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SYN-5,13-DIMETHYL[2.2]METACYCLOPHANE. SYNTHESIS, SPECTRA AND THERMAL STABILITY

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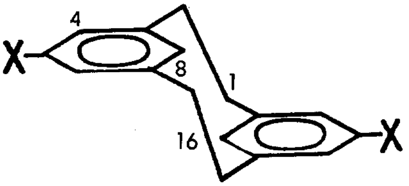
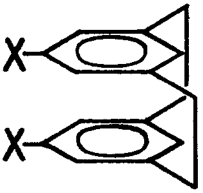
Abstract. The title compound was synthesized in 3 steps from trithia$[2_3]$(1,3,5)cyclophane. Activation parameters for its change to the anti conformer as well as its NMR, IR and UV spectra were secured.

[2.2]Metacyclophane **1** and its derivatives with at least one inner hydrogen at C-8 or C-16 are known to exist always in the stepped anti conformation (eg. **1a**) and all attempts to prepare the syn conformers (eg. **1s**) resulted in **1a**[1,2b)]. Thus syn conformers known till recently possess at smallest two methyl groups at the inner positions[1,3)]. Very recently, however, Mitchell et al. have reported an elegant synthesis of syn[2.2]metacyclophane (**1s**) and its bis(methylthio) derivative from syn-2,11-dithia[3.3]metacyclophane utilizing its bis(chromium tricarbonyl) derivative[2)]. We have succeeded in synthesizing its dimethyl homolog **2s** without complexation, and investigated its physical and dynamic properties. The result is reported herein.



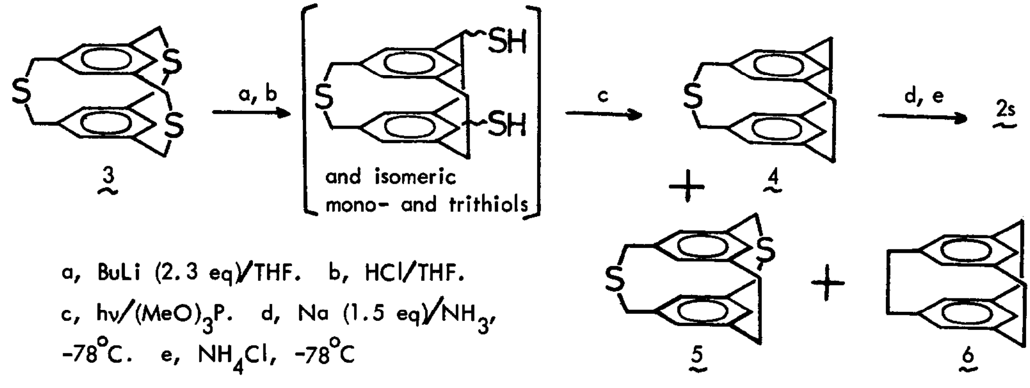
1a: X=H　**2a**: X=CH_3



1s: X=H　**2s**: X=CH_3

Synthesis　The compound **2s** was synthesized by the scheme shown in the next page. The known trithia$[3_3]$(1,3,5)cyclophane **3**[4)] was subjected to Wittig rearrangement with BuLi. After quenching by HCl a mixture of ring-contracted thiols was obtained in 90% yield. Without separation, the mixture was desulfurized photochemically in trimethyl phosphite[5)], and subsequent SiO_2 chromatography (benzene-hexane) yielded the thia[3.2.2] compound **4** (49% yield) and the dithia[3.3.2] compound **5** (26% yield) along with known $[2_3]$(1,3,5)cyclophane (**6**)[4)] (3% yield)[6)]. The same two-step reaction sequence on **5** afforded **4** in 48% yield. Finally, **4** was reduced with Na in NH_3 at -78°C. Work up and a short column chromatography (SiO_2, ether) at low temperature furnished in 88% yield the desired **2s**, colorless granules, which is stable at room temperature and sublimes at ~75°C to **2a** (prisms)[8)].

Spectra　The structure of **2s** was established by PMR [δ (THF-d_8, -60°C) 1.92 (6H, s, CH_3), 2.77, 2.98 (8H, AA'BB', CH_2), 6.13 (4H, s, H_4), 6.44 (2H, s, H_8)][7)] comparing with that of **2a** [δ (THF-d_8, 30°C) 2.31 (CH_3), 2.02, 2.97 (CH_2), 4.10 (H_8), 6.83 (H_4)] and by its facile change to **2a** occurring thermally at 0°C in THF. Diagnostic PMR features are 1) the signal due to H-8 appears at a lower field than that of H-4 in **2s** in contrast to those of **2a**, and 2) the methyl signal appear at a higher



a, BuLi (2.3 eq)/THF. b, HCl/THF.
c, hν/$(MeO)_3P$. d, Na (1.5 eq)/NH_3, -78°C. e, NH_4Cl, -78°C

field in 2s than in 2a. Electronic spectrum of 2s, showing a peak at 258 nm (log ε 3.28) and three shoulders (Fig.1) is similar to that of 6 and considerably different from that of 2a.

Conformational change 2s → 2a Activation parameters obtained by PMR time course at different temperatures are Ea=20.0 kcal/mol, and at 298K $\Delta H^{\neq}$=19.4 kcal/mol, $\Delta S^{\neq}$= -8.7 cal/K·mol, $\Delta G^{\neq}$=22.6 kcal/mol. The Ea is similar to that (18.9 kcal/mol) obtained for the bis(methylthio) derivative of 1s[2b]. Since Ea for anti→anti change was estimated to be ca. 27kcal/mol[9] and both conformational changes would proceed through ring-flipping, ΔH^{o} between 1a and 1s would be ca. 7 kcal/mol. Our molecular mechanics calculations revealed the difference of their strain energies to be ca. 5.7 kcal/mol[10].

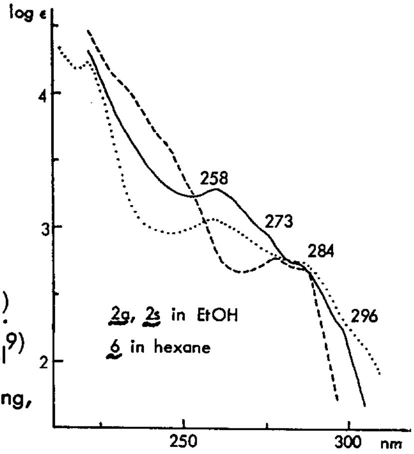


Fig. 1 Electronic spectra of 2s (at 0°C, ——), 2a (-----) and 6 (·······).

References and Notes

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6) 4, colorless prisms, m.p. 237-238°C, ν (KBr) 1450, 890, 730 cm^{-1}, δ 2.95 (8H, s), 3.79 (4H, s), 5.69 (2H, br.s), 6.46 (4H, d, J=1.5 Hz). 5, colorless prisms, m.p. 188-189°C, ν 1450, 880, 720 cm^{-1}, δ($CDCl_3$) 3.03 (4H, s), 3.84 (8H, s), 6.32 (4H, d, J=1.5 Hz), 7.01 (2H, br.s).

7) CMR: 2s, δ(THF, -60°C) 20.9 (CH_3), 35.9 (CH_2), 127.9 (C-4), 136.2 (C-8), 137.4 (C-5), 138.5 (C-3). 2a, δ(THF, 30°C) 21.5 (CH_3), 41.6 (CH_2), 126.7 (C-4), 134.9 (C-8), 137.4 (C-5), 139.6 (C-3).

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10) Molecular mechanics calculations (MMPI) revealed the strain energy as follows: 18.13 kcal/mol for 1s, 12.45 kcal/mol for 1a. Cf. N.L. Allinger and Y.H. Yuh, QCPE No. 318 (1983). N.L. Allinger and J.T. Sprague, J. Am. Chem. Soc., 95, 3893 (1973).

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