

Nitrolysis of Carboxylic *t*-Butyl and 1-Adamantyl Esters

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Received 3 July 1998; accepted 1 October 1998

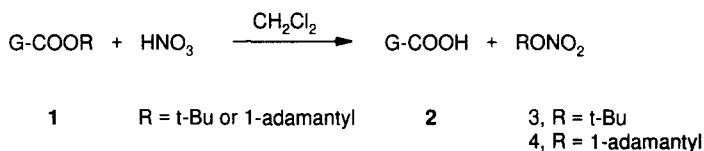
Abstract

A cheap, less problematic, efficient and selective reagent for the removal of the *t*-butyl and 1-adamantyl protecting groups from carboxylic esters was found to be commercial 100% HNO₃ in CH₂Cl₂. Incidentally, 1,1-dimethylethyl nitrate and tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) nitrate are coproducts in a clean reaction. The procedure is in many ways superior to the method employing CF₃COOH. © 1998 Published by Elsevier Science Ltd. All rights reserved.

Keywords: Carboxylic acids and derivatives; Deblocking; Nitric acid and derivatives; Protecting groups



t-Butylation of free carboxylic acids is a widespread procedure for the protection of the carboxyl function, receiving continuous attention in many fields of chemistry.² The same kind of protection of the carboxyl function is also achieved by formation of 1-adamantyl esters.³ Removal of the protecting groups is usually performed in a number of ways,^{2a,4} among which the procedure using excess CF₃COOH (TFA), neat or in its concentrated CH₂Cl₂ (or other suitable solvent) solution, is, by and large, the most common.⁵ Under these acidic conditions, reactive substrates may be attacked by *t*-butyl cations present in high concentrations:⁶ *inter alia*, thiols, thioethers, anisole and triethylsilane may be added as scavengers to avoid unwanted reactions with the substrate.⁷

Scheme 1



We now find that treating a number of *t*-butyl esters **1**, prepared from carboxylic acids with different steric properties and potentially reactive functionality, with only twice the stoichiometric amount of commercial 100% HNO₃ (d = 1.50) in CH₂Cl₂ at 0 °C for 2 h, yields, in a smooth reaction, the complete restoration of the free organic acid, accompanied by the almost quantitative formation of 1,1-dimethylethyl nitrate (**3**) (Scheme 1, Table 1).

Table 1Nitrolysis of *t*-butyl and 1-adamantyl esters of various carboxylic acids (Scheme 1) ^{a,10}

Entry	Substrate 1	Acid 2 (%) ^b
1	CH ₃ COO <i>t</i> -Bu (1a)	98 (n. d.) ^c
2	CH ₃ COCH ₂ COO <i>t</i> -Bu (1b)	92 (20) ^d
3	(CH ₃) ₃ CCOO <i>t</i> -Bu (1c)	99 (91)
4	CH ₃ (CH ₂) ₄ COO <i>t</i> -Bu (1d)	98 (95)
5	(<i>E</i>)-C ₂ H ₅ CH=CHCH ₂ COO <i>t</i> -Bu (1e)	97 (90)
6	PhCH ₂ COO <i>t</i> -Bu (1f)	99 (96)
7	(<i>E</i>)-PhCH=CHCOO <i>t</i> -Bu (1g)	98 (96)
8	PhCOO <i>t</i> -Bu (1h)	99 (97)
9	CH ₃ COO-  (1i)	97 (n. d.)
10	CH ₃ COO-  (1m)	0 (0)

^a Unless otherwise specified, the reaction was carried out by treating a chilled solution of the ester **1** (50 mmol) in CH₂Cl₂ (30 mL) at 0 °C for 2 h with a solution of commercial 100% HNO₃ (106 mmol) in CH₂Cl₂ (20 mL), pouring the reaction mixture into 10% aqueous Na₂CO₃ (100 mL), washing with Et₂O (2 x 30 mL), acidifying the separated aqueous phase with concentrated HCl, extracting with Et₂O (2 x 50 mL), drying over Na₂SO₄ and eventually evaporating the solvent. 1,1-Dimethylethyl nitrate (**3**) and tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) nitrate (**4**) were obtained by drying over Na₂SO₄, evaporating the solvent and finally distilling the residue of the combined ethereal phases resulting from the Na₂CO₃ solution washing.

^b Reported conversions were determined by ¹H NMR on intact reaction mixtures, after dilution with CDCl₃: the spectra for all reactions revealed only the resonances of unreacted **1** and the products **2**, **3**, and **4**. Yields of separated acids are in parentheses.

^c n. d. : not determined.

^d Isolated as the methyl ester after treating of the final ethereal solution with a suitable amount of ethereal CH₂N₂. The low separated yield of the methyl ester of **2b** is consistent with the work up procedure of isolation of the corresponding acid (**2b**), notoriously a very unstable compound, from the reaction mixture.

2-Methylpropene, a possible reaction product by proton abstraction from the intermediate *t*-butyl cation, was absent (< 1%), as well as 2-methyl-2-propanol. Tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) acetate (**1i**) reacted similarly under the same conditions, yielding tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) nitrate (**4**) as the sole fate of the protecting moiety.

The soft, but efficient nature of HNO₃ in CH₂Cl₂, is clearly apparent from the result of the reaction: oxidations of double bonds or benzylic hydrogens did not take place, nor was there any evidence for additions or aromatic substitutions, in sharp contrast to earlier reports.⁸ This latter fact is particularly notable for the reaction with 1,1-dimethylethyl benzeneacetate (**1f**), if one thinks that other esters of this acid underwent smooth 100% nitration with HNO₃ in CH₂Cl₂.⁹ The reaction appears particularly selective and efficient because of the prompt formation of the carbenium ion, followed by its fast capture by NO₃⁻. The observed higher efficiency of this system, in comparison with the solvolysis with TFA, may be attributed to a

higher concentration of NO_3^- , possibly closely associated with emerging *t*-butyl or 1-adamantyl cation, at hand than that of free CF_3COO^- in the case of CF_3COOH . Incidentally, the $\text{S}_{\text{N}}1$ reaction mechanism may be inferred by the unreactivity of 7,7-dimethylbicyclo[2.2.1]hept-1-yl (1-apocamphanyl) acetate (**1m**), which is unable to form the corresponding carbenium ion.

The superiority of the present procedure, compared to the TFA one, is evidenced, *inter alia*, by some rough rate measurements. Using the same molar ratio acid (Table 1, note a) vs. *t*-butyl acetate (**1a**), nitrolysis was found to occur much faster than trifluoroacetolysis (Table 2). A reduced concentration of acidic, hydrogen bonding and solvating material, as used in our experiments, offers the advantage of a medium less prone to catalyze carbenium ion formation and so any subsequent related reaction.

Table 2

Comparison of deprotection rates of *t*-butyl acetate (**1a**) using HNO_3 or CF_3COOH

Reaction conditions ^a	Conversion into 2a (%) ^b	
	HNO_3	CF_3COOH
0 °C, 1 h	92	15
0 °C, 2 h	97	37
rt, 1 h	-	58
rt, 72 h	-	97

^a See note a in Table 1.

^b Determined by ^1H NMR on intact reaction mixtures, after dilution with CDCl_3 .

Aknowledgements

This work was supported in part by grants to AGG (CNR 95.01044CT03, 96.02740CT03, 97.02807CT03) and to PS (MURST 1994, 40%). We are indebted to Prof. G. Verardo for MS data collection, Mr. P. Polese and Mr. V. Tosoratti for skillful assistance.

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10. All the compounds reported in the present work which were not commercially available were fully characterized by spectroscopic techniques (IR, ^1H and ^{13}C NMR, MS).
 100% HNO_3 was purchased from Hydro Chemicals France (Nanterre, France) and used as received.
 1,1-Dimethylethyl 2,2-dimethylpropanoate (**1c**). Prepared from 1,1-dimethylethanol and 2,2-dimethylpropanoyl chloride in pyridine: 88% yield, bp 47 °C/4000 Pa;^{2c} ν_{max} (KBr, film) 2979, 1727, 1481, 1394, 1369, 1292, 1149, 854, 758 cm^{-1} ; δ_{H} (200 MHz, CDCl_3 , TMS) 1.15 (9H, s), 1.43 (9H, s); ^{13}C NMR;¹¹ MS (EI, 70 eV, m/z (%)) 143 (5), 85 (19), 59 (7), 57 (100), 41 (18).
 1,1-Dimethylethyl hexanoate (**1d**). Prepared from 1,1-dimethylethanol and hexanoyl chloride in pyridine: 95% yield, bp 66 °C/1066 Pa;¹² ν_{max} (KBr, film) 2961, 2933, 1734, 1457, 1368, 1253, 1156 cm^{-1} ; δ_{H} (50 MHz, CDCl_3 , TMS) 173.21, 79.74, 35.48, 31.21, 28.01, 24.72, 22.28, 13.84; MS (EI, 70 eV, m/z (%)) 117 (49), 116 (11), 100 (10), 99 (100), 57 (21).
 1,1-Dimethylethyl (*E*)-3-hexenoate (**1e**). Prepared according to the procedure reported in ref. 2b: 41% yield, bp 71 °C/1466 Pa; ν_{max} (KBr, film) 2969, 1735, 1369, 1257, 1151, 968, 848 cm^{-1} ; δ_{H} (200 MHz, CDCl_3 , TMS) 0.99 (3H, t, $J = 7.4$ Hz), 1.45 (9H, s), 2.04 (2H, m), 2.94 (2H, d, $J = 5.5$ Hz), 5.40–5.66 (2H, m); δ_{C} (50 MHz, CDCl_3 , TMS) 171.56, 135.73, 121.12, 80.24, 39.17, 28.00, 25.45, 13.43; MS (EI, 70 eV, m/z (%)) 170 (M^+ , 1), 114 (100), 97 (89), 69 (91), 57 (84), 41 (58).
 1,1-Dimethylethyl benzeneacetate (**1f**).¹³
 1,1-Dimethylethyl (*E*)-benzenepropenoate (**1g**). Prepared from 1,1-dimethylethanol and (*E*)-benzenepropenoyl chloride in pyridine: 89% yield, bp 103 °C/133 Pa.¹⁴
 1,1-Dimethylethyl benzoate (**1h**). Prepared from 1,1-dimethylethanol and benzoyl chloride in pyridine: 92% yield, bp 115 °C/2933 Pa;¹⁵ ν_{max} (KBr, film) 2979, 1713, 1451, 1369, 1294, 1256, 1169, 1116, 1027, 849, 711 cm^{-1} ; ^1H and ^{13}C NMR;¹⁵ MS (EI, 70 eV, m/z (%)) 178 (M^+ , 1), 124 (18), 123 (100), 122 (19), 105 (76), 77 (14).
 Tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) acetate (**1i**) and 7,7-dimethylbicyclo[2.2.1]hept-1-yl (1-apocamphanyl) acetate (**1m**).¹⁶
 3-Oxobutanoic acid (**2b**).¹⁷ δ_{H} (200 MHz, CDCl_3 , TMS) 2.32 (3H, s), 3.53 (2H, s), 7.25 (1H, br s); δ_{C} (50 MHz, CDCl_3 , TMS) 201.74, 171.04, 49.08, 30.21.
 1,1-Dimethylethyl nitrate (**3**).¹⁸ See Table 1, note a: 60% yield, bp 24 °C/2000 Pa;¹⁹ IR;²⁰ δ_{H} (200 MHz, CDCl_3 , TMS) 1.55 (9H, s); δ_{C} (50 MHz, CDCl_3 , TMS) 89.93, 26.60; MS (EI, 70 eV, m/z (%)) 104 (14), 61 (38), 59 (36), 58 (35), 43 (100).
 Tricyclo[3.3.1.1^{3,7}]dec-1-yl (1-adamantyl) nitrate (**4**). See Table 1, note a: 66% yield, mp 104 °C (pentane).²¹
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