Reaction of Nitromethane with Aryl Isocyanates in the Presence of Triethylamine. A Formation of 1,3-Diaryl-5-(hydroxyimino)-imidazolidine-2,4-diones

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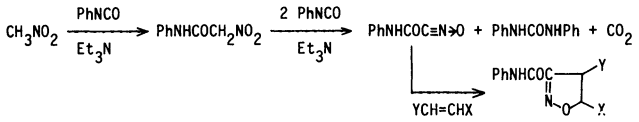
Synopsis. 1,3-Diaryl-5-(hydroxyimino)imidazolidine-2,4-diones were obtained from the reactions of nitromethane with several aryl isocyanates in the presence of a trace amount of triethylamine and their structures were established from spectroscopic evidence and their chemical behavior.

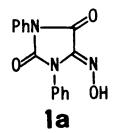
Many preparative methods of nitrile oxides by dehydration of primary nitro compounds have been known.[1-5] One of the most useful methods consists of the use of phenyl isocyanate as the dehydrating agent in the presence of a catalytic amount of triethylamine.[2a] While the reaction has been applied successfully to various types of primary nitro compounds, the reaction takes a slightly different course with nitromethane since nitromethane reacts with phenyl isocyanate to give α-nitroacetanilide.[2c] In fact, 2-isoxazoline-3-carboxanilides are formed via a cyanoformanilide *N*-oxide from the reaction of nitromethane with phenyl isocyanate in the presence of olefins and trace of triethylamine.[2c] We investigated the reaction



in expectation of obtaining a furazandicarboxanilide 2-oxide, a dimer of the cyanoformanilide *N*-oxide, in the absence of dipolarophiles. Though we could isolate none of the desired furazan oxides from the reaction mixture, we could isolate an unexpected and interesting compound. We report here the reaction in detail.

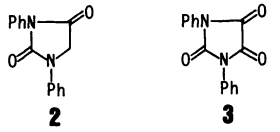
Results and Discussion

Treatment of an ethereal solution of nitromethane with two equivalents of phenyl isocyanate in the presence of a few drops of triethylamine gave colorless crystals (**1a**) in 27% yield besides a large amount of *N,N'*-diphenylurea and a small amount of phenyl isocyanate dimer. The structural assignment of **1a** as 5-(hydroxyimino)-1,3-diphenylimidazolidine-2,4-dione was based on the following results. The molecular ion



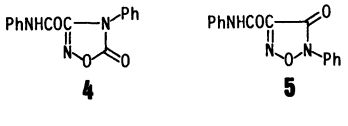
1a

peak (281.080) in the high resolution mass spectrum and the elemental analysis suggest its molecular formula as $C_{15}H_{11}N_3O_3$, formally a combination of 2 moles of phenyl isocyanate and one mole of formonitrile oxide (HCNO). Two singlets (δ 7.50 and 7.55) based on the protons of two phenyl groups and an acidic proton (δ 11.9) observed in the NMR spectrum and the formation of *N,N'*-diphenylurea by hydrolysis with ethanolic NaOH also suggested the structure of **1a**. 1,3-Diphenylimidazolidine-2,4-dione (**2**) and 1,3-diphenylimidazolidine-2,4,5-trione (**3**) were prepared by methods given in literatures for comparison. A sin-

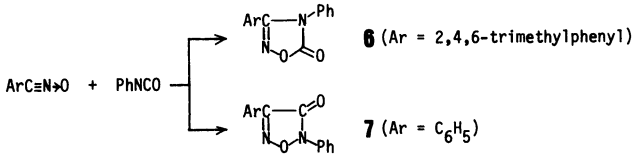


2 **3**

glet peak at δ 7.50 of phenyl protons of **3** in the NMR spectrum agreed well with that of **1a**. The product (**1a**) and the model compound (**3**) displayed carbonyl absorption peak in the IR spectra at a similar position (1730—1740 cm^{-1}). The structures of oxadiazole (**4** and **5**) are identical with those of the compounds expected from the 1,3-dipolar cycloaddition reaction of cyanoformanilide *N*-oxide with phenyl isocyanate.



4 **5**



The formation of analogous oxadiazoles (**6** and **7**) has been known in the reaction of aromatic nitrile oxides with phenyl isocyanate.[6] The possibility of the structures (**4** and **5**) for the product could be ruled out by the evidence that **6** and **7** showed its carbonyl absorption at 1770[6a] and 1720 cm^{-1},[6b] respectively. The structure (**1a**) for the product was also supported by the formation of *O*-acyl oximes (**8**) by the acylation with several acyl halides. The compounds (**8**) showed an absorption of ester group at 1770 cm^{-1} in their IR spectra which agreed well with the *O*-acyl oxime structure and not with *N*-acylated compounds (ureas) of **4** and **5**. The chemical shifts of the alkyl protons in the acyl group of **8** appeared at a field higher than that of normal ones in the NMR spectra, and the effect may be ascribed to *Z*-configuration of *O*-acyl oximes.

Analogous oximes (**1b** and **1c**) and the O-acyl oxi-

Table Elemental Analyses of Compounds **1** and **8**

Compd	Formula	Found (Calcd) (%)		
		H	C	N
1a	$C_{15}H_{11}N_3O_3$	4.18 (3.94)	64.32 (64.05)	14.72 (14.94)
1b	$C_{17}H_{15}N_3O_3$	4.97 (4.89)	66.30 (66.01)	13.42 (13.59)
1c	$C_{15}H_9N_3O_3Cl_2$	2.36 (2.59)	51.19 (51.45)	11.88 (12.00)
8a	$C_{17}H_{13}N_3O_4$	4.01 (4.05)	63.18 (63.15)	12.77 (13.00)
8b	$C_{18}H_{15}N_3O_4$	4.41 (4.48)	63.93 (64.09)	12.17 (12.46)
8c	$C_{19}H_{17}N_3O_4$	4.76 (4.88)	64.95 (64.95)	12.06 (11.96)
8d	$C_{21}H_{21}N_3O_4$	5.52 (5.58)	66.32 (66.48)	11.25 (11.08)
8e	$C_{22}H_{15}N_3O_4$	3.92 (3.92)	68.85 (68.56)	10.74 (10.91)
8f	$C_{19}H_{17}N_3O_4$	4.83 (4.88)	64.77 (64.95)	11.83 (11.96)
8g	$C_{17}H_{11}N_3O_4Cl_2$	2.70 (2.81)	52.11 (52.04)	10.69 (10.71)

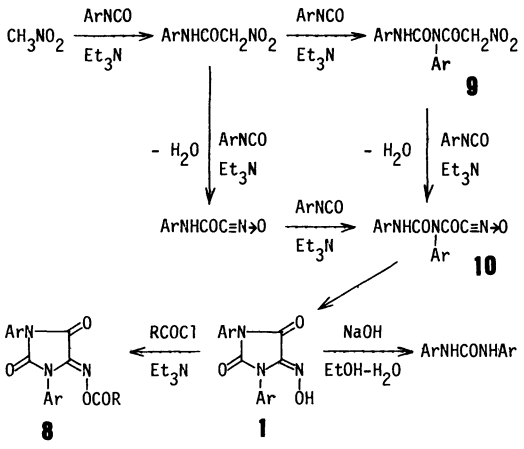
Table 1. Yields[a] and Melting Points of **1** and **8**

Compd	Ar	R	Yield %	Mp θ_m/°C
1a	C_6H_5	—	27	182—184
1b	$C_6H_4CH_3$-*m*	—	5	178—182
1c	C_6H_4Cl-*p*	—	32	215—219
8a	C_6H_5	CH_3	43	199—201
8b	C_6H_5	C_2H_5	25	218—221
8c	C_6H_5	C_3H_7-*n*	16	162—163
8d	C_6H_5	C_5H_{11}-*n*	20	154—155
8e	C_6H_5	C_6H_5	55	255—256
8f	$C_6H_4CH_3$-*p*	CH_3	4	208—209
8g	C_6H_4Cl-*p*	CH3	42	240—241

a) Yields of compounds (**1a**—**c**) were calculated on the basis of the aryl isocyanates. In the case of **8f**, the corresponding **1** (Ar=Tol-*p*) could not be isolated in crystalline state and the yield of **8f** is shown in over all yield from the isocyanate.

mes (**8f** and **8g**) were prepared by the reactions of nitromethane with some of aryl isocyanates and following acylation of the products. The results are shown in Table 1.

The mechanism of the formation of the oximes (**1**) is shown in Scheme 1; successive addition of aryl isocyanates to nitromethane gives *N*-(nitroacetyl)-*N,N'*-diarylureas (**9**), which undergo dehydration by the action of ArNCO/Et3N to give nitrile oxides (**10**) and then, the nitrile oxides undergo intramolecular cyclization giving **1**. A similar addition of amines to nitrile oxides is well-known.[7]



Scheme 1.

Experimental

Measurements. All melting points are uncorrected. The ^{1}H NMR spectra were measured on a Varian T-60A instrument with Me_4Si as an internal standard; chemical shifts are given in δ units and coupling constants (J) are in herz units: s=singlet; t=triplet; q=quartet; m=multiplet; br=broad singlet. The IR spectra were determined on a Hitachi 215 infrared spectrophotometer. The high-resolution mass spectra were measured on a Hitachi M-80 mass spectrometer. A part of these spectral data for all new compounds (**1** and **8**), 1,3-diphenylimidazolidine-2,4-dione (**2**), 1,3-diphenylimidazolidine-2,4,5-trione (**3**), 4-phenyl-3-(2,4,6-trimethylphenyl)-1,2,4-oxadiazol-5(4*H*)-one (**6**), and 2,4-diphenyl-1,2,5-oxadiazol-3(2*H*)-one (**7**) are shown in Table 2. All new products gave satisfactory elemental analyses (±0.3% for C, H, and N).

Materials. Nitromethane and isocyanates were commercially available and were without further purification. 1,3-Diphenylimidazolidine-2,4-dione (**2**)[8] and 1,3-diphenylimidazolidine-2,4,5-trione (**3**)[9] were prepared according to the methods described in the literatures.

Reactions of Nitromethane with Aryl Isocyanates. Typical Procedure. A few drops of triethylamine were added to a stirred dry ethereal solution (100 ml) of nitromethane (0.1 mol, 6.1 g) and phenyl isocyanate (0.2 mol, 24 g) at room temperature and the mixture was refluxed until an evolution of carbon dioxide ceased (ca. 6 h). Upon cooling to room temperature, a white solid crystallized out of the solution was filtered off. This colorless crystalline solid is a mixture of *N,N'*-diphenylurea, 5-(hydroxyimino)-1,3-diphenylimidazolidine-2,4-dione (**1a**), and phenyl isocyanate dimer. Upon exposing to atmosphere, the colorless products yellowed gradually at the surface owing to the presence of small amount of phenyl isocyanate dimer. The phenyl isocyanate dimer and a large part of **1a** could be extracted together with a small amount of *N,N'*-diphenylurea from the crystalline mixture by a Soxlet extractor using ethyl acetate. After evaporation of the solvent, the residual crystals were mixed with 100 ml of ethanol and the mixture was refluxed for 6 h for the purpose of conversion of phenyl isocyanate dimer into ethyl *N,N'*-diphenylallophanate[10] which shows better solubility in benzene than phenyl isocyanate dimer. Then, the solvent was evaporated and the crystalline residue was recrystallized from benzene to give analytically pure **1a**. The yields and melting points were shown in Table 1 along with those of analogous compounds prepared from similar reactions of nitromethane with other aryl isocyanates. Using a stoichiometric amount (0.4 mol) of phenyl isocyanate for the reaction, the yield of **1a** was not so varied.

Acylation of 1 with Acyl Chlorides. Typical Procedure. Seven mmol of acyl chloride was added to a stirred benzene solution (80 ml) of **1** (3.5 mmol) and triethylamine (7 mmol) at room termperature. The mixture was refluxed for 4 h and, then, washed with water several times. Evaporation of the solvent from the reaction mixture in a rotary evap-

Table 2. Spectral Data of **1**, **3**, **6**, **7**, and **8**

Compd	Ms; *m/z* Found (Calcd)	IR cm^{-1}	NMR[a] δ
1a	281.091 (281.091)	3270, 1740, 1670	7.50 (s, 5H), 7.55 (s, 5H), 11.9 (br, 1H, OH).
1b	309.126 (309.126)	3270, 1740, 1660	2.33 (s, 3H), 2.4 (s, 3H), 6.8—7.5 (m, 8H), 10.5 (s, 1H, OH).
1c	349.000 (349.000)	3250, 1725, 1660	7.45 (s, 4H), 7.55 (s, 4H), 11.9 (br, 1H, OH).
8a	323.103 (323.103)	1770, 1740, 1650	1.5 (s, 3H), 7.50 (s, 10H).
8b	337.121 (337.121)	1770, 1740, 1640	0.77 (t, 3H, J=7), 1.75 (q, 2H, J=7), 7.50 (s, 10H).
8c	351.138 (351.139)	1770, 1740, 1640	0.75 (t, 3H, J=7), 1.3 (sextet, 2H, J=7), 1.75 (t, 2H, J=7), 7.47 (s, 10H).
8d	379.174 (379.174)	1750, 1640	0.83 (t, 3H, J=7), 1.0—1.5 (m, 6H), 1.8 (t, 2H), 7.50 (s, 10H).
8e	385.121 (385.121)	1755, 1740, 1650	6.7—7.8 (m, 15H).
8f	351.138 (351.139)	1765, 1740, 1640	1.63 (s, 3H), 2.38 (s, 3H), 2.42 (s, 3H), 7.30 (s, 4H), 7.55 (s, 4H).
8g	391.012 (391.013)	1770, 1740, 1650	1.63 (s, 3H), 7.33 (s, 4H), 7.55 (s, 4H).
2	252.089 (252.090)	1700	4.3 (s, 2H), 7.47 (s, 5H), 7.1—7.8 (m, 5H).
3	226.069 (226.069)	1730	7.50 (s, 10H).
6[b]		1770	
7[b]		1720, 1650	about 7.25 (10H).

a) Compounds (**1b**, **8c**, **8d**, **8f**, and **2**) were dissolved in $CDCl_3$, the others were dissolved in DMSO-d_6. b) Spectral data of these compounds was cited from ref. 6.

orator gave crude crystalline product. The crude product was recrystallized from ethanol to give pure material of 5-(acyloxyimino)-1,3-diarylimidazolidine-2,4-dione (**8**) in the yields shown in Table 1.

Hydrolysis of 1a with Ethanolic NaOH. To a solution of sodium hydroxide (200 mg, 5 mmol) in 90% aqueous ethanol (50 ml) we added 280 mg (1 mmol) of **1a**, after which the mixture was stirred for 1 h at 50 °C. After evaporation of the solvent from the reaction mixture, the residue was treated with water and extracted with chloroform (100 ml). The organic layer was dried over anhydrous sodium sulfate. The evaporation of the solvent yielded *N,N'*-diphenylurea in 71% (150 mg) yield.

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