Conformational Study of Dibenzocyclo-octadiene Systems related to the Schizandrin-type Lignans

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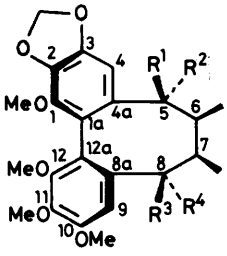
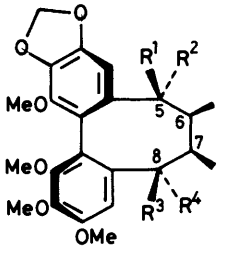
X-Ray and ^1H and ^{13}C n.m.r. data have been obtained for the dibenzocyclo-octadiene lignan kadsurin and several of its synthetic precursors, in which di-*ortho*-substitution of the aryl rings leads to high energy barriers for rotation around the biaryl bond. The crystallographic and spectral information shows that for compounds in this series the eight-membered ring adopts either a twist-boat (TB) or twist-boat-chair (TBC) conformation. The relative stability of ring conformers and/or biaryl rotamers is determined by three factors: (i) a preference for the TBC over the TB form, (ii) stabilization of the TB conformation by conjugation of the benzylic carbonyl groups with the aryl rings, and (iii) the presence of benzylic hydroxy (or acetoxy) substituents in *endo*/*exo* orientations.

THE schizandrin-type lignans, some of which show an interesting medicinal activity, are characterized by a dibenzocyclo-octadiene skeleton and one-carbon substitution at the C-6 and -7 positions. The stereochemistry of these natural compounds has been studied mainly by ^1H n.m.r. spectroscopy,[1,2] although in one case, involving a gomisin-D derivative, an *X*-ray analysis has been reported.[3]

During the recent synthesis of kadsurin,[4] a high stereoselectivity in reactions involving the eight-membered ring of some intermediates was observed. Moreover, it was found that some of these intermediates, which are isomeric by hindered biaryl rotation, have very different stabilities, and as a result one rotamer can be converted thermally into another;[4,5] these properties are undoubtedly related to well-defined conformations of the octacycle. We have tried to obtain a self-consistent conformational analysis of compounds (1)—(3) on which to base an explanation of these findings.

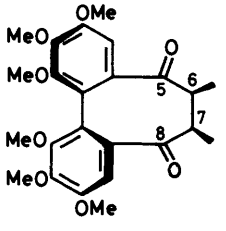


(1)



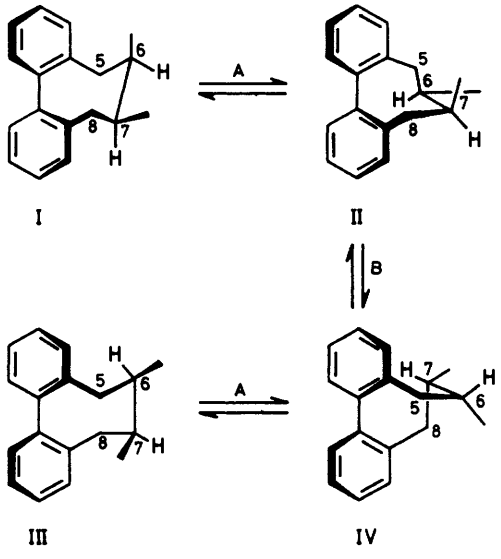
(2)

a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = OAc$, $R^2 = R^3 = R^4 = H$
c; $R^1,R^2 = R^3,R^4 = O$
d; $R^1,R^2 = O$, $R^3 = R^4 = H$
e; $R^1,R^2 = O$, $R^3 = OH$, $R^4 = H$
f; $R^3,R^4 = O$, $R^1 = OH$, $R^2 = H$



(3)

An analysis of the parent cyclo-octadiene ring has been performed by Anet and Yavari, utilizing dynamic ^1H n.m.r.[6] These authors show that the molecule exists in solution in two conformations, a twist-boat (TB) and a twist-boat-chair (TBC) with C_2 symmetry, in nearly equal populations. These forms interconvert *via* two processes: (A) TBC ⇌ TB and (B) TB ⇌ TB, with energy barriers of 38 and 30 kJ mol^{-1}, respectively.



SCHEME

The parallel picture for the dimethylated, dibenzo-fused cyclo-octadiene ring is shown in the Scheme. Process B, which involves biaryl rotation, has a high energy barrier (≥ 145 kJ mol^{-1} [7,8]) because of substitution of the aromatic rings *ortho* to the biaryl bond (the substituents are omitted in the Scheme for simplicity).

For all practical purposes, therefore, process B does not occur at room temperature and biphenyl rotamers are isolatable. The eight-membered ring conformation change (process A), on the other hand, is expected to have a barrier no higher than 60 kJ mol^{-1}, and should be

fast at room temperature. Indeed, in no case did a diphenyl rotamer show more than one set of signals in the n.m.r. spectrum. The conformational analysis of these substances can therefore be divided into two problems: (i) which form, the TBC or the TB, is the most stable for a particular biphenyl rotamer (process A); and (ii) which biphenyl rotamer (in whichever conformation it exists) is the more stable (process B). Data from *X*-ray diffraction and ^{1}H and ^{13}C n.m.r. spectra provide evidence for (i), while for (ii) the position of the equilibrium can be best ascertained for compounds with a benzylic carbonyl function (for which alumina has been shown to catalyze the biphenyl rotation [5,8]).

It should be pointed out *a priori* that previous evidence [1-3] and the present data indicate that the cyclooctadiene ring always exists in conformations similar to Anet and Yavari's [6] twist-boat-chair (I, III) or twist-boat (II, IV in Scheme) (*vide infra*), even in compounds with benzylic carbonyl groups. Moreover, an inspection of models indicates that the conjugation of such functions with the adjacent aromatic rings is only possible when they are located at C-5 in conformation II, or in the enantiomeric position, C-8, in conformation IV (see Scheme). A carbonyl bond at the other benzylic carbon in these TB forms, as well as in the TBC conformations I and III, would be nearly perpendicular to the plane of the aromatic ring making conjugation impossible. The existence of both conjugated and non-conjugated forms of the ketone function has been previously inferred from i.r. spectroscopic data (*vide infra*).[4]

RESULTS

X-Ray Crystallography.—Figures 1—4 show the results of crystallographic analyses of kadsurin (2b), the monoketone (1d), and the two biphenyl rotamers of a hydroxyketone (1f) and (2f). Full details of the *X*-ray study will be published elsewhere,[9] but several pertinent observations can be made. (*a*) The torsion angles about the carbon-carbon bonds of the octacycle are presented in Table 1. The absolute value of the angle about the biaryl bond C(12a)–C(1a), 66 ± 3°, is very similar in each of the four compounds examined [the angle has opposite signs for compounds (1) and (2), since they represent different biaryl rotamers]. This value is also close to those found in isosteganol (−70°) [10] and episteganol (68°),[11] in spite of the fact that these compounds lack the 1-methoxy-group, and in dibromogomisin-D (73°) [3] a derivative of a lignan with a six-atom bridge between C-1 and -8.

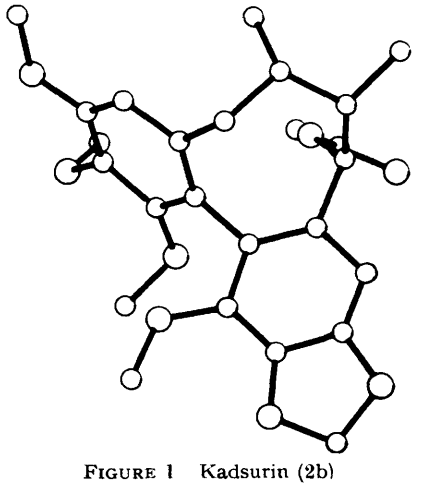


FIGURE 1 Kadsurin (2b)

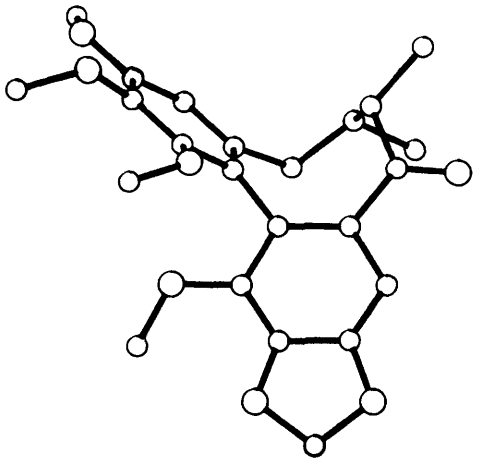


FIGURE 2 Monoketone (1d)

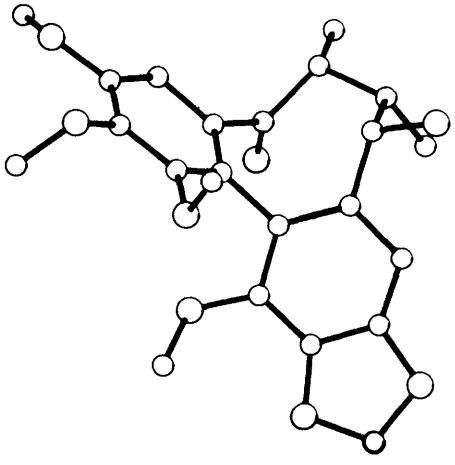


FIGURE 3 Hydroxyketone (1f)

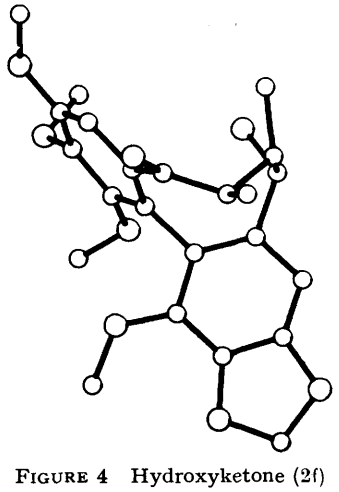


FIGURE 4 Hydroxyketone (2f)

(*b*) The torsional angles distinguish clearly between the TBC and TB forms. The former is characterized by the alternation of signs for the five bonds involving the non-aromatic carbons of the octacycle [*cf.* (2b) and (1f)]. In the latter, a pair of adjacent bonds [C(6)–C(5) and C(7)–C(6) in (2f) and C(7)–C(6) and C(8)–C(7) in (1d)] have torsion angles with signs opposite those of the other three bonds under consideration, a result of the boat-like shape of the ring.

TABLE 1

Torsion angles around the eight-membered ring (from *X*-ray diffraction data)

Bond	(2b)	(1f)	(2f)	(1d)
C(4a)–C(1a)	−3	−1	8	3
C(5)–C(4a)	87	−94	78	−13
C(6)–C(5)	−70	88	−24	−72
C(7)–C(6)	49	−58	−79	68
C(8)–C(7)	−89	95	55	44
C(8a)–C(8)	88	−98	31	−84
C(12a)–C(8a)	11	−3	−4	−15
C(1a)–C(12a)	−68	63	−68	64

(*c*) In the hydroxy-ketone (1f), the CO bond makes an angle of 96° with the plane of the adjacent aromatic ring, and conjugation between the two functions is absent. In its isomer (2f) and the ketone (1d), however, the corresponding angles are 29 and 11°, respectively, and conjugation is apparent from the spectral data (*vide infra*).

(*d*) Of the two possible TB forms (*cf.* Anet and Yavari [6]), compounds (2f) and (1d) adopt that in which the eight-membered ring equivalent of the stem-to-stern interaction involves a CH (C-6 in conformation II and C-7 in IV, see Scheme) rather than a CMe bond. This seems to be a general rule; an *endo*-methyl group would cause severe crowding with the corresponding benzene ring.

(*e*) The small differences in conformation between compounds (1d) and (2f) are the consequence of the presence of an *endo*-hydroxy-group in the latter. Inspection of the *X*-ray data shows that the small ring-twist that decreases the steric hindrance between the hydroxy-group and the opposite aryl ring increases the crowding between the hydrogen of the *endo*-methine [6-H in (1d) and 7-H in (2f)] and the other aryl moiety, and, in addition, makes the carbonyl function less coplanar with the adjacent π-system.

^{1}H *N.m.r. Spectra.*—A full analysis of the ^{1}H n.m.r. spectra of the diketone (2c), monoketones (1d) and (2d), and hydroxyketones (2c) and (2f) is presented in Table 2. We have already established in the previous section that compounds (2e and f) have TBC (Figure 3) and TB (Figure 4) conformations, respectively [the *X*-ray analysis of (1f) must apply to (2e) as well, since the two substances only differ in their aromatic-ring substitution]. The monoketone (1d) and diketone (2c) have been shown by i.r. spectroscopy (and ^{13}C n.m.r. *vide infra*) to possess one conjugated carbonyl group, and must therefore have a TB conformation; for (1d), this is in agreement with the *X*-ray data. As pointed out before, a benzylic carbonyl cannot conjugate with the aromatic ring in the TBC form.

An inspection of the vicinal hydrogen coupling constants (Table 2) corroborates this analysis. Indeed, the five compounds fall into two groups according to their $J_{5,6}$ values: 2.5—3.5 Hz for the three compounds established above as TB, and 5—6.5 Hz for the other two substances, indicating that the monoketone (2d) also has the TBC form. The similarities in *J* values within the two groups extend to the coupling constants between the C*H*Me and the neighbouring

TABLE 2

^{1}H N.m.r. data

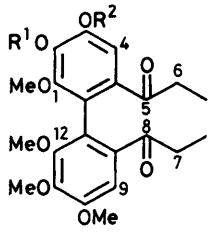
δ(H)	(2c)	(1d)	(2f)	(2d)	(2e)
4	6.41	7.45	6.38	6.35	6.34
5α			4.76		
6α	2.50	2.57	1.98	2.91	3.35
7α	3.34	1.54	2.95	2.31	2.28
8α		2.66		2.85	4.87
8β		2.23		2.58	
9	7.18	6.55	7.62	6.44	6.92
6-Me	0.92	1.01	0.92	1.05	1.12
7-Me	1.20	0.82	1.03	0.82	0.69
OCH_2O	6.06	6.05	6.03	6.02	6.01
	3.48	3.58	3.53	3.56	3.58
OMe	3.88	3.76	3.88	3.83	3.86
	3.89	3.91	3.94	3.89	3.91
	3.94	3.92	3.96	3.90	3.92
J_{HH} (Hz)					
5α-6α			6		
6α-Me	7	6.5	7.5	6.5	7
6α-7α	2.5	3.5	3.5	5	6.5
7α-Me	6.5	6.5	6.5	7	7
7α-8α		7		3.5	1
7α-8β		12		8.5	
8α-8β		13		14.5	

benzylic proton(s), if present. The range of the coupling-constant values gives an indication of the extent to which the conformations of the TB and TBC forms are defined which is independent of the substitution and/or the hybridization of the benzylic carbons.

While the extensive functionality in these molecules precludes the quantitative application of the Karplus equation, the experimental $J_{vic.}$ values are in qualitative agreement with the H–C–C–H dihedral angles obtained from the *X*-ray analysis. Thus, the larger coupling constant between 5-H and 6-H in the TBC relative to the TB conformation is paralleled by a smaller dihedral angle between these two protons in the former case [57 *vs.* 77° for (1f) (TBC) and (2f) (TB), respectively]. The coupling constants between the C*H*Me and the adjacent benzylic proton(s) can also be analyzed. Thus, in the TBC form, the *cis*-coupling is small [1 and 3.5 Hz for (2e) and (2d), respectively] and the *trans*-coupling is larger [8.5 Hz in (2d)]. From the *X*-ray structure of (1f), the dihedral angles with the C-8 substituents are, respectively, 85 and 34°. In the TB form, the *cis*-coupling [7 Hz in (1d), 6 Hz in (2f)] and the very large *trans*-coupling [12 Hz in (1d)] correspond to dihedral angles of 29 (2f) and 50° (1d), and 146 (2f) and 150° (1d), respectively.

The chemical shifts of the aromatic protons are also of diagnostic value. As noted previously,[2,4] a vicinal methylenedioxy-group shields the aromatic proton slightly more than a vicinal methoxy-group. Also, a neighbouring conjugated ketone causes a large deshielding, while a non-conjugated ketone leads to a small shielding. In addition to these observations, it may be pointed out that going from a TBC to a TB form causes up to 0.1 p.p.m. deshielding [compare δ 6.34 and 6.35 in (2d) and (2e) (TBC) to δ 6.41 in (2c) (TB), all for 4-H next to a non-conjugated ketone; or δ 6.44 (TBC) in (2d) to δ 6.55 in (1d) (TB), for 9-H next to a methylene at C-8]. Also, an *endo*-hydroxy-group has a small shielding effect on the aromatic proton [*cf.* 4-H in (2f) (δ 6.38, adjacent OH) *vs.* (2c) (δ 6.41, adjacent non-conjugated ketone), both TB forms], but an *exo*-hydroxy-group has a larger deshielding influence [*cf.* 8-H in (2e) (δ 6.92, adjacent OH) *vs.* (2d) (δ 6.44, adjacent methylene), both TBC forms], as might be expected.

^{13}C *N.m.r. Spectra.*—In order to be able to analyse the ^{13}C n.m.r. spectra of kadsurin and its precursors, it is useful to interpret the shift data for acyclic diketones such as (4a) and (4b). The assignment of the carbon signals of these and the other compounds presented in Table 3 was aided by



(4)

a; $R^1 = R^2 = Me$
b; $R^1, R^2 = CH_2$

recording single-frequency off-resonance decoupled (sford) spectra under different conditions which gave long-range coupling information (*e.g.* identifying *C*OMe peaks or signals due to carbons *meta* to the aromatic CH), as well as a correlation between carbon and proton signals.[12] As might be expected, the carbonyl functions in the diketones (4) are to a large extent conjugated with the aryl rings; compare, for instance, their absorption at *ca.* 203 p.p.m. with acetophenone (δ 195.6) and cyclohexyl methyl ketone (δ 210.2),[13] considering that additional substitution α to the carbonyl (Me→Et) has a deshielding effect of *ca.* 2.5 p.p.m.[13] Examination of the carbonyl band frequency in the i.r. spectrum leads to the same conclusion: *ca.* 1 677 cm^{-1} for compounds (4), as compared with 1 667 ± 1 and 1 703 ± 1 cm^{-1} for conjugated and non-conjugated carbonyls, respectively, in cyclic compounds (1)—(3).[4] Models (4) also lead to an assessment of the differences in chemical shifts of an aryl ring with dimethoxy as opposed to methylenedioxy as substituent. These differences are similar in direction, but increased in magnitude, to those observed in simple systems.[14]

The ^{13}C absorptions of the carbonyls in cyclic compounds (1)—(3) are clearly divided into two ranges, 201.1 ± 0.8 and 209.4 ± 0.2 p.p.m., which can be attributed to conjugated and non-conjugated carbonyl groups, respectively, in full agreement with the i.r. data (*vide supra* and ref. 4); as we have pointed out before, a conjugated carbonyl implies a TB conformation.

The chemical shifts of C-4 and -9 are strongly dependent on the substitution of the adjacent benzyl carbon. The signals under consideration appear at *ca.* 7 p.p.m. upfield when the function is a non-conjugated carbonyl, compared with its conjugated counterpart (101.0 *vs.* 108.3 ± 0.1 p.p.m. for a CH in a trimethoxy-substituted ring and 97.1 ± 0.1 *vs.* 104.1 ± 0.1 p.p.m. for a CH in a methoxy-methylenedioxy-substituted ring). It appears, therefore, that a non-conjugated ketone imparts a strong γ-effect on the aryl CH, while, with a nearly coplanar carbonyl group, this effect is almost completely balanced by the deshielding caused by electron-withdrawal from the ring. Furthermore, the γ-effect from a benzylic CHOR is small when the oxy-function is *endo* [*cf.* kadsurin (2b) and hydroxy-ketones (1e) and (2f)], but is slightly larger, at 3.5 p.p.m., for an *exo* conformation [compare C-9 in the hydroxy-ketone (2e) and in kadsurin (2b)].

The chemical shifts of the sp^3-hybridized carbons in the diketones (1c), (2c), and (3) are virtually identical; as expected, the different aryl substituents have no effect on the conformation of the octacycle. It is noteworthy that the methyl group near to the non-conjugated ketone is more shielded than the other one; this cannot result from a stronger γ-effect with the carbonyl oxygen, since the CH–Me and the C=O (conjugated) bonds are almost eclipsed [*X*-ray analysis gives dihedral angles of 3 (2f) and 17° (1d)]. The shielding is probably due to a *gauche* relationship with the *carbon* of the non-adjacent carbonyl; examination of a model shows that an analogous interaction does not exist in the other, *exo*-oriented methyl group. In the hydroxy-ketones (1e) and (2f), which also exist in the TB form, the methyl group adjacent to the conjugated carbonyl is invari-

TABLE 3

^{13}C N.m.r. data

C	(4a)	(4b)	(1c)	(2c)	(3)	(2f)	(1e)	(2e)	(2b) [a]
1a	122.9	123.2	122.6	117.8	122.3	119.5	125.8	115.7	120.6
1	151.3	141.3	141.2	142.1	151.7	142.2	140.9	140.9	141.4
2	144.8	139.0	141.0	137.0	146.5	136.2	141.3	136.7	136.0
3	152.6	148.8	149.8	150.1	153.4	149.5	149.2	149.6	148.4
4	107.2	102.9	104.2	97.1	108.2	101.5	104.0	97.2	102.5
4a	135.5	134.1	131.7	135.6	131.7	135.7	131.0	134.3	134.9
5	203.6	202.6	201.7	209.2	201.9	79.5	200.5	209.4	82.3
6	34.0	34.2	47.2	52.5	47.1	48.1	44.2	48.8	41.9
6-Me	8.4	8.4	15.5	8.4	15.5	10.3	16.0	14.1	19.6
7	34.0	34.0	52.4	47.2	52.4	44.0	47.8	43.2	34.9
7-Me	8.4	8.4	8.5	15.3	8.6	15.8	10.2	8.0	14.8
8	203.6	203.5	209.6	201.9	209.6	200.3	79.4	73.1	38.8
8a	135.5	135.4	137.0	131.8	137.0	130.9	137.3	134.3	133.3
9	107.2	107.3	101.0	108.4	101.0	108.2	105.7	106.9	110.4
10	152.6	152.5	154.6	153.4	154.5	152.8	153.6	152.7	151.6
11	144.6	144.7	142.4	146.3	142.3	146.4	141.3	141.3	139.7
12	151.3	151.4	152.8	151.7	152.5	151.7	152.9	151.7	151.0
12a	122.9	123.2	117.9	122.1	118.1	125.1	120.3	120.5	123.4
OCH_2O		102.0	102.2	101.7		101.5	102.0	101.5	101.2
1-OMe	60.8	59.5	59.9	59.8	61.0	59.8	59.8	59.9	59.7
2-OMe	60.4				60.5				
3-OMe	56.0				56.0				
10-OMe	56.0	55.9	56.1	55.9	56.1	55.9	56.0	55.9	56.0
11-OMe	60.4	60.5	61.3	60.5	61.2	60.5	61.0	61.1	60.3
12-OMe	60.8	60.8	61.1	61.0	61.0	61.0	61.0	60.8	60.7

[a] δ(CH_3COO) 20.7 and 170.1 p.p.m.

ant relative to the diketones, while the other methyl group is deshielded, indicating a weaker γ-effect from the hydroxy-group than from the ketone oxygen.

The interpretation of the carbon shifts of kadsurin (2b) and the hydroxy-ketone (2e), which adopt TBC conformations, is facilitated by the recently published data on the ' unsubstituted ' system (1a),[15, *] which has been shown to exist in the TBC form.[13] The chemical shifts of the CHMe (axial) and CHMe (equatorial) moieties in compound (1a) are 33.7 and 12.7 and 40.7 and 21.8 p.p.m. respectively.[15] The introduction of an *endo*-acetoxy-group adjacent to the equatorial methyl group [kadsurin (2b)] does not shield C-7 (which has an equatorial, *exo*-hydrogen) and affects only slightly the 6-methyl signal (the dihedral angle is 90° in the crystal). The acetoxy-group and the 7-methyl, however, have a ' *syn*-diaxial ' type of relationship, and the signal of the latter is deshielded by 2.1 p.p.m. (a δ effect [16]).

Finally, in the hydroxy-ketone (2e), an *exo*-hydroxy-group shields the adjacent, axial methyl group by 4.7 p.p.m., even though the dihedral angle in the crystal is 80°, indicating that the conformations in the solid and in solution may be slightly different. (This shielding is not caused by the ketone, since Ikeya *et al.* report a virtually identical shift, 8.0 p.p.m., for the analogous compound without a keto-group.[15]) As expected, the carbonyl strongly shields the adjacent, equatorial methyl group (14.1 *vs.* 21.8 p.p.m. in the deoxy-compound [15]).

DISCUSSION

In the unsubstituted 1,3-cyclo-octadiene the TBC and the TB conformations were found to have similar energies.[6] The parent *cis*-6,7-dimethyldibenzocyclo-octadiene (1a), however, adopts preferentially a TBC conformation, as determined by the use of ^{1}H–^{1}H nuclear Overhauser effect (n.O.e.).[2] It seems unlikely that the decreased stability of the TB form in the lignan derives from interaction between the 6- and 7-methyl groups; the dihedral angle, as determined by *X*-ray analysis, is in effect smaller in the TBC than in the TB conformation [45 and 54° for (2b) and (1f), respectively, both TBC, and 75 and 68° for (2f) and (1d), respectively, both TB]. The difference in stability must, therefore, result from increased stem-to-stern interactions between the eight-membered- and aromatic-rings, *e.g.* the interactions between 6-H and the bottom aryl ring and between the 7-methyl and the top aryl ring, respectively, in structure II (Scheme). The conformation of kadsurin (2b) is also TBC. This compound has an *endo*-acetoxy-group at C-5 (structure III, Scheme). Ring-flip to structure IV would leave the oxy-function *endo*-oriented and little, if any, strain would be relieved. The preference for a TBC form, therefore, still prevails.

In addition to the deoxy-compound (1a), another ' symmetrical ' case (*i.e.* one in which biaryl rotation would lead to an enantiomer except for the different aryl substitution, and therefore the two biaryl rotamers have virtually the same energy) is that of the diketones (1c), (2c), and (3); here the preferred conformer is a TB. The most probable reason is that the energy gained by the conjugation of one of the carbonyl groups with the ring (and this is only possible in the TB form) is more than enough to compensate for the inherent advantages of the TBC conformation (*vide supra*). This principle explains why the monoketone (1d) exists as a TB with a conjugated carbonyl [structure II in the Scheme with C(5)=O]. Its biaryl rotamer (2d), however, has a TBC conformation (III in the Scheme); a ring-flip to structure IV would not lead to conjugation as only a C(8)=O in this conformer would be coplanar with the adjacent aryl ring, and therefore TBC prevails over TB. Alumina-catalysed equilibration of compounds (1d) and (2d) shows that the former is more stable than the latter by 2.9 kJ mol^{-1} (an equilibrium constant of **3.2**),[3,4] again demonstrating that the energy gain by conjugation overrides the disadvantages of the TB form.

The same explanations apply to the 5- and 8-hydroxy-ketones. Isomers (1e) and (2f) are able to conjugate and do so, existing in TB forms II and IV (see Scheme), while their biaryl rotamers (2e) and (1f) cannot achieve conjugation and therefore prefer the TBC conformations (III and I, respectively). The hydroxy-group does not seem to significantly affect the A equilibria; indeed, it would be *endo*-oriented for compounds (1e) and (2f), and *exo*-oriented for (2e) and (1f), independently of the conformation of the octacycle (TB or TBC). Equilibrium B, however, is radically changed. Alumina-catalysis leads to essentially complete (1e) ⟶ (2e) and (2f) ⟶ (1f) conversions,[3,4] indicating that the non-conjugated, TBC form is more stable by at least 7 kJ mol^{-1} (<5% of the unstable isomer). It is conceivable that the additional strains introduced by the *endo*- vs. *exo*-hydroxy-group account for the >10 kJ mol^{-1} differences between the monoketone and the hydroxy-ketone systems, and lead to the surprising stability of the non-conjugated rotamers.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded on a Bruker WH 270 instrument, in the Fourier transform mode. Spectral widths of 2 400 Hz and the use of 16 K data points resulted in acquisition times (and pulse delays) of 3.413 s and a digital resolution of ±0.001 p.p.m. (±0.3 Hz); the pulse width used corresponds to a flip angle of 50°. For ^{13}C n.m.r. spectra, the spectrometer used was a Bruker WH 90 instrument (at 22.63 MHz), and the corresponding parameters were 4 200 Hz, 8 K data points, 0.974 s, ±0.05 p.p.m. and 20—40°. All the data in Tables 2 and 3 correspond to measurements for $CDCl_3$ solutions, and chemical shifts are in p.p.m. relative to internal tetramethylsilane; coupling constants are given in Hz. The normal probe temperature was 29 ± 2 °C.

Full characterizations of compounds (1)—(4) mentioned in the text are reported in ref. 4, unless otherwise specified.

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* This paper, which reports the carbon spectra of 13 natural dibenzocyclo-octadiene lignans, appeared when the analysis of our ^{13}C n.m.r. data had been completed. While there is no overlap between the compounds in ref. 15 and those presented in Table 3, the two sets of data are fully compatible.

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