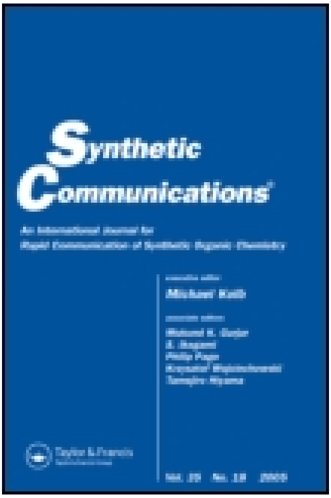

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A Facile Preparation of Methoxymethyl Ethers of Primary and Secondary Alcohols with Dimethoxymethane Catalysed by Expansive Graphite

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A FACILE PREPARATION OF METHOXYMETHYL ETHERS OF PRIMARY AND SECONDARY ALCOHOLS WITH DIMETHOXYMETHANE CATALYSED BY EXPANSIVE GRAPHITE

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Abstract: An easy preparation of methoxymethyl ethers of primary and secondary alcohols with dimethoxymethane has been carried out in excellent yield under catalysis of expansive graphite.

The methoxymethyl moiety is a commonly used protecting group for alcohols in organic synthesis.[1] It is stable to a variety of commonly used reagents such as strong bases, Grignard reagents, butyllithium, and lithium aluminium hydride and is readily removed by acid treatment.[2] The commonly employed method for the preparation of methoxymethyl ethers is based on the reaction of corresponding alkoxide anions with chloromethyl methyl ether.[3,4] However, the direct alkylation of an alcohol using chloromethyl methyl ether is restricted due to the reagent being highly carcinogenic. Acid catalysed condensation of dimethoxymethane

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with alcohols is a widely used approach for the preparation of methoxymethyl ethers. The catalysts for this reaction are phosphorous pentoxide,[5] *p*-toluenesulfonic acid,[6] Nafion-H,[7] iodotrimethylsilane,[8] lithium bromide/*p*-toluenesulfonic acid,[9] molybdenyl(VI) acetylacetone,[10] anhydrous iron (III) chloride,[11] Envirocat EPZG^{R},[12] sulphated zirconia[13] and K-10 montmorillonite.[14] While each of the above methods has its own merit and some shortcomings. Some methods have not been entirely satisfactory, owing to such drawbacks as low yield, long reaction time and the catalysts are not easily obtained, expensive and unrecoverable.

Expansive graphites have been used as efficient catalysts for a variety of organic reactions.[15, 16] Recently we have reported the use of expansive graphite as an efficient heterogeneous catalyst for preparation and cleavage of 1,1-diacetates.[17,18] Herein we report a simple, efficient and inexpensive method for methoxymethylation of alcohols catalysed by expansive graphite.

$$\mathrm{ROH} + \mathrm{CH_3OCH_2OCH_3} \xrightarrow[\text{60-95\%}]{\substack{\text{Expansive graphite} \\ \mathrm{CHCl_3}\text{ or }\mathrm{C_6H_6} \\ \text{reflux, 4-10 h}}} \mathrm{ROCH_2OCH_3} + \mathrm{CH_3OH}$$

As shown in Table 1, a series of methoxymethyl ethers (2) are synthesised under catalysis of expansive graphite. The reactions are carried out at refluxing temperature as they are sluggish at room temperature. Primary alcohols can be easily converted into corresponding methoxymethyl ethers(entries 1, 3, 4, 5, 8 and 9) in excellent yield. Dimethoxymethane is employed both as reagent and solvent. In the cases of secondary alcohols, the reactions progress slower than primary ones. Therefore, benzene or chloroform is used as solvent to raise the refluxing

Table 1. Preparation of Methoxymethyl Ethers form Alcohols with Dimethoxymethane in the Presence of Expansive Graphite

Entry	Alcohol	Solvent/ Time(h)	Yield[a] (%)	b.p./Torr or m.p.(°C) Found	Reported
1	1-Butanol	none/7	90	86-88/15	87/15[12]
2	2-Butanol	$CHCl_3$/9	85	78-80/20	80/20[12]
3	2-Chloroethanol	none/4	93	37-39/15	38/15[12]
4	1-Heptanol	none/8	95	111-113/10	35-36/0.05[8]
5	1-Octanol	none/8	94	96-98/15	97/15[12]
6	2-Decanol	C_6H_6/10	86	103-105/20	105/20[12]
7	Cyclohexanol	$CHCl_3$/8	82	63-65/10	32-34/1.6[7]
8	Benzyl alcohol	none/6	91	74-76/5	75/5[12]
9	Tetrahydrofurfuryl alcohol	none/6	92	74-76/20	75/20[12]
10	Cholesterol	$CHCl_3$/7	60	76-78	78[12]

[a]Isolated yield.

temperature and thus completing the reaction in a considerable time. Tertiary alcohols, however, afford dehydration products instead of the expected methoxymethyl ethers under these conditions.

In conclusion, we have developed an efficient and high yield method for the preparation of methoxymethyl ethers, which uses inexpensive and reusable catalyst, and does not require an aqueous workup.

Experimental

The catalyst of expansive graphite was prepared according to our reported method.[17,19] The products were identified by ^1H NMR spectra and by comparison of their melting or boiling points with literature values.

General procedure for the preparation of methoxymethyl ethers:

A mixture of alcohol(10.0 mmol), dimethoxymethane(30.0 mmol) and expansive graphite (200 mg) was stirred at refluxing temperature (41 °C) for the length of time as indicated in Table 1. For the reactions with solvent, $CHCl_3$ or C_6H_6 (5 mL) was also added. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and the expansive graphite was filtered off and washed with dichloromethane (2 x 10 mL). After evaporation of the solvent, the crude product was purified by distillation under reduced pressure or by column chromatography on silica gel using petroleum ether as eluent to afford the pure product.

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References

[1] Greene, T. W. and Wuts, P. G.M. "Protective Groups in Organic Synthesis," John Wiley & Sons, New York,**1991**, pp. 17-20.

[2] Yardley, J. P. and Fletcher, H. *Synthesis*, **1976**, 244.

[3] Kluge, A. F.; Untch, K. G. and Fried, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 7827.

[4] Kumar, P.; Raju, S. V. N.; Reddy, R. S. and Pandey, B. *Tetrahedron Lett.* **1994**, *35*, 1289.

[5] Fuji, K.; Nakano, S. and Fujita, E. *Synthesis*, **1975**, 276.

[6] Dieter, R. K. and Datar, R. *Org. Prep. Proced. Int.* **1990**, *22*, 63.

[7] Olah, G. A.; Husain, A.; Gupta, B. G. B. and Narang, S. C. *Synthesis*, **1981**, 471.

[8] Olah, G. A.; Husain, A. and Narang, S. C. *Synthesis*, **1983**, 896.

[9] Gras, J. L.; Chang, Y-Y. K. W. and Guerin, A. *Synthesis*, **1985**, 74.

[10] Kantam, M. L. and Santhi, P. L. *Synlett*, **1993**, 429.

[11] Patney, H. K. *Synlett*, **1992**, 567.

[12] Bandgar, B. P., Hajare, C. T. and Wadgaonkar, P. P. *J. Chem. Res. (S)*, **1996**, 90.

[13] Sarkar, A. *Indian J. Chem., Sect. B*, **1996**, *35B*, 862.

[14] Kantam, M. L. and Santhi, P. L. *Indian J. Chem., Sect. B*, **1996**, *35B*, 260.

[15] Susumu, T.; Kenji, F.; Tadashi, M.; Yoshihisa, S. and Hayao, L. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1011.

[16] Bertin, J.; Kagan, H. B.; Luche, J.-L. and Setton, R. *J. Am. Chem. Soc.* **1974**, *96*, 8113.

[17] Jin, T.-S.; Du, G.-Y.; Zhang, Z.-H. and Li, T.-S. *Synth. Commun.***1997**, *27*, 2261.

[18] Jin, T.-S.; Ma, Y.-R.; Zhang, Z.-H. and Li, T.-S. *Synth. Commun.* **1997**, *27*, (in press).

[19] Jin, T.-S.; Ma, Y.-R. and Li, Q. *Chin. J. Inorg. Chem.* **1997**, *13*, (in press).

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