Regiospecific Formation of 9,3-Propeno-8-aza-9*H*-xanthines and their Conversion into 3-(2,3-Dihydroxypropyl)-8-aza-9*H*-xanthine and Derivatives

Milan Jokić and Vinko Škarić *
Laboratory of Stereochemistry and Natural Products, 'Ruđer Bošković' Institute, 41001 Zagreb, Croatia, Yugoslavia

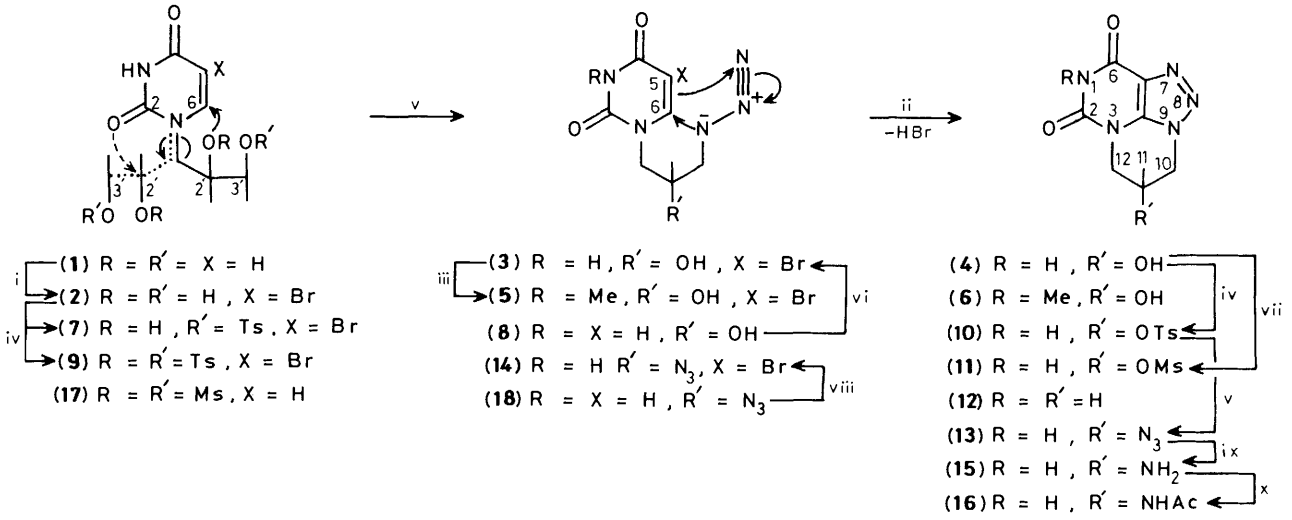
A novel series of C-11-functionalized 3,9-propano-8-aza-9*H*-xanthine and related compounds have been synthesized. With 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 11-methylsulphonyloxy-3,9-propano-8-aza-9*H*-xanthine (**11**) underwent a regiospecific elimination to give 9,3-propeno-8-aza-9*H*-xanthine (**19**). An equally interesting result was obtained from (**19**) on osmium tetraoxide oxidation, when 10,11-dihydroxy-3,9-propano-8-aza-9*H*-xanthine (**20**) was formed and then transformed into 3-(2,3-dihydroxypropyl)-8-aza-9*H*-xanthine (**22**) by aqueous $NaBH_4$ treatment. Reaction of compound (**19**) with bromine in methanol afforded 11-bromo-10-methoxy-3,9-propano-8-aza-9*H*-xanthine (**28**). The latter on stereochemically controlled elimination with DBU led to 10-methoxy-3,9-propeno-8-aza-9*H*-xanthine (**29**), easily converted into 11-bromo-10,12-dimethoxy-3,9-propano-8-aza-9*H*-xanthine (**30**).

In previous communications[1,2] we reported that the *syn*-cyclization (dotted lines) of 1-(2,3-dihydroxypropyl)uracil (**1**) (Scheme 1) depends on its activation at C-2′ and on the reaction conditions employed. On the other hand, the biotransformation of the antiviral 1-allyl-6-chloro-3,5-diethyluracil[3] to the corresponding 1-(2,3-dihydroxypropyl)uracil derivative is enhanced by an *anti*-cyclization process,[2] yielding the corresponding 2-hydroxymethyltetrahydro-oxazolo[3,2-*c*]-pyrimidine-5,7(6*H*)-dione compound.[4] It was also shown that the polarization of the C-5,C-6 double bond by the bromination of (**1**) to give 5-bromo-1-(2,3-dihydroxypropyl)uracil[2] (**2**) resulted in a marked increase of C-2′,C-6-cyclization-selectivity. The C-5 halogenation of the pyrimidine nucleosides, such as 5′-azido-5′-deoxyuridine, also gave easy access to the intramolecular C-5,C-6-cycloaddition processes.[5–7]

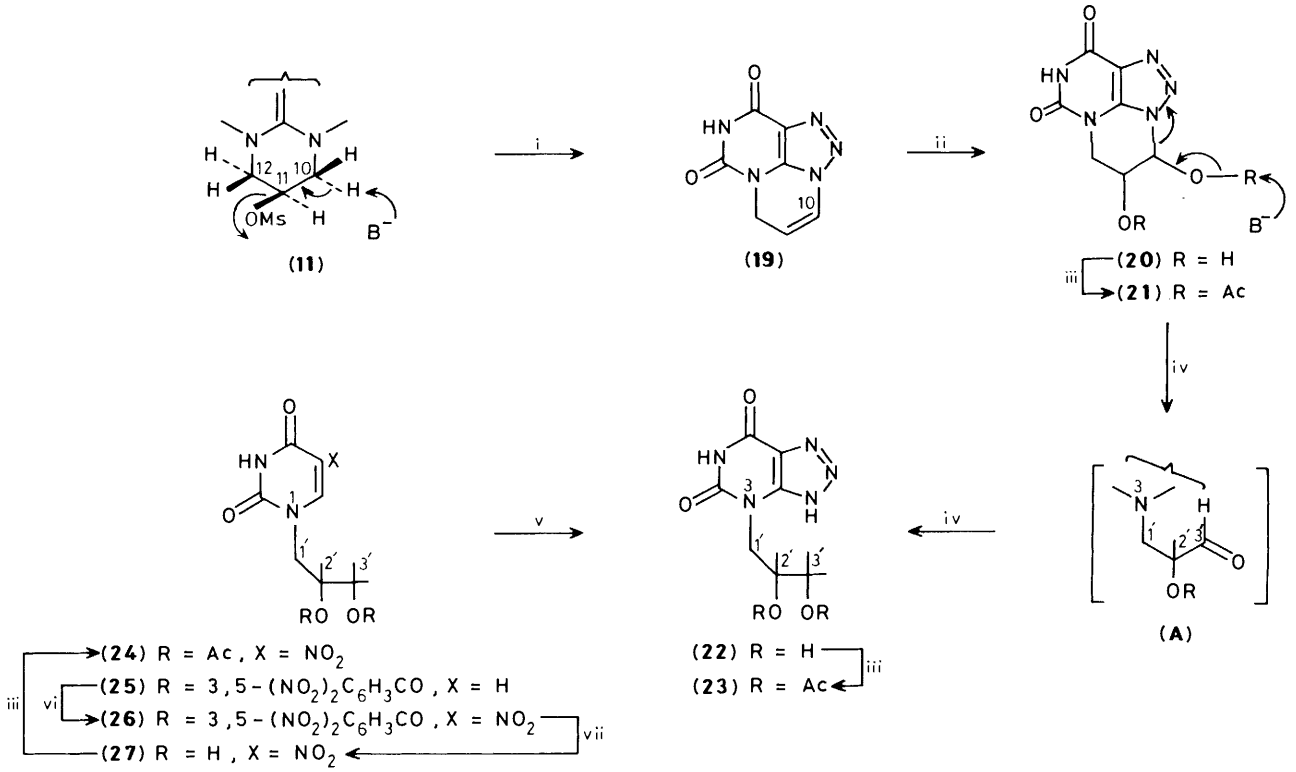
Results and Discussion

The intramolecular C-5,C-6-cycloaddition of 1-(3-azido-2-hydroxypropyl)-5-bromouracil (**3**) in dimethylformamide (DMF) produced the expected 11-hydroxy-3,9-propano-8-aza-9*H*-xanthine (**4**) (Scheme 1), *via* a dehydrobromination, in 74% yield, when the solution was carefully heated. Interestingly, Me-substitution at N-3, such as in 1-(3-azido-2-hydroxypropyl)-5-bromo-3-methyluracil (**5**) had no effect[8,9] on the cycloaddition. Thus, the latter compound was converted into 11-hydroxy-1-methyl-3,9-propano-8-aza-9*H*-xanthine (**6**) in 80% yield. The 3-methyl compound (**5**) was prepared by methylation of the 3′-azido-5-bromo compound (**3**). The latter was obtained from the 5-bromo-2′,3′-diol (**2**) *via* 5-bromo-1-[2-hydroxy-3-(*p*-tolylsulphonyloxy)propyl]uracil (**7**) which was then treated with sodium azide–DMF. Compounds (**3**) could also be prepared by a high-yielding bromination of 1-(3-azido-2-hydroxypropyl)-uracil[1] (**8**) (Scheme 1). It should be noted that compound (**2**) was shown to give 5-bromo-1-[2,3-bis-(*p*-tolylsulphonyloxy)-propyl]uracil (**9**) as a by-product on treatment with toluene-*p*-sulphonyl chloride in pyridine.

The tricyclic product (**4**) yielded ^1H and ^{13}C n.m.r. spectral data similar to those of the derived compounds, such as 11-(*p*-tolylsulphonyloxy)- (**10**) and 11-methylsulphonyloxy-(**11**)-



Scheme 1. *Reagents and conditions:* i, Br_2, EtOH–CH_2Cl_2; ii, DMF, 115 °C; iii, CH_2N_2–Et_2O; iv, TsCl, py; v, NaN_3, DMF; vi, Br_2, CH_2Cl_2–MeOH; vii, MsCl, py; viii, Br_2, CH_2Cl_2; ix, H_2, Pd 'black' in DMF; x, Ac_2O, py



Scheme 2. *Reagents and conditions:* i, DBU, DMF; ii, OsO_4, C_6H_6–DMF; iii, Ac_2O, py; iv, $NaBH_4$, water; v, NaN_3, DMF; vi, HNO_3–H_2SO_4; vii, Na, EtOH

3,9-propano-8-aza-9*H*-xanthine. According to Sasaki *et al.*[10] the C-11-unsubstituted 3,9-propano-8-aza-9*H*-xanthine (**12**) decomposed rapidly on heating in toluene at 110 °C to yield 1,N^6-trimethylene-6-aminouracil. This result, however, contrasted with our observation that the preparation of the 11-hydroxy-3,9-propano compound (**4**) as well as the transformations of C-11-functionalized derivatives in this series did not give rise to the ring-opened products.

In the present paper, we report our results on the nucleophilic and elimination reactions[11,12] of the 11-sulphonyloxy compounds (**10**) and (**11**). Thus, nucleophilic reaction of the 11-*O*-tosyl compound (**10**) with sodium azide has been shown to proceed to give 11-azido-3,9-propano-8-aza-9*H*-xanthine (**13**). This tricyclic compound was independently prepared by the intramolecular cyclization of 5-bromo-1-(2,3-diazidopropyl)-uracil (**14**) on heating in DMF. The azido compound (**13**) on reduction (H_2, Pd/C) afforded 11-amino-3,9-propano-8-aza-9*H*-xanthine (**15**), which then on acetylation was converted into the stable 11-acetamino-3,9-propano-8-aza-9*H*-xanthine (**16**) (Scheme 1). The 2′,3′-diazido-5-bromo compound (**14**), used for the above described cycloaddition reaction, was derived from 1-[2,3-bis(methylsulphonyloxy)propyl]uracil[1] (**17**) on reaction with sodium azide–DMF, followed by bromination of the thus obtained 1-(2,3-diazidopropyl)uracil (**18**).

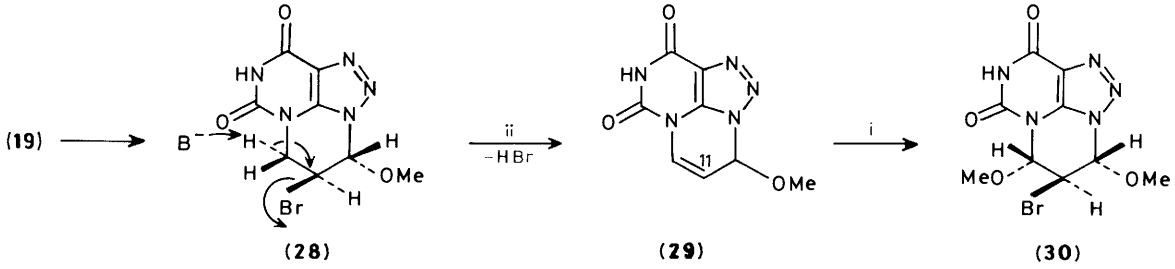
All tricyclic compounds here reported were characterized by u.v. (at 235 and 256 nm) and i.r. absorptions and ^{1}H n.m.r. spectral assignments (see Experimental section). The characteristic signals in the ^{13}C n.m.r. spectra at δ_C 149.8—148.8, 140.9—139.8, and 123.1—122.8 were attributable to C-2, C-6, and C-5, respectively.

The most interesting elimination reaction of the 11-methylsulphonyloxy derivative (**11**) with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) gave only one of the two possible propeno-products (Scheme 2). We assumed that this regiospecific formation of 9,3-propeno-8-aza-9*H*-xanthine (**19**) proceeded by loss of the more acidic and less hindered C-10 proton rather than that at C-12. The position of the propeno-double bond was then determined by osmium tetraoxide[13,14] oxidation of compound (**19**) to give 10,11-dihydroxy-3,9-propano-8-aza-9*H*-xanthine (**20**). The thus formed glycol contains a hydroxy group at C-10 which could serve to steer the ring-opening step at the C-10–N-9 bond. Therefore, the target, but chemically very sensitive, vicinal diol (**20**), formed as the major product on osmium tetraoxide oxidation of enamine (**19**), was acetylated to give 10,11-diacetoxy-3,9-propano-8-aza-9*H*-xanthine (**21**) as the stable model compound for further investigations.

The reactivity of the vicinal diol (**20**) may be considered as a spontaneous C-10–N-9 ring opening, similar to the glycosyl bond cleavages in nucleoside chemistry, a scission of the hemiacetal-like linkage to afford the very reactive intermediate aldehyde (A) (Scheme 2) which would then be very disposed to undergo condensation and polymerization processes. In order to avoid these unwanted reactions of the intermediates, we envisaged the transformation sequences of the 10,11-diacetoxy compound (**21**), shown in Scheme 2. Thus $NaBH_4$-treatment of 10,11-diacetoxy derivative (**21**) in water was found to be the method of choice. The success of this method rested on a moderate deacetylation, which then facilitated the C-10–N-9 ring opening and the reduction of the generated aldehyde intermediate (A). This picture was consistent with formation of the hitherto unknown 3-(2,3-dihydroxypropyl)-8-aza-9*H*-xanthine (**22**), characterized as the corresponding 2′,3′-diacetoxy derivative (**23**). These results confirmed the C-10,C-11 position of the double bond in the propeno-part of compound (**19**).

The ^{13}C n.m.r. spectrum of the 9,3-propeno structure (**19**) showed signals at δ_C 120.6 and 111.0 attributed to C-10 and C-11, respectively, and at δ_C 41.9 for C-12. The ^{1}H n.m.r. spectrum also confirmed the presence of the C-10,C-11 double bond by the coupling constant *J* 8.5 Hz.

The structure of 3-(2,3-diacetoxypropyl)-8-aza-9*H*-xanthine



Scheme 3. *Reagents and conditions:* i, Br_2, MeOH; ii, DBU, DMF

(**23**), obtained by the ring opening of 10,11-dihydroxy-3,9-propano-8-aza-9*H*-xanthine (**20**), was confirmed by an independent synthesis from 1-(2,3-diacetoxypropyl)-5-nitrouracil (**24**) with sodium azide–DMF.[15] The 5-nitro compound (**24**) was prepared from 1-[2,3-bis-(2,3-dinitrobenzoyloxy)propyl]uracil (**25**) by treatment with a nitric–sulphuric acid mixture.[16] 1-[2,3-Bis-(3,5-dinitrobenzoyloxy)propyl]-5-nitrouracil (**26**) thus obtained was then hydrolysed with sodium ethoxide–ethanol to 1-(2,3-dihydroxypropyl)-5-nitrouracil (**27**), which was then acetylated.

The structural features of the 9,3-propeno compound (**19**) were also determined by a *trans*-addition reaction with bromine in MeOH which yielded 11-bromo-10-methoxy-3,9-propano-8-aza-9*H*-xanthine (**28**) (Scheme 3). Assuming a *trans*-geometry between the 11-bromo and the 10-methoxy groups, (the elimination reaction of compound (**28**) with DBU–DMF has to be at C-11 and C-12. Indeed, 10-methoxy-3,9-propeno-8-aza-9*H*-xanthine (**29**) was unambiguously formed from compound (**28**) by DBU dehydrobromination. The structure of the 3,9-propeno compound was established by ^{13}C n.m.r. analysis, showing the characteristic chemical shifts for the ethylenic C-11 and C-12 at δ_C 120.4 and 105.3, respectively, and at δ_C 41.3 for C-10.

Treatment of the propeno compound (**29**) with bromine in MeOH gave 11-bromo-10,12-dimethoxy-3,9-propano-8-aza-9*H*-xanthine (**30**). As expected, the dehydrobromination of compound (**30**), containing a '*cis*' 11-bromo group with respect to C-12 and C-10 protons, failed. Stereochemical analysis of these compounds together with a detailed spectroscopic analysis of several possible intermediates in this series will be published in due course.

Experimental

M.p.s, uncorrected, were taken with a Kofler hot-stage apparatus. I.r. spectra were obtained for KBr pellets on a Perkin-Elmer 297 spectrophotometer. U.v. spectra were taken for solutions in MeOH on a Beckman DU-2 spectrophotometer. ^1H N.m.r. spectra were recorded for solutions in [$^2H_6$]Me_2SO on a JEOL FX 90 Q spectrometer operating at 89.55 MHz with $SiMe_4$ as internal standard. ^{13}C N.m.r. spectra were determined for solutions in [$^2H_6$]Me_2SO on a JEOL FX 90 Q spectrometer operating at 22.5 MHz. Multiplicities s, d, t, and q. refer to off-resonance decoupled spectra. The silica gel (Merck; 0.06—0.2 mm) which was used for column chromatography and silica gel (Merck; HF_{254}, type 60) which was used for t.l.c. and preparative t.l.c. (p.l.c.) were activated at 110 °C for 60 min. The R_F values of the products were determined by developments in CH_2Cl_2–MeOH (9:1) and rendered visible by u.v. illumination, unless otherwise stated.

Tosylation of 5-*Bromo*-1-(2,3-*dihydroxypropyl*)*uracil*[2] (**2**).—Toluene-*p*-sulphonyl chloride (335 mg, 1.76 mmol) was added to a solution of the glycol (**2**) (412 mg, 1.56 mmol) in anhydrous pyridine and the mixture was stirred at room temperature for 24 h. The solvent was evaporated off and the residue co-evaporated with toluene under reduced pressure several times. The resultant residue was subjected to p.l.c. to give two components [R_F 0.65 and 0.88; CH_2Cl_2–MeOH (9.5:0.5)]. The fraction with R_F 0.65 was identified as 5-*bromo*1-[2′-*hydroxy*-3′-(*p*-*tolylsulphonyloxy*)*propyl*]*uracil* (**7**) (346 mg, 53%), m.p. 175—176 °C (from acetone–ether) (Found: C, 40.25; H, 3.5; N, 6.7. $C_{14}H_{15}BrN_2O_6S$ requires C, 40.1; H, 3.6; N, 6.7%); $\lambda_{max.}$ 220 and 279 nm (log ε 4.16 and 3.91); $\lambda_{min.}$ 2.42 nm (log ε 3.32); $\nu_{max.}$ 3 400, 3 156, 3 146, 2 833, 1 695, 1 670, 1 617, 1 452, 1 367, 1 357, 1 190, 1 175, and 812 cm^{-1}; δ_H 11.58 (1 H, d, *J* 0.6 Hz, NH), 7.95 (1 H, s, 6-H), 7.78 and 7.47 (4 H, 2 d, *J* 8.5 Hz, ArH), 5.51 (1 H, br s, 2′-OH), 4.05—3.25 (5 H, m, 1′- and 3′-H_2 and 2′-H), and 2.43 (3 H, s, Me); δ_C 159.8 (s, C-4), 150.6 (s, C-2), 146.2 (d, C-6), 145.2, 132.3, 130.3, and 127.8 (ArC), 94.4 (s, C-5), 71.9 (t, C-3′), 65.9 (d, C-2′), 50.5 (t, C-1′), and 21.3 (q, Me).

The fraction with R_F 0.88 was identified as 5-*bromo*-1-[2′,3′-*bis*-(p-*tolylsulphonyloxy*)*propyl*]*uracil* (**9**) (105 mg, 11.7%), m.p. 171—172 °C (from MeOH) (Found: C, 43.95; H, 3.6; N, 4.65. $C_{21}H_{21}BrN_2O_8S_2$ requires C, 44.0; H, 3.7; N, 4.9%); $\lambda_{max.}$ 223 and 275 nm (4.39 and 3.86); $\lambda_{min.}$ 243 nm (3.46); $\nu_{max.}$ 3 452, 3 154, 3 072, 2 832, 1 715, 1 680, 1 623, 1 356, 1 346, 1 190, 1 180, 930, and 810 cm^{-1}; δ_H 11.57 (1 H, br s, NH), 7.90 (1 H, s, 6-H), 7.78, 7.56, 7.50, and 7.33 (8 H, 4 d, *J* 8.5 Hz, ArH), 4.96—4.88 (1 H, m, 2′-H), 4.26—4.22 (2 H, m, 3′-H_2), 3.93—3.84 (2 H, m, 1′-H_2), and 2.44 and 2.38 (6 H, 2 s, 2 × Me); δ_C 159.2 (C-4), 150.1 (C-2), 145.8 and 145.4 (ArC), 144.6 (C-6), 131.8, 131.6, 130.5, 130.3, 127.8, and 127.2 (ArC), 95.3 (C-5), 76.1 (C-2′), 68.9 (C-3′), 47.7 (C-1′), and 21.3 and 21.2 (2 × Me).

1-(3′-*Azido*-2′-*hydroxypropyl*)-5-*bromouracil* (**3**).—(*a*) Sodium azide (50 mg, 0.78 mmol) was added to a solution of the 3′-tolylsulphonyloxy derivative (**7**) (110 mg, 0.26 mmol) in DMF (2 ml) and the mixture was heated at 90 °C and stirred for 1 h. It was then filtered and the filtrate was evaporated to dryness under reduced pressure. P.l.c. gave the *product* (**3**) (61.5 mg, 78%), R_F 0.64, m.p. 145—147 °C (from MeOH–ether–hexane) (Found: C, 29.3; H, 3.1; N, 23.9. $C_7H_8BrN_5O_3$ requires C, 29.0; H, 2.8; N, 24.15%); $\lambda_{max.}$ 282 nm (3.95); $\nu_{max.}$ 3 426, 3 297, 2 827, 2 093, 1 679br, 1 617, 1 447, 1 317, and 870 cm^{-1}; δ_H 11.18 (1 H, s, NH), 8.05 (1 H, s, 6-H), 5.34 (1 H, m, 2′-OH), 3.91—3.84 (1 H, m, 2′-H), 3.80 (1 H, dd, *J* 13.8, 3.2 Hz, 3′-H_a), 3.35 (1 H, dd, *J* 13.8, 8.8 Hz, 3′-H_b), 3.35 (1 H, dd, *J* 12.6, 3.5 Hz, 1′-H_a), and 3.18 (1 H, dd, *J* 12.6, 6.5 Hz, 1′-H_b): δ_C 159.8 (s, C-4), 150.6 (s, C-2), 146.3 (d, C-6), 94.1 (s, C-5), 67.4 (d, C-2′), 53.6 (t, C-3′), and 51.5 (t, C-1′).

(*b*) A solution of 1-(3-azido-2-hydroxypropyl)uracil (**8**) (313 mg, 1.08 mmol) in a mixture of CH_2Cl_2 (14 ml) and MeOH (1 ml) was treated dropwise with a solution of bromine (0.1 ml, 2.13 mmol) in CH_2Cl_2 (16 ml). The mixture was then stirred at room temperature for 2 h and the solvent was removed under reduced pressure. P.l.c. gave the product (**3**) (363 mg, 85%), R_F 0.64, m.p. 146—147 °C (from MeOH–ether–hexane), identical (mixed m.p., i.r. and ^1H n.m.r. spectra) with that described under (*a*).

11-*Hydroxy*-3,9-*propano*-8-*aza*-9H-*xanthine** (**4**).—A solution of the 3′-azido compound (**3**) (399 mg, 1.38 mmol) in DMF (31 ml) was heated at 115 °C (oil-bath) and stirred for 16 h. The solvent was removed under reduced pressure and the residue was washed with MeOH–CH_2Cl_2 (9:1) (2 × 10 ml) to give the *product* (**4**) (213 mg, 74.1%), R_F 0.30, m.p. 280—281 °C (from 70% EtOH) (Found: C, 40.35; H, 3.55; N, 33.35. $C_7H_7N_5O_3$ requires C, 40.2; H, 3.35; N, 33.5%); $\lambda_{max.}$ 235 and 256 nm (3.57 and 3.81); $\lambda_{min.}$ 238 nm (3.56); $\nu_{max.}$ 3 448, 3 190, 3 070, 2 850, 1 730, 1 695, 1 657, 1 584, 1 426, 1 425, 1 322, 1 175, 886, and 743 cm^{-1}; δ_H 11.33 (1 H, br s, NH), 5.78 (1 H, d, *J* 3.8 Hz, 11-OH), 4.67—4.43 (2 H, m, 11-H and 10-H_a), 4.34 (1 H, dd, *J* 13.5, 2.9 Hz, 10-H_b), 4.09 (1 H, dd, *J* 12.9, 2.9 Hz, 12-H_a), and 3.62 (1 H, dd, *J* 12.9, 2.1 Hz, 12-H_b); δ_C 155.6 (s, C-6), 149.9 (s, C-2), 140.9 (s, C-4), 122.9 (s, C-5), 60.1 (d, C-11), 50.3 (t, C-10), and 44.9 (t, C-12).

1-(3′-*Azido*-2′-*hydroxypropyl*)-5-*bromo*-3-*methyluracil* (**5**).—The 3′-azido compound (**3**) (300 mg, 1.04 mmol) was treated with ethereal diazomethane [prepared from *N*-methyl-*N*-nitrosotoluene-4-sulphonamide (2.14 g, 10 mmol) in ether (30 ml)] at 0 °C and kept at room temperature for 6 h. The solvent was removed under reduced pressure and the residue was subjected to p.l.c. [CH_2Cl_2–MeOH (95:5)] to give the *product* (**5**) (280 mg, 89%), R_F 0.8, m.p. 104—105 °C (from CH_2Cl_2–ether–hexane) (Found: C, 31.8; H, 3.5; N, 23.25. $C_5H_{10}BrN_5O_3$ requires C, 31.6; H, 3.3; N, 23.05%); $\lambda_{max.}$ 280 nm (4.00); $\nu_{max.}$ 3 442, 3 052, 2 957, 2 101, 1 718, 1 659, 1 642, 1 462, 1 322, 1 238, 993, and 890 cm^{-1}; δ_H 8.13 (1 H, s, 6-H), 5.58 (1 H, d, *J* 5.3 Hz, 2′-OH), 3.9 (1 H, m, 2′-H), 3.80—3.60 (2 H, m, 3′-H_2), 3.3 (2 H, m, 1′-H_2), and 3.2 (3 H, s, Me).

11-*Hydroxy*-1-*methyl*-3,9-*propano*-8-*aza*-9H-*xanthine*† (**6**).—The 3′-azido-3-methyl compound (**5**) (82 mg, 0.28 mmol) was heated in DMF (6 ml) and the solution was stirred at 115—120 °C for 16 h (oil-bath). The solvent was removed under reduced pressure and the residue was triturated with MeOH–CH_2Cl_2 (9:1) (2 × 5 ml) to give the *product* (**6**) (51 mg, 81%), R_F 0.75, m.p. 281—283 °C (from 70% EtOH) (Found: C, 43.3; H, 4.35; N, 31.25. $C_8H_9N_5O_3$ requires C, 43.05; H, 4.05; N, 31.4%); $\lambda_{max.}$ 255 nm (3.96); $\nu_{max.}$ 3 497sh, 3 395, 2 958, 1 726, 1 683br, 1 592, 1 441, 992, and 838 cm^{-1}; δ_H 5.7 (1 H, d, *J* 3.5 Hz, 11-OH), 4.7—4.6 (1 H, m, 11-H), 4.5—4.4 (2 H, m, 10-H_2), 4.09 (1 H, ddd, *J* 12.9, 2.9, 1.5 Hz, 12-H_a), 3.7 (1 H, dd, *J* 12.9, 2.1 Hz, 12-H_b), and 3.22 (3 H, s, Me).

11-(p-*Tolylsulphonyloxy*)-3,9-*propane*-8-*aza*-9H-*xanthine*‡ (**10**).—Toluene-*p*-sulphonyl chloride (309 mg, 1.62 mmol) was added to a solution of 11-hydroxy-3,9-propano-8-aza-9*H*-xanthine (**4**) (113 mg, 0.54 mmol) in pyridine (7 ml) at 0 °C, and the mixture was stirred at room temperature for 5 h, then evaporated to dryness under reduced pressure, and the residue was triturated with CH_2Cl_2 (2 × 10 ml) and MeOH (2 × 10 ml). The resultant precipitate was isolated as the *product* (**10**) (170.5 mg, 86.9%), R_F 0.63, m.p. 254—255 °C (from Me_2SO–MeOH) (Found: C, 46.25; H, 3.8; N, 19.4. $C_{14}H_{13}N_5O_5S$ requires C, 46.3; H, 3.6; N, 19.3%); $\lambda_{max.}$ 228 and 256 nm (4.08 and 3.82); $\lambda_{min.}$ 242 nm (3.68); $\nu_{max.}$ 3 248br, 3 100, 3 020, 1 746, 1 720br, 1 686, 1 656, 1 583, 1 430, 1 368, 1 342, 1 322, 1 190, 1 181, 1 174, 942, 856, and 766 cm^{-1}; δ_H 11.44 (1 H, s, NH), 7.84 and 7.49 (4 H, 2 d, ArH), 5.59—5.73 (1 H, m, 11-H), 4.85—4.69 (1 H, m, 10-H_a), 4.52 (1 H, dd, *J* 14.3, 2.7 Hz, 10-H_b), 4.17—4.03 (1 H, m, 12-H_a), and 3.80—3.66 (1 H, m, 12-H_b).

11-*Methylsulphonyloxy*-3,9-*propano*-8-*aza*-9H-*xanthine*§ (**11**).—Methanesulphonyl chloride (0.029 ml, 0.39 mmol) was added to a solution of 11-hydroxy-3,9-propano-8-aza-9*H*-xanthine (**4**) (55 mg, 0.26 mmol) in pyridine (1 ml) and the mixture was stirred at 3—5 °C for 16 h. The solvent was removed under reduced pressure and the residue triturated with CH_2Cl_2 (2 × 5 ml) and MeOH (2 × 5 ml). The resultant precipitate was isolated as *compound* (**11**) (66 mg, 84.5%), R_F 0.39, m.p. 244—245 °C (from 50% EtOH) (Found: C, 33.7; H, 3.35; N, 24.2. $C_8H_9N_5O_5S$ requires C, 33.45; H, 3.15; N, 24.4%); $\lambda_{max.}$ 234 and 256 nm (3.66 and 3.88); $\lambda_{min.}$ 237 nm (3.65); $\nu_{max.}$ 3 209, 3 092, 3 019, 2 846, 1 740, 1 694br, 1 673, 1 589, 1 428, 1 363, 1 348, 1 326, 1 182, 1 154, 924, and 872 cm^{-1}; δ_H 11.50 (1 H, br s, NH), 5.83—5.77 (1 H, m, 11-H), 5.0 (1 H, ddd, *J* 14.4, 2.6, 1.2 Hz, 10-H_a), 4.62 (1 H, dd, *J* 14.4, 2.6 Hz, 10-H_b), 4.39 (1 H, ddd, *J* 14.1, 2.6, 1.2 Hz, 12-H_a), 3.87 (1 H, dd, *J* 14.1, 1.8 Hz, 12-H_b), and 3.37 (3 H, s, Me); δ_H 154.8 (s, C-6), 148.9 (s, C-2), 140.1 (s, C-4), 122.5 (s, C-5), 69.1 (d, C-11), 48.4 (t, C-10), and 43.1 (t, C-12).

1-(2′,3′-*Diazidopropyl*)*uracil* (**18**).—A solution of 1-[2,3-bis(methylsulphonyloxy)propyl]uracil[1] (**17**) (307 mg, 0.898 mmol) in DMF (8 ml) was treated with sodium azide (388 mg, 5.39 mmol) and the mixture was stirred and heated at 90 °C for 2 h. The precipitate was filtered off and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 ml) and partitioned with water (2 × 10 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. Column chromatography on silica gel (10 g) in CH_2Cl_2 [eluant CH_2Cl_2–MeOH (94:4)] afforded the *product* (**18**) (106 mg, 50.04%), R_F 0.62, m.p. 93—94 °C (from CH_2Cl_2–ether) (Found: C, 35.9; H, 3.65; N, 47.65. $C_7H_8N_8O_2$ requires C, 35.6; H, 3.4; N, 47.45%); $\lambda_{max.}$ 264 nm (3.90); $\nu_{max.}$ 3 140, 3 034, 2 830, 2 130, 2 090, 1 753, 1 695, 1 667br, 1 740, 1 425, 1 380, 1 273, 1 245, 871, and 764 cm^{-1}; δ_H 11.33 (1 H, br s, NH), 7.61 (1 H, d, *J* 7.7 Hz, 6-H), 5.60 (1 H, d, *J* 7.7 Hz, 5-H), 4.23—3.95 (1 H, m, 2′-H), 3.91 (1 H, dd, *J* 14.3, 4.8 (Hz, 3′-H_a) 3.86—3.72 (1 H, m, 3′-H_b), 3.70 (1 H, dd, *J* 13.2, 4.0 Hz, 1′-H_a), and 3.46 (1 H, dd, *J* 13.2, 7.0 Hz, 1′-H_b).

5-*Bromo*-1-(2′,3′-*diazidopropyl*)*uracil* (**14**).—A solution of bromine (0.066 ml, 1.28 mmol) in CH_2Cl_2 (9.5 ml) was added to a solution of 1-(2,3-diazidopropyl)uracil (**18**) (202 mg, 0.86 mmol) in CH_2Cl_2 (9 ml) and the mixture was worked up as described for the 3′-azido-5-bromo compound (**3**) [under (*b*)]. P.l.c. [CH_2Cl_2–MeOH (95:5)] gave *compound* (**14**) (211 mg, 78.3%), R_F 0.75, m.p. 128—130 °C (from CH_2Cl_2–ether) (Found: C, 26.75; H, 2.4; N, 35.5. $C_7H_7BrN_8O_2$ requires C, 26.7; H, 2.25; N, 35.55%); $\lambda_{max.}$ 277 nm (3.94); $\nu_{max.}$ 3 150, 3 008, 2 836, 2 126, 2 096, 1 701, 1 658, 1 612, 1 460, 1 426, 1 348, 1 246, 916, 866, and 746 cm^{-1}; δ_H 11.63 (1 H, br s, NH), 8.18 (1 H, s, 6-H), 4.18—4.0 (1 H, m, 2′-H), 3.85—3.76 (2, H, m, 3′-H_2), 3.71 (1 H, dd, *J* 12.9, 3.6 Hz, 1′-H_a), and 3.45 (1 H, dd, *J* 12.9, 6.7 Hz, 1′-H_b); δ_C 161.2 (C-4), 152.0 (C-2), 146.7 (C-6), 95.8 (C-5), 59.9 (C-2′), 51.8 (C-3′), and 48.7 (C-1′).

11-*Azido*-3,9-*propano*-8-*aza*-9*H*-*xanthine*¶ (**13**).—(*a*) A solution of 5-bromo-1-(2,3-diazidopropyl)uracil (**14**) (201 mg, 0.64 mmol) in DMF (15.6 ml) was stirred and heated at 110—

* *Systematic name:* 4-hydroxy-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

† *Systematic name:* 4-hydroxy-7-methyl-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

‡ *Systematic name:* 4-(*p*-tolylsulphonyloxy)-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

§ *Systematic name:* 4-methylsulphonyloxy-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

¶ *Systematic name:* 4-azido-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

120 °C for 14 h. The solvent was removed under reduced pressure and the residue was triturated with CH_2Cl_2 (2 × 10) and MeOH (10 ml). The resultant precipitate was identified as compound (**13**) (74 mg, 49.7%), R_F 0.56, m.p. 300 °C (from 30% EtOH) (Found: C, 36.0; H, 2.9; N, 47.65. $C_7H_6N_8O_2$ requires C, 35.9; H, 2.6; N, 47.85%); $\lambda_{max.}$ 236 and 257 nm (3.71 and 3.88); $\lambda_{min.}$ 239 nm (3.70); $\nu_{max.}$ 3 185, 3 060, 2 850, 2 130, 1 725, 1 705br, 1 655, 1 640, 1 586, 1 430, 1 327, 1 176, and 857 cm^{-1}; δ_H 11.40 (1 H, br s, NH), 5.02—4.89 (1 H, m, 11-H), 4.77 (1 H, ddd, *J* 13.5, 2.9, 1.2 Hz, 10-H_a), 4.52 (1 H, dd, *J* 13.5, 2.9 Hz, 10-H_b), 4.20 (1 H, ddd, *J* 13.5, 2.9, 1.2 Hz, 12-H_a), and 3.79 (1 H, dd, *J* 13.5, 2.9 Hz, 12-H_b); δ_C 155.4 (C-6), 149.5 (C-2), 140.6 (C-4), 122.9 (C-5), 51.6 (C-11), 47.7 (C-10), and 42.2 (C-12).

(*b*) A solution of 11-(*p*-tolylsulphonyloxy)-3,9-propano-8-aza-9*H*-xanthine (**10**) (32 mg, 0.088 mmol) in DMF (0.7 ml) was treated with sodium azide (17 mg, 0.264 mmol) and the mixture was stirred at 90 °C for 2 h, then filtered, and the filtrate was evaporated to dryness under reduced pressure. The residue was triturated with MeOH (2 × 5 ml) to give compound (**13**) (15 mg, 72.8%), R_F 0.56, m.p. 300 °C, identical (i.r. and ^1H n.m.r. spectra) with that obtained under (*a*).

11-*Acetamido*-3,9-*propano*-8-*aza*-9H-*xanthine** (**16**).—Pd 'black' (35 mg) was added to a solution of 11-azido-3,9-propano-8-aza-9*H*-xanthine (**13**) (162 mg, 0.26 mmol) in DMF (22 ml) and the mixture was stirred under H_2 (0.36 MPa) at room temperature for 3 h. The catalyst was then filtered off on a short Celite column and the filtrate was evaporated to dryness. Acetic anhydride (0.18 ml) was added to a solution of the thus obtained 11-amino-3,9-propano-8-aza-9*H*-xanthine (**15**) in water (1.3 ml) and the mixture was stirred at room temperature for 30 min, concentrated under reduced pressure, and evaporated with ethanol and toluene under reduced pressure. The residue was subjected to p.l.c. (two developments) to give *compound* (**16**) (79 mg, 45.7%), R_F 0.22, m.p. 185—186 °C (from MeOH) (Found: C, 43.25; H, 4.25; N, 33.65. $C_9H_{10}N_6O_3$ requires C, 43.2; H, 4.05; N, 33.6%); $\lambda_{max.}$ 235 and 256 nm (3.77 and 3.99); $\lambda_{min.}$ 238 nm (3.76); $\nu_{max.}$ 3 442br, 3 335, 3 175br, 3 092, 2 808, 1 727, 1 695, 1 661, 1 587, 1 535, 1 432, 1 427, 1 315, 1 275, 1 256, 1 243, 1 140, and 827 cm^{-1}; δ_H 11.34 (1 H, br, s, NH), 8.32 (1 H, d, *J* 7.1 Hz, 11-NH), 4.80—4.64 (1 H, m, 11-H), 4.50—4.41 (2 H, m, 10-H_2), 3.98 (1 H, dd, *J* 12.9, 3.2 Hz, 12-H_a), 3.76 (1, H, dd, *J* 12.9, 3.2 Hz, 12-H_b), and 1.76 (3 H, s, Me); δ_C 169.7 (CO, acetyl), 155.6 (s, C-6), 149.7 (s, C-2), 140.9 (s, C-4), 123.1 (s, C-5), 47.9 (t, C-10), 42.6 (t, C-12), 41.1 (d, C-11), and 22.5 (q, Me).

9,3-*Propeno*-8-*aza*-9H-*xanthine*† (**19**).—A solution of the 11-methylsulphonyloxy-3,9-propano compound (**11**) (175 mg, 0.6 mmol) in DMF (6 ml) was treated with DBU (0.1 ml, 0.67 mmol) and the mixture was stirred at 75—80 °C for 90 min. The solvent was removed under reduced pressure and the residue was triturated with CH_2Cl_2 (5 ml) and MeOH (5 ml) to afford the product (**19**) (93 mg, 80%), R_F 0.55, m.p. 270—271 °C (from 70% EtOH) (Found: C, 44.05; H, 2.9; N, 36.9. $C_7H_5N_5O_2$ requires C, 44.0; H, 2.65; N, 36.65%); $\lambda_{max.}$ 229 nm (4.17); $\lambda_{infl.}$ 250 nm (3.84); $\nu_{max.}$ 3 400br, 3 200, 3 095, 2 815, 1 724br, 1 664, 1 566, 1 413, 1 350, 1 295, 1 193, 1 154, 1 007, 928, and 873 cm^{-1}; δ_H 11.35 (1 H, br s, NH), 7.70 (1 H, dt, *J* 8.5, 2.6 Hz, 10-H), 5.76 (1 H, dt, *J* 8.5, 3.2 Hz, 11-H), and 4.49 (2 H, dd, *J* 3.2, 2.6 Hz, 12-H_2); δ_C 155.2 (s, C-6), 149.4 (s, C-2), 140.3 (s, C-4), 123.0 (s, C-5), 120.6 (d, C-10), 111.0 (d, C-11), and 41.9 (t, C-12).

10,11-*Diacetoxy*-3,9-*propano*-8-*aza*-9H-*xanthine*‡ (**21**).—Osmium tetraoxide (172 mg, 0.68 mmol) was dissolved in benzene (2 ml) and the solution was added dropwise to a solution of 9,3-propeno-8-aza-9*H*-xanthine (**19**) (85 mg, 0.45 mmol) in DMF (3 ml). The mixture was stirred at room temperature for 1 h, then filtered, and the filtrate was saturated with hydrogen sulphide to give a precipitate, which was filtered off and washed with DMF (2 × 1 ml). The combined filtrate and washings were evaporated to dryness. Acetic anhydride (1.1 ml) was then added to a solution of the residue (82 mg) in pyridine (3 ml). This mixture was stirred at room temperature for 16 h, and then worked up by the standard procedure. P.l.c. gave the *product* (**21**) (42 mg, 30.5%), R_F 0.65, m.p. 210—212 °C (from EtOH) (Found: C, 42.75; H, 3.85; N, 22.85. $C_{11}H_{11}N_5O_5$ requires C, 42.85; H, 3.6; N, 22.65%); $\lambda_{infl.}$ 237 nm (4.07); $\lambda_{max.}$ 250 nm (4.12); $\nu_{max.}$ 3 450br, 3 206, 3 086, 2 856, 1 776, 1 750, 1 706br, 1 662, 1 422, 1 374, 1 320, 1 230, 1 213, 1 186, 1 036, 936, and 820 cm^{-1}; δ_H 11.3 (1 H, br s, NH), 7.14 (1 H, dd, *J* 2.7, 1.0 Hz, 10-H), 5.65 (1, H, dd, *J* 2.7, 2.4 Hz, 11-H), 4.3 (1, H, ddd, *J* 14.7, 2.4, 1.0 Hz, 12-H_a), 3.9 (1 H, dd, *J* 14.7, 2.4 Hz, 12-H_b), and 2.13 and 1.98 (6 H, 2 s, 2 × Me); δ_C 169.0 and 168.0 (2 × CO, acetyl), 155.1 (C-6), 149.3 (C-2), 141.0 (C-4), 122.7 (C-5), 73.2 (C-10), 64.1 (C-11), 42.4 (C-12), and 20.6 and 20.5 (2 × Me).

3-(2,3-*Diacetoxypropyl*)-8-*aza*-9H-*xanthine* (**23**).—(*a*) $NaBH_4$ (12 mg, 0.36 mmol) was added to a solution of the 10,11-diacetoxypropano compound (**21**) (45 mg, 0.138 mmol) in water (3 ml) and the mixture was stirred at room temperature for 30 min. After filtration the filtrate was evaporated and the residue was co-evaporated with ethanol and toluene under reduced pressure. Acetic anhydride (0.525 ml, 0.57 mmol) was then added to a solution of the resultant residue in pyridine (3 ml). This mixture was stirred at room temperature for 16 h and then evaporated to dryness. P.l.c. (four developments) gave the *product* (**23**) (39 mg, 86%), R_F 0.35, m.p. 162—164 °C (from MeOH–ether–hexane) (Found: C, 42.25; H, 4.0; N, 22.3. $C_{11}H_{13}N_5O_6$ requires C, 42.45; H, 4.2; N, 22.5%); $\lambda_{max.}$ 266 nm (3.76); $\nu_{max.}$ 3 454, 3 186, 3 058, 2 854, 1 739, 1 687, 1 637, 1 581, 1 240, and 856 cm^{-1}; δ_H 10.85 (2 H, br s, 2 × NH), 5.34—5.32 (1 H, m, 2′-H), 4.22—4.05 (4 H, m, 1′- and 3′-H_2), and 2.00 and 1.86 (6 H, 2 s, 2 × Me); δ_H 170.3 and 170.0 (2 s, 2 × CO, acetyl), 157.1 (s, C-6), 151.4 (2 s, C-4 and -2), 124.0 (s, C-5), 68.9 (d, C-2′), 63.2 (t, C-3′), 43.5 (t, C-1′), and 20.8 and 20.7 (2 q, 2 × Me).

(*b*) Sodium azide (30 mg, 0.46 mmol) was added to a solution of 1-(2,3-diacetoxypropyl)-5-nitrouracil (**24**) (see later) (48 mg, 0.15 mmol) in DMF (3 ml) and the mixture was stirred at room temperature for 16 h. The solvent was removed under reduced pressure and the residue was dissolved in water (3 ml). Amberlite IRC-50 (H^+) was added to the neutral reaction, which was then filtered and the resin was washed with ethanol (4 × 15 ml), and the combined filtrate and washings were evaporated to dryness. P.l.c. [two developments; CH_2Cl_2–MeOH (8:2)] gave the product (**23**) (35 mg, 73.7%), identical (mixed m.p., i.r., and ^1H n.m.r. spectra) with that obtained in (*a*).

1-[2,3-*Bis*-(3,5-*dinitrobenzoyloxy*)*propyl*]*uracil* (**25**).—Freshly prepared 3,5-dinitrobenzoyl chloride (691 mg, 2.91 mmol) was added to a solution of 1-(2,3-dihydroxypropyl)uracil (**1**) (250 mg, 1.34 mmol) in pyridine (14 ml) and the mixture was stirred at room temperature for 2 days. The solvent was then removed under reduced pressure, and the oily residue was partitioned between water and CH_2Cl_2. The organic phase was evaporated to dryness. The residue was purified by p.l.c. [two developments, CH_2Cl_2–MeOH (95:5)] to give *compound* (**25**) (634 mg, 82%), R_F 0.63, m.p. 118—120 °C (on rechromatography) (Found: C, 43.9; H, 2.65; N, 14.55. $C_{21}H_{14}N_6O_{14}$ requires C, 43.9; H, 2.45; N, 14.65%); $\lambda_{infl.}$ 226 and 252 nm (4.76 and 4.58); $\nu_{max.}$ 3 433br, 3 093, 1 736, 1 683br, 1 627, 1 544,

* *Systematic name:* 4-acetamido-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

† *Systematic name:* 1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(5*H*,7*H*)-dione.

‡ *Systematic name:* 3,4-diacetoxy-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8-(3*H*,7*H*)-dione.

1 456, 1 343, 1 272, 1 155, 1 073, 965, 726, and 715 cm^{-1}; δ_H 11.27 (1 H, br s, NH), 9.08—8.88 (6 H, m, ArH), 7.90 (1 H, d, *J* 7.9 Hz, 6-H), 5.79—5.74 (1 H, m, 2′-H), 5.52 (1 H, d, *J* 7.9 Hz, 5-H), 4.89 (1 H, dd, *J* 12.9, 4.4 Hz, 3′-H_a), 4.68 (1 H, dd, *J* 12.9, 6.7 Hz, 3′-H_b), and 4.32—4.26 (2 H, m, 1′-H_2); δ_C 163.7 (s, C-4), 162.4 and 162.2 (2 s, 2 × COPh), 151.4 (s, C-2), 148.5 (s, C-1 arom.), 145.8 (d, C-6), 132.5 and 132.3 (2 s, C-3 and -5 arom.), 129.2 and 129.0 (2 d, C-2 and -6 arom.), 123.0 and 122.8 (2 d, 2 × C-4 arom.), 101.4 (d, C-5), 72.0 (d, C-2′), 65.0 (t, C-3′), and 47.6 (t, C-1′).

1-[2,3-*Bis*-(2,5-*dinitrobenzoyloxy*)*propyl*]-5-*nitrouracil* (**26**).—A mixture of fuming nitric and conc. sulphuric acids (1:1) (0.6 ml) was added portionwise to the 2′,3′-bis(dinitrobenzoyloxy) compound (**25**) (100 mg, 0.174 mmol) and the mixture was stirred at room temperature for 20 min. It was then poured into chilled water (5 ml) and the precipitate was separated by suction. After being washed with water (3 × 3 ml) to neutrality, the residue was subjected to p.l.c. [two developments, CH_2Cl_2–MeOH (95:5)] to give *compound* (**26**) (95 mg, 88%), R_F 0.77, m.p. 140—145 °C (on rechromatography) (Found: C, 39.55; H, 2.75; N, 15.2. $C_{21}H_{13}N_7O_{16}\cdot H_2O$ requires C, 39.55; H, 2.35; N, 15.4%); $\lambda_{infl.}$ 225 nm (4.51); $\lambda_{max.}$ 302 nm (3.90); $\lambda_{min.}$ 275 nm (3.79); $\nu_{max.}$ 3 441, 3 106, 1 735br, 1 626, 1 546, 1 458, 1 345, 1 325, 1 281, 1 261, 1 155, 1 072, 927, 727, and 715 cm^{-1}; δ_H 12.05 (1 H, br s, NH), 9.5 (1 H, s, 6-H), 9.1—8.9 (6 H, m, ArH), 5.7—5.6 (1 H, m, 2′-H), and 4.98—4.30 (4 H, 2 m, 1′-and 3′-H_2); δ_C 162.2 and 162.1 (2 s, 2 × COAr), 155.4 (s, C-4), 150.6 (d, C-6), 150.0 (s, C-2), 148.5 (s, C-1 arom.), 132.5 and 132.3 (2 s, C-3 and -5 arom.), 128.9 (d, C-2 and -6 arom.), 125.5 (s, C-5), 122.8 (d, C-4 arom.), 71.6 (d, C-2′), 64.6 (t, C-3′), and 48.3 (t, C-1′).

1-(2,3-*Diacetoxypropyl*)-5-*nitrouracil* (**24**).—Sodium ethoxide [sodium (20.8 mg, 0.92 mmol) in anhydrous ethanol (4.4 ml)] was added to a solution of the 2,3-bis(dinitrobenzoyloxy)-5-nitro compound (**26**) (281 mg, 0.46 mmol) in anhydrous ethanol (17 ml) and the mixture was heated under reflux for 3 h. The precipitate was separated by suction, washed with hot ethanol (2 ml), and the resultant residue was suspended in ethanol (2 ml) and treated with conc. sulphuric acid (0.01 ml). The precipitate was filtered off and the filtrate was evaporated to dryness. P.l.c. [two developments, CH_2Cl_2–MeOH (8:2)] gave an oily product presumed to be 1-(2,3-dihydroxypropyl)-5-nitrouracil (**27**) (65 mg, 62%), R_F 0.55.

A solution of compound (**27**) (65 mg, 0.28 mmol) in anhydrous pyridine (2 ml) was treated with acetic anhydride (1.05 ml, 1.12 mmol) and the mixture was stirred at room temperature for 16 h. The solvent was then removed under reduced pressure and the residue was subjected to p.l.c. to give *compound* (**24**) (60 mg, 68%), R_F 0.72, m.p. 207—208 °C (from MeOH) (Found: C, 41.75; H, 4.45; N, 13.55. $C_{11}H_{13}N_3O_8$ requires C, 41.9; H, 4.15; N, 13.35%); $\lambda_{max.}$ 236 and 302 nm (3.83 and 3.98); $\lambda_{min.}$ 258 nm (3.39); $\nu_{max.}$ 3 456, 3 179, 3 074, 2 844, 1 735, 1 683br, 1 641, 1 621, 1 516, 1 471, 1 326, 1 230, 1 055, and 820 cm^{-1}; δ_H 12.1 (1 H, s, NH), 9.25 (1 H, s, 6-H), 5.23 (1 H, m, 2′-H), 4.26—4.22 (2 H, m, 3′-H_2), 4.17—4.10 (2 H, m, 1′-H_2), and 2.04 and 1.98 (6 H, 2 s, 2 × Me); δ_C 170.1 and 169.9 (2 s, 2 × COMe), 155.5 (s, C-4), 150.5 (d, C-6), 149.8 (s, C-2), 125.3 (s, C-5), 68.9 (d, C-2′), 62.6 (t, C-3′), 48.8 (t, C-1′), and 20.7 and 20.5 (2 q, 2 × Me).

11-*Bromo*-10-*methoxy*-3,9-*propano*-8-*aza*-9H-*xanthine* * (**28**).—A solution of bromine (0.0185 ml, 0.34 mmol) in MeOH (10 ml) was added dropwise to a suspension of the propeno compound (**19**) (46 mg, 0.24 mmol) in MeOH (10 ml) and the mixture was stirred at room temperature for 20 min. The solvent was then recovered under reduced pressure and the residue was subjected to p.l.c. to give the *product* (**28**) (63 mg, 86%), R_F 0.78, m.p. 200—201 °C (from MeOH) (Found: C, 31.95; H, 2.9; N, 22.95. $C_8H_8BrN_5O_3$ requires C, 31.8; H, 2.65; N, 23.2%); $\lambda_{infl.}$ 236 nm (3.87); $\lambda_{max.}$ 253 nm (3.99); $\nu_{max.}$ 3 170, 3 060, 2 837, 1 720br, 1 696sh, 1 656, 1 570, 1 416, 1 356, 1 328, 1 249, 1 079, 1 067, 973, 894, 858, and 846 cm^{-1}; δ_H 11.59 (1 H, br s, NH), 6.25 (1 H, d, *J* 2.3 Hz, 10-H), 5.2 (1 H, ddd, *J* 2.3, 2.3, 2.3 Hz, 11-H), 4.36 (1 H, dd, *J* 14.7, 2.3 Hz, 12-H_a), 4.01 (1 H, dd, *J* 14.7, 2.3 Hz, 12-H_b), and 3.59 (3 H, s, OMe); δ_C 155.1 (s, C-6), 149.2 (s, C-2), 139.8 (s, C-4), 122.8 (s, C-5), 85.6 (d, C-10), 57.4 (q, Me), 42.4 (t, C-12), and 40.6—39.6 (C-11, obscured by signal of $[^2H_6]Me_2SO$).

10-*Methoxy*-3,9-*propeno*-8-*aza*-9H-*xanthine* † (**29**).—A solution of the 11-bromo-10-methoxy compound (**28**) (42 mg, 0.133 mmol) in anhydrous DMF (3.2 ml) was treated with DBU (0.032 ml, 0.22 mmol) and heated at 80 °C for 20 min. The solvent was removed under reduced pressure and the residue was subjected to p.l.c. to give the *product* (**29**) (18 mg, 62%), R_F 0.75, m.p. 170—171 °C (from MeOH) (Found: C, 43.45; H, 3.0; N, 31.55. $C_8H_7N_5O_3$ requires C, 43.45; H, 3.2; N, 31.65%); $\lambda_{infl.}$ 233 nm (4.19); $\lambda_{max.}$ 264 nm (4.36); $\lambda_{min.}$ 234 nm (4.08); $\nu_{max.}$ 3 442, 3 212, 3 084, 1 736, 1 712, 1 664, 1 632, 1 571, 1 417, 1 342, 1 310, 1 169, 1 110, 1 078, 960, and 888 cm^{-1}; δ_H 11.47 (1 H, br s, NH), 7.42 (1 H, dd, *J* 8.5, 1.2 Hz 12-H), 6.69 (1 H, dd, *J* 3.5, 1.2 Hz, 10-H), 5.65 (1 H, dd, *J* 8.5, 3.5 Hz, 11-H), and 3.45 (3 H, s, 10-OMe); δ_C 155.2 (s, C-6), 146.5 (s, C-2), 138.6 (s, C-4), 123.0 (s, C-5), 120.4 (d, C-12), 105.3 (d, C-11), 81.4 (d, C-10), and 55.5 (q, OMe).

11-*Bromo*-10,12-*dimethoxy*-3,9-*propano*-8-*aza*-9H-*xanthine* ‡ (**30**).—A solution of bromine (0.014 ml, 0.26 mmol) in MeOH (7.5 ml) was added to a solution of the propeno compound (**29**) (40 mg, 0.18 mmol) in MeOH (7.5 ml) and the mixture was worked-up as for the preparation of compound (**28**). P.l.c. gave *compound* (**30**) (48 mg, 80%), R_F 0.79, m.p. 260—262 °C (from MeOH–ether–hexane) (Found: C, 32.7; H, 2.9; N, 21.3. $C_9H_{10}BrN_5O_4$ requires C, 32.55; H, 3.05; N, 21.1%); $\lambda_{infl.}$ 234 nm (3.75); $\lambda_{max.}$ 248 nm (3.87); $\nu_{max.}$ 3 424, 3 214, 3 110, 3 014, 2 940, 2 840, 1 722, 1 650, 1 565, 1 415, 1 295, 1 198, 1 177, 1 106, 1 088, 1 063, 984, 952, 908, and 879 cm^{-1}; δ_H 11.71 (1 H, br s, NH), 6.25 (1 H, d, *J* 1.5 Hz, 10-H), 5.75 (1 H, d, *J* 1.75, 12-H), 5.3 (1 H, dd, *J* 1.75, 1.5 Hz, 11-H), and 3.6 and 3.5 (6 H, 2 s, 2 × OMe); δ_C 155.0 (s, C-6), 149.4 (s, C-2), 138.4 (s, C-4), 123.0 (s, C-5), 86.8 (d, C-10), 83.3 (d, C-12), 58.1 and 57.9 (2 q, 2 × Me), and 41.8 (d, C-11).

* *Systematic name:* 4-bromo-3-methoxy-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

† *Systematic name:* 3-methoxy-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

‡ *Systematic name:* 4-bromo-3,5-dimethoxy-4,5-dihydro-1,2,2a,5a,7-penta-aza-acenaphthylene-6,8(3*H*,7*H*)-dione.

References

1 V. Škarić and M. Jokić, *Croat. Chem. Acta*, 1983, **56**, 125.
2 V. Škarić and B. Kašnar, *Croat. Chem. Acta*, 1985, **58**, 583.
3 P. Fischer, R. Kaul, G. Kiefer, S. Erhardt, and B. Hempel, *Tetrahedron Lett.*, 1975, 3521.
4 K. K. Gawn and Rhode, *Klin. Wochenschr.*, 1969, **47**, 375.
5 M. Friedland and D. W. Visser, *Biochim. Biophys. Acta*, 1961, **51**, 148.
6 T. Sasaki, K. Minamoto, M. Kino, and T. Mizuno, *J. Org. Chem.*, 1976, **41**, 1100.
7 T. Sasaki, K. Minamoto, T. Suzuki, and T. Sugiura, *J. Am. Chem. Soc.*, 1978, **100**, 2248.
8 B. A. Otter, E. A. Falco, and J. J. Fox, *J. Org. Chem.*, 1968, **33**, 3593.

9 M. Márton-Merész, J. Kuszmann, J. Lango, L. Párkányi, and A. Kálmán, *Nucleosides Nucleotides*, 1984, **3**, 221.
10 T. Sasaki, K. Minamoto, T. Suzuki, and S. Yamashita, *Tetrahedron*, 1980, **36**, 865.
11 V. Škarić, J. Matulić-Adamić, and M. Jokić, *Nucleic Acid Res. Symp. Ser.*, 1987, **18**, 9.
12 V. Škarić, M. Škarić-Mlakar, M. Jokić, and D. Škarić, *Nucleosides Nucleotides*, 1987, **6**, 391.
13 K. C. Murdock and B. B. Angier, *J. Am. Chem. Soc.*, 1962, **84**, 3748.
14 V. Škarić and J. Matulić-Adamić, *Helv. Chim. Acta*, 1980, **63**, 2179.
15 H. Ulrich Blank and J. J. Fox, *J. Am. Chem. Soc.*, 1968, **90**, 7175.
16 I. Wempen, I. L. Doerr, L. Kaplan, and J. J. Fox, *J. Am. Chem. Soc.*, 1960, **82**, 1624.

Received 1*st August* 1988; *Paper* 8/03121E