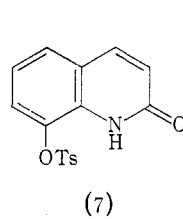
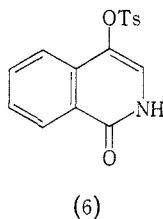
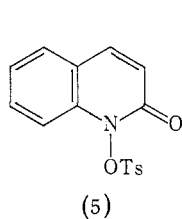
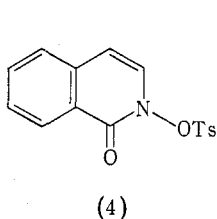
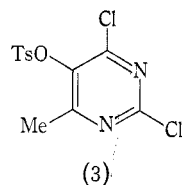
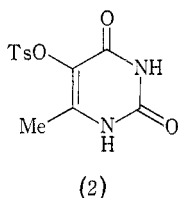
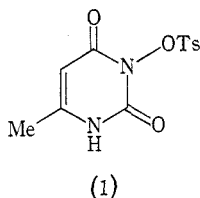


THE REARRANGEMENT OF 6-METHYL-3-TOSYLOXYURACIL

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During a study of the reactions of 3-hydroxyuracils it was observed that refluxing 6-methyl-3-tosyloxyuracil (1) in phosphorus oxychloride for 2½ hr produced a compound isomeric with the starting material, but lacking the p.m.r. signal corresponding to the C5 proton. The product was formulated as 6-methyl-5-tosyloxyuracil (2) and this structure was confirmed by comparison with the product obtained by tosylation of 5-hydroxy-6-methyluracil.



When the reflux time was extended to 17 hr there was, in addition to (2), a second compound isolated which lacked not only the p.m.r. signal corresponding to the C5 proton but also any carbonyl absorption bands in the infrared spectrum. This product was formulated as 2,4-dichloro-6-methyl-5-tosyloxypyrimidine (3) in agreement with high resolution mass spectral and analytical data. The structure was further supported by the near quantitative conversion of (2) into (3) in boiling phosphorus oxychloride containing catalytic amounts of diethylaniline.

It would appear from the product distribution obtained under the different conditions that the primary reaction involves the rearrangement of the tosyloxy group from the N3 to the C5 atom. 1,3-Rearrangements of this type¹ have been

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¹ Ogino, K., Kozuka, S., and Oae, S., *Tetrahedron Lett.*, 1969, 3559.

reported for *N*-tosyloxyisocarbostyryl (4) and *N*-tosyloxycarbostyryl (5) which when heated in acetonitrile or nitromethane gave rise to 4-tosyloxyisocarbostyryl (6) and 8-tosyloxycarbostyryl (7) respectively. Attempts to carry out the uracil rearrangement by refluxing (1) in either acetonitrile or dimethylformamide were unsuccessful, the starting product being recovered unchanged. The facile rearrangement of (1) in phosphorus oxychloride may be associated with adduct formation between that solvent and one of the carbonyl functions of the uracil.

Experimental

Analyses were performed by the Australian Microanalytical Service, Melbourne. The p.m.r. spectra were obtained on a Varian A60 spectrometer with tetramethylsilane as internal reference. Mass spectra were measured on an AEI MS902 instrument using the direct insertion probe. Accurate mass measurements were made using an on-line Raytheon 706 computer.

5-Hydroxy-6-methyluracil

This compound, m.p. $>270^\circ$ (Found: C, 42.5; H, 4.5; N, 19.7. $C_5H_6N_2O_3$ requires C, 42.3; H, 4.2; N, 19.7%) was prepared from 6-methyluracil using the procedure described by Hull for the preparation of 2-amino-4,5-dihydroxy-6-methylpyrimidine.²

Preparation of 6-Methyl-5-tosyloxyuracil (2)

5-Hydroxy-6-methyluracil (1.4 g) and *p*-toluenesulphonyl chloride (1.9 g) were refluxed in pyridine for 1 hr. The reaction mixture was poured into iced water and a solid separated. It was recrystallized from ethanol to give 6-methyl-5-tosyloxyuracil (2), m.p. $276-278^\circ$, $FeCl_3$ negative (Found: C, 48.6; H, 4.1; N, 9.3. $C_{12}H_{12}N_2O_5S$ requires C, 48.6; H, 4.1; N, 9.4%). P.m.r. spectrum in $(CD_3)_2SO$: δ 1.97 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 7.72 (q, 4H, aromatic), 11.13 (broad, 1H, NH), 11.38 (broad, 1H, NH). Mass spectrum: Found 296.04715. $C_{12}H_{12}N_2O_5S$ requires 296.04670.

Rearrangement of (1) with Phosphorus Oxychloride

(i) *Reflux time 2.5 hr.*—6-Methyl-3-tosyloxyuracil³ (1) (0.5 g) was refluxed for 2.5 hr with phosphorus oxychloride (10 ml). Some of the phosphorus oxychloride was removed by distillation and the remaining reaction mixture poured into ice-water. A solid precipitated which was recrystallized from ethanol to give a product (0.4 g) shown to be identical with 6-methyl-5-tosyloxyuracil (2) (infrared, p.m.r., mixed m.p.).

(ii) *Reflux time 17 hr.*—The uracil (1) (1 g) was refluxed for 17 hr with phosphorus oxychloride (20 ml). When the reaction mixture was treated as in (i) above, colourless crystals (0.7 g) were obtained which melted over a wide range. Of this material, 0.5 g proved to be soluble in chloroform and was recrystallized from ethanol to give 2,4-dichloro-6-methyl-5-tosyloxypyrimidine (3), m.p. $89-90^\circ$ (Found: C, 43.5; H, 3.4; Cl, 21.2; N, 8.3. $C_{12}H_{10}Cl_2N_2O_3S$ requires C, 43.2; H, 3.0; Cl, 21.3; N, 8.4%). P.m.r. spectrum in $(CD_3)_2SO$: δ 2.38 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 7.70 (q, 4H, aromatic). Mass spectrum: Found 331.98015. $C_{12}H_{10}Cl_2N_2O_3S$ requires 331.97892. The chloroform-insoluble residue was shown to be identical with (2) (infrared, p.m.r. mixed m.p.).

Conversion of (2) into (3)

Compound (2) (0.5 g) was refluxed for 17 hr in phosphorus oxychloride (10 ml) containing diethylaniline (0.5 ml). When the reaction mixture was treated as in (i) above, the product (0.4 g) was shown to be identical with 2,4-dichloro-6-methyl-5-tosyloxypyrimidine (3) (i.r., p.m.r., mixed m.p.).

² Hull, R., *J. chem. Soc.*, 1956, 2033.

³ Cossey, A. L., and Phillips, J. N., *Chem. Ind.*, 1970, 58.