

CONTRIBUTIONS TO THE KNOWLEDGE OF FOREST PRODUCTS.

VI. ON HYDRAZINO-2 CYMENE AND SOME OTHER COMPOUNDS DERIVED FROM AMINO-2 CYMENE.¹

BY W. A. DEMONBREUN AND R. E. KREMERS.

The amino-2 cymene prepared as previously described² was used in the following preparations.

Hydrazino-2 Cymene.—The diazotization of the base by hydrochloric acid and sodium nitrite and the subsequent reduction by stannous chloride were tried according to the usual method several times,³ but without much success. The following procedure gave better results.⁴

Two hundred and fifteen cc of concentrated hydrochloric acid was added to 25 grams of amino-2 cymene in a deep porcelain beaker placed in a freezing mixture of salt and ice. An electrically driven stirrer was then started in the mixture, causing most of the hydrochloride to go into solution. When the temperature had fallen to -5°C ., a solution of 15 grams ethyl nitrite in 15 cc of alcohol was added drop by drop from an ice-cooled burette. The temperature was kept below 0° . The diazotizing mixture passed through all the color changes just as in the diazotization of aniline.

After the nitrite solution had been added, a slight excess of nitrous acid was present. To the solution, still cooled and agitated, was added a solution of 150 grams stannous chloride in 125 cc of conc. hydrochloric acid, also cooled to 0° . The cymylhydrazine separated as a pinkish white precipitate which collected at the surface of the liquid on standing. It was filtered out by suction and when nearly dry was decomposed by the addition of an excess of strong caustic soda solution. When the decomposition was complete, the free base, which separated as a light red colored oil, was extracted with ether. This solution was dried over anhydrous sodium sulphate and the ether distilled off from the water-bath. The residual viscous oil was finally purified by vacuum distillation. The largest yield of crude hydrazine was 19 grams, or 69 per cent.

The data from a fractionation under 1.5 mm. pressure—considerable decomposition took place at 13 mm. pressure maintained by a water pump—are given as representative of our best results.

Fraction.	B. p. 1.5 mm.	Weight, Gm.	n_D^{20} .
1	-95°C .	12	1.5083
2	95-110	2	1.5260
3	110-15	3	...
4	115-20	7	1.5502
5	120-30	4	1.5443
6	130+	3	...

Fraction 1 was almost colorless, insoluble in hydrochloric acid, and without action on Fehling's solution.

¹ Based on part of a thesis submitted by W. A. D. to the Graduate Faculty of Vanderbilt University in partial fulfillment of requirements for the degree of M.S., June 1922.

² See Contribution V, *JOUR. A. PH. A.*, p. 296, April issue, 1923.

³ Cohen, "Practical Organic Chemistry."

⁴ Compare with Weyl, "Die Methoden der Organischen Chemie," pp. 817, 819.

Fraction 2 was partially soluble in hydrochloric acid, and reduced Fehling's solution.

Fractions 3 and 4 were completely soluble in hydrochloric acid, reduced Fehling's solution, and had a light yellow color.

Fraction 5 was darker in color and smelled of ammonia. The residue was a red tar.

Considering fractions 3 and 4 as pure hydrazine, the yield is 21 per cent. of the aminocymene.

Hydrazino-2 Cymene Hydrochloride.—The hydrochloride was prepared by adding a slight excess of concentrated hydrochloric acid to the free base. The resulting solid was dissolved in 5 per cent. alcohol and reprecipitated by the addition of conc. acid. The white needle-like crystals were separated from the mother liquor by filtration, washed with water, and dried. M. p. 186–7° C.

Aqueous or alcoholic solutions of this compound decompose during evaporation, even under diminished pressure.

Nitrogen by Dumas method = 14.16 p. c.

Nitrogen in $C_{10}H_{16}N_2.HCl$ = 13.97 p. c.

Acetylhydrazino-2 Cymene.—The acetyl derivative was prepared by adding a slight excess of acetic anhydride to the free base. The resulting reaction was completed by warming the solution for a few minutes on a water-bath. The new compound was isolated by pouring the warm reaction mixture into cold water. The precipitated straw colored solid was recrystallized from 50 per cent. alcohol, and then from ether. There resulted almost white, scaly crystals, of m. p. 125–6°.

Nitrogen by Dumas method = 13.87 p. c.

Nitrogen in $C_{10}H_{13}.N_2H_2.C_2H_3O$ = 13.59 p. c.

Glucose Cymylhydrazone.—One mole of cymylhydrazine hydrochloride was dissolved in a 1 per cent. solution of glucose containing one mole of sugar. The solution was then made acid with acetic acid by the addition of a slight excess of anhydrous sodium acetate. On standing the hydrazone precipitated. The compound was filtered out by suction, recrystallized from 50 per cent. alcohol, and dried as quickly as possible.

The product was a yellow mass of fibrous crystals. M. p. 92–3° C.

Nitrogen found by the Dumas method = 8.87 p. c.

Nitrogen in $C_{16}H_{26}O_5N_2$ (hydrazone) = 8.59 p. c.

Nitrogen in $C_{26}H_{33}O_4N_4$ (osazone) = 11.91 p. c.

Mannose Cymylhydrazone.—The mannose compound was prepared in the same manner as the preceding substance. M. p. 110–11° C.

Nitrogen found by the Dumas method = 9.09 p. c.

Nitrogen in $C_{16}H_{26}O_5N_2$ = 8.59 p. c.

Galactose Cymylhydrazone.—This compound was prepared by the same method as its analogues. M. p. 149–50° C.

Nitrogen found by the Dumas method = 9.42 p. c.

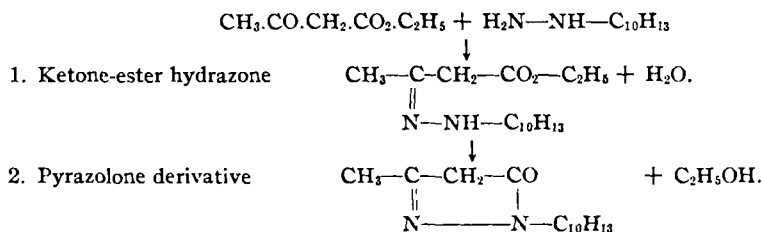
Nitrogen in $C_{16}H_{26}O_5N_2$ = 8.59 p. c.

Glucose Osazone.—In experimenting with the action of hydrazino-2 cymene on glucose, the conditions first chosen were analogous to those obtaining in the preparation of glucose phenylosazone. That is, 3 moles of the hydrazine hydrochloride to one mole of glucose were dissolved in water, treated with sodium acetate, and the filtered solution heated gently on a water-bath. The resultant precipitate was always grossly contaminated with a tar that could not be removed by recrystallization. Furthermore the nitrogen content was always too low, and the compound when partially purified began to approximate the properties of the glucose hydrazone described above.

In view of these facts, it seems reasonable to conclude that hydrazino-2 cymene reacts readily but once with aldose sugars; that is, the reaction practically stops with the formation of hydrazones. This is in decided contrast to the behavior of phenylhydrazine, which forms osazones very easily in certain cases, and is analogous to the behavior of *o*-tolyl hydrazine. The uniformly rather high nitrogen content may raise a question as to just what has happened. But the values lie closer to the hydrazone than to the osazone. And in view of the ready decomposition of these substances, a variation from the theoretical values is not surprising.

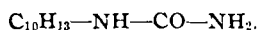
Benzaldehyde Cymylhydrazone. Furfural Cymylhydrazone.—The preparation of hydrazones of benzaldehyde and furfural was attempted as one of the first reactions in the study of our hydrazine fractions. It was thought that these compounds would be readily crystallizable and that they would aid in their characterization. While reactions undoubtedly took place, only red-colored tars resulted that defied crystallization.

Acetoacetic Ester Derivative.—Various fractions and preparations of hydrazino-2 cymene were involved in reaction with acetoacetic ester. It was thought that pyrazolone formation might result as in the case of phenylhydrazine. There can be no doubt that these two substances react because heat is evolved and drops of water separate when they are brought together. However it was not possible to effect the formation of a crystalline substance. The amount of material at our disposal was too small for purification by distillation *in vacuo*, hence no analysis was made. It is therefore impossible to decide whether a ketone ester hydrazone resulted, or a liquid pyrazolone. We are inclined to the supposition that the former is the case because of the behavior of hydrazino-2 cymene toward the aldohexoses

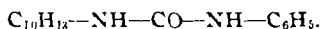


In addition to preparing hydrazino-2 cymene from amino-2 cymene, preliminary experiments were made with two other compounds.

Cymyl Urea.—Cymyl urea results when amino-2 cymene hydrochloride and potassium cyanate are allowed to react in the usual way. After recrystallization from hot alcohol, diluted with water, the compound forms white, needle-like crystals. M. p. 162-3° C.



Sym. Cymyl Phenyl Urea.—Phenylisocyanate and amino-2 cymene react vigorously on being brought together. The product recrystallized from 5 per cent. alcohol forms light, fluffy, white crystals of m. p. 192° C.



SUMMARY.

1. Hydrazino-2 cymene (synonyms; cymyl hydrazine, carvacryl hydrazine) has been prepared from amino-2 cymene, together with its hydrochloride; mono-acetyl derivative; glucose, mannose, and galactose hydrazones.
2. The cymyl hydrazones of benzaldehyde and furfural were not obtained in crystalline form.
3. Cymyl hydrazine reacts readily with acetoacetic ester, but the exact nature of the product has not been determined.
4. There is evidence that the side chains of the cymene residue exert a steric hindrance in some reactions of hydrazino-2 cymene.
5. Cymyl and sym. cymyl phenyl urea have been prepared.

SYNTHETIC DRUGS—IV.*

EXAMINATION OF AMERICAN-MADE CHLORAMINE-T, DICHLORAMINE-T, HALAZONE AND PREPARATIONS.

BY PAUL NICHOLAS LEECH, PH.D., CHICAGO.

Six years ago Dakin, Cohen and Kenyon¹ introduced into medicine the first "chloramine" antiseptic, "Chloramine-T;" the other members of the family, "Dichloramin-T" and "Halazone," followed soon afterward. The history of their introduction and of their commercial preparation has been detailed repeatedly in the pharmaceutical and medical literature; discussion now would be repetition.

The Council on Pharmacy and Chemistry of the American Medical Association kept pace with the therapeutic progress attendant on war times and described these chlorine antiseptics in "New and Nonofficial Remedies" after standards had been drawn up by the A. M. A. Chemical Laboratory. Since then a number of American firms have been marketing the products. It seemed opportune at this time to determine the purity of the market supply of those products described in "New and Nonofficial Remedies" and particularly to investigate the stability of the compounds containing a somewhat unstable atom. Hence this present report.

* Contribution from the Chemical Laboratory of the American Medical Association.

The previous articles were: "Examination of American-Made Acetylsalicylic Acid," *J. Ind. and Eng. Chem.*, April, 1918, p. 228 (see also editorial, *Ibid.*, April 1918, p. 225); "American-Made Synthetic Drugs—II. Examination of Procaine (Novocain), Barbitol (Veronal), Phenetidyl-acetphenetidin (Holocain), Cinchopen (Atophan), Manufactured under Federal Trade Licenses" (with Wm. Rabak and A. H. Clark), *J. A. M. A.*, 73, 754 (Sept. 6), 1919; "Synthetic Drugs—III. The Digestion of Tannin Compounds Used as Intestinal Astringents by Artificial Digestive Mixtures," *J. A. M. A.*, 75, 1120 (Oct. 23), 1920.

¹ *British Medical Journal*, Jan. 29, 1916, p. 160.