# PREPARATION OF N-SUBSTITUTED UREAS FROM NITROSOMETHYLUREAS<sup>1</sup>

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#### Abstract

Good yields of N-substituted ureas were obtained by reacting amines with N-nitroso-N-methylurea in aqueous solution. It has been shown that N-nitroso-N-methylurea decomposed into methylnitrosamide and isocyanic acid. Similarly, N-nitroso-N, N'-dimethylurea and amines gave rise to good yields of N-substituted-N'-methylureas.

#### Introduction

Davis and Blanchard (4) have shown that nitrourea (I) decomposed in aqueous solution into isocyanic acid (III) and nitramide (II) which is transformed into nitrous oxide (IV) and water. The formation of isocyanic acid was inferred from the reaction of nitrourea in aqueous solution with amines to yield N-substituted ureas, quantitatively in several instances.

The reaction of nitrosoureas with amines has not been studied. However, it may be postulated that N-methyl-N-nitrosourea (V) decomposes in aqueous solution into N-methyl-N-nitrosamide (VI) and isocyanic acid (III) according to the mechanism suggested by T. L. Davis (Equations (1) and (2)). In strongly alkaline solution compound V is known to yield diazomethane. When N-methyl-N-nitrosourea (V) was boiled in aqueous solution, the stoichiometric amount of nitrogen was evolved and the solution was found to contain isocyanic acid and methanol. With amines, as was expected, the isocyanic acid produced yielded N-substituted ureas (VII) according to the following equation:-

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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 ureas', RNHCONH2 (VII)

N-Sub- stituent R	Reaction time, min.	$rac{\mathrm{Yield,}}{c_c'}$	M.p. °C.		Solvents	Ref.
			Observed	Recorded	Solvents	Ker.
Methyl	5	96.1	101	102	Ethanol plus ether	4
Ethyl	5	92.1	92	92-92.4	Ethanol plus ether	-1
n-Propyl	5	86.8	107	107	Ethanol plus ether	3
n-Butyl	5	85.8	96	96	Ethanol plus ether	4
n-Amyl	3	70.8	$75^{2}$	75	Water	5
n-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	-1
Benzyl	15	80.0	147-147.5	147-147.5	Water	13
Amino	1	100	227-234d	214-235d	Ethanol	10
Anilino	5	100	172	171-172	Ethanol	8
p-Tolyl	20	85.3	181-182	181-182	Ethanol	12
p-Chlorophenyl	30	90.4	212d	212d	Ethanol	15
Diethyl	1	91.9	75	75-75.3	Ether	4

<sup>&</sup>lt;sup>1</sup> All melting points are uncorrected. <sup>2</sup> Isolated as the nitrate.

<sup>3</sup> 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:-

$$CH_{3}N - NO$$

$$C = O \longrightarrow CH_{3}N - NO + CH_{3}NCO$$

$$CH_{3}NH \qquad H$$

$$VIII$$

$$VI \qquad IX$$

$$+ HOH$$

$$CH_{2}N_{2} \longrightarrow CH_{3}OH + N_{2} \qquad (5)$$

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).

$$CH_3-N=C + RNH_2 \longrightarrow CH_3NC-NR \longrightarrow CH_3NC=O$$

$$OH \qquad NHR$$

$$IX \qquad X$$

$$(6)$$

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-Sub- stituent R	Reaction time, min.	Yield, %	M.p. °C.		Solvents	Ref.
			Observed	Recorded	Solvents	Kei.
Methyl	12	73.8	100	100	Ether	6
Ethyľ	3	88.0	52-53	52-53	Ether	14
n-Propyl <sup>1</sup>	5	84.3	67-68		Ether	
n-Amyl²	2	94.3	75-76		Diluted ethanol	
Cyclohexyl <sup>3</sup>	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
p-Tolyl	10	87.1	178	178	Ethanol	1
p-Chlorophenyl	10	88.7	200	200	Diluted ethanol	1

## 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 isocvanic acid. The formation and identification of methylamine and carbon dioxide indicated the transient formation of methyl isocvanate. 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-Nnitrosourea (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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