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Synthesis and studies of pyrazolo[3,4-*b*]pyridin-4-one derivatives

Hussain Ali Soleiman*, Ali Kamel Khalafallah and Hana'a Abd-Ellatif

Chemistry Department, Aswan Faculty of Science, South Valley University, Aswan, 81111, Egypt

**Corresponding author at: Chemistry Department, Aswan Faculty of Science, South Valley University, Aswan, 81111, Egypt. Tel.: +20.97.3480447; fax: +20.97.3480450. E-mail address: hsoleiman2001@yahoo.com (H.A. Soleiman).*

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ABSTRACT

A series of isolated/fused of pyrazole, isoxazolo, pyrimidine, pyrimidine thione, spiro thiazolodine and spiro β-lactam derivatives incorporating to 4-acetyl-5-imino-3-methyl-1-phenyl-2-pyrazoline have been synthesized by different methods. The structure of chemical reactions based on chemical and spectroscopic evidence. The detailed synthesis and spectroscopic data were reported.

1. Introduction

Pyrazole, isoxazole, pyrimidine, pyrimidinothione, spiro thiazolodine and Spiro β-lactam derivatives incorporating 4-acetyl-5-imino-3-methyl-1-phenyl-2-pyrazoline are biologically important molecules and natural products [1-5]. The reaction between benzaldehyde, aniline and cyclohexanone was studies as a model reaction in water in the presence of various amounts of first generation dendrimer [6-15]. It was found that only 2 mol % of the catalyst was required to drive the reaction smoothly to completion. The scope of the dendrimer catalyzed Mannish reaction was extended to other aldehydes, ketones and anilines [16-26]. In a similar manner condensation between other substrates like 1-(5-imino-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)ethanone (1) also a short period of time with excellent yield and high purity and no more purification was required. In a literature search, it has found that Mannich bases had antimicrobial activities [27,28] besides various activities. The pyrazole nucleus is present in a wide variety of biologically interesting compounds, which exhibit anti-hyperglycemic, analgesic, anti-inflammatory, antipyretic, antibacterial, hypoglycemic, sedative-hypnotic activity [29-42]. Pyrazoles and their derivatives are widely used as pharmaceutical [43-45] and agrochemical agents [46] and consequently a large number of synthetic routes to pyrazoles has been reported [47-51]. However, there is still great interest in finding milder and more efficient methods to these valuable compounds. Amino pyrazole derivative and imino pyrazole derivative undergo various reactions, and as such are excellent and general starting materials for the development of the heterocyclic compounds synthesis.

2. Experimental

2.1. Instrumentation

All melting points are uncorrected. IR spectra were recorded on a Pye Unicam SP-1100 Spectrophotometer KBr disc. ^{1}H NMR spectra were recorded on a Varian EM-390 90 MHz spectrophotometer using DMSO-d_6 as a solvent and TMS as an internal standard chemical shifts are expressed as ppm units. Mass spectra were obtained on a Shimadzu GCMS QP 1000 EX mass spectrometer at 70 eV. The microanalyses were performed by the microanalytical centers at Cairo University.

2.2. Synthesis of 1-(5-imino-3-methyl-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)ethanone (1)

The compound **1** was carried out according to Mohanty *et al*., 1977 [52] (Tables 1, 2).

2.3. Synthesis of 3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo 3,4-b]pyridin-4(3aH)-one (2)

A solution of compound (2.15 g, 0.01 mol) in DMF as a solvent in presence of piperidine (0.85 mL, 0.01 mol) and HCl (0.5 mL, 0.05 mol) with paraformaldehyde (0.3 g, 0.01 mol). The reaction mixture was heated under reflux for 3 hr. Then left to cool and was poured on ice/water with the stirring. The solid product so formed was collected by filtration and crystallized from the diluted dimethyl-formamide (Scheme 1, Tables 1, 2).

2.4. Synthesis of 5-benzylidene-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4(3aH)-one (3a), *5-(4-methoxybenzylidene)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4(3aH)-one* (3b), *5-(4-hydroxybenzylidene)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4(3aH)-one* (3c)

A solution of compound **2** (1.135 g, 0.005 mol) in DMF was treated with aromatic aldehyde compounds (**3a**: 0.53 mL, 0.005

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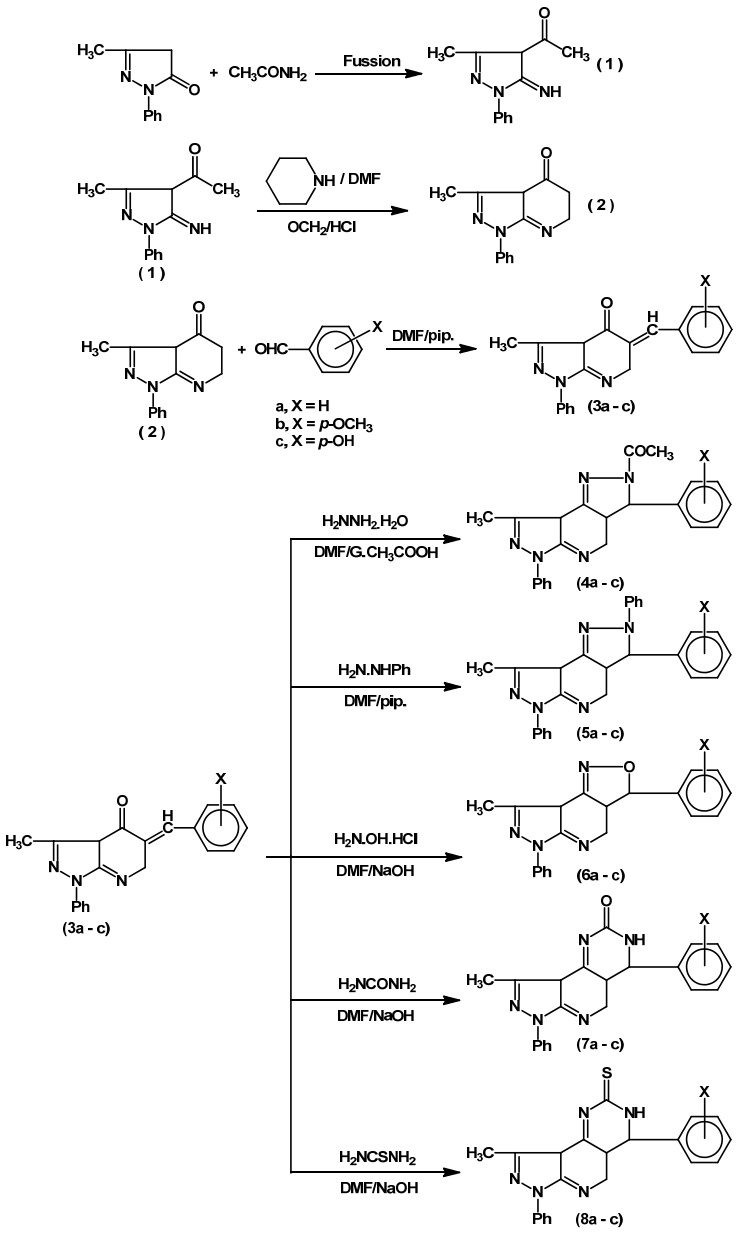


Scheme 1

mol; **3b**: 0.68 mL, 0.005 mol; **3c**: 0.61 g, 0.005 mol) in presence of piperidine as catalyst. The reaction mixture was heated under reflux for 4 hr., then left to cool and poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted dimethyl-formamide (Scheme 1, Tables 1, 2).

2.5. Synthesis of 1-(8-methyl-3,6-diphenyl-3a,4-dihydro dipyrazolo[3,4-b:3',4'-d]pyridin-2(3H,6H,8aH)-yl)ethanone (4a), *1-(3-(4-methoxyphenyl)-8-methyl-6-phenyl-3a,4-dihydrodipyrazolo[3,4-b:3',4'-d]pyridin-2(3H,6H,8aH)-yl) ethanone* (4b), *1-(3-(4-hydroxyphenyl)-8-methyl-6-phenyl-3a,4-dihydrodipyrazolo[3,4-b:3',4'-d]pyridin-2 (3H,6H,8aH)-yl)ethanone* (4c)

A solution of compounds **3a-c** (**3a**: 0.94 g, 0.003 mol; **3b**: 0.99 g, 0.003 mol; **3c**: 1.03 g, 0.003 mol) in dimethyl formamide was treated with hydrazine monohydrate (0.15 mL, 0.003 mol) in presence of (4 drops) of acetic acid as a catalyst. The reaction mixture was heated under reflux for 8 hr, then left to cool and poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

2.6. Synthesis of 8-methyl-2,3,6-triphenyl-2,3,3a,4,6,8a-hexahydrodipyrazolo[3,4-b:3',4'-d]pyridine (5a), *3-(4-methoxyphenyl)-8-methyl-2,6-diphenyl-2,3,3a,4,6,8a-hexahydrodipyrazolo[3,4-b:3',4'-d]pyridine* (5b), *3-(4-hydroxyphenyl)-8-methyl-2,6-diphenyl-2,3,3a,4,6,8a-hexahydrodipyrazolo[3,4-b:3',4'-d]pyridine* (5c)

A solution of compounds **3a-c** (**3a**: 0.3 g, 0.0009 mol, **3b**: 0.29 g, 0.0009 mol; **3c**: 0.3 g, 0.0009 mol) in dimethyl formamide was treated with phenyl hydrazine (0.1 mL, 0.0009

Table 1. Characterization of compounds (**2-11**).

Comp. No.	Yield, %	M.P., °C	Color	Mol. Formula, (M.wt., g)	Elemental Analysis, % Calculated (Found)			Mass, *m/z*
					C	H	N	
2	63	120-122	Light beige	$C_{13}H_{13}N_3O$ (227.27)	68.71 (68.72)	5.77 (5.72)	18.49 (18.50)	227
3a	35	134-136	Reddish brown	$C_{20}H_{17}N_3O$ (315.37)	76.19 (76.20)	5.39 (5.40)	13.30 (13.5)	316
3b	46	114-116	Dark red	$C_{21}H_{19}N_3O_2$ (345.40)	73.04 (73.05)	5.50 (5.52)	12.17 (12.15)	345
3c	99	148-150	Light brown	$C_{20}H_{17}N_3O_2$ (331.37)	72.50 (72.48)	5.31 (5.30)	12.68 (12.66)	331
4a	50	150-152	Light brown	$C_{22}H_{21}N_5O$ (371.44)	71.15 (71.17)	5.66 (5.65)	18.86 (18.85)	359
4b	25	145-147	Reddish brown	$C_{23}H_{23}N_5O_2$ (401.47)	68.81 (65.82)	5.77 (5.72)	17.44 (17.44)	400
4c	30	140-142	Dark beige	$C_{22}H_{21}N_5O_2$ (387.44)	68.20 (68.2)	5.46 (5.41)	18.00 (18.00)	389
5a	83	200-202	Brown	$C_{26}H_{23}N_5$ (405.50)	77.03 (77.05)	5.67 (5.69)	17.28 (17.30)	403
5b	48	114-116	Brown	$C_{27}H_{25}N_5O$ (435.53)	74.46 (74.48)	5.79 (5.72)	16.09 (16.07)	436
5c	34	>180	Dark brown	$C_{26}H_{23}N_5O$ (421.50)	74.09 (74.11)	5.50 (5.48)	16.62 (16.62)	422
6a	80	152-154	Dark brown	$C_{20}H_{18}N_4O$ (330.39)	72.72 (72.71)	5.45 (5.45)	16.96 (16.95)	331
6b	40	132-135	Brown	$C_{21}H_{20}N_4O_2$ (360.42)	69.98 (69.90)	5.59 (5.56)	15.55 (15.56)	360
6c	52	210-212	Reddish brown	$C_{20}H_{18}N_4O_2$ (346.39)	69.35 (69.35)	5.24 (5.19)	16.17 (16.17)	347
7a	45	138-140	Dark red	$C_{21}H_{19}N_5O$ (357.41)	70.58 (70.59)	5.32 (5.30)	19.60 (19.62)	359
7b	25	109-111	Dark brown	$C_{22}H_{21}N_5O_2$ (387.45)	68.20 (68.03)	5.46 (5.66)	18.08 (18.03)	387
7c	76	118-220	Brown	$C_{21}H_{19}N_5O_2$ (373.41)	67.55 (66.56)	5.13 (5.09)	18.75 (18.76)	375
8a	58	170-172	Light greenish yellow	$C_{21}H_{19}N_5S$ (373.48)	67.56 (67.55)	5.09 (5.08)	18.76 (18.75)	371
8b	63	212-214	Light brown	$C_{21}H_{19}N_5OS$ (389.47)	64.78 (64.77)	4.88 (4.86)	17.99 (17.98)	387
8c	40	119-120	Dark brown	$C_{22}H_{21}N_5OS$ (403.50)	65.50 (64.50)	5.21 (5.21)	17.36 (17.36)	403
9a	99	122-124	Dark brown	$C_{21}H_{21}N_5O$ (359.43)	70.19 (70.20)	5.84 (5.90)	19.49 (19.50)	359
9b	96	158-160	Dark brown	$C_{19}H_{16}N_4O_2$ (332.36)	68.67 (68.70)	4.81 (4.82)	16.86 (16.88)	330
9c	94	130-132	Brown	$C_{23}H_{18}N_4O_2$ (382.42)	72.25 (72.30)	4.71 (4.73)	14.65 (14.66)	381
10a	70	166-164	Dark brown	$C_{23}H_{23}N_5O_2S$ 433.53)	63.74 (63.76)	5.31 (5.32)	16.16 (16.16)	433
10b	20	110-112	Brown	$C_{21}H_{18}N_4O_3S$ (406.46)	62.06 (62.07)	4.43 (4.44)	13.79 (13.80)	405
10c	40	160-???	Dark brown	$C_{25}H_{20}N_4O_3S$ (456.52)	65.78 (65.80)	4.38 (4.40)	12.20 (12.30)	455
11a	20	190-192	Light brown	$C_{23}H_{22}N_5O_2Cl$ (435.91)	63.44 (64.45)	5.05 (5.06)	16.09 (16.10)	434
11b	20	175-177	Dark brown	$C_{21}H_{17}N_4O_3Cl$ (408.84)	61.76 (61.77)	4.16 (4.17)	13.72 (13.73)	407
11c	50	165-167	Brown	$C_{25}H_{19}N_4O_3Cl$ (458.90)	65.43 (65.48)	4.17 (4.20)	12.21 (12.00)	458

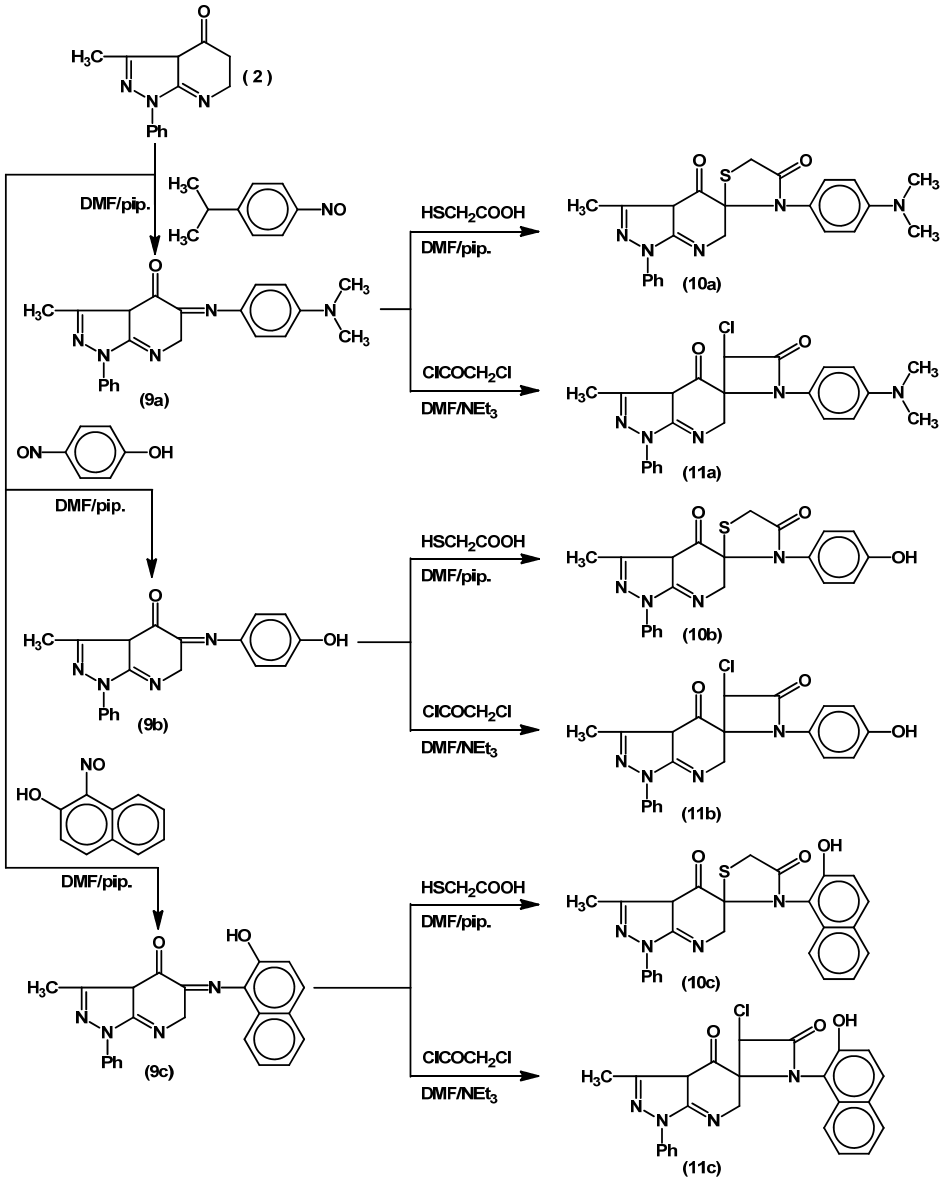
mol) in presence of 3 drops of piperidine as catalyst. The reaction mixture was heated under reflux for 8 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

2.7. Synthesis of 8-methyl-3,6-diphenyl-3a,4,6,8a-tetrahydro-3H-isoxazolo[3,4-d]pyrazolo[3,4-b]pyridine (6a), 3-(4-methoxyphenyl)-8-methyl-6-phenyl-3a,4,6,8a-tetrahydro-3H-isoxazolo[3,4-d]pyrazolo[3,4-b]pyridine (6b), 3-(4-hydroxyphenyl)-8-methyl-6-phenyl-3a,4,6,8a-tetrahydro-3H-isoxazolo[3,4-d]pyrazolo[3,4-b]pyridine (6c)

A solution of compounds **3a-c** (**3a**: 0.22 g, 0.0007 mol; **3b**: 0.22 g, 0.0007 mol; **3c**: 0.24 g, 0.0007 mol) in dimethyl formamide as a solvent was treated with hydroxylamine hydrochloride (0.05 g, 0.0007 mol), in the presence of sodium hydroxide as a catalyst. The reaction mixture was heated under reflux for 8 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

2.8. Synthesis of 9-methyl-4,7-diphenyl-3,4,4a,5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6]pyrido[4,3-d]pyrimidin-2-one (7a), 4-(4-methoxyphenyl)-9-methyl-7-phenyl-3,4,4a,5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6]pyrido[4,3-d]pyrimidin-2-one (7b), 4-(4-hydroxyphenyl)-9-methyl-7-phenyl-3,4,4a,5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6]pyrido[4,3-d]pyrimidin-2-one (7c)

A solution of compounds **3a-c** (**3a**: 1.57 g, 0.005 mol; **3b**: 1.59 g, 0.005 mol; **3c**: 1.72 g, 0.005 mol) in dimethyl formamide was treated with urea (0.3 g, 0.005 mol) in the presence of sodium hydroxide as a catalyst. The reaction mixture was heated under reflux for 8 hr, then left to cool and was poured on ice/water.



Scheme 2

The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

***2.9. Synthesis of 9-methyl-4,7-diphenyl-3,4,4a,5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6]pyrido[4,3-d]pyrimidine-2-thione* (8a), *4-(4-methoxyphenyl)-9-methyl-7-phenyl-3,4,4a, 5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6]pyrido[4,3-d] pyrimidine-2-thione* (8b), *4-(4-hydroxyphenyl)-9-methyl-7-phenyl-3,4,4a,5,7,9a-hexahydro-2H-pyrazolo[4',3':5,6] pyrido[4,3-d]pyrimidine-2-thione* (8c)**

A solution of compounds **3a-c** (**3a**: 0.5 g, 0.001 mol; **3b**: 0.4 g, 0.001 mol; **3c**: 0.34 g, 0.001 mol) in dimethyl formamide was treated with thiourea (0.1 g, 0.001 mol) in the presence of sodium hydroxide as a catalyst. The reaction mixture was heated under reflux for 8 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

***2.10. Synthesis of 5-((4-(dimethylamino)phenyl)imino)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4 (3aH)-one* (9a), *5-((4-hydroxyphenyl)imino)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4(3aH)-one* (9b), *5-((2-hydroxynaphthalen-1-yl)imino)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-b]pyridin-4(3aH)-one* (9c)**

A solution of compound **2** (0.5 g, 0.002 mol) in dimethyl formamide was treated with nitroso compounds (**9a**: 0.33 g, 0.002 mol; **9b**: 0.24 g, 0.002 mol; **9c**: 0.34 g, 0.002 mol) in presence of 2 drops of piperidine as a catalyst. The reaction mixture was heated under reflux for 8-10 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

Table 2. IR and ^{1}H NMR spectral data of compounds (**2-11**).

Comp. No	IR (cm^{-1})	^{1}H NMR (δ, ppm)
2	1707-1704 (C=O), 1629 (C=N)	1.20 (s, 3H, CH_3), 2.39 (t, *J* = 7.00 Hz, 2H, CH_2CO), 2.79 (s, 1H, CHCO), 3.70-3.90 (t, *J* = 7.30 Hz, 2H, CH_2N), 7.09-7.99 (m, 5H, Ar-H$^+$).
3b	3069 (OH), 1656 (C=O), 590 (C=N)	0.80 (s, 3H, CH_3), 1.19 (s, 1H, CH), 3.35 (s, 1H, CHCO), 7.12-8.00 (m, 9H, Ar-H$^+$), 8.71 (s, 2H, CH_2N), 9.90 (s, 3H, CH_3)
3c	1704-1717 (C=O), 3069 (OH), 1597 (C=N)	1.18 (s, 3H, CH_3), 1.60 (s, 1H, CH), 2.89 (s, 1H, CHCO), 3.39 (s, 2H, CH_2N), 6.96-7.94 (m, 9H, Ar-H$^+$), 9.78 (s, 1H, OH)
4a	1707 (C=O), 1627 (C=N)	1.24 (s, 3H, CH_3), 2.11 (s, 1H, CHCN), 2.35 (q, *J* = 7.30 Hz, 1H, CHCH), 2.74-2.89 (d, *J* = 7.00 Hz, 1H, CHPh), 3.38-3.85 (d, *J* = 7.00 Hz, 2H, CH_2N), 3.93 (s, 3H, OCH_3), 6.50-8.00 (m, 10H, Ar-H$^+$)
4c	3055 (OH), 1706 (C=O), 1599 (C=N),	0.76 (s, 3H, CH_3), 3.37 (s, 3H, CH_3O), 7.12-8.00 (m, 14H, Ar-H$^+$ + heterocyclic nuclei), 8.50 (s, 1H, OH)
5a	1590-1599 (C=N)	0.77 (s, 3H, CH_3), 1.17 (s, 1H, CHCN), 1.50 (q, *J* = 7.30 Hz, 1H, CHCHPh), 2.17-2.32 (d, *J* = 7.00 Hz, 1H, CHN), 3.35 (d, *J* = 7.00 Hz, 2H, CH_2N), 7.43-7.98 (m, 15H, Ar-H$^+$)
6c	3045 (OH), 1597 (C=N)	0.75 (s, 3H, CH_3), 6.50-8.00 (m, 14H, Ar-H$^+$ + heterocyclic nuclei), 8.50 (s, 1H, OH)
7c	3428 (NH), 3075 (OH), 1708-1707 (C=O), 1599 (C=N),	0.76 (s, 3H, CH_3), 3.33 (br, 1H, NH), 6.00-7.80 (m, 14H, Ar-H$^+$ + Heterocyclic nuclei), 8.50 (s, 1H, OH)
8c	3427 (NH), 1608 (C=N)	0.70 (s, 3H, CH_3), 1.17 (s, 1H, CHCN), 2.16 (q, *J* = 7.30 Hz, 1H, CHCH), 2.34 (d, *J* = 7.00 Hz, 1H, CHN), 3.35 (s, 1H, NH), 3.83 (d, *J* = 7.00 Hz, 2H, CH_2N), 3.35 (s, 3H, OCH_3), 7.43-7.99 (m, 9H, Ar-H$^+$)
9c	3060 (OH), 1705-1708 (C=O), 1625 (C=N)	0.87 (s, 3H, CH_3), 2.37 (s, 1H, CHCO), 3.43 (s, 2H, CH_2N), 7.43-7.99 (m, 11H, Ar-H$^+$), 8.93 (s, 1H, OH)
10a	1709 (C=O), 1626-1598 (C=N)	0.77 (s, 3H, CH_3), 1.19 (s, 1H, CHCO), 2.14 (s, 2H, SCH_2), 2.89 (s, 2H, CH_2N), 3.33 (s, 6H, CH_3N), 7.75-7.89 (m, 9H, Ar-H$^+$)
10c	3427-3060 (OH), 1627 (C=O), 1492 (C=N)	1.25 (s, 3H, CH_3), 6.50-8.00 (m, 16H, Ar-H$^+$ + Heterocyclic nuclei), 4.27 (s, 1H, OH)
11c	3428-3060 (OH), 1626-1598 (C=N)	0.78 (s, 3H, CH_3), 3.38 (s, 1H, CHCl), 7.10-8.00 (m, 14H, Ar-H$^+$ + Heterocyclic nuclei), 7.87 (s, 1H, OH)

2.11. Synthesis of 3'-(4-(dimethylamino)phenyl)-3-methyl-1-phenyl-3a,6-dihydrospiro[pyrazolo[3,4-b]pyridine-5,2'-thiazolidine]-4,4'(1H)-dione (10a), *3'-(4-hydroxyphenyl)-3-methyl-1-phenyl-3a,6-dihydrospiro[pyrazolo[3,4-b]pyridine-5,2'-thiazolidine]-4,4'(1H)-dione* (10b), *3'-(2-hydroxy naphthalen-1-yl)-3-methyl-1-phenyl-3a,6-dihydrospiro [pyrazolo[3,4-b]pyridine-5,2'-thiazolidine]-4,4'(1H)-dione* (10c)

A solution of compounds **9a-c** (**9a**: 0.72 g, 0.002 mol; **9b**: 0.74 g, 0.002 mol; **9c**: 0.8 g, 0.002 mol) in dimethyl formamide was treated with thioglycolic acid (0.2 mL, 0.002 mol) in presence of 2 drops of piperidine as a catalyst. The reaction mixture was heated under reflux for 8-10 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

2.12. Synthesis of 3-chloro-1-(4-(dimethylamino)phenyl)-3'-methyl-1'-phenyl-3a',6'-dihydrospiro[azetidine-2,5'-pyrazolo[3,4-b]pyridine]-4,4'(1'H)-dione (11a), *3-chloro-1-(4-hydroxyphenyl)-3'-methyl-1'-phenyl-3a',6'-dihydrospiro [azetidine-2,5'-pyrazolo[3,4-b]pyridine]-4,4'(1'H)-dione* (11b), *3-chloro-1-(2-hydroxynaphthalen-1-yl)-3'-methyl-1'-phenyl-3a',6'-dihydrospiro[azetidine-2,5'-pyrazolo[3,4-b] pyridine]-4,4'(1'H)-dione* (11c)

A solution of compounds **9a-c** (**9a**: 0.72 g, 0.002 mol; **9b**: 0.74 g, 0.002 mol; **9c**: 0.8 g, 0.002 mol) in dimethyl formamide was treated with chloroacetylchloride (0.23 mL, 0.002 mol) in presence of 2 drops of triethylamine as a catalyst. The reaction mixture was heated under reflux for 8-10 hr, then left to cool and was poured on ice/water. The solid product so formed was collected by filtration and crystallized from the diluted DMF (Scheme 1, Tables 1, 2).

3. Results and discussion

Our approach to the development of some synthetic applications of 1-phenyl-3-methyl-5-pyrazolone is based on the generation of building blocks containing fused, isolated, and Spiro heterocyclic compounds, each of which can be selectively reacted [51]. We have recently shown like reaction of 1-(5-imino-3-methyl-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)ethanone (**1**) wheras we have obtained an available compound **2**, Scheme 1. The structure of compound **2** was confirmed by IR spectra which revealed the presence of peaks at 1656-1707 (C=O) and 1596-1629 cm^{-1} (C=N), also ^{1}H NMR spectra of compound **2** revealed the presence of signals peaks at 1.2 (s, 3H, CH_3), 2.39 (t, 2H, CH_2CO), 2.79 (s, 1H, CHCO), 3.7-3.9 (t, 2H, CH_2N) and 7.09-7.99 (m, 5H, Ar-H$^+$) ppm, the mass spectrum showed the molecular ion peak at *m/z* = 227.28.

The active methylene group in compound **2** condensed with different aromatic aldehydes (benzaldehyde, anisaldehyde, *p*-hydroxy-benzaldehyde) in dimethylformamide under piperidine as catalyst to yield the corresponding 5-aryldino-4-tetrahydropyridinone derivatives (**3a-c**) Scheme 1. The structures of compounds **3a-c** were confirmed by IR spectra, ^{1}H NMR spectra.

The activity of exocyclic C=C conjugated with the α-carbonyl group in compound **3a-c** were determined by the reaction with hydrazines, hydroxyl amine hydrochloride, urea and thiourea, to yield the compounds **4-8a-c**, Scheme 1. The nature of the products obtained such as *N*-acetyl pyrazolo pyridine derivatives was confirmed by IR spectra, ^{1}H NMR spectra, and the mass spectra. The structure of isoxazolo-pyridine derivatives **6a-c**, pyridopyrimidinone derivatives **7a-c** and also pyrimidine thiano derivatives **8a-c** was confirmed by IR spectra, ^{1}H NMR spectra and mass spectra.

Other Schiff's base compounds were prepared through the condensation of 3-methyl-1-phenyl-5,6-dihydro-1*H*-pyrazolo

[3,4-*b*]pyridin-4(3*aH*)-one (**2**) with nitroso compounds such as (a) *p*-nitroso, *N*,*N*-dimethyl aniline, (b) *p*-nitrosophenol and (c) α-nitroso-β-naphthol in the presence of dimethylformamide as solvent under piperidine as catalyst, afforded to compounds 9a-c (Scheme 2).. Schiff's base compounds **9a-c** reacted with thioglycolic acid in dimethylformamide under piperidine as catalyst to yield the corresponding *N*-thiazole derivatives **10a-c** (Scheme 2). Also, when Schiff's base compounds **9a-c** reacted with chloroacetylchloride in dimethylformamide under triethylamine as catalyst to yield the corresponding *N*-β-lactam derivatives **11a-c** (Scheme 2).

4. Conclusions

We have reported the development of some synthetic applications of 1-phenyl-3-methyl-5-pyrazolone is based on the generation of building blocks containing fused, isolated and spiro pyrazole, isoxazole, pyrimidine, pyrimidinothione, thiazolodine and β-lactam derivatives incorporating 4-acetyl-5-imino-3-methyl-1-phenyl-2-pyrazoline.

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