Monatshefte für Chemie 115, 825—835 (1984)

Monatshefte für Chemie
Chemical Monthly

Diisophorone and Related Compounds. Part 14[1] ^{13}C-Nuclear Magnetic Resonance Spectra of Diisophorone Carboxylic Acids

Frederick Kurzer* and **Jayantilal N. Patel**

Royal Free Hospital School of Medicine (University of London), London, England

(Received 22 November 1983. Accepted 17 January 1984)

The ^{13}C-nmr spectra of a group of diisophorone carboxylic acids have been determined and fully assigned. The spectral data confirm, in some cases decisively, the formulation of members of this series of compounds. In the light of the spectral information, the stereochemistry of the C(4)-C(5)-region of the diisophorone ring-system is discussed, with special reference to the configuration of the 4-substituents.

(Keywords: Diisophorone carboxylic acids, ^{13}C-nmr spectra thereof; Tricyclo[7.3.1.0^{2,7}]tridecanes)

Diisophorone und verwandte Verbindungen, 14. Mitt.: ^{13}C-NMR Spektren von Diisophoron-carbonsäuren

Die ^{13}C-Kernresonanzspektren einer Anzahl von Diisophoron-carbonsäuren wurden aufgenommen und die Signale den Atomen des Kohlenstoffgerüstes zugeordnet. Die so erhaltenen Beziehungen ermöglichen ihrerseits die Bestätigung — und in gewissen Fällen die entscheidende Sicherung — der Struktur weiterer Beispiele dieser Verbindungsreihe. Die sterische Anordnung des C(4)-C(5)-Bereiches im Diisophoron-Ring-System, insbesondere die Konfiguration von 4-Substituenten, wird an Hand der spektroskopischen Ergebnisse erörtert.

Introduction

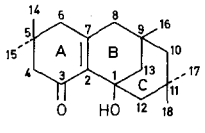
The ^{13}C-nmr spectrum of diisophor-2(7)-en-1-ol-3-one ("diisophorone", **1**), the ultimate source of all diisophorone derivatives so far described, has recently been studied[2] and a complete assignment of its signals attempted. The interpretation was based on the comparison and correlation of the spectra of a series of diisophorone derivatives of known structure. This empirical approach, used with success in the case of other

complex molecular patterns (e.g. terpenes[3], sterols[4], nucleotides[5] etc.) has provided reliable and self-consistent data for identifying the signals in the spectra of diisophorone-derivatives. On the basis of this information, the ^{13}C-nmr spectra of the diisophorone-carboxylic acids described in the foregoing papers[1,6] have now been interpreted. The results fully support the formulations of these compounds based on chemical methods, and provide decisive structural evidence in certain cases.

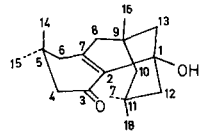
Results and Discussion

For the experimental determination of the ^{13}C-nmr spectra, the methyl esters were preferable to the free acids because of their ready solubility in deuteriochloroform. The spectra of the parent acid **2** and of two representative substituted acids **6** and **14** were obtained in deuteriopyridine; the near identity of the spectra of the methyl ester **3** measured in either deuterio-chloroform *or* -pyridine established that numerical results obtained in either solvent were directly comparable. Furthermore, the spectra of the free acids differed only very insignificantly from those of their methyl esters (viz. **2** and **3**; **6** and **7**; **14** and **15**), so that a knowledge of the chemical shifts of the latter provides all the information required for the present purpose.

The ^{13}C-nmr spectra of the diisophorone-carboxylic acids or their methyl esters are recorded in Table 1, which lists the proton noise decoupled chemical shifts (in ppm) and first order multiplicities, displayed in accordance with their proposed assignments. The spectrum of diisophorone (**1**)[2] is included for comparison.



1



1a

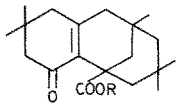
The task of interpreting the spectra of the diisophorone-carboxylic acids was greatly simplified by reference to the fully assigned signals of the parent ketol **1** and its derivatives[2]. The following brief discussion of the new spectra is therefore confined to their salient features, with special emphasis on their usefulness in providing structural information in this series of compounds.

1-Carboxydiisophor-2(7)-en-3-one (**2**)

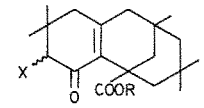
Singlets. The 1-carboxyl-carbon (C-19) gives rise to a new singlet within the appropriate range of the spectrum[7a,8,9] throughout the series of compounds. In the case of the methyl esters, the signal is found with striking regularity at 177 ppm, and that of the free acids at slightly lower field (179 ppm) as expected[7a,10]. The singlets of the olefinic carbon atoms (C2, C7) are readily identified, appearing near 135 and 155 ppm, as in the parent ketol **1**[2]. The emergence of the C-3 singlet consistently near 198 ppm (except in the 4-substituted examples) agrees well with the keto-resonances recorded for α,β-unsaturated ketones in general[7a], and for the closely related cyclohex-2-enone[11] (197 ppm) and its 2,3-dimethyl-homologue[8,12] (196.4 ppm) in particular; the upfield displacement from the usual keto-shift (near 210 ppm) is ascribed to electron-release from the conjugated π-system of the α,β-double bond. The signal due to the bridgehead C-1 carbon is displaced upfield (from ca. 70 to 45 ppm) upon the exchange of the 1-hydroxy- for the 1-carboxy-substituent by the increased shielding effect of the carboxy-group on the adjacent carbon atom, as has been established in both the alkane[13] and cycloalkane series[14]. This change in the substituents has little influence on the more remote C-5, C-9 and C-11 centres, but is nevertheless reflected in the consistent small upfield displacements (by 1.5–2 ppm) of the singlet resonances of C-9 and C-11 in comparison with those of the ketol series (32.4 and 31.4 ppm)[2]. A distinction between the three signals, all of which appear in the narrow range between 30 and 40 ppm, especially the selection of that associated with C-5, is made by the reasoning previously outlined for the ketols[2]. The displacement of the chemical shifts of the signals by the introduction of substituents into the parent acid **2** is examined collectively in the discussion of the spectra of suitable derivatives (see below).

Triplets. The 10- and 4-methylene-groups of the ring-system may be correlated, as in the ketols[2], with the triplets appearing invariably at 52 and 50 ppm, respectively; the latter give way to a doublet in the 4-substituted acids, and to a singlet in the 4-keto-acid **12**.

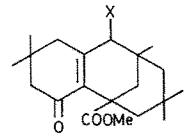
The remaining triplets (corresponding to C-6, 8, 12, 13) form a group of closely spaced signals in the range of 40–45 ppm; their individual allocation is therefore subject to some uncertainty, and the entries are marked accordingly in Table 1. The two signals near 45 ppm are attributed, in the parent acid (**2**, **3**) and its 4-substitution products, to the 6- and 8-methylene carbons (matching those of the parent ketols[2]) on the grounds that these more remote positions will be least affected by a change in the substituent at C-1. Of these, one is replaced by a doublet in the spectra of the 8-substituted acids **5**, **8**, and **11**. However, irrespective of the way in which the four triplets are distributed amongst



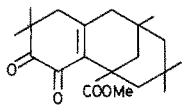
2: R = H
3: R = Me



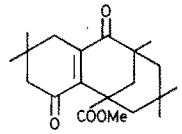
4: X = Br, R = Me
6: X = OH, R = H
7: X = OH, R = Me
9: X = αOAc, R = Me
10: X = βOAc, R = Me



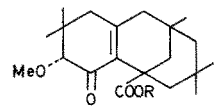
5: X = Br
8: X = OH
11: X = OAc



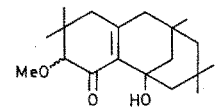
12



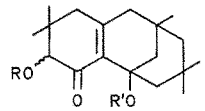
13



14: R = H
15: R = Me



16



17: R = Ac, R′ = H
18: R = R′ = Ac
19: R = R′ = H

Table 1. *Supplement*

	4-Acetyl		8-Acetyl		4-*Me*O
	CO (C-21)	*Me* (C-22)	CO (C-21)	*Me* (C-22)	(C-23)
9	170.4 s	20.7 q			
10	170.4 s	20.7 q			
11			170.7 s	20.8 q	
14					58.6 q
15					58.3 q
16 α					58.9 q
16 β					60.1 q

C-19 = carbonyl carbon of 1-carboxy- or methoxycarbonyl group;
C-20 = methyl carbon of 1-methoxycarbonyl group.

Table 1. ^{13}C *Chemical shifts in diisophorone-carboxylic acids and their assignments*[a]

Compound	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
1	71.4 s	135.4 s	200.7 s	51.8 t	32.2 s[b]	45.7 t[c]	157.5 s	44.6 t[c]	32.4 s[b]	52.1 t
2 (*py*)	44.9 s	135.7 s	196.4 s	51.6 t	32.5 s	45.3 t[b]	155.1 s	45.2 t[b]	30.7 s	52.6 t
3	44.3 s	134.7 s	196.6 s	51.1 t	32.5 s	45.3 t[b]	155.8 s	45.1 t[b]	30.6 s	52.4 t
(*py*)	44.6 s	134.8 s	196.4 s	51.3 t	32.5 s	45.0 t[b]	155.9 s	44.8 t[b]	30.6 s	52.3 t
4	44.5 s	132.7 s	189.3 s	60.8 d	36.1 s	40.7 t[b]	157.0 s	45.3 t[c]	30.5 s	52.4 t
5	44.5 s	134.8 s	197.6 s	51.4 t[b]	32.8 s	41.7 t	151.7 s	65.6 d	35.2 s	49.0 t[b]
6 (*py*)	45.7 s	134.1 s	199.6 s	80.2 d	39.4 s	45.2 t[b]	154.6 s	44.9 t[b]	30.7 s	52.7 t
7	45.2 s	132.9 s	198.9 s	79.7 d	39.7 s	44.9 t[b]	156.3 s	44.8 t[b]	30.6 s	52.6 t
8	44.4 s	135.6 s	198.1 s	51.4 t[b]	32.5 s	42.7 t[c]	153.8 s	75.5 d	35.5 s	50.1 t[b]
9	45.0 s	134.1 s	192.8 s	80.7 d	37.4 s	44.7 t[b]	154.0 s	45.1 t[b]	30.6 s	52.6 t
10	44.5 s	134.3 s	190.3 s	80.1 d	36.4 s	45.0 t[b]	155.3 s	45.2 t[b]	30.7 s	52.2 t
11	44.3 s	137.6 s	197.5 s	51.2 t[b]	32.5 s	42.0 t[c]	150.3 s	75.2 d	34.9 s	50.2 t[b]
12	46.5 s	137.9 s	199.2 s	180.9 s	44.9 s	45.8 t[b]	160.3 s	44.9 t[b]	30.7 s	52.2 t
13	44.2 s	145.4 s[b]	200.2 s[c]	51.4 t[d]	32.0 s	36.9 t	146.2 s[b]	205.5 s[c]	42.7 s	49.8 t[d]
14 (*py*)	45.3 s	134.2 s	195.8 s	88.5 d	37.2 s	45.2 t[b]	154.4 s	44.8 t[b]	30.7 s	52.7 t
15	44.5 s	132.8 s	194.8 s	87.7 d	36.3 s	45.0 t[b]	156.1 s	44.3 t[b]	30.6 s	52.6 t
16 α	71.8 s	134.1 s	200.7 s	89.4 d	36.9 s	46.6 t[b]	157.4 s	45.5 t[b]	32.3 s	52.5 t
16 β	71.7 s	134.7 s	199.3 s	88.6 d	36.9 s	46.7 t[b]	156.8 s	45.5 t[b]	32.4 s	52.3 t

Compound	C11	C12	C13	C14ax	C15eq	C16	C17ax	C18eq	C19	C20
1	31.4 s	50.3 t	46.6 t[c]	26.8 q	29.7 q	28.2 q	32.7 q	37.1 q	—	—
2 (*py*)	30.2 s	44.9 t[b,c]	42.5 t[c]	26.9 q	29.9 q	28.9 q	32.9 q	37.7 q	179.2 s	—
3	30.0 s	44.3 t[b,c]	41.4 t[c]	26.4 q	30.2 q	28.7 q	32.8 q	37.4 q	177.5 s	51.6 q
(*py*)	30.0 s	44.5 t[b,c]	42.1 t[c]	26.5 q	29.9 q	28.8 q	32.7 q	37.6 q	177.3 s	51.5 q
4	30.1 s	44.3 t[c]	41.0 t[b]	29.7 q	24.2 q	28.4 q	32.8 q	37.4 q	177.1 s	51.7 q
5	29.7 s	44.1 t	36.8 t	25.4 q	30.1 q	31.3 q	33.1 q	36.5 q	176.6 s	51.9 q
6 (*py*)	30.2 s	44.6 t[b,c]	42.9 t[c]	29.4 q	20.9 q	28.1 q	32.9 q	37.8 q	179.0 s	—
7	30.0 s	44.3 t[b,c]	41.9 t[c]	29.3 q	19.7 q	28.2 q	32.8 q	37.6 q	176.8 s	51.9 q
8	29.6 s	40.9 t[c]	38.7 t	26.3 q	30.2 q	27.5 q	30.2 q	37.3 q	177.2 s	51.8 q
9	30.0 s	44.2 t[b,c]	41.8 t[c]	27.5 q	21.6 q	29.1 q	32.8 q	37.6 q	176.8 s	51.7 q
10	30.0 s	44.1 t[b,c]	41.1 t[c]	19.8 q	27.3 q	28.9 q	32.7 q	37.4 q	177.0 s	51.8 q
11	29.6 s	40.8 t[c]	39.8 t	26.4 q	29.8 q	26.8 q	30.0 q	37.4 q	176.7 s	51.8 q
12	30.0 s	43.7 t[b]	40.9 t	23.5 q	24.3 q	28.7 q	32.6 q	37.3 q	176.3 s	52.0 q
13	30.0 s	44.8 t	39.3 t	26.0 q	29.8 q	26.6 q	29.2 q	37.1 q	175.6 s	52.1 q
14 (*py*)	30.3 s	43.3 t[b]	42.7 t[b]	25.9 q	23.5 q	29.1 q	33.0 q	37.9 q	179.3 s	—
15	30.1 s	42.3 t[b,c]	41.5 t[c]	24.8 q	24.3 q	28.7 q	32.9 q	37.6 q	177.7 s	51.7 q
16 α	31.7 s	50.4 t	43.8 t[b]	26.5 q	25.6 q	28.4 q	32.7 q	37.1 q	—	—
16 β	31.7 s	50.5 t	42.8 t[b]	21.7 q	23.3 q	28.5 q	32.8 q	37.3 q	—	—

[a] Chemical shifts are given in ppm downfield from *TMS*. The solvent was deuteriochloroform except where stated (*py* = deuteriopyridine).

[b, c, d] Signals may be reversed in horizontal line.

the methylene carbons, there emerges, in comparison with the corresponding ketols[2], a small upfield displacement of the chemical shifts of the 12- and 13-methylene triplets; the increased shielding of these centres is again attributable to the proximity of the 1-carboxyl group.

Quartets. New quartets due to the ester methyl group appear consistently within very narrow limits in the expected[15] range (C-20, at 51.5–52.1 ppm), as do those of the 4-methoxy-groups of **14**, **15**, and **16** (C-23, at 58.3–60.1 ppm)[7a]. The signals of the five ring-methyl groups conform closely to those of analogous ketols[2] and are identified accordingly. The 17- and 18-methyl groups, being generally remote from structural changes, produce signals having particularly constant resonances. Small but significant deviations in any of the quartets under the influence of neighbouring substituents are noticed in the appropriate context.

The Effect of 4-Substituents. The change in the ^{13}C-nmr spectra specifically indicative of 4-substitution in the diisophorone-1-carboxylic acids is the replacement by a doublet of the diagnostic triplet (at 51 ppm) associated invariably with this position. The deshielding of the 4-carbon by the substituents is considerable, and increases in the order Br > OH, O*Ac* > O*Me*, as has also been observed in alkane-[16a] and vinyl-compounds[16b]. The location of the substituents at C-4 is further confirmed by the displacements of the singlets of the adjacent 3-keto- and 5-carbon atoms, and by the absence of significant effects on the carbon framework elsewhere. The influence of the 4-substituents on the adjacent 5-dimethyl-group (C-14, 15) depends on the configuration of the former and is considered in the context of the stereochemistry of the C-4, C-5 region of the structure (see below).

The spectrum of 4-methoxydiisophor-2(7)-en-1-ol-3-one (**16**)[1], measured for comparison, consisted of 38 signals forming closely spaced pairs (some coinciding), showing this methanolysis product to be an approximately 1 : 1 mixture of its 4α- and 4β-epimers.

The Effect of 8-Substituents. Upon introduction of an 8-substituent into diisophorone, one of the three methylene triplets near 45 ppm is replaced by a doublet. That it is the 8-methylene-signal that has been so transformed, rather than the 6- or 12-methylene-triplets indistinguishable from it, is demonstrated by the fact that all other changes in the ^{13}C-nmr spectra concern carbon atoms surrounding the 8-position. Any remaining doubt that the present group of compounds may possibly be the 6-substituted isomers is dispelled by the constancy of the chemical shifts of their 5-carbon atoms (identical with that of **3**); these experience a distinct deshielding by identical substituents placed in the adjacent 4-position (see above).

The deshielding effect exerted by the 8-bromo-, hydroxy-, and acetoxy substituent on C-8 increases in the same order, but to a different degree, as in the 4-isomers. The influence extends on a diminished scale to the adjacent quaternary 9-carbon. Of the two carbon atoms flanking the central double bond, the adjacent C-7 is distinctly shielded, but the remoter C-2 position is unaffected. Minor shielding of the 10- and 13-methylene carbon atoms is also observed.

3,4- and 3,8-Diketocarboxylic Acids (**12**, **13**). The presence of an additional keto-group in conjugation with the existing α,β-unsaturated keto-system in **3** causes particularly marked changes in the ^{13}C-nmr spectra. The 4- *or* 8-methylene triplet (at 51.3 or ca. 45 ppm) gives way to a characteristic low-field singlet. The adjacent ring carbon atoms (C-5 in **12**, C-9 in **13**) are deshielded even more than in the 4- and 8-substitution products, presumably because of the strong polarisability of the keto-group[16c].

The symmetry of the conjugated diketone system (CO · C : C · CO) in the 3,8-diketo-acid **13** is apparent from the nearly identical chemical shifts of the two singlets associated with the carbon atoms flanking the double bond (145.4, 146.2 ppm) on the one hand, and the two keto-singlets (200.2, 205.5 ppm) on the other. This distribution of the keto-groups clearly exerts an equalising influence on the electron distribution over the "olefinic" carbon atoms, involving, in comparison with the parent acid **3**, deshielding of C-2 and the opposite effect on C-7. The chemical shift of the C-5 singlet remains unaffected by the newly entered keto-group: a possible 3,6-diketo-formulation of the acid (in which the CO · C : C · CO-system is restricted to ring A) is therefore excluded. The 5-gem-dimethyl group of **13** is sufficiently distant from the structural change (**3** → **13**) for its quartets to be unaffected. However, the 17-methyl group, projecting below rings A/B to a point opposite the centre of the conjugation, is subject to a small but distinct shielding (—3.5 ppm), as is the relatively close 16-methyl carbon (—2.2 ppm).

In the 3,4-diketo-acid **12**, the origin of the individual four low-field singlets is less clear. The two signals nearly coincident with those of C-2 and C-3 in the parent structure are reasonably assigned to the same centres in the 3,4-diketo-analogue **12**. Since carbonyl-signals appear at lower field than those of olefinic carbons[16c], the remaining two singlets (160.3, 180.9 ppm) are allocated in that order. In this (or any alternative) assignment, the chemical shift of one of the keto-groups is unusually low. The exceptionally close spacing of the quartets of the 5-gem-dimethyl-group of **12** reflects the nearly equal effect exerted by the adjacent 4-keto-group on the two methyl moieties: Unlike other substituents, the keto-oxygen is situated spatially midway between them in the plane of the more than usually flattened ring A.

Conformation of the C(4)-C(5)-Region of Diisophorone

Of the numerous stereochemical problems liable to be posed by the three-dimensional folded structure of diisophorone, the question of the configuration of 4-substituents has been encountered repeatedly in the present work. A brief consideration of this structural aspect, and the bearing on it of ^{13}C-nmr spectral data, concludes our discussion.

Conformation of Ring A. Whether a 4-substituent, be it axial or equatorial, is situated above (β) or below (α) the plane of rings A/B* depends on the conformation of the partially flattened flexible ring A itself. Apart from two possible boat forms, which may reasonably be rejected at once[17a,18], ring A may assume one of two pseudo-chair conformations (i or ii) by "flipping over" at the C(4)-C(5)-bond. Reference to a stereomodel shows that the 4- and 5-substituents will consequently appear in the following positions relative to the plane of rings A/B:

Conformation (i) C-4: α-ax, β-eq · C-5: α-eq, β-ax
Conformation (ii) C-4: α-eq, β-ax · C-5: α-ax, β-eq

A 4-axial substituent thus appears below the plane of rings A/B in conformer (i), and above this plane in conformer (ii).

Configuration of Substituents at C-4. According to the available spectral evidence, the *major* epimers of the 4-substituted diisophorones obtained in the present work[1,6,19] are *axial* conformers. This conclusion is based, in the first instance, on the multiplicity of the ester band (near 1200 cm^{-1}) in the i.r. spectra of 4-acetoxydiisophorones[1,19]. The predominating more readily formed epimers produce, in all the known cases (**9** and hence compounds relatable thereto, i.e. **4**, **6**, **7**; also **17**, **18**) a double or triple peak, indicative[20] of the axial configuration of the substituent.

Further information is obtained from the ^{13}C-nmr data, by examining the effect of introducing the 4-substituent on the chemical shifts of the adjacent 5-gem-dimethyl group (i.e. C-14 ax, C-15 eq). A *4-axial* substituent, occupying a position trans to C-14 ax and gauche to C-15 eq, should have little effect on that of the former, but would appreciably displace that of the latter. A *4-equatorial* substituent, being staggered with respect to both C-14 and C-15, should exert an approximately equal influence on both[7b]. However, in the present case, this approach is complicated by the fact that, in 4-substituted diisophorones, the quartets associated with C-14, C-15 are themselves not individually assignable: the usual guidelines that equatorial methyl

* The terms "above" (or "below") the plane of rings A/B are defined by specifying ring C to be situated *below* this plane.

carbons resonate at lower field than axial ones[2,21] are inapplicable because of the perturbing influence of the adjacent substituent.

We are thus led to consider separately and independently two alternative models, in which the C-14, C-15-quartets are allotted in each possible way. If the 4-substituent has the discriminating displacement effect specified above on the C-14 and C-15 resonances in *both* models, it cannot be situated "staggered" between the two methyl moieties of the 5-gem-dimethyl-group, but must be trans to one, and gauche to the other, and is therefore itself in the 4-axial configuration. The numerical data pertaining to a representative ketol (**19**, Table 2)[19] and a carboxylic acid (**7**, Table 3) illustrate the argument; these and other examples (e.g. **6**, **15**) support the view that our "major" isomers of 4-substituted diisophorones are the axial epimers.

Table 2. *4-Hydroxydiisophor-2(7)-en-1-ol-3-one* (**19**)[19] (δ/ppm from Ref.[2])

		Model A		Model B	
	δ (**1**)	δ (**19**)	δ (**1**)–(**19**)	δ (**19**)	δ (**1**)–(**19**)
14 ax	26.8	28.7	1.9	19.4	−7.4
15 eq	29.7	19.4	−10.3	28.7	−1.0

Table 3. *4-Hydroxy-1-methoxycarbonyldiisophor-2(7)-en-3-one* (**7**)

		Model A		Model B	
	δ (**3**)	δ (**7**)	δ (**3**)–(**7**)	δ (**7**)	δ (**3**)–(**7**)
14 ax	26.4	29.3	2.9	19.7	−6.7
15 eq	30.2	19.7	−10.5	29.3	−0.7

Once the axial configuration of the 4-substituent is adopted, the quartets of the 14- and 15-methyl carbons are readily assigned by choosing that model in which the chemical shift of the equatorial 15-methyl carbon has undergone the significant displacement. Under the influence of adjacent 4-axial substituents, equatorial methyls are thus seen to produce quartets at higher field than their axial counterparts, a situation opposite to that prevailing in the absence of this neighbouring effect (see Table 1, **4**, **6**, **7**, **9**).

Finally, the position of the 4-axial substituent relative to the plane of the rings A/B needs to be resolved: it depends on the spatial disposition

of ring A as a whole. In conformation (i) of the diisophorone structure, the gem-dimethyl group at C-5 is remote from that of C-11, but in (ii) these groups approach one another so closely as to nearly overlap. Conformation (i) is therefore considered the preferred one, and the 4-axial substituents consequently appear *below* (α) the plane of rings A/B.

The conclusion that the major (and sometimes only isolable) epimers of 4-substituted diisophorones are the 4α-axial conformers conflicts at first sight with the general experience that in cyclohexane, the less hindered equatorial derivatives are the preferred species[17b,22]. However, stable axial epimers do exist, both in the parent cyclohexane series[23], and more especially in the rigid condensed polycyclic systems derived therefrom, including steroids[24]; their formation is controlled by a number of complex factors[24]. The present steric assignment is given with the reservations imposed by the limits of the available data. Decisive confirmation may become available from an X-ray analysis of a suitable diisophorone derivative (e.g. **4**).

Acknowledgements

We are indebted to Mrs. *J. Elliot* and Miss *F. Mills*, of the University of London NMR Spectroscopy Service at King's College, London, for the production of the spectra.

Experimental

The ^{13}C-nmr spectra were determined on a Bruker WM 250 Fourier Transform instrument operating at 62.89 MHz, and the broad band proton noise decoupled and DEPT spectra recorded. The internal standard was tetramethylsilane, and the solvent deuteriochloroform or deuteriopyridine.

The preparation of the parent acid (**2**, **3**) and its 4-substituted derivatives are described in Part 12[6], and that of the 8-substituted isomers in Part 13[1] of this series of papers.

References

[1] Part 13, preceding paper.
[2] *Davies P. R., Morgan A. R., Kurzer F.*, Monatsh. Chem. **114**, 739 (1983).
[3] *Wenkert E., Clouse A. O., Cochran D. W., Doddrell D.*, J. Amer. Chem. Soc. **91**, 6879 (1969); *Jautelat M., Grutzner J. B., Roberts J. D.*, Proc. Nat. Acad. Sci. U.S. **65**, 288 (1970).
[4] *Reich H. J., Jautelat M., Messe M. T., Weigert F. J., Roberts J. D.*, J. Amer. Chem. Soc. **91**, 7445 (1969); *Eggert H., Van Antwerp C. L., Bhacca N. S., Djerassi C.*, J. Org. Chem. **38**, 3788 (1973); ibid. **41**, 71 (1976); *Ap Simon J. W., Beierbeck H., Saunders J. K.*, Canad. J. Chem. **51**, 3874 (1973).
[5] *Jones A. J., Grant D. M., Winkley M. W., Robins R. K.*, J. Amer. Chem. Soc. **92**, 4079 (1970); J. Phys. Chem. **74**, 2684 (1970); *Dorman D. E., Roberts J. D.*, Proc. Nat. Acad. Sci. U.S. **65**, 19 (1970).
[6] *Kurzer F., Patel J. N.*, Monatsh. Chem. **115**, 793 (1984).

[7] *Wehrli F. W., Wirthlin T.*, Interpretation of Carbon-13 NMR Spectra. London: Heyden & Son. 1978 (a) Chart at end, (b) pp. 38, 46.
[8] *Marr D. H., Stothers J. B.*, Canad. J. Chem. **45**, 225 (1967).
[9] *Johnson L. F., Jankowski W. C.*, Carbon-13 NMR Spectra. A Collection of Assigned Coded and Indexed Spectra. New York: Wiley-Interscience. 1972, e.g. nos. 230. 274, 318, 344, 439.
[10] *Stothers J. B., Lauterbur P. C.*, Canad. J. Chem. **42**, 1563 (1964).
[11] *Marr D. H., Stothers J. B.*, Canad. J. Chem. **43**, 596 (1965).
[12] *Weigert F. J., Roberts J. D.*, J. Amer. Chem. Soc. **92**, 1347 (1970).
[13] *Roberts J. D., Weigert F. J., Kroschwitz J. I., Reich H. J.*, J. Amer. Chem. Soc. **92**, 1338 (1970); *Hagen R., Roberts J. D.*, J. Amer. Chem. Soc. **91**, 4504 (1969).
[14] *Grutzner J. B., Jautelat M., Dence J. B., Smith R. A., Roberts J. D.*, J. Amer. Chem. Soc. **92**, 7107 (1970).
[15] *Lippmaa E., Pehk T.*, Eesti N.S.V. Tead Akad. Toim. Keem. Geol. **17**, 210 (1968).
[16] *Stothers J. B.*, Carbon-13 NMR Spectroscopy. New York: Academic Press. 1972 (a) pp. 56, 133, 140, 144, for CH_3CH_2X; (b) p. 184, (c) p. 280.
[17] *Hanack M.*, Conformation Theory. New York: Academic Press. 1965 (a) p. 43 et seq. (b) p. 89 et seq.
[18] *Shoppee C. W.*, J. Chem. Soc. **1946**, 1138.
[19] *Allen A. A., Kurzer F., Morgan A. R.*, J.C.S. Perkin I **1980**, 733.
[20] *Fieser L. F., Fieser M.*, Steroids, p. 171. New York: Reinhold. 1959.
[21] *Dalling D. K., Grant D. M.*, J. Amer. Chem. Soc. **89**, 6612 (1967); *Mason J.*, J. Chem. Soc. (A) **1971**, 1038.
[22] *Eliel E. L.*, Stereochemistry of Carbon Compounds, p. 204 et seq. New York: McGraw-Hill 1962.
[23] *Dauben W. G., Fonken G. J., Noyce D. S.*, J. Amer. Chem. Soc. **78**, 2579 (1956); *Kamernitzky A. V., Akhrem A. A.*, Izv. Akad. Nauk SSSR, Otdel Khim. Nauk **1959**, 740; Tetrahedron **18**, 705 (1962); *Stork G., Wagle S. S., Mukharji P. C.*, J. Amer. Chem. Soc. **75**, 3197 (1953).
[24] *Kirk D. N., Hartshorn M. P.*, Steroid Reaction Mechanisms, pp. 13, 19, 147. Amsterdam: Elsevier. 1968.