Transformation of Carboxylic Acid *t*-Butyl Esters *into the Corresponding Trimethylsilyl* Esters or Free Acids under Non-Acidic Conditions

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We report a method for the transformation, under non-acidic conditions, of *t*-butyl esters **6** to the corresponding trimethylsilyl esters **8** *or the respective free acids* **9**. *In a re*cent paper describing trimethylsilyl triflate (**2**) as a silylating agent[1], a "transalkylation" **1**→**3** is briefly mentioned to

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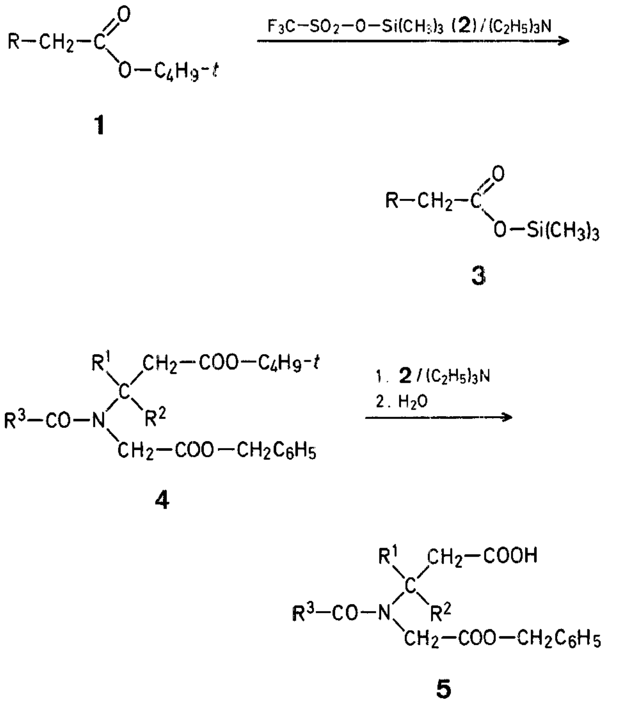
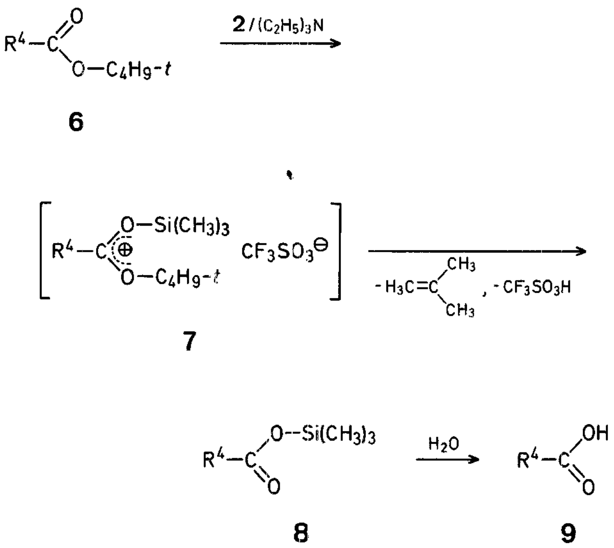
take place in ether at 0–5 °C, in the presence of triethylamine. We observed[2] the selective transformation of a mixed diester of the type **4** into a monoester of type **5** under similar conditions, but with a subsequent aqueous work up.

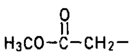
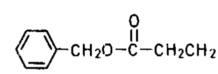
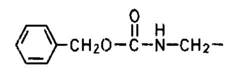
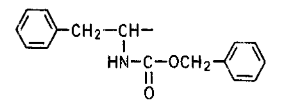
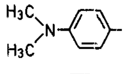
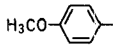
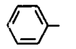
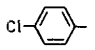
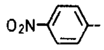


The species **5** is obviously formed via the corresponding mixed trimethylsilyl benzyl ester. These findings prompted us to study the scope and limitations of this type of reaction.



In most cases the reaction rate in ether is too slow for practical purposes. Boiling dioxan is the preferred reaction medium. Our results, obtained with ten different *t*-butyl esters under these conditions, are summarized in the Table. The

Table. Trimethylsilyl Esters **8** or Carboxylic Acids **9** from *t*-Butyl Esters **6**

Entry	R^4	Reaction time [min][a]	Trimethylsilyl ester **8**			Carboxylic Acid **9**		
			Yield [%]	b.p. [°C]/torr	Molecular Formula[b] or Lit. b.p. [°C]/torr	Yield [%]	m.p. [°C]	Lit. m.p. [°C]
1	$n\text{-}C_5H_{11}-$	20	82	95–100°/23	50–55°/0.5	—		
2	 $H_3CO-\overset{O}{\overset{\parallel}{C}}-CH_2-$	20	87	105–110°/19	$C_7H_{14}O_4Si$ (190.3)	—		
3		3	79	115–125°/0.05	$C_{14}H_{20}O_4Si$ (280.4)	—		
4		10	87	125–130°/0.05	148°/0.5	—		
5		30	—[c]			78	85–87°	85–87°
6[d]		5	>90	200°/21	$C_{12}H_{19}NO_2Si$ (237.4)	—		
7		30	—[c]			98	183–185°	182–184°
8		60	82	110–112°/10	221/760	—		
9		60	—[c]			89	237–239°	239–241°
10		240	—[c]			88	235–237°	237–239°

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[a] Reaction monitored by T.L.C. on silica gel plates with ether.

[b] The new products gave satisfactory microanalyses (C ±0.45, H ±0.20, N ±0.31).

[c] Not isolated.

[d] Starting material prepared by reacting 4-(dimethylamino)-benzoyl chloride with *t*-butyl alcohol in pyridine; yield: 57%; m.p. 56–57 °C.

$C_{13}H_{19}NO_2$	calc.	C 70.56	H 8.65	N 6.33
(221.3)	found	70.54	8.85	6.31

transformation of aliphatic *t*-butyl esters to the corresponding trimethylsilyl esters is completed within 3–20 min. α-Silylation[1] or ketene acetal formation[1] do not compete in the case of mixed esters (entry 3), or even with a mixed malonic ester (entry 2).

A benzyl ester grouping is stable under the reaction conditions (entry 3). In *N*-benzyloxycarbonyl-glycine *t*-butyl ester the *N*-protecting group is not affected (entry 4). *N*-Benzyloxycarbonyl-L-phenylalanine *t*-butyl ester can be transformed into *N*-benzyloxycarbonyl-L-phenylalanine without racemisation (78% yield).

The reaction rate of *t*-butyl benzoates depends upon the nature of the substituents (entries 6–10). Thus, the *p*-dimethylamino compound reacts roughly 50 times faster than the *p*-nitro derivative. This suggests transition states related to the carbenium ions **7**. Loss of isobutene and of a proton would lead to the trimethylsilyl esters **8**. – The free carboxylic acids **9** may be obtained after evaporation of the solvent from the crude reaction mixture by treatment with water.

Trimethylsilyl Benzoate from *t*-Butyl Benzoate; Typical Procedure:

To a mixture of *t*-butyl benzoate (**6**; $R^4 = C_6H_5$; 284.3 mg, 1.60 mmol) and triethylamine (193.7 mg, 1.91 mmol) in dry dioxan (10 ml) is added with stirring at room temperature under an argon atmosphere, trimethylsilyl triflate (**2**; 372.3 mg, 1.68 mmol). The mixture is heated under reflux for 1 h. The progress of the reaction is checked by T.L.C. (silica gel plates; ether; UV_{254} or vanillin/sulfuric acid). The dioxan is then removed in vacuo and the residue extracted with dry ether (3 × 5 ml). The ether layers are transferred with a pipet and evaporated. The crude trimethylsilyl benzoate (**8**; $R^4 = C_6H_5$) is purified by Kugelrohr distillation and obtained as an oil; yield: 241.7 mg (82%); b.p. 110–112 °C/10 torr (Lit.[3] b.p. 221 °C/760 torr).

***N*-Benzyloxycarbonyl-L-phenylalanine from *N*-Benzyloxycarbonyl-L-phenylalanine *t*-Butyl Ester:**

To a dioxan solution (5 ml) of *N*-benzyloxycarbonyl-L-phenylalanine *t*-butyl ester (515.8 mg, 1.45 mmol) and triethylamine (352.4 mg, 3.48 mmol) is added dropwise with stirring at room temperature under an argon atmosphere, trimethylsilyl triflate (**2**; 677.3 mg, 3.05 mmol). After 30 min of heating under reflux, the pink coloured solution is evaporated in vacuo, the residue diluted with water, and the resulting oil extracted with ether (2 × 25 ml). The ether solution is washed with brine, dried with sodium sulfate, filtered, and evaporated. The product is crystallized from ethyl acetate/petroleum ether (30–60 °C) to give *N*-benzyloxycarbonyl-L-phenylalanine, identical in every respect (including ORD) with an authentic sample[4]; yield: 341.3 mg (78%); m.p. 85–87 °C.

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[1] H. Emde, G. Simchen, *Synthesis* **1977**, 867.

[2] J. Borgulya, K. Bernauer, unpublished results.

[3] H. H. Anderson, *J. Am. Chem. Soc.* **74**, 2371 (1952).

[4] Sample from Fluka A. G., Buchs, Switzerland.