isoxazolone-5. Minunni obtained 3-phenylisoxazolone-5 from 3-phenyl-4-benzylidene-isoxazolone-5, but he considered it to be alpha-aminocinnamolactone, a compound which would have the same empirical formula.

Reaction with Phenylhydrazine.—The salt was prepared directly from 3-phenylisoxazolone and phenylhydrazine by the method described by Uhlenhuth.[8] It can be recrystallized in the form of white flakes from methanol; it melts with decomposition to a red liquid at 153–154°. The yield was quantitative. It easily reduced Fehling's solution, showing it to be a phenylhydrazine salt and not a phenylhydrazone. The same salt (plus the corresponding aldehyde phenylhydrazone) was obtained by mixing warm methanol solutions of 3-phenyl-4-benzylidene-isoxazolone-5 (1 mole) and phenylhydrazine (2 moles); the same was done with 3-phenyl-4-anisylidene-isoxazolone-5. The aldehyde phenylhydrazones were separated from the salt in each case by taking advantage of the greater solubility of the former in warm benzene. Mixed melting points showed no depression, and salts from the varying sources showed identical analyses.

Anal. Calcd. for $C_{15}H_{15}O_2N_3$: N, 15.61. Found: N, 15.52, 15.76.

When 3-methyl-4-benzylidene-isoxazolone-5 was treated as above, a 50% yield of compound II was obtained, plus benzaldehyde phenylhydrazone.

Preparation of Dimethyl-diisoxazolone.—The method of Hantzsch[9] was employed using 65.0 g. acetoacetic of ester. On recrystallization from ethanol a 33% yield (17.1 g.) of white flakes was obtained. It melts with decomposition to a red liquid at 168–169° (corr.).

Anal. Calcd. for $C_8H_8O_3N_2$: N, 15.56. Found: N, 15.58, 15.58.

Summary

1. It is shown that aromatic aldoximes and beta keto esters react in the presence of acids to form arylidene isoxazolones, and not arylidene amino lactones as previously reported.[2–4]

2. The action of phenylhydrazine and of an alkaline hydrolytic agent has been studied, and the earlier work has been corrected and extended.

3. The optimum conditions for condensation have been found. The probable mechanism of the reaction is discussed. It has been found that reaction occurs in the presence of strong acids in general.

4. An unsuccessful attempt was made to extend the reaction to aliphatic and alicyclic aldoxime and ketoximes. Acetone oxime did condense, however.

5. It is shown that the compound reported as 3-methylisoxazolone-5 in the literature has actually never been prepared. The product reported as such was actually dimethyldiisoxazolone. Its structure is demonstrated.

NEW HAVEN, CONN. RECEIVED MARCH 27, 1937

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

Two Forms of Anhydrous *l*-Rhamnose and a New Method for the Preparation of Crystalline β-Tetraacetyl-*l*-rhamnose[1]

BY ERNEST L. JACKSON AND C. S. HUDSON

l-Rhamnose usually crystallizes as a monohydrate of its α-modification having an initial specific rotation in water of −7.7°, which becomes constant at +8.9° after mutarotation is complete. This form is usually regarded as the configurational analog of α-*d*-mannose of initial rotation +30°, its final value being +14°. In 1895 Emil Fischer[2] crystallized a new form of rhamnose, anhydrous crystals of initial rotation about +31° which is regarded as β-rhamnose, the analog of β-*d*-mannose of initial rotation −17°. Minsaas[3] on repeating Fischer's preparation recently found "about +44°" as the initial rotation, and mentioned that the yield of this anhydrous form is small. We also had been engaged in studying this form and in devising methods for obtaining it in higher yields; our β-rhamnose showed +38° as the initial specific rotation.[4] After the publication of Minsaas' article we repeated our work and again obtained +38° for crystals which by appearance seemed to be of one form only. In the course of the preparation of these β-rhamnose crystals another anhydrous form of quite different crystalline appearance frequently separated. This third form of the sugar shows an initial rotation of about +14°, mutarotating in water at the

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[1] Publication authorized by the Surgeon General, U. S. Public Health Service. Presented before the Division of Organic Chemistry, at the Pittsburgh meeting of the American Chemical Society, Sept. 7–11, 1936.

[2] Fischer, *Ber.*, **28**, 1162 (1895); **29**, 324 (1896); Tanret, *Compt. rend.*, **122**, 86 (1896); Purdie and Young, *J. Chem. Soc.*, **89**, 1194 (1906).

[3] Minsaas, *Kgl. Norske Videnskab. Selskabs Forh.*, **6**, 177 (1933); *Chem. Zentr.*, **105**, I, 2738 (1934).

[4] Except where otherwise specified, all rotations in this article are specific rotations at 20° for sodium light.

same rate as the two other forms to the equilibrium value +8.9°. It is apparently a true chemical individual in the crystalline state. Its formula, on the assumption that its components are the known α- and β-forms, is α,β-rhamnose if the rotation of β-rhamnose is +38° (our value), or 3α,2β-rhamnose if the rotation of β-rhamnose is +44° (Minsaas' value). This is the second sugar for which a molecular combination of α- and β-forms in the crystalline state has been found; the other sugar, α,β-lactose, has been described by Hockett and Hudson.[5]

For a long period of years it was not possible to obtain a crystalline tetraacetate of rhamnose. In 1920 Fischer, Bergmann and Rabe[6] showed that crystalline β-tetraacetylrhamnose can be prepared in an indirect way through acetobromorhamnose. It is now shown that the acetylation of β-rhamnose with acetic anhydride and pyridine at low temperature gives a high yield (about 90%) of this crystalline β-tetraacetate. Since β-rhamnose may now be prepared in 85–90% yield from ordinary α-rhamnose hydrate, the present directions furnish the best way of obtaining the crystalline β-tetraacetate. The similar acetylation of α,β-rhamnose gives, besides a sirup, a 43% yield of the β-tetraacetate, which confirms the presence of the β-sugar as one component; the other constituent is presumably α-rhamnose, the tetraacetate of which is known only as a sirup.

Experimental

Dehydration of Rhamnose Monohydrate with Barium Monoxide.—A solution of 50 g. of pure rhamnose hydrate in 2 liters of pure acetone was refluxed with 100 g. of barium monoxide for two hours with exclusion of atmospheric moisture, the barium oxide was filtered off and the drying was repeated with fresh barium monoxide for three and one-half hours. The filtered solution, concentrated to about 700 cc. and kept overnight at 25°, deposited long prismatic needles (32.5 g.); the yield was increased to 40.3 g. (90%) by further concentration of the mother liquor. The crops rotated +8.5 to +10.3° (three minutes) in water and +8.9° (constant). On recrystallization from acetone, which had been dried by refluxing over barium monoxide, the initial rotation increased to an approximately constant value. In the course of three successive recrystallizations and drying in an evacuated desiccator over calcium chloride, the extrapolated initial rotation in water was respectively +13.2, +14.2 and +14.6°. The crystals from each recrystallization were characteristic long primatic needles with m. p. 112.5–113.5° (corr.) and rotation +8.9° (constant) in water.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.88; H, 7.37. Found:[7] C, 44.18, 44.13; H, 7.44, 7.36.

These crystals of α,β-rhamnose, from their appearance and repeated preparation with the same physical constants, might be mistaken for a homogeneous crystalline isomer of the sugar. Tanret[8] obtained crystals ($[\alpha]_D$ +10.1°) which may be the same as those here described; if so, he was mistaken in their identification, as is now generally recognized, since he considered his product to be anhydrous β-rhamnose.

Dehydration with Absolute Ethanol.—A solution of 10 g. of pure rhamnose hydrate in 25 cc. of absolute ethanol was concentrated on the steam-bath to a sirup. After repeating the process the sirup was crystallized by stirring it with 25 cc. of cold dry acetone, the solvent was evaporated on the steam-bath and the crystals were boiled thrice with 10-cc. portions of dry acetone. Recrystallization from 250 cc. of dry acetone gave long prismatic needles (4 g.) showing the extrapolated initial rotation +14.4° in water and +9.0° (constant); m. p. 112.5–113.5° (corr.). Concentration of the mother liquor increased the yield to 7.7 g. (85%).

After seeds of the two forms of anhydrous sugar were available, either form could be prepared by seeding the acetone solution of the crude dry sugar with the appropriate crystals.

β-Rhamnose.—The conversion of crystals of the lower rotating form (+14°) into the β-sugar was accomplished by adding some crystals of the β-form (fine needles) to an acetone solution from which a considerable quantity of long prismatic needles had separated, and keeping it tightly stoppered at 20° for several weeks when the prismatic needles had changed to clusters of fine needles showing an initial rotation of +37.9° in water. The conversion was effected more rapidly[9] by seeding the acetone solution of the lower rotating form with crystals of β-sugar. Samples of β-rhamnose for analysis and mutarotation were recrystallized twice from dry acetone and dried in a high vacuum at 76° in the presence of phosphorus pentoxide; m. p. 123.5–124.5° (corr.); extrapolated initial rotation +38.4° ($k_1 + k_2 = 0.045$ in minutes and decimal logarithms) in water at 20 ± 0.5° (*c*, 2.24).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.88; H, 7.37. Found:[10] C, 44.09; H, 7.19.

Acetylation.—To a mixture of 8 cc. of acetic anhydride and 8 cc. of pyridine at −12° was added 1.6 g. of powdered β-rhamnose of initial rotation +37.7°. It was shaken at −12° until the sugar dissolved, kept overnight at 0° and poured into 150 cc. of ice and water. After partial neutralization of the solution with sodium bicarbonate, the tetraacetate, which crystallized readily, was filtered off, washed with ice water and dried at 25° *in vacuo* over calcium chloride; weight 2.2 g., rotating +12.7° in chloroform. An additional 0.65 g. of crystals rotating +11.2° (yield, 89%) was obtained from the filtrate by thorough extraction with chloroform, followed

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(5) Hockett and Hudson, THIS JOURNAL, **53**, 4455 (1931).

(6) Fischer, Bergmann and Rabe, *Ber.*, **53**, 2362 (1920).

(7) By Dr. F. H. Goldman.

(8) Tanret, *Bull. soc. chim.*, [3] **15**, 203, 349 (1896).

(9) In occasional experiments, probably because of the presence of seeds of the lower rotating form, it was necessary to repeat the operation.

(10) By Dr. R. T. K. Cornwell.

by washing the chloroform solution twice with 3% hydrochloric acid, once with dilute sodium bicarbonate solution, and crystallization of the sirup, recovered from the dried extract, from ether–petroleum ether at 0°. After one recrystallization from 90% ethanol, the acetate rotated +13.4° in chloroform and melted at 98.5–99° (corr.) alone or mixed with pure β-tetraacetate prepared from β-triacetylrhamnose by the directions of Fischer, Bergmann and Rabe,[6] whose method gave a product rotating, after purification, +13.3° in chloroform (*c*, 3.87) and +14.2° in acetylene tetrachloride compared with their $[\alpha]^{16}_D$ +13.75° in the latter solvent.

The lower rotating form of anhydrous rhamnose was acetylated as described for the β-sugar. One gram of sugar with initial rotation +13.2° yielded 0.85 g. (43%) of β-tetraacetate, most of which melted at 97–98° (corr.) and rotated +12.5° in chloroform. The remainder of the product was a sirup.

Summary

Anhydrous rhamnose, hitherto obtainable only in small yield, has been prepared in 85–90% yield by two methods. The initial rotation of Fischer's β-rhamnose was found to be +38° in water; Minsaas recently reported about +44°. During the preparation of β-rhamnose a second form of the anhydrous sugar rotating about +14° in water frequently separated; this substance appears to be a molecular compound having the composition α,β-rhamnose if the rotation of β-rhamnose is +38° or 3-α,2-β-rhamnose if it is +44°. The presence of the β-isomer as one component of this molecular compound is confirmed by the preparation from it of crystalline β-tetraacetylrhamnose in 43% yield. Acetylation of β-rhamnose yields about 90% of the crystalline β-tetraacetate, which is now best obtained in this way.

WASHINGTON, D. C. RECEIVED APRIL 24, 1937

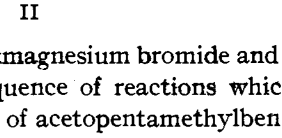
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Acetopentamethylbenzene[1]

BY LEE IRVIN SMITH, ISABELLA M. WEBSTER AND CYRUS GUSS

In a recent paper, Henri Clément[2] has discussed the properties of pentamethylphenylmagnesium bromide, which was prepared by the entrainment method of Grignard[3] by allowing an equimolecular mixture of bromopentamethylbenzene and ethyl bromide in ether to react with magnesium. Among other reactions discussed by Clément was that between acetyl chloride and pentamethylphenylmagnesium bromide, which was claimed to give acetopentamethylbenzene in 34% yield. This substance was described as crystallizing in small rods which melted at 110°. In view of the work of Kohler and Baltzly[4] and of Smith and Guss[1] upon the behavior toward Grignard reagents of diortho substituted aromatic ketones of the type of acetomesitylene and acetopentamethylbenzene, it seemed very unlikely that any enolizable ketone of this type could be prepared by dropping acetyl chloride into a highly hindered Grignard reagent especially when ethylmagnesium bromide also was present. When Smith and Guss[1] prepared acetopentamethylbenzene from the hydrocarbon by the Friedel–Crafts synthesis and found the substance to melt at 84°, it was obvious that Clément's compound which melted at 110° could not be acetopentamethylbenzene.

At first it was supposed that Clément's compound was the triketone I, formed from pentamethylphenylmagnesium bromide and acetyl chloride by a sequence of reactions which included: (a) formation of acetopentamethylbenzene, a slow reaction; (b) enolization of the ketone by excess Grignard reagent, a more rapid reaction; and (c) reaction of the enolate with acetyl chloride to give the triketone, also a reaction faster than (a). Accordingly acetopentamethylbenzene was con-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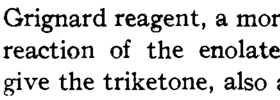
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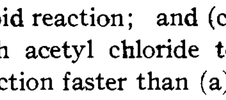
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(1) Polymethylbenzenes. XVII. Paper XVI. Smith and Guss, THIS JOURNAL, **59**, 804 (1937).

(2) Henri Clément, *Compt. rend.*, **202**, 425 (1936).

(3) (a) Grignard, *ibid.*, **198**, 625 (1934); (b) Clément and Grignard, *ibid.*, **198**, 665 (1934); (c) Grignard, *ibid.*, **198**, 2217 (1934); (d) see also Urion, *ibid.*, **198**, 1244 (1934).

(4) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).