modified with high-temperature inlet system) yielded a peak at m/e of 199 (parent ion), one at m/e of 154 (loss of $C_2H_5NH_2$) and one at m/e of 86 (loss of $C_2H_5NHCH_2CO$). The nuclear magnetic resonance of the product (Varian spectrophotometer, model No. *HR*-60) in tetramethylsilane indicated the presence of an ethyl amino group (6·17, 6·37 and 7·13τ), a methylene group α to the carbonyl function (7·72τ), a strong $(CH_2)n$ absorption (8·66τ), the terminal methyl group of the octyl linkage (9·04τ), and a slight trace of carbon–carbon unsaturation (4·54τ). Very small peaks at 6·92, 6·77 and 6·59τ in the ratio 4 : 2 : 1 were consistent with an octyl-morpholine structure. Attempts to separate the 2-isomers by chemical methods were unsuccessful. An estimation of the amount of each isomer was obtained on an Atlantic column (10 ft., 0·25 in. diam., 0·25 wt. per cent microcrystalline wax on 60/80 mesh glass beads) using an *F* and *M* flame ionization gas chromatography apparatus (model No. 609) temperature programmed at 13°/min from 75° to 260°. Both isomers were detectable above 250° but not completely resolved. Based on the ratio of the areas a conservative figure for the azaketone/octylmorpholine ratio was four.

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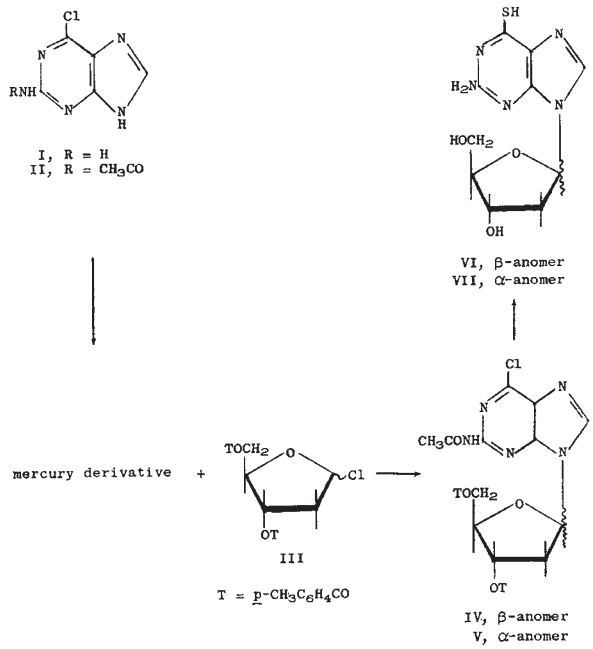
2′-Deoxythioguanosine and its α-Anomer

THE recent announcement[1] that 5-iodo-2′-deoxyuridine (IUDR) is effective against the herpes simplex virus, whereas the riboside, 5-iodo-uridine, is not, emphasizes the possible therapeutic differences between ribosides and 2′-deoxyribosides of a common heterocyclic base. As a result of our interest in preparing potentially better forms of certain common antitumour drugs, we have recently reported the synthesis of the 2′-deoxyriboside of 6-mercaptopurine[2]; we now describe the synthesis of 2′-deoxythioguanosine (DTG). In view of LePage's report[3] that the tumour-inhibitory properties of 6-thioguanine result from the incorporation of this guanine analogue into the nucleic acids (probably specifically the DNA), DTG is of especial interest since it represents the closest practical precursor of thioguanine as it is incorporated in the DNA; it by-passes some of the steps from thioguanine to its incorporation into DNA.

To prepare a properly blocked form of 2-amino-6-chloropurine for the synthesis of DTG, the base (I) was heated with acetic anhydride at reflux using phosphoric acid as catalyst[4] to form a polyacetylated base that could be converted to 2-acetamido-6-chloropurine (II) by careful treatment with methanolic ammonia. A mercury derivative suitable for nucleoside formation was prepared from II by reaction with 2 moles of mercuric chloride and 2 moles of sodium hydroxide.

The reaction of the mercury derivative of II with 1 mole of the chlorosugar (III) (ref. 5) in refluxing benzene for 20 min gave 25 per cent of the crystalline β-anomer (IV), $[\alpha]^{24}D$ −30°, and 24 per cent of the amorphous α-anomer (V), $[\alpha]^{24}D$ −55° (rotations in chloroform). Anomeric configurations for IV and V could be assigned by comparison of the nuclear magnetic resonance spectra with those of 6-chloro-9-(2′-deoxy-3′,5′-di-O-*p*-toluyl-α- and β-D-ribofuranosyl) purine[2], the structures of which had been proved chemically.



Treatment of IV with refluxing methanolic sodium hydrogen sulphide followed by methanolic sodium methoxide gave 80 per cent of VI, $[\alpha]^{25}D$ − 32° (0·1 N sodium hydroxide). Anal.: $C_{10}H_{13}N_5O_3S{\cdot}H_2O$ requires C, 39·9; H, 5·02; N, 23·2; S, 10·6. Found: C, 39·6; H, 5·11; N, 23·0; S, 10·6. Similar treatment of V gave 64 per cent of VII, $[\alpha]^{24}D$ +65° (0·1 N sodium hydroxide). Anal.: found: C, 39·9; H, 4·83; N, 23·2; S, 10·8.

The ultra-violet spectra of the crystalline *S*-benzyl derivatives of VI and VII were those of 9-substituted (and not the 7-substituted)[6] *S*-benzylthioguanines. The conversion of 2′-deoxythioguanosine (VI) to 2′-deoxyguanosine via the *S*-(β-hydroxyethyl) derivative[7] of VI provided a chemical proof of structure of VI.

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