Conformational Analysis of t-5-Methyl-t-2-(trimethylsilyl)cyclohexan-r-ol and its derived Esters

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The existence of significant σ–σ* interactions involving the C–Si bonding orbital and the C–O antibonding orbital, results in a strong preference for the diaxial conformation for the esters 6a–m.

The stabilising influence of a β-silyl substituent on an electron-deficient centre, the so called β effect, is one of the most important electronic effects of silicon in organic chemistry.[1,2] This effect is clearly demonstrated by the enhanced rates of unimolecular solvolyses of compounds bearing leaving groups situated β to a silicon substituent.[3,4] In addition to a small inductive effect, silicon is believed to stabilise developing positive charge (Scheme 1) either by hyperconjugation of the C–Si bond with the vacant β carbon p orbital (cation a) or by formation of the silacyclopropylium cation (cation b).[5] The demonstration of a marked dependence of unimolecular solvolyses rates upon the Si–C–C–Lg dihedral angle[5] (Lg = leaving group) in stereochemically constrained systems, and the observation of a secondary α deuterium isotope effect $k_H/k_D = 1.17(1)$ for the solvolysis of 1[6] suggests a significant involvement of the open cation (a) on the reaction pathway. We have recently shown from accurate X-ray structural studies on a selected range of β-trimethylsilyl esters that there are also significant ground-state effects when a silicon substituent is disposed β to a leaving group.[7] For example, when the Si–C–C–O dihedral angle is close to 180° as in 2 the C–O bond is lengthened, however, when they were gauche to one another as in 3 we found the C–O bond is shorter and essentially the same as that of the corresponding non-silylated compound.[8] The origin of this effect was proposed as being the result of σ–σ* interactions where the C–Si σ bonding orbital acts as the donor and the C–O σ* orbital acts as the acceptor. This evidence for the existence of σ–σ* interactions in these model systems led us to investigate the influence that such interactions would have on the conformational equilibria of flexible molecules containing the β-trimethylsilyl ester moieties. The $\sigma_{C–Si}$-σ* C–O interaction should stabilise
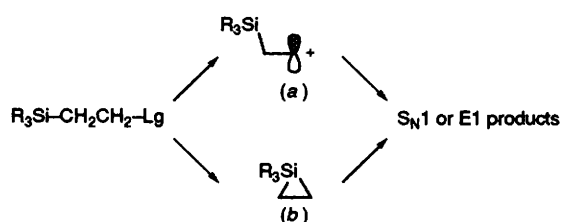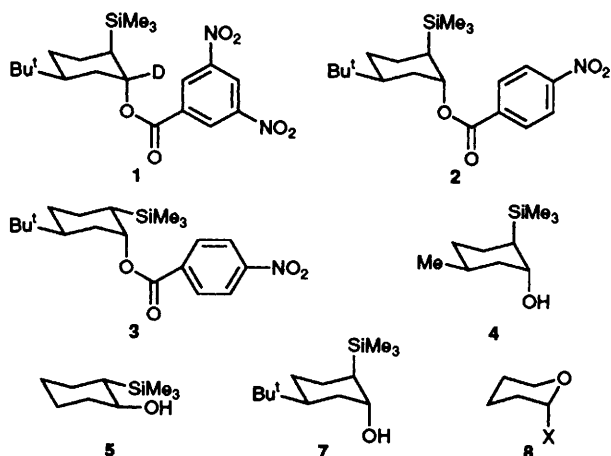
conformations having the Si–C–C–O dihedral angle close to 180°. We chose as our model system esters derived from the 5-methyl- substituted 2-trimethylsilylcyclohexanol 4.

Substrate 4 was synthesized according to the procedure in Scheme 2. Conversion of 4 to the esters 6a–6m was achieved by standard methods. With the exception of 6b–6d and 6k–6l, the esters were stable and readily handled and characterised, however, 6b–6d and 6k–6l, underwent a facile elimination of the trimethylsilyl group and ester function within several hours of preparation, giving 4-methylcyclohexene as the predominant product. Thus, although satisfactory spectral data (^{1}H, ^{13}C NMR) for 6b–6d and 6k–6l, could be obtained immediately upon their preparation, full characterisation was not possible. The 4-tert-butyl silacyclohexanol 7 and the 2-trimethylsilylcyclohexanol 5 which were required for spectral parameters were synthesized as previously described.[7]

The positions of the conformational equilibria between the diaxial and diequatorial conformations of 4 and 6a–m were measured using the coupling constant method,[10] where the total coupling to the C-1–H proton (J_{obs}) in the ^{1}H NMR spectrum was taken as the distance between the outside lines for this multiplet, which occured between δ 4–6 for these compounds in deuteriochloroform and was well removed from the rest of the spectrum. At room temperature this value of J_{obs} is a weighted average of the total coupling expected for the diaxial conformer and the diequatorial conformer (Scheme 3). Estimates of the couplings for the diaxial and diequatorial conformers were obtained from the measurement of the total coupling to the corresponding C-1–H proton in the conformationally biased structures 7 (8.7 Hz) and 5 (24.8 Hz). The measured values of J_{obs}, and the corresponding calculated conformational data for the parent alcohol 4 and the derived esters 6a–6m are presented in Table 1.
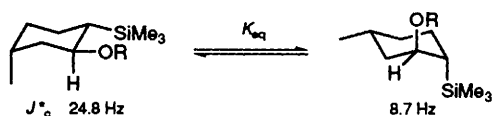
The conformational data summarised in Table 1 demonstrate that, with the exception of the parent alcohol 4, all substrates show a preference for the diaxial conformation. Closer inspection of the data for the esters 6a–6m reveals some interesting trends; for example the sequential replacement of the methyl hydrogens of the acetate 6a with chlorines (entries 6b–6d) is accompanied by an increasing proportion of the diaxial conformation. Thus, it is clear that the proportion of the diaxial conformation increases as the electronegativity of
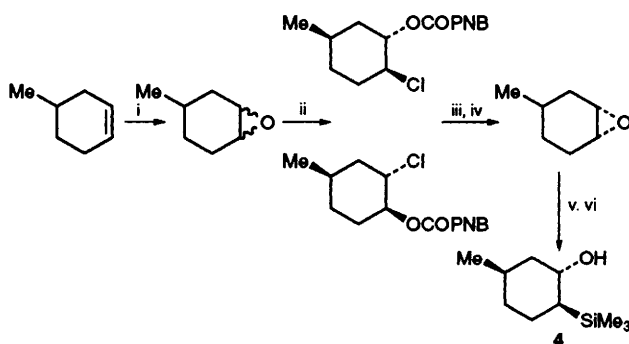
Scheme 1 Stabilisation of positive charge by β silicon

the ester function in the acetate derived series increases; this trend is the reverse of what we predict from steric and dipolar considerations alone.[9] This type of relationship is also apparent with the substituted benzoate esters (entries 6e–6m); a plot of log K_a of the parent acids vs. log K_{eq} for the corresponding esters shows a reasonably linear relationship, with a slope of 0.1 (correlation coefficient 0.91), again demonstrating a clear relationship between the electronegativity of the ester function and the proportion of the diaxial conformation present at equilibrium.

These results demonstrate the presence of significant σ–σ^* interactions between the σ_{C-Si} orbital and the σ^*_{C-O} orbital, which act to stabilise the diaxial conformation, the stabilisation resulting from this σ–σ^* interaction is proportional to $S^2/\Delta E$ where S is the orbital overlap and ΔE is the energy difference between the σ and σ^* orbitals.[11] The σ_{C-Si} orbital is a particularly effective σ donor orbital since it has a relatively high energy (the energy of a C–Si bonding orbital is similar to that of an oxygen p-type lone pair orbital[12]), resulting in a close energy match with the adjacent low lying σ^*_{C-O} orbital. Furthermore, the effect of increasing the electronegativity of the ester function is to decrease the energy of the σ^*_{C-O} orbital, resulting in a closer energy match with the σ_{C-Si}

4   R = H
6a R = MeCO
  b R = ClCH₂CO
  c R = Cl₂CHCO
  d R = Cl₃CCO
  e R = PhCO
  f R = 3-MeOC₆H₄CO

6g R = 4-MeOC₆H₄CO
  h R = 3-NO₂C₆H₄CO
  i R = 4-NO₂C₆H₄CO
  j R = 2,4-(NO₂)₂C₆H₃CO
  k R = 3,4-(NO₂)₂C₆H₃CO
  l R = 3,5-(NO₂)₂C₆H₃CO
  m R = 4-CNC₆H₄CO

* J_{calc} is the estimated H–H coupling to the indicated proton for each conformer, and is taken as the distance between the outside lines of this multiplet in the ¹H NMR spectrum. The indicated values come from those measured for the biased structures **5** and **9**.

Scheme 3 Conformational isomers of **4** and esters **6a–m**

Table 1 Conformational data for **4** and esters **6a–6m**

Compound	J_{obs}/Hz	Diaxial	Diequatorial	ΔG_{298}/kcal mol⁻¹	log K_{eq}
4	17.94	41.2	58.8	−0.21	−0.154
6a	15.14	58.0	42.0	0.19	0.140
6b	13.20	70.0	30.0	0.50	0.367
6c	11.40	80.8	19.2	0.85	0.624
6d	10.38	87.0	13.0	1.13	0.825
6e	13.43	68.5	31.5	0.46	0.337
6f	13.19	70.0	30.0	0.50	0.367
6g	13.67	67.0	33.0	0.42	0.307
6h	13.19	70.0	30.0	0.50	0.367
6i	12.70	72.9	27.1	0.59	0.429
6j	11.24	81.8	18.2	0.89	0.647
6k	12.45	74.5	25.5	0.64	0.466
6l	12.69	73.0	27.0	0.59	0.431
6m	12.70	72.9	27.1	0.59	0.429

orbital, and hence a greater interaction. This interaction also depends on the overlap integral S between the two interacting orbitals. The C–Si bond is polarised towards the carbon atom; $C^{\delta-}$–$Si^{\delta+}$, (the difference in the Pauling electronegativities of C and Si is 0.7) making overlap with the adjacent vacant orbital on carbon more effective. The electronegativity of the ester also influences the S term, thus as the ester function becomes more electronegative, the electronic density of the σ^*_{C-O} near the carbon increases[13] so that more effective overlap with the σ_{C-Si} results. The observed trend whereby the proportion of the diaxial conformer increases with increasing electronegativity of the ester function is fully consistent with these orbital energy and orbital overlap effects.

The influence of σ_{C-Si}–σ^*_{C-O} interactions on the conformational equilibria of flexible molecules containing the Si–C–C–O structural moiety act to stabilise the conformation where the Si–C–C–O dihedral angle is 180°. This is a new example of the so called repulsive *gauche* effect although, like many examples of compounds displaying this behavior, this is probably more accurately described as an 'attractive *trans* effect'. The magnitude of the σ_{C-Si}–σ^*_{C-O} interaction is not readily calculated from these results, however, it is likely that it is similar in magnitude to the anomeric effect observed for electronegative substituents at the 2-position of a tetrahydropyran ring **8** (1–3 kcal mol⁻¹).[14] Given that the accepted origin of this effect is the n-σ^* interaction between the p-type oxygen lone pair on the ring oxygen and the σ^*_{C-X} orbital (in addition to electrostatic effects), and since the oxygen p-type lone pair orbital has a similar energy to a C–Si σ orbital, and ignoring any differences in overlap S, one would expect these effects to be similar.

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