How to cite: *Angew. Chem. Int. Ed.* **2023,** *62,* e202213913
International Edition: doi.org/10.1002/anie.202213913
German Edition: doi.org/10.1002/ange.202213913

Hydroamination

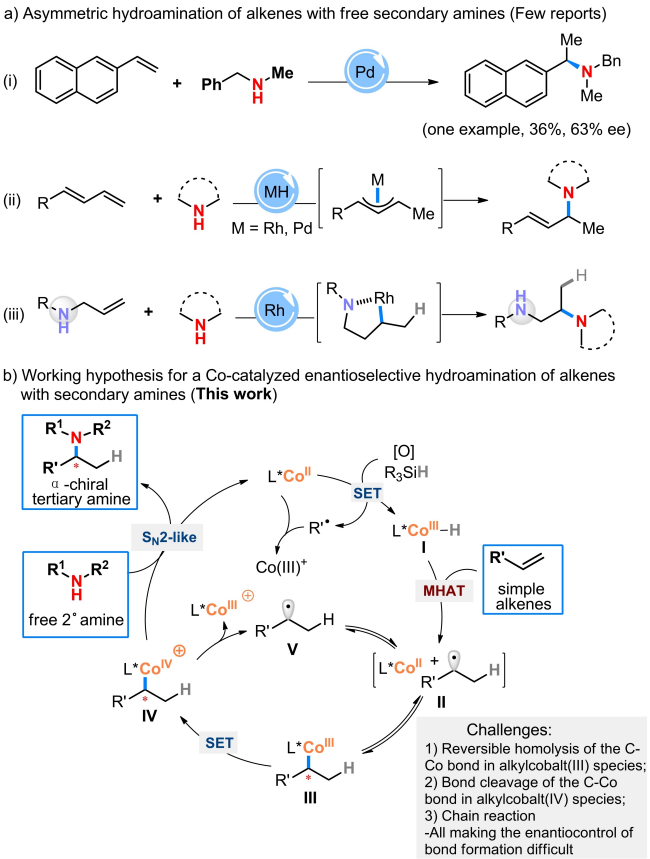
Cobalt-Catalyzed Enantioselective Hydroamination of Arylalkenes with Secondary Amines

Huanran Miao, Meihui Guan, Tao Xiong, Ge Zhang, and Qian Zhang*

Abstract: Catalytic asymmetric hydroamination of alkenes with Lewis basic amines is of great interest but remains a challenge in synthetic chemistry. Here, we developed a Co-catalyzed asymmetric hydroamination of arylalkenes directly using commercially accessible secondary amines. This process enables the efficient access to valuable *α*-chiral tertiary amines in good to excellent yields and enantioselectivities. Mechanistic studies suggest that the reaction includes a CoH-mediated hydrogen atom transfer (MHAT) with arylalkenes, followed by a pivotal catalyst controlled S_N2-like pathway between in situ generated electrophilic cationic alkylcobalt(IV) species and free amines. This radical-polar crossover strategy not only provides a straightforward and alternative approach for the synthesis of enantioenriched *α*-tertiary amines, but also underpins the substantial opportunities in developing asymmetric radical functionalization of alkenes with various free nucleophiles in oxidative MHAT catalysis.

Introduction

The enantioselective synthesis of *α*-chiral tertiary amine derivatives is an important undertaking due to the prevalence of this motif in a large number of biologically active natural products and pharmaceuticals as well as agrochemicals.[1] The asymmetric hydroamination of alkenes undoubtedly offers a direct, effective, and atom-economical approach to these important motifs from readily available starting materials.[2] However, the intermolecular enantioselective hydroamination of alkenes directly using Lewis basic amines as nucleophiles has long been a challenging task in synthetic chemistry. This is mainly due to the intrinsic strong coordination of Lewis basic amines with transition metal and the electrostatic repulsion between the olefin π-system and the nitrogen lone pair, thus most reported asymmetric alkene hydroamination are limited to reactions of amines preinstalled with an electron-withdrawing group.[3] Significant progress recently has been made in the intermolecular enantioselective hydroamination of alkenes with primary amine such as anilines and benzylamines since Togni's seminal report on the asymmetric Ir-catalyzed intermolecular hydroamination of norbornene.[4,5] Yet, the catalytic asymmetric variants directly using Lewis basic secondary amines, especially in an intermolecular manner, remain rarely reported.[6–10] In this respect, Hartwig pioneered a Pd-catalyzed asymmetric hydroamination of 2-vinylnaphthalene with *N*-methylbenzylamine lead to the chiral tertiary amines in moderate enantioselectivity in 2003 (one example, 63 % ee; Scheme 1a, i).[6] Recently, Dong[7] and Malcolmson[8] have demonstrated highly enantio- and regioselective hydroaminations of conjugated alkenes with secon-



Scheme 1. Enantioselective intermolecular hydroamination of alkenes with free secondary amines.

[*] H. Miao, M. Guan, Prof. T. Xiong, Prof. G. Zhang, Prof. Q. Zhang
Jilin Province Key Laboratory of Organic Functional Molecular Design & Synthesis, Department of Chemistry, Northeast Normal University
130024 Changchun (China)
E-mail: zhangg492@nenu.edu.cn
Prof. Q. Zhang
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Lingling Lu, 200032 Shanghai (China)

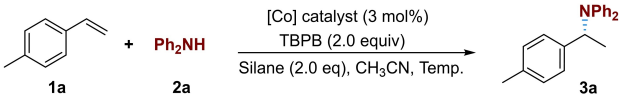
dary amines by leveraging a MH migratory insertion to generate a key metal-π-allyl complex, followed by amine attack, in the presence of chiral Pd and Rh catalysts, respectively (Scheme 1a, ii). By employing an amine-directing alkenes, Schultz and Hull successfully disclosed a Rh-catalyzed enantioselective intermolecular hydroamination of nonactivated alkenes with cyclic secondary amines (Scheme 1a, iii).[9] Despite with these advances, the development of efficient methods for enantioselective alkene hydroamination of secondary amines, especially using the cheap first-row transition metal catalysts, is still an ideal strategy for synthetically important *α*-chiral tertiary amines and particularly appealing.

As a cheap and biocompatible 3d-metal catalyst, cobalt recently was found to exhibit excellent catalytic activity in asymmetric transformation.[11] In particularly, cobalt-catalyzed oxidative functionalization via metal hydride-hydrogen atom transfer (MHAT) has emerged as a practical and promising approach for Markovnikov hydrofunctionalization of alkenes including aliphatic alkenes under mild conditions.[12–14] However, the highly enantioselective hydrofunctionalization of alkenes based on MHAT remains a significantly less explored, given the inherently challenging construction of a chiral carbon from a reactive prochiral radical. With the contribution of Shenvi[15] and Pronin,[16] leveraging an electrophilic alkylcobalt(IV) intermediate offers a rallying point for the asymmetric induction.[17,18] As shown in Scheme 1b, the [L*CoH] species could be generated from the reaction of Co^{II} precursor, oxidant and silanes in situ. Then, a [L*CoH]-mediated HAT to alkenes could give rise to the alkylcobalt(III) species,[15] which then deployed to a further SET oxidation to generate the pivotal alkylcobalt(IV) species.[17,19] Finally, a stereoinversed nucleophilic displacement of the diastereomeric alkylcobalt(IV) complex with nucleophiles occurred to afford the chiral products.[16b,18,20] However, the reversible homolysis of Co–C bonds in alkylcobalt(III) species[21] and the "spontaneous" decomposition of C–Co bonds in diastereometric alkylcobalt(IV) species,[22] as well as the potential radical chain reaction,[23] all of which make the enantiocontrol for new bond forming more complicated and challenging. Recently, we reported an enantioselective cobalt-catalyzed radical hydroamination of alkenes with *N*-fluorobenzenesulfonimides as both nucleophilic nitrogen source and oxidant, whereas sulfonamides were the only valid nitrogen nucleophiles.[18b,24] Therefore, we conceived that such a versatile cobalt hydride mediated asymmetric oxidative HAT strategy might allow the use of readily available amines as modular coupling fragments, thus solving the challenging enantioselective hydroamination using Lewis basic secondary amines. Herein we describe the successful development of enantioselective hydroamination of alkenes with secondary amines via a cobalt hydride-mediated oxidative HAT process. This approach furnishes an expedient and straightforward route to the synthesis of chiral *α*-tertiary amines with moderate to excellent yields and enantioselectivities.

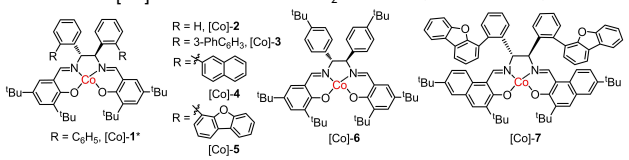
Results and Discussion

We initiated our study by subjecting styrene **1a** and diphenylamine **2a** as the model substrates with *tert-butyl* peroxybenzoate (TBPB), an excellent oxidant in our recently developed asymmetric alkylation,[18c] in the presence of a silane and a catalytic amount of chiral salen-cobalt(II) precatalyst for the asymmetric hydroamination of alkenes (Table 1). The reaction using enantioenriched *o*-phenyl-substituted salen complex ([Co]-**1**) integrated with tetramethyl disiloxane (TMDS), which had proven competent in our previous HAT-initiated asymmetric hydroamidation,[18b] provided the desired product **3a** in 76 % yield and 51 % enantioselective excess (entry 1). After extensive modification of the ethylenediamine-derived fragment in cobalt catalyst, we found that the *ortho*-biaryl substituents had a significant effect on the enantioselectivity (entry 2–6, also see Table S1). For example, switching *o*-phenyl to other more steric (hetero)aryl motifs (e.g. [Co]-**3**–[Co]-**5**) at the *ortho*-position of diamine substructure allowed for significant enhancement of the enantioselectivity; while hydrogen substituted complex, [Co]-**2**, resulted in a sharp decline in the enantiocontrol with moderate reactivity. Notably, the application of dibenzofuran-containing complex [Co]-**5** demonstrated optimal performance to deliver **3a** in 94 % yield with 81 % ee (entry 5). This is likely due to the increasing size of the arene fragment which leads

Table 1: Optimization of the reaction conditions.[a]



Entry[a]	Catalyst	Silane	Yield[b]	EE[c]
1	[Co]-**1**	TMDS	76 %	51 %
2	[Co]-**2**	TMDS	60 %	3 %
3	[Co]-**3**	TMDS	76 %	55 %
4	[Co]-**4**	TMDS	56 %	55 %
5	[Co]-**5**	TMDS	94 %	81 %
6	[Co]-**6**	TMDS	58 %	−17 %
7	[Co]-**7**	TMDS	48 %	35 %
8[d]	[Co]-**5**	TMDS	72 %	83 %
9[d]	[Co]-**5**	$PhSiH_3$	60 %	89 %
10[d]	[Co]-**5**	Et_2SiH_2	76 %	89 %
11[d]	[Co]-**5**	$PhMe_2SiH$	60 %	89 %
12[d]	[Co]-**5**	$PhMeSiH_2$	72 %	90 %
13[d,e]	[Co]-**5**	$PhMeSiH_2$	70 %	91 %



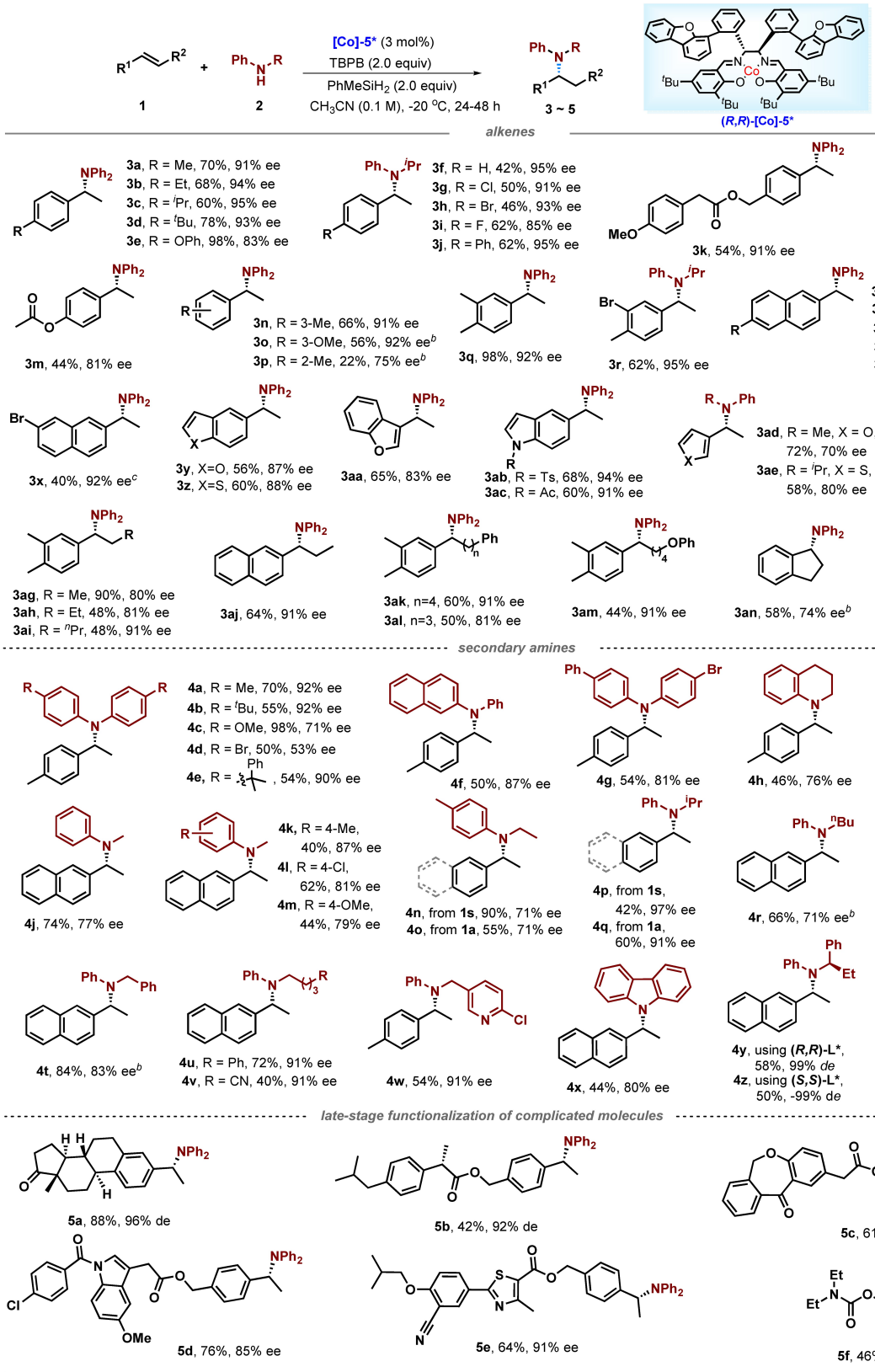
[a] Reaction conditions: styrene **1a** (0.2 mmol), amine **2a** (2.0 equiv), TBPB (2.0 equiv), silane (2.0 equiv) and [Co] catalyst (3 mol %) in CH_3CN (2.0 mL) at 0 °C for 24 h. [b] Yield determined by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard. [c] The ee values were determined by HPLC on a chiral stationary phase. [d] The reaction was conducted at −20 °C for 48 h. [e] Using 1.5 equiv of **2a**. TBPB = *tert-butyl* peroxybenzoate.

to the destabilization of the minor transition state assembly in the enantiodetermining step.[16b] We also altered the salicylaldehyde fragment ([Co]-**7*** vs [Co]-**5***), owing to the potential stabilizing noncovalent interactions in the relevant cobalt complex; however only moderate enantioselectivity and reaction efficiency was observed (entry 7). Lowering the reaction temperature was beneficial for the further improvement of enantioinduction, but required extended reaction time to achieve appreciable conversion (entry 8). In addition, several silanes were evaluated and among which $PhMeSiH_2$ is the best hydrogen supplier in terms of both reactivity and enantiocontrol, providing **3a** in good yield and excellent enantioselectivity (entry 9–12). To our delight, the process could also be conducted at low nucleophile loadings without detrimental effects on the reactivity and enantioselectivity (entry 13). Other conventional solvents (DCM, CF_3Ph, et al.) and oxidants were also examined and slightly inferior results under otherwise optimal reaction conditions were observed. In addition, control reactions demonstrated that all components (cobalt complex, oxidant, and hydrosilane) were required to obtain the product. Full details on the optimization are provided in the Supporting Information.

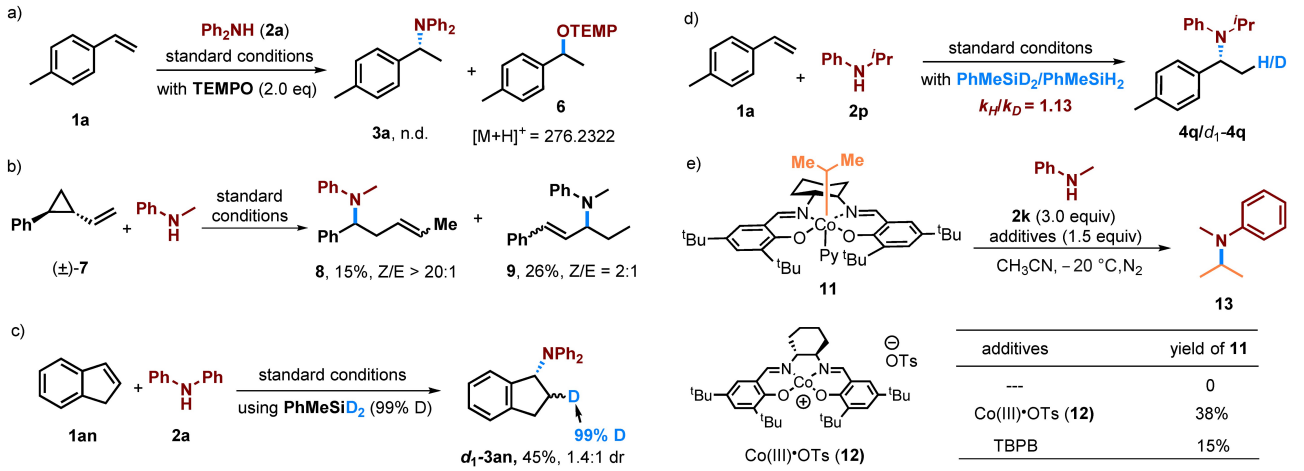
With optimized conditions in hand, we sought to investigate the generality and limitations of this CoH-catalyzed enantioselective hydroamination. As shown in Scheme 2, various styrenes with either electron-donating or electron-withdrawing substituents at *para*-, or *meta*-position on the phenyl ring could participate in this reaction, delivering α-chiral tertiary amines **3a**–**3o** in medium to good yields and uniformly good enantioselectivities. *Ortho*-substituted styrene is modestly effective with a relatively low yield and moderate enantiocontrol of the desired product (**3p**), likely due to the steric hindrance. Bis-substituted or naphthyl ethylenes were also suitable substrates, affording products **3q**–**3x** in good yields and high level of enantiocontrol (73–95 % ee). In the case of less electron-rich styrene, a mass of dimerization was observed, which is attributable to the slower oxidative trapping and elevated free radical concentration. Interestingly, the use of more electron-rich but bulky *N*-isopropyl aniline was found to alleviate this situation slightly, enabling the desired C–N bond formation to proceed smoothly with good yield and excellent enantioselectivity (**3f**–**3j**, **3r**). Reactions involving various heteroaryl-derived alkenes, such as 5-vinylbenzofuran, 5-vinylbenzo[*b*]thiophene, 3-vinylbenzofuran, protected 5-vinylindoles as well as simple 3-vinylfuran and 3-vinylthiophene showed good performance in producing **3y**–**3ae**. 2-Vinylpyridine was also feasible substrate and delivered the expected chiral amines **3af** in moderate yield and enantiocontrol. When a series of β-substituted internal arylalkenes, as well as indene, were applied, the target products **3ag**–**3an** could be obtained with respectable efficiency and enantioselectivity (74–91 % ee). Notably, unactivated alkene **1ao** also enabled this Co-catalyzed enantioselective hydroamination to provide **3ao** in 60 % yield, albeit with low enantioselectivity. This is mainly attributed to the small differentiation between the two alkyl groups, which makes the enanitocontrol more challenging.

The scope of simply secondary amines was next studied. It was found that the amine scope is similarly broad, with both 4-methyl styrene (**1a**) and 2-vinylnaphthalene (**1s**); the regiospecific, enantioselective hydroamination reactions generate a diverse array of highly enantioenriched α-branched tertiary alkylamines. For example, a range of diarylamines participated in this reaction to provide **4a**–**4g** with good to excellent enantioselectivities, albeit a relatively lower enantiomeric excess value for **4d**. Alkyl substituted anilines, such as tetrahydroquinoline and indoline, were suitable nucleophiles to deliver **4h** and **4i**. Acyclic secondary anilines with various *N*-alkyl substituents, including methyl, ethyl, and sterically hindered isopropyl, butyl as well as allyl and benzyl, were also viable nitrogen suppliers, affording the desired chiral tertiary amines **4j**–**4t** with a range of 71 % to 97 % ee. Generally, the more steric hindrance of alkyl in amines shows a high level of enantiocontrol (e.g. **4p** and **4q** versus **4j**, **4n**, and **4o**). The electronic property of the alkene partner also displayed a marginal effect because the enantiocontrol of styrene is slightly different from that of 2-vinyl naphthalene using the same nitrogen suppliers. Some secondary amines pendent a phenyl, or –CN were also effective partners, as well as pyridyl, which may coordinate with transition metal (see **4u**–**4w**). In addition, carbazole, a heterocycle that occurs in bioactive molecules and blockbuster drugs,[25] could be used to deliver **4x**. Gratifyingly, using enantiomeric amines provided the corresponding products with excellent diastereoselectivity, and the stereochemistry of the chiral catalyst, rather than the chiral nucleophile, primarily determined the stereochemistry of the products (see **4y** and **4z**). Importantly, the more Lewis basic dialkyl amine, such as dibenzyl amine, was also capable of participating in this hydroamination, with an enantioselectivity of up to 92 %, when the reaction conditions was slightly modified to add a catalytic amount of Lewis acid $Sc(OTf)_3$.[26] This result is a good complement to the recent dioxygen-promoted cobalt-catalyzed hydroamination of alkenes with free amines to yield racemic tertiary amines reported by Zhu,[27] wherein dialkyl amines were not viable substrates. However, dialkyl amines that without an aryl linked, such as n-Bu_2NH and pyrrolidine, were not viable substrates for the current method, likely due to the strong basicity and coordination with the cobalt catalyst. Furthermore, complexed alkenes containing bioactive skeletons, such as estrone, (+)-ibuprofen, isoxepac and indomethacin could undergo this reaction smoothly to deliver chiral amines derivatives (**5a**–**5e**) in 42–88 % yields, as well as a Rivastigmine analogue (**5f**), in good to excellent diastereo- and enantioselectivities, which exhibited the underlying feasibility in late-stage modification of complicated molecules.

Control experiments lent support to the proposed radical-polar crossover mechanism for this enantioselective hydroamination. First, the catalytic transformation of **1a** and **2a** was completely inhibited in the presence of stoichiometric TEMPO, and the corresponding TEMPO-trapped product **6** was detected (Scheme 3a), which suggests an alkyl radical is probably involved in this transformation, in line with the speculated $Co^{III}H$ mediated HAT.[12,15,18]



Scheme 2. Substrate scope of asymmetric hydroamination. [a] Unless otherwise noted, the reactions were carried out using alkenes **1** (0.20 mmol), amine **2** (1.5 equiv), TBPB (2.0 equiv), $PhSiMeH_2$ (2.0 equiv) and Co-**5** (3 mol%) in CH_3CN (2.0 mL) at −20 °C, isolated yield. The ee values were determined by HPLC on a chiral stationary phase. [b] Using 2.0 equiv amine as nucleophiles. [c] The reaction was conducted at −10 °C for 48 h. [d] Using 5 mol% [Co]-**5**·OTs. [e] Using 20 mol% $Sc(OTf)_3$ as the additives and 2.0 equiv TMDS. [f] The reaction was performed at room temperature.



additives	yield of **11**
---	0
Co(III)•OTs (**12**)	38%
TBPB	15%

Scheme 3. Control experiments: a) Radical inhibition experiment; b) Radical clock reaction; c) Control experiment without amine; d) Deuterium labeling experiment; e) Deuterium isotope effect; f) Stoichiometric reaction with a well-defined organocobalt(III).

This result was further confirmed by the "radical-clock" experiment with alkene **7** (Scheme 3b), which afforded the ring-opened amination products **8** and **9**.[28] In addition, the involvement of alkyl radical was also corroborated by the observation of a small dimerization in the case of electron-deficient styrenes (Supplementary Figure S7). Furthermore, a deuterium-labeled experimental reaction of indene using $PhMeSiD_2$ was conducted to afford ***d*-3an** in 45 % yield with 99 % D and 1.4 : 1 dr (Scheme 3c), which demonstrated that the hydrogen came from silanes and the deuterium incorporation of no more than 99 % indicated the irreversibility of $Co^{III}H$-mediated HAT process. A deuterium kinetic isotope effects (KIEs) were also conducted. The k_H/k_D value for $PhMeSiH_2$ and $PhMeSiD_2$ was found to be 1.13, revealing a secondary kinetic deuterium effect (Scheme 3d).[29] We next performed the stoichiometric reactions using a well-defined alkylcobalt(III) complex **11** (Scheme 3e). It was found that upon the addition of a cationic Co^{III} species **12**, the oxidative amination smoothly took place to afford product **13**, while no amination was observed by mixing **11** with an excess amount of amine. Replacing **12** with stoichiometric TBPB in a similar reaction also yield the amination product. These results suggest that both the cationic Cobalt(III) complex and oxidant (TBPB) could oxidative the alkylcobalt(III) species for the amination occurring.

To gain more insight into the mechanism, we further assessed the detailed kinetic analysis of this CoH-HAT initiated asymmetric hydroamination by conducting kinetic studies on the reaction of 4-methyl styrene **1a** with *N*-isopropyl substituted aniline **2p** as the model reaction. The kinetic profiles were obtained by measuring the initial rates of the reaction at different concentrations of catalyst or reactants (Scheme 4, also see Supplementary Figure S13–S22). The kinetic rate data indicated a second-order dependence on the concentration of cobalt catalyst, and first-order dependence on the concentration of alkene and oxidant, while a zeroth-order was found for the silane and amine. These results revealed that the oxidation of alkylcobalt(III) to the corresponding cationic Co^{IV} specie might be the turnover-limiting step. In addition, the Hammett analysis with a series of competition experiments between styrene and *para*- substituted styrene derivatives were performed, and a linear relationship between $\log(k_{Ar}/k_{Ph})$ and σ yield a negative slope ($\rho = -1.61$) with an R^2 of 0.98. These results implicate a transition state with significant partial positive charge in the rate-determining step, consistent with the formation of an electrophilic Co^{IV} intermediate (Figure 1A).[30] Finally, we also investigated the thermal dependence of the enantioselectivity of this transformation (Figure 1B). It was found that the ee variation was not monotonic with temperature, and a slightly convex Eyring plot is characterized by two lines with an inversion point ($T_{inv} = -20\,°C$), which is the same as the observation in our previous CoH-mediated alkylation of styrene with indoles,[18c] as well as the intramolecular enantioselective hydroalkoxylation reported by Shigehisa.[18a] This nonlinearity indicated that such CoH-HAT initiated enantioselective hydroamination may include no fewer than two enantiodetermining steps.[31] Indeed, there was a slightly decrease in enantioselectivity for the reaction with nondeoxygenated CH_3CN or silane-slow addition experiment (see Supplementary Figure S27–S28), which suggest that concentration of the downstream intermediates, such as a alkylcobalt(III) intermediate and alkyl radical, might affect the enantiocon-

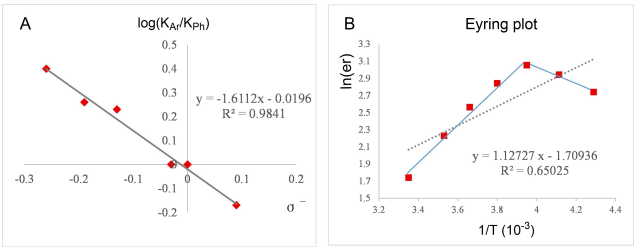
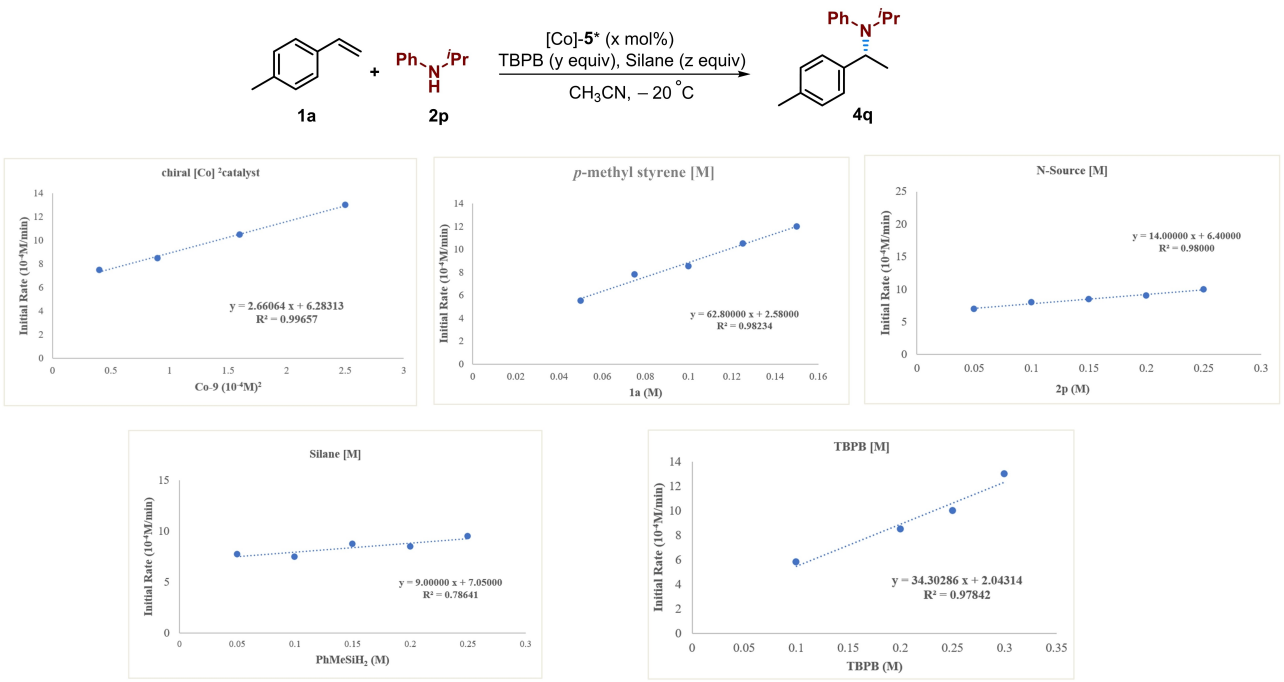


Figure 1. A) Hammett plot. B) Eyring plots. Activation parameters calculated from Eyring plots were $\Delta\Delta H^{\ddagger} = -1.98$ kcal mol^{-1} and $\Delta\Delta S^{\ddagger} = -2.51$ kcal/(mol·K).



Scheme 4. Kinetic studies of the Co-catalyzed enantioselective hydroamination of alkenes with amines.

trol of amination product. Combined with the derived activation parameters from Eyring analysis, as well as the partial influence of amine partner on the enantioselectivity, both the nucleophilic displacement of the cationic alkylcobalt(IV) complex with amines and the enantioselective radical capture to form alkylcobalt(III) species may be involved in enantiodetermining step(s) leading to chiral tertiary amines.[32]

Conclusion

In conclusion, by exploiting $Co^{III}H$ catalysis, we have accomplished an enantioselective radical hydroamination of arylalkenes with Lewis basic secondary amine, thereby enabling an efficient and alternative strategy for the asymmetric synthesis of α-branched tertiary amines in which the key chiral C–N bond formation via TM-HAT integrated with radical-polar crossover process. This mode reaction operates under mild conditions, displays good functional group tolerance, broad substrate scope, and can be used in the last-stage functionalization of complex bioactive compounds. Further investigations on the development of new cobalt catalytic systems and their application in oxidative MHAT with various free nucleophiles are underway in our laboratory.

Acknowledgements

We thank the Grants NSFC (22171043, 22193012, 21831002), and the Fundamental Research Funds for the Central Universities for generous financial support.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Asymmetric · Cobalt Catalysis · Hydroamination · Hydrogen Atom Transfer · Secondary Amines

[1] a) T. C. Nugent, *Chiral Amine Synthesis: Methods, Developments and Applications*, Wiley-VCH, Weinheim, **2010**; b) S. Funayama, G. A. Cordell, *Alkaloids: A Treasury of Poisons and Medicines*, Academic Press, Waltham, MA, **2014**.

[2] For selected reviews, see: a) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795–3892; b) A. L. Reznichenko, A. J. Nawara-Hultzsch, K. C. Hultzsch, *Top. Curr. Chem.* **2013**, *343*, 191–260; c) K. C. Hultzsch, *Adv. Synth. Catal.* **2005**, *347*, 367–391; d) M. T. Pirnot, Y.-M. Wang, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2016**, *55*, 48–57; *Angew. Chem.* **2016**, *128*, 48–57; e) J. Hannedouche, E. Schulz, *Chem. Eur. J.* **2013**, *19*, 4972–4985; f) A. Trowbridge, S. M. Walton, M. J. Gaunt, *Chem. Rev.* **2020**, *120*, 2613–2692; g) K. Hirano, M. Miura, *J. Am. Chem. Soc.* **2022**, *144*, 648–661.

[3] a) Z. Zhou, Y. Li, B. Han, L. Gong, E. Meggers, *Chem. Sci.* **2017**, *8*, 5757–5763; b) F. Yu, P. Chen, G. Liu, *Org. Chem. Front.* **2015**, *2*, 819–822; c) C. Lee, H.-J. Kang, H. Seo, S. Hong, *J. Am. Chem. Soc.* **2022**, *144*, 9091–9100; d) Q. Li, X. Fang, R. Pan, H. Yao, A. Lin, *J. Am. Chem. Soc.* **2022**, *144*, 11364–11376; e) C. B. Roos, J. Demaerel, D. E. Graff, R. R. Knowles, *J. Am. Chem. Soc.* **2020**, *142*, 5974–5979; f) Z. Zhang, S. D.

Lee, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2009**, *131*, 5372–5373.
[4] R. Dorta, P. Egli, F. Zürcher, A. Togni, *J. Am. Chem. Soc.* **1997**, *119*, 10857–10858.
[5] For examples of enantioselective intermolecular hydroaminations of alkenes with primary amines, see a) M. Kawatsura, J. F. Hartwig, *J. Am. Chem. Soc.* **2000**, *122*, 9546–9547; b) A. Hu, M. Ogasawara, T. Sakamoto, A. Okada, K. Nakajima, T. Takahashi, W. Lin, *Adv. Synth. Catal.* **2006**, *348*, 2051–2056; c) J. S. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 12220–12221; d) Y. Xi, S. Ma, J. F. Hartwig, *Nature* **2020**, *588*, 254–260; e) S. Ma, Y. Xi, H. Fan, S. Roediger, J. F. Hartwig, *Chem.* **2022**, *8*, 535–542; f) A. L. Reznichenko, H. N. Nguyen, K. C. Hultzsch, *Angew. Chem. Int. Ed.* **2010**, *49*, 8984–8987; *Angew. Chem.* **2010**, *122*, 9168–9171; g) G. Tran, W. Shao, C. Mazet, *J. Am. Chem. Soc.* **2019**, *141*, 14814–14822; h) J. Long, P. Wang, W. Wang, Y. Li, G. Yin, *iScience* **2019**, *22*, 369–379.
[6] a) M. Utsunomiya, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 14286–14287; b) C. S. Sevov, J. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 3200–3207.
[7] X.-H. Yang, V. M. Dong, *J. Am. Chem. Soc.* **2017**, *139*, 1774–1777.
[8] a) N. J. Adamson, E. Hull, S. J. Malcolmson, *J. Am. Chem. Soc.* **2017**, *139*, 7180–7183; b) S. Park, S. J. Malcolmson, *ACS Catal.* **2018**, *8*, 8468–8476.
[9] E. P. Vanableion, J. L. Kennemur, L. A. Joyce, R. T. Ruck, D. M. Schultz, K. L. Hull, *J. Am. Chem. Soc.* **2019**, *141*, 739–742.
[10] Chiral half-sandwich rare-earth metal complexes catalyzed asymmetric hydroamination of cyclopropane with secondary amines, see: H.-L. Teng, Y. Luo, B. Wang, L. Zhang, M. Nishiura, Z. Hou, *Angew. Chem. Int. Ed.* **2016**, *55*, 15406–15410; *Angew. Chem.* **2016**, *128*, 15632–15636.
[11] a) J. Guo, Z. Cheng, J. Chen, X. Chen, Z. Lu, *Acc. Chem. Res.* **2021**, *54*, 2701–2716; b) S. Ghorai, S. S. Chirke, W.-B. Xu, J.-F. Chen, C. Li, *J. Am. Chem. Soc.* **2019**, *141*, 11430–11434; c) Z. Jia, L. Zhang, S. Luo, *J. Am. Chem. Soc.* **2022**, *144*, 10705–10710; d) Y. Li, W. Nie, Z. Chang, J.-W. Wang, X. Lu, Y. Fu, *Nat. Catal.* **2021**, *4*, 901–911; For the selected examples for cobalt-catalyzed enantioselective C–N bonds construction, see: e) Y. Sun, J. Guo, X. Shen, Z. Lu, *Nat. Commun.* **2022**, *13*, 650; f) X. Shen, X. Chen, J. Chen, Y. Sun, Z. Cheng, Z. Lu, *Nat. Commun.* **2020**, *11*, 783; g) J. Chen, X. Shen, Z. Lu, *J. Am. Chem. Soc.* **2020**, *142*, 14455–14460; h) W. Yang, M. Pu, X. Lin, M. Chen, Y. Song, X. Liu, Y.-D. Wu, X. Feng, *J. Am. Chem. Soc.* **2021**, *143*, 9648–9656.
[12] a) H. Shigehisa, T. Aoki, S. Yamaguchi, N. Shimizu, K. Hiroya, *J. Am. Chem. Soc.* **2013**, *135*, 10306–10309; b) H. Shigehisa, N. Koseki, N. Shimizu, M. Fujisawa, M. Niitsu, K. Hiroya, *J. Am. Chem. Soc.* **2014**, *136*, 13534–13537; c) H. Shigehisa, M. Hayashi, H. Ohkawa, T. Suzuki, H. Okayasu, M. Mukai, A. Yamazaki, R. Kawai, H. Kikuchi, Y. Satoh, A. Fukuyama, K. Hiroya, *J. Am. Chem. Soc.* **2016**, *138*, 10597–10604; d) X.-L. Zhou, F. Yang, H.-L. Sun, Y.-N. Yin, W.-T. Ye, R. Zhu, *J. Am. Chem. Soc.* **2019**, *141*, 7250–7255; e) S. Date, K. Hamasaki, K. Sunagawa, H. Koyama, C. Sebe, K. Hiroya, H. Shigehisa, *ACS Catal.* **2020**, *10*, 2039–2045; f) T. Nagai, N. Mimata, Y. Terada, C. Sebe, H. Shigehisa, *Org. Lett.* **2020**, *22*, 5522–5527; g) S. Ohuchi, H. Koyama, H. Shigehisa, *ACS Catal.* **2021**, *11*, 900–906; h) X.-G. Zhang, Z.-X. He, P. Guo, Z. Chen, K.-Y. Ye, *Org. Lett.* **2022**, *24*, 22–26; i) K. Yahata, Y. Kaneko, S. Akai, *Org. Lett.* **2020**, *22*, 598–603; j) Y.-N. Yin, R.-Q. Ding, D.-C. Ouyang, Q. Zhang, R. Zhu, *Nat. Commun.* **2021**, *12*, 2552; k) E. Touney, R. Cooper, S. Bredenkamp, D. George, S. Pronin, *ChemRxiv*. **2021**, https://doi.org/10.26434/chemrxiv.14450580.v1.
[13] For the photoredox/Co-catalyzed oxidative hydrofunctionalization, see: a) M. Nakagawa, Y. Matsuki, K. Nagao, H. Ohmiya, *J. Am. Chem. Soc.* **2022**, *144*, 7953–7959; b) H.-L. Sun, F. Yang, W.-T. Ye, J.-J. Wang, R. Zhu, *ACS Catal.* **2020**, *10*, 4983–4989.
[14] For the electrocatalytic oxidative hydrofunctionalization reactions of alkenes with a nucleophilic partner, see a) F. Yang, Y.-C. Nie, H.-Y. Liu, L. Zhang, F. Mo, R. Zhu, *ACS Catal.* **2022**, *12*, 2132–2137; b) L. Song, N. Fu, B. G. Ernst, W. H. Lee, M. O. Frederick, R. A. DiStasio Jr, S. Lin, *Nat. Chem.* **2020**, *12*, 747.
[15] a) S. L. Shevick, C. Obradors, R. A. Shenvi, *J. Am. Chem. Soc.* **2018**, *140*, 12056–12068; b) S. A. Green, J. L. M. Matos, A. Yagi, R. A. Shenvi, *J. Am. Chem. Soc.* **2016**, *138*, 12779–12782; c) S. A. Green, S. Vásquez-Céspedes, R. A. Shenvi, *J. Am. Chem. Soc.* **2018**, *140*, 11317–11324; d) S. L. Shevick, C. V. Wilson, S. Kotesova, D. Kim, P. L. Holland, R. A. Shenvi, *Chem. Sci.* **2020**, *11*, 12401–12422.
[16] For pioneering works on catalytic transformation involving an alkylcobalt(IV) complex as a key intermediate, see: a) E. E. Touney, N. J. Foy, S. V. Pronin, *J. Am. Chem. Soc.* **2018**, *140*, 16982–16987; b) C. A. Discolo, E. E. Touney, S. V. Pronin, *J. Am. Chem. Soc.* **2019**, *141*, 17527–17532.
[17] For the first definitive evidence for alkylcobalt(IV) complex, see: C. V. Wilson, D. Kim, A. Sharma, R. X. Hooper, R. Poli, B. M. Hoffman, P. L. Holland, *J. Am. Chem. Soc.* **2022**, *144*, 10361–10367.
[18] a) K. Ebisawa, K. Izumi, Y. Ooka, H. Kato, S. Kanazawa, S. Komatsu, E. Nishi, H. Shigehisa, *J. Am. Chem. Soc.* **2020**, *142*, 13481–13490; b) T. Qin, G. Lv, Q. Meng, G. Zhang, T. Xiong, Q. Zhang, *Angew. Chem. Int. Ed.* **2021**, *60*, 25949–25957; *Angew. Chem.* **2021**, *133*, 26153–26161; c) T. Qin, G. Lv, H. Miao, M. Guan, C. Xu, G. Zhang, T. Xiong, Q. Zhang, *Angew. Chem. Int. Ed.* **2022**, *61*, e202201967; *Angew. Chem.* **2022**, *134*, e202201967; d) K. Yahata, Y. Kaneko, S. Akai, *Chem. Pharm. Bull.* **2020**, *68*, 332–335.
[19] a) J. Halpern, J. Topich, K. I. Zamaraev, *Inorg. Chim. Acta* **1976**, *20*, L21–L24; b) M. E. Vol′pin, I. Y. Levitin, A. L. Sigan, A. T. Nikitaev, *J. Organomet. Chem.* **1985**, *279*, 263–280.
[20] a) M. E. Vol′pin, I. Y. Levitin, A. L. Sigan, J. Halpern, G. M. Tom, *Inorg. Chim. Acta* **1980**, *41*, 271–277; b) R. H. Magnuson, J. Halpern, I. Y. Levitin, *J. Chem. Soc. Chem. Commun.* **1978**, 44–46; c) S. N. Anderson, D. H. Ballard, J. Z. Chrzastowski, D. Dodd, M. D. Johnson, *J. Chem. Soc. Chem. Commun.* **1972**, 685–686.
[21] T. T. Tsou, M. Loots, J. Halpern, *J. Am. Chem. Soc.* **1982**, *104*, 623–624.
[22] For discussion of homolysis of relevant alkylcobalt(IV) complexes, see: a) S. Fukuzumi, K. Miyamoto, T. Suenobu, E. Van Caemelbecke, K. M. Kadish, *J. Am. Chem. Soc.* **1998**, *120*, 2880–2889; b) J. Harmer, S. Van Doorslaer, I. Gromov, M. Bröring, G. Jeschke, A. A. Schweiger, *J. Phys. Chem. B* **2002**, *106*, 2801–2811.
[23] a) E. G. Samsel, J. K. Kochi, *J. Am. Chem. Soc.* **1986**, *108*, 4790–4804; b) S. Li, B. de Bruin, C. H. Peng, B. B. Fryd, M. Wayland, *J. Am. Chem. Soc.* **2008**, *130*, 13373–13381.
[24] Asymmetric hydroamination of alkenes using electrophilic diazo compounds as the nitrogen source, via cobalt-hydride mediated HAT followed by addition process, has been developed recently by Lu and co-workers, also see reference 11e–g for details.
[25] A. W. Schmidt, K. R. Reddy, H.-J. Knölker, *Chem. Rev.* **2012**, *112*, 3193–3328.
[26] C. C. Roberts, D. M. Matías, M. J. Goldfogel, S. J. Meek, *J. Am. Chem. Soc.* **2015**, *137*, 6488–6491.
[27] W.-T. Ye, R. Zhu, *Chem Catalysis* **2022**, *2*, 345–357.
[28] J. L. Male, B. E. Lindfors, K. J. Covert, D. R. Tyler, *J. Am. Chem. Soc.* **1998**, *120*, 13176–13186.

[29] M. Gómez-Gallego, M. A. Sierra, *Chem. Rev.* **2011**, *111*, 4857–4963.
[30] P. Guo, J.-F. Han, G.-C. Yuan, L. Chen, J.-B. Liao, K.-Y. Ye, *Org. Lett.* **2021**, *23*, 4067–4071.
[31] H. Buschmann, H.-D. Scharf, N. Hoffmann, P. Esser, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 477–515.
[32] The derived activation parameters from Eyring analysis are close to the activation enthalpy associated with this diffusion-controlled process (ca. 2 kcal mol^{-1}). In addition, the influence of radical chain reaction to the enantioselectivity could not be ruled out because of the rate of the radical chain disproportionation to the more stable scalemic alkylcobalt(III) intermediate depend on the concentration of a diffused alkyl radical and alkylcobalt(III) intermediate.

Manuscript received: September 20, 2022
Accepted manuscript online: November 7, 2022
Version of record online: December 5, 2022