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Magnesium Bromide Mediated Selective Conversion of Acetals into Thioacetals

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Magnesium bromide in ether is found to be a very effective and highly selective reagent for the conversion of acetals into the corresponding thioacetals in the presence of ketones.

Thioacetals have been widely used as carbonyl protective groups[1] and synthons[2] in a variety of synthetic operations, and various methods for the thioacetalization of acetals and carbonyl compounds using protic acids, Lewis acids, and some silicon reagents have been developed so far.[1] As a chemoselective method, silica gel treated with thionyl chloride[3] and bis(diisobutylaluminum) 1,2-ethanedithiolate[4] have been recently reported to be useful reagents for the conversion of aldehydes and acetals respectively into the corresponding thioacetals in the presence of ketones. Nevertheless, the requirement for a more convenient as well as highly selective thioacetalization method is still in existence.

Recently, we have reported that magnesium bromide is a mild and efficient reagent for the selective removal of tetrahydropyranyl ethers in the presence of tert-butyldimethylsilyl ethers.[5] On the basis of the mildness and potential oxygenophilicity[6] of magnesium bromide, we have investigated its possibility as a promotor for the conversion of acetals and carbonyl compounds into the corresponding thioacetals. In this communication, we wish to report a very effective and highly selective method for the thioacetalization of acetals without affecting

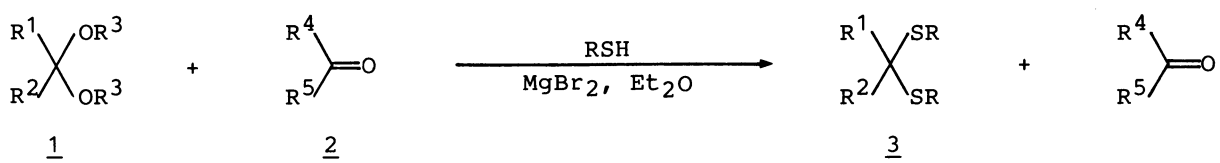

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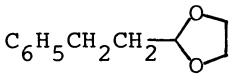
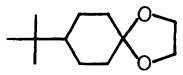
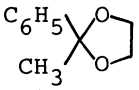
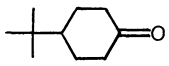
Table 1. Thioacetalization of Acetals, Aldehydes, and Ketones Using $MgBr_2$

Entry	Substrate	Thiol	Time/min	Yield/%[a]
1	$C_6H_5CH_2CH_2CH(OCH_3)_2$	C_6H_5SH	10	94
2		$n\text{-}C_4H_9SH$	10	90
3		$HS(CH_2)_3SH$	10	92
4	$C_6H_5CH(OCH_3)_2$	C_6H_5SH	10	93
5		$HS(CH_2)_2SH$	30	88
6		$HS(CH_2)_3SH$	30	97
7		$HS(CH_2)_2SH$	30	86
8		$HS(CH_2)_3SH$	30	96
9		$HS(CH_2)_2SH$	30	92
10	$CH_3(CH_2)_7CHO$	$HS(CH_2)_2SH$	10	94
11	C_6H_5CHO	C_6H_5SH	30	93
12		$HS(CH_2)_2SH$	30	92
13	$CH_3(CH_2)_8COCH_3$	$HS(CH_2)_2SH$	4 h	94
14	$C_6H_5COCH_3$	$HS(CH_2)_2SH$	12 h	0(85)[b]

a) Isolated yields. b) The yield in parenthesis refers to the recovered starting material.

ketones using magnesium bromide as an efficient catalyst.

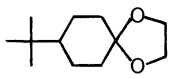
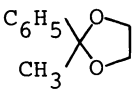
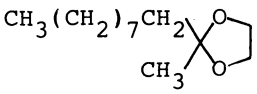
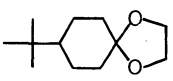
We have found that acetals and some carbonyl compounds can be cleanly converted into the corresponding thioacetals under very mild conditions. Table 1 summarizes some experimental results and illustrates the efficiency and scope of the present method. When acetals were treated with 2.1 equiv. of monothiols or 1.1 equiv. of dithiols in the presence of 2.1 equiv. of magnesium bromide in ether at room temperature, the corresponding thioacetals were obtained in high yields after simple aqueous workup (entries 1-9). Aromatic and aliphatic monothiols and dithiols gave the corresponding thioacetals in equally high yields. Acyclic acetals were quantitatively thioacetalized within 10 min and cyclic acetals within 30 min, respectively.

Furthermore, aldehydes and aliphatic ketones were found to be cleanly

converted into their thioacetals upon treatment of 1.1 equiv. of 1,2-ethanedithiol and 1.2 equiv. of magnesium bromide in ether at room temperature (entries 10-13). However, aromatic ketones were recovered unchanged even in the presence of 2.1 equiv. of this catalyst and for prolonged reaction time (entry 14). Under this enhanced conditions, 2-undecanone was slowly thioacetalized to afford the corresponding 1,3-dithiolane in 94% yield within 4 h.

Based on the difference in reactivity between acetals and ketones, we have also found that our approach allows for the selective conversion of acetals into the corresponding thioacetals in the presence of ketones. The following procedure is representative. To a solution of 1,2-ethanedithiol (91 μL, 1.1 mmol) and magnesium bromide (387 mg, 2.1 mmol) in ether (3 mL) at room temperature was added an equimolar mixture of ethylene glycol acetal of acetophenone (163 mg, 1.0 mmol) and 2-undecanone (170 mg, 1.0 mmol) in ether (2 mL). The reaction mixture was stirred at the same temperature for 30 min and diluted with ether (20 mL). The ether solution was washed successively with 10% NaOH, aq. NH_4Cl solution, and brine. Drying over $MgSO_4$, concentration, and flash chromatography using ethyl acetate and hexane (1:40) as an eluant gave 2-methyl-2-phenyl-1,3-dithiolane (162 mg, 91%) and unreacted 2-undecanone (153 mg, 92%) which were pure in careful

Table 2. Selective Thioacetalization of Acetals in the presence of Ketones[a)]

Acetal, 1	Ketone, 2	Yield of 3/%[b)]
$C_6H_5CH(OCH_3)_2$	$CH_3(CH_2)_8COCH_3$	93 (92)
		87 (93)
		91 (92)
	$C_6H_5COCH_3$	92 (89)
		89 (91)

a) All reactions were carried out with 1.1 equiv. of 1,2-ethanedithiol and 2.1 equiv. of magnesium bromide in ether at room temperature. b) Isolated yields and the numbers in parenthesis refer to the yields of recovered ketones.

^{1}H-NMR analysis. Some of the results that we have obtained for this selective conversion are summarized in Table 2. As illustrated above, cyclic as well as acyclic acetals were selectively converted into the desired 1,3-dithiolanes without thioacetalization of ketones. It is noteworthy that the reactivity of 2-undecanone and acetophenone toward the thioacetalization is reversed by modifying the latter compound into an acetal, thus ethylene glycol acetal of acetophenone was selectively converted into the corresponding thioacetal without affecting 2-undecanone. The present results are opposed to that obtained with boron trifluoride etherate.[4] Namely, using boron trifluoride etherate as a Lewis acid catalyst, the thioacetalization of ketones is usually faster than that of acetals.

The previously reported mildness and operational easiness of magnesium bromide appear to make the present method very attractive and further synthetic utility of this reagent in functional group transformation will be reported in due course.

References

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6) Aside from the cleavage of tetrahydropyranyl ethers, the oxygenophilicity of magnesium bromide was illustrated in the following references; J. P. McCormick and D. L. Barton, J. Org. Chem., 45, 2566 (1980); D. J. Goldsmith, E. Kennedy, and R. G. Campbell, ibid., 40, 3571 (1975); S. M. Naqvi, J. P. Horwitz, and R. Filler, J. Am. Chem. Soc., 79, 6283 (1957); H. O. House, ibid., 77, 3070, 5083 (1955).

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