Demethylation of aryl methyl ethers using pyridinium *p*-toluenesulfonate under microwave irradiation

Mandeep S. Lamba[a] and Jagdish K. Makrandi[b]

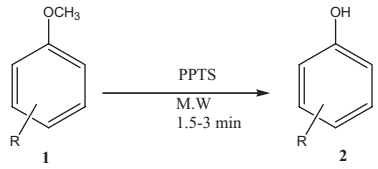
[a]*Ordnance Factory Chanda, Ministry of Defence, 442 501 India*

[b]*Department of Chemistry, M.D. University, Rohtak, India*

Aryl methyl ethers are deprotected in high yields using pyridinium *p*-toluenesulfonate under microwave irradiation and solvent-free conditions.

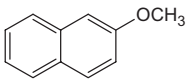
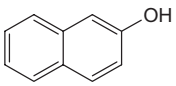
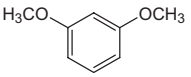
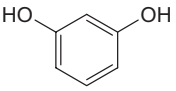
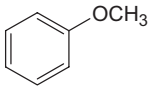
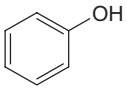
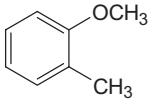
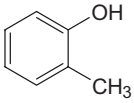
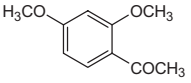
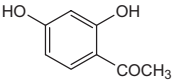
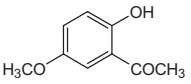
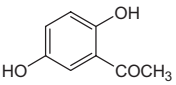
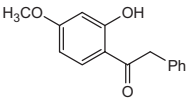
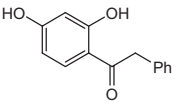
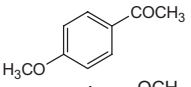
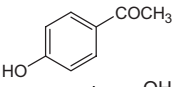
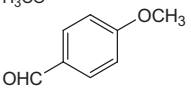
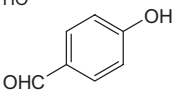
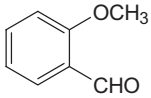
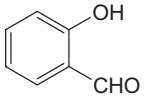
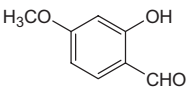
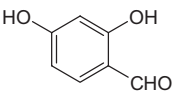
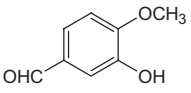
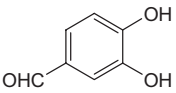
Keywords: aryl methyl ethers, demethylation, pyridinium *p*-toluenesulfonate, microwave irradiation

Protection of phenolic groups as methyl ethers during a reaction is considered to be an important step[1] to avoid the side reactions or rearrangements which may otherwise take place. Deprotection then follows to get the free hydroxyl groups. Large numbers of reagents have been used for demethylation under various conditions which include Lewis acids such as BBr_3,[2] $BeCl_2$,[3] $AlCl_3$,[4] pyridine hydrobromide perbromide,[5]



Scheme 1

Table 1 Microwave assisted demethylation of aryl methyl ethers using PPTS

Entry	Reactant	Product	Time/min	Yield/%	M.p./°C	(Lit. M.p.[17])/°C	B.p.(Lit B.p.[17])/°C
1			1.5	80	118–120	(120–121)	–
2			1.5	75	108–109	(109–110)	–
3			2.0	70	–	–	178–179 (180–181)
4			2.0	70	–	–	187–189 (190–192)
5			2.0	80	141–142	(143–145)	–
6			1.5	85	200–202	(204–206)	–
7			2.0	80	114	(115)	–
8			3.0	70	104–105	(106–108)	–
9			1.5	70	115–116	(117–119)	–
10			3.0	70	–	–	195–196 (197)
11			2.0	80	134–135	(135–37)	–
12			1.5	75	152–153	(155–157)	–

* Correspondent. E-mail: mandeep_lamba2001@yahoo.co.in

trimethylsilyliodide,[6] L-selectride,[7] KF-alumina,[8] pyridine hydrochloride[9,10] and HCl in the presence of surfactant.[11] These reagents require drastic conditions for demethylation of aryl methyl ethers and sometimes yields are also poor because of side reactions, including rearrangement, taking place along with demethylation.

In continuation of our work on the synthesis of naturally occurring polyphenolics, we were in search of a reagent which could be used for demethylation under milder conditions. Here we report the use of pyridinium *p*-toluene sulfonate (PPTS), a compound which is a weaker acid than acetic acid[12] and can be easily prepared[13] (Scheme 1). We report that it is a highly efficient demethylating agent under microwave conditions in solvent free conditions. PPTS has been used for the cleavage of some acetals,[14] cleavage of silyl ethers[15] and for various deprotections.[16] Using this reagent, demethylation of various aryl methyl ethers (Table 1) including methoxy substituted benzaldehydes and acetophenones has been carried out successfully. Demethylation takes place in a short time (1.5–3 min.).

This reagent could also be used as demethylating agent under conventional thermal conditions but it requires a higher temperature (200°C) and a longer reaction time, also yields are lower (60%).

Experimental

The reactions were carried out in a stoppered round bottom flask in a domestic microwave oven (Samsung, output energy 900W, frequency 2450 MHz, with temperature control arrangement, model No. CE118KF) using 30% power for all the experiments and maintaining oven temperature at 100°C.

General procedure for demethylation of methyl aryl ethers

A mixture of the aryl methyl ether (0.01 mol) and pyridinium *p*-toluenesulfonate (0.03 mol) [(0.06 mol) for entry 2] was placed in a 20 ml round bottom flask fitted with a stopper and subjected to microwave irradiation at 270W for various time intervals. Completion of the reaction was checked by TLC. After completion of the reaction, the reaction mixture was cooled, added to ice cold water and extracted with diethyl ether (3 × 20 ml). The ethereal layer was dried over anhydrous sodium sulfate and the solvent was removed by distillation to get the product.

In conclusion, the present method appears to be quick and highly efficient for demethylation of aryl methyl ethers under solvent-free conditions using PPTS, an easily obtainable reagent.

Received 28 August 2007; accepted 4 October 2007
Paper 07/4819 doi: 10.3184/030823407X255551

References

1 T.W. Green and P.G.M. Wutz, *Protective groups in organic synthesis*, 2nd Ed., John Wiley: New York, 1991.
2 F.L. Benton and T.E. Dillon, *J. Am. Chem. Soc.,* 1942**, 64**, 1128.
3 W. Gerrand and M.F. Lappert, *J. Chem. Soc.,* 1952, 1486.
4 R.L. Burwell and L. Robert, *Chem. Rev.,*1954, **54**, 615.
5 A.S. Ijaj, M. Alam and B. Ahmad, *Indian J. Chem.,* 1994, **33B**, 288.
6 N. Sato and Y. Kato, *J. Heterocycl. Chem.,* 1986**, 23,** 1677.
7 U. Dilger, B. Franz, H. Rottele and R. Herges, *J. Prakt. Chem.,* 1998, **340**, 468.
8 A.S. Radhakrishna, K.R.K. Prasad, S.K. Suri and B.B. Singh, *Synth. Commun.,* 1991**, 21**, 379.
9 F.W. Bachelor, A.A. Loman and L.R. Snowdon, *Can. J. Chem.,* 1970*,* **48**, 1554.
10 J. Branka, *J. Chem. Res(S).***,** 1989, 284.
11 P.P. Kulkarni, A.J. Dadam, R.B. Mane, U.V. Desai and P.P. Wadgaonkar, *J. Chem. Res(S).,* 1999, 394.
12 N. Miyashita, A. Yoshikoshi and P.A. Griew, *J. Org. Chem.,* 1977, **42**, 3772.
13 A.I. Vogel, *Textbook of practical organic chemistry,* 5th Ed.; ELBS: London, 1967.
14 R. Sterzycki, *Synthesis,* 1979, 724.
15 C. Prakash, S. Seleh and I.A. Blair, *Tetrahedron. Lett.*, 1994, **35,** 7565.
16 J.H. Zaidi, A.H. Faug and N. Ahmed, *Tetrahedron. Lett.,* 1998, **39,** 4137**.**
17 *Dictionary of Organic compounds*, 4th Ed.; I. Heilbron, A.H. Cook, H.M. Bunbury and D.H. Hey, Eds.; Oxford University Press, New York, 1956.