Medium-sized Cyclophanes. Part XVIII.[1] Iodine-induced Cycloisomerization of Methyl-, Ethyl-, and Isopropyl-[2.2]metacyclophanes. π-Basicity and Additional Strain Energy Terms as Controlling Factors

By **Takeo Sato** * and **Tetsuo Takemura,** Department of Chemistry, Tokyo Metropolitan University, Setagaya-ku, Tokyo, 158 Japan

Methyl-, ethyl-, and isopropyl-[2.2]metacyclophanes (4)—(14), in which up to eight alkyl groups are present. have been prepared. The relative rates of iodine-induced cycloisomerization were determined by competitive experiments and gave the order of reactivity as (12) > (9) ≃ (10) > (11) > (5) > (8) > (4) > (3). The presence of alkyl groups adjacent to the bridging methylene enhanced the rate. For the methyl series, the rate increased with increasing number of methyl groups except for (13) and (14) which were recovered unchanged. Though the ethyl compound (10) had reactivity similar with that of the methyl derivative (9), the isopropyl compound (11) had decreased reactivity in accord with lower equilibrium constant for π-complexation. The results were ascribed to two factors: (a) π-basicity of the substrate as determined by the tetracyanoethylene complexes and (b) additional strain imposed by the alkyl groups adjacent to the methylene bridge to the ten-membered ring.

THE strain energy of [2.2]paracyclophane (1) has been determined to be 31 kcal mol^{-1},[2] which is the largest among the cyclophane family (1)—(3) and almost identical with that of cyclopropane.

[1] Part XVII, K. Nishiyama, K. Hata, and T. Sato, *Tetrahedron*, 1975, **31**, 239.
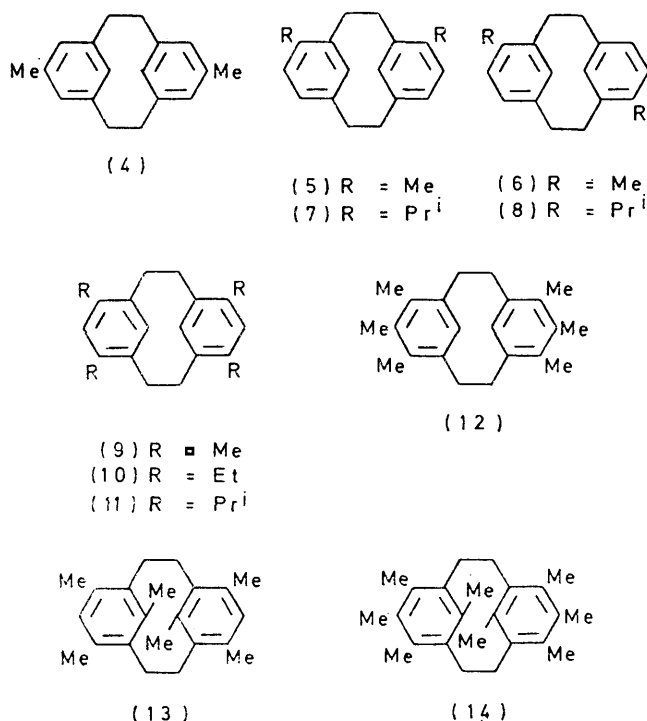
[2] R. H. Boyd, *Tetrahedron*, 1966, **22**, 119; C. Shieh, D. C. McMally, and R. H. Boyd, *ibid.*, 1969, **25**, 3653.

Cram and his co-workers [3] have observed ready ring cleavage reactions of (1). They attributed the driving force of the reaction to ring strain. The cyclophanes (1)—(3) are inter-related by an acid-catalysed isomerization reaction. [2.2]Metaparacyclophane (2), strain

(1)   (2)   (3)
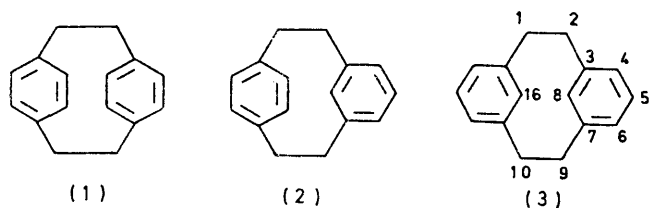
energy 24 kcal mol⁻¹,[2] results when (1) is treated with an acid. In addition, pyrene derivatives are obtained indicating that (2) is further isomerized to [2.2]meta-cyclophane (3), strain energy 12 kcal mol⁻¹.[2] The internal strain is successively relieved during the transformation (1) ⟶ (2) ⟶ (3).

Under a variety of conditions,[1,4,5] (3) has been shown to give pyrene derivatives. The reaction is favoured both by the strain energy term and the proximity between the reacting positions. The most efficient

(4)

(5) R = Me   (6) R = Me
(7) R = Pr^i (8) R = Pr^i

(9) R = Me
(10) R = Et
(11) R = Pr^i

(12)

(13)   (14)

reaction of these is an iodine-catalysed cycloisomerization to give 1,2,3,3a,4,5-hexahydropyrenes.[6] A quantitative conversion can be achieved, for example, by brief

warming of (3) and iodine in a non-polar solvent. The reaction involves an intermolecular hydrogen transfer *via* a π-complex between (3) and iodine as shown by experiments using a deuteriated precursor.[6]

In this paper we describe the iodine-catalysed trans-annular reaction of several alkyl derivatives (4)—(12). Overcrowded polyalkyl models were selected to impose an additional strain in the ten-membered ring. The correlation between the relative rates and the strain is examined by using the van der Waals shifts in ¹H and ¹³C n.m.r. The degree of π-basicity of the substrates is studied by the charge-transfer spectra between tetracyanoethylene (TCNE).

Syntheses.—Bis(chloromethyl) derivatives used for modified Wurtz coupling [7] were prepared by the chloromethylation of suitable alkylbenzenes using a para-formaldehyde–zinc chloride mixture.[8,9] *m*-Diethyl- and *m*-di-isopropyl-benzene gave the corresponding 4,6-bis(chloromethyl) derivatives. Similarly, cumene gave 2,4-bis(chloromethyl)cumene together with a small amount of 2,4,6-tris(chloromethyl)cumene. 1,2,3-Tri-methylbenzene also gave 4,6-bis- and 4,5,6-tris-(chloro-methyl) derivatives. Mesitylene gave a bis(chloro-methyl) derivative from which (13) was obtained.[8] Bischloromethylation of 1,2,3,5-tetramethylbenzene gave the starting material for (14).

The Wurtz dimerization using a sodium–tetraphenyl-ethylene adduct as the condensing agent was carried out under high dilution conditions.[7] Table 1 summarized physical data and analytical figures for the new alkyl derivatives. The dimeric structure is supported by the mass number of the parent ion. Compounds (3),[7] (4),[8] (5),[9] (9),[8] and (13) [8] were prepared by the reported method. The di-isopropyl compound (7) showed the expected parent ion in the mass spectrum but was not obtained entirely free from the geometrical isomer (8). Spectral data for (7) were recorded for a mixture with (8), which, in turn, was obtained in a sufficiently pure form.

¹H *and* ¹³C *N.m.r. Spectra.*—Table 2 shows the ¹H n.m.r. data for the alkyl derivatives. The cyclophane structure is readily assigned by an upfield shift of inner aryl proton resonances and an AA′BB′ pattern for the bridging methylene protons.

The isopropyl methyl resonances in (8) and (11) appeared as a double doublet due to the chirality induced by the rigid stepped conformation. The strain imposed by the four isopropyl groups in (11) is reflected in a large chemical shift difference between the axial and equatorial protons. The downfield shift of the equatorial protons is clearly correlated with the size of the alkyl group as illustrated in Figure 1. Steric compression between the bridging methylene and alkyl

[3] D. J. Cram and J. M. Cram, *Accounts Chem. Res.*, 1971, **4**, 204.
[4] T. Sato, *Nippon Kagaku Zasshi*, 1971, **92**, 277; F. Fögtle and P. Neumann, *Angew. Chem. Internat. Edn.*, 1972, **11**, 73.
[5] K. Nishiyama, K. Hata, and T. Sato, *J.C.S. Perkin II*, 1974, 577.
[6] T. Sato, K. Nishiyama, and A. Murai, *J.C.S. Chem. Comm.*, 1972, 163; T. Sato and K. Nishiyama, *J. Org. Chem.*, 1972, **37**, 3254.

[7] M. Fujimoto, T. Sato, and K. Hata, *Bull. Chem. Soc. Japan*, 1967, **40**, 600.
[8] T. Sato, S. Akabori, S. Muto, and K. Hata, *Tetrahedron*, 1967, **24**, 5557.
[9] T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Japan*, 1966, **39**, 856; S. Akabori, T. Sato, and K. Hata, *J. Org. Chem.*, 1968, **33**, 3277.

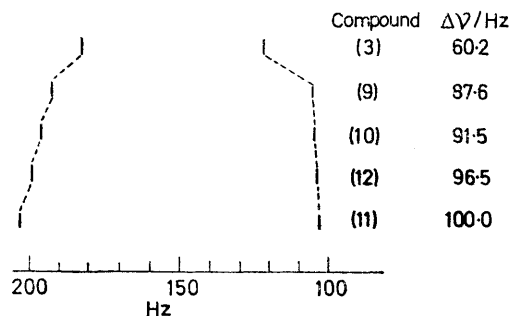group is responsible for the observed shift since an equatorial proton lies almost in the benzene plane in

Compound	$\Delta\nu$/Hz
(3)	60.2
(9)	87.6
(10)	91.5
(12)	96.5
(11)	100.0

FIGURE 1 Bridging methylene proton chemical shift (from Me$_4$Si) analysed by an AB approximation. High field signals correspond to axial and lower field ones to equatorial protons

these rigid molecules and severely interferes with the *ortho*-substituent.

For the hexamethyl derivative (12) the equatorial proton experiences a further downfield shift compared

aryl carbon resonances compared with acyclic models and was attributed to a direct *p*-orbital compression effect.[10]

The distinction between *cis*- and *trans*-structures [(5) and (6); (7) and (8)] is not easy by other means and the ^{13}C n.m.r. results provide the most convincing evidence. Table 3 shows proton-decoupled carbon resonances obtained by the pulse Fourier transform technique for (5)—(8). Assignments were aided by off-resonance decoupling and comparison with model compounds. Both *cis*-compounds, (5) and (7), showed two methylene carbon resonances indicating the presence of two types of bridge, one with very similar chemical shift to that of (3) and the other at appreciably higher field. The chemical shift difference between these resonances is 5.3 for (5) and 4.2 p.p.m. for (7). The upfield shift is caused by the interaction between the *o*-alkyl groups.

On the other hand, the *trans*-compounds (6) and (8) showed two absorptions for the bridging carbons with similar chemical shifts as expected from the substitution

TABLE 1

M.p.s and analytical data for [2.2]metacyclophanes

Compound	M.p. (°C)	Formula	M^+	C (%) Calc.	Found	H (%) Calc.	Found
(8)	169—170	$C_{22}H_{28}$	292	90.35	90.3	9.65	9.75
(10)	106—107	$C_{24}H_{32}$	320	89.95	89.8	10.05	10.2
(11)	277—278	$C_{28}H_{40}$	376	89.3	89.7	10.7	10.75
(12)	244—245	$C_{22}H_{28}$	292	90.35	90.45	9.65	9.8
(14)	314—316	$C_{24}H_{32}$	320	89.95	90.2	10.05	10.05

TABLE 2

^{1}H N.m.r. data for [2.2]metacyclophanes ^{a}

Compound	Aromatic protons 5,13-H	8,16-H	Others	Bridging methylene ^{b} eq-H	ax-H	Alkyl
(3) ^{d,e}	7.18 (m)	4.25 (t, 1.8)	6.97 (m)	3.05	2.05	
(8)	7.29 (d, 6)	4.28 (d, 2)	7.05 (dd, 6.2)	1.94 ^{c}		1.33 (d, 7), 1.27 (d, 7)
(9) ^{e}	6.98 (s)	4.20 (s)		3.22	1.76	2.30 (s)
(10)	6.95 (s)	4.25 (s)		3.28	1.75	2.67 (q, 7.6), 2.63 (q, 7.0), 1.27 (t, 7.3)
(11)	7.09 (s)	4.26 (s)		3.39	1.73	2.71 (h, 7.0), 1.32 (d, 7), 1.28 (d, 7.0)
(12)		4.23 (s)		3.33	1.72	2.25 (s)
(13) ^{e}	6.62 (s)			3.15	2.47	2.35 (s), 0.48 (s, H-8,16)
(14)				3.21	2.41	2.32 (s), 2.17 (s, H-5,13), 0.47 (s, H-8,16)

^{a} Spectra were recorded in CDCl$_3$. Chemical shifts are in δ values downfield from Me$_4$Si. Multiplicity: s, singlet, d, doublet, t, triplet, q, quartet, h, heptet. ^{b} First-order analysis by an AB-type approximation. ^{c} Centre of a multiplet of ABCD type. ^{d} Ref. 7. ^{e} Ref. 8.

with (9) and lies between the tetraethyl (10) and tetra-isopropyl derivatives (11), the fact suggesting a large buttressing effect of three vicinal methyl groups. An upfield shift of the axial protons in *o*-alkyl derivatives is due to a carbon–carbon anisotropy effect and is not affected by the size of the alkyl group (Figure 1).

The ^{13}C n.m.r. spectra of these compounds have been reported in preliminary form.[10] These data not only served as the direct structural proof but also provided interesting anomalous shifts for the compressed carbons. An upfield shift of the bridging methylene carbon signal occurs when an *o*-alkyl group is present due to steric overcrowding.[11] On the other hand, an anomalous downfield shift, 6—7 p.p.m., was observed for the inner

pattern. The upfield shift is less than that caused by two *o*-alkyl groups. The rest of the carbon resonances are surprisingly similar for the *cis*- and *trans*-compounds except for small differences in the methyl resonances of the isopropyl isomers ($\Delta\delta$ *ca.* 0.1 p.p.m.).

Charge-transfer Complexes with Tetracyanoethylene.— Comparison of the charge-transfer bands of cyclophane molecules with those of the corresponding acyclic models has been studied to correlate π-basicity with structure.[4] Compared with the large enhancement in

[10] T. Sato, T. Takemura, and M. Kainosho, *J.C.S. Chem. Comm.*, 1974, 97.
[11] N. K. Wilson and J. B. Stothers, *Topics Stereochem.*, 1974, **8**, 1.

the π-basicity in the lower membered paracyclophanes,[12] (3) showed only a moderate increase [13] reflecting decreased overlap between the two aryl groups.[10,14]

Thermodynamic data for a series of alkyl[2.2]metacyclophanes determined in methylene chloride at 19—20° are shown in Table 4 together with the data for several benzene models.

Comparison among the tetra-alkyl derivatives (9)—(11) revealed that (11) has the smallest equilibrium constant and the smallest heat of formation. This is

mixture of (17a) and (18a) were obtained. Compound (19a) was not obtained possibly due to an unfavourable 1,3-diaxial methyl interaction. Structural assignments were made by detailed examination of [1]H n.m.r. spectra using coupling constants, nuclear Overhauser effect, and solvent-induced chemical shifts using an aromatic solvent. Treatment of (10) and (11) with iodine gave the expected hexahydropyrenes. By repeated column chromatography (16b) and a diastereoisomeric mixture of (17b) and (18b) were obtained. Similarly, the isopropyl

TABLE 3

^{13}C N.m.r. data for [2.2]metacyclophanes [a]

Compound	Alkyl	C-1,2	C-9,10	C-1,9	C-2,10	C-3,7	C-4	C-5	C-6	C-8
(3) [b]		41.4				138.6	125.1	128.6	125.1	136.3
(5)	18.8	35.4	40.7			136.4 136.4	132.5	130.0	125.1	136.6
(6)	18.8			38.4	37.7	136.2 136.2	132.3	130.0	125.3	136.6
(7)	23.6 (Me) 25.1 (Me) 28.9 (CH)	36.2	40.4			134.9 135.6	143.2	125.0 125.5		136.8
(8)	23.7 (Me) 25.2 (Me) 28.9 (CH)			39.6	37.2	135.0 135.9	143.4	125.1 125.6		136.8

[a] Spectra were recorded by using the pulsed Fourier transform technique with proton-noise decoupling. Samples are dissolved in CDCl$_3$. Chemical shifts are in δ values downfield from internal Me$_4$Si. [b] Ref. 10.

TABLE 4

Spectral and thermodynamic parameters for charge-transfer complexes between [2.2]metacyclophanes and tetracyanoethylene [a]

Compound	λ_{max}/nm	ε	K/l mol^{-1}	$-\Delta H$/kcal mol^{-1}	IP/eV
(3)	486	260	17.5	2.8	8.41
(5)	520	1 140	12.1	4.7	8.24
(9)	538	2 890	15.1	5.6	8.14
(10)	550	890	15.0	6.8	8.1
(11)	570	361	5.0	4.0	8.0
4,6-Diethyl-m-xylene	490	1 123	3.8	4.6	8.4
4,6-Di-isopropyl-m-xylene	500	287	5.2	4.9	8.3

[a] Determined in CH$_2$Cl$_2$ at 19—20°, ref. 15.

explained by the steric bulk of the four isopropyl groups which hinder the approach of an acceptor. This is not the case with benzene models: 4,6-di-isopropyl-m-xylene is more basic than the ethyl homologue. In a simple benzene derivative an isopropyl group rotates freely while in the cyclophane molecule the motion is restricted due to the rigid, overcrowded molecular geometry.

Iodine-induced Reactions.—When a benzene solution of (3) and iodine was warmed for a short period of time, (15) was obtained in quantitative yield. Although a similar transformation occurs with bromine,[6] silver perchlorate,[6] aluminium chloride,[1] and sulphuric acid [1] these are less selective and less efficient compared with iodine. Alkyl derivatives gave diastereoisomeric mixtures. For example, possible structures resulting from a tetra-alkyl derivative are the four configurational isomers (16)—(19) (each exists as a racemate, one enantiomeric form shown).

With (9), for example, (16a) and an inseparable

derivatives (16c)—(18c) were obtained. As a side reaction, which was observed in (9)—(11), the corresponding 4,5,9,10-tetrahydropyrenes (20b and c) were obtained in appreciable amounts. The progress of the reaction was followed by g.l.c., which was also used to determine the relative rates using competitive experiments. The hexahydro- and tetrahydro-pyrene structures were easily distinguished by u.v. spectroscopy.

The di-isopropyl derivative (8) on treatment with iodine gave the isomeric di-isopropylhexahydropyrenes (21)—(23). Compound (12) gave (24) and (25). No attempt was made to separate the configurational isomers from (21), (22), and (24).

All new compounds have satisfactory analytical and spectral properties.

A marked enhancement in the reactivity of (9) com-

[12] D. J. Cram and R. H. Bauer, *J. Amer. Chem. Soc.*, 1959, **81**, 5971; L. A. Singer and D. J. Cram, *ibid.*, 1963, **85**, 1080; M. Sheehan and D. J. Cram, *ibid.*, 1969, **91**, 3553.

[13] D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *J. Amer. Chem. Soc.*, 1966, **88**, 1324; K. Burri and W. Jenny, *Helv. Chim. Acta*, 1967, **50**, 1978; R. Flammang, H. P. Figeys, and R. H. Martin, *Tetrahedron*, 1968, **24**, 1171; S. Hayashi and T. Sato, *Nippon Kagaku Zasshi*, 1970, **91**, 950; F. Vögtle and P. Neumann, *Angew. Chem.*, 1973, **84**, 75.
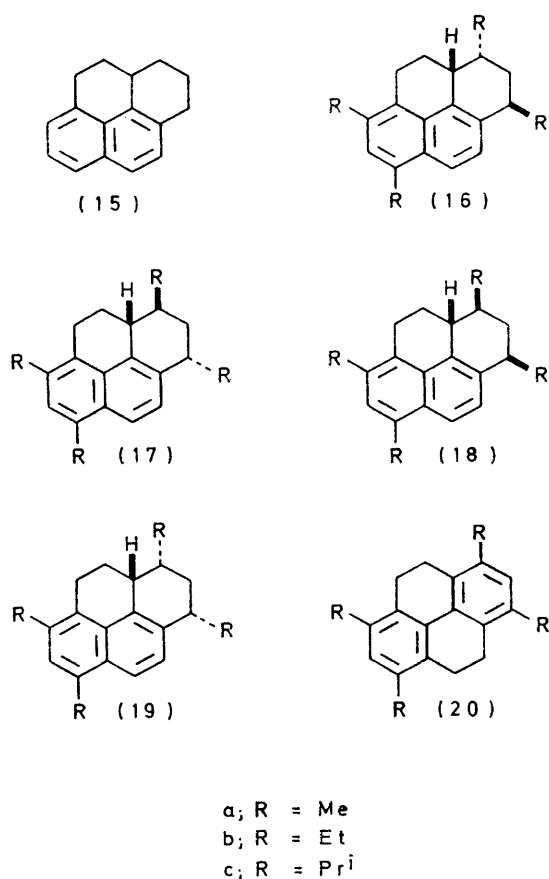
[14] E. Langer and H. Lehner, *Tetrahedron*, 1973, **29**, 375.

pared with (3) was noticed earlier. The difference is so great that (9) disappeared completely before (3) entered into the reaction.

Relative rates of the iodine-induced transannular reaction of polyalkyl derivatives were determined by competitive experiments. Relative rates are also compared by half lives of the substrates. The results are summarized in Table 5.

Tetrahydropyrene formation was observed for rapidly reacting polyalkyl cyclophanes and amounted to 20—30% for (9)—(12). For example, (25) was formed in 33% yield when (12) was treated with iodine. The


a; R = Me
b; R = Et
c; R = Pr^i

relative rates in Table 5 are expressed as the totals for the hexahydro- (isomerization) and tetrahydro-pyrenes (dehydrogenation).

Figure 2 illustrates the product distribution as determined by g.l.c. There is always a short induction period for the reaction presumably corresponding to the complex-forming stage. For this reason, the initial reaction product of the rapidly reacting polyalkyl derivatives contains higher proportions of the tetra-hydropyrene, the formation of which might involve a one-electron transfer mechanism.[1]

The relative ease of cyclization for the compounds examined is:

(12) > (9) ≃ (10) > (11) > (5) > (8) > (4) > (3)

The reactivity is governed by two factors: (a) the stability of the π-complex and (b) an additional strain energy term.
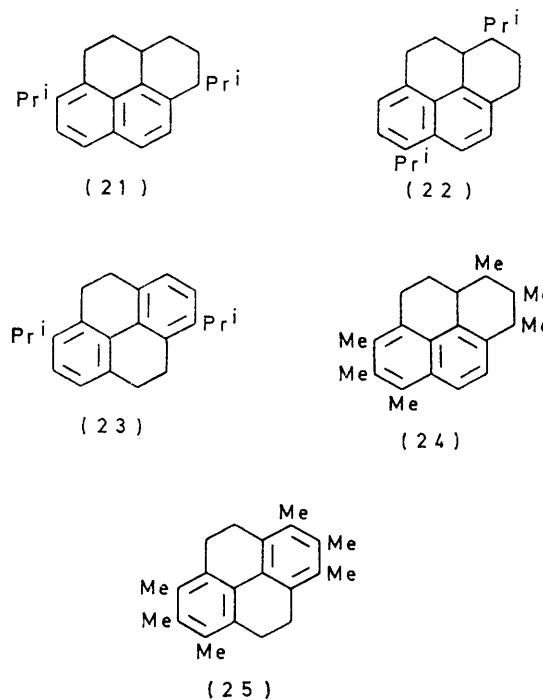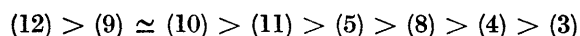
Although the transannular reaction should be dependent on the π-basicity of the substrate, the reactivity order is not explained by the base strength alone. For
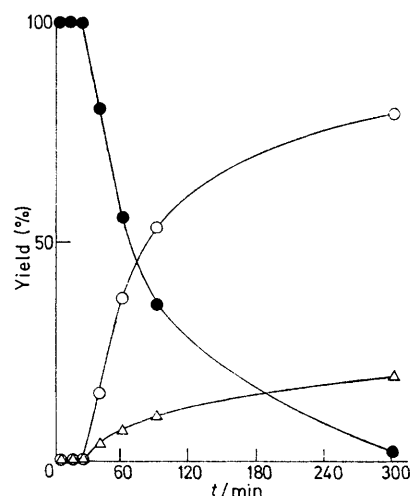

FIGURE 2 Products of reactions of the tetraisopropyl derivative (11) (0.2 mmol) and iodine (0.2 mmol) in benzene (18 ml) at 60°: ●, (11); ○, (16c)—(18c); △, (20c)

example, comparison among (3)—(5) reveals alkylation enhances the reactivity but the enhancement is apparently dependent on the type of substitution (Table 5).

The higher reactivity of (5) and, especially (9), compared with (3) suggest the importance of the additional strain energy term as an important driving force of the reaction. The reactivity difference between (3) and

(9) is most remarkable in that both have similar equilibrium constants yet the latter is far more reactive. Alkyl groups *ortho* to the bridge impose an additional strain on the ten-membered ring. An increased strain in the ground state will facilitate the reaction by decreasing the activation energy.

The fact that the isopropyl homologue (11) is the least reactive of the tetra-alkyl compounds indicates the reactivity is determined by a balance of the two factors above. A bulky isopropyl group exerts larger steric

TABLE 5

Relative rates of the iodine–[2.2]metacyclophane reaction

Compound	Rel. rate [a]	Rel. rate [b]	$t_{\frac{1}{2}}$/min [c]
(3)	1.0		
(4)	4.2		
(8)	6.6		
(5)	8.7		230
(11)			70
(9)	Very fast	1.0	10
(10)			10
(12)		5.1	

[a] Competitive experiments in benzene at 60°. [b] Competitive experiment at 35° for 3 min. [c] Determined in benzene at 60°.

strain on the ten-membered ring as shown by [1]H n.m.r. (Table 2 and Figure 1). The equilibrium constant for (11), however, is the smallest for the homologues. Evidently the molecule becomes unreactive toward various reagents. Compound (11) does not react with $CuCl_2$ in acetonitrile, which effects transannular dehydrogenation of (3).

Compound (12) is the most reactive of the compounds so far prepared. As Table 5 shows (12) gave 58% yield of the transannular products by reaction with iodine at 35° for only 3 min.

Both compounds (13) and (14) did not undergo cycloisomerization on treatment with iodine.

EXPERIMENTAL

Measurements.—[1]H N.m.r. spectra were recorded on Varian XL100 and Hitachi R-20B spectrometers using $CDCl_3$ as solvent. [13]C N.m.r. spectra were recorded on a Varian XL100 spectrometer using the pulsed Fourier transform technique with $CDCl_3$ as solvent; chemical shifts are shown downfield from internal tetramethylsilane. Both proton-decoupled and continuous wave off-resonance spectra were taken. Mass spectra were obtained with a Hitachi RMU-6E mass spectrometer with an ionization current of 70 eV.

1 : 1 Charge-transfer complexes between the cyclophanes and TCNE were formed in dichloromethane. No spectral changes occurred when a 4—12-fold excess of TCNE was added. Equilibrium constants were calculated by the Rose–Drago equation.[15] Thermodynamic parameters were calculated from Briegleb's equation which correlates the ionization potential of the electron donor and the energy of the charge-transfer band.

4,6-Bis(chloromethyl)-m-di-isopropylbenzene.— Hydrogen chloride was passed through a stirred mixture containing paraformaldehyde (120 g), anhydrous zinc chloride (90 g), and carbon tetrachloride (425 ml) at 70°. To the mixture *m*-di-isopropylbenzene (24 g, 1.5 mol) was added drop-

wisely during 1 h. Stirring and passage of hydrogen chloride were continued for 7 h under reflux. After the usual work-up, the chloride was distilled under reduced pressure, b.p. 144° at 3 mmHg. Crystalline material was obtained by recrystallization from n-hexane, *prisms* (68 g, 17.5%), m.p. 55—56° (Found: C, 65.15; H, 7.7. $C_{14}H_{20}Cl_2$ requires C, 64.9; H, 7.8%).

4,6-Bis(chloromethyl)-m-diethylbenzene.— *m*-Diethylbenzene gave the bischloromethyl compound, b.p. 126—127° at 3 mmHg, *prisms* (51%), m.p. 73—75° (from n-hexane) (Found: C, 62.45; H, 6.9. $C_{12}H_{16}Cl_2$ requires C, 62.35; H, 7.0%).

2,4-Bis(chloromethyl)cumene.—Starting from cumene (240 g, 1 mol), 4-chloromethyl- (154 g), b.p. 99° at 2 mmHg, 2,4-*bis(chloromethyl)*- (118 g), b.p. 120° at 2 mmHg (Found: C, 61.2; H, 6.45. $C_{11}H_{14}Cl_2$ requires C, 60.85; H, 6.5%), and 2,4,6-*tris(chloromethyl)-cumene* (12 g), b.p. 130° at 2 mmHg, were obtained. The trischloromethyl derivative gave plates, m.p. 60—62° (Found: C, 54.25; H, 5.6. $C_{12}H_{15}Cl_3$ requires C, 54.25; H, 5.7%).

4,6-Bis(chloromethyl)-1,2,3-trimethylbenzene.—The distillate, b.p. 150—160° at 2 mmHg, was recrystallized from n-hexane, *needles* (40%), m.p. 121—122° (Found: C, 60.85; H, 6.55. $C_{11}H_{14}Cl_2$ requires C, 60.85; H, 6.5%).

4,5,6-Tris(chloromethyl)-1,2,3-trimethylbenzene.—This was obtained as *plates* (4.5%), m.p. 119—121° (from n-hexane) (Found: C, 54.5; H, 5.7. $C_{12}H_{15}Cl_3$ requires C, 54.25; H, 5.7%).

4,6-Bis(chloromethyl)-1,2,3,5-tetramethylbenzene.—Needles (81%), m.p. 114° (from n-hexane), were obtained by bischloromethylation of 1,2,3,5-tetramethylbenzene (Found: C, 62.65; H, 7.05. $C_{12}H_{16}Cl_2$ requires C, 62.35; H, 7.0%).

Modified Wurtz Coupling of Bischloromethylarenes.—The intermolecular Wurtz dimerization of bischloromethylarenes was carried out in tetrahydrofuran (THF) under high dilution conditions using tetraphenylethylene–sodium adduct as condensing agent.[7-9] The high dilution conditions were realized by slow addition of the dihalide over 100—180 h through a modified Herschberg funnel to a THF solution containing the condensing agent at low temperatures (−50 to −60°). Analytical data are summarised in Table 1.

[2.2]Metacyclophane (3) and several alkyl derivatives used in this study were prepared according to the reported method: (3), m.p. 132—133°;[7] (4), m.p. 148—149°;[8] (5), m.p. 68—69°;[9] (9), m.p. 204—205°;[8] and (13), m.p. 244°.[8]

4,14-Di-isopropyl- (7) *and* 4,12-*Di-isopropyl-[2.2]metacyclophane* (8).—These compounds were prepared from 2,4-bis(chloromethyl)cumene. Column chromatography on Woelm neutral alumina using chloroform as eluant was followed by rechromatography on active alumina with n-hexane as eluant. After repeated purification using chromatography the transoid compound (8) was obtained as a fast moving fraction in 4.7% yield as plates, m.p. 169—170° (from π-hexane). The cisoid compound (7) was obtained as a slower moving fraction in small amounts. The structure was confirmed by the [13]C n.m.r. spectrum.

4,6,12,14-Tetraethyl[2.2]metacyclophane (10).—After 2,4-bis(chloromethyl)-*m*-diethylbenzene was subjected to the modified Wurtz reaction, the reaction mixture was chromatographed on alumina. Elution with n-hexane afforded (10) as plates (13%), m.p. 106—107°.

4,6,12,14-Tetraisopropyl[2.2]metacyclophane (11).—Starting from 2,4-bis(chloromethyl)-*m*-di-isopropylbenzene, com-

pound (11) (6.7%) was obtained as plates, m.p. 276—277° (from n-hexane containing a small amount of benzene). Chromatography was carried out on alumina eluting first with n-hexane–benzene (1 : 10) and then with n-hexane.

4,5,6,12,13,14-*Hexamethyl*[2.2]*metacyclophane* (12).— Using 4,6-bis(chloromethyl)-1,2,3-trimethylbenzene as starting material, compound (12) (5%) was obtained as needles, m.p. 244—245°.

4,5,6,8,12,13,14,16-*Octamethyl*[2.2]*metacyclophane* (14).— The crude reaction mixture obtained by the Wurtz reaction of 4,6-bis(chloromethyl)-1,2,3,5-tetramethyl was sublimed under reduced pressure. After tetraphenylethane sublimed at 140° and 0.8 mmHg, the temperature was raised to 180° at 0.5 mmHg. The sublimate was purified by chromatography on alumina using n-hexane as eluant. Prisms (11%), m.p. 314—316°, were obtained by recrystallization from n-hexane.

Iodine-induced Cycloisomerizations.—As a representative the reaction of (10) is given.

1,3,6,8-*Tetraethyl*-1,2,3,3a,4,5-*hexahydropyrenes* (16b)— (18b) *and* 1,3,6,8-*tetraethyl*-4,5,9,10-*tetrahydropyrene* (20b). A mixture of (10) (509 mg, 1.59 mmol) and iodine (363 mg, 1.44 mmol) in benzene (20 ml) was warmed at 60° for 30 min. After the usual work-up, the mixture was fractionated by column chromatography on neutral alumina. By elution with n-hexane (16b)—(18b) and (20b) were successively eluted and characterized by n.m.r. analysis.[6] Recrystallization of (16b) from n-hexane–ethanol gave needles, m.p. 87—88°. The mixture of (17b) and (18b) could not be

separated and had m.p. 60—70°. The tetrahydropyrene (20b) was obtained as plates, m.p. 176—178°.

Similarly, compound (11) gave 1,3,6,8-tetraisopropyl-1,2,3,3a,4,5-hexahydropyrene (16c), needles from ethanol–n-hexane, m.p. 112—113°, a mixture of (17c) and (18c), needles from methanol–ethanol, m.p. 120—127° and (20c), plates from n-hexane, m.p. 199—200°.

Reaction Rates.—Relative rates were determined by following the reaction by g.l.c. Competitive experiments were performed in most cases. With very rapidly reacting substrates, however, such experiments could not be run.

A solution of (11) (75.3 mg, 0.20 mmol) and iodine (51.4 mg, 0.20 mmol) in benzene (8 ml) was placed in a constant temperature bath at 60°. Aliquot samples were taken out at intervals. The reaction was quenched by adding sodium thiosulphate solution and organic layer was analysed by g.l.c. A typical example is shown in Figure 2.

For competitive experiments, a mixture of (3) (23.5 mg, 0.11 mol), (8) (28.4 mg, 0.10 mmol), and iodine (38.0 mg) in benzene (2 ml) was warmed at 60° for 1 h. After the usual work-up the mixture was analysed. The results are given in Table 5.

[15] S. Hayashi and T. Sato, *Bull. Chem. Soc. Japan,* 1972, **45,** 2360.