A General Convenient One-Pot Procedure for the Conversion of Carboxylic Acids into their *t*-Butyl Esters which is also Applicable to Aliphatic Carboxylic Acids

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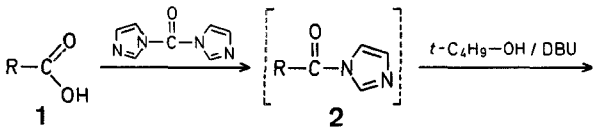
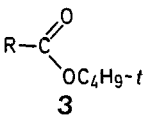
Although the *t*-butyl group is frequently used for carboxy-group protection in selective conversions of complex molecules, the known methods[1-8] for the direct synthesis of *t*-butyl carboxylates from the acids have several drawbacks such as the necessity to use inconvenient to handle reagents (e.g., phosgene, isobutene), tedious procedures, narrow range of applicability, etc. Thus, the otherwise useful method of treating a *N*-acylimidazole (**2**; formed from the carboxylic acid **1** and *N,N'*-carbonyldiimidazole) with *t*-butanol in the presence of 0.1–0.2 mol equiv of sodium *t*-butoxide[3] is not applicable to alkanoic acids having one or two H-atoms at C-2 because of the competitive formation of 3-oxoalkanoic esters. Similar limitations and probably also incompatibility with unsaturated carboxylic acids are encountered with a modification of this method in which an isolated *N*-acylimidazole (**2**) is treated with *t*-butanol in the presence of an equimolecular amount of *N*-bromosuccinimide[6]. We have now found that the reaction of *N*-acylimidazoles (**2**) with *t*-butanol can be accelerated by using DBU (1,8-diazabicyclo[5.4.0]-7-undecene) as base.





Our modification may be applied to carboxylic acids of various types: aromatic carboxylic acids, alkanoic acids having hydrogen atoms at C-2, and 2-alkenoic acids. It is not applicable, however, to pivalic acid (**1**, R = *t*-C_4H_9; less than 10% yield even after prolonged heating at 80 °C) and to *N*-acyl-α-amino acids (formation of complex mixtures, probably by oxazolone formation and subsequent reactions). The basic reaction medium used makes our method particularly useful for application to acid-sensitive compounds.

t-Butyl 2-Chlorobenzoate (3b):
N,N'-Carbonyldiimidazole (1.65 g, 10 mmol) is added to a solution of 2-chlorobenzoic acid (**1b**; 1.57 g, 10 mmol) in dimethylformamide (10 ml) under nitrogen and the mixture is stirred for 1 h at 40 °C. *t*-Butanol (1.48 g, 20 mmol) and DBU (1.52 g, 10 mmol) are added and the mixture is stirred at 40 °C for 24 h. Ether (100 ml) is then added, the solution is washed with 10% hydrochloric acid (20 ml), water (20 ml), and aqueous 10% potassium carbonate (20 ml), and it is dried with sodium sulfate. The solvent is removed and the oily residue distilled in vacuo; yield: 1.80 g (85%); b.p. 135–140 °C/2 torr.

t-Butyl Pyridine-3-carboxylate (3d, t-Butyl Nicotinate):
The procedure is performed as above using *N,N'*-carbonyldiimidazole (1.65 g, 10 mmol), nicotinic acid (**1d**; 1.23 g, 10 mmol), dimethylformamide (10 ml), *t*-butanol (1.48 g, 20 mmol), and DBU (1.52 g, 10 mmol).

Work-up: Ether (100 ml) is added to the mixture, the solution is washed with 10% acetic acid (20 ml), water (20 ml), and aqueous 10% potassium carbonate (20 ml), and is dried with sodium sulfate. The solvent is removed and the oily residue distilled in vacuo; yield: 1.51 g (84%); b.p. 130–135 °C/2 torr.

t-Butyl *trans*-2-(3,4-Methylenedioxyphenyl)-3-cyclohexene-1-carboxylate (3j):
The procedure is performed as above using *N,N'*-carbonyldiimidazole (0.83 g, 5 mmol), *trans*-2-(3,4-methylenedioxyphenyl)-4-cyclohexene-1-carboxylic acid (**1j**; 1.23 g, 5 mmol), *t*-butanol (0.74 g, 10 mmol), and DBU (0.76 g, 5 mmol). The reaction time is 5 h at 80 °C. Work-up is as described for **3b**; the crude oily product is distilled in vacuo; yield: 0.92 g (61%); b.p. 168–172 °C.

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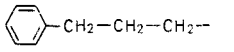
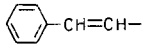
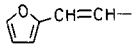
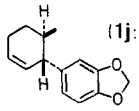
Table 1. *t*-Butyl Carboxylates (**3**) prepared

3	R	Reaction conditions [°C], [h]	Yield[a] [%]	b.p./torr[b] [°C]	n_D^{20}	Molecular formula or b.p./torr [°C] (Refractive Index) reported	High-Resolution M.S. *m/e* of M^+
a		40°, 5	91	128–130°/5	1.4911	94°/10[9] (n_D^{20}: 1.4908)[3]	
b	 (**3b**: Ref.[10])	40°, 24	85	135–140°/2	1.5052	131–132°/17[10] (n_D^{25}: 1.5024)[10]	
c		40°, 10	75	150–155°/2	1.4847	$C_{11}H_{14}O_3$ (220.14633)	220.14099
d		40°, 6	84	130–135°/2	1.4870	108°/8[11]	
e	n-C_6H_{13}	40°, 5	76	103–106°/2	1.4156	$C_{11}H_{22}O_2$ (186.16235)	186.16198
f	$H_3C-CH_2-CH_2-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-$	40°, 24	85	104–105°/8	1.4066	60–61°/59[10] (n_D^{25}: 1.3986)[10]	
g		40°, 15	74	109–110°/5	1.4399 (n_D^{25}: 1.4378)	82.5–85.5°/9[12] (n_D^{25}: 1.4370)[12]	
h		40°, 24	64	150–155°/2	1.5385 (n_D^{16}: 1.5402)	160°/4[13] (n_D^{16}: 1.5414)[13]	
i		40°, 24	54	120–125°/2	1.5247	$C_{11}H_{14}O_3$ (194.09429)	194.09149
j	 (**1j**: Ref.[14])	80°, 5	68	168–172°/1	1.5248	$C_{18}H_{22}O_4$ (302.15181)	302.15616

[a] Yield of isolated product.
[b] Bath temperature of Kugelrohr vacuum distillation.

Table 2. I.R.- and ^{1}H-N.M.R. Spectra of the New Compounds **3**

3	I.R. ($CHCl_3$) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (80 MHz, $CDCl_3$/TMS_{int}) δ [ppm]
c	1715	7.2 (m, 5 H_{arom}); 2.65 (t, 2H, CH_2—CO, J=8 Hz); 2.35–1.7 (m, 4H, CH_2—CH_2—CH_2—CO); 1.40 [s, 9H, $C(CH_3)_3$]
e	1725, 1717 (branched)	1.95 [s, 9H, —$C(CH_3)_3$]; 2.3–1.0 (m, 13H, other protons)
i	1700	7.40 (d, 1H, —O—CH=, J=2 Hz); 7.30 (d, 1H, —CH=CH—CO, J=12 Hz); 6.60 (d, 1H, O—CH=CH—CH=, J=4 Hz); 6.40 (dd, 1H, O—CH=CH—, J=2 Hz, 4 Hz); 6.35 (d, 1H, —CH=CH—COO, J=12 Hz); 1.55 [s, 9H, —$C(CH_3)_3$]
j	1715	6.65 (s, 3 H_{arom}); 5.90 (s, 2H, O—CH_2—O); 5.95–5.4 (m, 2 H_{olefin}); 3.75–3.4 (m, 1H, benzylic methine H); 2.55–1.5 (m, 5H, —CH_2—CH_2—CH—COO); 1.35 [s, 9H, —$C(CH_3)_3$]

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