimines.



Scheme 43 Synthesis of bispiropyrrolidone indanones from 2,3-dioxopyrrolidines and 2-isothiocyanato-1-indanones.

amino-squaramide **149** (Scheme 40).[74] The bispiro-oxindole indanone compounds **150** were produced *via* Michael addition/cyclization cascade in excellent yields with high enantioselectivity and diastereoselectivity (up to 99 : 1 er and 20 : 1 dr). Various arylidene-indanones with diverse steric and electronic character were compatible under ambient conditions. Notably, heteroarylidene-indanones were also well tolerated to form desired products in good selectivity. The protocol was equally efficient for different 3-isothiocyanato oxindoles containing varied *N*-substituents (Bn, Me, ^{n}Pr, PMB). The absolute configuration was determined by single crystal XRD analysis.

Construction of pyrrolidine–bispirooxindole frameworks bearing sterically congested two vicinal spiro-centers was realized *via* a three-component reaction between 2-arylidene-indanones **49**, isatins **62**, primary amino acids **151**.[75] The 1,3-dipolar cycloaddition reaction accomplished pyrrolidine–bispirooxindoles **152** in highly regio- and diastereoselective manner. In most of the cases, single diastereoisomer were obtained in good yields (up to 95%) at room temperature in DMSO solvent. Significantly, primary amino acids **151** acted as amine component (*via* decarboxylation) for the *in situ* generation of azomethine ylides from isatin (Scheme 41). The azomethine ylides underwent 1,3-dipolar cycloaddition reaction with 2-arylidene-indanones **49** offering bispiro skeleton **152**. Relative configurations of the products were determined by single crystal X-ray diffraction analysis. The practicality of the reaction was certified by gram-scale synthesis. Molecular docking studies revealed that the some products can act as inhibitors of the epidermal growth factor receptor (EGFR).

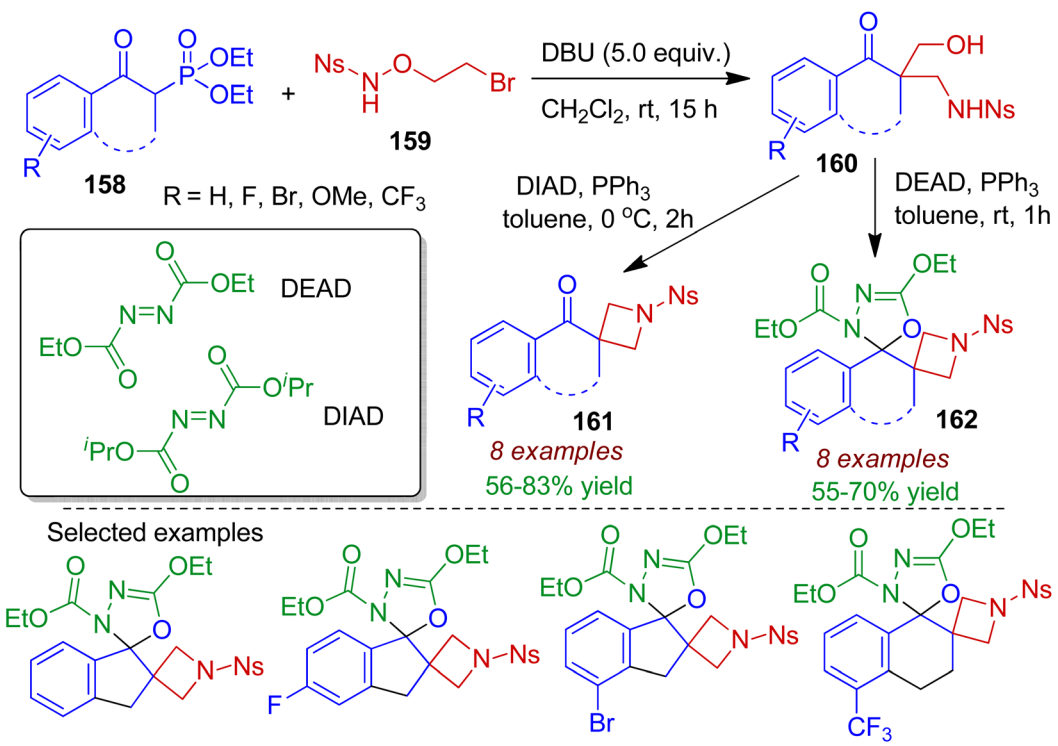
An efficient protocol for the stereoselective construction of bispiro indanon-thioimidazolidine-oxindoles bearing two adjacent spiro-quaternary stereocenters has been reported by Zhao and Du.[76] The cinchona alkaloid derived squaramide-

based chiral organocatalyst promotes reaction between 2-isothiocyanato-1-indanones **72** and isatinimines **153** to deliver desired thioimidazolidine-oxindole bispiro system **154** with excellent enantio- and diatereoselectivity (up to >99% ee, >25 : 1 dr). The reaction takes place *via* initial Mannich reaction followed by cyclization sequence (Scheme 42). Indanones and isatnimines containing electron-withdrawing (F, Cl, Br) and electron-donating substituents (Me, OMe) responds well under standard conditions. The synthesized bispiro products can easily be transformed into various bioactive compounds.

The authors also synthesized spiropyrrolidone indanone scaffolds using squaramide catalyst **156** using readily available 4-arylmethylidene-2,3-dioxopyrrolidines **155** and 2-isothiocyanato-1-indanones **72**.[77] This method provides mild access to bispirocyclic compounds **157** containing three contiguous stereocenters in excellent yields (up to 99%) and enantio-/diatereoselectivity (up to 99% ee, >20 : 1 dr). A plausible mechanism for the squaramide-triggered cycloaddition reaction is outlined in Scheme 43. Initially, the isothiocyanato-1-indanone **72** is enolized *via* quinidine amine in the Michael addition process. Meanwhile, dioxopyrrolidine **155** is activated by the catalyst through hydrogen bonding. The enol ion attacks the double bond of **155** from the *Si*-face *via* intermediate **A**. Subsequently, the newly formed anion on the α-carbon center of **155** attacks the carbon atom of the isothiocyanato group in the intramolecular cyclization fashion involving intermediate **B**. The desired bispiro skeleton **157** is constructed through protonation of intermediate **C** along with the regeneration of the catalyst for the next cycle.

A tandem hydroxymethylation and aminomethylation reaction of cyclic β-keto phosphonates **158** with *N*-nosyl-*O*-(2-bromoethyl)hydroxylamine **159** in the presence of DBU was devised by Hu *et al.*[78] The reaction led to the formation of 1,3-aminoalcohols **160** at room temperature through sequential Horner–Wadsworth–Emmons/Michael addition/aldol reactions. The resultant 1,3-aminoalcohols **160** could readily be transformed into biologically relevant spirocyclic azitidines **161** and azitidine-oxadiazoline bispirocycles **162** *via* Mitsunobu cyclization reaction (Scheme 44). It is worth mentioned that synthesis of bispirocyclic core bearing two vicinal azetidine and oxadiazoline rings otherwise difficult to achieve.

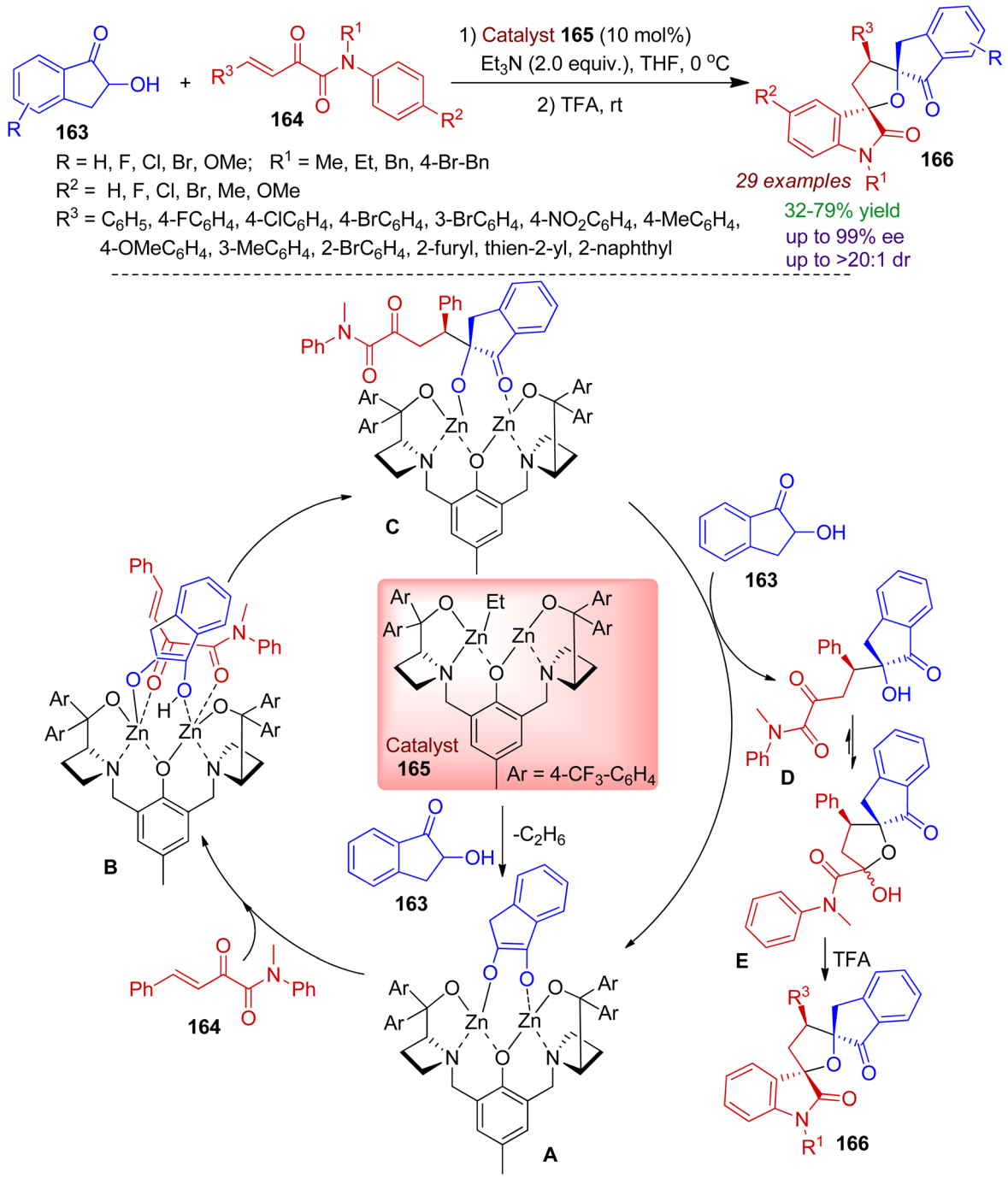
Recently, 2-hydroxy-1-indanone scaffold has been exploited by researchers to access diverse spiro heterocyclic frameworks. A facile synthesis of bispirotetrahydrofuran oxindoles **166** by cooperative bimetallic-catalyst is realized by Chang, Wang and co-workers *via* the reaction of 2-hydroxy-1-indanone **163** and β,γ-unsaturated α-ketoamide **164**.[79] The strategy involves cascade Michael/hemiketalization/Friedel–Crafts reaction sequence. The reaction is highly step-economic and can run on a gram scale with minimum catalyst loading. A plausible mechanism for the catalytic conversion is proposed in Scheme 45. Coordination and deprotonation of nucleophilic 2-hydroxy-1-indanone **163** with dinuclear zinc–ligand catalyst **165** gives intermediate **A**. Afterwards, electrophilic β,γ-unsaturated α-ketoamide **164** is activated by zinc–oxygen coordination to afford complex **B** from the sterically less hindered site. Subsequently, **B** undergoes Michael addition reaction to generate intermediate **C**. Next, proton transfer with another 2-hydroxy-1-indanone produces the Michael addition product **D** which is converted into its hemiketal form **E**. Finally, intramolecular Friedel–Crafts alkylation leads to bispiro indanone compound **166**.



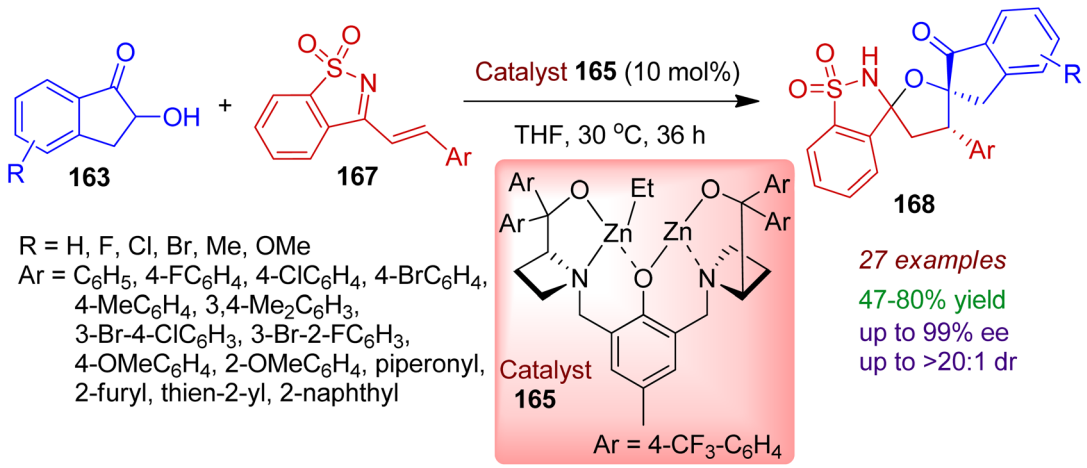
Scheme 44 Synthesis of spirocyclic azitidines starting from cyclic β-keto phosphonates and *N*-nosyl-*O*-(2-bromoethyl)hydroxylamine.

Very recently, an efficient synthesis of bispirocyclic saccharine system is realized involving asymmetric [3+2] spiroannulation reaction of saccharine-derived cyclic azadienes **167** with 2-hydroxy-1-indanones **163**.[80] The bimetallic cooperative catalytic conversion was attributed *via* Michael/O-Mannich cascade process resulting highly stereoselective formation of bispirocyclic compounds **168** in which indanone, tetrahydrofuran, and saccharine moieties are embedded (Scheme 46). 2-Hydroxy-1-indanones bearing electron-donating groups (Me, OMe) and electron-withdrawing groups (F, Cl, Br) underwent the [3+2] spiroannulation reaction with excellent enantioselectivity (up to 99% ee). A wide range of saccharine derivatives with varied aryl substitution including heterocycles (thienyl, furyl, piperonyl) was fruitful under the standard conditions. This strategy could be run on a gram scale without significant loss of stereoselectivities.

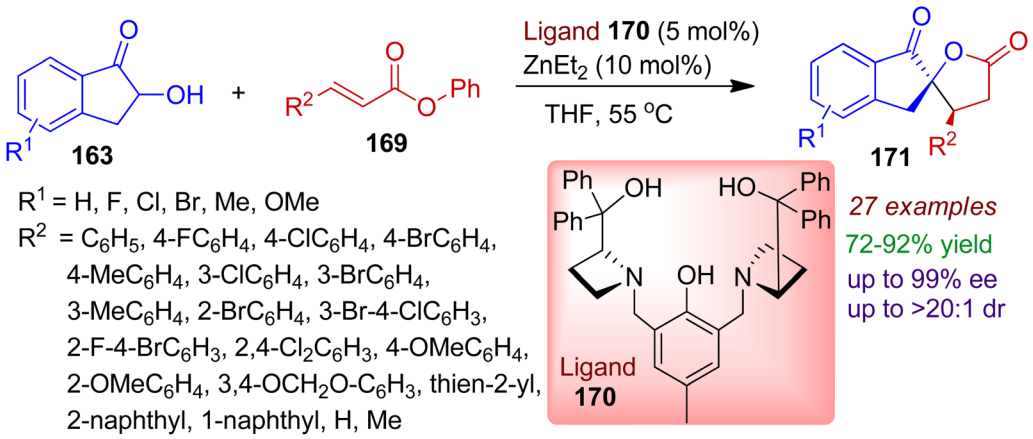
3.2.3. O-containing spiro-heterocycles. Stereoselective construction of spirolactones has attracted significant attention due to their great medicinal value as well as diverse synthetic applications. In 2019, Wang *et al.* developed a facile chiral



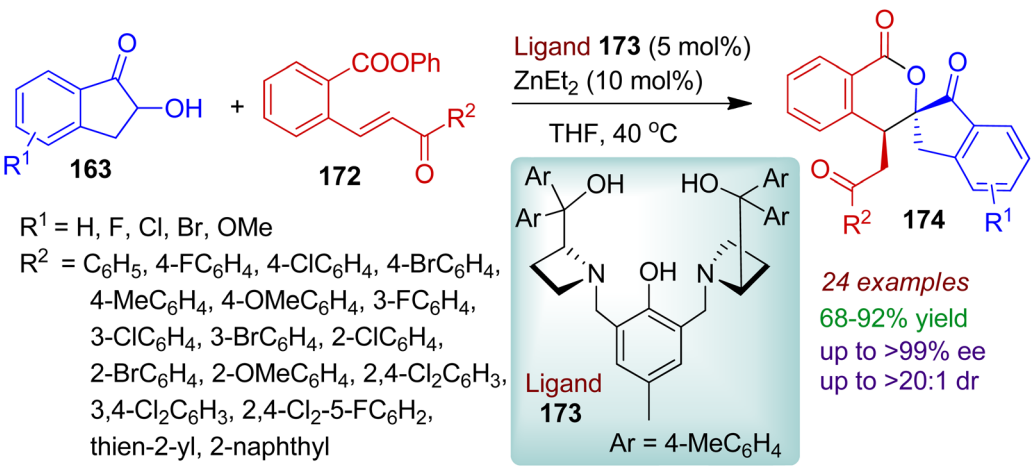
Scheme 45 Formation of chiral bispirotetrahydrofuran oxindoles *via* the reaction of 2-hydroxy-1-indanone and β,γ-unsaturated α-ketoamides.



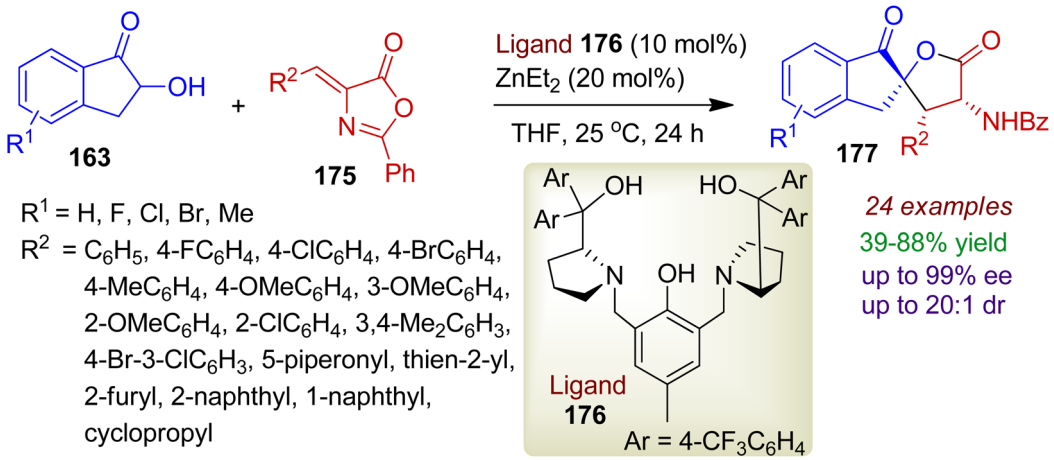
Scheme 46 Construction of bispirocyclic saccharine scaffolds *via* reaction of cyclic azadienes and 2-hydroxy-1-indanones.



Scheme 47 Dinuclear zinc-AzePhenol complex catalyzed synthesis of spiro[indanone-5,2′-γ-butyrolactones] from 2-hydroxy-1-indanones and α,β-unsaturated esters.



Scheme 48 Dinuclear zinc catalyzed synthesis of spiro[indanone-2,3′-isochromane-1-one] derivatives from 2-hydroxy-1-indanones and *ortho*-ester chalcones.

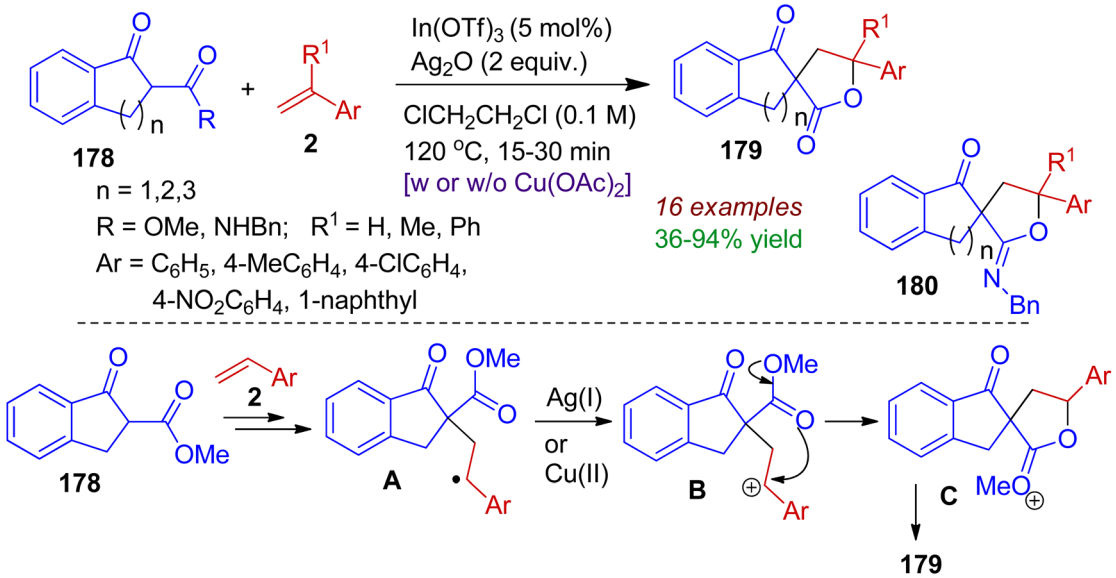


Scheme 49 Dinuclear zinc catalyzed synthesis of spirocyclic α-amino-γ-butyrolactones from 2-hydroxy-1-indanones and alkylidene azlactones.

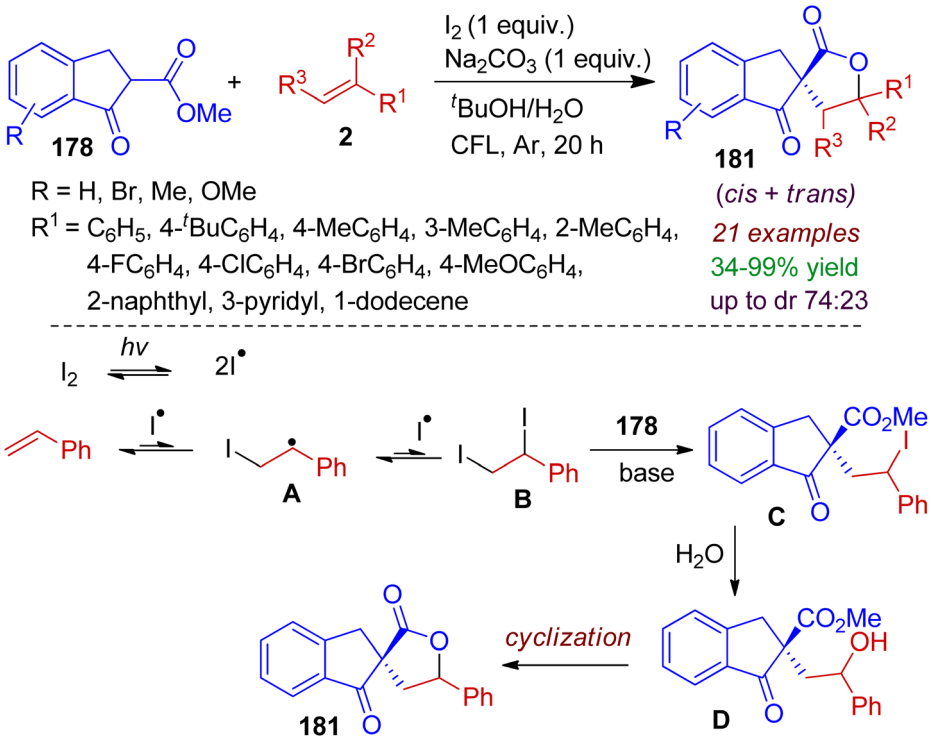
dinuclear zinc-AzePhenol complex catalytic reaction employing 2-hydroxy-1-indanones **163** and α,β-unsaturated esters **169** (Scheme 47).[81] The use of 5 mol% of ligand **170** and 10 mol% of Et_2Zn was found to be effective for cyclization in THF medium. The one-step cascade Michael addition/transesterification reaction well accomplished wide range of spiro[indanone-5,2′-γ-butyrolactones] **171** with contiguous stereocenters in excellent yields and stereoselectivities (up to >99% ee, >20 : 1 dr). α,β-Unsaturated esters bearing aromatic (aryl, naphthyl, piperonyl, thienyl) as well as nonaromatic moieties smoothly delivered corresponding products. The electronic natures and positions of substituents had very little influence on the stereoselectivities. The absolute configuration of the synthesized products was established by X-crystal structure.

The authors also successfully carried out similar type of asymmetric Michael addition/transesterification tandem reaction between 2-hydroxy-1-indanones **163** and *ortho*-ester chalcones **172** using a dinuclear zinc catalyst (ligand **173** and Et_2Zn).[82] A library of chiral spiro[indanone-2,3′-isochromane-1-one] derivatives **174** possessing two adjacent chiral centers was obtained up to >99% ee, >20 : 1 dr (Scheme 48). Notably, the *ortho*-ester chalcones **172** bearing mono, di, and trisubstituted aromatic rings (R^2 = aromatics) were proved to be suitable substrates for this conversion. However, the reaction failed for *ortho*-ester chalcones with aliphatic substituents (R^2 = Me). The practicality of the reaction was manifested by the gram-scale synthesis of the desired spiro products without affecting stereoselectivities.

Alkylidene azlactones may also be used for the preparation of spirolactone derivatives. An efficient enantioselective annulation of 2-hydroxy-1-indanones **163** and alkylidene azlactones **175** was realized with chiral dinuclear zinc catalyst (ligand **176**



Scheme 50 Indium(III)/silver(I)-catalyzed synthesis of spirolactones/spiroiminolactones from 2-substituted 1-indanones and styrene.



Scheme 51 Photooxidative reaction between substituted 1-indanones and olefins to afford spirolactones.

and Et_2Zn).[83] The reaction enabled the formation of polyfunctional spirocyclic α-amino-γ-butyrolactones **177** bearing three stereocenters *via* [3+2] cyclization (Scheme 49). A wide range of *ortho*-, *meta*-, *para*- and multisubstituted phenyl azlactone substrates **175** could be applied to afford α-amino-γ-butyrolactones **177** in good yields (up to 88%) and stereoselectivities (up to 99% ee, 20 : 1 dr). However, corresponding aliphatic substitution (R^2 = cyclopropyl) led to decreased yield (70%) and enantioselectivity (73% ee). The methodology was also amenable for α-hydroxyacetophenones and 3-hydroxychroman-4-ones.

During their synthetic programme, Ko and Youn realized a cooperative indium(III)/silver(I)-catalyzed synthesis of spirolactones **179** and spiroiminolactones **180** starting from readily available 2-substituted 1-indanones **178** and substituted styrenes **2**.[84] This method involves sequential formation of C–C and C–O (or C–N) bonds with good substrate scope within short time (15–30 min). Mechanistically, it is conceivable that (Scheme 50) the reaction of indanones **178** with styrene **2** in the presence of indium catalyst generates radical intermediate **A**. Then, intermediate **A** is oxidized to the benzylic carbocation **B** by Ag(I) alone or with the help of co-oxidant $Cu(OAc)_2$. Subsequent intramolecular cyclization (lactonization) furnishes spirolactone species **C**, which after hydrolysis produces spirolactone product **179**.

Finally, we discuss an interesting photooxidative intermolecular spirolactonization reaction as reported by Maejima, Yamaguchi and Itoh.[85] The visible light/molecular iodine-mediated reaction between 1-indanone derivative **178** (acts as β-keto ester) and olefins **2** proceeded to afford indeno spirolactones **181** in a single step. Iodine radical generation from molecular iodine triggered by visible light was the key step in this process. A plausible mechanism is outlined in Scheme 51. Initially, iodine radicals are generated *via* activation of molecular iodine by visible light. Afterwards, iodine radicals are added to the olefin to form radical intermediate **A**, which is added to another iodine radical, thereby producing *vic*-diiodide intermediate **B**. Subsequently, the diiodide **B** reacted with β-keto ester **178** in the presence of base to obtain compound **C**. Hydrolysis of **C** gives corresponding hydroxyl intermediate **D**, which after intramolecular cyclization forms desired spirolactone **181**. The reaction is cost effective, atom economic, without using transition-metal catalyst and environmentally benign.

4. Conclusion

Indanone scaffolds comprise key structural components of numerous bioactive natural products. Because of their versatile reactivity they are efficiently employed in various organic transformations. In the last few years, a number of novel methodologies have been adopted to access diverse annulated scaffolds involving 1-indanones. This review emphasizes recent (2016–2022) applications of 1-indanones for the construction of various fused- and spiro carbo-/heterocyclic compounds.

In the fused carbocycle section we discuss synthesis of benzocycloheptenones, fluorenones, dibenzo-azulenes, indanone fused cyclopentanes, and photodimerized products which are difficult to prepare otherwise.[86] In the next part, formation of fused N- and O-containing heterocycles, such as indeno-

indoles, indeno-pyridines, indenoquinoxalines, cyclopenta-isoquinolines, indeno[1,2-*b*]chromenes, indeno[1,2-*c*]furans, *etc.* is highlighted. The spirocarbocyclic sector consists of cyclopropane/cyclopentane/cyclohexane-spiroindanone compounds. Construction of various N-containing spiro heterocycles *viz.* spiroindeno-aziridines, spiroindeno-pyrrolidines, spiro-glutarimides, spiroindeno-pyrazoles, spiroindeno-pyridine-oxindoles, spiro-cyclopentaindeno-indolines, spiroindeno-morpholines as well as interesting bis-pirocyclic skeletons is demonstrated accordingly. Finally, methods of synthesis of several spiroindeno-γ-butyrolactones, spiroindeno-isochromanes are unveiled in the O-containing spiro-heterocycles section.

Interestingly, a large number of reactions described in this review are associated with stereoselective formation of annulated scaffolds. Moreover, mechanistic aspects of representative reactions have been illustrated for better understanding of the reaction pathways. Some of the reactions offer biologically relevant compounds as well as natural products, *viz.*, plecarpenene/plecarpenone, swinhoeisterol A, cephanolides A–D, diptoindonesin G and atlanticone C. We believe that the results presented in this article will attract the attention of organic and medicinal chemistry researchers for future developments of cyclization methods involving indanone analogues.

Conflicts of interest

The authors declare no conflict of interest.

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References

1 S.-H. Kim, S. H. Kwon, S.-H. Park, J. K. Lee, H.-S. Bang, S.-J. Nam, H. C. Kwon, J. Shin and D.-C. Oh, Tripartin, a Histone Demethylase Inhibitor from a Bacterium Associated with a Dung Beetle Larva, *Org. Lett.*, 2013, **15**, 1834–1837, DOI: **10.1021/ol4004417**.

2 X. Luo, C. Li, P. Luo, X. Lin, H. Ma, N. P. Seeram, C. Song, J. Xu and Q. Gu, Pterosin Sesquiterpenoids from *Pteris cretica* as Hypolipidemic Agents *via* Activating Liver X Receptors, *J. Nat. Prod.*, 2016, **79**, 3014–3021, DOI: **10.1021/acs.jnatprod.6b00558**.

3 G. Assante, R. Locci, L. Camarda and G. Nasini, Screening of the genus *Cercospora* for secondary metabolites, *Phytochemistry*, 1977, **16**, 243–247, DOI: **10.1016/S0031-9422(00)86794-1**.

4 S. Das, Recent applications of 1,3-indanedione in organic transformations for the construction of fused- and spiro scaffolds, *Tetrahedron*, 2022, **122**, 132954, DOI: **10.1016/j.tet.2022.132954**.

5 S. Das, Annulations involving 2-arylidene-1,3-indanediones: stereoselective synthesis of spiro- and fused scaffolds, *New J. Chem.*, 2020, **44**, 17148–17176, DOI: **10.1039/d0nj03968**.

6 S. Das, Recent applications of ninhydrin in multicomponent reactions, *RSC Adv.*, 2020, **10**, 18875–18906, DOI: **10.1039/d0ra02930k**.

7 S. Sutthivaiyakit, W. Mongkolvisut, S. Prabpai and P. Kongsaree, Diterpenes, Sesquiterpenes, and a Sesquiterpene-Coumarin Conjugate from *Jatropha integerrima*, *J. Nat. Prod.*, 2009, **72**, 2024–2027, DOI: **10.1021/np900342b**.

8 M. J. D. Peña, J. M. B. Ares, I. G. Collado and R. H. Galán, Biologically active diterpenes containing a *gem*-dimethylcyclopropane subunit: an intriguing source of PKC modulators, *Nat. Prod. Rep.*, 2014, **31**, 940–952, DOI: **10.1039/c4np00008k**.

9 K. E. Wilson, N. N. Tsou, Z. Guan, C. L. Ruby, F. Pelaez, J. Gorrochategui, F. Vincente and H. R. Onishi, Isolation and structure elucidation of coleophomone A and B, novel inhibitors of bacterial cell wall transglycosylase, *Tetrahedron Lett.*, 2000, **41**, 8705–8709, DOI: **10.1016/S0040-4039(00)01532-X**.

10 K. C. Nicolaou, T. Montagnon and G. Vassilikogiannakis, Total synthesis of celeophomone D, *Chem. Commun.*, 2002, 2478–2479, DOI: **10.1039/b208236p**.

11 J. A. Wendt, P. J. Gauvreau and R. D. Bach, Synthesis of (.+−.)-Fredericamycin A, *J. Am. Chem. Soc.*, 1994, **116**, 9921–9926, DOI: **10.1021/ja00101a013**.

12 S. Kotha and A. Fatma, Synthetic Approaches to the Anticancer Agent Fredericamycin A, *Asian J. Org. Chem.*, 2021, **10**, 129–148, DOI: **10.1002/ajoc.202000484**.

13 M. A. Ernst-Russell, C. L. L. Chai, J. H. Wardlaw and J. A. Elix, Euplectin and Coneuplectin, New Naphthopyrones from the Lichen *Flavoparmelia euplecta*, *J. Nat. Prod.*, 2000, **63**, 129–131, DOI: **10.1021/np9903245**.

14 H. L. Holland, D. B. MacLean, R. G. A. Rodrigo and R. F. H. Manske, A new synthesis of spirobenzylisoquinolines. Analogues of sibiricine and corydaine, *Tetrahedron Lett.*, 1975, **16**, 4323–4326, DOI: **10.1016/S0040-4039(00)91114-6**.

15 G. Blaskó, N. Murugesan, A. J. Freyer, D. J. Gula, B. Şener and M. Shamma, The indenobenzapine-spirobenzylisoquinoline rearrangement; stereocontrolled syntheses of (±)-raddeanine and (±)-yenhusomine, *Tetrahedron Lett.*, 1981, **22**, 3139–3142, DOI: **10.1016/S0040-4039(01)81847-5**.

16 X. Wang, T. Yang, X. Cheng and Q. Shen, Enantioselective Electrophilic Trifluoromethylthiolation of β-Ketoesters: A Case of Reactivity and Selectivity Bias for Organocatalysis, *Angew. Chem., Int. Ed.*, 2013, **52**, 12860–12864, DOI: **10.1002/anie.201305075**.

17 Q.-H. Deng, T. Bleith, H. Wadepohl and L. H. Gade, Enantioselective Iron-Catalyzed Azidation of β-Keto Esters and Oxindoles, *J. Am. Chem. Soc.*, 2013, **135**, 5356–5359, DOI: **10.1021/ja402082p**.

18 M. Majdecki, P. Grodek and J. Jurczak, Stereoselective α-Chlorination of β-Keto Esters in the Presence of Hybrid

Amide-Based Cinchona Alkaloids as Catalysts, *J. Org. Chem.*, 2021, **86**, 995–1001, DOI: 10.1021/acs.joc.0c02486.

19 S. Dai, F. Zhao, Q. Zhang, T.-K. Lau, T. Li, K. Liu, Q. Ling, C. Wang, X. Lu, W. You and X. Zhan, Fused Nonacyclic Electron Acceptors for Efficient Polymer Solar Cells, *J. Am. Chem. Soc.*, 2017, **139**, 1336–1343, DOI: 10.1021/jacs.6b12755.

20 Q. Liao, Q. Kang, Y. Yang, C. An, B. Xu and J. Hou, Tailoring and Modifying an Organic Electron Acceptor toward the Cathode Interlayer for Highly Efficient Organic Solar Cells, *Adv. Mater.*, 2019, **32**, 1906557, DOI: 10.1002/adma.201906557.

21 L. A. Estrada, J. E. Yarnell and D. C. Neckers, Revisiting Fluorenone Photophysics *via* Dipolar Fluorenone Derivatives, *J. Phys. Chem. A*, 2011, **115**, 6366–6375, DOI: 10.1021/jp200507j.

22 K.-C. Tang, M.-J. Chang, T.-Y. Lin, H.-A. Pan, T.-C. Fang, K.-Y. Chen, W.-Y. Hung, Y.-H. Hsu and P.-T. Chou, Fine Tuning the Energetics of Excited-State Intramolecular Proton Transfer (ESIPT): White Light Generation in A Single ESIPT System, *J. Am. Chem. Soc.*, 2011, **133**, 17738–17745, DOI: 10.1021/ja2062693.

23 Y. Cui, H. Ren, J. Yu, Z. Wang and G. Qian, An indanone-based alkoxysilane dye with second order nonlinear optical properties, *Dyes Pigm.*, 2009, **81**, 53–57, DOI: 10.1016/j.dyepig.2008.09.002.

24 K. Kolmakov, C. Wurm, M. V. Sednev, M. L. Bossi, V. N. Belov and S. W. Hell, Masked red-emitting carbopyronine dyes with photosensitive 2-diazo-1-indanone caging group, *Photochem. Photobiol. Sci.*, 2012, **11**, 522–532, DOI: 10.1039/C1PP05321C.

25 E. Benedetti, L. S. Kocsis and K. M. Brummond, Synthesis and Photophysical Properties of a Series of Cyclopenta[b]naphthalene Solvato-chromic Fluorophores, *J. Am. Chem. Soc.*, 2012, **134**, 12418–12421, DOI: 10.1021/ja3055029.

26 L. Fang, X.-Y. Zhang, Q. Yuan, D.-D. Li, Q.-C. Jiao, Y.-S. Yang and H.-L. Zhu, A novel indanone-derivated fluorescence sensor for Cysteine detection and biological imaging, *Dyes Pigm.*, 2020, **175**, 108122, DOI: 10.1016/j.dyepig.2019.108122.

27 C. R. Monzón-González, R. Corona-Sánchez, W. E. V. Narvaáez, T. Rocha-Rinza, M. E. Sánchez-Vergara, R. A. Toscano and C. Álvarez-Toledano, Synthesis and photophysical properties of conformationally restricted difluoroboron β-diketonate complexes of 1-indanone derivatives, *Tetrahedron*, 2020, **76**, 131457, DOI: 10.1016/j.tet.2020.131457.

28 S. Das and A. Dutta, Recent advances in transition-metal-catalyzed annulations for the construction of a 1-indanone core, *New J. Chem.*, 2021, **45**, 4545–4568, DOI: 10.1039/D0NJ06318E.

29 S. Das, Transition-Metal-Free Synthesis of 1-Indanone Skeleton: A Brief Update, *ChemistrySelect*, 2021, **6**, 4761–4781, DOI: 10.1002/slct.202101460.

30 T. Chanda and M. S. Singh, Developments toward the synthesis and application of 3-hydroxyindanones, *Org. Biomol. Chem.*, 2016, **14**, 8895–8910, DOI: 10.1039/C6OB01648K.

31 Y. Xia, S. Ochi and G. Dong, Two-Carbon Ring Expansion of 1-Indanones *via* Insertion of Ethylene into Carbon–Carbon Bonds, *J. Am. Chem. Soc.*, 2019, **141**, 13038–13042, DOI: 10.1021/jacs.9b07445.

32 R. Zhang, Y. Xia and G. Dong, Intermolecular [5+2] Annulation between 1-Indanones and Internal Alkynes by rhodium-Catalyzed C-C Activation, *Angew. Chem., Int. Ed.*, 2021, **60**, 20476–20482, DOI: 10.1002/ange.202106007.

33 Z. Xing, B. Fang, S. Luo, X. Xie and X. Wang, Generation of Fuesed seven-Membered Polycyclic Systems *via* Ring Expansion and Application to the Total Synthesis of Sesquiterpenoids, *Org. Lett.*, 2022, **24**, 4034–4039, DOI: 10.1021/acs.orglett.2c01401.

34 P. R. Throve, M. M. Guru and B. Maji, Manganese-Catalyzed Divergent Markovnikov Addition and [2+2+2] Cycloaddition of 2-Carbonyl Indanone with Terminal Alkyne, *J. Org. Chem.*, 2019, **84**, 8185–8193, DOI: 10.1021/acs.joc.9b01173.

35 K. Patel, U. K. Mishra, D. Mukhopadhyay and S. S. V. Ramasastry, Beyond the Corey-Chaykovsky reaction: synthesis of Unusual Cyclopropanoids *via* Desymmetrization and Thereof, *Chem.–Asian J.*, 2019, **14**, 4568–4571, DOI: 10.1002/asia.201901108.

36 T. Mita, M. Uchiyama and Y. Sato, Catalytic Intramolecular Coupling of Ketoalkenes by Allylic C(sp^3)–H Bond Cleavage: Synthesis of Five- and Six-Membered Carbocyclic Compounds, *Adv. Synth. Catal.*, 2020, **362**, 1275–1280, DOI: 10.1002/adsc.201901533.

37 M. E. Jung and G. Piizzi, gem-Disubstituent Effect: Theporetical basis and Synthetic Applications, *Chem. Rev.*, 2005, **105**, 1735–1766, DOI: 10.1021/cr940337h.

38 N. Uemura, H. Ishikawa, N. Tamura, Y. Yoshida, T. Mino, Y. Kasashima and M. Sakamoto, Stereoselective Photodimerization of 3-Arylindenones in Solution and in the Solid State, *J. Org. Chem.*, 2018, **83**, 2256–2262, DOI: 10.1021/acs.joc.7b03147.

39 N.-N. Zhou, S.-S. Ning, L.-Q. Li, J. Y. Zhang, M.-J. Fan, D.-S. Yang and H.-T. Zhu, Brønsted Acid-Catalyzed One-Pot Tandem Annulation/[5+2]-Cycloaddition of o-Propargyl Alcohol Benzaldehydes with Alkynes: Regioselective and Stereoselective Synthesis of Dibenzo[a,f]azulen-12-ones, *Org. Chem. Front.*, 2020, **7**, 2664–2669, DOI: 10.1039/D0QO00522C.

40 Z.-J. Shen, H.-N. Shi, W.-J. Hao, S.-J. Tu and B. Jiang, Visible-light photocatalytic bicyclization of β-alkynyl propenones for accessing diastereoenriched *syn*-fluoren-9-ones, *Chem. Commun.*, 2018, **54**, 11542–11545, DOI: 10.1039/c8cc06086j.

41 J. Zhang, H. Jiang and S. Zhu, Cascade One-pot Synthesis of Indanone-Fused Cyclopentanes from the Reaction of Donor-Acceptor Cyclopropanes and Enynals *via* a Sequential Hydrolysis/Knoevenagel Condensation/[3+2] Cycloaddition, *Adv. Synth. Catal.*, 2017, **359**, 2924–2930, DOI: 10.1002/adsc.201700345.

42 T. Kurzawa, K. Harms and U. Koert, Stereoselective Synthesis of the Benzodihydropentalene Core of the Fijiolides, *Org. Lett.*, 2018, **20**, 1388–1391, DOI: 10.1021/acs.orglett.8b00163.

43 A. Takano, Y. Zhao, T. Ohyoshi and H. Kigoshi, Synthetic studies toward swinhoeisterol A, a novel steroid with an unusual carbon skeleton, *Tetrahedron Lett.*, 2019, **60**, 591–593, DOI: 10.1016/j.tetlet.2019.01.027.

44 M. Kashyap, S. Kandekar, A. T. Baviskar, D. Das, R. Preet, P. Mohapatra, S. R. Satapathy, S. Siddharth, S. K. Guchhait, C. N. Kundu and U. C. Banerjee, Indenoindolone derivatives as topoisomeraseII-inhibiting anticancer agents, *Bioorg. Med. Chem. Lett.*, 2013, **23**, 934–938, DOI: 10.1016/j.bmcl.2012.12.063.

45 A. G. K. Reddy and G. Satyanarayana, A Facile, Superacid-Promoted Sequential Domino One-Pot Dual C–C Bond Formation and Fischer Indole Synthesis: Rapid Access to 10-Phenyl-5,10-dihydroindeno[1,2-*b*]indoles, *Synthesis*, 2015, 1269–1279, DOI: 10.1055/s-0034-1380287.

46 Z. Wang, M. Wang, S. Xu, M. Gu, Z. Meng, C. Li, P. Cai and L. Rong, Efficient and facile synthesis of 5-arylindeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidine-2,4(3*H*)-dione and 7-arylbenzo[*h*]pyrimido[4,5-*b*]quinoline-8,10(5*H*,9*H*)-dione under mild conditions, *Synth. Commun.*, 2016, **46**, 1887–1892, DOI: 10.1080/00397911.2016.1234621.

47 H. Nagarajaiah, A. K. Mishra and J. N. Moorthy, Mechanochemical Solid-State Synthesis of 2-Aminothiazoles, Quinoxalines and Bezoylbenzofurans from Ketones by One-Pot Sequential Acid- and Base-Mediated reactions, *Org. Biomol. Chem.*, 2016, **14**, 4129–4135, DOI: 10.1039/C6OB00351F.

48 T. M. Kadayat, S. Park, A. Shrestha, H. Jo, S.-Y. Hwang, P. Katila, R. Shrestha, M. R. Nepal, K. Noh, S. K. Kim, W.-S. Koh, K. S. Kim, Y. H. Jeon, T. C. Jeong, Y. Kwon and E.-S. Lee, Discovery and Biological Evaluations of Halogenated 2,4-Diphenyl Indeno[1,2-*b*]pyridinol Derivatives as Potent Topoisomerase IIα-Targeted Chemotherapeutic Agents for Breast Cancer, *J. Med. Chem.*, 2019, **62**, 8194–8234, DOI: 10.1021/acs.jmedchem.9b00970.

49 J.-Q. Zhao, S. Zhou, H.-L. Qian, Z.-H. Wang, Y.-P. Zhang, Y. You and W.-C. Yuan, Higher-order [10 + 2] cycloaddition of 2-alkylidene-1-indanones enables the dearomatization of 3-nitroindoles: access to polycyclic cyclopenta[*b*]indoline derivatives, *Org. Chem. Front.*, 2022, **9**, 3322–3327, DOI: 10.1039/d2qo00289b.

50 S. K. Sarkar, O. Osisioma, W. L. Karney, M. Abe and A. D. Gudmundsdottir, Using Molecular Architecture to Control the Reactivity of a Triplet Vinylnitrene, *J. Am. Chem. Soc.*, 2016, **138**, 14905–14914, DOI: 10.1021/jacs.6b05746.

51 D. F. Vargas, E. L. Larghi and T. S. Kaufman, Concise Synthesis of the ABC-Ring System of the Azafluoranthene, Tropoisoquinoline and Proaporphine Alkaloids: An Olefin Hydroacylation/Pomeranz–Fritsch Cyclization Approach, *Synthesis*, 2019, **51**, 2030–2038, DOI: 10.1055/s-0037-1611711.

52 X.-Q. Hou, Y. Lin and D.-M. Du, Organocatalytic domino annulation of *in situ* generated *tert*-butyl 2-hydroxybenzylidenecarbamates with 2-isothiocyanato-1-indanones for synthesis of bridged and fused ring heterocycles, *Org. Chem. Front.*, 2021, **8**, 4183–4187, DOI: 10.1039/d1qo00626f.

53 X. Liu, K. Wang, Y. Liu and C. Li, Divergent Asymmetric Reactions of *ortho*-Quinone Methides with α-Thiocyanato Indanones for the Synthesis of Spiro- and Fusedindanones, *Chem.–Eur. J.*, 2021, **27**, 735–739, DOI: 10.1002/chem.202003647.

54 B. Li, N. Shen, Y. Yang, X. Zhang and X. Fan, Tunable Synthesis of Indeno[1,2-*c*]furans and 3-Benzoylindenones *via* $FeCl_3$-Catalyzed Carbene/Alkyne Metathesis Reaction of *o*-Alkynylbenzoyl Diazoacetates, *Org. Lett.*, 2021, **23**, 388–393, DOI: 10.1021/acs.orglett.0c03882.

55 M. Haider, G. Sennari, A. Eggert and R. Sarpong, Total Synthesis of the Cephalotaxus Norditerpenoids (±)-Cephanolides A–D, *J. Am. Chem. Soc.*, 2021, **143**, 2710–2715, DOI: 10.1021/jacs.1c00293.

56 D. K. Singh and I. Kim, Skeletal Reorganization: Synthesis of Diptoindonesin G from Pauciflorol F, *J. Org. Chem.*, 2018, **83**, 1667–1672, DOI: 10.1021/acs.joc.7b03089.

57 J. Proessdorf, A. Zech, C. Jandl and T. Bach, Concise Total Synthesis of (+)-Atlanticone C, *Synlett*, 2020, **31**, 1598–1602, DOI: 10.1055/s-0040-1707215.

58 S. P. Midya, E. Gopi, N. Satam and I. N. N. Namboothiri, Synthesis of fused cyanopyrroles and spirocyclopropanes *via* addition of N-ylides to chalconimines, *Org. Biomol. Chem.*, 2017, **15**, 3616–3627, DOI: 10.1039/c7ob00529f.

59 J.-N. Wang, S.-Q. Chen, Z.-W. Liu and X.-Y. Shi, Divergent Syntheses of Spiroindanones and 2-Substituted 1-Indanones by Ruthenium-Catalyzed Tandem Coupling and Cyclization of Aromatic Acids with α,β-Unsaturated Ketones, *J. Org. Chem.*, 2019, **84**, 1348–1362, DOI: 10.1021/acs.joc.8b02820.

60 Y. Suzuki, N. Vatmurge, S. Tanaka and M. Kitamura, Enantio- and Diastereoselective Dehydrative "One-Step" Construction of Spirocarbocycles *via* a Ru/H+-Catalyzed Tsuji-Trost Approach, *Chem.–Asian J.*, 2017, **123**, 633–637, DOI: 10.1002/asia.201700013.

61 B. Lantaño, J. M. Aguirre, E. V. Drago, M. Bollini, D. J. De la Faba and J. D. Mufato, Synthesis of benzylidenecycloalkan-1-ones and 1,5-diketones under Claisen–Schmidt reaction: Influence of the temperature and electronic nature of arylaldehydes, *Synth. Commun.*, 2017, **47**, 2202–2214, DOI: 10.1080/00397911.2017.1367819.

62 S. Kotha, R. Ali, N. R. Panguluri, A. Datta and K. K. Kannaujiya, Synthesis and photophysical properties of star-shaped blue green emitting π-conjugated spirotruxenes, *Tetrahedron Lett.*, 2018, **59**, 4080–4085, DOI: 10.1016/j.tetlet.2018.10.005.

63 S. Kotha and S. R. Cheekatla, Synthesis and Acid Catalyzed Rearrangement of Cage Propellanes, *ChemistrySelect*, 2019, **4**, 13440–13445, DOI: 10.1002/slct.201903441.

64 S. Kotha, S. R. Cheekatla and A. Fatma, Synthetic Approach to the ABCD Ring System of Anticancer Agent Fredericamycin A *via* Claisen Rearrangement and Ring-Closing Metathesis as Key Steps, *ACS Omega*, 2019, **4**, 17109–17116, DOI: 10.1021/acsomega.9b01178.

65 S. Sabir, G. Kumar, V. P. Verma and J. L. Jat, Aziridine Ring Opening: An Overview of Sustainable Methods, *ChemistrySelect*, 2018, **3**, 3702–3711, DOI: 10.1002/slct.201800170.

66 K. T. Ashitha, P. P. Vinaya, A. Krishna, D. C. Vincent, R. Jalaja, S. Varughese and S. B. Somappa, I_2/TBHP Mediated Diastereoselective Synthesis of Spiroaziridines, *Org. Biomol. Chem.*, 2020, **18**, 1588–1593, DOI: 10.1039/C9OB02711D.

67 F. Beltran, I. Fabre, I. Ciofini and L. Miesch, Direct Spirocyclization from Keto-sulfonamides: An Approach to Azaspiro Compounds, *Org. Lett.*, 2017, **19**, 5042–5045, DOI: 10.1021/acs.orglett.7b02216.

68 Z. Ding, Y. Wang, W. Liu, Y. Chen and W. Kong, Diastereo- and Enantioselective Construction of Spirocycles by Nickel-Catalyzed Cascade Borrowing Hydrogen Cyclization, *J. Am. Chem. Soc.*, 2021, **143**, 53–59, DOI: 10.1021/jacs.0c10055.

69 S. Mondal, A. Ghosh, S. Mukherjee and A. T. Biju, N-Heterocyclic Carbene-Catalyzed Enantioselective Synthesis of Spiro-glutarimides *via* α,β-Unsaturated Acylazoliums, *Org. Lett.*, 2018, **20**, 4499–4503, DOI: 10.1021/acs.orglett.8b01799.

70 B.-X. Quan, J.-R. Zhuo, J.-Q. Zhao, M.-L. Zhang, M.-Q. Zhou, X.-M. Zhang and W.-C. Yuan, [4+1] Annulation reaction of cyclic pyridinium ylides with *in situ* generated azoalkenes for the construction of spirocyclic skeletons, *Org. Biomol. Chem.*, 2020, **18**, 1886–1891, DOI: 10.1039/C9OB02733E.

71 G. I. Shakibaei and A. Bazgir, A highly efficient one-pot synthesis of indenopyridine-fused spirocyclic systems, *RSC Adv.*, 2016, **6**, 22306–22311, DOI: 10.1039/C6RA00869K.

72 Y. Yang, Y. Jiang, W. Du and Y.-C. Chen, Asymmetric Cross [10+2] Cycloadditions of 2-Alkylidene-1-indanones and Activated Alkenes under Phase-Transfer Catalysis, *Chem.–Eur. J.*, 2020, **26**, 1754–1758, DOI: 10.1002/chem.201904930.

73 B. Wu, J. Yang, M. Gao and L. Hu, Ring-Strain-Enabled Catalytic Asymmetric Umpolung C–O Bond-Forming Reactions of 1,2-Oxazetidines for the Synthesis of Functionalized Chiral Ethers, *Org. Lett.*, 2020, **22**, 5561–5566, DOI: 10.1021/acs.orglett.0c01916.

74 S. Kayal and S. Mukherjee, Catalytic enantioselective cascade Michael/cyclization reaction of 3-isothiocyanato oxindoles with exocyclic α,β-unsaturated ketones en route to 3,2'-pyrrolidinyl bispirooxindoles, *Org. Biomol. Chem.*, 2016, **14**, 10175–10179, DOI: 10.1039/c6ob02187e.

75 K. Dutta, M. Kumar, S. K. Ghosh, A. Das and R. Chowdhury, Diastereoselective synthesis of diverse 3,2′-pyrrolidinyl bispirooxindoles *via* 1,3-dipolar cycloaddition reactions of azomethine ylides with exocyclic α,β-unsaturated ketones and *in silico* studies for prediction of bioactivity, *Synth. Commun.*, 2019, **49**, 444–455, DOI: 10.1080/00397911.2018.1560472.

76 B.-L. Zhao and D.-M. Du, Catalytic Asymmetric Mannich/Cyclization of 2-Isothiocyanato-1-indanones: An Approach to the Synthesis of Bispirocyclic Indanone-Thioimidazolidine-Oxindoles, *Org. Lett.*, 2018, **20**, 3797–3800, DOI: 10.1021/acs.orglett.8b01389.

77 X.-Q. Hou, J.-B. Wen, L. Yan and D.-M. Du, Squaramide-catalysed asymmetric Michael addition/cyclization cascade reaction of 4-arylmethylidene-2,3-dioxopyrrolidines with 2-isothiocyanato-1-indanones, *Org. Biomol. Chem.*, 2021, **19**, 7181–7185, DOI: 10.1039/d1ob01223a.

78 B. Wu, H. Chen, M. Gao, X. Gong and L. Hu, Synthesis of 1,3-Aminoalcohols and Spirocyclic Azetidines *via* Tandem Hydroxymethylation and Aminomethylation Reaction of β-Keto Phosphonates with *N*-Nosyl-*O*-(2-bromoethyl) hydroxylamine, *Org. Lett.*, 2021, **23**, 4152–4157, DOI: 10.1021/acs.orglett.1c01091.

79 M.-M. Liu, X.-C. Yang, Y.-Z. Hua, J.-B. Chang and M.-C. Wang, Synthesis of Chiral Bispirotetrahydrofuran Oxindoles by Cooperative Bimetallic-Catalyzed Asymmetric Cascade Reaction, *Org. Lett.*, 2019, **21**, 2111–2115, DOI: 10.1021/acs.orglett.9b00386.

80 S.-H. Chen, Y.-H. Miao, G.-J. Mei, Y.-Z. Hua, S.-K. Jia and M.-C. Wang, Dinuclear zinc catalyzed asymmetric [3+2] spiroannulation for the synthesis of diverse bispirocyclic saccharines, *Org. Chem. Front.*, 2022, **9**, 5010–5015, DOI: 10.1039/d2qo01039a.

81 M.-M. Liu, X.-C. Yang, Y. Z. Hua, J.-B. Chang and M.-C. Wang, Dinuclear Zinc-Catalyzed Asymmetric Tandem Reaction of α-Hydroxy-1-indanone: Access to Spiro[1-indanone-5,2′-γ-butyrolactones], *Org. Lett.*, 2019, **21**, 7089–7093, DOI: 10.1021/acs.orglett.9b02658.

82 X.-C. Yang, M. Xu, J.-B. Wang, M.-M. Liu, F. Mathey, Y.-Z. Hua and M. C. Wang, Enantioselective Synthesis of Indanone Spiro-Isochromanone Derivatives *via* Dinuclear Zinc-Catalyzed Michael/Transesterification Tandem Reaction, *Org. Biomol. Chem.*, 2020, **18**, 3917–3926, DOI: 10.1039/D0OB00541J.

83 W.-P. Yang, S.-K. Jia, T.-T. Liu, Y.-Z. Hua and M.-C. Wang, Dinuclear zinc-catalyzed asymmetric [3 + 2] cyclization reaction for direct assembly of chiral α-amino-γ-butyrolactones bearing three stereocenters, *Org. Chem. Front.*, 2021, **8**, 6998–7003, DOI: 10.1039/d1qo01338f.

84 T. Y. Ko and S. W. Youn, Cooperative Indium(III)/Silver(I) System for Oxidative Coupling/Annulation of 1,3-Dicarbonyls and Styrenes: Construction of Five-Membered Heterocycles, *Adv. Synth. Catal.*, 2016, **358**, 1934–1941, DOI: 10.1002/adsc.201600280.

85 S. Maejima, E. Yamaguchi and A. Itoh, Visible Light/Molecular-Iodine-Mediated Intermolecular Spirolactonization Reaction of Olefins with Cyclic Ketones, *J. Org. Chem.*, 2019, **84**, 9519–9531, DOI: 10.1021/acs.joc.9b01081.

86 H. Cao, F. Chen, C. Su and L. Yu, Construction of Carbocycles from Methylenecyclopropanes, *Adv. Synth. Catal.*, 2020, **362**, 438–461, DOI: 10.1002/adsc.201900615.