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Oxidation of Primary Alcohols and Aldehydes to Carboxylic Acids via Hydrogen Atom Transfer

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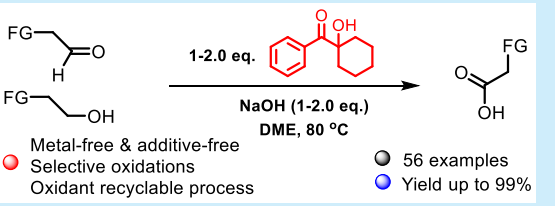
ABSTRACT: The oxidation of primary alcohols and aldehydes to the corresponding carboxylic acids is a fundamental reaction in organic synthesis. In this paper, we report a new chemoselective process for the oxidation of primary alcohols and aldehydes. This metal-free reaction features a new oxidant, an easy to handle procedure, high isolated yields, and good to excellent functional group tolerance even in the presence of vulnerable secondary alcohols and *tert*-butanesulfinamides.

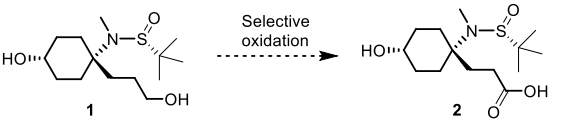


The oxidation of alcohols to the corresponding carbonyl compounds is one of the most important and useful reactions in functional group transformations.[1] Among the carbonyls, carboxylic acids are prevalent in natural products as well as synthetic organic chemicals, such as pharmaceuticals and agrochemicals.[2] Furthermore, carboxylic acids are versatile intermediates for the synthesis of peptides, esters, amine/amides, aldehyde/ketones, alcohols, and polymers in both academic research and industrial processes.[3] Traditionally, the oxidation of primary alcohols and aldehydes to carboxylic acids is achieved by stoichiometric or excess amounts of oxidants such as chromium salts,[4] potassium permanganate,[5] nickel peroxide,[6] and hypervalent iodines.[7] In the past decade, combinations of 2,2,6,6-tetramethylpiperidin-*N*-oxyl (TEMPO) and related *N*-oxyl mediators with diverse stoichiometric co-oxidants have been reported for this transformations.[8] Transition-metal-complex-mediated dehydrogenative oxidation of primary alcohols to carboxylic acids, those including W,[9] Ru,[10] Pd,[11] Rh,[12] Ir,[13] Ag,[14] Fe,[15] Mn,[16] Cu,[17] and Zn[18] complexes, have also been documented in the literature. Among the reactions mentioned above, only a few TEMPO-based oxidation conditions could be used for the chemoselective conversion of primary alcohols to carboxylic acids in the presence of secondary alcohols.[8a]

In our recent research program toward the synthesis of bioactive alkaloids,[19] we needed a selective oxidation to transfer primary alcohol **1** to the corresponding acid **2** in the presence of a secondary alcohol and a chiral *tert*-butanesulfinamide moiety. TEMPO-based selective oxidation conditions were initially used (Table 1).[8a,20] The reported oxidation conditions unfortunately failed to promote the desired transformation, with either a complex mixture or an undesired product (entry 1, the aldehyde was isolated in 25% yield; see the Supporting Information) being formed.

In order to realize the desired oxidation without introducing additional steps, we decided to investigate a new chemoselective method. We were especially interested in transition-metal-free procedures using small molecules as recyclable oxidants. In this regard, the Meerwein–Ponndorf–Verley–Oppenauer (MPVO) reaction[21] is an efficient organo-based oxidation. To the best of our knowledge, MPVO reactions have rarely been used in the oxidation of primary alcohols to the corresponding carboxylic acids. On a careful survey of the literature, we found a few examples employing Oppenauer oxidation to convert steroid-derived 1,4- and 1,5-diols to lactones.[22] Using the same 9-fluorenone-mediated conditions, however, we failed to effect the desired transformation (entry 6, Table 1). Although our synthetic route was altered to avoid this dilemma, the problem remained unsolved. It is highly

Table 1. Desired Oxidation of Primary Alcohol 1



entry	reagents and additives	solvents and temperature	yield of acid **2** (%)
1	TEMPO, $PhI(OAc)_2$	DCM, H_2O, rt	0
2	TEMPO, KBr, NaClO, $NaHCO_3$	H_2O, rt, or acetone, H_2O 0 °C	0
3	TEMPO, NaClO, $NaClO_2$ phosphate buffer (pH 6.8)	MeCN, 35 °C	0
4	TEMPO, *n*-Bu_4NCl, KBr, NaCl, NaClO, $NaHCO_3$	H_2O, DCM, 0 °C to rt	0
5	TEMPO, NaBr, $NaClO_2$, NaClO, NaH_2PO_4, H_2O	MeCN, rt, or MeCN, 60 °C	0
6	9-fluorenone, *t*-BuOK	xylene, reflux	0

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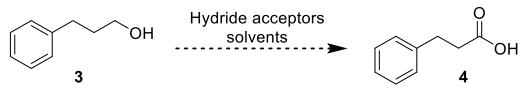
desirable to develop a new oxidation procedure to cope with this chemoselective transformation. In this paper, we report a hydrogen transfer method for the selective oxidation of primary alcohols and aldehydes to the corresponding acids.

We began screening with the oxidation of 3-phenylpropan-1-ol (**3**), and parts of the results are indicated in Table 2.

Table 2. Screening Oxidants and Reaction Conditions



3 4

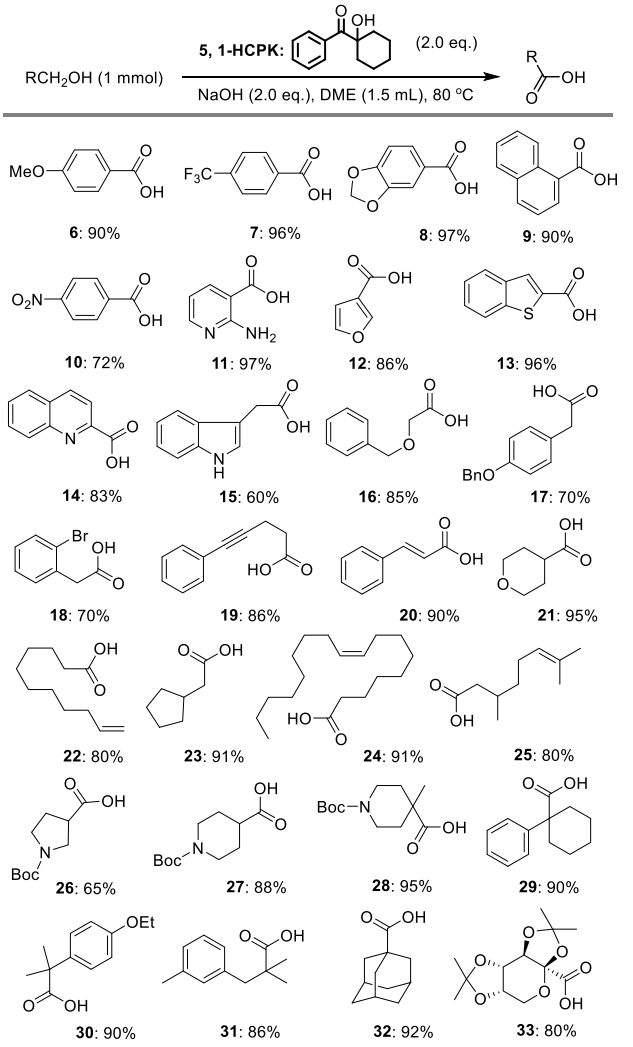
entry	hydrogen acceptors	solvents and additives	yield (%)[a]
1	cyclohexanone	toluene, $(i\text{-Pro})_3Al$	0[b]
2	1,1,1-trifluoroacetone	DCM, $EtOAlEt_2$	0[b]
3	9-fluorenone	xylene, *t*-BuOK	11[b]
4	9-fluorenone	DME, NaOH	15[c]
5	1-HCPK	DMSO, NaOH	14[c]
6	1-HCPK	pyridine, NaOH	67[c]
7	1-HCPK	poluene, NaOH	85[c]
8	1-HCPK	DME, NaOH	91[c]
9	1-HCPK	DME, $Mg(OH)_2$	0[c]
10	1-HCPK	DME, KOH	55[c]
11	open to air or O_2	DME, NaOH	trace[b]
12	1-HCPK	DME, NaOH	94[d]

[a]Yields are isolated yields. All reactions were performed with 1 mmol of alcohol and 2 mmol of hydrogen acceptors and bases in 1.5 mL of the solvents. [b]Reactions were conducted at reflux for 18 h. [c]Reactions were carried out at 80 °C (oil bath) for 18 h in a sealable tube (Teflon cap). [d]Reaction was performed on a gram scale (10 mmol of **3** and 20 mmol of 1-HCPK and NaOH in 15 mL of DME at 80 °C for 30 h).

Trifluoroacetone under the reported conditions[21e] did not provide the desired product; however, 9-fluorenone in the presence of sodium hydroxide in 1,2-dimethoxyethane (DME) afforded the acid in 15% yield. This result prompted us to test more hydrogen acceptors, and after a few experiments we finally found that 1-hydroxycyclohexyl phenyl ketone (entry 8, Table 2; structure of 1-HCPK shown in Scheme 1) was an excellent acceptor in this hydrogen transfer oxidation. When the reaction was mediated by commercially available 1-HCPK[23] and sodium hydroxide, the carboxylic acid **4** was obtained in 94% yield even on gram scale under the optimal reaction conditions (Table 2, entry 12). It should be noted that less solvent (1 mmol of the substrate in 1.5 mL of DME) provides the best yield, possibly increasing the concentration of both the substrates and the base.

With the optimal reaction conditions in hand, we next investigated the substrate scope and the generality of this reaction. Excellent yields were obtained with a range of primary benzylic alcohols bearing electron-donating or electron-withdrawing groups. Primary aliphatic alcohols were also oxidized to the corresponding carboxylic acids in good to excellent yields. A number of functional groups such as amine, ether, heterocycle, amide, alkene, and alkyne units are compatible under our oxidation conditions. Steric hindrance is well tolerated (**28**−**33**), with relatively longer reaction times being required. The workup procedures were simple for most reactions. Extracting the water-diluted reaction mixture with organic solvents (to remove byproducts) followed by acidification of the aqueous phases with HCl or acidic resins normally afforded the products in acceptable purities.

Scheme 1. Oxidation of Primary Alcohols with 1-Hydroxycyclohexyl Phenyl Ketone



Oxidation of aldehydes to the corresponding carboxylic acids is also one of the most common classes of functional group transformations.[2,3] We next investigated the oxidation of a number of aldehydes (Scheme 2). As expected, only 1 equiv of 1-HCPK was required. Benzylic aldehydes bearing different substituents at the aromatic rings were readily converted to benzoic acid derivatives within a couple of hours and in high yields, while the aliphatic aldehydes generally required longer times to be consumed. It is noteworthy that amine and heterocycle moieties are compatible, and the oxidation conditions can be used for the selective conversion of benzaldehydes to benzoic acids (e.g. **43** and **44**) in the presence of primary and secondary aliphatic alcohols.

Coming back to the initial target, the selective oxidation of alcohol **1** to the corresponding carboxylic acid **2**, we conducted the experiment under the optimal reaction conditions. To our delight, oxidation of **1** provided acid **2** in a 72% isolated yield (Scheme 3). To further demonstrate the selectivity, a number of functional alcohols were subjected to our oxidation conditions. The results in Scheme 3 indicated that substrates bearing vulnerable functional groups, including thioethers, amines, *tert*-butanesulfinamides, and secondary alcohols, are compatible. When the substrates (Scheme 2, **43**; Scheme 3,

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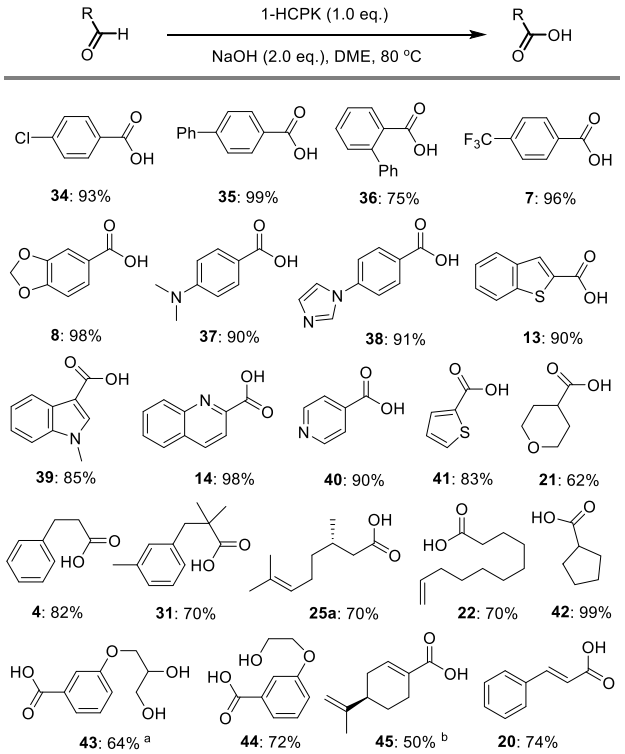
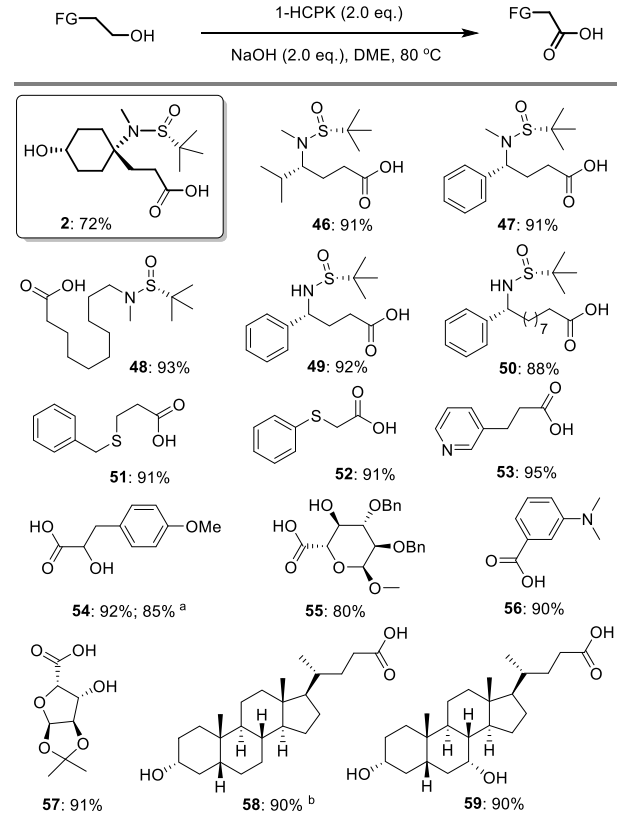
Scheme 2. Oxidation of Aldehydes Using 1-HCPK



a) Reaction was performed in pyridine (1.5 mL). b) Reaction was performed at 60 °C.

Scheme 3. Selective Oxidation of Primary Alcohols in the Presence of Vulnerable Functional Groups

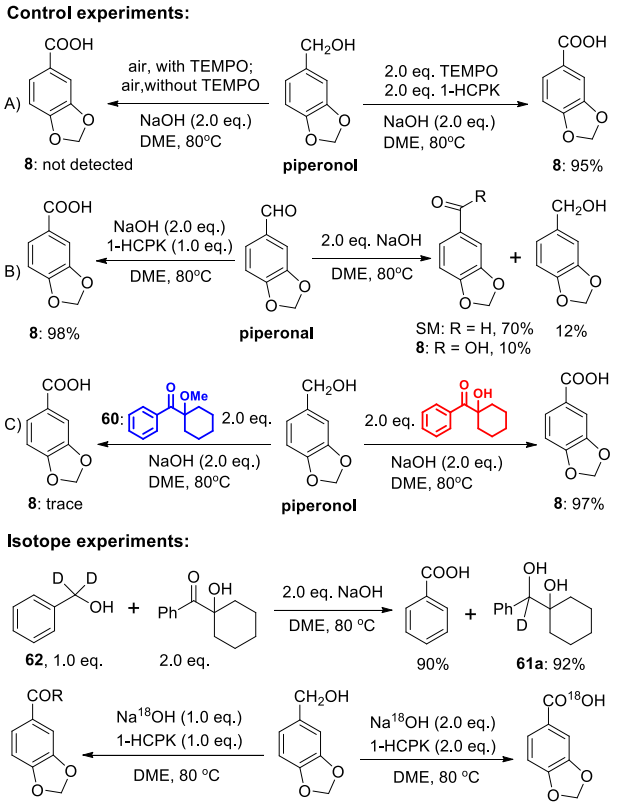


a) Reaction was performed in gram-scale.
b) Reaction was performed in pyridine (1.5 mL).

58) were difficult to dissolve in DME, pyridine could be used as the solvent without affecting the efficiency of the oxidation.

Next, we investigated the mechanism of this process. To exclude possible radical oxidation, control experiments were conducted (Scheme 4). None of the desired acid was detected

Scheme 4. Experiments to Elaborate the Mechanism



R = H, 2% yield; R = ^{18}OH, OH, 41% combine yields

in the absence of 1-HCPK (Scheme 4A), and addition of TEMPO did not interfere with the oxidation process. The effects of Cannizzaro disproportionation[2b] were also studied. Without 1-HCPK, the piperonal did undergo disproportionation under basic conditions; however, the reaction provided piperonylic acid (**8**) in less than 10% isolated yield together with piperonol (11% yield). The same reaction in the presence of 1-HCPK afforded piperonylic acid in 98% yield (Scheme 4B). To elaborate the function of the hydroxyl group in the oxidant, 1-hydroxycyclohexyl phenyl ketone was converted to the methyl ether **60** (see the Supporting Information) and used as a hydrogen acceptor. As predicted, only a trace of the acid was detected under identical reaction conditions (Scheme 4C). Therefore, a neighboring hydroxyl group present in the oxidant plays a decisive role, possibly enhancing the interaction with sodium hydroxide. Interestingly, we did not isolate any aldehyde products in the oxidation of primary alcohols under our optimal reaction conditions. Piperonal could be obtained under the conditions of less 1-HCPK (1.0 equiv) and less sodium hydroxide (1.0 equiv); however, only a 2% isolated yield was obtained (Scheme 4, ^{18}O isotope experiments). These results suggested that the oxidation of aldehydes to the corresponding acids was a fast process. To further confirm the hydrogen transfer process, deuterated benzyl alcohol **62** was subjected to oxidation under the optimal reaction conditions and we obtained the reduced product of 1-HCPK, namely

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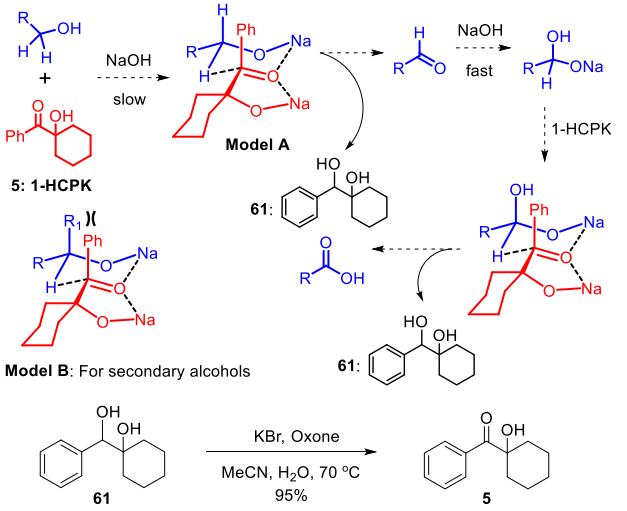
deuterated alcohol **61a**, in 92% yield. Although the oxidation of aldehydes obviously included a hydroxylation process with sodium hydroxide, we still performed experiments with ^{18}O-NaOH. As expected, the ^{18}O-containing acid was isolated as the major product (by LC-HRMS; see the Supporting Information). The proposed oxidation reaction pathway is shown in Scheme 5. Although the reaction follows the

Scheme 5. Proposed Pathway for 1-HCPK-Mediated Oxidations and Recycling of 1-HCPK



Oppenauer oxidation pathway,[21] the hydroxyl group present in the oxidant might form sodium alkoxide and further activate the adjacent carbonyl via coordination (for primary alcohols: model A, Scheme 5). The selective oxidation of primary alcohols (model A) rather than secondary alcohols might result from the steric interactions between the R_1-substituted group (present in secondary alcohols) and the benzene group (present in the oxidant), as indicated in Scheme 5 (model B).

Finally, recycling of 1-hydroxycyclohexyl phenyl ketone was conducted (Scheme 5). Although 1-HCPK is quite cheap, it is still desirable to recycle this organic compound. Thus, diol **61** produced from the reaction process (around 90−97% yields) was collected and subjected to oxidation under the conditions of KBr and oxone,[24] and 1-hydroxycyclohexyl phenyl ketone was obtained in 95% yield.

In conclusion, we have developed a new process for the chemoselective oxidation of primary alcohols and aldehydes to the corresponding carboxylic acids. The mechanism was also elaborated by isotope experiments. Features of this oxidation are a new hydrogen transfer acceptor, namely the commercially available and cheap material 1-hydroxycyclohexyl phenyl ketone, tolerance of a wide range of functional groups, including vulnerable *tert*-butanesulfinimades and secondary alcohols, an easy to handle procedure, and good to excellent yields. The oxidation process is practical and can be carried out on a gram scale. On the basis of our experience, this selective oxidation should find application in organic synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c02188.

Experimental procedures, characterization data, and spectra of all new compounds (PDF)

Accession Codes

CCDC 2092153 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected books and review chapters, see: (a) Bäckwall, J. E. *Modern Oxidation Methods*; Wiley-VCH: 2004. (b) Ley, S. V. *Comprehensive Organic Synthesis*, 3rd ed.; Pergamon: 1999; Vol. 7, Chapter 2, pp 251−327. (c) Arends, I. W. C. E.; Sheldon, R. A. Modern Oxidation of Alcohols Using Environmentally Benign Oxidants. In *Modern Oxidation Methods*, 2nd ed.; Bäckvall, J. E., Ed.; Wiley-VCH: 2010; pp 147−185.

(2) (a) Tojo, G.; Fernández, M. I. *Oxidation of Primary Alcohols to Carboxylic Acids: A Guide to Current Common Practice*; Springer: 2007. (b) Lappe, P.; Schulz, E. Aliphatic Carboxylic Acids via Aldehyde Oxidation. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: 1996; pp 424−464. (c) Tojo, G.; Fernández, M. Oxidation of Primary Alcohols to Carboxylic Acids. In *Basic Reactions in Organic Synthesis*; Springer: 2010. (d) Caron, S.; Dugger, R. W.; Ruggeri, S. G.; Ragan, J. A.; Ripin, D. H. B. Large-Scale Oxidations in the Pharmaceutical Industry. *Chem. Rev.* **2006**, *106*, 2943−2989.

(3) (a) Ogliaruso, M. A.; Wolfe, J. F. Synthesis of Carboxylic Acids, Esters and Their Derivatives. In *The Chemistry of Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley: 1991; pp 40−49. (b) Smith, M. B. *Compendium of Organic Synthetic Methods*; Wiley: 2001; Vol. 9. (c) Larock, R. C. *Comprehensive Organic Transformations, A Guide to Functional Group Preparations*, 2nd ed.; Wiley-VCH: 1999, and references cited therein.

(4) Zhao, M.; Li, J.; Song, Z.; Desmond, R.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. A Novel Chromium Trioxide Catalyzed Oxidation of Primary Alcohols to the Carboxylic Acids. *Tetrahedron Lett.* **1998**, *39*, 5323−5326.

(5) Mahmood, A.; Robinson, G. E.; Powell, L. An Improved Oxidation of an Alcohol Using Aqueous Permanganate and Phase-Transfer Catalyst. *Org. Process Res. Dev.* **1999**, *3*, 363−364.

(6) (a) George, M. V.; Balachandran, K. S. Nickel Peroxide Oxidation of Organic Compounds. *Chem. Rev.* **1975**, *75*, 491−519. (b) Grill, J. M.; Ogle, J. W.; Miller, S. A. An Efficient and Practical System for the Catalytic Oxidation of Alcohols, Aldehydes, and α,β-Unsaturated Carboxylic Acids. *J. Org. Chem.* **2006**, *71*, 9291−9296.

(7) Uyanik, M.; Akakura, M.; Ishihara, K. 2-Iodoxybenzenesulfonic Acid as an Extremely Active Catalyst for the Selective Oxidation of Alcohols to Aldehydes, Ketones, Carboxylic Acids, and Enones with Oxone. *J. Am. Chem. Soc.* **2009**, *131*, 251−262 and references cited therein.

(8) For selected reviews, see: (a) Shibuya, M. Nitroxyl radical-catalyzed chemoselective alcohol oxidation for the synthesis of polyfunctional molecules. *Tetrahedron Lett.* **2020**, *61*, 151515−151525. (b) Nutting, J. E.; Rafiee, M.; Stahl, S. S. Tetramethylpiperidine *N*-Oxyl (TEMPO), Phthalimide *N*-Oxyl (PINO), and Related *N*-Oxyl Species: Electrochemical Properties and Their Use in Electrocatalytic Reactions. *Chem. Rev.* **2018**, *118*, 4834−4885. For selected recent examples, see: (c) Rafiee, M.; Konz, Z. M.; Graaf, M. D.; Koolman, H. F.; Stahl, S. S. Electrochemical Oxidation of Alcohols and Aldehydes to Carboxylic Acids Catalyzed by 4-Acetamido-TEMPO: An Alternative to "Anelli" and "Pinnick" Oxidations. *ACS Catal.* **2018**, *8*, 6738−6744. (d) Jiang, X.; Zhang, J.; Ma, S. Iron Catalysis for Room-Temperature Aerobic Oxidation of Alcohols to Carboxylic Acids. *J. Am. Chem. Soc.* **2016**, *138*, 8344−8347.

(9) Noyori, R.; Aoki, M.; Sato, K. Green oxidation with aqueous hydrogen peroxide. *Chem. Commun.* **2003**, 1977−1986 and references cited therein.

(10) For selected recent examples, see: (a) Wang, Z.-Q.; Tang, X.-S.; Yang, Z.-Q.; Yu, B.-Y.; Wang, H.-J.; Sang, W.; Yuan, Y.; Chen, C.; Verpoort, F. Highly active bidentate *N*-heterocyclic carbene/ruthenium complexes performing dehydrogenative coupling of alcohols and hydroxides in open air. *Chem. Commun.* **2019**, *55*, 8591−8594. (b) Hu, P.; Ben-David, Y.; Milstein, D. General Synthesis of Amino Acid Salts from Amino Alcohols and Basic Water Liberating H_2. *J. Am. Chem. Soc.* **2016**, *138*, 6143−6146. (c) Balaraman, E.; Khaskin, E.; Leitus, G.; Milstein, D. Catalytic transformation of alcohols to carboxylic acid salts and H_2 using water as the oxygen atom source. *Nat. Chem.* **2013**, *5*, 122−125.

(11) (a) Ahmed, M. S.; Mannel, D. S.; Root, T. W.; Stahl, S. S. Aerobic Oxidation of Diverse Primary Alcohols to Carboxylic Acids with a Heterogeneous Pd−Bi−Te/C (PBT/C) Catalyst. *Org. Process Res. Dev.* **2017**, *21*, 1388−1393. (b) Mori, T.; Ishii, C.; Kimura, M. Pd-Catalyzed Dehydrogenative Oxidation of Alcohols to Functionalized Molecules. *Org. Process Res. Dev.* **2019**, *23*, 1709−1717. and references cited therein

(12) Sawama, Y.; Morita, K.; Yamada, T.; Nagata, S.; Yabe, Y.; Monguchi, Y.; Sajiki, H. Rhodium-on-carbon catalyzed hydrogen scavenger- and oxidant-free dehydrogenation of alcohols in aqueous media. *Green Chem.* **2014**, *16*, 3439−3443.

(13) (a) Fujita, K. I. Development and Application of New Iridium Catalysts for Efficient Dehydrogenative Reactions of Organic Molecules. *Bull. Chem. Soc. Jpn.* **2019**, *92*, 344−351. (b) Cherepakhin, V.; Williams, T. J. Iridium Catalysts for Acceptorless Dehydrogenation of Alcohols to Carboxylic Acids: Scope and Mechanism. *ACS Catal.* **2018**, *8*, 3754−3763.

(14) Ghalehshahi, H. G.; Madsen, R. Silver-Catalyzed Dehydrogenative Synthesis of Carboxylic Acids from Primary Alcohols. *Chem. - Eur. J.* **2017**, *23*, 11920−11926.

(15) (a) Nguyen, D. H.; Morin, Y.; Zhang, L.; Trivelli, X.; Capet, F.; Paul, S.; Desset, S.; Dumeignil, F.; Gauvin, R. M. Earth-abundant transition metals-catalyzed oxidative transformations of bio-sourced alcohols. *ChemCatChem* **2017**, *9*, 2652−2660. (b) Tang, Y.; Meador, R. I. L.; Malinchak, C. T.; Harrison, E. E.; McCaskey, K. A.; Hempel, M. C.; Funk, T. W. (Cyclopentadienone)iron-Catalyzed Transfer Dehydrogenation of Symmetrical and Unsymmetrical Diols to Lactones. *J. Org. Chem.* **2020**, *85*, 1823−1834.

(16) Shao, Z.; Wang, Y.; Liu, Y.; Wang, Q.; Fu, X.; Liu, Q. A general and efficient Mn-catalyzed acceptorless dehydrogenative coupling of alcohols with hydroxides into carboxylates. *Org. Chem. Front.* **2018**, *5*, 1248−1256. See also ref 15c.

(17) Jiang, N.; Ragauskas, A. J. Selective Aerobic Oxidation of Activated Alcohols into Acids or Aldehydes in Ionic Liquids. *J. Org. Chem.* **2007**, *72*, 7030−7033.

(18) Monda, F.; Madsen, R. Zinc Oxide-Catalyzed Dehydrogenation of Primary Alcohols into Carboxylic Acids. *Chem. - Eur. J.* **2018**, *24*, 17832−17837.

(19) Kong, X.-K.; Xiong, Z.-M.; Zhi, X.; Meng, X.-L.; Zhao, J.-F.; Chen, W.; Zhang, H. Lewis acid mediated cyclization: synthesis of 2-spirocyclohexylindolines. *Org. Biomol. Chem.* **2021**, *19*, 4043−4047.

(20) (a) Doi, R.; Shibuya, M.; Murayama, T.; Yamamoto, Y.; Iwabuchi, Y. Development of an Azanoradamantane-Type Nitroxyl Radical Catalyst for Class-Selective Oxidation of Alcohols. *J. Org. Chem.* **2015**, *80*, 401−413. (b) Ikunaka, M.; Matsumoto, J.; Nishimoto, Y. A concise synthesis of (2*S*,3*S*)-BocAHPBA and (*R*)-BocDMTA, chiral building blocks for peptide-mimetic HIV protease inhibitors. *Tetrahedron: Asymmetry* **2002**, *13*, 1201−1208. (c) Liu, J. Y.; Wang, L.; Zhang, J. F.; Xu, Z. S.; Ye, T. The total synthesis and stereochemical assignment of scytonemin A. *Chem. Commun.* **2016**, *52*, 1002−1005. (d) Chinthapally, K.; Baskaran, S. A chemoselective oxidation of monosubstituted ethylene glycol: facile synthesis of optically active α-hydroxy acids. *Org. Biomol. Chem.* **2014**, *12*, 4305−4309. (e) Furukawa, K.; Shibuya, M.; Yamamoto, Y. Chemoselective Catalytic Oxidation of 1,2-Diols to α-Hydroxy Acids Controlled by TEMPO−ClO_2 Charge-Transfer Complex. *Org. Lett.* **2015**, *17*, 2282−2285. (f) Hansen, T. M.; Florence, G. J.; Lugo-Mas, P.; Chen, J. H.; Abrams, J. N.; Forsyth, C. J. Highly chemoselective oxidation of 1,5-diols to δ-lactones with TEMPO/BAIB. *Tetrahedron Lett.* **2003**, *44*, 57−59.

(21) For selected books and review chapters, see: (a) Graves, C. R.; Campbell, E. J.; Nguyen, S. T. Aluminum-based catalysts for the asymmetric Meerwein−Schmidt−Ponndorf−Verley−Oppenauer (MSPVO) reaction manifold. *Tetrahedron: Asymmetry* **2005**, *16*, 3460−3468. (b) de Graauw, C. F.; Peters, J. A.; van Bekkum, H.; Huskens, J. Meerwein-Ponndorf-Verley Reduction and Oppenauer Oxidations: An Integrated Approach. *Synthesis* **1994**, 1007−1017.

https://doi.org/10.1021/acs.orglett.1c02188
Org. Lett. XXXX, XXX, XXX−XXX

(c) Djerassi, C. The Oppenauer Oxidation. *Org. React.* **2011**, *6*, 207−272. For selected recent examples, see: (d) Graves, C. R.; Zeng, B.-S.; Nguyen, S. T. Efficient and Selective Al-Catalyzed Alcohol Oxidation via Oppenauer Chemistry. *J. Am. Chem. Soc.* **2006**, *128*, 12596−12597. (e) Mello, R.; Martínez-Ferrer, J.; Asensio, G.; González-Núñez, M. E. Oppenauer Oxidation of Secondary Alcohols with 1,1,1-Trifluoroacetone as Hydride Acceptor. *J. Org. Chem.* **2007**, *72*, 9376−9378 and references cited therein.

(22) Eignerová, L.; Kasal, A. Intramolecular Hydride Shift in Oppenauer Oxidation of Some Dihydroxylsteroids. *Collect. Czech. Chem. Commun.* **1976**, *41*, 1056−1065.

(23) 1-Hydroxycyclohexyl phenyl ketone is commercially available and cheap, USD $50−80/kG. High-purity sodium hydroxide (99.99%) and normal sodium hydroxide (96%) were used in this oxidation, and no difference was observed.

(24) Moriyama, K.; Takemura, M.; Togo, H. Selective Oxidation of Alcohols with Alkali Metal Bromides as Bromide Catalysts: Experimental Study of the Reaction Mechanism. *J. Org. Chem.* **2014**, *79*, 6094−6104.

https://doi.org/10.1021/acs.orglett.1c02188
Org. Lett. XXXX, XXX, XXX−XXX