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Novel Synthesis of Imidazo[1,2-b]pyrazoles and Their Fused Derivatives

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4-Arylazo-1H-pyrazol-3,5-diamines **1a-c** reacted with bromomalononitrile (**2**) to yield the corresponding imidazo[1,2-b]pyrazoles **3a-c**. The latter reacted with some active methylene compounds and with α-cinnamonitriles to afford the corresponding pyrazoloimidazopyridines **6**, **8**, **9** and **15**, respectively. Compounds **3** reacted with each of formic acid, formamide, trichloroacetonitrile and with guanidine to yield the corresponding pyrazoloimidazopyrimidines **16-19**, respectively.

Key words: Imidazo[1,2-b]pyrazoles, Pyrazoloimidazo-pyridines and pyrimidines

INTRODUCTION

Polyfunctional nitriles are highly reactive reagents that have been extensively used as synthons for heterocyclic compounds (Elnagdi *et al.*, 1987; Galil *et al.*, 1986; Sherif *et al.*, 1988). In continuation of our efforts directed towards the development of new procedures for the synthesis of azoles, azines and their condensed derivatives utilizing readily obtainable polyfunctional nitriles (Sherif *et al.*, 1993; Shawali *et al.*, 1980; Mohareb *et al.*, 1992), we report herein, a new synthesis of polyfunctional substituted imidazo[1,2-b]pyrazoles together with their chemical transformations into pyrazoloimidazo-pyridines and pyrimidines of expected wide spectrum of biological activities.

MATERIALS AND METHODS

All melting points were determined on Gallenkamp melting point apparatus and are uncorrected. The infrared spectra were recorded in potassium bromide on Pye Unicam SP-1000 infrared spctrophotometer. The ^{1}H-NMR spectra were recorded in DMSO-d_6 on a Varian EM-390 90 MHz spectrometer using tetramethylsilane as internal reference. Mass spectra were recorded on a GCMS-QP 1000 Ex Shimadzu insturment at 70 eV. Elemental analyses were carried out at the Microanalytical Data Center at Cairo University, Giza, Egypt. 4-Arylazo-1H-pyrazole-3,5-diamines **1a-c** (Elnagdi *et al.*, 1973) were prepared as previously described in literature.

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Synthesis of 6-arylazo-2,5-diamino-1H-imidazo[1,2-b]-pyrazole-3-carbonitriles 3a-c

To a solution of each of **1a-c** (5 mmoles) in dry dioxane (50 ml) containing a catalytic amount of piperidine (3 drops) was added bromomalononitrile (**2**) (0.7 gm, 5 mmoles). The reaction mixture was heated under reflux for 4 h, cooled at room temperature and then poured onto ice/water mixture. The mixture was neutralized with dilute hydrochloric acid whereby, the solid product so formed, in each case, was filtered off, dried and crystallized from the proper solvent (Tables I and II).

Synthesis of 8-arylazo-2,7-diamino-pyrazolo[5',1' : 1, 2]imidazo[4,5-b]pyridine-3-carbonitriles 6a, b

To a solution of each of **3b, c** (5 mmoles) in glacial acetic acid (30 ml) malononitrile was added (**5a**) (0.33 gm, 5 mmoles). The reaction mixture was heated under reflux for 6 h, cooled at room temperature and then poured onto ice/water mixture. The solid product so precipitated, in each case, was collected by filtration, washed several times with water, dried and crystallized from the proper solvent (Tables I and II).

Table I. Physcial and analytical data of the newly prepared compounds

Compd. No. (Cryst. solvent)	M.P. ℃	Yield (%)	Mol. Formula (Mol. wt.)	Analysis (%)[a] Calcd/Found		
				C	H	N
3a	266	65	$C_{12}H_{10}N_8$	54.13	3.78	42.08
(dioxan/H_2O)			(266.25)	53.9	3.6	42.0
3b	271	69	$C_{13}H_{12}N_8O$	52.70	4.07	37.82
(dioxan/H_2O)			(296.27)	52.4	3.9	37.6
3c	288	62	$C_{12}H_9ClN_8$	47.93	3.01	37.26
(dioxan/H_2O)			(300.69)	47.8	3.0	37.0
6a	>320	59	$C_{16}H_{14}N_{10}O$	53.04	3.89	38.65
(DMF/H_2O)			(362.33)	52.8	3.7	38.6
6b	>320	51	$C_{15}H_{11}ClN_{10}$	49.12	3.02	38.19
(DMF/H_2O)			(366.75)	49.0	3.0	38.1
8a	298	34	$C_{15}H_{11}N_9O$	54.05	3.32	37.82
(dioxan)			(333.29)	54.0	3.1	37.6
8b	>320	49	$C_{15}H_{10}ClN_9O$	48.85	3.00	34.18
(dioxan)			(368.74)	48.7	2.8	33.8
9a	>320	61	$C_{28}H_{22}N_8O_2$	66.92	4.40	22.29
(dioxan/EtOH)			(502.50)	66.7	4.3	22.0
9b	>320	55	$C_{27}H_{19}ClN_8O$	63.97	3.77	22.10
(dioxan/H_2O)			(506.92)	63.8	3.7	22.0
10a	306	48	$C_{22}H_{17}N_9OS$	58.01	3.75	27.67
(DMF/H_2O)			(455.47)	58.0	3.6	27.5
10b	>320	63	$C_{21}H_{14}ClN_9S$	54.84	3.06	27.41
(DMF/H_2O)			(459.89)	54.7	3.0	27.2
11	310	49	$C_{21}H_{14}ClN_9S$	54.84	3.06	27.41
(DMF)			(459.89)	54.7	3.0	27.2
15a	269	49	$C_{21}H_{15}N_9$	64.12	3.84	32.04
(dioxan)			(393.39)	63.8	3.6	31.9
15b	306	67	$C_{22}H_{17}N_9O$	62.41	4.04	29.77
(DMF/H_2O)			(423.41)	62.4	3.8	29.7
15c	289	61	$C_{24}H_{22}N_8O_3$	61.13	4.71	23.81
(DMF/H_2O)			(470.46)	61.0	4.5	23.8
16a	>320	70	$C_{14}H_{12}n_8O_2$	51.85	3.73	34.55
(DMF/H_2O)			(324.28)	51.8	3.6	34.3
16b	295	66	$C_{13}H_9ClN_8O$	47.50	2.76	34.08
(DMF/H_2O)			(328.70)	47.5	2.7	34.0
17a	292	61	$C_{14}H_{13}N_9O$	52.01	4.04	38.99
(dioxan)			(323.29)	51.8	4.0	38.8
17b	>320	59	$C_{13}H_{10}ClN_9$	47.64	3.07	38.46
(dioxan/H_2O)			(327.72)	47.4	3.0	38.2
18	296	44	$C_{14}H_9Cl_4N_9$	37.78	2.03	28.32
(dioxan/EtOH)			(445.08)	37.6	1.9	28.4
19a	293	41	$C_{14}H_{14}N_{10}O$	49.70	4.16	41.39
(DMF/H_2O)			(338.31)	49.5	4.0	41.1
19b	312	49	$C_{13}H_{11}ClN_{10}$	45.55	3.23	40.86
(DMF/H_2O)			(342.73)	45.4	3.0	40.6

[a] S% of compounds **10a**, 7.04 (6.8); **10b**, 6.97 (6.8).

Synthesis of 8-arylazo-4,7-diamino-2-oxo-pyrazolo [5',1' : 1,2]imidazo[4,5-b]pyridine-3-carbonitriles 8a, b

To a solution of each of **3a, c** (5 mmoles) in dry dioxane (30 ml) containing a catalytic amount of triethylamine (3 drops) was added ethyl cyanoacetate (**5b**) (0.56 gm, 5 mmoles). The reaction mixture was heated under reflux for 6 h, cooled at room temperature, poured onto ice/water and neutralized with acetic acid (pH=7). The solid product so precipitated, in each case, was filtered off, dried and crystallized from the proper solvent (Tables I and II).

Table II. Spectroscopic data of the newly prepared compounds

Compd. No.	IR (cm^{-1}) (Selected bands)	^{1}H-NMR δ (ppm)
3a	3360-3230 (NH_2, NH); 2225 (CN)	3.35 (s, br, 2H, NH_2, D_2O-exchangeable); 6.91 (d, 2H, arom, protons); 7.28 (m, 3H, arom, protons); 8.31 (s, br, 2H, NH_2, D_2O-exchangeable); 9.24 (s, 1H, NH, D_2O-exchangeable)
3b	3350-3300 (NH_2, NH); 2940 (CH_3); 2220 (CN)	3.75 (s, 3H, OCH_3); 4.61 (s, br, 2H, NH_2, D_2O-exchangeable); 7.13 (d, 2H, arom. protons); 7.29 (d, 2H, arom. protons); 8.12 (s, br, 2H, NH_2, D_2O-exchangeable); 10.81 (s, 1H, NH, D_2O-exchangeable)
3c	3310-3250 (NH); 2225 (CN)	–
6a	3410-3250 (NH, NH_2); 2940 (CH_3); (CH_3); 2225 (CN)	2.81 (s, br, 2H, NH_2, D_2O-exchangeable); 3.85 (s, 3H, OCH_3); 6.21 (s, 2H, NH_2, D_2O-exchangeable); 7.21 (d, 2H, arom. protons); 7.33 (d, 2H, arom. protons); 8.29 (s, 2H, NH_2, D_2O-exchangeable); 1055 (s, 1H, NH, D_2O-exchangeable)
6b	3400-3200 (NH, NH_2); 2217 (CN)	–
8a	3420-3250 (NH, NH_2); 1700 (CO)	2.93 (s, br, 2H, NH_2, D_2O-exchangeable); 8.1 (s, 2H, NH_2, D_2O-exchangeable); 7.28-7.33 (m, 5H, arom. protons); 8.41 (s, 1H, NH, D_2O-exchangeable); 9.53 (s, 1H, NH, D_2O-exchangeable)
8b	3400-3180 (NH, NH_2); 1700 (CO)	3.54 (s, 2H, NH_2, D_2O-exchangeable); 5.32 (s, 2H, br, NH_2, D_2O-exchangeable); 7.21 (d, 2H, arom. protons); 7.32 (d, 2H, arom. protons); 8.55 (s, 1H, NH, D_2O-exchangeable); 9.32 (s, 1H, NH, D_2O-exchangeable)
9a	3400-3180 (NH, NH_2); 2940 (CH_3); 1680 (CO)	3.21 (s, br, 2H, NH_2, D_2O-exchangeable); 3.85 (s, 3H, OCH_3); 7.21-7.39 (m, 14H, arom. protons); 8.52 (s, 2H, NH_2, D_2O-exchangeable); 10.32 (s, 1H, NH, D_2O-exchangeable)
9b	3420-3270 (NH, NH_2); 1680 (CO)	–
10a	3470-3260 (NH, NH_2); 2940 (CH_3); 2220 (CN)	–
10b	3450-3260 (NH, NH_2); 2220 (CN)	3.72 (s, 2H, NH_2, D_2O-exchangeable); 6.32 (s, 1H, thiazole H-5); 7.25-7.31 (m, 9H, arom. protons); 9.21 (s, 1H, NH, D_2O-exchangeable); 10.51 (s, 1H, NH, D_2O-exchangeable)
11	3450-3250 (NH, NH_2)	–
15a	3450-3300 (NH, NH_2); 2210 (CN)	3.99 (s, 2H, NH_2, D_2O-exchangeable); 7.21-7.29 (m, 10H arom. protons); 8.11 (s, 2H, NH_2, D_2O-exchangeable); 9.92 (s, 1H, NH, D_2O-exchangeable)
15b	3410-3250 (NH, NH_2); 2940 (CH_3); 2210 (CN)	3.21 (s, 2H, NH_2, D_2O-exchangeable); 3.91 (s, 3H, OCH_3); 7.12-7.31 (m, 9H, arom. protons); 8.23 (s, 2H, NH_2, D_2O-exchangeable); 8.93 (s, 1H, NH, D_2O-exchangeable)
15c	3400-3220 (NH, NH_2), 1700 (CO)	1.24 (t, 3H, CH_3); 3.90 (s, 3H, OCH_3); 4.20 (q, 2H, CH_2); 5.11 (s, 2H, NH_2, D_2O-exchangeable); 7.11-7.34 (m, 9H, arom. protons); 8.41 (s, 2H, NH_2, D_2O-exchangeable); 8.83 (s, 1H, NH, D_2O-exchangeable)
16a	3400-3270 (NH, NH_2); 2945 (CH_3); 1680 (CO)	–
16b	3390-3270 (NH, NH_2); 1690 (CO)	3.12 (s, 2H, NH_2, D_2O-exchangeable); 7.13 (d, 2H, arom. protons); 7.27 (d, 2H, arom. protons); 7.83 (s, 1H, pyrimidine H-2); 9. 11 (s, 1H, NH, D_2O-exchangeable); 9.93 (s, 1H, NH, D_2O-exchangeable)
17a	350-3290 (NH, NH_2)	3.55 (s, 2H, NH_2, D_2O-exchangeable); 4.11 (s, 3H, OCH_3); 7.00-7.21 (m, 4H, arom. protons); 7.91 (s, 1H, pyrimidine H-2); 9.11 (s, 2H, NH_2, D_2O-exchangeable); 9.93 (s, 1H, NH, D_2O-exchangeable)
17b	3380-3250 (NH, NH_2)	–
18	3440-3310 (NH_2+NH)	5.31 (s, 2H, NH_2, D_2O-exchangeable); 7.12 (d, 2H, arom. protons); 7.33 (d, 2H, arom. protons); 8.10 (s, 2H, NH_2, D_2O-exchangeable); 9.53 (s, 1H, NH, D_2O-exchangeable)
19a	3400 (NH_2)	3.90 (s, 3H, OCH_3); 4.45 (s, 2H, NH_2, D_2O-exchangeable); 5.56 (s, 2H, NH_2, D_2O-exchangeable); 6.95 (d, 2H, arom. protons); 7.22 (d, 2H, arom. protons); 8.03 (s, 2H, NH_2, D_2O-exchangeable); 9.71 (s, 1H, NH, D_2O-exchangeable)
19b	3420 (NH_2)	4.12 (s, 2H, NH_2, D_2O-exchangeable); 6.33 (s, 2H, NH_2, D_2O-exchangeable); 7.13 (d, 2H, arom. protons); 7.26 (d, 2H, arom. protons); 8.93 (s, 2H, NH_2, D_2O-exchangeable); 9.55 (s, 1H, NH, D_2O-exchangeable)

Synthesis of 8-arylazo-3-benzoyl-2-phenyl-pyrazolo [5',1' : 1,2]imidazo[4,5-b]pyridine-3,7-diamines 9a, b

To a solution of each of **3b, c** (5 mmoles) in dimethylformamide (50 ml) containing a catalytic amount of piperidine (0.5 ml) was added dibenzoylmethane (**5c**) (1.2 gm, 5 mmoles). The reaction mixture was heated under reflux for 2 h, cooled at room temperature, poured onto ice/water and neutralized with acetic acid. The solid product so precipitated, in each case, was collected by filtration, dried anc crystallized from the proper solvent (Tables I and II).

Synthesis of 6-amino-7-arylazo-2-(4'-phenyl-thiazol-2'-yl)amino-1H-imidazo[1,2-b]pyrazole-3-carbonitriles 10a, b

To a solution of each of **3b, c** (5 mmoles) in dioxane (50 ml) containing concentrated hydrochloric acid (1 ml) was added phenacyl thiocyanate (**5d**) (0.87 gm, 5 mmoles). The reaction mixture was heated on a boiling water bath for 8 h, then left aside at room temperature overnight. The solid product so formed, in each case, upon trituration the reaction mixture with water was filtered off, dried and crystallized from the proper solvent (Tables I and II).

Synthesis of 11

A solution of **10b** (2.3 gm, 5 mmoles) in dioxane (30 ml) containing triethylamine as a catalyst (0.5 ml) was refluxed for 3 h and then left aside at room temperature overnight. The solid product that separated was collected by filtration, dried and crystallized from the proper solvent (Tables I and II).

Synthesis of 2-aryl-8-arylazo-4,7-diamino-pyrazolo[5', 1' : 1,2]imidazo[3,4-b]pyridines 15a-c

To a solution of each of **3a, b** (5 mmoles) in pyridine (30 ml) was added the appropriate α-cinnamonitrile **12a, b** (5 mmoles). The mixture was refluxed for 4 h, cooled at room temperature then poured onto ice/water. The solid product that precipitated, in each case, was collected by filtration, washed several times with water, dried and crystallized from the proper solvent (Tables I and II).

Synthesis of 8-arylazo-4-oxo-pryazolo[5',1' : 1,2]imidazo[4,5-d]pyrimidine-7-amines 16a, b

Each of **3b, c** (1 gm) was heated under reflux in formic acid (85%, 10 ml) for 12 h. The solid product so formed on cooling at room temperature was filtered off and crystallized from the proper solvent (Tables I and II).

Synthesis of 8-arylazo-pyrazolo[5',1' : 1,2]imidazo[4, 5-d]pyrimidine-4,7-diamines 17a, b

Each of **3b, c** (1 gm) was heated under reflux with a ternary mixture of formic acid (5 ml), formamide (5 ml) and dimethylformamide (5 ml) for 12 h. The reaction mixture was then left aside at room temperature overnight, where by the solid product so formed, in each case, was filtered off and crystallized from the proper solvent (Tables I and II).

Synthesis of 8-(p-chlorophenylazo)-2-trichloromethyl-pyrazolo[5',1' : 1,2]imidazo[4,5-b]pyrimidine-4,7-diamine 18

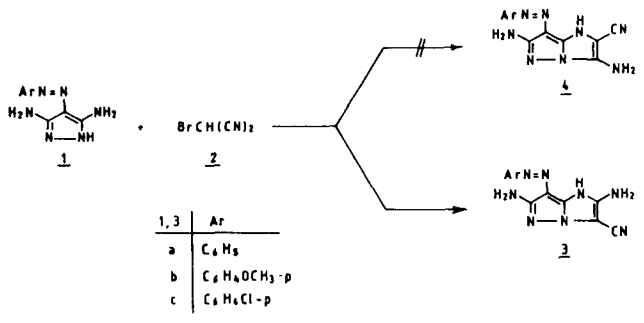
To a solution of **3c** (1.5 gm, 5 mmoles) in DMF (30 ml), trichloroacetonitrile (0.7 gm, 5 mmoles) was added together with a catalytic amount of triethylamine (0.5 ml). The reaction mixture was heated under reflux for 5 h, and then left overnight at room temperature. The mixture was then poured onto ice/water, and neutralized with few drops of hydrochloric acid. The solid product so formed, was filtered off, dried and crystallized from the proper solvent (Tables I and II).

Synthesis of 8-arylazo-pyrazolo[5',1' : 1,2]imidazo[4, 5-b]pyrimidine-2,4,7-triamines 19a, b

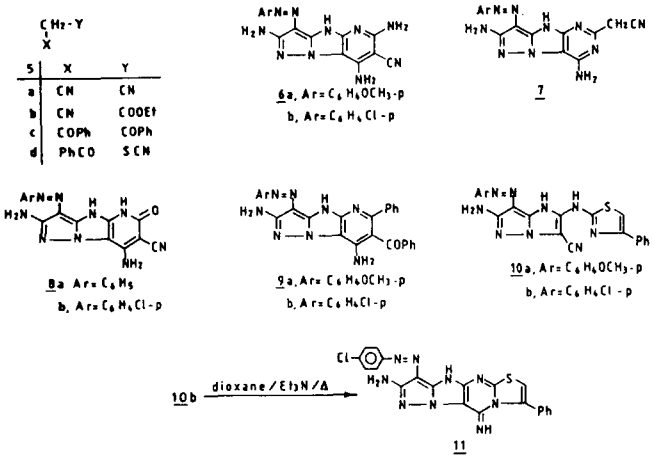
Guanidine nitrate (0.6 gm, 5 mmoles) in ethanolic sodium ethoxide (0.11 gm, 5 mmoles Na in 20 ml absolute EtOH) was stirred for 0.5 h and then treated with **3b, c**. The reaction mixture was refluxed for 24 h, cooled at room temperature and then poured onto ice/water. The solid product so precipitated was collected by filtration, washed with water, dried and crystallized from the proper solvent (Tables 1 and II).

RESULTS AND DISCUSSION

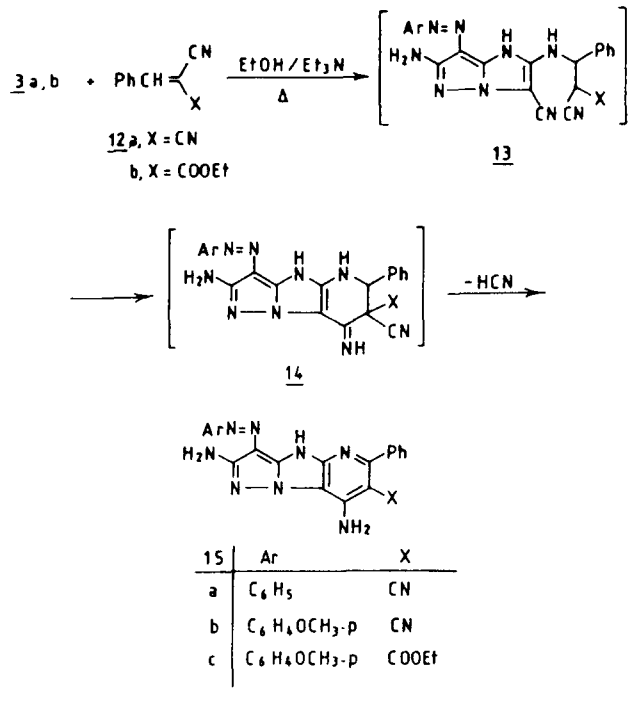
Treatment of the 4-arylazo-1H-pyrazole-3,5-diamines **1a-c** with equimolecular proportion of bromomalononitrile (**2**) in dry dioxane containing a catalytic amount of piperidine as HBr acceptor afforded the corresponding 1H-imidazo[1,2-b]pyrazole derivatives **3a-c**, respectively, in reasonably good yields (Scheme 1). Struture **3** was established for such products on the basis of correct elemental analyses and compatible spectroscopic data. Thus, as a representive example, the Ms spectrum of **3b** revealed a molecular ion (M^+) peak at m/z=296 with 30% relative abundance corresponding to the molecular formula $C_{13}H_{12}N_8O$. Its IR spectrum showed absorption peaks at 3350-3300 cm^{-1} (NH, NH_2) and 2220 (CN). Also its ^1H-NMR spectrum (DMSO-d_6) showed in addition to the aromatic protons signals, three types of D_2O-exchangeable protons at δ (ppm) 4.61 (s, 2H, NH_2), 8.21 (s, 2H, NH_2) and 10.81 (s, 1H, NH). Formation of **3** from the reaction



Shceme 1



Shceme 2



Shceme 3

of **1** with **2** is assumed to be proceeded via initially attack on the most basic ring-N in **1**. Although one may argue that the reaction of **1** with **2** may involve the exo-cyclic 3-amino group to yield the isomeric structure **4**, the involvement of the endo-cyclic pyrazole-N was considered based on literature reports (Elgemeie *et al.*, 1991; Shawali *et al.*, 1980; Mosby *et al.*, 1961) which revealed that the ring H-1 in amino pyrazoles is the most reactive centre in the molecule and consequently the ability of pyrazoles to be alkylated at the ring-N.

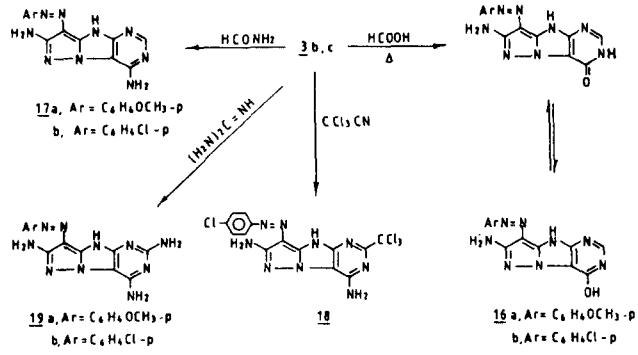
Compounds **3b, c** reacted with malononitrile (**5a**) in glacial acetic acid, under reflux, to yield 1 : 1 adducts. Such products may be formulated as the pyrazolo [5′,1′ : 1,2]imidazo[4,5-b]pyridines **6** or the isomeric pyrazolo[5′,1′ : 1,2]imidazo[4,5-d]pyrimidines **7**. Structure **6** was tentively preferred for such products based on ^{1}H-NMR spectra which revealed four types of D_2O-exchangeable protons (Scheme 2).

Compounds **3a, c** reacted with ethyl cyanoacetate (**5b**) in dry dioxane in the presence of a catalytic amount of triethylamine under reflux to yield the corresponding pyrazolo[5′,1′ : 1,2]imidazo[4,5-b]pyridine derivatives **8a, b** via elimination of ethanol. Structure **8** was established for such products on the basis of correct elemental analyses and compatible spectroscopic data. Thus the IR spectra of **8a, b** revealed bands corresponds to NH_2, CN and cyclic CO functions. ^{1}H-NMR spectrum (DMSO-d_6) of **8a**, as an example, revealed the presence of multiplet signal at δ (ppm) 7.28-7.33 (5H) corresponding to the aromatic protons together with D_2O-exchangeable signals at 2. 93 (s, 2H, NH_2), 8.1 (s, 2H, NH_2), 8.41 (s, 1H, NH) and 9.53 (s, 1H, NH).

Similarly, compounds **3b, c** reacted with dibenzoylmethane (**5c**) in refluxing DMF/piperidine solutions to yield the corresponding pyrazolo[5′,1′ : 1,2]imidazo[4, 5-d]pyridine derivatives **9a, b** via elimination of water elements. The IR spectra of the latter showed no CN absorption bands around 2200 cm^{-1}.

Compounds **3b, c** reacted with equimolecular amounts of phenacyl thiocyanate (**5d**) in refluxing dioxane containing a catalytic amount of hydrochloric acid to afford the corresponding 2-(4′-phenyl-thiazol-2′-yl) amino-1H-imidazo[1,2-b]-pryazole-3-carbonitriles **10a, b**, respectively. The IR spectra of **10a, b** revealed absence of the CO absorption and the presence of only one CN function. Compound **10b** underwent intramolecular cyclization into the fused tetracyclic compound **11** upon reflux in dioxane in presence of triethylamine as a catalyst (Scheme 2). The IR spectrum of **11** revealed the disappearance of the CN absorption band.

The reaction of compounds **3** with α-cinnamonitriles **12a, b** was also investigated. Thus compounds **3a, b** reacted with **12** in pyridine solutions, under reflux, to afford the corresponding pyrazolo[5′,1′: 1,2]imidazo[3,



Shceme 4

4-b]pyridines **15a-c** (Scheme 3). The identity of the product, in each case, was established based on analytical and spectral data (Experimental). Formation of **15** could be assumed via the anticipitated addition of the NH_2 function of the enaminonitrile moiety in **3** to the activated double bond of **12** to give the acyclic intermediate adduct **13**, which spontaneously cyclized into **14**. The latter, aromatized via loss of HCN under the reaction conditions to yield the final isolable end products **15a-c**. Similar phenomena has been previously reported in literature (Yamanaka *et al.*, 1987; Gupta *et al.*, 1987).

Long heating of compounds **3b, c** with excess of formic acid (85%), under reflux, yielded the corresponding pyrazolo[5',1' : 1,2]imidazo[4,5-b]pyrimidines **16 a, b** respectively. Analogously, compounds **3b, c** reacted with formamide in the presence of formic acid and dimethylformamide, on boiling under reflux, to yield the corresponding pyrazolo[5',1' : 1,2]imidazo[4, 5-d]pyrimidine-4,7-diamines **17a, b** (Scheme 4). The analytical and spectral data of **16** and **17** are entirely consistent with the proposed structures.

Likewise, compounds **3** seems to be an interesting candidates for further chemical transformations. Thus compound **3c** reacted with equimolecular proportions of trichloroacetonitrile in DMF catalysed by triethylamine on boiling under reflux, to afford the pyrazoloimidazopyrimidine derivative **18**. Formation of **18** is assumed to be formed via initial Michael-type addition of the NH_2 of the imidazole moiety in **3** to the CN moiety of CCl_3CN followed by intramolecular cyclization. Also, **3b, c** reacted with guanidine in boiling ethanolic sodium ethoxide solution, under reflux, to yield pyrazoloimidazopyrimidines **19a, b**.

In conclusion, we consider that the above results presented in this article, indirectly extend and broaden the knowledge in the area of enaminonitriles and demonstrate a general applicable methodology for constructing a polyfunctionally substituted imidazo[1,2-b] pyrazoles, pyrazoloimidazo-pyridines and pyrimidines.

REFERENCES CITED

Abdel-Galil, F. M., Sherif, S. M., and Elnagdi, M. H., Utility of cyanoacetamide and cyanothioacetamide in heterocyclic synthesis. *Heterocycles,* 24, 2023 (1986).

Elgemeie, G. E. H., Fathy, N. M., Fadah, L. M., Ebeid, M. Y. and Elsaid, M. K., Reactions with 3,5-diaminopyrazoles: New routes to pyrazolo[1,5-a]pyrimidines. *Arch. Pharm. (Weinheim),* 324, 149 (1991).

Elnagdi, M. H. and Abd-Allah, S. O., Reactions with the arylhydrazones of some α-cyanoketones. *J. Prak. Chemie,* 315, 109 (1973).

Elnagdi, M. H., Sherif, S. M., and Mohareb, R. M., The synthetic potentialities of nitriles in heterocyclic synthesis. *Heterocycles,* 26, 497 (1987).

Elnagdi, M. H., Elmoghayer, M. R. H. S. and Sadek, K. U., Pyrazoles condensed to five and six membered rigns. *Adv. Heterocycl. Chem.,* 48, 319 (1990).

Gupta, R. R., Kumar, R., Synthesis of 2-amino-3-fluorobenzenethiol and its conversion into different heterocycles. *Synthetic Commun.,* 17, 229 (1987).

Mohareb, R. M., and Sherif, S. M., Heterocyclic synthesis with isothiocyanates: A novel synthetic approach to polyfunctionally substituted pyrazoles and their fused derivatives. *Sulfur letters,* 15, 91 (1992).

Mosby, W. L., Heterocyclic systems with bridgehead nitrogen atoms. Interscience, New York, 1961, Part 1, p. 460.

Shawali, A. S., Sami, M., Sherif, S. M., and Parkanyi, C., Synthesis of some derivatives of imidazo[1,2-a] pyridine, pyrazolo[1,5-b]imidazole, and 4-(3H)-quinazolinone from α-ketohydrazidoyl bromides. *J. Hetrocycl. Chem.,* 17, 877 (1980).

Sherif, S. M., Mohareb, R. M., Elgemeie, G. E. H., and Sigh, R. P., Nitriles in heteroyclic synthesis: 1-Cyanoformamide as precursor for a variety of heterocyclic ring systems. *Heterocycles,* 27, 1579 (1988).

Sherif, S. M., Youssef, M. M., Mobarak, K. M., and Abdel-Fattah, A. M., A convenient synthesis of thiazolopyrimidines, thiazolodipyrimidines and heterocyclothiazolopyrimidines. *Tetrahedron,* 49, 9561 (1993).

Yamanaka, H., Ohba, S., and Konno, S., Reaction of 2,4-diphenyl-1,3,5-triazine derivatives with nucleophiles. *Heterocycles,* 26, 2853 (1987).