Physical Sciences Section

Pakistan J. Sci. Ind. Res., Vol. 30, No. 11, November 1987

REACTION WITH HETEROCYCLIC DIAZONIUM SALTS : SYNTHESIS OF SOME AZOLYLHYDRAZONE AND FUSED AZOLES DERIVATIVES

Mohamed Kamal Ahmed Ibrahim

Faculty of Science, Cairo University, Giza, Egypt

(Received April 8, 1986; revised October 17, 1987)

4-Bromo-3-phenylpyrazol-5-yl diazonium chloride (1) was coupled with different active methylene reagents such as 3-methylpyrazol-5-one, cyanoacetanilide, acetoacetanilide, rhodanine, 2-substituted thiazolin-4-one derivative (11) and 2-oxazolin-5-one derivative (21) in ethanol solution to give the corresponding coupling products (4), (6) (10), (12) and (22). Also aminoantipyrine was diazotized to diazonium chloride (2) and then coupled with the 2-substituted thiazolin-4-one derivative (11) to give the corresponding hydrazone derivative (16). Similarly 3-amino-4-phenylazopyrazol-5-yl diazonium chloride (3) was coupled with ethyl 1,1,1-trifluoroacetoacetate to give the corresponding hydrazone (18). Some of the acyclic hydrazones could be cyclized via reflux in acetic acid, such as hydrazones (6) and (12) to give pyrazolo [1,5-c] as-triazine derivatives (7) and (14) respectively. Also hydrazone (18) was treated with hydrazine hydrate and phenylhydrazine to give the corresponding pyrazolyl pyrazole derivatives (19) and (20) respectively. On the other hand, pyrazol-5-ylazo-oxazolin-5-one derivative (22) was converted into pyrazolo [1,5-c] as-triazine (23) via treatment with ammonia solution. All structures suggested are based on elemental analysis and spectral data.

Key words: Heterocyclic, salts, derivatives.

INTRODUCTION

Heterocyclic diazo compounds and their diazonium salts are versatile reagents and their chemistry has of late received considerable recent attention [1-4]. In a previous work we have reported that 3-phenylpyrazol-5-yl diazonium chloride reacted with active methylene reagents to yield pyrazolo-triazines [3-5]. Similar behaviour has also been noticed with products of reactions of diazotized 3-amino-indazole and 5-amino-1,2,4-triazoles with active methylene reagents [4,6-7]. In the present work we report the isolation of some hydrazones from the reaction of diazotized 5-amino-4-bromo-3-phenylpyrazole (1), 4-amino-antipyrine (2) and 3,5-diamino-4-phenylazopyrazole (3) with some active methylene reagents. Some of these hydrazones in contrast with the previous reports, are highly stable and did not cyclize to azolo-triazines under the reaction conditions, but others cyclized into azolotriazines on treatment with acids. Thus, diazonium salt (1) coupled with 3-methylpyrazole-5-one to yield the hydrazone (4). The latter hydrazone is highly stable and did not cyclize into an azolo-triazine derivative (5) under the coupling conditions. This contrasted with the previously obtained results with other coupling reagents [8].

MATERIALS AND METHOD

The diazonium salt (1) reacted with cyanoacetanilide to yield a product which may be formulated as the hydrazone (6) or the pyrazolo [1,5-c]-as-triazine derivative (7). Structure (6) was proposed for this product based on IR data which revealed absorption for –CN and –CONH groups. On the other hand, acyclic hydrazone (6) can be readily cyclized to the pyrazolo [1,5-c]-as-triazine derivative (7) on treatment with concentrated sulphuric acid or on boiling with acetic acid for 2 hr. Structure (7) was proposed for the cyclization product through IR data which revealed absorption for –CONH group and absence for –CN group. In contrast with these observations, formation of the cyclic triazine (8), occurred on the treatment of diazonium salt (1) with acetoacetanilide. The formation of cyclic or acyclic products from the coupling of active methylene compounds with diazonium salt (1) was explained on the basis of the mechanistic pathway of the reactions. Coupling with active hydrogen reagents which leads to the direct formation of cyclic products can take place with diazonium salts which exist in equilibrium with diazobetaine via 7 + 2 dipolar cycloaddition. When a usual coupling takes place hydrazones are formed [7].

On the other hand, the diazonium salt (1) was reacted with rhodanine to afford a product with molecular formula $C_{12}H_6N_5S_2Br$. Three theoretically isomeric possible structures were considered for the coupling product (cf. structure 9a, 9b and 10). Structures (9a) and (9b) are already eliminated on the basis of elemental analysis and IR spectrum which revealed the absence of C=O group Structure (10) is most likely for the reaction product. The formation of compound (10) is assumed as usual coupling takes place, to afford acyclic hydrazone (9) as intermediate, followed by cyclization under the same reaction conditions through loss of water to yield pyrazolo [3:4, 1:5]-as-triazino[5,6-b] thiazolthione (10). (cf. Chart 1).

In continuation of this work, the reaction of diazonium salt (1) with our newly synthesised 2-thiazolin-4-one derivative (11) has been reported. Thus, it has been found that the diazonium salt (1) reacts readily with (11) to yield the corresponding pyrazol-5-yl hydrazones. Two structures seemed possible for the reaction products [cf. structures (12) and (13)]. Structure (12) could be established on the basis of ready cyclization of the resulting hydrazone into the pyrazolo [1,5-c] as-triazine (14) on boiling the product in acetic acid. Structures of (12) and (14) could be confirmed with analytical and spectral data.

Also the diazonium salt (2) was coupled with compound (11) to yield the corresponding hydrazone (16) or (17). Structure (17) was excluded in view of a similar behaviour of (11) towards the heterocyclic diazonium salts [7]. The structure of hydrazone (16) was established on the basis of the analytical and spectral data (cf. Chart 2).

Moreover, it has been found that the diazonium salt (3) was coupled with ethyl 1,1,1-trifluoroacetoacetate to yield the corresponding hydrazone (18). Hydrazone (18) was obtained as usual coupling product and cannot be cyclized under the coupling conditions. But hydrazone (18) could be reacted with hydrazine hydrate and phenylhydrazine to field the corresponding pyrazolylpyrazole derivatives (19) and (20) respectively. Structures (19) and (20) were suggested on the evidence of elemental analysis, spectral data and the analogy of the reaction of hydrazines derivative toward the β-ketoester compounds [9]. (cf. Chart 2).

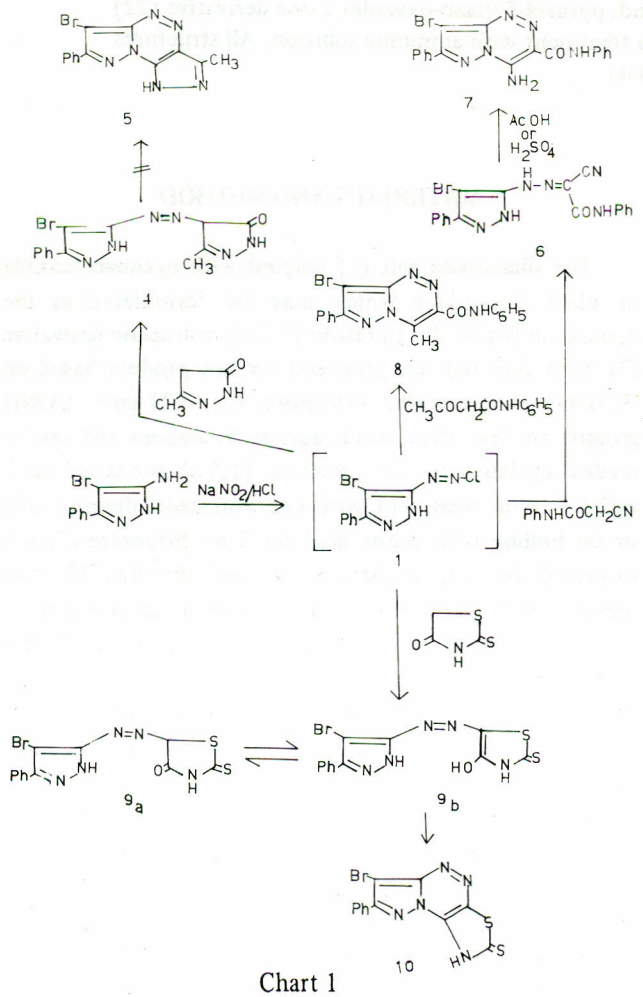

Chart 1

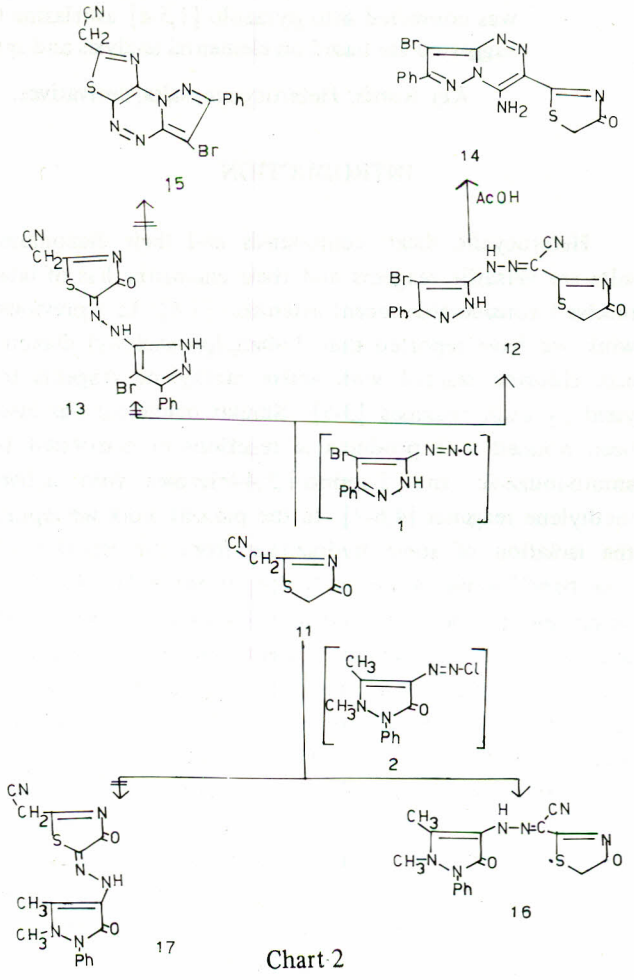

Chart 2

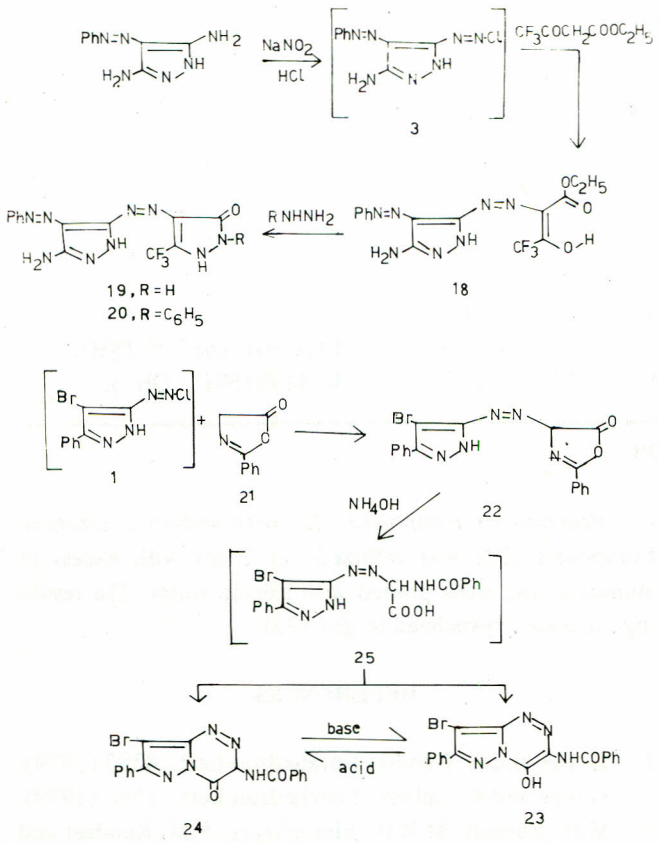

Chart 3

It has also been found that diazonium chloride (1) could be coupled with 2-oxazolin-5-one (21) in acetic acid to yield the corresponding hydrazone derivative (22). The formation of hydrazone (22) takes place via a usual coupling reaction on the active methylene group. The structure was established through elemental and spectral data. On the other hand, compound (22) was reacted with ammonium hydroxide to yield pyrazolo-[1,5-c] as-triazine derivative (23 or 24). The formation of (23) or (24) seemed via oxazole ring cleavage to give the intermediate hydrazone (25), followed by cyclization through the loss of water to yield structures (23) in basic medium or structure (24) in acid medium. Structure (23) was established through elemental and spectral data. (cf. Chart 3).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye-Unicam SP-1100 spectrophotometer. Analytical data were obtained from the Microanalytical Centre at Cairo University. Analytical, physical and spectral data of the compounds are given in Table 1.

Diazotization and coupling of amino-heterocyclic compounds with the active hydrogen compounds : (General Method). A suspension of amino-heterocyclic compounds

Table 1. Analytical, physical and spectral data of compounds:

Compd. No.	M.p. °C	Yield (%)	Mol. formula/ (mol. weight)	Analysis %: Calcd./Found C	H	N	cm^{-1} υmax (Selected bands)
4	260	68	$C_{13}H_{11}N6OBr$	44.9	3.2	24.2	1605 (C=N), 1660 (C=O),
			(387)	44.8	3.0	24.1	3100-3200 (NH)
6	190	76	$C_{18}H_{13}N_6OBr$	52.8	3.2	20.5	1610 (C=N), 1680 (C=O),
			(409)	52.6	3.1	20.4	2210 (CN), 3000-3100 (NH).
7	210	72	$C_{18}H_{13}N_6OBr$	52.8	3.2	20.5	1606 (C=N), 1680 (C=O),
			(409)	52.5	3.2	20.3	3000-3300 (NH , NH_2).
8	220	69	$C_{19}H_{14}N_5OBr$	55.9	3.4	17.1	———
			(408)	55.6	3.1	17.0	———
10	260	62	$C_{12}H_6N_5S_2Br$	39.5	1.6	19.2	1602 (C=N), 3100 (NH)
			(364)	39.3	1.5	19.1	
12	225	65	$C_{14}H_9N_6OSBr$	43.2	2.3	21.6	1600 (C=N), 1710 (C=O),
			(389)	43.0	2.1	21.4	2210 (CN), 3200 (NH).
14	242	63	$C_{14}H_9N_6OSBr$	43.2	2.3	21.6	1605 (C=N), 1710 (C=O),
			(389)	43.1	2.2	21.5	3300 (NH_2).
16	219	66	$C_{16}H_{16}N_6O_2S$	53.9	4.5	23.6	1630 (C=N), 1710, 1748-
			(356)	53.8	4.3	23.3	(2CO), 2210 (CN), 3150-
							3300(NH)

(continued . . . . .)

(Table 1, continued)

18	165	75	$C_{15}H_{14}N_7O_3F_3$	45.3	3.5	24.7	1600 (C=N), 1700 (ester),
			(397)	45.1	3.4	24.5	3100-3300 (NH, NH_2).
19	> 260	62	$C_{13}H_{10}N_9OF_3$	42.7	2.7	34.5	1603 (C=N), 1678 (C=O),
			(365)	42.5	2.6	34.3	3000-3300 (NH , NH_2).
20	> 260	68	$C_{19}H_{14}N_9OF_3$	51.7	3.2	28.6	1605 (C=N), 1675 (C=O),
			(441)	51.5	3.1	28.4	3100-3320 (NH , NH_2).
22	95	56	$C_{18}H_{12}N_5O_2Br$	52.7	2.9	17.1	---
			(410)	52.4	2.6	16.8	---
23	160	58	$C_{18}H_{12}N_5O_2Br$	52.7	2.9	17.1	1650 (C=N), 1685 (CONH),
			(410)	52.5	2.7	17.0	3150-3450 (NH , OH).

Solvent of crystallisation for all compounds is ethanol except (14) from AcOH.

like (5-amino-4-bromo-3-phenylpyrazole or 4-aminoantipyrine or 3,5-diamino-4-phenylazopyrazole) (0.1 mole) in hydrochloric acid (30 ml 37.5%) was heated to produce a clear solution of sodium nitrite (0.1 mole) in water (10 ml) was added dropwise with continuous stirring for 15 min. to give the corresponding diazonium chlorides (1-3) respectively. The diazonium salts 1, 2 or 3 were gradually added to cold solution of 3-methylpyrazol-5-one, cyanoacetanilide, acetoacetanilide, rhodanine, compounds (11) and (21) or (11) and ethyl 1,1,1-trifluoroacetoacetate (0.1 mole) in ethanol (50 ml) containing sodium acetate (0.2 mole) with continuous stirring for 30 min. The resulting products were collected and crystallized from ethanol to give the products (4,6,10,12,22) or (16) and or (18) respectively.

Cyclization of compounds (6) and (12) . A suspension of (6) or (12) (0.1 mole) in acetic acid (50 ml) was refluxed fo 2 hr, then poured in cold water. The solid products were collected and crystallized from AcOH to give compounds (7 or 14) respectively.

Reaction of compound (18) with hydrazine derivatives. Compound (18) was treated with excess of hydrazine hydrate or phenylhydrazine then heated for 3 hr at 100° The reaction mixture was poured into cold water. The products were crystallized to give (19 or 20) respectively.

Reaction of compound (22) with ammonia solution. Compound (22) was refluxed for 2 hrs with excess of ammonia sol., then poured into icecold water. The resulting solid was crystallized to give (23).

REFERENCES

1. G. Ege and K. Gilbert, Tetrahedron Lett., 4253 (1979).
2. G. Ege and K. Gilbert, Tetrahedron Lett., 1567 (1979).
3. M.H. Elnagdi, M.R.H. Elmoghayer, E.M. Kandeel and M.K.A. Ibrahim, J. Heterocyclic. Chem. **14**, 227 (1977).
4. M.H. Elnagdi, M.R.H. Elmoghayer, M.K.A. Ibrahim and H.H. Alnima, Z. Naturforsch, **33**b, 218 (1978).
5. M.H. Elnagdi, M.R.H. Elmoghayer, H.A. Elfaham, M.M.M. Sallam and H.H. Alnima, J. Heterocyclic Chem., **17**, 209 (1980).
6. M.K.A. Ibrahim, A.A. El-Agamey, A. Takaoka and N. Ishikawa, Heterocycles (in press).
7. M.K.A. Ibrahim, M.R.H. Elmoghayer and A.H.H. Elghandour, Indian Textile J. (1983).
8. M.R.H. Elmoghayer, M.K.A. Ibrahim, I. El-Sakka, A.H.H. Elghandour and M.H. Elgandi, Arch. Pharm., **315**, 697 (1982).
9. E.M. Kandeel, M.K.A. Ibrahim, K.U. Sadek and M.H. Elnagdi Arch. Phar., **316**, (1983).