A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

www.angewandte.org

Accepted Article

Title: Cobalt-Catalyzed Enantioselective Alkenylation of Aldehydes

Authors: Chuiyi Lin, Jiwu Zhang, Zhao Sun, Yinlong Guo, Qinglei Chong, Zhihan Zhang, and Fanke Meng

To be cited as: *Angew. Chem. Int. Ed.* **2024**, e202405290

Link to VoR: https://doi.org/10.1002/anie.202405290

WILEY VCH

10.1002/anie.202405290

COMMUNICATION

WILEY VCH

Cobalt-Catalyzed Enantioselective Alkenylation of Aldehydes

Chuiyi Lin,[a] Jiwu Zhang,[a] Zhao Sun,[a] Yinlong Guo,*[a] Qinglei Chong,*[a] Zhihan Zhang,*[b] and Fanke Meng*[a][c][d][e]

Dedication ((optional))

[a] C. Lin, J. Zhang, Z. Sun, Prof. Dr. Y. Guo, Prof. Dr. Q. Chong, Prof. Dr. F. Meng
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences
345 Lingling Road, Shanghai (China)
E-mail: ylguo@sioc.ac.cn, chongql@sioc.ac.cn, mengf@sioc.ac.cn

[b] Prof. Dr. Z. Zhang
College of Chemistry, Central China Normal University, 152 Louyu Road, Wuhan, Hubei, 430079, China.
E-mail: zhihanzhang@ccnu.edu.cn

[c] Prof. Dr. F. Meng
School of Chemistry and Materials Science, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, 1 Sub-lane Xiangshan, Hangzhou, 310024, China.

[d] Prof. Dr. F. Meng
Beijing National Laboratory for Molecular Sciences.

[e] Prof. Dr. F. Meng
State Key Laboratory of Elemento-Organic Chemistry, Nankai University.

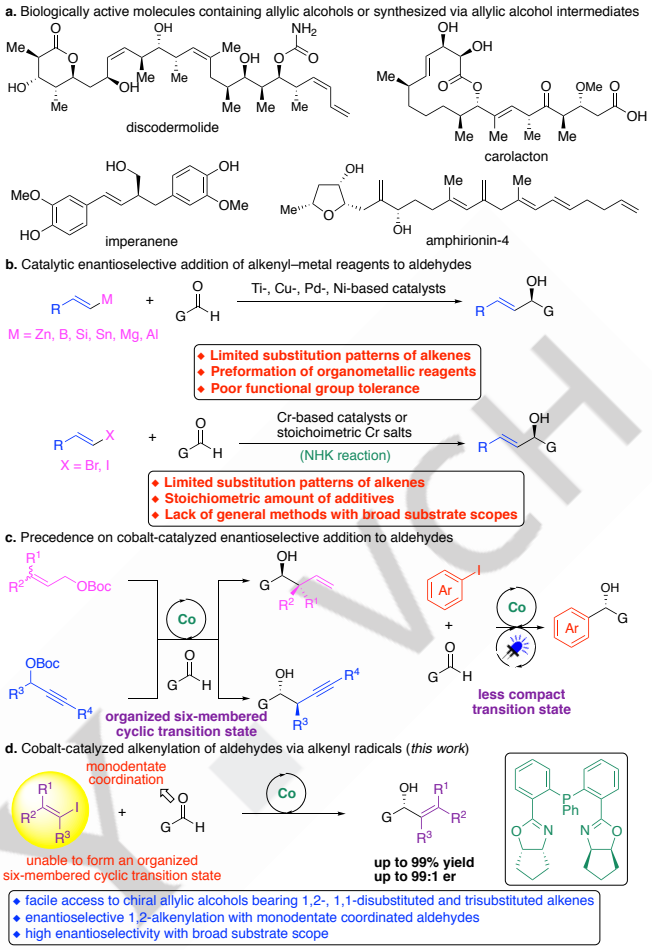
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate.))

Abstract: Catalytic enantioselective alkenylation of aldehydes with easily accessible alkenyl halides promoted by a chiral cobalt complex derived from a newly developed tridentate bisoxazolinephosphine is presented. Such processes represent an unprecedented reaction pathway for cobalt catalysis and a general approach that enable rapid construction of highly diversified enantioenriched allylic alcohols containing a 1,1-, 1,2-disubstituted and trisubstituted alkene as well as axial stereogenicity in up to 99% yield and 99:1 er without the need of preformation of alkenyl–metal reagents. DFT calculations revealed the origin of enantioselectivity.

Enantiomerically enriched allylic alcohols are an important class of chiral building blocks for organic synthesis, since they are versatile for a wide range of subsequent transformations. Particularly, the hydroxy group is able to direct a variety of highly diastereoselective reactions that can install multiple stereogenic centers.[1] Furthermore, chiral allylic alcohols are key structures that widely exist in natural products and biological active molecules (Scheme 1a). Therefore, development of an efficient and stereoselective catalytic process with readily available starting materials and an easily accessible catalyst to afford a broad scope of enantioenriched allylic alcohols containing alkenes with various substitution patterns is highly desirable.[2] Although numerous strategies, such as kinetic resolution of racemic allylic alcohols,[3] allylic C–H bond oxidation,[4] allylic substitution with O-based nucleophiles,[5] enantioselective addition of O-based nucleophiles to π-bond,[6] enantioselective addition of α,β-unsaturated carbonyls,[2] enantioselective reduction of α,β-unsaturated ketones,[7] reductive and alkylative coupling of aldehydes and unsaturated hydrocarbons,[8] have been revealed, catalytic enantioselective alkenyl addition of aldehydes with alkenyl–metal reagents that constitutes one of the most straightforward and modular approaches remained much less developed. In this context, preformation of alkenyl–metal (Zn, Mg, Al, Sn, Si, B) reagents was generally required (Scheme 1b).[2,9] Such approaches suffered from significant limitation of substrate scopes and functional group tolerance. Cr-mediated Nozaki-Hiyama-Kishi (NHK) reactions represent a crucial method to generate chiral allylic alcohols directly from alkenyl halides.[10] However, significant limitations on substrate scope of aldehydes and alkenyl halides as well as the requirement for stoichiometric amounts of additives remained unaddressed. The enantioselectivity was highly substrate-dependent. In the cases mentioned above, the substitution patterns of the alkenyl groups were restricted to mono- and disubstituted alkenes and incorporation of alkenes with different substitution patterns normally required different catalytic systems. There is a lack of a general approach promoted by a single catalyst for access a broad scope of enantioenriched allylic alcohols with diverse alkenyl substitution patterns.

Cobalt is an inexpensive earth-abundant transition metal of low toxicity.[11] Development of novel cobalt-catalyzed reactions to address longstanding issues has attracted increasing research interests utilizing the unique nature of cobalt catalysis. Our group has been focusing on developing new cobalt-catalyzed enantioselective transformations.[12] We have recently disclosed cobalt-catalyzed protocols for diastereo- and enantioselective allyl and propargyl additions to aldehydes via allyl and propargyl radicals generated from allylic and propargyl alcohol derivatives through well-organized six-membered transition states (Scheme 1c).[12a,f] The involvement of radical intermediates was crucial for the stereoconvergent processes. Xiao and co-workers reported

a photoredox/cobalt-catalyzed arylation of aldehydes with aryl iodides.[13] Such process is more challenging due to a less compact transition state, as orbital overlapping is not as good as that in the six-membered transition state. Zhao and co-wokers developed a cobalt-catalyzed method for enantioselective alkenylation of α-ketoesters, isatins and activated imines with alkenyl boronic acids.[14] During preparation of this manuscript, Chen and co-workers revealed cobalt-catalyzed approaches for enantioselective alkylation and alkenylation of α-imino esters with alkyl and alkenyl halides.[15] In comparison with α-ketoesters, isatins and α-imino esters that are able to chelate to the metal center, alkenylation of aldehydes is more challenging due to their nature of monodentate coordination to the cobalt center, resulting in difficulty to form a well-organized transition state. Moreover, the smaller size of alkenyl groups than aryls posed additional challenges for interaction with the chiral ligand and accurate control of enantioselectivity. We envisioned that increasing rigidity of the stereogenic fragments in the chiral ligand by introduction of additional carbocycles would provide better stereochemical induction and tolerate a wide range of alkenyl groups. The catalyst has to retard the potential alkene isomerization due the possible involvement of alkenyl radical intermediates as well. Herein, we disclosed an unprecedented cobalt-catalyzed protocol for enantioselective alkenylation of aldehydes with alkenyl iodides to afford a broad scope of enantioenriched allylic alcohols bearing 1,1-, 1,2-disubstituted and trisubstituted alkenes as well as simultaneous construction of central and axial stereogenicity in high efficiency and stereoselectivity.

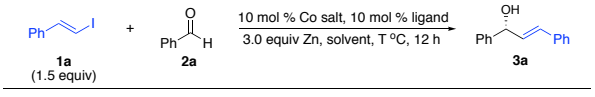


Scheme 1. Catalytic enantioselective alkenylation of aldehydes and reaction design.

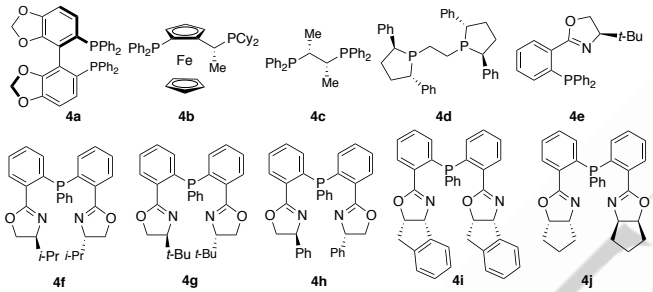
We commenced our studies with reaction of alkenyl iodide **1a** and benzaldehyde **2a** in the presence of chiral phosphine–Co complexes (Table 1). Unlike previous reports on cobalt-catalyzed allylation, propargylation and arylation of aldehydes,[12a,12f,13] bisphosphines and phosphinooxazoline ligands were not able to promote the reaction and/or induce enantioselectivity, suggesting that it was more difficult to obtain high enantioselectivity for alkenylation of aldehydes (entries 1–5). We found that tridentate bisoxazolinephosphine ligands were crucial for efficiency and enantioselectivity (entries 6–10).[16] Unlike transformations with α-imino esters,[15] bisoxazolinephosphines derived from amino alcohols containing a single acyclic stereogenic center (**4f–h**) provided low enantioselectivity (entries 6–8). As we expected, introduction of additional rigidity for the oxazoline fragment delivered higher enantioselectivity (entry 10), whereas deeper binding pocket resulted in diminished enantioselectivity (entry 9). Switching the cobalt salt to CoI_2 led to enhancement of enantioselectivity (entry 11). Higher efficiency resulted from lower reaction temperature (entry 12). Further screening of solvents indicated that reaction performed in MeCN gave the highest yield (entries 12–15). Lowering the catalyst loading to 5.0 mol % wouldn't

erode the efficiency and enantioselectivity (entry 16). It is worth mentioning that reaction of alkenyl bromides provided lower efficiency and enantioselectivity.

Table 1. Optimization of reaction conditions.

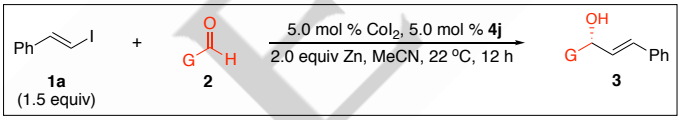


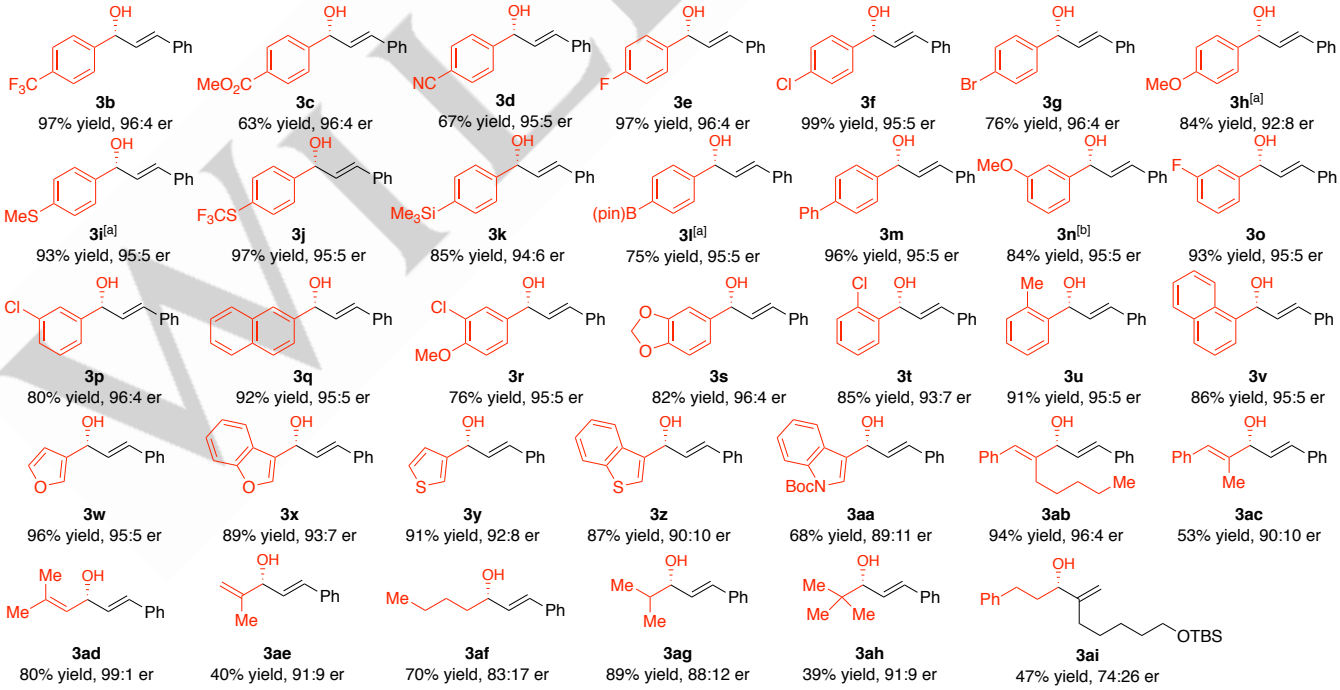
entry	ligand	Co salt	solvent	T [°C]	yield [%][a]	er[b]
1	**4a**	$Co(hfac)_2$	MeCN	80	<5	NA[c]
2	**4b**	$Co(hfac)_2$	MeCN	80	21	48:52
3	**4c**	$Co(hfac)_2$	MeCN	80	<5	NA[c]
4	**4d**	$Co(hfac)_2$	MeCN	80	<5	NA[c]
5	**4e**	$Co(hfac)_2$	MeCN	80	14	50:50
6	**4f**	$Co(hfac)_2$	MeCN	80	74	25:75
7	**4g**	$Co(hfac)_2$	MeCN	80	37	45:55
8	**4h**	$Co(hfac)_2$	MeCN	80	32	22:78
9	**4i**	$Co(hfac)_2$	MeCN	80	61	70:30
10	**4j**	$Co(hfac)_2$	MeCN	80	76	91:9
11	**4j**	CoI_2	MeCN	80	73	94:6
12	**4j**	CoI_2	MeCN	22	98	96:4
13	**4j**	CoI_2	CH_2Cl_2	22	8	51:49
14	**4j**	CoI_2	THF	22	73	93:7
15	**4j**	CoI_2	DMF	22	66	96:4
16[d]	**4j**	CoI_2	MeCN	22	92	95:5



[a] Yield of isolated product. [b] Determined by analysis of HPLC spectra. [c] Not available. [d] The reaction was performed in the presence of 5.0 mol % CoI_2, 5.0 mol % **4j** and 2.0 equiv of Zn.

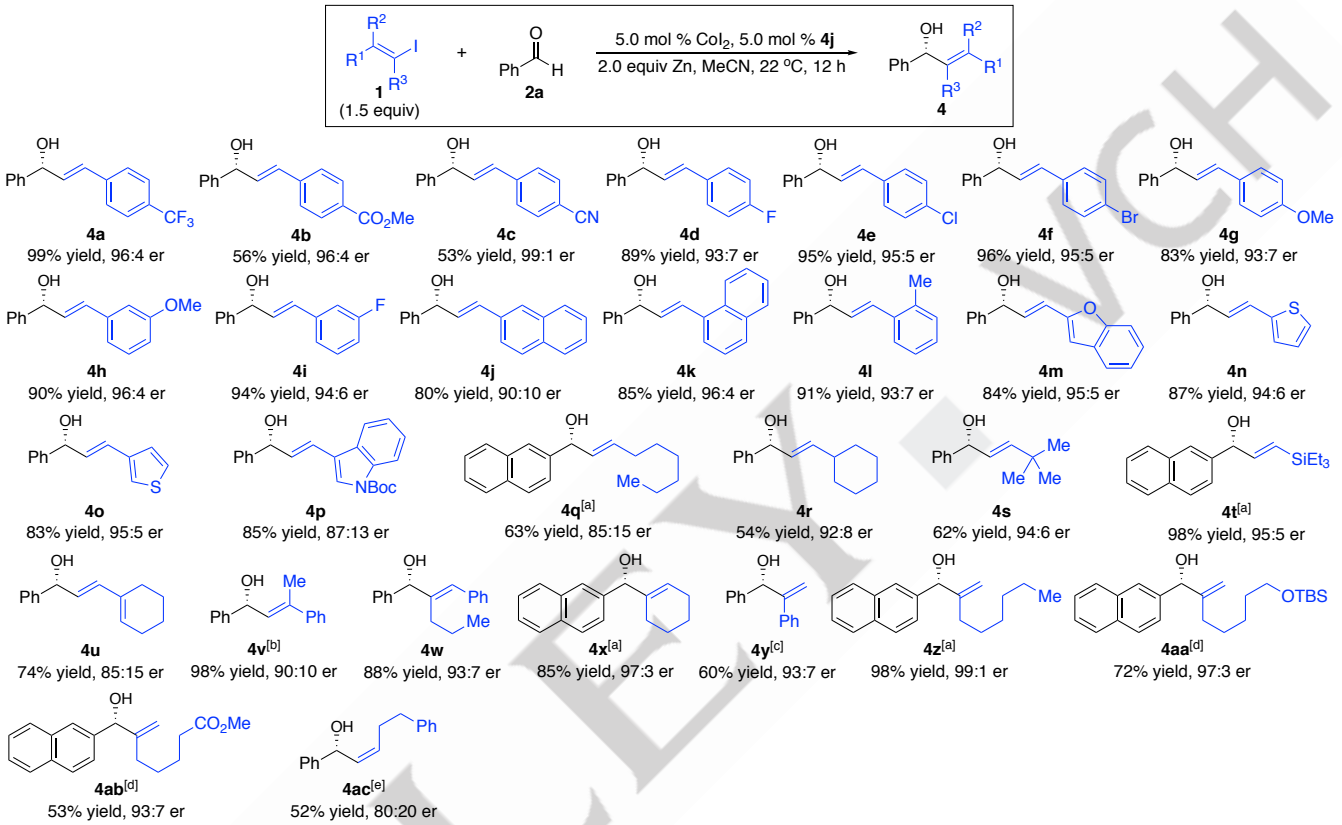
With the optimal conditions in hand, we investigated the scope of aldehydes (Scheme 2). Aldehydes bearing electron-deficient (**3b–g**, **3o–p**, **3t**), electron-rich (**3h–j**, **3m–n**, **3r–s**), halogenated (**3e–g**, **3o–p**, **3t**), and sterically congested (**3q**, **3t–v**) aryl groups underwent the enantioselective alkenylation, producing allylic alcohols in high efficiency and enantioselectivity (63–97% yield, 92:8–96:4 er). Silyl (**3k**) and boryl (**3l**) were well tolerated in the reaction conditions. Aldehydes containing pharmaceutically important heterocycles such as furan (**3w**), benzofuran (**3x**), thiophene (**3y**), benzothiophene (**3z**) and indole (**3aa**) served as suitable substrates that afforded products in 68–96% yield with 89:11–95:5 er. Reactions of α,β-unsaturated aldehydes with different substitution patterns furnished allylic alcohols **3ab–ae** in 40–94% yield with 90:10–99:1 er. Such type of enantioenriched allylic alcohols were difficult to access through other methods such as reduction of α,β-unsaturated ketones, coupling of aldehydes and unsaturated hydrocarbons and allylic C–H oxidation. Aliphatic aldehydes were transformed into desired products (**3af–ai**) albeit with lower enantioselectivity.





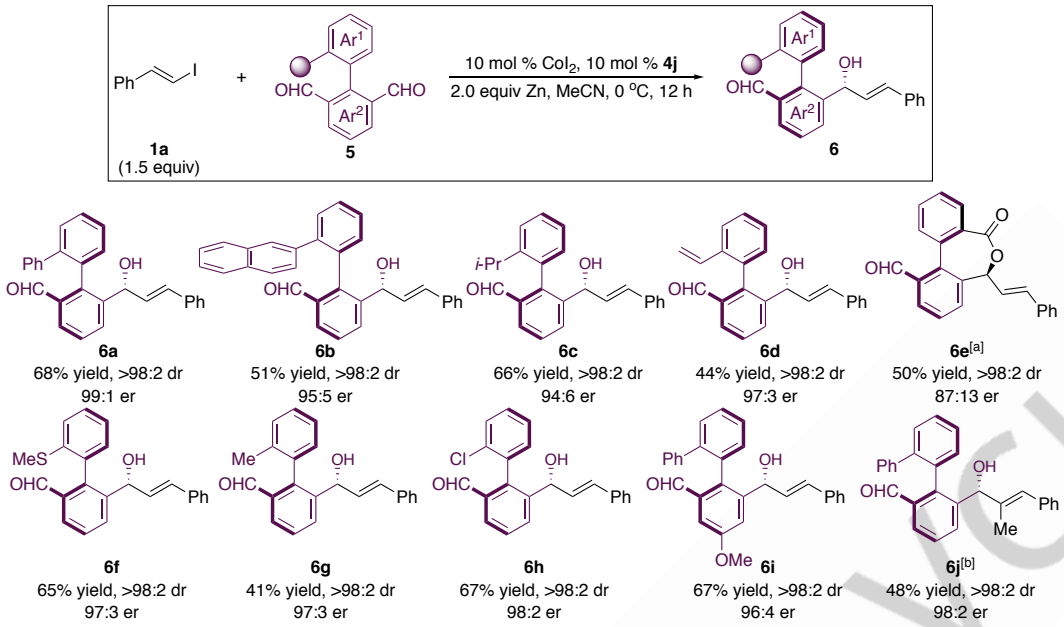
Scheme 2. Scope of aldehydes. [a] The reactions were performed for 5 h. [b] The reactions were performed for 8 h.

We next surveyed the scope of alkenyl iodides. A wide range of (*E*)-1,2-disubstituted alkenyl iodides bearing electron-deficient (**4a**–**f**, **4i**), electron-rich (**4g**–**h**), halogenated (**4d**–**f**, **4i**) and sterically congested (**4j**–**l**) aryl groups were able to convert into the allylic alcohols in 53–99% yield with 90:10–99:1 er. Heteroaryl groups (**4m**–**p**) were compatible with the reaction conditions. Alkyl-substituted alkenyl iodides (**4q**–**s**) were suitable substrates as well, while transformations of alkenyl iodides containing larger alkyl groups provided higher enantioselectivity. Reaction of silyl-substituted alkenyl iodide afforded the desired product **4t** in 98% yield with 95:5 er. Dienyl iodide was able to participate in the reaction albeit with lower enantioselectivity (**4u**). Trisubstituted alkenyl iodides with various substation patterns underwent the alkenylation, generating the allylic alcohols in 85–98% yield with 90:10–97:3 er (**4v**–**x**). Reactions of 1,1-disubstituted alkenyl iodides bearing aryl (**4y**) and alkyl (**4z**, **4aa**–**ab**) groups furnished products in 53–98% yield with 93:7–99:1 er. Although (*Z*)-1,2-disubstituted alkenyl iodide was also able to transform into the allylic alcohol **4ac**, lower enantioselectivity was obtained.



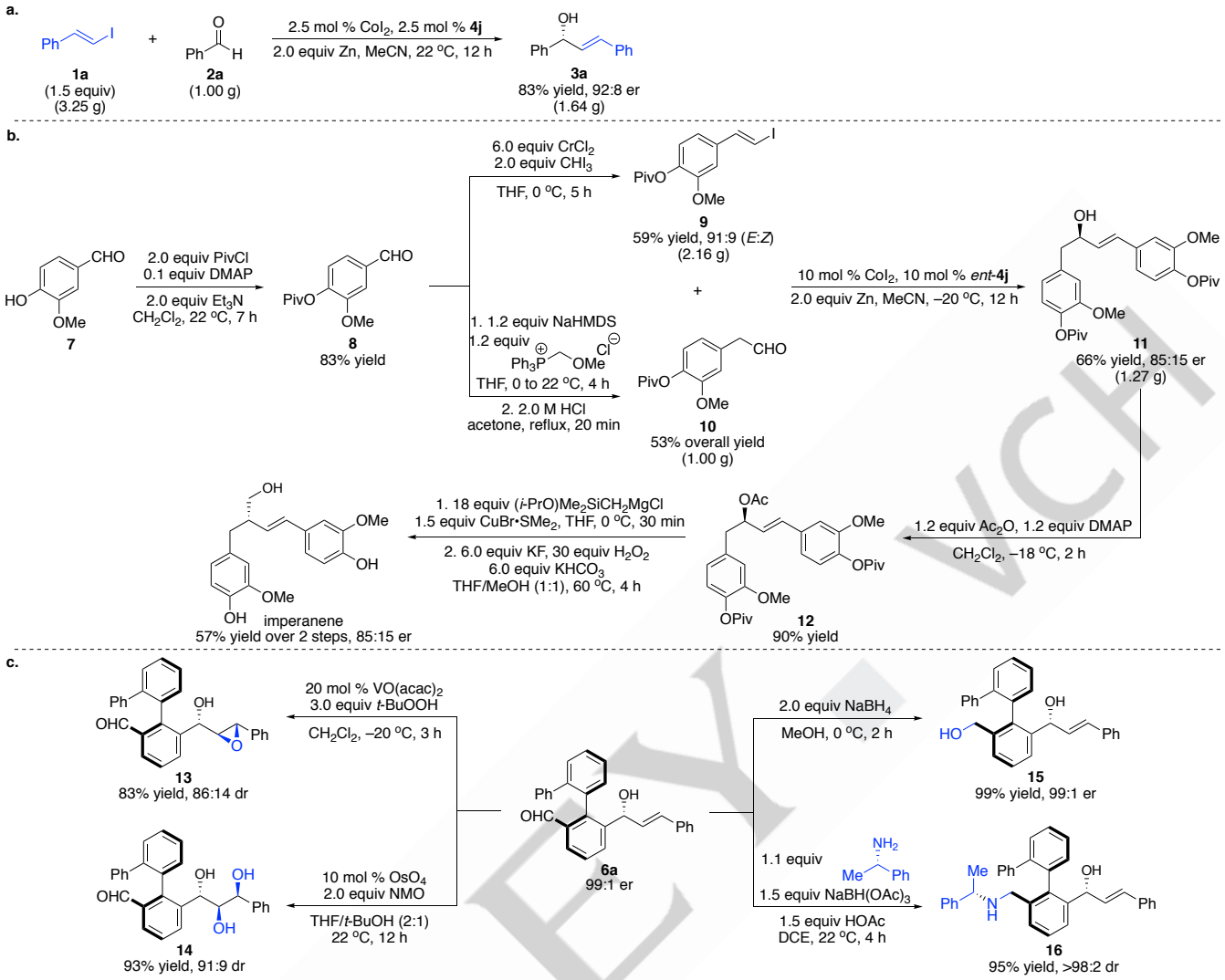
Scheme 3. Scope of alkenyl iodides. [a] The reactions were performed with 10 mol % catalyst loading. [b] The reactions were conducted in the presence of 10 mol % CoI_2 and 10 mol % **4j** at 0 °C. [c] The transformations were performed in the presence of 10 mol % CoI_2 and 10 mol % **4j** at 80 °C. [d] The reactions were performed in the presence of 7.5 mol % CoI_2 and 7.5 mol % **4j**. [e] The reactions were conducted in the presence of 10 mol % CoI_2 and 10 mol % **4j** for 24 h.

Molecules with axial stereogenicity have attracted increasing attentions due to their importance in catalysis, complex molecule synthesis and material science.[17] Development of new approaches for catalytic enantioselective synthesis of atropisomers is therefore sought after. Particularly, it is challenging for simultaneous construction of central and axial stereogenicity in a single step and accurate control of diastereo- and enantioselectivity in the process of generating multiple stereogenic elements. In this context, we attempted to apply our cobalt-catalyzed approach to desymmetrization of dialdehydes for simultaneous construction of axial and central stereogenicity (Scheme 4).[13b,18] A broad scope of dialdehydes containing various substituents and functional groups (**6a**–**i**) underwent the diastereo- and enantioselective alkenylation, affording multifunctional allylic alcohols in 44–68% yield with 87:13–99:1 er as a single diastereomer. Trisubstituted alkenyl iodides were tolerated as well (**6j**).[19] It is worth mentioning that simultaneous lactonization occurred with ester-containing dialdehyde in the reaction (**6e**).



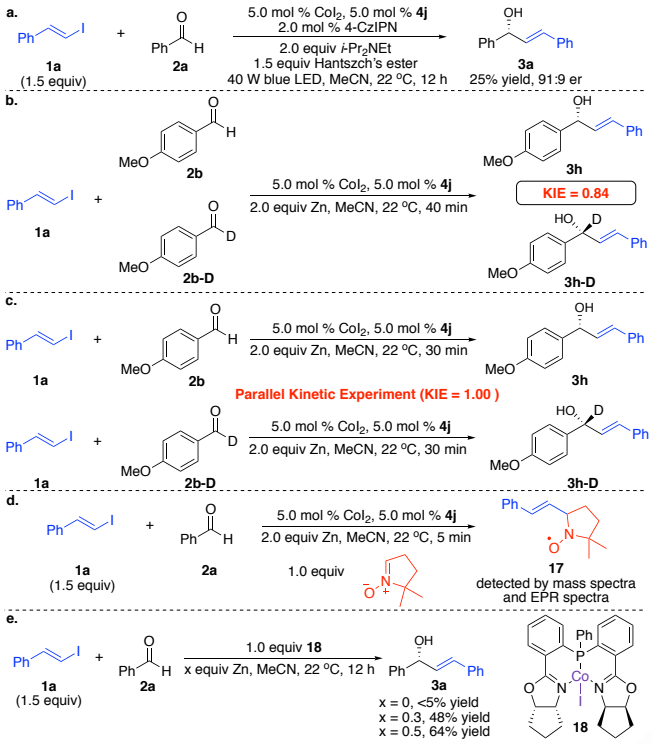
Scheme 4. Application to synthesis of allylic alcohols with axial stereogenicity. [a] The reactions were performed with the enantiomer of **4j**. [b] The reactions were conducted at 22 °C for 18 h.

The reaction can be performed on gram scale with 2.5 mol % catalyst loading (Scheme 5a). Taking advantage of the enantioselective alkenylation of aldehydes enabled a shortest synthesis of imperanene (Scheme 5b). Alkenyl iodide **9** and aldehyde **10** were easily prepared from vanillin **7** efficiently. Treatment of aldehyde **10** (1.00 g) with alkenyl iodide **9** (2.16 g) produced allylic alcohol **11** (1.27 g) in 66% yield with 85:15 er. The allylic C–O bond at the stereogenic center was converted to C–C bond through stereospecific allylic substitution with complete inversion of stereochemistry followed by global deprotection, delivering imperanene in 57% overall yield.[20] The densely functionalized allylic alcohol with axial stereogenicity can be easily transformed into a variety of axially stereogenic building blocks that are otherwise difficult to access (Scheme 5c). Directed epoxidation (**13**)[21] and dihydroxylation (**14**)[22] enabled introduction of two additional stereogenic centers without touching the aldehyde moiety. Reduction and reductive amination of **6a** provided diol **15** and amino alcohol **16** in high stereoselectivity.



Scheme 5. Gram scale reaction and functionalization.

To gain some preliminary insight into the mechanism, a series of experiments were conducted (Scheme 6). Replacement of reductant Zn with photoredox-catalyzed conditions afforded allylic alcohol **3a** in 25% yield with 91:9 er (Scheme 6a), suggesting that the enantioselectivity originated from addition of an alkenyl–Co complex rather than an alkenyl–Zn intermediate. Secondary kinetic isotope effect experiments indicated that addition of alkenyl–Co intermediates to aldehydes is involved of an irreversible rehybridization from sp^2 to sp^3, being consistent with our previous report (Scheme 6b).[12a] Parallel kinetic isotope experiment indicated that the aldehyde addition might not be the rate-determining step (Scheme 6c). Trapping the alkenyl radical with 5,5-dimethyl-1-pyrroline *N*-oxide and taking the EPR and mass spectra for the adduct, we detected the presence of an alkenyl radical (Scheme 6d, see Supporting Information for more details). We also observed that *E*/*Z* isomerization took place in some cases. About 10% *E*/*Z* isomerization occurred in the reaction with **4i** (Table 1, entry 9), implying that competitive isomerization of alkenyl radicals occurred if alkenyl addition to aldehyde was sluggish. Similar isomerization of alkenyl–Co intermediates were observed in the recent reports as well.[15b] We further conducted density functional theory (DFT) calculations on the energetic barriers for the possible alkenyl radical isomerization and radical rebounding to the metal center (see **Figure S1** for more details), implying that isomerization of alkenyl radical was off-cycle and slower than the rebounding process. Therefore, isomerization of the resulting products was not observed. Transformation promoted by Co(I) complex **18** in the absence of Zn resulted in no reaction, implying that alkenyl–Co(III) intermediates were not able to undergo addition to aldehydes (Scheme 6e). The presence of 0.3 equiv and 0.5 equiv of Zn led to 48% and 64% yield respectively, indicating that alkenyl–Co(II) might be the reactive species (Scheme 6e). Preliminary density functional theory (DFT) calculations show that the energy barrier for the dissociation of alkenyl radical from Co(III) intermediate is 27.2 kcal/mol and this process is endothermic by 26.2 kcal/mol, indicating the reversibility of the homolytic cleavage of Co–C bond (see **Figure S2** for more details).



Scheme 6. Preliminary mechanistic studies.

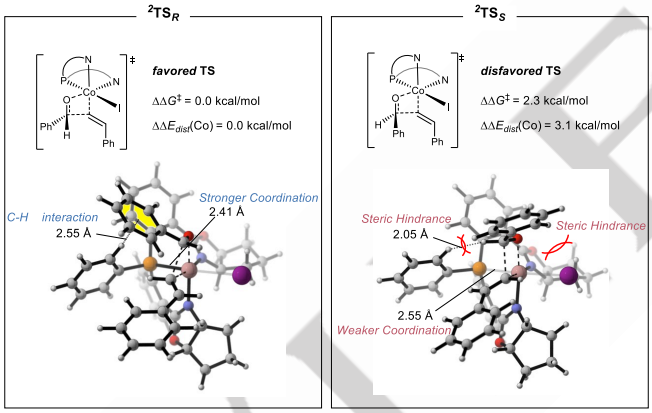
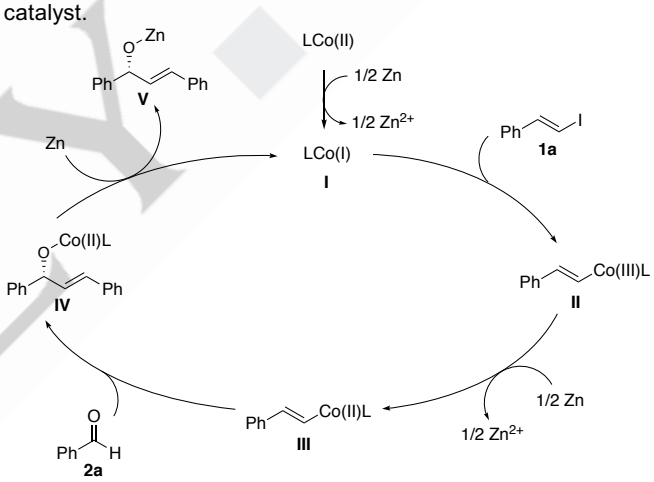


Figure 1. DFT calculations and the optimized geometries of enantioselective addition transition states.

To investigate the origin of enantioselectivity, we conducted DFT calculations, exploring enantioselective addition for both doublet and quartet spin states (Figure 1). While the alkenyl–Co intermediate exhibits a preference for the doublet spin state, our calculations revealed comparable energies of the transition states of enantioselective addition for both spin states, with a consistent preferred configuration (see **Figure S3**). As our primary interests are focused on the origin of enantioselectivity, we further compared the transition states on the energy surface of doublet spin state. The energy difference between ^{2}**TS**$_R$ and ^{2}**TS**$_S$ was calculated to be 2.3 kcal/mol, successfully predicting the configuration of the product. As depicted in Figure 1, in ^{2}**TS**$_R$, the phenyl group of **2a** adopts an orientation opposite to the highly electron-rich iodide ligand (see the electron surface potential map in **Figure S3**) and engages in a *C–H···π* interaction with phenyl group attached to phosphine ligand. Conversely, in the disfavored ^{2}**TS**$_S$, the phenyl group of **2a** locates on the same side with iodide ligand, necessitating a closer proximity to the ligand to mitigate strong repulsion with iodide. Aside from the identified close contact between H atoms in ^{2}**TS**$_S$, the bond distance of Co–P is significantly elongated by 0.14 Å compared to that of ^{2}**TS**$_R$ due to this steric hindrance. Further distortion/interaction-analysis confirmed that the destabilizing effects resulting from this geometric distortion contribute to a larger distortion energy of the Co-fragment in the disfavored ^{2}**TS**$_S$ (see **Table S1**).

Based on all the observations above and literature precedence, we proposed the catalytic cycle (Scheme 7). The Co(II) complex was reduced to Co(I) complex **I** by Zn, which underwent oxidative addition to alkenyl iodide **1a** to generate alkenyl–Co(III) **II** intermediate. Reduction of intermediate **II** to alkenyl–Co(II) complex **III** followed by enantioselective addition to aldehyde **2a** furnished alkoxide **IV**. Exchange with zinc salt and reduction of Co(II) complex released the product **V** and regenerated the catalyst.



Scheme 7. Proposed catalytic cycle.

In conclusion, a cobalt-catalyzed protocol for enantioselective alkenylation of aldehydes to furnish a wide range of allylic alcohols in high efficiency and enantioselectivity. To the best of our knowledge, it is the first time that enantioselective alkenylation of aldehydes promoted by a cobalt-based catalyst via alkenyl radicals has been developed. The starting materials are readily available or prepared easily. The formation of allylic alcohols without preformation of organometallic reagents and highly sensitive additives enabled enantioselective incorporation of alkenyl groups with diversified substitution patterns as well as simultaneous construction of axial and central stereogenicity. The catalyst is derived from an inexpensive sustainable cobalt salt and a newly developed tridentate bisoxazolinephosphine ligand. The synthetic utility was demonstrated by synthesis of imperanene and diverse functionalization of the axially stereogenic allylic alcohol, affording a variety of useful

enantioenriched building blocks that are otherwise difficult to access. Mechanistic studies revealed the addition of alkenyl–Co complex is the selectivity-determining step, and DFT calculations further provided the insights into the origin of enantioselectivity. Such discoveries unveiled a novel reaction pathway for cobalt catalysis, opening new opportunities for designing new reactions promoted by chiral cobalt-based catalysts and pushing forward the development of organocobalt chemistry. Further investigations on other cobalt-catalyzed enantioselective carbonyl addition reactions are underway.

Acknowledgements ((optional))

This work was financially supported by the National Key R&D Program of China (2022YFA1506100), National Natural Science Foundation of China (Grant No. 22371294, 21821002, and 22203034), the Strategic Priority Research Program of the Chinese Academy of Sciences (Grant No. XDB0610000), Beijing National Laboratory for Molecular Sciences (BNLMS202304), the Shanghai Science and Technology Innovation Action Plan (Grant No. 21142200800) and State Key Laboratory of Elemento-Organic Chemistry, Nankai University (Grant No. 202201).

Keywords: alkenylation • allylic alcohol • axial stereogenicity • cobalt • enantioselective catalysis

[1] For a comprehensive review, see: A. H. Hoveyda, D. A. Evans, G. C. Fu, *Chem. Rev*. **1993**, *93*, 1307–1370.

[2] For a comprehensive review, see: A. Lumbroso, M. L. Cooke, B. Breit, *Angew. Chem. Int. Ed*. **2013**, *52*, 1890–1932; *Angew. Chem.* **2013**, *125*, 1942–1986.

[3] For selected reviews, see: a) J. M. Keith, J. F. Larrow, E. N. Jacobsen, *Adv. Synth. Catal.* **2001**, 343, 5–26; b) M. Breuer, K. Ditrich, T. Habicher, B. Hauer, M. Keßeler, R. Stürmer, T. Zelinski, *Angew. Chem. Int. Ed.* **2004**, *43*, 788–824; *Angew. Chem.* **2004**, *116*, 806–843; c) E. Vedejs, M. Jure, *Angew. Chem. Int. Ed.* **2005**, *44*, 3974–4001; *Angew. Chem*. **2005**, *117*, 4040–4069; d) H. Pellissier, *Adv. Synth. Catal.* **2011**, *353*, 1613–1666; e) F. F. Huerta, A. B. E. Minidis, J.-E. Bäckvall, *Chem. Soc. Rev*. **2001**, *30*, 321–331; f) O. Pàmies, J.-E. Bäckvall, *Chem. Rev*. **2003**, *103*, 3247–3262; g) H. Pellissier, *Tetrahedron* **2003**, *59*, 8291–8327; h) A. Kamal, M. A. Azhar, T. Krishnaji, M. S. Malik, S. Azeeza, *Coord. Chem. Rev*. **2008**, *252*, 569–592; i) Y. Ahn, S.-B. Ko, M.-J. Kim, J. Park, *Coord. Chem. Rev*. **2008**, *252*, 647–658; j) B. L. Conley, M. K. Pennington-Boggio, E. Boz, T. J. Williams, *Chem. Rev*. **2010**, *110*, 2294–2312; k) J. H. Lee, K. Han, M.-J. Kim, J. Park, *Eur. J. Org. Chem.* **2010**, 999–1015; l) H. Pellissier, *Tetrahedron* **2011**, *67*, 3769–3802.

[4] For reviews, see: a) J. Eames, M. Watkinson, *Angew. Chem. Int. Ed*. **2001**, *40*, 3567–3571; *Angew. Chem*. **2001**, *113*, 3679–3683; b) M. B. Andrus, J. C. Lashley, *Tetrahedron* **2002**, *58*, 845–866. For selected Pd-catalyzed examples, see: c) D. J. Covell, M. C. White, *Angew. Chem. Int. Ed.* **2008**, *47*, 6448–6451; *Angew. Chem*. **2008**, *120*, 6548–6551; d) P.-S. Wang, P. Liu, Y.-J. Zhai, H.-C. Lin, Z.-Y. Han, L.-Z. Gong, *J. Am. Chem. Soc.* **2015**, *137*, 12732–12735; e) S. E. Ammann, W. Liu, M. C. White, *Angew. Chem. Int. Ed.* **2016**, *55*, 9571–9575; *Angew. Chem.* **2016**, *128*, 9723–9727.

[5] For a comprehensive review, see: a) Z. Lu, S. Ma, *Angew. Chem. Int. Ed.* **2008**, *47*, 258–297; *Angew. Chem.* **2008**, *120*, 264–303; For selected examples, see: b) B. M. Trost, M. L. Crawley, *J. Am. Chem. Soc.* **2002**, *124*, 9328–9329; c) S. F. Kirsch, L. E. Overman, *J. Am. Chem. Soc.* **2005**, *127*, 2866–2867; d) K. Onitsuka, H. Okuda, H. Sasai, *Angew. Chem. Int. Ed*. **2008**, *47*, 1454–1457; *Angew. Chem.* **2008**, *120*, 1476–1479; e) N. Kanbayashi, K. Onitsuka, *Angew. Chem. Int. Ed.* **2011**, *50*, 5197–5199; *Angew. Chem.* **2011**, *123*, 5303–5305; f) F. López, T. Ohmura, J. F. Hartwig, *J. Am. Chem. Soc*. **2003**, *125*, 3426–3427; g) C. Shu, J. F. Hartwig, *Angew. Chem. Int. Ed*. **2004**, *43*, 4794–4797; *Angew. Chem.* **2004**, *116*, 4898–4901; h) P. A. Evans, D. K. Leahy, *J. Am. Chem. Soc*. **2000**, *122*, 5012–5013; i) P. A. Evans, D. K. Leahy, *J. Am. Chem. Soc*. **2002**, *124*, 7882–7883.

[6] For a comprehensive review on reactions with allenes and alkynes, see: a) P. Koschker, B. Breit, *Acc. Chem. Res.* **2016**, *49*, 1524–1536; For recent examples on reactions with 1,3-dienes, see: b) S.-Q. Yang, A.-J. Han, Y. Liu, X.-Y. Tang, G.-Q. Lin, Z.-T. He, *J. Am. Chem. Soc.* **2023**, *145*, 3915–3925; c) L.-F. Fan, R. Liu, X.-Y. Ruan, P.-S. Wang, L.-Z. Gong, *Nat. Synth.* **2022**, *1*, 946–955.

[7] For a review, see: a) R. Noyori, *Angew. Chem. Int. Ed*. **2002**, *41*, 2008–2022; *Angew. Chem.* **2002**, *114*, 2108–2123. For a selection of recent examples, see: b) J. Guan, J. Chen, Y. Luo, L. Guo, W. Zhang, *Angew. Chem. Int. Ed.* **2023**, *62*, e202306380; *Angew. Chem*. **2023**, *135*, e202306380; c) Y. Shi, J. Wang, Q. Yin, X. Zhang, P. Chiu, *Org. Lett.* **2021**, *23*, 5658–5663; d) F. Chen, Y. Zhang, L. Yu, S. Zhu, *Angew. Chem. Int. Ed*. **2017**, *56*, 2022–2025; *Angew. Chem*. **2017**, *129*, 2054–2057; e) K. Zhang, Q. Liu, R. He, D. Chen, Z. Deng, N. Huang, H. Zhou, *Green Chem.* **2021**, *23*, 1628–1632; f) H.-Y. Bin, L. Cheng, X. Wu, C.-L. Zhu, X.-H. Yang, J.-H. Xie, Q.-L. Zhou, *Chem. Sci.* **2021**, *12*, 7793–7799; g) J. Ma, W. Li, L. He, H. Lv, *Chem. Commun.* **2022**, *58*, 5841–5844.

[8] For reviews on enantioselective reductive coupling, see: a) E. Ortiz, J. Shezaf, Y.-H. Chang, M. J. Krische, *ACS Catal.* **2022**, *12*, 8164–8174; b) E. Skucas, M.-Y. Ngai, V. Komanduri, M. J. Krische, *Acc. Chem. Res.* **2007**, *40*, 1394–1401; For examples on enantioselective alkylative coupling, see: c) Y. Yang, S.-F. Zhu, C.-Y. Zhou, Q.-L. Zhou, *J. Am. Chem. Soc.* **2008**, *130*, 14052–14053; d) M. Nie, W. Fu, Z. Cao, W. Tang, *Org. Chem. Front.* **2015**, *2*, 1322–1325.

[9] For a review, see: a) T. Bauer, Coord. *Chem. Rev.* **2015**, *299*, 83–150; For selected examples, see: b) W. Oppolzer, R. N. Radinov, *J. Am. Chem. Soc*. **1993**, *115*, 1593–1594; c) P. Wipf, S. Ribe, *J. Org. Chem.* **1998**, *63*, 6454–6455; d) Y. K. Chen, A. E. Lurain, P. J. Walsh, *J. Am. Chem. Soc*. **2002**, *124*, 12225–12231; e) A. E. Lurain, P. J. Walsh, *J. Am. Chem. Soc*. **2003**, *125*, 10677–10683; f) L. Salvi, S.-J. Jeon, E. L. Fisher, P. J. Carroll, P. J. Walsh, *J. Am. Chem. Soc.* **2007**, *129*, 16119–16125; g) Z. Chai, X.-Y. Liu, J.-K. Zhang, G. Zhao, *Tetrahedron: Asymmetry* **2007**, *18*, 724–728; h) J.-X. Ji, L.-Q. Qiu, C. W. Yip, A. S. C. Chan, *J. Org. Chem*. **2003**, *68*, 1589–1590; i) H.-L. Wu, P.-Y. Wu, B.-J. Uang, *J. Org. Chem*. **2007**, *72*, 5935–5937; j) D. Tomita, R. Wada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2005**, *127*, 4138–4139; k) D. A. Evans, Y. Aye, *J. Am. Chem. Soc.* **2006**, *128*, 11034–11035; l) K. Aikawa, Y. Hioki, K. Mikami, *J. Am. Chem. Soc.* **2009**, *131*, 13922–13923; m) D. Tomita, M. Kanai, M. Shibasaki, *Chem. Asian J.* **2006**, *1*, 161–166; n) T. Shono, T. Harada, *Org. Lett*. **2010**, *12*, 5270–5273; o) P. Wang, G.-R. Ma, S.-L. Yu, C.-S. Da, *Chirality* **2019**, *31*, 79–86.

[10] For reviews on NHK reactions, see: a) A. Fürstner, *Chem. Rev*. **1999**, *99*, 991–1046; b) G. C. Hargaden, P. J. Guiry, *Adv. Synth. Catal*. **2007**, *349*, 2407–2424; c) A. Gil, F. Albericio, M. Álvarez, *Chem. Rev*. **2017**, *117*, 8420–8446.

[11] a) M. Giedyk, K. Goliszewska, D. Gryko, *Chem. Soc. Rev*. **2015**, *44*, 3391–3404; b) A. Frei, A. P. King, G. J. Lowe, A. K. Cain, F. L. Short, H. Dinh, A. G. Elliott, J. Zuegg, J. J. Wilson, M. A. T. Blaskovich, *Chem. Eur. J*. **2021**, *27*, 2021–2029; c) K. S. Egorova, V. P. Ananikov, *Organometallics* **2017**, *36*, 4071–4090.

[12] a) L. Wang, C. Lin, Q. Chong, Z. Zhang, F. Meng, *Nat. Commun*. **2023**, *14*, 4825; b) Z. Liang, L. Wang, Y. Wang, L. Wang, Q. Chong, F. Meng, *J. Am. Chem. Soc*. **2023**, *145*, 3588–3598; c) W. Huang, J. Bai, Y. Guo, Q. Chong, F. Meng, *Angew. Chem. Int. Ed*. **2023**, *62*, e202219257; *Angew. Chem*. **2023**, *135*, e202219257; d) L. Wang, W. Lu, J. Zhang, Q. Chong, F. Meng, *Angew. Chem. Int. Ed*. **2022**, *61*, e202205624; *Angew. Chem*. **2022**, *134*, e202205624; e) W. Lu, Y. Zhao, F. Meng, *J. Am. Chem. Soc*. **2022**, *144*, 5233–5240; f) L. Wang, L. Wang, M. Li, Q. Chong, F. Meng, *J. Am. Chem. Soc*. **2021**, *143*, 12755–12765; g) Z. Liang, Q. Chong, F. Meng, *Sci. China Chem*. **2021**, *64*, 1750–1755; h) H. Zhang, J. Huang, F. Meng, *Cell Reports Physical Science* **2021**, *2*, 100406; i) W. Huang, F. Meng, *Angew. Chem. Int. Ed*. **2021**, *60*, 2694–2698; *Angew. Chem*. **2021**, *133*, 2726–2730; j) D. Zhu, Y. Zhao, Q. Chong, F. Meng, *Chin. J. Chem*. **2022**, *40*, 190–194; k) H. Zhang, W. Huang, T. Wang, F. Meng, *Angew. Chem. Int. Ed*. **2019**, *58*, 11049–11053; *Angew. Chem*. **2019**, *131*, 11165–11169.

[13] a) X. Jiang, H. Jiang, Q. Yang, Y. Cheng, L.-Q. Lu, J. A. Tunge, W.-J. Xiao, *J. Am. Chem. Soc*. **2022**, *144*, 8347–8354; b) H. Jiang, X.-K. He, X. Jiang, W. Zhao, L.-Q. Lu, Y. Cheng, W.-J. Xiao, *J. Am. Chem. Soc*. **2023**, *145*, 6944–6952; For a related Ni-catalyzed enantioselective reductive arylation of aldehydes, see: c) Z. Zhu, J. Xiao, M. Li, Z. Shi, *Angew. Chem. Int. Ed*. **2022**, *61*, e202201370; *Angew. Chem*. **2022**, *134*, e202201370.

[14] Y. Huang, R.-Z. Huang, Y. Zhao, *J. Am. Chem. Soc*. **2016**, *138*, 6571–6576.

[15] a) X. Wu, H. Xia, C. Gao, B. Luan, L. Wu, C. Zhang, D. Yang, L. Hou, N. Liu, T. Xia, H. Li, J. Qu, Y. Chen, *Nat. Chem*. **2023**, DOI: 10.1038/s41557-023-01378-9; b) T. Xia, Y. Wu, J. Hu, X. Wu, J. Qu, Y. Chen, *Angew. Chem. Int. Ed*. **2024**, e202316012.

[16] a) Y. Jiang, Q. Jiang, G. Zhu, X. Zhang, *Tetrahedron Lett*. **1997**, *38*, 215–218; For applications of bisoxazolinephosphines ligands in Co-catalyzed enantioselective reactions, see: b) S. Ghorai, S. S. Chirke, W.-B. Xu, J.-F. Chen, C. Li, *J. Am. Chem. Soc*. **2019**, *141*, 11430–11434; c) K. Li, L. Wei, M. Sun, B. Li, M. Liu, C. Li, *Angew. Chem. Int. Ed*. **2021**, *60*, 20204–20209; *Angew Chem*. **2021**, *133*, 20366–20371; d) S. Ghorai, S. U. Rehman, W.-B. Xu, W.-Y. Huang, C. Li, *Org. Lett*. **2020**, *22*, 3519–3523; e) J.-F. Chen, C. Li, *Org. Lett*. **2020**, *22*, 4686–4691.

[17] For a comprehensive review, see: H.-H. Zhang, T.-Z. Li, S.-J. Liu, F. Shi, *Angew. Chem. Int. Ed*. **2024**, *63*, e202311053.

[18] Y. Wu, M. Li, J. Sun, G. Zheng, Q. Zhang, *Angew. Chem. Int. Ed*. **2022**, *61*, e202117340; *Angew. Chem*. **2022**, *134*, e202117340.

[19] Deposition numbers 2349725 (for **6j**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[20] Y. Takashima, Y. Kobayashi, *J. Org. Chem*. **2009**, *74*, 5920–5926.

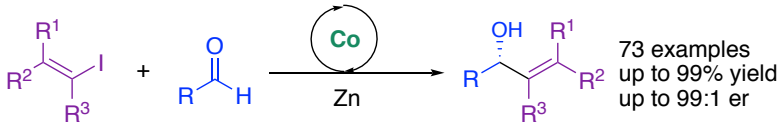
[21] C. Qiao, A. Villar-Yanez, D. Garay-Ruiz, J.-B. Buchholz, C. Bo, A. W. Kleij, *ACS Catal*. **2022**, *12*, 5464–5469.

[22] M.-Y. Chang, Y.-H. Kung, C.-C. Ma, S.-T. Chen, *Tetrahedron* **2007**, *63*, 1339–1344.

10.1002/anie.202405290

WILEY VCH

Entry for the Table of Contents



- Broad scope with diversified substitution patterns
- Applicable to construction of axial stereogenicity

A new approach for highly efficient and enantioselective alkenylation of aldehydes promoted by an easily accessible cobalt-based complex was developed. This protocol represents the first example of incorporating a wide range of alkenyl groups with diversified substitution patterns as well as axial stereogenicity into enantioenriched allylic alcohols.

Institute and/or researcher Twitter usernames: ((optional))