124–125 °C (cyclohexane) (lit.[15,16] 123–124, 134–135 °C); NMR (500 MHz) δ 4.98 (s, 2, H_6), 7.45 (dd, 2, $H_{5,7}$), 7.50 (t, 2, $H_{4,8}$), 7.72 (dd, 2, $H_{3,9}$), 7.76 (d, 2, $H_{1,11}$ or $H_{2,10}$), 7.80 (d, 2, $H_{1,11}$ or $H_{2,10}$); $J_{1,2} = J_{10,11} = 8.6$, $J_{3,4} = J_{4,5} = J_{7,8}$, $J_{8,9} = 7.1$, $J_{3,5} = J_{7,9} = 1.2$ Hz.

4,5,8,9,10,11-Hexahydro-7*H*-cyclopenta[*a*]pyrene. A solution of **8** (1 g, 3.8 mmol), hydrazine hydrate (1 g), and KOH (1 g) in diethylene glycol (100 mL) was heated at reflux overnight under N_2. The usual workup, followed by chromatography on silica gel, gave on elution with hexane 4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene (863 mg, 92%): mp 82–83 °C (ethanol); NMR δ 2.1 (m, 2, H_8), 2.7–3.1 (m, 4, $H_{7,9}$), 2.8 (s, 8, $H_{4,5,10,11}$), 7.1 (m, 4, $H_{1,2,3,6}$).

8,9-Dihydro-7*H*-cyclopenta[*a*]pyrene (10). A mixture of the product of the foregoing reaction (310 mg, 1.26 mmol) and 10% Pd/C (30 mg) was heated at 220 °C under N_2 for 2 h.[9] The usual workup, followed by chromatography on silica gel, gave, on elution with hexane–benzene (8:2), **10** (300 mg, hexane): NMR δ 2.25 (t, 2, H_8), 3.35 (q, 4, $H_{7,9}$), 7.9–8.25 (m, 8, aromatic).

7,8-Dihydro-9-oxo-9*H*-cyclopenta[*a*]pyrene (11). A solution of **10** (104 mg, 0.43 mmol) and DDQ (279 mg, 1.23 mmol) in 10% aqueous dioxane (50 mL) was heated at reflux overnight. The solution was cooled and chromatographed through a column of neutral alumina eluted with dioxane. Evaporation of the solvent afforded **11** (81 mg, 74%): mp 206–208 °C (EtOAc); NMR (500 MHz) δ 2.94 (t, 2, H_8), 3.48 (t, 2, H_7), 8.02 (d, 1, H_4 or H_5), 8.05 (d, 1, H_2), 8.11 (s, 1, H_6), 8.16 (d, 1, H_4 or H_5), 8.25 (d, 1, H_3), 8.29 (d, 1 H_1), 8.31 (d, 1, H_{11}), 9.49 (d, 1 H_{10}), $J_{1,2} = J_{2,3} = 7.6$, $J_{4,5} = 8.9$, $J_{10,11} = 9.1$ Hz.

7*H*-Cyclopenta[*a*]pyrene (1). A mixture of **11** (644 mg, 2.5 mmol) and $NaBH_4$ (380 mg, 10 mmol) was taken up in THF (70 mL) and MeOH (80 mL) and stirred at room temperature for 2.5 h. After the usual workup, evaporation of the solvent afforded the alcohol (60 mg, 93%): mp 148–149 °C (EtOAc); NMR δ 2.2–3.7 (m, 4 $H_{7,8}$), 6.1 (m, 1, H_9), 8.0–8.6 (m, 8, aromatic). A solution of the alcohol (90 mg, 0.35 mmol) and *p*-toluenesulfonic acid (10 mg) was heated in refluxing benzene for 30 min. The usual workup, followed by chromatography on 2% 2,4,7-trinitrofluorenone on silica gel,[17] furnished, on elution with hexane, **1** (49 mg, 58%); mp 125–127 °C; NMR (500 MHz) δ 3.78 (s, 2, H_7), 6.9 (m, 1, H_8), 7.7 (m, 1, H_9), 7.97 (t, 1, H_2), 8.0 (d, 1, H_4 or H_5), 8.1 (d, 1 H_4 or H_5), 8.1 (d, 1, H_{11}), 8.2 (d, 1, $H_{1,3}$), 8.3 (s, 1, H_6), 8.4 (d, 1, H_{10}), $J_{1,2} = J_{2,3} = 7.7$, $J_{4,5} = 8.9$, $J_{8,9} = 5.7$, $J_{10,11} = 9.0$ Hz; UV λ_{max} (EtOH) 222 nm (ε 24 440), 244 (36 000), 250 (42 200), 275 (20 800), 285 (30 000), 325 shoulder (11 800), 342 (28 300), 360 (40 300).

7-Acetoxy-4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene (12b). A mixture of **8** (1.3 g, 5 mmol) and $NaBH_4$ was taken up in THF (20 mL) and methanol (20 mL) and stirred at ambient temperature for 2.5 h. After the usual workup, evaporation afforded the alcohol **12a** (1.1 g, 85%): NMR δ 2.6–3.1 (m, 4, $H_{8,9}$), 2.9 (s, 8, $H_{4,5,10,11}$), 5.27 (t, 1, H_7), 6.15 (m, 4, $H_{1,2,3,6}$).

To a solution of acetic anhydride (15 mL) and pyridine (6 mL) was added **12a** (747 mg, 2.8 mmol), and the resulting solution was stirred at room temperature overnight. The usual workup, followed by chromatography on silica gel, gave, on elution with benzene, **12b** (860 mg, 99%): mp 85–87 °C (EtOAc–hexane); NMR δ 2.05 (s, 3, CH_3), 2.6–3.1 (m, 4, $H_{8,9}$), 2.85 (s, 8, $H_{4,5,10,11}$), 6.2 (m, 1, H_7) 7.1 (m, 4, aromatic).

7-Acetoxy-8,9-dihydro-7*H*-cyclopenta[a]pyrene (13). A solution of **12b** (804 mg, 2.6 mmol) and DDQ (1.31 g, 5.8 mmol) in anhydrous benzene (80 mL) was refluxed for 2 h under N_2. The solution was chromatographed on a silica gel column eluted with benzene. Evaporation of the solvent afforded 578 mg (73%) of a product consisting of **13** and **14** (or its 4,5-dihydro isomer) (10% by NMR). Recrystallization from ether–hexane gave the analytical sample of **13**: mp 100–102 °C; NMR δ 2.1 (s, 3, CH_3), 2.3–3.8 (m, 4, $H_{8,9}$), 6.6 (m, 1, H_7), 7.9–8.3 (m, 8, aromatic).

9*H*-Cyclopenta[*a*]pyrene (2). A solution of **13** (42 mg, 0.14 mmol) and *p*-toluenesulfonic acid (4 mg) was heated in refluxing benzene (20 mL) for 1 h under N_2. The usual workup, followed by chromatography on silica gel, yielded **2** (31 mg, 93%) as a white solid: mp 133–135 °C; NMR (500 MHz) δ 3.90 (s, 2, H_9), 6.89 (m, 1, H_8), 7.30 (m, 1, H_7), 8.02 (t, 1, H_2), 8.11 (d, 1, H_{10}), 8.16 (d, 1, H_{11}), 8.17 (d, 1, H_4), 8.22 (d, 1, H_1 or H_3), 8.23 (d, 1, H_1 or H_3), 8.26 (d, 1, H_5), 8.29 (s, 1, H_6); $J_{1,2} = J_{2,3} = 7.5$, $J_{4,5} = 9.0$, $J_{7,8} = 5.5$, $J_{10,11} = 8.9$ Hz; UV λ_{max} (EtOH) 263 nm shoulder (ε 55 960), 275 (68 600), 281 shoulder (33 200), 296 (25 270), 326 (20 940), 342 (36 800).

Conversion of **13** to **2** was also accomplished via methanolysis and dehydration. A suspension of **13** (65 mg, 0.22 mmol) in 30 mL of 5% KOH in MeOH was heated at reflux for 40 min. Conventional workup, followed by chromatography on a column of Florisil, gave the corresponding alcohol (46 mg, 82%): NMR δ 2.0–3.7 (m, 5, $H_{8,9}$, OH), 5.7 (t, 1, H_7), 7.2–8.3 (m, 8, aromatic). Dehydration of the alcohol was effected with *p*-toluenesulfonic acid (4 mg) in refluxing benzene (10 mL) for 20 min. The usual workup, followed by chromatography on a column of silica gel impregnated with 2% 2,4,7-trinitrofluorenone,[17] yielded **2** (30 mg, 58%) as a white solid identical by NMR with the sample obtained via the alternative route.

7,8-Dihydro-7,8-epoxy-9*H*-cyclopenta[*a*]pyrene (16). To a heterogeneous solution of CH_2Cl_2 (10 mL) and 0.5 M $NaHCO_3$ (10 mL) were added **2** (39 mg, 0.16 mmol) and *m*-chloroperbenzoic acid (41 mg, 0.24 mmol). The mixture was stirred at ambient temperature for 5 h and then worked up conventionally. Trituration of the product with ether–hexane gave **16** (21 mg, 53%) as a white solid: mp 158–160 °C; NMR (500 MHz) δ 3.51 (dd, 1, $H_{9\alpha}$ or $H_{9\beta}$), 3.84 (d, 1, $H_{9\alpha}$ or $H_{9\beta}$), 4.44 (t, 1, H_8), 4.66 (m, 1, H_7), 7.96 (t, 1, H_2), 8.0 (d, 1, H_{10}), 8.06 (m, 3, $H_{4,5,11}$), 8.16 (d, 1, H_1 or H_3), 8.18 (d, 1, H_1 or H_3), 8.31 (s, 1, H_6); $J_{1,2} = J_{2,3} = 7.3$, $J_{7,8} = J_{8,9} = 1.0$, $J_{10,11} = 7.5$, $J_{9\alpha,\beta} = 18$ Hz.

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Registry No. **1**, 189-80-0; **2**, 50861-05-7; **6a**, 3029-19-4; **6b**, 82979-67-7; **6c**, 82979-68-8; **7**, 82979-69-9; **8**, 82979-70-2; **9**, 82979-71-3; **10**, 82979-72-4; **11**, 82979-73-5; **12a**, 82979-74-6; **12b**, 82979-75-7; **13**, 82979-76-8; **14**, 82979-77-9; **15**, 82979-78-0; **16**, 82979-79-1; **17**, 82979-80-4; 5-hydroxy-1,2,2a,3,4,5,7,8,9-octahydrobenzo[*cd*]pyrene, 82979-81-5; 1,2,2a,3,7,8,9-hexahydrobenzo[*cd*]pyrene, 82979-82-6; 6*H*-benzo[*cd*]pyrene, 191-33-3; 4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene, 82979-83-7; 9-hydroxy-8,9-dihydro-7*H*-cyclopenta[*a*]pyrene, 82979-84-8.

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Synthesis of Psicofuranine Cyclic 4′,6′-Monophosphate

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Adenosine cyclic 3′,5′-monophosphate (cAMP) plays a key role in the regulation of a broad range of physiological processes.[1] The only known mechanism by which cAMP exerts its effects in eukaryotic cells is via the activation of cAMP-dependent protein kinases.[2] As part of our continuing studies on the ability of cAMP analogues to activate these enzymes,[3] we have synthesized the cyclic

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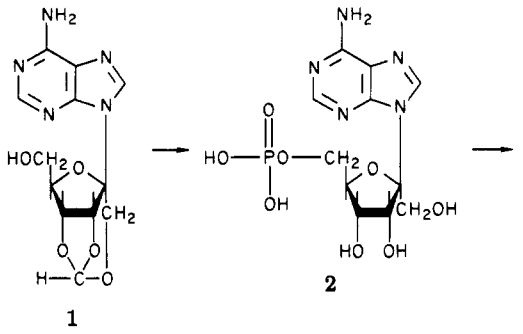
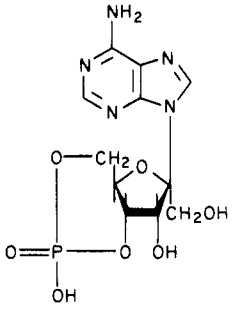
Scheme I



1 2



3

4′,6′-monophosphate of psicofuranine. To our knowledge this is the first nucleotide synthesis involving this both acid- and alkali- labile[4] nucleoside, although phosphorylation of psicose itself has been reported[5] along with extensive ^1H and ^{13}C NMR data. Furthermore, while numerous analogues of cAMP have been synthesized by modifying every other position in the molecule, this synthesis represents the first modification of the C-1′ carbon functionality.

The requisite C-1′, C-3′, C-4′ blocked intermediate 1 (Scheme I) required for phosphorylation was synthesized from psicofuranine according to McCarthy and co-workers[6] by a modification of their workup procedure. Crude 1 was obtained by ethyl acetate extraction of the aqueous reaction media. Recrystallization of this residue from ethanol afforded the cyclic ortho ester 1, homogenous by thin-layer chromatography. Phosphorylation of 1 with phosphoryl chloride in triethyl phosphate was effected with 4A molecular sieves to act as a neutral acid scavenger[7] and protect the labile glycosidic bond. Although trace amounts of adenine were visible by thin-layer chromatography of the reaction solution, its presence was considerably less than that present in a small probe reaction run without molecular sieves. The addition of ice–water to terminate the reaction and to hydrolyze the nucleoside phosphorochloridate reaction product, followed by adjustment of the pH to 4 with 1 N NaOH, was enough to remove the cyclic *ortho*formyl group. Mass spectral analysis of the trimethylsilyl derivative of the isolated material gave a parent peak of m/e 809, which represents the fully derivatized ($6Me_3Si$) **2**.

Cyclization of the crude 6′-monophosphate **2** in the traditional manner[8] with dicyclohexylcarbodiimide in refluxing pyridine yielded psicofuranine cyclic 4′,6′-monophosphate (**3**) as a hydrated partial ammonium salt. While the synthetic route employed should preclude the formation of anything but the 4′,6′-cyclic monophosphate, the mass spectrum of the Me_3Si derivative of **3** unequivocally confirmed the cyclic 4′,6′-monophosphate structure by demonstrating mass fragments m/e 440 and 338. These fragments correspond to ions "k + H" and "a + H" (Figure 1) in the fragmentation pattern of nucleotide trimethylsilyl derivatives reported by McCloskey and co-workers.[9] Thus, ion "k + H" contains the heterocyclic base and the C-1′ through C-3′ portion of the sugar plus their attached oxygens and Me_3Si groups; ion "a + H" contains the base and C-1′ to C-2′ portion of the sugar with their attached oxygens and Me_3Si groups. We have thus confirmed the presence of Me_3Si groups at C-1′ and C-3′. This, together with the parent peak for fully derivatized **3** at m/e 647, allows one to formulate a cyclic phosphate at positions 4′ and 6′ (structure **3**). In addition, the loss of $-CH_2O(Me_3Si)$ was strongly in evidence at m/e 544 (M − 103). This is as expected in light of the strong M − CH_2OH peak reported for psicofuranine.[10]

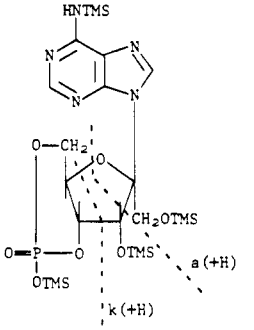


Figure 1. Partial mass spectral fragmentation pattern of the title compound (TMS = Me_3Si).

Generation of the free acid of **3** by passage through Dowex 50 (H^+) initially did not produce degradation, but on standing, the free acid slowly suffered glycosidic cleavage. The sodium salt of **3** obtained from Dowex 50 (Na^+) was examined both by ^1H and ^{13}C NMR. The proton NMR appeared little changed from the starting psicofuranine. Natural abundance ^{13}C NMR of the sodium salt of **3** in Me_2SO-d_6 and the partial ammonium salt in D_2O produced proton-decoupled spectra with assignments shown in Table I. These assignments are made in light of Ikehara's[11] reassignment of the 3′ and 4′ carbons in normal cyclic 3′,5′-phosphates as previously assigned by Smith and co-workers.[12] Ikehara's assignments were confirmed by Kainosho[13] via heteronuclear decoupling experiments. Ikehara's assignments revealed a pattern of chemical-shift changes for several cyclic 3′,5′-phosphates, wherein the carbons esterified with the cyclic phosphate group (3′ and 5′) show similar downfield (~6.5 ppm) chemical shifts when compared to the parent nucleoside. In addition, the anomeric carbon always showed a downfield shift, while the remaining sugar carbons exhibited upfield shifts. In particular, the carbon surrounded by the phosphate group (i.e., 4′ in cAMP) was markedly shielded,

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Table I. ^{13}C Chemical Shifts and ^{13}C-^{31}P Coupling Constants of Nucleotides and Their Parent Nucleosides

compd	solvent	chemical shift (from Me_3Si), ppm (J, Hz)										
		C-2	C-4	C-5	C-6	C-8	C-1′	C-2′	C-3′	C-4′	C-5′	
adenosine[a]	Me_2SO-d_6	153.09	149.85	120.11	156.87	140.68	88.75	74.24	71.42	86.65	62.49	
cAMP[a]	D_2O	153.24	148.38	118.90	155.70	140.05	92.05	72.93 (8)	77.81 (4)	72.30 (4)	67.86 (7)	
							C-2′	C-3′	C-4′	C-5′	C-6′	C-1′
psicofuranine	Me_2SO-d_6	151.64	148.05	119.88	155.95	140.53	97.86	74.16	69.21	83.70	60.31	62.03
3 (NH_4^+)	D_2O	150.39			154.09		99.71	72.50 (7.5)	76.65 (3.0)	71.54 (0)	67.37 (5.4)	61.42
3 (Na^+)	Me_2SO-d_6	152.00	147.89	119.90	155.98	139.8	99.70	71.73[b] (9)	76.83 (4)	72.10[b] (0)	66.06 (6.6)	61.35

[a] Data obtained from Table I in ref 11. [b] The signals of two carbons have coalesced such that half of the doublet of C-3′ is under the singlet of C-5′, which shows some asymmetry. Positions given are those of signal apexes.

showing upfield shifts of 12.5–15 ppm. Their assignments continued to support the results of Smith and co-workers concerning the dihedral angle dependency of vicinal ^{13}C–^{31}P coupling constants. Thus, in normal nucleoside cyclic 3′,5′-phosphates, the C-2′ and C-5′ signals are distinguished by their larger coupling constants (7–8 Hz) from the C-3′ and C-4′ signals (4–5 Hz). Bearing these relationships in mind, examination of the data for **3** in Table I indicates larger coupling constants (5.4–9 Hz) for C-3′ and C-6′. In the ^{13}C NMR spectrum of **3** (Na^+) in Me_2SO-d_6, the signals of two carbons have coalesced such that one-half of the doublet of C-3′ is obscured by the singlet of C-5′ with an estimated coupling of 9 Hz for C-3′. The lack of apparent coupling in C-5′ is particularly noteworthy, while C-4′ shows the expected small coupling (3 and 4 Hz in D_2O and Me_2SO-d_6 solvents, respectively).

The spectrum of psicofuranine itself (Me_2SO-d_6) gave sugar peaks that were tentatively assigned by analogy to the ^{13}C data for adenosine[11] (Table I). There arises the question of which of the two upfield signals is C-6′ and which is C-1′. The assignments were made such that, upon introduction of the cyclic phosphate group, the chemical-shift relationships demonstrated by Ikehara were maintained. Thus, the data for **3** in Table I show an upfield, though small, shift for C-1′. C-3′ and C-5′ also show upfield shifts, with that of C-5′ showing the large shift (~12 ppm) seen for the carbon situated between the esterified carbons. The esterified carbons, in turn, show similar downfield shifts (5.8–7.6 ppm). The adenine portion of the ^{13}C spectrum of psicofuranine and **3** varied little from each other, and assignments were made by analogy to adenosine and cAMP.

Experimental Section

Psicofuranine was obtained from the Upjohn Co. All evaporations were conducted at ≤30 °C. Thin-layer chromatograms on E. Merck Cellulose F were developed with isopropyl alcohol/ammonium hydroxide/water, 7:1:2, and visualized by ultraviolet light. ^{13}C and ^1H NMR spectra were obtained on a Varian XL-100 spectrometer with a Nicolet 1180 computer system for Fourier transform. Mass spectra were determined on an LKB Model 9000 mass spectrometer at 70 eV. HPLC data were obtained with a Waters Associates ALC 210 chromatograph interfaced with a Waters Data Module and a Schoeffel Instrument Model 770 variable-wavelength ultraviolet monitor. Ultraviolet spectra were obtained on a Perkin-Elmer 552 spectrophotometer. Altex low-pressure columns containing Whatman DE-52 diethylaminoethylcellulose (DEAE-cellulose) in the bicarbonate form were used for chromatographic separations. Linear gradients of water and ammonium bicarbonate were administered to the columns via peristaltic pump. Fractions were collected with an LKB 2070 collector; selected fractions were examined in the PE-552 spectrophotometer at 259λ to locate eluting peaks. Total absorbance is expressed as AU_{259} and is obtained by multiplying measured absorbance at 259 nm by the dilution factor required to obtain an on-scale reading and by the total volume of the solution.

Psicofuranine Cyclic 4′,6′-Monophosphate (3). To 1′,3′,4′-*O*-orthoformylpsicofuranine[6] (1; 954 mg, 3.1 mmol), dried in vacuo at 56 °C for 2 days, plus 1.0 g of 4A molecular sieves[7] stirring in 15 mL of triethyl phosphate (stored over 4A sieves) at 0 °C was added dropwise $POCl_3$ (1.13 mL in 2.5 mL of triethyl phosphate). The solution was stirred for 2 h at 0 °C when the reaction was terminated by careful addition of ice–water (40 mL), keeping the temperature below 8 °C. The pH was adjusted to 4 with 1 M NaOH with continued ice cooling. A fine white solid formed, which cleared upon warming to room temperature. Examination of the solution by TLC showed that starting material 1 and adenine were barely visible at R_f 0.71 and 0.63, respectively, while a strong spot at the origin indicated phosphorylated product. The molecular sieves were removed and washed with water. The filtrate (100 mL; 43 100 AU) was extracted 3 times with Et_2O to remove triethyl phosphate. The pH, which had fallen to 1.5, was readjusted to 4, and the solution began to cloud. After storage overnight at 3 °C, the flocculent material (443 mg, white powder, mp >250 °C) was removed by centrifugation and discarded. Rinses resulting from thorough H_2O washing of the residue were combined with the original filtrate. This solution (pH 3.4; 32 760 AU) was stirred with Barnebey–Cheney charcoal (28 g of UU 1064) for 2 h. UV examination indicated 99% absorption. The charcoal slurry was poured into a column, washed with H_2O to negative Cl^- test, and then eluted with $EtOH/H_2O/Et_3N$ (10:10:1). The first 300 mL (Solution A) contained 29 000 AU, while the next 775 mL (Solution B) contained 3000 AU (99% recovery from charcoal). Solution A was concentrated to 30 mL and then was filtered through Celite to eliminate charcoal fines. The filtrate was evaporated; the oily residue was dissolved in minimum H_2O, cooled in an ice bath, and brought to pH 3 with 1 M HCl. Addition of EtOH yielded crude product (414 mg; 12 260 AU, trace impurity by TLC). The mother liquor contained only 1300 AU. The mother liquor and solution B were concentrated to a small volume and chromatographed on a DEAE-cellulose column (0.9 × 46 cm) with a gradient of H_2O and 0.25 N NH_4HCO_3 (2 L each). Two bands were eluted, the first consisting of impurities (1260 AU) and the second (2440 AU) of desired product plus a trace of adenine as determined by TLC. The latter, upon evaporation and trituration in EtOH, yielded a white solid (66 mg, homogenous by TLC), which was added to the main crop for a crude yield of **2** (480 mg, 34%) that was ~85% pure: mass spectrum (Me_3Si derivative), *m/e* 809 [M^+ for $(Me_3Si)_6$ derivative], 794 ($M^+ - CH_3$), 587, 423, 315, 271.

An aqueous solution of **2** (~1 mmol, combined with *N*,*N*′-dicyclohexyl-4-morpholinecarboxamidine (294 mg, 1 mmol) in pyridine was evaporated in vacuo. The mixture was dried by twice repeating evaporation from pyridine. The residue, dissolved in dry (over 3A molecular sieves) pyridine (60 mL), was added dropwise to a solution of DCC (824 mg, 4 mmol) in pyridine (120 mL) at reflux under anhydrous conditions. After a total 3-h reflux, an equal volume of H_2O was added, and the reaction was stored at 3 °C overnight. A flocculent solid (*N*,*N*-dicyclohexylurea) was removed by filtration. The filtrate was evaporated to dryness, redissolved in H_2O, and again filtered. The aqueous filtrate was

applied to a DEAE-cellulose (0.9 × 46 cm) column, washed with 300 mL of water, and then eluted with a gradient of water (2 L) and 0.1 M NH_4HCO_3 (2 L), collecting 10-mL fractions. The water eluant contained 1580 AU and was discarded. The gradient eluant (200 mL) contained 5310 AU and weighed 135 mg after lyophilization. This material was rechromatographed on DEAE-cellulose with a H_2O (2 L)–0.02 M NH_4HCO_3 (2 L) gradient, and 20-mL fractions were collected. Fractions 65–73 (center cut of fractions containing UV-absorbing material) were combined and lyophilized to yield 61 mg (14%) of product as a white solid. Anal. Calcd for $C_{11}H_{14}N_5O_7P\cdot0.5NH_3\cdot H_2O$: C, 31.32; H, 5.13; N, 18.26; P, 7.34. Found: C, 30.96; H, 4.48; N, 18.42; P, 7.39. UV λ_{max} at pH 1, 258 nm (ϵ 14 700); at pH 7, 260 (15 400); at pH 11, 260 (15 400); mass spectrum (Me_3Si derivative), m/e 647 [M^+ of $(Me_3Si)_4$ derivative], 632 ($M^+ - CH_3$), 544 [$M^+ - CH_2O(Me_3Si)$], 440 (k + H), 338 (a + H), 270, 208 (M^+ – sugar moiety + 2 H); HPLC on 4.6 × 250 mm Partisil 10 SAX, 15% MeOH in 0.04 M KH_2PO_4 at 2 mL/min: 2.14 (99%) and 2.71 min (1%); ^{13}C NMR, see Table I; ^1H NMR (D_2O) δ 4.0–4.46 (m, 6 H, nonexchangable sugar protons other than 3′-CH), 5.03 (br s, 1 H, 3′-CH), 8.19 (very br s, 2 H, aromatic). Another 22 mg of impure material was obtained in fractions from DEAE-cellulose chromatography before and after the above-collected material. The free acid isolated from passage through Dowex 50 (H^+) slowly suffered glycosidic cleavage. The sodium salt isolated by chromatography on Dowex 50 (Na^+) gave ^1H NMR (Me_2SO-d_6–D_2O) δ 3.78–4.40 (m, 6 H, nonexchangable sugar protons other than 3′-CH), 5.0 (asym d, 1 H, 3′-CH), 7.18 (remnant of br s, NH_2), 8.02 (aromatic s, 1 H), 8.16 (aromatic s, 1 H); ^{13}C NMR, see Table I. Anal. Calcd for $C_{11}H_{13}N_5O_7PNa\cdot1.5H_2O$: C, 32.36; H, 3.95; N, 17.16. Found: C, 32.64; H, 3.73; N, 16.69.

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Registry No. 1, 23267-28-9; 2, 16638-76-9; 3, 83005-53-2; 3 NH_3, 83005-52-1; 3 Na, 83005-54-3.

Adducts Derived from Furan Macrocycles and Benzyne

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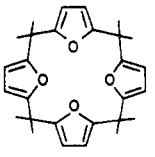
The macrocycle 1 is readily synthesized from furan and



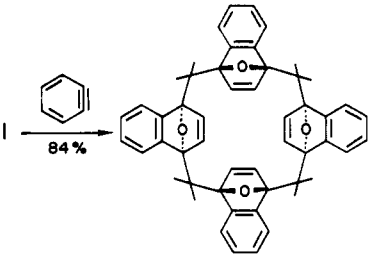
1

acetone.[1-5] Although 1 and related macrocycles are fairly accessible, attention has focused so far on their synthesis and not on their chemistry. Aside from catalytic hydrogenation,[2] the only exception is the recent elegant work of Williams and LeGoff,[6] who used 1 and related compounds as precursors for novel macrocyclic polyketones.

We have been exploring the use of bisaryne equivalents in the synthesis of novel compounds,[7] particularly through cycloadditions with dienes. It occurred to us that a bisaryne equivalent might react with two "opposite" furan moieties in 1 to give unique structures. Preliminary to such investigations, we examined and report here on the reaction of benzyne itself with 1.

Results and Discussion

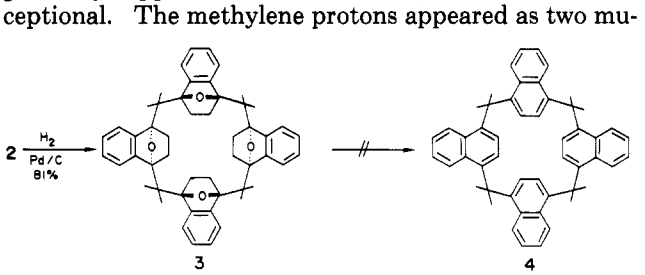
Treatment of 1 with 4 equiv of benzyne (generated from benzenediazonium carboxylate hydrochloride) gave a singlet adduct, 2, in 84% yield. The D_{2d} symmetry is assigned



2

to 2 on the basis of its NMR spectrum, which showed all methyl groups equivalent (singlet, δ 1.78). The ^{13}C NMR spectrum was consistent with the structure, showing only seven peaks for this C_{52} compound (see Experimental Section).

Attempts to directly deoxygenate 2 to produce the novel [1.1.1.1]paranaphthalenophane 4 were unsuccessful.[8] Accordingly, 2 was hydrogenated with the hope that the hydrogenation product could be dehydrated with acid. Catalytic hydrogenation of 2 over Pd/C gave a good yield of a single product, 3, whose NMR spectrum, though generally supportive of the structure, was somewhat exceptional. The methylene protons appeared as two mu-



3 4

tually coupled doublets at δ 3.00 and 1.23 (J = 7.0 Hz). It seemed unusual that one set of these methylene protons should appear at such an extrordinarily low field (δ 3.00). For comparison, model compound 5 was prepared and showed H_x at δ 1.92 and H_n at δ 1.50. Molecular models of 3 suggest that it has a geometry similar to what is shown in 3′. All of the aryl rings are oriented to the outside of

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(8) $LiAlH_4$–$TiCl_4$, BuLi–$TiCl_3$, and Zn–HOAc gave only recovered starting material. Lithium naphthalenide or thermolysis gave only oily decomposition products.

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