## MLD DEPROTECTION OF METHOXYMETHYL, METHYLTHIOMETHYL, METHOXYETHOXYMETHYL, AND β-(TRIMETHYLSILYL)ETHOXYMETHYL ESTERS WITH MAGNESIUM BROMIDE IN ETHER

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Abstract: MOM, MTM, MEM, and SEM esters are cleanly deprotected under mild conditions by treatment with magnesium bromide in ether at room temperature.

Methoxymethyl (MOM), methylthiomethyl (MTM), methoxyethoxymethyl (MEM), and  $\beta$ -(trimethylsilyl)ethoxymethyl (SEM) esters have not been widely utilized as ester protective groups in organic synthesis due in part to their similar reactivities with the methyl ester under acidic and basic conditions, although the particular advantage of this type of ester protective groups lies in their simple and easy preparation.<sup>1,2</sup> They are normally deprotected by simple acidic hydrolysis.<sup>1</sup> In addition to acidic hydrolysis, the deprotection of MTM esters involves HgCl<sub>2</sub>/H<sub>2</sub>S,<sup>3</sup> MeI<sup>4</sup> and (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>27</sub>-H<sub>2</sub>O<sub>2</sub>/NaOH.<sup>4</sup> We have previously reported that magnesium bromide in ether is a mild and efficient reagent for the selective deprotection of tetrahydropyranyl, MOM, MTM, and SEM ethers in the presence of *t*-butyldimethylsilyl and MEM ethers.<sup>5,6</sup> We wish to report a highly efficient method for the deprotection of MOM, MTM, MEM, and SEM esters with magnesium bromide in ether.

$$\begin{array}{c} O \\ R-C-O-CH_2-X & \underbrace{MgBr_2}_{Et_2O} \begin{bmatrix} O \\ R-C-OMgBr + BrCH_2X \end{bmatrix} \underbrace{H_2O}_{H_2O} & B \\ X = OMe, SMe, OCH_2CH_2OMe, OCH_2CH_2SiMe_3 \end{array}$$

As previously noticed in similar reactions,<sup>5,6</sup> the deprotection for this type of ester protective groups depends critically on the nature of solvents. The deprotection of MOM phenylacetate with 2 equiv of magnesium bromide in ether or in dichloromethane was complete within 1 h at room temperature, yielding phenylacetic acid in 94% and 82% yield, respectively. However, no reaction took place in tetrahydrofuran or in acetonitrile at room temperature for 12 h.<sup>7</sup> When the same reaction was carried out in the presence of 1 equiv of thiophenol in ether, an equimolar mixture of phenylacetic acid and phenylthiomethyl ether was obtained in essentially quantitative yields, indicating that the bond cleavage occurred at O-CH<sub>2</sub> rather than CH<sub>2</sub>-X. Deprotection of MOM, MTM and SEM esters was normally carried out with 2 equiv of magnesium bromide in ether at room temperature.

Table 1 summarizes our experimental results, showing the applicability and the efficiency of the present method. MOM, MTM and SEM esters of aliphatic acids were cleanly deprotected but the deprotection of

R-CO <sub>2</sub> H	R-CO2MOM		R-CO <sub>2</sub> MTM		R-CO2MEM		R-CO <sub>2</sub> SEM	
	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
PhCH <sub>2</sub> CO <sub>2</sub> H	1	94	1.5	88	24	91	1	94
CH <sub>3</sub> (CH <sub>3</sub> ) <sub>6</sub> CO <sub>2</sub> H	1	95	1.5	90	24	92	1	87
⊂ −CO <sub>2</sub> H	1	91	4	90	40	90	1	94
CO <sub>2</sub> H	1	82	4	84	24	90	2	85
CO <sub>2</sub> H	4	90	12	74	48	92	6	93
CO <sub>2</sub> H	0.3	77	1.5	75	24	75	0.3	77
Me - CO <sub>2</sub> H	16	94	24	92	30	94	16	91

Table 1. Deprotection of MOM, MTM, MEM, and SEM Esters with MgBr<sub>2</sub> in ether.

those of aromatic acids like *p*-toluic acid was relatively slow. Furthermore, the deprotection of MEM esters was very slow, as compared with that of MOM, MTM and SEM esters, and required more than 24 h for completion of the reaction. Furthermore, it was found that the use of 3 equiv of magnesium bromide was beneficial for optimal yields and completion of the reaction for the deprotection of MEM esters. Selective removal of MOM, MTM, or SEM ester in the presence of MEM ester was unsuccessful, even though a marked difference in the reaction rate was noticed.

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## **References and Notes**

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- MOM, MEM and SEM esters were prepared by treatment of acids with an equimolar amount of MOM, MEM or SEM chloride and Et<sub>3</sub>N at room temperature. Treatment of acids with NaH in HMPA followed by addition of chloromethylmethyl sulfide afforded MTM esters in high yields. (Zoretic, P.A.; Soja, P.; Conrad, W.E. J. Org. Chem. 1975, 40, 2962.)
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