Monatshefte für Chemie 114, 739—751 (1983)

Monatshefte für Chemie
Chemical Monthly

Di-isophorone and Related Compounds. Part 10[1] ^{13}C-Nuclear Magnetic Resonance Spectra of Di-isophorone Derivatives[2]

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(Received 2 December 1982. Accepted 30 December 1982)

^{13}C-Nuclear magnetic resonance spectra of a series of di-isophorone derivatives have been mapped and the individual resonances assigned. Assignments were obtained by comparing and correlating the spectra of closely related di-isophorones of known structure. Estimates, based on approximate calculations, of the chemical shifts of the six methylene moieties of the di-isophorone skeleton are in fair agreement with the observed values.

(Keywords: Di-isophorone; ^{13}C-Nmr spectra, assignment of; Tricyclo(7.3.1.0^{2,7})tridecanes)

Di-isophoron und verwandte Verbindungen, 10. Mitt.: ^{13}C-NMR-Spektren von Di-isophoron-Derivaten

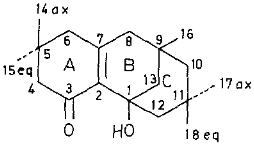
Die ^{13}C-Kernresonanzspektren einer Reihe von Di-isophoron-Derivaten wurden gemessen und die Signale den einzelnen Kohlenstoffatomen zugeteilt. Die Zuordnung erfolgte auf Grund des Vergleichs von Spektren verwandter Di-isophorone bekannter Struktur. Für die Resonanzen der Ringmethylen-Gruppen wurde eine befriedigende Übereinstimmung der gefundenen Werte mit errechneten Schätzungswerten festgestellt.

Introduction

The study of ^{13}C-nuclear magnetic resonance spectra as an aid in solving structural problems has attracted increasing attention in all branches of organic chemistry[3–6]. An example of the use of this method particularly relevant to our present interests has been the systematic examination and interpretation of the ^{13}C-nmr spectra of steroids[7–9].

0026-9247/83/0114/0739/$ 02.60

We have now studied and assigned the ^{13}C-nmr spectra of a representative series of di-isophorone derivatives by a similar approach and have obtained a set of assignments for use in dealing with structural questions in this field. The information has already been helpful in interpreting rearrangements involving bromodi-isophorones[10], the partial aromatisation of di-isophoranes[11], as well as other examples.



Di-isophorone (**2**)

Our first objective was the complete assignment of the spectrum of the parent ketol [di-isophor-2(7)-en-1-ol-3-one, "di-isophorone", (**2**)][12], the ultimate source of all other di-isophorone derivatives so far described. Because of the complexity of its three-dimensional ring-system, and the lack of spectral information on sufficiently closely related structures, its ^{13}C-nmr spectrum is not accessible by calculation. The required assignments were deduced empirically, as has been done in the case of steroids[7–9] and diterpenes[13,14] by a comparison of the spectra of a series of di-isophorone derivatives of established structure. The numerical values of the ^{13}C-nmr spectrum of **2** agree closely with those of a previously recorded[15] unassigned spectrum.

Results and Discussion

The present work thus involved the mapping of the ^{13}C-nmr spectra of a number of suitable di-isophorone derivatives and the study of the effect of structural changes in rings A and B on the chemical shifts of the individual atoms of the carbon skeleton. Assignments were obtained by a comparison and correlation of appropriately chosen data; although this empirical approach does not always provide unequivocal attributions, particularly for closely spaced signals, the results are highly self-consistent and the conclusions should require none but minor revisions.

The results for the whole series of model compounds are recorded in Table 1, which presents the proton noise decoupled chemical shifts (in ppm) and their first order multiplicities, together with the suggested assignments. In some cases, two or three closely spaced signals are

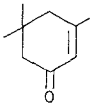
Table 1. ^{13}C *Chemical shifts in diisophorones and their assignments (ppm downfield from TMS; * + signals may be reversed in horizontal line)*

	C1	C2	C3	C4	C5	C6	C7	C8	C9
	71.4 s	135.4 s	200.7 s	51.8 t	*32.2 s	45.7 t	157.5 s	44.6 t	*32.4 s
	80.0 s	134.6 s	196.3 s	51.9 t	*32.3 s	45.4 t	153.6 s	45.0 t	*32.6 s
	73.3 s	129.6 s	141.4 s	35.5 t	29.4 s	45.5 t	155.8 s	44.4 t	32.4 s
	72.2 s	131.6 s	138.6 s	35.9 t	29.6 s	45.5 t	150.1 s	43.9 t	32.2 s
	70.9 s	135.1 s	200.5 s	79.9 d	39.6 s	45.4 t	157.6 s	44.3 t	32.5 s
	70.9 s	135.9 s	194.6 s	80.6 d	37.6 s	45.4 t	156.3 s	44.6 t	32.4 s
	79.8 s	134.4 s	191.0 s	80.0 d	37.2 s	44.7 t	150.4 s	44.4 t	32.7 s
	79.6 s	133.8 s	189.9 s	80.9 d	36.1 s	45.3 t	153.9 s	45.3 t	32.7 s
	71.4 s	134.5 s	202.1 s	52.2 t	32.6 s	*39.3 t	153.0 s	65.9 d	37.2 s
	71.8 s	133.4 s	192.9 s	63.6 d	37.1 s	*45.9 t	158.8 s	*41.0 t	32.7 s
2	71.5 s	64.1 s	209.5 s	51.2 t	*31.8 s	+41.7 t	68.9 s	+40.5 t	*32.5 s
3	83.4 s	66.3 s	206.4 s	50.3 t	*33.1 s	42.5 t	71.6 s	40.7 t	*34.7 s
4	70.9 s	69.8 s	+203.9 s	+195.1 s	44.1 s	*39.6 t	70.1 s	*40.6 t	33.2 s
5	72.0 s	64.7 s	192.3 s	137.9 s	35.6 s	42.0 t	68.6 s	39.9 t	32.8 s
6	71.4 s	138.4 s	184.8 s	137.4 s	37.3 s	*46.0 t	156.2 s	*45.0 t	32.4 s
7	72.1 s	132.2 s	129.4 s	199.4 s	40.6 s	42.3 t	139.0 s	139.4 d	36.5 s
8	79.5 s	137.4 s	130.2 s	196.0 s	41.5 s	42.2 t	141.3 s	141.8 d	36.5 s
9	71.8 s	131.8 s	121.1 d	73.4 d	36.6 s	39.6 t	135.3 s	143.9 d	34.2 s
0	67.3 s	135.9 s	195.7 s	51.4 t	*33.0 s	45.4 t	155.6 s	44.9 t	*32.9 s
1	62.4 s	136.8 s	196.0 s	*51.8 t	+33.9 s	45.6 t	155.2 s	45.1 t	+33.6 s

	C10	C11	C12	C13	C14 ax	C15 eq	C16	C17 ax	C18 eq
2	52.1 t	31.4 s	50.3 t	46.6 t	26.8 q	29.7 q	28.2 q	32.7 q	37.1 q
3	52.2 t	31.1 s	46.3 t	43.9 t	27.4 q	29.6 q	28.6 q	32.5 q	37.3 q
4	52.7 t	31.7 s	49.8 t	47.0 t	26.5 q	30.6 q	28.0 q	32.9 q	37.2 q
5	52.7 t	31.5 s	50.3 t	47.3 t	26.7 q	30.8 q	27.9 q	33.0 q	37.3 q
6	52.4 t	31.6 s	50.5 t	46.3 t	28.7 q	19.4 q	28.1 q	32.7 q	37.2 q
7	52.4 t	31.5 s	50.6 t	46.4 t	27.4 q	21.2 q	28.7 q	32.7 q	37.2 q
8	52.3 t	31.2 s	46.4 t	43.6 t	27.5 q	21.5 q	28.8 q	32.5 q	37.4 q
9	52.1 t	31.1 s	46.3 t	43.6 t	20.7 q	27.3 q	28.9 q	32.4 q	37.3 q
0	49.1 t	31.1 s	50.3 t	*44.0 t	25.6 q	29.9 q	+30.5 q	+33.4 q	36.6 q
1	52.2 t	31.6 s	50.3 t	46.7 t	*28.0 q	*24.5 q	*29.1 q	32.7 q	37.1 q
2	53.4 t	31.3 s	49.1 t	+41.7 t	32.5 q	29.4 q	30.3 q	32.9 q	36.5 q
3	53.4 t	31.8 s	42.5 t	39.1 t	32.8 q	29.3 q	31.5 q	32.9 q	36.5 q
4	53.2 t	31.4 s	48.0 t	42.2 t	*28.3 q	*27.3 q	*28.0 q	32.7 q	36.4 q
15	53.6 t	31.4 s	49.2 t	42.0 t	32.8 q	30.6 q	28.3 q	32.8 q	36.6 q
16	52.3 t	31.5 s	50.0 t	46.3 t	+27.3 q	+27.9 q	28.4 q	32.7 q	37.1 q
17	51.2 t	31.7 s	49.0 t	47.9 t	*26.0 q	*29.0 q	*24.6 q	30.1 q	37.1 q
18	48.3 t	31.4 s	47.6 t	44.6 t	*25.3 q	*28.9 q	*24.3 q	29.8 q	37.2 q
19	53.0 t	31.7 s	50.6 t	48.0 t	*25.8 q	*29.3 q	*24.5 q	30.2 q	37.4 q
20	52.3 t	31.5 s	52.0 t	50.4 t	27.7 q	29.3 q	27.9 q	32.4 q	36.9 q
21	54.0 t	32.4 s	*51.7 t	*51.3 t	27.8 q	29.5 q	27.7 q	32.6 q	36.8 q

Table 1. *Supplement*

	1-Acetyl		4-Acetyl	
	CO	*Me*	CO	*Me*
3	169.9 s	21.9 q		
7			170.0 s	20.5 q
8	*169.3 s	21.5 q	*169.9 s	20.5 q
9	*170.2 s	22.0 q	*170.5 s	20.1 q
13	170.0 s	22.7 q		
18	*168.3 s	21.4 q	*168.7 s	20.5 q



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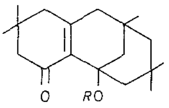
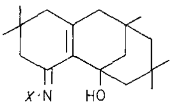
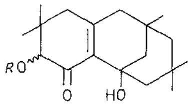


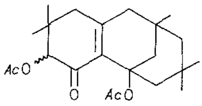
2: *R* = H
3: *R* = *Ac*



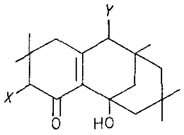
4: *X* = OH
5: *X* = NH_2



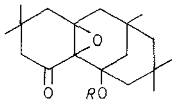
6: *R* = H
7: *R* = *Ac*



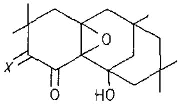
8: 4 α-*Ac*O
9: 4 β-*Ac*O



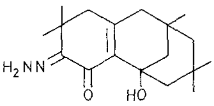
10: *X* = H *Y* = Br
11: *X* = Br *Y* = H



12: *R* = H
13: *R* = *Ac*



14: *X* = O
15: *X* = NNH_2



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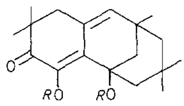
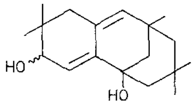


17: *R* = H
18: *R* = *Ac*



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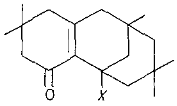

20: *X* = Cl
21: *X* = Br

assigned collectively to an equal number of specified carbon atoms, where the individuals of the group cannot be further matched: these are marked in Table 1 in the usual manner. A consideration of the sum of the data provided the following interpretation of the spectrum of the parent ketol (**2**).

*Di-isophor-2(7)-en-1-ol-3-one [“Di-isophorone”, (**2**)]*

Singlets. The ^{13}C nmr spectrum of the parent ketol **2** consisted of the expected 7 singlets, 6 triplets and 5 quartets. Two of the singlets, appearing in characteristic low-field ranges, are immediately assignable to the 3-ketonic- (200.7 ppm) and the 1-hydroxy-carbon (71.4 ppm)[3–6]. The two singlets of the carbon atoms flanking the olefinic 2,7-bond are similarly identifiable, and are differentiated by reference to the corresponding signals of isophorone (**1**), which appear at 125.3 (C-2) and 159.7 ppm (C-3)[3]. In di-isophorone (**2**), the singlet at 135.4 ppm is therefore attributed to C-2, and that at 157.5 to C-7. These assignments are in accord with the greater shielding of C-2 by its relatively higher electron density, and also with the observed lower intensity of the C-2 signal, reflecting its longer relaxation time due to its being bonded to three quaternary carbon atoms (viz. C-1, C-3, C-7)[16,17].

Of the remaining three high-field singlets of the di-isophorone derivatives, one appears almost invariably at ca. 31 ppm. This signal is attributed to C-11 on the grounds that structural changes in rings A and B are likely to have the smallest effect on the carbon atom most remote from these sites. The two remaining singlets at 32.4 and 32.2 ppm are therefore associated with C-5 and C-9, but are too closely spaced (in **2**) to be individually assigned; this is possible, however, in the case of most other derivatives (e.g. **6**–**11**, **17**–**19**, see below).

Quartets. A scrutiny of the chemical shifts of the quartets of the reference compounds (**2**–**16**) shows that the two lowest-field signals appear constantly near 32.7 and 37.2 ppm. They are therefore assigned, for the reasons given in the case of C-11, to the C-17 and C-18 methyl carbons; they are differentiated by the following two independent arguments:

(a) Equatorial methyl carbons of condensed cyclohexane systems are known[18] to resonate at lower field than axial ones (as, for example, in 1,1,10-trimethyl-trans-decalin[14], pimaradienes[13], and podocarpane[19]). In the present series, the signals at ca. 37 ppm are therefore assigned to the C-18 equatorial and those at ca. 33 ppm to the C-17 axial methyl carbons throughout.

(b) In passing from the parent ketol **2** to the dienolone **17**, the signal at 37.1 remains unaffected, but that at 32.7 ppm undergoes upfield displacement (by at least 2.6 ppm; see Table 1). The system of conjugated 2,7-double bonds (in **17**) may reasonably be expected to be without effect on the remote C-18 equatorial methyl carbon, but is sufficiently close to the C-17 axial carbon (situated *below* ring B) to cause the observed displacement.

The quartet appearing near 28 ppm in the parent ketol **2** and its immediate functional derivatives (**3**–**5**) persists upon introduction of a 4-substituent (e.g. in **6**–**9**), and is therefore attributed to the C-16 methyl carbon, the one least likely to be affected by such changes. In agreement with this conclusion, 8-substitution does displace this signal (e.g. in **10**).

The remaining two quartets are therefore allotted to the 5-*gem*-dimethyl-group (i.e. C-14 and C-15), an assignment that agrees with the observed displacement of these signals upon substitution at the adjacent 4-position (compare **2**-**5** with **6**-**9**). A distinction between the C-14 axial and C-15 equatorial carbons is again based on the higher-field resonances of the former (see above). In di-isophorone (**2**), the signals at 26.8 and 29.7 ppm are therefore attributed to C-14 and C-15, respectively. This conclusion is corroborated by a comparison of the appropriate quartets of the parent ketol **2** and its 2,7-epoxide **12**.

	Quartets (in ppm)		
Ketol **2**	26.8	28.2	**29.7**
Epoxide **12**	**29.4**	30.3	32.5

The signal that persists unchanged (i.e. 29.7 ppm) upon the introduction of the oxirane ring above the plane of rings A and B is allotted to the C-15 equatorial methyl carbon, as being least likely affected by this structural change, while its influence on the two closer methyl carbons (C-14, C-16) is reflected in the observed displacements.

Triplets. The six triplets of the di-isophorone framework are distributed over the range 35-53 ppm, but usually form two groups of three closely spaced signals near 45 and 52 ppm. Their emergence at lower field relative to those of cyclohexane (27.7 ppm) or decaline is due to the presence of substituents adjacent to the methylene groups concerned. Because of the close spacing of the signals, the interpretation of this part of the spectrum is the most difficult and further information may, in some cases, call for minor revisions of the assignments, especially those of C-6 and C-8.

A survey of all the spectra shows that the triplet at lowest field appears invariably at 52-53 ppm; being the one least affected by structural changes in rings A and B, it is assigned to the most remote methylene carbon, C-10.

The signal of C-4 is identifiable (at 51.8 ppm for **2**, **3**; 51.2 for **12**) by its replacement by a doublet upon 4-substitution (e.g. in **6**-**9**, **11**). It is also the only signal that is displaced appreciably (by ca. —15 ppm), when the parent ketol **2** is converted into its oxime **4** or hydrazone **5**, the adjacent 4-methylene carbon being most likely to be shielded. Additional confirmation is provided by a comparison with isophorone (**1**, see below).

On passing from di-isophorone (**2**) to its 2,7-epoxide **12**, the introduction of the oxirane ring should affect the adjacent C-6 and C-8 methylene signals, and probably to a lesser degree, that of the spatially close C-13 bridge-methylene; the remote C-12 should be largely unaffected. Of the four signals in question, three do indeed undergo upfield displacement by 4-5 ppm; the only one that changes but little (50.3 to 49.1 ppm) is therefore assigned to C-12.

		C-12	C-4	C-10
Di-isophorone **2**	44.6 ↔ 45.7 ↔ 46.6	50.3	51.8	52.1
Di-isophorone-2,7-epoxide **12**	40.5 ↔ 41.7 ↔ 41.7	49.1	51.2	53.4

Because of the almost identical structural and spatial environment of corresponding methylene groups in isophorone (C-6, C-4 in **1**) and di-isophorone (C-4, C-6 in **2**), a comparison of the spectra of the two compounds was indicated. The chemical shift of C-6 of isophorone (**1**, 50.7 ppm)[3] agrees closely with that attributed to C-4 in di-isophorone (**2**, 51.8 ppm), thus supporting the assignment based on the arguments restricted to the tricyclic di-isophorone structures alone. The remarkable coincidence of the 4-methylene signal of isophorone (**1**, 45.1 ppm) with the triplets that remain to be assigned to di-isophorone (**2**, viz. 44.6, 45.7, 46.6 ppm) is also apparent, and strongly suggests that one of these is associated with the C-6 methylene group (in **2**); however, because of their close spacing, a choice between them is precluded at this stage.

Although the structure of di-isophorone is too complex for the calculation of its ^{13}C nmr spectrum *ab initio*, approximate predictions may be made concerning its methylene resonances by the application of existing[4] empirical quantitative data. The introduction of substituents into the cyclohexane ring displaces the resonance of the adjacent methylene carbon to an extent that may be estimated by a comparison of the chemical shifts of the α-methylene carbon in cyclohexanol[20], cyclohexanone[21], methyl-[18,22] or 1,1-dimethylcyclohexane[18] and cyclohexene[23] with that of cyclohexane (28 ppm)[18,24]. According to the available figures, the insertion of a hydroxyl-, keto-, methyl- or 1,1-dimethyl-group, or an olefinic bond, into the cyclohexane ring displaces the signal of the adjacent methylene carbon by ca. 8, 13, 8.5, 13 and —2 ppm, respectively. The use of these parameters provides approximate estimates for the individual methylene resonances in di-isophorone (see Table 2). By choosing decalin as the basis for comparison, and taking as the "reference point" the average of the known resonances[3,25] of its *cis*- and *trans*-form (α- and β-methylene carbon atoms), a comparable set of figures is obtained, that may possibly approach the true values for di-isophorone even more closely (Table 2).

Table 2. *Estimated (calculated) methylene resonances in di-isophorone* (**2**)

Carbon Atoms	C-4	C-6	C-8	C-10	C-12	C-13
Calculated δ_C (based on hexane)*	54	39	34.5	49.5	49	44.5 ppm
Calculated δ_C (based on decalin)**	52	43.5	39	54	53.5	42.5 ppm

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* Referred to cyclohexane, δ_C 28 ppm.

** Referred to the average values of the shifts of the α- (30, 35 ppm) and β-methylene groups (25, 27.5 ppm) in *cis-* and *trans*-decalin, respectively (i.e. using 32.5 and 26 ppm). Average values are chosen because of the partly flattened conformation of ring A in **2**.

The resulting figures are subject to the obvious uncertainties that are the consequence of neglecting all effects except those, however predominant, of the α-substituents adjoining the methylene groups in question. They appear nevertheless to confirm in a remarkable way the assignments of the C-4, C-10 and C-12 methylene carbons made by the comparative approach, and to agree with the "collective" assignment of the three higher-field triplets to the remaining positions (i.e. C-6, C-8, and C-13). The relative magnitudes of the "calculated" resonances (Table 2) are thought to justify the allocation, in **2**, of the highest-field signal to the C-8 position (44.6 ppm). Since the structural environment of C-8 and C-6 is very similar, but that of C-13 is distinct, the signal closest to that of C-8 is next allotted to the C-6 methylene carbon, leaving the remaining one to the C-13 bridge-methylene carbon atom. Unless there is evidence to the contrary, the same sequence is adhered to for the other di-isophorone compounds. The complete assignment of the di-isophorone spectrum thus arrived at is included in Table **1**; it differs from the conclusions given in our preliminary note[2] in respect of the triplets associated with C-8, C-10 and C-13, which needed to be redistributed amongst themselves as a result of the wider survey.

In the light of the foregoing arguments, the ^{13}C nmr spectra of the derivatives of di-isophorone were similarly interpreted and correlated. The conclusions, presented in Table 1, are briefly discussed below.

Functional Derivatives of Di-isophorone

The conversion of di-isophorone (**2**) into its *oxime* **4**[12] and *hydrazone* **5**[10] is attended by a pronounced upfield shift (ca. 60 ppm) of the C-3 singlet, in line with the lower electron-withdrawing power of the modified 3-substituent. The C-5 and C-9 singlets, which are too closely spaced to be differentiated in the parent ketol **2** and some of its key-derivatives (e.g. **3**, **12**), are distinguishable in its ketonic derivatives by the deshielding (by ca. 3 ppm) of the C-5 ring carbon, while the more remote C-9 atom remains unaffected. Only one of the six triplets is significantly displaced (51.8 to ca. 36 ppm), a change that evidently involves the 4-methylene group.

Acetylation of the 1-hydroxy-group (in **2**) deshields the C-1 carbon (by 9.4 ppm) and affects to a minor extent the adjoining ring positions (C-2, C-3, C-7). The acetylation of cyclohexanol[3] and of sterols results in small upfield displacements of the resonances of the adjacent ring-methylene groups, amounting in the case of the secondary and tertiary hydroxy-groups of 3 α- and 5 β-cholestanol to ca. 3 and 6 ppm, respectively[7,8]. When the triplets of the *1-acetylated ketol* **3**[26] are assigned in line with this generalisation, the shielding of the 12- and 13-methylene carbons is seen to be somewhat unequal (4 and 2.7 ppm, respectively). The lesser change, associated with C-13, is thought to reflect the rigidity of this methylene group, which functions as the bridge in the bicyclo[3.3.1]nonane moiety (rings B, C) of the di-isophorone framework. It is noted, in passing, that the possible reverse assignment of these two triplets would indicate the unlikely displacement of the C-12 and C-13 signals by —6.4 and —0.3 ppm, respectively; this alternative is therefore not adopted. The same arguments apply to the attribution of the corresponding signals of the *diacetates*[27] **8** and **9**. The additional signals due to each acetyl-substituent are readily assignable (see Supplement to Table 1). In the monoacetates (**3**, **7**, **13**), **1**- and **4**-acetoxy-groups consistently produce quartets at ca. 22 and 20.5 ppm, respectively; those of the diacetates (**8**, **9**, **18**) may therefore be identified accordingly. The keto-singlets, however, appearing in the appropriate range for ester-carbonyl groups (ca. 170 ppm)[4,5], are too closely spaced to be similarly differentiated.

Substituted Di-isophorones

The spectrum of *1,4α-dihydroxydi-isophor-2(7)-en-3-one* (**6**)[27] shows that the only significant changes effected by the introduction of the 4 α-hydroxy-group occurs at the adjacent 5-position. The C-5 carbon, being deshielded (by 7.4 ppm), becomes distinguishable from C-9. The equatorial 15-methyl- and the axial 4 α-hydroxy-groups, occupying the same side of the partially flattened ring A, assume a quasi-eclipsed conformation. The 15-methyl carbon is therefore thought to be subject to a greater effect from the 4 α-substituent than its C-14 (axial) counterpart.

Accordingly, the quartet that has undergone the greater displacement is assigned to the equatorial 15-methyl carbon. The same effects, observed in the case of the two *4α-acetoxy-compounds* (**7**[28], **8**[27]) are similarly accommodated. In the *4β-acetoxy-epimer* (**9**[27]), the reverse configuration of the 4-substituent demands that the quartet subject to the greater displacement be attributed to C-14.

Monobromination of the parent ketol **2** yields *8-bromodi-isophor-2(7)-en-1-ol-3-one* (**10**)[26,29]. The fact that the C-3 resonance is barely affected excludes the possible alternative 4-bromo-structure. The consequent exceptional assignment of the displaced singlet (at ca. 37 ppm) to the C-9 ring carbon is noteworthy. Of the five quartets, one is displaced more significantly than the others, and is assigned to the 16-methyl group bonded to the position adjacent to the 8-substituent. Two triplets which are unaffected by the 8-halogenation are regarded to be associated with the 4- and 12-methylene groups. The other three undergo displacement to varying degrees and cannot be differentiated with certainty, the relevant methylene groups (C-6, C-10, C-13) being similarly placed with respect to carbon atom C-8. The 6-methylene position, differing from the others in occupying a less rigid environment, may be associated with the signal that has shifted most (to 39.3 ppm). The chief characteristic of the spectrum of *4-bromo-di-isophor-2(7)-en-1-ol-3-one* (**11**)[10] is the displacement of the signals associated with the 3- and 5-ring carbons flanking the new substituent, an observation that supports the formulation of the product. The two quartets of the remote 11-*gem*-dimethyl-group appear in their usual places; the remaining three are provisionally assigned, in analogy with **6**, **7**, and **8**, to express the likely maximum influence of the 4α-bromo-substituent on the equatorial 15-methyl carbon.

The spectra of the *2,7-epoxides* (**12**–**14**[30], **15**[28]) are distinguished by the pronounced upfield displacement of their C-2 and C-7 singlets into the oxirane-carbon range[3]. In each case, the lower resonance is allocated to the 2-position, on the assumption that the 3-keto-group confers a relatively higher elctron density on the adjacent carbon atom. In the absence of conjugation, the 3-keto-resonance moves downfield as expected[4], but this tendency is evidently opposed by the 4-keto-group in **14**, and overcome by the 4-hydrazono-group in **15**. The C-5 and C-9 singlets of the epoxide **12** and its acetate **13** are, as in the parent ketol **2**, too closely spaced to be differentiated, but in the 4-keto-(**14**) and 4-hydrazono-derivatives (**15**), one of them undergoes upfield displacement and is clearly assignable to C-5. The close agreement of the chemical shifts of the carbon atoms carrying the hydrazono-substituent (C-3 in **5**; C-4 in **15**, **16**) is noteworthy.

The epoxidation of the ketol (**2** → **12**) is without effect on two of the six triplets, which are assigned to the remote 4- and 10-positions; the relative displacement of the others provides the data for identifying the C-12 triplet in **2** (see above). The quartets associated with C-14 and C-16 in **12** cannot be individually allotted by a comparison with those of **2**, each having been displaced by an unknown amount. They may be differentiated by accepting that the epoxide-ring, situated above the plane of rings A/B, affects the axial C-14 more strongly than the C-16 methyl carbon, resulting in a greater downfield shift of the resonance of the former. Accordingly, the signals at 32.5 and 30.3 ppm are assigned to the 14-ax- and 16-methyl carbons, respectively; this order, the reverse of that in **2**, is also adopted in the case of the epoxides **13**–**15**.

The spectra of the *diethylenic di-isophorones* **17**[31], **18**[31], and **19**[28] prove the correctness of their conjugated heteroannular 2,7-diene structures, that had previously been proposed on chemical and uv spectral evidence[31]. Two fairly closely matched pairs of signals (appearing between ca. 130 and 145 ppm) arise clearly from the carbon atoms flanking the two double bonds[3–6]. They are assigned in decreasing numerical order to the 8-, 7-, 2- and 3-position, corresponding to the presumed relative electron densities. The double bond terminating at C-8 causes a downfield displacement of the signal of the adjacent C-9, a change seen elsewhere only in the 8-bromo-derivative **10**. Since four of the five quartets undergo small displacements (in comparison with **2**), their assignment is uncertain: the signals that appear to have changed most may reasonably be attributed to the 17- and 16-methyl carbons, as being nearest to the conjugated double bond system.

The general validity of the results and conclusions may finally be illustrated by the ready interpretation of the spectra of the 1-chloro- and 1-bromo-analogues (**20**, **21**) of diisophorone, on the basis of the assigned spectrum of the parent ketol **2**. The observed spectral changes on replacing the 1-hydroxy- (in **2**) by the 1-halogen-substituents are confined to the site of the substitution and its immediate environment; they include the shielding of C-1 itself (by 4.1, 9.0 ppm, the bromine having the greater effect as expected[4,6]), and of the neighbouring 3-carbonyl-carbon (by ca. 5 ppm). The signals of the adjacent 12- and 13-methylene carbons undergo small downfield displacements. Apart from these perturbations, the spectra display a consistency that reflects the preservation of the conformation of the rigid di-isophorone framework in substitution reactions previously concluded on chemical evidence. Conversely, ^{13}C nmr spectra have served to indicate the occurrence of rearrangements[10,11] that will be described subsequently.

Experimental

The ^{13}C nmr spectra were determined on a Bruker HF-X-90 *Fourier* Transform instrument operating at 22.63 Hz, and the broad band proton noise decoupled and off-resonance spectra recorded. The internal standard was tetramethylsilane, and the solvent deuteriochloroform.

The preparation of the compounds has been previously described as follows: **2**, **4**[12], **3**, **20**[26], **5**, **11**, **15**[10], **6**, 8, **9**[27], **7**, **16**, **19**[28], **10**[26,29], **12**, **13**, **14**[30], **17**, **18**[31], **21**[32].

Acknowledgements

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

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