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Levetiracetam analogs: chemoenzymatic synthesis, absolute configuration assignment and evaluation of cholinesterase inhibitory activities

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Spectra (^{1}H NMR, ^{13}C NMR, MS and IR) of all characterized compounds **2**, **3**, **4a**–**d**, **5a**–**b**, **5d**, **7**, **8a**–**d**, **9a**–**b** and **9d**, spectra (^{1}H, ^{13}C, ^{19}F NMR) of the synthesized ionic liquids and the ECD figures and the lower energy conformers.

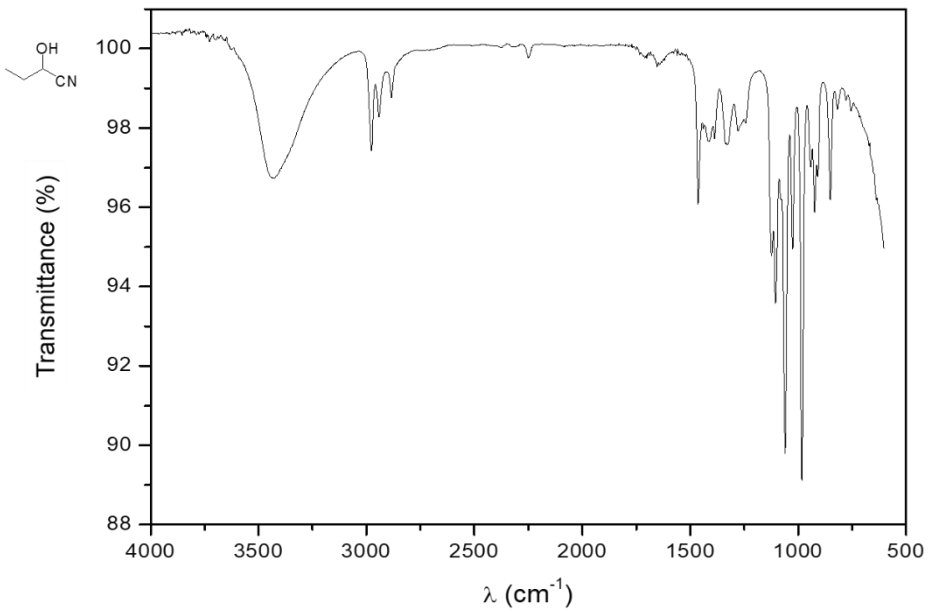

Figure S1. IR spectrum of compound **2**.

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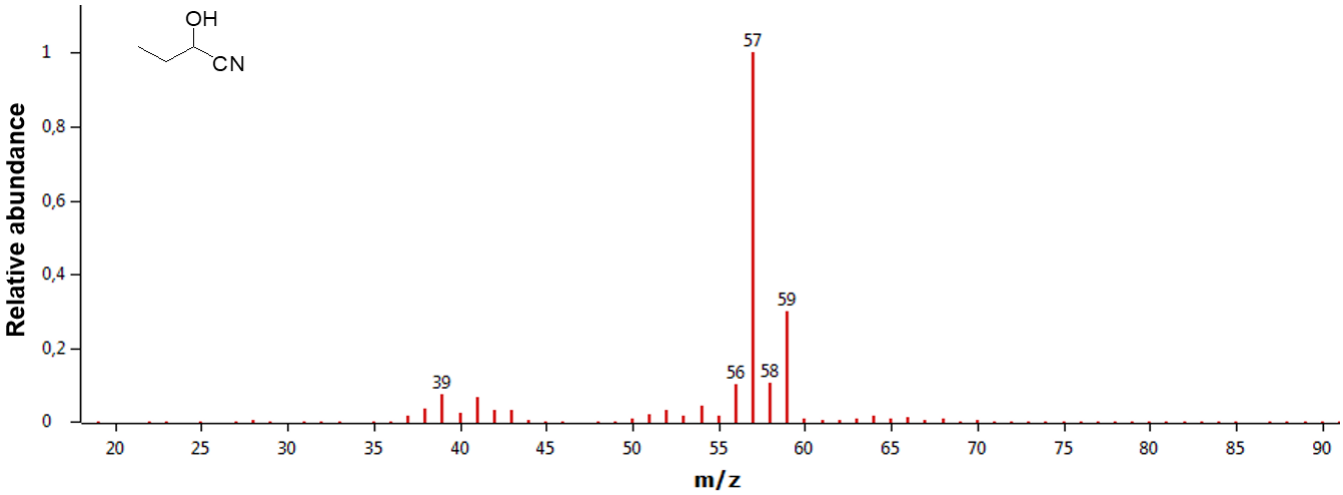

Figure S2. MS (EI, 70 eV) spectrum of compound **2**.

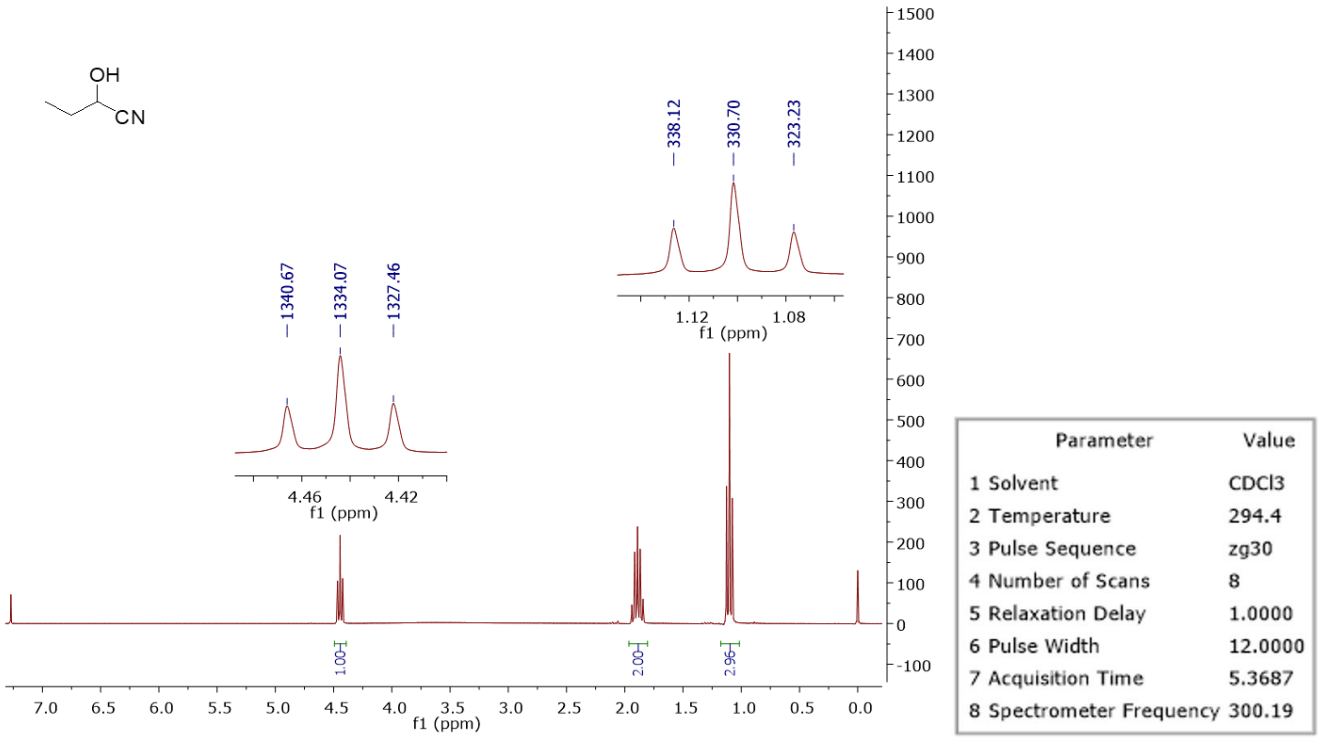

Figure S3. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **2**.

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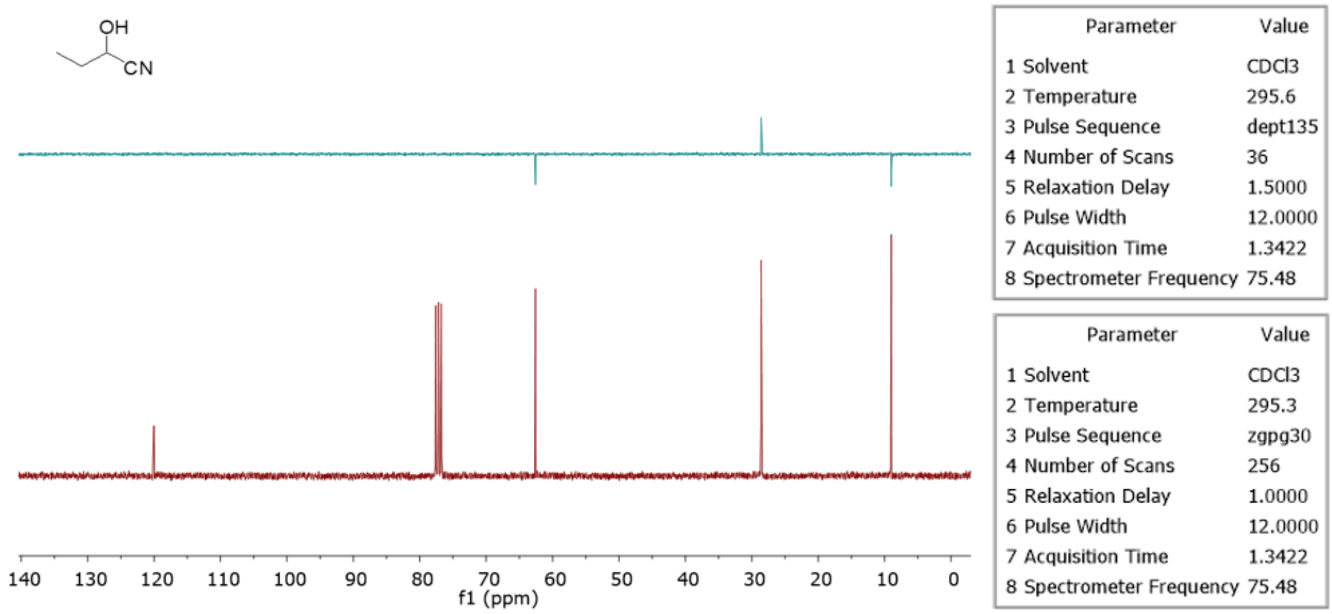

Figure S4. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **2**.

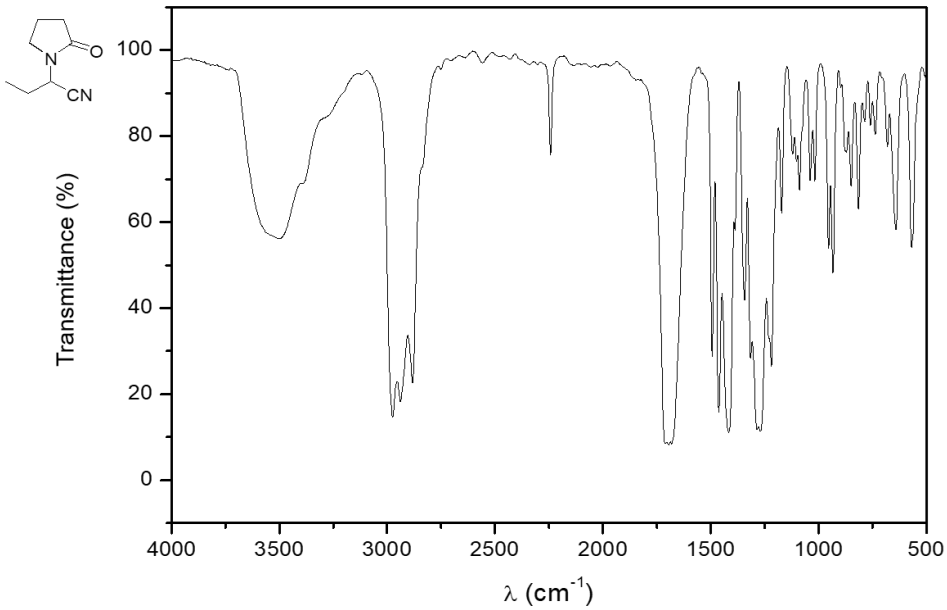

Figure S5. IR spectrum of compound **4a**.

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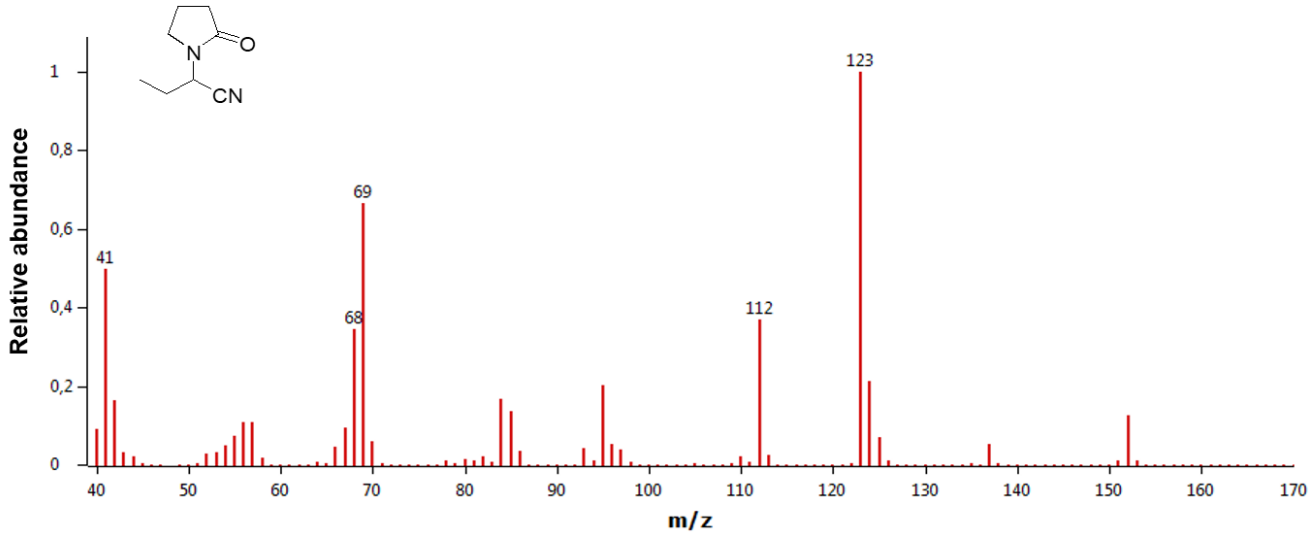

Figure S6. MS (EI, 70 eV) spectrum of compound **4a**.

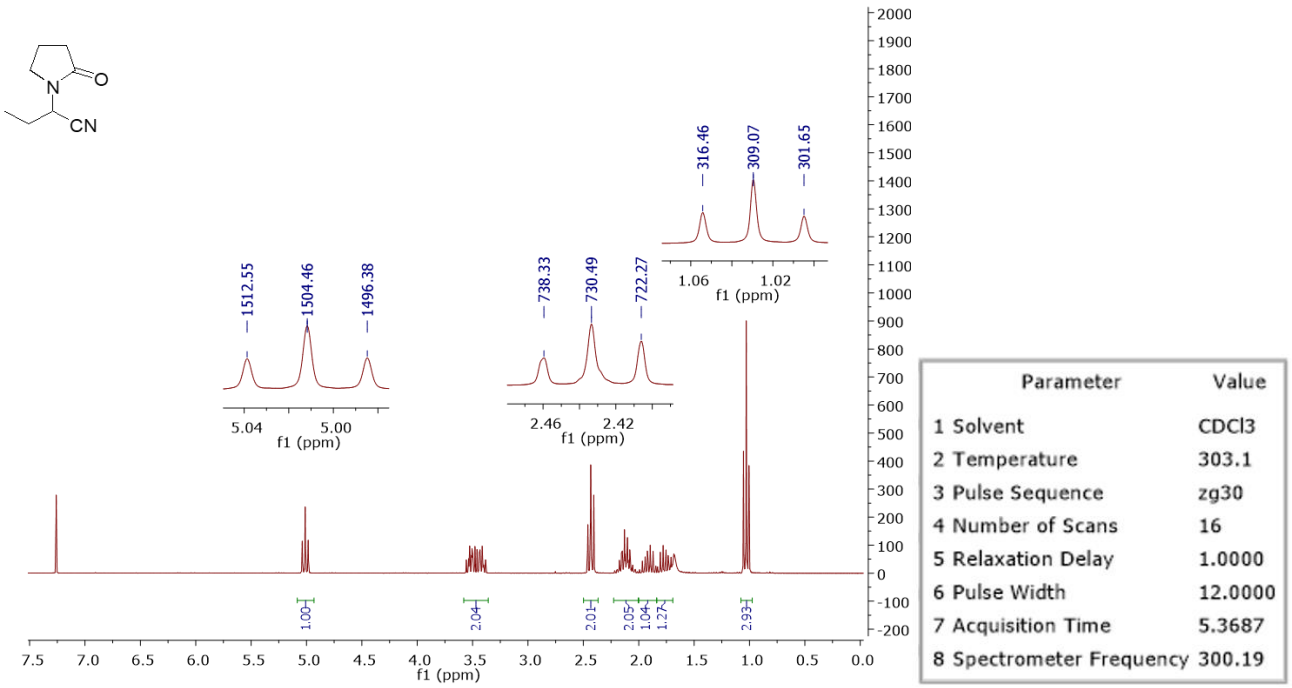

Figure S7. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **4a**.

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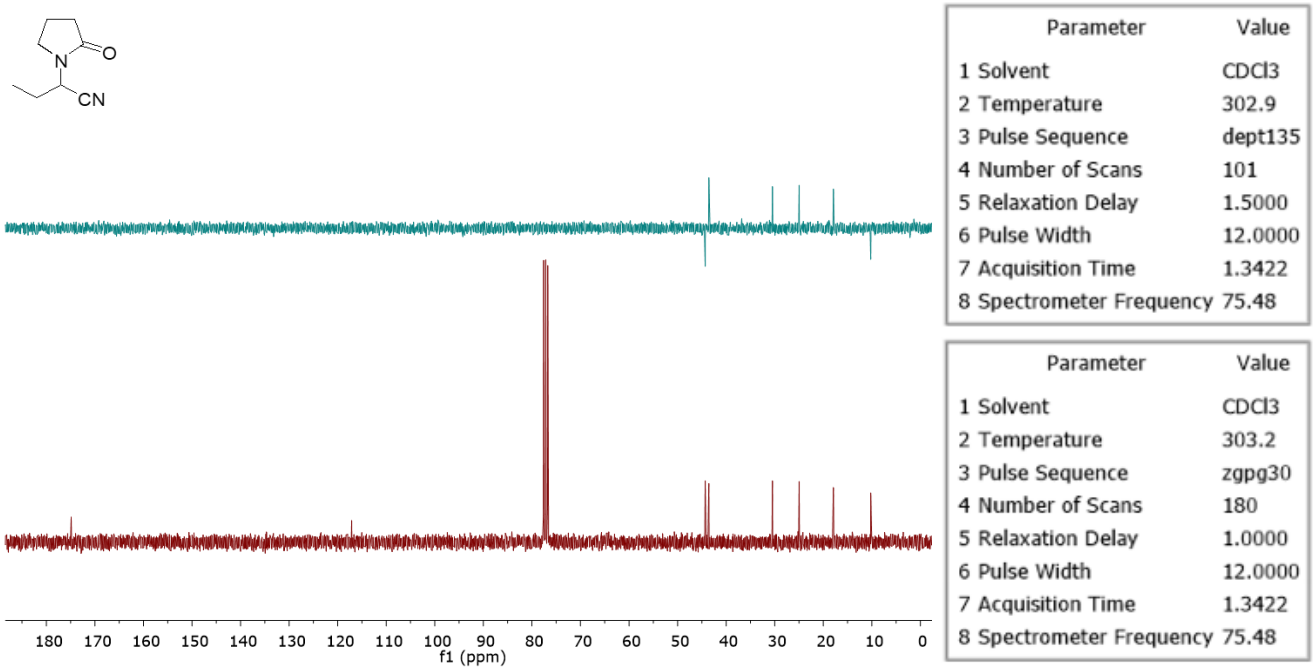

Figure S8. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **4a**.

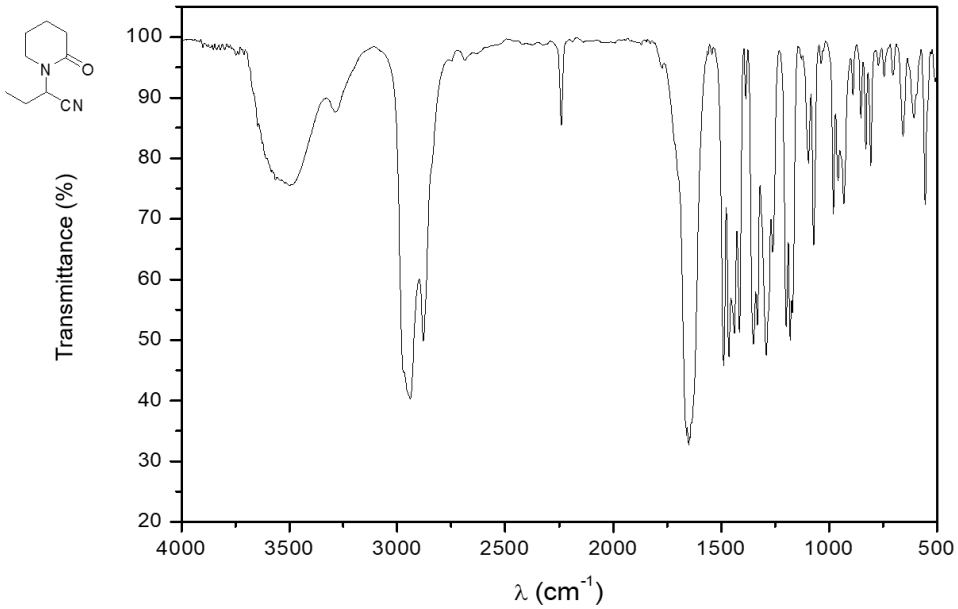

Figure S9. IR spectrum of compound **4b**.

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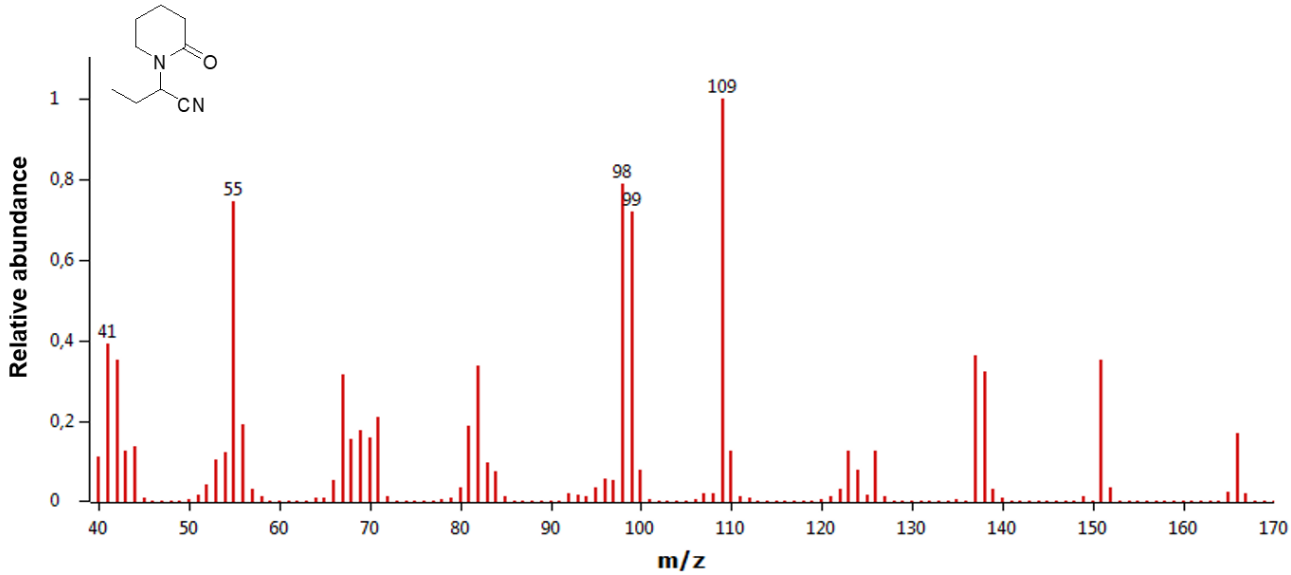

Figure S10. MS (EI, 70 eV) spectrum of compound **4b**.

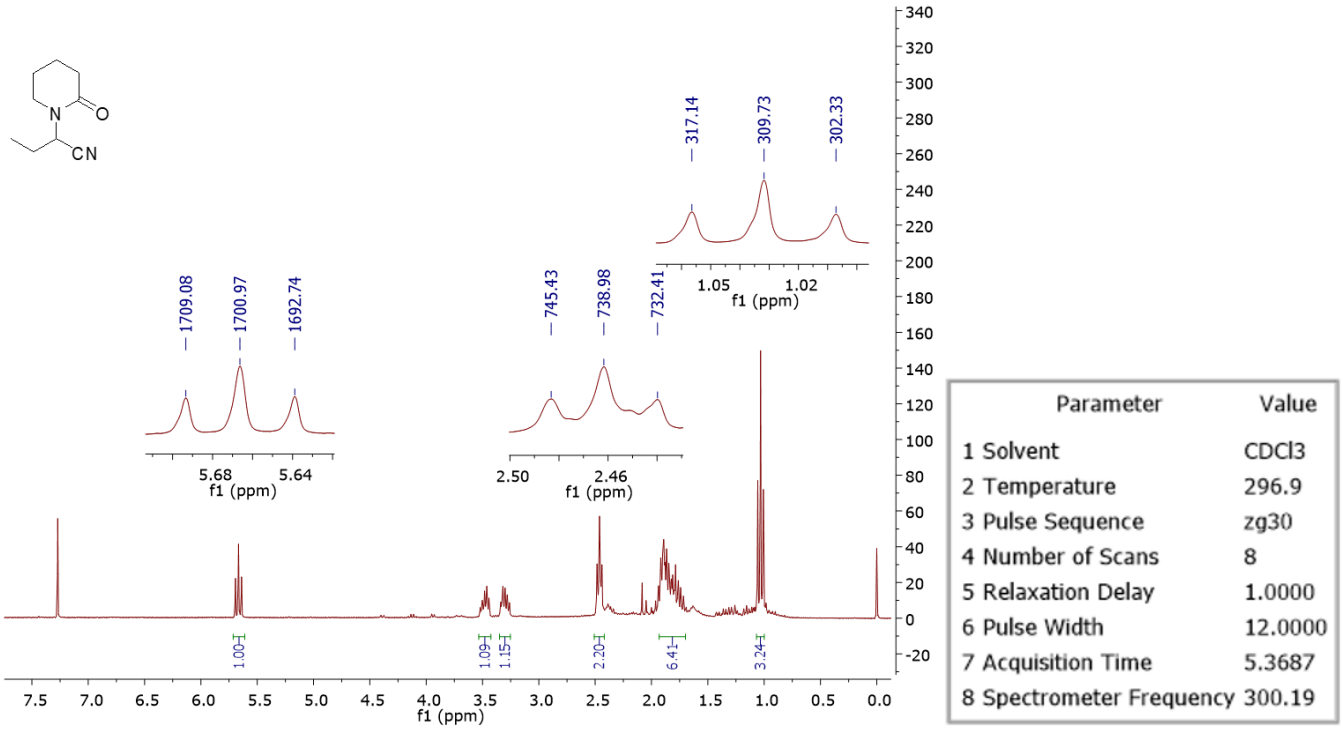

Figure S11. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **4b**.

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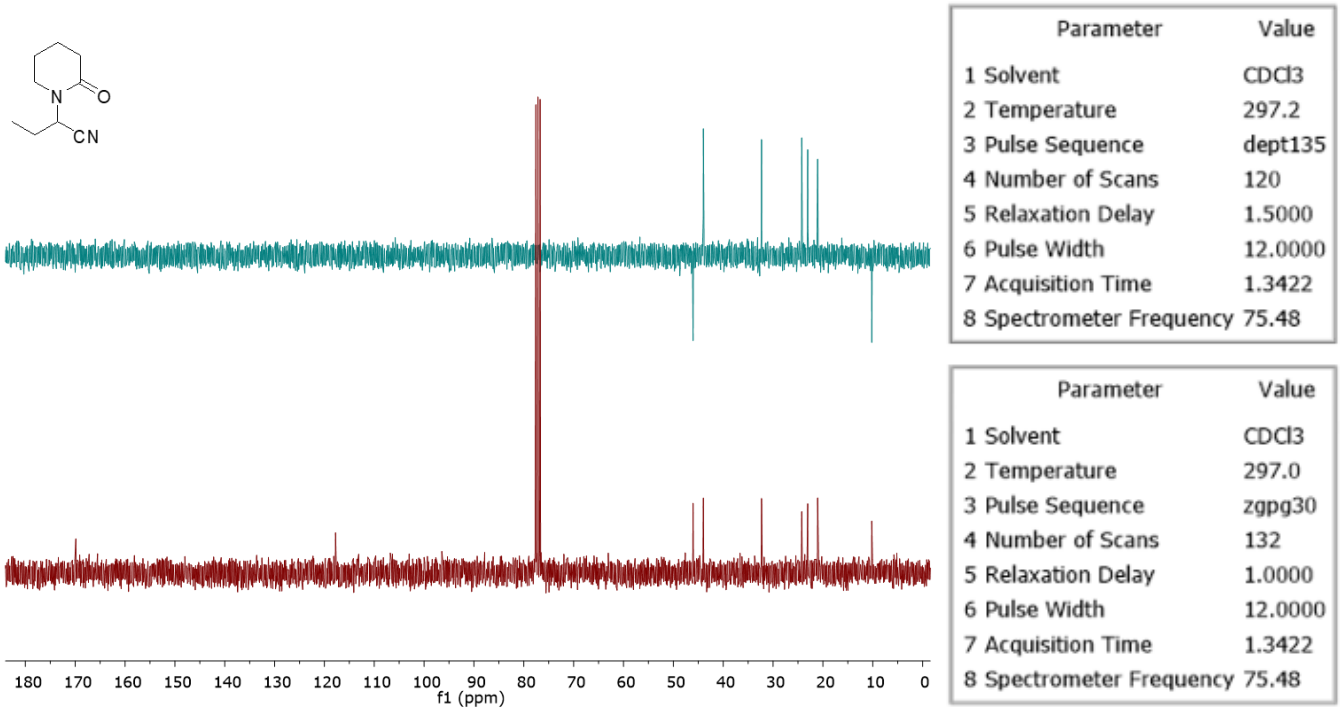

Figure S12. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **4b**.

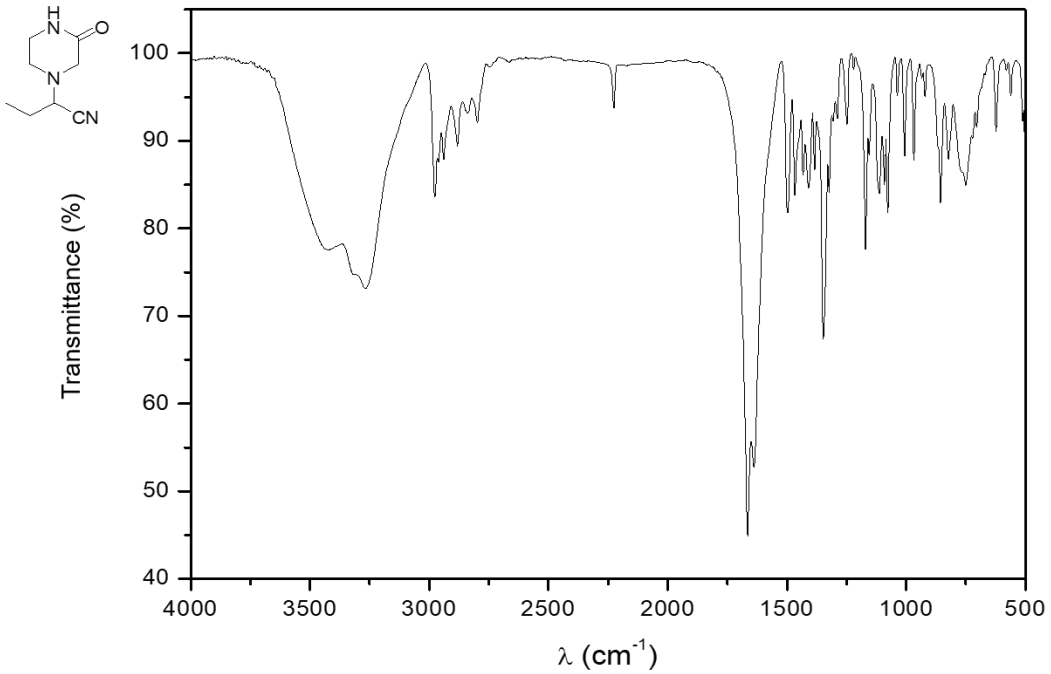

Figure S13. IR spectrum of compound **4c**.

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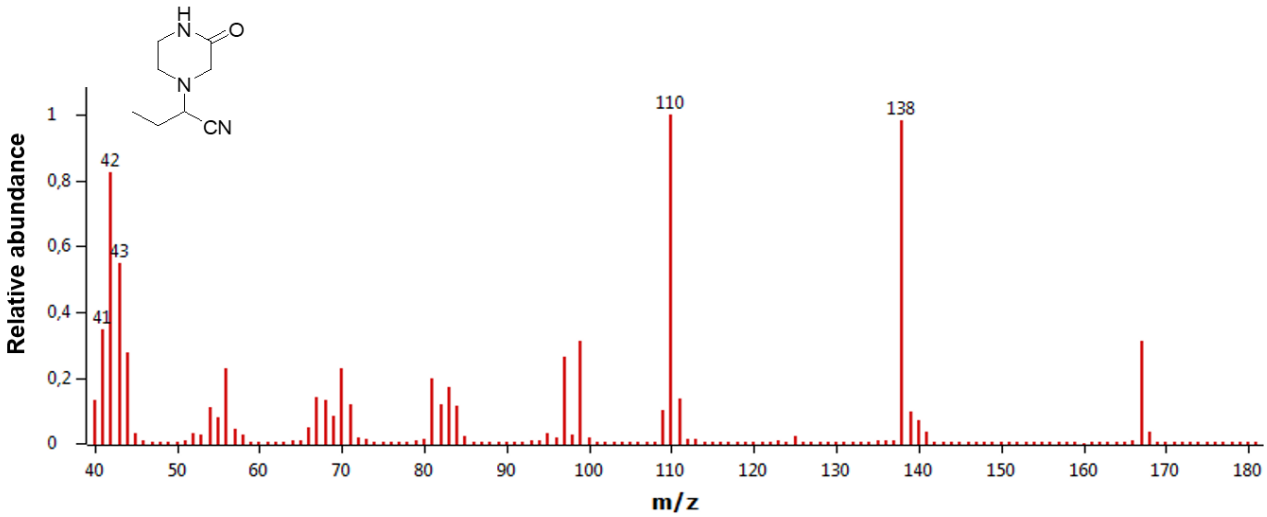

Figure S14. MS (EI, 70 eV) spectrum of compound **4c**.

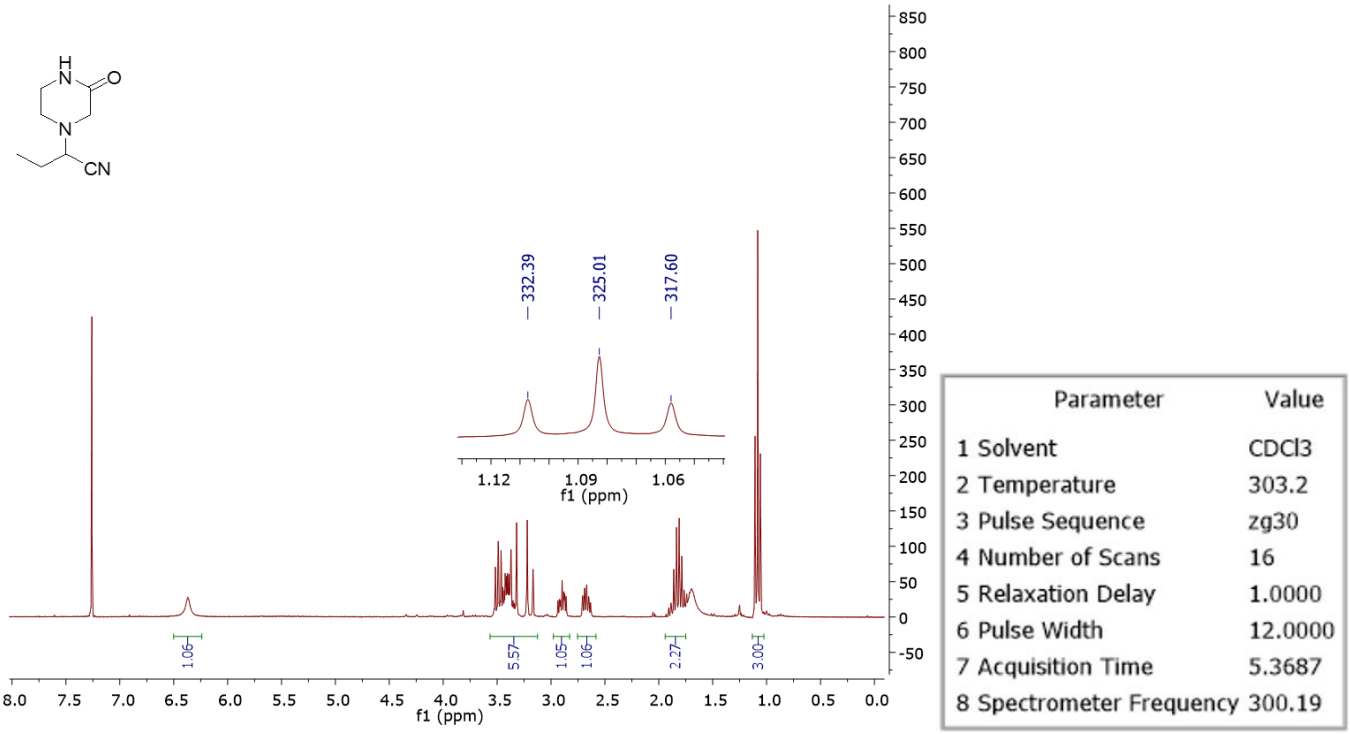

Figure S15. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **4c**.

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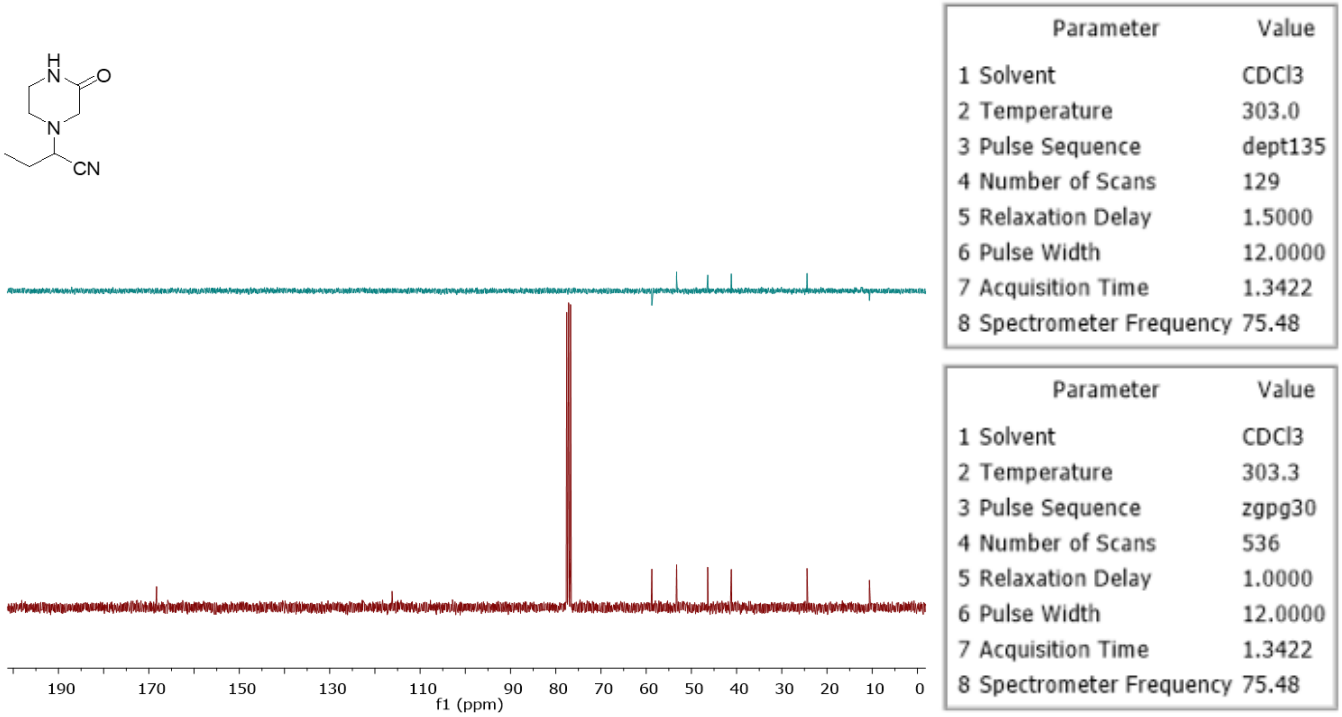

Figure S16. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **4c**.

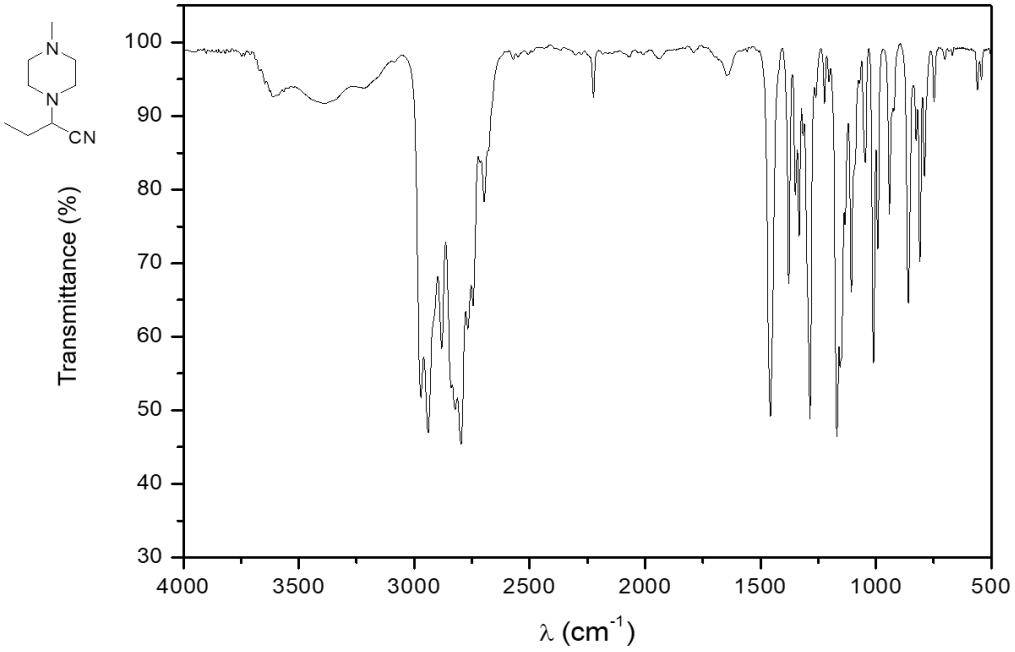

Figure S17. IR spectrum of compound **4d**.

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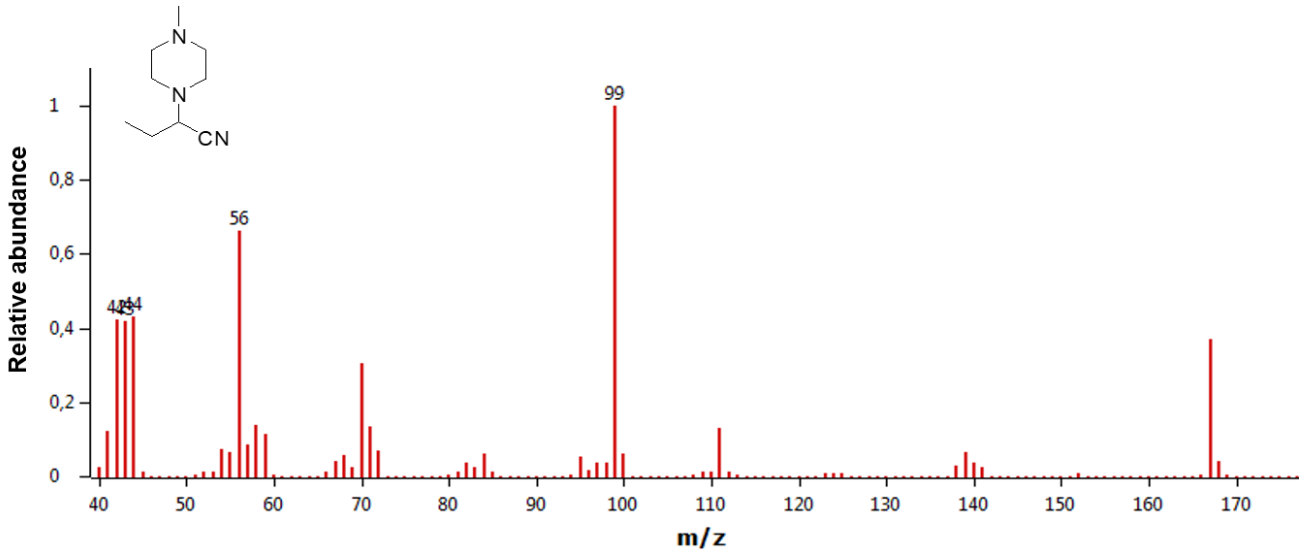

Figure S18. MS (EI, 70 eV) spectrum of compound **4d**.

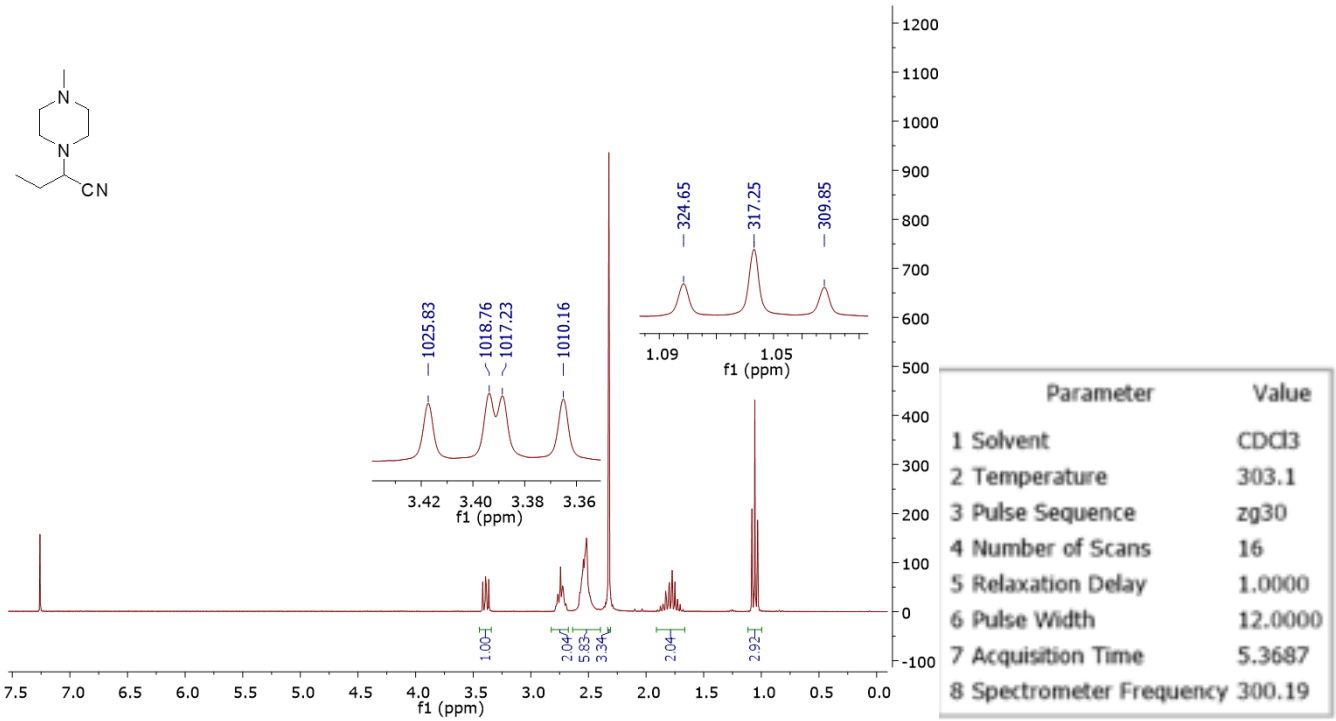

Figure S19. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **4d**.

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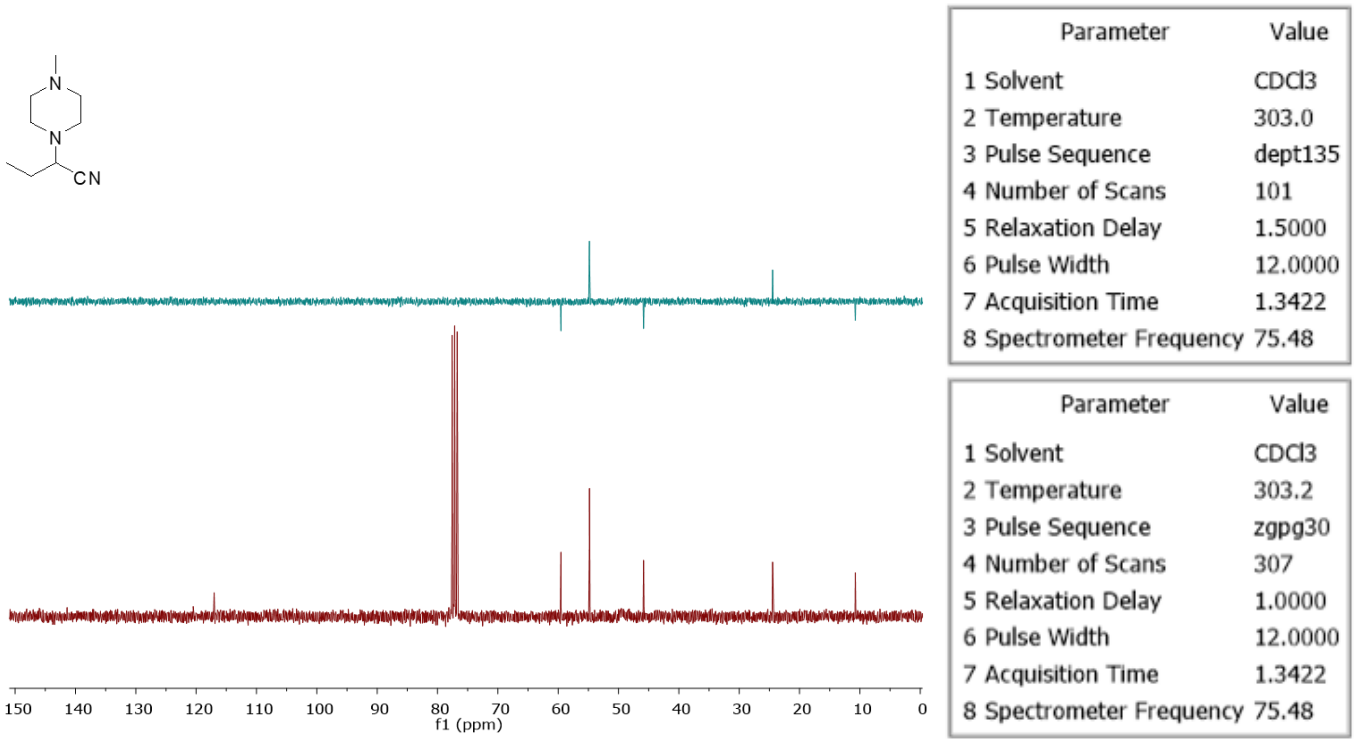

Figure S20. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **4d**.

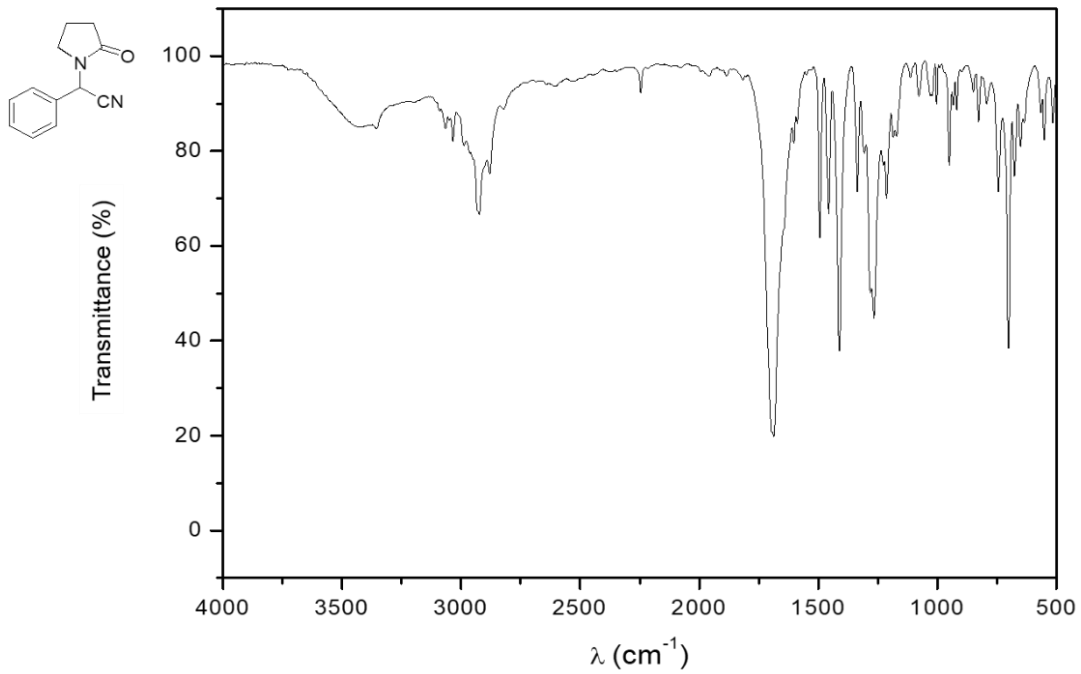

Figure S21. IR spectrum of compound **8a**.

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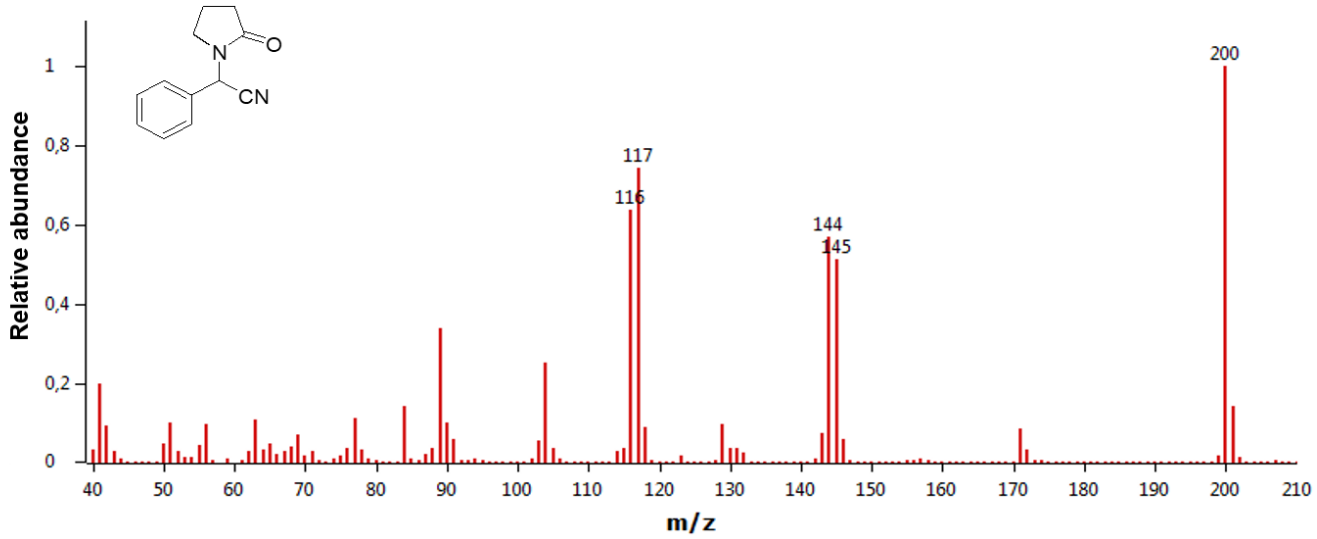

Figure S22. MS (EI, 70 eV) spectrum of compound **8a**.

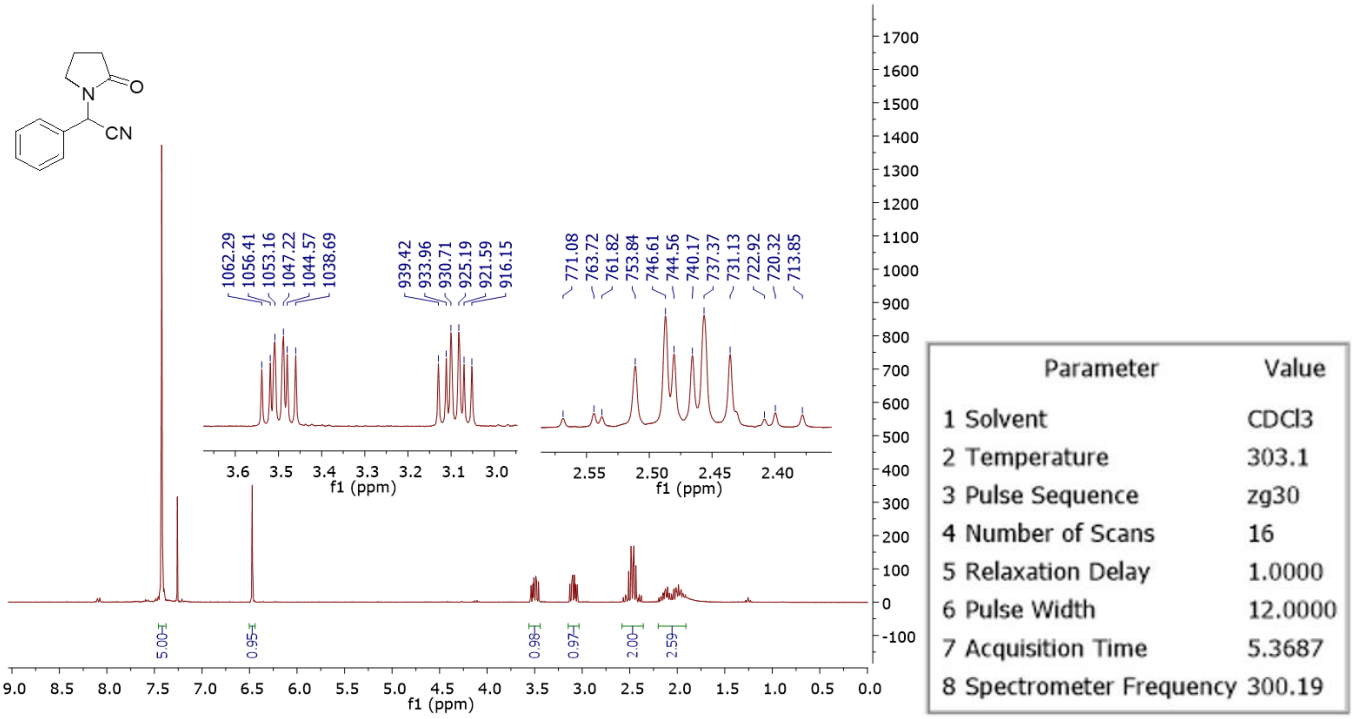

Figure S23. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **8a**.

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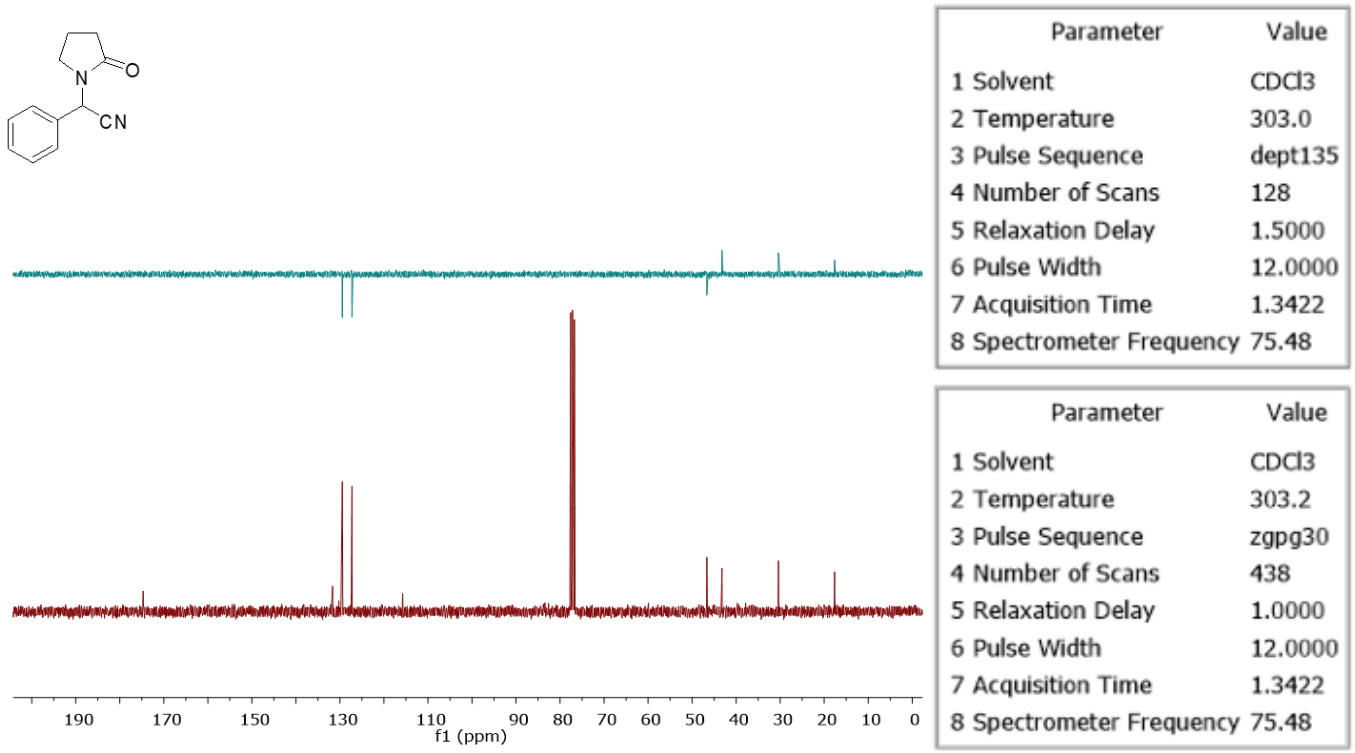

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6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

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3 Pulse Sequence	zgpg30
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5 Relaxation Delay	1.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S24. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **8a**.

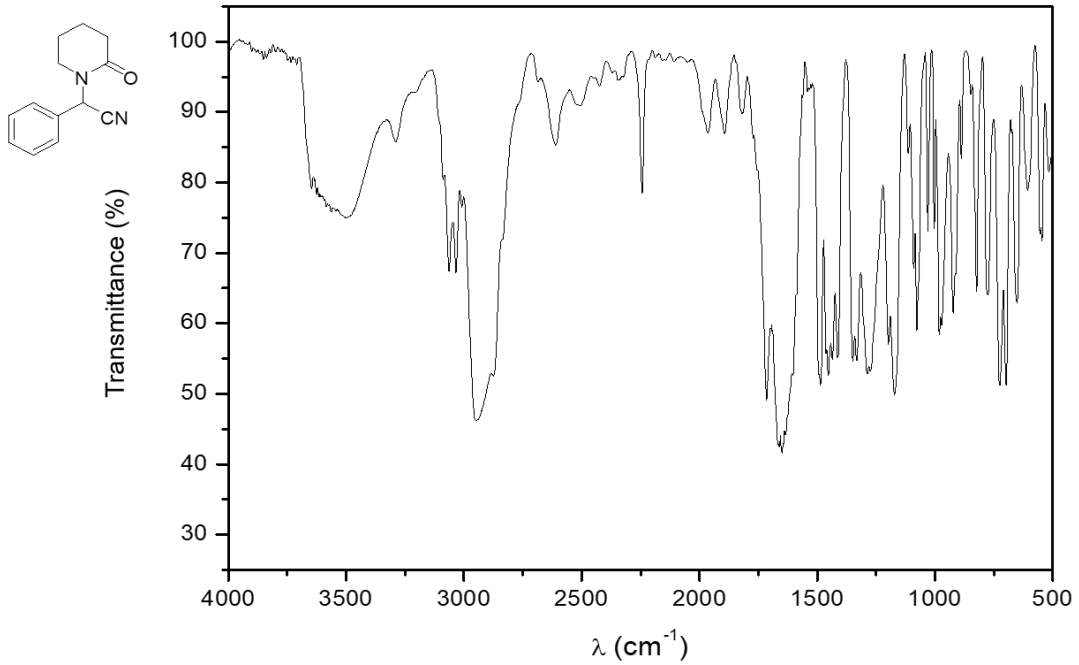

Figure S25. IR spectrum of compound **8b**.

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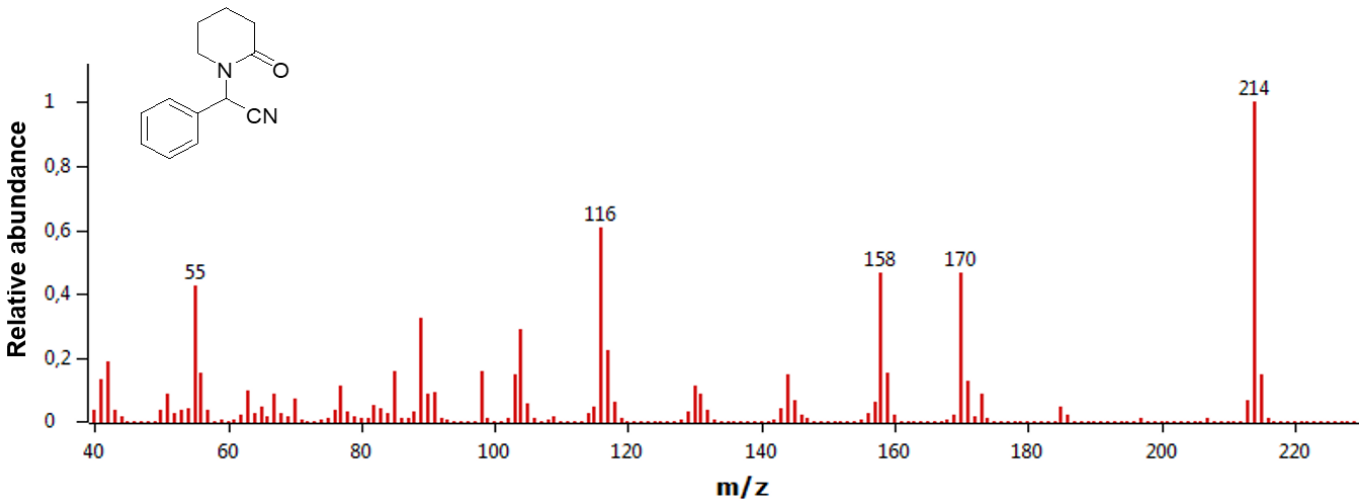

Figure S26. MS (EI, 70 eV) spectrum of compound **8b**.

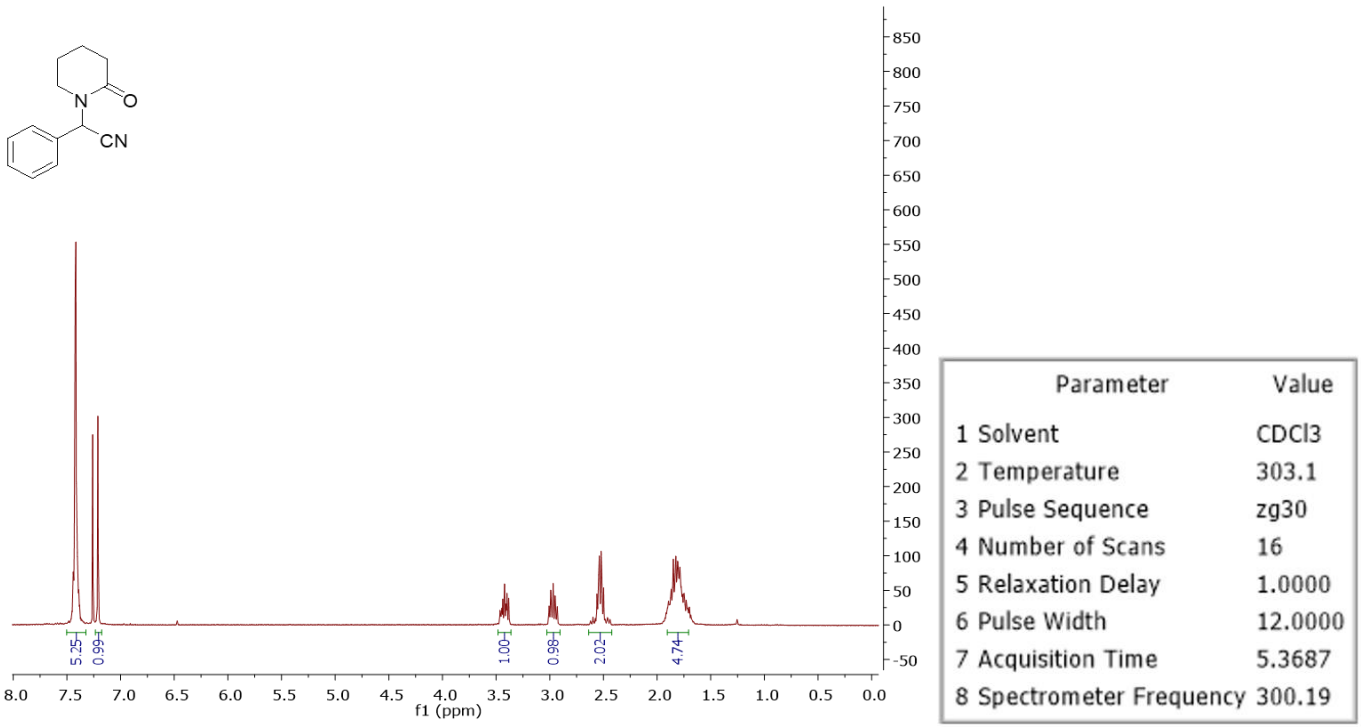

Figure S27. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **8b**.

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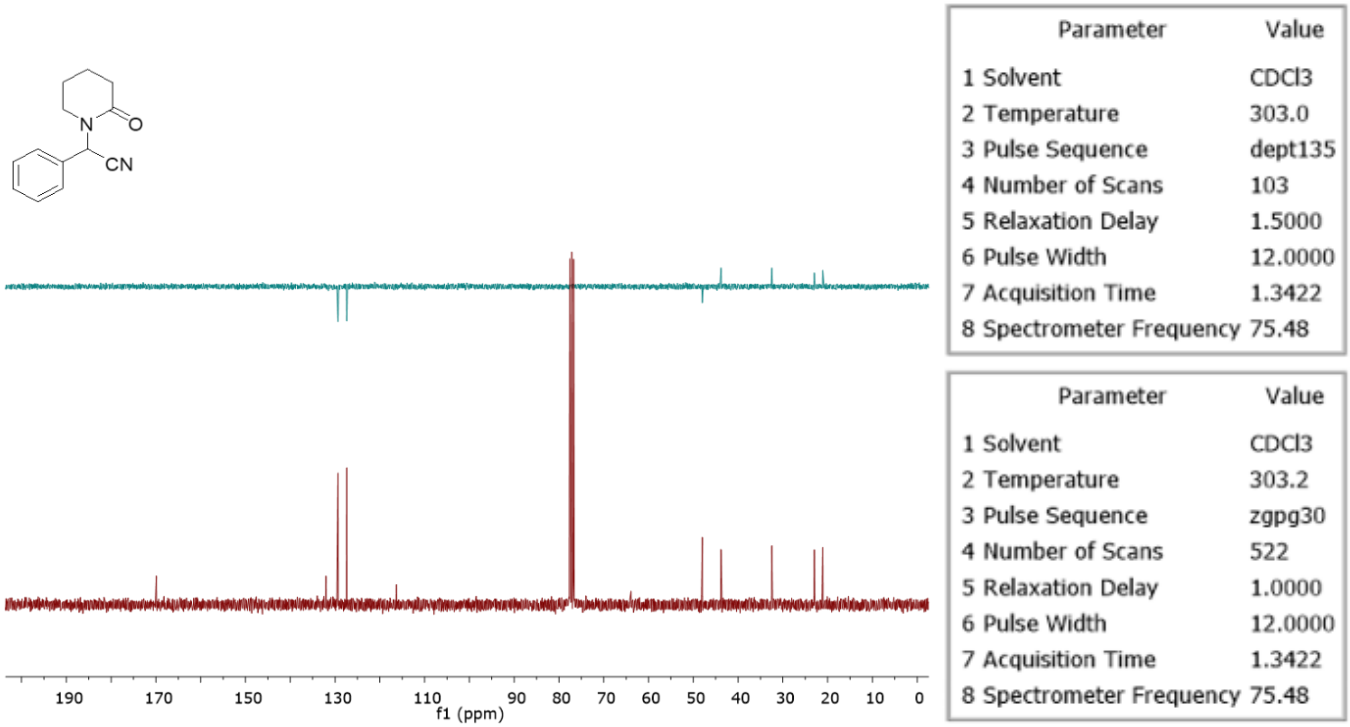

Figure S28. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **8b**.

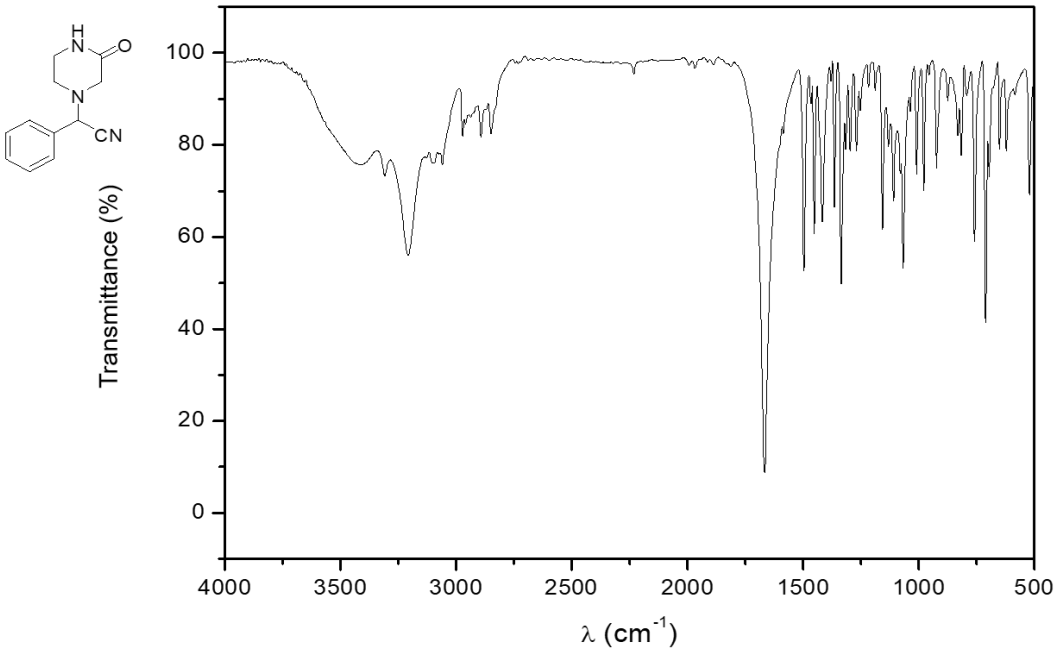

Figure S29. IR spectrum of compound **8c**.

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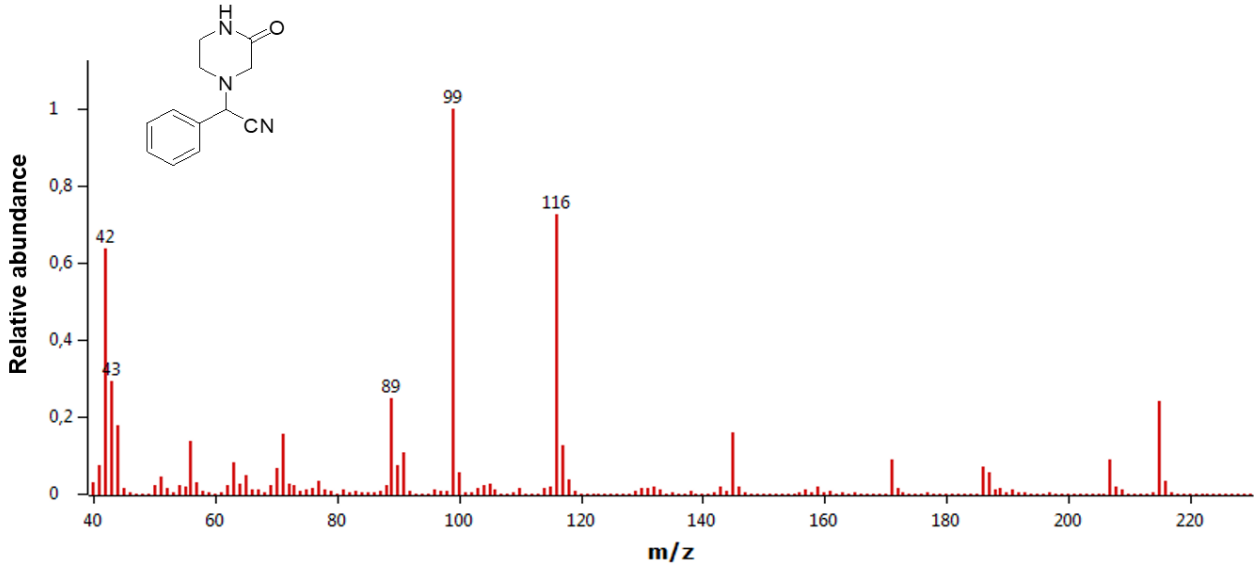

Figure S30. MS (EI, 70 eV) spectrum of compound **8c**.

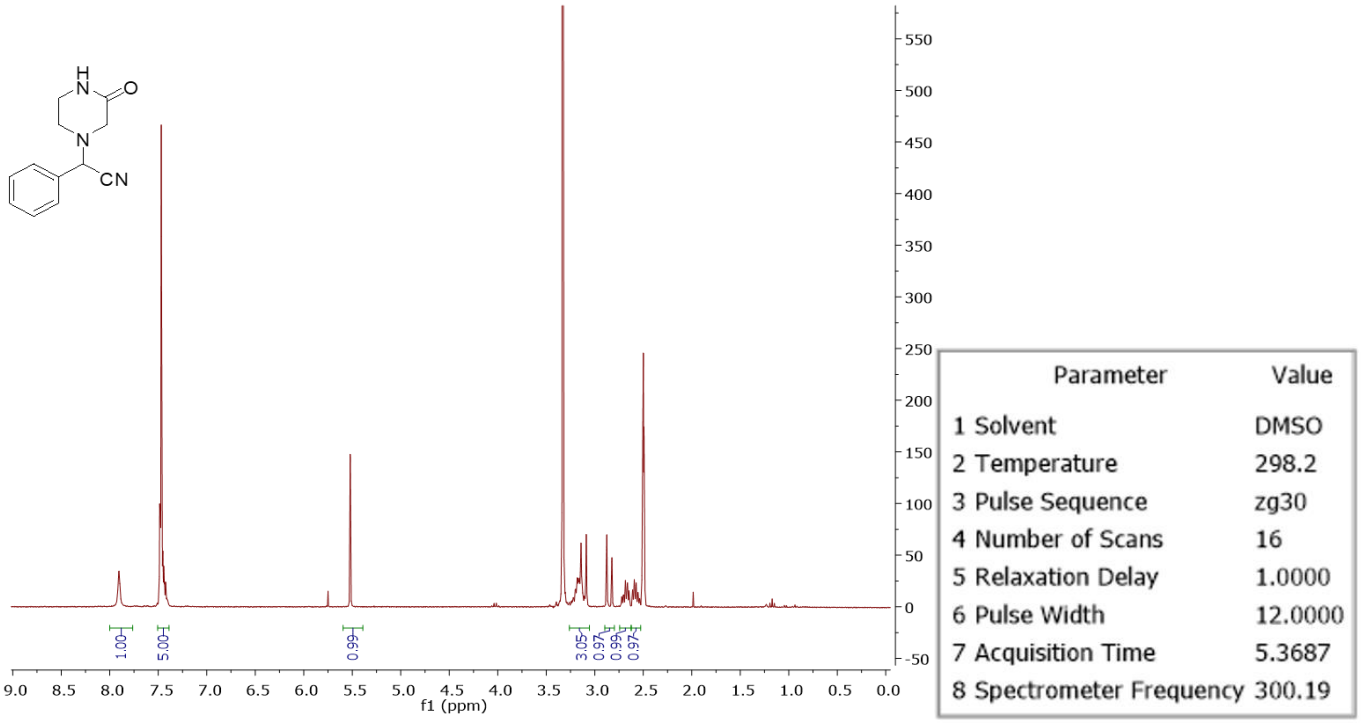

Figure S31. ^{1}H NMR (300.19 MHz, DMSO-d_6) spectrum of compound **8c**.

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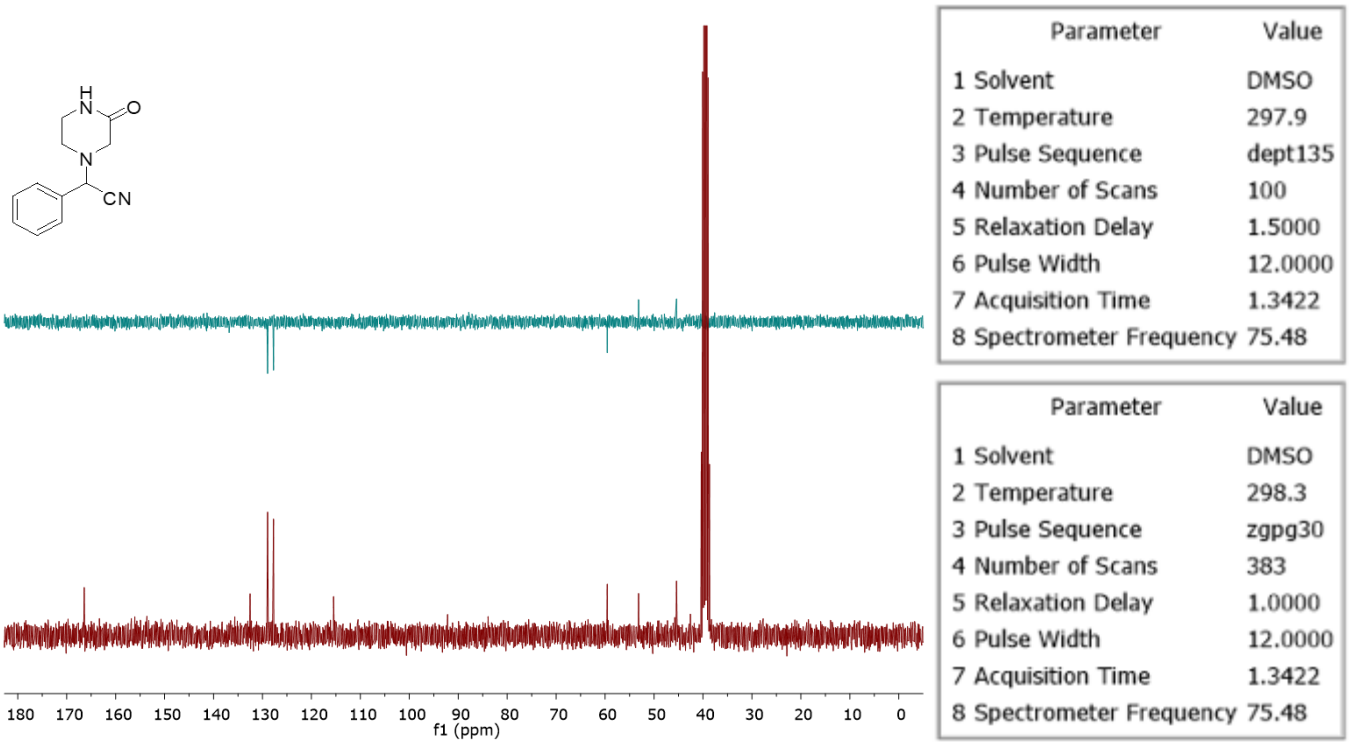

Figure S32. ^{13}C NMR (75.48 MHz, DMSO-d_6) spectrum and DEPT-135 experiment of compound **8c**.

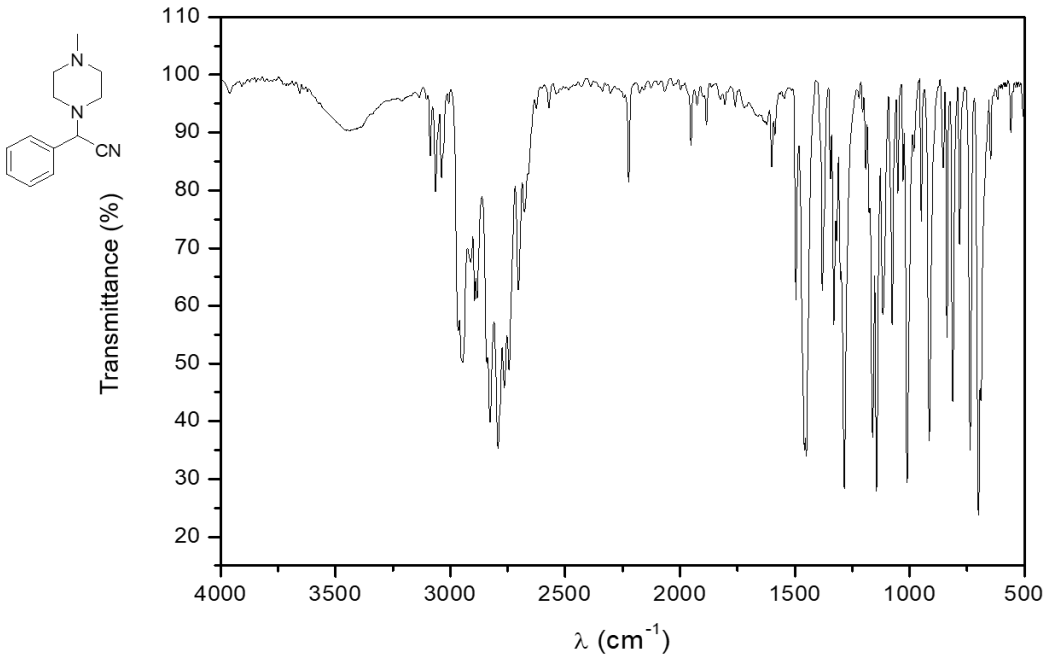

Figure S33. IR spectrum of compound **8d**.

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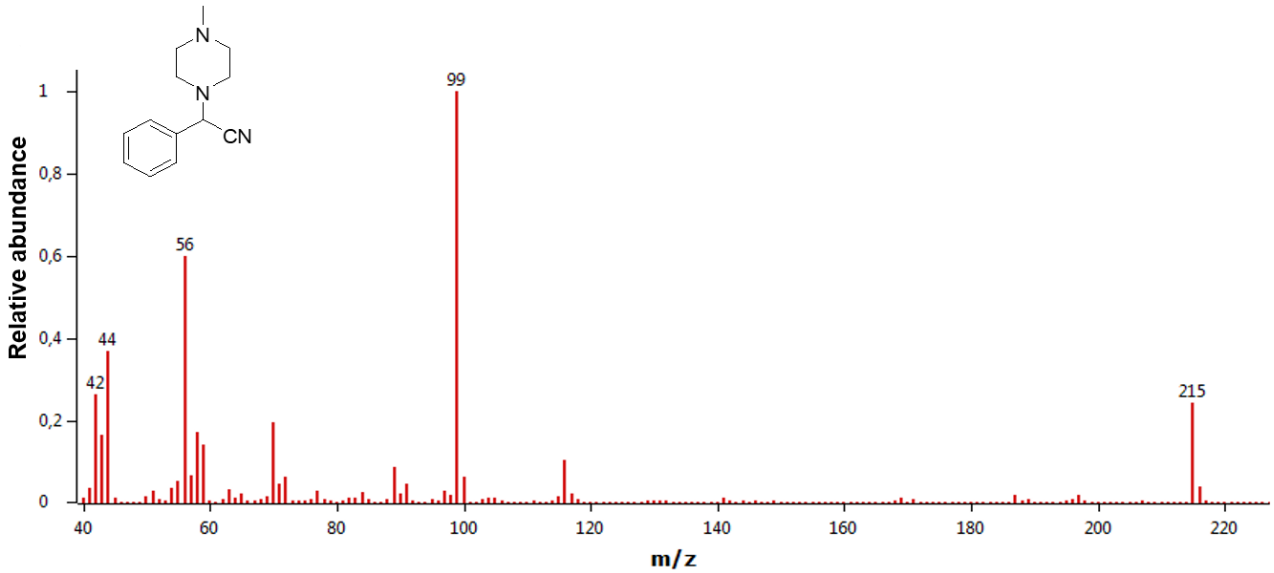

Figure S34. MS (EI, 70 eV) spectrum of compound **8d**.

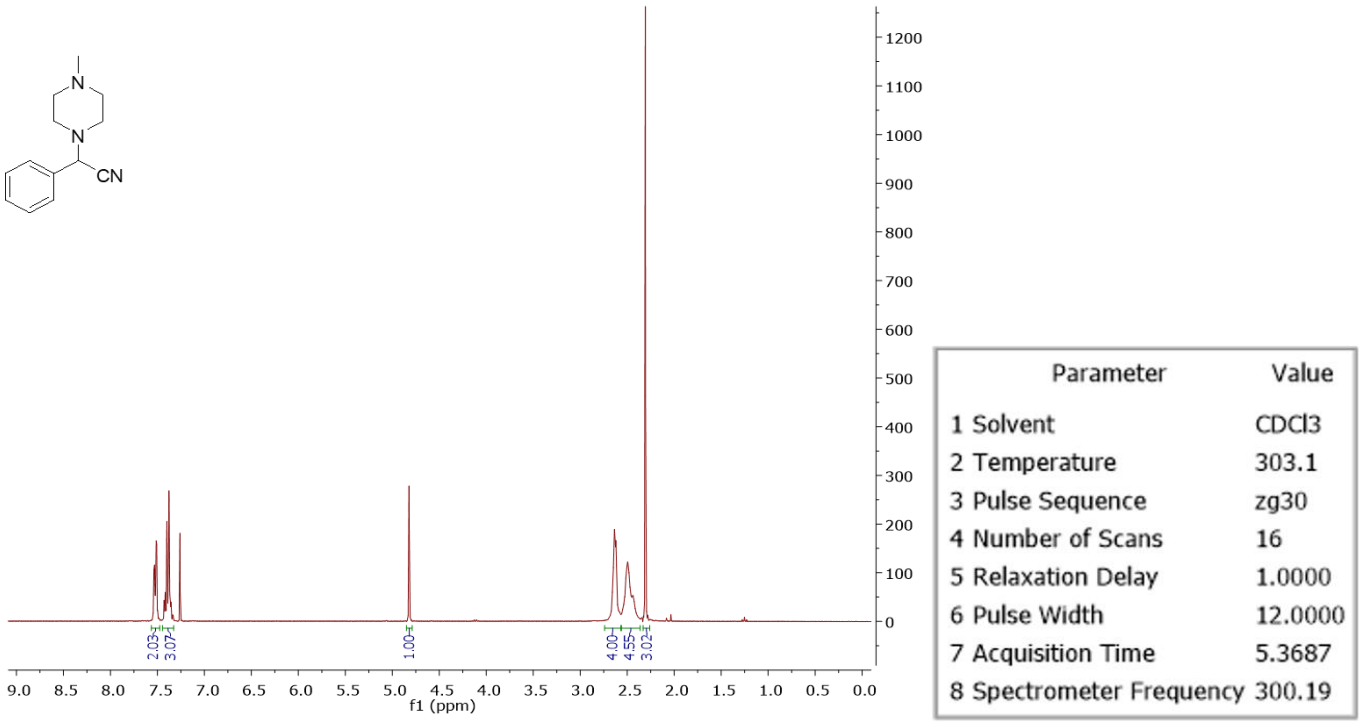

Figure S35. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **8d**.

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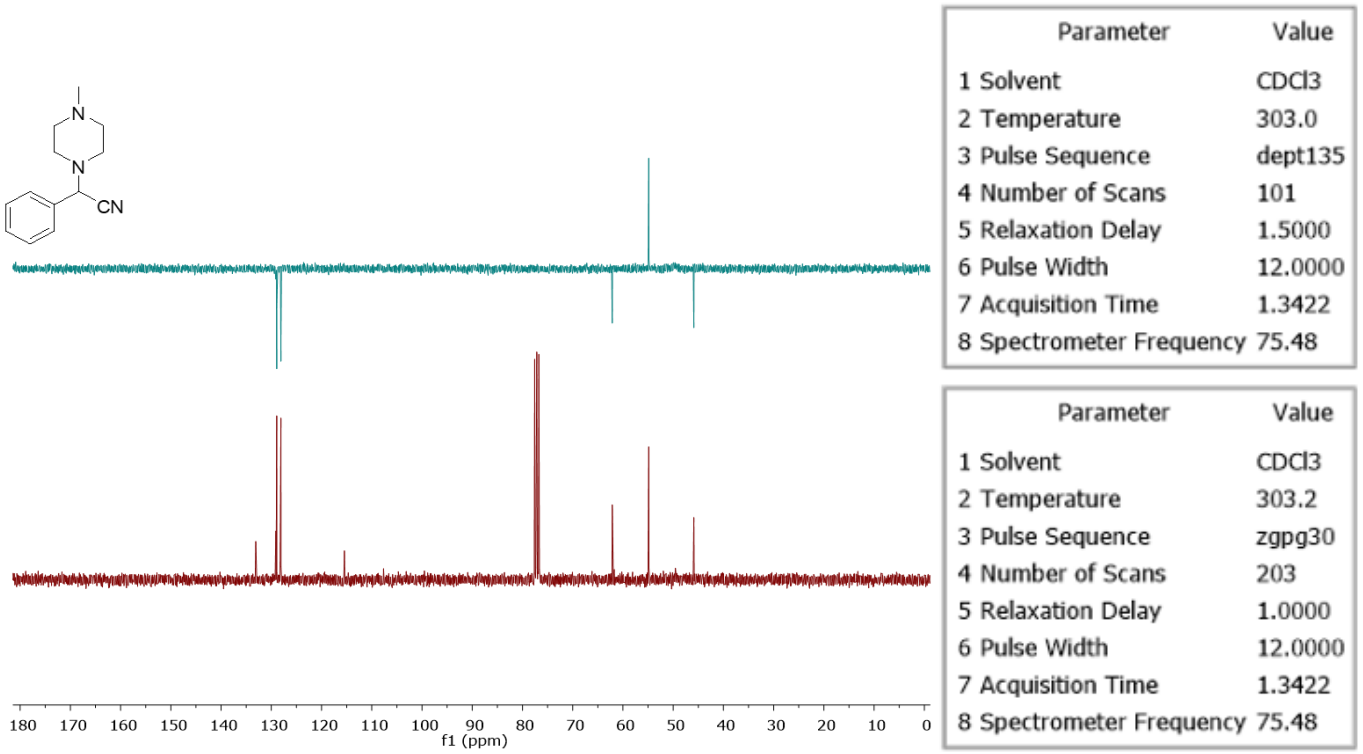

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7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

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6 Pulse Width	12.0000
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8 Spectrometer Frequency	75.48

Figure S36. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **8d**.

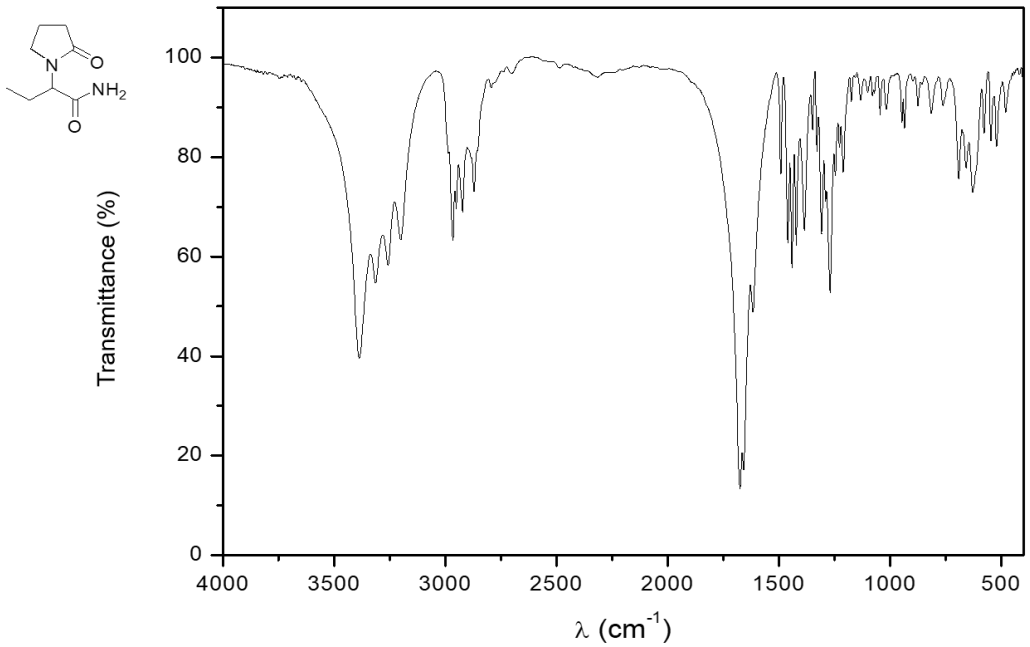

Figure S37. IR spectrum of compound **5a**.

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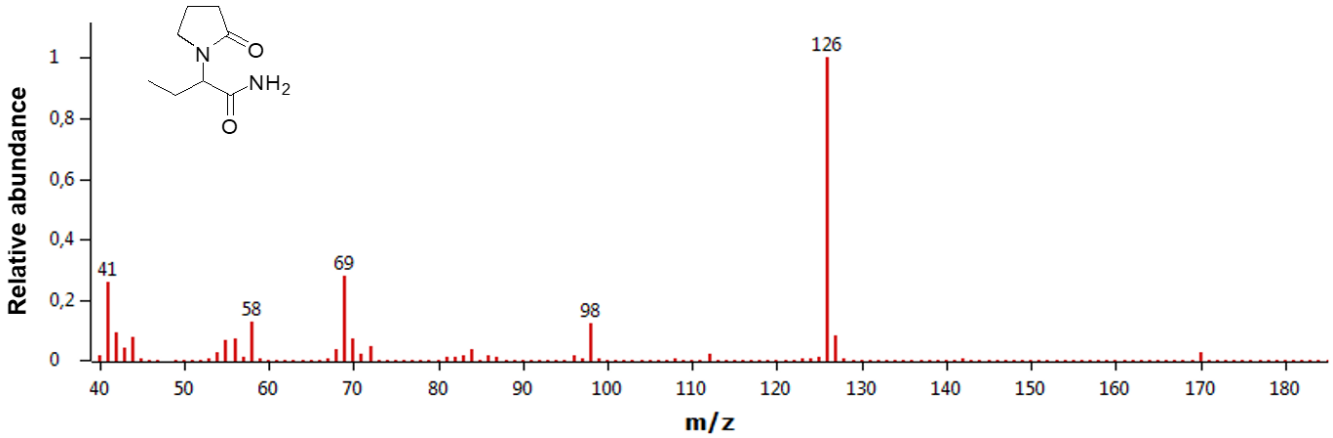

Figure S38. MS (EI, 70 eV) spectrum of compound **5a**.

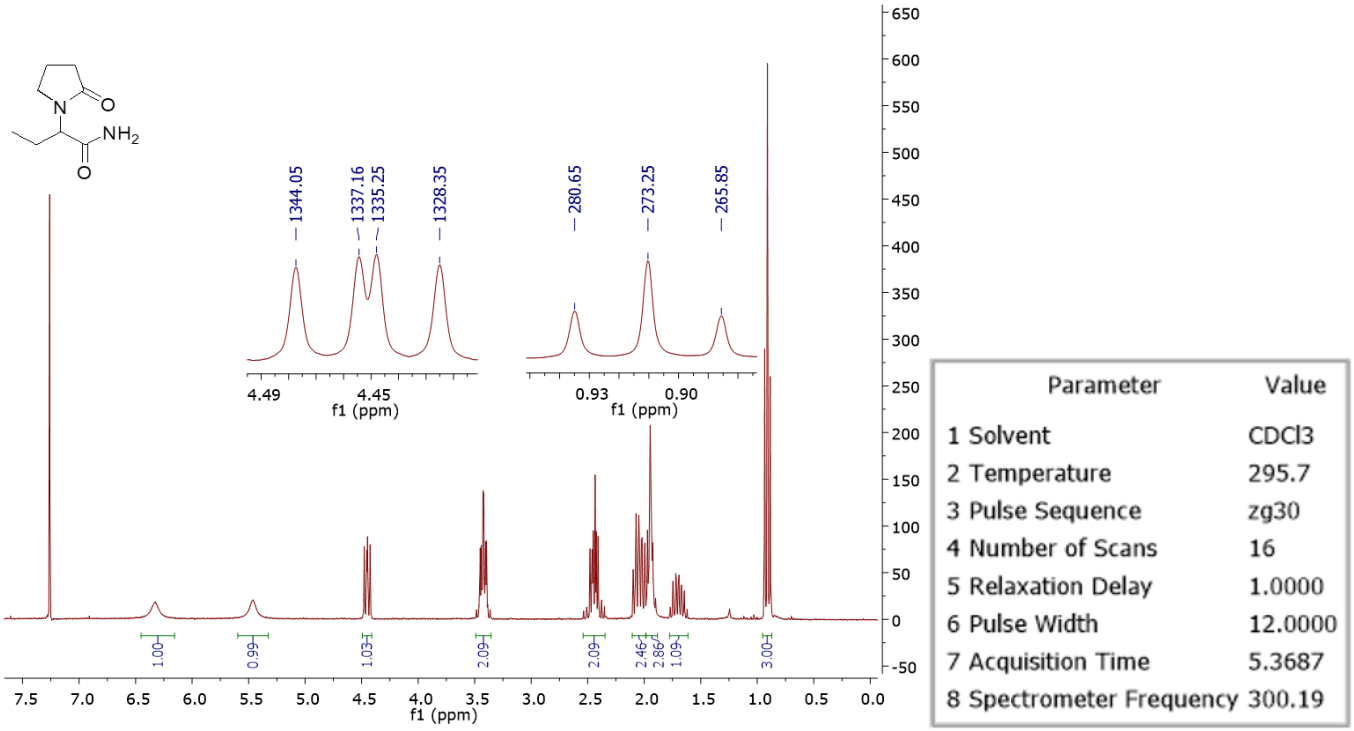

Figure S39. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **5a**.

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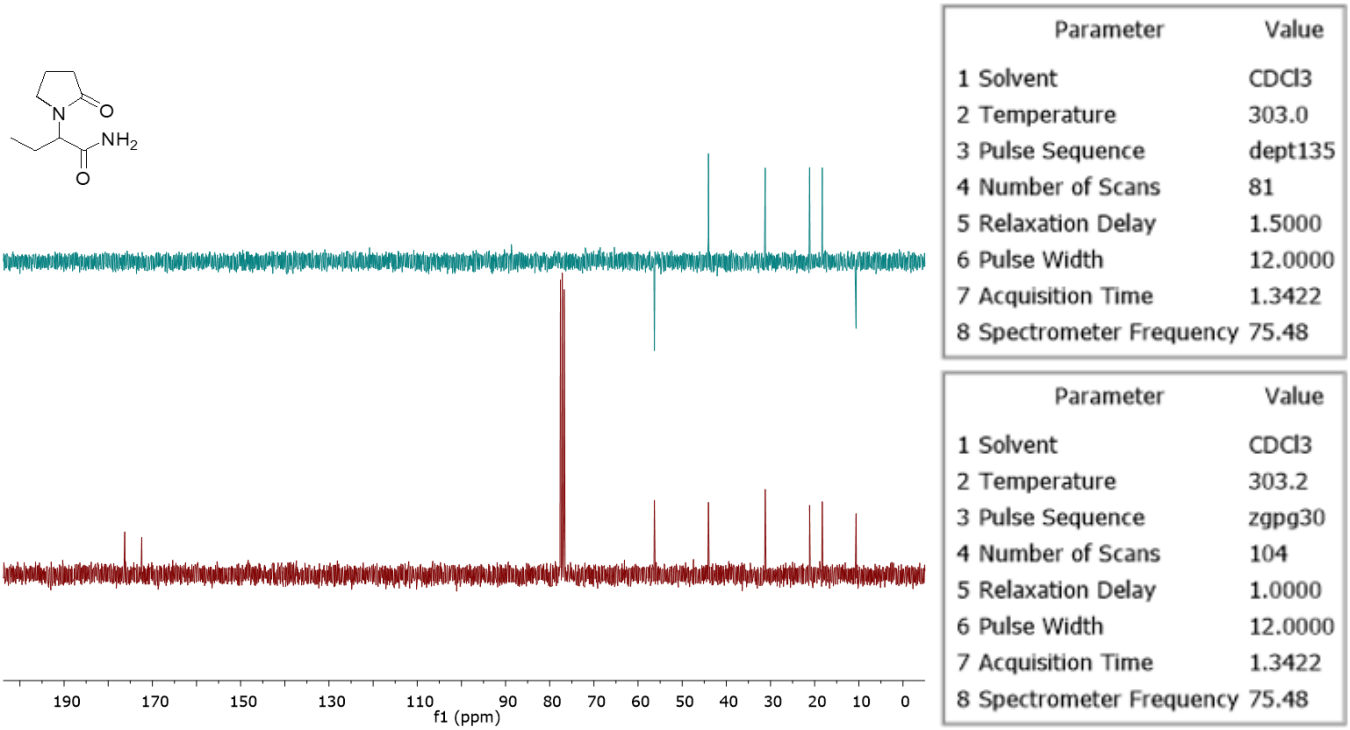

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.0
3 Pulse Sequence	dept135
4 Number of Scans	81
5 Relaxation Delay	1.5000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.2
3 Pulse Sequence	zgpg30
4 Number of Scans	104
5 Relaxation Delay	1.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S40. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **5a**.

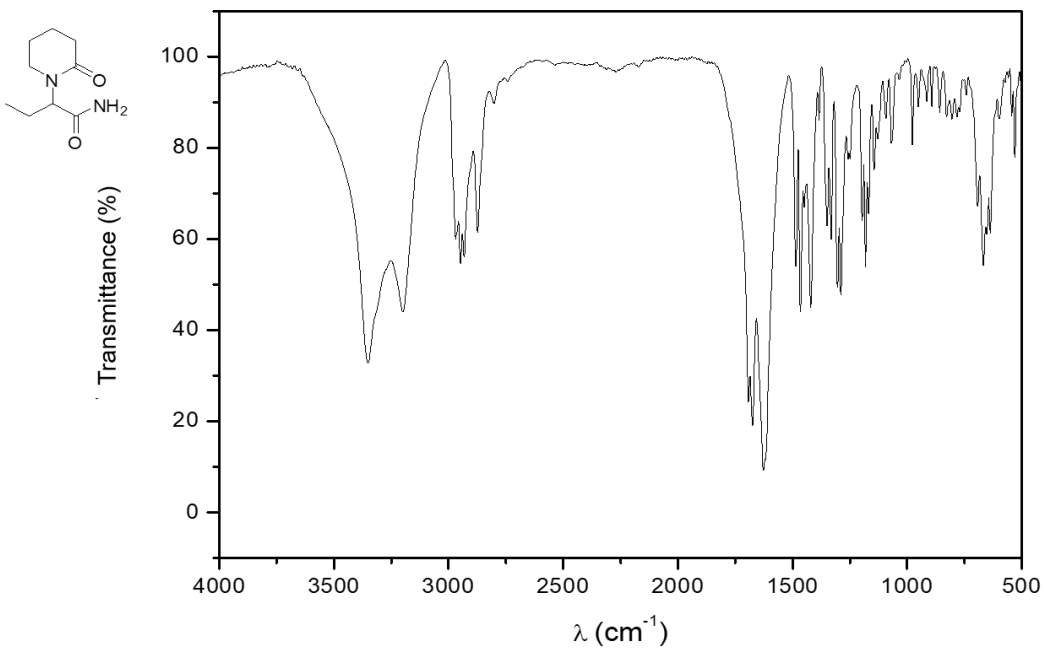

Figure S41. IR spectrum of compound **5b**.

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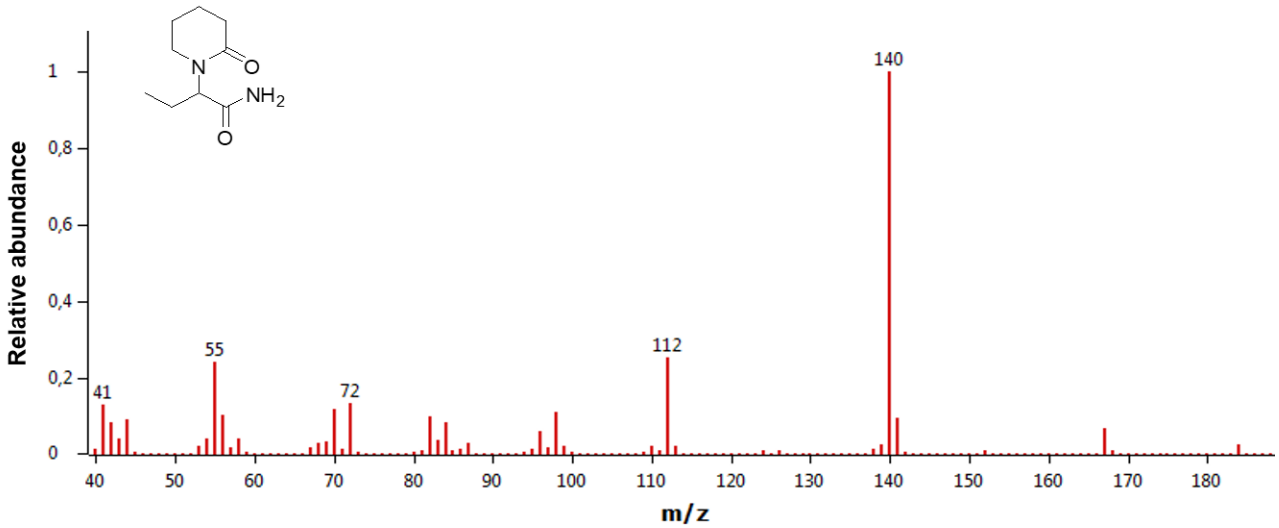

Figure S42. MS (EI, 70 eV) spectrum of compound **5b**.

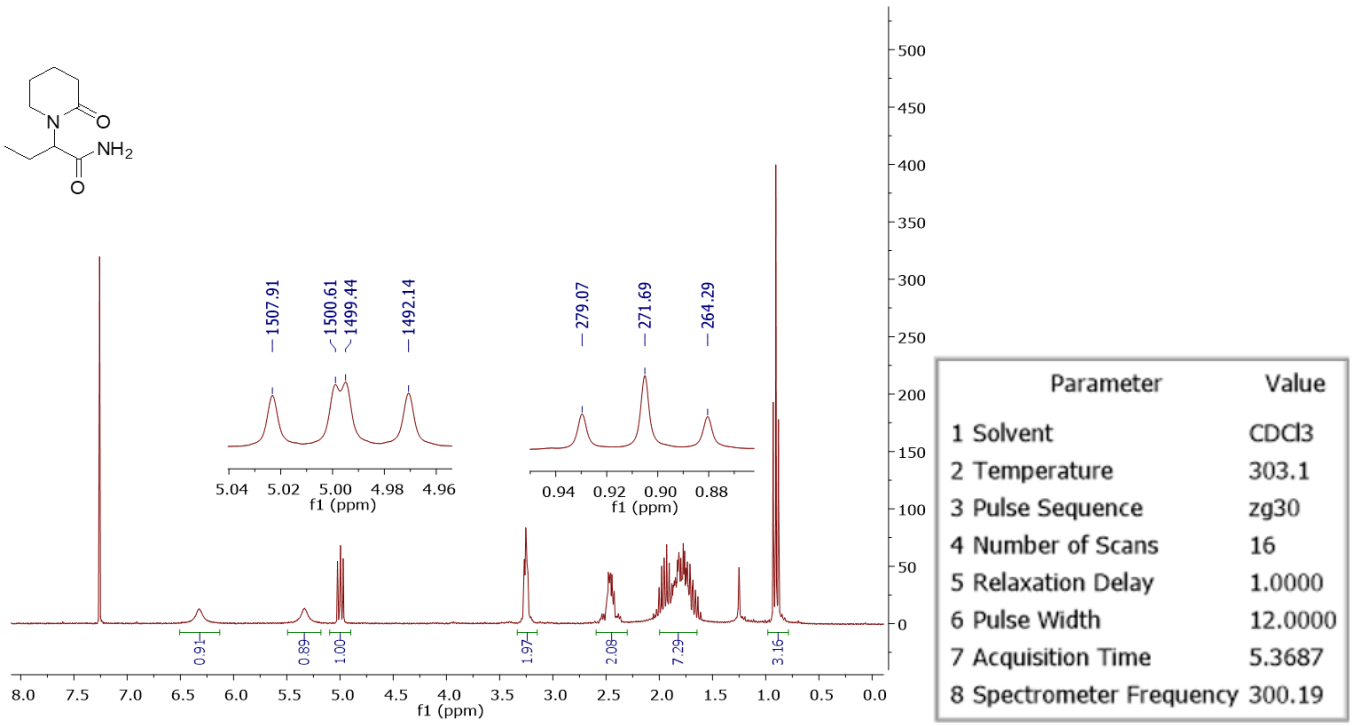

Figure S43. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **5b**.

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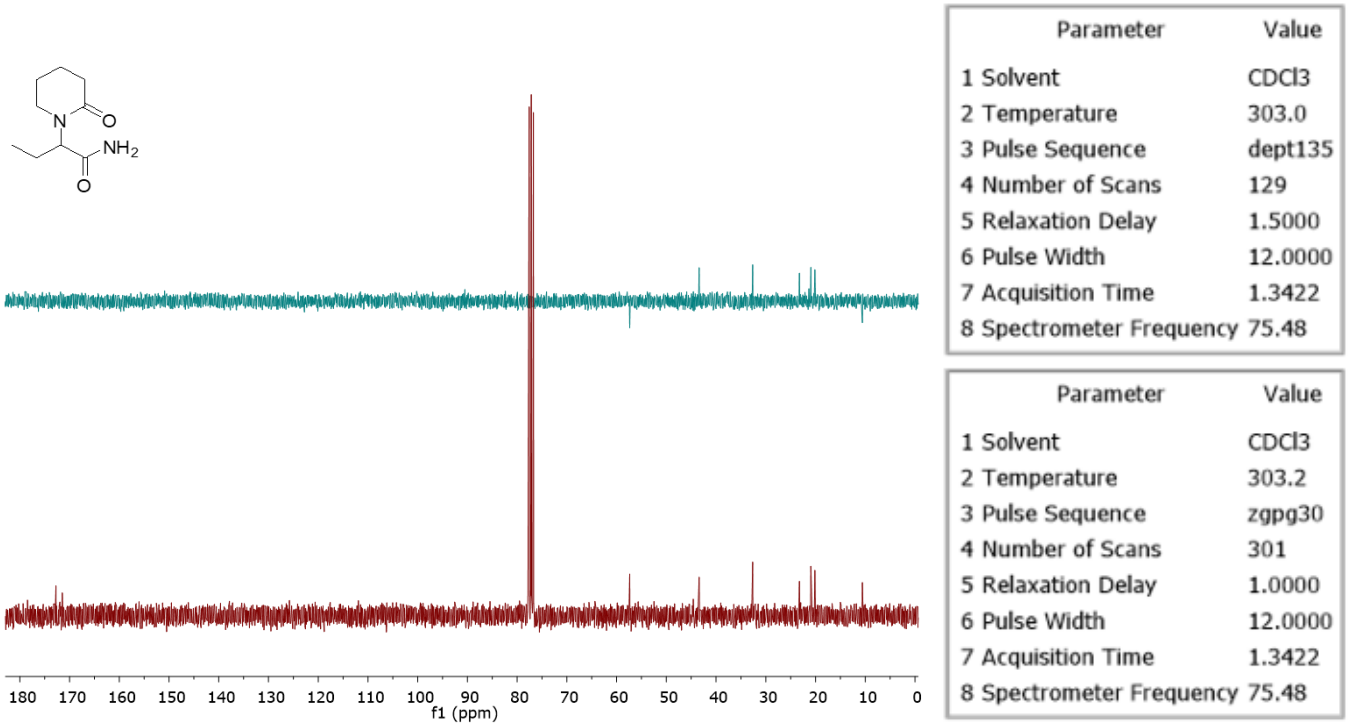

Figure S44. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **5b**.

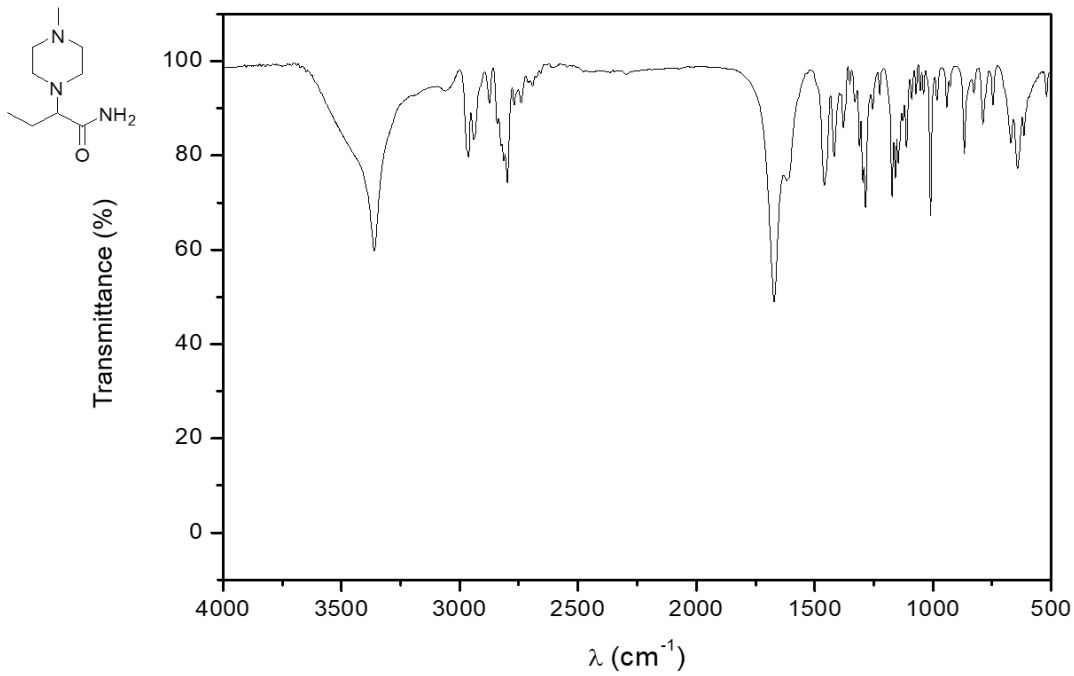

Figure S45. IR spectrum of compound **5d**.

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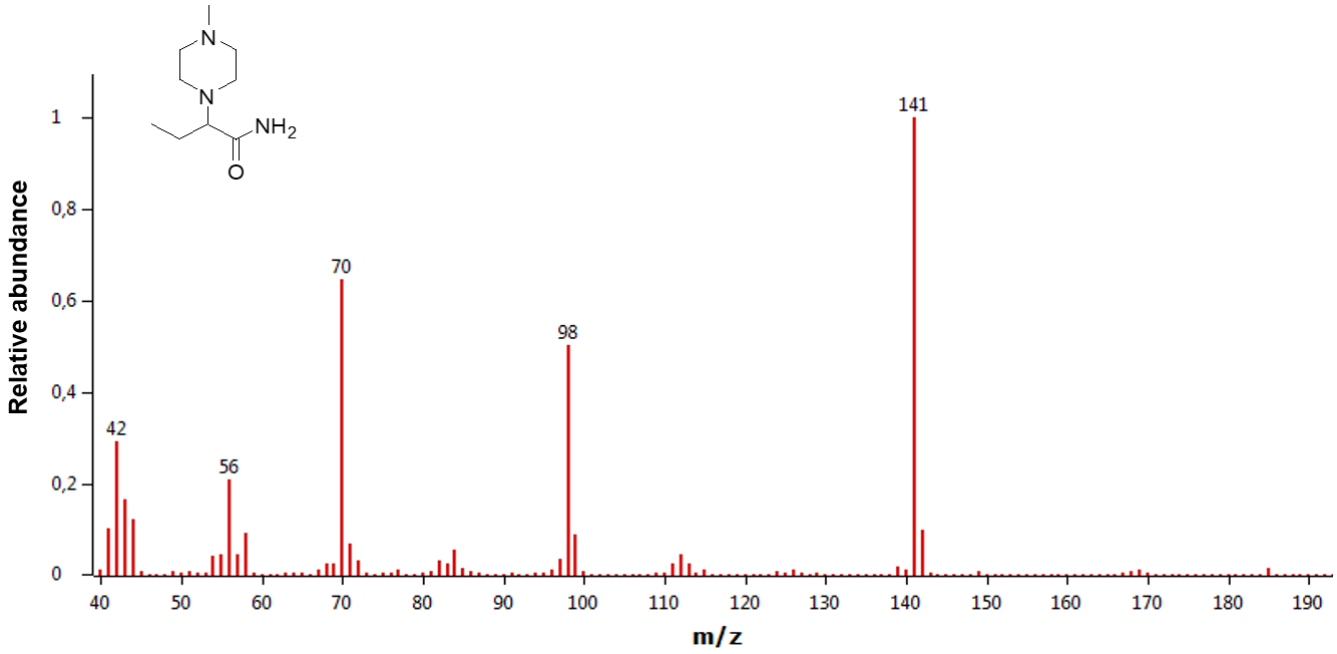

Figure S46. MS (EI, 70 eV) spectrum of compound **5d**.

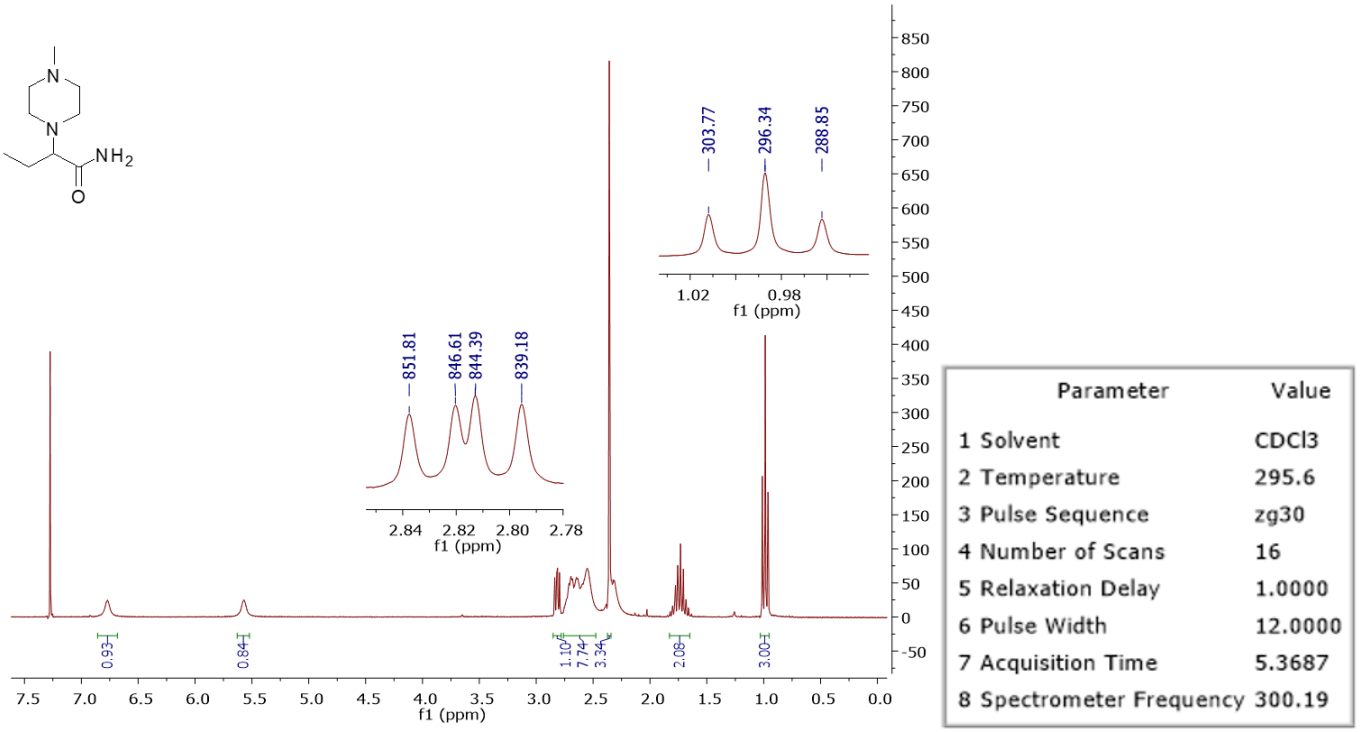

Figure S47. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **5d**.

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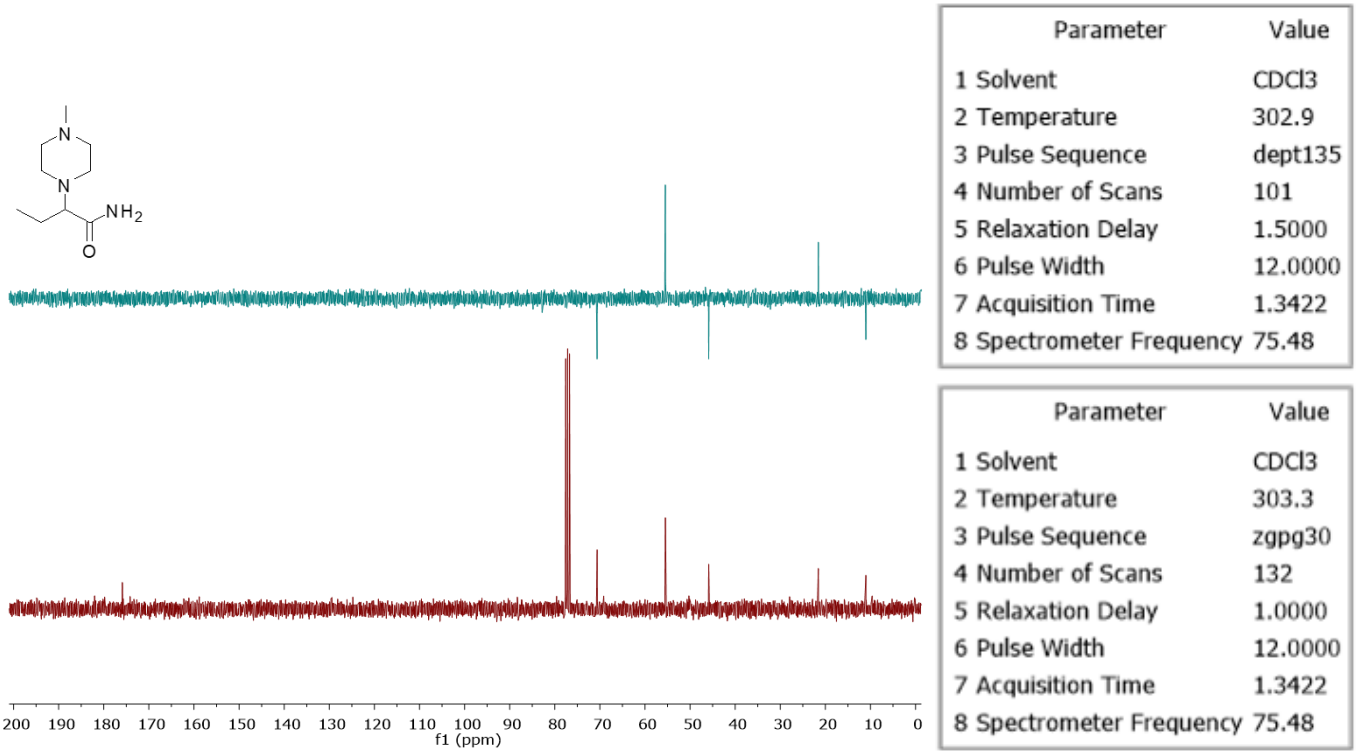

Figure S48. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **5d**.

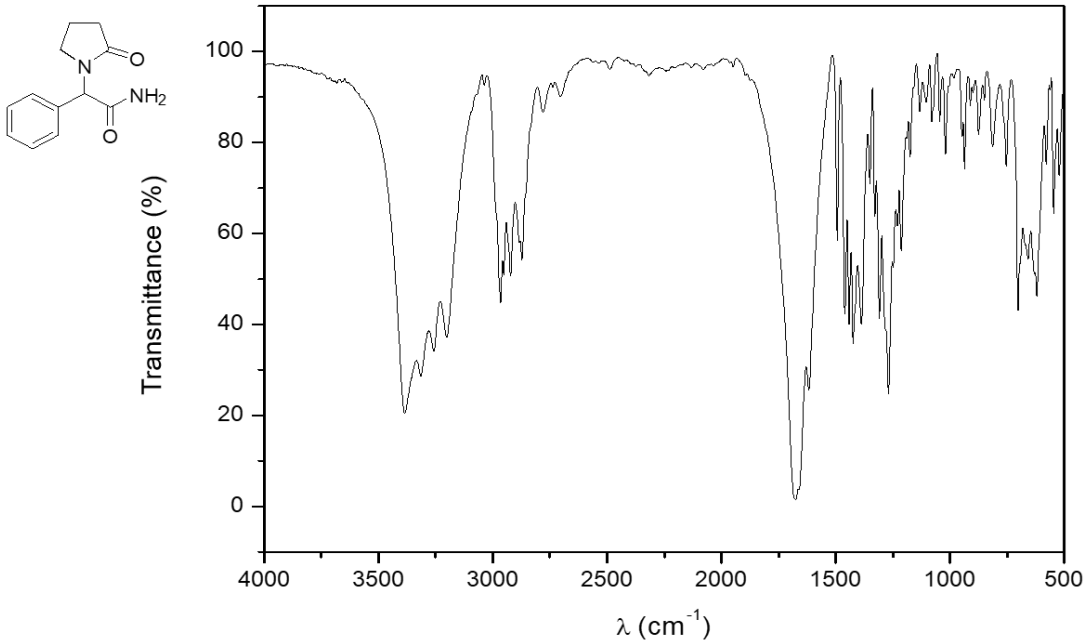

Figure S49. IR spectrum of compound **9a**.

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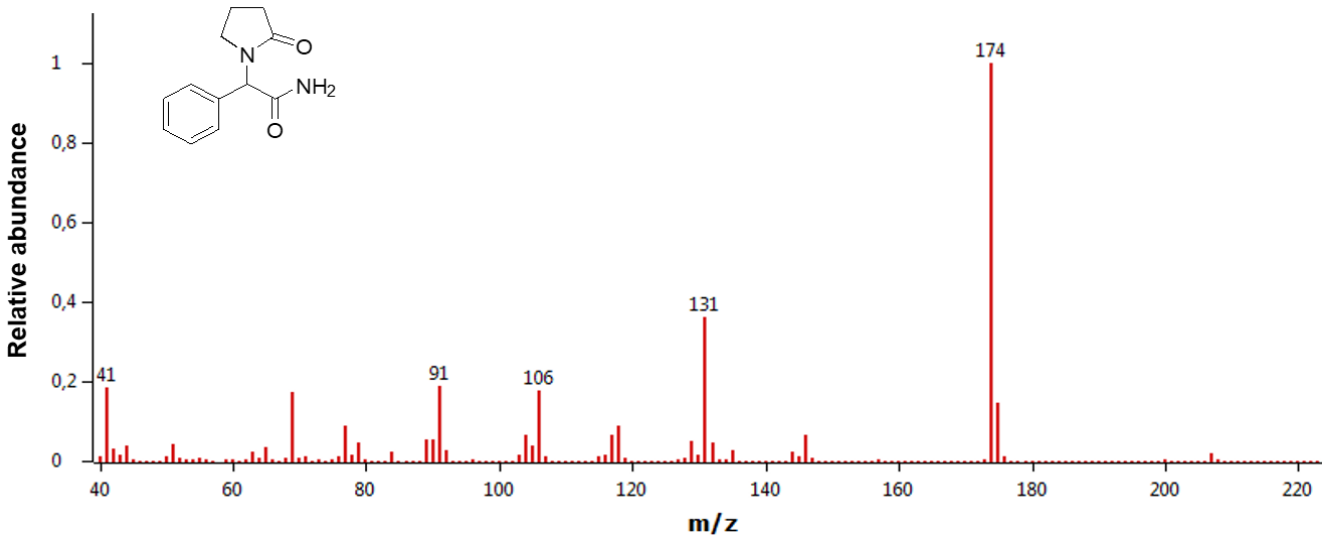

Figure S50. MS (EI, 70 eV) spectrum of compound **9a**.

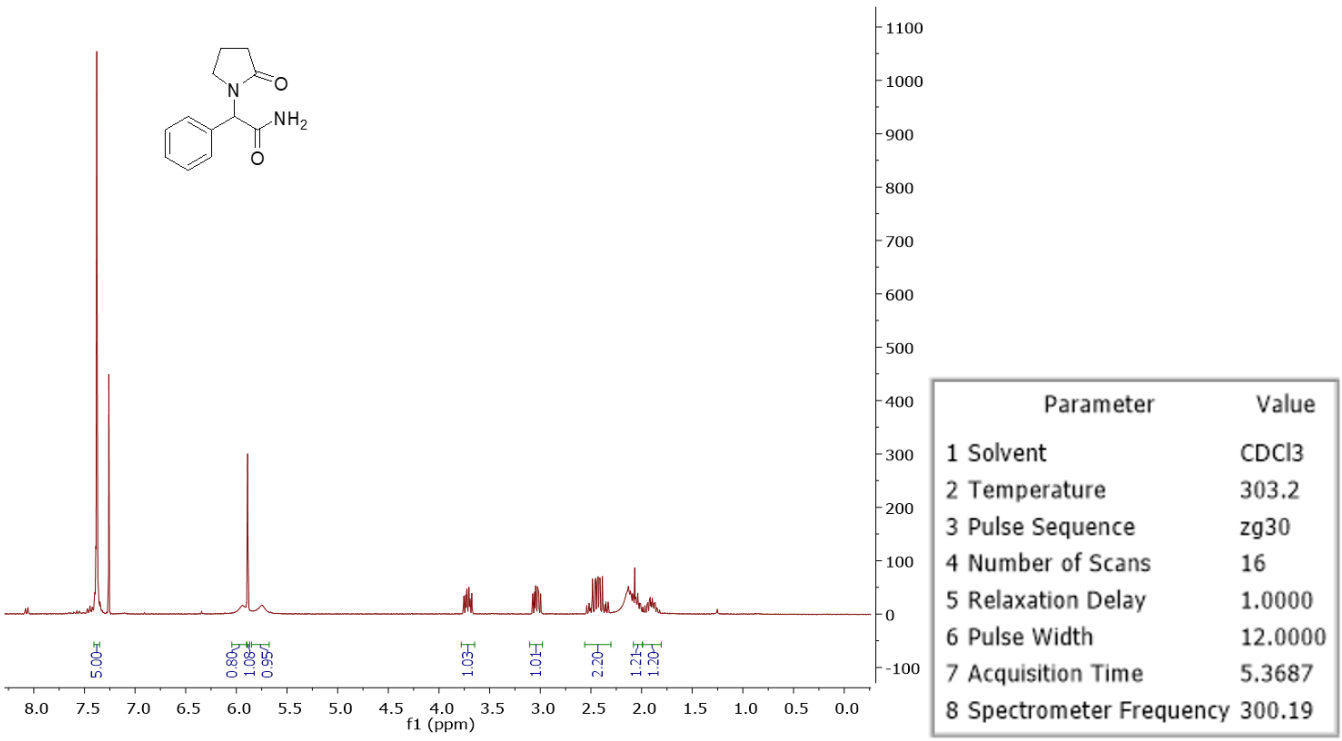

Figure S51. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **9a**.

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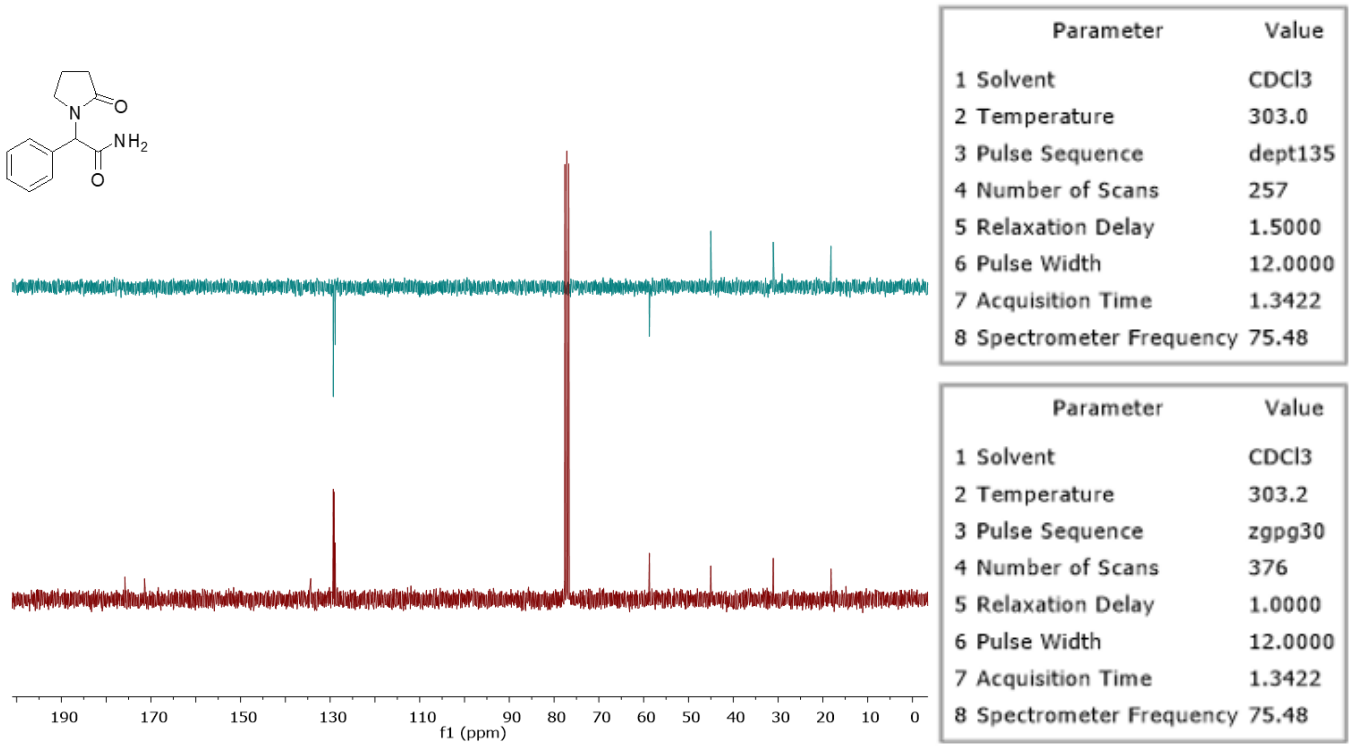

Figure S52. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **9a**.

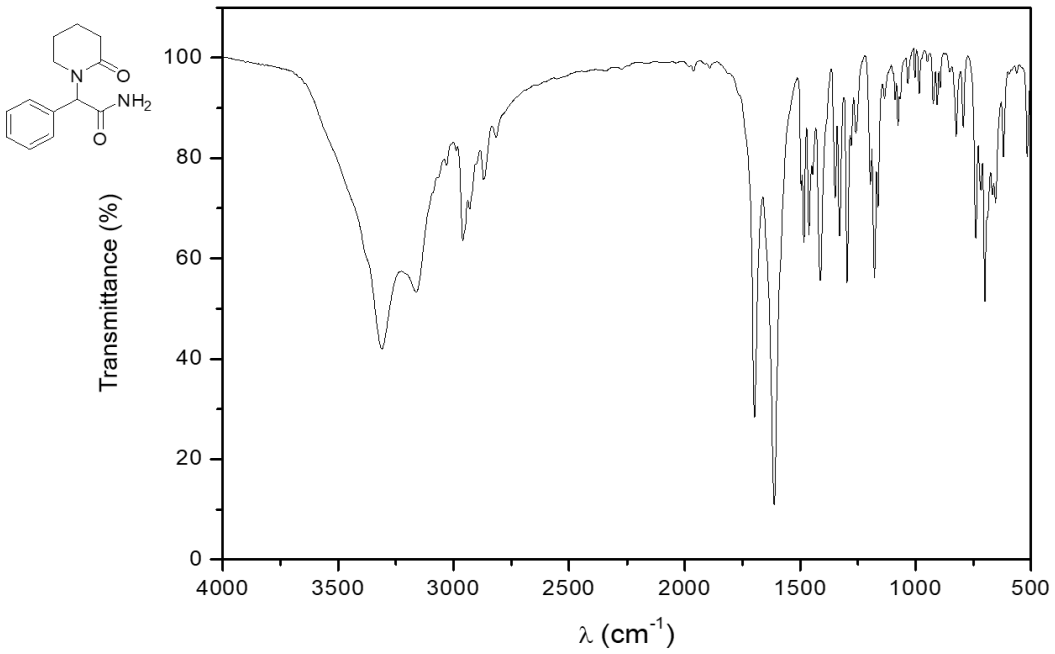

Figure S53. IR spectrum of compound **9b**.

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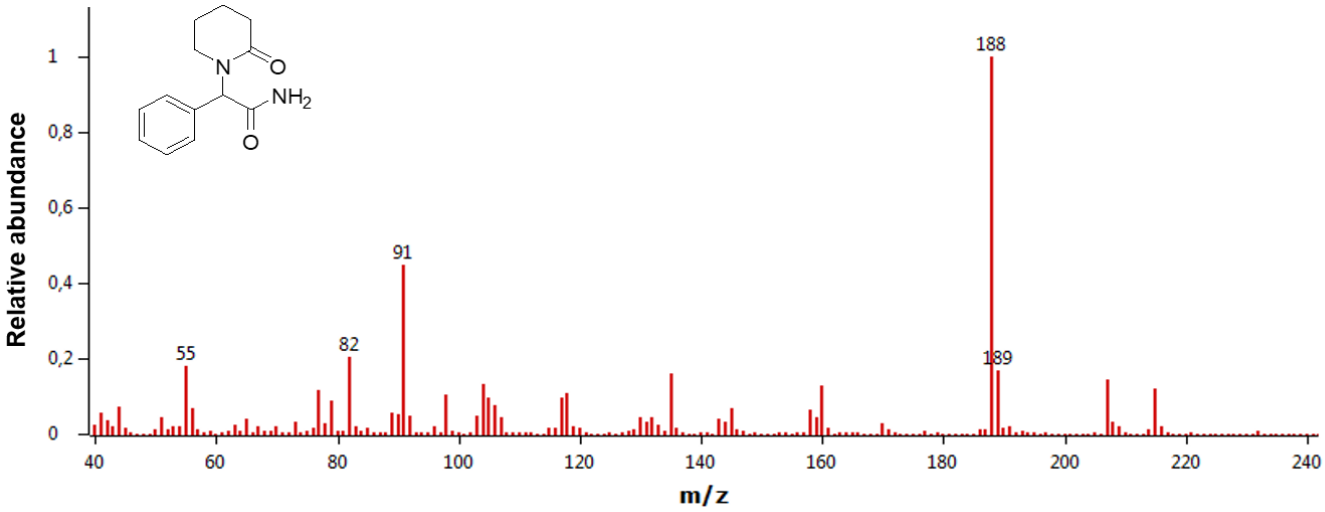

Figure S54. MS (EI, 70 eV) spectrum of compound **9b**.

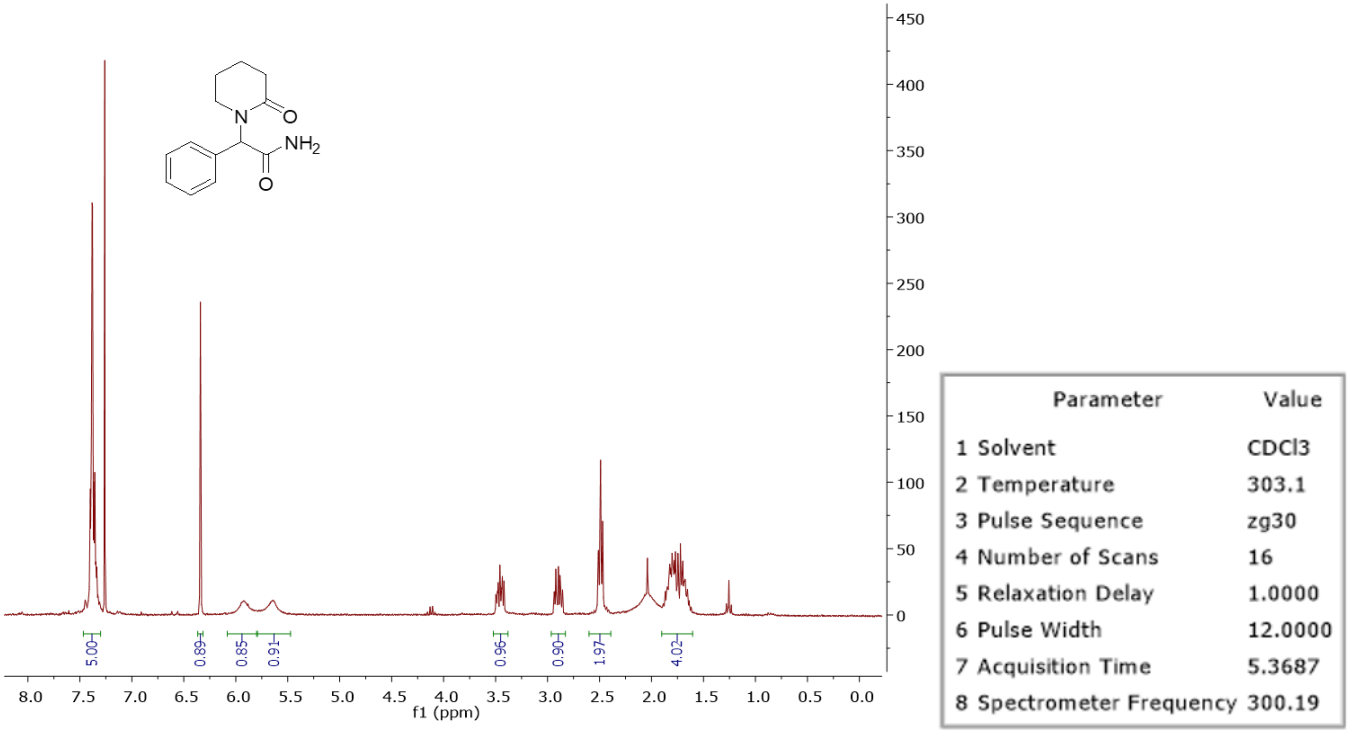

Figure S55. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **9b**.

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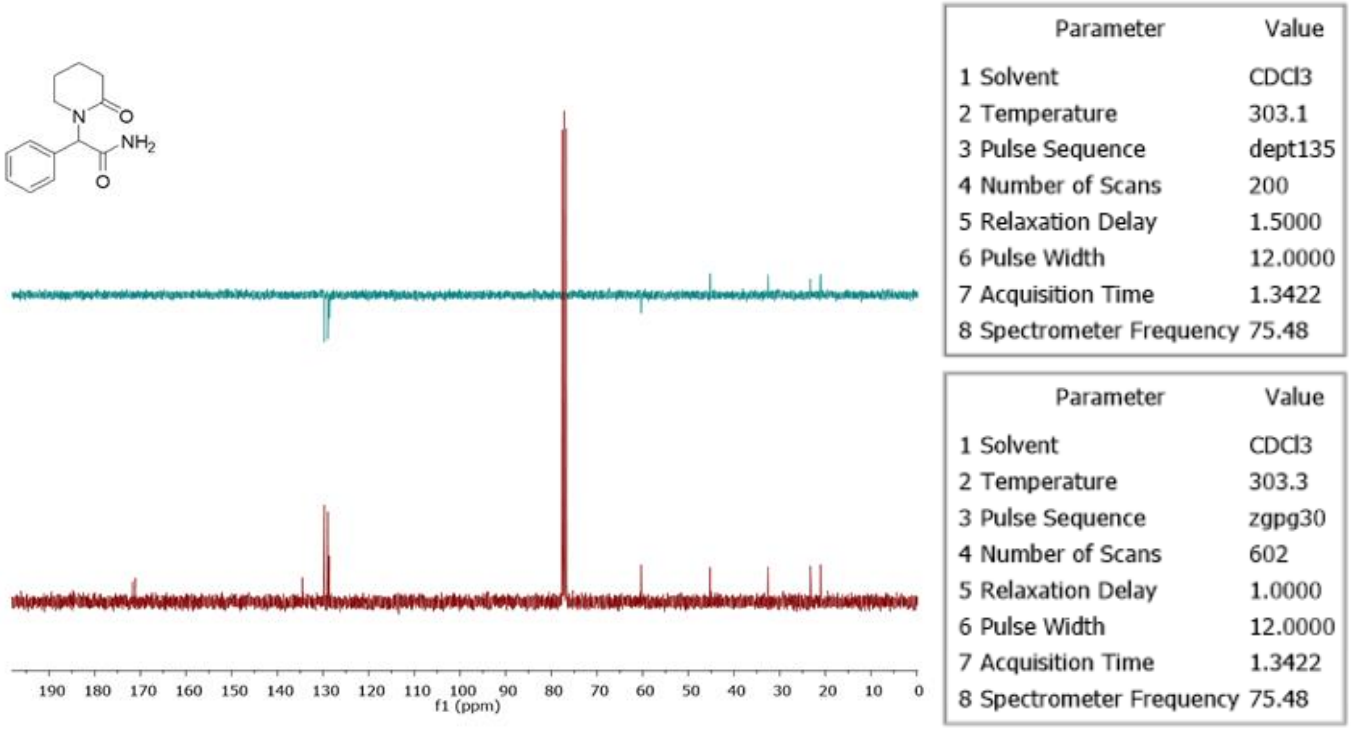

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.1
3 Pulse Sequence	dept135
4 Number of Scans	200
5 Relaxation Delay	1.5000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.3
3 Pulse Sequence	zgpg30
4 Number of Scans	602
5 Relaxation Delay	1.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S56. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **9b**.

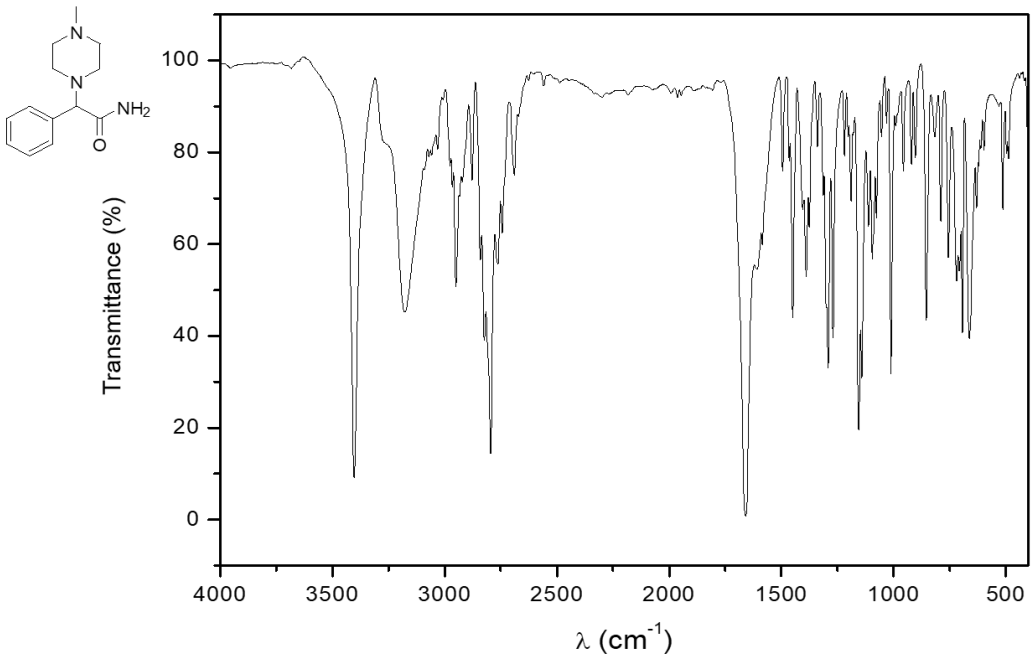

Figure S57. IR spectrum of compound **9d**.

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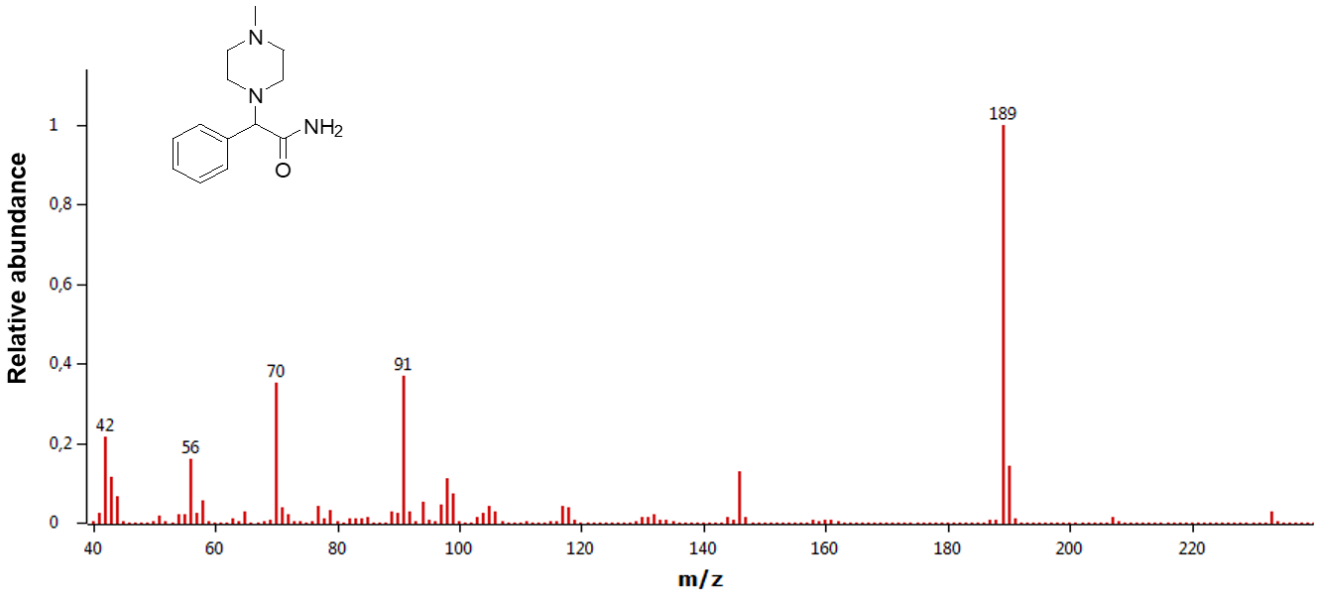

Figure S58. MS (EI, 70 eV) spectrum of compound **9d**.

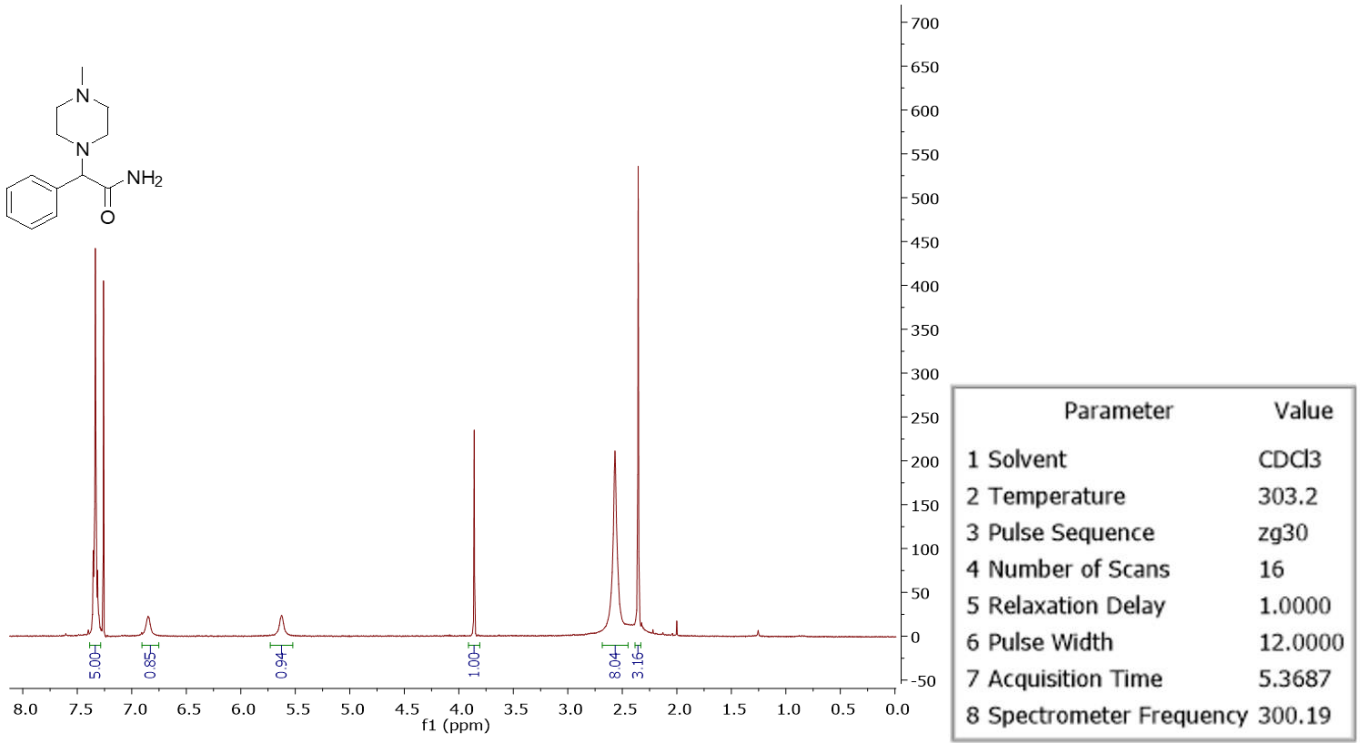

Figure S59. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **9d**.

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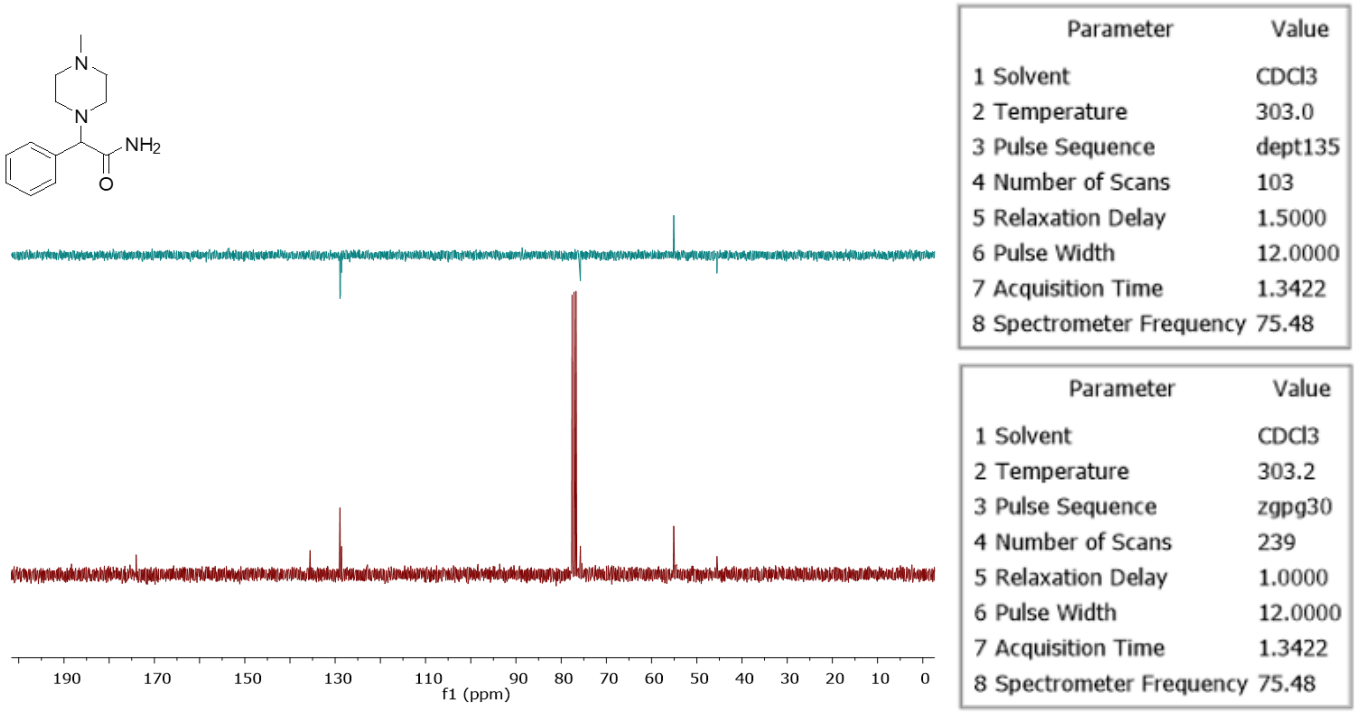

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.0
3 Pulse Sequence	dept135
4 Number of Scans	103
5 Relaxation Delay	1.5000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Parameter	Value
1 Solvent	CDCl3
2 Temperature	303.2
3 Pulse Sequence	zgpg30
4 Number of Scans	239
5 Relaxation Delay	1.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S60. ^{13}C NMR (75.48 MHz, $CDCl_3$) spectrum and DEPT-135 experiment of compound **9d**.

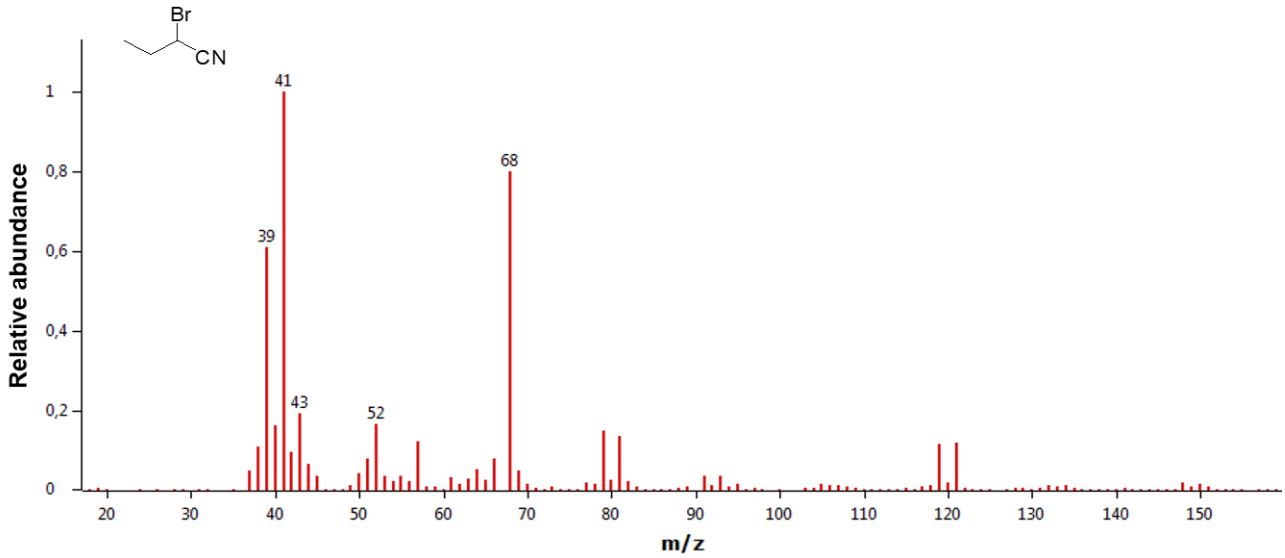

Figure S61. MS (EI, 70 eV) spectrum of compound **3**.

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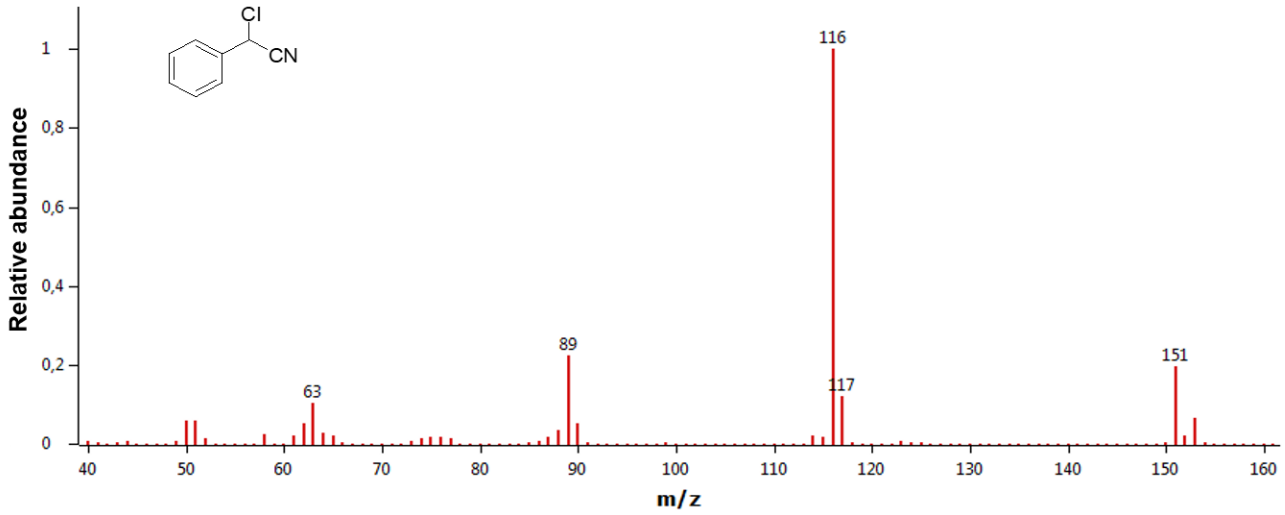

Figure S62. MS (EI, 70 eV) spectrum of compound **7**.

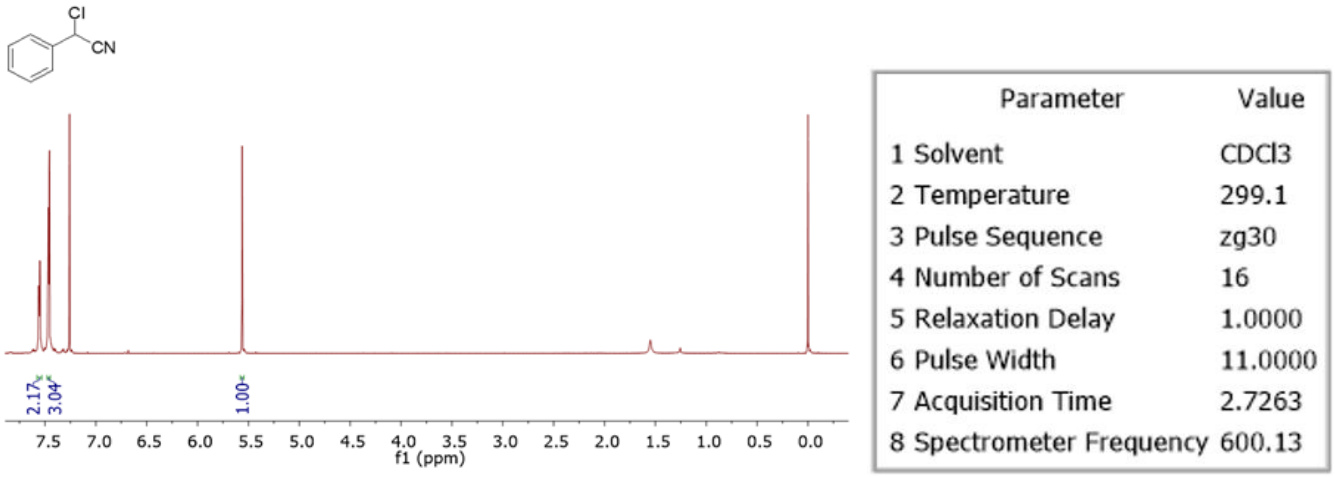

Figure S63. ^{1}H NMR (300.19 MHz, $CDCl_3$) spectrum of compound **7**.

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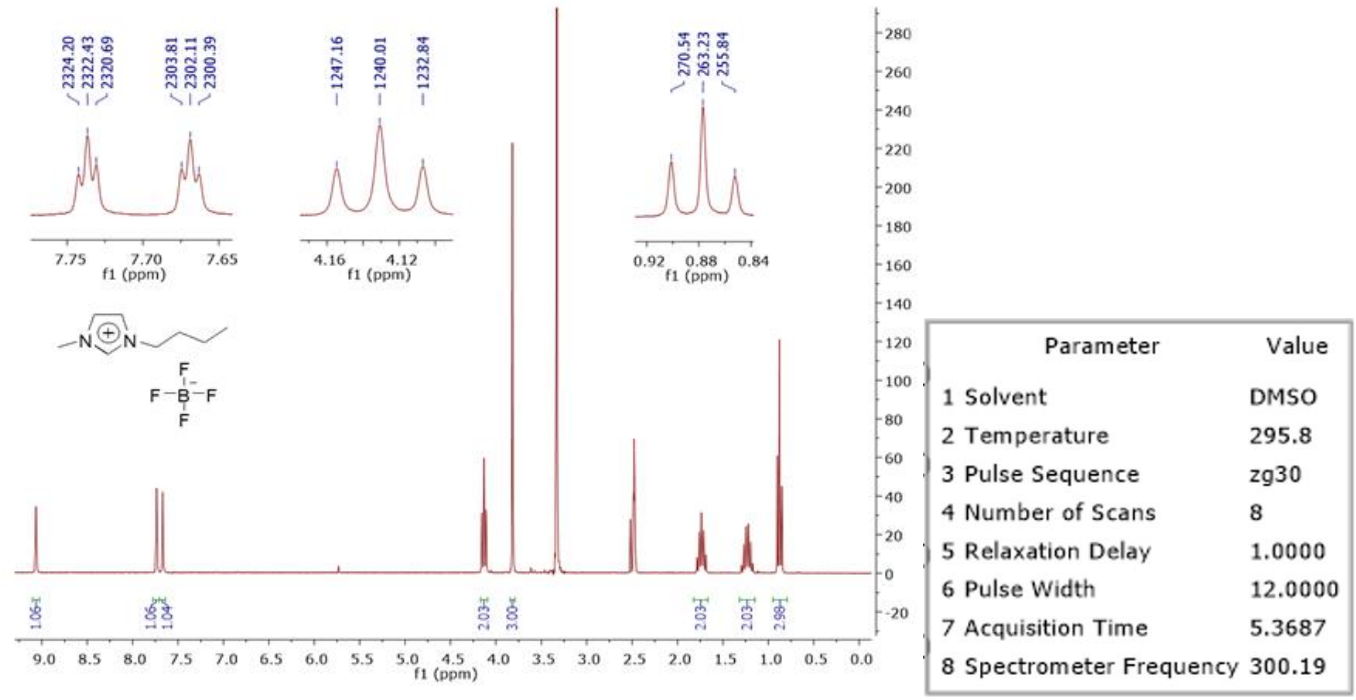

Figure S64. ^{1}H NMR (300.19 MHz, DMSO-d_6) spectrum of compound **BMIM.BF$_4$**.

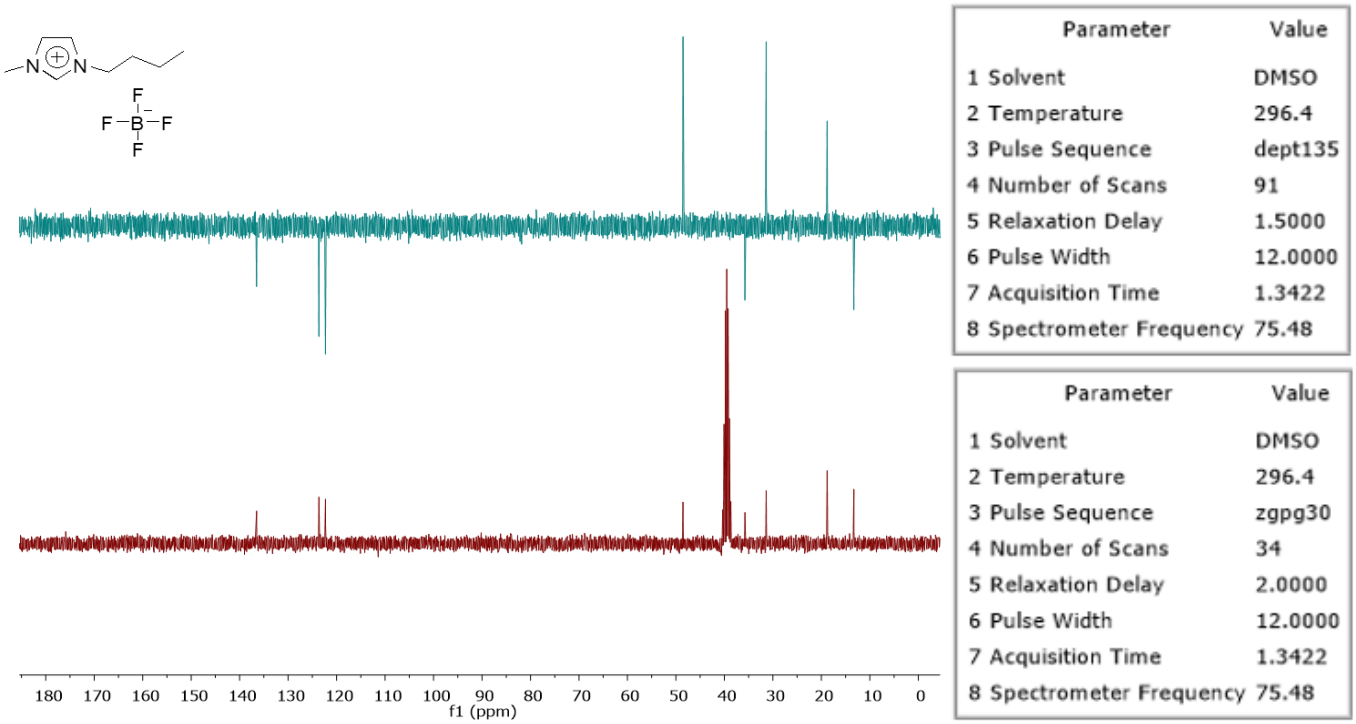

Figure S65. ^{13}C NMR (75.48 MHz, DMSO-d_6) spectrum and DEPT-135 experiment of compound **BMIM.BF$_4$**.

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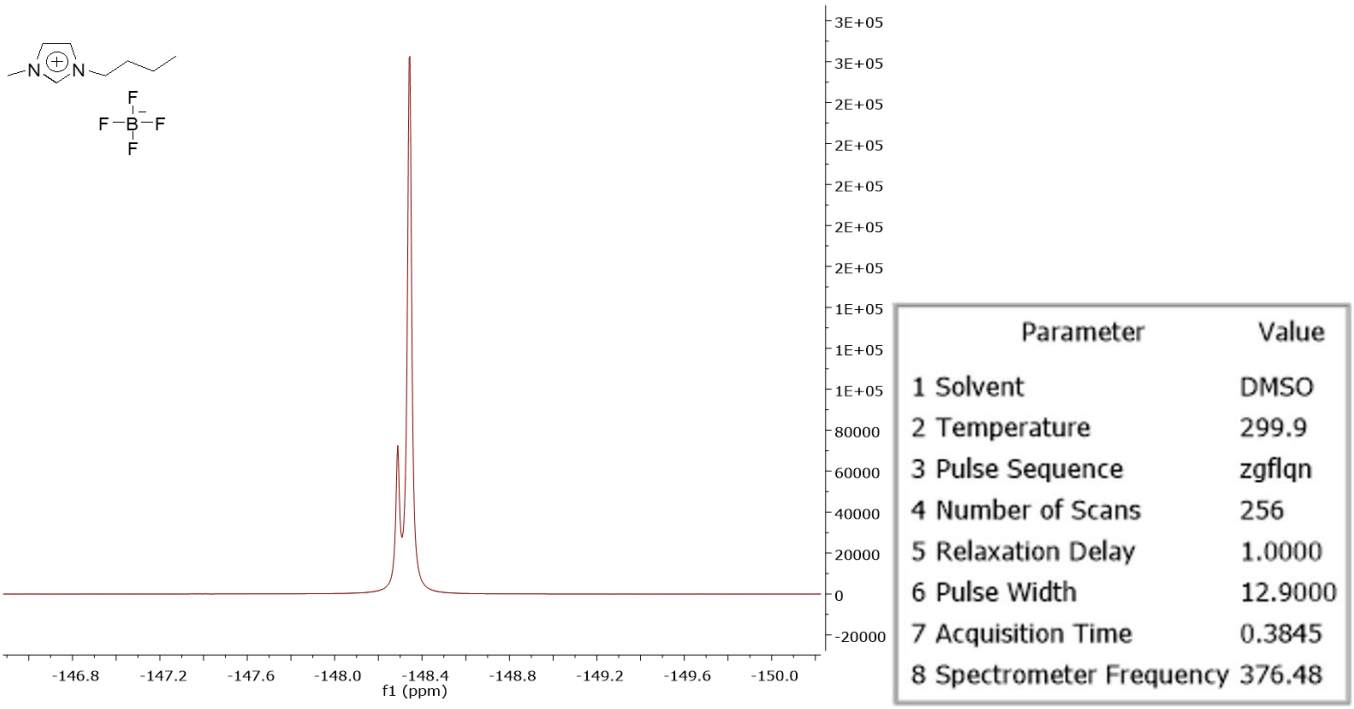

Figure S66. ^{19}F NMR (376.48 MHz, DMSO-d_6) spectrum of compound **BMIM.BF$_4$**.

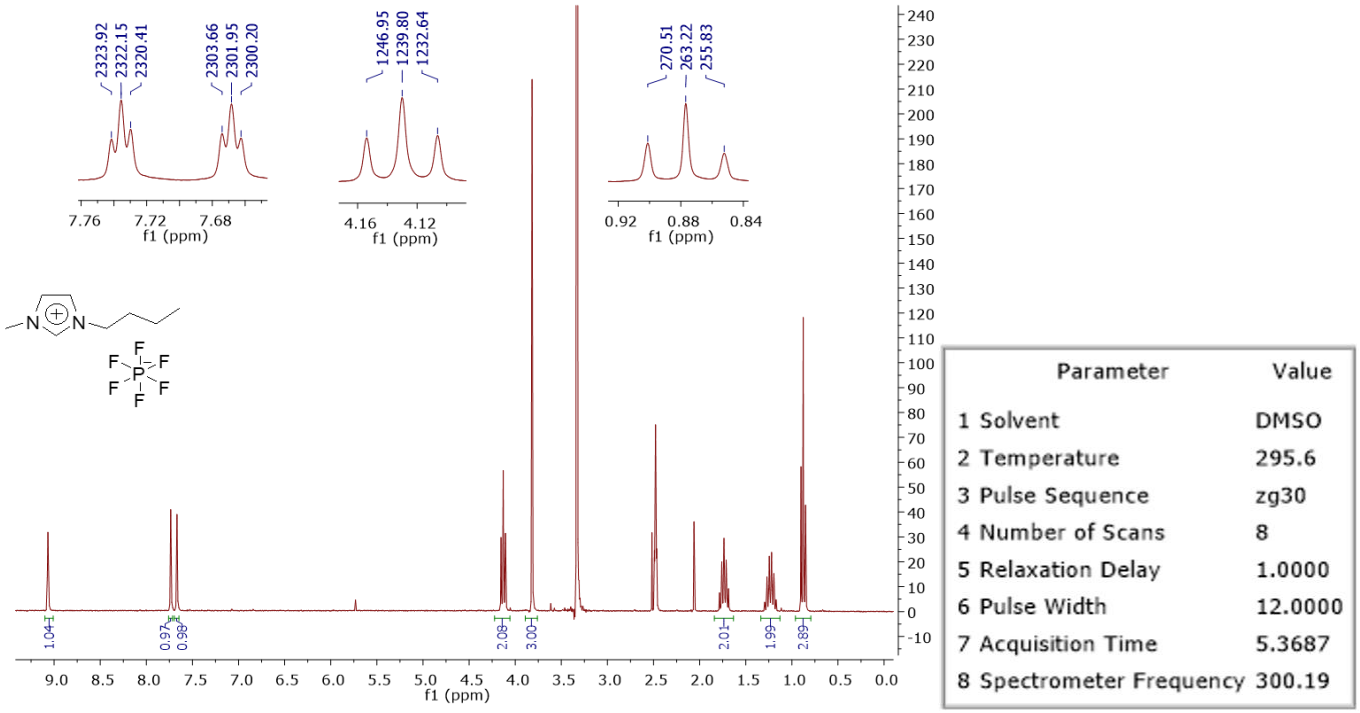

Figure S67. ^{1}H NMR (300.19 MHz, DMSO-d_6) spectrum of compound **BMIM.PF$_6$**.

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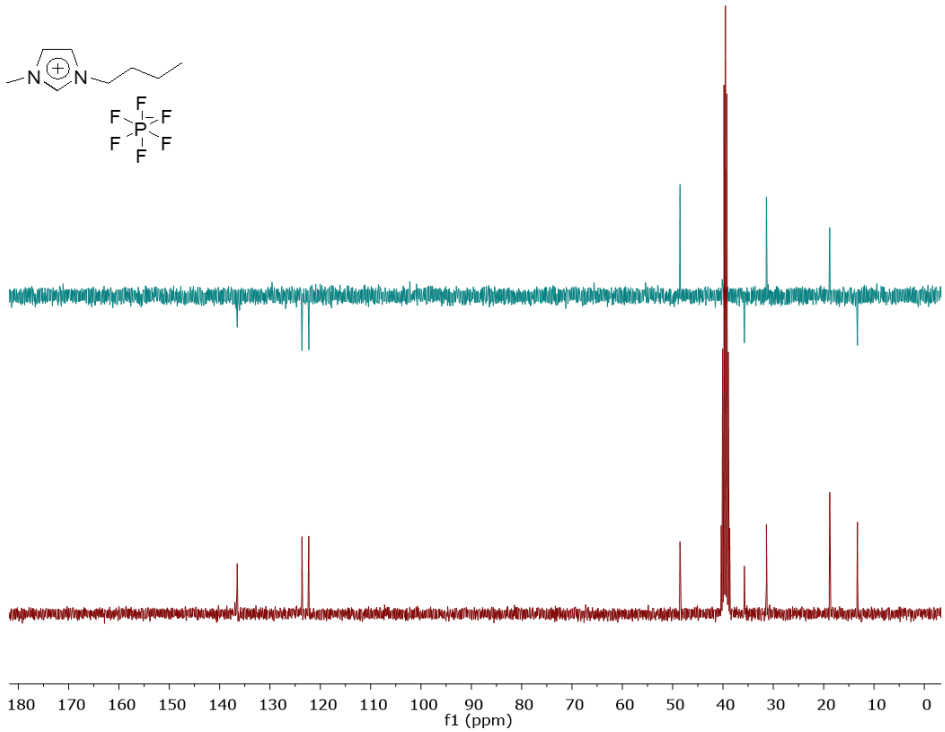
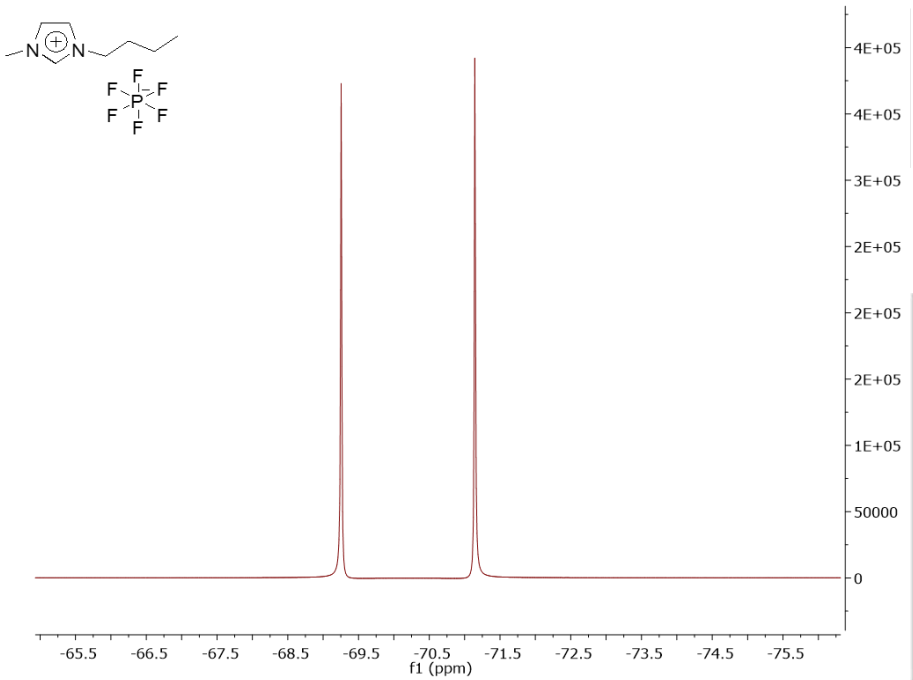


Parameter	Value
1 Solvent	DMSO
2 Temperature	296.5
3 Pulse Sequence	dept135
4 Number of Scans	91
5 Relaxation Delay	1.5000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Parameter	Value
1 Solvent	DMSO
2 Temperature	296.6
3 Pulse Sequence	zgpg30
4 Number of Scans	281
5 Relaxation Delay	2.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S68. ^{13}C NMR (75.48 MHz, DMSO-d_6) spectrum and DEPT-135 experiment of compound **BMIM.PF$_6$**.



Parameter	Value
1 Solvent	DMSO
2 Temperature	299.9
3 Pulse Sequence	zgflqn
4 Number of Scans	256
5 Relaxation Delay	1.0000
6 Pulse Width	12.9000
7 Acquisition Time	0.3845
8 Spectrometer Frequency	376.48

Figure S69. ^{19}F NMR (376.48 MHz, DMSO-d_6) spectrum of compound **BMIM.PF$_6$**.

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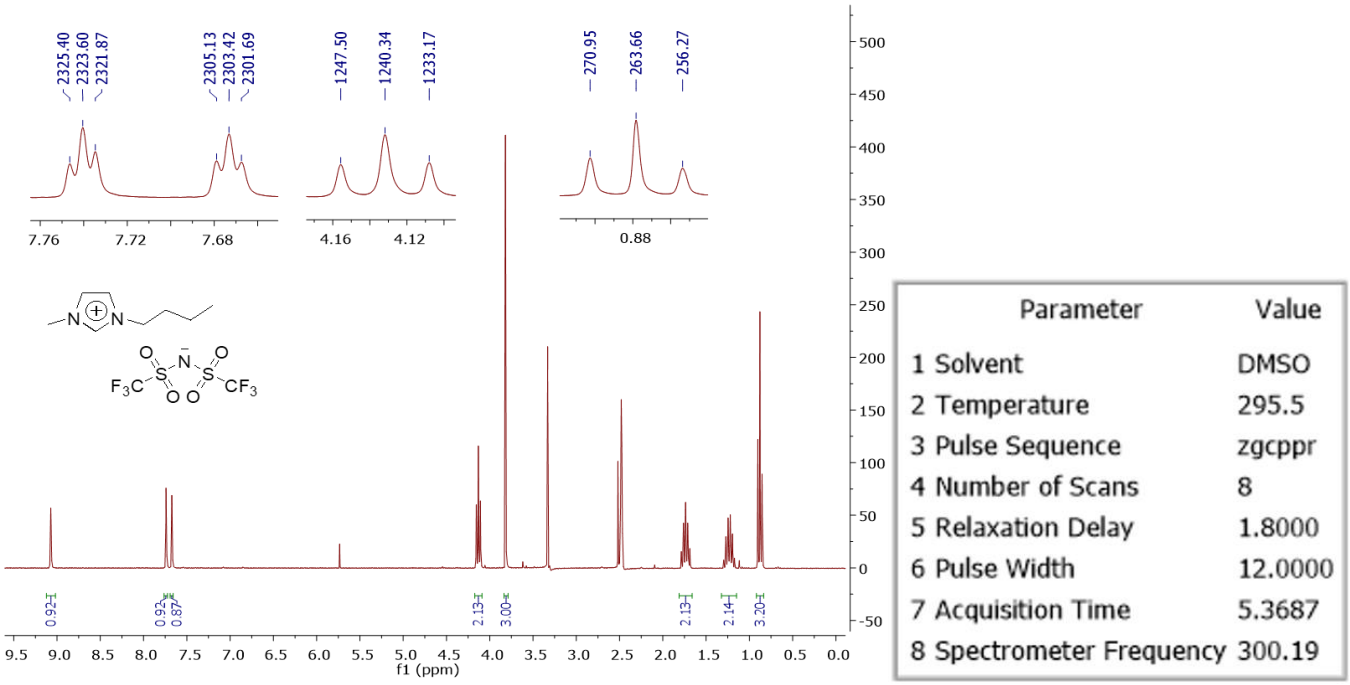
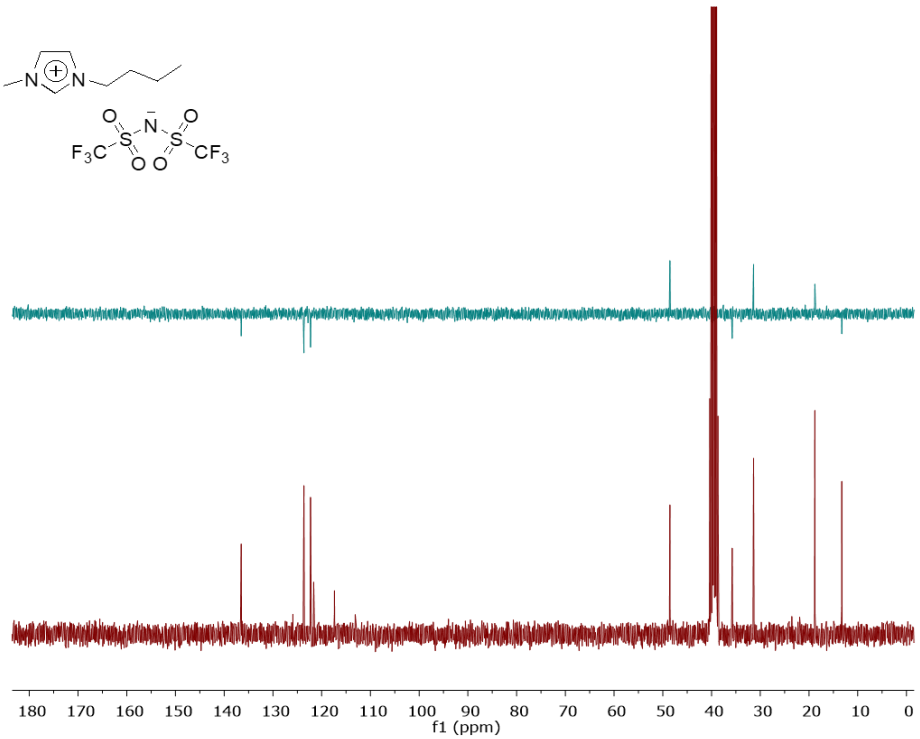


Parameter	Value
1 Solvent	DMSO
2 Temperature	295.5
3 Pulse Sequence	zgcppr
4 Number of Scans	8
5 Relaxation Delay	1.8000
6 Pulse Width	12.0000
7 Acquisition Time	5.3687
8 Spectrometer Frequency	300.19

Figure S70. ^{1}H NMR (300.19 MHz, DMSO-d_6) spectrum of compound **BMIM.NTf$_2$**.



Parameter	Value
1 Solvent	DMSO
2 Temperature	296.6
3 Pulse Sequence	dept135
4 Number of Scans	129
5 Relaxation Delay	1.5000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Parameter	Value
1 Solvent	DMSO
2 Temperature	296.3
3 Pulse Sequence	zgpg30
4 Number of Scans	500
5 Relaxation Delay	2.0000
6 Pulse Width	12.0000
7 Acquisition Time	1.3422
8 Spectrometer Frequency	75.48

Figure S71. ^{13}C NMR (75.48 MHz, DMSO-d_6) spectrum and DEPT-135 experiment of compound **BMIM.NTf$_2$**.

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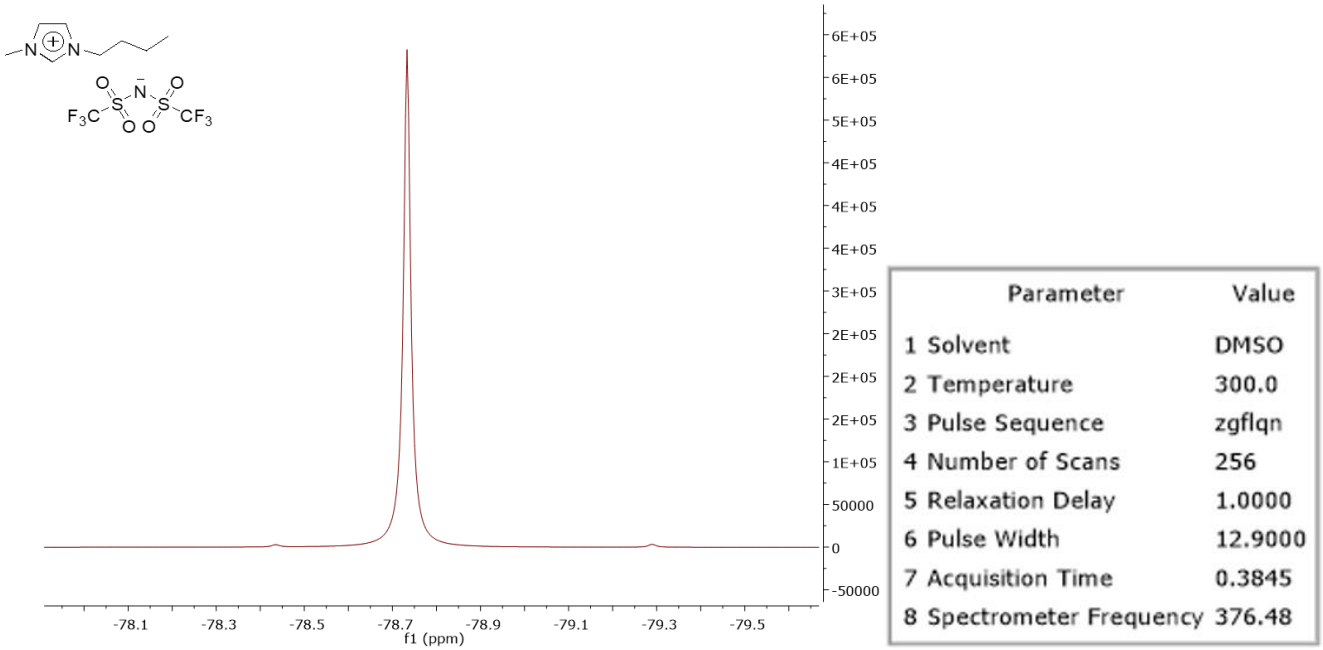

Figure S72. ^{19}F NMR (376.48 MHz, DMSO-d_6) spectrum of compound **BMIM.NTf$_2$**.

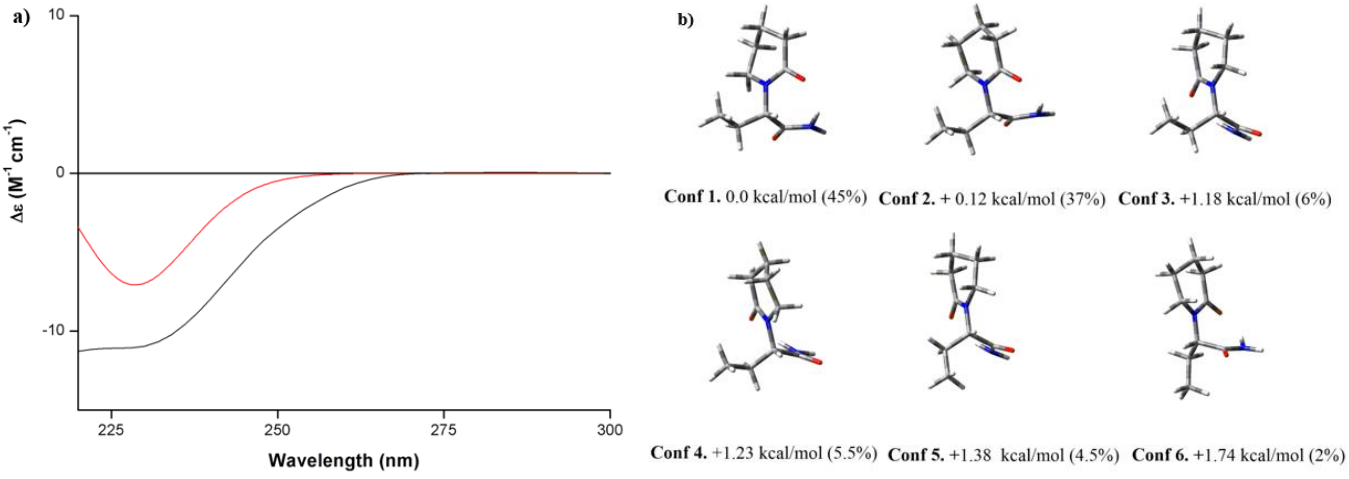

Figure S73. (a) Experimental (black) and calculated (CAM-B3LYP/TZVP, red) ECD spectra of (*S*)-**5b**. **(b)** Optimized structures, relative energies and Boltzmann populations of the lowest-energy conformers identified for (*S*)-**5b** at the B3LYP/6-31G(d)l level.

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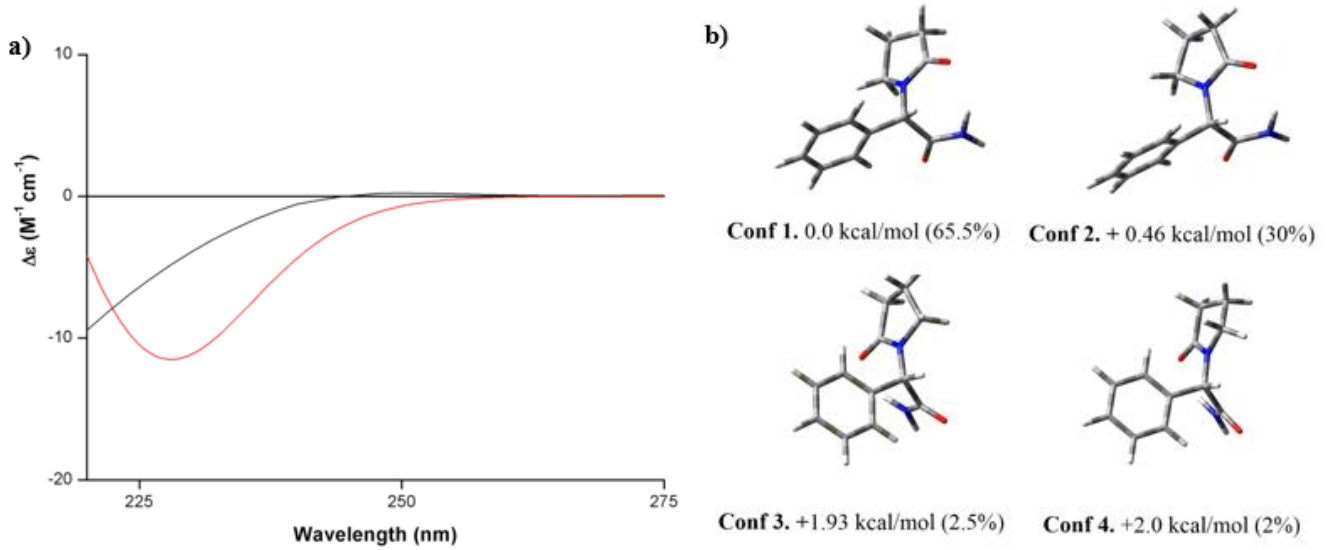

Figure S74. (a) Experimental (black) and calculated (CAM-B3LYP/TZVP, red) ECD spectra of (*S*)-**9a**. **(b)** Optimized structures, relative energies and Boltzmann populations of the lowest-energy conformers identified for (*S*)-**9a** at the B3LYP/6-31G(d)l level.

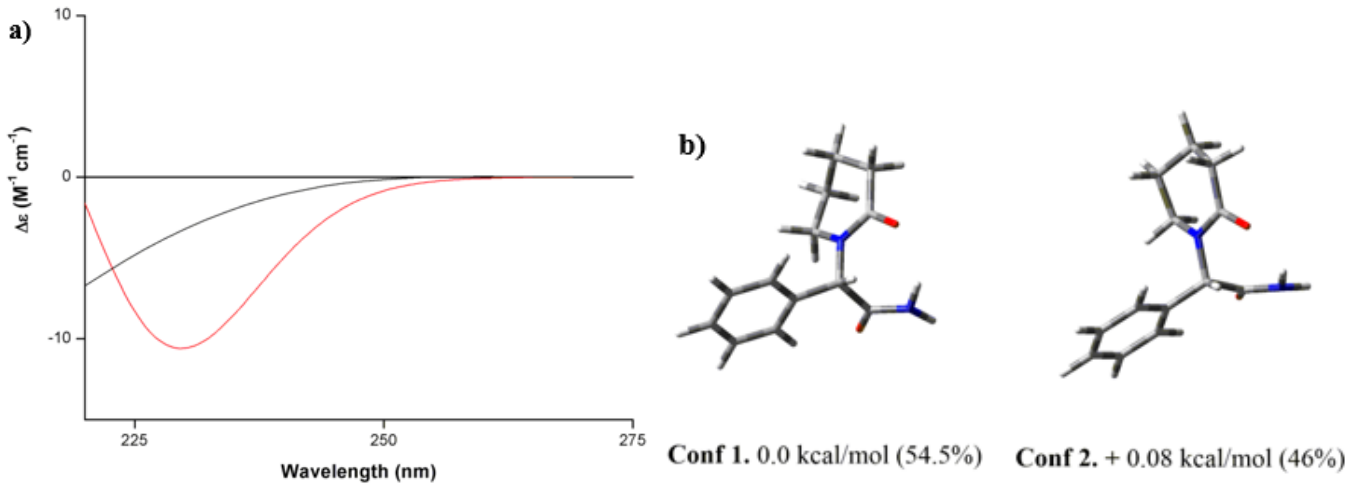

Figure S75. (a) Experimental (black) and calculated (CAM-B3LYP/TZVP, red) ECD spectra of (*S*)-**9b**. **(b)** Optimized structures, relative energies and Boltzmann populations of the lowest-energy conformers identified for (*S*)-**9b** at the B3LYP/6-31G(d)l level.

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