

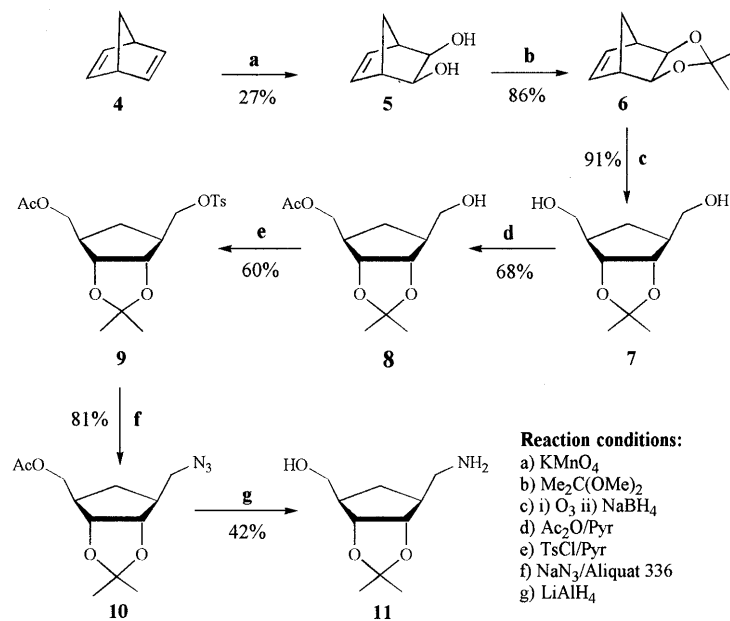


Chart 1

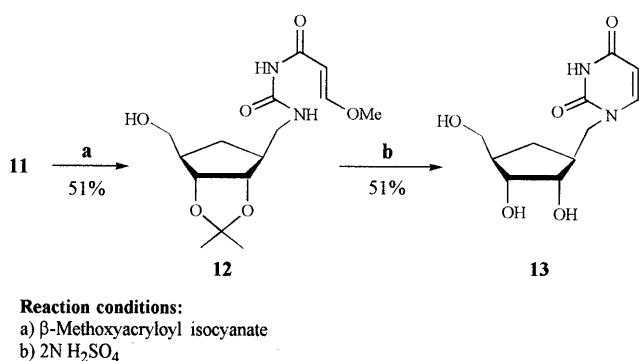


Chart 2

hydrolysis of the isopropylidene protecting group, thus affording the desired homouridine analogue **13**.

Experimental

Melting points are uncorrected and were determined in a Reichert Kofler thermopan. IR spectra of samples in KBr disc (for solids) or as films between NaCl plates (for oils) were obtained in a Perkin Elmer FT-IR 1640 spectrometer. ^1H - and ^{13}C -NMR spectra were recorded in a Bruker AMX-300 spectrometer, at 300 and 75 MHz, respectively, with tetramethylsilane (TMS) as an internal standard. Microanalyses were performed by a Perkin Elmer 240B Elemental Analyser. Column chromatography was done on Solvants Documentation Syntheses (SDS) silica chromagel 60 (70–230 mesh). Thin layer chromatography was performed on Merck GF₂₅₄ chromatoplates. Reagents and solvents were of commercial grade and were all supplied by Aldrich Chemical Co.

***exo-cis*-5-Norborene-2,3-diol (5)** Finely powdered KMnO_4 (15.8 g, 100 mmol) was slowly added in several portions, to a cooled (-65°C), vigorously stirred solution of norbornadiene (25 ml, 232 mmol) in acetone (300 ml), so that the reaction temperature did not exceed -60°C . After addition was complete, the reaction mixture was stirred at -65°C for 1 h, then treated with an ice-cold solution of $\text{Na}_2\text{S}_2\text{O}_5$ (21.75 g, 114 mmol) in water (100 ml) and stirred at -65°C for 30 min and at $+40^\circ\text{C}$ for 15 min. The cooled mixture was filtered through a bed of silica gel, which was then washed with 5:1 (v/v) acetone/water, and the combined filtrates and washings were concentrated under reduced pressure to eliminate acetone. The resulting aqueous solution was extracted with dichloromethane, and the organic layer was dried over anhydrous Na_2SO_4 and evaporated to leave a crystalline solid **5** (3.0 g, 27%), mp (cyclohexane) $114\text{--}116^\circ\text{C}$ (lit.⁸) $114\text{--}116^\circ\text{C}$. IR (KBr) ν (cm^{-1}): 3410,

3245, 2983, 1570, 1078. ^1H -NMR (CDCl_3) δ (ppm): 1.64 (1H, dt, $J_d=9.29$, $J_t=1.62$ Hz, 7-HH), 1.90 (1H, d, $J=9.29$ Hz, 7-HH), 2.70 (2H, br s, OH, D_2O exch.), 2.73 (2H, dd, $J=3.47$, 1.42 Hz, 1-H + 4-H), 3.72 (2H, d, $J=1.32$ Hz, 2-H + 3-H), 6.04 (2H, t, $J=1.73$ Hz, 5-H + 6-H). ^{13}C -NMR δ (ppm): 136.74, 69.35, 48.37, 42.56.

***exo-cis*-5,6-(Isopropylidenedioxy)bicyclo[2.2.1]hept-2-ene (6)** A solution of the diol **5** (5.00 g, 39.6 mmol) and a catalytic amount of *p*-toluenesulfonic acid in 2,2-dimethoxypropane was stirred until the diol was no longer detectable by TLC (ca. 3 h), whereupon the reaction mixture was poured into 5% (w/v) aqueous NaHCO_3 (200 ml). The whole was extracted with CH_2Cl_2 , and the organic phase was separated, washed with water, and dried over anhydrous Na_2SO_4 . The solvent was removed *in vacuo*, and the resulting oily residue (5.95 g) was chromatographed on silica gel with CH_2Cl_2 to afford **6** a colorless oil (5.67 g, 86%). IR (film) ν (cm^{-1}): 3064, 2985, 1635, 1531, 1299, 1234. ^1H -NMR (CDCl_3) δ (ppm): 1.23 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.63 (1H, dt, $J_d=8.98$, $J_t=1.50$ Hz, 7-anti-H), 1.93 (1H, d, $J=8.98$ Hz, 7-syn-H), 2.71 (2H, t, $J=1.48$ Hz, 1-H + 4-H), 4.14 (2H, d, $J=1.31$ Hz, 5-H + 6-H), 6.04 (2H, t, $J=1.67$ Hz, 2-H + 3-H).

***t*-4,5-(Isopropylidenedioxy)-*r*-1,3-cyclopentane-1,3-dimethanol (7)** In a Fischer 503 ozonolysis apparatus, a solution of **6** (4.00 g, 24.1 mmol) in 2:1 methanol/ CH_2Cl_2 was cooled (-78°C) and vigorously stirred while O_3 (6 g h^{-1}) was bubbled through it for 1 h (the O_3 was generated from 60 l h^{-1} of O_2 , in accordance with the technical specifications of the apparatus). Solid NaBH_4 (0.22 g, 5.79 mmol) was added portionwise while maintaining the reaction temperature at around -78°C , and then the temperature was raised to -5°C and further NaBH_4 (0.93 g, 24.6 mmol) was added. The mixture was stirred for 4 h, warmed to room temperature, and concentrated to afford a white, solid residue. This was triturated in ethyl acetate, collected by filtration, washed with more ethyl acetate, and then dissolved in methanol. This solution was adjusted to pH 7 with concentrated HCl, the solvent was evaporated, and the residue was chromatographed on silica gel with 2:1 CH_2Cl_2 /ethyl acetate to afford **7** as a colorless oil (4.44 g, 91%). IR (film) ν (cm^{-1}): 3392, 2931, 1377, 1058. ^1H -NMR (CDCl_3) δ (ppm): 1.19–1.29 (1H, m, 2-HH), 1.26 (3H, s, CH_3), 1.45 (3H, s, CH_3), 2.04 (1H, dt, $J_d=12.96$, $J_t=7.64$ Hz, 2-HH), 2.18–2.22 (2H, m, 1-H + 3-H), 3.39 (2H, br s, $2 \times \text{OH}$, D_2O exch.), 3.59 (2H, part A of a ABM system; $J_{AB}=10.60$, $J_{AM}=6.18$ Hz, 1,3-(CHH)₂), 3.61 (2H, part B of a ABM system, $J_{BA}=10.60$, $J_{BM}=5.85$ Hz, 1,3-(CHH)₂), 4.35 (2H, d, $J=3.05$ Hz, 4-H + 5-H). Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_4$: C, 59.40; H, 8.97. Found: C, 59.25; H, 9.03.

($\pm$)-*c*-4-(Hydroxymethyl)-*t*-2,*t*-3-(isopropylidenedioxy)-*r*-1-cyclopentylmethyl Acetate (8) A solution of **7** (3.95 g, 19.5 mmol) in pyridine (25 ml) and acetic anhydride (1.85 ml, 19.6 mmol) was stirred overnight at room temperature. The solvent was removed *in vacuo*, and the oily residue (4.40 g) was chromatographed on silica gel with 1:1 hexane/ethyl

acetate and then ethyl acetate. The diacetate of **7** (0.99 g, 25%) eluted first, and then the racemic monoacetate **8** (2.05 g, 52%); in the more polar eluent, some diol **7** (0.75 g, 19%) was recovered. For **8** (68%, on the basis of unrecovered **7**), IR (film), ν (cm^{-1}): 3462, 2986, 2937, 1737. $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 1.28 (3H, s, CH_3), 1.19–1.30 (1H, m, 5-HH), 1.48 (3H, s, CH_3), 2.05 (3H, s, COCH_3), 1.99–2.10 (1H, m, 5-HH), 2.18–2.29 (1H, m, 4-H), 2.31–2.41 (1H, m, 1-H), 3.61–3.69 (2H, m, 4- CH_2), 4.08 (2H, d, $J=6.38$ Hz, 1- CH_2), 4.13–4.44 (2H, m, 2-H + 3-H).

($\pm$)-*r*-2,*t*-3-(Isopropylidenedioxy)-*c*-4-(tosyloxymethyl)-*r*-1-cyclopentylmethyl Acetate (9**)** *p*-Toluenesulfonyl chloride (5.00 g, 26.5 mmol) was added to a cooled (0 °C) solution of **8** (4.56 g, 18.7 mmol) in dry pyridine (11 ml) under argon. The mixture was stirred at room temperature for 24 h, then poured into 2N HCl (70 ml) and extracted with diethyl ether (3 $\times$ 70 ml), and the combined extracts were washed with 5% (w/v) NaHCO_3 and water, then dried over anhydrous Na_2SO_4 . Removal of the solvent *in vacuo* gave an oil, which was chromatographed on silica gel with 9:1 (v/v) toluene/ethyl acetate to afford **9** as a colorless oil (4.41 g, 60%). IR (film) ν (cm^{-1}): 2936, 1740, 1189, 1177, 1070. $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 1.25 (3H, s, CH_3), 1.22–1.34 (1H, m, 5-HH), 1.45 (3H, s, CH_3), 2.05 (3H, s, COCH_3), 2.01–2.10 (1H, m, 5-HH), 2.28–2.35 (2H, m, 1-H + 4-H), 2.45 (3H, s, 4'- CH_3), 3.99–4.12 (4H, m, 1- CH_2 + 4- CH_2), 4.23–4.31 (2H, m, 2-H + 3-H), 7.34 (2H, d, $J=8.16$ Hz, 3'-H + 5'-H), 7.78 (2H, d, $J=8.16$ Hz, 2'-H + 6'-H).

($\pm$)-*c*-4-(Azidomethyl)-*r*-2,*t*-3-(isopropylidenedioxy)-*r*-1-cyclopentylmethyl Acetate (10**)** Compound **9** (2.92 g, 7.33 mmol) was added to a solution of sodium azide (0.96 g, 14.8 mmol) and methyltriethylammonium chloride (Aliquat 336) (0.30 g, 0.72 mmol) in water (4 ml), and the mixture was stirred at 75 °C for 5 h. The cooled mixture was diluted with ethyl acetate (16 ml), and the organic layer was separated, washed with saturated NaCl solution and dried over anhydrous Na_2SO_4 . Removal of the solvent *in vacuo* gave an oil (1.90 g), which was chromatographed on silica gel with ethyl acetate. Evaporation of the early eluate fractions gave **10** as a colorless oil (1.7 g, 81%). IR (film) ν (cm^{-1}): 2986, 2935, 1743, 1278, 1246. $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 1.30 (3H, s, CH_3), 1.21–1.33 (1H, m, 5-HH), 1.49 (3H, s, CH_3), 2.07 (3H, s, COCH_3), 2.04–2.15 (1H, m, 5-HH), 2.24–2.31 (1H, m, 4-H), 2.33–2.43 (1H, m, 1-H), 3.40 (1H, part A of a ABM system, $J_{\text{AB}}=12.22$, $J_{\text{AM}}=6.35$ Hz, 4-HH), 3.42 (1H, part B of a ABM system, $J_{\text{BA}}=12.22$, $J_{\text{BM}}=6.59$ Hz, 4-CHH), 4.10 (2H, d, $J=6.20$ Hz, 1- CH_2), 4.27–4.39 (2H, m, 2-H + 3-H). *Anal.* Calcd for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_4$: C, 53.35; H, 7.11; N, 15.60. Found: C, 53.07; H, 7.21; N, 15.48.

($\pm$)-*c*-4-(Aminomethyl)-*r*-2,*t*-3-(isopropylidenedioxy)-*r*-1-cyclopentylmethanol (11**)** A solution of LiAlH_4 (1.86 g, 48.8 mmol) in tetrahydrofuran (THF) (60 ml) was carefully added to a cooled (0 °C) solution of **10** (1.60 g, 5.94 mmol) in THF (100 ml). The mixture was warmed and left at reflux for 6 h, then cooled and treated with water (50 ml), and most of the THF was evaporated *in vacuo*. The remaining aqueous mixture was extracted with CH_2Cl_2 (2 $\times$ 50 ml), and the combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated to a brown oil, which was chromatographed on silica gel with 1:1 (v/v) methanol/ethyl acetate to afford **11** as an oil (0.50 g, 42%). $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 1.07–1.23 (1H, m, 5-HH), 1.31 (3H, s, CH_3), 1.51 (3H, s, CH_3), 1.96–2.02 (1H, m, 5-HH), 2.03–2.17 (1H, m, 4-H), 2.20–2.30 (1H, m, 1-H), 2.78 (2H, d, $J=6.19$ Hz, 4- CH_2), 3.67 (1H, part A of a ABM system, $J_{\text{AB}}=10.62$, $J_{\text{AM}}=6.52$ Hz, 1-CHH), 3.69 (1H, part B of a ABM system, $J_{\text{BA}}=10.62$, $J_{\text{BM}}=5.65$ Hz, 1-CHH), 4.30 (1H, dd, $J=6.89$, 4.89 Hz, 3-H), 4.41 (1H, dd, $J=6.89$, 5.20 Hz, 2-H). *Anal.* Calcd for $\text{C}_{10}\text{H}_{19}\text{NO}_3$: C, 59.68; H, 9.52; N, 6.96. Found: C, 59.45; H, 9.65; N, 7.18.

($\pm$)-*N*-[*c*-4-(Hydroxymethyl)-*r*-2,*t*-3-(isopropylidenedioxy)-*r*-1-cyclo-

pentylmethyl]-*N'*-(3-methoxyacryloyl)urea (12**)** A freshly prepared toluene solution of β -methoxyacryloyl isocyanate (1.9 ml, *ca.* 1.2 mmol),^{12,13} was added to a cooled (–15 °C) solution of **11** (0.17 g, 0.84 mmol) in dimethylformamide (4.0 ml) with stirring under argon, at such a rate that the reaction temperature remained < –10 °C. The mixture was allowed to warm to room temperature and further stirred overnight. The solvent was removed *in vacuo* (ethanol was added so as to form a low-boiling ternary azeotrope), and the resulting residue (0.24 g) was chromatographed on silica gel with 95:5 (v/v) CHCl_3 /methanol. Concentration of the eluate gave **12** as an oil (0.14 g, 51%). $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 1.29 (3H, s, CH_3), 1.21–1.31 (1H, m, 5'-HH), 1.48 (3H, s, CH_3), 2.02–2.21 (3H, m, 1'-H + 4'-H + 5'-HH), 2.25 (1H, br s, OH, D_2O exch.), 3.45–3.54 (2H, m, CH_2N), 3.70 (3H, s, OCH_3), 3.69–3.75 (2H, m, CH_2O), 4.23–4.27 (1H, m, 2'-H), 4.41–4.45 (1H, m, 3'-H), 5.30 (1H, d, $J=12.52$ Hz, OC–CH=), 7.68 (1H, d, $J=12.52$ Hz, =CH–O–), 8.72 (1H, s, NH, D_2O exch.), 9.34 (1H, s, N'H, D_2O exch.).

($\pm$)-1-[*r*-2,*t*-3-Dihydroxy-*c*-4-(hydroxymethyl)-*r*-1-cyclopentylmethyl]-1,2,3,4-tetrahydropyrimidine-2,4-dione (13**)** A mixture of **12** (100 mg, 0.30 mmol) and 2N H_2SO_4 (1.7 ml) was refluxed for 3 h, then the hot mixture was treated with a small amount of activated carbon and filtered. The filtrate was adjusted to pH 7 with 2N NaOH, the solvent was evaporated, and the residue was extracted with ethanol. The ethanolic extracts were concentrated *in vacuo*, and the resulting oil was chromatographed on silica gel with 9:1 (v/v) CHCl_3 /methanol. Concentration of the eluate gave **13** as an oil (40 mg, 51%). $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 0.85–0.95 (1H, m, 5'-HH), 1.71–2.02 (3H, m, 1'-H + 4'-H + 5'-HH), 3.30 (3H, br s, 3 $\times$ OH, D_2O exch.), 3.45–3.57 (2H, m, CH_2O), 4.07–4.21 (2H, m, CH_2N), 4.40–4.46 (1H, m, 3'-H), 4.62–4.67 (1H, m, 2'-H), 5.43 (1H, d, $J=7.64$ Hz, 5-H), 7.37 (1H, d, $J=7.64$ Hz, 6-H), 10.97 (1H, br s, NH, D_2O exch.). UV λ_{max} (MeOH) nm (log ϵ): 269.6 (4.05). HR-EI-MS m/z : Calcd for $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_5$: 256.1059. Found: 256.1048.

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