Photocatalysis

How to cite:
International Edition: doi.org/10.1002/anie.202105285
German Edition: doi.org/10.1002/ange.202105285

1,3-Alkyl Transposition in Allylic Alcohols Enabled by Proton-Coupled Electron Transfer

*Kuo Zhao, Gesa Seidler, and Robert R. Knowles**

Abstract: *A method is described for the isomerization of acyclic allylic alcohols into β-functionalized ketones via 1,3-alkyl transposition. This reaction proceeds via light-driven proton-coupled electron transfer (PCET) activation of the O–H bond in the allylic alcohol substrate, followed by C–C β-scission of the resulting alkoxy radical. The transient alkyl radical and enone acceptor generated in the scission event subsequently recombine via radical conjugate addition to deliver β-functionalized ketone products. A variety of allylic alcohol substrates bearing alkyl and acyl migratory groups were successfully accommodated. Insights from mechanistic studies led to a modified reaction protocol that improves reaction performance for challenging substrates.*

The allylic transposition of alkyl groups is an appealing synthetic transformation, providing opportunities to reconfigure C–C bonds in complex carbon frameworks. While thermal [1s,3s] alkyl shifts are forbidden by orbital symmetry,[1] numerous alkyl 1,3-transpositions have been reported that proceed via sequential C–C bond-cleavage and reformation pathways.[2–5] Seeking to expand on these advances, we recently aimed to develop general methods for the 1,3-transposition of alkyl groups in allylic alcohol substrates enabled by proton-coupled electron transfer (PCET) (Figure 1 a).[6] In these reactions, an excited-state oxidant and a weak Brønsted base jointly mediate the homolytic activation of a substrate alcohol O–H bond to generate a reactive alkoxy radical intermediate.[7] These unstable oxygen-centered radicals then prompt the cleavage of a vicinal C–C bond via β-scission to furnish an α,β-unsaturated carbonyl and an alkyl radical that may then recombine through radical conjugate addition.[8,9] From a synthetic perspective, these methods enable the products of 1,2-addition to enone electrophiles to be selectively transposed into their corresponding 1,4-isomers. Building on important precedents from Renaud and Galatsis,[10] we recently reported that this approach could be applied to numerous ring-expansion reactions of cyclic alkenols.[7c] Here we demonstrate that this protocol can be successfully adapted to enable both 1,3-alkyl transpositions with acyclic allylic alcohol substrates, as well as a variety of aliphatic ring isomerizations and ring contractions (Figure 1 b). The design, optimization, scope, and preliminary mechanistic investigations of these reactions are presented herein.

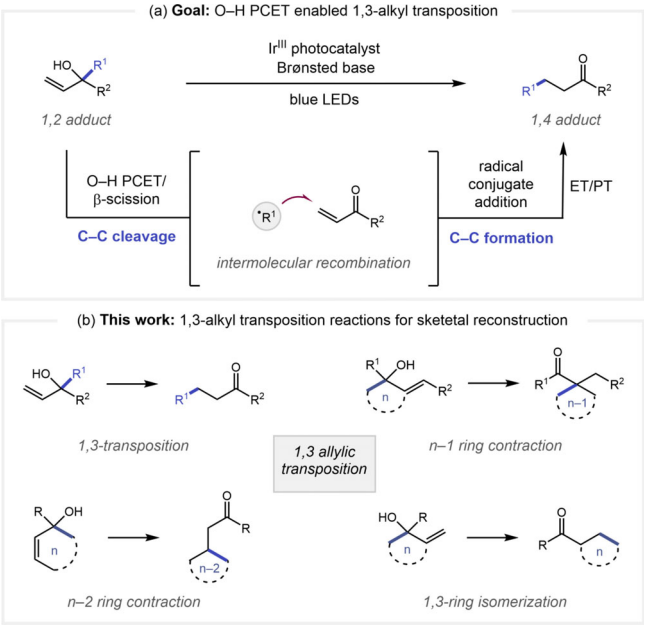


Figure 1. a) 1,3-alkyl transposition enabling useful skeletal rearrangements. b) 1,3-transposition of allylic alcohols via O–H PCET-mediated C–C bond cleavage.

The reaction design underlying the proposed allylic isomerization is presented in Figure 2. In line with our previous studies, we envisioned that under blue-light irradi-

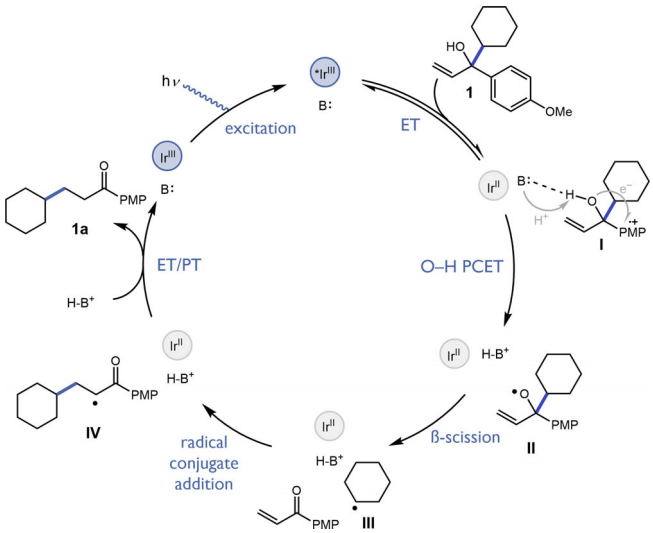


Figure 2. Reaction design for allylic transposition.

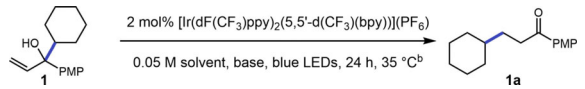
[*] K. Zhao, G. Seidler, Prof. R. R. Knowles
Department of Chemistry, Princeton University
Princeton, NJ 08544 (USA)
E-mail: rknowles@princeton.edu

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202105285.

ation the excited state of an Ir^{III} chromophore would first oxidize the electron-rich *p*-methoxyphenyl (PMP) group of substrate **1**, generating aryl radical cation intermediate **I**. Next, an intramolecular PCET event would occur between the alcohol adjacent to the radical cation **I** and an exogenous Brønsted base to furnish key alkoxy radical intermediate **II**.[7a,11] Radical **II** would then undergo C–C β-scission, leading to the concurrent formation of alkyl radical intermediate **III** and an α,β-unsaturated ketone. Intermolecular recombination of these scission products would then occur via radical conjugate addition to deliver a new C–C bond and electrophilic α-acyl radical **IV. IV** would accept an electron from the reduced Ir^{II} state of the photocatalyst and the resulting enolate would then be protonated by the conjugate acid of the Brønsted base to close the catalytic cycle and furnish the desired ketone product **1a** (Figure 2).

Our experimental investigations began with conditions adapted from our previous reports on O–H β-scission, employing allylic alcohol **1** as the model substrate.[7c] Upon treating **1** with 2 mol% $[Ir(dF(CF_3)ppy)_2(5,5'\text{-}d(CF_3)(bpy))](PF_6)$ and 25 mol% $PBu_4^+CF_3CO_2^-$ in $PhCF_3$ under blue-light irradiation for 24 hours, the desired ketone product **1a** was formed in 46% yield as judged by ^1H NMR analysis (Table 1, entry 1). Further optimization revealed that neutral 2,4,6-collidine (entry 5) was a superior Brønsted base (entries 1–4), and that increasing the loading of the base from 25 mol% to 300 mol% (entries 5–7) further benefitted the reaction yield. A survey of reaction solvents (entries 7–9) affirmed $PhCF_3$ as the optimal reaction medium, but reactions in toluene and dichloromethane also provided serviceable yields. Finally, control experiments revealed that the Ir photocatalyst and visible-light irradiation are essential for the observed reactivity (entries 10, 11), while the absence of the Brønsted base afforded a complex mixture of products and low yields of the desired ketone product **1a** (entry 12).

Table 1: Optimization Studies.[a]



Entry	Brønsted Base [mol%]	Solvent	Yield[c]
1	PBu_4^+ $CF_3CO_2^-$ (25)	$PhCF_3$	46%
2	PBu_4^+ $(PhO)_2P(O)O^-$ (25)	$PhCF_3$	68%
3	PBu_4^+ $(MeO)_2P(O)O^-$ (25)	$PhCF_3$	24%
4	PBu_4^+ $(n\text{-}BuO)_2P(O)O^-$ (25)	$PhCF_3$	32%
5	2,4,6-collidine (25)	$PhCF_3$	75%
6	2,4,6-collidine (100)	$PhCF_3$	85%
7	2,4,6-collidine (300)	$PhCF_3$	95%
8	2,4,6-collidine (300)	$PhCH_3$	84%
9	2,4,6-collidine (300)	CH_2Cl_2	79%
	Changes from the optimal conditions (entry 7)		
10	no light		0%
11	no Ir^{III} photocatalyst		0%
12	no Brønsted base		14%

[a] Optimization reactions were performed on 0.05 mmol scale. [b] Internal temperature of the reaction mixture under LED irradiation (see SI for details). [c] Yields were determined by ^1H NMR analysis of crude reaction mixtures relative to dimethylformamide as the internal standard.

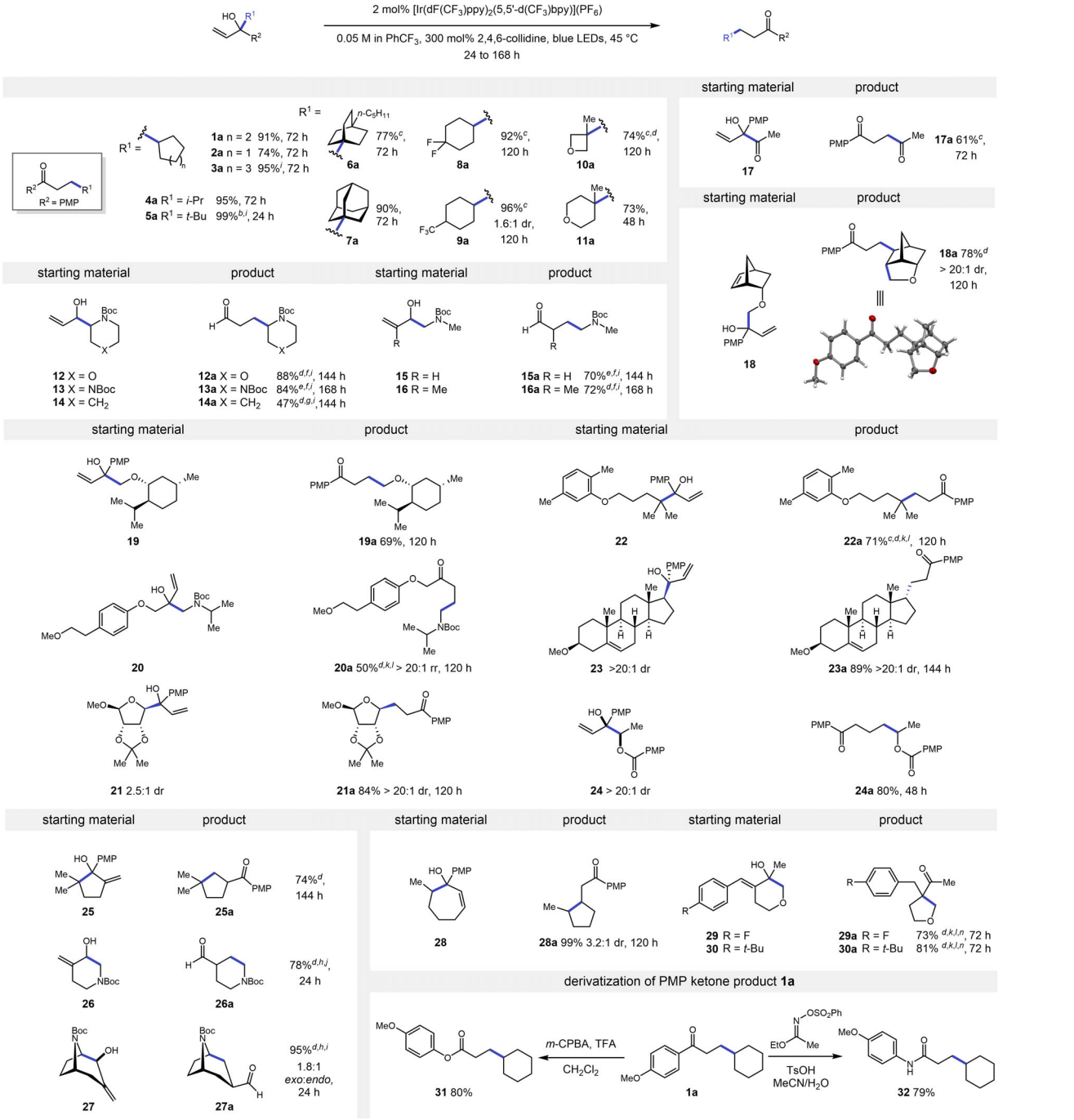
With these optimized conditions in hand, we examined the generality of this 1,3-transposition protocol (Table 2) and found that a variety of allylic alcohol substrates were accommodated. Substrates bearing secondary and tertiary aliphatic migratory groups (**1**–**11**) generally afforded the desired ketone products in good to excellent yields, though for **5** optimal results required the use of 2-methyl-2-oxazoline as the optimal base co-catalyst. Analogous substrates bearing primary aliphatic migratory groups proved to be inefficient, likely due to less favorable β-scission. Unsaturated β-amino alcohol derivatives (**12**–**16**) were also readily isomerized to furnish γ-amino aldehyde products (**12a**-**16a)**, albeit requiring increased loading of the photocatalyst for optimal performance.[12] Notably, for this class of substrates, the PMP group was not required for PCET activation, though optimal results required the use of diphenyl phosphate as a base in place of collidine. These reactions proceed through an alternative PCET mechanism which we have reported previously for non-benzylic alcohols involving a hydrogen-bonded complex between the alcohol and the phosphate base.[7b,c] In this class of substrates, the formation of a stabilized α-aminoalkyl radical intermediate enables the C–C β-scission step to compete effectively with non-productive back-electron transfer.

In addition to alkyl radicals, acyl radicals also proved to be viable migratory groups, as demonstrated by the isomerization of α-hydroxy ketone **17** into 1,4-diketone **17a**. Cascade cyclization reactions can also be accomplished as demonstrated by the reaction of norbornene derivative **18**. In this substrate, the alkyl radical intermediate formed in the β-scission event first undergoes intramolecular addition of a pendant alkene to form a new C–C bond, and the resulting alkyl radical is then captured by the ejected enone acceptor to afford the polycyclic product **18a** as a single diastereomer in 78% yield.

Further investigation revealed that derivatives of (–)-menthol (**19**), metoprolol (**20**), D-ribose (**21**), gemfibrozil (**22**), pregnenolone (**23**), and harmandianone (**24**) all furnished the desired 1,3-transposed ketone products (**19a**-**24a**) in synthetically useful yields, demonstrating that the method tolerates a variety of functional groups including electron-rich arenes (**20**, **22**), distal olefins (**23**), acetals (**21**), and esters (**24**). Notably, for **20** and **22**, a combination of 3% photocatalyst loading, acetonitrile solvent, and 2-methyl-2-oxazoline as the base co-catalyst provided optimal results. **21a** and **23a** were afforded as single diastereomers while **20a** was the sole product observed despite two potential sites for β-scission in substrate **20**—an outcome in line with the known preference for β-scission reactions to favor the ejection of the most stable radical intermediate.[9]

We then considered whether methylidenecycloalkanols might be prompted to undergo allylic ring reconstruction under these PCET conditions. As such, we were pleased to find that a variety of methylidenecycloalkanol substrates (**25**–**27**) rearranged readily, yielding transposed ketone (**25a**) or aldehyde products (**26a**, **27a**) in excellent yields, albeit with a slightly higher loading of photocatalyst (3 mol%). Reactions of **26** and **27** are thought to proceed through the hydrogen-bond-mediated PCET mechanism discussed for **12**–

Table 2: Scope of the allylic transposition reaction.[a][20]



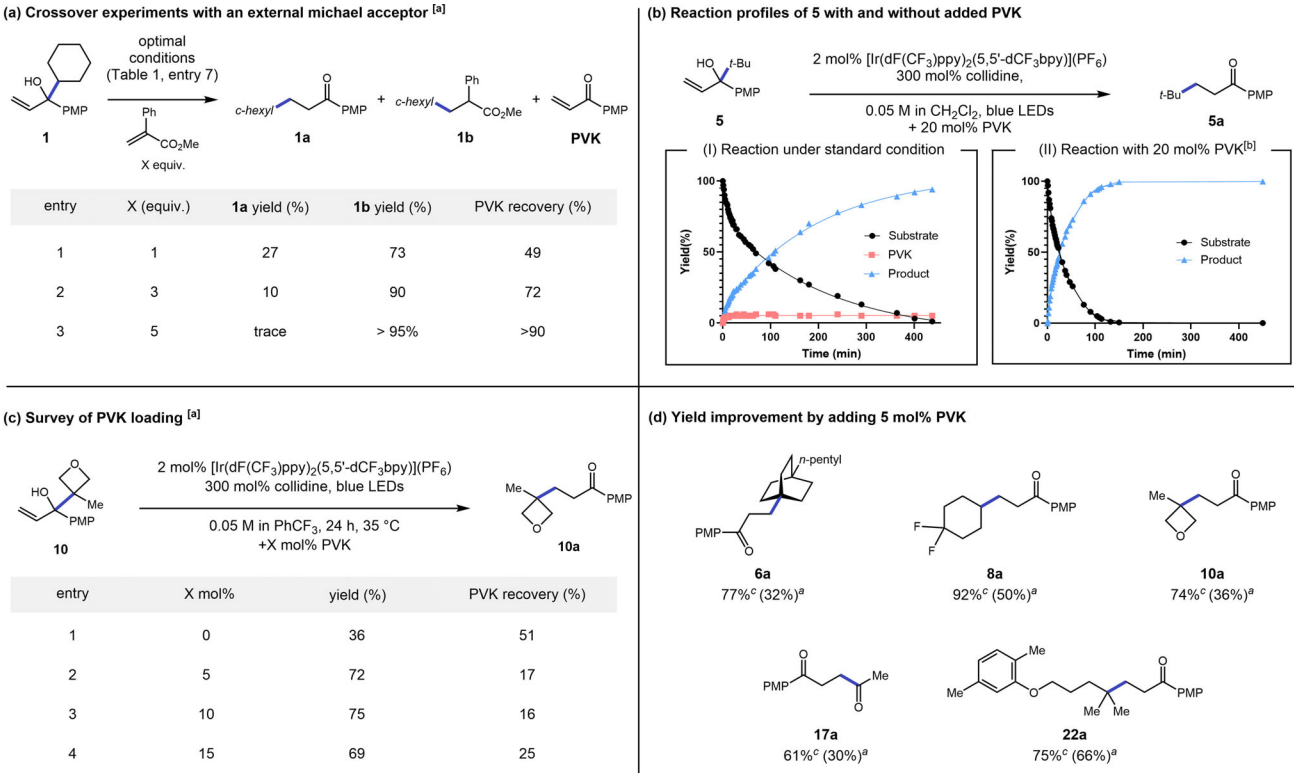
[a] Reactions were run on 0.5 mmol scale. Reported yields are for isolated and purified material and are the average of two experiments. Diastereomeric ratios were determined by ^{1}H NMR analysis of the crude reaction mixtures. The internal reaction temperature in the reaction setup was measured to be ≈45 °C. Details are provided in Supporting Information [b] 2-methyl-2-oxazoline (25 mol%) was used as the base. [c] 5 mol% phenyl vinyl ketone (PVK) was added. [d] 3 mol% photocatalyst was used. [e] 5 mol% photocatalyst was used. [f] $PBu_4^+(PhO)_2P(O)O^-$ (25 mol%) was used as the base. [g] $PBu_4^+(MeO)_2P(O)O^-$ (25 mol%) was used as the base. [h] $PBu_4^+CF_3CO_2^-$ (25 mol%) was used as the base. [i] in 0.1 M $PhCF_3$. [j] in 0.2 M $PhCF_3$. [k] in 0.05 M MeCN. [l] 2-methyl-2-oxazoline (300 mol%) was used as the base. [m] Relative configuration was determined by X-ray crystallographic analysis. [n] 2,4,6-triisopropylbenzenethiol (5 mol%) was added as a hydrogen-atom transfer co-catalyst.

16 with $PBu_4^+CF_3CO_2^-$ as the optimal base co-catalyst.[7a,c] Tropane **27** is particularly efficient in this rearrangement, furnishing aldehyde **27a** in 95% yield as a 1.8:1 mixture of *exo*:*endo* diastereomers. As will be detailed in the mechanistic discussion to follow, optimal yields for substrates **6**, **8**, **10**, **17**, and **22** were realized when 5 mol% of phenyl vinyl ketone (PVK) was added to the reaction mixture.

Next, we questioned whether allylic alcohols bearing endocyclic olefins might afford an opportunity to develop $n-2$ aliphatic ring contraction reactions. Indeed, under the standard reaction conditions cycloheptenol **28** was readily transformed into the ring-contracted cyclopentyl aldehyde product **28a**. In addition, we demonstrated analogous $n-1$ ring-contraction reactions of benzylidene tetrahydropyran cycloalkenols (**29**, **30**) through a formal 1,2-alkyl shift, which take advantage of the known preference for anti-Michael regioselectivity in alkyl radical additions to cinnamate derivatives.[13] In this case, incorporating a catalytic amount of a thiol hydrogen-atom transfer (HAT) co-catalyst is necessary to assist the reduction of benzyl radical intermediate formed up upon C–C bond formation, which cannot be reduced directly to its corresponding carbanion by the Ir^{II} complex.[7c] Additionally, we note that PMP ketone product **1a** can be readily converted to its respective ester (**31**) and amide (**32**) derivatives via Baeyer–Villiger oxidation and Schmidt-type rearrangement.[14] Lastly, while these isomerization reactions typically underwent full conversions within 24 hours on small scale (0.05 mmol), we observed notably diminished rates for preparative-scale runs (0.5 mmol). In addition to decreased photon flux for the larger reaction vessels, we hypothesize that the slow reaction rates may be due in part to the accumulation of a reduced and inactive state of the Ir photocatalyst under the reaction conditions.

In considering the mechanism of this transformation, we sought to ascertain whether the radical recombination step occurs within the solvent cage prior to the diffusional separation of the enone and the alkyl radical.[15] To do so, we performed a series of crossover experiments (Scheme 1a) wherein increasing equivalents of an exogenous acceptor alkene, methyl 2-phenylacrylate, were added to the reaction mixture. Upon addition of 1 equivalent of acrylate, the major product observed was the crossover product **1b** (73%) while the 1,3-transposition product **1a** was obtained in 27% yield. Increasing amounts of added olefin further suppressed the formation of **1a**, and when 5 equivalents of acrylate acceptor was employed, crossover product **1b** was the sole product observed with nearly quantitative recovery of PMP vinyl ketone (PVK). These results suggest that in-cage recombination is not operative in these reactions and that the ketone and radical intermediates formed upon β-scission diffuse apart into the solution at a rate faster than C–C bond formation. This result in turn raises an interesting question related to the apparent efficiency of these processes. Following β-scission, the concentrations of solvent-separated olefin and radical in solution are expected to be exceedingly low at any given time, implying that the rate of their bimolecular union may not be kinetically competitive with other non-productive processes that consume the radical intermediate.

To shed light on this issue, the reaction kinetics were studied by ^{1}H photo-NMR.[16] In reactions of substrate **5**, we observed that a small equilibrium concentration of PVK is established within the first 10 minutes of irradiation and persists until the reaction reaches completion (Scheme 1b-(I)).[17,18] While this in situ accumulation of PVK likely facilitates the key C–C bond-forming step, its formation



Scheme 1. Mechanistic studies and rate acceleration with additional alkene acceptor. [a] Yields were determined by ^{1}H NMR analysis of crude reaction mixtures. Reactions on 0.05 mmol scale. [b] PVK data points are removed for clarity [c] isolated yields with added 5 mol% PVK at 0.5 mmol scale.

implies that a majority of the photocatalyst may have also been converted into an inactive Ir^{II} state, thus decreasing the overall rate of reaction. To address this issue, we investigated reactions where small amounts of PVK were added solution prior to the beginning of the reaction. We reasoned that a higher olefin concentration would improve reaction performance by increasing the efficiency of the radical conjugate addition and thus mitigate the formation of a non-productive state of the photocatalyst. Gratifyingly, ^{1}H photo-NMR analysis of the rearrangement of **5** incorporating 20 mol% of added PVK revealed a significant rate enhancement, with the reaction reaching full conversion after only 2 hours as compared to 7 hours for reactions without added PVK (Scheme 1 b(II)).[19]

Building on these NMR observations, we questioned whether we could develop a modified protocol to improve the yields for challenging substrates by adding small amounts of exogenous PVK to the reaction mixture. Utilizing substrate **10** as a model, we were pleased to discover that product **10a** is formed in 72% yield with as low as 5 mol% of added PVK compared to only 36% yield under the standard conditions (Scheme 1 c). Using this simple modification of the reaction conditions, we were able to substantially improve the yields for several challenging substrates (**6a**, **8a**, **10a**, **17a**, and **22a**) by up to 45% (Scheme 1 d). While these reactions were more efficient with added PVK, we note they still required long reaction times to reach completion on preparative scale.

In summary, we have developed a light-driven, PCET-based method for the 1,3-transposition of acyclic allylic alcohols through sequential C–C bond dissociation and recombination steps. In addition to the reactions of acyclic substrates, previously unexplored ring isomerization reactions were described, including intra-annular transpositions and several novel ring contractions. Mechanistic studies revealed the in situ generation of low steady-state concentrations of the key enone acceptor, leading to a modified experimental protocol that significantly improved the performance for several challenging substrates. We are optimistic that these methods will provide new opportunities for remodeling C–C bond connectivity in a variety of complex contexts.

Acknowledgements

Financial support was provided by the NIH (R35 GM134893). We thank Kenji Yamashita for conducting preliminary experiments, Phil Jeffrey for assistance with X-ray crystallographic analysis, Laura Wilson for assistance with sample purification, and Kenith Conover for assistance with photo-NMR experiments.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: alkoxy radicals · C–C cleavage · isomerization · PCET · photocatalysis

[1] a) R. B. Woodward, R. Hoffmann, *J. Am. Chem. Soc.* **1965**, *87*, 2511 – 2513; b) R. Hoffmann, R. B. Woodward, *Acc. Chem. Res.* **1968**, *1*, 17 – 22; c) C. W. Spangler, *Chem. Rev.* **1976**, *76*, 187 – 217.

[2] For review of anion-mediated [1,3]-rearrangement, see: S. R. Wilson, *Org. React.* **2004**, *43*, 93 – 250, and references therein.

[3] For reviews of vinylcyclopropane rearrangements, see: a) Z. Goldschmidt, B. Crammer, *Chem. Soc. Rev.* **1988**, *17*, 229 – 267; b) J. E. Baldwin, *Chem. Rev.* **2003**, *103*, 1197 – 1212; c) J. E. Baldwin, P. A. Leber, *Org. Biomol. Chem.* **2008**, *6*, 36 – 47; d) P. A. Leber, J. E. Baldwin, *Acc. Chem. Res.* **2002**, *35*, 279 – 287; e) T. Hudlicky, J. W. Reed, *Angew. Chem. Int. Ed.* **2010**, *49*, 4864 – 4876; *Angew. Chem.* **2010**, *122*, 4982 – 4994.

[4] a) M. Nagel, G. Fráter, H.-J. Hansen, *Synlett* **2002**, 275 – 279; b) M. Nagel, G. Fráter, H.-J. Hansen, *Synlett* **2002**, 280 – 284; c) G. Rüedi, M. Nagel, H.-J. Hansen, *Org. Lett.* **2003**, *5*, 2691 – 2693; d) G. Rüedi, M. Nagel, H.-J. Hansen, *Org. Lett.* **2003**, *5*, 4211 – 4213; e) G. Rüedi, M. Nagel, H.-J. Hansen, *Synlett* **2003**, 1210 – 1212; f) G. Rüedi, M. A. Oberli, M. Nagel, H.-J. Hansen, *Org. Lett.* **2004**, *6*, 3179 – 3181; g) G. Rüedi, H.-J. Hansen, *Helv. Chim. Acta* **2004**, *87*, 1628 – 1665.

[5] a) K. C. Guérard, A. Guérinot, C. Bouchard-Aubin, M. A. Ménard, M. Lepage, M. A. Beaulieu, S. Canesi, *J. Org. Chem.* **2012**, *77*, 2121 – 2133; b) O. A. Ivanova, E. M. Budynina, V. N. Khrustalev, D. A. Skvortsov, I. V. Trushkov, M. Y. Melnikov, *Chem. Eur. J.* **2016**, *22*, 1223 – 1227; c) O. A. Ivanova, A. O. Chagarovskiy, A. N. Shumsky, V. D. Krasnobrov, I. I. Levina, I. V. Trushkov, *J. Org. Chem.* **2018**, *83*, 543 – 560; d) M. Thangamani, K. Srinivasan, *J. Org. Chem.* **2018**, *83*, 571 – 577; e) H. Kamiya, Y. Okada, *J. Org. Chem.* **2020**, *85*, 6551 – 6566.

[6] For reviews of PCET, see: a) S. Y. Reece, D. G. Nocera, *Annu. Rev. Biochem.* **2009**, *78*, 673 – 699; b) J. J. Warren, T. A. Tronic, J. M. Mayer, *Chem. Rev.* **2010**, *110*, 6961 – 7001; c) D. R. Weinberg, C. J. Gagliardi, J. F. Hull, C. F. Murphy, C. A. Kent, B. C. Westlake, A. Paul, D. H. Ess, D. G. McCafferty, T. J. Meyer, *Chem. Rev.* **2012**, *112*, 4016 – 4093; d) N. Hoffmann, *Eur. J. Org. Chem.* **2017**, 1982 – 1992; e) E. C. Gentry, R. R. Knowles, *Acc. Chem. Res.* **2016**, *49*, 1546 – 1556; f) D. C. Miller, K. T. Tarantino, R. R. Knowles, *Top. Curr. Chem.* **2016**, *374*, 30.

[7] a) H. G. Yayla, H. Wang, K. T. Tarantino, H. S. Orbe, R. R. Knowles, *J. Am. Chem. Soc.* **2016**, *138*, 10794 – 10797; b) E. Ota, H. Wang, N. L. Frye, R. R. Knowles, *J. Am. Chem. Soc.* **2019**, *141*, 1457 – 1462; c) K. Zhao, K. Yamashita, J. E. Carpenter, T. C. Sherwood, W. R. Ewing, P. T. W. Cheng, R. R. Knowles, *J. Am. Chem. Soc.* **2019**, *141*, 8752 – 8757; d) S. T. Nguyen, P. R. D. Murray, R. R. Knowles, *ACS Catal.* **2020**, *10*, 800 – 805; e) E. Tsui, A. J. Metrano, Y. Tsuchiya, R. R. Knowles, *Angew. Chem. Int. Ed.* **2020**, *59*, 11845 – 11849; *Angew. Chem.* **2020**, *132*, 11943 – 11947.

[8] Advances in alkoxyl radical-mediated β-scission chemistry: a) A. Hu, Y. Chen, J.-J. Guo, N. Yu, Q. An, Z. Zuo, *J. Am. Chem. Soc.* **2018**, *140*, 13580 – 13585; b) K. Zhang, L. Chang, Q. An, X. Wang, Z. Zuo, *J. Am. Chem. Soc.* **2019**, *141*, 10556 – 10564; c) Y. Chen, J. Du, Z. Zuo, *Chem* **2020**, *6*, 266 – 279; d) F. Cong, X.-Y. Lv, C. S. Day, R. Martin, *J. Am. Chem. Soc.* **2020**, *142*, 20594 – 20599; e) Y. Chen, X. Wang, H. Xu, Q. An, Z. Zuo, *J. Am. Chem. Soc.* **2021**, *143*, 4896 – 4902; f) P. Wu, S. Ma, *Org. Lett.* **2021**, *23*, 2533 – 2537.

[9] Reviews: a) P. Gray, A. Williams, *Chem. Rev.* **1959**, *59*, 239 – 328; b) C. Walling, *Pure Appl. Chem.* **1967**, *15*, 69 – 80; c) J. Hartung, T. Gottwald, K. Špehar, *Synthesis* **2002**, 1469 – 1498; d) J.-J. Guo, A. Hu, Z. Zuo, *Tetrahedron Lett.* **2018**, *59*, 2103 – 2111; e) K. Jia, Y. Chen, *Chem. Commun.* **2018**, *54*, 6105 – 6112; f) X. Wu, C. Zhu, *Chem. Commun.* **2019**, *55*, 9747 – 9756; g) E. Tsui, H. Wang, R. R. Knowles, *Chem. Sci.* **2020**, *11*, 11124 – 11141.

[10] a) R. Chuard, A. Giraud, P. Renaud, *Angew. Chem. Int. Ed.* **2002**, *41*, 4321 – 4323; *Angew. Chem.* **2002**, *114*, 4497 – 4499; b) R. Chuard, A. Giraud, P. Renaud, *Angew. Chem. Int. Ed.* **2002**, *41*, 4323 – 4325; *Angew. Chem.* **2002**, *114*, 4499 – 4501; c) P. Galatsis, S. D. Millan, T. Faber, *J. Org. Chem.* **1993**, *58*, 1215 – 1220.
[11] a) E. Baciocchi, M. Bietti, S. Steenken, *J. Am. Chem. Soc.* **1997**, *119*, 4078 – 4079; b) E. Baciocchi, M. Bietti, O. Lanzalunga, S. Steenken, *J. Am. Chem. Soc.* **1998**, *120*, 11516 – 11517; c) E. Baciocchi, M. Bietti, O. Lanzalunga, *Acc. Chem. Res.* **2000**, *33*, 243 – 251.
[12] The lower yield for substrate **14** was partially due to difficulty in purification.
[13] G. H. Lovett, B. A. Sparling, *Org. Lett.* **2016**, *18*, 3494 – 3497.
[14] a) N. Iranpoor, H. Firouzabadi, D. Khalili, S. Motevalli, *J. Org. Chem.* **2008**, *73*, 4882 – 4887; b) K. Hyodo, G. Hasegawa, N. Oishi, K. Kuroda, K. Uchida, *J. Org. Chem.* **2018**, *83*, 13080 – 13087.
[15] a) J. Franck, E. Rabinowitch, *Trans. Faraday Soc.* **1934**, *30*, 120 – 130; b) E. Rabinowitch, W. C. Wood, *Trans. Faraday Soc.* **1936**, *32*, 1381 – 1387; c) L. Herk, M. Feld, M. Szware, *J. Am. Chem. Soc.* **1961**, *83*, 2998 – 3005; d) D. A. Braden, E. E. Parrack, D. R. Tyler, *Coord. Chem. Rev.* **2001**, *211*, 279 – 294.
[16] a) C. Feldmeier, H. Bartling, E. Riedle, R. M. Gschwind, *J. Magn. Reson.* **2013**, *232*, 39 – 44; b) Y. Ji, D. A. DiRocco, C. M. Hong, M. K. Wismer, M. Reibarkh, *Org. Lett.* **2018**, *20*, 2156 – 2159.
[17] The steady-state concentration of PVK in the NMR studies was observed to be slightly higher than the loading of the photocatalyst, suggesting that a species in the solution other than the alpha-acyl radical is also able to re-oxidize the Ir^{II} complex.
[18] In the NMR kinetic studies, we observed that 2-methyl-2-oxazoline underwent partial decomposition, which complicated the analysis. 2,4,6-collidine was thus used instead as it was found to be equally efficient as a base co-catalyst and was stable under the reaction conditions.
[19] The faster rates in the NMR reactions can be attributed to increased photon flux relative to the preparative scale reactions.
[20] Deposition numbers 2025661 (for **18a**), 2025980 (for **21a**), and 1964649 (for **23a**) contain the supplementary crystallographic data for the indicated structures. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

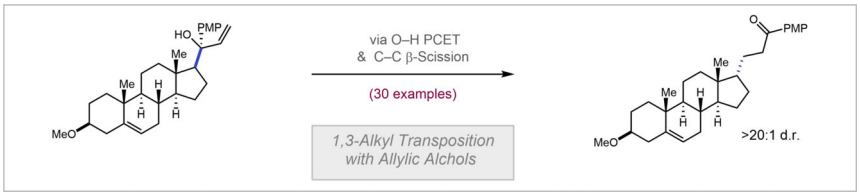
Manuscript received: April 18, 2021
Revised manuscript received: June 2, 2021
Accepted manuscript online: June 22, 2021
Version of record online: ■■ ■■, ■■■■

Communications

Photocatalysis

K. Zhao, G. Seidler,
R. R. Knowles* ——— ■■■■–■■■■

1,3-Alkyl Transposition in Allylic Alcohols Enabled by Proton-Coupled Electron Transfer



A method is described for the isomerization of acyclic allylic alcohols into β-functionalized ketones via 1,3-alkyl transposition. This reaction proceeds via light-driven proton-coupled electron transfer (PCET) activation of the O—H bond in an allylic alcohol substrate, followed by C—C β-scission of the resulting alkoxy radical to form an enone and an alkyl radical that may recombine via radical conjugate addition.