Aryl Methyl Ketones: Versatile Synthons in the Synthesis of Heterocyclic Compounds

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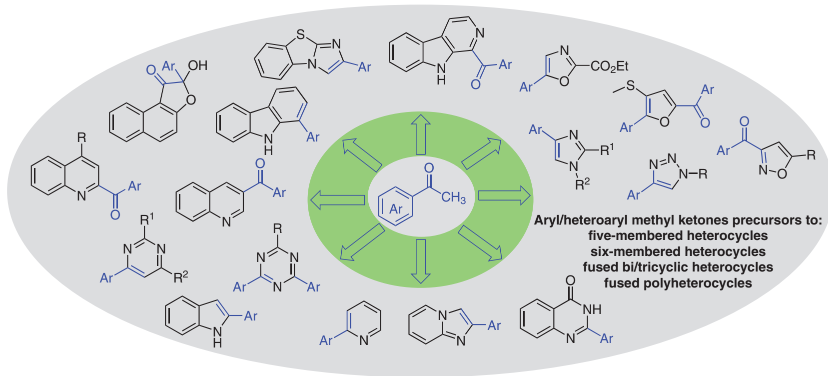

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Abstract The synthesis of aromatic heterocycles has attracted substantial attention due to the abundance of these heterocycles in drug molecules, natural products, and other compounds of biological interest. Accordingly, there is a demand for straightforward synthetic protocols toward such compounds using readily available starting materials. In the past decade, there have been substantial developments in heterocycle synthesis, especially in metal-catalyzed and iodine-assisted approaches. This graphical review focuses on notable reactions from the past decade using aryl and heteroaryl methyl ketones as starting materials, including representative reaction mechanisms.

Key words aromatic heterocycles, iodine, ketones, metal-free, fused bicycles, fused tricycles, fused polyheterocycles

Aromatic heterocycles are highly privileged structures in drug discovery and development. Such fragments are found very frequently in biologically active compounds and thus are common building blocks for drugs and natural product derivatives. Beyond their utility in eliciting biological activity, these heterocycles are also useful in modifying ADME (absorption, distribution, metabolism and excretion)/pharmacokinetic properties (introducing lipophilicity or hydrophilicity, improving solubility, fine-tuning hydrogen bonding, etc.) and reducing possible toxicity concerns. The increasing presence of various aromatic heterocycles in drugs is no doubt related to advances in synthetic methodology such as metal-catalyzed cross-couplings,[1a] hetero-couplings,[1b] and metal-free conditions,[1c,d] enabling rapid access to a wide variety of functionalized heterocyclic scaffolds.

Aryl methyl ketones (AMKs) (also including heteroaryl compounds) are attractive precursors that allow for the facile synthesis of aromatic heterocycles. Iodine, in combination with AMKs, can substitute for several transition metals used in previously reported transformations while also maintaining an excellent atom economy.[1e,f,j] This aspect, along with the commercial abundance and cost-effective nature of AMKs, provides an incentive to the research community to discover and further develop such processes for use in drug discovery. Despite the vast literature that has evolved on this topic, there has yet to be a succinct review of the important developments in this area. The present graphical review provides a comprehensive compilation (focused on 2012–2021) of synthetic approaches for 5- and 6-membered, as well as fused and poly-fused heterocycles. Herein, we detail the role of AMKs in the synthesis of such heterocycles. Brief examples of practical syntheses of AMKs are presented in Scheme 1. The application of AMKs to the synthesis of heterocycles follows in Schemes 2 through 111, with an overall organization focused on heterocycle type. Brief reaction mechanisms are highlighted in instructive examples, with colors to aid understanding. Yields and structural diversity are reported in numerous examples to reflect the substrate scope for these reactions, including the use of electron-donating and -withdrawing groups as well as heterocyclic starting materials.

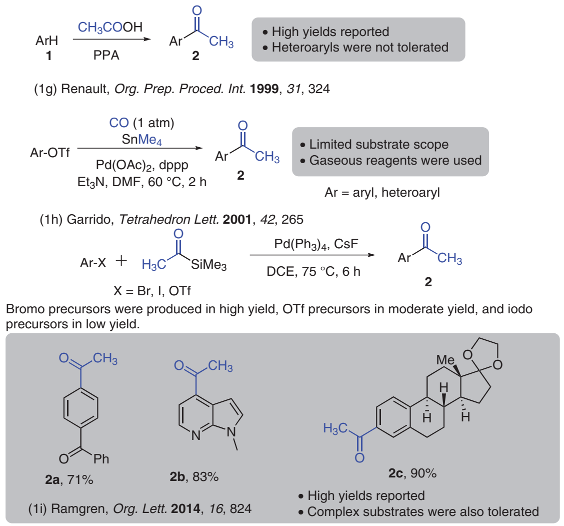
from left to right

Shabber Mohammed was born and raised in Telangana, India. He obtained B.Sc. and M.Sc. degrees from Osmania University (India). He completed his Ph.D. in chemical sciences under the joint supervision of Dr. Ram A. Vishwakarma and Dr. Sandip B. Bharate at the IIIM-Academy of Scientific and Innovative Research, India. After working as a research scientist for 1.3 years at GVK BIO and Piramal Life Sciences, he joined the group of Dr. Thota Ganesh at Emory University as a postdoctoral research scholar. He subsequently worked in the lab of Dr. Lee McDermott at the University of Pittsburgh for two years. His research has mainly focused on the medicinal chemistry of CNS drugs (EP2 receptors and 20-HETE inhibitors) and anticancer drugs (PI3K-mTOR inhibitors). At present, he is a postdoctoral researcher at The Ohio State University in the laboratories of Dr. Mark Mitton-Fry and Dr. Pui-Kai Li.

Jason S. West obtained his B.Sc. in pharmaceutical sciences from The Ohio State University in the spring of 2020. During his undergraduate studies, he conducted research in biomedical informatics, microbial engineering, and synthetic medicinal chemistry. He is presently a second-year graduate student at The Ohio State University, pursuing a Ph.D. in synthetic medicinal chemistry. He is currently researching novel bacterial topoisomerase inhibitors as a new therapeutic option for multidrug-resistant bacterial infections in the lab of Dr. Mark Mitton-Fry.

Mark J. Mitton-Fry graduated *summa cum laude* from Carleton College with a B.A. in chemistry, which was followed by a year as a fellow of the *Deutscher Akademischer Austauschdienst* (DAAD) in Würzburg, Germany. He completed his Ph.D. with Professor Tarek Sammakia at the University of Colorado Boulder before spending nine years in the pharmaceutical industry. He is currently an assistant professor in the Division of Medicinal Chemistry and Pharmacognosy at The Ohio State University. His research team is primarily focused on the discovery of bacterial topoisomerase inhibitors, with additional interests in novel anticancer approaches.

1 Synthesis of aromatic methyl ketones

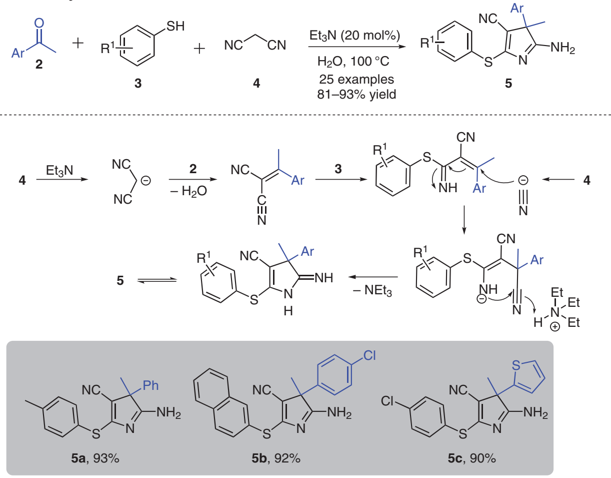


Scheme 1 Different approaches for the synthesis of aryl methyl ketones **2**

Recent review on aryl methyl ketones: (1j) Rajai-Daryasarei, *New J. Chem.* **2021**, *45*, 20486

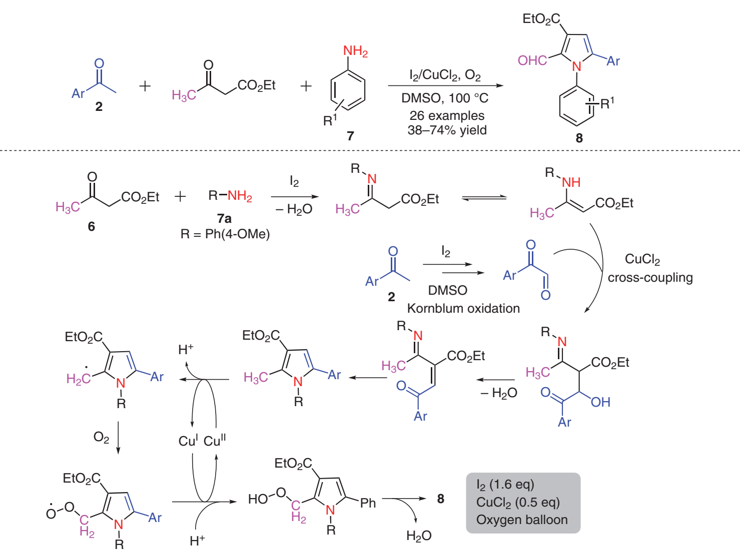
2 Synthesis of five-membered heterocycles using aryl methyl ketones

2.1 3*H*-Pyrroles



Scheme 2 Synthesis of 3*H*-pyrroles **5** by a multicomponent approach

(2a) Das, *Org. Lett.* **2013**, *15*, 5622

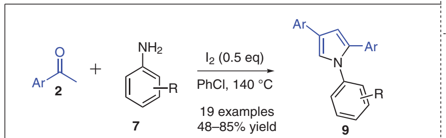


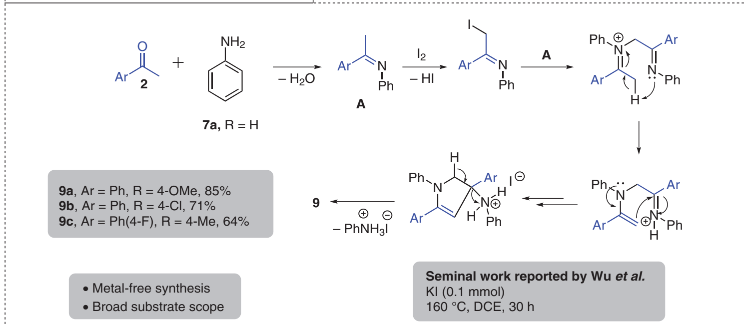
Scheme 3 Synthesis of pyrrole 2-carbaldehydes **8** by oxidative annulation

(2b) Wu, *Org. Lett.* **2018**, *20*, 688

De novo synthesis of pyrrole 2-carbaldehydes using $I_2/CuCl_2$-mediated oxidative cross-coupling/annulation/C–H oxidation. No stoichiometric hazardous oxidants were used and broad substrate scope was explored.

8a, R^1 = 4-OMe, Ar = Ph, 74%
8b, R^1 = 4-OMe, Ar = Ph(4-Br), 71%
8c, R^1 = 4-OMe, Ar = Ph(3-NO_2), 55%
8d, R^1 = 4-F, Ar = Ph(4-Cl), 61%
8e, R^1 = 4-I, Ar = Ph(4-Cl), 63%
8f, R^1 = 2-Ph, Ar = Ph(4-Cl), 71%





9a, Ar = Ph, R = 4-OMe, 85%
9b, Ar = Ph, R = 4-Cl, 71%
9c, Ar = Ph(4-F), R = 4-Me, 64%

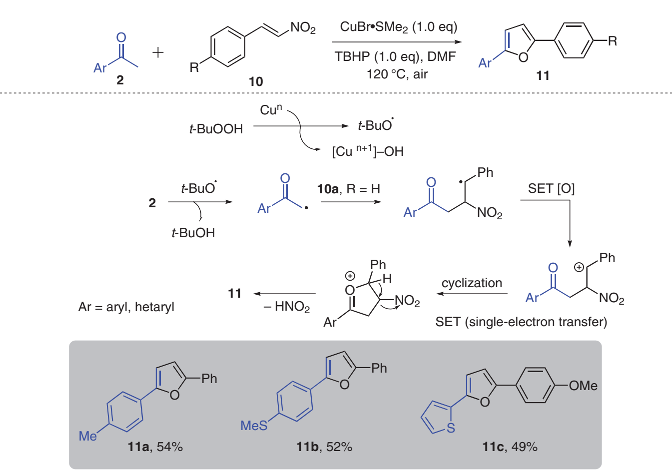
• Metal-free synthesis
• Broad substrate scope

Seminal work reported by Wu *et al.*
KI (0.1 mmol)
160 °C, DCE, 30 h

Scheme 4 Synthesis of 1,2,4-triarylpyrroles **9** by I_2-promoted condensation and cyclization

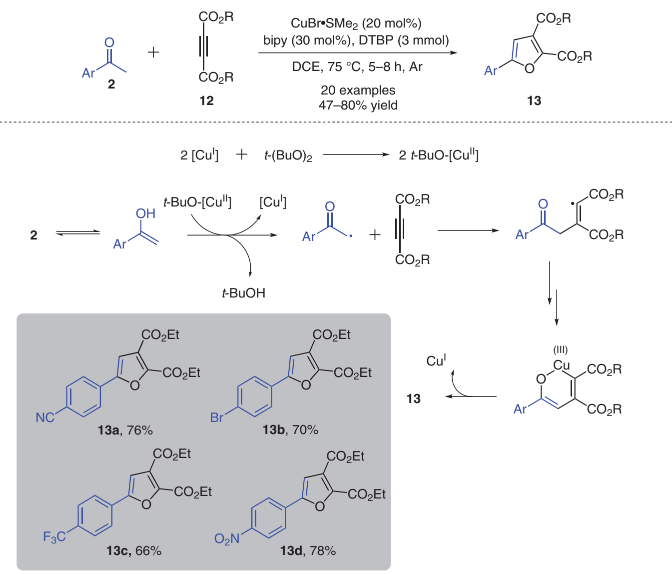
(2c) Xu, *Eur. J. Org. Chem.* **2016**, 925
(2d) Wu, *J. Org. Chem.* **2017**, *82*, 5743

2.2 Furans



Scheme 5 Synthesis of 2,5-disubstituted furans **11**

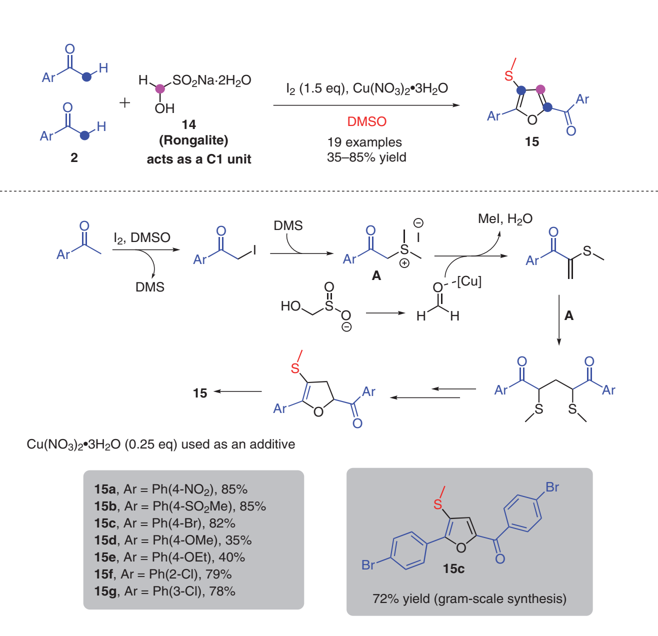
(2e) Ghosh, *J. Org. Chem.* **2015**, *80*, 5364



Scheme 6 Synthesis of furan analogues **13** by copper-catalyzed radical addition

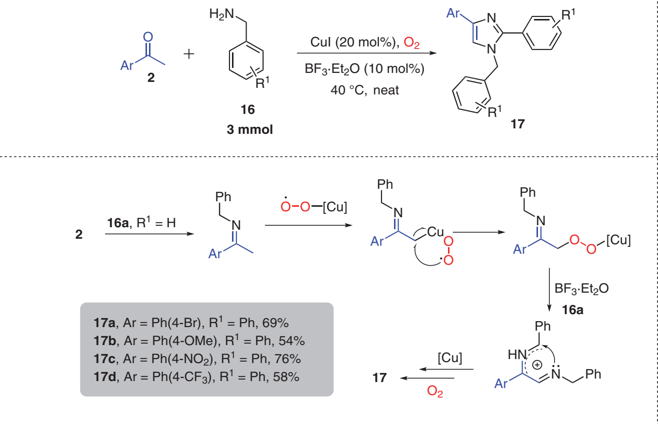
(2f) Manna, *Org. Lett.* **2015**, *17*, 4300

Figure 1 Synthesis of aryl methyl ketones[1g–j] and five-membered heterocycles, part I[2a–f]



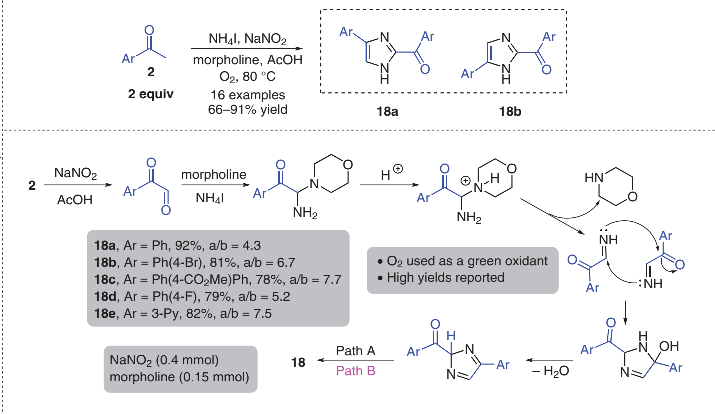
Scheme 7 Synthesis of 2,4,5-trisubstituted furans **15** (2g) Wang, *Org. Lett.* **2016**, *18*, 524

2.3 Imidazoles

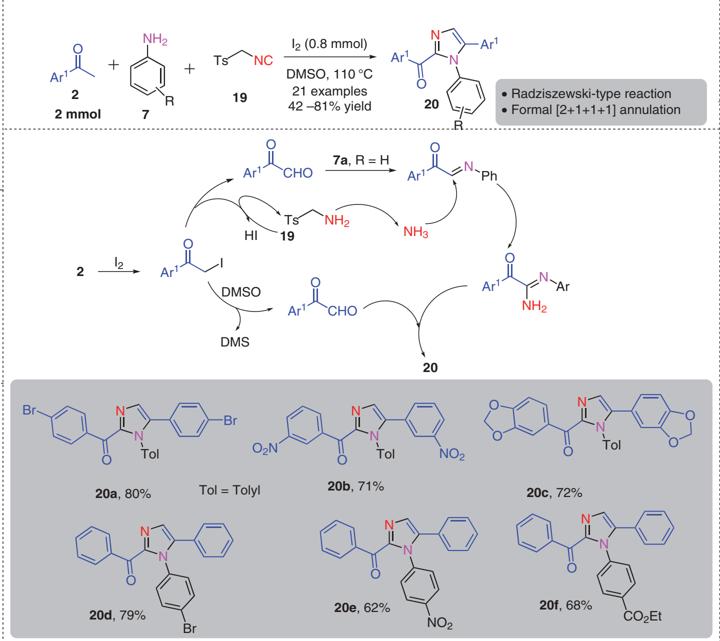


Scheme 8 Synthesis of 1,2,4-trisubstituted imidazoles **17** by dehydrogenative coupling

(2h) Cai, *Org.Lett.* **2012**, *14*, 6068

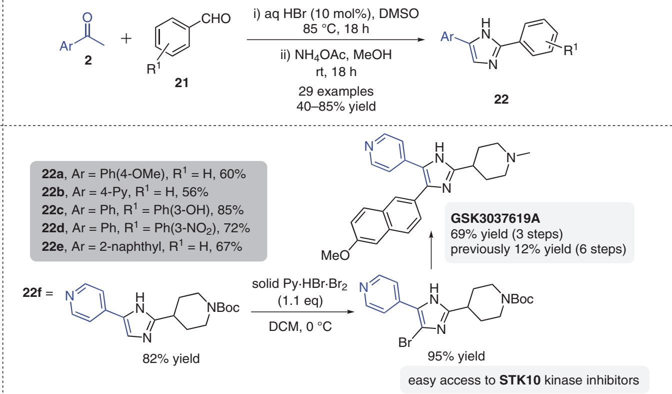


Scheme 9 Synthesis of 4/5-aryl-2-aroyl imidazoles **18** (2i) Liu, *Org. Chem. Front.* **2017**, *4*, 1508

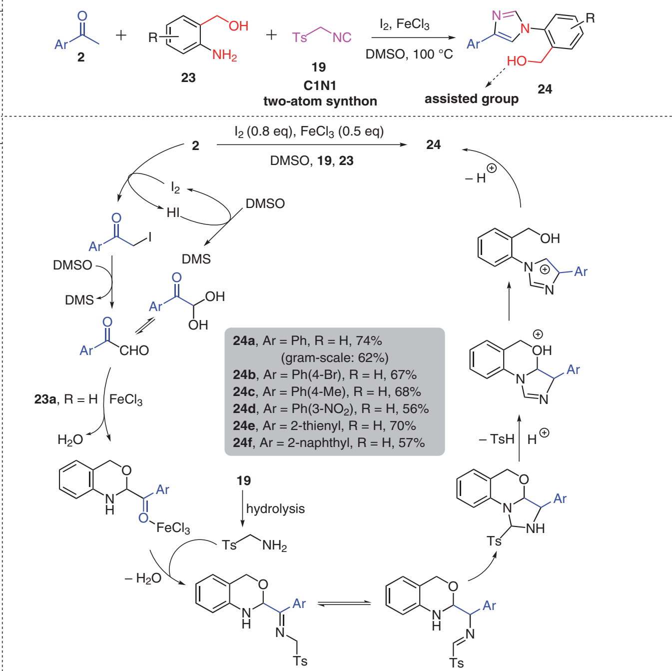


Scheme 10 Synthesis of 1,2,5-trisubstituted imidazoles **20** by formal [2+1+1+1] annulation

(2j) Zhang, *Org. Lett.* **2016**, *18*, 1686



Scheme 11 Synthesis of 2,4(5)-disubstituted imidazoles **22** (2k) de Toledo, *J. Org. Chem.* **2019**, *84*, 14187

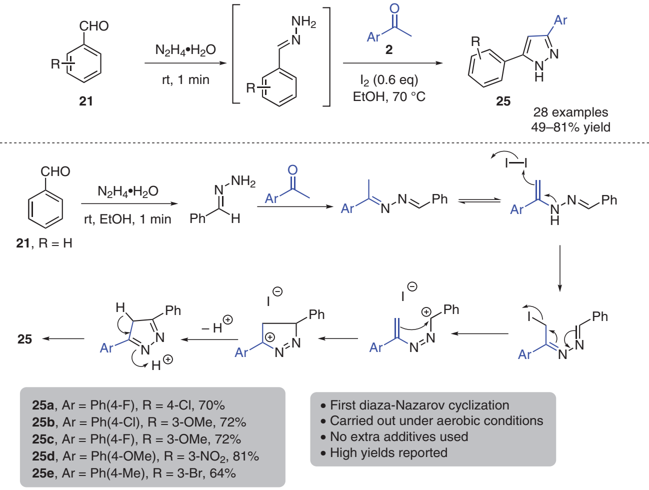


Scheme 12 Synthesis of 1,4-disubstituted imidazoles **24** by neighbouring-group-assistance strategy

(2l) Geng, *Org. Lett.* **2020**, *22*, 140

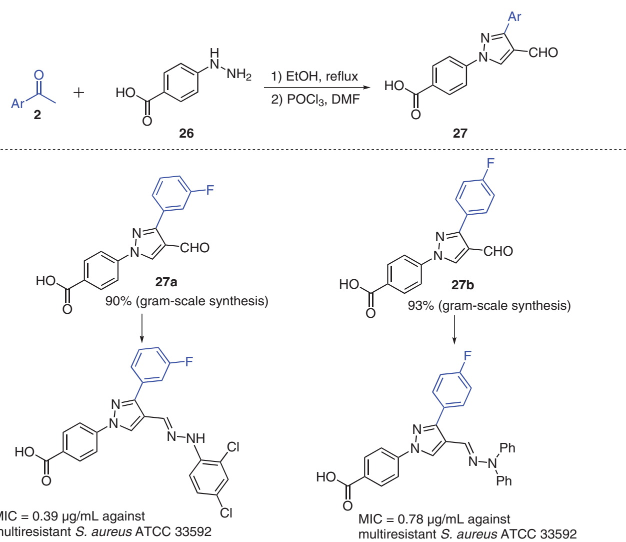
Figure 2 Synthesis of five-membered heterocycles, part II[2g–l]

2.4. Pyrazoles



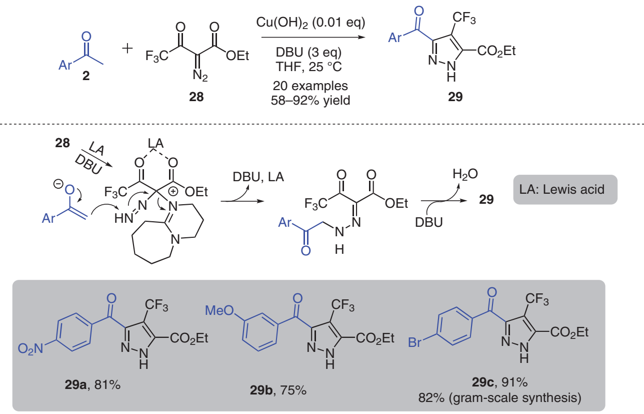
Scheme 13 Synthesis of polysubstituted pyrazoles **25** by a diaza-Nazarov cyclization

(2m) Aegurla, *Org. Biomol. Chem.* **2017**, *15*, 9643



Scheme 14 Synthesis of 4-formylpyrazole derivatives **27**

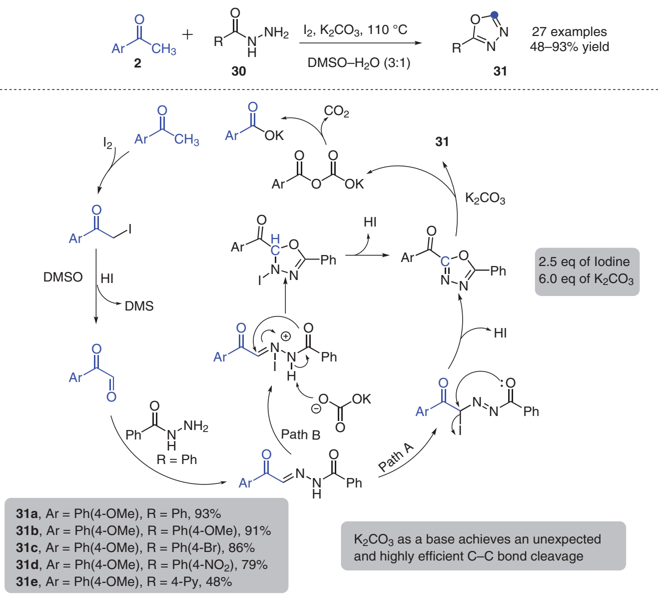
(2n) Whitt, *ACS Omega* **2019**, *4*, 14284



Scheme 15 Synthesis of polysubstituted 4-trifluoromethylpyrazoles **29**

(2o) Fang, *J. Org. Chem.* **2020**, *85*, 8714

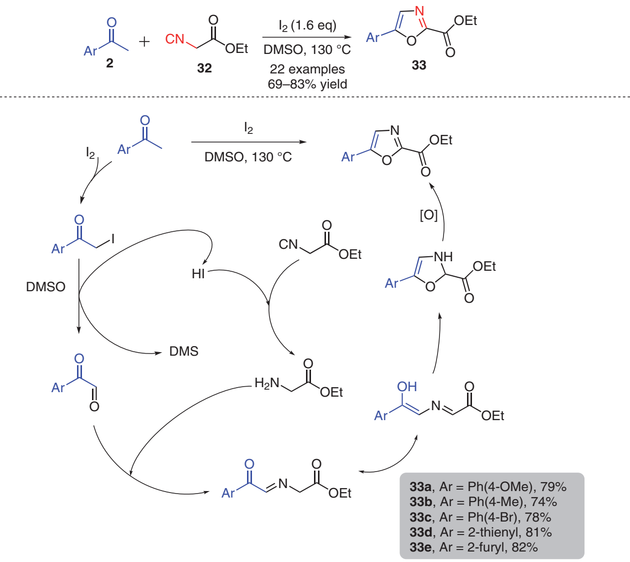
2.5. Oxadiazoles



Scheme 16 Synthesis of 1,3,4-oxadiazoles **31** via oxidative C(CO)–C(methyl) bond cleavage

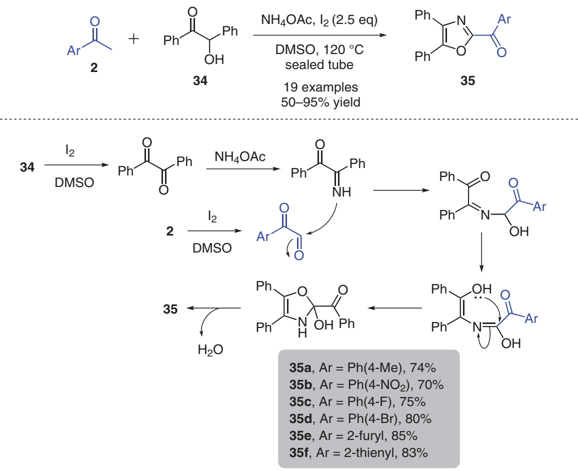
(2p) Gao, *Org. Lett.* **2015**, *17*, 2960

2.6 Oxazoles



Scheme 17 Synthesis of 2,5-disubstituted oxazoles **33** via I_2-promoted formal [3+2] cycloaddition

(2q) Wu, *Chem. Commun.* **2017**, *53*, 3438

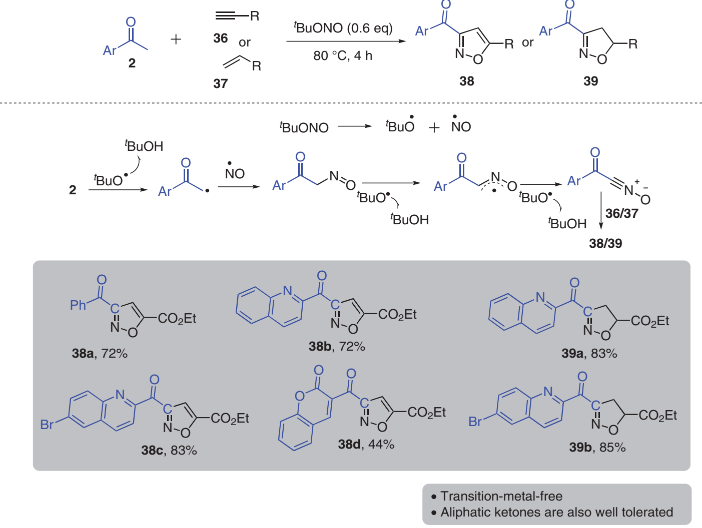


Scheme 18 Synthesis of oxazole derivatives **35**

(2r) Xue, *Chem. Commun.* **2012**, *48*, 3485

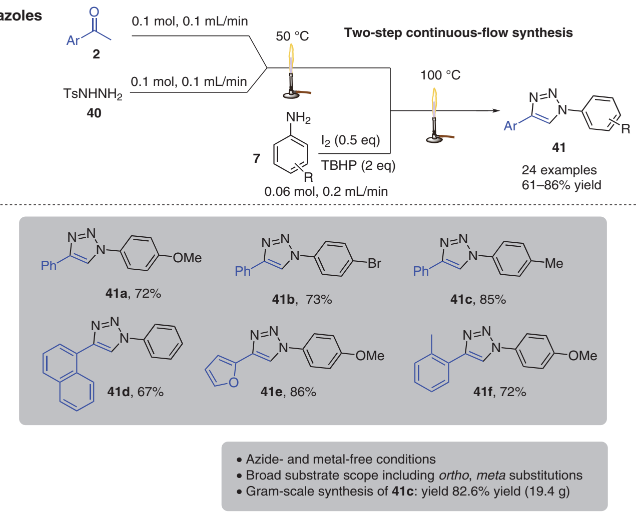
Figure 3 Synthesis of five-membered heterocycles, part III[2m–r]

2.7 Isoxazoles

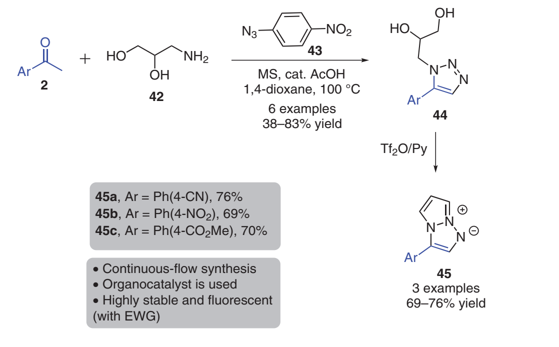


Scheme 19 Synthesis of 3-acyl-isoxazoles and isoxazolines **38/39** (2s) Dai, *Org. Lett.* **2019**, *21*, 5096

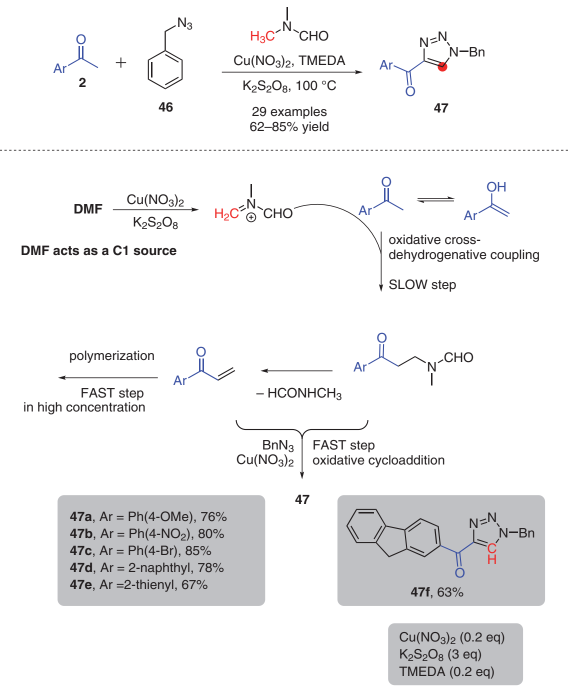
2.8 Triazoles



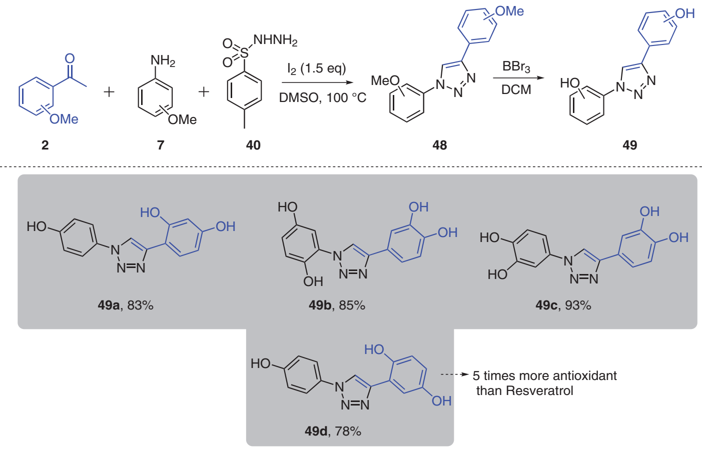
Scheme 20 Metal-free synthesis of 1,4-disubstituted triazoles **41** (2t) Gu, *RSC Adv.* **2016**, *6*, 89073



Scheme 21 Synthesis of triazole fluorescent probes **45** (2u) Verbelen, *Org. Lett.* **2016**, *18*, 6412

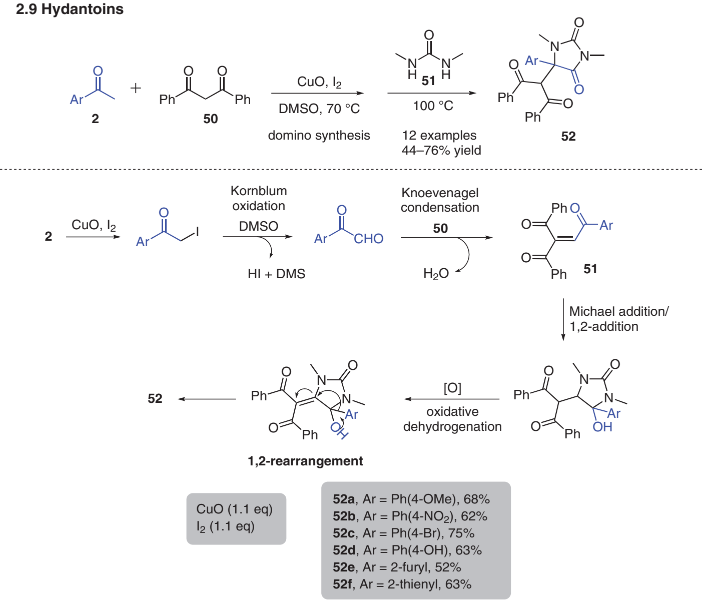


Scheme 22 Synthesis of 4-acyl-1,2,3-triazoles **47** (2v) Liu, *J. Org. Chem.* **2017**, *82*, 9198



Scheme 23 Synthesis of polyphenolic triazoles **49** (2w) Bonache, *ACS Comb. Sci.* **2018**, *20*, 694

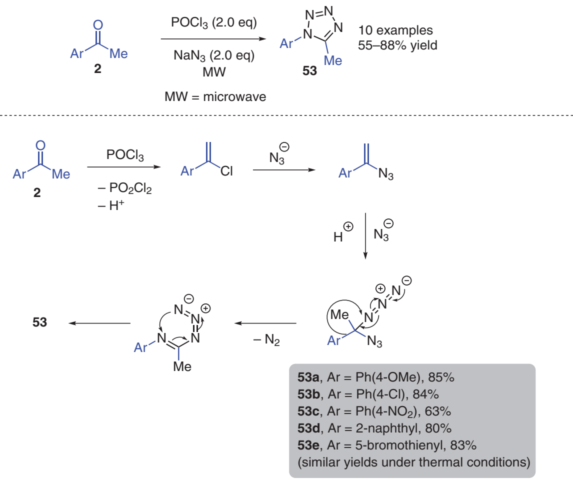
2.9 Hydantoins



Scheme 24 Synthesis of hydantoin analogues **52** (2x) Gao, *Org. Lett.* **2010**, *12*, 4026

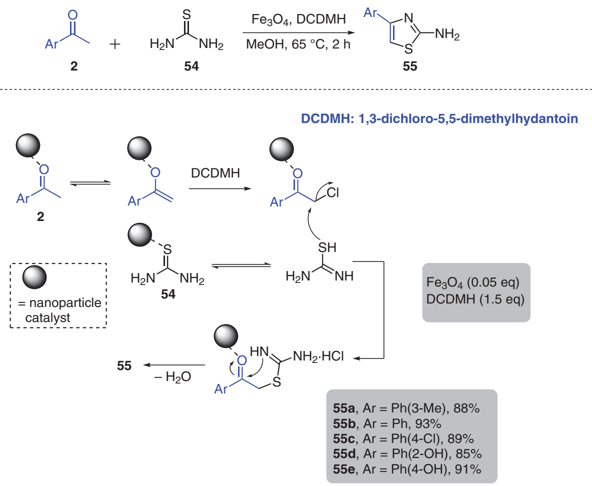
Figure 4 Synthesis of five-membered heterocycles, part IV[2s–x]

2.10 Tetrazoles



Scheme 25 Synthesis of tetrazole analogues **53** (2y) Sribalan, *New J. Chem.* **2017**, *41*, 3414

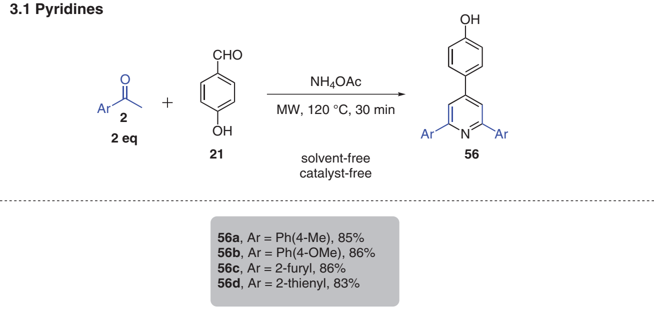
2.11 2-Aminothiazoles



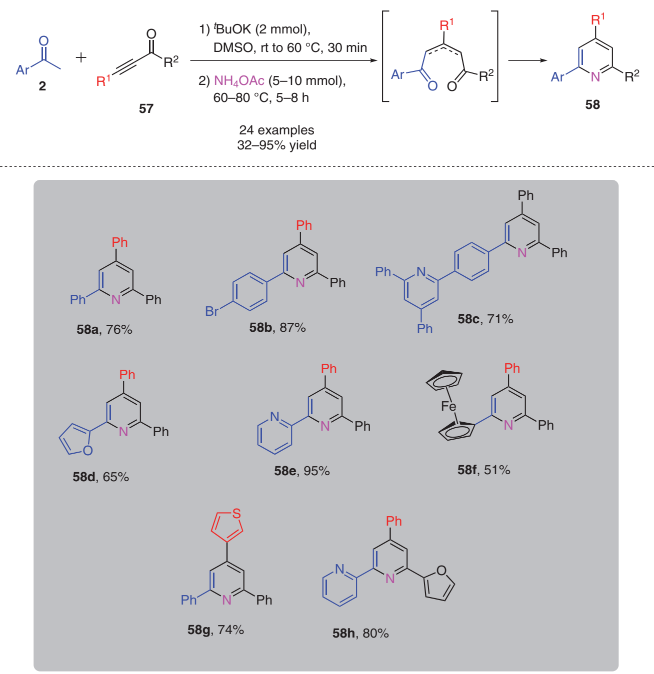
Scheme 26 Synthesis of 2-aminothiazoles **55** (2z) Sadeghi, *RSC Adv.* **2016**, *6*, 64749

3 Six-membered heterocycles

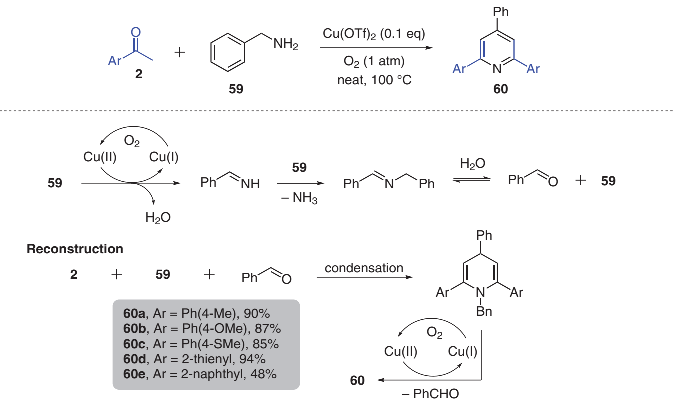
3.1 Pyridines



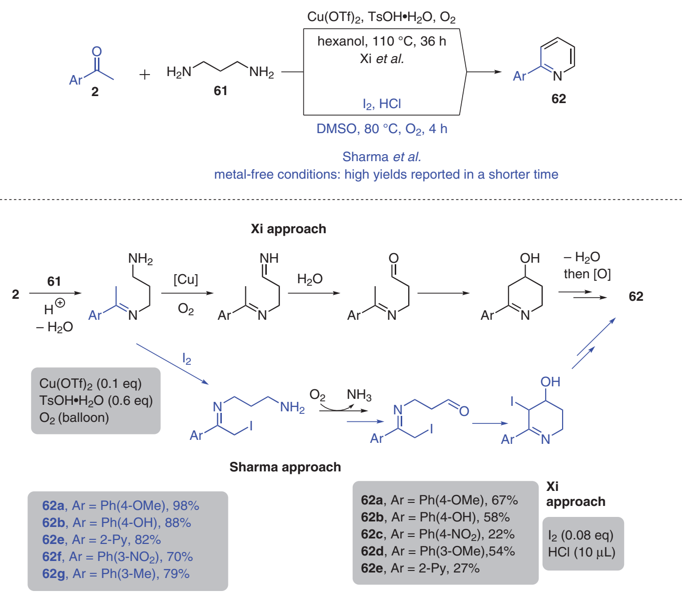
Scheme 27 Synthesis of trisubstituted pyridines **56** (3a) Yin, *Green Chem.* **2012**, *14*, 1796



Scheme 28 Regiocontrolled synthesis of 2,4,6-triarylpyridines **58** (3b) Shabalin, *Org. Biomol. Chem.* **2021**, *19*, 2703

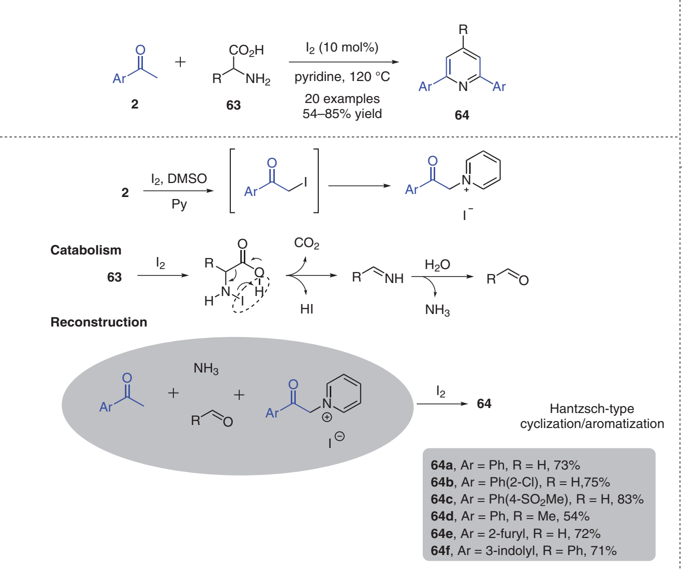


Scheme 29 Synthesis of 2,4,6-trisubstituted pyridine analogues **60** by C–N bond cleavage (3c) Huang, *J. Org. Chem.* **2013**, *78*, 3774

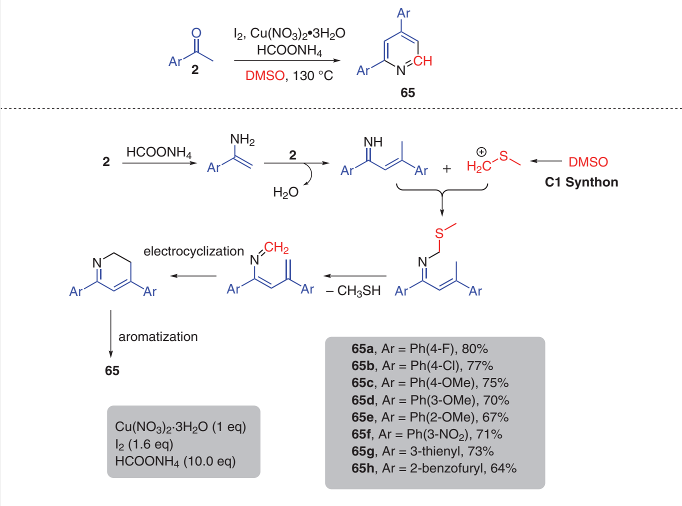


Scheme 30 Synthesis of 2-arylpyridines **62** (3d) Xi, *Org. Lett.* **2014**, *16*, 5269
(3e) Sharma, *Chem. Commun.* **2016**, *52*, 1009

Figure 5 Synthesis of five-membered heterocycles, part V,[2y,z] and six-membered heterocycles part I[3a–e]

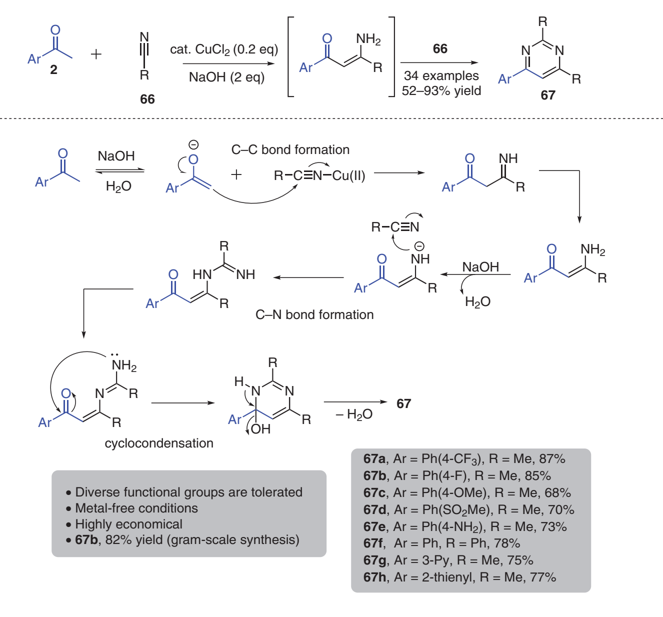


Scheme 31 Synthesis of multisubstituted pyridines **64** (3f) Xiang, *Org. Lett.* **2016**, *18*, 24

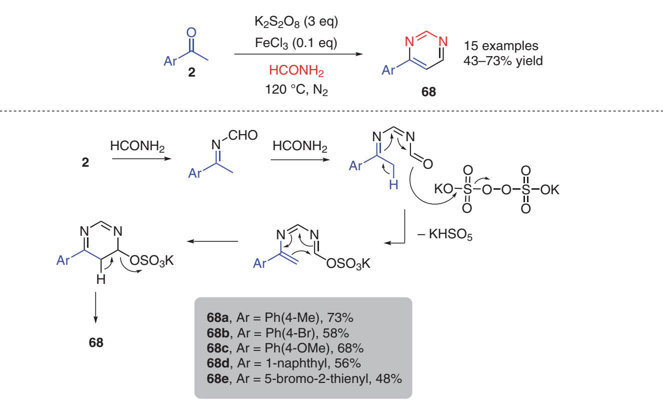


Scheme 32 Synthesis of polysubstituted pyridines **65** using DMSO as a carbon synthon (3g) Wu, *Adv. Synth. Catal.* **2016**, *358*, 218

3.2. Pyrimidines

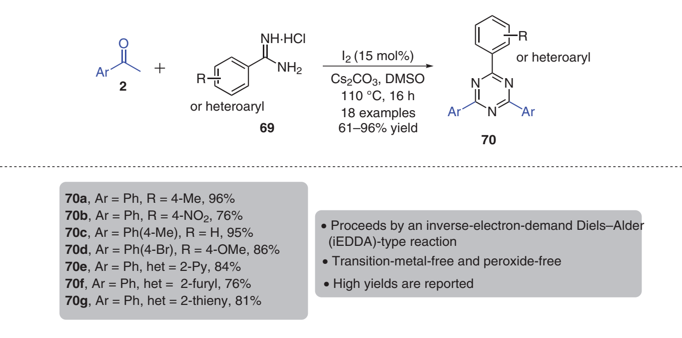


Scheme 33 Synthesis of pyrimidines **67** via cyclization of aryl methyl ketones and nitriles (3h) Su, *Org. Lett.* **2018**, *20*, 3399

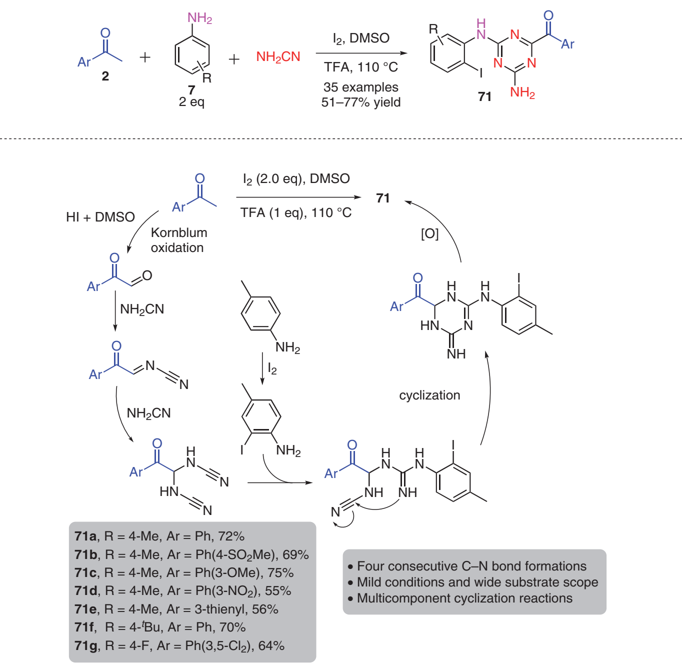


Scheme 34 Synthesis of pyrimidines **68** mediated by $K_2S_2O_8$ (3i) Jadhav, *Org. Lett.* **2017**, *19*, 5673

3.3 Triazines



Scheme 35 Synthesis of triazines **70** via sp^3 C–H functionalization (3j) Tiwari, *J. Org. Chem.* **2017**, *82*, 13239

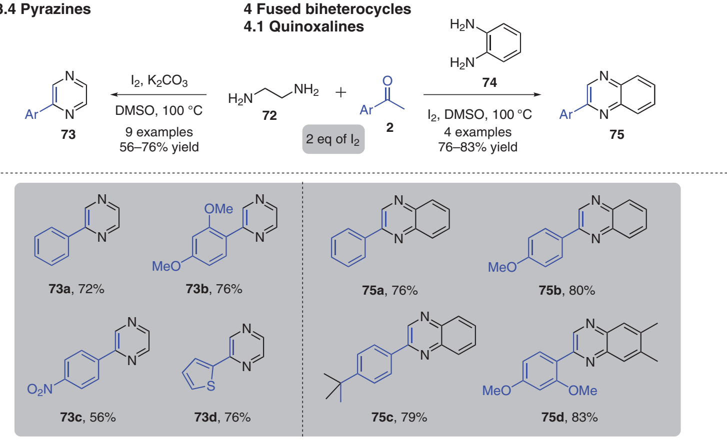


Scheme 36 Iodine-promoted multicomponent synthesis of 2,4-diamino-1,3,5-triazines **71** (3k) Zhao, *Org. Lett.* **2020**, *22*, 8528

Figure 6 Synthesis of six-membered heterocycles, part II[3f–k]

3.4 Pyrazines

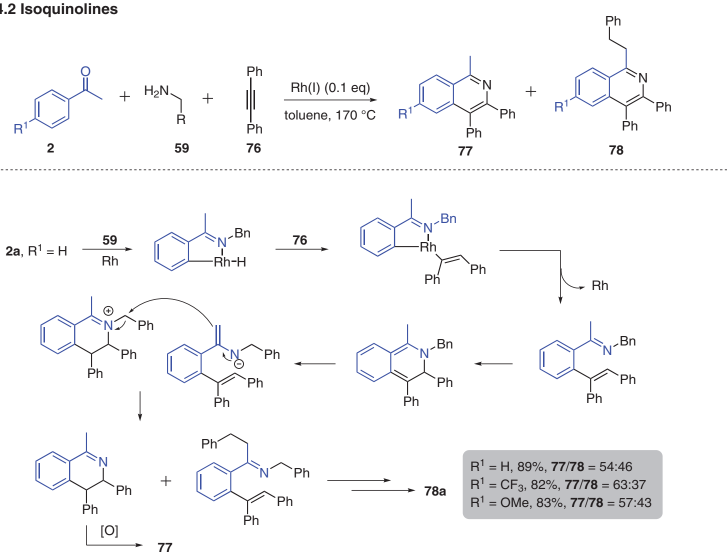
4 Fused biheterocycles
4.1 Quinoxalines



Scheme 37 Synthesis of pyrazines **73** and quinoxalines **75** by iodine-mediated oxidative annulation

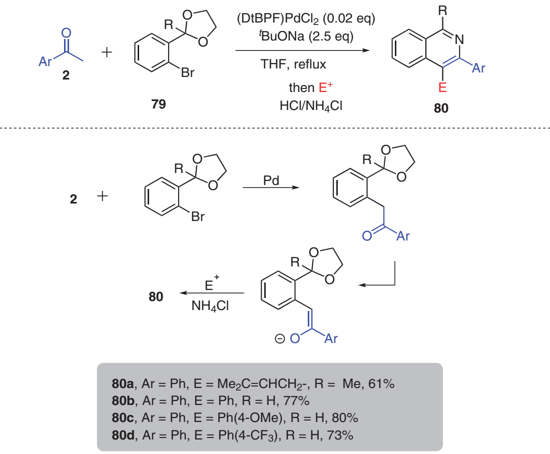
(3l) Viswanadham, *Chem. Commun.* **2014**, *50*, 13517

4.2 Isoquinolines



Scheme 38 Synthesis of isoquinolines **77** and **78** via Rh-catalyzed *ortho*-alkenylation

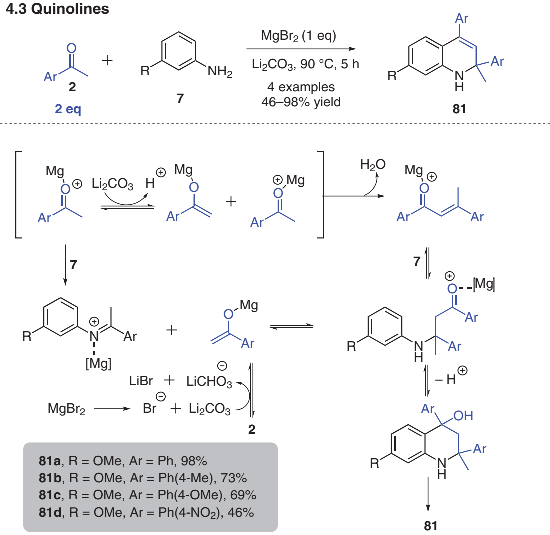
(3m) Lim, *Org Lett.* **2003**, *5*, 2759



Scheme 39 Synthesis of isoquinoline analogues **80** via catalytic enolate arylation

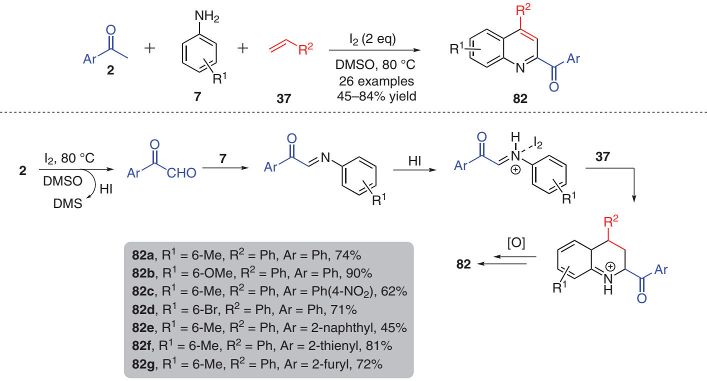
(3n) Pilgrim, *Org. Lett.* **2013**, *15*, 6190

4.3 Quinolines



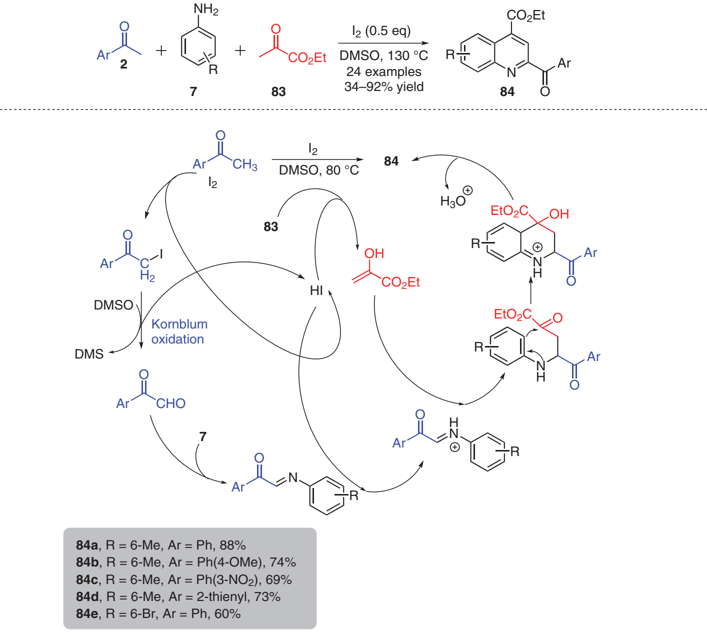
Scheme 40 $MgBr_2$-catalyzed synthesis of 1,2-dihydroquinolines **81**

(4a) Gutierez, *J. Org. Chem.* **2013**, *78*, 9614



Scheme 41 Synthesis of quinolines **82** by I_2-mediated formal [3+2+1] cycloaddition

(4b) Gao, *Org. Lett.* **2014**, *16*, 4582

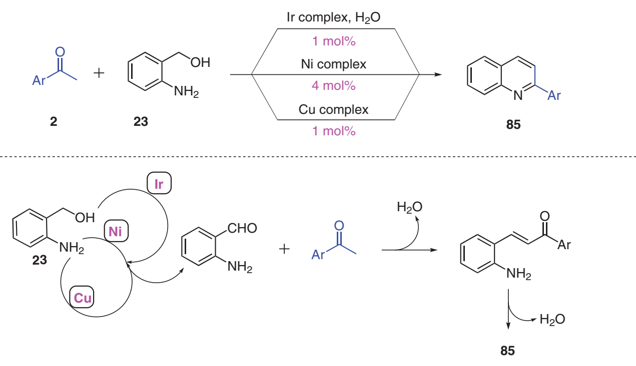


Scheme 42 Synthesis of substituted quinolines **84** via a co-product-promoted Povarov reaction

(4c) Gao, *J. Org. Chem.* **2015**, *80*, 5984

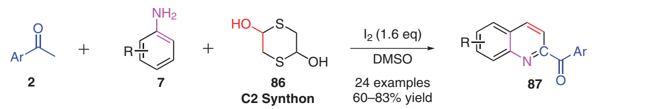
Figure 7 Synthesis of fused bi-heterocycles, part I[3l–n,4a–c]

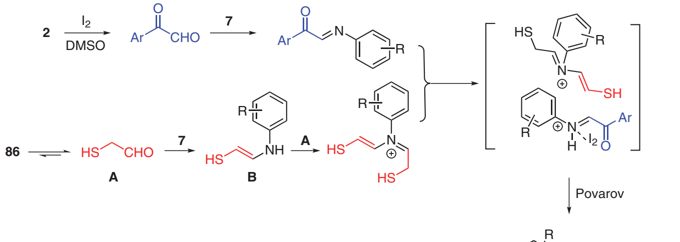
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany



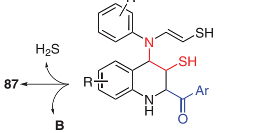
Ir	(4d) Wang, *Org. Lett.* **2016**, *18*, 3558
Ni	(4e) Chakraborty, *J. Org. Chem.* **2019**, *84*, 2626
Cu	(4f) Das, *J. Org. Chem.* **2019**, *84*, 10160

Scheme 43 Synthesis of 2-arylquinolines **85**



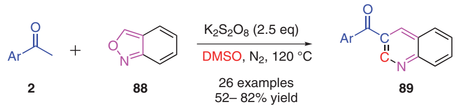


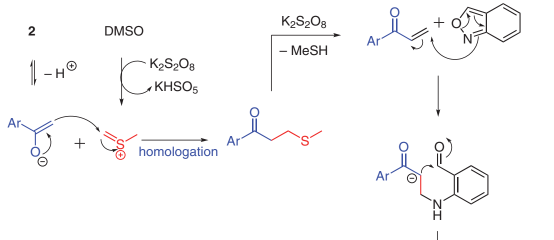
87a, R = 6-Me, Ar = Ph, 76%
87b, R = 6-Me, Ar = Ph(4-OMe), 76%
87c, R = 6-Me, Ar = Ph(4-NO2), 81%
87d, R = 6-CO2Et, Ar = Ph, 60%
87e, R = 6-Me, Ar = 2-Naphthyl, 82%
87f, R = 6-Me, Ar = 2-thienyl, 79%
87g, R = 6-Me, Ar = 2-furyl, 83%
87h, R = 6-Br, Ar = Ph, 61%



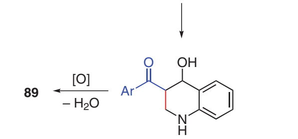
Scheme 44 Synthesis of quinoline analogues **87** through [4+2] cycloaddition

(4g) Wu, *Org. Lett.* **2017**, *19*, 1550



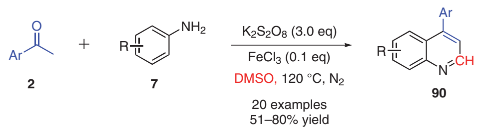


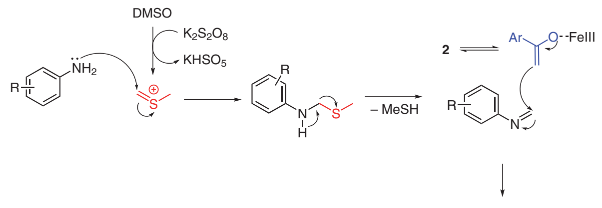
89a, Ar = Ph, 76%
89b, Ar = Ph(3-Br), 77%
89c, Ar = Ph(2-Br), 78%
89d, Ar = Ph(4-CN), 82%
89e, Ar = Ph(3-NO2), 78%
89f, Ar = 2-furyl, 73%



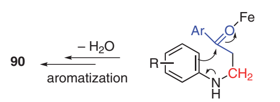
Scheme 45 Synthesis of quinoline analogues **89** via a sequential one-carbon homologation/conjugate addition/annulation cascade

(4h) Wakade, *Org. Lett.* **2017**, *19*, 4948



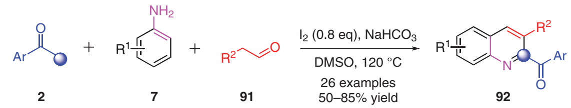


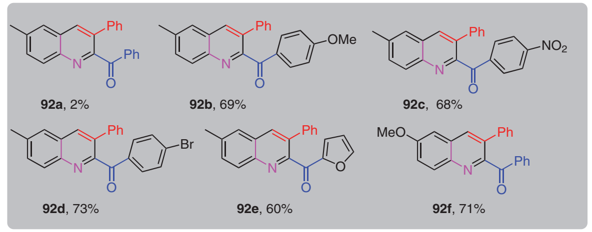
90a, R = 6-Me, Ar = Ph, 70%
90b, R = 6-Me, Ar = Ph(4-Me), 77%
90c, R = 6-Me, Ar = Ph(4-Br), 64%
90d, R = 6-Me, Ar = Ph(4-NO2), 69%
90e, R = 6-Me, Ar = 5-bromo-2-thienyl, 55%
90f, R = 6-F, Ar = Ph(4-OMe), 70%



Scheme 46 Synthesis of 4-substituted quinoline analogues **90** via oxidative annulations involving DMSO

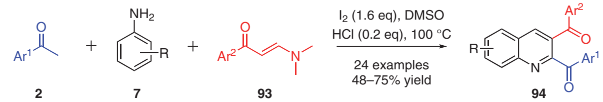
(3i) Jadhav, *Org. Lett.* **2017**, *19*, 5673

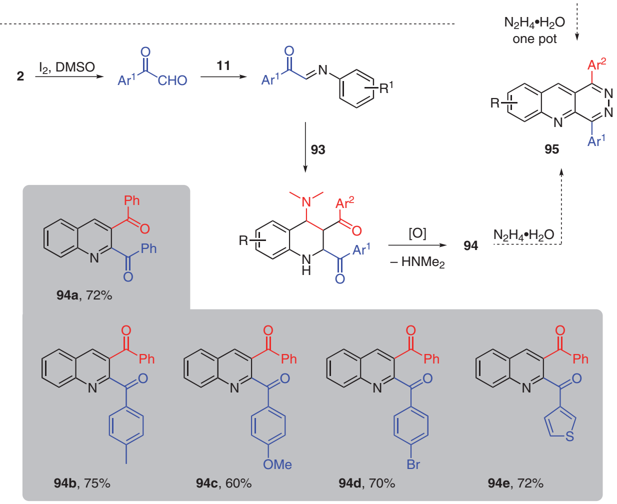




Scheme 47 Synthesis of 2-acyl-3-arylquinolines **92** via a synergistic I_2/amine-promoted Povarov-type reaction

(4i) Geng, *Org. Lett.* **2017**, *19*, 4179



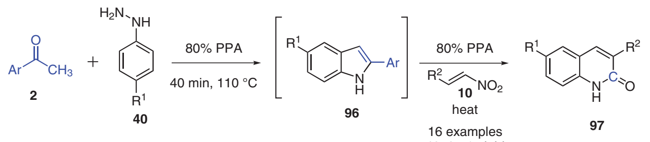


Scheme 48 Synthesis of 2,3-diaroylquinolines **94** via an I_2-promoted one-pot multicomponent reaction

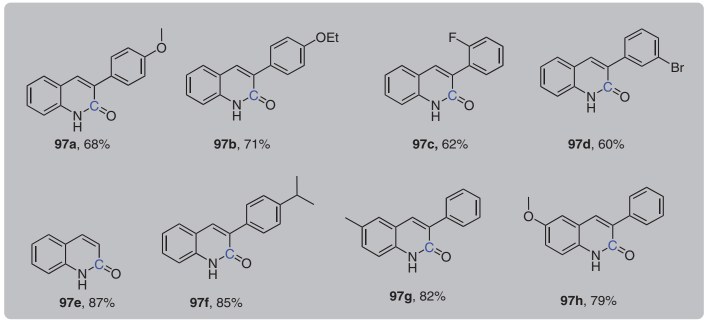
(4j) Zhao, *Org. Lett.* **2019**, *21*, 2708

Figure 8 Synthesis of fused bi-heterocycles, part II[3i,4d–j]

4.4 2-Quinolones



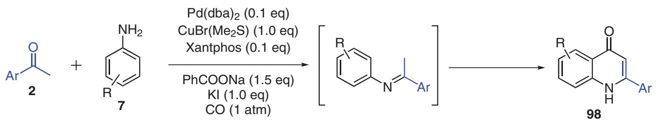
PPA: polyphosphoric acid

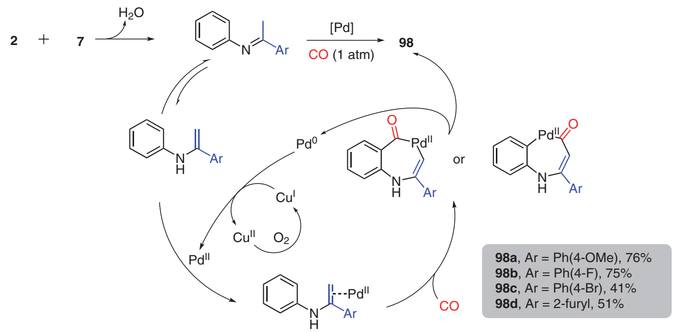


Scheme 49 Synthesis of 3-substituted 2-quinolones **97**

(4k) Aksenov, *RSC Adv.* **2015**, *5*, 8647

4.5 4-Quinolones

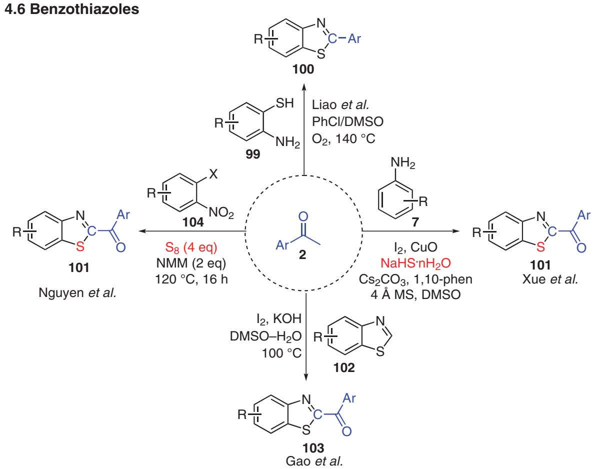




Scheme 50 Synthesis of 4-quinolones **98** via palladium-catalyzed oxidative carbonylation

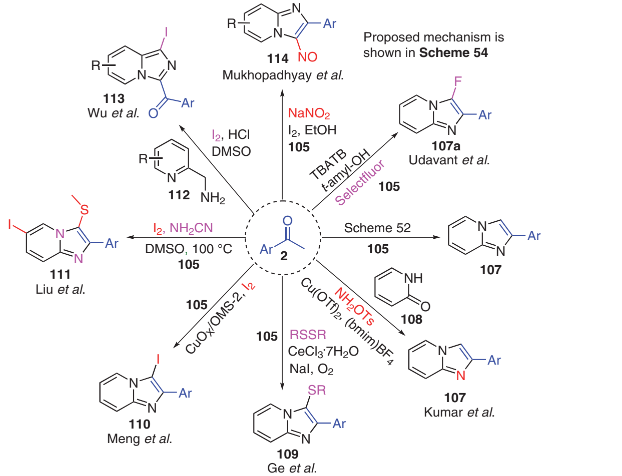
(4l) Wu, *Org. Lett.* **2017**, *19*, 6432

4.6 Benzothiazoles



Scheme 51 Synthesis of substituted benzothiazoles by various approaches

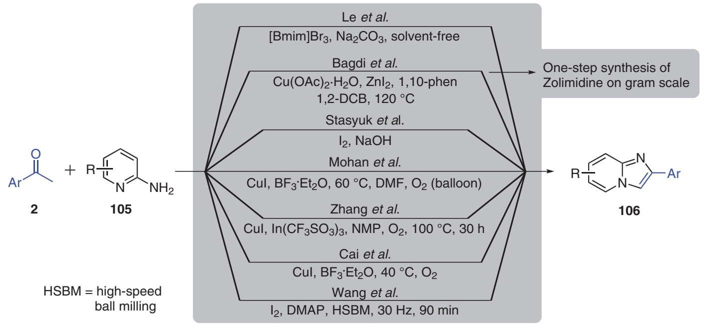
(4m) Liao, *Org. Lett.* **2012**, *14*, 6004
(4n) Xue, *Org. Lett.* **2013**, *15*, 890
(4o) Gao, *J. Org. Chem.* **2013**, *78*, 2792
(4p) Nguyen, *Org. Lett.* **2015**, *17*, 2562
Recent related work:
(4q) Huynh, *RSC Adv.* 2020, *10*, 18423



Scheme 53 Different approaches to access substituted imidazopyridines **107–114**

(5h) Kumar, *RSC Adv.* **2015**, *5*, 51576
(5i) Ge, *Eur. J. Org. Chem.* **2013**, 6015
(5j) Meng, *Catal. Sci. Technol.* **2015**, *5*, 372
(5k) Liu, *Org. Biomol. Chem.* **2015**, *13*, 8807
(5l) Wu, *Org. Chem. Front.* **2016**, *3*, 1430
(5m) Mukhopadhyay, *Eur. J. Org. Chem.* **2016**, 3836
(5n) Udavant, *Eur. J. Org. Chem.* **2018**, 3432
Recent related research work:
(5o) Okai, *Org. Lett.* **2020**, *22*, 8002

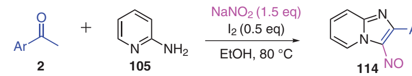
4.7 Imidazopyridines

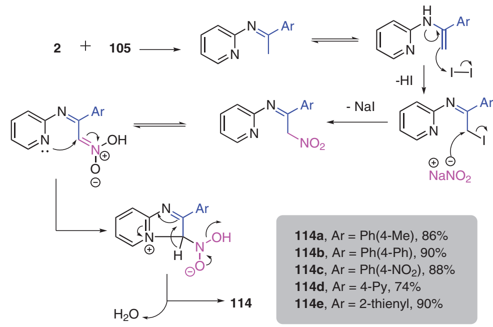


HSBM = high-speed ball milling

Scheme 52 Different approaches to access imidazopyridines **106**

(5a) Le, *Molecules* **2012**, *17*, 13368
(5b) Stasyuk, *J. Org. Chem.* **2012**, *77*, 5552
(5c) Bagdi, *Adv. Synth. Catal.* **2013**, *355*, 1741
(5d) Mohan, *Adv. Synth. Catal.* **2013**, *355*, 2217
(5e) Zhang, *J. Org. Chem.* **2013**, *78*, 12494
(5f) Cai, *Adv. Synth. Catal.* **2013**, *355*, 2686
(5g) Wang, *Mol. Diversity* **2016**, *20*, 659





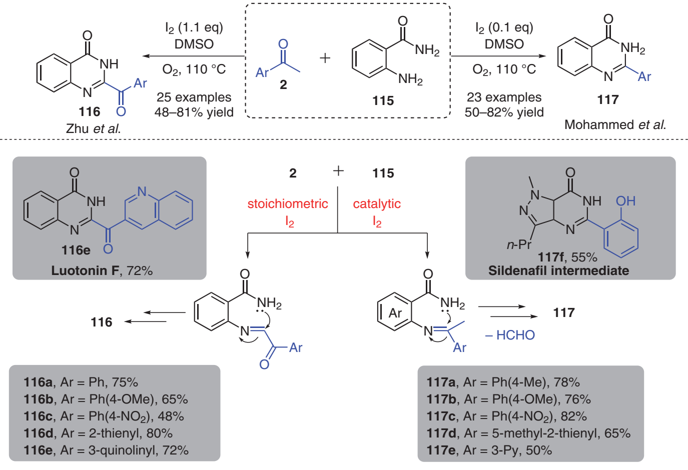
114a, Ar = Ph(4-Me), 86%
114b, Ar = Ph(4-Ph), 90%
114c, Ar = Ph(4-NO$_2$), 88%
114d, Ar = 4-Py, 74%
114e, Ar = 2-thienyl, 90%

Scheme 54 NaNO$_2$/I$_2$-mediated regioselective synthesis of nitrosoimidazopyridines **114**

(5m) Mukhopadhyay, *Eur. J. Org. Chem.* **2016**, 3836

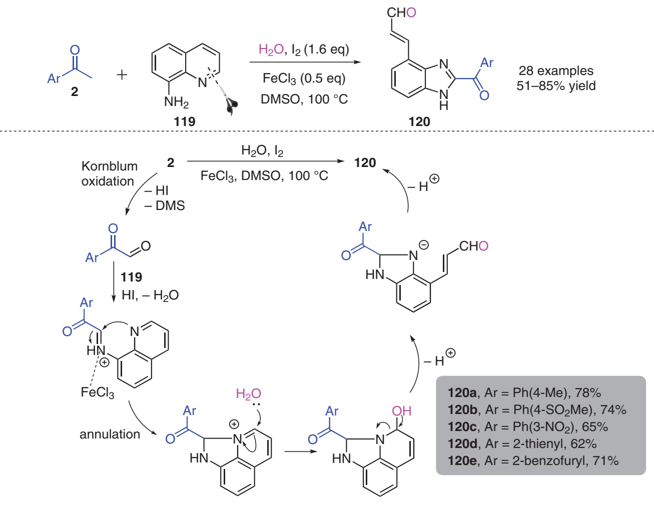
Figure 9 Synthesis of fused bi-heterocycles, part III[4k–q,5a–o]

4.8 Quinazolinones



Scheme 55 Synthesis of quinazolinones **116** and **117** by using catalytic/stoichiometric iodine

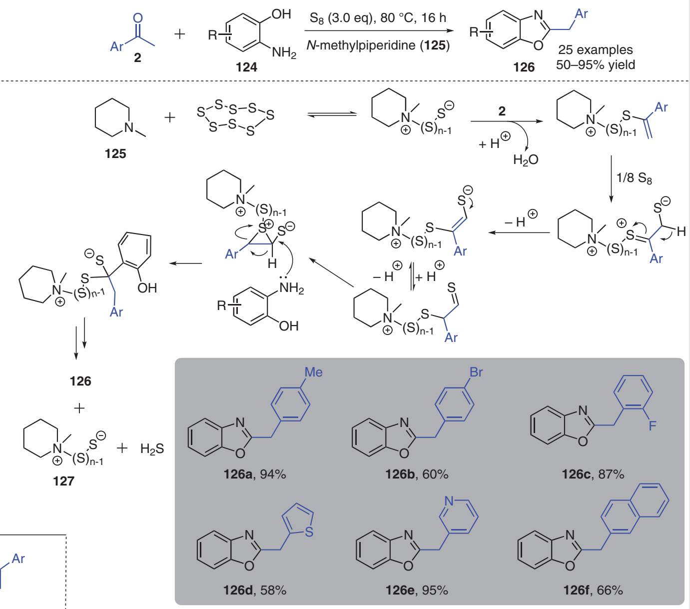
(5p) Zhu, *Org. Lett.* **2013**, *15*, 378
(5q) Mohammed, *J. Org. Chem.* **2015**, *80*, 6915



Scheme 57 Synthesis of (*E*)-3-(2-acyl-1*H*-benzo[*d*]imidazol-4-yl)acrylaldehyde derivatives **120**

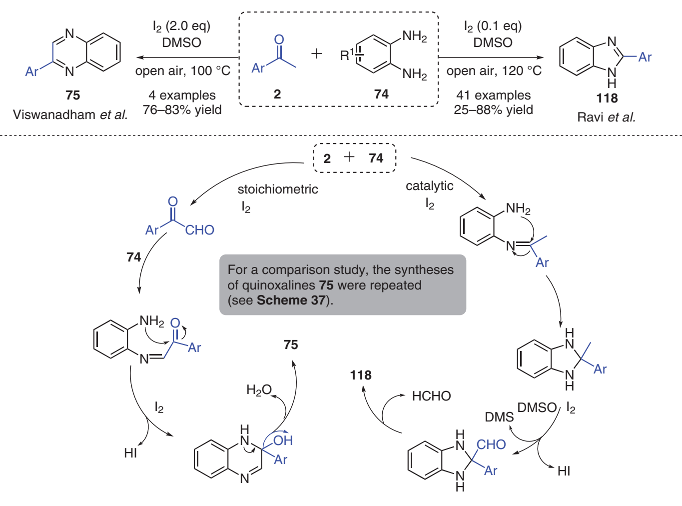
(6b) Xu, *Org. Lett.* **2021**, *23*, 2559

4.11 Benzoxazoles



Scheme 59 Synthesis of 2-alkylbenzoxazoles **120** (6d) Nguyen, *Org. Lett.* **2017**, *19*, 3887

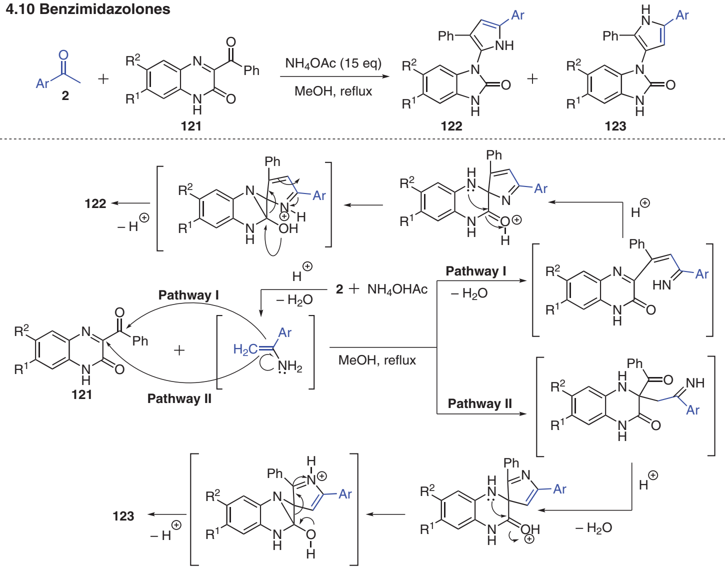
4.9 Benzimidazoles



Scheme 56 Synthesis of quinoxalines **75** and benzimidazoles **118** using catalytic or stoichiometric equivalents of iodine

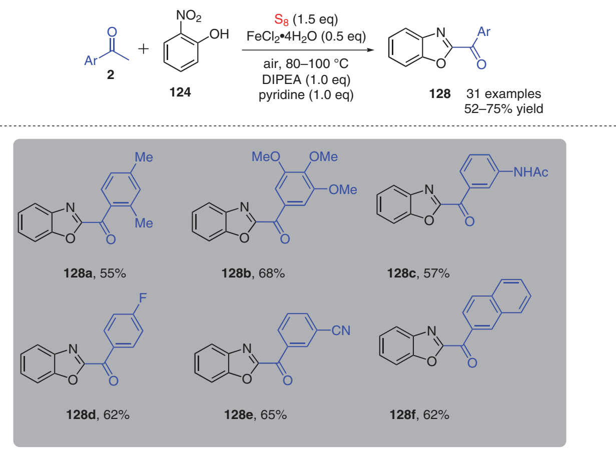
(3l) Viswanadham, *Chem. Commun.* **2014**, *50*, 13517
(6a) Ravi, *J. Org. Chem.* **2017**, *82*, 4422

4.10 Benzimidazolones



Scheme 58 Synthesis of 1-(pyrrolyl)benzimidazolones **122** and **123** by rearrangement of quinoxalin-2-ones

(6c) Mamedov, *J. Org. Chem.* **2015**, *80*, 1375

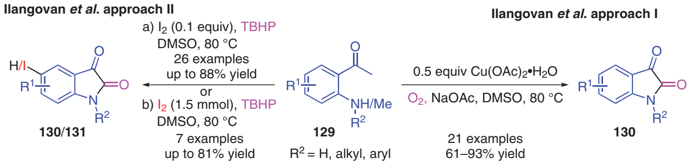


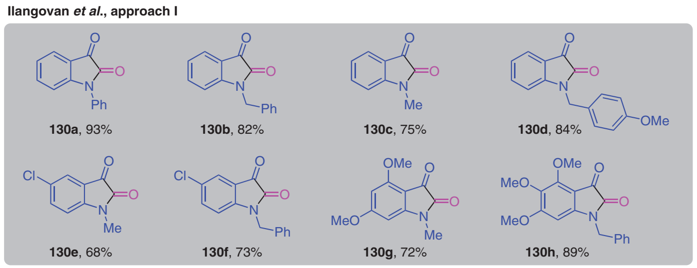
Scheme 60 Fe/S-catalyzed synthesis of 2-benzoylbenzoxazoles **128**

(6e) Nguyen, *Org. Biomol. Chem.* **2021**, *19*, 6015

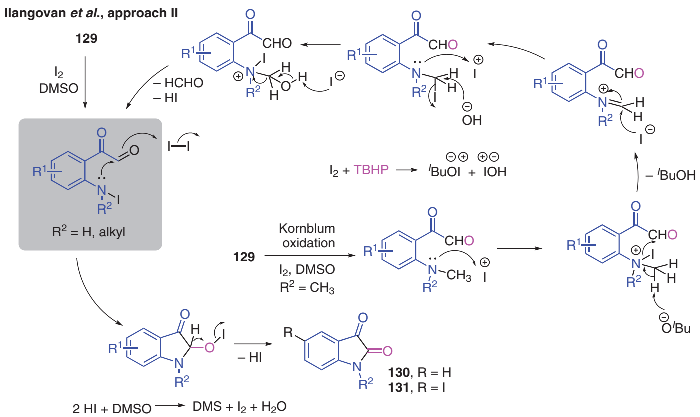
Figure 10 Synthesis of fused bi-heterocycles, part IV[5p,q,6a–e]

4.12 Isatins



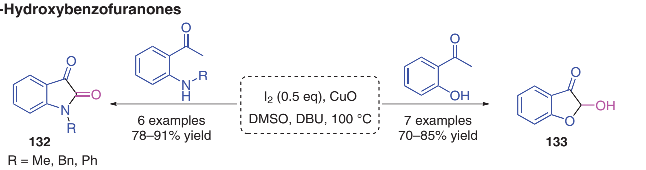


Scheme 61 Synthesis of isatins **130** by Ilangovan *et al.*, approach I (6f) Ilangovan, *Org. Lett.* **2013**, *15*, 5726



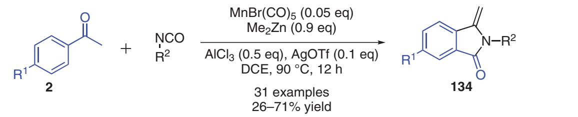
Scheme 62 Synthesis of isatins **130/131** by Ilangovan *et al.*, approach II (6g) Ilangovan, *J. Org. Chem.* **2014**, *79*, 4984

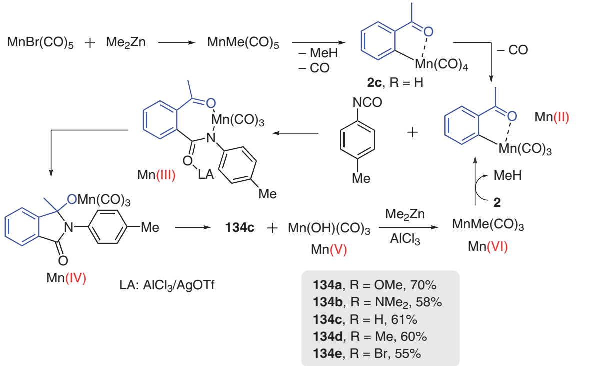
4.13 2-Hydroxybenzofuranones



Scheme 63 Synthesis of 2-hydroxybenzofuranones **130** and isatins **132** (6h) Gao, *Tetrahedron* **2014**, *70*, 4331

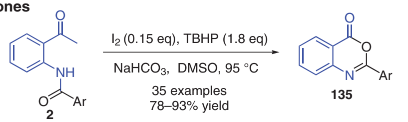
4.14 Phthalimidines

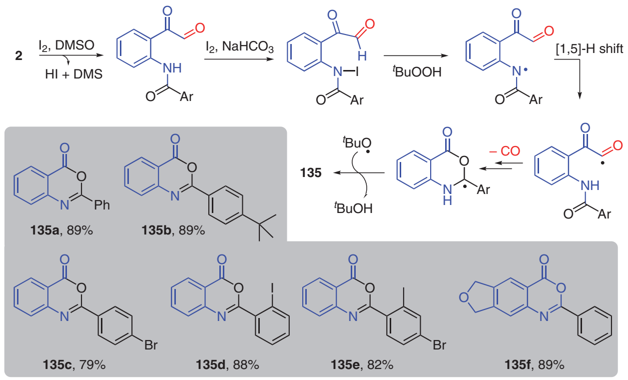




Scheme 64 Synthesis of phthalimidines **134** via manganese-catalyzed [3+2] cyclization (6i) Huo, *Org. Lett.* **2021**, *23*, 3384

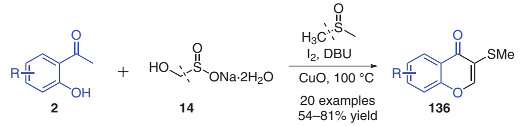
4.15 Benzoxazinones

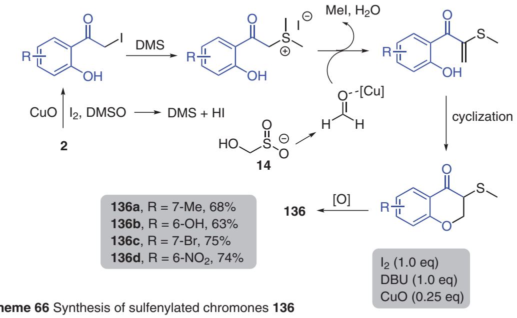




Scheme 65 Synthesis of substituted benzoxazinones **135** via decarbonylative cleavage of unstrained $C(sp^3)–C(sp^2)$ bonds (6j) Verma, *Org. Lett.* **2016**, *18*, 4388

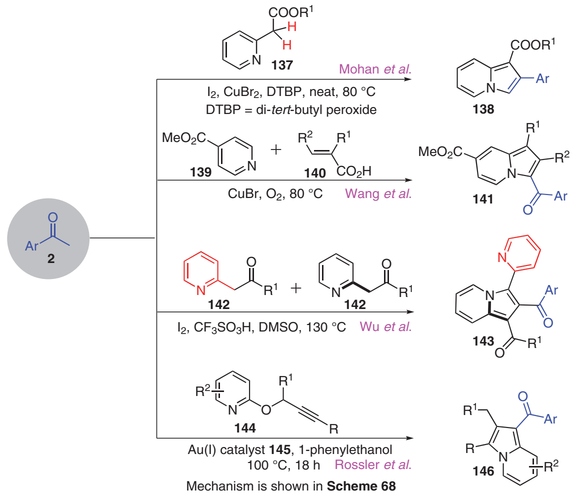
4.16 Chromenes





Scheme 66 Synthesis of sulfenylated chromones **136** (6k) Wang, *Org. Biomol. Chem.* **2019**, *17*, 1535

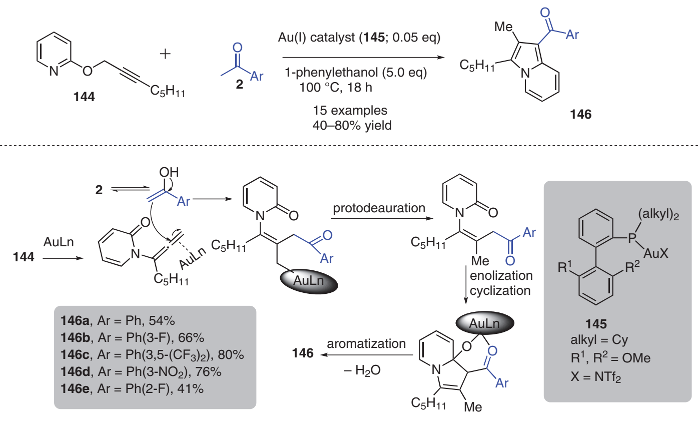
4.17 Indolizines



Scheme 67 Different approaches to access indolizines **138**, **141**, **143** and **146**

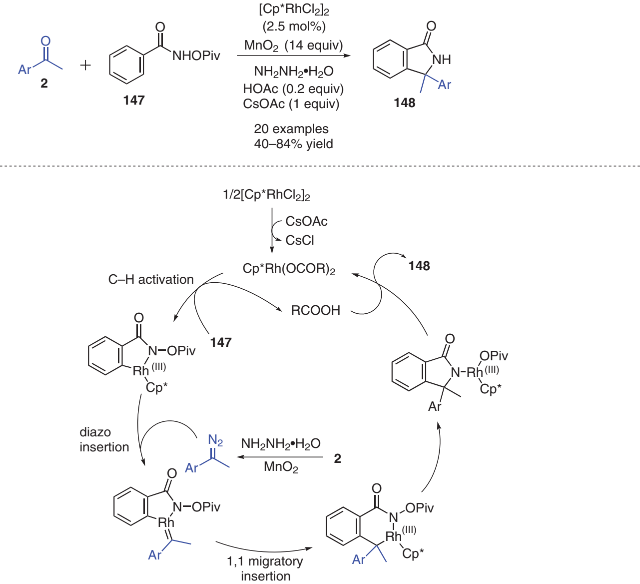
(6l) Mohan, *J. Org. Chem.* **2015**, *80*, 6846
(6m) Wang, *J. Org. Chem.* **2017**, *82*, 2835
(6n) Wu, *Org. Lett.* **2017**, *19*, 3319
(6o) Rossler, *Org. Lett.* **2019**, *21*, 5591

Figure 11 Synthesis of fused bi-heterocycles, part V[6f–o]



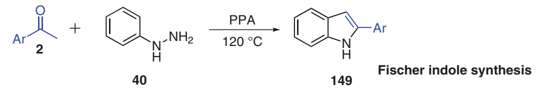
Scheme 68 Au(I)-catalyzed synthesis of trisubstituted indolizines **146** (6o) Rossler, *Org. Lett.* **2019**, *21*, 5591

4.18 Isoindolinones

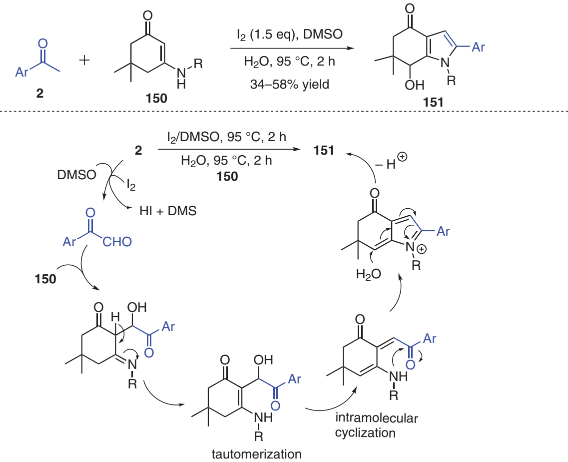


Scheme 69 Facile synthesis of isoindolinones **148** via a Rh(III)-catalyzed one-pot synthesis (7a) Zhang, *Org.Lett.* **2015**, *17*, 2494

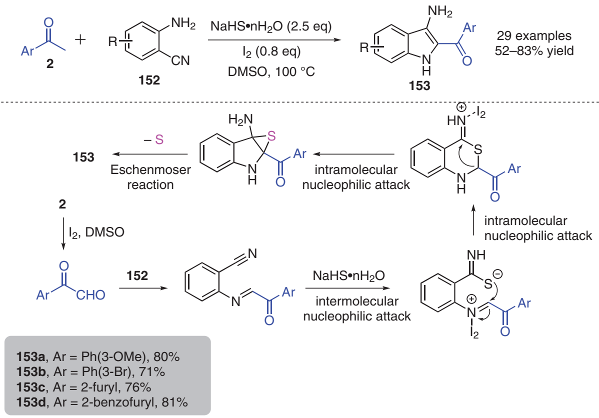
4.19 Indoles



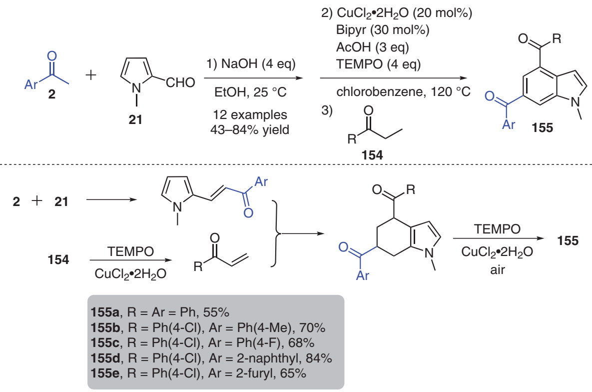
Scheme 70 Synthesis of 2-arylindoles **149** (7b) Fischer, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241 (7c) Kissman, *J. Am. Chem. Soc.* **1952**, *74*, 3948



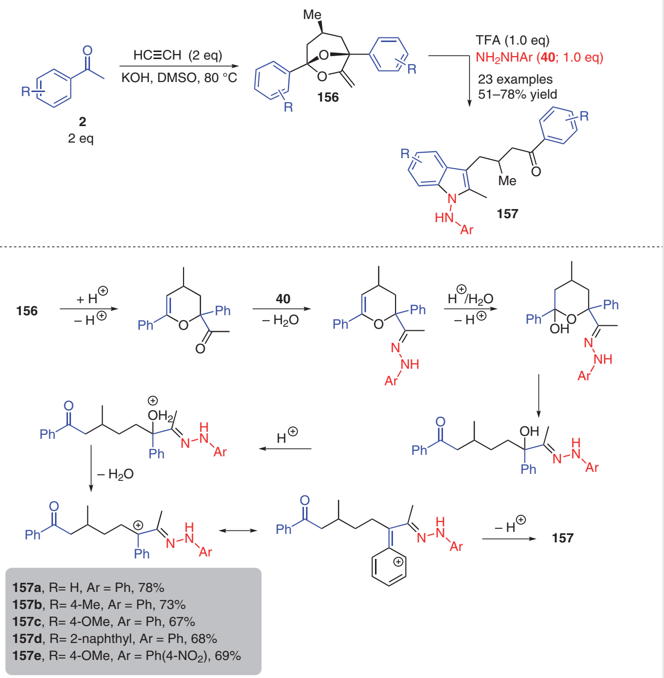
Scheme 71 Synthesis of 7-hydroxy-6,7-dihydroindole **151** (7d) Lu, *RSC Adv.* **2015**, *5*, 51501



Scheme 72 Synthesis of 2-acyl-3-aminoindoles **153** via $NaHS•nH_2O$-induced umpolung (7e) Geng, *Chem. Commun.* **2018**, *54*, 12730

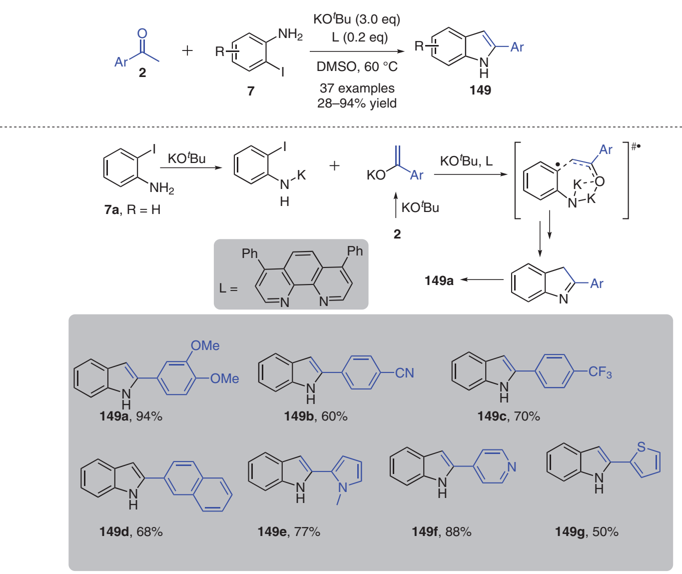


Scheme 73 Synthesis of 2-acyl-3-aminoindoles **149** via a copper-catalyzed three-component formal [3+1+2] benzannulation (7f) Guo, *J. Org. Chem.* **2020**, *85*, 9117

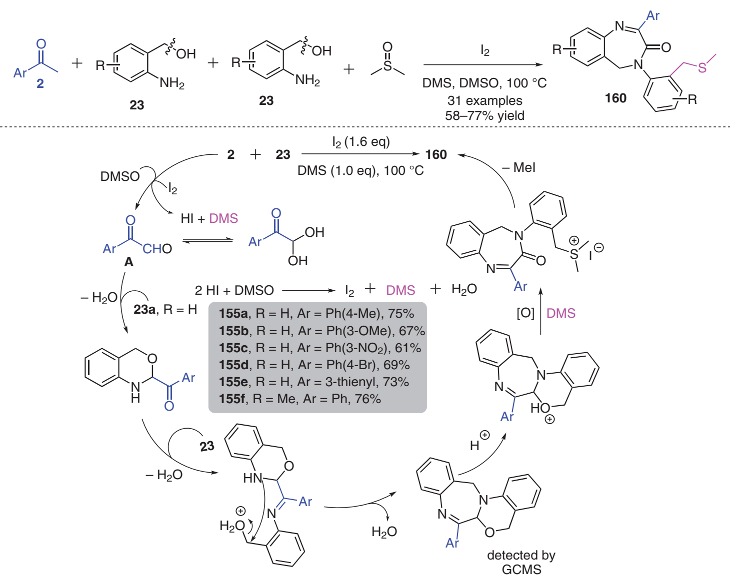


Scheme 74 Synthesis of *N*-aminoindoles **157** (7g) Schmidt, *Org. Lett.* **2019**, *21*, 4275

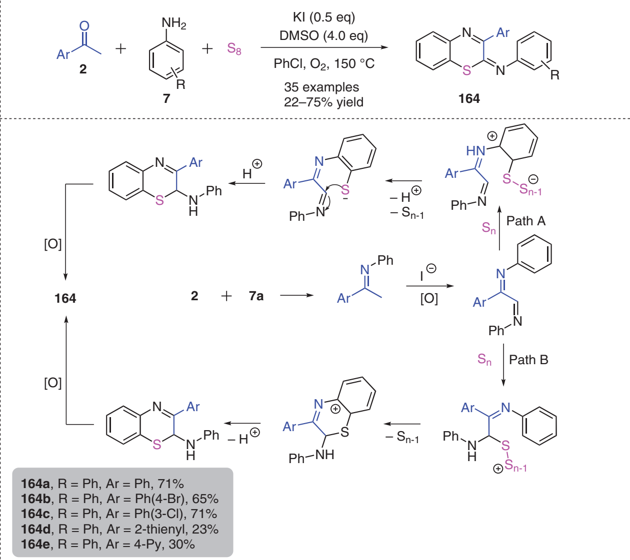
Figure 12 Synthesis of fused bi-heterocycles, part VI[6o,7a–g]



Scheme 75 Synthesis of 2-arylindoles **149** through radical enolate coupling
(7h) Chung, *Org. Lett.* **2021**, *23*, 1096

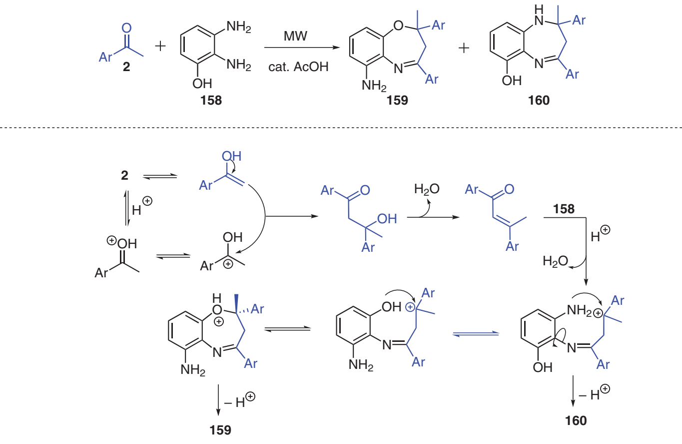


Scheme 77 Synthesis of 1,4-benzodiazepines **160** via dual C–O bond cleavage
(7j) Geng, *Org. Lett.* **2019**, *21*, 7504



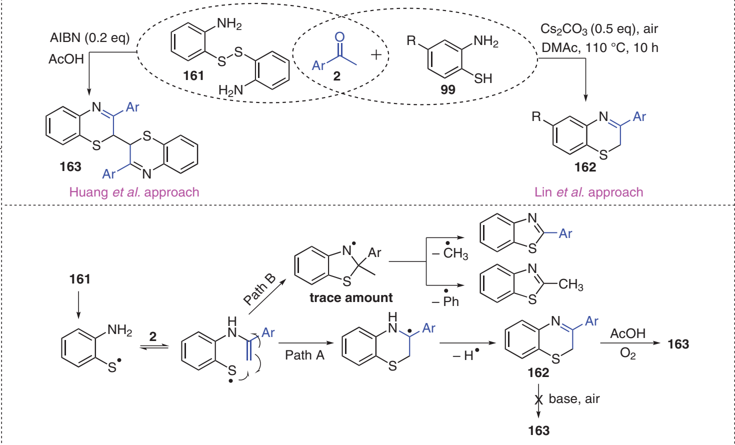
Scheme 79 Synthesis of 1,4-benzothiazines **164** via iodide-catalyzed aerobic C–H sulfuration with elemental sulfur
(7m) Jiang, *Org. Biomol. Chem.* **2020**, *18*, 3234

4.20 Benzoxazepines
4.21 Benzodiazepines



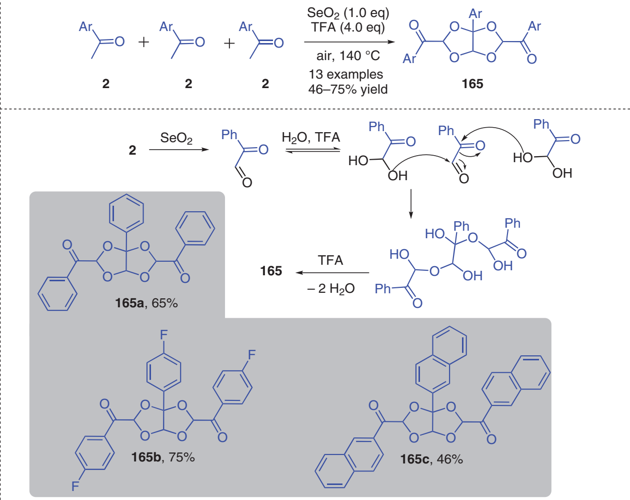
Scheme 76 One-pot synthesis of 1,5-benzoxazepines **159** and 1,5-benzodiazepines **160**
(7i) Neochoritis, *J. Med. Chem.* **2010**, *53*, 8409

4.22 Benzothiazines



Scheme 78 Synthesis of benzothiazines **162** and bibenzo[*b*][1,4]thiazines **163**
(7k) Lin, *Org. Lett.* **2016**, *18*, 6424
(7l) Huang, *Org. Lett.* **2018**, *20*, 3332

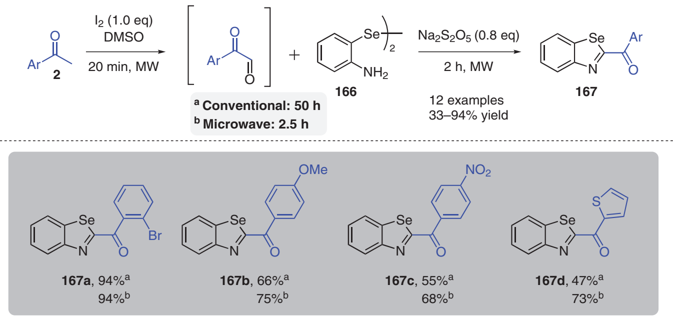
4.23 [1,3]Dioxolo[4,5-*d*][1,3]dioxoles



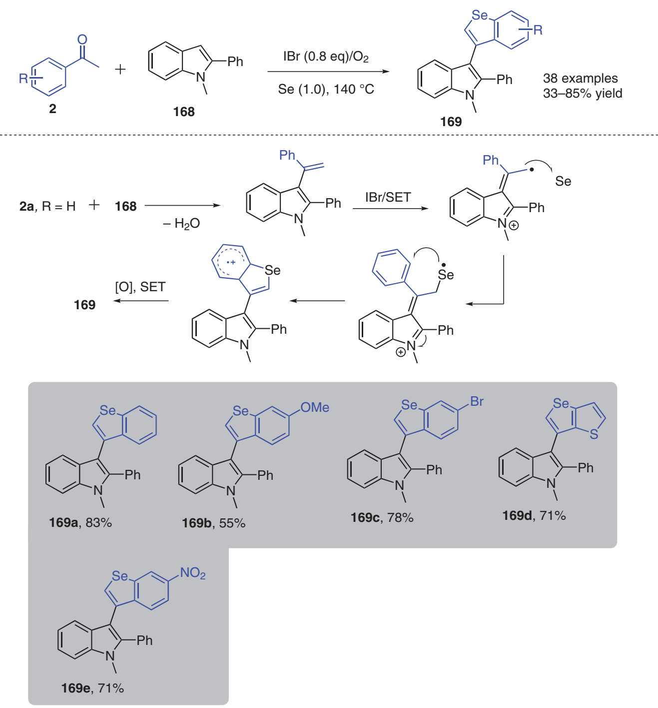
Scheme 80 Synthesis of fused [1,3]dioxolo[4,5-*d*][1,3]dioxoles **165** via trifluoroacetic acid mediated oxidative self-condensation of aryl methyl ketones
(7n) Marpna, *ACS Omega* **2021**, *6*, 14518

Figure 13 Synthesis of fused bi-heterocycles, part VII[7h–n]

4.24 Benzoselenazoles

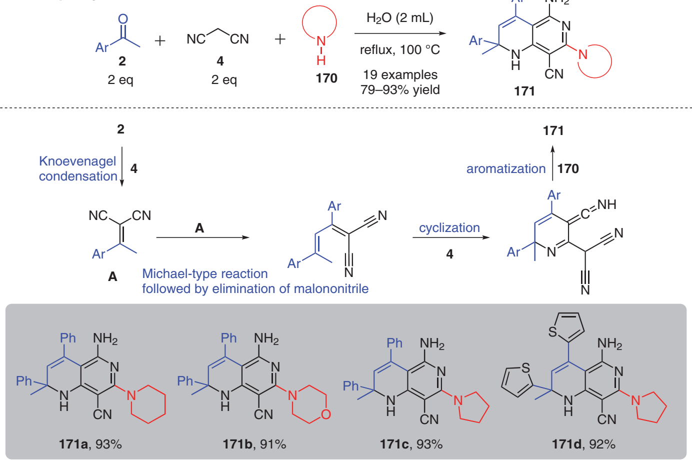


Scheme 81 Synthesis of 2-acylbenzo[1,3-*d*]selenazoles **167** via domino oxidative cyclization
(7o) Balaguez, *New J. Chem.* **2017**, *41*, 1483



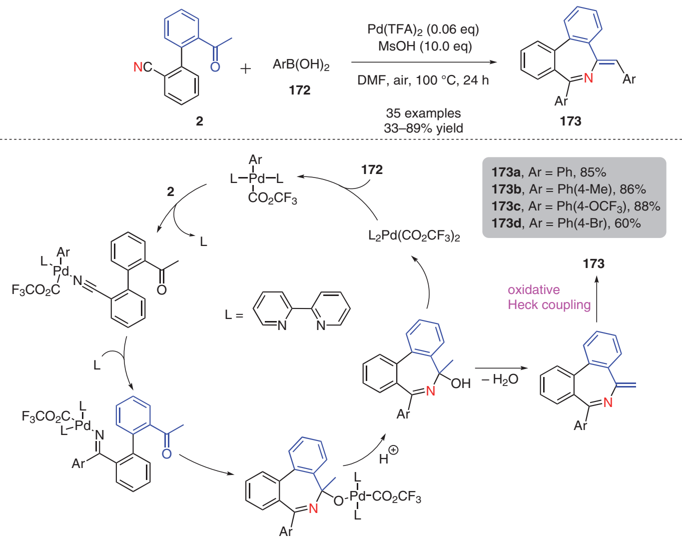
Scheme 82 Synthesis of benzoselenophenes **169** under metal-free conditions
(7p) Ni, *Org. Lett.* **2019**, *21*, 3518

4.25 Naphthyridines



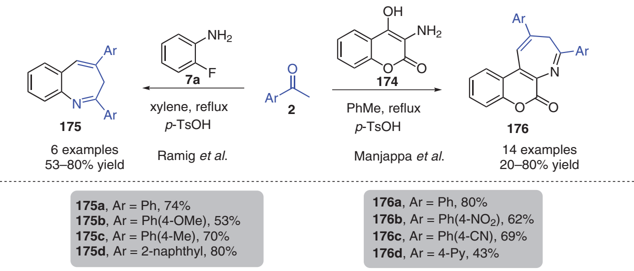
Scheme 83 Synthesis of dihydro[1,6]naphthyridines **171** (7q) Mukhopadhyay, *Org. Lett.* **2011**, *13*, 4664

5 Fused triheterocycles
5.1 Dibenzo[*c*,*e*]azepines



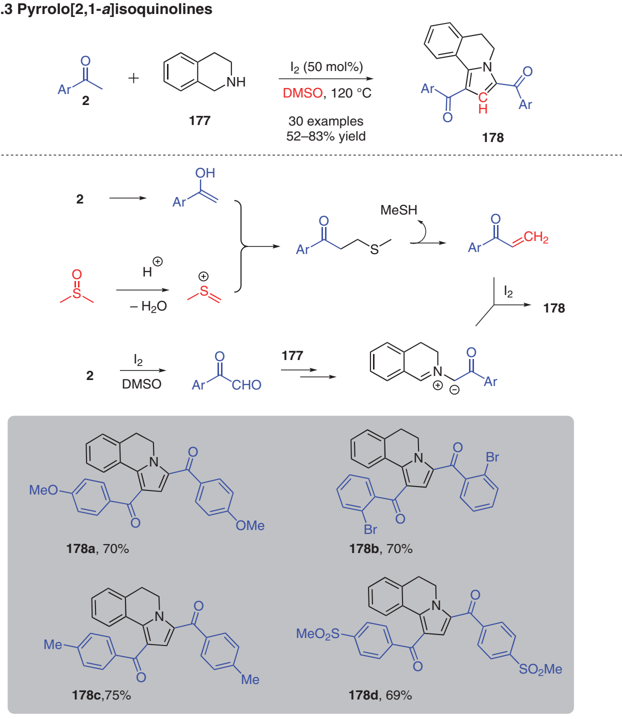
Scheme 84 Synthesis of 5-arylidene-7-aryl-5*H*-dibenzo[*c*,*e*]azepines **173**
(8a) Yao, *Org. Lett.* **2019**, *21*, 7697

5.2 Coumarin-annulated azepines



Scheme 85 Synthesis of 2,4-diaryl-3*H*-1-benzazepines **175** and coumarin-annulated azepines **176**
(8b) Ramig, *Synlett* **2007**, 2868
(8c) Manjappa, *RSC Adv.* **2017**, *7*, 45269

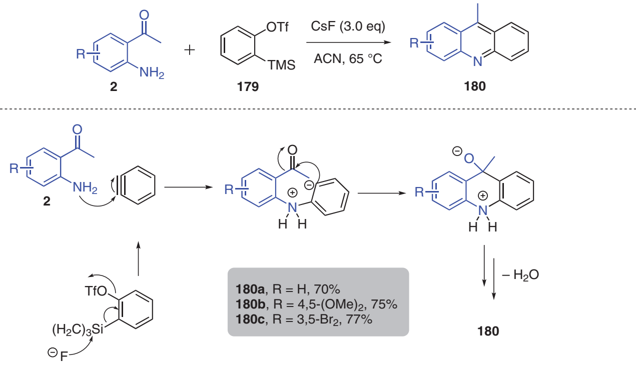
5.3 Pyrrolo[2,1-*a*]isoquinolines



Scheme 86 Synthesis of pyrrolo[2,1-*a*]isoquinolines **178** via molecular iodine mediated formal [2+1+1+1] cycloaddition
(8d) Zheng, *Chem. Commun.* **2018**, *54*, 11897

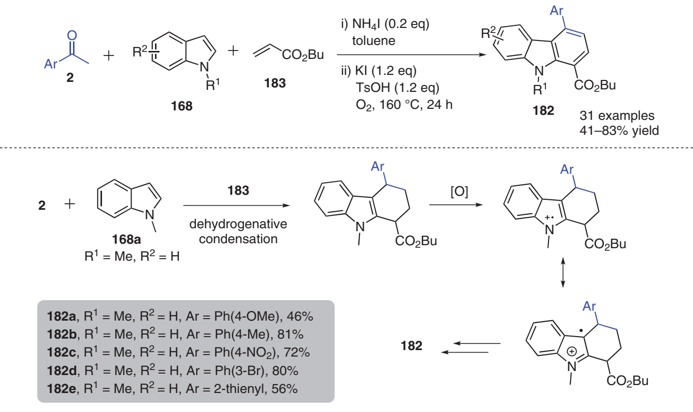
Figure 14 Synthesis of fused bi-heterocycles, part VII,[7o–q] and fused tri-heterocycles, part I[8a–d]

5.4. Acridines



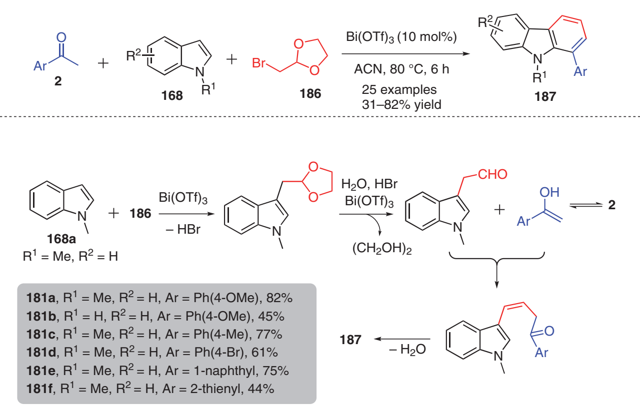
Scheme 87 Synthesis of acridines **180** via a [4+2] annulation

(8e) Rogness, *J. Org. Chem.* **2010**, *75*, 2289



Scheme 89 Synthesis of substituted carbazoles **182** via a one-pot synthesis

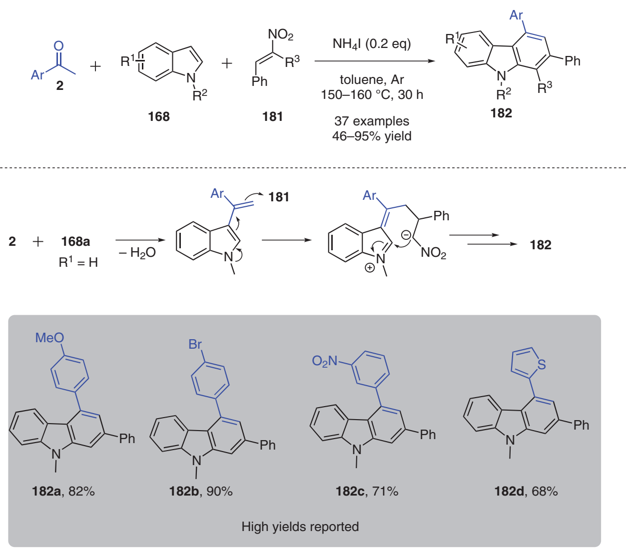
(8g) Chen, *J. Org. Chem.* **2017**, *82*, 2935



Scheme 91 Synthesis of carbazoles **187** catalyzed by bismuth(III) triflate via three-component reactions

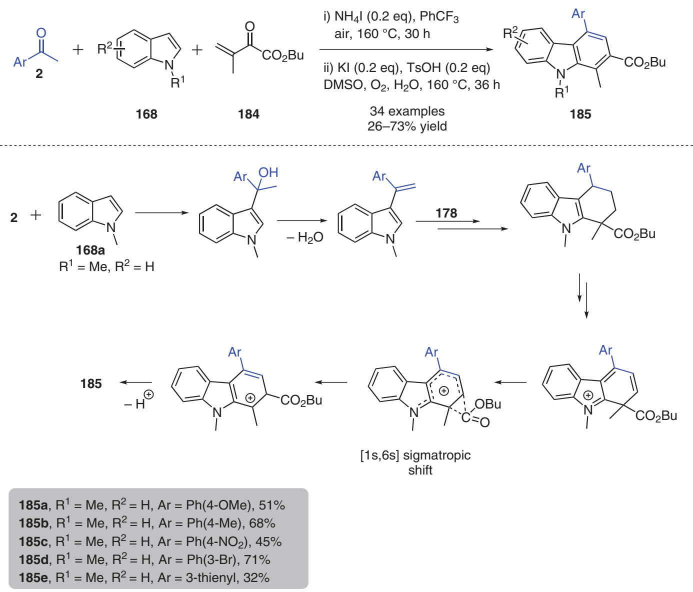
(8i) Gu, *Org. Lett.* **2018**, *20*, 4285

5.5. Carbazoles



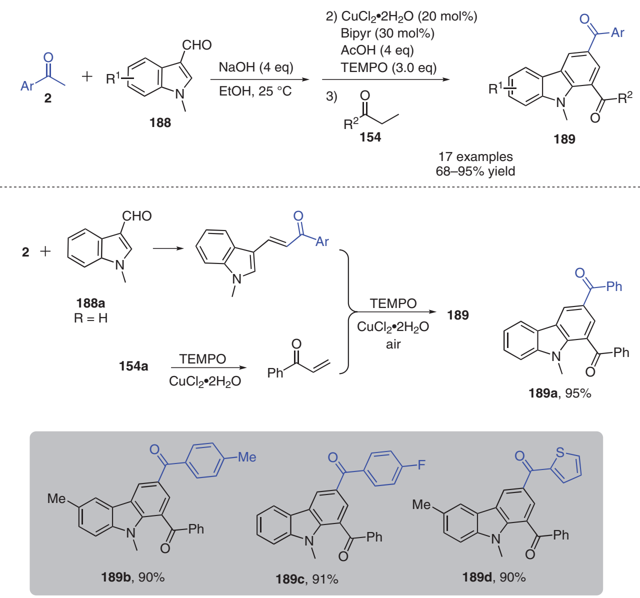
Scheme 88 Synthesis of substituted carbazoles **182** from indoles

(8f) Chen, *Org. Lett.* **2016**, *18*, 5384



Scheme 90 Synthesis of carbazoles **185** through a [1s,6s] sigmatropic shift

(8h) Chen, *J. Org. Chem.* **2019**, *84*, 3121

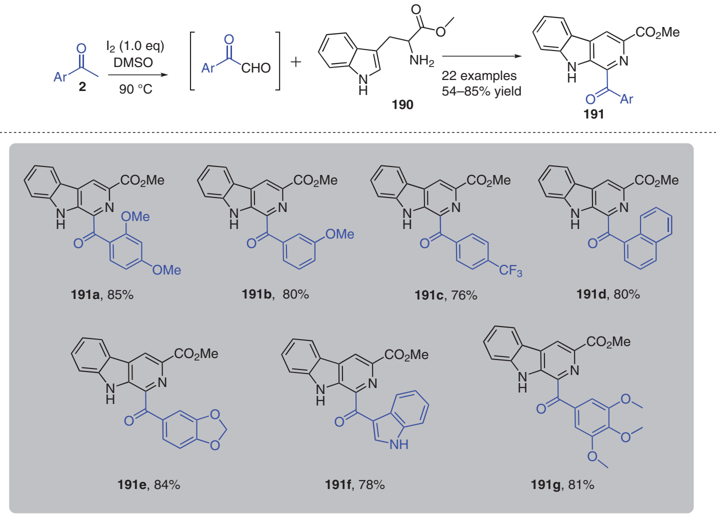


Scheme 92 Synthesis of carbazoles **189** by formal [3+1+2] benzannulation

(7f) Guo, *J. Org. Chem.* **2020**, *85*, 9117

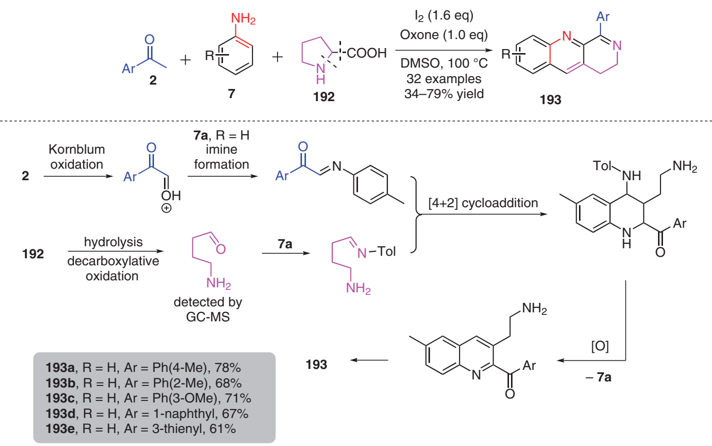
Figure 15 Synthesis of fused tri-heterocycles, part II[7f,8e–i]

5.6 β-Carbolines



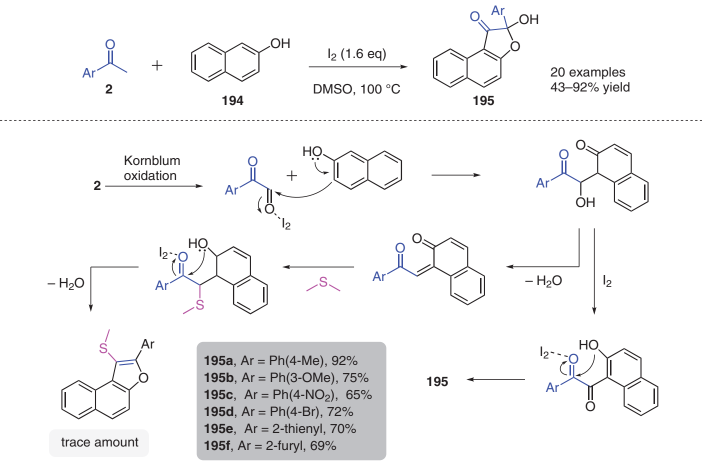
Scheme 93 Synthesis of β-carbolines **191** under Pictet–Spengler conditions
(8j) Battini, *RSC Adv.* **2014**, *4*, 26258

5.7 Dihydrobenzo[*b*][1,7]naphthyridines



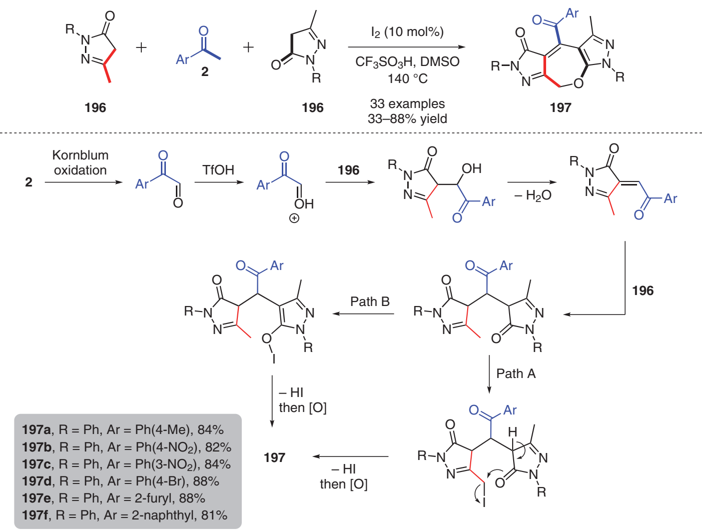
Scheme 94 Synthesis of 3,4-dihydrobenzo[*b*][1,7]naphthyridines **193** via consecutive decarboxylation/ring-opening/dicyclization
(8k) Geng, *Org. Lett.* **2019**, *21*, 4939

5.8 Naphtho[2,1-*b*]furan-1(2*H*)-ones



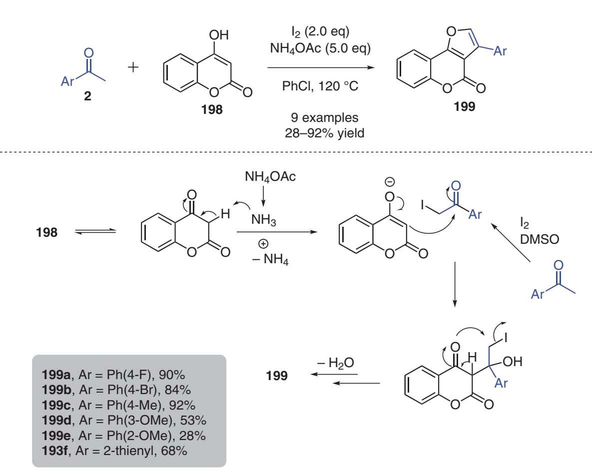
Scheme 95 Iodine-promoted synthesis of naphtho[2,1-*b*]furan-1(2*H*)-ones **195**
(8l) Gao, *Org. Lett.* **2014**, *16*, 1732

5.9 Dihydrooxepines



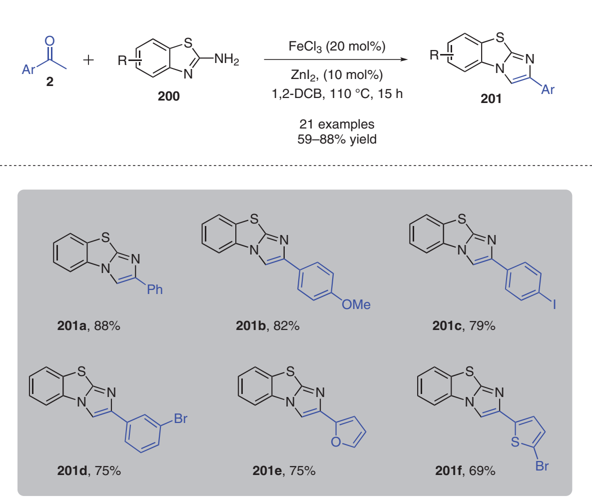
Scheme 96 Synthesis of 2,3-dihydrooxepines **197** by iodine-catalyzed oxidative coupling
(8m) Wu, *Org. Lett.* **2017**, *19*, 4584

5.10 Furocoumarins



Scheme 97 Metal-free synthesis of furocoumarins **199**
(8n) Pham, *Eur. J. Org. Chem.* **2018**, 4431

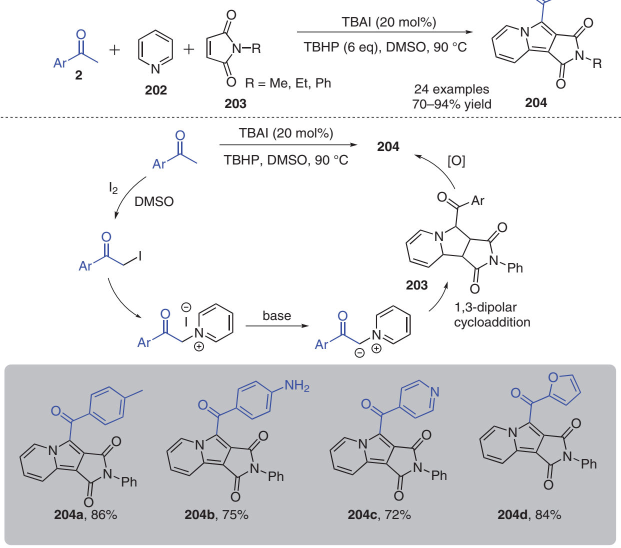
5.11 Benzo[*d*]imidazo[2,1-*b*]thiazoles



Scheme 98 $FeCl_3/ZnI_2$-catalyzed synthesis of benzo[*d*]imidazo[2,1-*b*]thiazoles **201**
(8o) Mishra, *Org. Lett.* **2014**, *16*, 6084

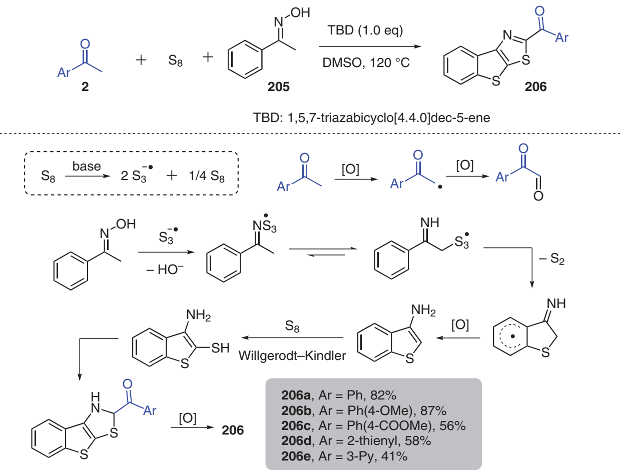
Figure 16 Synthesis of fused tri-heterocycles, part III[8j–o]

5.12 Annulated indolizines

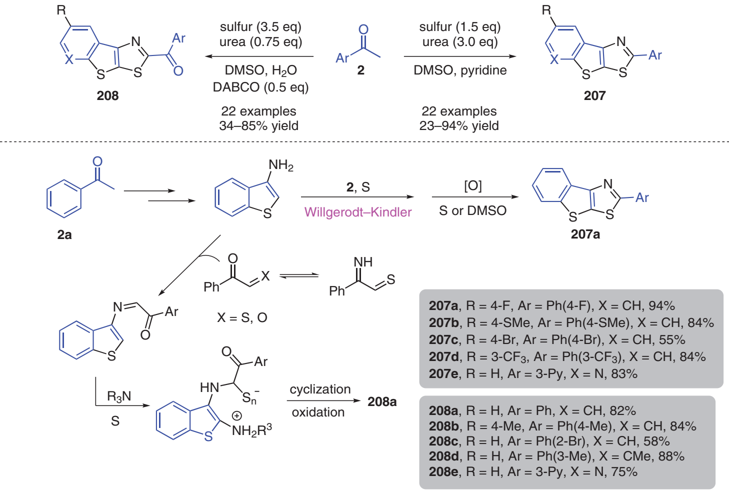


Scheme 99 Synthesis of annulated indolizines **204** via [3+2] cycloaddition
(8p) Zhang, *New J. Chem.* **2019**, *43*, 17000

5.13 Thienothiazoles

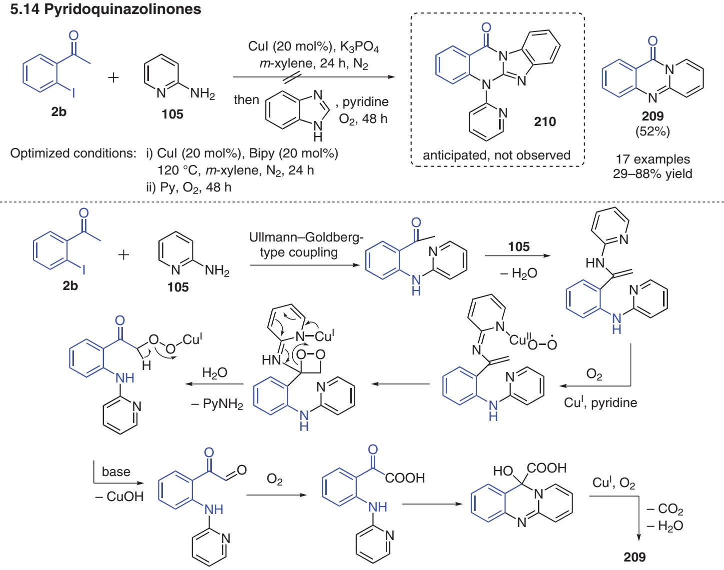


Scheme 100 Synthesis of 2-aroylthienothiazoles **206** via C–H/N–O bond functionalization of oximes
(8q) Zhou, *Org. Lett.* **2019**, *21*, 9976



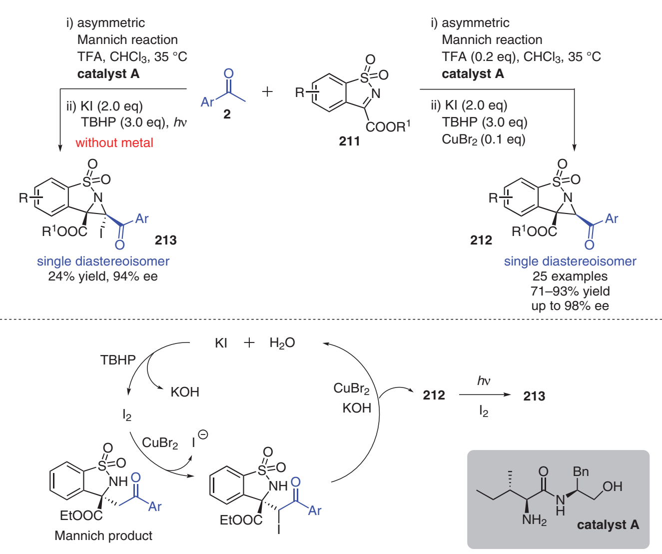
Scheme 101 Divergent synthesis of thienothiazoles **207**, **208**
(8r) Pham, *Org. Lett.* **2019**, *21*, 8795

5.14 Pyridoquinazolinones



Scheme 102 Synthesis of pyridoquinazolinones **209** via oxidative C-C bond cleavage
(8s) Brendel, *J. Org. Chem.* **2020**, *85*, 8102

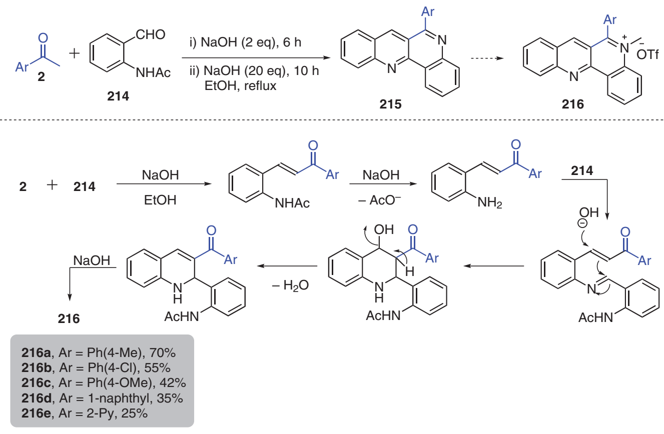
5.15 Aziridines



Scheme 103 A one-pot approach to multisubstituted, fused aziridines **212**, **213**
(8t) Zhang, *J. Org. Chem.* **2017**, *82*, 2399

6 Fused tetra-heterocycles

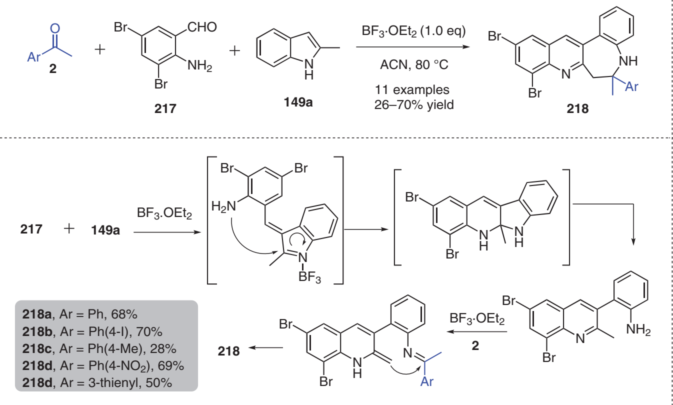
6.1 Dibenzo[*b*,*h*][1,6]naphthyridines



Scheme 104 One-pot synthesis of dibenzo[*b*,*h*][1,6]naphthyridines **216**
(9a) Okuma, *Chem. Commun.* **2014**, *50*, 15525

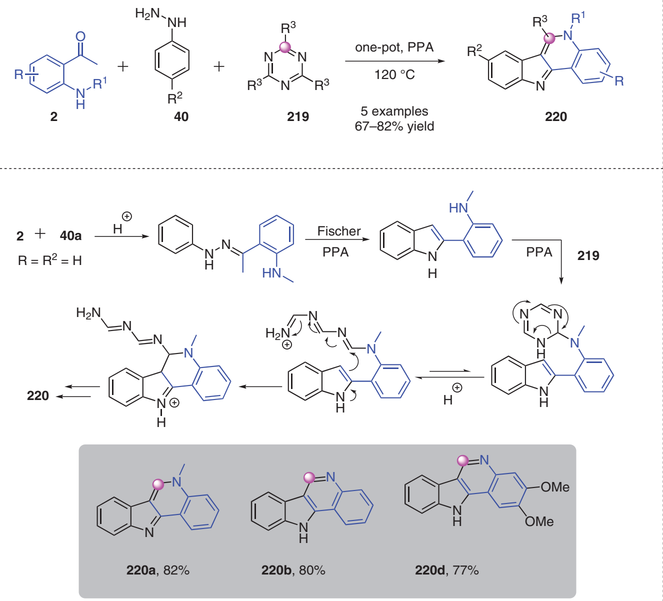
Figure 17 Synthesis of fused tri-heterocycles, part IV,[8p–t] and fused polyheterocycles, part I[9a]

6.2 Quinoline-fused 1-benzazepines



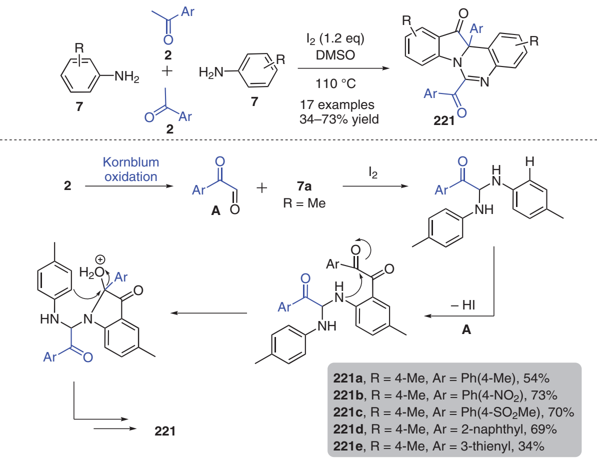
Scheme 105 Synthesis of quinoline-fused 1-benzazepines **218** (9b) Min, *Org. Lett.* **2016**, *18*, 364

6.3 Isocryptolepines



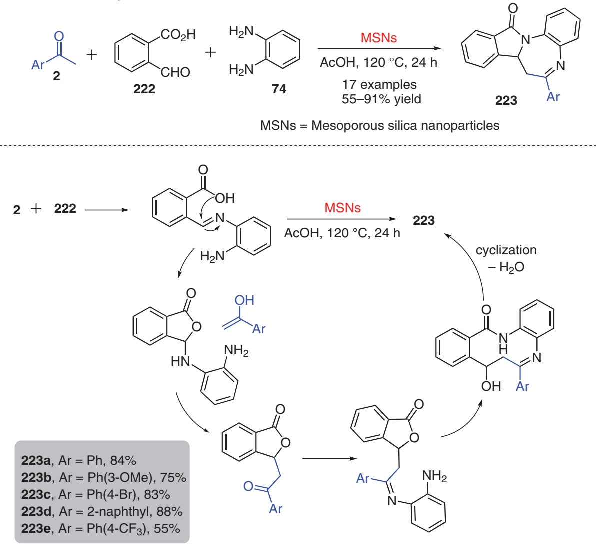
Scheme 106 Synthesis of isocryptolepine analogues **220** by a multicomponent approach (9c) Aksenov, *J. Org. Chem.* **2017**, *82*, 3011

6.4 Fused oxindoles



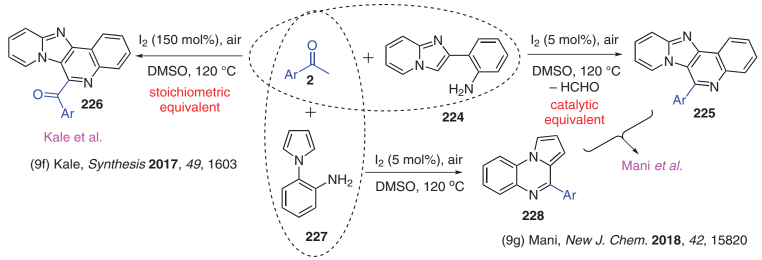
Scheme 107 Iodine-promoted synthesis of 1,2-fused oxindoles **221** (9d) Zhang, *Org. Lett.* **2017**, *19*, 408

6.5 Benzodiazepine-fused isoindolinones



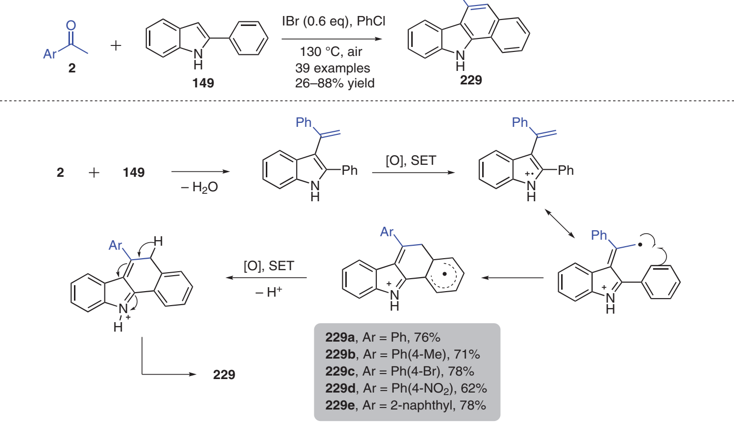
Scheme 108 Synthesis of tetracyclic benzodiazepine-fused isoindolinones **223** (9e) Yuan, *Chem. Commun.* **2020**, *56*, 11461

6.6 Pyrido-fused imidazo[4,5-*c*]quinolines



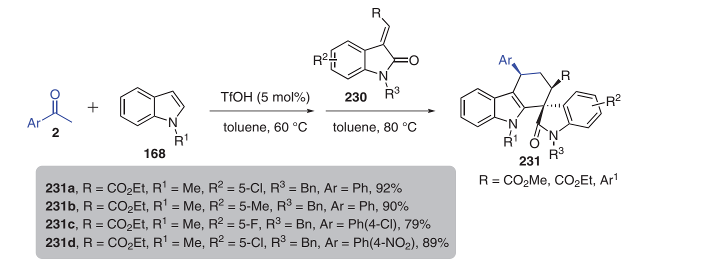
Scheme 109 Synthesis of pyrido-fused imidazo[4,5-*c*]quinolines **225**, **226** and pyrrolo[1,2-*a*]quinoxalines **227**

6.7 Benzo[*a*]carbazoles



Scheme 110 Synthesis of benzo[*a*]carbazoles **229** (9h) Ni, *Org. Lett.* **2019**, *21*, 3687

6.8 Tetrahydrospiro[carbazole-1,3'-indoline]s



Scheme 111 Synthesis of polysubstituted tetrahydrospiro[carbazole-1,3'-indoline]s **231** (9i) Yang, *J. Org. Chem.* **2017**, *82*, 13277

Figure 18 Synthesis of fused polyheterocycles, part II[9b–i]

Conflict of Interest

The authors declare no conflict of interest.

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References

(1) (a) Buskes, M. J.; Blanco, M. J. *Molecules* **2020**, *25*, 3493. (b) Zhang, T. Y. *The Evolving Landscape of Heterocycles in Drugs and Drug Candidates*, In *Advances in Heterocyclic Chemistry, Vol. 121*; Scriven, E. F. V.; Ramsden, C. A., Ed.; Academic Press: Cambridge, **2017**, Chap. 1, 1. (c) Khan, I.; Zaib, S.; Ibrar, A. *Org. Chem. Front.* **2020**, *7*, 3734. (d) Lasso, J. D.; Castillo-Pazos, D. J.; Li, C. J. *Chem. Soc. Rev.* **2021**, *50*, 10955. (e) Yasui, O.; Ishihara, K. *Science* **2010**, *328*, 1376. (f) Yusubov, M. S.; Zhdankin, V. V. *Resour.-Effic. Technol.* **2015**, *1*, 49. (g) Renault, O.; Dallemagne, P.; Rault, S. *Org. Prep. Proced. Int.* **1999**, *31*, 324. (h) Garrido, F.; Raeppel, S.; Mann, A.; Lautens, M. *Tetrahedron Lett.* **2001**, *42*, 265. (i) Ramgren, S. D.; Garg, N. K. *Org. Lett.* **2014**, *16*, 824. (j) Rajai-Daryasarei, S.; Gohari, M. H.; Mohammadi, N. *New J. Chem.* **2021**, *45*, 20486.

(2) (a) Das, P.; Ray, S.; Mukhopadhyay, C. *Org. Lett.* **2013**, *15*, 5622. (b) Wu, X.; Zhao, P.; Geng, X.; Wang, C.; Wu, Y.-d.; Wu, A.-x. *Org. Lett.* **2018**, *20*, 688. (c) Xu, H.; Wang, F.-J.; Xin, M.; Zhang, Z. *Eur. J. Org. Chem.* **2016**, 925. (d) Wu, J.; Chen, X.; Xie, Y.; Guo, Y.; Zhang, Q.; Deng, G.-J. *J. Org. Chem.* **2017**, *82*, 5743. (e) Ghosh, M.; Mishra, S.; Hajra, A. *J. Org. Chem.* **2015**, *80*, 5364. (f) Manna, S.; Antonchick, A. P. *Org. Lett.* **2015**, *17*, 4300. (g) Wang, M.; Xiang, J.-C.; Cheng, Y.; Wu, Y.-D.; Wu, A.-X. *Org. Lett.* **2016**, *18*, 524. (h) Cai, Z.-J.; Wang, S.-Y.; Ji, S.-J. *Org. Lett.* **2012**, *14*, 6068. (i) Liu, C.-K.; Yang, Z.; Zeng, Y.; Guo, K.; Fang, Z.; Li, B. *Org. Chem. Front.* **2017**, *4*, 1508. (j) Zhang, J.; Gao, Q.; Wu, X.; Geng, X.; Wu, Y.-D.; Wu, A. *Org. Lett.* **2016**, *18*, 1686. (k) de Toledo, I.; Grigolo, T. A.; Bennett, J. M.; Elkins, J. M.; Pilli, R. A. *J. Org. Chem.* **2019**, *84*, 14187. (l) Geng, X.; Wang, C.; Huang, C.; Bao, Y.; Zhao, P.; Zhou, Y.; Wu, Y.-D.; Feng, L.-l.; Wu, A.-X. *Org. Lett.* **2020**, *22*, 140. (m) Aegurla, B.; Peddinti, R. K. *Org. Biomol. Chem.* **2017**, *15*, 9643. (n) Whitt, J.; Duke, C.; Ali, M. A.; Chambers, S. A.; Khan, M. M. K.; Gilmore, D.; Alam, M. A. *ACS Omega* **2019**, *4*, 14284. (o) Fang, Z.; Yin, H.; Lin, L.; Wen, S.; Xie, L.; Huang, Y.; Weng, Z. *J. Org. Chem.* **2020**, *85*, 8714. (p) Gao, Q.; Liu, S.; Wu, X.; Zhang, J.; Wu, A. *Org. Lett.* **2015**, *17*, 2960. (q) Wu, X.; Geng, X.; Zhao, P.; Zhang, J.; Wu, Y.-d.; Wu, A.-x. *Chem. Commun.* **2017**, *53*, 3438. (r) Xue, W.-J.; Li, Q.; Zhu, Y.-P.; Wang, J.-G.; Wu, A.-X. *Chem. Commun.* **2012**, *48*, 3485. (s) Dai, P.; Tan, X.; Luo, Q.; Yu, X.; Zhang, S.; Liu, F.; Zhang, W.-H. *Org. Lett.* **2019**, *21*, 5096. (t) Gu, J.; Fang, Z.; Yang, Z.; Li, X.; Zhu, N.; Wan, L.; Wei, P.; Guo, K. *RSC Adv.* **2016**, *6*, 89073. (u) Verbelen, B.; Dehaen, W. *Org. Lett.* **2016**, *18*, 6412. (v) Liu, Y.; Nie, G.; Zhou, Z.; Jia, L.; Chen, Y. *J. Org. Chem.* **2017**, *82*, 9198. (w) Bonache, M. A.; Moreno-Fernández, S.; Miguel, M.; Sabater-Muñoz, B.; González-Muñiz, R. *ACS Comb. Sci.* **2018**, *20*, 694. (x) Gao, M.; Yang, Y.; Wu, Y.-D.; Deng, C.; Shu, W.-M.; Zhang, D.-X.; Cao, L.-P.; She, N.-F.; Wu, A.-X. *Org. Lett.* **2010**, *12*, 4026. (y) Sribalan, R.; Sangili, A.; Banuppriya, G.; Padmini, V. *New J. Chem.* **2017**, *41*, 3414. (z) Sadeghi, M.; Safari, J.; Zarnegar, Z. *RSC Adv.* **2016**, *6*, 64749.

(3) (a) Yin, G.; Liu, Q.; Ma, J.; She, N. *Green Chem.* **2012**, *14*, 1796. (b) Shabalin, D. A.; Dvorko, M. Y.; Schmidt, E. Y.; Trofimov, B. A. *Org. Biomol. Chem.* **2021**, *19*, 2703. (c) Huang, H.; Ji, X.; Wu, W.; Huang, L.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 3774. (d) Xi, L.-Y.; Zhang, R.-Y.; Liang, S.; Chen, S.-Y.; Yu, X.-Q. *Org. Lett.* **2014**, *16*, 5269. (e) Sharma, R.; Patel, N.; Vishwakarma, R. A.; Bharatam, P. V.; Bharate, S. B. *Chem. Commun.* **2016**, *52*, 1009. (f) Xiang, J.-C.; Wang, M.; Cheng, Y.; Wu, A.-X. *Org. Lett.* **2016**, *18*, 24. (g) Wu, X.; Zhang, J.; Liu, S.; Gao, Q.; Wu, A. *Adv. Synth. Catal.* **2016**, *358*, 218. (h) Su, L.; Sun, K.; Pan, N.; Liu, L.; Sun, M.; Dong, J.; Zhou, Y.; Yin, S.-F. *Org. Lett.* **2018**, *20*, 3399. (i) Jadhav, S. D.; Singh, A. *Org. Lett.* **2017**, *19*, 5673. (j) Tiwari, A. R.; Nath, S. R.; Joshi, K. A.; Bhanage, B. M. *J. Org. Chem.* **2017**, *82*, 13239. (k) Zhao, P.; Zhou, Y.; Yu, X.-X.; Huang, C.; Wu, Y.-D.; Yin, G.; Wu, A.-X. *Org. Lett.* **2020**, *22*, 8528. (l) Viswanadham, K. K. D. R.; Prathap Reddy, M.; Sathyanarayana, P.; Ravi, O.; Kant, R.; Bathula, S. R. *Chem. Commun.* **2014**, *50*, 13517. (m) Lim, S.-G.; Lee, J. H.; Moon, C. W.; Hong, J.-B.; Jun, C.-H. *Org. Lett.* **2003**, *5*, 2759. (n) Pilgrim, B. S.; Gatland, A. E.; McTernan, C. T.; Procopiou, P. A.; Donohoe, T. J. *Org. Lett.* **2013**, *15*, 6190.

(4) (a) Gutiérrez, R. U.; Correa, H. C.; Bautista, R.; Vargas, J. L.; Jerezano, A. V.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **2013**, *78*, 9614. (b) Gao, Q.; Liu, S.; Wu, X.; Wu, A. *Org. Lett.* **2014**, *16*, 4582. (c) Gao, Q.; Liu, S.; Wu, X.; Zhang, J.; Wu, A. *J. Org. Chem.* **2015**, *80*, 5984. (d) Wang, R.; Fan, H.; Zhao, W.; Li, F. *Org. Lett.* **2016**, *18*, 3558. (e) Chakraborty, G.; Sikari, R.; Das, S.; Mondal, R.; Sinha, S.; Banerjee, S.; Paul, N. D. *J. Org. Chem.* **2019**, *84*, 2626. (f) Das, S.; Sinha, S.; Samanta, D.; Mondal, R.; Chakraborty, G.; Brandaõ, P.; Paul, N. D. *J. Org. Chem.* **2019**, *84*, 10160. (g) Wu, X.; Geng, X.; Zhao, P.; Zhang, J.; Gong, X.; Wu, Y.-d.; Wu, A.-x. *Org. Lett.* **2017**, *19*, 1550. (h) Wakade, S. B.; Tiwari, D. K.; Ganesh, P. S. K. P.; Phanindrudu, M.; Likhar, P. R.; Tiwari, D. K. *Org. Lett.* **2017**, *19*, 4948. (i) Geng, X.; Wu, X.; Zhao, P.; Zhang, J.; Wu, Y.-D.; Wu, A.-X. *Org. Lett.* **2017**, *19*, 4179. (j) Zhao, P.; Wu, X.; Zhou, Y.; Geng, X.; Wang, C.; Wu, Y.-d.; Wu, A.-X. *Org. Lett.* **2019**, *21*, 2708. (k) Aksenov, A. V.; Smirnov, A. N.; Aksenov, N. A.; Aksenova, I. V.; Matheny, J. P.; Rubin, M. *RSC Adv.* **2015**, *5*, 8647. (l) Wu, J.; Zhou, Y.; Wu, T.; Zhou, Y.; Chiang, C.-W.; Lei, A. *Org. Lett.* **2017**, *19*, 6432. (m) Liao, Y.; Qi, H.; Chen, S.; Jiang, P.; Zhou, W.; Deng, G.-J. *Org. Lett.* **2012**, *14*, 6004. (n) Xue, W.-J.; Guo, Y.-Q.; Gao, F.-F.; Li, H.-Z.; Wu, A.-X. *Org. Lett.* **2013**, *15*, 890. (o) Gao, Q.; Wu, X.; Jia, F.; Liu, M.; Zhu, Y.; Cai, Q.; Wu, A. *J. Org. Chem.* **2013**, *78*, 2792. (p) Nguyen, T. B.; Pasturaud, K.; Ermolenko, L.; Al-Mourabit, A. *Org. Lett.* **2015**, *17*, 2562. (q) Huynh, T. V.; Doan, K. V.; Luong, N. T. K.; Nguyen, D. T. P.; Doan, S. H.; Nguyen, T. T.; Phan, N. T. S. *RSC Adv.* **2020**, *10*, 18423.

(5) (a) Le, Z.-G.; Xie, Z.-B.; Xu, J.-P. *Molecules* **2012**, *17*, 13368. (b) Bagdi, A. K.; Rahman, M.; Santra, S.; Majee, A.; Hajra, A. *Adv. Synth. Catal.* **2013**, *355*, 1741. (c) Stasyuk, A. J.; Banasiewicz, M.; Cyrański, M. K.; Gryko, D. T. *J. Org. Chem.* **2012**, *77*, 5552. (d) Mohan, D. C.; Donthiri, R. R.; Rao, S. N.; Adimurthy, S. *Adv. Synth. Catal.* **2013**, *355*, 2217. (e) Zhang, Y.; Chen, Z.; Wu, W.; Zhang, Y.; Su, W. *J. Org. Chem.* **2013**, *78*, 12494. (f) Cai, Z.-J.; Wang, S.-Y.; Ji, S.-J. *Adv. Synth. Catal.* **2013**, *355*, 2686. (g) Wang, F.-J.; Xu, H.; Xin, M.; Zhang, Z. *Mol. Diversity* **2016**, *20*, 659. (h) Kumar, G. S.; Ragini, S. P.; Kumar, A. S.; Meshram, H. M. *RSC Adv.* **2015**, *5*, 51576. (i) Ge, W.; Zhu, X.; Wei, Y. *Eur. J. Org. Chem.* **2013**, 6015. (j) Meng, X.; Yu, C.; Chen, G.; Zhao, P. *Catal. Sci. Technol.* **2015**, *5*, 372. (k) Liu, S.; Xi, H.; Zhang, J.; Wu, X.; Gao, Q.; Wu, A. *Org. Biomol. Chem.* **2015**, *13*, 8807. (l) Wu, Y.-D.; Geng, X.; Gao, Q.; Zhang, J.; Wu, X.; Wu, A.-X. *Org. Chem. Front.* **2016**, *3*, 1430. (m) Mukhopadhyay, S.; Dighe, S. U.; Kolle, S.; Shukla, P. K.; Batra, S. *Eur. J. Org. Chem.* **2016**, 3836. (n) Udavant, R. N.; Yadav, A. R.; Shinde, S. S. *Eur. J. Org. Chem.* **2018**, 3432. (o) Okai, H.; Tanimoto, K.; Ohkado, R.; Iida, H. *Org. Lett.* **2020**, *22*, 8002. (p) Zhu, Y.-p.; Fei, Z.; Liu, M.-c.; Jia, F.-c.; Wu, A.-x. *Org. Lett.* **2013**, *15*, 378. (q) Mohammed, S.; Vishwakarma, R. A.; Bharate, S. B. *J. Org. Chem.* **2015**, *80*, 6915.

(6) (a) Ravi, O.; Shaikh, A.; Upare, A.; Singarapu, K. K.; Bathula, S. R. *J. Org. Chem.* **2017**, *82*, 4422. (b) Xu, C.; Yin, G.; Jia, F.-C.; Wu, Y.-D.; Wu, A.-X. *Org. Lett.* **2021**, *23*, 2559. (c) Mamedov, V. A.; Zhukova, N. A.; Beschastnova, T. N.; Syakaev, V. V.; Krivolapov, D. B.; Mironova, E. V.; Zamaletdinova, A. I.; Rizvanov, I. K.; Latypov, S. K. *J. Org. Chem.* **2015**, *80*, 1375. (d) Nguyen, T. B.; Retailleau, P. *Org. Lett.* **2017**, *19*, 3887. (e) Nguyen, L. A.; Nguyen, T. T. T.; Ngo, Q. A.; Nguyen, T. B. *Org. Biomol. Chem.* **2021**, *19*, 6015. (f) Ilangovan, A.; Satish, G. *Org. Lett.* **2013**, *15*, 5726. (g) Ilangovan, A.; Satish, G. *J. Org. Chem.* **2014**, *79*, 4984. (h) Gao, F.-F.; Xue, W.-J.; Wang, J.-G.; Wu, A.-X. *Tetrahedron* **2014**, *70*, 4331. (i) Huo, J.; Yang, Y.;

Wang, C. *Org. Lett.* **2021**, *23*, 3384. (j) Verma, A.; Kumar, S. *Org. Lett.* **2016**, *18*, 4388. (k) Wang, M.; Tang, B.-C.; Ma, J.-T.; Wang, Z.-X.; Xiang, J.-C.; Wu, Y.-D.; Wang, J.-G.; Wu, A.-X. *Org. Biomol. Chem.* **2019**, *17*, 1535. (l) Mohan, D. C.; Ravi, C.; Pappula, V.; Adimurthy, S. *J. Org. Chem.* **2015**, *80*, 6846. (m) Wang, W.; Han, J.; Sun, J.; Liu, Y. *J. Org. Chem.* **2017**, *82*, 2835. (n) Wu, X.; Zhao, P.; Geng, X.; Zhang, J.; Gong, X.; Wu, Y.-d.; Wu, A.-x. *Org. Lett.* **2017**, *19*, 3319. (o) Rossler, M. D.; Hartgerink, C. T.; Zerull, E. E.; Boss, B. L.; Frndak, A. K.; Mason, M. M.; Nickerson, L. A.; Romero, E. O.; Van de Burg, J. E.; Staples, R. J.; Anderson, C. E. *Org. Lett.* **2019**, *21*, 5591.

(7) (a) Zhang, Y.; Wang, D.; Cui, S. *Org. Lett.* **2015**, *17*, 2494. (b) Fischer, E.; Jourdan, F. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241. (c) Kissman, H. M.; Farnsworth, D. W.; Witkop, B. *J. Am. Chem. Soc.* **1952**, *74*, 3948. (d) Lu, X.-M.; Cai, Z.-J.; Li, J.; Wang, S.-Y.; Ji, S.-J. *RSC Adv.* **2015**, *5*, 51501. (e) Geng, X.; Wu, X.; Wang, C.; Zhao, P.; Zhou, Y.; Sun, X.; Wang, L.-J.; Guan, W.-J.; Wu, Y.-D.; Wu, A.-X. *Chem. Commun.* **2018**, *54*, 12730. (f) Guo, T.; Han, L.; Wang, T.; Lei, L.; Zhang, J.; Xu, D. *J. Org. Chem.* **2020**, *85*, 9117. (g) Schmidt, E. Y.; Semenova, N. V.; Tatarinova, I. V.; Ushakov, I. A.; Vashchenko, A. V.; Trofimov, B. A. *Org. Lett.* **2019**, *21*, 4275. (h) Chung, H.; Kim, J.; González-Montiel, G. A.; Ha-Yeon Cheong, P.; Lee, H. G. *Org. Lett.* **2021**, *23*, 1096. (i) Neochoritis, C. G.; Tsoleridis, C. A.; Stephanidou-Stephanatou, J.; Kontogiorgis, C. A.; Hadjipavlou-Litina, D. J. *J. Med. Chem.* **2010**, *53*, 8409. (j) Geng, X.; Wang, C.; Huang, C.; Zhao, P.; Zhou, Y.; Wu, Y.-D.; Wu, A.-X. *Org. Lett.* **2019**, *21*, 7504. (k) Lin, Y.-m.; Lu, G.-p.; Wang, R.-k.; Yi, W.-b. *Org. Lett.* **2016**, *18*, 6424. (l) Huang, X.; Rong, N.; Li, P.; Shen, G.; Li, Q.; Xin, N.; Cui, C.; Cui, J.; Yang, B.; Li, D.; Zhao, C.; Dou, J.; Wang, B. *Org. Lett.* **2018**, *20*, 3332. (m) Jiang, J.; Tuo, X.; Fu, Z.; Huang, H.; Deng, G.-J. *Org. Biomol. Chem.* **2020**, *18*, 3234. (n) Marpna, I. D.; Shangpliang, O. R.; Wanniang, K.; Kshiar, B.; Lipon, T. M.; Laloo, B. M.; Myrboh, B. *ACS Omega* **2021**, *6*, 14518. (o) Balaguez, R. A.; Betin, E. S.; Barcellos, T.; Lenardão, E. J.; Alves, D.; Schumacher, R. F. *New J. Chem.* **2017**, *41*, 1483. (p) Ni, P.; Tan, J.; Zhao, W.; Huang, H.; Xiao, F.; Deng, G.-J. *Org. Lett.* **2019**, *21*, 3518. (q) Mukhopadhyay, C.; Das, P.; Butcher, R. J. *Org. Lett.* **2011**, *13*, 4664.

(8) (a) Yao, X.; Shao, Y.; Hu, M.; Xia, Y.; Cheng, T.; Chen, J. *Org. Lett.* **2019**, *21*, 7697. (b) Ramig, K.; Alli, S.; Cheng, M.; Leung, R.; Razi, R.; Washington, M.; Kudzma, L. V. *Synlett* **2007**, 2868. (c) Manjappa, K. B.; Peng, Y.-T.; Liou, T.-J.; Yang, D.-Y. *RSC Adv.* **2017**, *7*, 45269. (d) Zheng, K.; Zhuang, S.; Shu, W.; Wu, Y.; Yang, C.; Wu, A. *Chem. Commun.* **2018**, *54*, 11897. (e) Rogness, D. C.; Larock, R. C. *J. Org. Chem.* **2010**, *75*, 2289. (f) Chen, S.; Li, Y.; Ni, P.; Huang, H.; Deng, G.-J. *Org. Lett.* **2016**, *18*, 5384. (g) Chen, S.; Li, Y.; Ni, P.; Yang, B.; Huang, H.; Deng, G.-J. *J. Org. Chem.* **2017**, *82*, 2935. (h) Chen, S.; Jiang, P.; Wang, P.; Pei, Y.; Huang, H.; Xiao, F.; Deng, G.-J. *J. Org. Chem.* **2019**, *84*, 3121. (i) Gu, Y.; Huang, W.; Chen, S.; Wang, X. *Org. Lett.* **2018**, *20*, 4285. (j) Battini, N.; Padala, A. K.; Mupparapu, N.; Vishwakarma, R. A.; Ahmed, Q. N. *RSC Adv.* **2014**, *4*, 26258. (k) Geng, X.; Wang, C.; Zhao, P.; Zhou, Y.; Wu, Y.-D.; Wu, A.-X. *Org. Lett.* **2019**, *21*, 4939. (l) Gao, Q.; Wu, X.; Liu, S.; Wu, A. *Org. Lett.* **2014**, *16*, 1732. (m) Wu, X.; Geng, X.; Zhao, P.; Wu, Y.-d.; Wu, A.-x. *Org. Lett.* **2017**, *19*, 4584. (n) Pham, P. H.; Nguyen, Q. T. D.; Tran, N. K. Q.; Nguyen, V. H. H.; Doan, S. H.; Ha, H. Q.; Truong, T.; Phan, N. T. S. *Eur. J. Org. Chem.* **2018**, 4431. (o) Mishra, S.; Monir, K.; Mitra, S.; Hajra, A. *Org. Lett.* **2014**, *16*, 6084. (p) Zhang, Q.; Wang, B.; Ma, H.; Ablajan, K. *New J. Chem.* **2019**, *43*, 17000. (q) Zhou, P.; Huang, Y.; Wu, W.; Zhou, J.; Yu, W.; Jiang, H. *Org. Lett.* **2019**, *21*, 9976. (r) Pham, P. H.; Nguyen, K. X.; Pham, H. T. B.; Nguyen, T. T.; Phan, N. T. S. *Org. Lett.* **2019**, *21*, 8795. (s) Brendel, M.; Sakhare, P. R.; Dahiya, G.; Subramanian, P.; Kaliappan, K. P. *J. Org. Chem.* **2020**, *85*, 8102. (t) Zhang, S.; Li, L.; Xin, L.; Liu, W.; Xu, K. *J. Org. Chem.* **2017**, *82*, 2399.

(9) (a) Okuma, K.; Koga, T.; Ozaki, S.; Suzuki, Y.; Horigami, K.; Nagahora, N.; Shioji, K.; Fukuda, M.; Deshimaru, M. *Chem. Commun.* **2014**, *50*, 15525. (b) Min, L.; Pan, B.; Gu, Y. *Org. Lett.* **2016**, *18*, 364. (c) Aksenov, A. V.; Aksenov, D. A.; Orazova, N. A.; Aksenov, N. A.; Griaznov, G. D.; De Carvalho, A.; Kiss, R.; Mathieu, V.; Kornienko, A.; Rubin, M. *J. Org. Chem.* **2017**, *82*, 3011. (d) Zhang, J.; Wu, X.; Gao, Q.; Geng, X.; Zhao, P.; Wu, Y.-D.; Wu, A. *Org. Lett.* **2017**, *19*, 408. (e) Yuan, S.; Yue, Y.-L.; Zhang, D.-Q.; Zhang, J.-Y.; Yu, B.; Liu, H.-M. *Chem. Commun.* **2020**, *56*, 11461. (f) Kale, A.; Bingi, C.; Ragi, N. C.; Sripadi, P.; Tadikamalla, P. R.; Atmakur, K. *Synthesis* **2017**, *49*, 1603. (g) Mani, G. S.; Rao, A. V. S.; Tangella, Y.; Sunkari, S.; Sultana, F.; Namballa, H. K.; Shankaraiah, N.; Kamal, A. *New. J. Chem.* **2018**, *42*, 15820. (h) Ni, P.; Tan, J.; Zhao, W.; Huang, H.; Xiao, F.; Deng, G.-J. *Org. Lett.* **2019**, *21*, 3687. (i) Yang, R.-Y.; Sun, J.; Tao, Y.; Sun, Q.; Yan, C.-G. *J. Org. Chem.* **2017**, *82*, 13277.