

Facile and selective deprotection of aryl acetates using sodium perborate under mild and neutral conditions

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A variety of aryl acetates are cleaved to the corresponding phenols using sodium perborate in methanol under mild conditions (25 °C). The effectiveness of this protocol is manifested in its tolerance of different functional groups and selectivity of deprotection towards aryl acetates whereas alkyl acetates are found to be unreactive under these reaction conditions.

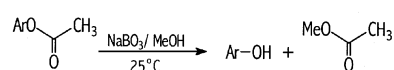
Protection or deprotection of a functional group is one of the important and widely carried out synthetic transformations in preparative organic chemistry.¹ In developing a synthesis of any phenol-containing product, protection is often mandatory to prevent reaction with oxidizing agents and electrophiles or reaction of the nucleophilic phenoxide ion with even mild alkylating and acylating agents. The protection of phenol as *O*-acyl derivatives has long played a key role in organic synthesis, because of the ease with which they are formed and cleaved. In the synthesis of multifunctional molecules, the problem regularly arises that a given functional group has to be deprotected in the presence of others. The methods available for deprotection of aryl acetates involve treatment with Zn–MeOH,^{1a} LiBH₄,^{1a} *p*-TsOH–SiO₂–H₂O,^{1a} bis(tributyltin)oxide,² NaHTe,³ borohydride exchange resin,⁴ Al₂O₃/microwaves,⁵ metal complexes,⁶ enzymes,⁷ metalloenzymes,⁸ antibodies,⁹ cyclodextrin,¹⁰ micelle-catalyzed saponification¹¹ and [tBu₂SnOH(Cl)]₂.¹² Alkaline hydrolysis is most commonly employed for deprotection of acetates, yet a number of other functional groups are not tolerated in this procedure.¹ In spite of several efforts, the methods available for selective removal of aryl acetates in the presence of other sensitive functional groups are very few,^{12–14} not general¹⁴ and most involve homogeneous conditions. The recently reported ytterbium triflate,¹⁵ unlike hafnium triflate,¹⁶ cleaves aryl acetates without Fries migration. However, it requires long reaction times, drastic conditions, aqueous work-up and does not discriminate between aryl and alkyl acetates. More recently reported natural kaolinitic clay¹⁷ and aromatic thiols in the presence of K₂CO₃ in dipolar aprotic solvents¹³ constitute an efficient protocol for selective cleavage of aryl acetates. However, the former method involves mild but acidic conditions whereas the latter method requires drastic reaction conditions and it does not discriminate between aryl acetates and aryl benzoates. The deacylation of acetates is carried out using [tBu₂SnOH(Cl)]₂ as a highly efficient catalyst under almost neutral conditions.¹² Though a variety of functional groups are tolerated and high selectivities are obtained in competition between primary, secondary and tertiary alcohol acetates, selective deprotection of acetates in the presence of benzoates is not achieved by this method.

The versatility of sodium perborate (SPB) in functional group oxidations has been highlighted in the literature.¹⁸ It is inexpensive and extensively used in the detergent industry as

a bleaching and antiseptic agent. Applications of SPB in various organic functional group transformations is well documented.¹⁸ The development of a new method that allows transformations under essentially neutral conditions should heighten the synthetic potentiality of the deprotection of aryl acetates. The useful common and cheap reagent, sodium perborate has not been studied so far for this transformation. This communication deals with a study of the scope of sodium perborate for the selective removal of aryl acetates in the presence of other sensitive functional groups under mild and neutral conditions (Scheme 1).

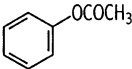

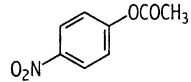
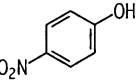
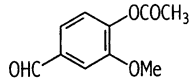
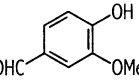
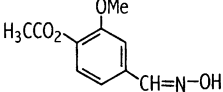
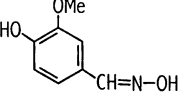
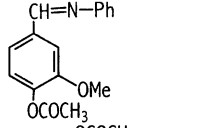
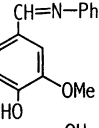
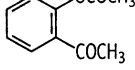
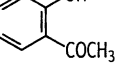
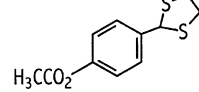
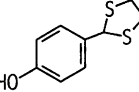
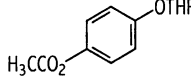
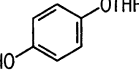
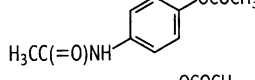
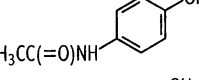
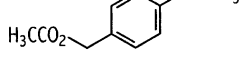
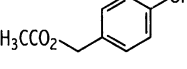
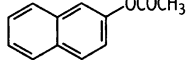
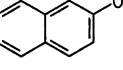
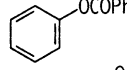

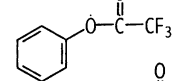

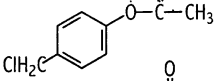
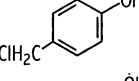
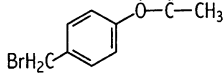
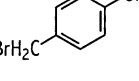
A variety of aryl acetates were subjected to the deprotection conditions with an equivalent amount of sodium perborate in methanol at 25 °C to give the corresponding phenols.¹⁹ Among the various solvents studied methanol is the solvent of choice. The results are presented in Table 1. It is important to note that this economically attractive and manipulatively simple protocol allows chemoselective deprotection of aryl acetates in the presence of several other protecting groups such as oximes (entry 4), thioacetals (entry 7), THP ethers (entry 8) and NH-acetyl (entry 9). Functional groups such as aldehyde (entry 3), ketone (entry 6), imine (entry 5) and benzoate (entry 12) remain unaltered under these reaction conditions. Furthermore, it is noticed that the aryl acetate group is removed selectively in the presence of benzyl acetate (entry 10) and no deacylation was observed for alkyl acetates (entries 10, 16–19). It is also noticed that aryl trifluoroacetates are cleaved readily to the corresponding phenols (entry 13). It may be also quite interesting that the presence of carbonyl groups (entries 3, 6), halogen atoms (entries 14, 15, 17–19) and ester groups (entries 10, 16–19), which may show some reactivity under the basic conditions of reported methods, did not disturb the reaction under the present reaction conditions. THP ethers, simple aryl ethers, anilides, oximes, thioacetals and benzoates generally do not tolerate acidic conditions. However, these protected groups remain intact under the present reaction conditions. This is attributed to the fact that the reaction is carried out under neutral conditions. The present reaction conditions allow exclusive aryl deacetylation with no trace of Fries migration products.

Excellent selectivities were observed during inter- and intramolecular competition between aryl esters and alkyl esters (Scheme 2). Thus, 4-methoxyphenyl acetate with ethyl benzoate [Scheme 2, eqn. (1)] and 2-naphthyl acetate with cinnamyl



Scheme 1

Table 1 Deprotection of aryl acetates using sodium perborate under mild and neutral conditions

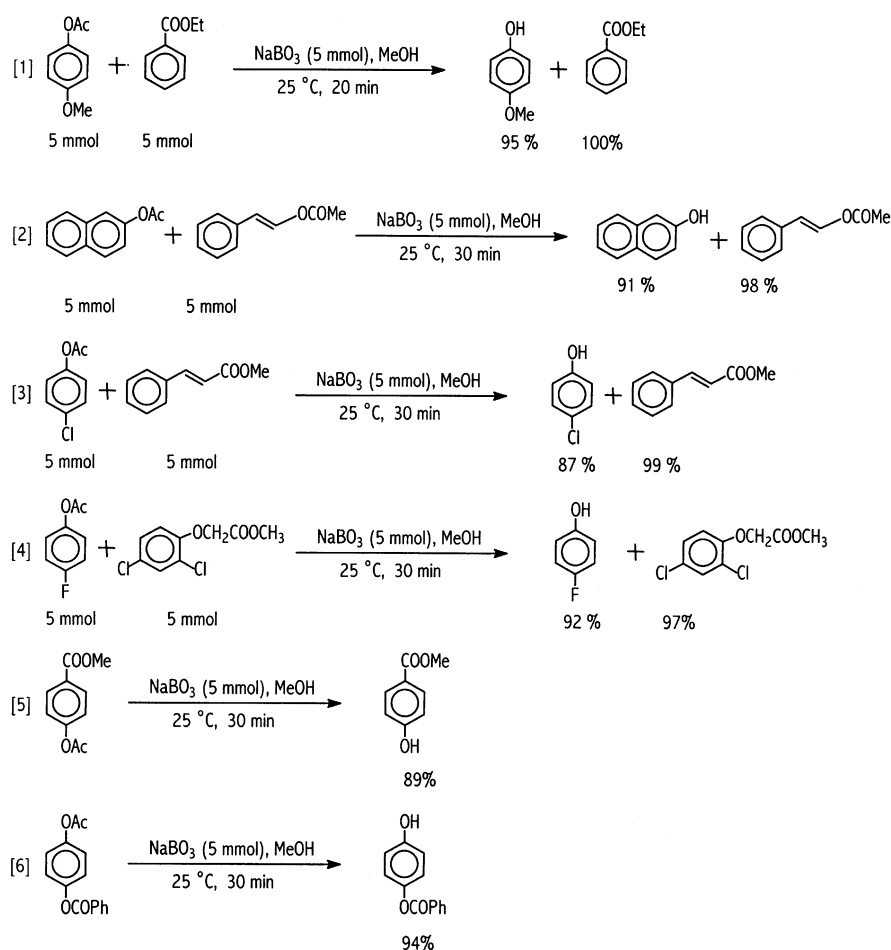
Entry	Substrate	Product	Time/min	Yield ^{a, b} /%
1			30	91
2			05	92
3			20	80
4			30	83
5			30	84
6			15	82
7			15	85
8			15	84
9			30	90
10			30	91
11			30	92
12			60	0
13			05	94
14			30	81
15			30	80
16	$\text{H}_3\text{C}-(\text{CH}_2)_7-\text{OCOCH}_3$	$\text{H}_3\text{C}-(\text{CH}_2)_7-\text{OH}$	60	0
17	$\text{F}_3\text{CCH}_2\text{OC}(=\text{O})\text{CH}_3$	$\text{F}_3\text{CCH}_2\text{OH}$	60	0
18	$\text{BuOC}(=\text{O})\text{CH}_2\text{Cl}$	BuOH	60	0
19	$\text{BuOC}(=\text{O})\text{CF}_3$	BuOH	60	0

^a Yields of pure isolated products. ^b Products are characterised by spectral analysis.

acetate [Scheme 2, eqn. (2)] showed selective deprotection of the aryl acetates. 4-Chlorophenyl acetate in the presence of methyl cinnamate [Scheme 2, eqn. (3)] and 4-fluorophenyl acetate in the presence of methyl 2,4-dichlorophenoxy acetate [Scheme 2, eqn. (4)] underwent selective cleavage of the aryl acetates. During intramolecular competitions, selective deprotection of the aryl acetate over that of benzyl acetate (entry 10), methyl ester [Scheme 2, eqn. (5)], and benzoate [Scheme 2, eqn. (6)] took place when 4-acetoxybenzyl acetate (entry 10),

methyl 4-acetoxybenzoate and 4-benzyloxy phenyl acetate were mixed with a stoichiometric amount of NaBO_3 in methanol at 25 °C for the specified time (Scheme 2). Selective deprotection of the aryl acetate took place in the competitions with aryl methyl ether and benzoate during which the aryl methyl ether and ethyl benzoate remained unaffected [Scheme 2, eqn. (1)].

The tolerance of different protecting groups to these reaction conditions illustrates the flexibility and generality of the



Scheme 2

protocol. The attempts to deprotect the aryl acetate using a catalytic amount of NaBO_3 failed and a catalytic amount of sodium perborate with H_2O_2 gave a complex mixture of products.

In conclusion the present results demonstrate a novel use of sodium perborate, which shows unique selectivity and constitutes a useful alternative to commonly accepted deacylation procedures. Moreover, the superiority and flexibility of the protocol lies in its ease of operation and simplicity in work-up, which involves mere filtration of the reagent. Clean deprotection under mild and neutral conditions using this cheap and easily available reagent make this simple protocol economically attractive.

Experimental

In the general procedure the aryl acetate (5 mmol) and sodium perborate (5 mmol) were stirred in methanol (10 ml) at 25 °C. After completion of the reaction (TLC), NaBO_3 was filtered off and washed with ethyl acetate (2×5 ml). The solvent was removed under vacuum to give the phenol in almost pure form, which was further purified by column chromatography on SiO_2 (hexane–ethyl acetate = 9 : 1) if necessary. All products are known compounds, which were characterized by their physical constants,¹⁹ spectral analysis and comparison with authentic samples.

Acknowledgements

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