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DIASTEREOISOMERIC BENZYLIDENENUCLEOSIDES

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THE specific rotation of benzylideneguanosine (I) was first reported by Michelson and Todd,[1] although the compound had been synthesized previously by two other groups of investigators.[2] In attempting to repeat the synthesis of this compound, Lipkin and McElheny[3] obtained a benzylideneguanosine (Ib) which differed from the 2':3'-isomer of Michelson and Todd[1] (Ia) in both its specific rotation and its solubility in pyridine. It was suggested at the time[3] that Ib was isomeric with Ia either because of a difference in the position of substitution of the benzylidene group or because of a difference in stereochemical configuration of the benzylidene carbon atom. It now is demonstrated conclusively that the latter explanation is the correct one. Furthermore, two 2':3'-benzylideneuridines (II) were

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[1] A. Michelson and A. R. Todd, J. Chem. Soc. 2476 (1949); D. M. Brown, L. J. Haynes and A. R. Todd, J. Chem. Soc. 3299 (1950).

[2] H. Bredereck and E. Berger, Ber. 73, 1124 (1940); J. M. Gulland and W. G. Overend, J. Chem. Soc. 1380 (1948).

[3] D. Lipkin and G. C. McElheny, Nature, Lond. 167, 238 (1951).

prepared and it was proved that their isomerism is also due only to a difference in the configuration of the benzylidene carbon. Experimental evidence for the existence of such diastereoisomerism in simpler benzylidene-substituted sugar derivatives has been presented.[4]

A benzylideneuridine (IIa) was prepared by shaking benzaldehyde and uridine with anhydrous zinc chloride for 7 days at 5°. Yield, 68°/o; m. p. 191-191.5°; $[\alpha]_D^{27}$ -93.3°(HCONMe$_2$, c 1.22). Found: C, 57.73; H, 4.68; N, 8.49. $C_{16}H_{16}N_2O_6$ requires C, 57.83; H, 4.85; N, 8.43°/o. By carrying out the reaction at 26° for 20 hrs. and then at 100° for 1 hr., an isomer (IIb) of the above was obtained. Yield, 74°/o; m. p. 193-194°; $[\alpha]_D^{26}$ -57.9°(HCONMe$_2$, c 1.35). Found: C, 57.86; H, 4.82; N, 8.23. Gulland and Smith reported no specific rotation, but gave m. p. 189-190°, for II.[5] Compounds IIa and IIb give different X-ray powder patterns and differ somewhat in their infrared spectra (KBr disks). Compound IIb does not depress the m.p. of IIa.

A sample of each of the isomers was subjected to Purdie methylation and the benzylidene group then was removed at room

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[4] A review of the literature on this subject is given by B. Dobinson, A. B. Foster and M. Stacey, Tetrahedron Letters 1 (1959).

[5] J. M. Gulland and H. Smith, J. Chem. Soc. 338 (1947).

temperature by means of 48°/o hydrofluoric acid.[6] The resulting methylated uridines (III) were found to be oxidizable by periodate. Samples of III were treated with hydrazine[7] and the O-methylriboses thus obtained were shown to be identical with authentic 5-O-methylribose[8] by means of paper chromatography and paper electrophoresis.[9,10] These observations demonstrated that IIa and IIb are 2';3'-benzylidenenucleosides. In order to demonstrate that changes in the parent nucleoside, such as an α-β or a furanoside-pyranoside interconversion, did not take place during the preparation of the benzylidenenucleosides, IIa and IIb were hydrolyzed by means of 48°/o hydrofluoric acid.[6] The recovered nucleosides were shown to be identical with authentic uridine by means of paper chromatography, measurements of their specific rotation, mixed melting points, ultraviolet absorption spectra and X-ray powder patterns.

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[6] D. Lipkin, W. H. Cook and R. Markham, J. Amer. Chem. Soc., in press.

[7] F. Baron and D. M. Brown, J. Chem. Soc. 2855 (1955).

[8] D. Lipkin, E. B. Rauch and W. H. Hunter, unpublished results.

[9] D. M. Brown, D. I. Magrath and A. R. Todd, J. Chem. Soc. 1442 (1954)

[10] G. R. Barker, T. M. Noone, D. C. C. Smith and J. W. Spoors, J. Chem. Soc. 1327 (1955).

It is worth noting that IIa is converted to IIb at room temperature by means of anhydrous zinc chloride in benzaldehyde solution. The reverse interconversion does not take place at 5°. Both isomers are stable, however, at room temperature in the presence of a methanol suspension of silver oxide.

Compounds Ia and Ib were prepared by using the two different reaction conditions described for the preparation of IIa and IIb.[11] Using essentially the same procedures as those which were used with II, including the recovery of guanosine by hydrolysis of Ia and Ib with 48°/o hydrofluoric acid, it was demonstrated that the two isomers are diastereoisomeric 2':3'-benzylideneguanosines in which the only difference is the configuration of the benzylidene carbon.

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[11] Many unsuccessful attempts were made in our laboratory to synthesize the Michelson-Todd isomer. Only after we recognized the fact that the average room temperature in Cambridge, England, was much lower than in Saint Louis, Missouri, were we able to obtain the low temperature isomer without any difficulty.