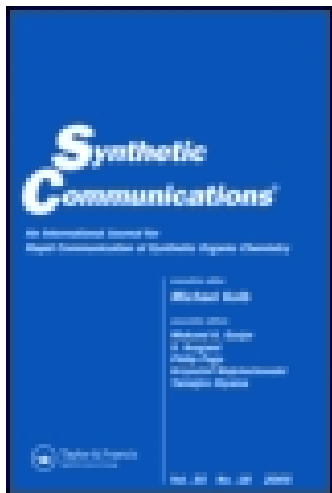


This article was downloaded by: [University of Chicago Library]  
On: 11 November 2014, At: 07:05  
Publisher: Taylor & Francis  
Informa Ltd Registered in England and Wales Registered Number: 1072954  
Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH,  
UK



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

### Cleavage or Acetyl-de-alkylation of 4-Methoxybenzyl (MPM) Ethers Using Acetic Acid

Kevin J. Hodgetts<sup>a</sup> & Timothy W. Wallace<sup>a</sup>

<sup>a</sup> Department of Chemistry and Applied Chemistry ,  
University of Salford , Salford, M5 4WT, U.K.

Published online: 23 Sep 2006.

To cite this article: Kevin J. Hodgetts & Timothy W. Wallace (1994) Cleavage or Acetyl-de-alkylation of 4-Methoxybenzyl (MPM) Ethers Using Acetic Acid, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:8, 1151-1155, DOI: [10.1080/00397919408011711](https://doi.org/10.1080/00397919408011711)

To link to this article: <http://dx.doi.org/10.1080/00397919408011711>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages,

and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

**CLEAVAGE OR ACETYL-DE-ALKYLATION OF 4-METHOXYBENZYL  
(MPM) ETHERS USING ACETIC ACID**

Kevin J. Hodgetts and Timothy W. Wallace\*<sup>1</sup>

*Department of Chemistry and Applied Chemistry, University of Salford,  
Salford M5 4WT, U.K.*

**Abstract:** Aryl (4-methoxyphenyl)methyl (MPM) ethers are cleaved by heating with acetic acid for a few hours at 90 °C, producing the corresponding phenols and (4-methoxyphenyl)methyl acetate. Under the same conditions alkyl MPM ethers are transformed directly into the corresponding alkyl acetates.

Methoxy-substituted benzyl ethers are of proven utility as protected hydroxyl compounds, strategic advantages of such systems being the possibility of selective oxidative removal in the presence of other benzylic groups, and their retention during the hydrogenolysis of unsubstituted benzyl groups.<sup>1,2</sup> Use of the (4-methoxyphenyl)methyl (MPM) moiety is widespread, and it is commonly cleaved with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in wet dichloromethane.<sup>3</sup> However, this deprotection protocol is quite expensive, and isolation of the desired

---

\* To whom correspondence should be addressed



TABLE 1 REACTIONS OF SUBSTITUTED BENZYL ETHERS IN ACETIC ACID<sup>a</sup>

	R	X	Y	Z	
1	MPM	CO <sub>2</sub> Me	H	H	2
4	DMPM	CO <sub>2</sub> Me	H	H	
6	CH <sub>2</sub> Ph	CO <sub>2</sub> Me	H	H	
7	MPM	Ac	H	AcO	8
9	MPM	H	CHO	H	10

ENTRY	SUBSTRATE	TIME (h)	PRODUCTS	YIELD (%) <sup>b</sup>
1	1	4	2	96
2	4	4	2	95
3	6	24	— <sup>c</sup>	—
4	7	16	8	91
5	9	24	10	88
6	11	72	12	>90 <sup>d</sup>
7	11	24–48	11, 12, 13	— <sup>e</sup>
8	14	24	15	93
9	16	72	17	89
10	18	4	— <sup>f</sup>	—

a The ethers (1 mmol) in acetic acid (10 ml) were heated at 90 °C.

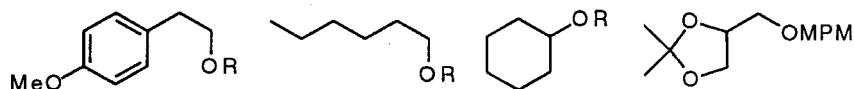
b Yields refer to isolated, chromatographically homogeneous material, except for entry 6. Other products 3 (entries 1, 4–9) and 5 (entry 2).

c The starting material 6 was recovered intact.

d Estimated by <sup>1</sup>H n.m.r. spectroscopy. The esters 3 and 12 were inseparable by t.l.c.

e Product distribution varied with reaction time, as judged by <sup>1</sup>H n.m.r. spectroscopy.

f The acetal group was no longer detectable by <sup>1</sup>H n.m.r. spectroscopy.



11 R = MPM

12 R = Ac

13 R = H

14 R = MPM

15 R = Ac

16 R = MPM

17 R = Ac

18

The cleavage of MPM ethers with acetic acid thus offers an economical alternative to the use of DDQ or other reagents. It is especially effective in the aryl series, and in the alkyl series induces a potentially useful direct route to the derived acetate.

### Experimental

Compounds **1**,<sup>7</sup> **3**,<sup>8</sup> **4**,<sup>7</sup> **5**,<sup>9</sup> **6**,<sup>10</sup> **12**,<sup>11</sup> and **18**<sup>12</sup> have been described, and **2**, **8**, **10**, **13**, **15**, and **17** are commercially available. The ethers **7**, **9**, **11**, **14**, and **16** were prepared from the corresponding alkanols using the conventional procedure,<sup>3</sup> and gave satisfactory spectroscopic data. Chromatography was carried out on silica gel (analytical on Camlab Polygram SIL G/UV<sub>254</sub> plates; preparative on Merck 9385).

**Procedure for cleaving MPM ethers with acetic acid:** A stirred solution of the MPM ether in acetic acid (10 ml/mmol) was heated at 90 °C for the time indicated in Table 1. The bulk of the acetic acid was then removed by rotary evaporation, and the residue partitioned between diethyl ether and water. The water layer was extracted with two more portions of ether, and the combined ethereal extract washed with saturated aqueous sodium chloride solution and dried over anhydrous MgSO<sub>4</sub>. The ether was removed by rotary evaporation, and the residue purified by flash chromatography over silica gel, eluting with a suitable mixture of petroleum (b.p. 40–60°) and ethyl acetate. The isolated product was characterised by comparison of its spectroscopic and t.l.c. properties with those of an authentic sample or published data. The by-product **3** had  $\nu_{\max}$  (neat) 1739 cm<sup>-1</sup>;  $\delta$  (300 MHz) 7.27 (1 H, d, *J* 8.6 Hz, ArH), 6.86 (1 H, d, *J* 8.6 Hz, ArH), 5.01 (2 H, s, OCH<sub>2</sub>Ar), 3.77 (3 H, s, OCH<sub>3</sub>), 2.05 (3 H, s, COCH<sub>3</sub>); *R*<sub>f</sub> 0.50 (petroleum/ethyl acetate 4:1).

**Acknowledgements.** We thank the SERC and Glaxo Group Research, Ware, for a CASE award, and Dr. Chris Wallis (Glaxo) for valuable discussions.

## References and Notes

- 1 Nakajima, N.; Abe, R.; Yonemitsu, O. *Chem. Pharm. Bull.* **1988**, *36*, 4244.
- 2 Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; pp. 53–56.
- 3 Horita, K.; Yoshioka, T.; Tanaka, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1986**, *42*, 3021, and references cited therein.
- 4 Hodgetts, K.J.; Wallace, T.W., unpublished observations.
- 5 An aryl MPM ether has been cleaved using stronger (trifluoroacetic) acid (White, J.D.; Amedio, J.C. *J. Org. Chem.* **1989**, *54*, 736). MPM ethers can also be cleaved with dimethylboron bromide (Hébert, N.; Beck, A.; Lennox, R.B.; Just, G. *J. Org. Chem.* **1992**, *57*, 1777). Acetyl-de-alkylation of ethers has also been effected using acetic anhydride/FeCl<sub>3</sub> (Ganem, B.; Small, V.R. *J. Org. Chem.* **1974**, *39*, 3728) and acetyl bromide/SnBr<sub>2</sub> (Oriyama, T.; Kimura, M.; Oda, M.; Koga, G. *Synlett* **1993**, 437).
- 6 The acetylation of benzyl alcohol under similar conditions (HOAc, reflux, 24 h) has been described; Kano, K.; Anselme, J.-P. *Tetrahedron* **1992**, *48*, 10075.
- 7 Saengchantara, S.T.; Wallace, T.W. *Tetrahedron* **1990**, *46*, 6553.
- 8 Belli, A.; Giordano, C.; Citterio, A. *Synthesis* **1980**, 477.
- 9 Lundquist, K.; Olsson, T. *Acta Chem. Scand. (B)* **1977**, *31*, 788.
- 10 Nagao, Y.; Miyusaka, T.; Hagiwara, Y. *J. Chem. Soc., Perkin Trans. I* **1984**, 183.
- 11 Taylor, R.; Smith, G.G.; Wetzel, W.H. *J. Am. Chem. Soc.* **1962**, *84*, 4817.
- 12 Horita, K.; Nagato, S.; Oikawa, Y.; Yonemitsu, O. *Chem. Pharm. Bull.* **1989**, *37*, 1705.

(Received in the UK 31 August 1993)