

Microwave assisted dealkylation of alkyl aryl ethers in ionic liquids

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Alkyl aryl ethers undergo selective dealkylation in 1-butyl pyridinium bromide and 1-butyl-3-methyl imidazolium bromide ionic liquids under microwave irradiation to give the corresponding phenols in high yields. The ionic liquids serve the dual purpose of solvent as well as reagent and allow easy isolation of products.

Keywords: alkyl aryl ethers, ionic liquids, microwave irradiation, dealkylation

A wide variety of reagents have been developed for the dealkylation of alkyl aryl ethers. Some of the ether-cleaving agents involve the use of Lewis acids such as BBr_3 ,¹ AlI_3 , AlCl_3 ,² bronsted acids like HI, HBr, py^+HCl , py^+HBr ,³ strong bases such as alkaline hydroxides⁴ and alkali metals⁵ and other reagents like iodotrimethylsilane,⁶ lithium diphenylphosphide⁷ and KF-alumina.⁸ The use of these reagents requires harsh reaction conditions, which usually brings about structural and stereochemical changes in the substrate and also lead to the formation of unwanted by-products. A great deal of inconvenience is also connected to their handling, removal, and work up to isolate pure products.

Microwave dielectric heating has become an important technique in organic synthesis as it offers the advantages of enhanced reaction rates, high yields, improved selectivity and reduction of thermal degradative products.^{9,10} Air- and moisture-stable room temperature ionic liquids have emerged as novel, environmentally friendly and recyclable alternatives to dipolar aprotic solvents in organic synthesis.¹¹ While much focus has been given to imidazolium based ionic liquids specially [bmim][Br], [bmim][BF₄] and [bmim][PF₆],^{12–17} ionic liquids based on other cations such as pyridinium and ammonium have found slightly less use in organic synthesis. Although pyridinium chloroaluminate ionic liquids have been used to carry out cationic and metal catalysed oligomerisation of alkenes,¹⁸ little has been explored with other pyridine-based ionic liquids.

Dealkylation reactions under microwave irradiation have been reported under solvent free conditions using pyridine hydrochloride¹⁹ and also using potassium *tert*-butoxide in presence of crown ether.²⁰ Lewis acidic ionic liquids, such as 1-ethyl-3-methylimidazolium halogenoaluminates

have been shown to be suitable solvents for the acylative cleavage of cyclic and acyclic ethers.²¹ Further, 3-methylimidazolium bromohydrogenates formed from one mole of 1-methylimidazole and two moles of anhydrous HBr have also been found to cleave ethers efficiently.²² However, there are no reports of a dealkylation reaction in a non-protonated pyridinium and imidazolium based ionic liquid. Herein we report a simple, quick, inexpensive and highly efficient method for chemoselective dealkylation of alkyl aryl ethers in ionic liquids under microwave irradiation.

The microwave irradiation of vanillin (entry 3, Table 1) in 1-butylpyridinium bromide [bpy][Br] for two minutes gave 3,4-dihydroxy benzaldehyde in 97% yield. The temperature of the reaction mixture during microwave irradiation was found to be 100–110°C. In a similar way, a variety of other ethers underwent smooth dealkylation under these reaction conditions to give the corresponding phenolic compounds in excellent yields (Table 1). The yield of 3,4-dihydroxy benzaldehyde was found to be 15% only when the reaction was carried out by heating vanillin with [bpy][Br] in an oil bath at 150°C for 8 hrs. This indicated that dealkylation took place at a lower temperature under microwave irradiation than under conventional heating and that the ionic liquids coupled with the microwave energy in an efficient manner and transferred energy rapidly by ionic conduction. Further, addition of *tert*-butyl hydroperoxide completely quenched the above reaction and no product was obtained even after 12 h. This suggested the reaction to be initiated by attack of the bromine radical generated during the reaction on the alkyl group of the ether. Further, vanillin, which possesses a 4-OH group, was found to undergo dealkylation faster than isovanillin having a 3-OH group. The microwave irradiation

Table 1 Dealkylation of alkyl aryl ethers in ionic liquids under microwave irradiation^a

Entry	Ether (1)	Product (3) ^b	Time/min	Yield ^c /%	M.p./(Lit. m.p.)/°C
1	Anisole	Phenol	4	80 (78)	43 (42) ²⁴
2	<i>p</i> -Anisaldehyde	4-Hydroxybenzaldehyde	3	90 (86)	113 (115–116) ²⁴
3	Vanillin	3,4-Dihydroxybenzaldehyde	2	97 (90)	153 (153–154) ²⁴
4	Isovanillin	3,4-Dihydroxybenzaldehyde	3	96 (90)	–
5	Veratraldehyde	3,4-Dihydroxybenzaldehyde	4	89 (85)	–
6	<i>p</i> -Anisic acid	4-Hydroxy benzoic acid	3	82 (76)	215 (213–214) ²⁴
7	4-Methoxy benzyl alcohol	4-Hydroxy benzyl alcohol	3	85 (78)	123 (124–125) ²⁴
8	4-Nitro anisole	4-Nitro phenol	4	80(76)	112(113–114) ²⁴
9	3-Nitro anisole	3-Nitro phenol	4	75(71)	96(97–98) ²⁴
10	Hydroquinone monomethyl ether	Hydroquinol	4	90 (88)	171 (172) ²⁴
11	4'-Methoxyphenyl acetonitrile	4'-Hydroxyphenyl acetonitrile	5	80 (77)	69(69–71) ²⁵
12	4-Methoxy stilbene	4-Hydroxy stilbene	5	82 (80)	187(188) ²⁶
13	Benzyl phenyl ether	Phenol	3	100(95)	–
14	4-Methoxy flavone	4-Hydroxy flavone	4	87 (82)	267–268(269) ²⁷
15	7-Methoxy isoflavone	7-Hydroxy isoflavone	5	81(78)	214(214–215) ²⁴
16	5,7,4'-Trimethoxy kaempferol	5,7,4'-Trihydroxy kaempferol	6	78(72)	276(277–278) ²⁴

^aReaction conditions: Ether (1.0 mmol), [bpy][Br] (1.0 mmol), 320 W. ^bAll products were characterised by NMR, IR and EI-MS spectroscopic methods. ^cYields are based on HPLC-analysis (μ -bondapack column, acetonitrile: water = 50: 50 v/v, flow rate = 0.5 ml/min, monitored at 350 nm) based on substrate; numbers in parenthesis denote isolated yields.

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of vanillin in [bmim][Br] for three minutes gave 3,4-dihydroxy benzaldehyde in 80% yield. Likewise for other products also, it was found that dealkylation was more facile in [bpy][Br] than in [bmim][Br]. The ease of dealkylation of various alkyl ethers was found to follow the order benzyl > methyl > ethyl. However, no dealkylation was observed when the reaction was carried out in [bpy][BF₄] and [bmim][BF₄] under same reaction conditions, indicating thereby that both the cation and anion played an important role in this transformation. A high level of chemoselectivity was observed in the dealkylation of tri- and tetra-methoxy flavones. 5,7, 4'-trimethoxy kaempferol (entry 16, Table 1) underwent selective dealkylation at 4' to give 5,7-dimethoxy kaempferol in 72% yield after 3 min. On increasing the irradiation time to 6 min and using an excess of [bpy][Br] (3.0mmol), dealkylation was found to occur at the 5 and 7 positions. In the dealkylation of 3,4-dimethoxybenzaldehyde, the 4-OCH₃ group underwent faster dealkylation to give first vanillin and only on extending the reaction time to 4 minutes did complete dealkylation occur to yield 3,4-dihydroxybenzaldehyde.

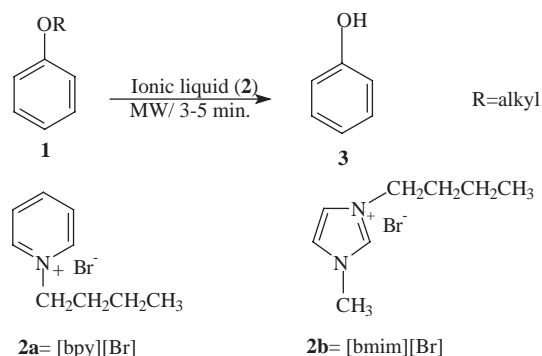
In conclusion, the present procedure provides a facile and efficient method for chemoselective dealkylation of alkyl aryl ethers in pyridinium- and imidazolium-based ionic liquids assisted by microwave irradiation. Unlike other methods, this method avoids the use of strong acidic as well as strong basic conditions for carrying out dealkylation, thereby making the method very general and applicable to substrates with acid and base sensitive groups along with the ether functionality in the molecule. Furthermore, simple experimental and work-up procedure, high yield of products in very short time and ease of handling of ionic liquids as compared to other dealkylating agents makes this procedure a useful, cost-effective and attractive alternative to conventional methods in synthetic organic chemistry.

Experimental

The ionic liquids [bpy][Br], [bpy][BF₄], [bmim][Br] and [bmim][BF₄] were synthesised by the literature procedures and were characterised by IR and NMR spectroscopic data.²³ A mixture of ionic liquid **2a** or **2b** (1.0 mmol) and alkyl aryl ether (1.0 mmol) was taken in a pyrex bottle and irradiated in an unmodified microwave oven at 320 W for an appropriate time (3–5 minutes) at an interval of 30 seconds (Scheme 1). After completion of reaction, the reaction mixture was cooled to room temperature, extracted with ethyl acetate (4×3 ml) and the extract dried over anhydrous sodium sulfate. The extract was concentrated under reduced pressure and the products were purified by column chromatography over silica gel and characterised by comparison with authentic sample (m.p., HPLC) and other spectroscopic data such as IR, ¹HNMR, EI-MS. The yields of the products are given in Table 1.

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Scheme 1 Microwave assisted dealkylation of alkyl aryl ethers in ionic liquids.

References

- 1 T. Taub, N.N. Girotra, R.D. Hoffsommer, C.H. Kuo, H.L. Slates, S. Weber and N.L. Wandler, *Tetrahedron*, 1968, **24**, 2443.
- 2 R.L. Burwell, *Chem. Rev.*, 1954, **45**, 54.
- 3 J.C. Sheehan, W.F. Erman and P.A. Cruickshank, *J. Am. Chem. Soc.*, 1957, **79**, 147.
- 4 J.H. Chesterfield, J.F.W. McOmie and M.S. Tute, *J. Chem. Soc.*, 1960, 4590.
- 5 A. Maercker, *Angew. Chem. Int. Ed. Engl.*, 1987, **26**, 972.
- 6 N. Sato and Y. Kato, *J. Heterocyclic Chem.*, 1986, **23**, 1677.
- 7 V. Giller and C. Andres, *Accross Organ. Acta*, 1995, **1**, 40.
- 8 A.S. Radhakrishna, K.R.K. Prasad, S.K. Suri, K. Sivaprakash and B.B. Sing, *Synth. Commun.*, 1991, **21**, 379.
- 9 S. Caddick, *Tetrahedron*, 1995, **51**, 10403.
- 10 P. Lidstrom, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, 2001, **57**, 9225.
- 11 P. Wasserschied and W. Keim, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 3772.
- 12 K.A. Srinivas, A. Kumar and S.M.S. Chauhan, *Chem. Commun.*, 2002, 2456.
- 13 T. Welton, *Chem. Rev.*, 1999, **99**, 2071
- 14 S.M.S. Chauhan, N. Jain, A. Kumar and K.A. Srinivas, *Synth. Comm.*, 2003, **33**, 3601.
- 15 S.M.S. Chauhan, A. Kumar and K.A. Srinivas, *Chem. Commun.*, 2003, 2348.
- 16 D.W. Kim, C.E. Song and D.-Y. Chi, *J. Org. Chem.*, 2003, **68**, 4281.
- 17 C.J. Boxwell, P.J. Dyson, D.J. Ellis and T. Welton, *J. Am. Chem. Soc.*, 2002, **124**, 9334.
- 18 J.D. Holbrey and K.R. Seddon, *Clean Prod. and Process.*, 1999, 223.
- 19 P.P. Kulkarni, A.J. Kadam, R.B. Mane, U.V. Desai and P.P. Wadgaonkar, *J. Chem. Res.(S)*, 1999, 394.
- 20 A. Oussaid, L.N. Thach and A. Loupy, *Tetrahedron. Lett.*, 1997, **38**, 2451.
- 21 L. Green, I. Hemeon and R.D. Singer, *Tetrahedron. Lett.*, 2000, **41**, 1343.
- 22 G. Driver and K.E. Johnson, *Green Chem.*, 2003, **5**, 2, 163.
- 23 R.S. Varma and V.V. Namboodiri, *Chem. Commun.*, 2001, 643.
- 24 *Dictionary of organic compounds*, 6th edn: Chapman and Hall: London, 1982.
- 25 M.A. Schwartz, M. Zoda, B. Vishnuvajjala and I. Mami, *J. Org. Chem.*, 1976, **41**, 14, 2502.
- 26 R.B. Chhor, K.A. Singh, B. Nosse and V.K. Tandon, *Synth. Commun.*, 2003, **33**, 14, 2519.
- 27 G.N. Dorofeenko, *Z. Organich. Khi.*, 1976, **12**, 432.