11. *Purines, Pyrimidines, and Glyoxalines. Part XI.* Some Oxazolidino- and Thiazolidino-[2 : 3-a]pyrimidines, and a Synthesis of Thymidine.*

By G. Shaw and R. N. Warrener.

Oxazolidino- and thiazolidino-[2 : 3-*a*]pyrimidines have been prepared by the reaction of 1-substituted hydroxyalkyl-uracils and -thiouracils respectively with methanesulphonyl chloride or toluene-*p*-sulphonyl chloride, and cyclisation of the resulting esters. Some properties of these compounds have been investigated and the method has been adapted to a synthesis of thymidine from 5-methyl-2-thiouridine.

When 2′-O-*p*-toluenesulphonyl or -methanesulphonyl derivatives of uridine and related pyrimidine ribofuranosides are heated with bases, the reaction $C_{(2)}{-}OH + C_{(2')}{-}O{\cdot}SO_2R \longrightarrow C_{(2)}{-}O{-}C_{(2')} + R{\cdot}SO_2{\cdot}OH$ occurs with liberation of the sulphonic acid and formation of a O^2 : 2′-*cyclo*nucleoside with simultaneous inversion of configuration at $C_{(2')}$. The *cyclo*-nucleosides can be hydrolysed to β-D-arabinofuranosides and this property has been used in the preparation of spongouridine [1] (1-β-D-arabinofuranosyluracil) and spongothymidine [2] (1-β-D-arabinofuranosylthymine) from uridine and 5-methyluridine respectively. *cyclo*-Nucleoside formation also provides conclusive proof of the β-configuration at the glycosidic centre of the above ribofuranosides. The analogous but hitherto unknown S^2 : 2′-*cyclo*-thiouridines (X) by similar reactions should lead to the 2′-deoxy-2′-thioarabinofuranosyl-uracils series which by desulphurisation would be a source of 2′-deoxyribofuranosyl-uracils.

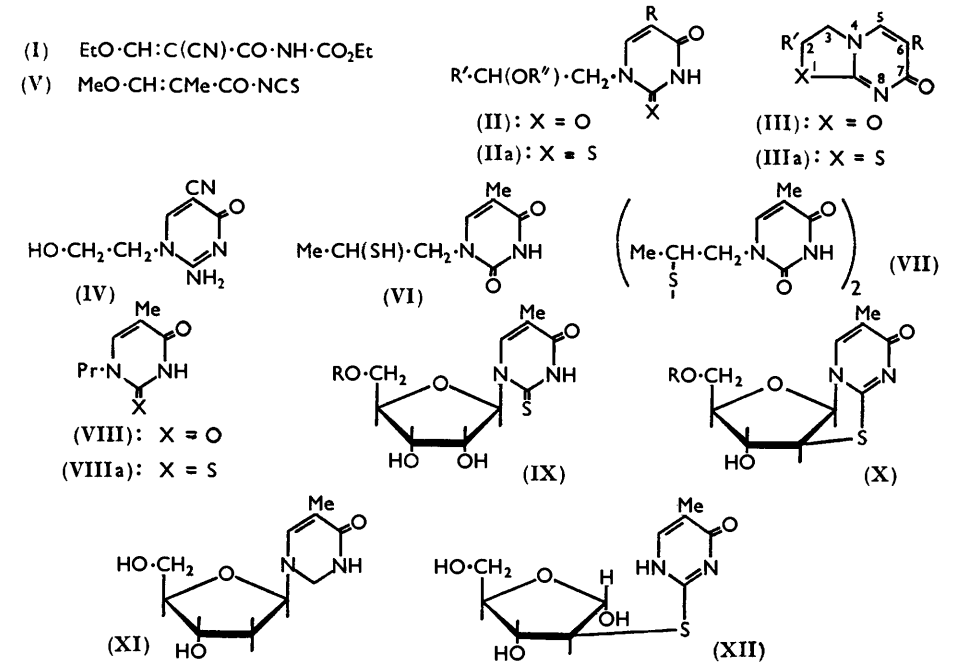
We examined initially some simpler compounds. 1-(Hydroxyalkyl)uracils and related compounds are now readily available by methods outlined in earlier papers, from primary amines and appropriate linear precursors of uracils or 2-thiouracils.[3] Reaction of ethanolamine and 2-hydroxypropylamine with the ethoxymethylene derivative (I) gave the 2′-hydroxyalkyluracils (II; R = CN, R′ = H or Me, R″ = H) which were readily converted into the sulphonates (II; R = CN, R′ = H and Me, R″ = $Me{\cdot}SO_2$ or *p*-$Me{\cdot}C_6H_4{\cdot}SO_2$). When either ester was heated in acetone with triethylamine an initial deep magenta-coloured solution was obtained which slowly faded as the oxazolidino-pyrimidines (III; R = CN, R′ = H or Me) separated from the solution. With methanolic ammonia the cyano-compound (III; R = CN, R′ = H) gave the *iso*cytosine derivative (IV), and the same compound was also obtained from the ester (II; R = CN, R′ = H, R″ = *p*-$Me{\cdot}C_6H_4{\cdot}SO_2$) and methanolic ammonia.

In a similar manner, reaction of ethanolamine and 2-hydroxypropylamine with the acyl *iso*thiocyanate (V) readily gave the thiothymines (IIa; R = Me, R′ = H or Me, R″ = H). These with methanesulphonyl chloride in pyridine at room temperature gave directly the thiazolidinopyrimidines (IIIa; R = Me, R′ = H or Me); intermediate *O*-methanesulphonyl derivatives could not be isolated. A positive reaction for the thiol group with sodium nitroprusside was rapidly obtained when the cyclic compound (IIIa; R = R′ = Me) was warmed with aqueous sodium hydroxide, and the thiol (VI) was readily isolated from the reaction mixture. Attempts to desulphurise this compound proved troublesome. With W7 Raney nickel catalyst or with iodine in aqueous alkali, the disulphide (VII) was obtained; however, reaction with W2 nickel catalyst gave 1-propylthymine (VIII), which was also prepared by the reaction of the *iso*thiocyanate (V) with propylamine and desulphurisation of the resulting 1-propyl-2-thiothymine (VIIIa) with chloroacetic acid.

* Part X, *J.*, 1958, 2299.

[1] Brown, Todd, and Varadarajan, *J.*, 1956, 2388.
[2] Fox, Yung, and Bendich, *J. Amer. Chem. Soc.*, 1957, **79**, 2775.
[3] (*a*) Shaw, *J.*, 1955, 1834; Shaw and Warrener, *J.*, 1958, (*b*) 153, (*c*) 157.

Adaptation of these reactions to a synthesis of thymidine (XI) required the preparation of 5-methyl-S^2 : 2′-*cyclo*thiouridine (X; R = H). Similar O^2 : 2′-*cyclo*uridines have been prepared by toluene-*p*-sulphonylation or methanesulphonylation of 5′-*O*-acetyluridine or 5-methyl-5′-*O*-trityluridine and cyclisation of the esters with ammonia;[1,2] in these experiments, no evidence for sulphonylation at the 3′-hydroxyl group was recorded.



5-Methyl-2-thiouridine[3d] (IX; R = H) in pyridine readily gave a good yield of crystalline 5′-*O*-triphenylmethyl derivative (IX; R = CPh_3), the position of the triphenylmethyl group appearing certain by analogy with similar compounds prepared from uridine and 5-methyluridine. Our material also gave a positive test for a vicinal glycol with the starch–periodate reagent but this is of doubtful diagnostic value for thiouracil derivatives in which the sulphur appears to reduce periodate.

The ether (IX; R = CPh_3) with methanesulphonyl chloride in pyridine gave a solid which from its elementary analysis and ultraviolet absorption spectrum, similar to that of the analogue (IIIa; R = R′ = Me), was undoubtedly the *cyclo*thionucleoside (X; R = CPh_3). Fox, Yung, and Bendich [2] obtained a similar solid by methanesulphonylation of 5-methyl-5′-*O*-trityluridine, but from a low sulphur content concluded that only 25% of esterification had occurred. Since an excess of methanesulphonyl chloride was used, this conclusion appears unlikely and we suggest that this substance may have been a mixture of the 2′-*O*-methanesulphonyl derivative and the corresponding *cyclo*nucleoside.

Hydrolysis of the ether (X; R = CPh_3) with dilute acid gave triphenylmethanol and a syrup whose ultraviolet absorption was very similar to that of compound (IIIa; R = R′ = Me), suggesting that it was largely the *cyclo*-compound (X; R = H), and this was confirmed by its further reactions. When the syrup was warmed with dilute sodium hydroxide solution, the solution soon gave a positive thiol test with sodium nitroprusside, and the ultraviolet absorption changed to that of a simple uracil derivative. When the syrup was warmed with dilute sodium hydroxide solution in the presence of W2 Raney nickel, the solution soon gave strong positive tests for 2-deoxy-sugars with the Dische and the cysteine–sulphuric acid reagent. Paper chromatograms of this solution showed the

presence of thymidine as an absorbing spot accompanied by two other spots, all three giving a positive test with the cysteine spray. A small amount of crystalline thymidine (XI) was isolated and its identity confirmed by comparison with an authentic specimen. The nature of the two cysteine-positive compounds which accompanied the thymidine is not clear: one of them gave tests for a reducing sugar and had the same R_F value as 2-deoxyribose—the formation of 2-deoxyribose would be readily accounted for if fission at the glycosidic link (X; R = H) is a competing reaction, leading to (XII), desulphurisation of which would give the free sugar.

The formation of thymidine, although only of academic value in its present form, conclusively proves the β-configuration assigned to 5-methyl-2-thiouridine.

Experimental

5-Cyano-1-2′-hydroxyethyluracil.—2-Hydroxyethylamine (1·2 ml.) was added to a suspension of α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide [3] (2·12 g.) in water (15 ml.), and the mixture heated on a water-bath for 5 min. The clear solution obtained was cooled and acidified with hydrochloric acid, to precipitate *5-cyano-1-2′-hydroxyethyluracil* (1·66 g.) which recrystallised from ethanol as needles, m. p. 194° (Found: C, 46·4; H, 4·1; N, 23·0. $C_7H_7O_3N_3$ requires C, 46·4; H, 3·9; N, 23·2%), $\lambda_{max.}$ 280 mμ (ε 12,950), $\lambda_{min.}$ 242 mμ (ε 1150) in water.

*5-Cyano-1-2′-toluene-*p*-sulphonyloxyethyluracil.*—A solution of the foregoing uracil (5·91 g.) and toluene-*p*-sulphonyl chloride (6·86 g.) in dry pyridine (10 ml.) was set aside at room temperature overnight, then treated with ice-water (200 ml.) and kept at 0° for 2 days, to give a crystalline precipitate. This was washed with ethanol (3 × 10 ml.) and ether (2 × 10 ml.), giving *5-cyano-1-2′-toluene-*p*-sulphonyloxyethyluracil* (5·6 g.) which recrystallised from a large volume of ethanol as needles, m. p. 238—240° (Found: C, 50·1; H, 4·05; N, 12·45. $C_{14}H_{13}O_5N_3S$ requires C, 50·15; H, 3·9; N, 12·5%). In a similar manner, the hydroxyethyluracil (1 g.) and methanesulphonyl chloride (0·46 ml.) in pyridine (7·5 ml.) afforded *5-cyano-1-2′-methanesulphonyloxyethyluracil* (1·09 g.), needles (from much methanol), m. p. 207° (Found: C, 37·3; H, 3·45; N, 16·15. $C_8H_9O_5N_3S$ requires C, 37·05; H, 3·5; N, 16·2%).

6-Cyano-7-oxo-oxazolidino[2 : 3-a]*pyrimidine.*—A solution of the foregoing toluene-*p*-sulphonate (1·5 g.) in acetone (75 ml.) containing triethylamine (4 ml.) was boiled under reflux for 2 hr. The mixture initially assumed a deep magenta colour which gradually faded, and a crystalline precipitate separated. The *cyclic compound* (0·62 g.) was sulphur-free and recrystallised from water as needles, m. p. 360° (Found: C, 51·9; H, 3·3; N, 25·5. $C_7H_5O_2N_3$ requires C, 51·55; H, 3·1; N, 25·75%), $\lambda_{max.}$ 277 (ε 7850), 227 mμ (ε 7300), $\lambda_{min.}$ 249 mμ (ε 2500) in water. The same substance (0·218 g.) was similarly prepared from the methanesulphonyl derivative (0·4 g.), acetone (50 ml.), and triethylamine (2 ml.).

*5-Cyano-1-2′-hydroxyethyl*isocytosine.—A suspension of the above-mentioned toluene-*p*-sulphonate (0·5 g.) in methanol (50 ml.) gave a clear red solution when treated with saturated methanolic ammonia (50 ml.). The solution was set aside for 16 hr., the red colour fading. Evaporation then gave *5-cyano-1-2′-hydroxyethyl*isocytosine (0·19 g.) which separated from water as needles, m. p. 248° (Found: C, 46·45; H, 4·4; N, 30·65. $C_7H_8O_2N_4$ requires C, 46·65; H, 4·5; N, 31·1%), $\lambda_{max.}$ 277 mμ (ε 8200), $\lambda_{min.}$ 252 mμ (ε 3600) in water. The same compound (0·084 g.) was similarly obtained from the foregoing cyclic compound (0·1 g.) and methanolic ammonia.

5-Cyano-1-2′-hydroxypropyluracil.—A solution of α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide (2·5 g.) in water (15 ml.) containing 2-hydroxypropylamine (2 g.) was heated on a water-bath for 5 min. The cooled solution was acidified with 10N-hydrochloric acid, then set aside for a few hr. A crystalline precipitate separated. *5-Cyano-1-2′-hydroxypropyluracil* (2·3 g.) recrystallised from ethanol as prisms, m. p. 223° (Found: C, 49·2; H, 4·65; N, 21·4. $C_8H_9O_3N_3$ requires C, 49·25; H, 4·65; N, 21·55%), $\lambda_{max.}$ 280 mμ (ε 14,900), $\lambda_{min.}$ 240 mμ (ε 3250) in water.

5-Cyano-1-2′-methanesulphonyloxypropyluracil.—The foregoing uracil (1 g.) in dry pyridine (7·5 ml.) at 0° was treated with methanesulphonyl chloride (0·44 ml.), and the solution set aside at room temperature for 24 hr. Excess of acid chloride was decomposed by addition of a few drops of water to the mixture which was then kept for 30 min., and treated with more water (25 ml.) to precipitate *5-cyano-1-2′-methanesulphonyloxypropyluracil* (1·13 g.). This

separated from methanol as prisms, m. p. 212° (Found: C, 39·85; H, 3·95; N, 15·25. $C_9H_{11}O_5N_3S$ requires C, 39·55; H, 4·05; N, 15·4%). Similarly the foregoing uracil (1·95 g.), pyridine (10 ml.), and toluene-*p*-sulphonyl chloride (2 g.) gave *5-cyano-1-2′-toluene-*p*-sulphonyloxypropyluracil* (2·7 g.), plates (from ethanol), m. p. 208° (Found: C, 51·6; H, 4·55; N, 12·0. $C_{15}H_{15}O_5N_3S$ requires C, 51·6; H, 4·35; N, 12·05%).

6-Cyano-2-methyl-7-oxo-oxazolidino[2 : 3-a]*pyrimidine.*—A solution of the last-mentioned toluene-*p*-sulphonate (2 g.) in acetone (50 ml.) and triethylamine (4 ml.) was boiled under reflux for 2 hr. during which crystals slowly separated. The *cyclic compound* (0·36 g.) was collected and recrystallised from water as plates, m. p. 248° (Found: C, 54·35; H, 4·15; N, 23·75. $C_8H_7O_2N_3$ requires C, 54·25; H, 4·0; N, 23·7%), $\lambda_{max.}$ 227 (ε 7900), 276 mμ (ε 8250), $\lambda_{min.}$ 249 mμ (ε 2900) in water. A further quantity of the compound (0·5 g.) was obtained by evaporation of the acetone solution.

1-2′-Hydroxyethyl-5-methyl-2-thiothymine.—A vigorous reaction occurred when β-methoxy-α-methylacryloyl *iso*thiocyanate [3b] (1·6 g.) was added to 2-hydroxyethylamine (1·2 g.) in water (5 ml.). The cooled solution was acidified and the precipitated solid collected. *1-2′-Hydroxyethyl-5-methyl-2-thiothymine* (1·3 g.) separated from ethanol as needles, m. p. 204° (Found: C, 45·45; H, 5·2; N, 14·8. $C_7H_{10}O_2N_2S$ requires C, 45·15; H, 5·4; N, 15·05%), $\lambda_{max.}$ 275 mμ (ε 15,380), $\lambda_{min.}$ 243 mμ (ε 4240).

6-Methyl-7-oxothiazolidino[2 : 3-a]*pyrimidine.*—The thiothymine (0·95 g.) in pyridine (5 ml.) with methanesulphonyl chloride (0·6 g.) was set aside for 24 hr., and the resulting crystals were collected. The *cyclic compound* (0·4 g.) separated from water as prisms, m. p. 262° (Found: C, 49·9; H, 4·75; N, 16·65. $C_7H_8ON_2S$ requires C, 50·0; H, 4·8; N, 16·65%), $\lambda_{max.}$ 228 mμ (ε 20,500), $\lambda_{infl.}$ 260 mμ (ε 6700) in water.

1-2′-Hydroxypropyl-2-thiothymine.—2-Hydroxypropylamine (2·5 g.) in ether (10 ml.) was added to β-methoxy-α-methylacryloyl *iso*thiocyanate (4·4 g.) in ether (30 ml.); a vigorous reaction occurred and a solid separated. This was heated with 2N-sodium hydroxide (12 ml.) on a water-bath for 5 min., then cooled and acidified to give *1-2′-hydroxypropyl-2-thiothymine* (4·05 g.) recrystallising from ethanol as prisms, m. p. 191° (Found: C, 47·9; H, 6·25; N, 13·55. $C_8H_{12}O_2N_2S$ requires C, 48·0; H, 6·05; N, 14·0%), $\lambda_{max.}$ 275 mμ (ε 16,100), $\lambda_{min.}$ 245 mμ (ε 5200) in water. A solution of the thiothymine (1 g.) in pyridine (3 ml.) containing benzoyl chloride (1 ml.) was set aside for 3½ hr., then acidified with hydrochloric acid to precipitate a gum which solidified when rubbed with ethanol; *1-2′-benzoyloxypropyl-2-thiothymine* (0·45 g.) separated from ethanol as needles, m. p. 202° (Found: C, 59·3; H, 5·1; N, 9·45. $C_{15}H_{16}O_3N_2S$ requires C, 59·2; H, 5·3; N, 9·2%). The benzoate (0·33 g.) in ethanol (30 ml.) and sodium ethoxide in ethanol (1·04 ml., 5%) were set aside for 20 hr., then evaporated, and the residue was treated with water (5 ml.) and extracted with ether. The aqueous solution was acidified, 1-2′-hydroxypropyl-2-thiothymine (0·195 g.), m. p. and mixed m. p. 186°, being precipitated.

2 : 6-Dimethyl-7-oxothiazolidino[2 : 3-a]*pyrimidine.*—Methanesulphonyl chloride (2·5 ml.) was added to 1-2′-hydroxypropyl-2-thiothymine (5·3 g.) in pyridine (20 ml.) at 0°, and the solution set aside for 24 hr. A crystalline precipitate was collected and washed with pyridine (2 × 3 ml.). The *cyclic compound* (1·75 g.) recrystallised from water as needles, m. p. 260° (Found: C, 52·7; H, 5·35; N, 15·9. $C_8H_{10}ON_2S$ requires C, 52·75; H, 5·55; N, 15·4%); a further quantity of the substance (1·05 g.) separated from the pyridine solution after 2 days. It had $\lambda_{max.}$ 229 (ε 22,400), 263 mμ (ε 7900), $\lambda_{min.}$ 256 mμ (ε 7800) in water.

1-2′-Mercaptopropylthymine.—The foregoing pyrimidine (3·4 g.) was warmed with 2N-sodium hydroxide (25 ml.) for 20 min., a homogeneous solution being obtained. This was cooled and acidified with hydrochloric acid, yielding *1-2′-mercaptopropylthymine* (2·26 g.) which recrystallised from water as needles, m. p. 158° (Found: C, 47·8; H, 5·8; N, 13·9. $C_8H_{12}O_2N_2S$ requires C, 48·0; H, 6·05; N, 14·0%), $\lambda_{max.}$ 272 mμ (ε 10,350), $\lambda_{min.}$ 238 mμ (ε 2470) in water, giving a deep purple colour with alkaline sodium nitroprusside solution. The thiol (0·05 g.) in 0·1N-sodium hydroxide (5 ml.) was added to 0·1N-iodine in aqueous potassium iodide (2·5 ml.); the solution which was rapidly decolorised was acidified and the *disulphide* (0·042 g.) was collected and recrystallised from ethanol as prisms, m. p. 224° (Found: C, 48·4; H, 5·6; N, 13·8. $C_{16}H_{22}O_4N_4S_2$ requires C, 48·25; H, 5·55; N, 14·05%).

1-Propyl-2-thiothymine.—Propylamine (2·5 ml.) in ether (10 ml.) was added to β-methoxy-α-methylacryloyl *iso*thiocyanate (3·05 g.) in ether (10 ml.); a vigorous reaction occurred and *N-(β-methoxy-α-methylacryloyl)-N′-propylthiourea* separated. It crystallised from ethanol as needles, m. p. 56° (Found: C, 50·2; H, 7·35; N, 12·8. $C_9H_{16}O_2N_2S$ requires C, 50·0; H, 7·45;

N, 12·95%). The thiourea was heated on a water-bath with 2N-sodium hydroxide (10 ml.) for 5 min. The clear solution obtained was cooled and acidified, to give 1-*propyl-2-thiothymine* (2·4 g.), needles (from ethanol), m. p. 200° (Found: C, 52·3; H, 6·45; N, 15·05. $C_8H_{12}ON_2S$ requires C, 52·15; H, 6·55; N, 15·2%).

1-*Propylthymine*.—A suspension of 1-propyl-2-thiothymine (0·5 g.) in water (30 ml.) and chloroacetic acid (0·6 g.) was boiled under reflux for 5 hr., then evaporated to an oil. This was evaporated twice with 10N-hydrochloric acid (2 ml.) and water (5 ml.), and the resulting residue dissolved in 5N-sodium hydroxide (4 ml.); the cooled filtered solution was acidified to give a crystalline precipitate. 1-*Propylthymine* (0·4 g.) recrystallised from water as needles, m. p. 138° (Found: C, 57·15; H, 7·2; N, 16·4. $C_8H_{12}O_2N_2$ requires C, 57·15; H, 7·2; N, 16·65%). The compound had R_F 0·82 on paper chromatograms (ascending) in a solvent system composed of butanol saturated with water.

Reaction of 1-2′-*Mercaptopropylthymine with Raney Nickel*.—(*a*) The thiol (0·262 g.) in ethanol (40 ml.) and W2 Raney nickel (2 g.) were heated together under reflux for 2 hr.; tests of the solution with alkaline sodium nitroprusside then showed absence of thiol groups. The solution was evaporated and the solid crystallised from water, to give 1-propylthymine (0·05 g.), m. p. and mixed m. p. 138°, R_F 0·82 in butanol saturated with water. One other absorbing substance (R_F 0·48) was also present. (*b*) The thiol (0·25 g.) in ethanol (40 ml.) and W7 Raney nickel (2 g.) were heated together under reflux, and additional amounts of the catalyst (3 × 0·5 g.) were added at hourly intervals until a negative reaction for the thiol group with alkaline sodium nitroprusside was obtained (5 hr.). The catalyst was filtered off and washed with ethanol, and the filtrate evaporated to a solid residue. This was washed with water to give the disulphide (0·112 g.) which recrystallised from ethanol as prisms, m. p. and mixed m. p. 224°, R_F 0·7 in butanol–water. In a similar experiment, the thiol (0·25 g.), W7 Raney nickel (1 g.), and ethanol were boiled together for 4 hr., then kept overnight at room temperature to give the disulphide (0·13 g.). Neither 1-propylthymine nor the substance of R_F 0·48 (see *a*) could be detected on paper chromatograms.

5-*Methyl-2-thio-5′*-O-*triphenylmethyluridine*.—Recrystallised chlorotriphenylmethane (1·77 g.) was added to a solution of 5-methyl-2-thiouridine[3d] (0·87 g.) in pyridine (15 ml.), and the solution set aside for 2 days, then heated on a water-bath for 2 hr. The cooled solution was added to water (10 ml.) to precipitate a gum. The mixture was kept at 0° for 2 hr. and the aqueous phase decanted. The remaining semi-solid gum was washed by decantation with water, then stirred with acetone (16 ml.), to precipitate 5-*methyl-2-thio-5′*-O-*triphenylmethyluridine* (0·87 g.) which recrystallised from ethanol as plates, m. p. 223° (Found: C, 67·3; H, 5·45; N, 5·5. $C_{29}H_{28}O_5N_2S$ requires C, 67·45; H, 5·45; N, 5·4%). A further quantity of the triphenylmethyl derivative (0·53 g.) was recovered by evaporation of the acetone filtrate and trituration of the residue with ether containing a little acetone; it had $\lambda_{max.}$ 277 mμ (ε 16,200), $\lambda_{min.}$ 247 mμ (ε 5000), in ethanol.

Reaction of 5-*Methyl-2-thio-5′*-O-*triphenylmethyluridine with Methanesulphonyl Chloride*.—Methanesulphonyl chloride (0·16 ml.) was added to a solution of the trityl derivative (0·97 g.) in pyridine (7 ml.), the mixture was set aside for 2 days, then evaporated to dryness *in vacuo*, and the residue rubbed with water (100 ml.) to give a solid (1 g.). This partly dissolved in benzene; the insoluble portion was collected and recrystallised from ethanol to give unchanged trityl derivative (0·21 g.), m. p. and mixed m. p. 223°. The benzene-soluble material was readily precipitated as a solid by addition of light petroleum (b. p. 40—60°). The solid, presumably a *hydrate* of 5-*methyl-5′*-O-*triphenylmethyl*-S[2]:2′-cyclo*thiouridine* (0·52 g.), was purified by several precipitations from benzene–light petroleum, then having m. p. 105° (to a glass) (Found: C, 66·5; H, 5·55; N, 5·4. $C_{29}H_{26}O_4N_2S,1\frac{1}{2}H_2O$ requires C, 66·4; H, 5·4; N, 5·35%), $\lambda_{max.}$ 270 mμ (ε 9050), $\lambda_{min.}$ 255 mμ (ε 7600), $\lambda_{infl.}$ 222 mμ (ε 26,450) in ethanol.

Thymidine.—The foregoing trityl compound (0·75 g.) in ethanol (100 ml.) and 0·1N-sulphuric acid (15 ml.) was heated on a water-bath for 2 hr. The solution was evaporated to a small volume *in vacuo* and water (25 ml.) added; triphenylmethanol (0·26 g.) was filtered off, and had m. p. and mixed m. p. 162—163°. The aqueous solution was just neutralised with "Deacidite FF," and evaporated *in vacuo* to a gum, $\lambda_{max.}$ 228 (ε 22,500), 266 mμ (ε 7850), $\lambda_{min.}$ 254 mμ (ε 7700) in water. A small amount of the gum was warmed for a few min. with 0·1N-sodium hydroxide; the solution then gave a purple colour with sodium nitroprusside and had $\lambda_{max.}$ 270 mμ and $\lambda_{min.}$ 240 mμ ($\varepsilon_{max.}$: $\varepsilon_{min.}$ 1·65). This gum (0·2 g.) in 0·1N-sodium hydroxide (10 ml.) was heated on a water-bath with W2 Raney nickel (1 g.) for 10 min.; the mixture was

filtered and the catalyst washed with water. The filtrate was just neutralised (to pH 7) with " Zeokarb 225." The solution then gave a deep blue colour with the Dische diphenylamine reagent, and paper chromatograms showed the presence of three spots which gave positive reactions with the cysteine spray reagent: R_F (butanol–water) 0·25, 0·36, 0·46 (butanol–acetic acid–water 5 : 2 : 3) 0·26, 0·45, 0·58. Thymidine had R_F 0·37 and 0·45 and 2-deoxyribose 0·25, 0·25 respectively in these solvent systems. The material of R_F 0·25 also gave positive tests for a reducing sugar with ammoniacal silver nitrate and aniline hydrogen phthalate. The above solution was evaporated *in vacuo* to a syrup which partly crystallised in 2 days. The solid was recovered after trituration with a little 80% aqueous ethanol and recrystallised from ethanol, to give thymidine (0·011 g.), m. p. and mixed m. p. 182—184° (Found: C, 49·8; H, 5·65; N, 11·95. Calc. for $C_{10}H_{14}O_5N_2$: C, 49·6; H, 5·85; N, 11·55%). The ultraviolet absorption spectra of the compound at different pH values were identical with those reported for thymidine in aqueous solution.[4]

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UNIVERSITY OF NEW SOUTH WALES,
SYDNEY, N.S.W., AUSTRALIA.

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[4] Fox and Shugar, *Biochim. Biophys. Acta*, 1952, **9**, 369.