

TABLE I.—FILTRATION RESULTS OF OIL CONTAMINATED WITH LOW COUNT LYOPHILIZED CULTURES

Microorganism	Days			
	1	3	5	7
<i>S. aureus</i>	0 ^a	+ ^b	+++	+++
<i>E. coli</i>	0	0	+	++
<i>B. subtilis</i>	0	+	++	+++

^a 0, No growth. ^b +, Growth.

DISCUSSION

Toxicity Studies on Triton X 100.—The detergent Triton X 100 at 0.1% concentration was nontoxic when in contact with vegetative forms of bacteria for several hours. The surfactant may be used at room or temperatures of $45 \pm 1^\circ$ during the membrane washing phase. An additional wash with peptone 0.1% is used to remove the excess detergent and sustain viability of microorganisms that were impinged on the membrane, thereby maintaining the sensitivity of the method (9, 10).

Bacteriological Validity of the Proposed Procedure.—Low count (approximately 25–125 in number), lyophilized cultures of *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis* spores were inoculated into 200 ml. of liquid coconut oil. The contaminated oils were treated as described under Procedure. (See Table I.)

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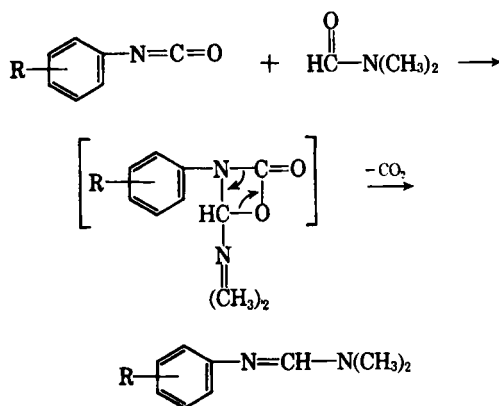
Convenient Synthesis of *N,N,N'*-Trisubstituted Formamidines

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The applicability of a method for preparing trisubstituted formamidines by treating isocyanates with an excess of formamides under neutral conditions at 150° was examined. This amidine-forming reaction was limited to the use of aryl isocyanates when treated with *N,N*-dimethylformamide as the solvent.

RECENT DISCLOSURE of the reaction of *p*-toluenesulfonyl isocyanate (1) and phenyl isocyanate (2) with *N,N*-dimethylformamide (DMF) to form amidines prompted a further investigation into the scope of this facile method for the preparation of trisubstituted formamidines. The synthesis of amidines and formamidines by the interaction of substituted amides with anilines in the presence of phosphorus pentachloride (3–5) or phosphorus oxychloride (6) has been reported previously. More recently, symmetrical *N,N'*-diarylacetylaminides were prepared by heating 2 moles of an aromatic amine with 1 mole of ethyl orthoacetate in the presence of *p*-toluenesulfonic acid (7) or, more effectively, acetic acid (8).

In the present investigation, the applicability of a method for preparing trisubstituted formamidines by treating isocyanates with an excess of formamides under neutral conditions at 150° was examined. This method was limited to the use of aryl isocyanates when treated with DMF as the solvent at 150° under neutral conditions. One mole of carbon dioxide was evolved per mole of isocyanate consumed in the reaction. By the removal of unreacted DMF, the *N,N*-dimethyl-*N'*-aryl formamidines could be isolated in 75–98% yield in a high state of purity.



The cyclic mechanism postulated by King (1) for the formation of the sulfonylamidine and by Weiner (2) for formamidine is supported by observations that groups on the benzene ring which tend to increase the electrophilicity of the isocyanate increase the rate of the reaction, whereas electron-donating groups have a tendency to decrease the rate of formation of the formamidine. 2,4,5,6-Tetrachlorophenylene diisocyanate readily formed the bis formamidine under the same reaction conditions. However, formamide failed to yield a formamidine with phenyl isocyanate under the conditions of our experiment, since formanilide was the isolated product.

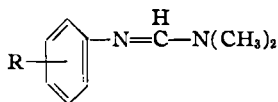
Similarly, the treatment of alkyl isocyanates with *N,N*-dimethylformamide or aryl isocyanates with

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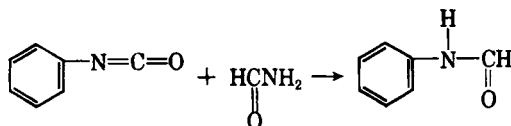
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TABLE I.—*N,N,N'*-TRISUBSTITUTED FORMAMIDINES

R	Salt	M.p., or B.p., °C., mm.	n_D^{25}	C, %		H, %		N, %	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
H	...	61-63 (0.01) ^a	1.5936
H	HCl	234-235 ^b
H	CH ₃ I	143-144
3-Cl	...	120 (0.4)	1.6041	59.18	59.11	6.07	6.38	15.34	15.08
3-Cl	HCl	234-235.5	...	49.33	49.60	5.52	5.64	12.79	13.06
3-Cl	CH ₃ I	208-209	...	37.00	36.72	4.35	4.38
2-Cl	...	157 (14)	1.6009	59.18	59.18	6.01	6.04
2-Cl	HCl	202-203	...	49.33	49.48	5.52	5.33
2-OCH ₃	...	136 (0.4)	1.5895	67.38	67.19	7.92	8.03	15.72	16.08
2-OCH ₃	HCl	208-209	...	55.94	55.78	7.04	6.70	13.05	13.16
2-OCH ₃	CH ₃ I	140-142	...	41.26	41.30	5.35	5.36
3-NO ₂	...	153 (0.35)	1.6250	55.95	56.23	5.74	6.05
3-NO ₂	HCl	260-261	...	47.05	47.05	5.27	5.47
4-Cl	...	160 (14)	1.6024	59.18	58.90	6.01	6.02
4-Cl	HCl	232-233	...	49.33	49.17	5.52	5.10
4-NO ₂	...	77-78	...	55.95	55.70	5.74	5.78
2-NO ₂	...	152-157 (0.4)	1.6153	55.95	55.78	5.74	5.74
3,4-diCl	...	140-148 (0.55)	1.6218	49.79	49.80	4.64	4.77	12.91	12.52
3,4-diCl	HCl	164-165	...	42.63	42.31	4.37	4.72	11.05	11.06
3,4-diCl	CH ₃ I	188-189	...	33.45	33.17	3.65	3.91	7.80	7.84
2,4,5,6-tetra Cl-
3-N=CH-N(CH ₃) ₂	...	157.5-158.5	...	40.47	40.28	3.96	4.04
2,4,5,6-tetra Cl-
3-N=CH-N(CH ₃) ₂	HCl	218-219 ^c	...	31.00	31.34	4.34	4.24

^a Lit. (2) b.p. 68-71° (0.05 mm.) and (4) 78-80° (0.1 mm.). ^b Lit. (6) m.p. 230-235°. ^c Dihydrate.



N,N-diethylformamide at 150° failed to yield the desired formamidines.

Table I summarizes the data on the reaction products obtained from the aryl isocyanates.

EXPERIMENTAL¹

The following example is representative of the method employed for the preparation of the formamidines and their salts.

***N,N*-Dimethyl-*N'*-3-chlorophenylformamidinium.**—A mixture of 51.5 Gm. (0.336 mole) of *m*-chlorophenyl isocyanate (Eastman White Label) and 161 Gm. (2.21 moles) of redistilled DMF was refluxed for 4 hours in a 250-ml. flask equipped with a condenser; provision was made for the absorption of any evolved carbon dioxide in aqueous potassium hydroxide solution in a 250-ml. conical flask connected to the condenser with a short length of rubber tubing. The titration of the evolved CO₂ served as

¹ Both the melting points and the boiling points were uncorrected. All melting points were obtained in a Thomas-Hoover silicone-filled capillary melting point apparatus. The technical assistance of Mr. Richard C. Pharo for the experimental portion of this work and of Mr. John E. Zarembo and his staff in carrying out the analyses reported is gratefully acknowledged.

an indication of the rate of the reaction and as a determination of when the reaction had been completed. The major portion of unreacted DMF was then removed by distillation. The residue was then distilled at reduced pressure to provide 54 Gm. (89% yield) of analytically pure product, b.p. 120° (0.4 mm.), n_D^{25} 1.6041.

The hydrochloride salt was prepared by treating an ethereal solution of the formamidinium with gaseous hydrogen chloride for 5 minutes; filtration of the resulting precipitate and recrystallization from ethanol yielded a white powder, m.p. 234-235.5°.

The methiodide was prepared by treating 10.0 Gm. (0.055 mole) of the amine with 15.6 Gm. (0.11 mole) of methyl iodide in 30 ml. of isopropyl alcohol in a 100-ml. flask equipped with a reflux condenser and a drying tube and heated at reflux for 60 hours. To the flask was added 200 ml. of ether, and the resulting precipitate was filtered and recrystallized from isopropyl alcohol to yield 12.0 Gm. of white crystals, m.p. 208-209°. Concentration of the mother liquor yielded an additional 2.8 Gm. of product, m.p. 204-209°.

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