Studies on 8,9,10,11-Tetrahydro-7*H*-cycloocta[*de*]naphthalenes. I. Conformations of 8,8,10,10-Tetrasubstituted Derivatives of 8,9,10,11-Tetrahydro-7*H*-cycloocta[*de*]naphthalene

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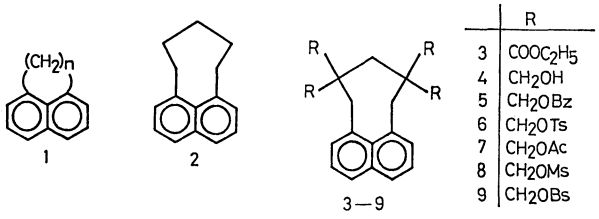
(Received June 28, 1975)

Several 8,8,10,10-tetrasubstituted 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalenes (**3**—**9**), novel pericyclic compounds of naphthalene, have been prepared through the alkylation reaction of 1,8-bis(bromomethyl)naphthalene and tetraethyl propane-1,1,3,3-tetracarboxylate, and the conformations of the cyclooctene ring in these compounds have been investigated on the basis of the PMR spectra. It is concluded that, at room temperature, the cyclooctene rings of (**3**—**9**) are frozen on the NMR time scale and exist exclusively in the boat form **15**, which is shown to be the most energetically stable conformation for the peri-eight-ring systems from models. Some discussion is also given on the configurations of the substituent groups in (**3**—**9**).

Although alicyclic ring systems, particularly six-membered rings, have been studied extensively by numerous investigators in the last two decades,[1] and although considerable attention has recently been focussed on the peri-interaction in naphthalene derivatives,[2] only a few reports have so far been presented on the pericyclic ring systems, in which methylene chains are fused to a naphthalene ring at the 1,8-positions, **1**. It seems that, in pericyclic naphthalene derivatives, the motions of the methylene chains of the peri-bridged ring are restricted by the naphthalene moiety, and that the rigid peri-bondings cause a large steric crowding in the molecules. This means that the peri-ring in these molecules exists under steric circumstances very different from those in the corresponding saturated cycloalkanes or structurally analogous benzo-derivatives. Among the pericyclic naphthalene derivatives **1**, little information has so far been available on the compounds with ring sizes larger than those of the commonly known acenaphthene (**1**, $n=2$), 2,3-dihydrophenalene (**1**, $n=3$) and 7,8,9,10-tetrahydrocyclohepta[*de*]naphthalene (**1**, $n=4$).[2]



	R
3	$COOC_2H_5$
4	CH_2OH
5	CH_2OBz
6	CH_2OTs
7	CH_2OAc
8	CH_2OMs
9	CH_2OBs

Our interest has been in the stereochemistry of these unknown pericyclic ring systems, particularly the 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene ring **2**, which is the next higher homolog of the cyclohepta[*de*]naphthalene compound. Recently, the unsubstituted hydrocarbon **2** was first synthesized by Nelsen and Gillespie, and some suggestion was given as to its conformation.[3] However, no information has yet been obtained on the substituted derivatives of this compound.

In this paper, some new derivatives of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene (**3**—**9**) have been prepared, and their stable conformations have been determined on the basis of the PMR spectra.

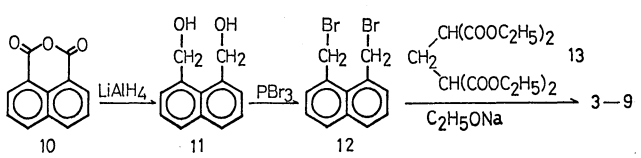
TABLE 1. PHYSICAL PROPERTIES OF 8,8,10,10-TETRASUBSTITUTED 8,9,10,11-TETRAHYDRO-7*H*-CYCLOOCTA[*de*]NAPHTHALENES (**3**—**9**)

Compd	Mp (°C)	Molecular formula	Mol wt M+ (Calcd)	Found (Calcd) C%	H%	S%	IR data[b] (Nujol, cm^{-1})
3	112—112.5	$C_{27}H_{32}O_8$	484.212 (484.209)	66.75 (66.92)	6.77 (6.66)		1739, 1240, 1100
4	234—234.5	$C_{19}H_{24}O_4$	316.164 (316.167)	71.51 (72.12)	7.69 (7.65)		3350, 1030
5	196.5—197	$C_{47}H_{40}O_8$	732.267 (732.272)	76.97 (77.03)	5.37 (5.50)		1715, 1286, 1115
6[a]	178.5—179	$C_{47}H_{48}O_{12}S_4$	..... (932.203)	60.82 (60.50)	5.23 (5.19)	13.46 (13.74)	1367, 1174
7	205—205.5	$C_{27}H_{32}O_8$	484.211 (484.209)	67.02 (66.92)	6.59 (6.66)		1728, 1250
8	230—231	$C_{23}H_{32}O_{12}S_4$	628.079 (628.078)	43.95 (43.95)	5.01 (5.13)	20.43 (20.37)	1340, 1170
9[a]	190—191	$C_{43}H_{36}O_{12}S_4Br_4$	..... (1187.782)	43.00 (43.31)	2.90 (3.04)		1377, 1189

a) Attemps were also made to obtain molecular ions for compounds (**6**) and (**9**), but unsuccessful. b) Absorptions due to substituent groups.

Results

Syntheses. The compounds (**3**—**9**) used in this study were synthesized in the following reaction sequence, outlined in Scheme 1. The starting material was commercially available 1,8-naphthalenedicarboxylic anhydride, **10**, which was reduced with lithium aluminum hydride to 1,8-bis(hydroxymethyl)naphthalene, **11**.[4] Treatment of **11** with phosphorus tribromide and pyridine in ether led to the dibromide, **12**.[5] The next step was the formation of the eight-membered peri-ring. For this purpose, **12** was allowed to react with tetraethyl propane-1,1,3,3-tetracarboxylate, **13**, which had been prepared from diethyl malonate and paraformaldehyde by the condensation reaction in the presence of potassium hydroxide.[6,7] By the reaction between equimolar amounts of **12** and **13** in ethanol-dimethyl sulfoxide at 0 °C, using sodium ethoxide as a condensing agent, tetraethyl 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene-8,8,10,10-tetracarboxylate, **3**, with the desired peri-8 ring, was obtained in 55% yield. Treatment of



Scheme 1.

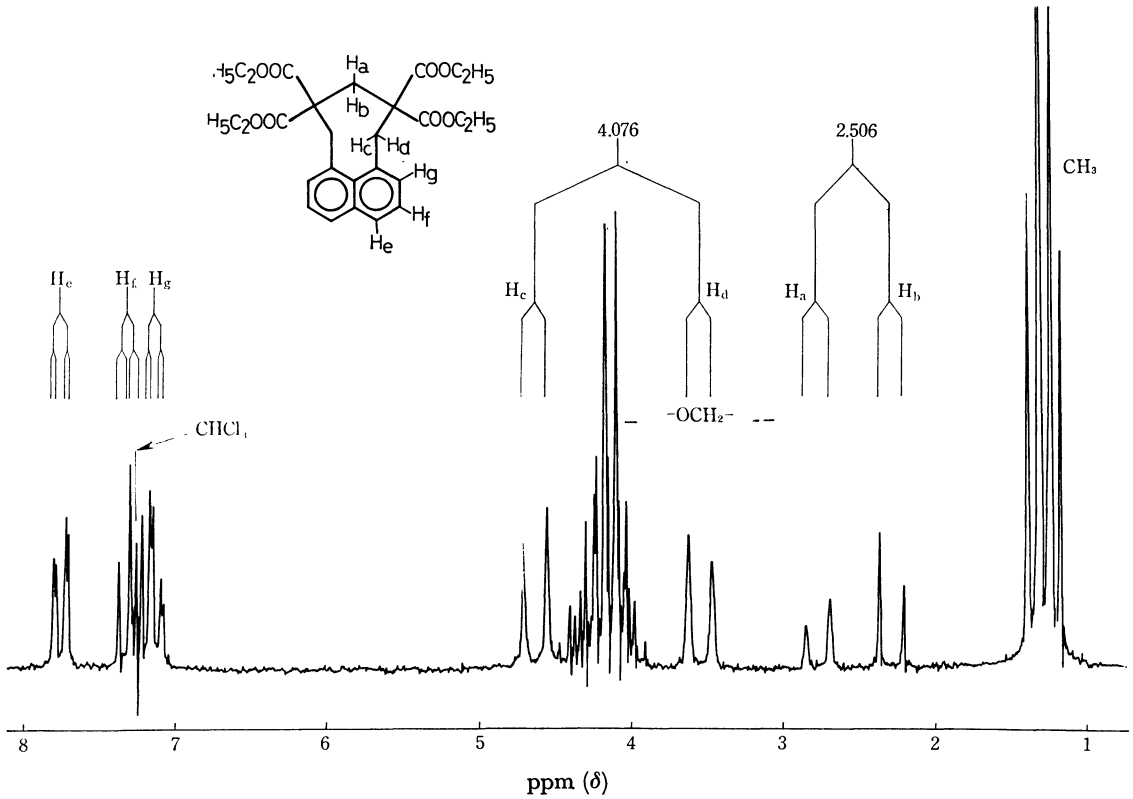


Fig. 1. PMR spectrum of tetraethyl 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene-8,8,10,10-tetracarboxylate (**3**) at 100 MHz in $CDCl_3$ solution.

3 with excess lithium aluminum hydride in ether gave the tetrol **4**, which was then converted to the esters in the usual fashion. Thus, by treating **4** in pyridine with such acylating agents as benzoyl chloride, *p*-toluenesulfonyl chloride, acetic anhydride, methanesulfonyl chloride, and *p*-bromobenzenesulfonyl chloride, the corresponding tetraesters of **4** were obtained- namely, benzoate **5**, tosylate **6**, acetate **7**, mesylate **8**, and brosylate **9** respectively.

After purification, each compound (**3**—**9**) was proved to have the desired structure by elemental analysis as well as by a study of the IR, PMR, and high-resolution mass spectra. The data are summarized in Table 1 except for PMR, which will be given fully later.

PMR Spectra. The room-temperature 100-MHz PMR spectrum of tetraethyl 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene-8,8,10,10-tetracarboxylate, **3**, in *ca.* 10% solution in deuteriochloroform consists of five distinct absorption groups, as is shown in Fig. 1. They are low-field naphthalene absorption bands (6H, e, f, g), a multiplet (8H) in the center of the spectrum due to the methylene protons of ester groups, a high-field methyl signal (12H), and two AB quartets centered at δ 4.076 (4H, c, d) and 2.506 (2H, a, b) respectively. From the positions and relative intensities of each peak, the low-field AB pattern can readily be assigned to the benzylic protons, and the high-field one, to the methylene protons on 9-carbon in the peri-ring. The lower-field portion, H_c, of the benzylic AB pattern can be assigned to hydrogens which point inward to the center of the molecule, since these hydrogens are expected to have a large steric interaction owing to their proximity with each other in the peri-eight ring systems.[8,9]

An important feature observed in the spectrum is that in the C_9-AB pattern, the higher-field methylene proton, H_b, appears as a sharp doublet, while the lower-field H_a affords a considerably broadened peak. The line broadening is also noted in the high-field H_d proton in the benzylic AB pattern, although it is not so remarkable as that for the C_9-methylene proton, H_a. An attempt to resolve these broadened lines by employing a degassed sample was unsuccessful. However, the line broadening in both AB patterns suggests that an appreciable long-range spin-spin interaction exists between one of the C_9-methylene protons, H_a, and an outward-pointing benzylic methylene proton, H_d. Actually, spin-decoupling experiments on **3** demonstrate the presence of this interaction, in which a sharpened doublet results for the C_9-methylene proton, H_a, upon irradiation at the higher-field portion, H_d, of the benzylic AB pattern.

The methyl and naphthalene absorptions are rather simple, as can be seen from the spectrum; thus, by a first-order analysis of the expanded spectra, two methyl groups at δ 1.287 and 1.208 (triplet, J=7.1 Hz, respectively), and three quartets for the aromatic protons at δ 7.730 (e, 2H, J=8.0 and 1.7 Hz), 7.279 (f, 2H, J=8.0 and 7.1 Hz), and 7.116 (g, 2H, J=7.1 and 1.7 Hz) are obtained. This means that two different types of methyl groups and three different types of aromatic protons are present in **3**. From the peak area and the values of the chemical shifts and the coupling constants, the aromatic protons can be assigned most reasonably as is shown in Fig. 1.

The methylene signals of the ester groups, appearing in the center of the spectrum as a complex multiplet rather than the usually observed simple pattern, can

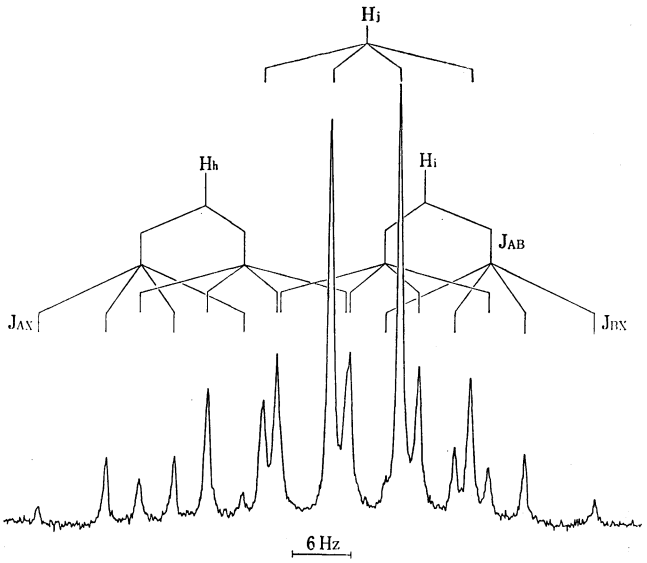


Fig. 2. *O*-Methylene proton signals of $-COOC_2H_5$ groups in compound (**3**). j; δ 4.131 (4H, quartet, $J=7.1$ Hz), h, i; δ 4.301 and 4.070, respectively (AB Part of ABX_3 system, 4H, $J_{AB}=10.8$, $J_{AX}=J_{BX}=7.1$ Hz).

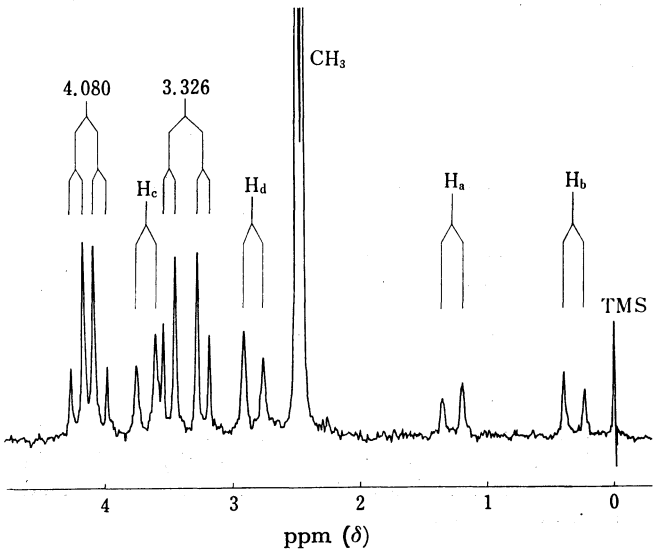
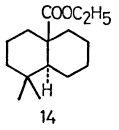


Fig. 3. PMR spectrum of aliphatic portion of tosylate (**6**).

also be completely analyzed, as is shown in Fig. 2. They consist of two distinct methylene groups, one of which resonates at δ 4.131, showing a simple, first-order quartet (j, 4H, $J=7.1$ Hz), while the other, with two components, resonates at δ 4.301 and 4.070, showing a multiplet of sixteen symmetric lines resulting from AB part of ABX_3 system (h, i, $J_{AB}=10.8$, $J_{AX}=J_{BX}=7.1$ Hz); *i.e.*, an AB quartet is formed, due to the nonequivalence of the methylene protons, and then each component further splits into a quartet by coupling with the neighboring methyl group. This is a fact of interest in connection with another previously reported compound, **14**, in which *O*-methylene protons of the ethoxycarbonyl group are known to be magnetically nonequivalent to each other.[10]



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The 100-MHz PMR spectrum of the aliphatic portions of the tosylate **6** at ambient temperature is given in Fig. 3. All the spectra of the oxymethyl derivatives (**4**—**9**) in this region resemble each other well; they all contain four AB quartets, as may be seen in the figure. The high-field AB pattern (a, b, 2H) is readily assigned to the C_9-methylene protons in a manner similar to that described above, while the AB pattern (c, d, 4H) in the low-field region, with a larger coupling constant and a larger chemical-shift difference, can be assigned to the benzylic methylene protons. The remaining two AB patterns (4H), centered at δ 4.080 and 3.326 respectively, are responsible for the protons of oxymethyl groups ($-CH_2O-$) attached to the carbons-8 and -10 of the peri-ring; this means that two different types of methylene groups, belonging to a $\begin{matrix}X\\Y\end{matrix}\!\!\times\!\!\begin{matrix}CH_2\\CH_2\end{matrix}$- moiety, are present in (**4**—**9**). The assignments of these methylene signals will be discussed later.

An additional doublet is also observed in the spctra of the tosylate **6** (δ 2.467 and 2.429), the acetate **7** (δ

Table 2. PMR spectra data of C_9 (a, b) and benzylic (c, d) methylene protons in compounds (**3**—**9**)[a]

Compd.	J_{gem}	$\delta_{a(c)}$	$\delta_{b(d)}$	$\triangle$	$\Delta\delta_{obsd}$	Solvent
3	16.0	2.735	2.277	2.506	0.458	$CDCl_3$
	(15.6	4.617	3.536	4.076	1.081)	
4	14.7	1.167	−0.032	0.568	1.199	DMSO-d_6
	(14.2	3.507	2.855	3.181	0.651)	
5	15.1	2.144	1.071	1.608	1.073	$CDCl_3$
	(14.9	4.163	3.466	3.815	0.697)	
6	15.0	1.261	0.330	0.796	0.931	$CDCl_3$
	(14.9	3.630	2.815	3.223	0.816)	
7	15.2	1.614	0.716	1.165	0.898	$CDCl_3$
	(14.9	3.881	2.965	3.423	0.916)	
8[b]	15.3	1.593	0.742	1.167	0.851	DMSO-d_6
	(15.1	4.111	2.940	3.526	1.171)	
9	15.2	1.390	0.540	0.965	0.850	$CDCl_3$
	(15.0	3.724	2.849	3.287	0.876)	
Cyclo-hexane	...	1.67[f]	1.21[f]	1.44[e]	0.46[d]	
Cyclo-hexane-d_8[e]	13.05	1.616	1.137	1.377	0.479	

J_{gem}; geminal coupling constant (Hz).
δ; chemical shift (ppm).
$\triangle$; absorption-center of AB protons (ppm).
$\Delta\delta_{obsd}$; differences in chemical shifts between AB protons (ppm).

a) In every compound, the data in parentheses correspond to those for the benzylic protons. b) Because of poor solubility in deuteriochloroform, the spectra of tetrol (**4**) and mesylate (**8**) were measured using dimethyl sulfoxide-d_6 as a solvent. The signals, however, seem little affected by this, since little change was observed in the spectra of brosylate (**9**) measured in both solutions. c) Ref. 11. d) Ref. 12. e) Ref. 13. f) Estimated from the values of $\triangle$ (1.44) amd $\Delta\delta_{obsd}$ (0.462) which were obtained from the high- and low-temperature spectra of cyclohexane, respectively.

TABLE 3. PMR SPECTRA DATA OF METHYLENE PROTONS OF $-CH_2O-$ GROUPS IN COMPOUNDS (**4**—**9**)[a]

Compound	J_{gem}	δ_A	δ_B	$\triangle$	$\Delta\delta$
4	11.0	3.813	3.654	3.733	0.158
	10.3	3.041	2.586	2.814	0.455
5	12.0	5.044	4.968	5.006	0.076
	11.2	4.402	4.185	4.294	0.217
6	10.0	4.156	4.003	4.080	0.152
	9.4	3.450	3.203	3.326	0.247
7	11.5	4.355	4.184	4.270	0.171
	10.9	3.735	3.464	3.599	0.271
8[b]	...	...	...	4.494	...
	9.8	3.749	3.654	3.702	0.094
9	9.9	4.223	4.104	4.164	0.119
	9.5	3.502	3.353	3.427	0.149

a) Symbols and units in this table are similar to those in Table 2. b) In the mesylate **8**, a methylene signal in the lower-field region appears as an unresolved broad singlet rather than an AB pattern.

TABLE 4. LINE-WIDTHS OF C_9- AND BENZILIC METHYLENE SIGNALS IN COMPOUNDS (**3**—**9**). (in Hz)

Compound	C_9-CH_2		Benzylic CH_2	
	H_a	H_b	H_c	H_d
3	3.0	1.1	2.1	2.7
4	3.8	3.1	3.9	3.0
5	3.5	2.6	a)	3.5
6	4.3	2.5	3.1	3.1
7	3.3	2.4	2.8	2.9
8	4.2	3.9	4.4	4.2
9	4.0	3.0	3.2	4.0

a) Because of overlapping of the peaks, line-width of this signal cannot be obtained.

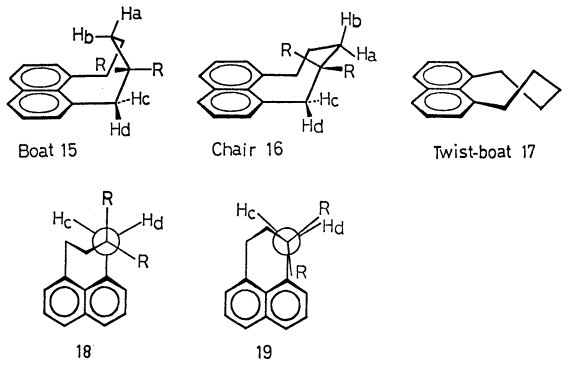
2.096 and 2.072), and the mesylate **8** (δ 3.304 and 3.166); all similarly arise from two different types of methyl protons in the tosyl, acetyl, and mesyl groups respectively.

Again, line broadening is also observed in all the low-field doublets, H_a, of the C_9-methylene AB pattern as in **3**, although to a lesser extent, due to long-range spin-spin interactions with benzylic methylene protons, H_d. This fact suggests that all the molecules of this series (**3**—**9**) have a geometry very similar to one another in solution; this can also be supported by the other analogous spectral features described above. The PMR data for Compounds (**3**—**9**) are summarized in Tables 2,3, and 4.

Discussion

The PMR spectra of Compounds (**3**—**9**) at ambient temperature always give an AB pattern for each of the benzylic and the C_9-methylene protons. This suggests that, in all the compounds, the inversion of the peri-ring has been slow enough at this temperature on the NMR time scale; it also suggests that the molecules always assume only a single energetically stable conformation in solution.

The fact that only a single AB pattern is observed for the benzylic methylene groups in all the spectra indicates the equivalence of the two diastereomeric methylene protons on the benzylic positions in all the compounds, *i.e.*, the equivalence of the positions at carbon-7 and carbon-11. A similar situation can be expected for the positions of C-8 and C-10 in all of this series, since always only two absorption groups are shown for the four substituents at these positions (see spectra). This indicates that the most stable conformation of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene derivatives (**3**—**9**) has either a mirror plane (C_s) or a two-fold symmetry axis (C_2) passing through the C-9 and angular carbon atoms of the naphthalene nucleus. The simplicity of the naphthalene signals observed in **3** can also be accounted for by the above symmetric conformations. Furthermore, the fact that all the compounds clearly show an AB pattern for the C_9-methylene protons rules out the two-fold axis of symmetry in Compounds (**3**—**9**). If it were not the case, one would expect to find an A_2 singlet for these protons. On the other hand, the models of the 8,8,10,10-tetrasubstituted derivatives of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene show that the molecules are capable of existing in three conformations: *i.e.*, the boat, **15**, and the chair, **16**, with a C_s symmetry, and the twist-boat, **17**, with a



C_2 symmetry, as was recently suggested by Nelsen and Gillespie for the unsubstituted hydrocarbon **2**.[3] It is understandable, however, that the twist-boat can hardly exist at the ground state in Compounds (**3**—**9**), since the twist-boat is much more strained than the boat or the chair conformation.

Symmetry considerations cannot distinguish between the boat and the chair conformations, but fortunately this distinction can be made by using the values of the chemical shifts and line-widths of the C_9-methylene protons, together with an evaluation of the ring-current effects induced by the naphthalene nucleus. From the data for the 8,8,10,10-tetrasubstituted derivatives of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene (**3**—**9**) in Table 2, it is apparent that, generally in all the compounds except **3**, the C_9-methylene proton signals, particularly that of the high-field portion, H_b, shift remarkably to the high-field region as compared to the axial protons of cyclohexanes (δ 1.21[11,12] and 1.137[13] ppm); this makes the chemical-shift difference between the protons, H_a and H_b, of the C_9-methylene group in (**4**—**9**) much larger ($\Delta\ \delta_{obsd}$ 0.85—1.20 ppm) than that between the equatorial and the axial protons in cyclohexane (0.46[12] and 0.479[13] ppm). This comparison is not always accurate, since it is made between compounds with different ring systems and different sub-

stituents. Nevertheless, the above data do indicate the trends of the C_9-methylene protons in the peri-8 ring systems.

The anomalously large chemical-shift difference, $\Delta\delta_{obsd}$, observed for the C_9-geminal protons in the alicyclic ring systems of (**4**—**9**) suggests that these compounds (**4**—**9**) assume a conformation in which either of the methylene protons on C-9 experiences rather large ring-current effects of naphthalene. An examination of the models reveals that the proton, H_a, on C-9 is quite remote from the naphthalene moiety in both the boat and chair conformations; it can be expected to be little affected by the ring-current of naphthalene, while the H_b proton, which is spatially closer to the naphthalene ring in the boat conformation, can be expected to undergo larger ring-current effects; little effect is expected for the H_b proton, in the chair conformation (see diagram). This suggests that there exists a large chemical-shift difference in the C_9-geminal protons in the boat conformation of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]-naphthalene ring.

Then, the effects of the ring-currents of naphthalene on the chemical shifts of the C_9-protons were evaluated for the boat and chair conformations of the 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene ring. The calculation was done according to the method of Goldstein *et al.*[14] using Eq. (1), where the distances of hydrogens from the naphthalene nucleus necessary for the calculation were obtained from the models:

$$\sigma = \frac{-3434}{R^3}\left[(1-3\cos^2\alpha) + \frac{0.735}{R^2}(35\cos^4\alpha - 30\cos^2\alpha + 3)\right] \quad (1)$$

From the results of the calculation, shown in Table 5, it is clear that, in the boat conformation, the *endo*-orienting C_9-methylene proton, H_b, is shielded to a greater extent (1.50 ppm) than the *exo*-orienting proton, H_a (0.28 ppm), by the effect of the ring-current of naphthalene, while in the chair conformation, the ring-current deshields both the axial (H_a) and the equatorial (H_b) protons of the C_9-methylene group and the effect is very small (0.44 and 0.08 ppm, respectively). Consequently, the chemical-shift difference in the C_9-geminal protons responsible for the ring-current of naphthalene is much larger in the boat conformation (δ_r 1.22 ppm) than in the chair (δ_r 0.36 ppm).

In addition, in order to evaluate the chemical-shift difference in the C_9-geminal protons more accurately, one must also consider the chemical-shift difference in the C_9-geminal protons when the ring-current effects of naphthalene are absent. Since both the boat and chair conformations of the 8,9,10,11-tetrahydro-7*H*-cycloocta-[*de*]naphthalene ring can be considered to have a geometry similar to that of the cyclohexane with respect to the arrangement of the C-8, C-9, and C-10 portions of the peri-ring, the effect of the different configuration on the chemical shifts of the protons in the saturated ring system can be estimated from the experimental values observed in cyclohexane derivatives, in which the signal of the axial protons appears in a field higher than the equatorial protons by 0.1—0.7 ppm (δ_{ae}).[15]

Thus, considering both the effects of the ring-current, δ_r, and the configurational difference, δ_{ae}, the chemical-shift difference in the C_9-geminal protons $\Delta\delta_{calcd}$ for the boat and chair conformations of the 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene ring are calculated as follows. Since, in the boat conformation, the hydrogens, H_a, and H_b, of the C_9-geminal group correspond to the equatorial and the axial protons of the cyclohexane respectively, the chemical-shift difference, $\Delta\delta_{calcd}$, is calculated to be 1.32—1.92 ppm. In the chair conformation, the H_a hydrogen corresponds to the axial, and the H_b hydrogen, to the equatorial; thus, the chemical-shift difference, $\Delta\delta_{calcd}$, is calculated to be —0.34—0.26 ppm (see diagram and Table 5). This result also indicates that the boat conformation has a large chemical-shift difference in the C_9-geminal protons, while the chair has a small one. A comparison of these calculated values $\Delta\delta_{calcd}$, with those observed, $\Delta\delta_{obsd}$, in (**4**—**9**) shows that the experimental values are much closer to that calculated for the boat conformation than that calculated for the chair. This makes it very possible that all the compounds (**4**—**9**) assume a boat form as the most stable conformation in solution at ambient temperature. Therefore, the high-field doublet (b) of the C_9-methylene signals observed in (**4**—**9**) can be assigned to the *endo*-orienting proton, H_b, and the low-field one (a), to the *exo*-orienting proton, H_a, of the boat conformation (see spectra).

The observed values in (**4**—**9**) ($\Delta\delta_{obsd}$ 0.85—1.20 ppm) are somewhat smaller than that calculated for the boat conformation ($\Delta\delta_{calcd}$ 1.32—1.92 ppm). In Compounds (**4**—**9**), however, the value of δ_{ae} is expected to be decreased to some extent by the effect of the axial $-CH_2O-$ groupings attached to the C-8 and C-10 positions.[15] Taking this fact into consideration, the chemical-shift difference calculated for the boat conformation can be expected to be a little smaller than that in Table 5; this results in a better agreement with the experimental values of (**4**—**9**).

It should be noted that there are some differences in the values of $\Delta\delta_{obsd}$ for (**4**—**9**), where **4** with hydroxyl groups exhibits a larger value than the others with more electronegative acyl or sulfonyl groups (**5**—**9**). From

Table 5. Calculation of chemical-shift difference in C_9–methylene protons in 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]-naphthalene ring (ppm unit)

	σH_a[a]	σH_b[a]	δ_r[b]	δ_{ae}[c]	$\Delta\delta_{calcd}$[d]
Boat	0.28	1.50	1.22	0.1—0.7	1.32—1.92
Chair	−0.44	−0.08	0.36	0.1—0.7	−0.34—0.26
Observed in (**4**—**9**)					0.85—1.20 ($\Delta\delta_{obsd}$)

a) Ring-current effect of naphthalene on the chemical shift of the C_9-methylene protons, calculated from Eq. (1). A minus sign indicates a low-field shift. b) Chemical-shift difference in C_9-methylene protons responsible for the ring-current effect of naphthalene. c) Chemical-shift difference in C_9-methylene protons caused by configurational difference between these two protons, estimated from Ref. 15. d) Chemical-shift difference in C_9-methylene protons calculated from the values of δ_r and δ_{ae} (see text).

Tables 2 and 3 it may be seen that the low-field shifts of all the AB absorption-centers (△) including oxymethyl, benzylic, and C_9-protons increase in this order of the compounds: **4**,**6**,**9**,**7**,**8**,**5**. This clearly means that, in all the (**4**—**9**) compounds, not only the oxymethyl groups but also the benzylic and the C_9-methylene groups are substantially affected by the substituents, although they are remote from the benzylic and the C_9-methylene groups in these molecules (**4**—**9**). Table 2 also shows that, in all the (**5**—**9**) compounds, the low-field shift of the absorption-centers (△) is always larger in the C_9-methylene signals than that in the benzylic signals; that is, the C_9-methylene groups are more affected than the benzylic methylene groups by the four substituent groups attached to C-8 and C-10. In the cyclohexane chair conformation, it is known that the equatorial electronegative groups shield both the axial and equatorial protons attached to the adjacent carbon atom, whereas the axial substituents shield the equatorial protons, but cause an appreciable low-field shift of the corresponding axial protons on the contiguous carbon atom.[16] This means that the C_9-methylene proton, H_a, in the tetrasubstituted derivatives of the 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene, with electronegative groupings at the C-8 and C-10 positions, is appreciably deshielded by the effect of the axial electronegative groups attached to the above positions, but the H_b proton is shielded, because the H_a proton in the boat conformation of the 8,9,10,11-tetrahydro-7*H*-cycloocta-[*de*]naphthalene ring corresponds to the equatorial proton of cyclohexane, and the H_b proton, to the axial. It is understandable, therefore, that the differences in chemical shifts between the C_9-methylene proton, H_a, and H_b, in **4** ($\Delta\delta_{obsd}$) are larger by 0.13—0.35 ppm than those in (**5**—**9**), since the signals of the H_b proton in Compounds (**5**—**9**) are expected to shift to a lower-field to a greater extent than in **4** as a result of the effect of acyl- or sulfonyloxymethyl groups on the carbon-8 and 10.

In the case of the benzylic methylene groups, the inward-pointing proton, H_c, is situated at the position *trans* to the equatorial substituents, and the spatial relationship between these two groups is similar to that between the H_b proton and the axial substituents described above. Thus, in contrast to the C_9-methylene protons, a large chemical-shift difference can be expected for the benzylic methylene protons in (**5**—**9**), since the inward-pointing proton, H_c, resonates at an appreciably lower field than the outward-pointing proton, H_d, because of the steric compression, and the H_c proton can be expected to be further deshielded by the acyl- or sulfonyloxymethyl groups in (**5**—**9**). The observed values of $\Delta\delta_{obsd}$ distinctly reveal this trend, where the value for **4** is smaller than those for (**5**—**9**) by 0.05—0.52 ppm (see Table 2). These results further support the predominance of the boat conformation over the chair in all the (**4**—**9**) compounds.

The only exception observed in Table 2 is the ethoxycarbonyl derivative, **3**, which shows a $\Delta\delta_{obsd}$ value of only 0.458 ppm, almost comparable to that of cyclohexane. However, as may be seen in the table, the absorption-centers of both the C_9- and benzylic methylene protons in **3** shift to a considerably lower field than those in other compounds (**4**—**9**); *i.e.*, in **3** both methylene groups are affected by the ethoxycarbonyl groups to a greater extent than in the other compounds, presumably because the electronegative ethoxycarbonyl groups directly attach to the ring carbons, C-8 and C-10, while in the other (**4**—**9**) compounds the acyloxy and sulfonyloxy groups attach to the substituent carbons. The chemical-shift difference in the C_9-methylene group in **3**, therefore, will be appreciably decreased by the effect of the ethoxycarbonyl groups, even if **3** exists in the boat conformation and even if the proton, H_b, in **3** is substantially shielded by the ring-current of naphthalene, as is observed in the other (**4**—**9**) compounds. This suggests a large possibility that the molecule of **3** also assumes the boat form as the most stable conformation at ambient temperature.

In the boat conformation, the four bonds between the C_9-methylene proton, H_a, and the outward-pointing benzylic methylene proton, H_d, lie in one plane in the W-arrangement, while in the chair such an arrangement is absent. Therefore, if the boat is the correct conformation for (**3**—**9**), an appreciably large long-range spin-spin interaction can be expected between these protons in all the (**3**—**9**) compounds.[17,18] Thus, as may be seen in the spectra and in Table 4, the fact that the signal of the C_9-methylene proton, H_a, is always broader than that of the proton, H_b, in (**3**—**9**) undoubtedly indicates the presence of this long-range coupling; hence, this is further evidence in favor of the boat conformation for (**3**—**9**). It may also be noted in Table 4 that the line-widths of both protons, H_a and H_b, are always larger in (**4**—**9**) than in **3**. This means that, in (**4**—**9**), both protons, H_a and H_b, are further coupled with oxymethyl groups attached to the contiguous carbon atoms, C-8 and C-10. It is also apparent from the table that this broadening of the signals is always more remarkable in the signals of H_b than those of H_a. This is presumably because the proton, H_b, in the boat conformation is coupled relatively strongly with the protons of the axial $-CH_2O-$ groups because of their *trans* arrangement.[19-22]

The effect of the substituents is also reflected in the geminal spin couplings of both the C_9- and the benzylic methylene groups in all the (**3**—**9**) compounds. Thus, as can be seen in Table 2, the geminal couplings, J_{gem}, of the C_9-methylene groups in (**3**—**9**) are appreciably larger (14.7—16.0 Hz) than those in the cyclohexanes (12—14 Hz). Moreover, the value of J_{gem} is much larger in the ethoxycarbonyl derivative, **3** (16.0 Hz), than those in the oxymethyl derivatives (**4**—**9**) (15.3—14.7 Hz), in which the value is the smallest in the hydroxy derivative **4**. Similar trends are also found in the geminal couplings of the benzylic methylene protons, in which, again, the value is the largest in **3** (15.6 Hz) and the smallest in **4** (14. 2Hz).

One point not yet discussed is the assignment of the two methylene signals arising from the 8- and 10-substituted groups ($-CH_2O-$ and $-COOC_2H_5$) to the axial and equatorial groups. In the oxymethyl derivatives (**4**—**9**), the axial methylene protons, involving the steric-compression effects, can be responsible for the low-field

AB quartet, and the equatorial ones, for the high-field signals.[16] This assignment is consistent with the results of the evaluation of the ring-current effect of the naphthalene nucleus on the methylene protons belonging to the axial and equatorial $-CH_2O-$ groups in (**4**—**9**), from which it is clear that the equatorial groups resonate at a field higher than the corresponding axials by *ca.* 0.46 ppm in the presence of the free rotations as a result of the ring-current effect.[10]

It is interesting that the nonequivalence of methylene protons is observed in the methylene signals of one of the $-COOC_2H_5$ groups in **3**. A detailed discussion of this point, however, as well as the assignment of methylene signals, must await further studies of the stereochemical properties inherent in these peri-8 ring systems.

All the results presented above provide conclusive evidence that all the (**3**—**9**) compounds exclusively exist in the boat conformation at room temperature in solution. Both the boat and chair conformations of (**3**—**9**) are expected to involve large van der Waals interactions caused by the two inward-pointing benzylic methylene protons, H_c,[8,9] and those caused by the two substituent groups in the 1,3-diaxial relationship to each other.[16] However, the chair conformation is expected to involve additional eclipsing interactions along the bonding between C-7 and C-8, and the bonding between C-10 and C-11 as well. Moreover, in the chair conformation, one can expect steric repulsions to be present between the axial substituents and the naphthalene ring because of their proximity to each other. On the other hand, the boat conformation lacks these additional interactions (see **15**, **16**, and the Newmann projections about the C_7–C_8 bonding, **18** for the boat and **19** for the chair conformation). The boat form, therefore, is the more energetically stable conformation for the 8,8,10,10-tetrasubstituted 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]-naphthalene ring, which well accounts for the predominance of the boat conformation over the chair observed in all the (**3**—**9**) compounds. A model of the boat conformation shows that the distance between the inward-pointing 7,11-hydrogens is *ca.* 0.7 Å, much smaller than the sum of the van der Waals radii of the two hydrogens (2.4 Å). Therefore, the molecules of (**3**—**9**) can be expected to assume a boat conformation which is strained to some extent in such a direction as to avoid the steric repulsions arising from the proximity of the two H_c hydrogens.

Experimental

All melting points were determined on a microscopic hot-stage melting-point apparatus and are reported uncorrected. All the solvents used in the reactions were dried and freshly distilled. Thin-layer chromatography was employed on silica gel to monitor the reactions and to check the purity of the products. After the solvents had been removed from the developed tlc sheets, the spots were detected by iodine vapor. The IR spectra were obtained on a JASCO Model IR-G Grating Infrared Spectrometer, using Uujol mulls. The positions of the absorption maxima are quoted in wave numbers (cm^{-1}), calibrated with polystyrene. The PMR spectra were obtained on a Varian HA-100 D spectrometer (100 MHz) at room temperature, using *ca.* 10% solution of compounds in deuteriochloroform or dimethyl sulfoxide-d_6; the chemical shifts are expressed in ppm (δ) downfield from the internal standard, tetramethylsilane, and the coupling constants (J), in Hz. High-resolution molecular-weight determinations were carried out on a CEC high-resolution mass spectrometer, Model 21-110 B, with a direct-inlet system and an ionization potential of 70 eV.

*1,8-Bis(hydroxymethyl)naphthalene (**11**).* Although Boekelheide and Vick[4] have previously reported the preparation of 1,8-bis(hydroxymethyl)naphthalene by the lithium aluminum hydride reduction of 1,8-naphthalenedicarboxylic anhydride, **11** was obtained in a more excellent yield by the method described below.

To a stirred suspension of 50 g of lithium aluminum hydride in a mixture of 1.2 l of absolute ether and 1 l of dry benzene, there was added 125 g of 1,8-naphthalenedicalbyxylic anhydride at a rate sufficient to maintain gentle boiling. After the addition was complete, the mixture was heated under reflux with stirring for an additional 6 days. After the reaction mixture had then been cooled, the excess metal hydride was destroyed by the addition of ethyl acetate and water. The further addition of 2M-aqueous hydrochloric acid to the slurry gave a white solid. This solid was collected, dried, and then heated with benzene containing ether. The benzene solution was separated and evaporated to give a white solid. After washing with dilute acid, the solid was recrystallized from benzene–methanol, giving the diol **11** (99 g; yield, 84%) as colorless needles; mp 156—156.5 °C (lit., mp 157—158 °C[4]) (Found: C, 76.39; H, 6.38%).

*1,8-Bis(bromomethyl)naphthalene (**12**).* 1,8-Bis(bromomethyl)naphthalene, **12**, was prepared in 84% yield by the bromination of 1,8-bis(hydroxymethyl)naphthalene, **11**, with phosphorus tribromide, essentially as has been described by Mitchell and Sondheimer.[5] Mp 131—132 °C (lit., mp 131—132 °C[5]) (Found: C, 46.00; H, 3.20; Br, 51.09%).

*Tetraethyl propane-1,1,3,3-tetracarboxylate (**13**).* Tetraethyl propane-1,1,3,3-tetracarboxylate, **13**, was prepared from diethyl malonate and paraformaldehyde according to the method of Welch.[6] Fractional distillation of the reaction product *in vacuo* using a Vigreux column afforded the tetraester **13**; bp 132—145 °C/0.3 mmHg; mostly distilled at 138 °C (lit., bp 194—198 °C/20 mmHg,[6] bp 190—200 °C/12 mmHg, 210—215 °C/20 mmHg[7]).

*Tetraethyl 8,9,10,11-tetrahydro-7H-cycloocta[de]naphthalene-8,8,10,10-tetracarboxylate (**3**).* A solution of 54 g of tetraethyl propane-1,1,3,3-tetracarboxylate, **13**, in 60 ml of absolute ethanol and 100 ml of dry dimethyl sulfoxide (distilled on calcium hydride) was added quickly to a stirred and cooled (0 °C) solution of sodium ethoxide in ethanol, obtained by dissolving 7.2 g of sodium in 660 ml of absolute ethanol. After 5 min, to this mixture, was added a solution of 54 g of 1,8-bis(bromomethyl)naphthalene, **12**, in 720 ml of dry dimethyl sulfoxide over a period of 12 min. After the addition was complete, stirring and cooling were continued for an additional 1.5 hr. The reaction mixture was then poured into cracked ice and water, and the resulting cloudy solution was extracted with ethyl acetate (500 ml × 5). The ethyl acetate solutions were combined, dried over anhydrous sodium sulfate, and evaporated to leave a yellow oil, which solidified on standing at room temperature. The solid was crushed in cool ethanol, filtered off, and then further purified by recrystallization from ethanol, giving the desired peri-eight-membered ring compound, **3** (43 g; yield, 55%) as colorless prisms.

*8,8,10,10-Tetrakis(hydroxymethyl)-8,9,10,11-tetrahydro-7H-cycloocta[de]naphthalene (**4**).* To a stirred slurry of 10 g of lithium aluminum hydride in 1 l of absolute ether, there was added a suspension of 30 g of the ester **3** in 200 ml of absolute

ether at a rate sufficient to maintain gentle boiling. After the addition was complete, the mixture was boiled under reflux, with vigorous stirring for an additional 120 hr. The excess lithium aluminum hydride was then decomposed by the addition of ethyl acetate, followed by that of 2M-aqueous hydrochloric acid. The resulting white precipitate was collected and extracted with 2 l of boiling ethyl acetate for 3 hr. The extracts and filtrate were then combined, and the solvent was evaporated. The residual solid was washed with 100 ml of diluted hydrochloric acid and recrystallized from methanol, giving the tetrol **4** (16 g; yield, 80%), as fine, colorless needles.

8,8,10,10-Tetrakis(benzoyloxymethyl)-8,9,10,11-tetrahydro-7H-cycloocta[de]*naphthalene (5).* The tetrol **4** (0.1 g), was treated with benzoyl chloride (2 ml) in pyridine (3 ml) at 60 °C for 1 hr, after which the mixture was left at room temperature for 2 days. After the reaction had been completed, the reaction mixture was poured into ice and water and extracted with ethyl acetate. The usual work-up of the ethyl acetate solution gave a brown oil, which crystallized on the addition of cool methanol. After separation, the crystals were further purified by two recrystallizations from benzene–methanol to give the benzoate **5** as colorless needles (0.16 g; yield, 70%).

*8,8,10,10-Tetrakis(*p*-toluenesulfonyloxymethyl)-8,9,10,11-tetrahydro-7H-cycloocta*[de]*naphthalene (6).* To a stirred suspension of 3 g of the tetrol **4** in 19 ml of pyridine, there was added a solution containing 12 g of *p*-toluenesulfonyl chloride and 12 ml of pyridine. The mixture was shaken vigorously for 1 min and then left at room temperature for 7 days. The reaction mixture was poured into 70 ml of ice and water, and the mixture was stirred well for 1 hr at 0 °C. The resulting precipitates were collected and recrystallized from methanol–benzene, yielding 8.6 g (yield, 97%) of the tosylate **6** as colorless needles.

8,8,10,10-Tetrakis(acetoxymethyl)-8,9,10,11-tetrahydro-7H-cycloocta[de]*naphthalene (7).* A mixture of the tetrol **4** (0.1 g), acetic anhydride (5 ml), and pyridine (5 ml) was heated at 60 °C on a water bath, with occasional shaking, for 30 min. The resulting clear solution was then allowed to stand at room temperature for 3 days to complete the reaction. The reaction mixture was poured into 50 ml of ice water; the mixture was stirred at 0 °C for 30 min and then left at room temperature for an additional 3 hr. The solid thus precipitated was collected and recrystallized from ethanol to give the acetate **7** (0.14 g; yield, 92%), as colorless needles.

8,8,10,10-Tetrakis(methanesulfonyloxymethyl)-8,9,10,11-tetrahydro-7H-cycloocta[de]*naphthalene (8).* To a suspension of 0.2 g of the tetrol **4** in 2 ml of pyridine, there was added 1 ml of methanesulfonyl chloride, after which the mixture was shaken vigorously for 10 min. After being left at 0 °C for 1 hr, the reaction mixture was poured into 100 ml of ice water and the mixture was stirred well at 0 °C for 30 min. The solid thus precipitated was filtered off, washed with methanol, and dried *in vacuo*. Recrystallization of this solid from dimethyl sulfoxide–methanol–water yielded the mesylate **8** as a colorless microcrystalline solid (0.3 g; 76%).

*8,8,10,10-Tetrakis(*p*-bromobenzenesulfonyloxymethyl)-8,9,10,-11-tetrahydro-7H-cycloocta*[de]*naphthalene (9).* To a stirred suspension of 0.2 g of the tetrol **4** in 2 ml of pyridine, was added a solution of *p*-bromobenzenesulfonyl chloride (1.2 g) in pyridine (2 ml). The mixture was stirred at room temperature for 30 min and then left at room temperature for an additional 2 days. The reaction mixture was poured into 50 ml of ice water, and the mixture was stirred well for 30 min. The white solid thus precipitated was filtered off, washed with methanol, and dried *in vacuo*. Then it was purified by recrystallization from chloroform–methanol–water to give the brosylate **9** (0.56 g; 75%), as microcrystals.

References

1) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y. (1965). (b) H. Hanack, "Conformation Theory," Academic Press, New York, N. Y. (1965). (c) G. Binsch, "Topics in Stereochemistry," Vol. 3, ed. by E. L. Eliel and N. L. Allinger, Interscience Publishers, New York, N. Y. (1968), p. 97. (d) H. Booth, "Progress in NMR Spectroscopy," Vol. 5, ed. by J. W. Emsley, J. Feeney, and C. H. Sutcliffe, Pergamon Press, Oxford (1969), p. 149.

2) V. Balasubramanian, *Chem. Rev.*, **66**, 567 (1966).

3) S. F. Nelsen and J. P. Gillespie, *J. Amer. Chem. Soc.*, **95**, 2940 (1973).

4) V. Boekelheide and G. K. Vick, *ibid.*, **78**, 653 (1956).

5) R. H. Mitchell and F. Sondheimer, *Tetrahedron*, **34**, 1397 (1968).

6) K. N. Welch, *J. Chem. Soc.*, **1931**, 673.

7) T. J. Otterbacher, "Organic syntheses," Coll. Vol. I, p. 290 (1941).

8) J. G. Colson, P. T. Lansbury, and F. D. Saeva, *J. Amer. Chem. Soc.*, **89**, 4987 (1967), and references cited therein.

9) A. W. Brinkmann, M. Gordon, R. G. Harvey, P. W. Rabideau, J. B. Stothers, and A. L. Ternay, Jr, *ibid.*, **92**, 5912 (1970).

10) W. L. Meyer, D. L. Davis, L. Foster, A. S. Levinson, V. L. Sawin, D. C. Shew, and R. F. Weddleton, *ibid.*, **87**, 1573 (1965).

11) G. V. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

12) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Amer. Chem. Soc.*, **82**, 1256 (1960).

13) E. W. Garbisch and M. G. Griffith, *ibid.*, **90**, 6543 (1968).

14) R. E. Mayo and J. H. Goldstein, *Mol. Phys.*, **10**, 301 (1966).

15) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London (1959), Chapter 7.

16) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco (1964), p. 183.

17) K. B. Wiberg, B. R. Lowry, and B. J. Nist, *J. Amer. Chem. Soc.*, **84**, 1594 (1962).

18) A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegell, *Tetrahedron Lett.*, **1964**, 233.

19) M. J. T. Robinson, *ibid.*, **1965**, 1685.

20) D. R. Davis and J. D. Roberts, *J. Amer. Chem. Soc.*, **84**, 2252 (1962).

21) D. H. Williams and N. S. Bhacca, *ibid.*, **85**, 2861 (1963).

22) N. S. Bhacca, J. E. Gurst, and D. H. Williams, *ibid.*, **87**, 302 (1965).