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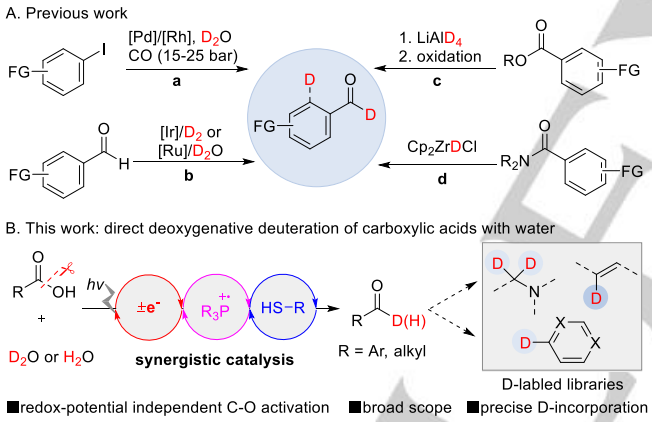
Deoxygenative Deuteration of Carboxylic Acids with D_2O

Muliang Zhang, Xiang-Ai Yuan, Chengjian Zhu and Jin Xie*

Abstract: We report a general, practical and scalable means of preparing deuterated aldehydes from aromatic and aliphatic carboxylic acids with D_2O as an inexpensive deuterium source. The use of Ph_3P as an O-atom transfer reagent can facilitate the deoxygenation of aromatic acids while Ph_2POEt is a better O-atom transfer reagent for aliphatic acids. Highly precise deoxygenation of complex carboxylic acids allows this protocol promising for late-stage deoxygenative deuteration of natural product derivatives and pharmaceutical chemicals.

Deuteration labeling technique has long been regarded as an important tool in analysis of drug metabolism[1] and investigation of reaction mechanism[2] as well as nuclear magnetic resonance spectroscopy[3] and mass spectrometry[4]. Incorporation of deuterium atom can dramatically enhance the metabolism and pharmacokinetic properties of parent drugs and drug candidates.[5] In 2017, FDA permission for the entry to market of the first deuterated drug, deutetrabenazine,[6] has significantly motivated the development of deuteration synthetic methodology,[7] and will certainly accelerate the discovery and development of deuterium-labeled drugs.



Scheme 1. Summary of previous and current work.

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Aromatic aldehydes are very useful building blocks in organic synthesis.[8] The development of a highly efficient protocol to construct aromatic aldehydes deuterated at the formyl position should enhance the library of deuterated lead compounds. Several methodologies that access deuterated aromatic aldehydes have been reported. Representative strategies include Pd/Rh co-catalyzed reductive carbonylation of arylhalides (Scheme 1Aa),[9] Ru- and Ir-catalyzed hydrogen isotope exchange (HIE) (Scheme 1Ab)[10] and careful reduction of carboxylic acid derivatives with deuterated reductants[11] (Schemes 1Ac and 1Ad). Given the importance of deuterated aromatic aldehydes, a convenient and step-economical synthetic approach is still highly desired. Moreover, late-stage introduction of deuterium into structurally complex aldehydes remains a challenge in organic synthesis.

Very recently, our group achieved the first direct synthesis of ketones from abundant aromatic acids and alkenes in aqueous solution by phosphoranyl radical-assisted deoxygenation enabled by visible-light photoredox catalysis.[12] We questioned if the generation of acyl radicals from aromatic acids has the potential to produce deuterated aldehydes with D_2O. However, the strong bond dissociation energy (BDE) of D-O-D bonds (BDE = 118 kcal mol^{-1}) prohibits a direct deuterium atom transfer (HAT) from D_2O.[13] Very recently, radical deuteration with D_2O was successfully reported by MacMillan[14a] and by Renaud[14b] using a HAT catalyst to bridge the energy gap. Our experience in synergistic thiol catalysis and photoredox catalysis[15] suggested that the thermodynamic property of thiols was an important factor in the success of such reactions. The use of a suitable thiol catalyst may be able to tune the equilibrium with D_2O as well as the HAT rate and possibly furnish deuterated aldehydes. With these considerations in mind, we herein report a general and practical radical deoxygenative deuteration of carboxylic acids with D_2O enabled by synergistic thiol catalysis, photoredox catalysis and phosphoranyl radical chemistry (Scheme 1B).

A synergistic mechanism for direct deoxygenative deuteration of carboxylic acids is proposed in Scheme 2. Density functional theory (DFT) calculations indicate that the pKa of thiols (**2a**-**d**) ranges from 10-16, and the proton of a thiol catalyst can exchange with excessive D_2O (pKa = 32)[16] to furnish a D-labeled thiol (**4**), which serves as the source of deuterium. The photoexcited $*Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ [$^{1/2}E_{red}$ ($*Ir^{III}/Ir^{II}$) = + 1.21 V vs SCE; τ = 2.3 μs][17] is a strong oxidant, which can achieve single electron oxidation of triphenylphosphine ($^{1/2}E_{red}$ = + 0.98 V vs SCE)[18] to generate a triphenylphosphine radical cation (**7**). This radical cation reacts with carboxylate ion to form an intermediate (**8**), which can proceed by β-scission[19] to produce triphenylphosphine oxides and a reactive acyl radical (**9**) as a result of the strong affinity between phosphine and oxygen atom. The DFT calculations also demonstrate that although the S-H bond in thiols (**2a-d)** varies significantly, the BDE for C-H of an aldehyde (94 kcal mol^{-1}) is still much higher than that of the S-H bond of these thiols (**2a**-**d**) (80-88 kcal mol^{-1}). The BDE gap between C-H and S-H bonds would be an important driving force for HAT processes (**4** → **5** and **9** → **3**). In this context, the nucleophilic acyl radical (**9**)[20] can readily undergo a HAT from the thiol (**4**) to form

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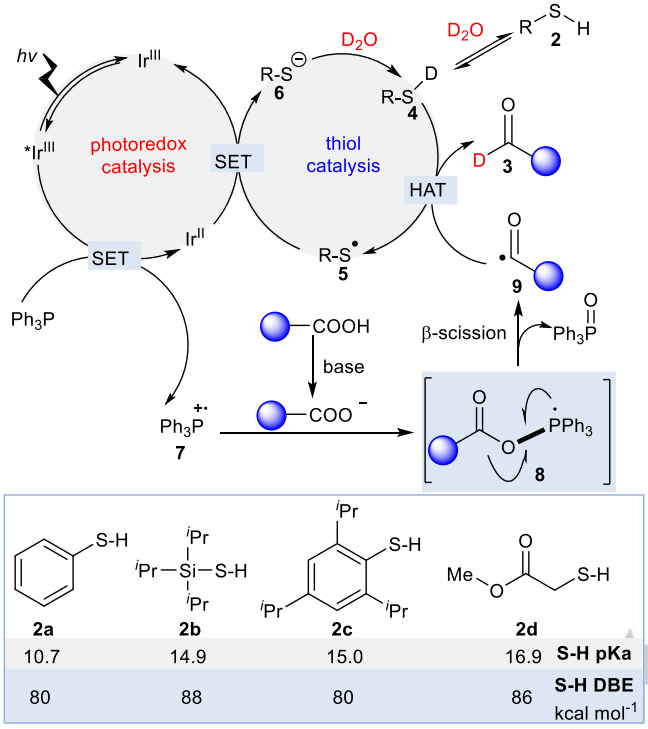
deuterated aldehydes, a reaction which is controlled by a polarity matching effect.[21] The generated electrophilic thiyl radical (**5**) subsequently accepts one electron from reducing Ir(II)-species to complete the photoredox cycle and the generated thiol anion (**6**) attracts one deuteron from D_2O to restart the thiol catalysis.

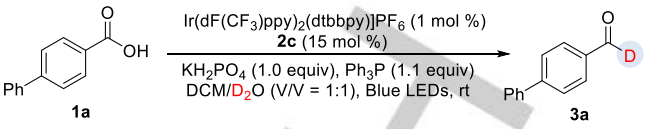


2a	2b	2c	2d	
10.7	14.9	15.0	16.9	**S-H pKa**
80	88	80	86	**S-H DBE** kcal mol^{-1}

Scheme 2. Mechanistic proposal.

Our investigation began with optimization of the deoxygenative deuteration of 4-phenylbenzoic acid with D_2O (Table 1). The optimized reaction conditions include of 1 mol% of Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 as the photocatalyst, 15 mol% of 2,4,6-triisopropylbenzenethiol (**2d**) as the HAT catalyst, 1.1 equiv Ph_3P as an oxygen-atom transfer reagent and DCM/D_2O (1:1, v/v) as solvent (Entry 1). The desired deuterated product (**3a**) was obtained in 86% yield with 96% D-incorporation using commercially inexpensive D_2O as an ideal deuterium source. The use of other relative electron-poor trivalent phosphorus compounds, such as Ph_2POEt and $P(OEt)_3$ led to decreased reaction yields (Entries 2 and 3), suggesting that the choice of O-transfer reagent was crucial for the success of the reaction (Entries 2-4). When other thiols were employed under the same conditions, the reaction yields significantly decreased, although the D-incorporation remained at a high level (Entries 5-7). The use of a lower oxidation potential photocatalyst, Ir(dF(Me)ppy)$_2$(dtbbpy)PF_6 [$^{1/2}E_{red}$ (*Ir^{III}/Ir^{II}) = + 0.97 V vs SCE; τ = 1.2 μs][22] resulted in a slightly declined yield and D-incorporation (Entry 8). Control experiments demonstrated that the deoxygenative deuteration reaction could not occur in the absence of either light or photocatalyst (Entry 9).

Table 1: Optimization of the reaction conditions



Entry	Variation of standard conditions	Yield[a]	D-Inc.[b]
1	none	86%	96%
2	Ph_2POEt instead of Ph_3P	12%	95%
3	$P(OEt)_3$ instead of Ph_3P	nd	nd
4	no Ph_3P	nd	nd
5	**2a** instead of **2c**	65%	95%
6	**2b** instead of **2c**	38%	96%
7	**2d** instead of **2c**	20%	94%
8	Ir(dF(Me)ppy)$_2$(dtbbpy)]PF_6	80%	92%
9	no light or no photocatalyst	nd	nd

Standard conditions: **1a** (0.2 mmol), Ir(dF(CF_3)ppy)$_2$(dtbbpy)]PF_6 (1 mol %), **2c** (15 mol %), Ph_3P (1.1 equiv), K_2HPO_4 (1.0 equiv) and DCM-D_2O (2 mL, v/v = 1:1), 5 W blue LEDs, 36 h. [a] Isolated yield. [b] Determined by ^{1}H NMR. nd = not detected.

With the optimized conditions in hand, we investigated the scope of carboxylic acids in this transformation (Scheme 3). In general, the developed phosphoranyl radical-assisted deoxygenation potentially could overcome the limitation of redox-potential of carboxylic acids and thus in principle, a wide variety of aromatic carboxylic acids should be competent substrates. A diverse range of electron-donating- (-Ph, *t*-Bu, -NMe_2, -BnO, -SMe and -NBoc), and electron-withdrawing- (-COOMe, -COMe and -pyridinyl) functional groups on the *ortho*-, *meta*- and *para*-position of phenyl rings are entirely compatible. Such substrates uniformly deliver the desired deuterated aryl aldehydes (**3a**-**r**) in moderate to good (up to 92%) yields with high D-incorporation (92-97% D) exclusively at the formyl position. Both 1-naphthoic acids and 2-naphthoic acids are efficient substrates (**3o**, **3p**). The reactive terminal alkene and alkyne units remain intact (**3s**, **3t**). Intriguingly, several relatively sensitive yet versatile functional groups, such as a free hydroxyl (**3u**), or amino group (**3x**), halogen (**3i** and **3j**), boronic esters (**3v**, **3w**), aldehyde (**3z**) and ketone (**3n**), tolerate the deoxygenative deuteration conditions well, and this should support promising broad-ranging applications in synthetic and medicinal chemistry. In addition, the reaction can be scaled up conveniently and the product **3x** was obtained in 76% yield with high D-incorporation when the reaction was carried out on an 8 mmol scale. The robustness of the reaction is illustrated by the precise synthesis of mono-deuterated *meta*-phthalaldehyde derivatives (**3z**). The quinoline- and indole-heteroaromatic acids (**3aa**, **3bb**) undergo this deoxygenative deuteration smoothly. In addition to aromatic acids, aliphatic

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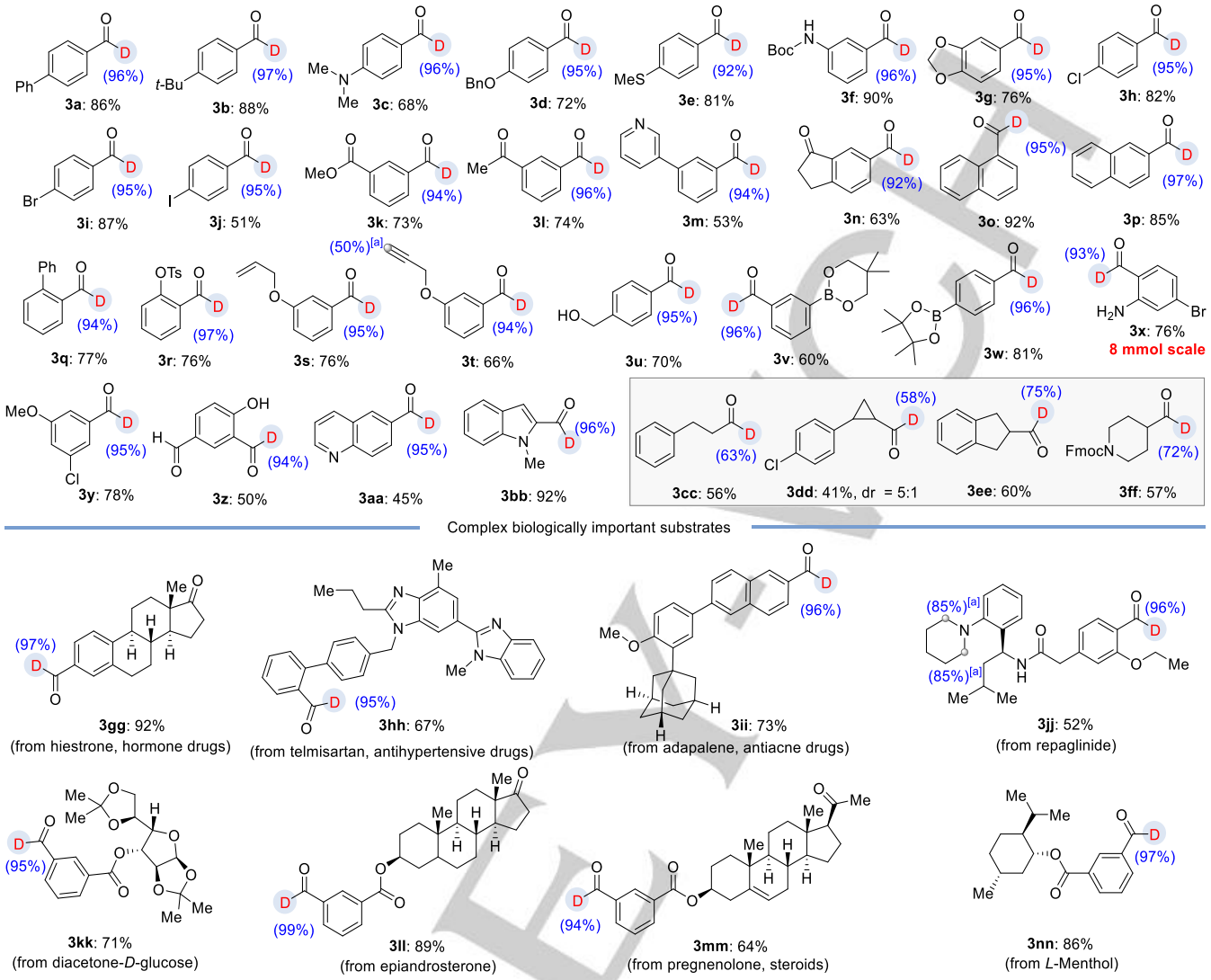

Scheme 3. Reaction scope: see Supporting Information (SI) for detailed reaction conditions. The yields are isolated yields after column chromatography on SiO_2 and D-content was determined by ^1H NMR. [a] Proton/deuterium exchange ratio of acidic protons with D_2O.

carboxylic acids are also good substrates and afford deuterated aliphatic aldehydes (**3cc**-**ff**) with moderate yields and D-incorporation under modified reaction conditions.[23] In such cases, the combination of $Ir(dF(Me)ppy)_2(dtbbpy)]PF_6$ as photocatalyst and Ph_2POEt as an O-atom transfer reagent is a key factor for control of deoxygenation as opposed to the well-studied decarboxylation.[24]

This excellent functional group tolerance enables potential application of the reaction in synthesis of complex deuterated aldehydes by late-stage functionalization of biologically active natural products, pharmaceuticals, and agrochemicals (Scheme 3, lower part). Deoxygenative deuteration of pharmaceuticals such as hiestrone (**3gg**), telmisartan (**3hh**) and adapalene (**3ii**) were successfully achieved in 67-92% yields with 95-97% D-incorporation. For complex carboxylic acids containing a tertiary amine motif, for example repaglinide, besides the expected deoxygenative deuteration, visible-light-induced HIE was observed at α-C(sp^3)-H of tertiary amines (**3jj**).[14a] The derivatives of diacetone-*D*-glucose (**3kk**), epiandrosterone (**3ll**), pregnenolone (**3mm**) and *L*-menthol (**3nn**) could achieve radical deuteration in 64-89% yields and high D-incorporation (up to 99% D), exclusively at the formyl position. These examples indicate that this protocol represents a practical late-stage modification in synthetic medicinal chemistry.

The versatility of aldehydes in organic transformations allows a practical strategy to access an enhanced library of deuterated compounds (Scheme 4). For example, the deuterium-labeled aldehydes obtained in this way are easily elaborated through Horner-Wadsworth-Emmons olefination and reductive amination to deliver β-deuterated, α,β-unsaturated esters (**10**) and highly valuable deuterated amines[7a] (**11**). The reaction of aminobenzaldehydes with D-labeled aldehydes provides an

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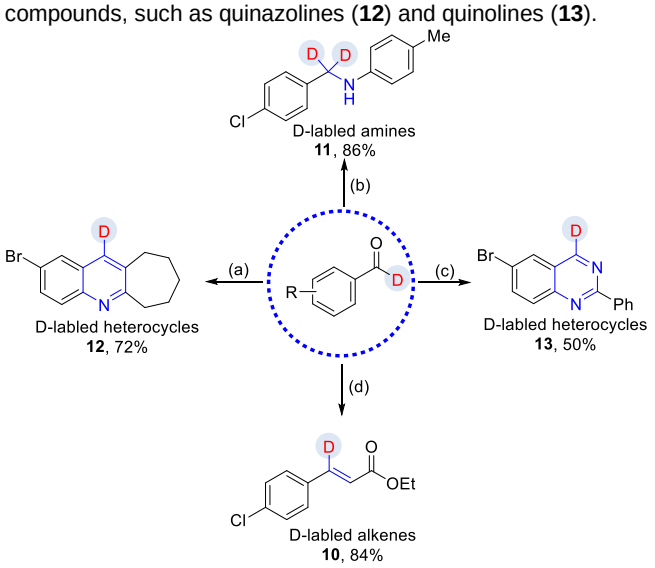
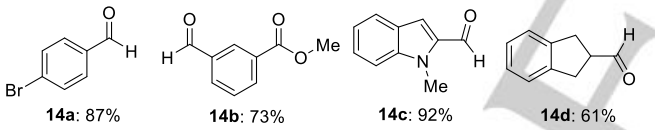
efficient route to D-labeled nitrogen-containing heterocycle compounds, such as quinazolines (**12**) and quinolines (**13**).



Scheme 4. Downstream transformations. See Supporting Information for detailed reaction conditions.

The mild reduction of carboxylic acids to aldehydes is one of the most important and challenging functional group conversions in organic synthesis. [25] Under the optimized conditions, and just replacing D_2O with H_2O,[26] our synergistic deoxygenation can serve as a powerful and general strategy for selective reduction of carboxylic acids to aldehydes under mild conditions, keeping a good selectivity and functional group compatibility (Scheme 5).



Scheme 5. Selective transformation of carboxylic acids to aldehydes.

To gain insight into the mechanism of this reaction, we performed radical inhibitor experiments by addition of 2,2,6,6-tetramethyl-1-piperidyloxy (TEMPO) and 2,6-di-*tert*-butyl-*p*-cresol (BHT) into the model reaction (see SI for details). Both these radical traps completely inhibit the deoxygenative deuteration, suggesting the possibility of a radical process. The trapping of acyl radicals by TEMPO further supports this claim. The ^{18}O-labeling experiments demonstrate that the oxygen atom in triphenylphosphine oxide comes from carboxylate group rather than from H_2O (see SI for details). Accordingly, the proposed mechanism in Scheme 2 is a promising candidate.

In conclusion, we have developed the first deoxygenative deuteration of both aromatic and aliphatic carboxylic acids with D_2O as an inexpensive deuterium source by synergistic photoredox catalysis, organocatalysis and phosphoranyl radical chemistry. A wide arrange of deuterated aldehydes are obtained in moderate to good yields with high D-incorporation. This reaction also provides a simple and promising reduction means of carboxylic acids to aldehydes using H_2O as a medium.

Acknowledgements

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Keywords: carboxylic acids • aldehydes • deuteration • deoxygenation • synergistic catalysis

[1] a) J. Helfenbein, C. Lartigue, E. Noirault, E. Azim, J. Legailliard, M. J. Galmier, J. C. Madelmont, *J. Med. Chem.* **2002**, *45*, 5806; b) C. S. Elmore, R. A. Bragg, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 167.

[2] a) J. Atzrodt, V. Derdau, W. J. Kerr, M. Reid, *Angew. Chem. Int. Ed.* **2018**, *57*, 3022; b) E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.

[3] S. E. Scheppele, *Chem. Rev.* **1972**, *72*, 511.

[4] a) L. S. Busenlehner, R. S. Armstrong, *Arch. Biochem. Biophys.* **2005**, *433*, 34; b) J. Atzrodt, V. Derdau, T. Fey, J. Zimmermann, *Angew. Chem. Int. Ed.* **2007**, *46*, 7744-7765.

[5] a) J. Atzrodt, V. Derdau, W. J. Kerr, M. Reid, *Angew. Chem. Int. Ed.* **2018**, *57*, 1758; b) Y. Zhu, J. Zhou, B. Jiao, *ACS Med. Chem. Lett.* **2013**, *4*, 349; c) A. Katsnelson, *Nat. Med.* **2013**, *19*, 656; d) A. Mullard, *Nat. Rev. Drug Discov.* **2016**, *15*, 219.

[6] C. Schmidt, *Nat. Biotechnol.* **2017**, *35*, 493.

[7] Selected deuteration and tritiation examples, see: a) L. V. A. Hale, N. K. Szymczak, *J. Am. Chem. Soc.* **2016**, *138*, 13489; b) J. L. Koniarczyk, D. Hesk, A. Overgard, I. W. Davies, A. McNally, *J. Am. Chem. Soc.* **2018**, *140*, 1990; c) X. Wang, M. H. Zhu, D. P. Schuman, D. Zhong, W. Y. Wang, L. Y. Wu, W. Liu, B. M. Stoltz, W.-B. Liu, *J. Am. Chem. Soc.* **2018**, *140*, 10970; d) J. Atzrodt, V. Derdau, W. J. Kerr, M. Reid, *Angew. Chem. Int. Ed.* **2018**, *57*, 3022; e) H. M. Xia, F. L. Zhang, T. Ye, Y. F. Wang, *Angew. Chem. Int. Ed.* **2018**, *57*, 11770; f) C. Liu, Z. Chen, C. Su, X. Zhao, Q. Gao, G. H. Ning, H. Zhu, W. Tang, K. Leng, W. Fu, B. Tian, X. Peng, J. Li, Q.-H. Xu, W. Zhou, K. P. Loh, *Nat. Commun.* **2018**, *9*, 80; g) R. P. Yu, D. Hesk, N. Rivera, I. Pelczer, P. J. Chirik, *Nature* **2016**, *529*, 195.

[8] Recent examples: a) H. Wang, X. J. Dai, C. J. Li, *Nat. Chem.* **2017**, *9*, 374-378; b) C. Min, Y. Lin, D. Seidel, *Angew. Chem. Int. Ed.* **2017**, *56*, 15353; c) M. Nakajima, E. Fava, S. Loescher, Z. Jiang, M. Rueping, *Angew. Chem. Int. Ed.* **2015**, *54*, 8828.

[9] M. Y. S. Ibrahim, S. E. Denmark, *Angew. Chem. Int. Ed.* **2018**, *57*, 10362.

[10] a) W. J. Kerr, M. Reid, T. Tuttle, *Angew. Chem. Int. Ed.* **2017**, *56*, 7808; b) E. S. Isbrandt, J. K. Vandavasi, W. Zhang, M. P. Jamshidi, S. G. Newman, *Synlett* **2017**, *28*, 2851.

[11] a) J. T. Spletstoser, J. M. White, A. R. Tunoori, G. I. Georg, *J. Am. Chem. Soc.* **2007**, *129*, 3408; b) H. V. Adcock, E. Chatzopoulou, P. W. Davies, *Angew. Chem. Int. Ed.* **2015**, *54*, 15525; c) E. P. K. Olsen, T. Singh, P. Harris, P. G. Andersson, R. Madsen, *J. Am. Chem. Soc.* **2015**, *137*, 834.

[12] M. Zhang, J. Xie, C. Zhu, *Nat. Commun.* **2018**, *9*, 3517.

[13] B. Ruscic, A. F. Wagner, L. B. Harding, R. L. Asher, D. Feller, D. A. Dixon, K. A. Peterson, Y. Song, X. Qian, C.-Y. Ng, J. Liu, W. Chen, D. W. Schwenke, *J. Phys. Chem. A* **2002**, *106*, 2727.

[14] a) Y. Y. Loh, K. Nagao, A. J. Hoover, D. Hesk, N. R. Rivera, S. L. Colletti, I. W. Davies, D. W. C. MacMillan, *Science* **2017**, *358*, 1182; b) V. Soulard, G. Villa, D. P. Vollmar, P. Renaud, *J. Am. Chem. Soc.* **2018**, *140*, 155.

[15] a) N. Zhou, X.-A. Yuan, Y. Zhao, J. Xie, C. Zhu, *Angew. Chem. Int. Ed.* **2018**, *57*, 3990; b) W. Xu, J. Ma, X.-A. Yuan, J. Dai, J. Xie, C. Zhu, *Angew. Chem. Int. Ed.* **2018**, *57*, 10357; c) J. Xie, K. Sekine, S. Witzel, P. Kramer,

M. Rudolph, *Angew. Chem. Int. Ed.* DOI: 10.1002/anie.201806427; d) Z. Yan, X.-A. Yuan, Y. Zhao, C. Zhu, J. Xie, *Angew. Chem. Int. Ed.* **2018**, *57*, 12906; e) W. Li, W. Xu, J. Xie, S. Yu, C. Zhu, *Chem. Soc. Rev.* **2018**, *47*, 654; f) P. Xu, W. Li, J. Xie, C. Zhu, *Acc. Chem. Res.* **2018**, *51*, 484; g) J. Xie, H. Jin, A. S. K. Hashmi, *Chem. Soc. Rev.* **2017**, *46*, 5193.

[16] A. K. Covington, R. A. Robinson, R. G. Bates, *J. Phys. Chem.* **1966**, *70*, 3820.

[17] C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322.

[18] G. Pandey, D. Pooranchand, U. T. Bhalerao, *Tetrahedron* **1991**, *47*, 1745.

[19] S. W. Lardy, V. A. Schmidt, *J. Am. Chem. Soc.* **2018**, DOI: 10.1021/jacs.8b06881.

[20] For recent representative examples about acyl radicals, see: a) V. Chudasama, R. J. Fitzmaurice, S. Caddick, *Nat. Chem.* **2010**, *2*, 592; b) X. Zhang, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2017**, *139*, 11353; c) K. Jia, Y. Pan, Y. Chen, *Angew. Chem. Int. Ed.* **2017**, *56*, 2478; d) S. Mukherjee, R. A. Garza-Sanchez, A. Tlahuext-Aca, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 14723; e) J. Liu, Q. Liu, H. Yi, C. Qin, R. Bai, X. Qi, Y. Lan, A. Lei, *Angew. Chem. Int. Ed.* **2014**, *53*, 502; f) G. Bergonzini, C. Cassani, C.-J. Wallentin, *Angew. Chem. Int. Ed.* **2015**, *54*, 14066.

[21] B. P. Roberts, *Chem. Soc. Rev.* **1999**, *28*, 25.

[22] K. Teegardin, J. I. Day, J. Chan, J. Weaver, *Org. Process Res. Dev.*, **2016**, *20*, 1156.

[23] The preparation of deuterated aliphatic carboxylic acids from corresponding aliphatic carboxylic acids with D_2O at the first step is necessary because aliphatic acids are prone to undergo radical decarboxylation in aqueous solution. See SI for detailed reaction conditions.

[24] a) X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 14330; b) J. Xuan, Z. G Zhang, W. J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 15632;

[25] a) L. J. Gooßen, K. Ghosh, *Chem. Commun.* **2002**, 836; b) F. Tinnis, A. Volkov, T. Slagbrand, H. Adolfsson, *Angew. Chem. Int. Ed.* **2016**, *55*, 4562; c) M. Zhang, N. Li, X. Tao, R. Ruzi, S. Yu, C. Zhu, *Chem. Commun.* **2017**, *53*, 10228; d) J. Xie, J. Li, T. Wurm, V. Weingand, H.-L. Sung, F. Rominger, M. Rudolph, A. S. K. Hashmi, *Org. Chem. Front.* **2016**, *3*, 841.

[26] The aliphatic carboxylic acids can deliver the corresponding aldehydes under modified conditions without addition of H_2O. Almost simultaneously, one study with similar conditions was reported, see: E. E. Stache, A. B. Ertel, T. Rovis, A. G. Doyle, *ACS Catal.* DOI: 10.1021/acscatal.8b03592.

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Layout 2:

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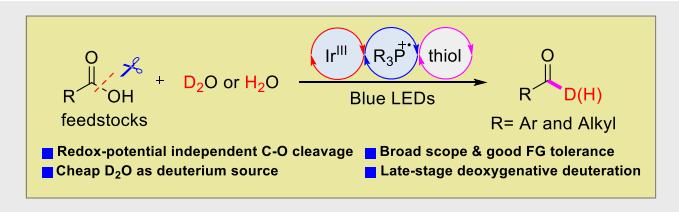

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Deoxygenative Deuteration of Carboxylic Acids with D_2O

Drink of Water: A general, practical and scalable means of preparing deuterated aldehydes from aromatic and aliphatic carboxylic acids has been achieved with D_2O as an inexpensive deuterium source enabled by synergistic photoredox catalysis, thiol catalysis and phosphoranyl radical chemistry.