Differential Reactivity of β-Amino Enones and 3-Dimethylaminoacrylaldehyde towards α-Amino Derivatives

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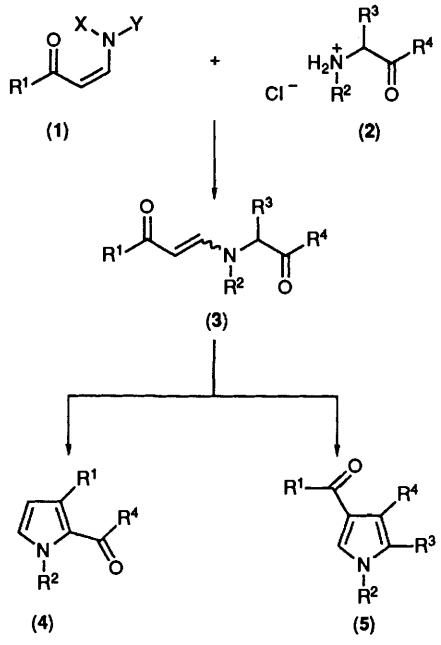
Unsubstituted β-amino enones react with α-amino derivatives by a well established route which implies a fast transamination process — 1,4-addition followed by elimination — and cyclodehydration of the intermediate to 3-functionalized pyrroles. In contrast, 3-dimethylaminoacrylaldehyde undergoes 1,2-addition followed by cyclization to give the final 2-substituted pyrroles. Isolation of the intermediates supports the proposed mechanism for each reaction.

The reaction of β-diketones,[1–3] β-chlorovinyl ketones,[4] β-alkoxyacrylaldehydes,[5] and β-amino enones[6] with α-amino derivatives has been widely exploited for the regioselective synthesis of 2-functionalized pyrroles. The regioselectivity of this two-step process is based in two facts: (i) The reaction starts by a fast addition–elimination step, leading to an isolable β-amino enone intermediate (**3**), and (ii) the regioselective cyclization of intermediates (**3**) to 2-functionalized pyrroles is always favoured by an additional substituent (R^3) of electron-withdrawing character at the α-position.

On the other hand, we have recently reported[7,8] that the less activated intermediates (**3**; R^3 = H or alkyl) cyclodehydrate, in both basic and thermal reactions to give 3-acylpyrroles as a single product or, in some cases, accompanied by small amounts of 2-acyl isomers. In contrast, the reactions of β-amino enones with α-amino esters, α-amino amides, and α-amino nitriles lead to 2-functionalized pyrroles regiospecifically (Scheme 1).

We have now directed our interest to the study of the reactivity of unsubstituted β-amino derivatives (**1A–H**) with both α-amino ketones (**2a–e**) and α-amino esters (**2f** and **g**). The reactions were carried out under different experimental conditions: (a) One-step formation of pyrrole derivatives from starting compounds (entries 1, 6, 10, 16, 19, and 23 in Table 1); (b) Isolation of transamination intermediates (**3**) with further purification and characterization (entries 7–9, 11, 17, 18, and 20–22); and (c) Isolation of the intermediates (**3**) without purification, and cyclodehydration to the pyrroles (entries 2–5 and 12–15).

Some special features of the results summarized in Table 1, on comparison with those previously described,[7,8] are worthy of note. Thus, unsubstituted β-amino enones (**1A–E**) and β-amino ester (**1H**) react with *N*-methylphenacylamine (**2e**) in the same way as the 3-alkyl-substituted substrates, leading directly to 3-functionalized pyrroles in refluxing ethanol. Nevertheless, transamination of compounds (**1A–H**) with α-amino derivatives (**2a–d**) and (**2f** and **g**) to the intermediates (**3**) is faster than that for 3-alkyl-substituted substrates, but, in the present case, compounds (**3**) decompose to complex mixtures of products when heated in ethanol. Otherwise, these intermediates can be initially isolated at 0 °C or at room temperature, and transformed into the final pyrroles, after treatment with sodium ethoxide in ethanol, in good yield except for the case of compounds (**3Bg**) and (**3Dg**), which lead to retrocondensations products (entries 9 and 18 in Table 1). Moreover, the cyclodehydration process of 'non-activated' intermediates (**3**) differs from that previously described for the activated ones, and leads to 3-functionalized pyrroles by nucleophilic attack of the β-enamino carbon on the carbonyl group of the α-amino ketone moiety. The only exception to this general behaviour is for compounds derived from ethyl glycinate (**2f**), which led to 2-functionalized pyrroles in low yield (entries 8, 11, and 17 in Table 1) because the evolution of intermediates (**3Bf**), (**3Cf**), and (**3Df**) would lead to the less stable 2-pyrrolidone derivatives.



	R^1	$-N<^{X}_{Y}$		R^2	R^3	R^4
(1)A;	Me	NH_2	(2)a;	H	H	Ph
B;	Et	NH_2	b;	H	H	*p*-$MeOC_6H_4$
C;	Pr^i	NH_2	c;	H	H	Me
D;	Ph	NH_2	d;	H	Me	Ph
E;	*p*-$MeOC_6H_4$	NH_2	e;	Me	H	Ph
F;	*p*-$NO_2C_6H_4$	NH_2	f;	H	H	EtO
G;	*p*-$NO_2C_6H_4$	NMe_2	g;	Me	H	EtO
H;	EtO	$N[CH_2]_4$				
I;	H	NMe_2				

Scheme 1.

3-Dimethylaminoacrylaldehyde (**1I**) reacts with ethyl glycinate hydrochloride (**2f**) (molar ratio 1:1) in ethanol at reflux, leading to an oily residue, which was transformed, in low yield, into ethyl pyrrole-2-carboxylate (**4If**) when refluxed in pyridine; the yield is slightly increased when the cyclization is carried out under irradiation, or when excess of substrate (**2f**) is used

Table 1. Reactions of β-amino enones (**1A–G**) and β-amino ester (**1H**) with α-amino derivatives (**2a–g**).

Entry	(1) + (2)	t_1(h)	T_1(°C)	Solvent$_1$	Yield (%) (3)	t_2(h)	T_2(°C)	Solvent$_2$	Products and yields (%) (4) + (5)
1	(1A) (2e)					1.5	78	EtOH	(5Ae) (32)
2	(1B) (2a)	0.5	0	MeOH		2	20	EtOH[a]	(5Ba) (45)
3	(1B) (2b)	0.5	0	MeOH		2	20	EtOH[a]	(5Bb) (47)
4	(1B) (2c)	0.5	0	MeOH		2	20	EtOH[a]	(5Bc) (22)
5	(1B) (2d)	1	0	MeOH		2	20	EtOH[a]	(5Bd) (54)
6	(1B) (2e)					3	78	EtOH	(5Be) (60)
7	(1B) (2e)	1	20	MeOH	(3Be) (90)				
8	(1B) (2f)	0.5	0	MeOH	(3Bf) (85)	3	78	EtOH[a]	(4Bf) (9)
9	(1B) (2g)	1	20	MeOH	(3Bg) (86)	3	78	EtOH[a]	*b*
10	(1C) (2e)					5	78	EtOH	(5Ce) (35)
11	(1C) (2f)	0.5	0	MeOH	(3Cf) (88)	3	78	EtOH[a]	(4Cf) (11)
12	(1D) (2a)	0.5	0	MeOH		6	20	EtOH[a]	(5Da) (38)
13	(1D) (2b)	0.5	0	MeOH		4	20	EtOH[a]	(5Db) (26)
14	(1D) (2c)	1	0	MeOH		4	20	EtOH[a]	(5Dc) (51)
15	(1D) (2d)	2	0	MeOH		6	20	EtOH[a]	(5Dd) (45)
16	(1D) (2e)					4	78	EtOH	(5De) (86)
17	(1D) (2f)	0.5	0	MeOH	(3Df) (86)	3	78	EtOH[a]	(4Df) (10)
18	(1D) (2g)	1	20	MeOH	(3Dg) (82)	6	78	EtOH[a]	*b*
19	(1E) (2e)					6	78	EtOH	(5Ee) (66)
20	(1F) (2e)	28	78	EtOH	(3Fe) (82)				
21	(1F) (2f)	7	20	EtOH	(3Ff) (92)	5	78	EtOH[a]	
22	(1G) (2f)	7	78	EtOH	(3Gf) (86)				
23	(1H) (2e)					18	78	EtOH	(5He) (65)

[a] Reactions with NaOEt (1 mol equiv.). [b] Only retrocondensation products were isolated after heating with NaOEt in ethanol.

Table 2. Reaction of 3-dimethylacrylaldehyde (**1I**) with α-amino derivatives (**2e–g**).

(**1I**) + (**2e–g**) $\xrightarrow[t_1(h)]{\text{EtOH, 78 °C}}$ (**6**)/(**7**) $\xrightarrow[t_2(h)]{\text{Pyridine, reflux}}$ (**4**)

Entry	Compd. (2)	Molar quotient (2)/(1I)	t_1(h)	t_2(h)	Pyrrole (%)
1	(2e)	1/1	14		(4Ie) (18)
2	(2e)	1/1	14	11	(4Ie) (34)
3	(2f)	1/1	12	4	(4If) (14)
4	(2f)	2.5/1	15	8	(4If) (19)
5	(2f)[a]	2.5/1	15	8	(4If) (25)
6	(2g)	1/1	11	8	(4Ig) (10)
7	(2g)[a]	2/1	11	8	(4Ig) (12)

[a] Reaction under irradiation.

[molar ratio (**1I**):(**2f**) 1:2.5] (entries 3–5 in Table 2). On the other hand, compound (**1I**) reacts with ethyl sarcosinate hydrochloride (**2g**) in a similar way, giving ethyl 1-methylpyrrole-2-carboxylate (**4Ig**) in low yield, and with *N*-methylphenacylamine (**2e**), leading to 2-benzoyl-1-methylpyrrole (**4Ie**) in 18% yield, or in 34% yield if the intermediate is refluxed in pyridine (entries 1 and 2 in Table 2).

Moreover, the intermediates of the reaction between substrates (**1I**) and (**2f**) were characterized as a mixture of diiminium salts (**6If**) and (**7If**), and both of them were separately transformed into ethyl pyrrole-2-carboxylate in 30 and 50% yield, respectively, in refluxing pyridine. The isolation of these intermediates allows us to confirm that the behaviour of 3-dimethylaminoacrylaldehyde (**1I**) towards α-amino derivatives differs from that previously described for the isoelectronic 3-chloro-[5] and 3-alkoxy-acrylaldehydes[9] or β-amino enones,[7,8] and to propose a different mechanism for its transformation into 2-functionalized pyrroles.

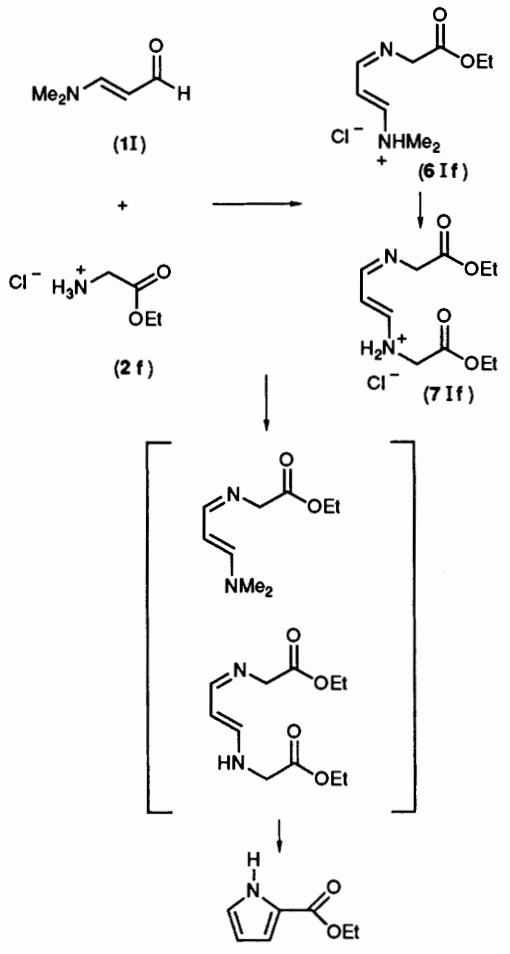
In this respect, the reaction is a two-step process; the first is a fast 1,2-addition of the α-amino derivative to the carbonyl group in compound (**1I**), leading to intermediate (**6If**), followed by transamination with formation of intermediate (**7If**). The second rate-limiting step is the cyclization of these intermediates, promoted by pyridine, with concomitant extrusion of diethylamine or ethyl glycinate, as previously described for azabutadiene derivatives[10] (Scheme 2).

On the other hand, attempts to liberate the azabutadienes from their salts by treatment with base failed, because autocondensation to the pyrrole (**4Ig**) and decomposition processes took place.

Experimental

M.p.s were determined on an open capillary tube and are uncorrected. The ^{1}H NMR spectra were recorded on a Bruker AC80 spectrometer at 80 MHz with $SiMe_4$ as internal standard. Mass spectra were obtained using a Hewlett-Packard 5988-A spectrometer by electronic impact at 70 eV.

β-Amino enones were prepared as previously described;[11] 3-dimethylaminoacrylaldehyde (**1I**) and α-amino derivatives (**2a**), (**2f**), and (**2g**) were commercially available, and compounds (**2b**)–(**2e**) were synthesized by literature methods.[12–14]



Scheme 2.

Reaction of β-*Amino Derivatives* (**1A–H**) *with* α-*Amino Compounds* (**2a–g**).—(a) *Reaction with* α-*amino compounds* (**2a–d**) (*entries* 2–5 *and* 12–15 *in Table* 1). A mixture of β-amino derivative (10 mmol) and the corresponding α-amino compound (11 mmol) in anhydrous methanol (30 ml) was stirred at 0 °C (ice–water-bath) until total disappearance of the starting compounds (TLC). The solvent was removed at room temperature (rotavapor) and the residue was taken up in anhydrous tetrahydrofuran (THF); the solid was separated by filtration and the filtrate was concentrated under reduced pressure. The residue, without further purification, was dissolved in anhydrous ethanol (20 ml) and treated with sodium ethoxide (0.68 g, 10 mmol) at room temperature. The mixture was stirred until reaction was complete (TLC) and was then hydrolysed by addition to a mixture of ice–water. The pyrrole product precipitated out and was collected by filtration, or by extraction with diethyl ether, the solvent was evaporated off, and the residue was purified by distillation or recrystallization.

(b) *Reaction with* N-*methylphenacylamine* (**2e**) (*entries* 1, 6, 10, 16, 19, *and* 23 *in Table* 1). A solution of β-amino derivative (10 mmol) and *N*-methylphenacylamine hydrochloride (**2e**) (2.04 g, 11 mmol) in anhydrous ethanol (30 ml) was refluxed until the reaction was finished (TLC). The ethanol was evaporated off under reduced pressure, the residue was taken up in anhydrous THF (15 ml), and the solids were eliminated by suction. The THF was distilled (rotavapor) and the oily residue was chromatographed on silica gel with CH_2Cl_2 as eluant.

(c) *Reaction with* α-*amino compounds* (**2f** *and* **g**), *with isolation of the intermediates* (*entries* 7–9, 11, 17, 18, *and* 20–22 *in Table* 1). A solution of β-amino derivative (10 mmol) and α-amino ketone (**2f**) or (**2g**) (11 mmol) in anhydrous methanol (30 ml) was stirred at the temperature given in Table 1 until consumption of the starting compounds (TLC). The solvent was eliminated under reduced pressure and the residue was redissolved in anhydrous THF. The insoluble salts were eliminated by filtration, the THF was evaporated off, and the residue was recrystallized from the appropriate solvent.

1-(N-*Methyl*-N-*phenacylamino*)*pent*-1-*en*-3-*one* (**3Be**). A *solid*, m.p. 103–104 °C (from hexane–benzene) (Found: C, 72.85; H, 7.2; N, 6.2. $C_{14}H_{17}NO_2$ requires C, 72.70; H, 7.41; N, 6.06%); δ($CDCl_3$) 1.03 (3 H, t, *J* 7 Hz, 5-H_3), 2.30 (2 H, q, *J* 7 Hz, 4-H_2), 2.95 (3 H, s, NMe), 4.70 (2 H, s, NCH_2), 5.07 (1 H, d, *J* 12 Hz, 2-H), and 7.30–8.00 (6 H, m, Ph and 1-H); *m*/*z* 231 (M^+, 18%) and 126 (100).

Ethyl N-(3-*oxopent*-1-*enyl*)*glycinate* (**3Bf**). An *oil*, b.p. 101–103 °C/0.5 mmHg (Found: C, 58.2; H, 8.25; N, 7.7. $C_9H_{15}NO_3$ requires C, 58.36; H, 8.16; N, 7.56%); δ(CCl_4) 1.03 (3 H, t, *J* 7 Hz, 5-H_3), 1.25 (3 H, t, *J* 7 Hz, OCH_2*Me*), 2.23 (2 H, q, *J* 7 Hz, 4-H_2), 3.98 (2 H, d, *J* 6 Hz, NCH_2), 4.18 (2 H, q, *J* 7 Hz, OCH_2), 5.02 (1 H, d, *J* 7 Hz, 2-H), 6.67 (1 H, dd, J_1 7, J_2 12 Hz, 1-H), and 9.70 (1 H, br, NH); *m*/*z* 199 (M^+, 29%) and 170 (100).

Ethyl N-*methyl*-N-(3-*oxopent*-1-*enyl*)*glycinate* (**3Bg**). A solid, m.p. 57–58 °C (from hexane–benzene) (lit.,[4] 58 °C); δ($CDCl_3$) 1.07 (3 H, t, *J* 7 Hz, 5-H_3), 1.27 (3 H, t, *J* 7 Hz, OCH_2*Me*), 2.38 (2 H, q, *J* 7 Hz, 4-H_2), 2.97 (3 H, s, NMe), 3.97 (2 H, s, NCH_2), 4.23 (2 H, q, *J* 7 Hz, OCH_2), 5.13 (1 H, d, *J* 12 Hz, 2-H), and 7.47 (1 H, d, *J* 12 Hz, 1-H); *m*/*z* 199 (M^+, 29%) and 170 (100).

Ethyl N-(4-*methyl*-3-*oxopent*-1-*enyl*)*glycinate* (**3Cf**). An *oil*, b.p. 85–87 °C/0.15 mmHg (Found: C, 60.4; H, 8.5; N, 7.1. $C_{10}H_{17}NO_3$ requires C, 60.28; H, 8.60; N, 7.03%); δ($CDCl_3$) 1.04 (6 H, d, *J* 7 Hz, 5-H_3), 1.26 (3 H, t, *J* 7 Hz, OCH_2*Me*), 2.48 (1 H, m, 4-H), 4.00 (2 H, d, *J* 6 Hz, NCH_2), 4.22 (2 H, q, *J* 7 Hz, OCH_2), 5.13 (1 H, d, *J* 8 Hz, 2-H), 6.77 (1 H, dd, J_1 8, J_2 12 Hz, 1-H), and 9.80 (1 H, br, NH).

Ethyl N-(3-*oxo*-3-*phenylprop*-1-*enyl*)*glycinate* (**3Df**). A *solid*, m.p. 91–92 °C (from EtOH) (Found: C, 66.7; H, 6.7; N, 6.2. $C_{13}H_{15}NO_3$ requires C, 66.94; H, 6.48; N, 6.00%); δ($CDCl_3$) 1.23 (3 H, t, *J* 7 Hz, OCH_2*Me*), 3.95 (2 H, d, *J* 6 Hz, NCH_2), 4.18 (2 H, q, *J* 7 Hz, OCH_2), 5.77 (1 H, d, *J* 8 Hz, 2-H), 6.83 (1 H, dd, J_1 8, J_2 12 Hz, 1-H), 7.20–8.00 (5 H, m, Ph), 10.30 (1 H, br, NH); *m*/*z* 233 (M^+, 38%) and 91 (100).

Ethyl N-*methyl*-N-(3-*oxo*-3-*phenylprop*-1-*enyl*)*glycinate* (**3Dg**). A solid, m.p. 85–86 °C (from hexane–benzene) (lit.,[4] 89.5 °C); δ($CDCl_3$) 1.25 (3 H, t, *J* 7 Hz, OCH_2*Me*), 3.00 (3 H, s, NMe), 3.97 (2 H, s, NCH_2), 4.18 (2 H, q, *J* 7 Hz, OCH_2), 5.77 (1 H, d, *J* 12 Hz, 2-H), 7.70 (1 H, d, *J* 12 Hz, 1-H), and 7.30–7.80 (5 H, m, Ph); *m*/*z* 247 (M^+, 30%) and 105 (100).

3-(N-*Methyl*-N-*phenacylamino*)-1-(p-*nitrophenyl*)*prop*-2-*en*-1-*one* (**3Fe**). *Yellow solid*, m.p. 221–222 °C (Found: C, 66.5; H, 4.9; N, 8.8. $C_{18}H_{16}N_2O_4$ requires C, 66.66; H, 4.97; N, 8.64%); *m*/*z* 324 (M^+, 8%) and 219 (100).

Ethyl N-[3-(p-*nitrophenyl*)-3-*oxoprop*-1-*enyl*]*glycinate* (**3Ff**). *Yellow solid*, m.p. 114–115 °C (from MeOH) (Found: C, 56.3; H, 5.2; N, 10.15. $C_{13}H_{14}N_2O_5$ requires C, 56.11; H, 5.07; N, 10.07%); δ($CDCl_3$) 1.30 (3 H, t, *J* 7 Hz, OCH_2*Me*), 4.07 (2 H, d, *J* 6 Hz, NCH_2), 4.23 (2 H, q, *J* 7 Hz, OCH_2), 5.75 (1 H, d, *J* 8 Hz, 2-H), 7.00 (1 H, dd, J_1 8, J_2 12 Hz, 1-H), 8.00 (2 H, d, *J* 9 Hz, *o*-H), 8.27 (2 H, d, *J* 9 Hz, *m*-H), and 10.40 (1 H, br, NH); *m*/*z* 278 (M^+, 34%) and 205 (100).

Ethyl 3-*ethylpyrrole*-2-*carboxylate* (**4Bf**). An *oil*, b.p. 125–129 °C/5 (Found: C, 64.8; H, 7.9; N, 8.5. $C_9H_{13}NO_2$ requires C, 64.65; H, 7.84; N, 8.38%); δ(CCl_4) 1.20 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.33 (3 H, t, *J* 7 Hz, OCH_2*Me*), 2.78 (2 H, q, *J* 7 Hz, CH_2), 4.33 (2 H, q, *J* 7 Hz, OCH_2), 6.03 (1 H, t, $J_{4,5} = J_{4,1} = 3$ Hz, 4-H), 6.77

(1 H, t, $J_{5,4} = J_{5,1} = 3$ Hz, 5-H), and 10.00 (1 H, br, 1-H); *m/z* 167 (M^+, 71%) and 120 (100). Hydrolysis with 2M-aq. KOH led to the corresponding acid, m.p. 149–150 °C (from aq. EtOH) (lit.,[15] 155 °C).

Ethyl 3-isopropylpyrrole-2-carboxylate (**4Cf**). An *oil*, b.p. 128–132 °C/2 mmHg (Found: C, 66.4; H, 8.5; N, 7.9. $C_{10}H_{15}NO_2$ requires C, 66.27; H, 8.34; N, 7.73%); δ(CCl_4) 1.23 (6 H, d, *J* 7 Hz, CH*Me*$_2$), 1.33 (3 H, t, *J* 7 Hz, OCH$_2$*Me*), 3.52 (1 H, m, C*H*Me$_2$), 4.33 (2 H, q, *J* 7 Hz, OCH$_2$), 6.08 (1 H, t, $J_{4,5} = J_{4,1} = 3$ Hz, 4-H), 6.75 (1 H, t, $J_{5,4} = J_{5,1} = 3$ Hz, 5-H), and 9.80 (1 H, br, 1-H); *m/z* 181 (M^+, 35%) and 120 (100). Hydrolysis with 2M-aq. KOH led to the corresponding *acid*, m.p. 152–153 °C (decomp.) (from aq. EtOH) (Found: C, 62.8; H, 7.4; N, 9.0. ($C_8H_{11}NO_2$ requires C, 62.73; H, 7.24; N, 9.14%).

Ethyl 3-phenylpyrrole-2-carboxylate (**4Df**). A *solid*, m.p. 66–67 °C (from hexane–benzene) (Found: C, 72.7; H, 6.2; N, 6.7. $C_{13}H_{13}NO_2$ requires C, 72.53; H, 6.09; N, 6.51%); δ(CCl_4) 1.23 (3 H, t, *J* 7 Hz, OCH$_2$*Me*), 4.27 (2 H, q, *J* 7 Hz, OCH$_2$), 6.30 (1 H, t, $J_{4,5} = J_{4,1} = 3$ Hz, 4-H), 6.93 (1 H, t, $J_{5,4} = J_{5,1} = 3$ Hz, 5-H), 7.10–7.70 (5 H, m, Ph), and 10.20 (1 H, br, 1-H); *m/z* 215 (M^+, 62%) and 169 (100).

3-Acetyl-1-methyl-4-phenylpyrrole (**5Ae**). A *solid*, m.p. 88.5–89.5 °C (from MeOH) (Found: C, 78.5; H, 6.7; N, 7.15. $C_{13}H_{13}NO$ requires C, 78.36; H, 6.58; N, 7.03%); δ(CCl_4) 2.08 (3 H, s, MeCO), 3.37 (3 H, s, NMe), 6.38 (1 H, d, *J* 2 Hz, 5-H), 7.05 (1 H, d, *J* 2 Hz, 2-H), and 6.90–7.50 (5 H, m, Ph); *m/z* 199 (M^+, 64%) and 184 (100).

3-Phenyl-4-propionylpyrrole (**5Ba**). A *solid*, m.p. 165–166 °C (from MeOH) (Found: C, 78.5; H, 6.7; N, 6.9. $C_{13}H_{13}NO$ requires C, 78.36; H, 6.58; N, 7.03%); δ[$CDCl_3$–$(CD_3)_2SO$] 1.10 (3 H, t, *J* 7 Hz, *Me*CH$_2$CO), 2.68 (2 H, q, *J* 7 Hz, CH$_2$CO), 6.67 (1 H, br s, 2-H), 7.10–7.60 (6 H, m, Ph and 5-H), and 10.80 (1 H, br, 1-H); *m/z* 199 (M^+, 33%) and 170 (100).

3-(p-Methoxyphenyl)-4-propionylpyrrole (**5Bb**). A *solid*, m.p. 175–176 °C (from MeOH) (Found: C, 73.2; H, 6.7; N, 6.04. $C_{14}H_{15}NO_2$ requires C, 73.34; H, 6.59; N, 6.11%); δ[$CDCl_3$–$(CD_3)_2SO$] 1.07 (3 H, t, *J* 7 Hz, *Me*CH$_2$CO), 2.70 (2 H, q, *J* 7 Hz, CH$_2$CO), 3.77 (3 H, s, MeO), 6.72 (1 H, m, 2-H), 6.85 (2 H, d, *J* 9 Hz, *m*-H), 7.40 (2 H, d, *J* 9 Hz, *o*-H), 7.46 (1 H, m, 5-H), and 11.10 (1 H, br, 1-H); *m/z* 229 (M^+, 48%) and 200 (100).

3-Methyl-4-propionylpyrrole (**5Bc**). A *solid*, m.p. 134–135 °C (from MeOH) (Found: C, 70.2; H, 8.15; N, 10.4. $C_8H_{11}NO$ requires C, 70.05; H, 8.08; N, 10.21%); δ($CDCl_3$) 1.17 (3 H, t, *J* 7 Hz, *Me*CH$_2$CO), 2.30 (3 H, d, *J* 1 Hz, Me), 2.74 (2 H, q, *J* 7 Hz, CH$_2$CO), 6.50 (1 H, br s, 2-H), 7.30 (1 H, m, 5-H), and 9.50 (1 H, br, 1-H); *m/z* 137 (M^+, 25%) and 108 (100).

2-Methyl-3-phenyl-4-propionylpyrrole (**5Bd**). A *solid*, m.p. 188–189 °C (from MeOH) (Found: C, 78.7; H, 7.2; N, 6.7. $C_{14}H_{15}NO$ requires C, 78.84; H, 7.09; N, 6.57%); δ[$CDCl_3$–$(CD_3)_2SO$] 1.02 (3 H, t, *J* 7 Hz, *Me*CH$_2$CO), 2.10 (3 H, s, Me), 2.57 (2 H, q, *J* 7 Hz, CH$_2$CO), 7.23 (5 H, s, Ph), 7.27 (1 H, d, *J* 3 Hz, 5-H), and 10.80 (1 H, br, 1-H); *m/z* 213 (M^+, 35%) and 184 (100).

1-Methyl-3-phenyl-4-propionylpyrrole (**5Be**). A *solid*, m.p. 78–79 °C (from hexane–benzene) (Found: C, 78.7; H, 7.2; N, 6.4. $C_{14}H_{15}NO$ requires C, 78.84; H, 7.09; N, 6.57%); δ(CCl_4) 0.97 (3 H, t, *J* 7 Hz, *Me*CH$_2$CO), 2.43 (2 H, q, *J* 7 Hz, CH$_2$CO), 3.30 (3 H, s, NMe), 6.35 (1 H, d, *J* 2 Hz, 2-H), 7.00 (1 H, d, *J* 2 Hz, 5-H), and 7.00–7.50 (5 H, m, Ph); *m/z* 213 (M^+, 33%) and 184 (100).

3-Isobutyryl-1-methyl-4-phenylpyrrole (**5Ce**). A *solid*, m.p. 83–84 °C (from MeOH) (Found: C, 79.1; H, 7.7; N, 6.0. $C_{15}H_{17}NO$ requires C, 79.26; H, 7.54; N, 6.16%); δ(CCl_4) 1.05 (6 H, d, *J* 7 Hz, *Me*$_2$CH), 2.96 (1 H, m, Me$_2$C*H*), 3.33 (3 H, s, NMe), 6.43 (1 H, d, *J* 2 Hz, 5-H), 7.13 (1 H, d, *J* 2 Hz, 2-H), and 7.00–7.50 (5 H, m, Ph); *m/z* 227 (M^+, 18%) and 184 (100).

3-Benzoyl-4-phenylpyrrole (**5Da**). A *solid*, m.p. 226–227 °C (from EtOH) (Found: C, 82.7; H, 5.2; N, 5.6. $C_{17}H_{13}NO$ requires C, 82.57; H, 5.30; N, 5.66%); δ[$CDCl_3$–$(CO_3)_2SO$] 7.00–7.80 (12 H, m, Ph, PhCO and 2 and 5-H) and 11.60 (1 H, br, 1-H); *m/z* 247 (M^+, 69%) and 170 (100).

3-Benzoyl-4-(p-methoxyphenyl)pyrrole (**5Db**). A *solid*, m.p. 222–223 °C (from EtOH) (Found: C, 77.8; H, 5.5; N, 5.2. $C_{18}H_{15}NO_2$ requires C, 77.96; H, 5.45; N, 5.05%); δ[$CDCl_3$–$(CD_3)_2SO$] 3.75 (3 H, s, MeO), 6.78 (2 H, d, *J* 9 Hz, *m*-H), 6.89 (1 H, t, $J_{5,2} = J_{5,1} = 2$ Hz, 5-H), 7.13 (1 H, t, $J_{2,1}$ 3, $J_{2,5}$ 2 Hz, 2-H), 7.31 (2 H, d, *J* 9 Hz, *o*-H), 7.40–7.80 (5 H, m, Ph), and 11.40 (1 H, br, 1-H); *m/z* 277 (M^+, 100%).

3-Benzoyl-4-methylpyrrole (**5Dc**). A *solid*, m.p. 116–117 °C (from hexane–toluene) (Found: C, 77.65; H, 6.1; N, 7.6. ($C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56%); δ($CDCl_3$) 2.33 (3 H, d, *J* 1 Hz, Me), 6.50 (1 H, m, 5-H), 6.98 (1 H, dd, $J_{2,1}$ 3, $J_{2,5}$ 2 Hz, 2-H), 7.20–7.80 (5 H, m, Ph), and 9.80 (1 H, br, 1-H); *m/z* 185 (M^+, 50%) and 108 (100).

4-Benzoyl-2-methyl-3-phenylpyrrole (**5Dd**). A *solid*, m.p. 222–223 °C (from EtOH) (Found: C, 82.6; H, 5.9; N, 5.5. ($C_{18}H_{15}NO$ requires: C, 82.73; H, 5.79; N, 5.36%); δ[$CDCl_3$–$(CD_3)_2SO$] 2.21 (3 H, s, Me), 7.00 (1 H, d, *J* 3 Hz, 5-H), 7.21 (5 H, s, Ph), 7.20–7.80 (5 H, m, PhCO), and 11.20 (1 H, br, 1-H); *m/z* 261 (M^+, 79%) and 184 (100).

3-Benzoyl-1-methyl-4-phenylpyrrole (**5De**). A *solid*, m.p. 81–82 °C (from MeOH) (Found: C, 82.9; H, 5.6; N, 5.5. $C_{18}H_{15}NO$ requires C, 82.73; H, 5.79; N, 5.36%); δ(CCl_4) 3.30 (3 H, s, NMe), 6.48 (1 H, d, *J* 2 Hz, 5-H), 6.75 (1 H, d, *J* 2 Hz, 2-H), and 6.90–7.80 (10 H, m, Ph and PhCO); *m/z* 261 (M^+, 90%) and 184 (100).

3-(p-Methoxybenzoyl)-1-methyl-4-phenylpyrrole (**5Ee**). A *solid*, m.p. 121–122 °C (from hexane–benzene) (Found: C, 78.5; H, 5.75; N, 4.7. $C_{19}H_{17}NO_2$ requires C, 78.33; H, 5.88; N, 4.81%); δ($CDCl_3$) 3.58 (3 H, s, NMe), 3.76 (3 H, s, OMe), 6.67 (1 H, d, *J* 2 Hz, 5-H), 6.80 (2 H, d, *J* 8 Hz, *m*-H), 6.96 (1 H, d, *J* 2 Hz, 2-H), 7.00–7.50 (5 H, m, Ph), and 7.80 (2 H, d, *J* 8 Hz, *o*-H); *m/z* 291 (M^+, 100%).

Ethyl 1-Methyl-4-phenylpyrrole-3-carboxylate (**5He**). A *solid*, m.p. 47–48 °C (from MeOH) (Found: C, 73.4; H, 6.5; N, 6.0. $C_{14}H_{15}NO_2$ requires C, 73.34; H, 6.59; N, 6.11%); δ(CCl_4) 1.13 (3 H, t, *J* 7 Hz, *Me*CH$_2$O), 3.36 (3 H, s, NMe), 4.06 (2 H, q, *J* 7 Hz, CH$_2$O), 6.38 (1 H, d, *J* 2 Hz, 5-H), and 7.00–7.60 (6 H, m, Ph and 2-H); *m/z* 229 (M^+, 49%) and 184 (100).

Reaction of 3-Dimethylaminoacrylaldehyde (**1l**) *with α-Amino Compounds* (**2e–g**).—3-Dimethylaminoacrylaldehyde (**1l**) (10 mmol) and an α-amino derivative (10 or 25 mmol) was refluxed in anhydrous ethanol (30 ml) until total disappearance of substrate (**1l**) (TLC). The solution was cooled to room temperature and the solvent was removed by distillation; the residue was dissolved in pyridine (20 ml) and the solution was refluxed for the time indicated in Table 2. The solution was cooled to room temperature and partitioned between a mixture of ice–hydrochloric acid (1 : 1) (150 g) and diethyl ether (150 ml). The aqueous layer was extracted twice with diethyl ether (50 ml); the combined ethereal phases were sequentially washed with aq. $NaHCO_3$ and water, and dried over anhydrous $MgSO_4$. The solvent was evaporated off (rotavapor) and the residue was purified by column chromatography on silica gel with CH_2Cl_2 as eluant.

The reactions under irradiation were carried out by heating of the mixture in pyridine under irradiation using a 125-W quartz lamp.

2-Benzoyl-1-methylpyrrole (**4Ie**). An oil, b.p. 105–108 °C/5 mmHg (lit.,[16] 159–160 °C/20 mmHg (Found: C, 77.95; H, 6.1; N, 7.4. Calc. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56%); δ($CDCl_3$) 3.98 (3 H, s, NMe), 6.09 (1 H, dd, $J_{4,3}$ 4, $J_{4,5}$ 2.5 Hz, 4-H), 6.67 (1 H, dd, $J_{3,4}$ 4, $J_{3,5}$ 1.5 Hz, 3-H), 6.82 (1 H, t, $J_{5,4}$ 2.5, $J_{5,3}$ 1.5 Hz, 5-H), and 7.30–7.90 (5 H, m, Ph); *m/z* 185 (M^+ 76%) and 184 (100).

Ethyl Pyrrole-2-carboxylate (**4If**). A solid, m.p. 39 °C (from

hexane–benzene) (lit.,[17] 38–40 °C); δCDCl$_3$) 1.31 (3 H, t, *J* 7 Hz, OCH_2Me), 4.30 (2 H, q, *J* 7 Hz, OCH_2), 6.18 (1 H, m, 4-H), 6.90 (2 H, 3- and 5-H), and 10.30 (1 H, br, 1-H); *m/z* 139 (M^+, 60%) and 94 (100).

Ethyl 1-*Methylpyrrole*-2-*carboxylate* (**4Ig**). An oil, b.p. 60–63 °C/5 mmHg (lit.,[18] 93–94 °C/16 mmHg) (Found: C, 62.9; H, 7.4; N, 9.3. Calc. for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14%); δ(CDCl$_3$) 1.34 (3 H, t, *J* 7 Hz, $MeCH_2O$), 3.91 (3 H, s, NMe), 4.26 (2 H, q, *J* 7 Hz, OCH_2), 6.07 (1 H, dd, $J_{4,5}$ 4, $J_{4,3}$ 2.5 Hz, 4-H), 6.73 (1 H, t, $J_{3,4}$ 2.5, $J_{3,5}$ 2 Hz, 3-H), and 6.91 (1 H, dd, $J_{5,4}$ 4, $J_{5,3}$ 2 Hz, 5-H); *m/z* 153 (M^+, 48%) and 108 (100).

Characterization of the Intermediates (**6Ig**) *and* (**7Ig**).—A solution of 3-dimethylaminoacrylaldehyde (**1I**) (0.99 g, 10 mmol) and ethyl glycinate hydrochloride (**2f**) (1.335 g, 11 mmol) in anhydrous ethanol (25 ml) was refluxed until reaction was complete (TLC). The reaction mixture was cooled to room temperature and the solvent was evaporated off (rotavapor). The residue was crushed in anhydrous THF, separated by filtration, and recrystallized from ethanol–THF, giving compound (**7Ig**) as crystals, m.p. 153–154 °C (Found: C, 47.6; H, 6.7; N, 9.8. $C_{11}H_{19}ClN_2O_4$ requires C, 47.40; H, 6.87; N, 10.05%); δ(D_2O) 1.42 (6 H, t, *J* 7 Hz), 4.39 (4 H, q, *J* 7 Hz), 4.44 (4 H, s), 5.78 (1 H, m), and 7.97 (2 H, m); *m/z* 242 (M^+, 27%) and 169 (100).

The pure compound (**6Ig**) could not be isolated from the mother liquor [90% (**6Ig**), 10% (**7Ig**)], but the structure was established by its spectral characteristics: δ(D_2O) 1.42 (3 H, t, *J* 7 Hz), 3.28 (3 H, s), 3.48 (3 H, s), 4.40 (2 H, q, *J* 7 Hz), 4.40 (2 H, s), 5.60 (1 H, m), and 7.90 (2 H, m).

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