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## Monosodium Urea and its Reactions

BY RALPH A. JACOBSON

The preparation of monopotassium urea and dipotassium urea by the reaction of potassium amide on urea in liquid ammonia solution has been described by Franklin and Stafford,<sup>1</sup> and more recently by Blair.<sup>2</sup> The corresponding sodium derivatives have been prepared by the action of sodium hydride on urea,<sup>3</sup> but the properties of the sodium compounds apparently have not been investigated. The present paper is concerned with the formation and properties of monosodium urea and its use for the synthesis of ureides.

Monosodium urea is obtained readily by the action of metallic sodium on urea in liquid ammonia solution, using ordinary laboratory equipment. The most convenient procedure consists in slowly adding the theoretical amount of sodium to a well-agitated solution of urea in ammonia. Evolution of hydrogen and precipitation of monosodium urea begin almost immediately and the blue color disappears as the sodium is utilized. The product is obtained either by evaporation of the liquid ammonia or by filtration of the ammonia suspension.

The monosodium urea obtained in this manner is a dusty white powder. It has no definite melting point but begins to decompose in a capillary tube at about 150–160°. It is insoluble in aliphatic and aromatic hydrocarbons, chlorinated hydrocarbons, ethers and other inert solvents. It dissolves with reaction in water, alcohols and in other compounds containing an hydroxyl group. It is rather hygroscopic but can be handled in the dry condition and can be retained indefinitely in a closed container.

Attempts to prepare disodium urea were only partly successful. While one equivalent weight of sodium reacted readily with urea in boiling liquid ammonia, sodium in excess of this amount reacted only very slowly. Presumably, the insolubility in ammonia of the monosodium derivative initially formed was an important inhibiting factor. By employing very dilute solutions of urea in liquid ammonia and permitting the reaction to

continue for several days, considerably more than one equivalent weight of sodium was finally introduced. The product was an exceedingly hygroscopic white powder which formed a dibenzoyl derivative upon reaction with benzoyl chloride. The analytical data, however, indicated that the product was not pure disodium urea but a mixture of the mono- and the disodium derivatives.

**Reaction of Monosodium Urea with Halogen Compounds.**—Benzoyl chloride, oleyl chloride and stearyl chloride reacted with sodium urea to yield the corresponding acyl derivatives. Benzyl chloride also reacted with monosodium urea to give benzyl urea. On the other hand, several unsuccessful attempts were made to prepare alkyl ureas by the reaction of monosodium urea with alkyl halides, *e. g.*, butyl iodide, butyl chloride and dodecyl bromide. These results indicate that a fairly active halogen is required for reaction.

**Reaction of Monosodium Urea with Esters.**—Esters reacted at room temperature with monosodium urea to yield acyl derivatives. It was usually necessary to add acetone or some other ketone (or an alcohol) to the mixture in order to obtain reaction. In a few instances condensation was effected in the absence of acetone by treating a solution of the ester and urea in liquid ammonia with sodium, thereby forming the monosodium urea *in situ*.

The reaction has been applied to simple esters such as ethyl acetate, ethyl benzoate and ethyl oleate for the preparation of the corresponding acyl derivatives. It has also been applied to dibasic esters such as malonic ester, ethylmalonic ester, isopropylmalonic ester, butylmalonic ester and to such higher esters as ethyl glutarate and ethyl pimelate. The malonic ester derivatives yielded the corresponding cyclic barbituric acids, whereas the higher esters appeared to yield straight chain diureides, *e. g.*, glutaryl diureide.

Another interesting application of the sodium urea-ester reaction is its use for the preparation of mixed long-chain acyl ureas by the reaction of monosodium urea with vegetable oils, *i. e.*, esters of glycerol. Such naturally-occurring ester de-

(1) Franklin and Stafford, *Am. Chem. J.*, **28**, 98 (1902).

(2) Blair, *THIS JOURNAL*, **48**, 96 (1926).

(3) Pfeiffer and Scheller, U. S. Patent 1,816,911.

rivatives as coconut oil, Chinawood oil and linseed oil react with monosodium urea in the presence of acetone to yield the corresponding mixed acyl ureas. The latter are white, crystalline, rather high-melting compounds of limited solubility in most organic solvents though crystallizable from hot acetic acid or dioxane. The acyl ureas from linseed and Chinawood oils retain the unsaturation of the oil acids and are characterized by rather high iodine numbers (around 130).

During this study the monosodium derivatives of a number of other amides and amines also were prepared, some of which have already been described by Franklin,<sup>1,4</sup> Titherley<sup>5</sup> and others.<sup>2,6</sup> In general, the condensation of these with esters followed the expected course, and furnished a convenient method for preparing certain acyl derivatives not readily obtained by other methods.

### Experimental Part

**Monosodium Urea.**—Two-mole lots of monosodium urea were prepared by slowly adding 46 g. of sodium to 120 g. of urea dissolved in 1.5 liters of liquid ammonia contained in a 3-necked 2-liter flask provided with a mercury-sealed stirrer. The product was obtained as a white powder upon evaporation of the ammonia; yield 160 g.

*Anal.* Calcd. for  $\text{CH}_2\text{ON}_2\text{Na}$ : Na, 28.05. Found: Na, 27.85 (as sodium sulfate), 28.40 (by titration with acid).

**Attempted Preparation of Disodium Urea.**—Sodium in excess of one atom reacted slowly and incompletely with a very dilute solution of urea in liquid ammonia. Apparently the product was a mixture of monosodium urea and disodium urea. *Anal.* Calcd. for  $\text{CH}_2\text{ON}_2\text{Na}_2$ : Na, 44.23. Found: Na, 34.72. Upon treatment of the product with benzoyl chloride, dibenzoyl urea (m. p. 204–205° from benzene) was obtained. *Anal.* Calcd. for  $\text{C}_{14}\text{H}_{12}\text{O}_2\text{N}_2$ : N, 10.44. Found: N, 10.70.

**Oleyl Urea.**—To 13.5 g. of monosodium urea was added, slowly during gentle warming, 50 g. of oleyl chloride. Boiling isobutanol was added to the mixture and then sufficient water to dissolve the sodium chloride formed in the reaction. The isobutanol layer deposited crystals of oleyl urea upon cooling; m. p. 155–160° (literature 161°).<sup>7</sup>

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{36}\text{O}_2\text{N}_2$ : C, 70.37; H, 11.11; N, 8.64. Found: C, 69.77; H, 10.65; N, 8.24.

(4) Franklin, *THIS JOURNAL*, **27**, 820 (1905); **37**, 2279 (1915); **44**, 490 (1922); **46**, 2143 (1924); **46**, 2148 (1924); *Am. Chem. J.*, **47**, 304 (1912); "The Nitrogen System of Compounds," Reinhold Publishing Corporation, New York, 1934.

(5) Titherley, *J. Chem. Soc.*, **71**, 460 (1897); **79**, 391 (1901); **81**, 1520 (1902); **85**, 1673 (1904); Titherley and Hicks, *ibid.*, **87**, 1216 (1905); **89**, 708 (1906).

(6) Blacher, *Ber.*, **28**, 432 (1895); Chablay, *Compt. rend.*, **154**, 364 (1912); Freer and Sherman, *Am. Chem. J.*, **18**, 580 (1896); *Parts. Ber.*, **60**, 2520 (1927); Priestley, *J. Chem. Soc.*, **93**, 454 (1909); Rakshit, *ibid.*, **103**, 1557 (1913); Werner, *ibid.*, **109**, 1126 (1916).

(7) Stendal, *Compt. rend.*, **196**, 1810 (1933). Oleyl urea (m. p. 161°) and stearyl urea (m. p. 176–178°) were obtained by heating urea with the corresponding esters in the presence of sodium ethylate and pyridine.

Stearyl urea (m. p. 175°) and benzoyl urea (m. p. 212°) were similarly prepared but satisfactory results were not obtained with some of the lower aliphatic acid chlorides.

Benzyl urea, m. p. 147–148°, was obtained from benzyl chloride and monosodium urea in liquid ammonia (literature m. p. 147°). *Anal.* Calcd. for  $\text{C}_8\text{H}_{10}\text{ON}_2$ : N, 18.66. Found: N, 18.24.

### Reaction of Monosodium Urea and Simple Esters

**Benzoyl Urea.**—To 30 cc. of methyl benzoate was added 10 g. of powdered sodium urea and 15 cc. of acetone. Considerable heat was evolved and the mixture became pasty. The mixture was allowed to stand overnight, diluted with water, and acidified with hydrochloric acid. The benzoyl urea thus obtained was filtered, washed in a beaker with boiling alcohol and dried. The product melted at 213–214° (literature 215°); yield 12 g. (60%).

Acetyl urea (m. p. 213°) and oleyl urea (m. p. 160°) were similarly prepared from ethyl acetate and methyl oleate, respectively.

**Reaction of Monosodium Urea and Esters of Dibasic Acids.**—Monosodium urea reacted with substituted malonic esters in the presence of acetone to yield substituted barbituric acid derivatives. Thus, butylbarbituric acid (m. p. 208° from alcohol)<sup>8</sup> was obtained in 79% yield from butylmalonic ester.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{12}\text{O}_3\text{N}_2$ : C, 52.17; H, 6.52; N, 15.21. Found: C, 52.46; H, 6.23; N, 14.79.

Ethylbarbituric acid (m. p. 185–186°, yield 79%), isopropylbarbituric acid (m. p. 212°) (*Anal.* Calcd. for  $\text{C}_7\text{H}_{10}\text{O}_3\text{N}_2$ : C, 49.41; H, 5.88. Found: C, 49.62; H, 5.94), and barbituric acid (m. p. 192°) were prepared from the corresponding malonic esters. The unsubstituted barbituric acid was obtained as the dihydrate.

*Anal.* Calcd. for  $\text{C}_4\text{H}_4\text{O}_2\text{N}_2 \cdot 2\text{H}_2\text{O}$ : N, 17.07. Found: N, 17.48.

The melting points given in the literature are: ethylbarbituric acid, m. p. 193–194° corr.; isopropylbarbituric acid 214–214.5°.<sup>8</sup>

The reaction of monosodium urea with esters of dibasic acids higher in the series than malonic yielded high melting insoluble products which appeared to be diureides. From ethyl glutarate a white compound melting at 247–248° was obtained. (*Anal.* Calcd. for  $\text{C}_7\text{H}_{12}\text{O}_4\text{N}_4$ : C, 38.88; H, 5.55; N, 25.92. Found: C, 38.75; H, 5.81; N, 24.62.)

A product of similar properties (m. p. 240–245°) was obtained from ethyl pimelate. A small amount of a compound melting at 205–206° (crystallized from acetic acid) was also obtained. This appeared to be the mono-ureide of pimelic acid ( $\text{NH}_2\text{CONHCO}(\text{CH}_2)_5\text{COOH}$ ).

*Anal.* Calcd. for  $\text{C}_8\text{H}_{14}\text{O}_4\text{N}_2$ : N, 13.86. Found: N, 13.48.

**Reaction of Monosodium Urea with Natural Oils.**—The mixed acyl ureas from coconut oil were prepared from 300 g. of coconut oil, 200 cc. of acetone and 100 g. of sodium urea. The white solid after an alcohol wash melted at 165–170°. Upon crystallization from acetic acid or dioxane, it melted at 172°; yield 150 g. The product contained 9.95% nitrogen.

(8) Volwiler, *THIS JOURNAL*, **47**, 2239 (1925), reported 208–209°.

The mixed acyl ureas from linseed oil and from China-wood oil were obtained in low yield. The former melted at 154–158° (from alcohol) and the latter at 155–162° (from alcohol). The iodine numbers were, respectively, 128 and 108.8, and the nitrogen contents 7.71 and 8.13%.

#### Summary

1. Monosodium urea has been prepared by the reaction of urea in liquid ammonia with one equivalent of sodium. It is a white powder insoluble in inert solvents. A mixture of disodium urea and monosodium urea was obtained from urea and two equivalents of sodium.

2. Several acyl ureas including stearyl, oleyl and benzoyl have been prepared by the reaction of monosodium urea with acid chlorides. Alkyl halides such as butyl iodide and dodecyl bromide did not react with monosodium urea.

3. Simple esters such as ethyl acetate and methyl benzoate reacted with monosodium urea in the presence of acetone to yield acyl ureas. Natural oils such as coconut, linseed and China-wood also reacted to yield high-melting mixed acyl ureas.

4. Malonic ester and its substituted derivatives reacted with monosodium urea to give barbituric acid derivatives. Barbituric acid, ethylbarbituric acid, isopropylbarbituric acid and butylbarbituric acid have been prepared in this manner.

5. Esters of higher dibasic acids, such as ethyl glutarate and ethyl pimelate, apparently yielded diureides.

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## The Interconversion of Mixed Benzoin

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The reduction of 2,4,6-trimethylbenzoin (II) and 2',4',6'-trimethylbenzoin (III) to the same desoxybenzoin, phenyl 2,4,6-trimethylbenzyl ketone,<sup>1</sup> can be explained on the basis of an initial transformation of one of the benzoin isomers into its isomer. If this explanation is correct, the benzoin isomers should be interconvertible under mild conditions. This has proved to be the case, for when either 2,4,6- or 2',4',6'-trimethylbenzoin was warmed in alcoholic sodium acetate solution, the corresponding isomer was formed. Isolation of starting material in each case indicated the existence of an equilibrium.

Because of this ease of interconversion, an investigation was made of the reaction of the two benzoin isomers toward reagents commonly employed in testing for the hydroxyl group. The benzoin isomers, when treated with benzoyl chloride, yielded a single benzoate instead of the expected isomeric benzoates. Presumably in one case benzoylation had been preceded by conversion of the benzoin into its isomer.

Such a conversion suggests the intermediate formation of the ene-diol. Longer treatment was, accordingly, attempted in the hope of obtaining the dibenzoate of the ene-diol. The mono-

benzoate was, however, the only product which could be isolated. The dibenzoate was made for reference by the action of benzoyl chloride on the sodium derivative of the diketone (I). Two forms (VI and VII) of the dibenzoate were isolated. The lower-melting form (139°) was converted into its isomer (170°) by heating above the melting point.

It was found possible, however, to obtain the diacetate of the ene-diol (V) by a method similar to that which was unsuccessful in the case of the corresponding dibenzoate. Subjection of either of the isomeric benzoin isomers to the action of acetic anhydride resulted in the formation of the diacetate. This structure was proved by preparing the compound by the action of acetyl chloride on the disodium salt of mesityl phenyl diketone (I). Compound III formed the diacetate more readily than did its isomer (II); when II was treated with acetic anhydride for five hours a monoacetate was formed while, under the same conditions, III formed the diacetate.

This implies that in the benzoylation III rather than II isomerizes. It is for this reason that the monobenzoate (IV), the structure of which is conjectural, is represented as a derivative of II rather than of III.

(1) Weinstock and Fuson, *THIS JOURNAL*, **58**, 1233 (1936).