

Scheme I

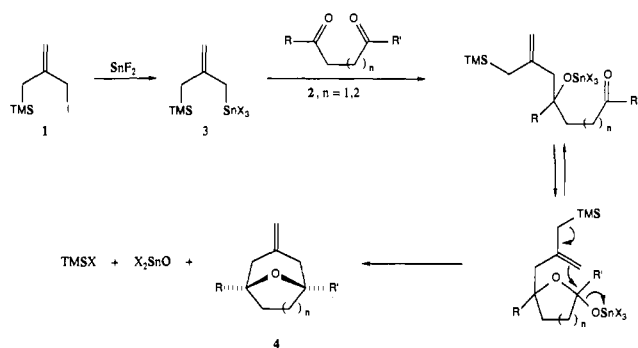


Table I. [3 + 4] Dianionic Annulation Reactions with 1,4-Dicarbonyl Substrates

entry	dicarbonyl substrate 2	product 4	% isolated yield ^a
1			91
2			66
3			60
4			70 ^b
5			100 ^c
6			85 ^d
7			74

^a Refers to material >98% pure by capillary GC analysis. ^b Isolated as a >15:1 mixture of diastereomers. ^c Isolated as a >10:1 mixture of diastereomers. ^d Isolated as a 3:1 mixture of diastereomers.

as well as synthetic materials¹⁶ possessing significant biological activity are also known which contain the same basic bicyclic ether structural units generated by this new approach. In addition, such bicyclic ethers have been utilized synthetically as key precursors to important natural products and other pharmacologically active materials.¹⁷ Because few general methods exist for construction of such molecules,^{4i,5a,8i,18} the present procedure represents a

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(17) (a) Cowling, A. P.; Mann, J.; Usmani, A. A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2116. (b) Sato, T.; Watanabe, M.; Kobayashi, H.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2680. (c) Sato, T.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2700.

(18) (a) Cope, A. C.; McKervey, M. A.; Weinshenker, N. M.; Kinnel, R. B. *J. Org. Chem.* **1970**, *35*, 2918. (b) Gras, J. L.; Bertrand, M. *Bull. Soc. Chim. Fr.* **1972**, 2024. (c) Barrelle, M.; Apparu, M. *Bull. Soc. Chim. Fr.* **1972**, 2016. (d) Gaude, D.; Barrelle, M.; Apparu, M. *Bull. Soc. Chim. Fr.* **1977**, 758. (e) Cekovic, Z.; Djokic, G. *Tetrahedron* **1981**, *37*, 4263.

Table II. [3 + 5] Dianionic Annulation Reactions with 1,5-Dicarbonyl Substrates

entry	dicarbonyl substrate 2	product 4	% isolated yield ^a
1			83
2			63
3			43
4			67 ^b

^a Refers to material >98% pure by capillary GC analysis. ^b Isolated as a 1.6:1 mixture of diastereomers.

promising new synthetic route into this exciting manifold of organic compounds.

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Supplementary Material Available: General synthetic procedure and complete spectral data for all compounds synthesized and tables of atomic coordinates and isotropic displacement parameters and bond lengths and bond angles (11 pages). Ordering information is given on any current masthead page.

Synthesis of *in*-[3^{4,10}][7]Metacyclophane: Projection of an Aliphatic Hydrogen toward the Center of an Aromatic Ring

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We recently noted that the previously prepared¹ 2,8,17-trithia[4^{5,12}][9]metacyclophane must have the structure **1**, in which the methine hydrogen lies inside the macrocycle.² Given this information, we immediately considered possible methods of triple ring contraction to form the exceptionally congested [3^{4,10}][7]-metacyclophane **3**, and the thermal extrusion of sulfur dioxide³ from the trisulfone **2** was chosen as the most promising route. Accordingly, compound **2** was prepared by heating **1** in a mixture of 30% aqueous hydrogen peroxide and acetic acid.⁴ Single

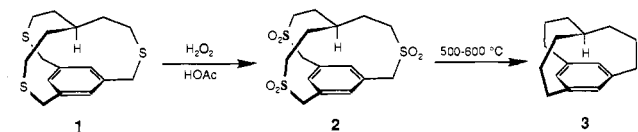
(1) Ricci, A.; Danieli, R.; Rossini, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1691-1693.

(2) Pascal, R. A., Jr.; Grossman, R. B. *J. Org. Chem.*, in press.

(3) Vogtle, F.; Rossa, L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 515-529.

(4) For **2**: melting point behavior—discoloration began at 250 °C, decomposition was gradual above 290 °C; ¹H NMR (250 MHz, DMSO-*d*₆) δ -2.79 [septet, 1 H, *J* = 6 Hz, methine H], 1.22 [m, 6 H, (RSO₂CH₂CH₂)₃CH], 2.96 [m, 6 H, (RSC₂H₂)₃CH], 4.67 [s, 6 H, Ar(CH₂)₃], 7.66 [s, 3 H, ArH₃]; MS, *m/z* 406 (M⁺, 4%), 342 (M - SO₂, 92), 213 (M - 3SO₂ - H, 48), 171 (66), 115 (100), 91 (65); exact mass 406.0574, calcd for C₁₆H₂₂S₃O₆ 406.0578.

crystals of **2** were obtained from DMSO solutions, and the structure was confirmed by X-ray crystallographic analysis.⁵ The distance from C(16) (see Figure 1) to the mean plane of the aromatic ring is 3.22 Å, and the methine H is 2.21 Å from the ring.⁶



To accomplish the ring contraction, compound **2** (37 mg) was placed in a 60 × 1 cm quartz tube. The tube was set at an incline and evacuated (0.25 Torr), and the lower end of the tube was heated in a Bunsen burner flame. After approximately 2 min a black cinder remained at the bottom, and a waxy solid (ca. 15 mg) had condensed a few centimeters higher in the tube. ¹H NMR analysis (CDCl₃) of this material showed four very high field resonances, δ -2.61, -3.03, -3.70, and -4.03 (all septets, *J* = 6 Hz; integral ratio 1:3:1:7), presumably corresponding to compound **2** and products having lost 1, 2, and 3 molecules of SO₂, respectively. The most abundant component was isolated in pure form by preparative VPC (10% OV-17, 145 °C; 2.2 mg, 11% yield). The low- and high-resolution mass spectra⁸ and the ¹H NMR spectrum⁹ (Figure 2) support the assignment of structure **3** to this material. Molecular mechanics calculations [MM2(85)¹⁰] indicate that the methine hydrogen should be only 1.78 Å from the aromatic ring, a proximity consistent with the δ -4.03 resonance for this proton.¹¹ These calculations also suggest that **3** should have C₃ symmetry in the ground state; thus the broadened methylene resonances in the room temperature ¹H NMR spectrum are a reflection of the relatively slow enantiomerization of the molecule on the NMR time scale. In the VT-NMR experiment illustrated in the inset of Figure 2, the widely separated resonances due to the diastereotopic benzylic hydrogens coalesce at approximately 320 K; therefore, Δ*G*_c^{*} for the exchange process is 14.8 kcal/mol.¹³ The UV spectrum of compound **3** [*n*-heptane,

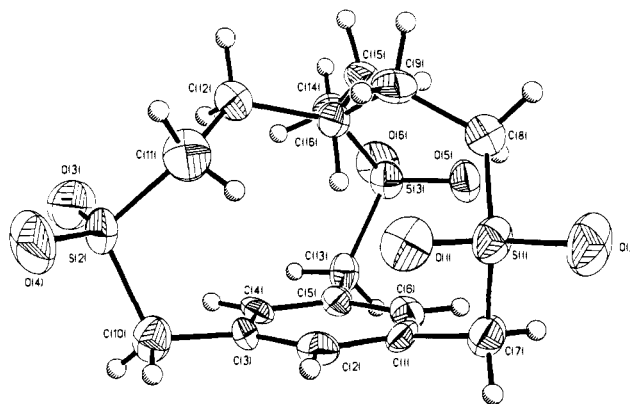


Figure 1. X-ray structure of compound **2**.

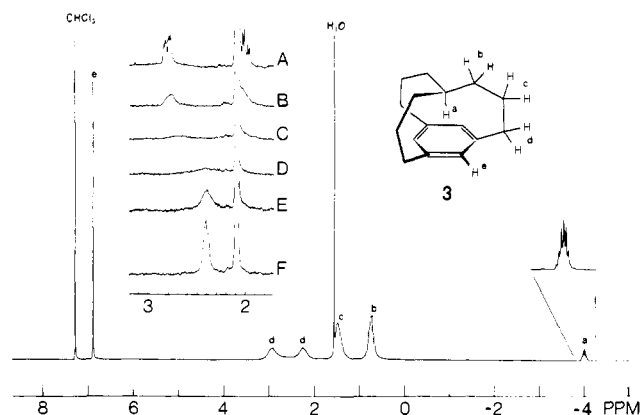


Figure 2. 250-MHz ¹H NMR spectrum (CDCl₃, 298 K) of compound **3**. The inset shows the benzylic proton region of the spectrum recorded in toluene-*d*₈ at a variety of temperatures: (A) 203 K; (B) 283 K; (C) 303 K; (D) 323 K; (E) 343 K; (F) 373 K. The off-scale signals at δ 2.09 in the inset spectra are from toluene-*d*₇.

(5) A crystal of compound **2** measuring 0.10 × 0.12 × 0.20 mm was used for the X-ray measurements. Crystal data: C₁₆H₂₂O₆S₃, *M_r* = 406.5; orthorhombic, space group *Pna*2₁; *a* = 16.984 (4) Å, *b* = 13.946 (3) Å, *c* = 7.540 (1) Å, *V* = 1785.9 (5) Å³, *Z* = 4, *d*_{calc} = 1.51 g/cm³. Intensity measurements were made with 3° < 2θ < 114° by using graphite-monochromated Cu Kα radiation (λ = 1.54178 Å) at room temperature on a Nicolet R3m diffractometer. A total of 1313 unique reflections were measured, and after Lorentz and polarization corrections were applied, 1248 were considered to be observed [*I*_o > 3σ(*F*_o)]. The structure was solved by direct methods using the SHELXTL software. Refinement with 230 parameters converged at *R* = 0.032 and *R_w* = 0.034 with goodness of fit = 1.18. Full details are provided in the supplementary material.

(6) The position of H(16), the inside hydrogen, was refined at 1.02 (5) Å from C(16), but X-ray crystallography tends to underestimate the length of C-H bonds.⁷ If the methine C-H distance is assumed to be 1.07 Å, then the inside hydrogen lies only 2.16 Å from the aromatic ring.

(7) Churchill, M. R. *Inorg. Chem.* **1973**, *12*, 1213-1214.

(8) For **3**: MS, *m/z* 214 (M⁺, 29%), 171 (M - C₃H₇, 100), 143 (M - C₅H₁₁, 40), 129 (M - C₆H₁₃, 43), 115 (M - C₇H₁₅, 41); exact mass 214.1724, calcd for C₁₆H₂₂ 214.1721.

(9) ¹H NMR (CDCl₃, 25 °C) δ -4.03 [septet, *J* = 6 Hz, 1 H, a (see Figure 2 for assignments); collapses to a singlet upon irradiation at δ 0.72], 0.72 [broad, 6 H, b], 1.45 [broad, 6 H, c], 2.23 and 2.91 [broad, 6 H, d], 6.86 [s, 3 H, e]; ¹H NMR (toluene-*d*₈, 70 °C) δ -4.00 [septet, *J* = 6 Hz, 1H, a], 0.65 [q, *J* = 6 Hz, 6 H, b], 0.86 [m, 6 H, c], 2.41 [broad, 6 H, d], 6.70 [s, 3 H, e].

(10) Allinger, N. L. *QCPE* MM2(85), 1986.

(11) This resonance is observed at a higher field than even the most highly shielded methylene protons of [9]- (δ 0.33), [8]- (0.19), [7]- (-0.3 to -0.9), [6]- (-0.6),^{12a} and [5]paracyclophane (0.01).^{12b}

(12) (a) Rosenfeld, S. M.; Cho, K. A. [*n*]Cyclophanes in Cyclophanes; Kechn, P. M., Rosenfeld, S. M., Eds.; Academic: New York, 1983; Vol. 1, p 339 and references cited therein. (b) Jenneskens, L. W.; de Kanter, F. J. J.; Kraakman, P. A.; Turkenburg, L. A. M.; Koolhaas, W. E.; de Wolf, W. H.; Bickelhaupt, F.; Tobe, Y.; Kakiuchi, K.; Odaira, Y. *J. Am. Chem. Soc.* **1985**, *107*, 3716-3717.

nm (log ε) 215 (4.4), 286 (2.3)] was typical of [*n*]cyclophanes with short methylene bridges,¹⁵ but the C-H stretching region of the IR spectrum (CCl₄) was unusual, exhibiting peaks at 2845, 2860, 2895, 2930, and 3325 cm⁻¹. The last signal we assign to the methine C-H stretch; the blue shift of ca. 400 cm⁻¹ is apparently an exceptional case of ν_{CH} frequency enhancement due to severe steric compression.¹⁷

When more of compound **3** becomes available, it will be interesting to see how the reactivities of the methine group and aromatic ring are influenced by their mutual proximity.

(13) *k_c* (462 s⁻¹) was calculated by using the equation appropriate for a coupled AB system (Δν_{AB} = 206 Hz, *J*_{AB} = 12 Hz) with equal populations,¹⁴ and a transmission coefficient of 1 was assumed for the Eyring equation.

(14) Kurland, R. J.; Rubin, M. B.; Wise, W. B. *J. Chem. Phys.* **1964**, *40*, 2426-2427.

(15) "Ultraviolet spectra of [*n*]cyclophanes are generally characterized by increasing bathochromic shifts and loss of fine structure as the length of the methylene bridge decreases, an effect ascribed to the bending of the aromatic ring."^{12a} The 286-nm band of **3** is featureless, and its shift is comparable to that in [6]metacyclophane (λ_{max} = 280 nm),^{16a} but not so much as in [5]-metacyclophane (306.5 nm).^{16b}

(16) (a) Hirano, S.; Hara, H.; Hiyama, T.; Fujita, S.; Nozaki, H. *Tetrahedron* **1975**, *31*, 2219-2227. (b) van Straten, J. W.; de Wolf, W. H.; Bickelhaupt, F. *Tetrahedron Lett.* **1977**, 4667-4670.

(17) Similar but smaller frequency enhancements have been observed for C-H stretches in many fused norbornane derivatives,^{18a-c} hexaisopropylbenzene,^{18d} and secododecahedrane.^{18e}

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