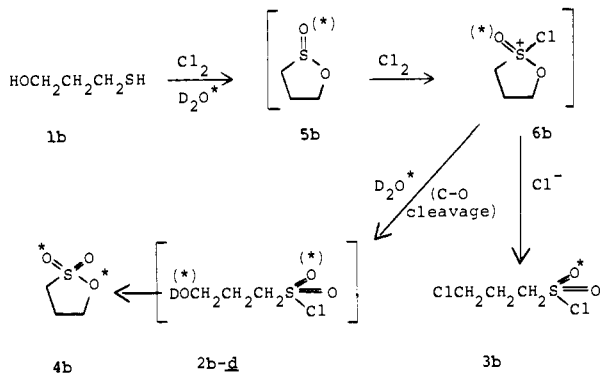
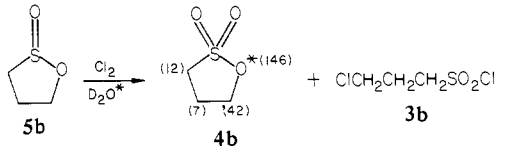
Scheme I



Similarly a 9-ppb shift in the C-1 signal in **3b** compared with the 18-ppb shift found for fully O-labeled[5] **3b** shows **3b** in the reaction product to have one heavy oxygen. The ^{17}O NMR spectrum[3] of natural abundance **4b** has signals at 175 and 146 ppm, assignable from their 2:1 ratio to the sulfonyl and endocyclic oxygens, respectively, while **3b** gives a single peak at 237 ppm; the product mixture had peaks at 146, 175, and 237 ppm in the ratio 2:2:1 thereby confirming the above labeling pattern and product composition. Scheme I gives a reaction pathway consistent with these observations.[6]

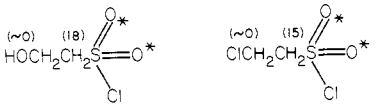
In accord with this picture, chlorination (in D_2O^*) of the sultine **5b** proceeded as follows:



the ^{18}O isotope effects in the ^{13}C NMR spectrum and the single ^{17}O signal (in parentheses, in ppb and ppm, respectively) establish the exclusively endocyclic labeling of **4b**, and the lack of both ^{18}O isotope shifts in the ^{13}C NMR spectrum and enhanced ^{17}O absorption at 237 ppm shows the absence of O label in the **3b**.

In excellent agreement with the notion that **6b** (Scheme I) is the precursor of both **3b** and **4b**, we found that starting with either the mercaptan **1b** or the sultine **5b** addition of NaCl increased the yield of **3b**. A plot of the ratio of **3b** to **4b** in the products vs. $[Cl^-]$ gave a straight line over the full range of chloride ion concentrations used (0.1-4 M); the reaction of **5b** gave essentially the same line[8] as that of **1b**.

In complete contrast to the reaction of **1b**, chlorination of 2-mercapto-1-ethanol (**1a**) proceeds without intramolecular oxygen migration, the products being **2a** (>95%) and a little **3a**, with the



labeling patterns shown deduced from the ^{18}O isotope shifts (in parentheses). We conclude that 2-hydroxyethanesulfonyl chloride (**2a**) is formed by a simple hydrolytic chlorination sequence without participation of the hydroxyl group (presumably because of strain in the four-membered ring counterpart of **5b**), and that the 2-chloroethanesulfonyl chloride arises by way of an *intermolecular* interaction of the reacting sulfur center and the alcohol function, e.g., via an acyclic sulfinic ester. This in turn suggests that the high-yield formation of **3a** by chlorination of **1a** plus a roughly equimolar amount of water,[9] which by its stoichiometry requires transfer of an oxygen from carbon to sulfur, also proceeds by an intermolecular process.

Acknowledgment. This work was supported by the Natural Sciences and Engineering Research Council of Canada.

Registry No. 1b, 19721-22-3; **5b**, 24308-28-9; ^{18}O, 14797-71-8; ^{17}O, 13968-48-4.

(5) The fully labeled samples were obtained from the chloromercaptan $Cl(CH_2)_nSH$ under conditions in which the only source of oxygen was D_2O^* (>95 atom % ^{18}O).

(6) Scheme I does not specify the origin of the sultine **5b**; the following gives the labeling shown and finds analogy for each step in the valuable pioneering studies of Douglass and co-workers.[7]

1b → $HO(CH_2)_3SCl$ → $HO(CH_2)_3SCl_3$ → $HO(CH_2)_3SOCl$ → **5b**

(7) (a) Douglass, I. B.; Farah, B. S.; Thomas, E. G. *J. Org. Chem.* **1961**, *26*, 1996-1999. (b) Douglass, I. B. *Ibid.* **1965**, *30*, 633-635.

(8) From **5b** the product ratio **3b**:**4b** = 1.01$[Cl^-]$ + 0.12; **3b**/**4b** from **1b** is given by 1.02$[Cl^-]$ + 0.06 with $r > 0.997$ in both cases.

(9) Gilbert, E. E. *Synthesis* **1969**, 3-10.

Perannulanes. A New Class of Fused Polycyclic Compounds

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Betweenanenes, by virtue of the crisscross arrangement of the two bridging chains, show highly attenuated olefinic reactivity.[1] The effect is most pronounced with the lower homologues (I, a = 10, b = 8; $a = b$ = 10) (Scheme I). These olefins survive even prolonged exposure to electrophiles such as peroxycarboxylic acids and dihalocarbenes.[2] As expected, double-bond reactivity is gradually restored with an increase in bridging chain length (e.g., I, a = 22, b = 10; a = 26, b = 10).[2]

For some time now we have been interested in preparing betweenanenes with functionalized bridges capable of transannular [2 + 1] cycloaddition to the encapsulated double bond. In the simplest case (Figure 1), a betweenanene carbene II could be expected to afford the addition products III or IV, depending upon the preferred geometry of the addition and the values of b and c. Likewise, the bicyclic carbene V of Z geometry could afford the isomeric products VI or VII. Extending the concept to transannular [2 + 2] and [2 + 2 + 2] cycloadditions of appropriate tricyclic dienes and tetracyclic trienes leads to the analogous polycyclic structures VIII and IX (Figure 2). We propose the name "perannulanes"[3] for the homologous series of polycyclics of which III-IX are members. Perannulanes are perceived as fully annulated cycloalkanes in which rings of varying size are fused to each side of a central ring. The prefix "tri, tetra, penta," etc. denotes the number of central ring sides and the bracketed numbers "a, b, c," etc. indicate the length of each bridging chain.

As a result of recent improvements in *trans*-cycloalkene synthetic methodology[4] we have been able to devise an efficient route to betweenanenes with features favorable to the transannular carbene addition depicted in eq 1 (figure 1). The sequence (Scheme II) employs S_N2' addition of a propargylmagnesium bromide-CuI complex to prepare the *trans*-cyclododecenylcarbinol **2** from the cyclododecylidene oxirane **1**.[4,5] As in previous cases, this addition was both stereoselective and regioselective. Addition of the same organocopper reagent to the phosphate derivative **3** afforded the bis(acetylene) **4**.[4] Hydroboration of this triisopropylsilyl-substituted acetylene with dicyclohexylborane followed

(1) Marshall, J. A.; Lewellyn, M. *J. Am. Chem. Soc.* **1977**, *99*, 3508-3510.

(2) Marshall, J. A. *Acc. Chem. Res.* **1980**, *13*, 213-218. Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Am. Chem. Soc.* **1979**, *101*, 147-151. Nakazaki, M., Yamamoto, K. *J. Synth. Org. Chem., Jpn.* **1981**, *39*, 624-632.

(3) "Per"—containing the largest possible or a relatively large portion of a (specific) element. "Annular"—relating to rings.

(4) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1983**, *105*, 3360-3362.

(5) Use of the ((trimethylsilyl)propargyl)magnesium bromide-CuI complex in this reaction led to appreciable allene product resulting from γ-substitution on the propargyl moiety. Cf.: Corey, E. J.; Ricker, C. *Tetrahedron Lett.* **1982**, *23*, 719-722.

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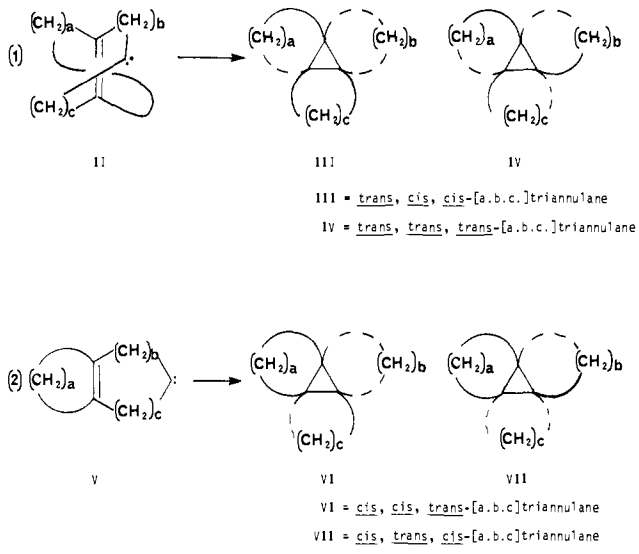


II III IV

III = trans, cis, cis-[a.b.c.]triannulane

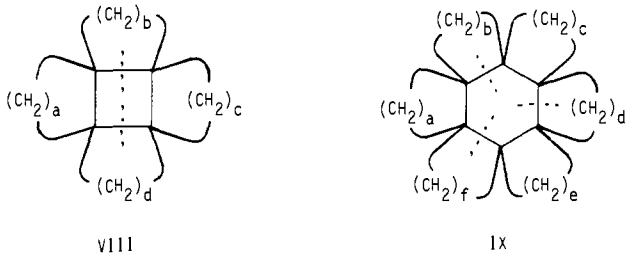
IV = trans, trans, trans-[a.b.c.]triannulane

V VI VII

VI = cis, cis, trans-[a.b.c]triannulane

VII = cis, trans, cis-[a.b.c]triannulane

Figure 1. Hypothetical routes to [*a.b.c*]triannulanes.



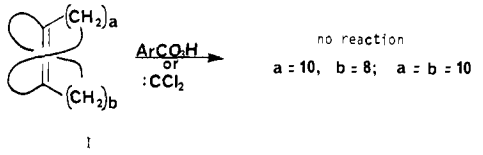
VIII IX

VIII = [a.b.c.d]tetraannulane

IX = [a.b.c.d.e.f]hexaannulane

Figure 2. Some perannulanes (dashed lines indicate possible bond disconnections).

Scheme I

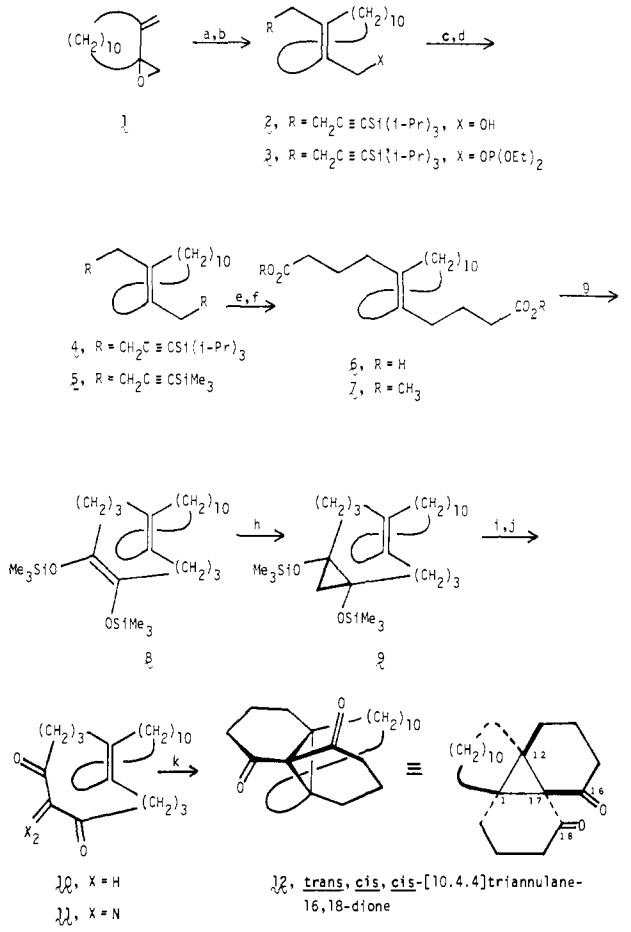


I

by oxidation led to a mixture of ketones and acids. The trimethylsilyl-substituted acetylene **5**,[5] however, was principally converted to diacid **6** by such treatment.

Acyloin cyclization of diester **7**, in the presence of trimethylsilyl chloride, gave the ene diol derivative **8**.[6] Cyclopropanation[7] and subsequent periodate cleavage[8] of the bis Me_3Si ether **9** yielded the 1,3-dione **10**, readily converted to the diazo derivative **11** by *p*-toluenesulfonyl azide.[9] Transannular cyclopropanation was effected through irradiation of diazo ketone **11** in benzene using benzophenone as a photosensitizer.[10] The [10.4.4]triannulanedione **12** was thereby obtained as a nicely crystalline solid: mp 109–110 °C; ^{13}C NMR 210.0, 47.0, 40.8, 40.3, 29.6, 28.3, 26.9, 24.5, 24.2, 24.1, and 22.6 ppm. Assuming retention of double-bond stereochemistry for the cycloaddition reaction, the cyclopropane product **12** could either possess the trans,cis,cis or the trans,trans,trans stereochemistry (cf. Figure 1, II → III/IV). While the latter possibility seems unlikely on steric grounds, the

Scheme II[a]



[a] (a) $(i\text{-Pr})_3SiC{\equiv}CCH_2MgBr$, CuI, THF, Me_2S, −78 to −20 °C; 79%. (b) $ClPO(OEt)_2$, C_5H_5N, −40 °C; 92%. (c) $(i\text{-Pr})_3SiC{\equiv}CCH_2MgBr$, CuI, DME, THF, −78 to −20 °C; 96%. (d) Bu_4NF, THF; *n*-BuLi, THF, −78 °C; Me_3SiCl; 80%. (e) $(C_6H_{11})_2BH{\cdot}THF$; H_2O_2, NaOH, MeOH; HCl. (f) CH_2N_2, Et_2O, EtOAc; 65%. (g) NaK, xylene, Me_3SiCl, reflux. (h) Et_2Zn, CH_2I_2, CH_3Ph, 80 °C. (i) $NaIO_4$, H_2O, THF; 40% overall. (j) *p*-TsN_3, Et_3N, MeCN. (k) Ph_2CO, $h\nu$, C_6H_6; 65%.

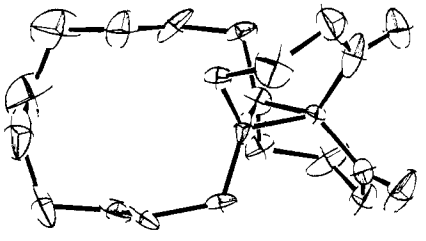


Figure 3. ORTEP drawing of *trans,cis,cis*-[10.4.4]triannulane-16,18-dione (**12**).

choice of the former as the correct structure was easily made through single-crystal X-ray analysis (Figure 3).[11]

The juxtaposition of quaternary centers in the triannulane **12** and derivatives thereof should foster interesting chemical behavior. We plan to examine such matters in due course.

Acknowledgment. Support for this work by the National Science Foundation through a research grant (CHE-8026013) is gratefully acknowledged.

Supplementary Material Available: Structural and physical data for Scheme I (3 pages). Ordering information is given on any current masthead page.

(6) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React.* **1976**, *23*, 259–403. See p 307.

(7) Ito, Y.; Saegusa, T. *J. Org. Chem.* **1977**, *42*, 2326–2327.

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(10) Jones, M.; Ando, W. *J. Am. Chem. Soc.* **1968**, *90*, 2200–2201.

(11) This analysis revealed the presence of at least two conformational isomers. The major conformer is shown in Figure 3. A detailed discussion of the crystal structure data will be presented in a full paper.

Stereocontrolled Synthesis of the C(1)–C(17) Half of Boromycin

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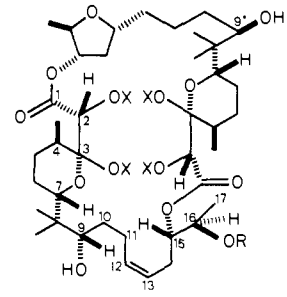
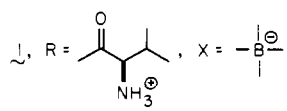
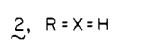
The ionophore boromycin (**1**)[1] consists of two stereochemically related halves linked head to tail to form a diolide, with a borate bridge spanning the macrocycle.[2] We recently described[3] the

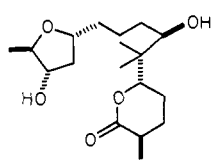




1, R = , X = $-B^{\ominus}$



2, R = X = H



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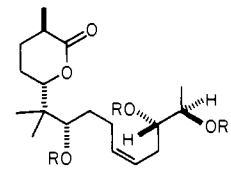
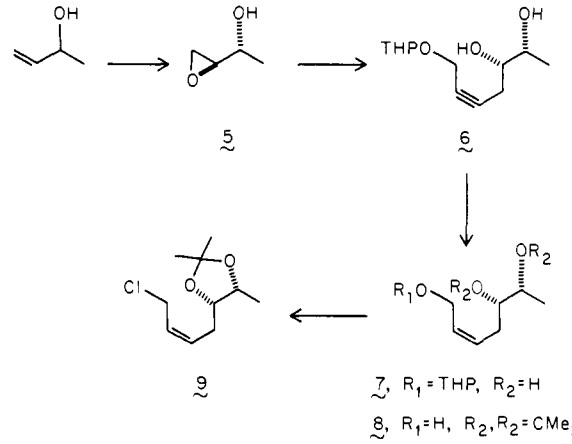


4, R = H

25, R = Ac

reconstitution of **1** from a degradation product **2**,[4] in which the macrodiolide nucleus was first converted to a borate and then selectively esterified with D-valine. In parallel with these efforts, we have pursued syntheses of the two halves of **2**[5] via a route that permits convergence with lactones **3** and **4** derived by further degradation of **2**.[2,3] Hanessian et al.[6] have independently reported chiral syntheses of these lactones, and recently, Corey et al.[7] announced the total synthesis of aplasmomycin,[8] a symmetrical macrocyclic borate structurally allied to **1**.

A synthesis of the chiral C(11)–C(17) segment of **2** was achieved from 3-buten-2-ol via enantioselective epoxidation with *tert*-butyl hydroperoxide in the presence of titanium tetraisopropoxide and diisopropyl D-(−)-tartrate.[9] The resulting epoxide **5**, which possessed the desired (2R,3S) configuration,[10] was alkylated with the tetrahydropyranyl ether of propargyl alcohol (*n*-BuLi, THF, −78 → 25 °C) to give **6** (91%). This acetylene was semihydrogenated (10% $Pd/BaSO_4$, quinoline, MeOH), affording cis olefin **7** (98%), and the latter was converted directly to **8** (91%) with 2,2-dimethoxypropane (*p*-TsOH, MeOH, C_6H_6). In preparation for coupling with the C(3)–C(10) segment, **8** was transformed to allylic chloride **9** (83%) with *N*-chlorosuccinimide and dimethyl sulfide.[11]



5 **6**

9

7, R_1 = THP, R_2 = H

8, R_1 = H, R_2,R_2 = CMe_2

Synthesis of the C(3)–C(10) moiety began from 3,3-dimethoxy-2,2-dimethylpropanol (**10**),[12] obtained via condensation of isobutyraldehyde with formaldehyde.[13] Oxidation of **10** (PCC) provided the malondialdehyde derivative **11** (66%, bp 55 °C (17 mm)), which was alkylated with the dianion[14] of tiglic acid (2.2 equiv of LDA, THF, −78 → 25 °C, 24 h) to give **12** (95%). This hydroxy acid was hydrogenated (94%, 10% Pd/C, EtOAc) and lactonized (DCC, DMAP) to yield **13** (80%) as a 40:60 mixture of cis/trans isomers.[15] Without separation, this mixture was taken to aldehyde **14** ($TiCl_4$, AcCl, CH_2Cl_2, 0 °C, 0.5 h)[16] and then to carboxylic acid **15** ($RuCl_3$, $NaIO_4$, CCl_4, CH_3CN, H_2O; 68% from **13**),[17] which, upon esterification (CH_2N_2), furnished **16** (96%). Treatment of **16** with (2*R*,3*R*)-(−)-butanediol (camphorsulfonic acid, C_6H_6) afforded the ortho ester **17**[18] in 84% yield as a mixture of four diastereomers, in which the trans/cis ratio was 3.7:1.[19] Condensation of this mixture with the *dianion*[20] of methyl phenyl sulfone (1.5 equiv, 3 equiv of *n*-BuLi, THF, 0 °C) gave a mixture of keto sulfones (92%), from which the desired diastereomer **18** (mp 96–98 °C) was obtained (35% from **16**) by HPLC on μPorasil.

Alkylation of the enolate of **18** (1.06 equiv of *n*-BuLi, Me_2SO–THF) with **9** in the presence of KI yielded **19** (97%) as a pair of diastereomers. The sulfonyl group was removed (Al/Hg,

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(4) Marsh, W.; Dunitz, J. D.; White, D. N. J. *Helv. Chim. Acta* **1974**, 57, 10.

(5) A portion of this work was communicated previously. See: White, J. D. "Abstracts of Papers", 179th National Meeting of the American Chemical Society, Houston, TX, March 24–28, 1980; American Chemical Society: Washington, DC, 1980; ORGN 48.

(6) (a) Hanessian, S.; Tyler, P. C.; Demailly, G.; Chapleur, Y. *J. Am. Chem. Soc.* **1981**, *103*, 6243. (b) Hanessian, S.; Delorme, D.; Tyler, P. C.; Demailly, G.; Chapleur, Y. *Can. J. Chem.* **1983**, *61*, 634.

(7) Corey, E. J.; Pan, B.-C.; Hua, D. H.; Deardorff, D. R. *J. Am. Chem. Soc.* **1982**, *104*, 6816. Corey, E. J.; Hua, D. H.; Pan, B.-C.; Seitz, S. P. *Ibid.* **1982**, *104*, 6818.

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(9) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

(10) It was established by an independent synthesis of **5** that epoxidation had taken place in 91% enantiomeric excess. See: White, J. D.; Sheldon, B. G.; Kang, M.-c. *Tetrahedron Lett.*, in press.

(11) Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339.

(12) Spath, E.; Pallan-Raschik, L. *Monatsh. Chem.* **1948**, *79*, 447.

(13) Hattori, S.; Tokizawa, M. Japan Pat. 21 687, 1970; *Chem. Abstr.* **1970**, *73*, 87460*d*.

(14) Katzenellenbogen, J. A.; Crumrine, A. L. *J. Am. Chem. Soc.* **1976**, *98*, 4925.

(15) Treatment of this mixture with LDA–THF gave an equilibrium composition of 80:20 in favor of *trans*-**13**.

(16) Berkowitz, W. F.; Choudhry, S. C.; Hrabie, J. A. *J. Org. Chem.* **1982**, *47*, 824.

(17) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

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(20) Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397.

0002-7863/83/1505-6517$01.50/0