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RESEARCH ARTICLE

DIRECT BENZYLIC OXIDATION OF ALKYL BENZENES USING CuBr AND HYDROGEN PEROXIDE

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ABSTRACT

A direct benzylic oxidation of alkylarenes via C-H bond abstraction was developed using copper bromide hydrogen peroxide mixture under mild conditions. This reaction proceeded with excellent selectivity by thermal oxidation.

Key words:

alkylbenzenes, CuBr and hydrogen peroxide, benzylic oxidation

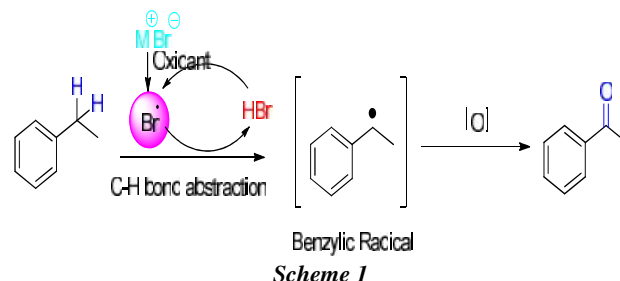
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INTRODUCTION

There is a necessary for the direct C-H bond functionalization of hydrocarbons via C-H bond activation in organic synthesis has attracted much interest in recent years.¹ Especially, chemoselective functionalization under metal-free conditions, which is one of the requirements for the realization of green chemical processes, remains a tremendous challenge in organic chemistry. Direct benzylic oxidation of alkylbenzenes to the corresponding carbonyl compounds which are useful as versatile building blocks in the synthesis of functionalized chemicals and pharmaceuticals.²

Several methods were reported for the direct benzylic oxidation of alkylarenes using heavy metals.³⁻¹¹ Further oxidation of arylbenzenes was performed using an organocatalyst¹² and a stoichiometric amount of hypervalent iodine¹³ have been developed as sustainable oxidation methods. However, in most cases, alkylarenes bearing an electron-withdrawing group on the aryl or alkyl moiety, whose C-H bond at the benzylic position is more inert, could not be used for the direct

oxidation. In this paper we report a metal-free direct and selective benzylic oxidation of alkylarenes via C-H abstraction using an alkali metal bromide/ oxidant system, focused towards green synthesis (Scheme 1). This oxidation proceeded smoothly under normal light in halogenated solvent.



Experimental

General Procedure for Direct Benzylic Oxidation of Alkylarenes

To a solution of 1a (1 mmol) in a mixture of DCM (19 vol) and H₂O (1 vol) was added CuBr (1.2 mmol) and 30% H₂O₂ (2

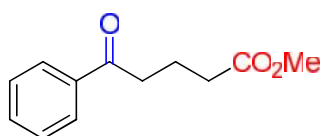
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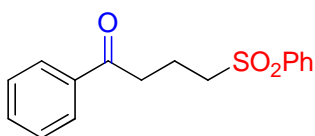
mmol) at room temperature, and stirred under visible light for 24 h. Saturated Na₂SO₃ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with DCM (20 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na₂SO₄. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: hexane/AcOEt = 20/1), to give the desired product 2a.

Representative Spectral data

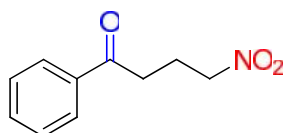
3-Acetoxypropylphenone (2k): ¹H NMR (400 MHz, CDCl₃) 2.05 (s, 3H), 3.34 (t, J = 6.2 Hz, 2H), 4.54 (t, J = 6.2 Hz, 2H), 7.48 (t, J = 7.4 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.94-7.98 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) 20.8, 37.2, 59.5, 128.1 (2C), 128.5 (2C), 133.3, 136.6, 171.1, 196.8. MS (ESI) calcd for C₁₁H₁₂NaO₃ [M+Na]⁺ 215.0679, found 215.0675.



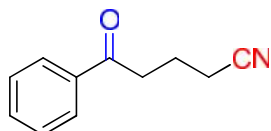
Methyl 4-phenyl-4-oxobutanoate (2l): ¹H NMR (400 MHz, CDCl₃) 2.79 (t, J = 6.4 Hz, 2H), 3.34 (t, J = 6.4 Hz, 2H), 3.72 (s, 3H), 7.48 (t, J = 7.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) 28.1, 33.2, 51.6, 128.1 (2C), 128.5 (2C), 133.3, 136.5, 173.3, 198.1. MS (ESI) calcd for C₁₁H₁₂NaO₃ [M+Na]⁺ 215.0679, found 215.0672.



4-Phenylsulfonyl-1-phenyl-1-butanone (2m): ¹H NMR (400 MHz, CDCl₃) 2.13-2.22 (m, 2H), 3.19 (t, J = 6.9 Hz, 1H), 3.20 (t, J = 6.9 Hz, 1H), 3.26 (t, J = 7.6 Hz, 2H), 7.43-7.49 (m, 2H), 7.54-7.62 (m, 3H), 7.63-7.69 (m, 1H), 7.89-7.96 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) 17.3, 36.3, 55.2, 127.9 (2C), 128.0 (2C), 128.7 (2C), 129.3 (2C), 133.4, 133.7, 136.4, 139.0, 198.4. MS (ESI) calcd for C₁₆H₁₇O₃S [M+H]⁺ 289.0893, found 289.0890.



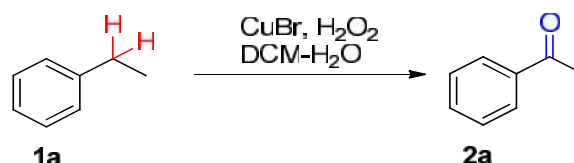
4-Nitro-1-phenyl-1-butanone (2n): ¹H NMR (400 MHz, CDCl₃) 2.46 (quin, J = 6.6 Hz, 2H), 3.16 (t, J = 6.6 Hz, 2H), 4.56 (t, J = 6.6 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.96 (d, J = 7.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) 21.5, 34.5, 74.7, 127.9 (2C), 128.7 (2C), 133.5, 136.3, 197.9. HRMS (FAB) calcd for S₇ C₁₀H₁₂NO₃ [M+H]⁺ 194.0817, found 194.0820.



4-Cyanobutylphenone (2o): ¹H NMR (400 MHz, CDCl₃) 2.13 (quin, J = 7.2 Hz, 2H), 2.55 (t, J = 7.2 Hz, 2H), 3.18 (t, J = 7.2 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) 16.6, 19.7, 36.3, 119.4, 127.9 (2C), 128.7 (2C), 133.5, 136.4, 198.1. MS (APCI) calcd for C₁₁H₁₂NO [M+H]⁺ 174.0913, found 174.0910.

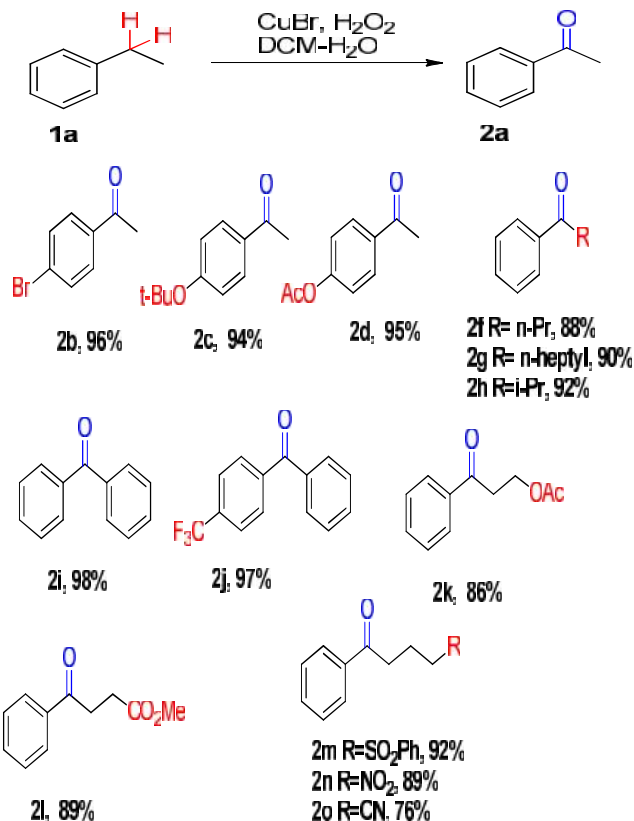
RESULTS AND DISCUSSION

To understand the reaction, we screened several bromo reagents, oxidants, and solvent for direct benzylic oxidation of alkylbenzenes (1a). The optimum reaction conditions were found to involve 1a, CuBr (1.2 equiv), and H₂O₂ (2.0 equiv) in DCM-H₂O at RT for 24 h (Scheme 2).



Scheme 2

To explore the scope of the direct benzylic oxidation, various alkylarenes 1 were examined using copper bromide under optimized conditions (Scheme 2). p-substituted alkylarenes bearing Br (1c), t-Bu (1d), and AcO (1e) were given oxidative products 2c, 2d, and 2e in good to excellent yields (88% to 96%). When the alkyl chain was increased there is a depreciation in the formation of the product (n-butylbenzene (1f), n-octylbenzene (1g)).



Reaction was carried out in a mixture of CH₂Cl₂ and H₂O (19:1) (3 mL) using CuBr and H₂O₂

The same was observed in branched alkyl chain (isobutylbenzene (1h)). Diarylmethanes (1i and 1j) were also efficiently converted into diarylketones (2i and 2j) in quantitative yields, respectively. Furthermore, various alkylarenes bearing functional groups, such as ester (1k and 1l), sulfonyl (1m), nitro (1n), nitrile (1o), and imide (1p and 1q), provided desired products 2k_2q in high yields (76% to 99%), respectively.

CONCLUSIONS

In conclusion, we have developed a direct benzylic oxidation of alkylarenes via benzylic C-H abstraction using the oxidation of alkalimetal bromides without heavy metals. This selective oxidation proceeds under normal light to give corresponding carbonyl compounds. This method is an environmental sustainability strategy for organic synthesis as it does not require heavy metals or organic reagents under mild conditions.

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References

- For recent reviews on C-H bond activation, see: (a) Lyons, T. W and Sanford, M. S (2010) Palladium-Catalyzed Ligand-Directed C-H Functionalization Reactions. *Chem. Rev.*, 110(2): 1147–1169. (b) Beccalli, E. M.; Broggini, G.; Martinelli, M and Sottocornola, S. (2007) C-C, C-O, C-N Bond Formation on sp² Carbon by Pd(II)-Catalyzed Reactions Involving Oxidant Agents. *Chem. Rev.*, 107(11): 5318–5365. (c) Alberico, D.; Scott, M. E and Lautens, M. (2007) Aryl-Aryl Bond Formation by Transition-Metal-Catalyzed Direct Arylation. *Chem. Rev.*, 107(1):174–238. (d) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J and Baudoin, O. (2010) Functionalization of Organic Molecules by Transition-Metal-Catalyzed C(sp³)-H Activation. *Chem.;Eur. J* 16(9): 2654–2672. (e) Giri, R.; Shi, B.-F.; Engle, K. M.; Mangel, N and Yu, J.-Q. (2009) Transition metal-catalyzed C-H activation reactions: diastereoselectivity and enantioselectivity. *Chem. Soc. Rev.*, 38 (11) 3242–3272. (f) Chen, X.; Engle, K. M.; Wang, D.-H and Yu, J.-Q. *Angew.* (2009) Palladium (II)-catalyzed C-H activation/C-C cross-coupling reactions: versatility and practicality. *Chem., Int. Ed.* 48(28): 5094–5115.
- Sheldon, R. A and Kochi, J. K. (1981) *Metal Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, (b) Cainelli, G and Cardillo, G. (1984) *Chromium Oxidations in Organic Chemistry*; Springer: Berlin, (c) Hudlicky, M. (1990) *Oxidation in Organic Chemistry*; American Chemical Society: Washington, DC, (d) Recupero, M and Punta, C. (2007) Free Radical Functionalization of Organic Compounds Catalyzed by *N*-Hydroxyphthalimide. *Chem. Rev.* 107 (9): 3800–3842.
- Rangarajan, R and Eisenbraun, E. J. (1985) Chromic acid oxidation of indans and tetralins to 1-indanones and 1-tetralones using Jones and other chromium (VI) reagents. *J. Org. Chem.* 50(14): 2435–2438. (b) Pearson, A. J and Han, G. R (1985) Benzylic oxidation using tert-butyl hydroperoxide in the presence of chromium hexacarbonyl. *J. Org. Chem.* 50(15); 2791–2792. (c) Rathore, R.; Saxena, N and Chandrasekaran, S. (1986) A Convenient Method of Benzylic Oxidation with Pyridinium Chlorochromate. *Synth. Commun.* 16 (12):1493-1498. (d) Muzart, J. (1986) Chromium^{VI} complex catalyzed benzylic oxidations in the presence of tert-butyl hydroperoxide. *Tetrahedron Lett.*, 27(27): 3139–3142. (e) Muzart, J. (1987) Practical chromium^{VI} oxide-catalyzed benzylic oxidations using 70% tert-butylhydroperoxide. *Tetrahedron Lett.* 28(19); 2131–2132. (f) Choudary, B. M.; Prasad, A. D.; Bhuma, V and Swapna, V. (1992) Chromium-pillared clay as a catalyst for benzylic oxidation and oxidative deprotection of benzyl ethers and benzylamines: a simple and convenient procedure. *J. Org. Chem.* 57(22): 5841–5844. (g) Das, T. K.; Chaudhari, K.; Nandan, E.; Chandwadkar, A. J.; Sudalai, A.; Ravindranathan, T and Sivasanker, S. (1997) Cr-MCM-41-catalyzed selective oxidation of alkylarenes with TBHP. *Tetrahedron Lett.* 38(20): 3631–3634. (h) Rothenberg, G.; Wiener, H and Sasson, Y. (1998) Pyridines as bifunctional co-catalysts in the CrO₃-catalyzed oxygenation of olefins by *t*-butyl hydroperoxide. *J. Mol. Catal. A: Chem.* 136(3): 253–262.
- Gannon, S. M and Krause, J. G. (1987) Phase-Transfer Permanganate Oxidation of Unfunctionalized Benzylic Positions. *Synthesis* 10: 915–917. (b) Li, W.-S and Liu, L. K. *Synthesis* 1989, 293–295. (c) Zhao, D and Lee, D. G. (1994) Heterogeneous Permanganate Oxidations; Part 6: Selective Oxidation of Arenes. *Synthesis* 9: 915–916. (d) Shaabani, A and Lee, D. G. (2001) Solvent free permanganate oxidations. *Tetrahedron Lett.* 42(34): 5833–5836. (e) Pan, J.-F and Chen, K. (2001) A facile catalytic oxidation of activated hydrocarbons to the carbonyl functionality mediated by Mn(II) complexes. *J. Mol. Catal. A: Chem.* 176(1-2): 19–22.
- Lee, N. H.; Lee, C.-S. and Jung, D.-S. (1998) Selective oxidation of benzylic hydrocarbons to carbonyl compounds catalyzed by Mn(III) salen complexes. *Tetrahedron Lett.* 39(11):1385–1388.
- Nagano, T and Kobayashi, S. (2008) Iron Catalyst for Oxidation in Water: Surfactant-type Iron Complex-catalyzed Mild and Efficient Oxidation of Aryl Alkanes Using Aqueous TBHP as Oxidant in Water. *Chem. Lett.* 37(): 1042–1043.
- Gonzalez, M. J.; Sullivan, A. C and Wilson, J. R. H. (2003) Allylic and benzylic oxidation using cobalt(II) alkyl phosphonate modified silica. *Tetrahedron Lett.* 44(22): 4283–4286. (b) Modica, E.; Bombieri, G.; Colombo, D.; Marchini, N.; Ronchetti, F.; Scala, A and Toma, L. *Eur.* (2003) Novel Estrones by Oxidation of the Benzylic Positions of the Estrane Skeleton with *tert*-Butyl Hydroperoxide and Cobalt Acetate. *J. Org. Chem.* 15: 2964–2971. (c) Jin, C.; Zhang, L and Su, W. (2011) Direct Benzylic Oxidation with Sodium Hypochlorite Using a New Efficient Catalytic System: TEMPO/Co(OAc)₂. *Synlett* 1435–1438.

8. Murahashi, S.; Oda, Y.; Naota, T and Kuwabara, T. (1993) Ruthenium-catalyzed cytochrome P-450 type oxidation of alkanes with alkyl hydroperoxides. *Tetrahedron Lett.* 34(8): 1299–1302. (b) Nikalje, M. D and Sudalai, A. (1999) Catalytic Selective Oxidation of Alkyl Arenes to Aryl tert. Butyl Peroxides with TBHP over Ru-Exchanged Montmorillonite K10. *Tetrahedron* 55(18): 5903–5908. (c) Yi, C. S.; Kwon, K.-H and Lee, D. W. (2009) Aqueous Phase C–H Bond Oxidation Reaction of Arylalkanes Catalyzed by a Water-Soluble Cationic Ru(III) Complex [(pymox-Me₂)₂RuCl₂]⁺BF₄⁻. *Org. Lett.* 11(): 1567–1569.
9. Catino, A. J.; Nichols, J. M.; Choi, H.; Gottipamula, S and Doyle, M. P. (2005) Benzylic Oxidation Catalyzed by Dirhodium(II,III) Caprolactamate. *Org. Lett.* 7(23): 5167–5170.
10. Bonvin, Y.; Callens, E.; Larrosa, I.; Henderson, D. A.; Oldham, J.; Burton, A. J and Barrett, A. G. M. (2005) Bismuth-Catalyzed Benzylic Oxidations with *tert*-Butyl Hydroperoxide. *Org. Lett.* 7(21): 4549–4552.
11. Li, H.; Li, Z and Shi, Z. (2009) Gold-catalyzed benzylic oxidation to carbonyl compounds. *Tetrahedron* 65(9): 1856–1858.
12. Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T and Nishiyama, Y. (1995) Novel Catalysis by N-Hydroxyphthalimide in the Oxidation of Organic Substrates by Molecular Oxygen. *J. Org. Chem.*, 60(13): 3934–3935. (b) Yang, G.; Zhang, Q.; Miao, H and Tong, X.; Xu, (2005) Selective Organocatalytic Oxygenation of Hydrocarbons by Dioxxygen Using Anthraquinones and N-Hydroxyphthalimide. *J. Org. Lett.* 7(2): 263–266.
13. Mahammad, T.; Shaikh, A.; Emmanuvel, L and Sudalai, A. (2006) NaIO₄-Mediated Selective Oxidation of Alkylarenes and Benzylic Bromides/Alcohols to Carbonyl Derivatives Using Water as Solvent. *J. Org. Chem.* 71(13): 5043–5046. (b) Dohi, T.; Takenaga, N.; Goto, A.; Fujioka, H and Kita, Y. (2008) Clean and Efficient Benzylic C–H Oxidation in Water Using a Hypervalent Iodine Reagent: Activation of Polymeric Iodosobenzene with KBr in the Presence of Montmorillonite-K10. *J. Org. Chem.* 73(18): 7365–7368. (c) Ojha, L. R.; Kudugunti, S.; Maddukuri, P. P.; Kommareddy, A.; Gunna, M. R.; Dokuparthi, P.; Gottam, H. B.; Botha, K. K.; Parapati, D. R and Vinod, T. K. (2009) (1) Benzylic Carbon Oxidation by an in situ Formed *o*-Iodoxybenzoic Acid (IBX) Derivative. *Synlett* 117–121.

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