consumption of starting material. The mixture was poured into cold 1 M phosphate buffer (100 mL, pH 2.5), ether (40 mL) was added, the layers were separated, and the aqueous portion was extracted with ether (2 × 25 mL). The combined ether phase was washed with water and saturated brine and dried, the solvent was evaporated, and the light yellow residue was Kugelrohr distilled at 80–85 °C (0.01 mm) to yield 3.1 g (0.012 mol, 60%) of product. To this diethyl *tert*-butyl triester (1.9 g, 7.3 mmol) dissolved in ether (8 mL) and cooled to 5 °C was added with stirring a solution of sodium in ethanol (2.9 mL of 2.5 M solution, 7.5 mmol, from dissolving 0.4 g of sodium in 7 mL of ethanol). After the addition was completed, the stirring was continued for 10 min. The white paste was transferred to a fritted glass funnel, washed with ether, and dried in vacuo; yield 1.7 g (6 mmol, 85%). Anal. Calcd for $C_{12}H_{19}O_6Na$: C, 51.1; H, 6.8. Found: C, 50.7; H, 6.7.

Diethyl *tert*-Butyl Pentane-1,1,1-tricarboxylate (14, R = C_2H_5, R′ = C_4H_9, R″ = $CH_3(CH_2)_3$). Diethyl *tert*-butyl sodiomethanetricarboxylate (3.0 g, 10.6 mmol) was dissolved in benzene/DMF (1/1, 30 mL). 1-Bromobutane (2.9 g, 20 mmol) was added, the solution was heated at 75 °C with stirring for 16 h and then cooled to room temperature, 50 mL of water and 40 mL benzene were added, and, after thorough mixing, the organic layer was separated and washed twice with water. After the solvent was dried and evaporated, the crude product was Kugelrohr distilled: bp 100–110 °C (0.1 mm); yield 2.7 g (8.6 mmol, 86%). Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.7; H, 8.9. Found: C, 60.4; H, 8.7.

Diethyl *n*-Butylmalonate (15) by Decarbo-*tert*-butoxylation of Diethyl *tert*-Butyl Pentane-1,1,1-tricarboxylate (14). The unsymmetrical triester in either 100% formic or trifluoroacetic acid (1.0 mL/0.1 g of triester) was stirred at room temperature for 3 h. An aliquot, quenched by addition of aqueous K_2CO_3 and extracted into CH_2Cl_2, was analyzed by GC and showed the presence of only diethyl *n*-butylmalonate as the product.

Benzyl Pipecolate (17). Pipecolic acid (52.7 g, 0.41 mol), *p*-toluenesulfonic acid monohydrate (85.5 g, 0.45 mol), and benzyl alcohol (130 g, 125 mL) were dissolved in 250 mL of toluene and heated at reflux for 48 h, with a Dean–Stark trap to remove water. The mixture was cooled, poured into 1.5 L of water, and extracted with ether (3 × 300 mL). The aqueous layer was made alkaline with excess solid K_2CO_3 and then extracted with ether (3 × 300 mL). After the ether extracts were washed with water (2 × 100 mL) and dried, the ether was evaporated to give a crude product containing the desired ester and benzyl alcohol. This product was Claisen distilled [bp 100–103 °C (0.05 mm)], followed by Kugelrohr distillation, to obtain 58 g (88%) of pure (GC) benzyl pipecolate: IR 2900, 1725, 1440, 1180 cm^{-1}; NMR δ 1.2–2.1 (m, 7 H), 2.3–3.4 (m, 3 H), 5.1 (s, 2 H), 7.35 (s, 5 H).

Benzyl *N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolate (18). Benzyl pipecolate (17; 4.15 g, 19 mmol), triethyl 5-bromopentane-1,1,1-tricarboxylate (8.7 g, 23.7 mmol), benzene/DMF (1/1, 65 mL), and anhydrous K_2CO_3 (9.75 g, 71 mmol) were heated at 85 °C with vigorous stirring for 17 h. The mixture was cooled, poured into 1 M H_3PO_4 (250 mL), and extracted with ether (3 × 100 mL). The aqueous acidic solution, cooled in an ice bath, was adjusted to pH 10 with K_2CO_3 and extracted with ether (3 × 100 mL). The ether was evaporated, benzene was added, and the benzene was washed with H_2O (2 × 75 mL), dried, and evaporated to yield 4.9 g (10.3 mmol, 53%) of **18**: NMR δ 1.25 (t, 9 H), 1.0–3.3 (m, 17 H), 4.2 (q, 6 H), 5.1 (s, 2 H), 7.3 (s, 5 H); IR 3000, 1745, 1360, 1255 cm^{-1}. Anal. Calcd for $C_{27}H_{39}NO_8$: C, 64.1; H, 7.8; N, 2.8. Found: C, 64.3; H, 7.7; N, 2.8.

***N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolic Acid (19).** Benzyl *N*-[5,5,5-tris(ethoxycarbonyl)-*n*-pentyl]pipecolate (**18**; 2.5 g, 5.0 mmol), dissolved in absolute ethanol (50 mL), was hydrogenated over Pd/C (10%, 0.25 g) for 20 h. After filtration and evaporation of the filtrate, the residue was triturated with ether/hexane (85/15, 5 mL). Cooling resulted in **19**: mp 91–94 °C; 1.9 g (4.6 mmol, 92%); NMR δ 1.3 (t, 9 H), 1.3–3.8 (m, 17 H), 4.2 (q, 6 H), 9.3 (br s, 1 H); IR ($CHCl_3$) 3075, 1740, 1630, 1380 cm^{-1}. Anal. Calcd for $C_{20}H_{33}NO_8$: C, 57.8; H, 8.0; N, 3.4. Found: C, 57.7; H, 7.9; N, 3.5.

***N*-[5,5-Bis(ethoxycarbonyl)-*n*-pentyl]pipecolic Acid (20) Hydrochloride.** *N*-[5,5,5-Tris(ethoxycarbonyl)-*n*-pentyl]pipecolic acid (**19**; 1.0 g, 2.4 mmol) was added to a solution of sodium (0.115 g, 5.0 mmol) in ethanol (10 mL) and stirred at room temperature for 10 min. The solution was then cooled in an ice bath, cold 2 N HCl (5 mL, 200 mol % based on sodium used) was added slowly, and the acidic ethanol/water solution was evaporated to give an oily solid. This material was triturated with hot *tert*-butyl alcohol, the NaCl was removed, and the *tert*-butyl alcohol was evaporated, leaving 0.85 g (2.24 mmol, 93%) of **20**·HCl as a glass: NMR δ 1.3 (t, 6 H), 1.0–3.6 (m, 18 H), 4.2 (q, 4 H), 9.2 (s, 1 H); IR ($CHCl_3$) 3100, 2480, 1735, 1600, 1520, 1200 cm^{-1}. Anal. Calcd for $C_{17}H_{30}NO_6Cl$: C, 53.8; H, 8.0; N, 3.7. Found: C, 54.0; H, 8.2; N, 3.6.

Registry No. **1**, 63972-17-8; **8**, 71170-77-9; **9**, 71170-78-0; **10**, 71170-79-1; (*Z*)-**11**, 71170-80-4; **12** (R = R′ = C_2H_5), 6279-86-3; **12** (R = C_2H_5; R′ = *t*-C_4H_9), 71170-90-6; **13** (R = R′ = C_2H_5), 68922-87-2; **13** (R = C_2H_5; R′ = *t*-C_4H_9), 71170-81-5; **14** (R = R′ = C_2H_5; R″ = $BrCH_2CH_2$), 71170-82-6; **14** (R = R′ = C_2H_5; R″ = $Br(CH_2)_4$), 71170-83-7; **14** (R = R′ = C_2H_5; R″ = $CH_3(CH_2)_3$), 3272-32-0; **14** (R = C_2H_5; R′ = *t*-C_4H_9; R″ = $CH_3(CH_2)_3$), 71170-84-8; **15** (R = C_2H_5; R″ = $CH_3(CH_2)_3$), 133-08-4; **17**, 38068-75-6; **18**, 71170-85-9; **19**, 71170-86-0; **20**·HCl, 71170-87-1; 2-(benzyloxy)ethyl chloride, 17229-17-3; 2-(benzyloxy)ethanol, 622-08-2; diethyl [2-(benzyloxy)ethyl]malonate, 41478-45-9; diethyl malonate, 105-53-3; 1,4-dichloro-2-butyne, 821-10-3; pipecolic acid, 535-75-1; *N*-(benzyloxycarbonyl)pipecolic acid, 71170-88-2; *tert*-butyl *N*-(benzyloxycarbonyl)pipecolate, 71170-89-3; 1,2-dibromoethane, 106-93-4; 1-bromobutane, 109-65-9; 1,4-dibromobutane, 110-52-1; ethyl *tert*-butyl malonate, 32864-38-3.

3,8-Thionanedione 1,1-Dioxide. Synthesis and Solid-State Conformation[1]

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Received March 8, 1979

The title compound is conveniently prepared in 80% overall yield by ozonolysis at −78 °C of the cycloadduct of SO_2 with 1,2-dimethylenecyclohexane. Single-crystal X-ray analysis establishes that the nine-membered ring adopts a twist-chair–chair conformation in which the sulfur atom and the midpoint of the C(5)–C(6) bond lie on a noncrystallographic C_2 axis, but the ring shape differs significantly from that of cyclononane in order to accommodate transannular dipole···dipole interactions. Crystals are orthorhombic, space group $P2_12_12_1$, with a = 8.963 (4) Å, b = 15.403 (7) Å, c = 6.724 (3) Å, and Z = 4. Atomic positional and thermal parameters were refined by full-matrix least-squares calculations to R = 0.032 over 913 statistically significant reflections.

We recently reported[2] a simple method to obtain diketo derivatives of the rare phosphorus heterocycles with seven to nine members in the ring. The method employs the cycloaddition of a diene with a trivalent phosphorus halide

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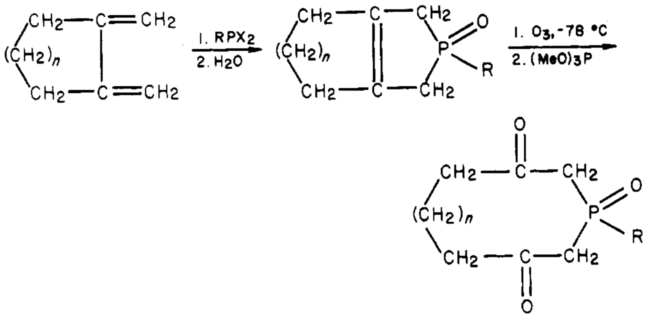
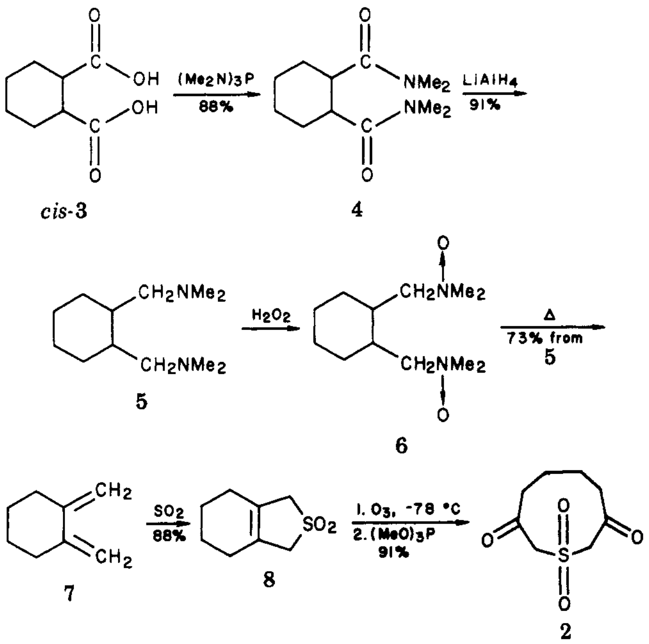
Scheme I



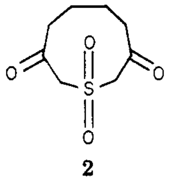
1

Scheme II



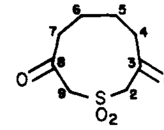
to establish a bicyclic system amenable to ring-opening ozonolysis (Scheme I). The method seemed applicable also to the synthesis of large-ring sulfur compounds, by using sulfur dioxide in the cycloaddition reaction, and in this paper we show that this is indeed a quite useful extension of the method.

To illustrate this process, we chose to prepare the nine-membered ring compound 3,8-thionanedione 1,1-dioxide (**2**), representative of a ring system for which only a few derivatives are known.[3] The keto groups of **2** could then conceivably participate in a number of reactions to provide a variety of new derivatives of this ring system. The compound also is of special interest in connection with structural and conformational studies being performed in this laboratory on other rings of nine members. The corresponding phosphine oxide (**1**, $n = 2$) has been shown[4] to exist in the solid state in an unusual conformation with all three oxygen atoms oriented syn with respect to the plane of the ring which has a form intermediate between C_2 and C_s conformations. We felt that with two oxygens on the heteroatom in sulfone **2** the locally symmetrical sulfur environment could lead to a conformational preference different from that of the corresponding phosphine oxide **1**, and this has proved to be the case.



2

Table I. NMR Spectral Properties of 3,8-Thionanedione 1,1-Dioxide



position	δ(¹H)	δ(¹³C)
2, 9	4.3 (s)	65.3
3, 8		201.7
4, 7	3.2 (m)	42.0
5, 6	1.7 (m)	23.2

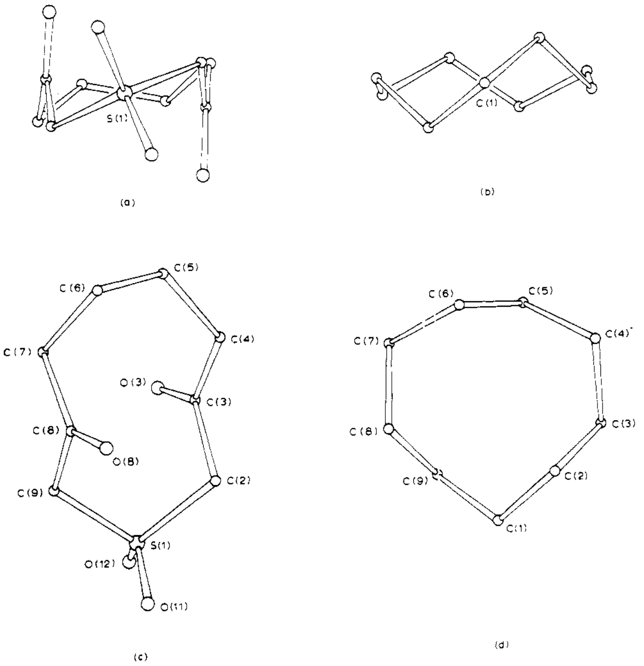


Figure 1. Views of the conformation of **2**: (a) in projection along the approximate C_2 axis; (c) perpendicular to the mean plane through the ring atoms. (b) and (d) are corresponding views of the cyclononane twist-chair-chair (TCC-C_2) conformation.

Synthesis and Characterization. The series of reactions used in the synthesis of **2** is given in Scheme II and involves six high-yield steps from the commercially available *cis*-cyclohexane-1,2-carboxylic acid (**3**).

The use of hexamethylphosphorous triamide as a reagent[5] for the one-step conversion of the cis acid **3** to the amide **4** deserves special comment as it proceeds in excellent yield and gives a product of such high purity that no further purification is required. The technique of converting the acid to the acid chloride for reaction with dimethylamine requires use of the more expensive trans acid to avoid the side reaction of dehydration to the anhydride. Other reactions in the sequence providing diene **7** are conventional, and this diene has previously been used[6] in the cycloaddition with sulfur dioxide to form

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(1) Supported in part by Public Health Service Research Grant CA-05507, National Cancer Institute.

(2) L. D. Quin and E. D. Middlemas, *J. Am. Chem. Soc.*, **99**, 8370 (1977).

(3) A. Müller, E. Funder-Fritzsche, W. Konar, and E. Rintersbacher-Wlasak, *Monatsh. Chem.*, 84, 1206 (1953); E. Vedejs, M. J. Arco, J. M. Renga, and S. P. Singer, *J. Org. Chem.*, 43, 4831 (1978); V. Cerè, C. Paolucci, S. Pollicino, E. Sandri, and A. Fava, *ibid.*, 43, 4826 (1978).

(4) A. T. McPhail and R. W. Miller, manuscript in preparation.

(5) R. Burgada, *Ann. Chim. (Rome)*, 8, 364 (1963).

(6) R. Jahn and U. Schmidt, *Chem. Ber.*, 108, 630 (1975).

sulfone 8. Ozonolysis occurred under the same conditions developed for the corresponding phosphine oxide[2] and gave a 91% yield of easily crystallized thionanedione 2, mp 131–134 °C. The structure of 2 was readily established by analysis and NMR spectroscopy (Table I). The symmetry of the molecule led to quite simple spectra, consisting of three signals in the ^{1}H spectrum and four in the ^{13}C spectrum, one of which was in the unique position of a ketone (δ 201.7). In further confirmation of the diketone structure, a bis(dinitrophenylhydrazone) was found to form with great ease.

X-ray Analysis of 2. The conformation of 2 in the solid state, as determined by single-crystal X-ray analysis, is shown in Figure 1 as viewed in projection along its approximate C_2 symmetry axis and perpendicular to the mean plane through the ring atoms; corresponding views of cyclononane in the twist-chair–chair (TCC-C_2)[7] conformation are included for comparison. Positional parameters for the nonhydrogen atoms are in Table II; bond lengths and valency and torsion angles are in Table III. Anisotropic thermal parameters (Table IV) and hydrogen atom parameters (Table V) are available as supplementary material.[8]

The nine-membered ring in 2 approximates to a twist-chair–chair (TCC-C_2) conformation in which the sulfur atom and the midpoint of the C(5)–C(6) bond lie on a noncrystallographic twofold axis. Since the individual ring parameters show small deviations from exact C_2 symmetry-related values (average deviations are 0.006 Å in bond lengths, 0.3° in valency angles, and 4.9° in torsion angles), only the mean values will be cited in the following discussions of the molecular geometry. Comparison of the endocyclic torsion angles in 2, −34° about bond S(1)–C(2), 133° about C(2)–C(3), −143° about C(3)–C(4), 79° about C(4)–C(5), and −66° about C(5)–C(6), with the corresponding values of −65, 124, −81, 91, and −124° characterizing the cyclononane[7,9,10] TCC-C_2 form reveals highly significant differences which appear to result principally from modifications occurring in the ring conformation of 2 in order to accommodate transannular dipolar interactions which are absent in cyclononane. Adoption by 2 of a conformation defined by the TCC-C_2 cyclononane torsion angles would result in an unfavorable, approximately parallel eclipsed orientation of the $S^+{=}O^-$ and $C^+{=}O^-$ dipoles but a favorable antiparallel orientation of the $C^+{=}O^-$ dipoles. In the form found for 2 in the solid state the pseudo torsion angle O(12)–S(1)···C(3)–O(3) of −32° reduces the unfavorable dipolar interaction but retains a favorable antiparallel orientation of the C=O groups. Further, concomitant diminution of the endocyclic torsion angle about the S(1)–C(2) bond in 2 compared with that in cyclononane is accompanied by conformationally transmitted alterations in the other ring torsion angles. That the combined effect of these torsion angle changes results in extension of the TCC-C_2 conformation along the C_2 axis and compression perpendicular to this direction is evident from the views presented in Figure 1 and from the C(3)···C(8) and S(1)···C(4)–C(5) midpoint distances of 2.84 and 4.80 Å in 2 compared with the more equal values of 3.84 and 3.93 Å in cyclononane. It would appear that the flattening which occurs at C(2) only partially alleviates the unfavorable S=O/C=O dipolar interactions in 2 for it is accompanied by slight increases in the S(1)–C(2) and C(2)–C(3) bond lengths over normal values. The S(1)–C(2) distance at 1.793 (3) Å in 2 may be contrasted with the slightly shorter value of 1.765 (5) Å in dimethyl sulfone;[11] in addition, although the mean C(sp^3)–C(sp^2) bond length of 1.516 Å is in excellent agreement with the accepted value (1.516 (5) Å),[12a] the C(2)–C(3) length at 1.533 (4) Å is significantly longer than the C(3)–C(4) distance of 1.499 (4) Å. The mean S=O bond length at 1.433 (2) Å and the O=S=O and C–S–C valency angles at 118.6 (1) and 106.1 (1)° accord well with those found in crystal structure analyses of other sulfones.[13]

Table II. Fractional Atomic Coordinates (×10^4) for the Nonhydrogen Atoms, with Estimated Standard Deviations in Parentheses

atom	*x*	*y*	*z*
S(1)	4325 (1)	−832 (1)	−37 (1)
C(2)	4477 (3)	−3 (2)	1812 (4)
C(3)	4102 (3)	896 (2)	978 (4)
C(4)	5100 (4)	1640 (2)	1528 (4)
C(5)	5378 (4)	2283 (2)	−157 (6)
C(6)	6481 (4)	1981 (2)	−1722 (5)
C(7)	5956 (3)	1203 (2)	−2960 (4)
C(8)	6169 (3)	342 (2)	−1963 (4)
C(9)	4977 (4)	−357 (2)	−2321 (4)
O(3)	3031 (2)	985 (1)	−101 (3)
O(8)	7218 (2)	184 (1)	−901 (3)
O(11)	5321 (3)	−1516 (1)	524 (4)
O(12)	2777 (2)	−1034 (1)	−316 (3)

Packing of molecules of crystals of 2 is shown in Figure 2,[8] and intermolecular separations less than 3.50 Å are in Table VI. The molecules are arranged such that there exist weak S=O···C=O and C=O···C=O interactions of the type first recognized by Dunitz et al.[14] from their surveys on O···C=O systems in crystals. Thus, O(12) and C(3) lie 2.997 and 0.004 Å to the same side of the C(2), C(4), O(3) plane while corresponding values for O(8) and C(8) are 3.111 and 0.003 Å with respect to the C(7), C(9), O(9) plane; the associated O···C=O angles are 92.5 and 95.1°. The other distances quoted correspond to normal van der Waals type interactions.

Experimental Section[15]

***cis*-*N*,*N*,*N'*,*N'*-Tetramethyl-1,2-cyclohexanedicarboxamide (4).** To a suspension of *cis*-1,2-cyclohexanedicarboxylic acid (86.4 g, 0.50 mol) in benzene (250 mL) was added hexamethylphosphorous triamide[16] (81.6 g, 0.50 mol) at a rate that maintained

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[7] J. B. Hendrickson, *J. Am. Chem. Soc.*, **89**, 7047 (1967).

[8] Supplementary material.

[9] The values found in 2 may also be contrasted with the corresponding means of −64, 118, −75, 85, −118°, derived by empirical force-field calculations [E. M. Engler, J. D. Andose, and P. von R. Schleyer, *J. Am. Chem. Soc.*, **95**, 8005 (1973)].

[10] A referee has criticized our use of cyclononane as a model for comparison with the observed conformation of 2 and contended that the distortions are exactly what would be expected to arise from replacement of the appropriate cyclononane sp^3-hybridized carbon atoms by sp^2-hybridized carbon atoms to give cyclononane-1,5-dione. It is, however, well established from studies on other medium ring systems that such a replacement results in only small conformational changes in contrast to the large effects observed in 2. To further support our conclusion regarding the origin of the unusual conformation adopted by 2, we have calculated torsion angles for the TCC-C_2 form of cyclononane-1,5-dione by means of an empirical force-field program which gives excellent agreement between the calculated and observed conformations of cyclooctane-1,5-dione (R. W. Miller and A. T. McPhail, *J. Chem. Soc., Perkin Trans. 2*, in press). As expected, the torsion angles thus derived for cyclononane-1,5-dione (−62, 121, −79, 86, −119°) are close to the corresponding cyclononane values.

[11] D. A. Langs, J. V. Silverton, and W. M. Bright, *J. Chem. Soc., Chem. Commun.*, 1653 (1970).

[12] "International Tables for X-Ray Crystallography", Vol. III, Kynoch Press, Birmingham, England, 1968: (a) p 276; (b) pp 213–216.

[13] I. Hargittai, "Lecture Notes in Chemistry", Vol. 6, Springer-Verlag, New York, 1978.

[14] H. B. Bürgi, J. D. Dunitz, and E. Shefter, *Acta Crystallogr., Sect. B*, **30**, 1517 (1974).

[15] Melting points were taken on a Mel-Temp apparatus and are corrected; boiling points are uncorrected. Ozonolysis was accomplished with a Welsbach T-23 laboratory ozonator. ^{1}H NMR spectra were taken with a JEOL MH-100 spectrometer and ^{13}C FT NMR spectra (proton decoupled) with a JEOL FX-60 spectrometer. Elemental analyses were performed by MHW Laboratories.

Table III. Interatomic Distances (Å) and Angles (deg), with Estimated Standard Deviations in Parentheses

(a) Bond Lengths			
S(1)-C(2)	1.787 (3)	C(4)-C(5)	1.526 (5)
S(1)-C(9)	1.799 (3)	C(5)-C(6)	1.517 (5)
S(1)-O(11)	1.432 (2)	C(6)-C(7)	1.533 (4)
S(1)-O(12)	1.434 (2)	C(7)-C(8)	1.498 (4)
C(2)-C(3)	1.532 (4)	C(8)-C(9)	1.535 (4)
C(3)-C(4)	1.500 (4)	C(8)-O(8)	1.206 (3)
C(3)-O(3)	1.211 (3)		
(b) Valency Angles			
C(2)-S(1)-C(9)	106.1 (1)	C(4)-C(3)-O(3)	122.3 (2)
C(2)-S(1)-O(11)	107.2 (1)	C(3)-C(4)-C(5)	114.2 (3)
C(2)-S(1)-O(12)	108.7 (1)	C(4)-C(5)-C(6)	115.0 (2)
C(9)-S(1)-O(11)	108.8 (1)	C(5)-C(6)-C(7)	114.6 (3)
C(9)-S(1)-O(12)	106.9 (1)	C(6)-C(7)-C(8)	114.2 (2)
O(11)-S(1)-O(12)	118.6 (1)	C(7)-C(8)-C(9)	117.5 (2)
S(1)-C(2)-C(3)	112.0 (2)	C(7)-C(8)-O(8)	122.9 (2)
C(2)-C(3)-C(4)	118.0 (2)	C(9)-C(8)-O(8)	119.6 (2)
C(2)-C(3)-O(3)	119.7 (2)	C(8)-C(9)-S(1)	112.2 (2)
(c) Torsion Angles			
C(9)-S(1)-C(2)-C(3)	36.8 (2)	S(1)-C(2)-C(3)-O(3)	43.7 (2)
S(1)-C(2)-C(3)-C(4)	−135.8 (2)	C(5)-C(4)-C(3)-O(3)	−37.9 (3)
C(2)-C(3)-C(4)-C(5)	141.6 (3)	S(1)-C(9)-C(8)-O(8)	49.7 (3)
C(3)-C(4)-C(5)-C(6)	−76.7 (3)	C(6)-C(7)-C(8)-O(8)	−35.2 (3)
C(4)-C(5)-C(6)-C(7)	66.4 (3)	O(11)-S(1)-C(2)-C(3)	152.9 (2)
C(5)-C(6)-C(7)-C(8)	−81.2 (3)	O(11)-S(1)-C(9)-C(8)	−84.7 (2)
C(6)-C(7)-C(8)-C(9)	144.3 (3)	O(12)-S(1)-C(2)-C(3)	−77.9 (2)
C(7)-C(8)-C(9)-S(1)	−129.9 (2)	O(12)-S(1)-C(9)-C(8)	146.2 (2)
C(8)-C(9)-S(1)-C(2)	30.3 (2)		

Table VI. Intermolecular Separations Less Than 3.50 Å[a]

C(3)···O(12^{I})	3.02	C(2)···O(3^{I})	3.41
C(8)···O(8^{II})	3.12	O(8)···O(8^{II})	3.45
C(2)···O(12^{I})	3.22	C(4)···O(12^{I})	3.47
O(3)···O(12^{I})	3.30	C(4)···O(11^{III})	3.48
C(7)···O(8^{II})	3.34	C(6)···O(11^{II})	3.49
O(8)···C(2^{II})	3.35	C(9)···O(8^{II})	3.49

[a] Roman numeral superscripts refer to the following transformations of the coordinates of Table II: I, $^1/_2 - x$, $-y$, $^1/_2 + z$; II. $^3/_2 - x$, $-y$, $-^1/_2 + z$; III, $1 - x$, $^1/_2 + y$, $-^3/_2 - z$.

reflux of the reaction mixture. The resulting cloudy solution was allowed to cool to room temperature and a saturated $NaHCO_3$ solution (200 mL) was added. The layers were separated and the aqueous layer was extracted with methylene chloride (3 × 100 mL). The organic solutions were combined, dried ($MgSO_4$), and concentrated to give a clear, colorless oil which solidified to a white solid. After the solid was washed with hexane, 99.3 g (88%) of diamide **4**, mp 74–75 °C, was obtained. Recrystallization from ether at −78 °C gave white needles: mp 76–77 °C; IR (KBr) $\nu_{C=O}$ 1630 cm^{-1}; NMR (CCl_4) δ 1.12–1.72 (m, 4 H, CH_2), 1.76–2.36 (m, 4 H, CH_2), 2.95 (br s, 14 H, NCH_3 and CH).

Anal. Calcd for $C_{12}H_{22}N_2O_2$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.81; H, 10.00; N, 12.29.

***cis*-*N*,*N*,*N'*,*N'*-Tetramethyl-1,2-cyclohexanebis(methaneamine) (5).** To a suspension of lithium aluminum hydride (21.3 g, 0.56 mol) in anhydrous ether (500 mL) was added a solution of diamide **4** (96.1 g, 0.43 mol) in dry tetrahydrofuran (500 mL) at a rate which maintained gentle reflux. The mixture was then refluxed for 1 h and hydrolyzed by the cautious addition of water (22 mL), 15% NaOH solution (22 mL), and finally water (66 mL). The fine, white precipitate which formed was filtered off, washed with ether (3 × 200 mL), and discarded. The filtrate was concentrated and the residue distilled to give 76.5 g (91%) of diamine **5**: bp 113–115 °C (21 mm); NMR (CCl_4) δ 1.25–1.52 (m, 8 H, $-CH_2$), 1.90–2.28 (m, 18 H, including a sharp singlet at δ 2.10, NCH_2, NCH_3, and CH).

Anal. Calcd for $C_{12}H_{26}N_2$: C, 72.66; H, 13.21; N, 14.13. Found: C, 72.68; H, 13.35; N, 14.35.

1,2-Dimethylenecyclohexane (7). The general procedure of Cope and Ciganek[17] was followed. To a solution of diamine **5** (73.4 g, 0.37 mol) in methanol (125.8 mL) at 0 °C was added hydrogen peroxide (83.9 mL of a 30% solution, 0.74 mol), followed by additional portions of 83.9 mL each at 3 and 5 h of elapsed time. The resulting solution was stirred for 36 h at room temperature after which a negative phenolphthalein test for basicity was obtained. The excess peroxide was destroyed by stirring the reaction mixture with 100 mg of platinum-on-carbon until the evolution of oxygen ceased. The catalyst was removed by filtration and the filtrate was concentrated at 50–60 °C by using a rotary evaporator at aspirator pressure followed by evacuation at 0.1 mm to give crude amine oxide **6** as a clear, highly viscous, pale yellow oil. Hydroquinone (0.5 g) was added and the resulting mixture was heated in an oil bath at 150–170 °C (100 mm). The pyrolysate was passed through a water-cooled condenser and then collected in a dry ice–acetone trap. Water (75 mL) was added to the pyrolysate and the two layers were separated. The upper layer of diene **7** was washed with water (2 × 25 mL), cold 10% HCl (10 mL), saturated $NaHCO_3$ (25 mL), and saturated NaCl (25 mL). The neat diene was dried over anhydrous K_2CO_3 followed by 4A molecular sieves and filtered through glass wool to give 29.3 g (73%) of product, the ^1H NMR spectrum[18] of which indicated that it was essentially free of impurities. The diene was used without further purification in the subsequent step.

1,3,4,5,6,7-Hexahydrobenzo[*c*]thiophene 2,2-Dioxide (8). A solution of 26.1 g (0.24 mol) of diene **7** and 25 mL of methanol containing a trace of hydroquinone was placed in a hydrogenation bottle in an ice bath, and 20 mL of liquid SO_2 was added. The reaction was exothermic and was accompanied by the precipitation of pale green solid. After the bottle was sealed, it was allowed to stand overnight. Volatiles were then removed on a rotary evaporator, followed by evacuation at 0.1 mm. The remaining solid (36.8 g, 88%) was recrystallized from methanol: mp 91–93 °C (lit.[6] mp 94 °C).

3,8-Thionanedione 1,1-Dioxide (2). A 4-g (0.023 mol) sample of cycloadduct **8** in 50 mL of CH_2Cl_2 and 25 mL of methanol was held at −78 °C while a stream of ozone was bubbled through until the solution was light blue. Excess ozone was removed by blowing the solution, still at −78 °C, with nitrogen. The cold ozonide was then reduced with trimethyl phosphite (4.1 g, 0.03 mol). The

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(16) V. Mark, *Org. Synth.*, **46**, 42 (1966). While the corresponding phosphoric acid derivative is classed as a carcinogen, this compound requires only routine precautions for an irritant; specifically all operations should be conducted in a hood.

(17) A. C. Cope and E. Ciganek, *Org. Synth.*, **39**, 40 (1959).

(18) P. D. Bartlett, A. S. Wingrove, and R. Owyang, *J. Am. Chem. Soc.*, **90**, 6067 (1968).

mixture was allowed to warm to room temperature and its volume then reduced to half on a rotary evaporator. When chilled in a -78 °C bath, the solution deposited 4.2 g (91%) of fine white solid. Recrystallization from methanol gave pure **2**: mp 131–134 °C; IR (KBr) $\nu_{C=O}$ 1690, ν_{SO_2} 1320 and 1130 cm^{-1}. ^{1}H and ^{13}C NMR data are given in Table I. Anal. Calcd for $C_8H_{12}O_4S$: C, 47.04; H, 5.92; S, 15.70. Found: C, 46.91; H, 5.81; S, 15.67.

A bis(2,4-dinitrophenylhydrazone) precipitated instantly on mixing a hot solution of 0.8 g (0.004 mol) of 2,4-dinitrophenylhydrazine, 4 mL of concentrated H_2SO_4, and 6 mL of water with a solution of diketone **2** (0.4 g, 0.0020 mol) in 25 mL of ethanol. The difficultly soluble, bright orange solid, mp 204–206 °C, was analyzed directly.

Anal. Calcd for $C_{20}H_{20}N_8O_{10}S$: C, 42.55; H, 3.57; N, 19.85; S, 5.68. Found: C, 42.84; H, 3.53; N, 19.96; S, 5.58.

Crystal Data: $C_8H_{12}O_4S$ (**2**), mol wt 204.25; orthorhombic, a = 8.963 (4) Å, b = 15.403 (7) Å, c = 6.724 (3) Å, U = 928.3 Å^3, d_{measd}(flotation) = 1.45 g cm^{-3}, Z = 4, d_{calcd} = 1.461 g cm^{-3}, $F(000)$ = 432; Cu Kα radiation, λ = 1.5418 Å; absorption coefficient for Cu Kα radiation, μ = 28.9 cm^{-1}. Space group $P2_12_12_1$ (D_2^4) was uniquely established from the systematic absences $h00$ when $h \neq 2n$, $0k0$ when $k \neq 2n$, $00l$ when $l \neq 2n$.

Crystallographic Measurements. Preliminary unit cell parameters and space group information were obtained from oscillation and Weissenberg photographs taken with Cu Kα radiation and precession photographs taken with Mo Kα (λ 0.7107 Å) radiation. For intensity measurements a crystal of dimensions ca. 0.20 × 0.36 × 0.40 mm was oriented on an Enraf-Nonius CAD-3 automated diffractometer (Ni-filtered Cu Kα radiation). Refined unit cell dimensions were derived by least-squares treatment of the θ, χ, and ϕ angles for 40 reflections widely separated in reciprocal space. One octant of intensity data to θ = 67° was surveyed by means of the θ–2θ scanning procedure with scan widths $(0.90 + 0.40 \tan \theta)°$; stationary background measurements were recorded at each end of the scan range for half the scan duration. Instrument and crystal stability were monitored throughout by remeasuring the intensity of a reference reflection after each batch of 99 reflections; no significant variation was noted. From a total of 1002 independent intensity measurements only those 913 for which $I > 2.0\sigma(I)$ [$\sigma^2(I)$ = scan count + total background count] were corrected for the usual Lorentz and polarization effects. Absorption corrections, derived from the ϕ dependence of the intensity of the 0,12,0 reflection measured at χ = 90°, were also applied to these data prior to their use in the structure analysis and refinement.

Structure Analysis. The structure was solved with difficulty by direct methods by use of MULTAN.[19] A seven-atom sulfur-containing fragment, obtained from the E map computed by using the phase angle set which gave the highest figure of merit and lowest residual, was used to phase a subsequent F_o Fourier map (R[20] = 0.418) which yielded positions for the remaining nonhydrogen atoms. Full-matrix least-squares refinement of atomic positional and isotropic thermal parameters reduced R from 0.241 to 0.082, and, when allowance was made for anisotropic thermal motion, R decreased further to 0.063. Hydrogen atom positions were then obtained from a difference Fourier synthesis and their positional and isotropic thermal parameters were included as variables in the subsequent least-squares iterations. In addition, when the anomalous scattering corrections for sulfur were included in the structure factor calculations, R for the coordinates corresponding to those listed in Table II was significantly lower than for the mirror image and so all later refinement was based on this coordinate set. Following several further rounds of least-squares adjustment of positional and thermal parameters, the refinement converged at R = 0.032. A listing of observed and calculated structure amplitudes (Table VII) is available as supplementary material.

In all structure factor calculations the atomic scattering factor for hydrogen was taken from ref 21 and for carbon, oxygen, and sulfur from ref 22 with that of sulfur corrected for anomalous scattering effects.[12b] In the least-squares iterations, $\sum w\Delta^2$ ($\Delta = ||F_o| - |F_c||$) was minimized with weights, w, assigned according to the following scheme: $(w)^{1/2} = 1$ when $|F_o| < 6.5$ and $(w)^{1/2} = 6.5/|F_o|$ when $|F_o| > 6.5$. The adequacy of this scheme was demonstrated by the fact that $\langle w\Delta^2 \rangle$ showed no systematic dependence when analyzed in ranges of $|F_o|$.

Registry No. 2, 71138-48-2; 2 bis(DNP), 71138-49-3; *cis*-3, 610-09-3; *cis*-4, 71138-50-6; *cis*-5, 71138-51-7; *cis*-6, 71138-52-8; 7, 2819-48-9; 8, 55370-42-8.

Supplementary Material Available: Tables of anisotropic thermal parameters (Table IV), hydrogen atom parameters (Table V), and observed and calculated structure amplitudes (Table VII) and a packing diagram of molecules of **2** in the crystal (Figure 2) (9 pages). Ordering information is given on any current masthead page.

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(20) $R = \sum||F_o| - |F_c||/\sum|F_o|$.

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Synthesis of (+)-*cis*-1-Methoxy-4β-carbomethoxy-4a,5,8,8a-tetrahydroisochroman, a Synthon for the Preparation of Alkaloids and Iridoids

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Received February 12, 1979

A synthesis of (+)-*cis*-1β-methoxy-4β-carbomethoxy-4a,5,8,8a-tetrahydroisochroman (**3b**) is carried out in seven steps from furfuryl alcohol in 8–16% overall yield. Detailed analyses of the ^{1}H NMR spectra of two intermediates prepared during this synthesis, **5b** and 1α-OMe-**6b**, plus other chemical evidence reveal that a preliminary report[7] concerning the preparation of **3b** and **5b** contained an incorrect assignment of relative stereochemistry. The results of the present study enable a correction of one literature report[8] describing the synthesis of **5b**. The bicyclic compound **3b** represents a potentially useful synthon for the preparation of certain indole alkaloids and iridoids.

Our continuing interest in the biosynthesis and pharmacology of several naturally occurring indole alkaloids and cyclopentanomonoterpenoids (iridoids) that have antitumor activity led us to consider the preparation of synthons that would be useful for the total synthesis of such natural products. Although our immediate objectives are the synthesis of the algucons of 16,17-dihydrostrictosamide (**1**) and of 3,4-dihydrosecologanin (**2**), we also

0022-3263/79/1944-3500$01.00/0