Chemistry of Substituted Pyrazolo[1,5-*a*]pyrimidines. Part 3.[1] A Structural Correction of a Pyrazolo[1,5-*a*][1,3]diazepine Derivative on the Basis of ^{13}C NMR Spectroscopy

Stefano Chimichi,*,[a] Barbara Cosimelli,[a] Fabrizio Bruni[b] and Annarella Costanzo[b]
[a] *Dipartimento di Chimica Organica e Centro CNR sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, Via Gino Capponi 9, I-50121 Firenze, Italy*
[b] *Dipartimento di Scienze Farmaceutiche, Via Gino Capponi 9, I-50121 Firenze, Italy*

The reaction of 3-amino-4-cyanopyrazole (**3**) with ethyl 3-ethoxymethylene-2,4-dioxopentanoate (**4**) has been reinvestigated and the nature of the condensation product firmly established. Ethyl 3-cyano-7-methylpyrazolo[1,5-*a*]pyrimidine-6-oxoacetate (**1**) and not, as formerly claimed, ethyl 3-cyano-7-methyl-6-oxopyrazolo[1,5-*a*][1,3]diazepine-8-carboxylate (**2**) is shown to be the final product in the reaction of ethyl 6-acetyl-3-cyanopyrazolo[1,5-*a*]pyrimidine-7-carboxylate (**6**) with aqueous acetic acid. The structure of **1** has been determined by ^{13}C NMR spectroscopy and confirmed by independent synthesis.

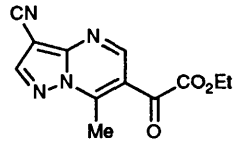
As part of our studies were devoted to the synthesis and the chemistry of heterocyclic systems condensed with a pyrazole ring,[1-4] we became interested in the pyrazolo[1,5-*a*][1,3]diazepines as potential pharmacologically active compounds.[5,6] A survey of the literature revealed that this class of compounds has received little attention to date, the only reported suitable preparation being a ring expansion of a pyrazolo[1,5-*a*]pyrimidine.[7,8] In order to assess the general applicability of this reaction, we have reinvestigated the procedure described by Kurihara[7] and we report here NMR results which require the structure of the final product to be amended to **1** and not, as formerly claimed, the diazepine **2**.

Results

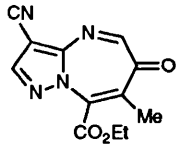
Reaction of the aminopyrazole **3** with ethyl 3-ethoxymethylene-2,4-dioxopentanoate (**4**) afforded the intermediate **5** as the sole reaction product in quantitative yield. This compound, while confirming the regioselective attack of the amino group of **3** on the ethoxymethylene moiety,[1,9] can be easily cyclised into a single product (TLC, ^1H and ^{13}C NMR spectra) to which the structure **6** [route (*a*)] or **1** [route (*b*)] could be attributed.

The structure of ethyl 6-acetyl-3-cyanopyrazolo[1,5-*a*]pyrimidine-7-carboxylate (**6**) was then attributed to the product on the basis of spectral evidence, the pyrazolopyrimidines **7**–**10**[2] being used as model compounds.

The ^1H NMR spectrum was of little value and the most convincing diagnostic data were obtained from the ^{13}C NMR spectra. In particular, the signal at δ 192.33 attributable to the ketonic C=O appears as a quartet of doublets ($^2J_{CO,Me}$ = 6.3 and $^3J_{CO,5}$ = 1.5 Hz) thus confirming, together with the chemical shift of the methyl group at δ 27.93, the presence of the acetyl group as in the reference compounds **7**–**10** (see Table 1). Moreover, the signal of the quaternary carbon at position 7, easily identified at 140.67 ppm, shows a fine structure of doublet

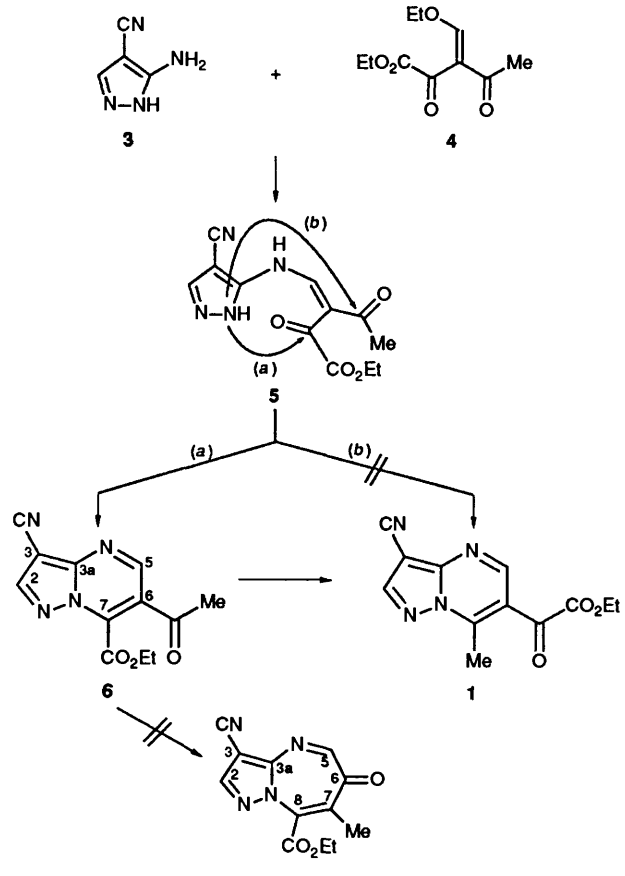


1



2

Fig. 1



Scheme 1

only ($^3J_{7,5}$ = 5.9 Hz) and not one of doublet of quartets (pseudo quintet, $^3J_{7,5} = {}^2J_{7,Me}$) as would be expected for the alternative structure **1** on the basis of the models **7**–**10** (see Table 1). As regards the attribution of the resonances of C-5 and C-2 in compound **6**, it has been achieved as follows. COLOC experiments showing connectivities between C-6 and H-5, and C-3 and H-2 allowed the distinction of H-5 and H-2 signals in the ^1H NMR spectrum, so that a subsequent HETCOR experiment led to the attribution of the resonance at higher

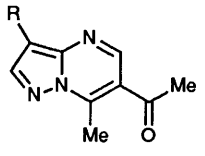
Table 1 Selected coupling constants (Hz) of model compounds **7–10**

Compound	C-2	C-5	C-7	6-CO
7	$^1J_{2,2}$ = 186.0	$^1J_{5,5}$ = 181.8	$^2J_{7,Me}$ = 6.2 $^3J_{7,5}$ = 6.2	$^2J_{CO,Me}$ = 6.0 $^3J_{CO,5}$ = 1.4
8	$^1J_{2,2}$ = 184.7	$^1J_{5,5}$ = 182.1	$^2J_{7,Me}$ = 6.4 $^3J_{7,5}$ = 6.4	$^2J_{CO,Me}$ = 5.9 $^3J_{CO,5}$ = 1.4
9	$^1J_{2,2}$ = 190.8	$^1J_{5,5}$ = 183.3	$^2J_{7,Me}$ = 6.4 $^3J_{7,5}$ = 6.4	$^2J_{CO,Me}$ = 5.8 $^3J_{CO,5}$ = 1.4
10	$^1J_{2,2}$ = 194.2	$^1J_{5,5}$ = 184.3	$^2J_{7,Me}$ = 6.4 $^3J_{7,5}$ = 6.4	$^2J_{CO,Me}$ = 5.6 $^3J_{CO,5}$ = 1.4

Table 2 Carbon-13 chemical shifts (δ) and coupling constants (Hz) of compounds **1** and **6**

Compound	δ	Assignment	Multiplicity[a] and J
1	183.41	C=O	d $^3J_{CO,5}$ = 2.0
	161.77	CO_2R	t $^3J_{CO,OCH_2}$ = 3.2
	153.90	C-7	dq[b] $^2J_{7,Me}$ = 6.3, $^3J_{7,5}$ = 6.3
	152.59	C-5[c]	d $^1J_{5,5}$ = 188.0
	150.10	C-3a	dd $^3J_{3a,5}$ = 14.2, $^3J_{3a,2}$ = 4.8
	149.08	C-2[c]	d $^1J_{2,2}$ = 194.7
	116.46	C-6	dq $^2J_{6,5}$ = 9.0, $^3J_{6,Me}$ = 3.4
	111.66	CN	d $^3J_{CN,2}$ = 1.0
	85.02	C-3	d $^2J_{3,2}$ = 9.0
	63.56	OCH_2	tq $^1J_{OCH_2}$ = 149.7, $^2J_{OCH_2,Me}$ = 4.4
	15.24	7-Me	q $^1J_{Me}$ = 133.0
	13.98	CH_2Me	qt $^1J_{Me}$ = 127.8, $^2J_{Me,CH_2}$ = 2.7
6	192.33	C=O	qd $^2J_{CO,Me}$ = 1.5, $^3J_{CO,5}$ = 6.3
	159.34	CO_2R	t $^3J_{CO,OCH_2}$ = 3.4
	152.55	C-5[c]	d $^1J_{5,5}$ = 187.2
	150.24	C-3a	dd $^3J_{3a,5}$ = 14.0, $^3J_{3a,2}$ = 5.0
	150.02	C-2[c]	d $^1J_{2,2}$ = 195.6
	140.67	C-7	d $^3J_{7,5}$ = 5.9
	117.14	C-6	dq $^2J_{6,5}$ = 9.6, $^3J_{6,Me}$ = 1.4
	111.43	CN	d $^3J_{CN,2}$ = 1.0
	84.76	C-3	d $^2J_{3,2}$ = 8.9
	64.19	OCH_2	tq $^1J_{OCH_2}$ = 149.8, $^2J_{OCH_2,Me}$ = 4.5
	27.93	COMe	q $^1J_{Me}$ = 128.8
	13.73	CH_2Me	qt $^1J_{Me}$ = 127.8, $^2J_{Me,CH_2}$ = 2.6

[a] Multiplicity in the coupled spectra, s = singlet, d = doublet, t = triplet, q = quartet. [b] Appears as a quintet. [c] Assignment made on the basis of COLOC experiments.



7; R = H
8; R = Ph
9; R = CO_2Et
10; R = CN

Fig. 2

frequency (152.55 ppm) to C-5 and, consequently, the signal at 150.02 ppm to C-2. Looking at the coupling constant values reported in Tables 1 and 2, it is of interest to note that for compound **6**, not only is $^1J_{2,2}$, as usual, larger than $^1J_{5,5}$ (195.6 *vs.* 187.2 Hz) but that its value is in full agreement with that of compound **10** (194.2 Hz).

The general rules outlined for similar[4] and other heterocyclic systems,[10] also hold for compounds **1** and **6–17**: for example, $^2J_{\beta\alpha}$ in which the coupled proton is geminal to an sp^2 nitrogen atom and $^3J_{CH}$ through a heteroatom are larger in comparison with other geminal or vicinal couplings, respectively.

As the nature of the starting material has been firmly established, we repeated many times the treatment of compound **6** with acetic acid and water as described by Kurihara,[7] always obtaining the same product.

To this compound, showing all the physical and spectroscopic data previously reported by the Japanese authors (see Experimental section), the structure of ethyl 3-cyano-7-methylpyrazolo[1,5-*a*]pyrimidine-6-oxoacetate (**1**) instead of that reported, pyrazolodiazepine **2** must be assigned. The structure **1** follows not only from a careful analysis of the coupled ^{13}C NMR spectrum, which was not previously examined,[7] but also from an unambiguous synthetic approach (see below).

As regards the proton-coupled carbon spectrum, two diagnostic coupling patterns must be highlighted. The signal of the quaternary carbon at 153.90 ppm (lit.,[7] 153.93, previously assigned to C-8 of **2** from the decoupled spectrum only) appears as a quintet (doublet of quartets) with a coupling constant of 6.3 Hz that cannot be ascribed to a four-bond pattern ($^4J_{8,5}$). On the other hand, the above resonance cannot be assigned to C-7 of **2** on the basis of chemical shift considerations. In contrast, if the signal is attributed to C-7 of compound **1**, a 6 Hz coupling appears in excellent agreement with those reported in Table 1 for similar structural patterns. Moreover, the signal at 116.46 ppm (lit.,[7] 116.54, assigned to C-7 of structure **2**) appears as a doublet of quartets but with coupling constants of 9 Hz and 3.4 Hz. Whereas these values are not in accord with C-7 of structure **2**, $^2J_{7,Me}$ having to be *ca.* 6 Hz for a $C(sp^2)$–$C(sp^3)$–H coupling,[4,11a] they agree well with the carbon at position 6 of compound **1** ($^2J_{6,5}$ and $^3J_{6,Me}$).[1,4]

Finally, we found it necessary to look also for a chemical proof of the nature of compound **1**. Thus, following our previously described procedure and starting from the 2-dimethylaminovinylpyrazolopyrimidine **11**,[2] we obtained, through compound **13**, the pyrazolo[1,5-*a*]pyrido[3,4-*e*]pyrimidine ester **17** (see Scheme 2). Both structures **13** and **17** follow from spectroscopic evidence. Owing to the easy attribution of the proton resonances, the carbon spectra of **13** and **17** have been completely assigned on the basis of proton coupled, HETCOR, and COLOC experiments (see Table 3).

On the other hand, reaction of compound **1** with dimethylformamide dimethyl acetal in anhydrous toluene afforded the vinyl derivative **16**, whose structure follows from spectroscopic evidence.[2] Ring closure of this compound in acetic acid–ammonium acetate gave a product identical (m.p., IR, ^1H, ^{13}C NMR and mass spectra) with compound **17** prepared as described above, thus confirming the structure of **1** to be ethyl 3-cyano-7-methylpyrazolo[1,5-*a*]pyrimidine-6-oxoacetate.

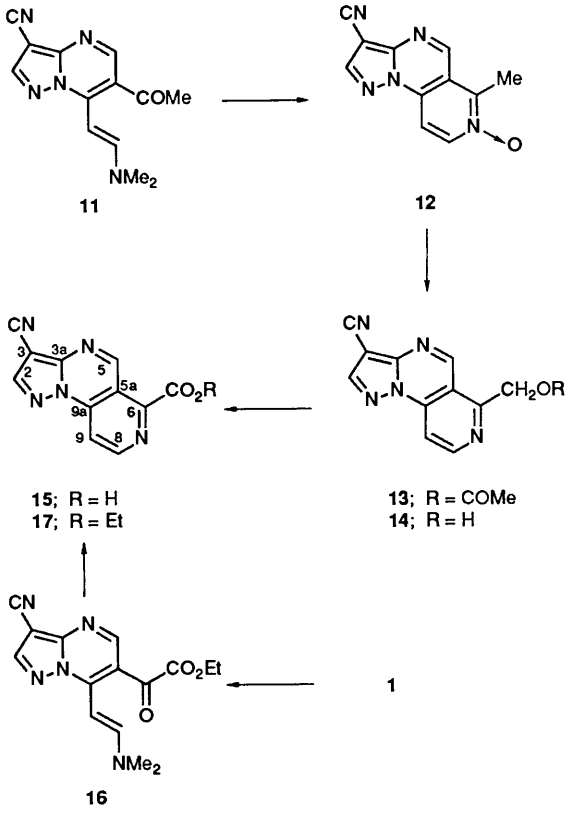
Experimental

All melting points were determined on a Gallenkamp MFB-595-010M melting point apparatus (accuracy ±0.5 °C) and are uncorrected. Infrared spectra were obtained with a Perkin-Elmer 881 spectrophotometer in KBr pellets. Mass spectra were recorded with a Carlo Erba QMD 1000 instrument at 70 eV. Carbon-13 and proton NMR spectra were measured on a Varian VXR-300 or a Varian Gemini-200 instrument in the

Table 3 Carbon-13 chemical shifts (δ) and coupling constants (Hz) of compounds **13** and **17**

13			**17**		
C	δ	J	C	δ	J
2[a]	146.37	$^1J_{2,2}$ = 195.5	2[a]	146.51	$^1J_{2,2}$ = 195.7
3	87.54	$^2J_{3,2}$ = 9.1	3	87.90	$^2J_{3,2}$ = 9.2
3a	147.97	$^3J_{3a,5}$ = 14.7, $^3J_{3a,2}$ = 4.8	3a[b]	147.64	$^3J_{3a,5}$ = 14.9, $^3J_{3a,2}$ = 5.1
5[a]	152.03	$^1J_{5,5}$ = 188.7	5[a]	153.45	$^1J_{5,5}$ = 195.9
5a	112.88	multiplet	5a	113.64	multiplet
6	156.80	$^3J_{6,8}$ = 11.5, $^2J_{6,CH_2}$ = 4.2, $^3J_{6,5}$ = 1.1	6[b]	149.12	$^3J_{6,8}$ = 11.3, $^3J_{6,5}$ = 1.1
8	152.51	$^1J_{8,8}$ = 184.3, $^2J_{8,9}$ = 2.1	8	151.92	$^1J_{8,8}$ = 186.2, $^2J_{8,9}$ = 2.2
9	109.15	$^1J_{9,9}$ = 173.8, $^2J_{9,8}$ = 8.7	9	111.80	$^1J_{9,9}$ = 174.5, $^2J_{9,8}$ = 9.1, $^4J_{9,5}$ = 0.9[c]
9a	140.71	multiplet	9a	140.93	multiplet
CN	111.73	$^3J_{CN,2}$ = 1.0	CN	111.59	$^3J_{CN,2}$ = 1.1
CH_2	64.61	$^1J_{CH_2}$ = 149.2	CH_2	63.35	$^1J_{CH_2}$ = 149.0, $^2J_{CH_2,Me}$ = 4.4
CO	170.11	$^2J_{CO,Me}$ = 7.0, $^3J_{CO,OCH_2}$ = 3.5	CO	163.78	$^3J_{CO,OCH_2}$ = 3.5
Me	20.65	$^1J_{Me}$ = 130.1	Me	14.19	$^1J_{Me}$ = 127.8, $^2J_{Me,CH_2}$ = 2.7

[a] Assignment made on the basis of HETCOR spectrum. [b] Assignment made on the basis of COLOC experiments. [c] Coupling constants of similar magnitude are reported in the literature.[11b]



Scheme 2

Fourier transform mode. All carbon spectra were recorded at 25 ± 0.5 °C for 0.5 mol dm^{-3} solutions in anhydrous $CDCl_3$. Proton coupled spectra were obtained in the 'gated decoupling' mode. Typical conditions were spectral width 16 000 Hz, 64 K data points (digital resolution of 0.5 Hz/point, i.e. 0.01 ppm), quadrature phase detection and pulse width 7 μs (≈30°). Chemical shifts are reported in ppm high frequency from tetramethylsilane as secondary internal reference and coupling constants in Hz. Solvents were removed under reduced pressure. Silica gel plates (Merck F_{254}) were used for analytical TLC.

3-Amino-4-cyanopyrazole (**3**) was commercially available (Aldrich) and was used without further purification; compounds **4**,[12] **6**,[7] **11**[2] and **12**[13] were obtained according to published procedures.

Ethyl 3-{[(4-*Cyano*-1H-*pyrazol*-5-*yl*)*amino*]*methylene*}-2,4-*dioxopentanoate* **5**.—Compound **4** (2.14 g, 10 mmol) in ethanol (10 cm^3) was added with stirring under ice cooling to a solution of the aminopyrazole **3** (1.08 g, 10 mmol) in ethanol (30 cm^3). The precipitate was collected by filtration, washed with cold ethanol and dried to give compound **5** as a yellowish solid (2.71 g, 98%), m.p. 162–163 °C (lit.,[7] 162–163 °C); (Found: C, 52.2; H, 4.45; N, 20.2. $C_{12}H_{12}N_4O_4$ requires C, 52.2; H, 4.4; N, 20.1%); δ_H[200 MHz, $(CD_3)_2SO$] 1.08 (3 H, t, *J* 7.0, OCH_2*Me*), 2.27 (3 H, s, CO*Me*), 4.09 (2 H, q, *J* 7.0, OCH_2Me), 7.25 (1 H, s, exch., NH), 7.88 (1 H, s, CH), 7.99 (1 H, s, H-3) and 11.96 (1 H, br s, exch., NH) [lit.,[7] 1.10 (3 H, t), 2.25 (3 H, s), 4.05 (2 H, q), 7.13 (1 H, s, CH), 7.80 (1 H, s, NH) and 7.93 (1 H, s, H-3)].

Ethyl 3-*Cyano*-7-*methylpyrazolo*[1,5-a]*pyrimidine*-6-*oxoacetate* **1**.—A solution of compound **6** (0.26 g, 1 mmol) in acetic acid (30 cm^3) containing water (1 cm^3) was heated at 70 °C for 5 h. Evaporation to dryness left a solid (0.26 g, 100%) consisting mainly (TLC and ^1H NMR spectrum) of compound **1** with a small amount of the starting material. An analytical sample obtained after crystallisation from ethanol (colourless needles) melted at 111–112 °C (lit.,[7] 112–113 °C) (Found: C, 55.8; H, 3.95; N, 21.5. $C_{12}H_{10}N_4O_3$ requires C, 55.9; H, 3.9; N, 21.7%); δ_H(200 MHz, $CDCl_3$) 1.46 (3 H, t, *J* 7.1, OCH_2*Me*), 3.19 (3 H, s, 7-Me), 4.51 (2 H, q, *J* 7.1, OCH_2Me), 8.54 (1 H, s, H-2) and 9.04 (1 H, s, H-5); *m/z* 258 (M^+, 12%), 185 ($M^+ - CO_2Et$, 100) and 157 ($M^+ - CO_2Et - CO$, 8).

6-*Acetoxymethyl*-3-*cyanopyrazolo*[1,5-a]*pyrido*[3,4-e]*pyrimidine* **13**.—A suspension of compound **12** (2.25 g, 10 mmol) was refluxed under stirring with acetic anhydride (6 cm^3) for 5 min. After concentration of the mixture, dilution with ethanol afforded compound **13** as a red solid (1.38 g, 52%), m.p. 205–206 °C (pink crystals from butan-2-one) (Found: C, 58.2; H, 3.55; N, 26.1. $C_{13}H_9N_5O_2$ requires C, 58.4; H, 3.4; N, 26.2%); ν_{max}(KBr)/ cm^{-1} 3118, 3096, 2233 (CN), 1790 (CO) and 1597; δ_H(200 MHz, $CDCl_3$) 2.18 (3 H, s, CO*Me*), 5.75 (2 H, s, 6-CH_2), 8.35 (1 H, dd, $^3J_{8,9}$ 5.9, $^5J_{5,9}$ 0.9, H-9), 8.44 (1 H, s, H-2), 9.03 (1 H, d, $^3J_{8,9}$ 5.9, H-8) and 9.49 (1 H, d, $^5J_{5,9}$ 0.9, H-5).

3-*Cyano*-6-*hydroxymethylpyrazolo*[1,5-a]*pyrido*[3,4-e]*pyrimidine* **14**.—Compound **13** (1.33 g, 5.0 mmol) in methanol (25 cm^3) was added to a solution of freshly prepared sodium methoxide (0.12 g of Na in 50 cm^3 of MeOH) and the mixture was stirred at room temperature for 30 min. After neutralisation, the solid which separated was filtered and dried to give compound **14** (0.95 g, 79%), m.p. 237 °C (decomp.) (from 2-

methoxyethanol) (Found: C, 58.6; H, 3.2; N, 31.0. $C_{11}H_7N_5O$ requires C, 58.7; H, 3.1; N, 31.1%); ν_{max}(KBr)/cm^{-1} 3420br (OH), 3090, 2220 (CN) and 1595; δ_H(200 MHz, $CDCl_3$) 1.57 (1 H, s, exch., OH), 5.38 (2 H, s, 6-CH_2), 8.33 (1 H, dd, $^3J_{8,9}$ 5.9, $^5J_{5,9}$ 0.8, H-9), 8.46 (1 H, s, H-2), 9.01 (1 H, d, $^3J_{8,9}$ 5.9, H-8) and 9.33 (1 H, d, $^5J_{5,9}$ 0.8, H-5).

3-*Cyanopyrazolo*[1,5-a]*pyrido*[3,4-e]*pyrimidine-6-carboxylic Acid* **15**.—Compound **14** (0.72 g, 3.2 mmol) was suspended in water (5 cm^3) and an aqueous solution of potassium permanganate (1.6% w/v; 40 cm^3) was added dropwise. The mixture was stirred at 40–50 °C for 1 h and filtered. Acidification with hydrochloric acid (6 mol dm^{-3}, pH 2) afforded the acid **15** as a yellowish solid which was not further purified (0.48 g, 62%). Compound **15** gradually darkened above 190 °C and melted at 225–230 °C (decomp.) (Found: C, 55.4; H, 2.0; N, 29.5. $C_{11}H_5N_5O_2$ requires C, 55.2; H, 2.1; N, 29.3%); ν_{max}(KBr)/cm^{-1} 3400–1900br (CO_2H), 3116, 3091, 2239 (CN), 1710 (CO) and 1600.

Ethyl 3-*Cyano*-7-(2-*dimethylamino*)*vinylpyrazolo*[1,5-a]*pyrimidine-6-oxoacetate* **16**.—Compound **1** (2.58 g, 10 mmol) in anhydrous toluene (160 cm^3) containing *N*,*N*-dimethylformamide dimethyl acetal (1.42 g, 11.9 mmol) was maintained at 60 °C under stirring for 20 min. Removal of the solvent left a yellow solid (2 g, 64%) which after crystallisation from ethanol melted at 211–212 °C (Found: C, 57.6; H, 4.8; N, 22.2. $C_{15}H_{15}N_5O_3$ requires C, 57.5; H, 4.8; N, 22.35%); ν_{max}(KBr)/cm^{-1} 2227 (CN), 1711 (2 × CO) and 1642; δ_H(200 MHz, $CDCl_3$) 1.43 (3 H, t, *J* 7.1, OCH$_2$*Me*), 3.20 (3 H, s, NMe), 3.41 (3 H, s, NMe), 4.45 (2 H, q, *J* 7.1, OCH_2Me), 7.34 (1 H, d, $^3J_{trans}$ 12.4, C*H*CHNMe$_2$), 8.26 (1 H, s, H-2), 8.57 (1 H, s, H-5) and 9.74 (1 H, d, $^3J_{trans}$ 12.4, CHC*H*NMe$_2$); δ_C(75 MHz, $CDCl_3$) 14.07 (q, OCH$_2$*Me*), 37.46 (q, NMe), 46.82 (q, NMe), 62.44 (t, OCH$_2$), 82.81 (s, C-3), 87.03 (d, C-α), 106.71 (s, C-6), 112.92 (s, CN), 146.68 (d, C-2), 147.50 (s, C-7), 151.67 (s, C-3a), 155.74 (d, C-5), 160.78 (d, C-β), 164.41 (s, CO_2Et) and 185.12 (s, CO).

Ethyl 3-*Cyanopyrazolo*[1,5-a]*pyrido*[3,4-e]*pyrimidine-6-carboxylate* **17**.—(*a*) To a stirred solution of compound **15** (0.48 g, 2.0 mmol) in absolute ethanol (40 cm^3), was added boron trifluoride etherate (0.8 cm^3) and the mixture was refluxed for 48 h. After cooling, the precipitate was filtered, washed with cold ethanol and dried to yield the ester **17** (0.38 g, 70%), m.p. 234–235 °C (white crystals from ethanol) (Found: C, 58.2; H, 3.55; N, 26.1. $C_{13}H_9N_5O_2$ requires C, 58.4; H, 3.4; N, 26.2%); ν_{max}(KBr)/cm^{-1} 3117, 3085, 2239 (CN), 1704 (CO) and 1598; δ_H(200 MHz, $CDCl_3$) 1.55 (3 H, t, *J* 7.1, OCH$_2$*Me*), 4.65 (2 H, q, *J* 7.1, OCH_2Me), 8.45 (1 H, s, H-2), 8.55 (1 H, dd, $^3J_{8,9}$ 5.7, $^5J_{5,9}$ 0.8, H-9), 9.13 (1 H, d, $^3J_{8,9}$ 5.7, H-8) and 10.14 (1 H, d, $^5J_{5,9}$ 0.8, H-5).

(*b*) The enamine **16** (0.62 g, 2.0 mmol) was refluxed for 2 h in acetic acid (10 cm^3) containing ammonium acetate (4 g). After cooling, the mixture was diluted with water (10 cm^3) and the precipitate was filtered and dried to afford compound **17** (0.39 g, 75%), identical (m.p., IR, ^{1}H and ^{13}C NMR spectra) with the material obtained as above.

References

1 S. Chimichi, B. Cosimelli, F. Bruni and S. Selleri, *Magn. Reson. Chem.*, 1992, **30**, 1117.
2 F. Bruni, S. Chimichi, B. Cosimelli, A. Costanzo, G. Guerrini and S. Selleri, *Heterocycles*, 1990, **31**, 1141.
3 F. Bruni, S. Chimichi, B. Cosimelli, A. Costanzo, G. Guerrini and S. Selleri, *Heterocycles*, 1990, **31**, 1635.
4 S. Chimichi, B. Cosimelli, F. Bruni and S. Selleri, *Can. J. Chem.*, 1992, **70**, 1093.
5 H. A. DeWald, S. Lobbestael and B. P. H. Poschel, *J. Med. Chem.*, 1981, **24**, 982.
6 M. Williams, *J. Med. Chem.*, 1983, **26**, 619.
7 T. Kurihara, K. Nasu, F. Ishimori and T. Tani, *J. Heterocycl. Chem.*, 1981, **18**, 163.
8 T. Kurihara, E. Kawasaki and K. Nasu, *Heterocycles*, 1983, **20**, 1913.
9 Y. Makisumi, *Chem. Pharm. Bull.*, 1962, **10**, 620; L. Pecori-Vettori, L. Cecchi, A. Costanzo, G. Auzzi and F. Bruni, *Farmaco*, 1981, **36**, 344.
10 S. Chimichi, P. Tedeschi, A. Camparini and F. Ponticelli, *Org. Magn. Reson.*, 1982, **20**, 141; S. Chimichi, P. Tedeschi, R. Nesi and F. Ponticelli, *Magn. Reson. Chem.*, 1985, **23**, 86; G. Miyajima, K. Takahashi and H. Sugiyama, *Org. Magn. Reson.*, 1974, **6**, 181; Y. Takeuchi, *Org. Magn. Reson.*, 1975, **7**, 181; G. W. H. Cheeseman, C. J. Turner and D. J. Brown, *Org. Magn. Reson.*, 1979, **12**, 212; C. J. Turner and G. W. H. Cheeseman, *Org. Magn. Reson.*, 1976, **8**, 357.
11 H. O. Kalinowski, S. Berger and S. Braun, *Carbon-13 NMR Spectroscopy*, Wiley, Chichester, 1988, (*a*) pp. 512–519; (*b*) p. 543 and references cited therein.
12 R. G. Jones, *J. Am. Chem. Soc.*, 1951, **73**, 8684.
13 S. Selleri, F. Bruni, A. Costanzo, G. Guerrini, P. Malberg-Aiello, G. Iavarone and C. Martini, *Eur. J. Med. Chem.*, in the press.

Paper 2/04283E
Received 7*th August* 1992
Accepted 14*th October* 1992