

Demethylation of Methyl Aryl Ethers using Pyridine Hydrochloride in Solvent-free Conditions under Microwave Irradiation†

P. P. Kulkarni,^a A. J. Kadam,^a R. B. Mane,^a Uday V. Desai^{*a} and P. P. Wadgaonkar^b

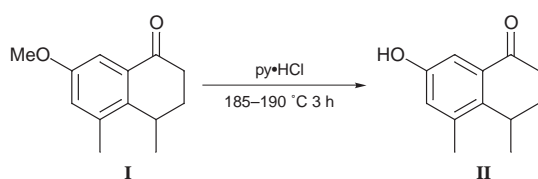
^aDepartment of Chemistry, Shivaji University, Kolhapur-416004, Maharashtra, India

^bNational Chemical Laboratory, Pune-8, India

Methyl aryl ethers are deprotected in high yields using pyridine hydrochloride in the absence of solvent under microwave irradiation

Ethers are the most useful protective groups in synthetic organic chemistry.¹ Methylation of phenolic hydroxy moieties is considered to be the most effective protection methodology owing to its high stability under a variety of reaction conditions and easy regeneration *via* demethylation. There are several reagents for the deprotection of methyl aryl ethers. Some of the classical reagents developed for this purpose include Lewis acids such as BBr₃,^{2a} AlI₃,^{2a} BeCl₂,^{2c}, AlCl₃,^{2d} AlH₂Cl,^{2e} Py⁺HBr₃^{-2f} as well as trimethylsilyliodide,^{2g} L-selectride,^{2h} lithium diphenylphosphide,²ⁱ KF-alumina,^{2j} pyridine hydrochloride^{2k} and CeTab with HCl.^{2l} Most of these reagents are expensive and require the use of solvents. Their use has been reviewed earlier,³ and amongst these, pyridine hydrochloride is the most favourable owing to its low cost, ready availability and the fact that no solvent is required.

Methyl aryl ethers are generally difficult to demethylate under mild reaction conditions and the drastic reaction conditions required usually brings about structural and stereochemical changes along with the formation of by-products. We came across this difficulty during demethylation of 4,5-dimethyl-7-methoxy-1-tetralone **I** (Scheme 1) an important intermediate in the synthesis of cacalol. The demethylation of **I** was achieved in 3 h using pyridine hydrochloride,^{4,2k} at 180–190 °C. During this, apart from the desired phenolic tetralone **II** several by-products were obtained which caused difficulties in the isolation of pure tetralone.



Scheme 1

Microwave dielectric heating has become an important technique in organic syntheses and many classical organic reactions are now carried out using it.⁵ This led us to attempt the demethylation of tetralone **I** with pyridine hydrochloride under microwave irradiation and the successful demethylation prompted us to undertake the demethylation of various methyl aryl ethers under similar conditions.

Various methyl aryl ethers were deprotected (Table 1) by heating a mixture of a methyl aryl ether and pyridine hydrochloride in a stoppered round bottom flask, under

Table 1 MW assisted demethylation of methyl aryl ethers

Entry	R	MW heating time/min	Yield ^a (%)	Mp/°C	Bp/°C	Lit./°C
1	H	14	87	—	178	182
2	<i>o</i> -Me	14	82	—	187	191
3	<i>m</i> -Me	14	82	—	196	202
4	<i>p</i> -Me	14	81	—	197	202
5	<i>p</i> -CHO	16	78	113	—	116
6	<i>p</i> -MeCO	16	74	106	—	109–111
7	<i>p</i> -Br	16	78	—	232	235
8	<i>p</i> -Cl	16	82	—	214	217
9	<i>o</i> -NO ₂	16	65	43	—	45
10	β -Naphthyl	14	95	118	—	122
11	4,5-Dimethyl-7-hydroxy-1-tetralone	16	76	110	—	—

^aYields refer to pure isolated products.

microwave irradiation (215 W) for 2 min. After each 2 min irradiation, the reaction mixture was cooled to room temperature and reirradiated. Demethylation in most cases was complete within 16 min. (2 × 8 pulses).

In conclusion, we have presented here a simple, quick and highly efficient method for demethylation of methyl aryl ethers using pyridine hydrochloride, an easily available reagent, in absence of solvent using microwave irradiation.

Experimental

General.—Microwave irradiation was carried out using a commercial microwave oven (BPL-Sanyo, BMO-700 T) operating at variable frequency and the products obtained were analyzed by IR and NMR spectroscopy.

Methyl aryl ethers and pyridine hydrochloride were prepared by standard methods.⁶

Microwave Assisted Demethylation of Methyl Aryl Ethers.—A mixture of methyl aryl ether (0.01 mol) and pyridine hydrochloride (0.05 mol) were placed in a stoppered round bottom flask and subjected to microwave irradiation at 215 W for various time intervals. After complete conversion the reaction mixture was decomposed using ice-water and extracted with diethyl ether. The ether extract was repeatedly washed with water, dried over anhydrous sodium sulfate and the ether removed to obtain the product.

Received, 16th February 1999; Accepted, 12th March 1999
Paper E/9/01278H

References

- 1 T. W. Green and P. G. M. Wutz, *Protective Groups in Organic Synthesis*, John Wiley, New York, 2nd edn., 1991.

* To receive any correspondence.

† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

- 2 (a) J. Ryohel, U. Hiroshi and K. Shiro, *Polym. Bull. (Berlin)*, 1997, **38**, 273; (b) S. Ichiro and T. Koho, *Jpn. Kokai Tokkyo Koho.*, JP-09-59202 (97-59202); *Chem. Abstr.*, 1997, **126**, 277; (c) H. Sharghi and F. Tamaddon, *Tetrahedron*, 1996, **52**, 13623; (d) R. L. Burwell, Jr., *Chem. Rev.*, 1954, **54**, 615; (e) Y. Takehiko, J. Hissataka, M. Kenji and T. Massahi, *J. Chem. Res. (S)*, 1996, 314; (f) A. S. Ijaz, M. Alam and B. Ahmad, *Indian J. Chem. Sect. B*, 1994, **33**, 288; (g) N. Sato and Y. Kato, *J. Heterocycl. Chem.*, 1986, **23**, 1677; (h) D. Ulrich, F. Baerbel, R. Herbert, S. Gerhard and H. Rainer, *J. Prakt. Chem.*, 1998, **340**, 468; (i) V. Giller and C. Andres, *Across Org. Acta*, 1995, **1**, 40; (j) A. S. Radhakrishna, K. R. K. Prasad, S. K. Suri, K. Sivaprakash and B. B. Sing, *Synth. Commun.*, 1991, **21**, 379; (k) V. Vishwanath and G. S. K. Rao, *J. Chem. Soc., Perkin Trans. I*, 1974, **21**, 450; (l) J. Branko, *J. Chem. Res. (S)*, 1989, 284.
- 3 (a) Y. Ming, J. Yaozhong and M. Qiqiao, *Huaxue Shizi*, 1996, **18**, 151; *Chem. Abstr.*, 1996, **125**, 328150c; (b) M. V. Bhat and S. U. Kulkarni, *Synthesis*, 1983, 249.
- 4 H. Wynberg, E. V. Echten and W. H. Ten, *Eur. Pat. Appl.*, 1991, EP 431, 561; *Chem. Abstr.*, 1991, **115**, 135698.
- 5 (a) R. A. Abramovich, *Org. Prep. Proceed. Int.*, 1991, **23**, 883; (b) S. Caddick, *Tetrahedron*, 1995, **51**, 10403; (c) S. A. Galena, *Chem. Soc. Rev.*, 1997, **26**, 233; (d) K. M. Luk, *Proceeding of 1997 Asia Pacific MW Conference*, 1998, **Vol. I**, 492.
- 6 A. I. Vogel, *Textbook of Practical Organic Chemistry*, ELBS, 5th edn., 1967.