oxide, and warmed on the steam-bath for 1.5 hours. The cooled solution was thrown into water, when 0.10 g. (72%) of crude diphenyl sulfone, m.p. 122–123°, precipitated. The product after recrystallization from a chloroform–ligroin mixture had m.p. 127–128° and showed no m.p. depression (128–128.5°) when mixed with authentic diphenyl sulfone (of m.p. 128–128.5°). Processing of the filtrate from the diphenyl sulfone produced only a negligible quantity of solid, m.p. 75–95°.

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A Suggestion on the Application of Hudson's Isorotation Rules[1]

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When α-anomers of glycoses and glycose derivatives are lacking, calculations involving Hudson's isorotation rules have been made using the rotations of the known β-anomer and a related anomeric pair of glycoses. It is here suggested that the related anomeric pair employed in such calculations should be a pair whose aglycon bears the greatest structural similarity to the aglycon of the unknown α-anomer. To test this suggestion Hudson's rule calculations have been applied to all known pairs of substituted aromatic glycosides, and it is found that the proposed principle of aglycon similarity leads to the closest prediction of the optical properties of the α-anomers in over 97% of the cases. Bromination and nitration reactions have been applied to several acetylated aromatic glucosides in the phenyl and naphthyl series. The position of the substituent in each new product has been established by hydrolysis and characterization of the aglycon.

In estimating the partial rotatory contribution, A, of the anomeric center in glycosides and related compounds by application of Hudson's isorotation rules,[2] precise calculations are frequently hampered by the unavailability of the required α-anomers. This difficulty has generally been circumvented by employing B values derived from a pair of related anomeric glycose derivatives for calculating the desired A value. Thus Purves[3] has calculated A values for a series of phenyl polyacetyl-D-thioglycosides and Hudson and co-workers[4] A values for 2-naphthyl polyacetyl-D-glycosides, typical instances where the α-anomers are lacking, by using B values calculated on the basis of the corresponding anomeric polyacetyl-D-glucoses. Similarly, the specific rotations of unknown α-glycosides have been estimated[2] by appropriately combining the rotation of the known β-anomer with the rotations of a related anomeric pair of glycoses.

In principle, any anomeric pair of a related glycose derivative might be employed in place of the glycose itself to accomplish such calculations. Because of the approximate validity[5] of the second isorotation rule, however, the figures calculated for unknown A values or specific rotations will vary widely depending on the nature of the second anomeric pair chosen for the calculations. The extent of such deviations can be seen in the tables.

While Professor Hudson has frequently emphasized the qualitative nature of the isorotation rules and while these have never led to an incorrect anomeric classification, it would nevertheless be desirable to have a guiding principle to ensure that predicted A values or predicted specific rotations be as accurate as possible. It is here suggested that such a guiding principle be the following: In the application of the isorotation rules to the calculation of unknown specific rotations or A values, that anomeric pair should be selected for the calculation whose aglycon bears the greatest structural similarity to the aglycon of the unknown substance in question.

The validity of this proposition has been tested as follows. The rotations and A values of all known anomeric pairs of substituted aromatic glycosides have been tabulated. The rotations and A values of each α-anomer have then been assumed to be unknown, and have been calculated by combining the rotation of the β-anomer with the rotations of all known anomeric pairs of derivatives of the parent glycose. The calculated values have then been compared with the known values to see which anomeric pair led to the closest prediction. The results of these calculations are presented in Tables II–V, with the closest prediction italicized in each case.

According to the proposed principle of aglycon similarity, the phenyl glycosides should be the most suitable pair on which to base predictions regarding optical properties of unknown substituted aryl glycosides. It is, of course, well known[6] that aromatic glycosides show anomalously high B values, but the present principle of aglycon similarity as a basis for isorotation rule calculations does not appear to have been suggested explicitly in the past.

Examination of Tables II–V shows that the principle of aglycon similarity leads to the best prediction of A values and specific rotations in all but four out of 163 calculations. Occasionally the agreement between calculated and known values is striking. The principle appears to be least valid in the case of *o*-substituted aryl glycosides. Thus the properties of the *o*-tolyl glycosides seem in general better predicted on the basis of some anomeric pair other than the phenyl glucosides. Similarly, while the phenyl tetraacetyl-D-glucosides

(1) Presented before the Division of Sugar Chemistry, 121st National Meeting, American Chemical Society, Milwaukee, March, 1952.

(2) C. S. Hudson, THIS JOURNAL, **31**, 66 (1909).

(3) C. B. Purves, *ibid.*, **51**, 3619, 3627 (1929).

(4) W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **69**, 1668 (1947).

(5) (a) W. W. Pigman and H. S. Isbell, *J. Research Natl. Bur. Standards*, **27**, 9 (1941); (b) W. W. Pigman, *ibid.*, **33**, 129 (1944); (c) E. M. Montgomery, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **64**, 690 (1942); (d) C. D. Hurd and W. A. Bonner, *J. Org. Chem.*, **10**, 604 (1945).

(6) W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, Inc., New York, N. Y., 1948, p. 80 ff.

TABLE I

MOLECULAR ROTATIONS OF ANOMERIC ARYL GLYCOPYRANOSIDE DERIVATIVES

Parent glycose	Substituent on phenyl aglycon	OH state	Solvent	Specific rotation α-Anomer	Specific rotation β-Anomer	Molecular rotation α-Anomer	Molecular rotation β-Anomer	Reference
Glucose	H	Free	H_2O	180.8	−71.9	46300	−18400	*a*
	p-NH_2			194.1	−65	52600(MeOH)	−17600	*b,c*
	p-OH			178.6	−63.5	48600	−17300	*d,e*
	o-MeO			156.4	−66.8	44700	−19100	*f,g,h*
	o-NO_2			206	106	62000	−31900	*5c,i*
	m-NO_2			189	−89	56900	−26800	*5b,i*
	p-NO_2			215	−103	64700	−32000	*5c,i,j,c*
	o-Me			156	−68.7	42100	−18550	*k,l*
	p-Me			178	−67.7	48050	−18300	*f,l,e*
Glucose	H	Acetylated	$CHCl_3$	168.7	−22.5	71500	−9540	*a,5c*
	p-PhCO			137.7	−14.5	74900	−7890	*d*
	p-Br			159.6	−17.8	80300	−8950	9
	m-Cl			160.5	−25.3	73650	−11600	
	p-Cl			165.5	−20.2	75950	−9270	
	o-MeO			170.5	−29	77400	−13170	*f,a,g,h*
	o-NO_2			167	45.0	78300	21100	*5c,i*
	m-NO_2			173	−37	81100	−17350	*5b,i*
	p-NO_2			200	−41.0	93800	−19230	*5c,j,i,c*
	2,4-di-NO_2			212	34.9	109000	17950	*5b,m,n*
	o-Me			155	−27.7	67850	−12130	*k,o,p*
	p-Me			164	−18.3	71800	−8010	*f,o*
Galactose	H	Free	H_2O	217	−39.8	55600	−10200	*q,u*
	p-MeCO			226.2	−51.69	67400	−15400(C_6H_6)	*f*
	o-MeO			211.4	−44.64	60500	−12750	*f*
	o-Me			188	−43.3	50800	−11700	*r,l*
	m-Me			207	−44.3	55900	−11950	*f,s*
Galactose	H	Acetylated	$CHCl_3$	175.5	−0.7	74400	−297	*a,t,u*
	o-MeO			227.6	−16.71	103000	−7580	*f*
	o-Me			173	−4	75800	−1750	*r,a*
	m-Me			178	2.7	78000	1180	*f,s*

[a] B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933). [b] W. F. Goebel, F. H. Babers and O. T. Avery, *J. Exptl. Med.*, **55**, 761 (1932). [c] B. Helferich and O. Peters, *J. prakt. Chem.*, [2] **138**, 281 (1933). [d] B. Helferich and W. Reischel, *Ann.*, **533**, 278 (1938). [e] Mme. Ramart-Lucas and J. Rabaté, *Bull. soc. chim.*, [5] **2**, 1596 (1935). [f] K. Nisizawa, *Bull. Chem. Soc. Japan*, **16**, 155 (1941). [g] B. Helferich and C. P. Burt, *Ann.*, **520**, 156 (1936). [h] T. Kariyone and K. Horino, *J. Pharm. Soc., Japan*, **51**, 854 (1931). [i] E. Glaser and W. Wulwek, *Biochem. Z.*, **145**, 514 (1924). [j] K. Aizawa, *J. Biochem. Japan*, **30**, 89 (1939). [k] B. Helferich, U. Lampert and G. Sparmberg, *Ber.*, **67**, 1808 (1934). [l] B. Helferich and H. E. Scheiber, *Z. physiol. Chem.*, **226**, 272 (1934). [m] B. Lindberg. *Acta Chem. Scand.*, 4, 49 (1950). [n] H. G. Latham, Jr., E. L. May and E. Mosettig, *J. Org. Chem.*, **15**, 884 (1950). [o] B. Helferich, E. Günther and S. Winkler, *Ann.*, **508**, 192 (1934). [p] A. Kunz, THIS JOURNAL, **48**, 262 (1926). [q] B. Helferich and H. Appel, *Z. physiol. Chem.*, **205**, 231 (1932). [r] B. Helferich, H. E. Scheiber, R. Streeck and F. Vorsatz, *Ann.*, **518**, 211 (1935). [s] B. Helferich and F. Philipp, *ibid.*, **514**, 228 (1934). [t] B. Helferich and H. Bredereck, *ibid.*, **465**, 166 (1928). [u] E. Fischer and E. F. Armstrong, *Ber.*, **35**, 833 (1902).

provide the best predictions about acetylated *o*-nitrophenyl and 2,4-dinitrophenyl α-D-glucosides, the agreement between calculated and known values is very poor. In addition, the states of acetylation or non-acetylation seem important with respect to the *o*-substituted aryl glycosides. Thus *o*-nitrophenyl D-glucoside is anomalous when acetylated and normal when non-acetylated, *o*-tolyl D-glucoside is anomalous either way, and *o*-tolyl D-galactoside is anomalous only in the unacetylated condition. In cases where *o*-, *m*- and *p*-substituted glycosides are available for comparison, it appears that the extent of deviation between known values and the optimum calculated values is at a minimum with the *m*-substituted isomer, suggesting that the presence or absence of conjugation between the substituent and the glycosidic oxygen is an important factor determining the accuracy with which the principle of aglycon similarity may be applied.

Another aspect of the present problem has been the attempt to synthesize substituted aryl glycosides by new methods. While aryl β-D-glycosides are readily available through the Koenigs–Knorr reaction[7] or the Helferich–Schmitz-Hillebrecht synthesis,[8,5c] the corresponding α-anomers are not generally available. Preparation of the α-anomers by the Helferich–Schmitz-Hillebrecht procedure gives an α,β-mixture from which the desired α-anomer is frequently inseparable. Our interest therefore has been to prepare substituted aryl glycosides by direct reaction at the aromatic nucleus of unsubstituted aryl glycosides which may more often be obtained in both anomeric forms. The only previous study of this sort has involved the bromination of certain acetylated phenyl D-glucosides.[9]

Bromination of 1-naphthyl tetraacetyl-β-D-glu-

(7) W. Koenigs and E. Knorr, *Ber.*, **34**, 957 (1901); E. Fischer and co-workers, *ibid.*, **34**, 2897 (1901); **42**, 1465 (1909); **45**, 2467 (1912).

(8) B. Helferich and E. Schmitz-Hillebrecht, *ibid.*, **66**, 378 (1933); K. Sisido, *J. Soc. Chem. Ind., Japan*, **39**, 217B (1936); B. Helferich, H. E. Scheiber and R. Hiltmann, *Ber.*, **73**, 1300 (1940).

(9) C. D. Hurd and W. A. Bonner, THIS JOURNAL, **67**, 1764 (1945).

TABLE II

CALCULATED A VALUES AND SPECIFIC ROTATIONS OF α-ANOMERS FOR SUBSTITUTED PHENYL D-GLUCOPYRANOSIDES USING B VALUES DERIVED FROM VARIOUS ANOMERIC PAIRS

Calculated A values and rotation based on B values from unacetylated D-glucopyranosyl derivatives containing at the anomeric center

Substituent	Known A value, $[\alpha]_D$,°	OH[a]	OMe[a]	OCH_2Ph[b]	OPh[b]
p-NH_2	35100	29390	29710	28075	*31550*
	194.1	152	154	142	*168*
p-OH	32950	29090	29410	27775	*31250*
	178.6	150	152	141	*166*
o-MeO	31900	30890	*31210*	29575	33050
	156.4	149	*151*	140	164
o-NO_2	46950	43690	44010	42375	*45850*
	206.0	184	186	176	*199*
m-NO_2	41850	38590	38910	37275	*40750*
	189.0	167	169	159	*182*
p-NO_2	48350	43790	44110	42475	*45950*
	215.0	185	187	176	*199*
o-Me	30325	*30340*	30660	29025	32500
	156.0	*156*	158	146	172
p-Me	33175	30090	30410	28775	*32250*
	178.0	155	157	145	*171*

[a] Values calculated from Tables in "Polarimetry, Saccharimetry and the Sugars," Circ. C440, Nat. Bur. Standards, Washington, 1942. [b] Values calculated from Tables in "Tabellen der Zucker und Ihrer Derivate," H. Vogel and A. Georg, J. Springer, Berlin, 1931.

and characterization of the aglucon. Bromination of 2-naphthyl tetraacetyl-β-D-glucoside under similar conditions produced the 1-bromo-2-naphthyl analog. Nitration of phenyl tetraacetyl-β-D-glucoside in acetic anhydride led to *o*-nitrophenyl tetraacetyl-β-D-glucoside, previously prepared[5c] only by the Helferich–Schmitz-Hillebrecht process. Similar nitration of 1-naphthyl tetraacetyl-β-D-glucoside gave 4-nitro-1-naphthyl tetraacetyl-β-D-glucoside, and nitration of the 2-naphthyl analog gave a 1-nitro-2-naphthyl product.

Experimental

Substituted Chlorophenyl Tetraacetyl-β-D-glucosides.—These were prepared according to the procedure of Helferich and Schmitz-Hillebrecht[8] by fusing β-D-glucose pentaacetate (20 g.), the appropriate chlorophenol (30 g.) and *p*-toluenesulfonic acid (0.3 g.) at 100° *in vacuo* for one hour. The mixtures were cooled, diluted with benzene, washed with alkali and with water, dried, and the solvent removed to yield 60–90% of the theoretical yield of crude products. The latter were recrystallized from 2-propanol until constant melting. *p*-Chlorophenyl tetraacetyl-β-D-glucoside had m.p. 123.5–124° and $[\alpha]^{25}D$ −20.2 (chloroform, *c* 2.527). These values are in agreement with those recorded by Dyfverman and Lindberg.[10]

m-Chlorophenyl tetraacetyl-β-D-glucoside had m.p. 112.5° and $[\alpha]^{25}D$ −25.3° (chloroform, *c* 2.209).

Anal. Calcd. for $C_{20}H_{23}O_{10}Cl$: C, 52.40; H, 5.06. Found: C, 52.32, 52.49; H, 5.04, 5.11.

o-Chlorophenyl tetraacetyl-β-D-glucoside had m.p. 143–144° and $[\alpha]^{25}D$ −41.3 (chloroform, *c* 2.711).

Anal. Calcd. above. Found: C, 53.17; H, 5.06.

TABLE III

CALCULATED A VALUES AND SPECIFIC ROTATIONS OF α-ANOMERS FOR SUBSTITUTED PHENYL TETRAACETYL-D-GLUCOPYRANOSIDES USING B VALUES DERIVED FROM VARIOUS ANOMERIC PAIRS

Calculated A value and rotation based on B values from acetylated D-glucopyranosyl derivatives containing at the anomeric center

Substituent	Known A value, $[\alpha]_D$,°	OH[a]	OCOMe[a]	OMe[a]	OCH_2Ph[b]	Cl[a]	F[a]	NO_2[a]	OCOEt[c]	Ph[d]	OPh[b]
p-PhCO	41395	32475	28480	28235	27835	35955	27540	34470	27090	23495	*38870*
	137.7	105	90.2	89.2	87.8	118	86.7	112	85.1	71.8	*128*
p-Br	44625	33535	29540	29295	28895	37015	28600	35530	28150	24555	*39930*
	159.6	116	99.6	98.6	97.0	130	95.9	124	94.1	79.8	*141*
m-Cl	42625	36185	32190	31945	31545	39665	31250	38180	30800	27205	*42580*
	160.5	133	115	114	112	148	111	141	109	93.2	*160*
p-Cl	42610	33855	29860	29615	29215	37335	28920	35850	28470	24875	*40250*
	165.5	127	110	109	107	143	106	136	104	88.2	*155*
o-MeO	45285	37755	33760	33515	33115	41235	32820	39750	32370	28775	*44150*
	170.5	137	120	119	117	153	116	146	114	97.8	*166*
o-NO_2	28600	3485	−510	−755	−1155	6965	−1450	5480	−1900	−5495	*9880*
	167.0	59.8	42.8	41.8	40.1	74.6	38.8	68.3	37.7	21.5	*87.1*
m-NO_2	49225	41935	37940	37695	37295	45415	37000	43930	36550	32955	*48330*
	173.0	142	125	124	122	157	121	150	119	104	*169*
p-NO_2	56515	43815	39820	39575	39175	47295	38880	45810	38430	34835	*50210*
	200.0	146	129	128	126	161	125	154	123	108	*173*
2,4-di-NO_2	45525	6635	2640	2395	1995	10115	1700	8630	1250	−2345	*13030*
	212.0	60.7	45.1	44.1	42.7	74.1	41.5	68.5	39.8	25.8	*85.6*
o-Me	39990	36715	32720	32475	32075	*40195*	31780	38710	31330	27735	43110
	155.0	140	122	121	119	*156*	117	149	115	98.9	169
p-Me	39905	32595	28600	28355	27955	36075	27660	34590	27210	23615	*38990*
	164.0	131	112	111	109	146	108	140	106	89.5	*160*

[a] Table II, ref. *a*. [b] Table II, ref. *b*. [c] W. A. Bonner, THIS JOURNAL, **73**, 2659 (1951). [d] W. A. Bonner and J. M. Craig, *ibid.*, **72**, 3480 (1950).

coside in acetic acid led to 4-bromo-1-naphthyl tetraacetyl-β-D-glucoside, identified by hydrolysis

(10) A. Dyfverman and B. Lindberg, *Acta Chem. Scand.*, **4**, 878 (1950).

TABLE IV

CALCULATED A VALUES AND SPECIFIC ROTATIONS OF α-ANOMERS FOR SUBSTITUTED PHENYL D-GALACTOPYRANOSIDES USING B VALUES DERIVED FROM VARIOUS ANOMERIC PAIRS

Calculated A value and rotations based on B values from unacetylated D-galactopyranosyl derivatives containing at the anomeric center

Substituent	Known A value, $[\alpha]_D$,°	OH[a]	OMe[a]	OPh[b]
p-MeCO	41400	33730	34510	*38100*
	226.2	175	180	*204*
o-MeO	36625	31080	31860	*35450*
	211.4	173	178	*203*
o-Me	31250	30030	*30810*	34400
	188	179	*185*	211
m-Me	33925	30280	31060	*34650*
	207	180	186	*212*

[a] Table II, ref. *a*. [b] Table II, ref. *b*.

TABLE V

CALCULATED A VALUES AND SPECIFIC ROTATIONS OF α-ANOMERS FOR SUBSTITUTED PHENYL TETRAACETYL-D-GALACTOPYRANOSIDES USING B VALUES DERIVED FROM VARIOUS ANOMERIC PAIRS

Calculated A value and rotations based on B values derived from acetylated D-galactopyranosyl derivatives containing at the anomeric center

Substituent	Known A value, $[\alpha]_D$,°	OCOMe[a]	OMe[a]	OPh[b]
o-MeO	55290	32955	29145	*44632*
	227.6	128	112	*180*
o-Me	38775	27125	23315	*38802*
	173.0	120	102	*173*
p-Me	38410	24195	20385	*35872*
	178.0	113	95.8	*166*

[a] Table II, ref. *a*. [b] Table II, ref. *b*.

Substituted Chlorophenyl Tetraacetyl-α-D-glucosides.—These were prepared as above, substituting zinc chloride as catalyst, conducting the fusion at 120°, employing freshly distilled phenols, and generally adopting the procedural modifications of Montgomery, Richtmyer and Hudson.[5c] The products were recrystallized from 2-propanol. The *o*-chloro isomer could not be induced to crystallize. *p*-Chlorophenyl tetraacetyl-α-D-glucoside had m.p. 99.5–100° and $[\alpha]^{25}D$ 165.5° (chloroform, *c* 2.380).

Anal. Calcd. for $C_{20}H_{23}O_{10}Cl$: C, 52.40; H, 5.06. Found: C, 52.37; H, 5.02.

m-Chlorophenyl tetraacetyl-α-D-glucoside had m.p. 105–107° and $[\alpha]^{25}D$ 160.5° (chloroform, *c* 2.119).

Anal. Calcd. above. Found: C, 52.42, 52.60; H, 5.04, 5.18.

4-Bromo-1-naphthyl Tetraacetyl-β-D-glucoside.—Bromine (0.6 cc.) in acetic acid (10.4 cc.) was dropped slowly into a stirred solution of 1-naphthyl tetraacetyl-β-D-glucoside (2 g.) in acetic acid (40 cc.). Each addition was made only after the preceding one had been decolorized. This avoided a large excess of bromine in the reaction mixture which caused intense and rapid darkening with subsequent inability to isolate the product desired. The addition was stopped when the bromine color persisted. The light amber solution was poured into water, and the resulting milky solution was extracted with chloroform. The chloroform solution was washed twice with water, once with sodium bisulfite solution to remove excess bromine, once with sodium bicarbonate solution, and twice again with water. After drying over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the residue dissolved in 2-propanol from which it crystallized as glistening colorless needles (1.91 g.), m.p. 133–136°. A single recrystallization from 2-propanol raised the melting point to 135–136°, unchanged by further recrystallization; $[\alpha]^{25}D$ −54.8° (chloroform, *c* 2.155).

Anal. Calcd. for $C_{24}H_{25}O_{10}Br$: C, 52.12; H, 4.56; Br, 14.45. Found: C, 52.06; H, 4.61; Br, 14.92.

Isolation of the Aglucon.—4-Bromo-1-naphthyl tetraacetyl-β-D-glucoside (1.93 g.) was refluxed with 1 *N* hydrochloric acid (50 cc.) for about 30 hours, when a large amount of undissolved material remained. The latter was removed by filtration, and the aqueous filtrate was extracted with ether. The solid on recrystallization from 2-propanol was shown to be 4-bromo-1-naphthyl tetraacetyl-β-D-glucoside, m.p. 133–135°, undepressed on admixture with an authentic sample. The ether extract was dried and the solvent evaporated. The residue crystallized as buff-colored needles which darkened in air. No definite melting point could be obtained. The material was therefore dissolved in a small amount of alcohol and the picrate prepared, m.p. 160–165°. The recorded melting point for the picrate of 4-bromo-1-naphthol[11] is 167°. The free naphthol was regenerated by dissolving the picrate in hot water. On cooling glistening colorless needles resulted, m.p. 122–124°. The values for the melting point of 4-bromo-1-naphthol given in the literature range from 121[12] to 129°.[13]

1-Bromo-2-naphthyl Tetraacetyl-β-D-glucoside.—When 2-naphthyl tetraacetyl-β-D-glucoside was brominated according to the procedure described above, the yields of bromination product did not exceed 20%. Carrying out the procedure at steam-bath temperatures raised the yield to only 25%. Bromination with aqueous bromine–potassium bromide, however, was found to give excellent yields. Bromine (0.6 cc.) in approximately 15% potassium bromide (40 cc.) was added slowly with shaking to a solution of 2-naphthyl tetraacetyl-β-D-glucoside (2.61 g.) in acetic acid (40 cc.). When the bromine color persisted, the product had separated in the flask and was filtered, washed with a solution of sodium bisulfite, and then with water; m.p. 162–167°. It was recrystallized from 2-propanol as sturdy, colorless needles (2.64 g.), m.p. 168–169°, $[\alpha]^{24.5}D$ −66.4° (chloroform, *c* 2.002).

Anal. Calcd. for $C_{24}H_{25}O_{10}Br$: C, 52.12; H, 4.56; Br, 14.45. Found: C, 51.95; H, 4.57; Br, 14.60.

Isolation of the Aglucon.—Two grams of the purified 1-bromo-2-naphthyl tetraacetyl-β-D-glucoside was refluxed with acetic acid (20 cc.) and 1 *N* hydrochloric acid (50 cc.). After an hour the mixture was a homogeneous yellow solution. This was poured into cold water, and the flocculent solid which separated was filtered and washed with water. After recrystallization from methanol–water it had a melting point of 82–83°. The melting point recorded for 1-bromo-2-naphthol[14] is 83°. The melting point of 6-bromo-2-naphthol,[15] the only other reasonable isomer, is reported as 122–124°.

The 1-bromo-2-naphthol was further characterized by its benzoate derivative which was prepared according to the procedure of Hazlet.[16] Benzoyl chloride (0.36 g.) was added slowly with agitation to a pyridine solution of the above naphthol (0.53 g.) cooled to 0°. The mixture was then heated at 60° for one-half hour, then gently refluxed for an equal length of time. The clear brown solution was poured into water and acidified with 1 *N* hydrochloric acid. The solid which separated was filtered, washed with water and recrystallized from methanol to give an almost quantitative yield of 1-bromo-2-naphthyl benzoate, long colorless needles, m.p. 98–99°. The recorded melting point of 1-bromo-2-naphthyl benzoate[14] is 98.5–99.5°.

***o*-Nitrophenyl Tetraacetyl-β-D-glucoside.**—The procedure followed in these nitrations is a modification of that used by Gilman and Wright for the nitration of furfural.[17] In a 100-cc. three-necked flask equipped with mechanical stirrer, thermometer and dropping funnel, acetic anhydride (4.3 g.) was cooled to 0°. Fuming nitric acid (1.35 g.) was slowly added. To this nitration mixture was added dropwise a solution of phenyl tetraacetyl-β-D-glucoside (3 g.) in acetic anhydride (21.6 g.). The addition was made over a period

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(14) S. E. Hazlet, THIS JOURNAL, **62**, 2156 (1940).
(15) J. A. Vona and P. C. Merker, *J. Org. Chem.*, **14**, 1049 (1949).
(16) S. E. Hazlet, THIS JOURNAL, **59**, 287 (1937).
(17) H. Gilman and G. F. Wright, *ibid.*, **52**, 2550 (1930).

of one-half hour while the reaction mixture was held at −5 to 0°. Stirring was continued for three hours longer. At the end of this time a thick cream-colored solid had separated. The mixture was poured over cracked ice and neutralized to litmus with 40% sodium hydroxide solution. The solid was removed by filtration, washed twice with ice-water, and dissolved in hot 2-propanol. Crystallization occurred at room temperature and after several recrystallizations a pure product, pale yellow shining platelets, was obtained, m.p. 156–157°, $[\alpha]^{24}D$ 40.5 (chloroform, *c* 2.002). The recorded physical properties of *o*-nitrophenyl tetraacetyl-β-D-glucoside have been stated as m.p. 150–152°, $[\alpha]^{20}D$ 45° (chloroform)[5c]; 160–162°, $[\alpha]^{20}D$ 45 (chloroform)[18]; m.p. 158–159°, $[\alpha]^{20}D$ 45° (chloroform)[19]; and m.p. 160.5–161.5°, $[\alpha]^{20}D$ 43.0° (chloroform).[20]

Although Lindberg[18] reported the isolation of both *o*-nitro- and *p*-nitrophenyl tetraacetyl-β-D-glucoside on nitration of phenyl tetraacetyl-β-D-glucoside using nitric acid in acetic acid, we have isolated only the ortho-isomer on successive recrystallization of the crude nitration mixture. Due to the isolation of lower melting material in impure form from the mother liquors in the present nitration, we feel that the para-isomer was also produced in our experiment.

Isolation of the Aglucon.—*o*-Nitrophenyl tetraacetyl-β-D-glucoside (1.08 g.) was refluxed for one hour with 1 *N* hydrochloric acid (100 cc.). At this time the *o*-nitrophenol had been steam distilled into the condenser as bright yellow needles, m.p. 45–47°. The reported melting point of *o*-nitrophenol[21] is 45°. The nitrophenol was further characterized by bromination with aqueous bromine–potassium bromide to yield the dibromo derivative, m.p. 116–117°. The melting point of 2,4-dibromo-6-nitrophenol given in the literature[22] is 117°.

4-Nitro-1-naphthyl Tetraacetyl-β-D-glucoside.—This compound was prepared from 1-naphthyl tetraacetyl-β-D-glucoside (3 g.) in acetic anhydride in the manner described above. The mixture was stirred for 2.5 hours after addition to the nitration mixture was completed. It was then poured into sodium bicarbonate (42 g.) in ice-water, at which point a deep yellow solid separated. This was filtered, washed with ice-water and dissolved in hot 2-propanol from which it crystallized as glistening yellow needles. Two recrystallizations from alcohol yielded a pure product, m.p. 176–177°, $[\alpha]^{25}D$ −67.2° (chloroform, *c* 2.025).

Anal. Calcd. for $C_{24}H_{25}O_{12}N$: C, 55.29; H, 4.82; N, 2.70. Found: C, 55.28; H, 4.86; N, 2.81.

Isolation of the Aglucon.—One gram of 4-nitro-1-naphthyl tetraacetyl-β-D-glucoside was refluxed with 1 *N* hydrochloric acid (50 cc.) for approximately 12 hours. The cooled mixture contained a flocculent yellow suspension which was extracted with ether. The ether solution was extracted with 10% sodium hydroxide and the resulting orange-red solution was acidified to yield the flocculent yellow solid once again. This was extracted into ether, the solution dried over anhydrous sodium sulfate, the solvent evaporated and the yellow residue recrystallized from water as very fine yellow needles, m.p. 159–164°. The recorded melting point of 4-nitro-1-naphthol is 164°.[23] The nitronaphthol was further identified by benzoylation after the procedure of Hazlet.[14] The benzoate crystallized from acetone as small pale yellow needles, m.p. 169–170°. The melting point reported for 4-nitro-1-naphthyl benzoate[24] is 176° (cor.).

1-Nitro-2-naphthyl Tetraacetyl-β-D-glucoside.—This compound was prepared, in the manner described previously, from 2-naphthyl tetraacetyl-β-D-glucoside (3 g.) dissolved in acetic anhydride. The product, pale yellow needles, m.p. 198–199°, crystallized from benzene, darkened to a green-yellow on exposure to light, and showed no optical activity in chloroform solution.

Anal. Calcd. for $C_{24}H_{25}O_{12}N$: C, 55.49; H, 4.82; N, 2.70. Found: C, 55.50; H, 4.82; N, 2.58.

Isolation of the Aglucon.—One gram of nitro-2-naphthyl tetraacetyl-β-D-glucoside was refluxed with 1 *N* hydrochloric acid for 48 hours. The free 1-nitro-2-naphthol steam distilled and collected in the condenser, m.p. 95–98°. On recrystallization from 2-propanol, the melting point was raised to 99–100.5°. The reported melting point for 1-nitro-2-naphthol[19] is 103°. The 1-nitro-2-naphthol was further characterized by its methyl ether, m.p. 123.5–125°. The recorded melting point is 128°.[25] The methyl ether was a pale yellow solid which turned to a green-yellow on standing in light, the characteristic shown by 1-nitro-2-naphthyl tetraacetyl-β-D-glucoside.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

The Stereochemistry of Raney Nickel Action. III. The Stereochemical Course of Dehydroxylations in the Benzyl Alcohol Series

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Since the stereochemical path followed during the Raney nickel catalyzed desulfuration of sulfides differed from that followed during sulfone desulfuration, we have undertaken a study of the stereochemical course of Raney nickel catalyzed dehydroxylations in the benzyl alcohol series. Derivatives of atrolactic acid were converted to derivatives of 2-phenylpropionic acid with Raney nickel in refluxing ethanol with what appeared to be practically complete retention of configuration. Such slight racemization as was noted seemed due to the fact that Raney nickel slowly racemizes derivatives of 2-phenylpropionic acid in refluxing ethanol. The dehydroxylation of ethyl mandelate appeared substantially complete in the course of 20 minutes reaction time.

The occurrence of carbon–oxygen bond cleavage in benzyl alcohol or substituted benzyl alcohols under conditions of catalytic hydrogenation at elevated temperatures and pressures is well known.[1] In 1944, while studying the effect of excess Raney nickel on potentially reducible groups other than sulfur, Mozingo and co-workers found[2] that this catalyst was also capable of converting both benzyl alcohol and benzaldehyde to toluene in a short time under the mild conditions of mere refluxing in ethanol ordinarily employed in Raney nickel catalyzed desulfurations.[3] Recently the stereochemical course of reductive desulfuration was investigated[4] with the discovery that sulfides were desulfurized with complete racemization whereas

(1) H. Adkins, "Reactions of Hydrogen with Organic Compounds Over Copper-Chromium Oxide and Nickel Catalysts," Univ. of Wisconsin Press, Madison, Wis., 1937, p. 69 ff.

(2) R. Mozingo, C. Spencer and K. Folkers, THIS JOURNAL, **66**, 1859 (1944).

(3) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *ibid.*, **65**, 1013 (1943).

(4) W. A. Bonner, *ibid.*, **74**, 1033, 1034 (1952). These papers constituted I and II in the present series.