

15. The ratio of ketone to alcohol was estimated by means of the refractive indices and by the comparison of the weight of 2,4-dinitrophenylhydrazone obtained from a sample of the mixture and from a sample of the pure ketone. The ketone (13 g.) was obtained distilling 138.5–140° (11 mm.) while the alcohol came over at 144–145° (11 mm.).

21. The basic and neutral compounds were separated from each other before fractionation. 3-Carbethoxy-2,4-dimethylpyrrole, b. p. 150–155° (7 mm.), was identified by a mixed melting point, 75–76°. 1-Ethyl-2,3,4-trimethylpyrrolidine was characterized by its neutral equivalent and nitrogen analysis. 1-Ethyl-3-carbethoxy-2,4-dimethylpyrrolidine gave a neut. equiv. of 198 (calcd. 199). The pyrrolidone fraction showed an analysis for carbon, hydrogen and nitrogen intermediate between the two compounds of formulas XIX and XX. Upon hydrogenation over copper chromite at 260° two moles of hydrogen (per average molecular weight) were taken up and a 40% yield of a mixture of pyrrolidines (b. p. 150–155°) was obtained which showed a neutral equivalent intermediate between the two pyrrolidines which would be produced by the hydrogenation of pyrrolidones of the structures XIX and XX.

22. The "carbethoxypyrrolidine" fraction boiled at 81–89° (7 mm.).

23. In order to obtain pure 1-ethyl-3-carbethoxy-2,4-dimethylpyrrolidine it was necessary to separate a small amount of a non-basic component in the fraction b. p. 86–89° (7 mm.).

24. The unchanged pyrrole in the residue from fractionation was obtained by crystallization from 70% ethanol.

25. 1-Ethyl-2-hydroxymethylpyrrolidine (b. p. 75–81° at 11 mm.) showed a neut. equiv. of 130 (calcd. 129) and its boiling point and refractive index were approximately in agreement with the values given by Signaigo.¹

Summary

It has been demonstrated in nine instances that the substitution of a carbethoxy group on the nitrogen of a pyrrole lowers the temperature required for the hydrogenation of the nucleus, thus making it possible to hydrogenate the pyrrole ring in preference to a carbonyl or carbethoxy group. This fact has made it possible to prepare five carbethoxy, two acetyl and three α -hydroxyethylpyrrolidines from acetyl or carbethoxy pyrroles. Methyl and ethyl groups on the nitrogen were relatively ineffective in lowering the temperature of hydrogenation of the ring. A benzoyl group on the nitrogen was in two of three cases so readily removed by hydrogenolysis that it was ineffective in facilitating the hydrogenation of the pyrrole nucleus.

In only one instance has it been possible to prepare a carbethoxypyrrolidine by the direct hydrogenation of a carbethoxypyrrole having a hydrogen on the nitrogen. In only one instance has it been possible to prepare a hydroxymethylpyrrolidine by the hydrogenation of a carbethoxypyrrole, the normal reaction being the reduction of the carbethoxy to a methyl group. The hydrogenation of a carbethoxy to a hydroxymethyl group in a pyrrolidine was carried out successfully.

Directions have been given for the preparation of a number of pyrroles, particularly those having a substituent on the nitrogen, and for the hydrolysis of N-carbethoxypyrrolidines.

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[CONTRIBUTION FROM THE INSTITUTO DE FISILOGIA, FACULTAD DE MEDICINA, BUENOS AIRES]

Acetylated Amides of Aldonic Acids

BY V. DEULOFEU AND E. RESTELLI DE LABRIOLA

Acetylated amides of aldonic acids were first prepared by Zemplén and Kiss,¹ who employed two different methods: (a) acetylation of the amide, (b) hydrolysis of the acetylated nitriles.

With the exception of the work of Miksic² in 1926 no other papers were published on those substances to this year, when almost simultaneously Hurd and Sowden,³ Zemplén, Balassa and Gardonyi,⁴ and Robbins and Upson⁵ published their

work on the preparation of the acetylated amides of aldonic acids. The first two groups of workers employed hydrolysis of the nitriles as a method of preparation; Robbins and Upson the acetylation of the amide with acetic anhydride and zinc chloride.

We were also engaged from the end of 1937 with the preparation of those substances by the acetylation of the amides with pyridine-acetic anhydride, a method that we have found very suitable for this work, as can be seen from our data in the experimental part, and in agreement with the findings of Robbins and Upson. Of course our work overlaps

(1) Zemplén and Kiss, *Ber.*, **60**, 165 (1925).

(2) Miksic, *Vestn. Kral. Ces. Spol. Nauk. Cl.*, **11**, 18 (1926); *from C. A.*, **23**, 2941 (1929).

(3) Hurd and Sowden, *THIS JOURNAL*, **60**, 235 (1938).

(4) Zemplén, Balassa and Gardonyi, *Ber.*, **71**, 768 (1938).

(5) Robbins and Upson, *THIS JOURNAL*, **60**, 1788 (1938).

most of that done by the three groups of workers named.

We also tried the hydrolysis of the acetylated nitriles of *l*-rhammonic and *d*-mannonic acids, and only in the first case were able to obtain a little quantity of the acetylated amide in crystalline form. As other authors^{1,3,4} have obtained good yields with that method, it follows that these are dependent on the nature of the sugar acid. By acetylation uniform results are obtained in every case, and if the lactone and amide are easy to obtain it is a very convenient method. Undoubtedly with some sugars the preparation by the way aldose oxime \rightarrow acetylated nitrile \rightarrow acetylated amide will be found easier by the facility of carrying out the reactions.

If one compares the change in rotation produced by the transformation of an acetylated nitrile into an acetylated amide, one can see that with the exception of *l*-rhammonic amide a diminution of the absolute value of the rotation is produced. If the nitrile has a low value of rotation (arabonic, mannonic) the amide has an opposite sign of rotation, a change that can be interpreted also as a diminution of the rotation of the nitrile.

| | Nitrile | Amide |
|--|---------|--------|
| <i>d</i> -Xylopic ⁶ | +50.3° | + 8.2° |
| <i>d</i> -Gluconic | +48.3° | +23° |
| <i>d</i> -Galactonic ⁷ | +43.2° | +26.4° |
| <i>d</i> - α -Glucosheptonic ¹ | +24.6° | +17.4° |
| <i>l</i> -Arabonic ⁷ | + 3.4° | -25.3° |
| <i>d</i> -Mannonic ⁸ | - 1.8° | +38.7° |
| <i>l</i> -Rhammonic ⁹ | - 4.5° | -48.8° |

The exceptional position of the pair, acetylated rhammonic nitrile-rhammonic amide, where the transformation of the nitrile into amide is accompanied by an augmentation of the absolute value of the rotatory power, is of interest because the rhammonic nitrile is also the only exception to a rule formulated by one of us⁶ that acetylated nitriles having an acetoxy group on the right of carbon 2 rotate to the right.

Experimental

Each gram of the aldonic amide was treated with 7 ml. of a mixture (1:1) of pyridine and acetic anhydride and gently heated to dissolution. After twenty-four hours at

(6) Deulofeu, *Nature*, **131** 548 (1933).

(7) Deulofeu, Wolfrom, Cattaneo, Christman and Georges, *THIS JOURNAL*, **55**, 3488 (1933).

(8) Wolfrom and Thompson, *ibid.*, **53**, 622 (1931).

(9) Deulofeu, Cattaneo and Mendivelzua, *J. Chem. Soc.*, 147 (1934).

room temperature the clear solution was evaporated to dryness in vacuum at low temperature (30-35°). Usually the acetylated amide crystallizes out, but if a sirup is obtained by treating it with a little alcohol or alcohol-ether and evaporating again it crystallizes easily. Yields are good (75-90%). These substances are very soluble in chloroform, less so in ether and alcohol.

Tetraacetyl-*l*-arabonamide.—Recrystallization from alcohol gave fine needles melting at 123°; (α)²⁴_D -25.3° (*c*, 4.282 in CHCl₃; 2 dm.).³

Anal. Calcd. for C₁₈H₁₉O₉N: CH₃CO, 51.65. Found: CH₃CO, 51.66.

Tetraacetyl-*d*-xylopicamide.—Recrystallized from alcohol, prisms melting at 112°, (α)²⁰_D +8.1 (*c*, 4.276 in CHCl₃; 2 dm.).³

Tetraacetyl-*l*-rhammonicamide.—This amide is very soluble in alcohol and was better recrystallized by dissolution in ether and precipitation with petroleum ether; long needles melting at 115°; (α)²⁰_D -48.8° (*c*, 1.4915 in CHCl₃; 1.894 dm.).

Anal. Calcd. for C₁₄H₂₁O₉N: N, 4.03. Found: N, 4.16.

This substance was also obtained, but with a very low yield, by hydrolysis of the tetraacetyl-*l*-rhammonitrile, with a solution of bromohydric acid in acetic acid, as indicated by Zemplén and Kiss.¹ No crystals were obtained when the hydrolyzing solution was poured into water. This was extracted with chloroform, the chloroform evaporated and the resulting sirup treated with alcohol and the evaporation repeated. Crystals were obtained that after recrystallization from ether-petroleum ether gave a melting point of 115° and were identical with those described above.

Pentaacetyl-*d*-mannonicamide.—Very soluble in alcohol, was also crystallized by dissolution in ether and addition of petroleum ether; long prisms melting at 112-113°, (α)²⁰_D +39.1° (*c*, 4.923 in CHCl₃, 2 dm.).⁵

Anal. Calcd. for C₁₆H₂₃O₁₁N: N, 3.45. Found: N, 3.40.

Attempts to obtain the acetylated amide by hydrolysis of the nitrile failed. The obtained sirup could not be induced to crystallize.

Pentaacetyl-*d*-galactonicamide.—From alcohol, as hexagonal plates melting at 166°; (α)²⁵_D +26.4 (*c*, 1.1912 in CHCl₃; 2 dm.).³⁻⁵

Anal. Calcd. for C₁₆H₂₃O₁₁N: N, 3.45. Found: N, 3.65.

Summary

A method has been studied for the direct acetylation of the amides of aldonic acids that can be employed in cases where the hydrolysis of the acetylated nitriles fails or gives low yields.

A comparison of the rotatory power of the acetylated amides of the aldonic acids and the corresponding nitriles has been made.

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