Pergamon

Tetrahedron Letters 39 (1998) 1799–1802

TETRAHEDRON LETTERS

Benzylation of Alcohols and Phenols with *N*-(4-methoxybenzyl)-*o*-benzenedisulfonimide

Per H.J. Carlsen

Department of Organic Chemistry, Norwegian University of Science and Technology

N-7034 Trondheim, Norway.

Received 3 October 1997; revised 6 January 1998; accepted 9 January 1998

Abstract. *N*-(4-methoxybenzyl)-*o*-benzene disulfonimide was prepared from *o*-benzenedisulfonyl chloride and 4-methoxybenzylamine in dichloromethane. Reaction of this compound with alcohols or phenols undere basic conditions gave the corresponding 4-methoxybenzyl ethers in good yields. Primary alkylamines were converted to the corresponding alcohols by treating the benzenedisulfonimido derivative with aqueous KOH in DMF solution. © 1998 Elsevier Science Ltd. All rights reserved.

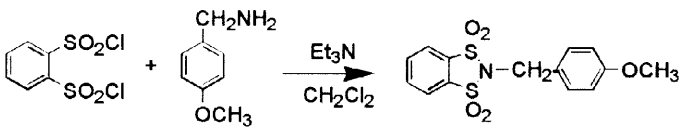
The 4-methoxybenzyl group is used for the protection of alcohols[1], phenols[2] and thiols[3]. Deprotection of the corresponding benzyl ethers may be readily accomplished under mild oxidative conditions with, *e.g.*, ceric ammonium sulfate (CAN) in acetonitrile[4] or with DDQ in dichloromethane[5]. We report here a new method for the protection of alcohols and phenols as the corresponding 4-methoxybenzyl ethers by the reaction with the new alkylation reagent, *N*-(4-methoxybenzyl)-*o*-benzenedisulfonimide, **1**.

The NH_2-group in the readily available 4-methoxybenzylamine, **2**, was transformed from a poor into a good leaving group by conversion to the corresponding *N*-benzylbenzene-sulfonimide. This is a variation on earlier reports on disulfonated amines, $(ArSO_2)_2NR$, which were found to undergo ready nucleophilic displacement with a number of nucleophiles with a high degree of inversion of stereochemistry[6]. The preparation of these disulfonated amines were in general associated with

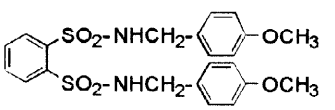
0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)00091-4

difficulties. However, we have found that the corresponding benzenesulfonimides were readily prepared. The cyclic structure of the disulfonimide moiety in **1** has also been argued to make it a better leaving group[7] compared to the non-cyclic $(ArSO_2)_2N$-group.

Pure *N*-(4-methoxybenzyl)-*o*-benzenedisulfonimide, **1**, was readily obtained by reacting *o*-benzenedisulfonyl chloride, **3**, with 4-methoxybenzylamine, **2**, in CH_2Cl_2 in the presence of Et_3N. The yield was 83 % after recrystallization from hexane/CH_2Cl_2[8]. The *o*-benzenedisulfonyl chloride was obtained in two steps from the readily available dipotassium salt of *o*-benzenedisulfonic acid[9]. Treatment of this salt with PCl_5 in refluxing xylene yielded *o*-benzenedisulfonyl chloride, **3**.



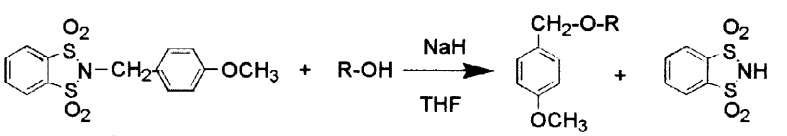
3 **2** **1**



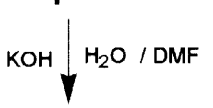
4

Compound **1** was a stable product with mp. 146-7 °C. Formation of the *o*-benzenedisulfonamide **4** was suppressed by the slow addition of the amine to a refluxing solution of **3** in dichloromethane.

Alcohols and phenols were converted into their corresponding 4-methoxybenzyl ethers by reaction with **1** in THF in the presence of sodium hydride at room temperature[10]. The acidic disulfonimide by-product **5** was easily soluble in water and removed during the aqueous work-up.



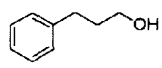
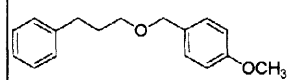
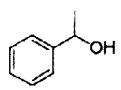
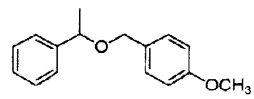
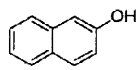
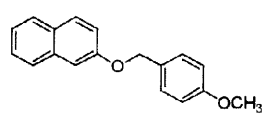
1 **5**



2 + **5**

The products were isolated by flash chromatography and identified by comparison of their spectroscopic properties with those of authentic samples. Representative examples are shown in Table 1.

Table 1. 4-Methoxybenzylation of Alcohols and Phenols with *1*.

Substrate	Product	Yield, %
		71
		78
		57

Treatment of *N*-(4-methoxybenzyl)-*o*-benzenedisulfonimide, **1**, with aqueous KOH in DMF yielded 4-methoxybenzyl alcohol. This, and other similar results, indicated that this reaction scheme may represent a new, general, mild procedure for the conversion of amines into the corresponding alcohols, and a versatile alternative to the classical deamination by diazotization.

Studies of the general formation of *o*-benzenedisulfonimides from other amines, including optically active, and their behavior in substitution and elimination reactions, are now in progress.

References and Notes

1 *a)* Takaku, H.; Kamike, K. *Chem. Lett.* **1982**, 189. *b)* Takaku, H.; Kamike. K.; Tsuchiya, H. *J. Org. Chem.* **1984**, *49*, 51.

2 Horita, K.; Yoshioka, T.; Tanaka, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1986**, *42*, 3021.

3 *a)* L.S. Richter, J.C. Masters and T.R. Gadek *Tetrahedron Lett.* **1994**, *35*, 1631. *b)* Akabori, S.; Sakakibara, S.; Shimonishi, Y.; Nobuhara, Y. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 433.

4 Fukuyama, T.; Laud, A.A.; Hotchkiss, L.M. *Tetrahedron Lett.* **1985**, *26*, 6391. *b)* Classon, B.; Garegg, P.J.; Samuelsson, B. *Acta Chem. Scand. Ser. B*, **1984**, *B38*, 419.

5 Tanaka, T.; Oikawa, Y.; Hamada,T.; Yonemitsu, O. *Tetrahedron Lett.* **1986**, *27*, 3651.

6 *a)* Seljestokken, B.; Fiksdahl, A. *Acta Chem. Scand.* **1993**, *47*, 1050. *b)* Johansen, C.; Fiksdahl, A. *Chirality* **1994**, *6*, 161. *c)* Oppedal, H.; Tveit, I.C.; Fiksdahl, A. *Tetrahedron Asymmetry* **1994**, *5*, 895.

7 Davis, F.A.; Han, W.; Murphy, C.K. *J. Org. Chem.* **1995**, *60*, 4730.

8 *Synthesis of N-(4-methoxybenzyl)-o-benzenedisulfonimide*, **1**. To a refluxing solution containing 2.75 g, (10 mmol) of *o*-benzenedisulfonyl chloride, *3*, in 20 ml of dry CH_2Cl_2 (mol. sieves, 3Å) was added a solution of 1.5 g, (11 mmol) of 4-methoxybenzylamine and 1.0 ml of Et_3N in 25 ml of CH_2Cl_2 over a period of 60 min. The resulting mixture was stirred overnight at room temperature. The reaction mixture was then washed with 0.1 M aqueous HCl, 5 % $NaHCO_3$, water and finally dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent under reduced pressure gave the crude product as a solid material. Recrystallization from hexane / CH_2Cl_2 (1 : 1) yielded 2.81 g, 83 % of the pure product. Mp. 146-7 ° C.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 4.83 (s, 2H), 6.9 (d, 2H), 7.45 (d, 2H), 7.9 (m, 2H), 8.0 (m, 2H) ppm.
^{13}C-NMR (75 MHz, $CDCl_3$): δ 45.1, 55.2, 114.2, 122.2, 125.0, 130.2, 134.7, 135.3, 159.8 ppm.
MS [*m/z* (rel.int.)]: 339(M^+, 28), 274(5), 244(5), 219(20), 210(9), 156(15), 136 (35), 135(17), 134(31), 133(9), 121(100), 108(9), 101(10), 92(11), 91(11), 86(43).
IR (KBr): 3085, 3011, 2935, 2849, 1615, 1588, 1515, 1484, 1448, 1345, 1329, 1300, 1275, 1264, 1245, 1201, 1171, 1129, 1029, 989, 831, 802, 758, 666, 578, 556, 521, 480 cm^{-1}.
Elemental anal. Calcd. for $C_{14}H_{13}NS_2O_5$: C, 49.55; H, 3.86; N, 4.13; S, 18.89. Found: C, 49.98; H, 4.00; N, 3.99; S, 18.81.

9 Meerwein, H.; Dittmar, G.; Göllner, R.; Hafner, K.; Mensch, F.; Steinfort, O. *Chem. Ber.* **1957**, *90*, 841.

10 *Benzylation of phenols and alcohols with* **1**. *General procedure.* To a solution containing 2.0 mmol of the alcohol or phenol and 3 mmol of NaH in 10 ml of dry THF was added dropwise a solution containing 0.68 g, 2.0 mmol, of *N-(*4-methoxybenzyl)-o-benzenedisulfonimide, **1**, in 5 ml of THF. The reaction mixture was then stirred overnight at room temperature. Then 25 ml of diethyl ether was added and the resulting solution was washed with water, 0.1 M NaOH solution, water and finally dried over anhydrous $MgSO_4$. Evaporation of the solvent and purification by flash chromatography yielded the pure product. The yields are shown in Table1. The spectroscopic properties of the products were in all cases in full agreement with the expected structures.