alcohol mixture gave the methyl ketone **3**. Reaction of **3** with the Grignard reagent formed from the benzyl ether derivative of 2-bromo-4-methylphenol gave the tertiary carbinol **4a** with the D-gluco configuration as the sole product in 80% yield. Neither the ^1H nor ^{13}C NMR spectra of this product showed the presence of any of the L-ido isomer, indicating that the second Grignard addition proceeded in a stereospecific manner.

The order of Grignard additions to the aldehyde **2** was reversed as shown in path B of Scheme I in order to establish if this observed specificity was general. The inverted process was expected to produce **7a** with the necessary stereochemistry in the tertiary carbinol fragment to furnish the oxocin **8** with the ido configuration. Addition of the Grignard reagent prepared from the benzyl ether derivative of 2-bromo-4-methylphenol to **2** followed by oxidation of the secondary alcohol mixture with Collins reagent[9] (CrO_3·2py, CH_2Cl_2) gave the phenyl keto sugar **6** in 58% overall yield. Reaction of **6** with methyllithium (THF, −78 °C) furnished the tertiary carbinol **7a** as the sole product of the reaction in 82% yield. The ^1H and ^{13}C NMR spectra of the crude and purified product showed only the presence of the L-ido isomer, again indicating that the addition proceeded stereospecifically.

The further conversion of the individually prepared tertiary carbinol epimers **4a** and **7a** to the respective optically active oxocins **5** and **8** was performed. Initial attempts to effect selective cleavage (Pd/C, EtOH) of the benzyl groups in the D-gluco compound **4a** gave approximately 30% of the product resulting from hydrogenolysis of the tertiary alcohol group. Careful monitoring of the reaction resulted in excellent selectivity and the debenzylated product **4b** was isolated in 96% yield.

Attempted hydrolysis of **4b** and rearrangement to the oxocin **5** with dilute mineral acids produced a complex mixture. The use of an acidic ion exchange resin (Amberlite IR-120) gave a much cleaner reaction, but again several products were evident by TLC. The initially received material was acetylated (Ac_2O, pyridine; room temperature) and then chromatographed in order to facilitate isolation of the products. A modest yield (16%) of the D-gluco isomer **5** along with a nearly equal amount (17%) of the L-ido compound **8** was obtained. Examination by TLC during the course of the hydrolysis showed the presence of material with an R_f corresponding to the acetonide of the L-ido compound **7b**, indicating that the loss of stereochemical integrity at the tertiary carbinol center was occurring prior to hydrolysis of the acetonide.

In contrast to the conversion of the D-gluco intermediate **4a** to the corresponding oxocin **5**, the transformation of intermediate **7a** to the oxocin **8** with L-ido configuration proceeded smoothly and with high stereoselectivity. Hydrogenolysis of **7a** (Pd/C, EtOH) was uneventful and gave the debenzylated product **7b** in 95% yield. Hydrolysis of **7b** (EtOH, H_2O, Amberlite IR-120, 12 h) followed by acetylation (Ac_2O, pyridine) and then chromatographic purification (silica) furnished a 57% yield of the L-ido compound **8** and a 4% yield of the D-gluco compound. The ^1H NMR spectrum of the L-ido oxocin triacetate **8** was striking. The methyl group of the axially oriented C-3 acetoxy functionality lies in the shielding cone of the aromatic moiety and was shifted upfield to 1.60 ppm.

Our observation that keto sugars **3** and **6** undergo stereospecific reaction with organometallic reagents in accordance with Cram's rule[11] indicates that the configurational and transition-state geometries are significantly more rigid than in a aldehyde sugar,[2] which undergoes only stereoselective addition. These findings have significant implications for the use of 5-ketofuranoses as precursors to other sugar configurations and also their utilization as chiral synthons to other classes of natural products.

While the origins of the enhanced reactivity of the gluco furanose intermediate **4** to acid are uncertain, the data indicate that the ido isomer **7** is thermodynamically more stable. Examination of models does not provide a straightforward explanation and further studies will be necessary to rationalize this observation. In conclusion, our studies show that optically active oxocins can be prepared by using sugars as synthons. The use of protective groups that can be cleaved under nonacidic conditions will likely enhance the feasibility of using this approach to prepare oxocins with the gluco configuration.

Acknowledgment. We thank Dr. J. D. White (Oregon State University) for the use of the polarimeter and the National Cancer Institute of the National Institutes of Health for support of this research (Grant CA 18141).

Supplementary Material Available: The entire experimental procedures for the accomplished study (7 pages). Ordering information is given on any current masthead page.

(9) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000.
(10) Kiely, D. E.; Walls, H., Jr.; Black, R. L. *Carbohydr. Res.* **1973**, *31*, 387.
(11) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245 and previous papers in this series.

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Silver Ion Assisted Acetolysis of the Tropenium Ion Analogue of *exo*-2-Bromobenzonorbornene, "*exo*-2-Bromotropenonorbornene" Hexafluoroantimonate

Summary: The preparation, characterization, and solvolysis (HOAc, CH_3CN, 3:1, v/v) of *exo*-5-bromobicyclo-[2.2.1]heptenotropenium (*exo*-2-bromotropenonorbornene) hexafluoroantimonate is described.

Sir: The pronounced solvolytic reactivity of exo-2-substituted benzonorbornenes is well-known.[1] Their solvolyses proceed with high exo/endo rate ratios and with complete exo product formation.[2] Mechanistic concensus implicates aryl π-participation in their solvolysis.[3] Also well-known is that tropenium ion (tropylium ion) is an "aromatic" analogue of benzene.[4] We have prepared the tropenium ion analogue of *exo*-2-bromobenzonorbornene (1-Br), dubbed "*exo*-2-bromotropenonorbornene",[5] as its

(1) Lancelot, C. J.; Cram, D. J.; Schleyer, P. v. R. in "Carbonium Ions"; ed. Olah, G. A., Schleyer, P. v. R., Ed.; Wiley-Interscience: New York, 1972; Vol. III, Chapter 27, pp 1420–1435.
(2) In 80% ethanol at 25 °C, the exo/endo ratio for the bromo derivatives is 2500. The exo bromide forms ~100% exo alcohol in aqueous dioxane. Cf. Wilt, J. W.; Chenier, P. J. *J. Org. Chem.* **1970**, *35*, 1571.
(3) Endemic to the area of *exo*-2-norbornyl and related solvolyses is the seemingly endless argument about the extent of this participation. Cf. Brown, H. C. "The Nonclassical Ion Problem"; Plenum Press: New York, 1977.
(4) Pietra, F. *Chem. Rev.* **1973**, *73*, 293.

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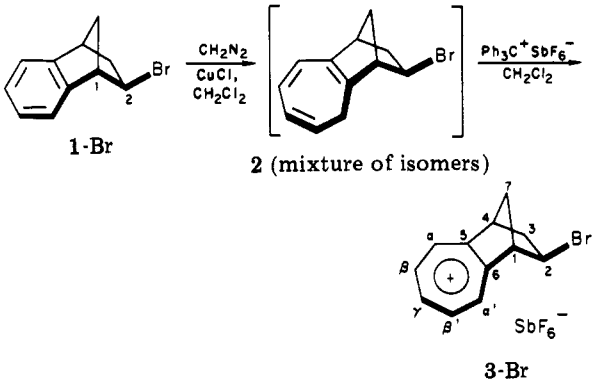
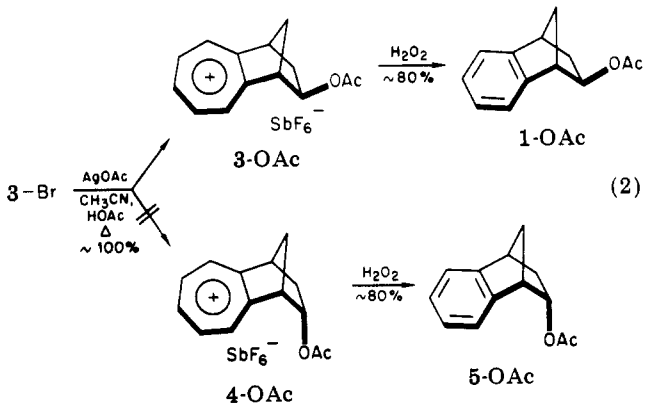
hexafluoroantimonate salt 3-Br (eq 1). Thus, in a typical



(1)

preparation, a mixture of *exo*-2-bromobenzonorbornene (1-Br,[6] 0.60 g, 2.7 mmol) and copper(I) chloride (freshly prepared, 30 mg) in dry methylene chloride (10 mL) was treated at room temperature with gaseous diazomethane (**CAUTION: carcinogen and explosion danger**) generated from *N*-nitrosomethylurea (3 g).[7] The heterogeneous material was filtered to remove solids and the mixture of tropilidenes **2**[8] treated with trityl hexafluoroantimonate[7] in further methylene chloride (20 mL). After having stood at room temperature overnight, the material was diluted with ether–hexane (1:1), v/v, 75 mL) to precipitate 3-Br. Dissolution in dry methylene chloride and reprecipitation with ether–hexane was repeated until no further physical change in 3-Br was observed, 125 mg (40% yield based upon 25% conversion of 1-Br to **2**). The salt is a white, microcrystalline solid; mp 173 °C; UV λ_{max} (CH_3CN) 223 (log ϵ 4.41), 281 (br, log ϵ 3.68), 300 (sh, log ϵ 3.64) nm; ^1H NMR (CD_3CN) δ (Me_4Si) 9.03 (near s, 5, tropenium Hs), 4.27 (sharp m, 1, CHBr), 4.07 (m, 2, H-1, 4), 2.67–2.30 (series of sharp m, 4, H-6, 7); ^{13}C NMR (CD_3CN), δ(Me_4Si) 179.3 (C-6), 173.9 (C-5), 154.5 (α'), 154.2 (α), 150.2 (γ), 148.5 (β'), 147.4 (β), 59.6 (C-1), 51.3 (C-4), 48.3 (C-7), 44.7 (C-2), 37.4 (C-3); IR (3% in KBr, ±3 cm^{-1}), 3140 w, 3090 w, 3020 m, 2950 w, 1560 w, 1450 s, 1340 w, 1300 m, 1280 m, 1270 m, 1250 sh, 1240 m, 1140 m, 1120 w, 980 m, 960 m, 910 m, 870 w, 800 w, 750 m, 720 m.

In contrast to 1-Br which reacted immediately,[6] 3-Br gave a precipitate with alcoholic silver nitrate very slowly at 25 °C. Reaction of 3-Br with silver acetate (each 0.0125 M) in dry acetic acid–acetonitrile (3:1, v/v) was followed kinetically[9] at 30.5 °C, 56 °C, and 76 °C, affording titrimetric rate constants 10^5k (M^{-1} s^{-1}) = 3.71 ± 0.08, 73.7 ± 1.3, and 377 ± 17, respectively. The calculated activation parameters were $\Delta H^{\ddagger}$ = 20.9 ± 0.9 kcal mol^{-1} and $\Delta S^{\ddagger}$ = −9.9 ± 2.8 eu. Treatment of the acetolyzed reaction material with excess hydrogen peroxide (30%)[11] produced *only* exo-2-acetoxybenzonorbornene (1-OAc).[12] The reactions are shown in eq 2. Synthesis of *exo*- and *endo*-



(2)

2-acetoxytropenonorbornene hexafluoroantimonates (3-OAc and 4-OAc, respectively) was accomplished from the corresponding benzo analogues[14] in the same way as was 3-Br. Their oxidation with hydrogen peroxide re-formed the benzo esters in good yield. Control studies showed that small amounts of 4-OAc (~1–2%) were readily detected in mixtures with 3-OAc by this oxidation technique followed by GLPC analysis.

To our knowledge these results are the first reported on the solvolysis of tropenium-related benzonorbornene substrates. To make any mechanistic comparison of the two systems is premature at this point and we resist the strong temptation to do so. Nonetheless it is clear that solvolytic data *can*[15] be obtained on such charged aromatic analogues and that product formation *can* be stereospecific. Intensive further work is in progress.

Acknowledgment. We thank the Loyola Research Committee for financial support of this work.

(5) This name was chosen in order to relate the tropenium ion and benzo cases. Its more orthodox name would be *exo*-5-bromo-1,2-bicyclo[2.2.1]heptenotropenium hexafluoroantimonate. The numbering system used was likewise selected to make the analogy more apparent.

(6) Wilt, J. W.; Chenier, P. J. *J. Org. Chem.* **1970**, *35*, 1562.

(7) The procedure used was that developed for the parent system by Thummel, R. P.; Chayangkoon, P. *J. Org. Chem.* **1983**, *48*, 596.

(8) As did Thummel and Chayangkoon,[7] we expanded 1-Br to **2** to the extent of only 20–25% (GLPC and ^1H NMR monitoring). Several isomers of **2** were evident but no detailed characterization was performed.

(9) No pretense is made that the kinetic data determined is uncomplicated. Silver ion mediated solvolyses are complex, with reactivity orders resembling those commonly associated with limiting solvolysis (S_N1).[10] However, silver ion (as the soluble salt) and silver bromide (as precipitated) undoubtedly enter the mechanism. The data given are therefore those from a second-order plot of the titrimetric data. Reaction in trifluoroacetic acid–acetonitrile (3:1, v/v) was dramatically *slower*.

(10) Gould, E. S. "Mechanism and Structure in Organic Chemistry"; H. Holt and Co.; new York, 1959; pp 273–274.

(11) Volpin, M. E.; Kursanov, D. N.; Dulova, V. G. *Tetrahedron* **1960**, *8*, 33. This reaction led to 1-Br from 3-Br in high yield (~80%).

(12) Prepared from the exo alcohol[13] and confirmed by comparison with reported material (Wilt and Chenier, ref 2).

(13) Bartlett, P. D.; Giddings, W. P. *J. Am. Chem. Soc.* **1960**, *82*, 1240.

(14) Ester 5-OAc was prepared from the endo alcohol.[13] Acetates 4-OAc and 5-OAc are readily distinguishable by GLPC (Carbowax 20 M, 180 °C) and by the δ values of their CHOAc resonances (1-OAc, 4.60 br t; 5-OAc, 5.15 dt). The tropeno salts 3-OAc and 4-OAc are similarly distinguishable by NMR. Their full characterization will be given later in the full paper.

(15) This report is dedicated to those anonymous referees of a research proposal who doubted this fact.

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Silylmethyl Radical Cyclization: New Stereoselective Method for 1,3-Diol Synthesis from Allylic Alcohols

Summary: Cyclizations of (bromomethyl)dimethylsilyl allylic ethers by treatment with tri-*n*-butyltin hydride in a free-radical process followed by oxidation in a one-pot manner with hydrogen peroxide gave the corresponding 1,3-diols predominantly with high stereoselectivity.

Sir: Free-radical cyclization has been currently visualized as a new potent methodology for ring construction via C–C bond-forming processes.[1] However, further development

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