Synthesis of Pyrazolo[1,5-*a*]-, 1,2,4-Triazolo[1,5-*a*]- and Imidazo[1,2-*a*]pyrimidines Related to Zaleplon, a New Drug for the Treatment of Insomnia

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This paper describes the preparation of some pyrazolo[1,5-*a*]-, 1,2,4-triazolo[1,5-*a*]- and imidazo[1,2-*a*]-pyrimidines substituted on the pyrimidine moiety by a 4-[(*N*-acetyl-*N*-ethyl)amino]phenyl group. A new synthesis of related benzo[*h*]pyrazolo[1,5-*a*]-, benzo[*h*]pyrazolo[5,1-*b*]- and benzo[*h*]1,2,4-triazolo[1,5-*a*]-quinazolines is also reported.

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The unsatisfactory use of benzodiazepines for the treatment of insomnia, often associated with several adverse effects, particularly with high doses and long-term use [1], has promoted new researches in benzodiazepine receptor pharmacology. The discovery of two central benzodiazepine receptor subtypes, BZ_1 or ω_1 , located in areas of the brain that are involved in sedation, and BZ_2 or ω_2 especially concentrated in areas responsible for cognition, memory and psychomotor functioning [2] has opened new perspectives for the pharmacological management strategy of insomnia, often associated with anxiety disorders [3]. Most benzodiazepines bind nonselectively at these sites, which may account for their unwanted central nervous system adverse effects. Over the last few years, the search has been undertaken for compounds chemically unrelated to benzodiazepines which display hypnotic properties with a better safety/efficacy profile. Typical of such compounds, which bind selectively to BZ_1 receptor subtypes, are the imidazopyridine zolpidem [4] and, more recently, the pyrazolopyrimidine zaleplon [5] approved in August 1999 by the Food and Drug Administration, and whose preparation has been reported only in an American Cyanamid patent [6].

This paper describes the synthesis and the physical properties of some pyrazolo[1,5-*a*]pyrimidines (**1**), 1,2,4-triazolo[1,5-*a*]pyrimidines (**2**), imidazo[1,2-*a*]pyrimidines (**3**) and some related tetracyclic derivatives (**4**) bearing on the pyrimidine moiety a phenyl ring substituted by the (*N*-acetyl-*N*-ethyl)amino group as the lead compound, though in position 4 instead of 3 (Figure 1), which were prepared in order to study their pharmacological activity.

The synthetical pathways to compounds **1** and **2** are summarized in Scheme 1.

The starting materials 3-dimethylamino-1-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-2-propen-1-one (**6a**) and ethyl 3-dimethylamino-2-[4-(*N*-acetyl-*N*-ethyl)aminobenzoyl]-propenoate (**6b**) were prepared respectively by reaction of 1-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]ethanone (**5a**) and ethyl 3-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-3-oxo-propanoate (**5b**) with *N*,*N*-dimethylformamide dimethyl acetal.

According to a conventional method, enaminone **6a** either by reaction with 3-aminopyrazoles or 3-amino-1,2,4-triazole gave the 7-aryl-pyrazolo[1,5-*a*]pyrimidines **7d-f** [7,8] and the corresponding 1,2,4-triazolo[1,5-*a*]pyrimidine **8a**, in high yield and in a regiospecific manner.

The 7-aryl substitution in compound **8a** was demonstrated on the basis of the coupling constant of pyrimidine protons whose value of 4.4 Hz was consistent with the proposed structure [9].

Under the same conditions enaminone **6b** by condensation with 4-substituted-3-aminopyrazoles and 3-amino-1,2,4-triazole afforded only the 7-aryl-6-ethoxycarbonylpyrazolo[1,5-*a*]pyrimidines **7h,i** and the 7-aryl-6-

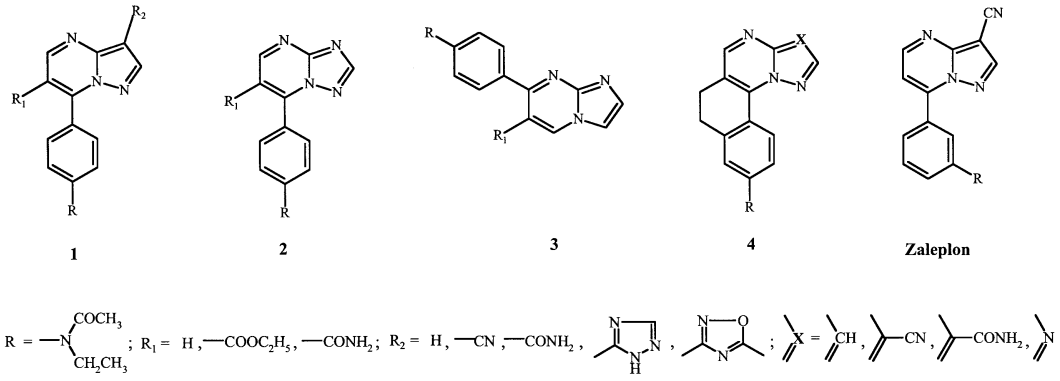
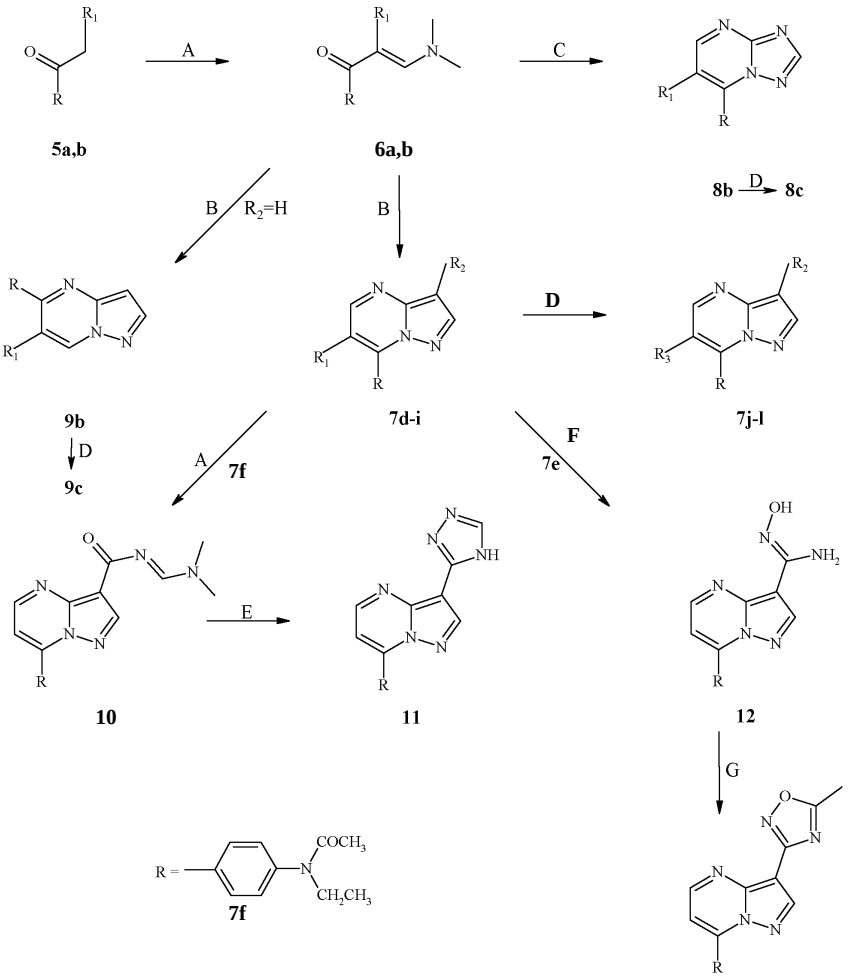
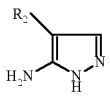
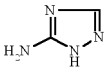


Figure 1

Scheme 1



a: R_1 = H
b: R_1 = –$COOC_2H_5$
c: R_1 = –$CONH_2$
d: R_1 = R_2 = H
e: R_1 = H, R_2 = –CN
f: R_1 = H, R_2 = –$CONH_2$
g: R_1 = –$COOC_2H_5$, R_2 = H
h: R_1 = –$COOC_2H_5$, R_2 = –CN
i: R_1 = –$COOC_2H_5$, R_2 = –$CONH_2$
j: R_2 = H, R_3 = –$CONH_2$
k: R_2 = –CN, R_3 = –$CONH_2$
l: R_2 = R_3 = –$CONH_2$

Reagents: A: $(CH_3)_2NCH(OCH_3)_2$; B:  , CH_3COOH, reflux; C:  , CH_3COOH, reflux; D: MeOH / NH_3 rt; E: $NH_2NH_2.H_2O$, CH_3COOH, 90°; F: $NH_2OH.HCl$, K_2CO_3, EtOH reflux; G: $(CH_3CO)_2O/CH_3COOH$.

ethoxycarbonyl-1,2,4-triazolo[1,5-*a*]pyrimidine **8b**, while by reaction with 3-aminopyrazole provided an isomeric 1:1 mixture of 7- and 5-aryl-6-ethoxycarbonyl derivatives **7g** and **9b,** easily separated by column chromatography.

The structure of isomers **7g** and **9b** could be determined by ^{1}H- and ^{13}C-nmr experiments on the basis of chemical shift evaluation. As reported in the literature [10] for analogue pyrazolo[1,5-*a*]pyrimidines, the H-5 and H-7 signals are characterized by a different chemical shift value, the first proton being shielded of about 0.5 ppm. In the protonic spectrum of compound **7g** the pyrimidine proton signal lies at 8.96 ppm (δ), while in the spectrum of compound **9b** the same signal appears at 9.31 ppm. This observation allowed to assign to **7g** the 7-arylsubstituted structure. The structure has been confirmed by the chemical shift values of the carbon atom bearing pyrimidine proton, whose signal is located downfield (150.1 ppm) for **7g** and upfield (139.4 ppm) for **9b**. This deshielded position of C-5 due to nearness of the sp^2 N-4 atom, in comparison with carbon C-7 adjacent to the sp^3 N-8 atom, has been already described for analogues heteroaromatic compounds [11]. Moreover, a complete assignment of ^{13}C signals of both compounds has

been performed by direct and long-range proton-carbon correlated spectroscopy HETCOR.

The structure of compound **8b** was determined by ^{1}H- and ^{13}C-nmr experiments. The Nuclear Overhauser Effect produced on the ethoxycarbonyl protons by irradiation of the aromatic signal at 9.28 ppm (δ) allowed to assign the position of the pyrimidine proton. Two-dimensional ^{1}H-^{13}C correlation spectroscopy and evaluation of the pyrimidine CH chemical shift (δ = 155.9 ppm) led to assignment of the 7-arylsubstitution for compound **8b**.

Amides **7j-l**, **8c** and **9c** were easily prepared from the corresponding ethoxycarbonyl derivatives **7g-i**, **8b** and **9b** allowed to react at room temperature in methanol saturated with ammonia for 72 hours.

Compound **7f** by reaction with *N*,*N*-dimethylformamide dimethyl acetal in refluxing ethylene glycol monomethyl ether gave the intermediate dimethylaminomethylenecarboxamide **10** which then reacted with hydrazine hydrate in acetic acid at 90° to give the 1,2,4-triazole derivative **11**.

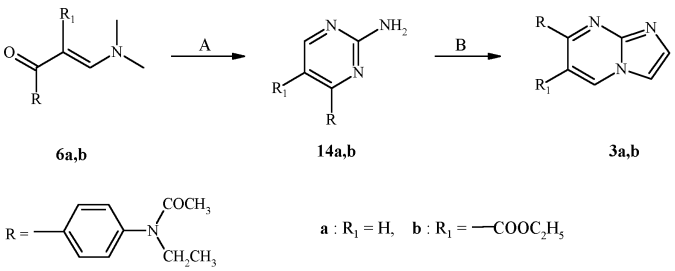
Treatment of nitrile **7e** with hydroxylamine in aqueous ethanol provided the amidoxime **12** which when heated with acetic anhydride in acetic acid afforded the 1,2,4-oxadiazole derivative **13**.

The preparation of imidazo[1,2-*a*]pyrimidines **3** is outlined in Scheme 2.

The 2-amino-4-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-pyrimidines **14**, obtained by condensing enaminones **6** with guanidine in refluxing ethanol, by cyclization with bromoacetaldehyde dimethyl acetal, gave the imidazo[1,2-*a*]-pyrimidines **3** in 32-38% yields. The structure of these compounds was confirmed by chemical shifts and proton-proton coupling constant values which are consistent with those reported in the literature for analogues 7-arylsubstituted imidazo[1,2-*a*]pyrimidines [9,12]. In fact, the ^{1}H-nmr spectrum of **3a**, showed for pyrimidine ring protons two doublets at 8.50 and 7.36 ppm (δ), whose coupling constant J = 7.0 Hz has been described as characteristic for the H-5 - H-6 sequence. In order to elucidate the structure of **3b**, the same considerations were made as reported above for **9b**: in the ^{13}C-nmr spectrum the pyrimidine CH signal at 137.8 ppm (δ) and the position of the carbon bearing the aryl substituent at 157.5 ppm (δ), are consistent with the 6,7-disubstituted imidazo[1,2-*a*]pyrimidine structure [11].

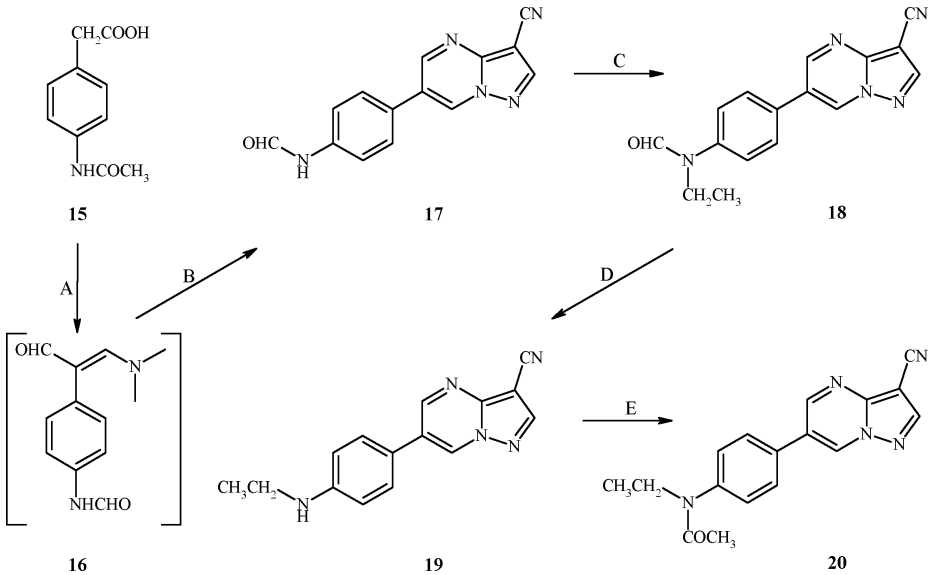
The synthesis of 6-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-3-cyanopyrazolo[1,5-*a*]pyrimidine (**20**) is illustrated in Scheme 3.

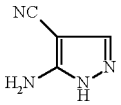
Scheme 2



Reagents: A: $(NH_2)_2C=NH.HCl$, EtONa, EtOH, reflux; B: $BrCH_2CH(OCH_3)_2$, CH_3COOH, CH_3COONa.

Scheme 3



Reagents: A: $POCl_3$, DMF; B:  , CH_3COOH reflux; C: C_2H_5I/NaH/DMF; D: HCl, MeOH reflux; E: $(CH_3CO)_2O/CH_3COOH$.

The 4-acetylaminophenylacetic acid (**15**), subjected to Vilsmeier-Haack condensation [13], was hydrolyzed in the acidic medium of the reaction mixture and the resulting ammonium ion was *N*-formylated to afford the 3-dimethylamino-2-[4-(*N*-formyl)aminophenyl]-2-propenal (**16**). This compound deteriorates considerably on standing with formation of tar products, so it was quickly used without purification in the following step. Treatment of crude **16** with 3-amino-4-cyanopyrazole in refluxing acetic acid led to 3-cyano-6-[4-(*N*-formyl)aminophenyl]pyrazolo[1,5-*a*]pyrimidine (**17**) which successively was first *N*-ethylated by ethyl iodide/sodium hydride in dimethylformamide to give compound **18**, then *N*-deformylated to obtain the 6-[4-(*N*-ethyl)aminophenyl]pyrazolo[1,5-*a*]pyrimidine (**19**). Finally, *N*-acetylation of **19** easily provided the expected compound **20**.

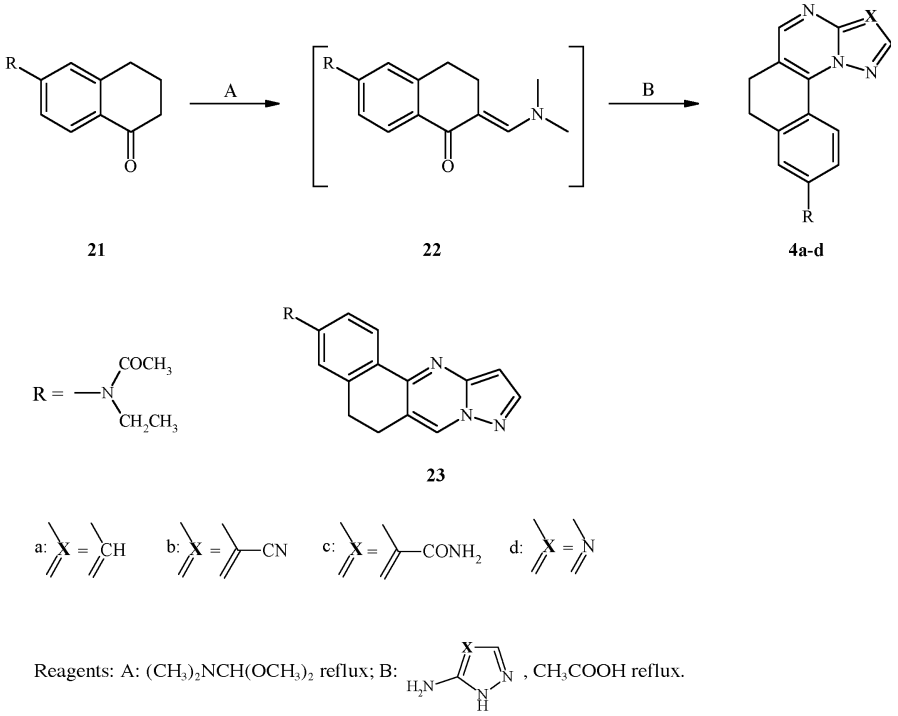
The 6-[(*N*-acetyl-*N*-ethyl)amino]-1-tetralone (**21**) was the key intermediate for the synthesis of benzo[*h*]pyrazolo[1,5-*a*]- and benzo[*h*]1,2,4-triazolo[1,5-*a*]quinazolines **4** outlined in Scheme 4. These tetracyclic compounds, which might be considered conformationally restricted analogues of compounds **7** and **8**, appear hitherto not to have been extensively studied, as only three references related to their preparation by different synthetical pathways are reported in the chemical literature [14-16].

Compound **21** in refluxing *N*,*N*-dimethylformamide dimethyl acetal provided a very unstable enaminone **22** which, without purification, was directly allowed to react with aminopyrazoles or 3-amino-1,2,4-triazole to give the desired compounds **4a-d**, according to the same procedure above reported for compounds **7** and **8**.

Likewise compounds **7g** and **9b**, the condensation of **22** with 3-aminopyrazole led to a 1:1 isomeric mixture of benzo[*h*]pyrazolo[1,5-*a*]- and benzo[*h*]pyrazolo[5,1-*b*]quinazolines **4a** and **23**. Their structures were supported by ^{1}H- and ^{13}C-nmr. The complete assignment of ^{13}C signals was obtained by performing direct and long-range heterocorrelated ^{1}H-^{13}C spectra. In the carbon spectrum of both compounds pyrimidine CH signals were observed to have the same chemical shift value (δ = 149.3 ppm for **4a** and 149.2 ppm for **23**) but this observation could not be used to support related structures. Final structural characterisation was achieved by ^{1}H-NOE experiments. The structure of compound **4a** was determined by the irradiation of doublet at 9.50 ppm (δ), assigned to H-11, which produced a NOE only on pyrazole H-2 proton 2.8 Å far from the irradiated proton, while no NOE was observed on H-3 and H-5 protons, respectively at 5.2 and 5.7 Å from H-11. On the contrary the irradiation of the analogue aromatic proton H-1 of compound **23** produced a NOE only on pyrazole H-11 proton at 4.5 Å from H-1, while no effect was observed on the farther protons H-7 and H-10.

Preliminary binding studies on membrane preparations from rat brain cortex, using [^{3}H]-Ro 15-1788 (flumazenil) as radioligand, indicate that only tetracyclic compound **4b** showed significant Ki value (145 nM) as compared to zaleplon (59 nM). All other tested compounds showed Ki values > 1µM.

Scheme 4



EXPERIMENTAL

Melting points and boiling points (mmHg as pressure unit) are uncorrected. The ^{1}H-nmr spectra were obtained on a Varian Gemini 200 MHz instrument; all values were reported in ppm (δ) and standard abbreviations were used (at = apparent triplet; b = broad; d = doublet; dd = doublet of doublets; m = multiplet; q = quadruplet; t = triplet; s = singlet, um = unresolved multiplet); peak assignments were also based on ^{13}C-APT, ^{1}H-NOE and ^{13}C-^{1}H HETCOR nmr experiments; electron ionization mass spectra were recorded on a HP 59580 B spectrometer operating at 70 eV. Column chromatographic separations were accomplished on Merck silica gel (70-230 mesh) or Merck aluminum oxide 90. The purity of each compound was checked on silica gel C. Erba 60 F_{254} or Merck aluminum oxide 60 F_{254} (type E) plates and spots were located by uv light. Sodium sulfate was used to dry organic solutions.

1-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]ethanone (**5a**).

To a stirred and cooled suspension of sodium hydride (2.8 g of 50% oil dispersion, 0.06 mole) in anhydrous dimethylformamide (80 ml), 1-(4-acetylaminophenyl)ethanone [17] (7.1 g, 0.04 mole) was added in several portions. After stirring 1 hour at room temperature, a solution of ethyl iodide (6.4 ml, 0.08 mole) in dimethylformamide (10 ml) was dropwise added, the mixture stirred for 3 hours at room temperature, then carefully poured into water and extracted with dichloromethane. The solvent was removed and the residue chromatographed over alumina eluting by 1:1 ethyl acetate/*n*-hexane mixture to give 6.3 g (77%) of a viscous oil. Analytical sample was obtained by distillation: bp 135-140°/0.05 mm; ^{1}H-nmr (deuteriochloroform): δ 7.98 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 7.23 (d, 2H, H-3' and H-5', J_{ortho} = 8.4 Hz), 3.73 (q, 2H, N-CH_2), 2.59 (s, 3H, aryl-$COCH_3$), 1.83 (s, 3H, *N*- $COCH_3$), 1.07 (t, 3H, *N*-ethyl CH_3).

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.38; H, 7.49; N, 6.66.

Ethyl 3-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-oxopropanoate (**5b**).

Sodium hydride (3.9 g of 50% oil dispersion, 0.08 mole) was added with stirring to a solution of diethyl carbonate (30 ml) in cyclohexane (80 ml). A mixture of the previously described **5a** (8.2 g, 0.04 mole) and diethyl carbonate (5 ml) was added dropwise and the whole was refluxed for 2 hours, then cooled. A small amount of isopropanol was added to the reaction mixture to destroy excess sodium hydride. The resulting mixture was poured into water and ice and the layers were separated. The organic phase was washed with water and the combined aqueous alkaline solutions were acidified with 10% hydrochloric acid, then extracted with diethyl ether. After evaporation of the solvent, the residue was purified by silica gel chromatography using ethyl acetate as eluent, to give the desired compound as a viscous oil, g 7.1 (64%); ^{1}H-nmr (deuteriochloroform): δ 7.99 (d, 2H, ketonic form H-2' and H-6'), 7.80 (d, 2H, enolic form H-2' and H-6', keto/enolic ratio = 3:1), 7.27 (d, 2H, ketonic form H-3' and H-5'), 7.20 (d, 2H, enolic form H-3' and H-5'), 5.63 (s, 1H, enolic H-2), 4.21 (two overlapped q, 2H, both forms O-CH_2), 3.97 (s, 2H, ketonic form H-2), 3.76 (two overlapped q, 2H, both forms N-CH_2), 1.85 (s, 3H, acetyl CH_3), 1.23 (two overlapped t, 3H, *O*-ethyl CH_3), 1.09 (two overlapped t, 3H, *N*-ethyl CH_3).

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.98; H, 7.00; N, 5.26.

3-Dimethylamino-1-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-2-propen-1-one (**6a**).

In a flask fitted with a Dean-Stark trap to remove methanol a mixture of 1-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]ethanone (**5a**) (8.2 g, 0.04 mole) and *N*,*N*-dimethylformamide dimethyl acetal (15 ml) was heated at reflux for 4 hours. The reaction mixture was evaporated to dryness *in vacuo* and the resulting **6a** cristallyzed from ethyl acetate 7.4 g (71%), mp 92-94°; ^{1}H-nmr (deuteriochloroform): δ 7.86 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 7.77 (d, 1H, H-3, $J_{2,3}$ = 12 Hz), 7.13 (d, 2H, H-3' and H-5', J_{ortho} = 8.4 Hz), 5.63 (d, 1H, H-2, $J_{2,3}$ = 12 Hz), 3.68 (q, 2H, N-CH_2), 3.10 (bs, 3H, N-CH_3), 2.88 (bs, 3H, N-CH_3), 1.77 (bs, 3H, acetyl CH_3), 1.03 (t, 3H, N-ethyl CH_3); ms: (m/z) 260 (M^+), 243, 201, 174.

Anal. Calcd. for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 68.98; H, 7.79; N, 10.56.

Ethyl 3-Dimethylamino-2-[4-(*N*-acetyl-*N*-ethyl)aminobenzoyl]-propenoate (**6b**).

Compound **6b** was obtained in 79% yield by reaction of ethyl 3-[4-(*N*-acetyl-*N*-ethyl)aminophenyl]-3-oxopropanoate (**5b**) with *N*,*N*-dimethylformamide dimethyl acetal following the same procedure previously reported for **6a**, mp 132-134° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 7.77 (um, 3H, H-2', H-6' and H-3), 7.13 (d, 2H, H-3' and H-5', J = 8.4 Hz), 3.91 (q, 2H, O-CH_2), 3.70 (q, 2H, N-CH_2), 2.92 (bs, 6H, $N(CH_3)_2$), 1.81 (bs, 3H, acetyl CH_3), 1.05 (t, 3H, *O*-ethyl CH_3), 0.85 (t, 3H, N-ethyl CH_3); ms: (m/z) 332 (M^+), 287, 243, 215, 190, 148, 132.

Anal. Calcd. for $C_{18}H_{24}N_2O_4$: C, 65.04; H, 7.28; N, 8.43. Found: C, 64.87; H, 7.12; N, 8.29.

General Procedure for the Preparation of Pyrazolo[1,5-*a*]pyrimidines **7d-i**, **9b** and 1,2,4-Triazolo[1,5-*a*]pyrimidines **8a,b**.

A mixture of each compound **6** (0.05 mole) and 3-aminopyrazole [18] (to obtain **7d,g** and **9b**), 3-amino-4-cyanopyrazole [19] (to obtain **7e,h**), 3-amino-4-carboxamidopyrazole [19] (to obtain **7f,i**) or 3-amino-1,2,4-triazole (to obtain **8a,b**) (0.05 mole) in glacial acetic acid (80 ml) was refluxed for 8 hours. After cooling, the reaction mixture was poured into water and extracted with dichloromethane. The organic phase was washed with 8% sodium hydroxide solution, then with brine. Evaporation of the solvent to dryness gave a crude product which was crystallized. The reaction of **6b** with 3-aminopyrazole provided an isomeric mixture of **7g** and **9b** separated by chromatography on silica gel by eluting with ethyl acetate. Compound **9b** was eluted first, followed by **7g**.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]pyrazolo[1,5-*a*]pyrimidine (**7d**).

This compound was obtained from **6a** in 64% yield, mp 171-173° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.51 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.15 (d, 1H, H-2, $J_{2,3}$ = 2.6 Hz), 8.11 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 7.34 (d, 2H, H-3' and H-5', J_{ortho} = 8.4 Hz), 6.89 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 6.77 (d, 1H, H-3, $J_{2,3}$ = 2.6 Hz), 3.77 (q, 2H, N-CH_2), 1.89 (bs, 3H, acetyl CH_3), 1.12 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.7 (C=O), 150.0 (C-3a), 149.1 (C-5), 145.7 (C-7), 145.4 (C-1'), 144.9 (C-2), 130.8 (C-2' and C-6'), 130.5 (C-4'), 128.6 (C-3' and C-5'), 107.6 (C-6), 97.5 (C-3), 44.3 (N-CH_2), 23.2 (acetyl CH_3), 13.5 (*N*-ethyl CH_3); ms: (m/z) 280 (M^+), 238, 223, 194, 140, 130.

Anal. Calcd. for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.66; H, 5.60; N, 20.18.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-cyanopyrazolo[1,5-*a*]-pyrimidine (**7e**).

This compound was obtained from **6a** in 91% yield, mp 169-171° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.80 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.45 (s, 1H, H-2), 8.14 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 7.43 (d, 2H, H-3' and H-5', J_{ortho} = 8.4 Hz), 7.24 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 3.82 (q, 2H, N-CH_2), 1.96 (bs, 3H, acetyl CH_3), 1.17 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.7 (C=O), 152.9 (C-5), 151.6 (C-3a), 147.4 (C-7), 147.3 (C-2), 146.4 (C-4'), 131.2 (C-2' and C-6'), 128.9 (C-1'), 128.8 (C-3' and C-5'), 112.8 (CN), 110.2 (C-6), 83.8 (C-3), 44.6 (N-CH_2), 23.3 (acetyl CH_3), 13.6 (*N*-ethyl CH_3); ms: (m/z) 305 (M^+), 263, 248, 219, 165, 155, 130.

Anal. Calcd. for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.59; H, 4.72; N, 22.81.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-carboxamidopyrazolo[1,5-*a*]pyrimidine (**7f**).

This compound was obtained from **6a** in 76% yield, mp 268-271° (methanol); ^{1}H-nmr (deuteriochloroform): δ 8.72 (s, 1H, H-2), 8.67 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.13 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 7.95 (bs, 1H, $CONH_2$), 7.38 (d, 1H, H-3' and H-5', J_{ortho} = 8.4 Hz), 7.09 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 5.97 (bs, 1H, $CONH_2$), 3.78 (q, 2H, N-CH_2), 1.93 (bs, 3H, acetyl CH_3), 1.14 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.8 (acetyl C=O), 164.2 ($CONH_2$), 151.1 (C-5), 147.8 (C-3a), 147.3 (C-7), 147.1 (C-2), 146.2 (C-4'), 131.1 (C-2' and C-6'), 129.4 (C-1'), 128.8 (C-3' and C-5'), 108.8 (C-6), 105.6 (C-3), 44.6 (N-CH_2), 23.3 (acetyl CH_3), 13.6 (*N*-ethyl CH_3); ms: (m/z) 323 (M^+), 295, 281, 266, 249, 237.

Anal. Calcd. for $C_{17}H_{17}N_5O_2$: C, 63.14; H, 5.30; N, 21.66. Found: C, 63.08; H, 5.55; N, 21.42.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-ethoxycarbonylpyrazolo[1,5-*a*]pyrimidine (**7g**).

This compound was obtained from **6b** in 37% yield, mp 142-144° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.96 (s, 1H, H-5), 8.15 (d, 1H, H-2, $J_{2,3}$ = 2.2 Hz), 7.55 (d, 2H, H-2' and H-6', J_{ortho} = 8.4 Hz), 6.78 (d, 1H, H-3, $J_{2,3}$ = 2.2 Hz), 4.11 (q, 2H, O-CH_2), 3.76 (q, 2H, NCH_2), 1.90 (bs, 3H, acetyl CH_3), 1.13 (t, 3H, *O*-ethyl CH_3), 1.04 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.5 (acetyl C=O), 164.2 (ethoxycarbonyl C=O), 150.1 (C-5), 149.4 (C-3a), 148.4 (C-7), 147.2 (C-2), 144.6 (C-4'), 130.5 (C-2' and C-6'), 129.6 (C-1'), 127.9 (C-3' and C-5'), 111.6 (C-6), 98.3 (C-3), 61.6 (O-CH_2), 44.2 (N-CH_2), 22.9 (acetyl CH_3), 13.8 (*O*-ethyl CH_3), 13.3 (*N*-ethyl CH_3); ms: (m/z) 352 (M^+), 310, 309, 295, 267, 249, 221.

Anal. Calcd. for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90. Found: C, 64.61; H, 5.49; N, 15.66.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-cyano-6-ethoxycarbonyl-pyrazolo[1,5-*a*]pyrimidine (**7h**).

This compound was obtained from **6b** in 58% yield, mp 229-232° (methanol); ^{1}H-nmr (deuteriochloroform): δ 9.20 (s, 1H, H-5), 8.40 (s, 1H, H-2), 7.58 (d, 2H, H-2' and H-6', J_{ortho} = 8.8 Hz), 7.37 (d, 2H, H-3' and H-5', J_{ortho} = 8.8 Hz), 4.20 (q, 2H, O-CH_2), 3.80 (q, 2H, N-CH_2), 1.94 (bs, 3H, acetyl CH_3), 1.16 (t, 3H, *O*-ethyl CH_3), 1.11 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.8 (acetyl C=O), 163.4 (ethoxycarbonyl C=O), 154.0 (C-5), 151.3 (C-3a), 149.8 (C-7), 148.9 (C-2), 145.7 (C-4'), 131.0 (C-2' and C-6'), 128.3 (C-3' and C-5'), 128.2 (C-1'), 114.9 (CN), 112.1 (C-6), 85.1 (C-3), 62.6 (O-CH_2), 44.7 (N-CH_2), 23.2 (acetyl CH_3), 14.1 (*O*-ethyl CH_3), 13.7 (*N*-ethyl CH_3); ms: (m/z) 377 (M^+), 335, 320, 292, 274, 246.

Anal. Calcd. for $C_{20}H_{19}N_5O_3$: C, 63.65; H, 5.08; N, 18.56. Found: C, 63.39; H, 5.30; N, 18.28.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-carboxamido-6-ethoxycarbonylpyrazolo[1,5-*a*]pyrimidine (**7i**).

This compound was obtained from **6b** in 51% yield, mp 235-236° (methanol); ^{1}H-nmr (deuteriochloroform): δ 9.14 (s, 1H, H-5), 8.70 (s, 1H, H-2), 7.82 (bs, 1H. $CONH_2$), 7.59 (d, 2H, H-2' and H-6'), 7.36 (d, 2H, H-3' and H-5'), 5.95 (bs, 1H, $CONH_2$), 4.18 (q, 2H, O-CH_2), 3.81 (q, 2H, N-CH_2), 1.95 (bs, 3H, acetyl CH_3), 1.17 (t, 3H, *O*-ethyl CH_3), 1.10 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.8 (acetyl C=O), 163.8 ($CONH_2$), 163.6 (ethoxycarbonyl C=O), 152.6 (C-5), 150.0 (C-3a), 149.1 (C-2), 147.3 (C-7), 145.5 (C-4'), 130.9 (C-2' and C-6'), 128.7 (C-1'), 128.3 (C-3' and C-5'), 113.5 (C-6), 106.5 (C-3), 62.4 (O-CH_2), 44.6 (N-CH_2), 23.2 (acetyl CH_3), 14.1 (*O*-ethyl CH_3), 13.7 (*N*-ethyl CH_3); ms: (m/z) 395 (M^+), 353, 338, 335, 321, 293, 275, 247.

Anal. Calcd. for $C_{20}H_{21}N_5O_4$: C, 60.75; H, 5.35; N, 17.71. Found: C, 60.66; H, 5.33; N, 17.59.

5-[4-(*N*-Acetyl-*N*-ethylamino)phenyl]-6-ethoxycarbonylpyrazolo[1,5-*a*]pyrimidine (**9b**).

This compound was obtained from **6b** in 32% yield, mp 134-136° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 9.32 (d, 1H, H-7, $J_{2,7}$ = 1.0 Hz), 8.26 (d, 1H, H-3, $J_{2,3}$ = 2.2 Hz), 7.61 (d, 2H, H-2' and H-6'), 7.23 (d, 2H, H-3' and H-5'), 6.76 (dd, 1H, H-2, $J_{2,3}$ = 2.2 Hz, $J_{2,7}$ = 1.0 Hz), 4.23 (q, 2H, O-CH_2), 3.77 (q, 2H, N-CH_2), 1.87 (s, 3H, acetyl CH_3), 1.17 (t, 3H, *O*-ethyl CH_3), 1.12 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.9 (acetyl C=O), 164.6 (ethoxycarbonyl C=O), 157.2 (C-5), 148.6 (C-2), 148.0 (C-3a), 144.1 (C-4'), 139.4 (C-7), 138.1 (C-1'), 130.1 (C-2' and C-6'), 128.1 (C-3' and C-5'), 112.7 (C-6), 98.4 (C-3), 62.2 (O-CH_2), 44.3 (N-CH_2), 23.2 (acetyl CH_3), 14.1 (*O*-ethyl CH_3), 13.4 (*N*-ethyl CH_3); ms: (m/z) 352 (M^+), 324, 310, 295, 267, 249, 221.

Anal. Calcd. for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90. Found: C, 64.58; H, 5.55; N, 15.88.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-1,2,4-triazolo[1,5-*a*]-pyrimidine (**8a**).

Compound **8a** was obtained from **6a** in 76% yield, mp 183-185° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.87 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.54 (s, 1H, H-2), 8.19 (d, 2H, H-2' and H-6'), 7.39 (d, 2H, H-3' and H-5'), 7.25 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 3.79 (q, 2H, N-CH_2), 1.92 (bs, 3H, acetyl CH_3), 1.33 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.7 (C=O), 156.5 (C-3a), 156.1 (C-5), 154.7 (C-2), 147.3 (C-7), 146.3 (C-4'), 131.0 (C-2' and C-6'), 129.1 (C-1'), 128.8 (C-3' and C-5'), 109.4 (C-6), 44.6 (N-CH_2), 23.2 (acetyl CH_3), 13.6 (*N*-ethyl CH_3); ms: (m/z) 281 (M^+), 239, 224, 211.

Anal. Calcd. for $C_{15}H_{15}N_5O$: C, 64.04; H, 5.37; N, 24.90. Found: C, 64.12; H, 5.20; N, 24.68.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-ethoxycarbonyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8b**).

Compound **8b** was obtained from **6b** in 68% yield, mp 150-152° (ethyl acetate/*n*-hexane);^{1}H-nmr (deuteriochloroform): δ 9.28 (d, 1H, H-5, $J_{2,5}$ = 2.6 Hz), 8.47 (d, 1H, H-2, $J_{2,5}$ = 2.6 Hz),

7.61 (d, 2H, H-2' and H-6'), 7.33 (d, 2H, H-3' and H-5'), 4.17 (q, 2H, O-CH_2), 3.76 (q, 2H, N-CH_2), 1.89 (s, 3H, acetyl CH_3), 1.12 (t, 3H, *O*-ethyl CH_3), 1.07 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.3 (acetyl C=O), 163.3 (ethoxycarbonyl C=O), 157.4 (C-2), 155.9 (C-5), 155.8 (C-3a), 149.4 (C-7), 145.3 (C-1' and C-4'), 130.7 (C-2' and C-6'), 128.0 (C-3' and C-5'), 114.2 (C-6), 62.2 (O-CH_2), 44.2 (N-CH_2), 22.9 (acetyl CH_3), 13.7 (*O*-ethyl CH_3), 13.3 (*N*-ethyl CH_3); ms: (m/z) 353 (M^+), 312, 296, 268, 250, 222.

Anal. Calcd. for $C_{18}H_{19}N_5O_3$: C, 61.18; H, 5.42; N, 19.82. Found: C, 61.41; H, 5.33; N, 19.59.

General Procedure for the Preparation of 6-Carboxamidopyrazolo[1,5-*a*]pyrimidines **7j-l** , **9c** and 6-Carboxamido-1,2,4-triazolo[1,5-*a*]pyrimidine **8c**.

A solution of each compound **7g-i**, **9b** or **8b** (0.01 mole) in methanol saturated with ammonia (100 ml) was stirred at room temperature until tlc on silica gel (ethyl acetate) indicated that the starting material had disappeared (about 3 days). The solvent was evaporated to dryness and the residue crystallized.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-carboxamidopyrazolo[1,5-*a*]pyrimidine (**7j**).

This compound was obtained from **7g** in 69% yield, mp 244-246° (ethyl acetate); ^{1}H-nmr (deuteriochloroform) δ 8.85 (s, 1H, H-5), 8.20 (d, 1H, H-2, $J_{2,3}$ = 2.2 Hz), 7.80 (d, 2H, H-2' and H-6', J_{ortho} = 8.0 Hz), 7.41 (d, 2H, H-3' and H-5', J_{ortho} = 8.0 Hz), 6.84 (d, 1H, H-3, $J_{2,3}$ = 2.2 Hz), 6.12 (bs, 1H, $CONH_2$), 5.87 (bs, 1H, $CONH_2$), 3.81 (q, 2H, N-CH_2), 1.97 (bs, 3H, acetyl CH_3), 1.19 (t, 3H, N-ethyl CH_3); ^{13}C-nmr (deuteriochloroform) δ 169.9 (acetyl C=O), 166.4 ($CONH_2$), 149.2 (C-5), 149.1 (C-3a), 147.0 (C-2), 145.6 (C-7), 145.3 (C-4'), 131.4 (C-2' and C-6'), 128.8 (C-3' and C-5'), 128.4 (C-1'), 115.9 (C-6), 98.4 (C-3), 44.8 (N-CH_2), 23.2 (acetyl CH_3), 13.7 (N-ethyl CH_3); ms: (m/z) 323 (M^+), 280, 266, 249, 221.

Anal. Calcd. for $C_{17}H_{17}N_5O_2$: C, 63.14; H, 5.30; N, 21.66. Found: C, 62.96; H, 5.29; N, 21.76.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-carboxamido-3-cyanopyrazolo[1,5-*a*]pyrimidine (**7k**).

This compound was obtained from **7h** in 81% yield, mp 287-290° (methanol); ^{1}H-nmr (deuteriochloroform) δ 11.70 (bs, 1H, $CONH_2$), 10.68 (bs, 1H, $CONH_2$), 8.25 (s, 1H, H-5), 7.87 (s, 1H, H-2), 7.77 (d, 2H, H-2' and H-6'), 7.54 (d, 2H, H-3' and H-5'), 3.88 (q, 2H, N-CH_2), 2.07 (bs, 3H, acetyl CH_3), 1.24 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform) δ 174.9 ($CONH_2$), 168.4 (acetyl C=O), 158.1 (C-5), 157.5 (C-3a), 153.8 (C-7), 145.7 (C-4' and C-2), 130.6 (C-2' and C-6'), 130.4 (C-1'), 128.2 (C-3' and C-5'), 113.5 (CN), 99.7 (C-6), 82.4 (C-3), 43.4 (N-CH_2); 22.7 (acetyl CH_3), 13.1 (N-ethyl CH_3); ms: (m/z) 348 (M^+), 306, 291, 263, 170, 161, 131.

Anal. Calcd. for $C_{18}H_{16}N_6O_2$: C, 62.06; H, 4.63; N, 24.13. Found: C, 62.12; H, 4.38; N, 23.98.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3,6-dicarboxamidopyrazolo[1,5-*a*]pyrimidine (**7l**).

This compound was obtained from **7i** in 59% yield, mp >300° (methanol); ^{1}H-nmr (DMSO-d_6): δ 11.23 (bs, 1H, $CONH_2$), 10.82 (bs, 1H, $CONH_2$), 8.21 (s, 1H, H-5), 7.95 (s, 1H, H-2), 7.74 (d, 2H, H-2' and H-6'), 7.56 (d, 2H, H-3' and H-5'), 7.52 (bs, 1H, $CONH_2$), 7.32 (bs, 1H, $CONH_2$), 3.75 (q, 2H, N-CH_2), 1.86 (s, 3H, acetyl CH_3), 1.04 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (DMSO-d_6): δ 174.6 (6-$CONH_2$), 168.4 (acetyl C=O), 162.9 (3-$CONH_2$), 158.0 (C-3a), 156.5 (C-5), 148.4 (C-7), 145.5 (C-4'), 144.7 (C-2), 130.6 (C-1'), 130.5 (C-2' and C-6'), 128.2 (C-3' and C-5'), 106.6 (C-6), 98.9 (C-3), 43.4 (N-CH_2), 22.7 (acetyl CH_3), 13.1 (*N*-ethyl CH_3); ms: (m/z) 366 (M^+), 350, 338, 324, 292, 280, 265.

Anal. Calcd. for $C_{18}H_{18}N_6O_3$: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.31; H, 4.68; N, 23.15.

5-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-carboxamidopyrazolo[1,5-*a*]pyrimidine (**9c**).

This compound was obtained from **9b** in 61% yield, mp 210-213° (ethyl acetate); ^{1}H-nmr (DMSO-d_6): δ 9.28 (s, 1H, H-7), 8.32 (d, 1H, H-2, $J_{2,3}$ = 2.2 Hz), 8.20 (bs, 1H, $CONH_2$), 7.76 (d, 2H, H-2' and H-6'), 7.75 (bs, 1H, $CONH_2$), 7.39 (d, 2H, H-3' and H-5'), 6.79 (d, 1H, H-3, $J_{2,3}$ = 2.2 Hz), 3.67 (q, 2H, N-CH_2), 1.79 (bs, 3H, acetyl CH_3), 1.02 (t, 3H, N-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 170.2 (acetyl C=O), 166.6 ($CONH_2$), 159.2 (C-5), 155.2 (C-3a), 147.7 (C-2), 144.7 (C-4'), 137.0 (C-7), 130.5 (C-2' and C-6'), 130.0 (C-1'), 128.6 (C-3' and C-5'), 116.6 (C-6), 98.4 (C-3), 44.6 (N-CH_2), 23.1 (acetyl CH_3), 13.5 (*N*-ethyl CH_3); ms: (m/z) 323 (M^+), 305, 281, 266, 248, 221.

Anal. Calcd. for $C_{17}H_{17}N_5O_2$: C, 63.14; H, 5.30; N, 21.66. Found: C, 63.34; H, 5.44; N, 21.60.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-carboxamido-1,2,4-triazolo[1,5-*a*]pyrimidine (**8c**).

Compound **8c** was obtained from **8b** in 68% yield, mp 252-255° (methanol); ^{1}H-nmr (DMSO-d_6): δ 11.26 (bs, 1H, $CONH_2$), 10.93 (bs, 1H, $CONH_2$), 8.28 (s, 1H, H-5), 8.07 (s, 1H, H-2), 7.73 (d, 2H, H-2' and H-6'), 7.57 (d, 2H, H-3' and H-5'), 3.68 (q, 2H, N-CH_2), 1.87 (s, 3H, acetyl CH_3), 1.04 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (DMSO-d_6): δ 175.0 ($CONH_2$),168.5 (acetyl C=O), 159.8 (C-5), 158.3 (C-3a), 153.9 (C-2), 145.7 (C-7 and C-4'), 130.6 (C-2' and C-6'), 130.5 (C-1'), 128.3 (C-3' and C-5'), 99.7 (C-6), 43.4 (N-CH_2), 22.7 (acetyl CH_3), 13.2 (*N*-ethyl CH_3); ms: (m/z) 324 (M^+), 281, 267, 254, 239, 146, 131.

Anal. Calcd. for $C_{16}H_{16}N_6O_2$: C, 59.25; H, 4.97; N, 25.91. Found: C, 59.37; H, 5.12; N, 25.69.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-[(dimethylaminomethylene)carboxamido]-pyrazolo[1,5-*a*]pyrimidine (**10**).

A solution of **7f** (3.2 g, 0.01 mole) in a 1:1 mixture of *N*,*N*-dimethylformamide dimethyl acetal and ethylene glycol monomethyl ether (40 ml) was stirred at 120° for 2 hours. After cooling, the precipitate which had formed was isolated by filtration and crystallized from methanol; yield 3.0 g (79%), mp 267-270°; ^{1}H-nmr (deuteriochloroform): δ 8.79 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.78 (s, 1H, H-2), 8.70 (s, 1H, amidinic CH), 8.11 (d, 2H, H-2' and H-6'), 7.37 (d, 2H, H-3' and H-5'), 7.03 (d, 1H, H-6 $J_{5,6}$ = 4.4 Hz), 3.78 (q, 2H, N-CH_2), 3.22 (s, 3H, N-CH_3), 3.17 (s, 3H, N-CH_3), 1.92 (bs, 3H, acetyl CH_3), 1.14 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 378 (M^+), 349, 335, 307, 280, 238, 211.

Anal. Calcd. for $C_{20}H_{22}N_6O_2$: C, 63.47; H, 5.86; N, 22.21. Found: C, 63.40; H, 5.57; N, 22.39.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-(1*H*-1,2,4-triazol-3-yl)-pyrazolo[1,5-*a*]pyrimidine (**11**).

To a solution of hydrazine hydrate (0.75 g, 0.015 mole) in acetic acid (25 ml) was added compound **10** (3.8 g, 0.01 mole). The reaction mixture was stirred at 90° for 2 hours, then evaporated under reduced pressure. The resulting solid was suspended in a sodium

carbonate solution, collected by filtration, washed with water and finally crystallized from methanol; yield 2.3 g (66%), mp 292-295°; ^{1}H-nmr (deuteriochloroform): δ 8.80 (s, 1H, H-2), 8.71 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.17 (d, 2H, H-2' and H-6'), 8.06 (s, 1H, triazole CH), 7.40 (d, 2H, H-3' and H-5'), 7.11 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 3.81 (q, 2H, N-CH_2), 1.94 (bs, 3H, acetyl CH_3), 1.16 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.8 (C=O), 151.1 (C-5), 150.6 (triazole C-5), 149.1 (C-3a), 147.3 (triazole C-3), 147.0 (C-7), 146.2 (C-4'), 143.6 (C-2), 131.1 (C-2' and C-6'), 129.4 (C-1'), 128.8 (C-3' and C-5'), 108.8 (C-6), 99.8 (C-3), 44.6 (N-CH_2), 23.3 (acetyl CH_3), 13.6 (*N*-ethyl CH_3); ms: (m/z) 347 (M^+), 305, 290, 248, 208.

Anal. Calcd. for $C_{18}H_{17}N_7O$: C, 62.23; H, 4.93; N, 28.23. Found: C, 62.38; H, 4.69; N, 28.18.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-[(*N*-hydroxy)carboxyimidamido]-pyrazolo[1,5-*a*]pyrimidine (**12**).

To a stirred suspension of potassium carbonate (5.6 g, 0.04 mole) and **7e** (6 g, 0.02 mole) in 10% aqueous ethanol (80 ml) hydroxylamine hydrochloride (2 g, 0.03 mole) was added. The reaction mixture was heated at reflux for 2 hours, then stirred overnight at room temperature. The precipitate which had formed was isolated by filtration, washed with water, then crystallized from ethanol; yield 3.5 g (52%), mp 266-269°; ^{1}H-nmr (DMSO-d_6): δ 9.38 (s, 1H, NOH), 8.68 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.42 (s, 1H, H-2), 8.20 (d, 2H, H-2' and H-6'), 7.54 (d, 2H, H-3' and H-5'), 7.35 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 6.02 (bs, 2H, NH_2), 3.72 (q, 2H, N-CH_2), 1.86 (bs, 3H, acetyl CH_3), 1.04 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 338 (M^+), 305, 248.

Anal. Calcd. for $C_{17}H_{18}N_6O_2$: C, 60.34; H, 5.36; N, 24.84. Found: C, 60.60; H, 5.18; N, 24.58.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-(5-methyl-1,2,4-oxadiazol-3-yl)-pyrazolo[1,5-*a*]pyrimidine (**13**).

To a stirred mixture of **12** (3.4 g, 0.01 mole) in glacial acetic acid (30 ml) a solution of acetic anhydride (1.5 g, 0.015 mole) in glacial acetic acid (10 ml) was dropwise added. The mixture was refluxed for 1 hour, cooled, poured into ice water and extracted with ethyl acetate. The organic phase was washed with 20% sodium carbonate solution and then water. The residue obtained after solvent evaporation was crystallized from ethyl acetate; yield g 1.7 (47%), mp 214-216°; ^{1}H-nmr (deuteriochloroform): δ 8.81 (d, 1H, H-5, $J_{5,6}$ = 4.4 Hz), 8.71 (s, 1H, H-2), 8.14 (d, 2H, H-2' and H-6'), 7.38 (d, 2H, H-3' and H-5'), 7.08 (d, 1H, H-6, $J_{5,6}$ = 4.4 Hz), 3.79 (q, 2H, N-CH_2), 2.68 (s, 3H, oxadiazole CH_3), 1.93 (bs, 3H, acetyl CH_3), 1.15 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 176.6 (oxadiazole C-5), 169.8 (C=O), 162.8 (oxadiazole C-3), 151.7 (C-5), 147.5 (C-3a), 146.8 (C-7), 145.9 (C-4'), 145.0 (C-2), 131.1 (C-2' and C-6'), 129.9 (C-1'), 128.7 (C-3' and C-5'), 109.0 (C-6), 99.4 (C-3), 44.6 (N-CH_2), 23.2 (acetyl CH_3), 13.6 (*N*-ethyl CH_3), 12.8 (oxadiazole CH_3); ms: (m/z) 362 (M^+), 320, 305, 263, 248, 209, 182.

Anal. Calcd. for $C_{19}H_{18}N_6O_2$: C, 62.97; H, 5.01; N, 23.19. Found: C, 63.10; H, 5.22; N, 22.98.

4-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-2-aminopyrimidine (**14a**).

4-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-2-amino-5-ethoxycarbonylpyrimidine (**14b**).

To a solution of sodium ethoxide in anhydrous ethanol (60 ml), prepared from sodium (1.0 g, 0.04 mole), guanidine hydrochloride (3.8 g, 0.04 mole) was added followed by a solution of each compound **6** (0.04 mole) in anhydrous ethanol (100 ml). The reaction mixture was refluxed for 4 hours, evaporated under reduced pressure and the residue treated with water (200 ml). The crystalline precipitate was isolated by filtration and crystallized.

Compound **14a** was obtained from **6a** in 60% yield, mp 165-167° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.33 (d, 1H, H-6, $J_{5,6}$ = 5.2 Hz), 8.00 (d, 2H, H-2' and H-6'), 7.22 (d, 2H, H-3' and H-5'), 6.98 (d, 1H, H-5, $J_{5,6}$ = 5.2 Hz), 5.39 (s, 2H, NH_2), 3.73 (q, 2H, N-CH_2), 1.82 (s, 3H, acetyl CH_3), 1.07 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 256 (M^+), 214, 199, 186, 170.

Anal. Calcd. for $C_{14}H_{16}N_4O$: C, 65.60; H, 6.29; N, 21.86. Found: C, 65.61; H, 6.18; N, 21.57.

Compound **14b** was obtained from **6b** in 75% yield, mp 202-204° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.86 (s, 1H, H-6), 7.56 (d, 2H, H-2' and H-6'), 7.20 (d, 2H, H-3' and H-5'), 5.66 (s, 2H, NH_2), 4.14 (q, 2H, O-CH_2), 3.75 (q, 2H, N-CH_2), 1.86 (s, 3H, acetyl CH_3), 1.10 (t, 6H, *O*-ethyl CH_3 and *N*-ethyl CH_3); ms: (m/z) 328 (M^+), 286, 271.

Anal. Calcd. for $C_{17}H_{20}N_4O_3$: C, 62.18; H, 6.14; N, 17.06. Found: C, 62.02; H, 6.30; N, 17.04.

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-imidazo[1,2-*a*]pyrimidine (**3a**).

7-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-6-ethoxycarbonylimidazo[1,2-*a*]pyrimidine (**3b**).

A mixture of bromoacetaldehyde dimethyl acetal (3.4 g, 0.02 mole), anhydrous sodium acetate (1.65 g, 0.02 mole) and the appropriate **14** (0.01 mole) in glacial acetic acid (15 ml) was stirred and refluxed for 20 hours, then poured into a saturated aqueous sodium carbonate solution (200 ml) and extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography over alumina using 5% methanol in ethyl acetate as eluent.

Compound **3a** was obtained from **14a** in 38% yield, mp 200-202° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 8.50 (d, 1H, H-5, $J_{5,6}$ = 7.0 Hz), 8.22 (d, 2H, H-2' and H-6'), 7.82 (d, 1H, H-2, $J_{2,3}$ = 1.6 Hz), 7.55 (d, 1H, H-3, $J_{2,3}$ = 1.6 Hz), 7.36 (d, 1H, H-6, $J_{5,6}$ = 7.0 Hz), 7.29 (d, 2H, H-3' and H-5'), 3.77 (q, 2H, N-CH_2), 1.87 (s, 3H, acetyl CH_3), 1.12 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.9 (C=O), 155.9 (C-8a), 148.8 (C-7), 145.1 (C-4'), 136.5 (C-1'), 136.1 (C-2), 133.9 (C-5), 128.8 (C-2', C-3', C-5' and C-6'), 111.0 (C-3), 106.3 (C-6), 44.2 (N-CH_2), 23.2 (acetyl CH_3), 13.5 (*N*-ethyl CH_3); ms: (m/z) 280 (M^+), 238, 223, 211, 194.

Anal. Calcd. for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.82; H, 6.01; N, 19.67.

Compound **3b** was obtained from **14b** in 32% yield, mp 150-152° (ethyl acetate/n-hexane);^{1}H-nmr (deuteriochloroform): δ 9.17 (s, 1H, H-5), 7.92 (d, 1H, H-2, $J_{2,3}$ = 1.8 Hz), 7.73 (d, 1H, H-3, $J_{2,3}$ = 1.8 Hz), 7.68 (d, 2H, H-2' and H-6'), 7.25 (d, 2H, H-3' and H-5'), 4.25 (q, 2H, O-CH_2), 3.78 (q, 2H, N-CH_2), 1.89 (s, 3H, acetyl CH_3), 1.16 (t, 3H, *O*-ethyl CH_3), 1.12 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.9 (acetyl C=O), 165.0 (ethoxycarbonyl C=O), 157.5 (C-8a), 148.0 (C-7), 144.1 (C-4'), 138.3 (C-1'), 138.1 (C-2), 137.8 (C-5), 130.3 (C-2' and C-6'), 127.9 (C-3' and C-5'), 114.2 (C-6), 111.7 (C-3), 62.3 (O-CH_2), 44.3 (N-CH_2), 23.2 (acetyl CH_3), 14.1 (*O*-ethyl CH_3), 13.4 (*N*-ethyl CH_3); ms: (m/z) 352 (M^+), 310, 295, 281, 267, 237, 221.

Anal. Calcd. for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90. Found: C, 64.74; H, 5.91; N, 15.69.

3-Cyano-6-[4-(*N*-formyl)aminophenyl]pyrazolo[1,5-*a*]pyrimidine (**17**).

Anhydrous dimethylformamide (7.3 g, 0.1 mole) was dropwise added with vigorous stirring to phosphorus oxychloride (8 ml, 0.087 mole) maintaining the temperature at about 30° by intermittent cooling. After the addition was complete, the mixture was stirred for 5 minutes, then a solution of 4-acetamidophenylacetic acid (**15**) (7.7 g, 0.04 mole) in dimethylformamide (20 ml) was added over a period of 5 minutes. The mixture was stirred and heated at 70° overnight, then poured into crushed ice (100 g) and first neutralized by addition of potassium carbonate then made strongly alkaline by 40% aqueous sodium hydroxide, maintaining the temperature at about 50°. After evolution of dimethylamine ceased, the mixture was cooled and extracted with ethyl acetate. Evaporation of the solvent gave crude compound **16** as a viscous dark red oil (4.7 g, 54%) which could not be purified by chromatography because of its instability. Moreover its spectral data were consistent with the proposed structure: ^{1}H-nmr (deuteriochloroform): δ 9.32 (s, 1H, aldehydic CHO), 8.96 (s, 1H, ethylenic CH), 8.17 (s, 1H, N-CHO), 7.39 (d, 2H, aryl protons), 6.99 (d, 2H, aryl protons), 6.84 (bs, 1H, NH), 2.53 and 1.96 (two s in a 2:1 ratio, 6H, $N(CH_3)_2$); ms: (m/z) 218 (M^+).

A mixture of crude **16** (4.4 g, 0.02 mole) and 3-amino-4-cyanopyrazole (2.2 g, 0.02 mole) in acetic acid was refluxed for 2 hours. After cooling the precipitate which had formed was collected by filtration, washed with methanol and dried to provide 2.1 g (40%) of **17**; mp 303-307°; ^{1}H-nmr (DMSO-d_6): δ 10.38 (bs, 1H, NH), 9.63 (s, 1H, H-7), 9.21 (s, 1H, H-5), 8.80 (s, 1H, N-CHO), 8.32 (s, 1H, H-2), 7.84 (d, 1H, H-3' and H-5'), 7.73 (H-2' and H-6'); ^{13}C-nmr (DMSO-d_6): δ 160.5 (N-CHO), 153.7 (C-5), 149.1 (C-3a), 148.8 (C-2), 139.5 (C-4'), 134.4 (C-7), 128.4 (C-2' and C-6'), 128.0 (C-1'), 124.5 (C-6), 120.3 (C-3' and C-5'), 114.0 (CN), 81.5 (C-3); ms: (m/z) 263 (M^+), 235, 207, 180, 148, 117.

Anal. Calcd. for $C_{14}H_9N_5O$: C, 63.87; H, 3.45; N, 26.61. Found: C, 63.62; H, 3.38; N, 26.31.

3-Cyano-6-[4-(*N*-ethyl-*N*-formyl)aminophenyl]pyrazolo[1,5-*a*]-pyrimidine (**18**).

Compound **17** (5.3 g, 0.02 mole) dissolved in anhydrous dimethylformamide (50 ml) was added over 10 minutes to a cooled and stirred suspension of sodium hydride (1 g, 50% oil dispersion, 0.022 mole) in dimethylformamide (50 ml). The mixture was allowed to warm to room temperature and stirred for 1 hour. It was then cooled in an ice water bath and ethyl iodide (1.6 ml, 0.02 mole) was dropwise added. The mixture was stirred at room temperature for 3 hours, then carefully diluted with ice water. The precipitate was collected by filtration, washed with water, dried and crystallized from ethyl acetate; yield 4.0 g (69%), mp 248-251°; ^{1}H-nmr (DMSO-d_6): δ 9.73 (d, 1H, H-7, $J_{5,7}$ = 2.2 Hz), 9.25 (d, 1H, H-5, $J_{5,7}$ = 2.2 Hz), 8.84 (s, 1H, CHO), 8.51 (s, 1H, H-2), 7.95 (d, 2H, H-3' and H-5'), 7.52 (d, 2H, H-2' and H-6'), 3.85 (q, 2H, N-CH_2), 1.07 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 291 (M^+), 263, 248, 236, 220, 165, 124.

Anal. Calcd. for $C_{16}H_{13}N_5O$: C, 65.97; H, 4.50; N, 24.04. Found: C, 66.00; H, 4.33; N, 23.80.

3-Cyano-6-[4-(*N*-ethyl)aminophenyl]-pyrazolo[1,5-*a*]pyrimidine (**19**).

A solution of **18** (2.9 g, 0.01 mole) in methanol (50 ml) containing concentrated hydrochloric acid (12 ml) was refluxed for 5 hours. After cooling the solvent was removed and the residue suspended in a saturated sodium carbonate solution (120 ml), filtered, washed with water then crystallized from ethyl acetate/*n*-hexane; yield 2.2 g (84%), mp 218-221°; ^{1}H-nmr (deuteriochloroform): δ 8.93 (d, 1H, H-7, $J_{5,7}$ = 2.2 Hz), 8.77 (d, 1H, H-5, $J_{5,7}$ = 2.2 Hz), 8.34 (s, 1H, H-2), 7.38 (d, 2H, H-2' and H-6'), 6.70 (d, 2H, H-3' and H-5'), 3.96 (bs, 1H, NH), 3.21 (q, 2H, N-CH_2), 1.28 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 153.6 (C-5), 149.9 (C-3a), 148.1 (C-2), 139.0 (C-4'), 131.8 (C-7), 128.6 (C-2' and C-6'), 126.5 (C-1'), 121.0 (C-6), 114.0 (C-3' and C-5'), 113.4 (CN), 83.5 (C-3), 38.9 (N-CH_2), 15.4 (*N*-ethyl CH_3); ms: (m/z) 263 (M^+), 248, 235, 165, 125.

Anal. Calcd. for $C_{15}H_{13}N_5$: C, 68.42; H, 4.98; N, 26.60. Found: C, 68.71; H, 4.73; N, 26.32.

6-[4-(*N*-Acetyl-*N*-ethyl)aminophenyl]-3-cyanopyrazolo[1,5-*a*]-pyrimidine (**20**).

A solution of **19** (2.6 g, 0.01 mole) in a mixture of acetic anhydride (100 ml) and glacial acetic acid (50 ml) was heated at 80° for 2 hours. After cooling, the mixture was poured into ice water and the precipitate filtered, washed with water, dried and crystallized from ethyl acetate; yield 2.6 g (85%), mp 186-188°; ^{1}H-nmr (deuteriochloroform): δ 8.98 (d, 1H, H-7, $J_{5,7}$ = 2.2 Hz), 8.92 (d, 1H, H-5, $J_{5,7}$ = 2.2 Hz), 8.42 (s, 1H, H-2), 7.65 (d, 2H, H-3' and H-5'), 7.36 (d, 2H, H-2' and H-6'), 3.78 (q, 2H, N-CH_2), 1.89 (bs, 3H, acetyl CH_3), 1.14 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 170.3 (C=O), 153.2 (C-5), 149.6 (C-3a), 148.7 (C-2), 144.7 (C-4'), 133.7 (C-7), 132.7 (C-1'), 130.2 (C-2' and C-6'), 129.1 (C-3' and C-5'), 125.0 (C-6), 113.0 (CN), 84.1 (C-3), 44.8 (N-CH_2), 23.6 (acetyl CH_3), 13.9 (*N*-ethyl CH_3); ms: (m/z) 305 (M^+), 263, 248, 235, 220, 165.

Anal. Calcd. for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.70; H, 5.23; N, 22.68.

6-[(*N*-Acetyl-*N*-ethyl)amino]-1-tetralone (**21**).

Part a) 6-[(*N*-acetyl-*N*-ethyl)amino]-1,2,3,4-tetrahydronaphtalene.

This compound was obtained in 70% yield by *N*-ethylation of the corresponding 6-acetamido derivative [20], according to the same procedure previously described for the preparation of 1-[(*N*-acetyl-*N*-ethyl)aminophenyl]ethanone (**5a**): mp: 45-46° (cyclohexane); ^{1}H-nmr (deuteriochloroform): δ: 7.04 (d, 1H, H-7), 6.80 (d and s, 2H, H-8 and H-5), 3.67 (q, 2H, N-CH_2), 2.73 (um, 4H, H-1 and H-4), 1.78 (s and um, 7H, acetyl CH_3, H-2 and H-3), 1.06 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 217 (M^+), 175, 160, 147, 132.

Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.40; H, 8.99; N, 6.18.

Part b)

To a solution of the above reported tetraline (6.5 g, 0.03 mole) in acetic acid (15 ml) and acetic anhydride (5 ml) was dropwise added a solution of chromium trioxide (4.5 g, 0.045 mole) in water (5 ml) and acetic acid (15 ml), maintaining the temperature below 10° by external cooling. After stirring overnight, the solution was poured into ice water and extracted with dichloromethane. The solvent was removed and the residue chromatographed on a silica gel column by eluting with ethyl acetate; yield 3.6 g (52%), viscous oil; ^{1}H-nmr (deuteriochloroform): δ 8.05 (d, 1H, H-8), 7.06 (d, 1H, H-7), 7.04 (s, 1H, H-5), 3.73 (q, 2H, N-CH_2), 2.96 (t, 2H, H-2), 2.65 (t, 2H, H-4), 2.14 (quintet, 2H, H-3), 1.86 (s, 3H, acetyl CH_3), 1.09 (t, 3H, *N*-ethyl CH_3); ms: (m/z) 231 (M^+), 189, 174, 161, 145, 133, 115.

Anal. Calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.52; H, 7.68; N, 6.00.

General Procedure for the Preparation of the Tetracyclic Compounds **4a-d** and **23**.

A solution of **21** (11.6 g, 0.05 mole) in *N*,*N*-dimethylformamide dimethyl acetal (60 ml) was refluxed for 8 hours. The reaction was monitored by tlc (silica gel, ethyl acetate). The solvent was removed under reduced pressure and the crude enaminone derivative **22** was immediately condensed with 3-aminopyrazole (to obtain **4a** and **23**), 3-amino-4-cyanopyrazole (to obtain **4b**), 3-amino-4-carboxamidopyrazole (to obtain **4c**) or 3-amino-1,2,4-triazole (to obtain **4d**) (0.05 mole) in refluxing glacial acetic acid (80 ml) for 3 hours. After cooling the solvent was evaporated and the residue purified by chromatography on silica gel with ethyl acetate. Isomers **4a** and **23** were separated by column chromatography using ethyl acetate as eluent. Compound **4a** was eluted first followed by the isomer **23.** The yields of all compounds have been calculated from starting tetralone **21**.

9-[(*N*-Acetyl-*N*-ethyl)amino]-6,7-dihydro-benzo[*h*]pyrazolo[1,5-*a*]-quinazoline (**4a**).

This compound was obtained by condensation of **21** with 3-aminopyrazole in 34% yield; mp 174-175° (ethyl acetate/*n*-hexane); ^{1}H-nmr (deuteriochloroform): δ 9.50 (d, 1H, H-11, $J_{10,11}$ = 8.4 Hz), 8.45 (s, 1H, H-5), 8.19 (d, 1H, H-2, $J_{2,3}$ = 2.4 Hz), 7.27 (dd, 1H, H-10, $J_{10,11}$ = 8.4 Hz, $J_{8,10}$ = 2.2 Hz), 7.17 (d, 1H, H-8, $J_{8,10}$ = 2.2 Hz), 6.78 (d, 1H, H-3, $J_{2,3}$ = 2.4 Hz), 3.81 (q, 2H, N-CH_2), 3.02 (s, 4H, H-6 and H-7), 1.94 (s, 3H, acetyl CH_3), 1.16 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.8 (C=O), 150.1 (C-3a), 149.3 (C-5), 145.0 (C-11b), 144.2 (C-2), 141.8 (C-9), 138.9 (C-7a), 130.7 (C-11), 127.6 (C-8), 126.7 (C-10), 126.3 (C-11a), 117.1 (C-5a), 97.2 (C-3), 44.3 (N-CH_2), 28.8 (C-7), 24.1 (C-6), 23.2 (acetyl CH_3), 13.6 (*N*-ethyl CH_3); ms: (m/z) 306 (M^+), 278, 264, 249, 236, 231, 189, 174, 161, 115.

Anal. Calcd. for $C_{18}H_{18}N_4O$: C, 70.56; H, 5.92; N, 18.29. Found: C, 70.30; H, 5.98; N, 18.02.

9-[(*N*-Acetyl-*N*-ethyl)amino]-3-cyano-6,7-dihydro-benzo[*h*]-pyrazolo[1,5-*a*]quinazoline (**4b**).

This compound was obtained by condensation of **21** with 3-amino-4-cyanopyrazole in 62% yield; mp 224-227° (methanol); ^{1}H-nmr (DMSO-d_6): δ 9.18 (d, 1H, H-11, $J_{10,11}$ = 8.4 Hz), 8.88 (s, 1H, H-5), 8.84 (s, 1H, H-2), 7.46 (s, 1H, H-8), 7.43 (d, 1H, H-10, $J_{10,11}$ = 8.4 Hz), 3.71 (q, 2H, N-CH_2), 3.02 (s, 4H, H-6 and H-7), 1.87 (s, 3H, acetyl CH_3), 1.04 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (DMSO-d_6): δ 168.4 (C=O), 153.5 (C-5), 150.6 (C-3a), 146.8 (C-2), 145.4 (C-11b), 142.4 (C-9), 139.9 (C-7a), 130.1 (C-11), 127.5 (C-8), 125.9 (C-10), 123.8 (C-11a), 120.5 (C-5a), 113.5 (CN), 80.9 (C-3), 43.3 (N-CH_2), 27.1 (C-7), 22.9 (C-6), 22.7 (acetyl CH_3), 13.2 (*N*-ethyl CH_3); ms: (m/z) 331 (M^+), 289, 274, 245, 218, 191, 140, 127.

Anal. Calcd. for $C_{19}H_{17}N_5O$: C, 68.86; H, 5.17; N, 21.14. Found: C, 68.68; H, 5.38; N, 21.08.

9-[(*N*-Acetyl-*N*-ethyl)amino]-3-carboxamido-6,7-dihydrobenzo-[*h*]pyrazolo[1,5-*a*]quinazoline (**4c**).

This compound was obtained by condensation of **21** with 3-amino-4-carboxamidopyrazole in 70% yield; mp >300° (methanol); ^{1}H-nmr (deuteriochloroform): δ 9.45 (d, 1H, H-11, $J_{10,11}$ = 8.4 Hz), 8.75 (s, 1H, H-5), 8.60 (s, 1H, H-2), 8.08 (bs, 1H, $CONH_2$), 7.31 (dd, 1H, H-10, $J_{10,11}$ = 8.4 Hz, $J_{8,10}$ = 2.2 Hz), 7.21 (d, 1H, H-8, $J_{8,10}$ = 2.2 Hz), 6.10 (bs, 1H, $CONH_2$), 3.83 (q, 2H, N-CH_2), 3.08 (s, 4H, H-6 and H-7), 1.97 (s, 3H, acetyl CH_3), 1.18 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 170.2 (acetyl C=O), 164.8 ($CONH_2$), 151.6 (C-5), 148.2 (C-3a), 146.8 (C-2), 146.4 (C-11b), 142.7 (C-9), 141.0 (C-7a), 131.8 (C-11), 128.2 (C-8), 127.3 (C-10), 125.7 (C-11a), 119.1 (C-5a), 105.3 (C-3), 44.8 (N-CH_2), 29.0 (C-7), 24.6 (C-6), 23.7 (acetyl CH_3), 14.1 (*N*-ethyl CH_3); ms: (m/z) 349 (M^+), 333, 307, 292, 275, 263, 247, 219.

Anal. Calcd. for $C_{19}H_{19}N_5O_2$: C, 65.31; H, 5.48; N, 20.05. Found: C, 65.05; H, 5.77; N, 20.05.

9-[(*N*-Acetyl-*N*-ethyl)amino]-6,7-dihydrobenzo[*h*]1,2,4-triazolo[1,5-*a*]quinazoline (**4d**).

This compound was obtained by condensation of **21** with 3-amino-1,2,4-triazole in 54% yield; mp 146-148° (methanol); ^{1}H-nmr (deuteriochloroform): δ 9.34 (d, 1H, H-11, $J_{10,11}$ = 8.6 Hz), 8.76 (s, 1H, H-5), 8.56 (s, 1H, H-2), 7.29 (dd, 1H, H-10, $J_{10,11}$ = 8.6 Hz, $J_{8,10}$ = 2.4 Hz), 7.21 (d, 1H, H-8, $J_{8,10}$ = 2.4 Hz), 3.79 (q, 2H, N-CH_2), 3.09 (s, 4H, H-6 and H-7), 1.94 (s, 3H, acetyl CH_3), 1.15 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 169.7 (C=O), 156.1 (C-3a), 155.5 (C-2), 154.7 (C-5), 146.1 (C-11b), 141.9 (C-9), 140.8 (C-7a), 131.1 (C-11), 127.9 (C-8), 127.0 (C-10), 125.2 (C-11a), 119.3 (C-5a), 44.4 (N-CH_2), 28.5 (C-7), 23.9 (C-6), 23.2 (acetyl CH_3), 13.7 (*N*-ethyl CH_3); ms: (m/z) 307 (M^+), 265, 250, 221, 174, 140.

Anal. Calcd. for $C_{17}H_{17}N_5O$: C, 66.43; H, 5.58; N, 22.79. Found: C, 66.35; H, 5.81; N, 22.58.

3-[(*N*-Acetyl-*N*-ethyl)amino]-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]-quinazoline (**23**).

This compound was obtained by condensation of **21** with 3-aminopyrazole in 30% yield; mp 125-127° (ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 9.40 (d, 1H, H-4, $J_{2,4}$ = 2.2 Hz), 8.45 (s, 1H, H-7), 8.19 (d, 1H, H-10, $J_{10,11}$ = 2.6 Hz), 7.41 (d, 1H, H-1, $J_{1,2}$ = 7.8 Hz), 7.26 (dd, 1H, H-2, $J_{1,2}$ = 7.8 Hz, $J_{2,4}$ = 2.2 Hz), 6.78 (d, 1H, H-11, $J_{10,11}$ = 2.6 Hz), 3.84 (q, 2H, N-CH_2), 3.03 (s, 4H, H-5 and H-6), 1.96 (s, 3H, acetyl CH_3), 1.18 (t, 3H, *N*-ethyl CH_3); ^{13}C-nmr (deuteriochloroform): δ 170.3 (C=O), 149.9 (C-12a), 149.2 (C-7), 144.3 (C-10), 141.7 (C-3), 139.4 (C-11a), 138.9 (C-4a), 130.5 (C-2), 129.6 (C-4), 129.2 (C-1), 128.1 (C-12b), 117.2 (C-6a), 97.2 (C-11), 44.2 (N-CH_2), 28.4 (C-5), 24.2 (C-6), 23.4 (acetyl CH_3), 13.4 (*N*-ethyl CH_3); ms: (m/z) 306 (M^+), 278, 264, 249, 220, 194, 166.

Anal. Calcd. for $C_{18}H_{18}N_4O$: C, 70.56; H, 5.92; N, 18.29. Found: C, 70.77; H, 5.71; N, 18.40.

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