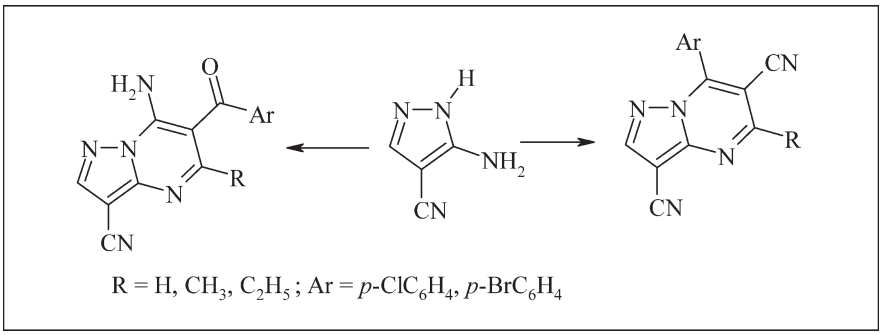
New One-Step Synthesis of Pyrazolo[1,5-*a*]pyrimidine and Pyrazolo[1,5-*a*]quinazoline Derivatives via Multicomponent Reactions

Bhausaheb K. Ghotekar, Madhukar N. Jachak, and Raghunath B. Toche*

Organic Chemistry Research Center, Department of Chemistry, K.R.T. Arts, B.H. Commerce and A.M. Science College, Gangapur Road, Nashik 422002, Maharashtra, India
*E-mail: bhausaheb.ghotekar@rediffmail.com

Received March 10, 2009
DOI 10.1002/jhet.128
Published online 13 July 2009 in Wiley InterScience (www.interscience.wiley.com).



A series of pyrazolopyrimidine and pyrazoloquinozoline derivatives has been synthesized in one step by multicomponent reactions using, 5-aminopyrazole, *p*-substitutedbenzoylacetonitrile/dimedone and triethylorthoesters. pyrazolopyrimidine derivatives were also studied for their absorption and fluorescence maxima.

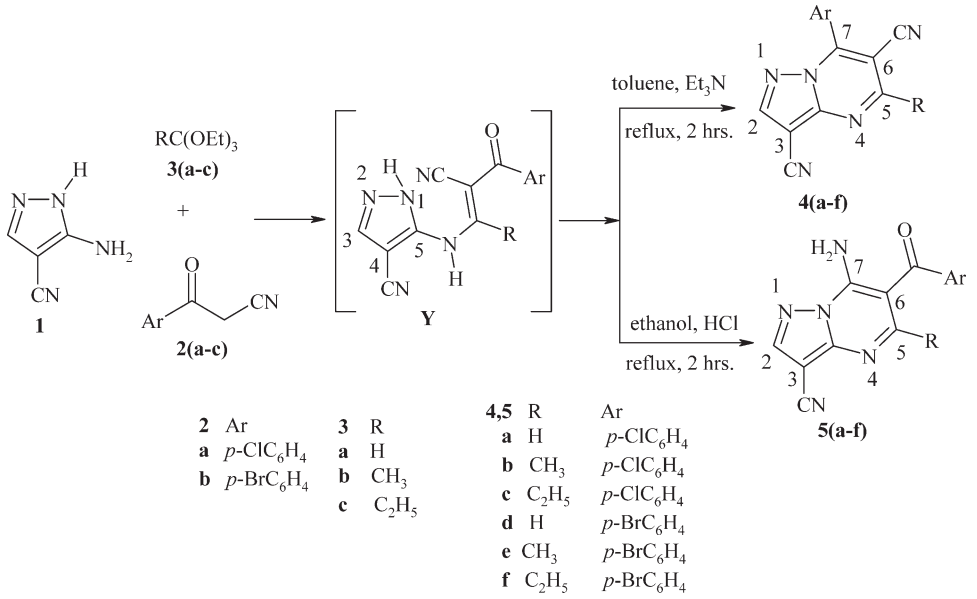
J. Heterocyclic Chem., **46**, 708 (2009).

INTRODUCTION

Heterocyclic ring systems that containing the pyrazole ring fused to pyrimidine or quinazoline rings are interesting classes of compounds both chemically and biologically. For example, pyrazolopyrimidines display significant chemical properties [1–7]. In particular, pyrazolo[1,5-*a*]pyrimidines structural motif may be found in a large number of pharmaceutical agents with a diverse range of physiological activities, such as, antiepileptic agents [8], anxiolytics [9], antidepressants [10], agents for treatment of sleep disorders [11], and oncolytics [12,13]. Whereas, several naturally occurring and synthetic compounds containing the quinazoline derivatives exhibit a wide range of biological properties [14,15]. In recent years an increasing interest has been focused on synthesis of fluorescent compounds owing to their significant biological applications in the medicinal chemistry [16,17]. In particular, these compounds have important applications in the field of dyes [18] and are used in the security papers [19]. In literature the synthesis of pyrazolo[1,5-*a*]pyrimidines has been reported [20,21] by using Michael addition reaction of 5-aminopyrazoles with enol ether of reactive methylene compounds and triethylorthoesters. The title compounds could be synthesized in one pot in which the synthesis of enol ether is not required.

On the other hand, multicomponent reactions (MCRs) are of increasing importance in organic and medicinal chemistry. MCR strategies offer significant advantages over conventional linear type synthesis [22–24]. As a part of our continued interest [25–27] in the synthesis of novel heterocyclic compounds, we have reported the synthesis of pyrazolo[3,4-*b*]pyridines, pyrazolo[3,4-*b*]quinolines, pyrazolonaphthyridines and pyrazolopyridopyrimidines by Friedlander condensation of 5-aminopyrazole-4-carbaldehyde with various reactive methylene compounds and the synthesis of fused pyrimidines [28] by using 2-aminoheterocycles and cyclic β-formylesters in ammonium acetate at 120°C. We have also reported the study of fluorescence properties of benzo[*h*]quinolines and dipyrazolopyridines [29,30]. In our recent communications [31,32], we have reported the synthesis of chromenes, quinolines, and pyrazolo[3,4-*b*]pyridines by multicomponent reaction strategy. These literature reports and increasing importance of multicomponent reactions in organic chemistry encourage us to synthesize, pyrazolo[1,5-*a*]pyrimidine and pyrazolo[1,5-*a*] quinazoline derivatives using multicomponent reactions and study the photophysical properties of pyrazolopyrimidine derivatives.

Scheme 1



RESULTS AND DISCUSSION

The cyclocondensation of 5-amino-1*H*-pyrazole-4-carbonitrile **1**, *p*-substituted benzoylacetonitriles **2** and triethylorthoesters **3** by refluxing in toluene containing catalytic amount of triethylamine for 2 h, afforded compounds **4** in good yield. The structure of **4a** was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectroscopy and elemental analysis for example the IR spectrum of **4a** showed bands at 2237 cm^{-1} for CN stretching. The ^{1}H-NMR of compound **4a** showed a multiplets at δ 7.85–7.89 for four aromatic protons and the two singlets at δ 8.87 and δ 9.16 corresponding to C_2H and C_5H aromatic protons. The ^{13}C-NMR spectrum of this compound exhibits a peaks of tertiary carbons at δ 128, 129, 138, 161 and of quaternary carbons at δ 66, 106, 117, 167, 131, 133, 134. Mass Spectrum of **4a** showed characteristic peaks for M^+ and M+2 at 279 and 281 *m*/*z*, due to presence of chlorine. The elemental analysis obtained is in agreement with molecular formula. Analogously, the cyclocondensation of 5-amino-1*H*-pyrazole-4-carbonitrile **1**, *p*-substituted benzoylacetonitriles **2** and triethylorthoesters **3** by refluxing in ethanol in the presence of catalytic amount of hydrochloric acid for 2 h, afforded compounds **5** in good yield. The structure of **5a** was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectroscopy and elemental analysis for example the IR spectrum of **5a** showed the bands at 1621 and 2231 cm^{-1} for C=O and CN stretching respectively and two bands for NH_2 groups were appears at 3328–3425 cm^{-1}. The 1H-NMR of compound **5a** showed a multiplet

Scheme 2

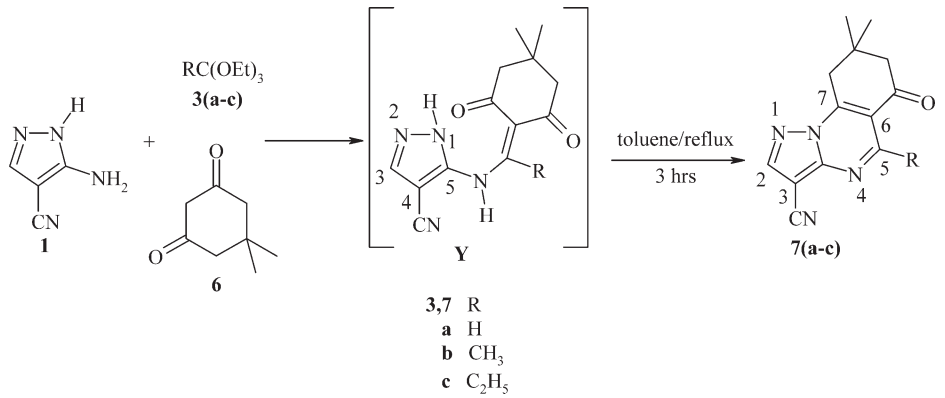


Table 1

The absorbance, emission λ_{max}, and quantum yield of pyrazolopyrimidines (**4a-f** and **5a-f**).

Compd.	Absorbance λ_{max} (nm)	Emission λ_{max} (nm)	Quantum yield (Φ_F)
(**4a**)	293	322	0.110
(**4b**)	280	316	0.109
(**4c**)	296	332	0.111
(**4d**)	279	306	0.108
(**4e**)	267	304	0.107
(**4f**)	284	312	0.112
(5a)	336	393	0.113
(5b)	342	398	0.114
(5c)	345	400	0.116
(5d)	360	414	0.117
(5e)	338	402	0.103
(5f)	350	407	0.104

between δ 7.71 and 7.97 for four aromatic protons and the two singlets at δ 6.84 and δ 8.63 for C2H and C5H aromatic protons. The two broad singlets appeared at δ 7.01 and δ 8.48 corresponding to NH_2 protons. The NH_2 protons are splits in to two broad singlets due to formation of hydrogen bonding between hydrogen atom of NH_2 group and oxygen atom of C=O group. The 13C-NMR spectrum of this compound exhibits a peaks of tertiary carbons at δ 129, 131, 138, 160, and of quaternary carbons at δ 68, 115, 133, 138, 168. The cyanide and carbonyl carbon appears at δ 126 and 196. The mass spectrum of a showed M+ and M+2 at 297 and 299 *m*/*z*. The elemental analysis obtained is in agreement with the molecular formula. Similarly, the structures of bromo-derivatives 4d and 5d were confirmed. It was observed that, the cyclocondensation of intermediate Y with —$COCH_2$— fragment of substrate 2 should give product 4 but cyclocondensation of Y with —CH_2CN— fragment of substrate 2 should give product 5 [21,33].

It was interesting to note that the cyclocondensaton reaction in presence of basic medium at pH 9–10 led 7-(4-aryl)pyrazolo[1,5-*a*] pyrimidine-3,6-dicarbonitriles **4**, where the cyclization on carbonyl carbon takes place, whereas the similar cyclocondensation reaction when carried out in presence of acidic medium at pH 3-4 gave 7-amino-6-(4-aroyl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitriles **5** in which the cyclization on nitrile carbon takes place [21,33]. The synthesis of pyrazolo[1,5-*a*]quinazolines **7** were also achieved in one step, by the cyclocondensation of 5-aminopyrazole **1**, dimedone **6** and triethyorthoesters **3** by refluxing in toluene for 3 h furnished the compound **7** in 75–80% yield. The structure of **7a** was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis for example the IR spectrum of **7a** showed bands at 2215, 1687 cm^{-1} for CN and carbonyl groups. The ^{1}H-NMR of compound **7a** showed a singlet at δ 1.25 for six methyl protons, singlet at δ 2.65 and δ 3.40 for four methylene protons, a singlet at 8.49 and 9.18 corresponding to C_2H and C_5H protons respectively. Further this structure was confirmed by ^{13}C-NMR which is in agreement with the structure proposed. Similarly, the structures of compound **7b** and **7c** were confirmed.

After synthesis of all these compounds, it was noted that the pyrazolo[1,5-*a*]pyrimidine derivatives showed good fluorescence properties. So, we further studied the photophysical properties of pyrazolopyrimidine derivatives **4** and **5**. It was observed that compounds **4** showed UV absorption in the range 267–296 nm and fluorescence maxima in the range of 304–332 nm. While the compounds **5** showed slightly better absorption and emission values. From Table 1. It is evident that the incorporation of amino group at C_7 position in compounds **5** markedly increases the absorption and emission properties compared with aryl group at C_7 position in compounds **4**. The compound **5d** showed good absorption and emission spectra as shown in Figure 1.

The reactions reported here represent new synthetic methods toward synthesis of novel pyrazolopyrimidine and pyrazoloquinozoline derivatives with simple workup and clean products in single step.

EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 in open capillary tubes and are uncorrected. The ^{1}H and ^{13}C-NMR spectra were recorded on a Varian XL-300 spectrometer (300 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given δ-units. The solvents for NMR spectra was duteriochloroform unless otherwise stated. Infrared spectra were taken on Shimadzu IR-408, a Shimadzu FTIR instrument in potassium bromide pellets unless otherwise stated. UV Spectra were recorded on a Shimadzu UV-1601 UV–visible

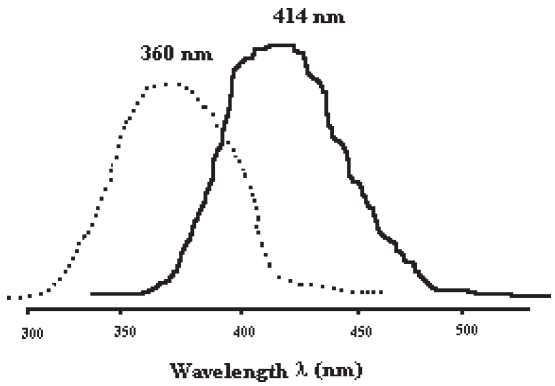


Figure 1. The absorption (dotted line) and emission spectra of compound **5d**.

Spectrophotometer. High-resolution mass spectra were obtained with a Mat 112 Varian Mat Bremen (70 eV) mass spectrometer. Compounds for UV scan were dissolved in methanol. Fluorescence spectra were recorded using RF-5301 PC Spectrofluorophotometer. Compounds for fluorescence measurements were dissolved in methanol. UV and fluorescence scans were recorded from 200 to 500 nm. Elemental analyses were performed on a Hosli CH-Analyzer and are within ±0.3 of the theoretical percentage. Solutions were concentrated in a rotary evaporator under reduced pressure. All reactions were monitored by thin layer chromatography, carried out on 0.2-mm silica gel 60 F_{254} (Merk) plates using UV light (254 and 366 nm) for detection. Common reagents-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

General procedure for the synthesis of 7-(4-aryl) pyrazolo[1,5-*a*]pyrimidine-3,6-dicarbonitrile (4). A mixture of 5-aminopyrazole **1** (1.08 g, 10 mmole), aroylacetonitriles **2** (10 mmole), and triethylorthoesters **3** (10 mmole) in toluene (20 mL) containing catalytic amount of triethylamine (0.5 mL) was refluxed for 2–3 h. The completion of reaction was monitored by thin layer chromatography (TLC). Then the excess of solvent was removed under reduced pressure. The solid obtained was stirred in ethanol (10 mL), filtered, washed with ethanol, dried and recrystallized from suitable solvent furnished compounds **4** in good yield.

7-(4-Chlorophenyl)pyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4a). This compound was obtained as colorless prism (ethanol), 2.15 g (77%), mp 223–224°C; IR: (Potassium bromide): 2237, 1654, 1606, 1590, 1525, 1486, 1264, 1065, 1012, 827, 637 cm^{-1}; 1H-NMR: (CDCl3) δ 7.85–7.89 (m, 4H, Ar—H), 8.87 (s, 1H, Ar—H), 9.16 (s, 1H, Ar—H); 13C-NMR: (CDCl3) δ 66, 106, 117, 119, 128, 129, 131, 133, 134, 138, 161, 167. MS: (70 eV) *m*/*z* (%) 281 (90) (M+2), 279 (100) (M+), 271 (80), 258 (65), 244 (70), 233 (80), 207 (10), 181 (20), 153 (40), 122 (30), 93 (50), 78 (70), 63 (80), 44 (40). *Anal*. Calcd for $C_{14}H_6ClN_5$: C, 60.12; H, 2.16; N, 25.04. Found: C, 60.29; H, 2.45; N, 25.33.

7-(4-Chlorophenyl)-5-methylpyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4b). This compound was obtained as yellow prism (ethanol/DMF), 2.58 g (88 %), mp 228–230°C; IR: (Potassium bromide): 2246, 1615, 1596, 1489, 1464, 1381, 1098, 1018, 832, 643 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 2.81 (s, 3H, CH_3), 7.74 (d, 2H, J = 8.7 Hz, Ar—H), 7.84 (d, 2H, J = 8.7 Hz, Ar—H), 8.89 (s, 1H, Ar—H). *Anal*. Calcd for $C_{15}H_8ClN_5$: C, 61.34; H, 2.75; N, 23.84. Found: C, 61.13; H, 2.45; N, 23.61.

7-(4-Chlorophenyl)-5-ethylpyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4c). This compound was obtained as colorless prism (ethanol/DMF), 2.43 g (79%), mp 174–175°C; IR: (Potassium bromide): 2233, 1622, 1587, 1492, 1463, 1385, 1094, 1021, 838, 642 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.41 (t, 3H, J = 7.2 Hz, CH_3), 3.19 (q, 2H, J = 7.2 Hz, CH_2), 7.83 (d, 2H, J = 8.7 Hz, Ar—H), 7.95 (d, 2H, J = 8.4 Hz, Ar—H), 8.91 (s, 1H, Ar—H); MS: (70 eV) *m*/*z* (%) 309 (40) (M+2), 307 (100) (M+), 280 (40), 272 (80), 252 (20), 245 (30), 229 (10), 218 (10), 187 (30), 179 (20), 161 (50), 152 (30), 126 (30), 113 (10), 111 (40), 88 (10), 75 (60), 63 (50), 51 (55), 40 (40). *Anal*. Calcd for $C_{16}H_{10}ClN_5$: C, 62.45; H, 3.28; N, 22.76. Found: C, 62.67; H, 3.53; N, 22.55.

7-(4-Bromophenyl)pyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4d). This compound was obtained as colorless prism (ethanol), 2.78 g (86%), mp 246–248°C; IR: (Potassium bromide): 2239, 1656, 1610, 1587, 1521, 1482, 1262, 1068, 1018, 828, 639 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 7.85 (d, 2H, J = 8.5 Hz, Ar—H), 7.89 (d, 2H, J = 8.4 Hz, Ar—H), 8.85 (s, 1H, Ar—H), 9.12 (s, 1H, Ar—H); ^{13}C-NMR: ($CDCl_3$) δ 67, 108, 118, 121, 125, 127, 131, 134, 136, 140, 163, 168. MS: (70 eV) *m*/*z* (%) 326 (90) (M+2), 324 (100) (M+), 323 (80), 322 (60), 298 (10), 271 (10), 258 (10), 244 (20), 233 (10), 207 (10), 183 (20), 181 (10), 153 (40), 122 (60), 102 (70), 91 (60), 75 (80), 63 (70), 44 (60). *Anal*. Calcd for $C_{14}H_6BrN_5$: C, 51.88; H, 1.87; N, 21.61. Found: C, 51.54; H, 1.62; N, 21.41.

7-(4-Bromorophenyl)-5-methylpyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4e). This compound was obtained as yellow prism (ethanol/DMF), 2.77 g (82%), mp 142–143°C; IR: (Potassium bromide): 2243, 1611, 1592, 1485, 1460, 1383, 1097, 1016, 830, 641 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 2.83 (s, 3H, CH_3), 7.76 (d, 2H, J = 8.7 Hz, Ar—H), 7.86 (d, 2H, J = 8.7 Hz, Ar—H), 8.85 (s, 1H, Ar—H). *Anal*. Calcd for $C_{15}H_8BrN_5$: C, 53.28; H, 2.38; N, 20.71. Found: C, 53.51; H, 2.49; N, 20.39.

7-(4-Bromophenyl)-5-ethylpyrazolo[1,5-a]pyrimidine-3,6-dicarbonitrile (4f). This compound was obtained as yellow prism (ethanol/DMF), 2.67 g (76%), mp 194–196°C; IR: (Potassium bromide): 2234, 1622, 1587, 1491, 1461, 1382, 1093, 1016, 836, 646 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.40 (t, 3H, J = 7.2 Hz, CH_3), 3.18 (q, 2H, J = 7.2 Hz, CH_2), 7.83 (d, 2H, J = 8.7 Hz, Ar—H), 7.94 (d, 2H, J = 8.4 Hz, Ar—H), 8.91 (s, 1H, Ar—H). *Anal*. Calcd for $C_{16}H_{10}BrN_5$: C, 54.56; H, 2.86; N, 19.89. Found: C, 54.29; H, 2.66; N, 19.65.

General procedure for the synthesis of 7-Amino-6-(4-aroyl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (5). A mixture of 5-aminopyrazole **1** (1.08 g, 10 mmole), aroylacetonitriles **2** (10 mmole) and triethylorthoesters **3** (10 mmole) in absolute ethanol (20 mL) containing catalytic amount of hydrochloric acid (0.1*N*, 0.5 mL) was refluxed for 2–3 h. The completion of reaction was monitored by thin layer chromatography (TLC). The solid obtained on cooling was filtered, washed with ethanol, dried, and recrystallized from suitable solvent furnished compounds **5** in good yield.

7-Amino-6-(4-chlorobenzoyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (5a). This compound was obtained as colorless prism (DMF), 2.64 g (89%), mp 273–274°C; IR: (Potassium bromide): 3425, 3328, 2887, 2874, 2554, 2231, 1660, 1621, 1499, 1368, 1313, 1200, 1076, 1011, 899, 821, 726, 627. cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 6.84 (s, 1H, Ar—H), 7.01 (bs, 1H, NH), 7.71 (d, 2H, J = 8.4 Hz, Ar—H), 7.97 (d, 2H, J = 8.4 Hz, Ar—H), 8.48 (bs, 1H, NH), 8.63 (s, 1H, Ar—H); ^{13}C-NMR: ($CDCl_3$) δ 68, 115, 126, 129, 131, 133, 138, 160, 164, 168, 169, 196. MS: (70 eV) *m*/*z* (%) 299 (70) (M+2), 297 (90) (M+), 275 (80), 243 (65), 236 (70), 233 (80), 205 (10), 173 (100), 151 (40), 119 (30), 91 (50), 74 (70), 61 (80), 42 (40). *Anal*. Calcd for $C_{14}H_8ClN_5O$: C, 56.48; H, 2.71; N, 23.52. Found: C, 56.29; H, 2.45; N, 23.33.

7-Amino-6-(4-chlorobenzoyl)-5-methylpyrazolo[1,5-a] pyrimidine-3-carbonitrile (5b). This compound was obtained as colorless prism (DMF), 2.43 g (78%), mp 275–277°C; IR: (Potassium bromide): 3427, 3330, 3086, 2888, 2524, 2235, 1660, 1623, 1400, 1367, 1310, 1200, 1069, 1011, 890, 820, 726, 626. cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 2.35 (s, 3H, CH_3), 5.29 (bs, 2H, NH_2), 7.60 (s 1H, Ar—H), 7.62 (d, 2H, J = 8.7 Hz, Ar—H), 7.70 (d, 2H, J = 8.7 Hz, Ar—H). *Anal*. Calcd for

$C_{15}H_{10}Cl\ N_5O$: C, 57.79; H, 3.23; N, 22.47. Found: C, 57.63; H, 3.41; N, 22.61.

7-Amino-6-(4-chlorobenzoyl)-5-ethylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (5c). This compound was obtained as colorless prism (DMF), 2.47 g (76%), mp 271–272°C; IR: (Potassium bromide): 3430, 3320, 3086, 2920, 2877, 2530, 2231, 1620, 1622, 1401, 1369, 1310, 1200, 1069, 1011, 890, 830, 710, 636. cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.24 (t, 3H, J = 7.2 Hz, CH_3), 2.55 (q, 2H, J = 7.2 Hz, CH_2), 5.62 (bs, 2H, NH_2), 7.89 (d, 2H, J = 8.7 Hz, Ar—H), 7.98 (d, 2H, J = 8.4 Hz, Ar—H), 8.96 (s, 1H, Ar—H). *Anal*. Calcd for $C_{16}H_{12}ClN_5O$: C, 58.99; H, 3.71; N, 21.50. Found: C, 58.76; H, 3.53; N, 21.69.

7-Amino-6-(4-bromobenzoyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (5d). This compound was obtained as colorless prism (DMF), 2.87 g (84%), mp 289–290°C; IR: (Potassium bromide): 3426, 3329, 2889, 2877, 2559, 2232, 1661, 1623, 1496, 1363, 1310, 1201, 1077, 1012, 890, 823, 722, 628. cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 6.86 (s, 1H, Ar—H), 7.12 (bs, 1H, NH), 7.77 (d, 2H, J = 8.2 Hz, Ar—H), 7.95 (d, 2H, J = 8.2 Hz, Ar—H), 8.52 (bs, 1H, NH), 8.65 (s, 1H, Ar—H); ^{13}C-NMR: ($CDCl_3$) δ 65, 120, 122, 123, 124, 128, 130, 133, 134, 165, 166, 192. MS: (70 eV) *m/z* (%) 344 (20) (M+2), 342 (90) (M+), 339 (30), 326 (10), 315 (60), 307 (10), 288 (10), 275 (10), 145 (25), 235 (20), 218 (60), 196 (65), 182 (45), 157 (10), 151 (05), 127 (20), 116 (15), 109 (100), 97 (60), 63 (40). *Anal*. Calcd for $C_{14}H_8BrN_5O$: C, 49.14; H, 2.36; N, 20.47. Found: C, 49.29; H, 2.48; N, 20.28.

7-Amino-6-(4-bromobenzoyl)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (5e). This compound was obtained as colorless prism (DMF), 2.77 g (78%), mp 292–293°C; IR: (Potassium bromide): 3429, 3331, 3089, 2890, 2221, 1660, 1619, 1400, 1369, 1315, 1200, 1069, 1013, 892, 823, 729, 628. cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 2.37 (s, 3H, CH_3), 5.21 (bs, 2H, NH_2), 7.63 (s 1H, Ar—H), 7.65 (d, 2H, J = 8.7 Hz, Ar—H), 7.73 (d, 2H, J = 8.7 Hz, Ar—H). *Anal*. Calcd for $C_{15}H_{10}BrN_5O$: C, 50.58; H, 2.83; N, 19.66. Found: C, 50.73; H, 2.68; N, 19.53.

7-Amino-(4-bromobenzoyl)-5-ethylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (5f). This compound was obtained as colorless prism (DMF), 2.73 g (74%), mp 277–278°C; IR: (Potassium bromide): 3433, 3316, 3086, 2921, 2879, 2530, 2233, 1620, 1623, 1401, 1363, 1319, 1200, 1069, 1011, 895, 830, 712, 630 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.21 (t, 3H, J = 7.2 Hz, CH_3), 2.59 (q, 2H, J = 7.2 Hz, CH_2), 5.62 (bs, 2H, NH_2), 7.85 (d, 2H, J = 8.7 Hz, Ar—H), 7.93 (d, 2H, J = 8.4 Hz, Ar—H), 8.91 (s, 1H, Ar—H). *Anal*. Calcd for $C_{16}H_{12}BrN_5O$: C, 51.91; H, 3.27; N, 18.92. Found: C, 51.77; H, 3.41; N, 18.73.

General procedure for the synthesis of 8,8-Dimethyl-6-oxo-6,7,8,9-tetrhydropyrazolo[1,5-*a*]quinazoline-3-carbo-nitrile (7). A mixture of 5-aminopyrazole **1** (1.08 g, 10 mmole), dimedone **2** (10 mmole) and triethylorthoesters **3** (10 mmole) was refluxed in toluene for about 3 h. Completion of reaction was monitored by thin layer chromatography (TLC). The excess of solvent was removed under reduced pressure. The solid obtained was stirred in ethanol (20 mL), filtered, washed with ethanol, dried, and recrystallized from suitable solvent furnished compounds **7** in good yield.

8,8-Dimethyl-6-oxo-6,7,8,9-tetrhydropyrazolo[1,5-a]quinazoline-3-carbonitrile (7a). This compound was obtained as colorless prism (ethanol), 1.96 g (82%), mp 162–163°C; IR: (Potassium bromide): 2215, 1687, 1609, 1537, 1367, 1310, 1261, 1175, 1096, 801, 683 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.25 (s, 6H, $2CH_3$), 2.65 (s, 2H, CH_2), 3.40 (s, 2H, CH_2), 8.49 (s, 1H, Ar—H), 9.18 (s, 1H, Ar—H); ^{13}C-NMR: 28, 32, 37, 50, 85, 111, 115, 149, 150, 151, 153, 193. *Anal*. Calcd for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.03; N, 23.32. Found: C, 65.29; H, 5.16; N, 23.56.

5,8,8-Trimethyl-6-oxo-6,7,8,9-tetrhydropyrazolo[1,5-a] quinazoline-3-carbonitrile (7b). This compound was obtained as colorless prism (ethanol), 2.13 g (84%), mp 186–187°C; IR: (Potassium bromide): 2217, 1689, 1610, 1539, 1369, 1312, 1264, 1177, 1098, 802, 684 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.23 (s, 6H, $2CH_3$), 2.63 (s, 2H, CH_2), 2.79 (s, 3H, CH_3), 3.38 (s, 2H, CH_2), 8.47 (s, 1H, Ar—H), 9.17 (s, 1H, Ar—H). *Anal*. Calcd for $C_{14}H_{14}N_4O$: C, 66.13; H, 5.55; N, 22.03. Found: C, 65.97; H, 5.31; N, 22.41.

5-Ethyl-8,8-dimethyl-6-oxo-6,7,8,9-tetrhydropyrazolo[1,5-a] quinazoline-3-carbonitrile (7c). This compound was obtained as colorless prism (ethanol), 2.38 g (89%), mp 205–206°C; IR: (Potassium bromide): 2216, 1688, 1610, 1538, 1366, 131 0, 1266, 1176, 1098, 801, 685 cm^{-1}; ^{1}H-NMR: ($CDCl_3$) δ 1.27 (s, 6H, $2CH_3$), 1.43 (t, 3H, J = 7.2 Hz, CH_3), 2.66 (s, 2H, CH_2), 3.19 (q, 2H, J = 7.1 Hz, CH_2), 3.41 (s, 2H, CH_2), 8.50 (s, 1H, Ar—H). *Anal*. Calcd for $C_{15}H_{16}N_4O$: C, 67.15; H, 6.01; N, 20.88. Found: C, 67.29; H, 6.16; N, 20.56.

Acknowledgment. The authors thank University Grant Commission (UGC), New Delhi, India for financial support and Prof. D. D. Dhavale, Department of Chemistry, University of Pune, Pune, India for his valuable cooperation for the measurement of fluorescence spectra and useful discussion.

REFERENCES AND NOTES

[1] Taylor, E.; Mc Killop, A. The Chemistry of Cyclic Enaminonitriles and *o*-Aminonitriles in Advanced Organic Chemistry; Wiley: New York, 1970; p 415.

[2] Taylor, E.; Loeffler, R. J Am Chem Soc 1960, 82, 3147.

[3] Baraldi, P.; Cacciari, B.; Romagnoli, R.; Spalluto, G.; Klotz, K.; Leung, E.; Varani, K.; Gessi, S.; Merighi S.; Borea, P. J Med Chem 1999, 42, 4473.

[4] Robins, R. J Am Chem Soc 1956, 78, 784.

[5] Cheng C.; Robins, R. J Org Chem 1956, 21, 1240.

[6] Cheng C.; Robins, R. J Org Chem 1958, 23, 191.

[7] Cheng C.; Robins, R. J Org Chem 1958, 23, 852.

[8] (a) Tomeufcik, A.; Albright, J.; Dusza, J. US Pat. 4,654,347, 1987; (b) Tomeufcik, A.; Albright, J.; Dusza, J. Chem Abstr 1985, 25, 220889m.

[9] (a) Chen, Y. Jpn. Pat. 2,000,502,723; (b) Chen, Y. Chem Abstr 1998, 17, 20490s; (c) Dusza, J.; Albright, J.; Tomcufcik, A. US Pat. 5,538,977, 1996; (d) Dusza, J.; Albright, J.; Tomcufcik, A. Chem Abstr 1996, 13, 168011c.

[10] (a) Boes, M.; Stadler, H.; Riemer, C. US Pat. 6,194,410, 2001; (b) Boes, M.; Stadler, H.; Riemer, C. Chem Abstr 1999, 16, 214304z.

[11] (a) O'Donnell, P.; Thiele, W. US Pat. 6,384,221, 2002; (b) O'Donnell, P.; Thiele, W. Chem Abstr 2001, 15, 212744f.

[12] (a) Kendall, R.; Rubino, R.; Rutledge, R.; Bilodeau, M.; Fraley, M.; Thomas, K., Jr.; Hungante, R. US Pat. 6,235,741, 2001; (b) Kendall, R.; Rubino, R.; Rutledge, R.; Bilodeau, M.; Fraley, M.; Thomas, K., Jr.; Hungante, R. Chem Abstr 1999, 4, 033028w; (c) Fraley, M.; Hoffman, W.; Rubino, R.; Hungate, R.; Tebben, A.;

Rutledge, R.; McFall, R.; Huckle, W.; Kendall, R.; Coll, K.; Thomas, K. Bioorg Med Chem Lett 2002, 12, 2767.

[13] Dalinger, I.; Vatsade, I.; Shevelev, S.; Ivachtchenko, A. J Comb Chem 2005, 7, 236.

[14] Kessler, M.; Baudry, M.; Lynch, G. Brain Res 1989, 489, 377.

[15] McQuaid, L.; Smith, E.; South, K.; Mitch, C.; Schoepp, D.; True, R.; Calligaro, D.; O'Malley, P.; Lodge, D.; Ornstein, P. J Med Chem 1992, 35, 3319.

[16] Shan, R.; Velazquez, C.; Knaus, E. J Med Chem 2004, 47, 254.

[17] Uray, G.; Niederreiter, K. S.; Belaj, F.; Fabin, W. Helv Chim Acta 1999, 82, 1408.

[18] Strohmeier, G.; Fabin, W.; Uray, G. Helv Chim Acta 2004, 87, 1.

[19] Basta, A.; Girgis, A.; Houssni, S. Dyes Pigment 2002, 54, 1.

[20] Ried, W.; Aboul-Fetouh, S. Tetrahedron 1988, 44, 7155.

[21] Elnagdi, M.; Kandeel, B.; Elmoghayar, M. Z Naturfosch B: Anorg Chem Org Chem 1977, 30B, 307.

[22] Zhu, J.;Bienayme, H., Eds.Multicomponent Reactions; Wiley-VCH: Weinheim, 2004.

[23] Ugi, I. Pure Appl Chem 2001, 73, 187.

[24] Blackburn, C.; Guan, B.; Fleming, P.; Shiosaki, K.; Tsai, S. Tetrahedron Lett 1998, 39, 3635.

[25] Jachak, M.; Avhale, A.; Tantak, C.; Toche, R.; Reidlinger, C.; Stadlbaur, W. J Heterocycl Chem 2005, 42, 1311.

[26] Jachak, M.; Avhale, A.; Medhane, V.; Toche, R. J Heterocycl Chem 2006, 43, 1169.

[27] Jachak, M.; Avhale, A.; Toche, R.; Sabnis, R. J Heterocycl Chem 2007, 44, 343.

[28] Toche, R.; Ghotekar, B.; Kazi, M.; Kendre, D.; Jachak, M. Tetrahedron 2007, 63, 8157.

[29] Jachak, M.; Kendre, D.; Avhale, A.; Toche, R.; Sabnis, R. J Heterocycl Chem 2007, 44, 1525.

[30] Kendre, D.; Toche, R.; Jachak, M. Tetrahedron 2007, 63, 11000.

[31] Kendre, D.; Toche, R.; Jachak, M. J Heterocycl Chem 2008, 45, 667.

[32] Jachak, M.; Avhale, A.; Ghotekar, B.; Kendre, D.; Toche, R. J Heterocycl Chem 2008, 45, 1221.

[33] Elnagdi, M.; Kandeel, B.; Elmoghayar, M. Z Naturfosch B: Anorg Chem Org Chem 1977, 32B, 1478.