was also isolated from the preparative tlc plate [ir spectrum identical to that obtained as described in (1), above].

Registry No.—**1**, 35158-78-2; **2**, 35158-79-3; **3a**, 35158-80-6; **3a** (precursor to), 13226-05-6; **3b**, 35158-82-8; **3c**, 35158-83-9; **3d**, 35158-84-0; **3e**, 35158-85-1; **3g** (one racemic isomer), 35158-86-2; **3g** (second racemic isomer), 35158-87-3; **3i** (one racemic isomer), 35158-88-4; **3i** (second racemic isomer), 35158-89-5; **3j**, 35158-90-8; **3k** (one racemic isomer), 35158-91-9; **3k** (second racemic isomer), 35158-92-0; **31**, 35158-93-1; **3m**, 35158-94-2; **3o**, 35191-47-0; **4**, 35158-95-3; **4** (precursor to), 35158-96-4; **5**, 35158-97-5; **5** (precursor to), 35158-98-6; **8**, 35158-99-7; **9a**, 35159-00-3; **9b**, 35159-01-4; **9b** (precursor to), 35159-02-5; **9c**, 35159-03-6; **9d**, 35159-04-7; **10**, 35159-05-8.

Acknowledgment.—The authors wish to thank Mrs. T. T. Sun for the preparation of **5**.

Medium-Sized Cyclophanes. XIII. A Highly Selective Cycloisomerization Reaction of [2.2]Metacyclophanes to 1,2,3,3a,4,5-Hexahydropyrenes Induced by Iodine[1]

TAKEO SATO* AND KOZABURO NISHIYAMA

Department of Chemistry, Tokyo Metropolitan University, Setagaya, Tokyo 158, Japan

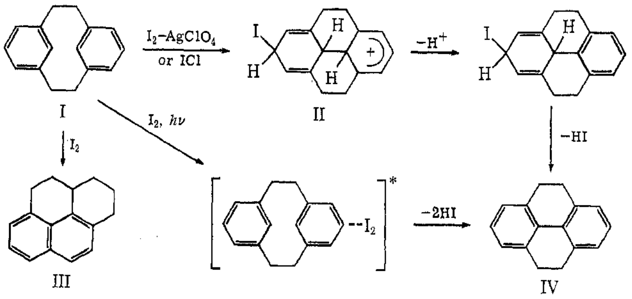
Received February 18, 1972

[2.2]Metacyclophane (I) underwent an iodine-induced cycloisomerization reaction to give 1,2,3,3a,4,5-hexahydropyrene (III) with remarkable ease and in high yield. The generality of the isomerization has been established using several alkyl derivatives (V–VII), which gave the corresponding hexahydropyrenes (VIII–XII), and efficacious reaction conditions have been broadly examined. Cross experiments using [2.2]metacyclophane-*8,16-d*$_2$ indicate the reaction might to involve intermolecular hydrogen transfer. Competitive experiments between I and alkyl derivatives suggest that a π-complex mechanism might apply.

Owing to electronic interactions between two benzene rings, the proximity of 8,16 positions, and the considerable strain energy, [2.2]metacyclophane (I) is prone to give transannular reaction products.[2] These are mostly explained by the initial formation of a dehydrogenation product, 4,5,9,10-tetrahydropyrene (IV) (Scheme I). It has been isolated under electrophilic,[3–6] radical,[7] and photolytic reaction conditions[4,8,9] together with other transformation products derived from IV.

Nitration with benzoyl nitrate[5] (reactive species, N_2O_5), which is preferred over nitric acid[3] for stoichiometric control and for homogeneous reaction conditions or bromination using iron catalyst[3,6] afforded substituted 4,5,9,10-tetrahydropyrene *via* IV. Attempted iodination of I using iodine and silver perchlorate[4,6] or iodine chloride[6] gave a high yield of IV. No further iodination occurred under the reaction conditions.

SCHEME I



A similar dehydrogenation–substitution scheme was postulated for a derivative of I.[3,10,11] Photolysis of I in the presence of iodine[4,8] or a suitable oxidant[9] afforded IV as the main product. Lack of conjugation between two aryl moieties in I demands a different mechanism from that postulated for *cis*-stilbene → phenanthrene.[12] It is likely to involve photoexcitation of the charge-transfer complex between I and iodine followed by dehydroiodination.[8] With iodine as a reactant the formation of IV is illustrated in Scheme I, where an addition–elimination mechanism is postulated for the attack of an electrophile.

We have found still another type of iodine-induced reaction of I which gives 1,2,3,3a,4,5-hexahydropyrene (III) with remarkable ease and with high selectivity.[1] When a benzene solution of I containing iodine was warmed at 60°, III[13] was produced in a quantitative yield. These reactions carried out in benzene and cyclohexane are summarized in Table I. No reaction

---

[1] Part XII: T. Sato, M. Wakabayashi, K. Hata, and M. Kainosho, *Tetrahedron*, **27**, 2737 (1971). For a preliminary account, see T. Sato, K. Nishiyama, and A. Murai, *Chem. Commun.*, 163 (1972).

[2] Reviews: R. W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963); B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964; T. Sato, *Kagaku no Ryoiki*, **23**, 672, 765 (1969); T. Sato, *Nippon Kagaku Zasshi*, **92**, 277 (1971).

[3] The formation of 2-nitro-4,5,9,10-tetrahydropyrene by the nitration with nitric acid was first explained by the oxidation of nitrated precursor and the possibility of an intermediacy of IV was eliminated [N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *J. Amer. Chem. Soc.*, **83**, 1947 (1961)]. In the revised mechanism, which conforms with our results, IV is postulated as an intermediate [N. L. Allinger, B. J. Gordon, H.-E. Hu, and R. A. Ford, *J. Org. Chem.*, **32**, 2272 (1967)].

[4] T. Sato, E. Yamada, Y. Okamura, T. Amada, and K. Hata, *Bull. Chem. Soc. Jap.*, **38**, 1049 (1965).

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

[6] T. Sato, M. Wakabayashi, Y. Okamura, T. Amada, and K. Hata, *ibid.*, **40**, 2363 (1967).

[7] For example, the reaction of I with BPO or diisopropyl peroxydicarbonate gave IV along with substituted I (unpublished results).

[8] T. Sato, M. Wakabayashi, S. Hayashi, and K. Hata, *Bull. Chem. Soc. Jap.*, **42**, 773 (1969); H. Shizuka, K. Sorimachi, T. Morita, K. Nishiyama, and T. Sato, *ibid.*, **44**, 1983 (1971); S. Hayashi and T. Sato, *ibid.*, **45**, 2360 (1972).

[9] T. Sato, K. Nishiyama, S. Shimada, and K. Hata, *ibid.*, **44**, 2858 (1971).

[10] T. Sato, S. Akabori, S. Muto, and K. Hata, *Tetrahedron*, **24**, 5557 (1967).

[11] R. W. Griffin, Jr., and R. A. Coburn, *J. Org. Chem.*, **32**, 3956 (1967).

[12] F. R. Stermitz in "Organic Photochemistry," Vol. 1, O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1967, p 249.

[13] J. W. Cook, C. L. Hewett, and I. Hieger, *J. Chem. Soc.*, 355, 396, 398 (1953).

Table I

The Formation of 1,2,3,3a,4,5-Hexahydropyrene (III) from [2.2]Metacyclophane (I)[a]

Expt no.	MCP (M)	I_2 (equiv)	Solvent	Temp, °C	Hydropyrene Hexa-	Tetra-
1	0.33	0.8	C_6H_6	80	95	1.9
2	0.32	0.14	C_6H_6	60	100	0
3	0.31	0.12	C_6H_6	80	63	4.9
4	0.24	0.11	C_6H_6	60	14	0
5	0.24	0.06	C_6H_6	60	0	0
6	0.16	0.82	C_6H_{12}	80	84	6.0
7	0.013	0.53	C_6H_{12}	60	0	0

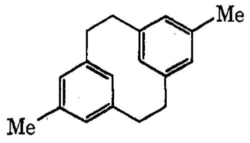
[a] Reaction time, 20 hr.

occurred in ethanol, acetic acid, carbon disulfide, or dimethylformamide.

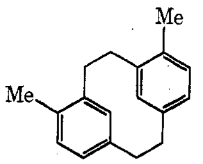
Concentration of both the substrate and iodine has a marked effect on the formation of III. Table I shows that the reaction rate is considerably lowered by using a lesser amount of iodine. Low concentration of I (<0.013 M) also retarded the reaction even when a sufficient amount of iodine was present. By contrast, a photocyclodehydrogenation reaction occurred in dilute benzene or cyclohexane solution ($\sim 4 \times 10^{-3}$ M) containing only a catalytic amount of iodine. The formation of III was not noticed in the photolysis mixture except for those cases where rather concentrated solutions were exposed to sunlight in summer.

A small amount of iodinated material was formed when nearly equimolar iodine was employed. The only other by-product was IV which was formed in a small amount depending on the reaction conditions. When these by-products were formed, hydrogen iodide was noticed in the reaction mixture, which itself, however, was ineffective in the isomerization reaction. Iodine was found to be recoverable after the reaction as determined by titration of an aqueous extract.

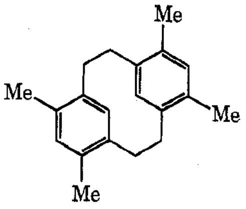
That the cycloisomerization reaction is general to this class of compounds has been confirmed by using 5,13-dimethyl- (V),[10] 4,14-dimethyl- (VI),[14] and 4,6,12,-14-tetramethyl[2.2]metacyclophanes (VII).[10] Under similar reaction conditions used for I they gave high yields of the corresponding 1,2,3,3a,4,5-hexahydropyrenes (VIII–XII; only one enantiomer is shown in the formula). Physical properties of the products are collected in Table II. There was no indication of skeletal change nor alkyl migration. The only side reaction was the formation of the corresponding 4,5-9,10-tetrahydropyrenes.



V



VI



VII

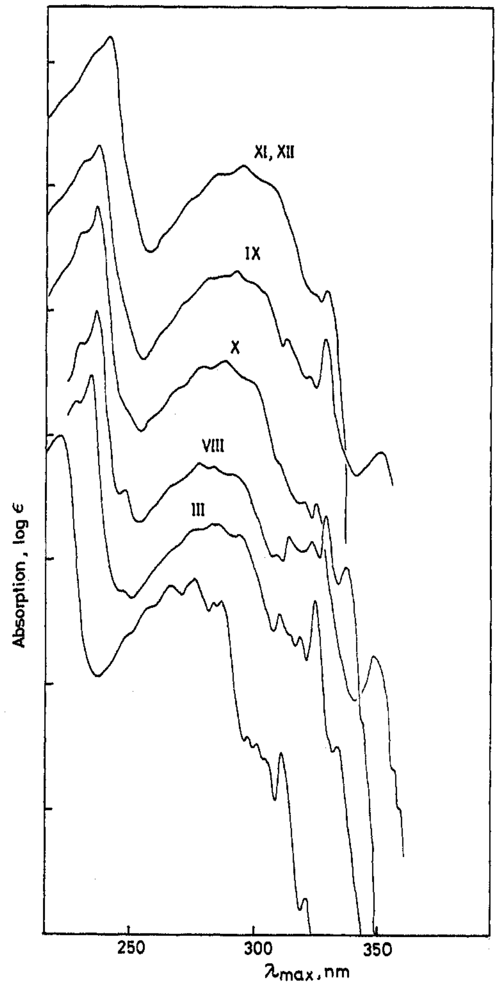


Figure 1.—Uv absorption spectra of naphthalene (bottom) and 1,2,3,3a,4,5-hexahydropyrenes in cyclohexane.

From combustion analysis and parent ion peaks in the mass spectra, the products were inferred to be isomeric with the starting materials. The gross structures were indicated from the ir and uv spectra, which showed absorptions due to typical alkylated naphthalene chromophores (Figure 1, Table III). Fragmentation patterns in the mass spectrum were also in accord with the naphthalene structures. Detailed structural information including stereochemistry was gained from nmr measurements (Table IV; see later section).

2,7-Dimethyl-1,2,3,3a,4,5-hexahydropyrene (VIII) was obtained by the similar treatment of V with iodine. The structure was confirmed by dehydrogenation into 2,7-dimethylpyrene[15] over palladium/charcoal. By repeated chromatography on alumina, VIII was separated into two configurational isomers, VIIIa and VIIIb. In VIIIa the methyl group at C-2 is cis to the hydrogen at bridgehead (C-3a) and exists in a quasiaxial arrangement, while the methyl group in VIIIb is trans to the hydrogen and takes a quasiequatorial position. The ratio of VIIIa and VIIIb was 46:54 as determined from nmr spectra of the reaction mixture by integrating

---

[14] T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Jap.*, **39**, 856 (1966); S. Akabori, T. Sato, and K. Hata, *J. Org. Chem.*, **33**, 3277 (1968).

[15] M. Orchin, L. Reggel, and R. A. Friedel, *J. Amer. Chem. Soc.*, **74**, 1094 (1952).

TABLE II

1,2,3,3a,4,5-HEXAHYDROPYRENES

Compd	Mp, °C	Yield,[a] %	Formula	Mol wt m/e	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found
III[b]	103–104	100[c]	$C_{16}H_{16}$	208	92.26	92.21	7.74	7.84
VIIIa	90–91	54	$C_{18}H_{20}$	236	91.47	91.14	8.53	8.31
VIIIb	163–164	46	$C_{18}H_{20}$	236				
IX	53–55	32	$C_{18}H_{20}$	236	91.47	91.02	8.53	8.74
X[d]	Liquid	68	$C_{18}H_{20}$	236				
XI	79–80	24	$C_{20}H_{24}$	264	90.85	91.04	9.15	9.48
XII[d]	136–141.5	52	$C_{20}H_{24}$	264				

[a] Determined by vpc and/or nmr. [b] See ref 14. [c] See Table I. [d] Mixture of diastereomers.

TABLE III

UV MAXIMA IN CYCLOHEXANE

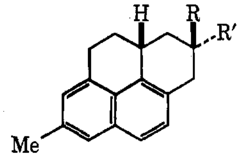
Compd	λ_{max}, nm (log ϵ)
III	227.5 (4.78), 234 (4.96), 269 (3.61), 275 (3.73), 283.5 (3.80), 289 (3.79), 294.5 (3.70), 311 (3.08), 315.5 (2.89), 319.5 (2.89), 325 (3.18), 335 (2.02)
VIII	230 (4.74), 236 (4.98), 248 (3.55), 268 (3.62), 278 (3.78), 283 (3.75), 291 (3.70), 296 (3.65), 309 (3.04), 315 (3.20), 324 (3.15), 330 (3.38), 338 (2.96)
IX	230 (4.81), 236 (5.01), 248 (3.43), 257 (3.30), 268 (3.57), 279 (3.75), 289 (3.80), 299 (3.63), 310 (2.98), 321 (2.66), 325.5 (2.66)
X	230 (4.73), 237 (4.87), 271 (3.60), 281 (3.81), 292 (3.86), 305 (3.66), 313 (3.33), 322 (3.03), 328 (3.32)
XI, XII	234 (4.76), 240 (4.90), 275 (3.60), 284 (3.79), 295 (3.86), 307 (3.70), 323 (2.85), 329 (2.88)

the methyl proton signals. The fact that VIIIb has a higher melting point and elutes from an alumina column slower than VIIIa provides additional evidence to support the assignment of the former to be the quasi-equatorial isomer.

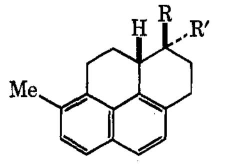
An attempted equilibration experiment between VIIIa and VIIIb using sulfuric acid failed since the 1,2,3,3a,4,5-hexahydropyrene structure isomerized to 1,2,3,6,7,8-hexahydropyrene (XIV, *sym*-hexahydropyrene). Lewis acid or metal catalysts were not examined since fragmentation, rearrangement, and dehydrogenation[16] reactions were anticipated.

For compound VI a dual way of cyclization is possible. Indeed, we obtained two types of naphthalene compounds IX and X, which were formed in a 32:68 ratio as determined by gas chromatography. As a by-product 1,8-dimethyl-4,5,8,10-tetrahydropyrene was formed in a trace amount and characterized by mass spectroscopy. Compound IXb was assigned the quasi-axial methyl isomer structure based on the high field methyl proton signal occurring at δ 0.89 in the nmr spectrum. No diastereomeric compound IXa was isolated.

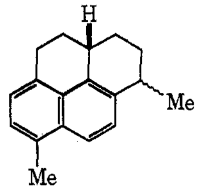
Compound X was obtained as an oily mixture of stereoisomers. A doublet signal at δ 1.29 and 1.36 indicates that each isomer has a methyl group at the benzylic position. The product ratio in the formation of IXa, IXb, and X was unchanged by increasing the reaction time up to 25 hr according to nmr. No epimerization appears to occur in the products on long contact with iodine.



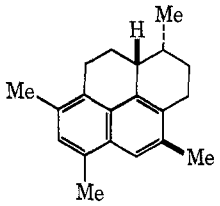
VIIIa, R = Me; R' = H
VIIIb, R = H; R' = Me



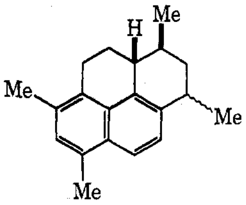
IXa, R = Me; R' = H
b, R = H; R' = Me



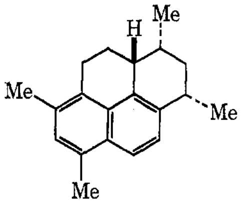
X



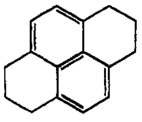
XI



XII



XIII



XIV

Compound VII gave three isomeric tetramethylhexahydropyrenes, XI and XII (mixture, 76%) and 1,3,6,8-tetramethyl-4,5,9,10-tetrahydropyrene (24%). The configurations of the methyl groups in XI and XII (mixture of diastereomers) was determined as shown in the formulae. The fourth isomer XIII, which would involve unfavorable 1,3-diaxial methyl interaction, was not detected.

Uv Spectra.—Uv data for hexahydropyrenes (III and VIII–XII) are summarized in Table III, and the absorption curves are shown in Figure 1. The number and location of alkyl substituents on a naphthalene ring has been correlated with band positions and absorption pattern.[17] Alkyl substitution at the α position, which extends conjugation in the transverse direction, causes both bathochromic and hyperchromic effects in the ^1L_a bands, whereas β substitution results in the red shift and intensifies the ^1L_b bands through

---

[16] E. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformation Analysis," Wiley-Interscience, New York, N. Y., 1965, p 141.

[17] W. L. Mosby, *J. Amer. Chem. Soc.*, **75**, 3348 (1953); H. H. Jaffè and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York, N. Y., 1962, p 303; R. W. Frank and E. G. Leser, *J. Org. Chem.*, **35**, 3932 (1970).

TABLE IV

NMR SPECTRAL DATA

	Aromatic proton,[a] ppm (J = Hz)					Methyl proton, ppm (J = Hz)	
Compd	C-6	C-7	C-8	C-9	C-10	Aliphatic	Aromatic[c]
III	7.17 (2.3, 7.7)	7.29 (7.4, 7.7)	7.58 (2.3, 7.4)	7.58 (8.5)	7.15 (8.5)		
VIIIa	7.05[b]		7.39[b]	7.50 (8.3)	7.12 (8.3)	1.11 (7.0)	2.43
VIIIb	7.03[c]		7.37[b]	7.45 (8.3)	7.15 (8.3)	1.13 (6.0)	2.43
IX		7.18 (8.3)	7.50 (8.3)	7.50 (8.3)	7.06 (8.3)	0.89 (7.0)	2.37
X	7.03 (7.6)	7.13 (7.6)		7.72 (8.8), 7.75 (8.8)	7.21 (8.8), 7.38 (8.8)	1.29 (7.5), 1.36 (7.0)	2.59
XI		7.08[c]		7.76 (9.0)	7.37 (9.0)	0.89 (7.0), 1.34 (7.0)	2.37, 2.60
XII		7.05[c]		7.70 (9.0), 7.73 (9.0)	7.16 (9.0), 7.34 (9.0)	1.15 (6.0), 1.22 (7.2), 1.35 (6.8)	2.35, 2.58

[a] Doublet or double doublet signals unless otherwise stated. [b] Broad singlet. [c] Singlet.

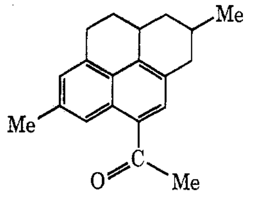
conjugation in the longitudinal direction. These have been studied in methyl-substituted naphthalenes.[17,18]

General trends are followed in the hexahydropyrenes. Compared with naphthalene, compound III which has two α and β substituents showed bathochromic shift of approximately 15 nm in all of three bands including ^1B_a. With additional β substituents VIII and IX showed a further red shift of 5 nm compared with III in the ^1L_b band. A similar red shift of a few nanometers in ^1L_a band was observed by going from III to X. For pentasubstituted naphthalenes XI and XII (determined as a mixture) further small bathochromic shifts and a loss of fine structure were observable. With highly overcrowded naphthalenes rather broad curves have been observed.[17,18]

Nmr Spectra.—Table IV summarizes spectral data for aryl and methyl protons determined in $CDCl_3$. Methylene and methine protons exhibited a complex pattern between about δ 1.2 and 3.3. Since an α proton in a naphthalene nucleus is known to be more deshielded than a β proton[19] and since there is virtually no coupling between protons in different rings,[19,20] aryl proton signals can be assigned by first-order analyses with the aid of benzyl decoupling.

Substitution of the C-7 hydrogen by a methyl group simplified the aromatic resonances and both VIIIa and VIIIb showed two broad singlets for each of the C-6 and C-8 protons. Methyl resonance signals for VIIIa and VIIIb appeared one as a singlet at δ 2.43 (C-8 methyl of both isomers), and the other as a doublet at δ 1.11 (J = 7.0 Hz) for VIIIa and at 1.13 (J = 6.0) for VIIIb. In methyl-substituted cyclohexanes and their heterocyclic analogs the vicinal coupling constants between methyl and methine protons are 5.6–6.3 Hz with equatorial and 6.3–7.2 Hz with axial isomers, and always smaller for equatorial isomers.[21] Accordingly VIIIb is assigned as possessing a quasiequatorial methyl group and VIIIa as a quasiaxial methyl group. On addition of C_6D_6 to a mixture of VIIIa and VIIIb in $CDCl_3$ the methyl signals shifted to a higher field, the magnitude of which was larger for VIIIb. This can be understood on the basis that the equatorial methyl is more exposed, and subject to an enhanced aromatic solvent induced shift.[22]

A varied amount of the shift reagent[23] was added to a $CDCl_3$ solution of 9-acetyl-2,7-dimethyl-1,2,3,3a,4,5-hexahydropyrene (XV, a mixture of configurational isomers), which was prepared by the Friedel–Crafts reaction[24] of VIII with acetyl chloride and aluminum chloride. In Figure 2 pseudocontact shifts of representative proton signals are shown as the function of the molar ratio of the reagent to XV. With $Eu(thd)_3$ the upfield shift was most prominent for the acetyl methyl and C-8 protons, while the C-10 proton showed a moderate shift. Remote protons such those at the C-6 and C-2 methyl did not show any significant change. It is noted that aryl methyl protons experience slight deshielding rather moving upfield. A similar phenomenon was noticed recently.[25] With $Pr(dpm)_3$ general downfield shifts were observed, especially the C-8 proton and acetyl methyl protons, which showed remarkable shifts as expected from the proximity of these to the metal.



XV

Of the two isomeric hexahydropyrenes derived from VI, IX has the 1,2,7,8-tetrasubstituted naphthalene structure and exhibits two sets of an AB quartet of nearly equal chemical shifts and coupling constants. On the other hand X shows unequal sets of two AB

---

(18) L. Ruzicka, H. Schinz, and P. H. Müller, *Helv. Chim. Acta*, **27**, 195 (1944); E. Heilbronner, U. Frolicher, and P. A. Plattner, *ibid.*, **32**, 2479 (1949); R. A. Morton and A. J. A. de Gouveia, *J. Chem. Soc.*, 916 (1934); B. J. Abadir, J. W. Cook, and D. T. Gibson, *ibid.*, 8 (1953).

(19) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Vol. 1, New York, N. Y., 1965, p 405; N. Jonathan, S. Gordon, and B. P. Dailey, *J. Chem. Phys.*, **36**, 2443 (1962).

(20) J. A. Pople, W. G. Schneider, and H. J. Bernstein, *Can. J. Chem.*, **35**, 1060 (1957).

(21) F. A. Bovey, "NMR Data Tables for Organic Compounds," Vol. 1, Wiley-Interscience, New York, N. Y., 1967; F. A. L. Anet, *Can. J. Chem.*, **39**, 2262 (1961); I. Kawasaki and T. Kaneko, *Bull. Chem. Soc. Jap.*, **35**, 697 (1962); T. M. Moynehan, K. Schofield, R. A. Y. Jones, and A. R. Katrizky, *J. Chem. Soc.*, 2637 (1962); W. Hofheinz, H. Griesebach, and H. Friebolin, *Tetrahedron*, **18**, 1265 (1962); A. Segre and J. I. Musher, *J. Amer. Chem. Soc.*, **89**, 706 (1967).

(22) K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon, and G. H. Wahl, Jr., *ibid.*, **86**, 1718 (1964); D. H. Williams and N. S. Bhacca, *Tetrahedron*, **21**, 2021 (1965); H. M. Fales and K. S. Warren, *J. Org. Chem.*, **32**, 501 (1967).

(23) C. C. Hinckley, *J. Amer. Chem. Soc.*, **91**, 5156 (1969); J. K. M. Sanders and D. H. Williams, *ibid.*, **93**, 641 (1971).

(24) G. Baddeley, *J. Chem. Soc.*, S 99 (1949).

(25) T. H. Siddall, III, *Chem. Commun.*, 452 (1971); P. H. Mazzocchi, H. J. Tamburin, and G. R. Miller, *Tetrahedron Lett.*, 1819 (1971); S. B. Tjan and F. R. Visser, *ibid.*, 2833 (1971).

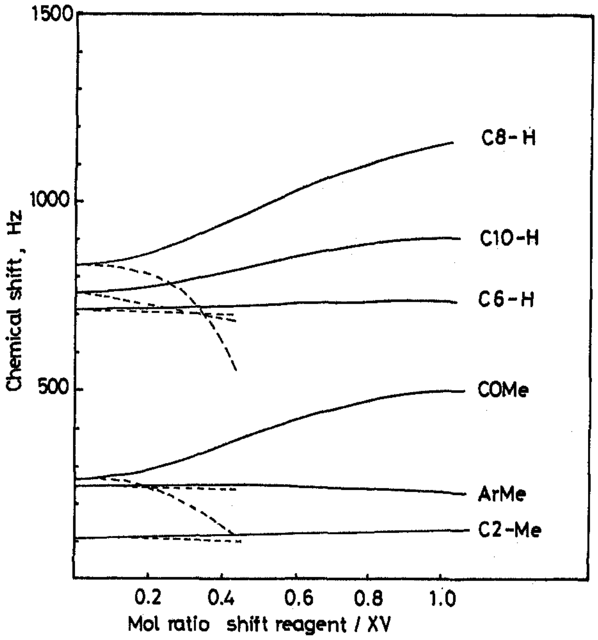
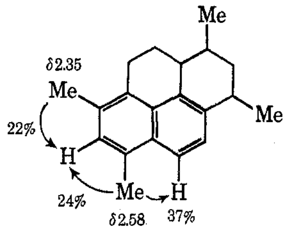


Figure 2.—Pseudo contact shifts in XV induced by Eu(dpm)$_3$ (———) and Pr(dpm)$_3$ (----) (CDCl$_3$).

quartets as expected from the structure. With IXb the methyl signal at C-3 absorbs at an unusually high field of δ 0.89, indicating the methyl group is axial and subject to a diamagnetic shift due to the naphthalene ring. The structures of X, XI, and XII were similarly determined. With XII the assignment of aryl methyl protons was achieved by NOE (see XVI).



XVI

Other Reagents.—Baker and coworkers[26] have noticed the formation of III by the treatment of I in carbon disulfide with aluminum chloride. By reexamination in our laboratory the reaction was found to give a complex mixture containing at least five materials besides III and XIV. The major product was pyrene. 4,5-Dihydropyrene (trace) and IV were also present. Those compounds preserving a cyclophane structure, such as [2.2]paracyclophane or [2.2]metaparacyclophane, were absent. The reaction of I with aluminum chloride involves fragmentation as well as disproportionation and is not so selective as the iodine-catalyzed reaction.

Cram and coworkers[27] reported the formation of III in small amount during the rearrangement of [2.2]paracyclophane to [2.2]metaparacyclophane by means of HAlCl$_4$ in dichloromethane. The reaction involves protonated [2.2]paracyclophane as an intermediate which rearranges to the [2.2]metaparacyclophane system. In view of facile cycloisomerization of I with iodine and aluminium chloride, the origin of III could be I formed by the further rearrangement of [2.2]paracyclophane. Although the cycloisomerization of I to III proceeds with aluminum chloride, whether there is a route *via* a protonated precursor is not known.

Other Lewis acids such as ferric chloride, cupric chloride (bromide), and nickel chloride were ineffective as catalysts for I → III.

Under electrophilic conditions bromination of I resulted in the formation of IV.[3,6] Boekelheide[28] reported that the irradiation of I with bromine gave pyrene. When I was treated with bromine in CCl$_4$ in the absence of catalyst, a 7% yield of III was obtained although the major product was IV. Bromine and particularly chlorine act as an electrophile to give IV *via* an addition–elimination mechanism. This may reflect the less electrophilic nature of iodine compared with other halogens and strongly suggests the participation of an iodine molecule rather than an iodonium ion. The reaction of I under ionic conditions (ICl or I$_2$–AgClO$_4$) gave IV in high yields, and not a trace of III was formed.[4,6] In view of a striking difference caused by the addition of silver perchlorate in the iodine reaction the effect of silver salts was examined. It is known that some silver salts promote strained σ bond rearrangement.[29] When I and silver perchlorate in benzene were warmed at 60° for 30 hr a trace of III resulted.

The treatment of I with concentrated sulfuric acid at room temperature produced IV, III, XIV, and pyrene together with sulfonated materials. Compound XIV was assumed to be formed from I *via* III since the latter was shown by a control experiment to be isomerized to XIV with sulfuric acid.[30]

Reaction Mechanism.—A marked difference in the rate of cycloisomerization among the methyl derivatives was noted. Accordingly, we carried out a series of competitive experiments between I and its methyl derivatives using an equimolar mixture of the substrates. The results are summarized in Table V. Figures indicate the rate of formation of the substituted hexahydropyrene relative to that of III. For comparison, the results for the ionic reaction using iodine–silver perchlorate are also shown. Cycloisomerization of V occured 4.2 times as fast as I, while under electrophilic conditions V underwent cyclodehydrogenation even more rapidly. For compound VI further enhancement in cycloisomerization was noticed but the cyclodehydrogenation rate was the same as that of V. It is noteworthy that VII undergoes very rapid cycloisomerization. Actually the rate is so rapid that VII was totally consumed after only 10 min at 60°, when only a few per cent of III was formed from I. These experiments provide three conclusions: (a) a methyl substituent enhances the rate of both cycloisomerization and cyclodehydrogenation; (b) the rate of enhancement is different between these two iodine-catalyzed reactions; (c) when methyl substituents are present at the position ortho to the bridging ethylene, cycloisomerization is anomalously accellerated. These

---

[26] W. Baker, J. F. W. McOmie, and J. M. Norman, *J. Chem. Soc.*, 1114 (1951).

[27] D. J. Cram, R. C. Helgeson, D. Lock, and L. A. Singer, *J. Amer. Chem. Soc.*, **88**, 1324 (1966); D. T. Hefelfinger and D. J. Cram, *ibid.*, **92**, 1073 (1970), **93**, 4754 (1971).

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

[29] L. A. Paquette, *Accounts Chem. Res.*, **4**, 280 (1971).

[30] Under similar conditions [2.2]paracyclophane underwent only sulfonation.

Table V

Competitive Reactions[a] between I and Methyl Derivatives and Stabilities for σ and π Complexes of Methylbenzenes[b]

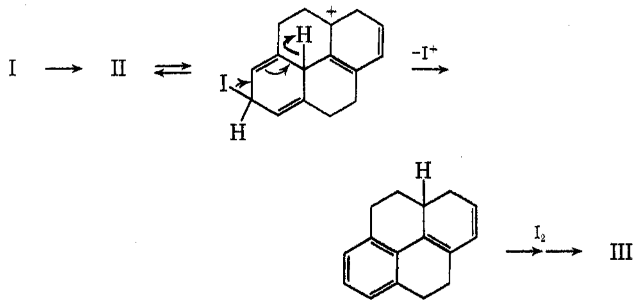
Compd	I_2 (heat)	I_2–$AgClO_4$	Compd	σ complex	π complex
I	1.0	1.0	*m*-Xylene	1.0	1.0
V	4.2	9.7	Mesitylene	630	1.3
VI	8.7	9.1	Pseudocummene	2.0	1.1
VII	Very fast		Durene	10	1.4

[a] Relative conversion to hexahydropyrenes taking I as 1 determined by treating an equimolar mixture of I and the methyl derivatives with iodine. [b] See ref 31.

data were compared with the reactivity of methylbenzenes corresponding to the half-part of the cyclophane molecules. Table V lists the stability of σ and π complexes for the model compounds.[31] The reactivities of I and V might be represented by those of *m*-xylene and mesitylene, respectively. Accordingly, one can expect strong enhancement in the reaction rate with V relative to I in a σ-complex mechanism. On the other hand moderate enhancement is to be expected with a π-complex mechanism. Strictly speaking, of course, one must consider transannular interaction and strain in the cyclophane compounds.

In electrophilic reactions, an iodonium ion attacks position 2 with concomittant bonding between C-8 and C-16 *via* σ complex II which then gives IV (Scheme I). The mechanism shown in Scheme II can be envisaged for the formation of III *via* a σ-complex mechanism. The scheme involves intramolecular hydride transfer in II followed by intermolecular hydride transfer and loss of iodonium ion.

Scheme II

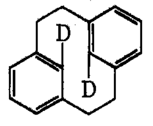


The results of competitive experiments coupled with the fact that cycloisomerization does not occur in protic solvents, however, strongly suggest involvement of the iodine molecule, possibly *via* π complexation.

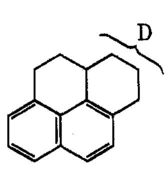
Indeed compound I and iodine in cyclohexane show a CT band at 334 nm. The band position is in agreement with the expected maximum, 336 nm, calculated from the ionization potential of I (8.41 eV).[32] The equilibrium constant was calculated to be 16.7 l./mol.[32]

For these cyclophanes having methyl groups ortho to the bridge ethylene one can not make reactivity comparisons with the methylbenzenes. Enhanced reactivity in VI and especially in VII can be taken as the indication of buttressing effects due to the *o*-methyl groups which raise the potential energy of the ground state by imposing additional strain.

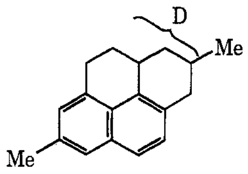
Formally the cycloisomerization involves a transfer of four hydrogens at C-1,2,8,16, to C-4,5,6,7 positions with concomittant bonding between C-8 and C-16. Marked effects of substrate and iodine concentration on the rate of cycloisomerization suggest an intermolecular hydrogen transfer process. To test this by cross-breeding experiments, [2.2]metacyclophane-8,16-d_2 (I-D) (for deuterium contents, see Table VI)[33] was prepared by the modified Wurtz dimerization of α,α'-dibromo-*m*-xylene-*2*-*d*. Compound I-D gave III-D by the treatment with iodine, whose deuterium content was determined by mass spectroscopy as shown in Table VI.



I-D



III-D



VIII-D

Table VI

Deuterium Distribution Per Cent

Compd	Source	d_0	d_1	d_2	d_3	d_4	d_5
I-D		1.7	21.3	77.0			
III-D	I-D	21.5	34.6	26.4	12.5	4.0	1.0
III-D	I-D + V	39.0	38.0	17.2	4.9	0.9	
VIII-D	I-D + V	52.3	34.7	10.7	2.1	0.2	

An equimolar mixture of I–D and V was similarly treated with iodine and the reaction mixture of III-D and VIII-D were separated. Their deuterium contents were determined by mass spectroscopy (Table VI). The results shows that a total of 48% of deuterium was transferred to VIII-D during the cross-breeding experiments suggesting an intermolecular mechanism. No deuterium transfer was observed in the control experiments in which a toluene-d_8–*m*-xylene–iodine system was similarly treated and analyzed. Owing to internal scrambling the position of labeling atoms in III-D and VIII-D could not be located from mass spectrometry.[34]

The formation of diastereomeric mixtures in approximately equal amounts in most cases during the cycloisomerization suggests that hydrogen transfer processes occur in a nonstereospecific manner. The fact that extended contact with iodine did not alter the product ratio shows that products formed are kinetically controlled. The driving force is ascribed to van der Waals and bond-bending strains in the ten-membered

---

(31) G. A. Olah, *Accounts Chem. Res.*, **4**, 240 (1971).

(32) S. Hayashi and T. Sato, *Nippon Kagaku Zasshi*, **91**, 950 (1970).

(33) K. Biemann, "Mass Spectrometry, Organic Chemical Applications," McGraw-Hill, New York, N. Y., 1962, p 223.

(34) T. K. Bradshaw, J. H. Bowie, and P. W. White, *Chem. Commun.*, 537 (1970); R. G. Cooks, I. Howe, and S. W. Tam, *J. Amer. Chem. Soc.*, **90**, 4064 (1968); R. G. Cooks, I. Howe, and D. H. Williams, *Org. Mass Spectrom.*, **2**, 137 (1969).

ring, which amounts to be 13 kcal/mol[35] for I and should be larger for more strained molecules such as VII.

Experimental Section

Methods.—Pmr spectra were obtained on a Varian XL-100 spectrometer operated by deuterium lock mode. Chemical shifts are reported in parts per million downfield from TMS. Spectra were run in deuteriochloroform unless otherwise stated. Mass spectra were obtained on a Hitachi RMU-6E mass spectrometer with ionization current of either 10 eV (for deuterium content determination) or 70 eV. To determine deuterium content, contribution of ^{13}C was corrected through M + 1 to M + 4 using average values of three scans.[33] Uv and ir spectra were recorded on Hitachi EPS-3T and EPI-G2 spectrometers, respectively. Gas chromatographic analyses were performed on a Hitachi K-53 equipped with a flame-ionization detector using 3 mm by 1-m stainless steel columns packed with SE-30 or Apiezon grease L both on Daichrom A. All melting points were obtained in liquid bath and uncorrected.

Materials.—[2.2]Metacyclophane (I) was prepared as previously described[5] and was purified by sublimation followed by column chromatography and recrystallization from ethanol, mp 132–133°. Alkyl[2.2]metacyclophanes (V–VII) were prepared according to the reported procedures: 5,13-dimethyl- (V), mp 148–149°;[10] 4,14-dimethyl- (VI), mp 68–69°;[15] 4,6,12,14-tetramethyl- (VII), mp 205–206°.[10]

***m*-Xylene-*2-d*.**—2-Bromo-*m*-xylene, prepared from 2,6-dimethylaniline by the diazo reaction, was converted to Grignard reagent in absolute THF, which was decomposed with excess deuterium oxide (99.8%). The resulting magnesium salt was treated with aqueous ammonium chloride solution. *m*-Xylene-*2-d* was distilled at 139–140°, and its deuterium content was determined by mass spectrometory to be 88.1%.

[2.2]Metacyclophane-*8,16*-d_2 (I-D).—α,α′-Dibromo-*m*-xylene-*2-d*, bp 160–180° (20 mm), crystals from *n*-hexane, prepared from *m*-xylene-*2-d* by the reaction with NBS, was subjected to high-dilution Wurtz dimerization reaction using a tetraphenylethylene–sodium adduct as a condensing reagent.[5] Addition of the bromide (10 g) took ~24 hr. After sublimation under reduced pressure the sublimate was purified by column chromatography on alumina followed by recrystallization from ethanol, mp 132–133°, $\nu_{\mathrm{C-D}}$ 2230 cm^{-1}. (For deuterium content see Table VI.)

9-Acetyl-2,7-dimethyl-1,2,3,3a,4,5-hexahydropyrene (XV).—With stirring, a 2-ml CH_2Cl_2 solution containing 533 mg (6.9 mmol) of acetyl chloride and 933 mg (7.0 mmol) of aluminum chloride was added to 700 mg (3.0 mmol) of VIII dissolved in 10 ml of CH_2Cl_2 at room temperature. After 30 min of stirring followed by usual work-up, the mixture was passed through an alumina column which gave 400 mg (48% yield) of XV, mp 124–125°, as pale yellow plates, $\nu^{\mathrm{KBr}}_{\mathrm{C-O}}$1660 cm^{-1}.

The Reaction of [2.2]Metacyclophanes (I and V–VII) with Iodine. The Formation of 1,2,3,3a,4,5-Hexahydropyrenes (III and VIII–XII).—Physical properties of III and VIII–XII are shown in Table II. Table III and IV list the spectral data. A typical example is shown by the case of I.

In a sealed tube a solution of 99.4 mg (0.48 mmol) of I and 16.6 mg (0.07 mmol) of iodine in 1.5 ml of benzene was warmed at 60° for 20 hr. After washing with sodium thiosulfate solution the benzene solution was evaporated and the residue was treated with picric acid in ethanol. The picrate, mp 147.5–148°, was then subjected to column chromatography on alumina, eluted with benzene, to give colorless plates, mp 103–104°. The yield was quantitative.

The reaction was studied under several conditions as shown in Table I. No reaction occurred in ethanol, acetic acid, carbon disulfide, or dimethylformamide.

2,7-Dimethyl-1,2,3,3a,4,5-hexahydropyrenes (VIIIa and VIIIb).—These were prepared in the same way as above starting from 60.2 mg (0.26 mmol) of V, 43.5 mg (0.17 mmol) of iodine, and 1.5 ml of benzene (60°, 20 hr). The fraction which formed the picrate was subjected to column chromatography on alumina using *n*-hexane as eluent. Fast eluting fractions contained VIIIa as colorless needles, mp 90–91°, recrystallized from methanol. As a slow moving part VIIIb was isolated, mp 163–164°, recrystallized from ethanol. The combined yield of VIIIa and VIIIb was 45 mg (70%). The ratio of VIIIa and VIIIb was determined by nmr spectra to be 46:54.

3,6-Dimethyl-1,2,3,3a,4,5-hexahydropyrenes (IXa and IXb) and 1,8-Dimethyl-1,2,3,3a,4,5-hexahydropyrene (X).—These were obtained from 641.0 mg (2.71 mmol) of VI, 153.4 mg (0.60 mmol) of iodine, and 10 ml of benzene by the same reaction conditions as above (60°, 15 hr). Repeated chromatography on alumina with *n*-hexane as eluent afforded X as viscous oil and IX as colorless plates, mp 53–55°, crystallized from ethanol. Yields were obtained by gas chromatography and nmr analysis (Table II).

In one experiment the product mixture was further treated with iodine for 25 hr at 60° but the product ratio was found to be unchanged.

1,3,6,8-Tetramethyl-1,2,3,3a,4,5-hexahydropyrenes (XI and XII).—These were obtained from 103.0 mg (0.39 mmol) of VII, 58.0 mg (0.23 mmol) of iodine, and 1 ml of benzene (60°, 20 hr). By repeated chromatographic separation, XI, mp 79–80°, and XII, mp 136–141.5°, were obtained both as colorless plates. XII was found to be an equimolar mixture of diastereomers (XIIa and XIIb). Yields were obtained by gas chromatography and nmr analysis (Table II). The cycloisomerization of VII was later found to be very rapid and was nearly complete after 10 min at 60°.

Cross-Breeding Experiment between I-D and V.—A solution of 107.4 mg (0.51 mmol) of I-D, 99.5 mg (0.42 mmol) of V, and 149.0 mg (0.59 mmol) of iodine in 2 ml of benzene was subjected to the above reaction conditions. Decomposition of the picrate afforded 130 mg of mixture, from which III-D and VIII-D were isolated by column chromatography on alumina, eluted with *n*-hexane–benzene.

Their deuterium analysis data are shown in Table VI.

Competitive Experiments. A. Cycloisomerization.—A mixture of 48.1 mg (0.23 mmol) of I, 52.2 mg (0.22 mmol) of V, and 40.4 mg (0.16 mmol) of iodine in 2.5 ml of benzene was warmed at 60° for 30 min in a sealed tube. Data in Table V were obtained by gas chromatographic analyses. For a competitive experiment between I and VI the reaction mixture was warmed at 41° for 30 min.

B. Cyclodehydrogenation.—A mixture of 44.1 mg (0.21 mmol) of I, 52.9 mg (0.22 mmol) of V, 60.4 mg (0.24 mmol) of iodine, and ~50 mg (excess) of silver perchlorate in 4 ml of ether was stirred for 2 hr at room temperature.[4,6] The product analysis was performed by gas chromatography (see Table V).

Registry No.—I, 2319-97-3; I-D, 35191-48-1; III, 5385-37-5; III picrate, 35191-50-5; VIIIa, 35191-51-6; VIIIb, 35191-52-7; IXa, 35191-53-8; IXb, 35191-54-9; Xa, 35191-55-0; Xb, 35191-56-1; XI, 35191-57-2; XIIa, 35191-58-3; XIIb, 35141-01-6; XIV, 1732-13-4.

Acknowledgment.—The authors are grateful to Dr. M. Kainosho and Mr. A. Murai, Central Research Laboratories, Ajinomoto Co., for measurements of nmr and mass spectra. Helpful discussions with Professor K. Hata and financial support from the Ministry of Education are gratefully acknowledged.

---

(35) C.-F. Shieh, D. McNally, and R. H. Boyd, *Tetrahedron*, **25**, 3653 (1969).