In summary, we have provided evidence for unique remote kinetic deuterium isotope effects of considerable variation in solvolytic systems. These values represent the largest and most remote secondary kinetic isotope effects reported to date. The unexpectedly large effects of 1.32 in the case of butadiynyl system **5** may involve a primary component whereas the expected inverse effects in 97% TFE are consistent with a rehybridization at the terminal center. The larger magnitude of remote isotope effects in these vinylic systems compared to saturated substrates is due to the greater need for stabilization of vinyl cations compared to saturated carbocations.[4]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 298 spectrometer. Deuterium content was determined on a Varian MAT GC-mass spectrometer. Solvents and reagents were purified and dried by standard procedures immediately prior to use. Vinyl triflates **3H**[8] and **5H**[9] were prepared and characterized as previously described.

Vinyl triflate 3D was prepared from the corresponding (trimethylsilyl)vinyl triflate (4) in a manner similar to the nondeuterated analogue.[3,8] This procedure gave **3D** as a colorless oil with a deuterium content of 96.2% d_1 (as determined by mass spectrometry): IR (neat) 2582 (C—D), 1977 cm^{-1} (C=C).

Vinyl triflate 5D was prepared from triflate 6 by following the same procedure as described for the preparation of triflate **3D**. It was obtained (200 mg; 60.3%) as a colorless oil with a deuterium content of 91.6% d_1 (as determined by mass spectrometry): IR (neat) 2585 (C—D), 1980 cm^{-1} (C=C).

Kinetic Studies. Solvents were prepared by weight from conductivity water (Millipore Systems) and appropriate organic solvents. Conductivity measurements were performed in sealed, paired cells by using a Hewlett-Packard Model 4274A LCR bridge, interfaced with a Hewlett-Packard Model 3497A multiplexer and a Hewlett-Packard Model 9826 BASIC microcomputer. From 1 to 10 μL (in-cell concentration was ca. 2×10^{-4} M) of a pentane solution of the triflate was utilized in the appropriate solvent buffered with 2,6-di*tert*-butylpyridine.

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Registry No. (**3H**), 84836-44-2; (**3D**), 98482-61-2; (**5H**), 79140-87-7; (**5D**), 98482-62-3; D_2, 7782-39-0.

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Facile Synthesis of the Four 3-Aminocyclopentane-1,2-diol Stereoisomers

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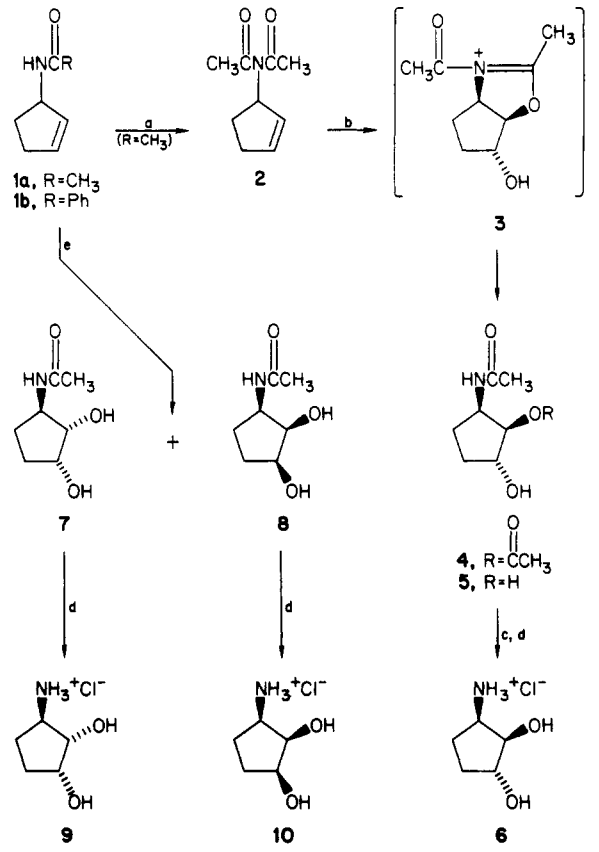
The 3-amino 1,2-diol functionality in five- and six-membered ring compounds occurs in many biologically active natural products, hence convenient synthetic routes to these compounds are desirable. For instance, the 3-amino 1,2-diol cyclopentyl function is not only present in both the parent[1] and reduced forms of nucleoside Q[2] but also has been used in the synthesis of nucleosides aristeromycin and neplanocin A.[3] Other examples of the occurrence of 3-amino 1,2-diol carbocyclic functionality are the aminocylitol antibiotics[4] such as 2-deoxyfortamine[5] and fortimicin aglycon[6] as well as the amino sugar antibiotics halacosamine[7] and garosaminide.[8]

Since none of the diastereomers of 3-aminocyclopentane-1,2-diol have been previously reported, we have developed convenient synthetic routes to all four isomers.

The synthesis of the first stereoisomer, (1α,2β,3β)-3-aminocyclopentane 1,2-diol (**6**) (Scheme I), was approached via a novel intramolecular rearrangement. Conventional routes for the synthesis of **6**, including the hydrolysis of the epoxide **12**,[9] would require forcing conditions in polar solvents making the isolation and purification of **6** difficult.[10]

A synthesis in which the nitrogen on 3-acetamidocyclopentene (**1a**) controls the regio- and stereochemistry of the trans diol to be formed was envisioned as a con-

Scheme I[a]



[a] (a) CH_3COCl, poly(4-vinylpyridine); (b) CF_3CO_3H; (c) K_2CO_3, MeOH; (d) $H_3O^+Cl^-$; (e) OsO_4, *N*-methylmorpholine *N*-oxide.

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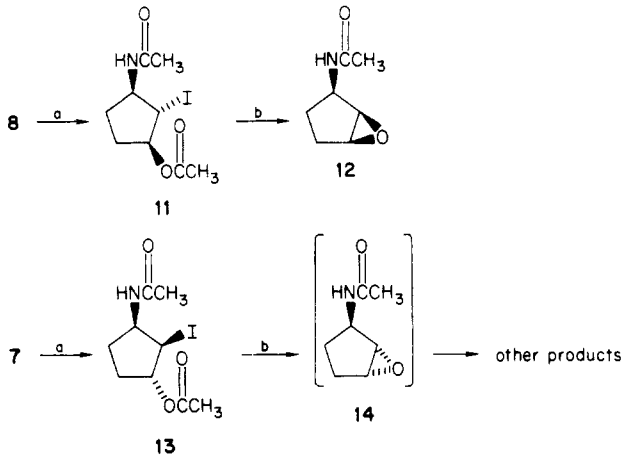
Scheme II[a]



[a] (a) $(CH_3)_2C(COCl)OCOCH_3$, NaI, CH_3CN; (b) NaOH, H_2O.

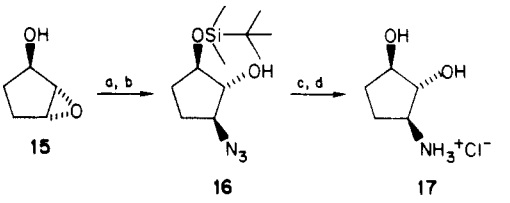
venient route based on the following two observations. Firstly, oxidation of 3-benzamidocyclopentene (**1b**) with *m*-chloroperbenzoic acid has been reported to yield both 3% of the *trans*-hydroxyoxazoline via β face oxidation as well as the cis epoxide in 90% yield, the product of allylic amide hydrogen bonding.[9] Secondly, imides also yield *N*-acyloxazolines via intramolecular O-alkylations by neighboring alkyl halides.[11] Thus it was postulated that peracid oxidation of the imide (**2**) derivative of **1a** would take place at the less hindered β face as allylic amide hydrogen bonding is no longer possible. The intermediate would then form the *trans*-hydroxy-*N*-acyloxazoline salt **3** via an intramolecular imide rearrangement. Workup of the reaction followed by mild hydrolysis would yield the desired amino diol **6**.

The imide **2** was prepared by treatment of 3-acetamidocyclopentene (**1a**) with acetyl chloride and poly(vinylpyridine) in benzene, followed by simple filtration and distillation. Subsequent reaction of **2** with peroxytrifluoroacetic acid in dichloromethane followed by chromatography yielded the bis-protected diol **4** in 39% yield. Selective deprotection of **4** to the amido diol **5** was readily accomplished by reaction with potassium carbonate in methanol. Acid treatment gave the desired amino diol **6** as the hydrochloride salt.

The amino diols **9** and **10** were prepared by reaction of **1a** with osmium tetraoxide and morpholine *N*-oxide.[12] The reaction yielded a mixture of stereoisomers **7** and **8** which were separated by flash chromatography. The ratio of the stereoisomers **7** to **8** was dependent on both temperature and concentration of osmium tetraoxide. Higher temperature and concentration increased the ratio of the amido cis diols **8** to **7** from 1:5 to 4:5 and the overall yield from 40% to 73%. Thus it was possible to maximize the isolation of the desired diol by careful control of the reaction conditions.

The stereochemistry of the amido cis diols **7** and **8** was demonstrated by treating the diols with α-acetoxyisobutyl iodide and base. These reagents have been shown to stereospecifically convert cis diols to their corresponding epoxides with retention of configuration.[13] Thus (1β,2β,3β)-amido cis diol **8** on reaction with α-acetoxyisobutyl iodide formed the intermediate acyl iodide **11** (Scheme II), which on treatment with base gave the known epoxide **12**[9] in 78% yield. This confirmed the stereochemistry of diol **8** as being all cis. Similar treatment of the (1β,2α,3α)-amido cis diol **7**, gave a mixture of compounds, but without any detectable quantities of epoxide **12**. The presumed product of this reaction, epoxide **14**, is known to be unstable and readily decomposes.[9] Thus the stereochemistry of the amido cis diol **7** was indicated to be trans. Acid hydrolysis of the amides **7** and **8** yielded the desired amino cis diols **9** and **10** in good yield.

Scheme III[a]



[a] (a) $(CH_3)_3CSi(CH_3)_2Cl$, 4-(dimethylamino)pyridine; (b) NaN_3, NH_4Cl, H_2O; (c) H_2, 10% Pd/C; (d) $H_3O^+Cl^-$.

The fourth amino diol **17** (Scheme III) was prepared by a regio- and stereospecific epoxide opening which was confirmed by ^1H NMR. Silylation of the readily available hydroxy epoxide **15**,[14] followed by reaction with azide and ammonium chloride, gave the azido alcohol **16**. The use of the *tert*-butyldimethylsilyl group avoided the diastereomer problem previously observed with a similar α-hydroxy epoxide.[15] Hydrogenolysis and mild acid hydrolysis of the crude azido alcohol **16** yielded the amino diol **17** by direct crystallization in satisfactory yield.

The regiochemistry of amino diol **17** was demonstrated by 300-MHz ^1H NMR spectroscopy using a combination of homonuclear decoupling and D_2O exchange. Thus the ^1H NMR spectrum of **17** consists of broad singlets at δ 8.23 (3 H, NH_3), δ 5.47 (1 H, OH), and δ 5.46 (1 H, OH) and two multiplets at δ 3.74 (2 H, C1–H, C2–H) and δ 3.08 (1 H, C3–H). Homonuclear decoupling of the individual OH resonances alters the signal at δ 3.74 only, verifying the assignment of the methine protons. Addition of D_2O separates the signal at δ 3.74 (C1–H, C2–H) to two distinct signals at δ_A 3.81 (1 H) and δ_B 3.74 (1 H). In addition, the third methine signal is also shifted slightly downfield to δ_C 3.15. The signals at δ_A and δ_C appear as broad quartets while the signal at δ_B appears as a triplet. Therefore δ_A was assigned to the methine proton C1, δ_B to C2, and δ_C to C3. Irradiation of δ_A or δ_C caused δ_B to collapse to a doublet while irradiation of δ_B caused both δ_A and δ_C to collapse to triplets, confirming the amino diol's regiochemistry (see Experimental Section).

All four amino diols were found to be easily handled as their hydrochloride salts. They are stable, nonhygroscopic compounds with very high water solubility.

In conclusion, all four stereoisomers of 3-aminocyclopentane-1,2-diols were synthesized via three reaction sequences, such that the pure isomers of unambiguous stereochemistry were obtained. The first route involved the use of a novel regio- and stereospecific rearrangement which could have general application for the stereospecific conversion of allylic amines to (1α,2β,3β)-3-amino 1,2-diols. The other three stereoisomers were synthesized by a stereospecific epoxide opening or by variation of reaction conditions during an osmium tetraoxide oxidation. The

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application of this methodology to antibiotic chemistry and the synthesis of biologically active compounds will be reported elsewhere.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 727B spectrophotometer, and band positions were calibrated by using polystyrene. Proton magnetic resonance (^{1}H NMR) spectra were recorded on Varian EM360, Perkin-Elmer R-32, and Varian XL-300 spectrometers. Chemical shifts are reported in δ in parts per million (ppm) downfield from tetramethylsilane as an internal standard. Mass spectra were obtained on a Finnigan 4000 gas chromatograph–mass spectrometer. For the chromatographic separations Merck silica gel 60 (0.062–0.0200 mm) was used.

***N*-(2-Cyclopenten-1-yl)-*N*-acetamidoacetamide (2).** A slurry of polymeric 4-vinylpyridine (60 g) was heated in benzene (250 mL) and stirred under reflux, and the water was separated and collected. The slurry was then cooled to 25 °C, and 3-acetamidocyclopentene (**1a**)[9] (18 g, 0.128 mol), acetyl chloride (25 g, 0.32 mol), and 4-(dimethylamino)pyridine (1 g) were added. The reaction was then heated and stirred under reflux for 3 h. The reaction was then cooled to 25 °C and filtered. The filtrate was evaporated to a residue which on distillation at 80 °C (0.1 mm) yielded **2** (17.9 g, 84%) as a colorless oil: IR (neat) 3060 and 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.8 and 5.6 (2 H, m), 2.8–1.6 (4 H, m), 2.5 (6 H, s); MS (CI), *m/e* 168 (M + 1), 140, 120, and 102 (base).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.64; H, 7.84; N, 8.38. Found: C, 64.75; H, 7.94; N, 7.92.

((1β,2β,3α)-2,3-Dihydroxycyclopentyl)acetamide (5). Trifluoroacetic acid (10 mL) and trifluoroacetic anhydride (12.5 g, 0.0595 mol) were mixed under an atmosphere of N_2 and cooled to 0 °C. A 90% H_2O_2 solution (2.3 mL, 0.0595 mol) was added, and the solution was stirred at 0 °C for 0.5 h. *N*-(2-Cyclopenten-1-yl)-*N*-acetamidoacetamide (**2**) (10 g, 0.0595 mol) in dichloromethane (250 mL) was added over 0.5 h and stirred under reflux for 0.5 h. The resulting solution was cooled to room temperature, and any excess peroxide decomposed by addition of 10% palladium on carbon (1 g). The resulting mixture was flash chromatographed using chloroform and acetone (9:1) to yield **4** (4.2 g, 39%) as an unstable oil: IR (neat) 3400, 1700, and 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.2 (1 H, exchangeable), 4.8 (1 H, m), 4.5 (1 H, m), 4.0 (1 H, m), 3.8 (1 H, exchangeable), 2.3–1.2 (4 H, m), 2.1 (3 H, s), 1.9 (3 H, s); MS (CI), *m/e* 202 (M + 1), 184 (base), 169, 142, 124, 100 (base), 82.

Compound **4** (4.0 g, 0.02 mol) was added to a slurry of methanol (100 mL) and potassium carbonate (10 g) and stirred at room temperature for 16 h. The resulting solution was filtered, and the filtrate was evaporated to a residue. On standing, the oil crystallized yielding **5** (3.2 g, 100%) as a white solid, mp 38–40 °C: IR (Nujol) 3300 and 1625 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 7.5 (1 H, exchangable), 3.9 (1 H, m), 3.7 (1 H, m), 1.8 (3 H, s), 1.7–1.0 (4 H, m); MS (CI), *m/e* 160 (M + 1), 142 (base), 124, 118, 100, 82.

Anal. Calcd for $C_{17}H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80. Found: C, 52.59; H, 8.25; N, 8.58.

((1β,2β,3β)-2,3-Dihydroxycyclopentyl)acetamide (8) and ((1β,2β,3α)-2,3-Dihydroxycyclopentyl)acetamide (7). 3-Acetamidocyclopentene (**1a**) (12.5 g, 0.1 mol) was added to a solution of osmium tetraoxide (0.2 g, 0.79 mmol) and *N*-methylmorpholine *N*-oxide (18.2 g, 0.13 mol) in acetone (20 mL) and water (50 mL). The reaction was stirred and heated at 35 °C for 24 h. The resulting mixture was evaporated to a residue which was chromatographed using chloroform and ethanol (20:1) to yield compound **8** (5.2 g, 33%) as a white solid which crystallizes from ethanol/acetonitrile [mp 102–104 °C; IR (Nujol) 3450, 3350, 3280, and 1640 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 6.8 (1 H, exchangable), 4.0 (1 H, m), 3.8 (1 H, m), 3.0 (1 H, m), 3.2 (2 H, exchangable), 2.1–1.6 (4 H, m), 1.8 (3 H, s); MS (CI), *m/e*, 160 (base M + 1), 142, 118, 100. Anal. Calcd for $C_{17}H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80. Found: C, 52.55; H, 8.37; N, 8.88.] and **7** (6.2 g, 40%) as an oil which crystallized on standing [mp 57–59 °C; IR (Nujol) 3300, 1665 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 5.0 (1 H, exchangable), 4.2 (1 H, m), 3.8 (1 H, m), 3.2 (1 H, m), 2.8 (1 H, exchangable), 0.9–2.3 (4 H, m), 1.8 (3 H, s); MS (CI), *m/e* 160 (M + 1) 142 (base 100). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80; Found: C, 52.60; H, 8.38; N, 8.62.]. Repeating the reaction at 20 °C yielded **8** (1.1 g, 17%) and **7** (2.1 g, 33%) and at 35 °C with 0.1 g of osmium tetraoxide (0.38 mmol) yielded **8** (4.1 g, 26%) and **7** (6.8 g, 43%).

***N*-(6-Oxabicyclo[3.1.0]hex-2-yl)acetamide (12).** α-Acetoxyisobutyl chloride[13] was added to a mixture of **7** (0.5 g, 0.32 mmol) and sodium iodide (1.5 g, 0.01 mol) in acetonitrile. The reaction was stirred for 1.5 h at room temperature and then evaporated to a residue. The residue was taken up in chloroform (100 mL) and washed with aqueous sodium bicarbonate (2 × 25 mL) and 10% sodium thiosulfate (2 × 25 mL), and the resulting organic layer was dried (Na_2SO_4) and evaporated to yield **13** as an oil: ^{1}H NMR ($CDCl_3$) δ 4.7 (1 H, m), 4.2 (1 H, m), 3.5 (1 H, m), 2.2–1.0 (4 H, m), 1.8 (3 H, s), 1.6 (3 H, s); IR (neat) 1760 and 1670 cm^{-1}. Stirring the oil with 1 M sodium hydroxide (10 mL) for 24 h at room temperature failed to yield any **12** as determined by TLC.

Repeating the above procedure with **8** (0.5 g, 3.2 mmol) yielded **11** as an oil: IR (neat) 3300, 1740, 1660 cm^{-1}; ^{1}H NMR δ 6.5 (1 H, exchangable), 5.2 (1 H, m), 4.8 (1 H, m), 4.2 (1 H, m), 2.8–1.5 (4 H, m), 2.2 (3 H, s), 2.0 (3 H, s). Stirring the oil with 1 M sodium hydroxide for 0.5 h after chloroform extraction yielded **12** (0.35 g, 78%), mp 92 °C (lit.[9] mp 92–93.5 °C).

Standard Hydrolysis Procedure. The amide diol was dissolved in ethanol (75 mL) and 5 M aqueous HCl (75 mL), and the resulting mixture was heated and stirred under reflux for 8 h. The resulting solution was then evaporated to a residue which was taken up in ethanol (7.5 mL) and crystallized by addition to diethyl ether (50 mL).

(1α,2β,3β)-3-Amino-1,2-cyclopentenediol Hydrochloride (6). With use of the standard hydrolysis procedure, **5** (3 g, 0.164 mol) yielded **6** (1.15 g, 46% as a white solid, mp 41–43 °C: IR (Nujol) 3380, 3320, and 1580 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 8.00 (3 H, s), 5.65 (1 H, br s), 5.09 (1 H, br s), 3.93 (1 H br s, $J_{1,2}$ = 2.8), 3.86 (1 H, br s, $J_{1,2}$ = 2.8, $J_{2,3}$ = 5.1), 3.46 (1 H, br q, $J_{2,3}$ = 5.1, $J_{3,4}$ = 5.4), 2.4–1.2 (4 H, m); MS (CI), *m/e* 118 (base), 100, 83, 82.

Anal. Calcd for $C_5H_{11}NO_2$·HCl: C, 39.09; H, 7.87; N, 9.11. Found: C, 38.94; H, 7.74; N, 9.63.

(1α,2α,3β)-3-Amino-1,2-cyclopentanediol Hydrochloride (9). With use of the standard hydrolysis procedure, **7** (3 g, 0.164 mol) yielded **9** (1.8 g, 72%), mp 48–50 °C: IR (Nujol) 3300 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 7.85 (3 H, s), 4.58 (1 H, s), 4.39 (1 H, s), 3.94 (1 H, m, $J_{1,2}$ = 4.3, $J_{2,3}$ = 7.3), 3.89 (1 H, m, $J_{2,3}$ = 7.3, $J_{1,2}$ = 4.6), 3.54 (1 H, br s, $J_{1,2}$ = 4.6), 1.96 (1 H, m), 1.78 (1 H, m), 1.47 (1 H, m), 1.18 (1 H, m); MS (CI), *m/e* 118 (M + 1), 100 (base), 82.

Anal. Calcd for $C_5H_{11}NO_2$·HCl; C, 39.09; H, 7.87; N, 9.11. Found: C, 39.26; H, 7.62; N, 8.93.

(1β,2β,3β)-3-Amino-1,2-cyclopentanediol Hydrochloride (10). With use of the standard hydrolysis procedure, **8** (3 g, 0.164 mol) yielded **10** (2.4 g, 96%) which recrystallized from ethanol and acetonitrile, mp 107 °C: IR (Nujol) 3310, 3230, and 3140 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 7.85 (3 H, s), 4.58 (1 H, s), 4.39 (1 H, s), 3.94 (1 H, m, $J_{2,3}$ = 4.3, 3.89 (1 H, m, $J_{1,2}$ = 4.6), 3.54 (1 H, br s, $J_{1,2}$ = 4.60), 1.96 (1 H, m), 1.78 (1 H, m), 1.47 (1 H, m), 1.18 (1 H, m); MS (CI), *m/e* 118 (M + 1 base); 100, 83, 82.

Anal. Calcd for $C_5H_{11}NO_2$·HCl: C, 39.09; H, 7.87; N, 9.11. Found: C, 38.75; H, 7.72; N, 9.18.

(1α,2β,5β)-5-Azido-2-(*tert*-butyldimethylsiloxy)cyclopentan-1-ol (16). *tert*-Butyldimethylsilyl chloride (15.1 g, 0.1 mol) was added to a solution of *trans*-6-oxabicyclo[3.1.0]hexan-2-ol (**15**)[14] (10 g, 0.1 mol) and 4-(dimethylamino)pyridine (13.4 g, 0.11 mol) in dichloromethane (100 mL). The reaction was stirred at room temperature for 16 h. The resulting mixture was filtered, and the filtrate was washed with saturated brine (50 mL) and then evaporated to a residue. Distillation at 120 °C (0.1 mm) yielded 15.2 g (71%) of a clear oil: ^{1}H NMR ($CDCl_3$) δ 4.1 (1 H, m), 3.3 (1 H, m), 3.0 (1 H, m), 1.8–1.2 (4 H, m), 0.8 (9 H, s), 0 (6 H, s); MS (CI), *m/e* 215 (M + 1), 199, 197 (base), 133.

Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.62; H, 10.34. Found: C, 61.33; H, 10.31.

The clear oil [(1α,2β,3α)-2-(*tert*-butyldimethylsiloxy)-6-oxabicyclo[3.1.0]hexane, (10 g, 0.047 mol)] was added to a solution

of sodium azide (20 g, 0.31 mol), ammonium chloride (0.5 g), water (50 mL), and ethanol (150 mL), heated, and stirred under reflux for 16 h. The resulting mixture was evaporated to a residue keeping the heating bath below 40 °C. The residue was suspended in chloroform (500 mL) and washed with saturated brine (2 × 50 mL). The organic layer was evaporated to an oil yielding 4.2 g of crude **16**.

(1β,2α,3β)-3-Amino-1,2-cyclopentanediol Hydrochloride (17). The crude **16** (4.2 g) was dissolved in methanol (150 mL), 10% Pd/C (0.5 g) was added, and the mixture was hydrogenated at 50 psi on a Parr hydrogenator for 2 h. The catalyst was removed by filtration, and the solution was evaporated to an oil. The oil was stirred with 5 M ethanolic HCl for 16 h and then evaporated to a residue. Crystallization from propan-1-ol yielded **17** (2.8 g, 38%), mp 34–37 °C: IR (Nujol) 3300 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.23 (3 H, br s), 5.47 (1 H, d), 5.16 (1 H, br s), 3.81 (1 H, t, $J_{1,2}$ = 5.4), 3.74 (1 H, q, $J_{1,2}$ = 5.4, $J_{2,3}$ = 5.9), 3.15 (1 H, br q, $J_{2,3}$ = 5.9), 1.55–1.9 (4 H, m); MS (CI), *m/e* 118 (M + 1), 100 (base), 82.

Anal. Calcd for $C_5H_{11}NO_2$·HCl; C, 39.09; H, 7.87; N, 9.11. Found, C, 38.95; H, 7.69; N, 9.18.

Synthesis of Mono and Unsymmetrical Bis Ortho Esters of *scyllo*-Inositol

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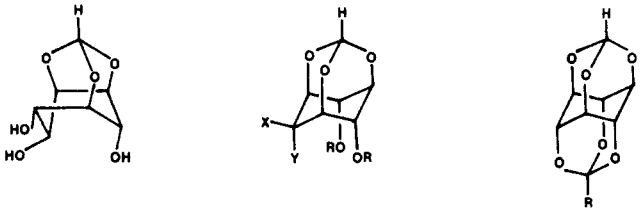
Related to an ongoing program, we needed a cyclohexane derivative bearing three axially disposed hydroxyl groups at the 1, 3, and 5 positions. An adamantane system obviously meets with this requirement because of its conformational rigidity. In particular, we have felt that mono ortho esters of *scyllo*-inositol ideally satisfies our requirement. In this paper, we would like to report a synthesis of mono and unsymmetrical bis ortho esters of *scyllo*-inositol.

Direct mono ortho ester preparation of *scyllo*-inositol did not seem promising since the rate of bis ortho ester formation was anticipated to be faster than that of mono ortho ester formation.[1] For this reason, we were interested in *myo*-inositol, which should form a mono ortho ester but not a bis ortho ester. Indeed, in 1966, Luk'yanov and Tolkachev disclosed the synthesis of monoorthoformate of *myo*-inositol by treatment with triethyl orthoformate in toluene containing *p*-toluenesulfonic acid and assigned the structure **1** to this product.[2] We were curious about the assigned structure and decided to reexamine this reaction. With modifications of the reported method,[3] we were able to isolate the monoorthoformate (mp 300–302 °C (sealed tube)) in 76% yield. The ^1H NMR spectra of both this product and its triacetate (mp 173–174 °C) clearly demonstrate that the monoorthoformate isolated must have a structure with a symmetry element, allowing assignment of the adamantane structure **2**. Unfortunately, however, there are no physical data available to conclude that this product is identical with the monoorthoformate previously reported.[2]

Selective protection of the equatorial hydroxyl group of **2** was readily achieved by treatment with *tert*-butyldimethylsilyl chloride in DMF in the presence of imidazole,[4] to yield **3** (mp 179–181 °C) in 48% yield.[5] The spectroscopic data show that **3** has only one *tert*-butyldimethylsilyl group, which was further confirmed from the fact that **3** yielded a diacetate (mp 64–65 °C) on treatment with acetic anhydride and pyridine. The ^1H NMR spectra of both **3** and its diacetate clearly establish that **3** was symmetrical, establishing the structure of this product as **3**. Benzylation of **3** under standard conditions gave the dibenzyl ether **4** (mp 124–125 °C; 93% yield), of which the desilylation furnished the dibenzyl ether alcohol **5** (viscous oil). Spectroscopic data of **4** and **5** are fully consistent with the assigned structures.



1

2: X=OH, Y=H, R=H
3: X=OSi(t-Bu)(Me)$_2$, Y=H, R=H
4: X=OSi(t-Bu)(Me)$_2$, Y=H, R=CH_2Ph.
5: X=OH, Y=H, R=CH_2Ph
6: X=Y=O(ketone), R=CH_2Ph.
7: X=H, Y=OH, R=CH_2Ph
8: X=H, Y=OH, R=H

9: R=H
10: R=Me

Swern oxidation[6] of **5** yielded the ketone **6**, which was, without purification, reduced with sodium borohydride in a mixture of tetrahydrofuran and methanol, to give exclusively the axial alcohol **7** (mp 98–99 °C), the epimeric alcohol of **5**, in 87% overall yield from **4**. The structures of **6** and **7** are established by their spectroscopic data. Debenzylation of **7** under standard hydrogenolysis conditions (5% or 10% Pd on C in methanol) or under catalytic transfer hydrogenation conditions[7] failed. However, in the presence of Pearlman's catalyst (20% $Pd(OH)_2$ on C)[8] hydrogenolysis did take place smoothly to yield the desired monoorthoformate **8** (mp 330 °C (sealed tube)) of *scyllo*-inositol in 94% yield. The ^1H NMR spectra of both **8** and its triacetate (mp 124–126 °C) establish the assigned structure. The overall yield of **8** from *myo*-inositol was about 28%.

Treatment of monoorthoformate **8** with triethyl orthoformate in THF containing a small amount of *p*-toluenesulfonic acid at room temperature smoothly gave quantitatively the known bis(orthoformate) **9** of *scyllo*-inositol.[9] Similarly, **8** yielded quantitatively unsymmetrical bis ortho ester **10** (mp 177–178 °C) of *scyllo*-inositol on treatment with triethyl orthoacetate. There was no product from

(1) Partial hydrolysis of the bis(orthoformate) of *scyllo*-inositol (for the preparation of this substance, see ref 9) was attempted under acidic conditions, but the starting material was either unchanged (aqueous AcOH/dioxane/90 °C) or only *scyllo*-inositol was, as expected, obtained (6 N HCl/dioxane/90 °C).

(2) Luk'yanov, A. V.; Tolkachev, O. N. USSR Patent 184 841, 1966; *Chem. Abstr.* **1967**, *66*, 95365.

(3) We attempted the orthoformate preparation in toluene containing *p*-toluenesulfonic acid but were unable to reproduce the reported results. The near insolubility of *myo*-inositol in toluene was obviously a problem in this reaction. For this reason, Me_2SO was chosen for the solvent.

(4) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(5) Attempted selective oxidation of **2** (O_2/Pd–C or Swern oxidation[6]) did not give encouraging results.

(6) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(7) Anantharamaiah, G. M.; Sivanandaiah, K. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 490.

(8) Rylander, P. N. "Catalytic Hydrogenation of Platinum Metals": Academic Press: New York, 1967; p 464.

(9) Vogl, O.; Anderson, B. C.; Simons, D. M. *J. Org. Chem.* **1969**, *34*, 204.

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