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STUDIES WITH POLYFUNCTIONALLY SUBSTITUTED HETERO- AROMATICS : SYNTHESES OF NEW 3-PYRAZOLIN-5-ONE DERIVATIVES.

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ABSTRACT

Diazotised 4-amino-I-phenyl-2,3dimethypyrazolin-5-one (4) coupled with active hydrogen containing reagents to yield the correspoding hydrazones (5-7). Compound (5) afforded 4-(4-antipyrinyl-hydrazono) -3-amino 2-pyrazolin- 5-one (10) on treatment with hydrazine hydrate. Thiazolyl hydrazone (12) was obtained by fusion of the hydrazone (11) with mercaptoacetic acid. Addition reactions of hydrazone (11) with aromatic primary amines, piperidine and morpholine are also reported.

INTRODUCTION

Polyfunctionally substituted heterocycles are interesting as potential biodegradable agrochemicals [1,2]. For this reason it seemed of value to develop new active and biodegradable pyrazoline compounds. In the present article I report on the synthesis of several new 3- pyrazolin-5-ones for biological testing in this area.

Thus, it has been reported that antipyrinyl hydrazones of type (I) readily cyclise on reflux in acetic acid in the presence of hydrochloric acid to pyrazolopyridazines (2) [3-5]. It seemed of value to see if this reaction is a general one and can thus constitute a new route for derivatives of this ring system.

The diazonium salt (4) couples readily with cyanoacetamide,

benzimidazol-2-ylacetonitrile or with salicylaldehyde to yield the corresponding coupling products (5-7). Whereas (5) and (6) were assigned the hydrazone form the coupling product of (4) with salicyladehyde was assigned structure (7) rather than the isomeric (8) based on its IR spectrum which revealed phenolic OH at 3500 cm^{-1}.

Diazotised (4) also couples with dimedone to yield the hydrazone (9). However, cyclohexanone failed to undergo similar reaction.

Attemppts to cyclise the coupling products (5, 6) into pyridazines failed under a variety of conditions.

Compound (5) reacted with hydrazine hydrate to yield the pyrazolohydrazone deravtive (10).

Attempted coupling of (4) with thiazolyl acetonitrile faild. The expected hydrazone (12) was, howerver, obtained on treatment of (11) with thioglcollic acid.

Compound (11) reacted also with primary amines, piperidine and morpholine to yield the imines (13) and (14).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded (KBr) on Pye Unicam Sp-1100 spectrophtometer. ^{1}H-NMR spectra were measured on a bruker AC 250 FT spectrometer using TMS as an internal standard and chemical shifts are expressed as ppm. Mass spectra were recorded on a Varian MAT 311 A spectrometer. The microanalyses were performed by the microanalytical unit at Cairo University

Coupling of diazotised 4-aminoantipyrine with active hydrogen containing compounds.

A solution of diazotised 4- aminoantipyrine (0.01mole) in the appropriate quantity of hydrochloric acid and sodium nitrire was added to a solution of the appropriate active hydrogen containing compound (0.01mole) in ethanol (20ml) end sodium acetate (1.5 g). The reaction mixture was left for I hr at room temperature. The solid product was filtered off, washed serveral times with water end crystallised from the suitable solvent. The aryl hydrazone derivatives (5-7) and 9 are listed in Table 1. the mass, IR and ^{1}H-NMR data are listed in Tanle 2.

Reaction of (5) with hydrazine hydrate : Formation of 4-(-antipyrinyl- hydrazono)-3-amino-2-pyrazolin-5-one (10).

A suspension of (5) (1.4 g; 0.005 mole) in 20ml ethanol was treated with hydrazine hydrate (0.5ml) and the reaction mixture was refluxed for I hr. the solid product, so formed, was filtered off and crystallised from ethanol. Compound (10) formed white crystsls, M.P. 203 °C, yield 87%, IR (cm^{-1}) 3455 (NH),1657 (CO) ^{1}H-NMR (δppm) (DMSO) :2.3 (s,3H,C-CH_3);3.5 (s,3H, N-CH_3); 7.2-7.7 (m, 6H aromatic protons and NH) and 11.2 (s, 3H, NH, and NH_2).-$C_{14}H_{15}N_7O_2$ (313.32) Calcd : C 53.67; H 4.83; N 13.29. Found : C 53.40; H 4.61; N 31.65. MS (m /z) : 313 (M^+ ,3), 111 (40), 56 (100).

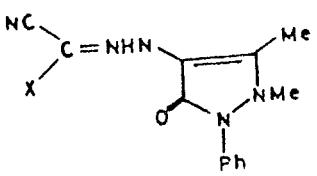
Reaction of (11) with mercaptoacetic acid, primary amines, piperidine and morpholine

Table 1: Compounds (5-7), (9), (13a,b) and (14a,b)

Com-pound	Cryst. Solvent	M.P. °C	Yield %	Molec. Formula (Molec. Weight)	Calcd Found	C	H %	N
(5)	EtOH	261	62	$C_{14}H_{14}N_6O_2$ (298.30)		56.4 56.0	4.7 4.9	28.2 27.8
(6)	EtOH	225	65	$C_{20}H_{17}N_7O$ (371.40)		64.6 64.3	4.6 4.8	26.4 26.0
(7)	AcOH	258	40	$C_{18}H_{16}N_4O_3$ (336.35)		64.2 64.6	4.7 4.9	16.6 16.4
(9)	MeOH	216	62	$C_{19}H_{22}N_4O_3$ (354.4)		64.3 64.0	6.2 6.1	15.8 16.1
(12)	AcOH	185	82	$C_{16}H_{14}N_6O_2S$ (354.39)		54.2 54.6	3.9 4.0	23.7 23.4
(13a)	EtOH	248	22	$C_{21}H_{21}N_7O$ (387.44)		65.1 65.3	5.4 5.2	25.3 25.5
(13b)	EtOH	245	25	$C_{21}H_{21}N_7O$ (387.44)		65.1 64.8	5.4 5.5	25.3 24.9
(14a)	EtOH	203	77	$C_{19}H_{23}N_7O$ (365.44)		62.4 62.1	6.3 6.6	26.8 27.2
(14b)	EtOH	230	60	$C_{18}H_{21}N_7O_2$ (367.41)		58.8 58.9	5.7 5.6	26.6 26.3

Table 2: Mass, IR and ^{1}H-NMR spectral data for compounds listed in Table 1.

Compound	Ms (m/z)	IR; cm^{-1} (Selected Bands)	^{1}H-NMR, δ (ppm) (DMSO)
(5)	298(M^+,26) 202 (16) 83 (54) 56 (100)	3369 (NH, NH_2) 2209 (CN) 1662 (CO)	2.3 (s, 3H, C-CH_3); 3.4 (s, 3H, N-CH_3); 7.2-7.6 (m, 5H, aromatic protons); 11.3 (s, 3H, NH_2 and NH).
(6)	371(M^+,36) 188 (19) 83 (34) 56 (100)	3300-3100 (NH) 2220 (CN) 1640 (CO)	2.4 (s, 3H, C-CH_3); 3.1 (s, 3H, N-CH_3); 7.1-7.7 (m, 10H, aromatic protons and NH).
(7)		3500 (6H); 1670 (CO)	
(9)	354(M^+,25) 202 (38.5) 83 (33.5) 56 (100)	3436 (NH) 1669 (CO)	1.05 (s, 6H, 2 CH_3); 2.55 (s, 3H, C-CH_3); 2.60 (s, 4H, 2 CH_2); 3.2 (s, 3H, N-CH_3); 7.2-7.7 (m, 6H, aromatic protons and NH)
(12)	354 (M^+,1.5) 188 (15)	3441 (NH)	2.2 (s, 3H, C-CH_3); 3 (s, 3H, N-CH_3); 3.7 (s, 2H, CH_2); 7.0-7.2 (m, 6H, aromatic protons and NH).
(13a)	387(M^+,0.3) 188 (52) 93 (100)	3436 (NH) 2219 (CN) 1662 (CO)	
(14a)	365(M^+,28) 214 (56) 188 (68) 84 (100)	3412 (NH) 2177 (CN) 1641 (CO)	1.7 (s, 6H, 3CH_2); 2.5 (s, 3H, C-CH_3); 3.1 (s, 4H, 2N-CH_2); 3,4 (s, 3H, N-CH_3); 7.1-7,7 (m, 6H, aromatic protons and NH)
(14b)	367(M^+,56.5) 214(10.5) 188 (26) 56 (100)	3362 (NH) 2184 (CN) 1641 (CO)	2.3 (s, 3H, C-CH_3); 2.8 (s, 4H, 2N CH_2); 3.3 (s, 3H, N-CH_3); 3.6(s, 4H, 2O-CH_2); 7.5-7.7 (m, 6H, aromatic protons and NH).



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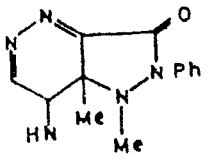

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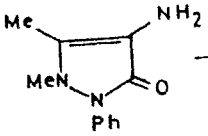

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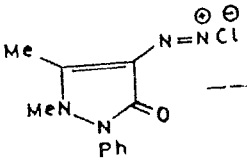

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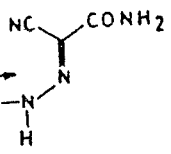

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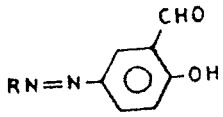

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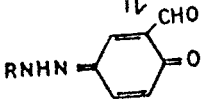

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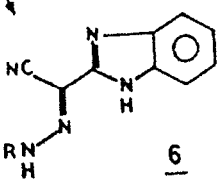

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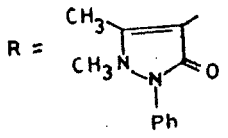

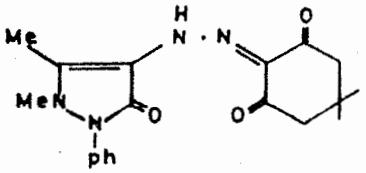

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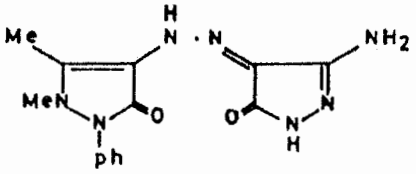

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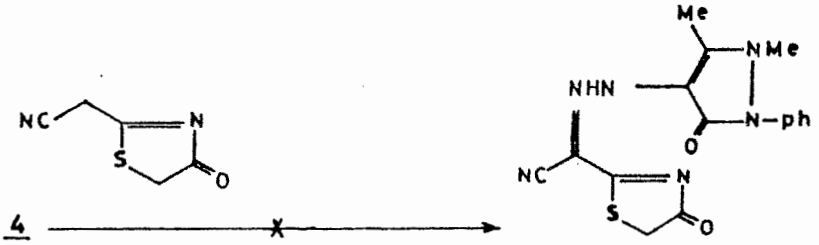

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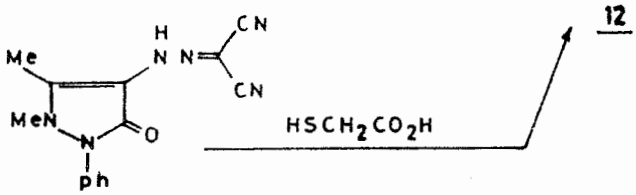

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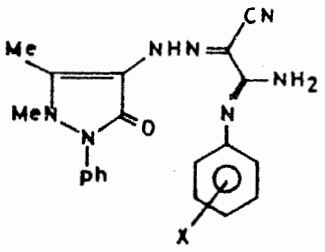
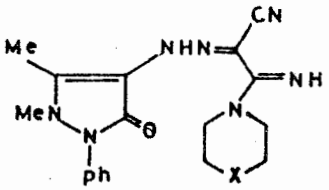


13

13 a, X = p - CH_3

b, X = m - CH_3



14

14 a, X = CH_2

b, X = O

A mixture of (II) (0.005 mole) and each of thioglycollic acid, p-toluidine, m- toluidine piperidine or morpholine (0.005 mole) was fused at 100°C (bath temperature) for 2 hrs. The oil formed was triturated with ethanol and the separated solid product was collected by filtration and crystallised from the proper solvent to give compounds (12) (13a, b) and (14a,b) which are listed in Table 1. The mass, IR and 1H-NMR spectral data are listed in Table 2.

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تخليق مشتقات جديدة من ٣-بيرازولين -٥- اون

إبراهيم أحمد السقا
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يتفاعل ملح الديازونيوم لمركب الأنتيبيرين مع الجواهر المحتوية علي ذرات هيدروجين نشطة لتعطي الهيدرازونات المقابلة.

وقد أمكن تحضير ثيازوليل هيدرازون نتيجة صهر مشتق الداي سيانو هيدرازون مع مركابتو حمض الخليك.

يتفاعل مشتق الداي سيانو هيدرازون أيضاً مع بعض الأمينات العطرية والقواعد مثل البيريدين والمورفولين لتكون مركبات إضافة .