for the substitution of ethanol as a washing agent, yield from 13 g. of 3-aminopyridine-1-oxide 2.3 g. of light yellow oil, b.p. 95–100° (2 mm.) which solidified on standing, m.p. 53°. It was unstable in air.

Anal. Calcd. for $C_{11}H_{18}N_2O_3$: N, 12.38. Found: N, 12.29.

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Reaction of Phenyl Isocyanate with *N,N*-Dimethylformamide

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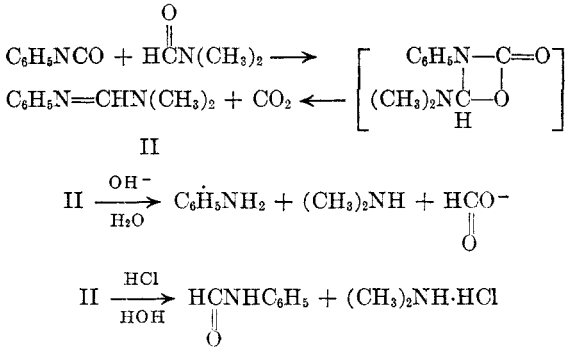
The reactions of phenyl isocyanate with *p*-dimethylaminobenzaldehyde to form *p*-dimethylaminobenzalaniline, and with nitrosobenzene to form azobenzene have been earlier reported.[2] In both reactions, the authors have postulated the intermediate formation of an unstable four-membered ring which loses carbon dioxide to form the final product.

In the present work, phenyl isocyanate was found to react readily with *N,N*-dimethylformamide (I) in excess I as solvent at 150°. The reaction proceeded analogously to the earlier reported reactions[2] with the evolution of nearly one mole of carbon dioxide per mole of isocyanate and led to the formation of *N,N*-dimethyl-*N'*-phenylformamidine (II) in 80% yield. A parallel instance of this amidine-forming reaction, one which involves the reaction of *p*-toluenesulfonyl isocyanate with *N,N*-dimethylformamide, has recently been reported.[3]

Alkaline hydrolysis of II led to the isolation of aniline, dimethylamine, and formic acid. Mild acidic hydrolysis of II permitted the isolation of the intermediate hydrolysis product, formanilide.



The reaction of an excess of phenyl isocyanate with I at 150° resulted in a reduced yield (25%) of the formamidine II and the concomitant recovery of a considerable quantity of a mixture of solid products. Fractional recrystallization of these solids led to the isolation of 1,1-dimethyl-3-phenylurea and a second material (III) that was not fully characterized.

EXPERIMENTAL[4]

N,N-Dimethyl-N'-phenylformamidine (II). A mixture of of 40 g. (0.336 mole) of phenyl isocyanate and 161 g. (2.21 moles) of redistilled *N,N*-dimethylformamide (I) was refluxed for 4 hr. with provision made for the absorption of any evolved carbon dioxide in aqueous potassium hydroxide solution. At the end of the reflux period, 0.312 mole of carbon dioxide was found to have been liberated. The major portion of the unchanged I was removed by distillation. The residue was then distilled to provide 41 g. (80%) of impure *N,N*-dimethyl-*N'*-phenylformamidine (II), b.p. 68–71° (0.05 mm.), n_D^{25} 1.5913, λ_{max} 6.12 and 9.05 μ.

Anal. Calcd. for $C_9H_{12}N_2$: C, 72.97; H, 8.11; N, 18.92. Found: C, 72.14; H, 7.82; N, 20.13.

Basic hydrolysis of the formamidine II. A mixture of 19.3 g. (0.132 mole) of II, 8.6 g. (0.131 mole) of potassium hydroxide, 30 ml. of water, and 100 ml. of methanol was refluxed for 16 hr. with provision made for the absorption of any evolved dimethylamine in dilute aqueous hydrochloric acid. The reaction mixture was distilled free of methanol the distillate being collected in another portion of dilute acid. The two acid solutions were combined, concentrated, and adjusted to a *p*H of 11 by the addition of 20% aqueous potassium hydroxide solution at 5°. The addition of 20 g. of phenyl isothiocyanate to the basic solution, with agitation, caused almost immediate solidification of the mixture. After standing at room temperature for several hours, the solids were filtered to provide 16.9 g. (0.093 mole) of crude 1,1-dimethyl-3-phenylthiourea, m.p. 116–126°. Repeated recrystallization from benzene raised the melting point to 133–136.5° (lit.[5] m.p. 135°), undepressed on admixture with an authentic sample prepared from dimethylamine and phenylisothiocyanate.

The basic residue from the distillation of the hydrolysis reaction mixture was steam distilled and the distillate was extracted with benzene. Addition of 20 g. of phenylisothiocyanate to the concentrated benzene extract resulted in the isolation of a 68% yield of aniline as thiocarbanilide, m.p. 151–152.5° (lit.[5] m.p. 154°), undepressed on admixture with an authentic sample.

The residue from the steam distillation of the reaction mixture was brought to *p*H 8 and, after dilution with an equal volume of ethanol, was refluxed with 16 g. of *p*-bromophenacyl bromide for 1 hr. The hot reaction mixture was filtered and the solids obtained were recrystallized from toluene to provide 7.9 g. (0.032 mole; 24%) of crude *p*-bromophenacyl formate, m.p. 128–133°. Repeated recrystallization from 95% ethanol raised the melting point to 138–141° (lit.[6] m.p. 140°), undepressed on admixture with an authentic sample.

Acid hydrolysis of the formamidine II. A mixture of 5 g. (0.038 mole) of II and 100 ml. of 0.38*N* aqueous hydrochloric acid was allowed to stand for 16 hr. and was then heated at 50° for 45 min. The cooled solution was saturated with sodium chloride and extracted with benzene. The benzene was evaporated at room temperature to leave an oil which subsequently solidified on standing in the freezer. The solidified oil was recrystallized from a mixture of toluene and ligroin to give 2.65 g. (65%) of formanilide, m.p.

(1) Kordite Company, Macedon, N. Y.
(2) H. Staudinger and R. Endle, *Ber.*, **50**, 1042 (1917).
(3) C. King, *J. Org. Chem.*, **25**, 352 (1960).
(4) All melting and boiling points are uncorrected.
(5) R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, John Wiley and Sons, Inc., New York, N. Y., 3rd Ed., 1948, p. 234.
(6) R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, John Wiley and Sons, Inc., New York, N. Y., 3rd Ed., 1948, p. 222.

45–47.5° (lit.[6] m.p. 47°), undepressed on admixture with an authentic sample.

Formation of solid byproducts in the reaction of phenylisocyanate with I. A mixture of 57.4 g. (0.482 mole) of phenyl isocyanate and 17.6 g. (0.241 mole) of I was heated at 160° for 13 hr. The reaction mixture was distilled to provide 3 g. of unchanged phenyl isocyanate and a 25% yield of the formamidine II. A considerable fraction of the reaction mixture remained as a solid residue in the distillation flask. This solid material was continuously extracted with ligroin (b.p. 66–75°) for 72 hr. at the end of which time 8.2 g. of impure 1,1-dimethyl-3-phenylurea had been extracted and was isolated as an insoluble solid in the extracting solvent, m.p. 118–126°. Repeated recrystallization from a benzene ligroin mixture raised the melting point to 132–135° (lit.[7] m.p. 134°), undepressed on admixture with an authentic sample prepared from the reaction of phenyl isocyanate with excess anhydrous dimethylamine.

The unextracted material remaining from the ligroin extraction was repeatedly recrystallized from a mixture of benzene and ligroin to yield 20.84 g. of a crystalline product (III), m.p. 227–228.5°, λ_{max} 5.73, 5.77, and 5.92 μ. Compound III, which was not further characterized, provided the following analysis.

Anal. Found: C, 72.28; H, 4.29; N, 12.52.

Acknowledgment. The author is indebted to D. L. Harms for the infrared spectral determinations.

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(7) R. Stolle, *J. prakt. Chem.*, **117**, 201 (1927).

Chemotherapeutic Nitrofurans. VI.[1] 3-(5-Nitrofurfurylideneamino)tetrahydro-2(1H)pyrimidinone

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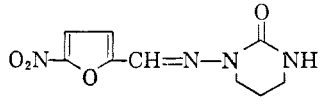
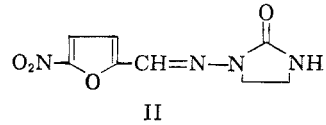
Interest in the chemotherapeutic activity of nitrofuran compounds has led to the preparation of 3-(5-nitrofurfurylideneamino)tetrahydro-2(1H)-pyrimidinone (I). A corresponding five-membered ring compound (II) has been reported.[2,3]



I



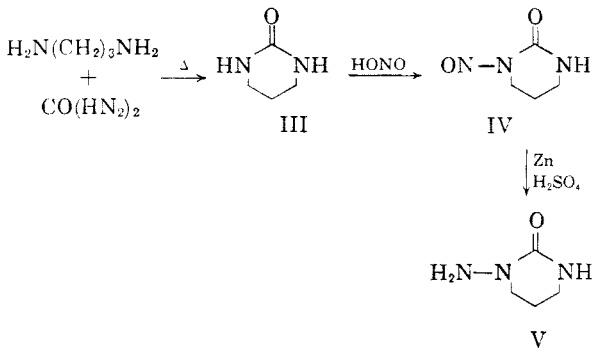
II

(1) For the previous paper in this series see Abstracts of Papers, 137th Meeting American Chemical Society, April 1960, p. 30N.

(2) J. G. Michels and G. Gever, *J. Am. Chem. Soc.*, **78**, 5349 (1956).

(3) G. Gever and J. G. Michels, U. S. Patent **2,746,960** (1956).

The method used for the synthesis of I is shown in the following scheme:



Tetrahydro-2-(1H)pyrimidinone (III) has been prepared by several methods[4–10] but none of these is particularly suited to large scale laboratory preparation. It was found most convenient to prepare III by heating a mixture of trimethylenediamine and urea. This general method of forming heterocyclic rings by heating urea with appropriately disubstituted aliphatic compounds has been used for the preparation of 2-oxazolidinones[11] and 2-thiazolidinone.[2]

The mononitrosation and reduction of III was carried out in the same manner described earlier for II.[2,3] Neither the intermediate nitroso compound IV nor the amino compound V was isolated. Treatment of the aqueous reduction solution containing the 3-aminotetrahydro-2(1H)pyrimidinone with an alcoholic solution of 5-nitrofurfural caused the direct precipitation of the desired product, I.

EXPERIMENTAL

Tetrahydro-2(1H)pyrimidinone. A mixture of 74 g. (1 mole) of trimethylenediamine, 43 g. (0.67 mole) of urea, and 18 ml. of water was heated under reflux (internal temperature 115°) for 4 hr. The water and excess amine were then distilled. The internal temperature rose slowly and after 2 hr. was 155°. During this heating period frothing occurred and a solid began to separate. After an additional 1.5 hr. heating, the solid was melted with a free flame, then allowed to cool. Recrystallization of the solid residue from 850 ml. of 95% alcohol using Darco gave 53 g. of the name compound, m.p. 258–262° (copper block; uncorr.). Evaporation of the alcoholic mother liquor and recrystallization of the residue from 450 ml. of 95% alcohol using Darco gave an additional 6 g. of product of the same melting point.

(4) E. Fischer and H. Koch, *Ann.*, **232**, 222 (1886).

(5) J. Tafel, *et al.*, *Ber.*, **33**, 3383 (1900); *Ber.*, **34**, 3286 (1901).

(6) A. P. N. Franchimont and H. Friedmann, *Rec. trav. chem.*, **26**, 218 (1907).

(7) Y. Iwakura, *Chem. High Polymers (Japan)*, **4**, 94 (1947); *Chem. Abstr.*, **45**, 2711g (1951).

(8) A. F. McKay, *et al.*, *J. Am. Chem. Soc.*, **71**, 766 (1949).

(9) C. W. Smith, U. S. Patent **2,662,080** (1953); *Chem. Abstr.*, **49**, 1110e (1955).

(10) J. J. Fox and D. Van Praag, *J. Am. Chem. Soc.*, **82**, 486 (1960).

(11) W. J. Close, *J. Am. Chem. Soc.*, **73**, 95 (1951).