

[7]- AND [6](3,7)TROPOLONOPHANES

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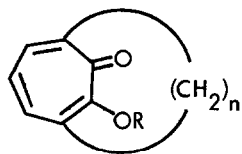
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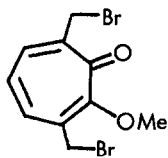
Abstract: Synthesis of the titled tropolonophanes has been attempted. Though the [7]- compound was obtained, the lower homolog was failed to be synthesized probably because of the strain imposed on the desired compound. The former tropolonophane was shown to exist in the enolone form. PMR and electronic spectra of [7] and [8]-homologs and their methylethers revealed some nonplanarity in the 7-membered rings. PMR spectrum also established the conformation of the bridge in the former compound.

In the previous paper¹⁾, we have reported the synthesis of [8](3,7)tropolonophane (1a), the first single-decked tropolonophane, and demonstrated that the compound possessed a nearly planar tropolone ring with a conformationally flexible bridge. In the continuous effort to impose strain on tropolone ring, we have attempted synthesis of two lower homologs of 1a. In this paper, we describe our synthetic effort toward [7]- and [6](3,7)tropolonophanes (1b and 1c), and some physical properties of the 1a and 1b and their methylethers (2a and 2b).

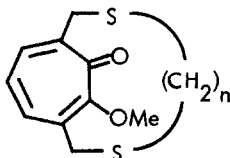
Synthesis: The synthesis of 1b followed the reaction sequence used in that of 1a¹⁾. 3,7-Bis(bromomethyl)-tropolone methylether (3) and disodium 1,5-pentanedithiolate were heated in refluxing methanol (high dilution) to give the dithia[9]tropolonophane 4b in 52% yield²⁾. *m*-Chloroperbenzoic acid oxidation of 4b afforded the corresponding methoxy-disulfone 5b in 95% yield. Acid hydrolysis (HBr) of 5b yielded the disulfotropolonophane 6b in 91% yield. Contrary to the case of 1a¹⁾, however, thermolysis of 6b at various temperatures induced only its decomposition. On the other hand, thermolysis of 5b at 470-480°C followed by flash column chromatography (Al₂O₃) gave the methoxy[7]tropolonophane 2b in 3% yield. Acid hydrolysis (HBr) of 2b afforded, after purification *via* Cu salt, the desired 1b as colorless needles in 41% yield.



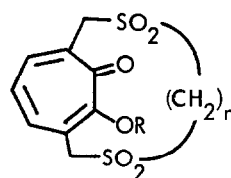
1: R=H, 2: R=Me



3



4



5: R=Me, 6: R=H

Suffixes a, b and c denote n=8, 7 and 6, respectively, through this paper.

Synthesis of 1c was then attempted by the same reaction sequence. The corresponding 4c (28%

yield), 5c (94%) and 6c (84%) were thus obtained. However all attempts to pyrolyze 5c or 6c at various temperatures yielded only intractable tar. The strain inherent in the desired 1c and 2c seems to have hampered the thermal C-C bond formation with SO₂ extrusion.

The present results coincide with the fact that the lowest known member of [n]cyclophanes synthesized by the SO₂ extrusion method is [8] for para series and [7] for meta series³⁾. Thus, 1b may be the lowest possible member of [n](3,7)tropolonophanes to be synthesized by this method.

Diketone-enolone problem in 1b: Although tropolone is known to have tendency to take a keto form when planarity is disturbed sterically^{1,4,5)}, the compound 1b exists in tropolone form judged from the following spectroscopic observations. General feature of IR spectrum is very similar to those of 1a and 3,7-dimethyltropolone (7), showing a broad OH band (3180 cm⁻¹) and strong CO bands (1552, 1537 cm⁻¹) and devoid of any band in normal carbonyl region. The low-field signals in PMR spectrum (Fig. 1) of 1b consist of a clear AB₂ pattern (J=10.0 Hz) at 6.86 (t, H₅ (tropolone numbering)) and 7.20 ppm (d, H₄). No signal except those due to the bridge protons is observed at around 3-4 ppm region where protons on a sp³ carbon in the keto form are expected to appear.

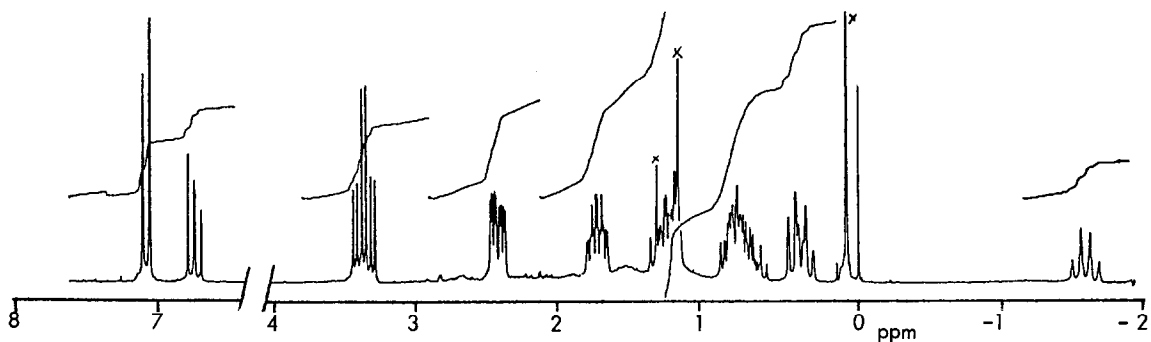


Fig. 1 PMR spectrum of 1b (200 MHz, in CD₂Cl₂)

Planarity of 7-membered rings in 1a, 1b, 2a and 2b: When chemical shifts of tropolone protons in 1a¹⁾ and 1b are compared with those of 7, a small but regular up-field shift is clearly observed for H₄, on

Table 1. Proton chemical shift in tropolone derivatives

Compd No.	<u>7</u>	<u>1a</u>	<u>1b</u>	<u>8</u>	<u>2a</u>	<u>2b</u>
H ₄	7.36	7.24	7.20	6.77	6.68	6.58
H ₅	6.86	6.86	6.86	6.56	6.63	6.58
H ₆	7.36	7.24	7.20	7.13	6.79	6.58

going from 7 through 1a to 1b, while H₅ remains constant (Table 1). A similar but amplified up-field shift is also observed for H₄ and H₆ in 2a and 2b compared with those of 2-methoxy-3,7-dimethyltropolone (8) (Table 1)⁶⁾. This is explicable by the increasing out-of-plane deformation of 7-membered ring

in the order. Shorter bridge, causing more deformation and reduction of the conjugation between the enolone part and the diene system, results in larger up-field shift of the hydrogens β and δ to the carbonyl group. The larger shifts in the methoxytropolones (2a and 2b) than in the corresponding tropolones (1a and 1b) suggest deeper bending of the 7-membered ring in the formers probably because of

their smaller delocalization energies.

All bands in electronic spectra of $1a$ and $1b$ (Fig. 2a) show, when compared with that of 7 , bathochromic shift in the same order and loss of fine structure, two common features observed in short-bridged phanes⁷⁾, in neutral, alkaline and acidic media. The spectra of $2a$ and $2b$ show the same trends compared with that of 8 (Fig. 2b). These changes would also reflect the nonplanarity of 7-membered rings in these phanes.

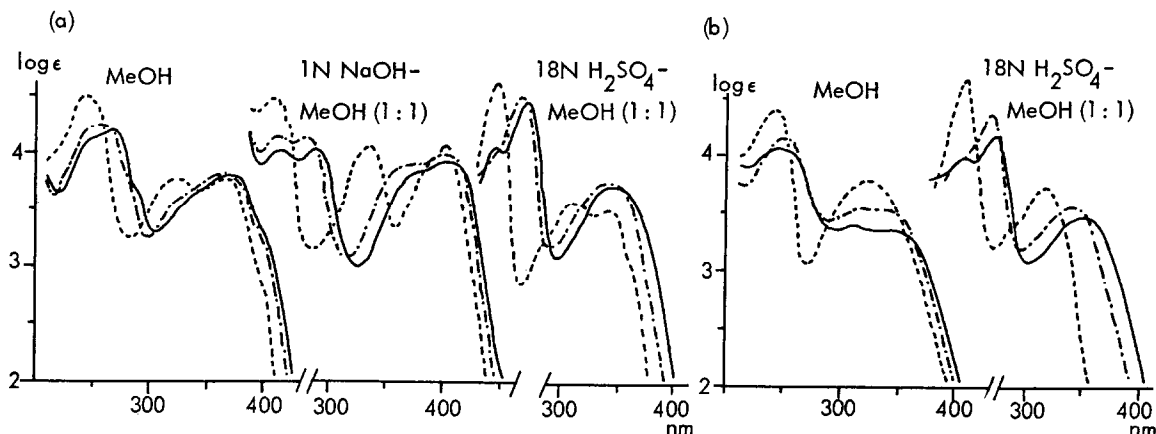


Fig. 2 Electronic spectra (a) of $1a$ (-----), $1b$ (—) and 7 (-----); (b) of $2a$ (-----), $2b$ (—) and 8 (-----)

Conformation of the bridge in $1b$: Seven signals are observed in NMR spectrum (Fig. 1) for bridge protons at -1.59 (1H, dt), 0.40 (2H, br.dt), 0.77 (1H, complex m), 0.85 (2H, complex m), 1.31 (2H, dt), 1.85 (2H, dddd), 2.54 (2H, ddd) and 3.48 (2H, td), suggesting that the bridge has a plane of symmetry within NMR time scale. The nonequivalence of two "benzylic" protons (H_a) suggests no flipping of the bridge across the plane of tropolone ring, though some conformational change may be inevitable. Detailed decoupling experiments disclosed the hydrogen sequence shown in Fig. 3a. Consideration of angular dependency of vicinal coupling constant⁸⁾ and anisotropy of tropolone ring suggested averaged conformation of the bridge. Of the two possible orientations of tropolone ring relative to the bridge, the one (Fig. 3b) with H_a at 3.48 ppm facing to the enolone part was considered more likely because of the anisotropic effect of that part⁹⁾. The most stable conformation obtained by molecular mechanics

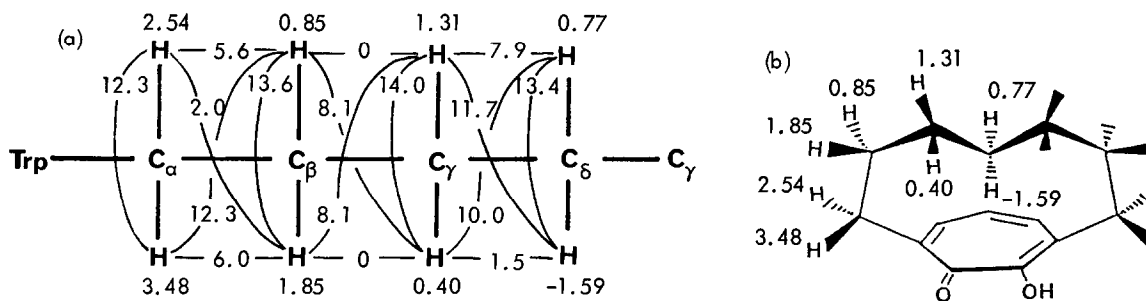


Fig. 3 (a) PMR parameters of bridge hydrogens in $1b$ (b) Conformation of $1b$ and assigned 1H chemical shifts

calculations¹⁰⁾ revealed the correctness of the assumption. The coupling constants calculated from the conformation^{8, 11)} are in good agreement with the experimental values.

No flipping of the 7-membered ring occurs at room temperature even in the dithia compound 4a¹⁾, the disulfones 5a¹⁾ and 6a¹⁾, as is judged from the presence of two sets (for 4a and 5a) or a set (for 6a) of AB signals for H_a. Apparently a bridge with 10 atoms is not long enough to allow the flipping in these cases.

References and Notes

- 1) H. Saito, Y. Fujise and S. Itô, *Tetrahedron Letters*, 24, 3879 (1983).
- 2) All new compounds gave satisfactory elemental analyses. Some of their physical properties follow (MS at 25 eV, 80–100°C, UV in methanol, IR in KBr, and NMR in CCl₄ unless otherwise stated).
 - 4b: Pale yellow prisms, m.p. 115–116°C; m/e 296 (M⁺), 108 (b); λ_{max} 249.5 (log ε 4.15), 309 (3.87), 352 nm (sh, 3.67); ν 1620, 1594 cm⁻¹; δ 6.38–6.84 (3H, m).
 - 4c: Pale yellow granules, m.p. 101–104°C; m/e 282 (M⁺), 108 (b); λ_{max} 252 (log ε 4.06), 273 (sh, 3.87), 305 (3.80), 356 nm (sh, 3.58); ν 1608, 1583 cm⁻¹; δ 6.50 (1H, dd, J=10.2, 7.5), 6.64 (1H, dd, J=7.5, 2.4), 6.72 (1H, dd, J=10.2, 2.4).
 - 5b: Pale yellow powder, m.p. 223–224°C; m/e 360 (M⁺), 108 (b); ν 1627, 1606, 1578, 1116 cm⁻¹.
 - 5c: Pale yellow powder, m.p. >300°C; m/e 346 (M⁺), 108 (b); ν 1621, 1602, 1110 cm⁻¹; δ (DMSO-d₆) 6.87 (1H, dd, J=11.3, 7.2), 7.11 (1H, br.dd, J=11.3, 1.5), 7.49 (1H, br.dd, J=7.2, 1.5).
 - 6b: Pale yellow powder, m.p. 266°C (dec.); m/e 345 (M⁺), 135 (b); ν 3165, 1591, 1552, 1121 cm⁻¹.
 - 6c: Pale yellow powder, m.p. ≥ 253°C (dec.); m/e 332 (M⁺), 91 (b); ν 3140, 1601, 1561, 1111 cm⁻¹.
 - 2b: Pale yellow oil; m/e 232 (M⁺, b), 217, 204, 189, 175, 161, 147, 134, 121, 105, 91; λ_{max} 243 (log ε 4.06), 250 (sh, 4.02), 258 (sh, 4.02), 310 (3.39), 346 nm (sh, 3.36), λ_{max} (H₂SO₄+MeOH) 246 (log ε 4.02), 275 (4.21), 352 nm (3.48); ν (oil) 1622, 1604 cm⁻¹; δ 0.60–2.03 (10H, m), 2.12 (1H, ddd, J=12.2, 4.5, 2.6), 2.52 (1H, br.dt, J=12.2, 3.9), 2.90 (1H, dd, J=12.2, 5.0), 2.99 (1H, ddd, J=12.2, 5.7, 4.5), 4.03 (3H, s), 6.58 (3H, br.s).
 - 1b: Colorless needles, m.p. 87.5–88.5°C; m/e 218 (M⁺, b), 190, 175, 172, 161, 130, 120, 107, 91; λ_{max} 253 (sh, log ε 4.13), 264 (sh, 4.17), 271 (4.19), 287 (sh, 3.68), 335 (sh, 3.57), 370 (3.78), 400 nm (sh, log ε 3.23); λ_{max} (NaOH+MeOH) 257 (log ε 4.01), 288 (4.04), 374 (sh, 3.80), 403 nm (3.91); λ_{max} (H₂SO₄+MeOH) 244 (log ε 4.04), 274 (4.48), 348 nm (3.72); ν 3180, 1593, 1552, 1537 cm⁻¹; ν (CHCl₃) 1597, 1535 cm⁻¹.
- 3) T. Otsubo and S. Misumi, *Synthetic Commun.*, 8, 285 (1978).
- 4) M. Yasunami, K. Takase and T. Nozoe, *Tetrahedron Letters*, 4327 (1970).
- 5) N. Kato, Y. Fukazawa and S. Itô, *ibid.*, 1113 (1979).
- 6) Assignment of protons in these compounds are based on the unambiguous analysis of specifically deuterated 2-methoxytropone. H. Sugiyama, Ph.D. Thesis, Tohoku University, 1963.
- 7) S.M. Rosenfeld and K. Ann Choe, in *Cyclophanes*, ed. by P.M. Keehn and S.M. Rosenfeld, Vol. 1, p. 311. Academic Press, New York (1983), and the references cited therein.
- 8) K. Kuriyama, E. Kondo and K. Tori, *Tetrahedron Letters*, 1485 (1963). R.U. Lemieux and J.W. Lown, *Can. J. Chem.*, 42, 893 (1964).
- 9) The same effect explains qualitatively the chemical shift difference of methine protons between α-thujaplicin (δ: 3.75), and hinokitiol (δ: 2.89) and γ-thujaplicin (δ: 2.90) (3-, 4-, and 5-isopropyl-tropolones, respectively). H. Sugiyama, Ph.D. Thesis, Tohoku University, 1963.
- 10) MMPI, QCPE=318, Indiana University (1983). N.L. Allinger and J.T. Sprague, *J. Am. Chem. Soc.*, 95, 3893 (1973), N.L. Allinger, J.T. Sprague and T. Liljefors, *ibid.*, 96, 5100 (1974).
- 11) Since PMR spectrum indicates C_s symmetry in NMR time scale, mean values of two corresponding dihedral angles in the calculated conformation were used for the calculation.