

A Simple Conversion of 5-Cyanouridine into Uridine

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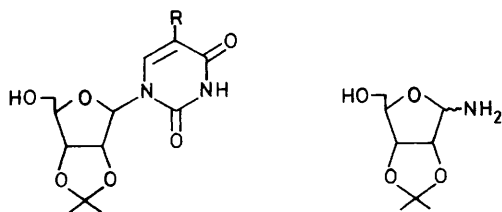
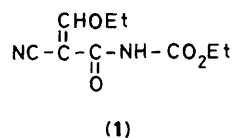
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2',3'-*O*-Isopropylideneuridine (**4**) was prepared in high yield from 5-cyano-2',3'-*O*-isopropylideneuridine (**2**) by the action of sodium dithionite in aqueous sodium hydrogen carbonate.

N(1)-Substituted uracils, including related *N*(1)-glycosyl-uracils, tend to be more difficult to synthesize than many related pyrimidine derivatives since direct alkylation or glycosylation of the aglycone often produces mixtures of the N(1)- and N(3)-substituted derivatives. Alternative routes to

such compounds involve less readily available intermediates.

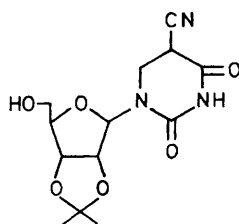
In contrast, 1-substituted 5-cyanouracils including several nucleosides are very readily obtained in high yield with unambiguous substitution of an alkyl, aryl, or glycosyl moiety at N(1) by condensation of an appropriate primary amine



(2); R = CN

(4); R = H

(3)



(5)

with the readily available α -cyano- β -ethoxy- N -ethoxycarbonylacrylamide (1).¹ Suitable glycopyranosyl (or furanosyl) amines required for nucleoside formation are equally easily

prepared^{2,3} in high yield. In this way³ 5-cyano-2',3'- O -isopropylideneuridine (2) was prepared by condensation of (1) with 2',3'- O -isopropylidene-D-ribofuranosylamine (3). We now report a simple and convenient conversion of (2) into 2',3'- O -isopropylideneuridine (4) which is of course readily deprotected with dilute acid to produce uridine.

A suspension of (2) (2 mmol) in a solution of sodium dithionite (10 m mol) in saturated aqueous sodium hydrogen carbonate (50 ml) at 95 °C during 15 minutes soon dissolved to a clear solution. The solution was evaporated *in vacuo* and a methanol extract of the residue filtered through a silica gel pad which was then eluted with ethyl acetate to give an excellent yield (95%) of 2',3'- O -isopropylideneuridine (4). The product was identical (t.l.c., i.r., mass, and ¹H n.m.r. spectra) to an authentic sample.

The reaction presumably involves initial reduction of (2) to the 5,6-dihydro derivative (5) followed by base catalysed elimination of hydrogen cyanide.

We believe that this constitutes a very convenient route to the preparation of a wide variety of uracil nucleosides and related substituted uracils.

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References

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