49. *Epimeric Alcohols of the* cyclo*Hexane Series. Part III. Glucoside Formation.*

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cis- and *trans*-Forms of alcohols of the *cyclo*hexane series both condense with bromotetra-acetylglucose to give glucosides. Miescher and Fischer's generalisation that glucoside formation can be applied as a criterion of *trans*-configuration is therefore untenable.

In a recent paper (*Helv. Chim. Acta*, 1938, **21**, 336) Miescher and Fischer showed that borneol reacted with bromotetra-acetylglucose to give the tetra-acetylglucoside, whereas *iso*borneol did not condense. It was further observed that certain epimeric alcohols of the sterol and sex-hormone series showed a similar behaviour, and Miescher and Fischer proceeded to the generalisation that glucoside formation could be applied as a criterion of *trans*-configuration in the series. Ruzicka, Furter, and Goldberg (*ibid.*, p. 498) disagreed with this conclusion and adduced evidence to show that the glucoside-forming alcohols could not invariably be regarded as having the *trans*-configuration.

In the *cyclo*hexane series the steric effect of other rings is absent, and it appeared to us that glucoside formation would probably take place with both the *cis*- and the *trans*-forms of such alcohols. This expectation has been realised in all the cases examined, and glucoside formation cannot therefore be applied as a discriminative test of configuration in the case of simple epimeric alcohols of the *cyclo*hexane series. The tetra-acetylglucosides of the following alcohols were prepared: *l*-menthol, *d-neo*menthol, *dl-iso*menthol, *dl-neoiso*-menthol, *cis*- and *trans*-cryptol, *cis*- and *trans*-dihydrocryptol, *cis*- and *trans-l*-3-methyl-*cyclo*hexanol, and *cis*- and *trans*-4-methyl- and -4-*iso*propyl-*cyclo*hexylcarbinols.

Experimental.

Tetra-acetyl l-*Menthyl*-d-*glucoside*.—Pure *l*-menthol (6 g.) was shaken at room temperature for 60—70 hours with bromotetra-acetylglucose (20 g.) and dry silver oxide (10 g.) in dry ether (25 c.c.). After filtration and washing of the silver salts with ether, the combined filtrates were successively washed with dilute nitric acid and water, and after removal of the ether on the water-bath any unchanged menthol was removed by steam-distillation. The residue, recrystallised from dilute methyl alcohol, gave fine needles (11 g.), m. p. 129·5°, $[\alpha]_D$ −90·3° (*c* 2·02, alcohol) (Found: C, 59·1; H, 7·9. Calc.: C, 59·2; H, 7·85%) (compare Fischer and Raske, *Ber.*, 1909, **42**, 1469).

Tetra-acetyl d-neo*Menthyl*-d-*glucoside*.—*d-neo*Menthol (6 g.), prepared by the Ponndorf reduction of *l*-menthone by the method of Grubb and Read (*J. Soc. Chem. Ind.*, 1934, **53**, 52T), when treated as above, gave the *tetra-acetyl glucoside* (7 g.), which separated from dilute methyl

alcohol in fine needles, m. p. 144·5°, $[\alpha]_D$ +3·3° (*c* 2·073, alcohol) (Found : C, 59·35; H, 7·9. $C_{24}H_{38}O_{10}$ requires C, 59·2; H, 7·85%).

Tetra-acetyl dl-iso*Menthyl*-d-*glucoside*.—*dl-iso*Menthol, prepared by reduction of *dl*-piperitone (Hughesdon, Smith, and Read, J., 1923, 2918), was purified by crystallisation of the hydrogen phthalate (m. p. 106—107°), which on hydrolysis gave the alcohol, m. p. 50—51°. The alcohol (1·2 g.) with bromotetra-acetylglucose (4 g.), silver oxide (2·5 g.), and ether (10 c.c.) gave by the above treatment the *tetra-acetyl glucoside* (2 g.) in slightly flattened needles, m. p. 103—105°, from methyl alcohol (Found : C, 59·4; H, 8·0. $C_{24}H_{38}O_{10}$ requires C, 59·2; H, 7·85%).

Tetra-acetyl dl-neoiso*Menthyl*-d-*glucoside*.—The compound of *dl-neoiso*menthol with phosphoric acid, having m. p. 60° after recrystallisation (thrice) from light petroleum, was prepared from the reaction product of the Ponndorf reduction of *iso*menthone (Read and Grubb, J., 1934, 316). The alcohol, m. p. 11—12°, obtained on hydrolysis (1·2 g.) was converted into the *tetra-acetyl glucoside*, which on crystallisation from methyl alcohol yielded 2·5 g. having m. p. 128—130° (Found : C, 59·4; H, 8·1. $C_{24}H_{38}O_{10}$ requires C, 59·2; H, 7·85%).

Tetra-acetyl trans-*Dihydrocryptylglucoside*.—*trans*-Dihydrocryptol (10 g.) (Cooke, Gillespie, and Macbeth, J., 1939, 518) was condensed in the usual way with bromotetra-acetylglucose (20 g.), silver oxide (20 g.), and dry ether (25 c.c.). The crude glucoside on recrystallisation from dilute methyl alcohol yielded the pure *tetra-acetyl glucoside* (11 g.) in plates, m. p. 107·5°, $[\alpha]_D^{24°}$ −25·8° (*c* 1·96, alcohol) (Found : C, 58·3; H, 7·8. $C_{23}H_{36}O_{10}$ requires C, 58·4; H, 7·7%).

Tetra-acetyl cis-*Dihydrocryptylglucoside*.—The pure alcohol (above reference), when condensed and worked up similarly, gave much the same yield (10 g.) of pure recrystallised *tetra-acetyl glucoside* in fine needles, m. p. 102°, $[\alpha]_D^{24°}$ −32·8° (*c* 1·93, alcohol) (Found : C, 58·3; H, 7·8. $C_{23}H_{36}O_{10}$ requires C, 58·4; H, 7·7%).

Tetra-acetyl trans-l-3-*Methyl*cyclo*hexyl*-d-*glucoside*.—*trans-l*-3-Methyl*cyclo*hexanol (1·2 g.), prepared by hydrogenation of 3-methyl*cyclo*hexanone obtained by the hydrolytic decomposition of pulegone (Wallach, *Annalen*, 1896, **289**, 340) and purified through the hydrogen phthalate, gave, as in the preceding experiments, the pure *tetra-acetyl glucoside* (1·8 g.), m. p. 103°, $[\alpha]_D^{24°}$ −31·5° (*c* 1·97, alcohol) (Found : C, 56·9; H, 7·45. $C_{21}H_{32}O_{10}$ requires C, 56·7; H, 7·25%).

Tetra-acetyl cis-l-3-*Methyl*cyclo*hexylglucoside*.—*cis-l*-3-Methyl*cyclo*hexanol recovered from the hydrogen phthalate crystallisations in the preceding experiment was purified by repeated crystallisation of its *p*-nitrobenzoate. The alcohol obtained on hydrolysis (0·6 g.) yielded on treatment the pure *tetra-acetyl glucoside* (1·1 g.), m. p. 105°, $[\alpha]_D^{24°}$ −38·9° (*c* 2·0, alcohol) (Found : C, 56·6; H, 7·5. $C_{21}H_{32}O_{10}$ requires C, 56·7; H, 7·25%).

Tetra-acetyl trans-4-*Methyl*cyclo*hexylcarbinylglucoside*.—The pure alcohol (1·5 g.) (Cooke and Macbeth, J., 1939, 1245) was shaken with bromotetra-acetylglucose (6 g.), silver oxide (3 g.), and dry ether (10 c.c.). The *tetra-acetyl glucoside*, worked up in the usual way, crystallised from dilute methyl alcohol in long, flat needles (2·4 g.), m. p. 113°, $[\alpha]_D^{20°}$ −28·6° (*c* 1·92, alcohol) (Found : C, 57·55; H, 7·45. $C_{22}H_{34}O_{10}$ requires C, 57·6; H, 7·5%).

Tetra-acetyl cis-4-*Methyl*cyclo*hexylcarbinylglucoside*.—The *cis*-alcohol (1·2 g.) (Cooke and Macbeth, *loc. cit.*) on condensation with bromotetra-acetylglucose (5 g.), silver oxide (3 g.), and dry ether (10 c.c.) gave after the usual treatment the *tetra-acetyl glucoside* (2·0 g.), which formed needles from dilute methyl alcohol, m. p. 72—73°, $[\alpha]_D^{20°}$ −23·4° (*c* 1·97, alcohol) (Found : C, 57·4; H, 7·3. $C_{22}H_{34}O_{10}$ requires C, 57·6; H, 7·5%).

Tetra-acetyl trans-4-iso*Propyl*cyclo*hexylcarbinylglucoside*.—The pure alcohol (1·5 g.) (Cooke and Macbeth, *loc. cit.*) was shaken for 60 hours at room temperature with bromotetra-acetylglucose (6 g.), silver oxide (3 g.), and dry ether (10 c.c.). The pure *tetra-acetyl glucoside* was isolated from dilute methyl alcohol in needles, m. p. 112°, $[\alpha]_D^{16°}$ −26·9° (*c* 2·08, alcohol) (Found : C, 59·3; H, 8·0. $C_{24}H_{38}O_{10}$ requires C, 59·2; H, 7·8%).

Tetra-acetyl cis-4-iso*Propyl*cyclo*hexylcarbinylglucoside*.—The pure alcohol (3 g.), bromotetra-acetylglucose (12 g.), silver oxide (6 g.), and dry ether (20 c.c.) were shaken for the usual time. The pure *tetra-acetyl glucoside* (6·8 g.), recrystallised from dilute methyl alcohol, had m. p. 103—104°, $[\alpha]_D^{16°}$ −25·8° (*c* 1·96, alcohol) (Found : C, 59·25; H, 7·5. $C_{24}H_{38}O_{10}$ requires C, 59·2; H, 7·8%).

Tetra-acetyl trans-l-*Cryptylglucoside*.—A sample of *l*-cryptol (4 g.), purified by rigorous crystallisation of the *p*-nitrobenzoate (Galloway, Dewar, and Read, J., 1936, 1595) and having $[\alpha]_D$ −129·6° (*c* 2·1, alcohol). was condensed in the usual way with bromotetra-acetylglucose (16 g.) and silver oxide (8 g.) in dry ether (25 c.c.). The pure *tetra-acetyl glucoside* (4·6 g.) crystallised from dilute alcohol in large plates, m. p. 99—99·5°, $[\alpha]_D$ −80·6° (*c* 2·27, alcohol) (Found : C, 58·55; H, 7·3. $C_{23}H_{34}O_{10}$ requires C, 58·7; H, 7·3%).

Tetra-acetyl cis-l-*Cryptylglucoside*.—A sample of *l*-cryptol (20 g.) prepared by the Ponndorf

reduction of *l*-cryptone, and having α_D −40·4° (homogeneous), was condensed with bromotetra-acetylglucose (40 g.) and silver oxide (20 g.) in dry ether (60 c.c.). After the usual preliminary treatment unchanged cryptol (10 g.) having α_D −49·3° was recovered on steam-distillation. The crude residual tetra-acetyl glucoside (17 g.) was dissolved in alcohol, and water added at 20° until precipitation just occurred. After the solution had been cleared by addition of a little alcohol, the mixture was placed in the refrigerator. The crystals collected (5·5 g.) were again crystallised in the same way, and a first fraction (2 g.) again collected. This had m. p. 96—99°, $[\alpha]_D$ −83·0° (*c* 1·87, alcohol), but a further crystallisation from dilute alcohol gave the pure *tetra-acetyl glucoside* in long needles (1·4 g.), m. p. 106·5°, $[\alpha]_D^{20°}$ −90·7°. Recrystallisation did not affect these constants. The substance is evidently a tetra-acetyl cryptylglucoside (Found : C, 58·8; H, 7·5. $C_{23}H_{34}O_{10}$ requires C, 58·7; H, 7·3%) and, as the Ponndorf reduction product of cryptone contains some 5% of the *cis*-alcohol, it appears probable that the fractional crystallisation has achieved a separation of tetra-acetyl *cis-l*-cryptylglucoside from the mixed reaction product.

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