Letters in Organic Chemistry, 2018, *15*, 895-898

RESEARCH ARTICLE

An Efficient Oxidation of Alcohols by Aqueous H_2O_2 with 1,3-Dibromo-5,5-Dimethylhydantoin

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ARTICLE HISTORY

Received: April 26, 2018
Revised: May 23, 2018
Accepted: June 01, 2018

DOI:
10.2174/1570178615666180613080548

Abstract: An efficient protocol is described for the oxidation of alcohols to the corresponding aldehydes or ketones with 1,3-dibromo-5,5-dimethylhydantoin in the presence of aqueous H_2O_2.

Keywords: Alcohols, aldehydes, hydrogen peroxide, ketones, oxidation, toxic reagent.

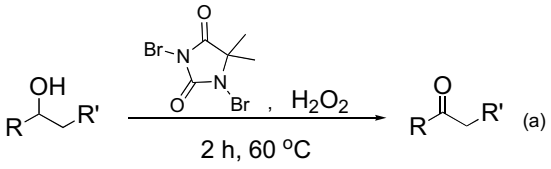
1. INTRODUCTION

The oxidative conversion of alcohols to the corresponding aldehydes or ketones is one of the most fundamental reactions in the field of organic synthesis [1-2]. Traditionally, the oxidation of alcohols is achieved in the presence of harmful chromate and permanganate reagents in hazardous organic solvents. Some of the recently reported protocols also involved the use of transition metal compounds such as chromium (VI) complexes [3], triphenylmethylphosphonium dichromate [4], manganese dioxide [5], trichloroisocyanuric acid/$RuCl_3$ [6], and Ru-hydrotalcite [7]. These methods have manydrawbacks such as use of toxic reagents, vigorous reaction conditions, long reaction times, and low yields. Hydrogen peroxide has been well known as an ideal green oxidant because it produced water as a sole by-product. To improve low oxidation ability of hydrogen peroxide, various complexes of transition metals such as gold [8], iron [9], manganese [10], molybdenum [11], tungsten [12, 13], or bismuth [14] have been utilized for the oxidation of alcohols. However, many of them used toxic and harmful transition metal complexes in volatile organic solvents which are problematic for a cleaner environment. Therefore, development of novel and alternative methods for the hydrogen peroxide promoted oxidation of the alcohol with more environmental friendly conditions is still highly desirable.

Water has attracted considerable attention as an eco-friendly alternative solvent to harmful and unsafe volatile organic solvents for the various reactions in organic synthesis [15]. Many organic reactions in aqueous conditions demonstrated uncommon solvent behaviors like accelerated reaction rate [16] and improved stereoselectivity [17] in comparison with the reactions in organic solvents. However, there has been reported only a few examples of selective benzylic alcohol oxidations reactions in pure aqueous reaction conditions up to now [18, 19]. 1,3-Dibromo-5,5-dimethyl hydatoin (DBDMH) has been -widely used as a green sterilizing disinfectant for various water purifications due to its very cheap and very low toxic properties [20]. DBDMH with a combination of chlorinated solvents has successfully been utilized in various bromination processes including benzylic bromination [21], dibromination of functionalized alkenes [22], oxidation of thiols [23], and bromination reactions of carboxylic acids [24]. In addition, DBDMH was utilized for the oxidation of benzylic alcohols in water mediated by TEMPO/$NaNO_2$ [25] and cyclodextrin [26]. Recently, DBDMH was applied for the oxidation of narrow ranges of secondary benzylic alcohols to carbonyl compounds in solvent-free conditions in lower yields [27]. Furthermore, this method was unsuccessful to give desired aldehydes products for the oxidation of primary benzylic alcohols.

2. RESULTS AND DISCUSSION

Our new protocol is based on the reaction of alcohols with DBDMH (0.5 equiv.) in 35% aqueous hydrogen peroxide solution for 2 h at 60°C (Scheme **1**).



Scheme (1). Oxidation of alcohols to carbonyl compounds.

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1875-6255/18 $58.00+.00

Initial attempts to oxidize benzyl alcohol with DBDMH with 35% aqueous hydrogen peroxide provided benzaldehyde in 85% yields. The reaction in the absence of hydrogen peroxide gave benzaldehyde in 50% yields after a prolonged reaction time of 5 h. Replacement of DBDMH by bromine or *N*-bromosuccinimide gave much lowered yields of benzaldehyde. Reaction temperatures below or above 60°C gave somewhat lowered yields or complicated products. The optimum amount of DBDMH proved to be less than stoichiometric amount (0.5 equiv.). As shown in Table **1**, both primary and secondary benzylic alcohols were smoothly converted to aldehydes or ketones in the present reaction conditions.

The products were isolated in high to excellent yields. In all cases of oxidation of primary benzylic oxidations, our conditions resulted in exclusive formation of aldehydes with the absence of carboxylic acids. Moreover, bromination reactions to the aromatic ring were not observed in all cases tested. In addition, electron releasing or electron-attracting substituents in the aromatic rings did not notably affect the effectiveness of the oxidative transformation reactions under the present reaction conditions. It was also observed that with acyclic and cyclic aliphatic alcohols, the oxidation reactions provided the desired products in high yields (entries 17-20). The oxidation probably occurred by the reactions of alcohols with bromine cation, formed *in situ* by the reaction of DBDMH and hydrogen peroxide, to give hypobromite ester intermediate in line with a previously reported analogous observation of oxidation of alcohols with NaBr-$NaBrO_3$ [28].

Table 1. Oxidation of Alcohols with DBDMH in Aqueous H_2O_2.

Entry	Substrate	Product	Yield (%)[a]
1	$PhCH_2OH$	PhCHO **(1a)**	85
2	$2\text{-}ClC_6H_4CH_2OH$	$2\text{-}ClC_6H_4CHO$ **(2a)**	82
3	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CHO$ **(3a)**	84
4	$4\text{-}BrC_6H_4CH_2OH$	$4\text{-}BrC_6H_4CHO$ **(4a)**	82
5	$4\text{-}FC_6H_4CH_2OH$	$4\text{-}FC_6H_4CHO$ **(5a)**	78
6	$4\text{-}MeC_6H_4CH_2OH$	$4\text{-}MeC_6H_4CHO$ **(6a)**	90
7	$4\text{-}MeOC_6H_4CH_2OH$	$4\text{-}MeOC_6H_4CHO$ **(7a)**	80
8	Piperonyl alcohol	Piperonal **(8a)**	78
9	$4\text{-}NO_2C_6H_4CH_2OH$	$4\text{-}NO_2C_6H_4CHO$ **(9a)**	85
10	$PhCH(OH)CH_3$	$PhCOCH_3$ **(10a)**	96
11	$C_6H_5CH(OH)CH_2CH_3$	$C_6H_5COCH_2CH_3$ **(11a)**	92
12	$4\text{-}MeC_6H_4CH(OH)CH_3$	$4\text{-}MeC_6H_4COCH_3$ **(12a)**	92
13	$4\text{-}ClC_6H_4CH(OH)CH_3$	$4\text{-}ClC_6H_4COCH_3$ **(13a)**	91
14	$4\text{-}BrC_6H_4CH(OH)CH_3$	$4\text{-}BrC_6H_4COCH_3$ **(14a)**	89
15	PhCH(OH)Ph	PhCOPh **(15a)**	96
16	9-Hydroxyfluorene	9-Fluorenone **(16a)**	90
17	a-Tetralol	a-Tetralone **(17a)**	85
18	Cyclohexanol	Cyclohexanone **(18a)**	78
19	1-Octanol	Octanal **(19a)**	70
20	2-Octanol	2-Octanone **(20a)**	76

[a] Yields of isolated product.

3. EXPERIMENTAL

A general experimental procedure is as follows: A mixture of alcohol (1.0 mmol) and DBDMH (0.5 mmol, 0.14 g) in aqueous hydrogen peroxide (3.0 mmol, 35% aq. 0.09 mL) solution was stirred for 2 h at 60°C in the open vessel. After cooling the mixture to room temperature, the product was extracted into dichloromethane (2 x 25 mL) and washed with water. The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash column chromatography (ethyl acetate/*n*-hexane = 1:3, v/v) to give the desired carbonyl compound. The spectral data of the products are as follows:

3.1. Benzaldehyde (1a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.87 (d, *J* = 1.5 Hz, 2H), 7.73 – 7.28 (m, 3H). Mass: 106(M^+) C_7H_8O

3.2. 2-Chlorobenzaldehyde (2a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.86-7.33(m, 2H-5H). Mass: 140(M^+) C_7H_5ClO.

3.3. 4-Chlorobenzaldehyde (3a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.84 (m, 2H) 7.45 (m, 2H).

Mass: 140(M^+) C_7H_5ClO.

3.4. 4-Bromobenzaldehyde (4a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.75 (d, *J* = 7.5Hz, 2H). 7.64(d, *J* =7.5Hz, 2H).

Mass: 185(M^+) C_7H_5BrO.

3.5. 4-Fluorobenzaldehyde (5a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (s,1H), 7.95 (m, 2H), 7.25 (m, 2H).

Mass: 124(M^+) C_7H_5FO.

3.6. 4-Methylbenzaldehyde (6a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.93-7.66 (m, 2H), 7.32 (dd, *J* = 7.9, 0.5 Hz, 2H), 2.43 (s, 3H).

Mass: 120(M^+) C_8H_8O.

3.7. 4-Methoxybenzaldehyde (7a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.84(d, 2H), 7.01(d, 2H), 3.90(s, 3H).

Mass: 136(M^+) $C_8H_8O_2$.

3.8. Piperonal (8a)

^{1}H NMR (300 MHz, $CDCl_3$) δ d 9.73 (s, 1H), 7.36 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 2H).

Mass: 150(M^+) $C_8H_6O_3$.

3.9. 4-Nitrobenzaldehyde (9a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.41(d, *J* = 8.6, 2H), 8.09(d, *J*=8.9 2H).

Mass: 151(M^+) $C_7H_5NO_3$.

3.10. Acetophenone (10a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.0 Hz, 2H), 7.69 – 7.30 (m, 3H), 2.59 (s, 3H).

Mass: 156(M^+) $C_{11}H_8O$.

3.11. Propiophenone (11a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.0 Hz, 2H), 7.60 – 7.26 (m, 3H), 2.97 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H).

Mass: 134(M^+) $C_9H_{10}O$.

3.12. 1-(p-Tolyl)ethanone (12a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (t, *J* = 8.6 Hz, 2H), 7.40 – 6.88 (m, 2H), 2.57 (s, 3H), 2.40 (s, 3H).

Mass: 136(M^+) $C_9H_{10}O$.

3.13. (4-Chlorophenyl)ethanone (13a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 –7.73 (m, 2H), 7.56 – 7.27 (m, 2H), 2.58 (s, 3H).

Mass: 155(M^+) C_8H_7ClO.

3.14. (4-Bromophenyl)ethanone (14a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.57 (m, 2H), 2.57 (s, 3H).

Mass: 197(M^+) C_8H_7BrO.

3.15. Benzophenone (15a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.49 (t, *J* = 7.5, 4H), 7.55-7.60 (t, *J* = 7.2, 2H), 7.79-7.81 (d, *J* = 7.5, 4H).

Mass: 182(M^+) $C_{13}H_{10}O$.

3.16. 9-Fluorene (16a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.4 Hz, 2H), 7.48-7.44 (m, 4H), 7.29-7.26 (m, *2*H).

Mass: 182(M^+) $C_{13}H_{10}O$.

3.17. α-Tetralone (17a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.34-7.11 (m, 2H), 3.17-2.84 (m, 2H), 2.78-2.47 (m, 2H), 2.14 (dd, *J* = 12.9, 6.7 Hz, 2H).

Mass: 146(M^+) $C_{10}H_{10}O$.

3.18. Cyclohexanone (18a)

1H NMR (300 MHz, $CDCl_3$) δ 2.34 (t, *J* = 6.6Hz, 4H), 1.87 (m, 4H), 1.42-1.72 (m, 2H).

Mass:98.07(M^+) $C_6H_{10}O$.

3.19. Octanal (19a)

1H NMR (300 MHz, D_2O) δ 9.767(s, 2H), 2.442-2.429 (d, 3H), 1.646-1.631 (m, 4H-8H), 1.321-1.307 (t, 9H).

Mass: 128.12(M^+) $C_8H_{16}O$.

3.20. 2-Octanone (20a)

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (t, *J* = 7.5Hz, 2H), 2.14 (s, 3H), 1.52-1.62 (m, 2H), 1.27-1.31 (m, 6H), 0.88 (t, *J* = 7.5Hz, 3H). Mass: 128.12(M^+) $C_8H_{16}O$.

CONCLUSION

In summary, we have demonstrated that primary, secondary benzylic alcohols, and aliphatic alcohols can be effectively converted to their corresponding carbonyl products with DBDMH in aqueous hydrogen peroxide. Thus, the present method may be served as a cost-effective, general and environmentally benign alternative to the existing methods for the oxidation of alcohols.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

This research was supported by the Chung-Ang University Research Scholarship Grants in 2017.

REFERENCES

[1] Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B.M.; Ley, S.V., Eds.; Pergamon, Oxford, **1991**, Vol. *7*.

[2] Tojo, G.; Fernández, M. (Eds.), *Oxidation of Alcohols to Aldehydes and Ketones: A Guide to Current Common Practice*, Springer, Berlin, **2006**.

[3] Hajipoure, A.R.; Mallakpour, S.E.; Khoee, S. *Synlett,* **2000**, *2*, 740.

[4] Hajipour, A.R.; Safaei, S.; Ruoho, A.E. *Synth. Comm.,* **2009**, *39*, 3687.

[5] Uchiyama, M.; Kimura, Y.; Ohta, A. *Tetrahedron Lett.,* **2000**, *41*, 10013.

[6] Yamaoka, H.; Moriya, N.; Ikunaka, M. *Prg. Proc. Res. Dev.,* **2004**, *8*, 931.

[7] Kaneda, K.; Yamashita, T.; Matsushita, T.; Ebitani, K. *J. Org. Chem.,* **1998**, *63*, 1750.

[8] Ni, J.; Yu, W-J.; He, L.; Sun, H.; Cao, Y.; He, H-Y.; Fan, K-N. *Green Chem.,* **2009**, *11*, 756.

[9] Martin, S.E.; Garrone, A. *Tetrahedron Lett.,* **2003**, *44*, 549.
[10] Mardani, H.R.; Golchoubian, H. *Tetrahedron Lett.,* **2006**, *47*, 2349.
[11] Bortolini, O.; Conte, V.; Furia, D.; Modena, G. *J. Org. Chem.,* **1986**, *51*, 2661.
[12] Sato, K.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.,* **1998**, *39*, 7549.
[13] He, Y.; Ma, X.; Lu, M. *ARKIVOC,* **2012**, *8,*187.
[14] Han, M.-K.; Kim, S.; Kim, S.T.; Lee, J.C. *Synlett,* **2015**, *26*, 2434.
[15] Li, C.-J. In *Handbook of Green Chemistry*; Anastas, P.T., Ed.; Wiley-VCH, Weinheim, **2010**, Vol. *5*.
[16] Narayan, S.; Muldoon, J.; Finn, M.G.; Fokin, V.V.; Kolb, H.C.; Sharpless, K.B. *Angew. Chem. Int. Ed.,* **2005**, *44*, 3275.
[17] González-Cruz, D.; Tejedor, D.; de Armas, P.; Morales, E.Q.; García-Tellado, F. *Chem. Comm.,* **2006**, 2789.
[18] Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.,* **1997**, *119*, 12386.
[19] Surendra, K.; Krishnaveni, N.S.; Reddy, M.A.; Nageswar, Y.V.D.; Rao, K.R. *J. Org. Chem.,* **2003**, *68*, 2058.
[20] Song, S.; Liu, P.; Song, Q.J. *Anal. Sci.,* **2007**, *23*, 327.
[21] Ishizumi, K.; Ohashi, N.; Tanno, N. *J. Org. Chem.,* **1987**, *52*, 4477.
[22] Hernández-Torres, G.; Tan, B.; Barbas, C.F. *Org. Lett.,* **2012**, *14*, 1858.
[23] Khazaei, A.; Zolfigol, M.A.; Rostani, A. *Synthesis*, **2004**, *18*, 2959-2961.
[24] Aurrbach, J.; Weissman, S.A.; Blacklock, J.T.; Angeles, M.R.; Hoogsteen, K. *Tetrahedron Lett.,* **1993**, *34*, 931.
[25] Liu, R.; Dong, C.; Liang, X.; Wang, X.; Hu, X. *J. Org. Chem.* **2005**, *70*, 729.
[26] Chaudhuri, S.; Zaki, H.; Levine, M. *Synth. Comm.* **2016**, *46*, 636.
[27] Khazaei, A.; Abbasi, F.; Kianiborazjani, M.; Saednia, S. *J. Braz. Chem. Soc.,* **2014**, *25*, 361.
[28] Pääkkönen, S.; Pursiainen, J.; Lajunen, M. *Synth. Comm.,* **2012**, *42*, 534.