Cationic Cyclocodimerization. 1. Novel Synthesis of the [3.3]Paracyclophane Skeleton from 1,3-Bis(*p*-vinylphenyl)propane

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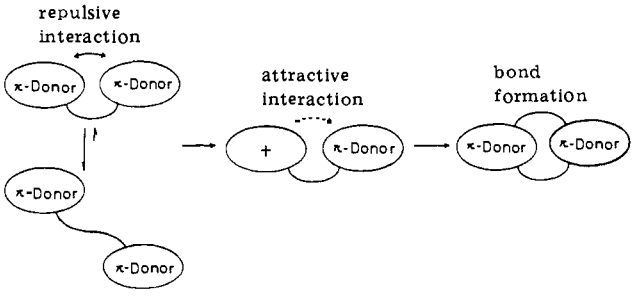
Abstract: The trapping of the cationic species, which was generated by the protonation of 1,3-bis(*p*-vinylphenyl)propane (St-C_3-St), was tried by using a number of olefins as nucleophiles. Among the olefins, styrene, *p*-methylstyrene, *p*-chlorostyrene, *m*-(trifluoromethyl)styrene, 2-phenylpropene, 1,1-diphenylethylene, indene, 1,3-cyclohexadiene, *trans*-1,3-pentadiene, and St-C_3-St itself were able to trap the cation to give *cis*- and *trans*-1-methyl-3-substituted[3.3]paracyclophanes (cis/trans ratio, 1.0-7.4) in 8-46% yields. 2-Phenylpropene gave the highest yield. Other α,ω-bis(*p*-vinylphenyl)alkanes (St-C_n-St, n = 4-6) also afforded *cis*- and *trans*-1-methyl-3-styryl[3.*n*]paracyclophanes (n = 4-6) in 43-61% yields in this cationic cyclocodimerization with styrene. From the consideration of the reaction mechanism, the propriety of olefins as a comonomer was clarified by using their ionization potentials and total delocalization energies, which were calculated for the face-to-face oriented benzyl cation-olefin pairs. Styrene derivatives and dienes of which ionization potentials lie in the range of 8.1 to 8.6 eV are concluded to be suitable for the comonomers. The methyl group of *trans*-1-methyl-3-X-substituted[3.3]paracyclophane (X = methyl, styryl, α-methylstyryl, or indenyl) showed temperature-dependent NMR resonance, which indicates conformational inversion at the disubstituted linkage. The line-shape analyses showed that the relative bulkiness of the substituents to the methyl group increased in the order of styryl < α-methylstyryl ≪ indenyl. Their activation free energies at 273 K were almost equal (11.5-11.9 kcal/mol), because of the compensative contribution of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. Especially the indenyl group substituted cyclophane showed remarkably small $\Delta H^{\ddagger}$ and largely negative $\Delta S^{\ddagger}$. These temperature-dependent NMR spectra also gave definite evidence for the cis/trans structural assignments of isomers.

Cationic cyclization, in which a carbocation intramolecularly reacts with unsaturation(s) to form a ring(s), is a general and useful method for the common-ring formation. Johnson's well-known biomimetic synthesis[1] of steroid skeletons from polyenes is one of the excellent and sophisticated applications of the method. However, carbocations are so labile in most organic solvents that the cationic C-C bond formations are often accompanied by several side reactions. Therefore, they are seldom used to make macrocyclic systems from open-chain starting materials that have little statistical advantage for the cyclization.

It is a quite common phenomenon[2] that a cation can form a donor-acceptor complex with a π-donor and stabilize itself. Hence, if the interaction is woven into an intramolecular system dexterously, a macrocyclic system or even a strained macrocyclic system can be envisioned to be prepared by the cationic method because of this stabilization.



When a molecule has donating systems at both sides that can be connected intramolecularly, any anionic C-C bond formation is scarcely suited because of the electrostatic repulsion between them. One of the typical cases in which the anionic C-C bond formation has such a difficulty is the synthesis of phanes which have two donating π-systems in a face-to-face arrangement. For such cases, however, it can be expected that the cationic method may form a C-C bond quite readily, since an attractive force as mentioned above can be generated between a donating π-system and a cationic center which may be derived from one of the π-systems and bring the two groups close to each other for the intramolecular bond formation. This is our working hypothesis adopted throughout the present study.

Within a large family of phanes,[3] [3.3]paracyclophane is quite unique. It has 12 kcal/mol of strain energy.[4] The strain is not that large compared with those of other homologues, but its synthesis was rather difficult and has experienced interesting progress: Cram and his associates[5] reported for the first time an ingenious preparation of the compound; i.e., they reduced a 1,3-diphenylpropane to a 1,3-dicyclohexylpropane system in order to avoid the repulsive interaction between two π-systems (benzene rings in this case) during the successive cyclization, namely intramolecular acyloin condensation, and applied, at the end of the synthesis, dehydrogenation to regenerate the benzene rings. The most general method for preparing the phane was recently reported,[6] in which sulfur extrusion after the oxidation of less strained and readily available dithia[4.4]paracyclophane was carried out thermally. Tsuji and Nishida[7] used the donor-acceptor interaction for the construction of the [3.3]paracyclophane skeleton. They successfully cyclized both tetracyanoquinodimethane and dispiro[2.2.2.2]deca-4,9-diene into the skeleton in surprisingly high yield (60%). Their evidence strengthens our working hypothesis mentioned above, as well as our results ac-

(1) As a review, see: Johnson, W. S. *Angew. Chem.* **1976**, *88*, 33-41.
(2) As a general reference, see: "Carbonium Ions" Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1972; Vol. III.
(3) As reviews, see: (a) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1971**, *4*, 204-13. (b) Misumi, S.; Otsubo, T. *Ibid.* **1978**, *11*, 251-6. (c) Boekelheide, V. *Ibid.* **1980**, *13*, 65-70.
(4) (a) Boyd, R. H. *Tetrahedron* **1966**, *22*, 119-22. (b) Boyd, R. H. *J. Chem. Phys.* **1968**, *49*, 2574-83. (c) Shieh, C.-F.; McNally, D.; Boyd, R. H. *Tetrahedron* **1969**, *25*, 3653-65.
(5) Cram, D. J.; Allinger, N. L.; Steinberg, H. *J. Am. Chem. Soc.* **1954**, *76*, 6132-41.
(6) (a) Otsubo, T.; Kitasawa, M.; Misumi, S. *Chem. Lett.* **1977**, 977-80. (b) Longone, D. T.; Küsefoglu, S. H.; Gladysz, J. A. *J. Org. Chem.* **1977**, *42*, 2787-8. (c) Haenel, M. W.; Flatow, A.; Taglieber, V.; Staab, H. A. *Tetrahedron Lett.* **1977**, 1733-6.
(7) (a) Tsuji, T.; Hienuki, Y.; Nishida, S. *Chem. Lett.* **1977**, 1015-6. (b) Tsuji, T.; Shibata, T.; Hienuki, Y.; Nishida, S. *J. Am. Chem. Soc.* **1978**, *100*, 1806-14.

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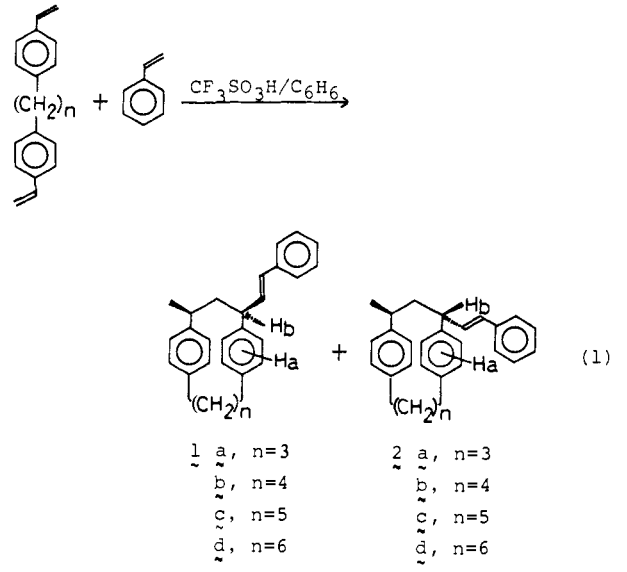
cumulated in cationic cyclopolymerization.[8]

We developed a novel and facile [3.3]paracyclophane-skeleton synthesis by cationic C–C bond formation following our working hypothesis, using readily available 1,3-bis(*p*-vinylphenyl)propane (St–C_3–St) as a starting material. In this paper, we would like to report the details of the reaction, focusing on its applicability, the mechanism including a discussion on the active species, and also a conformational change of some cyclophanes produced.

Results

Cationic Cyclocodimerization of St–C_n–St with Styrene. The intramolecular cationic cyclization of St–C_n–St by CF_3SO_3H[9] in benzene turned out to be practically useless, but the formations of the intermediate cyclic cations were certified by the data of cyclopolymerization.[8b] Therefore, the intermolecular trapping of the cyclic cation by some nucleophile was tried. The lifetime of the cation is considered to be short[10] so that its trapping must be done in situ, unless a rapid quenching technique is applied. The trapping of the cyclic cation by styrene was examined first, since it was expected to trap the cyclic cation and form the cation that may easily undergo deprotonation in the CF_3SO_3H–benzene system.[11]



(1)

1 a, n=3 b, n=4 c, n=5 d, n=6

2 a, n=3 b, n=4 c, n=5 d, n=6

From St–C_n–St (n = 3–6) and styrene, corresponding [3.n]-paracyclophane derivatives (**1** and **2**) were obtained in 38–61% yields. Results are summarized in Table I together with spectroscopic properties of the products. These products possess fully consistent spectroscopic evidence as cyclophanes, i.e., the high-fielded shift of stacked-aromatic protons in ^1H NMR spectroscopy,[12] the absorption at ca. 240 nm and the red-shifted broad B-band in UV spectroscopy,[5,13] the red-shifted charge-transfer band with tetracyanoethylene (TCNE) in visible spectroscopy,[14] and the characteristic emission in fluorescence spectroscopy.[15]

Table I. Cationic Cyclocodimerization of St–C_n–St with Styrene at 50 °C[a]

St–C_n–St, n	yield, %	isomer ratio, cis/trans	spectroscopic data for cis isomers: vis spectrosc,[b] nm	spectroscopic data for cis isomers: fluorescence spectrosc,[c] nm
3[d]	38	3.2	575 ± 5[e]	355 ± 2[f]
4	55	1.5	540 ± 5	326 ± 2
5	61	2.5	540 ± 5	310 ± 2
6	43	1.6	526 ± 5	309 ± 2

[a] Reaction conditions: [St–C_n–St]$_0$ = 6.6 mM; [St]$_0$ = 50 mM; [CF_3SO_3H] = 0.2 mM; 30 min. [b] CT complex with TCNE. Observed in methylene chloride. [c] Observed in nitrogenated cyclohexane. Excitation at 270 nm. [d] Reaction conditions: [St–C_3–St]$_0$ = 24 mM; [St]$_0$ = 120 mM; [CF_3SO_3H] = 0.02 mM; 30 h. [e] The trans isomer, 585 ± 5 nm. After hydrogenation, *cis*- and *trans*-1-methyl-3-(2-phenethyl)[3.3]paracyclophane showed CT bands at the same wavelength (595 ± 5 nm). [f] The trans isomer, 357 ± 2 nm.

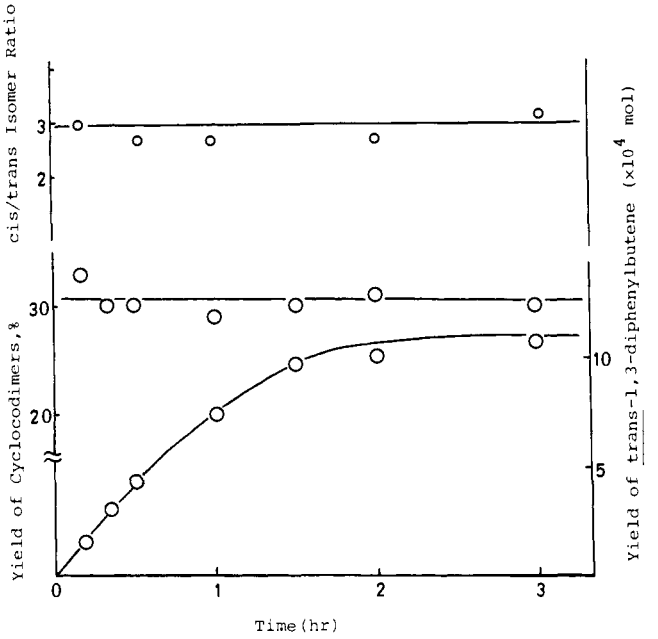


Figure 1. Time-course of cationic cyclocodimerization of St–C_3–St with styrene. Reaction conditions: [St–C_3–St]$_0$ = 0.024 M; [St]$_0$ = 0.12 M; [CF_3SO_3H] = 0.2 mM; in benzene at 50 °C. The yield of *trans*-1,3,5-triphenylhexene was trace.

As major byproducts besides polymer, a considerable amount of *trans*-1,3-diphenylbutene (styrene dimer) and a trace of *trans*-1,3,5-triphenylhexene (styrene trimer) were isolated. The time-course of the reaction of St–C_3–St with styrene is illustrated in Figure 1.

Products (**1** and **2**) are the cis and trans isomers with respect to the substituents of the linkage. The assignments of the isomers were done by ^1H NMR spectroscopy, using the chemical shift of the methyl group. It is clearly understood by a framework examination of the [3.3]paracyclophane structure that the quasiaxial (q-ax) methyl group of 1-methyl-3-styryl[3.3]paracyclophane lies in a stronger deshielding region[16] of the benzene nucleus than the

(8) (a) Furukawa, J.; Nishimura, J. *J. Polym. Sci., Polym. Lett. Ed.* **1976**, *14*, 85–90. (b) Furukawa, J.; Nishimura, J. *J. Polym. Sci., Polym. Symp.* **1976**, *56*, 437–46. (c) Nishimura, J.; Ishida, Y.; Mimura, M.; Nakazawa, N.; Yamashita, S. *J. Polym. Sci., Polym. Chem. Ed.* **1980**, *18*, 2061–70. (d) Nishimura, J.; Mimura, M.; Nakazawa, N.; Yamashita, S. *Ibid.* **1980**, *18*, 2071–84. (e) Nishimura, J.; Ishida, Y.; Hashimoto, K.; Shimizu, Y.; Oku, A.; Yamashita, S. *Polym. J.* **1981**, *13*, 635–9. (f) Nishimura, J.; Furukawa, M.; Yamashita, S.; Inazu, T.; Yoshino, T. *J. Polym. Sci., Polym. Chem. Ed.* **1981**, *19*, 3257–68. (g) Nishimura, J.; Ishida, Y.; Yamashita, S. *Kobunshi Ronbunshu* **1982**, *39*, 791–8. (h) Nishimura, J.; Yamashita, S. In "Cyclopolymerization and Polymers with Chain-Ring Structures"; Butler, G., Kresta, J. E., Ed.; American Chemical Society: Washington, DC, 1982; ACS Symp. Ser. No. 195, Chapter 14.

(9) St–C_3–St and St–C_4–St gave only polymeric material. St–C_5–St and St–C_6–St gave mixtures of cyclic products in 0.5 and 10.2% yield, respectively. St–C_2–St has been known to be unable to cyclopolymerize by cationic catalysts. See ref 8b.

(10) Nishimura, J.; Ishida, Y.; Yamashita, S.; Hasegawa, K.; Higashimura, T. *Polym. J.* **1983**, *15*, 303–7.

(11) The dimerization of styrene, namely the sequence of protonation followed by C–C bond formation and deprotonation, takes place very selectively by the treatment with CF_3SO_3H in benzene, according to Sawamoto et al.: Sawamoto, M.; Masuda, T.; Nishii, H.; Higashimura, T. *J. Polym. Sci., Polym. Lett. Ed.* **1975**, *13*, 279–82.

(12) Cram, D. J.; Helgeson, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 3515–21.

(13) In this case, the spectroscopic properties were clearly shown by the hydrogenated compounds of **1a** and **2a**.

(14) Cram, D. J.; Bauer, R. H. *J. Am. Chem. Soc.* **1959**, *81*, 5971–7.

(15) (a) Vala, M. T., Jr.; Haebig, J.; Rice, S. A. *J. Chem. Phys.* **1965**, *43*, 886–97. (b) Otsubo, T.; Kitasawa, M.; Misumi, S. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1515–20.

Table II. ^{1}H NMR Data of 1-Methyl-3-substituted[3.*n*]paracyclophane[a]

			chem shift δ,[b] ppm			Δδ, ppm		
n	substituent	isomer	H_a	H_b	Me (d; *J*, Hz)	H_a	H_b	Me
3	styryl	1a cis	6.62 (m)	3.34 (m)	1.27 (7.2)[c]	0.05	0.32	0.10
		2a trans	6.67 (bs)	3.66 (m)	1.37 (7.2)[d]			
3	α-methylstyryl	5 cis	6.70 (m)	3.55 (m)	1.26 (6.8)	0.03	0.31	0.09
		6 trans	6.73 (bs)	3.86 (m)	1.35 (7.4)			
3	indenyl	7 cis	6.62 (m)	3.60 (m)	1.29 (6.6)	0.08	0.18	0.15
		8 trans	6.70 (m)	3.78 (m)	1.44 (7.8)			
3	α-phenylstyryl	9 cis	6.46 (m)	3.27 (m)	1.18 (6.8)[e]	0.06	0.36	0.00
		10 trans	6.52 (m)	3.63 (m)	1.18 (7.0)[f]			
3	*n*-pentyl	11 cis	6.63 (m)		1.21 (6.8)	0.04		0.10
		12 trans	6.67 (m)		1.31 (6.8)			
3	cyclohexyl	13 cis	6.56 (m)		1.24 (7.0)	0.15		0.09
		14 trans	6.71 (m)		1.33 (6.8)			
3	methyl	15 cis	6.52 (m)		1.12 (6.6)	0.09		0.15
		16 trans	6.61 (bs)		1.27 (7.2)			
4	styryl	1b cis	6.58 (m)	3.37 (m)	1.27 (6.9)	0.06	0.30	0.12
		2b trans	6.64 (bs)	3.67 (m)	1.39 (6.6)			
5	styryl	1c cis	6.69 (m)	3.39 (m)	1.25 (6.6)	0.02	0.33	0.14
		2c trans	6.71 (bs)	3.72 (m)	1.39 (7.6)			
6	styryl	1d cis	6.77 (m)	3.40 (m)	1.23 (6.6)	0.03	0.35	0.13
		2d trans	6.80 (bs)	3.75 (m)	1.36 (7.2)			

[a] Only representative chemical shifts of protons on the cyclophane skeletons are listed. Recorded in $CDCl_3$ with Me_4Si as an internal standard on a Varian T60A NMR spectrometer. [b] For the designation, see structure (1 and 2). [c] ^{13}C NMR (δ, only sp^3 carbons): 49.99, 44.48, 41.40 36.05 (double intensity), 30.03, 24.62. All ^{13}C NMR spectra (20 MHz) were taken in $CDCl_3$ with Me_4Si as an internal standard on a Varian FT-80 NMR spectrometer. [d] ^{13}C NMR (δ, only sp^3 carbons): 44.51, 43.38, 36.11 (double intensity) 35.97, 29.96, 19.91. [e] ^{13}C NMR (δ, only sp^3 carbons): 46.78, 45.27, 40.72, 35.93 (double intensity), 29.88, 24.61. [f] ^{13}C NMR (δ, only sp^3 carbons): 44.04, 41.26, 35.97, 35.89, 35.79, 29.78, 20.10.

Table III. Cationic Cyclocodimerization of St–C_3–St with Various Olefins[a]

comonomer	concn, mM	time, min	yield,[b] %	isomer ratio,[c] cis/trans
p-methoxystyrene	24	30	0[d]	
	120	30	0[d]	
p-methylstyrene	24	30	21	*e*
	120	30	18	7.4
styrene	120	30	37[f]	2.7
p-chlorostyrene	120	30	20	1.9
	240	30	28	
m-(trifluoromethyl)-styrene	120	30	8	2.5
	240	30	17	2.4
p-nitrostyrene	120	30	0[g]	
indene	28	10	22	2.0
2-phenylpropene	120	20	46	1.3
1,1-diphenylethylene	120	20	36	1.0
1,3-cyclohexadiene	65	30	37	*h*
trans-1,3-pentadiene	58	30	22	*h*
St–C_3–St	*i*	60	8[j]	*e*

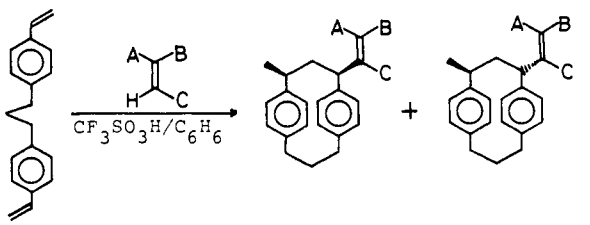
[a] Reaction conditions: [St–C_3–St]$_0$ = 24 mM; [CF_3SO_3H] = 0.2 mM; at 50 °C in benzene. [b] Isolated yield. [c] Determined by HPLC. [d] Only a high polymer was obtained. [e] Not determined. [f] The yield was determined by GC (SE30, 10%, 0.5 m, 200–250 °C). [g] *p*-Nitrostyrene was almost all recovered. [h] Isomers could not be separated by HPLC. [i] In the presence of allyl bromide (240 mM). [j] Products were 3d and 4d.

quasiequatorial (q-eq) methyl group. The methyl group of the cis isomer is always fixed at a q-eq position, whereas that of the trans isomer has the chance of being located at a q-ax position, because of the conformational change (vide infra). Hence, the methyl group of the cis isomer resonates at a higher field than that of the trans isomer.

Representative data of ^{1}H NMR spectra of these isomers are listed in Table II. The same tendency as that of the methyl group chemical shifts was observed for H_b chemical shifts. For this cis–trans structural assignment, variable-temperature NMR spectra gave additional but clearer evidence than the chemical shift differences, as mentioned below.

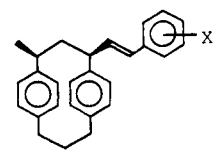
Cationic Cyclocodimerization of St–C_3–St with Various Olefins. Including styrene, 22 olefins were examined as comonomers to trap the cyclic cation of St–C_3–St.

In order to elucidate the electronic effect of the reaction, ring-substituted styrenes were employed as comonomers. Highly nucleophilic *p*-methoxystyrene did not give cyclic codimers, but

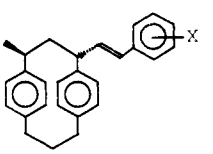


(2)

only a polymer with molecular weight 500–25000.[17] Highly electrophilic *p*-nitrostyrene did not trap the cyclic cation and almost all of it was recovered. On the other hand, *p*-methylstyrene, *p*-chlorostyrene, and *m*-(trifluoromethyl)styrene formed cyclic codimers with St–C_3–St. Results are summarized in Table III. Styrene has the most potential as a comonomer for the cyclocodimerization within its ring-substituted derivatives.



3 a, X=p-CH_3
b, X=p-Cl
c, X=m-CF_3
d, X=p-$(CH_2)_3$-C$_6$H$_4$-CH=CH_2



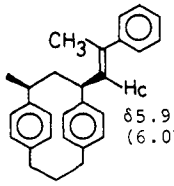
4 a, X=p-CH_3
b, X=p-Cl
c, X=m-CF_3
d, X=p-$(CH_2)_3$-C$_6$H$_4$-CH=CH_2

Among olefins examined, 2-phenylpropene gave the [3.3]-paracyclophane derivatives (**5** and **6**) in the highest yield (vide infra). In this case, the formation of *E* and *Z* isomers is possible. The calculated chemical shift[18] of H_c of the three-substituted olefin

(16) Emsley, J. W.; Feeney, J.; Sutcliffe, L. H. "High Resolution Nuclear Magnetic Resonance Spectroscopy"; Pergamon Press; Oxford, 1965; Vol. 1.

(17) Determined by gel permeation chromatography, using polystyrene as a standard.

suggests that the products are of the *E* configuration.



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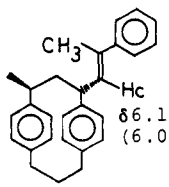

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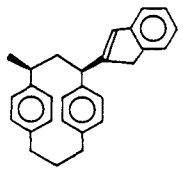
Indene was also successfully employed as a comonomer to afford the corresponding [3.3]paracyclophane derivatives (**7** and **8**).



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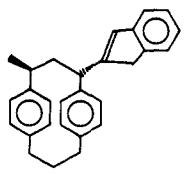

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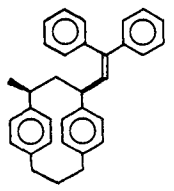
The cyclocodimerization of St–C_3–St and 1,1-diphenylethylene produced two [3.3]paracyclophane derivatives. Both showed a doublet of methyl protons at the same chemical shift, so that the criterium for assignment using methyl group resonance mentioned above was useless in this case. But the resonance of H_b indicates that one is the cis isomer (**9**) and the other the trans isomer (**10**) (see Table II). Moreover, in ^{13}C NMR spectroscopy, the methyl carbon of **10** resonates at a higher field (δ 20.10) than that of **9** (δ 24.61, see footnotes in Table II). This fact is also consistent with the above assignment, because the q-ax methyl group of **10** suffers 1,3-diaxial compression.



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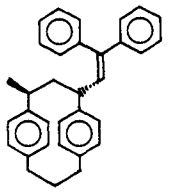

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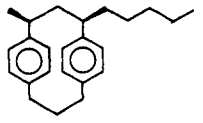
Dienes like *trans*-1,3-pentadiene and 1,3-cyclohexadiene were also cyclocodimerized with St–C_3–St. The cyclic dimers could not be separated by the reversed-phase HPLC and were slightly unstable, so that they were isolated after the hydrogenation. There are two possible attacking modes of *trans*-1,3-pentadiene to the cyclic cation with either its head or tail. According to ^1H NMR spectra, hydrogenated products (**11**, **12**) show a triplet-type resonance of three proton integrals for the methyl group of the *n*-pentyl group, but neither a doublet nor a triplet resonance of the methyl groups of the 1-methylbutyl group. Therefore, the tail attack of *trans*-1,3-pentadiene is concluded to take place in the cyclocodimerization.



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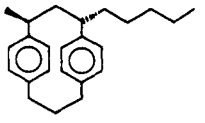

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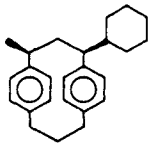

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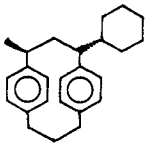


14

(18) Pascual, C.; Meier, J.; Simon, W. *Helv. Chem. Acta* **1966**, *49*, 164–168. For *Z* isomer, the calcd δ value was 5.63.

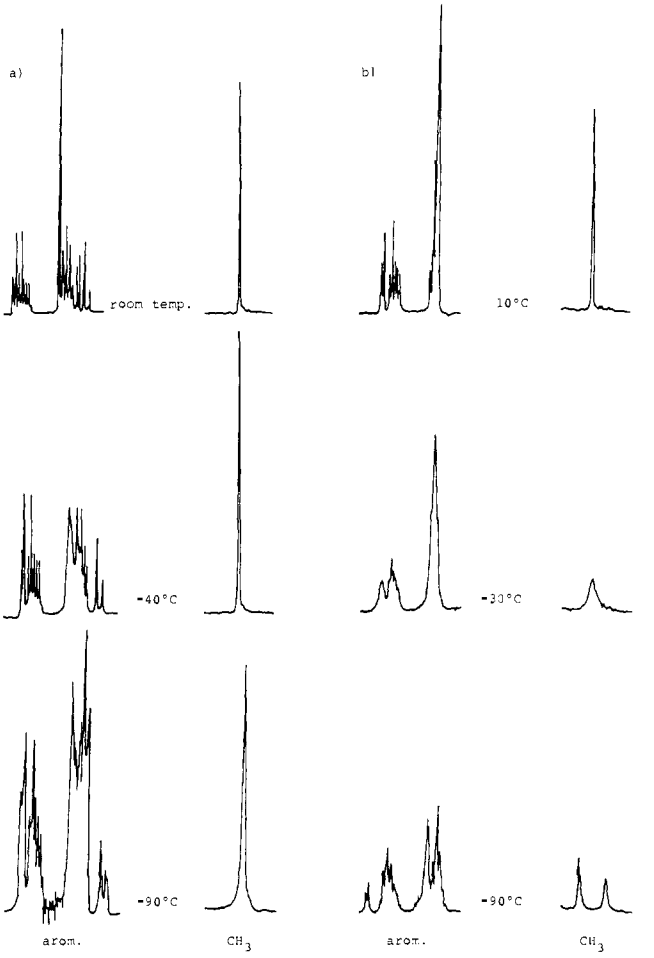


Figure 2. Variable-temperature NMR spectra of (a) **1a** and (b) **6**. The methyl group was observed as a singlet by the irradiation at the methine group. Recorded on a Varian XL 200 FT-NMR spectrometer.

Anethole, acenaphthylene, *trans*-1-phenylpropene, 2,3-dimethyl-2-butene, cyclopentadiene, 1,3-cyclooctadiene, cyclohexene, norbornene, 1-octene, 2-chloroethyl vinyl ether, and allyl bromide were not cyclocodimerized. In some cases when unreactive olefins like 1-octene, allyl bromide, and 2-chloroethyl vinyl ether were used, [3.3]paracyclophane derivatives **3d** and **4d** were formed from the cyclic cation and St–C_3–St itself instead of codimers derived from these olefins.

Dynamic NMR Study of *trans*-1-Methyl-3-substituted[3.3]paracyclophane. The dynamic NMR study of the conformational inversion of the linkage of [3.3]paracyclophane was done for the first time by Anet and his associate in 1969,[19] using a 100-MHz NMR spectrometer. They reported that for 1,1,2,2,10,10,11,11-octadeuterio[3.3]paracyclophane the coalescence temperature of the AB quartet of the benzylic protons was −33 °C, $\Delta G_c^{\ddagger} = 11.7 \pm 0.5$ kcal/mol, and the boat/chair ratio was 1:2[20] at −88 °C. For comparison with their results, it is quite interesting to examine how 1,3-disubstituted[3.3]paracyclophanes invert their conformations, focusing on the effect of the bulkiness of substituents.

The cis isomer is not expected to show a conformational inversion of the disubstituted chain at low temperature, because both substituents take q-eq positions, owing to the fact that the chain has the most stable conformation, whereas the trans isomer is expected to invert the conformation of the chain. In fact, variable-temperature NMR spectroscopy (VT NMR) corroborated the expectation (see Figure 2).

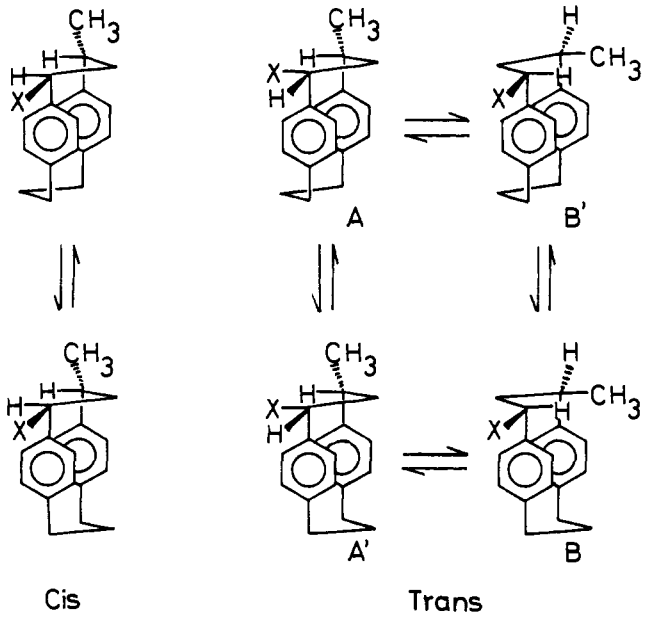
(19) Anet, F. A. L.; Brown, M. A. *J. Am. Chem. Soc.* **1969**, *91*, 2389–91.
(20) On the other hand, Benn et al. (Benn, R.; Blank, N. E.; Haenel, M. W.; Klein, J.; Koray, A. R.; Weidenhammer, K.; Ziegler, M. L. *Angew. Chem.* **1980**, *92*, 42–6) reported that the chair and boat form of (η^{12}-[3.3]paracyclophane)chromium(0) existed in a 1:1 ratio at −70 °C in toluene.

Table IV. Thermodynamic Parameters for the Interconversion of A and B Forms[a]

compound	chem shift (population) A	chem shift (population) B	T_c, °C	Arrhenius plot $\Delta E^{\ddagger}$, kcal/mol	Arrhenius plot ln A	Eyring plot $\Delta H^{\ddagger}$, kcal/mol	Eyring plot $\Delta S^{\ddagger}$, eu	Eyring plot $\Delta G^{\ddagger}_{273}$, kcal/mol
[3.3]paracyclophane[b]			−33					11.7 ± 0.5[c]
16	1.397 (0.50)	1.122 (0.50)	−43	7.4 ± 0.3	21.9 ± 0.5	7.0 ± 0.3	−16.6 ± 1.1	11.5 ± 0.6
2a	1.480 (0.53)	1.166 (0.47)	−40	7.4 ± 0.8	22.2 ± 1.8	6.9 ± 0.8	−15.9 ± 3.5	11.2 ± 1.8
6	1.540 (0.56)	1.176 (0.44)	−28	7.6 ± 0.4	22.4 ± 0.7	7.1 ± 0.4	−15.7 ± 1.5	11.4 ± 0.8
8	1.464 (0.85)	1.240 (0.15)	*d*	5.2 ± 0.6	16.9 ± 1.2	4.7 ± 0.6	−26.5 ± 2.4	11.9 ± 1.3

[a] In acetone-d_6 on a Varian XL200 FT NMR spectrometer. For simulation, generally $T_2 = 5$ s. [b] Reference 15. [c] For $\Delta G^{\ddagger}_c$. [d] Unable to be determined on spectra.

Scheme I



The trans isomers like **2a**, **6**, **8**, and **16** were proved to be conformationally less stable than the cis isomers like **1a**. Representative VT NMR spectra were illustrated in Figures 2 and 3. The preparation of **16** was shown in Scheme II. Rather complicated temperature-dependent NMR patterns of aromatic ring protons were observed for both cis and trans isomers. However, methyl resonance of cis isomer **1a** did not change its shape at temperatures between −90 °C and room temperature; i.e., the conformation of the disubstituted linkage is not inverted at low temperatures. On the other hand, the methyl groups of trans isomers showed temperature-dependent resonances. The line shapes were analyzed by using the CLATUX program reported by Binsch.[21] Representative results of the simulation are illustrated in Figure 3, and the data are summarized in Table IV.

The populations of A (and A′) and B (and B′) indicate that the relative bulkiness of substituents (X) at carbon-3 to the methyl group at carbon-1 increases in the order of styryl < α-methylstyryl ≪ indenyl. Especially the effect of the indenyl group is remarkable. Activation entropy suggests that the inversion in compound **8** occurred through a rather fixed transition state.[22] These results suggest that the steric repulsion between substituents on the α-carbon of X and the *o*-hydrogen of the adjacent benzene ring affects largely the population. When X is styryl or α-methylstyryl, the bulky group can lie far from the *o*-hydrogen, so that their steric contribution to the population becomes rather small (see side views in Figure 4).

The substituent effect on the activation free energy at 273 K was small, because of the compensation of activation entropy and enthalpy contributions. It is an interesting question how the conformational change of the disubstituted trimethylene linkage is affected by the synchronous conformational inversion of the opposite chain, if at all. Further investigation is needed on this aspect. The cyclocodimers that are prepared by reaction 2 and have a methyl group as a clue for the dynamic NMR method will be useful for this purpose.

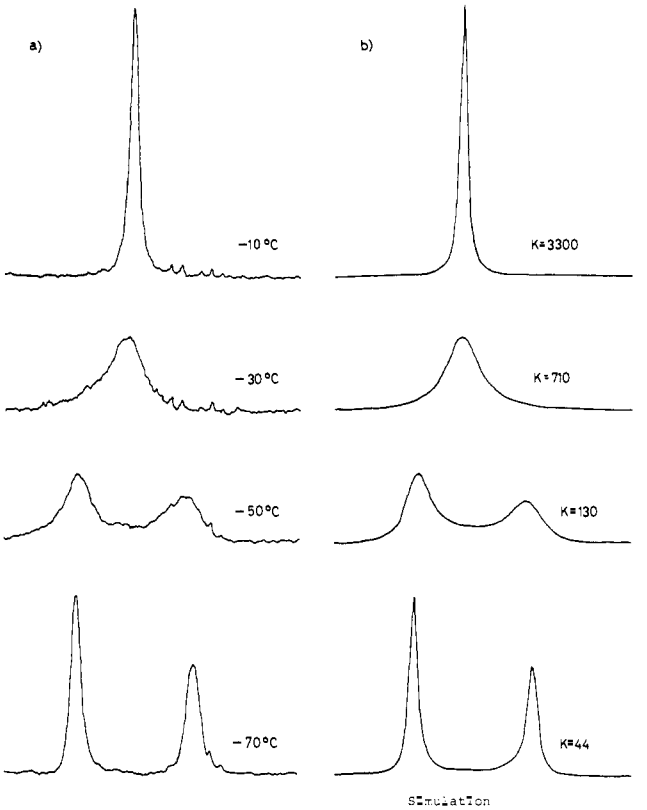


Figure 3. Simulation of variable-temperature NMR spectra of **6**: (a) observed and (b) simulation.

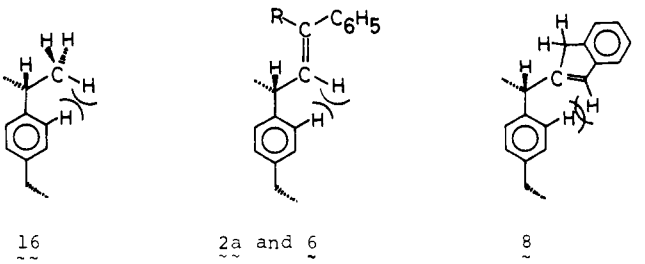


Figure 4. Side views of some trans isomers.

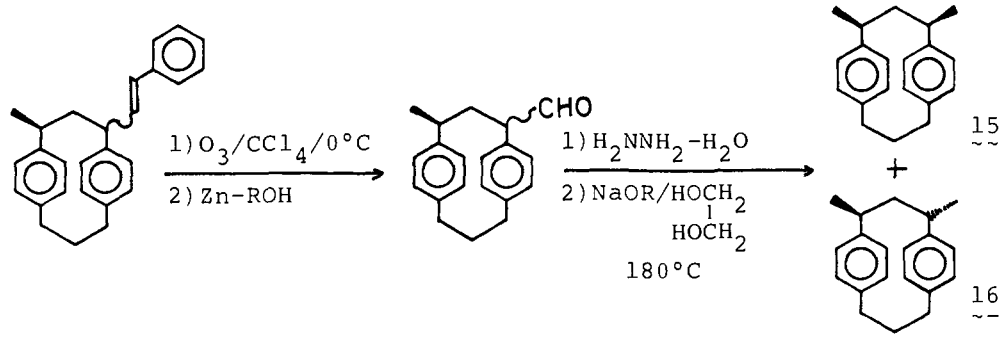
Discussion

The cationic cyclocodimerization is considered to proceed consecutively through the following four stages as shown in Scheme III: (a) protonation of St–C_n–St by a Brønsted acid, (b) subsequent intramolecular cyclization, (c) trapping of cyclic cation **18** by a comonomer, and (d) final deprotonation from codimer-

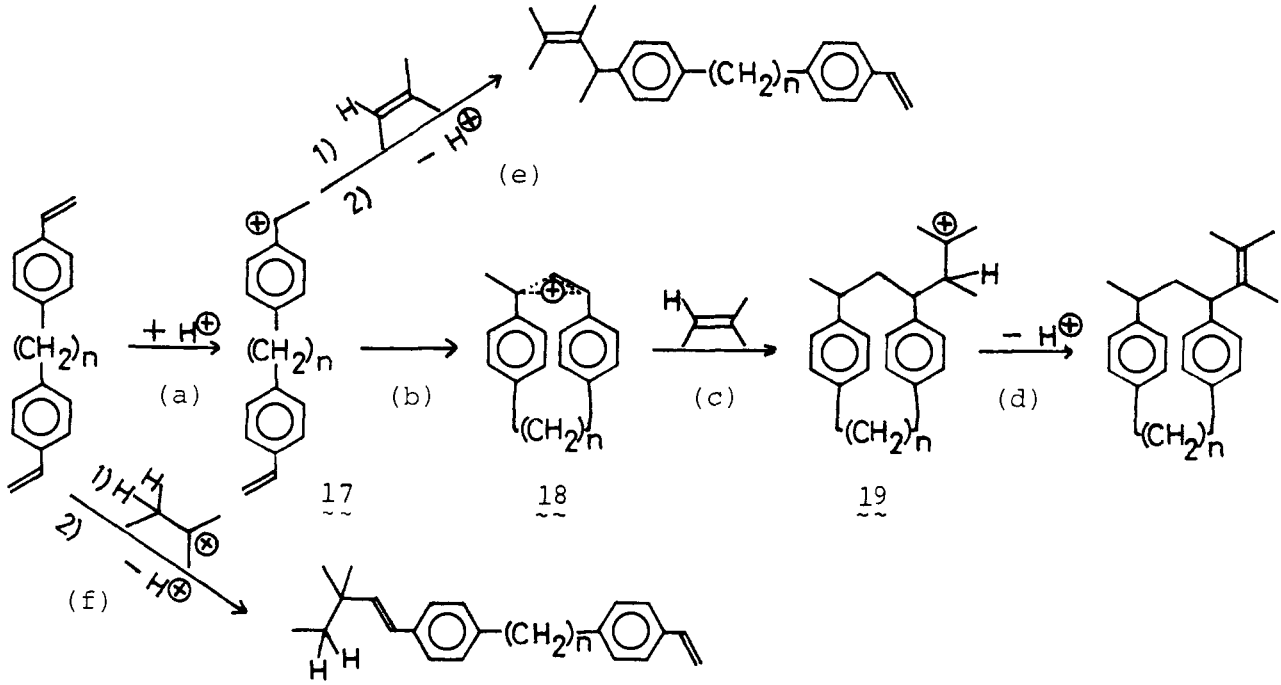
(21) Binsch, G. In "Topics in Stereochemistry": Eliel, E. L., Allinger, N. L. Eds.; Interscience Publisher: New York, 1968; Vol. 3, pp 97–192.

(22) This is supported by the framework examination; i.e., the indenyl group cannot move from the q-eq position to the q-ax position and vice versa, unless the group is accommodated at a limited space.

Scheme II



Scheme III



cation **19** to afford neutral cyclic codimers. Additionally, the following major side reactions can be expected: (e) trapping of linear cation **17** by the comonomer and (f), when a highly nucleophilic comonomer is employed, protonation taking place predominantly to it and the corresponding carbocation, thus formed, causing the formation of higher oligomers and/or linear codimers with St–C_n–St.[23]

As mentioned in the Experimental Section, steps a and d occurred as long as acid catalysts like CF_3SO_3H, acetyl perchlorate ($AcClO_4$),[24] FSO_3H, $ClSO_3H$, CH_3SO_3H, and Nafion-H[25] were used. And also the competition between steps b and e was not as serious as long as the reaction was carried out at less than 0.06 M St–C_3–St concentration above 0 °C.[26] Therefore, the competitive protonation between St–C_3–St and a comonomer olefin should be examined together with the competitive trapping (step c) of the cyclic cation between an olefin and remaining St–C_3–St. The examination of the protonation and step c clarified what kind of olefins are suitable for the cyclocodimerization, as mentioned below.

The ionization potential (IP) can be used as the reactivity parameter of olefins for the protonation and the addition of some cationic species, because IP normally represents the HOMO level[27] and olefins are considered to interact first with cationic species through this molecular orbital, although the discussion should be limited to kinetically controlled reactions. In the presence of an olefin of which the IP is higher than the 8.12 eV value of *p*-methylstyrene (a model of St–C_3–St), the protonation is supposed to occur mainly to St–C_3–St, and the cyclocodimerization goes well. The results of the cyclocodimerization with ring-substituted styrenes support this expectation; i.e., *p*-methoxystyrene gave no cyclocodimers and *p*-methylstyrene gave a rather lower product yield than styrene. According to the data summarized in Table V, olefins with IP's higher than 8.12 eV can be used as comonomers. This is the upper limitation of the reactivity of olefins toward cationic species for the cyclocodimerization. The reaction with 1,1-diphenylethylene (IP = 8.0 eV) is an exception: The diphenylethyl cation from this comonomer is stabilized and slowly propagates.[31] Therefore, the trapping of the cyclic cation with

(23) In fact, the formation of several linear telomers was observed in the reaction of St–C_3–St with styrene. See Experimental Section.
(24) Masuda, T.; Higashimura, T. *J. Macromol. Sci., Chem.* **1971**, *A5*, 549–56.
(25) This resin catalyst has an advantage in that it can be easily removed by a simple filtration and used repeatedly.
(26) The rate ratio between the cyclization and propagation of the linear cationic species of the polymerization, k_c/k_p, was determined to be 0.26 mol/L at 0 °C at the initial monomer concentration of 0.06 mol/L. See ref 8g.
(27) In this study, olefins are not always related to each other in the respect of their structures, so that any subtle discussion by comparison between their IP values could not be meaningful. Reactivity parameters such as Hammett σ, proton affinity in this specific solvent system, etc., could be more helpful for the intimate comparison of their reactivities than IP's. There are, however, no such parameters reported that can cover all olefins examined in this work, as far as we searched in literatures.
(28) "Kagaku Benran"; 2nd ed.; Japan Chemical Society, Maruzen; Tokyo, 1975; Part I.
(29) Heublein, G.; Spange, S.; Alder, P. *Faserforsch. Textiltech.* **1978**, *29*, 513–515.
(30) Herndon, W. C. *J. Am. Chem. Soc.* **1976**, *98*, 887–9 and references cited therein.

Table V. Reactivities of Olefins

entry no.	olefin	IP, eV	HOMO level,[a] eV	total delocalization energy,[b] eV	remarks[c]
1	anethole	7.68[d]			no
2	*p*-methoxystyrene	7.92[d]	−11.24	0.6216	no
3	acenaphthylene	8.02[e]	−11.63		no
4	*trans*-1-phenylpropene	8.17[d]	−11.66	0.5653	no
5	1,1-diphenylethylene	8.00[f]			yes
6	*p*-methylstyrene	8.12[d]	−11.73		yes
7	St-C_3-St				yes
8	indene	8.13[e]	−11.84		yes
9	2-phenylpropene	8.34[d]	−11.96	0.5828	yes
10	*p*-chlorostyrene	8.45[d]			yes
11	styrene	8.49[e]	−12.23	0.6443	yes
12	*m*-(trifluoromethyl)styrene				yes
13	*p*-nitrostyrene				no
14	1,3-cyclohexadiene	8.25[e]	−11.20	0.9992	yes
15	*trans*-1,3-pentadiene	8.56[e]	−12.22 (S-cis)	0.7551 (tail)[g]	yes
			−12.22 (S-cis)	0.3545 (head)[h]	
			−12.18 (S-trans)	0.5366 (tail)[i]	
			−12.18 (S-trans)	0.3354 (head)[i]	
16	cyclopentadiene	8.61[e]	−12.46	0.6314	no
17	1,3 cyclooctadiene	8.68[e]			no
18	2,3-dimethyl-2-butene	8.40[e]	−11.88	0.4685	no
19	norbornene	8.97[e]			no
20	cyclohexene	9.12[e]			no
21	1-octene	9.52[e]	−14.33[k]	0.1940[k]	no
22	2-chloroethyl vinyl ether	(9.97[e])[l]	−13.07[k]	0.2597[l]	no

[a] CNDO/2 method. [b] With benzyl cation. [c] Availability for the cyclocodimerization with St-C_3-St. [d] Reference 29. [e] Reference 28. [f] Reference 30. [g] For *S*-cis-tail attack. [h] For *S*-cis head attack. [i] For *S*-trans-tail attack. [j] For *S*-trans-head attack. [k] For propylene as a model. [l] For methyl vinyl ether as a model.

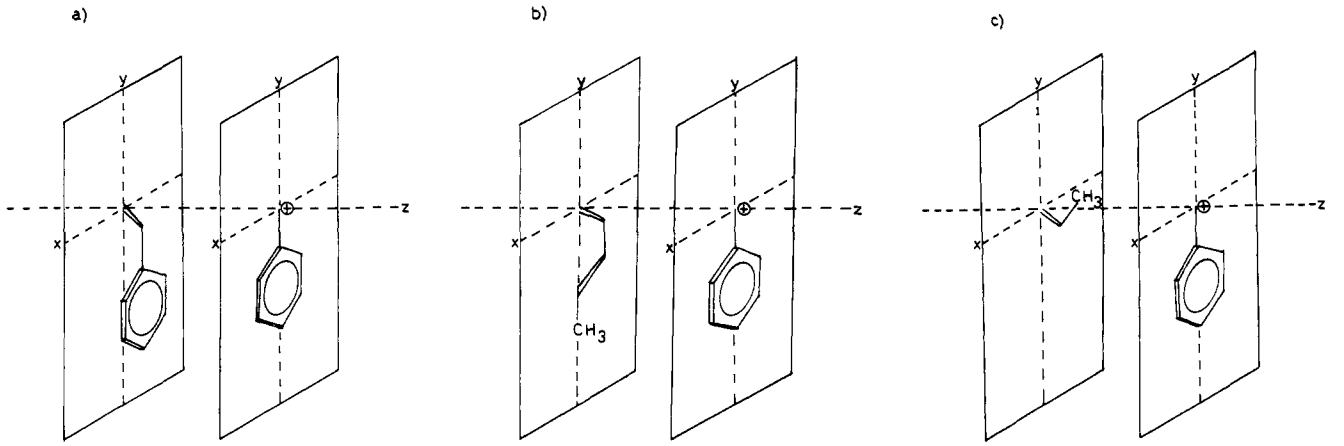


Figure 5. Models for the calculation of total delocalization energies: (a) styrene–benzyl cation pair, (b) *trans*-1,3-pentadiene (*S*-cis-tail)-benzyl cation pair, and (c) propylene–benzyl cation pair.

this olefin seems to be emphasized.

The examination of step c provides the lower limitation of the reactivities of olefins. The reactivities of olefins toward the cyclic cation were estimated by the total delocalization energy (DE) calculated by using a benzyl cation–olefin pair as a model for the transition state: Both molecules are arranged face-to-face with the distance of 3 Å between the cationic site and the reacting site of the olefin as shown in Figure 5.[32]

The experimental results are reasonably interpreted by the calculated DE values. Uneffective monoenes like 2,3-dimethyl-2-butene and 2-chloroethyl vinyl ether (methyl vinyl ether as a model) gave rather small total delocalization energies (0.19–0.47 eV), whereas pertinent styrene derivatives (entries 1–13 in Table V) and dienes (entries 14–17) like 2-phenylpropene and 1,3-cyclohexadiene gave large values of 0.6–1.00 eV, although these values may not be compared directly beyond each group—styrene derivatives, dienes, or monoenes.

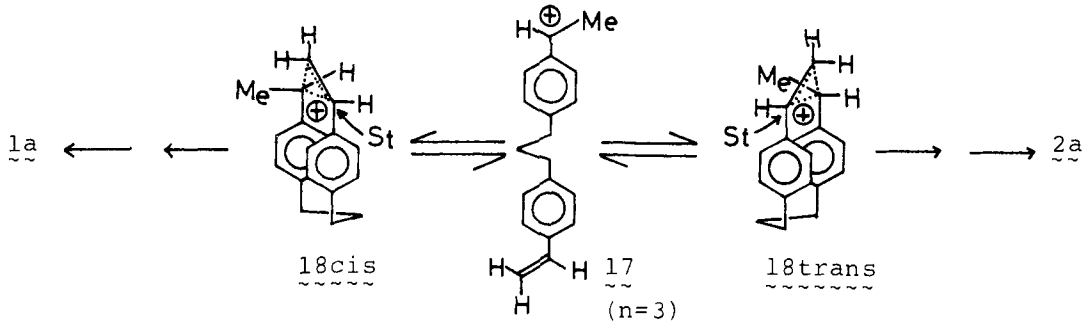
Among the three easily cationically polymerizable cyclic dienes tried, 1,3-cyclohexadiene has an almost planar 1,3-diene moiety and gives the largest DE value. It accounts well for the experimental results that only this cyclic diene was able to cyclocodimerize with St-C_3-St. The calculation can also predict the attacking mode of *trans*-1,3-pentadiene to the cyclic cation. Although several attacking modes are conceivable, the following four models were chosen for the total DE calculation as the most probable cases: *S*-cis-head, *S*-cis-tail, *S*-trans-head, and *S*-trans-tail attacks. The *S*-cis-head attack gives the highest total DE value, so that the contribution of this attacking mode may be significant in this cyclocodimerization.

Since this total delocalization energy depends largely on the HOMO level of olefins, the other end of the limitation can also be provided by IP's, ca. 8.6 eV, of *trans*-1,3-pentadiene and cyclopentadiene. Hence it can be said qualitatively that styrene derivatives and dienes having their IP in the range of 8.1 to 8.6 eV are suited for the reaction.

(31) Evans, A. G.; Owen, E. D. *J. Chem. Soc.* **1959**, 4123–5.

(32) A standard benzene ring geometry was employed throughout this study: C–C, 1.40 Å; C–H, 1.09 Å; benzylic C–C, 1.48 Å. Substituents replace appropriate hydrogen. CH_3: C–C, 1.54 Å; C–H, 1.09 Å. CH_3O: C–O, 1.36 Å; O–C, 1.43 Å; C–H, 1.09 Å; C–O–C, 121°. For styrene derivatives: C=C, 1.34 Å; =C—CH_3, 1.54 Å; C—H, 1.09 Å. For alkenes: C=C, 1.34 Å; =C—CH_3, 1.54 Å; =C—C=, 1.46 Å; C—H, 1.09 Å.

Scheme IV



Although *trans*-1-phenylpropene has a pertinent property with regard to the reactivity based on IP and DE, it did not cyclocodimerize. This can be due to the steric hindrance caused by the methyl group substituted at the double bond, when this olefin attacks the cyclic cation, because its homologue, indene, successfully gave the desired cyclocodimers.

The highest yield of cyclocodimers was obtained in the reaction with 2-phenylpropene. This result is ascribed to its ceiling temperature, in addition to its ideal properties which are promised by IP and DE. Near the ceiling temperature,[33] it propagates little. It has the same advantage as 1,1-diphenylethylene.

The rapid-scan absorption spectroscopic analysis[10] showed that the cationic species of St–C_3–St, which was generated by the protonation of the monomer by CF_3SO_3H in methylene chloride at 30 °C, absorbed light at 360 nm. On the other hand, the cationic species of St–C_2–St showed absorption at 345 nm. This monomer, St–C_2–St, is known not to be cyclopolymerized by any cationic catalysts,[8b] so that the absorption at 345 nm is ascribed to the linear cation **17** (n = 2) and/or the corresponding linear polymer cation.[34] Accordingly, the absorption of the cation of St–C_3–St was shifted bathochromically by 15 nm from that of the linear cation **17** (n = 2). Since through-bond inductive effects of the substituents on both cations are almost the same, the stabilization of the cationic species of St–C_3–St, recognized by this bathochromic shift, can be attributed to the through-space donor–acceptor interaction between an electron-donating aromatic ring and an electron-deficient or positively charged aromatic ring of the cyclic cation **18** (n = 3) and/or its polymerization counterpart.[34] This kind of stabilization seems to reduce substantially the strian that is involved in the transition state of the C–C bond formation of the cyclization.

At present there is no definite evidence for the structure of the cationic species in the cyclocodimerization. However, the following evidence seems to support the nonclassical form with a three-center two-electron bond: Classical cation **20** has the vacant p orbital which cannot fully conjugate with the π orbital of the adjacent benzene ring because of the strain. Therefore, the cation might be unstabilized by the cyclization. This is contrary to the spectroscopic observation mentioned above. On the other hand, nonclassical cation **18** can account for the experimental facts reasonably. Energetically, it is stabilized by the intramolecular complexation. There are two possible nonclassical cations, namely *cis*- and *trans*-**18**. Cation *cis*-**18** can be formed more favorably than *trans*-**18**, because *cis*-**18** does not experience any appreciable nonbonding interaction between the β position of the styryl group and the cationic site when two aromatic rings are overlapped for the successive bond formation, whereas in *trans*-**18** the interaction between the methyl group and the α-hydrogen of the styryl group is not negligible. Accordingly, by raising the concentration of styrene or by introducing electron-donating groups to styrene, the kinetically favored intermediate *cis*-**18** can be trapped preferably to *trans*-**18**, thus increasing the cis/trans isomer ratio.[35] The temperature-dependence study of the isomer ratio give an activation energy difference ($\Delta E^{\ddagger}_{trans} - \Delta E^{\ddagger}_{cis}$) of 2.2 kcal/mol for the formation of both isomers.

20

We have been discussing the active species of St–C_3–St, but the above conclusion also seems to be valid for other species of St–C_n–St (n = 4, 5, 6): For example, even the reaction of St–C_6–St gave a small amount of self-cyclized products in the absence of comonomers; i.e., the intermediate for these products, which should be the classical cation, is not considered to be generated as a major species.[9]

Further investigation of this intriguing cationic species is now in progress by means of solvolysis and other methods.

Conclusion

The cyclic cation formed from St–C_n–St (n = 3–6) by treatment with some strong Brønsted acids can be trapped sufficiently by some olefins in situ to afford [3.n]paracyclophane derivatives. Thus, the intramolecular cyclization of a linear molecule having donor sites at both ends that can be connected can be achieved successfully for the purpose of synthesizing even a strained macrocyclic system.

Styrene derivatives and dienes having IP in the range of 8.1–8.6 eV were effective as trapping agents or comonomers in this cationic cyclocodimerization. The range of the reactivity of olefins was recognized as above, because the protonation of St–C_n–St must occur mainly in the reaction system and the cyclic cation formed must be trapped by the olefin in competition with the remaining St–C_n–St, otherwise polymerization and/or linear codimerization occur substantially.

The cationic cyclocodimerization gave a mixture of *cis*- and *trans*-1-methyl-3-substituted[3.n]paracyclophane. The cis isomer did not show the conformational inversion of the disubstituted linkage below room temperature, whereas the trans isomer did. The inversion was easily examined by the dynamic NMR method, using the advantageously located methyl group as a clue. Therefore, we expect that the present cationic cyclocodimerization will give some intriguing materials not only for the further investigation of the conformational change of [3.n]paracyclophane systems but also for some other cyclophane chemistry.

Experimental Section

Methods. Elemental analysis was done at the Microanalysis Center of Kyoto University. Melting points were not corrected. UV and visible spectra were recorded on a Shimadzu UV-190 double-beam spectro-

(33) 61 °C, reported by: Kilroe, J. G.; Weale, K. E. *J. Chem. Soc.* **1960**, 3849–54.

(34) In this system used for the spectroscopic measurement, the presence of **17** and **18** was not proved, but the active end of the polymerization is likely to have a similar structure to **17** and **18**.

(35) As shown in Figure 1, the cis/trans isomer ratio and the total yield of cyclocodimers did not change within an experimental error after a prolonged heating for 3 h, although the increase of the amount of styrene dimer was observed. This result suggests that isomerization did not occur and the formation of isomers was kinetically controlled.

Table VI. Physical Properties and Analytical Data of Cyclophanes Produced[a]

compd	mp,[b] °C	$\nu_{C=C}$,[c] cm^{-1}	MS ($M^{+\cdot}$, m/z) calcd (found)	anal. calcd (found) C:H
1a	114.7-117.0 (E)	957	352 (352)	91.99 (92.07):8.01 (8.13)
2a	*hl*[d]	957	352 (352)	91.99 (91.50):8.01 (8.10)
1b	104.5-105.5 (E)	961	366 (366)	91.75 (92.02):8.25 (8.26)
2b	*hl*[d]	965	366.2346 (366.2323)	
1c	*hl*[d]	956	380.2502 (380.2488)	
2c	*hl*[d]	962	380.2502 (380.2483)	
1d	*hl*[d]	958	394.2659 (394.2642)	
2d	*hl*[d]	960	394.2659 (394.2655)	
5	89.0-90.5 (E)	820[e]	366.2346 (366.2323)	
6	141.5-143.0 (E)	820[e]	366.2346 (366.2349)	
7	153.0-155.0 (E)	825[e]	364 (364)	92.26 (92.19):7.74 (7.76)
8	84.0-85.0 (M)	825[e]	364.2190 (364.2198)	
9	212.0-215.0 (E)	825[e]	428 (428)	92.47 (92.63):7.53 (7.50)
10	142.5-143.5 (E)	825[e]	428.2502 (428.2497)	
11	*hl*[d]	*f*	320.2502 (320.2500)	
12	*hl*[d]	*f*	320.2502 (320.2497)	
13	90.0-95.0 (E)	*f*	332.2502 (332.2520)	
14	89.5-91.0 (E)	*f*	332.2502 (332.2480)	
15	130.0-131.0 (M)	*f*	264 (264)	90.85 (90.78):9.15 (9.30)
16	121.0-123.0 (M)	*f*	264.1877 (264.1863)	

[a] Compounds 3 and 4 were converted to 15 and 16 and compared with the authentic samples. [b] Solvents for recrystallization are given in parentheses: E, ethanol; M, methanol. [c] The out-of-plane vibration of C=C double bond. [d] Heavy liquid. [e] The absorption was designated by the comparison with those of 15 and 16 in the range of 790 to 840 cm^{-1}. [f] No olefinic absorption.

photometer. Fluorescence spectra were taken on a Hitachi MPF-4 spectrophotometer. NMR spectra were recorded on Varian T60A-, FT80-, and XL200 FT-NMR spectrometers. IR spectra were taken on JASCO IRA-1 spectrometers. Mass spectra were recorded on Hitachi RMU-6L and M80A mass spectrometers. High performance liquid chromatographic analysis (HPLC) was carried out by using an Altex Model 110A pump and a Hitachi wavelength tunable effluent monitor.

Total delocalization energies (ΔE_{rs}) with CNDO/2 molecular orbital energies and LCAO coefficients were computed by eq 3 and 4. Computation was done at the Data Processing Center of the Kyoto Institute of Technology.

$$\Delta E_{rs} = 2\left(\sum_{m}^{occ}\sum_{n}^{unocc} - \sum_{m}^{unocc}\sum_{n}^{occ}\right)\frac{(c_s^n)^2(c_r^m)^2}{\epsilon_n - \epsilon_m}\int \chi_s H' \chi_r \, d\tau \qquad (3)$$

$$H_{rs} = \int \chi_s H' \chi_r \, d\tau = \tfrac{1}{2} S_{rs}(\beta_r + \beta_s) \qquad (4)$$

In eq 3 and 4 c is the LCAO coefficient, ϵ is the molecular orbital energy, S_{rs} is the overlapping integral between atomic orbitals χ_r and χ_s, and β is the parameter of the CNDO/2 method.

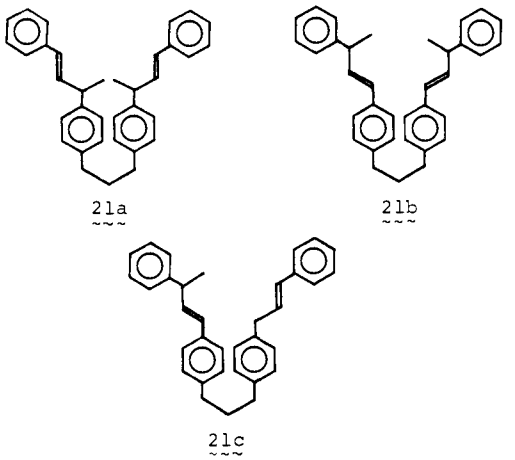
Materials. CF_3SO_3H was purified by distillation. Other commercially available highest-grade acid catalysts were used without further purification. Benzene was distilled over CaH_2 after a prolonged reflux. Olefins were dried and purified by distillation over CaH_2. St–C_n–St was prepared conveniently by our method[8e] from the corresponding alcohol.

Cationic Cyclocodimerization (General Procedure). St–C_3–St (0.60 g, 2.4 mmol) and 2-phenylpropene (1.4 g, 11.9 mmol) were dissolved in 100 mL of absolute benzene under a nitrogen atmosphere. To the mixture was added all at once at 50 °C with vigorous stirring 0.15 mL of the benzene solution of CF_3SO_3H (0.13 M). After the mixture had stirred for 20 min, 10 mL of 5% aqueous NaOH was added to stop the reaction. The reaction mixture was washed three times with water, dried over Na_2SO_4, and concentrated by evaporation. 1-Methyl-3-(α-methylstyryl)[3.3]paracyclophane (**5** and **6**; 0.403 g, 46%) was isolated as a mixture of cis and trans isomers, by column chromatography using a silica gel packed column and cyclohexane as eluent. Both were separated by HPLC (Cosmosil C-18 from Nakarai Chemicals Co. Ltd., methanol, 30 °C), in which the trans isomer (**6**) was eluted more slowly than the cis isomer (**5**). This tendency was generally observed in all cis and trans isomer combinations as long as the same kind of reversed-phase HPLC column was used. Isomer ratios were determined by HPLC with use of the monitor (λ 295 nm).

The reaction could be applied to a large-scale preparation: For example, **1a** and **2a** (total 5.3 g, 26%) were obtained by the reaction of St–C_3–St and styrene in 2 L of benzene.

Physical properties and analytical data were summarized in Table VI. Detailed data are available.[36]

The reaction was actually completed within 10 min. Further continuation of the reaction, however, increased the amount of the dimer of the comonomer itself, which was one of the major byproducts, so that a rather short reaction time is recommended (see Figure 1). In the reaction of St–C_3–St and styrene, *trans*-1,3-diphenylbutene (styrene dimer), *trans*-1,3,5-triphenylhexene (styrene trimer), and a small amount of cotrimers (St–C_3–St/St = 1:2) were obtained. The cotrimers were ozonized, treated by zinc powder in an ethanol–acetic acid–water mixture, and finally reduced under Wolff–Kishner–Huang–Minlon conditions to give a 2.5:1.0:1.6 mixture of 1,3-bis(*p*-isopropylphenyl)propane, 1,3-di-*p*-tolylpropane, and 1-(*p*-isopropylphenyl)-3-*p*-tolyl)propane, respectively. This result shows that in the products there existed three cotrimers, **21a**,**b**,**c**. Dilution of St–C_3–St beyond ca. 0.02 M did not affect the yield



significantly. The reaction was carried out conveniently at temperatures between 50 and 80 °C. Effective acids except for CF_3SO_3H were $AcClO_4$ (28), FSO_3H (9), $ClSO_3H$ (7), CH_3SO_3H (12), and Nafion-H (28); yields are given in parentheses. Other acids like BF_3OEt_2, $SnCl_4$, 95% H_2SO_4, and 70% $HClO_4$ were ineffective. The high acid concentration caused polymerization, or other unknown side reaction, to produce polymeric materials, because cyclic codimers themselves are not as stable to acids. Solvents other than benzene were not suited for the reaction as reported for the dimerization of styrene.[11]

1,3-Dimethyl[3.3]paracyclophane (15 and 16). 1-Methyl-3-styryl-[3.3]paracyclophane (0.29 g; cis/trans isomer ratio, 9.5) was dissolved in 50 mL of CCl_4. In the mixture, ozone (2% in oxygen; flow rate, 500 mL/min) was introduced for 15 min at 0 °C, and then excess ozone was expelled by a nitrogen stream. The solvent was evaporated. The residue was dissolved in a mixture of ethanol (20 mL), acetic acid (0.5 mL), and water (1.5 mL). Under vigorous stirring, zinc powder (0.3 g) was added to the mixture over 1 h at room temperature. After the solvent was evaporated, the residue was extracted by ether, washed with aqueous Na_2CO_3, and dried over Na_2SO_4. Without further purification, the products, isomeric 1-formyl-3-methyl[3.3]paracyclophanes, were reduced under Wolff–Kishner–Huang–Minlon conditions (diethylene glycohol, 5 mL; Na, 0.22 g; NH_2–NH_2–H_2O, 0.2 mL; 180 °C; 30 min). After the usual workup procedure, the reduced products (**15** and **16**) were isolated

(36) In supplementary material.

in 78% total yield (0.17 g) by column chromatography (silica gel, cyclohexane). The cis/trans isomer ratio was 2.5, indicating that the intermediate aldehyde was epimerized by the base.

Variable-Temperature NMR Measurement. Samples (ca. 10 mg) were dissolved in 0.4 mL of acetone-d_6. Using Me_4Si as an internal standard, NMR spectra were taken between 10 and −90 °C on a Varian XL200 FT-NMR spectrometer. The CLATUX program[21] was employed to analyze the line shapes of the methyl group resonance, which was observed as a singlet by the irradiation at the methine proton.

Acknowledgment. We thank Dr. Takuji Sugimoto, School of Medicine, Osaka University, for graciously providing the program for the computation of total delocalization energies and Dr. Nobuo Tanaka, Kyoto Institute of Technology, for helpful discussion on HPLC and graciously providing excellent reversed-phase HPLC columns packed by himself.

Registry No. 1a, 85781-42-6; **1b**, 85781-43-7; **1c**, 85781-44-8; **1d**, 85781-45-9; **2a**, 85848-69-7; **2b**, 85848-70-0; **2c**, 85848-71-1; **2d**, 85848-72-2; **3a**, 85781-46-0; **3b**, 85781-47-1; **3c**, 85781-48-2; **3d**, 85781-49-3; **4a**, 85848-73-3; **4b**, 85848-74-4; **4c**, 85848-75-5; **4d**, 85848-76-6; **5**, 85781-50-6; **6**, 85848-77-7; **7**, 85781-51-7; **8**, 85848-78-8; **9**, 85781-52-8; **10**, 85848-79-9; **11**, 85781-53-9; **12**, 85848-80-2; **13**, 85781-54-0; **14**, 85848-81-3; **15**, 85781-55-1; **16**, 85848-82-4; St-C_3-St, 58845-03-7; St-C_4-St, 41996-99-0; St-C_5-St, 79541-69-8; St-C_6-St, 32927-54-1; *p*-methoxystyrene, 637-69-4; *p*-methylstyrene, 622-97-9; styrene, 100-42-5; *p*-chlorostyrene, 1073-67-2; *m*-(trifluoromethyl)styrene, 402-24-4; *p*-nitrostyrene, 100-13-0; indene, 95-13-6; 2-phenylpropene, 98-83-9; α-phenylstryene, 530-48-3; 1,3-cyclohexadiene, 592-57-4; *trans*-1,3-pentadiene, 2004-70-8.

Supplementary Material Available: Table of ^1H NMR and mass spectroscopic data of cyclophane (4 pages). Ordering information is given on any current masthead page.

Rate-Controlling Two-Proton Transfer Coupled with Heavy-Atom Motion in the 2-Pyridinone-Catalyzed Mutarotation of Tetramethylglucose. Experimental and Calculated Deuterium Isotope Effects

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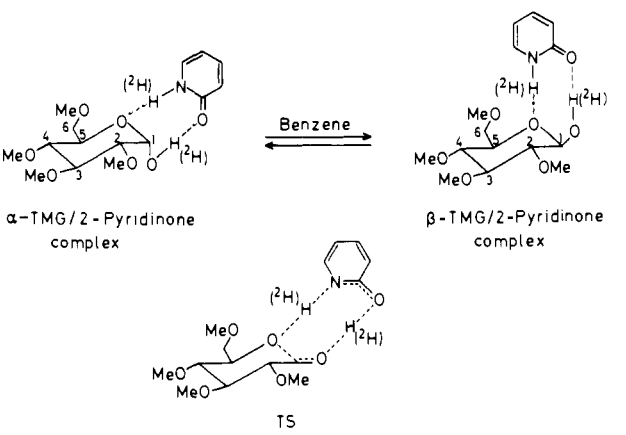
Abstract: Primary and secondary deuterium isotope effects have been measured by polarimetry, and primary isotope effects have been calculated for the classical bifunctional catalysis: 2-pyridinone-catalyzed mutarotation of 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranose (α-TMG) in benzene. From the positively curved plot of the specific rate of epimerization vs. the mole fraction of ^2H in the "pool" of OH and NH hydrogens, the isotope effects $k_{HH}/k_{DD} = 3.66 \pm 0.09$, $k_{HH}/k_{DH} = 1.5$, and $k_{HH}/k_{HD} = 2.4$ have been calculated. A secondary isotope effect of 1.14 ± 0.02 has been measured by using α-TMG and (1-^2H)-2,3,4,6-tetra-*O*-methyl-α-D-glucopyranose [(1-^2H)-α-TMG], the synthesis of which is described in detail, together with those for (*N*-^2H)-2-pyridinone and (1-*O*-^2H)-2,3,4,6-tetra-*O*-methyl-α-D-glucopyranose [(1-*O*-^2H)-α-TMG]. The rate data obtained have also been analyzed by fractionation theory, yielding approximately equal fractionation factors (0.5). The interpretation of the results has been assisted by calculations of the primary deuterium isotope effects using the BEBOVIB IV program. Two models involving small and considerable coupling, respectively, of the transferring protons to heavy-atom motion have been considered. In the favored structure for the transition state of the rate-limiting step, two protons are in transit, and their motion is governed either by a potential with a barrier or by one without. Their motion is considerably coupled to the heavy-atom motion (i.e., the breakage of the ring C–O bond), and tunnel corrections to the isotope effects are found to be negligible. The results uphold the principle behind the rule of the geometric mean, i.e., $(k_{HH}/k_{HD})(k_{HH}/k_{DH}) = k_{HH}/k_{DD}$, despite the strong couplings in the transition state. The calculated k_{HH}/k_{DD} values are found to be relatively insensitive to the extent and symmetry of the proton transfers.

Introduction

Thirty years ago Swain and Brown reported their discovery of the unusual catalytic activity of 2-pyridinone in the epimerization of α-TMG to β-TMG in benzene.[2] The extraordinary efficiency of this catalyst in relation to its weak basic and acidic properties was the basis for the formulation of the bifunctional mechanism shown in Scheme I. In the 2-pyridinone–hemiacetal (TMG) complex the two protons were assumed to be transferred simultaneously in the rate-controlling transition state. Since its discovery this type of catalysis has attracted considerable interest.[3]



To obtain a deeper understanding of the nature of two-proton transfers in bifunctional catalysis, we are investigating a number of reaction systems. We have studied *sec*-amidine catalyzed 1,3-proton transfers in substituted propenes in which protons are transferred from carbon to nitrogen and from nitrogen to carbon

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