Reactivity of 7-(2-Dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidines: Synthesis of Pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidine Derivatives as Potential Benzodiazepine Receptor Ligands. 2.

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A series of pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidin-6-ones was obtained by reaction of ammonium acetate with ethyl 7-dimethylaminovinylpyrazolo[1,5-*a*]pyrimidine-6-carboxylates and these had been prepared from ethyl 7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylates by reaction with dimethylformamide dimethylacetal. Under these conditions the compounds bearing a 2-hydroxy group were also *O*-alkylated. During the preparation of the ethyl 2-hydroxy-7-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate the corresponding 5-methyl isomer was isolated and identified.

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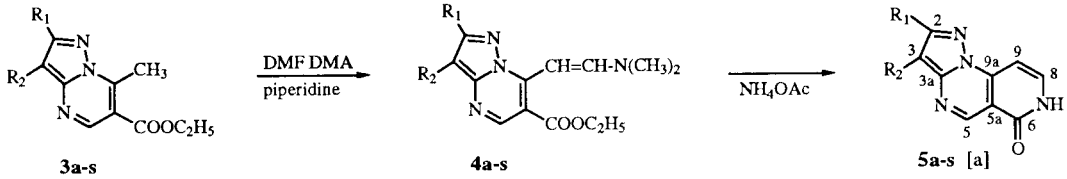
In connection with our ongoing program on the chemistry and pharmacology of pyrazolo[1,5-*a*]pyrido[3,4-*e*]-pyrimidines (as analogues of pyrazoloquinolines of the CGS series) we report here the synthesis of a number of derivatives of the former system, featured by the presence of a carbonyl function at the 6 position. Although a series of derivatives of this system has already been reported and studied [1], it seemed worthwhile to prepare an extensive series of analogues bearing various substituents on the pyrazole moiety.

Preparation of the pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidin-6-one derivatives was based upon a sequence previously described and outlined in Scheme 1 [2].

The pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidines **3a-s** depicted in Scheme 1 were prepared by reaction of 3- and/or 4-substituted 5-aminopyrazoles **2a-s** according to a

Scheme 1



3a-s **4a-s** **5a-s** [a]

3a	$R_1 = H$	$R_2 = H$	**4a**	$R_1 = H$	$R_2 = H$
3b	$R_1 = CH_3$	$R_2 = H$	**4b**	$R_1 = CH_3$	$R_2 = H$
3c	$R_1 = HC(CH_3)_2$	$R_2 = H$	**4c**	$R_1 = HC(CH_3)_2$	$R_2 = H$
3d	$R_1 = C(CH_3)_3$	$R_2 = H$	**4d**	$R_1 = C(CH_3)_3$	$R_2 = H$
3e	$R_1 = C_6H_5$	$R_2 = H$	**4e**	$R_1 = C_6H_5$	$R_2 = H$
3f	R_1 = 2-thienyl	$R_2 = H$	**4f**	R_1 = 2-thienyl	$R_2 = H$
3g	$R_1 = OH$	$R_2 = H$	**4h**	$R_1 = OCH_3$	$R_2 = H$
3h	$R_1 = OCH_3$	$R_2 = H$			
3i	$R_1 = OCH_2C_6H_5$	$R_2 = H$	**4i**	$R_1 = OCH_2C_6H_5$	$R_2 = H$
3j	$R_1 = H$	$R_2 = COOC_2H_5$	**4j**	$R_1 = H$	$R_2 = COOC_2H_5$
3k	$R_1 = H$	$R_2 = CN$	**4k**	$R_1 = H$	$R_2 = CN$
3l	$R_1 = H$	$R_2 = C_6H_5$	**4l**	$R_1 = H$	$R_2 = C_6H_5$
3m	$R_1 = H$	$R_2 = 3\text{-}OCH_3C_6H_4$	**4m**	$R_1 = H$	$R_2 = 3\text{-}OCH_3C_6H_4$
3n	$R_1 = H$	$R_2 = 3\text{-}ClC_6H_4$	**4n**	$R_1 = H$	$R_2 = 3\text{-}ClC_6H_4$
3o	$R_1 = H$	R_2 = 2-thienyl	**4o**	$R_1 = H$	R_2 = 2-thienyl
3p	$R_1 = H$	R_2 = 3-thienyl	**4p**	$R_1 = H$	R_2 = 3-thienyl
3q	$R_1 = HC(CH_3)_2$	$R_2 = CH_3$	**4q**	$R_1 = HC(CH_3)_2$	$R_2 = CH_3$
3r	$R_1 = OH$	$R_2 = C_6H_5$	**4r**	$R_1 = OCH_3$	$R_2 = C_6H_5$
3s	$R_1 = OH$	R_2 = tiadiazolyl	**4s**	$R_1 = OCH_3$	R_2 = tiadiazolyl

[a] For compounds **5a-s** R_1, R_2 are specified in Table I.

reported method [3-4]. The synthesis of 3- and/or 4-substituted 5-aminopyrazoles **2m-p** was hitherto unreported and their preparation was performed by reaction of 3-oxopropanenitriles **1m-p** with hydrazine hydrate according to a standard procedure as described in the Experimental.

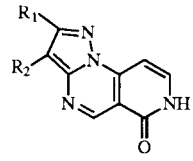
The following reaction with ethyl ethoxymethylenacetoacetate runs smoothly in high yield leading to ethyl 2- and/or 3-substituted-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylates **3a-s**. We have already pointed out the unambiguous mode of cyclization [5]. Yet, from 3-amino-4-phenylpyrazolidin-5-one a mixture of ethyl 7-methyl-2-oxo-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3r**) and ethyl 5-methyl-2-oxo-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3r'**) was obtained. The two compounds were separated by column chromatography and identified by comparison of their nmr spectral data. In fact, the regioisomers could be easily distinguished on the basis of the carbon chemical shift of the methyl groups, since **3r** exhibits a diagnostic upfield signal (δ 15.2), due to 7-methyl group, while the signal lying at a higher frequency (δ 25.7) can be reasonably attributed to the 5-methyl group of **3r'** [6].

Moreover, as regards the proton spectrum, in accordance with our previous findings which pointed out chemical shift values of H-5 and H-7, the downfield signal is to be attributed to H-7. To our knowledge this is the first example of a synthesis of a pyrazolo[1,5-*a*]pyrimidine, where the ketone carbonyl group of ethyl ethoxymethyleneacetoacetate reacts with 3(5)-aminopyrazoles as readily as the ethoxymethylene moiety.

As it appears in Scheme 1 the subsequent step is represented by the reaction of **3a-s** with DMF-DMA from which the corresponding 7-dimethylaminovinyl derivatives **4a-s** were obtained. The 2-hydroxy derivatives **3g, 3r, 3s** underwent simultaneous *O*-methylation giving 2-methoxy-7-dimethylaminovinyl derivatives **4h, 4r, 4s**. Compound **4h** was isolated with difficulty and in low yield. In order to circumvent this practical limitation, compound **3g** was alkylated *via* a classical procedure and the 2-methoxy intermediate obtained was subsequently reacted with DMF-DMA.

Table I

Physical Data of 7*H*-Pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidin-6-ones **5a-s**



Compound	R_1	R_2	Molecular Formula (% yield)	Mp (°C)	Crystalization Solvent	Elemental Analysis (Calcd./Found) C	H	N
5a [2]	H	H	$C_9H_6N_4O$ (59)	>300	ethanol	58.06/58.05	3.24/3.18	30.09/30.12
5b	CH_3	H	$C_{10}H_8N_4O$ (50)	>300	ethanol/water	58.89/59.16	4.02/4.02	27.98/27.77
5c	$HC(CH_3)_2$	H	$C_{12}H_{12}N_4O$ (41)	>300	ethanol	63.14/62.96	5.30/4.98	24.55/24.34
5d	$C(CH_3)_3$	H	$C_{13}H_{14}N_4O$ (42)	305	ethanol	64.44/64.60	5.82/5.48	23.12/22.95
5e	C_6H_5	H	$C_{15}H_{10}N_4O$ (69)	>300	ethanol	68.69/68.70	3.84/3.96	21.36/21.32
5f		H	$C_{13}H_8N_4OS$ (50)	>300	ethanol	58.19/58.32	3.00/3.13	20.88/20.64
5h	OCH_3	H	$C_{10}H_8N_4O_2$ (52)	299	i.propanol	55.55/55.54	3.72/3.69	25.91/25.99
5i	OCH_2-C_6H_5	H	$C_{16}H_{12}N_4O_2$ (11)	276-277	ethanol	65.74/65.53	4.13/4.22	19.16/19.38
5j [2]	H	$COOC_2H_5$	$C_{12}H_{10}N_4O_3$ (67)	>300	ethanol	55.81/55.67	3.90/4.00	21.69/21.56
5k	H	CN	$C_{10}H_5N_5O$ (60)	>300	DMF	56.87/56.70	2.38/2.43	33.16/33.31
5l	H	C_6H_5	$C_{15}H_{10}N_4O$ (67)	>300	DMF	68.69/68.53	3.84/3.96	21.36/20.96
5m	H	3-$OCH_3C_6H_4$	$C_{16}H_{12}N_4O_2$ (63)	238	ethanol	65.74/65.78	4.13/4.09	19.16/19.32
5n	H	3-ClC_6H_4	$C_{15}H_9N_4OCl$ (59)	>300	AcOH	60.72/60.75	3.05/2.91	18.88/18.79
5o	H		$C_{13}H_8N_4OS$ (55)	263-264	AcOH	58.19/58.11	3.00/2.83	20.88/20.82
5p	H		$C_{13}H_8N_4S$ (56)	>300	AcOH	58.19/58.04	3.00/3.30	20.88/20.48
5q	$HC(CH_3)_2$	CH_3	$C_{13}H_{14}N_4O$ (50)	>300	ethanol/water	64.44/64.58	5.82/5.88	23.12/23.15
5r	OCH_3	C_6H_5	$C_{16}H_{12}N_4O_2$ (42)	291-292	ethanol	65.74/65.53	4.13/4.24	19.16/19.00
5s	OCH_3		$C_{12}H_8N_6O_2S$ (47)	>300	AcOH	47.99/48.12	2.68/2.61	27.98/27.76

Table II

Spectral Data of 7*H* -Pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidin-6-ones **5a-s**

Compound	R_1	R_2	^{1}H-nmr Spectrum [a] [b]
5a	H	H	6.88 (d, J = 2.5 Hz, 1H, H-3), 7.01 (d, J = 7.3 Hz, 1H, H-9), 7.93 (d, J = 7.3 Hz, 1H, H-8), 8.36 (d, J = 2.5 Hz, 1H, H-2), 9.00 (s, 1H, H-5), 12.22 (s, 1H, NH exchangeable) [c]
5b	CH_3	H	3.32 (s, 3H, 2-CH_3), 6.67 (s, 1H, H-3), 7.02 (d, J = 7.0 Hz, 1H, H-9), 7.86 (d, J = 7.0 Hz, 1H, H-8), 8.92 (s, 1H, H-5), 12.12 (s, 1H, NH, exchangeable)
5c	$HC(CH_3)_2$	H	1.34 (s, 6H, $HC(CH_3)_2$), 3.14 (m, 1H, $HC(CH_3)_2$), 6.73 (s, 1H, H-3), 7.02 (d, J = 7.1 Hz, 1H, H-9), 7.86 (d, J = 5.9 Hz, 1H, H-8), 8.92 (s, 1H, H-5), 12.20 (s, 1H, NH, exchangeable [b]
5d	$C(CH_3)_3$	H	1.40, (t, 9H, $C(CH_3)_3$), 6.78 (s, 1H, H-3), 7.04 (d, 7.1 Hz, 1H, H-9), 7.85 (d, J = 7.1 Hz, 1H, H-8), 8.92 (s, 1H, H-5), 12.12 (s, 1H, NH, exchangeable)
5e	C_6H_5	H	7.16 (d, J = 7.5 Hz, 1H, H-9), 7.40 (s, 1H, H-3), 7.45-7.55 (m, 3H, ArH_3), 7.92 (d, J = 7.5 Hz, 1H, H-8), 8.14-8.18 (m, 2H, ArH_2), 8.98 (s, 1H, H-5), 12.15 (s, 1H, NH, exchangeable)
5f		H	7.15 (d, J = 7.0 Hz, 1H, H-9),7.22-7.30 (m, 2H; 1H, thienyl, 1H, H-3), 7.70-7.72 (m, 1H, thienyl), 7.81-7.83 (m, 1H, thienyl), 7.92 (d, J = 7.0 Hz, 1 H, H-8), 8.98 (s, 1 H, H-5), 12.20 (s, 1H, NH, exchangeable)
5h	OCH_3	H	3.99 (s, 3H, OCH_3), 6.32 (s, 1H, H-3), 6.87 (d, J = 5.0 Hz, 1H, H-9), 7.84 (t, J = 5.0 Hz, J = 2.0 Hz, after D_2O treatment it becomes a doublet, 1H, H-8), 8.89 (s, 1H, H-5), 12.05 bd, J = 2.0 Hz, 1H, NH exchangeable)
5i	$OCH_2C_6H_5$	CH_3	3 99 (s, 3H, OCH_3), 6.32 (s, 1H, H-3), 6.87 (d, J = 5.0 Hz, 1H, H-9), 7.84 (t, J = 5.0 Hz, J = 2.0 Hz, after D_2O treatment it becomes a doublet, 1H, H-8), 8.89 (s, 1H, H-5), 12.05 bd, J = 2.0 Hz, 1H, NH exchangeable)
5j	H	$COOC_2H_5$	1.35 (t, 3H, OCH_2CH_3), 4.36 (q, 2H, OCH_2CH_3), 7.20 (d, J = 7.6 Hz, 1H, H-9), 7.90 (d, J = 7.6 Hz, 1H, H-8), 8.72 (s, 1H, H-2), 9.21 (s, 1H, H-5), 12.40 (bs, 1H, NH exchangeable)
5k	H	CN	7.11 (d, J = 6.5 Hz, 1H, H-9), 8.04 (d, J = 6.5 Hz, 1H, H-8), 8.91 (s, 1H, H-2), 9.23 (s, 1H, H-5), 12.55 (bs, 1H, NH exchangeable)
5l	H	C_6H_5	7.07 (d, J = 7.2 Hz, 1H, H-9) 7.20-7.30 (m, 1H, ArH), 7.40-7.51 (m, 2H, ArH_2), 7.90 (d, J = 7.2 Hz, 1H, H9), 8.14-8.22 (m, 2H, ArH_2), 8.87 (s, 1H, H-2), 9.04 (s, 1H, H-5), 12.23 (bs, 1H, NH, exchangeable)
5m	H	3-$OCH_3C_6H_4$	3.83 (s, 3H, OCH_3), 6.86-6.91 (m, 1H, ArH), 7.13 (d, J = 6.5 Hz, 1H, H-9), 7.74-7.80 (m, 2H, ArH_2), 7.93 (t, J = 6.5 Hz, J = 3.0 Hz, 1H, H-8), 8.91 (s, 1H, H-2), 9.08 (s, 1H, H-5), 12.25 (bd, J = 3.0 Hz), 1H, NH, exchangeable)
5n	H	3-ClC_6H_4	3.90 (bs, 1H, OH exchangeable), 7.12 (d, J = 7.2 Hz, 1H, H-9), 7.31-7.34 (m, 1H, ArH), 7.45-7.53 (m, 1H, ArH), 7.93 (d, J = 7.2 Hz, 1H, H-8), 8.09-8.13 (m, 1H, ArH), 8.25-8.27 (m, 1H, ArH), 8.92 (s, 1H, H-2), 9.09 (s, 1H, H-5)
5o	H		7.10 (d, J = 7.12 Hz, 1H, H-9), 7.13-7.18 (m, 1H, thienyl) 7.51-7.53 (m, 1H, thienyl) 7.65, 7.67 (m, 1H, thienyl), 7.94 (t, J = 7.12 Hz, J = 2.0 Hz, 1H, H-8), 8.77 (s, 1H, H-2), 9.05 (s, 1H, H-5), 12.24 (bd, J = 2.0 Hz, 1H, NH exchangeable)
5p	H		7.12 (d, J = 7.30 Hz, 1H, H-9), 7.66-7.68 (m, 1H, thienyl) 7.85-7.88 (m, 1H, thienyl) (m, 1H, thienyl), 7.93 (d, J = 7.30 Hz, 1H, H-8), 8.06-8.08 (m, 1H, thienyl), 8.79 (s, 1H, H-2), 9.04 (s, 1H, H-5), 12.23 (bs, 1H, NH exchangeable)
5q	$HC(CH_3)_2$	CH_3	1.30 (s, 6H, $HC(CH_3)_2$), 2.30 (s, 3H, 3-CH_3), 3.15-3.30 (m, 1H, $HC(CH_3)_2$), 7.02 (d, J = 7.1 Hz, 1H, H-9), 7.80 (d, J = 7.1 Hz, 1H, H-8), 8.82 (s, 1H, H-5), 12.20 (bs, 1H, NH, exchangeable [b]
5r	OCH_3	C_6H_5	4.25 (s, 3H, OCH_3), 6.90 (d, J = 7.0 Hz, 1H, H-9), 7.24-7.28 (m, 1H, ArH), 7.40-7.47 (m, 2H, ArH_2), 7.85 (d, J = 7.0 Hz, 1H, H-8), 8.10-8.13 (m, 2H, ArH_2), 8.96 (s, 1H, H-5), 12.04 (bs, 1H, NH exchangeable)
5s	OCH_3		4.22 (s, 3H, OCH_3), 7.00 (d, J = 7.2 Hz, 1H, H-9), 7.97 (d, J = 7.2 Hz, 1H, H-8), 9.15 (s, 1H, H-5), 9.59 (s, 1H, thiadiazole), 12.26 (bs, 1H, NH exchangeable)

[a] All spectra were determined in dimethyl sulphoxide-d_6, as solvent. [b] Chemical shifts are given in ppm (δ), relative to internal tetramethylsilane; Coupling constants (J) are given in Hz; b = broad.

Surprisingly, the reaction of the latter with **3r'** afforded only ethyl 2-methoxy-5-methyl-3-phenylpyrazolo[1,5-*a*] pyrimidine-6-carboxylate (**3r''**) revealing the inertness of 5-methyl group toward the above reagent.

As was described in our previous paper [1] the 7-(2-dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidines react with excess ammonium acetate, giving with moderate to low yields a series of 2- and/or 3-substituted pyrazolo-[1,5-*a*]pyrido[3,4-*e*]pyrimidin-6-ones **5a-s**.

Compounds **5a-s** obtained together with a series of 6-methylpyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidines previously described in our paper [1] were evaluated for their ability to displace ^{3}H-flunitrazepam from bovine brain membranes [7-8]. They were tested at a concentration of 10 μ*M* in the presence of 2%, dimethyl sulphoxide as the solvent. From our results it appears that none of the tested compounds exhibit any interaction with the benzodiazepine receptor site.

Table III

^{13}C-nmr Spectral Data for Compounds **3r** and **3r'** [a]

Carbon	Compound **3r**	Compound **3r'**
C_2	165.4 (s)	166.4 (s)
C_3	94.2 (m)	93.0 (m)
C_{3a}	145.1 (m)	144.5 (m)
C_5	149.7 (d, $^1J_{C5-H5}$ = 187.1)	158.9 (dq)
C_6	109.2 (dq)	109.8 (m)
C_7	150.3 (m)	138.5 (d, $^1J_{C7-H7}$ = 188.7)
Others:	14.4 (qt, CH_2-CH_3)	15.6 (qt, CH_2-CH_3)
	15.2 (q, 7-CH_3)	25.7 (q, 5-CH_3)
	61.3 (tq, OCH_2)	61.2 (tq, OCH_2)
	125.8 (C_{meta})	126.8 (C_{meta})
	126.6 (C_{ortho})	127.0 (C_{ortho})
	128.5 (C_{para})	128.2 (C_{para})
	131.6 (C_{ipso})	131.6 (C_{ipso})
	164.7 (m, CO)	164.2 (m, CO)

[a] Chemical shifts (δ, ppm) and selected ^{n}J(C-H) values (Hz).

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The ir spectra were measured as nujol mulls with a Perkin Elmer 681 spectrophotometer. The ^{1}H and ^{13}C nmr spectra were recorded with a Varian Gemini 200 instrument; chemical shifts are reported in ppm high frequency from tetramethylsilane as secondary reference standard and coupling constants in Hz. Silica gel plates (Merck F_{254}) were used for analytical tlc. Solvents were removed under reduced pressure.

Microanalyses were performed with a Perkin Elmer Model 240 C Elemental Analyzer and values are within ± 0.4% of the theoretical values.

General Procedure for Preparing 3-Oxopropanenitriles **1m-p**.

A suspension of 50%, sodium hydride in mineral oil was added to anhydrous toluene (300 ml) in a 1 l round bottomed flask. After addition of *tert*-amyl alcohol (2 ml) the mixture was heated at 70° and a solution of a suitable acetonitrile (200 mmoles) and ethyl formate (200 mmoles, 17 ml) in anhydrous toluene (50 ml) was added dropwise in an hour. After 6 hours of stirring and heating at 70-80° the resulting solid was allowed to stand overnight. The mixture was treated with ice-water (400 ml) and the aqueous phase was separated and washed with diethyl ether. Acidification with concentrated chloridric acid causes the separation of an oil which was extracted with diethyl ether. The extracts were dried on anydrous sodium sulphate and evaporated to dryness and a brownish solid was obtained.

2-(3'-Methoxyphenyl)-3-oxopropanenitrile (**1m**).

This compound was obtained from 2,3'-methoxyphenylacetonitrile as ivory crystals from water, 32.2 g (92%), mp 100-101°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 3.78 (s, 3H, OCH_3), 6.80-6.97 (m, 3H, ArH_3), 7.24-7.33 (m, 2H, ArH_2), 7.67 (s, 1H, CH), 8.07 (s, 1H, CHO).

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.17; N, 7.99. Found: C, 68.38; H, 5.25; N, 8.2.

2-(3'-Chloroyphenyl)-3-oxopropanenitrile (**1n**).

This compound was obtained from 2,3'-chlorophenylacetonitrile as white crystals from water, 29.8 g (90%), mp 167-168°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 7.28-7.42 (m, 2H, ArH_2), 7.50-7.57 (m, 1H, ArH), 7.76-7.78 (m, 2H: 1H, ArH 1H, CH) 8.19 (s, 1H, CHO).

Anal. Calcd. for C_9H_6NOCl: C. 60.18; H, 3.36; N, 7.79. Found: C, 60.1; H, 3.49; N, 7.70.

2-(2'-Thienyl)-3-oxopropanenitrile (**1o**).

This compound was obtained from 2,2'-thienylacetonitrile as white crystals from water, 26 g (86%), mp 140-141°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 7.02-7.09 (m, 2H, thienyl), 7.28-7.30 (m, 1H, thienyl), 7.68 (s, 1H, CH), 8.09 (s, 1H, CHO).

Anal. Calcd. for C_7H_5NOS: C, 55.61; H, 3.39; N, 9.26. Found: C, 55.47; H, 3.33; N, 9.37.

2-(3'-Thienyl)-3-oxopropanenitrile (**1p**).

This compound was obtained from 2,3'-thienylacetonitrile as pink crystals from water, 29.6 g (98%), mp 117-118°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 7.30-7.50 (m, 2H, thienyl), 7.65 (s, 1H, thienyl), 7.69 (s, 1H, CH), 8.05 (s, 1H, CHO).

Anal. Calcd. for C_7H_5NOS: C, 55.61; H, 3.39; N, 9.26. Found: C, 55.53; H, 3.49; N, 9.37.

General Procedure for Preparing 3- or 4-Substituted 5-Aminopyrazoles **2m-p**.

A solution of a suitable 2-substituted-3-oxopropanenitrile (55 mmoles) in ethanol was added to hydrazine hydrate (110 mmoles, 5.5 ml) and acetic acid (5 ml) then refluxed for 6 hours. After cooling a precipitate was separated, filtered and washed with water.

4,3'-Methoxyphenyl-5-aminopyrazole (**2m**).

This compound was obtained from **1m** as ivory crystals from water, 8.6 g (83%), mp 120-121°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 3.82 (s, 3H, OCH_3), 4.80-4.83 (bs, 2H, NH_2, exchangeable), 6.84-6.88 (m, 1H, ArH), 7.34-7.42 (m, 2H, ArH_2), 7.63-7.67 (m, 1H, ArH), 8.50 (s, 1H, H-2), 11.80-12.00 (bs, 1H, NH, exchangeable).

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.47; H, 5.86; N, 22.20. Found: C, 63.60; H, 5.92; N, 22.34.

4,3'-Chlorophenyl-5-aminopyrazole (**2n**).

This compound was obtained from **1n** as ivory crystals from water, 6.4 g (60%), mp 137-138°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 4.75-4.80 (bs, 2H, NH2, exchangeable), 7.28-7.38 (m, 2H, ArH_2), 7.91-7.95 (m, 1H, ArH), 8.09 (m, 1H, ArH), 8.53 (s, 1H, H-2), 11.78-11.97 (bs, 1H, NH, exchangeable).

Anal. Calcd. for $C_9H_8N_3Cl$: C, 55.82; H, 4.16; N, 21.70. Found: C. 55.73; H, 4.18; N, 21.82.

4.2'-Thienyl-5-aminopyrazole (**2o**).

This compound was obtained from **1o** as pink crystals from water, 7.5 g (83%), mp 179-180°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 4.77-4.79 (bs, 2H, NH_2, exchangeable), 7.02-7.09 (m, 2H, thienyl), 7.27-7.30 (s, 1H, thienyl), 7.60 (bs, 1H, H-2), 11.76-11.77 (bs, 1H, NH, exchangeable).

Anal. Calcd. for $C_7H_7N_3S$: C, 50.88; H, 4.26; N, 25.43. Found: C, 50.82; H, 4.22; N, 25.56.

4,3'-Thienyl-5-aminopyrazole (**2p**).

This compound was obtained from **1p** as pink crystals from water, 8.17 g (90%), mp 201-202°; ^{1}H-nmr (dimethyl sulphoxide-d_6): δ 7.32-7.54 (m, 3H, thienyl), 7.70 (s, 1H, H-2), 11.45-11.55 (bs, 1H, NH, exchangeable).

Anal. Calcd. for $C_7H_7N_3S$: C, 50.88; H, 4.26; N, 25.43. Found: C, 51.01; H, 4.17; N, 25.55.

General Procedure for Preparing Ethyl 7-Methylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylates **3a-s**.

A mixture of ethyl-2-acetyl-3-ethoxyacrylate (55 mmoles) and 3- or 4-substituted 5-aminopyrazoles **2a-s** (50 mmoles) in ethanol (100 ml) was refluxed under magnetic stirring for 30 minutes. After cooling a precipitate was separated and filtered.

Ethyl 7-Methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3a**).

Compound **3a** has been described [9]. This compound was obtained from **2a**.

Ethyl 2,7-Dimethylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3b**).

This compound was obtained from **2b** as white crystals from ethanol, 10.6 g (88%), mp 103-104°; ^{1}H-nmr (deuteriochloroform): δ 1.43 (t, 3H, OCH_2CH_3), 2.55 (s, 3H, 2-CH_3), 3.18 (s, 3H, 7-CH_3), 4.42 (q, 2H, OCH_2CH_3), 6.53 (s, 1H, H-3), 8.89 (s, 1H, H-5).

Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.97; N, 19.16. Found: C, 60.18; H, 5.86; N, 19.30.

Ethyl 2-(1-Methylethyl)-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3c**).

This compound was obtained from **2c** as ivory crystals from cyclohexane, 9.65 g (71%), mp 48-50°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (m, 9H: 6H,$CH(CH_3)_2$, 3H, OCH_2CH_3), 3.2 (m, 4H, 3H,7-CH_3, 1H, $CH(CH_3)_2$), 4.42 (q, 2H, OCH_2CH_3), 6.57 (s, 1H, H-3), 8.91 (s, 1H, H-5).

Anal. Calcd. for $C_{13}H_{17}N_3O_2$: C, 63.13; H, 6.93; N, 16.99. Found: C, 63.20; H, 7.02; N, 16.76.

Ethyl 2-(1,1-Dimethylethyl)-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3d**).

This compound was obtained from **2d** as white crystals from ethanol, 9.62 g (67%), mp 68-70°; ^{1}H-nmr (deuteriochloroform): δ 1.41 (m, 12H: 3H, OCH_2CH_3, 9H, $C(CH_3)_3$), 3.19 (s, 3H, 7-CH_3), 4.41 (q, 2H,OCH_2CH_3), 6.59 (s, 1H, H-3), 8.88 (s, 1H, H-5).

Anal. Calcd. for $C_{14}H_{19}N_3O_2$: C, 64.34; H, 7.32; N, 16.07. Found: C, 64.55; H, 7.54; N, 15.76.

Ethyl 2-Phenyl-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3e**).

This compound has been described [3] and it was obtained from **2e**.

Ethyl 7-Methyl-2,2'-thienylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3f**).

This compound was obtained from **2f** as white crystals from ethanol, 10.95 g (78%), mp 155-157°; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.35 (t, 3H, OCH_2CH_3), 3.12 (s, 3H, 7-CH_3), 4.30 (q, 2H, OCH_2CH_3), 7.28 (m, 2H, 1H, thienyl, 1H, H-3), 7.80 (m, 2H, thienyl), 8.83 (s, 1H, H-5).

Anal. Calcd. for $C_{14}H_{13}N_3O_2S$: C, 58.52; H, 4.55; N, 14.62. Found: C, 58.45; H, 4.42; N, 14.83.

Ethyl 2-Hydroxy-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3g**).

This compound has been described [10] and it was obtained from **2g**.

Ethyl 2-Methoxy-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3h**).

This compound was obtained by treatment of **3g** (30 mmoles, 6.63 g) with methyl iodide (35 mmoles, 4.96 g) in anhydrous *N,N*-dimethylformamide (40 ml) in the presence of potassium carbonate (30 mmoles, 4.14, g). The mixture was heated to 40-50° with magnetic stirring for 4 hours. Exclusion of external moisture was achieved by insertion of a calcium chloride guard tube at the top of the condenser. On cooling, addition of water causes the formation of a precipitate, which was filtered and washed with water. Ivory crystals were obtained from ethanol/water, 4.23 g (60%), mp 92-93°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.12 (s, 3H, 7-CH_3), 4.06 (s, 3H, OCH_3), 4.41 (q, 2H, OCH_2CH_3), 6.10 (s, 1H, H-3), 8.87 (s, 1H, H-5).

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.04; H, 5.64; N, 17.65.

Ethyl 2-Benzyloxy-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3i**).

This compound was obtained by treatment of **3g** (30 mmoles, 6.63 g) with benzyl chloride (50 mmoles, 5.75 ml) in anhydrous dimethylformamide (40 ml) in the presence of potassium carbonate (30 mmoles, 4.14 g). The suspension was magnetically stirred for 5 hours at 50°. After cooling the precipitate was filtered and washed with water. White crystals were obtained from ethanol, 4.20 g (45%), mp 106-107°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.13 (s, 3H, 7-CH_3), 4.41 (q, 2H, OCH_2CH_3), 5.41 (s, 2H, OCH_2), 6.14 (s, 1H, H-3), 7.36-7.40 (m, 3H, ArH_3), 7.48-7.49 (m, 2H, ArH_2), 8.87 (s, 1H, H-5).

Anal. Calcd. for $C_{17}H_{17}N_3O_3$: C, 65.58; H, 5.50; N, 13.49. Found: C, 65.69; H, 5.66; N, 13.72.

Diethyl 7-Methylpyrazolo[1,5-*a*]pyrimidine-3,6-dicarboxylate (**3j**).

Compound **3j** has been described [2] and it was obtained from **2j**.

Ethyl 3-Cyano-7-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3k**).

This compound was obtained from **2k** as light yellow crystals from ethanol, 10.50 g (83%), mp 112-114°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.24 (s, 3H, 7-CH_3), 4.47 (q, 2H, OCH_2CH_3), 8.47 (s, 1H, H-2), 9.16 (s, 1H, H-5).

Anal. Calcd. for $C_{11}H_{10}N_4O_2$: C, 57.38; H, 4.37; N, 24.33. Found: C, 57.52; H, 4.21; N, 24.69.

Ethyl 7-Methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3l**).

This compound was obtained from **2l** as yellow crystals from ethanol, 11.13 g (72%), mp 95-97°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.23 (s, 3H, 7-CH_3), 4.45 (q, 2H, OCH_2CH_3), 7.45-7.49 (m, 3H, ArH_3), 8.02-8.05 (m, 2H, ArH_2), 8.54 (s, 1H, H-2), 9.03 (s, 1H, H-5).

Anal. Calcd. for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.93. Found: C, 68.40; H, 5.30; N, 15.14.

Ethyl 7-Methyl-3,3'-methoxyphenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3m**).

This compound was obtained from **2m** as yellow crystals from ethanol, 14.4 g (84%), mp 92-93°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.23 (s, 3H, 7-CH_3), 3.89 (s, 3H, OCH_3), 4.46 (q, 2H, OCH_2CH_3), 6.84-6.88 (m, 1H, ArH), 7.26-7.38 (m, 1H, ArH), 7.59-7.69 (m, 2H, ArH_2), 8.54 (s, 1H, H-2), 9.03 (s, 1H, H-5).

Anal. Calcd. for $C_{17}H_{17}N_3O_3$: C, 65.58; H, 5.50; N, 13.49. Found: C, 65.55; H, 5.59; N, 13.44.

Ethyl 7-Methyl-3,3'-chlorophenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3n**).

This compound was obtained from **2n** as yellow crystals from ethanol, 13.88 g (80%), mp 121-122°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.24 (s, 3H, 7-CH_3), 4.46 (q, 2H, OCH_2CH_3), 7.27-7.28 (m, 1H, ArH), 7.35-7.39 (m, 1H, ArH), 7.91-7.95 (m, 1H, ArH), 8.09 (m, 1H, ArH), 8.54 (s, 1H, H-2), 9.05 (s, 1H, H-5).

Anal. Calcd. for $C_{16}H_{14}N_3O_2Cl$: C, 60.86; H, 4.46; N, 13.30. Found: C, 61.12; H, 4.52; N, 13.48.

Ethyl 7-Methyl-3,2'-thienylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3o**).

This compound was obtained from **2o** as yellow crystals from ethanol, 12.32 g (78%), mp 121-122°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.23 (s, 3H, 7-CH_3), 4.45 (q, 2H, OCH_2CH_3), 7.13-7.15 (m, 1H, thienyl), 7.29-7.32 (m, 1H, thienyl), 7.57-7.59 (m, 1H, thienyl), 8.46 (s, 1H, H-2), 9.05 (s, 1H, H-5).

Anal. Calcd. for $C_{14}H_{13}N_3O_2S$: C, 58.52; H, 4.55; N, 14.62. Found: C, 58.70; H, 4.46; N, 14.86.

Ethyl 7-Methyl-3,3'-thienylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3p**).

This compound was obtained from **2p** as white crystals from ethanol, 12.95 g (82%), mp 97-98°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.21 (s, 3H, 7-CH_3), 4.45 (q, 2H, OCH_2CH_3), 7.40-7.44 (m, 1H, thienyl), 7.66-7.69 (m, 1H, thienyl), 7.90-7.91 (m, 1H, thienyl), 8.45 (s, 1H, H-2), 8.99 (s, 1H, H-5).

Anal. Calcd. for $C_{14}H_{13}N_3O_2S$: C, 58.52; H, 4.55; N, 14.62. Found: C, 58.68; H, 4.47; N, 14.38.

Ethyl 3,7-Dimethyl-2-(1-methylethyl)pyrazolo[1,5-*a*]pyrimidin-6-carboxylate (**3q**).

This compound was obtained from **2q** as white crystals from ethanol, 7.32 g (51%), mp 77-78°; ^{1}H-nmr (deuteriochloroform): δ 1.40 (m, 9H, 6H, $CH(CH_3)_2$, 3H, OCH_2CH_3), 2.33 (s, 3H, CH-3), 3.15 (s, 3H, 7-CH_3), 3.25 (m, 1H, $CH(CH_3)$ 2), 4.42 (q, 2H, OCH_2CH_3), 8.91 (s, 1H, H-5).

Anal. Calcd. for $C_{14}H_{19}N_3O_2$: C, 64.34; H, 7.32; N, 16.07. Found: C, 64.08; H, 7.41; N, 16.33.

Ethyl 2-Hydroxy-7-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3r**).

This compound was obtained together with the regioisomer **3r'** from **2r** (see below). The mixture was separated by column chromatography (silica gel column 3.0 x 60 cm, toluene:ethyl acetate 8:3 v/v as eluent) to give **3r** and **3r'** in 33 and 6.0% respectively. Yellow crystals were obtained from ethanol, mp 207-208°; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.37 (t, 3H, OCH_2CH_3), 3.04 (s, 3H, 7-CH_3), 4.36 (q, 2H, OCH_2CH_3), 7.23-7.26 (m, 1H, ArH), 7.40-7.47 (m, 2H, ArH_2), 8.19-8.23 (m, 2H, ArH_2), 8.85 (s, 1H, H-5), 12.20 (bs, 1H, OH exch.).

Anal. Calcd. for $C_{16}H_{15}N_3O_3$: C, 64.63; H, 5.08; N, 14.13. Found: C, 64.48; H, 4.99; N, 14.25.

Ethyl 2-Hydroxy-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**3r'**).

Yellow crystals were obtained from ethanol, mp 254-255°; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.37 (t, 3H, OCH_2CH_3), 2.79 (s, 3H, 5-CH_3), 4.33 (q, 2H, OCH_2CH_3), 7.21-7.25 (m, 1H, ArH), 7.39-7.47 (m, 2H, ArH_2), 8.21-8.25 (m, 2H, ArH_2), 9.20 (s, 1H, H-7), 12.21 (bs, 1H, OH exch.).

Anal. Calcd. for $C_{16}H_{15}N_3O_3$: C, 64.63; H, 5.08; N, 14.13. Found: C, 64.71; H, 5.05; N, 13.92.

Ethyl 2-Hydroxy-7-methyl-3-(1,3,4-thiadiazol-2-yl)pyrazolo-[1,5-*a*]pyrimidine-6-carboxylate (**3s**).

This compound was obtained from **2s** as light yellow crystals from acetic acid, 8.73 g (52%), mp 253-254°; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.34 (t, 3H, OCH_2CH_3), 3.04 (s, 3H, 7-CH_3), 4.37 (q, 2H, OCH_2CH_3), 8.97 (s, 1H, thiadazole), 9.54 (s, 1H, H-5), 12.10 (bs, 1H, OH exch.).

Anal. Calcd. for $C_{12}H_{11}N_5O_3S$: C, 47.20; H, 3.64; N, 23.00. Found: C, 46.86; H, 4.00; N, 22.97.

General Procedure for Preparing **4a-s**.

Compounds **4a-s** were prepared according to a reported procedure [2].

Ethyl 7-(2-Dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4a**).

Compound **4a** has been described [2] and it was obtained from **3a**.

Ethyl 7-(2-Dimethylaminovinyl)-2-methylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4b**).

This compound was obtained from **3b** as yellow crystals from cyclohexane, 3.01 g (55%), mp 103-104°; ^{1}H-nmr (deuteriochloroform): δ 1.43 (t, 3H, OCH_2CH_3), 2.54 (s, 3H, 2-CH_3), 3.15 (s, 3H, N-$(CH_3)_2$), 3.35 (s, 3H, N-$(CH_3)_2$), 4.42 (q, 2H, OCH_2CH_3), 6.53 (s, 1H, H-3), 7.00 (d, J_{trans} = 12.5 Hz, 1H, $CHN(CH_3)_2$), 8.89 (s, 1H, H-5), 9.70 (d, J_{trans} = 12.5 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{14}H_{18}N_4O_2$: C, 61.29; H, 6.61; N, 20.42. Found: C, 61.42; H, 6.52; N, 20.65.

Ethyl 7-(2-Dimethylaminovinyl)-2-(1-methylethyl)pyrazolo-[1,5-*a*]pyrimidine-6-carboxylate (**4c**).

This compound was obtained from **3c** as yellow crystals from cyclohexane, 3.14 g (52%), mp 95-96°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (m, 9H: 3H, OCH_2CH_3; 6H-$CH(CH_3)_2$), 3.2 (m, 7H: 6H, N-$(CH_3)_2$, 1H, $CH(CH_3)_2$), 4.37 (q, 2H, OCH_2CH_3), 6.34 (s, 1H, H-3), 7.03 (d, J_{trans} = 12.74 Hz, 1H, $CHN(CH_3)_2$), 8.83 (s, 1H, H-5), 9.8 (d, J_{trans} = 12.74 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{16}H_{22}N_4O_2$: C, 63.55; H, 7.33; N, 18.52. Found: C, 63.34; H, 7.30; N, 18.65.

Ethyl 7-(2-Dimethylaminovinyl)-2(1,1-dimethylethyl)pyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4d**).

This compound was obtained from **3d** as yellow crystals from cyclohexane, 3.05 g (48%), mp 118-120°; ^{1}H-nmr (deuteriochloroform): δ 1.43 (m, 12H, OCH_2CH_3, C-$(CH_3)_3$), 3.06 (s, 3H, N-$(CH_3)_2$), 3.24 (s, 3H, N-$(CH_3)_2$), 4.34 (q, 2H, OCH_2CH_3), 6.38 (s, 1H, H-3), 7.00 (d, J_{trans} = 13.00 Hz, 1H, $CHN(CH_3)_2$), 8.83 (s, 1H, H-5), 9.85 (d, J_{trans} = 13.00 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{17}H_{24}N_4O_2$: C, 64.53; H, 7.64; N, 17.70. Found: C, 64.67; H, 7.76; N, 17.46.

Ethyl 7-(2-Dimethylaminovinyl)-2-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4e**).

This compound was obtained from **3e** as yellow crystals from ethanol, 5 g (74%), mp 185-186°; ^{1}H-nmr (deuteriochloroform): δ 1.45 (t, 3H, OCH_2CH_3), 3.15 (s, 3H, N-$(CH_3)_2$), 3.35 (s, 3H, N-$(CH_3)_2$), 4.45 (q, 2H, OCH_2CH_3), 6.84 (s, 1H, H-3), 7.05 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 7.42-7.50 (m, 3H, ArH_3), 7.96-8.00 (m, 2H, ArH_2), 8.87 (s, 1H, H-5), 9.90 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{19}H_{20}N_4O_2$: C, 67.83; H, 5.99; N, 16.65. Found: C, 67.97; H, 5.92; N, 16.82.

Ethyl 7-(2-Dimethylaminovinyl)-2-2'-thienylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4f**).

This compound was obtained from **3f** as yellow crystals from ethanol, 5.5 g (81%), mp 170-173°; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 1.35 (t, 3H, OCH_2CH_3), 3.04 (s, 3H, N-$(CH_3)_2$), 3.32 (s, 3H, N-$(CH_3)_2$), 4.30 (q, 2H, OCH_2CH_3), 6.85 (d, J_{trans} = 12.4 Hz, 1H, $CHN(CH_3)_2$), 6.94 (s, 1H, H-3), 7.22 (m, 1H, thienyl), 7.66 (m, 1H, thienyl), 7.75 (m, 1H, thienyl), 8.70 (s, 1H, H-5), 9.77 (d, J_{trans} = 12.4 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{17}H_{18}N_4O_2S$: C, 59.63; H, 5.29; N, 16.36. Found: C, 59.41; H, 5.12; N, 16.67.

Ethyl 7-(2-dimethylaminovinyl)-2-methoxypyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4h**).

This compound was obtained from **3g** or **3h** as yellow crystals from cyclohexane, 1.91 g (33%) and 4.5 g (74%) respectively, mp 119-120°; ^{1}H nmr (deuteriochloroform): δ 1.40 (t, 3H, OCH_2CH_3), 3.06 (s, 3H, N-$(CH_3)_2$), 3.24 (s, 3H, N-$(CH_3)_2$), 4.04 (s, 3H, OCH_3), 4.35 (q, 2H, OCH_2CH_3), 5.94 (s, 1H, H-3) 6.95 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 8.82 (s, 1H, H-5), 9.58 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{14}H_{18}N_4O_3$: C, 57.91; H, 6.22; N, 19.29. Found: C, 57.79; H, 6.14; N, 19.47.

Ethyl-2-benzyloxy-7-(2-dimethylaminovinyl)pyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4i**).

This compound was obtained from **3i** as yellow crystals from ethanol, 5.5 g (76%), mp 144-146°; ^{1}H-nmr (deuteriochloroform): δ 1.43 (t, 3H, OCH_2CH_3), 3.03-3.16 (m, 6H, N-$(CH_3)_2$), 4.34 (q, 2H, OCH_2CH_3), 5.37 (s, 2H, OCH_2), 5.98 (s, 1H, H-3), 6.94 (d, J_{trans} = 12.82 Hz, 1H, $CHN(CH_3)_2$), 7.35-7.47 (m, 5H, ArH_5), 8.81 (s, 1H, H-5), 9.52 (d, J_{trans} = 12.82 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{20}H_{22}N_4O_3$: C, 65.55; H, 6.05; N, 15.29. Found: C, 65.27; H, 5.94; N, 15.15.

Diethyl 7-(2-Dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidin-3,6-dicarboxylate (**4j**).

Compound **4j** has been described [2] and it was obtained from **3j**.

Ethyl 3-Cyano-7-(2-dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4k**).

This compound was obtained from **3k** as yellow crystals from ethanol, 4.6 g (82%), mp 204-205°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.19 (s, 3H, N-$(CH_3)_2$), 3.33 (s, 3H, N-$(CH_3)_2$), 4.36 (q, 2H, OCH_2CH_3), 6.85 (d, J_{trans} = 12.6 Hz, 1H, $CHN(CH_3)_2$), 8.28 (s, 1H, H-2), 8.97 (s, 1H, H-5), 9.54 (d, J_{trans} = 12.6 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{14}H_{15}N_5O_2$: C, 58.93; H, 5.29; N, 24.54. Found: C, 58.67; H, 5.40; N, 24.86.

Ethyl 7-(2-Dimethylaminovinyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4l**).

This compound was obtained from **3l** as yellow crystals from ethanol, 5 g (74%), mp 183-184°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.08 (s, 3H, N-$(CH_3)_2$), 3.28 (s, 3H, N-$(CH_3)_2$), 4.36 (q, 2H, OCH_2CH_3), 7.06 (d, J_{trans} = 12.6 Hz, 1H, $CHN(CH_3)_2$), 7.41-7.45 (m, 3H, ArH_3), 8.03-8.07 (m, 2H, ArH_2), 8.40 (s, 1H, H-2), 8.98 (s, 1H, H-5), 9.68 (d, J_{trans} = 12.6 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{19}H_{20}N_4O_2$: C, 67.83; H, 5.99; N, 16.65. Found: C, 67.99; H, 6.10; N, 16.51.

Ethyl 7-(2-Dimethylaminovinyl)-3,3'-methoxyphenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4m**).

This compound was obtained from **3m** as yellow crystals from ethyl acetate, 4.97 g (68%), mp 169-170°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.08 (s, 3H, N-$(CH_3)_2$), 3.28 (s, 3H, N-$(CH_3)_2$), 3.89 (s, 3H, OCH_3), 4.37 (q, 2H, OCH_2CH_3), 6.79-6.84 (m, 1H, ArH), 7.00 (d, J_{trans} = 12.74 Hz, 1H, $CHN(CH_3)_2$), 7.32-7.39 (m, 1H, ArH), 7.61-7.69 (m, 2H, ArH_2), 8.38 (s, 1H, H-2), 8.97 (s, 1H, H-5), 9.67 (d, J_{trans} = 12.74 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{20}H_{22}N_4O_3$: C, 71.40; H, 6.59; N, 16.65. Found: C, 71.49; H, 6.53; N, 16.44.

Ethyl 7-(2-Dimethylaminovinyl)-3,3'-chlorophenylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4n**).

This compound was obtained from **3n** as yellow crystals from ethyl acetate, 4.4 g (60%), mp 180-181°; ^{1}H-nmr (deuteriochloroform): δ 1.42 (t, 3H, OCH_2CH_3), 3.08 (s, 3H, N-$(CH_3)_2$), 3.27 (s, 3H, N-$(CH_3)_2$), 4.37 (q, 2H, OCH_2CH_3), 7.00 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 7.18-7.39 (m, 2H, ArH_2), 7.93-7.98 (m, 1H, ArH_1), 8.07-8.08 (m, 1H, ArH_1), 8.35 (s, 1H, H-2), 8.98 (s, 1H, H-5), 9.65 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{19}H_{19}N_4O_2Cl$: C, 61.53; H, 5.16; N, 15.10. Found: C, 61.39; H, 5.17; N, 14.94.

Ethyl 7-(2-Dimethylaminovinyl)-3-2'-thienylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4o**).

This compound was obtained from **3o** as yellow crystals from ethanol, 5 g (73%), mp 180-181°; ^{1}H-nmr (deuteriochloroform): δ 1.41 (t, 3H, OCH_2CH_3), 3.07 (s, 3H, N-$(CH_3)_2$), 3.27 (s, 3H, N-$(CH_3)_2$), 4.36 (q, 2H, OCH_2CH_3), 6.90 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 7.12-7.15 (m, 1H, thienyl), 7.45-7.47 (m, 1H, thienyl), 7.60-7.62 (m, 1H, thienyl), 8.66 (s, 1H, H-2), 8.80 (s, 1H, H-5), 9.60 (d, J_{trans} = 12.7 Hz, 1 H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{17}H_{18}N_4O_2S$: C, 59.63; H, 5.29; N, 16.36. Found: C, 59.80; H, 5.20; N, 16.18.

Ethyl 7-(2-Dimethylaminovinyl)-3-3'-thienylpyrazolo[1,5-*a*]-pyrimidine-6-carboxylate (**4p**).

This compound was obtained from **3p** as yellow crystals from ethyl acetate, 3.9 g (58%), mp 191-192°; ^{1}H-nmr (deuteriochloroform): δ 1.41 (t, 3H, OCH_2CH_3), 3.07 (s, 3H, N-$(CH_3)_2$), 3.27 (s, 3H, N-$(CH_3)_2$), 4.37 (q, 2H, OCH_2CH_3), 7.00 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 7.38-7.42 (m, 1H, thienyl), 7.67-7.69 (m, 1H, thienyl), 7.88-7.90 (m, 1H, thienyl), 8.30 (s, 1H, H-2), 8.96 (s, 1H, H-5), 9.66 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{17}H_{18}N_4O_2S$: C, 59.63; H, 5.29; N, 16.36. Found: C, 59.70; H, 5.27; N, 16.45.

Ethyl 7-(2-Dimethylaminovinyl)-2-(1,1-methylethyl)-3-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4q**).

This compound was obtained from **3q** as yellow crystals from water, 4.4 g (71%), mp 132°; ^{1}H-nmr (deuteriochloroform): δ 1.40 (m, 9H: 3H, OCH_2CH_3; 6H-$CH(CH_3)_2$), 2.33 (s, 3H, 3-CH_3), 3.2 (m, 7H: 6H, N-$(CH_3)_2$, 1H-$CH(CH_3)_2$), 4.36 (q, 2H, OCH_2CH_3), 7.00 (d, J_{trans} = 12.8 Hz, 1H, $CHN(CH_3)_2$), 8.81 (s, 1H, H-5), 9.86 (d, J_{trans} = 12.74 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{17}H_{24}N_4O_2$: C, 64.53; H, 7.64; N, 17.70. Found: C, 64.42; H, 7.66; N, 17.73.

Ethyl 7-(2-Dimethylaminovinyl)-2-methoxy-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4r**).

This compound was obtained from **3r** as yellow crystals from ethanol, 3.8 g (52%), mp 116-117°; ^{1}H-nmr (deuteriochloroform): δ 1.40 (t, 3H, OCH_2CH_3), 3.06-3.22 (m, 6H, N-$(CH_3)_2$), 4.18 (s, 3H, OCH_3), 4.37 (q, 2H, OCH_2CH_3), 7.00 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 7.21-7.26 (m, 1H, ArH), 7.39-7.46 (m, 2H, ArH_2), 8.14-8.19 (m, 2H, ArH_2), 8.93 (s, 1H, H-5), 9.60 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{20}H_{22}N_4O_3$: C, 65.55; H, 6.05; N, 15.29. Found: C, 65.76; H, 6.03; N, 15.34.

Ethyl 7-(2-Dimethylaminovinyl)-2-methoxy-3-(1,3,4-thiadiazol-2-yl)pyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**4s**).

This compound was obtained from **3s** as yellow crystals from ethanol, 3.2 g (44%), mp 202-203°; ^{1}H-nmr (deuteriochloroform): δ 1.40 (t, 3H, OCH_2CH_3), 3.07 (s, 3H, N-$(CH_3)_2$), 3.26 (s, 3H, N-$(CH_3)_2$), 4.25 (s, 3H, OCH_3), 4.35 (q, 2H, OCH_2CH_3), 6.96 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$), 8.98 (s, 1H, H-5), 9.07 (s, 1H, thiadiazolyl), 9.53 (d, J_{trans} = 12.7 Hz, 1H, $CHN(CH_3)_2$).

Anal. Calcd. for $C_{16}H_{18}N_6O_3S$: C, 51.32; H, 4.84; N, 22.44. Found: C, 51.48; H, 4.80; N, 22.28.

General Procedure for Preparing Pyrazolo[1,5-*a*]pyrido[3,4-*e*]-pyrimidine-6-ones **5a-s**.

Compounds **5a-s** were prepared from ethyl 7-(2-dimethylaminovinyl) derivatives **4a-s** according to a reported method [2].

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REFERENCES AND NOTES

[1] F. Bruni, S. Selleri, A. Costanzo, G. Guerrini, and M. L. Casilli, Reactivity of 7-(2-Dimethylaminovinyl)pyrazolo[1,5-*a*]pyrimidines: Synthesis of Pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidine derivatives as Potential Benzodiazepine Receptor Ligands, **1**, *J. Heterocyclic Chem.*, **31**, 1193 (1994).

[2] S. Selleri, F. Bruni, A. Costanzo, G. Guerrini, P. Malmberg Aiello, and C. Martini, *Eur. J. Med. Chem.*, **27**, 985 (1992).

[3] G. Auzzi, L. Cecchi, A. Costanzo, L. Pecori Vettori, F. Bruni, R. Pirisino, and G. B. Ciottoli, *Farmaco, Ed. Sci.*, **34**, 478 (1979).

[4] G. Auzzi, L. Cecchi, A. Costanzo, L. Pecori Vettori, and F. Bruni, *Farmaco, Ed. Sci.*, **34**, 898 (1979).

[5] S. Chimichi, B. Cosimelli, F. Bruni, and S. Selleri, *Magn. Reson. Chem.*, **30**, 1117 (1992).

[6] S. Chimichi, B. Cosimelli, F. Bruni, and S. Selleri, *Can. J. Chem.*, **70**, 1093 (1992).

[7] C. Martini, T. Rigacci, and A. Lucacchini, *J. Neurochem.*, **41**, 1183 (1983).

[8] G. Palazzino, L. Cecchi, F. Melani, V. Colotta, G. Filacchioni, C. Martini, and A. Lucacchini, *J. Med. Chem.*, **30**, 1737 (1987).

[9] Y. Makisumi, *Chem. Pharm. Bull.*, **10**, 620 (1962).

[10] M. Ridi, P. Papini, and S. Checchi, *Gazz. Chim. Ital.*, **91**, 973 (1961).