

Summary

1. The vapor phase esterification of ethyl alcohol and acetic acid in the presence of silica gel has been studied over the temperature range of 150 to 300°.

2. The limits obtained with the equimolar mixture of the alcohol-acid have been approached from the other side by the hydrolysis of an acetate-water mixture.

3. Close checks by the two methods gave average conversions of from about 85% at 150° to 75% at 300° as limits in the presence of silica gel. These data would indicate that there is some variation of the equilibrium constant with the temperature, with the highest conversion at the lower temperatures.

BALTIMORE, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH]

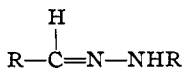
THE OPTICAL ROTATION OF RHAMNOSE AND MANNOSE PHENYLHYDRAZONES

BY C. L. BUTLER AND LEONARD H. CRETCHER

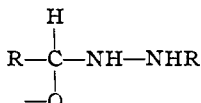
RECEIVED JULY 18, 1931

PUBLISHED DECEMBER 10, 1931

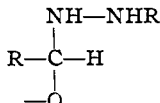
Very little is known of the structure of the sugar hydrazones. Although Behrend and collaborators¹ found evidence of structural isomerism among certain members of this group of substances, it has usually been assumed that the reaction between sugars and hydrazines results in the formation of true hydrazones. Since the sugars are complex substances capable of reacting in several different forms, no assumptions regarding the structure of the hydrazones or the course of reaction would seem to be justified. The only recent work done in this field is that of Wolfrom,² who reported results favoring a true hydrazone structure for several hydrazones of galactose. Formulas I (true hydrazone), II and III (hydrazide, or substituted hydrazine, corresponding to the α - and β -glucosides) were proposed by Behrend¹ and they appear to the present authors to be the most probable ones for the sugar hydrazones although others are possible. These structures are



I



II



III

¹ Behrend and others, *Ann.*, **353**, 106 (1907); **362**, 78 (1908); **366**, 277 (1909); **377**, 189 (1910); see also Lobry de Bruyn, *Ber.*, **28**, 3084 (1895); Simon and Benard, *Compt. rend.*, **132**, 564 (1901); Frèrejacque, *ibid.*, **180**, 1210 (1925).

² Wolfrom and Christman, *THIS JOURNAL*, **53**, 3413 (1931).

similar to those proposed by Wolfrom³ to explain the mutarotation of the alcoholate of aldehydo-galactose pentaacetate.

The present study of the optical rotation of rhamnose and mannose phenylhydrazones was undertaken in order to throw further light on the structure of these substances and for purposes of comparison in the work on the corresponding nitrophenylhydrazones, a report of which will be found in the following paper.

The Preparation and Mutarotation of Rhamnose and Mannose Phenylhydrazones.—Mannose phenylhydrazone was prepared by mixing 2 g. of the sugar and 2 g. of phenylhydrazine in 30 cc. of 95% alcohol and warming for one-half hour on a water-bath. The mixture was allowed to stand for two hours at room temperature and overnight in the ice box. The hydrazone was then filtered and washed thoroughly first with water, then with alcohol and finally with ether. The yield was 3.0 g. of glistening, snow white crystals melting at 199–200°. Crystallization from 60% alcohol gave a slightly colored product with melting point 3° lower.

When prepared in the usual way in dilute acetic acid solution at room temperature the substance, washed as described above, was slightly colored and melted at 188–189°. Crystallization from 60% alcohol raised the melting point several degrees but did not improve the color.

Rhamnose phenylhydrazone was prepared by mixing together 3 g. of the sugar, 3 cc. of water and 3 g. of phenylhydrazine.⁴ A clear solution was obtained. After standing for two hours at room temperature the hydrazone commenced to crystallize out. The product solidified after standing overnight in the ice box. It was ground under ether, filtered and thoroughly washed with ether. The yield was 3.5 g. of very slightly colored crystals melting at 158–159°.

Mannose phenylhydrazone has been previously reported not to mutarotate in pyridine solution.⁵ The rotation of our sample of this material in ordinary c. p. pyridine, however, changed in an unusual manner. The initial value, +26.3°,⁶ agrees with the figures given by Hofmann. It remained at this point for one and one-half hours, then dropped to a minimum value of about 6° and after passing through this point increased slowly to a point slightly higher than the initial rotation. If in the older work⁵ readings were taken during less than one and one-half or two hours, or if only initial and final readings forty to fifty hours apart were taken, it is easy to see how the mutarotation of this hydrazone could have escaped observation.

³ Wolfrom, *THIS JOURNAL*, **53**, 2275 (1931).

⁴ Van der Haar, "Anleitung zum Nachweis, zur Trennung und Bestimmung der Monosaccharide und Aldehydesäuren," Gebrüder Borntraeger, Berlin, 1920, p. 147.

⁵ Hofmann, *Ann.*, **366**, 277 (1909).

⁶ Levene and Mori, *J. Biol. Chem.*, **84**, 59 (1929), report $[\alpha]_D +32.5^\circ$ in pyridine-alcohol solution.

A similar but more pronounced change took place in 1:1 pyridine-alcohol solution. The initial value $+27.3^\circ$ dropped to -2.6° , then increased

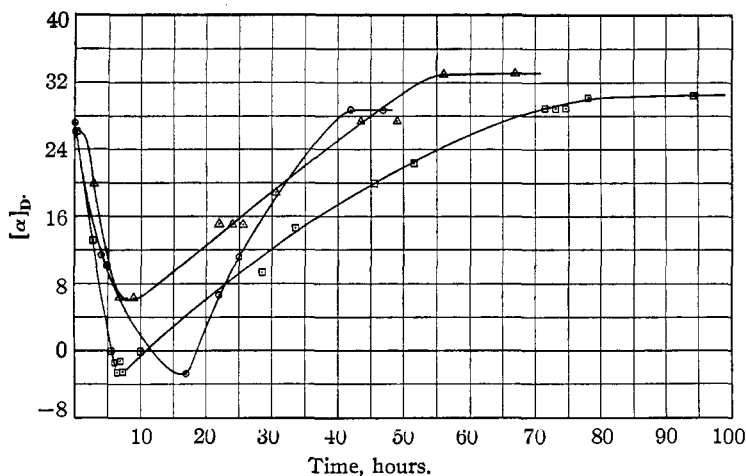


Fig. 1.—○, Mannose phenylhydrazone in 1:1 pyridine-alcohol mixture No. 1; □, mannose phenylhydrazone in 1:1 pyridine-alcohol mixture No. 2; Δ, mannose phenylhydrazone in c. p. pyridine.

slowly to a constant value slightly higher than the initial rotation. Two experiments were run and it was found that the rate of change was not the

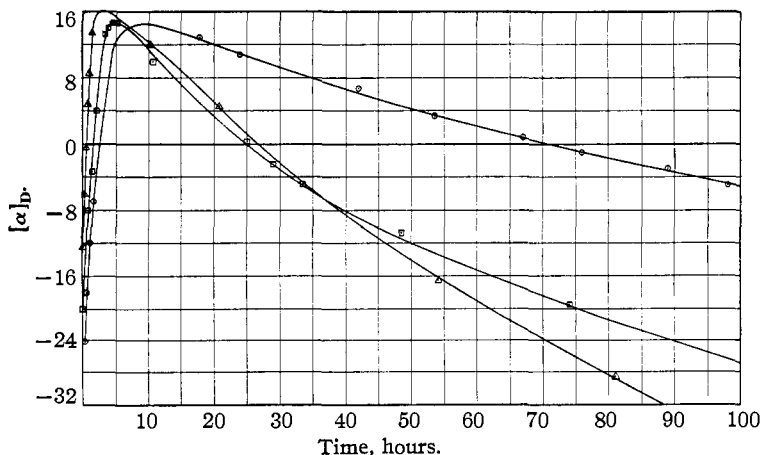


Fig. 2.—Rhamnose phenylhydrazone in 1:1 alcohol-pyridine mixture: Experiment 1 marked ○ came to equilibrium after 279 hours at -35.0° ; Experiment 2 marked □ came to equilibrium after 365 hours at -100.0° ; Experiment 3 marked Δ came to equilibrium after 246 hours at -67.3° .

same in the two cases although the initial, minimum and end values agreed. The only difference in the experimental conditions of the two determinations

was that in the second the sample was ten days older than in the first. It is possible that the material changes slightly on standing, and that the reaction is catalyzed by the presence of the resulting impurity.

The initial rotation of rhamnose phenylhydrazone in aqueous solution was found to be $+57.1^\circ$. This value gradually decreased until a constant rotation of $+44.3^\circ$ was reached. Jacobi⁷ reported $[\alpha]_D + 54.6^\circ$ with no mutarotation for rhamnose phenylhydrazone in aqueous solution.

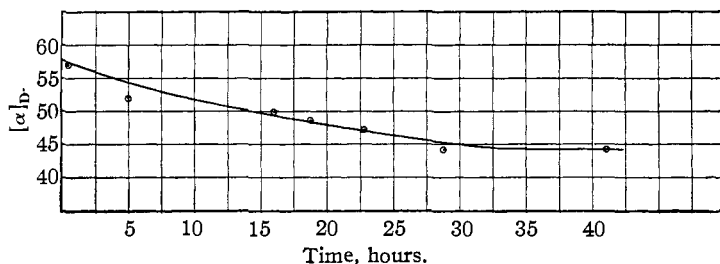


Fig. 3.—Rhamnose hydrazone in water.

The rotation of this substance was also determined in pyridine-alcohol mixture and the same type of curve was obtained as for mannose phenylhydrazone. Three determinations were made. The initial value was somewhat below -24° . This value rapidly increased until a maximum of about $+16^\circ$ was reached. It then fell off slowly and became constant at a larger negative value than the initial rotation. The rate of change was found to increase with the age of the sample. As shown in Table IV, it was so rapid initially that no agreement in the values for initial observed rotation could be obtained. Another peculiarity in the observations was that different final constant rotations, namely, -35.0 , -100.0 and -67.3° were obtained in the three experiments. No explanation for this behavior can be given at present.

TABLE I
THE MUTAROTATION OF MANNOSE PHENYLHYDRAZONE
Solvent 1:1 pyridine-alcohol mixture

Expt. 1		Expt. 2			
Time	$[\alpha]_D$	Time, hours	$[\alpha]_D$	Time, hours	$[\alpha]_D$
5 min.	$+27.3^\circ$	0.5	$+26.3^\circ$	22	$+6.6^\circ$
4 hours	$+11.4^\circ$	2.25	$+13.2^\circ$	28.5	$+9.2^\circ$
5 hours	$+10.2^\circ$	5.5	0.0°	33.5	$+14.5^\circ$
17 hours	-2.6°	5.75	0.0°	45.5	$+19.8^\circ$
25 hours	$+13.0^\circ$	6.25	-1.3°	51.5	$+22.4^\circ$
42 hours	$+28.6^\circ$	6.5	-2.6°	71.5	$+28.9^\circ$
47 hours	$+28.6^\circ$	6.75	-2.6°	73	$+28.9^\circ$
		7	-1.3°	74	$+28.9^\circ$
		7.5	-2.6°	78	$+30.2^\circ$
		10	-0.0°	94	$+30.2^\circ$

⁷ Jacobi, *Ann.*, 272, 170 (1893).

TABLE II
THE MUTAROTATION OF MANNOSE PHENYLHYDRAZONE

Solvent, c. p. pyridine			
Time	$[\alpha]_D$	Time, hours	$[\alpha]_D$
30 min.	+26.3°	24	+15.0°
45 min.	+26.3°	25.5	+15.0°
1 hour	+26.3°	30.5	+18.8°
3 hours	+20.0°	43.5	+27.5°
6.75 hours	+ 6.3°	49	+27.5°
9 hours	+ 6.3°	56	+33.8°
21 hours	+16.3°	67	+33.8°
22 hours	+15.0°		

TABLE III
THE MUTAROTATION OF RHAMNOSE PHENYLHYDRAZONE

Solvent, water	
Time, hours	$[\alpha]_D$
0.5	+57.1°
5	+52.1°
16	+50.0°
18.75	+48.6°
22.75	+47.1°
28.75	+44.3°
41	+44.3°

TABLE IV
THE MUTAROTATION OF RHAMNOSE PHENYLHYDRAZONE

Solvent 1:1 pyridine alcohol mixture					
Expt. 1		Expt. 2		Expt. 3	
Time, hours	$[\alpha]_D$	Time, hours	$[\alpha]_D$	Time, hours	$[\alpha]_D$
15 min.	-24.1	10 min.	- 20.0	5 min.	-12.5
30 min.	-18.0	40 min.	- 8.0	15 min.	- 6.0
1	-13.0	1.33	- 3.5	30 min.	- 0.4
1.33	- 7.0	2	+ 4.0	45 min.	+ 4.8
18	+12.8	3.5	+ 13.3	1	+ 8.5
24	+10.8	4	+ 14.0	1.5	+13.5
42	+ 6.8	4.5	+ 14.5	1.75	+14.5
53.5	+ 3.3	5.5	+ 14.5	2	+15.5
67	+ 0.8	8.5	+ 13.0	2.167	+16.0
76	- 1.0	10.75	+ 9.8	2.33	+16.0
89	- 3.0	25	+ 0.3	2.5	+16.5
98	- 5.0	29	- 2.5	3	+16.3
119.75	- 9.0	33.5	- 5.0	4.25	+15.5
138.25	-11.8	48.5	- 10.8	4.5	+15.0
150.25	-13.8	74	- 19.5	10.25	+12.0
168	-16.5	102.5	- 28.3	20.75	+ 4.5
186	-20.0	121	- 33.3	33.5	- 4.8
210	-23.8	143	- 39.5	54	-16.5
233	-28.0	169	- 46.3	81	-28.5
263	-33.0	190.5	- 53.0	99	-36.3
279	-35.0	223	- 62.5	148	-50.8
287	-35.0	239	- 66.0	165	-54.8
305	-35.0	264	- 71.8	189	-56.5
		288	- 74.5	201.5	-59.5
		311	- 77.8	224	-62.0
		335	- 84.5	246	-67.3
		365	- 98.5	266	-67.3
		383	-100.0°		

* The rate of change was very slow at this point. Further readings could not be taken due to coloring which developed in the solution.

The mutarotations in pyridine and pyridine-alcohol mixture described above and shown graphically in Figs. 1 and 2 indicate that at least two changes take place under the conditions of the experiments. These reactions are obviously more complicated than that of rhamnose phenylhydrazone in water since in this case a constant minimum rotation was reached. Whether the results obtained in pyridine and pyridine-alcohol mixture are due to rearrangements involving structures I, II and III shown above or similar ones, to shifts in the ring structure of the compounds, or to reactions of the hydrazones with the solvent cannot be stated at present. A curve similar in shape to those given here was obtained by Wolfrom³ in the work on the alcoholate of aldehydo-galactose pentaacetate.

Summary

A polarimetric study of rhamnose and mannose phenylhydrazones was made. These substances, previously reported to have constant rotations, were found to mutarotate in an unusual manner.

PITTSBURGH, PENNSYLVANIA

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH]

THE OPTICAL ROTATION OF THE ISOMERIC NITROPHENYLHYDRAZONES OF RHAMNOSE AND MANNOSE

By C. L. BUTLER AND LEONARD H. CRETCHER

RECEIVED JULY 18, 1931

PUBLISHED DECEMBER 10, 1931

Since the structure of the sugars and of most sugar derivatives is so complex, a strictly regular variation in the values for the optical rotation of isomeric sugar hydrazones might not be expected. The older data on the nitrophenylhydrazones, obtained by Van Ekenstein and Blanksma,¹ do in fact show peculiar variations. However, the published values for these compounds and for the unsubstituted derivatives vary so markedly in their relationship to each other, with the relationship found among other types of optically active position isomers, that further investigation of the subject appeared to be worth while.

Frankland,² after examination of the results of many investigations on the effect of position isomerism on rotation, deduced a rule which may be stated as follows. When the rotations of a monosubstituted benzene derivative and the three disubstitution products are compared, the para derivative has the highest rotation, the order of magnitude of the other three being meta, monosubstituted derivative, ortho. It was also pointed out by Cohen³ that the change in rotation due to substitution in the ortho

¹ Van Ekenstein and Blanksma, *Rec. trav. chim.*, **22**, 434 (1903); **24**, 33 (1905).

² Frankland, *J. Chem. Soc.*, **101**, 666 (1912).

³ Cohen, *ibid.*, **97**, 1737 (1910); **99**, 1060 (1911).