An Expeditious Synthetic Access to β-(Z)-[(1-Propynyl)amino]enones and β-[(Z)-(1-Propynyl)amino]enoates

David Gravestock,* Martin C. Dovey
School of Chemical and Physical Sciences, University of Natal, Pietermaritzburg, Private Bag X01, Scottsville 3209, South Africa.
Fax +27(33)260 5009; E-mail: GravestockD@nu.ac.za
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Abstract: The silver nitrate promoted reaction of propargyl bromide with (Z)-4-amino-3-penten-2-ones and (Z)-3-amino-2-butenoates provides rapid access to β-(Z)-[(1-propynyl)amino]enones and β-[(Z)-(1-propynyl)amino]enoates respectively.

Key words: β-aminoenones, β-aminoenoates, ynamines, microwave-mediated synthesis

Ynamines are a class of compounds whose exposure has increased in the past 40–50 years. This stems from their ability to function as a synthon for a variety of synthetic protocols. They are more valuable than traditional alkynes and are in their own right very useful compounds, due to the electron donating ability of the nitrogen atom which allows for regiospecific transformations.1 Ynamides are a subgroup of ynamines which contain an electron withdrawing group attached to nitrogen and show greater stability than their electron rich counterparts without great loss of reactivity.2 Ynamides have received much attention over the past decade with numerous accounts of their synthesis and reactivity.3

We now report our addition to this fascinating field of organonitrogen chemistry. We have prepared ynamines that are related to the ynamides discussed above by vinylogy. Thus in our systems (CH₃C≡C–N–C=C–COR) a carbon-carbon double bond is interpolated between the nitrogen atom and the electron withdrawing ketone or ester group. Nitrogen is thus linked conjugatively to both the alkyne and the electron withdrawing group. The ynamine moiety is stabilised by virtue of the conjugation of the nitrogen lone pair with the electron-withdrawing carbonyl group. The β-acylated enamine moiety offers attractive synthetic potential from its ability to function both as an ambident nucleophile and as an ambident electrophile in addition to its ability to participate in pericyclic and radical processes.4 In our system the electron-withdrawing acylic group serves to temper the reactivity of both the enamine and ynamine functional groups and thus improves the stability of these novel organonitrogen compounds. Our system marries ynamines and β-acylated enamines and their synergistic chemistry promises to be rich and useful.

We are particularly interested in the chemistry of N-propargylated enaminoes and have been developing synthetic methods to access these compounds for some time now. Initial endeavours in this regard involved the preparation of cyclic compounds and their subsequent transformation into 2,3-dihydro-7(1H)-indolizinones.5 Attempts to extend this methodology required the preparation of their acyclic analogues. Following the same protocols for the preparation of the cyclic compounds mentioned above would require synthesis of thioamide D (Scheme 1). N-Propargylation of various secondary amides A, using propargyl bromide and sodium hydride as base, was met with failure. Beak and Lee reported a method for the N-allylation of various secondary amides using tert-butyllithium as base.6 In accordance with this method, treatment of secondary amides A with propargyl bromide and tert-butyllithium afforded tertiary amides B. However, thionation using Brillon’s method (P₄S₁₀, Na₂CO₃, THF)⁷ did not yield the desired thioamides D. Previous attempts at thionation of N-propargyl lactams using Lawesson’s reagent⁸ appeared to harm the alkyne functionality and, therefore, this method was not attempted on the present amides. Using a different approach, alkylation of secondary thioamides C, accessed via thionation of secondary amides A using Brillon’s procedure, was not successful.

Scheme 1

Another possible alternative would be to prepare secondary β-enameinones, which could be propargylated to give the required compounds. Hamelin and co-workers reported the synthesis of secondary and tertiary enaminoketones by condensing β-diketones with amines, over an inert sup-
port, under microwave irradiation. Various amines were reacted with acetylacetone or ethyl acetoacetate and enaminones were obtained (Table 1). Equimolar quantities of the primary amine and β-dicarbonyl compound were mixed and poured onto a bed of silica gel. The mixture was irradiated in a domestic microwave oven to yield analytically pure samples of the desired enaminones. The reaction appears sensitive to steric effects alpha to nitrogen as consistently good yields (70–97%) were obtained with R = Me, n-Bu, Bn and cyclohexyl while the reaction of tert-butylamine and acetylacetone afforded a low 6% yield of the corresponding enaminone and its reaction with ethyl acetoacetate failed to give any detectable condensation product.

Table 1  Microwave Reaction Results of Primary Amines with β-Dicarbonyl Compounds

<table>
<thead>
<tr>
<th>Entry</th>
<th>β-Dicarbonyl Compound</th>
<th>R</th>
<th>Yield of 3a–k (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a (Z = COMe)</td>
<td>Me</td>
<td>80 (3a)</td>
</tr>
<tr>
<td>2</td>
<td>2b (Z = CO₂Et)</td>
<td>Me</td>
<td>82 (3b)</td>
</tr>
<tr>
<td>3</td>
<td>2a (Z = COMe)</td>
<td>n-Bu</td>
<td>76 (3c)</td>
</tr>
<tr>
<td>4</td>
<td>2b (Z = CO₂Et)</td>
<td>n-Bu</td>
<td>70 (3d)</td>
</tr>
<tr>
<td>5</td>
<td>2a (Z = COMe)</td>
<td>t-Bu</td>
<td>6 (3e)</td>
</tr>
<tr>
<td>6</td>
<td>2b (Z = CO₂Et)</td>
<td>t-Bu</td>
<td>– b</td>
</tr>
<tr>
<td>7</td>
<td>2a (Z = CO₃C₂H₅)</td>
<td>c-C₆H₁₁</td>
<td>88 (3f)</td>
</tr>
<tr>
<td>8</td>
<td>2b (Z = CO₃C₂H₅)</td>
<td>c-C₆H₁₁</td>
<td>76 (3g)</td>
</tr>
<tr>
<td>9</td>
<td>2a (Z = CO₃C₂H₅)</td>
<td>Ph</td>
<td>72 (3h)</td>
</tr>
<tr>
<td>10</td>
<td>2b (Z = CO₃C₂H₅)</td>
<td>Ph</td>
<td>70 (3i)</td>
</tr>
<tr>
<td>11</td>
<td>2a (Z = CO₃C₂H₅)</td>
<td>Bn</td>
<td>82 (3j)</td>
</tr>
<tr>
<td>12</td>
<td>2b (Z = CO₃C₂H₅)</td>
<td>Bn</td>
<td>97 (3k)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields of pure compounds based on 2.  
<sup>b</sup> No condensation product was detected.

Enaminones are ambident nucleophiles. They may attack electrophiles via their nitrogen atom or the carbon atom beta to nitrogen. The outcome of any given reaction (N- versus C-alkylation) will be determined to a large extent by the electronic character of the electrophile. Hard bases prefer hard acids and soft bases prefer soft acids according to hard and soft acid-base theory. In an ambident nucleophile the more electronegative atom is a harder base than the less electronegative atom. When applying these concepts to the enaminone system we can view the carbon atom as the soft base with the more electronegative nitrogen atom being the harder base. Therefore the reaction conditions shown in Scheme 2 favoured the soft-base/soft acid combination. The conversion (3a → 5) presumably takes place via an S₅₂ mechanism whereby the soft enamine attacks the soft electrophilic carbon atom of propargyl bromide with simultaneous expulsion of bromide. In order to induce attack via the more electronegative nitrogen atom the electrophile must be converted into a harder acid. This would favour the corresponding S₅₁ mechanism. Treatment of propargyl bromide with Ag⁺ should encourage the heterolytic cleavage of the carbon-bromine bond, favouring formation of a carbocation and thus rendering the propargyl bromide a harder acid and therefore attack by nitrogen would be preferred. This trend has been observed in the treatment of alkyl halides with the cyanide anion. Alkyl halides treated with NaCN give mostly nitriles (RCN), whereas alkyl halides treated with AgCN give mostly isonitriles (RNC). It was with these ideas in mind that the reactions summarized in Table 2 were performed.
Thus propargyl bromide was added to a stirred solution of an equimolar quantity of silver nitrate in anhydrous acetonitrile at ambient temperature. The appropriate enamino ne (0.5 equiv) was added immediately thereafter and the mixture stirred overnight. Workup and purification afforded not the desired N-(2-propynyl)enaminones, but instead the novel N-(1-propynyl)enaminones in moderate yields. This result is rather surprising and further studies to elucidate the mechanism of this reaction are currently being undertaken. Presumably a thermodynamic driving force for the rearrangement reaction will be the conjugation of the nitrogen atom to the alkyne group. These compounds are remarkably stable – they suffer very little degradation even when left exposed to the atmosphere for several weeks.

Various 2-D NMR spectra including GHMQC, GHSQC, and COSY facilitated the unambiguous assignment of NMR signals. A NOESY experiment on the benzyl analogue, 4-(benzylamino)-3-penten-2-one (3j) showed a correlation between the vinyl proton at $\delta$ 5.03 and the methyl group at $\delta$ 1.89 (Figure 1). By analogy a Z-configuration was assigned to all the other enamino products shown in Table 1. This finding is in agreement with the results of Hamelin et al.² To confirm that the geometry of the double bond had not changed during the course of the reaction summarized in Table 2 a NOESY experiment on the benzyl derivative, 4-[benzyl(1-propynyl)amino]-3-penten-2-one (6j) was performed. A correlation between the vinyl proton at $\delta$ 6.30 and the methyl group bonded to the double bond at $\delta$ 2.49 showed that the double bond had maintained its Z-geometry (Figure 1). By analogy a Z-configuration was assigned to all the other 1-propynylenaminone products listed in Table 2. The third structure in Figure 1 shows that if the compounds existed as the E-isomers then one would not expect a correlation between these groups (see highlighted regions).

Comparison of the NMR data showed some interesting effects (Figure 2). All protons of the enamines 3a–k experienced a downfield shift when converted into the corresponding N-(1-propynyl)enaminones 6a–k. The most marked shift being experienced by the vinyl protons (e.g. $\delta$ 4.42 in 3b versus $\delta$ 6.22 in 6b). Effects on the $^{13}$C signals were more erratic. Noteworthy though is the significant downfield shift experienced by the vinyl carbon beta to nitrogen (e.g. $\delta$ 81.7 in 3a versus $\delta$ 106.9 in 6b) and an even more pronounced upfield shift of the quaternary vinyl carbon alpha to nitrogen (e.g. $\delta$ 162.6 in 3b versus $\delta$ 135.2 in 6b). Comparison of the chemical shifts of the alkyl carbon atoms in N-2-propynyl compound (7)³ and the analogous N-1-propynyl compound (6b) reveals some startling differences (Figure 2). The carbon atoms in the N-1-propynyl compounds (6a–k) experience significant downfield shifts ($\Delta \delta = 40–50$). These NMR data serve as valuable clues to the electronic changes brought about when the enamino system (N=C=C–COR) is bonded to the propynyl group to form the corresponding $\beta$-(Z)-[(1-propynyl)amino]enones (MeC=C–C–N=C–COMe) and $\beta$-[Z)-(1-propynyl)amino]enoates (MeC=C–C–N=C–CO₂Et).

In conclusion we have developed a convenient synthetic access to $\beta$-(Z)-[(1-propynyl)amino]enones and Enoates. Future work involves conducting studies to elucidate the mechanism of the rearrangement reaction as well as to investigate the chemistry and the synthetic potential of these remarkable composite functional groups.

Table 2 Reaction Results of Enaminones 3a–k with Propargyl Bromide

<table>
<thead>
<tr>
<th>Entry</th>
<th>Enamine 3a–k</th>
<th>R</th>
<th>Z</th>
<th>Yield of 6a–k (%)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a</td>
<td>Me</td>
<td>COMe</td>
<td>16 (6a)</td>
</tr>
<tr>
<td>2</td>
<td>3b</td>
<td>Me</td>
<td>CO₂Et</td>
<td>21 (6b)</td>
</tr>
<tr>
<td>3</td>
<td>3c</td>
<td>n-Bu</td>
<td>COMe</td>
<td>24 (6c)</td>
</tr>
<tr>
<td>4</td>
<td>3d</td>
<td>n-Bu</td>
<td>CO₂Et</td>
<td>24 (6d)</td>
</tr>
<tr>
<td>5</td>
<td>3f</td>
<td>c-C₆H₁₁</td>
<td>COMe</td>
<td>25 (6f)</td>
</tr>
<tr>
<td>6</td>
<td>3g</td>
<td>c-C₆H₁₁</td>
<td>CO₂Et</td>
<td>24 (6g)</td>
</tr>
<tr>
<td>7</td>
<td>3h</td>
<td>Ph</td>
<td>COMe</td>
<td>7⁸ (6h)</td>
</tr>
<tr>
<td>8</td>
<td>3i</td>
<td>Ph</td>
<td>CO₂Et</td>
<td>–⁵</td>
</tr>
<tr>
<td>9</td>
<td>3j</td>
<td>Bn</td>
<td>COMe</td>
<td>21 (6j)</td>
</tr>
<tr>
<td>10</td>
<td>3k</td>
<td>Bn</td>
<td>CO₂Et</td>
<td>14⁴ (6k)</td>
</tr>
</tbody>
</table>

¹ Isolated yields of pure compounds based on 3.

² Starting material and product co-elute and therefore the yield is based on relative integral values of the vinyl protons in the $^1$H NMR spectrum.

³ Trace quantity detected by $^1$H NMR spectroscopy.

Figure 1
Methylamine and acetylacetone were mixed and irradiated to yield (Z)-4-(methylamino)-3-penten-2-one as a yellow oil (6%); Rf 0.47 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl₃): 3071, 2956, 2928, 2868, 1610, 1574, 1294, 735 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 10.93 (br s, 1 H, NH), 4.85 (s, 1 H, C=CH), 3.32 (m, 1 H, NCH₂), 1.92 (s, 3 H, COCH₃), 1.88 (s, 3 H, CH₃C=C). 13C NMR (125 MHz, CDCl₃): δ = 194.2 (C=O), 161.7 (C=CH), 94.7 (C=CH), 51.3 (NCH₂), 24.2 [2 C, NCH(CH₂)₂(CH₃)₂].

MS (EI): m/z (%) = 181 (M⁺, 100), 166 (37), 138 (57), 100 (44), 84 (48).

(Z)-4-(Butylamino)-3-acetylacetone-penten-2-one (3c)

Butylamine and acetyl acetone were mixed and irradiated to yield (Z)-4-(butylamino)-3-penten-2-one as a yellow oil (%); Rf 0.49 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl₃): 3071, 2956, 2928, 2868, 1610, 1574, 1294, 735 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 10.83 (br s, 1 H, NH), 4.91 (s, 1 H, C=CH), 3.19 (q, 2 H, J = 7.5 Hz, NCH₂), 1.96 (s, 3 H, COCH₃), 1.88 (s, 3 H, CH₃C=C), 1.53 (m, 2 H, NCH₂CH₂), 1.38 (m, 2 H, NCH₂CH₂), 0.90 (t, 3 H, J = 7.5 Hz, CH₃CH₂).

13C NMR (125 MHz, CDCl₃): δ = 194.5 (C=O), 163.1 (C=CH), 94.9 (C=CH), 42.6 (NCH₂), 32.0 (NCH₂CH₂), 28.6 (COCH₃), 19.9 (CH₃CH₂), 18.7 (CH₂CH₂), 13.6 (CH₃CH₂).

MS (EI): m/z (%) = 155 (M⁺, 100), 140 (85), 126 (36), 112 (51), 98 (26), 84 (42), 70 (21).

(Z)-4-(t-Butylamino)-3-penten-2-one (3e)

t-Butylamine and acetylacetone were mixed and irradiated to yield (Z)-4-(t-butylamino)-3-penten-2-one as a yellow oil (%); Rf 0.47 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl₃): 3070, 2950, 2935, 1610, 1591 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 11.34 (br s, 1 H, NH), 4.88 (s, 1 H, C=CH), 2.04 (s, 3 H, COCH₃), 1.97 (s, 3 H, CH₃C=C), 1.38 [s, 9 H, (CH₃)₃].

13C NMR (125 MHz, CDCl₃): δ = 193.9 (C=O), 163.2 (C=CH), 96.2 (C=CH), 52.2 [C(CH₃)₃], 30.7 [C(CH₃)₃], 28.6 (COCH₃), 20.4 (CH₂CH₂C).

MS (EI): m/z (%) = 155 (M⁺, 38), 140 (16), 84 (100).

(Z)-4-(Cyclohexylamino)-3-penten-2-one (3f)

Cyclohexylamine and acetylacetone were mixed and irradiated to yield (Z)-4-(cyclohexylamino)-3-penten-2-one as a yellow oil (%); Rf 0.52 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl₃): 3080, 2934, 2857, 1610, 1580, 1300, 732 cm⁻¹.

1H NMR (500 MHz, CDCl₃): δ = 10.9 (br s, 1 H, NH), 4.85 (s, 1 H, C=CH), 3.32 (m, 1 H, NCH₂), 1.92 (s, 3 H, COCH₃), 1.88 (s, 3 H, CH₃C=C), 1.28–1.77, 17.2–1.67, 1.55–1.48, 1.34–1.17 (m, 10 H, NCH₂H₃).

13C NMR (125 MHz, CDCl₃): δ = 194.2 (C=O), 161.7 (C=CH), 94.7 (C=CH), 51.3 (NCH₂), 33.6 [2 C, NCH₂CH₂], 28.5 (COCH₃), 25.2 [2 C, NCH₂CH₂(CH₂)], 24.2 [(CH₂)₂CH₂], 18.4 (CH₃CH₂C).

MS (EI): m/z (%) = 181 (M⁺, 100), 166 (37), 138 (57), 100 (44), 84 (48).

(Z)-4-(Benzylamino)-3-penten-2-one (3j)

Benzylamine and acetylacetone were mixed and irradiated to yield (Z)-4-(benzylamino)-3-penten-2-one as a yellow oil (%); Rf 0.51 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl₃): 3027, 1607, 1572, 1289, 735 cm⁻¹.
1H NMR (500 MHz, CDCl3): δ = 8.51 (br s, 1 H, NH), 4.37 (s, 1 H, C=CH), 4.03 (q, 2 H, J=7.0 Hz, OCH2CH3), 3.15 (q, 2 H, J=6.9 Hz, NCH3), 1.86 (s, 3 H, CH3C=C), 1.50 (m, 2 H, NCH2CH2), 1.35 (m, 2 H, CH2CH3), 1.19 (t, 3 H, J=7.2 Hz, OCH2CH3), 0.88 (t, 3 H, J=7.1 Hz, CH2CH3).

13C NMR (125 MHz, CDCl3): δ = 170.1 (C=O), 161.8 (C=C), 81.5 (C=C), 58.0 (OCH2CH3), 42.5 (NCH2CH2), 32.3 (NCH2CH2), 19.9 (CH2CH3), 19.2 (CH3C=C), 14.5 (OCH2CH3), 13.6 (CH2CH3).

MS (EI): m/z (%) = 185 (M+, 60), 142 (25), 130 (37), 124 (56), 84 (100), 57 (67).

Ethyl (Z)-3-(Cyclohexylamino)-2-butenoate (3g)

Cyclohexylamine (2 equiv) and ethyl acetoacetate were mixed and irradiated to yield ethyl (Z)-3-(cyclohexylamino)-2-butenoate as a colorless oil (76%); Rf 0.54 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl3): 3274, 2934, 2851, 1651, 1627, 1273, 814 cm–1.

1H NMR (500 MHz, CDCl3): δ = 8.58 (br s, 1 H, NH), 4.32 (s, 1 H, C=CH), 4.01 (q, 2 H, J=7.5 Hz, OCH2CH3), 3.25 (m, 1 H, NCH3), 1.87 (s, 3 H, CH3C=C), 1.83–1.77, 1.72–1.66, 1.56–1.49, and 1.32–1.20 (m, 10 H, NCH2CH2J), 1.18 (t, 3 H, J=7.5 Hz, OCH2CH3).

13C NMR (125 MHz, CDCl3): δ = 170.1 (C=O), 161.8 (C=C), 81.5 (C=C), 57.9 (OCH2CH3), 51.2 (NCH3), 34.1 [2 C, NCH2CH2], 25.2 [2 C, NCH2( CH2)2], 24.5 [(CH3)2CH2], 19.0 (CH3C=C), 14.5 (OCH2CH3).

MS (EI): m/z (%) = 211 (M+, 73), 166 (34), 138 (23), 130 (100), 84 (55).

Ethyl (Z)-3-(Benzyllamino)-2-butenoate (3k)

Benzyllamine (1.5 equiv) and ethyl acetoacetate were mixed and irradiated to yield ethyl (Z)-3-(benzyllamino)-2-butenoate as a colorless oil (97%); Rf 0.54 (EtOAc–hexanes, 1:1).

1H NMR (500 MHz, CDCl3): δ = 8.69 (br s, 1 H, NH), 7.34–7.24 (m, 5 H, C6H5), 5.45 (s, 1 H, CH=C), 4.20 (2 H, J=7.5 Hz, C6H5CH2), 4.10 (q, 2 H, J=7.1 Hz, OCH2CH3), 1.89 (s, 3 H, CH3C=C), 1.25 (t, 3 H, J=7.0 Hz, OCH2CH3).

13C NMR (125 MHz, CDCl3): δ = 170.3 (C=O), 161.6 (C=C), 138.5 (ipso-C6H5), 128.2 (2 C, m-C6H5), 127.1 (p-C6H5), 126.5 (2 C, o-C6H5), 83.0 (C=C), 58.1 (OCH2CH3), 46.5 (NCH3), 19.1 (CH3C=C), 14.4 (OCH2CH3).

MS (EI): m/z (%) = 219 (M+, 46), 190 (22), 172 (48), 146 (32), 91 (100).

Ethyl (Z)-3-(Phenylamino)-2-butenoate (3i)

Aniline and acetylacetone were mixed and irradiated to yield ethyl (Z)-3-(phenylamino)-2-butenoate as a colorless oil (79%); Rf 0.58 (EtOAc–hexanes, 1:1).

1H NMR (500 MHz, CDCl3): δ = 8.38 (br s, 1 H, NH), 7.41–7.33 (m, 5 H, C6H5), 4.25 (s, 1 H, CH=C), 4.19 (d, 2 H, J=6.9 Hz, C6H5CH2), 3.15 (q, 2 H, J=7.0 Hz, OCH2CH3), 1.86 (s, 3 H, CH3C=C), 1.25 (t, 3 H, J=7.0 Hz, OCH2CH3).

13C NMR (125 MHz, CDCl3): δ = 170.1 (C=O), 128.6 (2 C, m-C6H5), 125.0 (2 C, o-C6H5), 124.2 (2 C, NCH2CH2), 83.0 (C=C), 58.1 (OCH2CH3), 19.0 (CH3C=C), 14.5 (OCH2CH3).

MS (EI): m/z (%) = 194 (M+, 59), 142 (100), 82 (20), 71 (57), 56 (37).

Ethyl (Z)-3-(Methylamino)-2-butenoate (3b)

Methylamine (2 equiv) and ethyl acetoacetate were mixed and irradiated to yield ethyl (Z)-3-(methylamino)-2-butenoate as a colorless oil (82%); Rf 0.48 (EtOAc–hexanes, 1:1).

1H NMR (500 MHz, CDCl3): δ = 8.43 (br s, 1 H, NH), 4.42 (s, 1 H, C=CH), 4.03 (q, 2 H, J=7.0 Hz, OCH2CH3), 2.86 (d, 3 H, J=5.5 Hz, NCH3), 1.87 (s, 3 H, CH3C=C), 1.20 (t, 3 H, J=7.0 Hz, OCH2CH3).

13C NMR (125 MHz, CDCl3): δ = 170.5 (C=O), 162.6 (C=C), 81.7 (C=C), 58.1 (OCH2CH3), 29.4 (NCH3), 19.0 (CH3C=C), 14.5 (OCH2CH3).

MS (EI): m/z (%) = 143 (M+, 59) 98 (100) 82 (20) 71 (57) 56 (37).

Synthesis 2003, No. 4, 523–530 ISSN 0039-7881 © Thieme Stuttgart · New York
3-[Z]-1-(Methylamino)ethylidene]-5-hexyn-2-one as a yellow oil (24%) after radial chromatography (EtOAc–hexanes, 1:1).  

Preparation of N-(1-Propynyl) Enaminones 6a–k; General Procedure

Propargyl bromide (2 mmol) was added to a stirred solution of silver nitrate to yield (Z)-4-(methylamino)-3-penten-2-one as a white crystalline solid (mp 37–38 °C) after radial chromatography (EtOAc–hexanes, 1:4); R_f 0.56 (EtOAc–hexanes, 1:1).

13C NMR (125 MHz, CDCl_3); δ = 193.7 (C=O), 164.0 (CH=C=CH), 99.5 (C=CH), 83.8 (C=CH), 67.5 (C=CH), 29.8 (NCH), 27.6 (COCH), 18.9 (CH=CH=CH).

(Z)-4-[Cyclohexyl(1-propynyl)amino]-3-penten-2-one (6f)

(Z)-4-[Cyclohexyl(1-propynyl)amino]-3-penten-2-one was treated with propargyl bromide and silver nitrate to yield (Z)-4-[cyclohexyl(1-propynyl)amino]-3-penten-2-one as a red-brown oil (25%) after radial chromatography (EtOAc–hexanes, 1:4); R_f 0.56 (EtOAc–hexanes, 1:1).  

IR (thin film, CHCl_3): 2928, 2849, 1649, 1517, 1414 cm⁻¹.

HRMS (EI): m/z (%) = 219 (M⁺, 95), 204 (M⁺ – CH₃, 35), 138 (28), 137 (91), 122 (100), 55 (42), 41 (25).

HRMS (EI): m/z calcd for C₁₂H₁₀NO, 193.1464; found, 193.1464.

HRMS (EI): m/z calcd for C₁₄H₂₁NO, 219.1623; found, 219.1627.

HRMS (EI): m/z calcd for C₁₅H₁₇NO, 227.1302; found, 227.1302.

HRMS (EI): m/z calcd for C₁₆H₂₃NO, 235.1480; found, 235.1480.

HRMS (EI): m/z calcd for C₁₇H₂₅NO, 243.1657; found, 243.1657.

HRMS (EI): m/z calcd for C₁₈H₂₇NO, 251.1834; found, 251.1834.


HRMS (EI): m/z calcd for C₂₀H₃₁NO, 271.2157; found, 271.2157.

HRMS (EI): m/z calcd for C₂₁H₃₃NO, 279.2313; found, 279.2313.

HRMS (EI): m/z calcd for C₂₂H₃₅NO, 289.2459; found, 289.2459.

HRMS (EI): m/z calcd for C₂₃H₃₇NO, 297.2615; found, 297.2615.


HRMS (EI): m/z calcd for C₂₅H₄₁NO, 315.2927; found, 315.2927.

HRMS (EI): m/z calcd for C₂₆H₄₃NO, 325.3083; found, 325.3083.

HRMS (EI): m/z calcd for C₂₇H₄₅NO, 335.3239; found, 335.3239.

HRMS (EI): m/z calcd for C₂₈H₄₇NO, 345.3395; found, 345.3395.

HRMS (EI): m/z calcd for C₂₉H₄₉NO, 359.3601; found, 359.3601.

HRMS (EI): m/z calcd for C₃₀H₅₁NO, 369.3757; found, 369.3757.
MS (EI): m/z (%) = 213 (M+, 34), 198 (M+ – CH3, 100).
HRMS: m/z calc'd for C13H20NO2, 213.1154; found, 213.1144.

Ethyl (Z)-[3-Methyl(1-propynyl)amino]-2-butoenate (6h)
Ethyl (Z)-[3-(methylamino)-2-butoenate was treated with propargyl bromide and silver nitrate to yield ethyl (Z)-[3-methyl(1-propynyl)amino]-2-butoenate as a colorless oil (21%) after radial chromatography (EtOAc–hexanes, 1:4); Rf 0.59 (EtOAc–hexanes, 1:1).

IR (thin film, CHCl3): 2983, 2923, 1695, 1533, 1415, 1223, 1061 cm⁻¹.

13C NMR (125 MHz, CDCl3): δ = 6.22 (2 H, 1 H, C=CH), 1.43 (2 H, J = 7.3 Hz, OCH2CH3), 3.46 (3 H, NCH3), 2.53 (3 H, CH3C=C), 1.26 (3 H, CH3C=C), 1.31 (3 H, 3 H, OCH2CH3), 1.36 (3 H, 3 H, CH3CH2CH3), 1.31 (3 H, J = 7 Hz, OCH2CH3), 0.94 (3 H, J = 7.3 Hz, CH3CH2CH3).

IR (thin film, CHCl3): 2928, 2857, 1698, 1530, 1421, 1220, 1185, 807 cm⁻¹.

13C NMR (125 MHz, CDCl3): δ = 165.7 (C=O), 134.8 (C=CH), 127.2 (NC=C), 110.5 (NC=C), 107.4 (C=CH), 84.7 (OCH2CH3), 54.3 (NCH3), 72.0 (CH2CH3), 14.5 (OCH2CH3), 13.7 (CH3CH2CH3), 12.1 (C=CC), 11.2 (CH3C=C).

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References
(10) For a recent review on microwave-assisted synthesis see: Caddick, S. Tetrahedron 1995, 51, 10403.