

## Supporting Information

# Carbamoyl-*N*-aryl-imine-urea: A new framework to obtain a putative leishmanicidal drug-candidate

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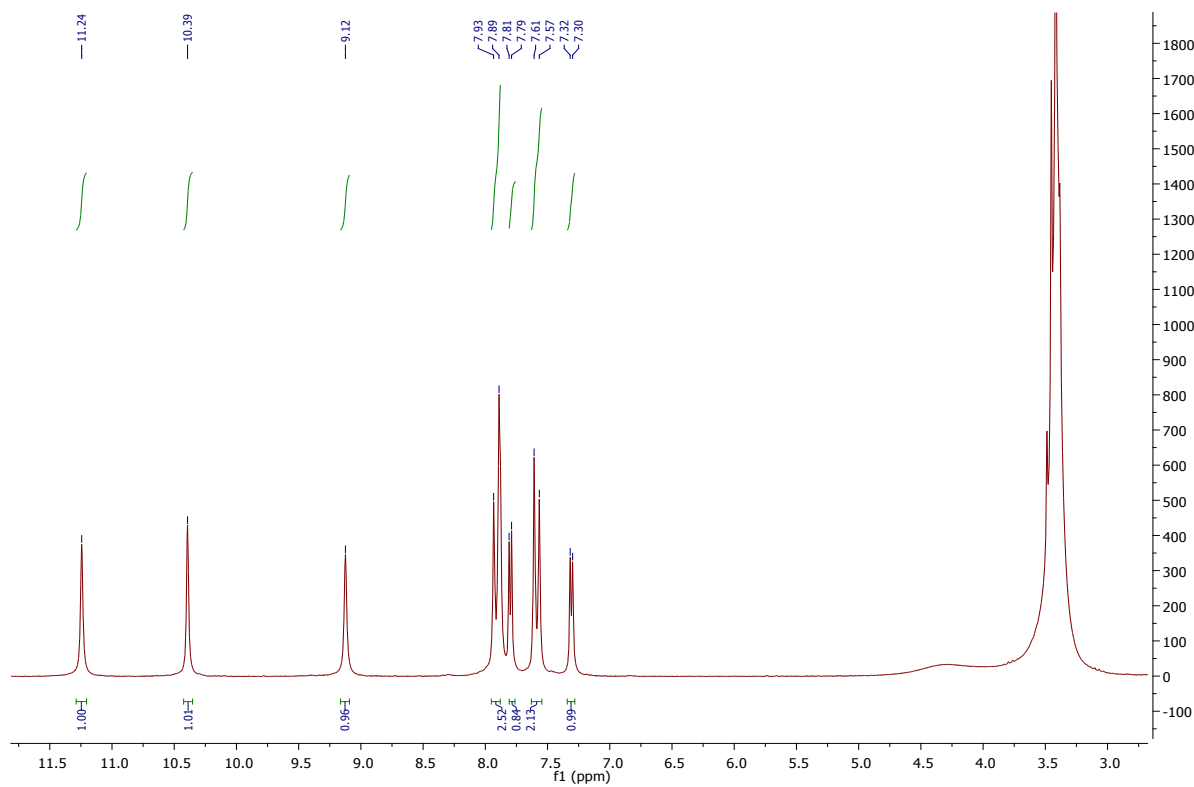
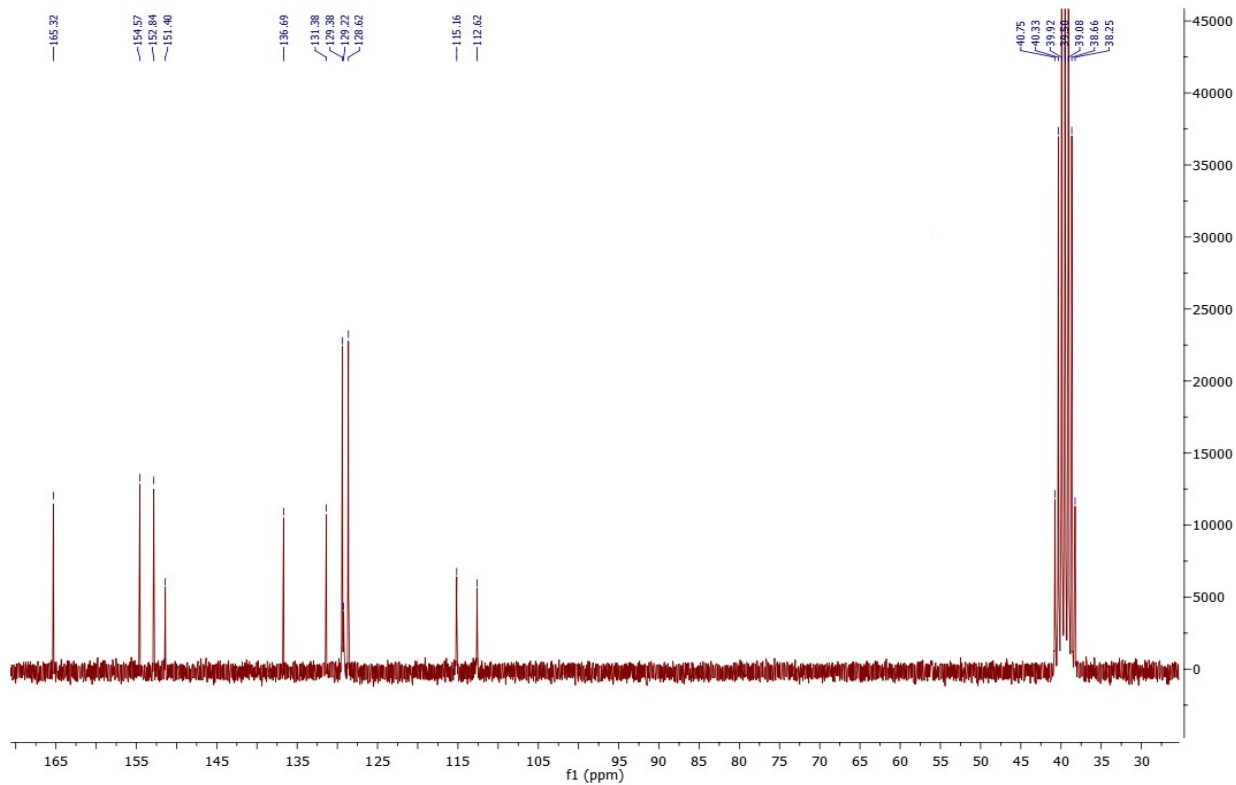
### Contents of SI

1 – <sup>1</sup>H and <sup>13</sup>C NMR Spectra, IR Spectra and HRMS analyses of Carbamoyl-*N*-aryl-imine-urea (9a-e)

2 – <sup>1</sup>H and <sup>13</sup>C NMR Spectra, IR Spectra and HRMS analyses of Carbamoyl-*N*-aryl-imine-urea (10a-e)

3- Table S1. Crystal data and refinement parameters of compound 9a (LASSBio-1491).

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Figure S1. Compound 9a (LASSBio-1491) <sup>1</sup>H NMRFigure S2. Compound 9a (LASSBio-1491) <sup>13</sup>C NMR

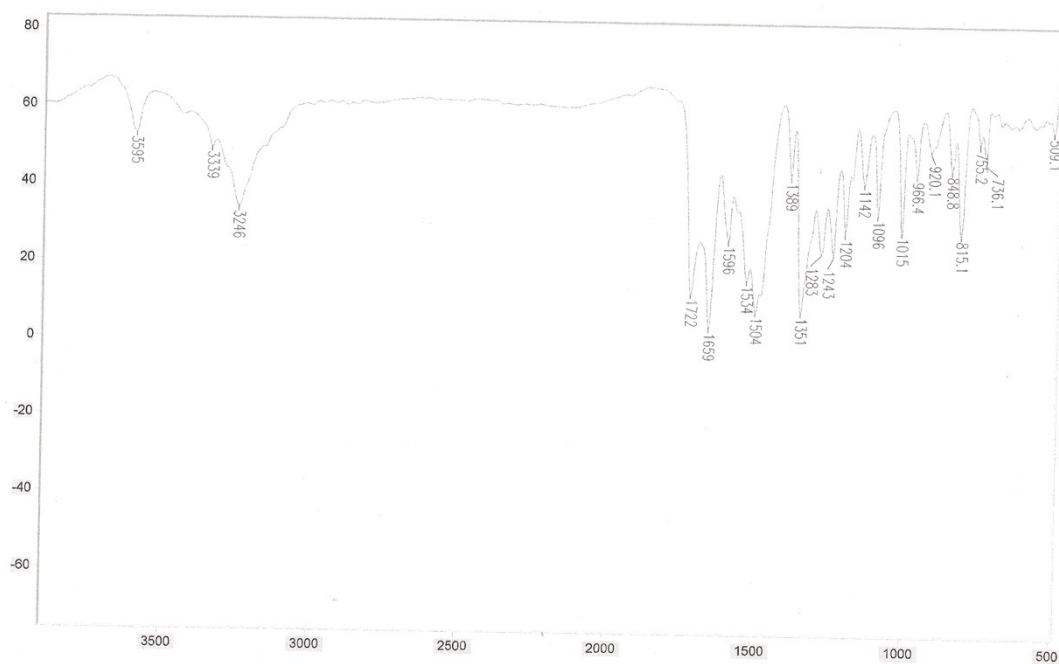


Figure S3. Compound 9a (LASSBio-1491) IR

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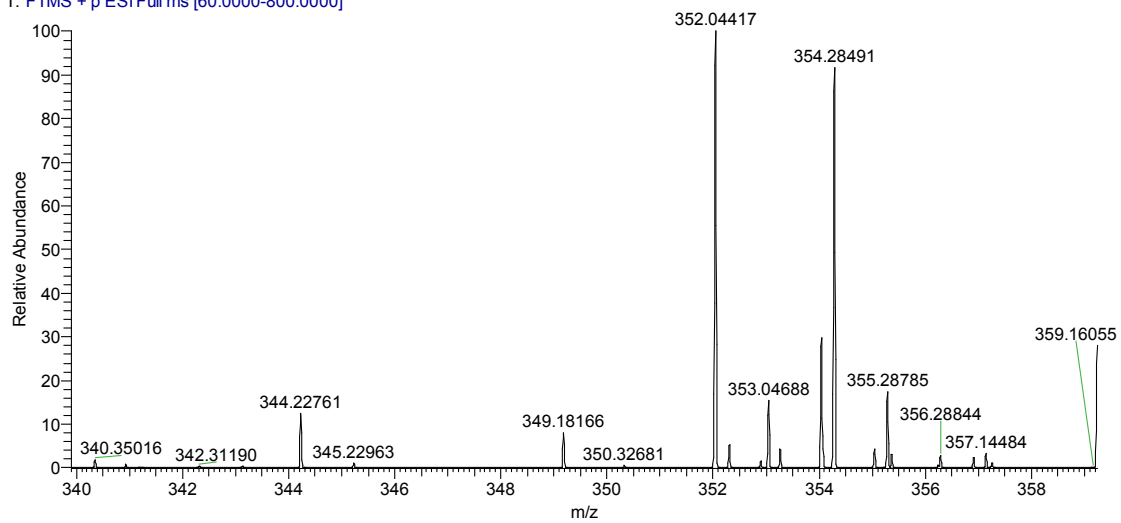
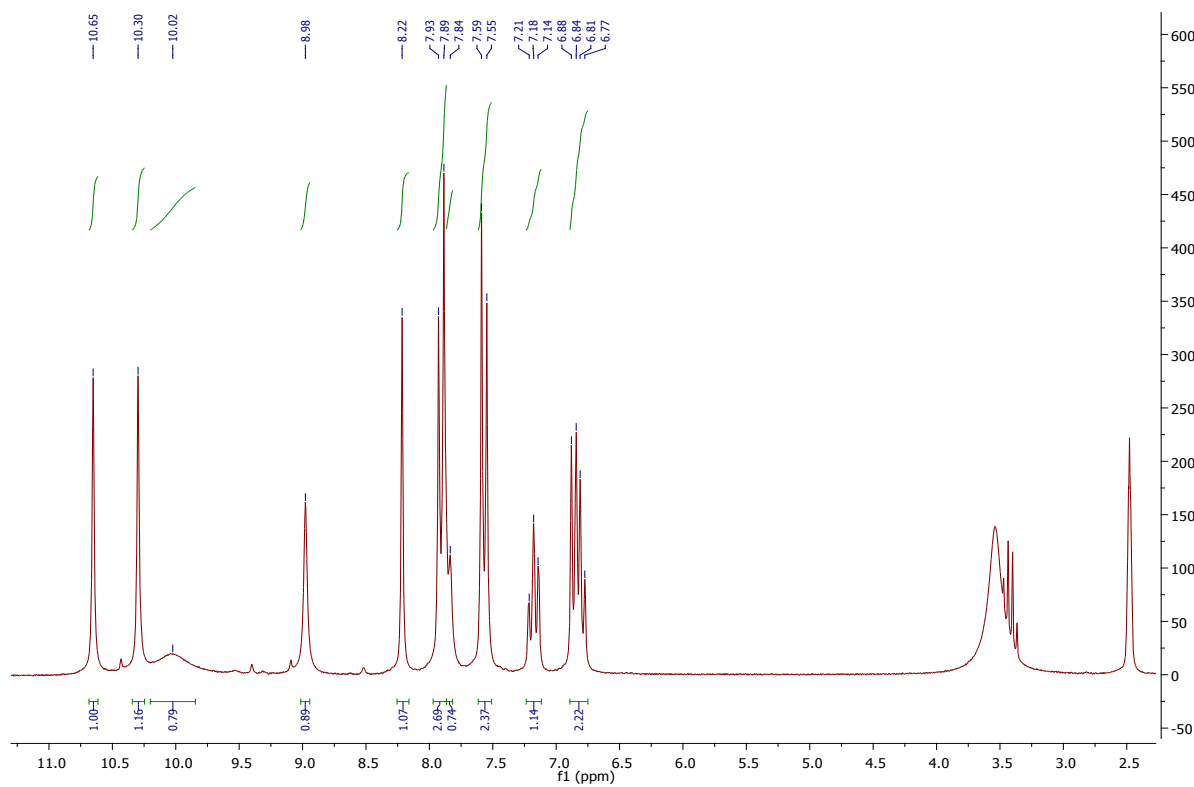
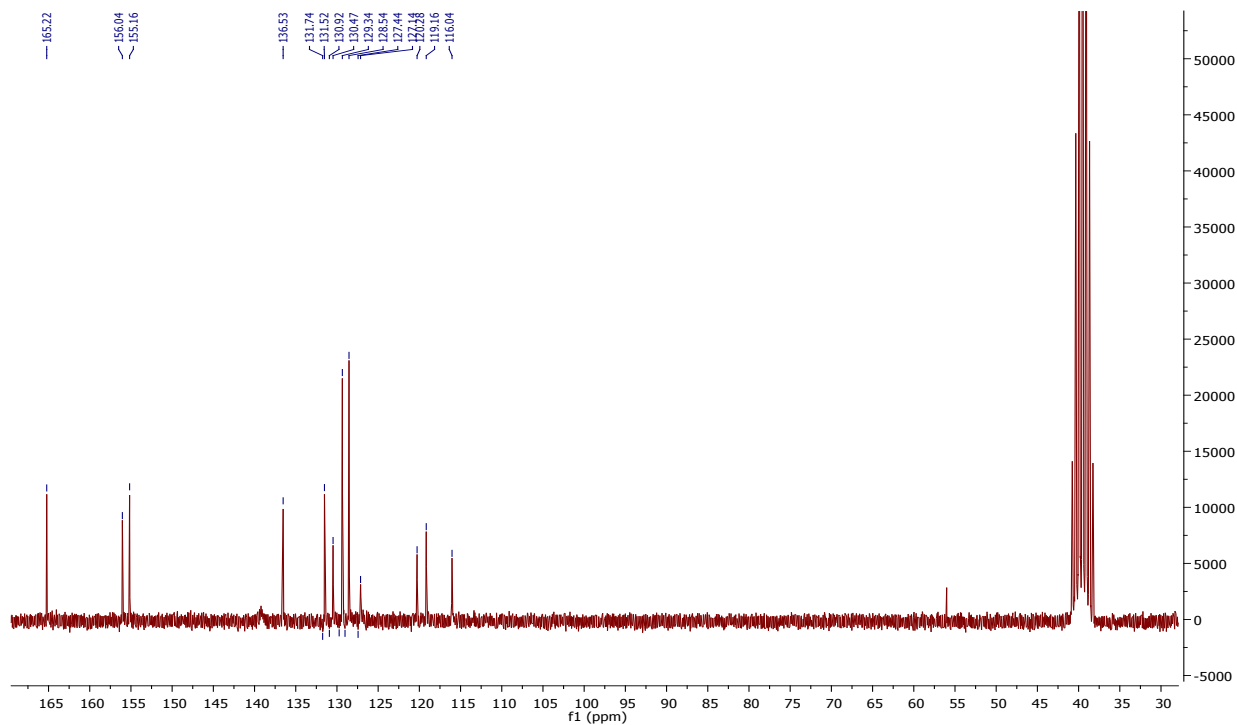


Figure S4. Compound 9a (LASSBio-1491) HRMS

Figure S5. Compound 9b (LASSBio-1704) <sup>1</sup>H NMRFigure S6. Compound 9b (LASSBio-1704) <sup>13</sup>C NMR

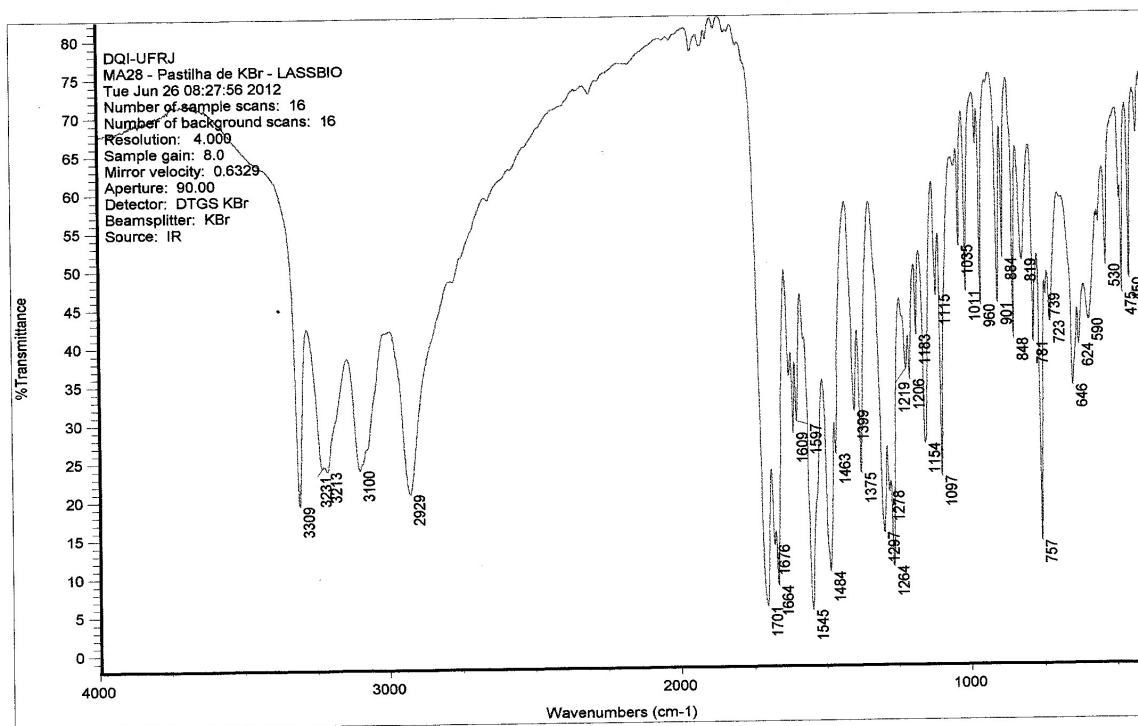


Figure S7. Compound 9b (LASSBio-1704) IR

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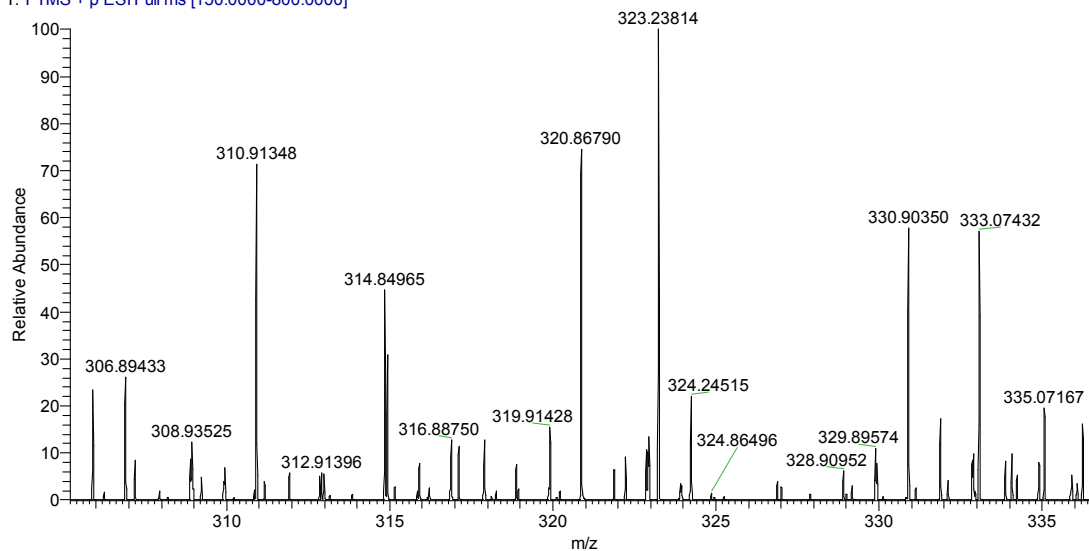


Figure S8. Compound 9b (LASSBio-1704) HRMS

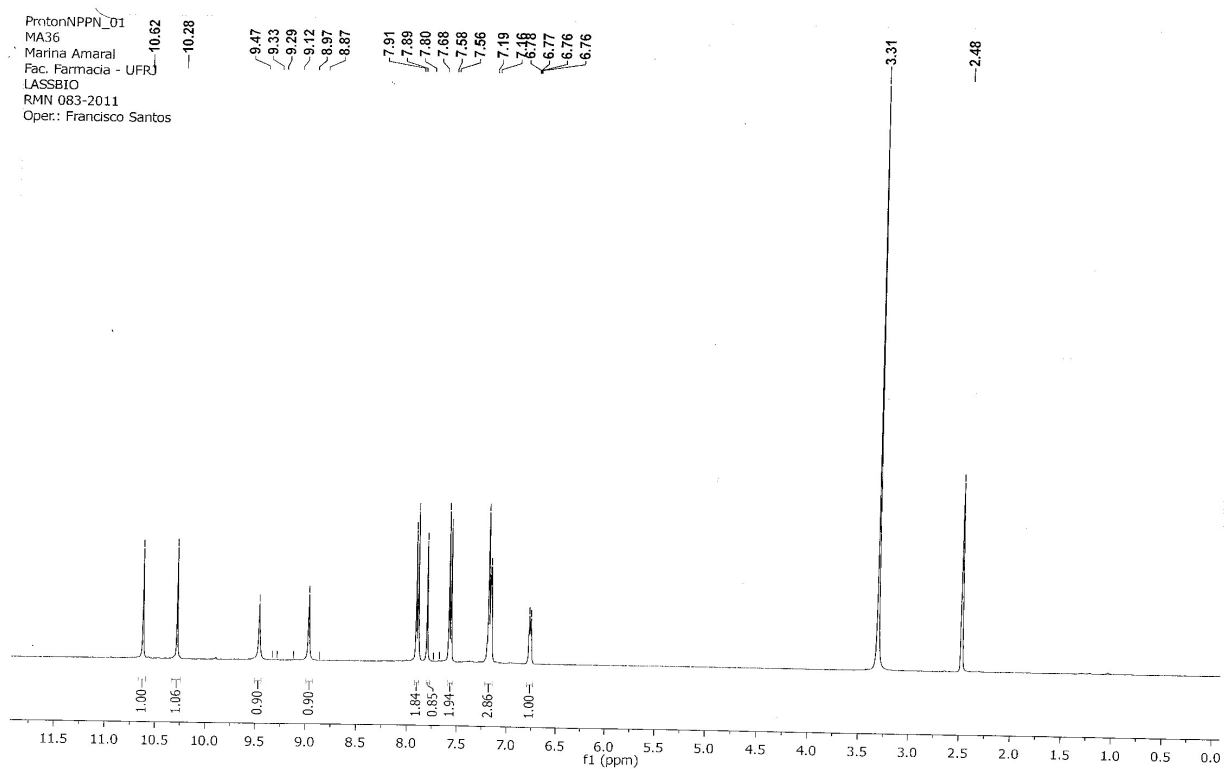
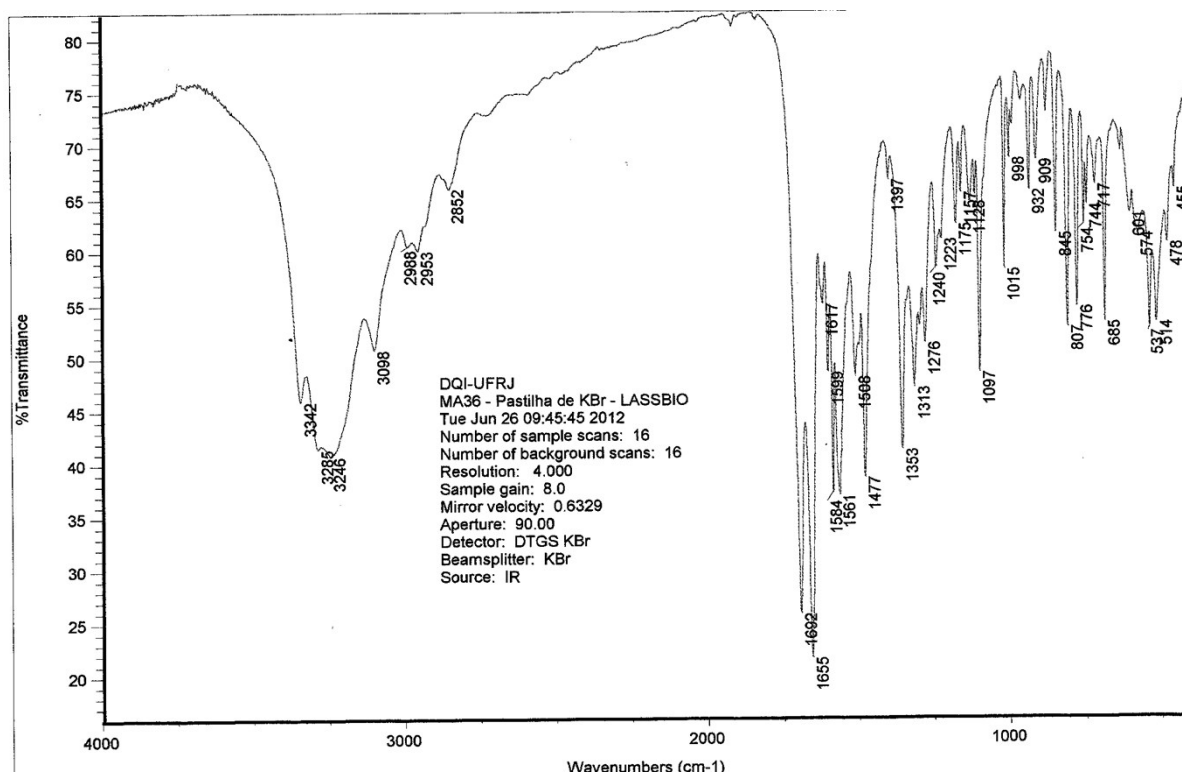
Figure S9. Compound 9c (LASSBio-1709)  $^1\text{H}$  NMR

Figure S10. Compound 9c (LASSBio-1709) IR

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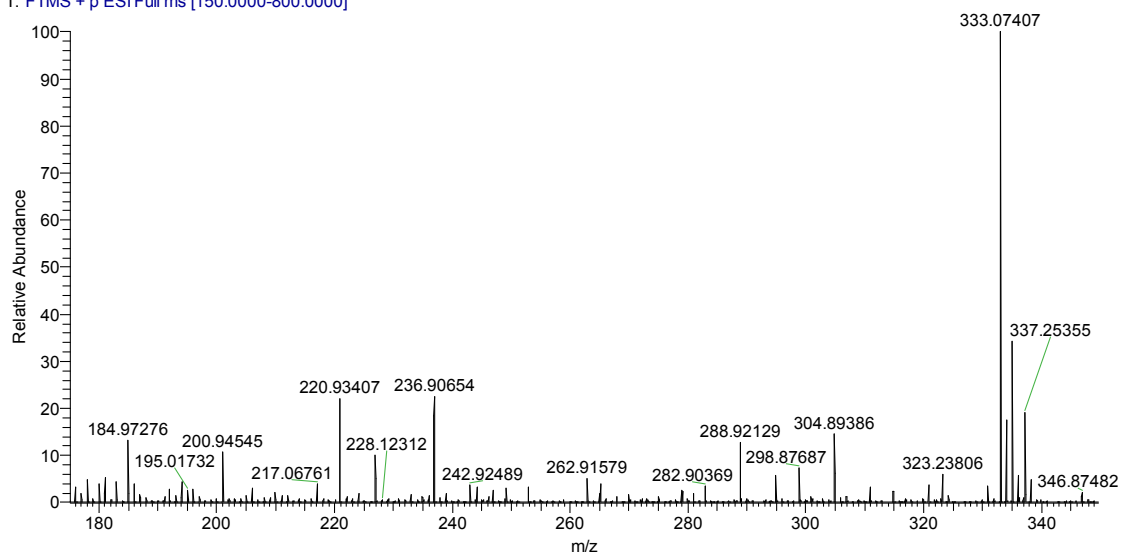
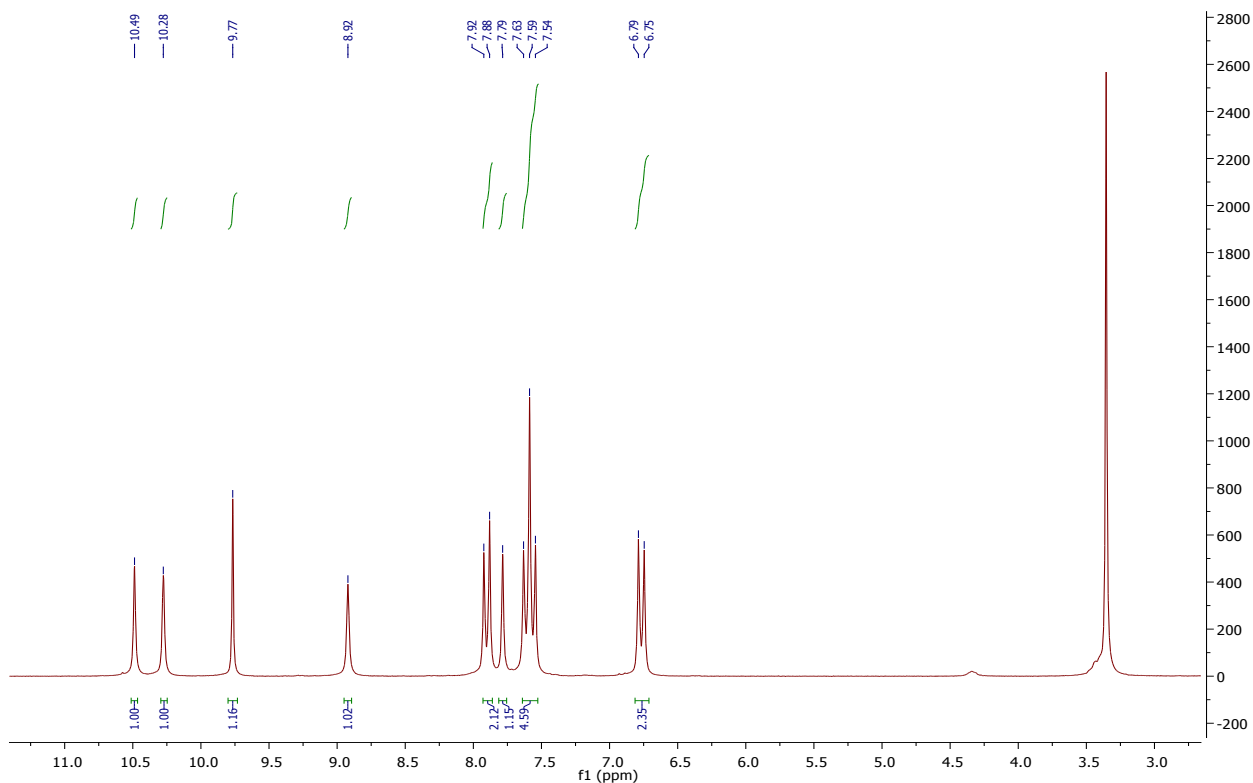
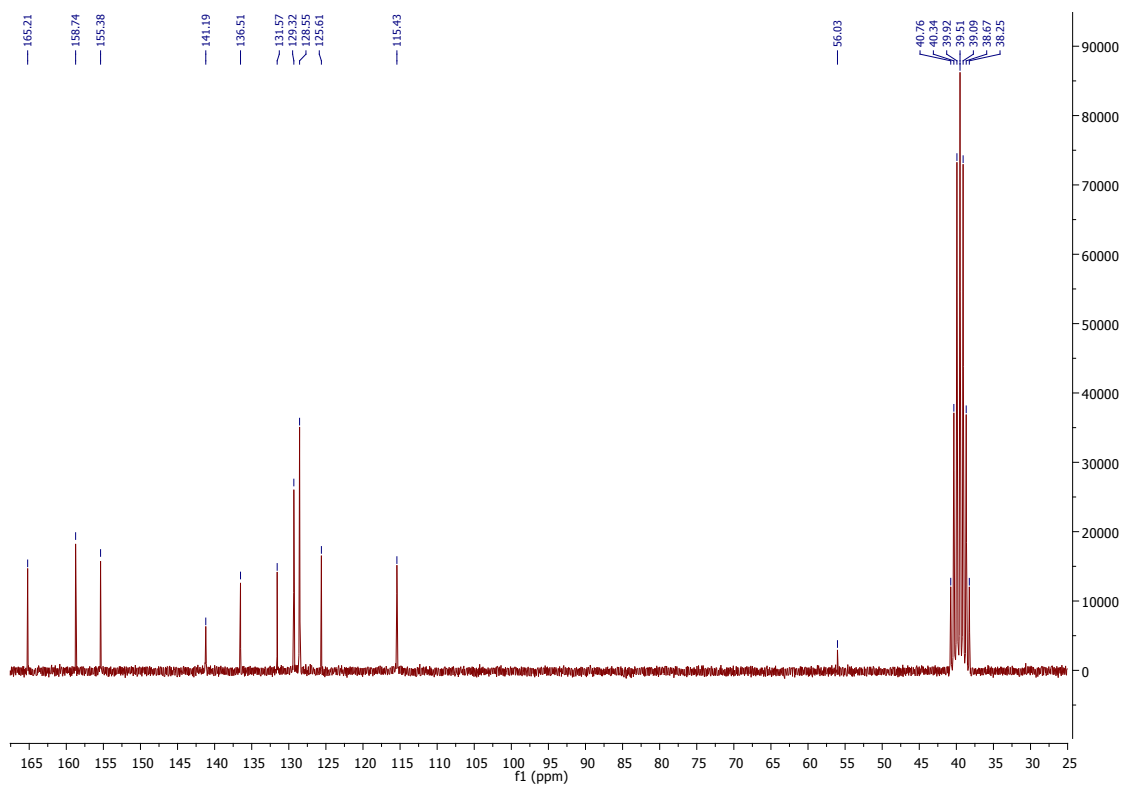
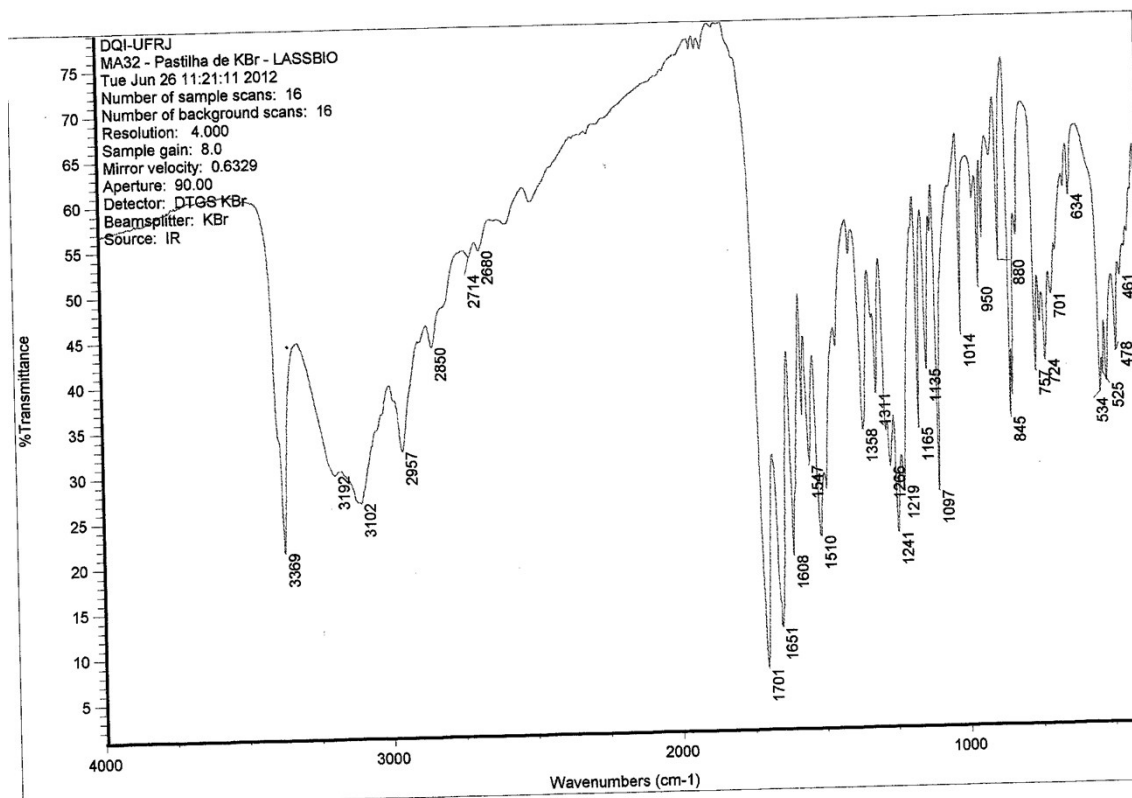
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T: FTMS + p ESI Full ms [150.0000-800.0000]

Figure S11. Compound 9c (LASSBio-1709) HRMS

Figure S12. Compound 9d (LASSBio-1706) <sup>1</sup>H NMR

Figure S13. Compound 9d (LASSBio-1706) <sup>13</sup>C NMRFigure S14. Compound 9d (LASSBio-1706) <sup>13</sup>C NMR



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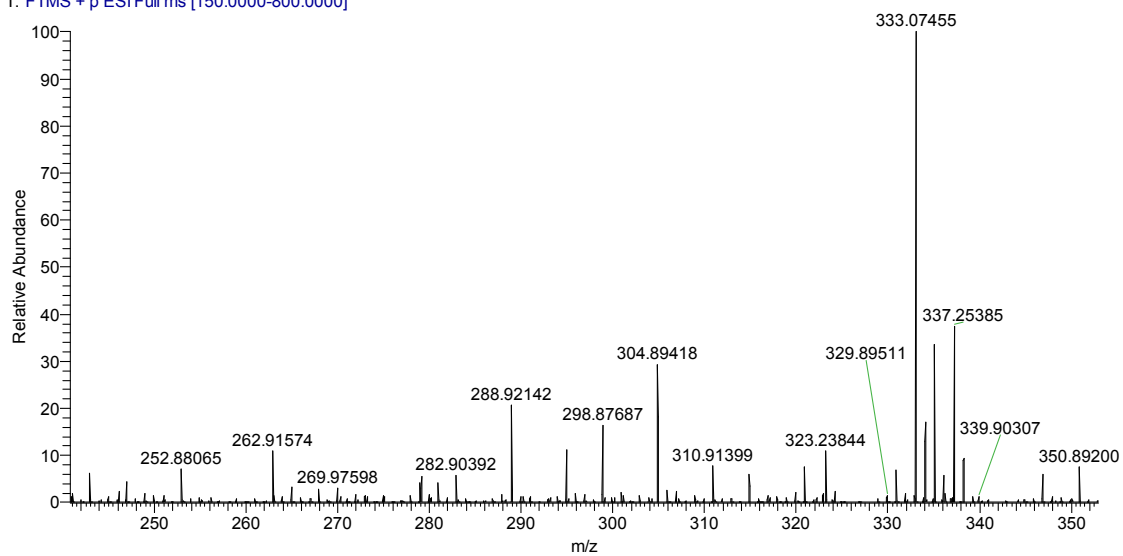
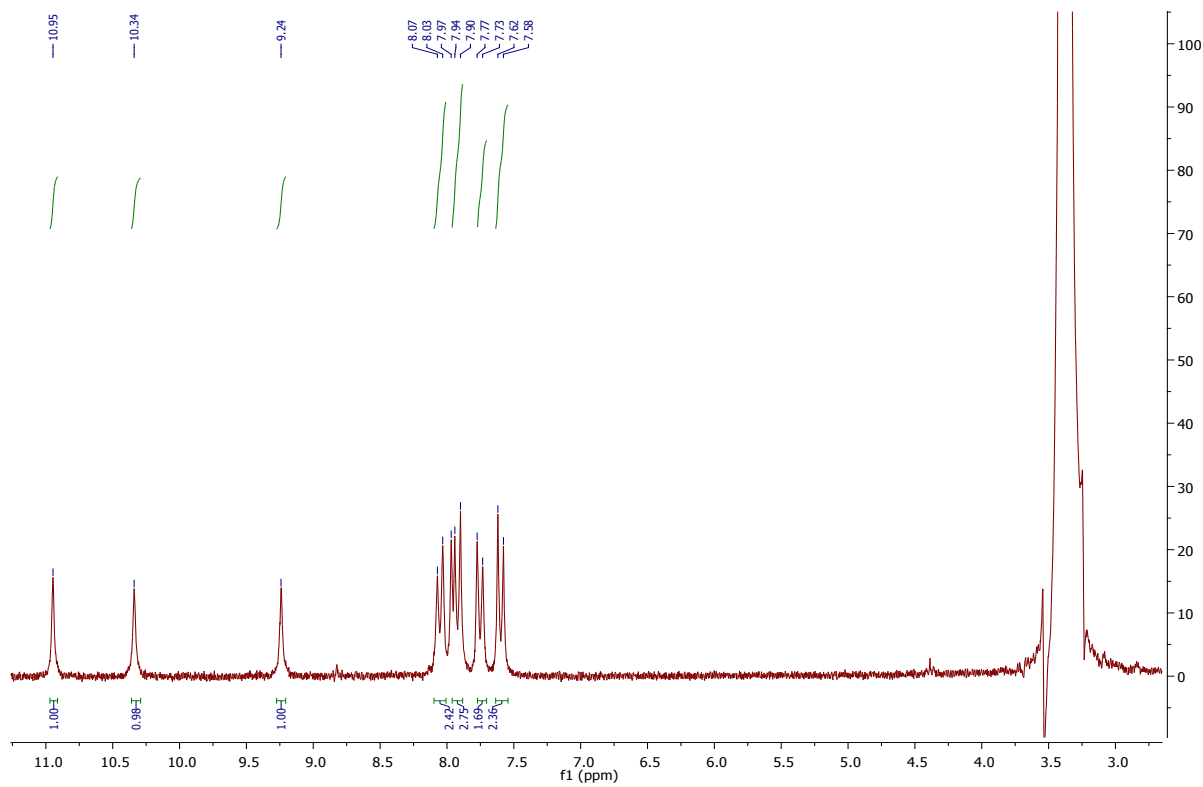
1706 #28-36 RT: 0.20-0.24 AV: 4 SM: 7G NL: 6.71E6  
T: FTMS + p ESI Full ms [150.0000-800.0000]

Figure S15. Compound 9d (LASSBio-1706) HRMS

Figure S16. Compound 9e (LASSBio-1737) <sup>1</sup>H NMR

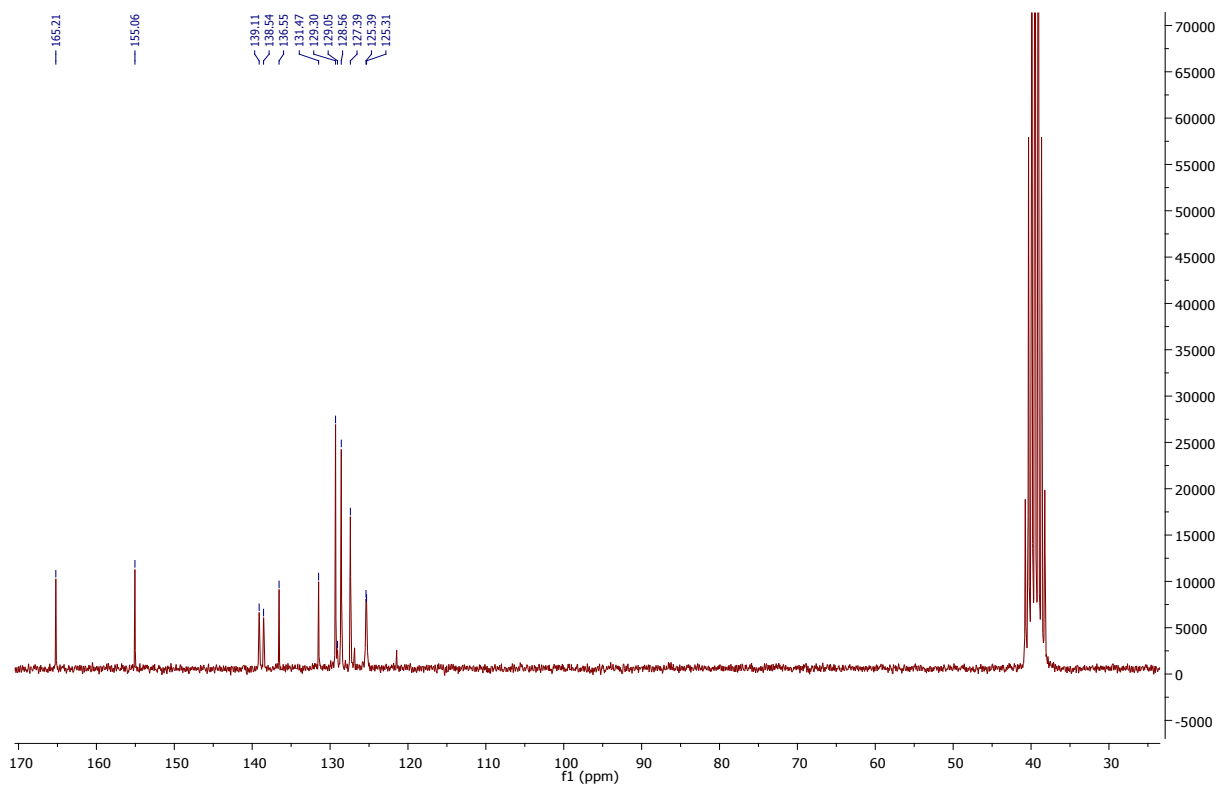
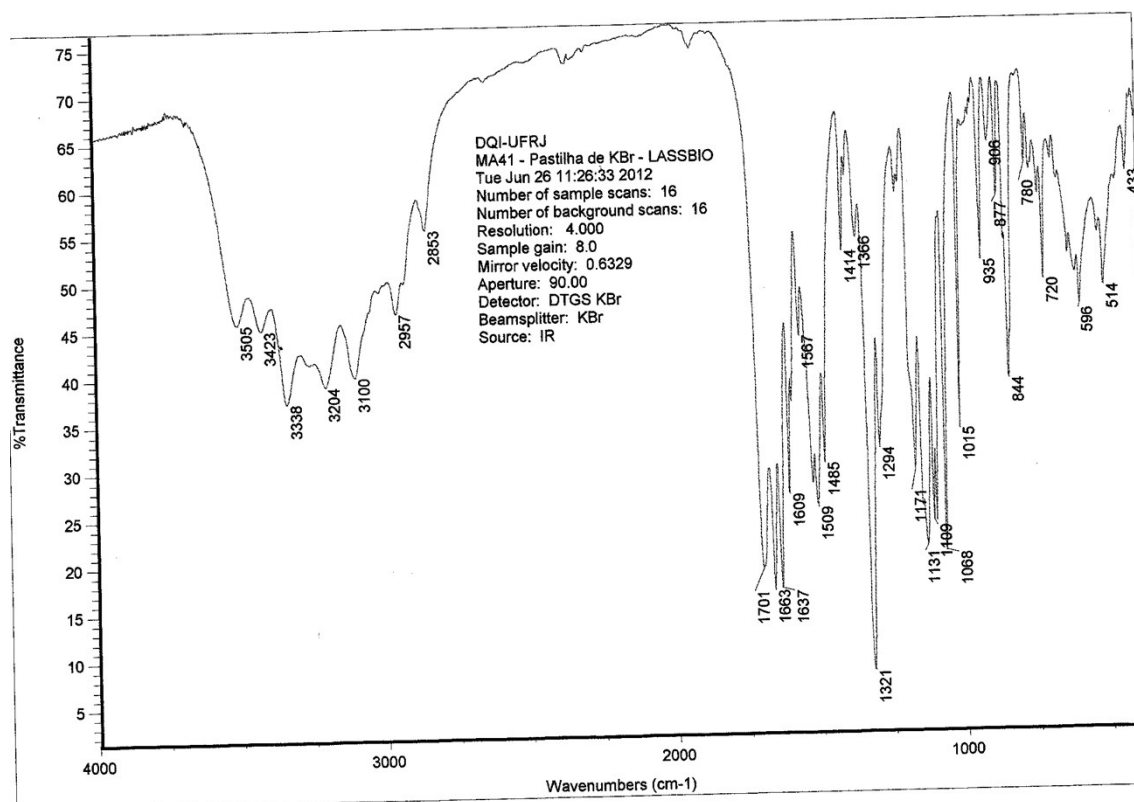
Figure S17. Compound 9e (LASSBio-1737)  $^{13}\text{C}$  NMR

Figure S18. Compound 9e (LASSBio-1737) IR

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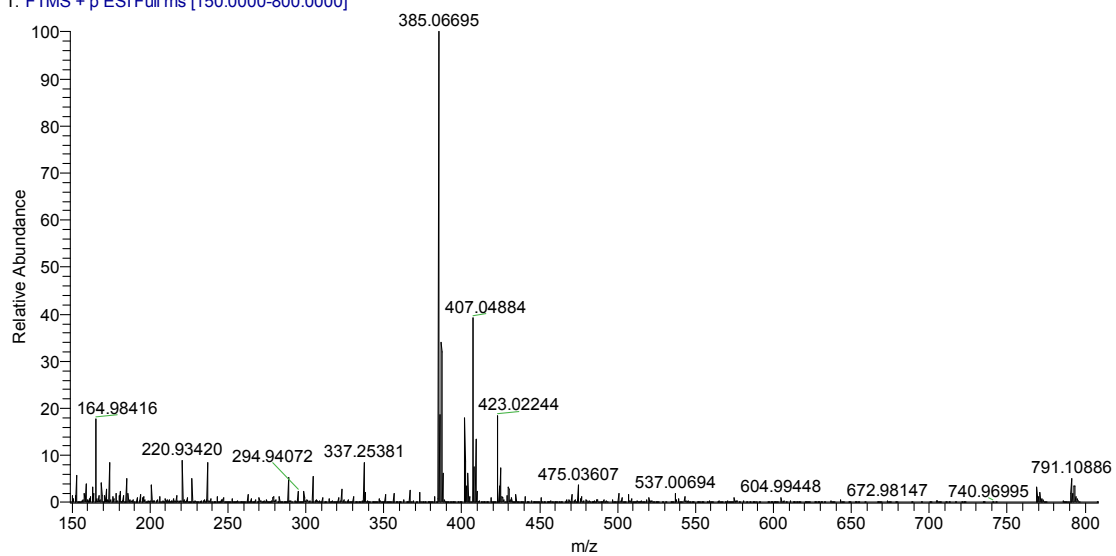
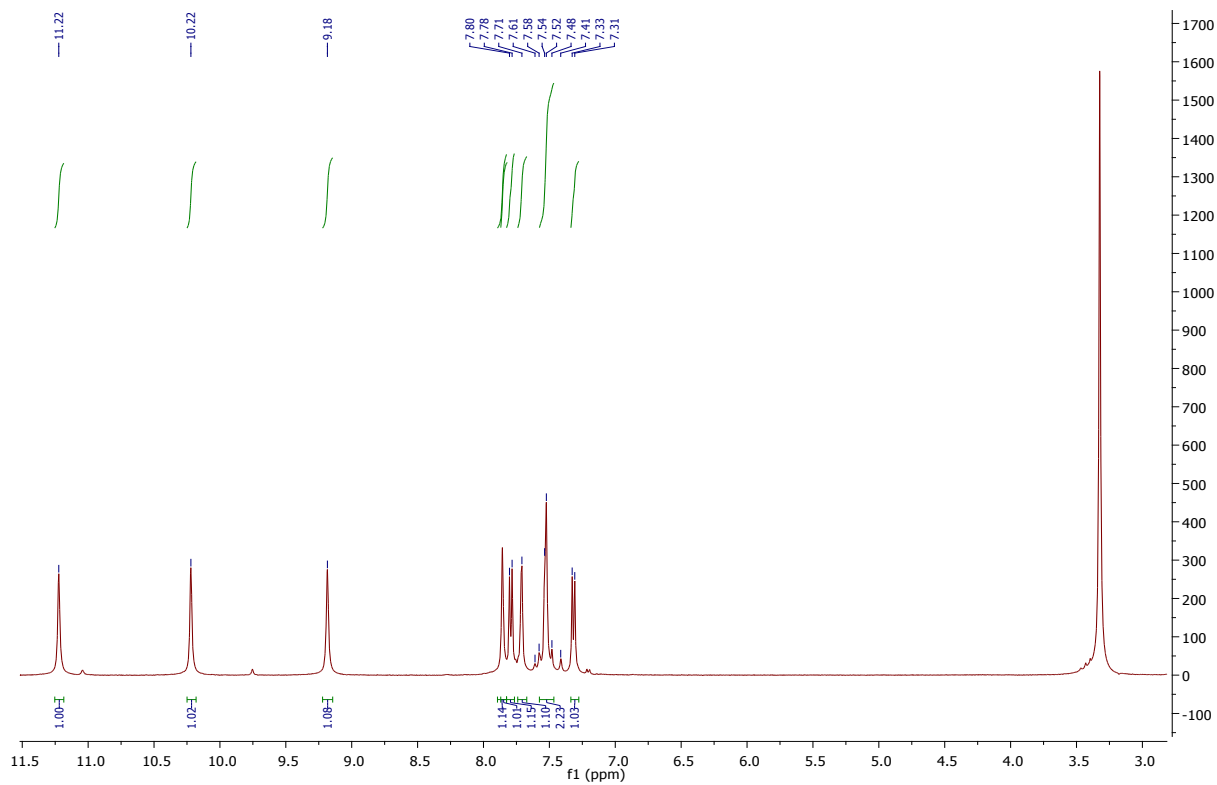
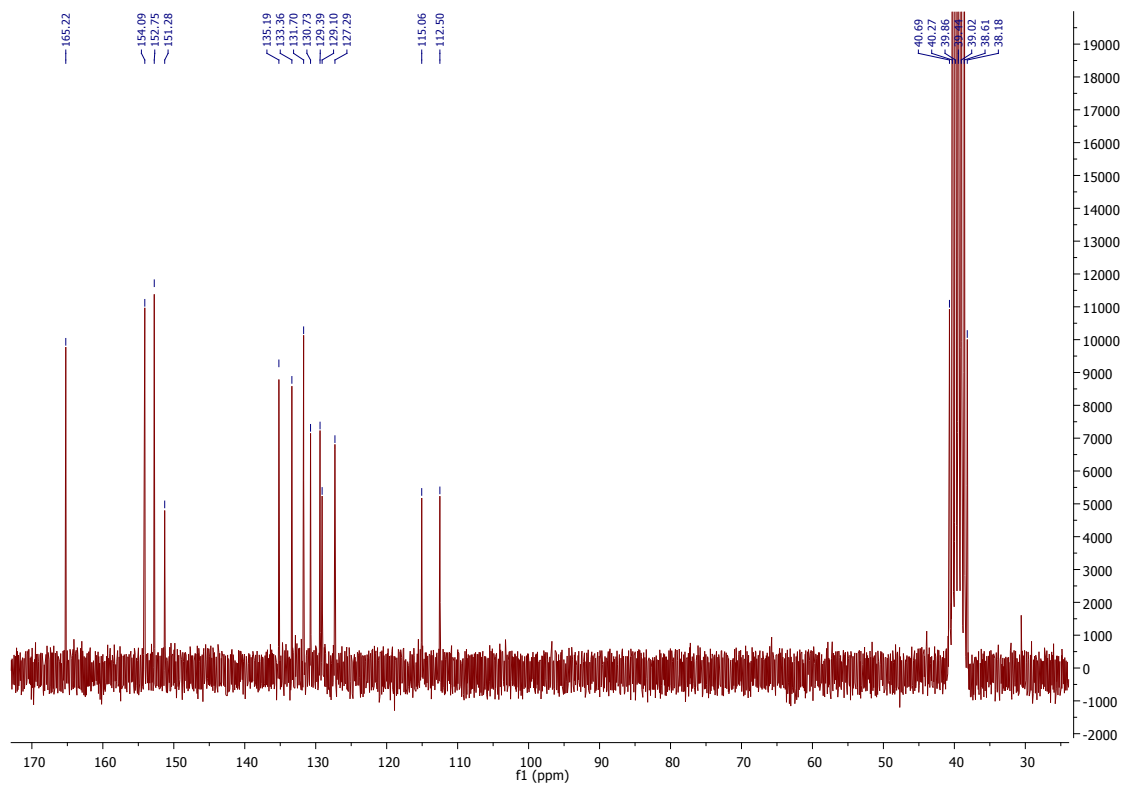
MA41 #23-35 RT: 0.16-0.24 AV: 7 SM: 7G NL: 3.12E7  
T: FTMS + p ESI Full ms [150.0000-800.0000]

Figure S19. Compound 9e (LASSBio-1737) HRMS

Figure S20. Compound 10a (LASSBio-1703)  $^1\text{H}$  NMRFigure S21. Compound 10a (LASSBio-1703)  $^{13}\text{C}$  NMR

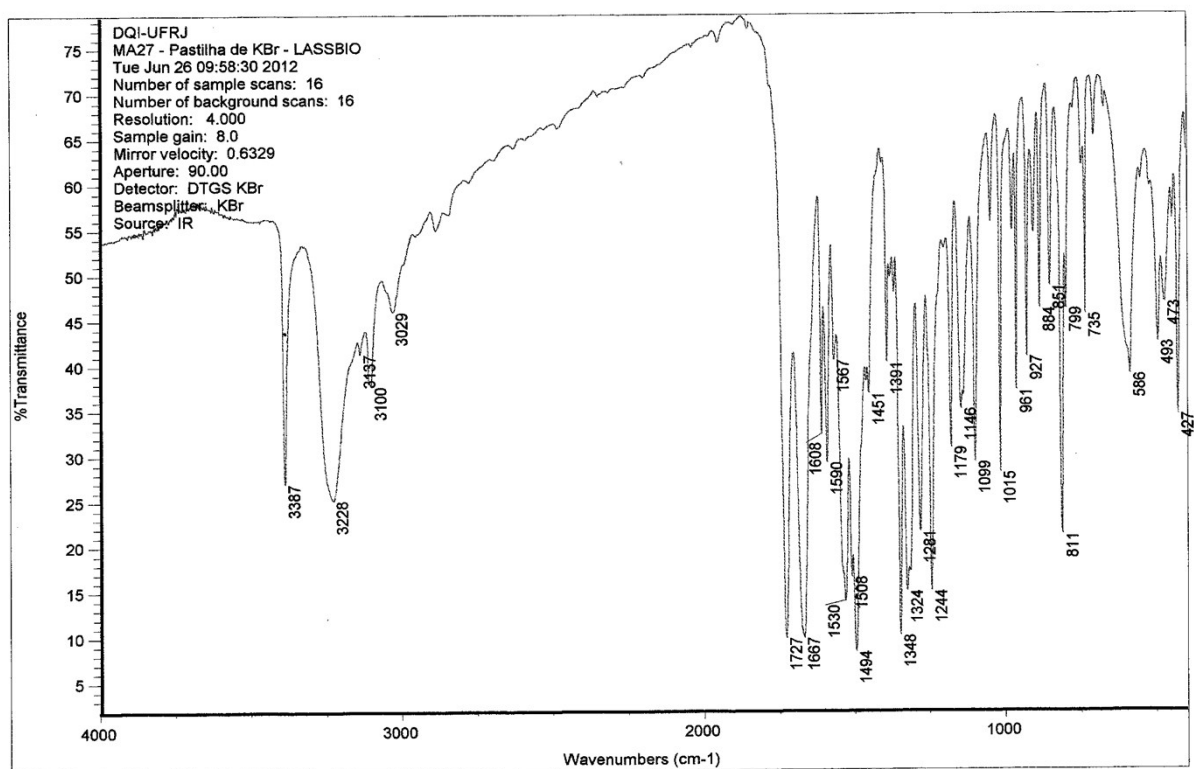


Figure S22. Compound 10a (LASSBio-1703) IR

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1703 #41-59 RT: 0.27-0.39 AV: 10 SM: 7G NL: 6.58E6  
T: FTMS + p ESI Full ms [60.0000-800.0000]

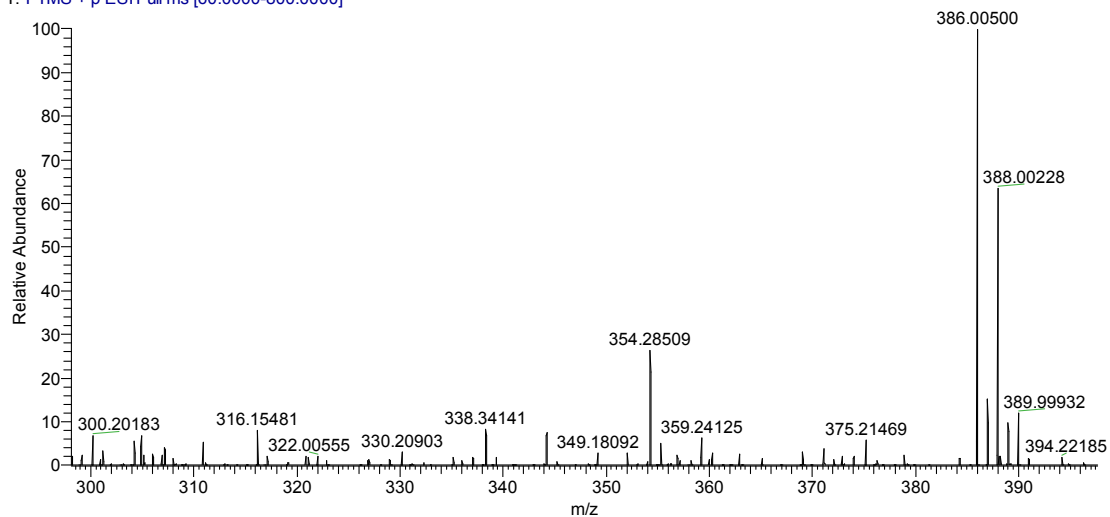
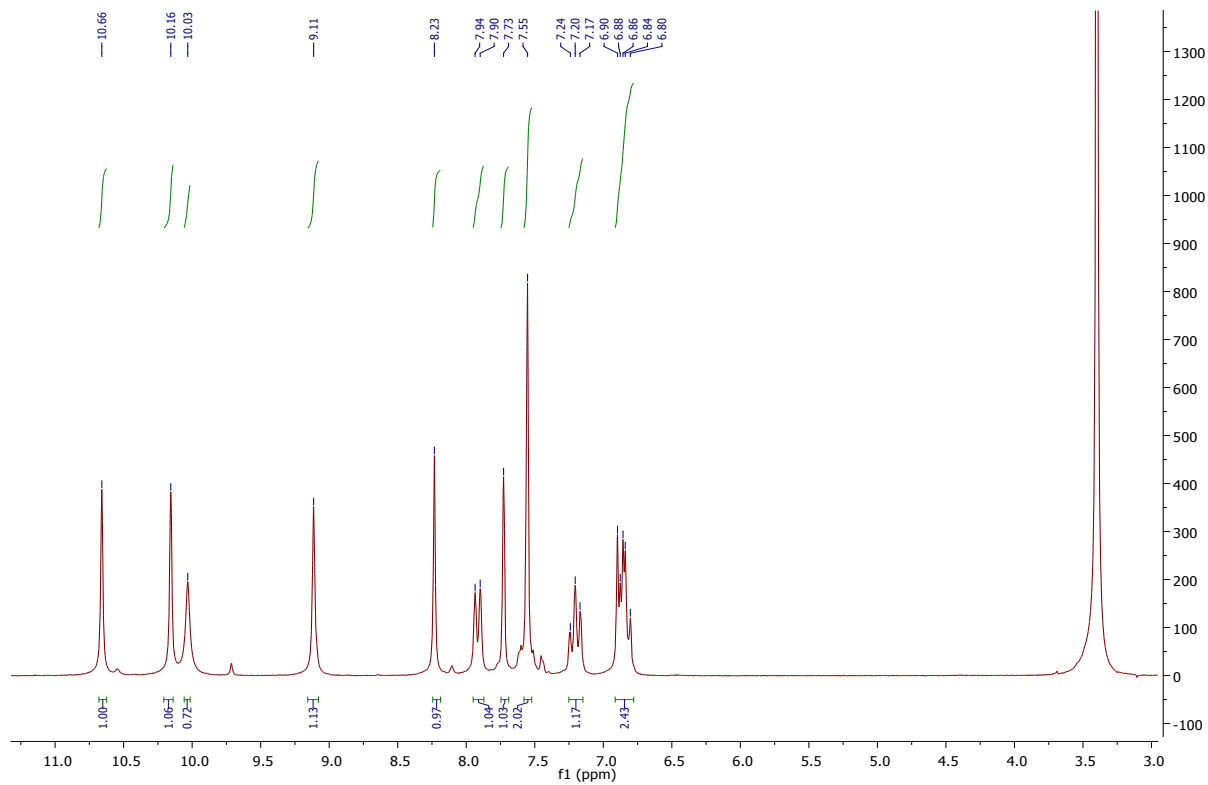
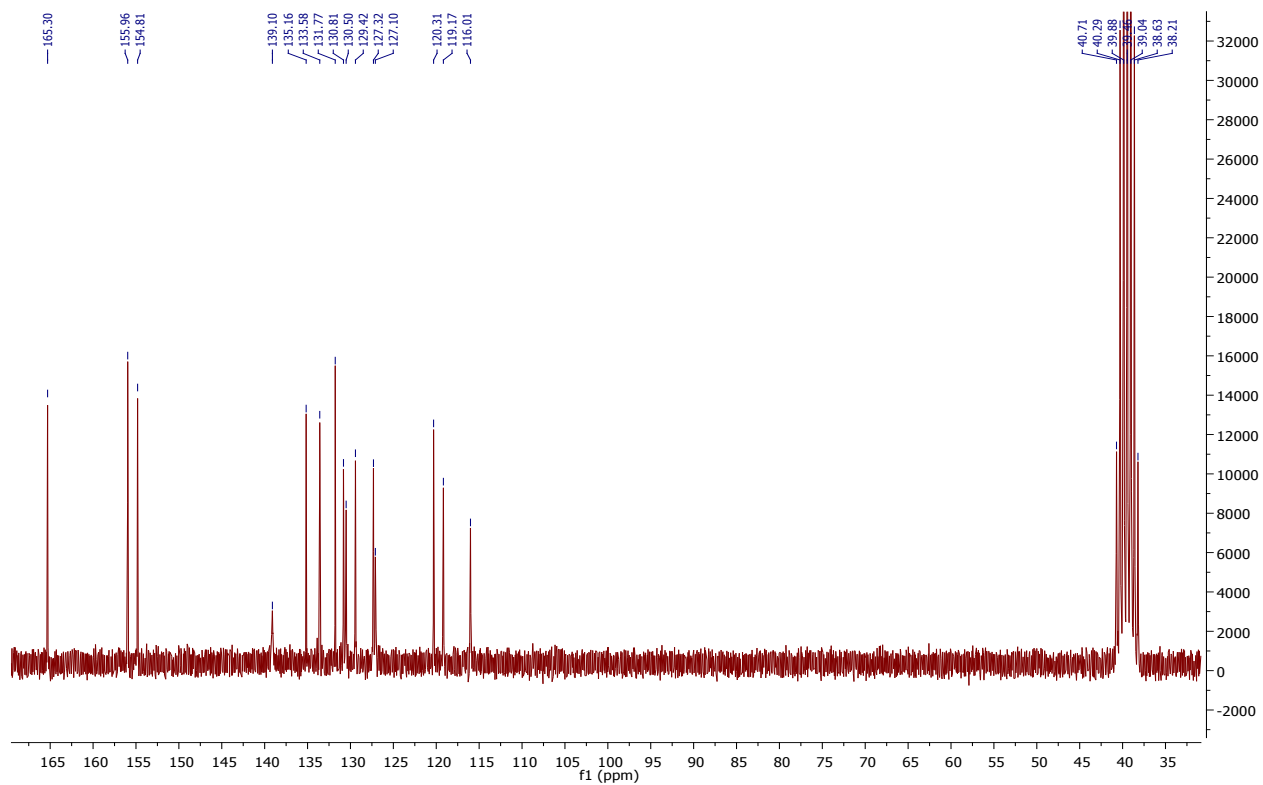


Figure S23. Compound 10a (LASSBio-1703) HRMS

Figure S24. Compound 10b (LASSBio-1705) <sup>1</sup>H NMRFigure S25. Compound 10b (LASSBio-1705) <sup>13</sup>C NMR

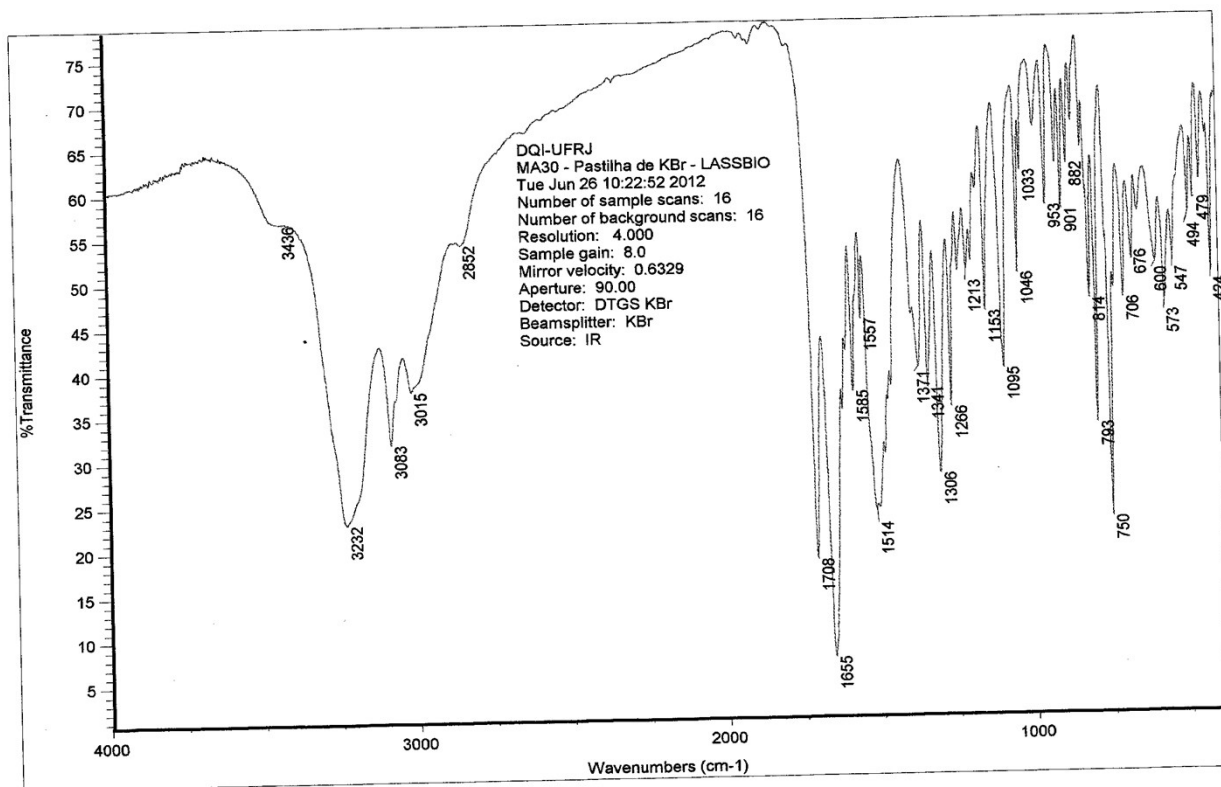


Figure S26. Compound 10b (LASSBio-1705) IR

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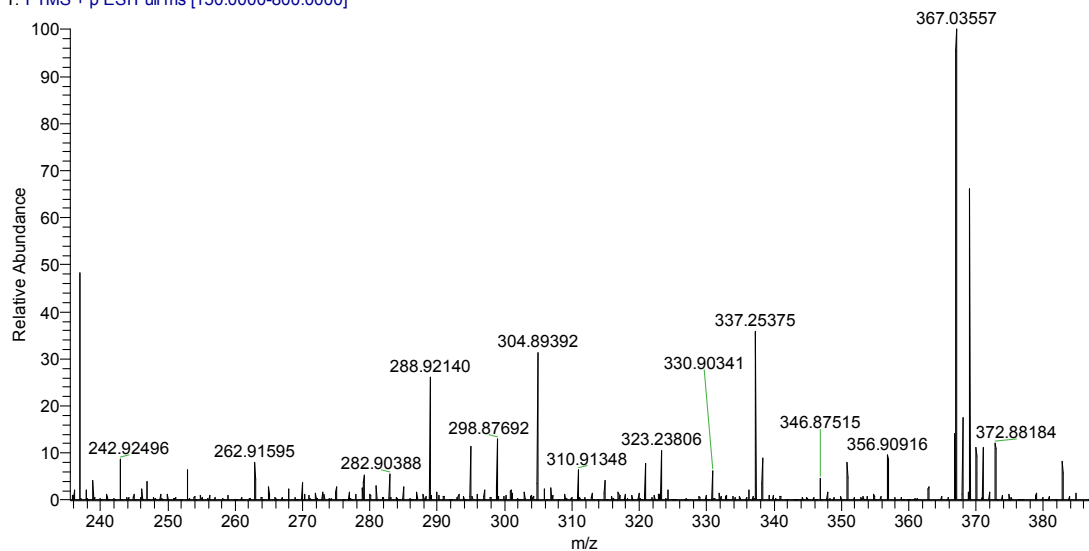
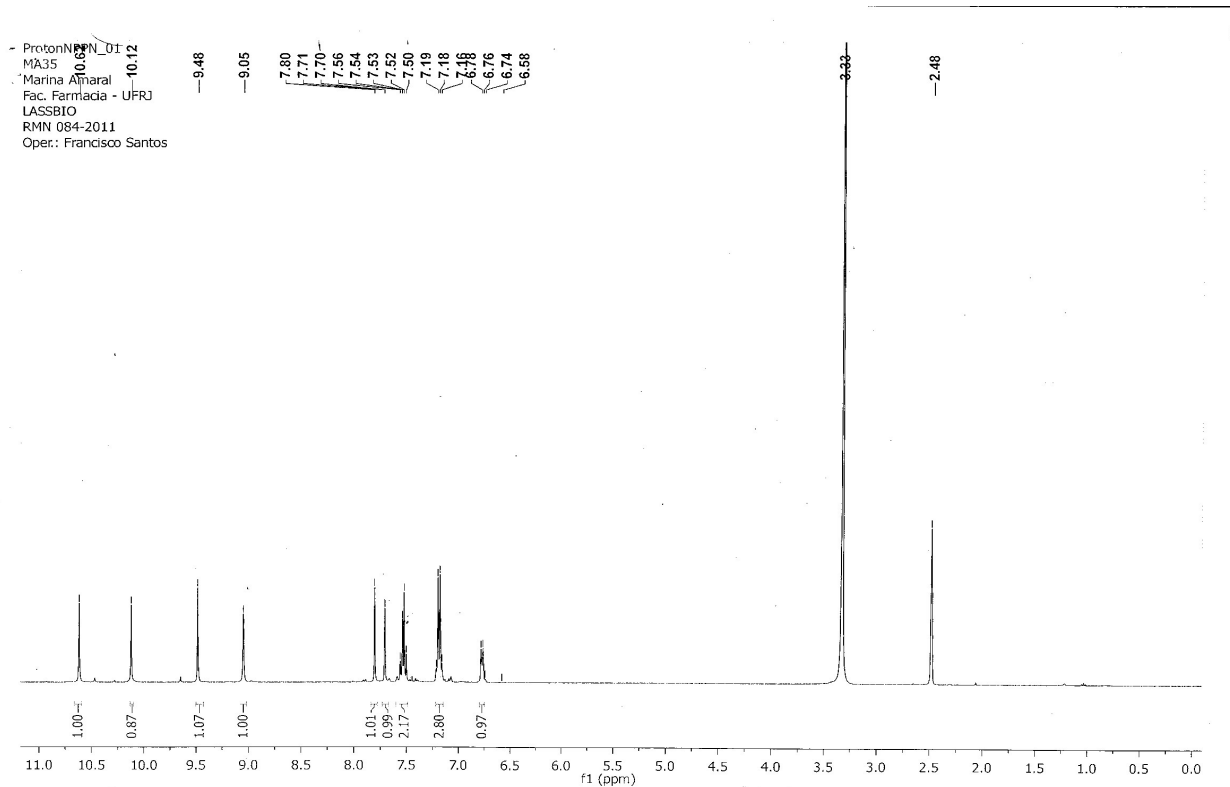


Figure S27. Compound 10b (LASSBio-1705) HRMS

Figure S28. Compound 10c (LASSBio-1708)  $^1\text{H}$  NMR

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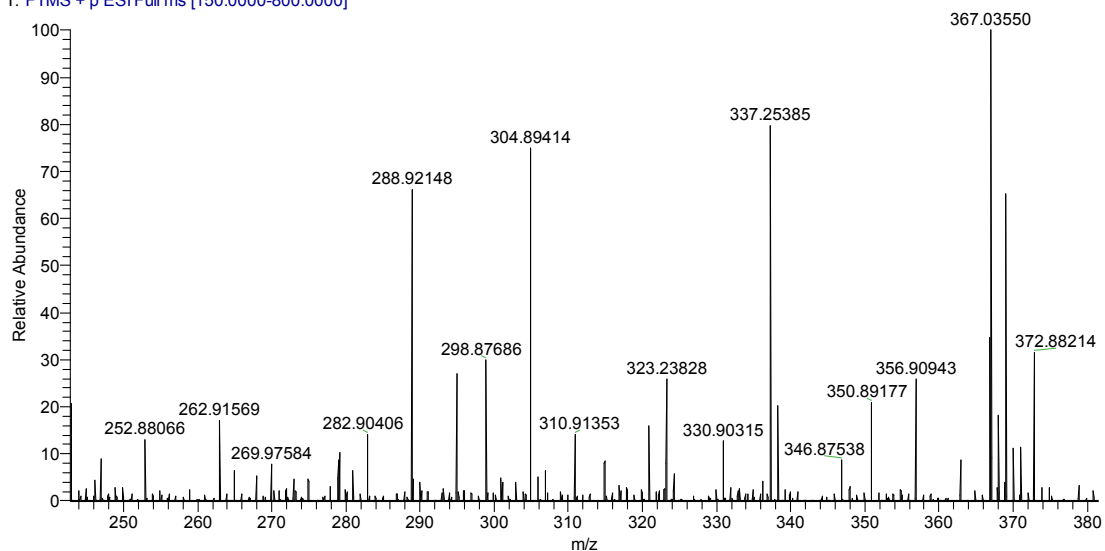
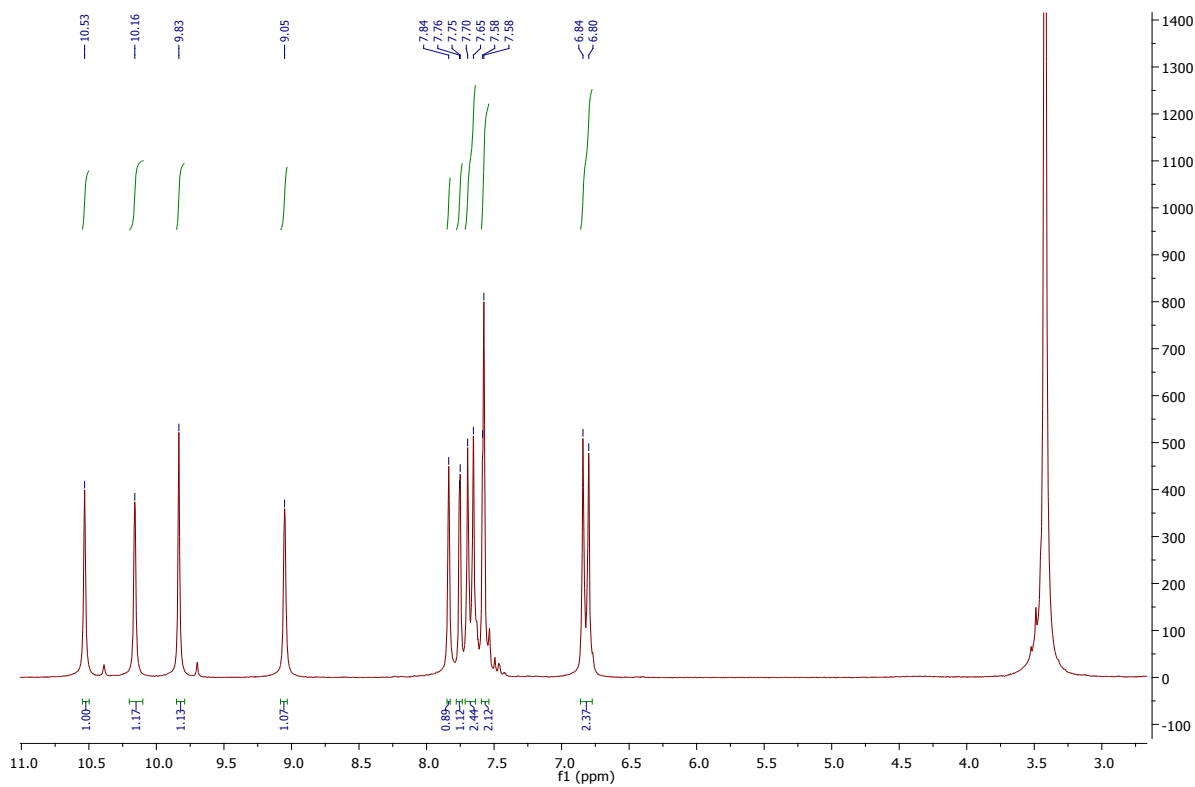
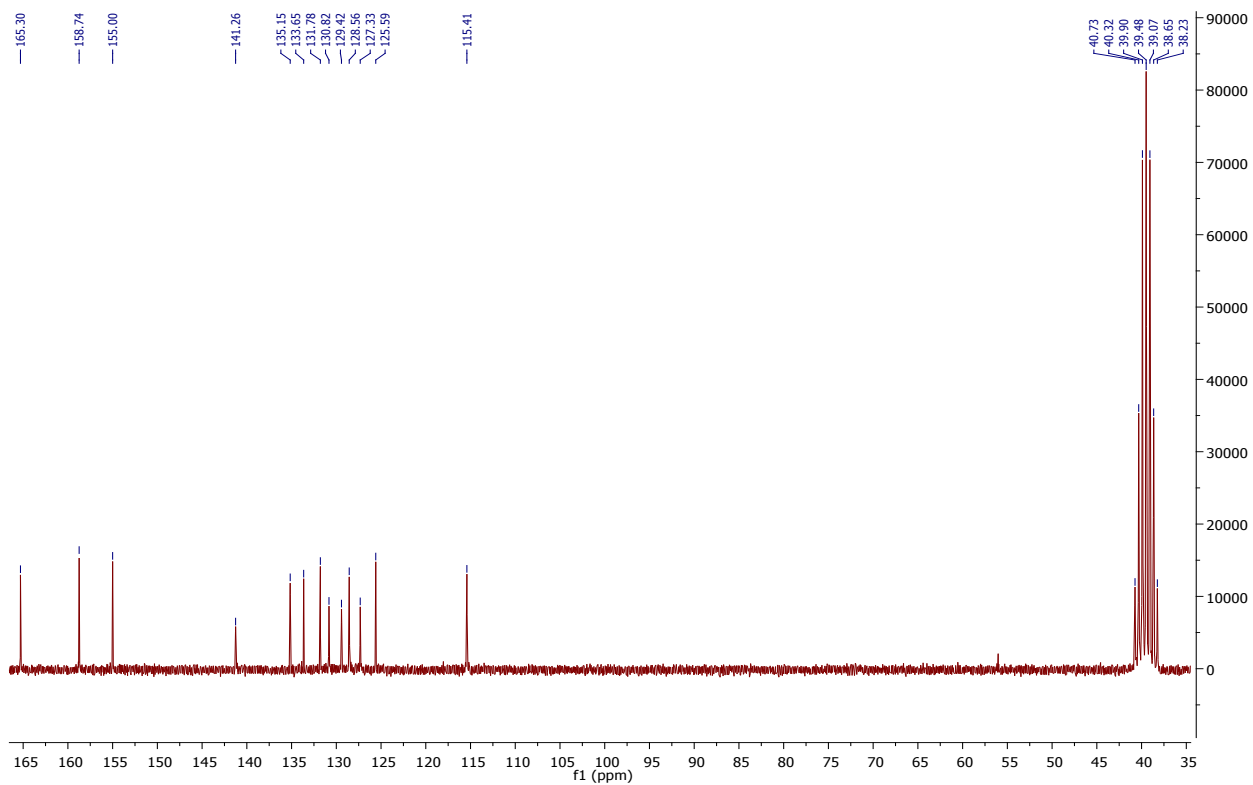
1708 #29-38 RT: 0.20-0.25 AV: 5 SM: 7G NL: 3.48E6  
T: FTMS + p ESI Full ms [150.0000-800.0000]

Figure S29. Compound 10c (LASSBio-1708) HRMS



Figure S30. Compound 10d (LASSBio-1707) <sup>1</sup>H NMRFigure S31. Compound 10d (LASSBio-1707) <sup>13</sup>C NMR

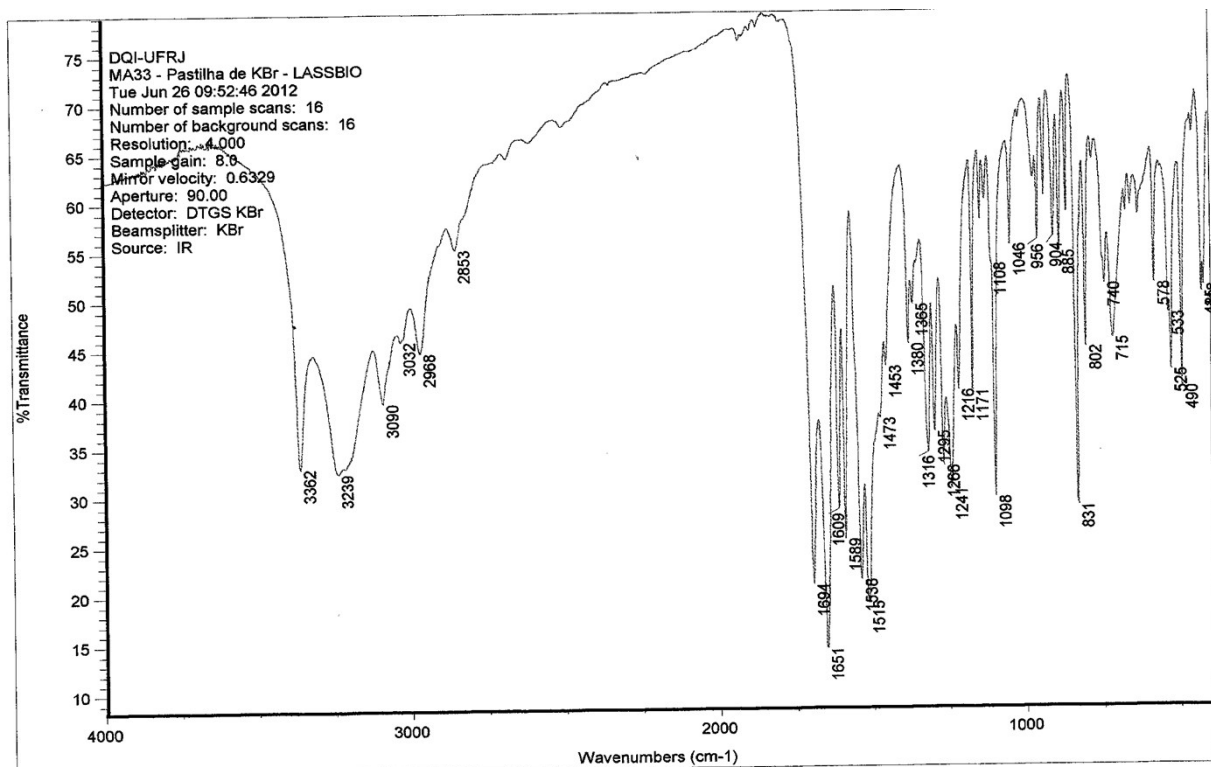


Figure S32. Compound 10d (LASSBio-1707) IR

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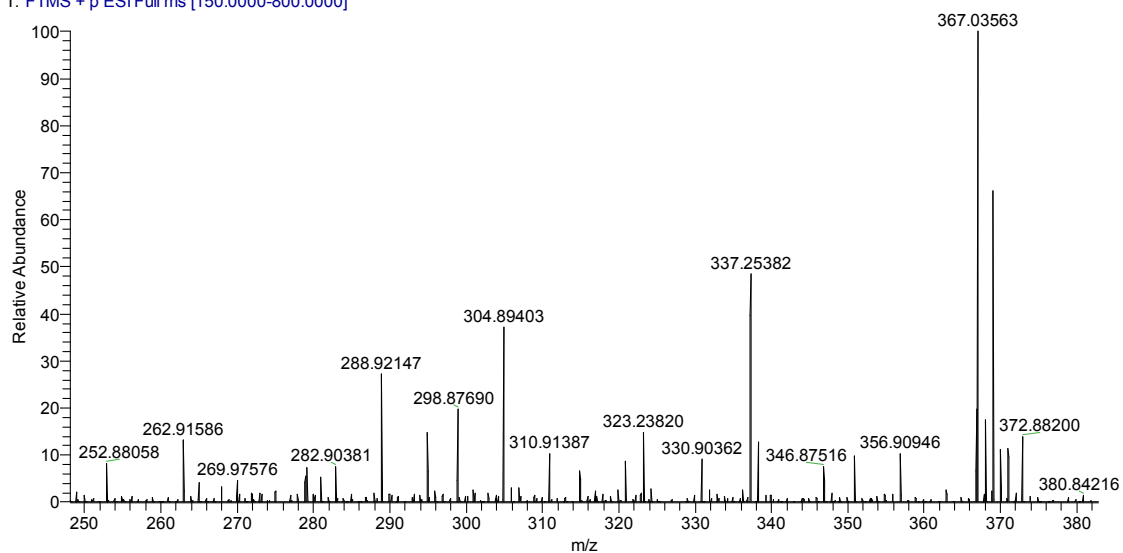
1707 #25-35 RT: 0.17-0.24 AV: 6 SM: 7G NL: 5.27E6  
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Figure S33. Compound 10d (LASSBio-1707) HRMS

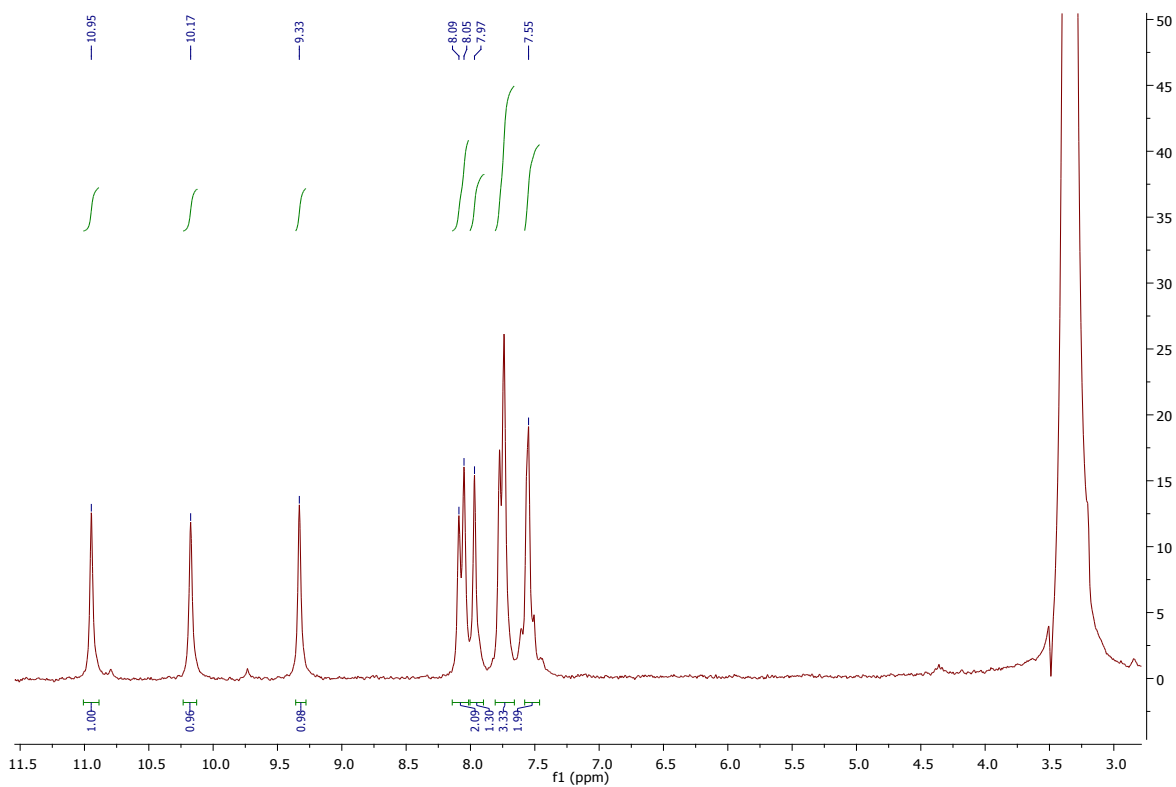
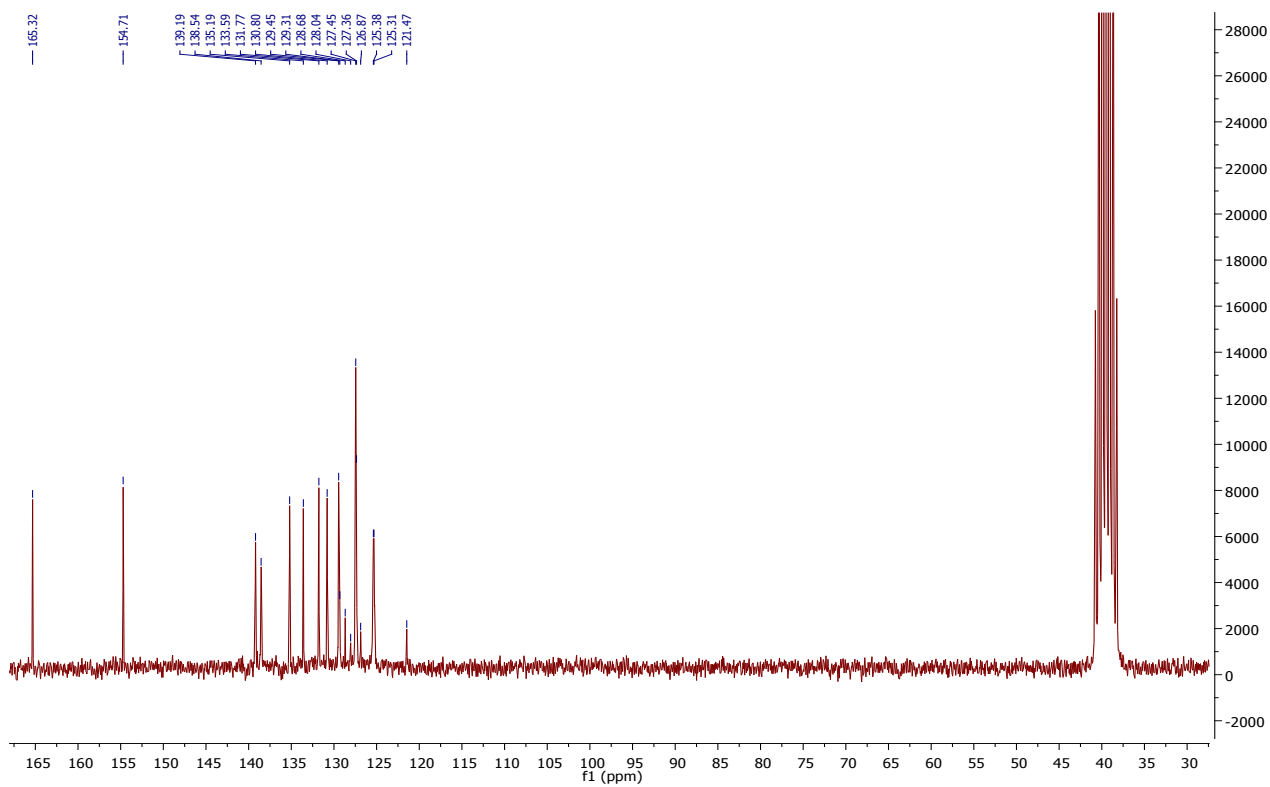
Figure S34. Compound 10e (LASSBio-1736)  $^1\text{H}$  NMR

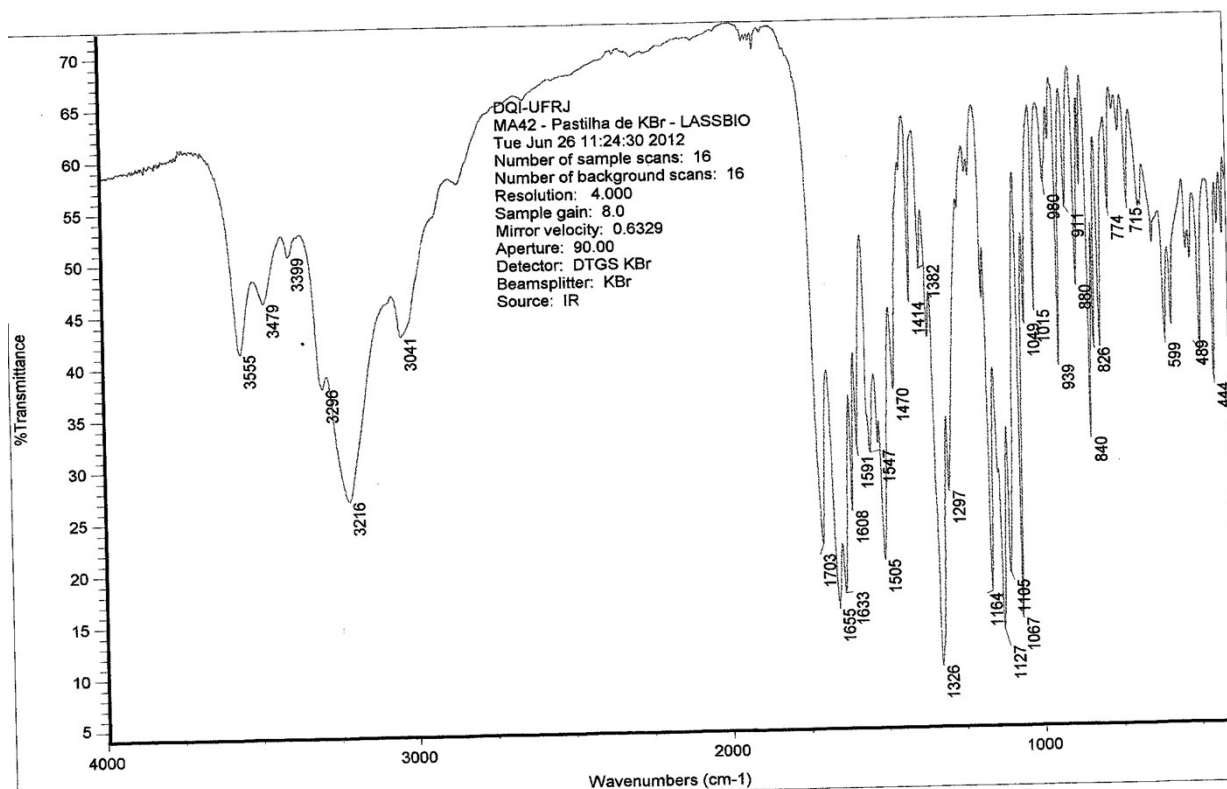
Figure S35. Compound 10e (LASSBio-1736)  $^{13}\text{C}$  NMR

Figure S36. Compound 10e (LASSBio-1736) IR

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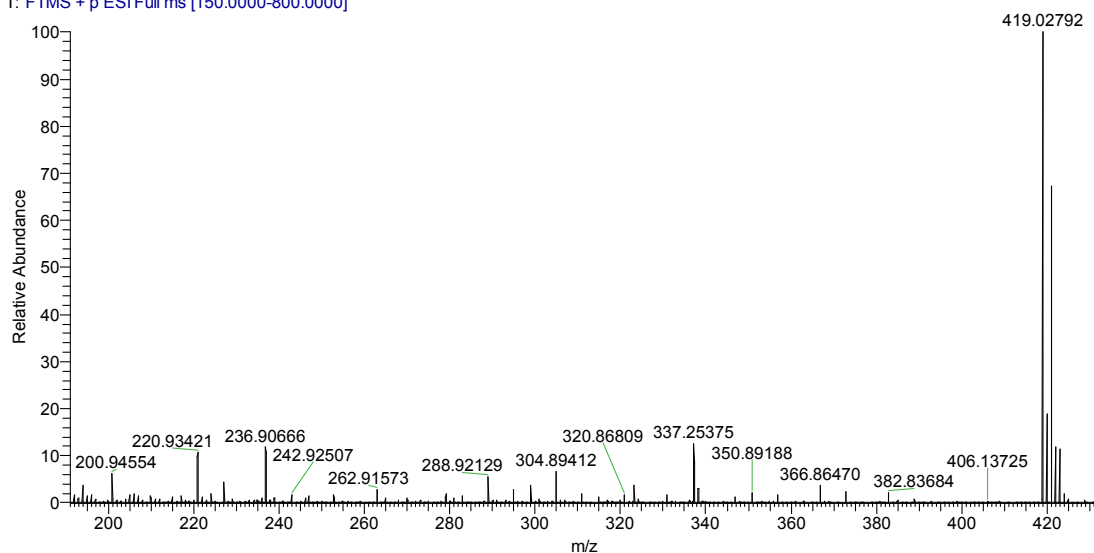
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T: FTMS + p ESI Full ms [150.0000-800.0000]

Figure S37. Compound 10e (LASSBio-1736) HRMS

Table S1. Crystal data and refinement parameters of compound 9a (LASSBio-1491).

structural formula	(C <sub>13</sub> H <sub>10</sub> ClN <sub>5</sub> O <sub>5</sub> ) <sub>2</sub> (H <sub>2</sub> O)	
fw (g/mol)	721.43	
cryst syst	monoclinic	
space group	<i>P2<sub>1</sub>/c</i>	
<i>Z</i> / <i>Z'</i>	4/2	
<i>T</i> (K)	296(2)	
unit cell dimensions	<i>a</i> (Å)	11.666(5)
	<i>b</i> (Å)	8.002(5)
	<i>c</i> (Å)	33.179(5)
	$\beta$ (°)	99.513(5)
<i>V</i> (Å <sup>3</sup> )	3055(2)	
calculated density (Mg/m <sup>3</sup> )	1.569	
absorption coefficient $\mu$ (mm <sup>-1</sup> )	0.291	
$\theta$ range for data collection (°)	3.101 to 26.154	
index ranges	<i>h</i>	-13 to 13
	<i>k</i>	-8 to 9
	<i>l</i>	-39 to 39
data collected	35580	
unique reflections	5317	
unique reflections with $I > 2\sigma(I)$	2282	
symmetry factor ( $R_{\text{int}}$ )	0.1930	
completeness to $\theta_{\text{max}}$ (%)	97.3	
<i>F</i> (000)	1480	
parameters refined	468	
goodness-of-fit on $F^2$	0.952	

final $R1$ factor for $I > 2\sigma(I)$	0.0594
final $wR2$ factor for all data	0.1689
largest diff. peak / hole ( $e/\text{\AA}^3$ )	0.220 and -0.256
CCDC deposit number	1824217

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#### Chemical stability pH 7.4

In a 10 mL tube, 5  $\mu\text{L}$  (250 ng/mL) of LASSBio-1736 (10e) (stock concentration = 10000 ng/mL solubilized in DMSO) was added in 195  $\mu\text{L}$  of PBS (pH=7.4), and the mixture was placed in a shaker at 37°C under vigorous stirring for 0 and 240 minutes. After each reaction time, the mixture was submitted to a liquid-liquid extraction method with 800  $\mu\text{L}$  TBME (tert-Butyl methyl ether)/ ethyl acetate (1:1) containing 100 ng/mL of ketoconazole (internal standard) which were then vortexed for 1 minute. The samples extracted were then centrifuged at 3000 rpm for 5 minutes and transferred 500  $\mu\text{L}$  of the organic phases to clean microtubes and evaporated under a nitrogen stream at 40 °C. The samples were resuspended with 100  $\mu\text{L}$  of a methanol:water mixture (7:3) containing and were placed in 2 mL vials, and analyzed by UPLC-MS.

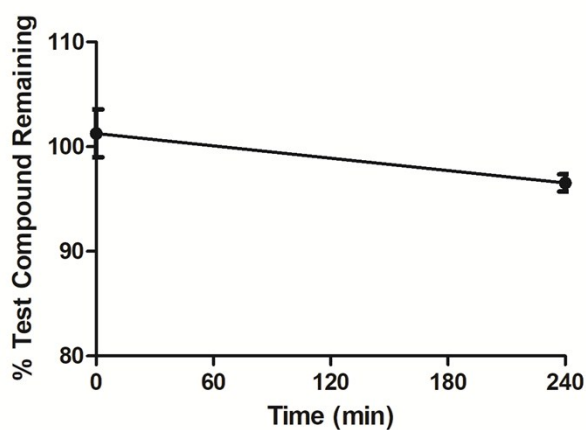


Figure S38. Chemical stability of 10e (LASSBio-1736). Data were analyzed by UPLC-MS and obtained through the compound recovery percentage expressed as mean  $\pm$  standard error average of triplicates of a representative experiment.