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REACTION WITH HETEROCYCLIC DIAZONIUM SALTS: SYNTHESIS OF PYRAZOLYLHYDRAZONE AND PYRAZOLO [1,5-C] AS-TRIAZINE DERIVATIVES

Mohamed Kamal Ahmed Ibrahim

Department of Chemistry, Faculty of Science, Cairo University, Giza, A.R. Egypt

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3-Amino-4-arylazopyrazol-5-yl diazonium chlorides (2 a,b) were coupled with different active methylene reagents such as benzenesulfonyl-acetophenone (i), *p*-toluenesulfonylacetophenone (ii), benzenesulfonylacetone (iii), dibenzolmethane and acetoacetanilide in sodium acetate/ethanol solution to give the corresponding pyrazole [1,5-c] as-triazine derivatives(5 a-d) and (6 a,b) respectively. Formation of pyrazole [1,5-c] as-triazines is assumed to be a dipolar cycloaddition reaction of diazobetaiene [3] and the enol form of the active methylene compounds. On the other hand, diazonium chlorides (2 a,b) were coupled with cyanoacetanilide, cyanoacetamide, β-naphthol, 3-methylpyrazol-5-one, 3-methyl-1-phenylpyrazol-5-one and (4-hydroxythiazol-2-yl)-acetonitrile [12] to give the corresponding hydrazones (7 a-c), (9 a,b), (11 a-c), and (13 a,b) respectively. The formation of hydrazones is assumed to occur by the normal coupling of diazonium chlorides (2 a,b) and active hydrogen reagents. Some of the acyclic hydrazones such as pyrazolylhydrazones (7 a-c), (9 a,b) and (13 a,b) could be cyclized by refluxing acetic acid to give pyrazole [1,5-c] as-triazine derivatives (8 a-c), (10 a,b) and (15 a,b) respectively. All structures suggested are based on elemental analysis and spectral data.

Key words: Heterocyclic, Salts, Pyrazoles.

INTRODUCTION

Heterocyclic diazo compounds and their diazonium salts are versatile reagents and recently their chemistry has received considerable attention [1-5]. In previous work [6], we have shown that diazotised aminopyrazoles react with active hydrogen reagents to yield either acyclic hydrazones (which could be readily cyclised into pyrazolo [1,5-c] as-triazines) or cyclic pyrazolo [1,5-c] as-triazines [3-7] directly. The formation of cyclic or acyclic products from the coupling of active methylene compounds with diazotised aminopyrazole was explained on the basis of the mechanistic pathway for 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 the diazobetaiene, via a 7+2 dipolar cycloaddition. When a usual coupling takes place, hydrazones are formed [3]. Dipolar addition to diazopyrazoles by electron poor dipolarophiles is now a well documented reaction. However, for a variety of systems it is difficult to predict the end product of reaction of diazoheterocycles, and whether the reaction would proceed mainly via a dipolar cycloaddition sequence or would lead to normal coupling.

MATERIALS AND METHODS

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye-Unicam SP-1100 spectrophotometer. Analytical data were obtained from the microanalytical center at Cairo University. Analytical, physical, and spectral data of the compounds are given in Tables 1 and 2.

Diazotization of 3,5-diamino-4-arylazopyrazole derivatives (1 a,b): A suspension of (1 a,b) (0.1 mole) in hydrochloric acid (30 ml, 37.5 %) was heated to produce a clear solution and then cooled to 0. A solution of sodium nitrite (0.1 mole) in water (30 ml) was added dropwise with continuous stirring for 5 min to give the diazonium chlorides (2 a,b).

Coupling of diazonium chlorides (2 a,b) with different active hydrogen reagents. A suspension of diazonium chlorides (2 a,b) (0.1 mole, prepared as described previously [3-8] was added gradually to cold solutions (0-5) of benzenesulfonylacetophenone (i), *p*-toluenesulfonylacetophenone (ii), benzenesulfonylacetone (iii), dibenzoylmethane, acetoacetanilide, cyanoacetanilide, cyanoacetamide, β-naphthol, 1-phenyl-3-methylpyrazol-5-one, 3-methylpyrazol-5-one and (4-hydroxythiazol-2-yl)acetonitrile [12] (0.1 mole) in ethanol (50 ml) containing sodium acetate (0.2 mole) with continous stirring for 30 min. The resulting products weee filtered off, washed with water, and crystallized from an appropriate solvent to give the coupling products (5 a-d), (6 a,b), (7 a-c), (9 a,b), (11 a-c) and (13 a,b).

Table 1. Analytical, physical and spectral data of synthetic pyrazolylhydrazones.

Compd. No.	M.p. °C	Yield %	Mol. formula/ (Mol. weight)	Analysis %. calcd./Found C	H	N	Cl	νmax cm^{-1} (Selected bands)
7 a	180	68	$C_{18}H_{15}N_9O$	57.9	4.0	33.8	–	1680 (C=O)' 2210 (C=N),
			(373)	57.8	4.1	33.6	–	2990-3200 (NH, NH_2)
7 b	138	56	$C_{12}H_{11}N_9O$	48.5	3.7	42.4	–	1685 (C=O), 2210 (C≡N),
			(297)	48.4	3.5	42.1		3000-3250 (NH, NH_2).
7 c	188	73	$C_{18}H_{14}N_9OCl$	53.0	3.4	30.9	8.7	1680 (C=O), 2210 (C≡N),
			(407.5)	52.8	3.3	30.8	8.6	3050-3300 (NH, NH_2).
9 a	182	82	$C_{19}H_{15}N_7O$	63.8	4.2	27.4	–	1605 (C=N), 3100-3380
			(357)	63.6	4.0	27.1	–	(NH, NH_2, OH).
9								
9 b	> 250	87	$C_{19}H_{14}N_7OCl$	58.2	3.6	25.0	9.1	1610 (C=N),
			(391.5)	57.9	3.4	24.8	8.8	3100-3450 (NH, NH_2, OH).
11 a	166	63	$C_{13}H_{13}N_9O$	50.1	4.2	40.5	–	
			(311)	49.8	3.9	40.2	–	
11 b	215	66	$C_{13}H_{12}N_9OCl$	45.1	3.5	36.5	10.3	1601 (C=N), 1663 (C=O),
			(345.5)	44.8	3.4	36.3	10.3	3100-3300 (NH, NH_2).
11 c	> 250	62	$C_{19}H_{16}N_9OCl$	54.1	3.8	29.9	8.4	1605 (C=N), 1660 (C=O),
			(421.5)	53.9	3.5	29.7	8.1	3100-3300 (NH, NH_2).
13 a	218	65	$C_{14}H_{11}N_9OS$	47.6	3.1	35.7	–	1600 (C=N), 1710 (C=O),
			(353)	47.4	2.9	35.6	–	2210 (C=N), 3200 (NH_2).
13 b	225	68	$C_{14}H_{10}N_9OSCl$	43.3	2.6	32.5	9.2	1605 (C=N), 1710 (C=O),
			(387.5)	43.1	2.4	32.4	9.0	2210 (C=N), 3190 (NH_2).

The solvent of crystallization for all hydrazones was ethanol except for (11 c) for which acetic acid was used.

Table 2. Analytical, physical and spectral data of synthesis pyrazolo [1,5-c] as-triazines.

Compd. No.	M.p. °C	Yield %	Mol. formula (Mol. weight)	Analysis % /. calcd./Found C	H	N	Cl	νmax cm^{-1} (Selected bands)
5 a	> 250	73	$C_{23}H_{17}N_7O_2S$	60.6	3.7	21.5	–	1150, 1340 (SO_2),
			(455)	60.4	3.6	21.2	–	3100-3200 (NH_2).
5 b	> 250	69	$C_{24}H_{19}N_7O_2S$	61.4	4.0	20.9	–	1155, 1345 (SO_2), 3000 (CH_3
			(469)	61.1	4.1	20.7	–	3200 (NH_2).
5 c	> 250	75	$C_{23}H_{16}N_7O_2SCl$	56.3	3.2	20.0	7.2	1150, 1345 (SO_2),
			(489.5)	56.1	3.1	20.2	7.0	3100-3200 (NH_2).
5 d	> 250	63	$C_{18}H_{14}N_7O_2SCl$	50.5	3.2	22.9	7.5	1155, 1340 (SO_2), 2900 (CH_3
			(427.5)	50.2	3.0	22.7	7.6	3150 (NH_2).

(Continued.....)

(Table 2, continued)

6 a	226	72	$C_{24}H_{17}N_7O$	68.7	4.1	23.4	–	1605 (C=N), 1661D(C=O),
			(419)	68.5	3.9	23.1	–	3100-3300 (NH_2).
6 b	155	55	$C_{19}H_{16}N_8O$	61.3	4.3	30.1	–	1600 (C=N), 1680 (C=O),
			(372)	61.1	4.1	29.8	–	3000-3300 (NH, NH_2).
8 a	>250	58	$C_{18}H_{15}N_9O$	57.9	4.0	33.8	–	1602 (C=N), 1680 (C=O),
			(373)	57.6	3.8	33.5	–	3100-3300 (NH, NH_2).
8 b	203	56	$C_{12}H_{11}N_9O$	48.5	3.7	42.4	–	1605 (C=N), 1685 (C=O),
			(297)	48.2	3.4	42.5	–	3100.3300 (NH_2).
8 c	>250	63	$C_{18}H_{14}N_9OCl$	53.0	3.4	30.9	8.7	1600 (C=N), 1680 (C=O),
			(407.5)	52.8	3.5	30.6	8.4	3000-3250 (NH, NH_2).
10 a	>250	85	$C_{19}H_{13}N_7$	67.2	3.8	28.9	–	1600 (C=N), 3100 (NH_2).
			(339)	67.1	3.6	28.7	–	
10 b	>250	88	$C_{19}H_{12}N_7Cl$	61.1	3.2	26.2	9.5	
			(373.5)	60.8	3.1	25.9	9.3	
15 a	>250	58	$C_{14}H_{11}N_9OS$	47.6	3.1	35.7	–	1601 (C=N), 1710 (C=O),
			(353)	47.4	3.0	35.6	–	2900-3300 (NH, NH_2).
15 b	>250	66	$C_{14}H_{10}N_9OSCl$	43.3	2.6	32.5	9.2	1610 (C=N), 1710 (C=O),
			(387.5)	43.1	2.4	32.4	9.1	3000-3300 (NH, NH_2).

The solvent of crystallization for all compounds was acetic acid except for (5 a-d) which was DMF and for (6 a,b) which was ethanol.

Cyclization of (7 a-c), (9 a,b) and (13 a,b). Suspensions of (7 a-c), (9 a,b), and (13 a,b) (0.1 mole) in acetic acid (50 ml) were refluxed for 2 hr, and then poured into water. The solid products were collected and crystallized to give the cyclic products (8 a-c), (10 a,b) and (15 a,b) respectively.

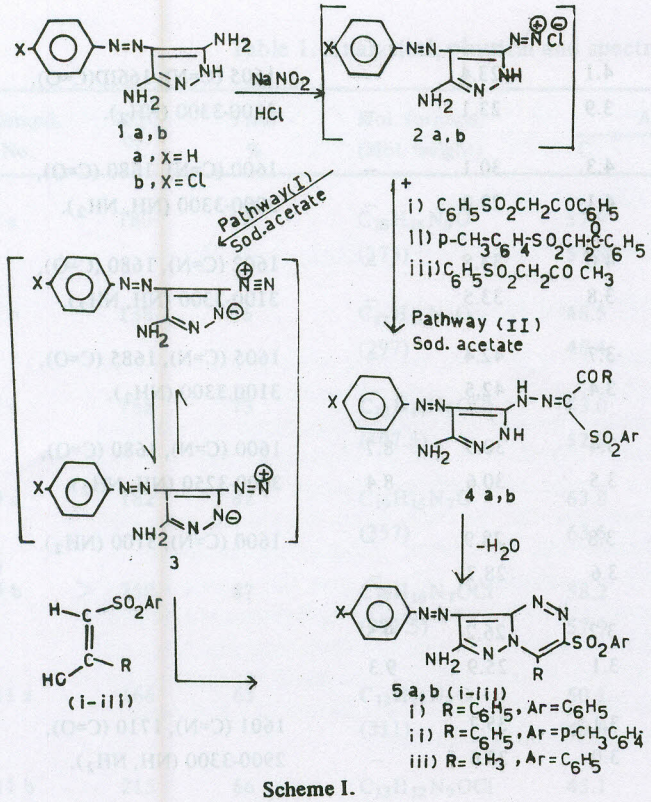
RESULTS AND DISCUSSION

In the present work we report the results of our investigations on the behaviour of diazotized 3,5diamino-arylazopyrazole (1 a,b) (a, aryl=C_6H_5– and b, aryl = *p*-Cl-C_6H_4-) toward a variety of reagents in order to get a better understanding of the nature of systems that would react preferentially via a cycloaddition sequence and those that would react via the normal coupling sequence.

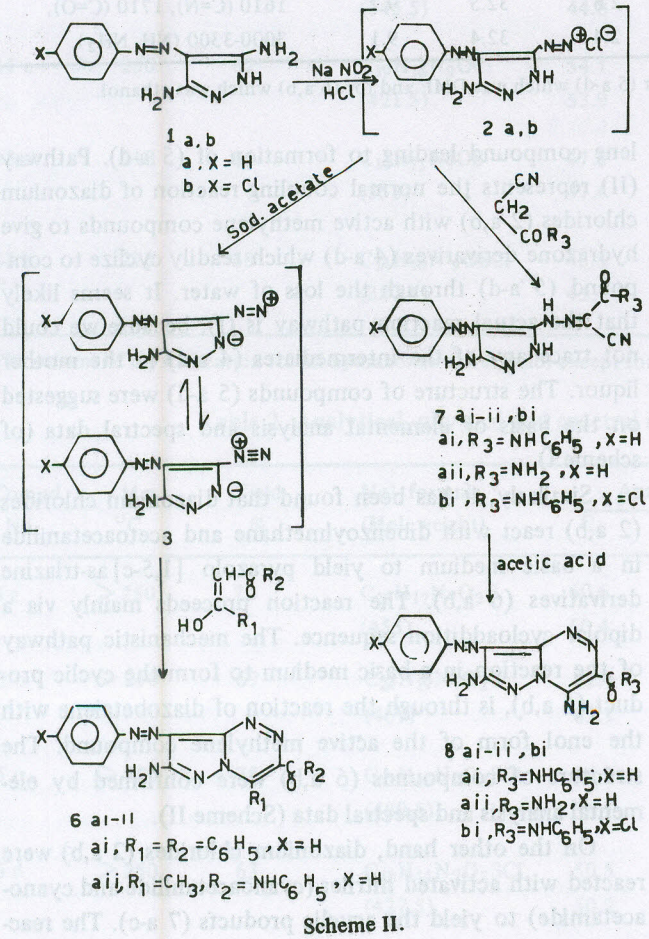
Thus, it has been found that diazonium chlorides (2 a,b) react with benzene sulfonylacetophenone (i), *p*-toluenesulfonylacetophenone (ii) and benzenesulfonylacetone (iii) in a basic medium to yield pyrazolo[1,5-c] astriazines derivatives (5 a-d). Two mechanistic pathways (I and II) lead to formation of pyrazolo [1,5-c] as-triazines (5-a-d). Pathway (I) represents a dipolar cycloaddition reaction of diazobetaiene [3] with the enol form of the active methylene compound leading to formation of (5 a-d). Pathway (II) represents the normal coupling reaction of diazonium chlorides (2 a,b) with active methylene compounds to give hydrazone derivatives (4 a-d) which readily cyclize to compound (5 a-d) through the loss of water. It seems likely that the actual reaction pathway is (I), because we could not trace any of the intermediates (4 a-d) in the mother liquor. The structure of compounds (5 a-d) were suggested on the basis of elemental analysis and spectral data (of scheme I).

Similarly, it has been found that diazonium chlorides (2 a,b) react with dibenzoylmethane and acetoacetanilide in a basic medium to yield pyrazolo [1,5-c] as-triazine derivatives (6 a,b). The reaction proceeds mainly via a dipolar cycloaddition sequence. The mechanistic pathway of the reaction in a basic medium to form the cyclic product (6 a,b), is through the reaction of diazobetaiene with the enol form of the active methylene compound. The structure of compounds (6 a,b) were confirmed by elemental analysis and spectral data (Scheme II).

On the other hand, diazonium chlorides (2 a,b) were reacted with activated nitriles (cyanoacetanilide and cyanoacetamide) to yield the acyclic products (7 a-c). The reac-



Scheme I.



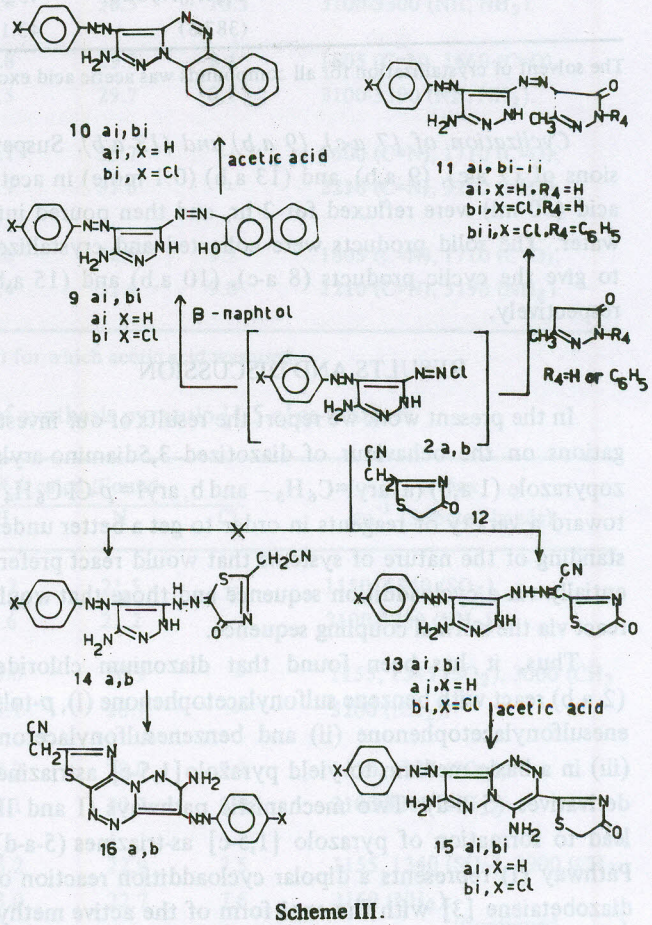
Scheme II.

tions take place via the normal coupling sequence. The structures of the products (7 a-c) were confirmed from the IR spectra which revealed a cyano peak at 2220 cm^{-1}, and by the fact that compounds (7 a–c) could be cyclized into pyrazole [1,5-c] as-triazines (8 a-c) on boiling with acetic acid. The structure of compounds (8 a-c) were confirmed from elemental analysis and spectral data (scheme II).

In contrast to the reported cycloaddition of naphthols to diazotised pyrazoles [8], diazonium chlorides (2 a,b) coupled with β-naphthol to afford the arylazo derivatives (9 a,b). The later compounds could be readily cyclised to (10 a,b) on refluxing with acetic acid (cf. scheme III).

In continuation of this work, the reaction of diazonium chlorides (2 a,b) with 2-pyrazolin-5-one derivatives was carried out resulting in formation of the hydrazones (11 a-c) only which could not be cyclised into the corresponding pyrazolo [1,5-c] as-triazines under a variety of conditions. The reaction takes place via the normal coupling sequence similar to that reported previously [3] (scheme III).

Also, diazonium chlorides (2 a,b) were reacted with the 2-thiazol-4-one derivative [12] 9,10 to yield the corres-



Scheme III.

ponding hydrazones. Two structures (13 a,b and 14 a,b. Scheme III) were possible for the reaction products. Structures (13 a,b) were established based on the ready cyclization of the hydrazones into the pyrazolo [1,5-c] as-triazines (15 a,b) on boiling the reaction products in acetic acid. The structures of (15 a,b) followed from an examination analytical and IR data.

These results when combined with our previous findings, indicate that the reaction of heterocyclic diazonium halides with active methylene reagents takes place via a dipolar cycloaddition reaction if the active methylene is either a β-diketo or β-ketosulfone or a β-ketoanilide. However, the reaction takes place via a normal coupling if the active methylene compound is either an α-cyano methylene compound, a β-ketoester, a β-ketonitrile, or an active hydrogen-containing aromatic or heterocyclic compound.

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