Preparation of Deoxyhalogenouridines

By YOSHIYUKI FUJISAWA and OYO MITSUNOBU*

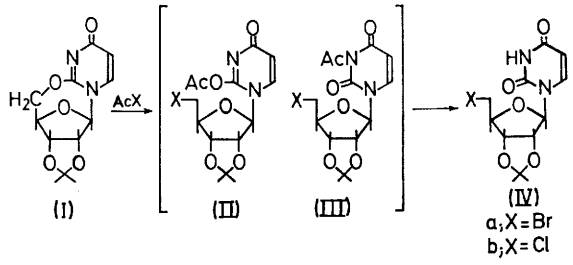
(*College of Science and Engineering, Department of Chemistry, Aoyama Gakuin University, Chitosedai, Setagaya-ku, Tokyo, Japan*)

Summary The cyclouridine (I) reacts with acetyl chloride or acetyl bromide at room temperature to give the corresponding deoxyhalogenouridines (IV) in good yield.

5'-DEOXY-5'-HALOGENONUCLEOSIDES have been prepared by various methods.[1] We have found that the cyclouridine (I) reacts readily with acetyl halides to give the corresponding 5'-deoxy-5'-halogenouridines (IV).

The relatively high reactivity of cyclonucleosides has been exploited since their discovery by Todd and his co-workers.[2] Thus, it was expected that the reaction of (I) with acyl halides would lead to the formation of the deoxyhalogenouridines (II) and/or (III), in which the active hydrogen atom of the uracil residue is protected by the acyl group to prevent intramolecular cyclization[3] in a subsequent displacement reaction.

When (I) (133 mg, 0·5 mmol) prepared from 2',3'-*O*-isopropylideneuridine, diethyl azodicarboxylate, and triphenylphosphine[4] was treated with acetyl bromide (246 mg, 2 mmol) in tetrahydrofuran (20 ml) at room temperature, (I) was dissolved in about 1 h. After stirring for 3 h and removal of the solvent, the residue was crystallized on treatment with a small amount of chloroform. T.l.c. of the compound indicated a single major component which was further purified by recrystallization from chloroform–n-hexane (138 mg, 80%, m.p. 181·5—182·5°). The structure of the product was shown to be (IVa) by elemental and u.v. analysis.† Similarly, the reaction of (I) with acetyl chloride in tetrahydrofuran for 12 h at room temperature produced (IVb) which was separated by preparative t.l.c. (90%, m.p. 175·5—176·5°).† Compounds (II) and (III) were not detected. On treatment with 90% acetic acid at 70° for 10 h (IVa) was converted into 5'-bromo-5'-deoxyuridine (m.p. 175·5—176·5°).



Based on the stability of the N^2-benzoyl group of uridine,[5] it is likely that the intermediate of the present reaction is (II) which is later deacetylated.

(*Received, 29th December* 1972; *Com.* 2154.)

† $\lambda_{max}(H_2O)$ 260 nm (ϵ 10,000), λ_{min} (H_2O) 230 nm.

[1] R. S. Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 107; J. E. G. Barnett, *ibid.*, 1967, **22**, 177; J. P. H. Verheyden and J. G. Moffatt, *J. Org. Chem.*, 1972, **37**, 2289, and refs. therein.

[2] V. M. Clark, A. R. Todd, and J. Zussman, *J. Chem. Soc.*, 1951, 2952; Y. Mizuno and T. Sasaki, *J. Amer. Chem. Soc.*, 1966, **88**, 863, and refs. therein; M. Ikehara, *Accounts Chem. Res.*, 1969, **2**, 47.

[3] D. M. Brown, A. R. Todd, and S. Varadarajan, *J. Chem. Soc.*, 1957, 868.

[4] M. Wada and O. Mitsunobu, *Tetrahedron Letters*, 1972, 1279.

[5] R. Lohrmann and H. G. Khorana, *J. Amer. Chem. Soc.*, 1964, **86**, 4188; J. P. H. Verheyden, D. Wagner, and J. G. Moffatt, *J. Org. Chem.*, 1971, **36**, 250.