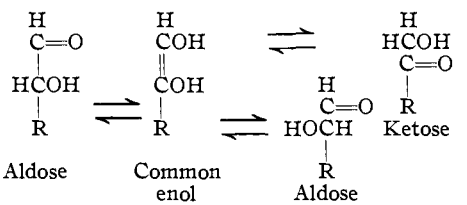
[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, LOYOLA UNIVERSITY, SCHOOL OF MEDICINE]

THE ACTION OF DILUTE ALKALI ON *d*-XYLOSE, *d*- AND *l*-ARABINOSE, *d*-α-GLUCOHEPTOSE AND *d*-GLUCOHEPTULOSE[1]

BY W. C. AUSTIN, C. J. SMALLEY AND M. I. SANKSTONE

RECEIVED NOVEMBER 9, 1931 PUBLISHED MAY 7, 1932

The recent investigations of Lewis[2] and co-workers have aroused new interest in the Lobry de Bruyn[3] conversion. Wolfrom and Lewis[2b] found that saturated calcium hydroxide induces rearrangements in sugar structures with minimal formation of caramel and saccharinic acids. Advantage was taken of this finding by Montgomery and Hudson[4] in the conversion of lactose to lactulose and by Austin[5] in the conversion of *d*-α-glucoheptose to *d*-glucoheptulose. The more widely accepted theory of the mechanism of the conversion is that the reducing sugar, when dissolved in alkali, forms a common enol which then rearranges to form new reducing sugars. The new reducing sugars so formed are predominantly those differing from the starting sugar only with respect to the configurations about the first and second carbon atoms.[6] The general structures shown in the formulas illustrate the extent and mechanism of the predominating interconversions between reducing sugars under the influence of alkali. The arrows indicate that the reactions are reversible and that the three remaining substances are formed from any one in solution with alkali.



[1] Abstracted in part from dissertations submitted by Smalley and Sankstone to the Graduate School of Loyola University in partial fulfilment of the requirements for the degree of Master of Science. A portion of the results described here was given on the program of the meeting of the American Chemical Society in Indianapolis, March 30–April 3, 1931, and on the program of the meeting of the American Society of Biological Chemists in Montreal, April 8–11, 1931. The authors desire to thank Mr. B. J. Gregory for valuable technical assistance.

[2] (a) Gustus and Lewis, THIS JOURNAL, **49**, 1512 (1927); (b) Wolfrom and Lewis, *ibid.*, **50**, 837 (1928); (c) Greene and Lewis, *ibid.*, **50**, 2813 (1928); (d) Gross and Lewis, *ibid.*, **53**, 2772 (1931).

[3] Lobry de Bruyn and van Ekenstein, *Rec. trav. chim.*, **14**, 156 (1895); **14**, 195 (1895); **14**, 207 (1895); **16**, 262 (1897); **19**, 1 (1900); **27**, 1 (1908).

[4] Montgomery and Hudson, THIS JOURNAL, **52**, 2101 (1930).

[5] Austin, *ibid.*, **52**, 2106 (1930).

[6] For more complete consideration of the theories of the Lobry de Bruyn conversion, the reader is referred to the papers cited by Gross and Lewis.[2d]

With *d*-xylose as the starting sugar it would be expected from the above theory that a common enol would be formed by the action of the alkali and from it *d*-lyxose and *d*-xyloketose would next form to constitute an equilibrated system.

In like manner *l*-arabinose in solution with alkali would be expected to form a common enol which would form *l*-ribose and *l*-araboketose and constitute another equilibrated system. Also *d*-α-glucoheptose would be expected to form a common enol which in turn would give rise to *d*-β-glucoheptose and *d*-glucoheptulose and constitute a third equilibrated system.

Before beginning experiments with the purpose of isolating products of rearrangement of *d*-xylose and of *l*-arabinose, it was thought advisable to follow quantitatively the changes which these sugars undergo when dissolved in saturated calcium hydroxide. It was found that the rotation of a solution of *d*-xylose in this medium changed from $[\alpha]_D^{20-35}$ +18.2° to the constant value of $[\alpha]_D^{20-35}$ +10° in twenty-four hours at 30–35°. The P_H changed in a month of observation from 10.19 to 6.01. During this longer period the percentage of reducing pentose fell from 99.73 to 91.53% of the used *d*-xylose, while the aldose concentration decreased from 97.5 to 88.2% of the used *d*-xylose. These concentrations of reducing pentose and aldopentose indicated that at no time was more than 5% of reducing ketose evident. Solutions of *d*-xylose which have attained such equilibrium values have been freed of unchanged *d*-xylose by evaporation and crystallization, leaving sirupy residues from which as yet no *d*-lyxose or *d*-xyloketose has crystallized. One such sirup showed a rotation of $[\alpha]_D^{20-35}$ −0.26°, with 118% apparent aldose pentose, with only 70% reducing pentose. When a portion of this sirup was dissolved in saturated calcium hydroxide, it changed from $[\alpha]_D^{20-35}$ −0.26 to +2.07° in rotation in one hundred forty-four hours.

It was found that the solution of *l*-arabinose in calcium hydroxide changed in rotation from $[\alpha]_D^{20-35}$ +99.6° to the constant value of +62.2° in seventy-two hours. The P_H changed in two months from 10.8 to 5.28. During this longer period of observation the percentage of reducing pentose fell from 94.5 to 86.4% of the used *l*-arabinose, while the aldose concentration decreased from 95.02 to 82.0% of the used *l*-arabinose. These concentrations of reducing pentose and aldopentose indicated that at no time was more than 5% of reducing ketose present. Solutions of *l*-arabinose which have attained equilibrium values have been freed of unchanged *l*-arabinose by evaporation and crystallization, leaving sirupy residues from which no *l*-ribose or *l*-araboketose has crystallized. A sirup so prepared has shown $[\alpha]_D^{20}$ +4.73° with 78.36% reducing pentose and 75.7% aldose pentose. Attempts to form the known *p*-bromophenylhydrazone of *l*-ribose from such sirups have met with uniform failure. Portions of the

sirups have been oxidized with bromine and the reaction products used in futile attempts to form the known phenylhydrazide and the cadmium salt of *l*-ribonic acid.

By solution of *d*-arabinose in saturated calcium hydroxide, the initial value of $[\alpha]_D^{20-35}$ $-100.4°$ changed in ninety-six hours to $[\alpha]_D^{20-35}$ $-54.4°$. Evaporation of this solution and removal of unchanged *d*-arabinose by crystallization left a sirup with the value of $[\alpha]_D^{20-35}$ $-7.4°$. This sirup showed 74.04% of reducing pentose and 60.32% of aldopentose. A portion of this sirup was dissolved in saturated calcium hydroxide and the rotation changed very slightly in one hundred twenty hours to the constant value of $[\alpha]_D^{20-35}$ $-4.9°$. Another portion of this sirup was seeded with *d*-ribose without any crystallization of this pentose resulting.

In contrast with the apparent lack of reversibility between *d*-xylose and its products, and between *d*-arabinose and its products, it has been found that alkali forms *d*-α-glucoheptose from *d*-glucoheptulose in a reversible manner. With either of these heptoses as the starting material in solution with alkali the final equilibrium value of $[\alpha]_D^{20-35}$ $+40$ to $+45°$ is attained. In the equilibrium mixture from the *d*-glucoheptulose there is about 23% aldose and 77% ketose. Resaturation of such an equilibrated solution with calcium hydroxide caused the value of the $[\alpha]_D^{20-35}$ $+45°$ to decrease further to the constant value of $[\alpha]_D^{20-35}$ $+36°$, when the solution contained 42% aldose and 58% ketose.

Experimental Part

The Action of Dilute Alkali on *d*-Xylose.—*d*-Xylose (37.5 g. with $[\alpha]_D^{20}$ $+19.9°$) was dissolved in calcium hydroxide solution, previously saturated at 30–35° and filtered, to make 500 cc. of solution, half-molal in concentration of the sugar. Before the sugar was dissolved the P_H of the solution of calcium hydroxide was 12.3, determined potentiometrically with the hydrogen electrode. Five minutes after solution of the *d*-xylose in this medium the P_H was 10.19. A portion of the solution was used to fill a 2-dm. tube and found to have the value of $[\alpha]_D^{20-35}$ $+18.19°$, five minutes after the solution of the sugar. A second portion of the solution was diluted and used for the iodine titration by the directions of Goebel,[7] employing a fifteen-minute oxidation time. This estimation accounted for 97.56% of the used *d*-xylose, five minutes after solution. At the same time interval a portion of the diluted solution was used to estimate the total reducing pentose by the directions of Bertrand,[8] and showed the value of 99.73% of the used *d*-xylose. The solution was preserved with xylene and kept at 30–35°. From time to time other portions of this stock solution were withdrawn for repetition of the analyses, with the addition of iodine oxidations on portions of the solution which had been deenolized by the directions of Wolfrom and Lewis,[2b] holding the sample in 2 *N* sulfuric acid for twenty-four hours before neutralization and oxidation with iodine in the usual manner. The changes in the solution are shown in Table I, and graphically in Fig. 1.

Further Studies of the Products from *d*-Xylose.—A solution, containing in 1180 cc. the products of the action of calcium hydroxide on 88.5 g. of *d*-xylose, was clarified and

[7] Goebel, *J. Biol. Chem.*, **72**, 801 (1927).

[8] Bertrand, *Bull. soc. chim.*, **35**, 1285 (1906).

TABLE I

CHANGES OF *d*-XYLOSE IN DILUTE ALKALI AT 30–35°

Time, hours	$[\alpha]_D^{20-35}$ [a]	Aldopentose, % A [b]	Aldopentose, % B [c]	Reducing pentose, %	P_H
0.08	18.19	97.56		99.73	10.19
.66	18.33				10.06
2.5	16.20				9.93
2.8		100.60	100.83	97.53	
4.5	13.72				9.01
5.6		100.60	96.92	97.33	
24.0	10.20	93.60	91.52	93.80	
51.0	10.41				9.24
72.0	10.35	90.40	90.29	93.33	9.65
142.0	10.01		88.39	92.23	7.69
166.0		87.30		92.0	
720.0	10.40	88.26	91.24	91.53	6.01

[a] $C = M/2$ solution of *d*-xylose in 0.04 N calcium hydroxide. [b] Before de-enolization. [c] After de-enolization.

evaporated to a thick sirup under reduced pressure. The sirup was diluted with 20 cc. of water and 480 cc. of hot methyl alcohol, filtered from an amorphous precipitate, and again reduced by evaporation to a sirup under reduced pressure. This sirup was thinned with 90–95% ethyl alcohol and allowed to crystallize overnight. Eighteen g. of

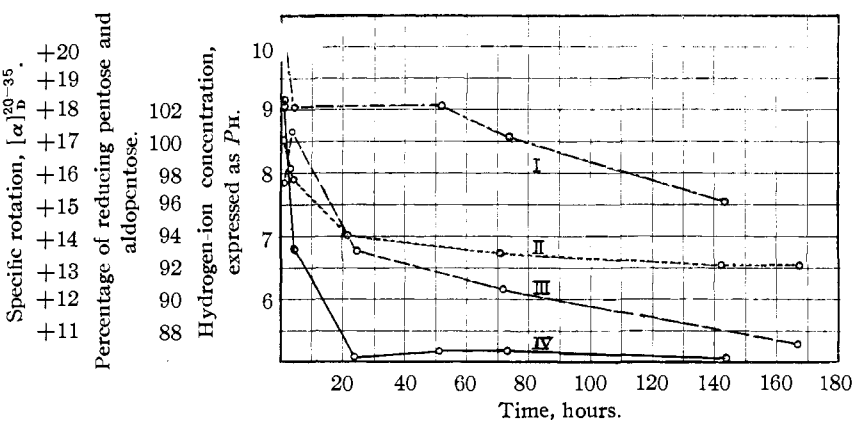


Fig. 1.—Changes in a solution of 37.5 g. of *d*-xylose in 0.04 N calcium hydroxide to 500 cc., at 30–35°: I, change in P_H; II, change in percentage of reducing pentose; III, change in percentage of aldopentose; IV, change in specific rotation, $[\alpha]_D^{20-35}$.

crude *d*-xylose was then removed by filtration. Concentration of the filtrate gave 6.0 g. more of crystalline *d*-xylose in three crops. The mother liquor of the last crop was dissolved in 50 cc. of methyl alcohol and the solution then diluted with 200 cc. of anhydrous ether. After one hour the supernatant solution was decanted from the hygroscopic brown precipitate and evaporated to a very clear and lightly colored sirup, from which 1.0 g. more of *d*-xylose was crystallized and removed. The sirup was then dried in a vacuum desiccator to 11.2 g. A sample of 1.9316 g. of the purified sirup was dissolved in water to 50 cc. A portion of this solution was saturated with calcium hydroxide and filtered into a 2-dm. tube for the reading $\alpha = -0.03°$, corresponding to $[\alpha]_D^{20-35}$

$-0.26°$. Seventy-two hours later the value was $[\alpha]_D^{20-35}$ $+1.67°$, and in 144 hours $+2.07°$. Before the solution was saturated with calcium hydroxide, the apparent aldopentose was 118.1%, with 69.37% reducing pentose. At the end of the one hundred and forty-four hour period the apparent aldopentose was 46.79%, with 45.72% reducing pentose.

The Action of Dilute Alkali on *l*-Arabinose.—*l*-Arabinose (37.5 g., $[\alpha]_D^{20}$ $+101.5°$) was dissolved in calcium hydroxide solution, previously saturated at 30–35° and filtered, to make 500 cc. of solution, half-molal in concentration of *l*-arabinose. Before the sugar was dissolved the P_H of the calcium hydroxide was 12.3, determined potentiometrically by the hydrogen electrode method. Twenty-five minutes after solution of the sugar the P_H was 10.80. A portion of the solution was used to fill a 2-dm. tube and found to have the value of $[\alpha]_D^{20-35}$ $+99.6°$. At the same time interval a second portion of the solution was used for the iodine titration by the method of Goebel,[7] employing fifteen minutes' time for oxidation. This estimation accounted for 95.02% of the used *l*-arabinose as aldopentose. A portion of the diluted solution was held for twenty-four hours in 2 *N* sulfuric acid, the solution then neutralized and oxidized with iodine in the usual manner. This estimation on the de-enolized sample accounted for 96.43% of the used *l*-arabinose as aldopentose. At the same time interval, twenty-five minutes after solution of the sugar, another portion of the diluted solution showed 94.56% of the used *l*-arabinose as reducing pentose, using the directions of Bertrand.[8] The remaining solution was preserved with xylene and kept at 30–35°. From time to time portions of this stock solution were withdrawn for repetition of the mentioned examinations. The changes in the *l*-arabinose are shown in Table II, and graphically in Fig. 2.

TABLE II

CHANGES OF *l*-ARABINOSE IN DILUTE ALKALI AT 30–35°

Time, hours	$[\alpha]_D^{20-35}$ [a]	Aldopentose, % A [b]	Aldopentose, % B [c]	Reducing pentose, %	P_H
0.42	99.60	95.02	96.43	94.56	10.80
3.25	95.23				
5.08		96.08	96.28	93.60	10.63
6.60	88.27				
9.00	85.20				
23.30	70.66	88.27	87.97	88.27	10.10
29.66	69.14				
47.00		85.33	83.84	87.20	9.60
48.33	65.00				
71.10	62.20				
119.20		82.40	83.69	86.27	7.84
191.20	61.66	81.24	82.51	85.43	7.21
1614.25	61.87	82.00	78.20	86.40	5.28

[a] $C = M/2$ solution of *l*-arabinose in 0.04 *N* calcium hydroxide. [b] Before de-enolization. [c] After de-enolization.

Further Studies of the Products from *l*-Arabinose.—Sixty grams of *l*-arabinose of $[\alpha]_D^{20}$ $+101.8°$ was dissolved in saturated calcium hydroxide solution and allowed to change to the final constant value $[\alpha]_D^{20-35}$ $+56.7°$ in seven days. The solution was then evaporated to a sirup under reduced pressure, diluted with 400 cc. of methyl alcohol, and filtered from an amorphous precipitate of 7 g. The filtrate was concentrated to a sirup again and allowed to crystallize overnight. Twenty grams of crude sugar was filtered out and recrystallized to 15.6 g. of crude *l*-arabinose of $[\alpha]_D^{20}$ $+97.7°$. From the sirup

5.2 g. more of *l*-arabinose was crystallized in three crops. The sirup was no longer crystallizable and showed the rotation of $[\alpha]_D^{20}$ +5.34° (0.6544 g. in water to 25 cc. to read α = +0.28°, using a 2-dm. tube). The sirup was diluted with 300 cc. of methyl alcohol and 300 cc. of anhydrous ether and the solution then filtered with carbon from an amorphous colored precipitate of 3 to 5 g. The solution was again reduced to a sirup from which 0.6 g. more of *l*-arabinose was removed after crystallization. The residual sirup showed $[\alpha]_D^{20}$ +4.73° (0.8455 g. in water to 25 cc. for reading α = +0.32°, using a 2-dm. tube). The sirup showed 78.36% of reducing pentose and 75.7% of aldopentose. The remaining 7.5 g. of the sirup was mixed with 5 g. of *p*-bromophenylhydrazine and 35 cc. of absolute alcohol. The mixture did not form any *l*-ribose *p*-bromophenylhydrazone crystals in forty-eight hours at 30–35°, as described by Fischer and Piloty.[9] The solution was freed of alcohol by evaporation and diluted with 300 cc. of water containing 19 cc. of 50% acetic acid, 20 g. more of *p*-bromophenylhydrazine hydrochloride and 15.0 g. of sodium acetate. No *l*-ribose *p*-bromophenylhydrazone formed in one hour of

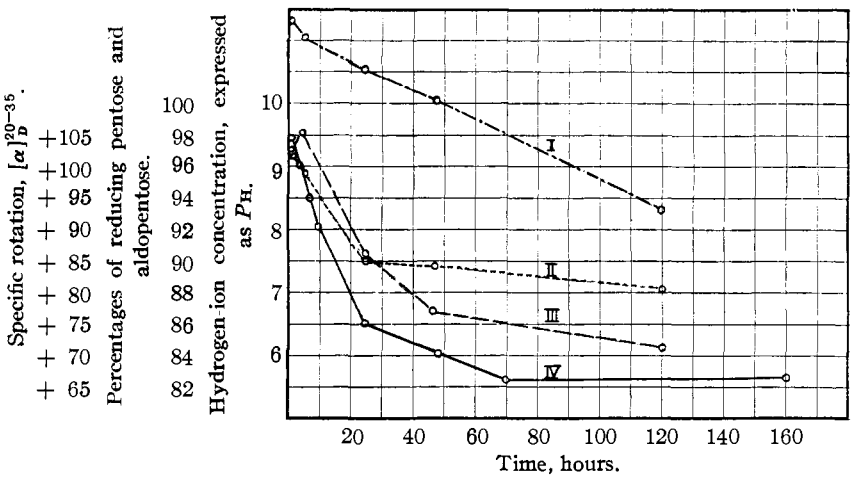


Fig. 2.—Changes in a solution of 37.5 g. of *l*-arabinose in 0.04 *N* calcium hydroxide to 500 cc. at 30–35°: I, change in P_H; II, change in percentage of reducing pentose; III, change in aldopentose; IV, change in specific rotation, $[\alpha]_D^{20-35}$.

standing as described by van Ekenstein and Blanksma[10] so 20 g. of *l*-arabinose in 30 cc. of water was added. The *l*-arabinose *p*-bromophenylhydrazone began to crystallize in two minutes. After one and one-half hours this insoluble hydrazone was filtered off and dried to 30 g., the customary yield from *l*-arabinose.

By the action of calcium hydroxide solution on 80 g. of *l*-arabinose, followed by removal of 26 g. of unchanged *l*-arabinose by crystallization, and purification of residual sirup, there was prepared 16 g. of sirup of $[\alpha]_D^{20}$ +10.1°. This sirup was oxidized by the directions of Hudson and Isbell[11] to form sugar acids of any remaining aldose and the solution freed from benzoate, bromide and silver ions. The solution of about 80 cc. was divided into two equal parts, each containing 3 to 4 g. of aldonic acids by estimate.

[9] Fischer and Piloty, *Ber.*, **24**, 4214 (1891).

[10] Van Ekenstein and Blanksma, *Chem. Centr.*, II, 1562 (1915); *Chem. Weekblad*, **10**, 664 (1913).

[11] Hudson and Isbell, THIS JOURNAL, **51**, 2225 (1929).

One portion was heated with an excess of cadmium hydroxide suspension, according to the directions of Fischer and Piloty,[9] who have described the crystalline cadmium salt of *l*-ribonic acid. The solution was filtered from the excess of base and evaporated to a brown sirup which contained dissolved cadmium, but which has deposited no crystalline salt of *l*-ribonic acid. The second portion of the solution suspected of containing *l*-ribonic acid was evaporated on the steam-bath, after the addition of 5 g. of phenylhydrazine, to a sirup which was heated for one hour longer in an attempt to form the *l*-ribonic acid phenylhydrazide described by Fischer and Piloty.[9] The mass deposited only a brown tarry residue on dilution with water. Attempts to crystallize material from this mass with the use of various solvents have resulted in uniform failure.

The Action of Dilute Alkali on *d*-Arabinose.—By the process of Clark[12] and Ruff,[13] degradation of calcium gluconate with 3% hydrogen peroxide and ferric acetate, 267 g. of pure *d*-arabinose was made with a yield of 11%. The *d*-arabinose showed $[\alpha]_D^{20}$ −103.7°, with m. p. 154–156°. The 267 g. of the sugar was dissolved in saturated calcium hydroxide to the volume of 3780 cc. Readings on a portion of the solution, kept at 30–35°, were $[\alpha]_D^{20-35}$ −100.4° after fifteen minutes, −68.2° after twenty-two hours, −55.1° after seventy hours, and constant at −54.4° after ninety-four hours. The solution was then clarified with carbon and concentrated to 170 cc. of sirup under reduced pressure. This sirup was diluted with 220 cc. of methyl alcohol and, after three days of refrigeration, filtered from 133 g. of *d*-arabinose of $[\alpha]_D^{20}$ −99.5°, m. p. 148–149°. The mother liquor and washes were concentrated to 75 cc., diluted with 250 cc. of methyl alcohol and saturated with 60 cc. of absolute alcohol. Two grams more of *d*-arabinose was crystallized and removed. The filtrate was seeded with *d*-ribose[14] without any crystallization being induced. The solution was held in the refrigerator for several days and did not crystallize. It was then diluted to 500 cc. with methyl alcohol and a 25-cc. portion evaporated under reduced pressure in a tared beaker to a residue of 5.1804 g., indicating that 100 to 105 g. of sirup was produced from the 267 g. of *d*-arabinose by rearrangement. The 5.1804 g. of sirup was dissolved in water to 50 cc. for reading ($[\alpha]_D^{20}$ −6.99°, α = −1.45°, using a 2-dm. tube). Analyses of this solution showed that the sirup contained 74.04% of reducing pentose and 60.32% of aldopentose. A solution of 1.2951 g. of this sample of sirup in 25 cc. of water was saturated with calcium hydroxide and showed $[\alpha]_D^{20-35}$ −7.42° fifteen minutes after saturation, −6.17° twenty-four hours later, and −4.91°, constant, one hundred and forty-four hours after saturation. The reducing pentose had decreased to 67.72% of the sample and the aldopentose to 56.49%.

The remaining larger portion of the solution of 95 to 100 g. of the sirup was evaporated under reduced pressure to a thick sirup of 90 cc. This was thinned with 35 cc. of methyl alcohol and 10 cc. of absolute alcohol and again seeded with *d*-ribose. Beyond the formation of 6 g. more of crystalline *d*-arabinose, no crystallization has occurred in three months.

The Action of Dilute Alkali on *d*-α-Glucoheptose and α-Glucoheptulose.—In order to determine whether the reaction *d*-α-glucoheptose ⟷ *d*-glucoheptulose is reversible in dilute alkali, a 10% solution of *d*-glucoheptulose in saturated calcium hydroxide was made at 30–35°. The $[\alpha]_D^{20-35}$ changed from an initial rotation of $[\alpha]_D^{20}$ +67.4°, the value of the ketose, to +66.9° in three hours, +64.7° in five hours, +55.9° in twenty-two hours, and became constant in one hundred and twenty hours at +45.4°. An iodine estimation of aldoses in this solution showed 23% aldoses, with 77% ketoses. The remainder of the solution was resaturated with alkali and the $[\alpha]_D^{20-35}$ value decreased

[12] Clark, *J. Biol. Chem.*, **31**, 605 (1921).

[13] Ruff, *Ber.*, **32**, 554 (1899).

[14] We are indebted to Mr. F. P. Phelps, U. S. Bureau of Standards, who kindly supplied crystalline *d*-ribose for this use.

further over six days to a new equilibrium rotation of +35.0°. The solution now showed that 42% of the ketose had been transformed to aldose capable of iodine consumption. The balance of 58% of unchanged ketose was shown by difference. These results are compared graphically in Fig. 3 with those published by Austin[5] on the extent of change of *d*-α-glucoheptose in dilute alkali. Taken together the results indicate reversibility of the interconversion between *d*-α-glucoheptose and *d*-glucoheptulose.

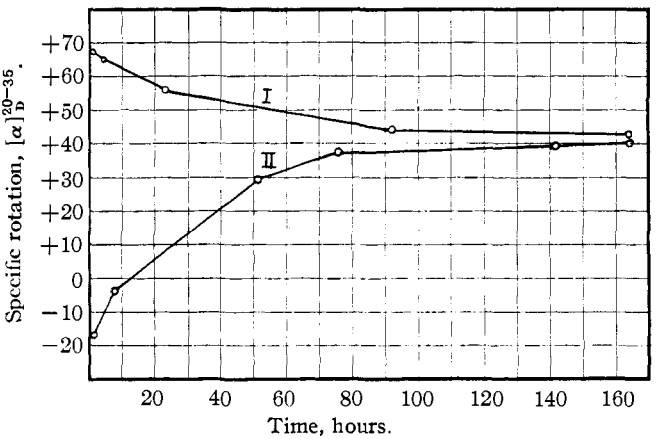


Fig. 3.—Changes in specific rotations of half-molar solutions of *d*-glucoheptulose and *d*-α-glucoheptose in 0.04 *N* calcium hydroxide, at 30–35°: I, *d*-glucoheptulose; II, *d*-α-glucoheptose.

In Table III is shown a summary of the changes observed in these sugars and their products by solution in saturated calcium hydroxide.

TABLE III

SUMMARY OF CHANGES CAUSED BY DILUTE ALKALI AT 30–35°

Substance	$[\alpha]_D^{20-35}$ Initial	$[\alpha]_D^{20-35}$ Final	Percentages of Reducing sugar Initial	Reducing sugar Final	Aldose Initial	Aldose Final
d-Xylose	+ 18.2	+10.0	99.7	91.5	98.5	88.2
Sirup from *d*-xylose	− 0.26	+ 2.1	70.0	46.0	118.0	47.0
l-Arabinose	+ 99.6	+60.0	95.0	86.4	95.0	82.0
Sirup from *l*-arabinose	+ 4.73		79.0		75.0	
d-Arabinose	−100.4	−54.4				
Sirup from *d*-arabinose	− 7.4	− 4.9	74.0	68.0	60.0	56.0
d-α-Glucoheptose	− 20.0	+40.0			99.0	40.0
d-Glucoheptulose	+ 67.5	+45.0 (35)[a]			0.0	23.0 (42.0)[a]

[a] The values shown in parentheses represent further changes observed after resaturation of the equilibrated solution with calcium hydroxide.

Discussion

Assuming that *d*-xylose formed only *d*-lyxose in alkali, it was calculated that the equilibrium mixture contained about 24% of the used *d*-xylose as *d*-lyxose, from a consideration of the rotation of the system and those of the two sugars. By similar assumptions the equilibrium mixture from

l-arabinose was calculated to contain about 37% of the used *l*-arabinose as *l*-ribose. These calculations are proved to be unwarranted by the behavior of the sirups from the two pentoses and by the findings of Gross and Lewis[2d] that polymerized xyloketose is present in the equilibrium mixture from *d*-xylose. A polymerized ketose of the nature described by Gross and Lewis would not be fully detected by the Bertrand copper reduction procedure, calculating results in terms of percentage of used *d*-xylose. The iodine titrations and copper reduction values are subject to the criticism that it is possible that still other substances than aldopentoses and reducing pentoses may have been present in small quantity to react with the reagents and introduce error. Thus Gross and Lewis have isolated the xyloketose in yield of 9.8% of the used *d*-xylose, while our results indicate that only about 5% of the used *d*-xylose was transformed into reducing ketose. Gross and Lewis have confirmed the findings of van Ekenstein and Blanksma[15] that *d*-lyxose is also formed from *d*-xylose by the action of dilute alkali, although the *d*-lyxose was not crystallized as such by either group of investigators. Although Gross and Lewis have employed molar solutions of *d*-xylose for rearrangement as compared with half molar in our experiments, the final rotations and quantitative studies on each system indicate formation of mixtures of the same nature.

The apparently slight degree of reversibility between the pentoses and the sirups produced from them by the action of alkali, and the apparently large degree of reversibility between the *d*-α-glucoheptose and *d*-glucoheptulose, are indications that the composition of the equilibrium mixture is determined to a large extent by the nature of the sugar dissolved in the alkali. Spoehr and Strain[16] have observed that *d*-glucose, *d*-mannose, and *d*-fructose are mutually interconvertible by the action of a weakly alkaline disodium phosphate solution. They have found, however, that the compositions of the equilibrium mixtures are determined by the nature of the sugar dissolved in the weak alkali.

Before it can be concluded that the systems *l*-arabinose $\longleftrightarrow$ *l*-ribose and *d*-xylose $\longleftrightarrow$ *d*-lyxose are not reversible by the action of the solution of calcium hydroxide, further experiments with *l*-ribose and *d*-lyxose as starting sugars are desirable. It is quite possible that these crystalline sugars would exhibit greater reversibility than the sirups made from *d*-arabinose and *d*-xylose have shown.

We have been unable to confirm the findings of van Ekenstein and Blanksma[17] that *l*-arabinose is partially transformed into *l*-ribose in alkaline solution. These workers have heated the *l*-arabinose in normal sodium hydroxide and then oxidized the mixture to *l*-arabonic and *l*-ribonic acids.

[15] Van Ekenstein and Blanksma, *Chem. Weekblad*, 11, 182 (1914).

[16] Spoehr and Strain, *J. Biol. Chem.*, **85**, 370 (1929).

[17] Van Ekenstein and Blanksma, *Chem. Weekblad*, **10**, 213–214 (1913).

The *l*-ribonic acid was separated from the *l*-arabonic acid by fractional crystallization of the mixed phenylhydrazides. We have employed 0.04 *N* calcium hydroxide, removed unchanged *l*-arabinose, oxidized the remaining sirup and attempted to form by their directions the phenylhydrazide of *l*-ribonic acid without success. In the light of our further negative experiments of seeding with *d*-ribose the sirups from the rearrangement of *d*-arabinose, the different findings can at present be best explained as due to differences in the temperatures, nature of the alkali and concentrations.

The authors are pleased to note here the recent findings of Neher and Lewis[18] on changes of a solution of *l*-arabinose in calcium hydroxide. Although they have studied changes in a molar solution of this sugar with respect to rotation and content of aldopentose, while we have measured changes of a half-molar solution with regard to rotation, contents of aldopentose and reducing pentose, and P_H, the results given by the two independent studies are close agreement.

The authors desire to thank Dr. C. S. Hudson for his helpful interest and valuable suggestions in connection with the above studies.

Summary

1. When a half molal solution of *d*-xylose was made in saturated calcium hydroxide at 30–35° the value of the $[\alpha]_D^{20-35}$ changed in twenty-four hours from +18.2° to the constant value of +10.2°. The P_H of the solution decreased more slowly from 10.19 to 6.01 during one month. The percentages of the reducing pentoses and of the aldopentoses decreased slowly from initial values of 99.73 and 97.5 to 91.53 and 88.20 during the month. The sirup prepared from *d*-xylose by the action of the alkali was dissolved again in calcium hydroxide solution and changed slightly from $[\alpha]_D^{20}$ −0.26° to +2.0° in one hundred forty-four hours, indicating very little reversibility toward the equilibrium value obtained from *d*-xylose.

2. When a half-molal solution of *l*-arabinose was made in saturated calcium hydroxide at 30–35°, the value of $[\alpha]_D^{20-35}$ changed in seventy-two hours from +100.0° to the constant value of +62.0°. The P_H of the solution decreased more slowly from the initial value of 10.8 to 5.28 during seventy days. The percentages of the reducing pentoses and of the aldopentoses decreased from beginning values of 94.5 and 95.0 to 86.4 and 82.0 during the seventy days. Sirups prepared from *d*- and *l*-arabinose by the action of the alkali have not been convertible to crystalline ribose, ribose *p*-bromophenylhydrazone, or to crystalline derivatives of ribonic acid (phenylhydrazide or cadmium salt). A sirup prepared from *d*-arabinose by the action of the alkali was dissolved again in calcium hydroxide solution. The $[\alpha]_D^{20-35}$ changed slightly from the initial value of

[18] Neher and Lewis, THIS JOURNAL, **53**, 4411 (1931).

$-7.5°$ to $-5.0°$ during five days, indicating very little reversibility toward the equilibrium value obtained from *d*-arabinose.

3. In contrast to the very small reversibility in the pentose systems, *d*-α-glucoheptose and *d*-glucoheptulose are mutually interconvertible by the action of saturated calcium hydroxide solution to give a common equilibrium value of $[\alpha]_D^{20-35}$ of approximately 45.0°.

CHICAGO, ILLINOIS

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

CERTAIN FACTORS INFLUENCING THE YIELD OF GRIGNARD REAGENTS AND THE RATIO OF R_2Mg TO RMgX

BY GEORGE O. JOHNSON AND HOMER ADKINS

RECEIVED NOVEMBER 16, 1931 PUBLISHED MAY 7, 1932

The ratio of Grignard reagent to hydrocarbon formed in the reaction of magnesium with alkyl halides is in part determined by the presence of compounds other than the two essential components of the reaction mixture. Metallic chlorides have long been known to modify this ratio of Grignard to Wurtz reactions and more recently copper has been shown to exert a similar influence.[1,2] It has sometimes been assumed that the hydrocarbon formation was dependent upon the reaction of the Grignard reagent with some of the alkyl halide which had not yet reacted with magnesium as illustrated in equation 1.

$$RMgX + RX \longrightarrow R_2 + MgX_2 \qquad (1)$$

Equation 1 represents a reaction known to occur, for example, between allylmagnesium bromide and allyl bromide.[3]

It has become increasingly evident that the Grignard reagent in many cases is not exclusively or even predominantly in the form RMgX but rather as R_2Mg, these compounds being in more or less stable combination with MgX_2 and the solvent.[4,5,6,7] Therefore, a possible explanation of the effect of copper in modifying the ratio of the Grignard and Wurtz reactions is that it modifies the ratio of RMgX and R_2Mg, thus increasing the amount of the former available for the reaction represented in equation 1. This explanation of the effect of copper upon the proportion of products would rest on the further assumption that R_2Mg does not react as rapidly, if at all, with RX. The foregoing hypothesis has now been tested.

[1] Johnson and Adkins, THIS JOURNAL, **53**, 1520 (1931).
[2] Gilman and Zoellner, *ibid.*, **53**, 1581 (1931).
[3] Späth, *Monatsh.*, **34**, 1965 (1913).
[4] Schlenk and Schlenk, *Ber.*, **62B**, 920 (1929).
[5] Gilman and Fothergill, THIS JOURNAL, **51**, 3149 (1929).
[6] Noller, *ibid.*, **53**, 635 (1931).
[7] Schlenk, *Ber.*, **64B**, 734 (1931).