Purines, Pyrimidines, and Imidazoles. Part 45.[1] Stereospecific Syntheses of Some 1-D-Ribofuranosyl- and 1-D-Xylofuranosyl-uracil Derivatives

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Ethyl *N*-[α-acetyl-β-(5,6-*O*-isopropylidene-D-glucofuranosylamino)acryloyl]carbamate and the corresponding α-ethoxycarbonyl derivative have been prepared from 5,6-*O*-isopropylidene-D-glucofuranosylamine with ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate and ethyl *N*-(α-ethoxycarbonyl-β-ethoxyacryloyl)carbamate, respectively. Ethyl *N*-[α-acetyl-β-(4,6-*O*-isopropylidene-L-sorbosylamino)acryloyl]carbamate was similarly prepared from 4.6-*O*-isopropylidene-L-sorbosylamine. which was produced as a crystalline toluene-*p*-sulphonate from L-sorbosylamine. acetone. dimethoxypropane, and toluene-*p*-sulphonic acid.

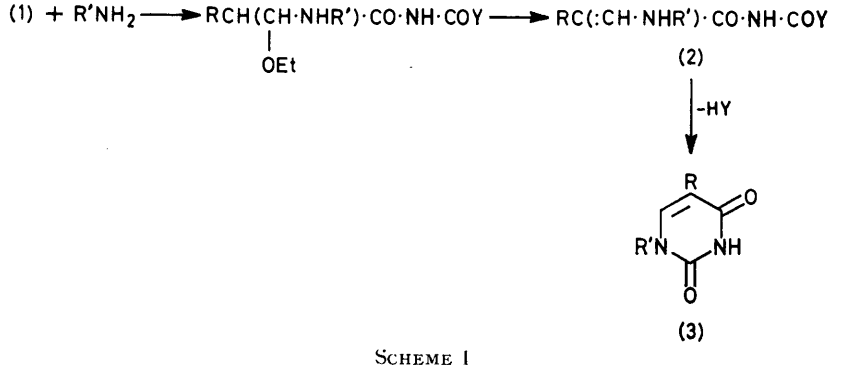
The anomeric ratios of α- and β-2',3'-*O*-isopropylidene-5-cyanouridines obtained from ethyl *N*-(α-cyano-β-ethoxyacryloyl)carbamate and 2,3-*O*-isopropylidene-D-ribofuranosylamine in aqueous solution have been found to vary with base concentration. Ethyl *N*-(α-cyano-β-dimethylaminoacryloyl)carbamate did not react readily with either 2,3-*O*-isopropylidene-D-ribofuranosylamine or 3,5-*O*-isopropylidene-D-xylofuranosylamine, whereas the corresponding α-acetyl derivative with the xylosylamine gave 5-acetyl-1-(2,3-*O*-isopropylidene-α-D-xylofuranosyl)uracil and with the ribosylamine gave 5-acetyl-2',3'-*O*-isopropylideneuridine; in each case only one anomer was formed. Mechanisms accounting for the stereospecificity of these reactions are proposed.

In other parts of this series [2] we have described a general method for the preparation of a wide variety of substituted uracils, by the reaction of a β-alkoxyacryloylcarbamate of type (1; X = Y = OEt) or a related acylurea [3,4] (1; X = OEt, Y = NHAc) with a primary amine. The reaction undoubtedly proceeds by prior addition of the amine to the C:C bond followed by elimination of ethanol to produce an intermediate aminomethylene derivative (2), which readily cyclises to a uracil (3) when heated or when treated with base (Scheme 1). The reaction has been adapted to include the use of glycopyranosylamines [5] and glycofuranosylamines,[6,7] which lead directly to 1-substituted glycosyluracils. The mechanism outlined is confirmed by the isolation of intermediates (2) where R is alkyl or aryl, but hitherto similar glycosylaminomethylene derivatives have not been isolated.

RC(:CHX)·CO·NH·COY

(1) a; R = MeCO, X = Y = OEt
b; R = CO_2Et, X = Y = OEt
c; R = CN, X = Y = OEt
d; R = CN, X = NHEt, Y = OEt
e; R = MeCO, X = OH, Y = OEt
f; R = CN, X = OEt, Y = NHAc
g; R = CN, X = NMe_2, Y = NHAc
h; R = CN, X = NMe_2, Y = OEt
i; R = MeCO, X = NMe_2, Y = OEt
j; R = MeCO, X = NC_4H_8O, Y = OEt

We now record the formation of the crystalline acyclic glucofuranosyl derivatives (4a and b) by the reaction of 5,6-*O*-isopropylidene-D-glucofuranosylamine [7] (5) with the acylurethanes (1a and b), respectively, and a molar amount of sodium methoxide in methanol solution. The structures of compounds (4) were confirmed by elemental analysis and mass spectra but the anomeric configurations are not known. In contrast to these reactions, under similar conditions the acyclic cyanoacrylamide (1c) with the glycofuranosylamine (5) gave the uracil glucofuranoside (6) directly.[7] Similarly the isopropylidene-L-sorbosylamine derivative, which probably has the



Scheme 1

[1] Part 44. S. Ahmed, R. Lofthouse, and G. Shaw, *J.C.S. Perkin I*, 1976. 1976.

[2] (*a*) G. Shaw, *J. Chem. Soc.*, 1955, 1834; (*b*) M. R. Atkinson, G. Shaw, and R. N. Warrener *ibid.* 1956 4118; (*c*) M. R. Atkinson, G. Shaw, K. Schaffner, and R. N. Warrener, *ibid.*, 1956, 3847; G. Shaw and R. N. Warrener, *ibid.*, 1958, 153, 157; D. J. Brown, 'The Pyrimidines,' Interscience, New York, and London, 1962; (*d*) J. H. Dewar and G. Shaw, *J. Chem. Soc.*, 1961, 3254.

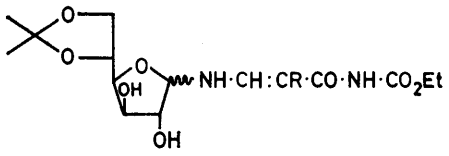
[3] J. H. Dewar and G. Shaw, *J. Chem. Soc.*, 1965, 1642.

[4] P. Lees and G. Shaw, *J. Chem. Soc.* (*C*), 1968, 1519.

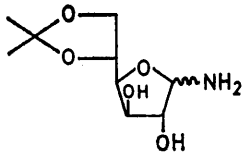
[5] R. K. Ralph and G. Shaw, *J. Chem. Soc.*, 1956, 1877.

[6] N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg, and G. Shaw, *J.C.S. Perkin I*, 1973, 1720.

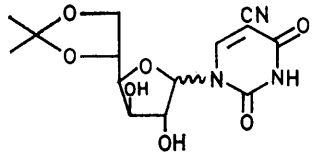
[7] N. J. Cusack, D. H. Robinson, P. W. Rugg, G. Shaw, and R. Lofthouse, *J.C.S. Perkin I*, 1974, 73.



(4) a; R=MeCO
b; R=CO_2Et



(5)



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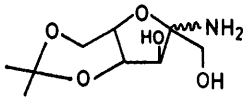
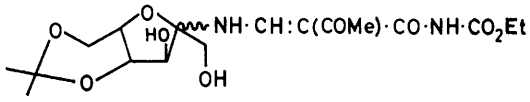


(7)



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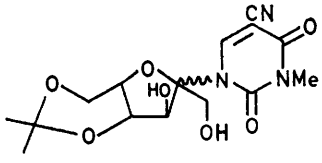

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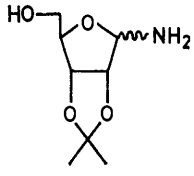

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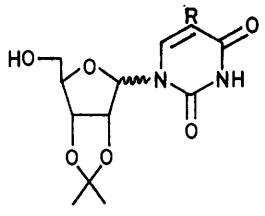
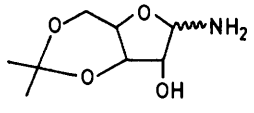


(11) a; R=MeCO; α-anomer
b; R=MeCO; β-anomer
c; R=CN; α-anomer
d; R=CN; β-anomer



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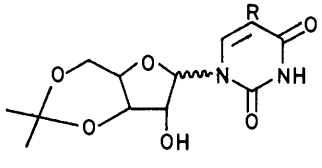


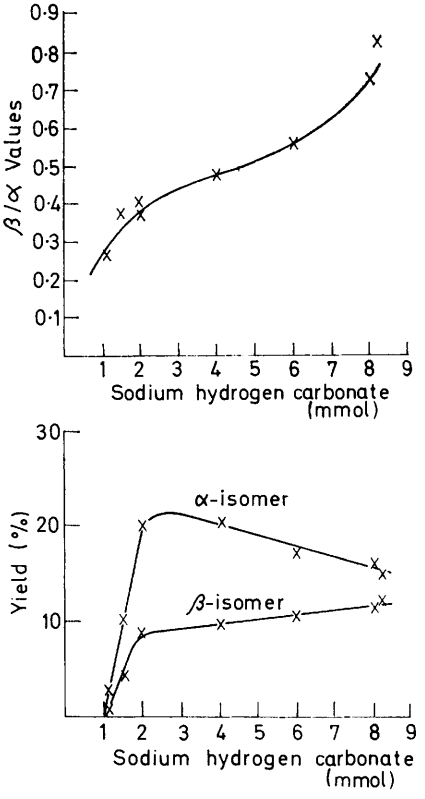
(13) a; R=CN; α-anomer
b; R=CN; β-anomer
c; R=MeCO; α-anomer
d; R=MeCO; β-anomer

furanose structure (7), prepared as a toluene-*p*-sulphonate from L-sorbosylamine, acetone, dimethoxypropane, and toluene-*p*-sulphonic acid, with the acetylacrylamide (1a) produced the acyclic glycoside (8) but with the *N*-methyl derivative of the cyanoacrylamide (1c) the L-sorbosyluracil (9) was obtained directly.

We have also recorded [6] that the reaction of the isopropylideneribofuranosylamine (10) with the acetylacrylamide (1a) gave a mixture of the α- and β-acetyluridine derivatives (11a and b) and a similar mixture of anomers (11c and d) was produced from (10) and the cyanoacrylamide (1c), in both alcoholic and aqueous solution.

We wished to examine the effect of variation of reaction conditions and of structures of acrylamides of type (1) on the ratios of anomeric pyrimidine nucleosides obtained in these reactions, in the hope of producing useful stereospecific or near stereospecific syntheses. In the case of D-xylose we have already shown that it is possible to prepare ethyl 5-amino-1-α-D-xylofuranosylimidazole-4-carboxylate (and hence by appropriate cyclisations purine xylosides) stereospecifically from an intermediate oxazoline,[8] and related sugar oxazoline derivatives have also been used to synthesise specific pyrimidine nucleosides, including α-cytidine.[9] In preliminary experiments we have investigated the reaction of the cyanoacrylamide (1c) with the isopropylideneribofuranosylamine (10) in aqueous solutions containing various concentrations of sodium hydrogen carbonate. The results (Figure) indicate that with increasing concentrations of the base the β : α anomer ratio increases and tends to 1 : 1. Although the results show that considerable enhancement of the α-anomer yield is possible at low base concentrations, there appears little likelihood of achieving more than about a threefold excess of α- to β-isomer in this particular reaction. In these reactions t.l.c. evidence was obtained for the formation of intermediates, considered to be acyclic nucleosides on the basis of comparison of u.v. data with those of the model acyclic compound (1d).[2b] It is uncertain whether the ethoxymethylene derivative is the major reactive species or whether the hydroxymethylene derivative is first produced. Hydrolysis of (1a) to (1e) by mild alkali has been shown to occur.[2d]

The ethoxyacryloylurea (1f) with the ribofuranosylamine (10) or the xylofuranosylamine (12) gave mixtures of corresponding pairs of α- and β-anomers (11c and d) and (13a and b) respectively in yields and ratios analogous to those obtained by using the acryloylcarbamate (1c). The acryloylurea (1f) with dimethylamine readily gave the dimethylaminomethylene derivative (1g), which with cyclohexylamine gave 5-cyano-1-cyclohexyluracil [4] (3; R = CN, R = C_6H_{11}), but with the ribofuranosylamine (10) under the conditions used with the acryloylurea (1f) or carbamate (1c) no nucleoside was formed. In a similar reaction of the dimethylaminomethylene derivative (1h) [prepared from (1c) and dimethylamine] and (10) in either aqueous or non-aqueous solution t.l.c. evidence was obtained for the formation of trace amounts of both α- and β-anomeric nucleosides. However, the reaction of the acetylcarbamate (1a) with dimethylamine produced (1i), which when treated with the xylofuranosylamine (12) gave the α-anomer (13c) only, with no evidence (t.l.c.) for the presence of the corresponding β-nucleoside (13d). In a similar manner the dimethylaminoethylene derivative (1i) or the related morpholino derivative (1j) with the ribofuranosylamine (10) gave the β-anomeric nucleoside (11b) as the sole product, with no evidence for any α-anomer. The structures of the nucleosides isolated were confirmed by comparison with authentic samples.

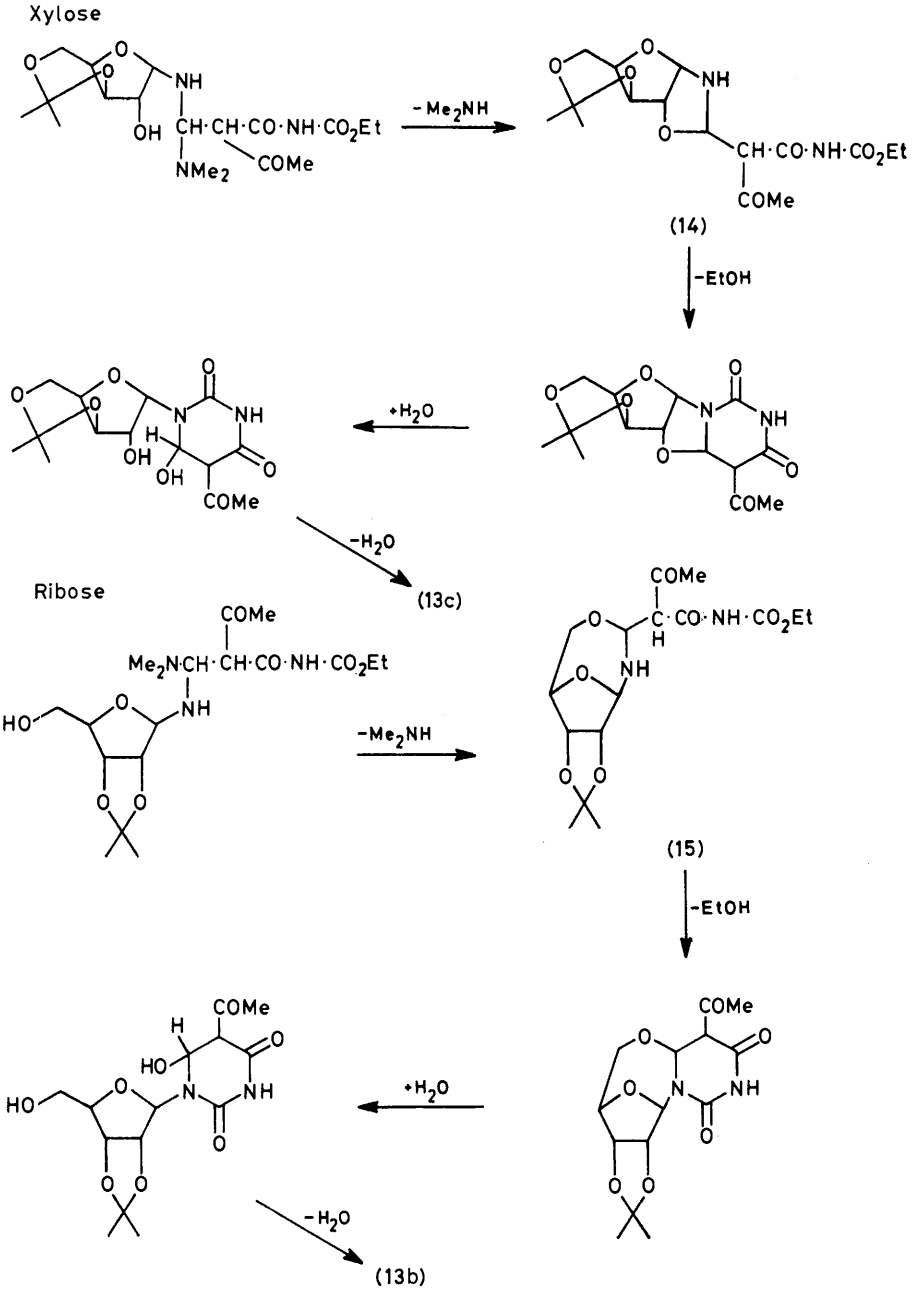


Formation of anomers of 5-cyano-2′,3′-*O*-isopropylideneuridine by reaction of ethyl *N*-(α-cyano-β-ethoxyacryloyl)carbamate with 2,3-*O*-isopropylidene-D-ribofuranosylamine in aqueous sodium hydrogen carbonate. The method used for the separation of the anomers has been described earlier.[6] If the reactions were carried out over a shorter period of time (<30 min), t.l.c. on large plates allowed separation of a u.v.-absorbing material with $\lambda_{max.}$ 283, $\lambda_{min.}$ 235 nm; *cf.* $\lambda_{max.}$ 276, $\lambda_{min.}$ 233 nm for 5-cyanouridine. The model acyclic derivative [2b] had $\lambda_{max.}$ 294, $\lambda_{min.}$ 245 nm; *cf.* $\lambda_{max.}$ 281, $\lambda_{min.}$ 239 nm for the model uracil (3; R = CN, R = Et).[2b] The shifts in absorption maxima are consistent with preliminary formation of an acyclic nucleoside. The starting material (1c) had $\lambda_{max.}$ 253, $\lambda_{min.}$ 227 nm

The stereospecificity involved in both reactions is clearly concerned with the structures of the intermediates produced by addition of the glycosylamine to the C:C bond and the greater basicity of NR_2 than of OR. In the case of the xylose derivative there is a free 2′-OH group which by interaction with the Me_2N group can produce a cyclic oxazolidine intermediate (14); this

[8] D. H. Robinson and G. Shaw, *J.C.S. Perkin I*, 1974, 774.
[9] R. A. Sanchez and L. E. Orgel, *J. Mol. Biol.*, 1970, **47**, 531.

restricts the configuration of the ultimate nucleoside to the α-form. In the case of the ribose derivative it is possible to invoke a similar mechanism which includes an intramolecular reaction involving the free 5'-OH group and formation of the cyclic intermediate (15), which can then only give the β-anomer (Scheme 2).



SCHEME 2

EXPERIMENTAL

Evaporations were carried out with a Büchi rotary evaporator under water pump vacuum with a flask temperature ⩽40 °C unless otherwise stated. U.v. absorption spectra were measured with a Unicam SP 800 spectrophotometer, i.r. spectra with a Perkin-Elmer 157 spectrophotometer, n.m.r. spectra with a JEOL-MH-100 spectrometer (tetramethylsilane or 3-trimethylsilylpropane-1-sulphonic acid as internal standard), mass spectra with an A.E.I. MS902 spectrometer, and optical rotations with a Perkin-Elmer 141 polarimeter. Silica gel (0.05—0.20 mm; 315—370 mesh; Machery Nagel and Co.) was used for column chromatography, and silica gel ($60F_{254}$; 0.25 mm thick) precoated glass plates (Merck) were used for t.l.c. with (A) chloroform–methanol (9 : 1) and (B) butan-1-ol–acetic acid–water (12 : 3 : 5) as development systems.

Ethyl N-[α-*Acetyl*-β-(5,6-O-*isopropylidene*-D-*glucofuranosyl*-

amino)acryloyl]carbamate (4a).—A mixture of 5,6-*O*-isopropylidene-D-glucofuranosylammonium toluene-*p*-sulphonate [7] (11.7 g, 0.03 mol) and ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate (6.9 g, 0.03 mol) was wetted with methanol (20 ml) and a solution of sodium methoxide in methanol (34.5 ml) [from sodium (0.69 g, 0.03 mol)] was added. The mixture was warmed to give a green solution, which was boiled for 10 min, cooled, then evaporated to dryness. The residue was swirled with methanolic dichloromethane (4 : 96; 30 ml) and the precipitate of sodium toluene-*p*-sulphonate filtered off and washed with more methanolic dichloromethane (total 70 ml) until all the orange colour had been washed into the filtrate. The filtrate was evaporated to dryness and treated with water (20 ml) to give a semicrystalline gel, which was filtered off, washed with water, and recrystallised from methanol–water (1 : 3) to give the *carbamate* (4a) (2.7 g, 22.5%), m.p. 210° (Found: C, 50.8; H, 6.65; N, 7.1%; *m/e* 402, 387. $C_{17}H_{26}N_2O_9$ requires C, 50.75; H, 6.5; N, 6.95%; *M*, 402, *M* − CH_3, 387).

Ethyl N-[α-*Ethoxycarbonyl*-β-(5,6-O-*isopropylidene*-D-*glucofuranosylamino)acryloyl]carbamate* (4b).—A mixture of 5,6-*O*-isopropylidene-D-glucofuranosylammonium toluene-*p*-sulphonate (11.8 g, 0.03 mol) and ethyl *N*-(α-ethoxycarbonyl-β-ethoxyacryloyl)carbamate (7.8 g, 0.03 mol) was wetted with methanol (15 ml) and sodium methoxide in methanol (34.5 ml) [from sodium (0.69 g, 0.03 mol)]. The mixture was heated to give a clear solution which was boiled for 10 min; the resulting orange solution was evaporated to dryness. The residue was swirled with methanolic dichloromethane (4 : 96; 30 ml) and the precipitate of sodium toluene-*p*-sulphonate filtered off and washed with methanolic dichloromethane (4 : 96; total 100 ml) until all the orange colour had been washed into the filtrate. The filtrate was evaporated to dryness and the residue swirled with water (20 ml) to give crystals of *compound* (4b) (1.92 g, 15% after recrystallisation from methanol) (Found: C, 50.1; H, 6.6; N, 6.65%; *m/e* 432, 417. $C_{18}H_{28}N_2O_{10}$ requires C, 50.0; H, 6.55; N, 6.5%; *M*, 432; *M* − CH_3, 417).

L-*Sorbosylamine*.—L-Sorbose (180 g) was added in 30 g portions to a solution of ammonium chloride (3 g) and ammonia in methanol (900 ml). During the addition the mixture was heated at 50 °C, and a strong stream of dry ammonia was bubbled through it. After 8 h dissolution was complete. The mixture was cooled, saturated with dry ammonia, and stored at 4 °C. Crystallisation commenced within 24 h. After 7 days the solid was collected, washed with methanol, and dried to give L-sorbosylamine (72 g, 40%) as a cream coloured solid, m.p. 119° (decomp.) [lit.,[10] 119° (decomp.)].

The filtrate was evaporated to *ca.* 500 ml, cooled, resaturated with ammonia, and again stored at 4 °C. After a further 7 days the resulting crystalline solid was broken up, collected, washed, and dried to give (presumably) di-(L-sorbosyl)amine (52 g) as a cream coloured crystalline solid, m.p. 130—131° (decomp.) [lit.,[10] 133° (decomp.)].

4,6-O-*Isopropylidene*-L-*sorbofuranosylammonium Toluene*-p-*sulphonate*.—A solution of dry toluene-*p*-sulphonic acid (30.4 g, 0.14 mol) in 2,2-dimethoxypropane (100 ml, 0.77 mol) and acetone (100 ml) was stirred at room temperature for 15 min. L-Sorbosylamine (14.4 g, 0.08 mol) was added and the mixture stirred for 0.5 h; dissolution was then complete. Dry ether (*ca.* 80 ml) was added and the mixture stored at 4 °C overnight. The resulting crystalline solid was collected, washed with acetone and ether, and dried to yield the *sorbofuranosylamine derivative* (17.4 g, 56%) as needles, m.p. 123—124° (decomp.). A portion recrystallised from ethanol–ether had m.p. 124° (decomp.), $[\alpha]_D^{20}$ +20° (after 5 min) (*c* 2.1 in Me_2SO) (Found: C, 49.0; H, 6.65; N, 3.45. $C_{16}H_{25}NO_8S$ requires C, 49.1; H, 6.45; N, 3.6%).

A solution of the product (100 mg) in 2N-hydrochloric acid (3 ml) was warmed at 80 °C for 5 min. Brady's reagent (3 ml) was added to the cooled solution and the mixture set aside at 0 °C for 1 h. The crystalline precipitate (40 mg) was recrystallised from methanol to give yellow-orange needles, m.p. and mixed m.p. (with acetone 2,4-dinitrophenylhydrazone) 126—127°.

Ethyl N-[α-*Acetyl*-β-(4,6-O-*isopropylidene*-L-*sorbofuranosyl amino)acryloyl]carbamate* (8).—Ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate (2.3 g, 0.01 mol) was added to a stirred solution of 4,6-*O*-isopropylidene-L-sorbofuranosylammonium toluene-*p*-sulphonate (3.9 g, 0.01 mol) in ethanolic sodium ethoxide [20 ml; from sodium (0.01 mol)] and the mixture set aside at room temperature overnight. T.l.c. (system A) showed the presence of one major u.v.-absorbing spot (R_F 0.50) and a minor spot (R_F 0.74). The solution was filtered and evaporated. The residue was swirled with dichloromethane (20 ml) and the precipitated sodium toluene-*p*-sulphonate filtered off. The solution was evaporated to *ca.* 3 ml and applied to a silica gel column (2 × 40 cm); u.v.-absorbing products were eluted by methanolic chloroform (2 : 98). The first fraction (R_F 0.74) was evaporated to a gum (300 mg). Evaporation of the second fraction gave a gum which when dissolved in a small amount of 1 : 1 ethyl acetate–light petroleum (b.p. 40—60 °C) soon yielded a crystalline solid. The carbamate (8) (450 mg, 11%) crystallised from ethyl acetate–light petroleum (b.p. 40—60 °C) as rods, m.p. 153° (softening at 149°) (Found: C, 50.45; H, 6.5; N, 7.0. $C_{17}H_{26}N_2O_9$ requires C, 50.75; H, 6.5; N, 6.95%).

5-*Cyano*-1-(4,6-O-*isopropylidene*-L-*sorbofuranosyl*)-3-*methyluracil* (9).—α-Cyano-β-ethoxycarbonyl-*N*-methylacrylamide [5] (2.25 g, 0.01 mol) was added to a stirred solution of 4,6-*O*-isopropylidene-L-sorbofuranosylammonium toluene-*p*-sulphonate (3.9 g, 0.01 mol) in ethanolic sodium ethoxide [20 ml; from sodium (0.01 mol)] and the mixture was set aside at room temperature overnight. T.l.c. (system A) showed one major u.v.-absorbing spot at R_F 0.66. The solution was filtered and evaporated to a gum. A solution of the gum in chloroform was applied to a silica gel column (2 × 40 cm) and the u.v. absorbing product eluted by ethanolic 2% chloroform. Evaporation gave a gum which, when dissolved in a small amount of 1 : 1 ethyl acetate–petroleum (b.p. 40—60 °C), soon gave a crystalline precipitate. The *sorbofuranosyluracil* (2.1 g, 60%) crystallised from ethyl acetate as rods, m.p. 178—179° (Found: C, 51.15; H, 5.6; N, 11.85%; M^+, 353. $C_{15}H_{19}N_3O_7$ requires C, 51.0; H, 5.4; N, 11.9%; *M*, 353).

In a subsequent experiment the reaction mixture was filtered and evaporated, the residue dissolved in a little methanol, and the solution seeded with crystals of the foregoing sorbofuranosyluracil. After 2 h at 0 °C the resulting precipitate was collected and recrystallised from ethyl acetate to give the uracil (55%) as rods, m.p. and mixed m.p. with the foregoing sample 178—179°.

5-*Cyano*-1-(2,3-O-*isopropylidene*-α-D-*ribofuranosyl)uracil* (11c).—*N*-Acetyl-*N*′-(α-cyano-β-ethoxyacryloyl)urea [4] (0.7

[10] K. Heyns, H. Paulsen, R. Eichstedt, and M. Rolle, *Chem. Ber.*, 1957, **90**, 2039.

g) and 2,3-*O*-isopropylidene-D-ribofuranosylammonium toluene-*p*-sulphonate [6] (1.1 g) were suspended in ethanol (10 ml), 1M-sodium ethoxide in ethanol (10 ml) was added, and the mixture was shaken until a clear solution was obtained. T.l.c. after 15 min showed the presence of the two anomeric nucleosides in similar amounts. The solution was evaporated to dryness, the residue dissolved in the minimum volume of water, and the resulting solution neutralised with a few drops of glacial acetic acid. On cooling in ice the title α-anomer was deposited; it crystallised from ethanol as needles (0.5 g), m.p. 268°, identical with a specimen prepared from α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide [6] (mixed m.p., t.l.c., and i.r., u.v., and mass spectra).

Ethyl N-(α-*Cyano*-β-*dimethylaminoacryloyl*)*carbamate* (1h).—Ethyl *N*-(α-cyano-β-ethoxyacryloyl)carbamate [2a] (1 g) in absolute ethanol (30 ml) was warmed for 15 min with ethanolic dimethylamine (33% w/v; 0.7 ml). The resulting solution was evaporated to dryness; the residue crystallised from ethanol as rods (0.5 g, 50%), m.p. 140° (lit.,[2b] 142°).

This acryloylcarbamate (1h) (0.45 g, 2.5 mmol) was added to a mixture of 2,3-*O*-isopropylidene-D-ribofuranosylammonium toluene-*p*-sulphonate (0.9 g, 2.5 mmol) and methanolic sodium methoxide [15 ml; from sodium (2.5 mmol)]. The mixture was refluxed for 1 h and evaporated to dryness. The residual gum was dissolved in water (5 ml), acidified with glacial acetic acid, and cooled in ice. T.l.c. (system A) showed a major u.v.-absorbing spot at R_F 0.76 which corresponded to the acrylamide starting material and two minor spots at R_F 0.53 and 0.60 which corresponded to authentic specimens [6] of 5-cyano-1-(2,3-*O*-isopropylidene-α- and β-D-ribofuranosyl)uracils, respectively.

The acryloylcarbamate (1h) (210 mg, 1 mmol) was added to a solution of 2,3-*O*-isopropylidene-D-ribofuranosylammonium toluene-*p*-sulphonate (360 mg, 1 mmol) and sodium hydrogen carbonate (170 mg, 2 mmol) in water (10 ml). The mixture was warmed at 70 °C for 5 min and set aside at room temperature overnight. The resulting solution was cooled in ice and adjusted to pH 7 with 0.1M-hydrochloric acid. T.l.c. (system A) showed a strong u.v.-absorbing spot at the origin and two faint spots at R_F 0.53 and 0.60 which corresponded to authentic specimens [6] of 5-cyano-1-(2,3-*O*-isopropylidene-α- and -β-D-ribofuranosyl)-uracils, respectively.

N-*Acetyl*-N′-(α-*cyano*-β-*dimethylaminoacryloyl*)*urea* (1g).—*N*-Acetyl-*N*′-(α-cyano-β-ethoxyacryloyl)urea (2 g) in ethanol (15 ml) with ethanolic dimethylamine (33 : 67; 5 ml) was warmed to 60 °C, then set aside for 15 min, and evaporated to a solid. The *acryloylurea* (1.3 g) crystallised from ethyl acetate as needles, m.p. 114° (Found: C, 48.1; H, 5.5; N, 24.9%; M^+, 224. $C_9H_{12}N_4O_3$ requires C, 48.2; H, 5.4; N, 25.0%; *M*, 224). On treatment of the product with 2,3-*O*-isopropylidene-D-ribofuranosylamine no evidence was obtained for the formation of a nucleoside.

5-*Cyano*-(3,5-O-*isopropylidene*-1-αβ-D-*xylofuranosyl*)*uracil* (13a *and* b).—(*a*) A suspension of 3,5-*O*-isopropylidene-D-xylofuranosylammonium toluene-*p*-sulphonate [7] (1.08 g) and ethyl *N*-(α-cyano-β-ethoxyacryloyl)carbamate (0.7 g) in methanol (10 ml) was shaken with M-sodium methoxide in methanol (10 ml) to produce a clear pale green solution, which was set aside overnight then evaporated to dryness. The residual foam was extracted with methanolic dichloromethane (4 : 96) and the precipitate of sodium toluene-*p*-sulphonate removed. The filtrate was evaporated, the residue dissolved in a little water, and the solution adjusted to pH 7 with acetic acid, then set aside at 0 °C. A solid slowly separated. The mixture of α- and β-D-*xylosyluracils* (0.2 g) separated from ethanol as needles, m.p. 270—280° (Found: C, 50.7; H, 5.1; N, 13.3%; M^+, 309. $C_{13}H_{15}N_3O_6$ requires C, 50.5; H, 4.9; N, 13.6%; *M*, 309). T.l.c. showed two spots of roughly equivalent intensity under a u.v. lamp. A similar mixture of anomers was obtained when the foregoing carbamate was replaced by *N*-acetyl-*N*′-(α-cyano-β-ethoxyacryloyl)urea.

Ethyl N-(α-*Acetyl*-β-*dimethylaminoacryloyl*)*carbamate* (1i).—Ethanolic dimethylamine (5 ml; 33%) was added to a suspension of ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate (2 g) in acetonitrile (10 ml) and the mixture set aside for 2 h at room temperature. The solution was evaporated to dryness and the residue dissolved in chloroform (100 ml). The solution was washed with water (40 ml), dried (Na_2SO_4), and evaporated to a gum. The *dimethylaminoacryloylcarbamate* (1.2 g) crystallised from ethyl acetate–ether as prisms, m.p. 140° (Found: C, 52.5; H, 7.0; N, 12.5%; M^+, 228. $C_{10}H_{16}N_2O_4$ requires C, 52.65; H, 7.0; N, 12.3%; *M*, 228), $\lambda_{max.}$ (H_2O) 299 nm (ε 21 280).

Ethyl N-(α-*Acetyl*-β-*morpholinoacryloyl*)*carbamate* (1j).—Morpholine (0.86 g) was added to a suspension of ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate (2 g) in acetonitrile; the mixture was set aside at room temperature for 2 h then evaporated to dryness. The residue was dissolved in chloroform (100 ml) and the solution washed with water (40 ml), dried (Na_2SO_4), and evaporated. The residual *morpholino-derivative* (1.6 g) crystallised from ethyl acetate as prisms, m.p. 144—146° (Found: C, 53.45; H, 6.85; N, 10.45. $C_{12}H_{18}N_2O_5$ requires C, 53.3; H, 6.7; N, 10.35%).

5-*Acetyl*-2′,3′-O-*isopropylideneuridine* (11b).—To a solution of 2,3-*O*-isopropylidene-D-ribosylammonium toluene-*p*-sulphonate (1.1 g) in methanol (10 ml) was added ethyl *N*-(α-acetyl-β-dimethylaminoacryloyl)carbamate (0.7 g) and a solution of methoxide [from sodium (0.14 g)] in methanol (10 ml). The solution was boiled under reflux for 1 h, cooled, and evaporated to dryness. The residue was dissolved in water (5 ml), cooled, and acidified with acetic acid (*ca.* 4 drops). A crystalline precipitate soon appeared. The acetyluridine (0.4 g) crystallised from ethanol as needles, m.p. 189°, identical (mixed m.p. and i.r., u.v., and mass spectra) with an authentic sample.[6] T.l.c. of the mother liquors (systems A and B) did not reveal the presence of any α-isomer. The same result was obtained when the dimethylaminoacryloyl derivative was replaced by the foregoing morpholinoacryloylcarbamate.

5-*Acetyl*-1-(3,5-O-*isopropylidene*-α-D-*xylofuranosyl*)*uracil* (13c).— 3,5-*O*-Isopropylidene-D-xylofuranosylammonium toluene-*p*-sulphonate (1.1 g) was dissolved in methanol (5 ml), ethyl *N*-(α-acetyl-β-dimethylaminoacryloyl)carbamate (0.7 g) was added, and the solution was refluxed for 1 h then evaporated to dryness. A solution of the solid residue in water (5 ml) was acidified with glacial acetic acid and cooled in ice to give a precipitate of 5-acetyl-1-(3,5-*O*-isopropylidene-α-D-xylofuranosyl)uracil (0.3 g), m.p. 205° (0.3 g) (needles from ethanol), identical with a specimen of the α-nucleoside [7] prepared from ethyl *N*-(α-acetyl-β-ethoxyacryloyl)carbamate (mixed m.p., t.l.c., and i.r., u.v., and mass spectra). T.l.c. the mother liquors (systems A and B) indicated the absence of any β-isomer.

We thank the S.R.C. (P. S. T., G. M., and D. H. R.), the M.R.C. (P. W. R.), and Allen & Hanburys (R. L.) for research studentships.

[6/1796 *Received*, 24*th September*, 1976]