alcohol), 10 ml. of *t*-butyl alcohol, 2.65 ml. of 1 *N* H_2SO_4, and 5.30 ml. of 30% H_2O_2 cooled in an ice–salt bath, a solution of 1.96 ml. of **2** in 10 ml. of *t*-butyl alcohol was added (the solution acquired a deep red-brown color). The temperature was maintained between 0 and −5°, and at the end of 2 hr., 10 ml. of water and 1.74 ml. of 5 *N* NaOH was added to neutralize the solution (phenolphthalein). Sodium metabisulfite (0.11 g.) was added and the mixture was stirred at reflux for 1 hr. After stripping off solvents, the residue was evaporatively distilled at 205° (20 μ). The 1.70-g. distillate on crystallization from *t*-butyl alcohol and acetone afforded 1.19 g. of white solid, m.p. 159–162° (46% yield). The analytical sample, recrystallized from methanol and dried at 100° (50 μ) had m.p. 166.5–167°.

Anal. Calcd. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.25; H, 9.02.

***trans*-2,5-Dihydroxy-1,4-dimethylenecyclohexane (5).**—To 7.6 g. (0.20 mole) of $LiAlH_4$ in 150 ml. of tetrahydrofuran at reflux, there was added gradually with stirring a solution of 10.3 g. (0.04 mole) of **4** in 100 ml. of warm tetrahydrofuran over an 11-min. period. After refluxing for 1 hr. 39 ml. of ethyl acetate was added dropwise followed by 15 ml. of water. Carbon dioxide was passed into the mixture from which, after filtration, evaporation of the filtrate, and crystallization from chloroform, there was obtained 2.09 g. of **5**, a white solid, m.p. 160–161°. The analytical sample, from chloroform, had m.p. 162.5–163°.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63; O, 22.83. Found: C, 68.80; H, 8.86; O, 22.87.

1,2,4,5-Tetrahydroxycyclohexanedimethanol-1,4 (6).—To a solution of 25 ml. of catalyst (0.005 g. of OsO_4/ml. of *t*-butyl alcohol), 40 ml. of *t* butyl alcohol, 20 ml. of acetone, 5 ml. of 1 *N* H_2SO_4, and 10 ml. of 30% H_2O_2 prechilled to −15°, there was added 3.85 g. of **5**. The mixture was stirred overnight at −15° (ice–salt bath) and filtered. The white solid obtained, after washing with acetone and air drying, weighed 3.00 g., m.p. 225.5–226.5° dec. (52% yield). The analytical sample, crystallized from water and dried at 100° *in vacuo*, m.p. 238.5–239.5° dec.

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.40; H, 7.63.

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New Compounds

Synthesis of β-5-Fluoro-2′-deoxyuridylyl-(5′→5′)-β-5-fluoro-2′-deoxyuridine[1]

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It is well known that nucleotides cannot penetrate Ehrlich ascites cells without degradation,[3] presumably because of their high negative charge. Since 5-fluoro-2′-deoxyuridine 5′-monophosphate (FUDRP) is the active intracellular form of 5-fluorouracil and 5-fluoro-2′-deoxyuridine (FUDR),[4] a number of derivatives were synthesized in which the phosphate group was altered in various ways.[5] However, none of these was more effective than the simple nucleotide at inhibiting the incorporation of labeled formate into DNA thymine in suspensions of Ehrlich ascites cells.[6] Hence, the report of Montgomery, *et al.*,[7] indicating that the 5′,5′-dinucleoside monophosphate of 6-mercaptopurine entered cells resistant to 6-mercaptopurine, stimulated us to synthesize the corresponding derivative of FUDRP, which is described below. This compound was less effective than FUDRP at inhibiting the above system and did not inhibit cells resistant to FUDR.[8] Consequently it does not enter these cells intact.

Experimental Section

Preparation of 3′-Acetyl-FUDRP.—5-Fluoro-2′-deoxyuridine 5-monophosphate diammonium salt[5] (100 mg.) was dissolved in 2 ml. of freshly distilled pyridine, and 1.0 ml. of distilled acetic anhydride was added. The mixture was stoppered, shaken vigorously, and allowed to remain at room temperature for 24 hr. The excess acetic anhydride was destroyed with 2 ml. of water, and the solution was evaporated *in vacuo* at 30°. When most of the pyridine and acetic acid had been removed, 5 ml. of water was added and evaporated to an oil; this process was repeated three times until all of the acetic acid had been removed. The residue was then evaporated *in vacuo* twice with dry pyridine to remove traces of water and was used for the next reaction without purification.

Condensation with 3′-Acetyl-FUDR.—The 3′-acetyl-FUDRP thus obtained (115 mg.) was dissolved in 2 ml. of dry pyridine, and 90 mg. of 3′-acetyl-FUDR[5] was added. A 4 molar excess (250 mg.) of dry dicyclohexylcarbodiimide was added, and the reaction was shaken at room temperature for 60 hr. The dicyclohexylurea was filtered and washed with a few drops of pyridine. Water (10 ml.) was added to the filtrate, and the aqueous solution was extracted three times with 10 ml. of heptane. The aqueous phase was evaporated to dryness *in vacuo*, and the residue was coevaporated three times water water to remove the pyridine. The residue was then shaken with 50 ml. of warm water, the insoluble material was filtered, and the filtrate was evaporated to 10 ml. This solution, containing the protected dinucleoside monophosphate was mixed with 10 ml. of 1 *N* NaOH and heated under reflux for 1 hr. The solution was cooled and Dowex 50 (H^+) was added to remove sodium ions. After filtration, the neutral, pale yellow solution was concentrated *in vacuo* to 5 ml.

A Dowex-1 formate column (2 × 25 cm.) was prepared, and the above product was added. The column was washed with water, and a peak of FUDR was eluted The column was then eluted with 0.5 *M* formic acid, and two small unidentified peaks were removed. A large peak was obtained on elution with 2 *M* formic acid, which contained the desired product. The fractions comprising this peak were combined (volume 1 l.) and evaporated in *vacuo* to 200 ml. Water was added and evaporated several times to remove formic acid. When the volume was reduced to 0.5 ml., ethanol was coevaporated twice, and excess ammonia was added. The ammonia was evaporated, and the residue was extracted with 90% ethanol. A small amount of insoluble, reddish brown material was removed and discarded, and the alcoholic solution was evaporated to a small volume. The ammonium salt was precipitated by the addition of ether, and the product was collected by centrifugation, washed with ether, and dried over P_2O_5 to give 59.2 mg. of **β-5-fluoro-2′-deoxyuridylyl-(5′→5′)-β-5-fluoro-2′-deoxyuridine ammonium salt.** This material gave a single spot on paper chromatography in isopropyl alcohol–ammonia–water (7:1:2, v./v.) (R_f 0.28). In this system FUDR has an R_f of 0.62 and FUDRP 0.14. The ultraviolet spectrum had a maximum at 269 mμ, which did not shift in alkali; the optical density was 21.0/mg. (molar extinction 15,700/g.-atom of phosphorus).

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