

Reactivity of Acyl Chloride Aryl-Hydrazones with some Diazines

Piero Dalla Croce

Istituto di Chimica Industriale dell'Università di Milano, C.N.R., Centro di studio sulla sintesi e stereochimica di speciali sistemi organici, Via Golgi, 19 20133 Milano, Italy

Received August 22, 1975

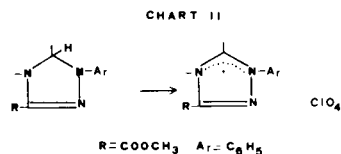
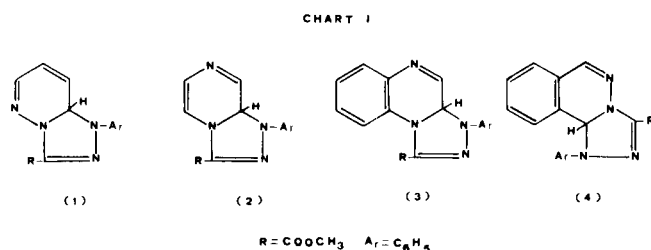
The reaction of methyl phenylhydrazonochloroacetate with pyridazine, pyrazine, quinoxaline and phthalazine gave the corresponding 1:1 cycloadducts (1-4) whose structure was proven by spectroscopic data and chemical transformations.

In continuation of our study of the reaction of acyl chloride arylhydrazones with heteroaromatic systems (1,2) we have investigated the behaviour of pyridazine, pyrazine, pyrimidine and their corresponding benzoderivatives towards such compounds. All the above azine-systems, a priori, had the possibility of undergoing the cycloaddition reaction on just one or both the C=N groups with the formation of 1:1 or 1:2 adducts. Methyl phenylhydrazonochloroacetate reacted, in the presence of triethylamine, with pyridazine, pyrazine, quinoxaline and phthalazine in chloroform solution at room temperature to give only 1:1 adducts (1-4). The principal characteristics of compounds 1-4 are summarized in Table 1.

The structure of cycloadducts 1-4 was assigned on the basis of elemental analysis and of spectroscopic data (Table 1). The infrared absorptions of the C=O groups

(1710-1690 cm^{-1}) (3) are consistent with the cyclic structure. The ^1H nmr spectrum showed aromatic protons signals, the hydrogen atom at the ring junction as a singlet at 4.1-4.9 τ and the singlet of methoxycarbonyl group (4.0-4.2 τ). Moreover, the chemical shifts of the signals related with H_5 in the series 1-4 and falling in the range 4.1-4.9 τ are similar to those observed for other analogous systems (5) and also support the bicyclic structure. The absence of any observed coupling between H_5 and H_6 in adducts 1-3 can be explained by assuming a dihedral angle of 90° between these protons in accord with the molecular models examination.

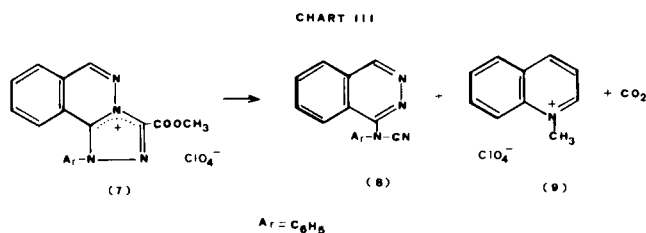
Accordingly to assigned structure, treatment of cycloadducts (1-4) with chromic anhydride in acetic acid gave the corresponding triazolium salts isolated as perchlorates 5-7. (Chart II). Heating 1-phenyl-3-methoxycarbonyl-



triazolo[3,4-*a*]phthalazinium perchlorate (7) with quinoxaline at 160° , *N*-phenyl-*N*-cyano-1-aminophthalazine (8) and *N*-methylquinolinium perchlorate (9) were obtained. (Chart III).

Table 1

Cyclo-adduct	M.p., °C.	Crystallization solvent	Yield %	Molecular formula	C	Calcd. H	Analysis			Ir ν CO cm^{-1}	Nmr (CDCl ₃) τ H ₅	
							N	C	H			
1	104-106	Methanol	65	C ₁₃ H ₁₂ N ₄ O ₂	60.93	4.72	21.87	60.80	4.67	21.82	1690	4.5
2	188-190	Methanol	62	C ₁₃ H ₁₂ N ₄ O ₂	60.93	4.72	21.87	60.88	4.56	21.72	1700	4.8
3	235-237	Acetic acid	68	C ₁₇ H ₁₄ N ₄ O ₂	66.65	4.61	18.19	66.55	4.50	18.06	1710	4.6
4	133-135	Methanol	80	C ₁₇ H ₁₄ N ₄ O ₂	66.65	4.61	18.19	66.40	4.58	18.38	1700	4.1



Such a behaviour is closely related to that previously observed for triazolium salts (6) of simpler structure. Treatment of adducts 1-4 with excess of methyl phenylhydrazonochloroacetate gave no further reaction. Probably the nucleophilicity of the imino nitrogen atom is so reduced by steric hindrance that the dimerisation of nitrile imine is, at this stage, easier than the cycloaddition (7).

Attempts to form the corresponding adducts with pyrimidine, quinazoline and cinnoline were unsuccessful and, in each case, the base was recovered unchanged.

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded with a Varian A-60 spectrometer (TMS as internal standard). Ir spectra were recorded on a Perkin-Elmer model 137 Infracord spectrophotometer as a ca. 2% chloroform solution.

General Procedure for the Preparation of Cycloadducts (1-4).

Triethylamine (0.01 mole) was added to a solution of the heterocyclic base (0.01 mole) and of the methyl phenylhydrazonochloroacetate (0.01 mole) in chloroform (50 ml.) and the mixture allowed to stand at room temperature for 24 hours. The chloroform was washed with water and dried (sodium sulfate). After evaporation the residue was taken up with diisopropyl ether, filtered off and crystallized (see Table 1).

General Oxidation Procedure of Cycloadducts.

A solution of chromic anhydride (0.02 mole) in aqueous 20% acetic acid (50 ml.) was added dropwise to a stirred solution of cycloadducts (0.03 mole) in acetic acid (50 ml.). The mixture was heated at 60-65° for 2 hours and then cooled. Addition of aqueous 60% perchloric acid (5 ml.) and dilution with water (50 ml.) gave, after filtration and crystallization, respectively, (a) 1-phenyl-3-methoxycarbonyl-*s*-triazolo[4,3-*b*]pyridazinium perchlorate (5), m.p. 208-210° from methanol, yield 55%;

(b) 1-phenyl-3-methoxycarbonyl-*s*-triazolo[4,3-*a*]pyrazinium perchlorate (6), m.p. 230° from acetic acid, yield 65%; (c) 1-phenyl-3-methoxycarbonyl-*s*-triazolo[3,4-*a*]phthalazinium perchlorate (7), m.p. 232° from acetic acid, yield 60%.

Anal. Calcd. for (a) $C_{13}H_{11}ClN_4O_6$: C, 44.12; H, 3.12; N, 15.82. Found: C, 44.10; H, 3.10; N, 15.62.

Anal. Calcd. for (b) $C_{13}H_{11}ClN_4O_6$: C, 44.12; H, 3.12; N, 15.82. Found: C, 44.17; H, 3.23; N, 15.33.

Anal. Calcd. for (c) $C_{17}H_{13}ClN_4O_6$: C, 50.49; H, 3.21; N, 13.81. Found: C, 50.19; H, 3.13; N, 13.73.

N-Cyano-*N*-phenyl-1-aminophthalazine (8) and *N*-Methylquinolinium Perchlorate (9).

A mixture of 7 (1 g.) and of quinoline (3 ml.) was heated at 160° for 20 minutes. After cooling the residue was taken up with benzene and water (50:10). The organic layer was washed with aqueous 10% hydrochloric acid (10 ml.) and dried over sodium sulfate. The solvent was evaporated and the residue crystallized from benzene to give 8, m.p. 145-147°, yield 65%.

Anal. Calcd. for $C_{15}H_{10}N_4$: C, 73.15; H, 4.09; N, 22.75. Found: C, 73.04; H, 4.02; N, 22.52.

The aqueous solution was boiled with Darco, filtered and evaporated under vacuum to dryness. Extraction with warm ethanol gave 9 (8).

REFERENCES

- (1) R. Fusco, P. Dalla Croce and A. Salvi, *Tetrahedron Letters*, 3071 (1967).
- (2) R. Fusco, P. Dalla Croce and A. Salvi, *Gazz. Chim. Ital.*, **98**, 511 (1968).
- (3) These values ruled out for the cycloadducts 1-4 an open ylidic structure that would show the carbonyl absorptions at 1620-1640 cm^{-1} (4).
- (4) A. W. Johnson, "Ylid Chemistry," Academic Press, 1966, pp. 1-65.
- (5) T. A. Crabb and R. F. Newton, *Tetrahedron Letters*, 3361 (1971).
- (6) R. Fusco and P. Dalla Croce, *Gazz. Chim. Ital.*, **99**, 69 (1969).
- (7) It must be pointed out that, in principle, the addition of a second mole of nitrile imine to adducts 1-4 should be easy since it does not imply loss of aromaticity of the system.
- (8) R. Eppele and T. Forster, *Z. Elektrochem.*, **58**, 783 (1954).