Tetrahedron Letters No. 32, pp 3345 - 3346, 1972. Pergamon Press. Printed in Great Britain.

2'- and 3'-O-Trityluridine

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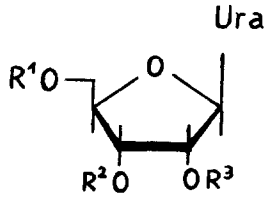
(Received in UK 30 June 1972; accepted for publication 6 July 1972)

The trityl group is a useful acid-labile protecting group for primary and secondary hydroxyl functions of carbohydrates and nucleosides. The most usual procedure for the detritylation is heating with 80 % aqueous acetic acid at reflux temperature.

We have found that milder heat treatment in some cases yields a partially selective detritylation of ditritylated nucleoside derivatives, e.g. in the case of 3',5'-(1) and 2',5'-di-O-trityluridine (2), and 2,3'-anhydro-1-(2,5-di-O-trityl-ß-D-xylofuranosyl)-uracil. Thus, 1 was partially detritylated to about the same extent at C-5' and C-3' by heating with 80 % acetic acid 1 hr at 50° giving 3'-O-trityluridine (3) and the known 5'-O-trityluridine[1] (4). Unreacted 1 and uridine were also present in the reaction mixture, but the time of reaction was optimal for a maximal yield (about 22 %) of 3; m.p. 180-186° (needles from chloroform); (Found: C, 63.01; H, 5.08; Cl, 9.16; N, 5.07. $C_{28}H_{26}N_2O_6 \cdot 1/2\ CHCl_3$ calc.: C, 62.67; H, 4.89; Cl, 9.74; N, 5.13 %). $\lambda_{max}^{methanol}$ 261 nm (ε 11,700), $\lambda_{min}^{methanol}$ 242.5 nm (ε 7,170); p.m.r. (CD_3SO, TMS, 100 MHZ): δ 5.90 (d, 2'-OH); δ 4.96 (s, 5'-OH); δ 8.32 (s, $CHCl_3$); highest peak in mass spectrometry m/e 486. The isomeric monotrityl derivatives 3 and 4 were clearly resolved by t.l.c. on "Kieselgel HF_{254}" (Merck) and by column chromatography on "Kieselgel zur Säulenchromatographie (0.05 - 0.2 mm)" (Merck), respectively, using chloroform-ethanol (95:5); R_F values (t.l.c.) 1 0.55; 3 0.30; 4 0.22; uridine 0.00.



1 $R^1 = R^2 = C(C_6H_5)_3$ $R^3 = H$
2 $R^1 = R^3 = C(C_6H_5)_3$ $R^2 = H$
3 $R^2 = C(C_6H_5)_3$ $R^1 = R^3 = H$
4 $R^1 = C(C_6H_5)_3$ $R^2 = R^3 = H$
5 $R^3 = C(C_6H_5)_3$ $R^1 = R^2 = H$

By contrast, compound 2 was not detritylated at 50°, but required a temperature of 80°. Then, part of 2 was selectively monodetritylated at C-5' giving 2'-O-trityluridine

(5), but yielded only traces of 4. Uridine was formed simultaneously, so that the time of the reaction had to be limited to 1 hr to obtain the best yield (about 20 %) of 5; m.p. 227 - 234° (dec.) (from absolute ethanol); (Found: C, 68.36; H, 5.89; N, 4.97. $C_{28}H_{26}N_2O_6 \cdot 1/2\ C_2H_5OH$ calc.: C, 68.35; H, 5.74; N, 5.50 %). $\lambda_{max}^{methanol}$ 261 nm (ε 9,400), $\lambda_{min}^{methanol}$ 243.5 nm (ε 6,070); p.m.r. (CD_3SO, TMS, 100 MHZ): δ 4.87 (d, 3'-OH); δ 4.99 (s, 5'-OH); δ 4.37 (OH from C_2H_5OH); highest peak in mass spectrometry m/e 486. 5 could be isolated as mentioned above for 3. R_F values (t.l.c.) 2 0.60; 5 0.50.

Analogously, 2,3'-anhydro-1-(2,5-di-O-trityl-ß-D-xylofuranosyl)uracil reacted with acetic acid at 80° in a similar manner giving two main products (checked by t.l.c.), presumably 2,3'-anhydro-1-(2-O-trityl-ß-D-xylofuranosyl)uracil and 2,3'-anhydro-1-ß-D-xylofuranosyluracil.

In view of these results, the preparation of 3 can be simplified by starting with the unseparated mixture of the ditrityl compounds 1 and 2 as obtained by reaction of uridine with trityl chloride according to Yung and Fox[2]. This mixture (difficult to separate into the components 1 and 2 by fractional crystallization and/or preparative t.l.c. or column chromatography) was treated as mentioned above for the preparation of 3. Under these conditions, 2 remains unaffected, and 4 readily gives 3 which can be easily separated from the other compounds of the reaction mixture by column chromatography in better total yield (14 %, related to uridine).

3 and 5 are appropriate starting compounds for special synthesis in the nucleoside and nucleotide field. Nucleosides with acid-labile groups at 3'-OH position are rare as yet.

In this context it is interesting to note that recently Verheyden and Moffatt[3] observed a selective loss of the 5'-O-trityl group from 2 and 1-(2,5-di-O-trityl-ß-D-xylofuranosyl)uracil during treatment with methyltriphenoxyphosphonium iodide in dimethylformamide giving in both cases 1-(2-O-trityl-ß-xylofuranosyl)uracil as a side product.

References

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