# Determination of *cis*-Methyldecalone and *cis*-Methylhydrindanone Conformation by Proton Nuclear Magnetic Resonance

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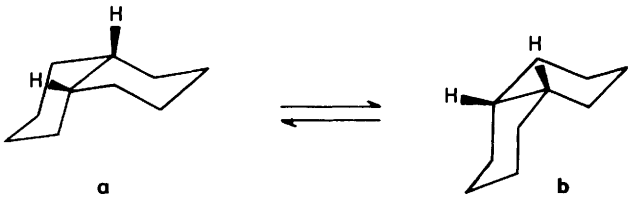
The position of the conformational equilibrium for *cis*-9-methyldecalones, *cis*-methyldecalindiones, *cis*-methylhydrindanones, and other polyfunctional compounds in these series has been determined by comparing the measured solvent effect induced by a carbonyl group on the angular methyl group by $^1$H n.m.r., and the corresponding values calculated for each conformer. If the methyl is in a γ position to the carbonyl group, Zürcher increments must then be considered.

The decalin skeleton occurs in many compounds. Functionalized derivatives of decalin are useful synthons for building more complex natural compounds (*e.g.* steroids, terpenes, and sesquiterpernes). *cis*-Decalin exists in an equilibrium between two conformers of the same energy. Interconversion between the two conformers requires ring inversion through a flexible 'twist boat' intermediate.[1,2] Axial substituents in one conformation become equatorial in the other (Scheme 1). As the




**Scheme 1.**

barrier of interconversion is 12—16 kcal mol$^{-1}$,[3,4] interconversion is fast at room temperature and an average spectrum is observed in $^1$H n.m.r.

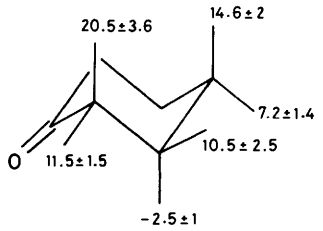
In the case of functionalized *cis*-decalins, the two conformers have different energies and therefore different populations. This problem has been frequently studied and various techniques have been employed, *e.g.* n.m.r.[5—7] and o.r.d. at variable temperature, the latter requiring optically active products.[3,8] No method can be considered as general, and inconsistent results have sometimes been obtained.

We report here a simple method based on solvent effects in $^1$H n.m.r. The position of the conformational equilibrium of the four possible *cis*-9-methyldecalones has been determined by this method. The same technique has been used to study *cis*-decalindiones and *cis*-hydrindanones which have a similar conformational equilibrium. It can be applied to other polyfunctional compounds in these two series.

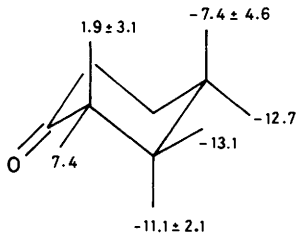
Solvent effects in $^1$H n.m.r. have many applications in conformational and structural studies.[9]

The chloroform–benzene solvent effect, $\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$, induced by a carbonyl on the methyl group in a methylcyclohexanone, has been shown[10,11] to depend on the position of the methyl group relative to the carbonyl group. Thus, solvent effects are of magnitude 18 and 0 Hz, respectively, for α-axial and α-equatorial methyl groups. The additivity of the solvent effects due to several carbonyl groups has also been shown in the 5α-androstane series.[10] In addition, the chemical shifts of angular methyl groups in the steroid series can be calculated from additive increments.[12,13] These increments can be employed with other types of compound having a rigid skeleton, provided that the geometry of the molecule is not modified by substituents. Finally, the use of additivity rules for chemical shifts has been shown[14] to be possible in solvents other than $CDCl_3$, such as $C_6H_6$, $C_5H_5N$, and $CCl_4$. Consequently, solvent effects can be considered as being the differences between Zürcher constants,[12,13] validating the additivity and equivalent position rules, provided that the solvent effect of the skeleton is taken into account. The chemical shift of a proton in the parent hydrocarbon can be different in the two solvents under consideration.[14,*]

It is possible, from the abundant literature data (Table 1) obtained from rigid models (steroids, *trans*-decalones, methylcyclohexanones), to calculate the average values of the Zürcher constants and the solvent effects induced by a carbonyl group on an α-, β-, or γ-axial or equatorial methyl group of a cyclohexanone (Schemes 2—4).




**Scheme 2.** Chemical-shift increment (Zürcher constant[12,13]) induced by the carbonyl group of a cyclohexanone on α-, β-, and γ-axial or equatorial methyl groups in $CDCl_3$ (Hz at 60 MHz)



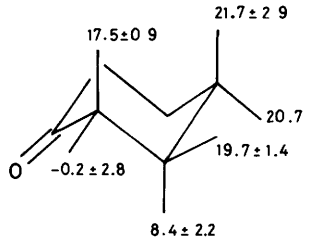

**Scheme 3.** Chemical-shift increment (Zürcher constant[12,13]) induced by the carbonyl group of a cyclohexanone on α-, β-, and γ-axial or equatorial methyl groups in $C_6H_6$ (Hz at 60 MHz)

* $\Delta^{CDCl_3}_{C_6H_6}$ (corr.) takes into account the solvent effect of the parent hydrocarbon which can be rather large in some instances: see compounds (**19**) and (**22**) (Table 4). Δ (corr.) is obtained either by subtracting the Zürcher constants in both solvents or by subtracting the measured Δ of the functionalized compound and of the parent hydrocarbon (see ref. 14*b*). The use of uncorrected data can lead to apparent discrepancies in the additivity rules[14] and wrong interpretations in stereochemical problems. Δ (corr.) can be used in the case of polyfunctional compounds.[14c]

**Table 1.** Chemical shifts (δ), Zürcher increments *Z*, and solvent effects $\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$, induced by a carbonyl group on an angular methyl group and corrected solvent effects $\Delta^{CDCl_3}_{C_6H_6}$ (corr.) (Hz at 60 MHz)

| Methyl position | Ketone | $\delta_{CDCl_3}$ | $\delta_{C_6H_6}$ | Parent compound | $\delta_{CDCl_3}$ | $\delta_{C_6H_6}$ | $Z_{CDCl_3}$ | $Z_{C_6H_6}$ | Average value $Z_{CDCl_3}$ | Average value $Z_{C_6H_6}$ | $\Delta^{CDCl_3}_{C_6H_6}$ | Average value $\Delta^{CDCl_3}_{C_6H_6}$ | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| α-Axial methyl | *trans*-9-Methyl-1-decalone | 67.3 | 48.3 | *trans*-9-Methyldecalin | 50.4 | 49.8 | 16.9 | −1.5 | | | 18.4 | | * |
| | 5α,14α-Androstan-1-one | 70.2 | 52.2 | 5α,14α-Androstane | 47.6 | 47.2 | 22.6 | +5.0 | | | 17.6 | | 10 |
| | 5α,14α-Androstan-1-one | 70.0 | | 5α,14α-Androstane | 47.5 | | 22.5 | | 20.5 | +1.9 | | 17.5 | 15 |
| | 5α,14α-Androstan-1-one | 68.1 | | 5α,14α-Androstane | 46.5 | | 21.6 | | | | | | 12 |
| | 5α,14α-Androstan-12-one | 60.6 | 45.0 | 5α,14α-Androstane (18-Me) | 41.9 | 42.9 | 18.7 | +2.1 | | | 16.6 | | 10 |
| α-Equatorial methyl | 5β-Androstan-1-one | 68.5 | | 5β-Androstane | 55.5 | | 13.0 | | | | | | 15 |
| | 2,2,6-Trimethylcyclohexanone | a 60.5 | a 61.3 | | | | | | | | −2.3 | | 16 |
| | (a:2-Me) (b:6-Me) | b 63.4 | b 65.7 | | | | | | 11.5 | +7.4 | −0.8 | −0.2 | 16 |
| | 2-Methylcyclohexanone | 62.2 | 59.5 | | 52.2 | 52.1 | 10.0 | +7.4 | | | +2.6 | | 16 |
| β-Axial methyl | *trans*-9-Methyl-2-decalone | 47.4 | | *trans*-9-Methyldecalin | 50.4 | 49.8 | −3.0 | | | | | | *17 |
| | *trans*-9-Methyl-4-decalone | 46.8 | 38.2 | *trans*-9-Methyldecalin | 50.4 | 49.8 | −3.6 | −11.6 | | | +8.0 | | * |
| | 5α-Androstan-2-one | 46.0 | | 5α-Androstane | 47.5 | | −1.5 | | | | | | 15 |
| | 5α-Androstan-2-one | 45.0 | 35.4 | 5α-Androstane | 47.6 | 47.2 | −2.6 | −11.8 | | | +9.2 | | 10 |
| | 5α-Androstan-4-one | 45.5 | | 5α-Androstane | 47.5 | | −2.0 | | | | | | 15 |
| | 5α-Androstan-6-one | 45.0 | 37.8 | 5α-Androstane | 47.5 | 47.2 | −2.6 | −9.4 | −2.5 | −11.1 | +6.8 | +8.4 | 10 |
| | 5α-Androstan-6-one | 44.5 | | 5α-Androstane | 47.5 | | −3.0 | | | | | | 15 |
| | 5α,10α-Androstan-2-one | 59.0 | 48.6 | 5α,10α-Androstane | 61.6 | 61.8 | −2.6 | −13.2 | | | +10.6 | | 14[b] |
| | 5α-Androstan-11-one | 40.2 | 33.6 | 5α-Androstane (18-Me) | 41.9 | 42.9 | −1.7 | −9.3 | | | +7.6 | | 10 |
| | 5α-Androstan-11-one | 39.5 | | 5α-Androstane (18-Me) | 41.5 | | −2.0 | | | | | | 15 |
| β-Equatorial methyl | 5β-Cholestan-4-one | 66.1 | | 5β-Cholestane | 54.6 | | 11.5 | | | | | | 12 |
| | 5β-Androstan-4-one | 67.5 | | 5β-Androstane | 55.5 | | 12.0 | | | | | | 13 |
| | 3,3,5-Trimethylcyclohexanone | a 62.8 | a 44.3 | | | | | | 10.5 | −13.1 | 18.5 | 19.7 | 18 |
| | (a:3-Me) (b:5-Me) | b 60.1 | b 40.7 | | | | | | | | 19.4 | | 18 |
| | 3-Methylcyclohexanone | 60.2 | 39.0 | Methylcyclohexane | 52.2 | 52.1 | +8.0 | −13.1 | | | 21.1 | | 18 |
| γ-Axial methyl | *trans*-9-Methyl-3-decalone | 63.9 | 39.0 | *trans*-9-Methyldecalin | 50.4 | 49.8 | 13.5 | −10.8 | | | 24.3 | | * |
| | 5α-Androstan-3-one | 62.0 | | 5α-Androstane | 47.5 | | 14.5 | | | | | | 15 |
| | 5α-Androstan-3-one | 61.7 | 39.7 | 5α-Androstane | 47.6 | 47.2 | 14.1 | −7.5 | | | 21.6 | | 14[b] |
| | 5α-Androstan-3-one | 61.2 | 39.2 | 5α-Androstane | 47.6 | 47.2 | 13.6 | −8.2 | | | 21.8 | | 10 |
| | 5α-Androstan-7-one | 64.0 | | 5α-Androstane | 47.5 | | 16.5 | | 14.6 | −7.4 | | 21.7 | 15 |
| | 5α-Androstan-7-one | 63.6 | 44.4 | 5α-Androstane | 47.6 | 47.2 | 16.0 | −2.8 | | | 18.8 | | 10 |
| | 5α,13α-Androstan-3-one | 57.1 | 35.1 | 5α,13α-Androstane | 42.7 | 42.6 | 14.4 | −7.5 | | | 21.9 | | 14[b] |
| | 5α-Androstan-3,17-dione | 62.2 | | 5α-Androstan-17-one | 48.3 | | 13.9 | | | | | | 12 |
| γ-Equatorial methyl | 4-Methylcyclohexanone | 60.8 | 39.4 | Methylcyclohexane | 52.2 | 52.1 | 8.6 | −12.7 | | | 20.7 | | 18 |
| | 5β-Androstan-3-one | 62.5 | | 5β-Androstane | 55.5 | | 7.0 | | 7.2 | −12.7 | | 20.7 | 15 |
| | 5β-Cholestan-3-one | 60.9 | | 5β-Cholestane | 54.9 | | 6.0 | | | | | | 12 |

* Present work.




**Scheme 4.** Corrected solvent effects $\Delta^{CDCl_3}_{C_6H_6}$ (corr.) induced by the carbonyl group of a cyclohexanone on α-, β-, and γ-axial or equatorial methyl groups (Hz at 60 MHz)

An axial methyl group is easily differentiated from an equatorial one if the measurements are made in two different solvents. This is precisely the case for the determination of the conformational equilibrium of methyldecalones, since the methyl group is axial in one conformer and equatorial in the other.

If the three series of values reported in Schemes 2—4 are compared, the differences in solvent effect between the axial and equatorial positions are *ca.* 18 Hz for the α-methyl groups and *ca.* 11 Hz for the β-methyl ones, differences larger than those of the corresponding Zürcher constants.[12,13] On the other hand, solvent effects in the γ-position are the same and so chemical-shift increments must be used.

## Results and Discussion

*Decalones.*—The chemical shifts of compounds (**1**)—(**15**) were measured in $CDCl_3$ and $C_6H_6$. These values, the corresponding Zürcher constants, and the corresponding solvent effect values are reported in Table 2. The angular methyl signals, which appeared as singlets, were assigned without difficulty, except in the following two cases.

cis- *and* trans-9-*Methyl*-4-*decalone* (**5**) *and* (**10**). The ring-junction hydrogen is enolizable. In solution, these two decalones

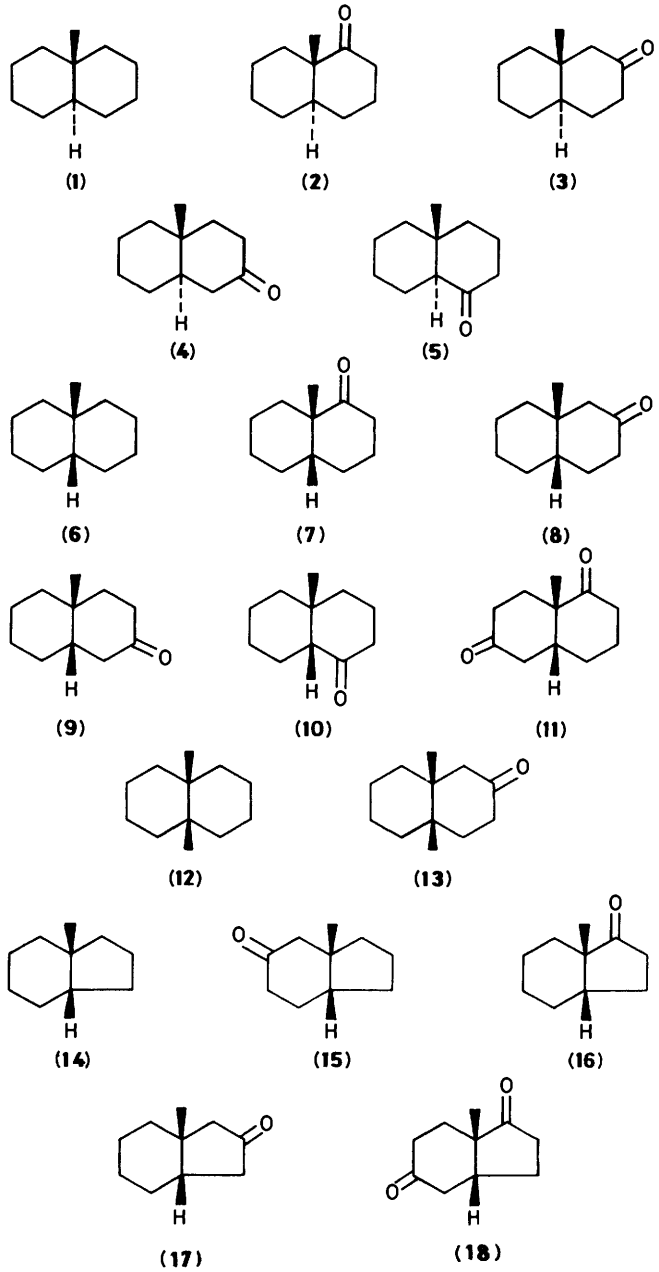


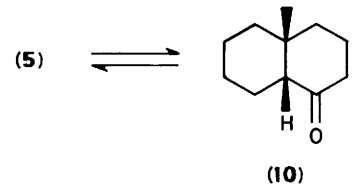
**Table 2.** Chemical shifts (δ), Zürcher increments *Z*, solvent effects $\Delta_{C_6H_6}^{CDCl_3} = \delta_{CDCl_3} - \delta_{C_6H_6}$ uncorrected and corrected [Δ (corr.)] from the solvent effect of the parent hydrocarbon, induced by a carbonyl group on an angular methyl group in *cis*-decalin and *cis*-hydrindane series (Hz at 60 MHz)

| Compounds | $\delta_{CDCl_3}$ | $\delta_{C_6H_6}$ | $Z_{CDCl_3}$ | $Z_{C_6H_6}$ | $\Delta_{C_6H_6}^{CDCl_3}$ | $\Delta_{C_6H_6}^{CDCl_3}$ (corr.) |
|---|---|---|---|---|---|---|
| (1) | 50.4 | 49.8 | | | 0.6 | |
| (2) | 67.3 | 48.3 | 16.9 | −1.5 | 19.0 | 18.4 |
| (3) | 47.4 | | −3.0 | | | |
| (4) | 63.9 | 39.0 | 13.5 | −10.8 | 24.9 | 24.3 |
| (5) | 46.8 | 38.2 | −3.6 | −11.6 | 8.6 | 8.0 |
| (6) | 57.9 | 59.2 | | | −1.3 | |
| (7) | 72.6 | 60.4 | 14.7 | +1.2 | 12.2 | 13.5 |
| (8) | 58.0 | 45.5 | +0.1 | −13.7 | 12.5 | 13.8 |
| (9) | 71.0 | 49.5 | 13.1 | −9.7 | 21.5 | 22.8 |
| (10) | 58.5 | 49.2 | 0.6 | −10.0 | 9.3 | 10.6 |
| (11) | 81.0 | 53.0 | 23.1 | −6.2 | 28.0 | 29.3 |
| (12) | 52.8 | 51.6 | | | 1.2 | |
| (13) β-Me | 55.2 | 41.1 | 2.4 | −10.5 | 14.1 | 12.9 |
| (13) γ-Me | 63.3 | 43.2 | 10.5 | −8.4 | 20.1 | 18.9 |
| (14) | 58.2 | 59.1 | | | −0.9 | |
| (15) | 60.8 | 46.8 | +2.6 | −12.3 | 14.0 | 14.9 |

**Table 3.** Conformation of *cis*-9-methyldecalones and *cis*-8-methylhydrindanones by comparison of the measured solvent effect $\Delta_{C_6H_6}^{CDCl_3}$ (mes.) induced by the carbonyl group on the angular methyl group, and the corresponding values Δ (calc.) (conformation **a**), Δ (calc.) (conformation **b**), calculated for conformers **a** and **b**

| Compounds | $\Delta_{C_6H_6}^{CDCl_3}$ (mes.) | Δ (calc.) (conformation **a**) | Δ (calc.) (conformation **b**) | % **a** | % **b** |
|---|---|---|---|---|---|
| (7) | 13.5 | 17.5 | −0.2 | 80 | 20 |
| (8) | 13.8 | 8.4 | 19.7 | 55 | 45 |
| (9)[a] | 22.8 | 21.7 | 20.7 | 80 | 20 |
| (10) | 10.6 | 8.4 | 19.7 | 80 | 20 |
| (11) | 29.3 | 38.2 | 21.5 | 50 | 50 |
| (13) β-Me | 12.9 | 8.4 | 19.7 | 60 | 40 |
| (13) γ-Me[a] | 18.9 | 20.7 | 21.7 | 55 | 45 |
| (15) | 14.9 | 8.4 | 19.7 | 40 | 60 |
| (16) | 8.7 | 14.5 | 4.1 | 45 | 55 |
| (17) | 21.4 | 17.5 | 24.8 | 45 | 55 |
| (18) | 22.6 | 36.2 | 24.8 | 0 | 100 |

[a] Δ (calc.) (**a**) and (**b**) being practically identical, the Zürcher increments were used to determine the conformer population at equilibrium.




**Scheme 5.**

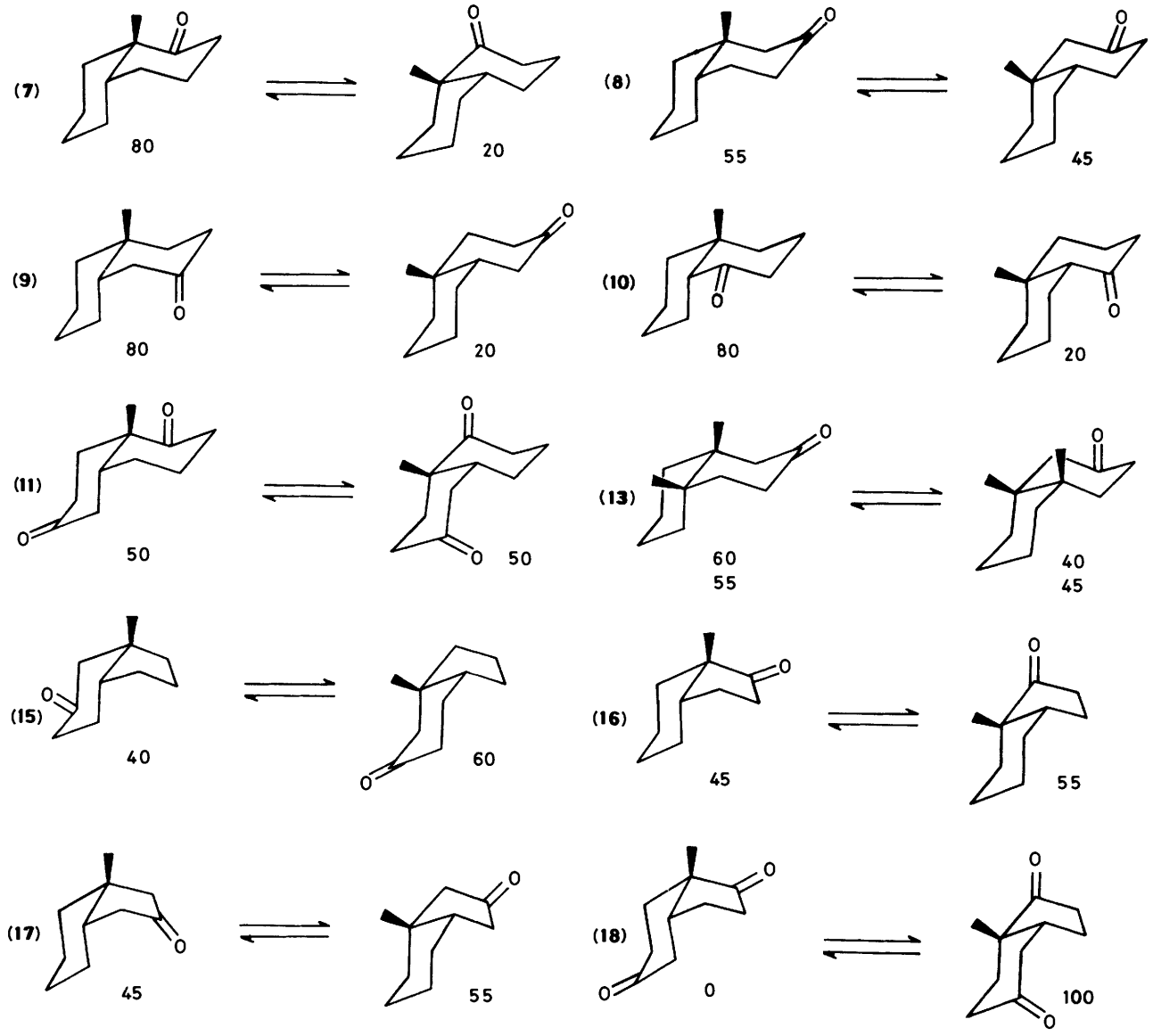
are present as an equilibrium mixture (Scheme 5). These two isomers were shown by the n.m.r. spectrum to be present in nearly equivalent quantities. The peaks of the methyl groups could therefore not be assigned in the different solvents on the basis of their height. In $CDCl_3$, the two singlets appeared at 46.8 and 58.5 Hz. In $C_6H_6$ they were at 38.2 and 49.2 Hz.

*trans*-Decalone is a conformationally rigid compound and the methyl shift can easily be calculated from Zürcher increments. In $CDCl_3$, the methyl resonance in *trans*-9-methyldecalin (**1**) (parent skeleton) appeared at 50.4 Hz. When the Zürcher increment for a carbonyl is added to a β-axial methyl group (−2.5 Hz) (Scheme 2), the chemical shift of the angular methyl group of (**5**) is estimated at 48 Hz. The peak at 46.8 Hz was therefore assigned to the *trans*-decalone (**5**) and the peak at 58.5 Hz to the *cis*-decalone (**10**). In $C_6H_6$, following the same argument, the peak at 38.2 Hz could be assigned to the rigid *trans*-decalone (**5**) and therefore the peak at 49.2 Hz to the *cis*-decalone (**10**).

cis-9,10-*Dimethyl-2-decalone* (**13**). Singlets corresponding to the two angular methyl groups were observed at 55.2 and 63.3 Hz in $CDCl_3$ and at 41.1 and 43.2 Hz in $C_6H_6$. Peak assignment in $CDCl_3$ was carried out as follows: the observed chemical shift was a mean of the chemical shifts of each of the two conformers, weighted by their relative populations. The expected chemical shift for each conformer can be calculated from the chemical shift of the angular methyl groups in dimethyldecalin (52.8 Hz) and from the Zürcher increments defined on rigid models. These data are given in Scheme 2. The shift of the β-methyl group should be between 50 and 65 Hz, and that of the γ-methyl group between 59 and 67 Hz. The peak at 55.2 Hz could therefore be assigned unequivocally to the β-methyl group and that at 63.3 Hz to the γ-methyl group.

The correspondence between the peaks in chloroform and in benzene was determined by the solvent mixture method, based on the linearity of the chemical shifts as a function of solvent composition.[14] In the case of (**13**), the signal at higher field in $CDCl_3$ was also shown to be the higher field peak in $C_6H_6$ (no peak 'crossing').

*Determination of Conformation.*—Whenever the experimental value $\Delta_{C_6H_6}^{CDCl_3}$, measured for a given decalone, was equal to one




**Scheme 6.** Position of the conformational equilibrium of decalones and hydrindanones (**7**)—(**11**), (**13**), and (**15**)—(**18**). Left, conformation **a**; right, conformation **b**

of the values corresponding to a rigid model (Scheme 4), then one of the conformers was predominant if not unique at equilibrium. If $\Delta^{CDCl_3}_{C_6H_6}$ was intermediate between these two values, the percentage at equilibrium of each conformer could be calculated using ratios (Table 3). The same reasoning is valid for decalone (**9**) in which Zürcher increments were used. The results are given in Table 3 and Scheme 6.

cis-9-*Methyl*-1-*decalone* (**7**). The measured solvent effect was 13.5 Hz. The solvent effect expected for conformer (**7a**) was 17.5 Hz and for (**7b**) −0.2 Hz. At 25 °C, the (**7a**):(**7b**) population ratio at equilibrium was deduced to be 80:20. The 'non-steroidal' conformer [*i.e.* (**7a**)] has been qualitatively shown by Djerassi[8] to be predominant (result obtained from Zürcher increments).

cis-9-*Methyl*-2-*decalone* (**8**). The measured solvent effect was 13.8 Hz and the solvent effect for the two conformers (**8a** and **b**) was, respectively, 8.4 and 19.7 Hz. The two conformers, according to calculation, are in practically equal amounts at room temperature.

cis-9-*Methyl*-3-*decalone* (**9**). The solvent effects induced by a carbonyl on an axial or equatorial γ-methyl group are practically identical (Scheme 4) and the method with Zürcher increments in $CDCl_3$ has to be used. The measured Zürcher constant was 13.1 Hz. The constants calculated from rigid models were 14.6 and 7.2 Hz, respectively, for (**9a** and **b**) (Scheme 2). The ratio (**9a**):(**9b**) was deduced to be 80:20.

This result agrees with that of Stothers[7] who showed by $^{13}C$ n.m.r. that at −50 °C, conformer (**9a**), with an axial methyl group, is formed in 85% by this ketone.

cis-9-*Methyl*-4-*decalone* (**10**). The measured solvent effect was 10.6 Hz. The solvent effect expected for (**10a**) was 8.4, and 19.7 Hz for (**10b**). At equilibrium, at 25 °C, the (**10a**):(**10b**) population ratio was deduced to be 80:20. At −70 °C conformer (**10a**) with an axial methyl group has been established[6] to be the major one (65—80%) by $^{13}C$ n.m.r. consistent with our result.

cis-9-*Methyldecalin*-1,6-*dione* (**11**). The solvent effect method can be applied to diketones by considering the sum of the solvent effects induced by each carbonyl group in each conformation. In the case of *cis*-9-methyldecalin-1,6-dione (**11**)

**Table 4.** Chemical shifts δ, Zürcher increments *Z*, solvent effects $\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$ uncorrected, and corrected ($\Delta_{corr.}$) from the solvent effect of the parent hydrocarbon, induced by a carbonyl group on the 18-methyl group, in the 5α,13α,14α- and 5α,13β,14β-androstane series (Hz at 60 MHz)

| Compounds | $\delta_{CDCl_3}$ | $\delta_{C_6H_6}$ | $\Delta^{CDCl_3}_{C_6H_6}$ | $Z_{CDCL_3}$ | $Z_{C_6H_6}$ | $\Delta^{CDCl_3}_{C_6H_6}$ (corr.) |
|---|---|---|---|---|---|---|
| (**19**) | 52.0 | 55.6 | −3.6 | | | |
| (**20**) | 60.0 | 46.1 | +13.9 | +8.0 | −9.5 | +17.5 |
| (**21**) | 58.2 | 47.3 | +10.9 | +6.2 | −8.3 | +14.5 |
| (**22**) | 59.4 | 64.5 | −5.1 | | | |
| (**23**) | 71.6 | 51.9 | +19.7 | +12.2 | −18.6 | +24.8 |
| (**24**) | 65.0 | 66.0 | −1.0 | +5.6 | +1.5 | +4.1 |

the experimental solvent effect was 29.3 Hz; the calculated value was 38.2 and 21.5 Hz respectively for conformers (**11a** and **b**). From the observed values the two conformers must be present in practically equal amounts at equilibrium.

cis-9,10-*Dimethyl*-2-*decalone* (**13**). In the case of this dimethyldecalone, measurements made on each angular methyl group were available, solvent effects on 9-methyl group and Zürcher increments on the 10-methyl group. The (**13a**):(**13b**) ratio was deduced to be 60:40 from the solvent effect measured for the 9-methyl group (12.9 Hz). A solvent effect of 18.9 Hz was observed for the 10-methyl group, as expected for an axial or equatorial γ-methyl group. The method based on Zürcher increments, applied as in decalone (**9**), gave a 55:45 ratio. These two results are consistent and show the limit of accuracy of the method to be *ca.* 5%. At −50 °C, Stothers *et al.*[7] have obtained an analogous result by $^{13}C$ n.m.r. [55% (**13a**)].

cis-8-*Methyl*-6-*hydrindanone* (**15**). *cis*-Hydrindanones exhibit a conformational equilibrium analogous to that observed for *cis*-decalones. The carbonyl group of the methylhydrindanone (**15**) is in the six-membered ring. If the deformations of this ring, induced by the junction with a five-membered ring, are neglected, the angular methyl group can be considered as axial in (**15a**) and equatorial in (**15b**). The same method can then be applied. The measured solvent effect was 14.9 Hz. The expected solvent effect for conformers (**15a** and **b**) was 8.4 and 19.7 Hz, respectively. The ratio (**15a**):(**15b**) was therefore 40:60.

*Hydrindanones.* There are three possible *cis*-methyl-8-hydrindanones bearing the carbonyl group on the five-membered ring. They have (like all other substituted *cis*-hydrindanes) a conformational equilibrium in which the angular methyl group takes either an equatorial or an axial position with respect to the six-membered ring.

To our knowledge, no experimental determination of the position of the equilibrium has been made, though Allinger and Tribble[4] have calculated the 'free energies' of the two conformers by using a 'force field method'. Thus the relative populations of the two conformers can be calculated.

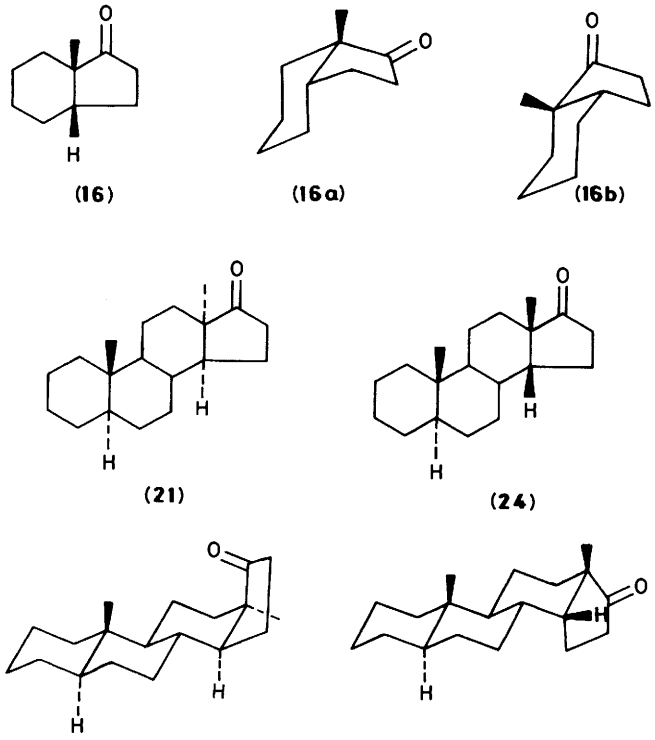
The solvent effect method permits a direct experimental determination of these populations. The two results can be compared to estimate the accuracy of the two methods.

Given the well known conformational mobility of five-membered rings the situation is more complicated than in the case of decalones where the conformation of the six-membered rings is well established.

Slight conformational changes can considerably modify the relative position of the angular methyl groups and of the carbonyl group, and hence the Zürcher increments and the solvent effects.

Rigid models of the two conformers, in which the angular methyl group has the same position relative to the carbonyl group in the five-membered ring, are necessary. As shown by molecular models, these are provided by the C and D rings of 16- and 17-androstanone in the 13α,14α (lumi) and 13β,14β series.

In the 13α,14α series (**21**) the angular methyl group is




equatorial relative to cyclohexane as in conformer (**16a**). In the 13β,14β series, the same methyl group is axial relative to cyclohexane, as in (**16b**).

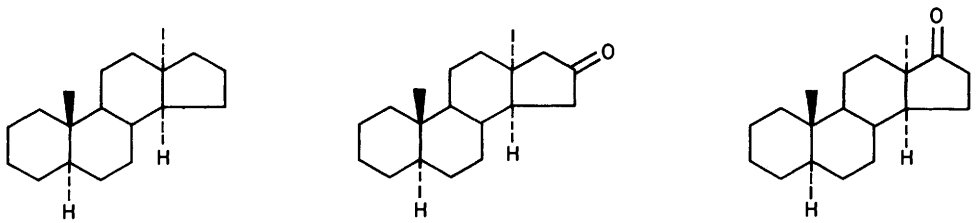
The 18-methyl chemical shifts of the androstanone models in $CDCl_3$ and $C_6H_6$ are given in Table 4. The 'corrected' solvent effects are different for the two possible conformations but these differences are smaller than in the case of cyclohexanones. A less accurate determination of the conformational equilibrium position is therefore inevitable.

cis-9-*Methylhydrindane* (**14**). Spectra were recorded in $CDCl_3$ and $C_6H_6$ to determine the chemical-shift values of the parent skeleton for calculations using Zürcher increments and the solvent effect of the skeleton. The methylhydrindanones (**16**) and (**17**) spectra were also recorded. The values of angular methyl chemical shifts in methylhydrindanedione (**18**) were taken from the literature.[19–21] These values are given in Table 5.

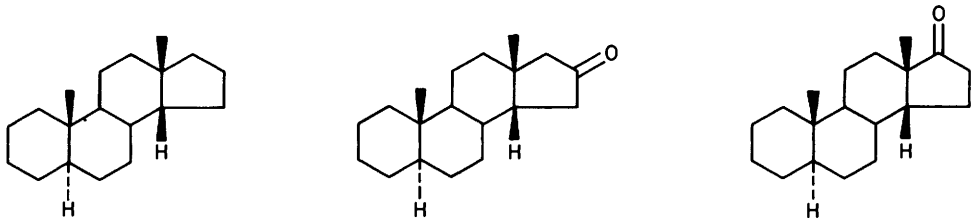
cis-8-*Methylhydrindan*-1-*one* (**16**). The measured solvent effect was 8.7 Hz for (**16**). This must be compared with that of 13α,14α-androstan-17-one (**21**), a model of conformer (**16a**) (14.5 Hz) and that of 13β,14β-androstan-17-one (**24**), a model of (**16b**) (4.1 Hz). Conformer (**16b**) was deduced to be slightly preponderant [(**16a**):(**16b**) *ca.* 45:55]. This population ratio corresponds to a difference of 'free energy' of *ca.* 0.1 kcal mol$^{-1}$. The 'free energy' difference has been calculated by Allinger and Tribble[4] to be 0.2 kcal mol$^{-1}$, conformer (**16a**) being the more

**Table 5.** Chemical shifts (δ), Zürcher increments *Z*, and solvent effects $\Delta_{C_6H_6}^{CDCl_3} = \delta_{CDCl_3} - \delta_{C_6H_6}$ uncorrected and corrected ($\Delta_{corr.}$) from the solvent effect of the parent hydrocarbon, induced by a carbonyl group on the angular methyl group in hydrindane series (Hz at 60 MHz)

| Compounds | $\delta_{CDCl_3}$ | $\delta_{C_6H_6}$ | $Z_{CDCl_3}$ | $Z_{C_6H_6}$ | $\Delta_{C_6H_6}^{CDCl_3}$ | $\Delta_{C_6H_6}^{CDCl_3}$ (corr.) |
|---|---|---|---|---|---|---|
| (**14**) | 58.2 | 59.1 | | | −0.9 | |
| (**16**) | 63.0 | 55.2 | +4.8 | −3.9 | +7.8 | +8.7 |
| (**17**) | 67.5 | 47.0 | +9.3 | −12.1 | +20.5 | +21.4 |
| (**18**) | 74.5 (20)<br>75.0 (19) | 53.0 (21) | 16.3<br>16.8 | −6.1 | +21.5<br>+22.0 | +22.4<br>+22.9 |



(**19**) (**20**) (**21**)



(**22**) (**23**) (**24**)

stable [which corresponds to (**16a**):(**16b**) 58:42]. There is therefore a difference of *ca.* 0.3 kcal mol$^{-1}$ between these two results which gives an indication of the limits of the two methods. It is obvious that a small error in energy leads to a larger variation in population ratios when these are practically equal than in the case when one conformer is strongly predominant. The 'free energies' of conformers (**16a** and **b**) can be concluded to be extremely close and therefore their populations practically identical.

cis-8-*Methylhydrindan*-2-*one* (**17**). The solvent effect measured for (**17**) was 21.4 Hz. It should be compared with that of 13α,14α-androstan-16-one (**20**), a model of (**17a**) (17.5 Hz) and that of 13β,14β-androstan-16-one (**23**), a model of (**17b**) (24.8 Hz). Conformer (**17b**) was deduced to be slightly preponderant [(**17a**):(**17b**) *ca.* 45:55]. According to Allinger and Tribble, (**17b**) should be more stable than (**17a**) by 0.2 kcal mol$^{-1}$, which corresponds to (**17a**):(**17b**) 42:58, in agreement with the experimental determination.

cis-8-*Methylhydrindane*-1,5-*dione* (**18**). The same type of calculation can be applied to this ketone, the solvent effects induced by the two carbonyl groups being added. The solvent effect measured for (**18**) was 22.6 Hz, those calculated from rigid models for (**18a** and **b**) were 36.2 and 24.8 Hz, respectively. Therefore, in solution, this hydrindanedione was deduced to adopt conformation (**18b**) exclusively.

The measured value of 22.6 Hz is outside the predicted range, 24.8—36.2 Hz. This difference of < 2 Hz could be due to the facts that only one value was available for the determination of the solvent effect of an γ-equatorial methyl group in cyclohexanone (Table 1), the experimental values for (**18**) had been taken from different literature sources and therefore depend on the calibration of the spectrometer, and, finally, fusing a six-membered ring to a five-membered ring perturbs the geometry of a cyclohexane ring and could result in a slightly different solvent effect. Nevertheless, this compound exists in solution almost exclusively as conformer (**18b**).

*Conclusions.*—The equilibrium position of the two possible conformers of *cis*-9-methyldecalones and *cis*-8-methylhydrindanones can be determined simply and directly by comparing the $^1$H n.m.r. spectra recorded in $CDCl_3$ and $C_6H_6$ provided that corresponding rigid models are available.

In all these compounds, with one exception, the population ratio of the two conformers varies between 50:50 and 80:20, which corresponds to small (< 0.8 kcal mol$^{-1}$) differences of 'free energy'. Because this difference is so small, the prediction of the position of this equilibrium by simple calculation is difficult and direct experimental determination is more accurate.

This method can be applied to the determination of conformational equilibria of polyfunctional compounds provided that there is no deformation of the carbon skeleton. It can also be extended to functional groups other than the carbonyl provided that the appropriate solvent pair is used (for example pyridine in the case of alcohols).[22]

## Experimental

$^1$H N.m.r. spectra were recorded at 25 °C on a JEOL C60 HL spectrometer of the n.m.r. service of the Centre Régional de Mesures Physiques. All spectra were obtained for $CDCl_3$ or $C_6H_6$ solutions (20—25 mg in 0.4 ml solvent) with $Me_4Si$ as internal standard. The bicyclic compounds used for this study were all known and were prepared using previously published methods unless otherwise indicated, in which case, their physical and spectral characteristics agreed with the literature data.

*trans*-9-Methyldecalin (**1**)[23] [Wolff–Kishner reduction of (**2**)], *trans*-9-methyldecalones (**2**),[24] (**3**)[25,26] (prepared according to the method of Fetizon *et al.*[27] using benzaldehyde), (**4**)[28] and (**5**),[29] *cis*-9-methyldecalin (**6**)[30] [Wolff–Kishner reduction of (**7**)], *cis*-9-methyldecalones (**7**),[24] (**8**),[31] (**9**),[28] and (**10**),[29] *cis*-9-methyldecalin-1,6-dione (**11**),[32] *cis*-9,10-dimethyldecalin (**12**),[33] *cis*-9,10-dimethyl-2-decalone (**13**),[34] *cis*-8-methylhydrindane (**14**)[30] [Wolff–Kishner reduction of (**17**)], *cis*-8-methylhydrindanones (**15**),[35] (**16**),[36] (**17**),[30] and steroids (**19**),[37] (**20**),[38] (**21**),[37] (**22**),[39] (**23**),[38] and (**24**)[39] were prepared as indicated.

*Note added in proof.* Since the acceptance of this paper, calculation of the conformational equilibrium of molecules (**7**)—(**11**), (**13**), and (**15**)—(**18**), using Allinger's MM2 force field (N. L. Allinger, *J. Am. Chem. Soc.*, 1977, **99**, 8127), has been performed by Dr. J. Bastard, Ecole Polytechnique, Palaiseau, whom we warmly thank. The relative ratio of conformers **a** and **b** at equilibrium are as follows: (**7**) 73:27, (**8**) 67:33, (**9**) 76:24, (**10**) 36:64, (**11**) 54:46, (**13**) 50:50, (**15**) 30:70, (**16**) 36:64, (**17**) 32:68, and (**18**) 18:82. There is a very good fit between those calculated figures and our experimental data given in Table 3. The only noticeable discrepancy concerns the decalone (**10**), although Blunt's results,[6] based on $^{13}C$ n.m.r spectral data, are consistent with our experimental determination.

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