How to cite: *Angew. Chem. Int. Ed.* **2022,** *61,* e202114556
International Edition: doi.org/10.1002/anie.202114556
German Edition: doi.org/10.1002/ange.202114556

Cross-Coupling

Reductive Alkylation of Alkenyl Acetates with Alkyl Bromides by Nickel Catalysis

*Rong-De He, Yunfei Bai, Guan-Yu Han, Zhen-Zhen Zhao, Xiaobo Pang, Xiaobo Pan, Xue-Yuan Liu, and Xing-Zhong Shu**

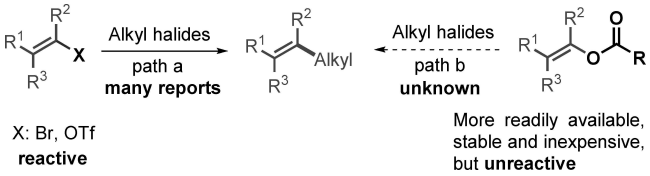
Dedicated to F. Dean Toste on the occasion of his 50th birthday

Abstract: *Catalytic alkylation of stable alkenyl C–O electrophiles is synthetically appealing, but studies to date have typically focused on the reactions with alkyl Grignard reagents. We report herein a cross-electrophile reaction of alkenyl acetates with alkyl bromides. This work has enabled a new method for the synthesis of aliphatic alkenes from alkenyl acetates to be established that can be used to add more structural complexity and molecular diversity with enhanced functionality tolerance. The method allows for a gram-scale reaction and modification of biologically active molecules, and it affords access to useful building blocks. Preliminary mechanistic studies reveal that the Ni^{I} species plays an essential role for the success of the coupling of these two reactivity-mismatched electrophiles.*

Cross-electrophile coupling has recently emerged as a powerful tool for forging Csp^2–Csp^3 bonds.[1] Reactions involving alkenyl electrophiles allow for facile and precise synthesis of aliphatic alkenes.[2] The majority of studies in this field describe coupling between alkenyl and alkyl halides (Scheme 1, path a),[3] and there are also several reports demonstrating coupling of alkenyl triflates.[4] However, the availability, stability, and cost issues associated with these alkenyl reagents have spurred ongoing efforts to develop new coupling fragments for alkene synthesis. Alkenyl carboxylates, especially alkenyl acetates, are readily available from abundant carbonyl compounds, and they are inexpensive, stable, easy to handle, and more environmentally friendly.[5] However, due to the low reactivity of these reagents,[5] their coupling reaction with alkyl halides remains to be disclosed (Scheme 1, path b).

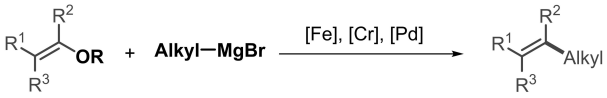
Stable enol derivatives, including carbamates, pivalates, and atom-economic acetates, have become attractive alternatives to organic halides within the cross-coupling arena.[6] Much of the focus in this field has been the development of arylation reactions for the synthesis of styrenes, where aryl metallic reagents (e.g., Ar–M, M=B and Zn),[7] aryl halides,[8] and arenes[9] proved to be effective coupling partners. By contrast, alkylation reactions that produce aliphatic alkenes are rare (Scheme 2a). In 2009, Shi and coworkers reported an iron-catalyzed alkylation reaction of alkenyl pivalates with alkyl Grignard reagents.[10] Lately, the groups of Jacobi von Wangelin and Knochel have reported the alkylation reactions of alkenyl acetates using iron and chromium catalysis, respectively.[11] The coupling of alkenyl carbamates was achieved by the Frantz group using iron catalysis and very recently by the So group using palladium catalysis.[12] Despite these formidable advances, these processes all rely on alkyl Grignard reagents as strong basic coupling partners. New coupling technology for the alkylation of alkenyl acetates under mild conditions that allow improved molecular diversity and functionality tolerance would have a substantial impact on organic synthesis.

Herein, we report a cross-electrophile coupling of alkenyl acetates with alkyl bromides (Scheme 2b). The reaction proceeds under mild conditions and tolerates



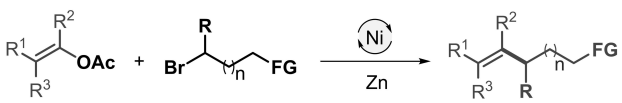
Scheme 1. Cross-electrophile Csp^2–Csp^3 coupling of alkenyl electrophiles with alkyl halides.

(a) Classic methods for alkylation of alkenyl carboxylates (ref. 5, 10–12)



OR: OAc, OPiv, $OCONR_2$

(b) Reductive coupling of alkenyl acetate with alkyl bromide (this work)



■ Mild conditions ■ Broad substrate scope ■ Gram-scale reaction
■ Great functionality tolerence ■ Improved structural complexity

Scheme 2. Transition-metal-catalyzed alkylation of alkenyl carboxylates.

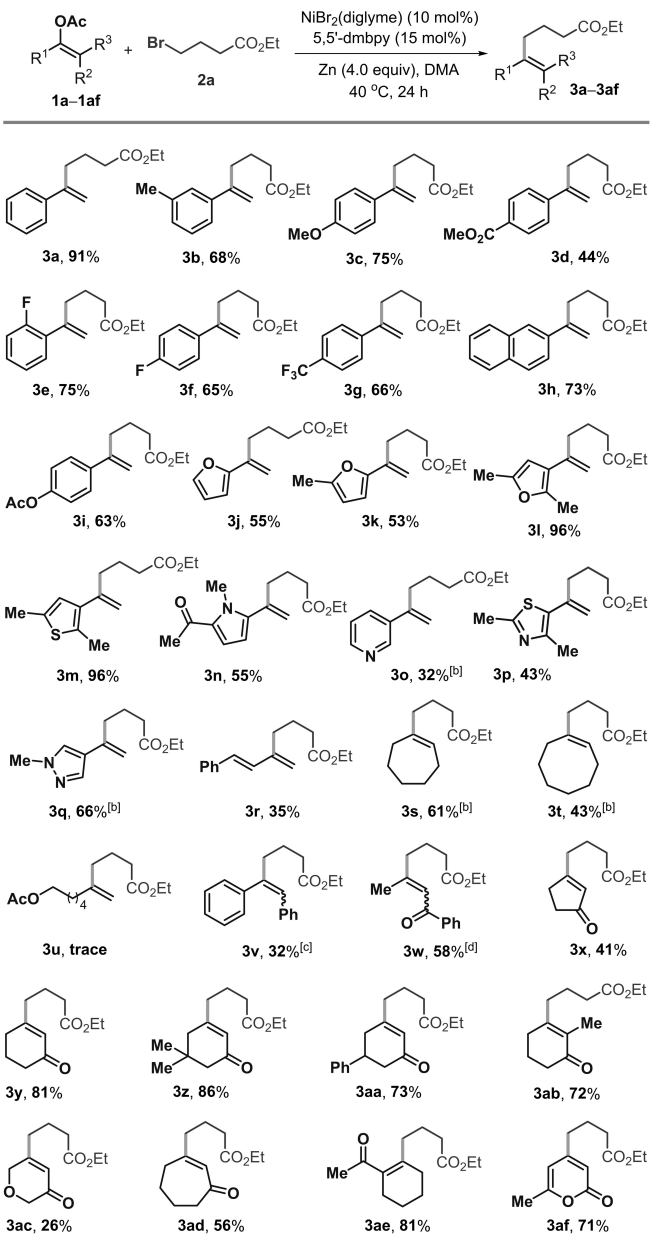
[*] R.-D. He, Y. Bai, G.-Y. Han, Z.-Z. Zhao, X. Pang, X. Pan, X.-Y. Liu, Prof. X.-Z. Shu
State Key Laboratory of Applied Organic Chemistry (SKLAOC)
College of Chemistry and Chemical Engineering
Lanzhou University
222 South Tianshui Road, Lanzhou 730000 (China)
E-mail: shuxingzh@lzu.edu.cn

various functionalities, including groups that are sensitive towards Grignard reagents (e.g., alkyl-Cl, RCON-H, R-CN, and RCHO). It thus offers access to aliphatic alkenes from readily available alkenyl acetates with a scope that is complementary to the established methods.[10–12]

We recently reported a reductive benzylation reaction of alkenyl acetates.[13] However, under these conditions, the reaction was only effective with primary benzylic ammonium salts to form allylarenes, and it failed to give any alkylation product when nonbenzylic substrates, either ammoniums or halides, were employed. This encouraged us to develop a new catalytic system for producing common aliphatic alkenes from alkenyl acetates. We found the ligand, solvent, and reductant all play essential roles for this reaction (see Table S1 in Supporting Information for details). After numerous trials, we determined that the combination of $NiBr_2$(diglyme), 5,5′-dmbpy (5,5′-dimethyl-2,2′-bipyridine) and Zn gave the best result, affording **3a** in 91 % yield (Scheme 3). Various styryl acetates were tolerated (**3a–i**). The reaction was selective for the alkylation of alkenyl over aryl acetate (**3i**). The reactions of heteroaryl-substituted alkenyl acetates, including furan (**3j–l**), thiophene (**3m**), pyrole (**3n**), pyridine (**3o**), thiazole (**3p**), and pyrazole (**3q**), generally afforded the target products in moderate to high yields. Dienyl acetate gave **3r** in a useful yield. The use of unactivated cyclic alkenyl acetates resulted in the formation of alkyl dimers and recovery of alkenyl acetates; this issue has been addressed by a slight modification of the conditions using Mn and DMF instead of Zn and DMA (**3s** and **3t**). However, the unactivated acyclic alkenyl acetate presently still does not work (**3u**). The 1,2-disubstituted alkenyl acetates were less effective, resulting in partial inversion of the stereochemistry.[14] For example, the reactions of (*Z*)-**1v** and (*E*)-**1w** gave **3v** (*Z*/*E* = 1.5:1) and **3w** (*Z*/*E* = 1:1.9) in 32 % and 58 % yield, respectively.

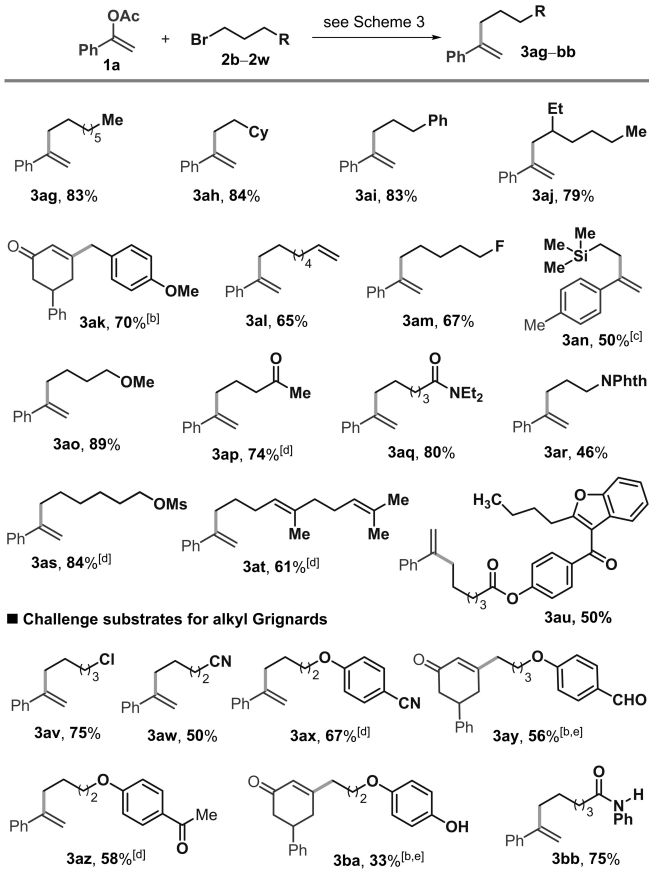
β-Alkyl-substituted cyclic enones are key building blocks in organic synthesis, but their synthesis often requires complex procedures.[15] Our method offers an alternative, direct approach to produce this class of compounds. Cyclic enones, ranging from five- to seven-membered rings, were coupled efficiently (**3x–ad**). Substituents at either the 2- or 5-positions were tolerated (**3z–ab**). The 2-acetylalkenyl acetate (**3ae**) and 2-pyrone substrate (**3af**) were alkylated in 81 % and 71 % yield, respectively.

The scope of reactions with primary alkyl bromides is shown in Scheme 4. Simple long-chain alkyl bromides gave products **3ag–aj** in high yields. The use of reactive alkyl halide, benzyl bromide, afforded **3ak** in 70 % yield. Alkyl bromides bearing functionalities such as terminal alkene (**3al**), alkyl fluoride (**3am**), alkylsilane (**3an**), ether (**3ao**), ketone (**3ap**), amide (**3aq** and **3ar**), mesylate (**3as**),[4a] and skipped diene (**3at**) were tolerated. The reaction of complex alkyl bromide afforded **3au** in 50 % yield. The Grignard-sensitive functionalities such as alkyl chloride (**3av**), nitrile (**3aw** and **3ax**), aldehyde (**3ay**), aryl ketone (**3az**), phenol (**3ba**), and secondary amide (**3bb**) were tolerated. The ability to introduce functionalized alkyl units makes this method complementary to the established methodologies for the alkylation of stable alkenyl C–O electrophiles.[10–13]

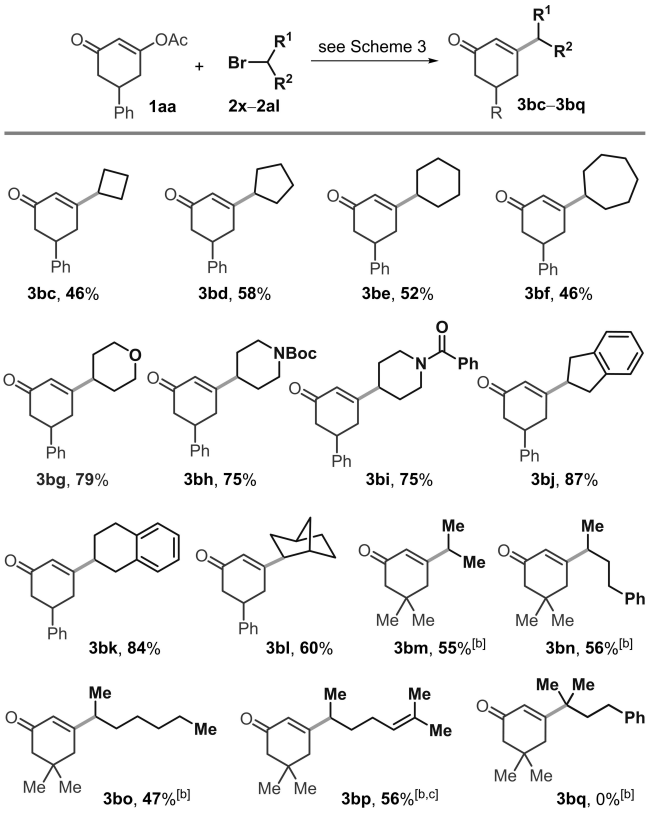


Scheme 3. Scope of the reaction with alkenyl acetates.[a] [a] Acetates **1a–af** (0.2 mmol) and bromide **2a** (3.5 equiv) were used, and the yields were isolated yields. b) Mn (4.0 equiv) and DMF (0.6 mL) were used. c) **3v** (*Z*/*E* = 1.5:1) was formed from (*Z*)-**1v**. d) **3w** (*Z*/*E* = 1:1.9) was formed from (*E*)-**1w.**

The reaction of alkenyl carboxylates with secondary alkyl species has been less investigated.[10–13] We then focused on this task (scheme 5). Cyclic alkyl bromides, ranging from four- to seven-membered rings, were coupled with **1aa** to afford the target products **3bc–bf** in moderate to high yields. Nonaromatic heterocycles, such as tetrahydropyran and piperidine, are prevalent in pharmaceuticals, and both were introduced efficiently via C–C bond formation (**3bg–bi**). The benzene-fused five- and six-membered rings afforded the desired products **3bj** and **3bk** in 87 % and 84 % yields, respectively. A bridged bicyclic molecule, 2-bromobi-



Scheme 4. Scope of the primary alkyl bromides.[a] [a] Reaction conditions as shown in Scheme 3; **1a** (0.2 mmol) was used, and the yields were isolated yields. [b] Alkenyl acetate **1aa** was used. [c] 1-(4-tolyl)alkenyl acetate **1ag** was used. [d] Reaction at 30 °C. [e] Reaction for 72 h.



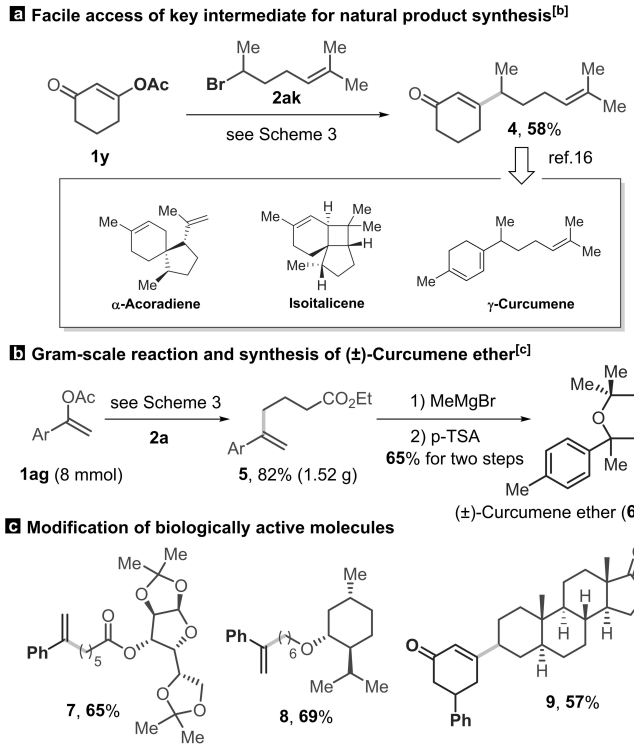
Scheme 5. Scope of the reaction with secondary and tertiary alkyl bromides.[a] [a] Reaction conditions as shown in Scheme 3, **1aa** (0.2 mmol) was used, isolated yields. [b] **1z** (0.2 mmol) was used. [c] 4,4′-Di-*tert*-butyl-2,2′-bipyridine (^{t}Bu-bpy) was used.

cyclo [2.2.1] heptane, afforded alkylated product **3bl** in 60 % yield. Besides cyclic substrates, many acyclic alkyl bromides were also coupled well, resulting in the target products **3bm–bp** in moderate yields. Attempts to perform the reaction with tertiary alkyl bromide have so far been unsuccessful (**3bq**). In this case, most of alkyl bromide was transferred to alkyl-H and β-hydride elimination products, with alkenyl acetate mostly protonated.

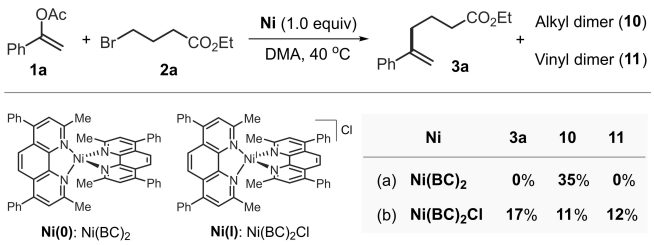
Synthetic applications of this method are demonstrated in Scheme 6. 1) Aliphatic enone **4** is the key intermediate for the synthesis of various biologically active molecules, including α-acoradiene, isoitalicene, and γ-curcumene (Scheme 6a).[16] However, its synthesis always requires complex procedures and harsh conditions (e.g., using lithium reagents). Our method offers a mild and simple protocol to obtain compound **4**. 2) Curcumene ether **6** was isolated from the plant Thuja orientalis, and its synthesis has been reported by several groups.[17] Here, we demonstrate an alternative approach, in which the gram-scale reaction of alkenyl acetate **1ag** and **2a** afforded alkene **5** in 82 % yield (1.52 g), which was then transformed into (±)-curcumene ether in 65 % yield for two steps (Scheme 6b). 3) The mild reaction conditions allow the method to be used for functionalizing structural complex molecules. For example, alkyl bromides derived from diacetone-d-glucose (**7**), l-menthol (**8**), and epiandrosterone (**9**) were coupled with alkenyl acetates readily (Scheme 6c).

To gain insight into the mechanism of this reaction, we prepared both Ni^0 and Ni^I species, $Ni(BC)_2$ and $Ni(BC)_2Cl$ (Scheme 7).[18] The use of BC as a ligand since the Ni^I complex of 5,5′-dmbpy failed to be purified,[19] and the reaction with BC also gave **3a** in 53 % yield, which is the second-best result (Table S1, **L11**). As is consistent with those observed for the reaction with $Ni(cod)_2$/**L3** (1.0/1.5 equiv) (Table S1, entry 8), the stoichiometric reaction of **1a** and **2a** with $Ni^0(BC)_2$ gave no product **3a** (Scheme 7a). However, the use of $Ni^I(BC)_2Cl$ resulted in **3a** in 17 % yield (Scheme 7b). This might be due to the fact that Ni^0 highly favors alkyl-Br **2a** over alkenyl acetate **1a** (35 % alkyl dimer and 0 % alkenyl derivatives), whereas Ni^I-Cl reacts with both reactants (11 % alkyl dimer and 12 % alkenyl derivatives).[20] Meanwhile, treating $Ni^{II}(BC)Cl_2$ and BC with Zn (50 equiv) in DMA, for either 2 or 12 hours, all gave $Ni^I(BC)_2Cl$ (Scheme S4 in Supporting Information). These results suggest that, unlike a common pathway of Csp^2–X electrophiles activated by Ni^0,[21] alkenyl acetate is activated by Ni^I under our conditions.[22]

The control experiments suggest that the alkyl bromide is activated via a radical mechanism. For example, 1) the



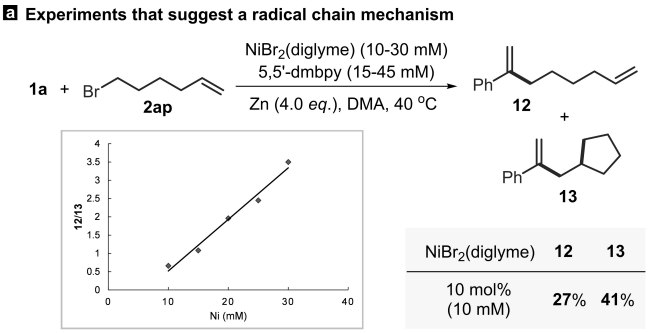
Scheme 6. Synthetic applications.[a] [a] Reaction conditions as shown in Scheme 3; alkenyl acetate (0.2 mmol) was used; yields are isolated yields. [b] ^{t}Bu-bpy (15 mol%) was used. [c] Acetate **1ag** (8.0 mmol) was used; see Supporting Information for detailed reaction conditions for the reaction of **5** to form **6**.



Ni	3a	10	11
(a) $Ni(BC)_2$	0%	35%	0%
(b) $Ni(BC)_2Cl$	17%	11%	12%

Scheme 7. Experiments to probe Ni^I catalysis.[a] [a] Acetate **1a** (0.1 mmol) and bromide **2a** (3.5 equiv) were used; reaction for 24 h; GC yields are given; the theoretical yields of **3a**, **10**, and **11** are 50%.

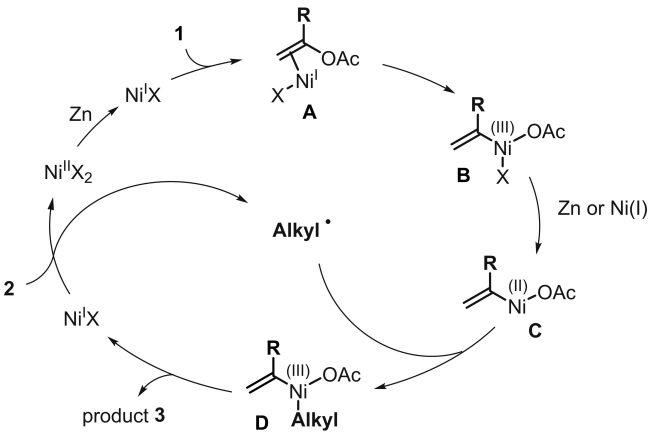
reaction of optically pure alkyl bromide (S)-**2ai** (95% ee) afforded product **3bn** in 54% yield with no enantiomeric excess (0% ee) (Scheme S9); 2) radical clock experiments showed that the reaction of alkene substrate **2ap** afforded the cyclized product **13** in 41% yield under the standard conditions (Scheme 8a). To investigate a possible radical chain mechanism, we evaluated the effect of catalyst concentration on the distribution of products **12** and **13**.[23] We anticipated that, if the postulated mechanism was valid, varying nickel concentration would result in a linear increase in the ratio of **12**/**13**. The results presented in Scheme 8a are consistent with this expectation, thereby supporting the conclusion that a radical chain mechanism may be involved.



Scheme 8. Radical chain process and secondary kinetic isotope effect.[a] [a] Acetate (0.2 mmol) and bromide **2ap**/**2a** (3.5 equiv) were used; reactions for 24 h; NMR yields are given. [b] Reaction for 5 h. [c] The value of k_H/k_D is an average of the two experiments.

Previous reports have shown that the coordination of alkenyl acetates to metal catalysts plays an essential role in their coupling reactions.[11] Our studies found that the use of a mixture of **1a** and **D-1a** resulted in a significant secondary kinetic isotope effects of $k_H/k_D = 1.20$ (Scheme 8b), suggesting a rate-determining step of oxidative addition of coordination complex **A** to form complex **B** (Scheme 9).[24]

On the basis of the above results and on previous reports, we tentatively propose a catalytic cycle as shown in Scheme 9.[25] The coordination of alkenyl acetate to Ni^I forms complex **A**.[11] The oxidative addition of this complex affords alkenyl-Ni^{III} **B**, which undergoes reduction with Zn or Ni^I to give alkenyl-Ni^{II} intermediate **C**.[22a] The following radical chain process is analogous to that previously proposed.[23] The combination of **C** with alkyl radical,



Scheme 9. Proposed mechanism.

followed by reductive elimination, yields the desired product **3**; the alkyl radical might be generated by reaction of alkyl bromide **2** with Ni^{I}-X species.[26] Reduction of $Ni^{II}X_2$ with Zn regenerates the Ni^{I}-X catalyst (Scheme S4).

In conclusion, we have reported the first cross-electrophile coupling of stable alkenyl C–O electrophiles with alkyl halides. This work has established a new method for the synthesis of aliphatic alkenes from alkenyl acetates with a scope that is complementary to those of the established methods. The reaction proceeds under very mild conditions and tolerates various functionalities. Primary, secondary, cyclic and acyclic alkyl bromides are tolerated. These features, as well as the ready availability of alkenyl acetates, make this method applicable for facile access to essential building blocks, and for the synthesis and modification of biologically active molecules. Detailed mechanistic studies and further expansion of the scope of the cross-electrophile coupling of alkenyl acetates are ongoing in our laboratory.

Acknowledgements

We thank the National Natural Science Foundation of China for their financial support (21772072, 22071084). We are grateful to Prof. Wei Yu for helpful discussions.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Alkenes · Alkenylation · Alkylation · Cross-coupling · Nickel

[1] Selected reviews: a) C. E. I. Knappke, S. Grupe, D. Gärtner, M. Corpet, C. Gosmini, A. Jacobi von Wangelin, *Chem. Eur. J.* **2014**, *20*, 6828; b) T. Moragas, A. Correa, R. Martin, *Chem. Eur. J.* **2014**, *20*, 8242; c) E. L. Lucas, E. R. Jarvo, *Nat. Chem. Rev.* **2017**, *1*, 0065; d) E. Richmond, J. Moran, *Synthesis* **2018**, *50*, 499; e) " Cross-Electrophile Coupling: Principles and New Reactions": M. J. Goldfogel, L. Huang, D. J. Weix in *Nickel Catalysis in Synthesis: Methods and Reactions* (Ed.: S. Ogoshi), Wiley-VCH, Weinheim, **2020**, p. 352; f) J. Liu, Y. Ye, J. L. Sessler, H. Gong, *Acc. Chem. Res.* **2020**, *53*, 1833; g) K. E. Poremba, S. E. Dibrell, S. E. Reisman, *ACS Catal.* **2020**, *10*, 8237.

[2] X. Pang, X. Peng, X.-Z. Shu, *Synthesis* **2020**, *52*, 3751.

[3] Selected references: a) D. A. Everson, B. A. Jones, D. J. Weix, *J. Am. Chem. Soc.* **2012**, *134*, 6146; b) A. H. Cherney, S. E. Reisman, *J. Am. Chem. Soc.* **2014**, *136*, 14365; c) K. A. Johnson, S. Biswas, D. J. Weix, *Chem. Eur. J.* **2016**, *22*, 7399; d) Y. Cai, A. D. Benischke, P. Knochel, C. Gosmini, *Chem. Eur. J.* **2017**, *23*, 250; e) J. Gu, C. Qiu, Q. Qian, K. Lin, H. Gong, *Synthesis* **2017**, *49*, 1867; f) X. Lu, Y. Wang, B. Zhang, J.-J. Pi, X.-X. Wang, T.-J. Gong, B. Xiao, Y. Fu, *J. Am. Chem. Soc.* **2017**, *139*, 12632; g) J. Liu, H. Gong, *Org. Lett.* **2018**, *20*, 7991; h) J. L. Hofstra, A. H. Cherney, C. M. Ordner, S. E. Reisman, *J. Am. Chem. Soc.* **2018**, *140*, 139.

[4] a) J. Duan, Y. F. Du, X. Pang, X. Z. Shu, *Chem. Sci.* **2019**, *10*, 8706; b) J.-B. Qiao, Z.-Z. Zhao, Y.-Q. Zhang, K. Yin, Z.-X. Tian, X.-Z. Shu, *Org. Lett.* **2020**, *22*, 5085; c) L. Su, G. Ma, Y. Song, H. Gong, *Org. Lett.* **2021**, *23*, 2493.

[5] An elegant work that details the advantages of alkenyl acetates and the challenge of their applications on the cross-coupling, see: D. Gärtner, A. L. Stein, S. Grupe, J. Arp, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed.* **2015**, *54*, 10545; *Angew. Chem.* **2015**, *127*, 10691.

[6] Selected reviews on the coupling of stable C–O electrophiles: a) B. M. Rosen, K. W. Quasdorf, D. A. Wilkson, N. Zhang, A.-M. Resmerita, N. K. Garg, B. Percec, *Chem. Rev.* **2011**, *111*, 1346; b) J. D. Sellars, P. G. Steel, *Chem. Soc. Rev.* **2011**, *40*, 5170; c) M. Tobisu, N. Chatani, *Top. Organomet. Chem.* **2012**, *44*, 35; d) T. Chen, L.-B. Han, *Angew. Chem. Int. Ed.* **2015**, *54*, 8600; *Angew. Chem.* **2015**, *127*, 8722; e) B. Su, Z.-C. Cao, Z.-J. Shi, *Acc. Chem. Res.* **2015**, *48*, 886; f) "Chapter Four—Phenol Derivatives: Modern Electrophiles in Cross-Coupling Reactions": C. Zarate, M. Van Gemmeren, R. J. Somerville, R. Martin, *Adv. Organomet. Chem.* **2016**, *66*, 143; g) M. Tobisu, N. Chatani, *Top. Curr. Chem.* **2016**, *374*, 41; h) Z. Qiu, C.-J. Li, *Chem. Rev.* **2020**, *120*, 10454.

[7] Selected references: a) B.-J. Li, Y.-Z. Li, X.-Y. Lu, J. Liu, B.-T. Guan, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2008**, *47*, 10124; *Angew. Chem.* **2008**, *120*, 10278; b) K. W. Quasdorf, X. Tian, N. K. Garg, *J. Am. Chem. Soc.* **2008**, *130*, 14422; c) J.-Y. Yu, R. Kuwano, *Angew. Chem. Int. Ed.* **2009**, *48*, 7217; *Angew. Chem.* **2009**, *121*, 7353; d) C.-L. Sun, Y. Wang, X. Zhou, Z.-H. Wu, B.-J. Li, B.-T. Guan, Z.-J. Shi, *Chem. Eur. J.* **2010**, *16*, 5844; e) J. Li, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 11436; *Angew. Chem.* **2018**, *130*, 11607; f) W.-J. Pan, Z.-X. Wang, *Org. Biomol. Chem.* **2018**, *16*, 1029; g) J. Becica, O. R. J. Heath, C. H. M. Zheng, D. C. Leitch, *Angew. Chem. Int. Ed.* **2020**, *59*, 17277; *Angew. Chem.* **2020**, *132*, 17430.

[8] a) P. Gomes, C. Gosmini, J. Périchon, *Tetrahedron* **2003**, *59*, 2999; b) M. Amatore, C. Gosmini, J. Périchon, *Eur. J. Org. Chem.* **2005**, 989.

[9] a) Y. Matsuura, M. Tamura, T. Kochi, M. Sato, N. Chatani, F. Kakiuchi, *J. Am. Chem. Soc.* **2007**, *129*, 9858; b) M. Moselage, N. Sauermann, S. C. Richter, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 6352; *Angew. Chem.* **2015**, *127*, 6450; c) K. D. Otley, J. A. Ellman, *Org. Lett.* **2015**, *17*, 1332.

[10] B.-J. Li, L. Xu, Z.-H. Wu, B.-T. Guan, C.-L. Sun, B.-Q. Wang, Z.-J. Shi, *J. Am. Chem. Soc.* **2009**, *131*, 14656.

[11] a) J. Li, Q. Ren, X. Cheng, K. Karaghiosoff, P. Knochel, *J. Am. Chem. Soc.* **2019**, *141*, 18127; b) Ref. [5].

[12] a) A. C. P. Rivera, R. Still, D. E. Frantz, *Angew. Chem. Int. Ed.* **2016**, *55*, 6689; *Angew. Chem.* **2016**, *128*, 6801; b) Z. Chen, C. M. So, *Org. Lett.* **2020**, *22*, 3879.

[13] R.-D. He, C.-L. Li, Q.-Q. Pan, P. Guo, X.-Y. Liu, X.-Z. Shu, *J. Am. Chem. Soc.* **2019**, *141*, 12481.

[14] The inversion of alkene geometry might be achieved through the reversible homolytic alkenyl-Ni bond dissociation and recombination of Ni^{III} intermediate. For related work, see: a) D. Anthony, Q. Lin, J. Baudet, T. Diao, *Angew. Chem. Int. Ed.* **2019**, *58*, 3198; *Angew. Chem.* **2019**, *131*, 3230; b) D. A. Cagan, G. D. Stroscio, A. Q. Cusumano, R. G. Hadt, *J. Phys. Chem. A* **2020**, *124*, 9915; c) J. R. Bour, N. M. Camasso, E. A. Meucci, J. W. Kampf, A. J. Canty, M. S. Sanford, *J. Am. Chem. Soc.* **2016**, *138*, 16105; d) G.-L. Xu, C.-Y. Liu, X. Pang, X.-Y. Liu, X.-Z. Shu, *CCS* **2021**, *43*, 1147. Stereoinversion through alkenyl radical, see: e) C. Galli, A. Guarnieri, H. Koch, P. Mencarelli, Z. Rappoport, *J. Org. Chem.* **1997**, *62*, 4072.

[15] a) C. Le Chapelain, *Org. Biomol. Chem.* **2017**, *15*, 6242; b) K.-S. Lee, M. K. Brown, A. W. Hird, A. H. Hoveyda, *J. Am. Chem. Soc.* **2006**, *128*, 7182.
[16] a) W. Oppolzer, F. Zutterman, K. Bättig, *Helv. Chim. Acta* **1983**, *66*, 522; b) P. Weyerstahl, H. Marschall-Weyerstahl, S. Scholz, *Liebigs Ann. Chem.* **1986**, 1021; c) S. Poplata, A. Bauer, G. Storch, T. Bach, *Chem. Eur. J.* **2019**, *25*, 8135.
[17] a) S. Serra, *Synlett* **2000**, 890; b) T. D. Vickers, B. A. Keay, *Synlett* **2003**, 1349.
[18] $Ni(BC)_2$ and $Ni(BC)_2Cl$ were prepared according to the literature procedures. a) D. C. Powers, B. L. Anderson, D. G. Nocera, *J. Am. Chem. Soc.* **2013**, *135*, 18876; b) M. Mohadjer Beromi, G. W. Brudvig, N. Hazari, H. M. C. Lant, B. Q. Mercado, *Angew. Chem. Int. Ed.* **2019**, *58*, 6094; *Angew. Chem.* **2019**, *131*, 6155.
[19] Treating (5,5′-dmbpy)$NiCl_2$ with Zn (50 equiv) in DMA at room temperature for either 3 h or 16 h gave the same dark blue solution of Ni^I-A. The Ni^I character of Ni^I-A was verified by EPR experiments. It exhibits a low-spin dx_2-y_2 ground state, with $g_x=2.05$, $g_y=2.08$ and $g_z=2.27$ (Scheme S7). The control experiments of **1a** and **2a** with $Ni(cod)_2$/5,5′-dmbpy and Ni^I-A gave the results similar to those obtained from $Ni(BC)_2$ and $Ni(BC)_2Cl$ in Scheme 7 (Scheme S8). However, this Ni^I species is failed to be purified. Consequently, we prepared $Ni(BC)_2$ and $Ni(BC)_2Cl$ for mechanistic studies.
[20] This result partially accounts for the failure of reaction under the conditions for reductive benzylation of alkenyl acetates in Ref. [13], because Mn prefers to generating Ni^0. Please see Ref. [1d] for the redox potentials of Mn^{2+}/Mn^0, Zn^{2+}/Zn^0, and $[Ni(bpy)_3]^{2+}/[Ni(bpy)_3]^+$.
[21] a) S. Biswas, D. J. Weix, *J. Am. Chem. Soc.* **2013**, *135*, 16192; b) D. J. Weix, *Acc. Chem. Res.* **2015**, *48*, 1767; c) X.-G. Jia, P. Guo, J. Duan, X.-Z. Shu, *Chem. Sci.* **2018**, *9*, 640; d) J. Duan, K. Wang, G.-L. Xu, S. Kang, L. Qi, X.-Y. Liu, X.-Z. Shu, *Angew. Chem. Int. Ed.* **2020**, *59*, 23083; *Angew. Chem.* **2020**, *132*, 23283.
[22] Limited reports on Csp^2–X activated by Ni^I species, see: a) Q. Lin, T. Diao, *J. Am. Chem. Soc.* **2019**, *141*, 17937; b) F. Yang, D. Ding, C. Wang, *Org. Lett.* **2020**, *22*, 9203; c) X. Huang, S. Teng, Y. R. Chi, W. Xu, M. Pu, Y.-D. Wu, J. S. Zhou, *Angew. Chem. Int. Ed.* **2021**, *60*, 2828; *Angew. Chem.* **2021**, *133*, 2864; d) P. Guo, K. Wang, W.-J. Jin, H. Xie, L. Qi, X.-Y. Liu, X.-Z. Shu, *J. Am. Chem. Soc.* **2021**, *143*, 513.
[23] a) J. Breitenfeld, J. Ruiz, M. D. Wodrich, X. Hu, *J. Am. Chem. Soc.* **2013**, *135*, 12004; b) N. D. Schley, G. C. Fu, *J. Am. Chem. Soc.* **2014**, *136*, 16588; c) Ref. [4a,21a].
[24] The alkene in coordination complex **A** is partial Csp^3 character. Transferring complex **A** to **B** results in the change in hybridization from Csp^3 to Csp^2, which leads to a normal secondary KIEs ($k_H/k_D>1$). For an elegant work discussing the secondary kinetic isotope effects, see: a) M. Gómez-Gallego, M. A. Sierra, *Chem. Rev.* **2011**, *111*, 4857; For related work: see: b) S. Gülak, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed.* **2012**, *51*, 1357; *Angew. Chem.* **2012**, *124*, 1386; c) Ref. [5].
[25] Alternatively, the reaction may proceed through the coupling of alkenyl acetates with in situ formed alkyl-Zn. However, this possibility is inconsistent with our observation. 1) The use of organic reductant, $(Bpin)_2$/LiOMe, instead of Zn also afforded desired product **3a** in 31 % yield (Table S1, entry 12). 2) The reaction of (*Z*)-**1v** with alkyl-Zn afforded **3v** (25 % yield, *Z*/*E* = 1:3.9; Scheme S14) with the stereochemistry opposite to that from alkyl-Br **2a** (32 % yield, *Z*/*E* = 1.5:1; Scheme 3, **3v**).
[26] This catalytic cycle only shows a possibility of generating the desired product. In addition to reacting with alkenyl-Ni–X to form the target products, alkyl radicals may also react with NiX_2 or Alkyl-$Ni^{II}X$ to deliver alkyl derivatives like alkyl dimers, which are major byproducts observed in the reactions.

Manuscript received: October 27, 2021
Accepted manuscript online: December 4, 2021
Version of record online: December 10, 2021