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Magtrieve™: a new agent for the deprotection/oxidation of acetals and ketals under neutral conditions

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Abstract

Magtrieve™ can be used for the deprotection of acetals and ketals or for the direct oxidation to carboxylic acids under neutral conditions. © 1999 Elsevier Science Ltd. All rights reserved.

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Acetals and ketals are important carbonyl protecting groups in organic synthesis and many methods have been introduced for both their formation and removal.¹ Usually, deprotection is accomplished by aqueous acid hydrolysis. Although the use of less acidic reagents such as $\text{MoO}_2(\text{acac})_2$,² montmorillonite K10,³ $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$,⁴ $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ⁵ and cerium ammonium nitrate⁶ have been reported, methods using neutral conditions will be required for the deprotection of acid-sensitive substrates.

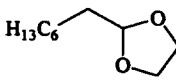
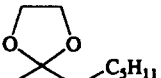
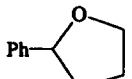
Magtrieve™ (Dupont Product), a magnetically retrievable oxidant (CrO_2) has been used for the oxidation of alcohols to aldehydes or ketones.⁷ Recently, we have reported that Magtrieve™ can oxidize 1,4-dihydropyridines to pyridines in good yield.⁸ We now report that wet Magtrieve™ can be also used for the deprotection of acetals and ketals or for the direct oxidation to carboxylic acids under neutral conditions.[†] When cinnamaldehyde dimethyl acetal (1 mmol) was allowed to react with Magtrieve™ (1.50 g) in chloroform (10 ml) at rt for 0.5 h, cinnamaldehyde was isolated as its oxime derivative in 95% yield.[‡] Also, the hydrolysis could be done using a smaller amount of Magtrieve™ in the presence of 5 equivalents of water (entries 1b and 1c). Encouraged by these results, acetals and ketals of aliphatic and aromatic carbonyl compounds were treated with Magtrieve™. The results are shown in Table 1. Dimethyl acetals of aromatic aldehydes (entries 3, 6) and dimethyl ketals of ketones (entries 4, 5) were converted into the corresponding carbonyl compounds in good yields. Deprotection of dimethyl acetal of α,β -unsaturated aliphatic aldehydes (entry 2) gave a mixture of aldehyde and acid, due to the overoxidation

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† Magtrieve™ used here contained 4.8% of water based on TGA (4.8% decrease in weight at 300°C), which amounts to 4.0 mmol of water in 1.50 g of Magtrieve™. When dry Magtrieve™ was used, the hydrolysis did not occur within one day under N_2 atmosphere.

‡ The formation of methanol as a coproduct was ascertained by GC-MS and ^1H NMR spectroscopy.

Table 1
Magtrieve™-mediated deprotection/oxidation of acetals and ketals

Entries	Substrates	Reaction Conditions ^a	Products (Yield%) ^b
1a	(<i>E</i>)-Ph-CH=CH-CH(OMe) ₂	1.50 g, r.t., 0.5 h	Aldehyde (97%)
1b		150 mg, r.t., 4 h ^c	Aldehyde (98%)
1c		30 mg, r.t., 8 h ^c	Aldehyde (98%)
2a	(<i>E</i>)-C ₅ H ₁₁ -CH=CH-CH(OMe) ₂	1.50 g, reflux, 4 h	Aldehyde (60%) + Acid (40%)
2b		1.50 g, r.t., 5 h	Aldehyde (50%) + Acid (50%)
3	PhCH(OMe) ₂	1.50 g, r.t., 10 min	Aldehyde (95%)
4	MeC(OMe) ₂ CH ₂ (CH ₂) ₄ Me	1.50 g, r.t., 0.5 h	Ketone (95%)
5	PhC(OMe) ₂ Me	1.50 g, reflux, 24 h	Ketone (92%)
6	<i>m</i> -NO ₂ C ₆ H ₄ -CH(OMe) ₂	3.00 g, reflux, 5 h	Aldehyde (77%)
7	Me(CH ₂) ₃ CH ₂ CH(OMe) ₂	1.50 g, r.t., 9 h	Acid (77%)
8	Me(CH ₂) ₄ CH ₂ CH(OMe) ₂	1.50 g, r.t., 9 h	Acid (74%)
9		1.50 g, r.t., 40 h	No Reaction
10a		1.50 g, r.t., 1 h	No Reaction
10b		1.50 g, r.t., 40 h	Ketone (32%) ^d
11a		1.50 g, r.t., 1 h	No Reaction
11b		1.50 g, r.t., 20 h	Aldehyde (43%) ^d

^a Deprotection was performed in chloroform under open air, except for entries 1b, 1c, 3, 11 where N₂ atmosphere was used. The weight represents the amount of Magtrieve™ used for 1 mmol of substrate.

^b Isolated yields.

^c Water (5 mmol) was added.

^d The rest is the starting compound.

of aldehyde. Dimethyl acetals (entries 7, 8) of simple aliphatic aldehydes were completely oxidized to give the carboxylic acids as a single product, probably via aldehydes.[§]

However, the 1,3-dioxolanes (entries 9–11) were inert to Magtrieve™ in a condition employed for the deprotection of dimethyl acetals and ketals (entries 7 vs 9, 4 vs 10a, 3a vs 11a). When an equimolar mixture (1 mmol each) of dimethyl acetal and 1,3-dioxolane of heptanal was treated with Magtrieve™ (1.50 g) in chloroform at rt, 1,3-dioxolane was recovered after 10 h, while dimethyl acetal was converted into the acid. Selective deprotection of dimethyl ketal group was also observed in a competitive reaction of dimethyl ketal and 1,3-dioxolane of 2-octanone in chloroform (rt, 6 h). Therefore, wet Magtrieve™ can be used for the chemoselective deprotection/oxidation of dimethyl acetals and ketals in chloroform.

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[§] Upon treatment with either dry or wet Magtrieve™ in chloroform (rt, 2 days), octanal was oxidized to the acid in 95% yield.

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