Electro-oxidative Neutral Deprotection of *S*-t-Butyl Thioates to give Carboxylic Acids

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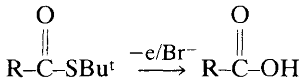
t-Butyl thioates are proposed as a convenient protecting group for carboxylic acids, because their deprotection under neutral conditions can be attained by electro-oxidation using bromide salts as electrolytes in aqueous acetonitrile.

A number of ester groups have been presented for the protection of carboxylic acids depending on deprotection requirements such as acidic or alkaline conditions.[1,2] Along with the frequently used reductive cleavage of benzylic esters, deprotection methods under neutral conditions have been devised using the electroreduction of 2,2,2-trichloroethyl esters,[3] photolyses of *o*-nitro aromatic esters,[4] and treatment of silyl esters with water.[5] Recently, an oxidative deprotection of *p*-methoxybenzylic esters was developed, where triarylamines were used as an electron transfer agent.[6] Here, t-butyl thioates (**1**) are proposed as a convenient way of protecting carboxylic acids because the neutral deprotection can be attained electro-oxidatively.



$$\mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}SBu^t} \xrightarrow[\mathrm{H_2O}]{-\mathrm{e/Br^-}} \mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH}$$

(**1**) (**2**)

Thioates can be readily prepared by the diimide condensation of carboxylic acids with thiols catalysed by 4-dimethylaminopyridine.[7] Electrolyses of *S*-alkyl or *S*-phenyl cyclohexanecarbothioate in aqueous acetonitrile† were found to cause hydrolysis to give the starting acid. As compared with the ethyl and phenyl analogues, the *S*-t-butyl ester was a promising protecting group, since it shows greater resistance towards hydrolyses under both alkaline and acidic conditions. Suitable electrolytes were bromide or chloride salts, and other applicable electrolytes were KF, LiI, $LiNO_3$, Bu_4NBF_4, and Bu_4NClO_4. Bromides and chlorides showed relatively high current efficiencies probably due to the mediation of bromonium or chloronium ions generated electrochemically.[8]

As a typical procedure, a solution of (**1**) (2 mmol) in $MeCN-H_2O$ (9:1 v/v, 25 ml) containing an appropriate electrolyte (0.1 M) was electrolysed at a constant current of 0.2 A in an undivided cell equipped with platinum electrodes (1 × 2 cm^2) at ambient temperature until almost all of (**1**) was consumed (*ca.* 2 h). The electrolysate was immediately extracted with diethyl ether to give the parent acid (**2**) after the usual work-up.

The results in Table 1 show that the deprotection of thioates can be accomplished using *ca.* 8 F mol^{-1} to afford high yields of acids. Products from the residue were water-soluble substance(s) identified as 2-methylpropane-2-sulphonic and/or -sulphinic acid. Hence, the present electrolysis involves an oxidative cleavage of the *S*-t-butyl group.

Electrolyses of (**1**; R = C_6H_{11}) were conducted in the presence of several kinds of compounds with different functional groups in order to examine their stability during the present deprotection. Sufficient stabilities were observed with tertiary-alcohols, ketones, esters, and α,β-unsaturated ketones or esters, but not with those compounds susceptible to oxidation such as primary or secondary alcohols, aldehydes, non-conjugated olefins, and amines. To avoid the hydrolysis of acid-sensitive functional groups, the use of weak bases is

Table 1. Electrolytic deprotection of (**1**) to give (**2**).

R in (**1**)	Electrolyte	F mol^{-1}	Yield of (**2**)/%[a]
cyclo-C_6H_{11}	LiBr	7	87
	Bu_4NBr	7	94
$Me[CH_2]_4$	LiCl	8	83
	LiBr	8	96
Ph	Bu_4NBr	11	94

[a] Yields were determined by g.l.c. of diethyl ether extracts after methylation with diazomethane.

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† As the aqueous organic solvent, acetonitrile was preferred to methanol to avoid any reactions with the solvent.

advantageous since acids formed as the byproducts are neutralized. For example, triphenylmethyl cyclohexanecarboxylate was completely hydrolysed to the starting acid and alcohol during the previous electrolysis of (**1**; R = C_6H_{11}); the electrolysis of the same mixture in the presence of an equivalent amount of sodium hydrogen carbonate resulted in a good yield of (**2**) and complete recovery of the trityl ester. The *p*-methoxybenzyl ester, which undergoes the electron transfer deprotection,[6] remained unchanged under the electrolytic conditions involving the weak base; thus, this electro-oxidative method enables a selective deprotection of t-butyl thioates.

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