Tetrahedron, 1966, Vol. 22, pp. 2275 to 2280. Pergamon Press Ltd. Printed in Northern Ireland

INVESTIGATIONS INTO THE CONFORMATION OF NON-AROMATIC RING COMPOUNDS—XI*

COUPLING CONSTANTS IN SOME *CIS*-2,3-DISUBSTITUTED-1,4-DIOXANS; A REASSIGNMENT OF THE STRUCTURE OF *TRANS*-NAPHTHODIOXAN

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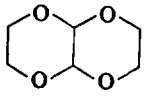
(*Received* 18 *December* 1965)

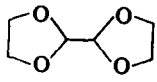
Abstract—Vicinal coupling constants (AA'BB' part) in *cis*-2,3-dichloro-1,4-dioxan (I, m.p. 54°), in *cis*-2,3-diphenyl-1,4-dioxan (II, m.p. 132°) and in so-called *trans*-1,4,5,8-naphtho-dioxan (III, m.p. 136°) are reported. The coupling constants of III provide unambiguous evidence that the structure of III is actually *cis*. The couplings of I, II and III clarify previous conflicting views and show that these compounds are rapidly inverting (ea) chair forms of closely similar geometry. The couplings in *cis*-2,5-diphenyl-1,4-dioxan (VII, m.p. 121°) support the previously assigned structure.

IN THE course of our work on the conformation and structure of 1,4-dioxans we analysed the NMR spectra of *cis*-2,3-dichlorodioxan (I, m.p. 54°), *cis*-2,3-diphenyl-dioxan (II, m.p. 132°) and of the so-called *trans*-1,4,5,8-naphthodioxan (III, m.p. 136°, hexahydro-1,4-dioxino-[2,3-b]-1,4-dioxin). The analysis of III, being of some interest since definite proof is presented here that the compound actually has the *cis*-structure, is selected as an example.

Compound III and a lower melting isomer IV were isolated by Boeseken *et al.*[1] by fractional crystallization of the reaction mixture from *trans*-2,3-dichlorodioxan and ethylene glycol. On the basis of dipole moment measurements the *trans*-structure was assigned[1] to III ($\mu = 0{\cdot}72$ D) and the *cis*-structure, pictured as two boat forms, to IV ($\mu = 1{\cdot}9$ D). Compound IV was later studied by X-ray analysis[2] and found to be 2,2'-bis-1,3-dioxolane. Interestingly, a similar mixture of III and IV is obtained from *cis*-2,3-dichlorodioxan and ethylene glycol.[3]



III



IV

The structure of III as the *trans*-fused chair form has generally been accepted up to the present, notwithstanding the fact that neither the low value of its dipole

* Part X, C. Altona, C. Knobler and C. Romers, *Rec. Trav. Chim.* **82**, 1089 (1963); part XII, A. Mossel, C. Romers and E. Havinga, *Tetrahedron Letters* 1247 (1963).

[1] J. Boeseken, F.Ph.A. Tellegen and P. Cohen Henriquez, *Rec. Trav. Chim.* **50**, 909 (1931); **54**, 733 (1935).

[2] S. Furberg and O. Hassel, *Acta Chem. Scand.* **4**, 1584 (1950); O. Hassel and C. Romming, *Ibid.* **10**, 136 (1956).

[3] R. K. Summerbell and H. E. Lunk, *J. Amer. Chem. Soc.* **79**, 4802 (1957).

moment, nor the single Fourier projection of its mercuric chloride complex,[2] offer conclusive evidence of its structure. Its NMR spectrum has recently been reported by two groups of workers[4,5] but an analysis in terms of coupling constants was still lacking. The spectrum[4] shows a single unsplit peak for the bridge protons at carbons 9 and 10 and a typical AA'BB' (or A_2B_2) multiplet for the methylene protons at carbons 2,3,5 and 6 (Fig. 1).

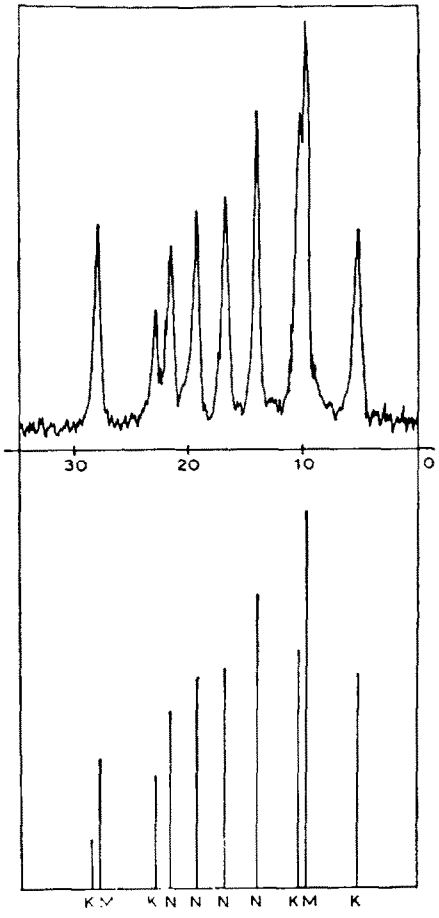
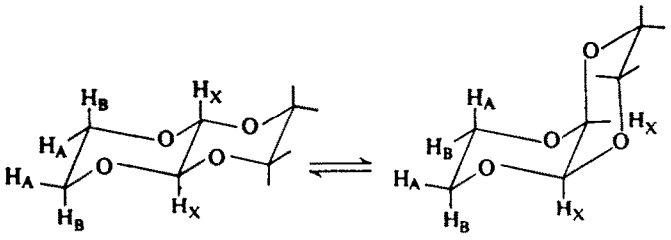


FIG. 1. Low-field half of the AA'BB' multiplet of compound III in benzene solution at 60 Mc. Frequencies are in c/s from the multiplet centre (ν_{AB} = 207 c/s from TMS). Line assignments (K, M and N, see text) are shown in the calculated spectrum.

At first sight, the appearance of a multiplet would seem to be due to the non-equivalence of equatorial protons (H_A and H_A') and axial protons (H_B and H_B'', Fig. 2A) as a consequence of both rings being *trans*-fused and therefore rigid chairs. The axial bridgehead protons are then magnetically equivalent by virtue of *symmetry* and show a single signal. The spectrum has been interpreted along these lines.[4,5]

[4] E. Caspi, Th. A. Wittstruck and D. M. Piatak, *J. Org. Chem.* **27**, 3183 (1962).
[5] C-Y. Chen and R. J. W. LeFèvre, *J. Chem. Soc.* 558 (1965).

However, a mobile molecule consisting of two *cis*-fused chairs in dynamic equilibrium with its inverted form (Fig. 2B) would give rise to exactly the same type of spectrum, but with different couplings and different internal chemical shift between the H_A and H_B ($\Delta\nu_{AB}$).



trans (A) *cis* (B)

FIG. 2. Two possible structures of 1,4,5,8-naphtodioxans.

The non-equivalence of H_A and H_B should arise from one species being *cis*, the other *trans*, with respect to the substituent C—O bonds of the second ring, H_A and H_B being differently shielded. Of course, in the case (B) the system is assumed to invert at a rate sufficiently rapid for the chemical shifts between H_A and H_A' (H_B and H_B') to be averaged, each proton alternating between axial and equatorial positions. The same reasoning applies to the bridgehead protons, which are also equivalent through rapid interconversion.

Analysis of the AA'BB' spectrum yielded the (absolute) values of five parameters:[6] N, L, K, M and $\Delta\nu_{AB}$. These parameters can be translated into coupling constants pertaining to the two cases: *trans* (A) and *cis* (B) (Table 1).

TABLE 1. RELATION OF AA'BB' PARAMETERS TO COUPLING CONSTANTS AND THE MEASURED DATA (c/s) OF COMPOUND III IN THREE SOLVENTS. J_{gem} IS THE GEMINAL COUPLING CONSTANT, J_{aa}, J_{ee} AND J_{ea} ARE THE USUAL *vic.* COUPLINGS

		trans (case A)	*cis* (case B)	CCl_4	$CDCl_3$	C_6H_6
N	$\lvert J_{AB} + J_{AB}' \rvert$	$J_{gem} + J_{ae}$	$J_{gem} + \frac{1}{2}(J_{aa} + J_{ee})$	5·17	5·47	5·45
L	$\lvert J_{AB} - J_{AB}' \rvert$	$J_{gem} - J_{ae}$	$J_{gem} - \frac{1}{2}(J_{aa} + J_{ee})$	17·96	18·03	18·11
K	$\lvert J_B + J_A \rvert$	$J_{aa} + J_{ee}$	$J_{ae} + J_{ea}$	6·0	6·0	5·8
M	$\lvert J_B - J_A \rvert$	$J_{aa} - J_{ee}$	$J_{ae} - J_{ea}$	0	0	0
$\Delta\nu_{AB}$		$\nu_a - \nu_e$	$\nu_{trans} - \nu_{cis}$	23·4	22·3	32·7

The application of three solvents greatly facilitated the interpretation of the spectrum because a change in $\Delta\nu_{AB}$ alters line positions and intensities whereas several line difference relations are invariant. In Fig. 1 lines 1–4 (N quartet) are designated N, 5–8 as K and 9–12 as M.[6] The values of K cannot be found directly from the measured spectrum but were approximated by calculation of a series of exact AA'BB' patterns with the aid of the Freqint IV computer program.* The line positions in the "best" calculated spectra correspond with the measured positions within an accuracy of about 0·1 c/s.

The AA'BB' spectra of *cis*-2,3-dichlorodioxan (I) and of *cis*-2,3-diphenyldioxan (II) were analysed in the same way as described for III and yielded similar results (Table 2). The line assignments and approximate coupling constants in the spectrum

* We are indebted to Mr. R. Kaptein of this laboratory for the ALGOL version of this program and for his help in carrying out the calculations on the X1 computer.

[6] J. A. Pople, W. G. Schneider and H. J. Bernstein, *High Resolution Nuclear Magnetic Resonance*. McGraw-Hill, New York, N.Y. (1959).

of *cis*-2,5-diphenyldioxan (VII) were initially based on the ABX approximation; the true coupling constants were determined with the aid of computer calculations of exact ABC spectra.[7]

DISCUSSION

Inspection of the measured parameters in Table 1 immediately shows that the previously accepted *trans*-structure of compound III must be rejected. In particular, the values of K and M do not agree with those established for J_{aa} (10–12 c/s) and J_{ee} (0–2 c/s) in dioxans with rigid conformations.[8] On the other hand, the data are in excellent agreement with the *cis*-structure B (two-chair model). From K and M we find $J_{ae} = J_{ea} = 2{\cdot}95$ c/s, close to J_{ae} in dioxan[9,10] (2·8 c/s); from N and L it follows that J_{gem} is negative (−11·7 c/s), as expected,[11] and that $(J_{aa} + J_{ee}) = 12{\cdot}7$ c/s, again in accordance with established values.

In Table 2 the coupling constants of I, II, III and VII are compared with those found for several other inverting chairforms of similar type, dioxan (V), morpholine (VIII), thioxan (IX) and dithian (X). The values of $(J_{aa} + J_{ee})$ and J_{ae} follow from the measurements and are given in Table 2. In current literature[9,10] J_{ee} is set equal to J_{ae}, thus yielding a value for J_{aa}. This practice is open to criticism, however, since in conformationally rigid dioxans and dithians J_{ee} is usually considerably different from J_{ae}.[8]

The finding that III is actually *cis*-naphthodioxan and that the *trans*-compound apparently never has been isolated from the reaction mixture is in accordance with recent views on the relative stability of *gauche* and *anti* C—O—C—O systems.[12] The *cis*-structure contains two *gauche* C—O—C—O— groups and should be rather more stable than the *trans*-structure which contains none.

The structure and conformation of compounds I and II have recently been the subject of some dispute. The NMR spectra were alternately interpreted in favor of *cis*-substituted rigid boat conformers[4] and as evidence for I and II being *trans*-diequatorial forms.[5] Neither interpretation fits the measured couplings and other

[7] It is of interest to note that an ABX treatment in this case yields approximately correct values for $J_{AX} + J_{BX}$ and J_{AB}, but would lead to a serious error in $J_{AX} - J_{BX}$.

This point was investigated by calculating a series of exact ABC spectra (varying the chemical shift of H_X and/or $\Delta\nu_{AB}$), which were subsequently analysed by means of the usual ABX line relationships.[6] Several parameters (e.g. $J_{AX} + J_{BX}$, J_{AB} etc.) that occur twice of four times in the spectrum were internally consistent within 0·02 c/s; nevertheless, the value of $J_{AX} - J_{BX}$ was erroneous by ±0·5 c/s or more (the sign depending on the relative magnitudes of $\Delta\nu_{AB}$ and J_{AB}).

An illustrative example is the following (all values in c/s);

	δ_{AB}	δ_X	$\Delta\nu_{AB}$	J_{AB}	$J_{AX} + J_{BX}$	$J_{AX} - J_{BX}$
Input	240·00	298·00	8·00	−12·00	9·00	2·00
From output, calc. as ABX	239·91	298·19	7·96	−11·98	8·98	1·52
From output, calc. as AMX	239·91	298·19	14·39	−11·98	8·98	0·84

Even when δ_X was moved up to 500 c/s, the calculated $J_{AX} - J_{BX}$ still deviated by −0·10 c/s from the input value.

[8] C. Altona, H. T. Kalff and E. Havinga, to be published.

[9] W. B. Smith and B. A. Shoulders, *J. Phys. Chem.* **69**, 579 (1965).

[10] A. D. Cohen, N. Sheppard and J. J. Turner, *Proc. Chem. Soc.* 118 (1958).

[11] R. Freeman, K. A. McLauchlan, J. I. Musher and K. G. R. Pachler, *Mol. Phys.* **5**, 321 (1962).

[12] C. Altona and M. Sundaralingam, to be published.

facts. In the first place, accurate X-ray analysis[13] has shown that I exists as a rigid (ea) chair form in the crystal. The NMR spectrum of I in solution shows an AA'BB' pattern closely similar to that of III (Table 2). In solution, at room temperature and down to −118° (the coalescence temp), the molecule interconverts rapidly between ea and ae chair forms;[13,14] the height of the energy barrier ($\Delta G^{\ddagger}$) was estimated to be about 7·5 kcals/mole.[14] Interestingly, the $\Delta\nu_{AB}$ values of I and III are practically equal in all solvents used, hence the almost identical patterns.[4] The $\Delta\nu_{AB}$ of II is

TABLE 2. COUPLING CONSTANTS (c/s) AND $\Delta\nu_{AB}$ (c/s) FOR A SERIES OF INVERTING SATURATED HETEROCYCLIC RING COMPOUNDS. THE SOLVENTS ARE : *a* = CARBON TETRACHLORIDE, *b* = DEUTERIOCHLOROFORM, *c* = BENZENE

	Compound	Solvent	$(J_{aa} + J_{ee})$	J_{ea}	J_{gem}	$\Delta\nu_{AB}$	Ref.
I	*cis*-2,3-Dichloro-1,4-dioxan	*a*	12·6[b]	3·1	−12·1[b]	23·3 c/s	
		b	12·6[b]	3·2	−12·1[b]	21·6	
		c	12·7[a]	3·2	−12·3[1]	32·6	
		av	12·6[g]	3·1[b]	−12·2[c]		
II	*cis*-2,3-Diphenyl-1,4-dioxan	*b*	12·7[7]	3·1	−11·9[c]	13·8	
		c	12·8[c]	3·0	−11·9[c]	17·1	
		av	12·7[8]	3·0[b]	−11·9[c]		
III	*cis*-Naphthodioxan	*a*	12·8[c]	3·0	−11·5[c]	23·4	
		b	12·5[c]	3·0	−11·7[b]	22·3	
		c	12·6[c]	2·9	−11·7[c]	32·7	
		av	12·6[7]	2·9[b]	−11·7[c]		
V	1,4-Dioxan[d]	*c*	13·0	2,8			9
		c	12·1	2·7[a]			10
VI	*cis*-2,5-Dimethyl-1,4-dioxan[f]		11·4	2·6	−11·8		*e*
VII	*cis*-2,5-Diphenyl-1,4-dioxan[f]	*b*	11·7[a]	3·0[c]	−11·9[b]	8·2[g]	
		c	11·0[7]	3·1[a]	−12·1	12·4[g]	
		av	11·4[c]	3·0[g]	−12·0[g]		
VIII	Morpholine	*c*	13·1	3·0[4]			9
IX	1,4-Thioxan	*c*	14·7	2·6[5]			9
X	1,4-Dithian	CS_2	16·4	2·1			8

[d] From ^{13}C—H satellite spectrum.

[e] M. J. Evans and E. B. Lord, communicated at the 8th Eur. Congress on Mol. spectroscopy, Aug. 14–20, 1965, Copenhagen, abstr. 301.

[f] J_{ea} for these compounds is in fact the average coupling constant $\frac{1}{2}(J_{ea} + J_{ae})$.

[g] The signal due to the proton *trans* to the phenyl group occurs at the highest field.

[13] C. Altona and C. Romers, *Acta Cryst.* **16**, 1225 (1963).

[14] C. Altona, Thesis, Leiden (1964).

considerably smaller resulting in a drastic change in the general shape of the AA'BB'-part. Secondly, the existence of boat or twisted boat forms in measurable amounts can be excluded for a number of reasons. The IR spectrum of I in solution is practically identical with that of the solid.[14] The couplings ($J_{aa} + J_{ee}$) and J_{ae} do not differ from those in dioxan itself (Table 2) and the latter compound is known to exist exclusively in a chair form. Furthermore, the J values are independent of the solvent used. The dipole moments of I, II and III[5,14] correspond well to the moments expected on the basis of the chair model. Of all the dioxan derivatives examined thus far, only the severely strained *trans-syn-trans*-(aa, aa)-2,3,5,6-tetrachloro compound (m.p. 101°) has been found to occur in solution as an equilibrium mixture that contains the (aa, aa) conformation together with a small amount of flexible forms.[14] The empirical relation between coupling constants and ring geometry in dioxans and dithians will be treated elsewhere.[8] We wish to remark here that the striking similarity of the coupling constants ($J_{aa} + J_{ee}$) and J_{ea} of compounds I, II, III, V and VIII points to a similar conformation angle about the O—CH_2—CH_2—O (O—CH_2—CH_2—N) moiety.

The lower value of ($J_{aa} + J_{ee}$) in VI and VII might be due to a slightly different geometry or to substituent effects. The "deviating" J's of (IX) and (X) are ascribed[8] partly to the larger puckering in these rings and partly to the lower electronegativity of sulphur compared to oxygen.

EXPERIMENTAL

Compounds I–III and VII were prepared and purified as described (cf. Refs 3, 4, 15). The NMR spectra were recorded on a Varian A-60 spectrometer at 60 Mc. The samples were 20–30% (wt. vol.) solutions except in a few cases where a saturated solution of lower concentration had to be used. The coupling constants are probably accurate to ±0·1–0·2 c/s. Some chemical shifts in $CDCl_3$ (ppm from tetramethyl silane) are listed as follows (δH_X and centre of multiplet δH_{AB}): I (5·71, 3·99); II (5·12, 3·85); III (4·65, 3·83); VII (4·74, 3·98). The IR spectra were in accord with those published previously.[3,4]

Note added in proof—After the present work was submitted, two publications appeared,[16,17] in which the AA'BB' spectrum of *cis*-2,3-dichlorodioxan (I) was analysed and similarly interpreted in favour of an inverting chair-chair (ea ⇌ ae) equilibrium. The three sets of coupling constants of (I) are in excellent agreement (within 0·1 c/s).

Acknowledgement—The authors thank Dr. H. T. Kalff for many fruitful discussions and Mr. P. Kranenburg for running the spectra. Compound VII was prepared by Mr. J. Vreeburg.

[15] L. A. Bryan, W. M. Smedley and R. K. Summerbell, *J. Amer. Chem. Soc.* **72**, 2206 (1950); M. J. Kland-English, R. K. Summerbell and I. M. Klotz, *Ibid*, **75**, 3709 (1953).
[16] R. R. Frazer and C. Reyes-Zamora, *Canad. J. Chem.* **43**, 3445 (1965).
[17] D. Jung, *Chem. Ber.* **99**, 566 (1966).