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Synthesis and Molecular Structure of Tetrathia[3^4](1,2,4,5)cyclophane

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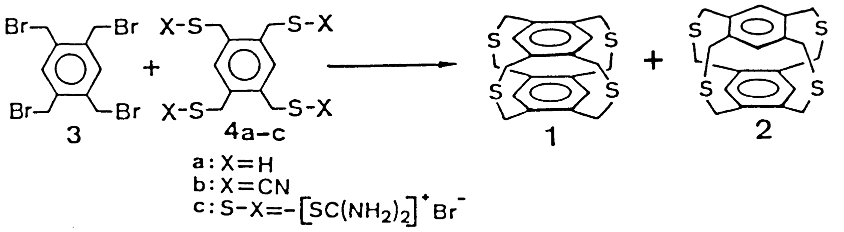
The titled tetrathiacyclophane was prepared by improved synthetic methods and its molecular structure previously reported was corrected by ^{1}H-NMR and X-ray analyses.

Multiple bridged cyclophanes such as superphane$^{1)}$ are useful model compounds to study the transannular interaction between benzenoid π-electron systems which are very closely overlapped with each other but highly strained. The method employed to synthesize superphane is unique but not so convenient for general synthesis of similarly constructed [2^n]cyclophanes due to multi-step procedure. Desulfurization of multi-bridged polythiacyclophanes,$^{2)}$ the popular method, is conceived as a shortcut way. Unfortunately general synthesis of polythiacyclophanes containing more than four sulfurs has not been developed so far.

In 1982, a coupling reaction using the cesium effect$^{3)}$ was reported as a one-step synthesis of polythiacyclophanes.$^{4)}$ The total yield of tetrathiacyclophanes **1** and **2** was less than 10% and their structures were determined by ^{1}H-NMR of the mixture because of hard separation into each isomer. In this paper we wish to report a synthesis of the titled tetrathia[3^4](1,2,4,5)cyclophane in excellent yield, successful separation of the isomers, and corrected assignment of their structures previously reported.

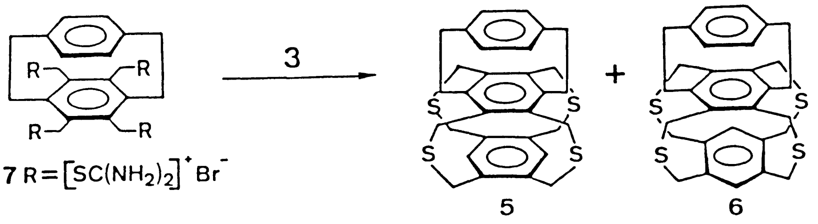


Scheme 1.

Table 1. Reaction of **3** with **4a-c**

	base solvents	Y/% **1**+**2**
4a	Cs_2CO_3 DMF	10$^{5)}$
4b	$NaBH_4$ THF-EtOH	30
4c	CsOH C_6H_6-EtOH	75
	KOH DMSO-EtOH	56

We have examined the coupling conditions of tetrabromide **3** with three kinds of tetrasubstituted durene derivatives, **4a-c**, to optimize the yield of tetrathiacyclophanes **1** and **2** as shown in Table 1. The reaction with **4a** also gave low yield as Vögtles', probably due to easy formation of reactive polythiolate anions, followed by oxygenative polymerization. In order to generate each thiolate anion stepwise and slowly in situ, we selected the coupling with tetrakis(thiocyanate) **4b**5) or tetrakis(isothiuronium)salt **4c**5) and carried out as follows: an equimolar mixture of **3** and **4b** in anhyd. DMF-THF (1:49 in v/v) was dropwise added to a suspension of excess $NaBH_4$ in anhyd. THF-EtOH (19:1) under nitrogen atmosphere using a high dilution technique at room temperature according to synthetic procedures for polyselenacyclophanes.6) The reaction mixture was chromatographed on silica gel with benzene-hexane (1:4) as an eluent to give **1** (21%) and **2** (9%).7) On the other hand, the reaction was carried out by dropwise addition of a solution of **3** and isothiuronium salt **4c** in DMF-benzene-EtOH (1:2:23) to a solution of CsOH (52 times moles) in benzene-EtOH (1:12) at 55 °C for 12 h under nitrogen atmosphere. The usual work up gave ca. 1:1 mixture of **1** and **2** in a surprisingly high yield of 75% despite such a quadruply bridging reaction, indicating the cesium effect compared to 56% yield (**1**:**2**=1:1) with KOH in DMSO-EtOH (1:74). Consequently, as shown in Table 1, the coupling of tetrabromide **3** with the corresponding isothiuronium salt using CsOH as a base (isothiuronium method) is now the most excellent synthetic method of tetrathiacyclophane.



7 $R=[SC(NH_2)_2]^+Br^-$ **5** **6**

Scheme 2.

By the use of this isothiuronium method, the more layered and new type tetrathiacyclophanes **5** and **6**, which couldn't be obtained by the conventional thiol method, were synthesized for the first time. The coupling of tetrabromide **3** with tetrakis(isothiuronium)salt **7**8) gave ca. 20% yield of **5**9) and **6**9) in a ratio of 1:4 and their structures were tentatively but reasonably assigned by ^{1}H-NMR spectra (vide infra).

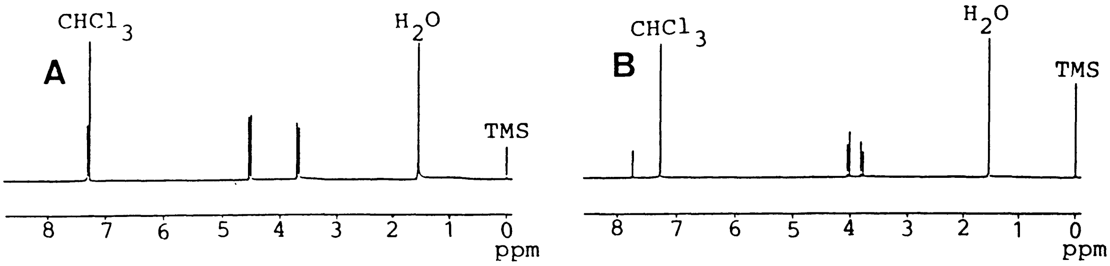


Fig.1. ^{1}H-NMR spectra of tetrathiacyclophanes **1** or **2** ($CDCl_3$).

Since tetrathiacyclophanes **1** and **2** were prepared by the isothiuronium method in ca. 8 times higher yield than that in the literature,[4)] each isomer could be separated and purified easily. Formerly, Vögtle assigned Fig. 1-A, where aromatic protons appear in relatively high field, to D_{2h} symmetric isomer **1** which is assumed to have longer interplanar distance between the two benzenes on the basis of molecular model examination, while Fig. 1-B to C_{2v} symmetric isomer **2** with shorter distance.[4)] We reexamined this assignment and present opposite assignment by considering the shielding field as well as the interplanar distances in molecular models, that is, Fig. 1-A to **2** and Fig. 1-B to **1**.

In order to confirm the NMR assignment of isomeric structures, **1** and **2**, a crystal of the isomer, which shows ^{1}H-NMR Fig. 1-B, was subjected to X-ray crystallography.[10)] As shown in Fig. 2, this compound is assigned to D_{2h} isomer and thereby another Fig. 1-A compound to C_{2v} isomer, indicating our proper assignment by NMR data. The figure also shows a parallel sliding of the two benzene rings to reduce their π - electron repulsion and a conformation of four $-CH_2-S-CH_2-$ bridges, in which all sulfur atoms are directed to unsubstituted aromatic hydrogens. In view of molecular structure that both two $-CH_2-S-CH_2-$ bridges of syn-2,11-dithia[3.3]metacyclophane and two $-CH_2-Se-CH_2-$ bridges of the corresponding diselenacyclophane are present as chair-chair conformer among three possible conformers in solid state,[11)] the structure in Fig. 2 suggests that it is the favorable conformation to avoid S-S and CH_2(nonbonded)-S repulsions between two ortho $-CH_2-S-CH_2-$ bridges.

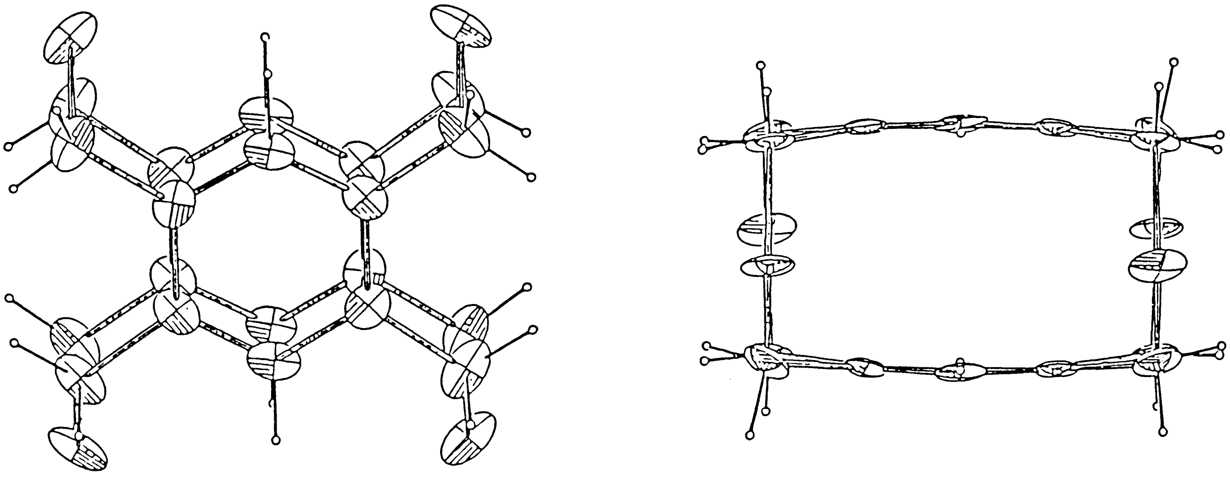


Fig.2. ORTEP drawings (top, side views) of tetrathiacyclophane **1**.

References

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4) B. Klieser and F. Vögtle, Angew. Chem., Int. Ed. Engl., 21, 618 (1982); Angew. Chem. Suppl., 1982, 1392.

5) **4b**: colorless fine crystals (DMF-benzene); mp 203-204 °C; ^{1}H-NMR (360 MHz, DMSO-d_6) δ =4.53(s,8H,CH_2), 7.53(s,2H,ArH); MS m/e 362 (M^+); Found C,46.17; H,2.86;N,15.58;S,35.22%. Calcd for $C_{14}H_{10}N_4S_4$: C,46.39;H,2.78;N,15.45; S,35.38%. **4c**: colorless powder; dec. 230 °C; ^{1}H-NMR (360 MHz, DMSO-d_6) δ =4.68 (s,8H,CH_2), 7.62(s,2H,ArH), 9.14, 9.34(both signals are broad,16H, $C(NH_2)_2Br$).

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7) **1**: colorless fine plates (benzene-hexane); dec.>310 °C; ^{1}H-NMR (360 MHz, $CDCl_3$) δ =3.78, 4.02(ABq, 16H, CH_2), 7.74(s, 4H, ArH); MS m/e 388 (M^+). **2**: colorless powder; dec.>300 °C; ^{1}H-NMR (360 MHz, $CDCl_3$) δ =3.68, 4.53 (AX,16H,CH_2), 7.30 (s,4H,ArH); MS m/e 388 (M^+).

8) **7**: colorless powder; dec.>260 °C; ^{1}H-NMR (360 MHz, DMSO-d_6) δ =3.23-3.24 ($A'_2B'_2$m,8H,$-CH_2CH_2$), 4.48-4.55 (m,8H,SCH_2), 6.69 (s,4H,ArH), 9.30-9.38 (bs, 16H,$C(NH_2)_2Br$).

9) **5**: colorless powder; mp >300 °C; ^{1}H-NMR (360 MHz, $CDCl_3$) δ =2.87-2.91, 3.36-3.40 ($A'_2B'_2$m,8H,$-CH_2-CH_2$), 3.60, 3.69 (ABq,8H,SCH_2), 3.70, 4.03 (ABq,8H, SCH_2), 6.25 (s,4H,ArH), 7.49 (s,2H,ArH); MS m/e 518 (M^+). **6**: colorless powder; mp >300 °C; ^{1}H-NMR (360 MHz, $CDCl_3$) δ =2.85-2.89, 3.22-3.26 ($A'_2B'_2$m, 8H,$-CH_2-CH_2$), 3.49 (d,4H,SCH_2), 3.53 (d,4H,SCH_2), 4.23 (d,4H,SCH_2), 4.40 (d,4H,SCH_2), 6.26 (s,4H,ArH), 7.23 (s,2H,ArH); MS m/e 518 (M^+).

10) The crystal of **1** is triclinic, space group $P\bar{1}$, with a=8.190(1), b=8.616(1), c=7.284(1)Å, α =109.37(1), β =115.06(1), γ =73.66(1) , V=433.2Å^3, d_c=1.490 g/cm^3, Z=1.
Intensity measurements were made on a Rigaku AFC-5FOS automated four-circle diffractometer (θ : 2θ scan, 2θ <55° , Mo ($K\alpha$), λ =0.71069 Å). The structure was solved by direct methods,[12] and refined by block diagonal least-squares to R=0.032, Rw=0.035 for 1835 reflections.

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