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STEREOCHEMICAL STUDIES—XVIII

CONFORMATIONAL STUDY OF HETEROANALOGUES OF BICYCLO[3.3.1]NONANE

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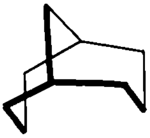
Abstract—A number of heteroanalogues of bicyclo[3.3.1]nonane containing heteroatoms in 3-, 3,7- and 3,7,9-positions has been synthesized. ^{1}H NMR measurement has shown that the compounds of the types **4**, **5** and **6** (Y = oxygen) are double-chairs with the "wings" of the molecule flattened. However, a new conformational effect has been found for the sulfur containing compounds of type **5** and **6** (X,Y = sulfur) which show substantially increased tendency to adopt boat–chair conformations.

Bicyclo[3.3.1]nonane itself may exist in any of the following three conformations: double-(or twin) chair **1**, chair–boat **2**, and double–boat **3**.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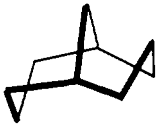
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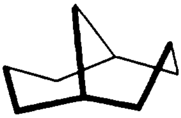
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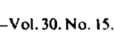
All these are subject to some destabilising interaction of non-bonded atoms. Various calculations[1] and experiments[2,3] show that the double–chair conformation **1** is the most stable. The difference between the energies of **1** and **2** was estimated[1,4,5] to be 2·7 to 3·7 kcal/mole. This is significantly lower than the ΔH value, 5 to 6 kcal/mole, associated with the chair–boat conversion in cyclohexane. The difference results from a strong destabilization of **1** due to a severe repulsion of 3- and 7-endo-hydrogens. The repulsion flattens the "wings" of the molecule and, consequently, distorts the valence angles substantially.[3]

Heteroanalogues of the types **4**, **5** or **6** have diminished destabilisation of the double–chair conformation particularly in compounds of the type **4**. Indeed, the compounds **4** (X = O)[6] and **4** (X = NR)[7,8] were shown experimentally to be double-chairs. What happens when a bulkier heteroatom X is introduced? This should destabilize the double-chair conformation; however, the destabilisation value is hardly predictable. Secondly, two more interactions of the heteroatoms may be assumed for the compounds containing two (**5**) or three (**6**) heteroatoms, namely, (a) the dipole–dipole repulsion (**7**) and (b) the overlap of the lone pair orbitals (**8**) (*cf* the "hockey-stick effect"[9,10]). Reportedly, the bispiperidine derivative **5** (X = Y = NCH$_3$) is a double-chair.[11] The present work is a study of the conformational behaviour of oxygen- and sulfur (selenium)-containing heteroanalogues (**4**–**6**) of bicyclo[3.3.1]nonane.



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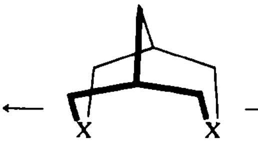

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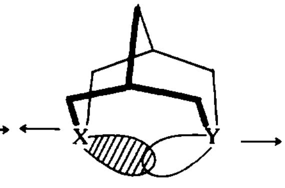

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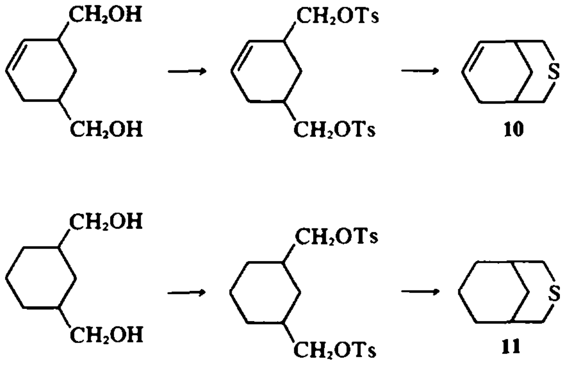
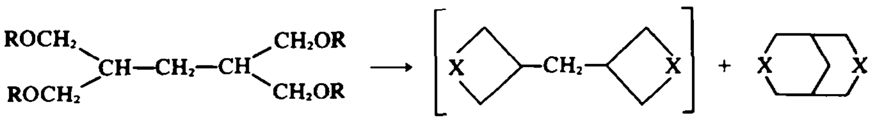
RESULTS AND DISCUSSION

3-Thiabicyclo[3.3.1]non-6-ene **10** and -nonane **11** were synthesized from a readily available cis-1,3-bis-hydroxymethylcyclohex-4-ene[12,13] (Scheme 1). 3,7-Dithiabicyclo[3.3.1]nonane **13** was a minor product of the tetratosylate **12b** cyclisation (Scheme 2). Analogously, tetraiodide **12c** gave diphenylbispiperidine **14**. Triheterosubstituted compounds of the type **6** were synthesized as shown in Scheme 3.

Conformations of heteroanalogues of bicyclo[3.3.1]nonane were studied by PMR. The PMR data are listed in Table 1. To facilitate the discussion, the coupling constants $^3J_{HH}$ reported for 6-membered heterocycles[14] are also included in the Table 2. Starting from the papers[14,15] where the value $|J_{aa} + J_{ee}|$ was found experimentally, we have calculated



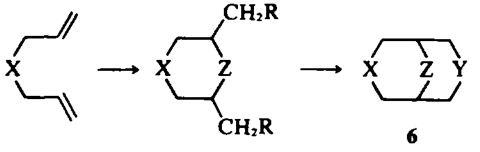
SCHEME 1



12a: R = OH
b: R = OTs
c: R = I

13: X = S
14: X = NC_6H_5

SCHEME 2



SCHEME 3.

J_{ee} for three cases (Table 2). J_{aa} has been assumed to be 9, 11 and 13 Hz. These J_{aa} values embrace practically the entire interval in which the constants observed for heterocyclic systems lie.

The methylene signal was assigned by assuming that the methylene system is an AB or AM part of the ABX or AMX system (the first-order analysis was sufficient in most cases, see e.g. **13**, Table 1). In some cases, however, additional splitting due to long-range coupling constants was observed (Table 1). Further, when the constant was so small that the splitting was unobservable, just the maximal possible value (usually, below ≤ 0.5 Hz) of the constant was measured. For **14** and **18**, the maximal limit of the constant was found from the line width. E.g., in the spectrum of **18**, the signal of the methylenes bonded to the oxygen was a narrow doublet centred at δ 3·9 ppm (the distance is 1·5 Hz) which may be interpreted as two intense signals associated with the parts A and B of the AB system. Since the AB system gives no signals of weak intensity, the coupling constant values (below 2·5 Hz) may be obtained from the doublet line widths. Also, the bridgehead proton signal was a wide singlet with $w_{1/2}$ of 11 Hz. Starting from the $J_{A'X}$ and $J_{B'X}$ values in Table 1, we estimate $|J_{AX} + J_{BX}|$ to be at or below 4 to 5 Hz.

The solvent affects the coupling constants rather weakly, however, the chemical shifts sometimes changed drastically when benzene was used instead of CCl_4. Special attention must be given to the assignment of the signals of axial and equatorial protons. Except for **14**, the signals of protons characterised by a greater vicinal coupling constant lie at lower fields in all cases. Our assignment criterion was the $^3J_{HH}$ value and we assumed that the proton having a greater coupling constant was axial (see below). This interrelation of axial and equatorial protons in six-membered heterocycles was noted in the literature repeatedly,[16] also for the bicyclo[3.3.1]nonane heteroanalogues.[17]

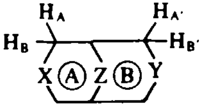
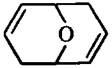
Conformational equilibrium of the compounds may be written as follows ($A \rightleftharpoons B \rightleftharpoons C$).

In terms of the equilibrium, the $^3J_{HH}$ value may be expressed by

$$^3J_{HH}\text{obs.} = \sum_i n_i J_i = n_A J_A + n_B J_B + n_c J_c \qquad (1)$$

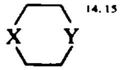
where n_i and J_i are fractions of coupling constants

Table 1. NMR- data for bicyclo[3.3.1]nonanes of heteroanalogs 4–6

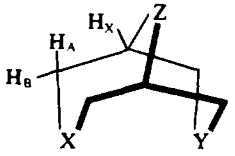
Formula 					ring A					ring B				
					Chemical shift ppm (±0·05)			$^{3}J_{HH}$ (cps) (±0·2 cps)		Chemical shift ppm (±0·05)		$^{3}J_{HH}$ (cps) (±0·2 cps)		
No	X	Z	Y	Spectrum type	δ_A	δ_B	δ_X	J_{AX}	J_{BX}	$\delta_{A'}$	$\delta_{B'}$	$J_{A'X}$	$J_{B'X}$	Solvent
15^{a}	O	CH_2	CH_2					2·7	1·7	—	—	—	—	
				ABX	3·65	3·45	2·8^{b}	2·7	≤0·5	3·65	3·45	2·7	≤0·5	C_6H_6
16	O	O	O											
				ABX	4·1	3·9	3·5^{b}	2·5	≤0·5	4·1	3·9	2·5	≤0·5	CCl_4
				AMX	4·05	3·9	3·75^{b}	3·3^{c,d}	≤0·5^{e}	3·4	2·45	4·0^{c}	1·5^{f,g}	$CHCl_3$
17	O	O	S	AMX	3·9	3·7	3·6^{b,h}	3·5^{c,g}	≤0·5^{e}	3·25	2·3	3·8^{c,g}	1·5^{f,g}	CCl_4
				AMX	3·65	3·4	3–3·2^{i}	3·5^{c,j}	≤0·5^{e}	3^{i}	1·85	4·2^{c,k}	1·0^{f,l}	C_6H_6
18	O	S	S	AMX	—	—	1·85^{b}	≤2·5	≤2·5	3·2	2·3	4·0	3·0^{g}	C_6H_6
19					2·35	1·6	4·2^{m}	6·0^{n}	0·5^{n}	2·35	1·6	6·0^{n}	≤0·5^{n}	CCl_4
10					2·9	—	—	3·2	—	—	—	—	—	CCl_4
				AMX	3·05	2·35	—	3·7	2·5^{o}	—	—	—	—	CCl_4
11	S	CH_2	CH_2											
				AMX	3·0	2·35	—	3·4	2·5^{o}	—	—	—	—	C_6H_6
				ABX	2·9	2·65	2·3^{b}	6·4	3·8	2·9	2·65	6·4	3·8	
13	S	CH_2^{p}	S											CCl_4
				AMX	2·9	2·65	2·3^{b}	6·2	4·0	2·9	2·65	6·2	4·0	
				ABX	3·1	2·65	4·2^{b}	6·5	3·1	3·1	2·65	6·5	3·1	$CDCl_3$
				ABX	2·55	2·1	3·65^{b}	6·4	3·2	2·55	2·1	6·4	3·2	C_6H_6
20	S	O	S											
				ABX	2·9	2·5	4·0^{b}	6·2	4·0	2·9	2·5	6·2	4·0	CCl_4
				ABX	2·9	2·5	4·05^{b}	6·7	4·0	2·9	2·5	6·7	4·0	C_6H_5–NO_2
21	S	O	Se	AMX	3·35	3^{i}	4·35^{q}	6·2	4·5	3·35	2·8^{i}	6·2	4·0	CCl_4
14	PhN	CH_2	PhN	AMX	3·0	3·6	—	3·6	≤2·0	3·0	3·6	3·6	≤2·0	CCl_4
22^{r}	MeN	CH_2	MeN	ABX	2·22	2·65	—	4·2	2·6	2·22	2·65	4·2	2·6	

^{a}Ref 6 ^{b}center of multiplet ^{c}doublet of quadruplets ^{d}long range constant 1·7 cps ^{e}doublet, $W_{1/2}$ 2 Hz ^{f}doublet of triplets ^{g}long-range constant 1·5 Hz ^{h}partial overlap ^{i}approximately, the signals are overlapped ^{j}long-range constant 2·0 Hz ^{k}based on one of the quadruplets ^{l}long-range constant 1 Hz ^{m}doublet, J = 6·0 Hz ^{n}by double resonance ^{o}based on extreme lines of the poorly resolved multiplet ^{p}triplet, 1·85 ppm, J = 3·7 Hz ^{q}3·55 ppm in benzene ^{r}Ref 11.

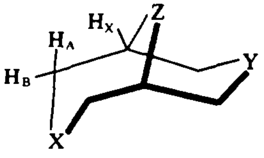
Table 2. $^3J_{HH}$ coupling constants for the heterocycles



X	Y	$J_{aa} + J_{ee}$ observ.	J_{ee} at: $J_{aa} = 9$ Hz	$J_{aa} = 11$ Hz	$J_{aa} = 13$ Hz	J_{ae} observ. Hz
O	O	12·2	3·2	1·2	—	2·8
NH	NH	13·1	4·1	2·1	0·1	3·04
S	O	14·7	5·7	3·7	1·7	2·65
S	S	16·2	7·2	5·2	3·2	2·4
Se	Se	17·0	8·0	6·0	4·0	2·43
CH_2	O	14·8	5·8	3·8	1·8	3·87
CH_2	NH	15·7	6·7	4·7	2·7	3·77
CH_2	S	17·0	8·0	6·0	4·0	3·26
CH_2	Se	16·9	7·9	5·9	3·9	3·09



A



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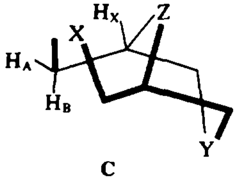

C

associated with the respective conformations. When X = Y and consequently $n_B = n_c$,* Eq (1) may be rewritten as

$$n_A = \frac{J_B + J_C - 2J_{obs}}{J_B + J_C - 2J_A}. \qquad (2)$$

At this stage, two problems are to be discussed, namely, (a) the effect of the conformational equilibrium on $^3J_{HH}$ obs. at known "standard" (or limiting) coupling constants assumed for each of the conformations and (b) the choice of the "standard" constants and their behaviour as a function of the geometry distortion.

The first problem may be resolved easily, by using the averaged values such as $J_{ae}(A) = J_{ae}(B) = 3$ Hz (Table 2), $J_{ee}(A) = J_{ee}(B) = 2$ Hz, $J_{ee}(C) = 10$ Hz and $J_{ae}(C) = 3$ Hz.[5-7] Evidently, J_{BX} is not sensitive to the conformational equilibrium and should be small, of the order of 2 to 3 Hz. In contrast, J_{AX} is appreciably variable in going from the conformations A and B to C. Eq (2) and the standard constants exposed above show that J_{AX}obs. is 3, 4·25 and 6·5 Hz when n_A is 100, 50 and 0%, respectively. Consequently, J_{AX} should increase with the fraction of the boat-like conformations **B** and **C**, however, two such conformations play the part, so the J_{AX} increasing should be rather smooth.

The second problem may be approached with the aid of the well-known Karplus equations, $^3J_{HH} = f(\varphi)$. Alongside with the dihedral angle, the substituent electronegativity with respect to hydrogen atom, ΔE, and the substituent orientation vis-à-vis the coupled protons (phase angle, θ) should be accounted for. The dependence $^3J_{HH} = (\varphi, \Delta E, \theta)$ was discussed by Pachler.[19] His equations are a good qualitative description of the coupling constants behaviour, however, they seem to be inapplicable to quantitative calculations.†

Let us consider a framework of the conformation **A** (**D** and **E** are the Newman projections). Appar-

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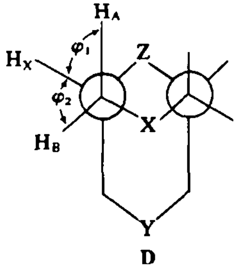
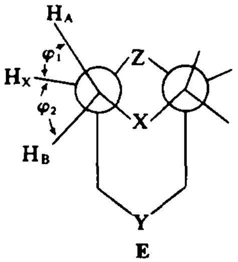
*The magnitudes of the chair-boat energy difference in 6-membered heterocycles are not well known (except 1,3-dioxan vs 1,3-dithiane[18]).

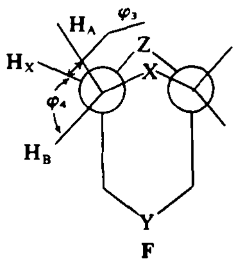
†To improve the calculations, a semi-empirical version[20] of the Pachler equations and a method based on the ratio of the Karplus equation coefficients (DAERM)[21] were proposed.



D

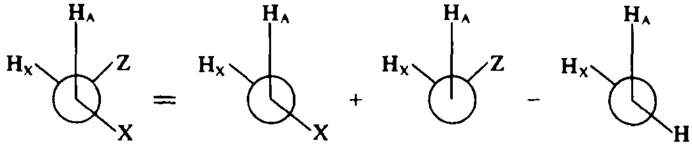


E



F

ently, the ideal structure has the angles $\varphi_1 = \varphi_2 = 60°$. Flattening the wings of the molecule leads, as e.g. due to **7** or **8**, to a decrease in φ_1 and an increase in φ_2 (E). Consequently, J_{BX} will decrease and J_{AX} increase.* The electronegativity effect may be included by analysing the Pachler equations. According to,[19,20] the electronegative substituent effects on J_{BX} may be reflected by a superposition of the fragments shown below.



Then, J_{AX} for the ideal framework will be:[19,20]

$$J_{AX} = [J^{300°}_{180°}]_X + [J^{60°}_{-60°}]_Z - [J^{300°}_{180°}]_H.$$

The flattening will raise the sub- and superscripts of the term $J^{300°}_{180°}$ and diminish these for $J^{60°}_{-60°}$. Consequently, if an electronegative substituent is present, the quantity $^3J_{HH} = f(\varphi)$ taken at 30° to 80° will exceed its value associated with the unsubstituted fragment. At 280° to 320°, in contrast, this function will be lower for the substituted fragment. Thus, contributions of the two terms to the total constant are directed oppositely, and the X and Z electronegativity effect upon J_{AX} somewhat smooths down.

A similar reasoning carried out for J_{BX} gives

$$J_{BX} = [J^{300°}_{180°}]_X + [J^{300°}_{180°}]_Z - [J^{300°}_{180°}]_H.$$

When the double chair is flattened, the sub- and superscripts of all the terms fall. Starting from the J_{HH} behaviour discussed above, we may expect that J_{BX} will decrease under the action of electronegativities of both X and Z. Therefore, even when the angles φ_1 and φ_2 are equal, J_{AX} should exceed J_{BX}.

For the chair–boat F, the electronegativity will affect both the constants more or less identically, the main contribution should be due to the difference between φ_3 and φ_4. The constants should differ strongly and J_{AX} should be much greater than J_{BX}. Analysis of the literature data shows that J_{AX} is 10 to 10·3 Hz[5,7] and J_{BX} is 2·1 Hz[7] for bicyclo[3.3.1]nonane derivatives whose chair–boat conformation **2** is fixed.

In the final analysis, the application of PMR techniques is hindered by the fact that (a) the coupling constants are not too sensitive to the conformational equilibrium and (b) alternative explanation of the J_{AX} increase is possible, namely, the flattening of the double chair.

Nevertheless, *reliable conclusions may be arrived at by considering both* J_{AX} *and* J_{BX}. To begin with, when both the constants are small, the double-chair conformation may be expected. Further, flattening the stable double chair requires that both J_{AX} increase and J_{BX} decrease whereas the conformational equilibrium requires that J_{AX} increase while J_{BX} be constant (or even rise a bit). Finally, a jump of J_{AX} to 9–11 Hz should say that the system prefers one of the alternative chair–boat conformations.

Let us consider the oxygen-containing compounds in Table 1. J_{AX} values for **15–18** are small and lie at 2·5 to 3·5 Hz. Table 2 demonstrates that the constant is 3·87, 2·8 and 2·65 Hz for tetrahydropyran, dioxan, and oxathian respectively. The data on the "standard" J_{ee} are less clear (Table 2). For substituted tetrahydropyrans or 1,4-dioxans, the constant lies between 0 to 2·5 Hz.[10] Consequently, the distinctly small values of both the constants, J_{AX} and J_{BX}, say explicitly that the compounds **15–18** prefer the chair conformation of their oxygen-containing rings. Note also that the molecule "wings" are strongly flattened when trigonal carbons **19** are introduced. As a result, one of the constants rises to 6·0 Hz, the other falls to zero, which fits well with the conclusion on the flattening effect upon coupling constants.

The problem of standard constants associated with sulphur derivatives is quite complicated. Table 2 shows that J_{ae} lies at 2·4 to 3·6 Hz. However, J_{ee} depends on the J_{aa} value assumed and may be equal to 3–6 Hz. The spectrum of **11** gives two constants, 3·4 and 2·5 Hz. This is a good argument in favour of the presence of the double chair. The spectrum of the unsaturated sulphide **10** reveals just one coupling constant 3·2 Hz. Judging from the chemical shift, this corresponds to the greater constant in **11**. Since the unsaturated ring in **10** is flattened, hence the 3,7-repulsion is sharply diminished,† the stereochemical consideration prompts that the tetrahydrothiopyran ring should be a chair. In going from **11** to **17**, J_{AX} (or $J_{A'X}$) rises from 3·4 to 4·0 Hz while J_{BX} (or $J_{B'X}$) falls from 2·5 down to 1·5 Hz, so that **17** undergoes additional flattening. This agrees with the fact that J_{AX} in the dioxan ring varies from 2·7 Hz in **16** to 3·5 Hz in **17**.

PMR spectra of **14** as collated with the data reported for **27** (Ref 11, Table 1) points to the double-chair conformation in the compounds.

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*For a detailed discussion for monocyclic systems, see.[14,15]

†**10** may also undergo the repulsion caused by the overlap of the sulphur p-orbital and the double bond π-orbital, as in **8**. However, the geometry is unfavourable for an overlap of the type.

However, the compounds containing sulphur (or selenium) in positions 3 and 7 reveal another regularity. Both J_{AX} and J_{BX} increase and this implies a conformational equilibrium with the proportion of double-chair being relatively small in accordance with the above criteria.* The alternative explanation might be as follows: the compounds adopt the double-chair conformation having anomalously high J_{ee} values.

Let us consider the problem of J_{BX} for **13**, **20**, and **21**. Anomalously high $^3J_{HH}$ values were reported for the H–C–C(H)–S–fragment. An example may be found in Table 2. An increase in the vicinal coupling constants was observed for derivatives of oxathian[22] (see, however[10]). Samitov and coworkers[23] introduced empirical electronegativity values of substituents, whereas a deviation of the experimental $^3J_{HH}$ (in olefins) from that calculated on the basis of this electronegativity was attributed to spatial effects. The steric parameter ("S"),[23] is often too high for sulphur-containing compounds, which may be explained alternatively by an insufficient decrease in $^3J_{HH}$ under the action of the sulphur electronegativity. Also, anomalously high $^3J_{HH}$ values were found for some sulphones. E.g., J_{aa} in the cyclohexane ring of derivatives of 4,9-dihydrothioxanthene-10,10-dioxide reached 18 Hz[24] while J_{ee} 8 Hz.[25]† However, this objection has to be rejected in the present case. The examples of the J_{ee} abnormal increase are extremely rare. More important is the fact that close structural analogy of all compounds investigated permits to treat **10**, **11**, **17** and **18** as the model compounds with double-chair conformation. As a result one may conclude that J_{ee} should be 2·5–3·5 Hz or below for the chair conformation of sulphur containing bicyclo[3.3.1]-nonanes.

Thus, the introduction of the sulphur atoms in 3,7-positions in bicyclo[3.3.1]nonane increases the relative proportions of the chair–boat conformations **B** and **C**. It is difficult to evaluate this increase quantitatively using "standard" coupling constants.

One may point out three reasons for the double-chair destabilisation effect associated with the heteroatoms in positions 3 and 7: (i) steric repulsion of the bulky heteroatoms (ii) dipole–dipole repulsion **7** and (iii) lone pair orbital overlap **8**. However, it is impossible to single out the main reason of the destabilisation without the quantitative data concerning both the geometry and equilibrium.

CONCLUSION

The double-chair is the most preferred conformation for **10**, **11**, **15–18**. Thus, both the O... O and O... S heteroatom repulsions are not sufficient to destabilize the double-chair, but they are sufficient to distort the geometry and to cause the flattening of the "wings" of molecules.

The repulsion associated with the sulphur atoms in positions 3 and 7 is sufficiently high to cause transformation into the chair-boat conformation. Our data show that the 3,7-repulsion rises across the series O... O < O... S ≪ S... S.

EXPERIMENTAL

PMR spectra were recorded on the Varian XL-100 and T-60 instruments with hexamethyldisiloxan as the internal standard. Synthesis of the following compounds was made according to **16**[26] **19**[27] and **20**.[28]

3-*Thiabicyclo*[3.3.1]*non-6-ene* **10**. Cis-1,3-bis (oxymethyl)-cyclohex-4-ene (1·3 g)[12,13] and toluene p-sulphonyl chloride (4 g) in 20 ml pyridine at − 15° gave ditosylate, **9**. M.p. 89–90° (methanol). (Found: C, 58·74; H, 5·76; S, 14·34. $C_{22}H_{26}O_6S_2$ requires: C, 58·67; H, 5·78; S, 14·22%).

Anhydrous sodium sulphide was extracted in a Soxhlet apparatus into a flask containing tosylate **9** (5·8 g) and 250 ml absolute alcohol. The mixture was refluxed for eight hours, cooled down to − 78°, filtered, the solvent was evaporated, the resulting oil was sublimed at 60–80°/8 mm. The sulphide **10** (0·55 g, 30%) melts at 111–115°. (Found: C, 68·21; H, 8·58; S, 22·7. $C_8H_{12}S$ requires: C, 68·57; H, 8·57; S, 22·85%).

3-*Thiabicyclo*[3.3.1]*nonane* **11** was obtained from cis-1,3-bis(hydroxymethyl)cyclohexane[12,13] in the same way as **10**. The yield was 20%. After subliming it at 70–80°/15 mm, sulphide **11** melts at 165–167°. (Found: C, 67·82; H, 9·90. $C_8H_{14}S$ requires: C, 67·70; H, 9·86%).

3,7-*Dithiabicyclo*[3.3.1]*nonane* **13**. Sodium sulphide 15 g) in 50 ml water was added to a stirred boiling solution of tetratosylate **12b**[29] (27 g) dissolved in 350 ml alcohol. The mixture was refluxed (1·5 h), cooled, poured into 300 ml water, and extracted twice by 70 ml portions of methylene chloride. The solvent was removed, the residue distilled at 109–110°/1 mm to give 2 g of a sulphide mixture out of which, after having kept it at 5° for a long time, sulphide **13** (25 mg) crystallised. This was filtered and washed with ether. M.p. 171–172° (softens at 140°). (Found: C, 52·84; H, 7·55. $C_7H_{12}S_2$ requires: C, 52·60; H, 7·50%).

1,5-*Diiodo*-2,4-*diiodomethylpentane* **12c**. Red phosphorus (6·3 g) and iodine (78 g) were stirred at 90° for an hour, the tetrahydroxyheptane **12a**[29] was added in small portions to the resulting system at 100–110°. The reaction mixture was heated at 120° for 5 h, cooled with ice, decomposed with 50 ml ice-cold water, the precipitate was filtered and washed with water. The crystallisation from CCl_4 gave tetraiodide **12c**, 30·6 g, m.p. 103–103·5°. (Found: C, 14·02; H, 2·11. $C_7H_{12}I_4$ requires: C, 13·90; H, 2·00%).

N,N-*Diphenyl*-3,7-*diazabicyclo*[3.3.1]*nonane* **14**. Tetraiodide **12c** (6 g) and aniline (9·4 ml) were refluxed in 70 ml toluene during 60 h, the precipitate was filtered off,

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*No lines broadening were observed in the spectrum of **20** at − 40°; at lower temperatures the spectrum could not be taken, owing to extremely low solubility of the compounds.

†Modern interpretation of the substituent effect is based on an analysis of the amplitude and phase shifts of the Karplus curves.[19] However, the facts cited above suggest that there exists sometimes a special mechanism which governs the effect of the sulfur atom in the H–C–C–(H)–S–fragment upon $^3J_{HH}$; this mechanism is not reducible to electronegativities, and leads to an increase in the coupling constants.

washed with benzene, the filtrate and the benzene solution were evaporated *in vacuo*, the main bulk of the unreacted aniline was distilled off. The residue was distilled *in vacuo* in a flask fitted with a sabre-shaped side arm. The resulting glass (3·2 g) was chromatographed on alumina (ether/ligroin 1:2) to give needles of **14**, 0·5 g, m.p. 137° (ligroin). (Found: C, 82·43; H, 8·10; N, 10·31. $C_{19}H_{22}N_2$ requires: C, 82·02; H, 7·91; N, 10·08%).

3-Oxa-7,9-dithiabicyclo[3.3.1]*nonane* **18.** 3,5-Bis(chloromethyl)-1,4-oxathian[30] (17·6 g) and anhydrous sodium sulphide (14 g) were refluxed in 150 ml methanol for 6 h, the solvent was removed *in vacuo*, the solid residue was extracted with hexane in a Soxhlet apparatus for 30 h. The solvent was removed *in vacuo*, the residual semi-crystalline bulk was separated from oil on a filter and washed with a minimal amount of cold benzene. The sublimation at 110–140°/6 mm gave **18**, 140 mg, sinters at 175°, melts at 183·5–184°. (Found: C, 44·61; H, 5·99; S, 39·45. $C_6H_{10}OS_2$ requires: C, 44·45; H, 6·17; S, 39·50%).

9-Oxa-3-thia-7-selenabicyclo[3.3.1]*nonane* **21.** Rongalite (40 g) dissolved in 40 ml water was added in a nitrogen atmosphere to a stirred mixture of selenium (8·25 g) and 60 ml water containing 23 g NaOH, the mixture was heated until selenium dissolution was complete. To the resulting suspension 75 ml alcohol were added, then the 2,6-bis(iodomethyl)-1,4-oxathian[28] (18 g) powder was poured in several portions, and the mixture was heated at 110–120° for 6 h. It was extracted several times with hexane, the solvent was removed to give 1·2 g of a crude **21**.

Before analysis **21** was sublimed three times at 120–140°/1 mm. It melts at 79–80°. (Found: C, 34·83; H, 4·18; Se, 15·45. $C_6H_{10}OSSe$ requires: C, 34·35; H, 4·31; Se, 15·32%).

3,9-Dioxa-7-thiabicyclo[3.3.1]*nonane* **17.** Bis-2,6-iodomethyl-1,4-dioxan (62 g)[31] and anhydrous sodium sulphide (40 g) were refluxed in 600 ml methanol. The reaction course was followed with the chromatography on silica gel ("Silufol" plates, $CHCl_3$ eluent, the R_f value of **17** is ca. 0·3; R_f of the initial diiodide is of about 0·8). After the reaction was complete (in *ca* 20 h), the mixture was filtered, methanol was removed *in vacuo*, the residue was treated with 200 ml water and extracted with chloroform (four 200 ml portions). The extracts were dried over sodium sulphate, the solvent was removed. The brown residue sublimed at 120–180°/1 mm to produce an oil which slowly crystallised from a hexane/chloroform mixture and gives large prisms. These were separated from smaller crystalline species. Two sublimations at 90–100°/1 mm gave **17**, 880 mg, m.p. 121·5–122·5° in a sealed capillary. (Found: C, 49·10; H, 7·07; S, 21·60. $C_6H_{10}O_2S$ requires: C, 49·34; H, 6·94; S, 21·91%).

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