Supporting Information

Direct/Reversible Amidation of Troponyl alkylglycinates via Cationic troponyl lactones and Mechanistic Insights

Chenikkayala Balachandra and Nagendra K. Sharma*

School of Chemical Sciences, National Institute of Science Education and Research (NISER), Jatani-752050, Odisha, India & HBNI-Mumbai, India.

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1. NMR and Mass spectra analysis of CTLs formation, reversible amidation and mechanistical investigations with control experiments:

I. All NMR experiments to study the cationic troponyl lactone (CTL) formation and reversible amidation and mechanistical investigations were performed in CD$_3$CN at 25 °C.

II. All characterized cationic troponyl lactones (CTLs) contains TFA or TFA-D peaks in their respective $^1$H and $^{13}$C NMR spectra.

III. $^1$H and $^{13}$C NMR spectra generated during reaction monitoring of reversible amidation is given Figure S1/2.
2. Stacked $^1$H/$^{13}$C NMR spectra obtained during reversible amidation reaction monitoring of 4a

Figure S1. A) $^1$H NMR spectra of 4a in CD$_3$CN without TFA. B) $^1$H NMR spectra of 4a in CD$_3$CN after addition of 6.0 equiv of TFA; spectra showing the formation of cationic troponyl lactone. C) $^1$H NMR spectra of 4a in CD$_3$CN after neutralization with 6.5 equiv of TFA; spectra showing the reformation of 4a through reversible amidation ($#$ = triethylamine peaks).

Figure S2. A) $^{13}$C NMR spectra of 4a in CD$_3$CN without TFA. B) $^{13}$C NMR spectra of 4a in CD$_3$CN after addition of 6.0 equiv of TFA; spectra showing the formation of cationic troponyl lactone. C) $^{13}$C NMR spectra of 4a in CD$_3$CN after neutralization with 6.5 equiv of TFA; spectra showing the reformation of 4a through reversible amidation ($#$ = TFA peaks).
3. Stacked $^1$H/$^13$C NMR spectra showing cationic troponyl lactone formation from 3b-OH

![Figure S3](image1)

**Figure S3.** A) $^1$H NMR spectra of 3b-OH after addition of TFA in CD$_3$CN; showing the formation of cationic troponyl lactone 5b. (B) $^1$H NMR spectra of 3b-OH in CD$_3$CN.

![Figure S4](image2)

**Figure S4.** A) $^13$C NMR spectra of 3b-OH after addition of TFA in CD$_3$CN; showing the formation of cationic troponyl lactone 5b. (B) $^13$C NMR spectra of 3b-OH in CD$_3$CN.
4. Comparative NMR spectra showing the formation of CTLs 5 from 3/3-OH/4 and only protonation in case of 3aa-\(\text{H}^+\) under same conditions.

Figure S5. Comparative \(^1\)H NMR spectra. A) \(^1\)H NMR of 3aa after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 3aa-\(\text{H}^+\). B) \(^1\)H NMR of 3b after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b and 3b-\(\text{H}^+\) after addition of TFA. C) \(^1\)H NMR of 3b-OH after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b. D) \(^1\)H NMR of 4b after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b.

Figure S6. Comparative \(^13\)C NMR spectra. A) \(^13\)C NMR of 3aa after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 3aa-\(\text{H}^+\). B) \(^13\)C NMR of 3b after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b and 3b-\(\text{H}^+\) after addition of TFA (synthesized from 3b). C) \(^13\)C NMR of 3b-OH after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b. D) \(^13\)C NMR of 4b after addition of 6.0 equiv of TFA in CD\(_3\)CN; showing the formation of 5b.
5. Time dependent conversion of 3b to 5b recorded in CD$_3$CN after addition of TFA with 15 min time intervals

**Figure S7.** Conversion of 3b into 3b-$\text{H}^+$ and 5b after addition of TFA in CD$_3$CN with time.
6. Comparative NMR spectra showing the formation of deuterated CTLs 5/5' from 3-OH/4 in presence of TFA-D in CD$_3$CN

![NMR spectra](image)

**Figure S8.** Comparative $^1$H NMR spectra. A) $^1$H NMR of 3b-OH after addition of 6.0 equiv of TFA-D in CD$_3$CN; showing the formation of 5b/b' after addition of TFA-D. B) $^1$H NMR of 3b-OH after addition of 6.0 equiv of TFA in CD$_3$CN; showing the formation of 5b after addition of TFA C) $^1$H NMR of 4b after addition of 6.0 equiv of TFA-D in CD$_3$CN; showing the formation of 5b/b'. D) $^1$H NMR of 4b after addition of 6.0 equiv of TFA in CD$_3$CN; showing the formation of 5b.

![Expanded NMR spectral regions](image)

**Figure S9.** Expanded $^1$H NMR spectral regions of 5b/b' and 5b: A) $^1$H NMR of 5b/b' in CD$_3$CN, showing the α-CHD (synthesized from 3b-OH in presence of TFA-D). B) $^1$H NMR of 5b in CD$_3$CN (synthesized from 3b-OH).
Figure S10. Comparative $^1$H NMR spectra. A) $^{13}$C NMR of 3b-OH after addition of 6.0 equiv of TFA-D in CD$_3$CN; showing the formation of 5b/b' after addition of TFA-D. B) $^{13}$C NMR of 3b-OH after addition of 6.0 equiv of TFA in CD$_3$CN; showing the formation of 5b after addition of TFA C) $^{13}$C NMR of 4b after addition of 6.0 equiv of TFA-D in CD$_3$CN; showing the formation of 5b/b'. D) $^{13}$C NMR of 4b after addition of 6.0 equiv of TFA in CD$_3$CN; showing the formation of 5b.

Figure S11. Expanded (δ 60-40) stacked $^{13}$C NMR spectra of 5b and 5b/b’ synthesized from 4b and 3b-OH A) $^{13}$C NMR of 5b/b’ obtained from 3b-OH in CD$_3$CN in presence of TFA-D, triplet represents α-CHD. B) $^{13}$C NMR of 5b obtained from 3b-OH in CD$_3$CN in presence of TFA. C) $^{13}$C NMR of 5b/b’ obtained from 4b in CD$_3$CN in presence of TFA-D, triplet represents α-CHD. D) $^{13}$C NMR of 5b obtained from 4b in CD$_3$CN in presence of TFA.
7. Assigned NMR spectra of **CTL 5b** (undeuterated and deuterated)

**Figure S12.** Assigned $^1$H NMR of 5b in CD$_3$CN (synthesized from 3b-OH)

**Figure S13.** Assigned $^1$H NMR of 5b/b’ in CD$_3$CN (synthesized from 3b-OH)
**Figure S14.** Assigned $^{13}$C NMR of 5b in CD$_3$CN (synthesized from 3b-OH)

**Figure S15.** Assigned $^{13}$C NMR of 5b/b' in CD$_3$CN (synthesized from 3b-OH)
Figure S16. A) $^{13}$CDEPT135 NMR of 5b/b' in CD$_3$CN (synthesized from 3b-OH in CD$_3$CN).
8. Time dependent stacked $^1$H NMR spectra/HRMS obtained during the time dependent reversible amidation: to demonstrate the formation of α-dideuterated amides

**Figure S17.** Stacked $^1$H NMR. A) $^1$H NMR spectra of $4b/b'/b''$, major $4b'/b''$ and reversible amidation reaction was performed after leaving in TFA-D for 12 h. B) $^1$H NMR spectra of $4b/b'/b''$, major $4b'$ and reversible amidation reaction was performed after leaving in TFA-D for 2 h. C) $^1$H NMR spectra of $4b/b'$, major $4b$ and reversible amidation reaction was performed after leaving in TFA-D for 0.5 h. D) $^1$H NMR spectra of Only $4b$ in CD$_3$CN.

**Figure S18.** Integrated spectral regions for above stacked NMR. Labelling is same as Figure SXX.
Figure S19. Stacked $^{13}$C NMR. A) $^{13}$C NMR spectra of 4b/b'/b''', major 4b'/b''' and reversible amidation reaction was performed after leaving in TFA-D for 12 h. B) $^{13}$C NMR spectra of 4b/b'/b''', major 4b' and reversible amidation reaction was performed after leaving in TFA-D for 2 h. C) $^{13}$C NMR spectra of 4b/b'', major 4b and reversible amidation reaction was performed after leaving in TFA-D for 0.5 h. D) $^{13}$C NMR spectra of Only 4b in CD$_3$CN.
ESI-MS spectra obtained during the time dependent reversible amidation:

**Figure S20.** ESI-MS spectral data showing increase in dideuterated product of α-deuterated 4b (4b'/b''/b') with time. A) HRMS spectra of isolated 4b/b'/b'', major 4b'/b'' and reversible amidation reaction was performed after leaving in TFA-D for 12 h. B) HRMS spectra of 4b/b'/b'', major 4b' and reversible amidation reaction was performed after leaving in TFA-D for 2 h. C) HRMS spectra of 4b/b', major 4b and reversible amidation reaction was performed after leaving in TFA-D for 0.5 h. D) HRMS spectra of Only 4b in CD$_3$CN.
ESI-MS spectra obtained during the time dependent direct amidation with 3c:

**Figure S21.** 3c was treated with 7.0 equiv of TFA-D for 6 hours in CH$_3$CN then amidation was performed to obtain α-deuterated 6c amide (6c/c'/c'').

**Figure S22.** 3c was treated with 7.0 equiv of TFA-D for 16 hours in CD$_3$CN then amidation was performed to obtain α-deuterated 6c amide (6c/c'/c'').

**Figure S23.** Picture of TLC obtained during the direct amidation reaction monitoring.
9. $^1$H/$^1$C NMR spectra of 3aa after 12 h of treatment with 7.0 equiv of TFA-D in CD$_3$CN

**Figure S24.** $^1$H/$^1$C NMR spectra in CD$_3$CN showing no deuteration at α-CH$_2$. 
10. $^1$H NMR spectral evidences for reversible reaction between protonated 3-H$^+$ and CTL 5:

**Figure S25.** A) Expanded spectral region of conversion of 3b into 5b/b' with TFA-D in CD$_3$CN. B) Expanded spectral region of conversion of 3b into 5b with TFA in CD$_3$CN. C) Expanded spectral region of conversion of 3b-OH into 5b/b' with TFA-D in CD$_3$CN. D) Expanded spectral region of conversion of 3b-OH into 5b with TFA in CD$_3$CN.

The peaks shown with red stars (*) are belongs to α-CH$_2$ of 3b-H$^+$/3b-OH-H$^+$. The peaks shown with blue solid circles in Figure A/C are belongs to α-CHD of 3b'-H$^+$/3b'-OH-H (chemical structures are highlighted in box).
11. Regioselective cleavage of *Trag* amide bond in presence of other amide bonds in *Trag* peptides 7/8:

**Figure S26.** Regioselective cleavage of *Trag* amide 7 in presence of 6.0 equiv of TFA in CH$_3$CN.

**Figure S27.** Regioselective cleavage of *Trag* amide 7 in presence of 6.0 equiv of TFA in CH$_3$OH.

**Figure S28.** Regioselective cleavage of *Trag* amide 8 in presence of 6.0 equiv of TFA in CH$_3$CN.
12. NMR ($^1$H/$^{13}$C) and HRMS spectra of troponyl alkylglycinates (3a-g and 3b/c-OH)

Figure S29. $^1$H NMR of 3a in CDCl$_3$.

Figure S30. $^{13}$C NMR of 3a in CDCl$_3$.
Figure S31. Mass Spectrum (ESI-MS) of 3a.
Figure S32. $^1$H NMR of 3b in CDCl$_3$.

Figure S33. $^{13}$C NMR of 3b in CDCl$_3$. 

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Figure S34. Mass Spectrum (ESI-MS) of 3b.
Figure S35. $^1$H NMR of 3b-OH in CD$_3$CN.

Figure S36. $^{13}$C NMR of 3b-OH in CD$_3$CN.
Figure S37. Mass Spectrum (ESI-MS) of 3b-OH.
Figure S38. $^1$H NMR of 3c in CDCl$_3$.

Figure S39. $^{13}$C NMR of 3c in CDCl$_3$. 
Figure S40. Mass Spectrum (ESI-MS) of 3c.
Figure S41. $^1$H NMR of 3c-OH in CDCl$_3$.

Figure S42. $^{13}$C NMR of 3c-OH in CDCl$_3$. 

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Figure S44. $^1$H NMR of 3d in CD$_3$CN.

Figure S45. $^{13}$C NMR of 3d in CD$_3$CN.
Figure S46. Mass Spectrum (ESI-MS) of 3d.
Figure S47. $^1$H NMR of 3e in CDCl$_3$.

Figure S48. $^{13}$C NMR of 3e in CDCl$_3$. 

Figure S49. Mass Spectrum (ESI-MS) of 3e.
Figure S50. $^1$H NMR of 3aa in CDCl$_3$.

Figure S51. $^{13}$C NMR of 3aa in CDCl$_3$. 
Figure S52. Mass Spectrum (ESI-MS) of 3aa.
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Figure S54. $^{13}$C NMR of 3ab in CDCl$_3$. 
**Figure S55.** Mass Spectrum (ESI-MS) of 3ab.
13. NMR ($^1$H/$^{13}$C) and HRMS spectra of dipeptides (4a-f and 4a’-c’)

**Figure S56.** $^1$H NMR of 4a in CDCl$_3$.

**Figure S57.** $^{13}$C NMR of 4a in CDCl$_3$. 
Figure S58. Mass Spectrum (ESI-MS) of 4a.
Figure S59. $^1$H NMR of 4a/a'/a'' in CDCl$_3$.

Figure S60. $^{13}$C NMR of 4a/a'/a'' in CDCl$_3$. 
Figure S61. Mass Spectrum (ESI-MS) of 4a/a'/a''.
Figure S62. $^1$H NMR of 4b in CDCl$_3$.

Figure S63. $^{13}$C NMR of 4b in CDCl$_3$. 
Figure S64. Mass Spectrum (ESI-MS) of 4b.
Figure S65. $^1$H NMR of $4b/b'/b''$ in CDCl$_3$.

Figure S66. $^{13}$C NMR of $4b/b'/b''$ in CDCl$_3$. 
Figure S67. Mass Spectrum (ESI-MS) of 4b/b'/b''.
Figure S68. $^1$H NMR of 4c in CDCl$_3$.

Figure S69. $^{13}$C NMR of 4c in CDCl$_3$. 
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Figure S71. $^1$H NMR of 4c/c'/c'' in CDCl$_3$.

Figure S72. $^{13}$C NMR of 4c/c'/c'' in CDCl$_3$. 
Figure S73. Mass Spectrum (ESI-MS) of 4c/c'/c''.
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Figure S75. $^{13}$C NMR of 4d in CDCl$_3$. 

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Figure S77. $^1$H NMR of 4e in CD$_3$CN.

Figure S78. $^{13}$C NMR of 4e in CD$_3$CN.
Figure S79. Mass Spectrum (ESI-MS) of 4e.
Figure S80. $^1$H NMR of 4f in CD$_3$CN.

Figure S81. $^{13}$C NMR of 4f in CD$_3$CN.
Figure S82. Mass Spectrum (ESI-MS) of 4f.
14. NMR ($^1$H/$^{13}$C/$^{13}$CDEPT135) and HRMS spectra of cationic troponyl lactones (5a-e and 5a’-c’)

**Figure S83.** $^1$H NMR of 5a in CD$_3$CN.

**Figure S84.** $^{13}$C NMR of 5a in CD$_3$CN.
Figure S85. Mass Spectrum (ESI-MS) of 5a.
Figure S86. $^1$H NMR of 5a/a’ in CD$_3$CN.

Figure S87. $^{13}$C NMR of 5a/a’ in CD$_3$CN.
Figure S88. DEPT135\(^{13}\)C NMR of 5a/\(a'\) in CD\(_3\)CN.
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Figure S92. $^1$H NMR of 5c in CD$_3$CN.

Figure S93. $^{13}$C NMR of 5c in CD$_3$CN.
Figure S94. Mass Spectrum (ESI-MS) of 5c.
Figure S95. $^1$H NMR of 5c/c' in CD$_3$CN.

Figure S96. $^{13}$C NMR of 5c/c'/c'' in CD$_3$CN
Figure S97. DEPT135$^{13}$C NMR of 5c/c' in CD$_3$CN.
Figure S98. Mass Spectrum (ESI-MS) of 5c/c'/c''.
Figure S99. $^1$H NMR of 5d in CD$_3$CN.

Figure S100. $^{13}$C NMR of 5d in CD$_3$CN.
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Figure S105. Mass Spectrum (ESI-MS) of 5e.
15. NMR ($^1$H/$^{13}$C) spectra of protonated control monomers (3aa-H$^+$/3ab-H$^+$)

Figure S106. $^1$H NMR of 3aa-H$^+$ in CD$_3$CN.

Figure S107. $^{13}$C NMR of 3aa-H$^+$ in CD$_3$CN
Figure S108. $^1$H NMR of 3ab-H$^+$ in CD$_3$CN.

Figure S109. $^{13}$C NMR of 3ab-H$^+$ in CD$_3$CN.
16. NMR (\(^{1}\text{H}/^{13}\text{C}/^{13}\text{CDEPT135}\)) and HRMS spectra of troponyl alkylglycinates (6a-e and 6a'-d')

**Figure S110.** \(^{1}\text{H} \text{NMR of 6a in CDCl}_3\)

**Figure S111.** \(^{13}\text{C} \text{NMR of 6a in CDCl}_3\)
Figure S112. Mass Spectrum (ESI-MS) of 6a.
Figure S113. $^1$H NMR of 6a/a'/a'' in CDCl$_3$.

Figure S114. $^{13}$C NMR of 6a/a'/a'' in CDCl$_3$.
Figure S115. Mass Spectrum (ESI-MS) of 6a/a’/a’’.
Figure S116. DEPT135$^{13}$C NMR of 6a in CDCl$_3$.

Figure S117. DEPT135$^{13}$C NMR of 6a/a'/a'' in CDCl$_3$. 
Figure S118. $^1$H NMR of 6b in CDCl$_3$.

Figure S119. $^{13}$C NMR of 6b in CDCl$_3$.
**Figure S120.** Mass Spectrum (ESI-MS) of 6b.
Figure S121. $^1$H NMR of 6b/b'/b'' in CDCl$_3$.

Figure S122. $^{13}$C NMR of 6b/b'/b'' in CDCl$_3$. 
Figure S123. Mass Spectrum (ESI-MS) of 6b/b'/b''.
Figure S124. DEPT135$^{13}$C NMR of 6b in CDCl$_3$.

Figure S125. DEPT135$^{13}$C NMR of 6b/b'/b'' in CDCl$_3$. 
Figure S126. $^1$H NMR of 6c in CDCl$_3$.

Figure S127. $^{13}$C NMR of 6c in CDCl$_3$.
Figure S128. Mass Spectrum (ESI-MS) of 6c.
Figure S129. $^1$H NMR of $6c/c'/c''$ in CDCl$_3$.

Figure S130. $^{13}$C NMR of $6c/c'/c''$ in CDCl$_3$.
Figure S131. Mass Spectrum (ESI-MS) of 6c/c'/c”.
Figure S132. DEPT135^{13}C NMR of 6c in CDCl₃.

Figure S133. DEPT135^{13}C NMR of 6c'/c'' in CDCl₃.
Figure S134. $^1$H NMR of 6d in CDCl$_3$.

Figure S135. $^{13}$C NMR of 6d in CDCl$_3$.
Figure S136. Mass Spectrum (ESI-MS) of 6d.
Figure S137. $^1$H NMR of 6d/d'/d'' in CDCl$_3$.

Figure S138. $^{13}$C NMR of 6d/d'/d'' in CDCl$_3$.
Figure S139. Mass Spectrum (ESI-MS) of 6d/d'/d''.
Figure S140. DEPT135$^{13}$C NMR of 6d in CDCl$_3$.

Figure S141. DEPT135$^{13}$C NMR of 6d/$d'/d''$ in CDCl$_3$. 
Figure S142. $^1$H NMR of 6e in CDCl$_3$.

Figure S143. $^{13}$C NMR of 6e in CDCl$_3$.
**Figure S144.** Mass Spectrum (ESI-MS) of 6e.
17. NMR ($^1$H/$^{13}$C) and HRMS spectra of peptides (7-15)

Figure S145. $^1$H NMR of 7 in CDCl$_3$.

Figure S146. $^{13}$C NMR of 7 in CDCl$_3$. 
Figure S147. Mass Spectrum (ESI-MS) of 7.
Figure S148. $^1$H NMR of 8 in CDCl$_3$.

Figure S149. $^{13}$C NMR of 8 in CDCl$_3$. 
Figure S150. Mass Spectrum (ESI-MS) of 8.
Figure S151. $^1$H NMR of 9 in CDCl$_3$.

Figure S152. $^{13}$C NMR of 9 in CDCl$_3$. 
Figure S153. Mass Spectrum (ESI-MS) of 9.
Figure S154. $^1$H NMR of 10 in CDCl$_3$.

Figure S155. $^{13}$C NMR of 10 in CDCl$_3$. 
Figure S156. Mass Spectrum (ESI-MS) of 10.
Figure S157. $^1$H NMR of 11 in CDCl$_3$.

Figure S158. $^{13}$C NMR of 11 in CDCl$_3$. 
**Figure S159.** Mass Spectrum (ESI-MS) of 11.
Figure S160. $^1$H NMR of 12 in CDCl$_3$.

Figure S161. $^{13}$C NMR of 12 in CDCl$_3$. 
Figure S162. Mass Spectrum (ESI-MS) of 12.
Figure S163. $^1$H NMR of 13 in CDCl$_3$.

Figure S164. $^{13}$C NMR of 13 in CDCl$_3$. 

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Figure S165. Mass Spectrum (ESI-MS) of 13.
Figure S166. $^1$H NMR of 14 in CDCl$_3$.

Figure S167. $^{13}$C NMR of 14 in CDCl$_3$. 
Figure S168. Mass Spectrum (ESI-MS) of 14.
Figure S169. $^1$H NMR of 15 in CDCl$_3$.

Figure S170. $^{13}$C NMR of 15 in CDCl$_3$. 
Figure S171. Mass Spectrum (ESI-MS) of 15.
18. $^1$H/$^{13}$C NMR and HRMS spectra of 8/11-OH in DMSO-d6

![NMR Spectra](image1)

Figure S172. $^1$H NMR of 8-OH in CDCl$_3$.

![NMR Spectra](image2)

Figure S173. $^{13}$C NMR of 8-OH in CDCl$_3$. 
Figure S174. Mass Spectrum (ESI-MS) of 8-OH.
**Figure S175.** $^1$H NMR of 11-OH in CDCl$_3$.

**Figure S176.** $^{13}$C NMR of 11-OH in CDCl$_3$. 
Figure S177. Mass Spectrum (ESI-MS) of 11-OH.
19. Traping the ketene intermediate via [2+2] cyclo addition with imine:

The Trag amide 10 and excess imine (N-benzylidene-1-phenylmethanamine, Scheme S1) was was taken in minimum amount of acetonitrile and treated with TFA. Then, the reaction mixture after addition of TFA and before addition of TFA was analysed by ESI-MS. In the mass spectrum of the reaction mixture after addition of TFA, corresponding β-lactam (Figure 2&3) peak was identified at m/z=469.28 along with CTL mass peak. However, the CTL formation was more prominent compared to β-lactam formation. This is probably due to faster intramolecular cyclization and also complete protonation of imine may led to the less availability of imine form in the reaction mixture.

Whereas, the reaction mixture without the addition of TFA has shown no peak in the mass spectrum representing the corresponding β-lactam.

Similar reaction was performed with two other Trag amides 6a/d and same imine (N-benzylidene-1-phenylmethanamine) and obtained spectral data is provided in Figure 4-7 (Scheme S2&3).

- Note: We have added less amount of TFA (compared to imine) to the reaction mixture of Trag amide and imine in acetonitrile. We observed the formation of corresponding lactam and presence of Trag amide also. This is most probably happening due to neutralization of the TFA (because excess imine is present in TFA) and as result facilitating reversible amidation (Figure 2).
- To the same reaction mixture we have added methanol:water mixture and analysed by ESI-MS, as expected CTLs were converted to Trag acid/methyl esters and the β-lactam mass peak was present as usual.
- Schemes and obtained data is provided below.

Overall, these experiments are also strongly supported the involvement of ketene intermediate in the conversion of Trag acid/ester/amide into CTLs.

**Trapping of ketene intermediate through [2+2] cycloaddition with imine:**

![Scheme S1](image)

**Scheme S1.** Reaction of Trag amide 10 with imine in presence of TFA.

![Scheme S2](image)

**Scheme S2.** Reaction of Trag amide 6a with imine in presence of TFA.
Scheme S2. Reaction of Trag amide 6c with imine in presence of TFA.
Figure S178. ESI-MS spectra of Trag amide (10) and imine. No peak was observed at \( m/z = 469 \)

![Figure S178](image)

Figure S179. ESI-MS spectra of Trag amide (10) and imine after treatment with TFA. Trag amide was also observed after the reaction. This most probably due to the instant neutralization of TFA and reversible amidation.

![Figure S179](image)

Figure S180. To the same reaction mixture (Figure 2; reaction mixture) was added further amount of TFA. Showing the complete cleavage of Trag amide (10) and formation corresponding beta-lactam.

![Figure S180](image)
Figure S181. ESI-MS spectra of Trag amide (6a) and imine. No peak was observed at \( m/z = 441 \).

Figure S182. ESI-MS spectra after addition of TFA. showing the formation of \( \beta \)-lactam.

Figure S183. To the same reaction mixture (Figure S180; reaction mixture) was added water and methanol mixture. Showing the conversion of CTL into Trag acid and methyl ester and presence of corresponding \( \beta \)-lactam.
Figure S184. ESI-MS spectra showing the formation of β-lactam. To the reaction mixture methanol:water mixture was added prior to analysis.