A Convenient Synthesis of α-Silyl Esters[1]

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Chlorosilanes have been found to react with α-bromo esters and zinc under Reformatsky conditions to yield α-silyl esters ($R_3SiCH_2CO_2C_2H_5$). Under these conditions, a chloroalkyl group on the silicon is inert. The ethyl esters prepared by this technique were the trimethyl-, chloromethyl-, dimethyl-, methyldiphenyl-, and triphenylsilylacetates and the α-trimethylsilylpropionate.

A variety of methods have been devised for the synthesis of α-silyl esters,[3] $R_3SiCH_2CO_2R$ (see eq 1-5).

$$(CH_3)_3SiCH_2MgBr + ClCO_2C_2H_5 \rightarrow \underset{\text{I, 75\%}}{(CH_3)_3SiCH_2CO_2C_2H_5}$$ (1)[4]

$$CH_3CO_2C_2H_5 \xrightarrow[\text{2. }(CH_3)_3SiCl]{\text{1. }NaC(C_6H_5)_3} \text{I}$$

27% (48% based on unrecovered $CH_3CO_2C_2H_5$) (2)[5]

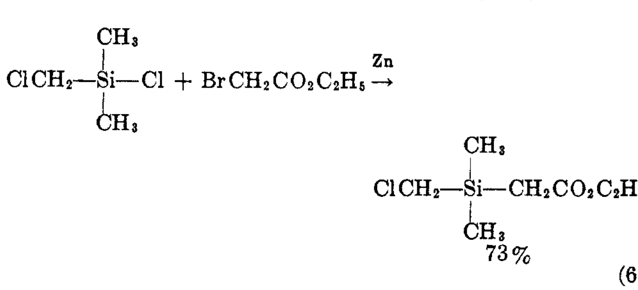
$$\underset{(R\,=\,C_2H_5,Ph)}{R(C_2H_5O)_2SiCl} + BrCH_2CO_2C_2H_5 \xrightarrow{\text{powdered Na}} \underset{33\%}{R(C_2H_5O)_2SiCH_2CO_2C_2H_5}$$ (3)[6]

$$(C_2H_5)_3SiH + N_2CH_2CO_2C_2H_5 \xrightarrow[\text{powder}]{\text{Cu}} \underset{40\%}{(C_2H_5)_3SiCH_2CO_2C_2H_5}$$ (4)[7]

$$(C_2H_5)_3SiI + (CH_3O_2CCH_2)_2Hg \rightarrow \underset{52\%}{(C_2H_5)_3SiCH_2CO_2CH_3}$$ (5)[8]

The procedures used for the preparation of these compounds suffer, for the most part, from the disadvantages of inconvenience or the impossibility of carrying functionality in the alkyl portions of the molecules.

In this laboratory we have found that α-silyl esters can be obtained by the reaction of a chlorosilane and an α-bromo ester with zinc under Reformatsky conditions (eq 6). This procedure is more convenient than the other methods reported and, at the same time, is useful for the synthesis of α-(chloroalkylsilyl) esters.



$$ClCH_2\text{—}\overset{CH_3}{\underset{CH_3}{Si}}\text{—}Cl + BrCH_2CO_2C_2H_5 \xrightarrow{Zn} \underset{73\%}{ClCH_2\text{—}\overset{CH_3}{\underset{CH_3}{Si}}\text{—}CH_2CO_2C_2H_5}$$ (6)

The esters prepared in this manner are summarized in Table I.

The reaction of a chlorosilane with ethyl bromoacetate and zinc was found to proceed smoothly with freshly sandpapered zinc strips and a benzene–ether solvent mixture. The distillation of a small amount of benzene was sufficient to dry the apparatus. The use of a nitrogen atmosphere did not improve the yield.

Commercial ethyl bromoacetate (or propionate) was used. Methyl chloroacetate was unreactive under these reaction conditions. The chlorosilanes were distilled before use, except for triphenylchlorosilane and methyldiphenylchlorosilane.[9]

The classical solvent for the Reformatsky reaction is benzene.[10] However, Cason and Fessenden[11] observed that a 1:1 mixture of ether–benzene improved the yield in the Reformatsky reaction, especially in the case of the reaction of a hindered ketone with an α-bromo ester. We found that the reaction of a chlorosilane and a bromo ester went in less time and in better yield with the addition of some ether (ether–benzene, ~ 1:5). When only benzene was used, zinc salts precipitated and coated the zinc strips.

Initiation of the reaction (evident by spots on the zinc and darkening of the solution) was sometimes difficult; therefore, in all cases, a small amount of iodine was added to the reaction mixture during the addition. The mixture generally required heating throughout the course of the reaction but occasionally became exothermic enough to require cooling. Addition times varied from 0.5 to 1 hr and reflux times, from 15 min (for ethyl methyldiphenylsilylacetate) to 6 hr (for ethyl triphenylsilylacetate). The reflux was continued until the zinc was consumed, although a small amount of black residue frequently remained. The initiation, necessary reflux time, and vigor of the reaction did not seem to depend on the structure of the reactants, but more probably are related to reaction conditions.[12]

A standard work-up procedure, involving treatment of the reaction mixture with 1 *N* hydrochloric acid to remove the zinc salts and washing with sodium bicarbonate solution, was found to be successful. Gold, Sommer, and Whitmore[4] found that at room temperature I is stable to 5% hydrochloric acid, although cleavage of the silicon–carbon bond (resulting in the formation of hexamethyldisiloxane and ethyl acetate)

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(3) Although some authors refer to R_3SiCO– and R_3SiCH_2CO– as α- and β-carbonyl compounds, respectively, we will refer to compounds of the type $R_3SiCH_2CO_2R'$ as α-silyl esters to be consistent with the nomenclature for α-bromo esters.

(4) J. R. Gold, L. H. Sommer, and F. C. Whitmore, *J. Am. Chem. Soc.*, **70**, 2874 (1948).

(5) C. R. Hance and C. R. Hauser, *ibid.*, **75**, 994 (1953), who also prepared in this manner $(CH_3)_3SiC(CH_3)_2CO_2C_2H_5$ in 38% yield, 65% based on unrecovered $(CH_3)_2CHCO_2C_2H_5$.

(6) K. A. Andrianov and L. I. Makarova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 702 (1956); *Chem. Abstr.*, **51**, 1877*d* (1957).

(7) F. Rijkens, M. J. Janssen, W. Drenth, and G. J. M. Van Der Kerk, *J. Organometal. Chem.*, **2**, 347(1964).

(8) Yu. I. Baukov and I. F. Lutsenko, *Zh. Obshch. Khim.*, **32**, 2746 (1962); *Chem. Abstr.*, **58**, 7964 (1963).

(9) Purchased from Peninsular ChemResearch.

(10) (a) R. L. Shriner, *Org. Reactions*, **1**, 12 (1942); (b) K. L. Rinehart, Jr., and E. G. Perkins, *Org. Syn.*, **37**, 37 (1957).

(11) J. Cason and R. J. Fessenden, *J. Org. Chem.*, **22**, 1326 (1957).

(12) In the case of triphenylchlorosilane, we found that the presence of silanol could change the course of the reaction. At reflux temperature, the triphenylsilanol apparently condensed to hexaphenyldisiloxane, cleaving out water, which, in turn, reacted with the chlorosilane to form the silanol and HCl, which then reacted with the zinc to liberate hydrogen.

TABLE I

YIELDS AND PHYSICAL PROPERTIES OF SOME α-SILYL ESTERS

α-Silyl ester[a]	Yield, %	Bp, °C (mm)	$n^{25}\text{D}$	Calcd, %		Found, %[i]	
				C	H	C	H
$(CH_3)_3SiCH_2CO_2C_2H_5$	72	76–77 (40)[g]	1.4136	...	...	...	...
$ClCH_2(CH_3)_2SiCH_2CO_2C_2H_5$[b]	73	65–67 (1.0)	1.4456	43.18	7.76	43.20	7.88
$(CH_3)_3SiCH(CH_3)CO_2C_2H_5$[c]	21	68–69 (13)	1.4230	55.13	10.41	55.16	10.55
$Ph(CH_3)_2SiCH_2CO_2C_2H_5$[d]	72	132–135 (9)[h]	1.4947	...	...	...	...
$Ph_2(CH_3)SiCH_2CO_2C_2H_5$[e]	50	184–185 (1.7)	1.5496	71.79	7.09	71.96	7.19
$Ph_3SiCH_2CO_2C_2H_5$[f]	33	...	...	76.26	6.40	76.31	6.21

[a] Analytical samples were obtained by glpc separation (see Experimental Section). [b] *Anal.* Calcd: Cl, 18.21. Found: Cl, 18.03. Infrared spectrum: 3.4 (CH), 5.81 (C=O), 8.0 (SiCH), 9.15, 11.5, and 11.9 μ. [c] Infrared spectrum: 3.4 (CH), 5.81 (C=O), 7.6, 8.0 (SiCH), 8.5, 8.75, and 11.8 μ. There was also observed 15% conversion to $CH_3CH_2COCH(CH_3)CO_2C_2H_5$, bp 84° (10 mm), $n^{25}\text{D}$ 1.4220 [lit. bp 85–86° (11 mm), R. O. Sauer, *J. Am. Chem. Soc.*, **69,** 2447 (1947); bp 62–63° (5 mm), $n^{20}\text{D}$ 1.4230, H. D. Zook, W. J. McAleer, and L. H. Horwin, *ibid.*, **68,** 2404 (1946)]. [d] Infrared spectrum: 3.3 and 3.4 (CH), 5.81 (C=O), 7.0 and 8.96 (SiPh), 8.0 (SiCH), 9.1, 9.6, 11.5, 12.0, 13.7, and 14.3 μ. [e] Infrared spectrum: 3.3 and 3.4 (CH), 5.81 (C=O), 7.0 and 8.95 (SiPh), 8.0 (SiCH), 9.7, 11.6, 12.3, 13.6, and 14.3 μ. An analytical sample was obtained by elution chromatography (see Experimental Section). [f] Mp 72–73°. Infrared spectrum: 3.4 and 3.5 (CH), 5.87 (C=O), 7.0 and 8.97 (SiPh), 8.0 (SiCH), 9.1, 12.6, 13.6, and 14.3 μ. (The C=O peak was relatively weak.) See Experimental Section for the work-up procedure. [g] Lit.[4] bp 75.5° (42 mm), $n^{20}\text{D}$ 1.4149. [h] R. A. Miller reports bp 82–93° (3 mm), $n^{25}\text{D}$ 1.4955 [University Publication No. 18869; *Dissertation Abstr.*, **17,** 2847 (1957); V. Bazant, V. Chvalovsky, and J. Rathousky, "Organosilicon Compounds," Vol. 2, Part 1, Academic Press Inc., New York, N. Y., 1965, p 480]. [i] The values reported are averages of duplicate analyses.

is observed at reflux. In 5% sodium hydroxide, however, cleavage is observed at room temperature. Attempts to improve the yield by milder work-up conditions (1% hydrochloric acid and several water washes rather than bicarbonate) were not successful, probably because of poor removal of the zinc salts. In an alternate synthesis of I, Hance and Hauser[5] (eq 2) did not use a water work-up, but filtered and distilled the reaction mixture. We found that the solubility of the zinc salts in the solvents used precluded this type of work-up. Fractional distillation presented no difficulty. The disiloxanes, which in some cases have boiling points very close to that of the silyl ester, were not observed in any quantity. Analytical samples of the α-silyl esters were obtained by glpc separation. In the case of the high-boiling ethyl methyldiphenylsilylacetate, some decomposition was observed during the distillation, but an analytical sample was easily obtained by elution chromatography.

In the case of the ethyl triphenylsilylacetate, distillation was not attempted. Attempted crystallization of the reaction mixture after water work-up gave only triphenylsilanol. However, the products of the reaction were easily separated by elution chromatography, affording 14% triphenylethoxysilane, 33% ethyl triphenylsilylacetate, and 42% triphenylsilanol, respectively. Since the ethyl bromoacetate used in the reaction contained only traces of ethanol (glpc) the origin of the ethoxysilane is unclear. The silanol may have been formed during the water work-up from unreacted chlorosilane. The decreasing yields as the number of phenyl groups on the silicon is increased (see Table I) are probably due to the decreased reactivity of the chlorosilane.

In the case of the reaction of trimethylchlorosilane with ethyl α-bromopropionate, a 21% yield of the α-silylpropionate was obtained. A 15% conversion to ethyl α-propionylpropionate was also observed. This type of condensation under similar conditions has been observed by other workers.[11,13]

The reaction appears to be limited to the monochlorosilanes. The attempted reaction of dimethyldichlorosilane with ethyl bromoacetate and zinc (1:2:2) did not provide the desired bis(carbethoxymethyl)dimethylsilane. The only product isolated was an unidentified low-melting solid. When the unstable nature of the compound (determined by glpc and changes in the nmr spectrum) was ascertained, structure proof was not pursued.

Because of the unusual spectral properties in the ultraviolet, visible, and infrared regions of compounds containing a carbonyl group adjacent to a silicon atom, these compounds have been the subject of several studies. The infrared spectra of α-ketosilanes (R_3SiCO–) show shifts of the carbonyl stretching vibration to abnormally low frequencies (see Table II).[14] Brook and Pierce[15] have further demonstrated that, while γ-ketosilanes ($R_3SiCH_2CH_2CO$–) show carbonyl absorption at the normal frequency, β-ketosilanes (R_3SiCH_2CO–) show a shift intermediate between normal and that of the α-ketosilanes. The esters prepared in this study, in every case except one, showed carbonyl absorption at 5.81 μ (*cf.* ethyl acetate, 5.75 μ). Ethyl triphenylsilylacetate exhibited carbonyl absorption at 5.87 μ, and, for this particular compound, the absorption was not so strong as is usually observed for the carbonyl group. In the light of the work of Brook, *et al.*,[14a] who observed no difference in the frequency of car-

TABLE II

INFRARED CARBONYL ABSORPTION OF SOME SILYL KETONES AND ESTERS

Compd	Infrared C=O, μ	Infrared C=O of carbon analog, μ
$Ph_3SiCH_2CH_2COPh$[a]	5.91	5.91
$R_3SiCOPh$ (R = CH_3 or Ph)[a,b]	6.18–6.19	5.93
R_3SiCOR' (R = CH_3 or Ph; R' = CH_3, Pr, or *t*-Bu)[b]	6.08–6.11	5.83
Ph_3SiCH_2COPh[a]	6.00	5.89
$R_3SiCH_2CO_2C_2H_5$[c]	5.81	5.75[e]
$Ph_3SiCH_2CO_2C_2H_5$[d]	5.87	5.75[e]

[a] Reference 15. [b] Reference 14. [c] The esters prepared in this study, with the exception of ethyl triphenylsilylacetate. [d] Prepared in this study. [e] Ethyl acetate, rather than the true carbon analog.

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(13) B. E. Hudson, Jr., and C. R. Hauser, *J. Am. Chem. Soc.*, **61,** 3568 (1939).

(14) (a) A. G. Brook, M. A. Quigley, G. J. D. Peddle, N. V. Schwartz, and C. M. Warner, *ibid.*, **82,** 5102 (1960); (b) E. J. Corey, D. Seebach, and R. Freedman, *ibid.*, **89:2,** 434 (1967).

(15) A. G. Brook and J. B. Pierce, *Can. J. Chem.*, **42,** 298 (1964).

TABLE III

NMR CHEMICAL SHIFTS OF SOME α-SILYL ESTERS[a]

	Chemical shift, δ, ppm					
Ester	$SiCH_3$	C_2H_5O		α-CH_2 or CH	$SiCH_2Cl$	C_6H_5
$(CH_3)_3SiCH_2CO_2CO_2C_2H_5$	0.15 (s)	1.24 (t)	4.02 (q)	1.87 (s)	...	...
$ClCH_2(CH_3)_2SiCH_2CO_2C_2H_5$	0.28 (s)	1.27 (t)	4.04 (q)	2.01 (s)	2.87 (s)	...
$(CH_3)_3SiCH(CH_3)CO_2C_2H_5$[b]	0.10 (s)	1.23 (t)	4.00 (q)	2.00 (q)	...	...
$Ph(CH_3)_2SiCH_2CO_2C_2H_5$	0.67 (s)	1.36 (t)	4.17 (q)	2.30 (s)	...	7.47 (m)
$Ph_2(CH_3)SiCH_2CO_2C_2H_5$	1.06 (s)	1.33 (t)	4.18 (q)	2.77 (s)	...	7.66 (m)
$Ph_3SiCH_2CO_2C_2H_5$	...	1.17 (t)	4.02 (q)	2.93 (s)	...	7.53 (m)

[a] The spectra were determined on a Varian A-60 spectrometer. Methylene chloride (singlet at δ 5.30) was used as solvent and internal standard. Values are reported downfield from TMS (s = singlet, t = triplet, q = quartet, m = multiplet). [b] The area ratios under the peaks (9.0:6.2:1.8:1.1) indicate that the doublet for the α-CH_3 group is masked by the triplet at 1.23.

bonyl absorption of triphenylsilyl phenyl ketone as the phenyl groups on the silicon were replaced by methyl groups, this anomalous behavior of the triphenylsilyl ester is rather surprising. Unfortunately, no silane carboxylate esters ($R_3SiCO_2C_2H_5$) were available for comparison, but it appears that the shift from the normal of the carbonyl absorption is not so pronounced for the α-silyl esters (0.06 μ), with the exception of the triphenylsilyl ester, as for the similar ketones (0.11 μ).

Experimental Section[16]

Ethyl Trimethylsilylacetate (I).—In a 2-l., three-necked round-bottom flask, equipped with a mechanical stirrer, dropping funnel, and condenser arranged for distillation, were placed 500 ml of benzene and 31.7 g (0.50 g-atom) of freshly sandpapered zinc strips. To ensure dryness, 75 ml of benzene was distilled. The condenser was replaced by a reflux condenser with a calcium chloride drying tube. A solution of 43.5 g (0.40 mole) of trimethylchlorosilane (redistilled, bp 57°) and 83.5 g (0.50 mole) of ethyl bromoacetate (Aldrich Chemical Co.) in 100 ml of dry benzene and 100 ml of anhydrous ether was added over a 30-min period to the gently refluxing mixture. During the addition, a crystal of iodine was added to help initiate the reaction. (Occasionally the reaction became vigorous, requiring cooling.) After the addition, the mixture was refluxed until the zinc was dissolved, 1–3 hr. The mixture was cooled in an ice bath, and 400 ml of 1 *N* hydrochloric acid was added over a 15-min period with stirring. The mixture was stirred for 5 min and separated. The organic layer was washed with 100 ml of 1 *N* acid and the combined aqueous layers were extracted with ether. The combined organic layers were washed with water, saturated bicarbonate, and water again, and dried. (Frequently, a precipitate formed in the bicarbonate solution, but was drawn off and discarded.) The solvents were distilled. Fractional distillation afforded 46.1 g (72%) of impure ethyl trimethylsilylacetate. (See Table I for the physical constants and references or analytical data, and Table III for the nmr data for this and succeeding α-silyl esters.) A run made without the ether in the reaction mixture gave a 55% yield of the silyl ester.

Purification of Ethyl Methyldiphenylsilylacetate.—The high boiling point of this compound prevented purification for analysis by redistillation or by glpc. Elution chromatography of 4 g of a fairly pure distillation fraction on 75 g silicic acid with benzene–petroleum ether (30–60°) (2:1) afforded an analytical sample.

Ethyl Triphenylsilylacetate.—The reaction was run as previously described, using 0.10 mole of triphenylchlorosilane (a 6-hr reflux was required). After the ether and benzene were distilled, 20 g of the residue (total weight, 72 g) was chromatographed on 300 g of silicic acid. As a solvent, mixtures of benzene and petroleum ether (bp 30–60°) from 2:1 to 4:1 were used.

There were eluted in the following order: (with 2:1 solvent) 1.25 g (extrapolated yield, 14%) of ethoxytriphenylsilane, mp 56–59° (lit.[17] mp 63°); (with 4:1 solvent) 3.2 g (33%) of ethyl triphenylsilylacetate, and 3.4 g (42%) of triphenylsilanol, mp 149.5–151° (lit.[18] mp 153–154°). The infrared and nmr spectra of the ethoxysilane and the silanol were consistent with the assigned structures.

An analytical sample of the silyl ester was obtained by recrystallization to a constant melting point, 72–73°, from petroleum ether.

Attempted Reaction of Trimethylchlorosilane with Methyl Chloroacetate.—After 2 days of reflux of the chlorosilane and the α-chloro ester under the usual conditions, the zinc was unchanged.

Reaction of Dimethyldichlorosilane with Ethyl Bromoacetate.—In the usual manner, a solution of 38.7 g (0.30 mole) of dimethyldichlorosilane, and 133 g (0.80 mole) of ethyl bromoacetate in benzene and ether was added to 50.6 (0.80 g-atom) of zinc and benzene. After a 3-hr reflux, the zinc was consumed. Work-up and distillation afforded 13.6 g of material, bp 66–76° (5 mm), which was redistilled. A center cut, bp 71–73° (5 mm), was further purified by glpc (DEGS column).

The purified product was a solid melting at about room temperature. This fact and the infrared and nmr spectra indicated that it was neither the desired bis(carbethoxymethyl)dimethylsilane nor ethyl acetoacetate. Infrared absorption was observed at 3.4, 5.8, and 6.15 (indicating conjugated C═O) 8.2, and 9.5 μ. Peaks were observed in the nmr at 2.65 (m), 3.63 (s), 4.75–5.62 (m), and 6.30 (s) ppm (δ). A second run of the reaction gave similar results. After the pure compound was allowed to stand overnight, it would not solidify on cooling. Glpc analysis showed two peaks and the nmr spectrum had become much more complex.

Registry No.—$(CH_3)_3SiCH_2CO_2C_2H_5$, 4071-88-9; $ClCH_2(CH_3)_2SiCH_2CO_2C_2H_5$, 13950-54-4; $(CH_3)_3SiCH(CH_3)CO_2C_2H_5$, 13950-55-5; $Ph(CH_3)_2SiCH_2CO_2C_2H_5$, 13950-56-6; $Ph_2(CH_3)SiCH_2CO_2C_2H_5$, 13950-57-7; $Ph_3SiCH_2CO_2C_2H_5$, 13950-58-8.

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[16] Melting points are corrected and were run on a Fisher-Johns melting point apparatus. Boiling points are uncorrected; fractional distillations were performed on a modified Podbielniak column (J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," 2nd ed, Prentice-Hall Co., Inc., Englewood Cliffs, N. J., 1962, p 289). Analyses were performed by the Berkeley Microanalytical Laboratory. Glpc separations were made on an Aerograph Autoprep Model A-700 with 30% SE-30 column, unless otherwise specified. Infrared spectra were recorded on a Beckman IR-5 spectrophotometer (neat or as mineral oil mulls).

[17] W. H. Daubt and J. F. Hyde, *J. Am. Chem. Soc.*, **74**, 386 (1952).

[18] R. West, R. H. Baney, and D. L. Powell, *ibid.*, **82**, 6269 (1960).