39.7, 55.3, 62.7, 81.1, 122.7, 123.9.

(3*R*,4*S*)- and (3*S*,4*S*)-(*E*)-Methyl 3-Hydroxy-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (24). To a solution of diisopropylamine (2.78 mL, 7.07 mmol) in Et_2O (5 mL) was dropwise added a 1 M *n*-hexane solution of *n*-BuLi (4.53 mL, 6.8 mmol) at 0 °C. After 20 min the reaction was cooled to −78 °C and methyl β-(dimethylamino) propionate (0.736 mL, 6.8 mmol) was added. After 30 min (2*S*)-**19** (0.772 g, 2.72 mmol) was added. After a further 10 min the reaction was treated with saturated aqueous NH_4Cl, extracted with Et_2O, dried, and evaporated to dryness. The crude product was dissolved in MeOH (10 mL) and K_2CO_3 (1.87 g, 13.6 mmol) and MeI (1.5 mL, 21.7 mmol) were added. After 3 h the mixture was filtered and the filtrate was worked up as described for **20**. The crude was purified by chromatography (*n*-hexane/AcOEt 9/1). Oil, 40%. IR ($CHCl_3$): 3500, 2910, 2830, 1705, 1430 cm^{-1}. ^1H NMR ($CDCl_3$): 0.87 (t, J = 9 Hz, 3 H), 1.15–1.68 (m, 1 H), 1.57 (s, 3 H), 1.9 (bt, J = 9 Hz, 4 H), 3.04 (bs, exchangeable, 1 H), 3.35 (s, 0.22 H, syn), 3.4 (s, 0.78 H, anti), 3.69–3.86 (m, 4 H), 4.6–4.8 (m, 3 H), 5.09 (bt, J = 7 Hz, 1 H), 5.84 (s, 0.22 H), 5.96 (s, 0.78 H), 6.64 (s, 0.22 H), 6.7 (s, 0.78 H).

The following compounds were synthesized analogously to the above reported corresponding *tert*-butyl ester derivatives.

(+)-(3*R*,4*S*)-(*E*)-Methyl 3-[(Methylsulfonyl)oxy]-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (25). Oil, (58% anti + syn, 45% anti). IR ($CHCl_3$): 2900, 2820, 1705, 1340, 1155. ^1H NMR ($CDCl_3$): 0.87 (bt, 3 H), 1.03–2.1 (m, 18 H), 1.55 (s, 3 H), 3.08 (s, 3 H), 3.42 (s, 3 H), 3.7–3.98 (m, 4 H), 4.75 (AB system, J = 6.7 Hz, 2 H), 5.07 (bt, J = 7 Hz, 1 H), 5.65 (m, 1 H), 6.10 (m, 1 H), 6.40 (m, 1 H). $[\alpha]^{20}_D$ +24° (c 1.025, $CHCl_3$).

(+)-(3*R*,4*S*)-(*E*)-Methyl 4-Hydroxy-10-methyl-2-methylene-3-[(methylsulfonyl)oxy]hexadec-9-enoate (26). Oil (30%). Anal. Found: C, 59.35; H, 9.0. Calcd for $C_{20}H_{36}SO_6$: C, 59.38; H, 9.0. IR ($CHCl_3$): 3400, 2920, 2840, 1720, 1350, 1170, 960 cm^{-1}. ^1H NMR ($CDCl_3$): 0.86 (bs, 3 H), 1.05–2.15 (m, 22 H), 3.03 (s, 3 H), 3.80 (s, 3 H), 3.85–4.10 (m, 1 H), 5.07 (bt, J = 6.7 Hz, 1 H), 5.45 (d, J = 4 Hz, 1 H), 6.1 (s, 1 H), 6.52 (s, 1 H). $[\alpha]^{20}_D$ +12° (c 0.53, $CHCl_3$).

(+)-(3*S*,4*S*)-(*E*)-Methyl 3,4-Epoxy-10-methyl-2-methylenehexadec-9-enoate (1, R = Me) (Conocandin methyl ester). Oil (25%). Anal. Found: C, 74.00; H, 10.40. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. IR ($CHCl_3$): 2900, 2820, 1710, 1420, 1265, 1130 cm^{-1}. ^1H NMR ($CDCl_3$): 0.88 (bt, 3 H), 1.0–2.1 (m, 21 H), 2.57–2.80 (m, 1 H), 3.4–3.52 (m, 1 H), 3.8 (s, 3 H), 5.1 (bt, J = 6.9 Hz, 1 H), 5.75 (dd, J_{3-4} = 1.6 Hz, 1 H), 6.2 (d, J = 1.6 Hz, 1 H). $[\alpha]^{20}_D$ +4.2° (c 0.3, $CHCl_3$).

Preparation of (+)-(3*S*,4*S*)-1 (R = Me) Starting from Natural Conocandin. To a solution of (+)-(3*S*,4*S*)-1 (R = H) (10 mg, 0.034 mmol) in $CHCl_3$ (1 mL) was added a 1 M CH_2N_2 ethereal solution at −70 °C until the reaction remained pale yellow. Evaporation under reducd pressure gave pure (+)-(3*S*,4*S*)-1 (R = Me); quantitative. Spectroscopical data as well as sign and value of rotation were identical with those obtained from the previous preparation.

Acknowledgment. The "Progetto Finalizzato Chimica Fine e Secondaria" of Consiglio Nazionale delle Ricerche is gratefully acknowledged. We also express our appreciation to Ciba-Geigy AG, Basel, for the generous gift of a strain of *Hormococcus conorum*.

Registry No. (+)-(3*S*,4*S*)-1 (R = H), 61371-61-7; (3*S*,4*S*)-1 (R = Me), 61417-68-3; (3*R*,4*R*)-1 (R = *t*-Bu), 109639-31-8; **2**, 28659-22-5; **3**, 109669-14-9; **4**, 33803-62-2; **5**, 103021-89-2; **6**, 103021-88-1; **7**, 103021-80-3; **8**, 103021-92-7; **9**, 109639-16-9; **10a**, 109639-17-0; **10b**, 109717-16-0; **10c**, 109717-17-1; **10d**, 109717-18-2; **11**, 109639-18-1; **12**, 109639-19-2; **13a**, 109639-20-5; **13b**, 109639-32-9; (2*R*)-**17**, 109639-21-6; (2*S*)-**17**, 109639-33-0; (2*R*)-**18**, 109639-22-7; (2*S*)-**18**, 109639-34-1; (2*R*)-**19**, 109639-23-8; (2*S*)-**19**, 109639-35-2; **20**, 109639-24-9; (3*S*,4*R*)-**21**, 109639-25-0; (3*R*,4*R*)-**21**, 109639-36-3; (3*S*,4*R*)-**22**, 109639-26-1; (3*R*,4*R*)-**22**, 109639-44-3; **23**, 109639-27-2; (3*R*,4*S*)-**24**, 109639-28-3; (3*S*,4*S*)-**24**, 109639-37-4; (3*R*,4*S*)-**25**, 109639-29-4; (3*S*,4*S*)-**25**, 109639-45-4; **26**, 109639-30-7; $CH_3(CH_2)_5C(CH_3)=CH(CH_2)_4CH(OCH_2OCH_3)CH(OH)C(=CH_2)CO_2H$, 109639-38-5; $CH_3(CH_2)_5CH(OH)CH(S\text{-}p\text{-}C_6H_4Me)S(O)\text{-}p\text{-}C_6H_4Me$, 86544-35-6; methyl β-(dimethylamino)propionate, 3853-06-3; 2-bromopropene, 75-26-3; *tert*-butyl β-(dimethylamino)propionate, 88722-74-1; (+)-(*R*)-1,1-bis(*p*-tolylthio)octan-2-ol, 109717-19-3; (−)-(*R*)-1,1-bis(*p*-tolylthio)-2-(methoxymethoxy)octane, 109717-20-6; (+)-(*R*)-2-(methoxymethoxy)octanal, 109717-21-7; (*R*)-2-(methoxymethoxy)octan-1-ol, 109639-39-6; (*R*)-1-[(methylsulfonyl)oxy]-2-(methoxymethoxy)octane, 109639-40-9; (*R*)-1-iodo-2-(methoxymethoxy)octane, 109639-41-0; (*S*)-2-(methoxymethoxy)octane, 109639-42-1; (*R*)-2-(methoxymethoxy)octane, 109639-43-2; (*R*)-octan-2-ol, 5978-70-1; (±)-2-(methoxymethoxy)octane, 109717-22-8; (±)-octan-2-ol, 4128-31-8; phenyllithium, 3525-31-3.

Supplementary Material Available: Experimental section describing the preparation of (−)-(*S*)-**16** from **15b** and related spectral data (5 pages). Ordering information is given on any current masthead page.

Synthesis of Analogues of Neplanocin A: Utilization of Optically Active Dihydroxycyclopentenones Derived from Carbohydrates

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The dihydroxycyclopentenones **1** and **2** were synthesized enantiomerically pure from D-ribonolactone and D-mannose, respectively. The synthesis involves the conversion of these carbohydrates to erythruronolactones, which are subsequently converted to the desired dihydroxycyclopentenones in good yields. The dihydroxycyclopentenone **1** was then used to synthesize analogues of neplanocin A.

Neplanocin A (NpcA, (−)-9-[*trans*-2′,*trans*-3′-dihydroxy-4′-(hydroxymethyl)cyclopent-4′-enyl]adenine) is a carbocyclic analogue of adenosine, which has been shown to possess both antitumor and antiviral activity.[1-3] The antitumor activity (cytotoxicity) of NpcA is believed to be mediated through the formation of NpcA nucleotides, catalyzed by adenosine kinase, which selectively inhibit RNA synthesis.[4] NpcA's antiviral activity has been cor-

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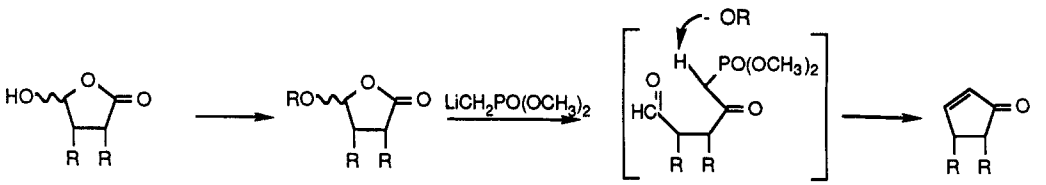
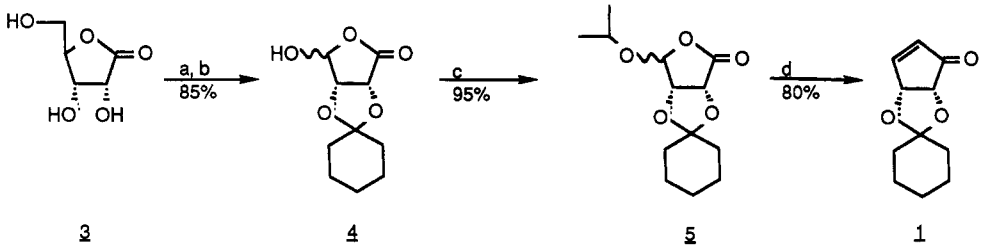
Scheme I

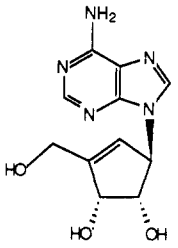


Scheme II[a]



[a] (a) Cyclohexanone, $FeCl_3$; (b) H_2O, NaOH, $NaIO_4$; (c) 2-propanol, pyridinium *p*-toluenesulfonate, 1.5 h, Δ; (d) $CH_3PO(OCH_3)_2$ *n*-BuLi, THF, 2.5 h, −78 °C to 20 °C.

related with the inhibition of *S*-adenosylhomocysteine (AdoHcy) hydrolase and subsequent perturbation of viral mRNA methylation.[5,6]



NpcA

In our continuing efforts to design and synthesize more selective and less cytotoxic inhibitors of AdoHcy hydrolase, we have synthesized the following analogues of NpcA: (−)-9-[*trans*-2′,*trans*-3′-dihydroxycyclopent-4′-enyl]adenine (**14**) and (−)-9-[*trans*-2′,*trans*-3′-dihydroxycyclopent-4′-enyl]-3-deazaadenine (**15**) (Scheme IV). These analogues have been shown to be selective and potent inhibitors of bovine liver and mouse L-929 cell AdoHcy hydrolase.[7,8] These analogues also displayed good antiviral activity with significantly reduced cytotoxicity.[9] The approach in designing these analogues was to remove the 4′-hydroxymethyl group of NpcA, which should reduce the substrate activity for adenosine kinase. In order to synthesize these analogues, we needed the (−)-dihydroxycyclopentenone **1** (Scheme II) in enantiomerically pure form.

There are few stereoselective procedures for the synthesis of optically pure hydroxylated cyclopentenones,[10-12] and many other procedures require that the cyclopentenones, at some point, be resolved into enantiomers.[13-15] We report here the synthesis of enantiomerically pure (−)-dihydroxycyclopentenone **1** from the inexpensive sugar lactone D-ribonolactone (Scheme II). The dihydroxycyclopentenone **1** has then been used to synthesize the two NpcA analogues (Scheme IV; compounds **14** and **15**). The synthesis of the (+)-dihydroxycyclopentenone **2** from D-mannose will also be described (Scheme III).

Results and Dicussion

It appeared to us that the uronolactone (Scheme I) would be an ideal intermediate for the synthesis of cyclic enones containing chiral centers. Since the uronolactone has two carbonyl functional groups, protection of this compound as the glycoside could allow for the selective attack at the lactone carbonyl group with lithium dimethyl methylphosphonate. Dimethyl methylphosphonate has been used in steriod synthesis to form simple five- and six-membered cycloalkenones from enol lactones.[16] The attack by lithium dimethyl methylphosphonate would result in the opening of the lactone ring and the elimination of alkoxide, giving an acyclic intermediate. This intermediate would then undergo base-promoted cyclization to the cyclopentenone by the alkoxide generated in situ.

The (−)-dihydroxycyclopentenone **1** (Scheme II) was synthesized with the L-erythruronolactone **4** as the starting material, which was synthesized from D-ribonolactone by using the procedure of Beer et al.[17] Compound **4** was converted to the L-glycoside **5** by refluxing it in 2-propanol with a catalytic amount of pyridinium *p*-toluenesulfonate (10 mol %) for 1.5 h. The glycoside **5** was then reacted with lithium dimethyl methylphosphonate at −78 °C to yield the optically active (−)-dihydroxycyclopentenone **1** in 65% overall yield.

The opposite enantiomer **2** (Scheme III) was synthesized from D-mannose (**6**) by converting it to the lactone **8**.[18] The selective deprotection of **7a** using a Dowex 50W (H^+) resin followed by treatment with NaOH and then $NaIO_4$

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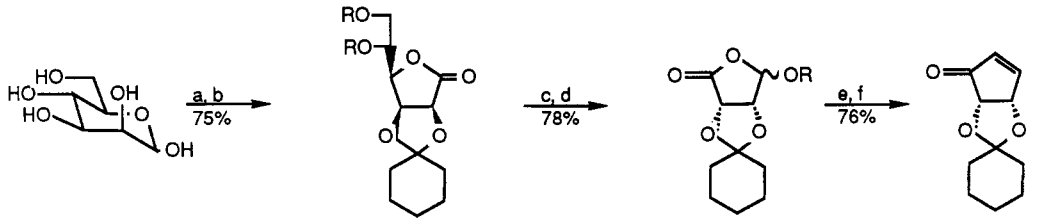
Scheme III[a]

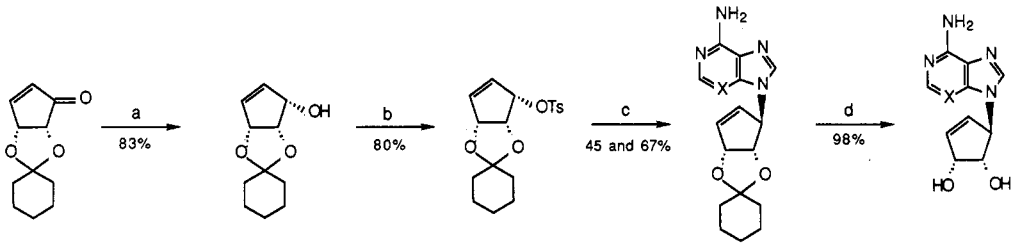


6 7a R=cyclohexylidene 8 R=H 2

7b R=H 9 R=CH(CH$_3$)$_2$

[a] (a) Cyclohexanone, H_2SO_4; (b) Collins reagent; (c) Dowex 50W, H_2O/EtOH, 16 h, 40 °C; (d) H_2O NaOH, $NaIO_4$, pH 7.0; (e) 2-propanol, pyridinium *p*-toluenesulfonate, 1.5 h, Δ; (f) $CH_3PO(OCH_3)_2$, *n*-BuLi, THF, 2.5 h, −78 to 20 °C.

Scheme IV[a]



1 10 11 12 X=N 13 X=CH 14 X=N 15 X=CH

[a] (a) $NaBH_4$, $CeCl_3$, MeOH, 0 °C, 20 min; (b) 1.2 equiv of TsCl, 2.4 equiv of Et_3N, CH_2Cl_2, 24 h; (c) 3 equiv of adenine or 3-deazaadenine, DMF, NaH, 50 °C, 2 days; (d) dilute HCl.

gave the D-erythruronolactone **8**. This compound was then converted to the cyclopentenone **5** in 44% overall yield.

Compound **1** was converted to the NpcA analogues **14** and **15** by first reducing it with sodium borohydride in the presence of cerium chloride,[19] which gave stereoselectively the cyclopentenol **10**. Compound **10** was tosylated to afford compound **11**, which was nucleophilically displaced with the sodium salts of adenine or 3-deazaadenine to give the protected nucleosides **12** and **13**, respectively.[20,21] Finally, deprotection of compounds **12** and **13** gave the desired nucleosides **14** and **15**.

Synthons similar to **2**, which were optically resolved and use a isopropylidene protecting group, have been recently utilized in a novel synthesis of prostaglandin E_2.[13] This compound has also been used in the synthesis of the queuine base in nucleoside Q.[22]

Protected uronolactones would appear to have a general use in the synthesis of functionalized five- and as well as six-membered cyclic enones on a large scale (>10 g). These cyclic enones would be desirable chiral building blocks to a variety of natural products.[23,24] We are currently exploring the usefulness of these cyclopentenones in the synthesis of carbocyclic nucleosides, such as aristeromycin and NpcA.

Experimental Section

Melting points were determined on a Fisher-Johns stage melting point apparatus and are uncorrected. NMR spectra were recorded on a Varian FT-80A (80 MHz for proton nuclei) spectrophotometer. Chemical shifts are reported in δ from the internal standard tetramethylsilane (TMS, δ 0.00). Mass spectra were recorded on a Ribermag R10-10 quadrupole spectrometer. Peak matching was performed by a Varian MAT CH5 magnetic deflection mass spectrometer. The optical rotations were carried out on a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed on an F and M Model 185 C, H, N analyzer in the Department of Medicinal Chemistry, Univeristy of Kansas. Ion-exchange chromatography was performed with a strong cation exchange resin Dowex 50W (H^+) stock no. 50×4-200, 4% crosslinked, 100–200 dry mesh size. This-layer chromatography was carried out with Analtech 0.25-mm silica gel GF glass-backed plates. Preparative-layer chromatography was performed with a Model 7924T chromatotron with 1-, 2-, or 4-mm silica gel PF-254 with $CaSO_4 \cdot {}^1/_2H_2O$ (Merck) plates.

2,3-(Cyclohexylidenedioxy)-4-hydroxy-4-(2-propyloxy)-butanoic Acid Lactone (5). The L-erythruronolactone[17] **4** (1.0 g, 4.7 mmol) was dissolved in 50 mL of dry 2-propanol containing a catalytic amount of pyridinium *p*-toluenesulfonate (10 mol %, 0.12 g, 0.47 mmol) and was refluxed for 1.5 h. The mixture was then concentrated to a syrup, which was then dissolved in 50 mL of Et_2O, extracted with H_2O (2×, 50 mL) and brine, dried over Na_2SO_4, and filtered. The filtrate was concentrated, and the syrup was dissolved in a minimum amount of hexane/Et_2O (5:1), which was applied to a small column of silica gel (5 g) and eluted with hexane/Et_2O (5:1) to give 1.15 g of compound **5** (97% yield): $[\alpha]_D$ +45.18° (*c* 1.55, MeOH); IR (neat) 1799 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.54 (s, 1 H, H-4), 4.81 (d, 1 H, H-2, J = 6 Hz), 4.51 (d, 1 H, H-3, J = 6 Hz), 4.02 (heptet, 1 H, $(CH_3)_2CHO$, J = 7 Hz), 1.58 (br s, 10 H, cyclohexyl), 1.24 and 1.18 (2 s, 6 H, 2 CH_3); MS (D-El, CH_2Cl_2), *m/e* 256 (M^+), 213 (Me_2CH), 81 (cyclohexyl). Anal. ($C_{13}H_{20}O_5$) C, H.

(−)-2,3-(Cyclohexylidenedioxy)-4-cyclopentenone (1). In an oven-dried 500-mL three-neck flask (fitted with a septum and a 125-mL addition funnel) was added dimethyl methylphosphonate (3.98 g, 31.4 mmol) in 200 mL of dry THF, and the lactone **5** (8.07 g, 31.4 mmol) dissolved in 25 mL of THF was poured into the addition funnel. The phosphonate solution was cooled to −78 °C with an acetone/dry ice bath, and then *n*-bu-

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tyllithium (1.6 M in hexane, 19.6 mL, 31.4 mmol) was added dropwise from a syringe over an 8–10 min period. When the addition was complete, the solution was stirred for 15 min, and the lactone was added rapidly. The solution was stirred for 2.5 h at −78 °C after which the dry ice bath was removed. When the solution came to room temperature (~30 min), the mixture was poured into 500 mL of Et_2O containing 100 mL of H_2O and shaken, and then the organic layer was separated. The aqueous layer was extracted with an additional 100 mL of Et_2O, and the organic layers were combined. The Et_2O layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated (<50 °C) to an oil (crude, 6 g, 90%). The oil was dissolved in Et_2O and added to a column of silica gel (10 g), which was eluted with Et_2O to give 4.85 g (80%) of a colorless liquid (solidified in the freezer and recrystallized from Et_2O/hexane): mp 65 °C; $[\alpha]_D$ −74° (*c* 3.0, MeOH); IR (neat) 1734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (dd, 1 H, H-4, *J* = 7 Hz), 6.19 (d, 1 H, H-5, *J* = 7 Hz), 5.26 (dd, 1 H, H-3, *J* = 6 Hz), 4.41 (d, 1 H, H-2, *J* = 6 Hz), 1.58 (m, 10 H); MS (D-El, CH_2Cl_2), *m/e* 194 (M^+). Anal. ($C_{11}H_{14}O_3$) C, H.

2,3:5,6-*O*-Dicyclohexylidene-D-mannonolactone (7a). To a solution of pyridine (53 g, 670 mmol) in 500 mL of CH_2Cl_2 was added in portions CrO_3 (33.5 g, 335 mmol), which was then stirred at room temperature for 1.5 h. The 2,3:5,6-di-*O*-cyclohexylidene-D-mannose[18] (19 g, 56 mmol) was dissolved in 50 mL of CH_2Cl_2 and added rapidly to the pyridine/CrO_3 complex. After 1.5 h, the solution was decanted, and the tar was throughly triturated with Et_2O (2×, 200 mL). The combined organic layers were filtered through a pad of Celite, and the filtrate was concentrated. The residue was taken up in 250 mL of Et_2O, extracted with dilute HCl (2×, 200 mL), H_2O (3×, 200 mL), and brine, dried over Na_2SO_4, and filtered. The filtrate was concentrated to dryness, and the resulting solid was dissolved in a minimum amount of Et_2O, which was applied to column of silica gel (30 g) and eluted with Et_2O/hexane (1:1) to give the desired compound **7a** (15.9 g, 84% yield): mp 108–109 °C (lit.[18] mp 108–110 °C).

2,3-*O*-Cyclohexylidene-D-mannonolactone (7b). The lactone **7** (4 g, 12 mmol) was dissolved in 100 mL of EtOH and 100 mL of H_2O, and 2 g of Dowex 50W (H^+) was added. The mixture was stirred for 16 h at 40 °C, after which the resin was removed by filtration, and the filtrate was concentrated. The oil that was obtained was dissolved in a minimum amount of EtOAc/hexane (1:1), and the solid (D-mannonolactone) that formed was removed by filtration. The filtrate was applied to a column of silica gel (10 g), and the starting material (<200 mg) that remained was removed by eluting with 75 mL of EtOAc/hexane (1:1), and the desired compound was removed by eluting with EtOAc to give 2.6 g of the desired compound as a viscous syrup (85% yield): $[\alpha]_D$ +41.6° (*c* 0.6, MeOH); IR (Nujol) 1780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.97 (d, 1 H, *J* = 1 Hz), 4.55–3.6 (m, 5 H), 2.88 (br s, 2 H, exchanged D_2O), 1.6 (br s, 10 H); MS (D-El), *m/e* 258 (M^+).

2,3-*O*-Cyclohexylidene-D-erythruronolactone (8). A solution of 2,3-*O*-cyclohexylidene-D-mannonalactone (2.6 g, 10 mmol) and NaOH (0.48 g, 12 mmol) in 30 mL of H_2O was heated at 40 °C until all the solid material dissolved. The mixture was then cooled to 0 °C, and $NaIO_4$ (5.12 g, 24 mmol) in 20 mL of H_2O was added dropwise (the pH was maintained at ~7.0 with dilute NaOH). After the addition was complete, the reaction was allowed to stir for 10 min. Then solid $BaCl_2$ (0.5 g) was added, and the resulting precipitate was filtered through a pad of Celite. The filtrate was acidified to pH 3.0 with 2 N HCl, the mixture was extracted with EtOAc (2×, 200 mL; 1×, 100 mL), and the extract was washed with brine, dried over Na_2SO_4, and filtered. The filtrate was concentrated to give 1.97 g of the desired compound **8** (92% yield): $[\alpha]_D$ +42° (*c* 1.1, $CHCl_3$). The compound was identical (mp, NMR, IR) with the 2,3-*O*-cyclohexylidene-L-erythruronolactone, which was previously reported by Beer et al.[17] (lit.[17] $[\alpha]_D$ −39.8° (*c* 1.65, $CHCl_3$) for the opposite enantiomer).

(−)-2,3-(Cyclohexylidenedioxy)-4-hydroxy-4-(2-propyloxy)butanoic Acid Lactone (9). Compound **8** (1.0 g, 4.7 mmol) was converted to **9** according to the procedure given for compound **5**. **9**: yield 1.17 g (98%); $[\alpha]_D$ −45.5° (*c* 5.75, MeOH). The physical data (bp, NMR, IR) were identical with that of the opposite enantiomer **5**.

(+)-4,5-(Cyclohexylidenedioxy)-2-cyclopentenone (2). Compound **2** was obtained from **9** (0.5 g, 2.0 mmol) by the same procedure described for compound **1**. **2**: yield 0.30 g (77%); $[\alpha]_D$ +74° (*c* 1.0, MeOH). The physical data were identical (mp, NMR, IR) with the opposite enantiomer **1**.

(−)-2,3-(Cyclohexylidenedioxy)-4-cyclopenten-1-ol (10). The cyclopentenone **1** (2.04 g, 10.5 mmol) and $CeCl_3 \cdot 7H_2O$ (3.91 g, 10.5 mmol) were added to 60 mL of MeOH cooled to 0 °C, $NaBH_4$ (0.48 g, 12.6 mmol) was added (foamed), and the mixture was allowed to stir for 20 min. The pH was then adjusted to 7.0 with 1 N HCl, 200 mL of Et_2O was added, and the organic layer was washed with a small amount of brine. The Et_2O layer was dried over Na_2SO_4, filtered, and concentrated to a yellow liquid. The liquid was dissolved in a small amount CH_2Cl_2 and added to a silica gel column (5 g), and the product was eluted to give 1.7 g (83%) of a colorless liquid: $[\alpha]_D$ −23.59° (*c* 4.45, MeOH); ^1H NMR ($CDCl_3$) δ 5.84 (s, 2 H, H-4 and H-5), 4.96 (d, 1 H, H-1, *J* = 6 Hz), 4.69 (t, 1 H, H-3, *J* = 6 Hz), 4.53 (dd, 1 H, H-2, *J* = 6 Hz) 1.55 (m, 10 H, cyclohexyl); MS (D-El, CH_2Cl_2), *m/e* 196 (M^+), 81 (cyclohexyl). Anal. ($C_{11}H_{16}O_3$) C, H.

(−)-2,3-(Cyclohexylidenedioxy)-1-[(*p*-tolylsulfonyl)oxy]-cyclopent-4-ene (11). The cyclopentenol **10** (0.22 g, 1.12 mmol) and *p*-toluenesulfonyl chloride (0.41 g, 2.14 mmol) were dissolved in 10 mL of CH_2Cl_2, and then Et_3N (0.46 g, 4.48 mmol) was added. The mixture was stirred for 24 h at room temperature, after which the mixture was extracted with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated to dryness. The solid was dissolved in a small amount of CH_2Cl_2/hexane (1:1) and loaded onto a 2-mm chromatotron (Model 7429T) plate (silica gel), which was eluted with CH_2Cl_2/hexane (1:1) to give 0.31 g (80%) of pure product: mp 110–111 °C; $[\alpha]_D$ −62.26° (*c* 2.65, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.85 (d, 2 H, aromatic, *J* = 8 Hz), 7.27 (d, 2 H, aromatic, *J* = 8 Hz), 5.87 (m, 2 H, H-4 and H-5), 5.3 (d, 1 H, H-1, *J* = 5 Hz), 4.87 (d, 1 H, H-3, *J* = 5 Hz), 4.53 (t, 1 H, H-2, *J* = 5 Hz), 2.42 (s, 3 H, CH_3), 1.50 (m, 10 H); MS (D-El, CH_2Cl_2), *m/e* 350 (M^+), 155 (tosylate), 81 (cyclohexyl). Anal. ($C_{18}H_{22}O_5S$) C, H.

(−)-9-[2′,3′-(Cyclohexylidenedioxy)cyclopent-4′-enyl]-adenine (12). The tosylate **11** (1.45 g, 4.1 mmol) dissolved in 3 mL of DMF was added to a solution of sodium adenine in 10 mL of DMF [sodium adenine was prepared by adding NaH (80%, 0.35 g, 12.3 mmol) to a slurry of adenine (1.66 g, 12.3 mmol) in 10 mL of DMF]. The mixture was stirred for 1–2 days at 50 °C, and then the DMF was removed by distillation. The residue was taken up in CH_2Cl_2 (50 mL), and the undissolved material was removed by filtration. The filtrate was concentrated to dryness, and the solid was dissolved in a small amount of CH_2Cl_2/EtOH (9:1) and loaded onto a 4-mm chromatotron (Model 7429T) plate, and 0.56 g (45%) of compound **12** was collected: mp 87 °C; $[\alpha]_D$ −200.95° (*c* 2.1, MeOH); ^1H NMR ($CDCl_3$) δ 8.36 (s, 1 H, H-2), 7.68 (s, 1 H, H-8), 6.58 (br s, 2 H, NH_2,exchanged D_2O), 6.33 (dd, 1 H, H-4′, *J* = 6 Hz, *J* = 2 Hz), 5.93 (dd, 1 H, H-5′, *J* = 6 Hz, *J* = 2 Hz), 5.63 (d, 1 H, H-1′, *J* = 1 Hz), 5.49 (d, 1 H, H-3′, *J* = 6 Hz), 4.71 (d, 1 H, H-2′, *J* = 6 Hz), 1.60 (m, 10 H); MS (D-El, MeOH), *m/e* 313 (M^+), 135 (base, adenine), 81 (cyclohexyl). Anal. ($C_{16}H_{19}N_5O_2 \cdot {}^3/_4H_2O$) C, H, N.

(−)-9-[2′,3′-(Cyclohexylidenedioxy)cyclopent-4′-enyl]-3-deazaadenine (13). Compound **13** was prepared in the same manner as **12** by starting from **11** (170 mg, 0.5 mmol), except adenine was replaced by 3-deazaadenine[25] (100 mg, 0.75 mmol): yield 100 mg (67%); mp 156–158 °C; $[\alpha]_D$ −164° (*c* 0.5, MeOH); UV_{max} 263 nm, 267 nm (sh); ^1H NMR ($CDCl_3$ + D_2O) δ 7.87 (d, 1 H, H-6, *J* = 6 Hz), 7.65 (s, 1 H, H-2), 6.79 (d, 1 H, H-7, *J* = 6 Hz), 6.38 (d, 1 H, H-4′, *J* = 5 Hz), 6.10 (d, 1 H, H-5′, *J* = 5 Hz), 5.36 (m, 1 H, H-1′ and H-3′, *J* = 6 Hz), 4.58 (d, H-2′, *J* = 6 Hz), 1.62 (m, 10 H); MS (D-El, CH_2Cl_2), *m/e* 312 (M^+), 134 (3-deazaadenine), 81 (cyclohexyl). Anal. ($C_{17}H_{20}N_4O_2 \cdot {}^1/_2H_2O$) C, H, N.

General Procedure for the Deprotection of Compounds 12 and 13. Compounds **12** or **13** were mixed with 20 mL of H_2O, and 1 mL of 6 N HCl was added. The mixture was stirred at room temperature for 3–6 h until TLC (CH_2Cl_2/EtOH, 9:1) showed no starting material remained. The solution was concentrated to dryness (azeotroped with EtOH), and the solid was dissolved in 1–2 mL of H_2O and applied to a Dowex 1×8-50 (H^+) column. The

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product was eluted with dilute ammomium hydroxide and concentrated to dryness. The compounds were dried azeotropically with ethanol.

(−)-9-(*trans*-2′,*trans*-3′-Dihydroxycyclopent-4′-enyl)-adenine (14): yield 230 mg (98%); mp 175–176 °C; $[\alpha]_D$ −170° (*c* 1.0, H_2O); ^1H NMR (DMSO-d_6 + D_2O) δ 8.47 (s, 2 H, H-2, H-8), 6.09 (m, 2 H, H-4′ and H-5′), 5.45 (d, 1 H, H-1′, *J* = 6 Hz), 4.55 (d, 1 H, H-3′, *J* = 6 Hz), 4.25 (dd, 1 H, H-2′, *J* = 6 Hz); MS (QP-El-Probe), *m/e* 233 (M^+ 1), 216 (− HO), 135 (base, adenine). Anal. ($C_{10}H_{11}N_5O_2 \cdot H_2O$) C, H, N.

(−)-9-(*trans*-2′,*trans*-3′-Dihydroxycyclopent-4′-enyl)-3-deazaadenine (15): yield 305 mg (98%); mp 140 °C; $[\alpha]_D$ −210° (*c* 1.1, MeOH); UV_{max} 263 nm, 267 nm (sh). ^1H NMR (DMSO-d_6 + D_2O) δ 8.03 (s, 1 H, H-2), 7.64 (d, 1 H, H-6, *J* = 6 Hz), 6.76 (d, 1 H, H-7, *J* = 6 Hz), 6.13 (m, 2 H, H-4′ and H-5′), 5.29 (d, 1 H, H-1′, *J* = 5 Hz), 4.49 (d, 1 H, H-3′, *J* = 5 Hz), 4.05 (dd, 1 H, H-2′, *J* = 5 Hz); MS (D-El, MeOH), *m/e* 232 (M^+) peak match Δ = 0.0007, 215 (− HO), 134 (base, 3-deazaadenine). Anal. ($C_{11}H_{12}N_4O_2 \cdot EtOH$) C, H, N.

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Generation and Nuclear Magnetic Resonance Studies of 9-Heteroanthracenide Anions: 9-Selena-, 9-Phospha-, and 9-Arsaanthracenides

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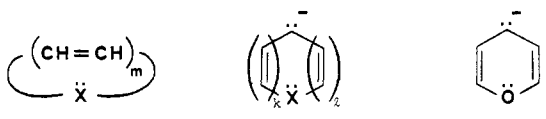
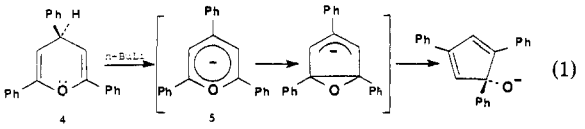
The thermally stable heteroanthracenide ions **9d–g** were generated upon exposure of the respective conjugate acids **8d–g** to KNH_2 in liquid NH_3 and were studied by ^1H, ^{13}C, and ^{31}P NMR. It is shown that **9d** possesses a paratropic molecular frame, while **9e** and **9f** exhibit no detectable paramagnetic ring current effect. Possible electronic and steric interactions that may give rise to the observed NMR characteristics of **9e–g** are discussed, and it is concluded that the carbanionic charge in these anions is substantially delocalized over the central ring involving the heteroatomic unit.

The influence of heteroatoms on the development of potential aromaticity (in "4*n* + 2" electron π-excessive[2] system **1**, *m* = even integer) and antiaromaticity (in "4*n*" electron counterpart **1**, *m* = odd integer) has been the subject of extensive theoretical[3] and experimental[4] work. Of considerable interest in this area is the direct observation and possible characterization of potentially delocalizable bis-π-excessive systems such as **2**, which incorporates a second π-excessive unit, namely, a carbanionic center in addition to a heteroatomic unit.



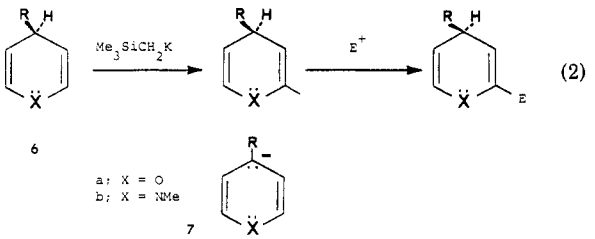
1 **2** **3**

Research aimed at the generation and direct observation of the potentially antiaromatic 8 π-electron anions **2** (*k* = *l* = 1) was pioneered by Schmidt and co-workers.[5] All attempts at observing **3** were unsuccessful, and in the case of substituted anion **5** were frustrated by its rapid ring-contractive reorganization to yield the cyclopentadiene derivative shown in eq 1.



(1)

In a related study,[6] metalation of **6** by the powerful metalating agent [(trimethylsilyl)methyl]potassium resulted in a slow hydrogen/potassium exchange at the α-position to the heteroatom rather than at the activated double allylic γ-position (eq 2), indicating the relative instability of the incipient eight π-electron anions **7a** and **7b**.



(2)

Our work in this area included a study (by NMR) of certain dibenzannulated variants of **2**, namely, anions **9a**[7] (4*n* π-electrons) and **11**[8] (4*n* + 2 π-electrons), which were

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