Further Investigation on the Reaction of Heterocyclic Ketene Aminals with Ethyl Propiolate: Ene-type Reaction of Enamines and an Unusual Substituent Effect

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The reaction between heterocyclic ketene aminals and ethyl propiolate **1** has been investigated and an unusual substituent effect observed. Although 2-(benzoylmethylene)-1,3-dimethylimidazolidines **2** failed to add to **1**, 2-(benzoylmethylene)imidazolidine **3** reacted with it to give the fused heterocycle **5** *via* the intermediate **4**. With one methylated nitrogen, the heterocyclic ketene aminals **6** or **7** reacted with **1** to afford the heterocyclic compounds **9** or **10** and ethoxycarbonylvinyl substituted heterocycles **11** or **12**. By controlling the reaction conditions, **9** or **10** and **11** or **12** can be synthesized selectively. The results are interpreted in terms of an ene–addition mechanism with steric interaction in the intermediates. A correlation between reactivity and intramolecular hydrogen bonding is also discussed.

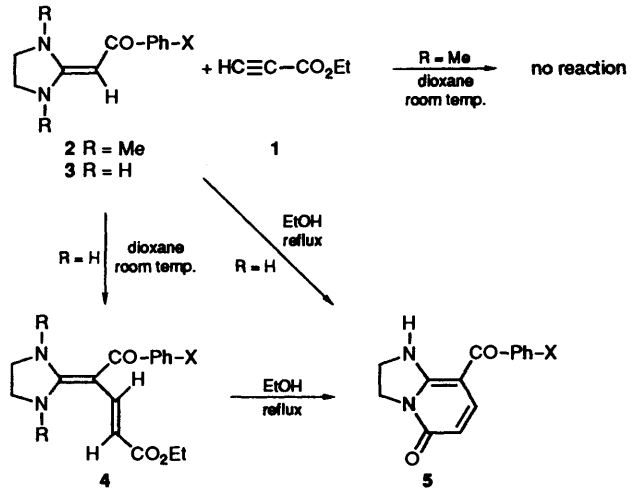
In contrast to enamines,[1,2] heterocyclic ketene aminals or cyclic 1,1-enediamines have been little studied until recently.[3–7] As enamines, heterocyclic ketene aminals show some intriguing structure characteristics and have demonstrated their potential in the synthesis of heterocycles.[3–5,7d–13] Owing to the conjugation effect of the electron-donating amino groups and electron-withdrawing substituents, the double bond is highly polarized and the electron density on the α-carbon is increased, leading to greater nucleophilicity at carbon than at the nitrogen. Thus, the carbon centre always attacks the electropositive site of electrophiles,[8,14–16] even 1,3-dipoles such as azides[3] and nitrile oxide.[9] Since, in addition, the secondary amino group in the molecule may also participate in the reaction, heterocyclic ketene aminals may serve as bis-nucleophilic reagents to give a wide variety of heterocyclic compounds by nucleophilic addition or substitution and cyclocondensation reaction sequences.[5,7d–11,13] Some cyclic 1,1-enediamines and their derivatives also possess certain biological activities.[17]

C-Alkylation of enamines with electron-deficient compounds has been well established.[1,2] Notably, reaction of enamines with activated acetylenes is strongly influenced by the structure of both reactants, solvent polarity and temperature. Enamines may undergo direct Michael addition through a dipolar intermediate or [2 + 2] cycloaddition to acetylenic esters, and different products have been obtained from these and further rearrangements.[18–23] *N*-Alkylation of secondary enamines formed by tautomerization of the corresponding imines has also been reported[24,25] on treatment of dimethyl acetylenedicarboxylate.

Earlier, we described the reaction of imidazolinyl and tetrahydropyrimidinyl substituted 1,1-enediamines with esters of α,β-unsaturated acids. *C*-Alkylation of 1,1-enediamines with methyl propiolate occurred to give vinylene adducts of *E* configuration, which were converted into fused heterocyclic compounds in refluxing ethanol.[13d,e] Although the ene reaction pathway was proposed for the addition, it is difficult to rule out other possible routes involving direct Michael addition or [2 + 2] cycloaddition followed by rearrangement, paths which are often encountered in the reactions of enamines.[18–23] Interest in the correlation between structure and reactivity and reaction mechanism of heterocyclic ketene aminals led us to further investigate their reactions with the propiolate. Herein we report our results.

Results and Discussion

In order to study the influence of the enediamine's structure on its addition to α,β-unsaturated compounds, heterocyclic ketene aminals of different heterocycle moieties were synthesized from the cyclocondensation of ketene mercaptals and diamines by a literature method.[3] 2-(Benzoylmethylene)-1,3-dimethylimidazolidines **2** failed to react with ethyl propiolate **1** in dioxane, only starting material being recovered after a lengthy reaction period. In contrast, under similar conditions, 2-(benzoylmethylene)imidazolidine **3** reacted readily with **1**, to give exclusively the (*E*)-(ethoxycarbonyl)vinylene substituted compound **4**, an intermediate which underwent intramolecular cyclocondensation in refluxing ethanol to afford the fused heterocycle **5**. The latter can be also obtained as the sole product from **3** and **1** in a one-pot reaction in refluxing ethanol (Scheme 1).



Scheme 1

The complexity of the reaction of *N*-methylated cyclic 1,1-enediamines **6** or **7** with **1** was unexpected, both fused heterocycles **9** or **10** and (*E*)-(ethoxycarbonyl)vinyl substituted heterocycles **11** or **12** being formed in refluxing ethanol. Product distribution was sensitive to the molar proportions of reactants used, increased proportions of acetylene **1** leading to higher yields of the products **11** or **12** (Table 1). Thus selective syntheses of **9** or **10** and **11** or **12** were possible (Table 2) by controlling the molar ratio of reactants.

In non-polar solvents such as 1,4-dioxane, **6** or **7** reacted

Table 1 Reaction of 2-(benzoylmethylene)-1-methylimidazolidine (**6a**) with ethyl propiolate **1**

Molar ratio **6a**:**1**	Solvent	Temp.	T/(day)	Yield[a] of product (%) 8	9a	11a
1:1	Dioxane	Room temp.	8	42[b]		19[b]
1:1	Dioxane	Room temp.	10	49[b]		5
2:1	Dioxane	Room temp.	7	64[c]		
1:8	Dioxane	Room temp.	7			50
1:1	EtOH	Reflux	2		78	6
1:1.1	EtOH	Reflux	2		69	11
1:2	EtOH	Reflux	2		37	47
1:4	EtOH	Reflux	2		19	63
1:8	EtOH	Reflux	2		8	72
2:1	EtOH	Reflux	2		89[d]	

[a] Isolated yield based on **6a**. [b] Measured by ^{1}H NMR based on **6a**. [c] Measured by ^{1}H NMR based on **1**. [d] Isolated yield based on **1**.

Table 2 Reaction between **1** and **6** or **7** in refluxing ethanol

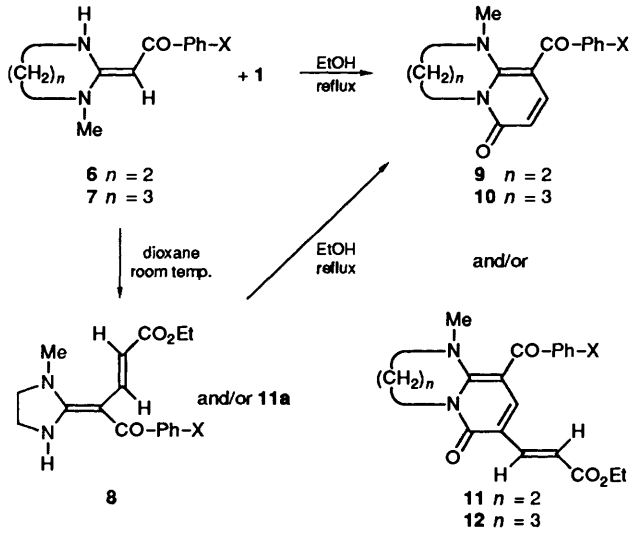
Starting material	**6** or **7**:**1** (1:1 molar ratio) yield[a] of product (%)	**6** or **7**:**1** = 1:8 (molar ratio) yield[a] of product (%)
6a	**9a** (78), **11a** (6)	**9a** (8), **11a** (72)
6b	**9b** (84), **11b** (4)	**9b** (10), **11b** (62)
6c	**9c** (73), **11c** (12)	**9c** (4), **11c** (63)
6d	**9d** (76), **11d** (6)	**9d** (7), **11d** (72)
7a	**10a** (58), **12a** (7)	**10a** (0), **12a** (74)
7b	**10b** (53), **12b** (6)	**10b** (0), **12b** (57)
7c	**10c** (35), **12c** (5)	**10c** (0), **12c** (73)
7d	**10d** (36), **12d** (6)	**10d** (0), **12d** (66)

[a] Isolated yield based on **6** or **7**.

sluggishly with **1** compared with the analogous reaction of **3** with **1**, and monitoring of this reaction by TLC and ^{1}H NMR spectroscopy showed it to be complex. Although the adduct **8** was detected after 10 days, the heterocycle **11** and starting material **6** were also present in the mixture; again, the reactant ratio, **1**:**6**, greatly affected the product distribution. Depending on whether an excess of **6** or **1** was used exclusive formation of the adduct **8** or heterocycle **11**, respectively, resulted. Attempted isolation of **8** from the reaction mixture failed because of its sensitivity to silica gel and polar solvents, but its formation was observed by ^{1}H NMR analysis of the reaction mixture. When heated in ethanol, the crude material obtained from the reaction in dioxane gave the heterocyclic compound **9** (Scheme 2).

Since the outcome of the reaction between **6** or **7** and **1** depended upon the conditions used, we varied the conditions for the reaction between **3** and **1**. Thus, varying the molar ratio of **3** to **1** from 1:1 to 1:8 in dioxane allowed shortening of the reaction period from 4 to 2 days, product **4** being formed exclusively. Use of ethanol instead of dioxane gave **5** as the sole product, although a large excess of **1** was necessary. Since no reaction occurred between **5**, **9** and **10** with **1**, **11** or **12** could not be derived from **9** or **10**.

The structures of all compounds were established on the basis of spectroscopic evidence and elemental analyses. The *E* configuration of the vinylene moiety in **4**, **8**, **11** and **12** was proven by ^{1}H NMR results with the vinylene hydrogens showing a coupling constant around 16 Hz. The *E* configuration about the enediamine double bond of **8** was determined based on the presence of an intramolecular hydrogen bond as indicated by the downfield shift of the nitrogen proton in the ^{1}H NMR spectra, while **5**, **9** and **10** showed AB quartet signals with *J* 10 Hz, consistent with a *cis*-geometry of the vinylene segment. All



6, 7, 9–12	a	b	c	d
X	H	Cl	Me	OMe

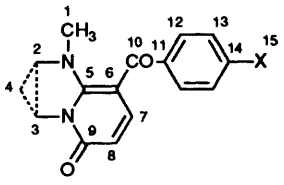
Scheme 2

fused heterocycles gave unsaturated lactam carbonyl signals around 160 ppm in the ^{13}C NMR spectra excluding the possibility of *N*-alkylation between **3**, **6**, **7** and **1**[24,25] (Table 3). The structures of heterocyclic compounds **11** or **12** were also confirmed unambiguously by X-ray analysis of 8-benzoyl-6-(ethoxycarbonyl)vinyl-1-methyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]-pyridin-5(4*H*)-one **11a**.[26]

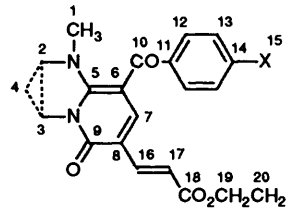
These results suggest that an unusual substituent effect operates during the reaction. Thus, with differently substituted heterocyclic ketene aminals, reactions differed considerably. It appears essential that the secondary amino group in heterocyclic ketene aminals add to the unsaturated compound, since the *N*,*N*′-dimethylated cyclic 1,1-enediamine **2** did not react with **1**. However, the secondary amino group does not attack the triple bond initially, only *C*-alkylated adducts being produced as evidenced by structural analyses. These indicated that the effective reaction unit is the secondary enamine moiety (H–N–C=C), rather than the double bond or tertiary enamine. It is concluded that the addition most probably proceeds *via* an ene reaction between the heterocyclic ketene aminals **3**, **6**, **7** and **1** rather than by direct Michael addition or [2 + 2] cycloaddition. *trans*-Vinylene adducts **4** and **8** isolated or detected are in accord with the ene process. The intermediates **4** and **8** were transformed into fused heterocycles **5**, **9** and **10** in protic solvents such as ethanol, by *trans-cis* isomerization and cyclocondensation sequences. Direct formation of the final products **5**, **9** and **10** in ethanol demonstrated that these steps were faster than that of the addition step. Unexpected products **11** or **12** must be formed from a second acetylene **1** and the intermediate *in situ*, since **9** or **10** itself did not react with **1**. Taking the configuration of both the intermediate **8** and of the products **11** or **12** into account, we suggest a possible reaction pathway involving [2 + 2] cycloaddition, symmetry-allowed conrotary ring opening[27] and cyclocondensation.

The mechanism depicted in Scheme 3 can best explain the experimental facts. The great difference in reaction rate between **3** and **6** or **7** may be attributed to the effect of intramolecular hydrogen bonds between carbonyl and secondary amine moieties in **3**, **6** or **7**. Intramolecular hydrogen bond formation decreases the ene addition rate (Fig. 1). The unusual *N*-substituent effect on the reaction outcome may result from subtle steric interactions in the intermediates **4** and **8**.

Table 1 ^{13}C NMR data of compounds **9–12**



9, 10



11, 12

Compd.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
9a	51.7	37.9	42.5		155.3	98.6	144.5	105.1	161.2	191.0
9b	51.6	37.7	42.4		155.3	98.1	143.9	105.3	161.0	189.4
9c	51.5	37.6	42.4		155.0	98.7	144.3	104.9	161.1	190.8
9d	51.6	37.6	42.5		154.9	98.7	144.4	105.0	161.4	192.0
10a	50.1	39.5	43.8	21.8	154.0	102.4	143.5	103.8	161.8	191.2
10b	50.2	39.6	43.8	21.7	154.1	102.0	143.2	103.9	161.7	189.7
10c	50.1	39.6	43.7	21.8	153.7	102.2	143.7	103.5	161.8	191.3
10d	50.1	39.7	43.6	21.9	153.5	102.1	143.6	103.4	161.8	190.6
11a	51.8	37.6	42.5		154.6	99.5	146.6	110.8	159.2	190.8
11b	51.7	37.5	42.4		154.4	99.0	146.0	110.8	159.0	189.2
11c	51.8	37.5	42.6		154.5	99.7	146.5	110.9	159.3	190.7
11d	51.7	37.3	42.6		154.2	99.6	146.4	110.6	159.2	189.8
12a	50.2	39.7	43.8	21.2	153.6	103.2	145.2	108.8	159.7	191.2
12b	50.3	39.8	43.8	21.3	153.7	102.8	144.6	109.1	159.6	189.6
12c	50.2	39.6	43.6	21.4	153.5	103.3	144.9	109.0	159.6	190.9
12d	50.2	39.6	43.5	21.4	153.3	103.2	144.7	108.8	159.5	190.2

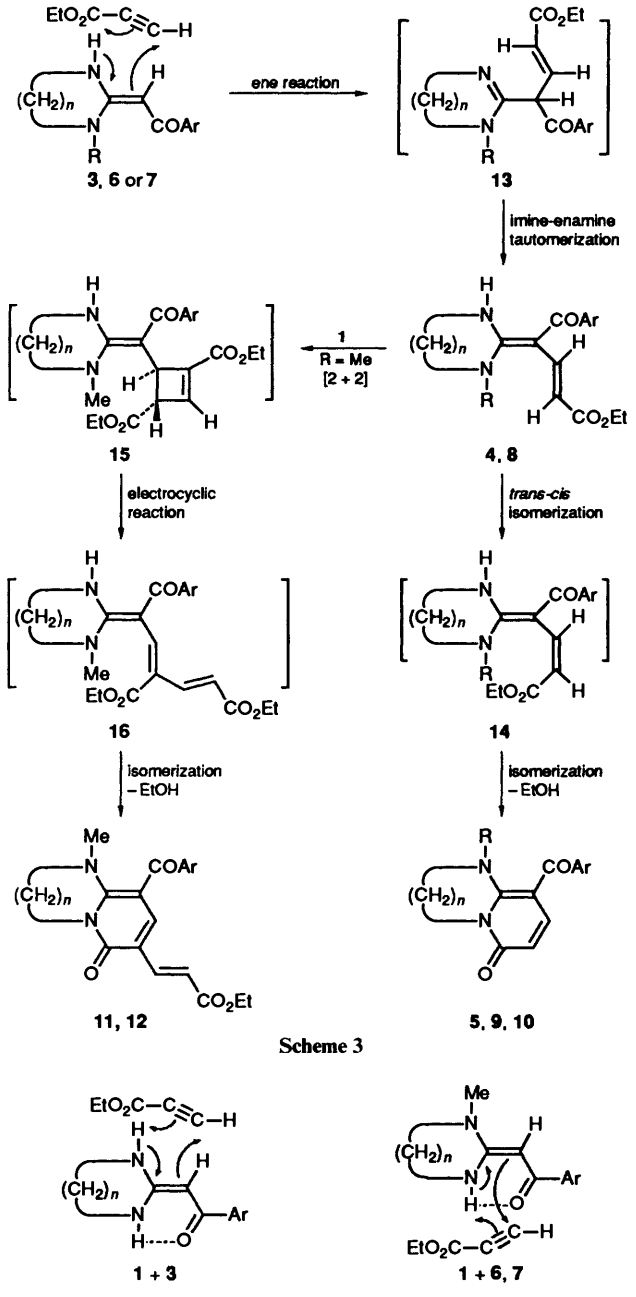
Compd.	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20
9a	138.6	129.6	128.5	132.2						
9b	136.9	130.9	128.6	138.3						
9c	142.8	129.7	129.0	135.9	21.5					
9d	131.2	131.9	113.7	163.0	55.5					
10a	138.9	129.4	128.4	131.9						
10b	137.3	130.8	128.7	138.2						
10c	142.8	129.7	129.2	136.0	21.6					
10d	131.1	131.6	113.7	163.0	55.5					
11a	138.0	129.7	128.6	132.6		140.2	115.7	168.3	59.9	14.3
11b	136.3	131.0	128.8	138.8		140.0	115.8	168.0	60.0	14.2
11c	143.6	129.9	129.4	135.3	21.7	140.1	115.8	168.3	60.0	14.4
11d	130.5	132.0	113.9	163.3	55.5	140.2	115.5	168.3	59.9	14.3
12a	138.0	129.6	128.6	132.5		140.8	115.2	168.4	59.9	14.3
12b	136.5	131.0	128.9	138.8		140.5	115.6	168.1	59.7	14.4
12c	143.1	129.8	129.3	135.4	21.6	140.7	115.3	168.1	59.7	14.4
12d	130.4	131.9	113.8	163.1	55.4	140.8	115.2	168.1	59.7	14.4

That few cases[28] of secondary enamines acting as an ene component have been reported previously is understandable in terms of imine tautomers being more stable than secondary enamines under standard conditions.[29] A study of the reaction between heterocyclic ketene aminals and ethyl propiolate suggests that heterocyclic ketene aminals are capable of acting as an ene component and adding to α,β-unsaturated compounds. Intramolecular hydrogen bonding of the secondary amino group, however, slows down the rate of ene reaction. In addition, by modifying the heterocyclic ketene aminal **3** to the *N*-methylated analogues **6** or **7**, the *E*-(ethoxycarbonyl)vinyl substituted heterocycles **11** or **12** as well as **9** or **10** are produced. This unusual substituent effect between **3** and **6** or **7** on the outcome of the reaction is rationalized in terms of steric interactions in the intermediates **4** and **8**. By controlling the reaction conditions, we have provided a simple route to the selective synthesis of the heterocyclic compounds **9**, **10** or **11**, **12**.

Experimental

M.p.s are uncorrected. ^1H NMR and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with Varian Unity 200 and JEOL FX-100 spectrometers. The chemical shifts are reported in ppm downfield from Me_4Si. *J* Values are given in Hz. IR spectra were recorded with Perkin-Elmer 782 and Hitachi 260–50 spectrometers. UV spectra were determined with a Hitachi 340 spectrometer. Mass spectra were recorded on a AEI MS-50 instrument. Elemental analyses were performed at the Analytical Laboratory of the Institute.

Preparation of Ethyl (E)-4-*Benzoyl*-4-(*imidazolidin*-2-*ylidene*)*but*-2-*enoate* **4**.—A mixture of **3** (380 mg, 2 mmol) and **1** (99%; 200 mg, 2 mmol) in dry 1,4-dioxane (20 cm^3) was stirred at ambient temperature for 4 days. The solvent was removed under reduced pressure and the residue was recrystallized from dry diethyl ether–ethyl acetate to provide **4** (530 mg, 92%) as yellow needles. Under the same conditions, with an excess of **1** (99%; 1.58 g, 16 mmol), the reaction afforded **4** (550 mg, 96%) after 2 days. **4**: m.p. 123–124 °C (Found: C, 67.1; H, 6.2; N, 9.9. $C_{16}H_{18}N_2O_3$ requires C, 67.12; H, 6.34; N, 9.78%); ν_{max}(KBr)/cm^{-1} 3225 (NH), 1700, 1605, 1571 and 1539; δ_H 8.24 (2 H, s, NH), 7.64 (1 H, d, *J* 15.9), 7.39 (5 H, s), 5.43 (1 H, d, *J* 15.9), 4.08 (2 H, q), 3.69 (4 H, s, CH_2CH_2) and 1.20 (3 H, t); *m*/*z* 286 (M^+, 1.6%), 240 (49) and 239 (100).



Scheme 3

Fig. 1

Preparation of 8-*Benzoyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **5**.—*Method A.* A solution of **4** (100 mg, 0.35 mmol) in ethanol (10 cm^3) was refluxed for 20 h after which removal of solvent gave **5** (69 mg, 82%) as pale yellow crystals.

Method B. A mixture of **3** (380 mg, 2 mmol) and **1** (99%; 200 mg, 2 mmol) in ethanol (20 cm^3) was heated for 2 days to give **5** (380 mg, 80%). Similarly, use of an excess of **1** (99%; 1.58 g, 16 mmol) also gave **5** (410 mg, 85%), m.p. 179–180.5 °C (Found: C, 70.0; H, 4.9; N, 11.7. $C_{14}H_{12}N_2O_2$ requires C, 69.99; H, 5.03; N, 11.66%); ν_{max}(KBr)/cm^{-1} 3355 (NH), 1664, 1592 and 1569; δ_H 8.72 (1 H, s, NH), 7.50 (1 H, d, *J* 9.5), 7.39–7.48 (5 H, m), 5.74 (1 H, d, *J* 9.5) and 3.89–4.32 (4 H, m, CH_2CH_2); δ_C 192.3 (C=O), 161.2 (O=C–N), 157.3, 97.0, 142.9, 106.1 (carbons of pyridinone ring), 139.0, 128.3, 128.0, 130.7 (carbons of phenyl ring), 42.7 and 43.3; *m/z* 240 (M^+, 56%) and 239 (100, M^+ − 1).

Reaction of 2-(*Benzoylmethylene*)-1-*methylimidazolidine* **6a** *with Ethyl Propiolate* **1** *in a Non-polar Solvent.*—A mixture of **6a** (400 mg, 2 mmol) and **1** (99%; 200 mg, 2 mmol) in 1,4-dioxane (20 cm^3) was stirred at room temperature, the reaction being monitored by TLC and ^1H NMR spectroscopy (Table 1).

Detection of Ethyl (E)-4-*Benzoyl*-4-(1-*methylimidazolidin*-2-*ylidene*)*but*-2-*enoate* **8**.—A mixture of **6a** (400 mg, 2 mmol) and **1** (99%; 99 mg, 1 mmol) in dry 1,4-dioxane was stirred at room temperature for 7 days. TLC analysis on silica gel, eluting with (EtOAc–EtOH, 40:1) indicated the presence of **8** (R_f 0.04) in addition to **6a** (R_f 0.33); δ_H 8.08 (1 H, s, NH), 7.31–7.90 (5 H, m), 7.70 (1 H, d, *J* 15.5), 5.02 (1 H, d, *J* 15.5), 4.09 (2 H, q), 3.42–3.48 (4 H, m, CH_2CH_2), 3.03 (3 H, s) and 1.21 (3 H, t).

General Procedure for the Preparation of 8-*Aroyl*-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **9a–d** *or* (9-*Aroyl*-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(7H)-*one* **10a–d**.—A mixture of **6** or **7** (2 mmol) and **1** (2 mmol) in ethanol (20 cm^3) was refluxed for 2 days after which solvent was removed and the resulting syrup purified by chromatography on silica gel column eluting with EtOAc–EtOH (50:3, v/v) to give **9a–d** or **10a–d** as major products. A minor product of **11a–d** or **12a–d** was also separated (Table 2).

8-*Benzoyl*-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **9a**. Yellow crystals (ethyl acetate), m.p. 130.5–132 °C (Found: C, 70.7; H, 5.55; N, 10.9. $C_{15}H_{14}N_2O_2$ requires C, 70.85; H, 5.55; N, 11.02%); ν_{max}(KBr)/cm^{-1} 1650, 1609 and 1560; λ_{max}(EtOH)/nm (log ε) 240sh (4.52) and 330 (4.33); δ_H 7.47–7.87 (5 H, m), 7.40 (1 H, d, *J* 9.3), 5.79 (1 H, d, *J* 9.3), 3.79–4.35 (4 H, m, CH_2CH_2) and 2.99 (3 H, s); *m/z* 254 (M^+, 100) 253 (31, M^+ − 1), 237 (39), 177 (62) and 91 (35).

8-(p-*Chlorobenzoyl*)-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **9b**. Yellow oil (Found: 288.0672. $C_{15}H_{13}ClN_2O_2$ requires 288.0664); ν_{max}(KBr)/cm^{-1} 1654, 1609, 1558 and 1550; λ_{max}(EtOH)/nm (log ε) 251 (4.85) and 328 (4.15); δ_H 7.72 (2 H, d, *J* 9.0), 7.46 (2 H, d, *J* 9.0), 7.35 (1 H, d, *J* 9.8), 5.77 (1 H, d, *J* 9.8), 3.81–4.32 (4 H, m, CH_2CH_2), 2.96 (3 H, s); *m/z* 290 (30), 288 (M^+, 100%), 271 (38), 177 (65) and 125 (36).

1-*Methyl*-8-(p-*toluoyl*)-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **9c**. Pale yellow powder, m.p. 129.5 °C (Found: C, 71.3; H, 6.0; N, 10.3. $C_{16}H_{16}N_2O_2$ requires C, 71.62; H, 6.01; N, 10.44%); ν_{max}(KBr)/cm^{-1} 1651, 1610, 1555 and 1545; λ_{max}(EtOH)/nm (log ε) 332 (4.55); δ_H 7.67 (2 H, d, *J* 8.0), 7.27 (2 H, d, *J* 8.0), 7.39 (1 H, d, *J* 9.8), 5.76 (1 H, d, *J* 9.8), 3.78–4.36 (4 H, m, CH_2CH_2), 2.94 (3 H, s) and 2.43 (3 H, s); *m/z* 268 (M^+, 100%), 267 (36, M^+ − 1), 251 (44), 177 (52), 105 (44) and 99 (33).

8-(p-*Methoxybenzoyl*)-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(8H)-*one* **9d**. Pale yellow powder, m.p. 119.5–120.5 °C (Found: C, 67.4; H, 5.5; N, 10.0. $C_{16}H_{16}N_2O_3$ requires C, 67.57; H, 5.67; N, 9.85%); ν_{max}(KBr)/cm^{-1} 1653, 1609, 1560 and 1549; λ_{max}(EtOH)/nm (log ε) 279 (3.96) and 330 (4.19); δ_H 7.76 (2 H, d, *J* 8.8), 6.98 (2 H, d, *J* 8.8), 7.41 (1 H, d, *J* 9.3), 5.77 (1 H, d, *J* 9.3), 3.78–4.33 (4 H, m, CH_2CH_2), 3.89 (3 H, s) and 2.92 (3 H, s); *m/z* 284 (M^+, 100), 283 (33, M^+ − 1), 267 (43), 177 (33) and 121 (46).

9-*Benzoyl*-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(7H)-*one* **10a**. Yellow crystals (ethyl acetate), m.p. 186–186.5 °C (Found: C, 71.65; H, 6.0; N, 10.4. $C_{16}N_{16}N_2O_2$ requires C, 71.62; H, 6.01; N, 10.44%); ν_{max}(KBr)/cm^{-1} 1660, 1644, 1617, 1568 and 1549; λ_{max}(EtOH)/nm (log ε) 252 (5.44) and 336 (5.25); δ_H 7.43–7.86 (5 H, m), 7.46 (1 H, d, *J* 9.5), 5.88 (1 H, d, *J* 9.5), 4.14 (2 H, t), 3.43 (2 H, t), 2.87 (3 H, s) and 2.16 (2 H, quin); *m/z* 268 (M^+, 28%) and 251 (100).

9-(p-*Chlorobenzoyl*)-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(7H)-*one* **10b**. Pale yellow crystals (ethyl acetate), m.p. 149–150 °C (Found: C, 63.55; H, 4.75; N, 9.1. $C_{16}H_{15}$-

ClN_2O_2 requires C, 63.47; H, 4.99; N, 9.25%; ν_{max}(KBr)/cm^{-1} 1658, 1613, 1570 and 1545; λ_{max}(EtOH)/nm (log ε) 255 (5.55) and 334 (5.3); δ_H 7.70 (2 H, d, *J* 8.8), 7.46 (2 H, d, *J* 8.8), 7.42 (1 H, d, *J* 9.3), 5.96 (1 H, d, *J* 9.3), 4.15 (2 H, t), 3.45 (2 H, t), 2.86 (3 H, s) and 2.17 (2 H, quin); *m*/*z* 304 (10), 302 (M^+, 27), 287 (33) and 285 (100).

1-*Methyl*-9-(p-*toluoyl*)-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(7H)-*one* **10c**. Yellow crystals (ethyl acetate), m.p. 163–165 °C (Found: C, 72.2; H, 6.4; N, 9.9. $C_{17}H_{18}N_2O_2$ requires C, 72.3; H, 6.45; N, 9.9%); ν_{max}(KBr)/cm^{-1} 1658, 1611, 1597, 1570 and 1544; λ_{max}(EtOH)/nm (log ε) 255 (4.33) and 336 (4.26); δ_H 7.67 (2 H, d, *J* 8.0), 7.27 (2 H, d, *J* 8.0), 7.46 (1 H, d, *J* 9.3), 5.97 (1 H, d, *J* 9.3), 4.15 (2 H, t), 3.43 (2 H, t), 2.84 (3 H, s), 2.43 (3 H, s) and 2.16 (2 H, quin); *m*/*z* 282 (M^+, 26%) and 265 (100).

9-(p-*Methoxybenzoyl*)-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(7H)-*one* **10d**. Yellow crystals (ethyl acetate), m.p. 129–130 °C (Found: C, 68.4; H, 6.1; N, 9.3. $C_{17}H_{18}N_2O_3$ requires C, 68.44; H, 6.08; N, 9.39%); ν_{max}(KBr)/cm^{-1} 1652, 1609, 1591, 1561 and 1540; λ_{max}(EtOH)/nm (log ε) 280 (4.10) and 334 (4.28); δ_H 7.76 (2 H, d, *J* 8.8), 7.00 (2 H, d, *J* 8.8), 7.47 (1 H, d, *J* 9.3), 6.08 (1 H, d, *J* 9.3), 4.17 (2 H, t), 3.43 (2 H, t), 3.89 (3 H, s), 2.83 (3 H, s) and 2.17 (2 H, quin); *m*/*z* 298 (M^+, 22%) and 281 (100).

General Procedure for the Preparation of 8-*Aroyl*-6-[(E)-*ethoxycarbonylvinyl*]-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(4H)-*one* **11a–d** *or* 1-*Methyl*-7-[(E)-*ethoxycarbonylvinyl*]-9-*aroyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(5H)-*one* **12a–d**.—A solution of **6** or **7** (2 mmol) and **1** (16 mmol) in ethanol (20 cm^3) was refluxed for 2 days and then cooled to room temperature when **11** or **12** were precipitated and filtered off. The filtrate was concentrated and chromatographed on a silica gel column [EtOAc–EtOH (50:3, v/v) as eluent] to give further **11a–d** or **12a–d** and a little **9a–d** or **10a–d** (Table 2).

8-*Benzoyl*-6-[(E)-*ethoxycarbonylvinyl*]-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(4H)-*one* **11a**. Yellow prisms (EtOAc–EtOH), m.p. 201–203 °C (Found: C, 68.3; H, 5.75; N, 7.8. $C_{20}H_{20}N_2O_4$ requires C, 68.17; H, 5.72; N, 7.95%); ν_{max}(KBr)/cm^{-1} 1685, 1651, 1618 and 1558; λ_{max}(EtOH)/nm (log ε) 249 (4.31), 290 (3.98) and 374 (4.53); δ_H 7.45–7.82 (5 H, m), 7.59 (1 H, s), 7.36 (1 H, d, *J* 15.8), 6.61 (1 H, d, *J* 5.8), 4.28 (2 H, t), 3.95 (2 H, t), 4.18 (2 H, q), 2.99 (3 H, s) and 1.27 (3 H, t); *m*/*z* 352 (M^+, 71%), 307 (29), 280 (46) and 279 (100).

8-(p-*Chlorobenzoyl*)-6-[(E)-*ethoxycarbonylvinyl*]-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(4H)-*one* **11b**. Yellow crystals (ethyl acetate), m.p. 161.5–163 °C (Found: C, 61.93; H, 5.0; N, 7.3. $C_{20}H_{19}ClN_2O_4$ requires C, 62.10; H, 4.95; N, 7.24%); ν_{max}(KBr)/cm^{-1} 1683, 1660, 1622, 1594 and 1558; λ_{max}(EtOH)/nm (log ε) 254 (4.44), 288 (4.03) and 371 (4.51); δ_H 7.20 (2 H, d, *J* 8.5), 7.49 (2 H, d, *J* 8.5), 7.52 (1 H, s), 7.35 (1 H, d, *J* 15.8), 6.77 (1 H, d, *J* 15.8), 4.25 (2 H, t), 3.96 (2 H, t), 4.16 (2 H, q), 2.96 (3 H, s) and 1.26 (3 H, t); *m*/*z* 388 (23), 386 (M^+, 76%), 341 (25), 315 (39), 314 (49) and 313 (100).

6-[(E)-*Ethoxycarbonylvinyl*]-1-*methyl*-8-(p-*toluoyl*)-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(4H)-*one* **11c**. Yellow crystals (ethyl acetate), m.p. 149.5–151.5 °C (Found: C, 68.6; H, 6.1; N, 7.4. $C_{21}H_{22}N_2O_4$ requires C, 68.84; H, 6.05; N, 7.65%); ν_{max}(KBr)/cm^{-1} 1680, 1660, 1619, 1597 and 1555; λ_{max}(EtOH)/nm (log ε) 248 (4.31), 290 (4.00) and 374 (4.52; δ_H 7.67 (2 H, d, *J* 9.0), 7.59 (1 H, s), 7.38 (1 H, d, *J* 15.8), 7.40 (2 H, d, *J* 9.0), 6.79 (1 H, d, *J* 15.8), 4.27 (2 H, t), 3.83 (2 H, t), 4.18 (2 H, q), 2.95 (3 H, s) and 1.25 (3 H, t); *m*/*z* 366 (M^+, 69%), 321 (24), 294 (46) and 293 (100).

6-[(E)-*Ethoxycarbonylvinyl*]-8-(p-*methoxybenzoyl*)-1-*methyl*-2,3-*dihydro*-1H-*imidazo*[1,2-a]*pyridin*-5(4H)-*one* **11d**. Yellow crystals (ethyl acetate), m.p. 148–149 °C (Found: C, 65.85; H, 6.0; N, 6.90. $C_{21}H_{22}N_2O_5$ requires C, 65.96; H, 5.80; N, 7.33%); ν_{max}(KBr)/cm^{-1} 1680, 1659, 1613, 1589 and 1556; λ_{max}(EtOH)/nm (log ε) 286 (4.27) and 373 (4.46); δ_H 7.77 (2 H, d, *J* 8.8), 7.60 (1 H, s), 7.40 (1 H, d, *J* 15.8), 6.99 (2 H, d, *J* 8.8), 6.80 (1 H, d, *J* 15.8), 4.27 (2 H, t), 3.92 (2 H, t), 4.18 (2 H, q), 3.91 (3 H, s), 2.95 (3 H, s) and 1.27 (3 H, t); *m*/*z* 382 (M^+, 78%), 337 (26), 310 (49) and 309 (100).

9-*Benzoyl*-7-[(E)-*ethoxycarbonylvinyl*]-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6-*one* **12a**. Yellow crystals (absolute ethanol), m.p. 196–198 °C (Found: C, 68.6; H, 6.1; N 7.6. $C_{22}H_{22}N_2O_4$ requires C, 68.84; H, 6.05; N, 7.65%); ν_{max}(KBr)/cm^{-1} 1695, 1665, 1629, 1602, 1570 and 1554; λ_{max}(EtOH)/nm (log ε) 249 (4.41), 295 (4.01) and 382 (4.52); δ_H 7.45–7.82 (5 H, m), 7.63 (1 H, s), 7.43 (1 H, d, *J* 15.8), 6.72 (1 H, d, *J* 15.8), 4.17 (2 H, q), 4.15 (2 H, t), 3.48 (2 H, t), 2.89 (3 H, s), 2.18 (2 H, quin) and 1.26 (3 H, t); *m*/*z* 366 (M^+, 87%), 349 (79), 321 (29), 303 (29), 293 (66) and 91 (100).

9-(p-*Chlorobenzoyl*)-7-[(E)-*ethoxycarbonylvinyl*]-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6-*one* **12b**. Yellow crystals (ethyl acetate), m.p. 142–144 °C (Found: C, 62.9; H, 5.15; N, 6.8. $C_{21}H_{21}ClN_2O_4$ requires C, 62.92; H, 5.28; N, 6.99%); ν_{max}(KBr)/cm^{-1} 1704, 1668, 1629, 1612 and 1570; ν_{max}(EtOH)/nm (log ε) 255 (4.37), 294 (3.95) and 381 (4.49); δ_H 7.72 (2 H, d, *J* 8.0), 7.58 (1 H, s), 7.47 (2 H, d, *J* 8.0), 7.30 (1 H, d, *J* 15.8), 6.73 (1 H, d, *J* 15.8), 4.19 (2 H, q), 4.14 (2 H, t), 3.47 (2 H, t), 2.88 (3 H, s), 2.17 (2 H, quin) and 1.27 (3 H, t); *m*/*z* 402 (35), 400 (M^+, 100%), 385 (33), 355 (27), 337 (29), 327 (70) and 125 (82).

7-[(E)-*Ethoxycarbonylvinyl*]-1-*methyl*-9-(p-*toluoyl*)-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(5H)-*one* **12c**. Yellow crystals [light petroleum (b.p. 60–90 °C)–ethyl acetate], m.p. 151–152.5 °C (Found: C, 69.7; H, 6.1; N, 7.43. $C_{22}H_{24}N_2O_4$ requires C, 69.46; H, 6.36; N, 7.36%); ν_{max}(KBr)/cm^{-1} 1705, 1669, 1632, 1605, 1576 and 1557; λ_{max}(EtOH)/nm (log ε) 253 (4.31), 293 (3.94) and 382 (4.52); δ_H 7.68 (2 H, d, *J* 8.0), 7.62 (1 H, s), 7.45 (1 H, d, *J* 15.8), 7.29 (2 H, d, *J* 8.0), 6.71 (1 H, d, *J* 15.8), 4.18 (2 H, q), 4.16 (2 H, t), 3.47 (2 H, t), 2.88 (3 H, s), 2.46 (3 H, s), 2.19 (2 H, quin) and 1.28 (3 H, t); *m*/*z* 380 (M^+, 86%), 363 (100), 335 (37), 317 (30), 307 (55) and 105 (89).

7-[(E)-*Ethoxycarbonylvinyl*]-9-(p-*methoxybenzoyl*)-1-*methyl*-1,2,3,4-*tetrahydropyrido*[1,2-a]*pyrimidin*-6(5H)-*one* **12d**. Brown needles [light petroleum (b.p. 60–90 °C)–ethyl acetate], m.p. 136.5–137 °C (Found: C, 66.7; H, 5.8; N, 7.05. $C_{22}H_{24}N_2O_5$ requires C, 66.65; H, 6.10; N, 7.07%); ν_{max}(KBr)/cm^{-1} 1708, 1663, 1624, 1605, 1579 and 1555; λ_{max}(EtOH)/nm (log ε) 289 (4.38) and 384 (4.56); δ_H 7.78 (2 H, d, *J* 8.8), 7.62 (1 H, s), 7.45 (1 H, d, *J* 15.8), 6.98 (2 H, d, *J* 8.8), 6.73 (1 H, d, *J* 15.8), 4.18 (2 H, q), 4.17 (2 H, t), 3.92 (3 H, s), 3.46 (2 H, t), 2.86 (3 H, s), 2.19 (2 H, quin) and 1.28 (3 H, t); *m*/*z* 396 (M^+, 70), 379 (100), 351 (23), 333 (23), 323 (38) and 121 (70).

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