Base mediated 5-endo-dig cyclization of N-propargyl proline derivatives: A facile entry to pyrrolizidine scaffolds

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A simple, base facilitated 5-endo-dig cyclization strategy has been exploited for the assembly of bicyclic core of pyrrolizidine alkaloids. This unprecedented protocol allows access to a diverse range of alkyl and aryl substituted pyrrolizidine scaffolds in moderate yields from readily available N-propargyl-L-proline ester derivatives under mild conditions. No catalyst or alkyne activator is required to effect this atom economical transformation.

Keywords: Bicyclic compounds, Cyclization, 5-endo-dig cyclization, Pyrrolizidine core, Propargyl amines

Pyrrolizidine alkaloids (PAs) are a class of nitrogen containing bicyclic natural products widely distributed in plants. Over six hundred alkaloids of this kind have been isolated from different families of plants including Boraginaceae, Asteraceae and Fabaceae. It is well documented in the literature that most of the PAs possess cytotoxicity in domestic animals and humans. The toxic behaviour of these alkaloids is due to the formation of pyrrolic metabolite, which is a strong alkylating agent that can bind with DNA and proteins during microsomal bio-activation in the liver. Although these secondary metabolites (PAs) are considered toxic substances, quite a few have some biological activity such as anticancer and neuro-active properties. In addition, some of the PAs have applications in agricultural industry due to the antifeedant activity against several insects. The structures of a few PAs are represented in Fig. 1. Most of the pyrrolizidine alkaloids are esters of necine bases (e.g. 1), which is the bicyclic core containing nitrogen at one of the bridge heads. The biological activities and the challenge associated with the formation of bicyclic core make these PAs attractive synthetic targets.

The assembly of bicyclic core of PAs has been approached by a number of research groups using different strategies. Most of the early approaches toward the construction of bicyclic core of PAs were based on the elaboration of Geissmann Waiss lactone derived from L-proline. Later, [3+2]-cycloaddition and radical cyclization methods were developed for the synthesis of natural products containing the pyrrolizidine core. Other interesting approaches to the synthesis of pyrrolizidine core involving intramolecular allylsilane or allylstannane ring closure, ring closing metathesis, intramolecular lactamization, palladium catalyzed tandem cyclization, rhodium catalyzed intramolecular carbenoid thioimide coupling, intramolecular domino oxidation – Wittig reaction and gold-catalyzed intramolecular allenyl amide cyclization have also been established.

Fig 1—Pyrrolizidine alkaloids found in plants.
Materials & Methods

All reactions were carried out under inert atmosphere. All the reagents used were purchased from commercial sources and used as such. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ using 400 MHz Bruker FT NMR spectrometer. Chemical shift values are reported in ppm relative to TMS. High resolution mass spectra (HRMS) were recorded on a Waters-Q-Tof spectrometer. IR spectra were recorded on a Brucker FTIR spectrometer. Thin layer chromatography was carried out on Merck silica gel 60 F254 TLC plates using EtOAc/hexane mixture as an eluent. Chromatographic separation was carried out through neutral alumina column.

General procedure for synthesis of pyrrolizidine scaffold (6)

A solution of LiHMDS (0.75 mmol) in hexane was added in a drop-wise manner to a solution of N-propargyl proline ester (0.5 mmol) in dry THF (5 mL) at RT under inert atmosphere. The resulting solution was stirred vigorously until the starting material was completely consumed. The solvent was evaporated under reduced pressure and the residue was purified through neutral alumina column using EtOAc/hexane mixture as an eluent.

Methyl-7-phenyl-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6a)

Yield: 70%; light yellow solid; M. pt. 97–99 °C; FTIR: 2930 (=CH), 1724 (C=O), 1497 (C=C) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.39-7.36 (m, 2H), 7.33-7.29 (m, 2H), 7.26-7.22 (m, 1H), 6.26 (t, $J = 2.2$ Hz, 1H), 4.14 (dd, $J = 16.6$ Hz, 2.2 Hz, 1H), 3.68 (s, 3H), 3.54 (dd, $J = 16.6$ Hz, 2.4 Hz, 1H), 3.32-3.29 (m, 1H), 2.92 (dd, $J = 12.2$ Hz, 6.8 Hz, 2.4 Hz, 1H), 2.56 (m, 1H), 2.02-1.91 (m, 1H), 1.90-1.81 (m, 1H), 1.80-1.69 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 175.2, 142.3, 133.1, 128.7, 127.8, 126.4, 124.3, 83.1, 61.4, 57.7, 52.8, 33.4, 26.5; HRMS (ESI): Calcd for C$_{13}$H$_{18}$NO$_2$ 244.1337; found 244.1333 [M+H]$^+$.  

Methyl-7-(thiophen-3-yl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6b)

Yield: 54%; yellow semi-solid; FTIR: 2930 (=CH), 1728 (C=O), 1432 (C=C) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.29-7.27 (m, 1H), 7.22 (dd, $J = 5.1$ Hz, 1.4 Hz, 1H), 7.19-7.18 (m, 1H), 6.06 (t, $J = 2.2$ Hz, 1H), 4.13 (dd, $J = 16.5$ Hz, 1.9 Hz, 1H), 3.67 (s, 3H), 3.54 (dd, $J = 16.5$ Hz, 2.4 Hz, 1H), 3.34-3.30 (m, 1H), 2.94-2.89 (m, 1H), 2.55-2.49 (m, 1H), 1.97-1.77 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 175.3, 138.0, 134.6, 126.6, 125.9, 123.3, 121.4, 83.5, 61.5, 57.7, 52.9, 33.4, 26.4; HRMS (ESI): Calcd for C$_{14}$H$_{16}$NO$_3$S 250.0901; found 250.0903 [M+H]$^+$.  

Methyl-7-(6-methoxynaphthalen-2-yl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6c)

Yield: 54%; light red solid; M. pt. 126 – 128 °C; FTIR: 2950 (=CH), 1731 (C=O), 1487 (C=C) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.75-7.68 (m, 2H), 7.65 (bs, 1H), 7.60 (dd, $J = 8.6$ Hz, 1.9 Hz, 1H), 7.15 (dd, $J = 8.6$ Hz, 2.6 Hz, 1H), 7.12 (d, $J = 2.6$ Hz, 1H), 6.35 (t, $J = 2.2$ Hz, 1H), 4.20 (dd, $J = 16.6$ Hz, 1.9 Hz, 1H), 3.94 (s, 3H), 3.71 (s, 3H), 3.61 (dd, $J = 16.6$ Hz, 2.5 Hz, 1H), 3.38-3.34 (m, 1H), 3.06 (dd, $J = 11.8$ Hz, 6.4 Hz, 1.8 Hz, 1H), 2.62-2.55 (m, 1H), 2.08-1.97 (m, 1H), 1.94-1.86 (m, 1H), 1.86-1.78 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 175.3, 158.1, 142.4, 134.0, 130.0, 128.8, 128.4, 127.1, 125.3, 124.9, 123.9, 119.1, 105.8, 83.2, 61.5, 57.7, 55.5, 52.8, 33.6, 26.6; HRMS (ESI): Calcd for C$_{30}$H$_{28}$NO$_3$ 324.1599; found 324.1592 [M+H]$^+$.  

Methyl-7-(3-fluorophenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6e)

Yield: 54%; yellow gel; FTIR: 2949 (=CH); 1730 (C=O); 1488 (C=C) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.32-7.28 (m, 1H), 7.16-7.10 (m, 2H), 6.99-6.94 (m, 1H), 6.27 (t, $J = 2.2$ Hz, 1H), 4.12 (dd, $J = 16.9$ Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, $J = 16.8$ Hz, 2.4 Hz, 1H), 3.33-3.28 (m, 1H), 2.89 (dd, $J = 12.3$ Hz, 6.9 Hz, 2.5 Hz, 1H), 2.56-2.50 (m, 1H), 1.99-1.90 (m, 1H), 1.88-1.82 (m, 1H), 1.74-1.69 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 174.9, 163.0 (d, $J_{C,F} = 243.5$ Hz), 141.5 (d, $J_{C,F} = 3$ Hz), 135.4 (d, $J_{C,F} = 8$ Hz), 130.2 (d, $J_{C,F} = 8.7$ Hz), 125.9, 122.0 (d, $J_{C,F} = 2.3$ Hz),
Yield: 38%; light yellow gel; FTIR: 2946 (=CH), 1732 (C=O), 1500 (C=C) cm\(^{-1}\); HRMS (ESI): Calcd for C\(_{13}\)H\(_{8}\)FNO\(_2\): 264.1965 [M+H]\(^+\).  

**Methyl-7-cyclopropyl-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6f)**  
Yield: 50%; light yellow semi solid; FTIR: 2949 (=CH), 1730 (C=O), 1505 (C=C) cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 6.98 (s, 1H), 6.73 (s, 1H), 5.76 (t, \(J = 2.0\) Hz, 1H), 4.16 (dd, \(J = 16.0\) Hz, 1.7 Hz, 1H), 3.72 (s, 3H), 3.56 (dd, \(J = 16.0\) Hz, 2.3 Hz, 1H), 3.33-3.29 (m, 1H), 2.62-2.53 (m, 2H), 2.29 (s, 3H), 1.89-1.81 (m, 2H), 1.73-1.67 (m, 1H); \(^1^3^C\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 175.6, 147.3, 120.3, 85.2, 61.6, 57.8, 52.4, 38.8, 33.2, 33.0, 26.0, 24.9; HRMS (ESI): Calcd for C\(_{13}\)H\(_{16}\)NO\(_2\): 236.1650; found 236.1653 [M+H]\(^+\).  

**Methyl-(4-methoxy-2-methylphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6i)**  
Yield: 20%; yellow gel; FTIR: 2946 (=CH), 1731 (C=O), 1500 (C=C) cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.44-7.41 (m, 2H), 7.26-7.23 (m, 2H), 6.26 (t, \(J = 2.2\) Hz, 1H), 4.11 (dd, \(J = 16.8\) Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, \(J = 16.8\) Hz, 2.5 Hz, 1H), 3.33-3.29 (m, 1H), 2.90 (ddd, \(J = 12.4\) Hz, 6.8 Hz, 2.5 Hz, 1H), 2.56-2.49 (m, 1H), 2.01-1.92 (m, 1H), 1.89-1.81 (m, 1H), 1.72-1.65 (m, 1H); \(^1^3^C\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 175.0, 141.4, 132.1, 131.8, 128.0, 125.2, 121.8, 83.1, 61.4, 57.6, 52.9, 33.4, 26.5; HRMS (ESI): Calcd for C\(_{13}\)H\(_{23}\)NO\(_2\): 322.0442; found 322.0442 [M+H]\(^+\).  

**Methyl-7-(p-tolyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate (6k)**  
Yield: 50%; light yellow liquid; FTIR: 2949 (=CH), 1730 (C=O), 1453 (C=C) cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.44-7.41 (m, 2H), 7.26-7.23 (m, 2H), 6.26 (t, \(J = 2.2\) Hz, 1H), 4.11 (dd, \(J = 16.8\) Hz, 1.9 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, \(J = 16.8\) Hz, 2.5 Hz, 1H), 3.33-3.29 (m, 1H), 2.90 (ddd, \(J = 12.4\) Hz, 6.8 Hz, 2.5 Hz, 1H), 2.56-2.49 (m, 1H), 2.01-1.92 (m, 1H), 1.89-1.81 (m, 1H), 1.72-1.65 (m, 1H); \(^1^3^C\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 175.6, 147.3, 120.3, 85.2, 61.6, 57.8, 52.4, 38.8, 33.2, 33.0, 26.0, 24.9; HRMS (ESI): Calcd for C\(_{13}\)H\(_{23}\)NO\(_2\): 236.1650; found 236.1653 [M+H]\(^+\).
Methyl-7-(4-pentylphenyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine-7a-carboxylate \((6m)\)

Yield: 60%; yellow liquid; FTIR: 2953 \((=\text{CH})\), 1731 \((\text{C}=\text{O})\), 1456 \((\text{C}=\text{C})\) cm\(^{-1}\); \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.29 (d, \(J = 8.4\text{ Hz}, 2\text{ H})\), 7.12 (d, \(J = 8.4\text{ Hz}, 2\text{ H})\), 6.20 (t, \(J = 2.2\text{ Hz}, 1\text{ H})\), 4.12 (dd, \(J = 16.5\text{ Hz}, 6.8\text{ Hz}, 2\text{ H})\), 3.68 (s, 3H), 3.52 (dd, \(J = 16.5\text{ Hz}, 2.5\text{ Hz}, 1\text{ H})\), 3.32-3.27 (m, 1H), 2.91 (dd, \(J = 12.2\text{ Hz}, 6.8\text{ Hz}, 2.4\text{ Hz}, 1\text{ H})\), 2.59-2.49 (m, 3H), 2.00-1.89 (m, 1H), 1.87-1.80 (m, 1H), 1.73-1.67 (m, 1H), 1.63-1.55 (m, 2H), 1.35-1.26 (m, 4H), 0.88 (t, \(J = 6.9\text{ Hz}, 3\text{ H})\);

\(^{13}\text{C}\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 175.2, 142.7, 142.2, 130.4, 128.7, 126.2, 123.2, 83.1, 61.4, 57.7, 52.8, 35.7, 33.4, 31.6, 31.2, 26.5, 22.7, 14.2; HRMS (ESI): Calcd for C\(_{20}\)H\(_{28}\)NO\(_2\) 314.2120; found 314.2120 \([\text{M}+\text{H}]^+\).

Results and Discussion

Since the 5-\textit{endo-dig} cyclization strategy has proved to be a prevalent strategy for the assembly of cyclic or bicyclic core of many valuable molecules,\(^{20}\) we were interested in employing this approach for the construction of the pyrrolizidine scaffold. Our proposed synthetic approach towards the pyrrolizidine skeleton is represented in Scheme 1. It is evident from Scheme 1 that the bicyclic core of pyrrolizidine \((6)\) could be easily assembled from N-propargyl-L-proline ester \((5)\) through base facilitated 5-\textit{endo-dig} cyclization. The N-propargyl-L-proline ester \((5)\) could be readily accessed from L-proline by adapting a precedent method.\(^{21}\) To the best of our knowledge, this particular 5-\textit{endo-dig} cyclization strategy towards pyrrolizidine core remains unknown in the literature.

The optimization studies were carried out using \((5a)\) (which was obtained in a single step via a three component reaction of L-proline with HCHO and phenylacetylene)\(^{21}\) under different conditions using various bases (Table 1). Initial efforts toward cyclization of \((5a)\) were discouraging as the starting material \((5a)\) was decomposed when bases like NaH or sodium tert-butoxide were used. Organic bases such as DBU and Hüning’s base also did not help the cyclization process. When the reaction was performed in DMF using NaH as a base, instead of \((6a)\), cinnamaldehyde was obtained as the sole product in 37% yield. The formation of cinnamaldehyde is probably due to isomerization of

![Proposed synthetic approach towards pyrrolizidine scaffold](image)

Table 1—Optimization studies for cyclization reaction

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Base (equiv.)</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield of ((6a)) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaH (1.5)</td>
<td>THF</td>
<td>2</td>
<td>Decomposed</td>
</tr>
<tr>
<td>2</td>
<td>NaO'Bu (1.5)</td>
<td>THF</td>
<td>24</td>
<td>Decomposed</td>
</tr>
<tr>
<td>3</td>
<td>DBU (1.5)</td>
<td>THF</td>
<td>2</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>DIPEA (1.5)</td>
<td>THF</td>
<td>24</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>LDA (1.2)</td>
<td>THF</td>
<td>2</td>
<td>Decomposed</td>
</tr>
<tr>
<td>6(^a)</td>
<td>NaH (1.2)</td>
<td>DMF</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>LiHMDS (1.5)</td>
<td>DMF</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>LiHMDS (1.5)</td>
<td>Toluene</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td>LiHMDS (1.5)</td>
<td>CH(_2)Cl(_2)</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>LiHMDS (1.5)</td>
<td>THF</td>
<td>1</td>
<td>70</td>
</tr>
<tr>
<td>11</td>
<td>LiHMDS (1.5)</td>
<td>Et(_2)O</td>
<td>1</td>
<td>50</td>
</tr>
</tbody>
</table>

\(^a\) Cinnamaldehyde was observed in 37% yield.

RT = Room temperature.

NR = No reaction.
(5a) to allene enamine followed by decomposition during water work-up (See supporting data for mechanism). Surprisingly, the required product (6a) was obtained in 10% yield when a little excess of LiHMDS was used as a base. Encouraged by this observation, we carried out further optimization studies using LiHMDS in different solvents. Of the solvents screened, satisfactory outcome was attained in THF (Entry 10, Table 1), and the product (6a) was isolated in 70% yield after chromatographic separation. Fortunately, cinnamaldehyde was detected only in trace quantities in most of the reactions, wherever LiHMDS was used as a base.

The structure of (6a) was confirmed by all the spectroscopic techniques. Since the concept of “memory of chirality”22 is often observed in α-alkylation chemistry of amino acids, we expected transfer of chirality to the newly formed quaternary center of the product (6a). Unfortunately, the product was found to be racemic as it didn’t show any specific rotation in polarimetry. It is documented in the literature that most of the transformations involving “memory of chirality” were performed at much lower temperatures (usually –78 °C) to retain the chirality.23 However in the present case, all reactions were carried out at room temperature, which is probably not suitable for retaining the chirality at the enolate stage, thus giving the racemic mixture. To check the transfer of chirality at lower temperature in the present method, cyclization reaction of (5a) using LDA or LiHMDS in THF at –78 °C was carried out. However, in both the cases no product was observed even after 12 h. This observation clearly indicates that the enolate did not react with alkynyl as the alkynyl moiety does not behave as a good electrophile at lower temperatures. Fortunately, one of the enantiomers could be crystallized from the racemic mixture (6a) and characterized by X-ray crystallography (Fig. 2).

With the optimized reaction condition identified, (Entry 10, Table 1), attention was focussed towards the substrate. In this regard, a wide array of N-propargyl-L-proline ester derivatives (5b-m) were prepared using a variety of terminal acetylenes, and finally subjected to LiHMDS mediated 5-endo-dig cyclization (Table 2). In all the cases, the desired bicyclic derivatives were formed in moderate yields. Maximum yield of 72% was attained in the case of proline ester derived from p-phenoxy phenylacetylene (6b) Table 2). This methodology was also applied for the cyclization of proline ester derivatives prepared from substituted phenyl acetylenes with various electronic properties (electron poor and electron rich). Even unactivated propargyl derivatives, synthesized from aliphatic and cycloalkyl acetylenes underwent smooth cyclization under the optimized conditions (6f, 6g, 6k). Unfortunately, the cyclized product was not observed in the case of N-propargyl proline ester derived from highly electron rich alkynes such as 4-N,N-dimethylamino phenylacetylene (entry (6n)) even after 24 h. In the cases of propargyl alcohol derived substrates, complex mixtures were obtained under the standardized condition (6o) and (6p). Although, in most of the cases, the conversion was more than 90% (by TLC), the products were isolated only in moderate yields after purification through column chromatography. It is well documented in the literature that pyrrolizidine derivatives are prone to undergo decomposition during column chromatography. This explains the lower yield of products after chromatographic purification. In most of the cases, traces of cinnamaldehyde derivatives were also detected.

Conclusions

A mild, base promoted 5-endo-dig cyclization strategy has been explored for the synthesis of bicyclic core of pyrrolizidine alkaloids. A diverse range of N-propargyl-L-proline esters, prepared from aliphatic and aryl substituted terminal alkynes, underwent smooth conversion to the respective cyclized products under the reaction conditions. Further exploration of this methodology to introduce chirality in the bicyclic compound through “memory of chirality” using various alkynyl activators is currently under investigation.
Table 2—Substrate scope of base mediated 5-endo-dig cyclization

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Reaction Conditions</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5b-5p</td>
<td>LiHMDS (1.5 equiv.) THF (5 mL), RT</td>
<td>6b-6p</td>
<td>58%</td>
</tr>
<tr>
<td>6b</td>
<td>MeOCO MeOCO MeOCO MeOCO OMe</td>
<td>6b</td>
<td>72%</td>
</tr>
<tr>
<td>6c</td>
<td>1.5 h, 58%</td>
<td>6c</td>
<td>54%</td>
</tr>
<tr>
<td>6d</td>
<td>24 h, 54%</td>
<td>6d</td>
<td></td>
</tr>
<tr>
<td>6e</td>
<td>1.5 h, 54%</td>
<td>6e</td>
<td></td>
</tr>
<tr>
<td>6f</td>
<td>2 h, 38%</td>
<td>6f</td>
<td></td>
</tr>
<tr>
<td>6g</td>
<td>1 h, 32%</td>
<td>6g</td>
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<tr>
<td>6h</td>
<td>1 h, 35%</td>
<td>6h</td>
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<tr>
<td>6i</td>
<td>1 h, 20%</td>
<td>6i</td>
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</tr>
<tr>
<td>6j</td>
<td>4 h, 45%</td>
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<td>6k</td>
<td>1 h, 50%</td>
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<td>6l</td>
<td>1 h, 60%</td>
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<td>6m</td>
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<td>6n</td>
<td>24 h, 0%</td>
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<td>1 h, 0%</td>
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</tr>
<tr>
<td>6p</td>
<td>0.5 h, 0%</td>
<td>6p</td>
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</tr>
</tbody>
</table>

Supplementary Data

CCDC 916511 contains the supplementary crystallographic data for (6a). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Other supplementary data associated with this article, viz., X-ray crystallographic data of (6a), experimental procedures for the synthesis of starting materials, $^1$H and $^{13}$C NMR of all the starting materials and products, are available in the electronic form at http://www.niscair.res.in/jinfo/ijca/IJCA_52A(8-9)1086-1092_SupplData.pdf.

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