176. *Optical Superposition and the* 4 : 6-*Benzylidenemethylglucosides.*

By David S. Mathers and George J. Robertson.

In the course of an investigation on the synthesis of 4 : 6-dimethyl glucose we had occasion to prepare 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene-α-methylglucoside. The substance had been described by Ohle and Spencker (*Ber.*, 1928, **61**, 2387), who stated that it had m. p. 149° and $[\alpha]_D + 66{\cdot}5°$ in chloroform ($c = 3{\cdot}068$). Our material melted at 148—149° and had $[\alpha]_D + 13°$ in chloroform ($c = 1{\cdot}505$), and this marked discrepancy in the specific rotation led us to submit our material to systematic fractional crystallisation. A specimen of m. p. 148—149° and $[\alpha]_D + 12{\cdot}9°$ was crystallised four times (see p. 698), but the specific rotations of the first fraction from each successive crystallisation and of the second and third fractions from the individual mother-liquors were practically unaltered. As the m. p. remained unchanged, there can be no doubt that our material is homogeneous. Further investigation proved that the optical properties of this substance are somewhat unusual, as it shows $[\alpha]_D + 71{\cdot}4°$ in dry methyl alcohol ($c = 0{\cdot}084$) and $- 8{\cdot}6°$ in dry acetone ($c = 1{\cdot}984$), and we suggest that Ohle and Spencker have misquoted the solvent employed. The above authors, however, use their value as the basis of a criticism of the theory of optical superposition with particular reference to the generalisation due to Hudson, which states that if the proportions of the molecular rotation of a sugar contributed respectively by the terminal asymmetric carbon atom and the remainder of the molecule be represented by A and B, the molecular rotations of the α- and the β-form may be regarded as having the values $+ A + B$ and $- A + B$, from which it follows that the molecular-rotation difference ($2A$) should be constant. The data given by Ohle and Spencker were :

Derivative of benzylidene-α- or -β-methylglucoside.	$[\alpha]_D$ in $CHCl_3$.	M.	$[M]_D$.	Diff. ($2A$).
α-Dibenzoyl	+ 96·9°	490	+47,500°	
β-Dibenzoyl	+ 15·8	490	+ 7,750	+39,750°
α-Di-*p*-toluenesulphonyl	+ 66·5	590	+39,250	
β-Di-*p*-toluenesulphonyl	− 54·7	590	−32,250	+71,500

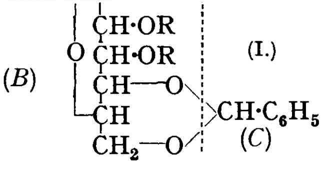
When, however, our value of + 13° in chloroform is substituted for 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene-α-methylglucoside, the corrected value of $[M]_D$ becomes + 7,650° and the corresponding difference is + 39,900°.

The close agreement in the values of 2*A* obtained for the above two pairs of isomerides encouraged us to pursue the investigation, and accordingly the parent substances, together with the corresponding diacetates and dimethyl ethers, were prepared and their optical behaviour in chloroform solution was examined. The results are summarised below (headings as for first table) :

α-Dibenzoyl	+ 98·6	490	+48,300	
β-Dibenzoyl	(+ 15·8)*	490	+ 7,750	+40,550
α-Di-*p*-toluenesulphonyl	+ 13·0	590	+ 7,650	
β-Di-*p*-toluenesulphonyl	(− 54·7)*	590	−32,250	+39,900
α-Dimethyl	+ 94·6	310	+29,350	
β-Dimethyl	− 59·6	310	−18,500	+47,850
α-Diacetyl	+ 75·5	366	+27,650	
β-Diacetyl	− 90·9	366	−33,250	+60,900
α-Methylglucoside (unsubstituted)	+117·5	282	+33,150	
β-Methylglucoside (unsubstituted)	− 62·3	282	−17,550	+50,700

* The values in parentheses are due to Ohle and Spencker (*loc. cit.*).

It therefore appears that the agreement in the values of 2*A* for the dibenzoyl and di-*p*-toluenesulphonyl derivatives is fortuitous, and that Hudson's rule does not apply to the benzylidene derivatives of α- and β-methylglucoside. Ohle and Spencker have pointed out that the specific rotation in such compounds is controlled by three factors owing to the introduction of a new asymmetric centre with the benzylidene residue. They suggest that benzaldehyde condenses in one optical sense in the α-series, and in the opposite sense in the β-series, so that each pair of isomerides may be looked upon as *cis*- and *trans*-compounds in which the optical rotation may be expressed as $+ A + B + C$ and $- A + B - C$ respectively [see (I)]. The available evidence, although incomplete, is distinctly adverse to this view. In the passage from α-methylglucoside to its 4 : 6-benzylidene-derivative the specific rotation changes from + 159° to + 117·5°, and this lævo-effect is likewise evident in the corresponding β-compounds, where the rotation changes from − 33° to − 62·3°. From this it might be argued that *C* has the same orientation in both series of compounds, in which case Hudson's reasoning should be applicable.



(I.)

It is, unfortunately, impossible to compare the above values of 2*A* with those derived by Hudson for the methylglucosides, methylxylosides, etc., owing to the difficulty in obtaining a common solvent for both series. Through the kindness of Dr. J. W. H. Oldham, however, we are enabled to give the following data for the α- and the β-form of 2 : 3-dimethyl methylglucoside and for the corresponding 4 : 6-dibenzoyl derivatives in chloroform solution :

2 : 3-Dimethyl derivative of	$[\alpha]_D$.	*M*.	$[M]_D$.	Diff. (2*A*).
α-Methylglucoside	+146·3°	222	+32,500°	
β-Methylglucoside	− 47·8	222	−10,600	+43,100°
4 : 6-Dibenzoyl α-methylglucoside	+108·5	430	+46,650	
4 : 6-Dibenzoyl β-methylglucoside	− 8·2	430	− 3,550	+50,200

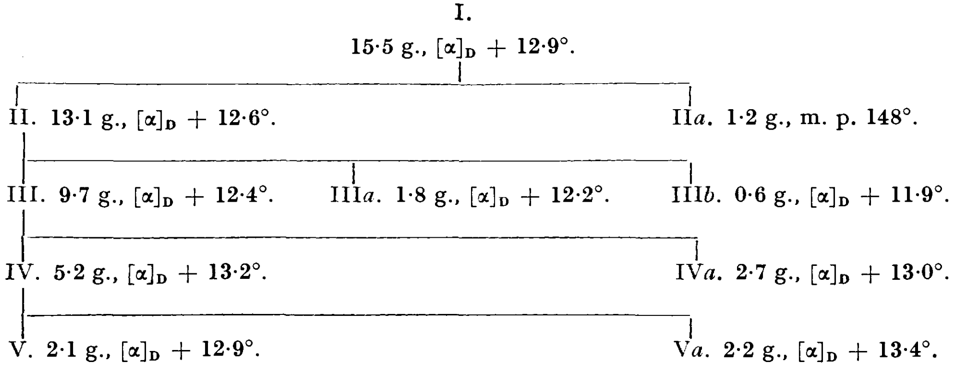
These values are directly comparable with those obtained by Hudson (*J. Amer. Chem. Soc.*, 1915, **37**, 1264) for α- and β-tetra-acetyl methylglucosides in chloroform, for which he found a difference (2*A*) of 53,900. It is therefore apparent that the optical value of the terminal asymmetric or glucosidic carbon atom is not constant, but in certain cases is dependent upon the constitution of the remainder of the molecule.

The reasonable conclusion to be drawn from our work is that Hudson's generalisation ought not to be applied to sugar derivatives so complicated as those now under consideration. The problem is complicated by the fact that, in addition to the sections of the molecule denoted as *A* and *B*, there are two new factors, *viz.* (*a*) the specific effect of the benzylidene residue in altering the rotation of the molecule as a whole, and (*b*) the further effect of *d*- and *l*-configurations within the benzylidene residue.

EXPERIMENTAL.

2 : 3-Dibenzoyl 4 : 6-benzylidene-α-methylglucoside was prepared by the method of Ohle and Spencker (*loc. cit.*). It crystallised in colourless needles, m. p. 152—153°, and had $[\alpha]_D$ + 98·6° in $CHCl_3$ (c = 2·820); + 95·7° in acetone (c = 1·022); + 154·6° in abs. EtOH (c= 0·119); and + 107·6° in MeOH (c = 0·112). Ohle and Spencker give m. p. 148°.

2 : 3-Di-*p*-toluenesulphonyl 4 : 6-benzylidene-α-methylglucoside was also prepared by the method of Ohle and Spencker (*loc. cit.*). The yield may be greatly improved by using a 50% excess of *p*-$C_6H_4Me{\cdot}SO_2Cl$ and allowing reaction to proceed at room temp. for 4 days. The substance crystallised from MeOH in colourless needles, m. p. 148—149°, and had $[\alpha]_D$ as given on p. **696** (Found : OMe, 5·2. Calc. for $C_{28}H_{30}O_{10}S_2$: OMe, 5·25%). The material was fractionally crystallised, and the crops had m. p. 148—149° in every case except the one noted (II*a*).



Solvent $CHCl_3$ (c = 3·03—3·07); l = 2.

2 : 3-Dimethyl 4 : 6-benzylidene-α-methylglucoside was prepared by the method of Irvine and Scott (J., 1913, **103**, 578); m. p. 121—122°; $[\alpha]_D$ + 94·6° in $CHCl_3$ (c = 1·997), + 95·4° in acetone (c = 1·677).

2 : 3-Dimethyl 4 : 6-benzylidene-β-methylglucoside was prepared by Freudenberg's method (*Ber.*, 1928, **61**, 1758); m. p. 140—141°; $[\alpha]_D$ − 59·6° in $CHCl_3$ (c = 1·980). Freudenberg gives $[\alpha]_D$ − 61° in EtOH.

2 : 3-Diacetyl 4 : 6-benzylidene-α-methylglucoside was prepared by treating 4 : 6-benzylidene-α-methylglucoside with a 10% excess of Ac_2O in pyridine. The mixture was kept at room temp. for 2 days, and then treated with H_2O and C_6H_6. The C_6H_6 extract was thoroughly washed and dried over anhyd. Na_2SO_4. The C_6H_6 was evaporated, and the residue crystallised from rectified spirit; yield 80%; colourless needles, m. p. 108—109°; $[\alpha]_D$ + 75·5° in $CHCl_3$ (c = 1·987), − 10·2° in acetone (c = 1·475), + 91·5° in abs. EtOH (c = 0·164) (Found : OMe, 8·2. Calc. for $C_{18}H_{22}O_8$: OMe, 8·47%).

2 : 3-Diacetyl 4 : 6-benzylidene-β-methylglucoside was prepared by Oldham and Rutherford's method (*J. Amer. Chem. Soc.*, 1932, **54**, 374); m. p. 171—172°; $[\alpha]_D$ − 90·1° in $CHCl_3$ (c = 1·931), − 84·2° in acetone (c = 1·994). Oldham and Rutherford give m. p. 169—170°, $[\alpha]_D$ − 95·2° in $CHCl_3$ (c = 5·214).

4 : 6-Benzylidene-α-methylglucoside, prepared by Irvine and Scott's or Freudenberg's method (*locc. cit.*), had m. p. 164—165°; $[\alpha]_D$ + 117·5° in $CHCl_3$ (c = 1·030), + 95·5° in MeOH (c = 1·016).

4 : 6-Benzylidene-β-methylglucoside, m. p. 199—201° (from Dr. J. W. H. Oldham), was examined in $CHCl_3$ solution and had $[\alpha]_D$ − 62·3° (c = 1·012).

The authors acknowledge their indebtedness to the Carnegie Trust for the grant of a Scholarship to one of them (D. S. M.).

THE UNIVERSITY, ST. ANDREWS.

[*Received, April* 29*th*, **1933**.]