

TAUTOMERISM OF UREA

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THE problem of the tautomerism of urea has been the subject of some controversy. A number of authors advanced the idea of the existence of zwitterionic structure.^{1,2} X-Ray examination of interatomic distances in urea by Wyckoff and Corey³ gave support to this concept and to the idea of the resonance structures of the compound.⁴ Dipole moment measurements⁵ also indicated a resonance hybrid of urea. Resonance in urea was also evidenced by former calculation of the values of force constants⁶ and magnetic susceptibility.⁷

Further support was given by investigation of the structure of urea salts^{8,9,10} - and by infra-red investigation of urea inclusion compounds in the independent papers of Kutzelnigg and Mecke¹¹ and Daniewski *et al.*¹².

Also comparative examination of infra-red spectra of crystalline urea kept

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⁵ W.D. Kumler and G.M. Fohlen, J. Amer. Chem. Soc. **64**, 1944 (1942).

⁶ J. Lellner, Proc. Roy. Soc. **A177**, 456 (1941).

⁷ G.W. Bhagavantam, Indian J. Phys. **4**, 1 (1929).

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¹¹ W. Kutzelnigg and R. Mecke, B. Schrader, F. Nerdel and G. Kresse, Z. Elektrochem. **63**, 109 (1961).

¹² W. Daniewski, U. Dąbrowska, Z. Piasek and T. Urbański, J. Chem. Soc. in press (1962).

dry for a longer time, freshly crystallized from methanol and dissolved in methanol seems to support the concept of zwitterionic (imidol) structure¹³ and explain the experimental observations, reported by McAdie and Frost¹⁴, that urea possesses altered properties in presence of water, methanol and ethanol.

Although the concept of zwitterionic structure of urea seems to be highly reasonable in the light of the foregoing considerations no final proof could be alleged and some authors did not agree with this concept.

Thus Ebert¹⁵ considered zwitterionic structure rather improbable and Hermanns¹⁶ pointed out that tautomerism of urea has never been demonstrated. Thiourea on the contrary can furnish S-alkyl derivatives of isothioureia through the action of simple alkylating agents upon thiourea in polar solvents.¹⁷

In the present investigation we examined infra-red spectra of urea dissolved in polar solvents, and we succeeded in alkylating urea to obtain O-alkyl derivatives of iso-urea. This experiential fact gives final evidence of the tautomerism of urea.

Infra-red Spectra

It has been now found that urea dissolved in water, methanol or ethanol gives a medium intensity band with the frequency 1650 cm^{-1} forming a shoulder with a higher intensity band $1629\text{--}1620\text{ cm}^{-1}$ produced by bending NH vibrations.^{9,18-20}

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¹⁴ H.G. McAdie and G.B. Frost, Canad. J. Chem. 33, 1275 (1955).

¹⁵ L. Ebert, Ber. Dtsch. Chem. Ges. 64, 679 (1931).

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¹⁸ H.J. Becher, Chem. Ber. 89, 1593 (1956).

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²⁰ A. Yamaguchi, T. Miyazawa, T. Shimanouchi and S. Mizushima, Spectrochim. Acta 10, 170 (1957).

As described in our previous paper,¹² a very strong band 1650 cm^{-1} is present in O-alkyl derivatives of iso-urea and is absent in dry, crystalline urea, and should be assigned to the vibrations of C=N present in the imidol form of urea, i.e. in "iso-urea".

The same shoulder 1650 cm^{-1} is present in urea freshly crystallized from any of the polar solvents mentioned above or in urea kept for several hours in an atmosphere saturated with the same solvent.

Judging from the intensity of the shoulder 1650 cm^{-1} in the solution of urea in methanol or ethanol, the concentration of imidol form of urea is of the order of a few per cent. This low concentration should account for the absence of the band c. 3.600 cm^{-1} (characterizing OH group vibrations) in the spectrum of solutions of urea. Moreover the use of methanol or ethanol as solvent makes the finding of the OH group in the dissolved substance difficult. A special investigation will be dedicated to this problem.

O-Alkylation of Urea

We found that urea dissolved in methanol and ethanol can react with diazomethane and diazoethane to give O-methyl and O-ethyl-iso-urea respectively; yield 11-12 per cent.

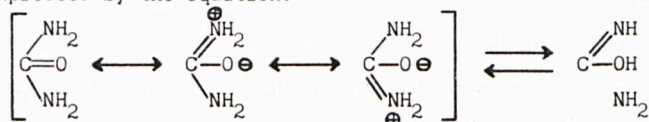
Both O-alkyl derivatives proved to be identical with those prepared from cyanamide according to Stieglitz²¹. The identification was based on the identity of physical properties including infra-red absorption spectra and chemical composition.

It was also stated that no methylation or ethylation of urea occurred when the reaction was carried out in a less polar solvent such as ethyl-ether.

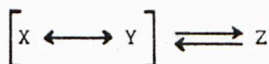
²¹ J. Stieglitz and R.A. McKee, Ber. Dtsch. Chem. Ges. **33**, 1517 (1900).

Discussion

These experiments seem to suggest that the tautomerism of urea exists and occurs in polar solvents such as water or alcohols. The tautomerism can be expressed by the equation:



It should be considered as a novel type of tautomerism, combined with resonance of a general type:



Experimental

Infra-red absorption spectra were determined in a double-beam recording Hilger spectrophotometer model H-800 with optics of rock salt.

The substances were examined either as thin films of crystalline solids or in solution. The solutions were nearly saturated and applied as films of capillary thickness.

Reaction of urea with diazomethane. Diazomethane prepared from nitroso-methylurea (25 g) in ether (150 ml) dried over potassium hydroxide was added to pure urea (m.p. 133°, 15 g) in freshly distilled methanol (200 ml) and all was kept for several hours at room temperature. Steady evolution of nitrogen ceased after 24-28 hr. Then ether and alcohol were distilled off under reduced pressure and the residue was extracted with dry ether. The crude product (3.5 g) was distilled at 78-82° (6-9 mm) to yield pure O-methylisourea, m.p. 44-45° (2.1 g, 11.3%).

There was no change in m.p. when mixed with a standard sample prepared according to the literature.²¹

The infra-red spectrum was taken and proved to be identical with that of the standard sample.

The product was dissolved in dry ether, saturated with dry hydrochloride to obtain O-methylisourea hydrochloride, m.p. 128-130°, unchanged when mixed with a standard sample²¹ (Found: N, 25.2. Calc. for $C_2H_7ON_2Cl$: N, 24.8%).

Reaction of urea with diazoethane was carried out as with diazomethane. Diazoethane was prepared from nitrozoethylurea (30 g) in ether and added to urea (15 g) in ethanol. The crude product (3.8 g) was purified by distillation (b.p. 90-92.9 mm) to yield pure O-ethylisourea, m.p. 42° (2.6 g, 11.8%). There was no change of m.p. when mixed with the standard sample prepared according to the literature.²¹

The infra-red spectrum proved to be identical with that of the standard sample.

The product was transformed into its hydrochloride as above, m.p. 122°, unchanged when mixed with a standard sample,²¹ (Found: N, 23.1. Calc. for $C_3H_9ON_2Cl$: N, 22.65%).

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