resulting amylopectin solution was concentrated under reduced pressure to a thick paste which was precipitated by pouring slowly with vigorous stirring into ethanol (1 part of paste to 5 parts of ethanol). The precipitate was filtered, thrice vigorously stirred with fresh portions of ethanol, and dried in a vacuum desiccator over calcium chloride.

Acknowledgments.—We are indebted to Dr. N. Cyril Schieltz for the X-ray data and to Mrs. Jane Rehn Von Korff and Messrs. Stanley A. Watson and William D. Johnson for carrying out parts of the experimental work.

Summary

In addition to alcohols, as found by Schoch, representatives of many different classes of organic compounds such as esters, ketones, mercaptans, carboxylic acids, nitroparaffins, and pyridine, which are capable of forming hydrogen bonds with amylose, have been found to form complexes with this carbohydrate and can serve as agents for fractionating starch.

"Crystalline" amylose–nitroparaffin complexes are formed when starches are fractionated with nitroethane, 1-nitropropane, and 2-nitropropane. The yields of amylose, using 1-nitropropane and 2-nitropropane as fractionating agents, from corn starch, potato starch, tapioca starch, and wheat starch are about the same as those obtained using butanol. Some of the properties of amylose–nitroparaffin complexes are described. The X-ray diffraction patterns of the three nitroparaffin complexes are identical. The amylose fractions have been characterized by potentiometric iodine titration, retrogradation, and the film-forming properties of the triacetate derivative.

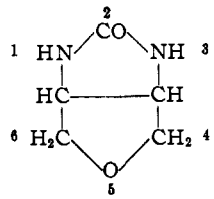
PEORIA, ILLINOIS RECEIVED APRIL 16, 1945

[CONTRIBUTION NO. 564 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

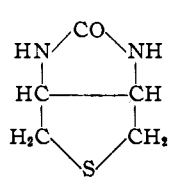
Furan and Tetrahydrofuran Derivatives. V. The Synthesis of a Racemic Hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole[1,2]

BY KLAUS HOFMANN AND ANNA BRIDGWATER

The ring system of hexahydro-2-oxo-1-furo-[3,4]imidazole (I)[3] has so far not been studied, and as it is closely related to hexahydro-2-oxo-1-thieno[3,4]imidazole (II),[3] the nucleus of biotin, the preparation of certain representatives of this class of compounds was desirable.



(I)



(II)

This report describes a new procedure for the synthesis of a hexahydro-2-oxo-4-methyl-1-furo-[3,4]imidazole isomer (VII), which is applicable to the preparation of a variety of 4-substituted hexahydro-2-oxo-1-furo[3,4]imidazoles, and thus makes these compounds easily available.

Recently, a number of 3,4-diaminocarbethoxy-2-substituted furans have been prepared[4] with the expectation that the introduction of aminocarbethoxy groups would labilize the furan nucleus and make it susceptible to low pressure catalytic hydrogenation.

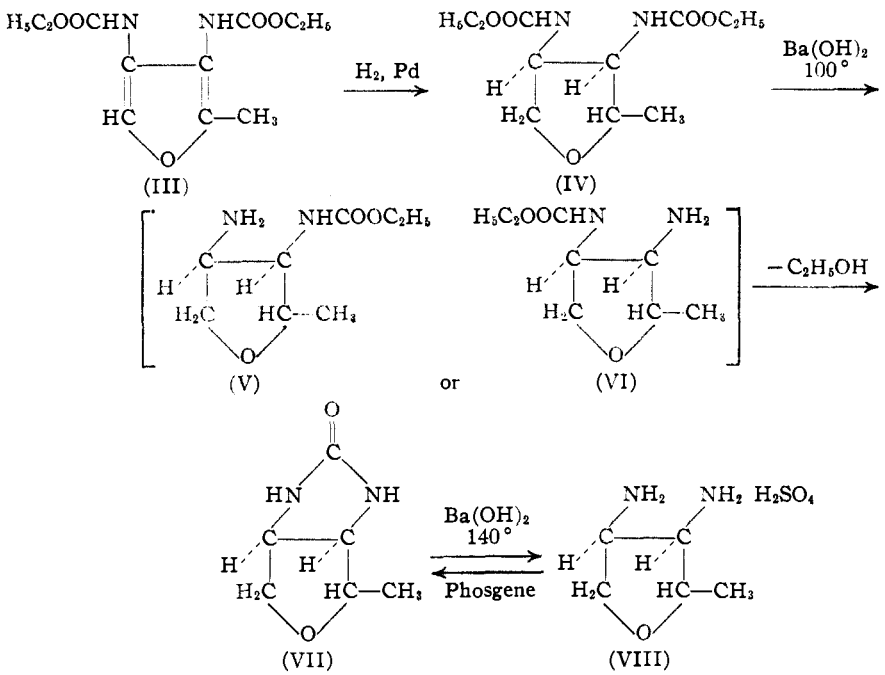
This has now been found to be the case, and it was observed that 3,4-diaminocarbethoxy-2-methylfuran (III) absorbed two moles of hydrogen with remarkable ease and was transformed into a mixture of hydrogenation products from which *cis* - 3,4 - diaminocarbethoxy - 2 - methyltetrahydrofuran (IV) could be isolated. Attempts to remove the carbethoxy groups from this compound by mild hydrolysis with dilute barium hydroxide did not afford the expected 3,4-diamino-2-methyltetrahydrofuran, but gave a substance which analyzed for $C_6H_{10}O_2N_2$. The structure of this new material was established as hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole (VII) by the following reactions. Drastic hydrolysis with strong barium hydroxide opened the urea ring with the formation of *cis*-3,4-diamino-2-methyltetrahydrofuran, which was characterized as the crystalline sulfate (VIII). Treatment of a sodium bicarbonate solution of (VIII) with phosgene reintroduced the CO group into the molecule and the resulting bicyclic urea derivative was identical with (VII). Thus, treatment of the urethan (IV) with dilute barium hydroxide effected a ring closure and resulted in the formation of the desired bicyclic urea derivative (VII). The great tendency of (IV) to undergo this ring closure provides direct chemical proof for the *cis* position of the aminocarbethoxy groups in compound (IV) and consequently establishes the *cis* configuration of the rings in compound (VII). Treatment of compound (IV) with strong barium hydroxide at 140° for six hours gave a small amount of (VIII), most of the material being transformed into (VII). Only prolonged hydrolysis at 140° resulted in a complete transformation of (IV) into (VIII), indicating that (IV) is even under these

(1) A preliminary report of this work has appeared in THIS JOURNAL, **67**, 694 (1945).

(2) The authors wish to express their appreciation to Ciba Pharmaceutical Products, Inc., and to the Buhl Foundation for their generous support of this work.

(3) These ring systems are named and numbered according to the rules followed by Chemical Abstracts and the Ring Index (American Chemical Society Monograph No. 84).

(4) Hofmann and Bridgwater, THIS JOURNAL, **67**, 738 (1945).



drastic conditions first transformed into (VII), which in turn yields (VIII).

The most logical explanation for the mechanism of this cyclization reaction is the assumption of a preferential hydrolysis of one of the carbethoxy groups in compound (IV) with the formation of either *cis*-3-aminocarbethoxy-4-amino-2-methyltetrahydrofuran (V) or *cis*-3-amino-4-aminocarbethoxy-2-methyltetrahydrofuran (VI), which in turn loses one molecule of alcohol to give (VII).

The molecule of hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole (VII) with a *cis* configuration of the rings may exist in four optically active forms which give two racemic mixtures. One of these contains its methyl group in *cis* and the other in *trans* configuration with respect to the nitrogen in position 3. Compound (VII) represents one of these two racemic mixtures, but small amounts of the other isomer also may be present.

Additional studies of a number of different *cis* diaminocarbethoxy compounds will be necessary in order to elucidate the mechanism of the above cyclization reaction and to determine its general applicability to the preparation of bicyclic urea derivatives.

The aforementioned procedures have been applied successfully to the synthesis of *dl*-oxybiotin (hexahydro-2-oxo-1-furo[3,4]imidazole-4-valeric acid), which will be described in a forthcoming publication.

Experimental[5]

***cis*-3,4-Diaminocarbethoxy-2-methyltetrahydrofuran (IV).**—3,4-Diaminocarbethoxy-2-methylfuran (III)[4] (5.12 g.) was dissolved in 100 cc. of glacial acetic acid, and the solution was shaken with hydrogen at room temperature and atmospheric pressure in the presence of 4 g. of a palladium on barium sulfate catalyst.[6] Two moles of hydrogen were absorbed within four hours when the hydrogenation came to an end. The catalyst was filtered off, the glacial acetic acid was removed *in vacuo* and the resulting oil was dissolved in ether. The ether solution was extracted with five 20-cc. portions of 2 *N* hydrochloric acid, which were combined, neutralized with 10% sodium bicarbonate, and concentrated to a small volume *in vacuo*. The residue was extracted with several portions of ether, the combined ether extracts were dried over sodium sulfate, the ether was removed on the steam-bath, and the resulting oil (2.9 g.) crystallized on standing. The crystals were washed with ice-cold ether, and were recrystallized from the same solvent; 1.5 g. (28.8% of the theoretical yield) of colorless needles was obtained which melted at 95–96°.

Anal. Calcd. for $C_{11}H_{20}O_5N_2$: C, 50.75; H, 7.74; N, 10.75; OC_2H_5, 34.62. Found: C, 50.80; H, 7.79; N, 10.68; OC_2H_5, 34.87.

Hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole (VII)

(a) From *cis*-3,4-Diaminocarbethoxy-2-methyltetrahydrofuran (IV) by Treatment with Dilute Barium Hydroxide.—A mixture of 500 mg. of compound (IV) and 30 cc. of a 10% aqueous solution of $Ba(OH)_2 \cdot 8H_2O$ was heated on the steam-bath for two hours. A slow stream of carbon dioxide was then passed through the hot solution for thirty minutes and the precipitated barium carbonate was removed by filtration through a mat of filter-cel. The clear filtrate was concentrated to dryness *in vacuo* and the resulting crystals were purified by recrystallization from 95% alcohol; 195 mg. (71.4% of the theoretical yield) of crystals was obtained which melted at 235–238° (sealed capillary tube). A sample of the recrystallized material for analysis was sublimed at 170–180° and 0.005 mm.

Anal. Calcd. for $C_6H_{10}O_2N_2$: C, 50.71; H, 7.09; N, 19.70. Found: C, 51.10; H, 7.04; N, 19.38.

The compound exhibits polymorphism, and crystallizes in either needles or diamond-shaped crystals. Both of these forms are interchangeable and sometimes appear simultaneously during recrystallization.

(b) By Phosgene Treatment of (VIII).—A solution of 400 mg. of compound (VIII) in 10 cc. of 10% sodium bicarbonate was cooled in an ice-bath and was treated with phosgene until it became acid to congo red. The clear solution was neutralized with 10% sodium bicarbonate, was evaporated to dryness *in vacuo*, and the crystalline residue extracted with hot 95% alcohol. The combined alcohol extracts were filtered, the alcohol was removed on the steam-bath, and the product was sublimed at 160–170° and 0.005 mm. pressure; 208 mg. (78.4% of the theoretical yield) of sublimate was obtained which melted at 234–237°. The material was recrystallized from 95% alcohol and melted at 235–238°. It crystallized in two polymorphic forms (needles and diamonds) and was

(5) The microanalyses were performed by the Microchemical Laboratory, California Institute of Technology, Pasadena, California. All melting points are corrected.

(6) Schmidt, *Ber.*, **52**, 409 (1919).

by the mixed melting point identical with the material prepared according to procedure (a). A sample of the recrystallized material for analysis was sublimed at 170–180° and 0.005 mm.

Anal. Calcd. for $C_6H_{10}O_2N_2$: C, 50.71; H, 7.09; N, 19.70. Found: C, 50.82; H, 7.07; N, 19.66.

cis-3,4-Diamino-2-methyltetrahydrofuran Sulfate (VIII)

(a) **By Drastic Hydrolysis of Hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole (VII).**—A mixture of 726 mg. of (VII), 9.0 g. of $Ba(OH)_2 \cdot 8H_2O$ and 44 cc. of water was sealed into a pressure tube and the tube was heated to 130–140° for twenty hours. The resulting suspension was removed from the tube, brought to a boil, and carbon dioxide was passed into the hot solution for thirty minutes. The barium carbonate was removed by filtration through filter-cel, the clear filtrate was concentrated to a small volume *in vacuo*, and was acidified to congo red with 2 *N* sulfuric acid. The precipitate of barium sulfate was filtered off, most of the water was removed *in vacuo*, and 823 mg. (75.2% of the theoretical yield) of the crystalline sulfate (VIII) was precipitated from the concentrated solution by the addition of hot methanol. The material was purified by several recrystallizations from dilute methanol, and melted at 270–275° with decomposition.

Anal. Calcd. for $C_5H_{14}O_5N_2S$: C, 28.03; H, 6.59; N, 13.07; S, 14.97. Found: C, 27.82; H, 6.38; N, 12.89; S, 15.35.

(b) **By Drastic Hydrolysis of *cis*-3,4-Diaminocarbethoxy-2-methyltetrahydrofuran (IV).**—A mixture of 214 mg. of (IV), 4.2 g. of $Ba(OH)_2 \cdot 8H_2O$ and 22 cc. of water was heated to 140–150° for six hours in a sealed tube, and 33 mg. (18.7% of the theoretical yield) of the sulfate (VIII) was isolated from the reaction mixture by the method outlined above.

The mother liquors from (VIII) were neutralized with 10% sodium bicarbonate and were concentrated to dryness *in vacuo*. Sublimation of the residue at 150–160° and 0.005 mm. gave 73 mg. (62.4% of the theoretical yield) of crystals which melted at 235–238° and were identical with compound (VII).

In another experiment in which 642 mg. of (IV) was hydrolyzed for twenty hours at 140–150° with 12.6 g. of $Ba(OH)_2 \cdot 8H_2O$ and 66 cc. of water, 381 mg. (72.1% of the theoretical yield) of (VIII) was obtained.

Summary

A procedure for the synthesis of a hexahydro-2-oxo-4-methyl-1-furo[3,4]imidazole isomer has been described. This synthesis involves catalytic hydrogenation of the appropriate furan derivative to the corresponding *cis*-3,4-diaminocarbethoxytetrahydrofuran and cyclization of this compound by treatment with dilute barium hydroxide.

PITTSBURGH, PENNSYLVANIA RECEIVED APRIL 26, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ROCHESTER]

The Action of Some Benzyl Halides on Salts of Phenylnitromethane and Phenylnitroacetonitrile

BY LEONARD WEISLER[1] AND R. W. HELMKAMP

Treatment of metallic derivatives of primary and secondary nitro compounds with alkyl halides either has failed to produce alkylation or, if alkylation has occurred, has given rise preferentially to nitronic esters rather than C-alkylated products. The nitronic esters frequently have not been isolated in the pure state because of the tendency of a nitronic ester to disproportionate into an oxime and an aldehyde or a ketone.

$$RCH{=}NO_2M + R'CH_2X \longrightarrow RCH{=}NO_2CH_2R' \longrightarrow RCH{=}NOH + R'CHO$$

To further the elucidation of the influence of constitutional and environmental factors on the course of the alkylation of nitronate ions (and of resonating anions in general), it was decided to investigate the action of some benzyl halides, in particular *p*-nitrobenzyl chloride, on salts of phenylnitromethane and phenylnitroacetonitrile. That these nitro compounds might react with *p*-nitrobenzyl chloride to form, at least to some extent, C-benzylated products was suggested by the fact that Posner[2] had been able to separate 2-nitro-1,3-bis-(*o*-nitrophenyl)-propane from the oil produced by the action of *o*-nitrobenzyl chloride on the sodium salt of nitromethane.

Action of Benzyl Halides on Salts of Phenylnitromethane.[3]—No evidence of C-benzylation could be found when equimolecular amounts of benzyl chloride and the sodium salt of phenylnitromethane were refluxed in absolute alcohol solution. That the reaction leads mainly, if not solely, to nitronic ester formation was shown by the isolation of a 76.5% yield of benzaldehyde and an 80% yield of the stereoisomeric benzaldoximes. On the other hand, when *p*-nitrobenzyl chloride was allowed to react under similar conditions, it was possible to separate not only *p*-nitrobenzaldehyde and a mixture of the benzaldoximes but also a 37% yield of a product which by analysis and chemical behavior was shown to be 1-nitro-2-

(1) Present address: Distillation Products, Incorporated, Rochester, New York.

(2) Posner, *Ber.*, **31**, 657 (1898); *cf.* the formation of 1,2-dinitro-1,2-diphenylethane and 1,2-dinitro-1,2-diphenyleneethane (Nenitzescu and Isacescu, *ibid.*, **63**, 2484 (1930)) and of dinitroparaffins (Hass and Seigle, *J. Org. Chem.*, **5**, 100 (1940)).

(3) Nenitzescu and Isacescu (ref. 2) failed to obtain a reaction on treating the sodium salt of phenylnitromethane with methyl iodide. They found, however, that the action of *t*-butyl bromide yielded the decomposition products of the nitronic ester. The methyl nitronic ester was obtained by Auwers and Otten (*Ber.*, **57**, 456 (1924)) and by Arndt and Rose (*J. Chem. Soc.*, 6 (1935)) through the use of dimethyl sulfate. Brown and Shriner (*J. Org. Chem.*, **2**, 376 (1937)) were unsuccessful in their attempt to bring about a reaction between the sodium salt and diphenylmethyl bromide. The only recorded instance of C-alkylation of phenylnitromethane is that reported by Wieland and Höchtlen (*Ann.*, **505**, 237 (1933)), who isolated triphenylmethylphenylnitromethane in 33% yield from the reaction of triphenylmethyl chloride on the mercury derivative. In a repetition of this work, we obtained a 40% yield.