[Contribution from the Department of Chemistry of The Ohio State University]

# The Hydrolytic Instability of the Aldonamides

By M. L. Wolfrom, R. B. Bennett and J. D. Crum[1]

Received September 20, 1957

The aldonamides are unstable in dilute aqueous solution at room temperature. When properly purified, they may show an apparent stability for many hours but eventually they will exhibit an abrupt polarimetric change. This change is catalyzed by acids and bases, and especially by bases; it also appears to be catalyzed by traces of metals (or metallic oxides). The product of the reaction is the ammonium salt of the aldonic acid. Specific data are given for the amides of D-galactonic, D-gluconic, L-mannonic and D-ribonic acids.

In the field of carbohydrate chemistry the aldonamides have been extensively used as intermediates, particularly in the synthesis of the higher ketoses.[2] In a recent report on the synthesis of L-mannoheptulose, the hydrolytic instability, at room temperature, of an aqueous solution of L-mannonamide was recorded.[3] This is in contrast to the more drastic hydroxyl or hydronium ion catalysis employed for the hydrolysis of the amides of the simple carboxylic acids. Although Kiliani[4] prepared the first carbohydrate amide, L-mannonamide, in 1886, it was not until 1918 that Weerman[5] prepared a considerable number of the aldonamides. He noted a change in specific rotation with time for some of them and attributed this change to the hydrolysis of the amide to the ammonium salt. However, no rotation data or isolation of the ammonium salt was reported to substantiate this conclusion. Irvine and co-workers[6] had previously prepared D-gluconamide in crude form along with ammonium D-gluconate, but no indication of the hydrolytic instability was reported. Hudson and Komatsu[7] re-examined Weerman's work and as a result of this study, Hudson[8] formulated his amide rule of rotation. Hudson and Komatsu did not note any hydrolytic instability of these amides. Glattfeld and Macmillan,[9] in the development of the amide synthesis utilizing liquid ammonia, prepared numerous aldonic and saccharinic acid amides, but no hydrolytic data were recorded. Renfrew and Cretcher[10] reported that an aqueous solution of D-talonamide shows a change of rotation from $[\alpha]_D$ $-13.1°$ to a slightly dextrorotatory value after several days. The ammonium salt was prepared and showed $[\alpha]_D$ $+2.9°$, but no data were advanced to show the identity of the ammonium salt to the final hydrolytic product of the amide.

We report herein the results of an investigation to determine the extent to which a number of aldonamides undergo hydrolysis with time and to determine some of the factors affecting the rate of this hydrolysis as well as the nature of the final hydrolytic product.

The aldonamides employed were purified by recrystallization from di-*O*-methyl-1,2-ethanediol (Methyl Cellosolve) as recommended by Hockett.[11] It was remarkable that these purified aldonamides, with the exception of D-gluconamide, exhibited a stable rotation in dilute aqueous solution at 25° for several hours. This is well illustrated for the case of D-ribonamide, Fig. 1, where this period of arrest persisted for 17 hours and then suddenly the downward rotation change was initiated. As might be expected, such a curve probably involves some type of accidental catalysis and is therefore generally difficult to reproduce in detail, as the data of Fig. 2 for L-mannonamide demonstrate. Figure 3 shows two curves for D-gluconamide, the lower of which was run in once-distilled water and the upper in demineralized and doubly-distilled water. The latter was a little slower, but the difference between the two is not great. When an aqueous solution of D-galactonamide was observed in a metal polarimeter tube (Fig. 4, curve C), no period of arrest was found and the downward rotation change was rapid. This is in accord with previous experience in observing sugar mutarotations in metal tubes.[12] The presence of these initial plateaus may account for the fact that the hydrolytic instability of the aldonamides was not remarked upon by Hudson and Komatsu[7] nor by Hockett and associates.[11]

That the final product of the reaction, which the polarimetric curve delineated, was solely the ammonium salt, was established for the case of D-gluconamide by isolation techniques.

In the case of D-galactonamide (Fig. 4), the period of arrest was established and then sufficient 0.2 *N* ammonium hydroxide was added to make the resultant solution 0.008 *N* in ammonium hydroxide. The resultant curve (Fig. 4, curve D) had a steeper slope than the control in water (curve B). An even steeper slope (curve E) was found on the addition of an equivalent amount of sodium hydroxide. Like results were obtained with D-gluconamide and sodium hydroxide (Fig. 5, curves B and C), although in this structure no period of arrest could be established. The addition of an equivalent amount of hydrochloric acid (curves A of Figs. 4 and 5) had a dramatic effect in slowing down the reaction but not in stopping it (see especially curve A of Fig. 4). The amide alone undoubtedly exerts a somewhat basic effect

---

[1] Charles F. Kettering Research Foundation Fellow, 1957–1958.

[2] M. L. Wolfrom, J. M. Berkebile and A. Thompson, This Journal, **71**, 2360 (1949); M. L. Wolfrom and P. W. Cooper, *ibid.*, **71**, 2668 (1949).

[3] M. L. Wolfrom and H. B. Wood, *ibid.*, **73**, 730 (1951).

[4] H. Kiliani, *Ber.*, **19**, 3029 (1886).

[5] R. A. Weerman, *Rec. trav. chim.*, **37**, 16 (1918).

[6] J. C. Irvine, R. F. Thomson and C. S. Garrett, *J. Chem. Soc.*, **103**, 238 (1913).

[7] C. S. Hudson and S. Komatsu, This Journal, **41**, 1141 (1919).

[8] C. S. Hudson, *ibid.*, **40**, 813 (1918).

[9] J. W. E. Glattfeld and D. Macmillan, *ibid.*, **56**, 2481 (1934).

[10] Alice G. Renfrew and L. H. Cretcher, *ibid.*, **54**, 4402 (1932).

[11] R. C. Hockett, J. B. Ames, H. A. Hill and A. Scattergood, *Abstracts Papers Am. Chem. Soc.*, **114**, 3Q (1948); R. C. Hockett, private communication.

[12] F. J. Bates and Associates, "Polarimetry, Saccharimetry and the Sugars," Natl. Bur. Standards Circular C440, 1942, p. 451.

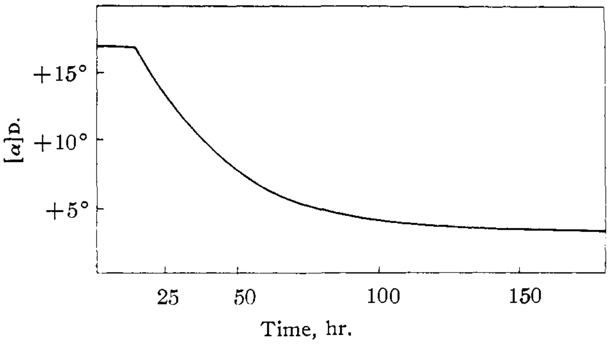


Fig. 1.—Hydrolytic mutarotation of D-ribonamide at 25° in water (*c* 3.0).

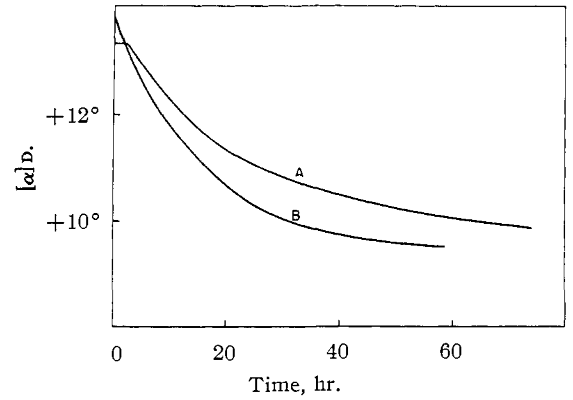


Fig. 2.—Hydrolytic mutarotation of L-mannonamide at 25° in water (*c* 1.0); "duplicate" runs.

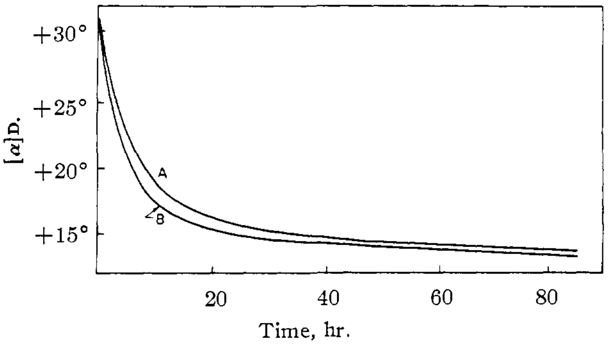


Fig. 3.—Hydrolytic mutarotation of D-gluconamide at 25° in water (*c* 3.0); A, demineralized and doubly-distilled water; B, ordinary distilled water.

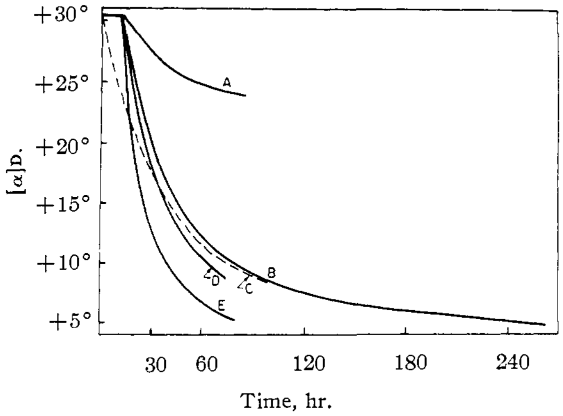
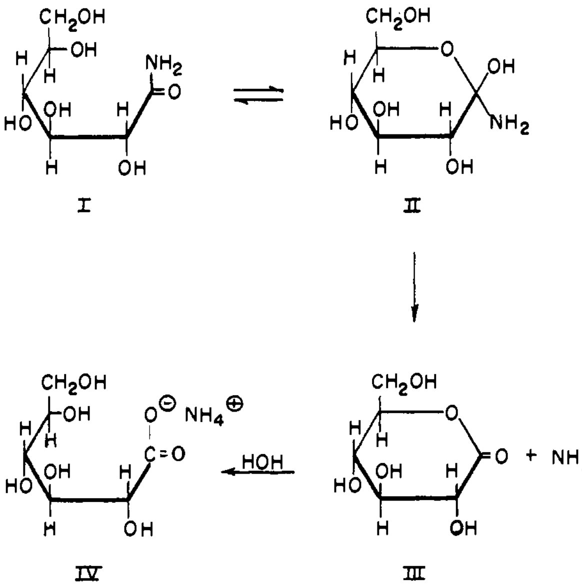


Fig. 4.—Hydrolytic mutarotation of D-galactonamide at 25° in water; C, metal polarimeter tube, *c* 3.0; B, glass polarimeter tube. After plateau was established in water (*c* 1.9); A, HCl added to make 0.008 *N*; D, $NH_4OH$ added to make 0.008 *N*; E, NaOH added to make 0.008 *N*.

in water which the acid neutralizes. Amide hydrolysis is known to be acid-base catalyzed but, as usual, the effect of bases is very much greater (40,000 times[13] in sugar mutarotation at 25°) than that of acids. The *p*H values of these solutions dropped during the course of the reaction and the data were therefore not amenable to kinetic evaluation.

The amides of the simple carboxylic acids, as acetamide, are not as readily hydrolyzed as are the aldonamides. Therefore the presence of hydroxyl groups in the latter would seem to be the accelerating factor. A postulated course of reaction is shown below as illustrated for D-gluconamide (I).



The intermediate II is that commonly proposed for general amide hydrolysis.[14] Interaction with the C5-hydroxyl to form the 1,5-lactone III, immediately unstable in the presence of ammonia,[15] would be a reasonable course for the formation of the final ammonium salt IV established by experiment. In the cyanohydrin reaction as applied to the aldoses, the nitrogen functions are hydrolyzed slowly under basic catalysis. The slow reaction must then be due to hydrolysis of the hydroxynitriles formed, which process could be further complicated by the known isomerism[16] of the aldonitrile function.

(13) C. S. Hudson, THIS JOURNAL, **29**, 1572 (1907). T. M. Lowry and G. F. Smith, "Mutarotation," Rapports sur les Hydrates de Carbone (Glucides), Dixieme Conférence de l'Union Internationale de Chimie, Liége, 1930, p. 106.

(14) M. L. Bender, R. D. Ginger and K. C. Kemp, *ibid.*, **76**, 3350 (1954); M. L. Bender and R. D. Ginger, *ibid.*, **77**, 348 (1955).

(15) P. A. Levene and H. S. Simms, *J. Biol. Chem.*, **65**, 31 (1925).

(16) P. E. Papadakis and H. J. Cohen, THIS JOURNAL, **60**, 765 (1938); P. E. Papadakis, *ibid.*, **64**, 1950 (1942); J. O. Deferrari and V. Deulofeu, *J. Org. Chem.*, **22**, 802 (1957).

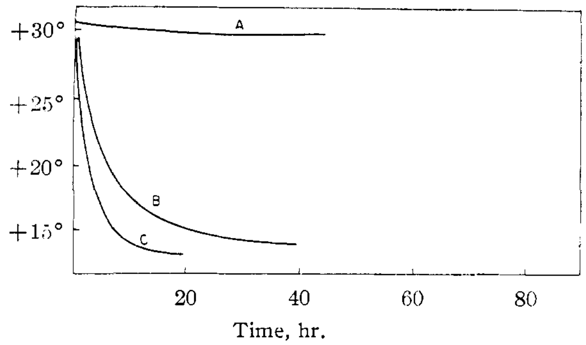


Fig. 5.—Hydrolytic mutarotation of D-gluconamide at 25° ($c$ 3); A, 0.008 $N$ HCl; B, water; C, 0.008 $N$ NaOH.

## Experimental

**Aldonamides.**—These were prepared from the lactones by reaction with liquid ammonia followed by solvent evaporation[9] or by reaction with concentrated ammonium hydroxide (sp. gr. 0.880) with subsequent precipitation by ethanol.[17] They were purified by recrystallization from di-$O$-methyl-1,2-ethanediol (Methyl Cellosolve) as recommended by Hockett.[11] The constants determined were: D-galactonamide, m.p. 170–171° dec., $[\alpha]^{25}\mathrm{D}$ + 30.6°; D-gluconamide, m.p. 142–143°, $[\alpha]^{25}\mathrm{D}$ +31.4°; L-mannonamide, m.p. 170–171° dec., $[\alpha]^{25}\mathrm{D}$ +13.8°; D-ribonamide, m.p. 136–137°, $[\alpha]^{25}\mathrm{D}$ +17°. The rotations were determined in aqueous solution ($c$ 3, $c$ 1 for L-mannonamide) and were extrapolated to initial time where required.

**Identification of Ammonium D-Gluconate as a Hydrolytic Product of D-Gluconamide.**—D-Gluconamide (1.500 g.) was dissolved in water and the volume adjusted to 50.00 ml. The solution was transferred to a 4-dm. glass polarimeter tube and the rotation followed until it became constant (+30.7 → +13.8°, 80 hr.). The solution was removed from the polarimeter tube and evaporated to dryness under reduced pressure. Recrystallization of the crystalline residue from 95% ethanol gave a quantitative yield of a white crystalline solid, m.p. 153–154°, $[\alpha]^{25}\mathrm{D}$ +11.8° ($c$ 3, water). Comparison of this compound with authentic ammonium D-gluconate, $[\alpha]^{25}\mathrm{D}$ +11.2° ($c$ 3, water), by melting point, melting point on admixture, and X-ray powder diffraction pattern showed them to be identical; X-ray powder diffraction data[18]: 8.92m, 5.10s(3,3), 4.88m, 4.66m, 4.44s(3,3), 3.85s(1,1), 3.34s(1,1), 3.21m, 3.11m, 2.91m, 2.56w, 2.51w, 2.43w, 2.30w.

**Mutarotation Data.**—The mutarotations were determined in 4-dm. or 6-dm. glass polarimeter tubes, unless otherwise noted. The data obtained are recorded in Figs. 1–5. The smooth curves shown were established by many points accurately determined by polarimetry; the complete data are on record.[19] The $p$H values of the solutions dropped during the rotation change.

---

[17] J. W. W. Morgan and M. L. Wolfrom, THIS JOURNAL, **78**, 1897 (1956).

[18] Interplanar spacings, Å., λ 1.5418 Å., and relative intensities, estimated visually: s, strong; m, medium; w, weak; first three strongest lines noted, (1) strongest, (1,1) about equal.

[19] R. B. Bennett, M. Sc. Thesis (M. L. Wolfrom, preceptor), The Ohio State University, 1955.

COLUMBUS 10, OHIO

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

# The Controlled Thermal Decomposition of Cellulose Nitrate. III[1,2]

BY M. L. WOLFROM, ALAN CHANEY AND P. MCWAIN

RECEIVED SEPTEMBER 23, 1957

The presence of α-hydroxynitriles among the reduced pressure ignition products of cellulose nitrate has been established. The absence of other non-gaseous nitrogenous substances has been demonstrated. The previously reported yield data for carbonyl compounds has been shown to be slightly low as the result of α-hydroxynitrile formation which occurred under the prevailing acidic conditions before the earlier analyses were carried out. Determination of the yield of carbon monoxide under the ignition conditions employed indicates an over-all carbon recovery (all identified products) from cellulose nitrate of 88%; unidentified carbonyl compounds presumably account for the remainder. Acetic acid (and possibly ethanol) are the only ignition products found which can be ascribed to traces of the residual ethyl acetate casting solvent in the cellulose nitrate sheets; cellulose nitrate is the sole precursor of all of the other substances identified. Reignition, at 200 mm. pressure, of the solid oxycellulose nitrate of a low degree of polymerization, obtained by the ignition of cellulose nitrate at 2 mm. pressure, afforded formaldehyde, glyoxal and formic acid in amounts closely agreeing with those predictable as arising from a cellulose nitrate of like nitrogen (9.5%) content. These results are employed to interpret further the nature of cellulose nitrate ignition.

The previous communications in this series have described the ignition of cellulose nitrate under reduced pressure. At the lowest pressures investigated, a white fragmented oxycellulose nitrate was isolated in good yield.[3] The yield of this material decreased rapidly with increasing pressure and the easily condensable product was collected as a red-orange liquid. After dilution of this liquid with water, the amounts of the major organic components (formic acid, glyoxal, formaldehyde and hydrogen cyanide )were determined.[2] Of these components, hydrogen cyanide is the product concerning which the least has been reported and whose formation is least explicable by the postulated[2] reaction sequences. Suggestions were made[2] concerning the role of the fragmented oxycellulose nitrate in the formation of the small organic molecules from cellulose nitrate. Further evidence concerning these matters has been obtained and is reported herein.

## Experimental

**Apparatus for the Ignition of Cellulose Nitrate.**—The ignition apparatus previously described[3] for the preparation of the solid fragmented oxycellulose nitrate was modified by the attachment of a 50/30 standard glass semi-ball inner-joint at the large end of the combustion tube and the rubber

---

[1] This work was performed under contracts DA-33-019-ord-2025 (Aberdeen Proving Ground) and DA-33-019-ord-2042 (Office of Ordnance Research) between the U. S. Army Ordnance Corps (technical supervising agency, Ballistic Research Laboratories of Aberdeen Proving Ground) and The Ohio State University Research Foundation (Projects 675 and 679). Preliminary communication: *Abstracts Papers Am. Chem. Soc.*, **132**, 16D (1957).

[2] Previous communication: M. L. Wolfrom, J. H. Frazer, L. P. Kuhn, E. E. Dickey, S. M. Olin, R. S. Bower, G. G. Maher, J. D. Murdock, A. Chaney and Eloise Carpenter, THIS JOURNAL, **78**, 4695 (1956).

[3] M. L. Wolfrom, J. H. Frazer, L. P. Kuhn, E. E. Dickey, S. M. Olin, D. O. Hoffman, R. S. Bower, A. Chaney, Eloise Carpenter and P. McWain, *ibid.*, **77**, 6573 (1955).