A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

www.angewandte.org

Accepted Article

Title: Precatalyst-Enabled Selectivity: Enantioselective NiH-catalyzed anti-Hydrometalative Cyclization of Alkynones to endo- and Hetero-cyclic Allylic Alcohols

Authors: Xiao-Wen Zhang, Ming-Hui Zhu, Hai-Xiang Zeng, Qi-Yang Li, and Wen-Bo Liu

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202110815

Link to VoR: https://doi.org/10.1002/anie.202110815

WILEY-VCH

10.1002/anie.202110815

WILEY-VCH

COMMUNICATION

Precatalyst-Enabled Selectivity: Enantioselective NiH-Catalyzed *anti*-Hydrometalative Cyclization of Alkynones to *endo*- and Hetero-cyclic Allylic Alcohols

Xiao-Wen Zhang,[a] Ming-Hui Zhu,[a] Hai-Xiang Zeng,[a] Qi-Yang Li,[a] and Wen-Bo Liu*[a],[b]

[a] X.-W. Zhang, M.-H. Zhu, H.-X. Zeng, Q.-Y. Li, Prof. W.-B. Liu
Sauvage Center for Molecular Sciences, Engineering Research Center of Organosilicon Compounds & Materials (Ministry of Education), and College of Chemistry and Molecular Sciences
Wuhan University
299 Bayi Rd, Wuhan 430072, China
E-mail: wenboliu@whu.edu.cn

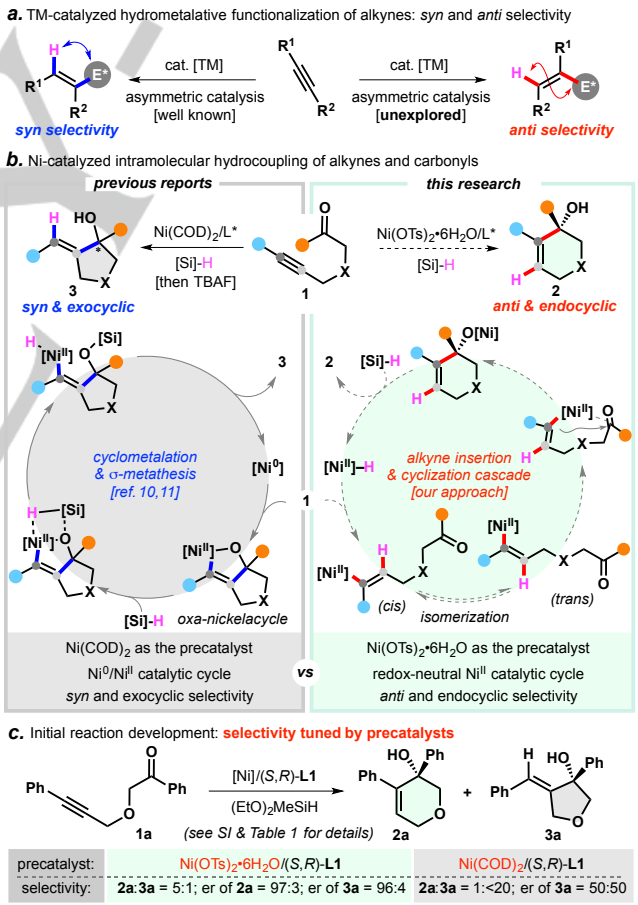
[b] Prof. W.-B. Liu
State Key Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Lingling Rd, Shanghai 200032, China

Supporting information for this article is given via a link at the end of the document.

Abstract: A highly enantioselective NiH-catalyzed hydrocyclization of alkynones with unparalleled *anti*- and endocyclic selectivities is described. The choice of the precatalysts has significant influence in tuning the regio- and enantio-selectivity. Using $Ni(OTs)_2$/Phox as a precatalyst and $(EtO)_2MeSiH$ as a hydride source, an array of enantioenriched O-, N-, and S-containing heterocyclic tertiary allylic alcohols are obtained in 24–81% yields with 80:20–99:1 er. Mechanistic investigations and synthetic application are also carried out. This study represents an efficient access to a set of allylic alcohols that are unable to access by the state-of-the-art coupling reactions.

Transition-metal-catalyzed hydrofunctionalization of alkynes is a straightforward method for the rapid synthesis of functional group-enriched alkenes from readily accessible materials.[1] Plentiful achievements have been made in last decades enabling enantioselective *syn*-hydrofunctionalization of alkynes which introduces a hydrogen atom and a functional group with a *cis* relationship (Scheme 1a).[2,3] In contrast, processes of the complementary *anti*-hydrofunctionalization are synthetically appealing but more challenging in addressing regio- and stereoselectivities.[2a,4] In particular, their asymmetric variants are still unexplored to date.

Allylic alcohols are ubiquitous units in natural products and pharmaceuticals.[2b,c] Since the seminal contributions by the groups of Montgomery,[5] Jamison,[6] and others,[7] nickel-catalyzed reductive coupling of alkynes and aldehydes is a powerful strategy for the construction of allylic alcohols.[8] In particular, its intramolecular version allows the regio- and enantio-selective access to heterocyclic allylic alcohols.[9–11] Recent reports by Tang[10] and Liu[11] elegantly illustrated the capability of nickel complexes derived from $Ni(COD)_2$ and chiral phosphine ligands in catalyzing enantioselective cyclization of alkynones (Scheme 1b, left). These examples intrinsically operate through an oxidative cyclometalation of Ni^0 with the two π-components to form an oxa-nickelacycle followed by reduction with silanes, therefore allylic alcohols with exocyclic double bond and *syn* stereochemical relationships of the two newly formed bonds are uniformly obtained.[5b,7d] We envisioned that this



Scheme 1. Transition-metal-catalyzed hydrofunctionalization of alkynes.

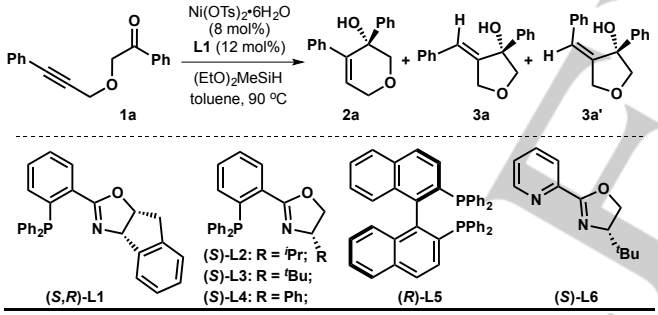
mechanistic paradigm could be altered if to initiate the reaction with a Ni^{II}–H catalyst, which could convert the same type of alkynones **1** into stereochemically and topologically complementary endocyclic products **2** (Scheme 1b, right). We proposed that this approach could undergo a regioselective migratory insertion of alkynes into Ni^{II}–H species,[12] followed by a

10.1002/anie.202110815

cis/*trans* isomerization of the resulting alkenylnickel[13] and concomitant addition onto carbonyls.

From a mechanistic standpoint, this *anti*-hydrometalative transformation is of considerable challenges. A judicious choice of Ni^{II} precatalysts and hydride sources to directly form Ni^{II}–H affecting the rapid alkyne insertion to avoid the formation of low-valent nickel (i.e., Ni^0) that leads to undesired pathways[10,11] is key to the success of this reaction. Additionally, the isomerization of the putative 1,2-disubstituted *cis*-alkenylnickel species to the corresponding *trans* one requires overriding the steric repulsion between the nickel and the substituent on the neighboring carbon.[13] Indeed, such isomerization of 1,2-disubstituted alkenylnickel has been rarely investigated, although strategies involving *cis*/*trans* isomerization of fully substituted alkenylnickel species formed via alkyne insertion into arylnickel species and sequential cyclization were successfully demonstrated by Liu,[14] Lam,[15] and our group.[16] Gratifyingly, a preliminary proof was obtained by the use of $Ni(OTs)_2$•$6H_2O$ as the nickel precursor predominately resulting endocyclic product **2a** with 97:3 er (Scheme 1c). As expected, a Ni^0 precursor, $Ni(COD)_2$, exclusively provided the exocyclic product **3a** with no enantio-induction. The results support our idea of tuning the regio- and enantio-selectivities by precatalysts. Herein, we report our study toward this unprecedented nickel-catalyzed enantio-, regio-, and *anti*-selective intramolecular coupling of alkynones to construct O-, N-, S-containing endocyclic allylic alcohols.

Table 1. Selected results of condition optimizations.



entry[a]	variation	**2a**/**3a**/**3a'** (%)[b]	er of **2a**[c]
1	none	61/15/–	96:4
2	**L2** instead of **L1**	65/12/–	95.5:4.5
3	**L3** instead of **L1**	22/19/7	94.5:5.5
4	**L4** instead of **L1**	52/12/8	89.5:10.5
5	**L5** or **L6** instead of **L1**	trace/–/–	–
6[d]	DME instead of THF	75 (68)[e]/15/–	97:3

[a] Reactions conducted with $Ni(OTs)_2$•$6H_2O$ (8 mol%), **L1** (12 mol%), $(EtO)_2MeSiH$ (0.2 mmol), and **1a** (0.1 mmol, 0.1 M) for 20–23 h. [b] Determined by ^1H NMR. [c] Determined by HPLC analysis (Chiralpak AD-H). [d] With 0.05 M of **1a** on a 0.2 mmol scale. [e] Isolated yield.

Our further extensive explorations (Tables S1–6) of nickel precursors, ligands, solvents, and hydride reagents revealed that using $Ni(OTs)_2$•$6H_2O$/InPhox (**L1**) as the precatalyst in the presence of $(EtO)_2MeSiH$ in toluene delivered **2a** as the major product in 61% yield with 96:4 er (entry 1, Table 1). It should be mentioned that Phox-type ligands[17] play a significant role in the productivity (entries 1–4), while the bulkier ^{t}Bu-Phox (**L3**) showed slightly poor results (entry 3). In a sharp contrast, no product was observed with either BINAP or Pyox (**L5** or **L6**, entry 5). Finally, we were pleased to identify the optimal reaction conditions by using DME as the solvent (entry 6).

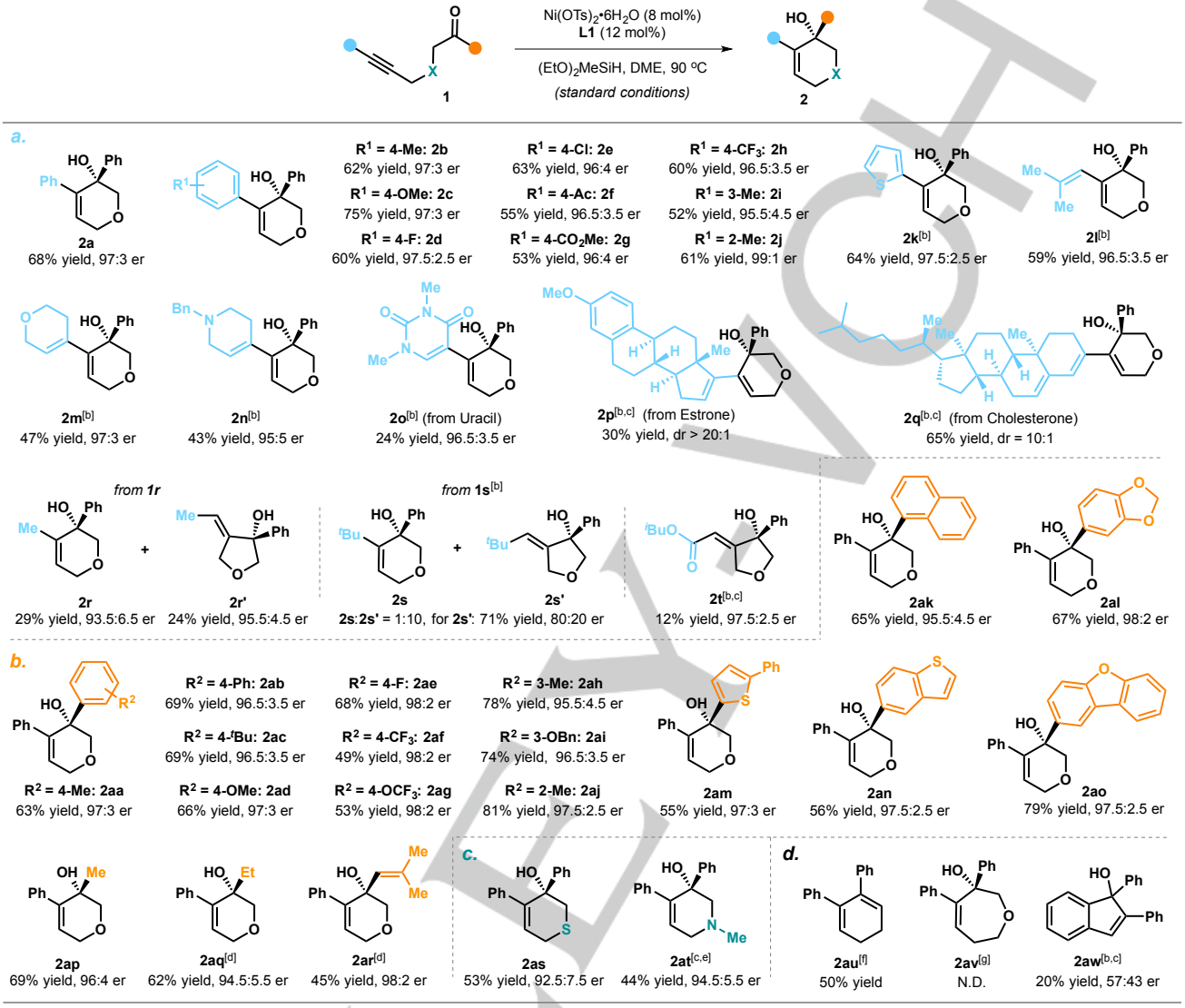
Next, the generality of the reaction was elucidated. The compatibility of substituents on the alkyne moiety was first examined (Table 2a). Substrates with various substituents including electron-rich and electron-deficient aromatics (**2b**–**2j**) afforded the corresponding products in 52%–75% yields with 95.5:4.5–99:1 er. Acetyl and ester functionalities were well tolerated by this neutral reaction conditions (**2f** and **2g**). It is notable that thienyl substituted alkynone reacted smoothly affording alcohol **2k** in 64% yield and 97.5:2.5 er. Alkenes are proven to undergo migratory insertion into Ni–H species,[18] but are remarkably compatible in this system. A few alkenyl-substituted alkynones were converted into the corresponding 1,3-diene products **2l**–**2q** with comparable enantioselectivities to those of the aryl substrates. Bio-important heterocycles, for instance, dihydropyranyl-, tetrahydropyridyl-, and uracil-substituted alkynones (**2m**–**2o**) were feasible substrates as well resulting in good enantioselectivities (95:5–97:3 er), albeit with lower yields. Interestingly, steroid-derived substrates (**2p** and **2q**) were amenable to generate their structurally complicated derivatives in good diastereoselectivities. Unfortunately, substrates with pendant alkyl-substituted alkynes underwent the cyclization in a much less regioselective manner (**2r** and **2s**). In particular, 5-*exo* cyclization product **2s'** was primarily obtained when sterically hindered ^{t}Bu-substituted alkyne **1s** was applied. These results demonstrate that the steric hindrance of the alkyne moiety is detrimental to the regioselectivity in the hydrometalation step. An ester-substituted alkyne **1t** was also investigated, but resulting in exclusive exocyclic product **2t** in 12% yield with 97.5:2.5 er.

The scope of ketones was then explored (Table 2b). Aromatic ketones with various steric and electronic properties were well compatible with this reaction (**2aa**–**2al**, 49%–81% yields, 95.5:4.5–98:2 er). The reaction seems less sensitive to the sterics of the ketone moiety, and *ortho*-methylphenyl- (**2aj**) and 1-naphthyl- (**2ak**) substituted ketones were successfully cyclized in good yields and enantioselectivities. Gratifyingly, heteroaryl ketones bearing thiophene (**2am**), benzothiophene (**2an**), and dibenzofuran (**2ao**), were also appropriate substrates. Subjecting alkyl substituted (methyl and ethyl) ketones to the conditions delivered **2ap** and **2aq** in 62%–69% yields with 94.5:5.5–96:4 er. Importantly, allyl-substituted ketone underwent the reaction with concomitant isomerization of the terminal olefin to internal (**2ar**, see Scheme S1). In addition, this approach also provided access to other heteroatom-containing allylic alcohols, for instance, thiopyran **2as** and tetrahydropyridine **2at** (Table 2c). It should be noted that although the regioselectivity of the reaction ranges from moderate to good (see SI), the corresponding isomers are readily separated by column chromatography. Some unsuccessful examples were included in Table 2d and Scheme S2 of the SI.

10.1002/anie.202110815

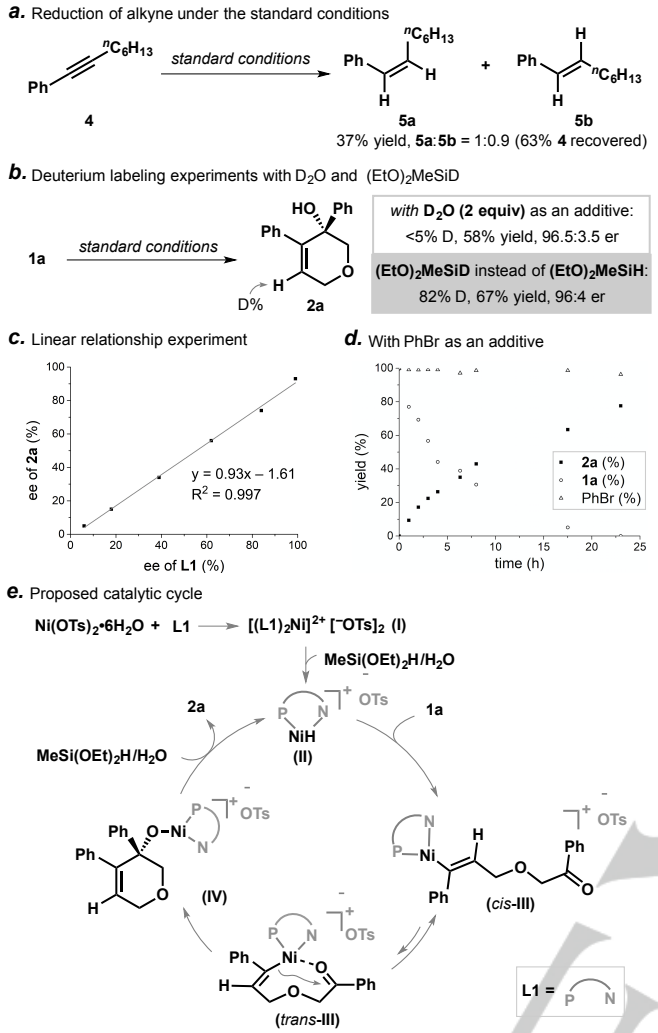
WILEY-VCH

Table 2. Substrate scope.[a]



[a] Reactions conducted on a 0.2 mmol scale under the *standard conditions*. Enantiomeric ratio (er) determined by HPLC. [b] With $Ni(OTs)_2•6H_2O$ (10 mol%) and **L1** (12 mol%). [c] 0.1 mmol scale. [d] With (*S*,*R*)-4-MeO-InPhox (**L7**). [e] With (*S*)-Bn-Phox (**L8**). [f] With 4:1 of regioselectivity and formed through the Ni-catalyzed cyclization followed by dehydration of the alcohol. [g] Complex mixture and *semi*-reduction of alkyne to alkene was observed. See SI for details.

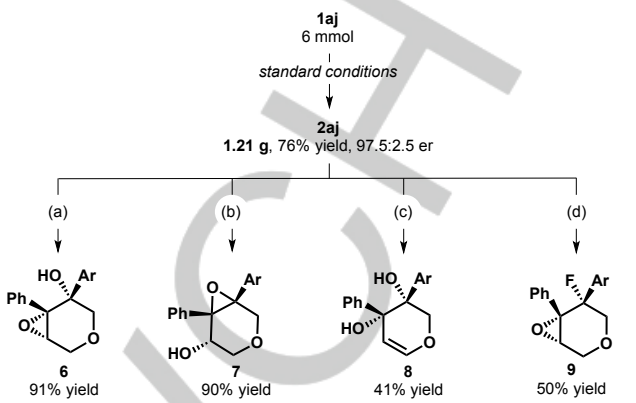
A series of experiments were then conducted to gain insights into the mechanism (Scheme 2 and Schemes S3–8 in SI). To probe the alkyne insertion step, alkyne **4** was subjected to the standard conditions, generating a *cis*/*trans* mixture of *semi*-reduction products **5a** and **5b** (Scheme 2a), which indicates the involvement of isomerization of the alkenylnickel species formed by the alkyne insertion into the Ni–H species. Further insights were obtained by deuterium scrambling experiments (Scheme 2b). With D_2O added, no detectable deuterium incorporation was observed. On the other hand, the reaction employing $(EtO)_2MeSiD$ delivered the allylic alcohol **2a** with 82% deuterium incorporation. These results clearly indicate that the alkenyl hydrogen atom of the product **2a** is mainly from the silane. ^{31}P NMR studies of the in situ complexation of the catalyst were also carried out (Scheme S4). The formation of Ni(**L1**)$_2$ was observed as the solo form regardless of the molar ratio of $Ni(OTs)_2•6H_2O$ to **L1**, which is consistent with previous observation by Lloyd-Jones et al.[19] However, the proportionality of the enantiomeric excess of **2a** and **L1** indicates the active catalytic nickel complex likely involves a single ligand (Scheme 2c),[20,21] which is also in line with the fact that constant enantioselectivity was observed when varying the ratio of $Ni(OTs)_2•6H_2O$ versus **L1** (Scheme S3d). Finally, the standard reaction with stoichiometric phenyl bromide or hexyl bromide as an additive resulting in little consumption of the bromides (Scheme 2d and Schemes S6–7), as well as using $Ni(COD)_2$ as the nickel precursor exclusively forming racemic **3a** (Scheme 1c), could rule out the formation of low-valent nickel species during the cycle.[22]



Scheme 2. Mechanistic investigations.

Taken all these clues together, a postulated mechanism is depicted in Scheme 2e. Reaction of Ni(**L1**)$_2$ (**I**) and (EtO)$_2$MeSiH forms Ni^{II}–H species **II**, followed by alkyne insertion to deliver *cis*-alkenylnickel *cis*-**III**.[15d] Then reversible *cis*/*trans* isomerization provides *E*-alkenylnickel *trans*-**III** followed by coordination of ketone to the nickel center and an intramolecular addition affording the allylic alkoxide nickel **IV**. Although the isomerization of *cis*-**III** to *trans*-**III** is sterically less favored, the coordination/addition step probably is the driving force of this reaction.[4d] Finally, the nickel species **II** is regenerated in the presence of H_2O and silane.[23] This reaction pathway is distinct from the known coupling of alkynes and carbonyls involving the an oxanickelacyclic intermediate,[5b,10] which provides conceptually new inputs to the enantioselective coupling chemistry.

The synthetic potential was showcased in Scheme 3. A gram-scale reaction of **1aj** furnished **2aj** without loss of efficiency. Treating **2aj** with *m*-CPBA produced an epoxide **6**, containing three contiguous stereocenters, in 91% yield with perfect diastereoselectivity (>20:1 dr).[24] Isomerization of the epoxide **6** with $TiCl_4$ produced a tetrasubstituted epoxide **7** in quantitative yield. In contrast, ring-opening product of **6** was obtained in the presence of LDA, giving rise to pinacol **8** bearing two adjacent stereocenters. Fluorination of the epoxide **6** using DAST generated a bulky tertiary alkyl fluoride **9** in moderate yield.[25]



Scheme 3. Gram-scale synthesis and product derivatization. Conditions: (a) *m*CPBA (1.5 equiv), $NaHCO_3$ (2.5 equiv), DCM, 0 °C to rt; (b) i) as (a); ii) $TiCl_4$ (1.1 equiv), DCM, –78 °C; (c) i) as (a); ii) LDA (3.0 equiv), THF, rt; (d) i) as (a); ii) DAST (2.4 equiv), DCM, –78 °C to rt. Ar = 2-Me-C_6H_4. See SI for conditions.

In conclusion, an enantio- and regio-selective nickel-catalyzed *anti*-hydrocyclization of alkynones was developed. With a Phox ligand-derived nickel complex as the precatalyst and methyldiethoxysilane as the hydride source, a broad range of enantioenriched heterocyclic tertiary allylic alcohols were efficiently synthesized in good yields with excellent enantioselectivities. This study offers conceptually distinct alternative to coupling alkynes and carbonyls, as well as a new mode for *anti*-selective and enantioselective hydrofunctionalization of alkynes. Further mechanistic studies in detail and expanding of this reaction mode are currently ongoing in our laboratory.

Acknowledgements

We thank NSFC (21971198 and 21772148), the Natural Science Foundation of Hubei Province (Grant No. 2020CFA036), and the Fundamental Research Funds for the Central Universities (2042021kf0193) for financial support. Dr. Hengjiang Cong is thanked for X-ray crystallographic analysis. We acknowledge the Core Research Facilities of CCMS (WHU) for access to analytic equipment. We are grateful to Dr. Yiyang Liu (Pfizer) and Prof. Xiaotian Qi (WHU) for useful discussions.

Keywords: NiH catalysis • hydrofunctionalization of alkynes • asymmetric cyclization • heterocycles • allylic alcohols

[1] Selected reviews: a) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079; b) R. Severin, S. Doye, *Chem. Soc. Rev.* **2007**, *36*, 1407; c) X. Zeng, *Chem. Rev.* **2013**, *113*, 6864; d) Y. Yamamoto, *Chem. Soc. Rev.* **2014**, *43*, 1575; e) A. M. Suess, G. Lalic, *Synlett* **2016**, *27*, 1165; f) J. Corpas, P. Mauleón, R. G. Arrayás, J. C. Carretero, *ACS Catal.* **2021**, *11*, 7513.

[2] Selected reviews: a) Y. Zheng, W. Zi, *Tetrahedron Lett.* **2018**, *59*, 2205; b) M. Holmes, L. A. Schwartz, M. J. Krische, *Chem. Rev.* **2018**, *118*,

6026; c) C. C. Meyer, E. Ortiz, M. J. Krische, *Chem. Rev.* **2020**, *120*, 3721.

[3] Selected examples: a) J.-R. Kong, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2006**, *128*, 718; b) K. Masuda, N. Sakiyama, R. Tanaka, K. Noguchi, K. Tanaka, *J. Am. Chem. Soc.* **2011**, *133*, 6918; c) C. C. Bausch, R. L. Patman, B. Breit, M. J. Krische, *Angew. Chem. Int. Ed.* **2011**, *50*, 5687; *Angew. Chem.* **2011**, *123*, 5805; d) M.-Y. Ngai, A. Barchuk, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 280; e) P. Gandeepan, C.-H. Cheng, *Acc. Chem. Res.* **2015**, *48*, 1194; f) Y.-L. Li, S.-Q. Zhang, J. Chen, J.-B. Xia, *J. Am. Chem. Soc.* **2021**, *143*, 7306; g) J. Montgomery, *Angew. Chem. Int. Ed.* **2004**, 43, 3890; *Angew. Chem.* **2004**, 116, 3980; h) R. M. Moslin, K. Miller-Moslin, T. F. Jamison, *Chem. Commun*. **2007**, 4441; i) M. R. Chaulagain, G. J. Sormunen, J. Montgomery, *J. Am. Chem. Soc.* **2007**, *129*, 9568; j) A. B. Bahadoor, A. Flyer, G. C. Micalizio, *J. Am. Chem. Soc.* **2005**, *127*, 3694; k) K. Shen, X. Han, X. Lu, *Org. Lett.* **2013**, *15*, 1732; l) X.-T. Liu, X.-Y. Han, Y. Wu, Y.-Y. Sun, L. Gao, Z. Huang, Q.-W. Zhang, *J. Am. Chem. Soc.* **2021**, *143*, 11309.

[4] Selected examples: a) B. M. Trost, Z. T. Ball, *J. Am. Chem. Soc*. **2005**, *127*, 17644; b) B. Sundararaju, A. Furstner, *Angew. Chem. Int. Ed.* **2013**, *52*, 14050; *Angew. Chem.* **2013**, 125, 14300. c) C. Gunanathan, M. Hölscher, F. Pan, W. Leitner, *J. Am. Chem. Soc.* **2012**, *134*, 14349; d) M. Hari Babu, G. Ranjith Kumar, R. Kant, M. Sridhar Reddy, *Chem. Commun*. **2017**, *53*, 17644; e) A. Yamamoto; M. Suginome, *J. Am. Chem. Soc.* **2005**, *127*, 15706. f) X. Wang, Y. Liu, R. Martin, *J. Am. Chem. Soc*. **2015**, *137*, 6476; g) K. Tanaka, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 11492; h) K. Tanaka, G. C. Fu, *Angew. Chem. Int. Ed.* **2002**, *41*, 1607; *Angew. Chem.* **2002**, *114*, 1677; i) For a review: S. E. Bottcher, L. E. Hutchinson, D. J. Wilger, *Synthesis* **2020**, *52*, 2807.

[5] a) E. Oblinger, J. Montgomery, *J. Am. Chem. Soc.* **1997**, *119*, 9065; b) E. P. Jackson, H. A. Malik, G. J. Sormunen, R. D. Baxter, P. Liu, H. Wang, A.-R. Shareef, J. Montgomery, *Acc. Chem. Res.* **2015,** *48*, 1736.

[6] a) W.-S. Huang, J. Chan, T. F. Jamison, *Org. Lett.* **2000**, *2*, 4221; b) K. M. Miller, W.-S. Huang, T. F. Jamison, *J. Am. Chem. Soc.* **2003**, *125*, 3442; c) E. A. Standley, S. Z. Tasker, K. L. Jensen, T. F. Jamison, *Acc. Chem. Res.* **2015**, *48*, 1503.

[7] a) Y. Sato, M. Takimoto, K. Hayashi, T. Katsuhara, K. Takagi, M. Mori, *J. Am. Chem. Soc.* **1994**, *116*, 9771; b) S. Ikeda, *Angew. Chem. Int. Ed.* **2003**, *42*, 5120; *Angew. Chem.* **2003**, *115*, 5276; c) Y. Yang, S.-F. Zhu, H.-F. Duan, C.-Y. Zhou, L.-X. Wang, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007,** *129*, 2248; d) S. Ogoshi, T. Arai, M. Ohashi, H. Kurosawa, *Chem. Commun.* **2008**, 1347.

[8] H. A. Malik, R. D. Baxter, J. Montgomery in *Catalysis without Precious Metals*, 1st ed. (Ed.: R. M. Bullock), Wiley-VCH: Weinheim, Germany, **2010**, pp 181.

[9] a) E. A. Colby, K. C. O'Brien, T. F. Jamison, *J. Am. Chem. Soc.* **2004**, *126*, 998; b) B. Knapp-Reed, G. M. Mahandru, J. Montgomery, *J. Am. Chem. Soc.* **2005**, *127*, 13156; c) C. C. Chrovian, B. Knapp-Reed, J. Montgomery, *Org. Lett.* **2008**, *10*, 811; d) A.-R. Shareef, D. H. Sherman, J. Montgomery, *Chem. Sci.* **2012**, *3*, 892; e) S. Kitahata, A. Katsuyama, S. Ichikawa, *Org. Lett.* **2020**, *22*, 2697.

[10] a) W. Fu, M. Nie, A. Wang, Z. Cao, W. Tang, *Angew. Chem. Int. Ed.* **2015**, *54*, 2520; *Angew. Chem.* **2015**, *127*, 2550; b) G. Liu, W. Fu, X. Mu, T. Wu, M. Nie, K. Li, X. Xu, W. Tang, *Commun. Chem.* **2018**, *1*, 90.

[11] a) Y. Mu, T. Zhang, Y. Cheng, W. Fu, Z. Wei, W. Chen, G. Liu, *Catal. Sci. Technol.* **2021**, *11*, 2306; b) W. Chen, Y. Cheng, T. Zhang, Y. Mu, W. Jia, G. Liu, *J. Org. Chem.* **2021**, *86*, 5166.

[12] a) L. She, X. Li, H. Sun, J. Ding, M. Frey, H.-F. Klein, *Organometallics* **2007**, *26*, 566; b) G. L. Wilson, M. Abraha, J. A. Krause, H. Guan, *Dalton Trans.* **2015**, *44*, 12128.

[13] J. M. Huggins, R. G. Bergman, *J. Am. Chem. Soc.* **1979**, *101*, 4410.

[14] X. Zhang, X. Xie, Y. Liu, *Chem. Sci.* **2016**, *7*, 5815.

[15] a) C. Clarke, C. A. Incerti-Pradillos, H. W. Lam, *J. Am. Chem. Soc.* **2016**, *138*, 8068; b) C. Yap, G. M. J. Lenagh-Snow, S. N. Karad, W. Lewis, L. J. Diorazio, H. W. Lam, *Angew. Chem. Int. Ed.* **2017**, *56*, 8216; *Angew. Chem.* **2017**, *129*, 8328; c) S. N. Karad, H. Panchal, C. Clarke, W. Lewis, H. W. Lam, *Angew. Chem. Int. Ed.* **2018**, *57*, 9122; *Angew. Chem.* **2018**, *130*, 9260; d) H. Green, S. P. Argent, H. W. Lam, *Chem. Eur. J.* **2021**, *27*, 5897; e) For a recent example, J. Tian, W. Li, R. Li, L. He, H. Lv, *Chinese Chemical Letters* **2021**, 10.1016/jcclet.2021.06.006.

[16] Z. Lu, X.-D. Hu, H. Zhang, X.-W. Zhang, J. Cai, M. Usman, H. Cong, W.-B. Liu, *J. Am. Chem. Soc.* **2020**, *142*, 7328.

[17] G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336.

[18] C. F. Lochow, R. G. Miller, *J. Org. Chem.* **2002**, *41*, 3020.

[19] a) G. C. Lloyd-Jones, C. P. Butts, *Tetrahedron* **1998**, *54*, 901; b) K. L. Bray, C. P. Butts, G. C. Lloyd-Jones, M. Murray, *J. Chem. Soc. Dalton Trans.* **1998**, 1421.

[20] T. Satyanarayana, S. Abraham, H. B. Kagan, *Angew. Chem. Int. Ed.* **2009**, *48*, 456; *Angew. Chem.* **2009**, *121*, 464.

[21] The possibility of a homochiral complex Ni(**L1**)$_2$, formed by self-recognition of **L1**, as the catalytic species cannot be ruled out by the linear effect experiment.

[22] a) K. W. Shimkin, J. Montgomery, *J. Am. Chem. Soc.* **2018**, *140*, 7074; b) Z. Zhou, W. Liu, W. Kong, *Org. Lett.* **2020**, *22*, 6982; c) Y. He, Y. Cai, S. Zhu, *J. Am. Chem. Soc.* **2017**, *139*, 1061; d) Y. Zhang, B. Han, S. Zhu, *Angew. Chem. Int. Ed.* **2019**, *58*, 13860; *Angew. Chem.* **2019**, *131*, 13998; e) J. Diccianni, Q. Lin, T. Diao, *Acc. Chem. Res.* **2020**, *53*, 906; f) Y. Chen, Z. Ding, Y. Wang, W. Liu, W. Kong, *Angew. Chem. Int. Ed.* **2021**, *60*, 5273; *Angew. Chem.* **2021**, *133*, 5333.

[23] For mechanisms regard to the formation of the minor products, see Scheme S8 in SI.

[24] R. Guo, X. Zheng, D. Zhang, G. Zhang, *Chem. Sci.* **2017**, *8*, 3002.

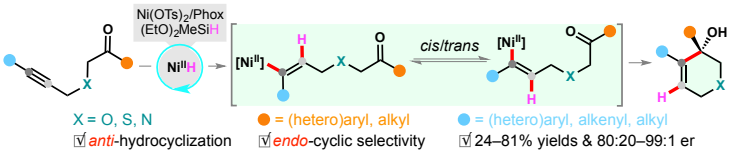
[25] F. Serpier, J.-L. Brayer, B. Folléas, S. Darses, *Org. Lett.* **2015,** *17*, 5496.

10.1002/anie.202110815

WILEY-VCH

COMMUNICATION

Entry for the Table of Contents



Metal precursor matters: An unprecedented NiH-catalyzed enantio-, regio-, and *anti*-selective intramolecular coupling of alkynones to construct O-, N-, S-containing endocyclic allylic alcohols was developed. The choice of metal precursors plays a key role in tuning the regio- and enantio-selectivity. This study offers a new *anti*-hydrocyclization mode for enantioselective hydrofunctionalization of alkynes.