of a Dowex 50W-X4 cation exchanger (2 M HCl). The resultant solution was analyzed to give S/W = 1.29 + 0.05 (four determinations).[14] The yield was ca. 17% based on tungsten. An HPTS (*p*-toluenesulfonic acid) solution was obtained as described elsewhere.[6]

The charge of the ion was estimated to be 4+ on the basis of its behavior, similar to that of the $Mo_3S_4^{4+}$ aqua ion on the ion exchanger.

The W/S ratio and the electronic spectrum of the purple solution ($\lambda_{max,nm}$ (ϵ/M^{-1} cm^{-1} per trimer) 315 (8650) and 560 (546) in 2 M HPTS) indicate the probable existence of a $W_3S_4^{4+}$ aqua ion. The aqua ion in 2 M HPTS is stable toward air oxidation as can be expected from the preparative method. X-ray structure analysis[15] of $(bpyH)_5[W_3S_4(NCS)_9]\cdot 3H_2O$[16] prepared from the aqua ion revealed the presence of an incomplete cubane-type trinuclear tungsten core structure, $W_3S_4^{4+}$, in the $[W_3S_4(NCS)_9]^{5-}$ anion (Figure 1).

The W–W distance is distinctly longer than those of compounds with a W_3O_4[17] or Mo_3O_4[18] core and similar to those of compounds with a Mo_3S_4[19] or bi-oxo-capped-Mo_3O_2[20] or -W_3O_2[21] core. The X-ray structure analysis supports the existence of a $W_3S_4^{4+}$ ion (probably $[W_3S_4(H_2O)_9]^{4+}$) in solution.

The electronic spectra of the $W_3S_4^{4+}$ aqua ion and $[W_3S_4(NCS)_9]^{5-}$ are shown in Figure 2. The maximal peak position of the aqua ion in the visible region is red-shifted by ca. 100 nm as compared to that of $W_3O_4^{4+}$ (λ_{max} = 455 nm), and this is similar to the case of $Mo_3S_4^{4+}$ (λ_{max} = 602 nm) compared to that of $Mo_3O_4^{4+}$ (λ_{max} = 505 nm).[22]

A cyclic voltammogram of the aqua ion (0.05 M in 2 M HPTS) shows no appreciable peak in the 0.7 to –0.7 V region (vs. SCE). The reactivity of the aqua ion with Hg is very low in contrast to the case of the $Mo_3S_4^{4+}$ aqua ion.[9b] The $W_3S_4^{4+}$ aqua ion in 2 M HCl reacts rapidly with reductants (e.g., $NaBH_4$, Sn, and $W_2Cl_9^{3-}$) to give an orange solution which comes back to the former blue-violet solution on exposure to air; the reactivity of the aqua ion in HPTS with the above-metnioned reductants is very low. Characterization of these reactions is in progress.

Registry No. $(bpyH)_5[W_3S_4(NCS)_9]\cdot 3H_2O$, 101652-56-6; $(NH_4)_2WS_4$, 13862-78-7.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles (2 pages). Ordering information is given on any current masthead page.

(14) Sulfur was determined gravimetrically as $BaSO_4$ and tungsten by the thiocyanate photometric method (*ASTM E* 146-64).

(15) Crystal data: triclinic system, space group $P\bar{1}$, a = 12.611 (5) Å, b = 24.927 (8) Å, c = 12.138 (4) Å, α = 93.05 (3)°, β = 91.06 (3)°, γ = 77.36 (3)°, V = 3718 (2) Å^3, Z = 2, Intensity data were collected on an automated four-circle diffractomer by use of graphite-monochromated Mo Kα radiation on the $4 \le 2\theta \le 45$ range. The coordinates of W's were determined by means of MULTAN, and the remaining non-hydrogen atoms were located from difference maps. The current R value is 0.102 for 7009 reflections ($F_o \ge 3\sigma(F_o)$).

(16) Excess KSCN (15 g) was added to the aqua ion (100 mL, 0.002 M per trimer in 1 M HCl). The color of the solution turned immediately from blue-violet to green. The solution was heated at 50 °C for 90 min to promote the reaction and allowed to stand overnight at room temperature. After filtration, 2,2′-bipyridine in 2 M HCl was added to the solution. On standing at room temperature, dark green crystals deposited. Anal. Found (calcd): N, 13.01 (13.01); C, 33.92 (34.67); H, 2.35 (2.52)%. Infrared spectrum of the complex shows absorption bands at 484, 466, 443, and 346 cm^{-1} due to W–S stretching.

(17) $[W_3O_4(NCS)_9]^{5-}$ (2.534 Å)[3] and $[W_3O_4F_9]^{5-}$ (2.514 Å: Matter, R.; Mennemann, K. *Z. Anorg. Allg. Chem.* **1977**, *437*, 175–182).

(18) For example, $[Mo_3O_4(mida)_3]^{2-}$ (2.495 Å)[5b] and $[Mo_3O_4(C_2O_4)_3(H_2O)_3]^{2-}$ (2.486 Å).[5a]

(19) For example, $[Mo_3S_4(ida)_3]^{2-}$ (2.754 Å)[9b] and $[Mo_3S_4(CN)_9]^{5-}$ (2.765 Å: Howlader, N. C.; Haight, G. P., Jr.; Hambley, T. W.; Lawrance, G. A.; Rahomoller, G. A.; Snow, M. R. *Aust. J. Chem.* **1983**, *36*, 377–383).

(20) For example, $[Mo_3O_2(O_2CCH_3)_6(H_2O)_3]^{2+}$ (2.759 Å: Cotton, F. A.; Dori, Z.; Marler, D. O.; Schwotzer, W. *Inorg. Chem.* **1983**, *22*, 3104–3106).

(21) For example, $[W_3O_2(O_2CC_3H_7)_6(H_2O)_3]^{2+}$ (2.742 Å: Cotton, F. A.; Dori, Z.; Marler, D. O.; Schwotzer, W. *Inorg. Chem.* **1984**, *23*, 4728–4742).

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Stereocontrolled Access to the Octosyl Acids: Total Synthesis of Octosyl Acid A

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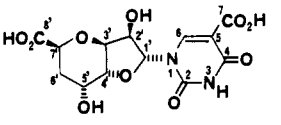
The octosyl acids, isolated from culture filtrates of *Streptomyces cacaoi* var. asoerisis,[1] have been shown to be anhydrooctose uronic acid nucleosides[2] consisting of an unusual trans- or cis-fused bicyclic perhydrofuropyran-type (dioxahydrindane) structure.[3] Related compounds can be found in the ezomycin complex[4] of nucleosides which have antifungal and antibiotic properties. Previous studies in our laboratories were concerned with developing methodology to construct the bicyclic ring systems found in such compounds[3,5] as well as in quantamycin, a computer-derived model for ribosomal binding.[6]

We now report on the first total synthesis of octosyl acid A (**1**)



OCTOSYL ACID A

1

from uridine in 15 steps. The synthetic challenge was heightened by the presence of a number of stereochemically demanding features, not the least of which was the presence of a strained bicyclic system. An expedient route, unlike those already published,[3,6,7] was therefore developed, based on an assembly strategy that utilized uridine as a template, and subsequently built the tetrahydropyran ring (with its appendages) in a stereocontrolled fashion. The readily available aldehyde **2**[8] was treated with allylmagnesium bromide to give the desired chain-extended crystalline nucleoside derivative **3**, mp 155–157 °C, $[\alpha]^{25}_D$ –3.5° (*c* 1.0, AcOEt), as the major isomer (16:1)[9,10] (Scheme I). Sequential protection and hydrolysis of the acetonide function gave derivative **5**, $[\alpha]^{25}_D$ +3.1° (*c* 1.07, CH_2Cl_2).

The ring-closure strategy was based on an alkoxymercuration–oxidation sequence, which had precedence albeit in sterically and stereochemically less demanding systems.[11,12] Clearly the adaptation of this sequence to our polyfunctional substrate was crucial to the successful completion of the synthesis. Toward this end, treatment of the O,N-protected diol **5** with mercuric acetate, followed by oxidative removal of the intermediate C_8' alkylmercurial bromide gave the expected bicyclic nucleoside **6**, $[\alpha]^{25}_D$ +52.3° (*c* 0.95, AcOEt) in 54% overall yield from **5**. The stereochemistry of the ring junction was unambiguously established by 400-MHz ^{1}H NMR spectroscopic analysis of **6** as

(1) Isono, K.; Nagatsu, J.; Kawashima, Y.; Suzuki, S. *Agric. Biol. Chem.*, **1965**, *29*, 848.

(2) Isono, K.; Crain, P. F.; McCloskey, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 943.

(3) Hanessian, S.; Dixit, D.; Liak, T. J. *Pure Appl. Chem.* **1981**, *53*, 129.

(4) Sakata, K.; Sakurai, A.; Tamura, S. *Tetrahedron Lett.* **1974**, 4327. Sakata, K.; Sakurai, A.; Tamura, S. *Tetrahedron Lett.* **1975**, 3191.

(5) Hanessian, S.; Liak, T. J.; Dixit, D. *Carbohydr. Res.* **1981**, *88*, C14.

(6) Hanessian, S.; Sato, K.; Liak, T. J.; Danh, N.; Dixit, D.; Cheney, B. V. *J. Am. Chem. Soc.* **1984**, *106*, 6114.

(7) See, for example: Anzai, K.; Saita, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 169. Kim, K. S.; Szarek, W. A. *Can. J. Chem.* **1981**, *59*, 878.

(8) Corey, E. J.; Samuelsson, B. *J. Org. Chem.* **1984**, *49*, 4735.

(9) All new compounds were characterized by standard spectroscopic methods; see supplementary material. Crystalline compounds gave correct microanalyses.

(10) Although **3** could be separated by fractional crystallization, separation of isomers was effected by flash chromatography on silica (CH_2Cl_2–MeOH, 99:1) at the diol stage, **5**.

(11) Hill, C. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 870.

(12) Pougny, J.-R.; Nassr, M. A. M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1981**, 375.

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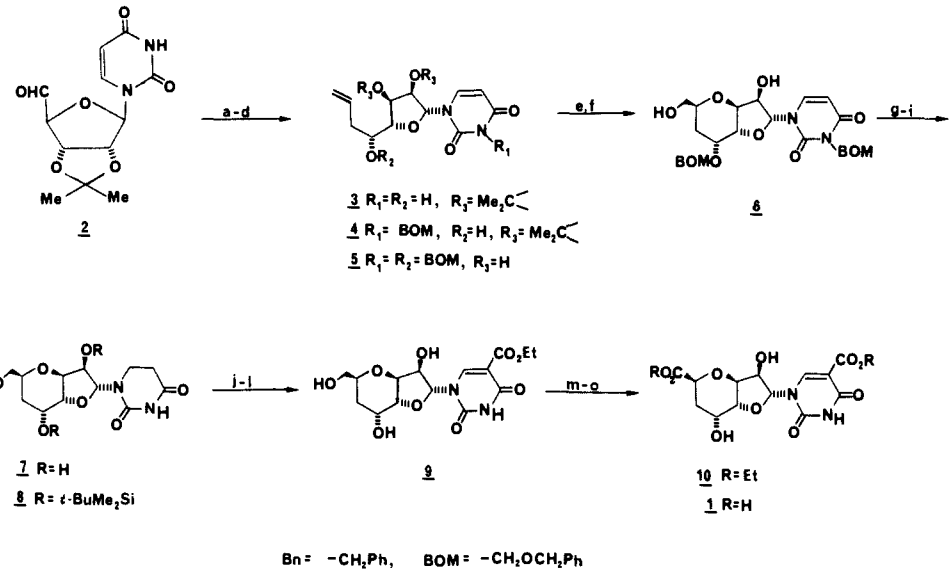
Scheme I[a]



[a](a) AllylMgBr, THF, 100 °C (70% both isomers). (b) BOMCl, DBU, DMF, 0 °C (94%). (c) BOMCl, *i*-Pr_2NEt, THF, 70 °C (85%). (d) THF-HOAc-H_2O (1:2:1) 65 °C (70%). (e) $Hg(OAc)_2$, THF, 36 h, then NaBr. (f) $NaBH_4$, O_2, DMF, (54% from **5**). (g) 20% $Pd(OH_2)/C$, H_2, MeOH, (99%). (h) 5% Rh on alumina, MeOH, (99%). (i) *t*-$BuMe_2SiCl$, *i*-Pr_2NEt, DMAP, DMF, (68%). (j) LDA, $ClCO_2Et$, THF, -78 °C. (k) PhSeCl, pyr, CH_2Cl_2, then H_2O_2 (88% from **8**). (l) *n*-Bu_4NF, THF, (97%). (m) PtO_2, $NaHCO_3$, H_2O, 90 °C. (n) H^+, EtOH. (o) LiOH, H_2O, then Dowex-50 (H^+) (70% from **9**).

well as of its diacetate.[13] Subsequent critical operations involved the introduction of a carboxyl group at C_5 and oxidation at C_8'. Deprotection of **6** and catalytic reduction gave the dihydrouridine derivative **7**. Treatment of the enolate derived from the corresponding silylated nucleoside **8** with ethyl chloroformate[14] gave the corresponding C_5 carboethoxy derivative, which was subjected to an oxidative elimination[15] to reinstate the C_5-C_6 double bond. After desilylation, the resulting triol derivative **9** was then catalytically oxidized[16] to the corresponding half-ester derivative. Saponification gave octosyl acid A as a colorless solid (**1**), mp 285-288 °C dec, $[\alpha]^{25}_D$ +9.8° (*c* 0.5, *N* NaOH),[17] whose identity was confirmed by 400-MHz ^1H NMR spectroscopy and comparison with authentic material. On the other hand, esterification of the half-ester gave the diethyl ester **10**, $[\alpha]^{25}_D$ +3.0° (*c* 1.0, EtOH).

The total synthesis of octosyl acid A from uridine was possible in large measure due to the successful application of the intramolecular alkoxymercuration reaction[11,18] for the construction of the strained dioxahydrindane ring system. The methodology developed in this work should also provide an expedient route to octosyl acid C and other structurally and stereochemically demanding nucleosides such as the ezomycins.[4]

Acknowledgment. We thank the National Scientific and Engineering Council of Canada and the Ministère de l'éducation du Québec for Financial support. We also thank Drs. Phan Viet Tan, A. Ugolini, and P. Beaulieu for assisting in the ^1H NMR spectroscopic studies and Michael Evans for mass spectra. We thank Professor K. Isono for samples of the octosyl acids.

Supplementary Material Available: Spectroscopic data and physical constants for new compounds reported in this paper (21 pages). Ordering information is given on any current masthead page.

(13) ^1H NMR of **6** (400 MHz, $CDCl_3$) δ (multiplicity, integration, assignment, coupling constants) 7.709 (d, 1 H, H-6, *J* = 8.2 Hz), 7.38-7.24 (m, 10 H, 2 Ph), 5.748 (s, 1 H, H-1'), 5.702 (d, 1 H, H-5, *J* = 8.2 Hz), 5.474 (s, 2 H, NCH_2O), 4.911 (dd, 2 H, OCH_2O, *J* = 6.9, 9.5 Hz), 4.693 (s, 2 H, OCH_2Ph), 4.640 (dd, 2 H, OCH_2Ph, *J* = 11.8, 17.2 Hz), 4.63-4.57 (m, 1 H, H-5'), 4.256 (d, 1 H, H-2', *J* = 4.6 Hz), 4.034 (dd, 1 H, H-4', *J* = 2.5, 10.3 Hz), 4.01-3.92 (m, 1 H, H-7'), 3.849 (dd, 1 H, H-3', *J* = 4.6, 10.3 Hz), 3.794 (dd, 1 H, H-8'A, *J* = 2.2, 12.2 Hz), 3.526 (dd, 1 H, H-8'B, *J* = 4.3, 12.2 Hz), 1.85-1.82 (m, 2 H, H-6'). ^1H NMR of the diacetate of **6** (400 MHz, $CDCl_3$) δ 7.51 (d, 1 H, H-6, *J* = 8 Hz), 7.2-7.4 (m, 10 H, 2 Ph), 5.87 (s, 1 H, H-1'), 5.70 (d, 1 H, H-5, *J* = 8 Hz), 5.47 (s, 2 H, NCH_2O), 5.34 (d, 1 H, H-2', *J* = 5 Hz), 4.90 (s, 2 H, OCH_2Ph), 4.89 (s, 2 H, OCH_2Ph), 4.63 (dd, 2 H, OCH_2O, *J* = 11, 14 Hz), 4.55-4.59 (m, 1 H, H-5'), 4.05-4.15 (m, 3 H, H-7', -8'), 4.02 (dd, 1 H, H-3', *J* = 5, 10 Hz), 3.88 (dd, 1 H, H-4', *J* = 3, 10 Hz), 2.07 2.16 (2s, 6 H, 2 OAc), 2.04-2.10 (ddd, 1 H, H-6'e *J* = 3, 3, 15 Hz), 1.60 (ddd, 1 H, H-6'a, *J* = 3, 12, 15 Hz).

(14) Hayakawa, H.; Tanaka, H.; Miyasaka, T. *Tetrahedron* **1985**, *41*, 1675.

(15) See, for example: Liotta, D.; Barnum, C.; Puleo, R.; Zima, G.; Bayer, C.; Kesar, H. S., III. *J. Org. Chem.* **1981**, *46*, 2920.

(16) Heyns, K.; Paulsen, H. *Newer Methods of Preparative Organic Chemistry*; Foerst, W., Ed.; Academic Press: New York, 1963; Vol. II.

(17) Reported physical constants for natural octosyl acid A[2] hydrate: mp 290-295 °C dec; $[\alpha]^{25}_D$ +13.3° (*c* 0.425, *N* NaOH). There is a discrepancy in the optical rotation value of our synthetic octosyl acid A sample, even though its structure and purity have been ascertained beyond any doubt (see supplementary material). Professor Danishefsky has made a similar observation in his independent synthesis of octosyl acid A (private communication).

(18) Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 5842.

Determination of Equilibrium ^{18}O Isotope Effects on the Deprotonation of Phosphate and Phosphate Esters and the Anomeric Effect on Deprotonation of Glucose 6-Phosphate

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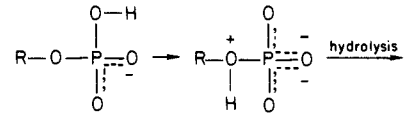
In conjunction with an investigation of the mechanism(s) of phosphate-transfer reactions, we have determined equilibrium ^{18}O isotope effects on the deprotonation of phosphate and phosphate esters. The first step in the hydrolysis of phosphate monoesters is thought to be a preequilibrium proton transfer to the bridge oxygen:[1]



(1)

We have determined the secondary kinetic ^{18}O isotope effect on the hydrolysis of glucose 6-phosphate labeled with ^{18}O only in the

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