Co(III)-Catalyzed, *N*-Amino-Directed C-H Coupling with 4-Hydroxy-2-Alkynoates for Indole Synthesis

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Abstract: Conventional synthetic organic chemistry typically relies on site-centered reactivity for reaction discovery. Herein, skeleton-chaperoned reactivity is exploited for reaction development, with skeleton utilized as a structural scaffold for assisting functional group activation into a proper reactivity sequence. A Co(III) catalytic method has been developed for *N*-amino-directed C-H coupling with 4-hydroxy-2-alkynoates, allowing convenient access to 2-alkene-3-carboxylic acid type indole derivatives. This reaction features phenyl/pyrrole/lactone skeleton-chaperoned reactivity and simultaneous conversions of five functional groups. Given the vast pool of skeletons available for structural scaffolding, skeleton-chaperoned reactivity promises to become a powerful tool for divergent entry into distinct chemical space.

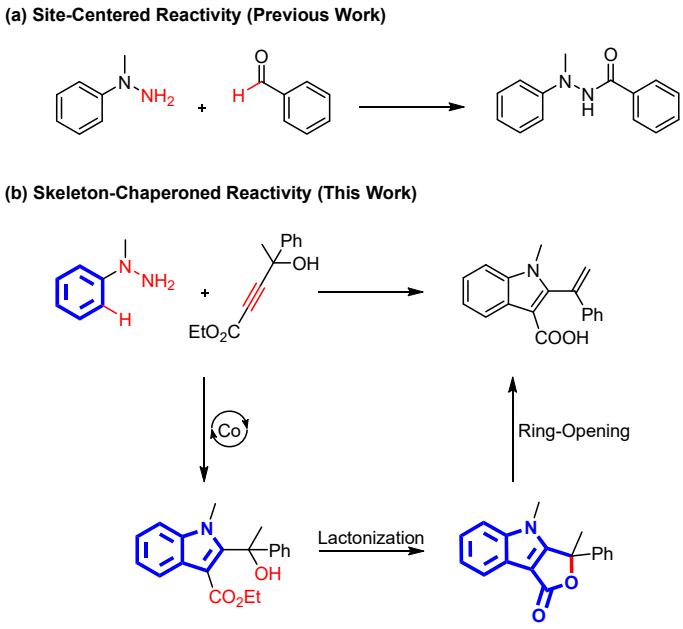
Keywords: Site-Centered Reactivity; Skeleton-Chaperoned Reactivity; Cobalt Catalysis; C-H Bond Activation; Indole Derivative.

Organic synthesis is a core discipline of chemical synthesis that is concerned with the creation of organic compounds via organic transformations. Organic transformations are structure-changing conversions of functional groups from the substrate forms to product forms in reactions.[1,2] In this regard, the number of functional groups that are transformed during a reaction can be taken as a metric, transformation economy as termed herein, for the measurement of degree of structural changes for the reaction. A higher transformation economy, corresponding to a higher number of functional group conversions and a higher degree of structural changes, can be a powerful enabler for the expedient divergence into distinct chemical space. Conventional reaction development methods typically rely on site-centered reactivity (Scheme 1a) for the discovery of organic transformations, with discrete functional group sites as the center of focus for eliciting reactivity and conversions.[3-5] This synthetic practice, although being useful for the establishment of reaction mechanism concepts and reaction analysis frameworks due to its simplicity, is inherently a self-limiting approach that confines the discovery to low transformation economy reactions. In our view, a self-liberating synthetic practice, with a collection of functional groups as the prospective cohort of sites for consolidation into a coherent reaction channel, can expand the discovery to high transformation economy reaction regime. In particular, skeleton-chaperoned reactivity (Scheme 1b), with skeleton as a structural scaffold for assisting the activation of functional group sites into a proper reactive sequence, can be a viable strategy to this end.

With skeleton-chaperoned reactivity as an entry mode into high transformation

economy reactions in mind, we have turned our attention to *N*-amino (hydrazine) group.[6] *N*-amino group alone, in a site-centered reactivity mode as reported previously, can, for example, react with aldehyde for transformation into acyl hydrazide, an apparently low transformation economy reaction (Scheme 1a).[7-9] In contrast, herein, in the skeleton-chaperoned reactivity mode, with the assistance of phenyl skeleton, *N*-amino group can direct the activation of *ortho* C-H bond and reaction with 4-hydroxy-2-alkynoates under Co(III) catalysis (Scheme 1b). A high transformation economy reactive sequence for 2-alkene-3-carboxylic acid type indole derivative synthesis can be effected as the following: phenyl skeleton-chaperoned C-H coupling reactivity with alkyne group, and conversion, via further internal oxidation ring closure coupling reactivity of *N*-amino group, into pyrrole skeleton; pyrrole skeleton-chaperoned reactivity between hydroxyl group and ester group, and conversion into lactone skeleton; lactone skeleton-chaperoned ring-opening self-reactivity, and conversion into

Scheme 1. Organic Transformations Based on *N*-Amino Group: (a) Site-Centered Reactivity (Previous Work), (b) Skeleton-Chaperoned Reactivity (This Work).

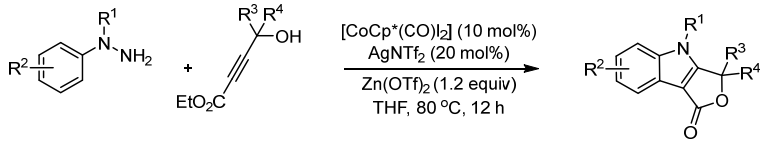


open-chain alkene and carboxylic acid groups. This single high transformation economy reaction amounts to the simultaneous conversions of five functional groups, demonstrating the significant chemical space diverging capability empowered by skeleton-chaperoned reactivity.

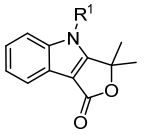
We commence the reaction development by the coupling of 1-methyl-1-phenylhydrazine (**1a**) with ethyl 4-hydroxy-4-methylpent-2-ynoate (**2a**).[10] Initial screening of reaction conditions allows the identification of [CoCp*(CO)I_2] (10 mol%), $AgNTf_2$ (20 mol%), and $Zn(OTf)_2$ (1.2 equiv) as the catalyst precursor components for the synthesis of 3,3,4-trimethyl-3,4-dihydro-1*H*-furo[3,4-*b*]indol-1-one (**3aa**), revealing lactonization reactivity mode as the termination step. The reaction toward **3aa** can progress to 20% after 12 h of 60 ºC reaction in tetrahydrofuran (THF) with the 1:1 equiv participation of **1a** and **2a**, and 36% when the temperature is raised to 80 ºC. The yield can be increased to 73% at 80 ºC with a 3:1 **1a**-to-**2a** ratio. A control experiment carried out in the exclusive absence of [CoCp*(CO)I_2] fails to produce any **3aa**. Taken together, mechanistically, it is expected that [CoCp*(CO)I_2] and $AgNTf_2$ (as an iodide abstraction reagent) together act as the catalyst for *N*-amino-directed C-H activation in **1a** and coupling with **2a**, and $Zn(OTf)_2$ acts as a Lewis acid for activation of alkyne group in **2a**.

With the optimized synthetic condition for **3aa** established, we next perform the survey of relevant substrate scope (Scheme 2). The hydrazine side is examined first, with **2a** fixed as the coupling partner. The reaction can proceed for a variety of 1-substitution patterns, with the extension of chain length from methyl (**1a**) to ethyl

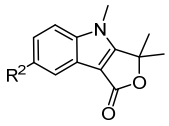
Scheme 2. Substrate Scope for Lactonization.[a,b]

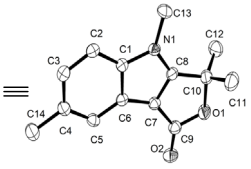


1 2 3

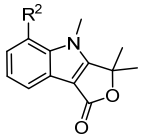


R^1=Me, **3aa**: 73%
R^1=Et, **3ba**: 61%
R^1=^{i}Pr, **3ca**: 36%

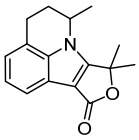




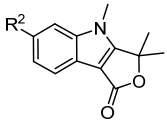
R^2=Me, **3da**: 60%
R^2=Ph, **3ea**: 76%
R^2=OMe, **3fa**: 37%
R^2=F, **3ga**: 67%
R^2=Cl, **3ha**: 56%
R^2=Br, **3ia**: 71%
R^2=CO_2Me, **3ja**: 63%
R^2=CF_3, **3ka**: 82%
R^2=CN, **3la**: 84%



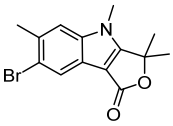
R^2=Me, **3ma**: 55%
R^2=Ph, **3na**: 71%
R^2=F, **3oa**: 56%



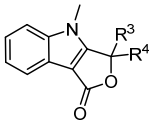
3pa: 39%



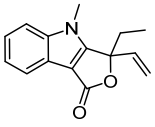
R^2=Me, **3qa**: 59%
R^2=F, **3ra**: 65%
R^2=Cl, **3sa**: 83%
R^2=Br, **3ta**: 88%
R^2=CF_3, **3ua**: 71%



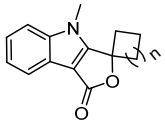
3va: 69%



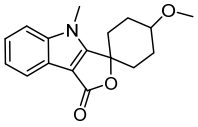
R^3=Me, R^4=Et, **3ab**: 64%
R^3=Me, R^4=^{n}Pr, **3ac**: 59%
R^3=Me, R^4=^{i}Pr, **3ad**: 53%
R^3=Me, R^4=^{t}Bu, **3ae**: 45%
R^3=Et, R^4=Et, **3af**: 71%



3ag: 39%



n=1, **3ah**: 29%
n=2, **3ai**: 45%
n=3, **3aj**: 65%
n=4, **3ak**: 60%



3al: 39%

[a]Reaction condition: **1** (0.6 mmol), **2** (0.2 mmol), [CoCp*(CO)I_2] (10 mol%), $AgNTf_2$ (20 mol%), $Zn(OTf)_2$ (0.24 mmol), THF (1 mL), 80 °C, 12 h. [b]Isolated yields.

(**1b**, 61%) and *iso*-propyl (**1c**, 36%) leading to a reduction of product yield.[11] The reaction is also compatible with a broad range of substitution patterns on the phenyl ring of **1a**. For the *para* substitution, both electron-donating and electron-withdrawing groups can be tolerated. Whereas the methyl group (**1d**, 60%; with the structure unambiguously determined by single-crystal X-ray diffraction) imparts a lower yield, the phenyl group (**1e**, 76%) bestows a slightly higher yield, and the yield is substantially reduced for the methoxy group (**1f**, 37%). For the halide group series, the yield first goes down from fluoro (**1g**, 67%) to chloro (**1h**, 56%) and then rises back up at bromo (**1i**, 71%). Whereas a lower yield is observed for the methoxycarbonyl group (**1j**, 63%), the yield is notably boosted for the trifluoromethyl (**1k**, 82%) and cyano (**1l**, 84%) groups. For the *ortho* substitution (methyl, **1m**, 55%; phenyl, **1n**, 71%; fluoro, **1o**, 56%), the yield is decreased as compared to the *para* counterpart. The 1, *ortho* fused ring substitution (whole structure: 2-methyl-3,4-dihydroquinolin-1(2*H*)-amine, **1p**, 39%) results in a marked drop in the product yield. For the *meta* substitution, the yield varies as compared to the *para* and *ortho* substitutions. Whereas the yield for the methyl (**1q**, 59%) and fluoro (**1r**, 65%) groups is in between the *para* and *ortho* counterparts, the yield for the chloro (**1s**, 83%) and bromo (**1t**, 88%) groups is higher than the *para* counterparts, and the yield for the trifluoromethyl group (**1u**, 71%) is lower than the *para* counterpart. The reaction can also proceed smoothly with the disubstitution (*para* bromo, *meta* methyl, **1v**, 69%). The 4-hydroxy-2-alkynoate side is examined second, with **1a** fixed as the coupling partner. **2a** can be viewed as an alkyne substituted on one side with ethoxycarbonyl, and on the other side with double methyl group-derivatized

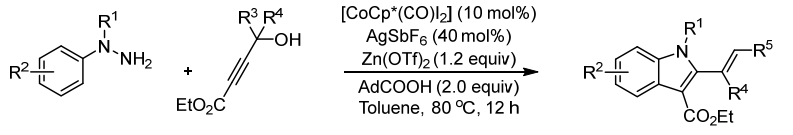
hydroxymethyl group. With one methyl group intact, the reaction can accept the switch of other methyl group to a variety of alkyl groups with different chain lengths and branching patterns. Thus, the yield is decreased in the order of ethyl (**2b**, 64%), *n*-propyl (**2c**, 59%), *iso*-propyl (**2d**, 53%), and *tert*-butyl (**2e**, 45%) groups. Interestingly, the yield is restored back to a comparable level with the double switch of methyl groups to ethyl groups (**2f**, 71%), likely reflecting the effect of local structural symmetry on the reaction outcome. With one ethyl group in **2f** altered to a vinyl group (**2g**, 39%), the yield is considerably lowered. With the complete integration of double methyl groups of **2a** into an alkyl ring motif, the reaction can also advance toward the product formation. The yield rises up with the ring size changed from four (**2h**, 29%) to five (**2i**, 45%) to six (**2j**, 65%) and goes slightly back down at seven (**2k**, 60%). A methoxy substitution on the alkyl ring of **2j** (**2l**, 39%) causes a vast drop in yield.

With the lactonization reactivity mode validated, we then initiate the search for an alternative reactivity mode. The screening of reaction conditions shows that with **1a** and **2a** as the reactants, [CoCp*(CO)I_2] (10 mol%) and $Zn(OTf)_2$ (1.2 equiv) as part of the catalyst precursor components, the alteration of $AgNTf_2$ to $AgSbF_6$ (40 mol%) allows the synthesis of ethyl 1-methyl-2-(prop-1-en-2-yl)-1*H*-indole-3-carboxylate (**4aa**),[12] showcasing alcohol dehydration reactivity mode as the termination step. The yield can reach 27% after 12 h of 80 °C reaction in toluene with the 1:1 equiv participation of **1a** and **2a**, and 46% with a 1.5:1 **1a**-to-**2a** ratio. An addition of carboxylic acid is beneficial and a 58% yield can be obtained in the presence of 2 equiv 1-adamantanecarboxylic acid (AdCOOH). Again, a control experiment confirms the

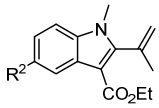
essential role played by [CoCp*(CO)I_2], in the production of **4aa**.

With the reaction condition for **4aa** optimized, we next investigate the applicable substrate scope (Scheme 3). The hydrazine side is interrogated first, with **2a** designated as the coupling partner. A wide spectrum of substitution patterns on the phenyl ring of **1a** are compatible with the reaction. Thus, for the *para* substitution, whereas the methyl group (**1d**, 24%) confers a low yield, the halide group series affords a relatively higher yield in the ascending order of chloro (**1h**, 54%), bromo (**1i**, 61%), and fluoro

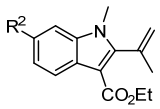
Scheme 3. Substrate Scope for Alcohol Dehydration.[a,b]



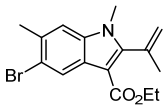
1 **2** **4**



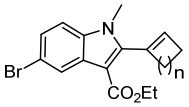
R^2=H, **4aa**: 58%
R^2=Me, **4da**: 24%
R^2=F, **4ga**: 71%
R^2=Cl, **4ha**: 54%
R^2=Br, **4ia**: 61%
R^2=CO_2Me, **4ja**: 46%
R^2=CF_3, **4ka**: 66%



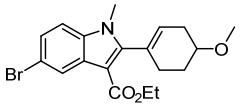
R^2=Cl, **4sa**: 29%
R^2=Br, **4ta**: 61%
R^2=CF_3, **4ua**: 62%



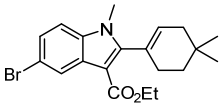
4va: 51%



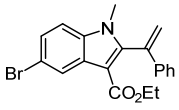
n=1, **4ih**: 47%
n=2, **4ii**: 39%
n=3, **4ij**: 54%
n=4, **4ik**: 51%



4il: 55%



4im: 53%



4in: 34%

[a]Reaction condition: **1** (0.3 mmol), **2** (0.2 mmol), [CoCp*(CO)I_2] (10 mol%), $AgSbF_6$ (40 mol%), $Zn(OTf)_2$ (0.24 mmol), AdCOOH (0.4 mmol), Toluene (1 mL), 80 °C, 12 h. [b]Isolated yields.

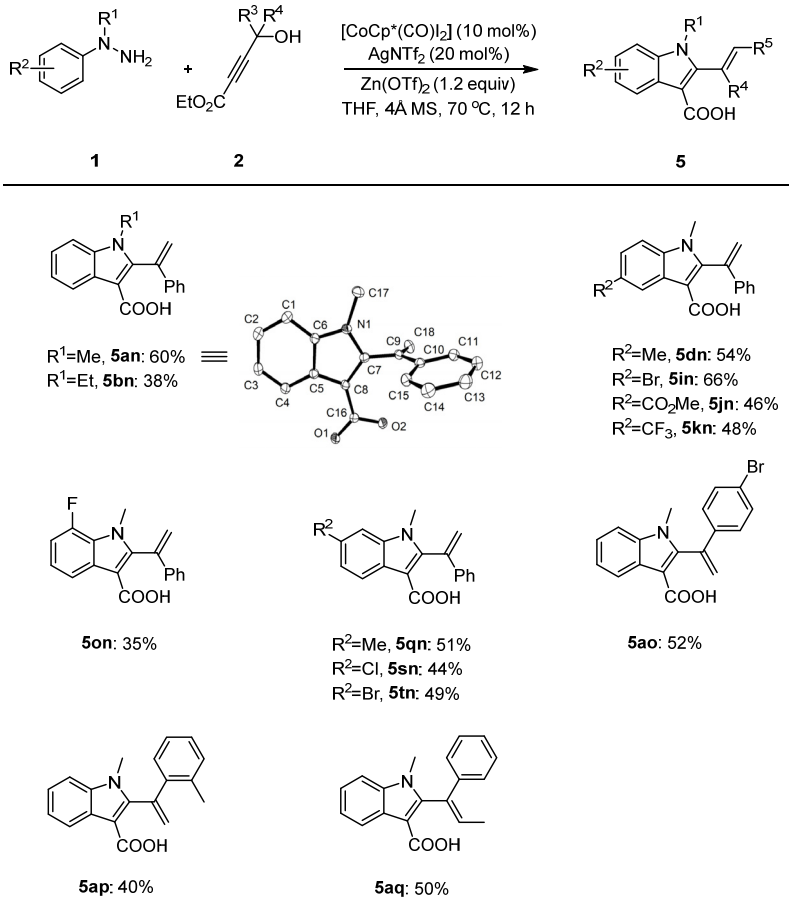
(**1g**, 71%). The methoxycarbonyl group (**1j**, 46%) offers a lower yield than the trifluoromethyl group (**1k**, 66%). For the *meta* substitution, the yield is low for the chloro group (**1s**, 29%), and at a comparably high level for the bromo (**1t**, 61%) and trifluoromethyl group (**1u**, 62%). The reaction is also viable with the disubstitution (*para* bromo, *meta* methyl, **1v**, 51%). The 4-hydroxy-2-alkynoate side is scrutinized second, with **1i** as the designated coupling partner. With the alkyl ring substitution motif, the reaction can invariably proceed. The yield dips at the five-membered ring (**2i**, 39%), peaks at the six-membered ring (**2j**, 54%), and is in between for the four-membered (**2h**, 47%) and seven-membered (**2k**, 51%) rings. For the six-membered ring motif, a methoxy substitution (**2l**, 55%) and a double methyl substitution (**2m**, 53%) retain the product yield. The change of **2a** to ethyl 4-hydroxy-4-phenylpent-2-ynoate (**2n**, 34%), which can be viewed as a switch of one methyl group to the phenyl group, causes a negative impact on the yield.

With the lactonization and alcohol dehydration reactivity modes verified, we launch an effort to yet further expand the reactivity scope.[13] Indeed, the reaction between **1a** and **2n** can, with [CoCp*(CO)I_2] (10 mol%), $AgNTf_2$ (20 mol%), and $Zn(OTf)_2$ (1.2 equiv) as the catalyst precursor components, provide 1-methyl-2-(1-phenylvinyl)-1*H*-indole-3-carboxylic acid (**5an**; with the structure unambiguously determined by single-crystal X-ray diffraction) as the product (2-alkene-3-carboxylic acid type indole derivative), featuring lactonization/ring-opening as the termination step (*vide infra*). With 1:1 equiv **1a** and **2n**, the yield can reach 53% after 12 h of 70 °C reaction in THF, and 60% in the extra presence of 4 Å molecular sieves (MS). A control

experiment once more corroborates the critical importance of [CoCp*(CO)I_2], in the formation of **5an**.

With the favored reaction condition for **5an** in hand, we next probe the applicable substrate scope (Scheme 4). The hydrazine side is inspected first, with **2n** specified as the coupling partner. The reaction is compatible with the chain extension of 1-substitution from methyl (**1a**) to ethyl (**1b**, 38%) group, albeit at a reduced yield. The reaction can also tolerate a diversity of substitution patterns on the phenyl ring of **1a**. For the *para* substitution, the methyl group (**1d**, 54%) gives a lower yield, and the

Scheme 4. Substrate Scope for Lactonization/Ring-Opening.[a,b]

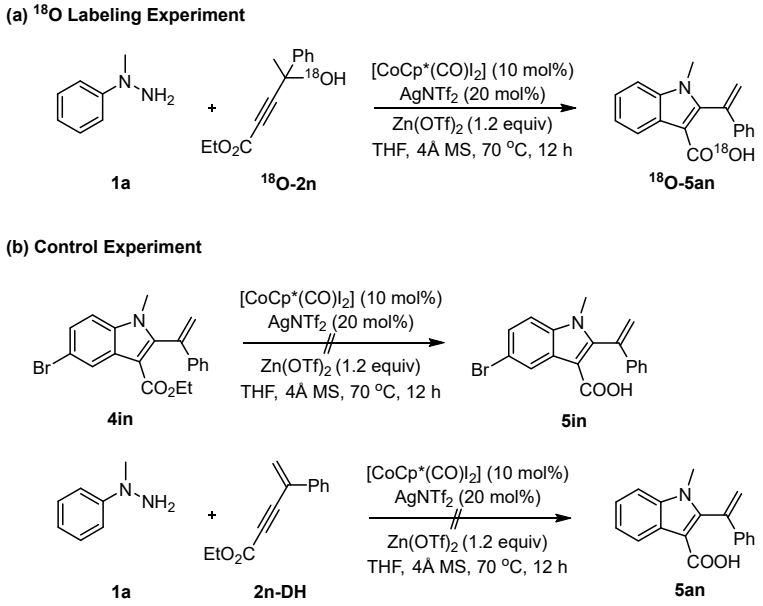


[a]Reaction condition: **1** (0.2 mmol), **2** (0.2 mmol), [CoCp*(CO)I_2] (10 mol%), $AgNTf_2$ (20 mol%), $Zn(OTf)_2$ (0.24 mmol), THF (1 mL), 4Å MS (200 mg), 70 °C, 12 h. [b]Isolated yields.

bromo group (**1i**, 66%) furnishes a higher yield. The yield for the methoxycarbonyl group (**1j**, 46%) is essentially on par with that for the trifluoromethyl group (**1k**, 48%). For the *ortho* substitution, the reaction can proceed for the fluoro group (**1o**, 35%). For the *meta* substitution, the yield is lower for the methyl (**1q**, 51%) and bromo (**1t**, 49%) groups as compared to the *para* counterparts, and is the lowest for the chloro group (**1s**, 44%) among the *meta* counterparts. The 4-hydroxy-2-alkynoate side is explored second, with **1a** as the specified coupling partner. For the substitution on the phenyl ring of **2n**, both *para* bromo group (**2o**, 52%) and *ortho* methyl group (**2p**, 40%) can be accepted. The chain extension of methyl group (**2n**) to ethyl group (**2q**, 50%) can also afford the product.

Mechanistically, three lines of evidence support the operation of skeleton-chaperoned reactivity sequence (phenyl skeleton-chaperoned formation of pyrrole skeleton, pyrrole skeleton-chaperoned formation of lactone skeleton, lactone skeleton-chaperoned self-ring-opening formation of alkene and carboxylic acid groups) in the conversion of hydrazine and 4-hydroxy-2-alkynoate to 2-alkene-3-carboxylic acid type indole derivative (e.g., **5an**) (Scheme 5): 1. The reaction between **1a** and a hydroxyl ^{18}O-labeled **2n** (**^{18}O-2n**) generates, exclusively, a carboxylic acid ^{18}O-labeled **5an** (**^{18}O-5an**);[14] 2. An attempted reaction of **4in** under the synthetic condition for 2-alkene-3-carboxylic acid type indole derivative fails to deliver any product; 3. An attempted reaction between **1a** and ethyl 4-phenylpent-4-en-2-ynoate (**2n-DH**) under the synthetic condition for 2-alkene-3-carboxylic acid type indole derivative is also not successful.

Scheme 5. Mechanistic Experiments.



In summary, a Co(III) catalytic method has been developed for *N*-amino-directed C-H coupling with 4-hydroxy-2-alkynoates, allowing the construction of 2-alkene-3-carboxylic acid type indole derivatives.[15] The reaction features skeleton-chaperoned reactivity as a high transformation economy synthetic mode for the simultaneous conversions of five functional groups. Given the vast number of skeletons available for facilitating the coordination of functional groups into a proper reactive channel, skeleton-chaperoned reactivity promises to become a powerful tool for the expedient diversity generation of chemical space.[16]

References

(1) (a) Zhang, Z.; Zhu, Q.; Pyle, D.; Zhou, X.; Dong, G. Methyl ketones as alkyl halide surrogates: a deacylative halogenation approach for strategic functional group conversions. *J. Am. Chem. Soc.* **2023**, *145*, 21096-21103. (b) Li, Y.; Liu, L.; Shan, D.; Liang, F.; Wang, S.; Yu, L.; Liu, J.-Q.; Wang, Q.; Shao, X.; Zhu, D. Exploration on metal-catalytic conversion of culfinyl sulfones. *ACS Catal.* **2023**, *13*, 13474-13483.

(2) (a) Liu, J.; Jia, X.; Huang, L. Sulfilimines as transformable and retainable directing groups in rhodium-catalyzed ortho-C-H bond functionalization. *Org. Lett.* **2022**, *24*, 6772-6776. (b) Kang, Y. C.; Wetterer, R. T.; Karimov, R. R.; Kojima, M.; Surke, M.; Martín-Torres, I.; Nicolai, J.; Elkin, M.; Hartwig, J. F. Substitution, elimination, and integration of methyl groups in terpenes Initiated by C-H bond functionalization. *ACS Cent. Sci.* **2024**, *10*, 2016-2027. (c) Ren, X.; Wang, Z.; Shen, C.; Tian, X.; Tang, L.; Ji, X.; Dong, K. Asymmetric alkoxy- and hydroxy-carbonylations of functionalized alkenes assisted by *β*-carbonyl groups. *Angew. Chem., Int. Ed.* **2021**, *60*, 17693-17700.

(3) Zhu, S.; Wang, H.; Liu, S.; Yu, R.; Ma, Y.; Zhang, R.; Fang, Y.; Lan, Y.; Shen, R. Access to indenofluorene skeletons via Pd-catalyzed sequential reaction involving cyclization of indenone-allenyne intermediates. *Org. Chem. Front.* **2024**, *11*, 5884-5889.

(4) Song, Y.; Li, C.; Hu, X.; Zhang, H.; Mao, Y.; Wang, X.; Wang, C.; Hu, L.; Yan, J. Light-promoted photocatalyst-free and redox-neutral hydrosulfonylation of unactivated alkenes using sulfinic acid. *Green Chem.* **2024**, *26*, 6578-6583.

(5) (a) Tian, Y.; Tian, L.; Li, C.; Jia, X.; Li, J. Temperature-dependent double isocyanide insertion reaction to construct a polycyclic skeleton. *Org. Lett.* **2016**, *18*, 840-843. (b)

Zech, A.; Jandl, C.; Bach, T. Concise access to the skeleton of protoilludane sesquiterpenes through a photochemical reaction cascade: total synthesis of atlanticone C. *Angew. Chem., Int. Ed.* **2019**, *58*, 14629-14632.

(6) (a) Zhou, S.; Wang, J.; Zhang, F.; Song, C.; Zhu, J. A Versatile, Traceless C-H activation-based approach for the synthesis of heterocycles. *Org. Lett.* **2016**, *18*, 2427-2430. (b) Zhou, S.; Wang, J.; Wang, L.; Chen, K.; Song, C.; Zhu, J. Co(III)-catalyzed, internal and terminal alkyne-compatible synthesis of indoles. *Org. Lett.* **2016**, *18*, 3806-3809.

(7) Zheng, L.; Zhuo, X.; Wang, Y.; Zou, X.; Zhong, Y.; Guo, W. Photocatalytic cross-dehydrogenative coupling reaction toward the synthesis of *N,N*-disubstituted hydrazides and their bromides. *Org. Chem. Front.* **2022**, *9*, 3012-3021.

(8) Moseley, D. F.; Kalepu, J.; Willis, M. C. Azine-*N*-oxides as effective controlling groups for Rh-catalysed intermolecular alkyne hydroacylation. *Chem. Sci.* **2021**, *12*, 13068-13073.

(9) Su, W.; Qiao, R..; Jiang, Y.; Zhen, X.; Tian, X.; Han, J.; Fan, S.; Cheng, Q.; Liu, S. Ligand-free iron-catalyzed regioselectivity-controlled hydroboration of aliphatic terminal alkenes. *ACS Catal.* **2020**, *10*, 11963-11970.

(10) (a) Hanchate, V.; Kumar, A.; Prabhu, K. R. Synthesis of naphthols by Rh(III)-catalyzed domino C-H activation, annulation, and lactonization using sulfoxonium ylide as a traceless directing group. *Org. Lett.* **2019**, *21*, 8424-8428. (b) Von Münchow, T.; Dana, S.; Xu, Y.; Yuan, B.; Ackermann, L. Enantioselective electrochemical cobalt-catalyzed aryl C-H activation reactions. *Science* **2023**, *379*, 1036-1042. (c) Liu, Y.;

Yang, Z.; Chauvin, R.; Fu, W.; Yao, Z.; Wang, L.; Cui, X. One-pot synthesis of furo[3,4-*c*]indolo[2,1-*a*]isoquinolines through Rh (III)-catalyzed cascade reactions of 2-phenylindoles with 4-hydroxy-2-alkynoates. *Org. Lett.* **2020**, *22*, 5140-5144.

(11) Muniraj, N.; Kumar, A.; Prabhu, K. R. Cobalt-catalyzed regioselective [4+2] annulation/lactonization of benzamides with 4-hydroxy-2-alkynoates under aerobic conditions. *Adv. Synth. Catal.* **2020**, *362*, 152-159.

(12) Song, X.; Gao, C.; Li, B.; Zhang, X.; Fan, X. Regioselective synthesis of 2-alkenylindoles and 2-alkenylindole-3-carboxylates through the cascade reactions of *N*-Nitrosoanilines with propargyl alcohols. *J. Org. Chem.* **2018**, *83*, 8509-8521.

(13) Jeyakannu, P.; Senadi, G. C.; Chiang, C.; Dhandabani, G. K.; Chang, Y.-C.; Wang, J.-J. An efficient approach to functionalized indoles from λ-Iodanes via acyloxylation and acyl transfer. *Adv. Synth. Catal.* **2020**, *362*, 2911-2920.

(14) Chen, H.; Yang, W.; Zhang, J.; Lu, B.; Wang, X. Divergent geminal alkynylation-allylation and acylation-allylation of carbenes: evolution and roles of two transition-metal catalysts. *J. Am. Chem. Soc.* **2024**, *146*, 4727-4740.

(15) (a) Bouayad-Gervais, S.; Scattolin, T.; Schoenebeck, F. *N*-trifluoromethyl hydrazines, indoles and their derivatives. *Angew. Chem., Int. Ed.* **2020**, *59*, 11908-11912. (b) Bariwal, J.; Voskressensky, L. G.; Van der Eycken, E. V. Recent advances in spirocyclization of indole derivatives. *Chem. Soc. Rev.* **2018**, *47*, 3831-3848. (c) Zhang, H.; Shi, F. Organocatalytic atroposelective synthesis of indole derivatives bearing axial chirality: strategies and applications. *Acc. Chem. Res.* **2022**, *55*, 2562-2580.

(16) CCDC 2418369 (**3da**) and 2418370 (**5an**) contain the supplementary

crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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