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Synthesis of disazo pyrazolo[1,5-*a*]pyrimidines

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Abstract

p-Substituted anilines were diazotized and coupled with 3-aminocrotononitrile, malononitrile, ethyl cyanoacetate or ethyl acetoacetate to give the 2-arylhydrazone-3-ketimino-butyronitriles, 2-arylhydrazonomalononitriles, ethyl 2-arylhydrazonocyanoacetates and ethyl 2-arylhydrazonoacetoacetates, respectively. Cyclization of these arylhydrazone derivatives with 5-amino-4-arylazo-3-methyl-1H-pyrazoles or 3,5-diamino-4-arylazo-1H-pyrazoles in pyridine moiety afforded the corresponding disazo pyrazolo[1,5-*a*]pyrimidine derivatives.

Keywords: Pyrazolopyrimidine; Disazo; Intermolecular cyclization; Diazo-coupling reaction; Condensation reaction

1. Introduction

Simple nitrogen-containing heterocycles receive a large amount of attention in the literature, as a consequence of their exciting biological properties and their role as pharmacophores of considerable historical importance. Of these heterocycles, the synthesis, reactions and biological activities of pyrimidine containing molecules stand as an ever-expanding area of research in heterocyclic chemistry and this structural motif appears in a large number of pharmaceutical agents and natural products [1–6]. These interesting activities have stimulated chemists to develop the chemistry of this class of compounds. Also, it is well known that nitriles are widely used as intermediates for a large number of heterocyclic compounds. The aminopyrazole compounds have been easily obtained by the reaction of nitrile derivatives with hydrazine [7–12], and are very useful as precursors for the synthesis of fused heterocyclic ring systems. The fused heterocyclic compounds can also be used as intermediates in the dyestuff industry [13–18]. In the present study, we report the synthesis of some new disazo pyrazolo[1,5-*a*]pyrimidine derivatives.

2. Results and discussion

Aniline, *p*-nitroaniline and *p*-anisidine were diazotised to afford the diazonium salts **1a–1c**. Coupling of **1a–1c** with 3-aminocrotononitrile (**2**), malononitrile (**3**), ethyl cyanoacetate (**4**) or ethyl acetoacetate (**5**) in sodium acetate buffered solution afforded the 2-arylhydrazone-3-ketiminobutyronitriles **6a–6c**, 2-arylhydrazonomalononitriles **7a–7c**, ethyl 2-arylhydrazonocyanoacetates **8a–8c** and ethyl 2-arylhydrazonoacetoacetates **9a–9c**, respectively, in good yields (Scheme 1, Table 2). 5-Amino-4-arylazo-3-methyl-1H-pyrazoles **10a–10c** and 3,5-diamino-4-arylazo-1H-pyrazoles **10d–10f** were synthesized by the cyclization, involving the reaction of 2-arylhydrazone-3-ketiminobutyronitriles **6a–6c** and 2-arylhydrazonomalononitriles **7a–7c** with hydrazine hydrate in ethanol under reflux for 4 h (Scheme 2). The prepared compounds were characterized by elemental analyses and spectroscopic techniques. The IR spectra of **6a–6c** showed the presence of two NH groups stretching at 3234–3221 cm^{-1} and CN group stretching at 2221–2205 cm^{-1}. ^1H NMR spectra of **6a–6c** revealed a singlet at δ 2.47–2.51 ppm (s, 3H, CH_3), singlets at δ 8.41–8.63 ppm (s, 1H, NH) and δ 8.82–9.12 ppm (s, 1H, NH) (Table 1). Compounds **6a–6c** reacted with hydrazine hydrate in refluxing absolute ethanol, to yield 5-amino-4-arylazo-3-methyl-1H-pyrazoles **10a–10c** (Scheme 2, Table 4). Structures **10a–10c** were assigned based on analytical and spectral

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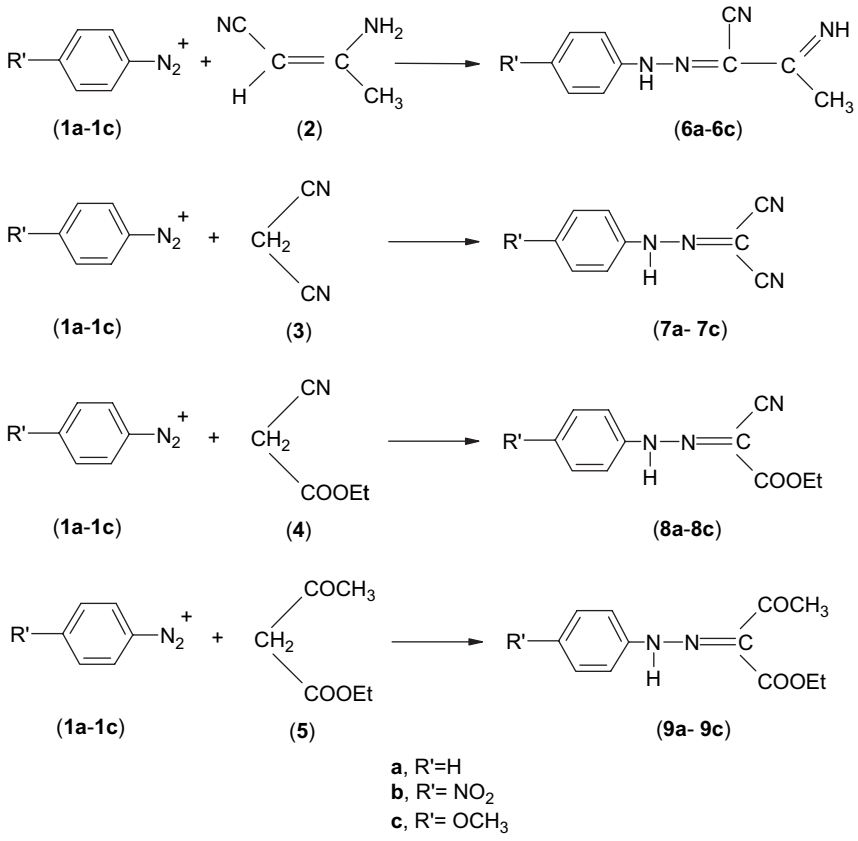
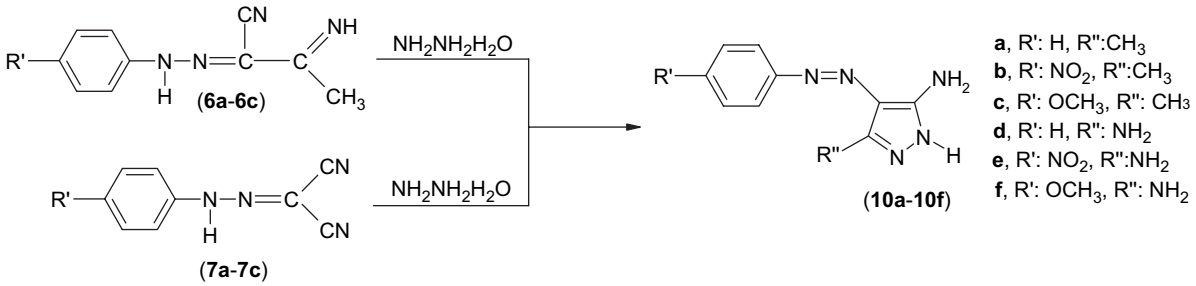


Scheme 1.

data. The IR spectra of **10a–10c** showed the absence of any CN stretching absorption that might be expected to appear at the range of ν 2221–2205 cm^{-1}, while they showed the presence of NH_2 group stretching at 3425–3410 and 3375–3360 cm^{-1}, NH group stretching at 3250–3215 cm^{-1}. Additionally, the ^1H NMR spectra of **10a–10c** showed a singlet at δ 3.00–3.12 ppm (s, 3H, CH_3), a singlet at δ 6.00–7.10 ppm (s, 2H, NH_2), a singlet at δ 11.50–12.30 ppm (s, 1H, NH) (Table 3).

The IR spectra of **7a–7c** indicated the presence of NH group stretching at 3234–3219 cm^{-1}, two CN groups stretching at 2233–2228 cm^{-1}. Moreover, ^1H NMR spectra of **7a–7c** indicated a singlet at δ 8.80–9.00 ppm for the NH group. Treatment of **7a–7c** with hydrazine hydrate in refluxing absolute ethanol yielded 3,5-diamino-4-arylazo-1H-pyrazoles **10d–10f** (Scheme 2). The structures of **10d–10f** were established on the basis of their elemental analyses and spectral data. For example, their IR spectra showed absorption bands at ν 3432–3415 cm^{-1} and 3371–3330 cm^{-1} due to two NH_2 (3-NH_2 and 5-NH_2) groups, at 3235–3208 cm^{-1} due to NH group and ^1H-NMR spectra showed two singlets at δ 5.96–6.52 ppm for two NH_2 (3-NH_2 and 5-NH_2) groups, δ 10.75–10.95 ppm for NH groups (Table 3).

The IR spectra of **8a–8c** indicated the presence of NH group stretching at 3230–3227 cm^{-1}, CN group stretching at 2221–2218 cm^{-1} and C=O group stretching at 1740–1730 cm^{-1}. The ^1H NMR spectra of **8a–8c** indicated a triplet δ 1.27–1.30 ppm due to ethoxy CH_3 group, a quartet at δ 4.09–4.15 ppm for the ethoxy CH_2 group and a singlet at δ 8.87–9.10 ppm for the NH group. Similarly, the IR spectra of **9a–9c** showed absorption bands at 3230–3215 cm^{-1}, 1740–1716 cm^{-1}, 1694–1682 cm^{-1} due to NH and two



Scheme 2.

Table 1
Spectral data for dyes **6a–6c**, **7a–7c**, **8a–8c** and **9a–9c**

Dye no.	MS *m/z* (M^+)	FT-IR (cm^{-1}) in KBr								^{1}H NMR (δ, ppm)			
		ν_{N-H}	$\nu_{C-H\ (alip.)}$	$\nu_{C-H\ (Arop.)}$	$\nu_{C\equiv N}$	$\nu_{C=O}$	$\nu_{C=N}$	ν_{NO_2}	ν_{C-O}	Arom.-H	Alip.-H	X–H	Solvent
6a	186	3234–3224	3037	2981	2218	–	1621	–	–	7.10–7.50 (5H, m, C_6H_5)	2.47 (CH_3, s)	8.41 (NH, s) 8.82 (NH, s)	$CDCl_3$
6b	231.2	3230–3221	3045	2973	2221	–	1634	1554, 1328	–	7.60 (2H, d, 3,5-PhH) 8.30 (2H, d, 2,6-PhH)	2.51 (CH_3, s)	8.63 (NH, s) 9.12 (NH, s)	DMSO-d_6
6c	216	3229–3221	3058	2965	2205	–	1635	–	1092	6.90–7.75 (4H, m, C_6H_4)	2.49 (CH_3, s) 3.85 (p-OCH_3, s)	8.44 (NH, s) 8.91 (NH, s)	$CDCl_3$
7a	170	3228	3109	–	2233	–	1634	–	–	7.02–7.43 (5H, m, C_6H_5)	–	8.90 (NH, s)	$CDCl_3$
7b	215.1	3234	3089	–	2230	–	1628	1513, 1344	–	7.79 (2H, d, 3,5-PhH) 8.40 (2H, d, 2,6-PhH)	–	9.00 (NH, s)	DMSO-d_6
7c	200.1	3219	3051	2968	2228	–	1636	–	1116	6.83–7.17 (4H, m, C_6H_4)	3.60 (p-OCH_3, s)	8.80 (NH, s)	$CDCl_3$
8a	217	3228	3071	2985, 2860	2218	1734	1626	–	1105	7.12–7.64 (5H, m, C_6H_5)	1.27 (CH_3, t) 4.10 (–OCH_2–, q)	8.87 (NH, s)	$CDCl_3$
8b	262.2	3230	3086	2971, 2852	2221	1740	1634	1559, 1331	1120	7.63 (2H, d, 3,5-PhH) 8.15 (2H, d, 2,6-PhH)	1.30 (CH_3, t) 4.15 (–OCH_2–, q)	9.10 (NH, s)	DMSO-d_6
8c	247.2	3227	3075	2953, 2875	2221	1730	1656	–	1098	7.02–7.78 (4H, m, C_6H_4)	1.28 (CH_3, t) 3.82 (p-OCH_3, s) 4.15 (–OCH_2–, q)	8.90 (NH, s)	$CDCl_3$
9a	234	3228	3092	2977, 2855	–	1734, 1688	1630	–	1114	7.12–7.83 (5H, m, C_6H_5)	1.27 (CH_3, t) 2.26 ($COCH_3$, s) 4.25 (–OCH_2–, q)	8.90 (NH, s)	$CDCl_3$
9b	279	3230	3105	2981, 2863	–	1740, 1694	1642	1561, 1335	1105	7.70 (2H, d, 3,5-PhH) 8.35 (2H, d, 2,6-PhH)	1.30 (CH_3, t) 2.32 ($COCH_3$, s) 4.27 (–OCH_2–, q)	9.10 (NH, s)	DMSO-d_6
9c	264	3215	3078	2963, 2868	–	1716, 1682	1627	–	1093	6.88–7.52 (4H, m, C_6H_4)	1.25 (CH_3, t) 2.30 ($COCH_3$, s) 3.75 (p-OCH_3, s) 4.27 (–OCH_2–, q)	8.85 (NH, s)	$CDCl_3$

Table 2
Element analysis of dyes **6a–6c**, **7a–7c**, **8a–8c** and **9a–9c**

Dye no.	Molecular formula (m. wt)	m.p. (°C) (color)	Solvent cryst. (yield %)	Elemental analysis: calc. (found)		
				C	H	N
6a	$C_{10}H_{10}N_4$ (186.2)	166–167 (greenish yellow)	C_2H_5OH–H_2O (82)	64.50 (64.41)	5.41 (5.44)	30.09 (29.97)
6b	$C_{10}H_9N_5O_2$ (231.2)	260–261 (brown)	DMF–H_2O (89)	51.95 (51.81)	3.92 (3.88)	30.29 (30.18)
6c	$C_{11}H_{12}N_4O$ (216.2)	123–124 (greenish yellow)	C_2H_5OH–H_2O (73)	61.10 (61.25)	5.59 (5.43)	25.91 (25.85)
7a	$C_9H_6N_4$ (170.2)	134–135 (yellow)	C_2H_5OH (74)	63.52 (63.65)	3.55 (3.61)	32.92 (32.86)
7b	$C_9H_5N_5O_2$ (215.2)	140–141 (yellow)	DMF–H_2O (92)	50.24 (50.32)	2.34 (2.19)	32.55 (32.48)
7c	$C_{10}H_8N_4O$ (200.2)	118–119 (yellow)	C_2H_5OH (72)	59.99 (60.11)	4.03 (3.93)	27.99 (27.81)
8a	$C_{11}H_{11}N_3O_2$ (217.2)	109–110 (yellow)	C_2H_5OH–H_2O (80)	60.82 (60.97)	5.10 (5.05)	19.34 (19.15)
8b	$C_{11}H_{10}N_4O_4$ (262.2)	246–247 (brown)	DMF–H_2O (91)	50.38 (50.56)	3.84 (3.67)	21.37 (21.13)
8c	$C_{12}H_{13}N_3O_3$ (247.3)	114–115 (yellow)	C_2H_5OH–H_2O (76)	58.29 (58.15)	5.30 (5.18)	17.00 (16.89)
9a	$C_{12}H_{14}N_2O_3$ (234.3)	69–70 (yellow)	C_2H_5OH–H_2O (84)	61.53 (61.74)	6.02 (6.09)	11.96 (11.77)
9b	$C_{12}H_{13}N_3O_5$ (279.2)	145–146 (reddish brown)	DMF–H_2O (89)	51.61 (51.48)	4.69 (4.73)	15.05 (14.88)
9c	$C_{13}H_{16}N_2O_4$ (264.3)	120–121 (yellow)	C_2H_5OH–H_2O (77)	59.08 (58.84)	6.10 (6.18)	10.60 (10.47)

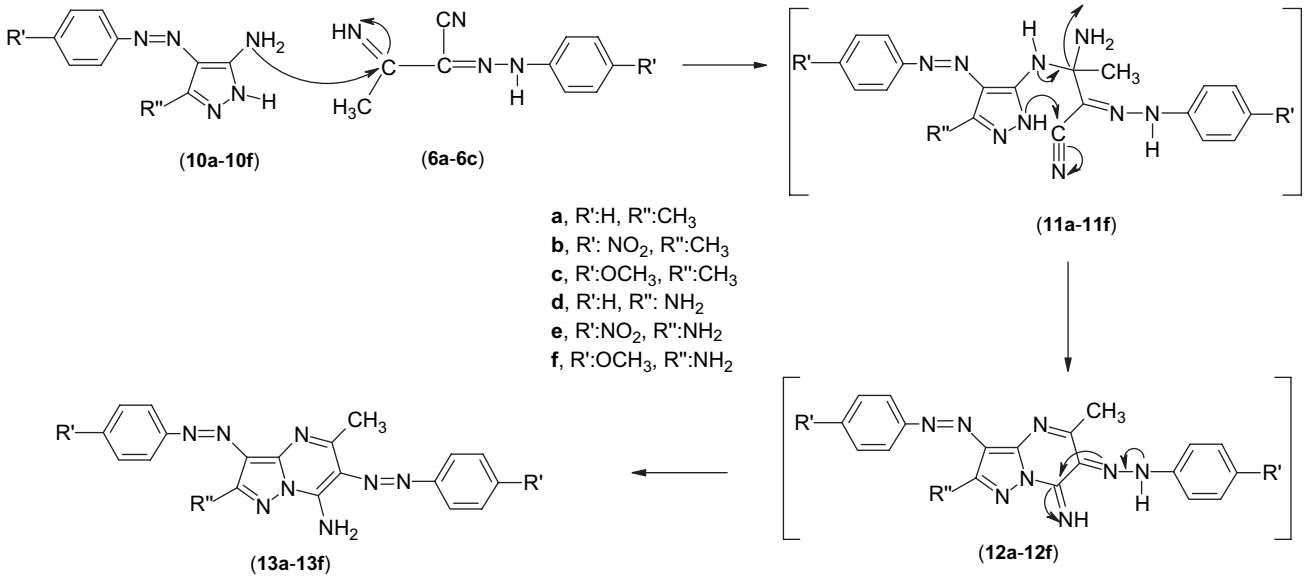
C=O functions, respectively. The ^{1}H NMR spectra of **9a–9c** showed a triplet at δ 1.25–1.30 ppm due to ester group, a singlet at δ 2.26–2.32 ppm for the $COCH_3$ group, a quartet at δ 4.10–4.27 ppm for the ester CH_2 group and a singlet at δ 8.85–9.10 ppm for the NH group.

The reaction of 5-amino-4-arylazo-3-methyl-1H-pyrazoles (**10a–10c**) and 3,5-diamino-4-arylazo-1H-pyrazoles (**10d–10f**) with 2-arylhydrazone-3-ketiminobutyronitriles (**6a–6c**) in refluxing ethanol containing a catalytic amount of pyridine yielded 3,6-diarylazo-7-amino-2,5-dimethylpyrazolo[1,5-*a*] pyrimidines (**13a–13c**) and 3,6-diarylazo-2,7-diamino-5-methylpyrazolo[1,5-*a*]pyrimidines (**13d–13f**), respectively (Scheme 3, Table 6). We suggest a mechanism for formation of **13a–13f** in which the intermediates **11a–11f** are obtained first. The first step of the mechanism involves the condensation of the 5-NH_2 group of the pyrazole ring with imino group of **6a–6c** [19], then an internal nucleophilic attack by 1-NH group of the pyrazole ring on the cyano group takes place and accompanied by deamination to yield the nonisolable **12a–12f**, which tautomerizes to the final isolable **13a–13f** (Scheme 3). The IR spectra of **13a–13f** showed the presence of NH_2 groups 3430–3414 and 3362–3318 cm^{-1} and CH_3 groups stretching at 2982–2946 cm^{-1}. Additionally, their ^{1}H NMR spectra revealed singlets at δ 3.12–3.20 or 5.98–6.50, 12.10–12.86 ppm due to CH_3, 2-NH_2 and 7-NH_2 protons, respectively (Table 5).

Treatment of 5-amino-4-arylazo-3-methyl-1H-pyrazoles (**10a–10c**) with 2-arylhydrazonomalononitriles (**7a–7c**) in

Table 3
Spectral data for dyes **10a–10f**

Dye no.	MS *m/z* (M^+)	FT-IR (cm^{-1}) in KBr							^{1}H NMR (δ, ppm)			
		ν_{NH_2}	ν_{N-H}	$\nu_{C-H\ (arom.)}$	$\nu_{C-H\ (alip.)}$	$\nu_{C=N}$	ν_{NO_2}	ν_{C-O}	Arom.-H	Alip.-H	X–H	Solvent
10a	201.2	3418, 3362	3230	3056	2977	1630	–	–	7.10–7.50 (5H, m, C_6H_5)	3.08 (CH_3, s)	6.60 (5-NH_2, s) 12.10 (1-NH, s)	$CDCl_3$
10b	246.2	3425, 3375	3250	3095	2981	1633	1558, 1327	–	7.70 (2H, d, 3,5-PhH) 7.75 (2H, d, 2,6-PhH)	3.12 (CH_3, s)	7.10 (5-NH_2, s) 12.30 (1-NH, s)	DMSO-d_6
10c	231	3410, 3360	3215	3067	2962	1628	–	1096	6.90–7.50 (4H, m, C_6H_4)	3.00 (CH_3, s) 3.82 (p-OCH_3, s)	6.00 (5-NH_2, s) 11.50 (1-NH, s)	$CDCl_3$
10d	202.2	3430–3420, 3362–3330	3219	3068	–	1618	–	–	7.28–7.76 (5H, m, C_6H_5)	–	5.96 (3-NH_2, s) 6.25 (5-NH_2, s) 10.75 (1-NH, s)	$CDCl_3$
10e	247	3432–3423, 3371–3358	3235	3094	–	1620	1561, 1331	–	7.83 (2H, d, 3,5-PhH) 7.76 (2H, d, 2,6-PhH)	–	6.31 (3-NH_2, s) 6.52 (5-NH_2, s) 10.95 (1-NH, s)	DMSO-d_6
10f	232	3424–3415, 3366–3353	3208	3065	2975	1617	–	1108	6.85–7.30 (4H, m, C_6H_4)	3.72 (p-OCH_3, s)	5.98 (3-NH_2, s) 6.10 (5-NH_2, s) 10.80 (1-NH, s)	$CDCl_3$



Scheme 3.

refluxing ethanol–pyridine solutions yielded 3,6-diarylazo-5,7-diamino-2-methylpyrazolo[1,5-*a*]pyrimidines (**16a–16c**) (Scheme 4, Table 6). Synthesis of 3,6-diarylazo-2,5,7-triaminopyrazolo[1,5-*a*]pyrimidine derivatives has been reported by Tsai and Wang [17]. Tsai and Wang synthesized symmetrical and asymmetrical 3,6-diarylazo-2,5,7-triaminopyrazolo[1,5-*a*]pyrimidines by the cyclization of 4-arylazo-3,5-diaminopyrazoles with different arylhydrazonomalononitriles. The first step of the mechanism involves the condensation of the 5-NH_2 group of the pyrazole ring with cyano group of **7a–7c**, in which the intermediates **14a–14c** are obtained first, then, an internal nucleophilic attack by the 1-NH group of the pyrazole ring on the cyano group takes place and accompanied by a migration of 5-NH proton of the pyrazole ring to the nitrogen atom of the imino group to yield the nonisolable **15a–15c**. The latter can tautomerize, forming the final isolable 3,6-diarylazo-5,7-diamino-2-methylpyrazolo[1,5-*a*]pyrimidines (**16a–16c**) (Scheme 4). The IR spectra of **16a–16c** showed absorption bands at 3436–3418 and 3370–3316 cm^{-1} due to NH_2 functions and 2972–2941 cm^{-1} for the CH_3 group. Moreover, their ^1H NMR spectra revealed singlets at δ 3.00–3.14, 6.64–7.18, 12.14–12.80 ppm for CH_3, 5-NH_2 and 7-NH_2 protons, respectively.

Compounds **10a–10f** reacted with ethyl 2-arylhydrazonocyanoacetates **8a–8c** in refluxing ethanol–pyridine solutions to yield 3,6-diarylazo-7-amino-2-methyl-4H-pyrazolo[1,5-*a*]pyrimidine-5-ones (**19a–19c**) and 3,6-diarylazo-2,7-diamino-4H-pyrazolo[1,5-*a*]pyrimidine-5-ones (**19d–19f**) (Scheme 5, Table 6). The first step of the mechanism involves the condensation of the 5-NH_2 group of the pyrazole ring with ester group of **8a–8c** [19], in which intermediates **17a–17f** are obtained first, then, accompanied by an internal nucleophilic attack by the 1-NH group of the pyrazole ring on the cyano group to yield the nonisolable **18a–18f**. Finally, tautomerization leads to the formation of **19a–19f** (Scheme 5). The IR spectra of **19a–19f** revealed the absence of any CN stretching absorption that might be expected to appear at the range of 2221–2218 cm^{-1}, while they showed the presence of NH_2 group stretching at 3435–3417 cm^{-1} and 3380–3343 cm^{-1}, NH group stretching at 3260–3235 cm^{-1} and C=O group stretching at 1694–1680 cm^{-1}. Moreover, their ^1H NMR spectra showed a singlet at δ 3.02–3.14 ppm for CH_3 protons or δ 5.90–6.65 ppm for 2-NH_2 protons, δ 10.14–10.20 ppm for 4-NH proton and a singlet at δ 11.20–11.92 ppm for NH_2 protons.

The reaction of 5-amino-4-arylazo-3-methyl-1H-pyrazoles (**10a–10c**) and 3,5-diamino-4-arylazo-1H-pyrazoles (**10d–10f**) with ethyl 2-arylhydrazonoacetoacetates **9a–9c** in refluxing ethanol containing a catalytic amount of pyridine yielded 3,6-diarylazo-2,5-dimethylpyrazolo[1,5-*a*]pyrimidine-7-ones (**22a–22c**)

Table 4
Element analysis of dyes **10a–10f**

Dye no.	Molecular formula (m. wt)	m.p. (°C) (color)	Solvent cryst. (yield %)	Elemental analysis: calc. (found)		
				C	H	N
10a	$C_{10}H_{11}N_5$ (201.2)	165–166 (yellow)	C_2H_5OH–H_2O (84)	59.69 (59.78)	5.51 (5.47)	34.80 (34.67)
10b	$C_{10}H_{10}N_6O_2$ (246.2)	226–227 (reddish brown)	DMF–H_2O (91)	48.78 (48.92)	4.09 (4.00)	34.13 (33.96)
10c	$C_{11}H_{13}N_5O$ (231.3)	187–188 (red)	C_2H_5OH–H_2O (72)	57.13 (57.28)	5.67 (5.49)	30.28 (30.13)
10d	$C_9H_{10}N_6$ (202.2)	261–262 (pale yellow)	C_2H_5OH–H_2O (54)	53.46 (53.64)	4.98 (4.83)	41.56 (41.45)
10e	$C_9H_9N_7O_2$ (247.2)	255–256 (reddish brown)	DMF–H_2O (60)	43.73 (43.68)	3.67 (3.61)	39.66 (39.47)
10f	$C_{10}H_{12}N_6O$ (232.2)	228–229 (yellow)	C_2H_5OH–H_2O (57)	51.72 (51.65)	5.21 (5.11)	36.19 (35.96)

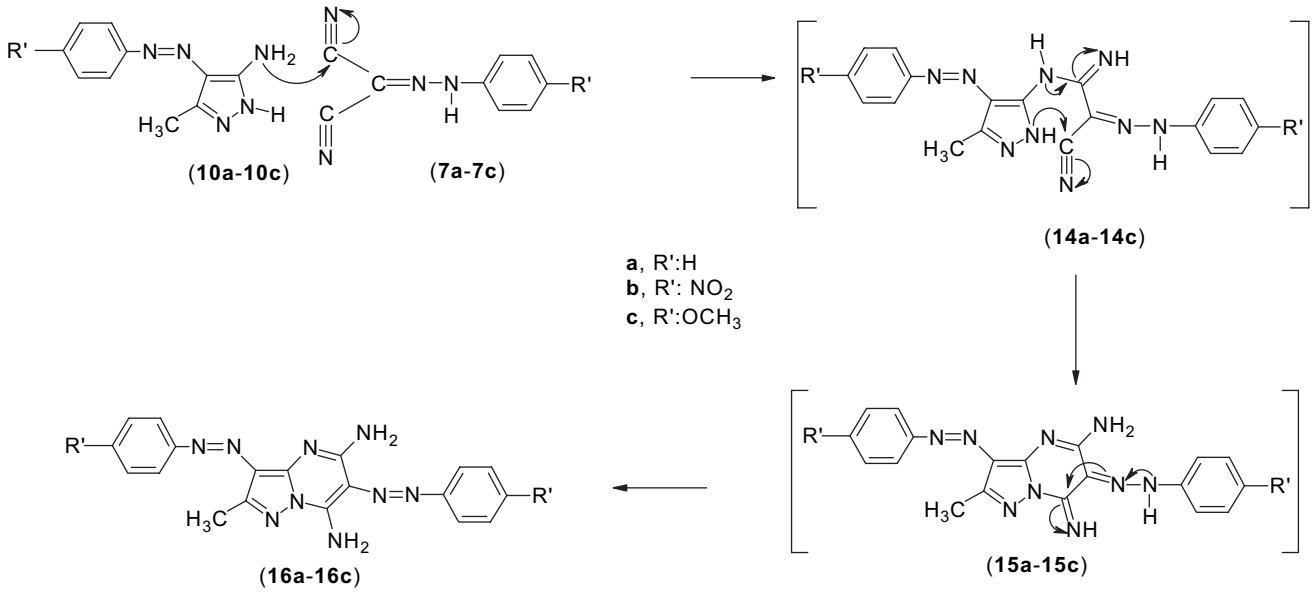
Table 5
Spectral data for dyes **13a–13f**, **16a–16c**, **19a–19f** and **22a–22f**

Dye no.	MS m/z (M^+)	FT-IR (cm^{-1}) in KBr								^{1}H NMR (δ, ppm)			
		ν_{NH_2}	ν_{N-H}	$\nu_{C-H\ (arom.)}$	$\nu_{C-H\ (alip.)}$	$\nu_{C=O}$	$\nu_{C=N}$	ν_{NO_2}	ν_{C-O}	Arom.-H	Alip.-H	X–H	Solvent
13a	370.4	3428, 3351	–	3087	2971	–	1618	–	–	7.10–7.50 (10H, m, 2 C_6H_5)	3.14 (6H, s, 2 CH_3)	12.20 (7-NH_2, s)	$CDCl_3$
13b	460.4	3430, 3362	–	3098	2988	–	1622	1563, 1333	–	7.70 (2H, d, 3,5-PhH) 8.30 (2H, d, 2,6-PhH)	3.20 (6H, s, 2 CH_3)	12.86 (7-NH_2, s)	DMSO-d_6
13c	430	3414, 3318	–	3076	2975	–	1620	–	1105	6.90–7.73 (8H, m, 2 C_6H_4)	3.12 (6H, s, 2 CH_3) 3.83 (6H, s, 2 p-OCH_3)	12.10 (7-NH_2, s)	$CDCl_3$
13d	371	3427–3412, 3361–3347	–	3083	2966	–	1620	–	–	7.18–7.54 (10H, m, 2 C_6H_5)	3.15 (3H, s, CH_3)	5.98 (2-NH_2, s) 12.35 (7-NH_2, s)	$CDCl_3$
13e	461.4	3429–3415, 3360–3345	–	3098	2972	–	1623	1560, 1327	–	7.60 (2H, d, 3,5-PhH) 8.20 (2H, d, 2,6-PhH)	3.18 (3H, s, CH_3)	6.50 (2-NH_2, s) 12.79 (7-NH_2, s)	DMSO-d_6
13f	431	3426–3414, 3352–3320	–	3077	2954	–	1617	–	1081	6.85–7.62 (8H, m, 2 C_6H_4)	3.14 (3H, s, CH_3) 3.87 (6H, s, 2 p-OCH_3)	6.15 (2-NH_2, s) 12.50 (7-NH_2, s)	$CDCl_3$
16a	371	3432–3420, 3365–3343	–	3086	2968	–	1621	–	–	7.12–7.68 (10H, m, 2 C_6H_5)	3.09 (3H, s, CH_3)	6.82 (5-NH_2, s) 12.62 (7-NH_2, s)	$CDCl_3$
16b	461	3436–3424, 3370–3349	–	3095	2972	–	1628	1563, 1336	–	7.75 (2H, d, 3,5-PhH) 8.25 (2H, d, 2,6-PhH)	3.14 (3H, s, CH_3)	7.18 (5-NH_2, s) 12.80 (7-NH_2, s)	DMSO-d_6
16c	431.5	3425–3418, 3347–3316	–	3065	2941	–	1623	–	1102	7.00–7.57 (8H, m, 2 C_6H_4)	3.00 (3H, s, CH_3) 3.85 (6H, s, 2 p-OCH_3)	6.64 (5-NH_2, s) 12.14 (7-NH_2, s)	$CDCl_3$
19a	372	3428, 3372	3241	3083	2975	1687	1622	–	–	6.95–7.48 (10H, m, 2 C_6H_5)	3.07 (3H, s, CH_3)	10.16 (4-NH, s) 11.45 (7-NH_2, s)	$CDCl_3$
19b	462.3	3432, 3379	3260	3093	2987	1693	1628	1565, 1334	–	7.78 (2H, d, 3,5-PhH) 8.32 (2H, d, 2,6-PhH)	3.10 (3H, s, CH_3)	10.20 (4-NH, s) 11.90 (7-NH_2, s)	DMSO-d_6
19c	432	3425, 3354	3238	3077	2966	1682	1621	–	1074	6.82–7.25 (8H, m, 2 C_6H_4)	3.02 (3H, s, CH_3) 3.82 (6H, s, 2 p-OCH_3)	10.18 (4-NH, s) 11.20 (7-NH_2, s)	$CDCl_3$
19d	373	3430–3422, 3371–3355	3245	3088	–	1690	1624	–	–	7.10–7.55 (10H, m, 2 C_6H_5)	–	6.20 (2-NH_2, s) 10.16 (4-NH, s) 11.40 (7-NH_2, s)	$CDCl_3$

(*continued on next page*)

Table 5 (*continued*)

Dye no.	MS m/z (M^+)	FT-IR (cm^{-1}) in KBr								^{1}H NMR (δ, ppm)			
		ν_{NH_2}	ν_{N-H}	$\nu_{C-H\ (arom.)}$	$\nu_{C-H\ (alip.)}$	$\nu_{C=O}$	$\nu_{C=N}$	ν_{NO_2}	ν_{C-O}	Arom.-H	Alip.-H	X−H	Solvent
19e	463	3435−3424, 3380−3368	3260	3099	–	1694	1630	1561, 1332	–	7.80 (2H, d, 3,5-PhH) 8.45 (2H, d, 2,6-PhH)	–	6.65 (2-NH_2, s) 10.20 (4-NH, s) 11.92 (7-NH_2, s)	DMSO-d_6
19f	433.4	3429−3417, 3356−3343	3235	3061	–	1680	1618	–	1081	6.80−7.27 (8H, m, 2 C_6H_4)	3.80 (6H, s, 2 *p*-OCH_3)	5.90 (2-NH_2, s) 10.14 (4-NH, s) 11.25 (7-NH_2, s)	$CDCl_3$
22a	371.4	–	–	3078	2970	1721	1620	–	–	7.15−7.72 (10H, m, 2 C_6H_5)	3.10 (6H, s, 2 CH_3) 7.42 (1H,s, 6-H)	–	$CDCl_3$
22b	461	–	–	3091	2978	1736	1627	1565, 1329	–	7.76 (2H, d, 3,5-PhH) 8.34 (2H, d, 2,6-PhH)	3.17 (6H, s, 2 CH_3) 7.44 (1H,s, 6-H)	–	DMSO-d_6
22c	431	–	–	3063	2957	1718	1618	–	1092	6.82−7.50 (8H, m, 2 C_6H_4)	3.08 (6H, s, 2 CH_3) 3.87 (6H, s, 2 *p*-OCH_3) 7.40 (1H,s, 6-H)	–	$CDCl_3$
22d	372	3422, 3364	–	3082	2976	1725	1622	–	–	7.14−7.65 (10H, m, 2 C_6H_5)	3.14 (3H, s, CH_3) 7.40 (1H,s, 6-H)	6.35 (2-NH_2, s)	$CDCl_3$
22e	462.3	3428, 3375	–	3097	2981	1740	1625	1565, 1328	–	7.72 (2H, d, 3,5-PhH) 8.30 (2H, d, 2,6-PhH)	3.16 (3H, s, CH_3) 7.44 (1H,s, 6-H)	6.60 (2-NH_2, s)	DMSO-d_6
22f	432.4	3407, 3342	–	3052	2959	1715	1617	–	1105	6.95−7.66 (8H, m, 2 C_6H_4)	3.08 (3H, s, CH_3) 3.90 (6H, s, 2 *p*-OCH_3) 7.35 (1H,s, 6-H)	5.92 (2-NH_2, s)	$CDCl_3$



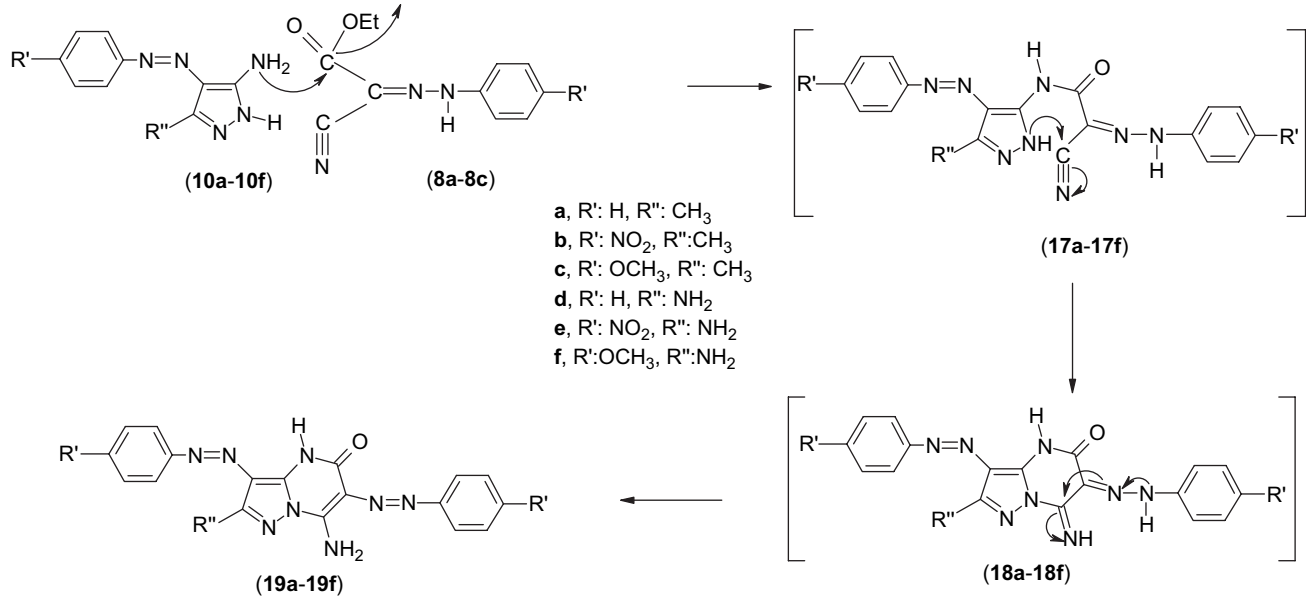
Scheme 4.

and 3,6-diarylazo-2-amino-5-methylpyrazolo[1,5-*a*]pyrimidine-7-ones (**22d–22f**), respectively (Scheme 6, Table 6). The first step of the mechanism involves the condensation of the 5-NH_2 group of pyrazole ring with the carbonyl group adjacent to the methyl group, in which the intermediates **20a–20f** are obtained first, followed by dehydration and cyclization with loss of ethanol [18] to yield nonisolable **21a–21f**. The latter can tautomerize to the final isolable **22a–22f** (Scheme 6). The IR spectra of **22a–22f** revealed absorption bands at 2981–2957 cm^{-1} for CH_3 group and 1740–1715 cm^{-1} for C=O group. Additionally, their ^1H NMR spectra showed singlets at δ 3.08–3.17 and 7.40–7.44 ppm for CH_3, and 6-H of pyrazolo[1,5-*a*]pyrimidine-7-one protons, respectively.

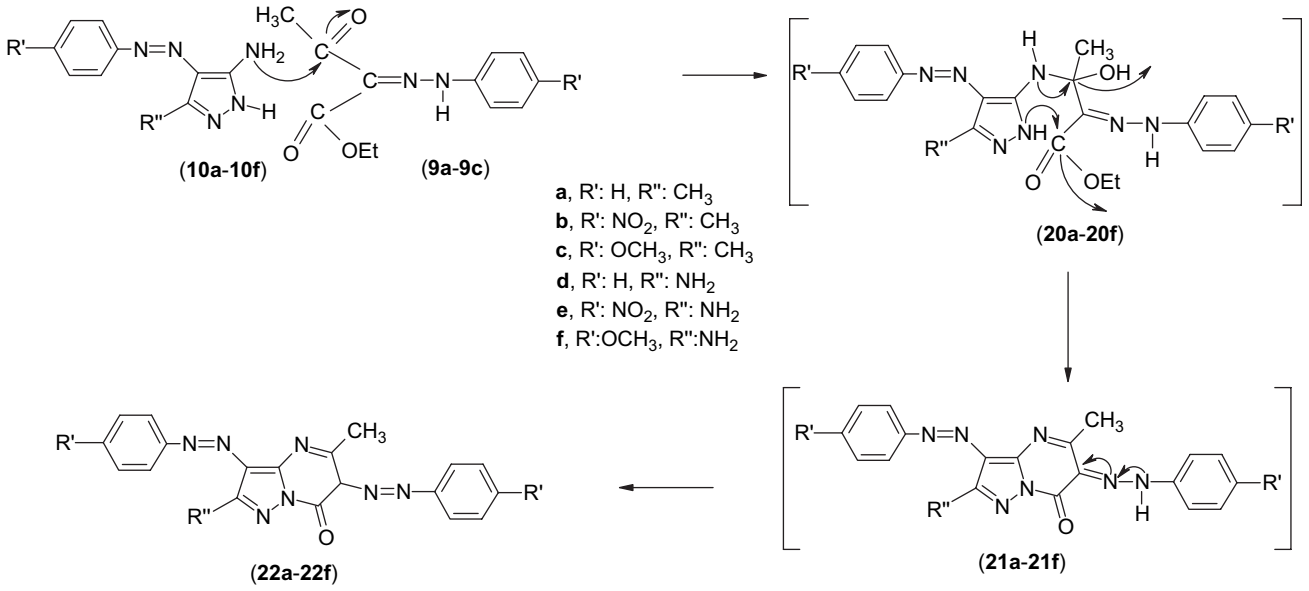
3. Experimental

The chemicals used for the synthesis of the compounds were obtained from Merck Chemical Company or Aldrich Chemical Company and were used without further purification. The solvents were of spectroscopic grade.

Infrared spectra were determined using a Mattson 1000 Fourier Transform-infrared (FT-IR) spectrophotometer on a KBr disc. Nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker-Spectrospin Avance DTX 400 Ultra-Shield in deuterated dimethylsulphoxide (DMSO-d_6) and deuterated chloroform ($CDCl_3$) using trimethylsilane (TMS) as the internal reference; chemical shifts (δ) given in



Scheme 5.



Scheme 6.

ppm. Mass spectra were measured on a GCMS-QP1000EX spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Center of TUBITAK. Melting points were uncorrected. 2-Arylhydrazono-3-ketiminobutyronitriles (**6a–6c**) [18], 2-arylhydrazonomalononitriles (**7a–7c**) [17], ethyl 2-arylhydrazonocyanoacetates (**8a–8c**) [20] and ethyl 2-arylhydrazonoacetoacetates (**9a–9c**) [20] were prepared according to the procedures reported in the literature.

*3.1. Synthesis of 2-arylhydrazone-3-ketiminobutyronitriles (**6a–6c**), 2-arylhydrazono-malononitriles (**7a–7c**), ethyl 2-arylhydrazonocyanoacetates (**8a–8c**) and ethyl 2-arylhydrazonoacetoacetates (**9a–9c**)*

The procedures used for the synthesis of compounds **6a–6c**, **7a–7c**, **8a–8c** and **9a–9c** are represented by the preparation of compound **6a** below.

*3.1.1. 2-Phenylhydrazone-3-ketiminobutyronitrile (**6a**)*

Aniline (0.93 g, 0.01 mole) was dissolved in concentrated hydrochloric acid (10 ml) and the solution was then cooled to 0–5 °C. Sodium nitrite (0.01 mole) in water (3 ml) was then added to this solution dropwise with vigorous stirring, during about 1 h, while cooling at 0–5 °C. The clear diazonium salt solution was then added dropwise to a well-cooled (0–5 °C) and stirred solution of 3-aminocrotononitrile (0.82 g, 0.01 mole) in sodium acetate (2 g, dissolved in 10 ml of 50% aqueous ethanol). The pH of the coupling mixture, in each case, was maintained at 5–6 through the coupling process by adding sodium acetate. Stirring was continued for 4 h at 0–5 °C and the precipitated products separated upon dilution with cold water (50 ml) were filtered off, washed with water several times, dried, and recrystallized from ethanol–H_2O to give 2-phenylhydrazone-3-ketiminobutyronitrile (**6a**).

*3.2. Synthesis of 5-amino-4-arylazo-3-methyl-1 H-pyrazoles (**10a–10c**) and 3,5-diamino-4-arylazo-1 H-pyrazoles (**10d–10f**)*

The synthesis of **10a–10f** was carried out as described below for the synthesis of **10a**.

*3.2.1. 5-Amino-4-phenylazo-3-methyl-1H-pyrazole (**10a**)*

Hydrazine hydrate (0.5 g, 0.01 mole) was added to a solution of **6a** (1.86 g, 0.01 mole) and pyridine 0.5 ml in 30 ml ethanol. The reaction mixture was heated under reflux for 3–4 h, then cooled to room temperature and the precipitated products that separated upon dilution with water were filtered off, washed with water several times, dried and recrystallized from ethanol–H_2O to give 5-amino-4-phenylazo-3-methyl-1H-pyrazole (**10a**).

3.3. Synthesis of disazo pyrazolo[1,5-a]pyrimidines

The procedures used for the synthesis of compounds **13a–13f**, **16a–16c**, **19a–19f** and **22a–22f** are represented by the preparation of compound **13a** below.

*3.3.1. 3,6-Bis-phenylazo-7-amino-2,5-dimethylpyrazolo[1,5-a]pyrimidine (**13a**)*

To solution of **10a** (2.01 g, 0.01 mole) and pyridine 0.5 ml in 30 ml ethanol was added compound **6a** (1.86 g, 0.01 mole). The reaction mixture was heated under reflux for 4 h, then cooled to room temperature and the precipitated products that separated upon dilution with water were filtered off, washed with water several times, dried and recrystallized

Table 6
Element analysis of dyes **13a**-**13f**, **16a**-**16c**, **19a**-**19f** and **22a**-**22f**

Dye no.	Molecular formula (m. wt)	M.p. (°C) (color)	Solvent. cryst.(yield %)	Elemental analysis: calc. (found)		
				C	H	N
13a	$C_{20}H_{18}N_8$ (370.4)	161-162 (brown)	C_2H_5OH-H_2O (62)	64.85 (64.93)	4.90 (4.95)	30.25 (30.08)
13b	$C_{20}H_{16}N_{10}O_4$ (460.4)	253-254 (red)	DMF-H_2O (69)	52.17 (52.29)	3.50 (3.41)	30.42 (30.33)
13c	$C_{22}H_{22}N_8O_2$ (430.5)	126-127 (yellow)	C_2H_5OH-H_2O (58)	61.38 (61.29)	5.15 (5.21)	26.03 (25.91)
13d	$C_{19}H_{17}N_9$ (371.4)	215-216 (brown)	C_2H_5OH-H_2O (65)	61.44 (61.35)	4.61 (4.65)	33.94 (33.72)
13e	$C_{19}H_{15}N_{11}O_4$ (461.4)	249-250 (red)	DMF-H_2O (71)	49.46 (49.32)	3.28 (3.35)	33.39 (33.27)
13f	$C_{21}H_{21}N_9O_2$ (431.5)	201-202 (orange)	C_2H_5OH-H_2O (63)	58.46 (58.33)	4.91 (4.97)	29.22 (29.15)
16a	$C_{19}H_{17}N_9$ (371.4)	192-193 (yellow)	C_2H_5OH-H_2O (68)	61.44 (61.32)	4.61 (4.53)	33.94 (33.77)
16b	$C_{19}H_{15}N_{11}O_4$ (461.4)	253-254 (reddish brown)	DMF-H_2O (74)	49.46 (49.54)	3.28 (3.33)	33.39 (33.20)
16c	$C_{21}H_{21}N_9O_2$ (431.5)	208-209 (orange)	C_2H_5OH-H_2O (61)	58.46 (58.43)	4.91 (4.85)	29.22 (29.20)
19a	$C_{19}H_{16}N_8O$ (372.4)	112-113 (yellow)	C_2H_5OH-H_2O (56)	61.28 (61.37)	4.33 (4.41)	30.09 (29.86)
19b	$C_{19}H_{14}N_{10}O_5$ (462.4)	171-172 (orange)	DMF-H_2O (63)	49.35 (49.23)	3.05 (3.10)	30.29 (30.20)
19c	$C_{21}H_{20}N_8O_3$ (432.4)	143-144 (yellow)	C_2H_5OH-H_2O (50)	58.33 (58.41)	4.66 (4.56)	25.91 (25.83)
19d	$C_{18}H_{15}N_9O$ (373.4)	184-185 (orange)	C_2H_5OH-H_2O (65)	57.90 (57.83)	4.05 (4.13)	33.76 (33.68)
19e	$C_{18}H_{13}N_{11}O_5$ (463.4)	222-223 (reddish brown)	DMF-H_2O (76)	49.66 (49.54)	2.83 (2.87)	33.25 (33.18)
19f	$C_{20}H_{19}N_9O_3$ (433.4)	167-168 (orange)	C_2H_5OH-H_2O (61)	55.42 (55.49)	4.42 (4.36)	29.08 (28.91)
22a	$C_{20}H_{17}N_7O$ (371.4)	172-173 (yellow)	C_2H_5OH-H_2O (70)	64.68 (64.77)	4.61 (4.57)	26.40 (26.33)
22b	$C_{20}H_{15}N_9O_5$ (461.4)	197-198 (red)	DMF-H_2O (76)	52.06 (51.95)	3.28 (3.20)	27.32 (27.23)
22c	$C_{22}H_{21}N_7O_3$ (431.4)	151-152 (yellow)	C_2H_5OH-H_2O (66)	61.24 (61.11)	4.91 (4.84)	22.73 (22.60)

from ethanol–H_2O to give 3,6-bis-phenylazo-7-amino-2,5-dimethylpyrazolo[1,5-*a*]pyrimidine (**13a**).

References

[1] Zeng H, Lin ZP, Sartorelli AC. Biochemical Pharmacology 2004;68:911.
[2] Sharma P, Rane N, Gurram VK. Bioorganic and Medicinal Chemistry Letters 2004;14:4185.
[3] Huang CQ, Wilcoxen KM, Grigoriadis DM, McCarthy JR, Chen C. Bioorganic and Medicinal Chemistry Letters 2004;14:3943.
[4] Dhavale DD, Matin MM, Sharma T, Sabharwal SG. Bioorganic and Medicinal Chemistry 2004;12:4039.
[5] West TP. Microbiological Research 2004;29:159.
[6] Devesa I, Alcaraz MJ, Riguera R, Ferrandiz ML. European Journal of Pharmacology 2004;488:225.
[7] Elnagdi MH, Kandeel EM, Zayed EM, Kandeel ZE. Journal of Heterocyclic Chemistry 1977;14:155.
[8] Elnagdi MH, Fahmy SM, Hafez EAZ, Elmoghayar MRH, Amer SAR. Journal of Heterocyclic Chemistry 1979;16:1109.
[9] Zvilichovsky G, David M. Journal of the Chemical Society of Perkin Transactions I 1983;11.
[10] Kandeel ZE, Abdelrazek FM, Eldin NEMS, Elnagdi MH. Journal of the Chemistry Society of Perkin Transactions I 1985;1499.
[11] Elfahham HA, Elgemeie GEH, Ibraheim YR, Elnagdi MH. Liebigs Annals of Chemistry 1988;819.
[12] Kandeel ZE. Journal of Chemical Research (S) 1995;290.
[13] Masoud MS, Khalil EA, Hindawy AM, Ali AE, Mohamed EF. Spectrochimica Acta. Part A: Molecular and Biomolecular Spectroscopy 2004;60:2807.
[14] Nasr MR. Spectrochimica Acta. Part A: Molecular and Biomolecular Spectroscopy 2004;60:1917.
[15] Nag JK, Santra PK, Sinha C, Liao FL, Lu TH. Polyhedron 2001;20:2253.
[16] Santra PK, Ray U, Pal S, Sinha C. Inorganic Chemistry Communications 2001;4:269.
[17] Tsai PC, Wang IJ. Dyes and Pigments 2005;64:259.
[18] Ho YW. Dyes and Pigments 2005;64:223.
[19] Ho YW, Yao CT. Journal of Chinese Chemical Society 2003;50:283.
[20] Mohareb RM, Sherif SM, Gaber HM, Ghabrial SS, Aziz SI. Heteroatom Chemistry 2004;15:15.