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Diisophorone and Related Compounds, Part 16[1] ^{13}C-Nuclear Magnetic Resonance Spectra of 5,11-Bisnordiisophorones

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The ^{13}C-nuclear magnetic resonance spectra of a number of 5,11-bisnordiisophorones have been mapped and assigned. The results indicate that compounds of this structure usually consist of mixtures of two stereoisomers, the existence of which is ascribed to the different conformation of their ring A and the 5-methyl group attached to it. Further stereochemical implications of the spectrometric observations are discussed.

(Keywords: 5,11-Bisnordiisophorones, ^{13}C-nmr spectra, assignment of; Tricyclo[7.3.1.0^{2,7}]tridecanes)

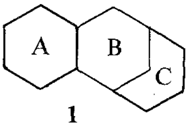
Diisophoron und verwandte Verbindungen, 16. Mitt.: ^{13}C-NMR von 5,11-Bisnordiisophoronen

Die ^{13}C-Kernresonanzspektren einiger 5,11-Bisnordiisophorone wurden aufgenommen und die Signale dem Kohlenstoffgerüst zugeordnet. Nach diesen Messungen bestehen die Verbindungen dieser Reihe gewöhnlich aus zwei Stereoisomeren, deren Vorkommen auf Konformationsunterschiede ihres Rings A und der daran haftenden 5-Methylgruppe zurückzuführen ist. Weitere stereochemische Folgerungen werden auf Grund der spektrometrischen Beobachtungen erörtert.

Introduction

3-Methylcyclohex-2-enones (**3**) readily undergo base-catalysed self-condensation to yield one or more of several possible dimeric or trimeric products[2]. Dimerisation of **3** by strong alkalis under controlled conditions gives access, in one operation, to compounds (**4**) having the tricyclo[7.3.1.$0^{2,7}$]tridecane structure (**1**). This three-dimensional condensed homocyclic ring-system incorporates the bicyclo[3.3.1]nonane carbon skeleton (**2**), which has featured prominently in stereochemical investigations[3].

The use, in the dimerisation **3**→**4**, of a 3-methylcyclohex-2-enone bearing one additional substituent in position 4, 5, or 6 (e.g. as in **3b**) introduces two new asymmetric centres into the resulting dimer (e.g. **4b**), thus leading theoretically to at least four stereoisomeric forms of the tricyclic ketol (**4**). In order to exclude this steric complication, the preferred starting monomers are 3-methylcyclohex-2-enones (**3**) either unsubstituted or identically disubstituted in the positions concerned. Isophorone (3,5,5-trimethylcyclohex-2-enone, **3c**) satisfies this requirement, is easily accessible and undergoes the desired dimerisation readily in satisfactory yield. Accordingly, the bulk of the work by the present approach[4] has been performed using diisophor-2(7)-en-1-ol-3-one[5]



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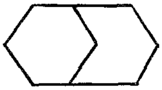

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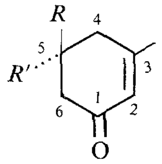
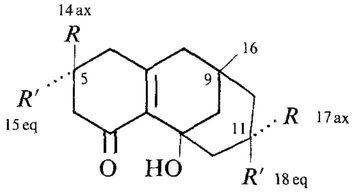
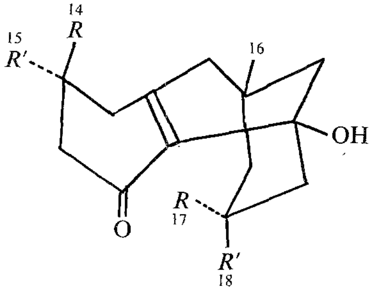


3a $R=R'=H$
3b $R=H$, $R'=Me$
3c $R=R'=Me$



4a $R=R'=H$
4b $R=H$, $R'=Me$
4c $R=R'=Me$



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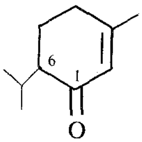

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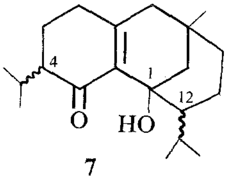

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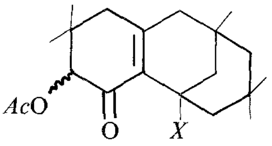


8 $X=OAc$
9 $X=COOMe$

("diisophorone", **4c**) rather than the ultimate parent ketol (**4a**), the synthesis of which is less convenient in practice both at the production and dimerisation stage of the monomer (**3a**)[6].

However, in order to confirm the general validity of the established reactions, homologues of **4a** have been employed in selected examples. Next to diisophorone (**4c**), 5,11-bisnordiisophorone[5] (**4b**) is a suitable and fairly readily accessible[2,7–9] compound for this purpose; its production from 3,5-dimethylcyclohex-2-enone (**3b**)[10] and its further conversions[4,7–9,11] take the expected course leading generally to stereochemically non-uniform products.

The formation of more than one isomer in the dimerisation of substituted 3-methylcyclohex-2-enones has occasionally been observed. In the case of piperitone[12] (6-isopropyl-3-methylcyclohex-2-enone, **6**), the "α- and β-dipiperitone" (**7**) obtainable by fractionation were regarded[7,13] as stereoisomers differing in the configuration of their 4-isopropyl-substituent. 5,11-Bisnordiisophorone (**4b**), the dimerisation product of **3b**, has been separated into two isomers[8], and a single conformer is on occasion isolable from an epimeric mixture (e.g. **14**, **21**, below).

Results and Discussion

Consistent physical evidence for the usual occurrence of 5,11-bisnordiisophorones (**4b**) in at least two isomeric forms has now been obtained in the course of a survey of their ^{13}C-nmr spectra, undertaken partly with this objective in view, and with the wider aim of mapping and assigning the spectra of this series of tricyclo[7.3.1.0^{2,7}]tridecanes by the usual correlation[14,15] of spectral variation with structural change. The more extensive data established for diisophorones[14,15] helped materially in arriving at or supporting the present attributions.

As an additional point of reference, the ^{13}C-nmr spectrum of 3,5-dimethylcyclohex-2-enone (**3b**), the ultimate source of all 5,11-bisnordiisophorones, was compared with the assigned spectrum of its 3,5,5-trimethylhomologue[16a] ("isophorone", **3c**) (Table 1). The exchange in this structure of the 5,5-dimethyl- for the 5-methyl-moiety produces the expected[14,17,18] shielding of the adjacent 4- and 6-methylene-carbons (by ca. 5 ppm[14]), and of the 8-methyl carbon (by ca. 7 ppm[17,18]). The chemical shifts settled for this simple model confirmed the assignments of the corresponding positions in ring A in the 5,11-bisnordiisophorones derived from it (i.e. C-4, C-6 and C-15 of **4b**). Unlike the latter, 3,5-dimethylcyclohex-2-enone gave rise to a single-line spectrum.

The assigned ^{13}C-nmr spectra of the 5,11-bisnordiisophorones (**11**–**21**) are presented in the usual way[14,15], together with that of diisophorone (**4c**)

Table 1. ^{13}C-*Chemical shifts in 3,5-dimethyl-* (**3b**) *and 3,5,5-trimethyl-cyclohex-2-enone (isophorone,* **3c***)*[a]

Carbon atom	**3b**	**3c**[b]
1	199.8 s	199.0 s
2	126.3 d	125.3 d
3	161.9 s	159.7 s
4	39.4 t	45.1 t
5	30.0 d	33.3 s
6	45.2 t	50.7 t
7	24.3 q	24.3 q
8	21.1 q	28.2 q
9	—	28.2 q

[a] Chemical shifts are given in ppm downfield from *TMS*. The solvent was deuteriochloroform. For numbering, see structure **3**. 7-Methyl is attached to C-3, and 8- and 9-methyl to C-5.

[b] Figures taken from Ref.[16a].

for comparison (Table 2). The numbering of the structure (**10**) is that of diisophorone[5], except for the omission of C-14 and C-17 so as to preserve the immediate comparability of entries for the two series. In all but two of the examples examined (**14**, **21**), the signals consist of *pairs of lines*, indicative of the presence of two stereoisomeric forms, corresponding carbon atoms showing resonance signals differing slightly in chemical shift. This interpretation is in accord with the established variation of the ^{13}C-nmr spectra of alkylcyclohexanes[17, 18] and cyclohexanols[16b, 19] with the conformation of their substituents; it recalls our previous observation, that individual 4α- and 4β-substituted diisophorones (**8**[14], **9**[15]) produce distinct spectra, corresponding signals, especially those of the more proximate carbon atoms, differing slightly but consistently in their chemical shifts. The steric heterogeneity of 4$\alpha\beta$-bromodiisophor-2(7)-en-1-ol-3-one has been similarly recognised[20].

The unequal intensities of the constituent lines of the signal pairs reflect the predominance of one stereoisomer over the other. Thus, the parent ketol (**4b**) arising in the dimerisation (**3b** → **4b**) is isolated as a mixture containing its components in the approximate ratio 3 : 1. The cause of this inequality may be sought in differences of the solubility and crystallisability of the constituents as much as in their respective rate of formation. Separate quantitative studies, taking account of side-reactions and partial resinification, would be needed to estimate the contribution of the latter factor. In subsequent reactions, the parent-ketol mixture (**4b**) gives products that may have a conspicuously altered isomer composition, presumably due to the operation of the same effects (see Table 2). Stereochemically uniform products (e.g. **14**, **21**) are in fact occasionally obtained from their non-homogenious source (**4b**).

Assignment of Spectra

In assigning the ^{13}C-nmr spectra of the 5,11-bisnordiisophorones, the reasoning used successfully in the interpretation of those of the diisophorones[14] and their 1-carboxylic acids[15] was again followed. The present discussion is therefore restricted to new aspects specifically relevant to the bisnor-series (**4b**). All numerical values of chemical shifts refer to the more intense signals of the major stereoisomers.

Singlets. The chemical shifts of the singlets of 5,11-bisnordiisophorones (**11**–**21**) closely resemble those of the corresponding diisophorones (**4c** and derivatives), and are readily assigned accordingly, leading to the following conclusions: Carbon C-9, situated in an almost identical structural environment in either homologous series (**4b**, **4c**), gives rise to closely matching signals in both, but a consistent deshielding of C-7 (by 1–3 ppm), and a lesser one of C-3 (by ca. 1 ppm) is evident in the bisnor-homologues, due to the removal of one of the 5-methyl-groups. The slight deshielding of C-1 seen throughout the 5,11-bisnor-series (0.3–1 ppm) is similarly attributable to the exchange of the 11-CMe_2—for the 11-CHMe—moiety. The C-3 carbon atom of the oximes (**18**, **19**) and the hydrazone (**20**) produces a low field singlet within the expected range[21a, 22–24].

Spacing of line pairs. The observed lateral spacing of the line pairs forming the individual signals agrees with the view that the stereoisomerism of 5,11-bisnordiisophorones is due to conformational differences in their 5- (and not their 11-) methyl-group. Thus, signal pairs due to C-1 are nearly coincident throughout the series (see Table 2); this is expected if the *same* conformation of the 11-methyl-group (i.e. 18 β-eq) exerts in both stereoisomers the same effect on the near C-1 bridgehead-carbon; any unequal influences of the 5 α- and 5 β-methyl groups fail to be transmitted to C-1 because of the relative remoteness of these centres from one another. The even closer spacing of the singlet line-pairs of C-9 is similarly explicable. In contrast, the distinct separation of the singlet pairs of C-7, C-3 and C-2 (by 1–3 ppm) is attributable to the unequal effect on these carbon atoms of the more proximate 5 α- and 5 β-substituents.

Doublets. The two new high-field doublets generated by the tertiary C-5 and C-11 carbons are distinguished by reference to compounds having identical cyclohexenone rings A (**11**, **12**, **14**–**16**). Their doublets appearing over the narrower range (30–31 ppm) are assigned to C-5, i.e. to the carbon atom situated in a less variable structural environment than C-11. This allocation agrees with the *spacing* of the line-pairs of individual signals; the two lines due to the C-5 signals are on average 1.5 ppm apart, indicating an effect on C-5 of the differing configuration of the 15-methyl groups, while those due to C-11 are coincident or nearly so, in accord with a non-varying configuration of the 18 β-eq methyl group. The two new doublets of the 5,11-bisnor-series replace the singlets appearing at 29–33 ppm, and at 31.5 ppm in diisophorones, thus confirming the asignment of the latter[14].

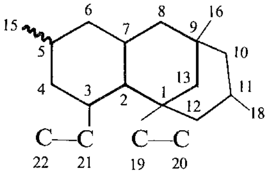
Triplets. The allocation of the triplets is difficult because of the location of four or more of them within a very narrow spectral range (43–

48 ppm). A comparison of the spectra of the homologous series (**4b**, **4c**) provides initial guidance, in that the triplets of positions C-4, 6, 10 and 12, adjacent to a $.CMe_2./.CHMe.$-exchange, move upfield by an amount close to the standard value established for cyclohexane rings (viz. 13–8.5 = 4.5 ppm[14]). Triplets resonating at 50–52 ppm in diisophorones (two or three in number) are thus displaced, in the 5,11-bisnor-series, into the spectral range near 46 ppm already occupied by those of C-8 and C-13; these carbon atoms should differ little in their chemical shifts in either homologous series (**4b**, **4c**), appearing in the same structural environment in both. The assignment of the triplets is thus proposed on the basis of the following reasoning:

The lowest field triplet (δ ca. 49 ppm) is allotted, in accordance with the foregoing guidelines. to C-10, its chemical shift showing an almost constant shielding (of ca. 3 ppm) relative to that of corresponding diisophorones (see Table 2 and Refs.[14, 15]). The triplet of C-4 is revealed by its shielding by an adjacent 3-oximino-group, or a 2,7-conjugated diene-system. In cyclohexanone[16c, 25, 26] and ketones generally[23], the exchange of the keto- by an oximino-group displaces the triplets of the adjacent *syn*- and *anti*-methylene carbons upfield by ca. 16 and 10 ppm respectively. In the present spectra, one of the narrow-range triplets (appearing nearest 46 ppm) conforms to this pattern, moving upfield (by 16 ppm) in the oximes **18** and **19**, and is therefore allocated to C-4. The asignment establishes, at the same time, the *syn*-configuration (with respect to C-4) of the 3-oximes (**18**, **19**), a conclusion conformable to the likely resistance to the formation of the *anti*-isomers by the operation of steric hindrance. A similar though lesser shielding is exerted on C-4 by a neighbouring 2,7-diene-system (in **13** and **21**), thus presenting consistent results in both homologous diisophorone series[1, 14]. Final support for the assignment of the C-4 triplet emerges from the very close agreement of its resonance and that of the comparable centre in 3,5-dimethylcyclohex-2-enone (**3b**, $\delta_{C\text{-}6} = 45.2$ ppm; Table 1).

The signal allotted to C-8 appears constantly near 47 ppm, except when shielded (by 5 ppm) in the 2,7-epoxide (**17**), or when giving place to a doublet (in **13**, **16** and **21**). The two remaining triplets of the narrow range are allocated to C-12 and C-13, providing a signal at 47 ppm for each of these positions in the parent ketol (**11**), in agreement with the introductory argument. Changes in the adjacent 1-substituent (in **11**–**21**) are duly reflected in displacements of both these signals in a manner parallel with those occurring in the diisophorone series[14, 15].

The final triplet, appearing with insignificant variation near 39 ppm, is assigned to C-6: of all triplets, its chemical shift approaches most closely the estimate based on the known[14] C-6 resonance in diisophorone (viz. 45–



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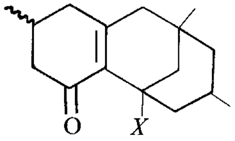
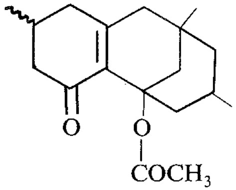


11 $X = OH$
14 $X = COOMe$
15 $X = Cl$



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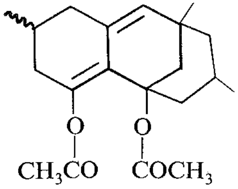

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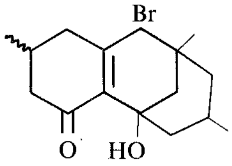

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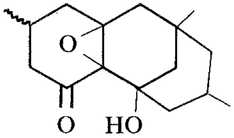

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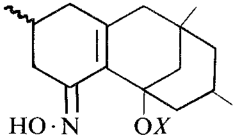
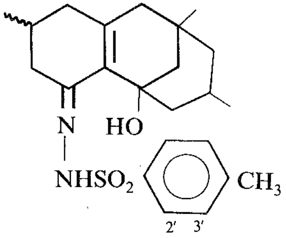


18 $X = H$
19 $X = Me$



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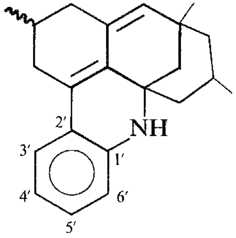

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Table 2. ^{13}C *Chemical shifts in*

Compound	C 1	C 2	C 3	C 4	C 5	C 6	C 7	C 8
4c[d]	71.4 s	135.4 s	200.7 s	51.8 t	*32.2 s	45.7 t	157.5 s	44.6 t
11	72.3 s	134.6 s	201.6 s	*46.2 t	30.2 d	39.1 t	160.1 s	*46.8 t
	72.4 s	135.0 s	201.0 s	—	29.0 d	38.8 t	160.6 s	46.0 t
12	80.5 s	134.2 s	197.3 s	*45.9 t	30.1 d	39.2 t	154.5 s	*46.8 t
	80.4 s	133.8 s	196.0 s	45.8 t	28.6 d	38.9 t	156.1 s	46.5 t
13	81.1 s	134.1 s	124.5 s	36.9 t	29.0 d	39.1 t	143.5 s	132.7 d
	81.0 s	133.0 s	124.1 s	37.0 t	27.8 d	37.9 t	143.2 s	132.5 d
14	45.3 s	133.9 s	197.1 s	*46.1 t	30.3 d	39.3 t	158.1 s	*46.2 t
15	67.3 s	135.1 s	195.0 s	*46.0 t	30.9 d	39.0 t	156.8 s	*46.4 t
	67.0 s	134.4 s	196.9 s	45.9 t	29.2 d	39.5 t	159.3 s	46.7 t
16	72.4 s	133.5 s	203.0 s	*46.5 t	30.2 d	39.3 t	156.3 s	65.5 d
	—	133.6 s	202.2 s	46.2 t	29.3 d	38.0 t	156.4 s	65.4 d
17	71.3 s	64.8 s	209.8 s	*44.9 t	31.1 d	38.3 t	70.7 s	41.3 t
	71.8 s	66.3 s	208.5 s	46.9 t	—	38.0 t	—	41.5 t
18	74.0 s	128.8 s	156.6 s	30.3 t	27.5 d	38.5 t	143.5 s	*46.8 t
	73.9 s	129.2 s	156.5 s	30.7 t	26.9 d	38.3 t	144.0 s	46.3 t
19	79.0 s	128.3 s	152.3 s	30.2 t	27.2 d	39.0 t	144.9 s	46.9 t
	78.7 s	—	152.8 s	—	—	39.2 t	147.1 s	46.3 t
20	73.0 s	130.4 s	156.6 s	32.7 t	28.3 d	38.0 t	147.0 s	*46.5 t
	72.8 s	130.9 s	155.8 s	33.3 t	31.4 d	37.8 t	147.8 s	46.0 t
21[e]	53.8 s	129.7 s	126.0 s	33.3 t	29.2 d	38.9 t	134.9 s	132.8 d
	—	131.0 s	125.7 s	34.0 t	28.7 d	38.1 t	134.0 s	132.3 d

[a] For numbering, see structure **10**.

[b] Chemical shifts are given in ppm downfield from *TMS*. The solvent was deuteriochloroform.

[c] This column records the approximate ratio of the intensities of the lines of the signal pairs. The upper line gives in each case the more intense signals of the more abundant stereoisomer.

[d] The chemical shifts of diisophorone are given for comparison.

4.5 = 40.5 ppm), and agrees strikingly with that of the comparable methylene-carbon in 3,5-dimethylcyclohex-2-enone (**3b**, $\delta_{C\text{-}4}$ = 39.4 ppm; Table 1). Its constancy reflects the non-variant environment of the 6-methylene grouping throughout the series.

Quartets. One of the three quartets of the 5,11-bisnordiisophorones appears in a range (28–31 ppm) close to that of the signals of the

5,11-bisnordiisophorones[a] *and their assignments*[b]

C 9	C 10	C 11	C 12	C 13	C 15	C 16	C 18	Relative Intensity[c]	Compound
*32.4 s	52.1 t	31.4 s	50.3 t	46.6 t	29.7 q	28.2 q	37.1 q		**4 c**[d]
32.4 s	49.2 t	28.4 d	*47.0 t	*46.9 t	$^{+}$21.0 q	31.2 q	$^{+}$21.7 q	3	**11**
—	49.1 t	28.6 d	46.4 t	46.3 t	20.9 q	31.3 q	21.8 q	1	
32.7 s	49.2 t	27.2 d	$^{+}$43.7 t	$^{+}$43.0 t	21.2 q	30.9 q	21.6 q	1	**12**
—	49.1 t	27.0 d	43.6 t	42.6 t	20.7 q	31.0 q	21.7 q	1	
35.7 s	45.8 t	26.6 d	$^{+}$45.2 t	$^{+}$44.1 t	21.2 q	28.9 q	21.8 q	3	**13**
36.0 s	45.9 t	—	45.3 t	44.2 t	20.3 q	—	21.9 q	1	
30.9 s	49.5 t	26.4 d	$^{+}$44.1 t	$^{+}$38.5 t	21.1 q	31.2 q	21.9 q	—	**14**
33.3 s	48.2 t	28.3 d	51.7 t	47.8 t	21.5 q	31.0 q	21.5 q	1	**15**
33.2 s	48.4 t	29.0 d	51.9 t	47.2 t	20.7 q	31.1 q	21.6 q	1	
37.1 s	47.3 t	28.8 d	*46.1 t	40.6 t	20.9 q	32.3 q	21.7 q	8	**16**
37.3 s	46.8 t	28.6 d	46.0 t	40.3 t	—	32.4 q	—	1	
32.4 s	50.1 t	27.9 d	*44.8 t	*43.4 t	21.6 q	31.1 q	22.3 q	4	**17**
—	49.9 t	—	45.1 t	41.7 t	20.9 q	—	22.7 q	1	
32.3 s	49.5 t	28.3 d	*46.9 t	*46.7 t	21.0 q	31.3 q	21.8 q	3	**18**
32.4 s	—	28.5 d	46.5 t	45.9 t	21.4 q	31.4 q	—	1	
32.4 s	49.8 t	28.2 d	*43.7 t	*43.3 t	21.0 q	31.7 q	22.0 q	5	**19**
—	49.5 t	—	—	43.0 t	21.4 q	—	—	1	
32.0 s	49.3 t	27.5 d	*47.0 t	*47.0 t	21.6 q	31.3 q	21.8 q	6	**20**
32.1 s	—	27.1 d	46.2 t	—	21.1 q	—	21.7 q	1	
35.0 s	47.8 t	26.5 d	*47.3 t	*46.8 t	21.5 q	29.1 q	21.7 q	2	**21**[e]
35.2 s	47.7 t	26.9 d	47.6 t	47.0 t	—	—	—	1	

[e] This compound was originally isolated[33] as (i) a less soluble fraction, m. p. 162–164°, and (ii) a more soluble fraction, m. p. 146–148°, which were surmised to be stereoisomers. The former, producing the signals given in the upper line, is now shown to be sterically uniform, but the latter, displaying the *additional* signals given in the lower line, is the usual mixture of the two conformers. The very close spacing of the signal pairs is noteworthy.

$^{+}$* Figures may be interchanged horizontally.

analogously placed 16-methyl-group in diisophorones, and is therefore assigned accordingly. In conformity with the fixed configuration of the 16-methyl-group, the line pairs of its signal arising from the two epimeric constituents are coincident, or nearly so, in all the derivatives examined.

The other two quartets emerge in the region of the spectrum appropriate to the . CH*Me* .-moiety in cyclohexanes (20–22 ppm)[16b, 17, 28]

Table 2. *Supplement*

Compound	C 19	C 20	C 21	C 22	Aromatic Signals					
					C 1′	C 2′	C 3′	C 4′	C 5′	C 6′
12	170.3 s	21.9 q								
13	*168.9 s	21.7 q	*168.8 s	20.8 q						
14	177.4 s	51.7 q								
19	49.9 q									
									(*Me*)	
20					144.5 s	128.3 d	130.0 d	135.3 s	20.7 q	
					—	128.4 d	—	—	—	
21					143.7 s	122.9 s	128.0 d	117.9 d	123.5 d	113.8 d
					143.8 s	124.0 s	127.9 d	118.3 d	—	113.7 d

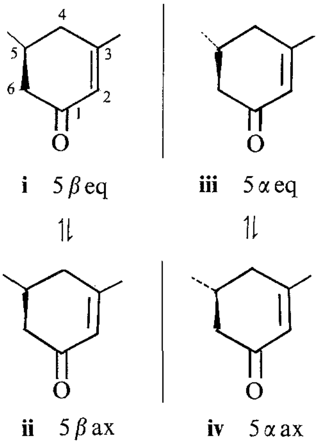
including 3,5-dimethylcyclohex-2-enone (Table 1). Though placed closely together, they may be identified by the lateral spacing of their individual line pairs: The quartet consisting of a pair of wholly or nearly coincident lines is assigned to the sterically invariant C-18 equatorial methyl group. The other line-pair shows small differences in the chemical shifts, consistent with the opposite configuration of the C-15 carbon atoms. The quartet of C-15 thus appears, in each case, at slightly higher field than that of C-18, a fact that is made us of in assigning the signals of the sterically uniform compounds (**16**, **21**).

The invariable β-equatorial configuration of the 18-methyl group is confirmed by the fact that its chemical shift is unaffected by the introduction of the 2,7-conjugated diene-system; in diisophorone, this structural change leaves the chemical shift of the C-18 β equatorial methyl unaffected, but displaces upfield (by ca. 3 ppm) that of its C-17 α axial counterpart[14].

Extranuclear and aromatic signals. The signals of the extranuclear acetate and carboxy-groups in 5,11-bisnordiisophorones (C-19 – C-22 in **12**, **13**, **14**) and of aromatic substituents (in **20**, **21**) were assigned by reference to standard spectra[14—16d,e,f] and require no comment (see Table 2, Supplement).

Stereochemical Implications

(a) *3,5-Dimethylcyclohex-2-enone.* It is expedient, in the first place, to define the stereoisomeric forms of 3,5-dimethylcyclohex-2-enone (**3b**), being the ultimate source of all the compounds described, and the pattern

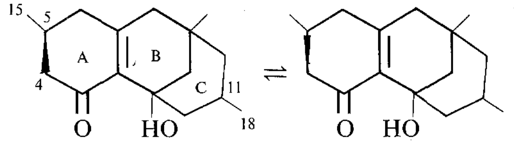


i 5βeq **iii** 5αeq

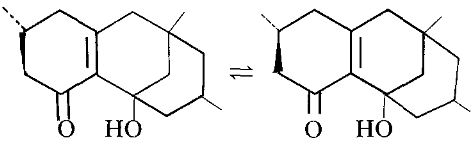
ii 5βax **iv** 5αax

reappearing in ring A of the 5,11-bisnordiisophorones (**4b**). Discounting boat conformations, the molecule may assume two "half-chair" structures[28, 29a], in which carbon atoms 1–4 are substantially coplanar, while the conformationally mobile carbon atoms 5 and 6 occupy positions "staggered" in opposite ways with respect to that plane (i.e. **i** and **ii**). Either ring pattern may bear the 5-substituent in the axial or equatorial conformation, resulting in the four stereoisomers **i**–**iv**. Structures **i** and **ii** are interconvertible into each other by "flipping" of the C-5–C-6 bond (as are also **iii** and **iv**), but in accord with established principles[29b] the 5-equatorial forms **i** and **iii** are likely to predominate. Rapid interconversion between the equatorial and axial conformers averages their ^{13}C-chemical shifts, the respective contribution of each being determined by its relative abundance[17]. Structures **i** and **iii** are not interconvertible, but are mirror-images of one another (as is the pair **ii**, **iv**). Because of this additional relationship, the stereoisomers **i** and **iii** (or equilibrium mixtures **i** $\rightleftharpoons$ **ii** and **iii** $\rightleftharpoons$ **iv**) produce ^{13}C-nmr signals having identical chemical shifts.

(b) *5,11-Bisnordiisophorones**. The existence of two stereoisomeric forms in individual 5,11-bisnordiisophorones is traced to differences in their rings A by the fact that rings B/C form a rigid bicyclo[3.3.1]nonane system, in which the 11-methyl group (i.e. C-18) assumes invariably the β-equatorial conformation (see structure **5**, $R = \mathrm{H}$). The alternative 11 α-axial conformation is disfavoured presumptively by the steric hindrance which the closeness of rings A/B would exert upon it, and is excluded fairly conclusively by the foregoing analysis of the ^{13}C-nmr signals (of carbon atoms C-1, 9, 5, 11, 15, and C-18). The results of previous ^{1}H-nmr measurements[9] have likewise indicated the equatorial conformation of the 11-methyl-group in the parent 5,11-bisnor-ketol (**4b**). The stereoisomers of 5,11-bisnordiisophorones thus differ in the nature of their ring A. Although the available evidence is as yet inadequate to select their structures with certainty, the following proposals may be made.



I 5βeq **II** 5βax



III 5αeq **IV** 5αax

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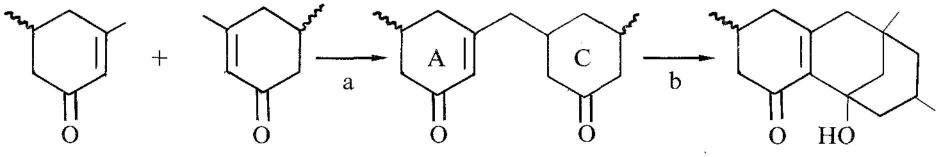
* The statements made in this section are verifiable by reference to molecular (e.g. *Dreiding*) models.

Four stereoisomers of 5,11-bisnordiisophorones (**I**–**IV**) corresponding to the 3,5-dimethylcyclohex-2-enones (**i**–**iv**) are obtained by incorporating the latter as ring A into the tricyclic structures. Conformational mobility about C-4–C-5 still permits interconversion between **I** and **II**, and between **III** and **IV** by "flipping". However, owing to the presence of the B/C ring system, structure **I** and **III** (or **II** and **IV**) are no longer mirror images, and thus give rise to non-identical ^{13}C-nmr spectra.

It therefore seems plausible that the most likely structures of the two stereoisomers that constitute individual 5,11-bisnordiisophorones are **I** and **III**, each of which bears the 5-methyl group in the favoured equatorial conformation. Though distinct from one another, these two stereoisomers differ only very insignificantly in the relative positions in space of the carbon atoms of their ring systems*. The appreciable differences in the ^{13}C-nmr chemical shifts of corresponding signal pairs are therefore ascribed to contributions to the structures **I** and **III** by their respective 5-axial conformers (**II** and **IV**), the steric differences between which are very apparent. Relative to the plane of rings A/B, the 5 β-ax-methyl group (of **II**) appears opposite ring C, while the 5 α-ax-methyl group (of **IV**) occupies the same side, and may therefore be correspondingly disfavoured. These considerations thus lead to the final postulate, that the two stereoisomers are represented by **I** (with a contribution by **II**), and by **III** (with a lesser contribution by **IV**), respectively. There appear to be grounds for the supposition, that the former is the more abundant conformer.



3b **3b** **4b**

The formation of the two stereoisomers is readily accountable in terms of the accepted[9] dimerisation mechanism (**3b** → **4b**) involving a successive *Michael* (a) and aldol condensation (b) between two molecules of the monomer. In the *Michael* intermediate, the configuration of ring A is that of the monomer **3b**, but its saturated ring C has a measure of conformational mobility, and assumes at the aldol condensation stage the chair conformation, with the 11-methyl group placed in the β-equatorial configuration. As a racemate[30], (±)-3,5-dimethylcyclohex-2-enone (**3b** = **i** + **iii**) will consequently yield both stereoisomeric forms of the tricyclic ketol **4b**.

Experimental

The ^{13}C-nmr spectra were determined at 302 K 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 solutions employed contained 100–150 mg of the compound in 0.75 ml of deuteriochloroform. The internal standard was tetramethylsilane.

The preparation of the 5,11-bisnordiisophorones used in the spectral measurements has previously been described as follows: **11**[2,8,9], **14**[31], **15**[8], **16**[7], **17**[32], **18**[2], **21**[33].

The acetates **12**, m. p. 97–98° and **13**, m. p. 102–103° were obtained from the parent ketol (**11**) by perchloric acid-catalysed acetylation at room temperature, and isolated after chromatographic separation[34]. The 1-methoxy-3-oximino-compound **19**, m. p. 224–225° was obtained by the standard procedure[2] from 1-methoxy-5,11-bisnordiisophor-2(7)-en-3-one[34]. The 3-toluene-*p*-sulphonylhydrazone (**20**), m. p. 212–213° was the product of the interaction of the parent ketol **11** and toluene-*p*-sulphonylhydrazide in boiling ethanol[34]. Full details concerning these compounds will be given in the appropriate context in due course.

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