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Synthesis of [3"]Cyclophanes and Related Compounds by Alkylation of Tosylmethyl Isocyanide with Bis(bromomethyl)benzenes

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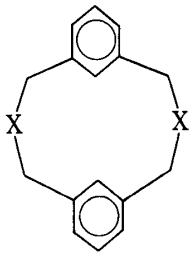
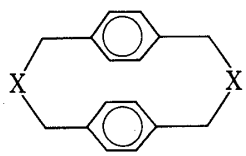
Bis(2-isocyano-2-tosylethyl)benzenes (**12a**, **12b**, and **12c**), synthesized by the reaction of tosylmethyl isocyanide (**7**) with bis(bromomethyl)benzenes (**11a**, **11b**, and **11c**) in 2:1 molar ratio, reacted again with **11a**, **11b**, and **11c** under phase-transfer conditions to form 2,11-diisocyano-2,11-ditosyl[3^2]cyclophanes of *ortho*, *meta*, and *para* types (**14**, **15**, and **17**), 2,11,20-triisocyano-2,11,20-tritosyl[3^3]paracyclophane (**19**), and 2,11,20,29-tetraisocyano-2,11,20,29-tetratosyl[3^4]cyclophanes of *meta* and *para* types (**16** and **18**). [3^2]Metacyclophane (**1**), [3^3]paracyclophane (**31**), and [3^4]meta- and paracyclophanes (**32** and **33**) could be obtained by hydrolysis and Wolff–Kishner reduction of the above intermediates (**15**, **16**, **18**, and **19**). Hydrolysis of 2,11-diisocyano-2,11-ditosyl[3^2]orthocyclophane (**14**) yielded 5,6,11,12-tetrahydro-dibenz[*b*,*g*]-azulen-5-one (**30**) instead of the corresponding ketone (**26**). Structural properties of the prepared cyclophanes (**15**, **17**, **21**, **23**, **24**, **31**, and **33**) are described on the basis of the proton magnetic resonance (PMR) spectra.

Keywords——tosylmethyl isocyanide; paracyclophane; metacyclophane; isocyanide; dibromide; macrocyclic ketone; indane; 5,6,11,12-tetrahydro-dibenz[*b*, *g*]azulen-5-one; phase-transfer alkylation; hydrolysis

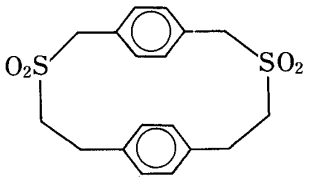
In a number of reports related to the preparation of [3^2]metacyclophane (**1**) and [3^2]paracyclophane (**3**), including a quite recent reference,[1] it has been shown that the corresponding chlorides (**2** and **5**),[2] ketones (**4**),[3] sulfones (**6**),[4] and other compounds[5] as important precursors can be synthesized by several methods. van Leusen has separately reported[6] that tosylmethyl isocyanide (TosMIC; **7**) can react with alkyl halides under basic conditions to give mono- and dialkylated TosMIC derivatives (**8** and **9**), and hydrolysis of **9** under acidic conditions converts it to the corresponding ketone (**10**) (Chart 1).



1: X=CH_2
2: X=CH–Cl



3: X=CH_2
4: X=C=O
5: X=CH–Cl



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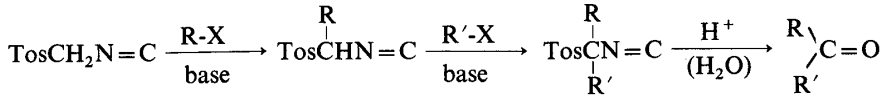


7 R, R′=alkyl **8** X=halogen **9** **10**

Chart 1

TABLE I. Bis(2-isocyano-2-tosylethyl)benzenes (**12a—c**)

Compd. No.	Yield (%)	mp (dec.) °C	IR (KBr) cm^{-1} (N=C)	PMR (δ, $CDCl_3$)						Formula	Analysis (%) Calcd (Found)		
				$-CH_3$	$-CH_2-$[a]		$-CH-$[a]	Benzene nucleus	Tos[b]		C	H	N
12a	48	(165—166)	2145	2.48 6H s	3.10 2H dd	3.60 2H dd	4.64 2H dd	7.24 4H s	7.66 8H q	$C_{26}H_{24}N_2O_4S_2$	63.39 (63.11)	4.91 (4.96)	5.69 (5.40)
12b	70	(146—147)	2145	2.48 6H s	2.98 2H dd	3.60 2H dd	4.56 2H dd	7.23 4H m	7.65 8H q	$C_{26}H_{24}N_2O_4S_2$	63.39 (63.13)	4.91 (4.89)	5.69 (5.78)
12c	67	(175—176)	2145	2.48 6H s	2.98 2H dd	3.60 2H dd	4.56 2H dd	7.22 4H s	7.65 8H q	$C_{26}H_{24}N_2O_4S_2$	63.39 (62.77)	4.91 (4.87)	5.69 (5.60)

a) ABX type absorption; $J_{gem}=14$ Hz, $J_{vic}=3$ Hz and 11 Hz.
b) AB quartet; $J=8$ Hz.

In continuation of our studies on the reaction of **7** with aldehydes,[7a,b] acetylenes,[7c] and isothiocyanates,[7d] van Leusen's results prompted us to examine the possibility that bis(2-isocyano-2-tosylethyl)benzenes (**12a**, **12b**, and **12c**) may react with bis(bromomethyl)benzenes (**11a**, **11b**, and **11c**) to form [3²]cyclophane derivatives (**14**, **15**, and **17**), if intermediates of type **12**, **12a**, **12b**, and **12c**, can first be obtained by the alkylation of TosMIC (**7**) with **11a**, **11b**, and **11c** in 2:1 molar ratio.

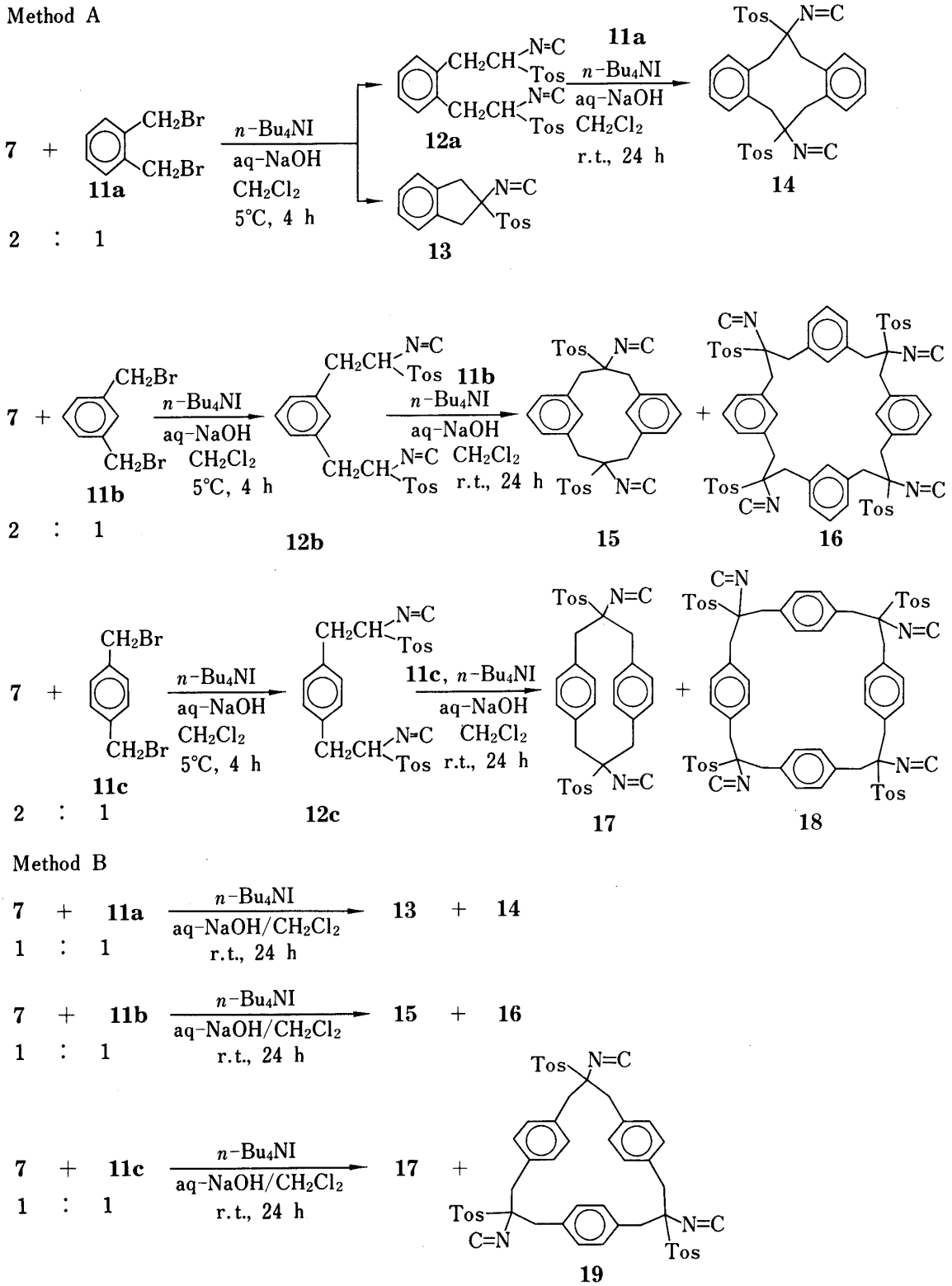


Chart 2

TABLE II. IT[3^n]cyclophanes (**14**, **15**, **17**, and **19**)

Compd. No.	n	Yield (%) Methods A[a] ( )[b]	Yield (%) Methods B[a]	mp (dec.) °C	IR (KBr) cm^{-1} (N=C)	PMR (δ, $CDCl_3$) $-CH_3$	PMR (δ, $CDCl_3$) $-CH_2-$	PMR (δ, $CDCl_3$) Benzene nucleus	PMR (δ, $CDCl_3$) Tos	Formula	Analysis (%) Calcd (Found) C	H	N
14	2	22 (47)	7	(201—203)	2120	2.50 6H s	3.65 8H q[c]	6.82 4H m; 7.20 4H m	7.82 8H q	$C_{34}H_{30}N_2O_4S_2$	68.66 (68.53)	5.09 (4.93)	4.71 (4.44)
15	2	44 (63)	14	(171—173)	2125	2.48 6H s	3.37 8H s	6.70—7.15 8H m	7.72 8H q	$C_{34}H_{30}N_2O_4S_2$	68.66 (—)	5.09 (—)	4.71 (—)[d]
17	2	4.7 (7)	0.6	(177—179)	2130	2.49 6H s	3.38 8H q[c]	6.75 4H m; 7.11 4H m	7.72 8H q	$C_{34}H_{30}N_2O_4S_2$	68.66 (—)	5.09 (—)	4.71 (—)[d]
19	3	—	12	(156—158)	2120	2.50 6H s; 2.56 3H s	3.33 12H m	5.92 and 6.80—8.20 24H m		$C_{51}H_{45}N_3O_6S_3$	68.66 (68.43)	5.09 (5.00)	4.71 (4.41)

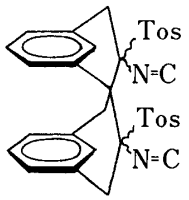
a) Calculated on the basis of TosMIC (**7**) as a starting material.
b) Calculated on the basis of **12a**—**c** as starting materials.
c) AB type absorption; $J_{gem}=14$ Hz.
d) See ref. 10.

Thus a first attempt to synthesize 1,2-bis(2-isocyano-2-tosylethyl)benzene (**12a**) by the reaction of 2 eq of TosMIC (**7**) with 1 eq of **11a** in the presence of tetra-*n*-butylammonium iodide (*n*-Bu_4NI) in a mixture of 7.5 N sodium hydroxide (NaOH) solution and dichloromethane (CH_2Cl_2) for 4 h at 5 °C provided the desired product in 48% yield, together with 2-isocyano-2-tosylindane (**13**) in 26% yield. As shown in Table I, the other 2:1 adducts (**12b** and **12c**) were also prepared under the same phase-transfer conditions.

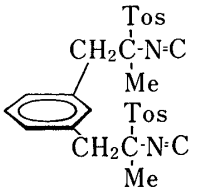
Subsequently one of the 2:1 adducts, **12b**, was reacted with 1,3-bis(bromomethyl)-benzene (**11b**) once again under similar phase-transfer catalysis for 24 h at room temperature to give 2,11-diisocyano-2,11-ditosyl[3^2]metacyclophane (IT[3^2]metacyclophane,[8] **15**; 44%) together with IT[3^4]metacyclophane (**16**) as a crude product[9] (method A). The other IT[3^2]cyclophanes (**14** and **17**) were synthesized in a similar manner in 22% and 4.7% yields, respectively.

When the reaction of TosMIC (**7**) with **11c** was carried out in 1:1 molar ratio, rather than 2:1, with *n*-Bu_4NI and 7.5 N NaOH (phase-transfer catalysis) for 24 h at room temperature (method B), not only **17** but also IT[3^3]paracyclophane (**19**) was directly obtained in 0.6% and 12% yields, respectively. Under the same reaction conditions, **7** reacted with **11b** to give IT[3^2]metacyclophane (**15**; 14%) together with **16** as a crude product, and also reacted with **11a** to yield **13** (39%) as a 1:1 adduct and IT[3^2]orthocyclophane (**14**; 7%). A comparison of the yields of IT[3^2]cyclophanes (**14**, **15**, and **17**) by methods A and B (Table II) indicates that method A (two-step procedure) rather than method B (one-pot procedure) is preferable for **14**, **15**, and **17**.

The PMR spectrum of **15** showed an inner aryl proton absorption as a broad singlet at δ 7.05. Since this δ value is similar to that of the corresponding proton (δ 7.11) of a model compound, 1,3-bis(2-isocyano-2-tosylpropyl)benzene (**20**),[11] the inner aryl protons of **15** are not shielded by the opposite benzene ring. Thus, it is reasonable to assume that the preferred conformation of **15** in solution at room temperature is a *syn* form. A comparison of the



15 (*syn*)



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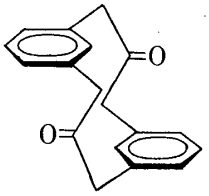

21 (*anti*)

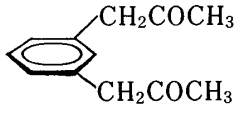

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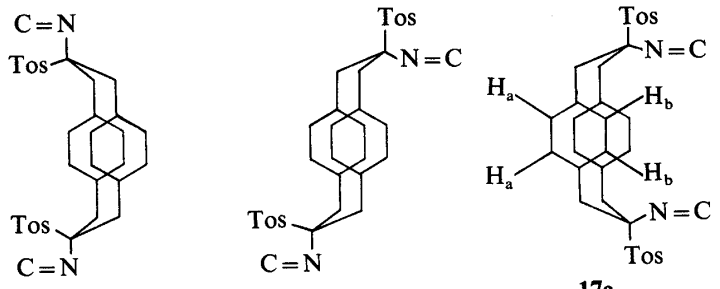
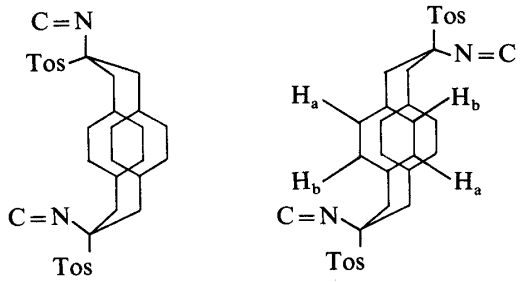
Chart 3

absorption pattern of the methylene protons of **15** with those of **14** and **17** revealed that the signal of **15** at δ 3.37 was a singlet, whereas those of **14** and **17** at δ 3.65 and 3.38 were AB quartets. These data suggest that some conformational changes might occur involving the methylene groups of **15**.

The most significant feature of the PMR spectrum of **17** is that aromatic protons are observed as two multiplets at δ 6.75 and 7.11, and methylene protons are observed as an AB quartet (J = 14 Hz) at δ 3.38. These findings suggest that inversion of the benzene ring and conformational change about the methylene groups are "frozen," probably because of the presence of the bulky tosyl groups at the 2- and 11-positions. Assuming that the bulky tosyl groups are attached at "equatorial" positions,[4a] **17c** would be preferred as a conformer for **17** on the basis of the value of the coupling constant between aromatic protons (H_a and H_b); this value for **17** is estimated at *ca.* 1.5 Hz, which is similar to the *meta* coupling constant in chromium complex of [3^2]paracyclophane[12] or 2,11-bis(phenylthia)[3^2]paracyclophane[4a] existing in a boat form. Thus, the relative position of H_a and H_b of **17** should be *meta*, but an



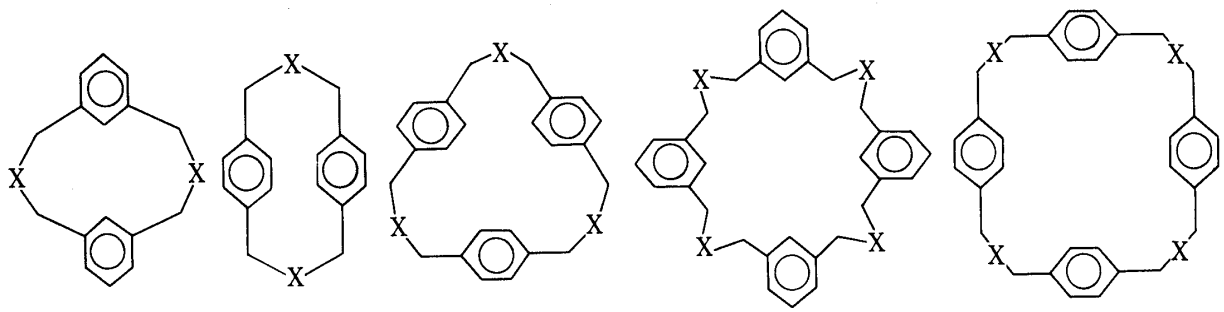
17a (boat) **17b** (chair) **17c** (boat)



17d (boat) **17e** (chair)

Chart 4

15, **16**, **17**, **18**, and **19** $\xrightarrow{H^+(H_2O)}$ **4**, **21**, **22**, **23**, and **24** $\xrightarrow{\text{reduction}}$ **1**, **31**, **32**, and **33**



21: X=C=O **4**: X=C=O **24**: X=C=O **22**: X=C=O **23**: X=C=O
1: X=CH_2 **3**: X=CH_2 **31**: X=CH_2 **32**: X=CH_2 **33**: X=CH_2

Chart 5

acceptable assignment for H_a and H_b on this basis could not be obtained.

Hydrolysis of **15** was smoothly accomplished in the presence of hydrochloric acid in CH_2Cl_2 for 1 h at room temperature to give the corresponding ketone (**21**; 81%).[13] The other ketones (**4**,[3] **22**, **23**, and **24**) prepared by similar hydrolysis, are summarized in Table III. In the case of the hydrolysis of **14**, the corresponding ketone (**26**) could not be obtained; the reaction mixture deposited a large amount of tarry material as soon as hydrochloric acid was added, whereas addition of methanol with the mixture of concentrated hydrochloric acid and CH_2Cl_2 resulted in the formation of a tetracyclic compound (**30**) (Chart 6). The formation of **30** can be rationalized in terms of hydrolysis of **14** to **26**, followed by acid-catalyzed transannular condensation of **26**.[14]

In the PMR spectrum of **21**, the inner aryl protons appeared as a broad singlet at δ 5.80.

TABLE III. Oxo[3^n]metacyclophanes (**21** and **22**) and Oxo[3^n]paracyclophanes (**4**, **23**, and **24**)

Compd. No.	n	Yield (%)	mp °C	IR (KBr) cm^{-1} (C=O)	PMR (δ, $CDCl_3$) $-CH_2-$	PMR (δ, $CDCl_3$) Ar-H	Formula	Analysis (%) Calcd (Found) C	Analysis (%) Calcd (Found) H	MS M^+ (m/e)
4[a]	2	83	276—278	1695	3.67 (8H, s)	6.83 (8H, s)	$C_{18}H_{16}O_2$	81.79 (81.80)	6.10 (5.99)	264
21[b]	2	81	207—208	1695	3.54 (8H, s)	5.82 (2H, br s) 7.25 (6H, m)	$C_{18}H_{16}O_2$	81.79 (81.79)	6.10 (5.81)	264
22	4	3[c]	220—222	1715	3.64 (16H, s)	6.80 (4H, br s) 7.15 (12H, m)	$C_{36}H_{32}O_4$	81.79 (81.72)	6.10 (5.83)	528
23	4	13[c]	292—294	1712	3.63 (16H, s)	6.88 (16H, s)	$C_{36}H_{32}O_4$	81.79 (81.53)	6.10 (5.96)	528
24	3	72	230—232	1712	3.63 (12H, s)	6.70 (12H, s)	$C_{27}H_{24}O_3$	81.79 (81.70)	6.10 (6.14)	396

a) See ref. 3. *b*) See ref. 13.
c) Overall yields calculated on the basis of TosMIC (**7**) as a starting material.

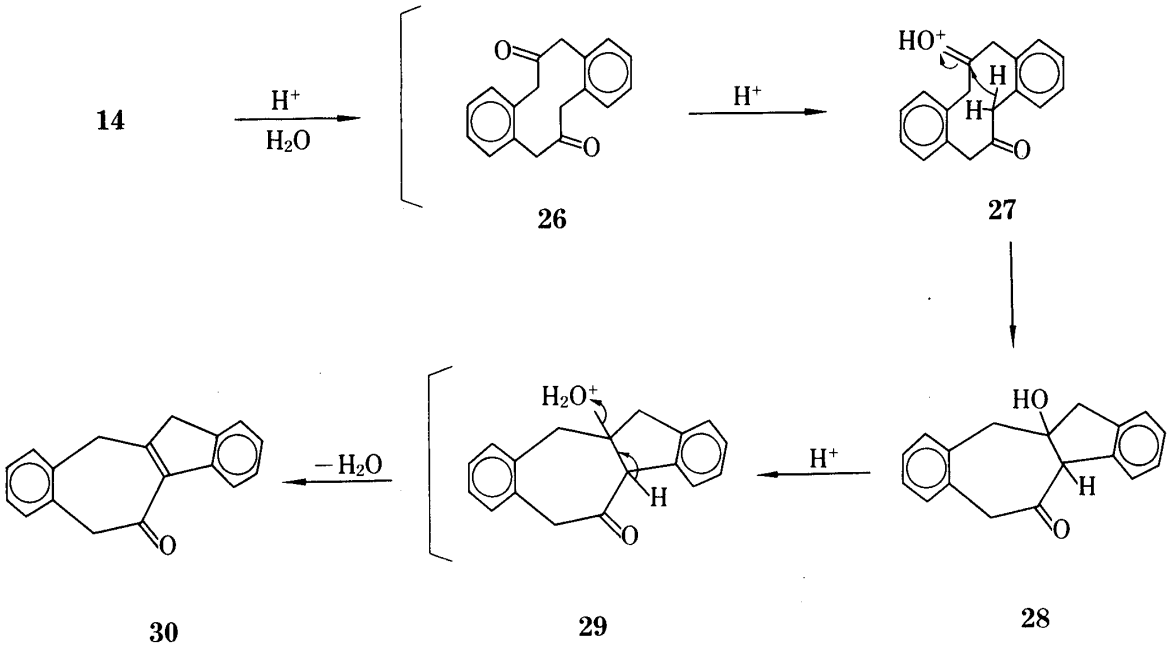


Chart 6

This δ value is higher than that of the corresponding proton (δ 7.06) of the model compound, 1,3-diacetonylbenzene (**25**).[15] Thus, the preferred conformation of **21** in solution at room temperature is assumed to be an *anti* form, because of the shielding effect of the opposite benzene ring. On the other hand, dioxo[3^2]-, trioxo[3^3]-, and tetraoxo[3^4]paracyclophanes (**4**, **24**, and **23**) are expected to exist in various conformations in solution at room temperature, since the aromatic and aliphatic protons appear as only two singlets at around δ 6.80 and 3.64 as shown in Table III.

Finally, reduction of the resulting ketones (**21**, **22**, **23**, and **24**) using hydrazine hydrate and potassium hydroxide in diethylene glycol for 3 h at 190 °C gave the corresponding [3^2]- and [3^4]metacyclophanes (**1** and **32**), and [3^3]- and [3^4]paracyclophanes (**31** and **33**) (Table IV).

TABLE IV. [3ⁿ]Metacyclophanes (**1** and **32**) and [3ⁿ]Paracyclophanes (**31** and **33**)

Compd. No.	n	Yield (%)	mp °C	IR (KBr) cm^{-1}	PMR (δ, $CDCl_3$) C-CH_2-C	PMR (δ, $CDCl_3$) Ar-CH_2-C	PMR (δ, $CDCl_3$) Ar-H	Formula	Analysis (%) Calcd (Found) C	Analysis (%) Calcd (Found) H	MS M^+ (m/e)
1[a]	2	93	85—87	822, 740, 582, 520	2.03, 4H, m	2.73, 8H, t like	6.53—6.90, 8H, m	$C_{18}H_{20}$	91.47 (91.17)	8.53 (8.53)	236
31	3	55	129—131	794, 720, 697, 442	1.91, 6H, m	2.53, 12H, t like	6.65, 12H, s	$C_{27}H_{30}$	91.47 (91.47)	8.53 (8.50)	354
32	4	30	131—133	798, 750, 698, 446	1.88, 8H, m	2.62, 16H, t like	6.90—7.12, 16H, m	$C_{36}H_{40}$	91.47 (91.30)	8.53 (8.47)	472
33	4	60	170—172	838, 803, 582, 538	1.83, 8H, m	2.52, 16H, t like	6.84, 16H, s	$C_{36}H_{40}$	91.47 (91.63)	8.53 (8.57)	472

a) See ref. 2*a*.

The spectral properties of **1** are in good agreement with those reported earlier by Yoshino.[2a] As shown in Table IV, aromatic protons of the parent [3ⁿ]paracyclophanes ($n=2$; **3**,[3] $n=3$; **31**, and $n=4$; **33**) were observed as singlets at δ 6.60, 6.65, and 6.84, respectively. This finding indicates that the larger the size of the paracyclophane ring, the smaller the shielding effect on the target benzene protons by the other benzene ring. This trend of shielding effect observed in our PMR spectra of **3**, **31**, and **33** is in good agreement with the findings of the PMR studies of [2ⁿ]paracyclophanes reported by Tabushi.[16]

Experimental[17]

Preparation of Bis(2-isocyano-2-tosylethyl)benzenes (12a, 12b, and 12c)——Typical Procedure for **12a**; A 7.5 N NaOH solution (80 ml) was added dropwise to a solution of TosMIC (**7**) (19.5 g, 0.1 mol), 1,2-bis(bromomethyl)benzene (**11a**) (13.2 g, 0.05 mol), and *n*-Bu_4NI (7.4 g, 0.02 mol) in CH_2Cl_2 (80 ml) with vigorous stirring at 5 °C. After being stirred for 4 h at 5 °C, the reaction mixture was filtered with suction to collect the precipitated product (**12a**), which was recrystallized from CH_2Cl_2 to give 11.8 g (48%) of **12a**; colorless needles, mp (dec.) 165—166 °C.

According to the same procedure as described for **12a**, the reaction of **7** with **11b** and **11c** gave crude products, which were recrystallized from CH_2Cl_2 to yield **12b** and **12c**, respectively. The yields, mp, infrared (IR), PMR, and elemental analysis data for **12a**—**c** are given in Table I.

2-Isocyano-2-tosylindane (13)——Method 1: In the preparation for **12a** described above, the filtrate that remained after collecting the crude product (**12a**), was worked up as follows; a mixture of water (500 ml) and CH_2Cl_2 (50 ml) was added to the filtrate. The CH_2Cl_2 layer was separated, washed with two 50 ml portions of water, and then dried over anhydrous magnesium sulfate ($MgSO_4$). The organic solvent was removed *in vacuo*, and the residue was extracted with three 30 ml portions of cold ether. The extracts were combined, and concentrated *in vacuo* to afford a crude product, which was recrystallized from methanol (MeOH) to yield 5.4 g (26%) of **13**; colorless prisms, mp 126—127 °C. *Anal.* Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.09; N, 4.71. Found: C, 68.41; H, 5.20; N, 4.60. PMR ($CDCl_3$) δ: 2.50 (3H, s, $-CH_3$), 3.65 (4H, AB q, $J=16$ Hz, $-CH_2-$), 7.25 (4H, s, phenyl-H), and 7.68 (4H, AB q, $J=8$ Hz, tosyl phenyl-H). IR ν_{max}^{KBr} cm^{-1}: 2125 (N=C) and 1320 and 1150 (SO_2).

Method 2: A 7.5 N NaOH solution (50 ml) was added dropwise to a solution of TosMIC (**7**) (9.75 g, 0.05 mol),

11a (13.2 g, 0.05 mol), and *n*-Bu_4NI (3.69 g, 0.01 mol) in CH_2Cl_2 (500 ml) with vigorous stirring at 0 °C to 5 °C. When the addition was over, the mixture was vigorously stirred for 24 h at room temperature, and then the CH_2Cl_2 layer was separated. The organic layer was washed with two 200 ml portions of water, and dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a heavy syrup. The residue was developed on a silica gel column with (1) benzene, (2) a mixture of benzene–ethyl acetate (AcOEt) (5 : 1). Fraction 1; concentration of the benzene eluate gave a crude product, which was recrystallized from MeOH to yield 5.8 g (39%) of **13**. Fraction 2; concentration of the benzene–AcOEt eluate gave a crude product (**14**) (see also method B in the following experiment with **14**).

2,11-Diisocyano-2,11-ditosyl[3²]orthocyclophane (14)——Method A: A 7.5 N NaOH solution (50 ml) was added dropwise to a solution of 1,2-bis(2-isocyano-2-tosylethyl)benzene (**12a**) (4.92 g, 0.01 mol), **11a** (2.64 g, 0.01 mol), and *n*-Bu_4NI (0.74 g, 0.002 mol) in CH_2Cl_2 (500 ml) with vigorous stirring at room temperature. The mixture was stirred for 24 h at room temperature, then the CH_2Cl_2 layer was separated. The organic layer was washed with three 200 ml portions of water, and dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a heavy syrup. Benzene (30 ml) was added to the residue, and the resulting solution was allowed to stand overnight at room temperature. The solution contained a crystalline mass, which was filtered off with suction and recrystallized from a mixture of CH_2Cl_2–MeOH (1 : 1) to give 2.79 g (47%) of **14**; colorless plates, mp (dec.) 201—203 °C.

Method B: In the manner described under preparation method 2 for **13**, the crude product (**14**) obtained by the reaction of **7** (9.75 g, 0.05 mol) with **11a** (13.2 g, 0.05 mol), was recrystallized from a mixture of CH_2Cl_2–MeOH (1 : 1) to give 1.04 g (7%) of **14**; colorless plates. A mixed melting point determination of this compound and the product obtained by method A show no depression. The IR spectra of the two samples were identical.

2,11-Diisocyano-2,11-ditosyl[3²]metacyclophane (15) and 2,11,20,29-Tetraisocyano-2,11,20,29-tetratosyl[3⁴]-metacyclophane (16)——Method A: According to method A described above for the preparation of **14**, the reaction of **12b** (4.92 g, 0.01 mol) with **11b** (2.64 g, 0.01 mol) in the presence of *n*-Bu_4NI (0.74 g, 0.002 mol) in a mixture of 7.5 N NaOH (50 ml) and CH_2Cl_2 (500 ml) afforded a syrupy material, which was worked up with benzene to leave crude **15** as a crystalline mass. The benzene solution was filtered with suction to collect the crude **15**, which was recrystallized from a mixture of CH_2Cl_2–MeOH (1 : 1) to give 3.74 g (63%) of **15**; colorless plates. Concentration of the benzene filtrate gave crude **16**, which was used as such for the next hydrolysis without further purification.

Method B: A 7.5 N NaOH solution (50 ml) was added dropwise to a solution of **7** (9.75 g, 0.05 mol), **11b** (13.2 g, 0.05 mol), and *n*-Bu_4NI (3.69 g, 0.01 mol) in CH_2Cl_2 (500 ml) with vigorous stirring at 0 °C to 5 °C. When the addition was over, the mixture was vigorously stirred for 24 h at room temperature, and then the CH_2Cl_2 layer was separated. The organic layer was washed with two 200 ml portions of water, and dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a heavy syrup. The residue was developed on a silica gel column with (1) benzene, (2) AcOEt. Fraction 1; concentration of the benzene eluate gave 2.08 g (14%) of **15**; colorless needles from chloroform ($CHCl_3$). Fraction 2; concentration of the AcOEt eluate gave a syrup containing **16**, which was used as such for the next hydrolysis without further purification.

2,11-Diosocyano-2,11-ditosyl[3²]paracyclophane (17), 2,11,20,29-Tetraisocyano-2,11,20,29-tetratosyl[3⁴]paracyclophane (18), and 2,11,20-Triisocyano-2,11,20-tritosyl[3³]paracyclophane (19)——Method A: According to method A described above for the preparation of **14**, the reaction of **12c** (4.92 g, 0.01 mol) with **11c** (2.64 g, 0.01 mol) in the presence of *n*-Bu_4NI (0.74 g, 0.002 mol) in a mixture of 7.5 N NaOH (50 ml) and CH_2Cl_2 (500 ml) afforded a syrupy material, which was worked up with benzene to leave crude **17** as a crystalline mass. The benzene solution was filtered with suction to collect **17**, which was recrystallized from $CHCl_3$ to yield 0.42 g (7%) of **17**; colorless needles. Concentration of the benzene filtrate gave crude **18**, which was used as such for the next hydrolysis without further purification.

Method B: According to method B described above for the preparation of **15**, the syrupy residue obtained after the reaction of **7** (9.75 g, 0.05 mol) with **11c** (13.2 g, 0.05 mol) in the presence of *n*-Bu_4NI (3.69 g, 0.01 mol) in a mixture of 7.5 N NaOH (50 ml) and CH_2Cl_2 (500 ml) was developed on a silica gel column with (1) benzene, (2) a mixture of benzene–AcOEt (4 : 1). Fraction 1; concentration of the benzene eluate gave 0.09 g (0.6%) of **17**. Fraction 2; concentration of the benzene–AcOEt eluate gave 1.78 g (12%) of **19**; colorless prisms from $CHCl_3$, mp (dec.) 156—158 °C (see Table II).

Hydrolysis of 15, 16, 17, 18, and 19 to 2,11-Dioxo[3²]metacyclophane (21) and Related Compounds (4, 24, 22, and 23)——The procedure of van Leusen[6b] was used with some modifications.

Typical Procedure for **21**: Concentrated hydrochloric acid (about 35%, 1 ml) was added dropwise to a solution of **15** (594 mg, 1 mmol) in CH_2Cl_2 (30 ml) with stirring at room temperature. The mixture was stirred for 1 h at room temperature, then the CH_2Cl_2 layer was washed with two 30 ml portions of 6 N NaOH and two 30 ml portions of water, and dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a crude product, which was recrystallized from benzene to yield 214 mg (81%) of **21**; colorless plates.

Hydrolysis of **16** (594 mg, 1 mmol) was carried out under the same conditions as described for **21** to give a crude product, which was recrystallized from CH_2Cl_2 to yield 219 mg (83%) of **4**; colorless prisms.

According to the same procedure as described for **21**, **17**, **18**, and **19** were hydrolyzed to give crude products, which were each developed on a silica gel column with (1) benzene, (2) a mixture of benzene–AcOEt (1 : 1). Fraction 1;

the benzene eluate gave *p*-toluenesulfinic acid. Fraction 2; concentration of the benzene–AcOEt eluates gave 285 mg (72%) of **24** from **17**; 114 mg (3%; on the basis of **7**) of **22** from **18**; and 502 mg (13%; on the basis of **7**) of **23** from **19**. These products were recrystallized from CH_2Cl_2 for **24** and **22**, and from 1,2-dichloroethane for **23**; colorless plates for **24** and colorless needles for **22** and **23**. The yields, mp, IR, PMR, mass spectra (MS), and elemental analysis data for **4**, **21**, **24**, **22**, and **23** are given in Table III. UV λ_{max}^{EtOH} nm (log ε): **4**; 220 (4.02), 271 (sh.) (2.76), 282 (sh.) (2.60), 299 (2.54), 312 (sh.) (2.40). **21**; 221 (sh.) (4.27), 276 (3.13), 294 (sh.) (2.96), 303 (sh.) (2.90), 313 (sh.) (2.73). **24**; 226 (sh.) (4.45), 275 (3.44), 283 (sh.) (3.41), 300 (sh.) (3.29), 312 (3.07).

Hydrolysis of 2,11-Diisocyano-2,11-ditosyl[3²]orthocyclophane (14) to 5,6,11,12-Tetrahydro-dibenz[*b*, *g*]azulen-5-one (30)——Concentrated hydrochloric acid (about 35%, 1 ml) was added dropwise to a solution of **14** (594 mg, 1 mmol) in a mixture of CH_2Cl_2 (20 ml) and MeOH (10 ml) with stirring at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was poured into 1 N NaOH (20 ml), and the CH_2Cl_2 layer was separated. The organic layer was washed again with two 20 ml portions of 1 N NaOH and two 30 ml portions of water, and then dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a crystalline mass, which was recrystallized from ether to yield 111 mg (45%) of **30**; pale yellow prisms, mp 186—188 °C. *Anal.* Calcd for $C_{18}H_{14}O$: C, 87.77; H, 5.73. Found: C, 88.07; H, 6.01. PMR ($CDCl_3$) δ: 3.66 (2H, s, $-CH_2-$), 4.00 (4H, s, $-CH_2-$), 7.10—7.50 (7H, m, phenyl-H), 8.17 (1H, m, phenyl-H). IR ν_{max}^{KBr} cm^{-1}: 1650 (C=O). MS (*m/e*): 246 (M^+). UV λ_{max}^{EtOH} nm (log ε): 238.5 (4.26), 280 (3.47), 288 (3.49), 298 (3.48).

[3²]Meta- (1), [3³]Para- (31), [3⁴]Meta- (32), and [3⁴]Para- (33) Cyclophanes——The procedure described for [3²]paracyclophane (**3**) by Cram[3] was used with some modifications.

Typical Procedure for **1**: A suspension of **22** (264 mg, 1 mmol), KOH (740 mg, 13.2 mmol), and hydrazine hydrate (about 100%, 1.26 g, 25 mmol) in diethylene glycol (20 ml) was stirred for 3 h at 190 °C. After being cooled, the mixture was poured into water (300 ml). The resulting mixture was extracted with three 50 ml portions of ether. The extracts were combined, washed with sat. aq. NaCl, and dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* to give a crude product, which was recrystallized from MeOH to yield 219 mg (93%) of **1**; colorless prisms.

According to the same procedure as described for **1**, the reductions of **24**, **22**, and **23** using hydrazine hydrate and KOH were carried out to give the crude products (**31**, **32**, and **33**), which were recrystallized from a mixture of MeOH–pet. ether (5 : 1) for **31**, from MeOH for **32**, and from a mixture of MeOH–pet. ether (3 : 1) for **33** to obtain analytical samples; colorless needles in all cases, **31**, **32**, and **33**. The yields, mp, IR, PMR, MS, and elemental analysis data for **1**, **31**, **32**, and **33** are given in Table IV. UV λ_{max}^{EtOH} nm (log ε): **1**; 262 (sh.) (2.49), 266 (sh.) (2.41), 275 (sh.) (2.14). **31**; 262 (2.55), 268 (3.11), 275 (3.07). **32**; 258 (3.02), 265 (3.11), 269 (2.97), 273 (3.01). **33**; 261 (3.16), 266 (3.26), 268 (3.25), 274 (3.25).

References and Notes

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8) The obtained [3ⁿ]cyclophane derivatives (**14—19**) possessing isocyano and tosyl groups at the 2, 11, 20, and 29 positions, are abbreviated as "IT[3ⁿ]ortho-, IT[3ⁿ]meta-, or IT[3ⁿ]paracyclophanes."
9) Attempts to isolate **16** and **18** by chromatography failed completely. Thus, we made no further attempt to isolate **16** and **18**, but isolated the corresponding ketones (**22** and **23**) after hydrolysis.
10) Of the isolated IT[3ⁿ]cyclophanes (**14**, **15**, **17**, and **19**), **15** and **17** were too unstable for elemental analysis to be possible.

11) According to method A described for the preparation of **14**, compound **20** was prepared by the reaction of **12b** with methyl iodide in 84% yield; pale yellow prisms, mp (dec.) 103—104 °C, PMR ($CDCl_3$) δ: 1.50 (6H, s, C–CH_3), 2.48 (6H, s, tosyl –CH_3), 3.22 (4H, s, –CH_2–), 7.11 (1H, br s, inner aryl-H), 7.20—7.36 (3H, m, other phenyl-H), 7.67 (8H, AB q, J=8 Hz, tosyl phenyl-H). IR ν_{max}^{KBr} cm^{-1}: 2110 (N=C), 1310 and 1145 (SO_2).
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15) According to the typical procedure for **1**, compound **25** was prepared by the hydrolysis of **20** in 76% yield; oil. PMR ($CDCl_3$) δ: 2.13 (6H, s, –CH_3), 3.70 (4H, s, –CH_2–), 7.06 (1H, br s, inner aryl-H), 7.10—7.40 (3H, m, other phenyl-H). IR ν_{max}^{KBr} cm^{-1}: 1710 (C=O). MS (*m/e*): 190 (M^+).
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17) All melting points are uncorrected. IR spectra were measured on a Hitachi model 260-30 infrared spectrophotometer. PMR spectra were measured on a Hitachi R-22 spectrometer (90 MHz) using tetramethylsilane as an internal reference, and chemical shifts were recorded as δ-values. MS were measured on a Hitachi mass spectrometer, model RMU-6MG. Ultraviolet spectra were measured on a Hitachi 323 spectrometer.