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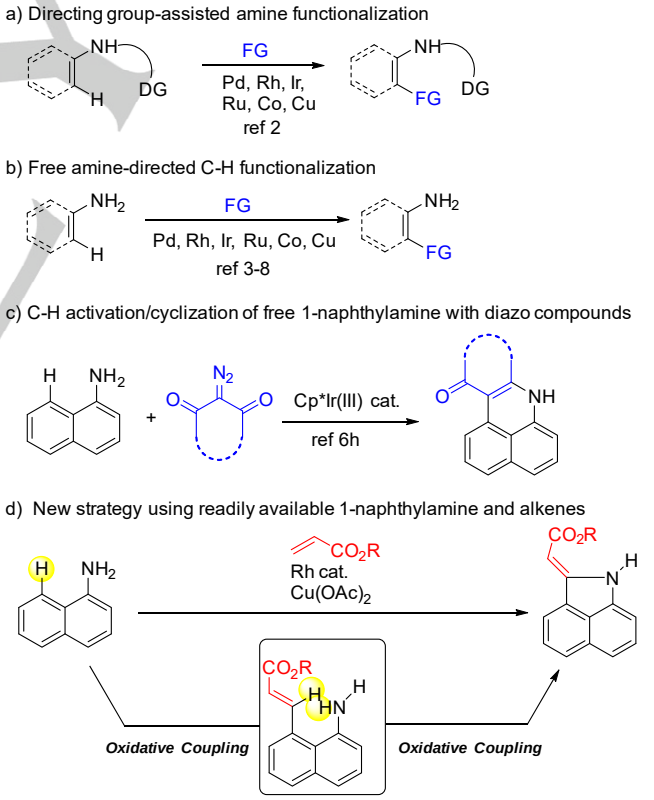
Rh(III)-catalyzed Double Dehydrogenative Coupling of Free 1-Naphthylamines with α,β-Unsaturated Esters

Supriya Rej and Naoto Chatani*

Abstract: The Rh(III)-catalyzed, consecutive double C-H oxidative coupling of free 1-naphthylamine and α,β-unsaturated esters through C-H/C-H and C-H/N-H coupling is reported. The one step reaction leads to the formation of biologically important alkylidene-1,2-dihydrobenzo[*cd*]indoles scaffolds. This efficient process is much more synthetically convenient and useful than others because the starting materials, such as 1-naphthylamine derivatives are readily available and the free amine serves as a directing group.

In the field of C–H bond activation chemistry, significant progress has been made in the development of strategies for the direct functionalization of organic compounds by incorporating a suitable directing group.[1] In this regard, the C–H bond activation of amine derivatives is a reaction of major interest because amines are an industrially and synthetically important class of organic compounds. Many pioneering studies on the selective functionalization of C–H bonds in amines in which a directing group strategy is used have been reported (Scheme 1a).[2] However, in such cases, the introduction of a directing group prior to the actual functionalization and its removal after the C-H functionalization are needed, leading to multi-step processes. Hence, to solve this problem, many research groups have focused their studies on the direct C–H bond activation of free amines (Scheme 1b).[3-8] A variety of functionalizations including arylation, alkylation, alkenylation, alkynylation, annulation, acetoxylation, carbonylation, intramolecular or intermolecular amination, and trifluoromethylation using Pd,[3] Rh,[4] Ru,[5] Ir,[6] Co,[7] and Cu complexes[8] as catalysts have been reported. Although a variety of free amines can be used in C-H functionalization reactions, the use of free 1-naphthylamine as a substrate is currently limited due to the regio-selectivity issue between the C2 and C8-position. Conversely, to achieve functionalization at the C8-position of 1-naphthylamines, directing group strategies using various directing groups have been extensively explored.[9] To the best of our knowledge, only one example is available that deals with the Ir-catalyzed C8-H activation and cyclization of free 1-naphthylamine with diazo compounds to afford naphtha[1,8-*bc*]pyridine derivatives (Scheme 1c).[6h] Therefore, functionalizing C-H bonds of free 1-naphthylamine derivatives is a subject of considerable interest.

In the family of *N*-heterocyclic compounds, alkylidene-1,2-dihydrobenzo[*cd*]indoles are one of the important structural cores that are found in various biologically useful compounds such as antitumor drugs and kinase inhibitors.[10] These scaffolds are also useful for the synthesis of dyes, which are used as fluorescent materials and cell-imaging probes.[11] A few known synthetic methods have been reported for the synthesis of these compounds,[12] but all of them require the use of pre-functionalized starting materials. To address the step economic issue, we were prompted to develop a suitable single step route for the synthesis of alkylidene-1,2-dihydrobenzo[*cd*]indoles from readily available starting materials. Due to the substantial importance of this class of compounds and having a continuous interest in the functionalization of 1-naphthylamine,[9l] we, for the first time, report on the direct Rh(III)-catalyzed C8-H functionalization of free 1-naphthylamines with α,β-unsaturated esters via two consecutive double C–H oxidative coupling reactions to afford alkylidene-1,2-dihydrobenzo[*cd*]indole derivatives (Scheme 1d).



Scheme 1. (a) Directing group assisted C-H bond functionalization of amines, (b) free amine-assisted C-H bond functionalization, (c) C-H activation/cyclization of free 1-naphthylamine with diazo compounds, and (d) this work: two consecutive double oxidative couplings of 1-naphthylamine and acrylate esters to give an alkylidene-1,2-dihydrobenzo[*cd*]indole.

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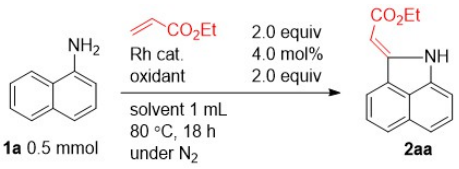
Table 1. Optimization of the consecutive double C-H oxidative coupling of 1-naphthylamine (**1a**) and ethyl acrylate [a]

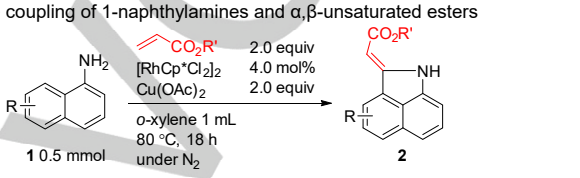


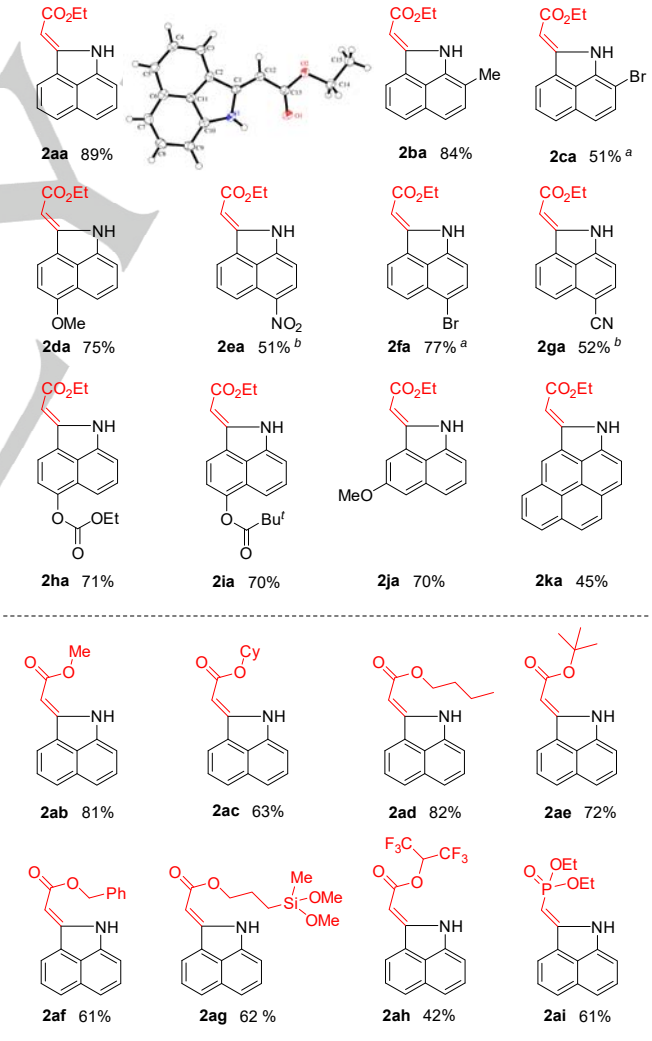
entry	Rh cat.	oxidant	solvent	**2**
1	$[RhCp^*Cl_2]_2$ (2.0 mol%)	-	*o*-xylene	n.d.
2[b]	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	38
3	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	63
4[c]	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	58
5[d]	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	55
6	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	toluene	52
7	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	chloro-benzene	51
8	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	DCE	38
9	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	DMF	45
10	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	HFIP	n.d.
11	$[RhCp^*Cl_2]_2$ (4.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	88
12	$[RhCp^*Cl_2]_2$ (4.0 mol%)	Ag_2CO_3	*o*-xylene	n.d.
13	$[RhCp^*Cl_2]_2$ (4.0 mol%)	$Cu(OAc)_2$	*o*-xylene	92 (89)
14[e]	$[RhCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	18
15	-	$Cu(OAc)_2$	*o*-xylene	n.d.
16	$[Rh(OAc)(cod)]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	n.d.
17	$Pd(OAc)_2$ (4.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	n.d.
18	$[IrCp^*Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	n.d.
19	$[Ru(p\text{-cymene})Cl_2]_2$ (2.0 mol%)	$Cu(OAc)_2•H_2O$	*o*-xylene	n.d.

Reaction conditions: 1-naphthylamine (0.5 mmol), oxidant (1.0 mmol), Rh cat. (0.01 mmol, 2 mol% or 0.02 mmol, 4 mol%), ethyl acrylate (1.0 mmol) in solvent (1 mL) under N_2 at 80 °C for 18 h. [a] Yields were determined from ^1H NMR spectra of crude mixtures. Isolated yield is given in parentheses. n.d. refers to not detected. [b] 1.0 equiv $Cu(OAc)_2•H_2O$. [c] 2.2 equiv of $Cu(OAc)_2•H_2O$. [d] 3.0 equiv ethyl acrylate. [e] Under air.

We began our studies by investigating suitable conditions for the reaction of 1-naphthylamine with ethyl acrylate using $[RhCp^*Cl_2]_2$ as a catalyst, as shown in Table 1. An initial experiment was done in the absence of an oxidant, which resulted in no product (entry 1). The use of 1 equiv. of $Cu(OAc)_2•H_2O$ as an oxidant gave **2aa** in 38% yield (entry 2). The use of 2 equiv. of $Cu(OAc)_2•H_2O$ resulted in an increase in product yield to 63% (entry 3). The necessity for 2 equiv. of oxidant was due to the fact that the product is formed through two oxidative coupling of C–H/C–H and C–H/N–H. The use of excess oxidant (more than 2 equiv.) or coupling partner did not increase the product yield (entries 4 and 5). *o*-Xylene was the best solvent over toluene, chlorobenzene, DCE, DMF, and HFIP (entry 3 vs entries 6–10). Increasing the catalyst loading to 4 mol% sharply increased the product yield (entry 11). After a screening of oxidants was performed (entries 12 and 13), we found that the use of 4 mol% $[RhCp^*Cl_2]_2$ and 2 equiv of $Cu(OAc)_2$ in *o*-xylene at 80 °C for 18 h produced **2aa** in 89% isolated yield (entry 13). Product yields were poor when the reaction was carried out in the presence of air (entry 14) and, as expected, no product was formed in the absence of a catalyst (entry 15). Various other catalysts such as $[Rh(OAc)(cod)]_2$, $Pd(OAc)_2$, $[IrCp^*Cl_2]_2$, $[Ru(p\text{-cymene})Cl_2]_2$ were also tested but none of them gave the desired product (entries 16-19).

Table 2. Substrate scope for Rh(III)-catalyzed, consecutive double C-H oxidative coupling of 1-naphthylamines and α,β-unsaturated esters





Amine (0.5 mmol), $Cu(OAc)_2$ (1.0 mmol), $[RhCp^*Cl_2]_2$ (0.02 mmol, 4 mol%), acrylate ester (1.0 mmol) in *o*-xylene (1 mL) under N_2 at 80 °C for 18 h. Isolated yields are reported. [a] 5 mol % catalyst. [b] 8 mol% catalyst.

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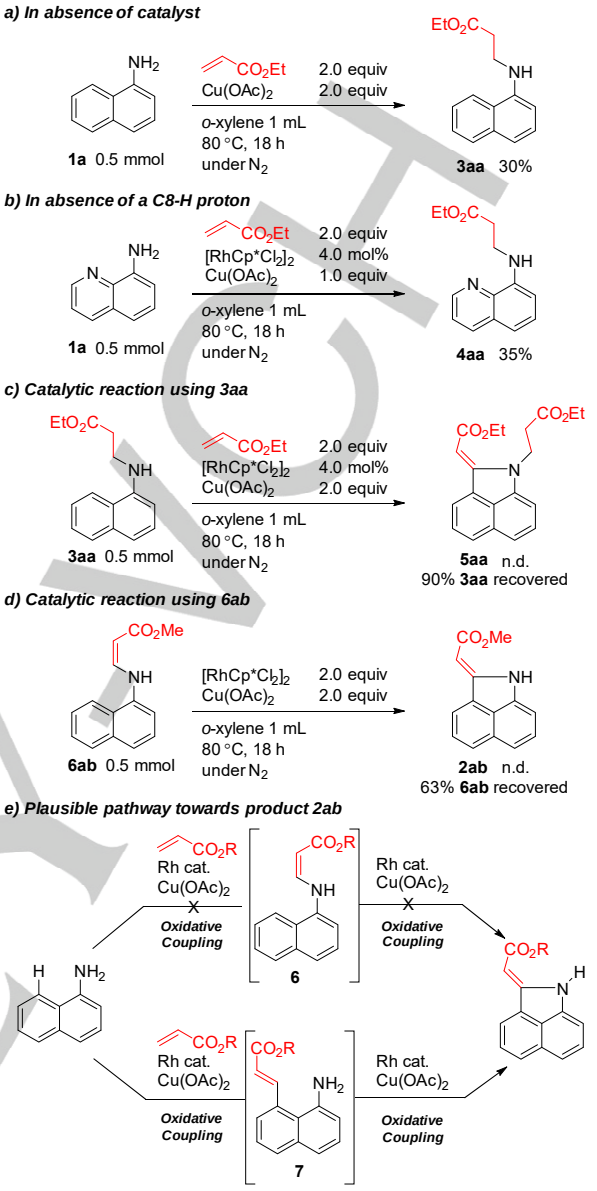
With the optimized reaction conditions in hand, substrate scope was examined for this double C–H oxidative coupling of 1-naphthylamine derivatives and α,β-unsaturated esters (Table 2). Notably, the reaction displayed a good substrate applicability with a high functional group tolerance for substituent groups such as –OMe, –NO_2, –Br, –CN, –OC(O)OEt, and –OC(O)^{t}Bu to give the corresponding products in good yields in the range of 51-84% (**2ca-ja**). Notably, along with C4, C5, C6-substituted 1-naphthylamine derivatives, –Br or –Me substituted 1-naphthylamines at the C2-position also gave impressive results despite steric effects (**2ba** and **2ca**). This protocol was applicable for use with a pyrene derivative, which gave the desired product **2ka**. Other α,β-unsaturated esters, such as methyl acrylate, cyclohexyl acrylate, *n*-butyl acrylate, *t*-butyl acrylate, benzyl acrylate, 3-[dimethoxy(methyl)silyl]propyl acrylate, and 1,1,1,3,3,3-hexafluoroisopropyl acrylate were examined as coupling partners for this cyclization reaction with the desired products being produced in good yields in the range of 42-81%. Diethyl vinylphosphonate was also found to react smoothly with 1-naphthylamine to give the desired product **2ai**.

In order to shed light on the pathway for this reaction, a series of control experiments were performed, as shown in Scheme 2. A reaction of 1-naphthylamine and ethyl acrylate was performed under the optimized reaction conditions, but in the absence of the Rh(III) catalyst (Scheme 2a). As expected, the desired product was not formed as indicated in entry 15, Table 1, instead a simple 1,4-addition product **3aa** was formed. The fact that amines react readily with acrylate esters prompted us to assume that the first step in the reaction involved the dehydrogenating coupling of the N–H of 1-naphthylamine and β-C–H of the acrylate ester, with **6ab** being formed as an intermediate.[13] To trap this proposed intermediate, 8-aminoquinoline that contains no C8–H bond was used as a substrate, however, only **4aa** was formed, which is similar to **3aa** (Scheme 2b). Even when **3aa** was used as a substrate, the corresponding product **5aa** was not formed (Scheme 2c). When **6ab** was synthesized by following a literature protocol[13] and exposed to the catalytic conditions, the expected cyclized product **2ab** was not formed (Scheme 2d). From these control experiments, we concluded that, instead of **6**, compound **7** is formed as an intermediate (Scheme 2e). All attempts to trap **7** were unsuccessful due to the rapid cyclization that occurred through C-H/N-H annulation. Therefore, we anticipated that, instead of the free amine **7** being formed, a Rh-complex coordinated with an alkene part in **7** might be generated as an intermediate (*vide infra*, Scheme 4, intermediate **C**).

Next, deuterium labeling studies was carried out (Scheme 3). When 1-naphthylamine was reacted with a catalytic amount of $[RhCp^*Cl_2]_2$ in the presence of ethanol-d_6, H/D exchange took place at all positions of the naphthalene ring (Scheme 3a). In addition to the activated positions in 1-naphthylamine, such as C2 and C4, significant amounts of H/D exchange were detected at the C8-position (0.18 D). This result suggests that a five-membered rhodacycle is formed via the activation of the C8–H bond. Surprisingly, when deuterated benzyl acrylate was used as an alkene, a significant amount of deuterium loss (0.06 D) was observed at the α-position in the product **2af** (Scheme 3b). In this reaction, when the unreacted benzyl acrylate was isolated, almost no D/H scrambling had taken place.



Scheme 2. Control experiments.

To investigate the reason for why D/H scrambling occurs at the α-position of the product **2af**, we performed a control reaction in which **2af** was reacted with a catalytic amount of $[RhCp^*Cl_2]_2$ in the presence of ethanol-d_6. We eventually observed significant H/D exchange (0.40 D) at the α-position of the product **2af'**, even within a short reaction period (Scheme 3c). This result explains the reason for the unusual H-incorporation in product **2af**, as mentioned in Scheme 3b. Conversely, since H/D exchange at the α-position of **2af'** was slightly lower than expected, we anticipated that D/H exchange also proceeds in the catalytic cycle because a stoichiometric amount of a carboxylic acid is generated during the reaction and the acid appears to promote D/H exchange through an unknown process.

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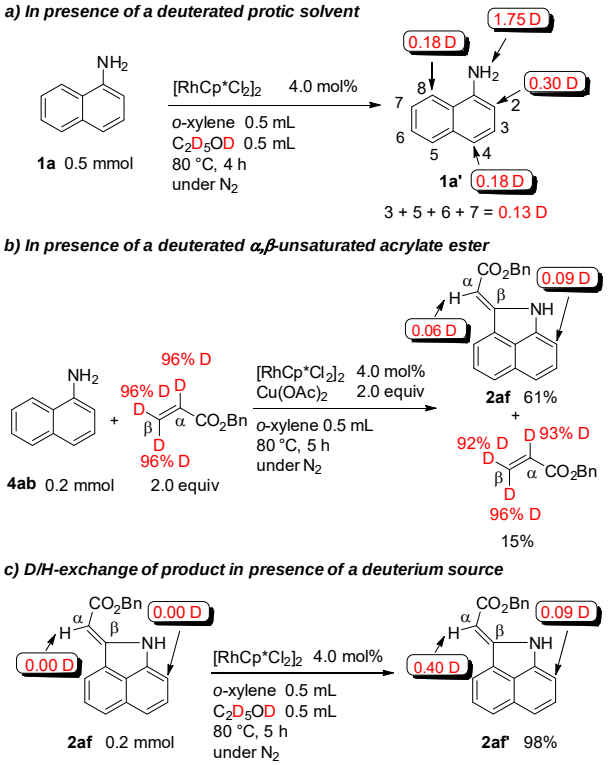
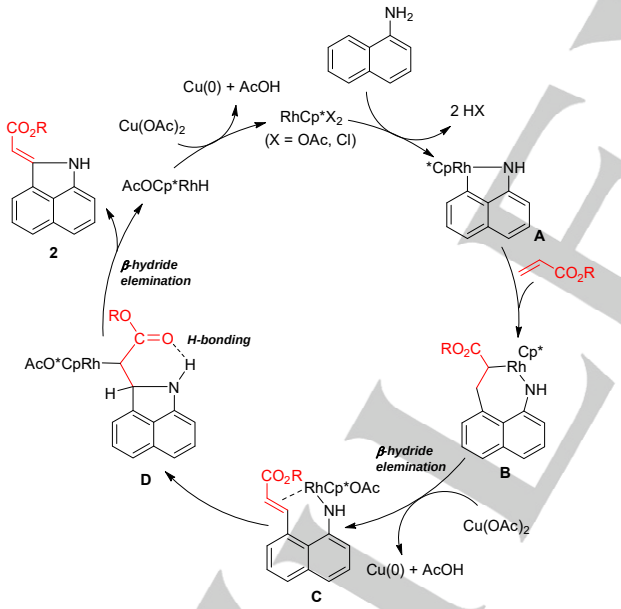


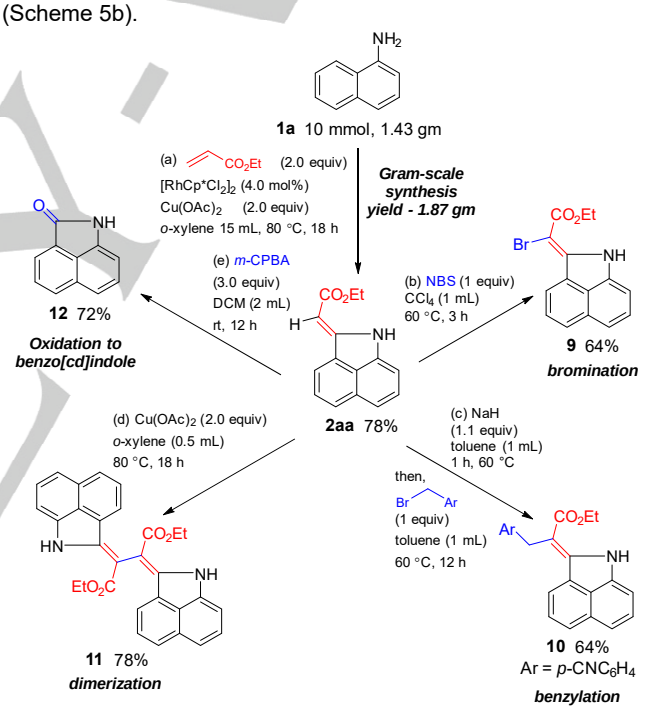
Scheme 3. Deuterium labelling experiments.



Scheme 4. Proposed catalytic cycle

Based on the control experiments and deuterium labeling studies, we propose a plausible mechanism for this consecutive double oxidative coupling of C–H/C–H and C–H/N–H bonds (Scheme 4). The coordination of an amine to a Rh-center initiates directed C–H bond activation at the C8-position to form intermediate **A**, along with the generation of two equivalents of acid. The migratory insertion of the acrylate ester into a Rh–C bond in **A** forms **B**.[4e] β-Hydride elimination, followed by the oxidation of the Rh-hydride species by $Cu(OAc)_2$ gives intermediate **C**.[14a,c] The insertion of an alkene into a N-Rh bond subsequently forms intermediate **D**. The second β-hydride elimination then takes place to produce the product **2**, along with the Rh-H species, which is oxidized by $Cu(OAc)_2$ to regenerate the catalytically active species. The exclusive *Z*-configuration of **2** can be explained by the formation of an intramolecular hydrogen bond which forms a favorable six-membered ring (intermediate **D**).[14]

It should also be noted that this Rh(III)-catalyzed, consecutive double oxidative coupling of 1-naphthylamine and acrylate ester can be used on a gram-scale. When **1a** (10.0 mmol) was reacted with ethyl acrylate under the optimization reaction conditions, the desired product **2aa** was obtained in 78% yield (Scheme 5a). Due to the high reactivity of the α-C-H bond of **2aa** (as observed in Scheme 3c, compound **2af**), a bromination reaction using *N*-bromosuccinimide (**9**; Scheme 5b) and a benzylation reaction using a benzyl bromide derivative (**10**; Scheme 5c) were successfully achieved. A dimerization reaction was also accomplished when the reaction was performed with $Cu(OAc)_2$ as an oxidant (**11**; Scheme 5d). Alkylidene-1,2-dihydrobenzo[cd]indole **2aa** was successfully oxidized to benzo[*cd*]indol-2(1*H*)-one (**12**) using *m*-CPBA as the oxidant (Scheme 5b).



Scheme 5. (a) Gram-scale synthesis and (b-e) application of coupling product

In summary, we report herein on the first example of the synthesis of biologically important 1,2-dihydrobenzo[*cd*]indole scaffolds in one step by the reaction of readily available free 1-naphthylamines with α,β-unsaturated esters in the presence of Rh(III) as a catalyst and $Cu(OAc)_2$ as an oxidant. A large window of functional group tolerance was observed, with the desired products being formed in good yields. Due to the high reactivity of the products, they can be easily transformed to a variety of important compounds.

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Keywords: C-H activation • Oxidative coupling • Rh(III) catalyst • 1-Naphthylamine • Acrylate esters

[1] Recent reviews on C-H bond activation, see: (a) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, *Org. Chem. Front.* **2015**, *2*, 1107–1295. (b) Z. Huang, H. N. Lim, F. Mo, M. C. Young, G. Dong, *Chem. Soc. Rev.* **2015**, *44*, 7764–7786. (c) T. Gensch, M. N. Hopkinson, F. Glorius, J. Wencel-Delord, *Chem. Soc. Rev.* **2016**, *45*, 2900–2936. (d) J. He, M. Wasa, K. S. L. Chan, Q. Shao, J.-Q. Yu, *Chem. Rev.* **2017**, *117*, 8754–8786. (e) J. R. Hummel, J. A. Boerth, J. A. Ellman, *Chem. Rev.* **2017**, *117*, 9163–9227. (f) Y. Park, Y. Kim, S. Chang, *Chem. Rev.* **2017**, *117*, 9247–9301. (g) Y. Yang, J. Lan, J. You, *Chem. Rev.* **2017**, *117*, 8787–8863. (h) C. Sambiagio, D. Schönbauer, R. Blieck, T. Dao-Huy, G. Pototschnig, P. Schaaf, T. Wiesinger, M. F. Zia, J. Wencel-Delord, T. Besset, et al., *Chem. Soc. Rev.* **2018**, *47*, 6603–6743. (i) A. Dey, S. K. Sinha, T. K. Achar, D. Maiti, *Angew. Chem. Int. Ed.* **2019**, *58*, 10820–10843. (j) P. Gandeepan, T. Muller, D. Zell, G. Cera, S. Warratz, L. Ackermann, *Chem. Rev.* **2019**, *119*, 2192–2452. (k) S. M. Khake, N. Chatani, *Trends Chem.* **2019**, *1*, 524–539. (l) S. Rej, Y. Ano, N. Chatani, *Chem. Rev.* **2020**, *120*, 1788–1887.

[2] Reviews on the directing group assisted C-H activation of amine derivatives, see: (a) S. Agasti, A. Dey, D. Maiti, *Chem. Commun.* **2017**, *53*, 6544–6556. (b) J. C. K. Chu, T. Rovis, *Angew. Chem. Int. Ed.* **2018**, *57*, 62–101. (c) C. He, W. G. Whitehurst, M. J. Gaunt, *Chem* **2019**, *5*, 1031–1058. (d) S. Rej, N. Chatani, *Angew. Chem. Int. Ed.* **2019**, *58*, 8304–8329.

[3] For the Pd-catalyzed C-H functionalization of free amines, see: (a) B. López, A. Rodriguez, D. Santos, J. Albert, X. Ariza, J. Garcia, J. Granell, *Chem. Commun.* **2011**, *47*, 1054–1056. (b) B. Haffemayer, M. Gulias, M. J. Gaunt, *Chem. Sci.* **2011**, *2*, 312–315. (c) Z. Liang, L. Ju, Y. Xie, L. Huang, Y. Zhang, *Chem. Eur. J.* **2012**, *18*, 15816–15821. (d) Z. Liang, R. Feng, H. Yin, Y. Zhang, *Org. Lett.* **2013**, *15*, 4544–4547. (e) J. Albert, X. Ariza, T. Calvet, M. Font-Bardia, J. Garcia, J. Granell, A. Lamela, B. López, M. Martinez, L. Ortega, et al., *Organometallics* **2013**, *32*, 649–659. (f) M. Miura, C.-G. Feng, S. Ma, J.-Q. Yu, *Org. Lett.* **2013**, *15*, 5258–5261. (g) Z. Liang, J. Yao, K. Wang, H. Li, Y. Zhang, *Chem. Eur. J.* **2013**, *19*, 16825–16831. (h) A. McNally, B. Haffemayer, B. S. L. Collins, M. J. Gaunt, *Nature* **2014**, *510*, 129–133. (i) A. Rodríguez, J. Albert, X. Ariza, J. Garcia, J. Granell, J. Farràs, A. La Mela, E. Nicolás, *J. Org. Chem.* **2014**, *79*, 9578–9585. (j) C. He, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2015**, *54*, 15840–15844. (k) J. Calleja, D. Pla, T. W. Gorman, V. Domingo, B. Haffemayer, M. J. Gaunt, *Nat. Chem.* **2015**, *7*, 1009–1016. (l) Z. Zuo, J. Liu, J. Nan, L. Fan, W. Sun, Y. Wang, X. Luan, *Angew. Chem. Int. Ed.* **2015**, *54*, 15385–15389. (m) H. Taneda, K. Inamoto, Y. Kondo, *Org. Lett.* **2016**, *18*, 2712–2715. (n) S. Yugandar, S. Konda, H. Ila, *J. Org. Chem.* **2016**, *81*, 2035–2052. (o) K. Chen, D. Wang, Z.-W. Li, Z. Liu, F. Pan, Y.-F. Zhang, Z.-J. Shi, *Org. Chem. Front.* **2017**, *4*, 2097–2101. (p) J. Zhu, W. Hu, S. Sun, J. T. Yu, J. Cheng, *Adv. Synth. Catal.* **2017**, *359*, 3725–3728. (q) T. U. Thikekar, C.-M. Sun, *Adv. Synth. Catal.* **2017**, *359*, 3388–3396. (r) A. Mancinelli, C. Alamillo, J. Albert, X. Ariza, H. Etxabe, J. Farràs, J. Garcia, J. Granell, F. J. Quijada, *Organometallics* **2017**, *36*, 911–919. (s) D.-Y. Li, S. Liu, S. Chen, A. Wang, X.-P. Zhu, P.-N. Liu, *ACS Catal.* **2018**, *8*, 6407–6412. (t) C. Zhang, Y. Ding, Y. Gao, S. Li, G. Li, *Org. Lett.* **2018**, *20*, 2595–2598. (u) G. Jiang, W. Hu, J. Li, C. Zhu, W. Wu, H. Jiang, *Chem. Commun.* **2018**, *54*, 1746–1749.

[4] For the Rh-catalyzed C-H functionalization of free amines, see: (a) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2011**, *40*, 600–602. (b) K. Morimoto, M. Itoh, K. Hirano, T. Satoh, Y. Shibata, K. Tanaka, M. Miura, *Angew. Chem. Int. Ed.* **2012**, *51*, 5359–5362. (c) D.-S. Kim, J.-W. Park, C.-H. Jun, *Adv. Synth. Catal.* **2013**, *355*, 2667–2679. (d) Q. Jiang, D. Duan-Mu, W. Zhong, H. Chen, H. Yan, *Chem. Eur. J.* **2013**, *19*, 1903–1907. (e) C. Suzuki, K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Adv. Synth. Catal.* **2014**, *356*, 1521–1526. (f) C.-Y. Tang, Y. Tao, X.-Y. Wu, F. Sha, *Adv. Synth. Catal.* **2014**, *356*, 609–615. (g) H. Baars, Y. Unoh, T. Okada, K. Hirano, T. Satoh, K. Tanaka, C. Bolm, M. Miura, *Chem. Lett.* **2014**, *43*, 1782–1784. (h) S. Peng, S. Liu, S. Zhang, S. Cao, J. Sun, *Org. Lett.* **2015**, *17*, 5032–5035. (i) P. Bai, X.-F. Huang, G.-D. Xu, Z.-Z. Huang, *Org. Lett.* **2016**, *18*, 3058–3061. (j) A. B. Weinstein, J. A. Ellman, *Org. Lett.* **2016**, *18*, 3294–3297. (k) H. Chu, P. Xue, J.-T. Yu, J. Cheng, *J. Org. Chem.* **2016**, *81*, 8009–8013. (l) Q. Wang, X. Li, *Org. Chem. Front.* **2016**, *3*, 1159–1162. (m) X. Lin, R. Chauvin, Y. Yu, L. Wang, L. Xu, X. Cui, *ChemistrySelect* **2017**, *2*, 2383–2387.

[5] For Ru-catalyzed free amine's C-H functionalization, see: (a) C. Suzuki, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2013**, *15*, 3990–3993. (b) P. Villuendas, E. P. Urriolabeitia, *J. Org. Chem.* **2013**, *78*, 5254–5263. (c) S. Ruiz, P. Villuendas, M. A. Ortuño, A. Lledós, E. P. Urriolabeitia, *Chem. Eur. J.* **2015**, *21*, 8626–8636. (d) S. Ruiz, F. J. Sayago, C. Cativiela, E. P. Urriolabeitia, *J. Mol. Catal. A Chem.* **2017**, *426*, 407–418.

[6] For the Ir-catalyzed C-H functionalization of free amines, see: (a) H. He, W.-B. Liu, L.-X. Dai, S.-L. You, *J. Am. Chem. Soc.* **2009**, *131*, 8346–8347. (b) K.-Y. Ye, H. He, W.-B. Liu, L.-X. Dai, G. Helmchen, S.-L. You, *J. Am. Chem. Soc.* **2011**, *133*, 19006–19014. (c) K.-Y. Ye, L.-X. Dai, S.-L. You, *Asian J. Org. Chem.* **2013**, *2*, 244–249. (d) C. Suzuki, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2015**, *17*, 1597–1600. (e) H. Chen, M. P. Huestis, *ChemCatChem* **2015**, *7*, 743–746. (f) A. Boelke, L. D. Caspers, B. J. Nachtsheim, *Org. Lett.* **2017**, *19*, 5344–5347. (g) L. D. Caspers, P. Finkbeiner, B. J. Nachtsheim, *Chem. Eur. J.* **2017**, *23*, 2748–2752. (h) K. Yan, Y. Lin, Y. Kong, B. Li, B. Wang, *Adv. Synth. Catal.* **2019**, *361*, 1570–1575.

[7] For the Co-catalyzed C-H functionalization of free amines, see: (a) T.-H. Zhu, S.-Y. Wang, Y.-Q. Tao, T.-Q. Wei, S.-J. Ji, *Org. Lett.* **2014**, *16*, 1260–1263. (b) P. Xu, T.-H. Zhu, T.-Q. Wei, S.-Y. Wang, S.-J. Ji, *RSC Adv.* **2016**, *6*, 32467–32470.

[8] For a paper on the Cu-mediated C-H functionalization of free amines, see: R. Morioka, K. Hirano, T. Satoh, M. Miura, *Chem. Eur. J.* **2014**, *20*, 12720–12724.

[9] For selected papers on the C8-functionalization of 1-naphthylamines, see: (a) X. Li, X. Gong, M. Zhao, G. Song, J. Deng, X. Li, *Org. Lett.* **2011**, *13*, 5808–5811. (b) X. Wang, X. Li, J. Xiao, Y. Jiang, X. Li, *Synlett* **2012**, *23*, 1649–1652. (c) E. T. Nadres, G. I. F. Santos, D. Shabashov, O. Daugulis, *J. Org. Chem.* **2013**, *78*, 9689–9714. (d) R. Odani, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2013**, *78*, 11045–11052. (e) L. Huang, Q. Li, C. Wang, C. Qi, *J. Org. Chem.* **2013**, *78*, 3030–3038. (f) L. Huang, X. Sun, Q. Li, C. Qi, *J. Org. Chem.* **2014**, *79*, 6720–6725. (g) M. Iwasaki, W. Kaneshika, Y. Tsuchiya, K. Nakajima, Y. Nishihara, *J. Org. Chem.* **2014**, *79*, 11330–11338. (h) R. Shang, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2015**, *137*, 7660–7663. (i) Z. Li, S. Sun, H. Qiao, F. Yang, Y. Zhu, J. Kang, Y. Wu, Y. Wu, *Org. Lett.* **2016**, *18*, 4594–4597. (j) J. Lan, H. Xie, X. Lu, Y. Deng, H. Jiang, W. Zeng, *Org. Lett.* **2017**, *19*, 4279–4282. (k) S. Pradhan, P. B. De, T. Punniyamurthy, *J. Org. Chem.* **2017**, *82*, 4883–4890. (l) S. Rej, N. Chatani, *ACS Catal.* **2018**, *8*, 6699–6706. (m) X. Yu, F. Yang, Y. Wu, Y. Wu, *Org. Lett.* **2019**, *21*, 1726–1729. (n)

[10] For the importance of alkylidene-1,2-dihydrobenzo[cd]indoles derivatives as drugs or kinase inhibitors, see: (a) X. Li, Q. Wang, Y. Qing, Y. Lin, Y. Zhang, X. Qian, J. Cui, *Bioorganic Med. Chem.* **2010**, *18*, 3279–3284. (b) S. H. Sinha, E. A. Owens, Y. Feng, Y. Yang, Y. Xie, Y. Tu, M. Henary, Y. G. Zheng, *Eur. J. Med. Chem.* **2012**, *54*, 647–659. (c) M. Yan, J. Zhao, D. Sun, W. Sun, B. Zhang, W. Deng, D. Zhang, L. Wang, *Tetrahedron* **2017**, *73*, 3355–3362.

[11] For the importance of alkylidene-1,2-dihydrobenzo[cd]indoles as dye, see: (a) C. Cheng, N. Gao, C. Yu, Z. Wang, J. Wang, E. Hao, Y. Wei, X. Mu, Y. Tian, C. Ran, et al., *Org. Lett.* **2015**, *17*, 278–281. (b) D. Gao, A. Li, L. Guan, X. Zhang, L. Y. Wang, *Dye. Pigment.* **2016**, *129*, 163–173. (c) M. Matsui, Y. Haishima, Y. Kubota, K. Funabiki, J. Jin, T. H. Kim, K. Manseki, *Dye. Pigment.* **2017**, *141*, 457–462.

[12] For the synthetic procedure of alkylidene-1,2-dihydrobenzo[cd]indoles see: (a) A. Kamal, G. Ramakrishna, V. Lakshma Nayak, P. Raju, A. V. Subba Rao, A. Viswanath, M. V. P. S. Vishnuvardhan, S. Ramakrishna, G. Srinivas, *Bioorganic Med. Chem.* **2012**, *20*, 789–800. (b) Q. Wang, L.

10.1002/chem.202000706

Zhang, J. Yao, G. Qiu, X. Li, H. Zhou, *J. Org. Chem.* **2018**, *83*, 4092–4098. (c) C. Bi, L. Zhang, G. Qiu, X. Li, J. Yao, H. Zhou, *Org. Biomol. Chem.* **2018**, *16*, 3006–3011.

[13] X. Ji, H. Huang, W. Wu, X. Li, H. Jiang, *J. Org. Chem.* **2013**, *78*, 11155–11162.

[14] (a) F. W. Patureau, T. Besset, F. Glorius, *Angew. Chem. Int. Ed.* **2011**, *50*, 1064–1067. (b) M. C. Reddy, M. Jeganmohan, *Org. Lett.* **2014**, *16*, 4866–4869. (c) X. G. Li, M. Sun, K. Liu, P. N. Liu, *Adv. Synth. Catal.* **2015**, *357*, 395–399

10.1002/chem.202000706

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The Rh(III)-catalyzed double oxidative coupling of free 1-naphthylamines and α,β-unsaturated esters were achieved, leading to the formation of a class of biologically important alkylidene-1,2-dihydrobenzo[*cd*]indoles scaffolds.

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Rh(III)-catalyzed Double Dehydrogenating Coupling of Free 1-Naphthylamines with α,β-Unsaturated Esters