Synthesis of New Fused and Spiro Heterocyclic Systems from 3,5-Pyrazolidinediones

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4-Bromo-1-phenyl-3,5-pyrazolidinedione **2** reacted with different nucleophilic reagents to give the corresponding 4-substituted derivatives **3-8**. The cyclized compounds **9-11** were achieved on refluxing compounds **3**, **4** or $\mathbf{6_a}$ in glacial acetic acid or diphenyl ether. 4,4-Dibromo-1-phenyl-3,5-pyrazolidinedione **12** reacted with the proper bidentates to give the corresponding spiro 3,5-pyrazolidinediones **13-15**, respectively. The 4-aralkylidine derivatives $\mathbf{16_{a-c}}$, were subjected to Mannich reaction to give Mannich bases $\mathbf{17_{a-c}}$-$\mathbf{22_{a-c}}$, respectively. 4-(*p*-Methylphenylaminomethylidine)-1-phenyl-3,5-pyrazolidinedione **23** or 4-(*p*-methylphenylazo)-1-phenyl-3,5-pyrazolidinedione **29** were prepared and reacted with active nitriles, cyclic ketones and N,S-acetals to give pyrano[2,3-c]pyrazole, pyrazolo[4′,3′:5,6]pyrano[2,3-c]pyrazole, spiropyrazole-4,3′-pyrazole and spiropyrazole-4,3′-[1,2,4]triazolane derivatives **24-34**, respectively.

Keywords: 3,5-Pyrazolidinedione; Pyrazolo[3,4-b][1,4]thiazine; Imidazo[4,5-c]pyrazole and spiro pyrazole-4′,2-thiadiazole derivatives.

INTRODUCTION

The early discovery of biological effects for pyrazolidinediones as analgesics,[1] antipyretics,[2] antrheumatics,[3] antiphlogistic agents,[4] for treatment of various other diseases[5-9] and as antiinflammatory drugs,[10,11] prompted us to continue our previous work on the synthesis of pyrazolo-[3,4-b]pyridines,[12] pyrazolo[3,4-b]thieno[3,2-e]pyridines,[12] pyrazolodithiane[13] and spiro heterocyclic systems.[13] We report herein synthesis of pyrazolothiazine, pyrano[2,3-c]pyrazole, spiro[imidazolidine-, oxazolidine-, thiazolidine-, oxathiolane]-2′,4-pyrazole derivatives, spiro pyrazole-4′,2-benzimidazole, spiro pyrazole-4′,2-thiadiazole, spiro pyrazolopyrazole, and spiro pyrazole-triazolane derivatives.

RESULTS AND DISCUSSION

The parent compounds 1-phenyl-3,5-pyrazolidinedione (**1**),[14] 4-bromo- (**2**)[15] and 4,4-dibromo-1-phenyl-3,5-pyrazolidinedione (**12**)[16] were prepared according to known methods.

4-Bromo-1-phenyl-3,5-pyrazolidinedione (**2**) reacted with cystamine, guanidine, ethyl glycinate, *o*-aminothiophenol, *o*-phenylenediamine, *p*-aminobenzoic acid or hydroquinone in dioxane in the presence of K_2CO_3 to give the corresponding 4-substituted derivatives **3-8**, respectively. Mass spectrum of compound **4** showed a molecular ion peak at *m/z* = 233.37 which is in agreement with its molecular formula (cf. Scheme I, Table 1).

Refluxing of compounds **3** and **4** in glacial acetic acid afforded the corresponding cyclized products pyrazolo[3,4-b][1,4]thiazine (**9**) and imidazo[4,5-c]pyrazole (**10**) derivatives, respectively, whereas pyrazolo[3,4-e][1,4]benzo[b]-thiazine derivative (**11**) was obtained by refluxing compound $\mathbf{6_a}$ in diphenyl ether.[17] Mass spectrum of compound **9** showed a molecular ion peak at *m/z* = 235.18 (M^++2) which is in agreement with its molecular formula (cf. Scheme I, Table 1).

4,4-Dibromo-1-phenyl-3,5-pyrazolidinedione (**12**) is a building block for the synthesis of spiro heterocyclic systems[13] attached to pyrazolidinedione moiety, where it was treated with ethylenediamine, ethanolamine, cystamine, 2-mercaptoethanol, *o*-phenylenediamine, *o*-aminophenol, *o*-aminothiophenol or thiosemicarbazide to give the corresponding spiro [imidazolidine-, oxazolidine-, thiazolidine-, (1,3)oxathiolane]-2′,4-pyrazole derivatives ($\mathbf{13_{a-d}}$), spiro pyrazole-4′,2-[benzimidazole, benzoxazole, benzothiazole, (1,3)benzodioxole] ($\mathbf{14_{a-d}}$), and spiro pyrazole-4′,2-thiadiazole (**15**), respectively. Mass spectra of compounds $\mathbf{13_b}$, $\mathbf{14_c}$ and **15** showed a molecular ion peak at *m/z* = 233 (M^+), 300 (M^++2), 263.29 (M^+) which is in agreement with its molecular structure (cf. Scheme II, Table 1).

4-Aralkylidene derivatives $\mathbf{16_{a-c}}$,[18] were subjected to Mannich reaction, using amines such as piperidine, morpholine, piprazine, *n*-butylamine, *n*-propylamine or *iso*-propylamine to give the corresponding Mannich bases 4-aralkyl-

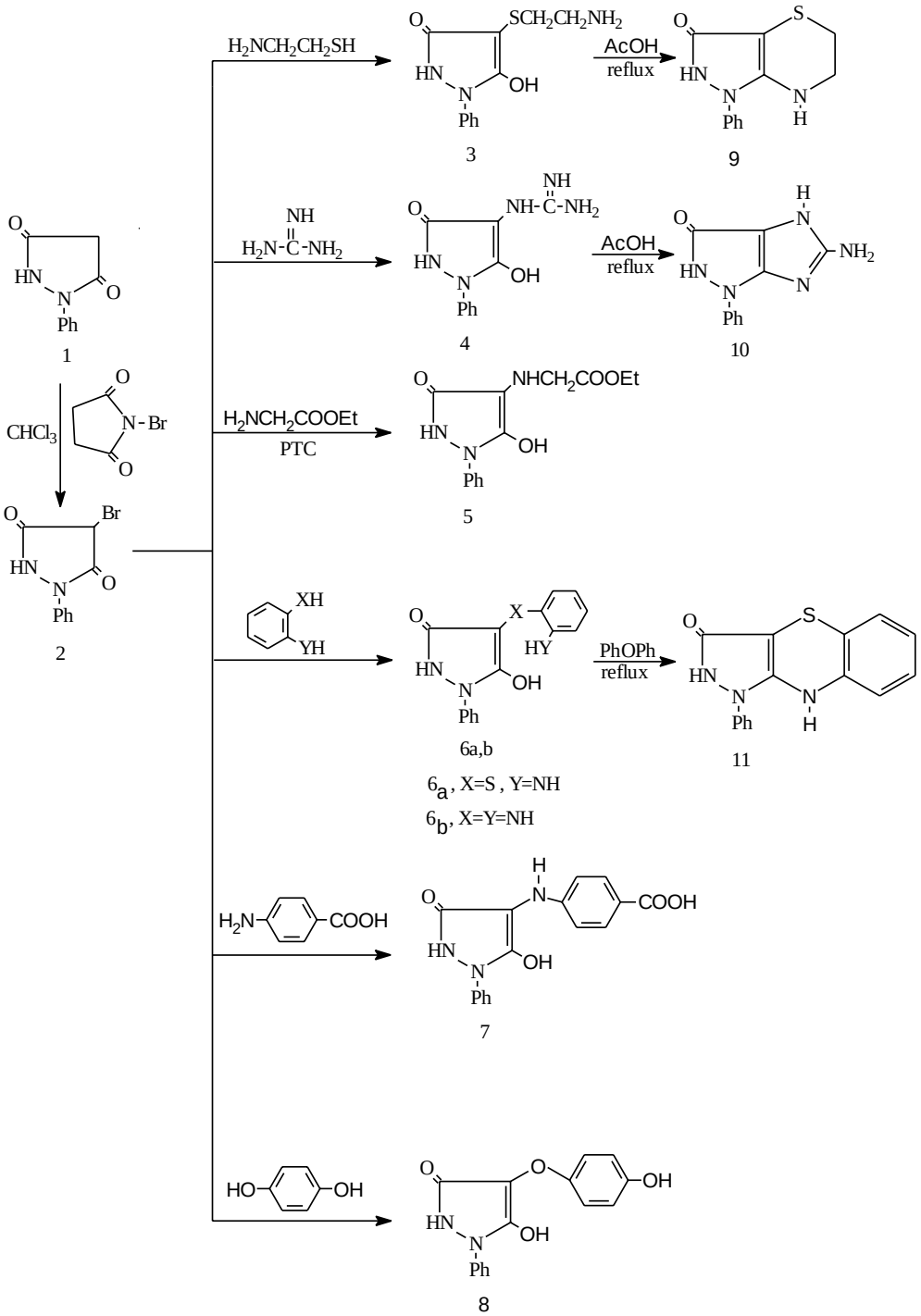
Table 1. Characterization Data of the Prepared Compounds

Comp No.	M.P(°C)[a] Crys. Solvent	Yield (%)	Mol. For. (Mol. Wt)	Analytical Data [b] Cal./ found				Spectral data
				C	H	N	S	
3	195 (Benzene)	80	$C_{11}H_{13}N_3O_2S$ (251.30)	52.57 52.39	5.21 5.34	16.72 16.99	12.76 12.64	IR: 3300 (NH); 3240; 3100 (NH_2), 1710 (CO), 1670 $(CO)_{amidic}$.
4	187 Benzene	82	$C_{10}H_{11}N_5O_2$ (233.23)	51.50 51.54	4.75 4.73	30.03 30.19		IR: 3300-3100 (NH_2+NH), 1708 (CO), 1676 $(CO)_{amidic}$. Ms: 233.37 (M^+, 0.7%); 216.4 (19.1%); 200.5 (13.5%); 190.5 (1.1%); 175.5 (69.8%); 77.8 (22%); 27.9 (16.9%).
5	285 Benzene	60	$C_{13}H_{15}N_3O_4$ (277.28)	56.31 56.58	5.45 5.26	15.15 15.32		IR: 3240, 3160 (2NH), 1740 $(CO)_{ester}$, 1708 (CO), 1676 $(CO)_{amidic}$.
6_a	230 Benzene	89	$C_{15}H_{13}N_3O_2S$ (299.35)	60.19 60.07	4.38 4.48	14.04 13.89	10.71 10.98	IR: 3300-3180 (NH_2+NH), 1710 (CO), 1676 $(CO)_{amidic}$ ^{1}H-NMR 7.4-6.5 (m, 11H, arom +NH); 4.3-3.8 (br., 2H, NH_2), 1.8 (s, 1H, CH).
6_b	205 Ethanol	76	$C_{15}H_{14}N_4O_2$ (282.30)	63.82 63.75	5.00 5.18	19.85 19.83		IR: 3380, 3280 (NH_2), 3100 (NH), 1700 (CO), 1660 $(CO)_{amidic}$. ^{1}H-NMR 7.2-6.3 (m, 10H, arom. + NH); 5.8-5.6 (br., 2H, NH_2), 2.3 (s, 1H, CH).
7	175 Methanol	55	$C_{16}H_{13}N_3O_4$ (311.29)	61.73 61.90	4.21 4.53	13.50 13.26		IR: 3420 (OH), 3200 (NH), 1720 $(CO)_{acid.}$; 1705 (CO); 1680 $(CO)_{amidic}$.
8	190 Benzene	65	$C_{15}H_{12}N_2O_4$ (284.27)	63.38 63.26	4.25 4.55	9.85 9.62		IR: 3400 (OH); 3180 (NH); 1700 (CO); 1670 $(CO)_{amidic}$. ^{1}H NMR 7-6.1 (m, 10H, arom +NH); 2.3 (s, 1H, CH); 1.2 (s, 1H, OH).
9	220 Methanol	70	$C_{11}H_{11}N_3OS$ (233.29)	56.63 56.84	4.75 4.56	18.01 17.88	13.74 13.98	IR: 3300-3100 (NH); 1660 $(CO)_{amidic}$. Ms: 235.18 (M^++2, 0.1 %); 231.18 (M^+-2, 0.1%); 219 (0.2%); 204.29 (0.5%); 192.3 (0.4%); 176.4 (0.8%); 76.8 (10.2%); 27.9 (16.1%).
10	185 Ethanol	75	$C_{10}H_9N_5O$ (215.21)	55.81 55.68	4.21 4.40	32.54 32.28		IR: 3320-3100 (NH_2+2NH); 1687 $(CO)_{amidic}$.
11	230 Methanol	76	$C_{21}H_{13}N_5OS$ (383.43)	64.04 63.98	3.94 3.72	14.94 15.12	11.40 1156	IR: 3300 (NH), 3100 (NH), 1680 $(CO)_{amidic.}$; ^{1}H NMR 7.2-6.4 (m, 11H, arom +2NH).
13_a	220 Ethanol	56	$C_{11}H_{12}N_4O_2$ (232.24)	56.89 56.67	5.21 5.43	24.12 24.34		IR: 3300-3100 (3NH), 2980 $(CH)_{aliph.}$ 1706 (CO); 1660 $(CO)_{amidic}$.
13_b	194 Ethanol	79	$C_{11}H_{11}N_3O_3$ (233.22)	56.65 56.46	5.19 5.43	24.12 24.30		IR: 3300, 3180 (2NH); 1710(CO); 1680 $(CO)_{amidic}$. ^{1}H-NMR 7.4-6.5 (m, 7H, arom +2NH); 4.5-4.2 (t, 2H, CH_2); 3.8-3.6 (t, 2H, CH_2). Ms: 236(M^++3, 21%); 176 (18%); 77 (100%); 58(52%) 27.9 (16.1%).
13_c	240 Ethanol	81	$C_{11}H_{11}N_3O_2s$ (249.29)	53.00 53.25	5.21 5.11	24.12 24.43	12.86 12.64	^{1}H-NMR 7.8-7.2 (m, 7H, arom +2NH); 4.3-4.1 (t, 2H, CH_2); 3.3-3.0 (t, 2H, CH_2).
13_d	210(decom) Ethanol	65	$C_{11}H_{10}N_2O_3S$ (233.23)	52.79 52.90	4.03 4.22	11.19 11.00	12.81 12.90	^{1}H-NMR 7.9 (s, 1H, NH); 7.7-6.8 (m, 5H, arom); 3.6-3.3 (t, 2H, CH_2); 2.9-2.7 (t, 2H, CH_2).
14_a	262 Ethanol	70	$C_{15}H_{12}N_4O_2$ (280.28)	64.28 64.45	4.32 4.13	19.99 19.82		IR: 3388, 3306, 3200 (3NH); 3072 (CH) arom., 1700 (CO); 1660 $(CO)_{amidic}$
14_b	240 Ethanol	60	$C_{15}H_{11}N_3O_3$ (281.27)	64.10 64.00	3.94 3.75	14.94 15.12		IR: 3300-3100 (2NH); 3060 (CH) arom., 1705 (CO); 1676 $(CO)_{amidic}$
14_c	180 Benzene	84	$C_{15}H_{10}N_3O_2S$ (298.31)	60.40 60.24	3.38 3.59	14.09 14.17	10.75 10.62	IR: 3330-3160 (2NH); 3040 (CH) arom., 1700 (CO); 1665 $(CO)_{amidic}$
14_d	230 Benzene	72	$C_{15}H_{10}N_2O_4$ (282.25)	63.83 63.68	3.57 3.80	9.93 9.67		IR: 3280 (NH); 3050 (CH) arom., 1710 (CO); 1676 $(CO)_{amidic}$
15	240 Benzene	52	$C_{10}H_9N_5O_2S$ (263.27)	45.62 45.48	3.45 3.22	26.60 26.95	12.18 12.34	IR: 3420-3280 (NH_2, -NH); 3100 (NH); 1710 (CO); 1670 $(CO)_{amidic}$

17_a	285	65	$C_{18}H_{23}N_3O_2$	68.99	7.40	13.41	IR: 3060 (CH) arom., 2972, 2860 $(CH)_{aliph.}$,
	Pet. ether		(313.40)	68.69	7.62	13.52	1708 (CO); 1685 $(CO)_{amidic}$
17_b	250	68	$C_{20}H_{22}N_4O_2$	68.55	6.33	15.99	IR: 3200 $(NH)_{pyrrole}$; 3060 $(CH)_{arom.}$; 2940
	Benzene		(350.42)	68.96	6.03	15.66	$(CH)_{aliph.}$ ^{1}H-NMR: 9.3 (s, 1H, =CH); 7.8-7.2 (m, 9H, 5H of arom., 3H of pyrrole and 1H of NH); 4.1 (s, 2H, CH_2-N); 3.1-2.8 (br., 10H, $5CH_2$).
17_c	254	70	$C_{23}H_{25}N_3O_3$	70.57	6.44	10.73	^{1}H-NMR: 7.3 (s, 1H, =CH); 7.1-6.3 (m, 9H,
	Ethanol		(391.47)	70.98	6.54	10.43	arom.); 4.4 (s, 2H, N-CH_2-N), 3.8 (s, 3H, CH_3), 3.6-3.2 (br., 4H, 2N-CH_2); 2.3 (m, 6H, $3CH_2$).
18_a	250	80	$C_{17}H_{21}N_3O_3$	64.75	6.71	13.32	IR: 3050 $(CH)_{arom.}$; 2965 $(CH)_{aliph.}$; 1705 (CO);
	Pet. ether		(315.37)	64.56	6.43	13.63	1679 $(CO)_{amidic}$.
18_b	255	77	$C_{19}H_{20}N_4O_3$	64.67	5.72	15.90	IR: 3225 $(NH)_{pyrrole}$; 1700 (CO), 1660
	Ethanol		(352.39)	64.92	5.94	15.63	$(CO)_{amidic}$. MS: *m/z* = 353.3 (M+1, 11%); 282 (18%); 274 (64%); 257 (100%); 241 (29%).
18_c	240	82	$C_{22}H_{23}N_3O_4$	67.16	5.48	12.03	IR: 3050 $(CH)_{arom.}$; 2965 $(CH)_{aliph.}$; 1705 (CO);
	Benzene		(393.44)	67.39	5.24	12.23	1679 $(CO)_{amidic.}$. ^{1}H-NMR; 7.3-6.2 (m, 10H, arom., + =CH); 4.6 (s, 2H, N-CH_2-N); 4.1 (s, 3H, CH_3); 3.8-3.6 (t, 4H, O.$(CH_2)_2$); 3.5-3.2 (t, 4H, -N$(CH_2)_2$).
19_a	175	89	$C_{40}H_{38}N_6O_6$	68.76	5.48	12.03	IR: 3050 $(CH)_{arom.}$; 1700 (CO); 1676
	Methanol		(698.77)	68.43	5.98	12.31	$(CO)_{amidic}$. MS: *m/z* = 545.3 (M^++1, 18%); 491.3 (7%); 477.3 (43%); 417.2 (86%); 387.2 (100%); 369.2 (46%); 274 (7%); 257 (27%); 241.1 (23%).
19_b	240	88	$C_{34}H_{32}N_8O_4$	66.32	5.23	10.38	^{1}H-NMR; 7.6 (s, 2H, 2=CH); 7.2-6.4 (m, 18H,
	Ethanol		(616.68)	66.64	5.14	10.63	arom. +2NH); 4.1 (s, 4H, 2-N-CH_2N); 3.6-3.2 (br., 8H, $4CH_2$).
19_c	260	92	$C_{30}H_{34}N_6O_4$	66.41	6.32	15.49	^{1}H-NMR; 7.3-6.5 (m, 18H, arom. + =CH); 4.2-
	Ethanol		(542.63)		6.13	15.98	4 (br., 4H, 2 N-CH2-N); 3.6-3 (br., 8H, $4CH_2$); 1.3 (s, 6H, $2CH_3$).
20_a	285	85	$C_{17}H_{23}N_3O_2$	67.75	7.69	13.94	IR: 3059 $(CH)_{arom.}$, 2867 $(CH)_{aliph.}$, 1710 (CO);
	Dioxane		(301.39)	67.54	7.97	13.69	1668 $(CO)_{amidic}$. MS: *m/z* =301 (39%); 278.2 (21%); 276.2 (80%); 271.2 (100%); 257 (21%); 241.2 (45%); 216 (24%); 215.2 (71%).
20_b	270	78	$C_{19}H_{22}N_4O_2$	67.44	6.55	16.65	IR: 3070 $(CH)_{arom.}$, 2965 $(CH)_{aliph.}$, 1710 (CO);
	Dioxane		(338.41)	67.88	6.35	16.42	1656 $(CO)_{amidic}$.
20_c	140	87	$C_{22}H_{25}N_3O_3$	69.64	6.64	11.07	IR: 3040 $(CH)_{arom.}$, 2856 $(CH)_{aliph.}$, 1700 (CO);
	Ethanol		(379.46)	69.92	6.41	11.35	1676 $(CO)_{amidic}$.
21_a	240	70	$C_{16}H_{21}N_3O_3$	66.88	7.37	14.62	MS: *m/z* =286.2 (M-1, 6%); 285.2 (11%); 274
	Benzene		(324.39)	66.42	7.54	14.98	(35%); 262 (32%); 257 (42%); 243.2 (100%); 241 (27%); 215.1 (47%).
21_b	175	82	$C_{18}H_{20}N_4O_2$	66.44	6.20	17.22	IR: 3065 $(CH)_{arom.}$, 2940 $(CH)_{aliph.}$, 1708 (CO);
	Methanol		(325.39)	66.76	6.02	17.64	1665 $(CO)_{amidic}$.
21_c	240	76	$C_{21}H_{14}N_3O_3$	69.02	6.34	11.50	^{1}H-NMR; 9.6 (s, 1H, =CH); 8.5-8.1 (m, 9H,
	Ethanol		(365.43)	69.32	6.65	11.21	arom.); 7.1 (s, 1H, NH); 5.5-5.2 (br., 2H, N-CH_2-N); 3.7 (s, 3H, OCH_3); 3.1 (s, 2H, CH_2-NH); 1.6-1.4 (br., 4H, $2CH_2$); 1.1 (t, 3H, CH_3).
22_a	260	68	$C_{16}H_{21}N_3O_2$	66.68	7.37	14.62	IR: 3045 $(CH)_{arom.}$, 2961, 2860 $(CH)_{aliph.}$, 1706
	Ethanol		(287.36)	66.24	7.53	14.76	(CO); 1684 $(CO)_{amidic}$.
22_b	285	73	$C_{18}H_{20}N_4O_2$	66.44	6.20	17.22	IR: 3050 $(CH)_{arom.}$, 2887 $(CH)_{aliph.}$, 1700 (CO);
	Dioxane		(325.39)	66.86	60.42	17.03	1657 $(CO)_{amidic}$.
22_c	270	78	$C_{21}H_{23}N_3O_3$	69.02	6.34	11.50	MS: *m/z* = 366,4 (M+1, 15%); 364.4 (15%);
	Dioxane		(265.43)	69.41	6.13	11.87	347.3 (17%); 334.2 (21%); 319 (43%); 276.2 (47%); 274 (43%); 257 (100%); 241 (42%); 15.1 (56%).

23	310 Dioxane	93	$C_{17}H_{15}N_3O_2$ (293.32)	69.61 69.41	5.50 5.33	14.33 14.47	IR: 3280, 3120 (2NH); 2930 ($CH_{aliph.}$); 1708 (CO), 1665 (CO_{amidic}). ^{1}H-NMR: 9.2 (s, 1H, NH); 7.8-6.4 (m, 10H, arom.+ NH), 5.6 (s, 1H,=CH); 1.8 (s, 3H, CH_3). MS: 294 (M^++1; 2.5%), 293 (M^+; 12.4%), 292 (M^+-1; 1%).
24	247 ethanol	80	$C_{20}H_{17}N_5O_2$ (359.39)	66.84 66.98	4.77 4.59	19.49 19.38	IR: 3240 (NH); 3140 (NH); 3050 $(CH)_{arom.}$; 2857 $(CH)_{aliph.}$; 2203 (CN); 1705 (CO); 1647 $(CO)_{amidic}$. ^{1}H NMR; 9.1 (s, 1H, NH); 7.1-6.4 (m, 10H, arom. +NH); 4.2 (s, 1H, CH); 3.3 (s, 2H, NH_2); 1.6 (s, 3H, CH_3).
25	280 methanol	67	$C_{20}H_{17}N_5O_3$ (375.38)	63.99 64.10	4.57 4.36	18.66 18.54	IR: 3340-3140 (4NH);1678, 1647 (2 $CO)_{amidic.}$ MS: 373.94 (M^+-1; 0.2%), 360.96 (2.0%), 345 (0.7%), 326 (0.6%),293.2 (24.9%), 292.2 (100%), 278.25 (0.8%), 177.49 (12.3%), 175.53 (11.1%), 76.8 (76.8%), 27.92 (8.5%).
26	185 methanol	67	$C_{26}H_{21}N_5O_3$ (451.48)	69.17 69.34	4.69 4.54	15.51 15.46	IR: 3320-3160 (3NH); 3040 $(CH)_{arom.}$; 2957 $(CH)_{aliph.}$; 1670, 1647 $(2CO)_{amidic.}$
27	180 methanol	60	$C_{27}H_{23}N_5O_2$ (449.51)	72.15 72.03	5.16 5.30	19.85 19.83	IR: 3260 (NH); 3150 (NH); 3055 $(CH)_{arom.}$; 2860 $(CH)_{aliph.}$; 1647 $(CO)_{amidic.}$
28$_a$	262 ethanol	68	$C_{22}H_{21}N_3O_2$ (359.43)	73.52 73.46	5.89 5.76	11.69 11.98	IR: 3121 (NH); 3045 $(CH)_{arom.}$; 2941, 2858 $(CH)_{aliph.}$; 1705 (CO); 1647 $(CO)_{amidic}$ ^{1}H-NMR: 7.2-6.3 (m, 10H, arom. +NH); 4.1 (s, 2H, CH_2); 3.5-3.2 (m, 2H, CH_2); 2.6-2.4 (m, 4H, $2CH_2$); MS: 360.7 (M^++1, 0.2%); 341.7 (1.9%); 292.7 (20.0%); 271.8 (20.4%); 270.8 (100.0%); 197.9 (5.3%); 176.8 (0.4%); 76.9 (9.7%).
28$_b$	185 methanol	82	$C_{23}H_{23}N_3O_2$ (373.45)	73.97 73.84	6.21 6.34	11.25 11.34	IR: 3280 (NH); 3160 (NH); 3040 $(CH)_{arom.}$; 2932, 2850 $(CH)_{aliph.}$; 1643 $(CO)_{amidic.}$
28$_c$	265 ethanol		$C_{24}H_{25}N_3O_2$ (387.48)	74.40 74.56	6.50 6.38	10.84 10.96	IR: 3240 (NH); 3110 (NH); 3031 $(CH)_{arom.}$; 2946, 2863 $(CH)_{aliph.}$; 1649 $(CO)_{amidic.}$
30	270 ethanol	62	$C_{19}H_{16}N_6O_2$ (360.39)	63.32 63.20	4.48 4.63	23.32 23.40	IR: 3300-3100 (NH_2 + 2NH); 2880 $(CH)_{aliph.}$; 2193 (CN); 1710 (CO);1662 $(CO)_{amidic}$ ^{1}H NMR; 8.3 (s, 1H, NH); 7.8-7.2 (m, 10H, arom. + NH); 4.8-4.4 (br., 2H, NH_2); 1.8 (s, 3H, CH_3) MS: 359 (M^+-1, 4.1%); 294 (80%); 2.3 (4.1%); 176.8 (2.5%); 119 (29.5%); 108 (88.1%) 91 (79.1%); 77 (86%); 28 (100%).
31	324 ethanol	62	$C_{27}H_{20}N_6O_2$ (460.49)	70.42 70.40	4.38 4.23	18.25 18.40	IR: 3139 (NH); 3069 $(CH)_{arom.}$; 2850 $(CH)_{aliph.}$;2196 (CN); 1710 (CO); 1641 $(CO)_{amidic}$
32	236 ethanol	70	$C_{25}H_{20}N_6O_3$ (452.47)	66.36 66.21	4.46 4.62	18.57 18.48	IR: 3280, 3150 (2NH); 3057 $(CH)_{arom.}$; 2853 $(CH)_{aliph.}$; 1700 (CO); 1674 $(CO)_{amidic}$ ^{1}H NMR: 8.3 (s, 2H, 2NH); 8.0-7.3 (m, 11H, arom. +NH); 4.2 (s, 1H, NH); 1.7 (s, 3H, CH_3)
33	200 benzene	42	$C_{26}H_{22}N_6O_2$ (450.50)	69.32 69.21	4.92 5.07	18.66 18.78	IR: 3150 (NH); 3065 $(CH)_{arom.}$; 2920 $(CH)_{aliph.}$; 1710 (CO); 1651 $(CO)_{amidic}$
34	278 ethanol	68	$C_{28}H_{24}N_6O_4$ (508.53)	66.13 66.25	4.76 4.98	16.53 16.37	IR: 3360, 3200 (2NH); 3060 $(CH)_{arom.}$; 2860 $(CH)_{aliph}$; 2210 (CN); 1740 $(CO)_{ester}$; 1700 (CO); 1660 $(CO)_{amidic}$

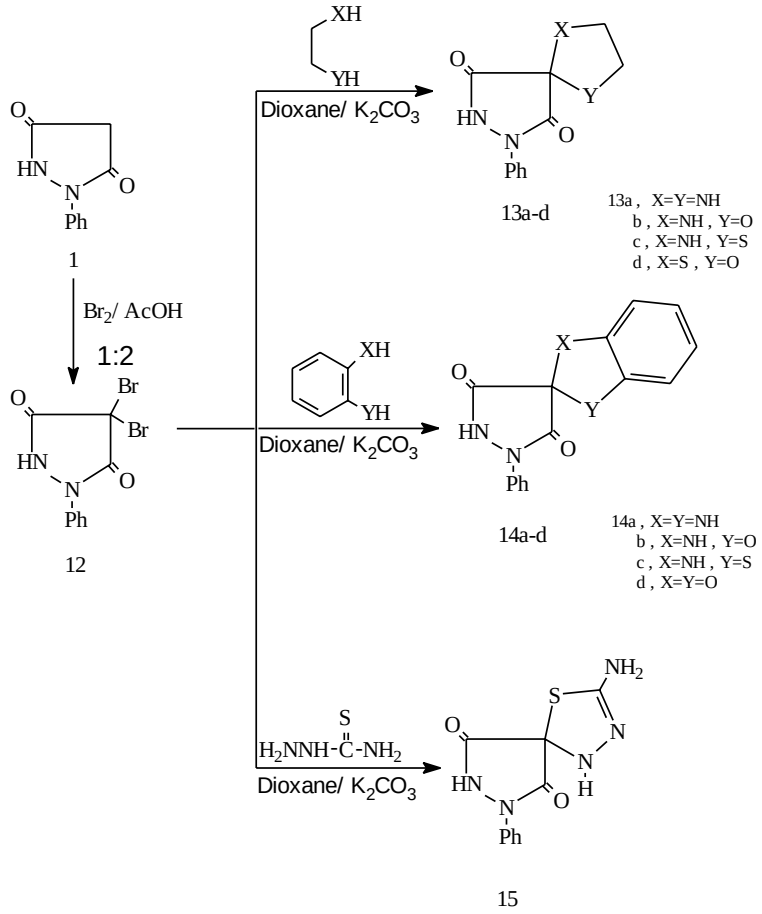
Scheme I



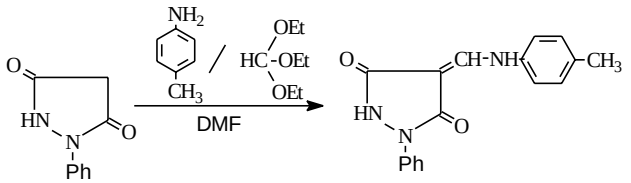
idene-2-(N-piperidino-, morpholino-, piprazine, n-butyl-, n-propyl- and isopropyl)aminomethyl-1-phenylpyrazolidine-3,5-diones (**17**$_{a\text{-}c}$-**22**$_{a\text{-}c}$), respectively. Mass spectra of compounds **17**$_b$, **18**$_b$, **19**$_a$, **20**$_a$, **21**$_a$ and **22**$_c$ showed the molecular ions at *m/z* (rel. int. %): 350 (77), 352 (11), 342 (18), 301 (54), 287 (12) and 365 (21), respectively (cf. Scheme III, Table 1).

4-(*p*-Methylphenylaminomethylidine)-1-phenyl-3,5-pyrazolidinedione (**23**) was prepared from the reaction of compound **1** with ethyl orthoformate and *p*-toluidine in boil-

Scheme II



ing dimethylformamide (Eq. 1). Mass spectrum of the product showed a molecular ion peak at *m/z* = 294 (M^++1) which is in agreement with its molecular structure.



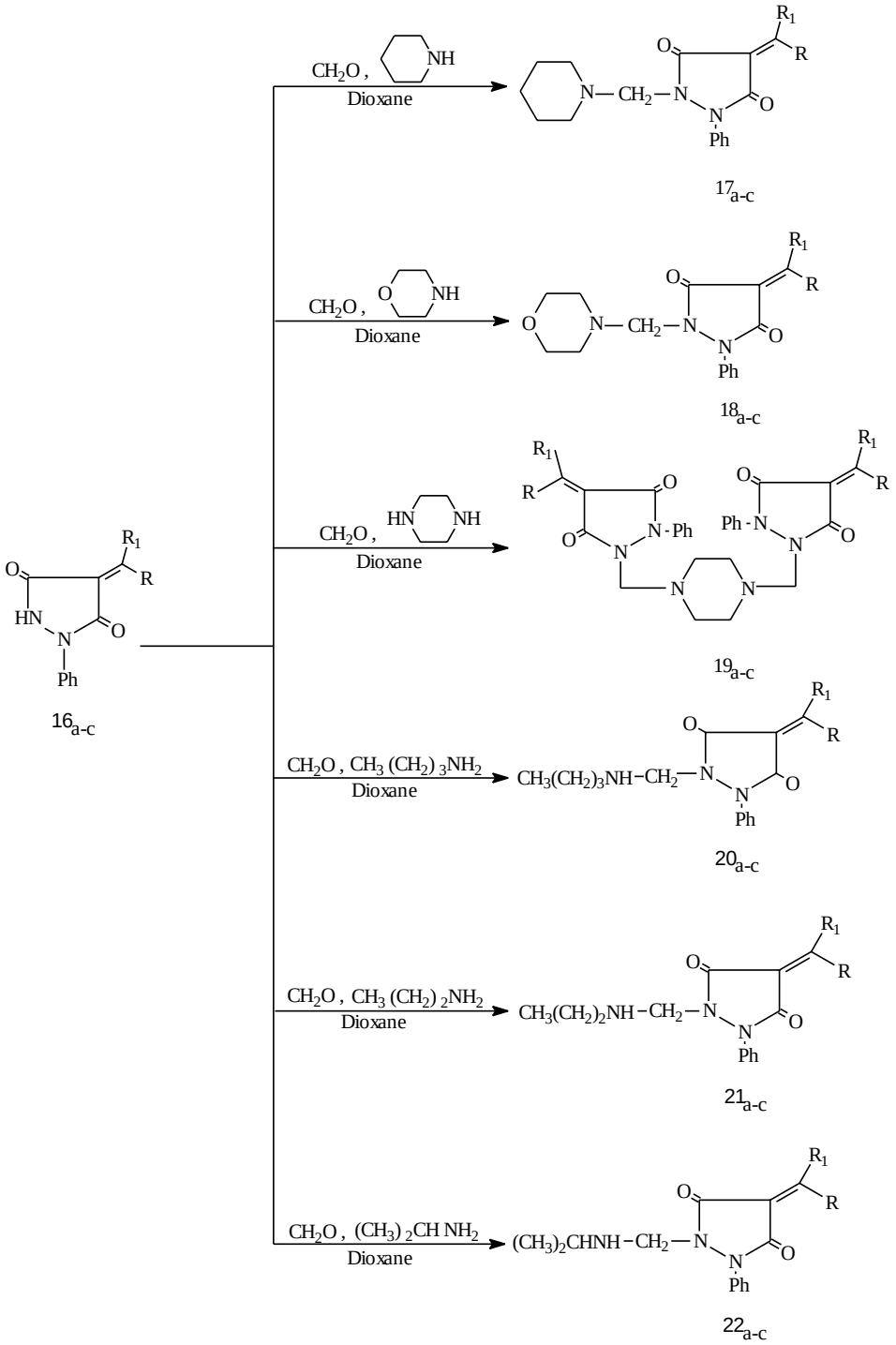
(1)

The reaction of compound **23** with active nitriles and cyclic ketones, namely malononitrile, cyanoacetamide, cyanothioacetamide, cyanoacetic hydrazide, 1-phenyl-3,5-pyrazolidinedione, 3-methyl-1-phenyl-5-pyrazolone, cyclopentanone, cyclohexanone and cycloheptanone in the presence of a catalytic amount of triethyl amine gave pyrano[2,3-c]pyrazoles derivatives (**24**-**28**), respectively. Mass spectra of compounds **24**, **25** and **28$_a$** showed molecular ion peaks at *m/z* = 359.05 (M^+), 373.94 (M^+-1), and 360.7 (M^++1) which are in agreement with their molecular formulae (cf. Scheme IV, Table 1).

The reaction pathway of compound **24** was assumed to follow a preliminary formation of carbanion of the active methylene reagent, which was added to the double bond followed by a nucleophilic attack of the NH group at the CN, CO, and CS groups with the elimination of a water molecule in the case of cyanoacetamide and a H_2S molecule in the case of cyanothioacetamide.[19] In the case of reaction of compound **23** with cyanoacetic hydrazide, evolution of NH_3 gas was observed with subsequent formation of fused pyrazolone ring most probably via a nucleophilic attack of the $NHNH_2$ group at the C-NH_2 linkage of the pyran nucleus followed by cyclization into compound **25**[20] (cf. Scheme V).

The reaction of 4-(*p*-methylphenylazo)-1-phenyl-3,5-pyrazolidinedione **29**[21,22] with active methylene reagents, namely malononitrile, cyanoacetamide, cyanothioacetamide, 1-phenyl-3,5-pyrazolidinedione and 3-methyl-1-phenyl-5-pyrazolone in the presence of a catalytic amount of triethyl

Scheme III

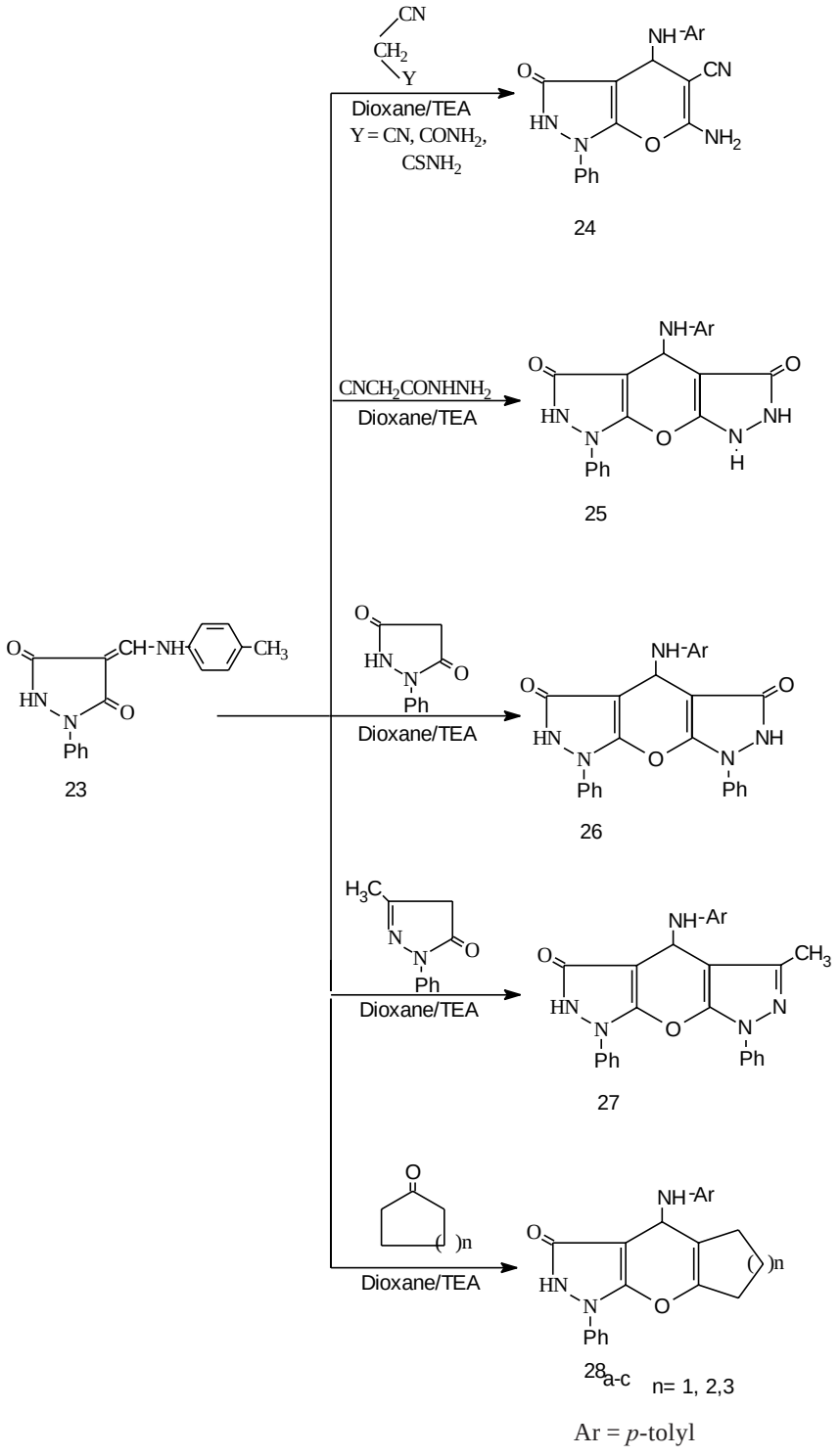


a, R , R_1= CH_3; b, R= H, R_1= pyrrolyl;
c, R= H, R_1= *p*-methoxyphenyl

amine gave spiropyrazole derivatives **30**-**32**, respectively. Mass spectrum of compound **30** showed a molecular ion peak at *m/z* = 359 (M^+-1) which is in agreement with its molecular structure (cf. Scheme VI, Table 1).

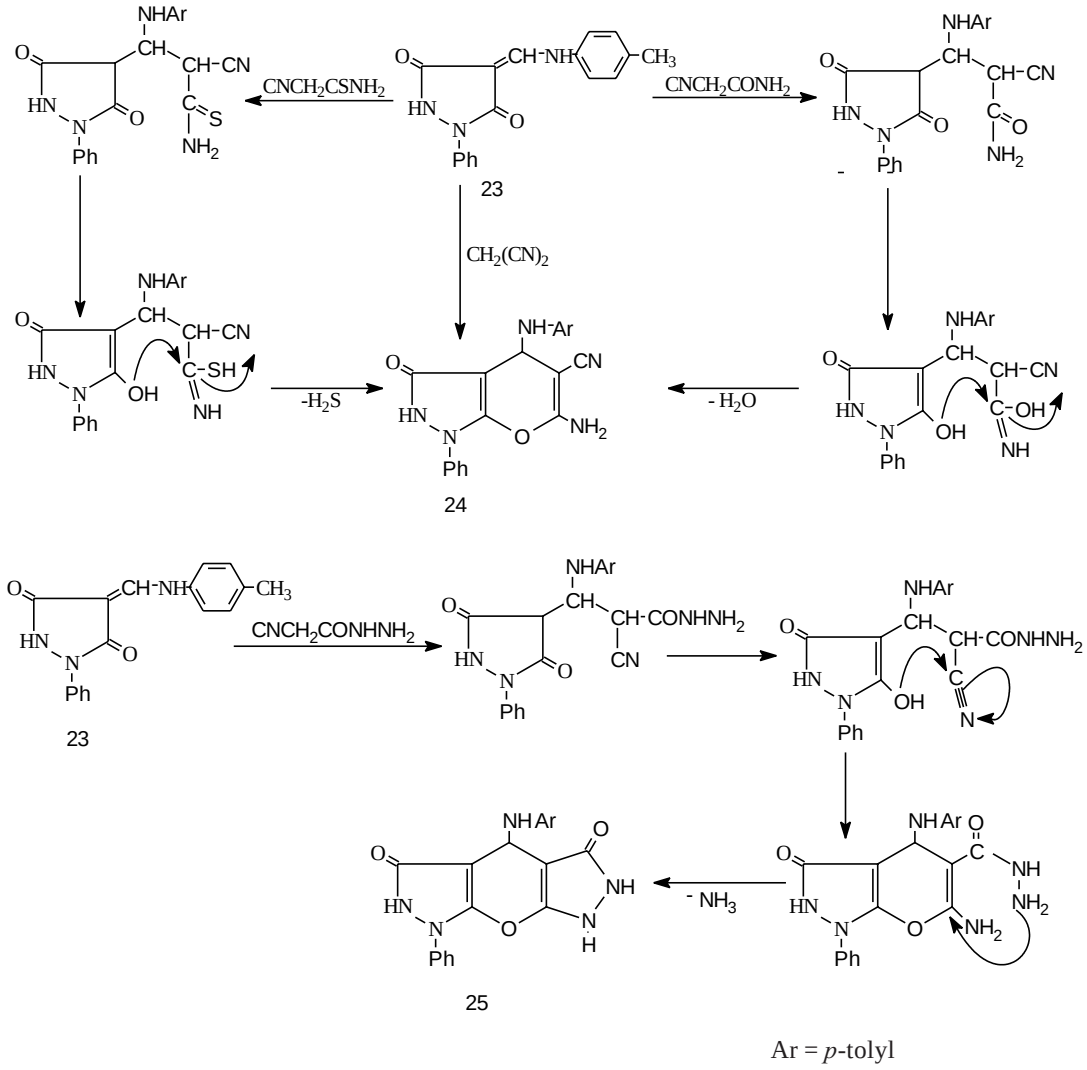
Suggested mechanism for the formation of compound **30** is illustrated as follows[19] (cf. Scheme VII).

Scheme IV



The reaction of compound **29** with PhNCS and ethyl cyanoacetate in 1:1:1 molar ratio under phase transfer catalysis conditions (PTC)[13,23] [dioxane/K_2CO_3/tetrabutylammonium bromide (TBAB)] gave the corresponding spiro pyrazole-4,3′-[1,2,4]triazolane **33** and spiro pyrazole-4,3′-[1,3,4]thiadiazolane **34** derivatives, respectively. Compound **33** was also obtained from the reaction of compound **29** with N-,S-acetal in glacial acetic acid. IR spectrum of compound

Scheme V



Ar = *p*-tolyl

33 showed the absorption bands at 2210 cm^{-1} corresponding to the CN group and at 1740 cm^{-1} due to $(CO)_{ester}$. Mass spectrum of compound **33** showed a molecular ion peak at *m/z* = 508.96 (M^++1) which is in agreement with its molecular formula (cf. Scheme VIII, Table 1).

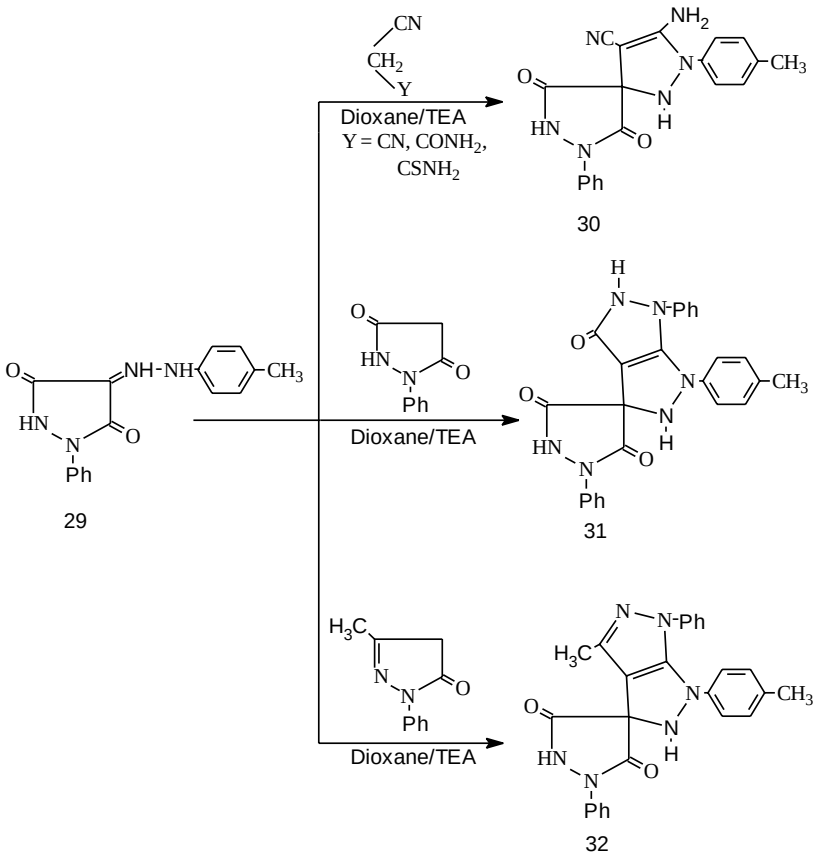
EXPERIMENTAL

All melting points were determined on a Kofler melting points apparatus and were uncorrected. IR spectra were obtained on a Nicolet 710 FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian EM 360 A at 60 MHz using TMS as an internal reference and (DMSO-d_6) as a solvent. The MS were measured on a Jeol JMS-600 Shimadzu spectrophotometer operating at 70 eV, using a direct inlet system. Elemental analyses (C,H,N) were carried out on a Perkin-Elmer 240 C elemental analyzer. Sulfur analyses were determined using the oxygen flask method by the Microanalytical Unit at Assiut University.

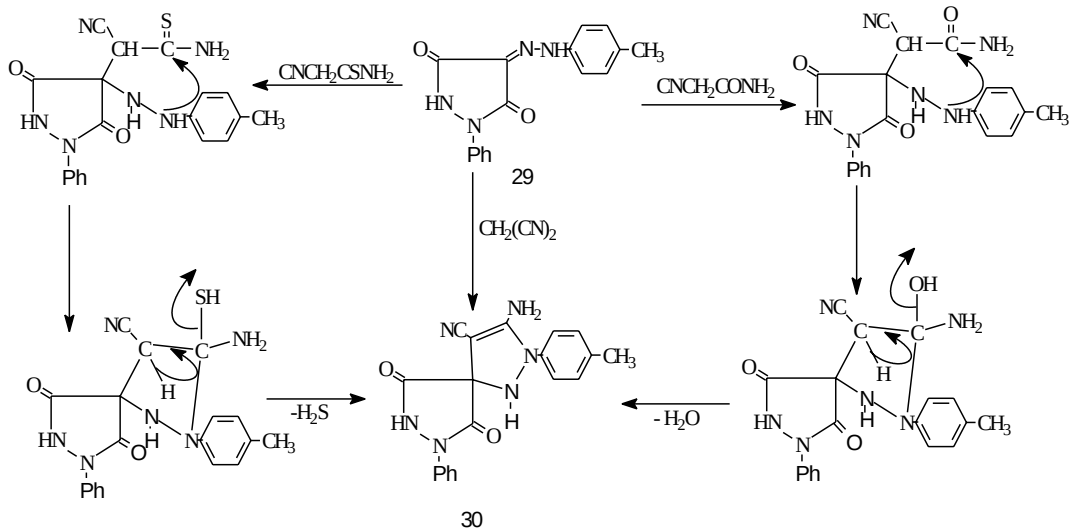
Synthesis of 1-phenyl-4-substituted-3,5-pyrazolidinediones (3-8): (General procedure)

A mixture of anhydrous potassium carbonate (3 gm), dry dioxane (30 mL), compound **2** (0.01 mol, 2.55 gm) and the appropriate reactant (0.01 mol), namely cystamine hydrochloride (0.99 gm), guanidine hydrochloride (1.02 gm), ethyl glycinate hydrochloride (1.40 gm), *o*-phenylenediamine

Scheme VI

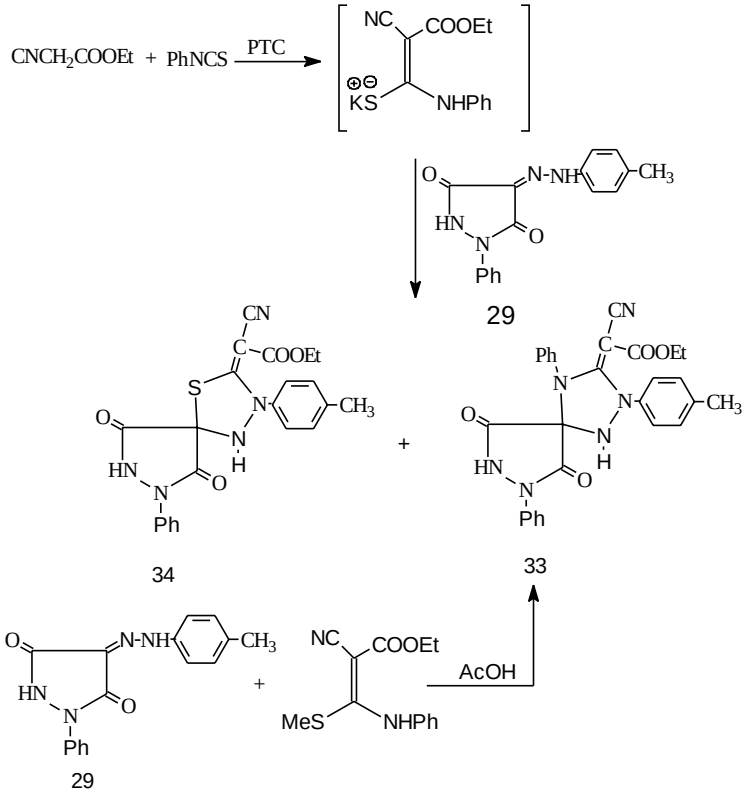


Scheme VII



(1.08 gm), *o*-aminothiophenol (1.25 mL), *p*-aminobenzoic acid (1.37 gm) or hydroquinone (1.10 gm) was refluxed for 4 hrs.; the reaction mixture was filtered off, and the filterate evaporated. The residue was triturated with pet. ether (40-60 °C) to give a solid, which crystallized from the appropriate solvent to give the corresponding compounds **3-8**, respec-

Scheme VIII



tively (cf. Scheme I, Table 1).

Synthesis of 3-oxo-1-phenyl-1,2,3,5,6,7-hexahydropyrazolo[3,4-b][1,4]thiazine (9) and 5-amino-3-oxo-1-phenyl-1,2,3,4-tetrahydroimidazo[4,5-c]pyrazole (10): (General procedure)

0.005 Mol of compound **3** (1.23 gm) or **4** (1.17 gm) was refluxed in glacial acetic acid for 4 hrs.; after cooling, the reaction mixture was poured into ice. The separated solid was collected by filtration and recrystallized from the suitable solvent to give the corresponding compounds **9** and **10**, respectively (cf. Scheme I, Table 2).

Synthesis of 3-oxo-1-phenyl-1,2,3,9-tetrahydrobenzo[b]-pyrazolo[3,4-e][1,4]thiazine (11)

0.005 Mol of compound $\mathbf{6_a}$ (1.41 gm) was dissolved in diphenyl ether (15 mL) and refluxed for 1.5 hr.; after cooling, the reaction mixture was poured into pet. ether (40-60 ºC). The separated solid was collected by filtration and recrystallized from benzene to give compound **11** (cf. Scheme I, Table 2).

Synthesis of componds 13-15: (General procedure)

A mixture of compound **12** (0.01 mol, 3.34 gm), dry dioxane (30 mL), and anhydrous potassium carbonate (3.0 gm) was treated with a suitable reactant (0.01 mol), namely ethylenediamine (0.60 mL), ethanolamine (0.61 mL), cystamine hydrochloride (0.99 gm), 2-mercaptoethanol (0.78 mL), *o*-phenylenediamine (1.08 gm), *o*-aminophenol (1.10 gm), *o*-aminothiophenol (1.24 gm), catechol (1.10 mg) or thiosemicarbazide (0.91 gm). The reaction mixture was refluxed for 5 hrs.; the reaction mixture was filtered off and the filterate evaporated. The solid residue was washed with water and crystallized from the appropriate solvent to give the corresponding compounds **13-15**, respectively (cf. Scheme II, Table 2).

Synthesis of compounds $\mathbf{17_{a-c}}$-$\mathbf{22_{a-c}}$: (General procedure)

To a stirred solution of compounds $\mathbf{16_{a-c}}$ (0.01 mol) in dioxane (20 mL), formaline solution (1 mL) and the appropriate amine, namely (0.01 mol) including, piperidine (0.85 mL), morpholine (0.87 mL), piperazine (0.005 mol, 0.43 gm), *n*-butylamine (0.73 mL), *n*-propylamine (0.59 mL) or isopropylamine (0.59 mL) were added. The reaction mixture was refluxed for 3 hours. The precipitated solid was filtered off, washed with water, and crystallized from the appropriate solvent to give the corresponding compounds $\mathbf{17_{a-c}}$ -$\mathbf{22_{a-c}}$, re-

spectively (cf. Scheme III, Table 2).

Synthesis of 4-(*p*-methylphenylaminomethylidine)-1-phenyl-3,5-pyrazo-lidinedione (23)

A mixture of compound **1** (0.01 mol, 1.76 gm), *p*-toluidine (0.01 mol, 1.08 gm) and ethyl orthoformate (0.01 mol, 1.67 mL) was heated for 0.5 hr.; the reaction mixture was cooled to room temperature, and the formed precipitate was filtered off and recrystalized from dioxane to give compound **23** (cf. Eq. 1, Table 2).

Synthesis of Compounds 24-28: (General procedure)

Compound **23** (0.005 mol, 1.47 gm) was added to a stirred solution of the appropriate reagent (0.005 mol), such as malononitrile (0.33 mL), cyanoacetamide (0.42 gm), cyanothioacetamide (0.5 gm), cyanoacetic hydrazide (0.50 gm), 1-phenyl-3,5-pyrazolidinedione (0.88 gm), 3-methyl-1-phenyl-5-pyrazolone (0.88 gm), cyclopentanone (0.42 mL), cyclohexanone (0.49 mL) and cycloheptanone (0.61 mL) in dry dioxane (30 mL), in the presence of a catalytic amount of triethylamine. The reaction mixture was refluxed for 5 hours, then cooled to room temperature; the solid was filtered off and recrystallized from the appropriate solvent to give compounds **24-28**, respectively. (cf. Scheme IV, Table 2).

Synthesis of Compounds 30-32: (General procedure)

Compound **29** (0.005 mol, 1.47 gm) was added to a stirred solution of the appropriate reagent (0.005 mol), namely malononitrile (0.33 mL), cyanoacetamide (0.42 gm), cyanothioacetamide (0.5 gm), cyanoacetic hydrazide (0.50 gm), 1-phenyl-3,5-pyrazolidinedione (0.88 gm) and 3-methyl-1-phenyl-5-pyrazolone (0.88 gm) in dry dioxane (30 mL), in the presence of a catalytic amount of triethylamine. The reaction mixture was refluxed for 5 hours, then cooled to room temperature; the solid was filtered off and recrystallized from the proper solvent to give compounds **30-32**, respectively. (cf. Scheme VII, Table 2).

Synthesis of 5-cyanoethoxycarbonylmethylidene-1,1′,2′,3,3′,4,5′-heptahydro-1′,4-diphenyl-1-*p*-tolylspiro-(pyrazole-4′,3-[1,2,4]triazole)-3′,5′-dione] (33) and 5-cyanoethoxycarbonylmethylidene-1,1′,2′,3,3′,5′-hexa-hydro-1′-phenyl-1-*p*-tolylspiro(pyrazole-4′,3-[1,2,4]-thiadiazole)-3′,5′-dione] (34)

A mixture of anhydrous potassium carbonate (3 gm), dry dioxane (30 mL), a catalytic amount of tetrabutylammonium bromide [TBAB] (0.005 mol), ethylcyanoacetate (0.005 mol, 0.53 mL) and phenyl isothiocyanate (0.005 mol, 0.68 mL) was stirred for 2 hours at 60 °C. Compound **29** (0.005 mol, 1.47 gm) was added to the reaction mixture, stirred for 5 hours at 70 °C. The reaction mixture was filtered off and the filterate evaporated in *vacuo*. The residual solid was washed with water, and dried and crystallized from ethanol to give compound **33**. The cabonate layer was dissolved in water (100 mL); the precipitated product was filtered off, dried and crystallized from ethanol to give compound **34** (cf. Scheme VIII, Table 2).

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