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Trioxazolo$[2^3]$metacyclophane. Synthesis and Properties of a Novel $[2^3]$Metacyclophane Annelated with Three Oxazole Rings[1)]

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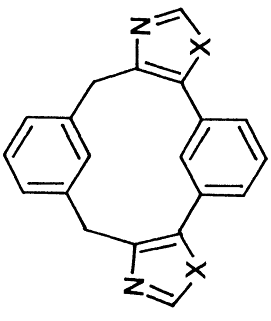
The title compound (**6**) was synthesized by the base-induced condensation of 3-(isocyanotosylmethyl)benzaldehyde as a new bifunctional reactant for the synthesis of $[2^n]$metacyclophanes. The treatments of **6** with silver triflate in several molar ratios in THF at room temperature afforded only 2:1 silver triflate complex on the basis of the ^{1}H NMR and the analytical data.

Previously, we have reported the synthesis and the conformational properties of dioxazolo$[3^2]$metacyclophane (**1a**)[2a)] and diimidazolo$[3^2]$metacyclophane (**1b** and **1c**).[2b,c)] The feature of these preparation methods for **1a** and **1c** was that the ring closure reaction to oxazole or imidazole rings was applied to the construction of the $[3^2]$metacyclophane ring. It is interested in utilization of these methods for the synthesis of $[2^n]$metacyclophanes annelated with azole rings to the methylene bridges. Since the resulting $[2^n]$cyclophanes have a classical conjugated system extended over all aromatic rings, their structures and physical properties are particularly interesting.

Here we wish to report the synthesis and the properties of trioxazolo$[2^3]$-metacyclophane (**6**) as a novel $[2^3]$metacyclophane derivative annelated with three oxazole rings by the base-induced condensation of 3-(isocyanotosylmethyl)benzaldehyde (**4**). The preparation of **6** was outlined in Scheme 1. Thus, the reaction of isophthalaldehyde (**2**, 0.2 mol) with sodium p-toluenesulfinate (0.22 mol) and large excess formamide (4 mol) in the presence of formic acid afforded 3-(formamidotosylmethyl)benzaldehyde (**3**) in 70% yield.[3)] Bifunctional reactant, 3-(iso-



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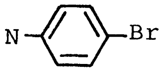
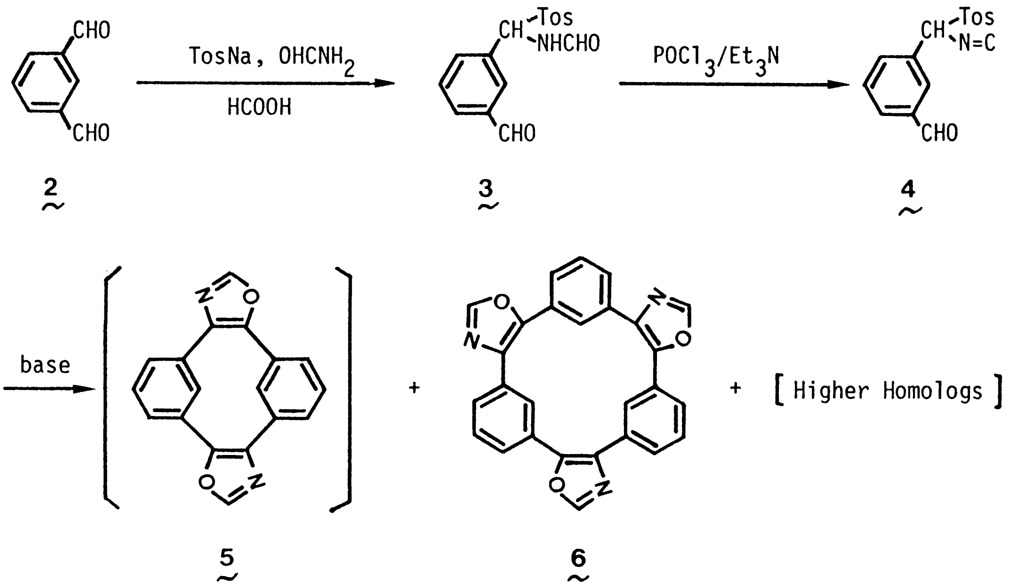
Compd. No.	X
1a	O
1b	NH
1c	

cyanotosylmethyl)benzaldehyde (4) was obtained in 53% yield by the dehydration of 3 (0.02 mol) with phosphorous oxychloride (0.04 mol) in the presence of triethylamine.[4)] Subsequently, the treatment of 4 (0.01 mol) with sodium ethoxide (0.01 mol) in refluxing ethanol (200 ml) for 3 h gave trioxazolo[2^3]metacyclophane (6) in 63% yield.[5)] Under several different conditions as summarized in Table 1, 6 was only one cyclization product and other cyclophanes such as 5 were not formed. The IR spectrum shows the characteristic absorption of oxazole C2-H at 3120 cm^{-1},[6)] and the MS indicates appropriate molecular ion peak (M^+) as a trimer of 4. The assignment of the ^1H NMR spectrum of 6 was achieved by the coupling pattern and the intensity of signals, as summarized in Table 3. In UV spectra, whereas a reference compound 4,5-diphenyloxazole shows a high intensity absorption at 275 nm (log ε =4.09),[7)] the absorption band of 6 [255 nm (4.42)] exhibits significant hypsochromic shift as compared with those of 4,5-diphenyloxazole. This fact suggests that the aromatic rings of 6 are less coplanar than those of 4,5-diphenyloxazole.

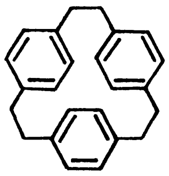


Scheme 1.

Table 1. Effect of Concentration and Base Solvent Systems on the Synthesis of 6

Run	Cyclization conditions Base	Solvent	Concn of 4/mM	Time/h	Temp	Yield of 6/%
1	EtONa	EtOH	50	3	reflux	63
2	EtONa	EtOH	5	3	reflux	62
3	EtONa	EtOH	125	3	reflux	57
4	K_2CO_3	MeOH	50	3	reflux	42
5	NaH	DMSO	250	3	80 °C	46

Pierre et al. first reported that [2^3]paracyclophane (7) formed 1:1 complex with silver triflate.[8a)] Moreover, it was demonstrated that cyclophanes 8 and 9 also produced 1:1 and 2:1 silver triflate complexes, respectively.[8b,c)] In the light of the CPK molecular model, the diameter of the cavity of 6 surrounded by the three benzene walls is ca. 2.5 nm which is close to that of 7 (ca. 2 nm).[8a)] Therefore, the complexation of 6 with silver triflate was examined. Typically, a solution of silver triflate (0.2 mmol) in THF (5 ml) was added at once to a solution of 6 (0.2 mmol) in THF (15 ml) at room temperature. The precipitate immediately appeared and was filtered on suction. The crude product was recrystallized from acetonitrile to afford 10 as colorless needles in 35% yield. Although the molar ratios between 6 and silver triflate on the complexation were changed as summarized in Table 2, each run afforded the identical product to 10 on account of the observation of the same physical properties. Thus, their IR spectra indicate the characteristic absorptions of oxazole C2-H and organic sulfate anion at 3124 and around 1256 cm^{-1}, respectively. On the other hand, it is suggested on the



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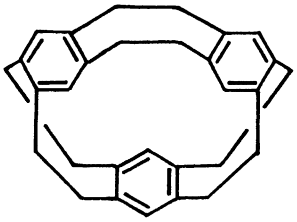

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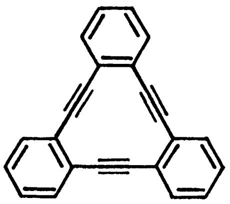

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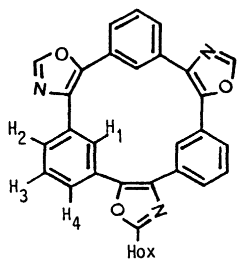
Table 2. Effect of Molar Ratios on the Complexation of 6 with Silver Triflate and Yield and Physical Properties of the Product (10)

Run	Molar ratio 6	Molar ratio CF_3SO_3Ag	Yield/%	Mp/°C	IR(KBr)/cm^{-1}	Analysis(%), Calcd for $2\ (C_{27}H_{15}N_3O_3)\cdot CF_3SO_3Ag\cdot CH_3CN$ (Found) C	H	N
						59.18	2.88	8.48
1	1	1	35	262-264	3124, 1257	(59.37)	(2.72)	(8.70)
2	1	2	66	262-264	3124, 1256	(59.31)	(2.81)	(8.95)
3	2	1	75	261-262	3124, 1254	(59.11)	(2.83)	(8.68)
4	3	1	44	262-263	3124, 1254	(59.20)	(2.78)	(8.51)

Table 3. ^1H NMR Data for Trioxazolo[2^3]metacyclophane (6) and 2:1 Silver Triflate Complex (10) (DMSO-d_6, 400 MHz)

Compound No.	Benzene ring H_1	Benzene ring H_2 and H_3	Benzene ring H_4	Oxazole ring H_{ox}
6	7.41	7.61	7.70	8.50
10	7.42	7.62	7.71	8.52



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basis of analytical data that these products are 2:1:1 adduct of 6, silver triflate, and acetonitrile. Furthermore, the ^{1}H NMR spectrum of 10 shows a slight down-field shift of the oxazole C2-H as compared with that of 6. These findings suggest that the product can be assigned as a 2:1 silver triflate complex of 6 and the silver atom is present in close position to the oxazole C2-H.

References

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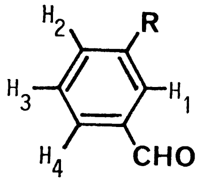
3) Data of 3: colorless prisms; mp 146-147 °C; IR(KBr) 3264(NH), 1698(CHO), 1664(NHCHO), 1320,1146 cm^{-1}(SO_2); ^{1}H NMR($CDCl_3$, 400 MHz) δ =10.00(1H, s, CHO), 8.13(1H, m, NHCHO), 7.96(1H, m, H_1), 7.94(1H, m, H_4), 7.75(2H, d, J=8.3 Hz, Tos-H), 7.73(1H, m, H_2), 7.60(1H, t, J=7.6 Hz, H_3), 7.34(2H, d, J=8.3 Hz, Tos-H), 7.28(1H, m, NHCHO), 6.42(1H, d, J= 10.5 Hz, CH), 2.45(3H, s, CH_3). Found: C, 60.27; H, 4.71; N, 4.26%. Calcd for $C_{16}H_{15}NO_4S$: C, 60.55; H, 4.76; N, 4.41%.

4) Data of 4: colorless prisms; mp 128-129 °C; IR(KBr) 2136(N=C), 1694(CHO), 1336, 1154 cm^{-1}(SO_2); ^{1}H NMR($CDCl_3$, 400 MHz) δ =10.00(1H, s, CHO), 8.00(1H, m, H_4), 7.83(1H, s, H_1), 7.67(1H, m, H_2), 7.65(2H, d, J=8.3 Hz, Tos-H), 7.61(1H, m, H_3), 7.35(2H, d, J=8.3 Hz, Tos-H), 5.70(1H, s, CH), 2.48(3H, s, CH_3); Found: C, 63.92; H, 4.44; N, 4.55%. Calcd for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68%.



3: R=CH(Tos)NHCHO

4: R=CH(Tos)N=C

5) Data of 6: colorless prisms; mp 249-250 °C; IR(KBr) 3120 cm^{-1}(oxazole C2-H); MS m/z: 429(M^+); UV(EtOH) λ max 225 nm(log ε 4.42), 255(4.42); Found: C, 76.86; H, 3.90; N, 9.06%. Calcd for $C_{27}H_{15}N_3O_3 \cdot 1/2C_6H_6$: C, 76.91; H, 3.87; N, 8.97%.

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