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A NEW METHOD FOR THE PREPARATION OF TERTIARY BUTYL ETHERS AND ESTERS

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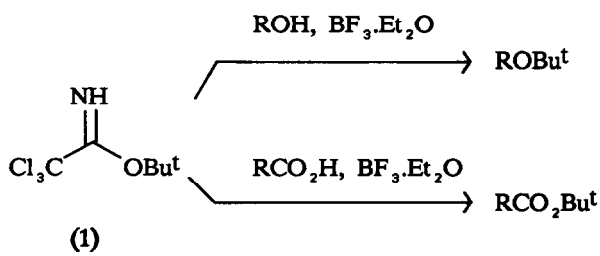
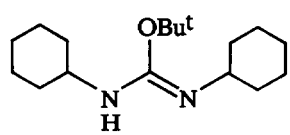
Summary: T-butyl 2,2,2-trichloroacetimidate **(1)**, *readily prepared by addition of t-butanol to trichloroacetonitrile, is an efficient reagent for the preparation of t-butyl ethers and esters in the presence of a catalytic amount of boron trifluoride etherate.*

Traditional methods for the preparation of t-butyl ethers and esters rely upon the use of isobutene in the presence of strong acid (*e.g.* concentrated sulphuric acid[1,2] or phosphoric acid in the presence of boron trifluoride etherate[3]) for generation of the t-butyl cation. More recent methods for the preparation of t-butyl esters involve conversion of a carboxylic acid to a mixed anhydride, followed by addition of t-butanol.[4] An alternative approach, due to Vowinkel,[5] involves treatment of the carboxylic acid with O-t-butyl-N,N'-dicyclohexyl isourea **(2)**. Unfortunately **(2)** cannot be easily purified, and yields of t-butyl esters are only moderate. In addition, it is necessary to free the product from dicyclohexyl urea, which can be difficult. We now report a mild and effective method for the conversion of alcohols and acids directly to the corresponding t-butyl derivatives using t-butyl trichloroacetimidate **(1)** in the presence of a catalytic amount of boron trifluoride etherate (Scheme 1). This method has the advantage that it is more compatible with acid sensitive functionality than the traditional methods using isobutene, is more amenable to small scale work (avoiding the handling of gaseous isobutene), and has allowed the selective protection of the less hindered hydroxyl group of a diol.



(1)



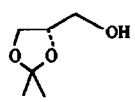
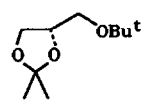
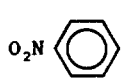
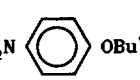
(2)

Scheme 1

Alkyl trichloroacetimidates were first prepared by Cramer,[6] who further investigated their rearrangement to N-alkyl trichloroacetamides.[7] More recently, trichloroacetimidates have found use in the synthesis of allylic amines,[8] the formation of glycosidic bonds[9] and the preparation of benzyl and allyl ethers in the presence of trifluoromethanesulphonic acid.[10–12] We envisaged that t-butyl trichloroacetimidate (1) would be a more convenient source of t-butyl cation than isobutene in the preparation of tertiary butyl ethers and esters. The required t-butyl trichloroacetimidate (1) was prepared by a modification[13] of the literature method.[6]

Primary alcohols are converted to the corresponding t-butyl ethers by treatment with t-butyl trichloroacetimidate (1.1 eq.) in cyclohexane (2 ml/mmol of alcohol) at room temperature, on addition of a catalytic amount of boron trifluoride etherate (20 μl/mmol). Work-up involves addition of solid $NaHCO_3$, filtration of the reaction mixture through a short plug of silica to remove trichloroacetamide, and finally removal of solvent. If the alcohol is insoluble in cyclohexane alone, use of a mixture of cyclohexane (2 ml/mmol) and dichloromethane (1 ml/mmol) is possible.[14] Secondary alcohols generally require 2 equivalents of acetimidate (1) for complete conversion. This must reflect the slower rate of reaction of the more sterically congested hydroxyl group, which competes less effectively with the decomposition of t-butyl trichloroacetimidate (1) to isobutene.[6] In the absence of a nucleophilic group, treatment of t-butyl trichloroacetimidate in cyclohexane with a catalytic amount of boron trifluoride etherate at room temperature led to complete decomposition of (1) within 10 minutes. Our results for the preparation of t-butyl ethers are detailed in Table 1.

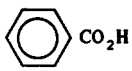
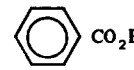
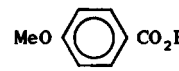
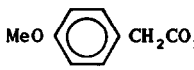
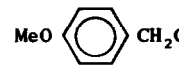
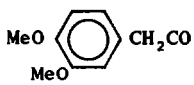
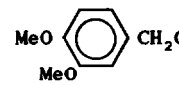
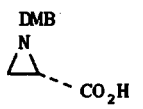
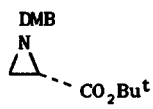
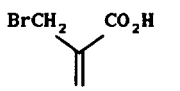
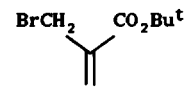
TABLE 1

Substrate	(1), Equiv.	Time, h	Product	Yield, %[a]
$PhCH_2OH$	1.1	21	$PhCH_2OBu^t$	72
$Ph(CH_2)_2OH$	1.1	19	$Ph(CH_2)_2OBu^t$	91
$C_{15}H_{29}CH_2OH$	1.1	16	$C_{15}H_{29}CH_2OBu^t$	69
	1.1	19		58
$PhCH_2OCH_2CH(OH)CH_2OH$ [b]	1.1	21	$PhCH_2OCH_2CH(OH)CH_2OBu^t$	67
$PhCH(OH)CH_3$	2	21	$PhCH(OBu^t)CH_3$	72
 [c]	4	16		68

[a] Yields of homogeneous isolated material. [b] Solvent: CH_2Cl_2 (1 ml/mmol) and Cyclohexane (4 ml/mmol). [c] Solvent: CH_2Cl_2 (2 ml/mmol) and Cyclohexane (4 ml/mmol).

Treatment of carboxylic acids with t-butyl trichloroacetimidate (1) constitutes a straightforward method for the preparation of t-butyl esters. Since most carboxylic acids are insoluble in cyclohexane, the carboxylic acid is first dissolved in dichloromethane (1 ml/mmol of acid), then a solution of (1) (2 eq.) in cyclohexane (2 ml/mmol) is added, followed by boron trifluoride etherate (20 μl/mmol). Work-up as for the t-butyl ethers leads to good yields of the corresponding t-butyl esters. Our results are detailed in Table 2.

TABLE 2

Substrate	Time, h	Product	Yield, %[a]
	16		92
 [b]	16		83
	16		74
	16		97
$PhCH(CH_3)CO_2H$	16	$PhCH(CH_3)CO_2Bu^t$	85
$CH_3CO(CH_2)_2CO_2H$	16	$CH_3CO(CH_2)_2CO_2Bu^t$	83
$BrCH_2CO_2H$	16	$BrCH_2CO_2Bu^t$	71
	16		70
DMB = 4,4'-dimethoxybenzhydryl			
	16		54

[a] Yields of homogeneous isolated material. [b] Solvent: CH_2Cl_2 (2 ml/mmol) and Cyclohexane (4 ml/mmol).

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13. Potassium t-butoxide (1.68 g, 15 mmol) was dissolved in t-butanol (30 ml) and dry diethyl ether (30 ml) and this solution was added over 15 min to a stirred solution of trichloroacetonitrile (21.6 g, 15 ml, 150 mmol) in dry diethyl ether (30 ml) cooled to 0 °C under nitrogen. The yellow mixture was allowed to warm to 20 °C over 1 h, and then heated at reflux for 1 h. After the reaction mixture had been cooled to room temperature, volatiles were removed on the rotary evaporator and the residual oil was dissolved in n-pentane (30 ml). The solution was filtered and pentane was removed on the rotary evaporator. The residue was then distilled to yield t-butyl trichloroacetimidate (23 g, 70 %), b.p. 65-69 °C/12 mm Hg, which solidified on storage. ^{1}H N.m.r. (60 MHz, $CDCl_3$) δ 1.55 (9H, s, *But*) and 8.2 (1H, br. s, N*H*).
14. We have found that the use of more polar solvent mixtures gives poor results due, presumably, to the more rapid decomposition of t-butyl trichloroacetimidate (**1**) in solvents in which ionisation is favoured.

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