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The aza–ene or the Michael addition? Examination of an unusual substituent effect on the reaction of heterocyclic ketene aminals with ethyl propiolate

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Abstract—Heterocyclic ketene aminals having at least one secondary amino group underwent the aza–ene reaction with ethyl propiolate under various conditions to yield the corresponding adducts, which were readily transformed into the δ-lactam fused heterocyclic products with or without the aid of sodium ethoxide in refluxing ethanol, while the ester- and cyano-substituted tertiary enediamines acted as the strong Michael donor to add to ethyl propiolate in a polar or a protic solvent. The unusual substituent effect on the reactivity and mechanism was discussed.

1. Introduction

The chemistry of enamines has been extensively developed since the pioneering work conducted by Stork and colleagues,[1] and it has become an important aspect of organic chemistry.[2] Heterocyclic ketene aminals or cyclic 1,1-enediamines **1** (Fig. 1), as members of the enamine family, are versatile synthons for the synthesis of various types of heterocyclic compounds and they have received increasing attention recently.[3] Owing to the conjugation effect of the electron-donating amino groups and the electron-withdrawing substituent, the double bond is highly polarized and the electron density on the α-carbon is greater than that of the nitrogen atom. Considerable effort has been made during the past decades to investigate enaminic reactions such as nucleophilic additions and substitutions with a variety of electrophiles,[4] even 1,3-diploes.[5] As an ambident nucleophile, however, the secondary amino group in the molecule can also participate in reactions such as *N*-alkylation[6] and *N*-acylation[7] in the presence of a strong base. Further interest in heterocyclic ketene aminals has been generated by their interesting biological activities.[8]

Figure 1. Structure of heterocyclic ketene aminals.

Through a systematic study of the reaction of aroyl-substituted heterocyclic ketene aminals with α,β-unsaturated compounds, we have proposed that heterocyclic ketene aminal is an aza–ene component able to undergo an aza–ene addition reaction with electron deficient alkenes and alkynes.[9] The aza–ene adduct between **1** (R=H or R=Me) and ethyl propiolate can undergo further isomerization and cyclocondensation to afford lactam-fused heterocycles.[9a] Surprisingly, however, mono-ester substituted heterocyclic ketene aminal **2** has been reported to exhibit a different reaction pattern towards electrophiles.[10] In contrast to **1**, for example, heterocyclic ketene aminal **2** reacted with electrophiles to give an exclusive *C*-alkylation product even under basic conditions. Furthermore, the *C*-adducts between **2** and methyl propiolate could not undergo cyclocondensation reaction in refluxing ethanol. Interest in the chemistry of heterocyclic ketene aminals, particularly the correlation between structure and reactivity, promoted us to undertake the current study. By utilizing ethyl propiolate as a reactive probe, we have found a great effect of the electron-withdrawing group at α-carbon and the substituent at nitrogen on the reactivity and reaction pathway of heterocyclic ketene aminals. The nature of the solvents, on the other hand, also plays an important role on the reaction.

2. Results and discussion

In order to examine the effect of the structure of heterocyclic ketene aminals on the reactivity, a number of compounds

Keywords: heterocyclic ketene aminals; ethyl propiolate; substituent effect; addition reaction.

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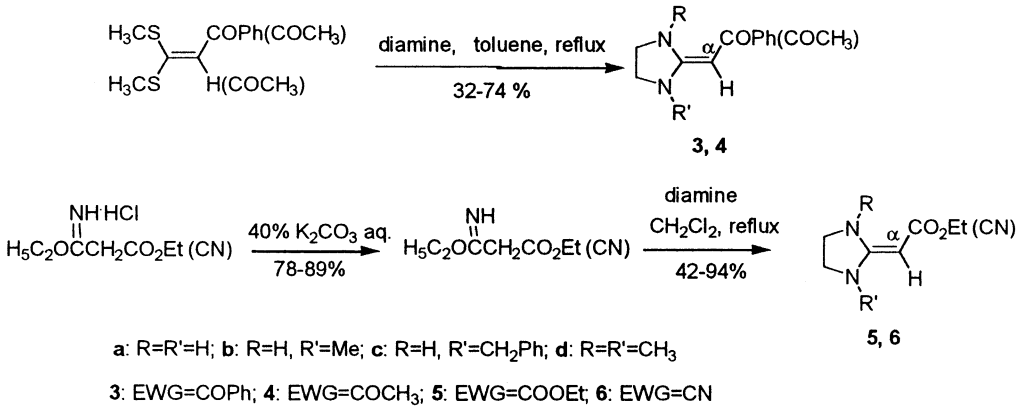


Scheme 1.

3–**6** having a different electron-withdrawing group and different *N*-substituents were designed. The aroyl[11] and acetyl-substituted[12] heterocyclic ketene aminals were synthesized from the corresponding ketene dithioacetals and diamines in an open or closed system, while the cyano- and ester-substituted heterocyclic ketene aminals were synthesized from the reaction of imino esters with diamines (Scheme 1). It is worth noting that the reaction of imino ester hydrochloride[13] did not give the desired product as those reported in the literature. Only when imino ester, derived from the treatment of imino ester hydrochloride salt with a base, was used, did the preparative reaction proceed readily to produce compounds **5** and **6**.

It is interesting to point out that both the chemical shift of the vinyl proton and the α-carbon of compounds **3**–**6** were influenced dramatically by the nature of the substituents on the α-carbon and on the nitrogen of imidazoline. The stronger the electron-withdrawing group, the higher the electron density on the α-carbon. As illustrated in Table 1, with the electron-withdrawing group being varied from benzoyl, acetyl, ester to cyano, the chemical shift of the vinyl proton decreased from 5.20–5.42 to 2.93–3.20 ppm. Similar upfield shift of the α-carbon in ^{13}C NMR was also observed with the exception of the acetyl-substituted analog which gave δ_C signal in the region of 74.9–76.1 ppm, higher than that of benzoyl-substituted heterocyclic ketene aminals. The substitution of methyl or benzyl on the nitrogen also led to the downfield shift of the vinyl proton in the ^1H NMR spectra. Since the chemical shifts of both δ_H and δ_C reflect the electron density of the α-carbon, therefore, they can be used a parameter to correlate the nucleophilicity of the α-carbon under certain circumstances.[14]

Heterocyclic ketene aminals **3**–**6a**–**c** reacted with ethyl propiolate effectively and the outcome, however, was strongly dependent upon the structure of the reactant **3**–**6** and upon the reaction conditions employed (Scheme 2, Table 2).

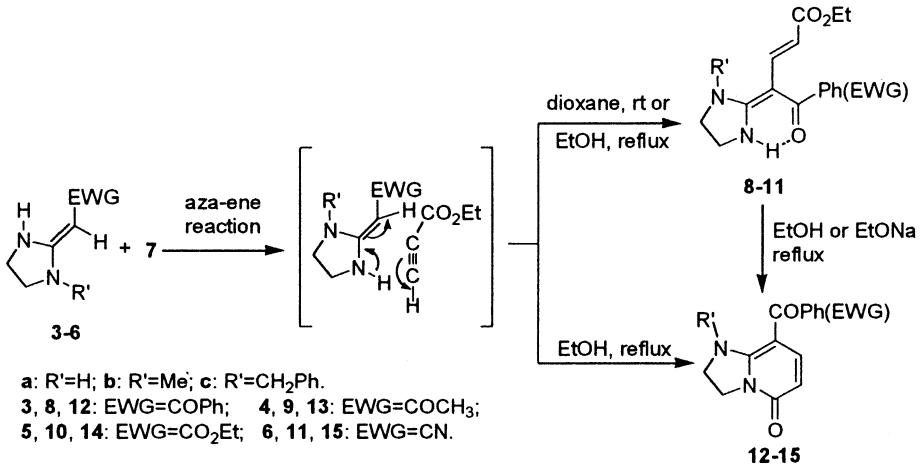
Benzoyl-substituted heterocyclic ketene aminals **3a**–**c** having at least one secondary amino moiety reacted with ethyl propiolate **7** in both 1,4-dioxane and ethanol solution to yield the corresponding adducts **8a**–**c** as the sole or major product. The configurations of both vinylene and enediamine moieties were assigned as *E*-form on the basis of the ^1H NMR spectrum. An AB quartet signal of coupling constant 15.0–15.9 Hz corresponding to the *trans*-configuration of the vinylene protons was observed, while a downfield N–H resonance peak at 8.24–9.70 ppm indicated intramolecular hydrogen bonding between N–H and carbonyl groups. Adducts **8a**–**c** were readily transformed into the δ-lactam-fused heterocyclic products **12a**–**c** in high yields. Compounds **12a**–**c** can also be prepared conveniently in one-pot reaction through refluxing **3a**–**c** with **7** in ethanol for a prolonged time.

Acetyl-substituted heterocyclic ketene aminals **4a**, which have two secondary amino moieties, underwent similar reaction with ethyl propiolate **7** in refluxing ethanol to afford a mixture of adduct **9a** and the fused heterocyclic product **13a**. Prolonged refluxing led to the conversion of **9a** into **13a**. Ester- or cyano-substituted heterocyclic ketene aminals **5a** or **6a**, however, gave the adduct **10a** or **11a** as the sole product. Prolonged refluxing led to the conversion of most **10a** into **14a**, however, no cyclized compound **15a** was found even in a longer reaction period. Only in the presence of sodium ethoxide, did transformation of **11a** into **15a** take place efficiently.

Having one methyl or benzyl group attached on the nitrogen of imidazoline, all heterocyclic ketene aminals **4**–**6b**,**c** were

Table 1. δ_H and δ_C values of the α-carbon in heterocyclic ketene aminals

δ (ppm)		**3** EWG=COPh	**4** EWG=$COCH_3$	**5** EWG=CO_2Et	**6** EWG=CN
a: R=H	δ_H	5.20	4.52	3.35	2.93
R′=H	δ_C	73.0	76.1	60.3	33.7
b: R=H	δ_H	5.30	4.62	3.36	3.01
R′=Me	δ_C	71.4	75.2	60.0	32.9
c: R=H	δ_H	5.42	4.77	4.01	3.20
R′=CH_2Ph	δ_C	72.9	74.9	60.1	34.6



Scheme 2.

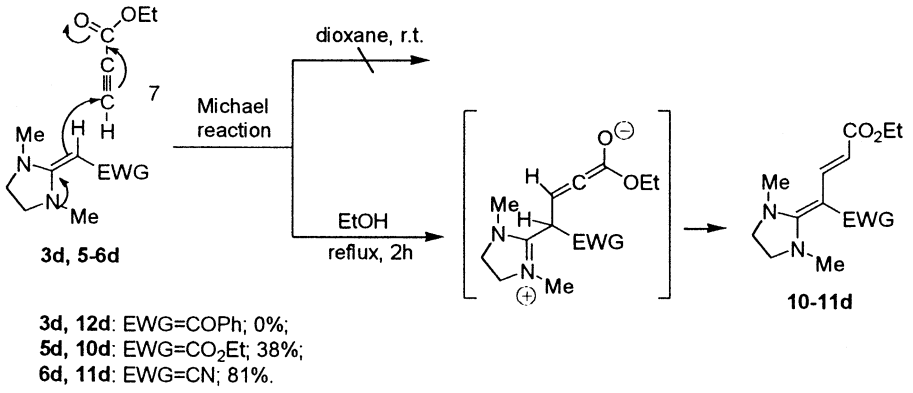
Table 2. Reaction of heterocyclic ketene aminals **3–6** with ethyl propiolate **7**

Entry	Reactant	EWG	R′	Reaction conditions	Product (%)[a]	
					Adduct	Heterocycle
1	**3a**[b]	COPh	H	1,4-Dioxane, rt 4 d	**8a** (92)	**12a** (0)
2	**3a**			EtOH, reflux, 2 h	**8a** (54)	**12a** (33)
3	**3a**[b]			EtOH, reflux, 2 d	**8a** (0)	**12a** (80)
4	**3b**		Me	EtOH, reflux, 1 h	**8b** (59)	**12b** (0)
5	**3b**			EtOH, reflux, 2 d	**8b** (0)	**12b** (78)
6	**3c**		CH_2Ph	EtOH, reflux, 1 h	**8c** (56)	**12c** (0)
7	**3c**			EtOH, reflux, 2 d	**8c** (0)	**12c** (79)
8	**4a**	$COCH_3$	H	EtOH, reflux, 2 h	**9a** (49)	**13a** (23)
9	**4a**			EtOH, reflux, 2 d	**9a** (0)	**13a** (62)
10	**4b**		Me	EtOH, reflux, 2 h	**9b** (63)	**13b** (0)
11	**4c**		CH_2Ph	EtOH, reflux, 2 h	**9c** (65)	**13c** (0)
12	**5a**	CO_2Et	H	EtOH, reflux, 2 h	**10a** (69)	**14a** (0)
13	**5a**			EtOH, reflux, 2 d	**10a** (17)	**14a** (65)
14	**5b**		Me	EtOH, reflux, 2 h	**10b** (80)	**14b** (0)
15	**5c**		CH_2Ph	EtOH, 20°C, 48 h	**10c** (68)	**14c** (0)
16	**6a**	CN	H	EtOH, reflux, 2 h	**11a** (69)	**15a** (0)
17	**6b**		Me	EtOH, reflux, 2 h	**11b** (75)	**15b** (0)
18	**6c**		CH_2Ph	EtOH, 20°C, 48 h	**11c** (80)	**15c** (0)
19	**9b**	$COCH_3$	Me	EtONa/EtOH, reflux, 2 h		**13b** (70)
20	**9c**		CH_2Ph	EtONa/EtOH, reflux, 2 h		**13c** (95)
21	**10b**	CO_2Et	Me	EtONa/EtOH, reflux, 2 h		**14b** (49)
22	**10c**		CH_2Ph	EtONa/EtOH, reflux, 2 h		**14c** (62)
23	**11a**	CN	H	EtONa/EtOH, reflux, 1 h		**15a** (quant.)
24	**11b**		Me	EtONa/EtOH, reflux, 1 h		**15b** (quant.)
25	**11c**		CH_2Ph	EtONa/EtOH, reflux, 1 h		**15c** (80)

[a] Isolated yields.
[b] See Ref. 9a.

exclusively transformed into the adducts **9–11b,c**. Prolonged reaction only led to a complex reaction mixture and no cyclized products were observed. Cyclocondensation of the adducts **9–11b,c** was similarly effected as that for **11a** by using sodium ethoxide. The structures of the fused heterocyclic compounds were established on the basis of spectroscopic evidence and elemental analyses. The imidazo[1,2-*a*]pyridinone structure was confirmed by the NMR spectra which showed an AB quartet signal of coupling constant around 9.3 Hz in ^{1}H NMR and amide carbonyl signal around 160 ppm in ^{13}C NMR. The lactam structure was also supported by the IR spectrum in which an amide carbonyl vibration band was evident in the region of 1600–1700 cm^{-1}.

To shed further light on the reaction mechanism, heterocyclic ketene aminals bearing two tertiary amino moieties were subject to the reaction with ethyl propiolate. As illustrated in Scheme 3, benzoyl-substituted heterocyclic ketene aminal **3d** did not add to ethyl propiolate **7** in both protic and aprotic solvents such as ethanol and 1,4-dioxane, respectively.[9a] By using ester- and cyano-substituted heterocyclic ketene aminal analogs **5d** and **6d**, we did not observe the addition reaction in 1,4-dioxane either. This is consistent with our previous finding that the reaction of heterocyclic ketene aminals with α,β-unsaturated compounds proceeds via an aza–ene addition mechanism (Scheme 2).[9] In other words, without a secondary enamine segment (H–N–C=C) such as those of *N*,*N*-dimethylated heterocyclic ketene



Scheme 3.

aminals **3**–**6d**, no aza–ene addition reaction takes place. Surprisingly, however, **5d** and **6d** were able to react with **7** in refluxing ethanol to afford products **10d** and **11d** in 38 and 81%, respectively. The formation of **10d** and **11d** most probably resulted from the well-known Michael addition reaction of **5d** and **6d** to ethyl propiolate **7**, and heterocyclic ketene aminals **5d** and **6d** appear as strong Michael donors (Scheme 3).

All the results obtained suggested that the reaction of heterocyclic ketene aminals with ethyl propiolate could proceed in a different manner depending not only on the structure of the reactant but also on the reaction conditions employed with the former being the dominant factor. In most cases, heterocyclic ketene aminals having at least one secondary amino group undergo the aza–ene addition reaction when treated with ethyl propiolate under various conditions. No addition reaction was found in general when *N*,*N*′-disubstituted heterocyclic ketene aminals were used because of the lack of secondary enamine moiety. Only in the case of ester- and cyano-substituted tertiary enediamines using a polar and protic solvent, did the reaction proceed in a Michael addition fashion. The higher Michael addition reactivity of the ester- and cyano-substituted tertiary enediamines **5d** and **6d** than that of the benzoyl-substituted analog **3d** is not surprising, since the nucleophilicity of α-carbon of **5d** and **6d** is greater than that of **3d**, which has been revealed by the comparison of the chemical shifts of both vinyl proton and α-carbon among compounds **3**–**6** (vide supra). It is also important to note that the higher nucleophilicity of α-carbon concomitantly lead to the lower nucleophilicity of the enamine nitrogen because of the ambident conjugation effect within the enediamine segment. This accounts not only for the easy aza–ene addition of ester-, and particularly cyano-substituted heterocyclic ketene aminals **6a**–**c** to ethyl propiolate but also for the difficulty of the consecutive δ-lactam formation reaction. The presence of sodium ethoxide increased the nucleophilicity of the secondary amino group and therefore facilitated the cyclocondensation reaction.

3. Conclusion

Heterocyclic ketene aminals or heterocyclic enediamines are a unique enamine analog exhibiting intriguing reaction properties. The addition reaction of heterocyclic ketene aminals to α,β-unsaturated compounds proceeds via the aza–ene mechanism or the Michael addition pathway depending on both the nature of the substituents at the α-carbon and at amino group and the reaction conditions used. Heterocyclic ketene aminals with a secondary enamine moiety (HN–C═C) undergo aza–ene reaction with ethyl propiolate to give the corresponding adduct which is readily transformed into δ-lactam fused heterocyclic products with or without the aid of sodium ethoxide in refluxing ethanol. Only ester and cyano-substituted tertiary enediamines act as the strong Michael donor to add to ethyl propiolate in a polar and protic solvent. This investigation has provided not only a convenient synthetic route to imidazo[1,2-*a*]pyridinone heterocycles but also the better understanding of the reaction mechanism which are important in guiding further study.

4. Experimental

4.1. General

Melting points are uncorrected. IR spectra were obtained on a Perkin–Elmer 782 instrument as KBr discs. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or d_6-DMSO solution with $SiMe_4$ as internal standard on Bruker DMX-300 spectrometers. Chemical shifts are reported in ppm and coupling constants are in Hz. Mass spectra were measured on an AEI MS-50 spectrometer. HR mass spectra were measured on a Bruker APEXR spectrometer. Elemental analyses were carried out at the Analytical Laboratory of the Institute. All solvents and chemicals were commercially available and, unless otherwise indicated, were used as received. The heterocyclic ketene aminals **3**[11] and **4**[12] were prepared according to literature methods.

4.1.1. 2-(Acetylmethylene)-1-benzyl-imidazolidine (4c). A mixture of ketene dithioacetals[11] derived from acetyl acetone (10 mmol) and *N*-benzyl-1,2-ethylenediamine (12 mmol) in 30 mL of toluene was heated at 110°C for 9 h in a closed system. The solvent was removed under vacuum and the residue was chromatographed over a silica gel column using ethyl acetate/petroleum ether as an eluant to give **4c**. White crystals; yield: 32%; mp 115–116°C; (Found: C, 72.29; H, 7.48; N, 13.05. $C_{13}H_{16}N_2O$ requires C, 72.19; H, 7.46; N, 12.96%); ν_{max} (KBr) cm^{-1}: 3288 (NH), 1603, 1544; δ_H (d_6-DMSO): 9.07 (1H, s, NH),

7.38–7.24 (5H, m, ArH), 4.77 (1H, s, =CH), 4.34 (2H, s, benzyl of CH_2), 3.48 (2H, t, J=7.8 Hz, NCH_2), 3.30 (2H, t, J=7.8 Hz, NCH_2), 1.78 (3H, s, $COCH_3$); δ_C (d_6-DMSO): 189.1, 163.0, 137.1, 128.9, 127.9, 127.7, 74.9, 48.4, 47.1, 42.0, 29.0; *m/z* (EI): 216 (M^+, 57%), 201 (45), 173 (51), 91 (100).

4.2. General procedure for the synthesis of imino ester

Imino ester hydrochloride[13] (50 mmol) was added to a mixture of 70 mL 40% K_2CO_3 solution and 50 mL cold diethyl ether. The organic layer was separated quickly and the water layer was extracted by diethyl ether twice. Combined the organic layer and poured it into anhydrous K_2CO_3 and then the organic layer was dried by anhydrous Na_2SO_4 for 4 h again. After removal of solvent under vacuum, the crude product was recrystallized from ethyl ether to give the imino ester as white crystals which can be used in the next step reaction directly.

4.3. General procedure for the synthesis of 5 and 6

A solution of imino ester (3 mmol) and diamine (3.3 mmol) in dry CH_2Cl_2 was refluxed for 10 h under nitrogen. After removal of the solvent under vacuum, the residue was recrystallized from ethyl acetate or fractionated by chromatography on a silica gel column using ethyl acetate or ethyl acetate/petroleum ether as an eluant to give products **5** and **6**.

4.3.1. 2-(Ethoxycarbonylmethylene)imidazolidine (5a). White crystals; yield: 94%; mp 112–113°C; (Found: C, 53.62; H, 7.89; N, 18.11. $C_7H_{12}N_2O_2$ requires C, 53.83; H, 7.75; N, 17.94%); ν_{max} (KBr) cm^{-1}: 3379 (NH), 3310 (NH), 1628, 1574; δ_H (d_6-DMSO): 7.39 (1H, s, N*H*), 6.84 (1H, s, N*H*), 3.87 (2H, q, J=6.9 Hz, OCH_2CH_3), 3.35 (1H, s, =C*H*), 3.46–3.28 (4H, m, 2×NCH_2), 1.09 (3H, t, J=6.9 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 169.8, 165.0, 60.3, 57.0, 43.7, 42.4, 15.4; *m/z* (EI): 156 (M^+, 66%), 127 (55), 111 (100).

4.3.2. (*E*)-2-(Ethoxycarbonylmethylene)-1-methylimidazolidine (5b). White crystals; yield: 75%; mp 98–100°C (lit.[15] 98–101.5°C); ν_{max} (KBr) cm^{-1}: 3368 (NH), 1639, 1584; δ_H (d_6-DMSO): 7.40 (1H, s, N*H*), 3.91 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.36 (1H, s, =C*H*), 3.41–3.28 (4H, m, 2×NCH_2), 2.67 (3H, s, NCH_3), 1.11 (3H, t, J=7.2 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 169.7, 164.1, 60.0, 57.2, 50.3, 42.1, 32.6, 15.2.

4.3.3. (*E*)-2-(Ethoxycarbonylmethylene)-1-benzylimidazolidine (5c). White crystals; yield: 70%; mp 106–108°C (lit.[17] 105–107°C); ν_{max} (KBr) cm^{-1}: 3365 (NH), 1645, 1591; δ_H (d_6-DMSO): 7.52 (1H, s, N*H*), 7.37–7.23 (5H, m, Ar*H*), 4.30 (2H, s, benzyl of CH_2), 4.01 (1H, s, =C*H*), 3.90 (2H, q, J=6.9 Hz, OCH_2CH_3), 3.46–3.29 (4H, m, 2×NCH_2), 1.10 (3H, t, J=6.9 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 169.9, 163.4, 137.4, 128.8, 127.7, 127.5, 60.1, 57.2, 48.8, 48.0, 42.1, 15.2.

4.3.4. 2-(Ethoxycarbonylmethylene)-1,3-dimethylimidazolidine (5d). Yellow viscous liquid; yield: 61%; MS (high resolution, positive FAB) *m/z*: 185.1284 [$(M+H)^+$]; $C_9H_{17}N_2O_2^+$ required 185.1284; ν_{max} (KBr) cm^{-1}: 1737, 1644; δ_H ($CDCl_3$): 3.85 (2H, q, J=6.9 Hz, OCH_2CH_3), 3.70 (1H, s, =C*H*), 3.22 (4H, s, 2×NCH_2), 2.74 (6H, s, 3×NCH_2), 1.05 (3H, t, J=6.9 Hz, OCH_2CH_3); δ_C ($CDCl_3$): 165.4, 164.1, 59.9, 55.9, 48.3, 34.4, 12.7; *m/z* (EI): 184 (M^+, 36%), 139 (100), 112 (72).

4.3.5. 2-(Cyanomethylene)imidazolidine (6a). White crystals; yield: 42%; mp 104–106°C (lit.[16] 106°C); δ_H (d_6-DMSO): 6.84 (1H, s, N*H*), 6.74 (1H, s, N*H*), 3.50–3.46 (4H, m, 2×NCH_2), 2.93 (1H, s, =C*H*); δ_C (d_6-DMSO): 166.6, 124.6, 43.9, 43.4, 33.7; *m/z* (EI): 109 (M^+, 60%), 80 (100).

4.3.6. (*E*)-2-(Cyanomethylene)-1-methylimidazolidine (6b). White crystals; yield: 76%; mp 120–121°C; (Found: C, 58.38; H, 7.23; N, 34.28. $C_6H_9N_3$ requires C, 58.51; H, 7.37; N, 34.12%); ν_{max} (KBr) cm^{-1}: 3268 (NH), 2165 (CN), 1601, 1520; δ_H (d_6-DMSO): 6.71 (1H, s, N*H*), 3.32–3.24 (4H, m, 2×NCH_2), 3.01 (1H, s, =C*H*), 2.63 (3H, s, NCH_3); δ_C (d_6-DMSO): 165.8, 124.0, 51.1, 41.8, 34.4, 32.9; *m/z* (EI): 123 (M^+, 100%), 95 (27), 80 (51).

4.3.7. (*E*)-2-(Cyanomethylene)-1-benzylimidazolidine (6c). White crystals; yield; 78%; mp 141–143°C; (Found: C, 72.08; H, 6.59; N, 21.32. $C_{12}H_{13}N_3$ requires C, 72.33; H, 6.57; N, 21.09%); ν_{max} (KBr) cm^{-1}: 3294 (NH), 2170 (CN), 1588, 1506; δ_H (d_6-DMSO): 7.33 (5H, m, Ar*H*), 6.73 (1H, s, N*H*), 4.20 (2H, s, benzylic CH_2), 3.32–3.23 (4H, m, 2×NCH_2), 3.20 (1H, s, =C*H*); δ_C (d_6-DMSO): 165.0, 137.0, 128.9, 128.0, 127.7, 124.0, 49.2, 48.7, 41.9, 34.6; *m/z* (EI): 199 (M^+, 33%), 91 (100).

4.3.8. 2-(Cyanomethylene)-1,3-dimethylimidazolidine (6d). Yellow oil; yield: 67%; MS (high resolution, positive FAB) *m/z*: 138.1027 [$(M+H)^+$]; $C_7H_{12}N_3^+$ required 138.1026; ν_{max} (KBr) cm^{-1}: 2180, 1591, 1503; δ_H ($CDCl_3$): 3.07–3.01 (4H, m, 2×NCH_2), 2.83 (3H, s, NCH_3), 2.68 (1H, s, =C*H*), 2.39 (3H, s, NCH_3); δ_C ($CDCl_3$): 164.2, 123.3, 50.5, 49.0, 35.4, 35.1, 34.0; *m/z* (EI): 137 (M^+, 50%), 97 (39), 81 (48), 56 (100).

4.4. General procedure for the reaction of heterocyclic ketene aminals with ethyl propiolate

A mixture of heterocyclic ketene aminals **3**–**6** (1 mmol) and ethyl propiolate **7** (1 mmol) was refluxed (or was stirred at 20°C) in ethanol or 1,4-dioxane for some period. After removal of the solvent under vacuum, the residue was chromatographed on a silica gel column using ethyl acetate/petroleum ether or ethyl acetate/methanol as an eluant to give the corresponding adducts. Prolonged reaction time, some adducts can be converted to the fused δ-lactam heterocycles.

4.4.1. 2-(1-Benzoyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (8a). Yellow crystals; yield: 54%; mp 122–124°C (lit.[9a] 123–124°C); δ_H ($CDCl_3$): 8.18 (2H, s, N*H*), 7.68 (1H, d, J=15.9 Hz, =CH), 7.39–7.38 (5H, m, ArH), 5.43 (1H, d, J=15.9 Hz, =CH), 4.09 (2H, q, J=7.2 Hz, OCH_2CH_3), 3.74 (4H, s, 2×NCH_2), 1.20 (3H, t, J=7.2 Hz, OCH_2CH_3).

4.4.2. 1-Methyl-2-(1-benzoyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (8b). Yellow crystals; yield: 59%; mp 142–144°C (Found: C, 67.91; H, 6.64; N, 9.38. $C_{17}H_{20}N_2O_3$ requires C, 67.98; H, 6.71; N, 9.33%); ν_{max} (KBr) cm^{-1}: 3239 (NH), 1656, 1561; δ_H ($CDCl_3$): 8.88 (1H, s, N*H*), 7.59 (1H, d, *J*=15.0 Hz, =C*H*), 7.37–7.36 (5H, m, Ar*H*), 5.05 (1H, d, *J*=15.3 Hz, =C*H*), 3.95 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.79–3.67 (4H, m, 2×NCH_2), 2.74 (3H, s, NCH_3), 1.11 (3H, t, *J*=6.9 Hz, OCH_2CH_3); δ_C ($CDCl_3$): 186.2, 168.8, 168.1, 145.6, 143.0, 129.4, 128.2, 128.1, 97.4, 90.3, 58.4, 50.9, 42.0, 35.1, 15.0; *m/z* (EI): 300 (M^+, 8%), 271 (9), 254 (100).

4.4.3. 1-Benzyl-2-(1-benzoyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (8c). Yellow crystals; yield: 56%; mp 62–64°C; MS (high resolution, positive FAB) *m/z*: 377.1860 [$(M+H)^+$]; $C_{23}H_{25}N_2O_3^+$ required 377.1860; ν_{max} (KBr) cm^{-1}: 3400 (NH), 1687, 1551; δ_H ($CDCl_3$): 9.70 (1H, br, N*H*), 7.74 (1H, d, *J*=15.6 Hz, =C*H*), 7.49–7.22 (5H, m, Ar*H*), 5.18 (1H, d, *J*=15.6 Hz, =C*H*), 4.64 (2H, s, CH_2), 4.04 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 3.74–3.55 (4H, m, 2×NCH_2), 1.15 (3H, t, *J*=7.2 Hz, OCH_2CH_3); δ_C ($CDCl_3$): 190.8, 168.7, 167.7, 144.7, 141.2, 135.3, 129.4, 128.9, 128.1, 128.0, 127.9, 127.8, 102.6, 90.8, 59.1, 52.6, 47.2, 42.2, 14.3; *m/z* (EI): 376 (M^+, 4%), 330 (28), 105 (17), 91 (100).

4.4.4. 2-(1-Acetyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (9a). Pale yellow solid; yield: 49%; mp 141–143°C; (Found: C, 58.88; H, 7.11; N, 12.52. $C_{11}H_{16}N_2O_3$, requires C, 58.91; H, 7.19; N, 12.49%); ν_{max} (KBr) cm^{-1}: 3250 (NH), 1691, 1562; δ_H (d_6-DMSO): 8.75 (1H, s, N*H*), 8.70 (1H, s, N*H*), 7.70 (1H, d, *J*=15.6 Hz, =C*H*), 5.45 (1H, d, *J*=15.6 Hz, =C*H*), 4.05 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.55 (4H, s, 2×NCH_2), 2.13 (3H, s, $COCH_3$), 1.18 (3H, t, *J*=6.9 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 191.9, 168.7, 164.6, 143.2, 119.2, 102.9, 91.5, 59.1, 43.2, 28.3, 14.9; *m/z* (EI): 224 (M^+, 27%), 178 (26), 163 (36), 151 (100), 44 (40).

4.4.5. 1-Methyl-2-(1-acetyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (9b). Yellow viscous liquid; yield: 63%; mp 101–103°C; MS (high resolution, positive FAB) *m/z*: 239.1390 [$(M+H)^+$]; $C_{12}H_{19}N_2O_3^+$ required 239.1390; ν_{max} (KBr) cm^{-1}: 3178 (NH), 1682, 1617, 1576; δ_H ($CDCl_3$): 8.88 (1H, s, N*H*), 7.75 (1H, d, *J*=15.0 Hz, =C*H*), 4.88 (1H, d, *J*=15.0 Hz, =C*H*), 4.03 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.86–3.69 (4H, m, 2×NCH_2), 2.83 (3H, s, NCH_3), 2.05 (3H, s, $COCH_3$), 1.19 (3H, t, *J*=6.9 Hz, OCH_2CH_3); δ_C ($CDCl_3$): 186.2, 168.7, 167.8, 143.9, 96.0, 90.9, 58.2, 50.7, 41.8, 35.3, 26.3, 14.9; *m/z* (EI): 238 (M^+, 16%), 192 (31), 177 (56), 165 (100), 58 (42).

4.4.6. 1-Benzyl-2-(1-acetyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (9c). Yellow viscous liquid; yield: 65%; mp 101–103°C; MS (high resolution, positive FAB) *m/z*: 315.1707 [$(M+H)^+$]; $C_{18}H_{23}N_2O_3^+$ required 315.1703; ν_{max} (KBr) cm^{-1}: 3200 (NH), 1679, 1561, 1502; δ_H ($CDCl_3$): 9.82 (1H, br, N*H*), 7.88 (1H, d, *J*=15.6 Hz, =C*H*), 7.34–7.25 (3H, m, Ar*H*), 7.18 (2H, t, *J*=6.9 Hz, Ar*H*), 5.31 (1H, d, *J*=15.6 Hz, =C*H*), 4.49 (2H, s, CH_2), 4.13 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 3.66 (2H, t, *J*=9.3 Hz, NCH_2), 3.50 (2H, t, *J*=9.3 Hz, NCH_2), 2.33 (3H, s, $COCH_3$), 2.05 (3H, s, $COCH_3$), 1.13 (3H, t, *J*=7.2 Hz, OCH_2CH_3); δ_C ($CDCl_3$): 192.1, 168.7, 167.2, 142.7, 135.5, 128.6, 127.9, 127.6, 104.5, 91.2, 59.2, 53.0, 47.2, 42.3, 27.0, 14.3; *m/z* (EI): 314 (M^+, 3%), 268 (13), 216 (14), 91 (100).

4.4.7. 2-(1-Ethoxycarbonyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (10a). White crystals; yield: 69%; mp 166–167°C; (Found: C, 56.59; H, 7.24; N, 11.17. $C_{12}H_{18}N_2O_4$ requires C, 56.68; H, 7.13; N, 11.02%); ν_{max} (KBr) cm^{-1}: 3350 (NH), 1669, 1634, 1551; δ_H (d_6-DMSO): 8.14 (1H, s, N*H*), 7.55 (1H, s, N*H*), 7.55 (1H, d, *J*=15.3 Hz, =C*H*), 5.80 (1H, d, *J*=15.3 Hz, =C*H*), 4.08 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 4.03 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.54 (4H, s, 2×NCH_2), 1.21 (3H, t, *J*=6.9 Hz, OCH_2CH_3), 1.17 (3H, t, *J*=6.9 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 169.2, 168.4, 165.4, 141.3, 101.3, 78.3, 58.8, 58.7, 43.5, 43.4, 15.1, 15.0; *m/z* (EI): 254 (M^+, 100%), 209 (88), 181 (45), 163 (92).

4.4.8. 1-Methyl-2-(1-ethoxycarbonyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (10b). Pale yellow crystals; yield: 80%; mp 77–79°C; (Found: C, 58.11; H, 7.61; N, 10.22; $C_{13}H_{20}N_2O_4$ requires C, 58.19; H, 7.51; N, 10.44%); ν_{max} (KBr) cm^{-1}: 3318 (NH), 1687, 1632, 1583, 1556; δ_H (d_6-DMSO): 8.28 (1H, s, N*H*), 7.63 (1H, d, *J*=15.3 Hz, =C*H*), 5.33 (1H, d, *J*=15.3 Hz, =C*H*), 4.03 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.99 (2H, q, *J*=6.9 Hz, OCH_2CH_3), 3.76–3.71 (2H, m, NCH_2), 3.69–3.57 (2H, m, NCH_2), 2.84 (3H, s, NCH_3), 1.19 (3H, t, *J*=6.9 Hz, OCH_2CH_3), 1.16 (3H, t, *J*=6.9 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 169.1, 167.6, 166.5, 144.0, 98.6, 76.7, 58.4, 51.8, 41.7, 37.2, 15.2, 15.1; *m/z* (EI): 268 (M^+, 25%), 222 (43), 177 (43), 170 (47), 125 (100).

4.4.9. 1-Benzyl-2-(1-ethoxycarbonyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (10c). Yellow viscous liquid; yield: 68%; MS (high resolution, positive FAB) *m/z*: 345.1810 [$(M+H)^+$]; $C_{19}H_{25}N_2O_4^+$ required 345.1809; ν_{max} (KBr) cm^{-1}: 3344 (NH), 1642, 1590, 1546, 1148; δ_H (d_6-DMSO): 8.61 (1H, s, N*H*), 7.65 (1H, d, *J*=11.4 Hz, Ar*H*), 7.47–7.30 (5H, m, Ar*H*+=C*H*), 5.46 (1H, d, *J*=15.0 Hz, =C*H*), 4.42 (2H, s, NCH_2), 4.13–3.93 (4H, m, 2×OCH_2CH_3), 3.58–3.56 (4H, m, 2×NCH_2), 1.18–1.09 (6H, m, 2×OCH_2CH_3); δ_C (d_6-DMSO): 169.0, 168.3, 166.7, 143.7, 136.6, 129.0, 128.0, 127.9, 99.2, 76.9, 58.5, 58.4, 53.0, 48.7, 42.1, 15.2, 15.0; *m/z* (EI): 344 (M^+, 9%), 271 (14), 257 (40), 246 (100), 211 (22), 201 (27), 173 (45), 132 (16), 104 (17), 91 (27), 65 (20).

4.4.10. 1,3-Dimethyl-2-(1-ethoxycarbonyl-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (10d). Yellow viscous liquid; yield: 38%; MS (high resolution, positive FAB) *m/z*: 283.1650 [$(M+H)^+$]; $C_{14}H_{23}N_2O_4$ required 283.1652; ν_{max} (KBr) cm^{-1}: 1637, 1571, 1530; δ_H (d_6-DMSO): 8.00 (1H, d, *J*=15.0 Hz, =C*H*), 4.67 (1H, d, *J*=15.0 Hz, =C*H*), 4.19–4.08 (4H, m, 2×OCH_2CH_3), 3.74 (4H, s, 2×NCH_2), 2.91 (6H, s, 2×NCH_3), 1.28–1.17 (6H, m, 2×OCH_2CH_3); δ_C (d_6-DMSO): 168.8, 167.6, 165.3, 144.4, 93.3, 73.1, 58.0, 58.0, 48.9, 35.2, 15.1, 14.9; *m/z* (EI): 282 (M^+, 60%), 237 (48), 209 (52), 178 (54), 150 (86), 123 (100).

4.4.11. 2-(1-Cyano-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (11a). White solid; yield: 69%; mp 218–220°C; (Found: C, 57.90; H, 6.45; N, 20.02. $C_{10}H_{13}N_3O_2$ requires C, 57.96; H, 6.32; N, 20.28%); ν_{max} (KBr) cm^{-1}: 3250 (NH), 2181 (CN), 1663, 1573; δ_H (d_6-DMSO): 8.25 (1H, s, N*H*), 7.51 (1H, s, N*H*), 7.52 (1H, d, *J*=14.4 Hz, =C*H*), 5.11 (1H, d, *J*=14.4 Hz, =C*H*), 4.00 (2H, q, *J*=7.2 Hz, OCH_2CH$_3$), 3.51 (4H, s, 2×NCH_2), 1.15 (3H, t, *J*=7.2 Hz, OCH$_2$CH_3); δ_C (d_6-DMSO): 167.8, 164.3, 142.5, 120.1, 100.2, 58.9, 57.9, 43.8, 43.7, 14.9; *m/z* (EI): 207 (M^+, 44%), 162 (100).

4.4.12. 1-Methyl-2-(1-cyano-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (11b). White crystals; yield: 75%; mp 131–133°C; (Found: C, 59.33; H, 6.81; N, 19.00. $C_{11}H_{15}N_3O_2$ requires C, 59.71; H, 6.83; N, 18.99%); ν_{max} (KBr) cm^{-1}: 3312 (NH), 2174 (CN), 1680, 1572; δ_H (d_6-DMSO): 7.98 (1H, s, N*H*), 7.50 (1H, d, *J*=14.4 Hz, =C*H*), 5.18 (1H, d, *J*=14.4 Hz, =C*H*), 3.99 (2H, q, *J*=6.9 Hz, OCH_2CH$_3$), 3.59 (2H, m, NCH_2), 3.41 (2H, m, NCH_2), 3.08 (3H, s, NCH_3), 1.13 (3H, t, *J*=6.9 Hz, OCH$_2$CH_3); δ_C (d_6-DMSO): 165.9, 161.3, 141.8, 118.3, 99.2, 57.1, 55.4, 51.0, 39.3, 33.0, 13.0; *m/z* (EI): 221 (M^+, 80%), 175 (100).

4.4.13. 1-Benzyl-2-(1-cyano-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (11c). Pale yellow crystals; yield: 80%; mp 134–136°C; (Found: C, 68.44; H, 6.44; N, 14.24. $C_{17}H_{19}N_3O_2$ requires C, 68.67; H, 6.44; N, 14.13%); ν_{max} (KBr) cm^{-1}: 3330 (NH), 2179 (CN), 1668, 1549, 1526; δ_H (d_6-DMSO): 8.17 (1H, s, N*H*), 7.56 (1H, d, *J*=14.4 Hz, =C*H*), 7.37–7.24 (5H, m, Ar*H*), 5.21 (1H, d, *J*=14.4 Hz, =C*H*), 4.80 (2H, s, CH_2), 3.99 (2H, q, *J*=6.9 Hz, OCH_2CH$_3$), 3.57–3.31 (4H, m, 2×NCH_2), 1.13 (3H, t, *J*=6.9 Hz, OCH$_2$CH_3); δ_C (d_6-DMSO): 167.5, 162.5, 143.4, 136.3, 129.0, 127.8, 127.5, 119.8, 101.4, 58.8, 57.0, 50.2, 50.1, 41.0, 14.7; *m/z* (EI): 297 (M^+, 2%), 251 (18), 91 (100).

4.4.14. 1,3-Dimethyl-2-(1-cyano-3-ethoxycarbonylprop-2-enylidene)-2,3,4,5-tetrahydroimidazole (11d). Yellow crystals; yield: 81%; mp 102–104°C; (Found: C, 60.95; H, 7.24; N, 17.79. $C_{12}H_{17}N_3O_2$ requires C, 61.25; H, 7.28; N, 17.86%); ν_{max} (KBr) cm^{-1}: 2172 (CN), 1688, 1587, 1538; δ_H (d_6-DMSO): 7.41 (1H, d, *J*=14.7 Hz, =C*H*), 5.59 (1H, d, *J*=14.7 Hz, =C*H*), 4.16 (2H, q, *J*=7.2 Hz, OCH_2CH$_3$), 3.63 (4H, s, 2×NCH_2), 3.12 (6H, s, 2×NCH_3), 1.28 (3H, t, *J*=7.2 Hz, OCH$_2$CH_3); δ_C (d_6-DMSO): 168.8, 166.5, 142.7, 120.4, 102.5, 59.3, 55.6, 50.5, 37.9, 14.5; *m/z* (EI): 235 (M^+, 60%), 190 (75), 162 (29), 148 (100).

4.4.15. 8-Benzoyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyridin-5-one (12a). Pale yellow crystals; yield: 80%; mp 179–181°C (lit.[9a] 179–180.5°C); δ_H ($CDCl_3$): 8.67 (1H, s, N*H*), 7.56–7.44 (6H, m, Ar*H*+=C*H*), 5.77 (1H, d, *J*=9.6 Hz, =C*H*), 4.29 (2H, t, *J*=9.0 Hz, NCH_2), 4.02 (2H, t, *J*=9.0 Hz, NCH_2).

4.4.16. 1-Methyl-8-benzoyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyridin-5-one (12b). Yellow green crystals; yield: 78%; mp 130–132°C (lit.[9a] 130–132.5°C); δ_H ($CDCl_3$): 7.74 (2H, d, *J*=7.5 Hz, Ar*H*), 7.53–7.42 (3H, m, Ar*H*), 7.38 (1H, d, *J*=9.3 Hz, =C*H*), 5.74 (1H, d, *J*=9.3 Hz, =C*H*), 4.20 (2H, t, *J*=9.3 Hz, NCH_2), 3.86 (2H, t, *J*=9.3 Hz, NCH_2), 2.94 (3H, s, NCH_3).

4.4.17. 1-Benzyl-8-benzoyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyridin-5-one (12c). Pale yellow crystals; yield: 79%; mp 138–140°C; (Found: C, 76.15; H, 5.50; N, 8.41. $C_{21}H_{18}N_2O_2$ requires C, 76.34; H, 5.49; N, 8.48%); ν_{max} (KBr) cm^{-1}: 1672, 1624, 1556; δ_H ($CDCl_3$): 7.55–7.16 (10H, m, Ar*H*), 7.35 (1H, d, *J*=9.3 Hz, =C*H*), 5.79 (1H, d, *J*=9.3, =C*H*), 4.66 (2H, s, CH_2), 4.26 (2H, t, *J*=9.6 Hz, NCH_2), 3.91 (2H, t, *J*=9.6 Hz, NCH_2); δ_C ($CDCl_3$): 191.8, 161.3, 153.9, 144.3, 138.5, 134.7, 131.9, 129.3, 128.7, 128.2, 127.8, 105.2, 99.6, 77.4, 52.6, 49.5, 42.4; *m/z* (EI): 330 (M^+, 39%), 91 (100).

4.4.18. 8-Acetyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (13a). White crystals; yield: 62%; mp 206–208°C; (Found: C, 60.25; H, 5.56; N, 15.85; $C_9H_{10}N_2O_2$ requires C, 60.66; H, 5.66; N, 15.72%); ν_{max} (KBr) cm^{-1}: 3321 (NH), 1668, 1607, 1581; δ_H ($CDCl_3$): 8.77 (1H, s, N*H*), 7.69 (1H, d, *J*=9.3 Hz, =C*H*), 5.51 (1H, d, *J*=9.3 Hz, =C*H*), 3.97 (2H, t, *J*=9.3 Hz, NCH_2), 3.72 (2H, t, NCH_2), 2.24 (3H, s, COCH_3); δ_C ($CDCl_3$): 192.9, 161.1, 155.6, 142.3, 104.7, 97.5, 43.2, 43.0, 26.4; *m/z* (EI): 178 (M^+, 93%), 163 (100).

4.4.19. 8-Ethoxycarbonyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyridin-5-one (14a). White crystals; yield: 65%; mp 153–155°C; (Found: C, 57.69; H, 5.80; N, 13.52; $C_{10}H_{12}N_2O_3$ requires C, 57.68; H, 5.81; N, 12.46%); ν_{max} (KBr) cm^{-1}: 3359 (NH), 1683, 1614, 1570; δ_H (d_6-DMSO): 7.99 (1H, s, N*H*), 7.53 (1H, d, *J*=9.3 Hz, =C*H*), 5.50 (1H, d, *J*=9.3 Hz, =C*H*), 4.14 (2H, q, *J*=10.8 Hz, OCH_2CH$_3$), 3.97 (2H, t, *J*=9.0 Hz, NCH_2), 3.69 (2H, t, *J*=9.0 Hz, NCH_2), 1.21 (3H, t, *J*=10.8 Hz, OCH$_2$CH_3); δ_C (d_6-DMSO): 164.9, 161.2, 155.8, 140.8, 105.0, 86.4, 59.6, 43.6, 42.8, 14.7; *m/z* (EI): 208 (M^+, 100%), 161 (80).

4.5. General procedure for the cyclization of adducts in the presence of sodium ethoxide

To a solution of the adduct (1 mmol) in ethanol (15 mL) was added sodium ethoxide (1 mmol) and the reaction mixture was refluxed for 1–2 h. Removal of solvent under vacuum gave a residue that was fractionated by chromatography on a silica gel column using petroleum ether/ethyl acetate or ethyl acetate/methanol as an eluant to give the fused imidazo[1,2-*a*]pyridinone products.

4.5.1. 1-Methyl-8-acetyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (13b). White crystals; yield: 70%; mp 106–108°C; (Found: C, 62.06; H, 6.32; N, 14.53; $C_{10}H_{12}N_2O_2$ requires C, 62.48; H, 6.29; N, 14.58%); ν_{max} (KBr) cm^{-1}: 1671, 1616, 1555; δ_H ($CDCl_3$): 7.65 (1H, d, *J*=9.3 Hz, =C*H*), 5.83 (1H, d, *J*=9.3 Hz, =C*H*), 4.16 (2H, t, *J*=9.3 Hz, NCH_2), 3.83 (2H, t, *J*=9.3 Hz, NCH_2), 3.05 (3H, s, NCH_3), 2.41 (3H, s, COCH_3); δ_C ($CDCl_3$): 192.3, 161.0, 154.7, 142.5, 105.7, 99.9, 51.8, 42.1, 38.8, 27.6; *m/z* (EI): 192 (M^+, 62%), 177 (100).

4.5.2. 1-Benzyl-8-acetyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (13c). White crystals; yield: 95%; mp 121–123°C; (Found: C, 71.68; H, 6.02; N, 10.44;

$C_{16}H_{16}N_2O_2$ requires C, 71.62; H, 6.01; N, 10.44%); ν_{max} (KBr) cm^{-1}: 1672, 1624, 1527, 1541; δ_H (d_6-DMSO): 7.72 (1H, d, *J*=9.3 Hz, =C*H*), 7.34–7.23 (5H, m, Ar*H*), 5.63 (1H, d, *J*=9.3 Hz, =C*H*), 4.66 (2H, s, CH_2), 4.00 (2H, t, *J*=9.3 Hz, NCH_2), 3.72 (2H, t, *J*=9.3 Hz, NCH_2), 2.19 (3H, s, $COCH_3$); δ_C (d_6-DMSO): 191.8, 159.7, 153.1, 142.4, 135.7, 127.8, 127.1, 126.7, 104.2, 99.4, 52.2, 48.8, 41.7, 27.3; *m/z* (EI): 268 (M^+, 29%), 91 (100).

4.5.3. 1-Methyl-8-ethoxycarbonyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (14b). White crystals; yield: 49%; mp 92–94°C (lit.[15] 88–92°C); δ_H (d_6-DMSO): 7.77 (1H, d, *J*=9.6 Hz, =C*H*), 5.83 (1H, d, *J*=9.6 Hz, =C*H*), 4.25 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.15 (2H, t, *J*=9.3 Hz, NCH_2), 3.78 (2H, t, *J*=9.3 Hz, NCH_2), 1.34 (3H, t, *J*=7.2 Hz, OCH_2CH_3).

4.5.4. 1-Benzyl-8-ethoxycarbonyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (14c). White crystals; yield: 62%; mp 66–68°C; MS (high resolution, positive FAB) *m/z*: 299.1391 [$(M+H)^+$]; $C_{17}H_{19}N_2O_3^+$ required 299.1390; ν_{max} (KBr) cm^{-1}: 1699, 1650, 1546; δ_H (d_6-DMSO): 7.85 (1H, d, *J*=9.6 Hz, =C*H*), 7.37–7.29 (5H, m, Ar*H*), 5.90 (1H, d, *J*=9.6 Hz, =C*H*), 4.84 (2H, s, CH_2), 4.21 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.13 (2H, t, *J*=9.0 Hz, NCH_2), 3.67 (2H, t, *J*=9.0 Hz, NCH_2), 1.28 (3H, t, *J*=7.2 Hz, OCH_2CH_3); δ_C (d_6-DMSO): 163.5, 161.0, 153.3, 142.3, 134.7, 127.5, 126.6, 126.5, 105.6, 89.5, 59.1, 52.9, 47.4, 41.3, 13.0; *m/z* (EI): 298 (M^+, 29%), 91 (100).

4.5.5. 8-Cyano-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (15a). White crystals; yield: quant.; mp 220–222°C; (Found: C, 59.59; H, 4.41; N, 26.04; $C_8H_7N_3O$ requires C, 59.62; H, 4.38; N, 26.07%); ν_{max} (KBr) cm^{-1}: 3277 (NH), 2213 (CN), 1668, 1561; δ_H (d_6-DMSO): 8.64 (1H, s, N*H*), 7.34 (1H, d, *J*=9.3 Hz, =C*H*), 5.54 (1H, d, *J*=9.3 Hz, =C*H*), 4.02 (2H, t, *J*=9.3 Hz, NCH_2), 3.67 (2H, t, *J*=9.3 Hz, NCH_2); δ_C (d_6-DMSO): 159.2, 156.4, 140.8, 116.7, 104.9, 64.4, 43.3, 41.1; *m/z* (EI): 161 (M^+, 100%), 133 (52).

4.5.6. 1-Methyl-8-cyano-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (15b). Pale yellow crystals; yield: quant.; mp 181–183°C; (Found: C, 61.41; H, 5.08; N, 24.12; $C_9H_9N_3O$ requires C, 61.70; H, 5.18; N, 23.99%); ν_{max} (KBr) cm^{-1}: 2200 (CN), 1661, 1595, 1571; δ_H (d_6-DMSO): 7.35 (1H, d, *J*=9.3 Hz, =C*H*), 5.60 (1H, d, *J*=9.3 Hz, =C*H*), 3.93 (2H, t, *J*=9.3 Hz, NCH_2), 3.70 (2H, t, *J*=9.3 Hz, NCH_2), 3.17 (3H, s, NCH_3); δ_C (d_6-DMSO): 160.2, 155.2, 143.2, 118.6, 106.6, 65.4, 50.3, 42.5, 33.6; *m/z* (EI): 175 (M^+, 100%), 147 (36).

4.5.7. 1-Benzyl-8-cyano-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one (15c). White needle crystals; yield: 80%; mp 104–106°C; (Found: C, 71.94; H, 5.28; N, 16.69. $C_{15}H_{13}N_3O$ requires C, 71.70; H, 5.21; N, 16.72%); ν_{max} (KBr) cm^{-1}: 2215 (CN), 1658, 1587, 1562; δ_H ($CDCl_3$): 7.42–7.31 (6H, m, Ar*H*+=C*H*), 5.88 (1H, d, *J*=9.6 Hz, =C*H*), 4.94 (2H, s, CH_2), 4.12 (2H, t, *J*=9.0 Hz, NCH_2), 3.66 (2H, t, *J*=9.0 Hz, NCH_2); δ_C ($CDCl_3$): 160.7, 153.9, 143.0, 134.1, 129.1, 128.4, 128.0, 117.7, 108.0, 66.7, 50.2, 47.2, 42.2; *m/z* (EI): 251 (M^+, 17%), 91 (100).

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