

THE STRUCTURE OF UREA AND ITS DERIVATIVES.

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For many years, attention has been paid to the problem whether urea has the classical formula (I) or an isomeric one as (II)¹ or a "Zwitterion"-structure (III).² The divergent results given by different methods have recently been reviewed thoroughly by Taylor and Baker.³ The chemical evidence is inconclusive. In the case of thiourea and its derivatives Lecher⁴ has emphasised that the high m.p. of thiourea, its insolubility in non-polar solvents, its behaviour towards acids and on alkylation or acylation seemed to point to a Zwitterion-formula (III), and the same conclusion has been reached by Hynd and MacFarlane⁵ on the basis of the reaction between urea and nitrous acid—but afterwards Lecher suggested rather a tautomeric equilibrium between (Ia) and (IIIa), and finally abandoned completely the scheme (IIIa) in favour of the classical formula (Ia).

The dielectric behaviour of urea and thiourea in their aqueous solutions indicates the presence of some molecules at least of type (III);⁶ therefore it seemed interesting to study the dipole moments of urea and

¹ Meyer-Jacobsohn, *Lehrbuch*, Vol. I, Part 2, pp. 1428, 1441, 1445.

² Formula of E. A. Werner, *J.C.S.*, 1912, **101**, 2185; 1913, **103**, 1010; as modified by Langmuir, *J. Amer. Chem. Soc.*, 1920, **42**, 244.

³ *The Organic Chemistry of Nitrogen*, Oxford, 1937.

⁴ Liebig's *Annalen*, 1924, **438**, 169; 1925, **445**, 77; 1927, **456**, 192.

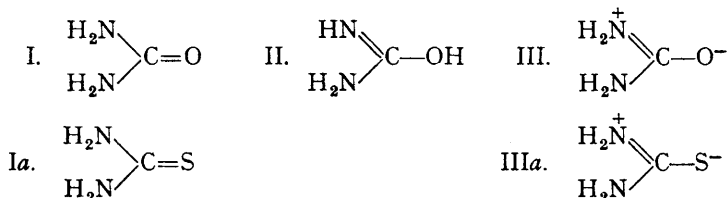
⁵ *Biochemical J.*, 1926, **20**, 1264.

⁶ Fuerth, *Annalen Physik* (4) 1923, **70**, 63; Blusch, *Z. physikal. Chem.*, 1923, **106**, 341; Devoto, *Gaz.*, 1930, **60**, 520; Ebert, *Ber.*, 1931, **64**, 679; Devoto, *ibid.*, 1329.

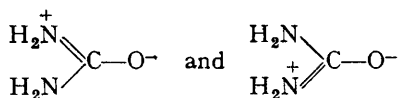
784 STRUCTURE OF UREA AND ITS DERIVATIVES

its derivatives. Such contributions to the problem have been made by Partington and Hunter,⁷ and by Devoto.⁸ Their figures which are of normal magnitude, seem to show that increasing substitution lowers the moment of the molecule (dimethyl-urea *e.g.* $\mu = 5.1$ D, tetramethyl urea $\mu = 3.3$ D, both in benzene solution). But urea and thiourea themselves have never been measured, so a comparison was impossible. We have found, now, that both these substances, although very slightly soluble in dioxane, are soluble enough to make possible an approximate determination of their moments, and have therefore determined the moments of the following series of substances :

urea	$\mu \sim 8.6$	
phenyl-urea	$= 3.6$	
(sym. diphenyl-urea	$= 4.6$	Partington and Hunter).
asym. diphenyl-urea	$= 2.7$	
N. N-diethyl-N-phenyl-urea	$= 3.2_5$	
sym. diphenyl-dimethyl-urea	$= 3.6$	
thiourea	~ 7.6	
methylthiourea	$= 4.2$	
sym. diphenyl-thiourea	$= 4.9$	



The value given for sym. diphenyl-thiourea compares satisfactorily with that reported by Partington and Hunter ($\mu = 4.85$ D), and that of Kremann and Fruhwirth for allyl-piperidyl-thiourea ($\mu = 4.61$ D). The latter authors have shown that these values (and that of methyl-thiourea above) are satisfactorily explained on the basis of the "classical" formula (I), so in terms of the "Zwitterion" theory it is obvious that increasing substitution of the urea or thiourea molecule prevents increasingly the electron transfer from the nitrogen to the oxygen atom. On the basis of our figures, it is difficult to say, which percentage of the molecules occurs in the "Zwitterion" state, but it seems safe in view even of the absolute magnitude of the observed moments, to assume that urea and thiourea are "Zwitterions" to a large extent, while their substitution products are increasingly less inclined to become "Zwitterions." According to Kohlrausch and co-workers,^{10a} the Raman spectrum of urea indicates the presence of a C=N—bond, and our conclusion is also, at least in some way, in accordance with the spectroscopic findings of Rivier and Borel.¹⁰ The X-ray analysis of solid urea points to a symmetrical formula in the solid state, but as Taylor and Baker³ have already pointed out, we have to assume, in any case, resonance between the two states



⁷ J.C.S., 1933, 87.

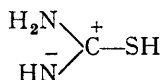
⁸ Monatshefte, 1936, 69, 319.

¹⁰ Helv. chim. acta, 1928, 11, 1219.

⁹ Gazz. chim. Ital., 1933, 63, 495.

^{10a} Z. physikal. Chem. (B), 1937, 38, 72.

which makes the two nitrogen atoms equivalent with regard to the C—O—bond. With regard to thiourea, the X-ray investigations have not yet led to definite conclusions.¹² It may be, that in the case of thiourea a "zwitterion" form of the structure



contributes towards the high dipole moment, which structure has been advocated recently by Clow.¹³ This cannot be decided by dipole measurements only, but it may be pointed out that according to Gilman and Nelson¹⁴ thiourea does not give the sulfhydryl reaction with triethylbismuth or tetraethyl-lead.

Experimental.

Urea and thiourea were purified by repeated recrystallisation from propyl alcohol and dioxane respectively, the sym. diphenyl derivatives from xylene and toluene, N, N-diphenylurea from amyl alcohol.

Sym. Diphenyl-dimethyl-urea was prepared according to the recipe of Michler and Zimmermann,¹⁵ but with certain alterations: A solution of monomethyl-aniline (50 g.) in benzene was saturated with phosgene gas, irrespectively of the occurring rise in temperature. Then the solvent was evaporated and the residue directly distilled in a good vacuum. Up to 100°/6 mm. monomethyl-aniline went over, then at 110–115°/0.6 mm. the desired urea derivative, which solidified spontaneously and was recrystallised from 50 per cent. acetic acid, then from 50 per cent. methyl alcohol. Long needles; m.p. 127.5°; yield, 14–20 g.

Methyl thiourea. According to Andreasch,¹⁶ methyl isothiocyanate (10 g.) and concentrated (20 per cent.) aqueous ammonia solution (100 c.c.) were kept at room temperature for twelve hours. The solvent was evaporated in vacuo and the residue recrystallised from propyl alcohol. Prisms; m.p. 130–131°.

Phenyl-urea was prepared according to "Organic syntheses."¹⁷ From amyl alcohol, m.p. 149°.

N.N.-Diethyl-N'-phenyl-urea was prepared according to Gebhardt¹⁸ from phenyl isocyanate (5 g.) and diethylamine (6.1 g.), which reacted smoothly at zero temperature in benzene solution (5 c.c.). From a mixture of benzene and light petroleum (b.p. 40–60°) needles, m.p. 90°.

Measurements.

All measurements were carried out in dioxane solution. The solutions of urea and thiourea were prepared by shaking the finely-powdered substances with dioxane at the proposed temperature of the measurement, cooling down by about 10° and filtering. The concentration was determined by evaporating an aliquot part of the solution. In the tables, the figures have the following significance: c = molar fraction, ρ = density, ϵ = dielectric constant, n = refractive index, $P_{1,2}$ ($P_{E1,2}$) = total (electronic)

¹¹ Becker and Jancke, *Z. physikal. Chem.*, 1921, **99**, 242. Mark and Weissenberg, *Z. Physik*, 1923, **16**, 1; *Ber.*, 1924, **57**, 1820; Hendricks, *J. Amer. Chem. Soc.*, 1928, **50**, 2455; Wyckoff, *Ztschr. Krystallogr.*, 1930, **75**, 529.

¹² Demény and Nitta, *Chem. Centralbl.*, 1928, II, 1970; Wyckoff and Corey, *Z. Kristallogr.*, 1933, **81**, 386.

¹³ Clow, *Trans. Faraday Soc.*, 1938, **34**, 457.

¹⁴ *J. Amer. Chem. Soc.*, 1937, **59**, 935.

¹⁶ *Monatshefte*, 1881, **2**, 277.

¹⁷ *Collective volume*, **1**, 442; New York, 1932.

¹⁵ *Ber.*, 1879, **12**, 1165.

¹⁸ *Ber.*, 1884, **17**, 3039.

786 STRUCTURE OF UREA AND ITS DERIVATIVES

polarisation of the solution $P(P_E)$ = the same for the solute, P_{A+0} = (atomic +) orientation polarisation, which is extrapolated graphically for infinite dilution.

ϵ .	ρ .	ϵ .	n^2 .	$P_{1,2}$.	$P_{E1,2}$.	P .	P_E .	P_{A+0} .
Urea ($t = 47.1^\circ$).								
0	1.0216	2.2241	—	24.962 ₈	—	—	—	—
0.00057	1.0239	2.2856	—	25.777 ₁	—	1444	15.9	1428
				$\mu \sim 8.6$ D.		(Calc.).		

Phenyl-urea ($t = 17.3^\circ$).								
0	1.0343	2.2361	2.0235	24.826 ₇	21.652 ₈	—	—	—
0.00507	1.0350	2.3385	2.0278	26.304 ₄	21.757 ₀	316.51	42.28	274.23
0.01644	1.0366	2.5594	2.0363	29.295 ₈	21.991 ₈	296.24	42.25	253.99
				$P_{A+0}^\infty = 280$		$\mu = 3.6 \pm 0.2$ D.		

Asym. Diphenyl-urea ($t = 17.0^\circ$).								
0	1.0343	2.2362	2.0238	24.826 ₇	21.645 ₇	—	—	—
0.00538	1.0351	2.2963	2.0289	25.847 ₁	21.876 ₈	214.47	64.21	150.26
0.00718	1.0354	2.3157	2.0311	26.173 ₈	21.960 ₀	212.31	65.15	147.16
				$P_{A+0}^\infty = 155$		$\mu = 2.7 \pm 0.1$ D.		

N. N-Diethyl-N'-phenyl-urea ($t = 16.8^\circ$).								
0	1.0343	2.2363	2.0235	24.826 ₇	21.642 ₈	—	—	—
0.00572	1.0345	2.3288	2.0275	26.271 ₄	21.834 ₀	277.24	55.10	221.12
0.01116	1.0347	2.4160	2.0309	27.630 ₈	22.038 ₈	276.17	57.14	220.05
						average 56.12		
$P_{A+0}^\infty = 225.$				$\mu = 3.2 \pm 0.1$ D.				

sym. Diphenyl-dimethyl-urea ($t = 23.7^\circ$).								
0	1.0306	2.2345	2.0164	24.948 ₈	21.608 ₈	—	—	—
0.00398	1.0307	2.3100	2.0200	26.128 ₈	21.812 ₈	334.8	72.7	262.1
0.00849	1.0309	2.4055	2.0243	27.231 ₉	22.045 ₈	347.5	73.1	274.4
				P_{A+0}^∞ (average) = 268.		$\mu = 3.6 \pm 0.1$ D.		

Thiourea ($t = 46.9^\circ$).								
0	1.0217	2.2242	—	24.960 ₈	—	—	—	—
0.00181	1.0249	2.3864	—	27.003 ₁	—	1153	24.3	1129
0.00213	1.0245	2.3987	—	27.3056	—	1128	24.3	1104
						(Calc.).		
				P_{A+0}^∞ (average) = 1117.		$\mu \sim 7.6$ D.		

Methyl-thiourea ($t = 17.5^\circ$).								
0	1.0343	2.2360	2.0235	24.826 ₇	21.642 ₈	—	—	—
0.00339	1.0343	2.3338	2.0246	26.188 ₀	21.661 ₈	426.19	27.24	398.9
0.00462	1.0343	2.3556	2.0249	26.482 ₈	21.667 ₀	383.06	26.94	356.1
				P_{A+0}^∞ (average) = 378.		$\mu = 4.2 \pm 0.1$ D.		

Sym. Diphenyl-thiourea ($t = 25.5^\circ$).								
0	1.0295	2.2364	2.0108	24.945 ₉	21.541 ₈	—	—	—
0.00677	1.0308	2.4925	2.0221	28.667 ₈	21.928 ₀	574.55	78.62	495.9
				$\mu = 4.9$ D.				

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