C-Nucleosides. 10. Synthesis of 1,3-Dimethyl-7-(β-D-ribofuranosyl)lumazine

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The synthesis of 1,3-dimethyl-7-(β-D-ribofuranosyl)lumazine (8) from 6-hydroxy-6-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2*H*-pyran-3(6*H*)-one (1) is described. Treatment of 1 with 5,6-diamino-1,3-dimethyluracil (2) in toluene at 80 °C afforded three compounds, 1,3-dimethyl-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)lumazine (3), 1,3-dimethyl-6-[3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-3-oxopropyl]lumazine (4), and 6,8-dimethyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[1,2-*f*]pteridine-7,9-dione (5), in 5%, 16%, and 30% yields, respectively. The position of the ribofuranosyl groups in 3–5 was confirmed by ^1H–^{13}C long-range COSY experiments. Deblocking of 3 with aqueous sodium carbonate in methanol gave 8 and dihydrofuran 9 in 32.7% and 38.6% yields, respectively. However, treatment of 3 with methanolic sodium methoxide gave 9 with no trace of 8.

The structural relationship between the pteridine nucleus on one hand and the purine and pyrimidine systems on the other has been responsible for many efforts aimed at synthesis of pteridine nucleosides as structural analogues of the nucleic acid components. Pfleiderer and his collaborators[1] have synthesized many *N*-nucleoside and nucleotide analogues of pteridine. Despite this, no *C*-nucleoside related to pteridine has previously been synthesized. It therefore seemed desirable to synthesize such pteridine *C*-nucleosides, which may have interesting and improved biological effects. The most widely used method[2] for the synthesis of such a ring system involves the condensation of a 5,6-diaminouracil with a 1,2-dicarbonyl compound. We now report the synthesis of pteridine *C*-nucleoside by a novel ring transformation of 6-hydroxy-6-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2*H*-pyran-3(6*H*)-one (1) with diaminopyrimidine derivatives. The key synthetic intermediate pyranulose 1 can be obtained readily from 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)furan by our previously published procedure.[3]

In order to investigate the feasibility of a condensation of 5,6-diamino-1,3-dimethyluracil hydrate (2) with the protected pyranulose 1, a solution of the two reactants in a variety of solvents was heated at 80 °C. In toluene, complete disappearance of starting material 1 was observed after 5 h. When the progress of the reaction in toluene was monitored by thin-layer chromatography (TLC), the gradual disappearance of 1 and 2 was accompanied by the appearance of three distinct products, 6,8-dimethyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[1,2-*f*]pteridine-7,9-dione (5) as the main product and small amounts of 1,3-dimethyl-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-lumazine (3) and 1,3-dimethyl-6-[3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-3-oxopropyl]lumazine (4) in 30%, 5%, and 16% yields, respectively (Scheme I). In ethylene glycol, 3 was obtained in 35% yield as the main product and 5 was obtained in 13% yield. However, in acetonitrile containing boron trifluoride diethyl etherate at room temperature, 4 was obtained in 29% yield with no trace of 3 and 5. To ascertain the structures, the position of the ribofuranosyl groups in 3–5 was confirmed by the following facts: (1) In ^1H–^{13}C long-range COSY experiments of 3, a correlation was observed between H-6 at δ 8.75 and C-4a at δ 127.59. Other long-range correlations are shown by arrows in Figure 1. While 4 gave satisfactory ^1H and ^{13}C NMR spectra, it appeared to be unstable. Hence, compound 4 was converted into a stable furan derivative 6 by treatment with *p*-toluenesulfonic acid. The ^1H–^{13}C long-range COSY spectrum of 6 exhibited a correlation between H-7 at δ 8.67 and C-8a at δ 146.66. (2) In the ^{13}C NMR spectra of 3 and 4, the C-7 signal is characteristically found at lower field than that of C-6 due to the stronger electron-attracting power of the 4-carbonyl function on the C-7 center;[4] the C-6 signal of 3 (δ 138.61) occurs at higher field than the C-7 of 4 (δ 147.89). (3) Hydrogenation of 5 with 10% palladium–carbon in methanol gave 7, which was gradually converted to 5 at room temperature. Irradiation of the NH signal (δ 4.77) of 7 gave an 11.1% enhancement of the signal at δ 3.29 assignable to N_1-CH_3 and a 4.4% enhancement of the signal at δ 4.23 assignable to H-4; furthermore, H-4 of 5 at δ 8.76 was correlated with C-5a at δ 145.38.

A plausible explanation for the formation of 4 involves nucleophilic attack by the more basic 5-amino group of 2 on the carbonyl carbon of the pyranulose moiety of 1 with subsequent formation of a Schiff's base I (Scheme III), which then isomerizes to give II. Dehydration of II would lead to tricyclic compound III, which is then opened to give the unstable ring-opened intermediate IV. IV is converted to 4 by a proton shift. We think that the formation of 3 and 5 proceeds by the same mechanism for formation of quinoxalines and pyrroloquinoxalines in a previous paper.[3]

Removal of protecting groups in compound 3 with aqueous sodium carbonate in methanol was readily accomplished and afforded 1,3-dimethyl-7-(β-D-ribofuranosyl)lumazine (8) and dihydrofuran 9 in 32.7% and 38.6% yields, respectively (Scheme II). The configuration of 8 was firmly established as β by formation of an acetonide. The ^{13}C NMR signals of the isopropylidene methyls in the acetonides of nucleosides occur at δ 25.5 ± 0.2 and 27.5 ± 0.2 ppm for β anomers and at δ 24.9 ± 0.3 and 26.3 ± 0.2 ppm for α anomers.[5] The 2,3-*O*-isopropylidene derivative 10 exhibited chemical shifts at δ 25.50 and 27.49 consistent with a β assignement. Interestingly, when the deprotection was carried out in methanol containing sodium methoxide, dihydrofuran 9 was obtained with no trace of 8. Structure assignment 9 was supported by the ^1H NMR spectrum, which exhibited the signal of an olefinic proton at δ 6.27 ($J_{2',3'}$ = 3.0 Hz). The ^{13}C NMR

(1) Ritzmann, G.; Ienaga, K.; Kiriasis, L.; Pfleiderer, W. *Chem. Ber.* **1980**, *113*, 1535. Bannwarth, W.; Pfleiderer, W. *Liebigs Ann. Chem.* **1980**, 50.

(2) Elion, G. B.; Hitchings, G. H. *J. Am. Chem. Soc.* **1947**, *69*, 2553.

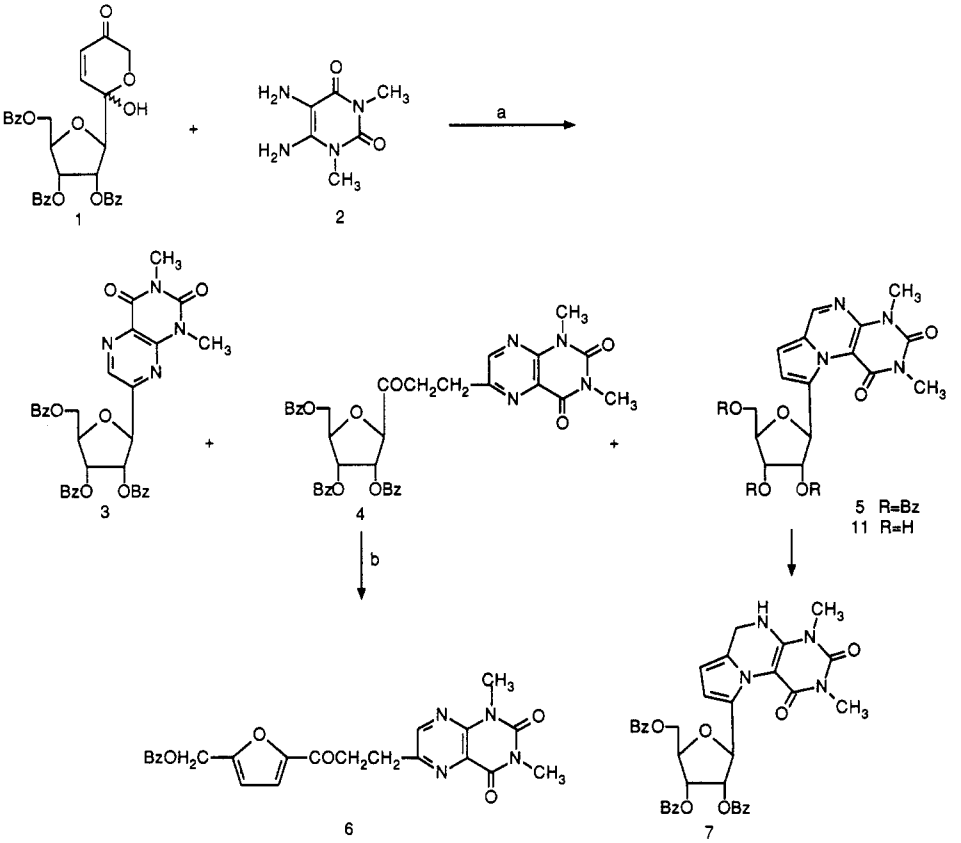
(3) Maeba, I.; Takeuchi, T.; Iijima, T.; Furukawa, H. *J. Org. Chem.* **1988**, *53*, 1401.

(4) Muller, G.; Philipsborn, W. *Helv. Chim. Acta* **1973**, *56*, 2681.

(5) Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensene, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602. Cousineau, T. J.; Secrist, J. A., III *J. Org. Chem.* **1979**, *44*, 4351.

0022-3263/89/1954-3927$01.50/0

Scheme I[a]



[a] (a) Toluene, 80 °C; (b) *p*-TsOH–CH_3Cl; (c) 10% Pd-C/CH_3OH.

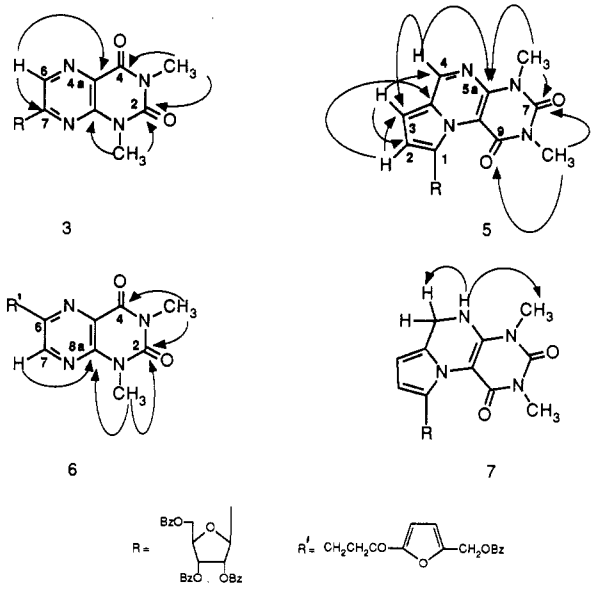
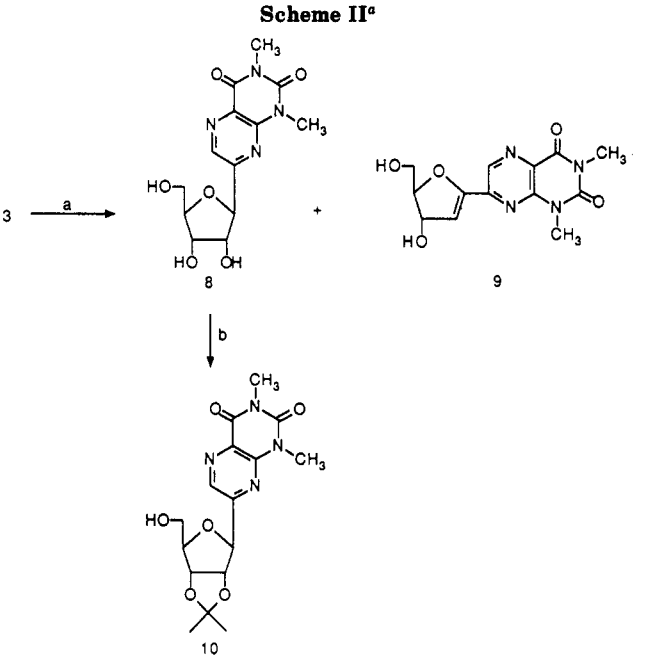


Figure 1. The ^1H–^{13}C long-range COSY experiments with **3**, **5**, and **6**. NOE experiment with **7**.

spectrum and elemental analysis were consistent with the structure of **9** being 1,3-dimethyl-7-(1,4-anhydro-2-deoxy-D-*erythro*-pent-1-enofuranosyl)lumazine. Several instances of *C*-glycosyl compounds containing a dihydrofuran moiety have been reported where side reactions gave furan derivatives.[6] The formation of **9** occurs at room temperature

Scheme II[a]

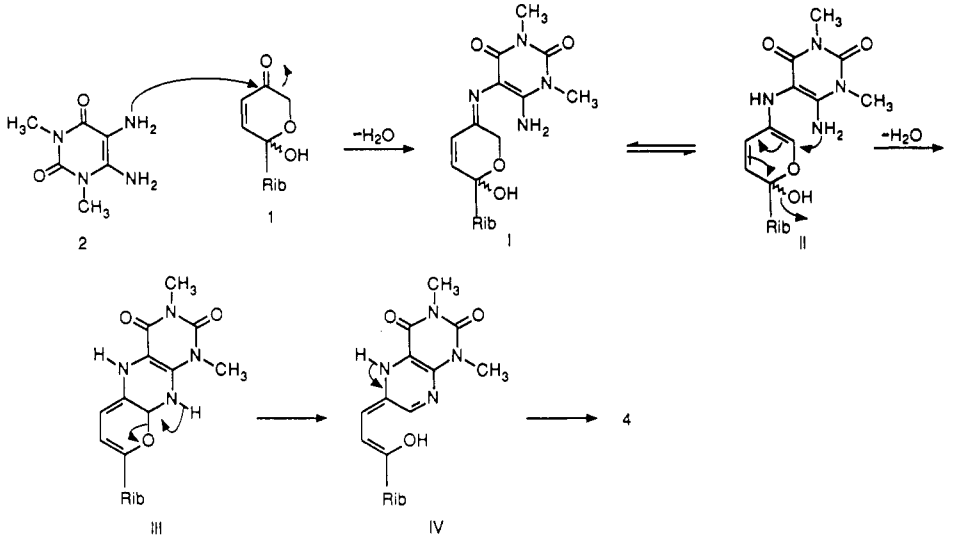


[a] (a) 1 N Na_2CO_3–CH_3OH; (b) *p*-TsOH–acetone.

and undoubtedly results from abstraction by base of H-1′, which has been rendered more acidic by the stronger electron-attracting power of the 4-carbonyl function on the C-7 center. Deprotection of **5** with methanolic sodium methoxide afforded 6,8-dimethyl-1-(β-D-ribofuranosyl)-pyrrolo[1,2-*f*]pteridine-7,9-dione (**11**) (Scheme I). The stereochemistry of **11** was determined by NOE experiment.[7] Irradiation of the two H-5′ signals gave en-

(6) Tam, S.; Klein, R. S.; Heras, F. G.; Fox, J. J. *J. Org. Chem.* **1979**, *44*, 4854. Hennen, W. J.; Robins, R. K. *J. Heterocycl. Chem.* **1985**, *22*, 1747. Fuertes, M.; Garcia-Lopez, T.; Garcia-Munoz, G.; Stud, M. *J. Org. Chem.* **1976**, *41*, 4074.

Scheme III



hancement at H-4′ (6.7%) but none at H-1′, H-3′, or H-2. Irradiation of H-1′ gave enhancement at H-4′ (5.5%), H-2′ (6%), and H-2 (1.6%). This indicated that **11** was the β glycoside.

Experimental Section

Melting points were determined on a Yanagimoto apparatus and are uncorrected. ^{1}H NMR spectra were measured with a JNM-GX-270 spectrometer, with tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on JEOL JNM-FX-100 and JEOL GX-400 spectrometers operating at 25.00 MHz, with tetramethylsilane as an internal standard. Mass spectra were obtained on Hitachi M-52 and M-80 spectrometers. Elemental analyses were determined by the analytical center of this faculty. Analytical thin-layer chromatography was performed on glass plates coated with a 0.5-mm layer of silica gel GF_{254} (Merck). The compounds were detected with UV light (254 nm). Column chromatography was performed on silica gel C-200 (74-149 μm, Wakogel).

1,3-Dimethyl-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)lumazine (3), 1,3-Dimethyl-6-[3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-3-oxopropyl]lumazine (4), and 6,8-Dimethyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[1,2-*f*]pteridine-7,9-dione (5). A solution of pyranulose **1** (224 mg, 0.4 mmol) and 5,6-diamino-1,3-dimethyluracil hydrate **2** (82 mg, 0.5 mmol) in dry toluene (20 mL) was heated at 80 °C for 5 h. After this time, three new compounds were detected (TLC) in the reaction mixture which had R_f values of 0.31, 0.27, and 0.26 (chloroform–methanol, 99:1), respectively. The solvent was removed under reduced pressure. The mixture was separated by preparative TLC with ethyl acetate–hexane (3:1) as the eluent after three elutions.

Compound **3**: R_f 0.27; colorless needles, mp 195–197 °C; 5% (35% from ethylene glycol); SIMS, m/z 637 ([M + H]$^+$, 60); ^{1}H NMR ($CDCl_3$) δ 3.50, 3.52 (each s, 3 each, CH_3), 4.57 (dd, 1, H-5′a, $J_{4',5'a}$ = 3.7 Hz, $J_{5'a,5'b}$ = 12.1 Hz), 4.84 (apparent q, 1, H-4′), 4.92 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.4 Hz), 5.47 (d, 1, H-1′, $J_{1',2'}$ = 2.7 Hz), 5.94 (t, 1, H-2′), 6.09 (t, 1, H-3′), 7.32–8.09 (m, 15, Ar H), 8.75 (s, 1, H-6); ^{13}C NMR ($CDCl_3$) δ 28.94, 29.13 (CH_3), 63.50 (C-5′), 72.86 (C-2′), 75.15 (C-3′), 81.15 (C-4′), 81.40 (C-1′), 127.59 (C-4a), 128.44–133.68 (Ar C), 138.61 (C-6), 147.29 (C-8a), 150.45 (C-4), 156.23 (C-7), 159.54 (C-2), 165.17, 165.45, 165.86 (C=O).

Anal. Calcd for $C_{34}H_{28}N_4O_9$: C, 64.14; H, 4.43; N, 8.80. Found: C, 64.34; H, 4.20; N, 8.59.

Compound **4**: R_f 0.26; colorless foam, 16%; SIMS, m/z 693 ([M + H]$^+$, 47); ^{1}H NMR ($CDCl_3$) δ 3.23–3.48 (m, 4, CH_2CH_2), 3.36, 3.67 (each s, 3 each, CH_3), 4.56–4.79 (m, 3, H-4′, H-5′), 4.89 (d, 1, H-1′, $J_{1',2'}$ = 2.7 Hz), 5.60 (q, 1, H-3′, $J_{2',3'}$ = 5.0 Hz, $J_{3',4'}$ = 5.3 Hz), 6.03 (q, 1, H-2′), 7.26–8.10 (m, 15, Ar H), 8.54 (s, 1, H-7); ^{13}C NMR ($CDCl_3$) δ 27.50, 29.25 (CH_2CH_2), 28.72, 28.90 (CH_3), 64.23 (C-5′), 72.30, 73.41, 79.86, 85.76 (C-1′, C-2′, C-3′, C-4′), 126.48–133.44 (Ar C, C-4a), 147.89 (C-7), 146.55, 151.17, 157.96, 159.89 (C-2, C-4, C-6, C-8a), 165.27, 166.03, 191.94 (C=O).

A solution of pyranulose **1** (22.7 mg, 0.04 mmol) and **2** (8.3 mg, 0.05 mmol) in acetonitrile (2 mL) containing boron trifluoride etherate (15 mg) was stirred at room temperature for 24 h. Workup as above gave compound **4** (5.5 mg, 29%). Due to the unstable nature of this compound, good elemental analysis could not be obtained.

Compound **5**: R_f 0.31; yellow needles; mp 240–242 °C; 30% (13% from ethylene glycol); SIMS, m/z 675 ([M + H]$^+$, 23); ^{1}H NMR ($CDCl_3$) δ 3.24 (s, 3, CH_3-6), 3.73 (s, 3, CH_3-8), 4.48–4.82 (m, 3, H-4′, H-5′), 5.42 (t, 1, H-3′, $J_{2',3'}$ = $J_{3',4'}$ = 5.0 Hz), 5.82 (q, 1, H-2′, $J_{1',2'}$ = 2.7 Hz), 6.70 (d, 1, H-1′), 7.10 (d, 1, H-2, $J_{2,3}$ = 4.4 Hz), 7.26–8.05 (m, 16, Ar H, H-3), 8.76 (s, 1, H-4); ^{13}C NMR ($CDCl_3$) δ 28.72 (CH_3-8), 30.54 (CH_3-6), 63.53 (C-5′), 71.78 (C-3′), 73.71 (C-2′), 78.19 (C-4′), 79.54 (C-1′), 105.95 (C-9a), 116.28 (C-2), 117.65 (C-3), 129.76 (C-3a), 129.78 (C-1), 130.10–134.79 (Ar C), 145.38 (C-5a), 147.95 (C-4), 150.29 (C-9), 153.31 (C-7), 165.29, 165.33, 166.15 (C=O).

Anal. Calcd for $C_{37}H_{30}N_4O_9 \cdot {}^3/_2H_2O$: C, 63.33; H, 4.74; N, 7.97. Found: C, 63.40; H, 4.53; N, 7.63.

Treatment of 4 with *p*-Toluenesulfonic Acid. To a solution of **4** (20 mg, 0.03 mmol) in chloroform (2 mL) was added *p*-toluenesulfonic acid (5 mg), and the resulting solution was stirred at reflux for 6 h. The reaction mixture was neutralized with saturated sodium bicarbonate solution and then extracted with chloroform (3 × 10 mL). The extracts were combined, washed with water, dried over magnesium sulfate, and evaporated in vacuo to a syrup. The residue was purified by preparative TLC with chloroform as the eluent. This afforded 8.1 mg of furan **6** (58%) as a colorless syrup: ^{1}H NMR ($CDCl_3$) δ 3.43–3.49 (m, 4, CH_2CH_2), 3.52, 3.70 (each s, 3 each, CH_3), 5.33 (s, 2, CH_2), 6.60 (d, 1, furan H-4, $J_{3,4}$ = 3.7 Hz), 7.18 (d, 1, furan H-3), 7.28–8.06 (m, 5, Ar H), 8.67 (s, 1, H-7); ^{13}C NMR ($CDCl_3$) δ 28.14, 37.20 (CH_2CH_2), 29.02, 29.72 (CH_3), 58.33 (CH_2), 112.68, 118.18 (furan C-3, C-4), 126.66 (C-4a), 128.57, 129.47, 129.82, 133.39 (phenyl), 146.66 (C-8a), 148.36 (C-7), 150.64 (C-4), 152.11, 152.34 (furan C-2, C-5), 153.98 (C-6), 160.24 (C-2), 165.91, 187.62 (C=O); high-resolution mass spectrum, m/z 448.1363 ($C_{23}H_{20}N_4O_6$ requires 448.1381).

6,8-Dimethyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4,5-dihydropyrrolo[1,2-*f*]pteridine-7,9-dione (7). To a suspension of 10% palladium–carbon (8 mg) in dry methanol (1 mL) was added a solution of tricyclic compound **5** (66 mg, 0.1 mmol) in dry methanol (10 mL), and the mixture was stirred under hydrogen at atmospheric pressure and room temperature for 4 h. After the catalyst was removed by filtration, the solvent was evaporated under reduced pressure. This residue was chromatographed over a column of silica gel with chloroform as the eluent. This afforded 31 mg of **7** (50%) as a yellow syrup. Due to the unstable nature of this compound, good elemental analysis could

(7) Macdonald, S. J. F.; Huizinga, W. B.; McKenzie, T. C. *J. Org. Chem.* **1988**, *53*, 3371.

not be obtained: ^{1}H NMR ($CDCl_3$) δ 3.21, 3.29 (each s, 3 each, CH_3), 4.23 (apparent s, 2, H-4), 4.43 (dd, 1, H-5′a, $J_{4',5'a}$ = 5.1 Hz, $J_{5'a,5'b}$ = 12.0 Hz), 4.56–4.65 (m, 1, H-4′), 4.68 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.4 Hz), 4.77 (br s, 1, NH, exchanges with D_2O), 5.67 (dd, 1, H-3′, $J_{2',3'}$ = 5.4 Hz, $J_{3',4'}$ = 6.8 Hz), 5.83 (dd, 1, H-2′, $J_{1',2'}$ = 3.9 Hz), 5.86 (d, 1, H-1′), 6.21 (d, 1, H-2 or H-3, $J_{2,3}$ = 3.7 Hz), 6.41 (d, 1, H-2 or H-3), 7.26–8.08 (m, 15, Ar H); ^{13}C NMR ($CDCl_3$) δ 28.42, 28.90 (CH_3), 41.23 (CH_2), 64.36 (C-5′), 72.44, 74.81, 78.08, 78.46 (C-1′, C-2′, C-3′, C-4′), 98.50 (C-9a), 103.38, 108.85 (C-2, C-3), 126.01–133.50 (Ar C, C-1, C-3a), 146.87, 149.78, 156.36 (C-5a, C-7, C-9), 165.44, 165.55, 166.30 (C=O).

1,3-Dimethyl-7-(β-D-ribofuranosyl)lumazine (8) and 1,3-Dimethyl-7-(1,4-anhydro-2-deoxy-D-*erythro*-pent-1-enofuranosyl)lumazine (9). To a solution of 1,3-dimethyllumazine **3** (201 mg, 0.33 mmol) in methanol (10 mL) was added a 1 N sodium carbonate aqueous solution (2 mL) at 0 °C for 2 h, and then the reaction mixture was rendered neutral with acetic acid and evaporated to dryness in vacuo. TLC (chloroform–methanol, 9:1) showed that the colorless syrup contained two major components (R_f 0.35 and 0.32). The mixture was separated by preparative TLC with chloroform–methanol (9:1) as the eluent after three elutions.

Compound **8**: R_f 0.32; colorless needles, mp 220–222 °C; 32.7%; CIMS, m/z 325 ([M + H]$^+$, 5); ^{1}H NMR (CD_3OD) δ 3.35, 3.48 (each s, 3 each, CH_3), 3.74 (dd, 1, H-5′a, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 12.1 Hz), 3.88 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.0 Hz), 4.05–4.20 (m, 2, H-3′, H-4′), 4.25 (dd, 1, H-2′, $J_{1',2'}$ = 5.1 Hz, $J_{2',3'}$ = 4.7 Hz), 5.01 (d, 1, H-1′), 8.08 (s, 1, H-6); ^{13}C NMR (CD_3SOCD_3) δ 28.31, 28.72 (CH_3), 61.25 (C-5′), 71.02, 76.64, 83.37, 84.89 (C-2′, C-3′, C-4′, C-1′), 128.30 (C-4a), 137.60 (C-6), 147.02 (C-8a), 150.41 (C-4), 152.81 (C-7), 159.01 (C-2).

Anal. Calcd for $C_{13}H_{16}N_4O_6$: C, 48.15; H, 4.97; N, 17.28. Found: C, 48.54; H, 5.30; N, 17.32.

Compound **9**: R_f 0.35; yellow needles, mp 225–226 °C; 38.6%; SIMS, m/z 307 ([M + H]$^+$, 16); ^{1}H NMR (CD_3OD) δ 3.48, 3.70 (each s, 3 each, CH_3), 3.73 (d, 2, H-5′, $J_{4',5'}$ = 5.7 Hz), 4.57 (q, 1, H-4′), 4.95 (dd, 1, H-3′, $J_{2',3'}$ = 3.0 Hz, $J_{3',4'}$ = 5.7 Hz), 6.27 (d, 1, H-2′), 8.78 (s, 1, H-6); ^{13}C NMR (CD_3OD) δ 29.95, 30.33 (CH_3), 64.12 (C-5′), 76.87, 92.86 (C-3′, C-4′), 109.98 (C-2′), 129.39 (C-4a), 138.48 (C-6), 149.44, 150.00 (C-1′, C-8a), 153.03 (C-4), 157.37 (C-7), 162.56 (C-2).

Anal. Calcd for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.66; H, 4.63; N, 18.06.

Methanolic sodium methoxide (16 mg, 0.3 mmol) was added to the protected *C*-nucleoside **3** (20 mg, 0.03 mmol) in 2 mL of methanol. The mixture was allowed to stand at 0 °C for 1.5 h, then rendered neutral with acetic acid, and evaporated. The residue was chromatographed over a column of silica gel with chloroform–methanol (4:1) as the eluent. This afforded 8.8 mg of **9** (82%) as yellow needles.

1,3-Dimethyl-7-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)lumazine (10). To a solution of **8** (91 mg, 0.3 mmol) in acetone (5 mL) was added *p*-toluenesulfonic acid (10 mg), and the resulting solution was stirred at room temperature for 1 h. The reaction mixture was neutralized with satruated sodium bicarbonate solution and then extracted with chloroform (3 × 10 mL). The extracts were combined, washed with water, dried over magnesium sulfate, and evaporated in vacuo to a syrup. The residue was purified by preparative TLC with chloroform as the eluent. This afforded 71 mg of **10** (72%) as a colorless syrup: ^{1}H NMR ($CDCl_3$) δ 1.40, 1.65 (each s, 3 each, isopropylidene CH_3), 3.55, 3.72 (each s, 3 each, CH_3), 3.70 (dd, 1, H-5′a, $J_{4',5'a}$ = 3.0 Hz, $J_{5'a,5'b}$ = 11.7 Hz), 3.93 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.0 Hz), 4.46 (apparent q, 1, H-4′), 4.88 (q, 1, H-3′, $J_{2',3'}$ = 4.1 Hz, $J_{3',4'}$ = 2.3 Hz), 4.93 (t, 1, H-2′), 5.18 (d, 1, H-1′), 8.70 (s, 1, H-6); ^{13}C NMR ($CDCl_3$ partial) δ 25.50, 27.49 (isopropylidene CH_3), 29.07, 29.49 (CH_3), 63.36 (C-5′), 82.72, 85.90, 85.94, 86.23 (C-1′, C-2′, C-3′, C-4′), 138.77 (C-6).

6,8-Dimethyl-1-(β-D-ribofuranosyl)pyrrolo[1,2-*f*]pteridine-7,9-dione (11). To a solution of tricyclic compound **5** (50 mg, 0.07 mmol) in methanol (4 mL) was added methanolic sodium methoxide (36 mg, 0.7 mmol) at 0 °C for 1.5 h, and then the reaction mixture was rendered neutral with acetic acid and evaporated. The residue was purified by preparative TLC with chloroform–methanol (9:1) as the eluent. This afforded 15.3 mg of **11** (55%) as yellow needles: mp 236–238 °C; SIMS, m/z 363 ([M + H]$^+$, 52); ^{1}H NMR (CD_3SOCD_3) δ 3.35, 3.62 (each s, 3 each, CH_3), 3.37–3.48 (m, 2, H-5′), 3.71–3.75 (m, 2, H-2′, H-3′), 3.85 (t, 1, H-4′, $J_{3',4'}$ = $J_{4',5'}$ = 5.1 Hz), 5.74 (d, 1, H-1′), 7.25, 7.29 (each d, 1 each, H-2 or H-3, $J_{2,3}$ = 4.8 Hz), 8.99 (s, 1, H-4); ^{13}C NMR (CD_3SOCD_3) δ 28.52, 30.07 (CH_3), 61.54 (C-5′), 70.78, 74.67, 78.26, 83.75 (C-1′, C-2′, C-3′, C-4′), 105.16 (C-9a), 110.27, 116.96 (C-2, C-3), 129.29 (C-3a), 137.48 (C-1), 144.59 (C-5a), 147.75 (C-4), 150.01, 156.38 (C-7, C-9).

Anal. Calcd for $C_{16}H_{18}N_4O_6$: C, 53.03; H, 5.01; N, 15.46. Found: C, 53.37; H, 5.06; N, 15.65.

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Synthesis and Reactivity of Benzylic Epoxides Derived from 1,2,3,9,10,10a-Hexahydrophenanthrene. Search for a Unified Mechanism for the Ring Opening of 2-Aryloxiranes

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The diastereoisomeric benzylic epoxides **4a** and **4b** were synthesized, and their ring-opening reactions under acidic conditions were compared with those of the known epoxides **2** and **3**. The chemical behavior of **4** more nearly resembles that of **3**, thus suggesting that the differences in chemical behavior between **2** and **3** could be ascribed to the different conformational rigidity of the aryl in these systems. The ring opening of **4** forms significant amounts of unsaturated alcohol and ketone in addition to the diastereoisomeric diols. The results obtained in the present study are difficult to explain by means of either of the two mechanistic schemes suggested for 2-aryloxiranes.

Introduction

Studies on polycyclic aromatic hydrocarbons have indicated that diol epoxides of type **1**, with the oxirane ring in the "bay region", are the metabolites responsible for the mutagenic and carcinogenic activity of these hydrocarbons.[1] Accordingly, there is interest in the mechanism

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