SYNOPSIS

The thesis entitled “Total synthesis of Pachastrissamine, C10-C24 fragment of (+)-Cannabisativine and asymmetric Michael reactions using proline based organocatalyst” has been divided into three chapters.

CHAPTER-I : Chapter I describes the synthesis of C10-C24 fragment of (+)-cannabisativine.

CHAPTER-II : Chapter II is further divided into two sections (Section-A and Section-B).

SECTION-A : This section deals with the total synthesis of (+)-pachastrissamine.

SECTION-B : This section describes the concise synthesis of (+)-pachastrissamine (truncated) and its enantiomer.

CHAPTER-III : Chapter III is again divided into two sections (Section-A and Section-B).

SECTION-A : This section encompasses a brief introduction to organocatalysis.

SECTION-B : This section describes the development of a new pyrrolidine-triazole conjugate catalyst for asymmetric Michael reactions.
CHAPTER-I:

This Chapter describes the synthesis of C10-C24 fragment of (+)-cannabisativine.

(+)-Cannabisativine 1 is a macrocyclic spermidine alkaloid containing a \textit{trans}-2,6-disubstituted-1,2,5,6-tetrahydropyridine ring annulated to a 13-membered lactam ring. This was the first reported nonquaternary alkaloid possessing the pyrido[1,2-$d$]-[1,5,9]-triazacyclotridecine nucleus isolated from \textit{Cannabis sativa} L and perhaps the most challenging alkaloid of its class. These unique as well as challenging structural features along with our interest in synthesizing heterocyclic compounds especially, containing nitrogen and oxygen, prompted us to undertake the synthesis of (+)-cannabisativine. Moreover, the 2,6-disubstituted tetrahydropyridine framework can be regarded as a valuable basic unit since the possibility of modification and functionalization of the double bond enables the preparation of polysubstituted piperidines. From the retrosynthetic perspective, disconnection of 1 at the amide bond and C1-N17 bond led to the fragment 2 and target fragment (C10-C24) 3 comprising of all the stereocenters of 1. The fragment 3 can be derived from 4 and 5. The subtarget 4 can be realized from the Garners aldehyde 6 obtainable from the commercially available D-serine 7. The aldehyde 5 can be synthesized from 1,3-propane diol 8. The crucial reactions involved in the synthesis are Sharpless asymmetric dihydroxylation, diastereoselective allylation of imine and ring-closing metathesis reaction (RCM).

\begin{align*}
\text{Scheme 1. Retrosynthetic analysis of (+)-cannabisativine 1.}
\end{align*}
Synthesis of fragment 4:

The synthesis of fragment 4 commenced with the preparation of (R)-Garner’s aldehyde 6 from the commercially available and cheap starting material D-serine 7. The esterification of D-serine 7 using acetyl chloride in MeOH and protection of amine functionality using (Boc)₂O and Et₃N in THF afforded compound 10 in 96% yield (Scheme 2). The amino alcohol 10 was protected as its acetonide derivative using 2,2-DMP in acetone and BF₃.Et₂O as Lewis acid catalyst to give compound 11. The ester functionality of compound 11 was reduced to alcohol using LAH in THF to get compound 12 in 82% yield. The alcohol was subjected to Swern oxidation using DMSO, (COCl)₂ and Et₃N as the base in CH₂Cl₂ to afford (R)-Garner’s aldehyde 6 in 87% yield.

Scheme 2.

The aldehyde 6 was subjected to Wittig olefination using n-hexyltriphenylphosphonium bromide and n-BuLi to furnish the olefin 13 in 72% yield. The acetonide group in 13 was cleaved in presence of 70% aqueous acetic acid at 60 ℃ to give the amino alcohol 14 (84%).

Scheme 3.
The amino alcohol 14 was selectively protected as its pivaloyl ester 15 (PivCl, Py, CH₂Cl₂) in 93% yield. The Pivaloyl protected olefin 15 was exposed to Sharpless asymmetric dihydroxylation using AD mix-α, methansulphonamide in t-BuOH/H₂O (1:1) to give the diol 16 along with another diastereomer (92:8) in 86% yield (for both diastereomers) (Scheme 3).

The two hydroxyl groups in 16 were protected as their MOM-ether to yield 17 using MOMCl, DIPAE in CH₂Cl₂ in 96% yield. The reductive removal of the pivaloyl group in 17 with DIBAL-H at 0 °C provided the alcohol 18 in 95% yield. The alcohol 18 was oxidized to the corresponding aldehyde using Dess-Martin periodinane followed by Wittig olefination to furnish the olefinic product 19 in 74% yield over two steps (trans:cis = 92:8). Finally, the fragment 4 was realized by deprotection of both the MOM and Boc groups in single step using 5% HCl in MeOH in 89% yield (Scheme 4).

**Scheme 4.**

**Synthesis of fragment 5:**

The synthesis of fragment 5 began with the mono protection of 1,3-propane diol 8. The diol 8 was mono protected as its PMB ether 20 using NaH and PMBBr in dry THF in 72% yield. The mono protected alcohol 20 was subsequently oxidized to the corresponding aldehyde 5 (IBX, DMSO/THF) (Scheme 5).

**Scheme 5.**
**Synthesis of the C10-C24 fragment 3:**

The synthesis of the target fragment 3 started with the coupling of fragment 4 and 5 subsequently followed by diastereoselective allylation. This was the most crucial step in the synthetic strategy. The aminoalcohol 4 and the aldehyde 5 were condensed in anhydrous Et\(_2\)O in presence of anhydrous MgSO\(_4\) to generate the imine 21. This reaction mixture containing 21 was filtered under argon atmosphere and without any concentration or purification, and was added to a freshly prepared solution of allylmagnesium bromide in Et\(_2\)O at \(-78^\circ\)C to obtain two diastereomers, the trans-22 (major) and cis-23 (minor) in the ratio of 82:18 (separated by column chromatography) in 73% yield over two steps (Scheme 6).

\[
\text{4} + \text{5} \rightarrow \text{21} \\
\text{AllMgBr, Et}_2\text{O, -78 to -40 }^\circ\text{C, 6 h, 73%}
\]

**Scheme 6.**

It is believed that the reaction proceeded through any one of the proposed transition states in Figure 1. The attack of the incumbent allyl group was more facile from a side opposite to the orientation of bulky phenyl group leading to the observed diastereoselectivity in favor of trans configuration at 2,6-position of the piperidine ring.

\[
\text{\textbullet Favored} \quad \text{\textbullet Disfavored}
\]

**Figure 1.**
The amine group along with the adjacent hydroxyl group in 22 was protected as cyclic carbamate using (Im)$_2$CO and Et$_3$N in CH$_2$Cl$_2$ to give 24 with 98% conversion. Finally, the ring closing metathesis on 24 proceeded smoothly with II$^{nd}$ generation Grubbs catalyst to furnish the required C10-C24 fragment 3 in 88% yield. The stereochemistry at the centres adjacent to nitrogen (2,6-position) of the piperidine ring was confirmed by 2D NOE study and found to be trans as predicted on the basis of transition state model (Scheme 7).

![Scheme 7](image-url)

**CHAPTER-II, SECTION-A:**

This section describes the total synthesis of (+)-pachastrissamine.

In 2002, pachastrissamine 1 was isolated from the marine sponge Pachastrissa sp. found around the Okinawan islands by Higa and coworkers. Almost simultaneously, a French group, Debitus et al. working on the ethanolic extracts of a Vanuatuan marin sponge, Jaspis sp. isolated the same compound and named as jaspine B. Pachastrissamine (jaspine B) 1 displayed marked cytotoxicity (IC$_{50} = 0.24$ µM) against the A549 human lung carcinoma cell line using the ATP lite assay. It has been proved to be the most potent compound yet isolated from the jaspis genus on this cell line. The important biological activity, novel structural features and our interest in total synthesis of aminols, chiral tetrahydropyran and tetrahydrofuran skeleton containing bioactives, encouraged us to take up the total synthesis of pachastrissamine. The retrosynthetic plan of pachastrissamine 1 is outlined in Scheme 1. The compound 1 was envisaged to obtain from the ester 2 using Julia olefination. The tetrahydrofuran ring in 2 can be realized from the
aldehyde 3 involving Wittig olefination and oxa–Michael ring closing reaction. The aldehyde 3 itself can be derived from (-)-tartaric acid 4.

\[
\begin{align*}
\text{H}_2\text{N} - \text{OH} & \quad \text{HO} - \text{OBn} \\
\text{HO} & \quad \text{HO} - \text{OBn} \\
\text{O} & \quad \text{O} - \text{O} \\
3 & \quad \text{4}
\end{align*}
\]

**Scheme 1.** Retrosynthetic analysis of pachastrissamine 1.

**Synthesis:**

The synthetic sequence commenced with the esterification of commercially available D(-)-tartaric acid 4 to its dimethyl ester 5 using SOCl₂ in MeOH. The hydroxyl functionalities in 5 were protected as their benzal acetal in presence of C₆H₆CHO and catalytic p-TSA in benzene under Dean-Stark condition to furnish the diester 6 with 70% conversion over two steps. AlH₃ (LiAlH₄, AlCl₃) mediated one step reduction of ester groups and acetal ring opening led to the benzyl protected triol 7 in 80% yield. The 1,2-diol in 7 was selectively converted to pentylidene acetal 8. The alcohol 8 was oxidized to the corresponding aldehyde 3 in presence of IBX in 89% yield (Scheme 2).

\[
\begin{align*}
\text{MeO}_2\text{C} - \text{CO}_2\text{Me} & \quad \text{MeO}_2\text{C} - \text{CO}_2\text{Me} \\
\text{OH} & \quad \text{PhCHO, C}_6\text{H}_6, \text{Dean Stark, 6 h, 70% (two steps)} \\
\text{5} & \quad \text{6}
\end{align*}
\]

**Scheme 2.**

The standard two carbon homologation of aldehyde 3 using ethyl tristriphenylphosphorane in benzene afforded the \(\alpha,\beta\)-unsaturated ester 9 in 86% yield. The 1,2-diol was released in 9 with the aid of formic acid to realize 10 (81%) (Scheme 3).

\[
\begin{align*}
\text{Ph}_3\text{P}=\text{CHCO}_2\text{Et} & \quad \text{HCO}_2\text{H, CH}_2\text{Cl}_2, 0^\circ \text{C-rt, 2 h, 81%} \\
\text{3} & \quad \text{9}
\end{align*}
\]

**Scheme 3.**
With the $\alpha,\beta$-unsaturated ester 10 in hand, the substrate was ready for the key and the most crucial step, oxa-michael ring closing reaction (Scheme 4). Several bases and various reaction conditions were attempted for this key reaction and NaH was found to be optimal in terms of yields, however with no control on diastereoselectivity to realize easily separable diastereomeric mixture 2 and 2a in almost equal ratio (Table 1).

**Scheme 4.**

**Table 1.** Study of oxa-Michael ring closure under different conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction condition</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaH, THF, 0 °C, 10 min</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>TBAF, THF, -10 °C, 2 h</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>KO′Bu, THF, -20 °C, 1 h</td>
<td>complex reaction mix.</td>
</tr>
<tr>
<td>4</td>
<td>DBU, EtOH, 0 °C, 6 h</td>
<td>46</td>
</tr>
<tr>
<td>5</td>
<td>NaHMDS, THF, -10 °C, 1 h</td>
<td>66</td>
</tr>
<tr>
<td>6</td>
<td>Pd(PPh$_3$)$_4$, toluene, r.t., 24 h</td>
<td>43</td>
</tr>
</tbody>
</table>

These two diastereomers 2 and 2a were characterized using NOE study and the desired 2 was carried forward (Figure 1).

**Figure 1.** I) NOEs observed in compound 2; II) Energy minimized Structure of 2.

The silylation of secondary alcohol in 2 to 11 was rather routine (TBSCl, imidazole, CH$_2$Cl$_2$, 96% yield). Reduction of ester group in 11 with LiBH$_4$ produced tetrahydrofuranyl alcohol 12 in 91% yield. IBX assisted oxidation of the alcohol 12 produced the corresponding aldehyde, which was subjected to Julia olefination using dodecyl sulphonyl benzothiazole 13 and KHMDS at -78 °C to get the $E/Z$ (9:1) mixture of 14. The selective deprotection of silyl ether in 14 was achieved using $p$-TSA in MeOH to get 15 in quantitative yield (Scheme 5).
The tosylation of \( \text{15} \) to \( \text{16} \) was carried out using TsCl and \( \text{Et}_3 \text{N} \) in \( \text{CH}_2\text{Cl}_2 \) in 97% yield. The \( \text{S}_2\text{N}_2 \) displacement of tosyl group in \( \text{16} \) with azido group (\( \text{NaN}_3 \), \( \text{DMF} \), 110 °C) provided \( \text{17} \) in 81% yield. A one pot debenzylation, olefin and azide reduction using \( \text{Pd(OH)}_2 \) under the influence of \( \text{H}_2 \) yielded the target natural product \( \text{pachastriassamine 1} \) in quantitative yield (Scheme 6). The \( ^{1}\text{HNMR} \), \( ^{13}\text{CNMR} \) and specific rotation were all in agreement with the literature values, confirming the successful total synthesis \( \text{pachastrissamine 1} \).

\[ \text{Scheme 5.} \]

\[ \text{Scheme 6.} \]

\text{CHAPTER-II, SECTION-B:}  

This section describes the concise synthesis of (+)-pachastrissamine (truncated) and its enantiomer.

As mentioned in the previous section, pachastrissamine \( \text{1} \) possess cytotoxicity at a level of \( \text{IC}_{50} \) 0.01 µg/mL against P388, A549, HT29 and Mell 28 cell lines and exhibits submicromolar cytotoxic activity against human lung carcinoma cell line using the ATP lite assay. Cancer, being incurable disease, has been a subject of intensive study around the world for the last several decades and search for an advanced lead is still on. In that regard we planned to synthesize analogs of pachastrissamine \( \text{1} \) and evaluate their activity. Pachastrissamine \( \text{1} \) in its original structure contains fourteen carbon long aliphatic chain. From synthetic point of view, it has
always been a difficult and yield degrading to attach a long chain thereby putting a hurdle in the large scale preparation required for biological testing at various levels. Thus, we planned to prepare analogs with a short side chain i.e. fourteen carbon long chain replaced with a five carbon (truncated at the side chain) one keeping the stereocentres intact as in the original molecule and examine the change in the activity. In other words, we planned to synthesise (+) and (-) pachastrissamine (truncated) (figure 2).

Figure 2.

Having interest in carbohydrate chemistry in general and the target molecule looking to be a matching case in particular, with sugar molecules, prompted us to explore a new synthetic route with raw materials derived from the chiral pool of sugar molecules. The retrosynthetic analysis revealed that the (+)-enantiomer 18 could be derived from the azide 21 through reductive removal of methoxy group followed by hydrogenation. The azide 21 could be realized from the olefin 23 by S_N^2 displacement of sulfonyl imidazylate obtained in situ with N_3 group. The olefin 114 could be obtained from L-xylene. Similarly, (−) pachastrissamine (truncated) 111 could be envisaged to obtain from D-glucose via similar intermediates (Scheme 7).

Scheme 7. Retrosynthetic plan for (+) and (−)- pachastrissamine (truncated).

Synthesis of (+)-pachastrissamine (truncated) (18):

The synthesis of (+)-pachastrissamine (truncated) began with the diacetonide protection (CuSO_4, H_2SO_4, acetone) of commercially available L-xylene to give 1,2,3,5-di-O-isopropylidene-L-xyloluranose 25 in 84% yield in a well documented procedure. The 3,5-O-isopropylidene group in 25 was selectively cleaved with 5% HCl (aqueous) leading to the diol 26. The diol 26 was converted to its acetal 27 using PhCH(OOMe)_2, catalytic p-TSA in CH_2Cl_2 in 92% yield.
DIBAL-H mediated reductive opening of the acetal 27 furnished the alcohol 28 having secondary hydroxyl protected as its benzyl ether in 92% yield. The alcohol 28 was oxidized to the corresponding aldehyde 29 in presence of IBX (Scheme 8).

Scheme 8.

The aldehyde 29 was subjected to Wittig olefination with n-butyl triphenylphosphonium bromide in THF-HMPA and n-BuLi at –40 °C to give olefin 23 with E/Z ratio of 7:93 in 86% yield. The hydrolysis of acetonide linkage in 23 and in situ formation of the methyl glycoside 30 (mixture of both anomers in 1:1 ratio) was successfully achieved using catalytic CH$_3$COCl in methanol. The alcohol 30 on treatment with $N$, $N'$-sulfonyldiimidazole and sodium hydride in DMF at –40 °C furnished imidazole sulfonate ester 31. Heating of this sulfonate ester 31 with Bu$_4$NN$_3$ resulted azide 21 in 68% overall yield for two steps. Bu$_4$NN$_3$ was generated in situ from tetrabutylammonium chloride (TBACl) and NaN$_3$ as it is not commercially available.

Scheme 9.
The reductive removal of methoxy group of 21 with triethylsilane in the presence of BF₃·OEt₂ proceeded smoothly to give tetrahydrofuran derivative 32 in 95% yield. Finally, reduction of the azide group as well as olefin hydrogenation and cleavage of benzyl ether was successfully achieved in one-pot by Pd/C in methanol under hydrogen atmosphere to furnish the target molecule 18 (Scheme 9).

**Synthesis of (−)-pachastrissamine (truncated) (20):**

The synthesis of (−)-pachastrissamine (truncated) 20 was initiated with conversion of D-glucose to its diacetonide, 1,2;5,6-Di-O-isopropylidene-α-D-glucofuranose 33 using known procedure in the literature in 83% yield. The free secondary hydroxyl functionality in 33 was protected as its benzyl ether 34. The 5,6-O-isopropylidene in 34 was released with the aid of 0.8% H₂SO₄ in methanol to furnish the diol 35 in 88% yield. The diol 35 was chopped (NaIO₄) to furnish the aldehyde 36 (Scheme 10).

![Scheme 10.](image)

The aldehyde 36 was strategically subjected to the same sequence of reactions as in case of aldehyde 29 in Scheme 9, finally producing the (−)-pachastrissamine (truncated) 20 (Scheme 11).
Cytotoxicity study:

Cytotoxicities of the compounds 18 (S-1) and 20 (S-2) were evaluated by the 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reduction assay. They were treated continuously for 48 h on A549 lung cancer cell and compared with the commercially available anticancer drug Doxorubicin shown in Figure 3. From the graph it is evident that both compounds 18 and 20 displayed very low cytotoxicity. Hence, it was concluded that the side chain in pachastrissamine 1 has a significant contribution in its cytotoxicity and can not be altered.

Figure 3.

CHAPTER-III, SECTION-A:

This section contains a brief introduction to organocatalysis.

CHAPTER-III, SECTION-B:

This chapter describes the development of a pyrrolidine-triazole conjugate catalyst for asymmetric Michael reactions.

The desire for new synthetic methodologies for the rapid construction of enantiomerically pure compounds has been a fruitful driving force for chemical research. Last few years have seen an exponential growth in the synthesis and application of various asymmetric organocatalysts,
especially in the area of proline derivatives or pyrrolidine based catalysts. These derivatives have been shown to exhibit catalytic activities in a diverse range of organic reactions. Our interest in proline-catalyzed asymmetric reactions as well as in the copper (I)-catalyzed 1,3-dipolar cycloaddition reaction directed us to prepare a new pyrrolidine based organocatalyst 1. The retrosynthetic analysis as shown in Scheme 1, revealed that the trizole catalyst 1 could be obtained from the alkyne 2 using 1,3-dipolar cycloaddition reaction. The alkyne 2 itself could be synthesized in bulk scale from the commercially available natural α-amino acid L-proline 4 via the intermediate alcohol 3.

Scheme 1. Retrosynthetic analysis for organocatalyst 1.

Synthesis:

The synthesis of the organocatalyst 1 commenced with L-proline 4. Proline was converted to its methyl ester hydrochloride using CH$_3$COCl in MeOH. The crude white solid product was subjected to Boc-protection in presence of (Boc)$_2$O and TEA in THF to furnish the ester 5 in 86% overall yield for the two steps. The ester 5 was treated with LiBH$_4$ in THF/EtOH (1:1) furnishing the corresponding alcohol 3 in 89% yield. The alcohol 3 on IBX-oxidation lead to the corresponding aldehyde which was subsequently subjected to Corey-Fuchs protocol (TPP, CBr$_4$, CH$_2$Cl$_2$) at 0 °C to furnish the olefinic dibromo product 6 in 63% yield over two steps. Exposing the dibromo compound 6 to $n$-BuLi at −78 °C for 30 min resulted the alkyne 2 in 82% yield.

Scheme 2.
The alkyne 2 was treated with benzyl azide under copper (I) catalyzed-Huisgen 1,3-dipolar cycloaddition reaction condition to give the pyrrolidine-triazole derivative 7 in 70% yield. Finally, the deprotection of Boc-group in the triazole derivative 7 was carried out using 5M HCl to furnish the desired organocatalyst 1 in 90% yield.

Scheme 3.

**Optimization of reaction condition:**

After preparation of the catalyst 1, we tested its efficiency in asymmetric Michael addition reaction, which is one of the most important C-C bond forming reactions in organic chemistry. As a model reaction, Michael addition of cyclohexanone 8 to β-nitrostyrene 9a was studied at various temperature and 0 °C was found to be the most optimal in terms of yields and selectivities. The effect of additives is well known for Michael reactions. So, the above reaction was carried out in the presence of various additives such as CSA, p-TSA, TFA at 0 °C and the results are summarized in Table 1. We were pleased to find that the 5 mol% of pyrrolidine-triazole 1 was able to catalyze the reaction efficiently in the presence of trifluoroacetic acid (entry 4, Table 1). Interestingly, the yield of the product and enantioselectivity improved with the 10 mol% of 1 (entry 5, Table 1).

**Table 1.**

<table>
<thead>
<tr>
<th>entry</th>
<th>additive</th>
<th>catalyst (mol%)</th>
<th>yield (%)</th>
<th>syn/anti (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>10</td>
<td>76</td>
<td>7:3</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>CSA</td>
<td>10</td>
<td>87</td>
<td>9:1</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>p-TSA</td>
<td>10</td>
<td>86</td>
<td>9:1</td>
<td>73</td>
</tr>
<tr>
<td>4</td>
<td>TFA</td>
<td>05</td>
<td>90</td>
<td>98:2</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>TFA</td>
<td>10</td>
<td>95</td>
<td>98:2</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>TFA</td>
<td>20</td>
<td>95</td>
<td>98:2</td>
<td>92</td>
</tr>
</tbody>
</table>

*a*Isolated yields;  *b*Determined by 1H NMR of the crude product;  *c*Determined by chiral HPLC of the syn product
However, further increase in the loading of the catalyst had no effect on the yield and selectivity (entry 6, Table 1). After running the above reaction in different solvents such as MeOH, DMSO, DMF and CH₂Cl₂, it was concluded that the reaction was most efficient under solvent-free condition.

Under this optimized condition, the reactions of a variety of nitroolefin substrates with ketones such as cyclohexanone 8, cyclopentanone 11 and acetone 12 were investigated to check the generality of this procedure. All the β-nitrostyrenes (9a-9g) bearing electron donating aryl groups as well as electron withdrawing aryl groups were reacted smoothly with cyclohexanone 8 to give the corresponding Michael adducts (10a-10g) in good yields with high diastereoselectivity and enantioselectivity (entries 1-7, Table 2). However, the other ketones such as cyclopentanone 11 and acetone 12 gave the Michael adduct 10h and 10i respectively with β-nitrostyrene in moderate to low yield and selectivity and took longer reaction times (entries 8 and 9, Table 2).

Table 2.

<table>
<thead>
<tr>
<th>entry</th>
<th>nitrostyrene</th>
<th>t (h)</th>
<th>Product</th>
<th>Yield (%)</th>
<th>syn/anti (ratio)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9a</td>
<td>12</td>
<td>10a</td>
<td>95</td>
<td>98:2</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>9b</td>
<td>16</td>
<td>10b</td>
<td>96</td>
<td>99:1</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>9c</td>
<td>19</td>
<td>10c</td>
<td>92</td>
<td>99:1</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>9d</td>
<td>13</td>
<td>10d</td>
<td>90</td>
<td>98:2</td>
<td>94</td>
</tr>
</tbody>
</table>
In conclusion, we developed a new proline derived organocatalyst for the asymmetric Michael addition reaction of ketones to nitroolefins, which was easily prepared from the alkyne using ‘click’ reaction. The reactions were highly efficient in terms of yield and selectivity for Michael addition. Further applications to extend the scope of the catalyst are under progress.