

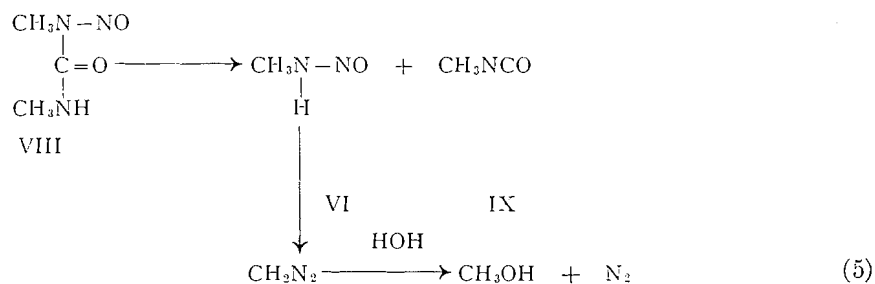
Table I shows some of the substituted ureas prepared, together with their physical properties and yields. Nearly quantitative yields were obtained and in several cases purification was unnecessary.

TABLE I
N-SUBSTITUTED UREAS¹, RNHCONH₂ (VII)

N-Substituent R	Reaction time, min.	Yield, %	M.p. °C.		Solvents	Ref.
			Observed	Recorded		
Methyl	5	96.1	101	102	Ethanol plus ether	4
Ethyl	5	92.1	92	92-92.4	Ethanol plus ether	4
<i>n</i> -Propyl	5	86.8	107	107	Ethanol plus ether	3
<i>n</i> -Butyl	5	85.8	96	96	Ethanol plus ether	4
<i>n</i> -Amyl	3	70.8	75 ²	75	Water	5
<i>n</i> -Hexyl	5	88.6	109.5	109.5	Water	7
Cyclohexyl	12	86.8	195-196	195-196	Water	11
Phenyl	20	91.0	146-147	147	Water	4
Benzyl	15	80.0	147-147.5	147-147.5	Water	13
Amino	1	100	227-234 ^d	214-235 ^d	Ethanol	10
Anilino	5	100	172	171-172	Ethanol	8
<i>p</i> -Tolyl	20	85.3	181-182	181-182	Ethanol	12
<i>p</i> -Chlorophenyl	30	90.4	212 ^d	212 ^d	Ethanol	15
Diethyl	1	91.9	75	75-75.3	Ether	4

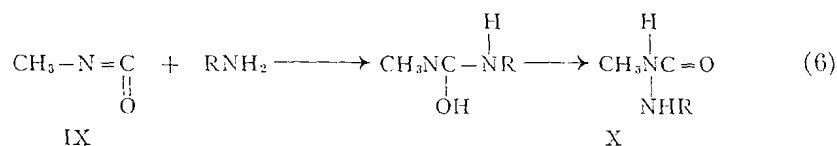
¹ All melting points are uncorrected. ² Isolated as the nitrate.
³ Semicarbazide isolated as its benzal derivative.

In addition to this series of N-substituted ureas, other derivatives of ureas were made from N, N'-dimethyl-N-nitrosourea (VIII). This starting material has been found to decompose in aqueous solution according to the following scheme:-



When compound VIII was boiled with water, nitrogen was evolved quantitatively in accordance with Equation (5), and methyl isocyanate (IX) was formed as was shown by its hydrolysis to methylamine and carbon dioxide. Similarly to N-nitroso-N-methylurea, the reaction of amines with N-nitroso-N, N'-dimethylurea proceeded through the formation of methyl nitrosoamide

(VI) and methyl isocyanate (IX), the latter reacting with amines to yield N-methyl-N'-substituted ureas (X).



The yields were excellent and, in most cases, the N-substituted-N'-methylureas did not require further purification. The results are given in Table II.

TABLE II
N-SUBSTITUTED-N'-METHYLUREAS, RNHCONHCH₃ (X)

N-Substituent R	Reaction time, min.	Yield, %	M.p. °C.		Solvents	Ref.
			Observed	Recorded		
Methyl	12	73.8	100	100	Ether	6
Ethyl	3	88.0	52-53	52-53	Ether	14
<i>n</i> -Propyl ¹	5	84.3	67-68		Ether	
<i>n</i> -Amyl ²	2	94.3	75-76		Diluted ethanol	
Cyclohexyl ³	3	90.4	157-158		Diluted ethanol	
Phenyl	12	77.7	150.5-151.5	150.5-151.5	Diluted ethanol	6
Benzyl	4	84.2	98-99	98-99	Diluted ethanol	9
Anilino	20	76.0	154-155	154-155	Water	6
Amino	2	92.1	114-115	112-118	Ethanol plus ether	2
<i>p</i> -Tolyl	10	87.1	178	178	Ethanol	1
<i>p</i> -Chlorophenyl	10	88.7	200	200	Diluted ethanol	1

¹Calc. for C₅H₁₂ON₂: N, 24.1%. Found: N, 23.8%.

²Calc. for C₇H₁₆ON₂: N, 19.4%. Found: N, 19.3%.

³Calc. for C₈H₁₆ON₂: N, 17.9%. Found: N, 17.2%.

Experimental

Effect of Boiling Water on N-methyl-N-nitrosourea

In a flask equipped to measure the gas evolved was placed N-methyl-N-nitrosourea (3.8450 gm.; 0.0414 mole) and water (125 ml.). The mixture was boiled and the solid dissolved with evolution of gas. The volume of gas which was collected over a solution of sodium hydroxide (20%) was found to be 808 ml. (calc. 816 ml.). The presence of isocyanic acid was shown in the following way: A slight excess of silver nitrate was added to the solution and a white precipitate soluble in ammonia and nitric acid was formed. However, the amount of isocyanic acid produced was not quantitative.

The presence of methyl alcohol was shown by the oxidation of a portion of the solution with potassium dichromate in strong sulphuric acid. After distilling a portion of this solution, the distillate contained formaldehyde as was shown by the derivative obtained with 2, 4-dinitrophenylhydrazine, m.p. 166-167°C.

Effect of Boiling Water on N-Nitroso-N, N'-dimethylurea

Using the procedure described above, N-nitroso-N, N'-dimethylurea (2.6920 gm.) was boiled with water. Nitrogen evolved: 542 ml. (calc. 552 ml.). No precipitation took place with a silver nitrate solution, indicating the absence of isocyanic acid. The formation and identification of methylamine and carbon dioxide indicated the transient formation of methyl isocyanate. The presence of methyl alcohol was demonstrated as described above.

Preparation of N-substituted ureas (VII)

N-Methyl-N-nitrosourea (0.1 mole) was reacted with an amine (0.1 mole) in aqueous solution (200 ml.). The solution was boiled until the evolution of gas ceased. Then it was evaporated under reduced pressure and the residue recrystallized from a suitable solvent. Results are listed in Table I. In several cases, recrystallization did not change the melting point of the product.

Preparation of N-Substituted-N, N'-dimethylurea (X) from N, N'-Dimethyl-N-nitrosourea (VIII)

The procedure used for the preparation of these substances was the same as the one described above for the preparation of N-substituted ureas (VII). The results are listed in Table II.

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References

1. BOEHMER, J. W. *Rec. trav. chim.* 55: 379. 1936.
2. BOUGAULT, J. *Compt. rend. acad. sci. U.R.S.S.* 160: 625. 1915.
3. CHANCEL, F. *Bull. soc. chim.* 9 (3): 102. 1893.
4. DAVIS, T. L. and BLANCHARD, K. C. *J. Am. Chem. Soc.* 51: 1797. 1929.
5. DAVIS, T. L. and CONSTAN, N. D. *J. Am. Chem. Soc.* 58: 1800. 1936.
6. DEGNER, O. and PECHMANN, H. *Ber.* 30: 651. 1897.
7. NORSTEDT, C. and WAHLFORSS, H. A. *Ber.* 25: 637. 1892.
8. PELLIZZARI, G. *Ber.* 20: 2359. 1887.
9. SCHMIDT, E. and HENNIG, W. *Arch. Pharm.* 251: 400. 1913.
10. THIELE, J. *Ann.* 270: 34. 1892.
11. WALLACH, O. *Ann.* 343: 46. 1905.
12. WALTHER, R. and WLODKOWSKI, S. *J. prakt. Chem.* 59 (2): 275. 1899.
13. WERNER, E. A. *J. Chem. Soc.* 1115: 1101. 1919.
14. WURTZ, M. A. *Compt. rend. acad. sci. U.R.S.S.* 32: 417. 1851.
15. YOUNG, G. and DUNSTAN, A. E. *J. Chem. Soc.* 93: 1058. 1908.