Studies on Nitrile Imines. Synthesis of Some New Five-Membered Heterocyclics *via* *N*-(2,4-Dinitrophenyl)-*C*-alkyl Nitrile Imines

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Reaction of *N*-(2,4-dinitrophenyl)-*C*-alkyl hydrazonyl chlorides with diverse dipolarophiles gave a variety of novel heterocyclics, which are expected to possess biological activities. The ring closure is brought about by a concerted process involving nitrile imine as an intermediate. The structures of the resulting products are supported by nmr and ir spectral data.

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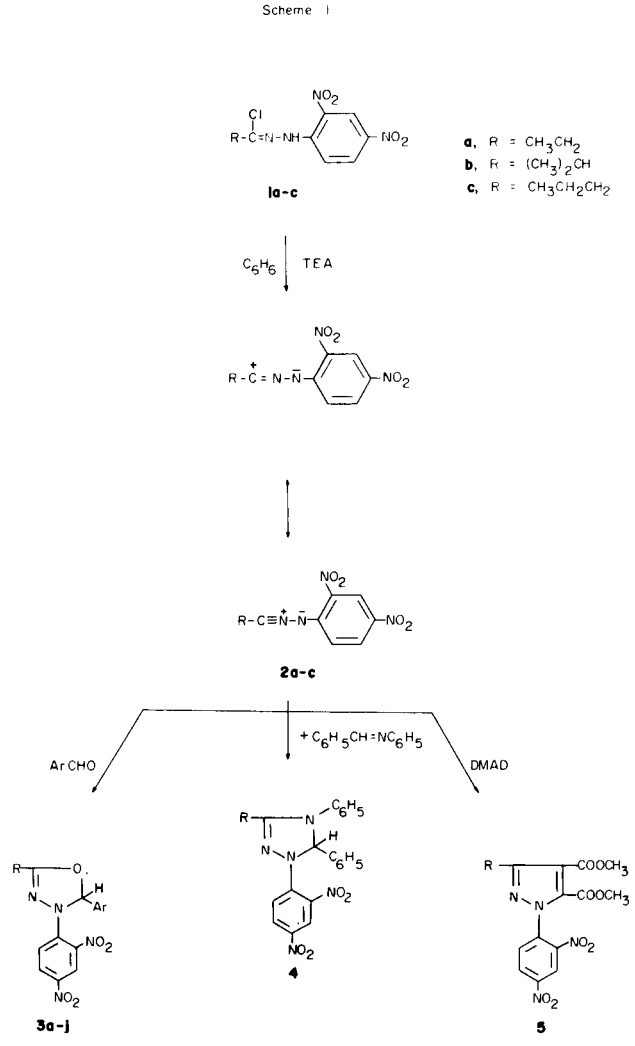
Although considerable work has been done by Huisgen and his coworkers (1-4), in order to explore the synthetic applicability of diphenylnitrile imine towards diverse dipolarophiles, the reactivity of 2,4-dinitrophenyl-*C*-alkyl nitrile imines has not been reported in the literature so far. In continuation of our previous researches (5-8), the present work was conducted in order to determine the effect of dipolarophiles on these species and also to synthesize the novel heterocyclics, which are expected to possess potential pharmaceutical values. *N*-(2,4-Dinitrophenyl)-*C*-ethyl nitrile imine (**2a**), *N*-(2,4-dinitrophenyl)-*C*-isopropyl nitrile imine (**2b**) and *N*-(2,4-dinitrophenyl)-*C*-*n*-propyl nitrile imine (**2c**), were generated *in situ* by the action of triethylamine (TEA) from their respective precursors, *i.e.*, hydrazonyl chlorides (**1a-c**, Scheme I) and were allowed to react with a variety of aromatic aldehydes in dry benzene, to afford a novel 1,3,4-oxadiazoline system (**3a-j**).

Scheme I



All the oxadiazolines (Table I) synthesized during this study gave adequate elemental analysis. Structural assignments of these products are made on the basis of nmr and ir spectral data. The presence of hydroxyl proton was further confirmed by deuterium exchange study (Table II).

Interestingly, it was found during the course of these investigations that the carbonyl group of normal ketones failed to respond to such 1,3-cycloaddition reactions with nitrile imines. Similarly, the reaction of the nitrile imine **2b** with benzylidene aniline and dimethylacetylene dicarboxylate (DMAD) yielded the Δ^2-triazoline **4** and pyrazole **5**, respectively, in good yields (Scheme I).

The results indicate that the compounds **3-5** are formed by the (3 + 2) addition of multiple bond system onto the nitrile imine intermediate **2a-c**. The orientation of the cycloaddition can be interpreted in a manner similar to that proposed for diphenyl nitrile imine, which seems to be influenced more strongly by steric than by electronic factors.

EXPERIMENTAL

Uncorrected melting points were determined on a Gallen-Kamp apparatus. The ir spectra were recorded on Perkin-Elmer infracord spectrophotometer and ^{1}H-nmr spectra were recorded on a Varian A-60 spectrometer using TMS as an internal standard. Analytical samples were purified by column chromatography over neutral alumina and purity was checked by tlc.

N-(2,4-Dinitrophenyl)-*C*-ethylhydrazonyl chloride *N*-(2,4-dinitrophenyl)-*C*-isopropylhydrazonyl chloride and *N*-(2,4-dinitrophenyl)-*C*-*n*-propyl-

Table I

Physical Properties of Cycloadducts **3-5**

Compound No.	R	Ar	Mp °C	Yield (%)	Recrystallizing Solvent	Molecular Formula	Analysis % Calcd. (Found) C	H	N
3a	$(CH_3)_2CH$	C_6H_5	213-214	70	Ethanol	$C_{17}H_{16}N_4O_5$	57.30 (57.25)	4.49 (4.40)	15.73 (15.69)
3b	$(CH_3)_2CH$	4-$OCH_3C_6H_4$	240-241	60	Acetone	$C_{18}H_{18}N_4O_6$	55.95 (55.89)	4.66 (4.71)	14.50 (14.51)
3c	$(CH_3)_2CH$	3-OH-C_6H_4	139-140	60	Benzene-petroleum ether	$C_{17}H_{16}N_4O_6$	54.83 (54.82)	4.30 (4.35)	15.05 (15.02)
3d	$(CH_3)_2CH$	4-OH-3-OCH_3-C_6H_3	132-133	70	Benzene-hexane	$C_{18}H_{18}N_4O_7$	53.73 (53.71)	4.47 (4.47)	13.93 (13.91)
3e	$CH_3(CH_2)_2$	4-Cl-C_6H_4	105-107	60	Chloroform-methanol	$C_{17}H_{15}N_4O_5Cl$	53.73 (53.70)	4.47 (4.49)	13.93 (13.59)
3f	$CH_3(CH_2)_2$	4-OH-C_6H_4	144-145	45	Chloroform-methanol	$C_{17}H_{16}O_6N_4$	54.83 (54.79)	4.28 (4.32)	15.05 (15.12)
3g	$CH_3(CH_2)_2$	3-OH-C_6H_4	135-136	64	Chloroform-methanol	$C_{17}H_{16}O_6N_4$	54.83 (54.79)	4.28 (4.39)	15.05 (15.42)
3h	$CH_3(CH_2)_2$	4-OH-3-OCH_3-C_6H_3	110-112	60	Ethyl acetate-ethanol	$C_{18}H_{18}N_4O_7$	53.73 (53.91)	4.47 (4.32)	13.93 (13.72)
3i	CH_3CH_2	3-OH-C_6H_4	174-175	58	Ethyl acetate-ethanol	$C_{16}H_{14}O_6N_4$	53.63 (53.54)	3.91 (3.48)	15.64 (15.72)
3j	CH_3CH_2	4-OH-3-OC_2H_5-C_6H_3	100-103	80	Chloroform-methanol	$C_{18}H_{18}O_7N_4$	53.73 (53.70)	4.47 (4.40)	13.93 (13.90)
4	$(CH_3)_2CH$	—	229-230	60	Ethanol	$C_{23}H_{21}N_5O_4$	64.03 (64.01)	4.87 (4.88)	16.24 (16.43)
5	$(CH_3)_2CH$	—	187-188	65	Ethanol	$C_{16}H_{16}N_4O_8$	47.64 (47.60)	4.18 (4.20)	14.65 (14.60)

Table II

NMR and IR Data for Cycloadducts **3-5**

Compound No.	^{1}H-NMR Data (deuteriochloroform) (δ ppm)	No. of Protons	Assignment	IR Data (potassium bromide) cm^{-1} Vibrations	Assignment
3a	0.86, d	6H	Methyl		
	2.07-2.54, m	1H	Methine		
	7.17-8.83, m	8H	Aromatic		
	10.70, s	1H	Methine		
3b	1.23, d	6H	Methyl		
	2.50-2.97, m	1H	Methine		
	3.36, s	3H	Methoxy		
	6.90-9.03, m	7H	Aromatic		
	11.43, s	1H	Methine		
3c				3340	OH
				1630	C=N
				1500, 1335	NO_2
				1590, 1530	C=C
3d	1.25, s	3H	Methyl		
	2.20-2.80, m	1H	Methine		
	3.97, s	3H	Methoxy		
	7.27-9.10, m	6H	Aromatic		
	10.03, s	1H	Methine		
	11.48, s (a)	1H	Hydroxyl		
3e	1.0, t	3H	Methyl		
	1.24-1.87, m	2H	Methylene		
	2.41, t	2H	Methylene		
	7.2-9.19, m	7H	Aromatic		
	10.99, s	1H	Methine		
3f	0.96, t, J = 7.0 Hz	3H	Methyl		
	1.36-2.10, m	2H	Methylene		
	2.31, t, J = 7.0 Hz	2H	Methylene		
	7.80-9.03, m	7H	Aromatic		
	10.00, s (a)	1H	Hydroxyl		
	11.46, s	1H	Methine		
3g	0.93, t, J = 7.0 Hz	3H	Methyl		
	1.47-1.97, m	2H	Methylene		
	2.20-2.45, t, J = 7.0 Hz	2H	Methylene		
	7.26-9.10, m	7H	Aromatic		
	9.10, s (a)	1H	Hydroxyl		
	11.53, s	1H	Methine		
3h	1.01, t, J = 7.0 Hz	3H	Methyl		
	1.20-1.97, m	2H	Methylene		
	2.30, t, J = 7.0 Hz	2H	Methylene		
	3.89, s	3H	Methoxy		
	7.1-9.17	6H	Aromatic		
	9.97 (a)	1H	Hydroxyl		
	11.52	1H	Methine		
3i	1.18, t, J = 7.0 Hz	3H	Methyl		
	2.19-2.59, q, J = 7.0 Hz	2H	Methylene		
	7.22-9.07, m	7H	Aromatic		
	10.00, s (a)	1H	Hydroxyl		
	11.50, s	1H	Methine		
3j	1.06-1.62, m	6H	Methyl		
	2.09-2.46, q, J = 7.0 Hz	2H	Methylene		
	3.96-4.32, q, J = 7.0 Hz	2H	Methylene		
	7.09-9.09, m	6H	Aromatic		
	9.96, s (a)	1H	Hydroxyl		
	10.46, s	1H	Methine		
4				1615	C=N
				1580, 1510	C=C
				1500, 1330	NO_2
				1420, 1130	C-N

(a) The presence of hydroxyl proton was confirmed by their deuterium exchange study also.

hydrazonyl chloride (**1a-c**) were prepared by the chlorination of their respective hydrazones in chloroform.

Preparation of Cycloadducts **3-5**. General Method.

To a solution of hydrazonyl chloride (0.005 mole) in 50 ml of dry benzene was added dipolarophiles (0.005 mole) and allowed to stir under cooled condition. Triethylamine (0.005 mole) in 5 ml of the same solvent was added dropwise under nitrogen. The reaction starts immediately and a red colour appears with the separation of white gelatinous mass of triethylamine hydrochloride. The mixture was further refluxed for 4 hours on a water-bath and then left overnight at room temperature. The resulting precipitate was filtered off and the filtrate was concentrated under reduced pressure. The products were finally purified and recrystallized from appropriate solvents (Table I).

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