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ALUMINIUM HALIDE-THIOL SYSTEM: A USEFUL REAGENT FOR DEMETHYLATION OF ALIPHATIC AND AROMATIC METHYL ETHERS AND DEMETHYLENATION OF METHYLENEDIOXY COMPOUNDS

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A new efficient procedure for demethylation of methyl ethers and demethylenation of methylenedioxy compounds under mild conditions has been exploited by the use of aluminium halide-thiol system.

We have published a reagent system, BF_3-etherate and thiol, for demethylation of aliphatic methyl ethers[1] and its application.[2] This reagent system has also been shown to be effective for debenzylation.[3] Now, we wish to report an exploitation of a new reagent system, AlX_3 and EtSH. As shown in Table 1, demethylation with aluminium halide-thiol system was tried with success on several aliphatic and aromatic methyl ethers. Also for the aromatic methyl ethers, demethylation proceeded very easily. (*Cf*. Selective demethylation of 17-OMe group in estradiol dimethyl ether (4) with BF_3-etherate-thiol[1]). A partial demethylation was successful on treatment of dimethyl ether (7) with $AlCl_3$ at -15°C for 5 min, which was applied to the total synthesis of lythranidine.[4] Selective demethylation of the aromatic methyl ether from the compound having both aromatic methoxy and aliphatic or aromatic alkoxycarbonyl groups was also successful under the conditions indicated [see reactions of (8), (9), and (10)], although this system is available for dealkylation of esters under stronger conditions.[5] By contrast, demethylation of the methoxycarbonyl group has been known to be prior to demethylation of methyl ether in (8), when RS^- was used.[6]

Application of this system was expanded to demethylenation of the methylenedioxy group. The methylenedioxy compounds, (21), (22), and (23), on treatment with $AlBr_3$-EtSH gave satisfactory yields of the corresponding catechols in a short time under mild conditions, as summarized in Table 2.

These reactions proceed *via* initial coordination of "hard" Lewis acid [Al(III)] to "hard" base (oxygen) followed by attack of thiol, a "soft" base, to the activated less hindered carbon atom ("soft" acid) through an S_N2-type pattern.

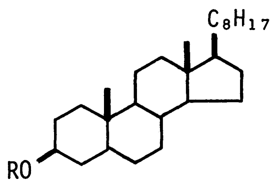
Table 1. Demethylation of aliphatic and aromatic methyl ethers with AlX_3 in EtSH

Substrate	AlX_3 (mol equiv.)	Temp.	Reaction time (hr)	Product and yield (%)
(1)	$AlBr_3$ (1.8)	r.t.	3	(11) 98.4
(2)	$AlBr_3$ (3)	r.t.	14[a]	(12) 98.3
(3)	$AlBr_3$ (3)	r.t.	< 1	(13) 90.0
(4)	$AlBr_3$ (5)	r.t.	< 1	(14) 94.3
(5)	$AlCl_3$ (3.4)	r.t.	< 0.5	(14) 97.5
(6)	$AlCl_3$ (2)	0°	< 0.5	(15) 95.0
(7)	$AlCl_3$ (3)[b]	-15°	0.1	(16) 80, (17) 5.0
"	$AlCl_3$ (2.7)	r.t.	< 0.5	(17) 97.4
(8)	$AlCl_3$ (3)[b]	0°	6	(18) 98.6
(9)	$AlCl_3$ (5)[b]	0°-r.t.	2.5	(19) 98.0
(10)	$AlCl_3$ (5)[b]	r.t.	2	(20) 95.2

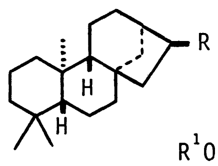
a Because of water of crystallisation in the substrate, the reaction took such a long time.
b Ethanethiol (5-10%) in dichloromethane was used.

Table 2. Demethylenation of methylenedioxy compounds with $AlBr_3$ in EtSH

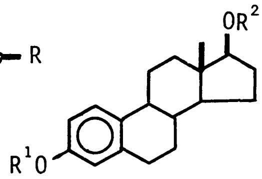
Substrate	Mol equiv. of $AlBr_3$	Temp.	Reaction time (hr)	Yield (%) of catechol
(21)	2.4	0°	< 0.5	78.4
(22)	2.4	0°	< 0.5	73.0
"	1.2	r.t.	2	60.2
(23)	4	0°	1	72.4



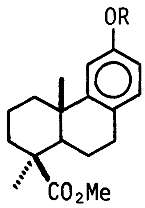
(1) R=Me
(11) R=H



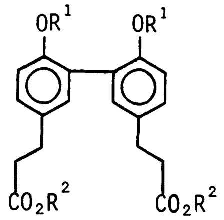
(2) $R=CH_2OMe$
(3) R=OMe
(12) $R=CH_2OH$
(13) R=OH



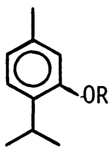
(4) $R^1=R^2=Me$
(5) $R^1=Me$; $R^2=H$
(14) $R^1=R^2=H$



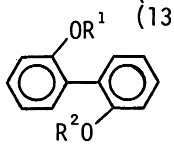
(8) R=Me
(18) R=H



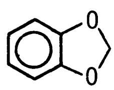
(9) $R^1=R^2=Me$
(10) $R^1=Me$; $R^2=Et$
(19) $R^1=H$; $R^2=Me$
(20) $R^1=H$; $R^2=Et$



(6) R=Me
(15) R=H



(7) $R^1=R^2=Me$
(16) $R^1=Me$; $R^2=H$
(17) $R^1=R^2=H$



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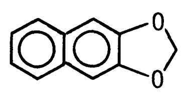

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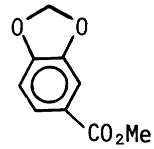

(23)

References and notes

1 M. Node, H. Hori, and E. Fujita, *J. C. S. Perkin I*, 1976, 2237.
2 E. Fujita, M. Node, and H. Hori, *J. C. S. Perkin I*, 1977, 611.
3 K. Fuji, K. Ichikawa, M. Node, and E. Fujita, unpublished.
4 K. Fuji, K. Ichikawa, and E. Fujita, unpublished.
5 It will be published elsewhere.
6 T. R. Kelly, H. M. Dali, and W. -G. Tsang, *Tetrahedron Letters*, 1977 3859.

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