

Novel Isoniazid-Carborane Hybrids Active *in vitro* Against *Mycobacterium tuberculosis*

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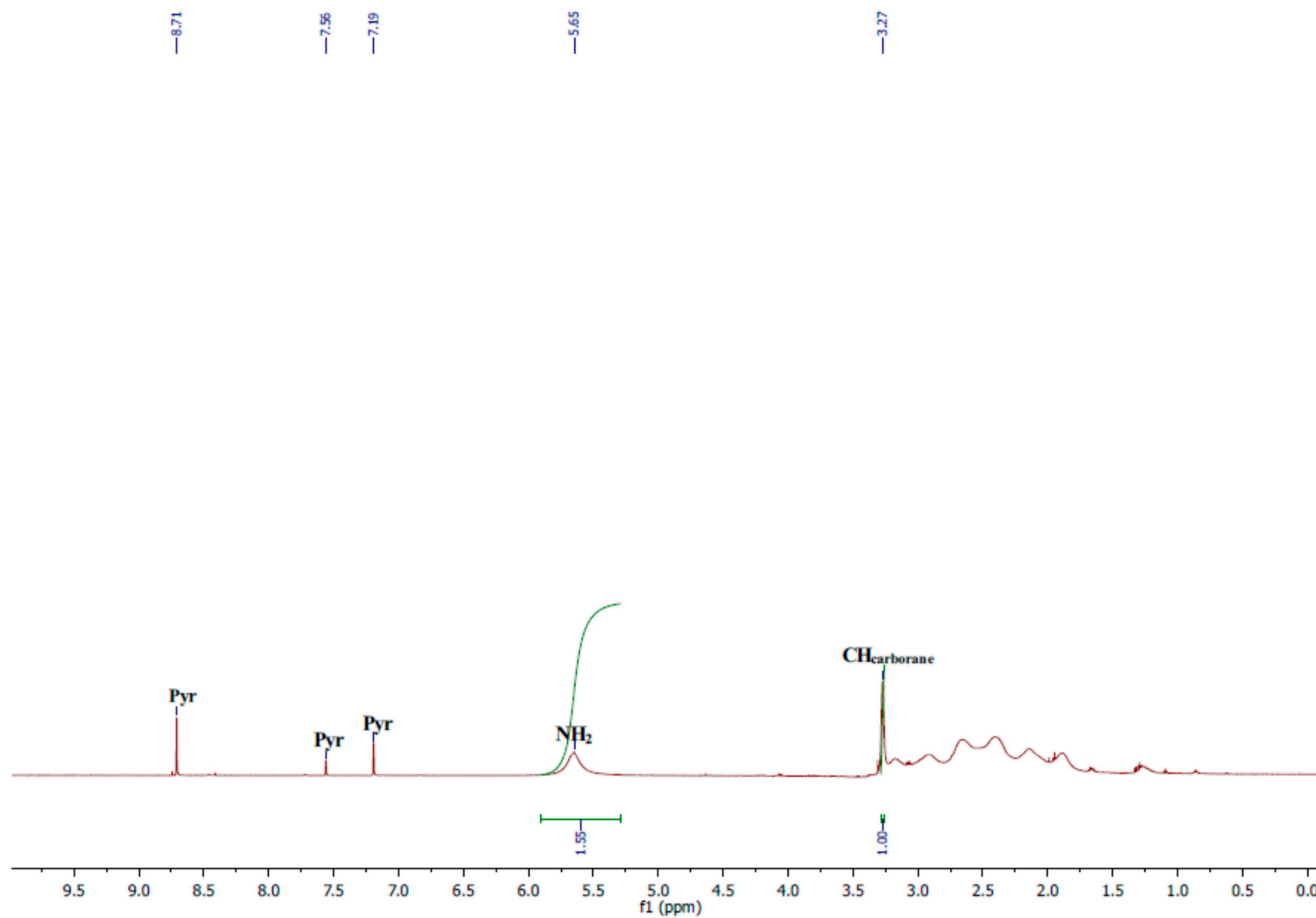


Figure S1. ¹H NMR spectrum of compound 3.

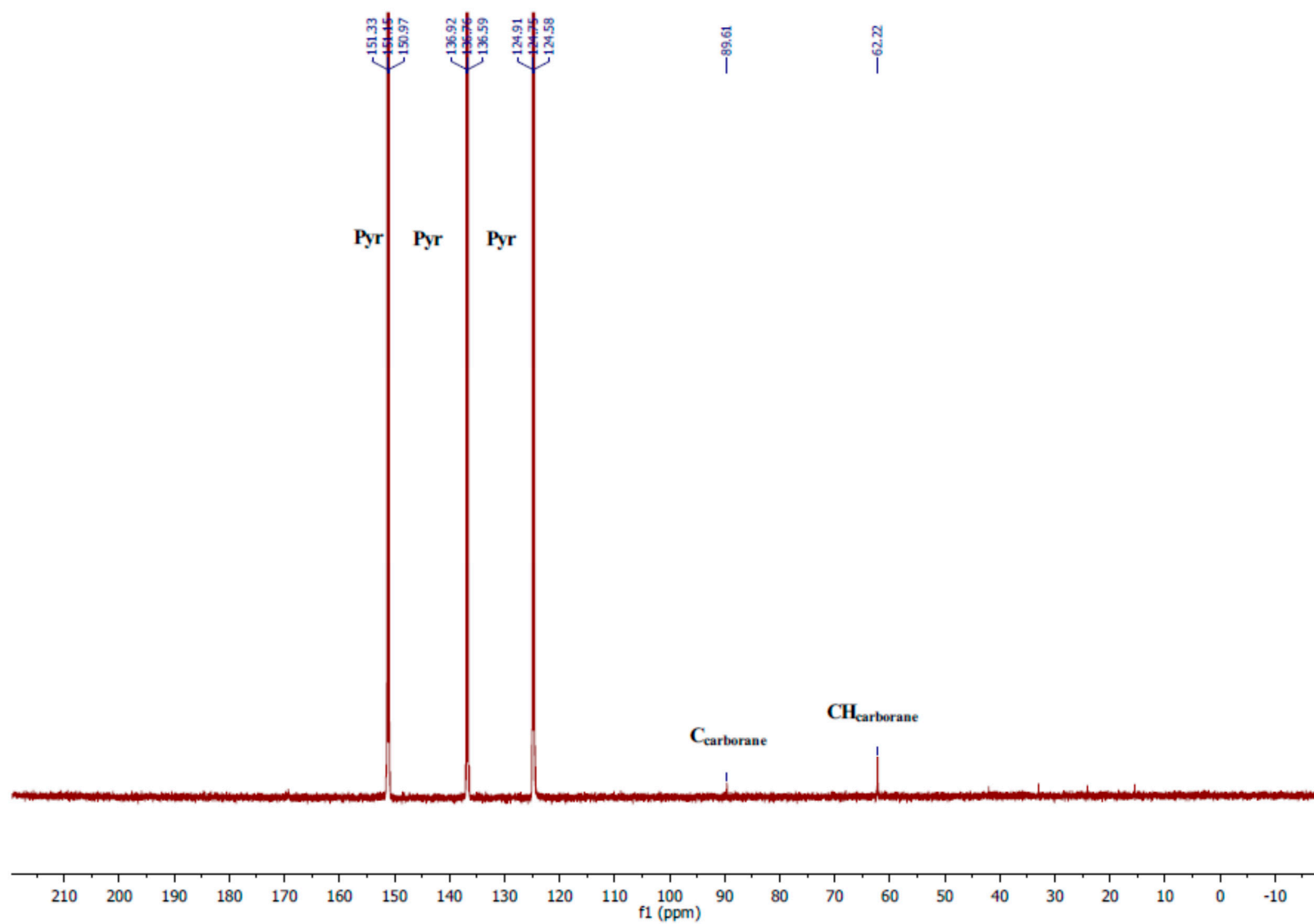


Figure S2. ^{13}C NMR spectrum of compound 3.

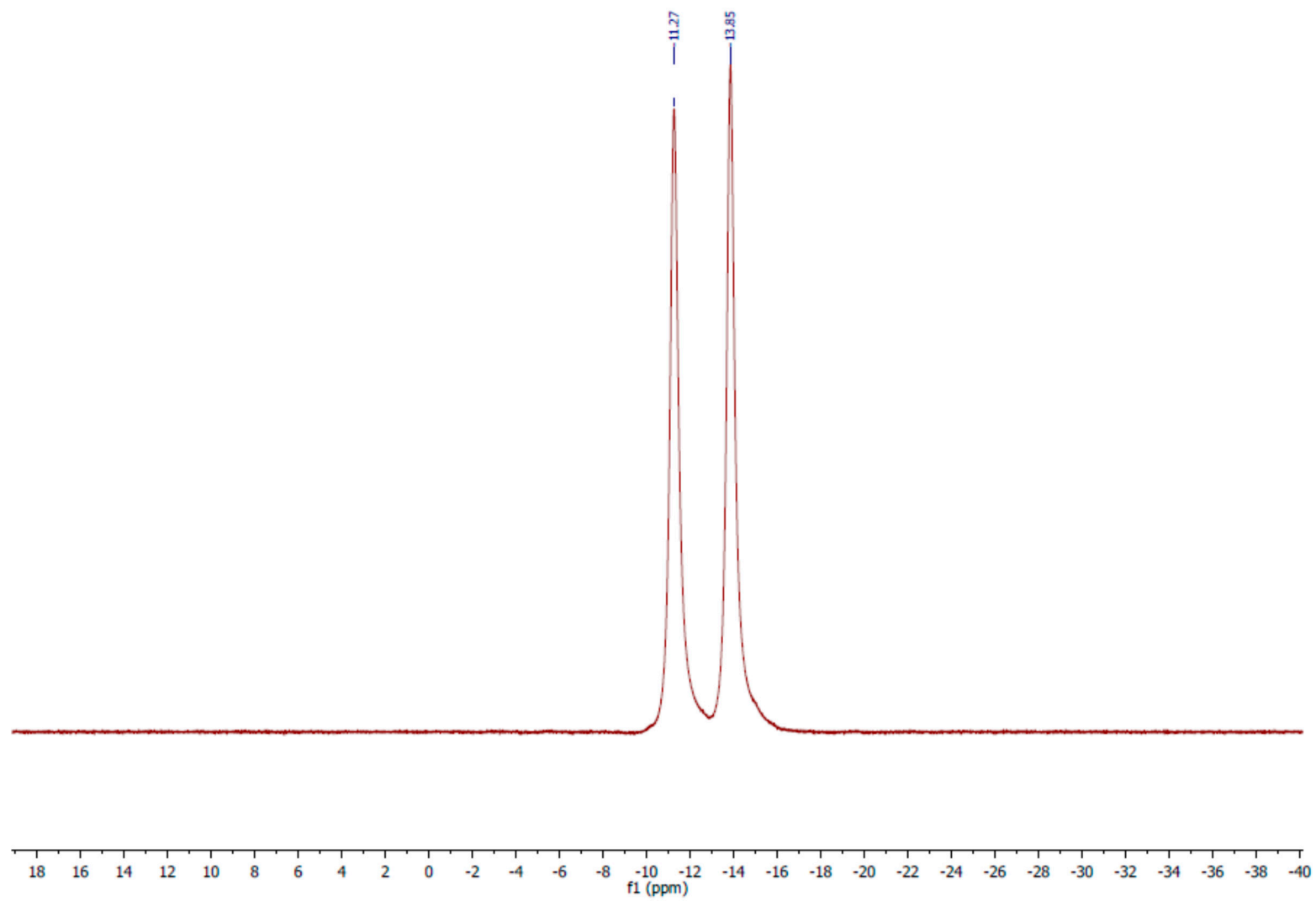


Figure S3. ^{11}B NMR {H BB} spectrum of compound 3.

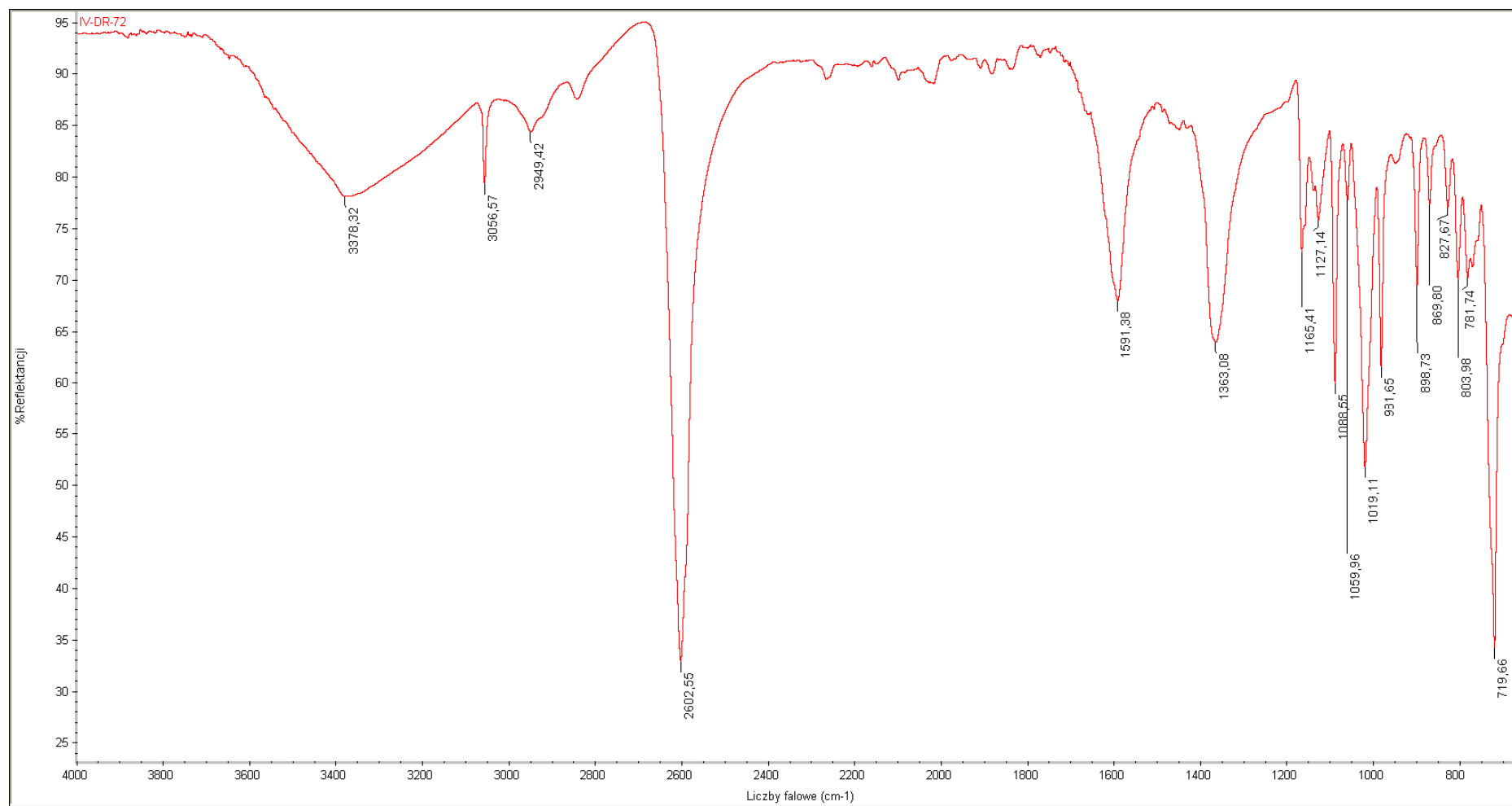


Figure S4. IR spectrum of compound 3.

Spectrum Name: iv-dr-56-t3_g
Start Ion: 100
End Ion: 250
Source: APCI + 10.0 μ A 400C
Capillary: 150V 300C Offset: 25V Span: 0V

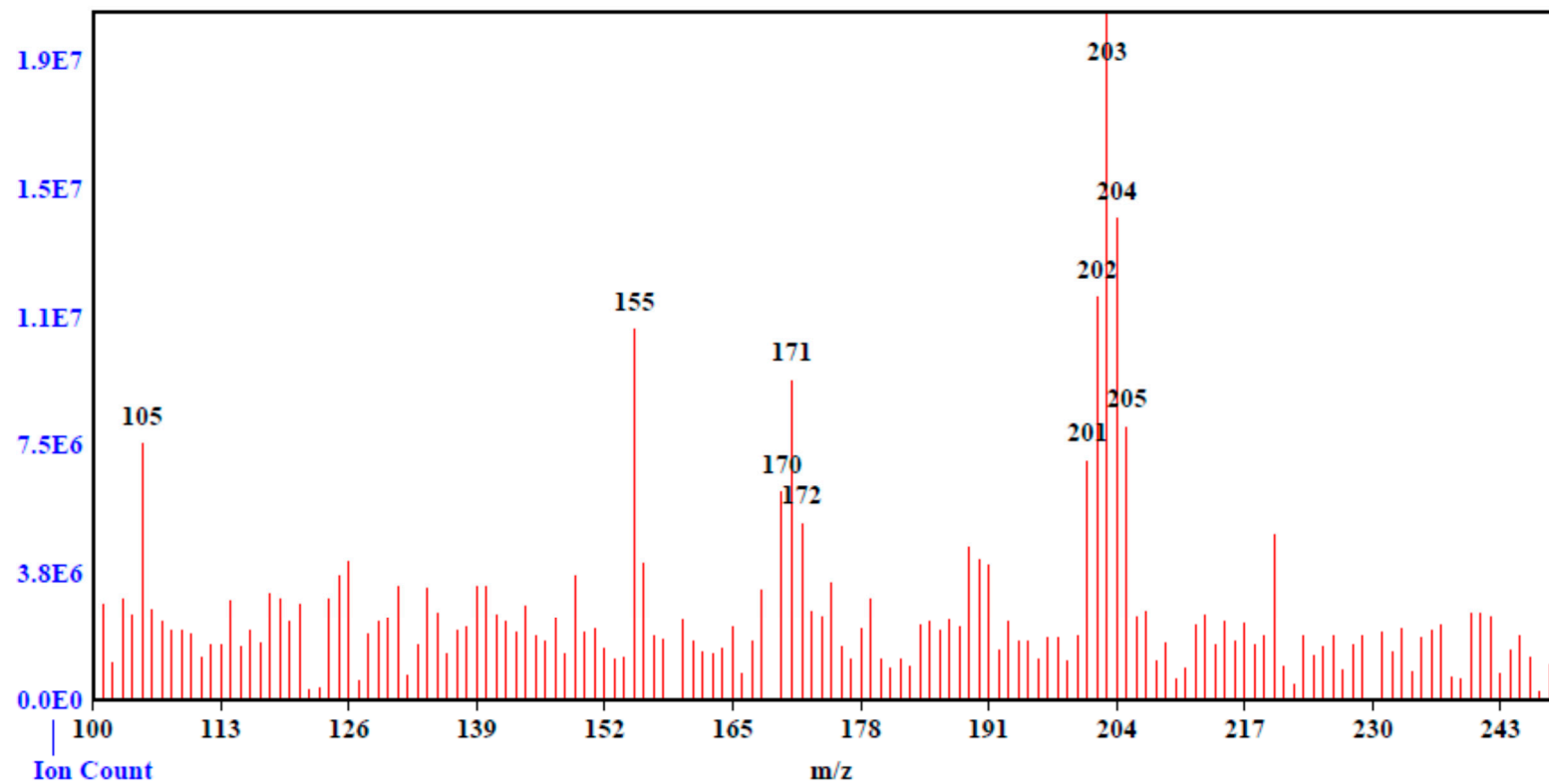


Figure S5. APCI-MS spectrum of compound 3.

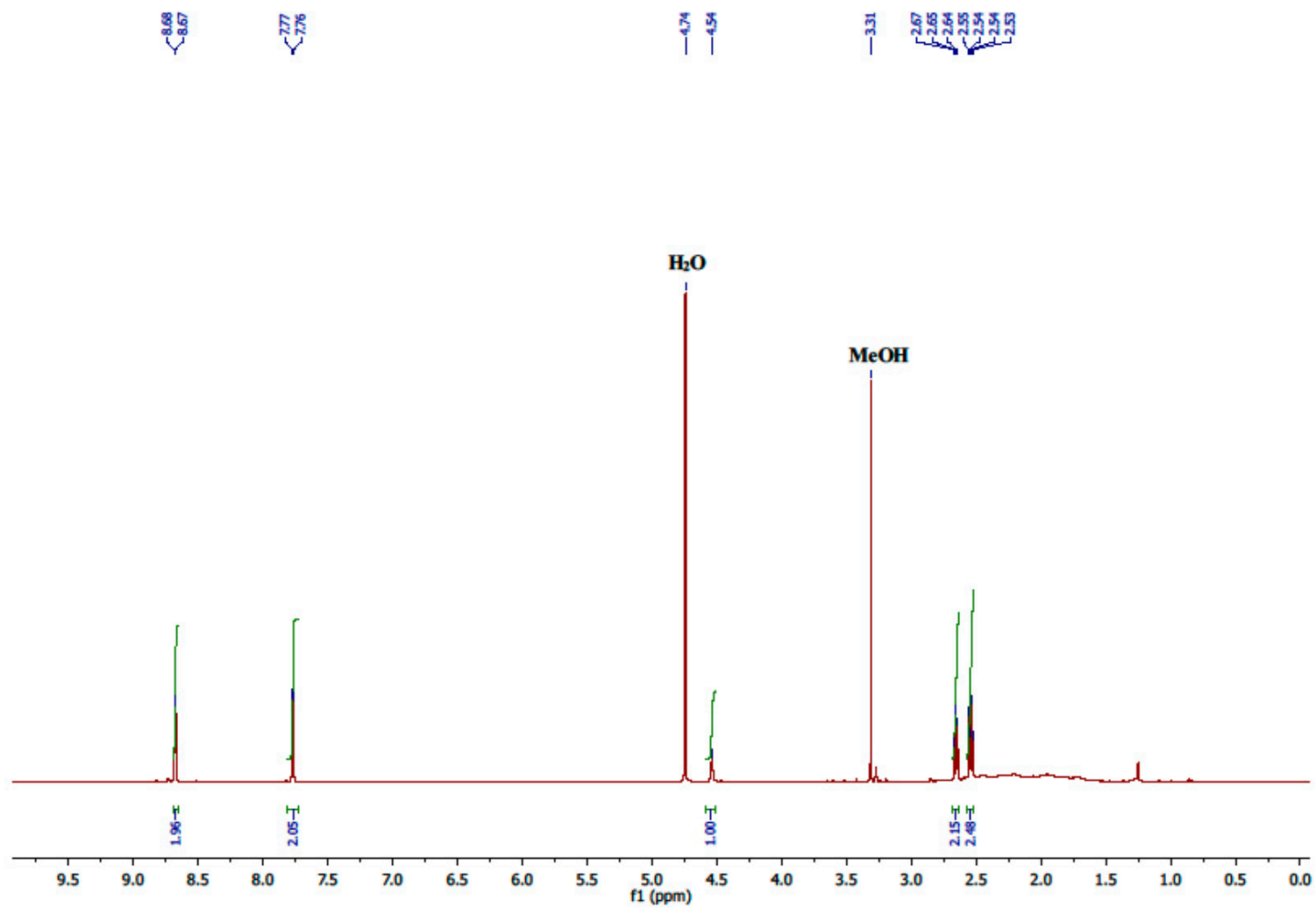


Figure S6. ¹H NMR spectrum of compound 8.

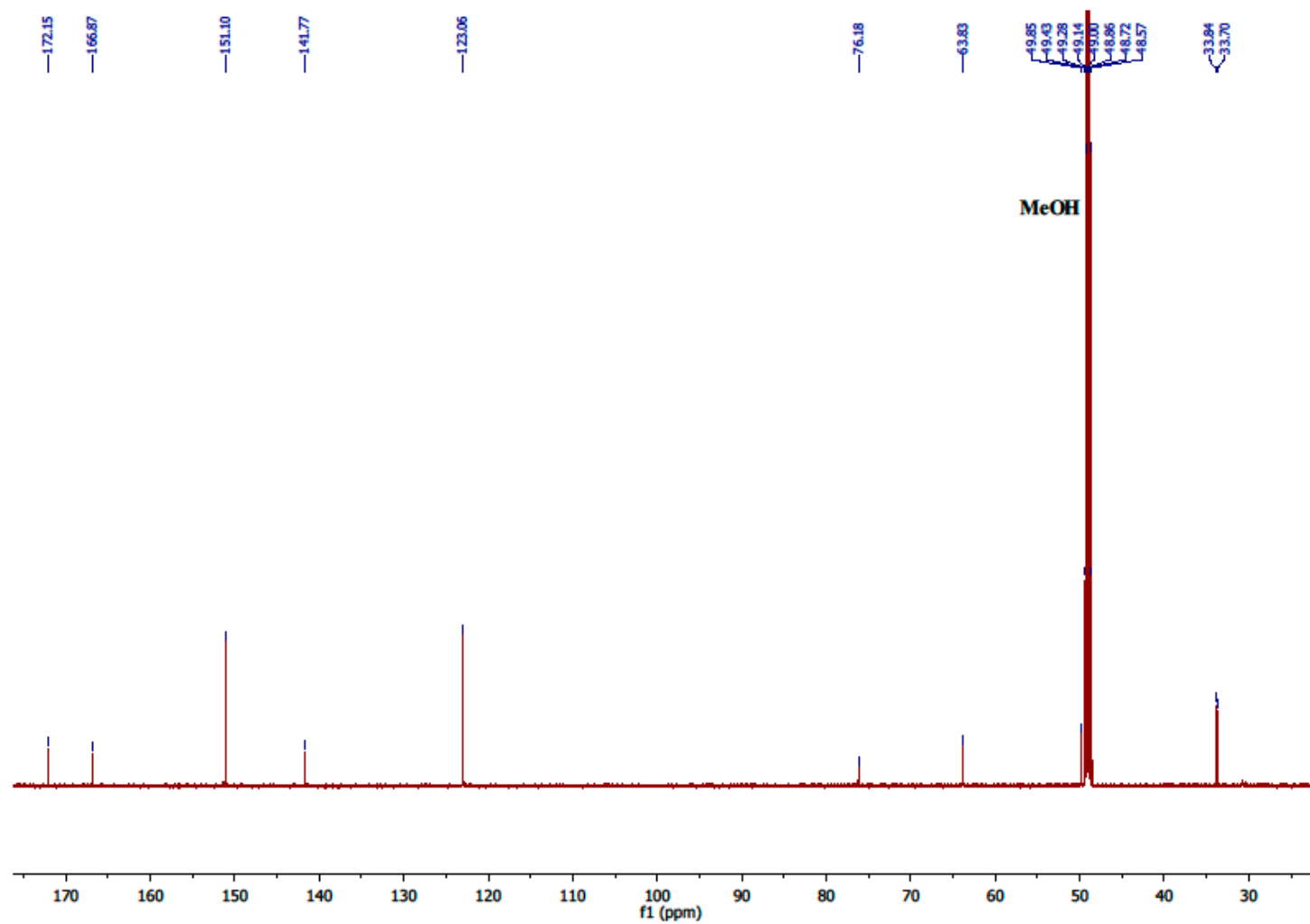


Figure S7. ¹³C NMR spectrum of compound 8.

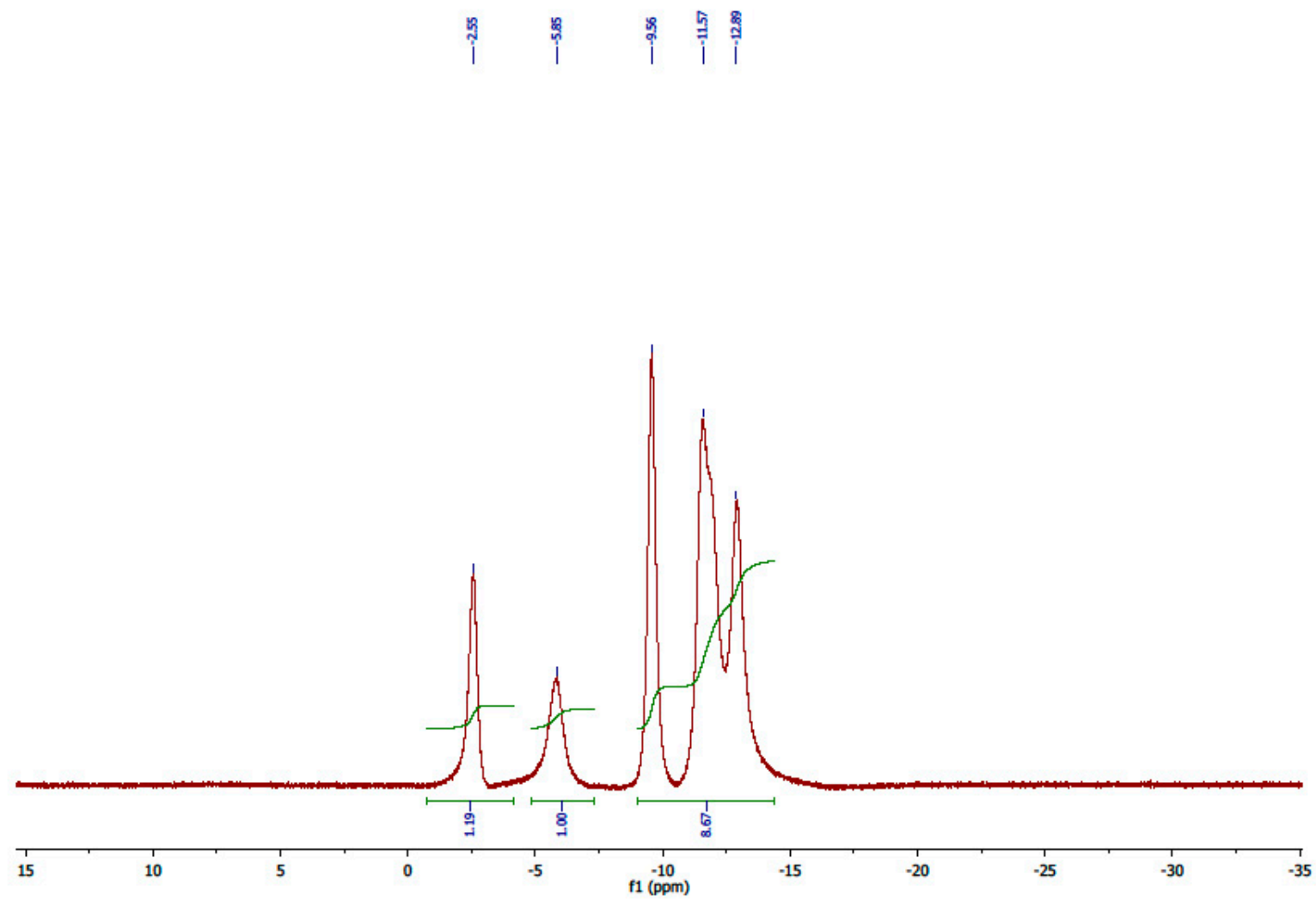


Figure S8. ^{11}B NMR {H BB} spectrum of compound 8.

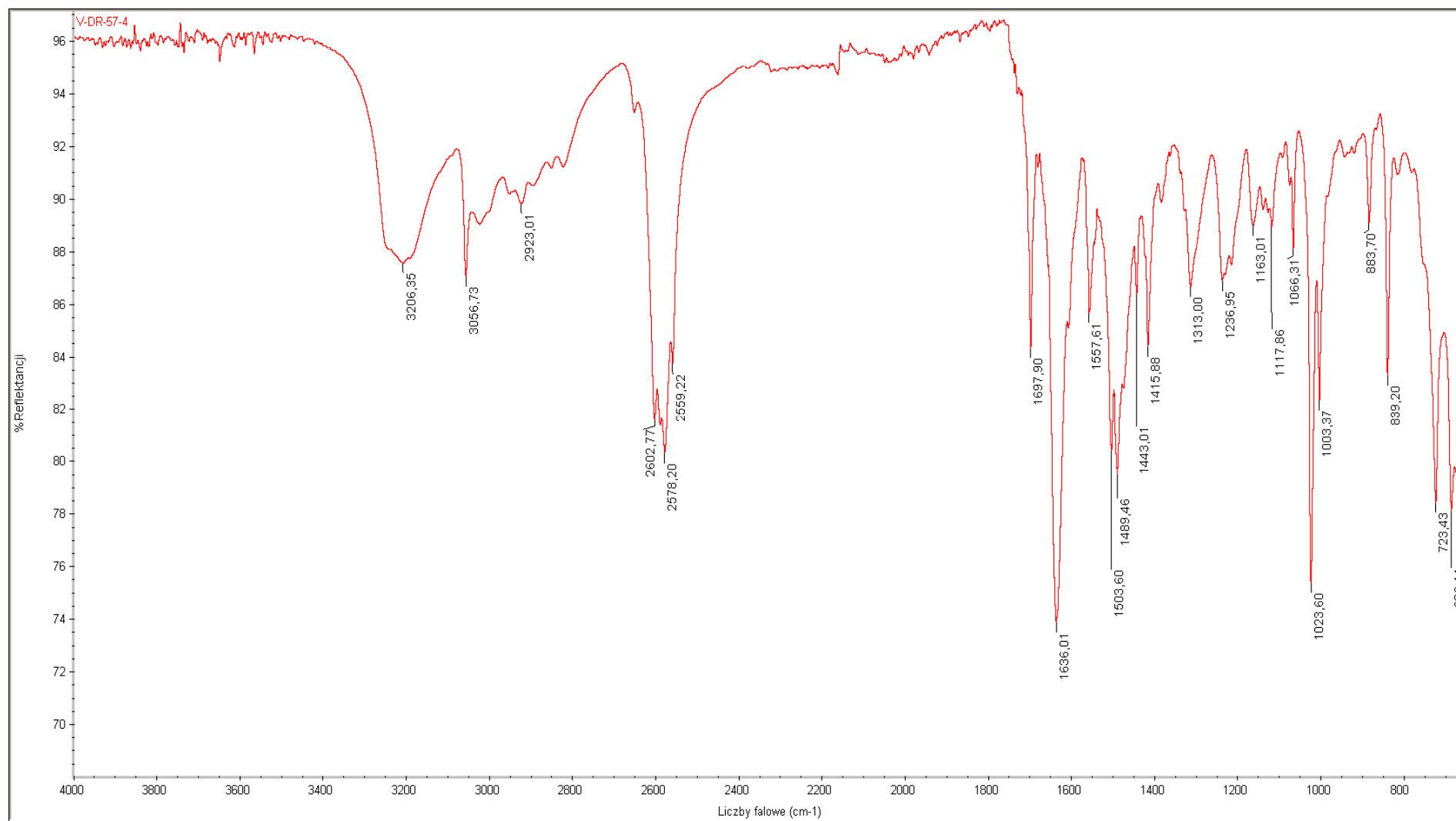


Figure S9. IR spectrum of compound 8.

Spectrum Name: V-DR-57-4_typ_dod2
Start Ion: 200
End Ion: 450
Source: APCI + 10.0 μ A 400C
Capillary: 150V 300C Offset: 25V Span: 0V

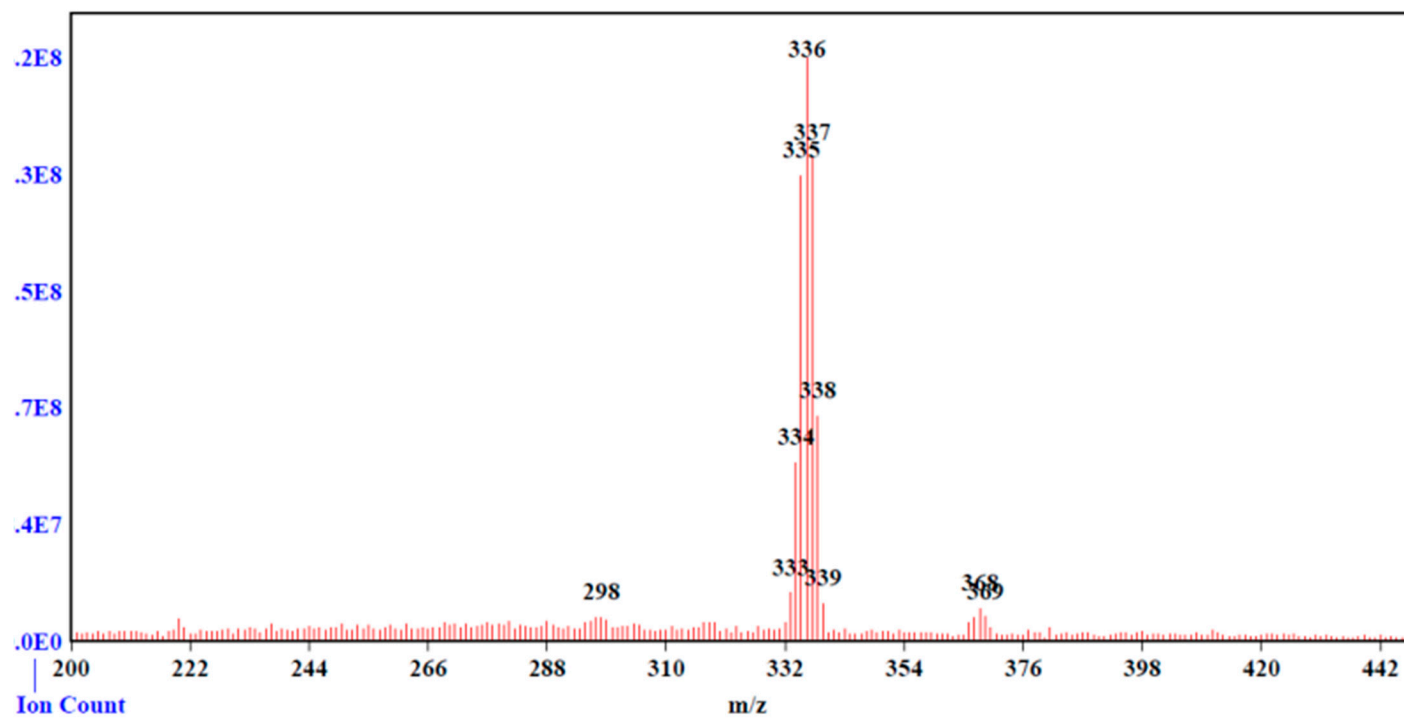


Figure S10. APCI-MS spectrum of compound 8.

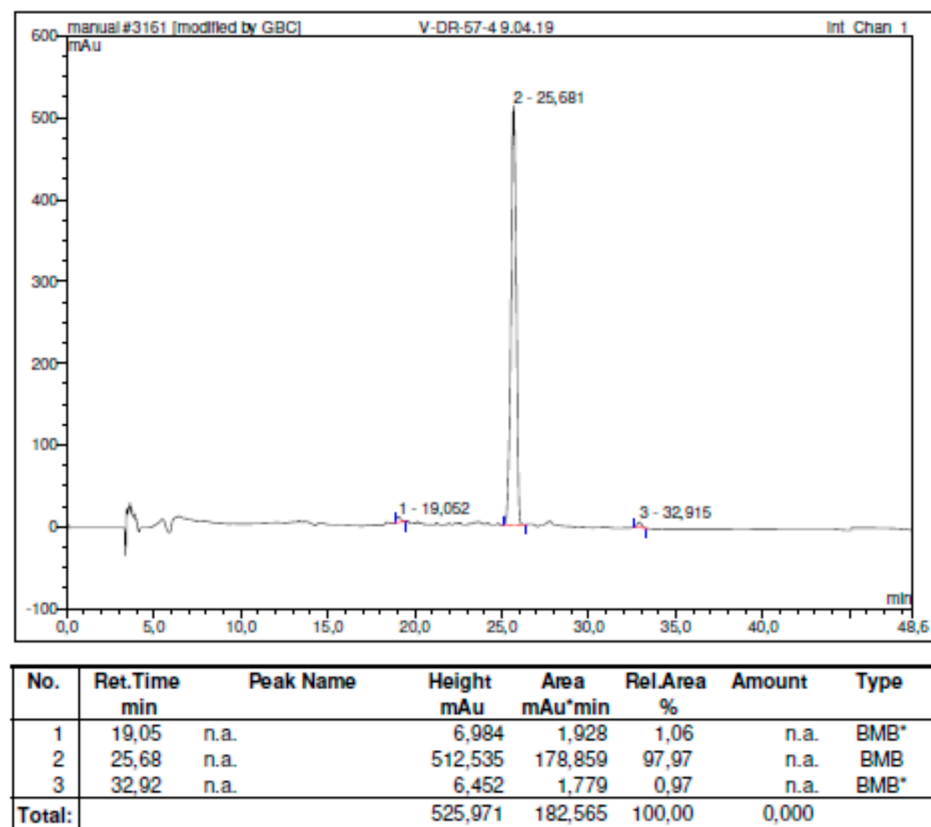


Figure S11. HPLC analysis of compound 8.

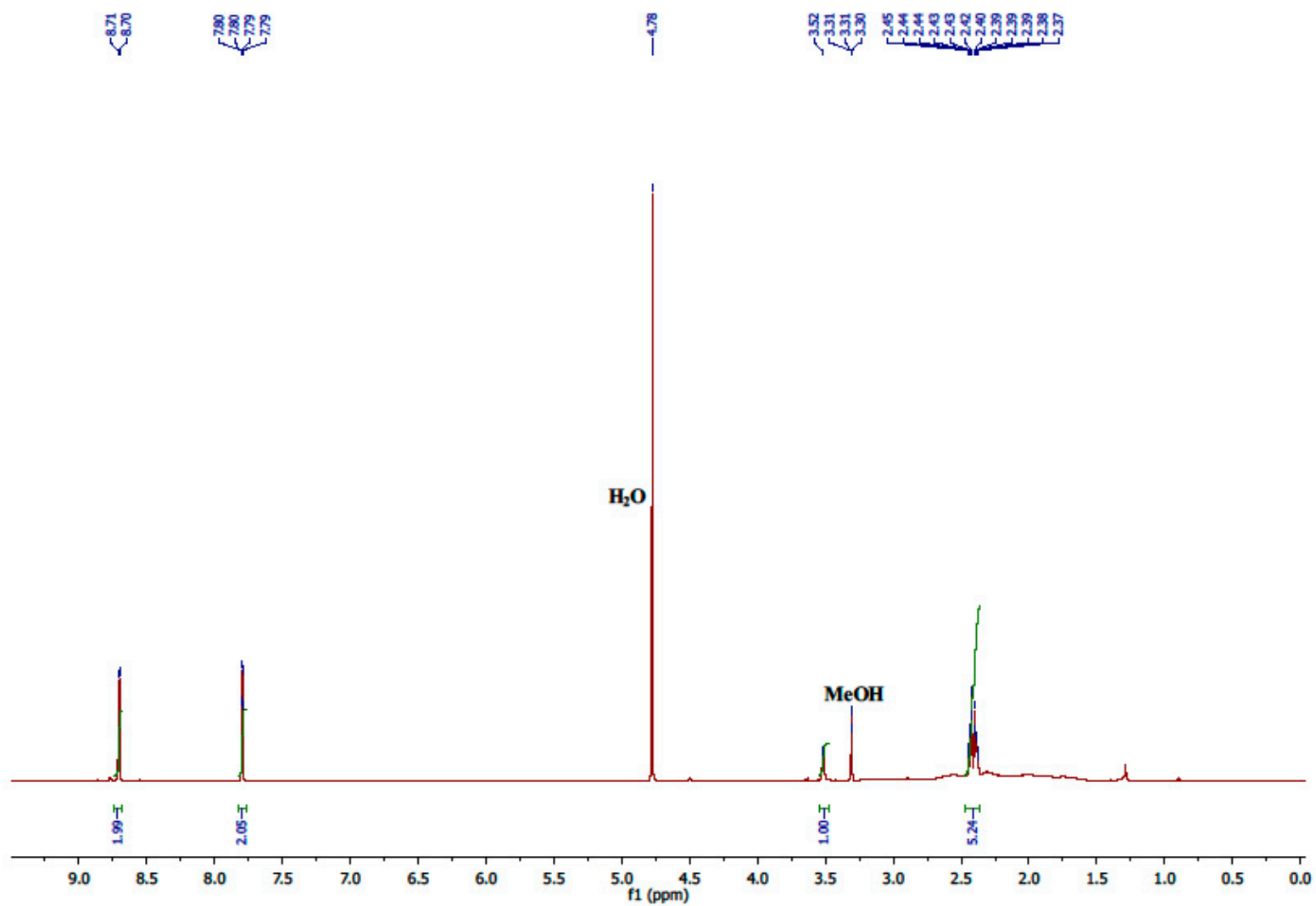


Figure S12. ¹H NMR spectrum of compound 9.

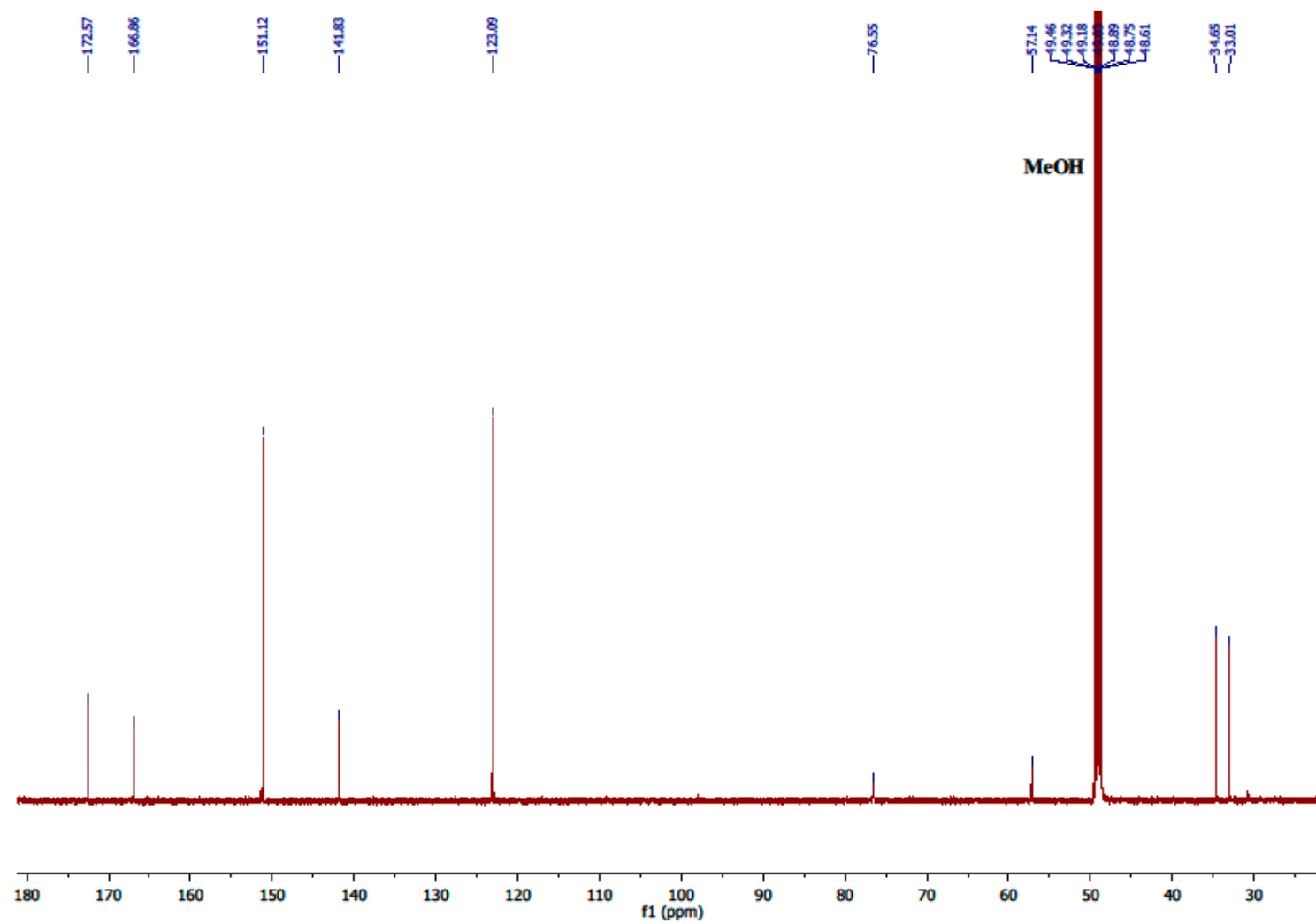


Figure S13. ¹³C NMR spectrum of compound 9.

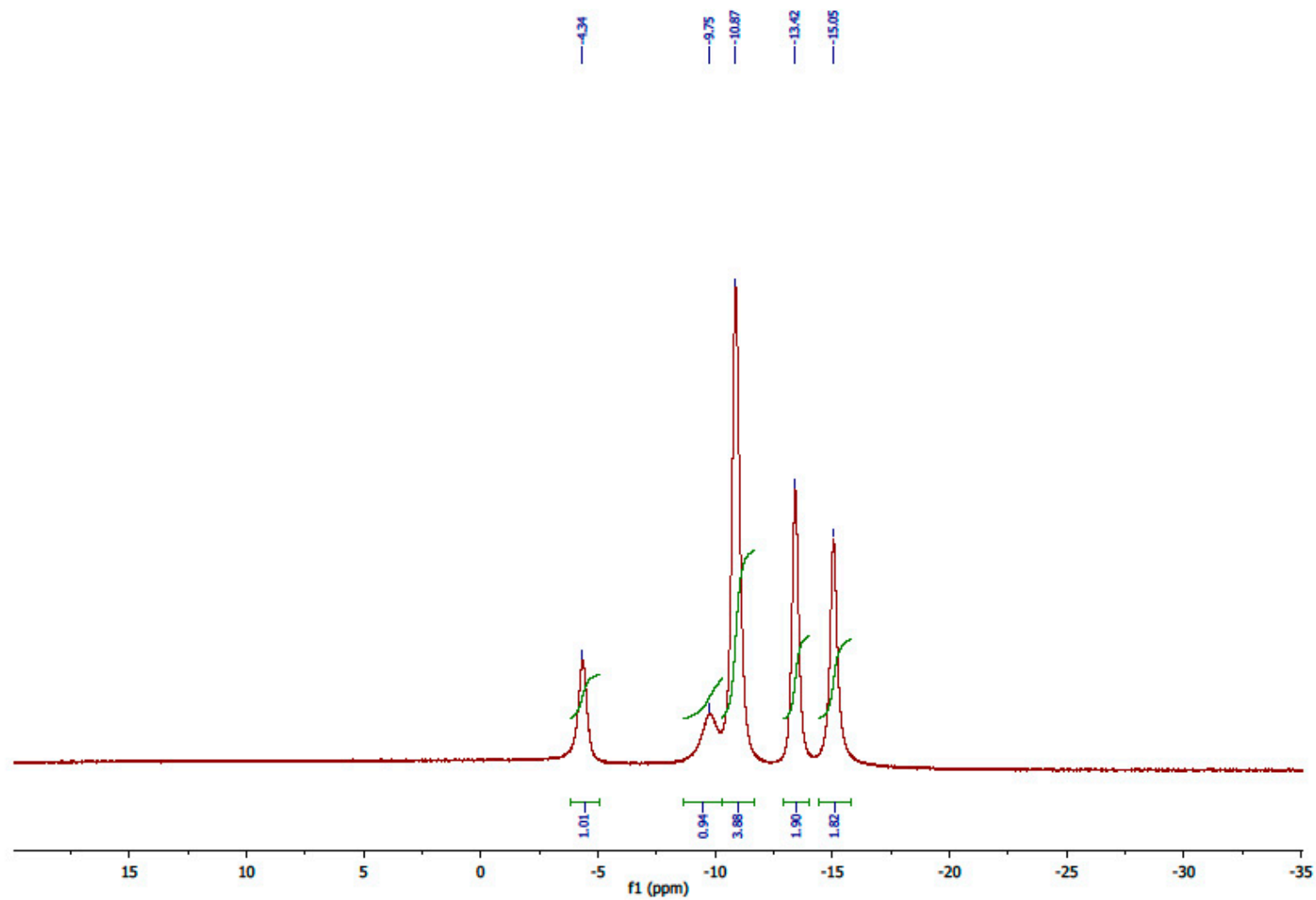


Figure S14. ^{11}B NMR {H BB} spectrum of compound 9.

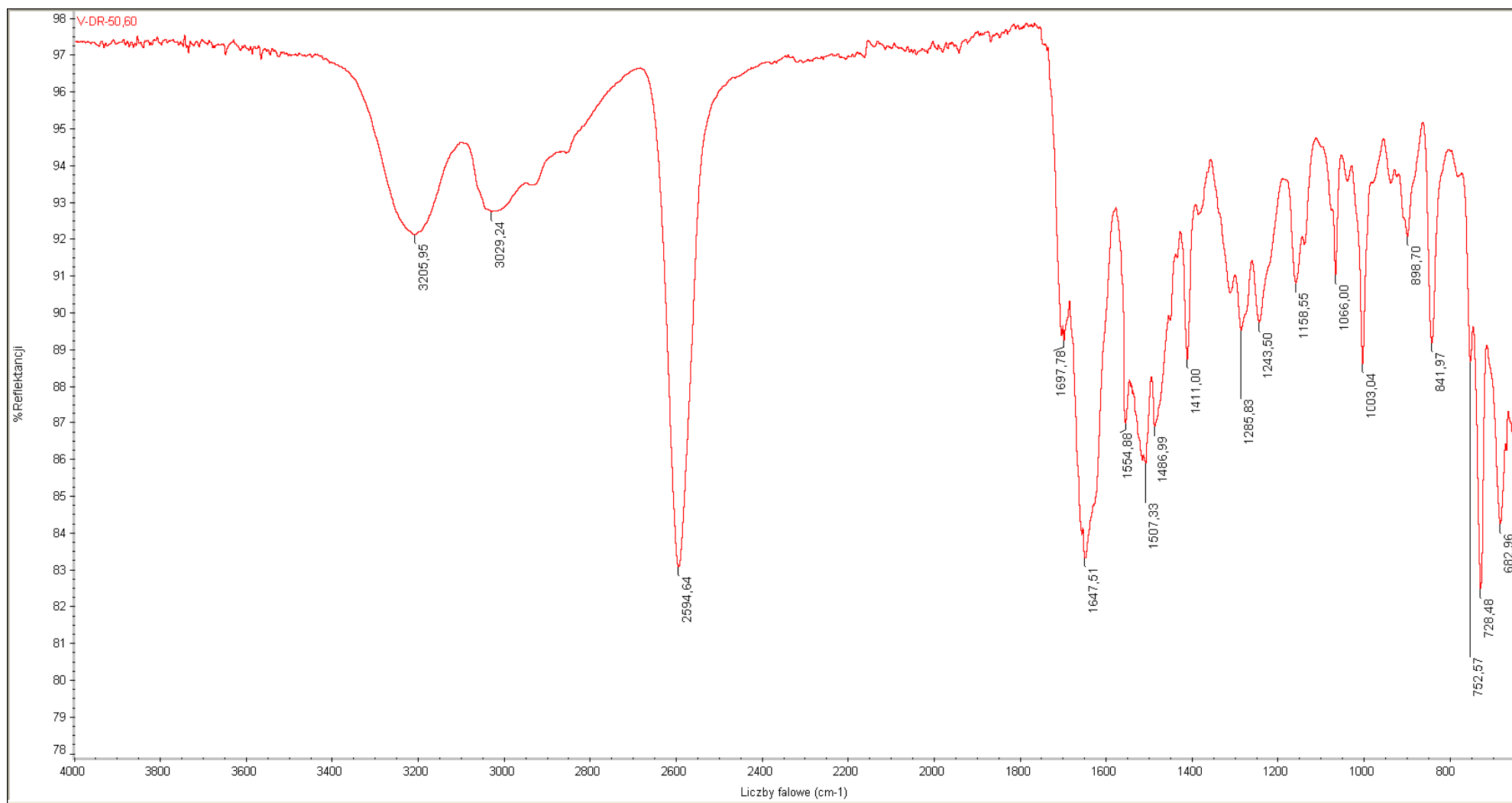


Figure S15. IR spectrum of compound 9.

Spectrum Name: V-DR-50_60_typ_dod2
Start Ion: 100
End Ion: 500
Source: APCI + 10.0 μ A 400C
Capillary: 150V 300C Offset: 25V Span: 0V

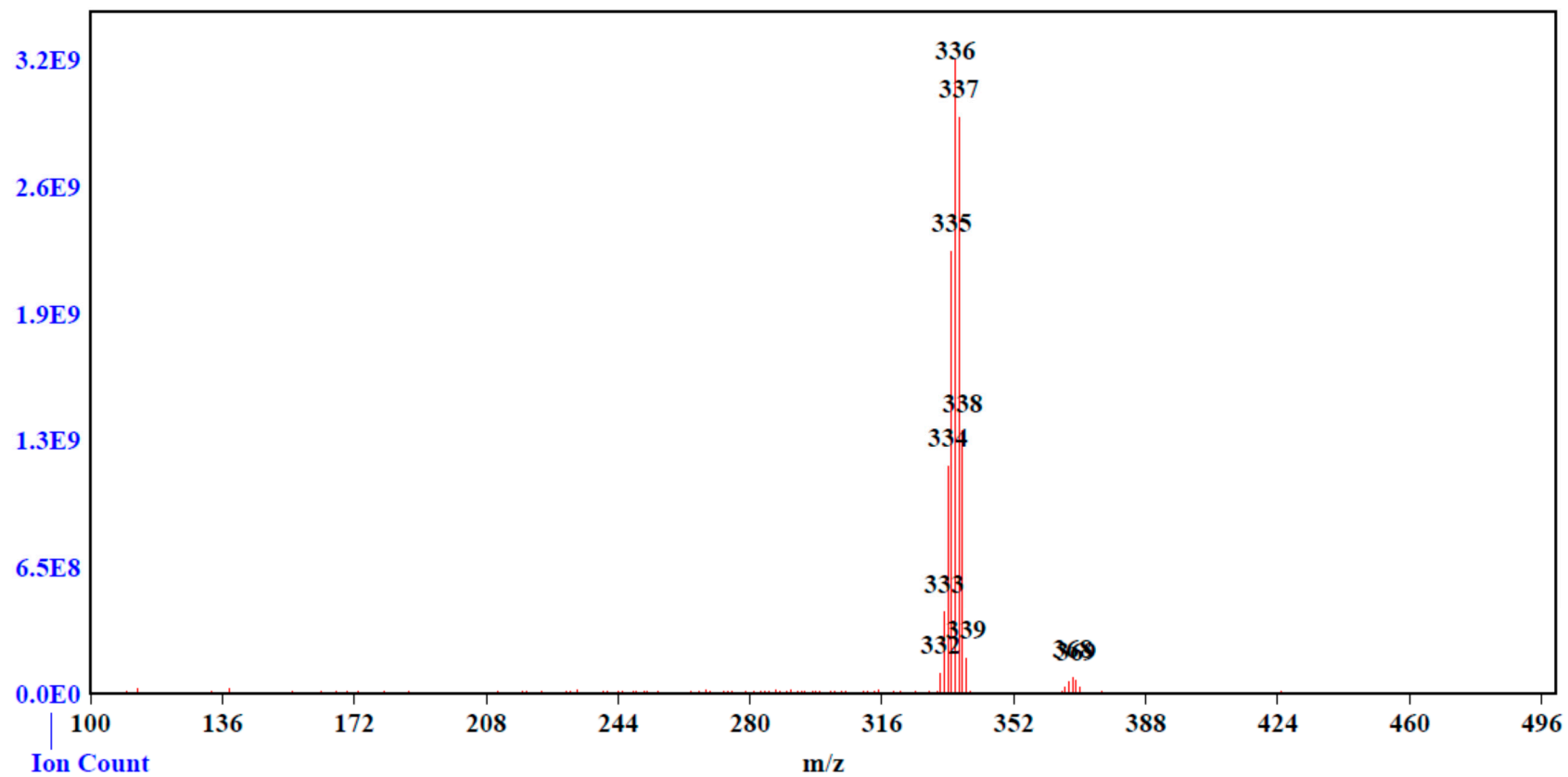


Figure S16. APCI-MS spectrum of compound 9.

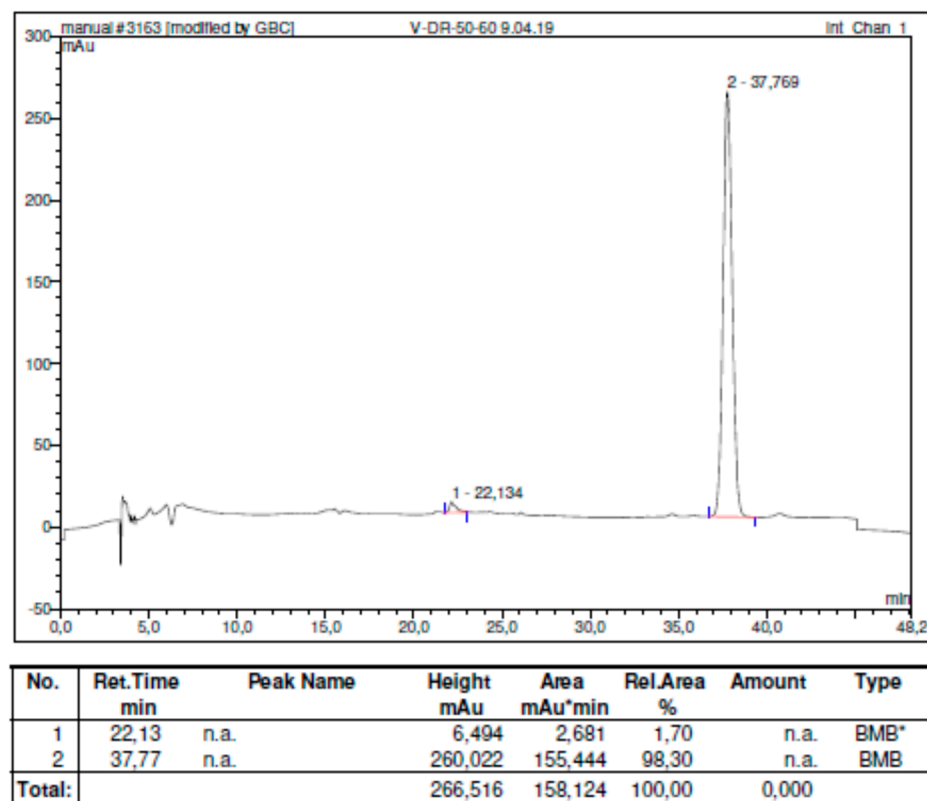


Figure S17. HPLC analysis of compound 9.

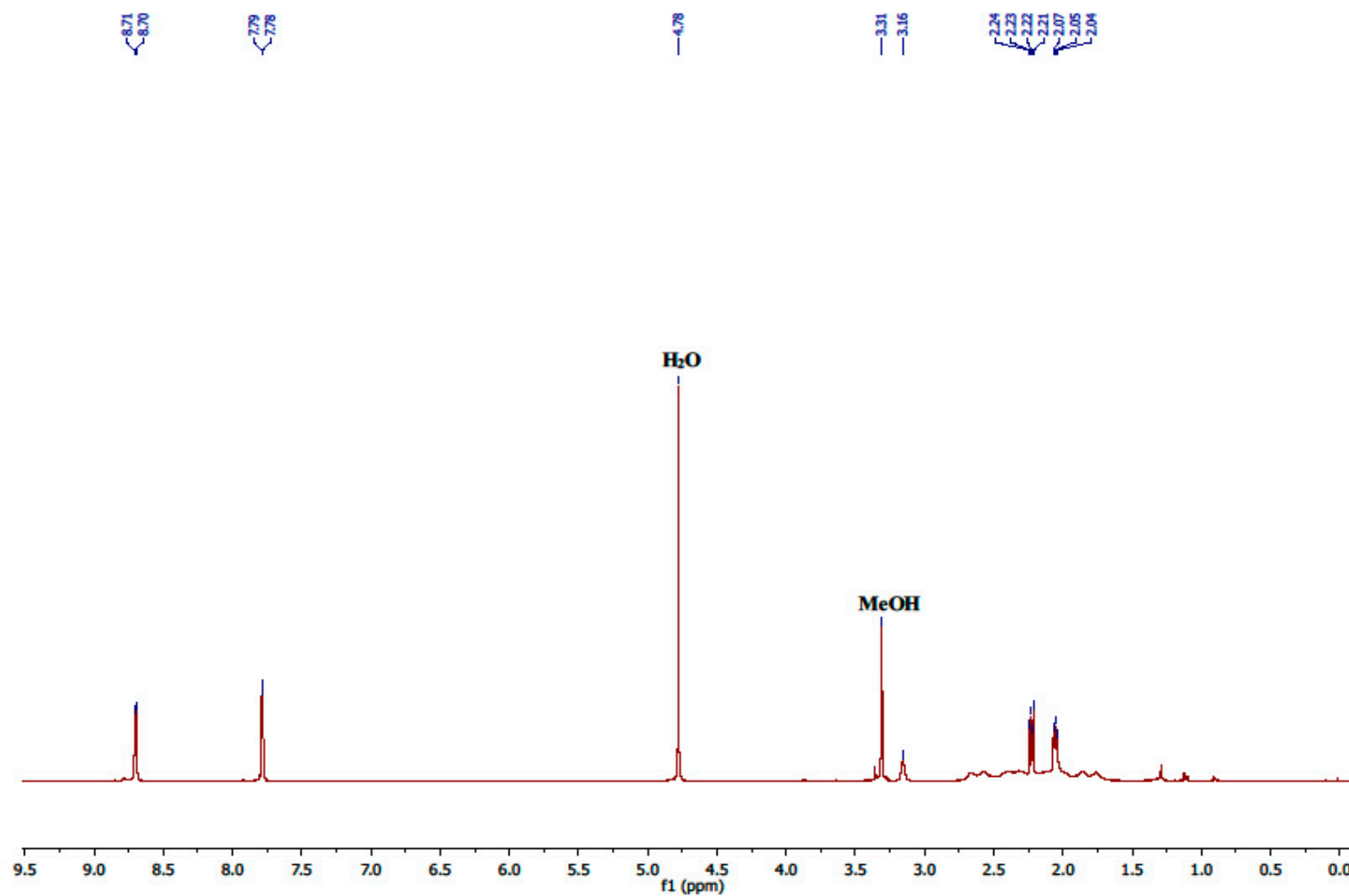


Figure S18. ¹H NMR spectrum of compound 10.

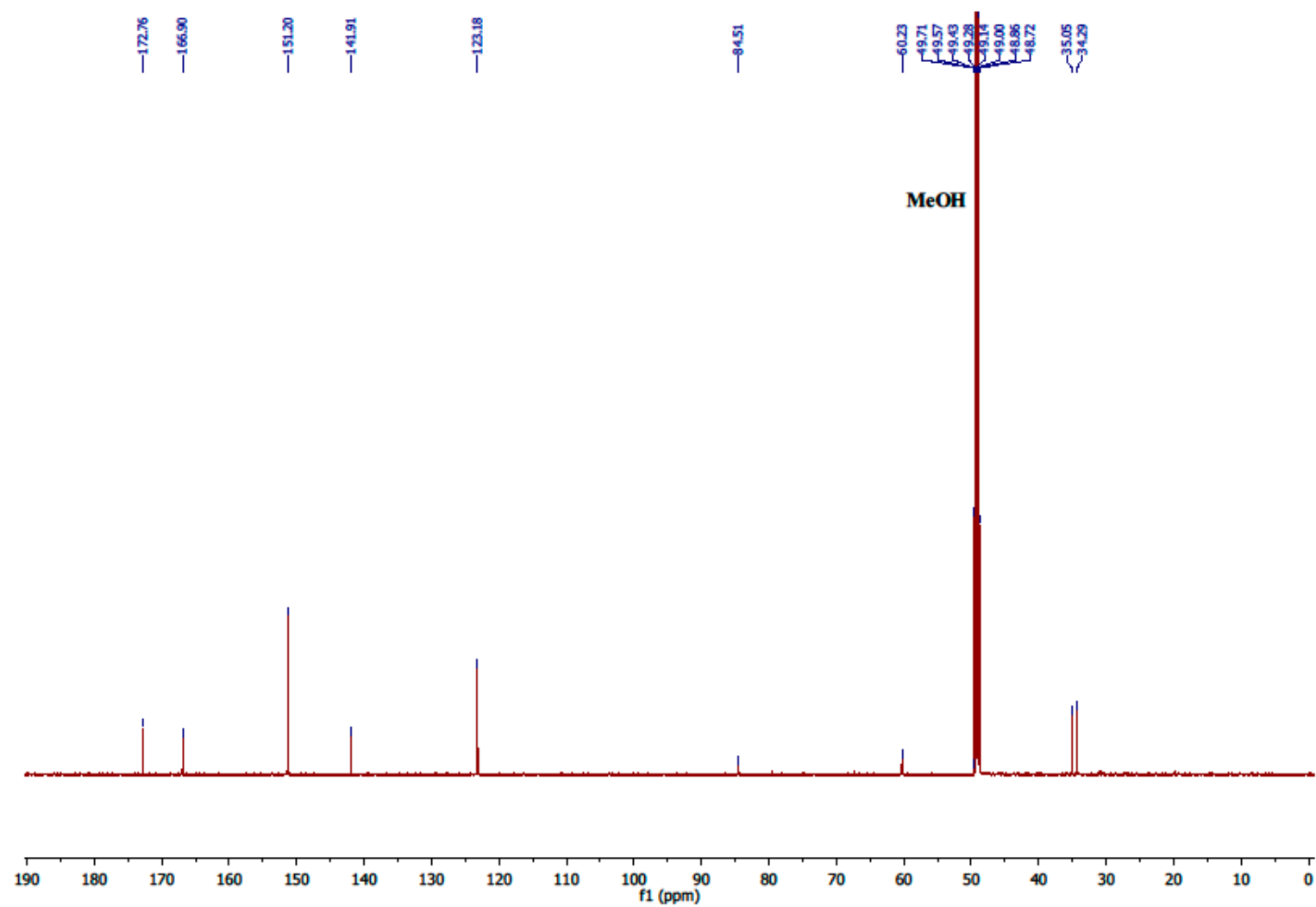


Figure S19. ¹³C NMR spectrum of compound 10.

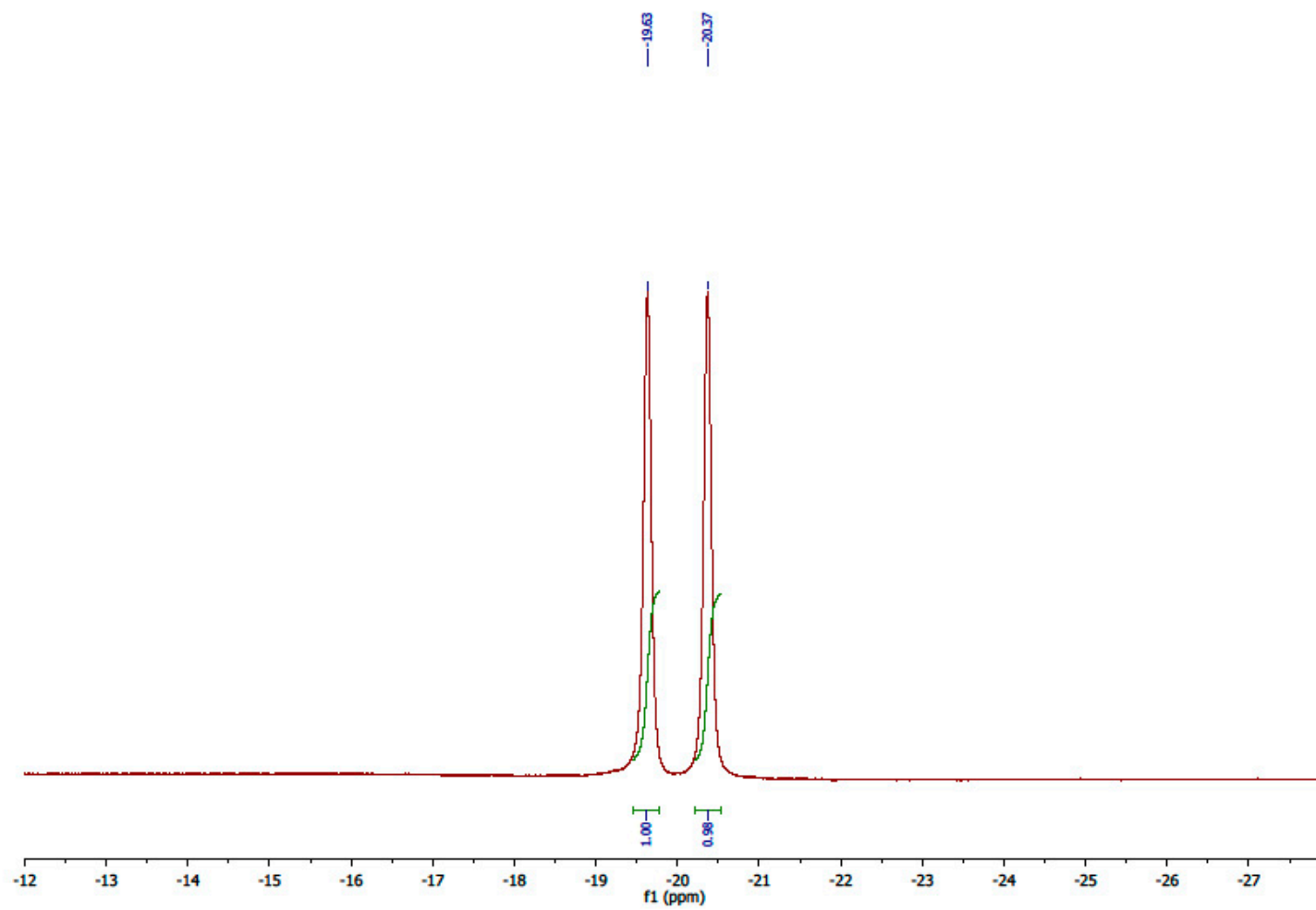


Figure S20. ^{11}B NMR {H BB} spectrum of compound 10.

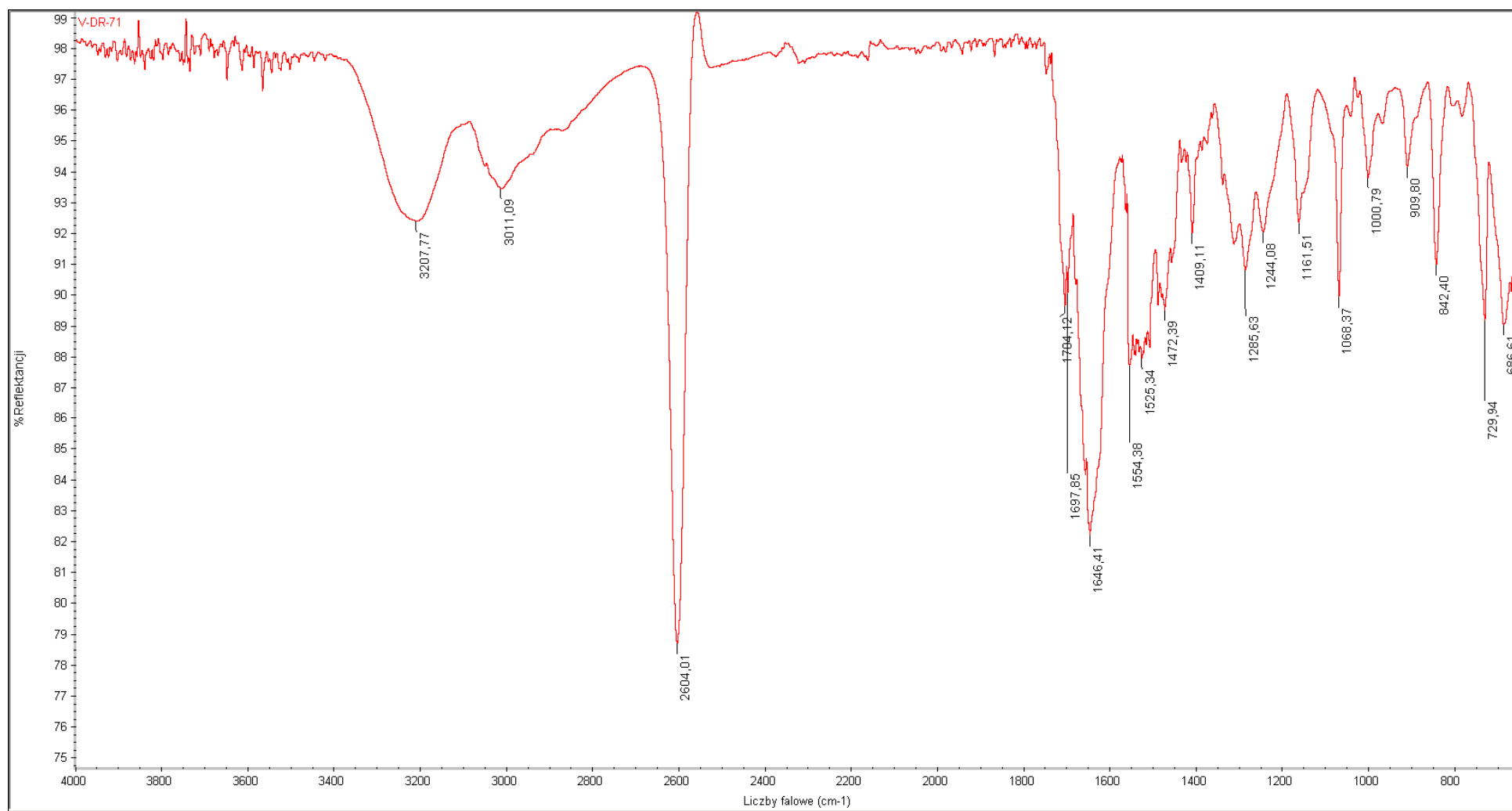


Figure S21. IR spectrum of compound 10.

Spectrum Name: V-DR-71_typ_dod
Start Ion: 100
End Ion: 600
Source: APCI + 10.0 μ A 400C
Capillary: 150V 300C Offset: 25V Span: 0V

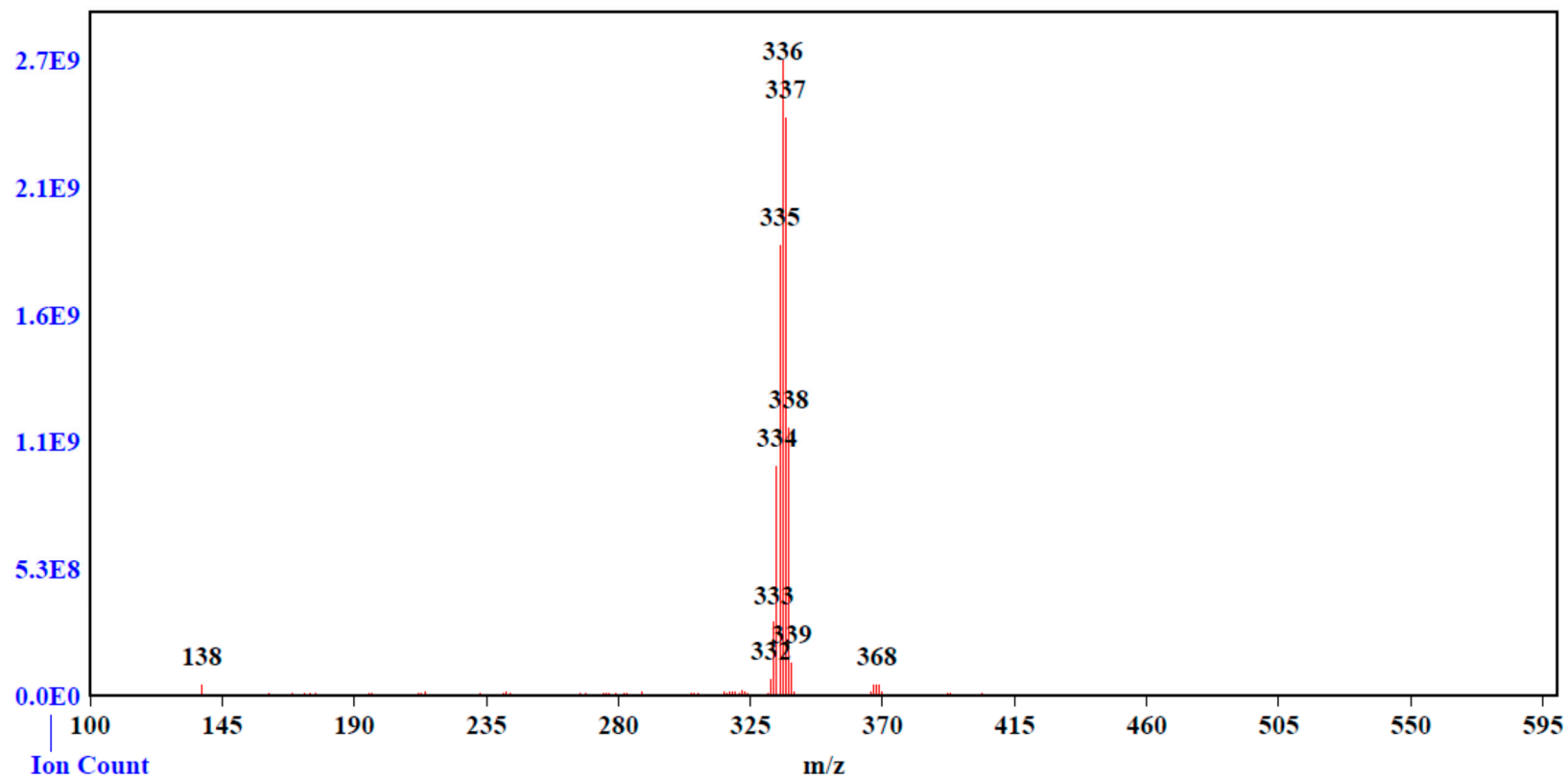


Figure S22. APCI-MS spectrum of compound 10.

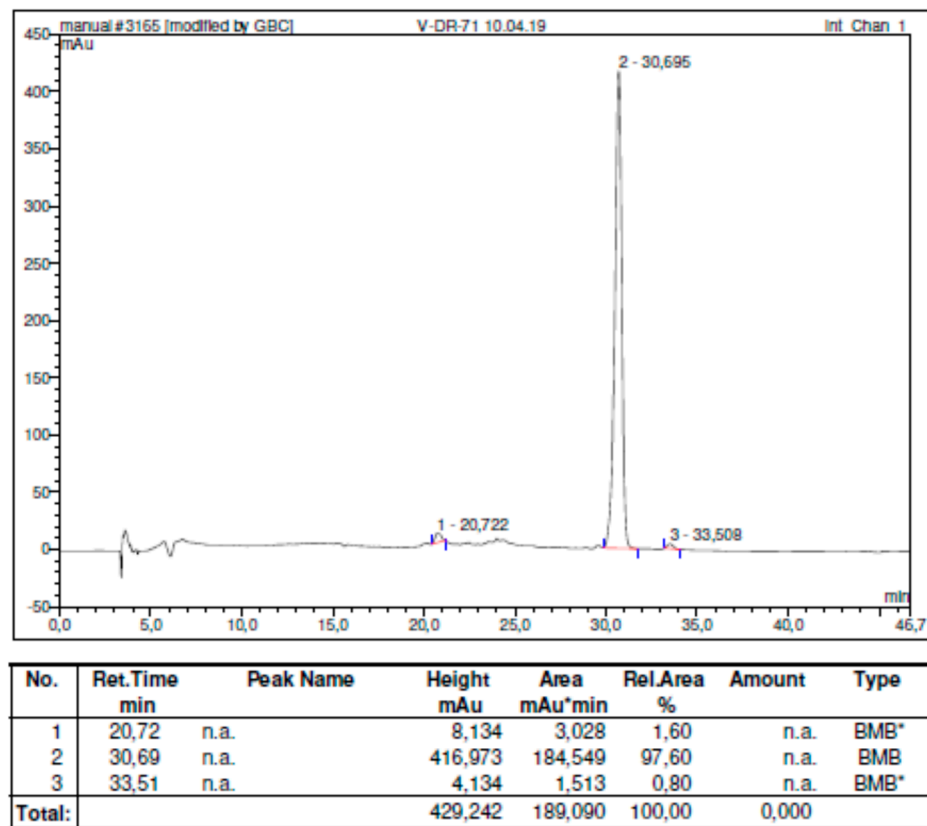


Figure S23. HPLC analysis of compound 10.

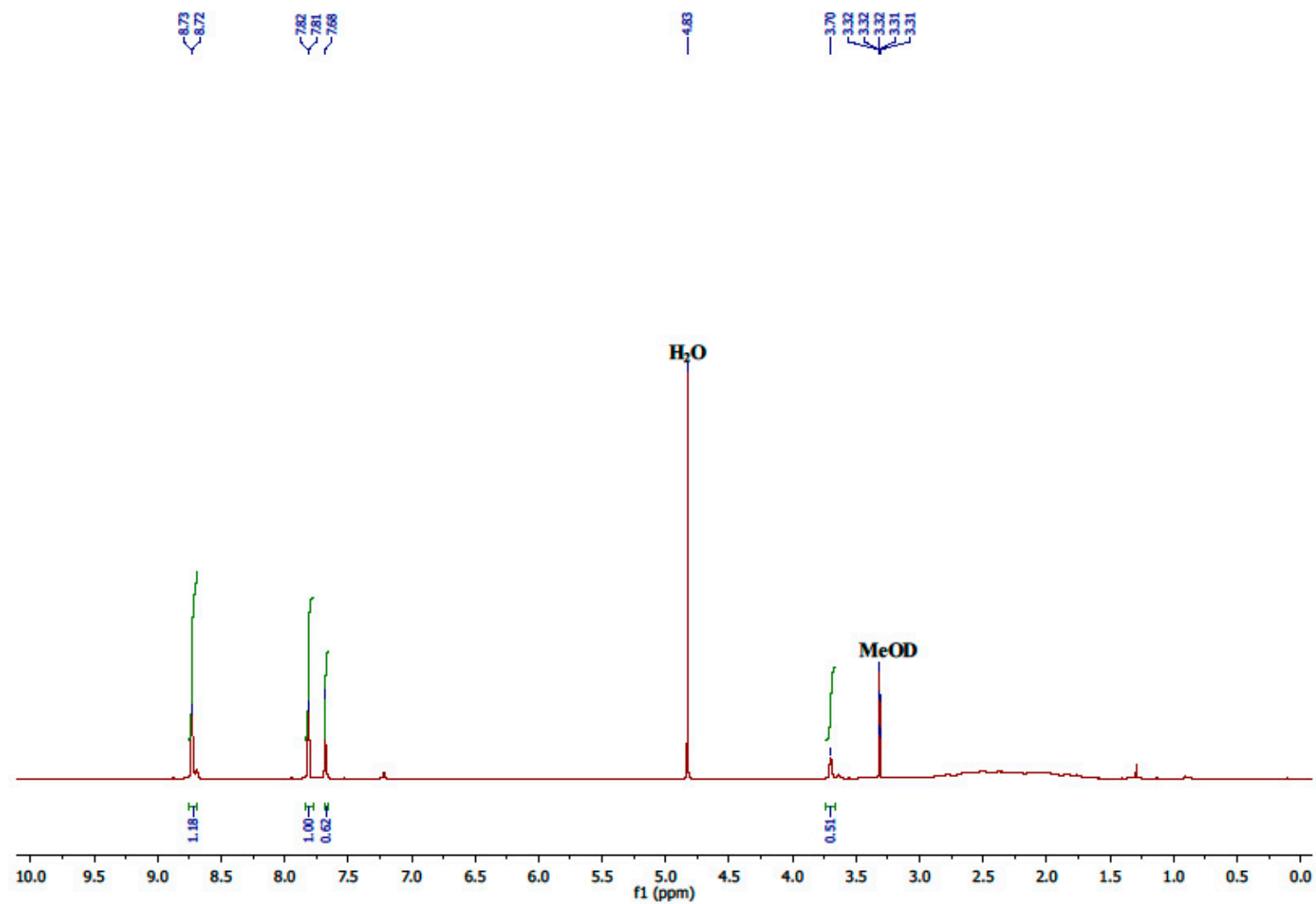


Figure S24. ¹H NMR spectrum of compound 14.

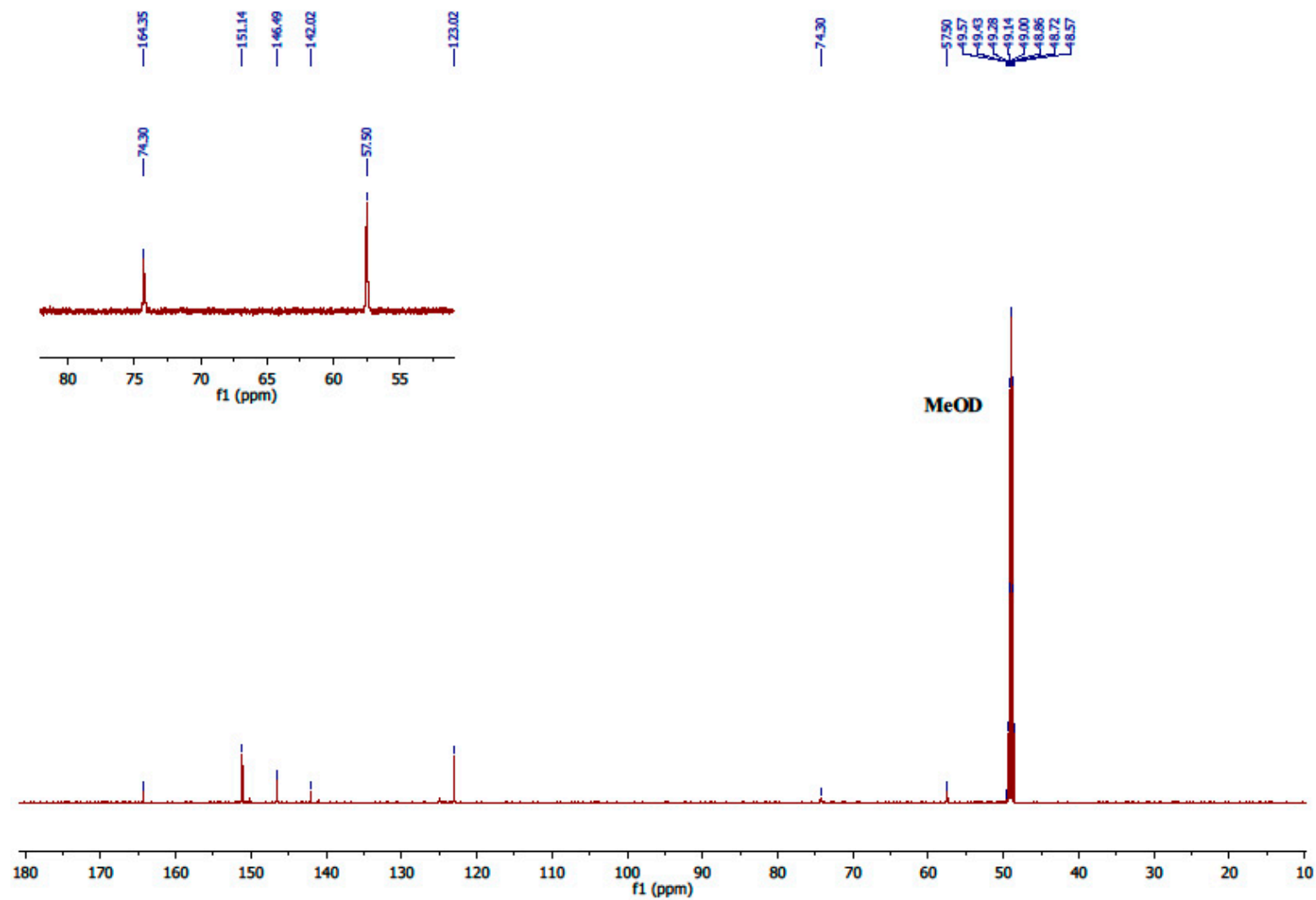


Figure S25. ^{13}C NMR spectrum of compound 14.

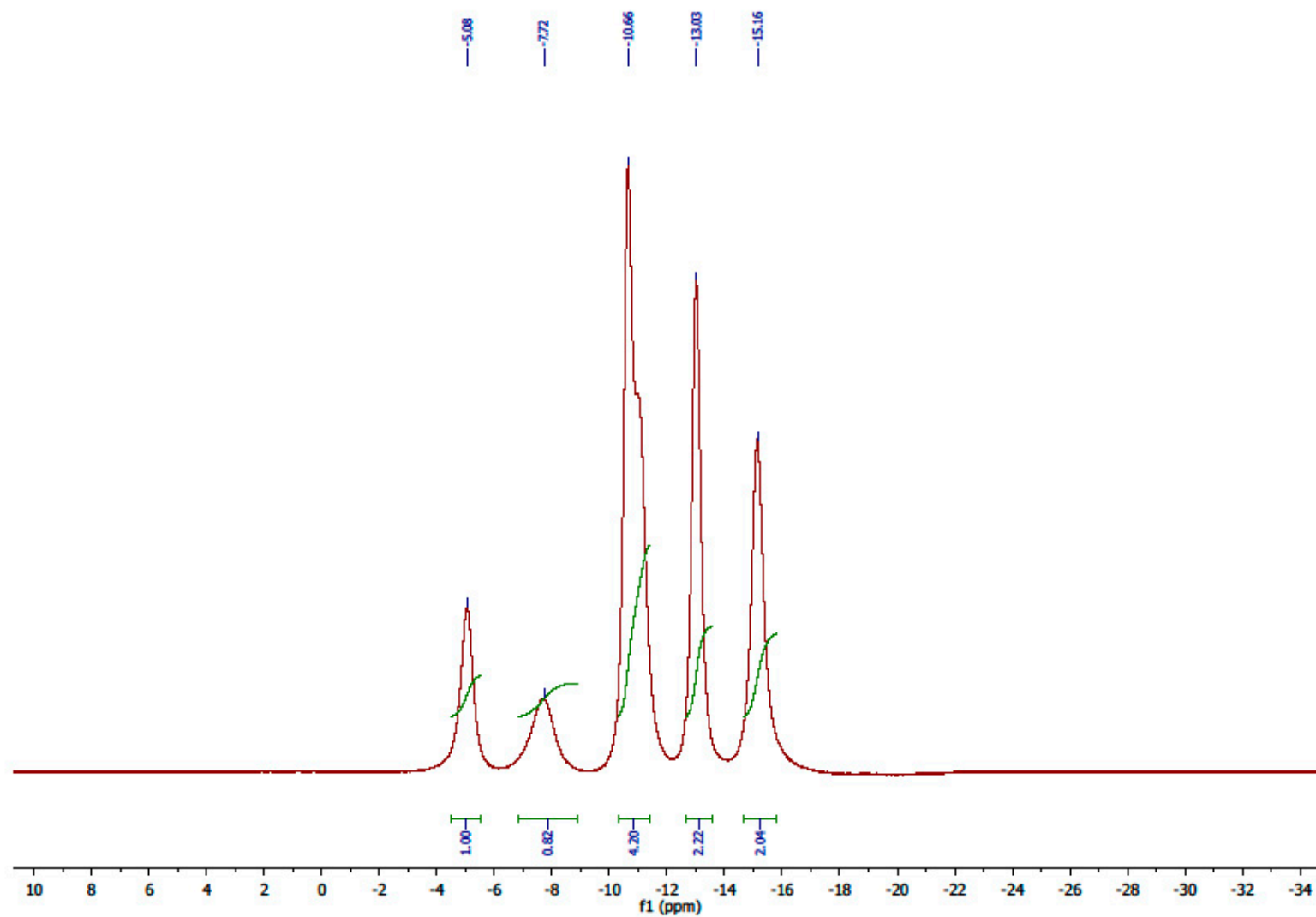


Figure S26. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 14.

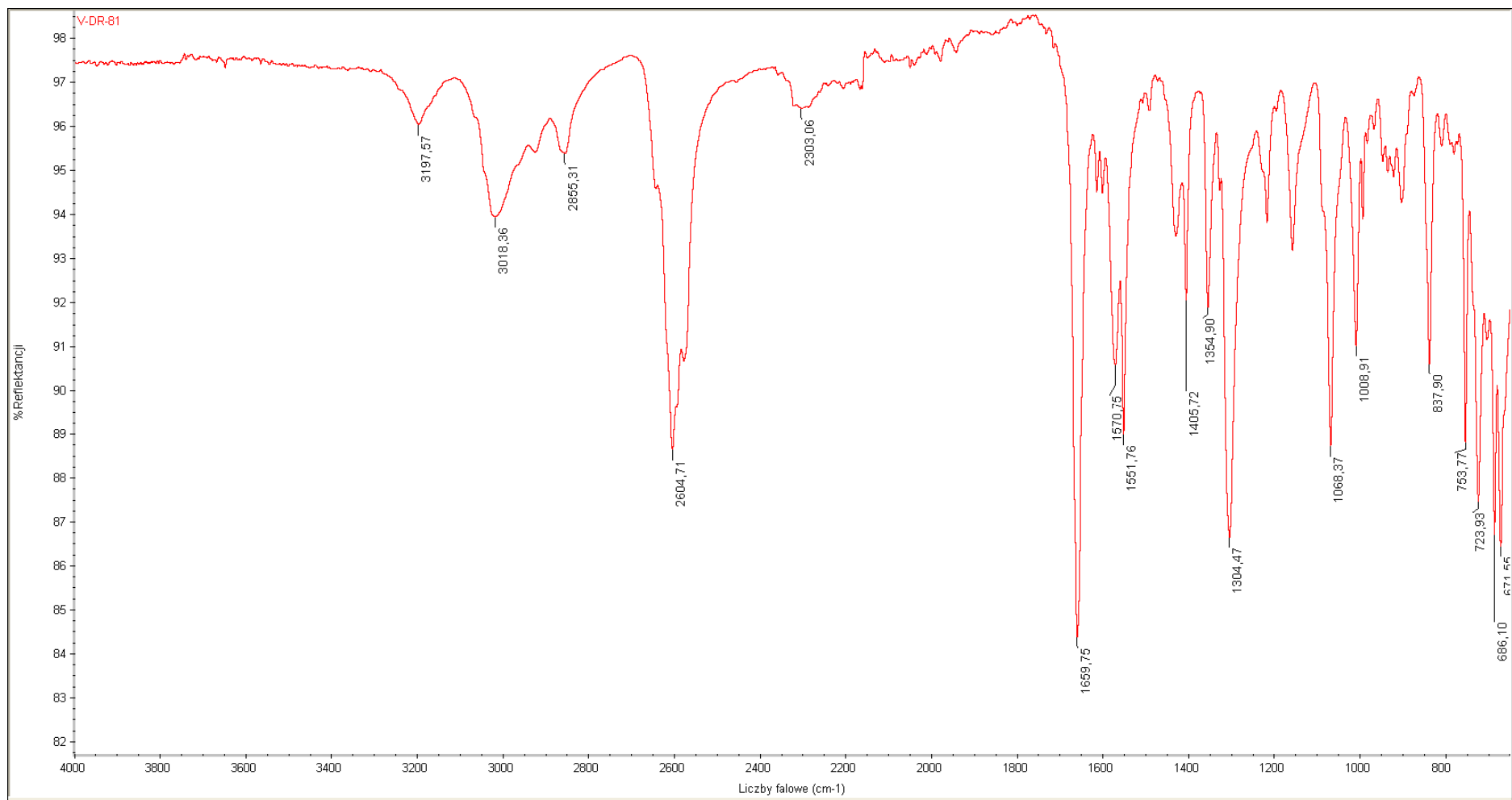


Figure S27. IR spectrum of compound 14.

Spectrum Name: V-DR-81_rob_dod
Start Ion: 200
End Ion: 400
Source: APCI + 10.0 μ A 400C
Capillary: 180V 300C Offset: 30V Span: 20V

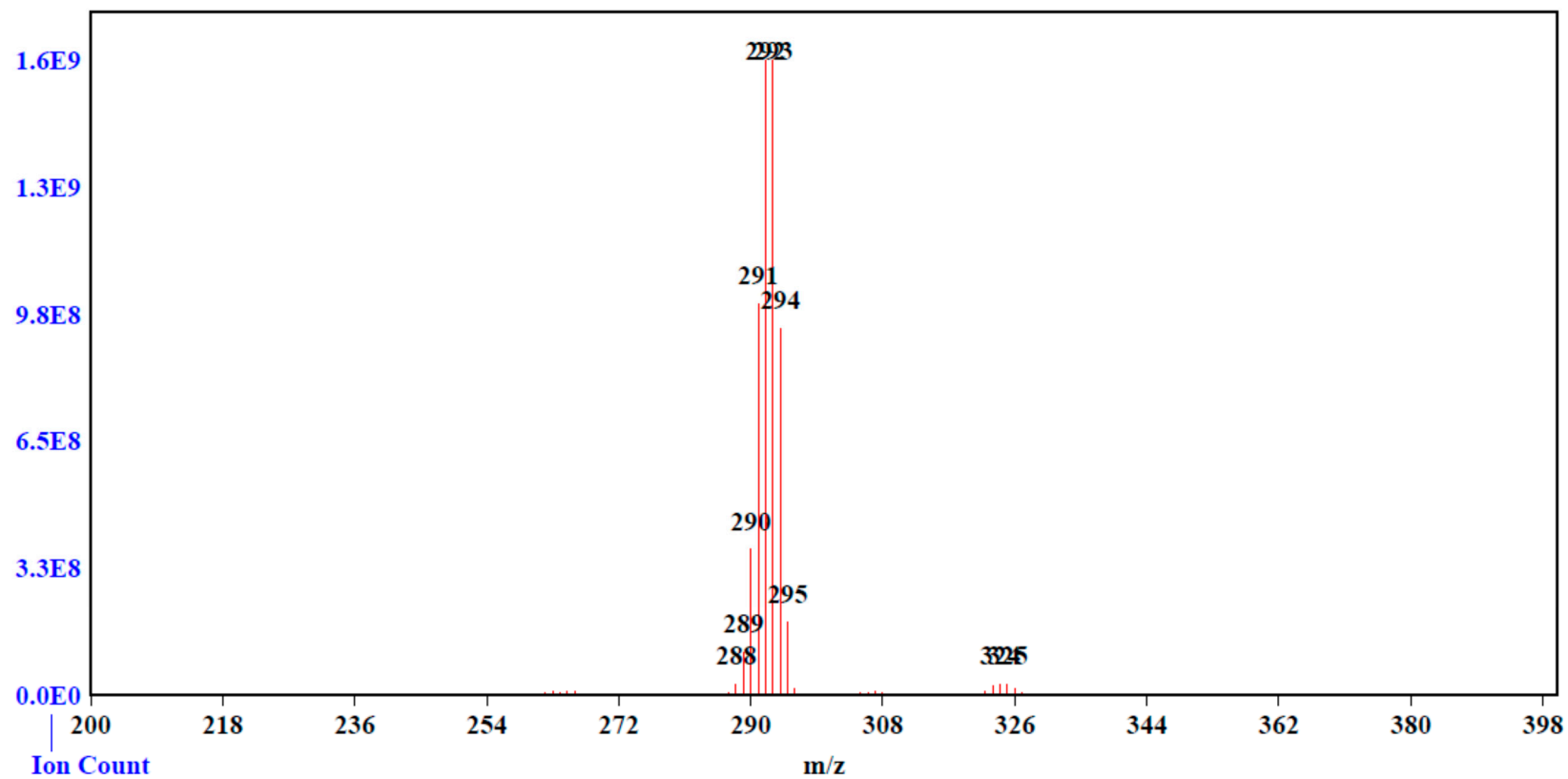


Figure S28. MS spectrum of compound 14.

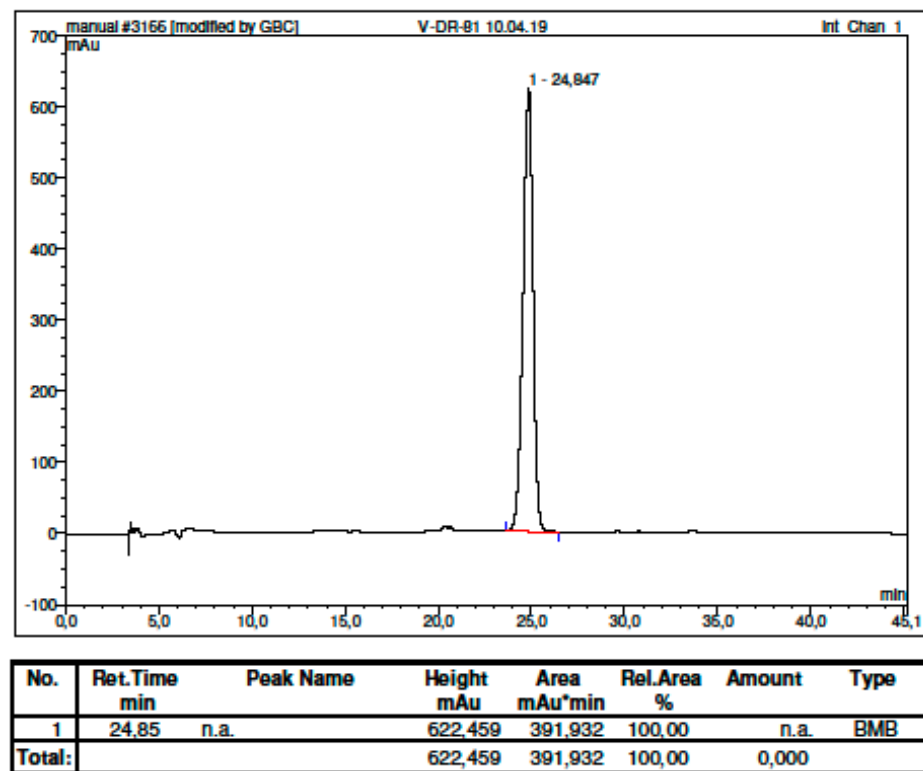


Figure S29. HPLC analysis of compound 14.

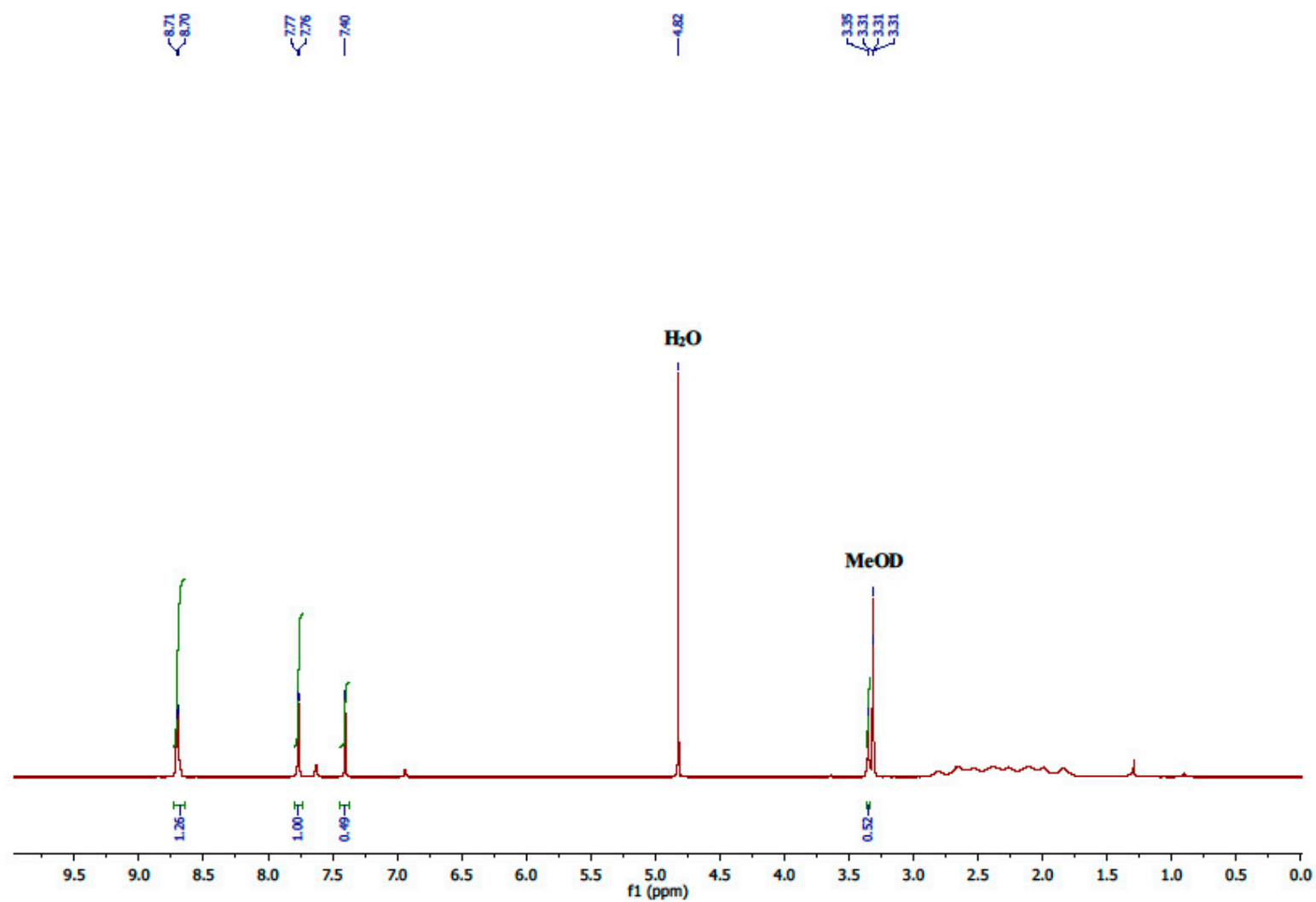


Figure S30. ¹H NMR spectrum of compound 15.

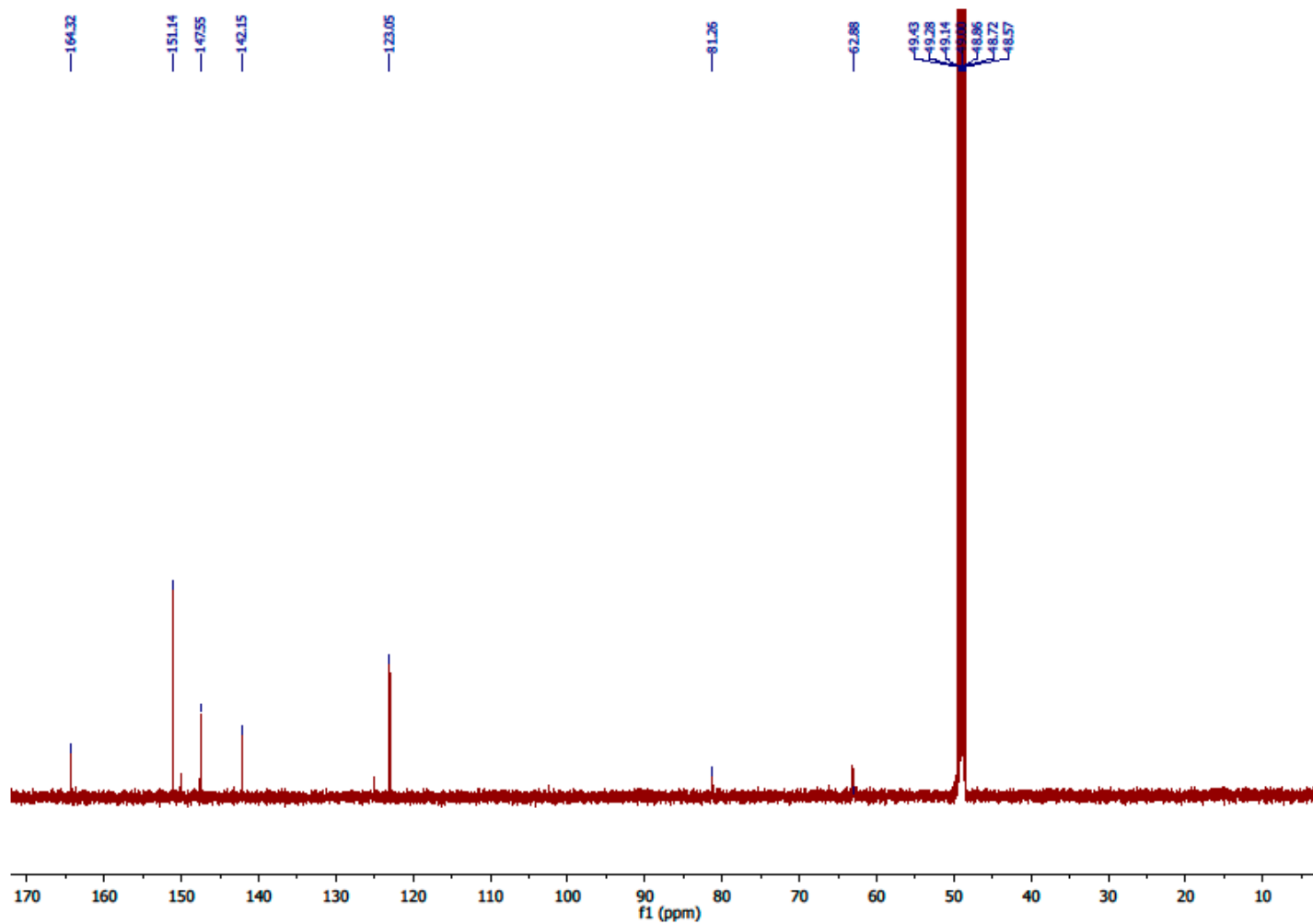


Figure S31. ¹³C NMR spectrum of compound 15.

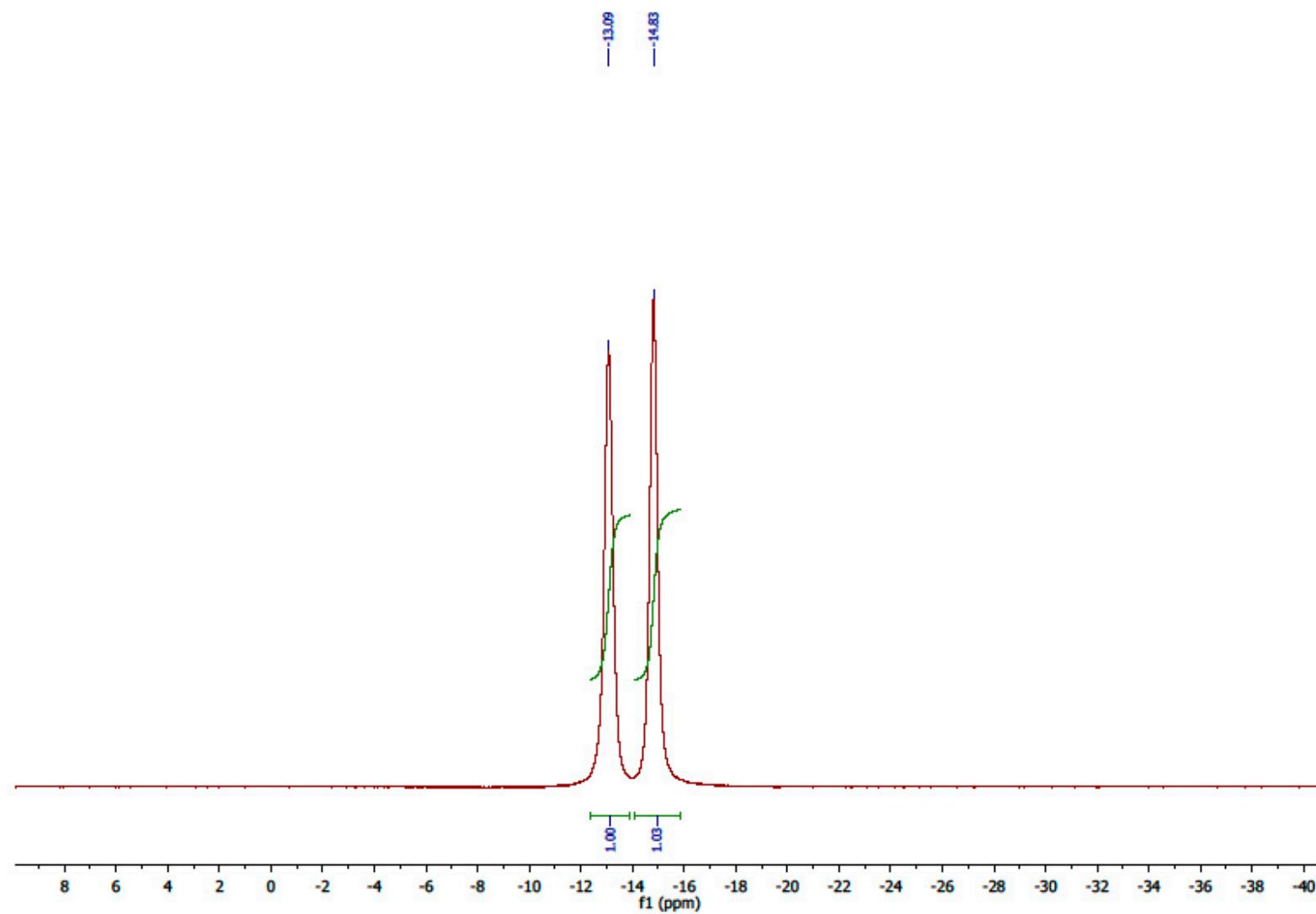


Figure S32. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 15.

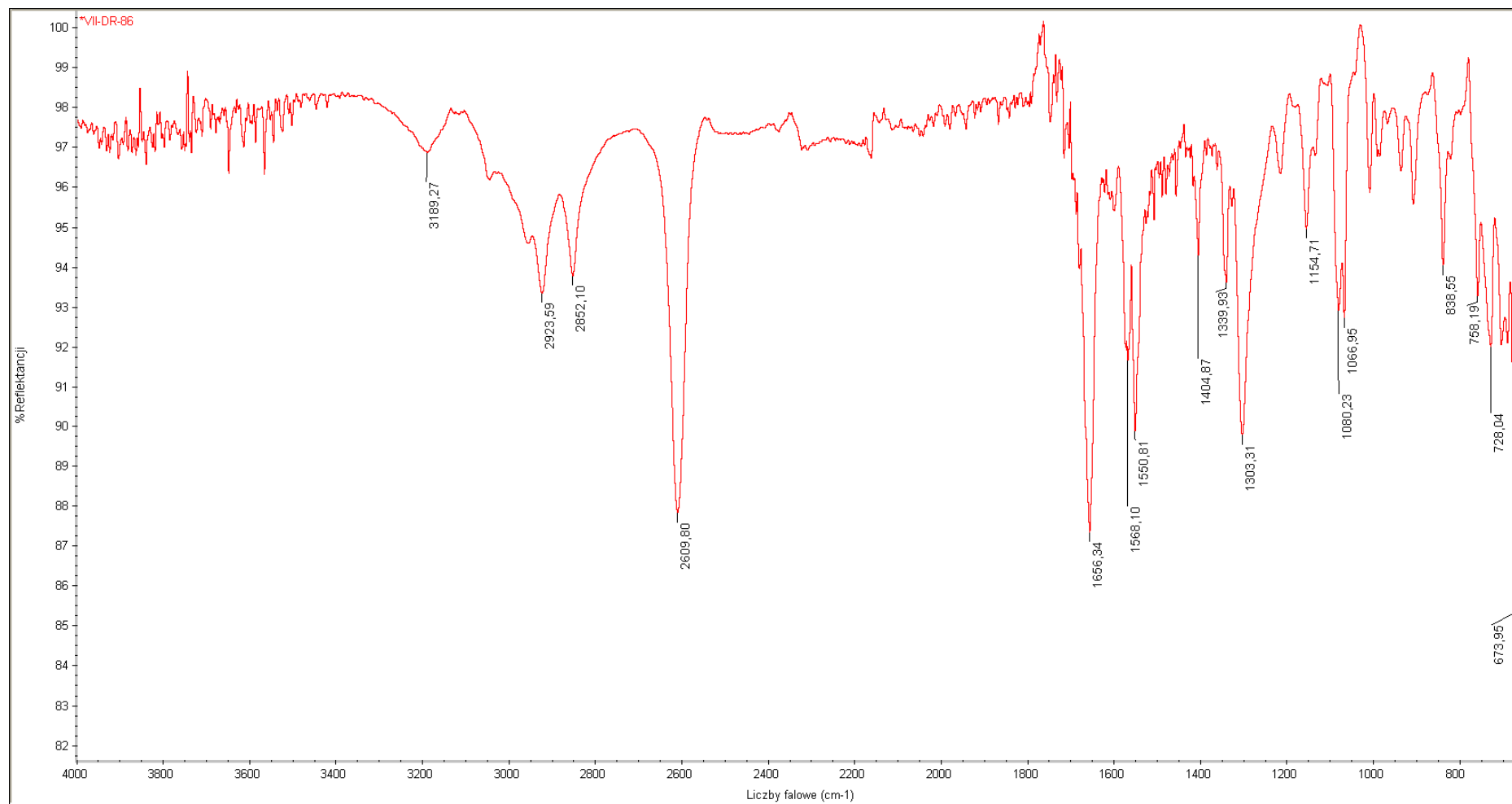


Figure S33. IR spectrum of compound **15**.

Spectrum Name: VII-DR-86_typ_dod
Start Ion: 100
End Ion: 500
Source: APCI + 10.0μA 400C
Capillary: 150V 300C Offset: 25V Span: 0V

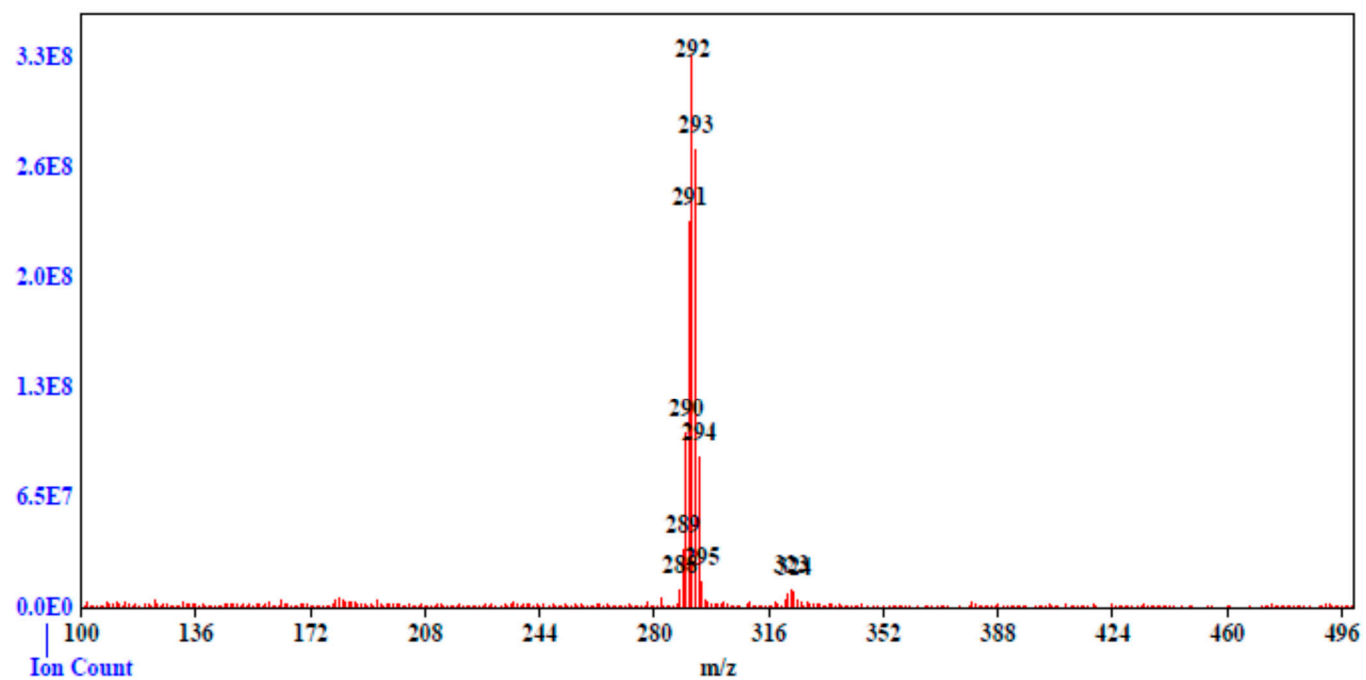


Figure S34. MS spectrum of compound 15.

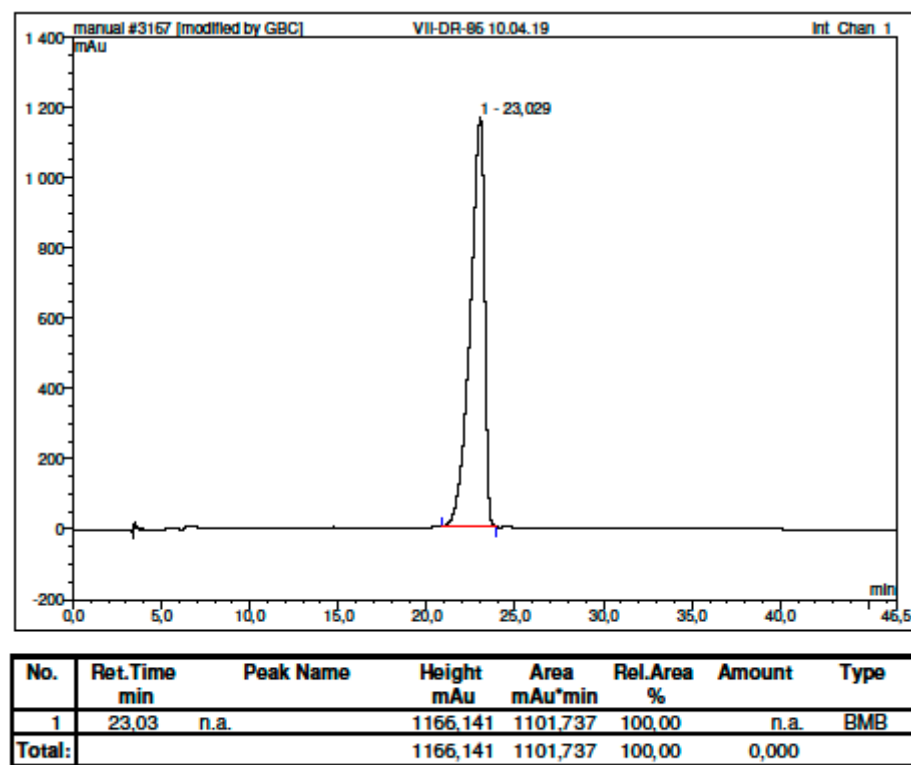


Figure S35. HPLC analysis of compound 15.

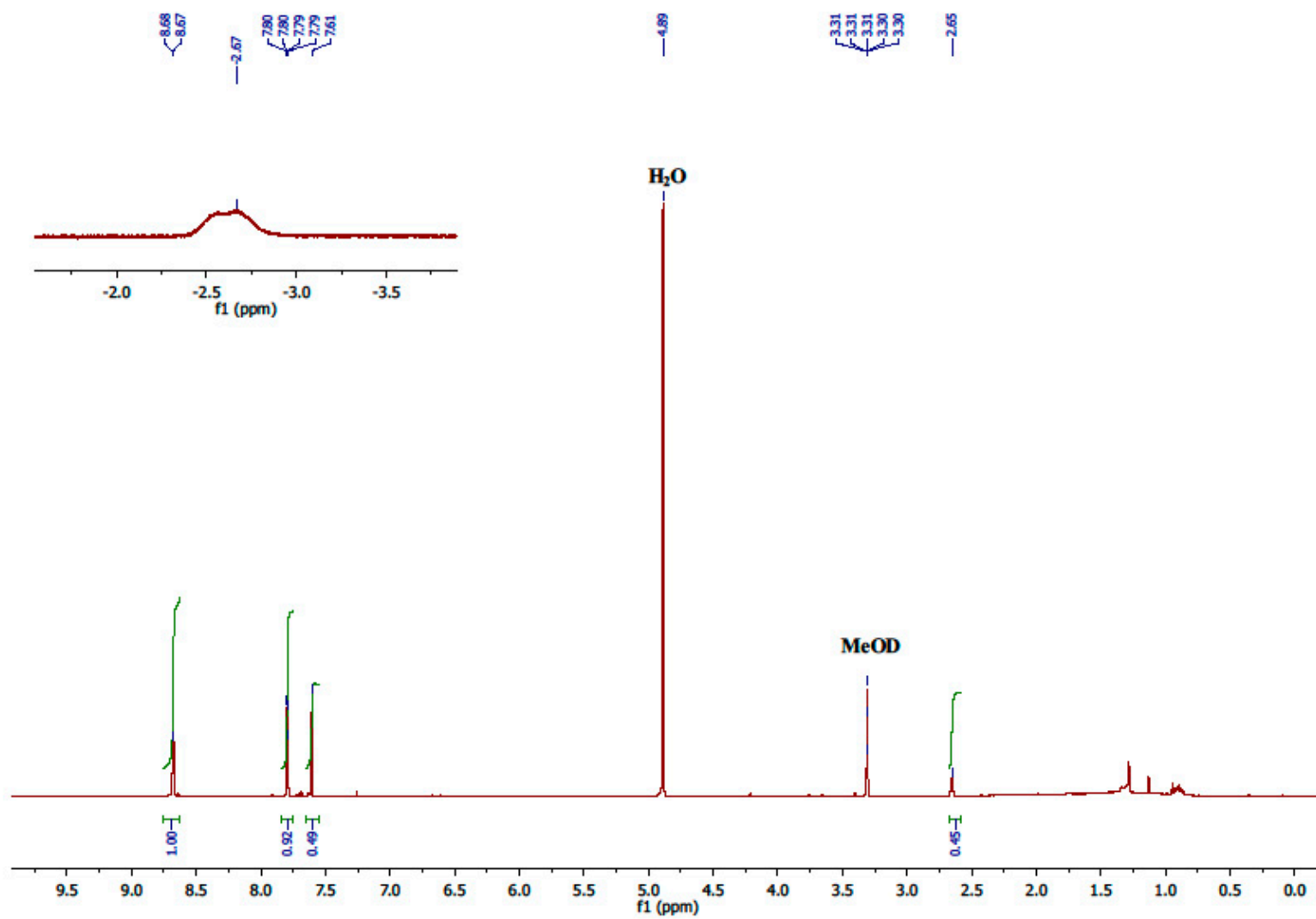


Figure S36. ¹H NMR spectrum of compound 16.

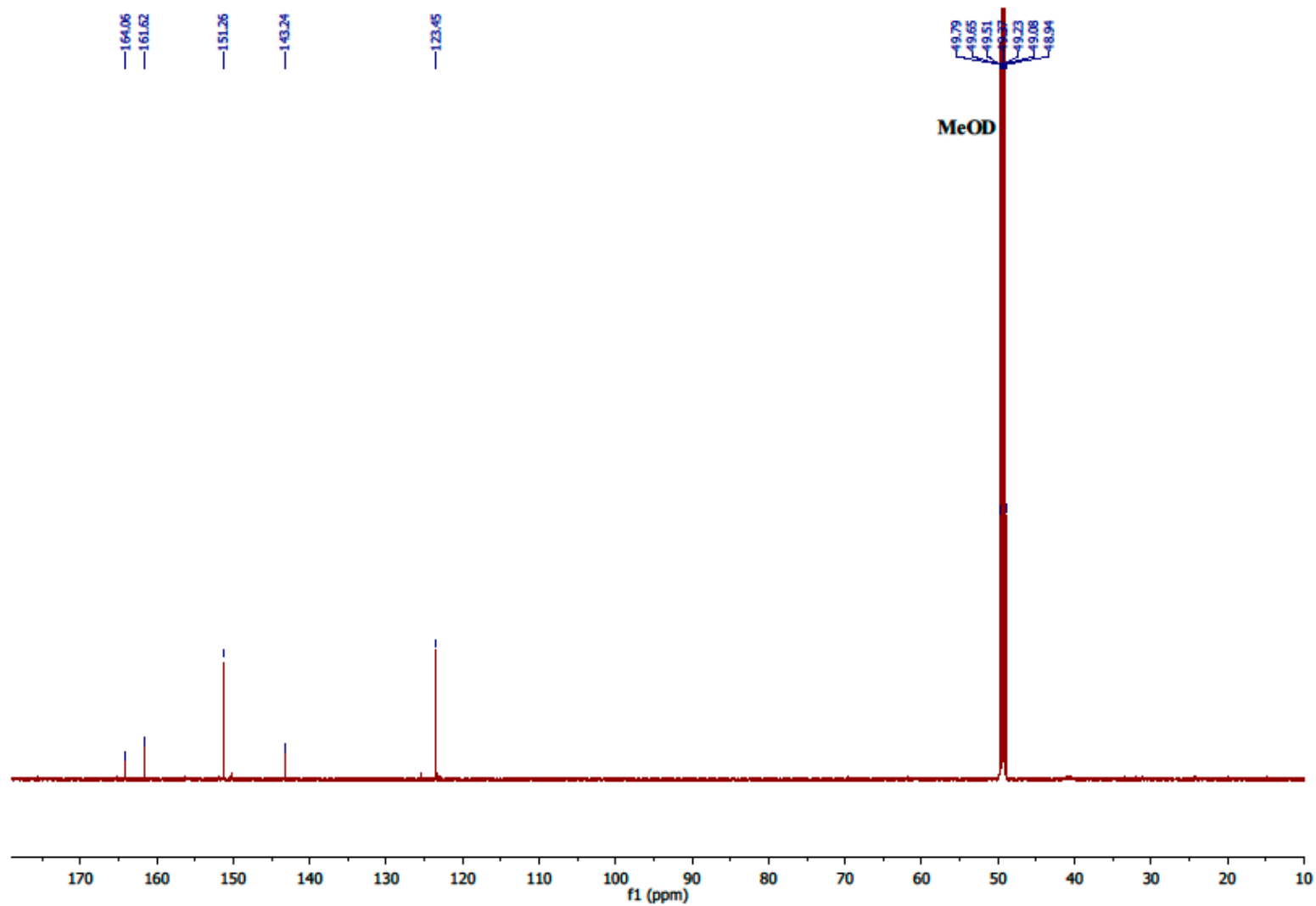


Figure S37. ^{13}C NMR spectrum of compound **16**.

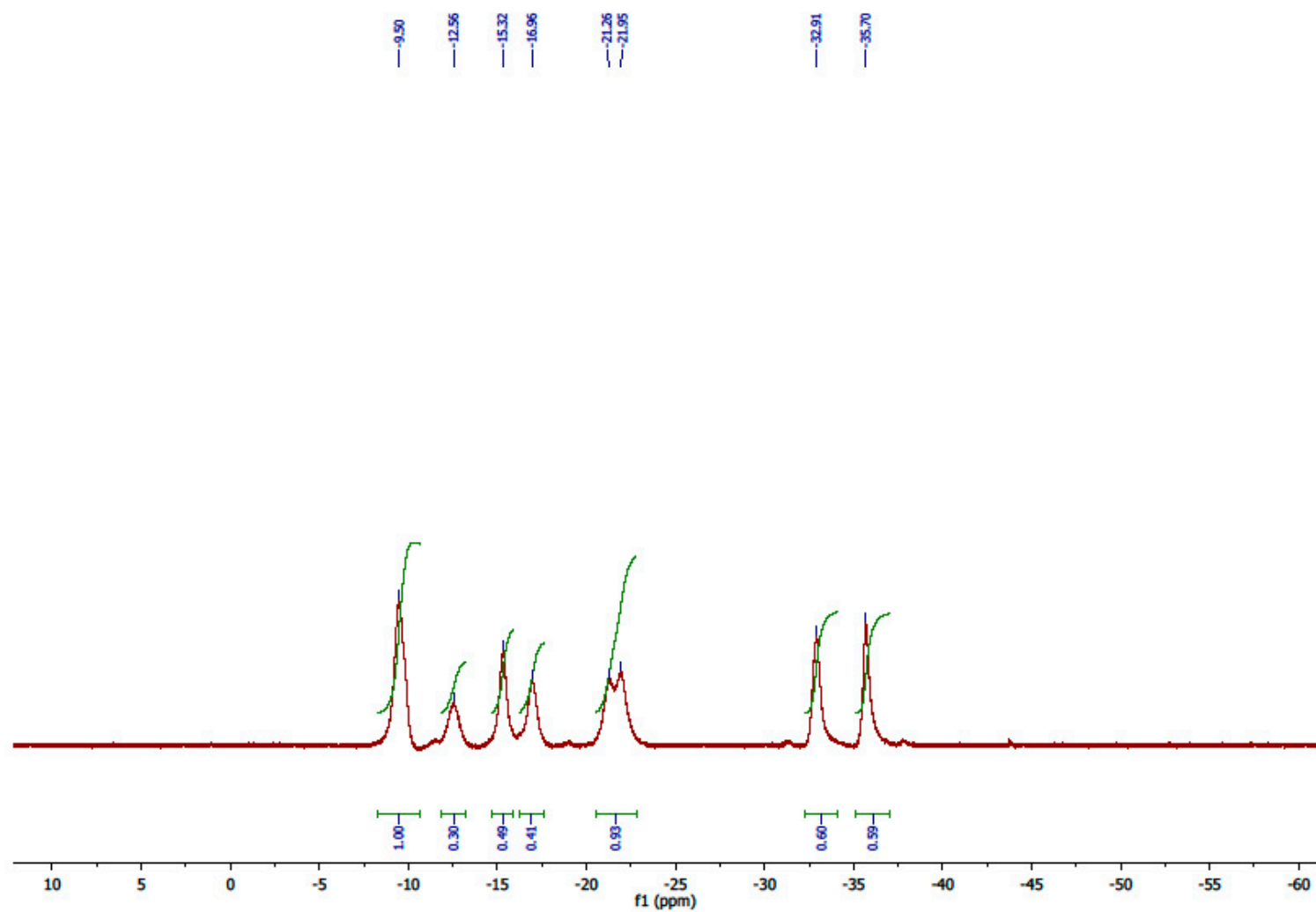


Figure S38. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 16.

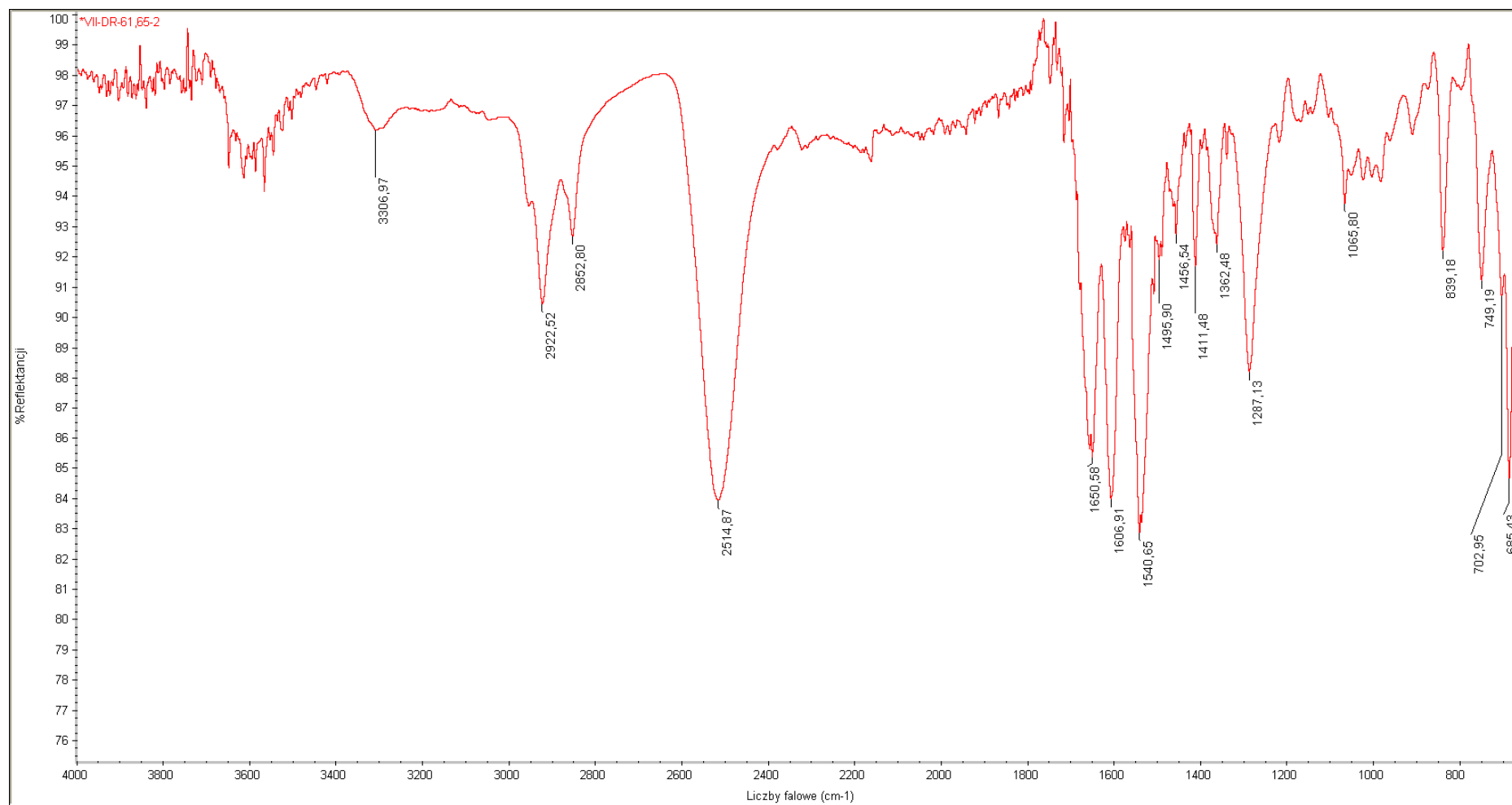


Figure S39. IR spectrum of compound 16.

Spectrum Name: VII-DR-46_fr3_rob_min
Start Ion: 100
End Ion: 400
Source: ESI - 2.5kV 350C
Capillary: 180V 300C Offset: 30V Span: 20V

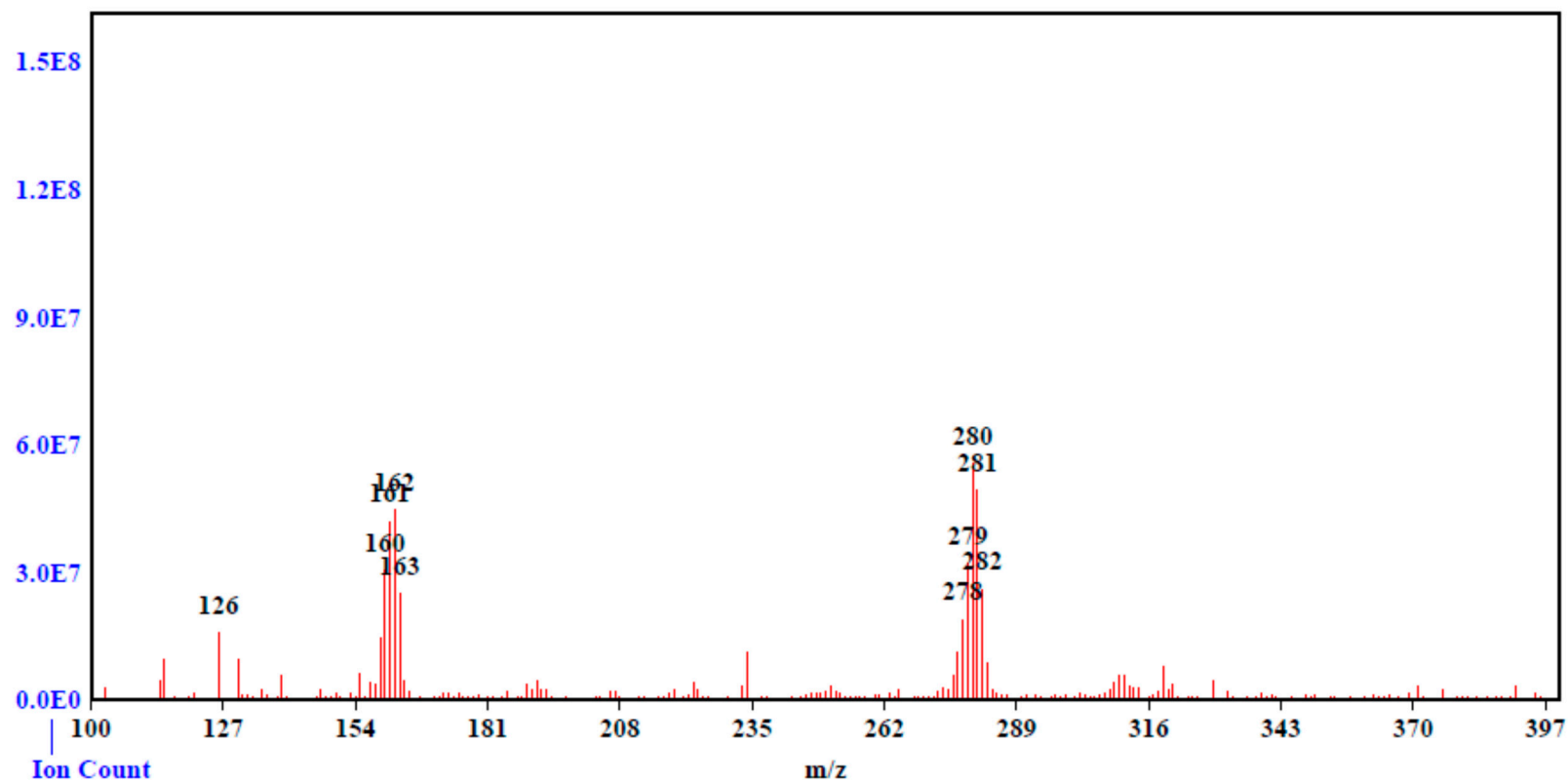


Figure S40. MS spectrum of compound 16.

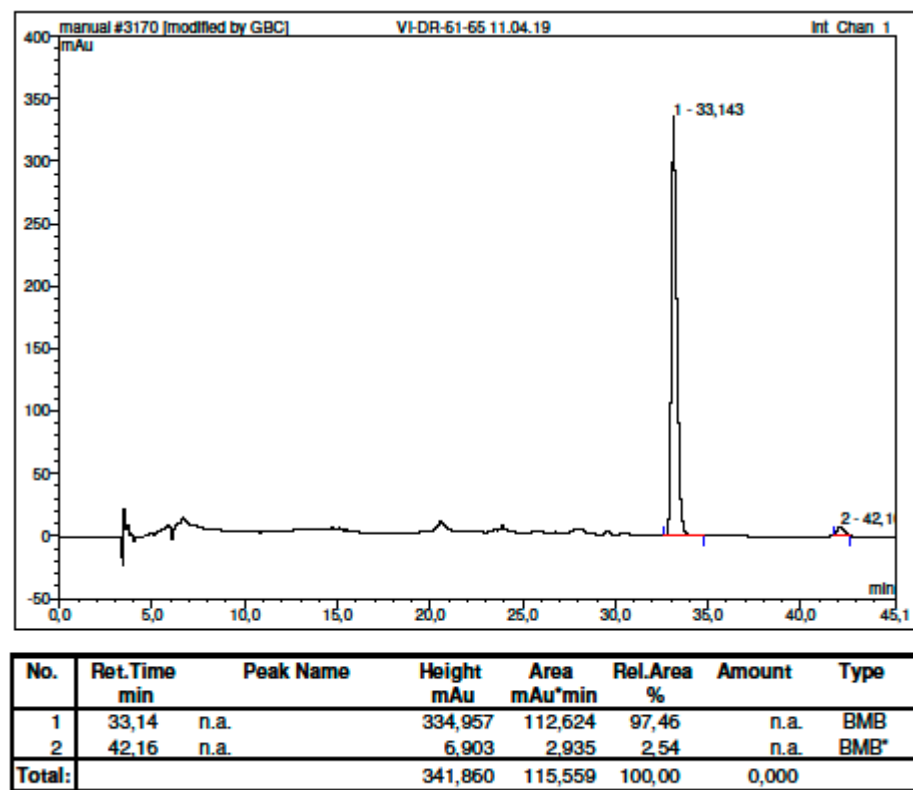


Figure S41. HPLC analysis of compound 16.

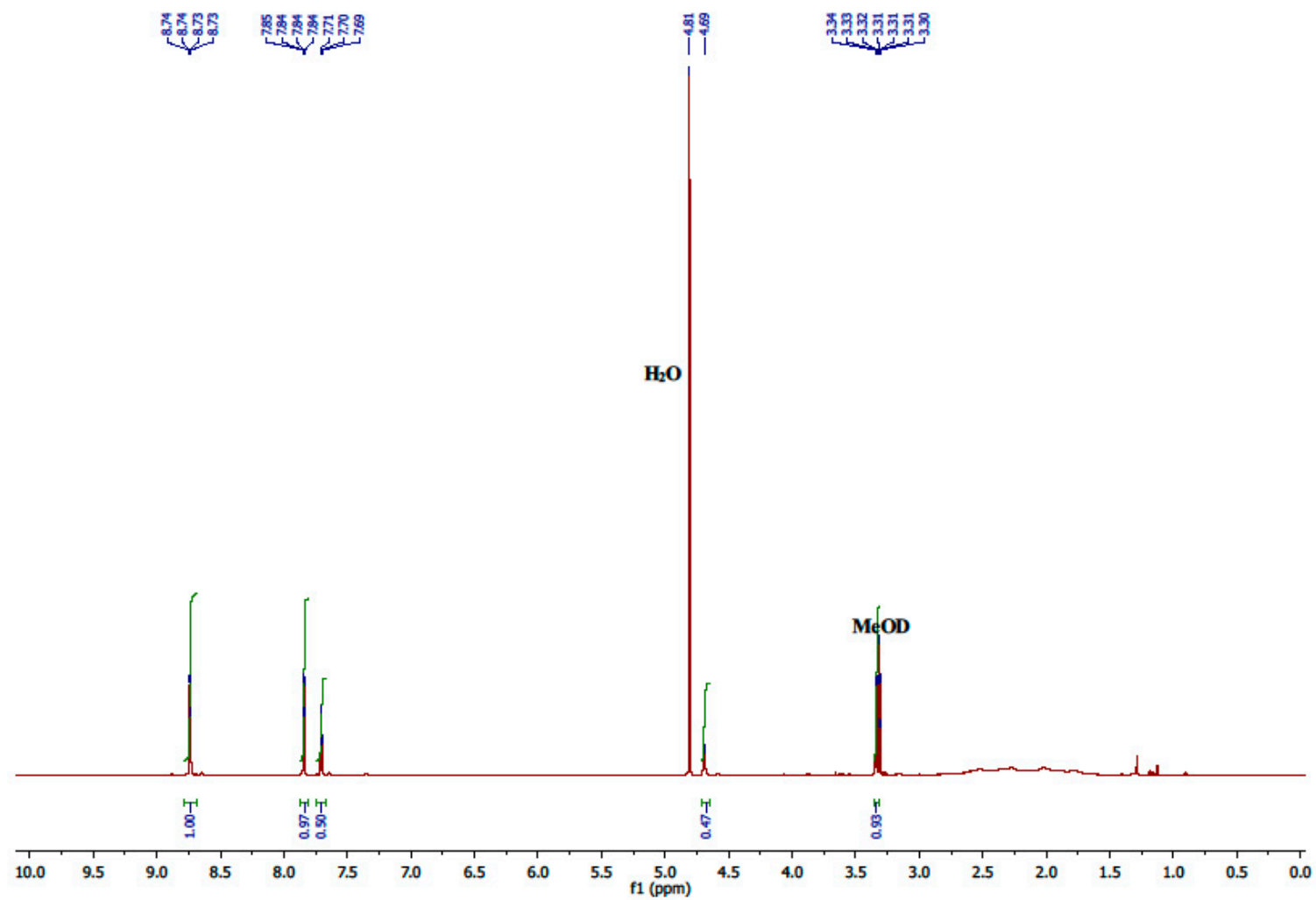


Figure S42. ¹H NMR spectrum of compound 20.

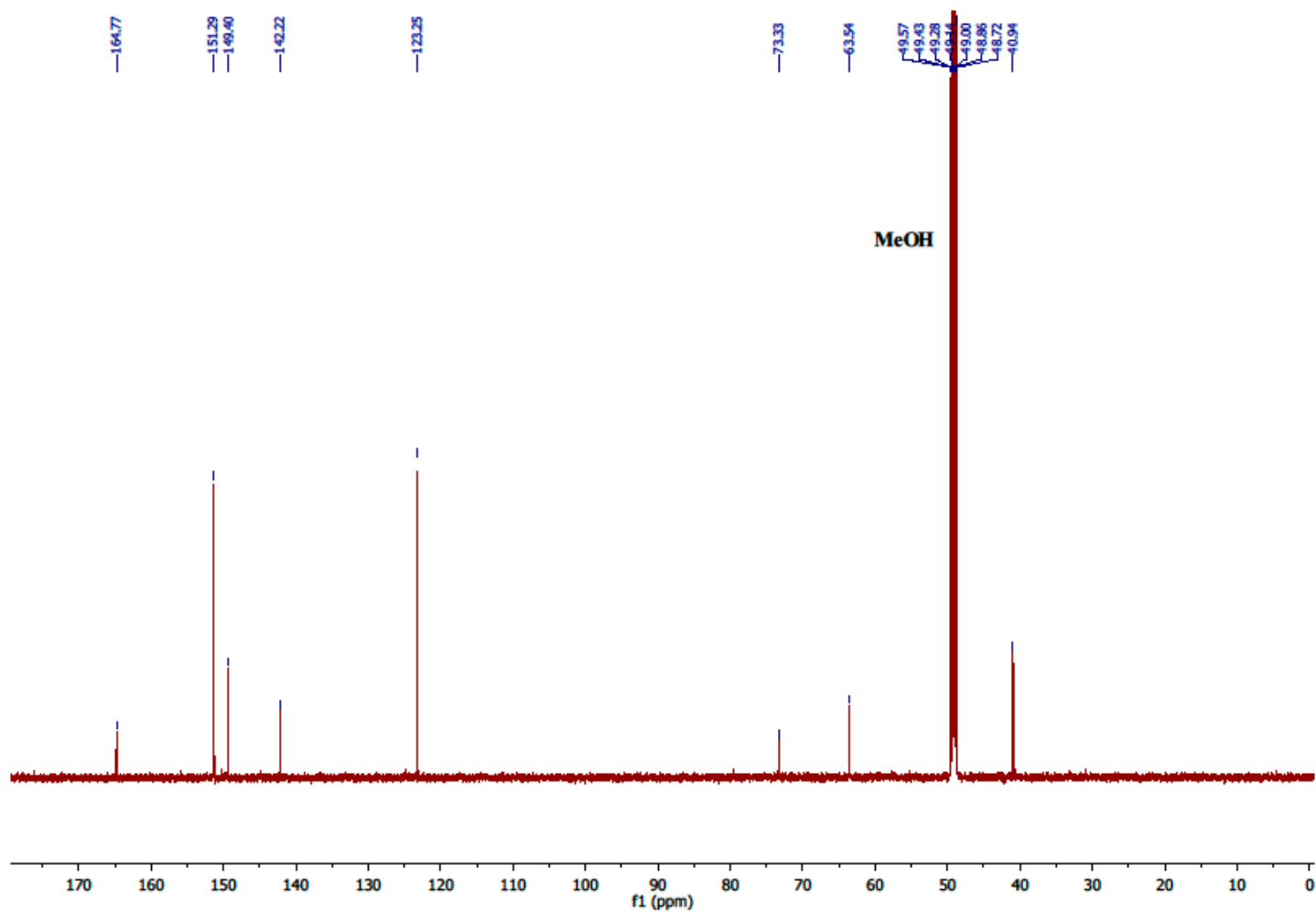


Figure S43. ¹³C NMR spectrum of compound 20.

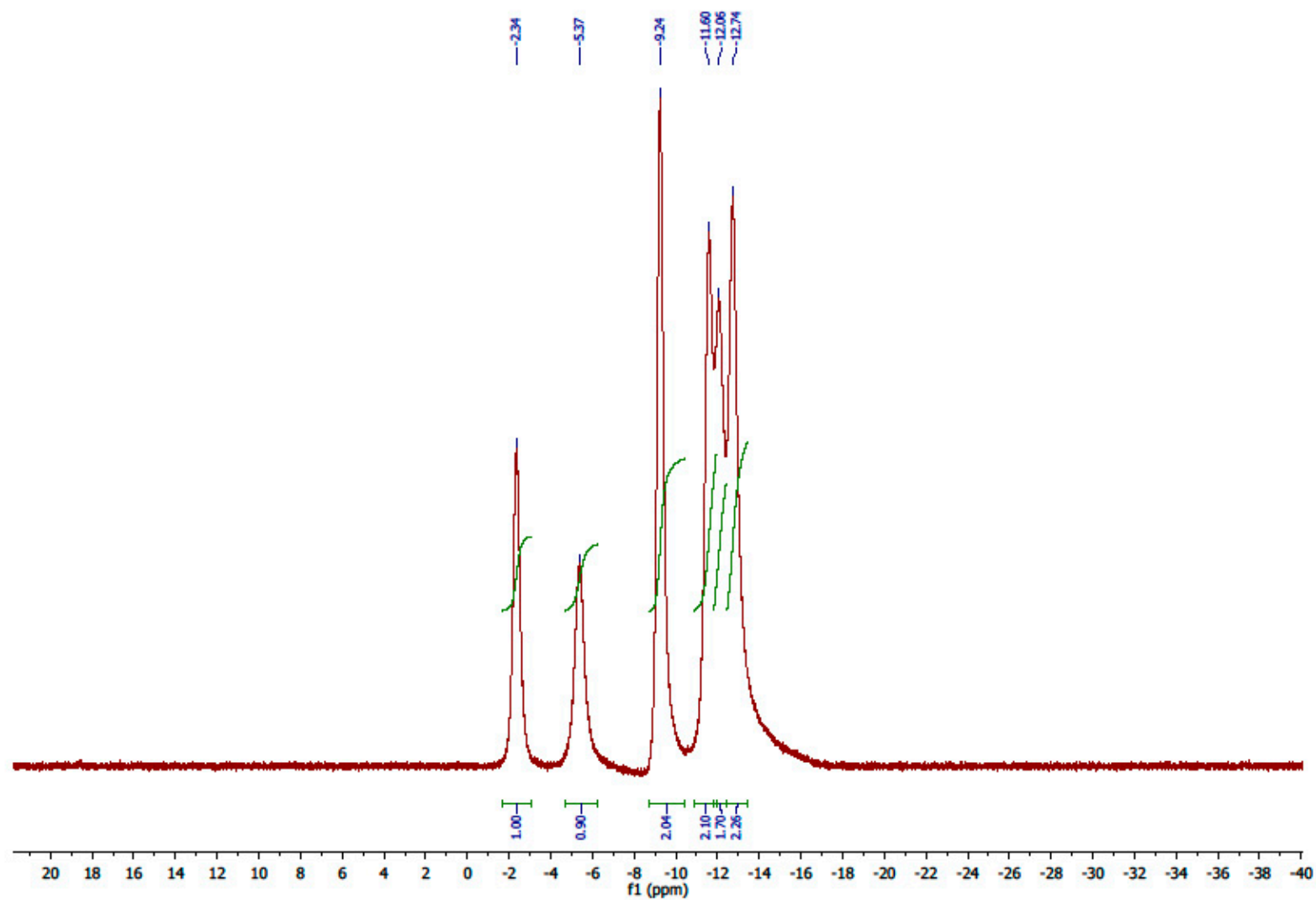


Figure S44. ^1H B NMR $\{^1\text{H BB}\}$ spectrum of compound 20.

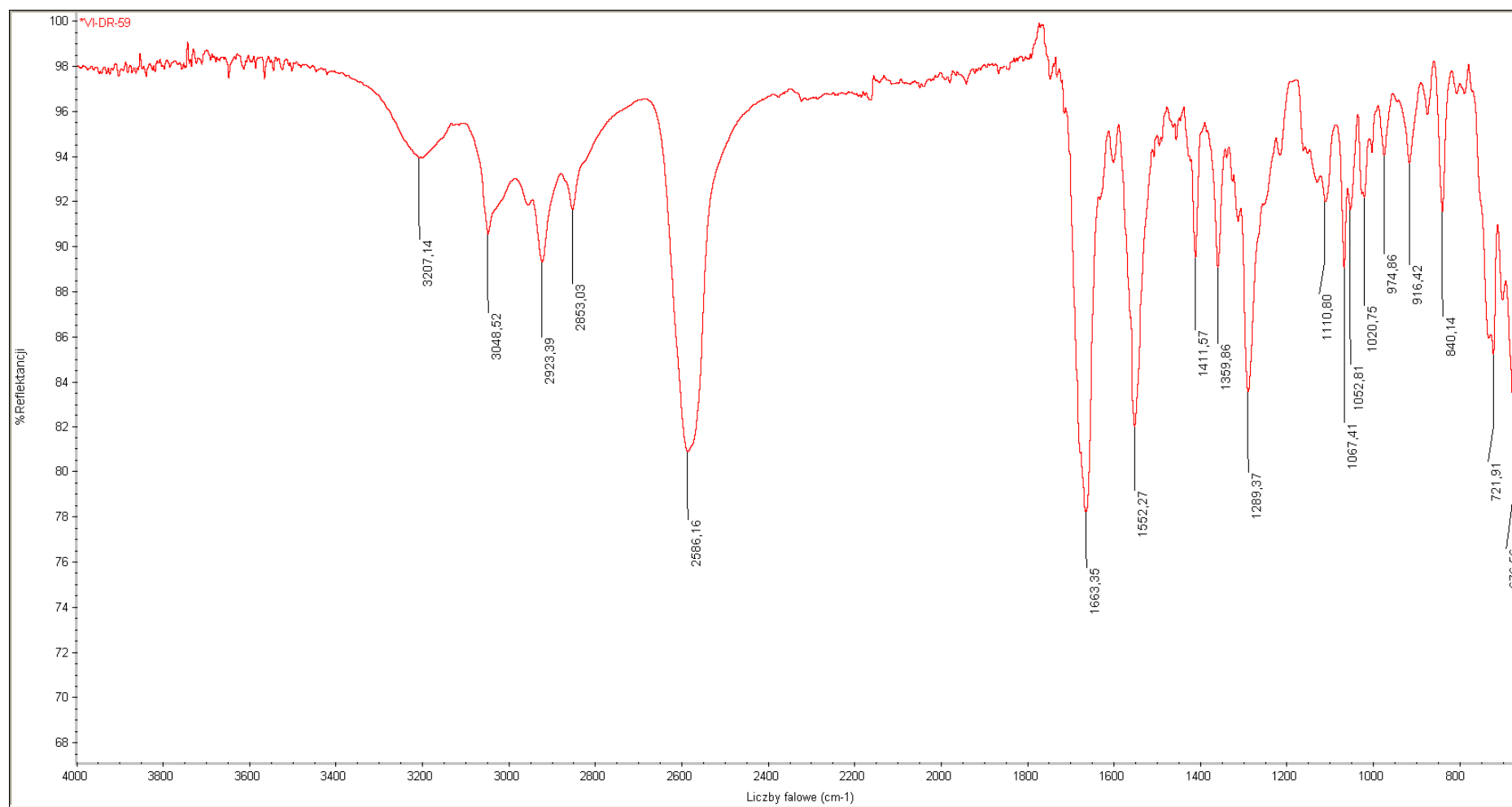


Figure S45. IR spectrum of compound 20.

Spectrum Name: VI-DR-59_frg_dod2
Start Ion: 100
End Ion: 500
Source: APCI + 10.0 μ A 250C
Capillary: 150V 200C Offset: 15V Span: 0V

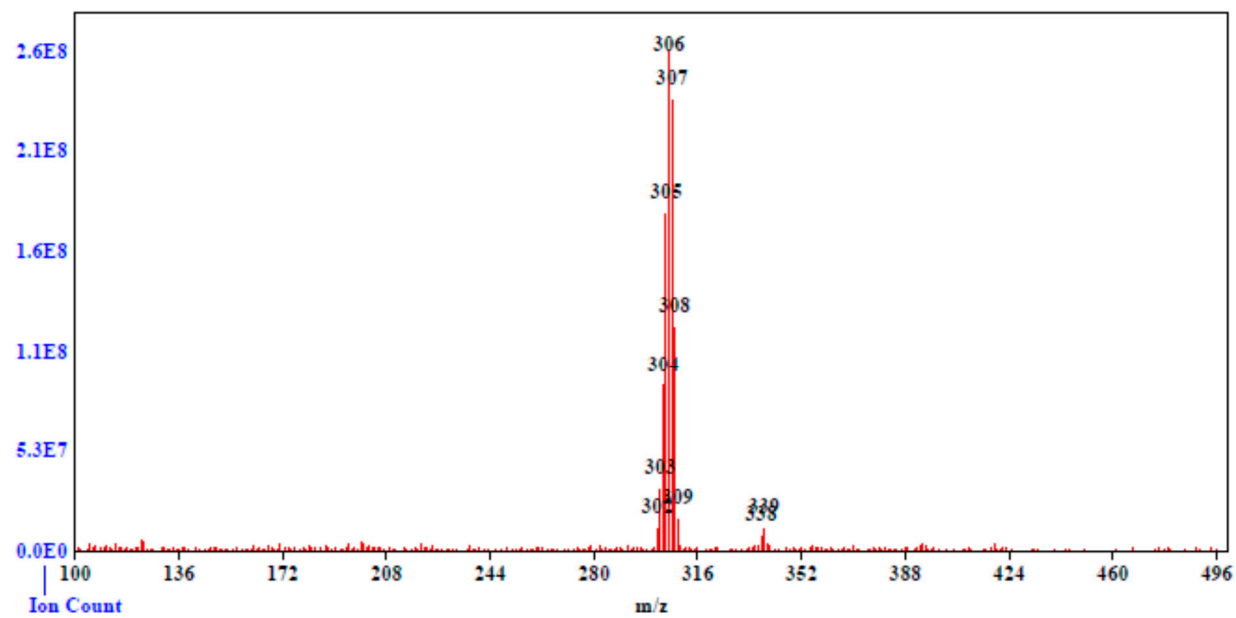


Figure S46. MS spectrum of compound 20.

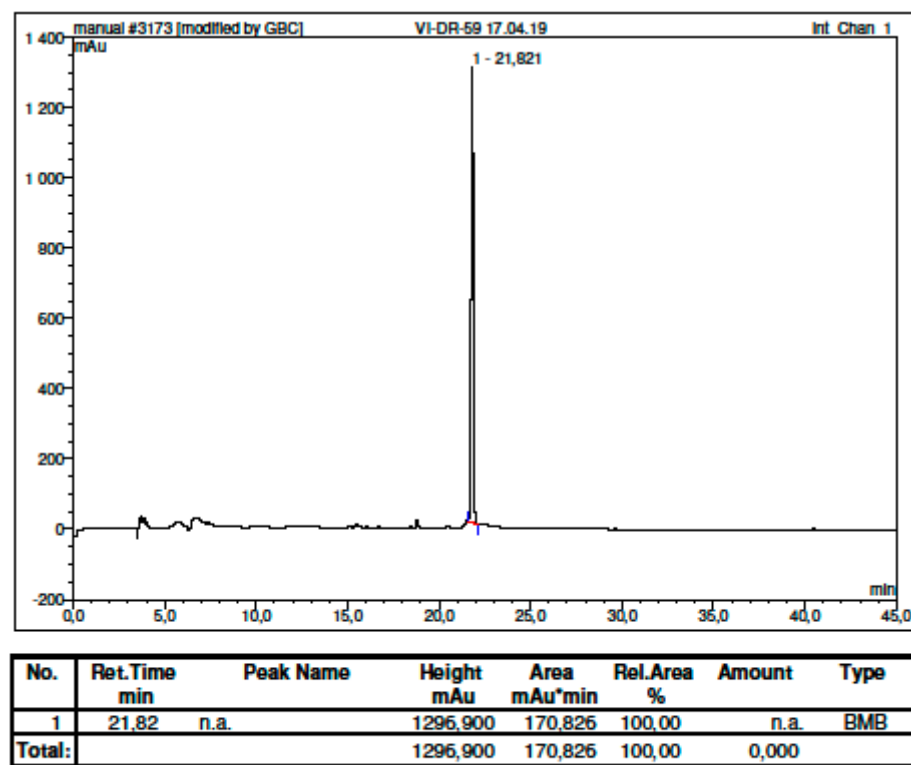


Figure S47. HPLC analysis of compound 20.

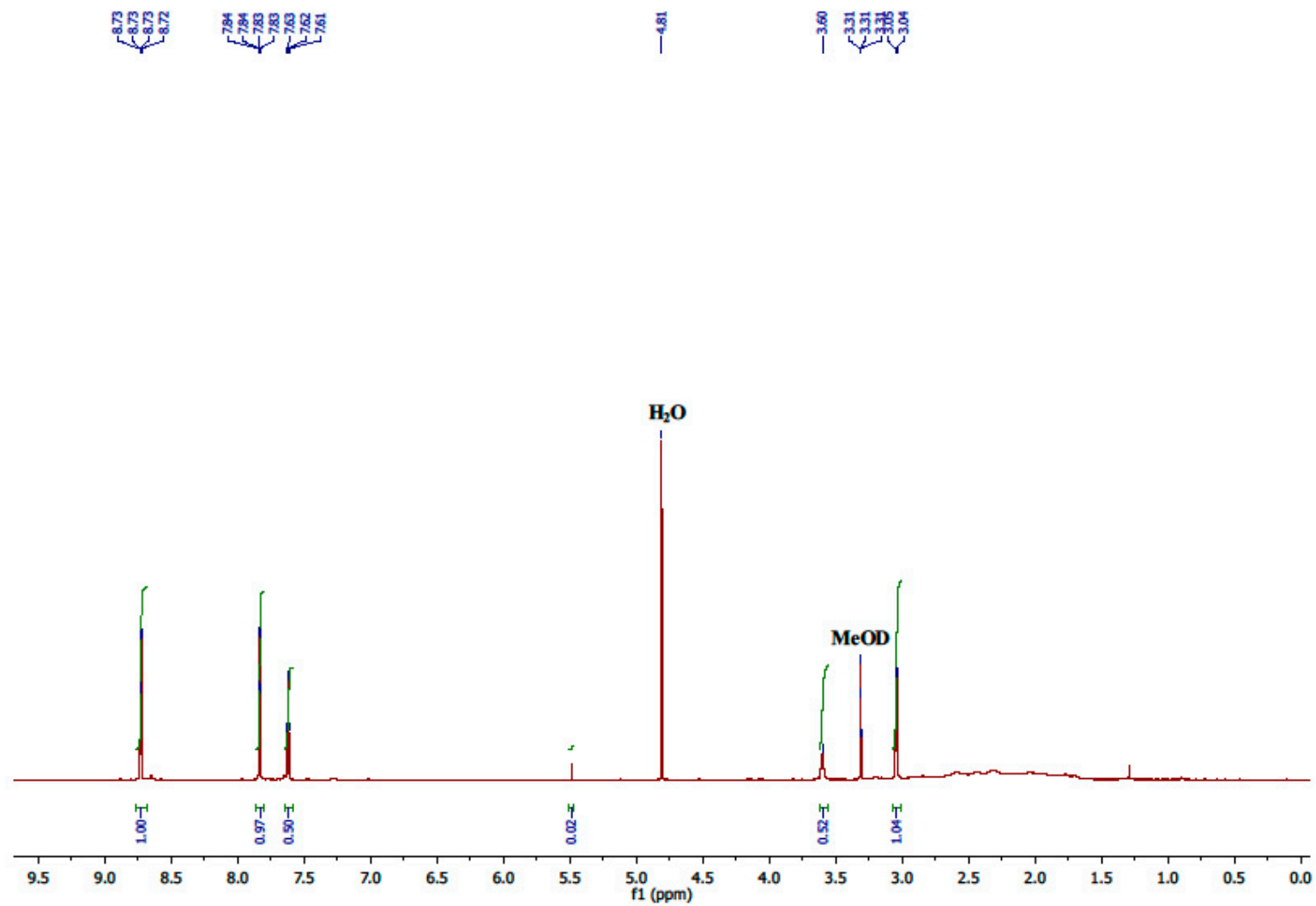


Figure S48. ¹H NMR spectrum of compound 21.

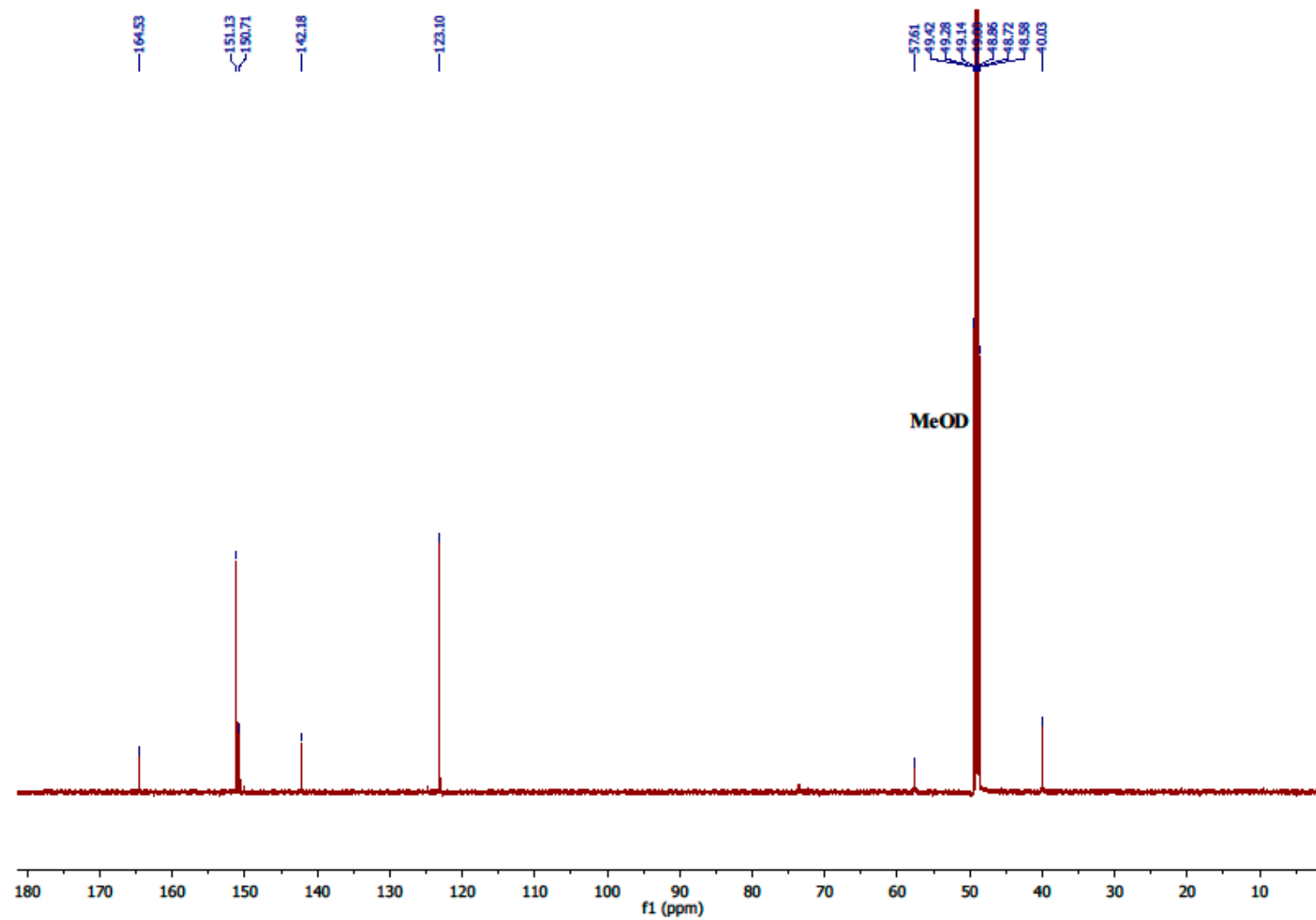


Figure S49. ¹³C NMR spectrum of compound 21.

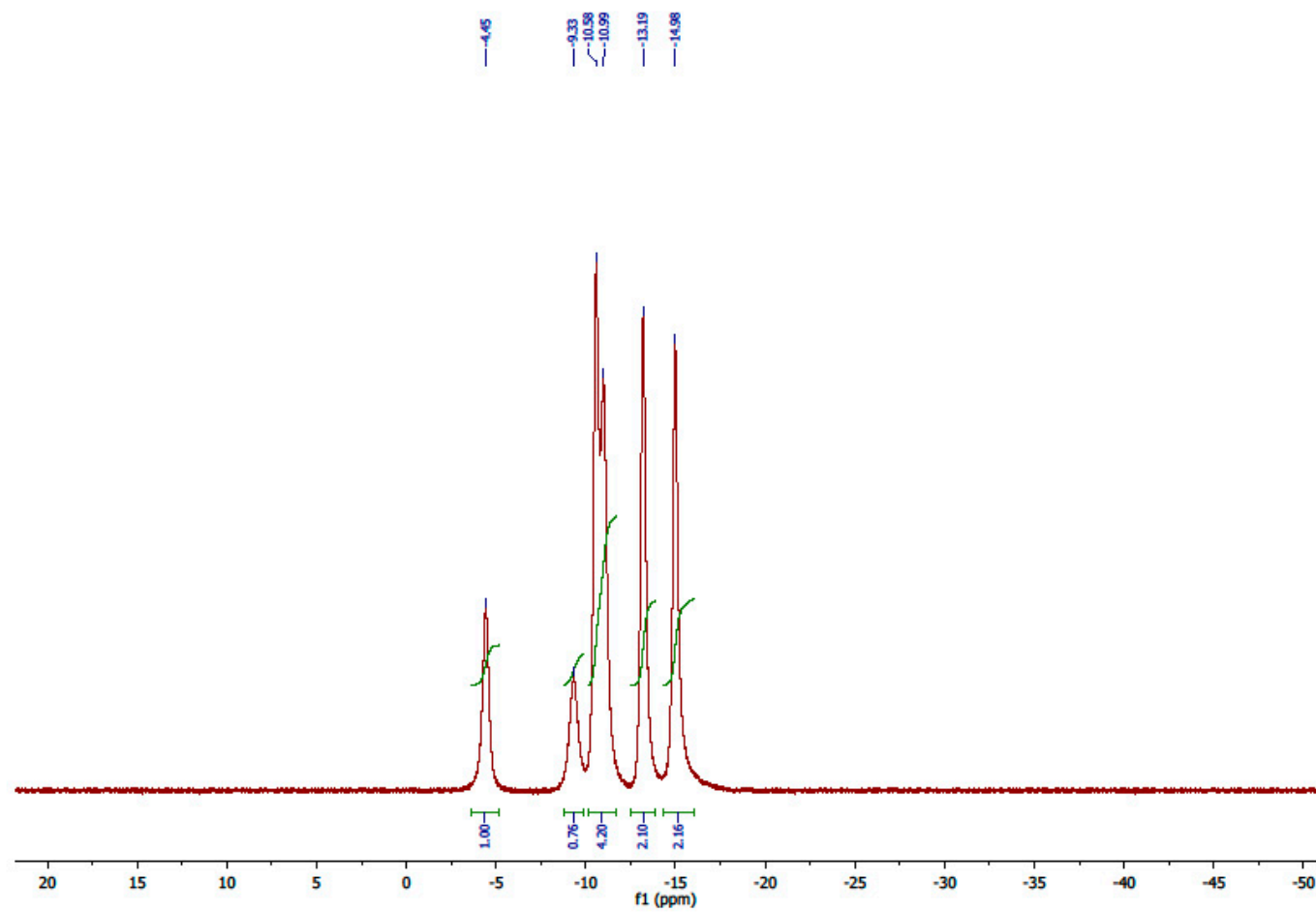


Figure S50. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 21.

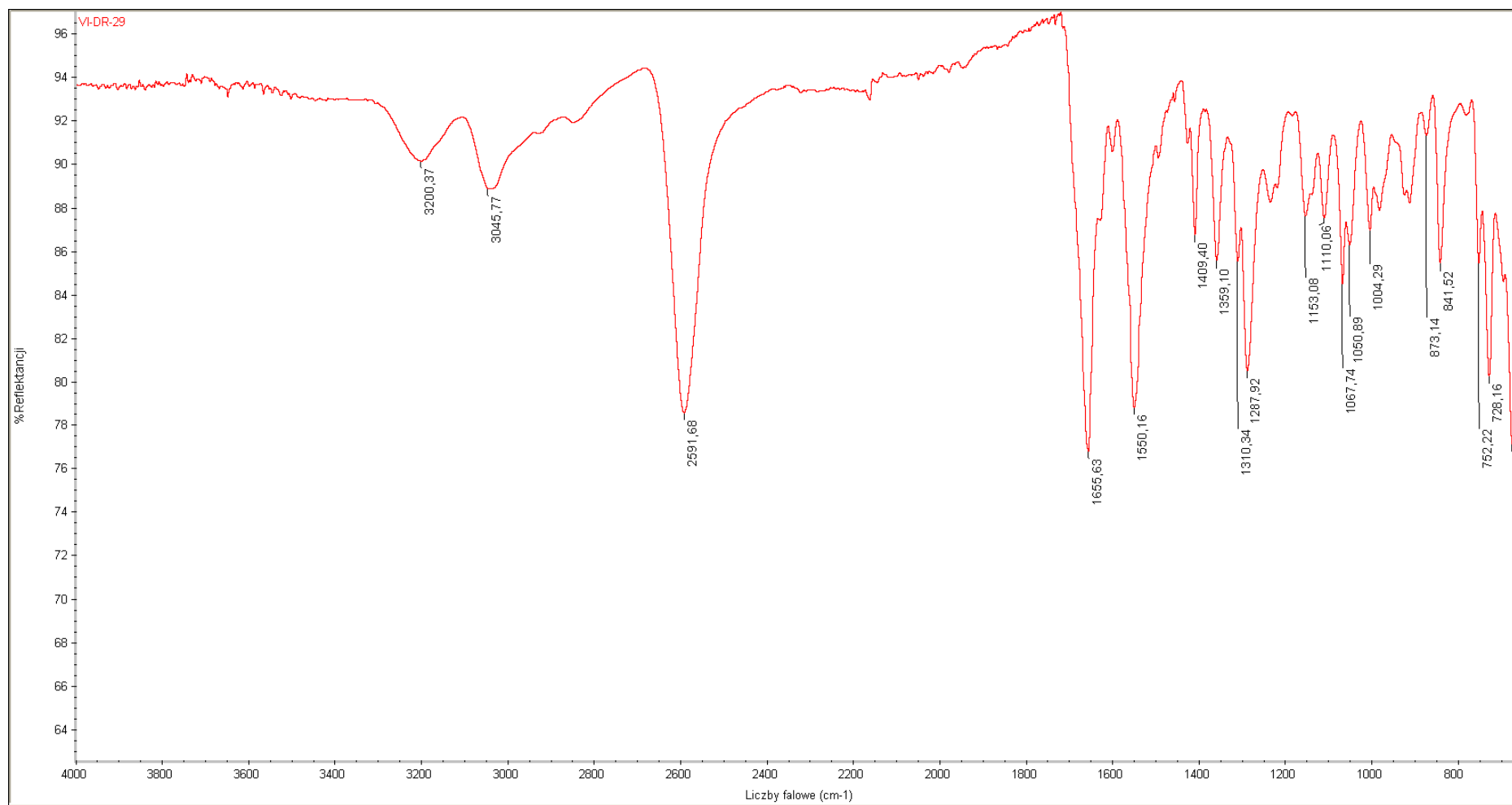


Figure S51. IR spectrum of **21**.

Spectrum Name: VI-DR-29_frg_dod
Start Ion: 200
End Ion: 500
Source: APCI + 10.0μA 250C
Capillary: 150V 200C Offset: 15V Span: 0V

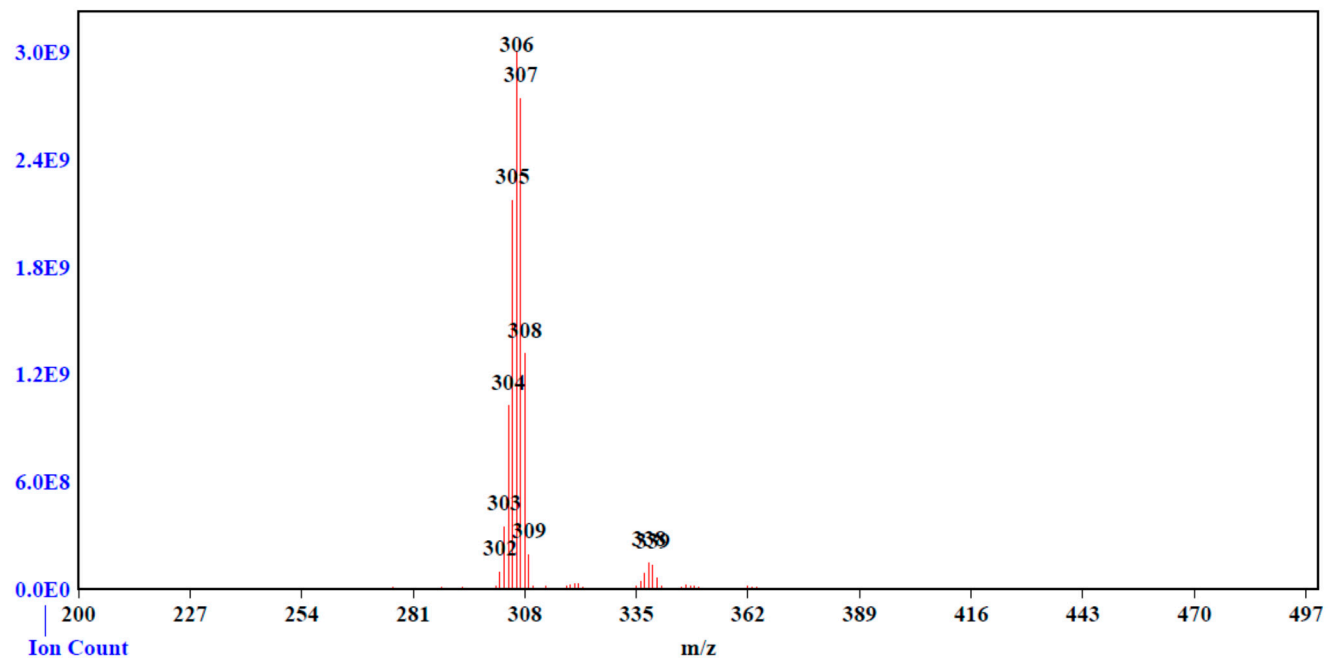


Figure S52. MS spectrum of compound 21.

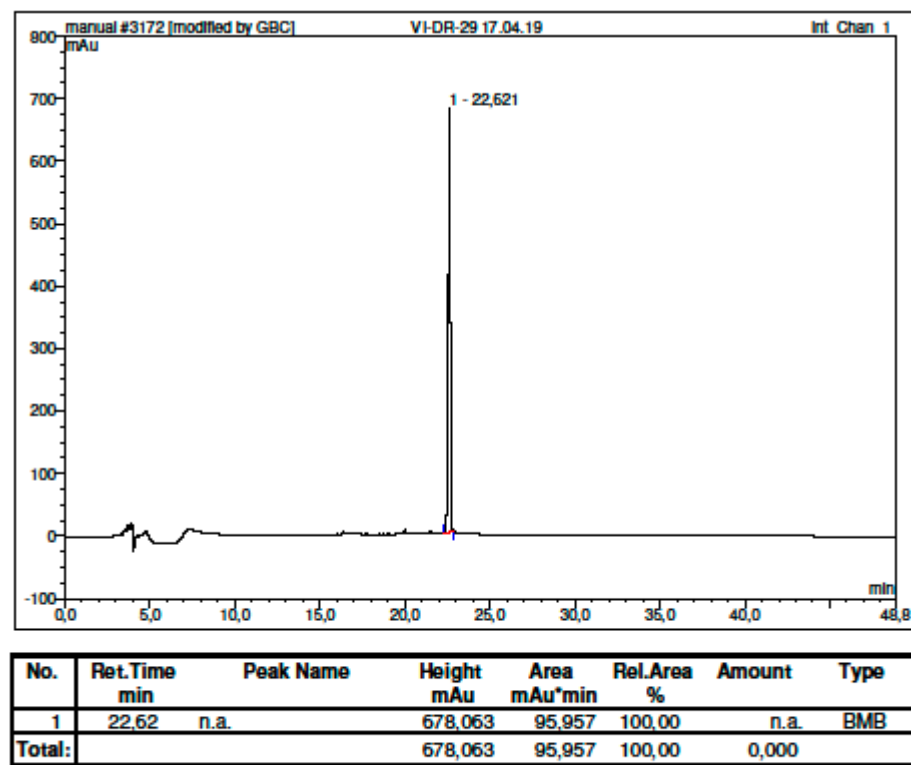


Figure S53. HPLC analysis of compound 21.

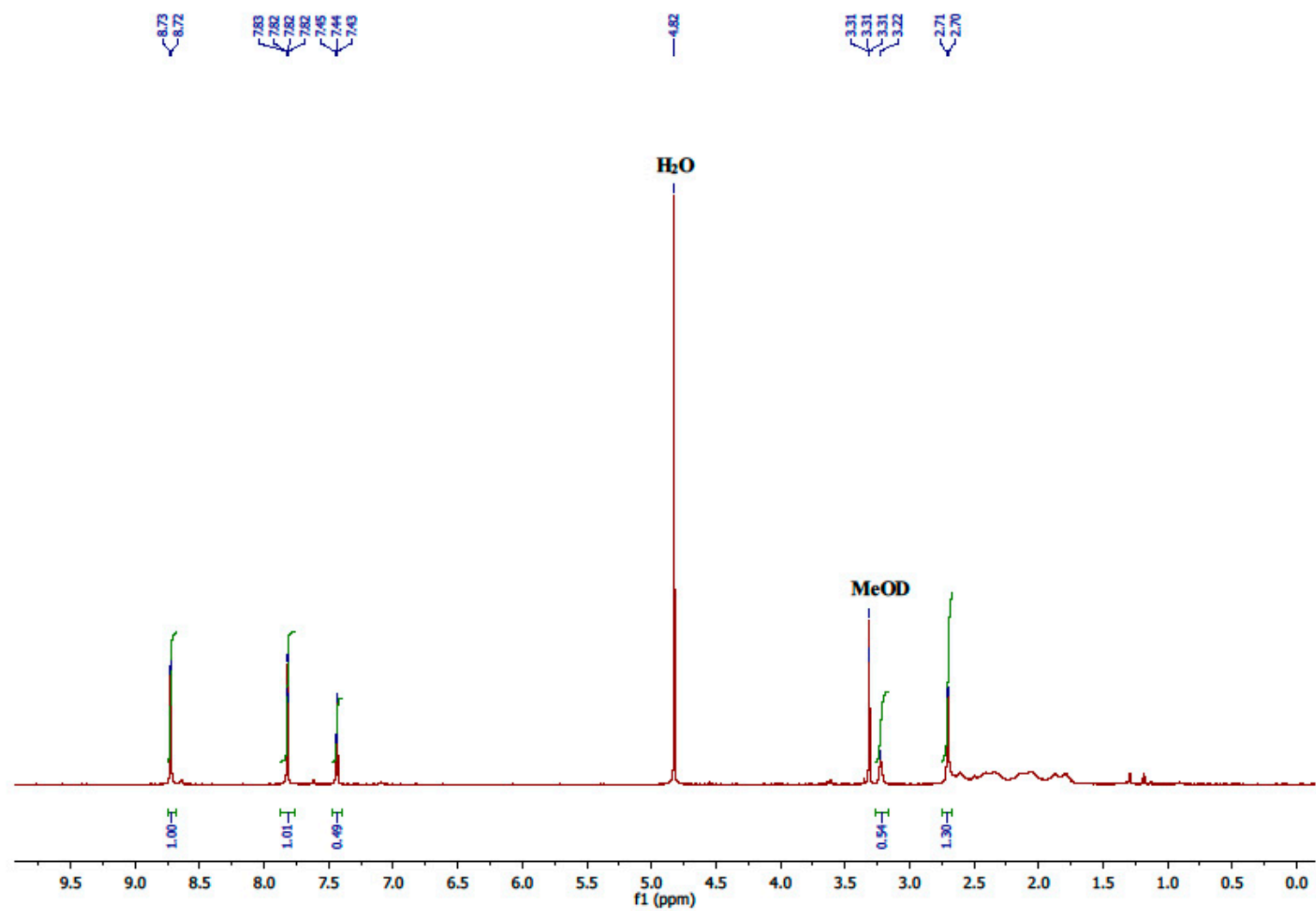


Figure S54. ¹H NMR spectrum of compound 22.

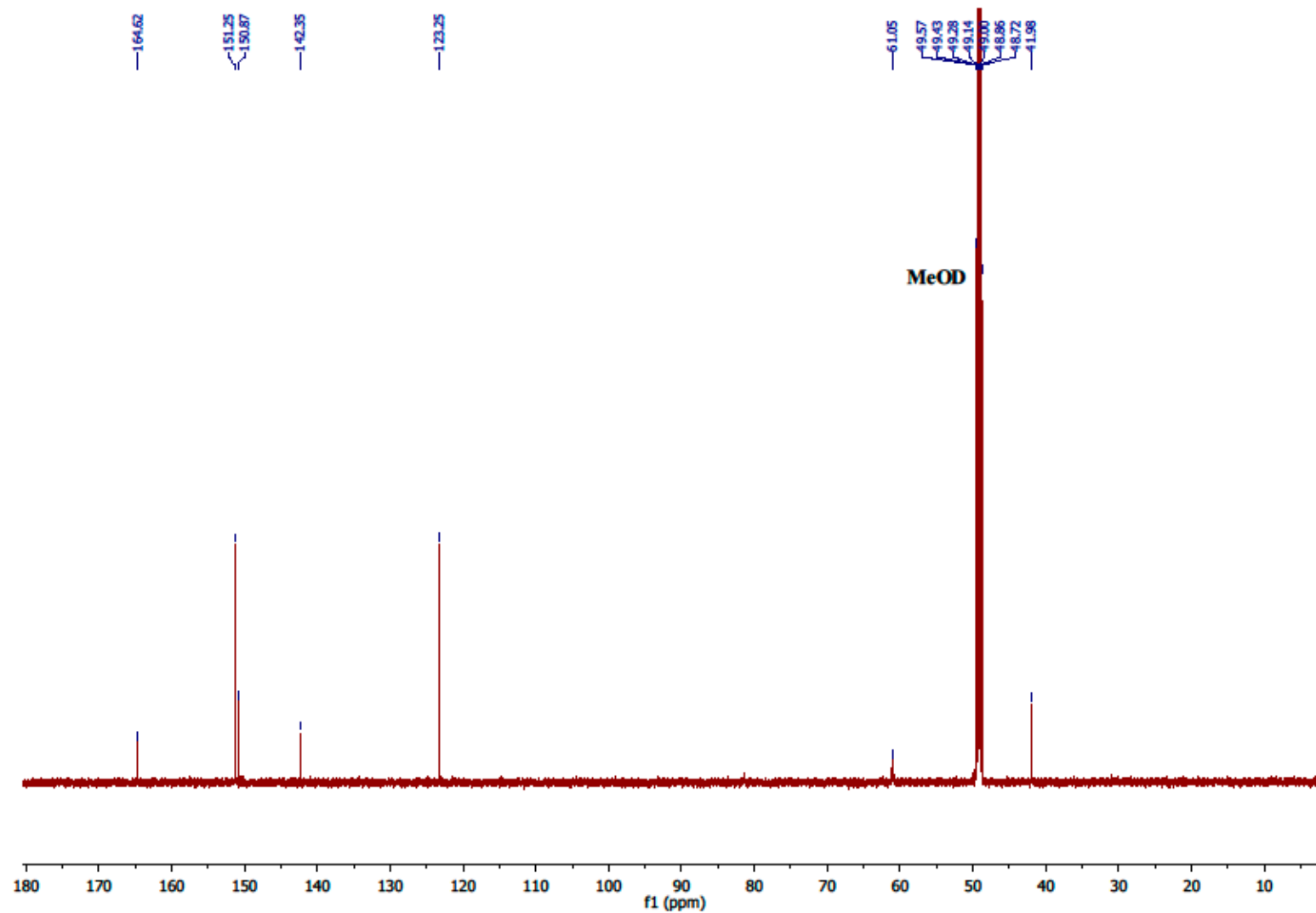


Figure S55. ¹³C NMR spectrum of compound 22.

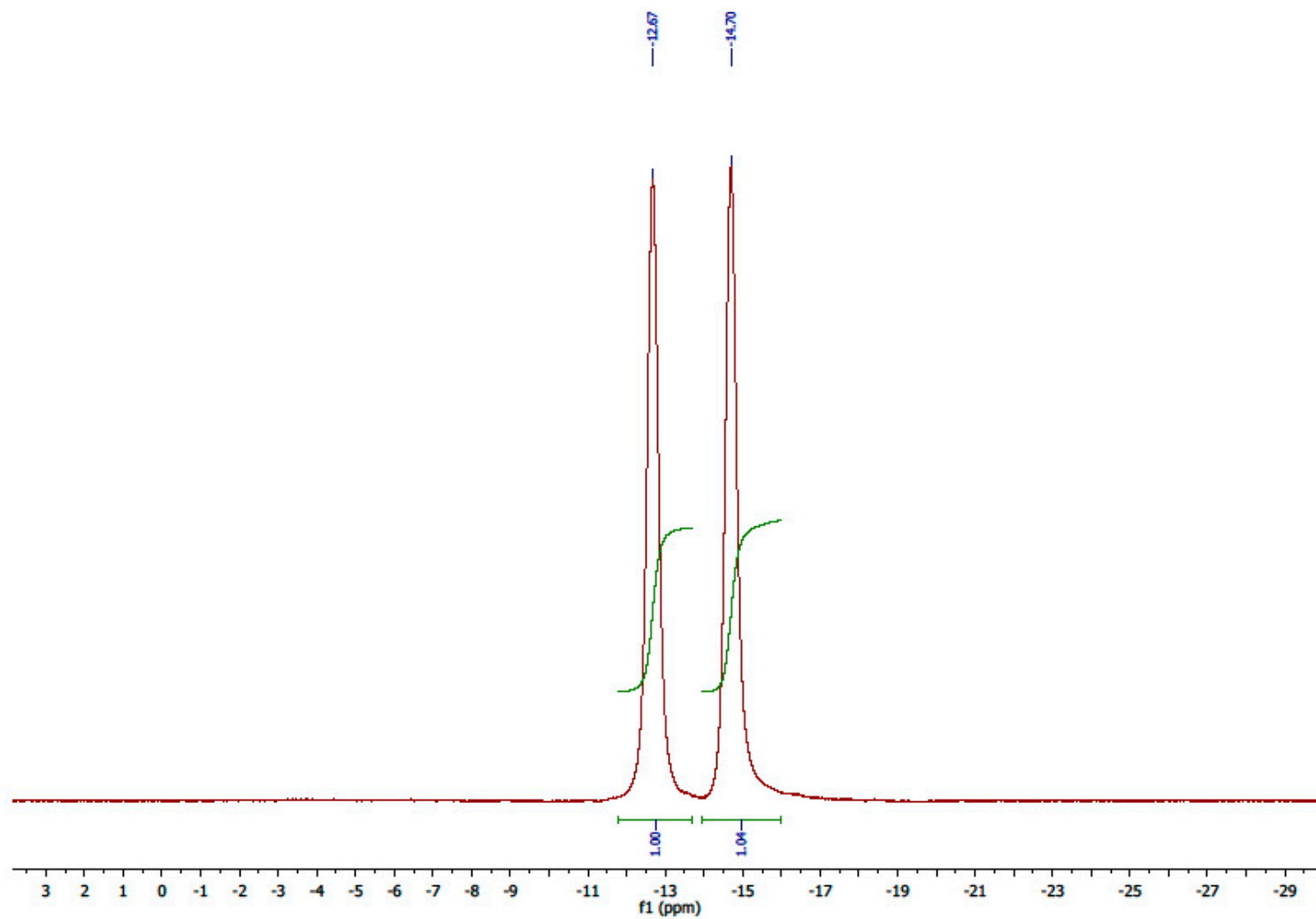


Figure S56. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 22.

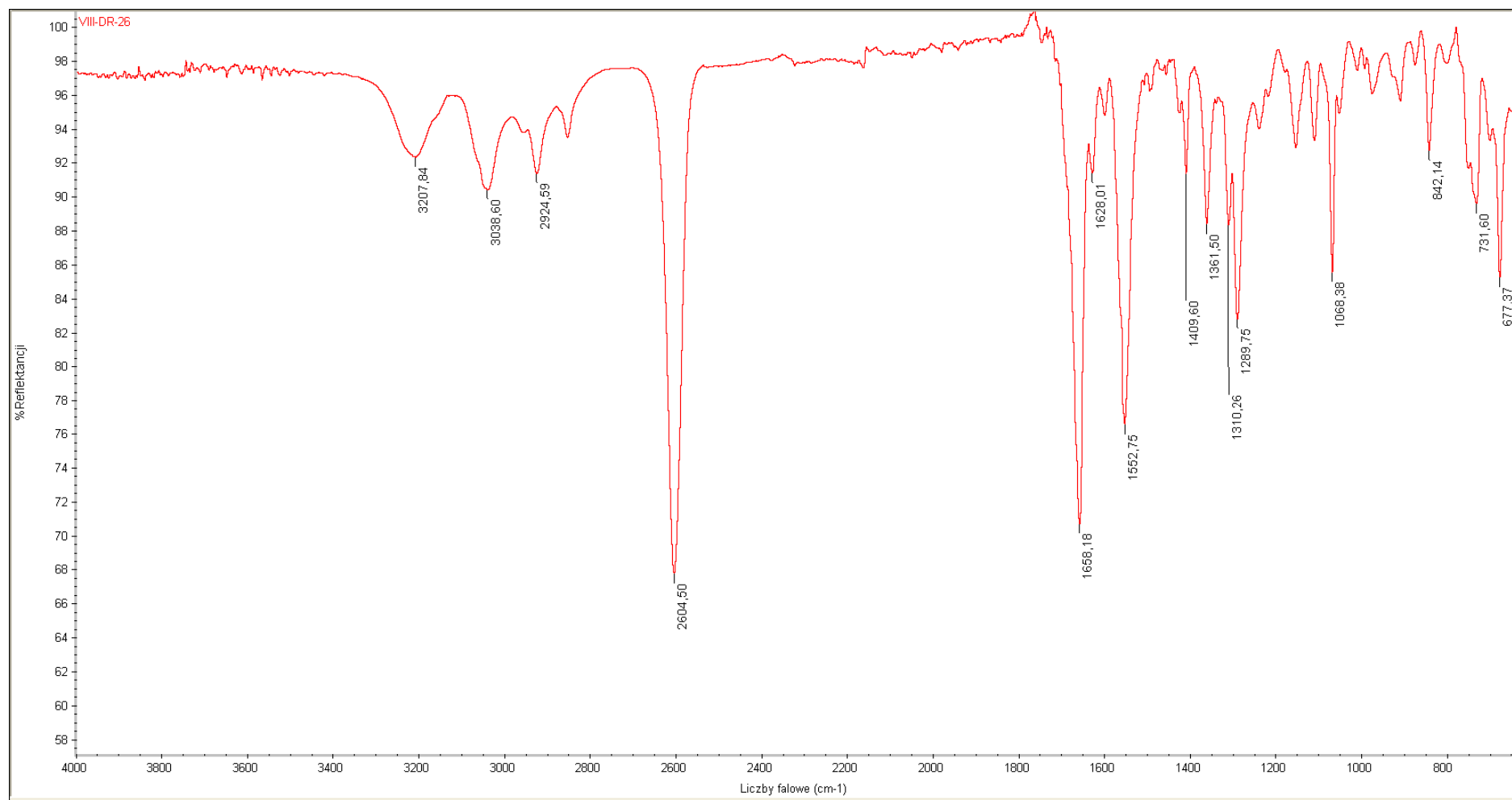


Figure S57. IR spectrum of compound 22.

Spectrum Name: VIII-DR-26_frg_dod
Start Ion: 100
End Ion: 500
Source: APCI + 10.0µA 250C
Capillary: 150V 200C Offset: 15V Span: 0V

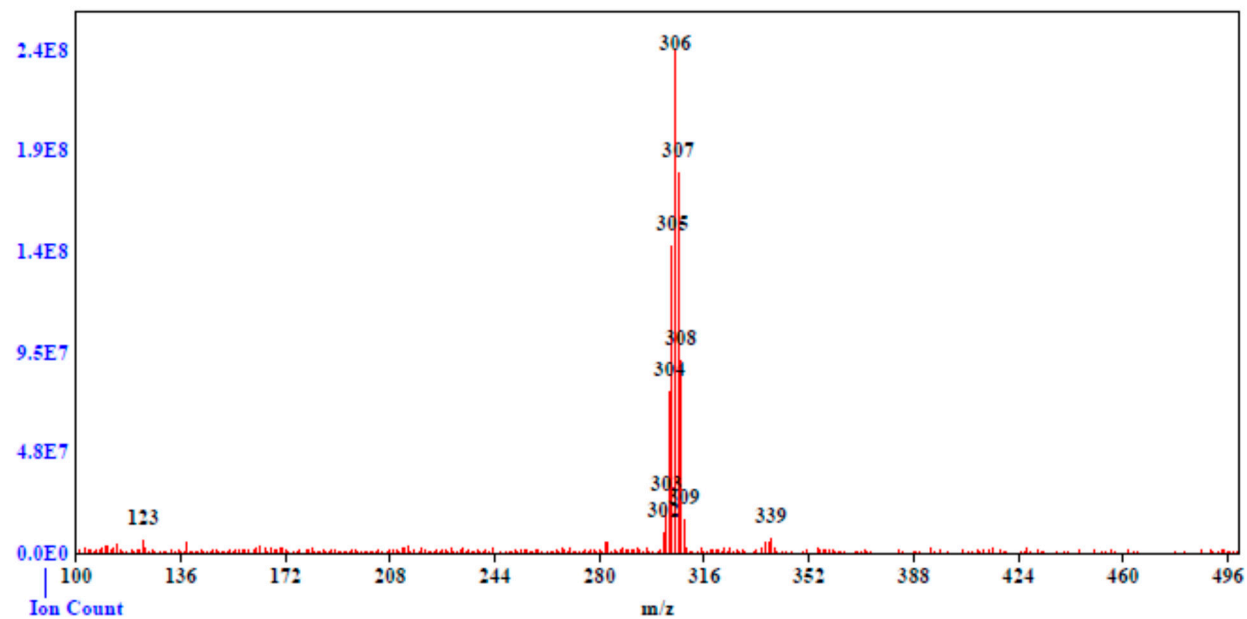


Figure S58. MS spectrum of compound 22.

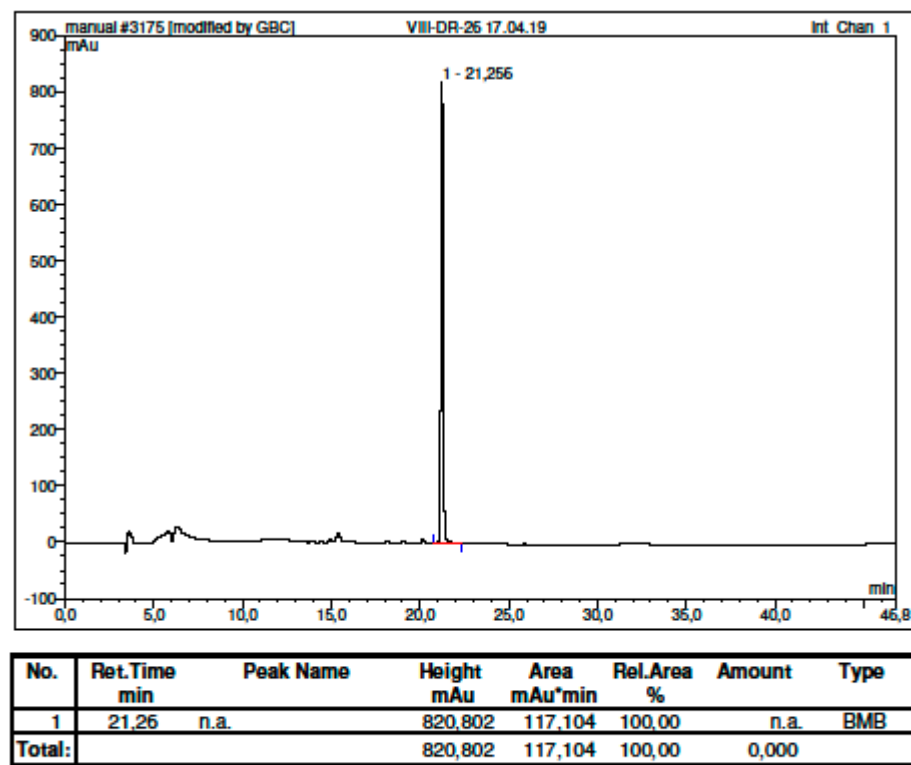


Figure S59. HPLC analysis of compound 22.

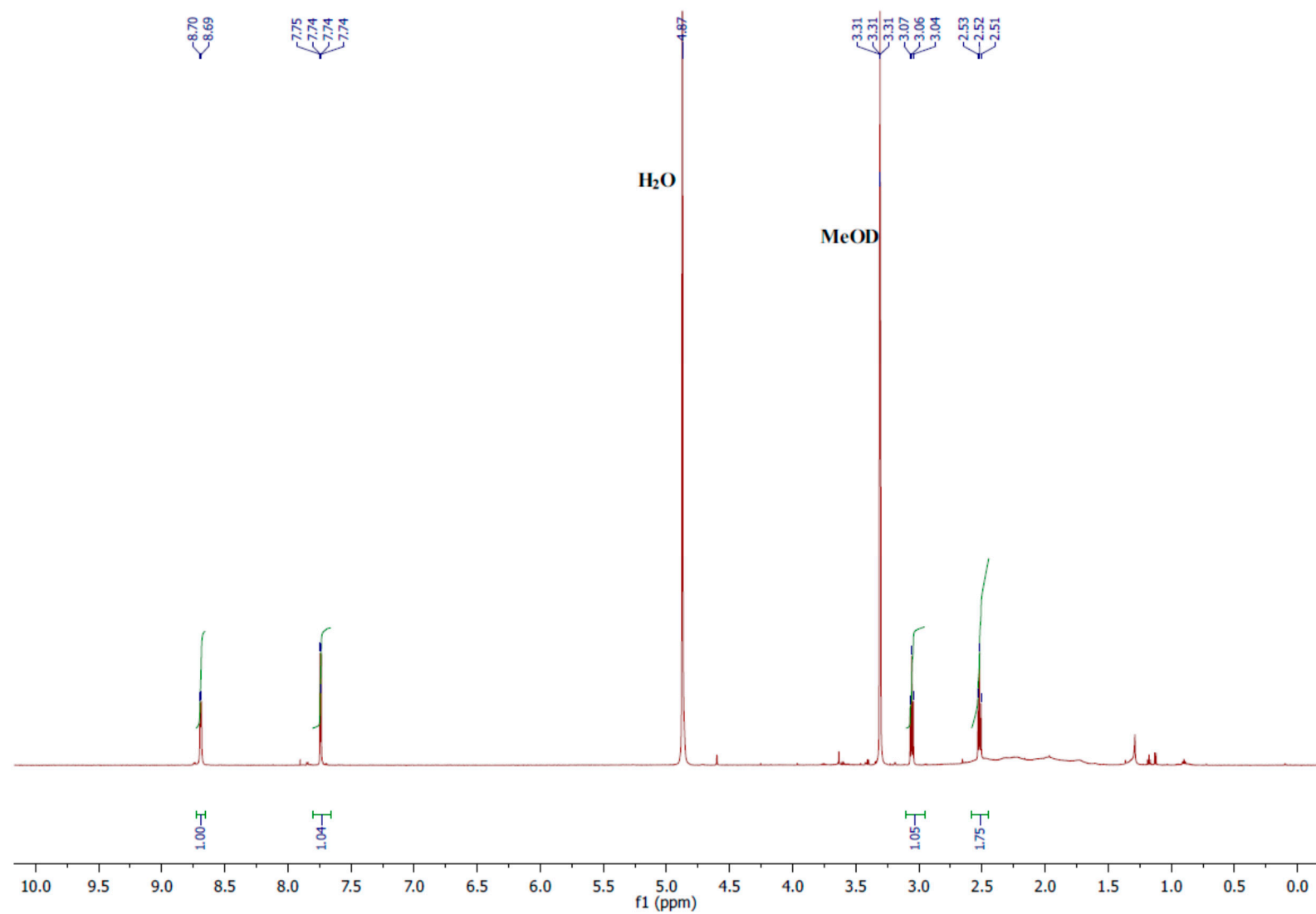


Figure S60. ¹H NMR spectrum of compound 23.

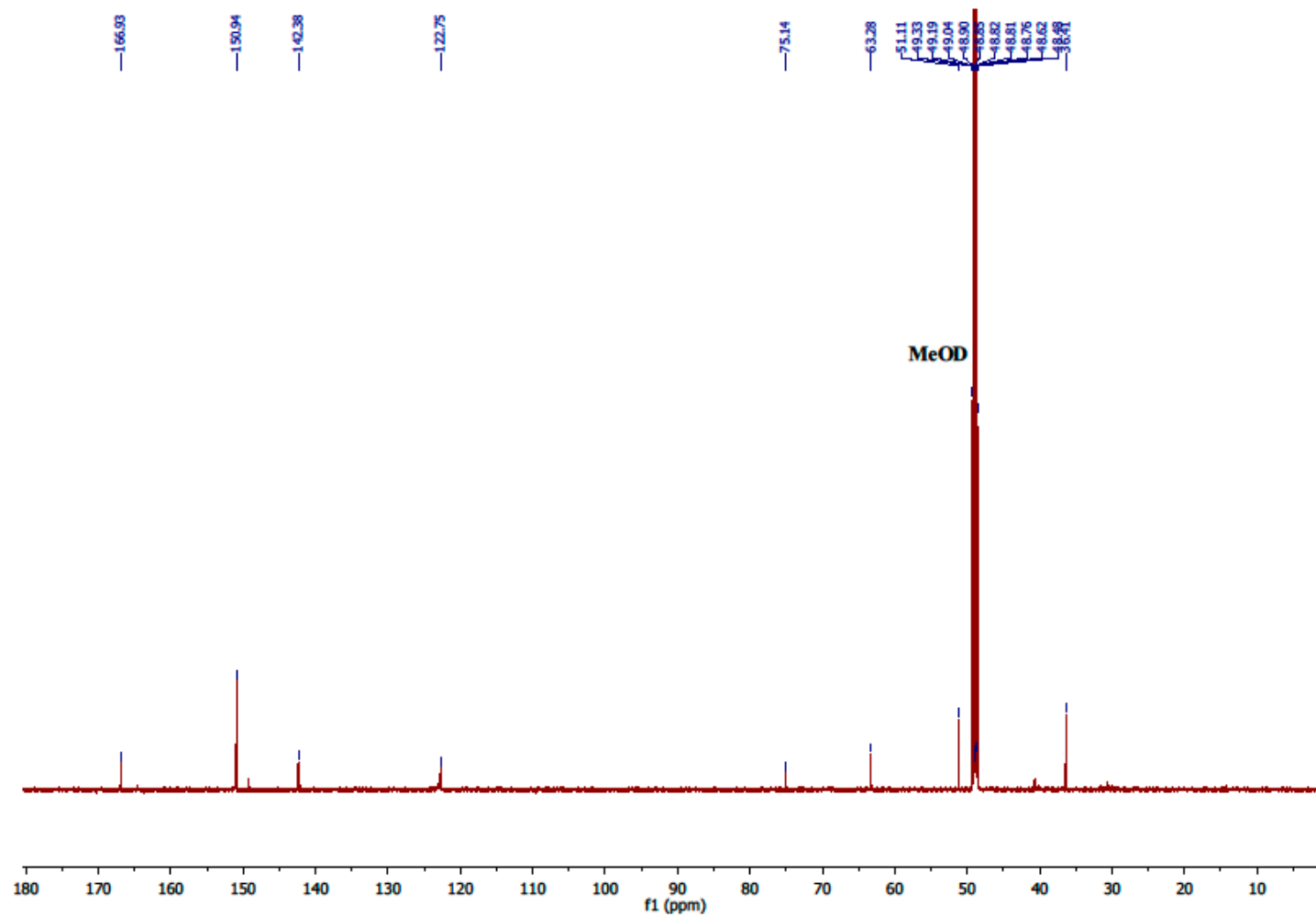


Figure S61. ¹³C NMR spectrum of compound 23.

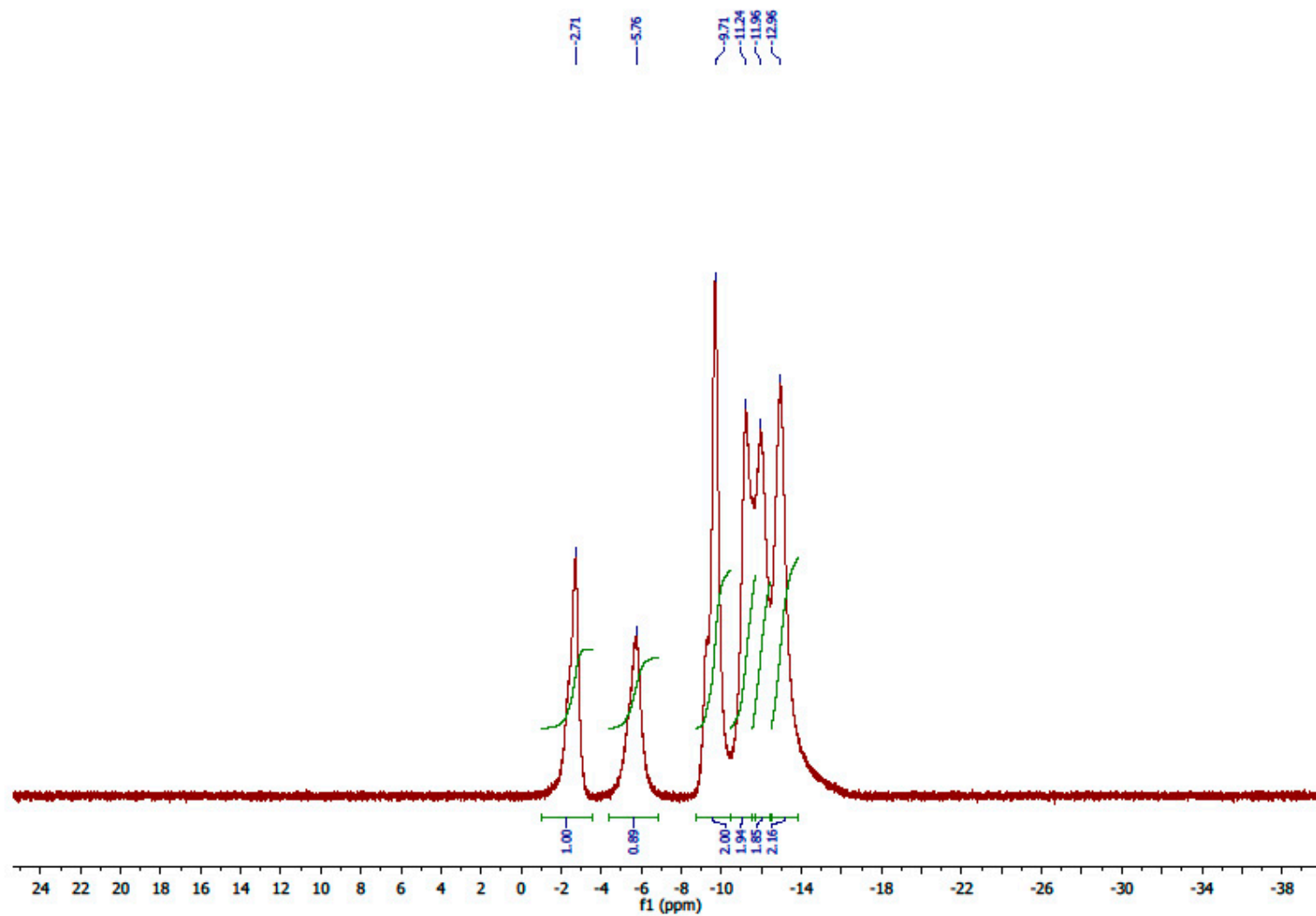


Figure S62. ^1B NMR $\{^1\text{H BB}\}$ spectrum of compound 23.

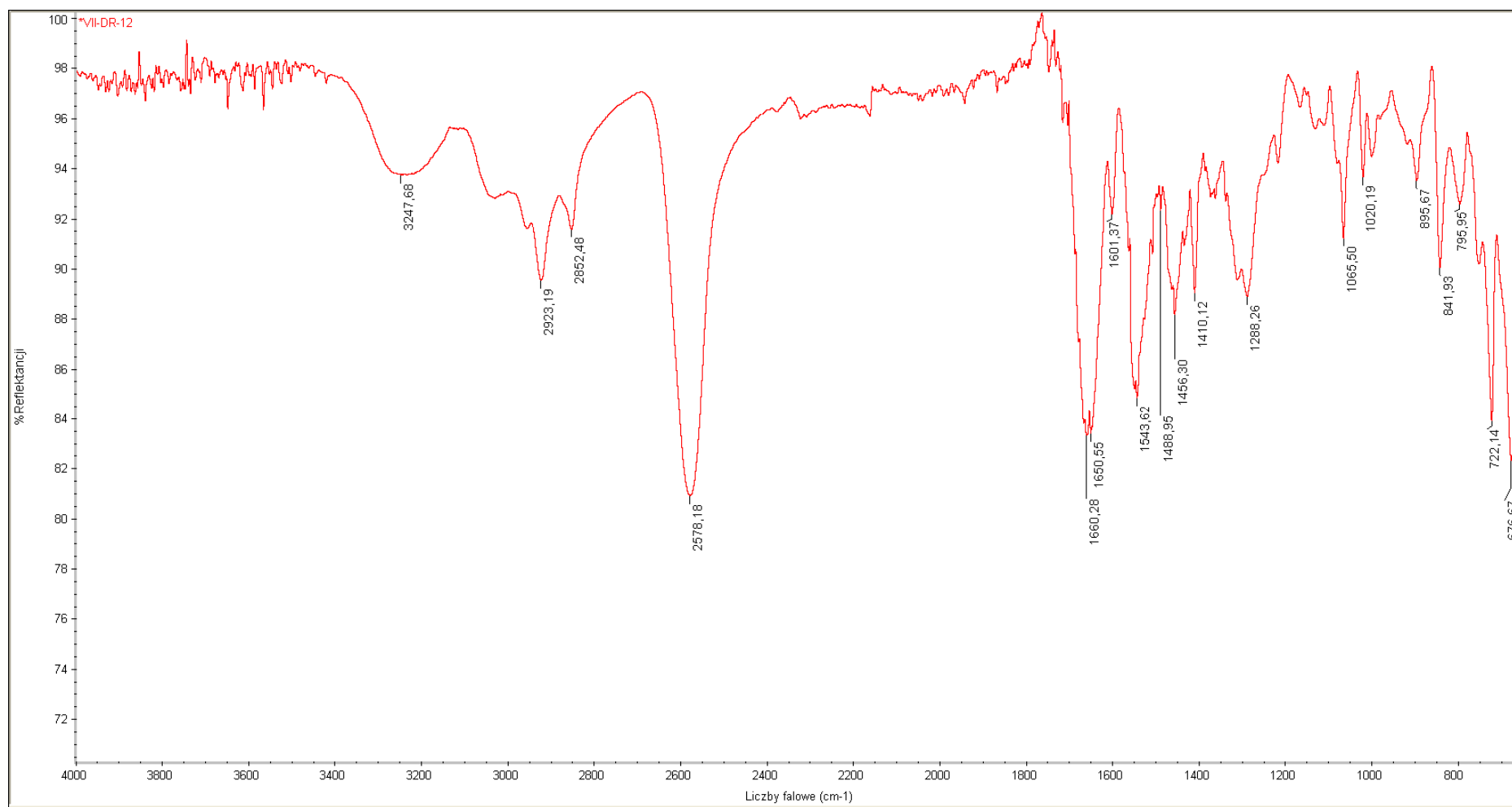


Figure S63. IR spectrum of compound 23.

Spectrum Name: VII-DR-12_rob_dod
Start Ion: 100
End Ion: 500
Source: APCI + 10.0 μ A 400C
Capillary: 180V 300C Offset: 30V Span: 20V

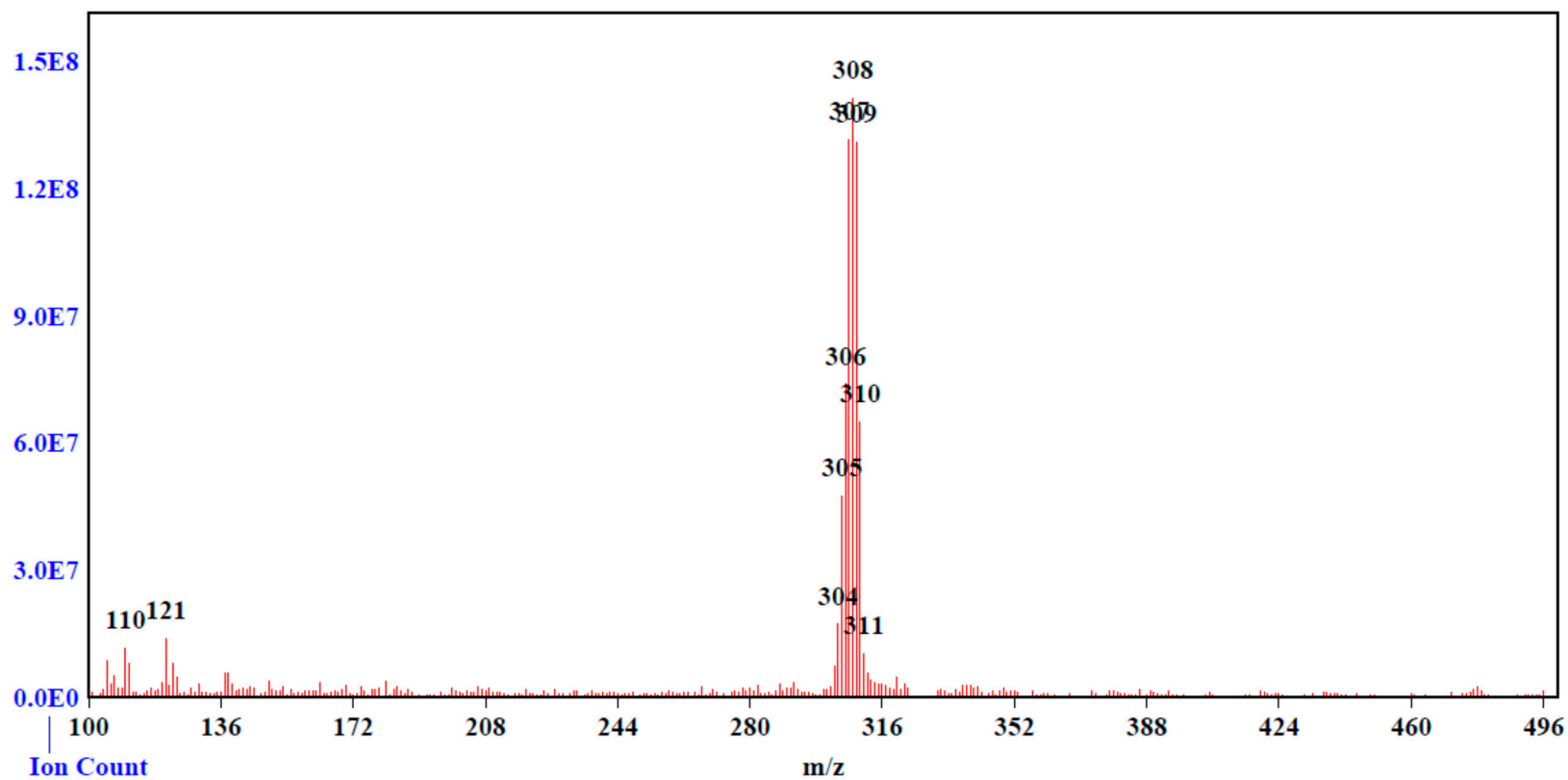


Figure S64. MS spectrum of compound 23.

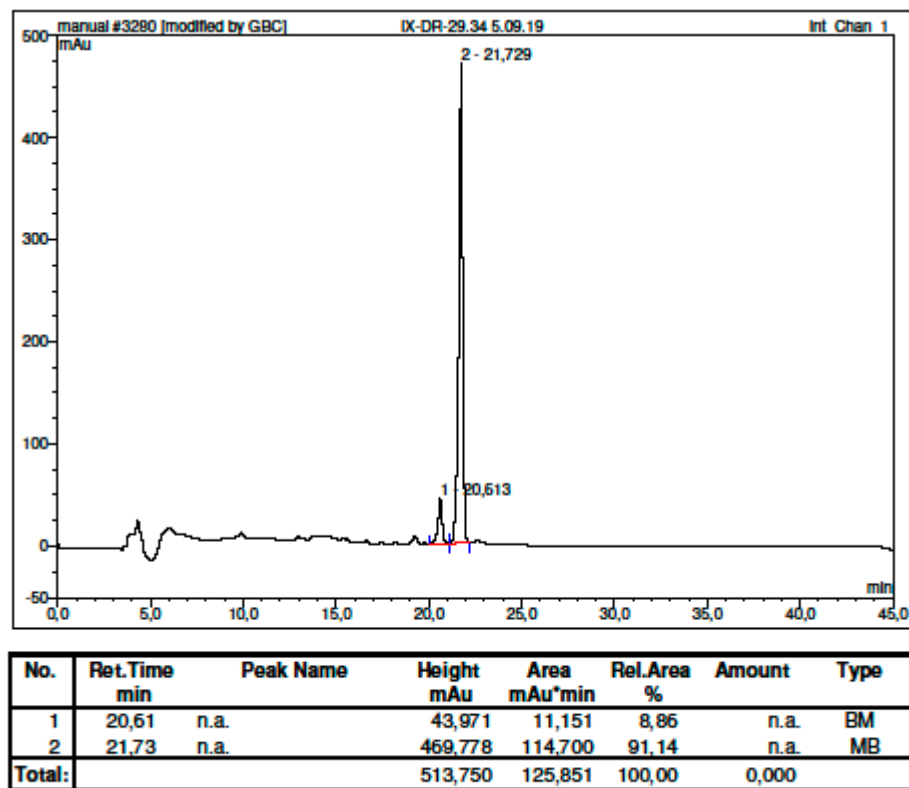


Figure S65. HPLC analysis of compound 23.

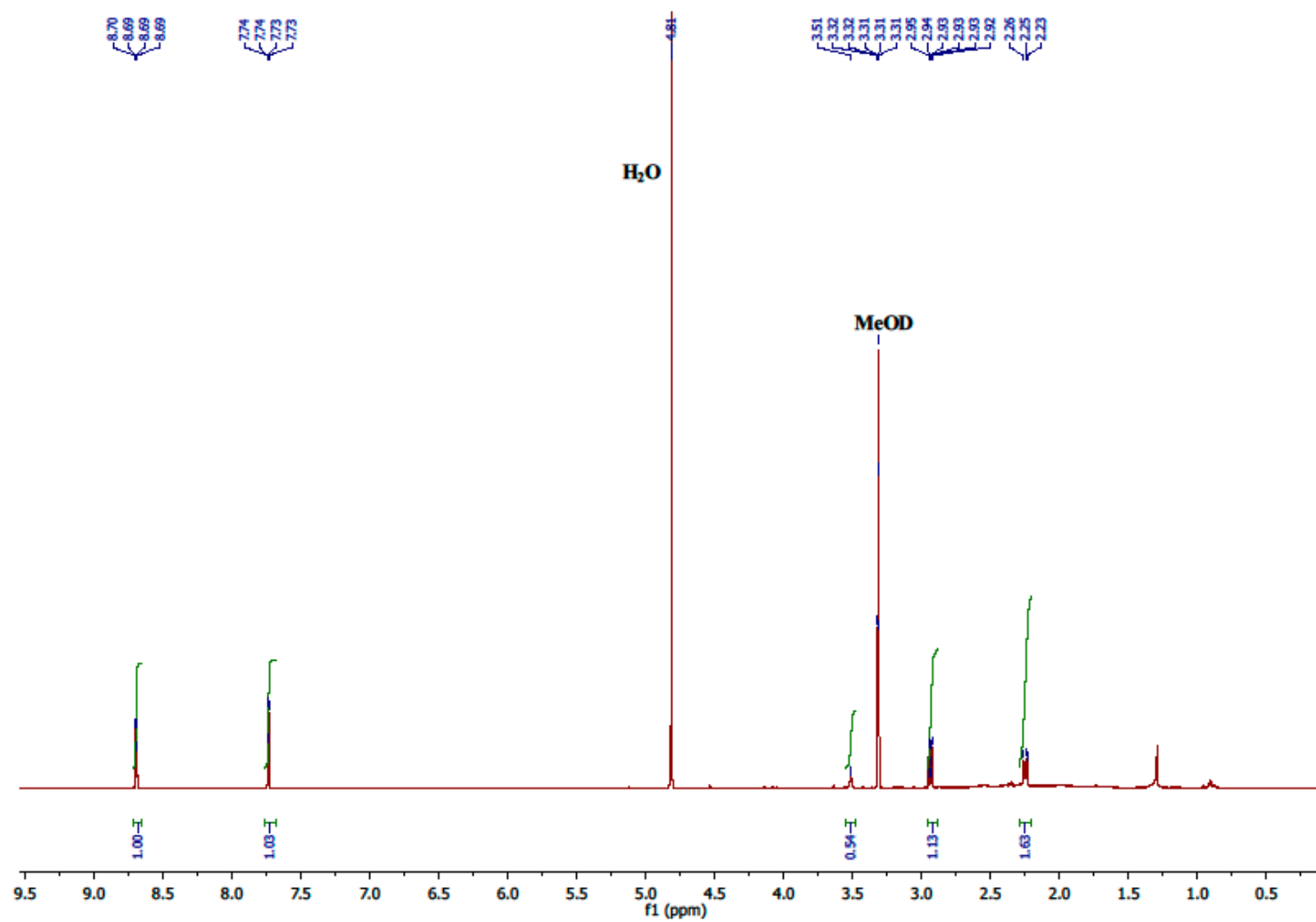


Figure S66. ¹H NMR spectrum of compound 24.

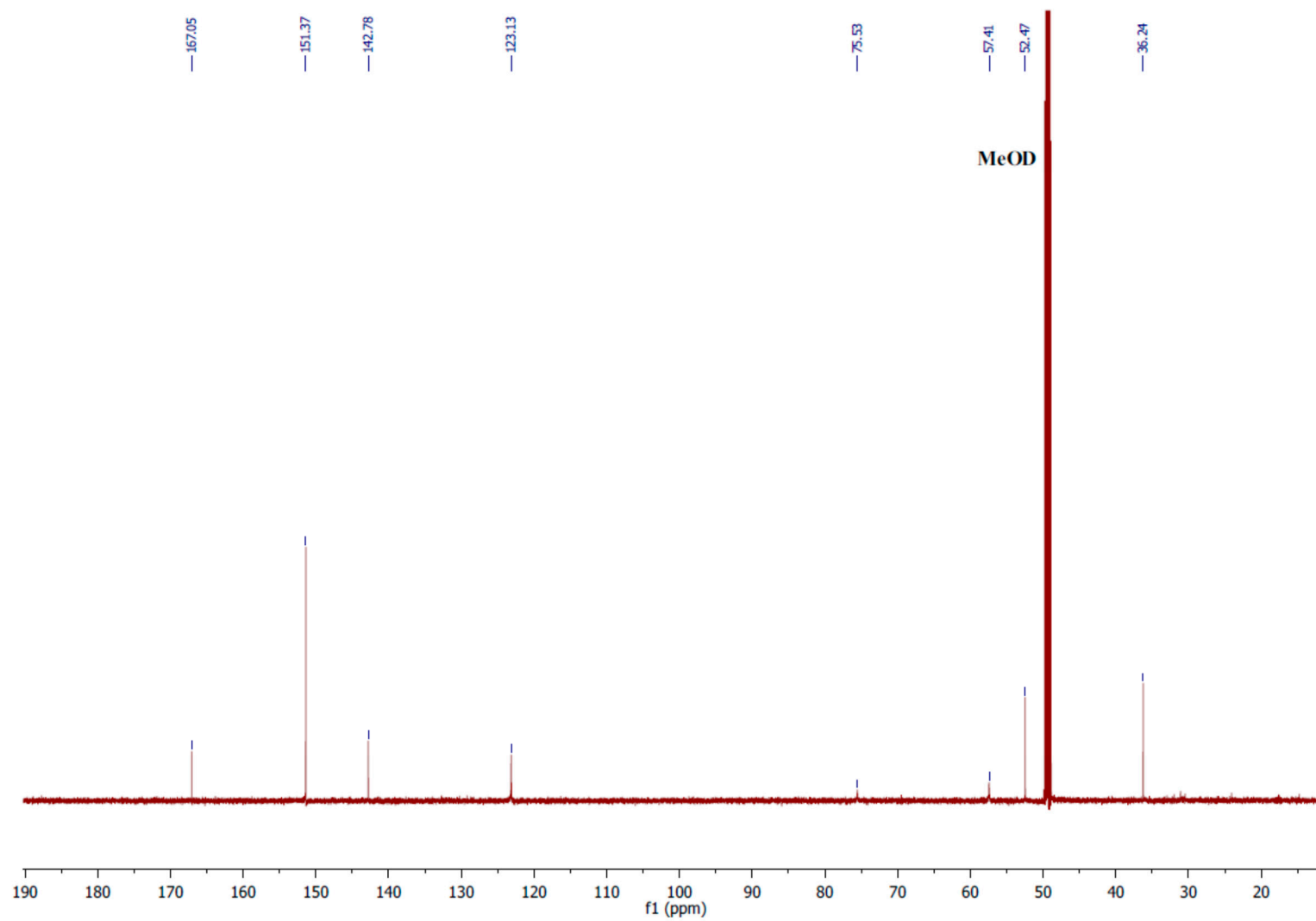


Figure S67. ¹³C NMR spectrum of compound 24.

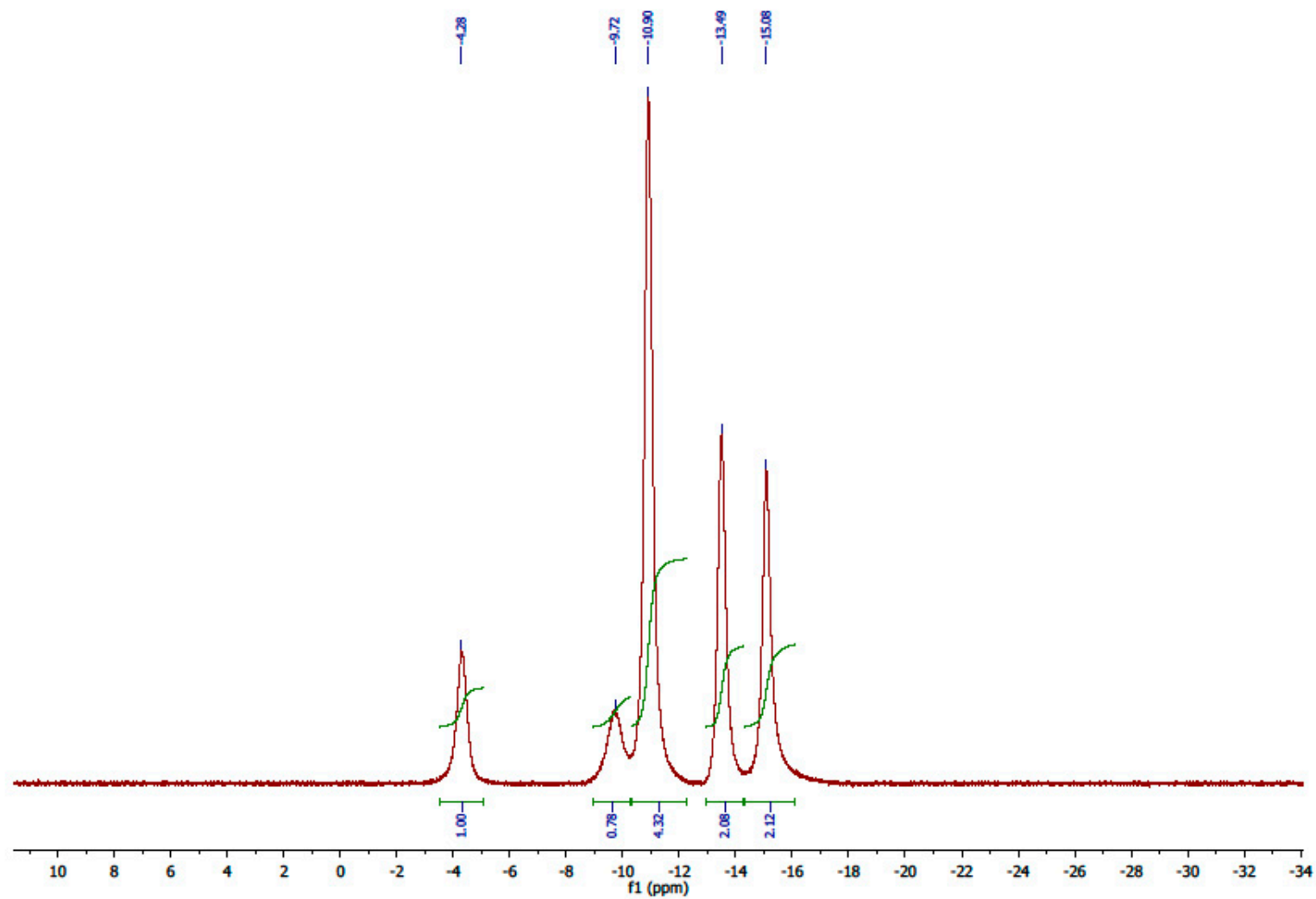


Figure S68. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 24.

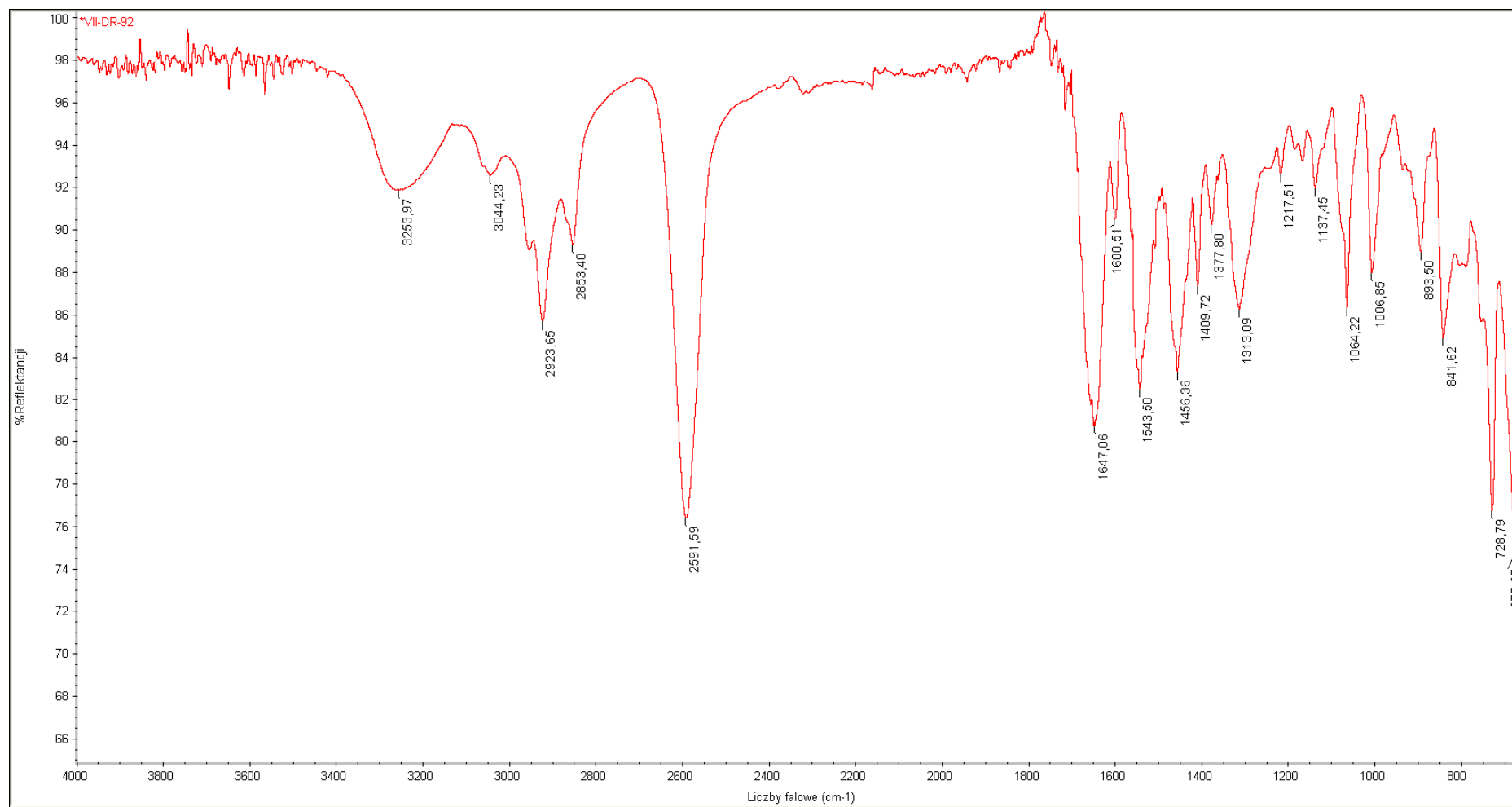


Figure S69. IR spectrum of compound **24**.

Spectrum Name: VI-DR-92_frg_dod
Start Ion: 200
End Ion: 450
Source: APCI + 10.0 μ A 250C
Capillary: 150V 200C Offset: 15V Span: 0V

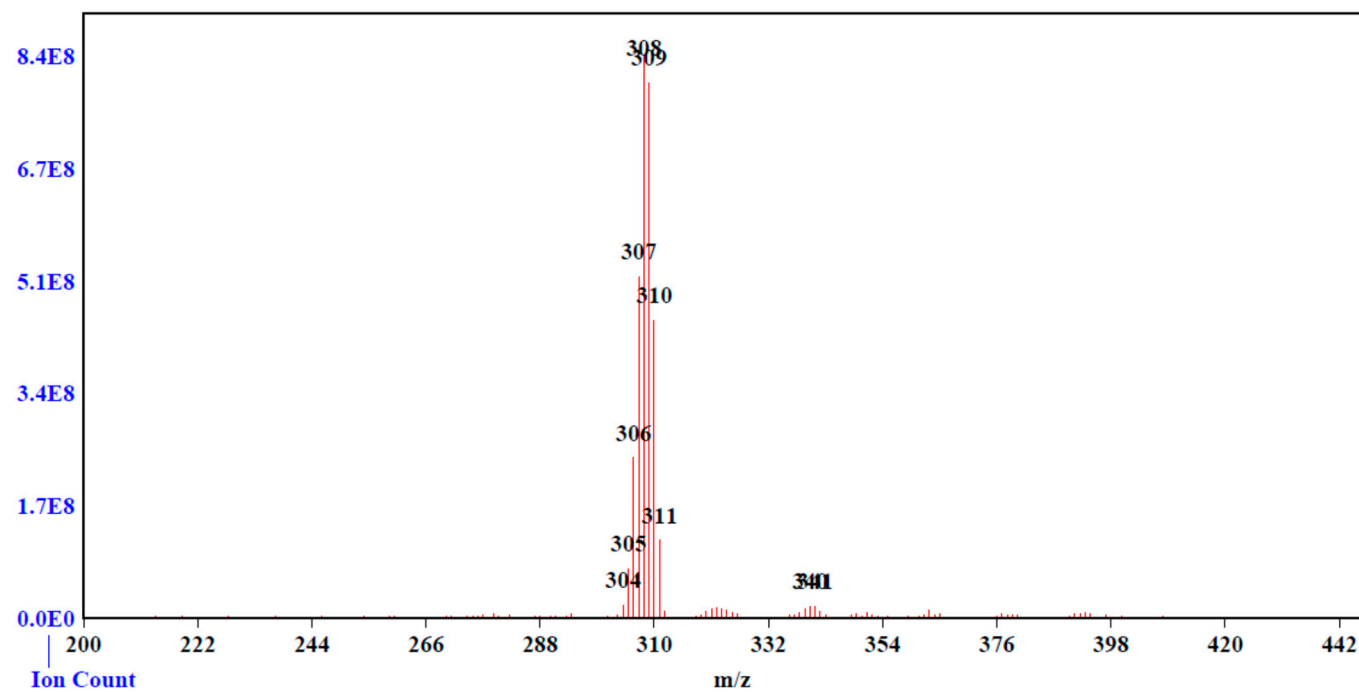


Figure S70. MS spectrum of compound 24.

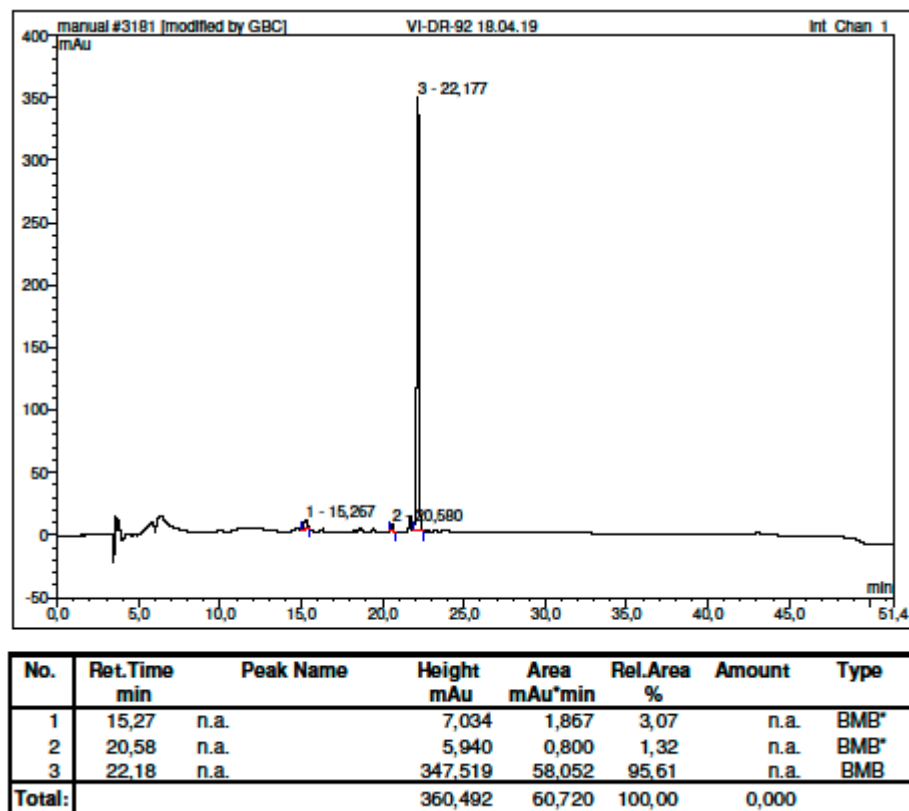


Figure S71. HPLC analysis of compound 24.

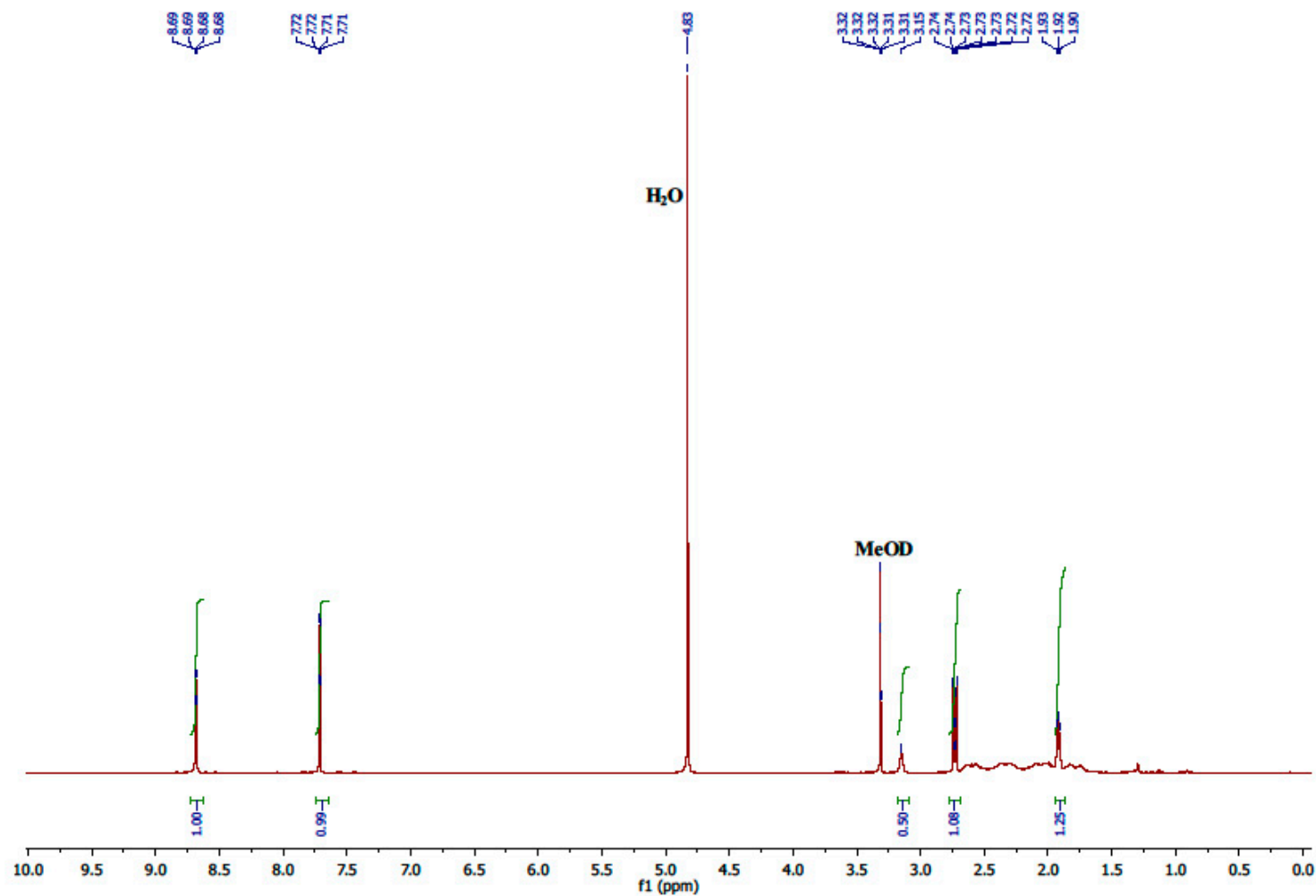


Figure S72. ¹H NMR spectrum of compound 25.

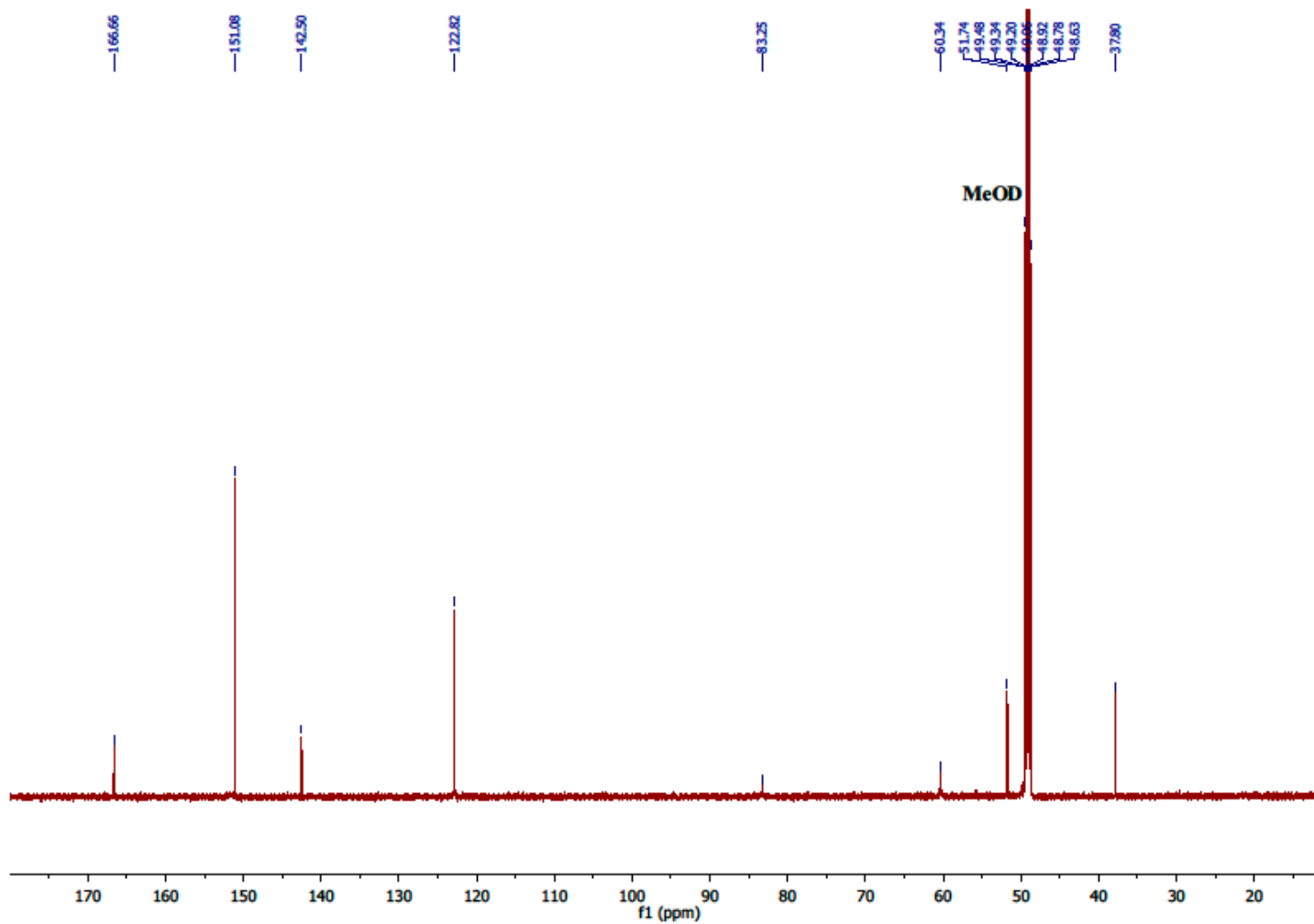


Figure S73. ¹³C NMR spectrum of compound 25.

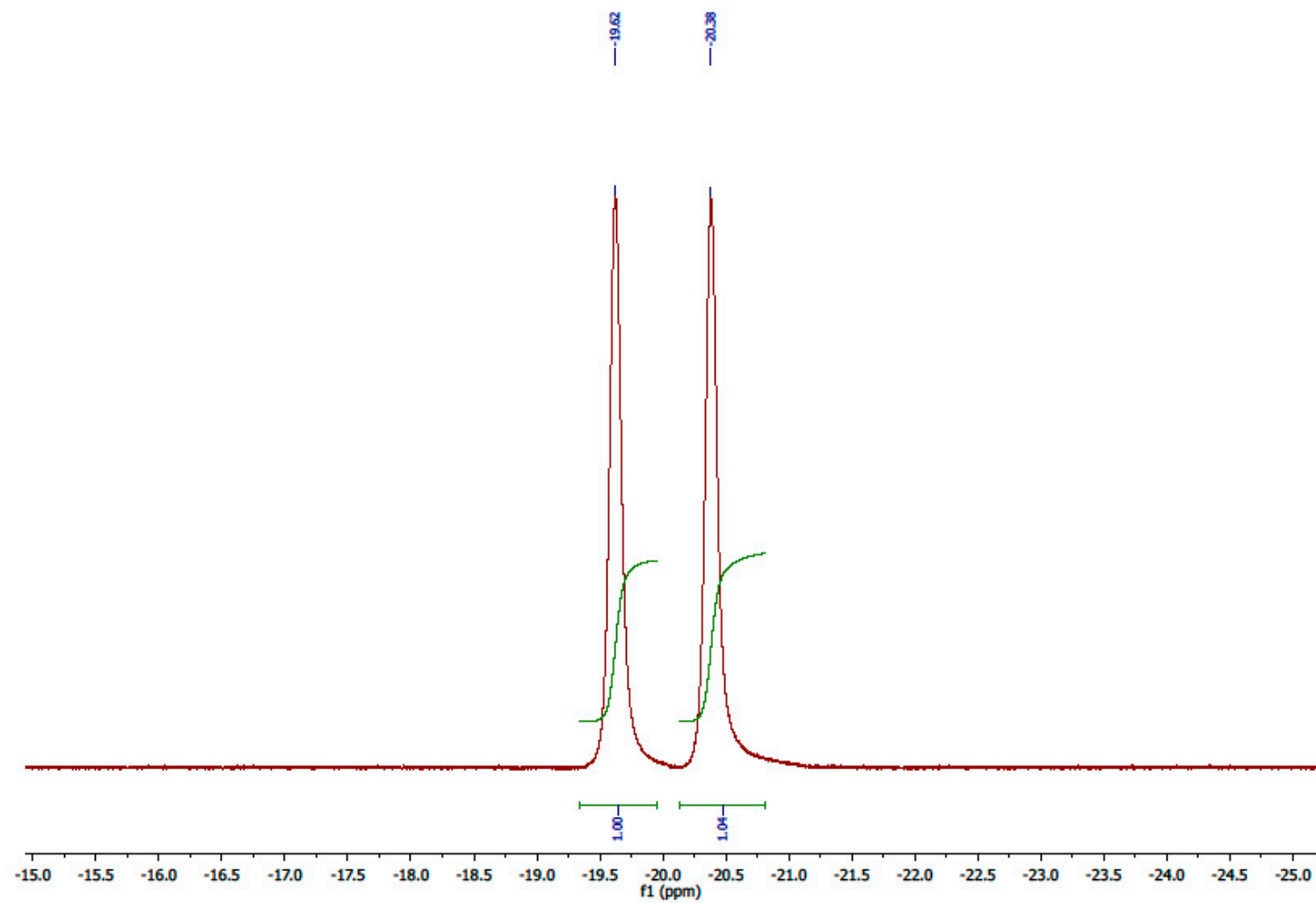


Figure S74. ^{11}B NMR $\{^1\text{H BB}\}$ spectrum of compound 25.

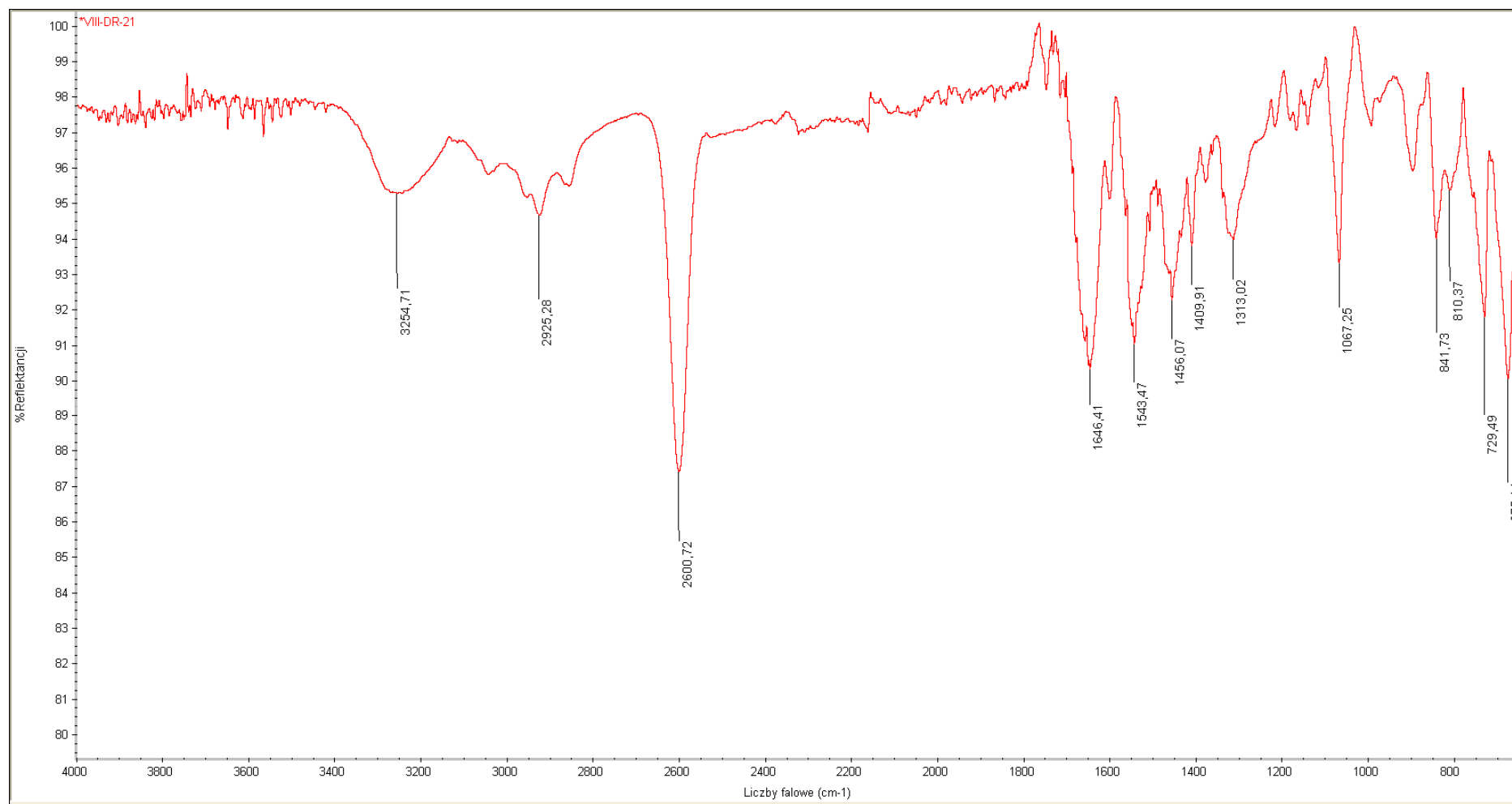


Figure S75. IR spectrum of compound 25.

Spectrum Name: VIII-DR-21_typ_dod
Start Ion: 100
End Ion: 500
Source: APCI + 10.0 μ A 400C
Capillary: 150V 300C Offset: 25V Span: 0V

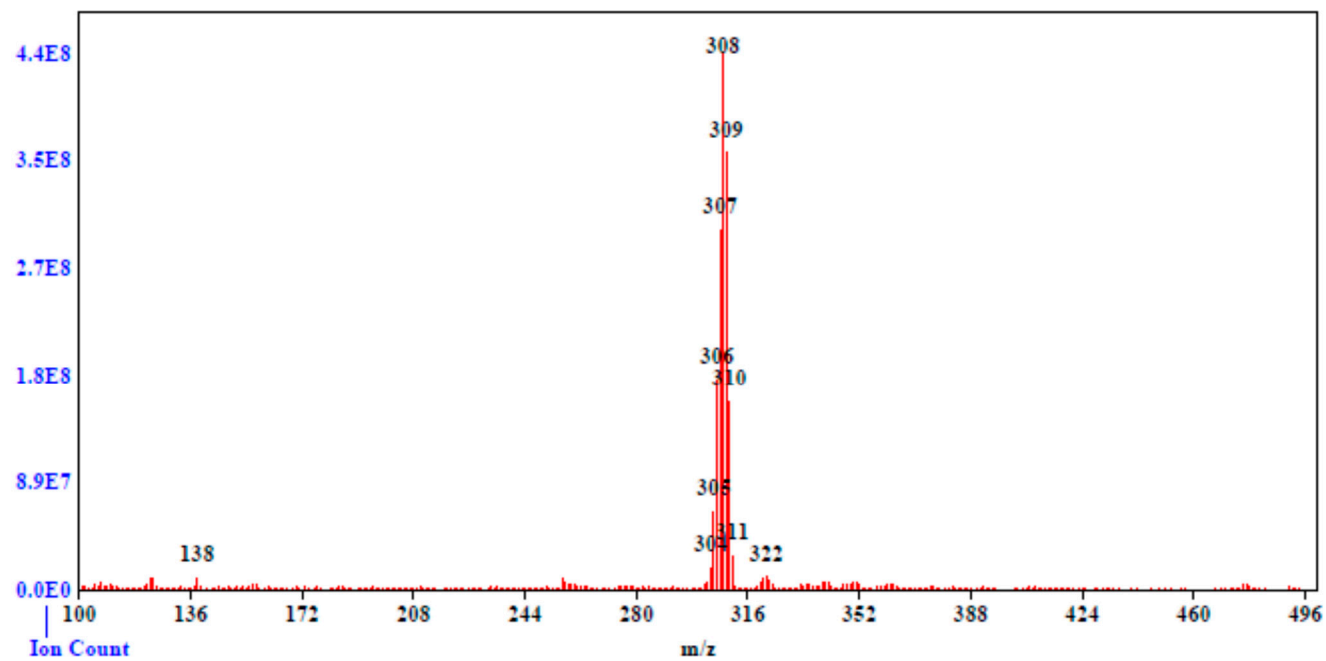


Figure S76. MS spectrum of compound 25.

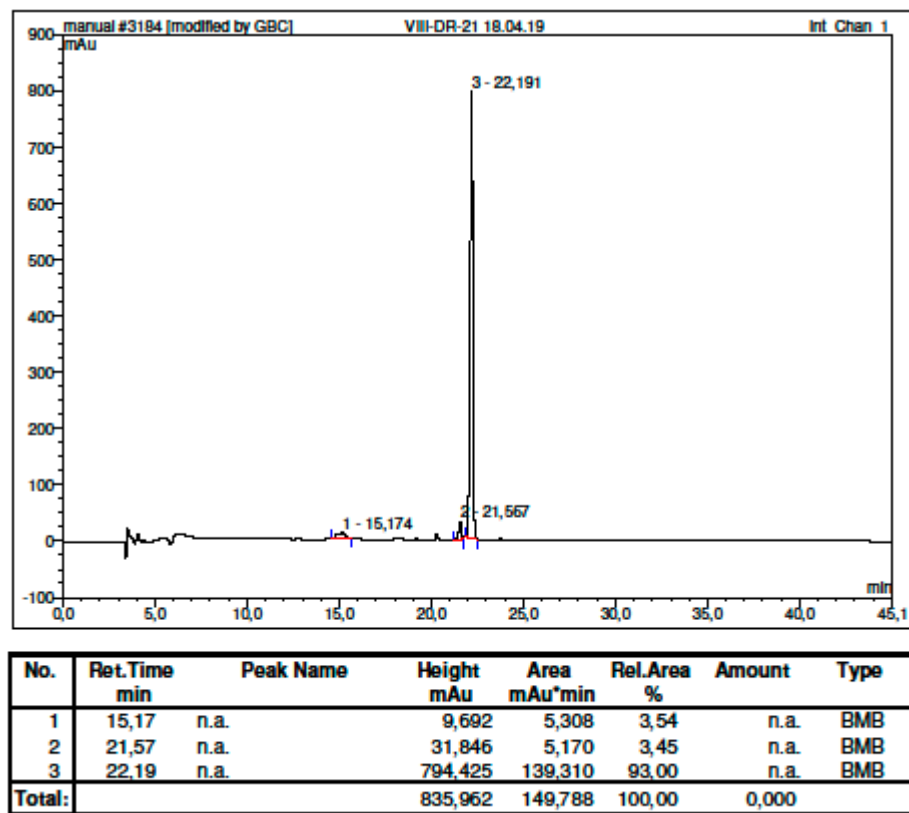


Figure S77. HPLC analysis of compound 25.

Table S1. Crystallographic data.

Compound	14	15	21
Wavelength [Å]	0.71073 (Mo K α)	0.71073 (Mo K α)	1.54184 (Cu K α)
Temperature [K]	132	131	130
Space group	Pbcn	P2 ₁ /c	C2/c
Z	8	4	8
<i>a</i> [Å]	20.6123(11)	10.9141(5)	21.3660(4)
<i>b</i> [Å]	7.7069(4)	20.0103(9)	6.47800(10)
<i>c</i> [Å]	20.7512(9)	7.6763(5)	27.1899(5)
β [°]	90	108.904(15)	103.552(2)
R _{int}	0.0565	0.0331	0.0295
Resolution [Å]	0.77	0.77	0.79
% completeness	94	90.3	98
Independent reflections	3522	3239	3772
R/R(for F _o >4 σ)	0.0890/0.0556	0.0502/0.0429	0.0482/0.0443
CSD code	2012276	2012274	2012277

General procedure for competitive trapping

Compound (1.45-3.45 mg, 4.7-11.4 μmol), TEMPO (1 eq.), and Mn catalyst ($[\text{Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}(\mu\text{-O})_3\text{L}_2](\text{PF}_6)_2$ (L = 1,4,7-trimethyl-1,4,7-triazacyclononane) (6×10^{-3} mmol, 1.6 mol%) was dissolved in degassed ($\text{Ar}_{(\text{g})}$) solution of MeOH/ACN (1:99, v/v). Periodic acid (2 eq.) was added slowly and the reaction mixture stirred for further 15 min. The solvent was removed and the reaction was quenched by H_2SO_4 (1 M, 20-25 μL), potassium bicarbonate (0.5 M, 20-25 μL) and saturated sodium sulfite solution (20-25 μL). The mixture was made alkaline with sodium carbonate and extracted with dichloromethane (3×0.1 mL). The organic phase was separated, dried over MgSO_4 , filtered and evaporated to dryness. Then, the product was purified by column chromatography on silica gel (230-400 mesh) using a gradient elution from 0 to 10% MeOH in CH_2Cl_2 to afford pure product.

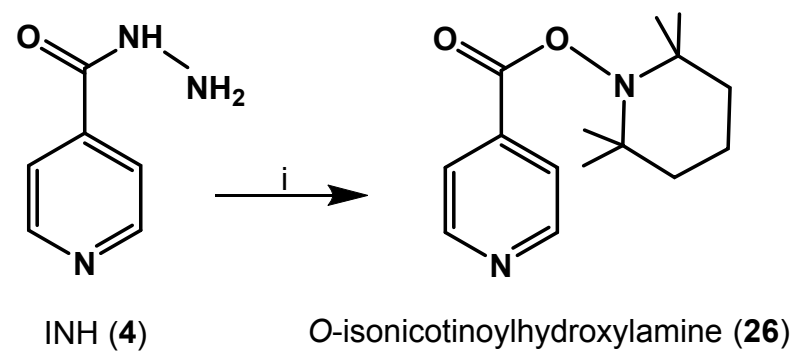


Figure S78. The resulting trapped product *O*-isonicotinoylhydroxylamine (**26**): i) TEMPO, MeOH/ACN (1:99, v/v), [Mn^{IV}-Mn^{IV}(μ-O)₃L₂](PF₆)₂ (L=1,4,7-trimethyl-1,4,7-triazacyclononane)/H₅IO₆.

Spectrum Name: X-DR-89_fg_
Start Ion: 100
End Ion: 500
Source: APCI + 10.0 μ A 250C
Capillary: 150V 200C Offset: 15V Span: 0V

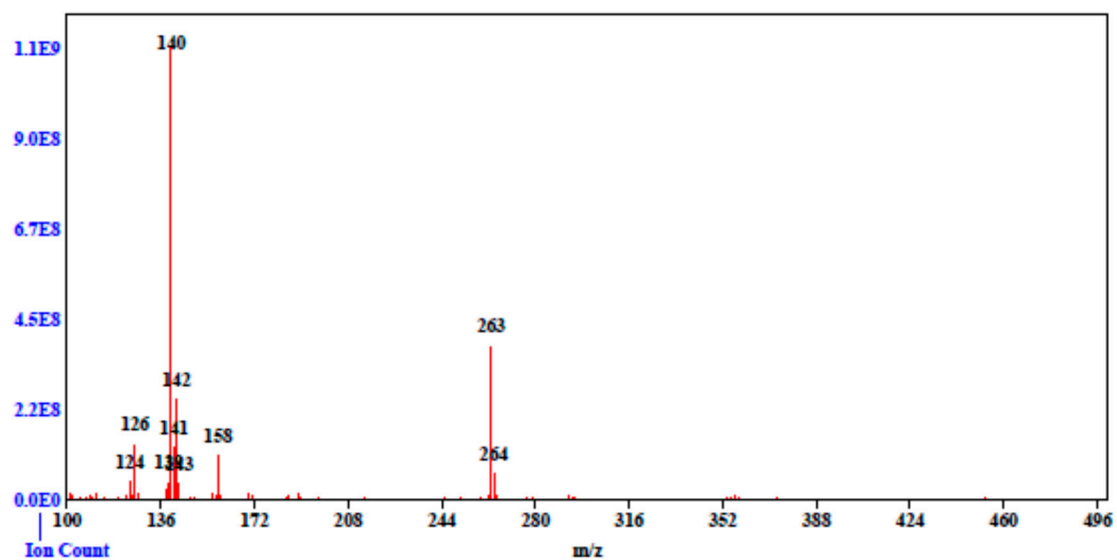


Figure S79. MS spectrum of reaction of INH with TEMPO, and manganese catalyst: APCI-MS: m/z 263, calcd for $C_{15}H_{22}N_2O_2 = 262$ (product **26**).

Spectrum Name: X-DR-85_fg
Start Ion: 100
End Ion: 400
Source: APCI + 10.0µA 250C
Capillary: 150V 200C Offset: 15V Span: 0V

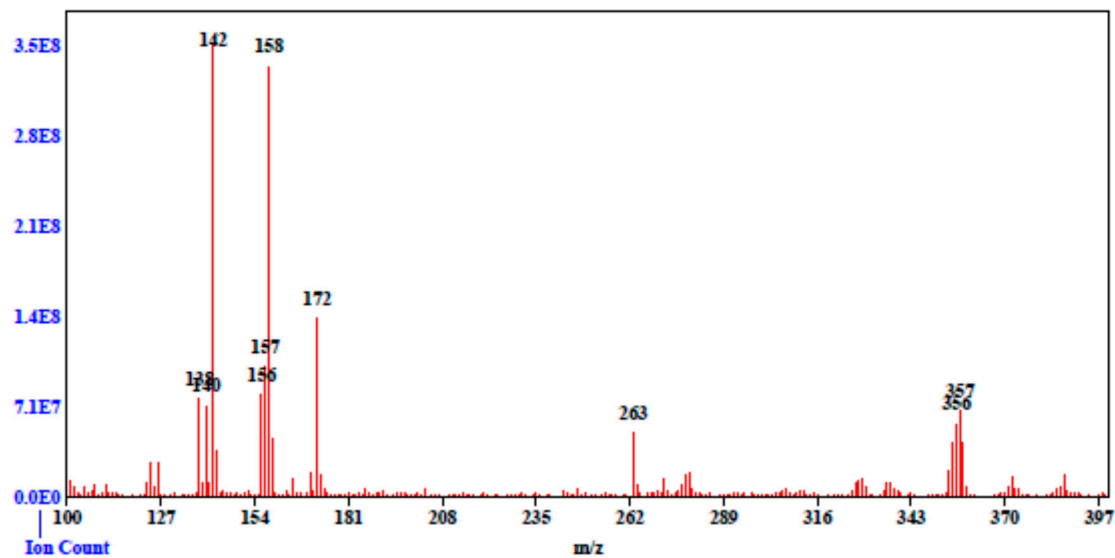


Figure S80. MS spectrum of reaction of 8 with TEMPO, and manganese catalyst.

Spectrum Name: X-DR-S7_fg
Start Ion: 100
End Ion: 400
Source: APCI + 10.0µA 250C
Capillary: 150V 200C Offset: 15V Span: 0V

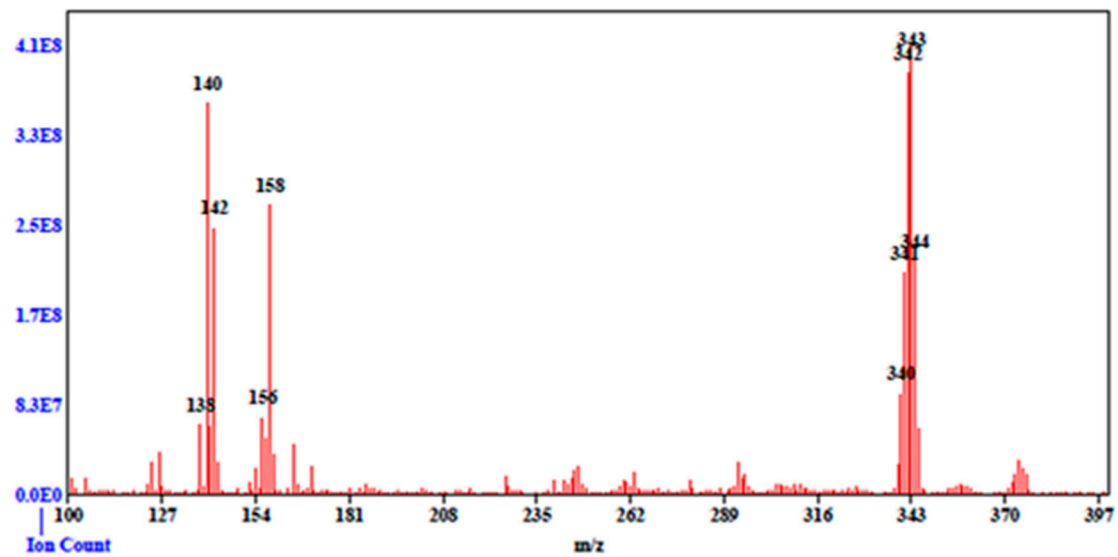


Figure S81. MS spectrum of reaction of **21** with TEMPO, and manganese catalyst.

Spectrum Name: X-DR-93_fg
Start Ion: 100
End Ion: 400
Source: APCI + 10.0μA 250C
Capillary: 150V 200C Offset: 15V Span: 0V

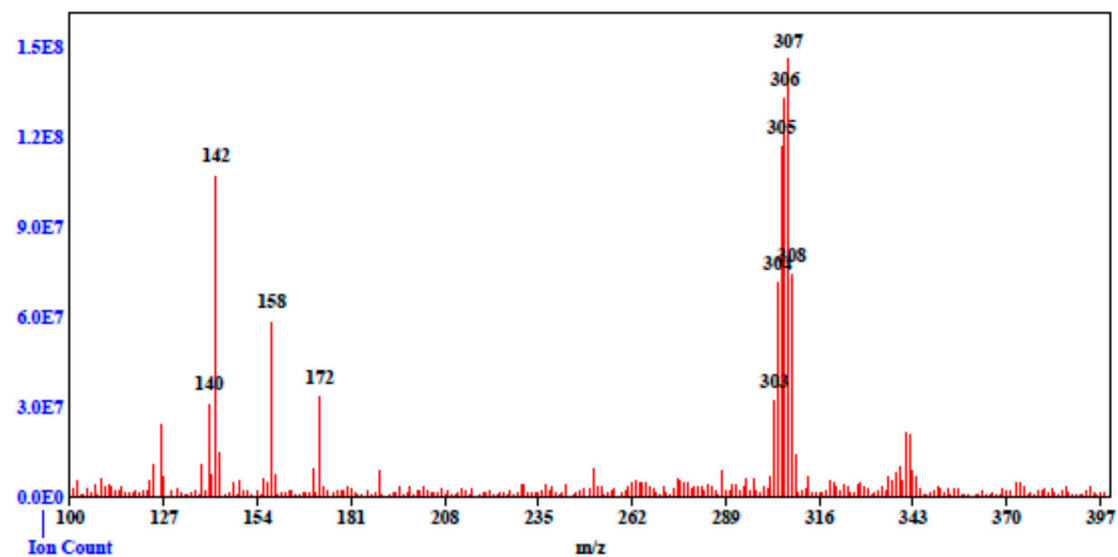


Figure S82. MS spectrum of reaction of **25** with TEMPO, and manganese catalyst.

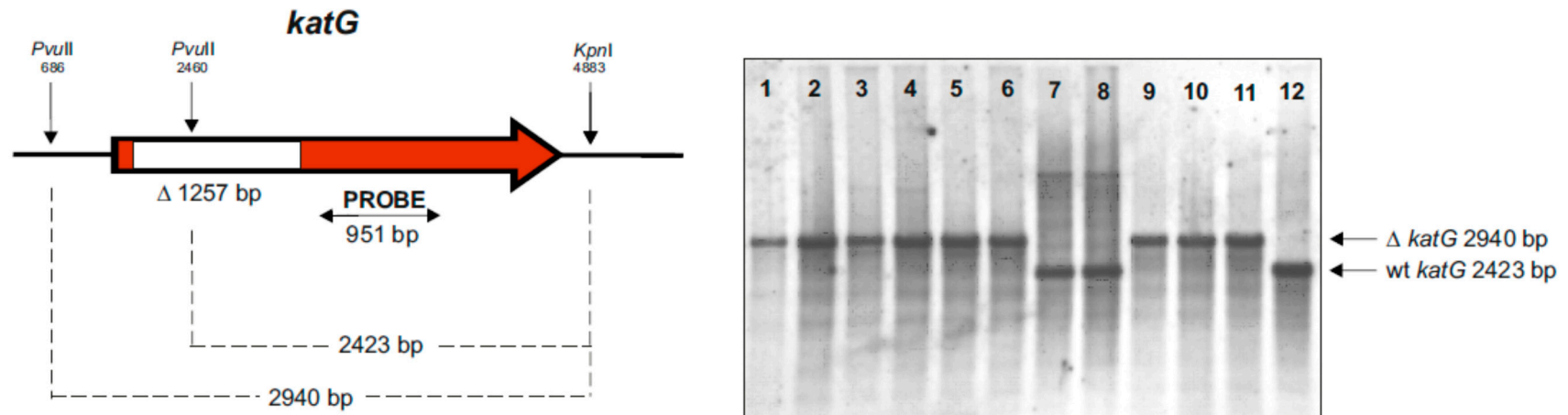


Figure S83. Confirmation of mutant construction by Southern blotting analysis. The *katG* was presented as red arrow. Restriction sites and internal deletion fragments (white rectangle) are indicated. DNA was digested with *PvuII* and *KpnI* restrictions enzymes. Lanes 1-6, 9-11 – *M. tuberculosis* H37Rv $\Delta katG$ DCO (double cross-over mutants), lanes 7-8 – *M. tuberculosis* H37Rv SCO (single cross-over mutants), lane 12 – *M. tuberculosis* H37Rv wild-type strain.