Notes

Reactions of Aryl Isocyanates with Substituted Formamides and Formamidines

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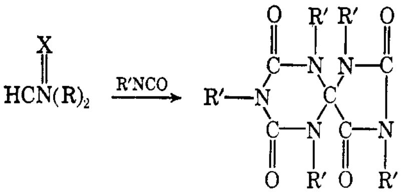
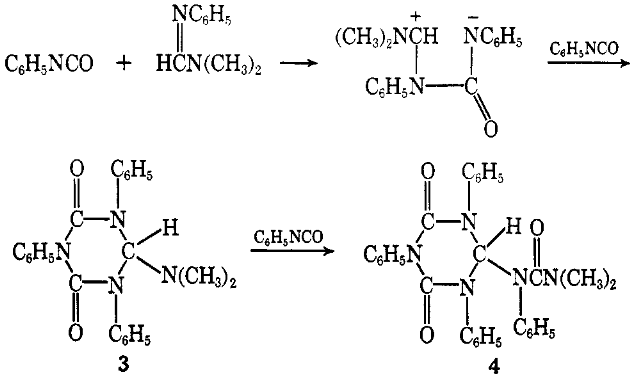
Cognizant of the work of Ulrich, Tucker, Stuber, and Sayigh,[2] we wish to summarize our results on the reactions of phenyl isocyanate with N,N-dialkylformamides and with N,N,N′-trisubstituted formamidines. The product **1**, obtained from the reaction of N,N-dimethylformamide with phenyl isocyanate, was first described in this laboratory by Majewski,[3] although the structure was incorrectly assigned. At that time, **1** was also prepared from N,N-diethylformamide, N-phenyl-N′,N′-dimethylformamidine, and N-phenyl-N′,-N′-diethylformamidine.[3] Weiner[4] reported **1** as a by-product in the formation of amidines from isocyanates, but did not determine its structure. We have prepared **1** and the analogous compound **2** in better than 90% yield by the reaction of N,N-dimethylformamide with the isocyanate (in a 1:10 molar ratio) at 140–150°.



1, X = O, NC_6H_5; R = CH_3; CH_3CH_2; R′ = C_6H_5
2, X = O, R = CH_3; R = *p*-$CH_3CC_6H_4$

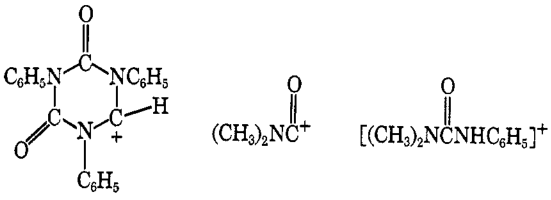
The structure of **1** was assigned on the basis of the molecular weight of 579 found by mass spectrometry, other spectral evidence in accord with and discussed by Ulrich and coworkers,[2] and the isolation of the intermediate compounds **3** and **4** shown to be the precursors of **1**. The intermediate 2-dimethylamino-1,3,5-triphenylhexahydro-1,3,5-triazine-4,6-dione (**3**) probably results from the addition of the 1,4-dipole derived from phenyl isocyanate and N-phenyl-N′,N′-dimethylformamidine to a second mole of phenyl isocyanate as shown in Scheme I. This reaction seems to be general for isocyanates and compounds containing the azomethine group.[5] Our evidence agrees with that given by Ulrich for the structure of **3**.[2]

SCHEME I

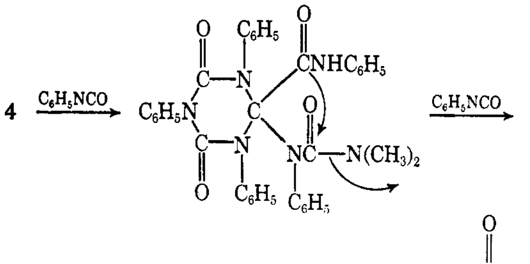


3 **4**

By limiting the quantity of phenyl isocyanate and controlling the reaction conditions, we isolated the second intermediate, **4**, which was predicted, but not obtained by Ulrich and coworkers.[2] This would arise from an insertion of phenyl isocyanate in the C–$N(CH_3)_2$ bond, a type of reaction recently observed in structurally similar acyclic compounds.[6–9] An alternative structure for **4** resulting from reaction of phenyl isocyanate at the C–H bond was discarded, since the ir spectrum showed no N–H absorption, and the mass spectrum indicated the following ions



It is proposed that **4** yields **1** by carbamoylation followed by ring closure as shown in eq 1.



Compound **1** was pyrolyzed at 330–360° to yield 2 mol of phenyl isocyanate and an unidentified solid of molecular formula $C_{21}H_{15}N_3O_2$. The loss of two molecules of phenyl isocyanate from the triazine ring of **1** would be expected to produce 1,3-diphenylparabanic

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[1] Armstrong Cork Company Research Fellow.

[2] H. Ulrich, B. Tucker, F. A. Stuber, and A. A. R. Sayigh, *J. Org. Chem.*, **33**, 3928 (1968).

[3] T. E. Majewski, Ph.D. Dissertation, University of Delaware, June 1960.

[4] M. L. Weiner, *J. Org. Chem.*, **25**, 2245 (1960).

[5] R. Huisgen, K. Herbig, and M. Morikawa, *Chem. Ber.*, **100**, 1107 (1967).

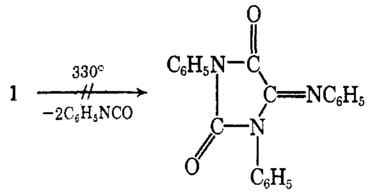
[6] H. v. Brachel and R. Merten, *Angew. Chem. Intern. Ed. Engl.*, **1**, 592 (1962).

[7] H. Biener, *Ann.*, **686**, 102 (1965).

[8] H. Bredereck, G. Simchen, and E. Göknel, *Angew. Chem. Intern. Ed. Engl.*, **3**, 704 (1964).

[9] H. Ulrich and A. A. R. Sayigh, *ibid.*, **5**, 844 (1966).

acid 5-anil (**5**). However, the pyrolysis product was shown not to be **5** by comparison with an authentic sample.



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Experimental Section[10]

1,3,6,8,10-Pentaphenyl-1,3,6,8,10-pentazaspiro[4,5]decane-2,-4,7,9-tetranone (1).—A solution of 3.7 g (0.05 mol) of N,N-dimethylformamide and 59.5 g (0.50 mol) of phenyl isocyanate was heated at 140–150° for 16 hr. Excess phenyl isocyanate was removed by distillation *in vacuo*. The residue was dissolved in boiling chloroform, the chloroform was removed by azeotropic distillation with ethanol, and the product was allowed to precipitate from ethanol. Thorough washing with ether gave colorless crystals, containing alcohol of crystallization, which after drying at 100° (3 mm) for 24 hr consisted of 28.5 g (96%) of **1**: mp 228–230° (unchanged by recrystallization); ir (KBr), 1790 (C=O), 1730 (C=O), 1685 cm^{-1} (C=O); nmr ($CDCl_3$), δ 7.0–8.1 (m, 23) 6.5–6.7 (m, 2). This unusual distribution of nmr signals was also observed by Ulrich, *et al.*[2]

Anal. Calcd for $C_{35}H_{25}N_5O_4$: C, 72.53; H, 4.32; N, 12.09; O, 11.05; mol wt, 579. Found: 72.84; H, 4.27; N, 12.26; O, 10.91; mol wt (mass spectroscopy), 579.

The same compound resulted in lower yield when prepared at 75–85°. Cyclohexyl isocyanate and phenyl isothiocyanate failed to react at 140–150°.

1,3,6,8,10-Penta-*p*-methoxyphenyl-1,3,6,8,10-pentazaspiro[4,-5]decane-2,4,7,9-tetraone (2).—This derivative was prepared in the same way as **1**, from the reaction of 0.05 mol of N,N-dimethylformamide with 0.50 mol of *p*-methoxyphenyl isocyanate. The yield of **2** was 34.0 g (93%), mp 286–287°, when dried. Recrystallization from ethanol–acetonitrile (2:1) raised the melting point to 287–288°.

Anal. Calcd for $C_{40}H_{35}N_5O_9$: C, 65.83; H, 4.83; N, 9.59. Found: C, 65.79; H, 4.78; N, 9.48.

2-Dimethylamino-1,3,5-triphenylhexahydro-1,3,5-triazine-4,6-dione (3).—A solution of 24.0 g (0.16 mol) of N-phenyl-N′,N′-dimethylformamidine[4] and 34.0 ml (0.32 mol) of phenyl isocyanate was heated at 80–85° for 12 hr. The resulting solid, after washing with ether, consisted of 40.0 g (64%) of **3**, mp 178–179°. Recrystallization from methanol and drying at 60° *in vacuo* (3 mm) for 12 hr raised the melting point to 181–182°: ir (KBr), 1712 (C=O), 1663 cm^{-1} (C=O); nmr ($CDCl_3$), δ 2.4 (s, 6, $(CH_3)_2N$), 5.95 (s, 1, C—H), 7.0–7.7 (m, 15, C_6H_5).

Anal. Calcd for $C_{23}H_{22}N_4O_2$: C, 71.50; H, 5.74; N, 14.50. Found: C, 71.84; H, 5.95; N, 14.62.

2-[1-(1-Phenyl-3,3-dimethylureido)]-1,3,5-triphenylhexahydro-1,3,5-triazine-4,6-dione (4).—A mixture of 3.0 g (0.0078 mol) of **3** and 15 ml (0.138 mol) of phenyl isocyanate was heated at 80–95° for 18 hr. The solid crystalline product, after washing with ether, consisted of 1.8 g (46%) of **4**, mp 239–240°. Recrystallization from ethanol and drying *in vacuo* at 60° for 24 hr gave tiny white needles melting at 242–243°: ir (KBr), 1712 (C=O), 1662 (C=O), 1655 cm^{-1} (C=O); nmr ($CDCl_3$), δ 2.4 (s, 6, $(CH_3)_2N$), 6.32–6.70 (m, 2, C_6H_5), 7.0–8.0 (m, 19, C_6H_5 and CH); mass spectrum (70 eV) *m/e* 342, 194, 164, 119, 91, 72.

Anal. Calcd for $C_{30}H_{27}N_5O_3$: C, 71.01; H, 5.32; N, 13.81. Found: C, 71.07; H, 5.41; N, 14.01.

Acid hydrolysis of **4** gave N,N′,N″-triphenylbiuret (95%), mp 150–151°.

Compound **4** was converted into **1** by heating a mixture of 2.0 g (0.004 mol) of **4** with 15 ml (0.138 mol) of phenyl isocyanate at 140–150° for 3 hr. The excess phenyl isocyanate was removed under reduced pressure, the residual gum was stirred with acetone, and the resulting precipitate was ground with ether and dried as before. The yield was 2.1 g (91%) of product, mp 228–230°, undepressed by mixing with **1**.

The acetone filtrate on evaporation yielded a gummy residue which was extracted three times with boiling water. The cooled aqueous extracts yielded needles (0.5 g, 76%) of 1-phenyl-3,3-dimethylurea, mp 129–130° (undepressed on mixture melting with an authentic sample).

Pyrolysis of 1.—Heating of 21.2 g (0.036 mol) of **1** at 330–360° and at a pressure of 50 mm gave as distillate 8.4 g (0.071 mol) of phenyl isocyanate. The residue, washed with acetone and recrystallized from methylene chloride, gave 11.0 g of a white solid **5**, which did not melt below 360° and was not hydrolyzed by aqueous alcoholic HCl: ir (KBr), 1705 (C=O), 1740 cm^{-1} (C=O).

Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.88; H, 4.42; N, 12.30; mol wt, 341. Found: C, 73.61; H, 4.40; N, 12.34; mol wt, 357 (boiling point elevation in bromobenzene).[11]

1,3-Diphenylparabanic Acid 5-Anil (5).—A mixture of 17.0 g (0.050 mol) of 1,3-diphenyl-5,5-diethoxyhydantoin,[12] 5.0 g (0.053 mol) of aniline, and 1 drop of concentrated HCl was heated at 135–140° for 1.5 hr with continuous distillation of the ethanol as formed. The resulting yellow glass was dissolved in a large volume of ether and treated with dry HCl to precipitate the hydrochloride. Decomposition of the hydrochloride with water gave 15.0 g (89%) of the free anil, a yellow solid melting at 105–108°. The compound was recrystallized from petroleum ether (bp 30–60°)–ethanol (2:1) with difficulty; after drying *in vacuo* at 50° for 12 hr, it melted at 122–123°: ir (KBr), 1792 (C=O), 1742 (C=O), 1672 cm^{-1} (C=N).

Compound **5** was hydrolyzed in aqueous ethanolic HCl to aniline hydrochloride and 1,3-diphenylparabanic acid.

Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.88; H, 4.42; N, 12.30. Found: C, 74.22; H, 4.76; N, 12.01.

Registry No.—**1**, 17350-46-8; **2**, 17350-47-9; **3**, 17350-48-0; **4**, 17350-49-1; **5**, 17350-50-4.

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[10] Melting points (corrected) determined on a Fisher-Johns apparatus; ir spectra on Perkin-Elmer 337 or 137 spectrophotometer; nmr spectra on a Varian A-60A spectrometer with TMS as internal standard, mass spectra on a 21-110B CEC double focus mass spectrometer.

[11] Subsequent mass spectral data suggest that the pyrolysis product has a molecular weight twice that found by boiling point elevation.

[12] C. W. Whitehead and J. Traverso, *J. Amer. Chem. Soc.*, **80**, 962 (1958).

The Reaction of Ethylene- and Propylenediamine with Esters of Trihaloacetic Acids

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The dihydroimidazole **1** was reportedly prepared by the reaction of ethyl trichloroacetate with ethylenediamine.[1] Several attempts to repeat this preparation gave a product whose melting point was similar to that reported for **1**, but which was, in fact, compound **2** (X = Cl) as shown by its ir and nmr spectra, elemental analyses, and molecular weight. Compound **2** (X = Cl) was the only product isolated (80% yield) under a variety of reaction conditions. The product from the reaction of trichloroacetyl chloride and ethylenediamine was identical with that from the above reaction, *i.e.*, **2** (X = Cl).

The ir spectrum of 1,6-bis(trichloroacetamido)hexane, prepared by the reaction of hexamethylenediamine with ethyl trichloroacetate,[2] was completely analogous to that of **2** (X = Cl). Cyclization would not compete with bisamide formation in this case.

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[1] M. M. Joullie and A. R. Day, *J. Amer. Chem. Soc.*, **76**, 2990 (1954).

[2] A. R. Surrey and J. R. Meyer, *J. Med. Pharm. Chem.*, **3**, 419 (1961).