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LETTERS

Efficient, selective deprotection of aromatic acetates catalyzed by Amberlyst-15 or iodine☆

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Abstract—Aromatic acetates were selectively deprotected in the presence of aliphatic acetates to the corresponding phenols in excellent yields using Amberlyst-15 or iodine as catalysts in methanol at room temperature. The first catalyst can be recovered.

Phenolic hydroxy groups are present in several bioactive naturally occurring compounds, hence protection and subsequent deprotection of this group is necessary for multistep transformations and syntheses of these compounds.[1] A routinely used method for the protection of the phenolic hydroxy group involves conversion to the corresponding acetate which can be cleaved under acidic or basic conditions or by hydrogenolysis.[1] However, these deprotection methods may affect different sensitive functional groups and selectivity is poor. A limited number of methods exist for the selective deprotection of aromatic acetates in the presence of aliphatic acetates (these include the use of specific micelles,[2a] Zn–MeOH,[2b] cyclodextrin,[2c] metalloenzymes,[2d] metal complexes,[2e] antibodies[2f] and NH_4OAc[2g]). Although these methods have certain applicabilities most have associated drawbacks such as operational complexity, harsh reaction conditions, use of costly and difficult to obtain reagents, long reaction times and low yields. The recovery of catalysts is also a problem. Recently natural kaoline clay has been applied,[3] however, the clay was collected from a specific geographical region. Thus, there is a need for suitable methods for selective deprotection of aromatic acetates which make use of readily available catalysts and which work efficiently under mild reaction conditions.

We have recently discovered a simple process for facile cleavage of aromatic acetates over a wide range of functional groups in the presence of Amberlyst-15 or iodine as catalysts in methanol. Several aromatic acetates were selectively deprotected to the corresponding phenols (Table 1) using these catalysts at room temperature. The yields of the regenerated phenols were typically excellent. Alkyl acetates were unaffected by both catalysts under the present experimental conditions. Ethers, esters and lactones also remained unaffected. Amberlyst-15 showed similar activity towards the deprotection of aromatic acetates containing electron-donating and electron-withdrawing groups but iodine showed weak or no activity towards deprotection of aromatic acetates possessing electron-withdrawing groups (except when in the presence of another –OAc group). Thus, *p*-nitrophenyl acetate (entry g) was easily converted into *p*-nitrophenol (time 3.0 h, yield 87%) using Amberlyst-15 but was unaffected in the presence of iodine. Amberlyst-15 also showed high chemoselectivity for the cleavage of phenyl acetates without affecting electron-withdrawing groups such as an aldehyde, ketone, benzoate, *N*-acetyl and tosylate. To demonstrate the selectivity, some intermolecular experiments were also carried out. Thus, when a mixture of *p*-methylphenyl acetate and phenylethyl acetate in methanol (entry u) was treated with Amberlyst-15 and iodine separately, the first compound underwent deprotection in each case to *p*-methylphenol, but the second compound remained unchanged. However, when the reaction was carried out with a mixture of phenyl acetate and *p*-formylphenyl acetate (entry v) in the presence of these two catalysts separately, both compounds were deprotected with Amberlyst-15 but only the first compound with iodine.

Keywords: aromatic acetates; deprotection; Amberlyst-15; iodine; chemoselectivity.

☆ Part 29 in the series, 'Studies on Novel Synthetic Methodologies'.

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0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
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The present method has also been utilized for the deprotection of acetates of some naturally occurring bioactive phenols. Thus rhododendrol diacetate[4] (entry s) and diphyllin acetate[5] (entry t) were converted into rhododendrol monoacetate and diphyllin respectively in very high yields. The first product can be utilized for the preparation of various analogues of rhododendrol with modifications at the phenolic hydroxyl group.

The catalysts, Amberlyst-15 and iodine are readily available and inexpensive. They catalyze the deprotection of aromatic acetates at room temperature via a simple experimental procedure.[6] The first catalyst works under heterogeneous conditions and can easily be removed from the reaction mixture simply by filtration and can be activated and reused.

In conclusion, we have developed a mild, efficient and facile process for the deprotection of aromatic acetates using Amberlyst-15 and iodine as catalysts. The process is associated with high yields of the parent phenols and high chemoselectivity. The method is also useful for

Table 1. Deprotection of aryl acetates with Amberlyst-15 and iodine[#]

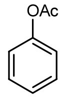
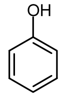
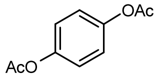
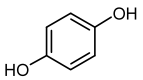
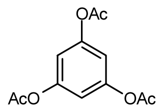
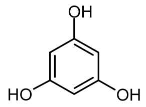
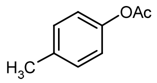
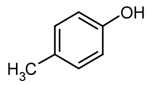
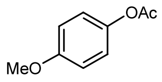
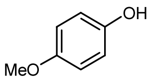
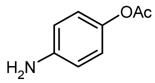
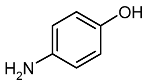
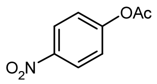
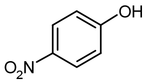
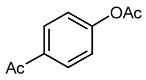
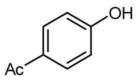
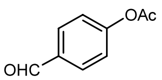
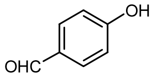
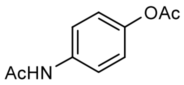
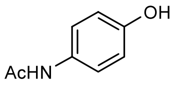
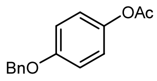
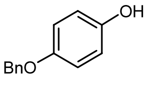
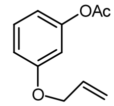
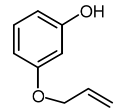
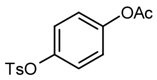
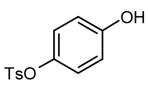
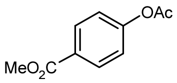
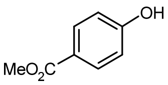
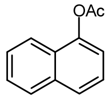
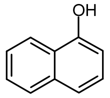
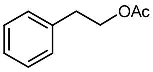
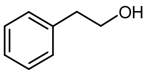
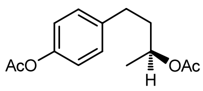
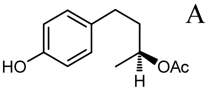
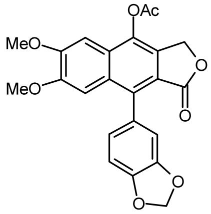
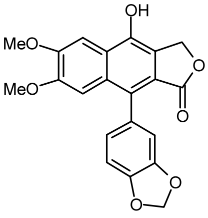
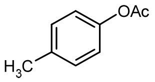
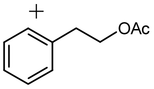
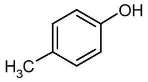
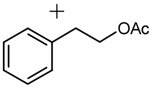
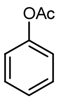
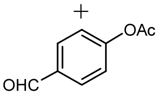
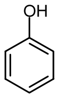
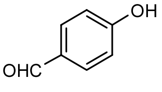
Entry	Acetate	Product	Catalyst	Time (h)	Isolated yield (%)
a			Amberlyst-15	2.5	95
			Iodine	2.5	93
b			Amberlyst-15	4.0	90
			Iodine	4.0	89
c			Amberlyst-15	4.0	87
			Iodine	4.0	85
d			Amberlyst-15	3.0	92
			Iodine	3.0	90
e			Amberlyst-15	3.0	93
			Iodine	3.0	92
f			Amberlyst-15	3.0	90
			Iodine	3.0	90
g			Amberlyst-15	3.0	87
			Iodine	3.0	0
h			Amberlyst-15	2.5	95
			Iodine	2.5	0
i			Amberlyst-15	3.0	90
			Iodine	3.0	0
j			Amberlyst-15	4.0	89
			Iodine	6.0	50
k			Amberlyst-15	3.0	87
			Iodine	3.0	87
l			Amberlyst-15	3.0	85
			Iodine	3.0	80
m			Amberlyst-15	4.0	90
			Iodine	6.0	48

Table 1. (*Continued*)

n			Amberlyst-15	3.0	89
			Iodine	3.0	0
o			Amberlyst-15	2.5	92
			Iodine	2.5	90
p			Amberlyst-15	3.0	0
			Iodine	3.0	0
q	CH_3-$(CH_2)_9$-OAc	CH_3-$(CH_2)_9$-OH	Amberlyst-15	3.0	0
			Iodine	3.0	0
r	AcO-$(CH_2)_4$-OAc	HO-$(CH_2)_4$-OH	Amberlyst-15	3.0	0
			Iodine	3.0	0
s			Amberlyst-15	3.0	85
			Iodine	3.0	85
t			Amberlyst-15	4.0	90
			Iodine	4.0	85
u	 + 	 + 	Amberlyst-15	3.0	92+100 (respectively)
			Iodine	3.0	90+100 (respectively)
v	 + 	 + 	Amberlyst-15	2.5	95+90 (respectively)
			Iodine	2.5	93+0 (respectively)

#The structures of all the products were determined from their spectroscopic (^{1}H NMR and MS) data.

deprotection of the acetates of bioactive natural phenols (chiral and non-chiral) containing sensitive functional groups.

Acknowledgements

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Giorgi, I. B. *J. Org. Chem.* **1994**, *59*, 7602; (d) Crampton, M. R.; Holt, K. E.; Perey, J. M. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1701; (e) Beisselier, V. L.; Postal, M.; Dunach, E. *Tetrahedron Lett.* **1997**, *38*, 2981; (f) Guo, J.; Huang, W.; Scanlan, T. S. *J. Am. Chem. Soc.* **1994**, *116*, 6062; (g) Ramesh, C.; Mahender, G.; Ravindranath, N.; Das, B. *Tetrahedron* **2003**, *59*, 1049.

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4. Das, B.; Padma Rao, S.; Srinivas, K. V. N. S.; Yadav, J. S. *Phytochemistry* **1993**, *33*, 2529.
5. Murakami, T.; Matsushima, A. *J. Pharm. Soc. Jpn.* **1961**, *81*, 1596.
6. Experimental procedure:

   (a) Treatment of aryl acetate with Amberlyst-15: Aryl acetate (1 mmol) and Amberlyst-15 (100 mg) were taken in MeOH (10 ml). The mixture was stirred at room temperature. After completion of the reaction (TLC) the catalyst was filtered off and washed with MeOH (2×5 ml). The filtrate was concentrated under reduced pressure and the residue was extracted with EtOAc (3×10 ml). The concentrated extract was purified by column chromatography over silica gel to give the parent phenol.

   (b) Treatment of aryl acetate with iodine: A mixture of aryl acetate (1 mmol), MeOH (10 ml) and I_2 (100 mg) was stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, MeOH was removed under reduced pressure and the residue was extracted with EtOAc (3×10 ml). The extract was washed with a solution of sodium thiosulfate (3×10 ml) and subsequently with water (3×10 ml). The concentrated extract was subjected to column chromatography over silica gel to afford the parent phenol.