Medium-Sized Cyclophanes. VII. 4,14-Disubstituted [2.2]Metacyclophanes[1]

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The stereoselective syntheses of 4,14-dimethyl- and 4,14-dimethoxy[2.2]metacyclophanes have been achieved by the modified Wurtz dimerization reaction carried out under extremely mild conditions. A series of further 4,14-disubstituted [2.2]metacyclophanes have been derived from the dimethyl derivative **4**. The nmr spectra of these compounds were examined in relation to the electronic and long-range effects of the substituents to the aryl and methylene signals. The chemical shift difference in protons *meta* to the substituent was correlated with Hammett σ_m constant; $-\rho_{6,12\text{-H}} = 28.2$ cps/σ_m and $-\rho_{8,16\text{-H}} = 14.5$ cps/σ_m. Whereas 1,2-methylene protons, especially those in the equatorial position, deviated largely, good linear relations were observed in 9,10-methylene absorption; $-\rho_{9,10\text{-ax}} = 6.88$ cps/σ_p and $-\rho_{9,10\text{-eq}} = 14.4$ cps/σ_p.

As the results of improvement[2,3] in the synthesis of [2.2]metacyclophane (**1**), a number of structural, spectroscopic, and chemical studies were carried out.[3] However, only a little is known about the chemistry of its derivatives. Attempts to introduce a functional group by means of electrophilic substitution reactions all failed and were led to the formation of 4,5,9,10-tetrahydropyrene or its derivatives.[2,4,5] Attempted reactions of **1** with various reagents, including alkyl metal, halogen, and oxidants, have also failed, so far, to introduce functionality into the side chain.[3] These results may be compared with the *para* counterpart in which nuclear[6] as well as side-chain[7] substitution reactions have been successfully applied to obtain a number of the derivatives.

Boekelheide and his coworkers have prepared 8,16-dimethyl[2.2]metacyclophane[8] and its derivatives[9] either by the bimolecular Wurtz method or by using multistepped reactions taking advantage of an efficient cyclization reaction of 3,3′-bis(bromomethyl)bibenzyl derivatives. They have also prepared[10] 5,13-dimethyl and -dimethoxy derivatives **2** (R = CH_3 or CH_3O) in 7 and 2.5% yields, respectively, by the dimerization of appropriate bis(bromomethyl) compounds, whereby noticing a marked decrease in the yields especially in the case of the preparation of **2** with electronegative substituents.

Isomeric 4,12- or 4,14-disubstituted [2.2]metacyclophanes may also be prepared by the similar dimerization method. An attempted reaction of 2,4-bis(bromomethyl)toluene with sodium and tetraphenylethylene, however, has resulted in the formation of trimer or tetramer.[11]

This paper will describe the preparation of these unknown isomers, and particularly the stereochemistry of the syntheses of 4,14-dimethyl and -dimethoxy derivatives **4** and **6** and 4,12-dimethoxy derivative **7** and nmr spectra of these as well as several derivatives derived from dimethyl compound **4**. A part of the results have already appeared in a preliminary form.[12]

Stereoselective Syntheses of 4,14-Disubstituted [2.2]-Metacyclophanes.—The chloromethylation[13] under forced conditions of toluene or anisole afforded the corresponding bis(chloromethyl) derivatives **3**. Bimolecular Wurtz condensation reaction of **3** may be conceived to afford 4,14 (**4** or **6**) and 4,12 derivatives (**5** or **7**). The reaction of **3** (R = CH_3) with disodium tetraphenylethane in a tetrahydrofuran solution after the method of Müller and Röscheisen[14] was carried out under high-dilution conditions which were realized by the slow addition of the halide (68 hr) at −60 to −70° to the condensing agent. By distillation under reduced pressure of the reaction mixture, a crystalline material, mp 68–69°, was obtained. Molecular weight determination and elemental analyses supported the formula $C_{18}H_{20}$.

The structural determination was achieved by the nmr spectral studies. As is shown in Figure 1 the compound showed a methyl proton signal as a singlet at δ 2.36 and intraannular aryl protons at δ 4.22 as a doublet (J = 1.8 cps) together with the rest of aryl proton signals at about δ 7.0 as an ABX pattern (not shown). The appearance of the doublet at an unusually high field is indicative of the generation of the [2.2]metacyclophane structure, since the intraannular protons (8,16 protons), which are extended over the diametrical benzene ring, should experience shielding by the diamagnetic ring current. It has already been shown that the ten-membered ring in **1** exists in a rigid-chair conformation as is evidenced by the appearance of an A_2B_2 type signal,[4,15,16] which is not affected over a wide range of temperatures between *ca.* −80 and 190°,[1,12] arising from axial and equatorial protons in the methylene group. In such compounds as **4**, in which two substituents are located in both of the *ortho* positions of one of the ethylene bridges, the methylene signals should be composed of two sets of A_2B_2 pattern, while in the *trans* compound such as **5** they would no longer be a simple A_2B_2 type but an ABCD type. An examination of the nmr spectra of the dimethyl derivative (Table II) re-

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[1] Part VI: T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Jap.*, **41**, 218 (1968).

[2] M. Fujimoto, T. Sato, and K. Hata, *ibid.*, **40**, 600 (1967).

[3] R. W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963).

[4] N. L. Allinger, M. A. Da Rooge, and R. B. Hermann, *J. Amer. Chem. Soc.*, **83**, 1974 (1961); N. L. Allinger, B. J. Gordon, S.-E. Hu, and R. A. Ford, *J. Org. Chem.*, **32**, 2272 (1967).

[5] T. Sato, M. Wakabayashi, Y. Okamura, T. Amada, and K. Hata, *Bull. Chem. Soc. Jap.*, **40**, 2363 (1967).

[6] For recent papers see D. J. Cram and H. P. Fischer, *J. Org. Chem.*, **30**, 1815 (1965); D. J. Cram and A. C. Day, *ibid.*, **31**, 1227 (1966); B. E. Norcross, D. Becker, R. I. Cukier, and R. M. Schutz, *ibid.*, **32**, 220 (1967); S. C. Dickerman and N. Milstein, *ibid.*, **32**, 852 (1967).

[7] *Cf.* E. Hedaya and L. M. Kyle, *J. Amer. Chem. Soc.*, **88**, 3667 (1966).

[8] W. S. Lindsay, P. Stokes, L. G. Humber, and V. Boekelheide, *ibid.*, **83**, 943 (1961).

[9] V. Boekelheide and J. B. Phillips, *ibid.*, **85**, 1545 (1963); **89**, 1695 (1967); J. B. Phillips, R. J. Molyneux, E. Sturm, and V. Boekelheide, *ibid.*, **89**, 1704 (1967); V. Boekelheide and T. Miyasaka, *ibid.*, **89**, 1709 (1967).

[10] V. Boekelheide and R. W. Griffin, Jr., unpublished work cited in ref 3.

[11] R. W. Griffin, Jr., and C. R. Slator, unpublished work cited in ref 3.

[12] T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Jap.*, **39**, 856 (1966).

[13] R. C. Fuson and C. H. McKeever, *Org. Reactions*, **1**, 63 (1942).

[14] E. Müller and G. Röscheisen, *Chem. Ber.*, **90**, 543 (1957).

[15] D. J. Wilson, V. Boekelheide, and R. W. Griffin, Jr., *J. Amer. Chem. Soc.*, **82**, 6302 (1960).

[16] H. S. Gutowsky and C. Juan, *J. Chem. Phys.*, **37**, 120 (1962).

Table I

Physical Properties of 4,12- and 4,14-Disubstituted Derivatives

Compd	Mp, °C	Formula	Mol wt		Carbon, %		Hydrogen, %	
			Calcd	Found	Calcd	Found	Calcd	Found
4	68–69	$C_{18}H_{20}$	236.34	236[a] 235[b]	91.47	91.34	8.53	8.34
6	132–134	$C_{18}H_{20}O_2$	268.34	268[a] 266[b]	80.56	80.60	7.51	7.45
7	182	$C_{18}H_{20}O_2$	268.34	268[a]				
8	170	$C_{18}H_{18}Br_2$[c]	394.16	394[a]	54.85	54.61	4.60	4.33
9	>300	$C_{18}H_{16}O_4$	296.31		72.96	72.60	5.44	5.51
10	117–120	$C_{18}H_{16}O_2$	264.31		81.79	80.99	6.10	5.98
12	196–197	$C_{18}H_{14}N_2$	258.31		83.69	83.36	5.46	5.78

[a] Determined by mass spectrometry. The measurements were carried out with Hitachi RMU-6D high-resolution mass spectrometer using an electron current of either 40 or 70 eV. The authors are grateful to the members of Naka works of Hitachi Co. for providing us with the data. [b] Determined by the Rast method. [c] Calcd: Br, 40.55. Found: 40.42.

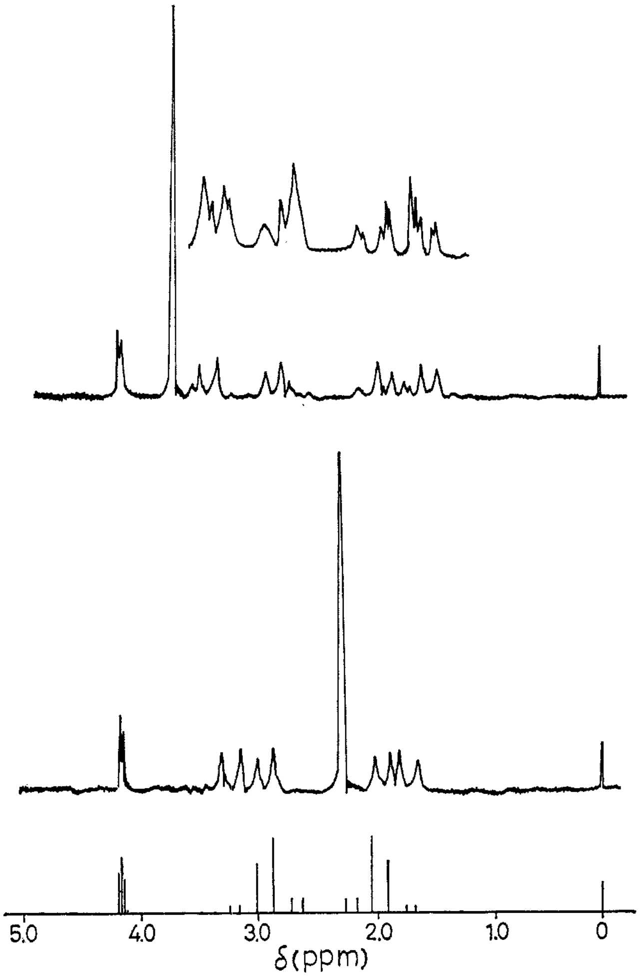


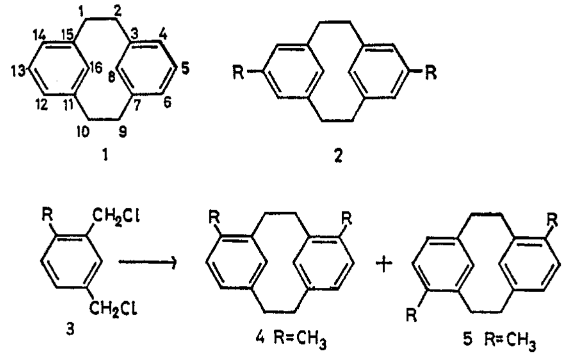
Figure 1.—Nmr spectra of 4,12-dimethoxy[2.2]metacyclophane (7), 4,14-dimethoxy[2.2]metacyclophane (6), and 4,14-dimethyl-[2.2]metacyclophane (4) from top to bottom. For comparison a line spectrum of [2.2]metacyclophane (1) is also shown.

vealed that the methylene region absorption could be analyzed as an overlap of an A_2B_2 pattern similar to 1 occurring at δ 2.99 and 1.99 (unsubstituted side, 9,10-H) and an $A'_2B'_2$ pattern at δ 3.28 and 1.76 (substituted side, 1,2-H). The structure **4** was thus assigned to the compound, which was formed in a 21% yield. A more direct evidence in favor of the structure was obtained by the optical resolution of **4**[1,12,17] which was achieved by a complex formation with the Newman's reagent.[18]

Careful examination of the reaction product either by alumina column chromatography or by gas chromatography[19] using SE-30 on Chromosorb W, Carbowax 20M on Chromosorb W, or neopentyl glycol adipate on Chromosorb G column revealed that the material was uniform.

The stereoselectivity observed in the formation of **4** was further experienced in the synthesis of dimethoxy analogs **6** and **7**. A similar condensation reaction of **3** (R = CH_3O) which was carried out over 184 hr at −20 to −40° furnished two products by chromatography on alumina. *n*-Hexane first eluted a minor compound, mp 182°, which was followed by the major product, mp 132–134°, both having expected analytical values and molecular weight as dimethoxy[2.2]metacyclephane (Table I). The low-melting isomer, formed in a 9% yield, was assigned the structure 4,14-dimethoxy compound (**6**)[20] from nmr spectrum (Figure 1) which consisted of signals at δ 6.92, 6.70 (ABX-type absorption, 5,6,12,13-H), 4.25 (doublet, J = 1.8 cps, 8,16-H), 3.80 (singlet, CH_3O) together with two sets of A_2B_2 patterns at δ 2.94 and 2.00 (9,10-H) and δ 3.50 and 1.59 (1,2-H). On the other hand, the high-melting isomer showed a complex absorption in the methylene region as is shown in Figure 1 indicating that the compound be isomeric 4,12-dimethoxy compound **7** (Scheme I).

Scheme I



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[17] Due to restricted inversion of a ten-membered ring in the [2.2]metacyclophane system, 4,14-disubstituted derivatives and also other suitably substituted compounds may exist as racemic molecules.

[18] M. S. Newman and W. B. Lutz, *J. Amer. Chem. Soc.*, **78**, 2469 (1956).

[19] The authors are grateful to Dr. N. Ikekawa of the Institute for Physical and Chemical Research for the measurements.

[20] As a possible clue to the structure, the dipole moment was measured in a benzene solution at 20° and was found to be μ = 0.79 D. The value, although compatible with structure **6**, may not, however, be used positively for the distinction between **6** and **7**, since the dipole moment of the *trans* compound **7** may not necessarily be zero due to conformational mobility of the methoxyl group. For detailed studies on the conformation of methoxyl group in several condensed ring systems deduced from dipole moment data see: K. B. Everard and L. E. Sutton, *J. Chem. Soc.*, 2312 (1949); 16 (1951).

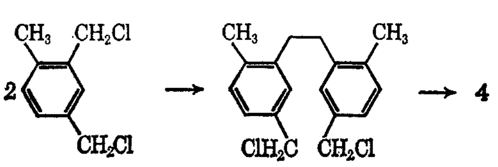
TABLE II

NMR DATA FOR [2.2]METACYCLOPHANE (1) AND 4,14-DISUBSTITUTED DERIVATIVES[a]

		Aryl protons					Methylene protons			
							9,10-H[d]		1,2-H[d]	
Compd	Substituent	5,13-H[b]	6,12-H[b]	$J_{5,6(12,13)}$	8,16-H[c]	$J_{8,6(12,16)}$	Equatorial	Axial	Equatorial	Axial
6	OCH_3	402.1	415.5	9.0	255.0	1.8	176.1	119.7	210.3	95.6
4	CH_3	424.5	411.3	8.0	252.9	1.8	179.5	119.5	197.0	105.6
1	H	430.8[e]	418.2[e,f]	8.0	254.8	1.8	182.9	122.7	182.9	122.7
8	CH_2Br	431.4	419.7	8.0	260.1	1.8	184.0	122.6	211.3	137.3
9	COOH	450.7	432.3	8.0	264.7	1.8	189.0	124.6	218.3	121.3
12	CN	451.2	434.0	8.0	264.0	1.8	196.2	128.6	225.0	133.4
10	CHO	477.6	440.8	8.0	261.0	1.8	199.0	131.2	277.3	108.7

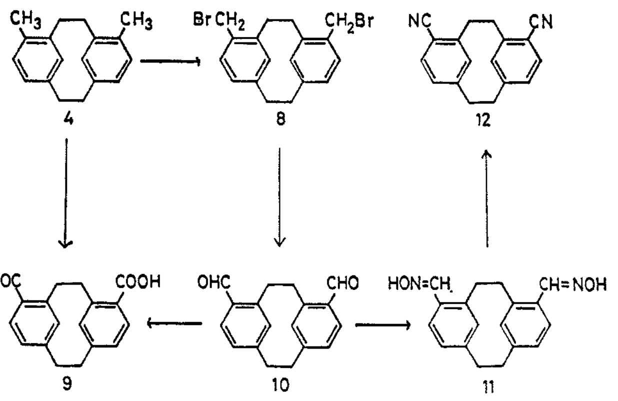
[a] The spectra were recorded with a Varian A-60 spectrometer on a *ca.* 10% (w/v) carbon tetrachloride solution except for **9** which was dissolved in an alkaline deuterium oxide solution. Chemical shifts are expressed in cycles per second (cps) relative to internal TMS as zero. [b] An ABX-type absorption having 6(12)-H weakly coupled with 8(16)-H. [c] Appeared as a doublet except for **1** which showed a triplet. [d] An A_2B_2-type absorption analyzed by AB approximation. [e] An AB_2X-type absorption. [f] Signal for 4,14-H included.

The bimolecular condensation reaction of **3** under extremely mild conditions was thus shown to be highly stereoselective. A combination of low temperature and slow addition is assumed to provide the minimum of the reaction conditions which permit a guiding of the product formation in the desired direction. Especially by using low temperature, a sufficient difference in the activation energies and hence the reactivities between the *o*- and *p*-chloromethyl groups could be realized. The first stage of the condensation of **3** then would afford symmetrical bis(chloromethyl)bibenzyl in preference to the unsymmetrical one no matter which chloromethyl group is more reactive than the other. Further condensation reaction of the intermediate would produce *cis* structure such as **4** or **6**. The relative reactivities of *o*- and *p*-chloromethyl groups were examined by carrying out the competitive Wurtz reaction between *o*- and *p*-methylbenzyl chlorides. Disodium tetraphenylethane solution was added to an equimolar mixture of the methylbenzyl chlorides at −40 to −50°, and the resulting mixture was analyzed by gas chromatography using 5% silicone gum XE-60 on Chromosorb W column. By comparing retention time with the standard samples, the mixture was found to contain 2,2′-dimethylbibenzyl as the major product but not any 4,4′-dimethylbibenzyl. Although the peak was not symmetrical, probably owing to the presence of 2,4′-dimethyl isomer, it was clearly demonstrated that *o*-chloromethyl group was more reactive compared with *p*-chloromethyl group. It may therefore be concluded that the dimerization of 2,4-bis(chloromethyl)toluene would first result in the condensation between *o*-chloromethyl groups to give 5,5′-bis(chloromethyl)-2,2′-dimethylbibenzyl which is then cyclized to the cyclophane **4**.



A series of 4,14-disubstituted [2.2]metacyclophanes bearing various substituents has been prepared for the nmr spectral studies starting from dimethyl compound **4** as is shown in Scheme II. The treatment of **4** with 2 mol of NBS in a carbon tetrachloride solution furnished bis(bromomethyl) derivative **8** in a 60% yield. The preferential bromination of methyl group over methylene group, in contrast to the usual reactivity order, may be ascribed to the inertness of the latter group due to inherent steric restriction that the bridging methylene group is deviated from the plane of benzene ring to discourage the usual charge stabilization associated with a benzyl methylene group.[3] Dialdehyde **10** was obtained either by the Sommelet reaction[21] of **8** in a 57% yield or preferably by the reaction with 2-nitropropane and sodium ethoxide in DMSO[22] in a 89% yield. Dicarboxylic acid **9**, which was obtained with difficulty and only in a poor yield by the direct oxidation of **4** due to the accompanying side reaction,[23] was formed in a high yield by the oxidation of **10** with potassium permanganate. The treatment of **10** with hydroxylamine hydrochloride gave dioxime **11** as a mixture of geometrical isomers, which on dehydration by heating with acetic anhydride afforded dinitrile **12**, the over-all yield from **10** being 37%. The results of molecular weight determinations and elemental analyses for these compounds are summarized in Table I. Infrared spectra were consistent with the structure assigned, and further, nmr spectra (Table II) which showed an intraannular 8,16-proton signal as a doublet (J = 1.8 cps) at δ 4.3–4.4 together with other typical signals, indicated that during these transformations the [2.2]metacyclophane structure was not affected.

SCHEME II



Nmr Spectra Studies.—The molecular geometry of **1** was elucidated by Brown[24] in 1953 using X-ray measurements and was reported to have a steplike arrangement in which two slightly distorted benzene rings lie on

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(21) S. J. Angyal, *Org. Reactions*, **8**, 197 (1954).

(22) B. H. Klanderman, *J. Org. Chem.*, **31**, 2618 (1966).

(23) Attempted reactions of **1** with various oxidizing reagents are summarized in ref 3.

(24) C. J. Brown, *J. Chem. Soc.*, 3278 (1953).

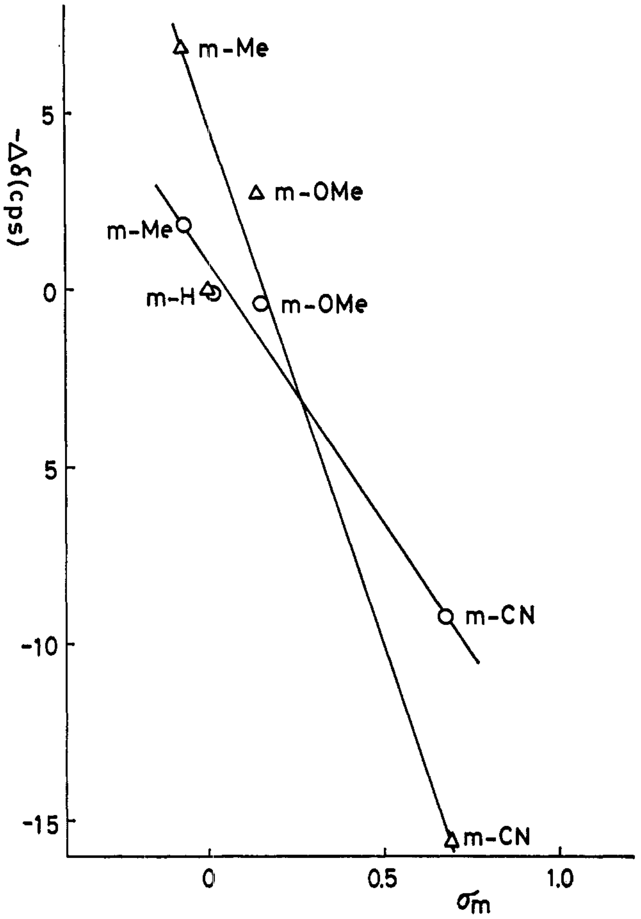

Figure 2.—Plot of chemical shift difference Δδ (cps) against Hammett σ_m: ○, 8,16-H; △, 6,12-H.

parallel planes. As a consequence the ten-membered ring in **1** exists as a rigid-chair form, intraannular 8,16-hydrogens being extended over, or even into, the π-electron cloud of the opposite benzene ring. These structural features have been shown to be well reflected in the nmr spectra.[25] In an effort to test ring current theory, Boekelheide and his coworkers[15] have examined the nmr spectra of **1** and also several derivatives. Their results indicated that shielding predicted on the basis of ring current anisotropy alone is not adequate to account for the observed shifts such as those between the nonequivalent methylene protons or AB_2-type aryl protons. They could, however, provide a qualitative explanation for the unusual upfield shift of almost 3 ppm exhibited by 8,16 protons, by assuming an induced diamagnetic ring current, which predicted a shift of 2.82 ppm. The ethylene bridge protons showed a typical A_2B_2 pattern consisting of two sets of multiplets, each of which was symmetrical about the midpoint of the spectrum. The most prominent peaks in each of the multiplets appeared as doublet. Owing to a rather large difference in the AB chemical shift, which amounted to almost 60 cps, the analysis of the ethylene bridge signal as a simple AB-type absorption seemed to be feasible. In fact, the calculated values[26] obtained in this way, $\delta_A = 2.04$ and $\delta_B = 3.05$, were in good agreement with those obtained by Boekelheide, *et al.*,[15] $\delta_A = 2.03$ and $\delta_B = 2.99$. Thus the analyses of the ethylene bridge proton signals of 4,14-disubstituted derivatives were achieved by this approximation. The main peaks used for the calculations were tabulated in Table III. The difference of 1.01 ppm in the chemical shift between the methylene protons of **1** is far greater than expected since the calculated value assuming ring current anisotropy was only 0.28 ppm.[15] It is considered, however, that the value is underestimated by neglecting ring-current effect of the second benzene ring to which the methylene group is not directly attached. An examination of the molecular model of **1** indicated that the particular methylene group is situated within the influence of the ring current of both of the benzene rings due to the rigid nature of the molecule. The sum of these two terms estimated from the Johnson–Bovey table[27] was found to be 0.50 ppm. Even regarding approximate nature of the ring-current theory, the difference between the observed and the estimated values, which was as large as 0.51 ppm (1.01 − 0.50), indicated the importance of other contributing factors such as methylene–methylene, ring–methylene,[28] and double bond anisotropy terms.

Table III

The Main Peaks of A_2B_2 and $A'_2B'_2$ Systems

	9,10-H (A_2B_2)				1,2-H ($A'_2B'_2$)			
Compd	Equatorial		Axial		Equatorial		Axial	
6	115.3	123.4	172.3	180.5	91.5	100.0	206.1	214.9
4	115.0	123.0	175.9	184.0	100.7	110.2	192.4	202.0
1	118.0	126.5	179.1	187.1				
8	118.2	126.4	180.3	188.5	132.9	141.4	207.2	216.0
9	120.5	128.5	186.2	194.5	116.5	125.5	214.0	223.0
12	128.8	137.5	182.2	200.5	124.8	132.7	221.0	230.0
10	125.0	134.2	195.2	203.2	105.7	115.7	270.2	279.9

That the spectral features of derivatives of **1** are reminiscent of those of the parent hydrocarbon has been well established.[25] Since the authors have prepared a series of 4,14-disubstituted derivatives bearing electron-releasing as well as electron-withdrawing substituents, the nmr spectra of these compounds were examined in relation to the electronic and long-range shielding effects of the substituents to the aryl and methylene proton signals. These derivatives appeared to be particularly suited to study the effect of anisotropy of the substituent, separately from other terms, on each of the axial and equatorial proton signals of conformationally locked methylene group at the *ortho* position. The spectral data, which are summarized in Table II, were determined[29] in a 10% (w/v) carbon tetrachloride solution except for **9**, which was measured in an alkaline deuterium oxide solution using a Varian A-60 spectrometer, and were expressed downfield from TMS in cycles per second or δ (parts per million) units. Aryl protons showed two groups of signals: The outer aryl protons at 5,6(12,13) positions showed an ABX-type absorption, of which assignment was unequivocal since 6(12) protons coupled weakly ($J = 1.8$ cps) with intraannular 8(16) protons. The latter protons appeared as a doublet at unusually high field of 253–265 cps, thus serving as a diagnostic purpose of the genera-

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(25) B. H. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y., 1964, p 407.

(26) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 119.

(27) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

(28) Diamagnetic term due to ring-methylene anisotropy may cause an upfield shift of 0.20 ppm as is estimated from McConnel's equation.

(29) The authors are indebted to Mr. M. Kainosho of Ajinomoto Co., Inc., for the measurements.

tion and transformation of the metacyclophane structure.

Both the 6 and 8 protons are situated in the *meta* position of the 4 substituent just as the 12,16 protons are for the 14 substituent. It has been well established[30,31] that the Hammett σ constant could be correlated with chemical shifts of *meta* and *para* protons in substituted benzene derivatives. In Figure 2, a plot of the chemical shift difference of the 8,16 and 6,12 protons against σ_m[32] is shown. Except for compounds **9** and **10**, there were obtained good linear correlations whereby

$$-\rho_{6,12\text{-H}} = 28.2 \text{ cps}/\sigma_m \text{ and } -\rho_{8,16\text{-H}} = 14.5 \text{ cps}/\sigma_m$$

A rather large difference has been shown to exist between these two values indicating that the effect of the substituents on 8,16 proton signals are less pronounced as compared with the 6,12 proton case. This may indicate that the 8,16 protons, which are much more shielded compared with the usual aryl protons by being extended over the π-electron cloud of the opposite benzene ring, are influenced by the nature of the *meta* substituent in a more or less equalized manner.

The assignment of the bridge methylene protons are summarized in Table II. Of the nonequivalent methylene protons in **1**, one at the high field was ascribed to be due to axial, and one at the low field to equatorial protons. Since 4,14-disubstituted derivatives have no plane of symmetry about the plane bisecting both of the benzene rings, they would show two sets of axial and equatorial proton signals, which, actually, were observed as an overlap of two sets of A_2B_2 patterns. One of these occurring at an approximately similar position to **1** was assigned to be due to the methylene protons of the unsubstituted side, namely the 9,10 protons. The chemical shift difference, $\delta_{\text{ax}} - \delta_{\text{eq}}$, was found to be kept around 1 ppm as in the parent compound. The 9,10-methylene proton signals were affected in a minor degree by changing the substituent. The presence of an electron-withdrawing group caused a downfield shift, whereas an electron-releasing group exhibited an upfield shift. Except for dialdehyde **10**, a good linear correlation was observed between the chemical shift difference and the Hammett σ_p, affording $-\rho_{9,10\text{-ax}} = 9.96 \text{ cps}/\sigma_p$ and $-\rho_{9,10\text{-eq}} = 20.1 \text{ cps}/\sigma_p$. This calculation may, however, be oversimplified by neglecting the contribution from the substituent in the opposite benzene ring, since the benzyl methylene grouping at the 9 or 10 position is regarded also as the β-methylene group in the phenethyl moiety. Thus by taking into account the $-\rho$ value of methyl protons[31] for *para*-substituted toluenes (12.5 cps/σ_p) as well as that for *para*-substituted ethylbenzenes (6.76 cps/σ_p), the substituent effect was correlated with better precision by using a modified Hammett relationship $\delta_R - \delta_H = \rho(\sigma_p - 6.76/12.5\sigma_p)$ instead of the usual Hammett equation used above. The calculated values, $-\rho_{9,10\text{-ax}} = 6.78 \text{ cps}/\sigma_p$ and $-\rho_{9,10\text{-eq}} = 14.4 \text{ cps}/\sigma_p$ (Figure 3), not only had higher consistency and less deviation but are more compatible with $-\rho$ of *para*-substituted toluenes, in which the methyl protons are conformationally equalized. The difference in ρ_{ax} and ρ_{eq} indicates that axial protons, which are more shielded than equatorial ones and make an angle of about 60° with a benzene plane, are less sensitive to the electronic effect than the equatorial ones which lie approximately in the plane of benzene ring. The cause of the phenomena, which is not explainable on the basis of ring-current effect, may be due partly to the σ–π interaction between the rear lobe of the sp^3 orbital of the bridge carbon used in the bonding with equatorial hydrogen and the π-electron system of the aromatic ring as in the case of the anti proton at C-9 of substituted benzonorbornenes.[33]

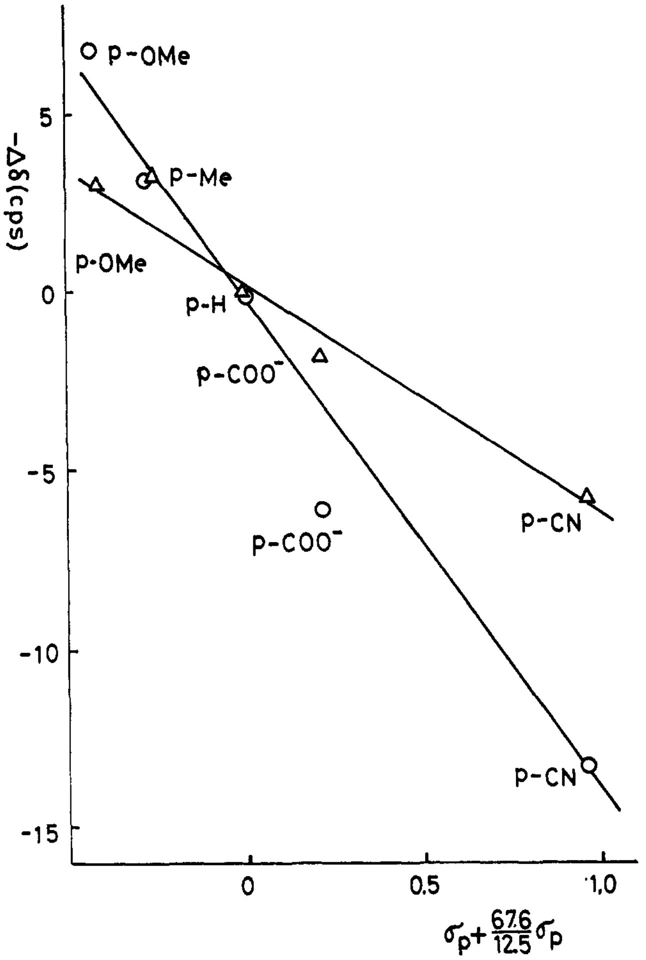

Figure 3.—Plot of chemical shift difference $\Delta\delta$ (cps) of 9,10-methylene protons against Hammett $\sigma_p + 6.76/12.5\ \sigma_p$: O, equatorial H; Δ, axial H.

In Figure 4, chemical shifts of axial and equatorial protons at 1,2 positions relative to various substituents are illustrated. If the chemical shift is only dependent on the inductive and mesomeric effect of the substituents, a linear correlation similar to the 9,10 proton case may be expected. It was found, however, that the difference in the chemical shift between the axial and equatorial protons increased and varied widely. For example, the difference reached 114.7 and 168.6 cps in dimethyl ether **6** and dialdehyde **10**, respectively. Although the axial proton did not suffer from a large deviation, except for **6** and **10**, the equatorial proton experienced a marked downfield shift which amounted to

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[30] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High-Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Ltd., London, 1966, p 752.

[31] S. H. Marcus, W. F. Reynolds, and S. I. Miller, *J. Org. Chem.*, **31**, 1872 (1966).

[32] L. P. Hammett, *J. Amer. Chem. Soc.*, **59**, 96 (1937).

[33] N. Inamoto, S. Masuda, K. Tori, K. Ando, and H. Tanida, *Can. J. Chem.*, **45**, 1185 (1967).

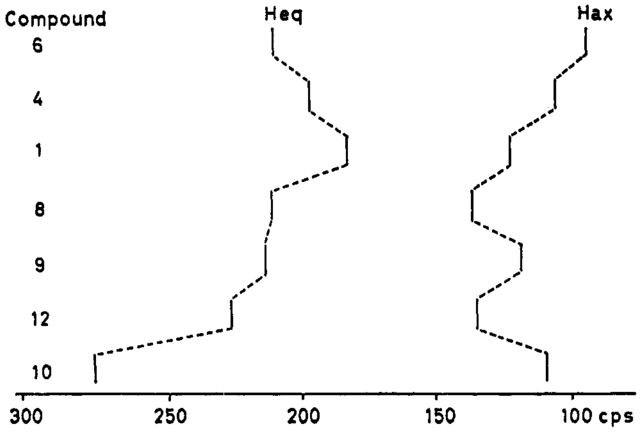

Figure 4.—Chemical shifts (cycles per second downfield from TMS) of axial (H_{ax}) and equatorial (H_{eq}) protons of 1,2-methylene group in [2.2]metacyclophane and its 4,14-disubstituted derivatives.

24.2 and 78.3 cps in the case of **6** and **10** (the chemical shift difference between $1,2_{eq}$ and $9,10_{eq}$ protons). These deviation may be caused by long-range shielding effects which are governed by the conformational preference of the substituent and the anisotropy terms of benzene ring and the substituent group.

Experimental Section[34]

4,14-Dimethyl[2.2]metacyclophane (4).—According to the method of Müller and Roscheisen,[14] disodium tetraphenylethane solution was prepared from 5 g (excess) of sodium and 3.5 g (0.011 mol) of tetraphenylethylene in 300 ml of absolute tetrahydrofuran (THF). To the above mixture was added, with stirring, a solution of 12 g (0.064 mol) of 2,4-bis(chloromethyl)toluene[35] [bp 146–160° (14–15 mm), mp 43–45° (from hexane)] dissolved in 500 ml of tetrahydrofuran at −60 to −70° through a specially designed dropping funnel over a period of 68 hr, the whole operation being conducted under a current of nitrogen. After the addition was completed a small amount of ethanol was added, and the reaction mixture was filtered. The concentrated mixture was then extracted with ether. The distillation of extract at 183° (12 mm) gave 1.56 g of colorless oil, which crystallized as colorless needles: mp 68–69°; $\lambda_{max}^{C_6H_{12}}$ 276 mμ (ε 673); ν_{max}^{KBr} 2900, 2810, 1490, 1170, 812, and 742 cm^{-1}.

The crude distillate was examined carefully by gas chromatography. By using a 5-ft column of 2.0% CNSi on Anakrom U with a nitrogen flow rate of 36 cc/min or a 6-ft column of 1.5% SE-30 on Anakrom U with a nitrogen flow rate of 80 cc/min only a sharp peak due to **4** was detectable: retention times for each column were 8.1 and 5.6 min, respectively.[19] It was also examined by several other columns including 10% SE-30 on Chromosorb W (6 ft), 10% Carbowax 20M on Chromosorb W (6 ft), and 4% neopentyl glycol adipate on Chromosorb G (6 ft). In no case was another peak due to isomeric **5** detectable.

The Competitive Wurtz Reaction of *o*-Methylbenzyl Chloride and *p*-Methylbenzyl Chloride.—A mixture of 1.24 g (9.1 mmol) of *o*-methylbenzyl chloride and 1.14 g (8.3 mmol) of *p*-methylbenzyl chloride was dissolved in 250 ml of tetrahydrofuran. In another vessel a solution of sodium–tetraphenylethylene adduct was prepared from 2.0 g (0.087 g-atom) of sodium in 200 ml of THF. The solution of condensing agent was added, with stirring and under a nitrogen current, into the competing mixture in the course of 13 hr, while the reaction temperature was maintained at −40 to −50°. The analysis of the reaction mixture by gas chromatography (Hitachi K-53 gas chromatography with a hydrogen flame ionization detector) using 5% silicone gum XE-60 on a Chromosorb W (60–80 mesh) column operated at 130° with a flow rate of 50 cc/min of nitrogen showed the presence of a material having a retention time of 23.6 min. The gas chromatography of the standard sample under the same conditions revealed that 4,4′-dimethylbibenzyl, mp 82–83° (lit.[36] mp 82–83°), and 2,2′-dimethylbibenzyl, mp 65–66° (lit.[37] mp 66–67°), had retention times of 21.4 and 23.4 min, respectively. Hence the main product was deduced to be 2,2′-dimethylbibenzyl.

4,14- and 4,12-Dimethoxy[2.2]metacyclophanes (6 and 7).—A solution of 40 g (0.20 mol) of 2,4-bis(chloromethyl)anisole,[38] bp 130–150° (2 mm), mp 64–66° (from petroleum ether (bp 30–60°)), in 760 ml of tetrahydrofuran was added dropwise, in the course of 184 hr, to a solution of the condensing agent, which was prepared from 16 g of sodium added to 5.0 g (0.015 mol) of tetraphenylethylene in 300 ml of absolute tetrahydrofuran at −40 to −20° under a current of nitrogen. After working up as described for the methyl analog, ether extract was subjected to vacuum sublimation at 100–130° (0.3–0.7 mm), thus obtaining 3.7 g of colorless crystalline material, which was then passed through an alumina column using *n*-hexane as an eluent. Tetraphenylethylene and tetraphenylethane came out first, followed by a compound which was found to be **7** as evidenced by its nmr spectrum (see Figure 1): mp 182° (recrystallized from ethanol); ν_{max}^{KBr} 1239, 1099, and 810 cm^{-1}.

The next few fractions contained a mixture of **6** and **7**. Then compound **6**, which was isolated in a 9.2% yield, followed: colorless needles; mp 132–134°; $\lambda_{max}^{C_6H_{12}}$ 290 mμ (ε 3380); ν_{max}^{KBr} 1238, 1088, and 796 cm^{-1}; dipole moment μ = 0.79 D (benzene solution at 20°).

Gas chromatography, carried out using a 1-m column of 5% silicone XE-60 on Chromosorb W, could not distinguish between **6** and **7** since both compounds had equal retention times (6.2 min).

4,14-Bisbromomethyl[2.2]metacyclophane (8).—To a solution of 2.6 g (0.011 mol) of **4** in 40 ml of carbon tetrachloride was added 4.0 g (0.023 mol) of N-bromosuccinimide and a few milligrams of benzoyl peroxide. After being kept at reflux for 8 hr, the mixture was filtered and the filtrate was concentrated to about 10 ml. A crude material, mp 161–166°, was obtained as colorless needles, which on repeated recrystallizations from carbon tetrachloride melted at 170°. An optimum yield of 60% was obtained by this method: ν_{max}^{KBr} 2940, 2840, 1600, 1580, and 1430 cm^{-1}.

[2.2]Metacyclophane-4,14-dicarbaldehyde (10). **A.**—A mixture of 2.4 g (6.1 mmol) of **8**, 2 ml of water, 40 ml of glacial acetic acid, and 2.0 g (0.014 mol) of hexamethylenetetramine was heated under reflux for 2 hr. An additional 25 ml of water was added and reflux was continued for 15 min. The reflux was further continued for 5 min by adding 2 ml of concentrated hydrochloric acid. After being diluted with water, the whole was extracted with several portions of ether. A crude material, mp 110–120°, was obtained in a 57% yield. Three recrystallizations from ethanol afforded colorless powder, mp 117–120°.

B.—A sodium ethoxide solution made by adding 0.46 g (0.02 g-atom) of sodium to 30 ml of ethanol, containing 3.0 g (0.034 mol) of 2-nitropropane, was added to a solution of 3.3 g (8.5 mmol) of **8** dissolved in 50 ml of DMSO in the course of 30 min. After the reaction mixture was kept at room temperature for 4 hr under stirring, it was diluted with 200 ml of water and allowed to stand overnight in the refrigerator. A crude material, mp 110–120°, which totaled 1.99 g (89% yield), was obtained as colorless powder by filtration of mixture. Final purification was achieved either by repeated recrystallizations or by column chromatography on alumina: mp 117–120°; $\lambda_{max}^{C_6H_{12}}$ 266 mμ (ε 19,200), and 300 (3250); ν_{max}^{KBr} 1688 cm^{-1}.

4,14-Dicyano[2.2]metacyclophane (12).—A mixture of 100 mg (0.38 mmol) of **10**, 70 mg (1 mmol) of hydroxylamine hydrochloride, and 3 ml of ethanol was warmed at 30–40° for 20 hr. On concentration a white solid separated, which consisted of oxime **11** (ν_{max}^{KBr} 3535 and 930 cm^{-1}) containing a small amount of dinitrile **12** which exhibited an additional absorption at 2200 cm^{-1}. Without further purification, the material was refluxed with 3 ml of acetic anhydride for 2 hr. On cooling a crystalline material, 33 mg (34% yield), found to be **12**, mp 185°, was separated. A purified material, mp 196–197°, was obtained as colorless needles on recrystallization from ethanol or acetic anhydride: λ_{max}^{EtOH} 286 mμ (ε 2330) and 245 (sh); ν_{max}^{KBr} 2200 cm^{-1}.

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(34) All melting and boiling points are uncorrected. The authors are grateful to Mr. S. Hayashi of Nihon University for providing uv data.

(35) M. G. Blanc, *Bull. Soc. Chim. Fr.*, [4] **33**, 313 (1923).

(36) E. I. du Pont de Nemours and Co., British Patent 583,634; *Chem. Abstr.*, **41**, 2749*d* (1947).

(37) J. Meisenheimer, O. Beisswenger, H. O. Rauffman, U. V. Rummer, and J. Link, *Ann.*, **468**, 216 (1929).

(38) R. Quelet and M. Anglade, *Bull. Soc. Chim. Fr.*, [5] **3**, 2200 (1936).

[2.2]Metacyclophane-4,14-dicarboxylic Acid (9). A.—A mixture of 250 mg (1.1 mmol) of **4**, 900 mg (5.7 mmol) of potassium permanganate, and 10 ml of water containing 1 ml of sulfuric acid was heated under reflux for 1 hr. The reflux was further continued for 30 min by adding additional 500 mg of potassium permanganate. After being made acidic with hydrochloric acid, the mixture was extracted continuously with benzene. A small amount of **9**, which did not melt below 300°, was obtained by extraction with a sodium hydroxde solution, $\nu_{\max}^{\mathrm{KBr}}$ 1680 cm^{-1}.

B.—To a solution of 200 mg (0.76 mmol) of **10** in 7.5 ml of acetone, 8 ml of 3.2% potassium permanganate solution was added with stirring during the course of 1 hr at 50–80°. After filtration, the filtrate was made acidic and 192 mg (86% yield) of a crystalline material was collected. It was recrystallized from acetic acid as colorless plates: mp >300°; $\lambda_{\max}^{\mathrm{EtOH}}$ 250 mμ (sh), 286 (ϵ 2330), and 355 (43); $\nu_{\max}^{\mathrm{KBr}}$ 1680 cm^{-1}.

Registry No.—**1,** 2319-97-3; **4,** 16620-99-8; **6,** 10125-36-7; **7,** 16621-01-5; **8,** 16621-02-6; **9,** 16621-03-7; **10,** 16621-04-8; **12,** 16621-05-9.

Acenaphthene Chemistry. IX.[1,2] The Synthesis and Epoxidation of 2a,3,4,5-Tetrahydroacenaphthylene

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2a,3,4,5-Tetrahydroacenaphthylene (I) was synthesized. This compound, when treated with *m*-chloroperbenzoic acid, formed *trans*-1-(2-hydroxy-2a,3,4,5-tetrahydroacenaphthyl) *m*-chlorobenzoate, *via* the intermediate epoxide. Hydrolysis of the ester formed *trans*-1,2-dihydroxy-2a,3,4,5-tetrahydroacenaphthene.

Only two attempts to epoxidize an acenaphthylene are described in the literature. In 1939, Wittig and Henkel[4] treated 1,2-diphenylacenaphthylene with perbenzoic acid in chloroform but were only able to isolate 1,8-dibenzoylnaphthalene. Bartlett and Brown[5] found the reaction to lead to the formation of a complex mixture from which they isolated 1,2-diphenylacenaphthylene glycol, 1,2-diphenyl-1,2-dichloroacenaphthene, 1,1-diphenylacenaphthenone, and 1,8-dibenzoylnaphthalene.

It is possible that, in acenaphthylene, delocalization of the electrons of the double bond is sufficient to reduce its nucleophilic character such that the molecule is sensitive to gross oxidative effects such as radical attack, but insensitive toward less electrophilic systems. This is reasonable in view of the fact that Bartlett and Brown found, among their products, 1,2-dichloro-1,2-diphenylacenaphthene which could arise from radical breakdown of the solvent chloroform.

We treated acenaphthylene with the nitrile–hydrogen peroxide system described by Payne,[6] but the starting material was recovered nearly quantitatively. 1,2-Diphenylacenaphthylene was similarly unreactive.

Base-catalyzed elimination of HX from *trans* halohydrins offers another possible route to epoxides. Even though the halohydrin formed by addition of hypohalite to acenaphthylene could not assume a *trans* coplanar arrangement, since the bridge substituents are in an eclipsed conformation, the possibility that HX elimination would proceed to give an epoxide could not be excluded. The treatment of acenaphthylene with a solution of "hypochlorous acid"[7] resulted in no change.

The properties of acenaphthylene[8] suggest that the double bond is not epoxidized since it is part of an essentially aromatic system. The 2a,3,4,5-tetrahydroacenaphthylene ring system, however, resembles the readily epoxidized indene and thus we visualized a synthesis of acenaphthylene oxide through its tetrahydro derivative.

Only one example of a 2a,3,4,5-tetrahydroacenaphthene ring system is reported in the literature. Buchta and Maar[9] described the synthesis of the 1,2-diphenyl-2a,3,4,5-tetrahydroacenaphthylene (II). We find that, when this compound was treated with benzonitrile–50% hydrogen peroxide, buffered with solid potassium bicarbonate, for 142 hr, 90% of the starting material was recovered. When II was treated with *m*-chloroperbenzoic acid, a yellowish oil was recovered. Chromatography of this oil gave a yellow glass. An infrared (ir) spectrum of the glass indicated that the tetrahydro ring was still intact, but no chemical entity could be isolated.

Attention was then directed toward the synthesis of an unsubstituted tetrahydroacenaphthylene. Utilizing a procedure similar to that of Buchta and Maar, we prepared 1,2,3,4-tetrahydronaphthyl-1-acetic acid (III) by the condensation of α-tetryl chloride and diethyl sodiomalonate, followed by hydrolysis and decarboxylation. Ring closure was effected in high yield by briefly heating the acid in polyphosphoric acid. The resulting 1-oxo-2a,3,4,5-tetrahydroacenaphthene (IV) was reduced with sodium borohydride to the alcohol V and then treated with phosphorous tribromide to form 1-bromo-2a,3,4,5-tetrahydroacenaphthene (VI). The bromide was found to be unstable as a marked discoloration appeared after 3 days at room temperature.

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[1] Paper VIII: H. J. Richter, R. L. Dressler, and S. F. Silver, *J. Org. Chem.*, **30**, 4078 (1965).

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[4] G. Wittig and K. Henkel, *Ann.*, **542**, 130 (1939).

[5] P. D. Bartlett and R. F. Brown, *J. Amer. Chem. Soc.*, **62**, 2927 (1940).

[6] G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, **26**, 659 (1961); G. B. Payne, *Tetrahedron*, **18**, 763 (1962).

[7] G. H. Coleman and H. J. Johnstone, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p 158.

[8] R. H. Boyd, R. L. Christensen, and R. Pua, *J. Amer. Chem. Soc.*, **87**, 3554 (1965).

[9] E. Buchta and H. Maar, *Ber.*, **95**, 1826 (1962); E. Buchta and H. Maar, *Ann.*, **674**, 129 (1964).