rotamer of the methylbenzyl group places the phenyl ring in a shielding position over the methylene protons in **5** but not in **6**. On this basis, structure **5** was assigned to the major isomer and **6** to the minor one. This assignment was confirmed by an X-ray crystallographic analysis of **5**. *To our knowledge, this represents the first example where the preference of the nitrone oxygen to add to the oxygen-bearing carbon of enol ethers or esters has been reversed.*[6]

Transformation of the chiral intermediate **5** to the amino sugars was carried out first by reduction of the N-O bond using zinc in aqueous acetic acid to give lactone **7a** [89%, mp 58-60 °C, $[\alpha]^{25}_D$ -17.11° (*c* 0.900, CH_3OH)] and followed by *N*-carbomethoxylation to **7b** [54%, mp 124.5 °C, $[\alpha]^{25}_D$ -82.10° (*c* 1.0378, $CHCl_3$)] with methyl chloroformate in aqueous tetrahydrofuran and sodium carbonate (Scheme II). Reduction with diisobutylaluminum hydride produced lactol **7c** which on stirring with Amberlite CG 120 resin (H^+ form) in methanol generated a 4:1 mixture of pyranose anomers (89% for the two steps). For simplification of the characterization of further intermediates, the major anomer **8a** [$[\alpha]^{25}_D$ -106.10° (*c* 0.9020, $CHCl_3$)] was isolated by chromatography. Debenzylation of **8a** to **8b** [75%, mp 143 °C, $[\alpha]^{25}_D$ -162.64° (*c* 0.7071, $CHCl_3$)] was accomplished with sodium in liquid ammonia. Basic hydrolysis then provided L-α-methyl acosaminide (**8c**) identical with authentic material by NMR and mass spectral properties as well as TLC characteristics and mixed melting point [$[\alpha]^{25}_D$ -140.4° (*c* 0.225, CH_3OH); lit.[2] -145.1° (*c* 0.61, CH_3OH)].[12] The hydrolysis of methyl acosaminide has been reported previously.[2]

The synthesis of L-α-methyl daunosaminide (**9b**) was completed by inversion of the C4 hydroxyl group of a methyl acosaminide derivative.[13] The mesylate **8d** [69% from **8b**, mp 141 °C, $[\alpha]^{25}_D$ -109.50° (*c* 0.9717, $CHCl_3$)] was exposed to aqueous dimethylformamide (bath temperature 105 °C) to give the C4 α-hydroxy carbamate **9a** [50% unoptimized, mp 90 °C, $[\alpha]^{25}_D$ -166.71° (*c* 0.3983, $CHCl_3$)] which was then hydrolyzed with aqueous barium hydroxide to give L-α-methyl daunosaminide **9b** (46% unoptimized) which was identical with authentic material by NMR, TLC, and mixed melting point.[12] The hydrolysis to daunosamine has been carried out previously.[2]

An alternate, more direct route to L-methyl acosaminide from the initial cycloadduct **5** was also investigated. Reduction of **5** with diisobutylaluminum hydride in tetrahydrofuran (-78 °C) gave lactols **10a** as a 2:1 mixture which on treatment with Amberlite CG 120 (H^+ form) in methanol gave a 3:1 mixture of acetals **10b** (mp 105 °C, 80% for the two steps). Cleavage of both the N-O and *N*-benzyl bonds in **10b** was carried out by catalytic hydrogenation (50 psi, 5% Pd/C, CH_3OH) to give a mixture of furanose anomers **11** (94%)[14] which on exposure to Amberlite CG 120 (H^+ form) in methanol isomerized to the pyranose anomers **12** (90%). For the purpose of comparison, this mixture was converted to the *N*-trifluoroacetyl derivatives and separated by silica gel chromatography (hexane/ethyl acetate 2:1). The major anomer was found to be identical with an authentic sample of **8e** by NMR, TLC, and mixed melting point [$[\alpha]^{25}_D$ -122° (*c* 0.56, $CHCl_3$); lit.[2] -123° (*c* 0.5, $CHCl_3$)].[15,16] Since anomeric mixtures at this stage are of no consequence for the linking of the sugars to the anthracyclinones, the above is a highly efficient route to acosamine (**2b**).

We are presently examining intramolecular [3 + 2] cycloadditions of chiral nitrones related to **4** in order to gain some insight on the source and the generality of the observed enantioselectivity as well as to develop other applications for such chiral cycloadducts.

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(11) **5**: NMR ($CDCl_3$, 100 MHz) δ 7.24 (s, 5 H), 4.52 (dd, *J* = 5, 8 Hz, 1 H), 4.02 (dq, *J* = 5, 7 Hz, 1 H) 3.69 (q, *J* = 7 Hz, 1 H, 3.44 (dt, *J* = 2, 8 Hz, 1 H), 1.98 (AB, J_{gem} = 18 Hz, J_{vic} = 8 Hz, 1 H), 1.69 (AB, J_{gem} = 18 Hz, J_{vic} = 2 Hz, 1 H), 1.52 (d, *J* = 7 Hz, 3 H), 1.37 (d, *J* = 7 Hz, 3 H); IR ($CHCl_3$) 1782 cm^{-1}; mp 138.5 °C; $[\alpha]^{25}_D$ +17.16 (*c* 0.6876, $CHCl_3$). **6**: NMR ($CDCl_3$, 100 MHz) δ 7.25 (s, 5 H), 4.56 (dd, *J* = 4, 7 Hz, 1 H), 3.99 (dq, *J* = 4, 7 Hz, 1 H), 3.85 (q, *J* = 7 Hz, 1 H), 3.52 (dt, *J* = 7,6 Hz, 1 H), 2.60 (d, *J* = 6 Hz, 2 H), 1.40 (d, *J* = 7 Hz, 3 H), 1.28 (d, *J* = 7 Hz, 3 H); IR ($CHCl_3$) 1785 cm^{-1}; mp 133 °C; $[\alpha]^{25}_D$ -54.34° (*c* 0.8303, $CHCl_3$).

(12) Authentic methyl 3-amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**8c**) and methyl 3-amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranoside (**9b**) were prepared by Dr. G. Grethe.

(13) For a similar inversion process, see: Marsh, J. P.; Mosher, C. W.; Acton, E. M.; Goodman, L. *J. Chem. Soc., Chem. Commun.* **1967**, 973.

(14) The major isomer crystallized from ether; mp 59-62 °C; $[\alpha]^{25}_D$ -120.82° (*c* 0.9982, CH_3OH).

(15) The minor isomer was converted to the major isomer by exposure to Amberlite CG 120 (H^+ form) in methanol.

(16) We are grateful to F. Arcamone for sending an authentic sample of methyl 2,3,6-trideoxy-3-trifluoroacetamido-α-L-*arabino*-hexopyranoside (**8e**).

Tetrakis(trifluoromethyl)semibullvalenes. Could Cope Degeneration Be Frozen Out?

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There are many reports concerning semibullvalene, an interesting "fluxional" cage compound.[1] Hoffmann et al.[2] and Dewar et al.[3] examined the effects of substituents theoretically and forecasted some substituents to favor one tautomer or lower the activation energy of the "fluxional" tautomerism. However, according to Hoffmann, the substituent effect of a trifluoromethyl group was not easily classified and remained to be worked out.[2] Therefore, we tried to synthesize trifluoromethylated semibullvalenes and have obtained two tetrakis(trifluoromethyl)-semibullvalenes from tetrakis(trifluoromethyl)cyclooctatetraene. Interestingly, one was nearly limited to one isomer, while the other was fluctuating very rapidly between two tautomers even at -90 °C or seemed to be frozen out in the transition state of the tautomerism.

As mentioned in the previous paper,[4] we synthesized 1,2,3,8-tetrakis(trifluoromethyl)cyclooctatetraene (**1**). Photolysis of **1** mainly gave [2 + 2] reaction products.[4,5] Therefore, we tried a [4a + 2a] intramolecular cycloaddition reaction of **1** to semibullvalene.[6] The thermolysis of the solution of **1** in pentane at 170-180 °C for 6 days gave three isomers, which were separated by preparative GLC.[7] One isomer was identified as 1,2,7,8-tetrakis(trifluoromethyl)bicyclo[4.2.0]octa-2,4,7-triene (**2**) by comparison of its spectral data with those of the authentic sample.[4] The other two isomers (**3** and **4**)[8] were found to be tetrakis(tri-

(1) (a) H. E. Zimmerman and G. L. Grunewald, *J. Am. Chem. Soc.*, **88**, 183 (1966); (b) L. T. Scott and M. Jones, Jr., *Chem. Rev.*, **72**, 181 (1972); (c) H. E. Zimmerman, R. W. Binkley, R. S. Givens, G. L. Grunewald, and M. A. Sherwin, *J. Am. Chem. Soc.*, **91**, 3316 (1969); (d) A. K. Cheng, F. A. L. Anet, J. Mioduski, and J. Meinwald, *ibid.*, **96**, 2887 (1974).

(2) R. Hoffmann and W. D. Stohrer, *J. Am. Chem. Soc.*, **93**, 6941 (1971).

(3) M. J. S. Dewar and D. H. Lo, *J. Am. Chem. Soc.*, **93**, 7201 (1971).

(4) Y. Kobayashi, A. Ando, K. Kawada and I. Kumadaki, *J. Chem. Soc., Chem. Commun.*, submitted for publication.

(5) Photolysis of the unsubstituted cyclooctatetraene to semibullvalene is well-known. See N. J. Turro, J.-M. Liu, H. E. Zimmerman, and R. E. Factor, *J. Org. Chem.*, **45**, 3511 (1980), and references therein.

(6) Concerning thermal isomerization of cyclooctatetraenes to semibullvalenes, see R. Criegee, and R. Askani, *Angew. Chem., Int. Ed. Engl.* **7**, 537 (1968); H. E. Zimmerman, and H. Iwamura, *J. Am. Chem. Soc.*, **92**, 2015 (1970). A theoretical aspect was given by H. Iwamura, *Tetrahedron Lett.*, 369 (1973).

(7) The preparative GLC Ohkura Gas Chromatograph (Model 701) (3 m × 3 mm in 10% SE 30 on 60/80 Uniport B, 60 °C). Order of elution is **4** (18%), **2** (trace), **1** (10%), and **3** (51%).

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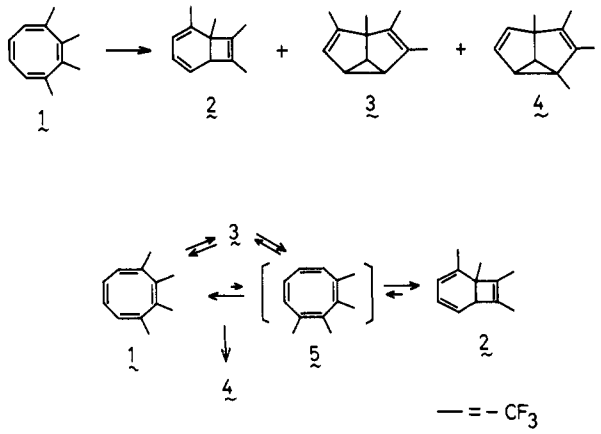
Chart I



fluoromethyl)semibullvalenes. Compound **3** showed four multiplets at 6.44, 3.74, 3.42, and 3.30 ppm in ^{1}H NMR spectra. The last peak was assigned to be a methine proton at C-8 by the decoupling experiments. Chemical shifts and coupling pattern of these protons were quite similar to those of benzosemibullvalene.[9]

Next, we examined the variable-temperature ^{1}H NMR spectra from −90 to +120 °C, but any essential changes were not observed. Therefore, **3** was limited to one tautomer. Its ^{19}F and ^{13}C NMR spectra were consistent with this fixed structure. This might be due to the steric repulsion between the two trifluoromethyl groups on the 4 and 6 carbons, which inhibited its tautomerism. Compound **4** contrasted sharply with **3**. In the ^{1}H NMR spectra, one proton was in the olefinic region and another was in the methine region, while the other two were in the middle of these two regions. Therefore, **4** seemed to be in a very rapid Cope degeneration. However, its variable-temperature ^{1}H NMR spectra did not show any significant changes in the chemical shift and coupling pattern from −90 to 120 °C;[10] namely, **4** seemed to be a frozen-out intermediate of the Cope degeneration. Its ^{19}F and ^{13}C NMR spectra were consistent with this degenerate structure. This result shows a very interesting effect of trifluoromethyl groups. This might be due to the interaction between two allyl systems, one of which is substituted with three electronegative trifluoromethyl groups and the other is not.

Thermolysis of **3** at 170–180 °C gave a mixture of **1**, **2**, and **4**, which were ultimately converted to **4** on a prolonged heating, while the ratio of **1** and **2** was constant throughout the reaction. These results might be explained reasonably by the equilibrium shown in Chart I. Thus, **1** was in a thermal equilibrium with the bond-shift isomer **5**, which cyclized rapidly to **2**. Compound **1** and/or **5** were in a equilibrium with **3** and isomerized to the most stable isomer **4** among these compounds. The comparison of molecular models suggests that repulsion between the trifluoromethyl groups on 4 and 6 positions in **3** may explain the higher stability of **4**. However, this should not be the only reason for this stability, since prolonged thermolysis of **4** did not give the cyclooctatetraene **1** at all. Therefore, this stability might be gained partially by the degenerate structure.

(8) 3,4,5,6-Tetrakis(trifluoromethyl)tricyclo[3.3.0.0^{2,8}]octa-3,6-diene (**3**): colorless oil; IR (CCl_4) 1635, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.44 (7-H, br s), 3.74 (2-H, dd, $J_{1,2} = J_{2,8} = 6$ Hz), 3.42 (1-H, dd, $J_{1,2} = J_{1,8} = 6$ Hz), 3.3 (8-H, m); ^{19}F NMR ($CDCl_3$) δ (upward from $C_6H_5CF_3$) −7.92 (4-CF_3, m), −3.92 (6-CF_3, sept), −1.52 (3-CF_3, q), 5.6 (5-CF_3; qq); ^{13}C NMR ($CDCl_3$) δ 137.4, 136.3, 135.8 (d), 134.5, 122.6 (q), 120.7 (q), 119.8 (q), 70.6 (t), 55.1 (d), 40.2 (d), 39.5 (d); *m/e* 376 (M^+). 2,3,4,5-Tetrakis(trifluoromethyl)-tricyclo[3.3.0.0^{2,8}]octa-3,6-diene (**4**): colorless oil; IR (CCl_4) 1640, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.85 (7-H, dd, $J_{6,7} = J_{7,8} = 4$ Hz), 5.33 (6-H, d, $J_{6,7} = 4$ Hz), 4.75 (8-H, dd, $J_{1,8} = J_{7,8} = 4$ Hz), 3.78 (1-H, d, $J_{1,8} = 4$ Hz), ^{19}F NMR ($CDCl_3$) δ −4.8 (4-CF_3, sept), −3.2 (3-CF_3, sept), −2.6 (2-CF_3, q), 4.2 (5-CF_3, q); ^{13}C NMR ($CDCl_3$) δ 127.0 (d), 122.7 (q), 121.9 (q), 120.7 (q), 119.3 (q), 104.3 (q), 98.5 (d), 88.4 (q), 83.4 (d), 66.0 (q), 52.9 (d); *m/e* 376 (M^+).

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(10) At the temperature below −90 °C, compounds **3** and **4** crystallized from the solution. We could not observe their NMR spectra below this temperature.

Ethylene Glycol from Synthesis Gas via Ruthenium Melt Catalysis

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The preparation of ethylene glycol directly from synthesis gas (eq 1) via homogeneous rhodium,[1] ruthenium,[2] and cobalt[3] ca-

$$2CO + 3H_2 \rightarrow (CH_2OH)_2$$

$$\Delta G_{500} = +15.8 \text{ kcal/mol}, \log K_p = -6.9 \qquad (1)$$

talysis has generally been limited by the high pressures necessary to effect reaction[4] and the modest turnover frequencies.[1,5] The problem of high pressure can be partially overcome through the intermediate formation of vicinal glycol esters,[6-8] such as ethylene glycol diacetate (eq 2), where thermodynamic parameters are more

$$2CO + 3H_2 + 2HOAc \rightarrow (CH_2OAc)_2 + 2H_2O$$

$$\Delta G_{500} = +4.7 \text{ kcal/mol}, \log K_p = -2.0 \qquad (2)$$

favorable.[8] In this paper we disclose a unique, highly active catalyst system for the direct synthesis of ethylene glycol (eq 1) involving ruthenium "melt" catalysis,[9] where the ruthenium source, such as ruthenium(IV) oxide or ruthenium(III) acetylacetonate, is dispersed in a molten quaternary phosphonium or ammonium salt such as tetrabutylphosphonium bromide.

While it is preferable that the ruthenium source and quaternary group 5B salt be solids at ambient temperatures, the melting point of the salt must lie well below the temperature necessary to effect CO hydrogenation[9] (ca. 220 °C). Under typical reaction temperature/pressure conditions then, the quaternary salt provides a highly polar, fluid medium for solubilization of the ruthenium active catalyst (vide infra) and effecting the desired conversion of synthesis gas to ethylene glycol. Alkanols plus diol are the major products. Data in Table I illustrate the preparation of ethylene glycol, together with glycol monoalkyl ethers and C_1–C_2 alkanols from CO/H_2 for a variety of ruthenium catalyst precursors and quaternary Group 5B salts.

The important features of this catalysis are the following: (a) The productivity of the melt catalysts—liquid weight gains[10] routinely exceed 100 wt% (see Table I, column 10) and turnover frequencies may surpass 7.8×10^{-3} s^{-1} at 220 °C (expt 16). (b) Glycol/alkanol weight ratios up to 1/1.65 have been noted, where ethylene glycol plus its monoalkyl ethers constitute >30 wt% of the liquid organic product. (c) Both alkanol and diol products may be readily isolated, by fractional distillation of the crude liquid

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(10) Liquid weight gains, defined as (total liquid organic + aqueous products)/(total ruthenium catalyst + quaternary salt charged) × 100.

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