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Synthesis, NMR spectroscopy, and conformational analysis of α-dimethylsilyl esters

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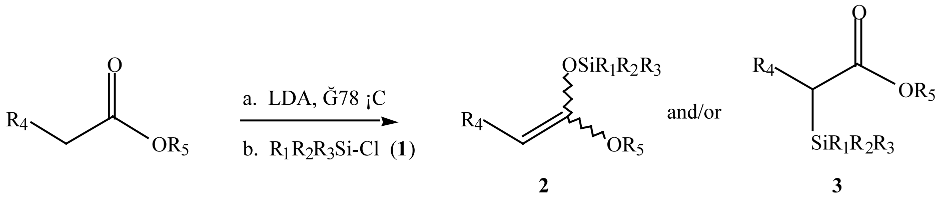
Abstract

The conformational properties of α-dimethylsilyl esters, synthesized in excellent yields by reaction of ester enolates with chlorodimethylsilane (DMSCl), have been explored by both molecular mechanics calculations and a variety of ^{1}H- and ^{29}Si-NMR spectroscopic experiments.

Keywords: ^{29}Si-NMR spectroscopy; Conformational analysis; α-Dimethylsilyl esters

The chemistry of enol silyl esters (**2**) has been the subject of extensive investigation [1–5]. These are generally produced by O-silylation of ester enolates using a trialkylchlorosilane (**1**) such as trimethylchlorosilane [6,7]. C-Silylation to afford α-silyl esters (**3**) has generally been regarded as an undesirable side reaction and therefore most efforts in this area have focused on methods to avoid it [8,9].



2

3

a ,$R_1 = R_2 = R_3 = CH_3$
b, $R_1 = CH_3$; $R_2 = R_3 = C_6H_5$
c, $R_1 = R_2 = CH_3$; $R_3 = H$

The literature indicates that C-silylation is favored with esters of acetic acid, or with zinc enolates [10], or when the ester bears a bulky alkoxy group such as *t*-butyl [7], or by proper choice of solvent [11]. These approaches rarely yield the α-silyl ester cleanly, except for esters of acetic acid. Larson et al. [12] have shown, however, that C-silylation is generally clean when the silylating agent is methyldiphenylchlorosilane (**1b**). Miura et al. [13] have also recently shown that the lithium enolates of ethyl acetate and ethyl propionate are C-silylated by chlorodimethylsilane (DMSCl, **1c**). We have explored the latter reaction further and found

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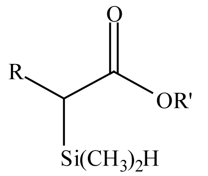
Table 1
Yields and spectroscopic properties of α-silyl esters

Ester	Yield (%)	C-silyl (%)	C=O stretch (cm^{-1})	SiH (δ)	Si*CH* (δ)	Si*C*H (ppm)	*C*=O (ppm)
4a	91	100	1716	3.90	2.1	66.8	175.4
4b	93	99.5	1715	3.91	1.85	77.0	174.4
4c	95	99.5	1717	3.90	1.83	59.8	174.3
4d	89	98.3	1718	4.03	2.47	51.2	175.2

it to be a good general method for preparation of α-dimethylsilyl esters (**4**) (Table 1). These slowly isomerize to the corresponding enol silyl ethers (**2**) (1–2%) and hydrolyze back to the starting ester in the presence of water or acid.



4a, R = Me; R' = *i*-Pr
b, R = Et; R' = *i*-Pr
c, R = Pentyl; R' = Et
d, R = $C_6H_5CH_2$; R' = Me

1. ^{1}H-NMR spectroscopy

Several characteristic spectroscopic properties of these substances require comment. The molecular ion is very weak or nonexistent in the mass spectrum, though a very small [M − 1] peak is seen; the most common fragmentation path is loss of Me_2SiH [M − 59]. The methyl groups attached to silicon are diastereotopic and are always seen as a pair of doublets near δ 0 in the ^{1}H-NMR spectrum. The ^{1}H-NMR spectrum of **4d** will be discussed in detail since it is representative of certain common features. The diastereotopic pair of protons H_a and H_b, together with H_c (see structure **A**, which represents the lowest energy conformation of **4d**) constitute a well-resolved AMX system (Fig. 1) assigned as follows. Proton A: δ 3.17 (dd, $J_{AX} = 11.0$ Hz; $J_{AM} = 14.5$ Hz; H_a or H_b); proton M: δ 2.78 (dd, $J_{AM} = 14.5$ Hz; $J_{MX} = 4.2$ Hz; H_b or H_a); proton X δ 2.47 (ddd, $J_{AX} = 11.0$ Hz; $J_{MX} = 4.2$ Hz; $J_{cd} = 2.1$ Hz; H_c). The apparent 2.1 Hz splitting of H_c was initially of concern.

Although it seemed likely that it was due to coupling of H_d, the proton attached to silicon, this could not be confirmed from the 1D experiment because H_d is not well resolved; it appears as an incompletely resolved multiplet because it is coupled separately to the two diastereotopic methyl groups with slightly different coupling constants. Surprisingly, a ^{1}H–^{1}H COSY NMR experiment exhibited no cross-peaks between H_c and H_d even at high magnification. However, spin-decoupling of H_c by saturation of H_d did cause the eight-line multiplet at δ 2.47 to collapse to a doublet of doublets ($J = 11.0$ and 4.2 Hz) as expected. The absence of cross-peaks between H_c and H_d in the COSY experiment was explained by an inversion recovery experiment [14a,15a]. The T_1's of H_c and H_d (3.8 and 4.7 s, respectively) were found to be both unusually large and substantially longer than those of other protons in the molecule. The intensities of cross-peaks in COSY spectra are dependent upon the magnitudes of the individual T_1's of the coupled peaks [14]; in this case, both the coupled peaks relax slowly. These long relaxation times and the small coupling [14b] (2.1 Hz) between H_c and H_d should both reduce the size of the COSY cross-peaks. DQCOSY and 2D-TOCSY [15b] experiments were then carried out with a long delay between individual repetitions, to allow full relaxation of all protons. Gratifyingly, both these experiments exhibited cross-peaks establishing the coupling between H_c and H_d.

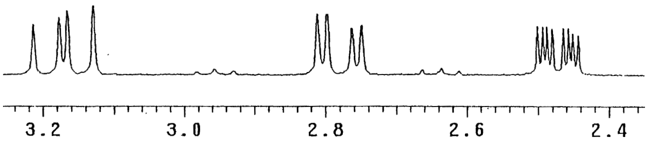


Fig. 1. ^{1}H-NMR spectrum of silyl ester **4d** showing protons a–c.

2. ^{29}Si-NMR spectroscopy

The ^{29}Si-NMR spectra of the silyl esters **4** (measured at 79.4423 Hz) consist of a doublet ($J_{Si-H} = 190–195$ Hz) at ca. −9 ppm relative to internal Me_4Si. Each component of the doublet is further broadened by longer range coupling to the diastereotopic methyl groups and H_c. Upon standing, the silyl esters slowly hydrolyze to afford a volatile substance (doublet, $J_{Si-H} = 204$ Hz, at −5.6 ppm), presumably either dimethylsilanol or dimethylsiloxane.

3. Conformational analysis

A series of molecular mechanics calculations were carried out in the course of attempts to understand the ^{1}H- and ^{13}C-NMR spectra of **4d**. The results demon-

Table 2
Lowest energy conformations of silyl ester **4d**[a], [b]

Energy (kcal mol^{-1})[c]	H_c–C_α–C_β–H_a dihedral angle (°)	H_c–C_α–C_β–H_b dihedral angle (°)	H_c–C_α–Si–H_d dihedral angle (°)	H_c–C_α–$C_{C=O}$–OR dihedral angle (°)
0	60	180	180	180
0.08	60	180	−59	163
0.15	−64	179	−60	155
0.4	59	176	62	164
0.7	64	180	69	152
0.9	56	173	−61	−12
0.95	54	171	12	−35

[a] There are four other conformations within 2 kcal of the minimum.

[b] If the four-atom sequence is written in a Newman projection, the angle is positive one proceeds clockwise from the front group to the rear, and conversely for negative angles.

[c] Relative to the lowest energy conformation.

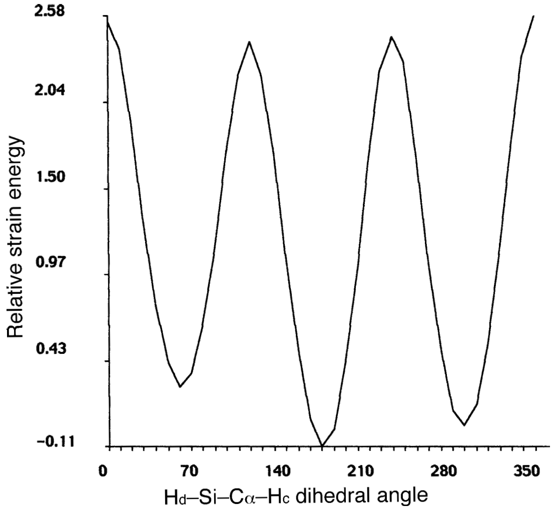


Fig. 2. Conformational energy (kcal mol^{-1}) for the lowest energy conformation of **4d** as a function of rotation around the α-carbon–silicon bond.

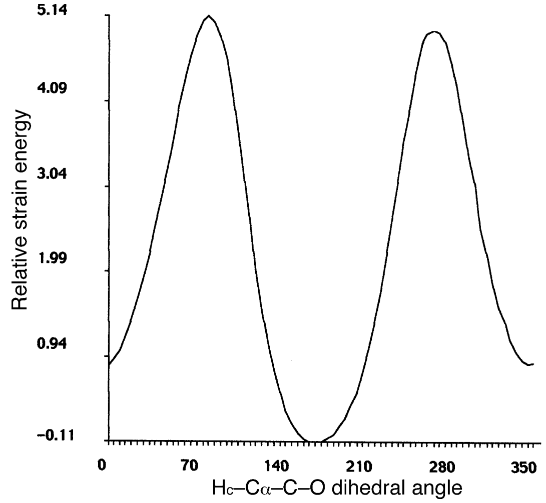
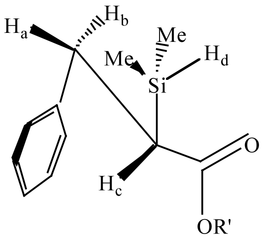


Fig. 3. Conformational energy (kcal mol^{-1}) for the lowest energy conformation of **4d** as a function of rotation around the α-carbon–carbonyl carbon bond.

strated that **4d** is conformationally heterogeneous. Structure **A** was identified as the lowest energy conformation for this compound. In this conformation, H_b, H_d, and the carbonyl oxygen atom are all *anti* to H_c.



A

However, six other conformations were also identified within 1 kcal mol^{-1} of the lowest energy conformation (Table 2). Furthermore, not only does **4d** exist in a variety of conformations, but the barriers between the individual conformations are very low such that all conformations readily interconvert. This was established by a series of dihedral driver calculations, in which the energy calculated as various bonds was rotated in increments. Figs. 2 and 3 represent the result of rotating around the bonds connecting α-carbon of the ester (in the minimum energy conformation) to the silicon and carbonyl atoms, respectively. The conformational heterogeneity of these compounds and the low interconversion barriers (similar results were found for the other silyl esters) are undoubtedly associated with the low steric demands of the ester group and the length of the carbon–silicon bond, which reduces steric interactions in the vicinity of silicon [16]. It may seem at first sight surprising that a substance as conformationally heterogeneous as **4d** should exhibit the well-resolved spectrum shown in Fig. 1. However, it may be noted from Table 2 that the dihedral angles between H_a and H_c and between H_b and H_c are almost unaffected by other conformational changes which take place, hence the coupling constants, which depend upon these dihedral angles, are essentially the same in all conformations.

4. Experimental

^{1}H- and ^{13}C-NMR spectra were recorded at 300 MHz (^{1}H) and 75 MHz (^{13}C) in $CDCl_3$ in a Varian Mercury pulsed field gradient spectrometer. Spectral assignments were confirmed by COSY (^{1}H) and APT (^{13}C) experiments. Infrared spectra were recorded on a Perkin–Elmer spectrum BX FT-IR spectrophotometer. Gas chromatography–mass spectrometry (GC–MS) was carried out on a Hewlett-Packard model 5890 spectrometer. DMSCl was redistilled from CaH_2 at 34 °C. Microanalyses were carried out by Chemisar Laboratories of Guelph, Ont., Canada. Samples for microanalysis were purified by preparative gas chromatography; GC–MS and NMR spectra of purified compounds showed them to be highly homogeneous substances. However, the microanalytical laboratory reported difficulty obtaining reproducible data on some of these compounds because of their volatility. Molecular mechanics calculations were carried out using PCMODEL7 (Serena Software, Bloomington, IN).

4.1. General procedure for synthesis of α-dimethylsilyl esters (**4**)

Lithium diisopropylamide mono-tetrahydrofuran complex (55 mmol) was added dropwise over a period of 10 min to a solution of ester (50 mmol) in anhydrous THF (50 ml) at −78 °C under nitrogen atmosphere, and allowed to stir for 4 h while maintaining a constant temperature. A slight excess of DMSCl (60 mmol) was then added dropwise, after which the mixture was allowed to warm to r.t. while stirring. The reaction mixture was filtered through dry Celite twice and concentrated in vacuo. The silyl ester was purified by vacuum distillation as a colorless liquid. Samples for microanalysis were purified by preparative gas chromatography on a Gow-Mac Model 580 chromatograph.

4.2. Isopropyl-2-dimethylsilylpropionate (**4a**)

B.p. 34 °C (0.5 mm); IR (neat) 1716 (C=O), 2129 (Si–H) cm^{-1}; ^{1}H-MR ($CDCl_3$): δ 0.13 (d, 3H), 0.16 (d, 3H), 1.18 (d, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.3$ Hz, 3H), 1.22 (d, $J = 5.7$ Hz, 3H), 2.10 (qd, $J = 7.2$ and 2.4 Hz, 1H), 3.90 (m, 1H), 5.00 (sept, $J = 6.3$ Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 175.4, 67.2, 66.8 (Si^{29} satellites, $J = 55$ Hz), 28.56, 22.32, 11.62, −5.01, −6.35; mass spectrum, m/e (%): 173 ($m-1$) (1), 115 (15), 75 (100). Anal. Calcd for $C_8H_{18}O_2Si$: C, 55.12; H, 10.41; Found: C, 55.59; H, 10.85%. HRMS: Calcd for [M−1]: 173.099783; Found: 173.100121.

4.3. Isopropyl-2-dimethylsilylbutyrate (**4b**)

B.p. 44 °C (0.5 mm); IR (neat) (cm^{-1}): 1715 (C=O), 2126 (Si–H); ^{1}H-NMR ($CDCl_3$): δ 0.13 (d, 3H, $J = 3.6$ Hz), 0.16 (d, 3H), 0.96 (t, $J = 7.0$ Hz, 3H), 1.21 (d, $J = 6$ Hz, 3H), 1.23 (d, $J = 6$ Hz, 3H), 1.82 (m, 1H), 1.92 (m, 1H),1.94 (m, 1H), 3.91 (m, 1H), and 5.02 (sept, $J = 6.3$ Hz, 1H); ^{13}C-NMR ($CDCl_3$): 174.4, 77.1, 77.0 (Si^{29} satellites, $J = 55$ Hz), 37.8, 22.2, 21.0, 14.8, −4.9, −5.6; mass spectrum, m/e (%): 187 ($m-1$) (1), 129 (100), 75 (68). Anal. Calcd for $C_9H_{20}O_2Si$: C, 57.40; H, 10.70; Found: C, 57.90; H, 11.40%. HRMS: Calcd for [M]: 188.123528, Found: 188.123949.

4.4. Ethyl-2-dimethylsilylheptanoate (**4c**)

B.p. 70 °C (0.5 mm); IR (neat): 1717 (C=O), 2128 (Si–H) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.13 (d, 3H), 0.16 (d, 3H), 0.75 (t, $J = 6.4$ Hz, 3H), 1.22 (t, 3H), 1.25–1.3 (m, 4H), 1.32 (m, 2H), 1.38 (m, 1H), 1.83 (m, 1H), 2.03 (qd, 1H), 3.90 (m, 1H), 4.12 (m, 2H); ^{13}C-NMR ($CDCl_3$): 174.3, 59.8 (Si^{29} satellites, $J = 55$ Hz), 35.6, 31.9, 30.2, 27.6, 22.8, 14.7, 14.2, −5.00, −5.66. Anal. Calcd for $C_{11}H_{24}O_2Si$: C, 61.06; H, 11.18; Found: C, 57.90; H, 11.40%. HRMS: Calcd for [M−1]: 215.146734, Found: 215.147689.

4.5. Methyl-2-dimethylsilylhydrocinnamate (**4d**)

B.p. 44 °C (0.1 mm); IR (neat): 1718 (C=O), 2129 (Si–H) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.17 (d, 3), 0.19 (d, 3H), 2.47 (ddd, 1H), 2.78 (dd, 1H), 3.17 (dd, 1H), 3.6 (s, 3H), 4.03 (m, 1H), 7.22 (m, 5H); ^{13}C-NMR ($CDCl_3$): δ 175.2, 142.6, 129–126 (5C), 51.2 (Si^{29} satellites, $J = 60$ Hz), 37.9, 35.9, −5.1, −6.2; mass spectrum, m/e (%): 222 (m) (5), 221 ($m-1$) (35), 131 (100), 91 (90). Anal. Calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16; Found: C, 64.84; H, 8.12%.

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