α-Substitution of 2-Alkenoic Esters via α-Carbanion Intermediates

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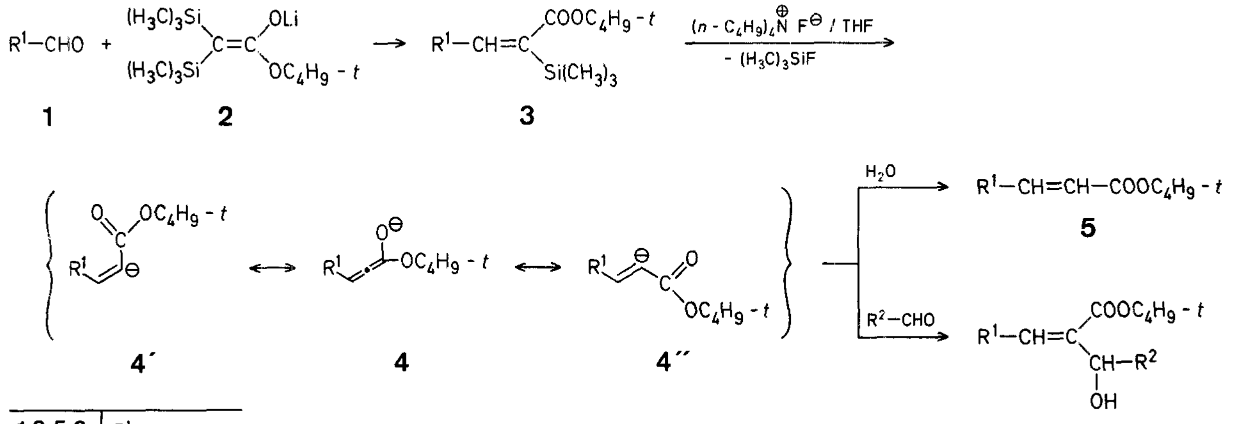
A direct method for the α-substitution of 2-alkenoic esters would consist of the generation of the α-carbanion followed by the addition of an appropriate electrophile. However, the usefulness of such an anion intermediate has not been generally recognized in synthetic chemistry because the removal of a proton from a 2-alkenoic ester having an H-atom at C-4 does not afford a vinyl anion but an allyl anion[1].

We recently reported that the fluoride ion-induced desilylation of (*E*)-2-trimethylsilyl-2-alkenenitriles gives stereospecifically (*Z*)-1-cyano-1-alkenyl anion intermediates, which may be converted into (*Z*)-2-alkenenitriles or (*E*)-2-(1-hydroxyalkyl)-2-alkenenitriles with retention of configuration[2]. We now describe the formation of the α-carbanions of *t*-butyl 2-alkenoates by a similar desilylation and the reaction of these carbanions with water or aldehydes as electrophiles.

The *t*-butyl 2-trimethylsilyl-2-alkenoates (**3**) used as startin compounds were prepared from aldehydes (**1**) and the lithiu enolate of *t*-butyl bis[trimethylsilyl]acetate (**2**) by a modification of the method of Ref.[3] (Table 1). All products **3** were obtained as mixtures of stereoisomers.

The C—Si bond in **3** is readily cleaved by treatment of compounds **3** with tetrabutylammonium fluoride in tetrahydrofuran even at low temperature (−20°C or −78°C). Desilylatio in moist tetrahydrofuran leads to the formation of *t*-butyl 2-alkenoates (**5**) in high yields (Table 2) whereas desilylation of in the presence of an aldehyde affords *t*-butyl 2-(1-hydroxyalkyl)-2-alkenoates (**6a–e, 7a, 7b**) in good yields (Table 3).

The (*Z*/*E*)-ratios of products **5, 6,** and **7** differ considerabl from those of the starting compounds **3.** As was found for tw representative examples (**6c, 6d**) these (*Z*/*E*)-ratios are nearl the same for reaction temperatures of −20°C and −78°C This suggests that the intermediate anion exists in a keten acetal form (**4**) rather than in a (*Z*)- or (*E*)-1-*t*-butoxycarbonyl-1-alkenyl anion form (**4′** or **4″**, respectively).



1,3,5,6	R¹
a	$n\text{-}C_3H_7\text{—}\underset{CH_3}{\underset{\vert}{CH}}\text{—}$
b	$n\text{-}C_7H_{15}$
c	$n\text{-}C_4H_9\text{—}\underset{C_2H_5}{\underset{\vert}{CH}}\text{—}$
d	$c\text{-}C_6H_{11}$
e	C_6H_5

6 $R^2 = C_6H_5$

7a $R^1 = R^2 = n\text{-}C_3H_7\text{—}\underset{CH_3}{\underset{\vert}{CH}}\text{—}$

7b $R^1 = n\text{-}C_3H_7\text{—}\underset{CH_3}{\underset{\vert}{CH}}\text{—}\,;\ R^2 = c\text{-}C_6H_{11}$

Table 1. *t*-Butyl 2-Trimethylsilyl-2-alkenoates (**3**) prepared

Product	Yield [%]	*E*/*Z*-Ratio[a]	b.p. [°C]/torr[b]	Molecular formula[c]	¹H-N.M.R. (CDCl₃/TMS$_{int}$) δ [ppm]		
						SiCH₃	—CH=
3a	96	92/8	112–113°/47	$C_{15}H_{30}O_2Si$ (270.5)	(*E*) (*Z*)	0.13 0.22	5.74 6.81
3b	81	62/38	143–144°/17	$C_{17}H_{34}O_2Si$ (298.5)	(*E*) (*Z*)	0.14 0.23	6.06 7.07
3c	97	93/7	100–102°/18	$C_{17}H_{34}O_2Si$ (298.5)	(*E*) (*Z*)	0.13 0.23	5.63 6.83
3d	95	86/14	110–112°/20	$C_{16}H_{30}O_2Si$ (282.5)	(*E*) (*Z*)	0.12 0.22	5.82 6.85
3e	91	97/3	102–103°/15	[d]	(*E*)	0.24	6.75

[a] Determined by G.L.C. analyses (Triton X-305).

[b] Kugelrohr distillation.

[c] Satisfactory microanalyses obtained: C, ±0.30; H, ±0.37.

[d] Ref.[3], no b.p. reported.

Table 2. *t*-Butyl 2-Alkenoates (**5a–e**) prepared

Product	Yield [%]	(*E*/*Z*)-Ratio[a]	n.p. [°C]/torr[b]	Molecular formula[c]		¹H-N.M.R. (CDCl₃/TMS$_{int}$) δ [ppm] R—CH=	=CH—CO	$J_{H_\alpha\text{-}H_\beta}$ [Hz]
5a	91	49/51	111°/65	$C_{12}H_{22}O_2$	(*E*)	6.79	5.69	16.2
				(198.3)	(*Z*)	5.84	5.60	11.8
5b	88	50/50	129–130°/39	$C_{14}H_{26}O_2$	(*E*)	6.85	5.72	15.6
				(226.4)	(*Z*)	6.10	5.65	11.1
5c	93	37/63	142°/50	$C_{14}H_{26}O_2$	(*E*)	6.68	5.70	15.7
	(94)[d]	(38/62)[d]		(226.4)	(*Z*)	(5.6–5.9, multiplet)		
5d	79	54/46	133–134°/69	$C_{13}H_{22}O_2$	(*E*)	6.80	5.53	16.0
	(82)[d]	(57/43)[d]		(210.3)	(*Z*)	5.87	5.48	11.8
5e	71	77/23	106–107°/15	$C_{13}H_{16}O_2$[e]	(*E*)	7.57	6.33	15.9
				(204.2)	(*Z*)	6.82	5.84	13.3

[a] Determined by G.L.C. analyses (Triton X-305).
[b] Kugelrohr distillation.
[c] Satisfactory microanalyses obtained: C, ±0.30; H, ±0.28.
[d] The reaction was carried out at −78°C.
[e] Ref.[4], (*E*)-isomer, b.p. 144°C/8 torr.

Table 3. *t*-Butyl 2-(α-Hydroxybenzyl)-2-alkenoates (**6a–e**) and *t*-Butyl 2-(1-Hydroxyalkyl)-4-methyl-2-heptenoates (**7a, b**)

Product	Yield [%]	(*E*/*Z*)-Ratio[a]	b.p. [°C]/torr[b] or m.p. [°C]	Molecular formula[c]		I.R. (film) ν [cm⁻¹] $\nu_{C=C}$	ν_{CO}	ν_{OH}	¹H-N.M.R. (CDCl₃/TMS$_{int}$) $\delta_{-CH=}$ [ppm]
6a	76	25/75	b.p. 115°/2	$C_{19}H_{28}O_3$		1640	1710	3350	(*E*) 6.62
				(304.4)					(*Z*) 5.85
6b	75	29/71	b.p. 136–137°/0.15	$C_{21}H_{32}O_3$		1645	1710	3420	(*E*) 6.82
				(332.5)					(*Z*) 6.04
6c	90	11/89	b.p. 108–109°/0.15	$C_{21}H_{32}O_3$		1635	1700	3420	(*E*) 6.65
	(90)[d]	(13/87)[d]		(332.5)					(*Z*) 5.79
6d	73	33/67)	b.p. 102°/0.3	$C_{20}H_{28}O_3$		1635	1700	3420	(*E*) 6.73
	(66)[d]	(34/66)[d]		(316.4)					(*Z*) 5.96
6e	48	43/57	(*E*) m.p. 82–83°[e]	$C_{20}H_{22}O_3$	(*E*)	1640	1700	3420[f]	(*E*) 7.86
			(*Z*) m.p. 108–110°[e]	(310.4)	(*Z*)	1630	1670	3420[f]	(*Z*) 6.96
7a	75	12/88	b.p. 105°/0.7	$C_{18}H_{34}O_3$		1640	1710	3440	(*E*) 6.42
									(*Z*) 5.59
7b	77	17/83	b.p. 125°/0.8	$C_{19}H_{34}O_3$		1640	1700	3440	(*E*) 6.48
									(*Z*) 5.64

[a] Determined by G.L.C. analyses (Triton X-305).
[b] Kugelrohr distillation.
[c] Satisfactory microanalyses obtained: C, ±0.35; H, ±0.31.
[d] The reaction was carried out at −78°C.
[e] Separated by preparative T.L.C. (silica gel; hexane/chloroform/ether = 5/15/1) and recrystallized from hexane.
[f] Nujol.

All experiments are carried out under an atmosphere of argon.

t-Butyl 2-Trimethylsilyl-2-alkenoates (3); Improved Procedure[3]:
To a stirred solution of *t*-butyl bis[trimethylsilyl]acetate (1.50 g, 5.75 mmol) in dry tetrahydrofuran (12 ml) at −78°C is added a 15% solution of butyllithium in hexane (3.65 ml, 5.7 mmol). After 1 h, the aldehyde (**1**; 5 mmol) in dry tetrahydrofuran (8 ml) is added dropwise and stirring is continued for 0.5 h and then at room temperature for 1 h. Citric acid (10%; 20 ml) is added and the mixture is extracted with ether (3 × 20 ml). The organic extract is washed with water (20 ml), dried with calcium chloride, and concentrated. The residual oil is distilled under reduced pressure to give the pure product **3**.

t-Butyl 2-Alkenoates (5); General Procedure:
To a stirred solution of a *t*-butyl 2-trimethylsilyl-2-alkenoate (**3**; 1 mmol) and water (0.03 ml, 1.7 mmol) in tetrahydrofuran (5 ml) is added a solution of tetrabutylammonium fluoride (310 mg, 1.2 mmol) in tetrahydrofuran (6 ml) at −20°C or −78°C. Stirring is continued for 45 min at the same temperature and then for 30 min at room temperature. The mixture is poured into 5% hydrochloric acid (10 ml) and extracted with ether (3 × 15 ml). The ether layer is washed with water (15 ml), dried with magnesium sulfate, and concentrated. Kugelrohr distillation of the residual oil affords the pure alkenoate **5**.

t-Butyl 2-(1-Hydroxyalkyl)-2-alkenoates (6 and 7); General Procedure:
A solution of tetrabutylammonium fluoride (310 mg, 1.2 mmol) in tetrahydrofuran (6 ml) is dried with molecular sieves 4A overnight and added dropwise to a mixture of a compound **3** (1 mmol) and the aldehyde (**1a, d, e**; 1.5 mmol) in dry tetrahydrofuran (5 ml) at −20°C or −78°C. The reaction is continued and the mixture worked up as described above.

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