Reaction of 5-Aminopyrazole Derivatives with Ethoxymethylenemalononitrile and its Analogues

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A one-pot synthesis using 5-aminopyrazole derivatives **1** with ethoxymethylenemalononitrile (EMMN), ethyl ethoxymethylenecyanoacetate (EMCA) or diethyl ethoxymethylenemalonate (DEMM) gave pyrazolo[1,5-*a*]pyrimidine compounds **2,4,8**. Also, the one step reaction of EMCA with hydrazine hydrate afforded ethyl(4-ethoxycarbonyl-5-pyrazolyl)aminomethylenecyanoacetate **3c**. On the other hand, the reaction of 1-substituted 5-aminopyrazole-4-carboxamide **9** with EMMN afforded pyrazolo[3,4-*d*]pyrimidine compounds **10**.

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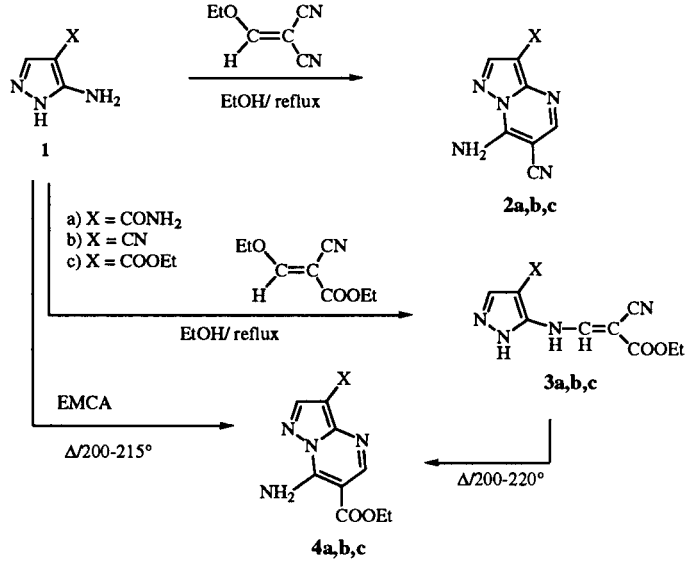
In a previous papers [1-3] from our laboratory we described a new synthesis of 3,4-dihydro-4-quinazolone derivatives by the reaction of 2-aminobenzamides with EMMN or EMCA. We have now found a one step synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives **2,4,8** by the reactions of 5-aminopyrazole compounds **1** with EMMN, EMCA or DEMM, and a one-pot synthesis of **3c** by the treatment of EMCA with hydrazine hydrate. We have also found that the reaction of 1-substituted 5-aminopyrazole-4-carboxamide **9** with EMMN afforded pyrazolo[3,4-*d*]-pyrimidin-4(5*H*)-ones **10**.

The reaction of 5-aminopyrazole-4-carboxamide **1a** [4] with an equivalent amount of EMMN afforded 7-amino-6-cyanopyrazolo[1,5-*a*]pyrimidine-3-carboxamide **2a**. Similarly, treatment of 5-amino-4-cyanopyrazole **1b** [4] or ethyl 5-aminopyrazole-4-carboxylate **1c** [5] with EMMN under the same reaction conditions gave the corresponding 7-amino-3,6-dicyanopyrazolo[1,5-*a*]pyrimidine **2b** and ethyl 7-amino-6-cyanopyrazolo[1,5-*a*]pyrimidine-3-carboxylate **2c**, respectively (Scheme 1). Also, **2b** was prepared by the reaction of hydrazine hydrate with excess EMMN [6]. Next, heating of **1a** with an equivalent amount of EMCA afforded a mixture of two geometric isomers of ethyl (4-carbamoyl-5-pyrazolyl)aminomethylenecyanoacetate, *cis*-and *trans*-enamines **3a** (88%). The structure of **3a** was assigned by its ir spectrum [3160 cm^{-1} (side chain NH) and 2240 cm^{-1} (C≡N)] and mass spectrum (m/z 249), confirmed by the satisfactory elemental analysis. In particular, the nmr spectra of two isomeric enamines of **3a** show the doublet signal due to the vinyl proton coupled with the adjacent NH proton [7-10]. The vinyl proton of the *cis*-enamine is at higher field than that of the *trans*-enamine [7]. The downfield NH signal attributed to an intramolecular hydrogen bonding between the amino and ester groups was assigned to that of the *cis*-enamine type (Table I). Similarly, refluxing of **1b,c** with EMCA under the same reaction conditions gave ethyl (4-cyano-5-pyrazolyl)aminomethylenecyanoacetate **3b** [8] and ethyl (4-ethoxycarbonyl-5-pyrazolyl)aminomethylenecyanoacetate **3c** [9].

Scheme 1



On the other hand, the pyrolysis of **1a** with an equivalent amount of EMCA at 200-215° afforded only ethyl 7-amino-3-carbamoylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate **4a** (76%), while the addition product of type **3** was not obtained. Also, the pyrolysis of compound **3a** at 200-220° gave product **4a** in 78% yield. Furthermore, the pyrolysis of **1b,c** with an equivalent amount of EMCA at 200-215° as well as the pyrolysis of **3b,c** at 200-220° gave the corre-

Table 1

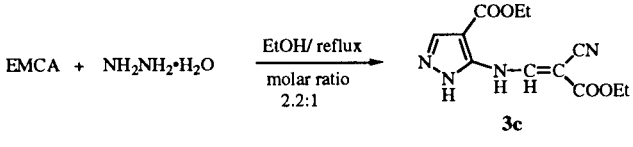
Characteristic NMR of 4-Substituted Ethyl 5-Pyrazolyl-aminomethylenecyanoacetates **3a,b,c** (δ values in DMSO-d_6)

Compound	*cis*-Enamine =CH	*cis*-Enamine NH (Exo)	*trans*-Enamine =CH	*trans*-Enamine NH (Exo)	Approximate Ratio of *cis*-and *trans*-Enamine [a]
3a	8.28 (1H, d) J = 13.5Hz	11.76 (1H, d)	8.57 (1H, d) J = 14.5 Hz	10.43 (1H, d)	75:25
3b	8.21 (1H, d) J = 13.0 Hz	11.52 (1H, d)	8.37 (1H, d) J = 13.0 Hz	10.87 (1H, d)	80:20
3c	8.35 (1H, d) J = 13.5Hz	11.40 (1H, d)	8.55 (1H, d) J = 14.5 Hz	9.50 (1H, d)	83:17

[a] This number was measured by nmr spectroscopy and is probably accurate with ±5.

sponding ethyl 7-amino-3-cyanopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **4b** [8] and diethyl 7-aminopyrazolo[1,5-*a*]-pyrimidine-3,6-dicarboxylate **4c** [9], respectively. Moreover, the one step synthetic method using hydrazine hydrate with 2.2-fold molar amount of EMCA afforded **3c** (68%) (Scheme 2).

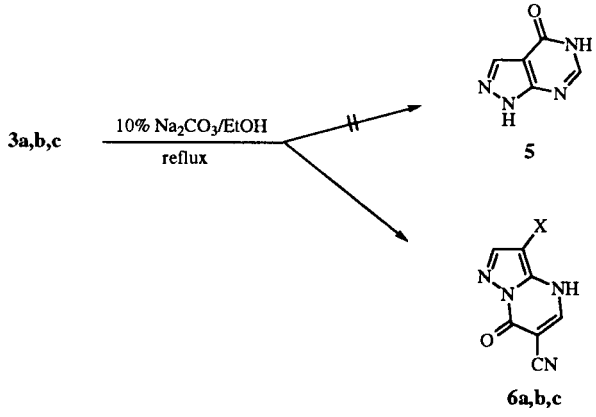
Scheme 2



3c

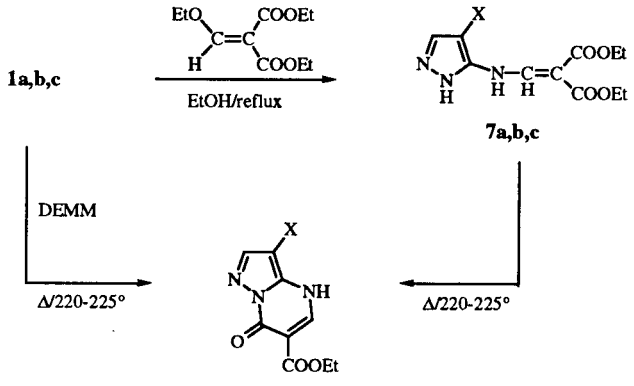
Next, when **3a** was treated with an aqueous solution of sodium carbonate, high yield (93%) of 6-cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-3-carboxamide **6a** was obtained instead of the expected pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **5**. The structure of **6a** established by its satisfactory spectral data and elemental analysis. Also, treatment of **3b,c** under the same reaction conditions afforded the corresponding 3,6-dicyanopyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one **6b** and ethyl 6-cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]-pyrimidine-3-carboxylate **6c**, respectively (Scheme 3).

Scheme 3



In view of the above facts, the reaction of compound **1** with an equivalent amount of DEMM gave the corresponding 4-substituted diethyl 5-pyrazolylaminomethylenemalonate [7]. Also, a one-pot synthesis using **1** with an equivalent amount of DEMM at 200-225° afforded 3-substituted ethyl 4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **8**. Similarly, the pyrolysis of **7** at 200-225° gave **8** (Scheme 4).

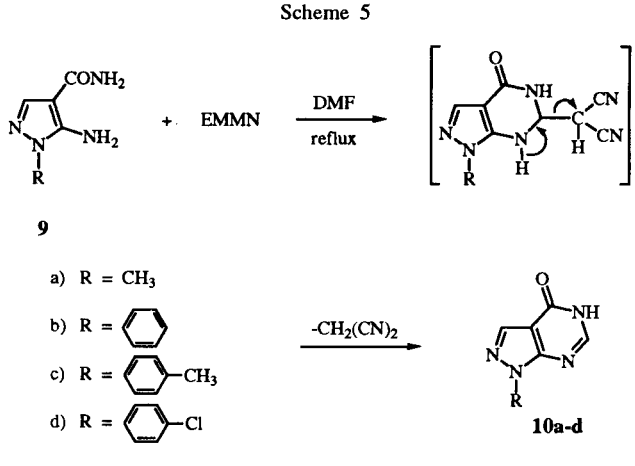
Scheme 4



8a,b,c

On the other hand, heating of 1-alkyl(aryl)-5-aminopyrazole-4-carboxamide **9** [4] with an equivalent amount of EMMN in DMF at 140-150° afforded 51-61% yield of 1-alkyl(aryl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **10** as the allopurinol derivatives, which was isolated by concentration of the reaction mixture and addition of water. The structure of **10** was established by its satisfactory spectral data and elemental analysis. In contrast with the above result, the EMCA or DEMM did not react with compound **9** and the starting material was recovered unchanged (Scheme 5).

Scheme 5



9

a) R = CH_3

b) R =

c) R =

d) R =

10a-d

EXPERIMENTAL

All melting points were determined on a Ishii melting point apparatus and are uncorrected. The ir spectra (potassium bro-

mide) were recorded with a JASCO IRA-1 spectrometer. The nmr spectra were measured in deuteriodimethyl sulfoxide with a Varian VXR-300 spectrometer. Chemical shifts are given in the δ scale. The mass spectra (ms) were determined with a JEOL JMS-DX300 spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

7-Amino-6-cyanopyrazolo[1,5-*a*]pyrimidine-3-carboxamide **2a**.

To a solution of 0.8 g (6.3 mmoles) of 5-aminopyrazole-4-carboxamide **1a** [4] in 15 ml of ethanol was added 0.8 g (6.3 mmoles) of ethoxymethylenemalononitrile (EMMN), and the mixture was refluxed on a water bath for 3 hours. The resulting precipitates were recrystallized from DMF-water to give 1.1 g (86%) of **2a** as a colorless powder, mp >300°; ir: ν 3340, 3380, 3300, 3160 (NH_2), 2240 (C≡N), 1670 (C=O) cm^{-1}; ms: (EI) m/z 202 (M^+); ^1H nmr: 7.45 (2H, s, $CONH_2$), 8.51 (1H, s, C_2-H), 8.58 (1H, s, C_5-H), 9.01 (2H, br, NH_2).

Anal. Calcd. for $C_8H_6N_6O$: C, 47.52; H, 2.99; N, 41.57. Found: C, 47.28; H, 3.07; N, 41.28.

7-Amino-3,6-dicyanopyrazolo[1,5-*a*]pyrimidine **2b**.

A mixture of 5-amino-4-cyanopyrazole **1b** [4] (0.8 g, 7 mmoles) and EMMN (0.9 g, 7 mmoles) in ethanol (15 ml) was refluxed on a water bath for 3 hours. The precipitates which resulted were collected and recrystallized from DMF-water to give 0.74 g (54%) of **2b**, mp >300°. Compound **2b** was identified by mixed melting point test and comparison of the ir spectrum with that of the authentic samples prepared by the reported procedure [6].

Ethyl 7-Amino-6-cyanopyrazolo[1,5-*a*]pyrimidine-3-carboxylate **2c**.

To a solution of 3.1 g (2.0 mmoles) of ethyl 5-aminopyrazole-4-carboxylate **1c** [5] in 30 ml of ethanol was added 2.4 g (2.0 mmoles) of EMMN. The mixture was refluxed on a water bath for 3 hours. The solid product was recrystallized from DMF-water to give 2.9 g (63%) of **2c** as a colorless powder, mp 301-302°; ir ν 3400, 3300 (NH), 2240 (C≡N), 1710 (C=O) cm^{-1}; ms: (EI) m/z 231 (M^+); ^1H nmr: 1.29 (3H, t, CH_2CH_3), 4.27 (2H, q, CH_2CH_3) 8.54 (1H, s, C_2-H), 8.57 (1H, s, C_5-H), 9.19 (2H, s, NH_2).

Anal. Calcd. for $C_{10}H_9N_5O_2$: C, 51.94; H, 3.92; N, 30.29. Found: C, 51.98; H, 3.88; N, 30.33.

4-Substituted Ethyl 5-Pyrazolylaminomethylenecyanoacetate **3a-c**.

General Procedure.

A mixture of **1a-c** (55 mmoles) and ethyl ethoxymethylenecyanoacetate (EMCA) (55 mmoles) in ethanol (50 ml) was refluxed on a water bath for 3 hours. The solid product was recrystallized from aqueous ethanol to give **3a-c**.

Ethyl (4-Carbamoyl-5-pyrazolyl)aminomethylenecyanoacetate **3a**.

This compound was obtained in 88% yield as a colorless powder, mp 203-205°; ir: ν 3460, 3420, 3340, 3260, 3160 (NH_2, NH), 2220 (C≡N), 1670, 1650 sh (C=O) cm^{-1}; ms: (EI) m/z 249 (M^+); ^1H nmr 1.27 (3H, t, CH_2CH_3), 4.21 (2H, q, CH_2CH_3), 7.26, 7.74 (2H, s, $CONH_2$), 8.24 (1H, s, C_3-H), 13.01 (1H, s, ring NH).

Anal. Calcd. for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 48.15; H, 4.32; N, 28.03.

Ethyl (4-Cyano-5-pyrazolyl)aminomethylenecyanoacetate **3b**.

This compound was obtained in 55% yield as a pale brown powder, mp 198-199°; mp 286° [5] ir: ν 3240, 3160 (NH), 2260, 2220 (C≡N), 1720, 1680 (C=O) cm^{-1}; ms: (EI) m/z 231 (M^+); ^1H nmr: 1.25 (3H, t, CH_2CH_3), 4.21 (2H, q, CH_2CH_3), 8.55 (1H, s, C_3-H), 13.60 (1H, br, ring NH).

Anal. Calcd. for $C_{10}H_9N_5O_2$: C, 51.94; H, 3.92; N, 30.29. Found: C, 51.72; H, 4.02; N, 30.07.

Ethyl (4-Ethoxycarbonyl-5-pyrazolyl)aminomethylenecyanoacetate **3c**.

This compound was obtained in 81% yield as a colorless powder, mp 178-179°, *cis*-enamine mp 178-182°, *trans*-enamine, mp 181.5-183° [9]; ir: ν 3220, 3180 sh (NH), 2220 (C≡N), 1670 (C=O) cm^{-1}; ms: (EI) m/z 278 (M^+); ^1H nmr: 1.30 (6H, t, 2 CH_2CH_3), 4.25 (4H, q, 2 CH_2CH_3), 8.34 (1H, s, C_3-H), 13.38 (1H, br, ring NH).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.92; H, 5.05; N, 20.09.

One-pot Synthesis of **3c**.

To a solution of 10 g (5.9 mmoles) of EMCA in 50 ml of ethanol was added 1.3 g (2.6 mmoles) of hydrazine hydrate. The mixture was refluxed on a water bath for 5 hours. The solid product was treated by aqueous ethanol to give 11.4 g (68%) of **3c**.

3-Substituted Ethyl 7-aminopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **4a-c**.

General Procedure.

Method A.

A mixture of **1a-c** (3 mmoles) and EMCA (3 mmoles) was heated on an oil bath for 10 minutes at 210-215°. After cooling, the solid product was recrystallized from DMF-water to give **4a-c**.

Method B.

One g of **3a-c** was heated on an oil bath for 10 minutes at 200-220°. After cooling, the solid product was treated as described in method A.

Ethyl 7-Amino-3-carbamoylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate **4a**.

The yield by method A was 76% and it was a colorless powder, mp 269-270°; the yield by method B was 78%; ir: ν 3360, 3300 (NH_2), 1680, 1660 (C=O) cm^{-1}; ms: (EI) m/z 249 (M^+); ^1H nmr: 1.34 (3H, t, CH_2CH_3), 4.35 (2H, q, CH_2CH_3), 7.44, 7.55 (2H, s, $CONH_2$), 8.50 (1H, s, C_2-H), 8.76 (1H, s, C_5-H), 9.15 (2H, s, NH_2).

Anal. Calcd. for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.09. Found: C, 47.89; H, 4.41; N, 28.06.

Ethyl 7-Amino-3-cyanopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **4b**.

The yield of **4b** by method A was 83% and by method B it was 89% and was obtained as a pale yellow powder, mp 302-304°, mp 350° [5]; ir: ν 3300, 3280 (NH_2), 2240 (C≡N), 1690 (C=O) cm^{-1}; ms: (EI) m/z 281 (M^+); ^1H nmr: 1.35 (3H, t, CH_2CH_3), 4.35 (2H, q, CH_2CH_3), 8.76 (1H, s, C_2-H), 8.78 (1H, s, C_5-H), 9.00 (2H, br, NH_2).

Anal. Calcd. for $C_{10}H_9N_5O_2$: C, 51.94; H, 3.92; N, 30.29. Found: C, 52.23; H, 3.83; N, 30.28.

Diethyl 7-Aminopyrazolo[1,5-*a*]pyrimidine-3,6-dicarboxylate **4c**.

Compound **4c** was obtained in 79% yield by method A and in 75% yield by method B as a colorless powder, mp 244-245°, mp 243-244° [9]; ir: ν 3380, 3260 (NH_2), 1710, 1680 (C=O) cm^{-1}; ms: (EI) m/z 278 (M^+); ^1H nmr: 1.33 (6H, t, 2 CH_2CH_3), 4.32 (4H, q, 2 CH_2CH_3), 8.58 (1H, s, C_2-H), 8.80 (1H, s, C_5-H), 9.06 (2H, br, NH_2).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.73; H, 4.84; N, 19.96.

3-Substituted 6-Cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine **6a-c**.

General Procedure.

To a solution of **3a-c** (8 mmoles) in 100 ml of ethanol was added 100 ml of 10% sodium carbonate solution. The mixture was refluxed on a water bath for 6 hours. After evaporation of ethanol, the residue was acidified with hydrochloric acid to precipitate crystals, which were filtered off, washed with water and dried.

6-Cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-3-carboxamide **6a**.

This compound was obtained in 93% yield as a colorless powder, mp >300°; ir: ν 3440, 3340, 3180 (NH_2, NH), 2240 (C≡N), 1720, 1710, 1660 (C=O) cm^{-1}; ms: (EI) m/z 203 (M^+); ^1H nmr: 7.49, 8.02 (2H, s, $CONH_2$), 8.45 (1H, s, C_2-H), 8.49 (1H, s, C_5-H), 10.00 (1H, br, NH).

Anal. Calcd. for $C_8H_5N_5O_2$: C, 47.29; H, 2.48; N, 34.48. Found: C, 47.23; H, 2.48; N, 34.46.

3,6-Dicyanopyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one **6b**.

This compound was obtained in 86% yield (pale yellow powders); mp >320° (mp 350° [8]); ir: ν 3420, 3180 (NH), 2240 (C≡N); 1710sh, 1690 (C=O) cm^{-1}; ms: (EI) m/z 185 (M^+); ^1H nmr: 8.45 (1H, s, C_2-H), 8.75 (1H, s, C_5-H), 10.62 (1H, br, NH).

Anal. Calcd. for $C_8H_3N_5O \cdot 1/4H_2O$: C, 50.66; H, 1.86; N, 36.93. Found: C, 50.70; H, 1.77; N, 37.22.

Ethyl 6-Cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-3-carboxylate **6c**.

This compound was obtained in 50% yield from aqueous ethanol as a colorless powder, mp 309-311°; ir: ν 3420, 3140 (NH), 2240 (C≡N), 1700, 1680sh (C=O) cm^{-1}; ms: (EI) m/z 232 (M^+); ^1H nmr: 1.31 (3H, t, CH_2CH_3), 4.31 (2H, q, CH_2CH_3), 8.28 (1H, s, C_2-H), 8.62 (1H, s, C_5-H), 10.60 (1H, br, NH).

Anal. Calcd. for $C_{10}H_8N_4O_3 \cdot 1/4H_2O$: C, 50.74; H, 3.62; N, 23.67. Found: C, 50.65; H, 3.37; N, 23.40.

4-Substituted Diethyl 5-Pyrazolylaminomethylenemalonates **7a-c**.

General Procedure.

A mixture of **1a-c** (2.6 mmoles) and diethyl ethoxymethylenemalonate (DEMM) (2.6 mmoles) in ethanol 50 ml was refluxed on a water bath for 3 hours. The solid product was recrystallized from a suitable solvent.

Diethyl (4-Carbamoyl-5-pyrazolyl)aminomethylenemalonate **7a**.

This compound was obtained in 51% yield from aqueous ethanol as a colorless powder, mp 243-245°; ir: ν 3460, 3320, 3260 (NH_2, NH), 1730, 1690, 1650 (C=O) cm^{-1}; ms: (EI) m/z 296 (M^+); ^1H nmr: 1.25 (6H, t, 2 CH_2CH_3), 4.16 (4H, q, 2 CH_2CH_3), 7.22, 7.70 (2H, s, $CONH_2$), 8.24 (1H, s, C_3-H), 8.70 (1H, d, J = 14.0 Hz, -CH=), 11.52 (1H, d, J = 14.0 Hz, NH), 12.85 (1H, br, ring NH).

Anal. Calcd. for $C_{12}H_{16}N_4O_5$: C, 48.64; H, 5.44; N, 18.91. Found: C, 48.38; H, 5.43; N, 19.16.

Diethyl (4-Cyano-5-pyrazolyl)aminomethylenemalonate **7b**.

This compound was obtained in 46% yield from aqueous ethanol as pale brown needles, mp 213-215°; ir: ν 3300, 3140 (NH), 2240 (C≡N), 1700, 1660 (C=O) cm^{-1}; ms: (EI) m/z 278 (M^+); ^1H nmr: 1.25 (6H, t, 2 CH_2CH_3), 4.17 (4H, q, 2 CH_2CH_3), 8.49 (1H, s, C_3-H), 8.53 (1H, s, -CH=), 10.73 (1H, br, NH), 13.54 (1H, br, ring NH).

Anal. Calcd. for $C_{12}H_{14}N_4O_4$: C, 51.79; H, 5.07; N, 20.14. Found: C, 51.60; H, 5.03; N, 20.10.

Diethyl (4-Ethoxycarbonyl-5-pyrazolyl)aminomethylenemalonate **7c**.

This compound was obtained in 67% yield from ethanol as a colorless powder, mp 173-175°; ir: ν 3240 (NH), 1730, 1690, 1660 (C=O) cm^{-1}; ms: (EI) m/z 325 (M^+); ^1H nmr: 1.28 (9H, t, 3 CH_2CH_3), 4.23 (6H, q, 3 CH_2CH_3), 8.23 (1H, s, C_3-H), 8.69 (1H, d, J = 13.5 Hz, -CH=), 11.31 (1H, d, J = 13.5 Hz, NH), 13.26 (1H, s, ring NH).

Anal. Calcd. for $C_{14}H_{19}N_3O_6$: C, 51.68; H, 5.89; N, 12.92. Found: C, 51.63; H, 5.66; N, 12.87.

3-Substituted Ethyl 4,7-Dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-6-carboxylates **8a-c**.

General Procedure.

Method A.

A mixture of **1a-c** (3.6 mmoles) and DEMM (3.6 mmoles) was heated on an oil bath for 10 minutes at 200-225°. After cooling, the solid product was recrystallized from DMF-water to give **8a-c**.

Method B.

One g of **7a,b,c** was heated on an oil bath 10 minutes at 200-225°. After cooling, the solid product was treated as described in method A.

Ethyl 3-Carbamoyl-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **8a**.

This compound was obtained in 55% yield by method A and in 61% yield by method B as a colorless powder, mp 318-320°; ir: ν 3380, 3180 (NH_2, NH), 1730, 1690, 1650 (C=O) cm^{-1}; ms: (EI) m/z 250 (M^+); ^1H nmr: 1.28 (3H, t, CH_2CH_3), 4.24 (2H, q, CH_2CH_3), 7.45, 7.96 (2H, s, $CONH_2$), 8.36 (1H, s, C_2-H), 8.39 (1H, s, C_5-H), 12.60 (1H, br, NH).

Anal. Calcd. for $C_{10}H_{10}N_4O_4$: C, 48.00; H, 4.02; N, 22.39. Found: C, 47.78; H, 3.97; N, 22.43.

Ethyl 3-Cyano-4,7-dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-6-carboxylate **8b**.

This compound was obtained in 57% yield by method A and in 67% yield by method B as a colorless powder, mp 309-310°, mp 315° [8]; ir: ν 3440, 3160 (NH), 2240 (C≡N), 1730, 1700, 1670 (C=O) cm^{-1}; ms: (EI) m/z 232 (M^+); ^1H nmr: 1.29 (3H, t, CH_2CH_3), 4.25 (2H, q, CH_2CH_3), 8.44 (1H, s, C_2-H), 8.55 (1H, s, C_5-H), 8.96 (1H, br, NH).

Anal. Calcd. for $C_{10}H_8N_4O_3$: C, 51.73; H, 3.43; N, 24.12. Found: C, 51.78; H, 3.50; N, 23.94.

Diethyl 4,7-Dihydro-7-oxopyrazolo[1,5-*a*]pyrimidine-3,6-dicarboxylate **8c**.

This compound was obtained in 80% yield by method A and in 70% yield by method B as a colorless powder, mp 303-304°; ir: ν 3400, 3180 (NH), 1730, 1670 (C=O) cm^{-1}; ms: (EI) m/z 279 (M^+); ^1H nmr: 1.30 (6H, t, 2 CH_2CH_3), 4.29 (4H, q, 2 CH_2CH_3), 8.25 (1H, s, C_2-H), 8.36 (1H, s, C_5-H), 12.77 (1H, br, NH).

Anal. Calcd. for $C_{12}H_{13}N_3O_5$: C, 51.61; H, 4.69; N, 15.05. Found: C, 51.45; H, 4.63; N, 15.18.

1-Alkyl(aryl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **10a-d**.

General Procedure.

To a solution of 15 mmoles of 1-alkyl(aryl)-5-aminopyrazole-4-carboxamide **9a-d** [4] in 40 ml of DMF was added of 15 mmoles of EMMN. The mixture was refluxed on an oil bath for 6 hours at 140-150°. The reaction mixture was concentrated *in vacuo* and the residue was added with water to precipitate crystals, which were filtered off, washed with water and dried.

1-Methylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **10a**.

This compound was obtained in 56% yield from aqueous ethanol, mp 287-288°, mp >300° [4]; ir: ν 3420, 3140 (NH), 1670 (C=O) cm^{-1}; ms: (EI) m/z 150 (M^+); ^1H nmr: 3.89 (3H, s, CH_3), 8.02 (1H, s, C_2-H), 8.06 (1H, s, C_6-H), 12.13 (1H, br, NH).

Anal. Calcd. for $C_6H_6N_4O$: C, 48.00; H, 4.03; N, 37.32. Found: C, 47.92; H, 4.07; N, 37.46.

1-Phenylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **10b**.

This compound was obtained in 61% yield from acetonitrile, mp 302-303°, mp 299° [4]; ir: ν 3440, 3160 (NH), 1730, 1650 (C=O) cm^{-1}; ms: (EI) m/z 212 (M^+); ^1H nmr: 7.35-8.06 (5H, m, Ph), 8.19 (1H, s, C_2-H), 8.32 (1H, s, C_6-H), 12.44 (1H, br, NH).

Anal. Calcd. for $C_{11}H_8N_4O$: C, 62.25; H, 3.80; N, 26.40. Found: C, 62.29; H, 3.77; N, 26.70.

1-(*p*-Chlorophenyl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **10c**.

This compound was obtained in 59% yield from DMF-water, mp >300°, mp >300° [4]; ir: ν 3440, 3160 (NH), 1670 (C=O) cm^{-1}; ms: (EI) m/z 246 (M^+), 248 (M^++2); ^1H nmr: 7.65, (2H, d, J = 8.5 Hz, Ph), 8.11 (2H, d, J = 8.5 Hz, Ph), 8.22 (1H, s, C_3-H), 8.35 (1H, s, C_6-H), 12.50 (1H, br, NH).

Anal. Calcd. for $C_{11}H_7N_4OCl$: C, 53.56; H, 2.86; N, 22.72. Found: C, 53.35; H, 3.07; N, 23.00.

1-(*p*-Tolyl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **10d**.

This compound was obtained in 51% yield from DMF-water, mp 302-304°; ir: ν 3420, 3140 (NH), 1660 (C=O) cm^{-1}; ms: (EI) m/z 226 (M^+); ^1H nmr: 2.36 (3H, s, Me), 7.34 (2H, d, J = 8.5 Hz, Ph), 7.90 (2H, d, J = 8.5 Hz, Ph), 8.17 (1H, s, C_3-H), 8.29 (1H, s, C_6-H), 2.41 (1H, s, NH).

Anal. Calcd. for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.46; N, 24.77. Found: C, 63.59; H, 4.53; N, 25.05.

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