Heteroatom Chemistry
Volume 14, Number 3, 2003

One-Pot PTC Synthesis of Polyfused Pyrazoles

Gamal A. El-Saraf, Ahmed M. El-Sayed, and Ahmed M. M. El-Saghier

Department of Chemistry, Faculty of Science, South Valley University, Sohag, Egypt

Received 25 May 2002; revised 22 June 2002

ABSTRACT: *Thienopyrazole* **2, 3, 5**, *or* **6** *and thienopyrazolothiazepine* **7, 9**, *and* **11** *derivatives were prepared via the reaction of the 3-aminopyrazoline-5-one* **1** *with* CS_2 *and different molar ratio of a variety of halo compounds having an active methylene under PTC conditions. Also, treatment of* **1** *with* CS_2 *and alcoholic KOH in 2:1:1 molar ratio afforded dipyrazolopyridine derivatives* **12** *and* **14**. *On other hand, the pyrazolothiadiazineone derivative* **13** *was obtained by treating compound* **1** *with* CS_2 *and alcoholic KOH in 1:2:2 molar ratio. Under PTC conditions, compound* **1**, CS_2, *and ethyl cyanoacetate or malononitrile to gave the pyrazolopyridine derivatives* **16** *and* **17**. *Coupling of compound* **1** *with diazonium acetates afforded the hydrazone derivatives* **18a,b**, *which were oxidized with bromine to give pyrazolotriazoles* **19a,b** *or cyclized with aldehydes to give pyrazolotriazine derivatives* **20a–e**. *Bromination of compound* **1** *afforded monobromopyrazole derivative* **21**, *which could be condensed to a dipyrazolopyrazindione* **23**. *Finally, the dibromopyrazole derivative* **22** *was cyclized with 2-mercaptoethanol or* o*-phenylenediamine to give the spiropyrazoles* **24a,b**. © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:211–217, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10129

Correspondence to: Gamal A. El-Saraf; e-mail: saraf-g@lycos.com.

INTRODUCTION

Pyrazoles and their derivatives are used as pharmaceuticals and agrochemicals, the earliest example, antipyrine, dating from 1884 [1]. Also, fused pyrazoles have fungicidal [2,3], herbicidal [4,5], virucidal [6], insecticidal [7,8] activity and used for the treatment of rheumatoid arthritis [9–11]. The chemistry of pyrazoles has received much attention and many methods for their synthesis have been developed [12]. Various heterocyclic systems containing a pyrazole moiety have been prepared by 1,3-dipolar cycloaddition of iminonitriles to activated olefins [13–16]. This motivated us to synthesize some new fused and spiropyrazoles under PTC conditions.

RESULTS AND DISCUSSION

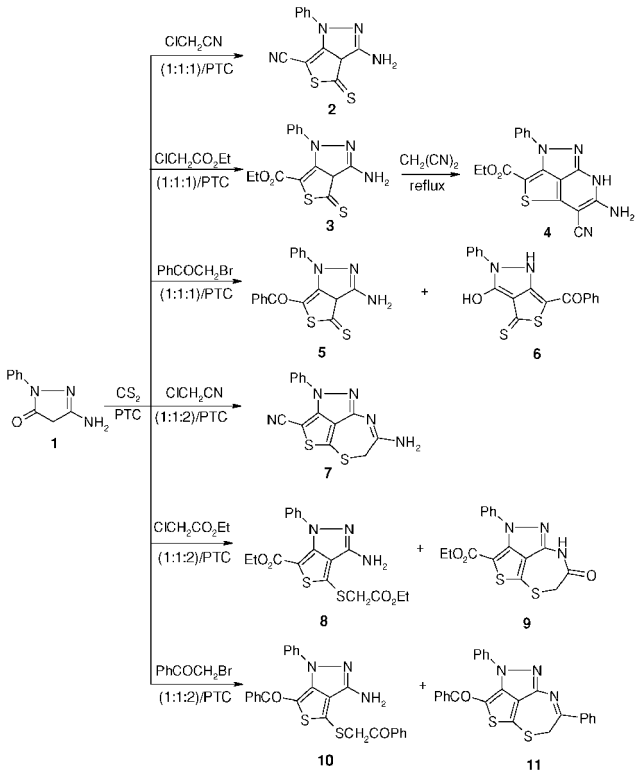
In an extension of our recent studies [17–23] on the application of PTC in heterocyclic synthesis, starting with an active methylene compounds containing α-keto or α-cyano group, herein we report the synthesis of some new fused and spiro pyrazole heterocycles starting with 3-amino-1-phenyl-2-pyrazolin-5-one (**1**). Compound **1** was allowed to react with CS_2 and a variety of halo compounds having an active methylene, including chloroacetonitrile, ethyl chloroacetate, or phenacyl bromide in 1:1:1 molar ratio, under PTC conditions [K_2CO_3/dioxane/tetrabutylammonium bromide (TBAB)], where 3-amino-1-phenyl-4-thioxo-3a,4-dihydro-1*H*-thieno[3,4-*c*]pyrazol-6-ylcarbonitrile (**2**), ethoxy(3-amino-1-phenyl-4-thioxo-3a,4-dihydro-1*H*-thieno[3,

4-*c*]pyrazo-6-yl)-1-methanone (**3**) or 3-amino-1-phenyl-4-thioxo-3a,4-dihydro-1*H*-thieno[3,4-*c*]pyrazol-6-ylphenyl-1-methanone (**5**), and 3-hydroxy-2-phenyl-4-thioxo-2,4-dihydro-1*H*-thieno[3,4-*c*]-pyrazol-6-ylphenyl-1-methanone (**6**) were obtained. The reaction is assumed to involve a nucleophilic attack of the generated carbanion of the pyrazole ring on CS_2, followed by alkylation of the formed dithiocarboxylate group with halo compounds and cyclization. On refluxing compound **3** with malononitrile in presence of piperidine as catalyst, 3-ethoxycarbonyl-6-amino-2-phenyl-2-hydro-4-thia-1, 2,7-triazacyclopenta[*cd*]-inden-5-ylcarbonitrile (**4**) was obtained. Moreover, the reaction of compound **1** with CS_2 and the same halo compounds but in 1:1:2 molar ratio under the same PTC conditions afforded 7-amino-2-phenyl-2,6-dihydro-4,5-dithia-1,2,8-triazacyclopenta[*cd*]azulen-3-ylcarbonitrile (**7**), 3-ethoxcarbonyl-2-phenyl-2,6,7,8-tetrahydro-4,5-dithia- 1,2, 8-triazacyclopenta[*cd*]azulen-7-one (**9**), or 2,7-diphenyl-2,6-dihydro-4,5-dithia-1,2,8-triazacyclopenta[*cd*]-azulen-3-ylphenyl-1-methanone (**11**) along with S-alkylated thienopyrazole derivative **8** or **10** as an intermediate (Scheme 1).

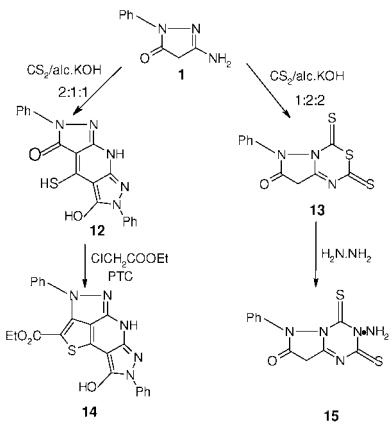
The reaction of compound **1** with CS_2 and alcoholic KOH in 2:1:1 molar ratio gave 5-hydroxy-4-mercapto-2,6-diphenyl-2,3,6,8-tetrahydrodipyrazolo-[3,4-*b*:4,3-*e*]pyridin-3-one (**12**), which was treated with ethyl chloroacetate under the proceeding PTC conditions to give ethoxy(8-hydroxy-3,7-diphenyl-5,7-dihydro-3*H*-1-thia-3,4,5,6,7-pentaaza-cyclopenta[*cd*]-*s*-indacen-2-yl)-1-methanone (**14**). On the other hand, 6-phenyl-2,4-dithioxo-2,6,7,8-tetrahydropyrazolo[1,5-*c*][1,3,5]-thiadiazin-7-one (**13**) was obtained by treating compound **1** with CS_2 and alcoholic KOH in 1:2:2 molar ratio, which was reacted with hydrazine hydrate [16,17] in refluxing ethanol, where H_2S gas was evolved to afford 3-amino-6-phenyl-2,4-dithioxo-2,3,4,6,7,8-hexahydropyrazolo[1,5-*a*][1,3,5]triazin-7-one (**15**) (Scheme 2). The structure of these compounds were confirmed using IR, ^{1}H-NMR, MS, and elemental analysis (Table 1).

Treatment of compound **1** with CS_2 under PTC conditions afforded pyrazole dithioc acid, which was allowed to react in situ with equimolar ratio of active nitriles including ethyl cyanoacetate or malononitrile to give 6-amino-5-ethoxycarbonyl-2-phenyl-4-thioxo-3,3a,4,7-tetrahydro-2*H*-pyrazolo-[3,4-*b*]pyridin-3-one (**16**) or 6-amino-3-oxo-4-mercapto-2-phenyl-3,3a,4,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridin-5-ylcarbonitrile (**17**), respectively (Scheme 3).

p-Chloro- and *p*-methylbenzenediazonium acetate was coupled with **1** to afford 3-amino-4-arylhydrazono-1-phenylpyrazol-5-one derivatives **18a** or **18b**, respectively. The mass spectrum of compound **18b** showed *m*/*z* 293 (relative intensity 100). Oxidation of compounds **18a,b** with bromine in acetic acid gave the 2,5-diphenyl-2,3,5,6-tetrahydropyrazolo[3,4-*d*][1,2,3]triazol-6-ones (**19a,b**). Also, treatment of **18a,b** with benzaldehyde, *p*-anisaldehyde, or *p*-nitrobenzaldehyde afforded the 2,3,6-tri-phenyl-3,4,6,7-tetrahydro-2*H*-pyrazolo[3,4-*e*][1,2,4]-triazin-7-ones (**20a–e**). The mass spectrum of **20a** showed *m*/*z* 401.5 (relative intensity 0.9) (Scheme 4).



SCHEME 1



SCHEME 2

TABLE 1 Analytical and Spectral Data of the Prepared Compounds

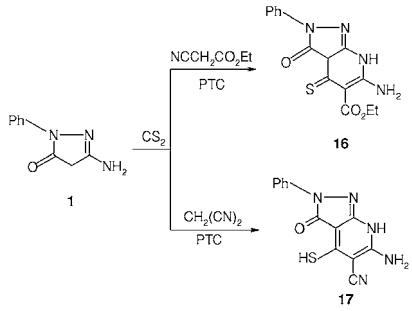
Compound	mp (°C)[a]	Solvent	Yield (%)	Mol. Formula	Mol. wt.	Anal Data Calc[b] C	H	N	S	IRν (cm⁻¹)	δ¹ H[c]
2	175–177	MeOH	56	$C_{12}H_8N_4S_2$	272.33	52.94 (52.80)[d]	2.94 (2.90)[d]	20.59 (20.20)[d]	23.55 (23.40)[d]	3368, 3252 (NH_2), 2243 (CN), 1617 (C=N), 1205 (C=S), 720 (C–S–C)	7.00–6.44 (m, 5H, arom), 3.74 (s, 2H, NH_2), 2.90 (s, 1H, CH)
3	167–168	EtOH/H_2O	50	$C_{14}H_{13}N_3O_2S_2$	319.41	52.66 (52.70)	4.08 (4.00)	13.17 (13.00)	20.08 (20.00)	3277, 3149 (NH_2), 1719 (CO), 1619 (C=N), 1196 (C=S), 737 (C–S–C)	7.04–6.60 (m, 5H, arom), 6.38–6.06 (br, 2H, NH_2), 3.94–3.60 (q, 2H, CH_2), 2.38 (s, 1H, CH), 1.46–1.04 (t, 3H, CH_3)
4	190–192	EtOH/H_2O	75	$C_{17}H_{13}N_5O_2S$	351.39	58.12 (58.00)	3.70 (3.70)	19.94 (19.80)	9.12 (8.80)	3279, 3200, 3153 (NH,NH_2), 2202 (CN), −1715 (CO), 736 (C–S–C)	7.80–7.60 (br, 1H, NH), 7.11–6.44 (m, 5H, arom), 4.54 (s, 2H, NH_2), 3.88–3.38 (q, 2H, CH_2), 1.32–1.00 (t, 3H, CH_3)
5	180–182	EtOH	32	$C_{18}H_{13}N_3OS_2$	351.45	61.54 (61.40)	3.70 (3.70)	11.97 (11.70)	18.25 (17.70)	3185, 3063 (NH_2), 1665 (CO), 1615 (C=N), 718 (C–S–C)	7.34–6.24 (m, 10H, arom), 5.08–4.08 (br, 2H, NH_2), 2.49 (s, 1H, CH)
6	207–208	EtOH/H_2O	44	$C_{18}H_{12}N_2O_2S_2$	352.44	61.36 (61.20)	3.41 (3.40)	7.95 (7.80)	18.20 (18.00)	3420 (OH), 3115 (NH), 1632 (CO), 694 (C–S–C)	7.25–6.48 (m, 12H, arom + NH + OH)
7	254–256	MeOH	75	$C_{14}H_9N_5S_2$	311.39	54.02 (53.80)	2.89 (2.80)	22.51 (22.30)	20.59 (20.48)	3235, 3125 (NH_2), 2210 (CN), 1630 (C=N), 698 (C–S–C)	7.82–7.22 (m, 5H, arom), 4.58 (s, 2H, NH_2), 3.45 (s, 2H, CH_2)
8	202–204	EtOH	45	$C_{18}H_{19}N_3O_4S_2$	405.47	53.33 (53.20)	4.69 (4.50)	10.37 (10.20)	15.82 (15.70)	3283, 3153 (NH_2), 1716 (CO), 1621 (C=N), 741 (C–S–C)	7.14–6.40 (m, 5H, arom), 3.95–3.58 (q, 4H, $2CH_2$), 3.65 (s, 2H, CH_2), 3.58–3.05 (br, 2H, NH_2), 1.37–0.99 (t, 6H, $2CH_3$)
9	300–302	dec. MeOH	68	$C_{16}H_{13}N_3O_3S_2$	359.43	53.48 (53.40)	3.62 (3.50)	11.70 (11.60)	17.84 (17.78)	3206 (NH), 1727, 1650 (2CO), 1627 (C=N), 758 (C–S–C)	7.45–6.50 (m, 6H, arom + NH), 3.22–2.62 (q, 2H, $-CH_2$), 2.88 (s, 2H, CH_2), 1.32–0.98 (t, 3H, CH_3)
10	152–154	beneze/pet. ether 60/80	55	$C_{26}H_{19}N_3O_2S_2$	469.59	66.52 (66.50)	4.05 (4.00)	8.96 (8.80)	13.66 (13.50)	3170, 3060 (NH_2), 1633 (CO), 659 (C–S–C)	7.34–6.30 (m, 15H, arom), 4.24 (s, 2H, NH_2), 3.14 (s, 2H, CH_2)
11	192–154	benzene	40	$C_{26}H_{17}N_3OS_2$	451.57	69.18 (69.00)	3.77 (3.70)	9.31 (9.20)	14.20 (14.33)	1634 (CO), 696 (C–S–C)	7.36–6.45 (m, 15H, arom), 2.68 (s, 2H, CH_2)
12	134–137	EtOH/H_2O	70	$C_{19}H_{13}N_5O_2S$	375.48	60.80 (60.80)	3.47 (3.40)	18.67 (18.50)	7.87 (7.70)	3320 (OH), 3197 (NH), 1655 (CO), 1602 (C=N)	8.28–8.00 (br, 2H, NH + OH), 7.35–6.78 (m, 10H, arom), 2.40 (s, 1H, SH)
13	224–226	EtOH/H_2O	55	$C_{11}H_7N_3OS_3$	293.39	45.05 (45.00)	2.39 (2.40)	14.33 (14.10)	32.79 (32.68)	1645 (CO), 1608 (C=N), 725 (C–S–C)	7.85–6.70 (m, 5H, arom), 4.20 (s, 2H, CH_2)
14	134–137	EtOH/H_2O	70	$C_{23}H_{17}N_5O_3S$	443.49	62.30 (62.20)	3.84 (3.90)	15.80 (15.40)	7.23 (7.20)	3424 (OH), 3120 (NH), 1726 (–CO), 1638 (C=N)	8.00–7.50 (br, 1H, NH), 7.04–6.44 (m, 10H, arom), 4.65–4.10 (br, 1H, OH), 3.94–3.60 (q, 2H, CH_2), 1.38–1.02 (t, 3H, CH_3)
15	262–264	EtOH	63	$C_{11}H_9N_5OS_2$	291.36	45.36 (45.00)	3.09 (3.10)	24.05 (23.90)	22.01 (22.80)	3238, 3128 (NH_2), 1650 (CO)	7.44–6.15 (m, 5H, arom), 5.35–4.30 (br, 2H, NH_2), 2.30 (s, 2H, CH_2)
16	170–172	EtOH	84	$C_{15}H_{14}N_4O_3S$	330.37	54.55 (54.40)	4.24 (4.10)	16.97 (16.60)	9.71 (9.60)	3260, 3158 (NH_2), 3120 (NH), 1720 (CO) 1632 (CO), 1610 (C=N), 1196 (C=S)	7.32–6.42 (m, 6H, arom + NH), 4.08–3.64 (q, 2H, CH_2), 3.02 (s, 2H, NH_2), 2.48 (s, 1H, CH), 1.36–1.02 (t, 3H, CH_3)

Continued

TABLE 1 *Continued*

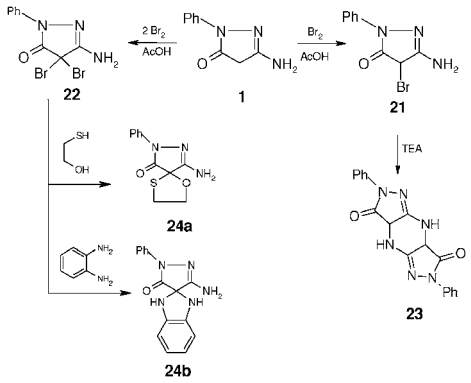
Compound	mp (°C)[a]	Solvent	Yield (%)	Mol. Formula	Mol. wt.	Anal. Data Calc[b] C	H	N	S	IRν (cm^{-1})	δ^1 H[c]
17	253–255	decomp. benzene	55	$C_{13}H_9N_5OS$	283.31	55.12 (55.00)	3.18 (3.20)	24.73 (24.50)	11.32 (11.20)	3267, 3149 (NH_2), 3120 (NH), 2207 (CN), 1665 (CO), 1625 (C=N)	8.50 (s, 1H, NH), 7.34–6.35 (m, 5H, arom), 3.34 (s, 2H, NH_2), 2.40 (s, 1H, SH)
18a	190–192	EtOH/H_2O	65	$C_{15}H_{12}ClN_5O$	313.80	57.42 (57.20)	3.83 (3.70)	22.33 (22.00)		3300, 3210 (NH_2), 3129 (NH), 1658 (CO)	7.70–6.45 (m, 9H, arom), 6.28 (s, 2H, NH_2), 5.950–5.82 (br, 1H, NH)
18b	172–174	EtOH/H_2O	76	$C_{16}H_{15}N_5O$	293.34	65.53 (65.30)	5.12 (5.40)	23.89 (23.60)		3135 (NH), 3500, 3380 (NH_2), 1650 (CO)	12.75–12.20 (br, 1H, NH), 7.50–6.45 (m, 9H, arom), 6.78 (s, 2H, NH_2), 2.20 (s, 3H, Ar–CH_3)
19a	271–273	EtOH	68	$C_{15}H_{10}ClN_5O$	311.78	57.78 (57.50)	3.21 (3.00)	22.47 (22.30)		3150 (NH), 1659 (CO)	8.00–6.30 (m, 10H, arom + NH)
19b	294–296	EtOH	65	$C_{16}H_{13}N_5O$	291.32	65.98 (65.50)	4.47 (4.40)	24.05 (24.50)		3146 (NH), 1658 (CO)	9.30–8.45 (br, 1H, NH), 7.70–6.64 (m, 9H, arom), 2.70 (s, 3H, CH_3)
20a	197–198	EtOH/H_2O	78	$C_{22}H_{16}ClN_5O$	401.91	65.75 (65.50)	3.99 (3.40)	17.43 (17.00)		3260 (NH), 1659 (CO);	8.40–8.15 (br, 1H, NH), 7.44–6.55 (m, 14H, arom), 4.90 (s, 1H, CH)
20b	196–198	EtOH/H_2O	75	$C_{23}H_{18}ClN_5O_2$	431.94	63.96 (63.70)	4.17 (4.00)	16.22 (16.40)		3238 (NH), 1647 (CO)	9.15–9.00 (br, 1H, NH), 7.52–6.50 (m, 13H, arom), 4.50 (s, 1H, CH), 3.85 (s, 3H, OCH_3)
20c	235–237	MeOH	82	$C_{22}H_{15}ClN_6O_3$	446.91	59.13 (58.80)	3.36 (3.30)	18.81 (18.50)		3242 (NH), 1651 (CO)	7.90–6.60 (m, 14H, arom + NH), 4.54 (s, 1H, CH)
20d	186–188	EtOH/H_2O	63	$C_{23}H_{19}N_5O$	381.44	72.44 (72.20)	4.99 (4.60)	18.37 (18.30)		3226 (NH), 1641 (CO)	7.60–6.40 (m, 15H, arom + NH), 4.62 (s, 1H, CH), 2.20 (s, 3H, CH_3)
20e	192–194	EtOH/H_2O	85	$C_{24}H_{21}N_5O_2$	411.47	70.07 (70.10)	5.11 (5.00)	17.03 (16.40)		3241 (NH), 1642 (CO)	9.15 (s, 1H, NH), 7.52–6.50 (m, 13H, arom), 4.80 (s, 1H, CH), 3.85 (s, 3H, OCH_3), 2.15 (s, 3H, CH_3)
21	128–130	dioxane	85	$C_9H_8BrN_3O$	254.18	42.52 (42.30)	3.15 (3.10)	16.54 (16.50)		3290, 3180 (NH_2), 1655 (CO)	7.55–6.30 (m, 5H, arom), 4.25 (s, 2H, NH_2), 2.80 (s, 1H, –CH–Br)
22	176–178	dioxane	65	$C_9H_7Br_2N_3O$	333.18	32.43 (32.30)	2.10 (2.20)	12.61 (12.00)		3300, 3180 (NH_2), 1649 (CO)	7.48–6.42 (m, 5H, arom), 4.75 (s, 2H, NH_2)
23	256–258	benzene	60	$C_{18}H_{14}N_6O_2$	246.35	62.79 (62.50)	3.49 (3.30)	24.42 (24.40)		3118 (NH), 1640 (CO)	8.50–8.10 (br, 2H, 2NH), 7.34–6.85 (m, 10H, arom), 4.64–3.95 (br, 2H, 2CH)
24a	155–157	benzene/ pet. ether	94	$C_{11}H_{11}N_3O_2S$	249.29	53.01 (53.00)	4.42 (4.20)	16.87 (16.60)	12.86 (12.70)	3300, 3190 (NH_2), 1638 (CO)	7.28–6.64 (m, 5H, arom), 6.10 (s, 2H, –NH_2), 3.62–3.38 (t, 2H, –O–CH_2), 2.94–2.50 (t, 2H, S–CH_2)
24b	184–186	benzene/ pet. ether	65	$C_{15}H_{13}N_5O$	279.27	64.52 (64.40)	4.66 (4.30)	25.09 (24.80)		3180, 3300 (NH_2), 3240 (NH), 1657 (CO)	7.98–7.00 (m, 9H, arom), 6.70–6.52 (br, 2H, NH_2), 5.25 (s, 2H, NH)

[a]Melting points are uncorrected.
[b]Satisfactory microanalysis obtained: C, +0.35; H, +0.4; N, +0.2.
[c]Measured by a Varian EM 360L spectrometer at 60 MHz using TMS as internal standard and DMSO-d_6 as a solvent.
[d]Values given in parentheses indicate found values.



SCHEME 3

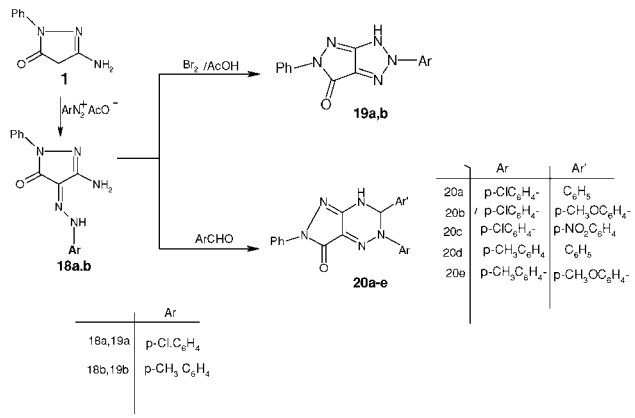
Bromination of compound **1** in 1:1 or 1:2 molar ratio afforded 3-amino-4-bromo-1-phenyl-2-pyrazol-5-one (**21**) or 3-amino-4,4-dibromo-1-phenyl-2-pyrazol-5-one (**22**), respectively. Refluxing of compound **21** in ethanol with triethylamine in 1:2 molar ratio gave 2,6-diphenyl-2,3,3a,4,6,7,7a,8-octahydrodipyrazolo[3,4-*b*:3,4-*e*]pyrazin-3,7-dione (**23**). 3′-Amino-1′-phenylspiro[perhydro[1,3]oxathiolane-2,4′-(1′,5′-dihydropyrazol)]-5′-one (**24a**) and 3′-amino-1′-phenylspiro[1,3-dihydrobenzo[*d*]imidazole-2,4′-(1′,5′-dihydropyrazole)]-5′-one (**24b**) were obtained by treating compound **21** with mercaptoethanol or *o*-phenylenediamine, respectively (Scheme 5).



SCHEME 5

EXPERIMENTAL

All melting points were determined on a Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Nicolet710 FT-IR spectrophotometer, using the KBr wafer technique. ^{1}H NMR spectra were measured on a Varian EM 360L, 60 MHz NMR spectrometer in a suitable deuterated solvent, using TMS as internal standard. Elemental analyses were performed on a Perkin–Elmer 240 C microanalyzer.



	Ar	Ar′
20a	p-ClC$_6$H$_4$-	C$_6$H$_5$
20b	p-ClC$_6$H$_4$-	p-CH$_3$OC$_6$H$_4$-
20c	p-ClC$_6$H$_4$-	p-NO$_2$C$_6$H$_4$
20d	p-CH$_3$C$_6$H$_4$	C$_6$H$_5$
20e	p-CH$_3$C$_6$H$_4$-	p-CH$_3$OC$_6$H$_4$-

	Ar
18a,19a	p-Cl.C$_6$H$_4$
18b,19b	p-CH$_3$ C$_6$H$_4$

SCHEME 4

Synthesis of Compounds **2, 3, 5–11**

General Procedure. To a solution of compound **1** (0.01 mol) in dioxane (30 ml) was added anhydrous potassium carbonate (3 g), TBAB (0.5 mmol), and carbon disulfide (0.01 mol), and finally chloroacetonitrile, ethyl chloroacetate or phenacyl bromide (0.01 or 0.02 mol). The reaction mixture was stirred for 10–12 h, filtered, and the solid potassium carbonate layer was dissolved in water and filtered. The filterate was acidified with acetic acid and the separated solid was crystallized from the suitable solvent to give compounds **2, 3, 6, 7, 9**, or **11** as yellow needles. The organic layer was evaporated *in vacuo* and the residue was treateds with water filtered, and crystallized from the suitable solvent to give compounds **5, 8**, or **10** as orange needles (Table 1).

^{13}C NMR of **2, 5, 9**, and **11** (dimethyl sulfoxide-d_6, δ ppm): **2**: 38.86, 40.13, 100.10, 114.08, 118.10, 120.06, 123.33, 128.55, 180.95, 205.11. **5**: 38.87, 93.12, 117.43, 118.86, 127.43, 127.92, 128.50, 128.75, 128.87, 129.66, 133.48, 135.33, 194.61, 203.09. **9**: 31.79, 57.53, 61.33, 107.23, 118.23, 123.17, 128.47, 140.00, 149.00, 159.46, 166.00, 168.02, 183.92, 211.23. **11**: 40.12, 103.47, 107.92, 117.69, 118.01, 118.76, 123.13, 124.37, 128.56, 128.90, 137.53, 139.88, 145.26, 157.34, 159.12, 160.31,168.02, 188.63, 191.76, 201.31.

MS of **6**: *m/e* (relative intensity) 352 (2.50), 319 (1.40), 247 (1.10), 234 (2.73), 223 (9.55), 142 (48.36), 129 (2.90), 105 (100.00), 100 (33.55), 93 (20.00), 77 (82.93), 55 (10.20).

*3-Ethoxycarbonyl-6-amino-2-phenyl-2,7-dihydro-4-thia-1,2,7-triazacyclopenta[cd]-inden-5-yl Carbonitrile (***4***)*

A mixture of compound **3** (0.003 mol, 1.053 g) and malononitrile (0.003 mol) in 30 ml of dioxane and a

few drops of piperidine was refluxed until H_2S gas ceased (7 h). The solvent was evaporated and the residue was diluted with water and acidified with hydrochloric acid. The precipitate was collected by filteration and crystallized from ethanol/water to give compound **4** as dark brown needles.

Synthesis of Compounds **12** *or* **13**

General Procedure. To a solution of **1** (0.01 mol) in 40 ml alcoholic potassium hydroxide (0.005 mol or 0.02 mol), carbon disulfide (0.005 mol or 0.02 mol) was added. The reaction mixture was refluxed for 10–12 h (until H_2S ceased), concentrated, diluted with water, and filtered. The filtrate was acidified with dilute hydrochloric acid, and the separating solid was collected by filtration and crystallized from ethyl alcohol to give compounds **12** or **13** as orange needles (Table 1).

*Ethoxy(8-hydroxy-3,7-diphenyl-5,7-dihydro-3H-1-thia-3,4,5,6,7-pentaazacyclopenta[cd]-s-indacen-2-yl)-1-methanone (***14***)*

A mixture of compound **12** (0.01 mol), anhydrous potassium carbonate (3 g), and a catalytic amount of TBAB (0.5 mmol) in dioxane (20 ml) was stirred for 45 min at 40°C, then ethyl chloroacetate (0.01 mol) was added. The reaction mixture was stirred for 8 h at 60°C, and filtered. The organic layer was dried over anhydrous sodium sulphate and evaporated *in vacuo* and the residual solid was crystallized from ethanol to give compound **14** as pale yellow needles (Table 1).

*3-Amino-6-phenyl-2,4-dithioxo-2,3,4,6,7,8-hexahydro-pyrazolo[1,5-a][1,3,5]triazin-7-one (***15***)*

To a solution of compound **13** (0.003 mol) in water (30 ml), hydrazine hydrate (0.006 mol) was added. The reaction mixture was refluxed for 4 h and filtered hot. The filterate was cooled and acidified with dilute hydrochloric acid. The precipitate was collected by filtration and crystallized from ethyl alcohol to give compound **15** as yellow needles.

*5-Ethoxycarbonyl-6-amino-2-phenyl-4-thioxo-3,3a,4,5-tetrahydro-2H-prazolo[3,4-b]pyridin-3-one(***16***) and 6-Amino-3-oxo-2-phenyl-4-thioxo-3,3a,4,5-tetrahydro-2H-prazolo[3,4-b]pyridin-5-yl Carbonitrile (***17***)*

A mixture of **1** (0.01 mol), anhydrous potassium carbonate (3 g), a catalytic amount of TBAB, dioxane (40 ml), carbon disulfide (0.01 mol) and ethyl cyanoacetate or malononitrile (0.01 mol) was stirred for 4 or 2 h at 60°C, and then filtered. The solid potassium carbonate was dissolved in water and filtered. The filtrate was acidified with acetic acid. The precipitate was crystallized from a suitable solvent to give compound **16** as yellow needles or **17** as orange needles (Table 1).

^{13}C NMR of compounds **16** and **17** (dimethyl sulfoxide-d_6,δ ppm): **16**: 38.87, 47.49, 47.91, 108.06, 117.98, 123.03, 128.56, 140.06, 143.81, 159.26, 188.83, 191.44, 213.80. **17**: 119.26, 127.90, 127.95, 128.08, 128.50, 128.60, 128.74, 133.11, 145.62, 174.92, 203.72.

*3-Amino-4-arylhydrazono-1-phenyl-2-pyrazolin-5-ones (***18a,b***)*

A solution of the diazonium salt synthesized from *p*-chloroaniline or *p*-toluidine, sodium nitrite, and sodium acetate/acetic acid (0.01 mol) was added to a solution of **1** (1.75 g, 0.01 mol) in acetic acid (20 ml) at 0–4°C with stirring. The reaction mixture was kept at room temperature for 24 h and the obtained solid was filtered and crystallized from ethanol/water to give compound **18a** as red needles or compound **18b** as violet needles.

^{13}C NMR of (**18b**) (dimethyl sulfoxide-d_6, δ ppm): 20.52, 115.63, 117.07, 122.21, 123.68, 128.83, 129.89, 134.24, 138.56, 139.48, 150.72, 155.45.

MS of **18b**: *m*/*z* (relative intensity) 293 (100), 202 (7.2), 187 (1.0), 174 (1.9), 132 (1.5), 106 (15.7).

*2,5-Diphenyl-2,3,5,6-tetrahydropyrazolo[3,4-d]-[1,2,3]triazol-6-ones (***19a,b***)*

To a solution of **18a** or **18b** (0.004 mol) in 20 ml of acetic acid was added bromine (0.21 ml; 0.004 mol) in 5 ml acetic acid dropwise (10 min). The reaction mixture was stirred for 24 h at room temperature, then poured into water, filtered, and the product crystallized from ethanol to give compound **19a** or **19b** as orange needles.

*2,3,6-Triphenyl-3,4,6,7-tetrahydro-2H-pyrazolo[3,4-e][1,2,4]triazin-7-ones (***20a–e***)*

Benzaldehyde, anisaldehyde, or *p*-nitrobenzaldehyde (0.005 mol) was added to compound **18a** or **18b** (0.005 mol) in absolute ethanol (20 ml) in presence of two drops of piperidine. The reaction mixture was refluxed for 3 h, filtered hot, concentrated, and cooled. The precipitate were collected by filteration and crystallized from a suitable solvent to give **20a–e** as yellow needles.

^{13}C NMR of **20e** (dimethyl sulfoxide-d_6, δ ppm): 23.08, 57.55, 97.65, 98.78, 116.30, 116.77, 120.73, 121.95, 123.17, 128.18, 128.39, 140.24, 141.46, 143.90, 151.22, 153.65, 163.41, 178.04.

MS of **20a**: *m/z* (relative intensity) 401.5 (0.9), 311.5 (0.9), 278 (1.2), 202 (7.5).

*3-Amino-4-bromo-1-phenyl-2-pyrazolin-5-one (**21**) and 3-Amino-4,4-dibromo-1-phenyl-2-pyrazolin-5-one (**22**)*

Bromine (1.03 ml, 0.02 mol or 2.06 ml, 0.04 mol) in 15 ml of acetic acid was added to **1** (3.5 g, 0.02 mol) in acetic acid (20 ml). The reaction mixture stirred at room temperature for 24 h, poured onto ice-water. The precipitate was filtered and crystallized from dioxane to give **21** as a deep yellow powder or **22** as pale brown fine needles.

*2,6-Diphenyl-2,3,3a,4,6,7,7a,8-octahydrodipyrazolo[3,4-b:-3,4-e]pyrazin-3,7-dione (**23**)*

A solution of **21** 0.875 g (0.005 mol) in 20 ml of absolute ethanol was treated with triethylamine (1.3 ml, 0.01 mol) with stirring and the reaction mixture was refluxed for 3 h, evaporated *in vacuo*, and the solid residue was crystallized from benzene to give **23** as yellow needles.

*3′-Amino-1′-phenyl-spiro[perhydro[1,3]-oxathiolane-2,4′-(1′,5′-dihydropyrazole)]-5′-one (**24a**) and 3′-Amino-1′-phenylspiro[1,3-dihydro-benzo-[d]-imidazol-2,4′-(1′,5′-dihydropyrazol)]-5′-one (**24b**)*

A mixture of **22** (0.525 g, 0.003 mol) and 2-mercaptoethanol (0.22 ml, 0.003 mol) or *o*-phenylenediamine (0.324 g, 0.003 mol) was refluxed in the presence of triethylamine (0.62 ml, 0.006 mol) for 2 h. The solvent was evaporated and the solid residue was washed with water, and crystallized from benzene/pet.ether 40:60 to give **24a** or **24b** as yellow needles.

MS of **24a**: *m/z* (relative intensity) 249 (4.2), 173 (15.6), 172 (21.7), 171 (100), 156 (8.7), 145 (7.5), 119 (9.1), 91 (24.3), 77 (22.4), 76 (15.9), 44 (38.8), 28 (30.0).

REFERENCES

[1] Acheson, R. M. An Introduction to the Chemistry of Heterocyclic Compounds, 2nd ed.; Wiley: New York, 1967; p. 309.

[2] Sasse, K.; Haenssler, G.; Schmidt, H. G.; Paulus, W. Ger Offen DE 1987, 3 , 327; CA 1987,106, 133794u.

[3] Pulido, M. L.; Fenyes, J. G. Eur Pat Appl 467,708, 1991; CA 1992, 116, 146150 J.

[4] Ohyama, H.; One, T.; Terakawa, T. Eur Pat Appl 202,169, 1986; CA 1987,106, 33046t.

[5] Igai, T. Jpn Kokai Tokkyo Koho 6157, 505, 1985: CA 1986,105, 92923r.

[6] Zikan, V.; Radl, S.; Smejkal, F.; Zelena, D.; Czech CS 233445, 1986; CA 1987, 106, 138437q.

[7] Hasan, R.; Nishimura, K.; Veno, T. Pestic Sci 1994, 42, 291.

[8] Roberts, D. A.; Hawkins, D.; Ross, W. Eur Pat Appl 403,309, 1991; CA 1991, 114, 185494c.

[9] Harlin, W.; Linke, A.; Messer, E. Deut Arch Klin Med 201, 690, 1955; CA 1956, 50, 11519c.

[10] Pacousky, V.; Holecek, V. Casopis Lekaru Ceskych 95, 300, 1956; CA 1956, 50, 7306c.

[11] Stanfield, A. B.; Brodie, E. C.; Yeoman, E. E. Proc Soc Exptl Biol Med 83, 254, 1953; CA 1953, 47, 10712d.

[12] Hanefeld, U.; Rees, C. W.; White, A. J. P.; Williams, D. J.; J Chem Soc, Perkin Trans 1 1996, 1546.

[13] Padmavathi, V.; Reddy, A. V. B.; Sumathi, R. P.; Padmaja, A.; Reddy, D. B. Indian J Chem 1998, 37B, 1286.

[14] Padmavathi, V.; Sumathi, R. P.; Reddy, A. V. B.; Reddy, D. B. Heterocyclic Commun 1998, 4, 163.

[15] Padmavathi, V.; Sumathi, R. P.; Chandrasekhar, N. B.; Reddy, D. B. J Chem Research (S) 1999, 610.

[16] Padmavathi, V.; Sumathi, R. P.; Balasah, A.; Somasekhar, A. R.; Reddy, D. B. Synth Commun 2001, 31, 2119.

[17] El-Saraf, G. A.; El-Sayed, A. M. Synth Commun 1996, 26, 3827.

[18] El-Shafei, A. K.; Abdel-Ghany, H.; Sultan, A. A.; El-Saghier, A. M. M. Phosphorus Sulfur Silicon 1992, 73, 15.

[19] El-Sayed, A. M.; Abdel-Ghany, H. J Heterocycl Chem 2000, 37, 1233.

[20] El-Saghier, A. M. M. Bull Chem Soc Jpn 1993, 66, 2011.

[21] El-Shafei, A. K.; El-Saghier, A. M. M.; Soliman, A. M.; Sultan, A. Phosphorus Sulfur Silicon 1992, 80, 72.

[22] El-Shafei, A. K.; El-Saghier, A. M. M.; Ahmed, E. A. Synthesis 1994, 152.

[23] El-Saghier, A. M. M. Phosphorus Sulfur Silicon 2002, 177, 1213.