Conformational Analysis of α-Alkyl-ββ-di-isopropylstyrenes. A Dynamic ^1H Nuclear Magnetic Resonance Spectroscopic and Molecular Mechanics Investigation

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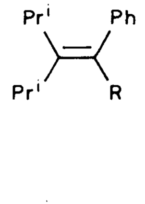
The conformational equilibria and barriers to rotation in α-R-ββ-di-isopropylstyrenes with R = H, Me, Et, Pr^i, CH_2Bu^t, and Bu^t, and in tri-isopropylethylene and 1,1,2-tri-isopropylpropene investigated by dynamic ^1H n.m.r. spectroscopy and molecular mechanics (MM2, MMP2 force fields) are reported. The following conclusions are drawn: (i) the phenyl group is twisted *ca.* 70—90° out of the ethylene plane, (ii) the conformational populations of the geminal isopropyl groups indicate that the effective steric size of the phenyl group is larger than that of methyl, ethyl, isopropyl, and neopentyl groups, but smaller than that of the t-butyl group, (iii) barriers ($\Delta G^\ddagger$) to interchange of the isopropyl groups fall in the range 10.5—12.2 kcal mol^{-1}, (iv) molecular mechanics calculations fail to reproduce the experimentally determined conformational populations but satisfactorily reproduce the barriers to rotation of the isopropyl and phenyl groups. According to these calculations the isopropyl group rotations are not correlated.

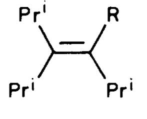
The stereochemistry of styrenes is highly dependent upon the substitution pattern in the α and β positions. While styrene is a planar molecule with a barrier of *ca.* 3 kcal mol^{-1} to rotation about the phenyl–olefin bond,[1] derivatives substituted in the α and β positions are twisted about the C–Ph bond, with substantial torsional barriers through a planar transition state.[2,3] Further substitution in one *ortho* position leads to chiral molecules with high optical stability.[4,5] This behaviour is a manifestation of the steric anisotropy of the phenyl group. The spatial requirement of aromatic rings has been examined in several cases and, not surprisingly, very divergent results have been obtained. This depends, among other factors, on the conformation of the aromatic ring, since the effective size of such a ring is quite different laterally and orthogonally.

Isopropyl groups attached to a planar framework usually assume two well defined conformations with the C–H bond eclipsing the sp^2 plane, and two adjacent isopropyl groups exist in four general types of rotamers, **A**—**D** (Scheme 1), of which the two 'gear-meshed' conformations **A** and **B** are in most cases lowest in energy.[6] The equilibrium between the rotamers is determined by the effective sizes of X and Y, and the study of the equilibrium constant offers a way to obtain information about the relative sizes of these groups.

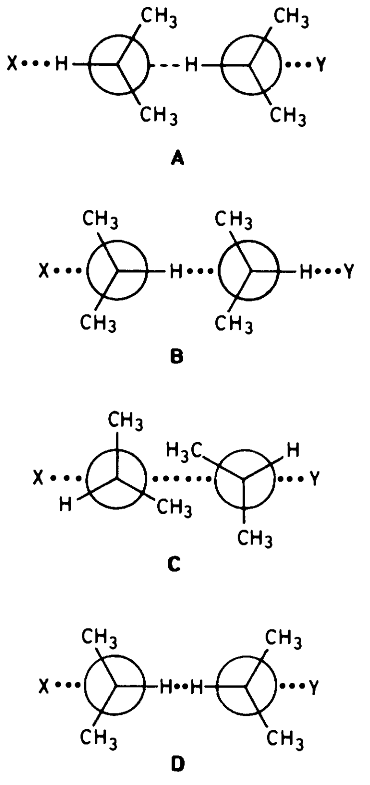
We report here a ^1H n.m.r. spectroscopic and molecular mechanics investigation of a series of α-R-ββ-di-isopropylstyrenes (**1**)—(**6**) in which the phenyl group is twisted relative to the ethylene plane and where the face of the phenyl group is exposed to its flanking isopropyl group.



R	
H	(1)
CH_3	(2)
C_2H_5	(3)
$(CH_3)_2CH$	(4)
$(CH_3)_3CCH_2$	(5)
$(CH_3)_3C$	(6)



R	
H	(7)
CH_3	(8)



Scheme 1.

The two simple ethylene derivatives (**7**) and (**8**) were studied for comparison, and one derivative of (**4**), selectively deuteriated on the isopropyl group geminal to the phenyl, was prepared as an aid in n.m.r. assignments.

Experimental

Syntheses.—The compounds were prepared by reductive coupling of the pertinent ketones with low-valent titanium reagent according to the method of McMurry and his co-workers[7,8] or its modifications.[9,10] If not stated otherwise, the procedure of Dams[9] was followed. Complicated product mixtures of various coupled products as well as reduced ketones (alcohols, hydrocarbons, and pinacols) were obtained. In all cases the desired compound was isolated and purified by preparative g.c. (OV 101, 40—60 mesh, 3 m).

ββ-Di-isopropylstyrene (**1**) was prepared from 2,4-dimethylpentan-3-one (2.85 g, 0.025 mol) and benzaldehyde (2.65 g, 0.025 mol) in 10% yield (g.l.c.).

1-Benzyl-1-isopropyl-2-methylpropanol was prepared from benzylmagnesium chloride [from benzyl chloride (25.3 g, 0.20 ml) and magnesium (4.8 g, 0.20 mol)] and 2,4-dimethylpentan-3-one in diethyl ether giving liquid (39 g, 94%), b.p. 95—100 °C at 0.9 mmHg, δ_H (60 MHz; $CDCl_3$) 7.22 (5 H, s), 2.82 (2 H, s), 1.93 (3 H, br sept, J 7.0 Hz), 0.98 (6 H, d, J 7.0 Hz), and 0.90 (6 H, d, J 7.0 Hz), $\nu_{max.}$ 3 580 (OH), 3 500 (OH), 3 080, 3 060, 3 020, 2 960, 2 880, 1 940, 1 870, 1 800, 1 700, and 1 600 cm^{-1}, *m/e* 188 ($M - H_2O$, 2%), 163 (9), 145 (7), 119 (9), 115 (40), 105 (6), 97 (6), 91 (74), 77 (6), 71 (100), 65 (15), 59 (14), 55 (30), 51 (7), and 45 (32).

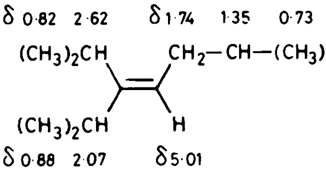
ββ-Di-isopropylstyrene (**1**) was prepared from 1-benzyl-1-isopropyl-2-methylpropanol and Amberlyst 15 in methylene dichloride at room temperature in almost quantitative yield, $\nu_{max.}$ 3 080, 3 060, 3 020, 2 960, 2 930, 2 870, 1 640, 1 600, 1 570, 1 490, 1 460, and 1 440 cm^{-1}, *m/e* 188 (M^+, 5%), 145 (100), 131 (12), 117 (17), 105 (8), 91 (25), 77 (8), 65 (6), and 51 (7), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 1.05 (6 H, d, J 6.8 Hz), 1.20 (6 H, d, J 6.8 Hz), 2.50 (1 H, sept, J 6.8 Hz), 3.10 (1 H, sept, J 6.8 Hz), 6.40 (1 H, s), and 7.1—7.3 (5 H, m).

ββ-Di-isopropyl-α-methylstyrene (**2**) was prepared from 2,4-dimethylpentan-3-one (5.7 g, 0.050 mol) and acetophenone (6.0 g, 0.050 mol), $\nu_{max.}$ 3 080, 3 060, 3 010, 2 960, 2 930, 2 870, 1 600, 1 490, 1 460, and 1 440 cm^{-1}, *m/e* 202 (M^+, 9%), 159 (100), 145 (14), 128 (19), 117 (83), 105 (22), 91 (29), 77 (22), 61 (12), and 55 (22), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.86 (6 H, d, J 6.8 Hz), 1.27 (6 H, d, J 6.8 Hz), 1.96 (3 H, s), 2.49 (1 H, sept, J 6.8 Hz), 2.57 (1 H, sept, J 6.8 Hz), and 7.0—7.3 (5 H, m).

α-Ethyl-ββ-di-isopropylstyrene (**3**) was prepared from 1-phenylpropan-1-one (1.41 g, 0.0105 mol) and 2,4-dimethylpentan-3-one (1.2 g, 0.0105 mol) in 25% yield (g.l.c.), $\nu_{max.}$ 3 080, 3 060, 2 960, 2 930, 2 870, 1 600, 1 490, 1 460, and 1 440 cm^{-1}, *m/e* 216 (M^+, 8%), 173 (54), 145 (17), 131 (80), 117 (31), 105 (12), 97 (5), 91 (44), 77 (15), 65 (9), and 57 (100), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.83 (3 H, t, J 7.2 Hz), 0.86 (6 H, d, J 6.9 Hz), 1.29 (6 H, d, J 6.9 Hz), 2.43 (2 H, q, J 7.2 Hz), 2.42 (1 H, sept, J 6.9 Hz), 2.60 (1 H, sept, J 6.9 Hz), and 7.0—7.3 (5 H, m).

αββ-Tri-isopropylstyrene (**4**) was prepared from 2,4-dimethylpentan-3-one (2.85 g, 0.025 mol) and 2-methyl-1-phenylpropan-1-one (3.7 g, 0.025 mol) in 15% yield (g.l.c.), m.p. 86—87 °C, $\nu_{max.}$ 3 080, 2 960, 2 930, 2 870, 1 600, 1 460, and 1 440 cm^{-1}, *m/e* 230 (M^+, 8%), 187 (28), 145 (68), 131 (34), 117 (21), 105 (22), 91 (42), 77 (15), 67 (11), and 57 (100), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.82 (6 H, d, J 6.9 Hz), 0.89 (6 H, d, J 6.9 Hz), 1.30 (6 H, d, J 6.9 Hz), 2.23 (1 H, sept, J 6.9 Hz), 2.57 (1 H, sept, J 6.9 Hz), 3.23 (1 H, sept, J 6.9 Hz), and 6.9—7.3 (5 H, m).

[2-^{2}H]-2-Methyl-1-phenylpropan-1-one was prepared when D_2O (1.0 ml) and 2-methyl-1-phenylpropan-1-one (4.4 g, 0.030 mol) were added to CD_3OD (5 ml) and a catalytic amount of sodium. The mixture was allowed to stand with stirring at room temperature for 24 h and was then poured into D_2O. The solution was extracted with ether. The ether solution was dried ($MgSO_4$) and evaporated to give a liquid, (3.5 g, 80%), δ_H (60 MHz; $CDCl_3$) 1.17 (6 H, s) and 7.17—8.17 (5 H, m).



α-([2-^{2}H]Isopropyl)-ββ-di-isopropylstyrene {[^{2}H]-(**4**)} was prepared from [2-^{2}H]-2-methyl-1-phenylpropan-1-one (3.5 g, 0.024 mol) and 2,4-dimethylpentan-3-one (2.7 g, 0.024 mol) in 17% yield (g.l.c.), m.p. 85—86 °C, δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.82 (6 H, d, J 7.0 Hz), 0.88 (6 H, s), 1.30 (6 H, d, J 7.0 Hz), 2.24 (1 H, sept, J 7.0 Hz), 2.58 (1 H, sept, J 7.0 Hz), and 6.9—7.3 (5 H, m).

3,3-Dimethyl-1-phenylbutan-1-one was prepared from phenylmagnesium bromide [from magnesium (2.4 g, 0.1 mol) and bromobenzene (15.7 g, 0.1 mol)] and 3,3-dimethylbutyryl chloride (13.4 g, 0.1 mol) in ether in 22% yield, b.p. 132—133 °C at 15 mmHg, *m/e* 176 (M^+, 4%), 120 (48), 105 (100), 77 (57), 57 (20), and 51 (29), δ_H (60 MHz; $CDCl_3$) 1.07 (9 H, s), 2.83 (2 H, s), and 7.2—8.0 (5 H, m).

ββ-Di-isopropyl-α-neopentylstyrene (**5**) was prepared from 3,3-dimethyl-1-phenylbutan-1-one (3.6 g, 0.020 mol) and 2,4-dimethylpentan-3-one (2.1 g, 0.018 mol) in 23% yield (g.l.c.), $\nu_{max.}$ 3 080, 3 060, 3 010, 2 950, 2 870, and 1 600 cm^{-1}, *m/e* 258 (M^+, 3%), 215 (7), 159 (19), 145 (26), 131 (9), 117 (9), 105 (9), 91 (15), 83 (9), 69 (10), 65 (6), and 57 (100), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.73 (9 H, s), 0.88 (6 H, d, J 7.2 Hz), 1.24 (6 H, d, J 7.2 Hz), 2.51 (2 H, s), 2.62 (1 H, sept, J 7.2 Hz), 2.83 (1 H, br sept), and 7.10—7.15 (5 H, m).

α-t-Butyl-ββ-di-isopropylstyrene (**6**) was prepared from 2,4-dimethylpentan-3-one (2.85 g, 0.025 mol) and 2-dimethyl-1-phenylpropan-1-one (4.4 g, 0.0275 mol) in 4% yield (g.l.c.), *m/e* 244 (M^+, 1%), 201 (8), 159 (19), 145 (35), 131 (14), 117 (12), 105 (15), 91 (26), 77 (8), 69 (9), and 57 (100), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.78 (6 H, d, J 7.1 Hz), 1.08 (9 H, s), 1.13 (6 H, d, J 6.8 Hz), 2.39 (1 H, sept, J 7.1 Hz), 3.47 (1 H, sept, J 6.8 Hz), and 6.9—7.2 (5 H, m).

3-Isopropyl-2,5-dimethylhex-3-ene (**7**) was prepared from 2-methylpropanal (2.2 g, 0.030 mol) and 2,4-dimethylpentan-3-one (2.8 g, 0.025 mol) in 7% yield (g.l.c.), $\nu_{max.}$ 2 960, 2 930, 2 870, and 1 460 cm^{-1}, *m/e* 154 (M^+, 5%), 111 (37), 97 (5), 87 (11), 83 (37), 73 (15), 69 (100), 55 (50), and 45 (19), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.92 (6 H, d, J 6.8 Hz), 1.00 (6 H, d, J 6.8 Hz), 1.02 (6 H, d, J 6.8 Hz), 2.27 (1 H, sept, J 6.8 Hz), 2.83 (1 H, sept, J 6.8 Hz), 2.65 (1 H, sept of d, ^3J 9.3, ^3J 6.8 Hz), and 4.95 (1 H, d, J 9.3 Hz).

3-Isopropyl-2,4,5-trimethylhex-3-ene (**8**) was prepared according to ref. 10 from 3-methylbutan-2-one (3.0 g, 0.035 mol) and 2,4-dimethylpentan-3-one (4.0 g, 0.035 mol) in 27% yield (g.l.c.), $\nu_{max.}$ 2 960, 2 930, 2 870, and 1 460 cm^{-1}, *m/e* 168 (M^+, 7%), 125 (24), 97 (8), 83 (47), 69 (100), and 55 (39), δ_H (360 MHz; [$^2H_6$]dimethyl ether) 0.97 (6 H, d, J 7.0 Hz), 1.02 (6 H, d, J 7.0 Hz), 1.10 (6 H, d, J 7.0 Hz), 1.56 (3 H, s), 2.66 (1 H, sept, J 7.0 Hz), 2.74 (1 H, sept, J 7.0 Hz), and 3.01 (1 H, sept, J 7.0 Hz). Attempts to prepare (**8**) by the method with $TiCl_3$ and $LiAlH_4$ gave a by-product [1:1 compared to (**8**)] which could not be separated from (**8**) even after repeated preparative g.l.c. treatments. The impurity was only observed on capillary gas chromatography and in the n.m.r. spectrum. It was identified through its n.m.r. spectrum as an isomer of (**8**), 3-isopropyl-2,6-dimethylhept-3-ene. Assignments were verified by double-resonance experiments. The vinylic proton couples with the methylene group, ^3J 7.0 Hz.

^{1}H N.m.r. spectra were recorded on a Nicolet 360 WB spectrometer. The samples were *ca.* 0.04M in [$^2H_6$]dimethyl ether and they were degassed by the high-vacuum freeze–thaw technique before being sealed off. Me_4Si was used as internal reference. The temperature scale of the instrument was calibrated by the use of a methanol–[$^2H_6$]acetone sample, which in turn had been calibrated by the technique described in ref. 11. using a JEOL MH-100 instrument.

N.O.e. difference experiments were run by automatic frequency alteration using the sequence: preirradiation (6 s), delay (50 ms), pulse, and acquisition of one transient. After *ca.* 100 passes through the cycle the f.i.d.s were Fourier transformed, identically phased, and the spectra subtracted. The n.O.e. experiments were performed on degassed and sealed samples in [$^2H_6$]dimethyl ether.

Bandshape analysis was performed as previously described.[11] The free energy differences and the free energies of activation were calculated using equations (1) and (2) where p_A is the

$$\Delta G^\circ = 1.987 \times 10^{-3} T \ln \frac{p_A}{p_B} \text{ kcal mol}^{-1} \quad (1)$$

$$\Delta G^\ddagger = 4.575 \times 10^{-3} T [10.319 + \log T/k] \text{ kcal mol}^{-1} \quad (2)$$

fractional molar population of conformer A. The calculations were performed on a PDP 11/34 computer with a GT 42 graphics terminal and a Printronix lineprinter–plotter of the Computer Graphics Laboratory for Organic Chemistry at the University of Lund.

Molecular mechanics calculations were performed using the MM2 or MMP2 programs developed by Allinger and his co-workers, employing their 1977 force field.[12–14] The calculations were carried out with full relaxation techniques, and all input structures were optimized without symmetry or other constraints. The energy profiles for the rotation of the isopropyl and phenyl groups were obtained using bond-drive techniques.

Results

Dynamic ^1H N.m.r. Spectroscopy.—At ambient temperature the 360 MHz ^1H n.m.r. spectra of (1)—(8) display signals corresponding to fast conformational inversion on the n.m.r. timescale.

The spectrum of (1) remained unchanged down to −100 °C, indicating the existence of one single conformation.

The spectrum of (2) exhibited selective broadening of the isopropyl methine septet at δ 2.56 below −20 °C. At −80 °C this signal resharpened as one single septet displaced *ca.* 0.1 p.p.m. to higher field. No trace of a second septet coming from a minor conformer could be found, and the other signals remained sharp in the whole temperature interval.

The α-ethyl and α-isopropyl derivatives (3) and (4) behaved quite similarly to (2) (Figure 1). In addition the lowfield methyl doublets [δ 1.28 for (3) and 1.30 for (4)] broadened and resharpened in the same temperature interval, 0 to −70 °C. Attempts to identify signals from minor conformers by decoupling through irradiation at the methyl doublets failed. Apparently a very small population of a minor conformer, perhaps lessened by unfavourable entropies at low temperatures, is present for all three compounds (2)—(4). Bandshape analyses of the broadened isopropyl septets of (2)—(4), with the assumption that the chemical shift difference between major and minor conformations is between 0.5 and 2.2 p.p.m., indicate that the minor conformers constitute 0.5—3% at the coalescence temperature.

ββ-Di-isopropyl-α-neopentylstyrene (5) displayed exchange-broadened spectra even at ambient temperature. Below −40 °C all signals from the isopropyl and neopentyl groups except the highfield isopropyl doublet decoalesced into two sets of signals corresponding to two conformations of the isopropyl groups with the population ratio 65:35. The septets from the minor constituent were hidden under the solvent peak and were found by irradiation at several frequencies with observation of the decoupling of their corresponding doublets.

Below −70 °C a second process appeared as a selective decoalescence of one isopropyl doublet (δ 0.86) and the methylene signal of the minor conformation. The detailed shape of these signals at −125 °C, at the slow exchange limit, was not resolved due to broad spectra probably caused by a third

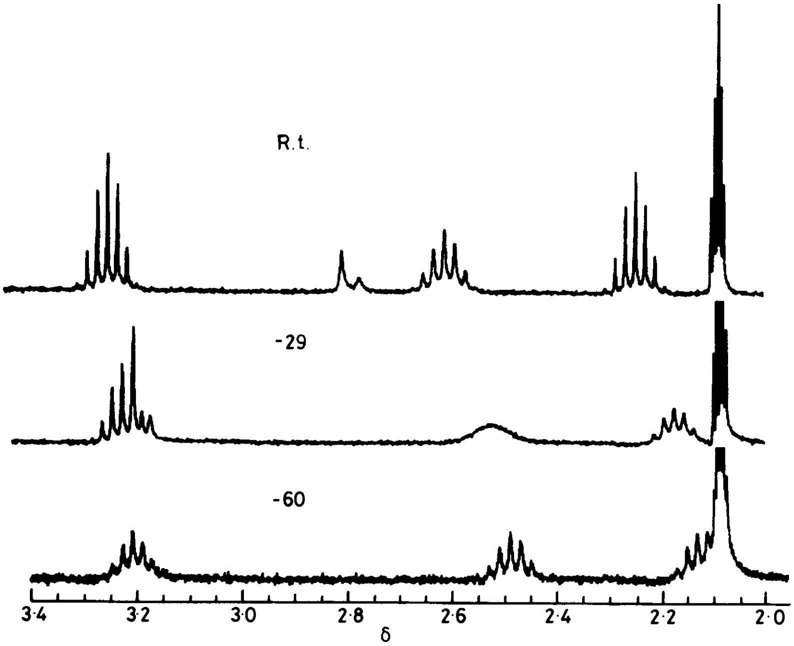


Figure 1. 360 MHz ^1H N.m.r. spectrum of (4) in [$^2H_6$]acetone at different temperatures showing the isopropyl septet region. Peaks at δ 2.8 at room temperature and amidst the septet at δ 3.2 at −29 °C are impurities

Table 1. Fractional populations, $\Delta G°$, and $\Delta G^{\ddagger}$ (major → minor) for compounds (1)—(8)

Compound	Major conf. (%)	Minor conf. (%)	$\Delta G°$ [a]	T [b]	$\Delta G^{\ddagger}$ [a]	T [b]
(1)	A ≥ 99		> 1.5			
(2)	A 97—99.5	(B) 0.5—3	≥ 1.3 ≤ 2.2	225	11.3	225
(3)	A 97—99.5	(B) 0.5—3	≥ 1.3 ≤ 2.2	225	11.1	225
(4)	A 97—99.5	(B) 0.5—3	≥ 1.3 ≤ 2.21	253	12.0	253
(5)	A 65	B 35	0.27 ± 0.05	218	11.5	240
(6)	B 91	C 9	0.75 ± 0.10	164	10.5	210
(7)	B ≥99		≥1.5			
(8)	A 73	B 27	0.60 ± 0.10 [c]	203	12.2	234

[a] kcal mol^{-1}. [b] K. [c] $\Delta H°$ 0.49 ± 0.10 kcal mol^{-1}, $\Delta S°$ −0.50 ± 0.05 cal mol^{-1} K^{-1}.

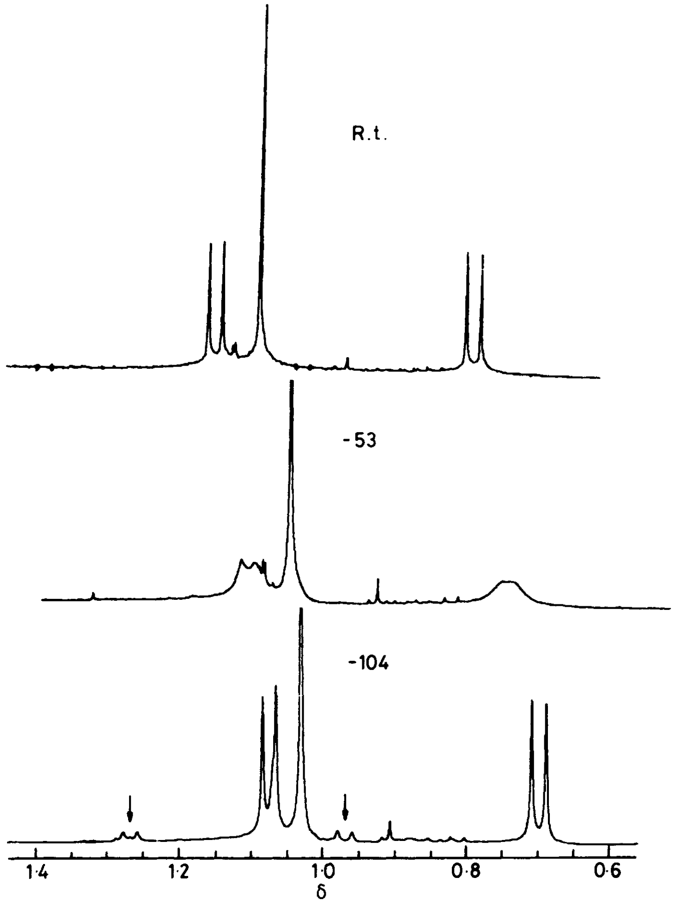


Figure 2. 360 MHz ^{1}H N.m.r. spectrum of (6) in [$^2H_6$]dimethyl ether at various temperatures showing the isopropyl–methyl region and the Bu^t signal. Arrows indicate the doublets from the minor conformation

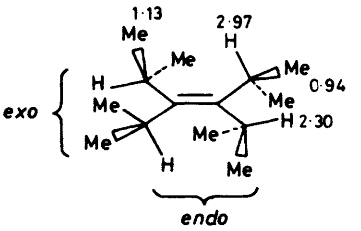
process becoming slow on the n.m.r. timescale. The barrier was estimated to be 9.4 ± 0.4 kcal mol^{-1} at −90 °C.

The spectrum of ββ-di-isopropyl-α-t-butylstyrene (6) displayed changes of the isopropyl signals in the temperature range −20 to −105 °C while the t-butyl signal remained essentially unchanged. At −110 °C two sets of signals with the intensity ratio 9:91 appeared (Figure 2). The septets of the minor conformation were just about recognizable but appeared clearly by decoupling through irradiation of the appropriate doublets.

No sign of changes was observed in the spectrum of 3-isopropyl-2,5-dimethylhex-3-ene (7) down to −100 °C, while 3-isopropyl-2,4,5-trimethylhex-3-ene (8) gave rise to decoalescence of all signals. At −70 °C two sets of signals with relative intensities 73:27 were obtained (Figure 3). The temperature dependence of the equilibrium was followed in the range −55 to −125 °C and gave $\Delta H°$ 0.49 ± 0.10 kcal mol^{-1} and $\Delta S°$ −0.50 ± 0.05 cal mol^{-1} K^{-1}.

A summary of the dynamic n.m.r. results and the derived energy parameters is found in Table 1.

Conformational and N.m.r. Assignments.—The conformational attributions in Table 1 are based on chemical shift considerations, double resonance, and n.O.e. difference techniques as well as on results of the MM calculations. The relative n.m.r. chemical shifts of the isopropyl methyl and methine signals are primarily determined by the anisotropy of the double bond and the phenyl group and by van der Waals shifts of proximate alkyl groups. Two idealized positions can be visualized for each of the methyl and methine groups, here called *endo* and *exo*.



The difference in chemical shift between *endo* and *exo* positions for the methyl and methine protons, due to the anisotropy of the double bond, may be illustrated by tetraisopropylethylene,[15] for which the proposed assignments are based upon the conclusions from this work. The anisotropic shielding effects of the phenyl group are strongly dependent upon the twist angle between this group and the double bond. However, chemical shift considerations alone do not allow for conclusive attributions, and we had to seek additional evidence. First, the combination of couples of doublets and septets for all isopropyl groups in all conformations was established by decoupling. A powerful technique, which has become available

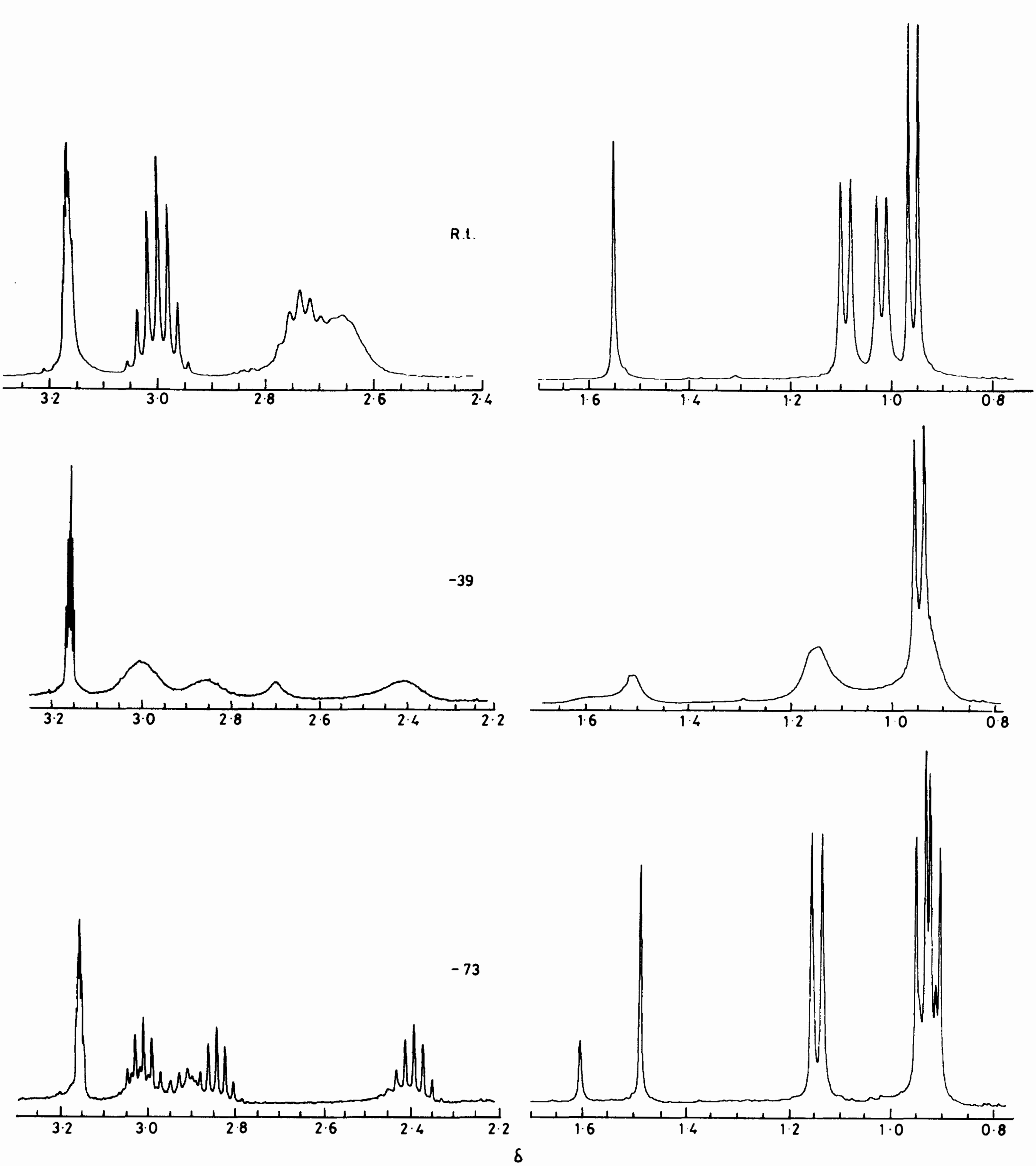


Figure 3. 360 MHz ^1H N.m.r. spectrum of (**8**) in [$^2H_6$]dimethyl ether at various temperatures. Solvent peak at δ 3.15

by modern pulse n.m.r. instrumentation, is n.O.e. difference spectroscopy.[16] This was applied to compounds (**1**)—(**8**) both at room temperature and at temperatures where the exchange rate is slow, below −75 °C in most cases.

In compound (**1**) only one rotamer is observed, which we allocated to conformation *a* (Scheme 2). An n.O.e. enhancement of the vinylic proton signal was caused by preirradiation of the doublet at δ 1.14 thus establishing the proximity between these groups.

There is a striking similarity between (**2**)—(**4**) both in dynamic behaviour and in chemical shifts of the β-isopropyl groups. Conformational assignment of the strongly dominant rotamer was supported by the following n.O.e. experiments. Partial saturation of the methyl signal at δ 1.96 of (**2**) led to enhancement of the doublet at δ 1.27 and *vice versa.* In (**3**) preirradiation of the doublet at δ 0.86 caused enhancement of the septet at δ 2.50 and in (**4**) preirradiation of the doublet at δ 1.29 gave enhancement of the septet at δ 3.23. The latter septet was identified by selective deuteriation of the methine proton of the isopropyl geminal to the phenyl group. All these experiments point towards A as the dominant rotamer. Compounds (**2**)—(**4**) have very similar chemical shifts of the β-isopropyl groups with the exception that the *endo* proton *cis* to phenyl in (**4**) appears at somewhat higher field. This upfield shift could be semi-quantitatively reproduced by screening constant calculations[17] using the geometries from the MM calculations according to which this proton is situated in a more shielding position than the corresponding protons in (**2**) and (**3**). More striking is the deviation of the chemical shifts of the *cis*-isopropyl group in (**1**). This is explained by a much smaller angle around the phenyl–olefin bond in (**1**), placing the *cis*-isopropyl protons in the deshielding region of the phenyl anisotropy. MM calculations and u.v. spectra also support a more planar arrangement in (**1**).

The α-neopentyl derivative (**5**) exists in at least two rotamers. Preirradiation of the doublet, at δ 1.29, of the major constituent enhanced the singlet at δ 2.54 for the methylene group. Furthermore, the chemical shifts of the isopropyl protons in the major constituent are quite similar to the corresponding values in (**2**)—(**4**). The shifts of the methylene protons experience the expected van der Waals' shift in rotamer *a*, whereas the t-butyl group shifts in the opposite direction, probably because of a change of conformation with respect to the phenyl group.

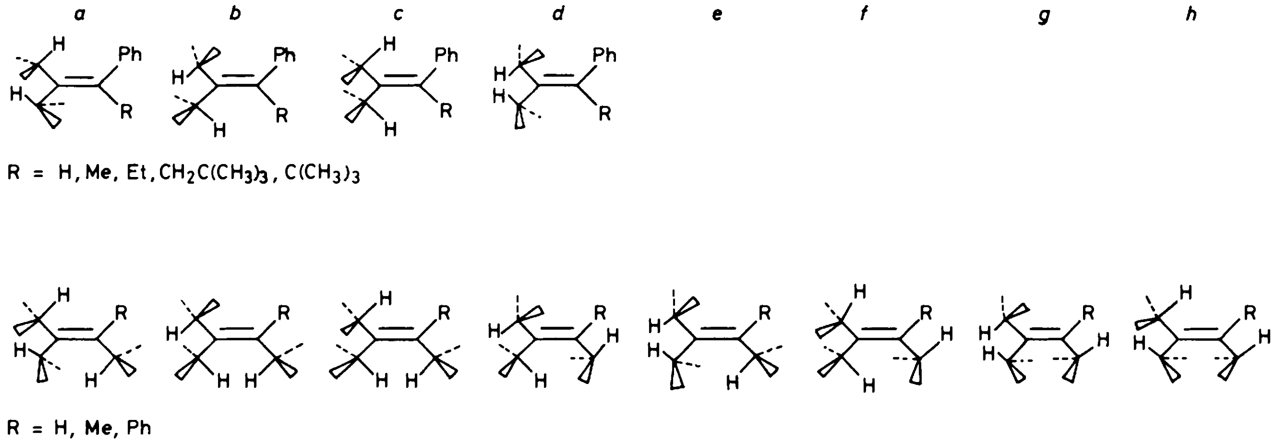
The attribution of the major constituent of (**6**) (to *b*, Scheme 2) was confirmed by n.O.e. enhancement of the septet at δ 3.42 on preirradiation of the t-butyl signal at δ 1.02. For the attribution of the minor constituent to rotamer *c* we had to resort to MM calculations, but the chemical shifts are also in best agreement with this conformation. Thus, the shift of the *trans*-isopropyl methine proton is hardly compatible with any other conformation of this isopropyl group.

In (**7**) a relatively large three-bond coupling of 9.3 Hz between the olefinic proton and the geminal isopropyl methine proton assigns this isopropyl group. No significant n.O.e. effects were obtained, and the assignment of the only observed conformation to rotamer *b* was based on MM calculations and chemical shift comparisons.

The resonance of the isopropyl group geminal to the methyl group of (**8**) is easily identified, since this group maintains the same conformation in the two possible rotamers *a* and *b*, and thus a very small splitting is observed. Furthermore, a selective n.O.e. enhancement of the doublet at δ 0.94 was observed on preirradiation of the methyl resonance at δ 1.49. In order to decide among the alternative rotamers *a* and *b* we use the following arguments. First, the chemical shifts of the $C{=}C{-}CH_3$ group in the two conformations are best understood by a van der Waals effect caused by the *cis*-isopropyl methyls in a conformation as in *b*. Second, preirradiation of the methyl group at δ 1.49 led to enhancement of only one septet, the one at δ 2.84.

Molecular Mechanics Calculations.—In order to treat the conformational situation in the present set of molecules, a computational procedure which includes the conjugation in the π-electron system must be applied. We have used the MMP2 force field,[13] in which a π-electron selfconsistent-field calculation generates the necessary force constants for stretching and torsion for the bonds connecting the π-system atoms. A crucial parameter in the calculations is the torsional angle about the phenyl–ethylene bond. Fortunately, the MMP2 force-field satisfactorily reproduces the planarity of styrene as well as the torsional barrier.[18]

Throughout the series (**1**)—(**8**) the calculations predict four types of minima when the energy is mapped as a function of the two dihedral angles defining the conformations of the geminal

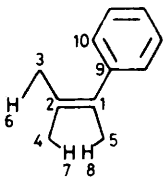


Scheme 2.

Table 2. Relative calculated energies of the rotamers *a*—*h* in kcal mol^{-1}

Compound	*a*	*b*	*c*	*d*	*e*	*f*	*g*	*h*
(**1**)	0.00	2.91	3.51	2.54				
(**2**)	0.19	0.00	1.36	2.35				
(**3**)	0.23	0.00	1.83	2.79				
(**4**)	0.00	0.49	1.29	2.65	3.43	4.03	10.91	8.14
(**5**)	0.21	0.00	0.74	3.48				
(**6**)	5.76	0.00	1.06	9.72				
(**7**)	0.92	0.00	2.59	1.16	1.81	5.09	8.07	8.17
(**8**)	0.13	0.00	1.49	1.69	2.78	3.96	10.55	8.58

Table 3. Selected calculated structural parameters



Compound	Conformation	2-1-9-10^a	1-2-3-6^a	1-2-4-7^a	2-1-5-8^a	1-2^b	2-1-9^c
(1)	*a*	51.9	2.0	176.3		1.349	126.8
	d	71.0	144.3	169.3		1.346	127.2
(2)	*a*	86.4	6.6	167.2		1.352	120.4
	b	85.1	176.4	2.6		1.352	124.0
(3)	*a*	77.9	4.7	172.0		1.353	120.2
	b	89.5	174.0	4.4		1.353	123.4
(4)	*a*	88.2	0.7	178.8	2.8	1.353	119.0
	b	89.5	168.6	8.3	40.2	1.356	121.9
(5)	*a*	69.7	2.7	176.1		1.356	119.7
	b	76.7	159.5	15.0		1.356	122.2
(6)	*b*	87.2	179.9	0.1		1.358	119.3
	c	88.0	20.6	13.8		1.361	117.4
(7)	*b*		180.0	0.1	0.2	1.347	
	a		0.1	179.9	0.3	1.348	
(8)	*a*		10.1	172.0	7.2	1.356	
	b		170.0	11.4	30.4	1.357	

[a] Torsional angle, degree. [b] Bond length, Å. [c] Bond angle, degree.

Table 4. U.v. spectra in hexane

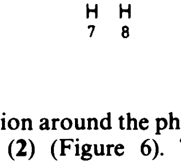
Compound	$\lambda_1{}^a$ (ε_1)	$\lambda_2{}^a$ (ε_2)	$\lambda_3{}^a$ (ε_3)
Benzene^b	203.5 (7 400)	254 (204)	
Styrene^c	248 (14 000)	282 (750)	291 (500)
(1)	242 (27 800)		
(2)	231 (5 400)		
(3)	230 (6 100)		
(4)	223 (sh)	254 (3 000)	
(5)	246 (18 900)		
(6)	218 (sh)	262 (4 400)	

[a] nm. [b] In hexane. [c] In ethanol.

isopropyl groups, giving rise to the rotamers *a*—*d*. In **(4)**, **(7)**, and **(8)** another four rotamers, *e*—*h*, are obtained due to the two possible conformations of the third isopropyl group (Scheme 2). The calculated energies of all stable rotamers are found in Table 2 and geometrical parameters of the two low-energy forms of each compound are given in Table 3.

The calculated dihedral angles at the phenyl–ethylene bond (2–1–9–10) are mostly close to 90°. The largest deviation is found for **(1)** in which the absence of an α-substituent enables a reduction of the dihedral angles to 52°. In the two α-primary-alkyl derivatives **(3)** and **(5)** the ethyl.and neopentyl groups project towards one side of the ethylene plane, thus introducing an unsymmetrical buttressing of the phenyl group leading to a reduction of the angle to 78° and 70°, respectively. The geminal isopropyl groups deviate only slightly from the ideal bisected conformation in the gear-meshed rotamers *a* and *b*, somewhat more in *c* and *d*. These calculated rotamer geometries are in harmony with the chemical shift features discussed above. The calculated structures and chemical shift assignments are shown in Figure 4.

The conformational change of the isopropyl groups between two gear-meshed conformations may proceed through a stepwise mechanism, where the isopropyl groups rotate one at a time over intermediates such as *c* or *e*, or through a correlated rotation over a single transition state. By use of the incremental group driving technique, one might get information to aid a decision among these alternatives. Such calculations were performed on **(8)** by driving the torsional angles C(1)–C(2)–C(3)–H(6), C(1)–C(2)–C(4)–H(7), and C(2)–C(1)–C(5)–H(8). The results are given in Figure 5. The favoured pathway is an uncorrelated rearrangement over the rotamer *e* with a calculated barrier of 11.0 kcal mol^{-1} ($b \longrightarrow a$). Any correlated rotation of the isopropyl groups (two or three) requires barriers which are at least twice as high as the uncorrelated mechanism.



The barrier to rotation around the phenyl-ethylene bond was studied for **(1)** and **(2)** (Figure 6). The calculations were performed on rotamers *a* in both cases, corresponding to the experimental minimum-energy conformations. Compound **(1)** has a calculated angle between the ring and ethylene planes of 52° and two barriers corresponding to the planar and 90°

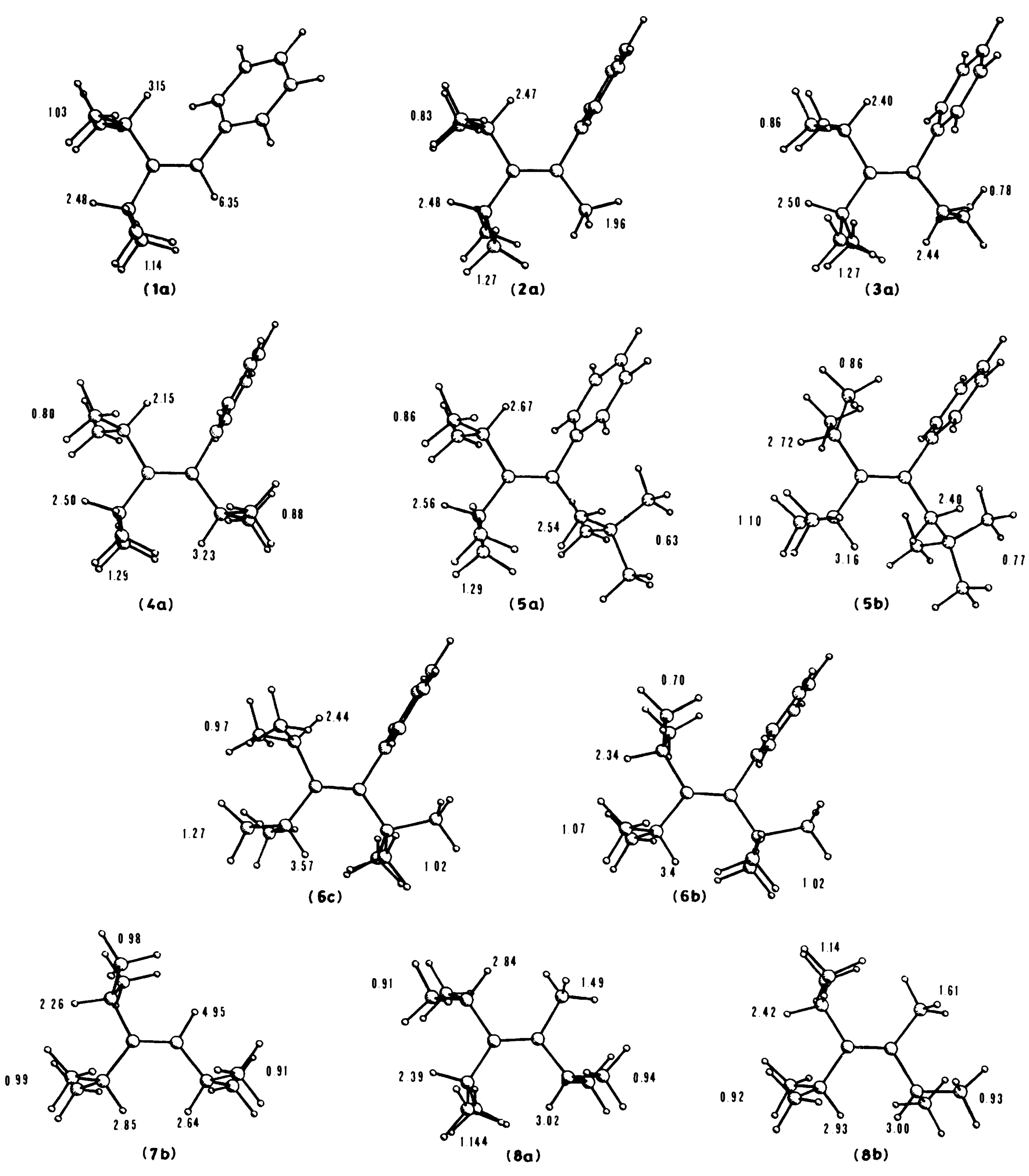


Figure 4. Structures of all conformers of (**1**)—(**8**), that are appreciably populated, calculated by the MM2 or MMP2 force fields. Numerical values are chemical shifts at low temperature in [$^2H_6$]dimethyl ether for all signals except those from the aromatic protons

twisted arrangements of 4.7 and 0.8 kcal mol^{-1}, respectively. In (**2**) there is a rather shallow minimum around the 90° twisted conformation and a barrier of 12.6 kcal mol^{-1} for passage of the planar form.

Ultraviolet Spectroscopy.—The u.v. spectra of the styrenes (**1**)—(**6**) in hexane are given in Table 4. The most interesting band, the K band, appears at 248 nm in styrene. The hypsochromic shifts of this band correlate well with the calculated twist angles about the phenyl–olefin bond, (**1**) and (**5**) being the only structures for which the angle significantly deviates from 90°.

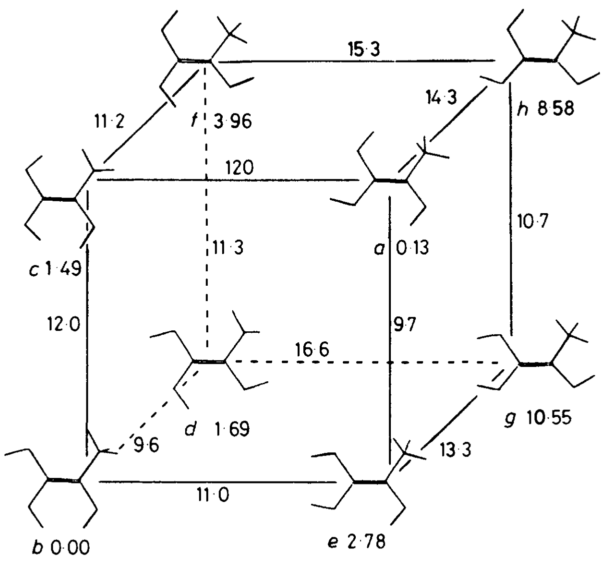


Figure 5. Rearrangement graph for (**8**) showing the calculated relative energies of the conformers and the barriers to rotation from the more stable to the less stable rotamer

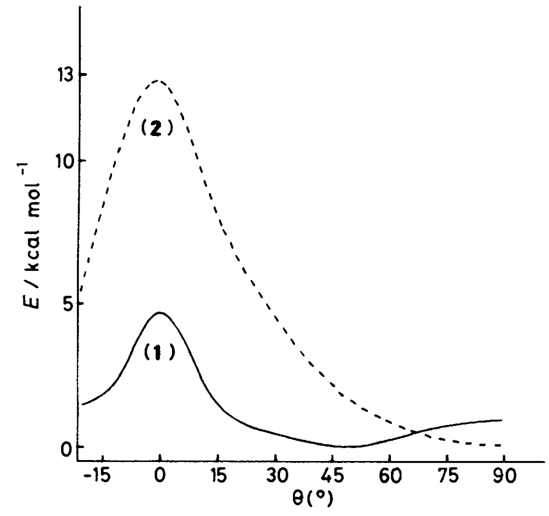
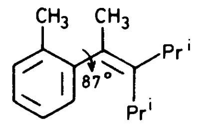
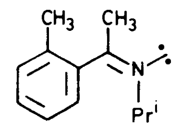


Figure 6. Relative steric energy of (**1**) and (**2**) as a function of the torsional angle between the benzene and ethylene planes calculated by the MMP2 force field



$\Delta G^{\ddagger}_{340}$ 25·4 kcal mol^{-1}

(**9**)



$\Delta G^{\ddagger}_{347}$ 18·3 kcal mol^{-1}

(**10**)

Discussion

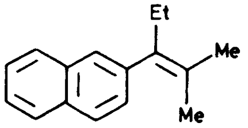
The conformation of two geminal isopropyl groups has been extensively studied in *NN*-di-isopropyl-amides, -thioamides, and one -selenoamide.[6,19–21] Rotamers corresponding to *a* and *b* are observed in the majority of the cases, and the equilibrium between them, and the barrier separating them are determined by the effective sizes of X and Y (Scheme 1). When both X and Y are large, as for X = CH_3Se and Y = Se or X = CH_2Ph and Y = S, rotamer C appears, while D has not been found so far. However, D is predicted by molecular mechanics calculations in cases of small flanking substituents, and it has been observed in cases with vicinal isopropyl groups.[22]

The general pattern observed for the conformation of geminal isopropyl groups in amides and thioamides is also found in the series (**1**)—(**8**), *i.e.* the 'gear-meshed' rotamers *a* and *b* are preferred. Only for (**6**), and, possibly (**5**), is rotamer *c* appreciably populated. The systems (**4**), (**7**), and (**8**) bear vicinal isopropyl groups, and for this configuration the conformation in which the isopropyl groups present their methine protons towards each other turns out to be at least as favourable as the 'gear-meshed' ones. Such a conformation is governed by the eclipsing of the double bond by both methine protons and is also found for simple analogues, such as *cis*-but-2-ene.[23]

The most striking aspect of the results summarized in Table 1 is the reluctance of the systems (**1**)—(**6**) to take up conformations in which the *cis*-isopropyl group exposes its bulkier face, the methyl groups, towards the phenyl group. Using the populations of the rotamers as a measure of the effective size in these systems the following order is obtained: $H \ll CH(CH_3)_2 < CH_3 \leq C_2H_5 < CH_2C(CH_3)_3 < Ph < C(CH_3)_3$. In energy terms, given by the $\Delta G°$ values in Table 1, the phenyl–methyl difference is at least 1.3 kcal mol^{-1} and the phenyl–neopentyl difference at least 0.27 kcal mol^{-1}. Very recently, several papers have appeared treating the steric interactions between the phenyl group and alkyl groups in various systems.[24–27] It turns out that, whenever the phenyl ring can expose its planar face towards a flanking methyl without interfering with other substituents, or with the framework, it behaves as if it were 'smaller' than or of about the same size as the methyl group,[28] in salient contrast to our findings. Must we conclude, then, that the phenyl group is considerably more coplanar with the ethylene plane than was concluded from both experimental and computational considerations in this work? The experimental evidence, including n.m.r. chemical shifts and u.v. spectra, is a rather coarse measure of the phenyl–olefin angles. Further evidence is found in a comparison of the behaviour of (**2**)—(**4**) with that of ββ-di-isopropyl-α,2-dimethylstyrene (**9**),[5] and *N*-[1-(2-methylphenyl)ethylidene]isopropylamine (**10**),[29] which are strongly twisted in the ground state and have high torsional barriers around the phenyl–olefin bond. Compound (**9**) has n.m.r. and u.v. spectra which are very similar to those of (**2**)—(**4**).

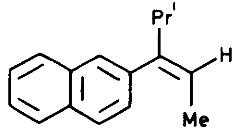
How reliable, then, are the MM calculations on this point? The energy profile for rotation around the phenyl–ethylene bond, and particularly, the shape of the curves around the minima, may give information about the reliability of the calculated phenyl–ethylene dihedral angles. As seen in Figure 6, a change of the dihedral angle in (**2**) by *ca.* 30° from the minimum energy value (86°) raises the energy by 1 kcal mol^{-1}. A minor deficiency in the force field may thus cause erroneous values of these dihedral angles. Furthermore, since the potential energy surface around the minimum certainly is much steeper in rotamer *b* than in *a*, due to the stronger interaction between the phenyl ring and the *cis*-isopropyl group, torsional liberation of the phenyl group may entropically favour rotamer *a*.

Thus, although deviation from orthogonality and torsional libration may contribute to increase the apparent size of the phenyl group, we believe that the major origin is to be sought in the specific interactions between the isopropyl group and the phenyl group. When polyhedral substituents interact with each other, strain accommodation takes place mainly by rotation of the polyhedral groups, so as to find a conformation of comparably low energy (gear effect).[6] In this work, that is manifested by the interaction between the β-isopropyl groups. In the isopropyl–phenyl interaction of the styrenes there is no



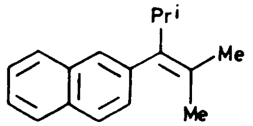
(11)

$\Delta G^{\ddagger}$ 6·6 kcal mol^{-1}



(12)

$\Delta G^{\ddagger}$ 5·2 kcal mol^{-1}



(13)

$\Delta G^{\ddagger}$ 12·9 kcal mol^{-1}

such effective relaxation mechanism, and thus the bulkier dimethyl side of the isopropyl group and the face of the phenyl group experience considerable strain when they interact in a *cis*-vicinal arrangement. This illustrates that important energy differences can appear depending upon how conveniently various groups can get on together sterically. In a recent gas chromatographic study it was shown that alkyl–phenyl interactions depend upon the shape of the alkyl group.[30] Furthermore, the geometry of the framework and the substitution pattern also have a profound influence on the interaction between phenyl and alkyl groups. Thus, the aromatic ring face presents a very small hindrance to geminal isopropyl and neopentyl groups in *N*-alkyl(thio)anilides[27] in agreement with our finding for (**4**), in which the isopropyl group geminal to the phenyl group prefers a conformation in which it turns its bulkier face toward the phenyl.

Comparison of the data in Table 1 with those of Table 2 shows that only four out of eight entries agree as to the most stable rotamer. A closer look reveals that in (**2**)—(**5**) the calculations unjustifiedly tend to favour the conformation, in which the *cis*-isopropyl group exposes its bulkier face, the methyl groups, towards the phenyl group, by 0.5—1.5 kcal mol^{-1}. Although a minor part of this discrepancy can be ascribed to effects such as differential solvation or to an entropy term, we believe that the major role is to be found in some inadequacy in the force field. One possibility is that the standard MMP2 force field underestimates the steric requirements of the faces of the benzene ring. However, the rather poor agreement between experimental ΔH° (0.5 kcal mol^{-1}) and calculated ΔE (-0.13 kcal mol^{-1}) values for (**8**) is an indication that other factors may also contribute.

The calculated barriers to rotation of the phenyl group in (**1**) and (**2**), 4.7 and 12.6 kcal mol^{-1}, respectively, conform with experimental barriers in β-naphthylethylenes, such as (**11**)—(**13**),[3] but a closer comparison is not possible, since the barrier is extremely sensitive to the substitution pattern in the α and β positions.[2,3] However, methyl substitution in the *ortho* position of (**2**) renders the molecule chiral and thus the barrier experimentally accessible, $\Delta H^{\ddagger}$ 18.9 $\pm$ 1.0 kcal mol^{-1}, a value somewhat lower than the calculated one, 21.4 kcal mol^{-1}.[5]

The barriers to interchange of the isopropyl groups fall in the rather narrow range of 10.5—12.2 kcal mol^{-1}. The highest barrier [(**8**), 12.2 kcal mol^{-1}] is obtained for the conceptually less strained molecule and the lowest barrier [(**6**), 10.5 kcal mol^{-1}] for the most strained one. This is a typical 'ground-state effect', *i.e.* a lower ground-state strain in (**8**) is not compensated for by a higher transition-state strain in (**6**). According to the calculations on (**8**), these processes proceed through stepwise rotation of the isopropyl groups *via* rotamer *e*, in agreement with several earlier findings.[6,19—21,31,32] The calculated barrier, 11.0 kcal mol^{-1}, is *ca.* 1 kcal mol^{-1} lower than the experimental value, as frequently observed in similar calculations.[33]

Finally, the low-temperature features of the n.m.r. spectrum of (**5**) deserve some comment. As was mentioned above, signs of further exchange processes were observed in the temperature range -70 to -135 °C, which could not be satisfactorily analysed due to unresolved spectra. We envisage two possible processes to account for the observations; the rotation of the neopentyl group and the rotation of the isopropyl group *cis* to the phenyl. The latter alternative implies that the first decoalescence to be ascribed the freezing of the rotation of only one isopropyl group, the one *trans* to the phenyl, the *cis*-isopropyl group still rotating fast. Actually, this alternative is not unreasonable, considering the calculated rotamer energies of (**5**) (Table 2), and that the stability of rotamer *c* seems to be exaggerated by *ca.* 1 kcal mol^{-1} in the MM calculation.

In summary, conformational analysis of a series of α-alkyl-ββ-di-isopropylstyrenes leads to the following conclusions: (i) the phenyl group is twisted *ca.* 70—90° out of the ethylene plane and (ii) the conformational populations of the geminal isopropyl groups indicate that the effective steric size of the phenyl group is larger then those of methyl, ethyl, isopropyl, and neopentyl groups, but smaller than that of the t-butyl group.

This unexpectedly large apparent size of the phenyl group, in view of the large twist angle, is rationalized by reluctance of a phenyl group and the bulkier face of the isopropyl group to tolerate each other sterically, when placed *cis*-vicinal to each other.

Molecular mechanics calculations fail to reproduce the experimentally determined conformational populations and seem to underestimate the steric requirements of the phenyl group in *cis*-vicinal interactions with the methyl groups of an isopropyl group by *ca.* 1 kcal mol^{-1}. The calculations reproduce barriers to rotation of the isopropyl and phenyl groups to within *ca.* $\pm 10\%$ of $\Delta H^{\ddagger}$ (or $\Delta G^{\ddagger}$) values.

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References

1 H. Musa, T. Ridley, P. H. Turner, K. H. Weisenberger, and V. Fawcett, *J. Mol. Spectrosc.*, 1982, **94**, 437.
2 J. E. Anderson and C. J. Hazlehurst, *J. Chem. Soc., Chem. Commun.*, 1980, 1188.
3 J. E. Anderson, D. J. D. Barkel, and C. J. Cooksey, *Tetrahedron Lett.*, 1983, **24**, 1077.
4 R. Adams and J. W. Mecorney, *J. Am. Chem. Soc.*, 1945, **67**, 798.
5 I. Pettersson and U. Berg, *J. Chem. Res.* (*S*), 1984, 208.
6 U. Berg, T. Liljefors, C. Roussel, and J. Sandström, *Acc. Chem. Res.*, 1985, **18**, 80.
7 J. E. McMurry and M. P. Flemming, *J. Am. Chem. Soc.*, 1974, **96**, 4708.
8 J. E. McMurry, M. P. Flemming, K. L. Kees, and L. R. Krepski, *J. Org. Chem.*, 1978, **43**, 3255.

9 R. Dams, M. Malinowski, I. Westdorp, and H. Y. Geise, *J. Org. Chem.*, 1982, **47**, 248.

10 D. Lenoir, *Synthesis*, 1977, 553.

11 U. Berg and U. Sjöstrand, *Org. Magn. Reson.*, 1978, **11**, 555.

12 N. L. Allinger, *J. Am. Chem. Soc.*, 1977, **99**, 8127.

13 J. Kao and N. L. Allinger, *J. Am. Chem. Soc.*, 1977, **99**, 975.

14 U. Burkert and N. L. Allinger, 'Molecular Mechanics,' ACS Monograph 177, Washington, 1982.

15 (*a*) R. F. Langler and T. T. Tidwell, *Tetrahedron Lett.*, 1975, 777; (*b*) D. S. Bomse and T. H. Morton, *ibid.*, p. 781.

16 See *e.g.* D. Neuhaus, R. N. Sheppard, and I. R. Bick, *J. Am. Chem. Soc.*, 1983, **105**, 5996.

17 C. W. Haigh and R. B. Maillion, *Org. Magn. Reson.*, 1972, **4**, 203.

18 S. Andersson, Thesis, University of Lund, 1982, p. 98.

19 A. Lidén, C. Roussel, T. Liljefors, M. Chanon, R. E. Carter, J. Metzger, and J. Sandström, *J. Am. Chem. Soc.*, 1976, **98**, 2853.

20 T. Liljefors and J. Sandström, *Org. Magn. Reson.*, 1977, **9**, 276.

21 H. Fritz, P. Hug, H. Sauter, T. Winkler, S.-O. Lawesson, B. S. Pedersen, and S. Scheibye, *Org. Magn. Reson.*, 1981, **16**, 36.

22 C. Roussel, A. Lidén, M. Chanon, J. Metzger, and J. Sandström, *J. Am. Chem. Soc.*, 1976, **98**, 2847.

23 F. Bernardi, A. Bottoni, and G. Tonachini, *J. Chem. Soc., Perkin Trans. 2*, 1983, 15.

24 M. Charton, *J. Org. Chem.*, 1983, **48**, 1011, 1016.

25 (*a*) L. A. Paquette, J. M. Gardlik, K. J. McCullough, and Y. Hanzawa, *J. Am. Chem. Soc.*, 1983, **105**, 7644; (*b*) L. A. Paquette, J. M. Gardlik, K. J. McCullough, R. Samodral, G. Dehucca, and R. J. Ouellette, *ibid.*, p. 7649.

26 M. Manoharan and E. L. Eliel, *J. Am. Chem. Soc.*, 1984, **106**, 367.

27 I. Pettersson and J. Sandström, *Acta Chem. Scand. B*, 1984, **38**, 397.

28 J. Bjögo, D. R. Boyd, C. G. Watson, and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 2*, 1974, 757, 1081.

29 D. R. Boyd, S. Al-Showiman, and W. B. Jennings, *J. Org. Chem.*, 1978, **43**, 3335.

30 T. Endo, M. M. Ito, Y. Yamada, H. Saito, K. Miyazawa, and M. Nishio, *J. Chem. Soc., Chem. Commun.*, 1983, 1430.

31 O. Ermer, *Angew. Chem.*, 1983, **95**, 1010; *Suppl.* 1983, 1353.

32 L. Lunazzi, M. Guerra, D. Macciantelli, and G. Cerioni, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1527.

33 B. Tiffon and J. S. Lomas, *Org. Magn. Reson.*, 1984, **22**, 29.

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