Chinese Journal of Catalysis 39 (2018) 1881–1889

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/chnjc

Article

Co(III)/Zn(II)-catalyzed dearomatization of indoles and coupling with carbenes from ene-yne ketones via intramolecular cyclopropanation

Na Li [a,b], Junbiao Chang [a,*], Lingheng Kong [c], Shuangjing Wang [a], Dandan Wang [a], Miao Cheng [a], Xingwei Li [a,c,#]

[a] *Henan Key Laboratory of Organic Functional Molecule and Drug Innovation, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang 453007, Henan, China*

[b] *School of Pharmacy, Xinxiang Medical University, Xinxiang 453003, Henan, China*

[c] *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, Liaoning, China*

ARTICLE INFO

Article history:
Received 21 June 2018
Accepted 26 July 2018
Published 5 December 2018

Keywords:
Co(III)/Zn(II) catalysis
Dearomatization
Cyclopropanation
Carbene
Indole

ABSTRACT

A straightforward and efficient protocol for dearomatizing indoles is described. The reaction, catalyzed by an inexpensive Co(III)/Zn(II) catalyst, starts from easily accessible *N*-pyrimidinyl indoles and ene-yne ketones. Mild reaction conditions, high diastereoselectivity, a broad substrate scope, effective functional group tolerance, and reasonable to remarkable yields were observed.

1. Introduction

Indoline skeletons have been considered as characteristic structures owing to their widespread use as key building blocks and chiral auxiliaries in asymmetric synthesis [1]. They are also widely present in alkaloids and other natural products with diverse biological activities [2–9], such as pentopril, which is a potent angiotensin enzyme inhibitor [3], strychnine, which is used as a pesticide [2], and lundurine A, which is effective for overcoming multidrug resistance in vincristine-resistant KB cells (Fig. 1) [10–12]. Chiral cyclopropanes are important motifs for the diverse functionality and reactivity provided by donor-acceptor substituents, which can be transformed into valuable synthetic intermediates via ring opening or ring expansion [13–20]. A hexacyclic ring system that includes a unique cyclopropyl ring fused to an indoline accompanied by three quaternary carbon stereocenters such as lundurines are attractive targets. Traditional methods to construct cyclopropane-fused indoline derivatives include transition-metal-mediated reactions [21–36], the classic Simmons-Smith reaction and so on [34–41]. However, highly efficient, environmentally friendly, and atom-economic methods

* Corresponding author. Tel: +86-411-84379089; E-mail: changjunbiao@zzu.edu.cn
# Corresponding author. Tel: +86-411-84379089; E-mail: xwli@dicp.ac.cn
This work was supported by the National Natural Science Foundation of China (21525208, 21472186) and the research fund from Henan Normal University (5101034011009).
DOI: 10.1016/S1872-2067(18)63154-7 | http://www.sciencedirect.com/science/journal/18722067 | Chin. J. Catal., Vol. 39, No. 12, December 2018

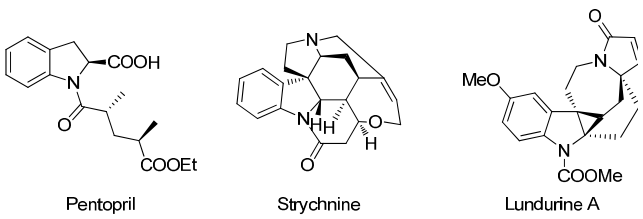
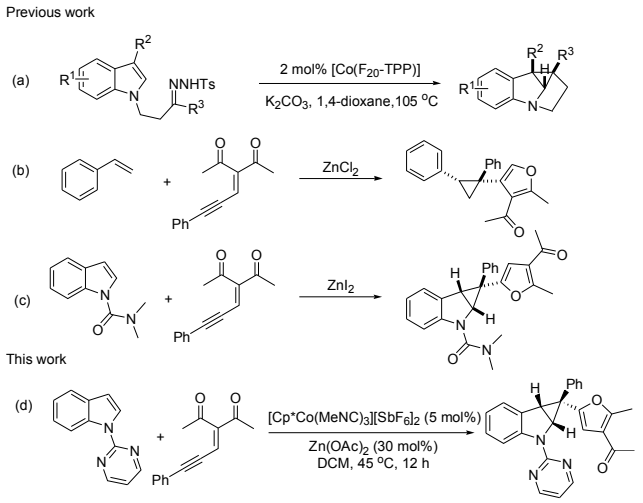


Fig. 1. Some examples of bioactive indolines.

for generating available carbenoids precursors in a catalytic fashion continue to be highly limited [42]. The catalytic generation of M-furylcarbenes derived from carbonyl ene-yne compounds and zinc salts were explored for its versatile character [43–48]. Che et al. [21] reported cobalt(II) porphyrin-catalyzed intramolecular cyclopropanation of *N*-alkyl indoles/pyrroles with alkyldiazomethanes generated in situ from hydrazones (Scheme 1(a)). Lopez et al. [47] reported the catalytic generation of zinc(II) furylcarbenes derived from carbonyl ene-yne compounds and zinc salts, as well as their reactivity in addition and insertion processes with styrene (Scheme 1(b)). Recently, while collating the data for the present article, Xu et al. [49] explored the access to similar products via ZnI_2-catalyzed cyclopropanation of indole with enynone. Notwithstanding the success, the investigation is limited to low functional group tolerance; certain *N*-substituent of indole failed to generate the desired product (Scheme 1(c)). As well-established and efficient catalysts for various organic transformations, Cp*Co(III) complexes have attracted increasing attention owing to their earth-abundance, cost-effectiveness, low toxicity, and unique catalytic reactivity [50–55]. However, the catalytic generation of efficient cyclopropanating intermediates from ene-yne ketone and Co(III)/Zn(II) remains largely underexplored. Herein, we report the intramolecular cyclopropanation of indoles with ene-yne ketones through zinc(II)/Co(III) furylcarbenes. A series of indolines bearing three-dimensional cyclic structures could be obtained with remarkable yields with high to very high diastereoselectivities.



Scheme 1. Cyclopropane reactions of olefins and indoles with metal carbenes.

2. Experimental

2.1. General

All the chemicals were obtained from commercial sources and were used as-received unless otherwise noted. All the reactions were carried out under N_2 atmosphere using standard Schlenk technique. The ^{1}H NMR spectra were recorded on a 400-MHz or 600-MHz NMR spectrometer. The ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz. The ^{19}F NMR spectra were recorded at 565 MHz. The chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane and were reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), dt (doublet of triplet), m (multiplet), br s (broad singlet), etc. The residual solvent signals were used as references, and the chemical shifts were converted to the TMS scale. High resolution mass spectra were obtained on an Agilent Q-TOF 6540 spectrometer. Column chromatography was performed on silica gel (300–400 mesh) using ethyl acetate (EA)/petroleum ether (PE).

Substrate 1v was synthesized according to a literature report [56]; the others were prepared following published procedures [57–59]. Compounds **2a**–**2m** were prepared according to a literature report [47].

2.2. General procedure for synthesizing compounds 3

N-pyrimidinylindole (0.2 mmol), ene-yne ketones (0.24 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol%), and $Zn(OAc)_2$ (30 mol%) were charged into a Schlenk tube; anhydrous CH_2Cl_2 (2 mL) was added to this mixture under N_2 atmosphere. The reaction mixture was stirred at 45 °C for 12 h. After being cooled to room temperature, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography using PE/EA to obtain the product.

2.3. Spectral data for products

3aa was obtained according to the general procedure, with 94% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, J = 4.7 Hz, 2H), 8.17 (d, J = 8.2 Hz, 1H), 7.43 (d, J = 7.3 Hz, 1H), 7.34 (m, 2H), 7.29–7.21 (m, 3H), 7.14 (t, J = 7.8 Hz, 1H), 6.94 (t, J = 7.4 Hz, 1H), 6.78 (t, J = 4.7 Hz, 1H), 5.75 (s, 1H), 5.20 (d, J = 6.5 Hz, 1H), 3.51 (d, J = 6.5 Hz, 1H), 2.15 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.8, 157.7, 147.8, 143.8, 142.0, 130.6, 128.7, 127.6, 126.7, 126.6, 124.8, 121.5 121.3, 115.6, 112.7, 111.1, 51.9, 35.9, 28.8, 27.2, 14.0. HRMS calculated for $C_{26}H_{22}N_3O_2^+$ (M + H)$^+$: 408.1707; observed: 408.408.1709.

3ba was obtained according to the general procedure, with 62% yield, dr = 15:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.8 Hz, 2H), 7.80 (d, J = 8.2 Hz, 1H), 7.37–7.31 (m, 2H), 7.29–7.22 (m, 3H), 7.09 (t, J = 8.2 Hz, 1H), 6.78 (t, J = 4.8 Hz, 1H), 6.52 (d, J = 8.2 Hz, 1H), 5.80 (s, 1H), 5.14 (d, J = 6.6 Hz, 1H), 3.91 (s, 3H), 3.62 (d, J = 6.6 Hz, 1H), 2.17 (s, 3H), 2.04 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.8, 157.7 (d, J = 7.4 Hz), 156.6, 148.1, 145.2, 142.1, 128.8, 128.6,

126.8, 126.5, 121.3, 118.5, 112.7, 110.9, 108.9, 104.4, 55.8, 52.3, 32.9, 28.8, 26.8, 14.1. HRMS calculated for $C_{27}H_{24}N_3O_3^+$ (M + H)$^+$: 438.1812; observed: 438.1819.

3ca was obtained according to the general procedure, with 92% yield, dr = 7:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 2H), 8.34 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 7.0 Hz, 1H), 7.47 (dd, J = 8.1, 2.0 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.23–7.18 (m, 1H), 7.14 (t, J = 8.0 Hz, 1H), 6.78 (t, J = 4.8 Hz, 1H), 5.63 (s, 1H), 5.12 (d, J = 6.4 Hz, 1H), 4.15 (d, J = 6.4 Hz, 1H), 3.95 (s, 3H), 2.03 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 167.1, 159.8, 157.6, 148.5, 144.9, 141.3, 132.9, 128.7, 128.2, 127.5, 127.0, 126.8, 122.8, 121.3, 119.5, 112.9, 110.2, 52.1, 51.8, 35.0, 28.8, 27.8, 14.0. HRMS calculated for $C_{28}H_{24}N_3O_4^+$ (M + H)$^+$: 466.1761; observed: 466.1767.

3da was obtained according to the general procedure, with 44% yield, dr = 5:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 4.7 Hz, 2H), 8.00 (d, J = 8.2 Hz, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.31 (d, J = 7.1 Hz, 2H), 7.29–7.24 (m, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.79 (t, J = 4.7 Hz, 1H), 6.76 (d, J = 7.5 Hz, 1H), 5.71 (s, 1H), 5.15 (d, J = 6.7 Hz, 1H), 3.47 (d, J = 6.7 Hz, 1H), 2.51 (s, 3H), 2.16 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.9, 157.7, 147.99 (s), 143.6, 142.1, 134.3, 129.5, 128.7, 127.7, 127.3, 126.6, 122.5, 121.3, 113.1, 112.6, 110.6, 51.9, 34.3, 28.8, 27.2, 18.8, 14.0. HRMS calculated for $C_{27}H_{24}N_3O_2^+$ (M + H)$^+$: 422.1863; observed: 422.1866.

3ea was obtained according to the general procedure, with 80% yield, dr = 16:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.8 Hz, 2H), 8.07 (d, J = 8.2 Hz, 1H), 7.44–7.33 (m, 4H), 7.31–7.25 (m, 1H), 7.07 (t, J = 8.1 Hz, 1H), 6.94 (d, J = 8.0, 1H), 6.85 (t, J = 4.8 Hz, 1H), 5.81 (s, 1H), 5.20 (d, J = 6.6 Hz, 1H), 3.66 (d, J = 6.6 Hz, 1H), 2.16 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.6, 157.9, 157.7, 147.9, 145.0, 141.3, 130.6, 129.2, 128.8, 128.7, 127.4, 126.9, 121.3, 113.8, 113, 110.7, 51.6, 33.9, 28.8, 27.2, 14.0. HRMS calculated for $C_{26}H_{21}ClN_3O_2^+$ (M + H)$^+$: 442.1317; observed: 442.1316.

3fa was obtained according to the general procedure, with 66% yield, dr = 11:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.8 Hz, 2H), 7.88 (d, J = 8.2 Hz, 1H), 7.33–7.25 (m, 4H), 7.24–7.16 (m, 1H), 7.02 (td, J = 8.3, 5.9 Hz, 1H), 6.78 (t, J = 4.8 Hz, 1H), 6.60 (t, J = 8.5 Hz, 1H), 5.76 (s, 1H), 5.15 (d, J = 6.6 Hz, 1H), 3.58 (d, J = 6.6 Hz, 1H), 2.10 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.1, 160.6, 159.6, 158.9, 157.9 157.7, 147.8, 146.1 (d, J = 7.9 Hz), 141.3, 129.1 (d, J = 8.1 Hz), 128.7, 127.2, 126.9, 121.3, 117.3 (d, J = 21.5 Hz), 113.1, 111.5, 110.8, 108.2 (d, J = 19.7 Hz), 52.1, 31.4, 28.8, 26.9, 14.0. ^{19}F NMR (565 MHz, $CDCl_3$) δ –121.76 (1F). HRMS calculated for $C_{26}H_{21}FN_3O_2^+$ (M + H)$^+$: 426.1612; observed: 426.1613.

3ga was obtained according to the general procedure, with 94% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, J = 4.7 Hz, 2H), 7.94 (dd, J = 8.2, 2.6 Hz, 1H), 7.24 (t, J = 7.7 Hz, 2H), 7.15 (dd, J = 14.7, 7.3 Hz, 4H), 6.85 (d, J = 8.2 Hz, 1H), 6.66 (t, J = 4.7 Hz, 1H), 5.67 (s, 1H), 5.07 (d, J = 6.5 Hz, 1H), 3.37 (d, J = 6.5 Hz, 1H), 2.23 (s, 3H), 2.08 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.8, 157.7 (d, J = 10.3 Hz), 147.9, 142.1 141.6, 131.0, 130.6, 128.6, 128.0, 126.7, 126.5, 125.4, 121.3, 115.4, 112.3, 111.0, 52.1, 35.9, 28.8, 27.5, 20.9, 14.0. HRMS calculated for $C_{27}H_{24}N_3O_2^+$ (M + H)$^+$: 422.1863; observed: 422.1866.

3ha was obtained according to the general procedure, with 84% yield, dr = 4:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 2H), 8.07 (d, J = 8.9 Hz, 1H), 7.35 (m, 2H), 7.29–7.22 (m, 4H), 7.04 (d, J = 2.7 Hz, 1H), 6.76 (t, J = 4.8 Hz, 1H), 6.70 (dd, J = 8.9, 2.7 Hz, 1H), 5.79 (s, 1H), 5.19 (d, J = 6.5 Hz, 1H), 3.80 (s, 3H), 3.49 (d, J = 6.5 Hz, 1H), 2.18 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.4, 158.0, 157.9, 157.4, 155.4, 140.2, 130.9, 130.2, 128.9, 128.7, 127.1, 125.2, 122.1, 120.4, 117.3, 115.8, 112.5, 108.3, 102.2, 55.7, 44.8, 29.2, 14.6. HRMS calculated for $C_{27}H_{24}N_3O_3^+$ (M + H)$^+$: 438.1812; observed: 438.1813.

3ia was obtained according to the general procedure, with 77% yield, dr = 9:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, J = 3.4 Hz, 2H), 8.11 (d, J = 5.1 Hz, 1H), 8.01 (s, 1H), 7.77 (d, J = 1.5 Hz, 1H), 7.34–7.02 (m, 5H), 6.76 (s, 1H), 5.68 (s, 1H), 5.11 (d, J = 6.5 Hz, 1H), 3.79 (s, 3H), 3.41 (d, J = 6.5 Hz, 1H), 2.04 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.8, 167.0, 159.5, 157.8, 147.6, 141.32 (s), 130.7, 130.1, 128.7, 127.1, 126.9, 126.2, 123.0, 121.3, 114.8, 113.6, 111.0, 52.1, 51.9, 35.0, 28.8, 27.1, 14.1. HRMS calculated for $C_{28}H_{24}N_3O_4^+$ (M + H)$^+$: 466.1761; observed: 466.1763.

3ja was obtained according to the general procedure, with 62% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 4.8 Hz, 2H), 8.06 (dd, J = 9.0, 4.8 Hz, 1H), 7.30–7.25 (m, 2H), 7.26–7.15 (m, 3H), 7.08 (dd, J = 8.1, 2.7 Hz, 1H), 6.76 (ddd, J = 9.6, 8.2, 3.7 Hz, 2H), 5.72 (s, 1H), 5.15 (d, J = 6.5 Hz, 1H), 3.42 (d, J = 6.5 Hz, 1H), 2.11 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.6, 158.9, 157.9, 157.7, 157.3, 147.6, 141.6, 139.9, 132.1 (d, J = 8.8 Hz), 128.7, 126.8 (d, J = 2.9 Hz), 121.3, 116.3 (d, J = 8.0 Hz), 113.8 (d, J = 22.7 Hz), 112.7, 111.9 (d, J = 24.3 Hz), 111.0, 52.3, 35.5, 28.8, 27.4, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ –122.30 (1F). HRMS calculated for $C_{26}H_{21}FN_3O_2^+$ (M + H)$^+$: 426.1612; observed: 426.1618.

3ka was obtained according to the general procedure, with 64% yield, dr = 16:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.8 Hz, 2H), 7.99 (d, J = 8.7 Hz, 1H), 7.47 (d, J = 2.1 Hz, 1H), 7.38–7.23 (m, 2H), 7.22–7.13 (m, 4H), 6.75 (s, 1H), 5.72 (s, 1H), 5.12 (d, J = 6.5 Hz, 1H), 3.40 (d, J = 6.5 Hz, 1H), 2.11 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.6, 157.9 157.7, 147.5, 142.8, 141.4, 132.8, 130.3, 128.7, 127.7, 126.8, 126.8, 121.3, 117.0, 113.7, 113.0, 111.1, 52.0, 35.1, 28.8, 27.2, 14.0. HRMS calculated for $C_{26}H_{21}BrN_3O_2^+$ (M + H)$^+$: 486.0812; observed: 486.0810.

3la was obtained according to the general procedure, with 66% yield, dr = 16:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 4.8 Hz, 2H), 8.18 (d, J = 8.6 Hz, 1H), 7.61 (d, J = 1.3 Hz, 1H), 7.35–7.26 (m, 3H), 7.24–7.16 (m, 3H), 6.81 (t, J = 4.8 Hz, 1H), 5.69 (s, 1H), 5.19 (d, J = 6.5 Hz, 1H), 3.48 (d, J = 6.5 Hz, 1H), 2.07 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.8, 159.5, 157.9, 157.8, 147.4, 146.2, 141.2, 131.2, 128.8, 126.9 (d, J = 4.1 Hz), 125.0 (d, J = 3.8 Hz), 121.8 (d, J = 3.7 Hz), 121.3, 115.2, 113.6, 111.3, 52.0, 35.0, 28.7, 26.9, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ –61.24 (3F). HRMS calculated for $C_{27}H_{21}F_3N_3O_2^+$ (M + H)$^+$: 476.1580; observed: 476.1583.

3ma was obtained according to the general procedure, with 58% yield, dr = 7:1; pale yellow solid. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 8.52 (d, J = 4.8 Hz, 2H), 8.07 (d, J = 8.9 Hz, 1H), 7.43 (m, 2H), 7.34 (m, 5H), 7.24 (m, 3H), 7.10 (d, J = 2.6 Hz, 1H), 6.76 (dt, J = 8.1, 3.7 Hz, 2H), 5.77 (s, 1H), 5.17 (d, J = 6.5 Hz, 1H), 5.06 (s, 2H), 3.47 (d, J = 6.5 Hz, 1H), 2.17 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.7, 157.7, 154.0, 147.8, 141.9, 138.0, 137.3, 131.8 128.7, 128.6, 127.9, 127.4, 126.7, 126.6, 121.3, 116.2, 113.8, 112.2, 110.9, 70.7, 52.3, 36.0, 28.9, 27.7, 14.1. HRMS calculated for $C_{32}H_{26}N_3O_3^+$ (M + H)$^+$: 500.1969; observed: 500.1974.

3pa was obtained according to the general procedure, with 72% yield, dr = 18:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.8 Hz, 2H), 7.93 (s, 1H), 7.30–7.21 (m, 3H), 7.17 (dd, J = 6.4, 2.0 Hz, 3H), 6.74–6.66 (m, 2H), 5.68 (s, 1H), 5.10 (d, J = 6.6 Hz, 1H), 3.39 (d, J = 6.6 Hz, 1H), 2.25 (s, 3H), 2.10 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.2, 159.8, 157.7, 157.6, 148.0, 144.0, 142.2, 137.4, 128.6, 127.8, 126.7, 126.5, 124.4, 122.3, 121.3, 116.2, 112.5, 111.1, 52.3, 35.7, 28.8, 27.4, 21.9, 14.1. HRMS calculated for $C_{27}H_{24}N_3O_2^+$ (M + H)$^+$: 422.1863; observed: 422.1861.

3qa was obtained according to the general procedure, with 40% yield, dr = 5:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 4.8 Hz, 2H), 7.88 (d, J = 2.4 Hz, 1H), 7.37–7.28 (m, 3H), 7.26 (s, 2H), 7.24 (s, 1H), 6.81 (t, J = 4.8 Hz, 1H), 6.50 (dd, J = 8.2, 2.4 Hz, 1H), 5.77 (s, 1H), 5.18 (d, J = 6.7 Hz, 1H), 3.79 (s, 3H), 3.46 (d, J = 6.7 Hz, 1H), 2.18 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.1, 159.7, 157.7, 148.0, 145.1, 142.1, 128.6, 126.6, 124.9, 123.1, 121.3, 112., 111.0, 106.8, 102.6, 55.5, 52.6, 35.3, 28.8, 27.5, 14.1. HRMS calculated for $C_{27}H_{24}N_3O_3^+$ (M + H)$^+$: 438.1812; observed: 438.1813.

3ra was obtained according to the general procedure, with 77% yield, dr = 9:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.55 (d, J = 4.8 Hz, 2H), 7.62 (dd, J = 7.8, 1.5 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.33–7.26 (m, 2H), 7.24–7.20 (m, 3H), 6.79 (t, J = 4.8 Hz, 1H), 5.72 (s, 1H), 5.20 (d, J = 6.4 Hz, 1H), 3.84 (s, 3H), 3.49 (d, J = 6.4 Hz, 1H), 2.09 (s, 3H), 1.96 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 193.8, 167.0, 159.5, 157.8, 147.6, 141.3, 130.7, 130.1, 128.7, 127.1, 126.9, 126.2, 123.0, 121.3, 114.8, 113.6, 111.0, 52.1, 51.9, 35.0, 28.8, 27.1, 14.0. HRMS calculated for $C_{28}H_{24}N_3O_4^+$ (M + H)$^+$: 466.1761; observed: 466.1764.

3sa was obtained according to the general procedure, with 62% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 4.8 Hz, 2H), 8.32 (d, J = 1.7 Hz, 1H), 7.27 (m, 2H), 7.18 (m, 4H), 7.00 (dd, J = 7.9, 1.8 Hz, 1H), 6.77 (t, J = 4.8 Hz, 1H), 5.70 (s, 1H), 5.12 (d, J = 6.6 Hz, 1H), 3.39 (d, J = 6.6 Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.5, 157.9, 157.7, 147.6, 144.9, 141.6, 129.7, 128.7, 126.8, 125.8, 124.3, 121.4, 121.1, 118.7, 113.2, 111.1, 52.2, 35.3, 28.9, 27.09, 14.1. HRMS calculated for $C_{26}H_{21}BrN_3O_2^+$ (M + H)$^+$: 486.0812; observed: 486.0819.

3ta was obtained according to the general procedure, with 84% yield, dr =16:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.8 Hz, 2H), 7.90 (dd, J = 11.2, 2.4 Hz, 1H), 7.26 (m, 3H), 7.21–7.11 (m, 3H), 6.75 (t, J = 4.8 Hz, 1H), 6.55 (td, J = 8.7, 2.5 Hz, 1H), 5.70 (s, 1H), 5.13 (d, J = 6.6 Hz, 1H), 3.39 (d, J = 6.6 Hz, 1H), 2.10 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 163.4, 161.8, 159.5, 157.8, 147.7, 144.9, 141.7, 128.7 , 126.7, 126.2, 125.1, 121.4, 113.2, 111.1, 107.9, 107.8, 103.9, 103.8, 52.6, 35.1, 28.8, 27.1, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.52 (1F). HRMS calculated for $C_{26}H_{21}FN_3O_2^+$ (M + H)$^+$: 426.1612; observed: 426.1615.

3ua was obtained according to the general procedure, with 88% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (s, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.27 (t, J = 7.7 Hz, 3H), 7.14 (d, J = 7.2 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.87 (s, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.16 (s, 1H), 5.12 (d, J = 6.5 Hz, 1H), 3.68 (s, 3H), 3.57 (d, J = 6.5 Hz, 1H), 2.26 (s, 3H), 2.17 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 159.5, 157.9, 157.7, 147.6, 144.9, 141.6, 129.7, 129.7, 126.8, 125.8, 124.3, 121.4, 121.1, 118.7, 113.2, 111.1, 52.2, 35.3, 28.9, 27.0, 14.1. HRMS calculated for $C_{27}H_{24}N_3O_3^+$ (M + H)$^+$: 438.1812; observed: 438.1819.

3va was obtained according to the general procedure, with 90% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.2 Hz, 1H), 7.30 (m, 4H), 7.19 (d, J = 3.2 Hz, 1H), 7.05 (td, J = 8.0, 1.4 Hz, 1H), 7.00 (dd, J = 5.3, 3.4 Hz, 2H), 6.94 (td, J = 7.4, 1.0 Hz, 1H), 5.77 (s, 1H), 4.77 (d, J = 6.8 Hz, 1H), 3.56 (d, J = 6.8 Hz, 1H), 2.30 (s, 3H), 2.05 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 177.2, 157.8, 146.7, 145.4, 141.1, 130.1, 129.2, 128.8, 128.1, 128.0, 126.8, 125.4, 124.4, 123.5, 121.4, 117.9, 112.2, 52.6, 40.7, 37.8, 28.9, 28.1, 27.8, 14.2. HRMS calculated for $C_{27}H_{24}N_3O_3^+$ (M + H)$^+$: 438.1812; observed: 438.1819.

3ab was obtained according to the general procedure, with 66% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.7 Hz, 2H), 8.10 (d, J = 8.0 Hz, 1H), 7.78 (td, J = 7.6, 1.8 Hz, 1H), 7.44 (dd, J = 7.3, 0.8 Hz, 1H), 7.24–7.17 (m, 1H), 7.15–7.06 (m, 2H), 7.00 (ddd, J = 10.1, 8.2, 1.2 Hz, 1H), 6.90 (td, J = 7.4, 1.0 Hz, 1H), 6.75 (t, J = 4.8 Hz, 1H), 5.64 (s, 1H), 5.19 (d, J = 6.7 Hz, 1H), 3.47 (d, J = 6.7 Hz, 1H), 2.02 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.06 (s), 162.9, 161.3, 160.0, 157.6, 157.3, 147.9, 143.9, 132.2 (d, J = 3.4 Hz), 130.0, 129.4 (d, J = 8.3 Hz), 127.8 (d, J = 13.2 Hz), 127.7, 125.1, 124.4 (d, J = 3.6 Hz), 121.6, 121.2, 116.1 (d, J = 21.2 Hz), 115.6, 112.6, 110.0, 50.1, 33.1, 28.8, 23.7, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.19 (1F). HRMS calculated for HRMS calculated for $C_{26}H_{21}FN_3O_2^+$ (M + H)$^+$: 426.1612; observed: 426.1612.

3ac was obtained according to the general procedure, with 74% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (d, J = 4.7 Hz, 2H), 8.17 (t, J = 7.0 Hz, 1H), 7.43 (d, J = 7.3 Hz, 1H), 7.30–7.19 (m, 1H), 7.14 (t, J = 7.8 Hz, 1H), 7.10–7.03 (m, 3H), 6.94 (t, J = 7.4 Hz, 1H), 6.78 (t, J = 4.7 Hz, 1H), 5.74 (d, J = 5.7 Hz, 1H), 5.20 (d, J = 6.5 Hz, 1H), 3.50 (d, J = 6.5 Hz, 1H), 2.36 (s, 3H), 2.16 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.1, 159.9, 157.7 147.9, 143.7, 141.9, 138.3, 130.7, 128.6, 127.5, 127.4, 127.3, 124.8, 123.8, 121.5, 121.3, 115.6, 112.6, 111.1, 51.9, 35.9, 28.8, 27.1, 21.6, 14.0. HRMS calculated for $C_{27}H_{24}N_3O_2^+$ (M + H)$^+$: 422.1863; observed: 422.1869;.

3ad was obtained according to the general procedure, with 90% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 4.7 Hz, 2H), 8.17 (d, J = 8.2 Hz, 1H), 7.44 (d, J = 7.3 Hz, 1H), 7.31 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 7.15 (t, J = 7.8 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.81 (t, J = 4.7 Hz, 1H), 5.73 (s, 1H), 5.16 (d, J = 6.6 Hz, 1H), 3.49 (d, J = 6.6 Hz, 1H),

2.16 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9 9, 159.79, 157.89, 157.7, 147.4, 143.7, 140.5, 132.5, 130.2, 128.7, 128.2, 127.7, 124.9, 121.6, 121.3, 115.6, 112.8, 111.2, 51.9, 35.9, 28.8, 26.7, 14.0. HRMS calculated for calculated for $C_{26}H_{21}ClN_3O_2^+$ $(M + H)^+$: 442.1317; observed: 442.1319.

3ae was obtained according to the general procedure, with 91% yield, dr = 15:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, J = 4.7 Hz, 2H), 8.16 (d, J = 8.2 Hz, 1H), 7.42 (d, J = 7.3 Hz, 1H), 7.18 (d, J = 8.2 Hz, 2H), 7.17–7.11 (m, 3H), 6.93 (td, J = 7.5, 0.8 Hz, 1H), 6.78 (t, J = 4.7 Hz, 1H), 5.72 (d, J = 2.4 Hz, 1H), 5.17 (d, J = 6.5 Hz, 1H), 3.48 (d, J = 6.5 Hz, 1H), 2.33 (s, 3H), 2.15 (s, 3H), 2.01(s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.9, 157.6 (d, J = 2.3 Hz), 148.2, 143.8, 138.9, 136.3, 130.6, 129.4, 127.5, 126.8, 124.8, 121.5, 121.2, 115.6, 112.6, 110.8, 51.8, 35.6, 28.8, 26.9, 21.0, 14.0. HRMS: calculated for $C_{27}H_{24}N_3O_2^+$ $(M + H)^+$: 422.1863; observed: 422.1865.

3af was obtained according to the general procedure, with 76% yield, dr = 15:1; pale yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, J = 4.7 Hz, 2H), 8.08 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 7.3 Hz, 1H), 7.13–7.08 (m, 4H), 7.05 (t, J = 7.8 Hz, 1H), 6.85 (t, J = 7.4 Hz, 1H), 6.69 (t, J = 4.7 Hz, 1H), 5.65 (d, J = 1.9 Hz, 1H), 5.09 (d, J = 6.5 Hz, 1H), 3.40 (d, J = 6.5 Hz, 1H), 2.55 (q, J = 7.6 Hz, 2H), 2.07 (s, 3H), 1.93 (s, 3H), 1.14 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.9, 157.77, 148.1, 143.8, 142.7, 139.2, 130.7, 128.2, 127.5, 126.8, 124.8, 121.5, 121.2, 115.6, 112.6, 110.9, 51.8, 37.2, 28.8, 28.5, 26.9, 15.7, 14.0. HRMS calculated for $C_{26}H_{26}N_3O_2^+$ $(M + H)^+$: 436.2020; observed: 436.2025.

3ag was obtained according to the general procedure, with 67% yield, dr = 18:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 4.8 Hz, 2H), 8.10 (d, J = 8.2 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.36 (dd, J = 7.6, 0.8 Hz, 1H), 7.21 (d, J = 8.2 Hz, 2H), 7.08 (td, J = 8.1, 1.3 Hz, 1H), 6.87 (td, J = 7.4, 1.0 Hz, 1H), 6.73 (t, J = 4.8 Hz, 1H), 5.69 (s, 1H), 5.12 (d, J = 6.6 Hz, 1H), 3.46 (d, J = 6.6 Hz, 1H), 2.08 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.8, 1597, 158.0, 157.7, 146.8, 146.4, 143.7, 130.1, 128.7, 128.5, 127.8, 126.7, 125.5 (d, J = 3.7 Hz), 124.9, 121.7, 121.3, 115.7, 112.9, 111.8, 52.5, 36.7, 28.8, 26.9, 14.0. ^{19}F NMR (565 MHz, $CDCl_3$) δ –62.39 (s, 1F). HRMS calculated for $C_{27}H_{21}F_3N_3O_2^+$ $(M + H)^+$: 476.1580; observed: 476.1584.

3ah was obtained according to the general procedure, with 68% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.7 Hz, 2H), 8.09 (d, J = 8.2 Hz, 1H), 7.36 (d, J = 7.4 Hz, 1H), 7.25–7.19 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 6.96 (t, J = 8.7 Hz, 2H), 6.87 (t, J = 7.0 Hz, 1H), 6.73 (t, J = 4.0 Hz, 1H), 5.64 (d, J = 1.0 Hz, 1H), 5.07 (d, J = 6.6 Hz, 1H), 3.40 (d, J = 6.6 Hz, 1H), 2.08 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 162.6, 160.9, 159.8, 157.7 (d, J = 9.3 Hz), 147.9, 143.8, 137.5, 130.3, 128.8 (d, J = 8.0 Hz), 127.6, 124.9, 121.6, 121.3, 115.6 (d, J = 6.7 Hz), 115.5, 112.7, 110.8, 51.7 35.4, 28.8, 26.8, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ –115.97 (1F). HRMS calculated for $C_{26}H_{21}FN_3O_2^+$ $(M + H)^+$: 426.1612; observed: 426.1613.

3ai was obtained according to the general procedure, with 67% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 4.8 Hz, 2H), 8.09 (d, J = 8.2 Hz, 1H), 7.42–7.28 (m, 1H), 7.23 (dd, J = 4.9, 3.1 Hz, 1H), 7.06 (s, 1H), 6.89–6.82 (m, 1H), 6.72 (t, J = 4.8 Hz, 3H), 5.69 (s, 1H), 5.09 (d, J = 6.5 Hz, 1H), 3.41 (d, J = 6.5 Hz, 1H), 2.11 (s, 3H), 1.96 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.7, 157.7, 147.8, 143.5, 143.2, 130.2, 127.6, 126.0, 125.9, 124.8, 121.6, 121.2, 119.2, 115.6, 112.7, 110.9, 52.0, 36.3, 28.8, 24.3, 14.0. HRMS calculated for $C_{24}H_{20}N_3O_2S^+$ $(M + H)^+$: 414.1271; observed: 414.1273.

3aj was obtained according to the general procedure, with 85% yield, dr > 20:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 4.7 Hz, 2H), 7.97 (d, J = 8.2 Hz, 1H), 7.13 (s, 1H), 6.94 (s, 1H), 6.76 (d, J = 7.4 Hz, 1H), 6.64 (s, 1H), 5.28 (s, 1H), 4.73 (d, J = 6.0 Hz, 1H), 3.03 (d, J = 6.0 Hz, 1H), 1.99 (s, 3H), 1.87 (s, 3H), –0.00 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.2, 160.0, 157.5, 156.7, 149.3, 142.7, 130.7, 126.9, 124.6, 121.3, 121.2, 115.5, 112.25, 108.7, 47.3, 29.2, 28.8, 14.4, 13.9, –2.9. HRMS calculated for $C_{23}H_{26}N_3O_2Si^+$ $(M + H)^+$: 404.1789; observed: 404.1784.

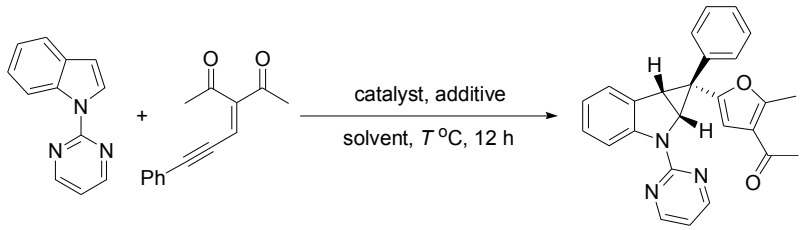
3ak was obtained according to the general procedure, with 38% yield, dr = 10:1; pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.8 Hz, 2H), 8.05 (d, J = 8.2 Hz, 1H), 7.27 (d, J = 7.4 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 6.82 (t, J = 7.4 Hz, 1H), 6.69 (t, J = 4.8 Hz, 1H), 5.46 (s, 1H), 4.62 (d, J = 6.5 Hz, 1H), 2.90 (d, J = 6.5 Hz, 1H), 2.13 (s, 3H), 1.94 (s, 3H), 1.76–1.62 (m, 1H), 1.59–1.49 (m, 1H), 1.34 (m, 4H), 0.83 (M, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.2, 159.9, 157.6, 157.1, 148.9, 143.7, 130.6, 127.1, 124.5, 121.3, 121.1, 115.5, 112.3, 109.8, 49.5, 35.8, 32.2, 28.9, 28.8, 23.9, 22.6, 14.1, 14.0. HRMS calculated for $C_{24}H_{26}N_3O_2^+$ $(M + H)^+$: 388.2020; observed: 388.2021.

5 was obtained with 96% yield, pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.7 Hz, 2H), 8.21 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 1.8 Hz, 1H), 7.59 (d, J = 7.3 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.41–7.33 (m, 4H), 7.32–7.26 (m, 3H), 6.83 (t, J = 4.7 Hz, 1H), 5.79 (s, 1H), 5.25 (d, J = 6.5 Hz, 1H), 3.59 (d, J = 6.5 Hz, 1H), 2.15 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.0, 159.8, 157.8, 157.7, 147.8, 143.1, 141.9, 141.2, 134.8, 131.3, 128.8, 128.7, 126.8, 126.7, 126.7, 126.5, 121.3, 115.7, 112.8, 111.2, 52.1, 35.8, 29.7, 29.3, 27.5, 14.0. HRMS calculated for $C_{32}H_{26}N_3O_2^+$ $(M + H)^+$: 484.2020; observed: 484.2027.

3. Results and discussion

We initiated our investigation by screening the reaction conditions of the coupling of *N*-pyrimidinylindole (**1a**) with ene-yne ketone (**2a**) under Co(III)/Zn(II) catalysis (Table 1). The preliminary experimentation highlighted the effectiveness of the combined Co(III)/Zn(II) catalysis. The control experiments revealed that both Co(III) and Zn(II) were important for this transformation. The omission of Co(III) resulted in trace formation of the desired product (entries 1 and 3), whereas the exclusion of Zn(II) resulted in a lower yield (entries 2 and 4). Note that the transformation proceeded in a highly regioselective manner. Neither Co(III) nor Zn(II) is effective against depression when applied alone (entries 1–4). The solvent was observed to exert a dramatic impact on the efficiency. Notably, dichloromethane was identified as the optimal solvent in terms of both the yield and diastereoselectivity, for the formation of **3aa** (entries 5–9). Lowering the reaction temperature further resulted in low efficiency (entry 10), and extending the reaction

Table 1
Optimization studies. [a]



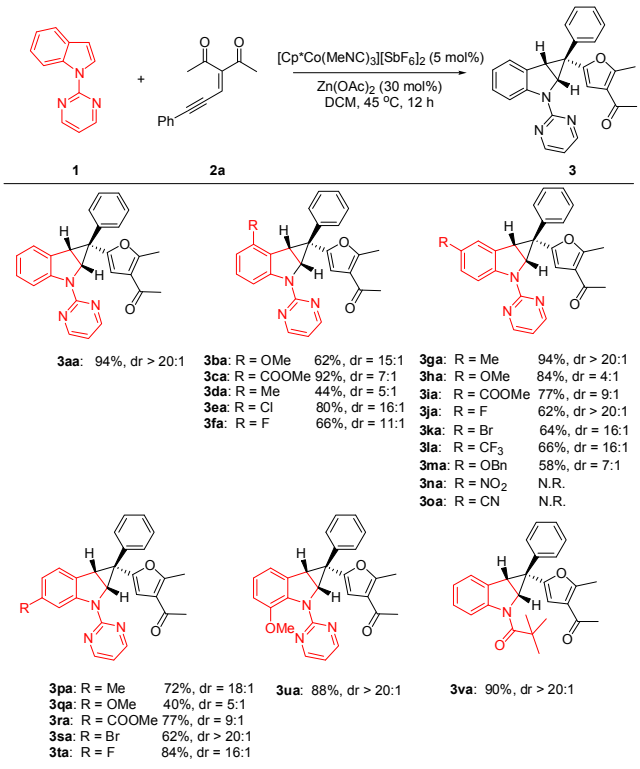
1a **2a** **3aa**

Entry	Catalyst (mol%)	Solvent (mL)	T/°C	t/h	Yield [b] (%)	dr [c]
1	$Zn(OAc)_2$ (30)	TFE (2)	45	12	trace	—
2	$[Cp^*Co(MeCN)_3][SbF_6]_2$ (5)	TFE (2)	45	12	13	15:1
3	$Zn(OAc)_2$ (30)	DCM (2)	45	12	6	12:1
4	$[Cp^*Co(MeCN)_3][SbF_6]_2$ (5)	DCM (2)	45	12	34%	10:1
5	$[Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	TFE (2)	45	12	81	14:1
6	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	THF (2)	45	12	12	15:1
7	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	MeCN (2)	45	12	16	12:1
8	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	1,4-dioxane (2)	45	12	trace	—
9	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	DCM (2)	45	12	94	> 20:1
10	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	DCM (2)	30	12	86	> 20:1
11	$Cp^*Co(MeCN)_3][SbF_6]_2$ (5) / $Zn(OAc)_2$ (30)	DCM (2)	45	24	95	> 20:1

[a] The reaction was carried out using **1a** (0.2 mmol), **2a** (0.24 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol%), and $Zn(OAc)_2$ (30 mol%) in DCM (2 mL) at 30–45 °C for 12–24 h. [b] Isolated yield. [c] Determined by ^1H NMR.

time resulted in a yield (entry 11) approximately equal to that under the optimized reaction conditions (entry 9).

After obtaining the optimized reaction conditions, we investigated the scope of *N*-pyrimidinyl indoles in the coupling with **2a** (Scheme 2). The introduction of substituents with different



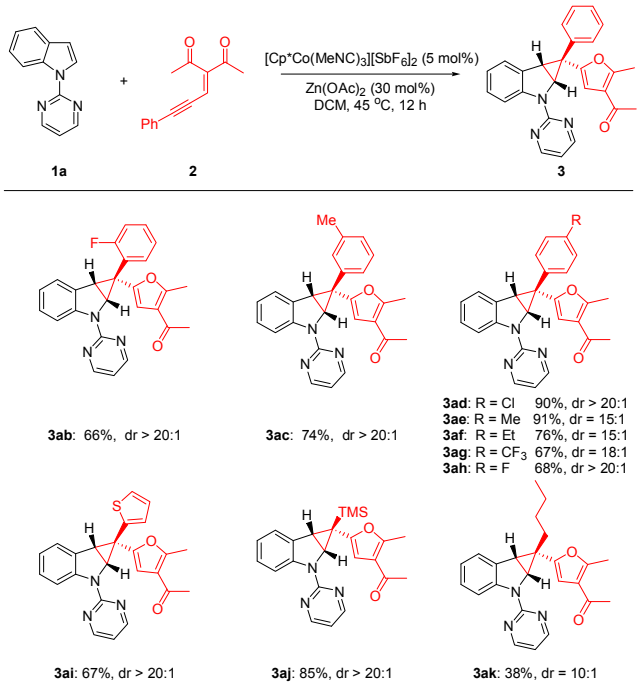
Scheme 2. Scope of indoles. Reaction conditions: **1a** (0.2 mmol), **2** (0.24 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol%), and $Zn(OAc)_2$ (30 mol%) in DCM (2 mL) at 45 °C for 12 h.

electronic effects, to different positions of the *N*-pyrimidinylindole is completely tolerated. With electron-donating groups (Me, OMe, and OBn), electron-withdrawing groups (CF_3 and CO_2Me), and halogen (F, Cl, Br) group at the C4-, C5-, or C6-positions of the indole ring, the coupling resulted in the corresponding products at moderate to high yields (**3ba–3fa**, **3ga–3ma**, and **3pa–3ta**). The 5-NO_2 and 5-CN indoles failed to yield the desired products. Moreover, a C7-substituted indole is tolerated in the isolation of the products **3ua** with 88% yield. The indole substrates are not limited to *N*-pyrimidinyl indoles; *N*-acyl also proceeded smoothly, and the desired product was obtained with 90% yield.

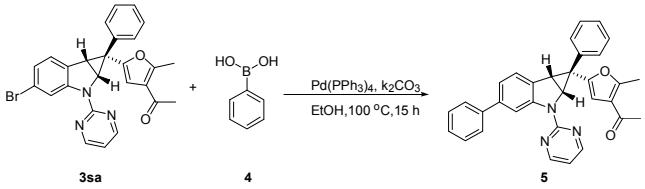
Next, the scope of the ene-yne ketones was examined in the coupling with *N*-pyrimidinylindole (Scheme 3). Both the electron-rich and electron-poor ene-yne ketones at the *para* position could react with **1a** to yield the target products **3ad–3ah** with reasonable to remarkable yields. Notably, ene-yne ketones bearing methyl (**3ab**) and fluorine (**3ac**) at both the *ortho* and *meta* positions were established to be viable coupling partners (66% and 74% yield, respectively). Heterocycle-based (**3ai**), TMS (**3aj**), and alkanes (**3ak**) substituted substrates coupled smoothly with **1a** to produce the desired products with reasonable yields and remarkable diastereoselectivity.

The scale-up (5 mmol) synthesis of **3aa** has also been performed, which was isolated with 90% yield. The derivatization reaction was also examined to demonstrate the utility of this reaction (Scheme 4). The Suzuki cross-coupling reaction of **3sa** (0.25 mmol) with benzeneboronic acid **4** (0.25 mmol) in the presence of $Pd(PPh_3)_4$ produced product **5** at the C5 position of the indoline with 96% yield.

On the basis of our experimental results presented above and literature precedents [21,45,51,54,55], a proposed catalytic

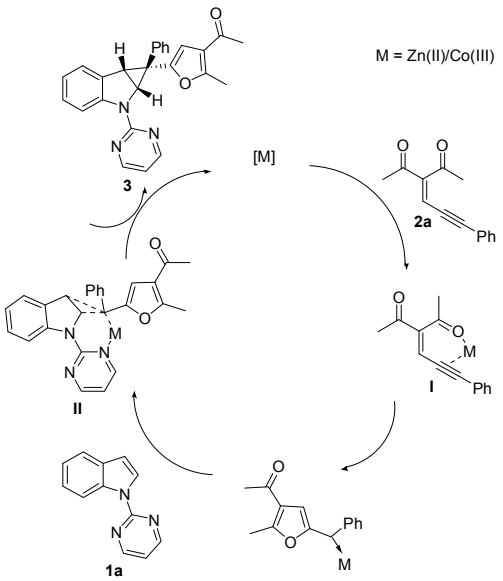


Scheme 3. Scope of ene-yne ketones. Reaction conditions: **1a** (0.2 mmol), **2** (0.24 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol%), and $Zn(OAc)_2$ (30 mol%) in DCM (2 mL) at 45 °C for 12 h.



Scheme 4. Derivatization reaction.

cycle is shown in Scheme 5. The electrophilic M-carbene intermediate **I** is produced by cyclometalation of carbonyl ene-yne with zinc/cobalt salt; then, Zn(II)/Co(III) furylcarbenes is obtained through an intramolecular 5-exo-dig cyclization by the nucleophilic attack of the carbonyl oxygen atom on the C4 carbon atom of complex **I**. Subsequent coordinates to indole **1a** to give intermediate **II,** which undergoes cyclization and elimination to form the desired product **3.** Further interaction regenerates the active Zn(II)/Co(III) catalyst for the subsequent catalytic cycle.



Scheme 5. Proposed mechanism.

4. Conclusions

We have realized Co(III)/Zn(II)-catalyzed dearomatization of indoles. The reactions are highly efficient and showed diastereoselectivities under mild reaction conditions to produce a series of highly functionalized cyclopropane fused indolines; these indolines are effective for the synthesis of indoline alkaloids. The scope of the protocols was investigated. Considering the mild conditions, broad scope, diastereoselectivities, and high catalytic efficiency, this method is likely to find applications in the synthesis of functionalized-cyclopropane-fused indolines derivatives.

References

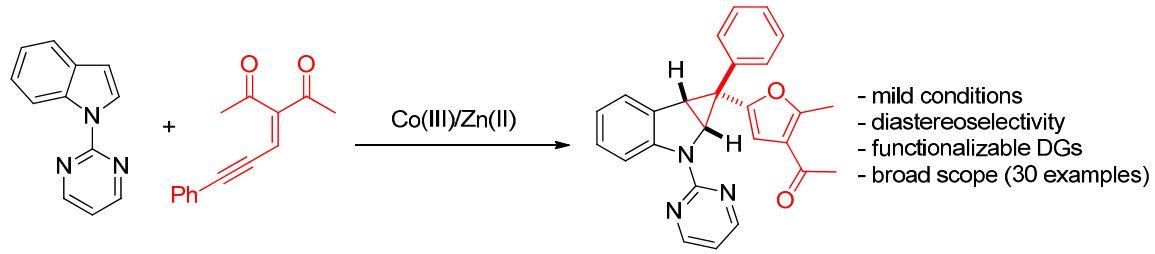
[1] D. Jin, F. Zhang, D. C. Zhang, *Chin. J. Org. Chem.*, **2010**, 30, 1005–1009.

Graphical Abstract

Chin. J. Catal., 2018, 39: 1881–1889 doi: 10.1016/S1872-2067(18)63154-7

Co(III)/Zn(II)-catalyzed dearomatization of indoles and coupling with carbenes from ene-yne ketones via intramolecular cyclopropanation

Na Li, Junbiao Chang*, Lingheng Kong, Shuangjing Wang, Dandan Wang, Miao Cheng, Xingwei Li*
Henan Normal University;
Xinxiang Medical University;
Dalian Institute of Chemical Physics, Chinese Academy of Sciences



A straightforward and efficient protocol for dearomatizing indoles is described. The reaction, catalyzed by an inexpensive Co(III)/Zn(II) catalyst, starts from conveniently accessible *N*-pyrimidinyl indoles and ene-yne ketones. Mild reaction conditions, high diastereoselectivity, a broad substrate scope, reasonable functional group tolerance, and reasonable to remarkable yields were observed.

[2] D. Y. Liu, G. W. Zhao, L. Xiang, *Eur. J. Org. Chem.*, **2010**, 2010, 3975–3984.
[3] S. Anas, H. B. Kagan, *Tetrahedron: Asymmetry*, **2009**, 20, 2193–2199.
[4] J. Bonjoch , D. Solé, S. García-Rubio, J. Bosch, *J. Am. Chem. Soc.*, **1997**, 119, 7230–7240.
[5] D. Zhang, H. Song, Y. Qin, *Acc. Chem. Res.*, **2011**, 44, 447–457.
[6] X. Deng, K. J. Liang, X. G. Tong, M. Ding, D. S. Li, C. F. Xia, *Org. Lett.*, **2014**, 16, 3276–3279.
[7] T. Wang, Q. G. Xu, P. Yu, X. X. Liu, J. M. Cook, *Org. Lett.*, **2001**, 3, 345–348.
[8] X. Y. Fu, J. M. Cook, *J. Am. Chem. Soc.*, **1992**, 114, 6910–6912.
[9] J. Li, T. Wang, P. Yu, A. Peterson, R. Weber, D. Soerens, D. Grubisha, D. Bennett, J. M. Cook, *J. Am. Chem. Soc.*, **1999**, 121, 6998–7010.
[10] S. J. Jin, J. Gong, Y. Qin, *Angew. Chem. Int. Ed.*, **2015**, 54, 2228–2231.
[11] H. X. Huang, S. J. Jin, J. Gong, D. Zhang, H. Song, Y. Qin, *Chem. Eur. J.*, **2015**, 21, 13284–13290.
[12] M. S. Kirillova, M. E. Muratore, R. Dorel, A. M. Echavarren, *J. Am. Chem. Soc.*, **2016**, 138, 3671–3674.
[13] L. A. Paquette, *Chem. Rev.*, **1986**, 86, 733–750.
[14] H. N. C. Wong, M. Y. Hon, C. W. Tse, Y. C. Yip, J. Tanko, T. Hudlicky, *Chem. Rev.*, **1989**, 89, 165–198.
[15] O. G. Kulinkovich, *Pol. J. Chem.*, **1997**, 71, 849–882.
[16] A. de Meijere, S. I. Kozhushkov, L. P. Hadjiarapoglou, *Top. Curr. Chem.*, **2000**, 207, 149–227.
[17] H. Lebel, J. F. Marcoux, C. Molinaro, A. B. Charetter, *Chem. Rev.*, **2003**, 103, 977–1050.
[18] D. Gagnon, C. Spino, *J. Org. Chem.*, **2009**, 74, 6035–6041.
[19] H. Song, J. Yang, W. Chen, Y. Qin, *Org. Lett.*, **2006**, 8, 6011–6014.
[20] B. He, H. Song, Y. Du, Y. Qin, *J. Org. Chem.*, **2009**, 74, 298–304
[21] A. R. Reddy, F. Hao, K. Wu, C. Y. Zhou, C. M. Che, *Angew. Chem. Int. Ed.*, **2016**, 55, 1810–1815.
[22] B. Zhang, A. G. H. Wee, *Chem. Commun.*, **2008**, 4837–4839.
[23] B. Zhang, A. G. H. Wee, *Org. Biomol. Chem.*, **2012**, 10, 4597–4608.
[24] G. Özüduru, T. Schubach, M. M. K. Boysen, *Org. Lett.*, **2012**, 14, 4990–4993.
[25] D. Gagnon, C. Spino, *J. Org. Chem.*, **2009**, 74, 6035–6041.
[26] W. J. Welstead Jr, H. F. Stauffer Jr, L. F. Sancilio, *J. Med. Chem.*, **1974**, 17, 544–547.
[27] E. Wenkert, M. E. Alonso, H. E. Gottlieb, E. L. Sanchez, R. Pellicciari, P. Cogolli, *J. Org. Chem.*, **1977**, 42, 3945–3949.
[28] H. Keller, E. Langer, H. Lehner, *Monatsh. Chem.*, **1977**, 108, 123–131.
[29] F. Gnad, M. Poleschak, O. Reiser, *Tetrahedron Lett.*, **2004**, 45, 4277–4280.
[30] X. J. Zhang, S. P. Liu, M. Yan, *Chin. J. Chem.*, **2008**, 26, 716–720.
[31] D. Zhang, H. Song, Y. Qin, *Acc. Chem. Res.*, **2011**, 44, 447–457.
[32] H. M. L. Davies, J. E. Spangler, *Adv. Heterocycl. Chem.*, **2013**, 110, 43–72.
[33] H. M. L. Davies, S. J. Hedley, *Chem. Soc. Rev.*, **2007**, 36, 1109–1119.
[34] H. Xu, Y. P. Li, Y. Cai, G. P. Wang, S. F. Zhu, Q. L. Zhou, *J. Am. Chem. Soc.*, **2017**, 139, 7697–7700.
[35] W. T. Wu, L. Zhang, S. L. You, *Acta Chim. Sinica.*, **2017**, 75, 419–438.
[36] D. C. Wang, M. S. Xie, H. M. Guo, G. R. Qu, M. C. Zhang, S. L. You, *Angew. Chem. Int. Ed.*, **2016**, 55, 14111–14115.
[37] W. Du, Q. S. Gu, Z. L. Li, D. Yang, *J. Am. Chem. Soc.*, **2015**, 137, 1130–1135.
[38] Y. Y. Zhou, C. Uyeda, *Angew. Chem. Int. Ed.*, **2016**, 55, 3171–3175.
[39] H. Rudler, T. Durand-Réville, *J. Organomet. Chem.*, **2001**, 617–618, 571–587.
[40] D. Dhanaka, R. Kurodab, C. B. Reese, *Tetrahedron Lett.*, **1987**, 28, 1827–1830.
[41] H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.*, **1958**, 80, 5323–5324.
[42] S. R. Goudreau, A. B. Charette, *J. Am. Chem. Soc.*, **2009**, 131, 15633–15635.
[43] K. Miki, T. Yokoi, F. Nishino, K. Ohe, S. Uemura, *J. Organomet. Chem.*, **2002**, 645, 228–234.
[44] K. Miki, F. Nishino, K. Ohe, S. Uemura, *J. Am. Chem. Soc.*, **2002**, 124, 5260–5261.
[45] K. Miki, T. Yokoi, F. Nishino, Y. Kato, Y. Washitake, K. Ohe, S. Uemura, *J. Org. Chem.*, **2004**, 69, 1557–1564.

[46] K. Miki, S. Uemura, K. Ohe, *Chem. Lett.*, **2005**, 34, 1068–1072.
[47] R. Vicente, J. Gonzalez, L. Riesgo, J. Gonzalez, L. A. Lopez, *Angew. Chem. Int. Ed.*, **2012**, 51, 8063–8067.
[48] C. X. Zhuo, W. Zhang, S. L.You, *Angew. Chem. Int. Ed.*, **2012**, 51, 12662–12686.
[49] W. Chen, D. S. Ji, Y. C Luo, Z. Y. Wang, P. F. Xu, *Org. Chem. Front.*, **2018**, 5, 1768–1771.
[50] N. Yoshikai, *ChemCatChem.*, **2015**, 7, 732–734.
[51] M. Moselage, J. Li, L. Ackermann, *ACS Catal.*, **2016**, 6, 498–525.
[52] X. L. Han, C. J. Zhou, X. G. Liu, S. S. Zhang, H. G. Wang, Q. J. Li, *Org. Lett.*, **2017**, 19, 6108–6111.
[53] W. Zhang, F. Han, J. Tong, C. Xia, J. Liu, *Chin. J. Catal.*, **2017**, 38, 805-812.
[54] F. Wang, Q. Wang, M. Bao, X. W. Li, *Chin. J. Catal.*, **2016**, 37, 1423-1430.
[55] Y. Chen, J. V. Ruppol, X. P. Zhang, *J. Am. Chem. Soc.*, **2007**, 129, 12074–12075.
[56] W. J. Kerr, D. M. Lindsay, P. K. Owens, M. Reid, T. Tuttle, S. Campos, *ACS Catal.*, **2017**, 7, 7182–7186.
[57] L. Ackermann, A.V. Lygin, *Org. Lett.*, **2011**, 13, 3332–3335.
[58] M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.*, **2012**, 51, 6993–6997.
[59] N. Li, J. B. Chang, L. H. Kong, X. W. Li, *Org. Chem. Front.*, **2018**, 5, 1978–1982.

Co(III)/Zn(II)催化吲哚的分子内环丙烷化

李　娜[a,b], 常俊标[a,*], 孔令恒[c], 王栓景[a], 王丹丹[a], 程　淼[a], 李兴伟[a,c,#]
[a]河南师范大学化学化工学院, 河南省有机功能分子和药物创新重点实验室, 河南新乡453007
[b]新乡医学院药学院, 河南新乡453003
[c]中国科学院大连化学物理研究所, 辽宁大连116023

摘要: 二氢吲哚骨架被广泛用作不对称合成中的关键结构单元和手性助剂, 也广泛存在于具有多种生物活性的生物碱和其他天然产物中. 其中2,3位取代的吲哚啉衍生物因其存在的广泛性和生物活性良好而备受关注. 手性环丙烷可通过开环或环扩展转化为有价值的合成中间体, 构建类似天然产物Lundurines的包含三个季碳立体中心的二氢吲哚并环丙烷结构是很有吸引力的目标. 传统构建此类化合物的方法包括过渡金属催化和经典的Simmons-Smith反应等. 然而, 更有效、环境友好和原子经济性的生成卡宾前体的催化方法研究仍然非常有限. 目前由羰基炔化合物和锌盐催化合成多功能性锌-呋喃卡宾的研究引起了人们的关注. 而Cp*Co(III)由于其地球丰度、成本效益、低毒性和独特的催化活性已引起越来越多的注意, 但Cp*Co(III)作为路易斯酸用于催化反应的报道仍然较少.

本文报道了吲哚与烯炔酮通过Zn(II)/Co(III)呋喃卡宾可以实现分子内环丙烷化, 得到一系列具有三维环状结构的二氢吲哚化合物. 研究从Co(III)/Zn(II)催化*N*-嘧啶吲哚与烯炔酮偶联反应开始, 条件筛选实验验证了Co(III)/Zn(II)催化联合使用的强大功能. 反应体系中不加Co(III)导致目标产物的痕量形成, 而排除Zn(II)会使收率降低. 本文共完成了30个不同官能团取代的二氢吲哚并环丙烷骨架结构的合成, 目标产物收率从中等到良好, 最高收率可达94%. 反应有较好的普适性, 吲哚基底物不局限于*N*-吡啶, *N*-酰基反应也进行得很顺利, 达到90%的收率. 为了提高反应的实用性, 我们进行了放大实验. 结果表明, 当嘧啶吲哚用量由0.2 增大至5 mmol时, 反应仍能以较高的收率(90%)得到目标产物. 此外, 目标产物还可以进一步衍生转化为其他杂环类化合物, 如在$Pd(PPh_3)_4$作用下发生Suzuki偶联反应.

总之, 我们在Co(III)/Zn(II)催化下成功实现了吲哚的分子内环丙烷化, 合成了一系列含有三个季碳立体中心的二氢吲哚并环丙烷化合物, 为新药开发奠定了基础. 该催化体系反应条件温和, 底物适用范围广, 非对映体选择性高, 催化效率高.

关键词: Co(III)/Zn(II)催化; 去芳构化; 环丙烷化; 卡宾; 吲哚

收稿日期: 2018-06-21. 接受日期: 2018-07-26. 出版日期: 2018-12-05.
*通讯联系人. 电话: (0411)84379089; 电子信箱: changjunbiao@zzu.edu.cn
#通讯联系人. 电话: (0411)84379089; 电子信箱: xwli@dicp.ac.cn
基金来源: 国家自然科学基金(21525208, 21472186); 河南师范大学研究基金(5101034011009).
本文的电子版全文由Elsevier出版社在ScienceDirect上出版(http://www.sciencedirect.com/science/journal/18722067).