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Cyclophanes. IV. Synthesis of New [3⁴]Paracyclophanes Containing Four Imidazole Rings

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New [3⁴]paracyclophanes, 5,14,29,38-tetrakis(4-halophenyl)tetraimidazolo[3⁴]paracyclophanes (**9**), were synthesized by the convenient one-pot coupling reaction of 1,4-bis(2-isocyano-2-tosylethyl)benzene (**1b**) with 1,4-bis[(4-halophenyl)iminomethyl]benzenes (**7**). On the basis of the proton nuclear magnetic resonance and the ultraviolet spectra it was suggested that the products **9**, as well as the open-chain reference compounds (**11**), maintain coplanarity of the three linked aromatic rings, *i.e.*, imidazole, benzene, and imidazole.

Keywords——[3⁴]paracyclophane; paracyclophane; cyclophane; cyclization; imidazole; isocyanide; imine

Recently, we reported the synthesis and the conformational properties of [3²]metacyclophane derivatives, such as dioxazolo[3²]metacyclophane (**3**)[1] and diimidazolo[3²]-metacyclophanes (**4** and **6**).[2] The successful application of diisocyanides of type **1a**[1,2b] for the preparation of **6** along with a higher homolog prompted us to examine the synthesis of [3ⁿ]paracyclophanes (**8** and **9**) from diisocyanides (**1b**)[1] and diimines (**7**)[3] as *para*-substituted reactants.

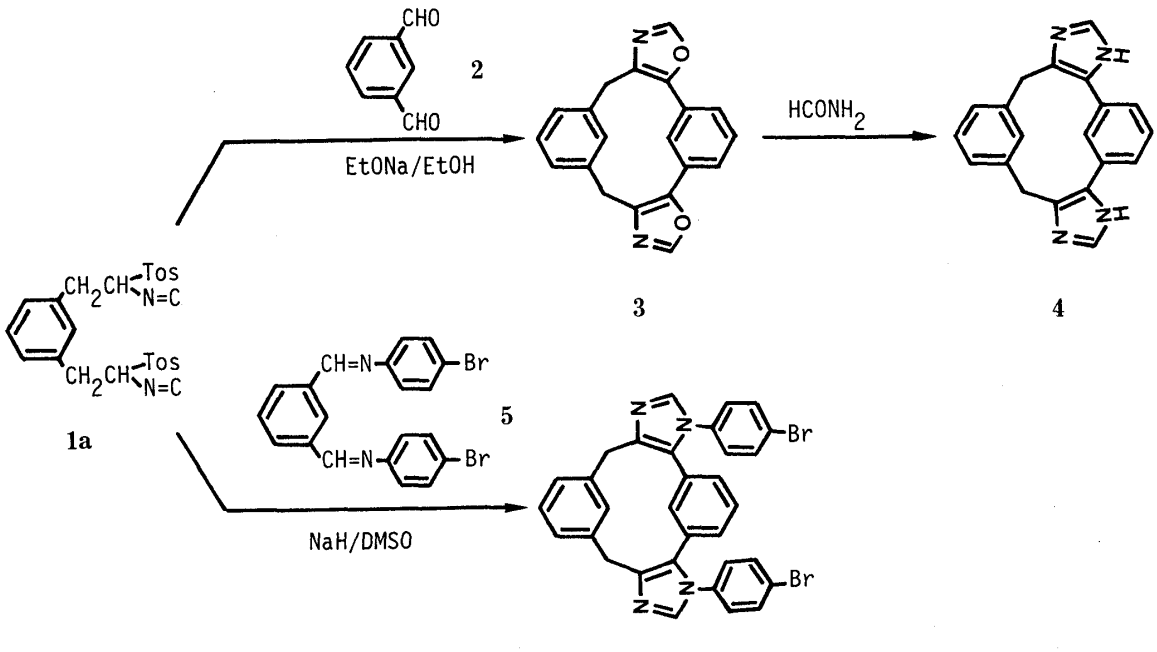


Chart 1

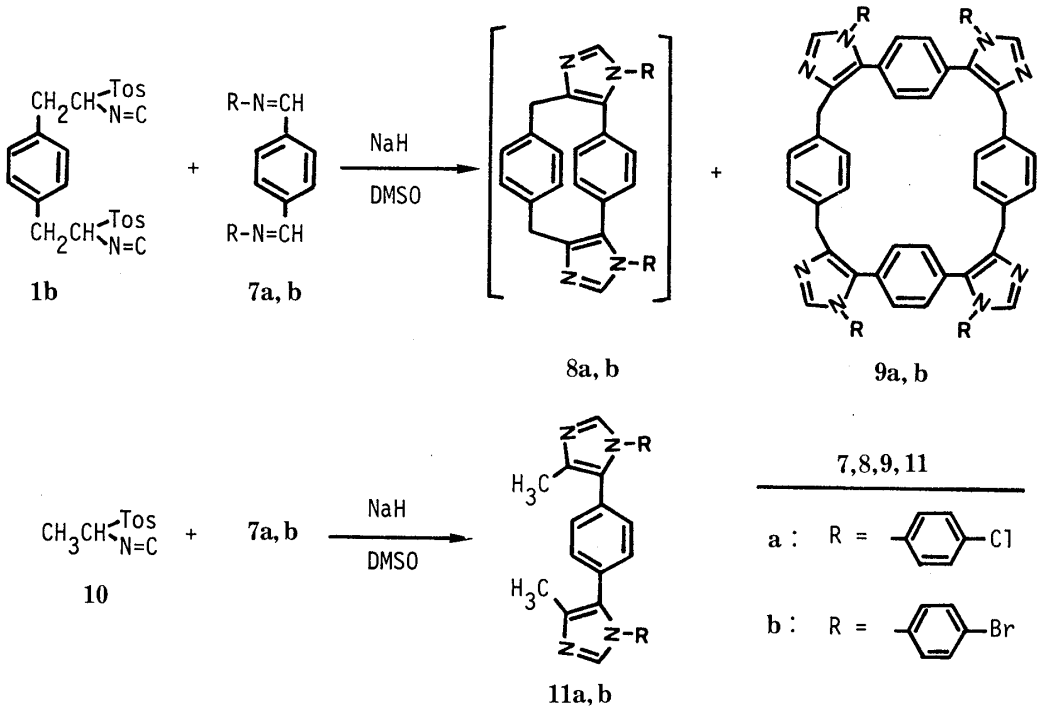
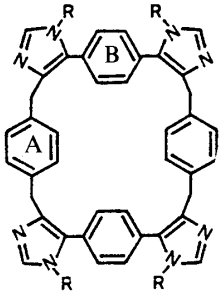
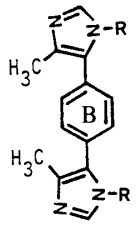


Chart 2

In this paper, we wish to report the synthesis of 5,14,29,38-tetrakis(4-halophenyl)-tetraimidazolo[3⁴]paracyclophanes (**9**)[4] as a new class of [3⁴]paracyclophanes by an one-pot coupling reaction. Thus, the reaction of 1,4-bis(2-isocyano-2-tosylethyl)benzene(**1b**)[1] with 1,4-bis[(4-chlorophenyl)iminomethyl]benzene(**7a**)[3] in the presence of 2 eq of sodium hydride (NaH) in dimethyl sulfoxide (DMSO) for 4 h at 80 °C afforded **9a** as a 2:2 adduct in 8.0% yield. Similarly, the cyclophane **9b** was obtained in 5.0% yield by the reaction of **1b** with **7b**[3] under the same conditions. However, [3²]paracyclophanes of type **8** could not be detected. On the basis of Corey-Pauling-Koltun (CPK) molecular models, it was considered that the [3²]paracyclophane ring annelated with two imidazole rings to the two methylene bridges could not be constructed by this cyclization because of the presence of large ring strain.[1] The reference compounds (**11**) were readily synthesized by the reaction of 2 eq of 1-tosylethyl isocyanide (**10**)[5] with **7** under the same conditions.

The structural assignments of these cyclophanes (**9**) were based on the spectroscopic properties and the analytical data. The infrared (IR) spectra show the imidazole ring C=N stretching absorption at 1498 cm^{-1},[6] and the field desorption mass spectra (FD-MS) show the appropriate molecular ion peaks (M^+). The proton nuclear magnetic resonance (^{1}H-NMR) signals of **9** were readily assigned from the coupling patterns and the intensity, and by comparison with those of reference compounds (**11**), as summarized in Table I. The A ring protons (H_A) of **9a** appear as a sharp singlet at δ 6.91, which is in the usual range for arene hydrogen (δ 6.98, in *p*-xylene).[7] The B ring protons (H_B) of **9a** exhibit a sharp singlet at δ 7.23, slightly shifted downfield compared with the corresponding protons (δ 7.00) of **11a**. Moreover, a similar trend for H_A and H_B of **9b** was observed, as shown in Table I. The ultraviolet (UV) spectral data for **9** and **11** in ethanol are summarized in Table I. Compound **11a** shows a high-intensity absorption at 288 nm ($\log \varepsilon = 4.21$) because of the presence of an extended conjugated system over the three aromatic rings, *i.e.*, imidazole, benzene, and imidazole.[8] Since the absorption bands of **9a** exhibit a significant hyperchromic effect and no hypsochromic shift as compared with those of **11a**, it was suggested that **9a** as well as **11a** maintains coplanarity of the three aromatic rings. A similar trend, as expected, was observed

TABLE I. ^{1}H-NMR and UV Spectral Data for 5,14,29,38-Tetrakis(4-halophenyl)tetraimidazolo-[3^4]paracyclophanes (**9**) and Reference Compounds (**11**)

Structure	R Compd. No.	^{1}H-NMR (400 MHz, $CDCl_3$) –CH_3	–CH_2–	A ring-H	B ring-H	4-Halophenyl-H	Imidazole C2-H	UV λ_{max}^{EtOH} (log ε) nm
	Cl **9a**	—	3.96 (s, 8H)	6.91 (s, 8H)	7.23 (s, 8H)	6.92, 7.24 (each d, J= 8.8 Hz, 16H)	7.65 (s, 4H)	223 (4.91) 288 (4.49)
	Br **9b**	—	3.96 (s, 8H)	6.92 (s, 8H)	7.23 (s, 8H)	6.86, 74.0 (each d, J= 8.8 Hz, 16H)	7.65 (s, 4H)	225 (4.86) 288 (4.42)
	Cl **11a**	2.35 (s, 6H)	—	—	7.00 (s, 4H)	7.00, 7.30 (each d, J= 8.7 Hz, 8H)	7.61 (s, 2H)	224 (sh) (4.47) 288 (4.21)
	Br **11b**	2.35 (s, 6H)	—	—	7.01 (s, 4H)	6.94, 7.45 (each d, J= 8.7 Hz, 8H)	7.62 (s, 2H)	224 (sh) (4.47) 287 (4.22)

in the UV spectra of **9b** and **11b**. These findings suggested that the structure of [3^4]paracyclophanes (**9**) involves simple linking of the two parts, *i.e.*, *p*-xylene and 1,4-bis[1-(4-halophenyl)-4-methyl-5-imidazolyl]benzene moieties, with hardly any ring strain or transannular interaction.

Finally, it is considered that the cyclophanes **9** have a rigid and deep hydrophobic cavity (diameter, *ca.* 0.62 nm) on the basis of the ^{1}H-NMR and UV spectra and a consideration of CPK models. Studies of the new [3^4]paracyclophanes (**9**) as inclusion hosts are in progress.

Experimental

All melting points were taken on a Yanagimoto micro melting point determination apparatus and are uncorrected. IR spectra were recorded on a Hitachi model 270—30 infrared spectrophotometer. ^{1}H-NMR spectra were measured on a Bruker AM-400 (400 MHz) instrument using tetramethylsilane as an internal reference. MS and FD-MS were measured on a Hitachi RMU-6MG mass spectrometer and a JEOL JMS-D300 mass spectrometer, respectively. UV spectra were measured on a Hitachi 340 spectrometer.

5,14,29,38-Tetrakis(4-chlorophenyl)tetraimidazolo[3^4]paracyclophane (9a)——A solution of 1,4-bis(2-isocyano-2-tosylethyl)benzene (**1b**, 4.92 g, 10 mmol) and 1,4-bis[(4-chlorophenyl)iminomethyl]benzene (**7a**, 3.53 g, 10 mmol) in DMSO (200 ml) was added to a stirred suspension of NaH (0.48 g, 20 mmol) in DMSO (200 ml) at room temperature. After the mixture had been heated for 4 h at 80 °C, it was cooled to room temperature, poured into ice-water (2000 ml), and then extracted with three 200 ml portions of $CHCl_3$. The extracts were combined, washed with three 200 ml portions of brine, and dried over anhydrous $MgSO_4$. After removal of the organic solvent under reduced pressure, the residue was chromatographed on silica gel with $CHCl_3$: MeOH (9 : 1) to give a crude product, which was recrystallized from MeOH to afford 0.43 g (8.0%) of **9a**, colorless prisms, mp >300 °C. IR (KBr): 1498 (C=N) cm^{-1}. FD-MS (*m/z*): 1066 (M^++2), 1064 (M^+). *Anal.* Calcd for $C_{64}H_{44}Cl_4N_8$: C, 72.05; H, 4.16; N, 10.50. Found: C, 72.12; H, 4.07; N, 10.50.

5,14,29,38-Tetrakis(4-bromophenyl)tetraimidazolo[3^4]paracyclophane (9b)——According to the procedure described above for **9a**, the reaction of **1b** (4.92 g, 10 mmol) with 1,4-bis[(4-bromophenyl)iminomethyl]benzene (**7b**, 4.42 g, 10 mmol) gave a crude product, which was recrystallized from $CHCl_3$ to afford 0.31 g (5.0%) of **9b**, colorless

plates, mp >300 °C. IR (KBr): 1498 (C=N) cm^{-1}. FD-MS(*m/z*): 1244 ($M^+ + 4$), 1242 ($M^+ + 2$), 1240 (M^+), *Anal.* Calcd for $C_{64}H_{44}Br_4N_8$: C, 61.76; H, 3.56; N, 9.00. Found: C, 61.89; H, 3.43; N, 8.92.

1,4-Bis[1-(4-chlorophenyl)-4-methyl-5-imidazolyl]benzene (11a)——A solution of 1-tosylethyl isocyanide (**10**, 4.18 g, 20 mmol)[5] and **7a** (3.53 g, 10 mmol) in DMSO (100 ml) was added to a stirred suspension of NaH (0.48 g, 20 mmol) in DMSO (50 ml). After the mixture had been heated for 4 h at 80 °C, the resulting mixture was cooled to room temperature, poured into ice-water (500 ml), and then extracted with three 50 ml portions of $CHCl_3$. The extracts were combined, washed with three 50 ml portions of brine, and dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel with $CHCl_3$: MeOH (19 : 1) to give a crude product, which was recrystallized from CH_2Cl_2 to afford 2.6 g (56%) of **11a**, colorless needles, mp >300 °C. IR (KBr): 1498 (C=N) cm^{-1}. MS (*m/z*): 458 (M^+). *Anal.* Calcd for $C_{26}H_{20}Cl_2N_4$: C, 67.98; H, 4.39; N, 12.20. Found: C, 67.94; H, 4.27; N, 12.18.

1,4-Bis[1-(4-bromophenyl)-4-methyl-5-imidazolyl]benzene (11b)——According to the procedure described above for **11a**, the reaction of **10** (4.18 g, 20 mmol) with **7b** (4.42 g, 10 mmol) gave a crude product, which was recrystallized from CH_2Cl_2 to afford 2.5 g (45%) of **11b**, pale yellow needles, mp >300 °C. IR (KBr): 1498 (C=N) cm^{-1}. MS (*m/z*): 548 ($M^+ + 2$), 546 (M^+). *Anal.* Calcd for $C_{26}H_{20}Br_2N_4$: C, 56.96; H, 3.68; N, 10.22. Found: C, 56.81; H, 3.58; N, 10.09.

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References and Notes

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