Radical Reactions

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Transforming Olefins into γ,δ-Unsaturated Nitriles through Copper Catalysis

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Abstract: *We have developed a strategy to transform olefins into homoallylic nitriles through a mechanism that combines copper catalysis with alkyl nitrile radicals. The radicals are easily generated from alkyl nitriles in the presence of the mild oxidant di-tert-butyl peroxide. This cross-dehydrogenative coupling between simple olefins and alkylnitriles bears advantages over the conventional use of halides and toxic cyanide reagents. With this method, we showcase the facile synthesis of a flavoring agent, a natural product, and a polymer precursor from simple olefins.*

While radicals play a key role in biochemistry,[1] their potential for use in organic synthesis remains vast, with new concepts continually emerging,[2] including applications in cross-coupling.[3] By combining Cu catalysis with radicals, Heck-type transformations have been achieved, including allylic trifluoromethylation,[4] arylation,[5] and alkylation.[6] These radical transformations enable bond construction patterns that were previously impossible and provide an attractive approach for olefin synthesis (Figure 1). Inspired by the versatility of nitriles,[7] we designed a strategy for transforming simple olefins into γ,δ-unsaturated nitriles by taming the reactivity of the cyanoalkyl radical. Rather than requiring functionalized halides and toxic cyanide reagents, this transformation enables olefin feedstocks to be coupled with alkyl nitriles to generate homoallylic nitriles in a single step, using an earth-abundant metal catalyst (Figure 1).[8]

The nitrile functional group is common in both materials[9] and medicines,[10] and is also a useful handle for elaboration.[7] As shown in Figure 1, we proposed a cross-dehydrogenative coupling (CDC)[11] between an olefin and acetonitrile.[12] Initial oxidation of an alkylnitrile forms the corresponding cyanoalkyl radical, which can add to an olefin to give the alkyl radical **A**.[13–16] Radicals such as **A** have been implicated in olefin hydrocyanoalkylations[13] and bifunctionalizations.[14–16] In the presence of a copper(II) catalyst, Koichi showed that radicals can be trapped to generate the alkylcopper(III) intermediate **B** with rate constants in excess of $10^{6}\,\mathrm{M}^{-1}\,\mathrm{s}^{-1}$.[17] Theoretical studies on the CF_3 allylic functionalization invoke a triflate-counterion-assisted elimination.[4b] On the basis of these studies, we reasoned that the appropriate counterion would be critical for controlling regio- and stereochemistry in the final elimination.[18]

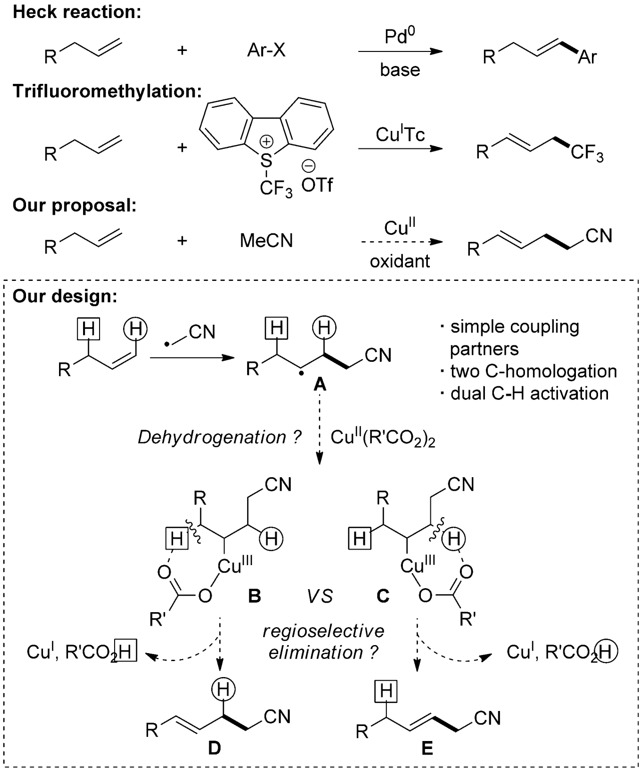

Figure 1. Allylic cyanoalkylation using alkylnitrile.

With this mechanistic hypothesis in mind, we focused on the copper-catalyzed allylic cyanoalkylation of 1-dodecene in acetonitrile, using di-*tert*-butyl peroxide (DTBP) as the oxidant. DTBP is a convenient and inexpensive radical initiator in synthetic and polymer chemistry, and is commonly used for generating radicals from acetonitrile.[13–16] Zhu and co-workers demonstrated that Cu/peroxide can generate cyanoalkyl radicals from alkylnitriles, which can then add to alkenes through an intermolecular process.[14a,b,d,e,16] In Zhu's work, the generated alkyl radicals are typically trapped to afford bifunctionalizations, such as oxycyanoalkylations[14a,b,d,e] and arylcyanoalkylation.[16] Rather than addition reactions across the olefin, we envisaged diverting **A** to achieve dehydrogenative olefin functionalization.

In the absence of copper, treatment of 1-dodecene with DTBP afforded the known hydrocyanoalkylation product **4a** in 25 % yield, with no desired cyanoalkene **3a**. Copper(I) and copper(II) complexes bearing weak counterions provided **4a** as the major product (28–70 % yields; Table 1), in accordance with reported studies on hydrocyanoalkylation.[13] The cata-

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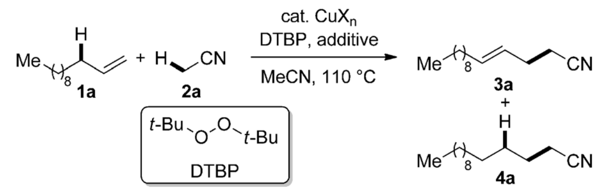
Table 1: Counterion effects on Cu-catalyzed allylic cyanoalkylation.[a,b]

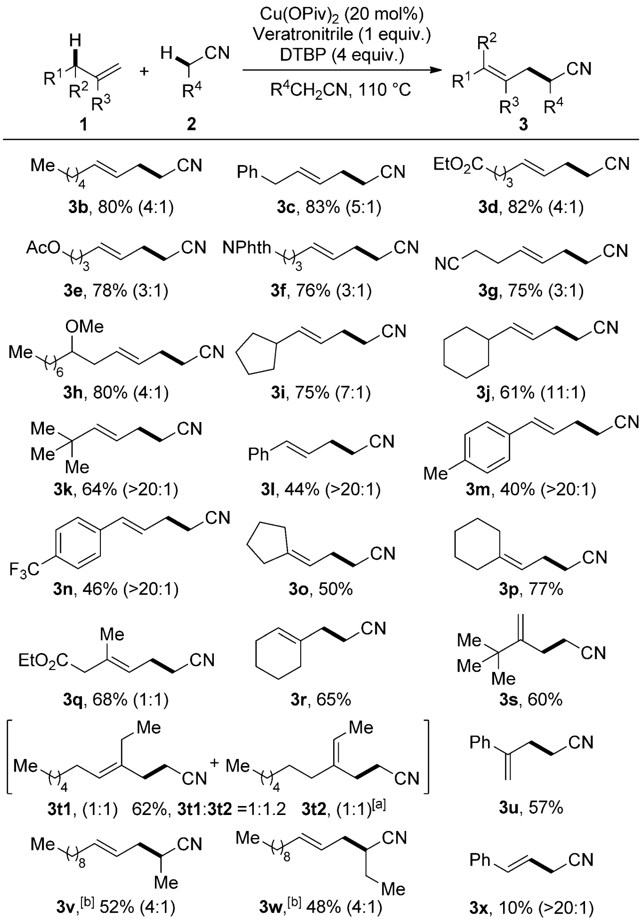


		CuOTf[c]	CuI	CuTc	CuOAc	
Cu(I)	3a	0%	0%	30%	35%	
	4a	47%	28%	10%	7%	
more coordinating →						
		Cu(OTf)$_2$	Cu(OAc)$_2$	Cu(*i*PrCO$_2$)$_2$	Cu(OPiv)$_2$	
Cu(II)	3a	0%	47%	58%	65%	90%(86%)[d]
	4a	70%	<5%	<5%	<5%	<5%c

[a] Reaction conditions: **1a** (0.20 mmol), CuX$_n$ (20 mol%) and DTBP (0.80 mmol) in acetonitrile **2a** (1.5 mL), 110 °C, 6 h. The transformation was performed in a 1 dram vial (diameter 1.4 cm/height 4.3 cm) which was sealed using a screw cap with a Teflon septum. [b] Yields were determined by NMR analysis of the unpurified reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. Yield of isolated product is shown within parentheses. [c] (CuOTf)$_2$·PhMe (10 mol%). [d] With veratronitrile (0.20 mmol). A 4:1 *E*/*Z* ratio was determined by NMR analysis of the unpurified reaction mixture.

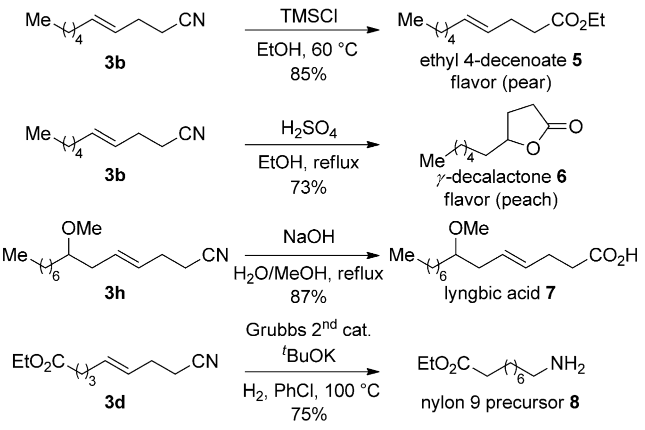
lysts used by Zhu and co-workers were not effective in our proposed allylic cyanoalkylation.[14a,b,d,e,16] In contrast, (thiophene-2-carbonyloxy)copper(I) (CuTc, previously used as a catalyst in allylic trifluoromethylation[4b]) provided cyanoalkene **3a** as the major product in 30% yield. In comparison to copper(I) acetate, we found that copper(II) acetate showed higher efficiency and chemoselectivity, providing **3a** in 47% yield with $>20{:}1$ regioselectivity. By replacing acetate with the more basic pivalate, the desired alkene was obtained in 65% yield, $>20{:}1$ regioselectivity. Other oxidants such as *tert*-butyl hydroperoxide (TBHP) and dicumyl peroxide (DCP) were ineffective. Using an electron-rich benzonitrile derivative as an additive further improved efficiency, presumably by improving catalyst solubility. In the presence of one equivalent of veratronitrile, **3a** was obtained in 90% yield, greater than 20:1 *rr*, and 4:1 *E*/*Z*. Only trace amounts of **4a** were observed (<5% yield). These results support the notion that a carboxylate counterion facilitates the elimination and enables $>20{:}1$ regioselectivity to provide the γ,δ-unsaturated nitrile. A *syn* elimination affords the *E* isomer as the major product.[19]

With this method, we elaborated a wide-range of terminal olefins (Scheme 1). Unactivated linear terminal olefins gave the corresponding γ,δ-unsaturated nitriles (**3a–c**) in 80–86% yields with $>20{:}1$ *rr* and 4:1 *E*/*Z*. For the substrates bearing ester (**3d**, **3e**), amide (**3f**), cyano (**3g**), and ether (**3h**) groups, regioselective CDC reactions with acetonitrile provided the corresponding products in 75–82% yields. Increasing the steric hindrance at the 4-position of the olefins slightly decreased the yields but increased the *E*/*Z* ratios of the products (**3i** 7:1 *E*/*Z*; **3j** 11:1 *E*/*Z*; **3k** $>20{:}1$ *E*/*Z*). With a *tert*-butyl group at the 3-position, we observed $>20{:}1$ regioselectivity and $>20{:}1$ *E*/*Z* selectivity (**3k**). The regioselectivity was unaffected by increased steric hindrance at the 4-position of the olefins. 3-Aryl-substituted substrates gave the corresponding nitriles (**3l–n**) in 40–46% yields with $>20{:}1$ *E*/*Z* selectivity. A substrate with an electron-withdrawing group on the phenyl ring (**3n**) showed slightly higher reactivity than one with an electron-donating group (**3m**). Trisubstituted alkenyl nitriles were synthesized in 50–77% yields from 3,3- and 1,1-disubstituted olefins (**3o–r** and **3t**). A series of nitriles were also tested as coupling partners and solvent. Propionitrile and butyronitrile showed decreased reactivity compared to acetonitrile, most likely due to steric effects and the lower solubility of the copper catalyst in these nitriles (**3v**, **3w**). Transformation with styrene, which has no allylic C−H bond, gave β,γ-unsaturated nitrile **3x** in 10% yield. Only trace amounts of the hydrocyanoalkylation product **4** were observed with the olefins shown in Scheme 1. Having established facile access to various nitriles, we next focused on applying them as building blocks.



Scheme 1. Allylic cyanoalkylation of terminal olefins. Reaction conditions: **1** (0.20 mmol), Cu(OPiv)$_2$ (20 mol%), DTBP (0.80 mmol). and veratronitrile (0.20 mmol) in alkylnitrile **2** (1.5 mL), 110 °C, 6 h. *E*/*Z* ratios determined by NMR analysis of the unpurified reaction mixture are shown in parentheses. [a] **3t1** and **3t2** were isolated as a mixture. [b] 24 h.

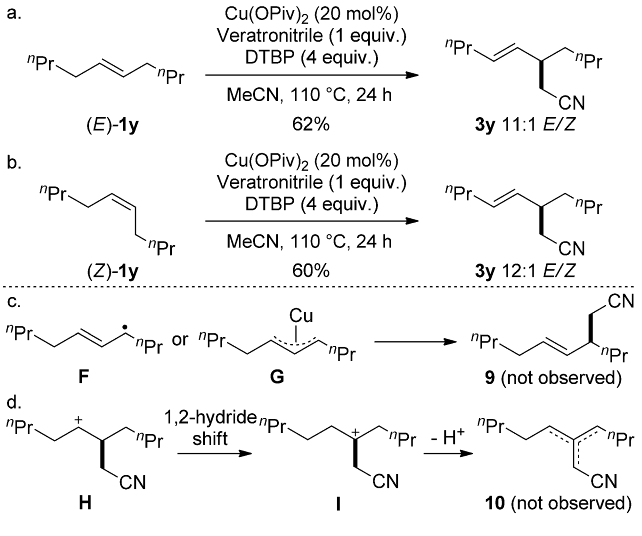
Owing to the versatility of the cyano group, we were able to use simple olefins to access a range of motifs, including an industrial flavor agent, a natural product, and a polymer precursor (Scheme 2). For example, treatment of **3b** with TMSCl in ethanol provided the pear flavoring ethyl 4-



Scheme 2. Application of the γ,δ-unsaturated nitriles. TMS = trimethylsilyl.

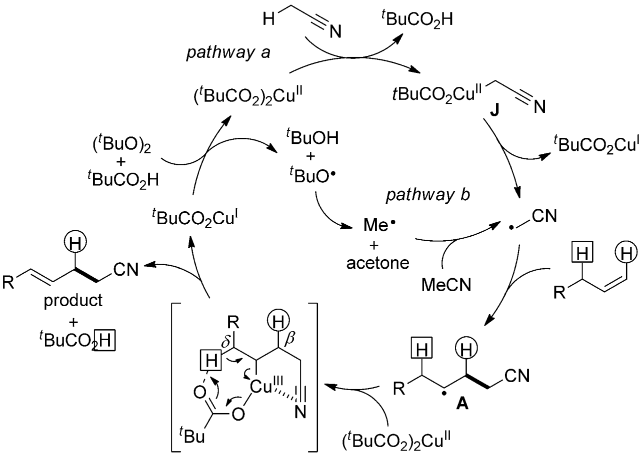
decenoate (**5**) in 85 % yield.[20] The 4-alkyl γ-lactones are members of a large family of natural flavors that are widely used in food industry.[21] From the same compound **3b**, γ-decalactone (**6**) was obtained in 73 % yield through a one-pot, hydrolysis and intramolecular hydroacyloxylation. Our strategy provides an efficient route to fatty acids. For example, lyngbic acid, which is isolated from the marine cyanophyte *Lyngbya majuscule*,[22] exhibits antimicrobial activity.[23] Through hydrolysis of the cyano group in compound **3h**, lyngbic acid (**7**) can be obtained in 87 % yield. Ru-catalyzed hydrogenation of **3d** provided the nylon-9 precursor **8** in 75 % yield.[24]

Next, we examined internal olefins (Scheme 3). With (*E*)-5-decene, the transformation gave cyanoalkene **3y** in 62 % yield with > 20:1 *rr* and 11:1 *E*/*Z* after 24 h (Scheme 3 a). With (*Z*)-5-decene, the *E* isomer **3y** was obtained as the major product in a similar yield and *E*/*Z* selectivity as the *E*-olefin substrate (60 % yield, 12:1 *E*/*Z*) (Scheme 3 b). The C–C bonds were formed at the 5-position of the substrates. No 3-propylnon-4-enenitrile (**9**) was observed from either the potential allylic radical **F** or π-allylcopper intermediate **G** through allylic C–H bond activation (Scheme 3 c). We observed no carbocation-rearrangement-type products (**10**), which would arise from the carbocation intermediate **H** (Scheme 3 d).[25] Nor were these 1,2-hydride shift products detected in experiments yielding compounds **3o–q** (Scheme 1). These observations suggest that allylic radicals or carbocations are most likely not key intermediates in our cross-coupling.



Scheme 3. Allylic cyanoalkylation of internal olefins.

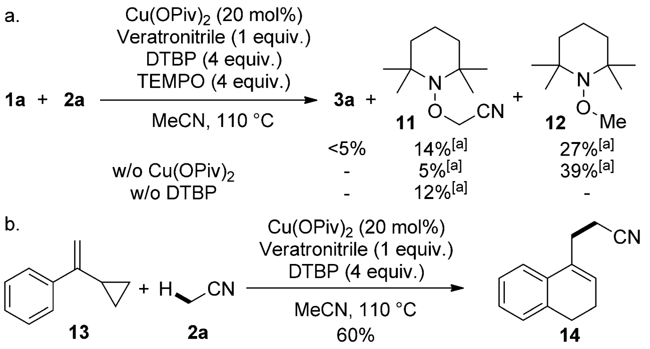
On the basis of further experiments and previous reports,[14–16] we propose the mechanism shown in Scheme 4.



Scheme 4. Proposed mechanism and rationale for the regioselectivity.

Pivalate-assisted deprotonation of alkylnitrile with copper(II) pivalate produces the cyanoalkylcopper(II) species **J** (pathway a). Homolytic cleavage of **J** gives the cyanoalkyl radical and copper(I) species. Addition of the cyanoalkyl radical to the olefin generates the radical intermediate **A**. Concerted carboxylate elimination of **A** provides the γ,δ-unsaturated nitrile product and a copper(I) species. To explain the regioselectivity, we propose that π-bonding of the cyano group to copper(III)[26] shields the H at the β position to direct the pivalate to abstract the H at the δ position. The copper(I) species decomposes DTBP through a single-electron-transfer redox reaction to regenerate copper(II) and a methyl radical. The methyl radical could also abstract hydrogen from alkylnitrile to produce the cyanoalkyl radical (pathway b).

The following radical-trapping and radical-clock experiments support the proposed mechanism (Scheme 5). Formation of the allylic cyanoalkylation product was suppressed in the presence of TEMPO, a known radical inhibitor. Instead, the products of cyanomethyl radical trapping (**11**) and methyl trapping (**12**) were both observed in 14 % and 27 % yields, respectively. These results support the notion that cyanomethyl radical and methyl radical intermediates are involved in the transformation. In the absence of $Cu(OPiv)_2$, the products **11** and **12** were also observed (in 5 % and 39 % yields, respectively). However, in the absence of DTBP, only **11** was observed (12 % yield). These results support the idea that pathways a and b are responsible for the activation of acetonitrile. Next, we found that the compound **14** was



Scheme 5. Intermediate-trapping and radical-clock experiments. [a] Yields based on TEMPO.

obtained in 60 % yield from (1-cyclopropylvinyl)benzene (**13**) through sequential ring opening of cyclopropylmethyl radical intermediate and cyclization (Scheme 4 b).[6e,13b,18] This radical-clock experiment supports the generation of **A**.

In summary, we have developed a copper-catalyzed cross-dehydrogenative coupling of unactivated olefins with alkylnitriles through dual sp^3 C−H bond cleavage. High chemo- and regioselectivity for E_2-type elimination is conferred by 1) the pivalate counterion and 2) the directing effect of cyano group. By using a catalyst derived from earth-abundant salts, we can access 4-alkenylnitriles from simple olefins. Both terminal and internal olefins can be transformed into γ,δ-unsaturated nitriles, which are versatile synthetic building blocks. These studies contribute to the emerging use of radicals for catalytic cross-coupling.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: alkenes · alkylnitriles · copper · cross-coupling · radicals

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[1] a) "Free Radical in Biochemistry and Medicine": B. Halliwell in *Molecular Biology and Biotechnology*, (Eds.: R. A. Meyers), VCH, New York, **1995**, p. 327; b) "Oxygen in Biology and Biochemistry: Role of Free Radicals": M. Hermes-Lima in *Functional Metabolism: Regulation and Adaptation* (Eds.: K. B. Storey), Wiley, Hoboken, **2004**, p. 319.

[2] A recent review: a) M. Yan, J. C. Lo, J. T. Edwards, P. S. Baran, *J. Am. Chem. Soc.* **2016**, *138*, 12692; Recent examples: b) I. Ghosh, T. Ghosh, J. I. Bardagi, B. Konig, *Science* **2014**, *346*, 725; c) J. C. Lo, J. Gui, Y. Yabe, C.-M. Pan, P. S. Baran, *Nature* **2014**, *516*, 343; d) J. L. Jeffrey, J. A. Terrett, D. W. C. MacMillan, *Science* **2015**, *349*, 1532; e) J. Gui, C.-M. Pan, Y. Jin, T. Qin, J. C. Lo, B. J. Lee, S. H. Spergel, M. E. Mertzman, W. J. Pitts, T. E. La Cruz, M. A. Schmidt, N. Darvatkar, S. R. Natarajan, P. S. Baran, *Science* **2015**, *348*, 886; f) D. S. Müller, N. L. Untiedt, A. P. Dieskau, G. L. Lackner, L. E. Overman, *J. Am. Chem. Soc.* **2015**, *137*, 660; g) C. C. Nawrat, C. R. Jamison, Y. Slutskyy, D. W. C. MacMillan, L. E. Overman, *J. Am. Chem. Soc.* **2015**, *137*, 11270; h) G. J. Choi, Q. Zhu, D. C. Miller, C. J. Gu, R. R. Knowles, *Nature* **2016**, *539*, 268; i) J. J. Murphy, D. Bastida, S. Paria, M. Fagnoni, P. Melchiorre, *Nature* **2016**, *532*, 218; j) Z. G. Brill, H. K. Grover, T. J. Maimone, *Science* **2016**, *352*, 1078; k) A. J. Musacchio, B. C. Lainhart, X. Zhang, S. G. Naguib, T. C. Sherwood, R. R. Knowles, *Science* **2017**, *355*, 727.

[3] Recent examples: a) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566; b) S. Biswas, D. J. Weix, *J. Am. Chem. Soc.* **2013**, *135*, 16192; c) J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433; d) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437; e) C. P. Johnston, R. T. Smith, S. Allmendinger, D. W. C. MacMillan, *Nature* **2016**, *536*, 322; f) W. Zhang, F. Wang, S. D. McCann, D. Wang, P. Chen, S. S. Stahl, G. Liu, *Science* **2016**, *353*, 1014; g) M. H. Shaw, V. W. Shurtleff, J. A. Terrett, J. D. Cuthbertson, D. W. C. MacMillan, *Science* **2016**, *352*, 1304; h) B. J. Shields, A. G. Doyle, *J. Am. Chem. Soc.* **2016**, *138*, 12719; i) S. A. Green, J. L. M. Matos, A. Yagi, R. A. Shenvi, *J. Am. Chem. Soc.* **2016**, *138*, 12779.

[4] a) A. T. Parsons, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2011**, *50*, 9120; *Angew. Chem.* **2011**, *123*, 9286; b) J. Xu, X. Fu, D.-F. Luo, Y.-Y. Jiang, B. Xiao, Z.-J. Liu, T.-J. Gong, L. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15300; c) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 16410; d) L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106; e) R. Beniazza, F. Molton, C. Duboc, A. Tron, N. D. McClenaghan, D. Lastécouères, J.-M. Vincent, *Chem. Commun.* **2015**, *51*, 9571.

[5] R. J. Phipps, L. McMurray, S. Ritter, H. A. Duong, M. J. Gaunt, *J. Am. Chem. Soc.* **2012**, *134*, 10773.

[6] a) Y. Zhu, Y. Wei, *Chem. Sci.* **2014**, *5*, 2379; b) D. Liu, C. Liu, H. Li, A. Lei, *Chem. Commun.* **2014**, *50*, 3623; For other Cu-catalyzed allylic alkylation, see: c) H. Bao, L. Bayeh, U. K. Tambar, *Angew. Chem. Int. Ed.* **2014**, *53*, 1664; *Angew. Chem.* **2014**, *126*, 1690; For Cu-catalyzed Heck type alkylations, see: d) T. W. Liwosz, S. R. Chemler, *J. Am. Chem. Soc.* **2012**, *134*, 2020; e) T. W. Liwosz, S. R. Chemler, *Org. Lett.* **2013**, *15*, 3034; f) M. T. Bovino, T. W. Liwosz, N. E. Kendel, Y. Miller, N. Tyminska, E. Zurek, S. R. Chemler, *Angew. Chem. Int. Ed.* **2014**, *53*, 6383; *Angew. Chem.* **2014**, *126*, 6501.

[7] a) Z. Rappoport, *The Chemistry of the Cyano Group*, Wiley, London, **1970**; b) "Supplement C: The Chemistry of Triple-Bonded Functional Groups, Part 2": A. J. Fatiadi in *The Chemistry of Functional Groups* (Eds.: Z. Pappoport, S. Patai), Wiley, London, **1983**, p. 1057; c) F. F. Fleming, Q. Wang, *Chem. Rev.* **2003**, *103*, 2035; d) R. López, C. Palomo, *Angew. Chem. Int. Ed.* **2015**, *54*, 13170; *Angew. Chem.* **2015**, *127*, 13366.

[8] For recent reviews, see: a) X.-X. Guo, D.-W. Gu, Z. Wu, W. Zhang, *Chem. Rev.* **2015**, *115*, 1622; b) J. Miao, H. Ge, *Eur. J. Org. Chem.* **2015**, 7859.

[9] P. Hu, J. Chai, Y. Duan, Z. Liu, G. Cui, L. Chen, *J. Mater. Chem. A* **2016**, *4*, 10070.

[10] a) F. Fleming, *Nat. Prod. Rep.* **1999**, *16*, 597; b) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, *J. Med. Chem.* **2010**, *53*, 7902.

[11] Selected reviews: a) C.-J. Li, *Acc. Chem. Res.* **2009**, *42*, 335; b) C. J. Scheuermann, *Chem. Asian J.* **2010**, *5*, 436; c) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780; d) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; e) B.-J. Li, Z.-J. Shi, *Chem. Soc. Rev.* **2012**, *41*, 5588; f) S. A. Girard, T. Knauber,

C.-J. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 74; *Angew. Chem.* **2014**, *126*, 76.

[12] Cross-dehydrogenative coupling of acetonitriles through dual sp^3 C−H bond cleavage: a) Y. Liu, K. Yang, H. Ge, *Chem. Sci.* **2016**, *7*, 2804; b) W. Zhang, S. Yang, Z. Shen, *Adv. Synth. Catal.* **2016**, *358*, 2392.

[13] a) J. W. Bruno, T. J. Marks, F. D. Lewis, *J. Am. Chem. Soc.* **1981**, *103*, 3608; b) J. W. Bruno, T. J. Marks, F. D. Lewis, *J. Am. Chem. Soc.* **1982**, *104*, 5580; c) H. R. Sonawane, N. S. Bellur, V. G. Shah, *J. Chem. Soc. Chem. Commun.* **1990**, 1603; d) Z. Li, Y. Xiao, Z.-Q. Liu, *Chem. Commun.* **2015**, *51*, 9969.

[14] a) A. Bunescu, Q. Wang, J. Zhu, *Org. Lett.* **2015**, *17*, 1890; b) C. Chatalova-Sazepin, Q. Wang, G. M. Sammis, J. Zhu, *Angew. Chem. Int. Ed.* **2015**, *54*, 5443; *Angew. Chem.* **2015**, *127*, 5533; c) X.-Q. Chu, X.-P. Xu, H. Meng, S.-J. Ji, *RSC Adv.* **2015**, *5*, 67829; d) T. M. Ha, C. Chatalova-Sazepin, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 9249; *Angew. Chem.* **2016**, *128*, 9395; e) T. M. Ha, Q. Wang, J. Zhu, *Chem. Commun.* **2016**, *52*, 11100; f) Y.-Y. Liu, X.-H. Yang, R.-J. Song, S. Luo, J.-H. Li, *Nat. Commun.* **2017**, *8*, 14720.

[15] a) J. Li, Z. Wang, N. Wu, G. Gao, J. You, *Chem. Commun.* **2014**, *50*, 15049; b) S. Tang, D. Zhou, Z.-H. Li, M.-J. Fu, J. Li, R.-L. Sheng, S.-H. Li, *Synthesis* **2015**, 1567.

[16] A. Bunescu, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2015**, *54*, 3132; *Angew. Chem.* **2015**, *127*, 3175.

[17] a) J. K. Kochi, *J. Am. Chem. Soc.* **1962**, *84*, 3271; b) J. K. Kochi, A. Bemis, C. L. Jenkins, *J. Am. Chem. Soc.* **1968**, *90*, 4616; c) C. L. Jenkins, J. K. Kochi, *J. Am. Chem. Soc.* **1972**, *94*, 843; d) C. L. Jenkins, J. K. Kochi, *J. Am. Chem. Soc.* **1972**, *94*, 856; e) J. K. Kochi, *Acc. Chem. Res.* **1974**, *7*, 351.

[18] a) T. W. Liwosz, S. R. Chemler, *Chem. Eur. J.* **2013**, *19*, 12771; b) P. Xiong, F. Xu, X.-Y. Qian, Y. Yohannes, J. Song, X. Lu, H.-C. Xu, *Chem. Eur. J.* **2016**, *22*, 4379.

[19] F. A. Carey, R. J. Sundburg, *Advanced Organic Chemistry: Reaction and Synthesis*, *5th ed.*, *Part B*, Springer, New York, **2010**.

[20] S. McDonald, M. Schulze, M. Peltz, D. Bolliet, L. Burroughs, *Perfum. Flavor.* **2011**, *36*, 24.

[21] a) P. Schreier, F. Drawert, Z. Kerényi, A. Junker, *Z. Lebensm.-Unters. Forsch.* **1976**, *161*, 249; b) M. Lübke, E. Guichard, A. Tromelin, J. L. L. Quéré, *J. Agric. Food Chem.* **2002**, *50*, 7094.

[22] J. J. Cardellina, D. Dalietos, F. Marner, J. S. Mynderse, R. E. Moore, *Phytochemistry* **1978**, *17*, 2091.

[23] W. H. Gerwick, S. Reyes, B. Alvarado, *Phytochemistry* **1987**, *26*, 1701.

[24] G. Ameh Abel, K. O. Nguyen, S. Viamajala, S. Varanasi, K. Yamamoto, *RSC Adv.* **2014**, *4*, 55622.

[25] F. C. Whitmore, *J. Am. Chem. Soc.* **1932**, *54*, 3274.

[26] a) R. M. Bullock, C. E. L. Headford, S. E. Kegley, J. R. Norton, *J. Am. Chem. Soc.* **1985**, *107*, 727; b) R. A. Michelin, M. Mozzon, R. Bertani, *Coord. Chem. Rev.* **1996**, *147*, 299.

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Communications

Radical Reactions

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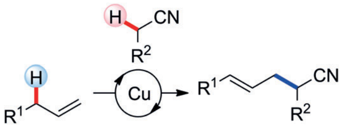
Transforming Olefins into γ,δ-Unsaturated Nitriles through Copper Catalysis



When two become one: A strategy was developed for transforming olefins into homoallylic nitriles through a mechanism that combines copper catalysis with alkyl nitrile radicals. The radicals are easily generated from alkyl nitriles in the presence of the mild oxidant di-*tert*-butyl peroxide. This cross-dehydrogenative coupling between simple olefins and alkylnitriles bears advantages over the conventional use of halides and toxic cyanide reagents.