

Cyclobutanone Inhibitors of Diaminopimelate Desuccinylase (DapE) as Potential Antibiotics

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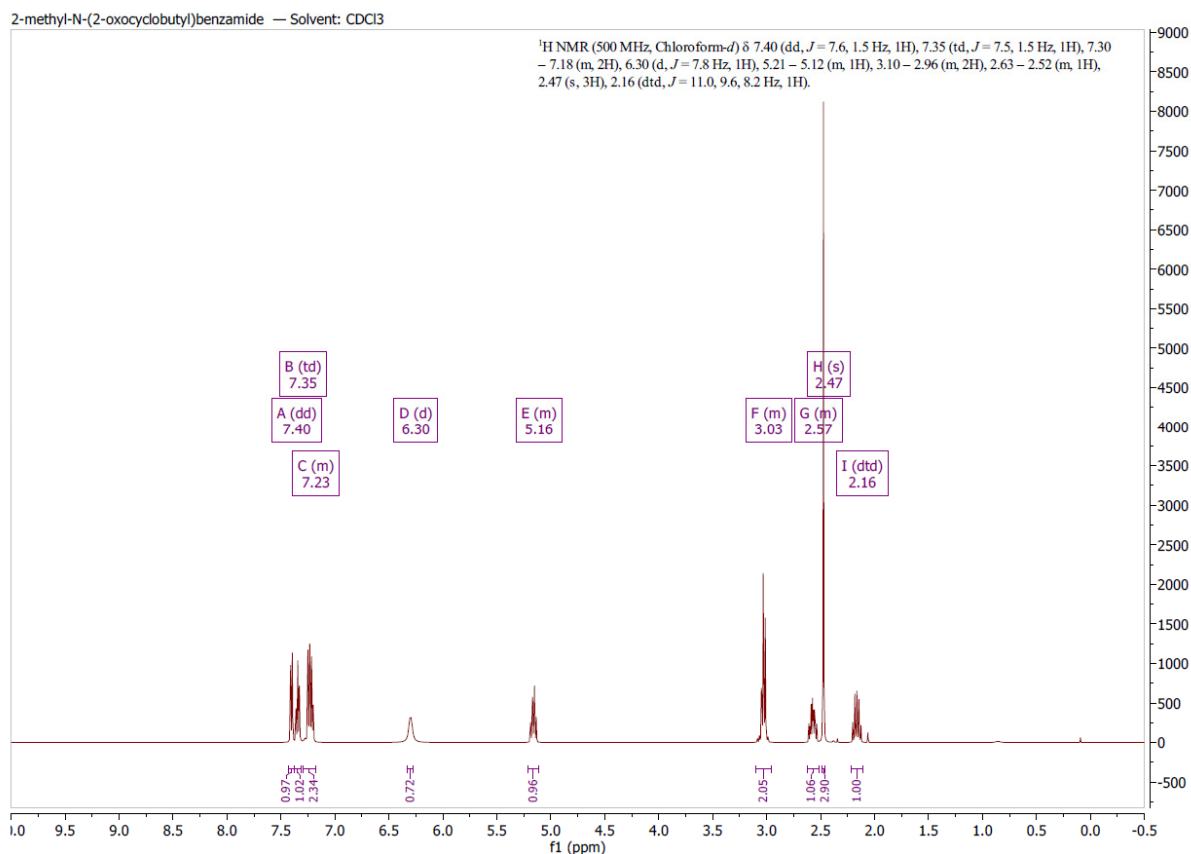
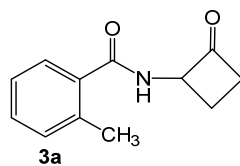


Figure S1. ¹H NMR (500 MHz CDCl₃) of 2-methyl-N-(2-oxocyclobutyl)benzamide (**3a**).

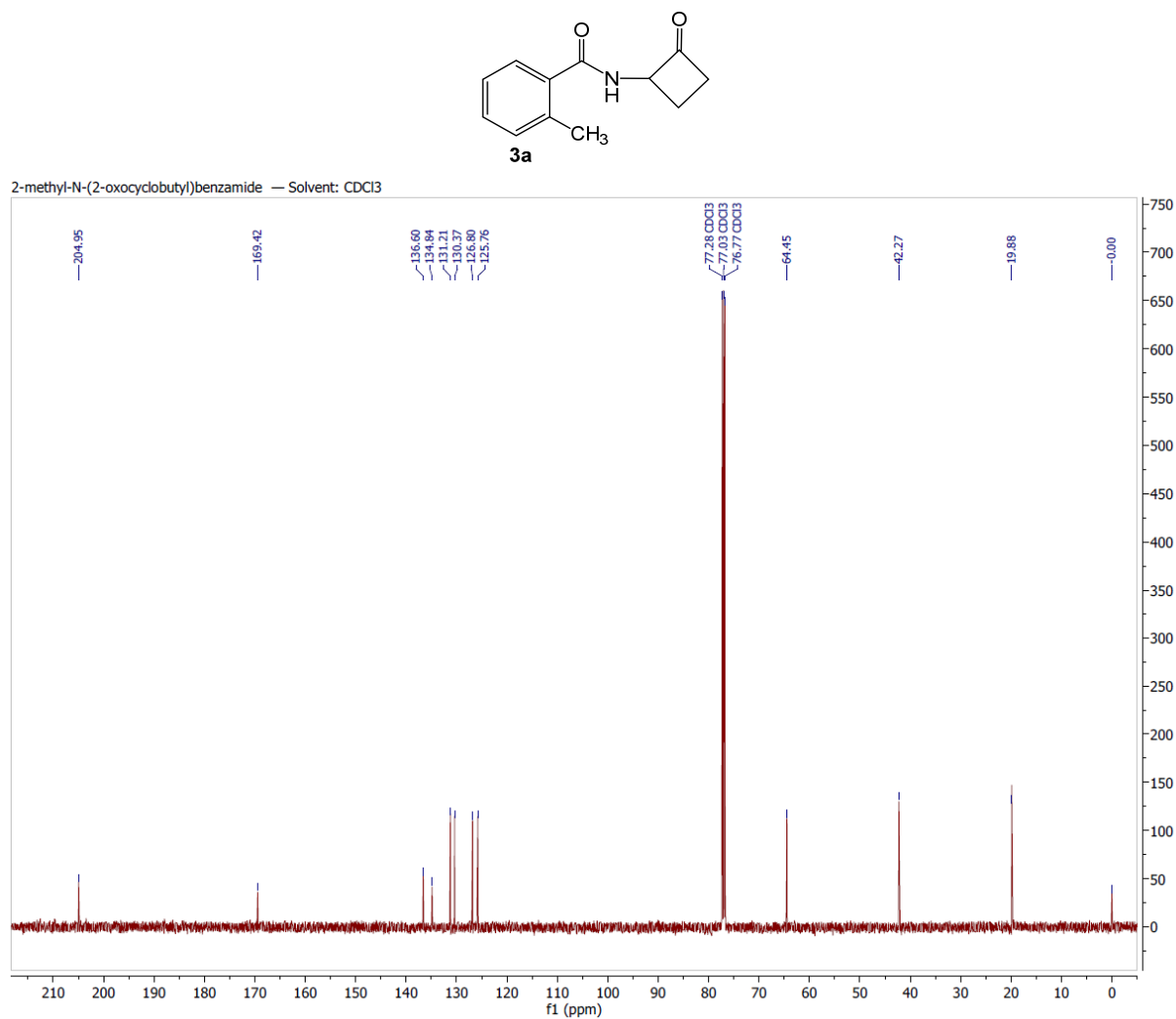


Figure S2. ¹³C NMR (126 MHz, CDCl₃) of 2-methyl-N-(2-oxocyclobutyl)benzamide (**3a**).

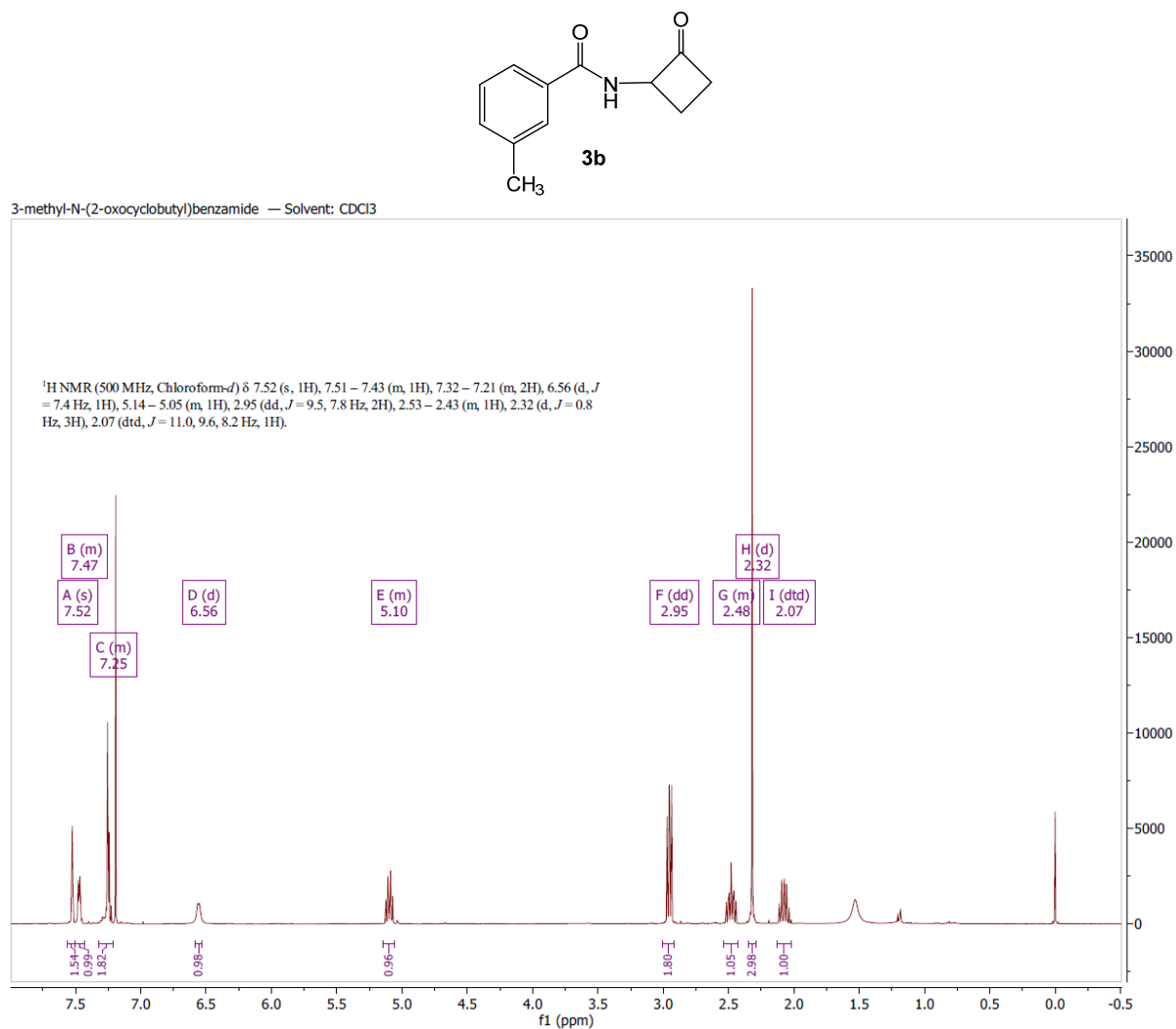


Figure S3. ¹H NMR (500 MHz CDCl₃) of 3-methyl-N-(2-oxocyclobutyl)benzamide (**3b**).

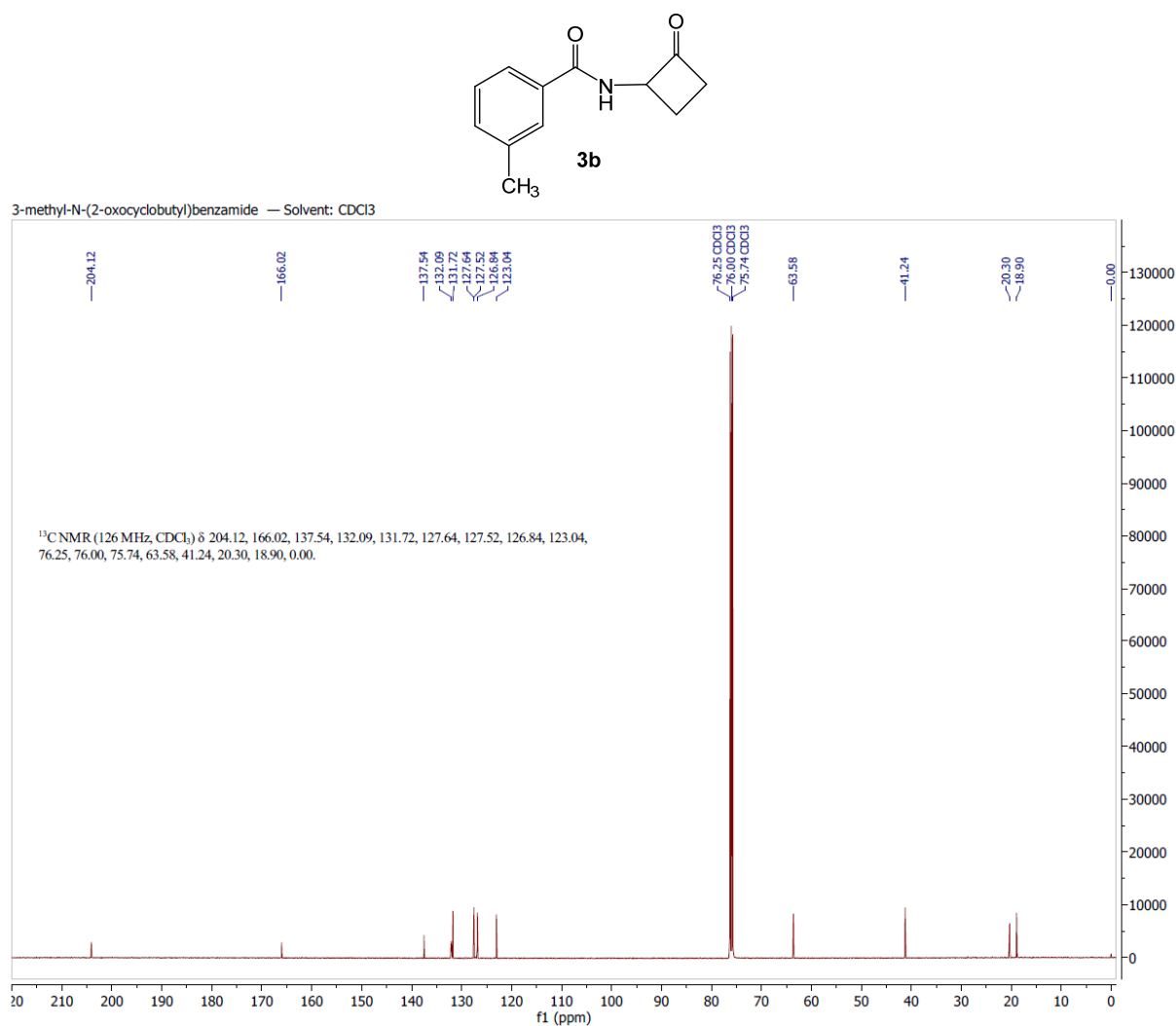


Figure S4. ¹³C NMR (126 MHz, CDCl₃) of 3-methyl-N-(2-oxocyclobutyl)benzamide (**3b**).

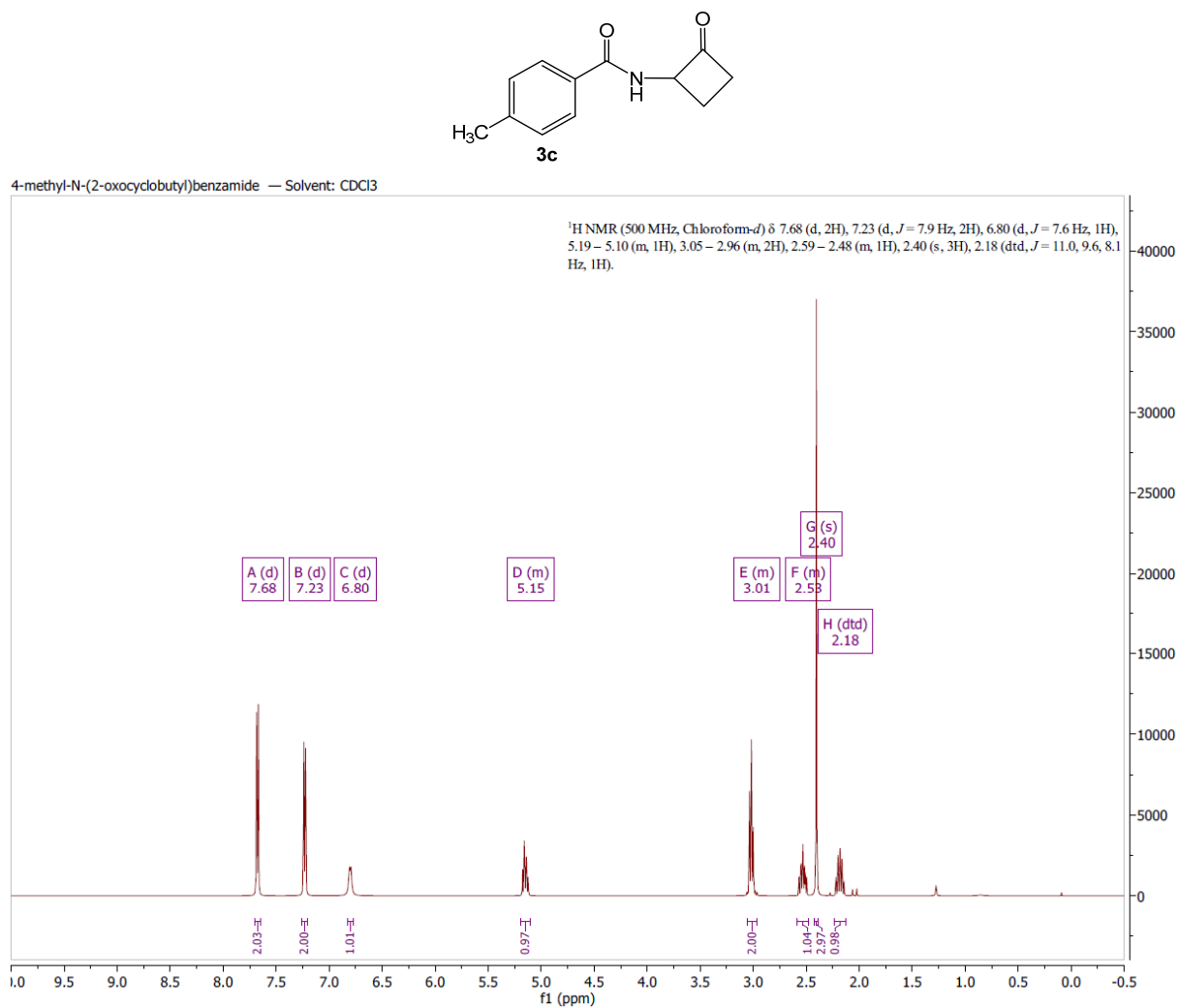


Figure S5. ¹H NMR (500 MHz CDCl₃) of 4-methyl-N-(2-oxocyclobutyl)benzamide (**3c**).

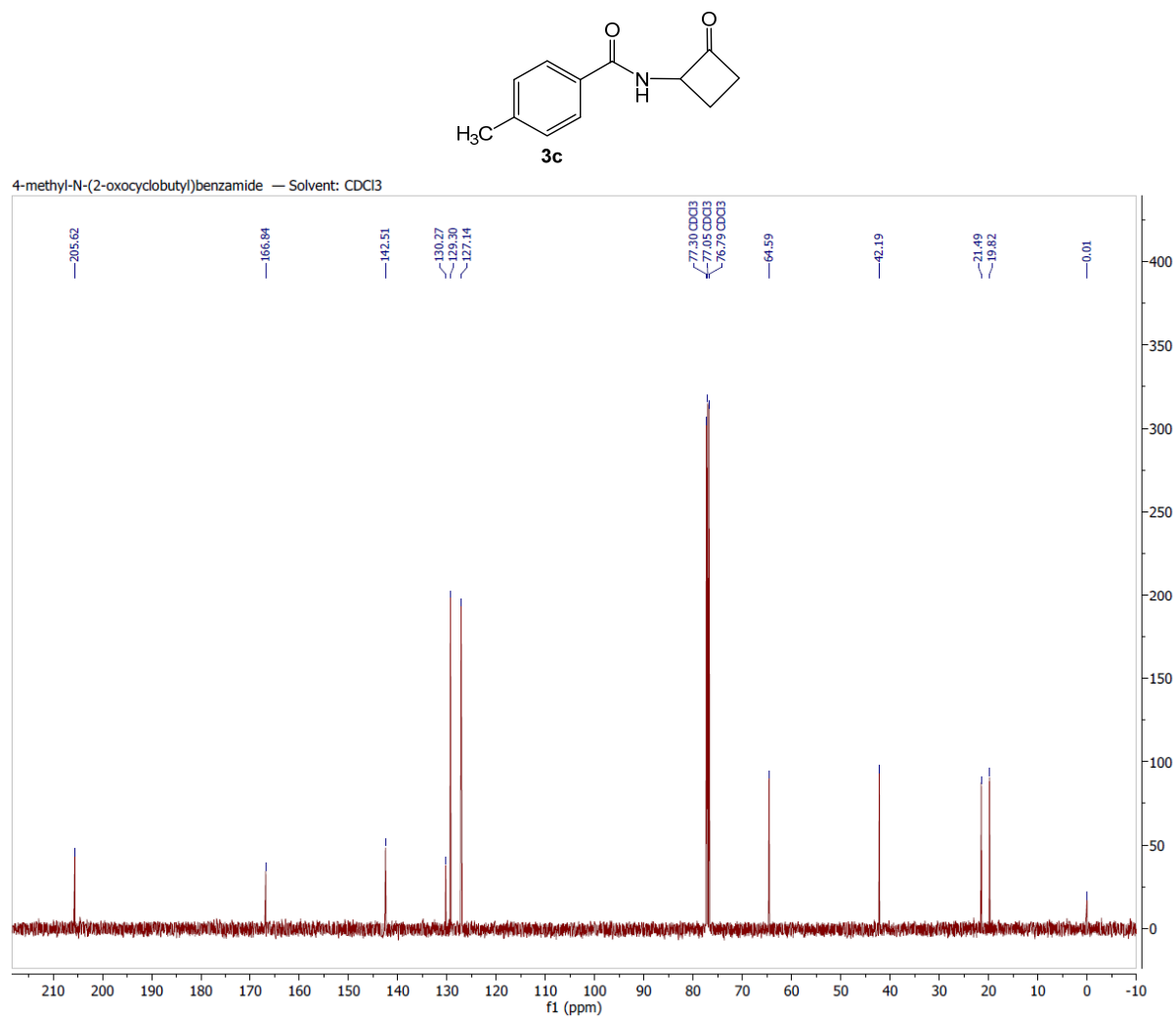


Figure S6. ¹³C NMR (126 MHz, CDCl₃) of 4-methyl-N-(2-oxocyclobutyl)benzamide (**3c**).

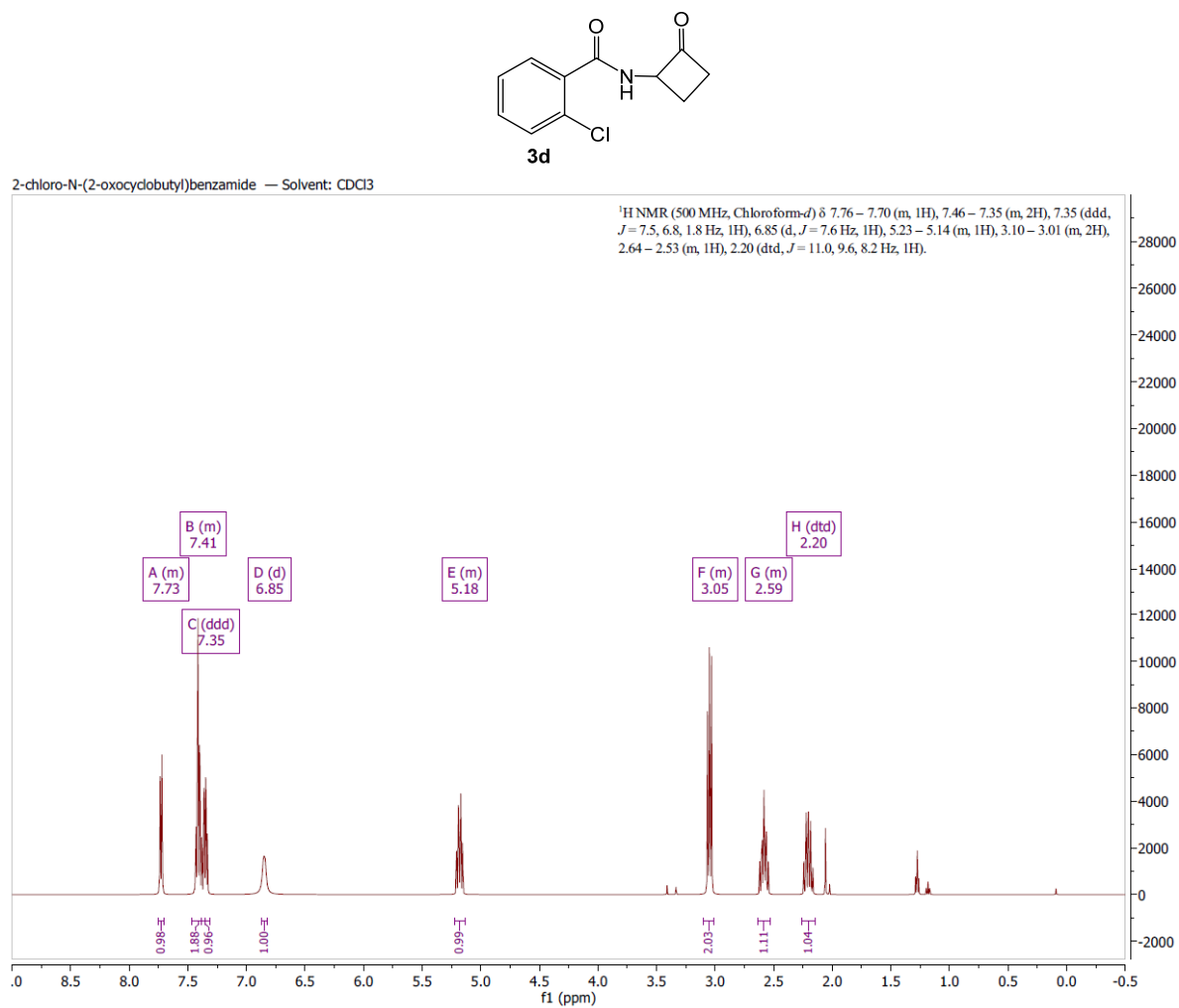


Figure S7. ¹H NMR (500 MHz CDCl₃) of 2-chloro-N-(2-oxocyclobutyl)benzamide (**3d**).

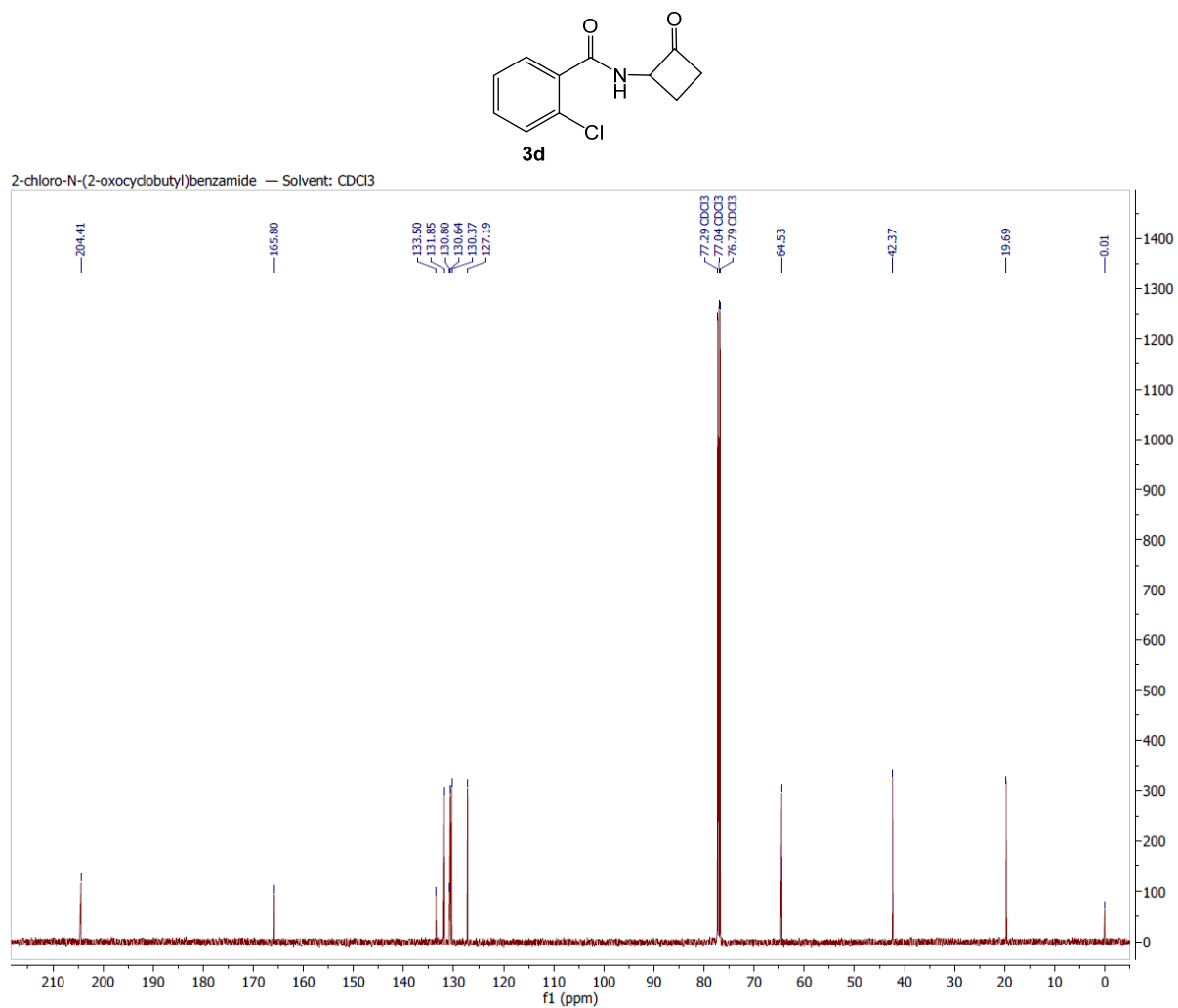


Figure S8. ¹³C NMR (126 MHz, CDCl₃) of 2-chloro-N-(2-oxocyclobutyl)benzamide (**3d**).

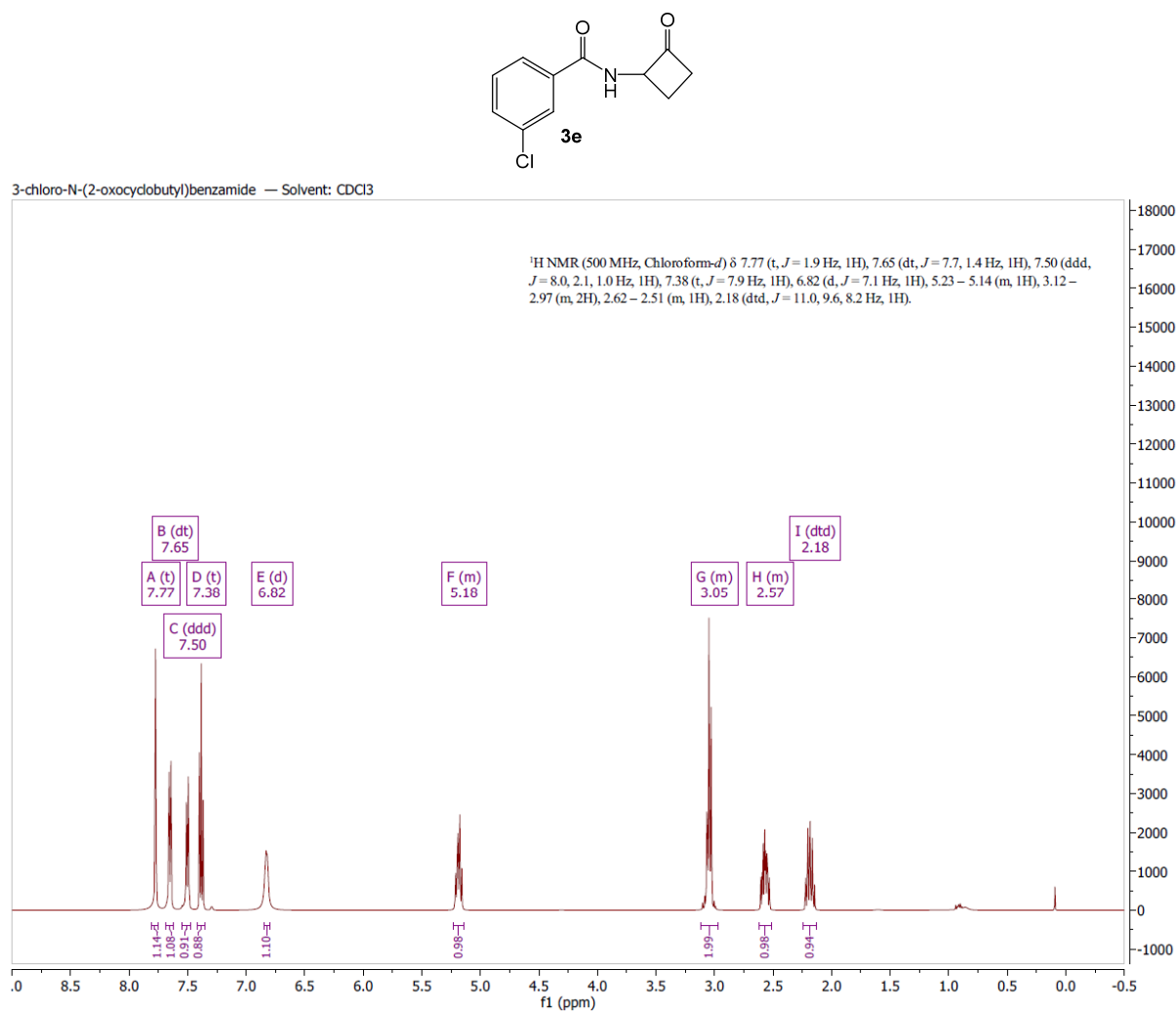


Figure S9. ¹H NMR (500 MHz CDCl₃) of 3-chloro-N-(2-oxocyclobutyl)benzamide (**3e**).

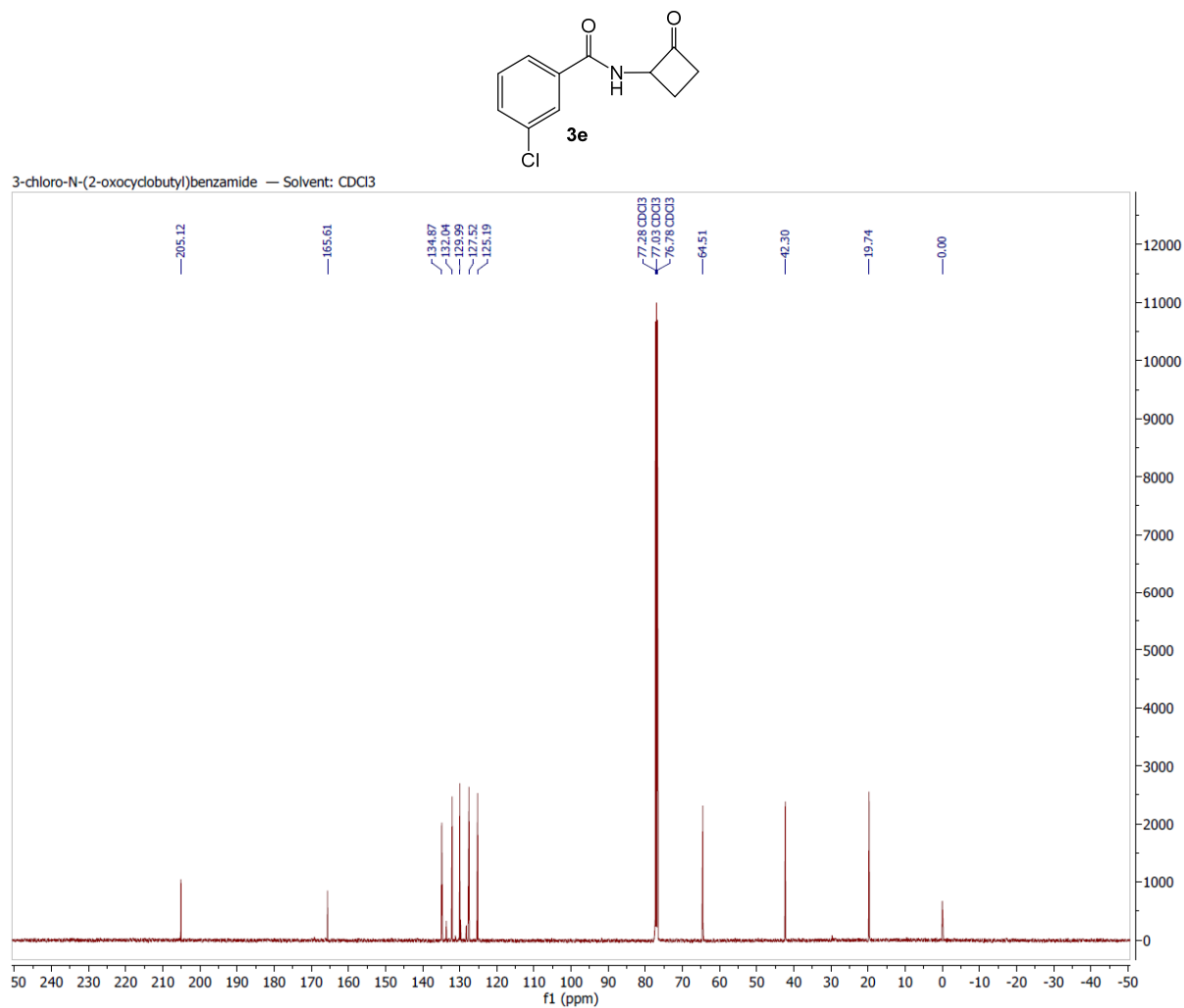


Figure S10. ¹³C NMR (126 MHz, CDCl₃) of 3-chloro-N-(2-oxocyclobutyl)benzamide (**3e**).

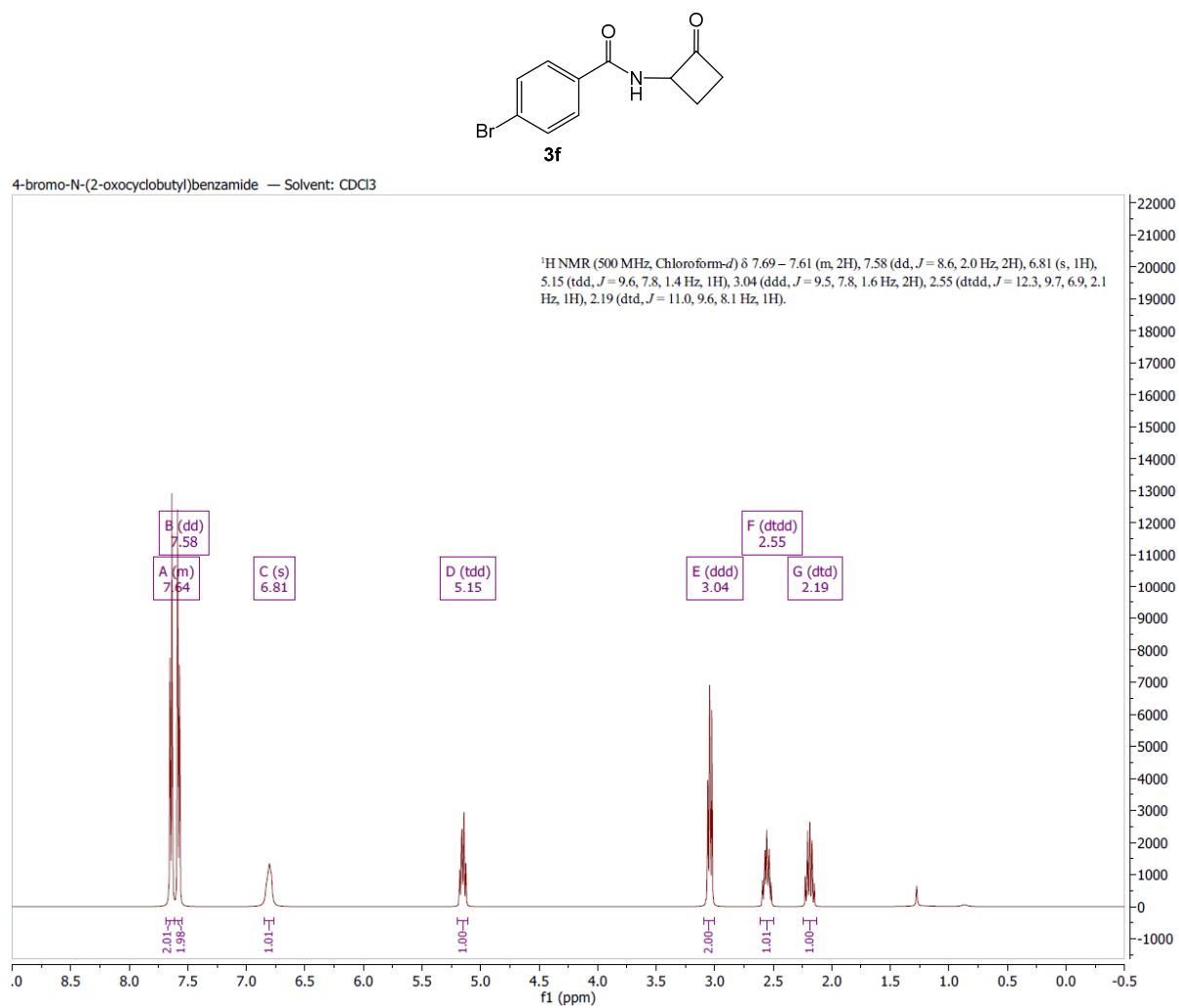


Figure S11. ¹H NMR (500 MHz CDCl₃) of 4-bromo-N-(2-oxocyclobutyl)benzamide (**3f**).

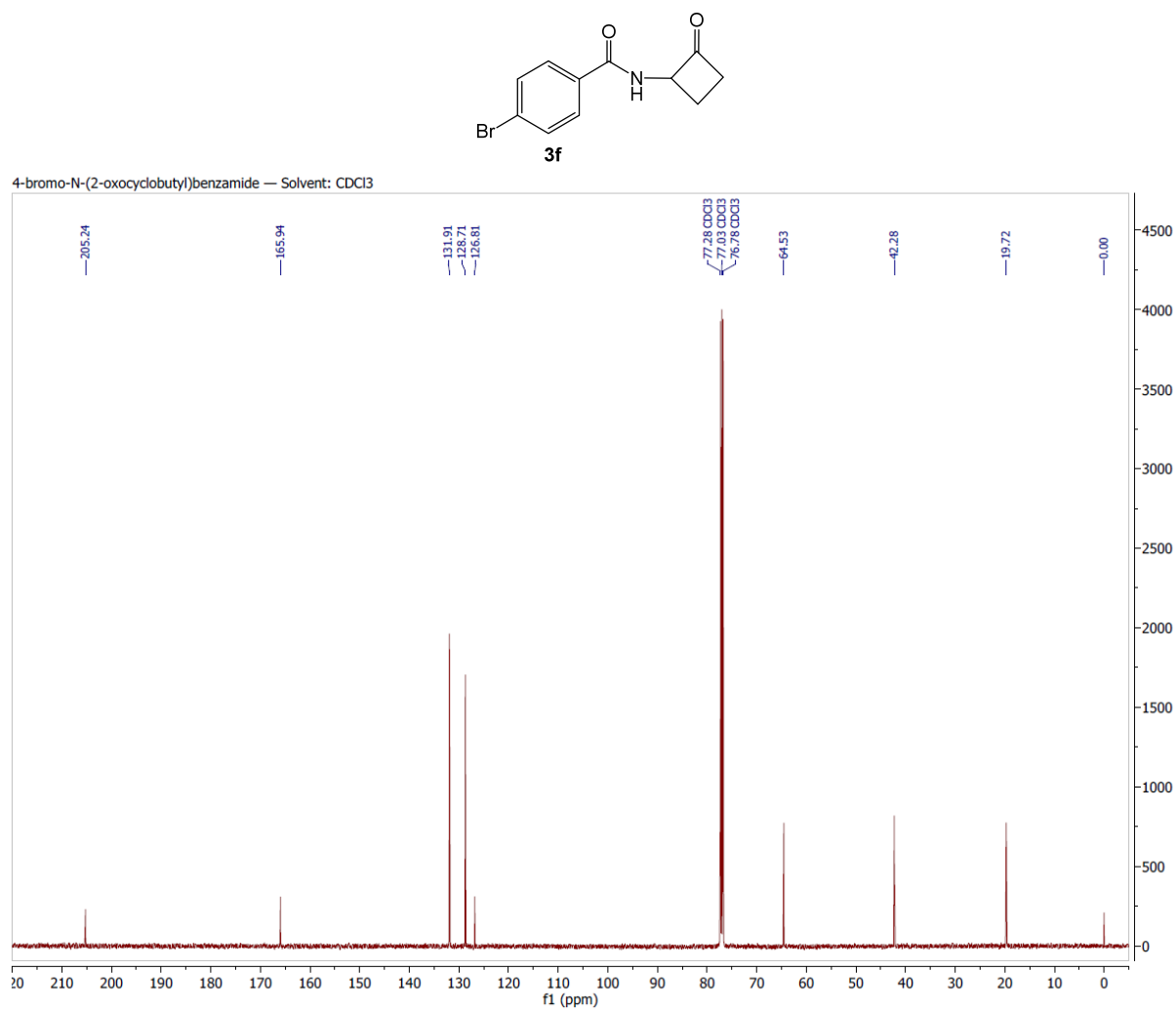


Figure S12. ¹³C NMR (126 MHz, CDCl₃) of 4-bromo-N-(2-oxocyclobutyl)benzamide (**3f**).

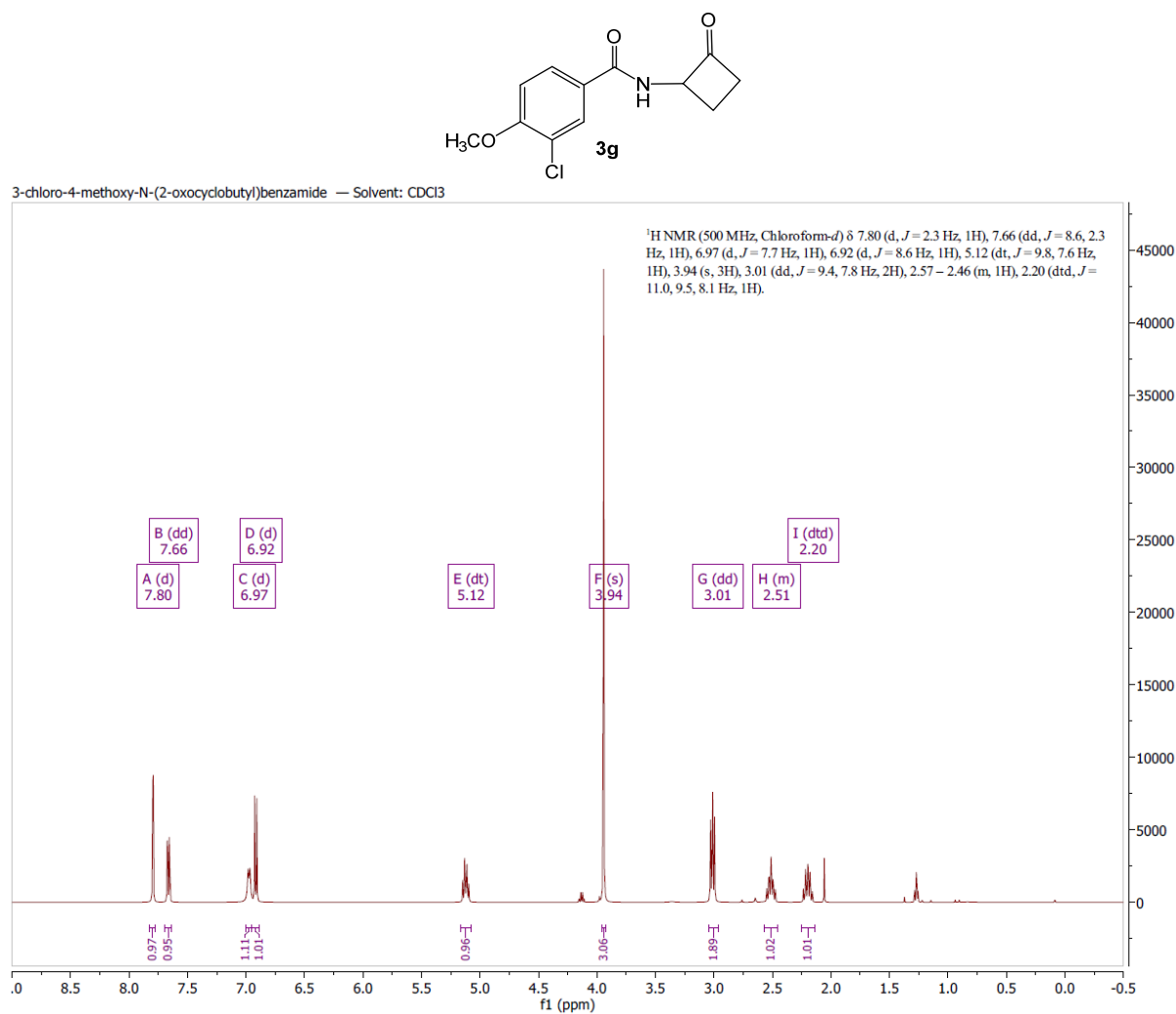


Figure S13. ¹H NMR (500 MHz CDCl₃) of 3-chloro-4-methoxy-N-(2-oxocyclobutyl)benzamide (**3g**).

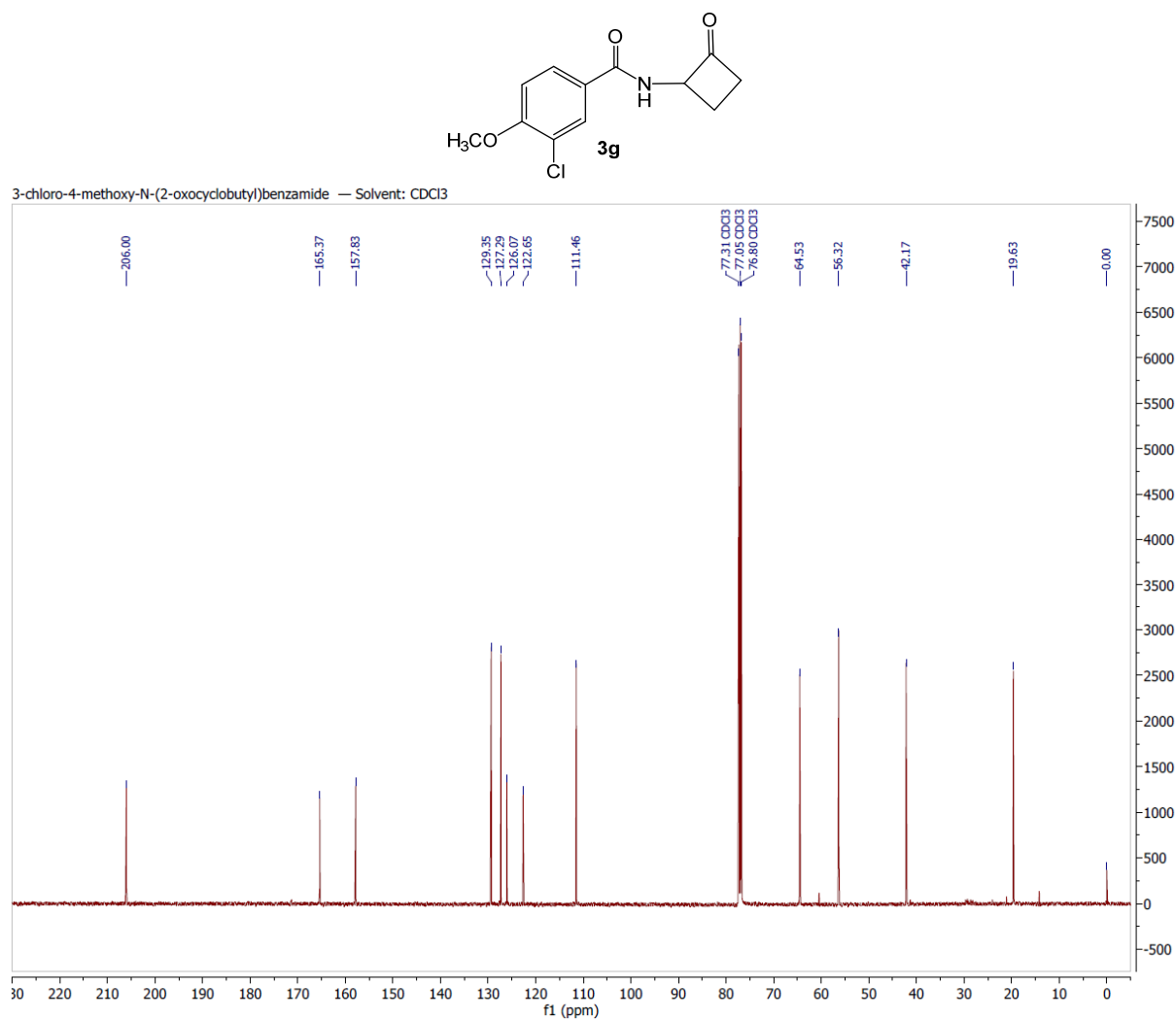


Figure S14. ¹³C NMR (126 MHz, CDCl₃) of 3-chloro-4-methoxy-N-(2-oxocyclobutyl)benzamide (**3g**).

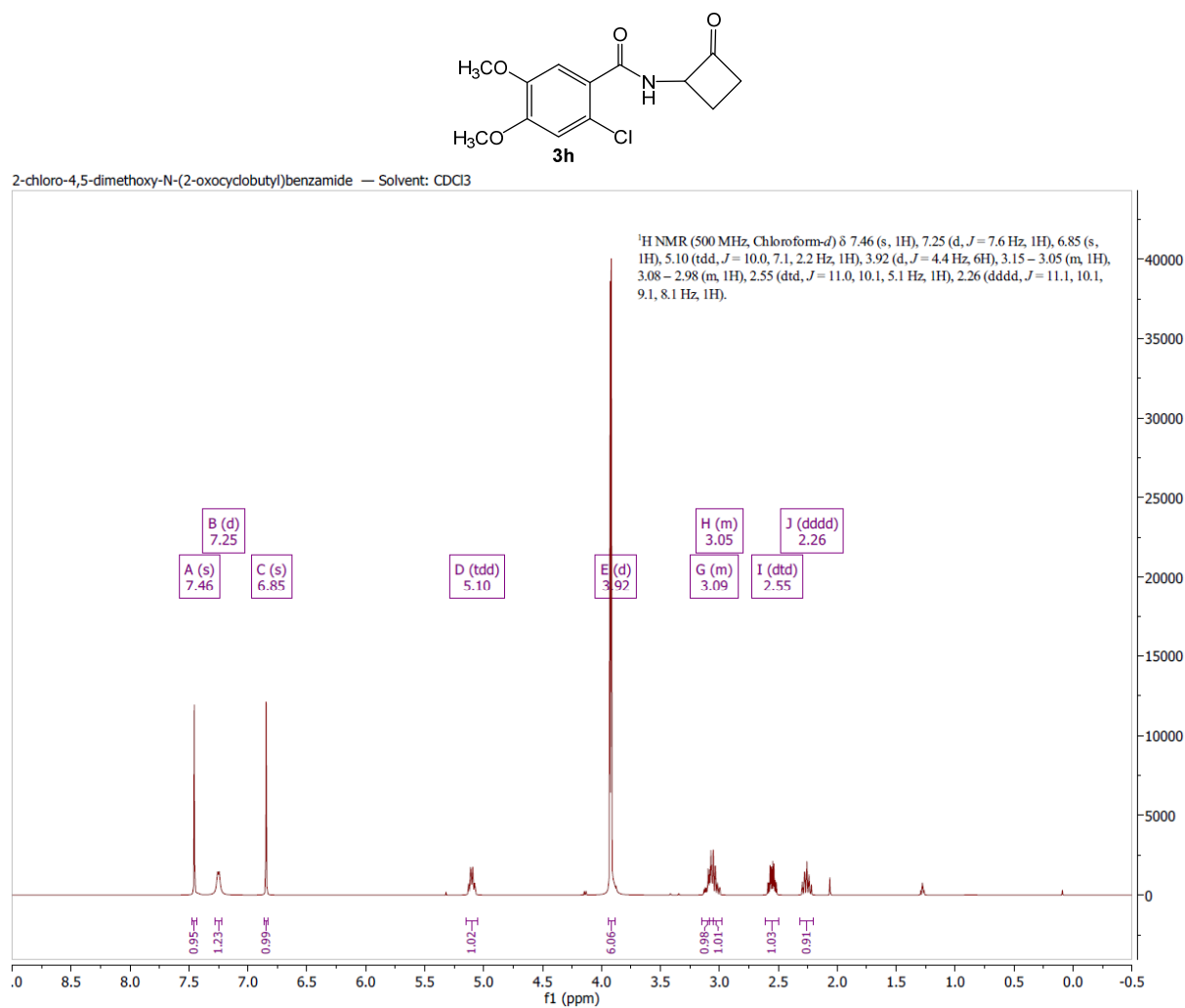


Figure S15. ¹H NMR (500 MHz CDCl₃) of 2-chloro-4,5-dimethoxy-N-(2-oxocyclobutyl)benzamide (**3h**).

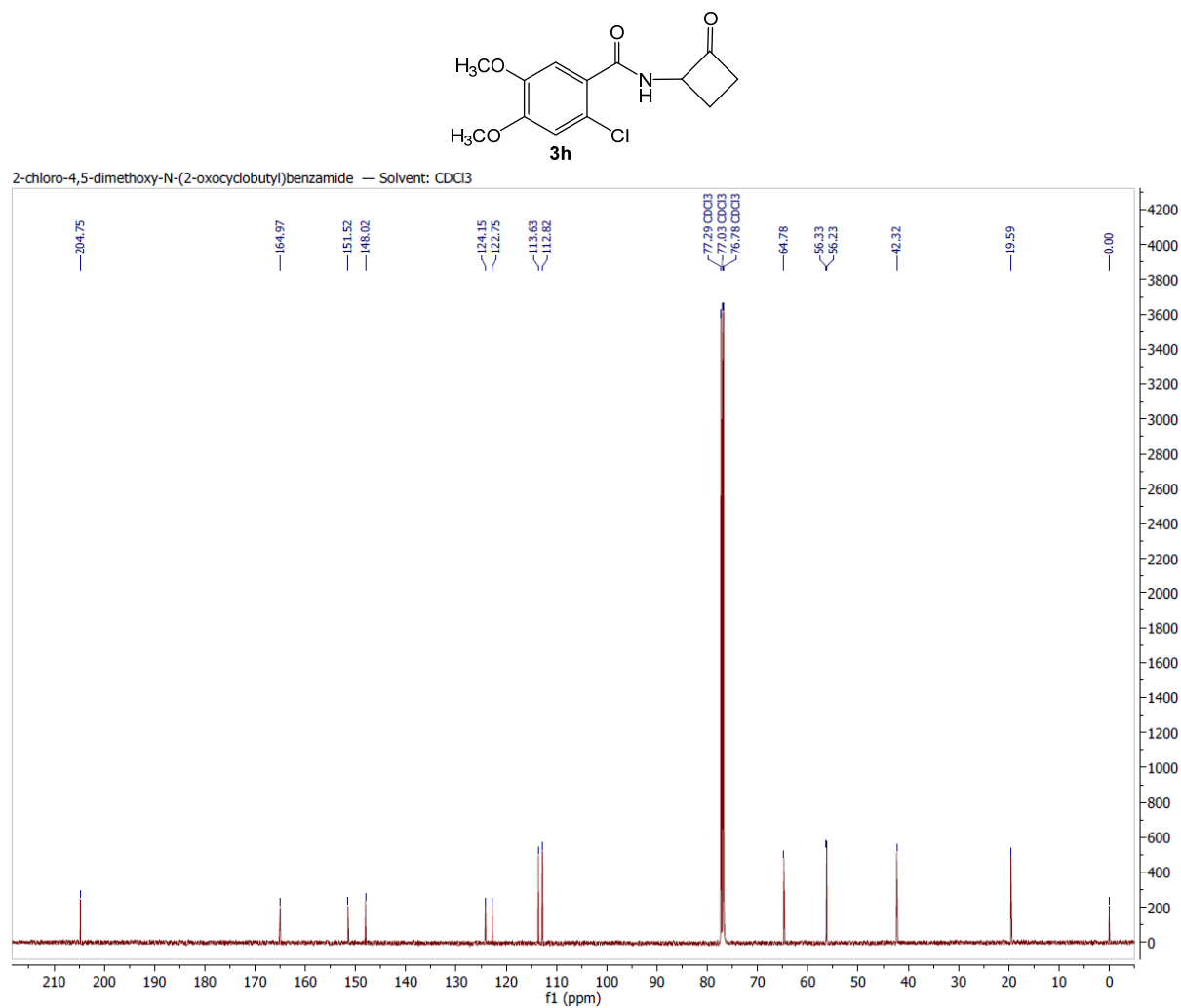


Figure S16. ¹³C NMR (126 MHz, CDCl₃) of 2-chloro-4,5-dimethoxy-N-(2-oxocyclobutyl)benzamide (**3h**).

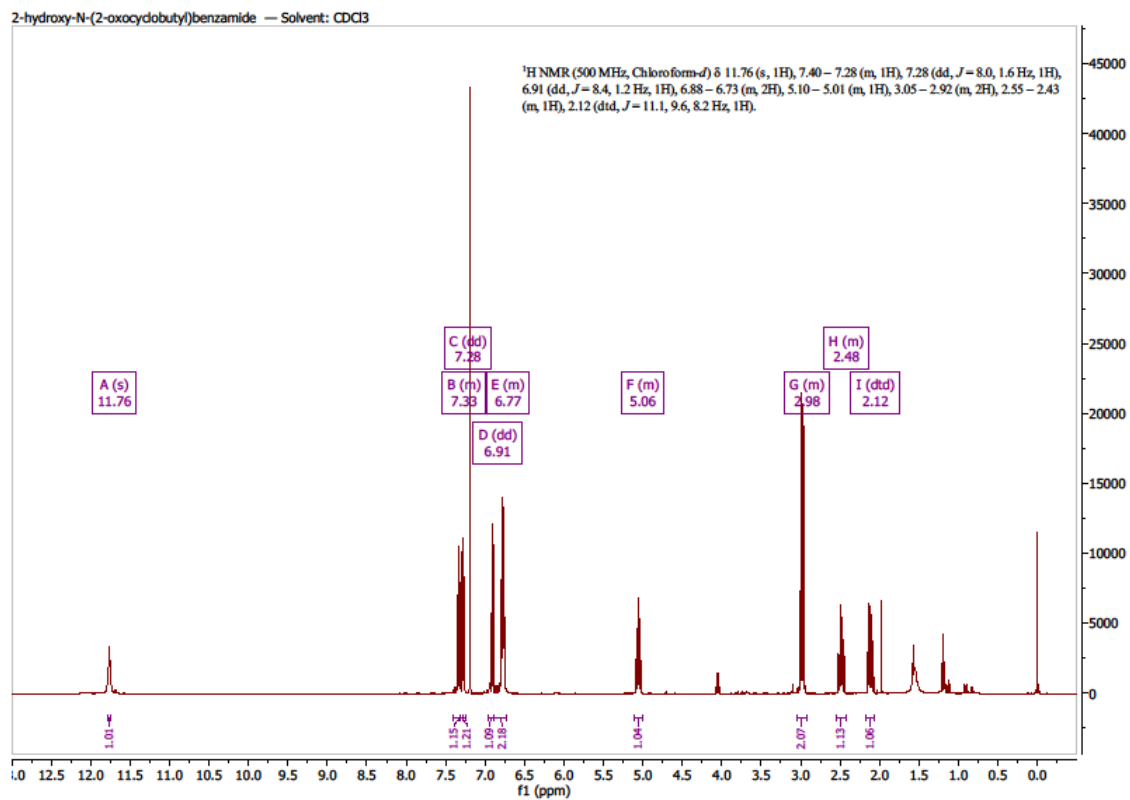
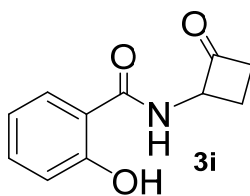


Figure S17. ¹H NMR (500 MHz CDCl₃) of 2-hydroxy-*N*-(2-oxocyclobutyl)benzamide (**3i**)

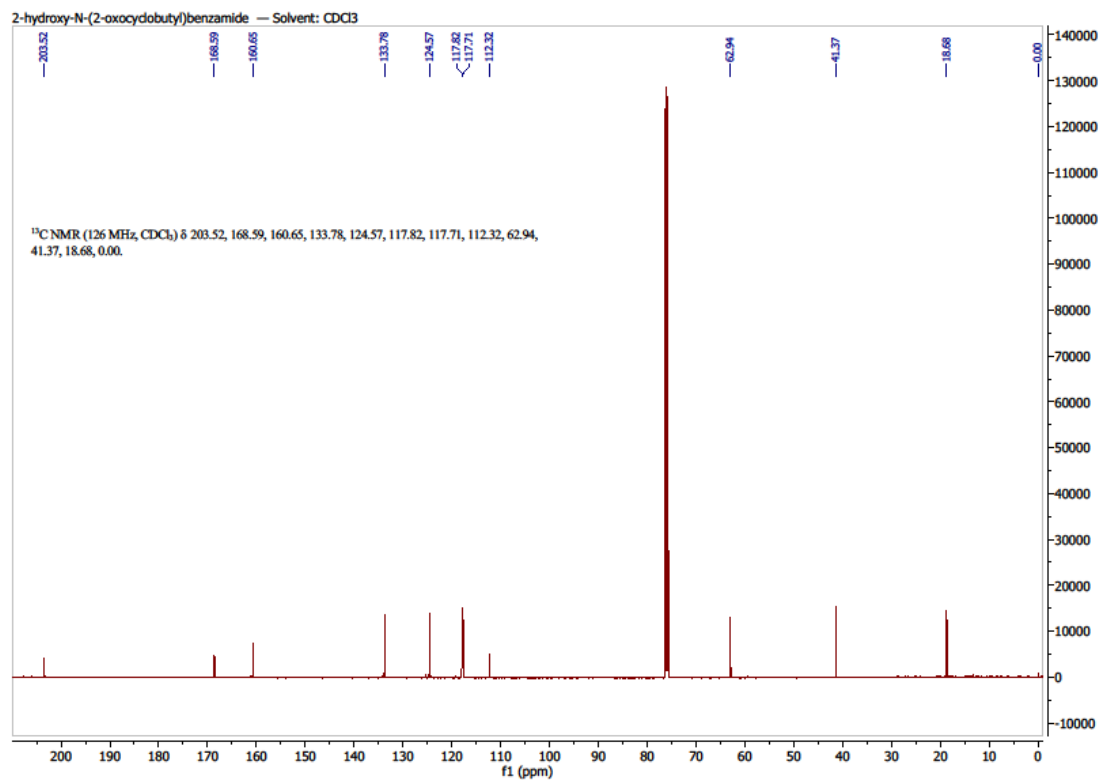
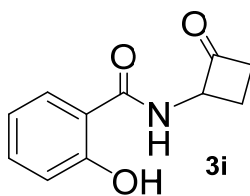


Figure S18. ¹³C NMR (126 MHz, CDCl₃) of 2-hydroxy-*N*-(2-oxocyclobutyl)benzamide (**3i**)

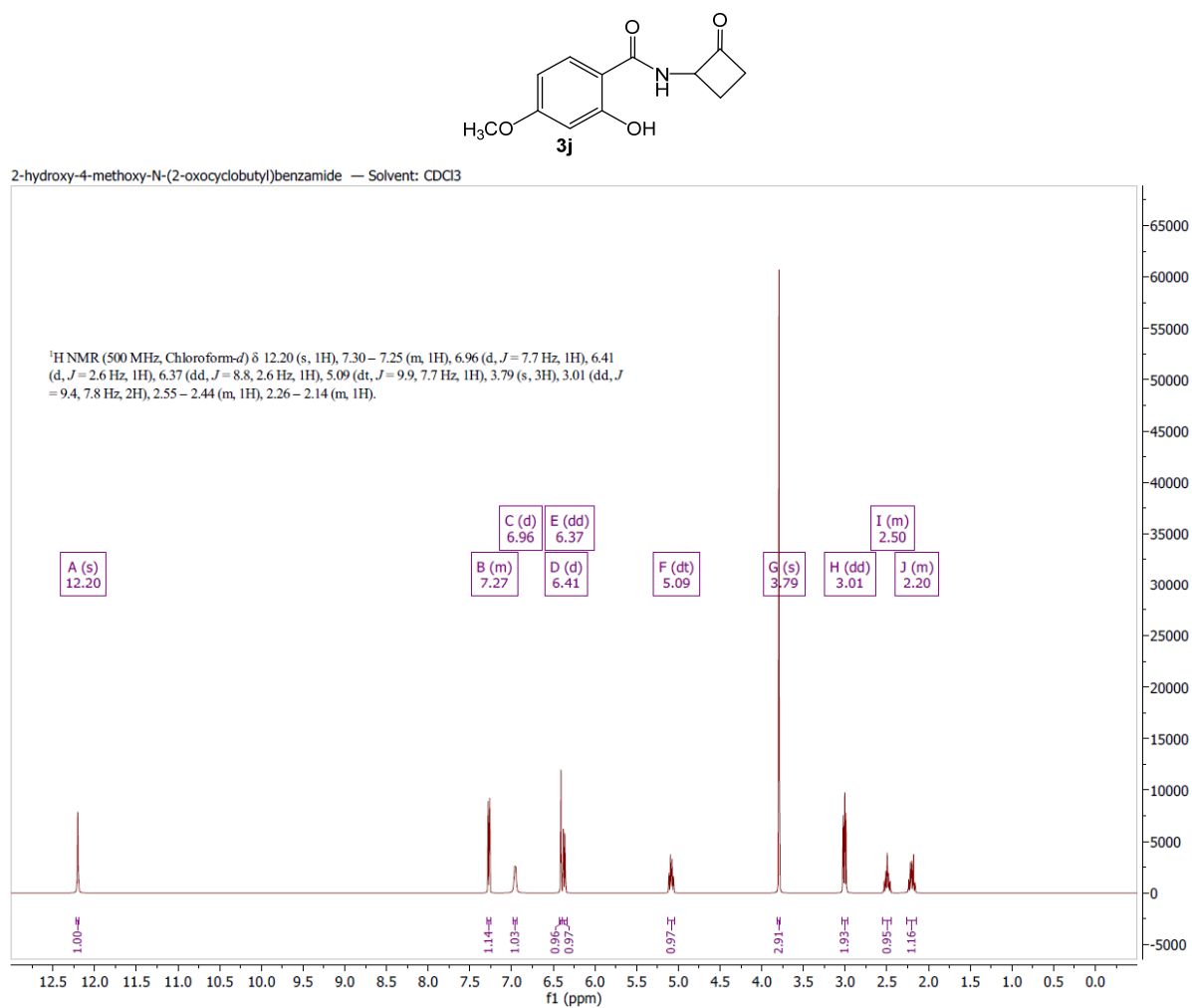


Figure S19. ¹H NMR (500 MHz CDCl₃) of 2-hydroxy-4-methoxy-*N*-(2-oxocyclobutyl)benzamide (**3j**).

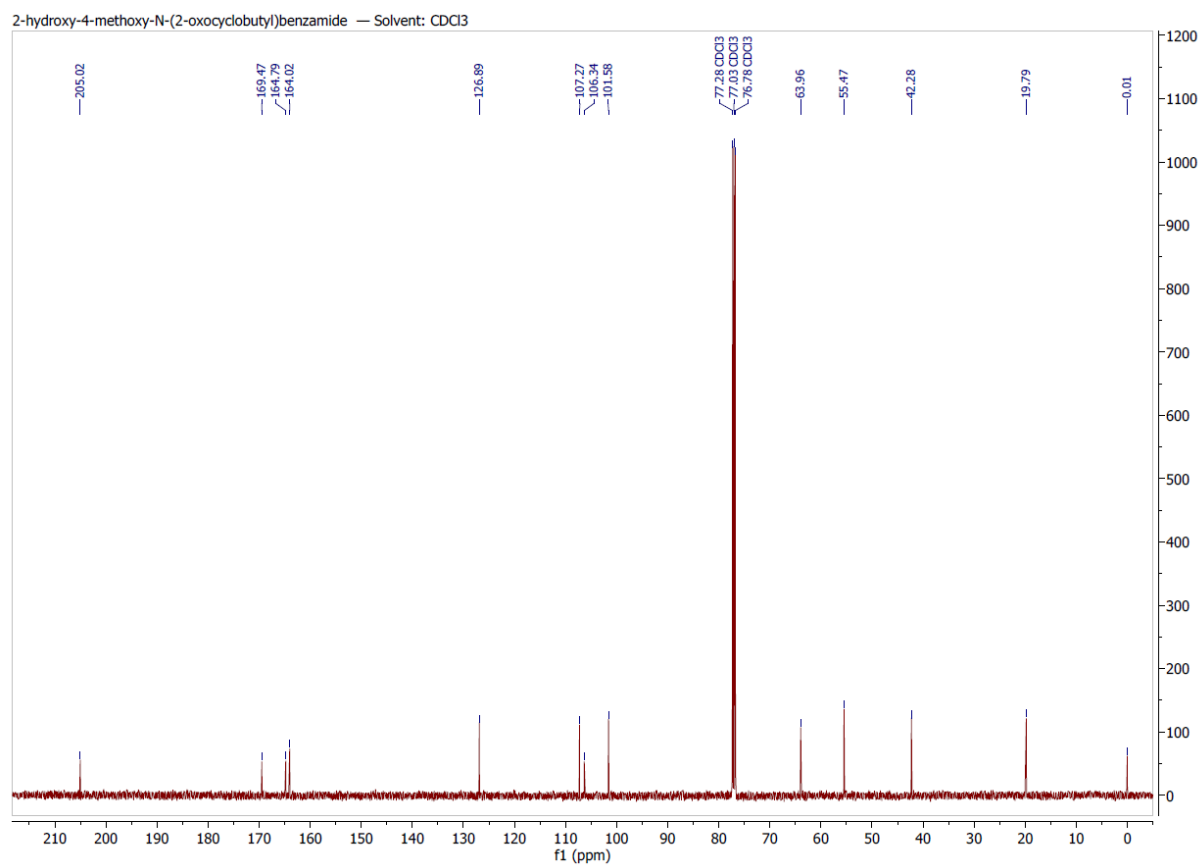
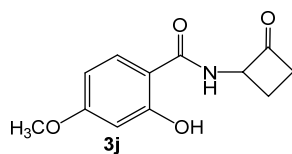


Figure S20. ¹³C NMR (126 MHz, CDCl₃) of 2-hydroxy-4-methoxy-N-(2-oxocyclobutyl)benzamide (**3j**).

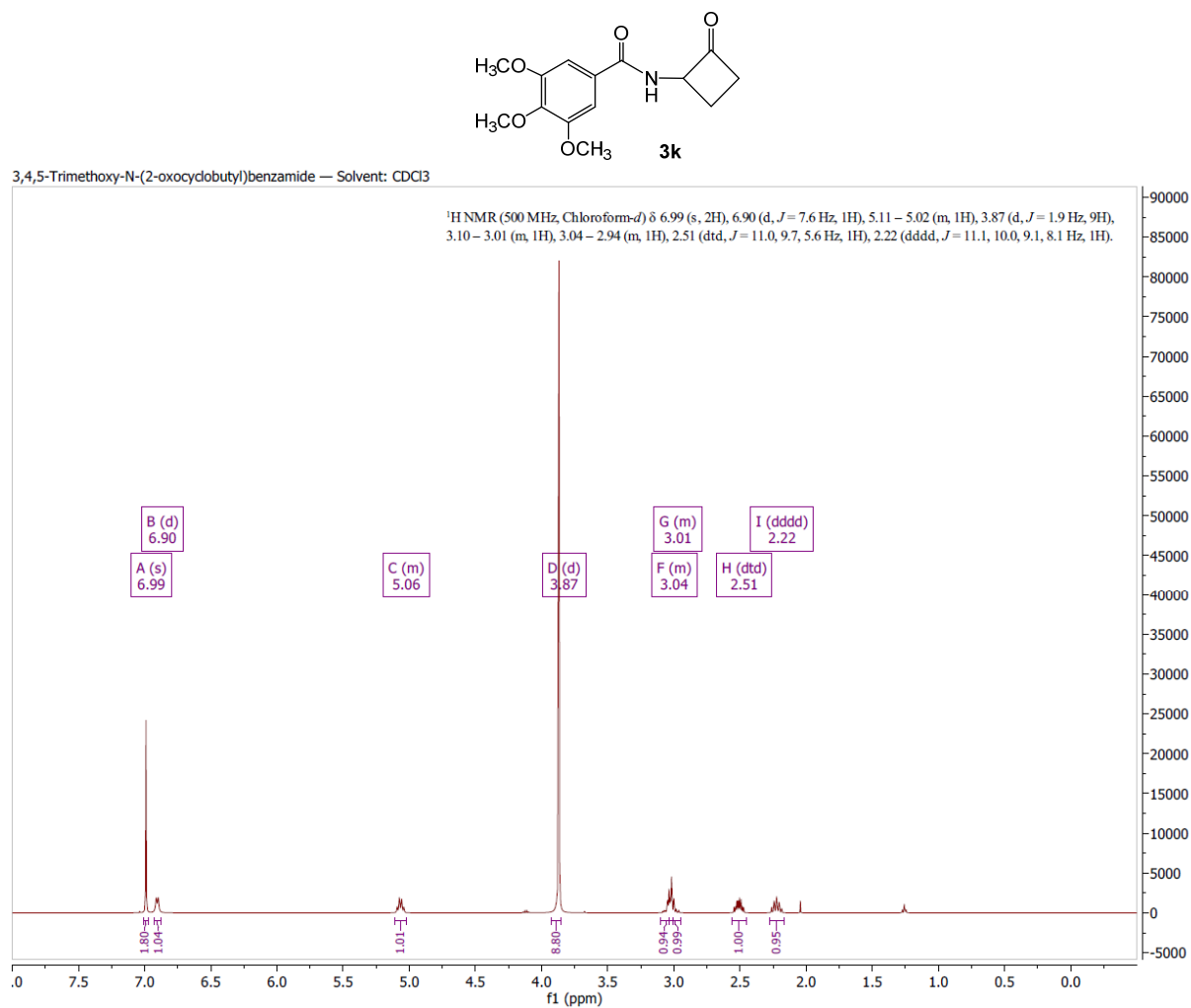
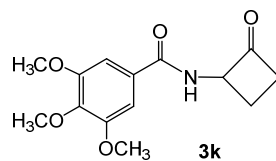
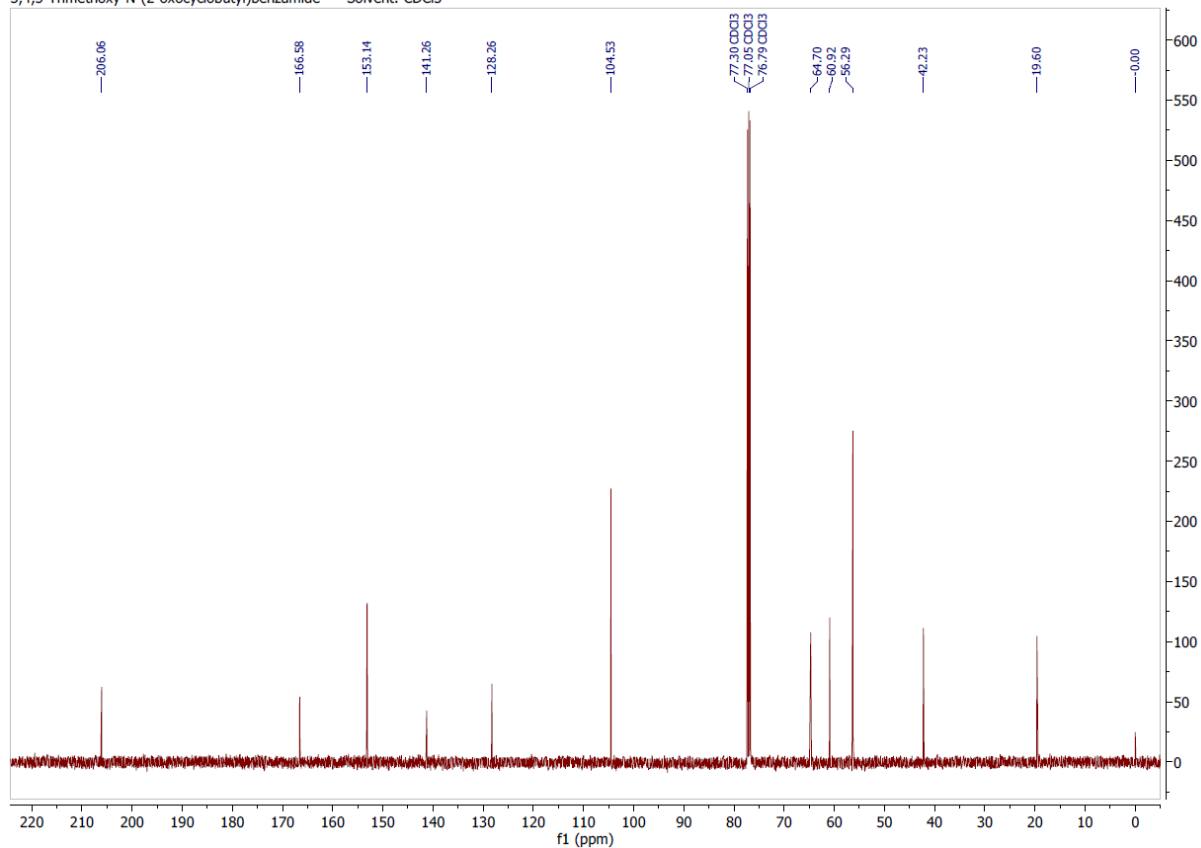
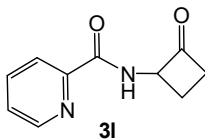
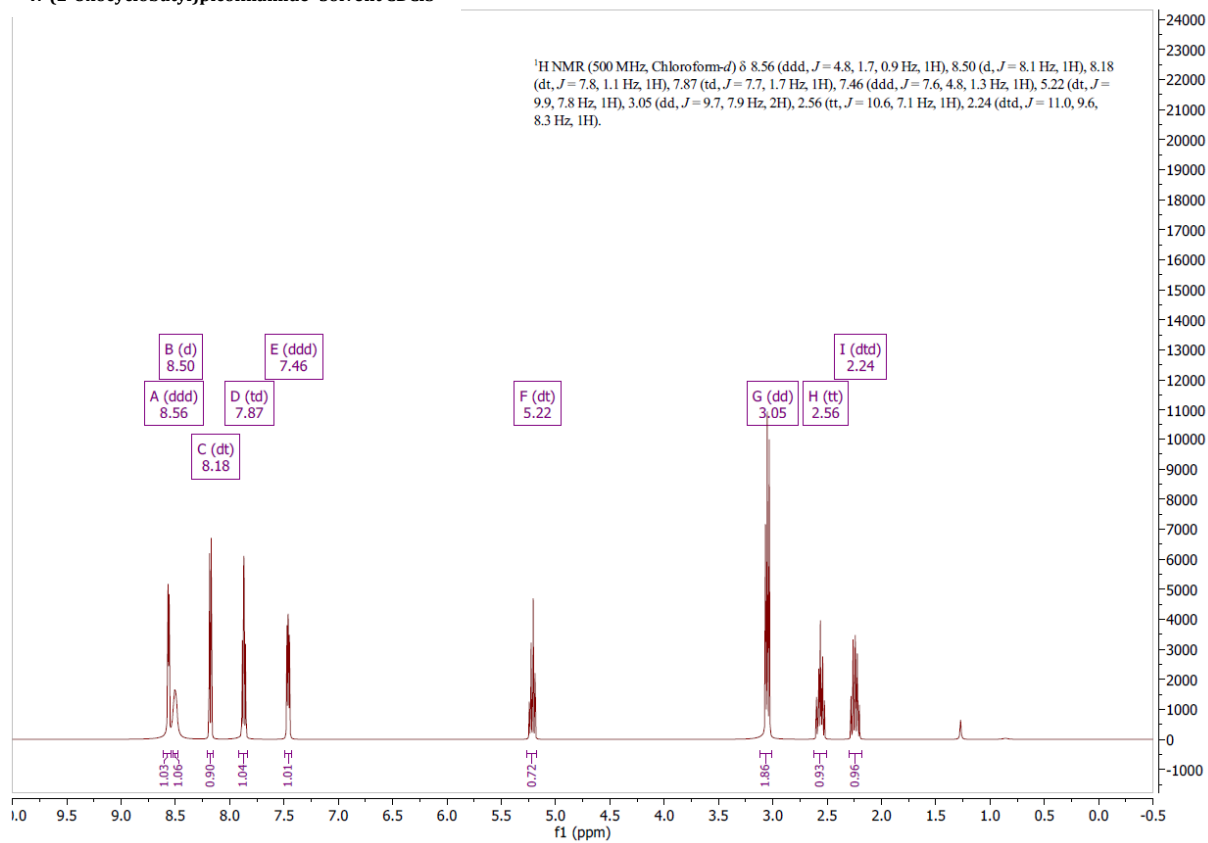


Figure S21. ¹H NMR (500 MHz CDCl₃) of 3,4,5-trimethoxy-N-(2-oxocyclobutyl)benzamide (**3k**).

3,4,5-Trimethoxy-N-(2-oxocyclobutyl)benzamide — Solvent: CDCl₃**Figure S22.** ¹³C NMR (126 MHz, CDCl₃) of 3,4,5-trimethoxy-N-(2-oxocyclobutyl)benzamide (**3k**).

***N*-(2-Oxocyclobutyl)picolinamide -Solvent CDCl₃****Figure S23.** ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)picolinamide (**31**).

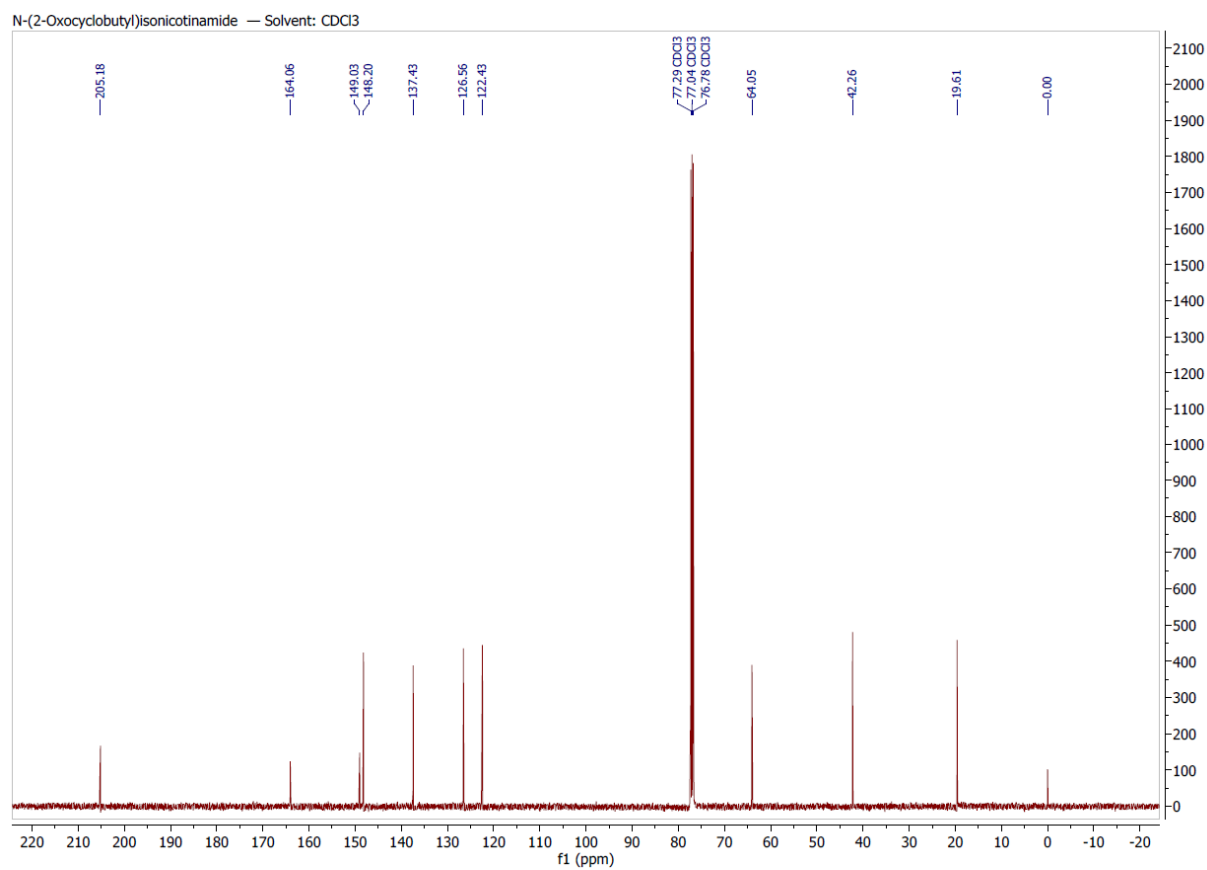
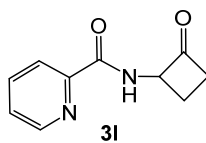
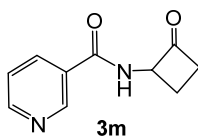
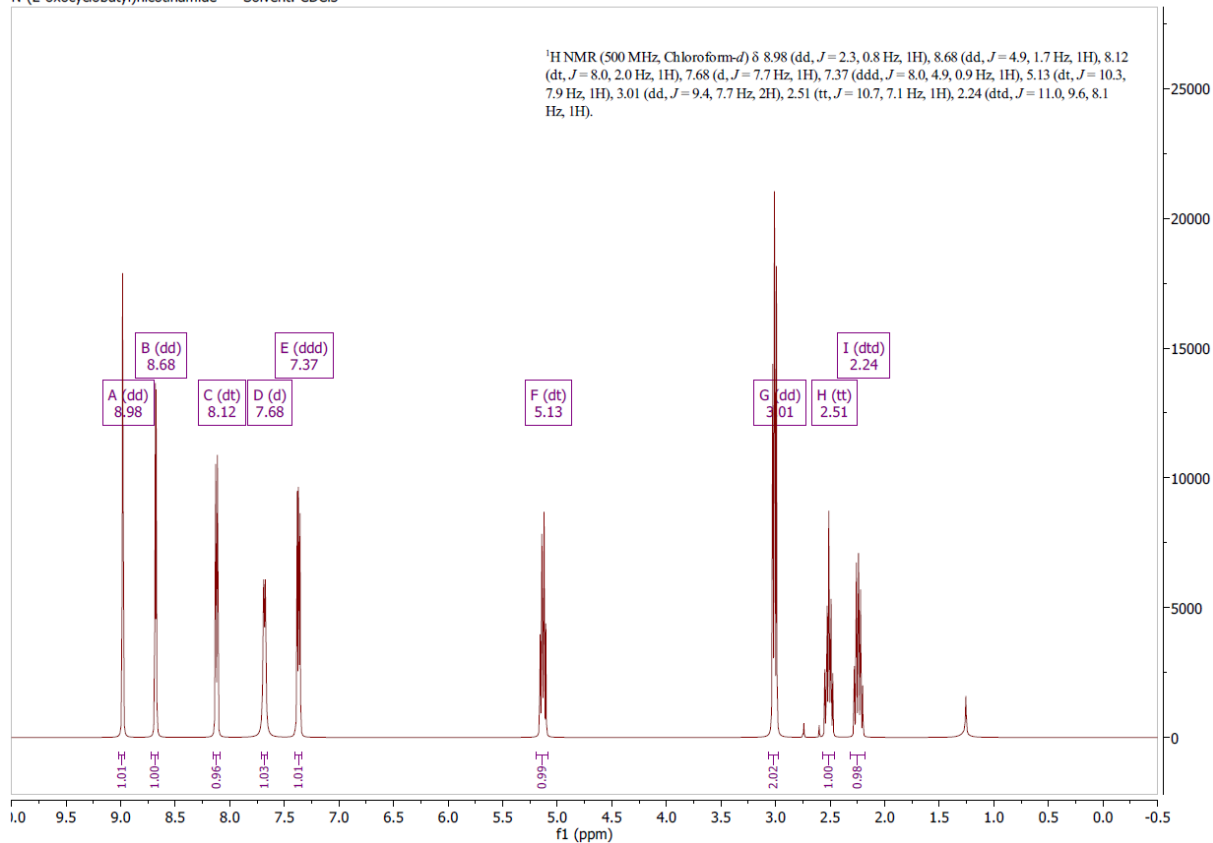


Figure S24. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)picolinamide (**31**).

N-(2-oxocyclobutyl)nicotinamide — Solvent: CDCl₃**Figure S25.** ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)nicotinamide (**3m**).

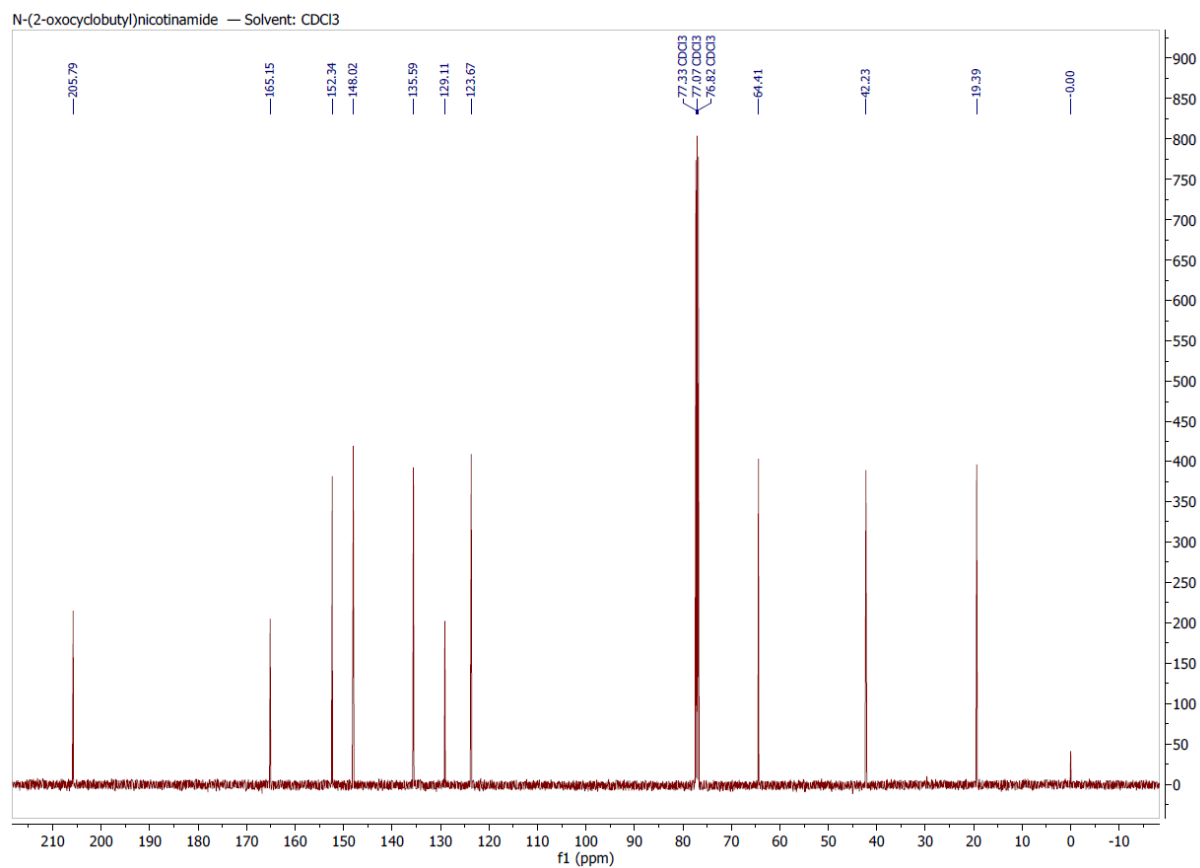
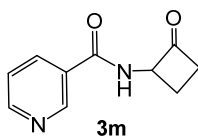


Figure S26. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)nicotinamide (**3m**).

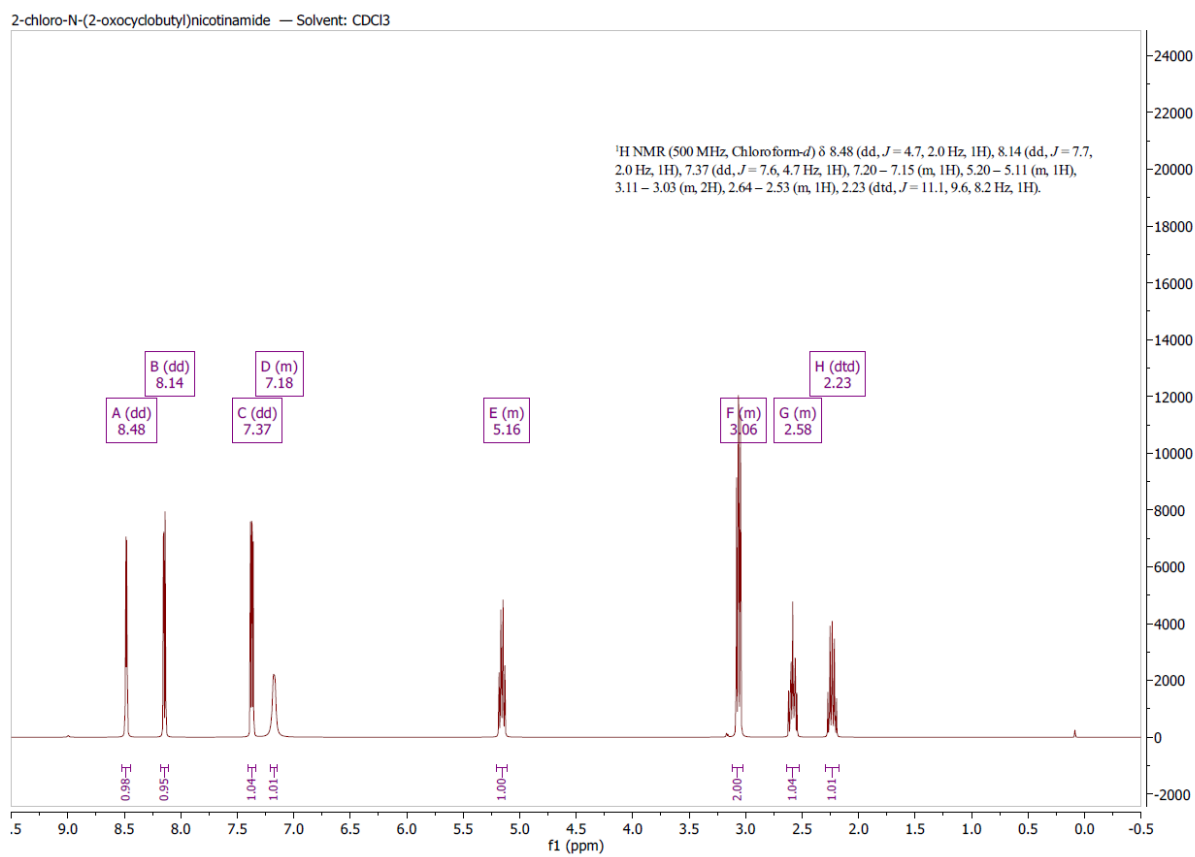
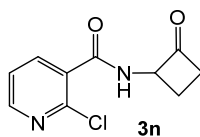


Figure S27. ¹H NMR (500 MHz CDCl₃) of 2-chloro-N-(2-oxocyclobutyl)nicotinamide (**3n**).

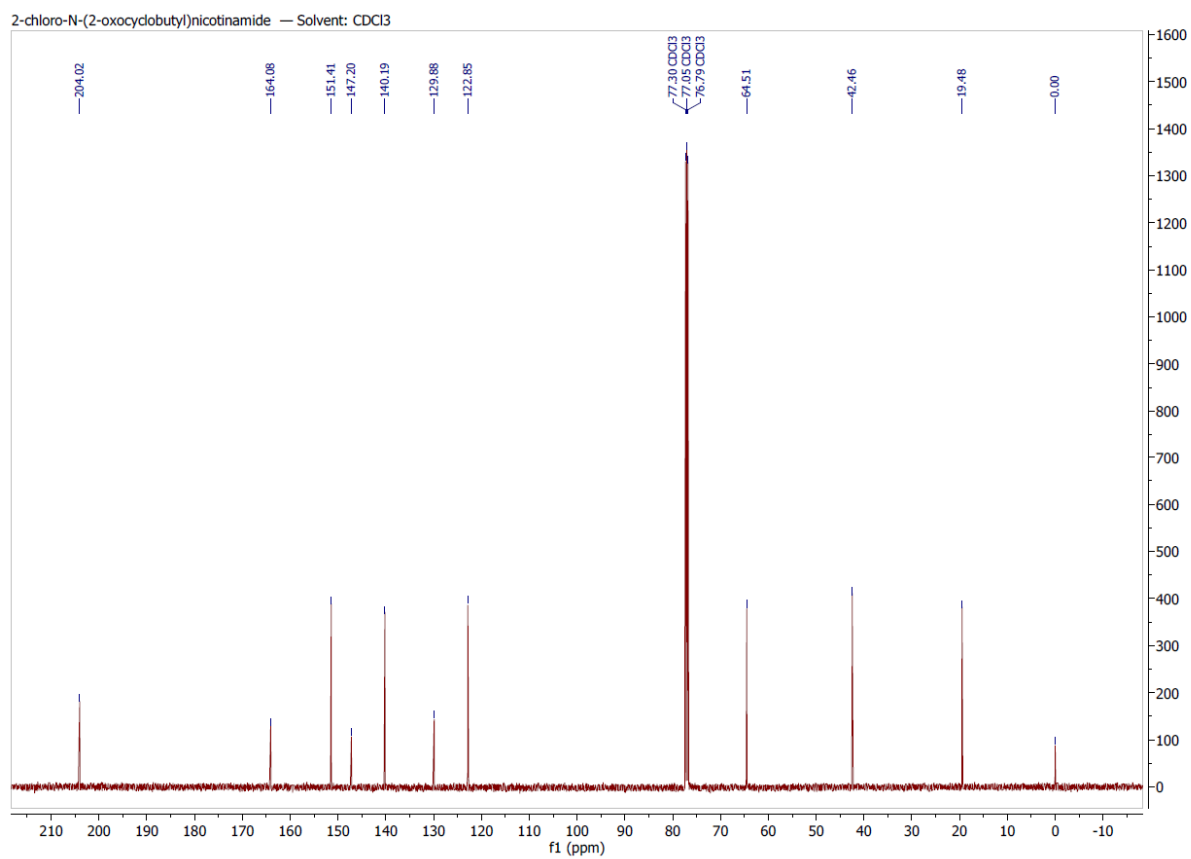
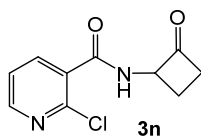


Figure 28. ¹³C NMR (126 MHz, CDCl₃) of 2-chloro-N-(2-oxocyclobutyl)nicotinamide (**3n**).

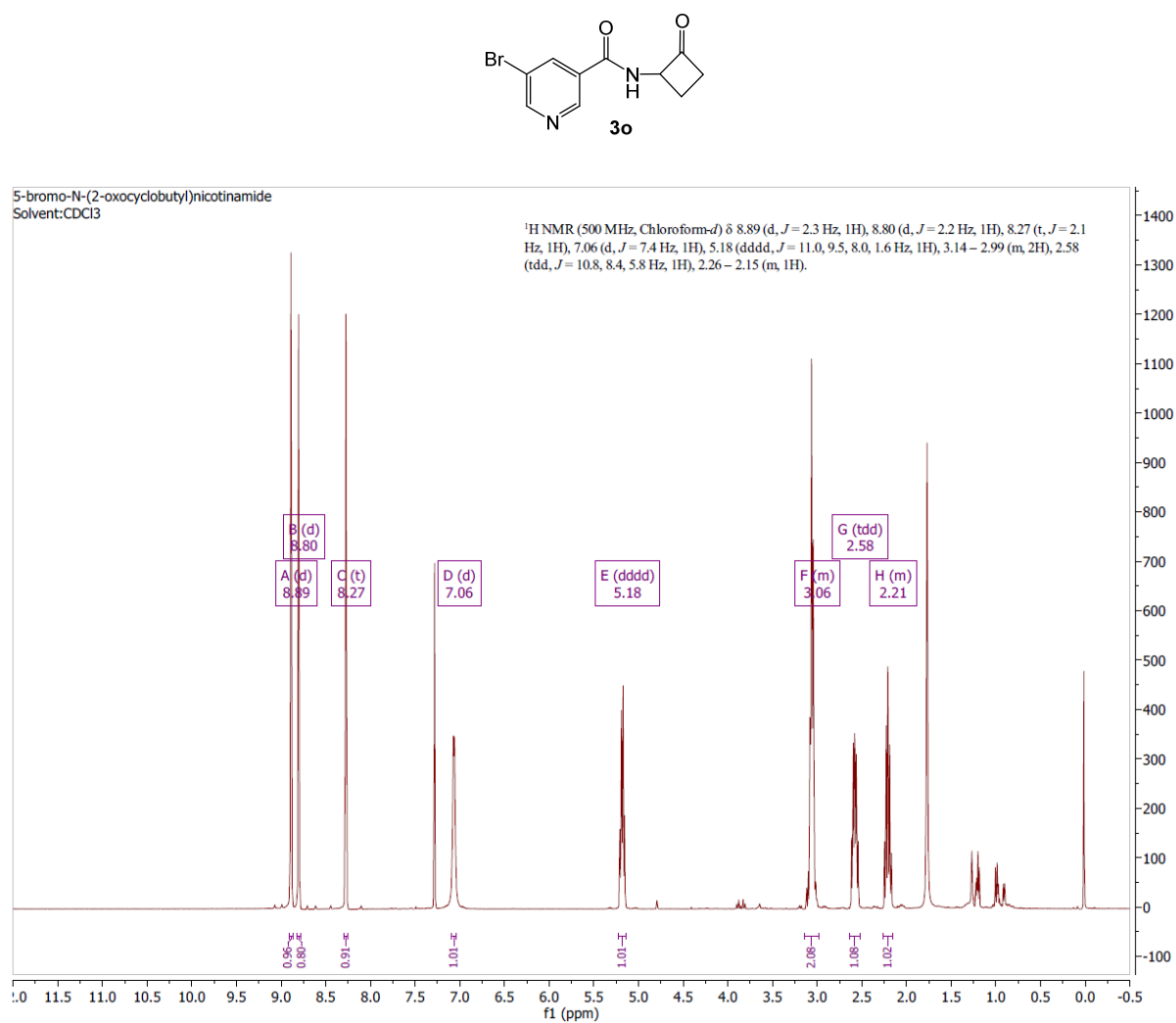


Figure S29. ¹H NMR (500 MHz CDCl₃) of 5-bromo-N-(2-oxocyclobutyl)nicotinamide (**3o**).

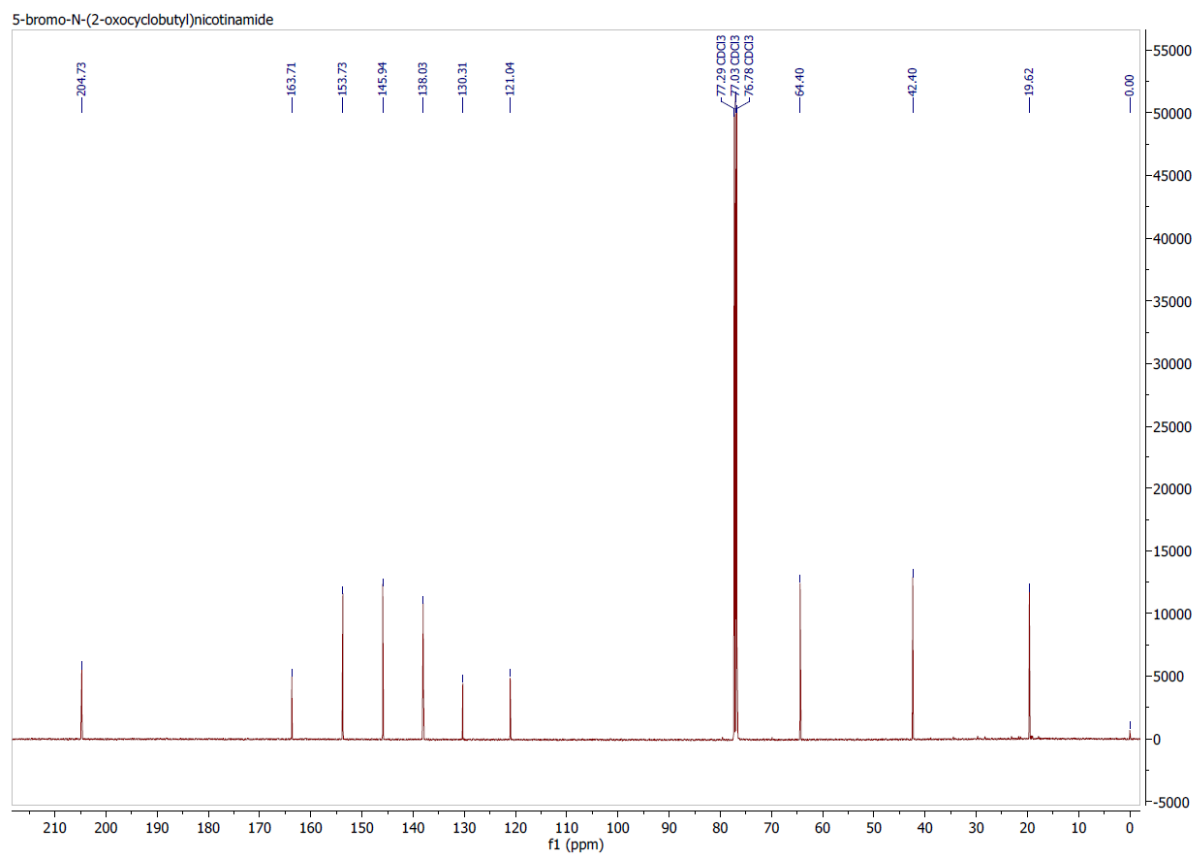
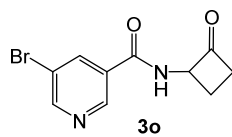


Figure S30. ^{13}C NMR (126 MHz, CDCl_3) of 5-bromo-*N*-(2-oxocyclobutyl)nicotinamide (**3o**).

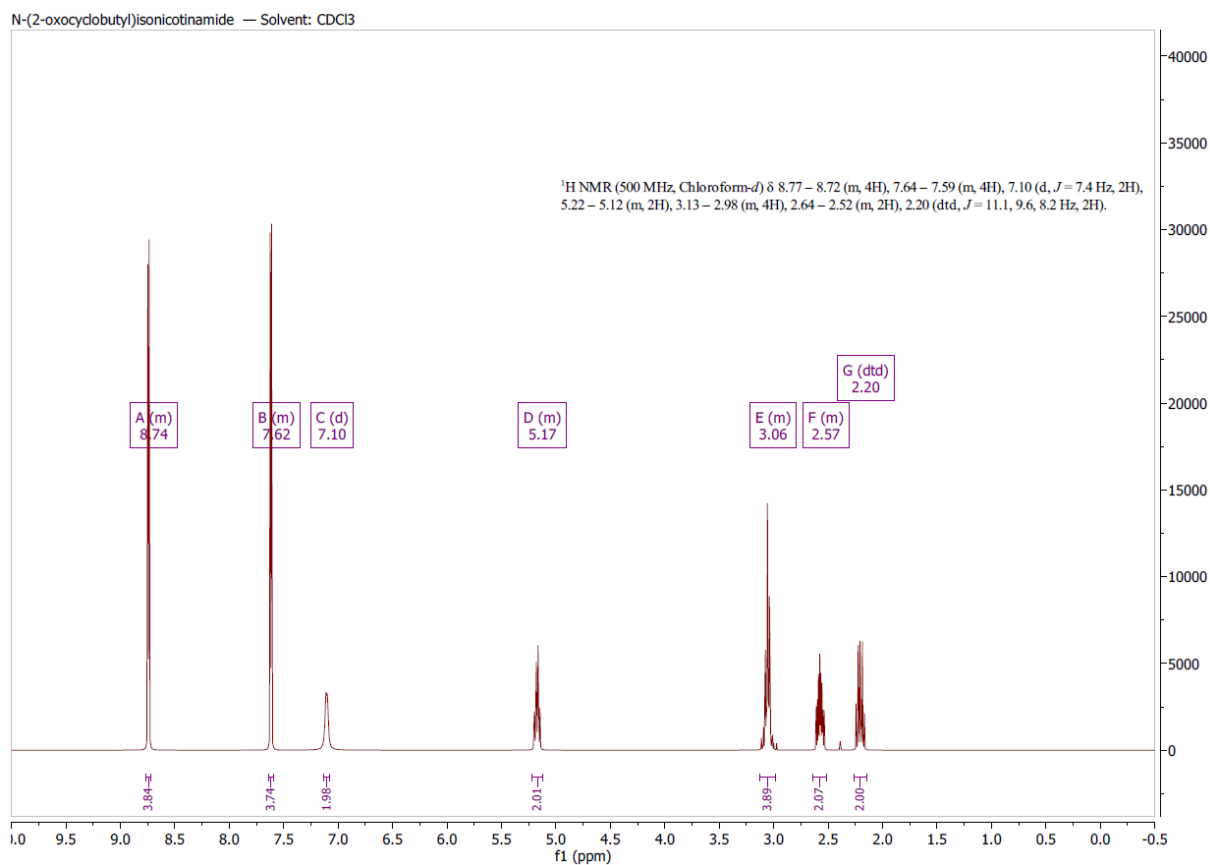
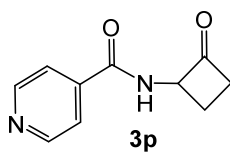


Figure S31. ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)isonicotinamide (**3p**).

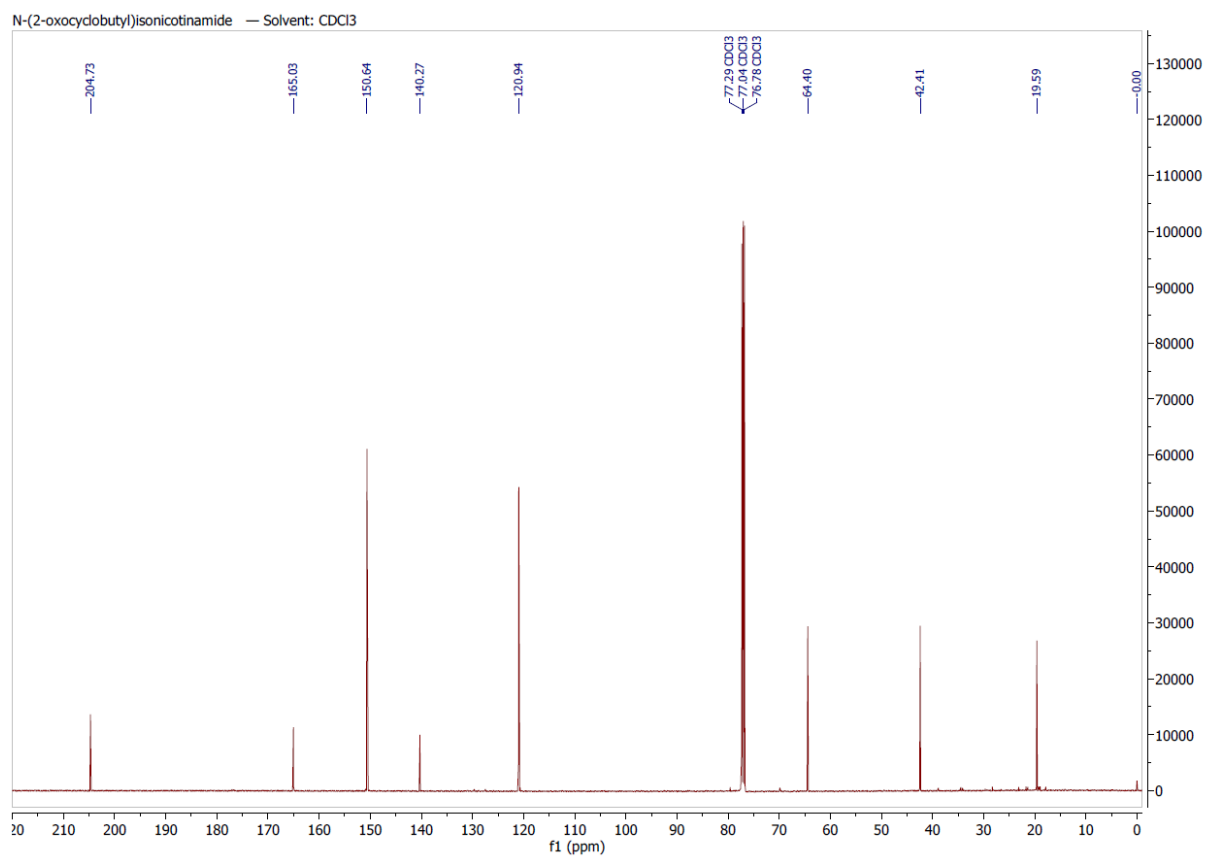
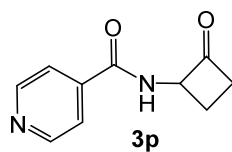


Figure S32. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)isonicotinamide (**3p**).

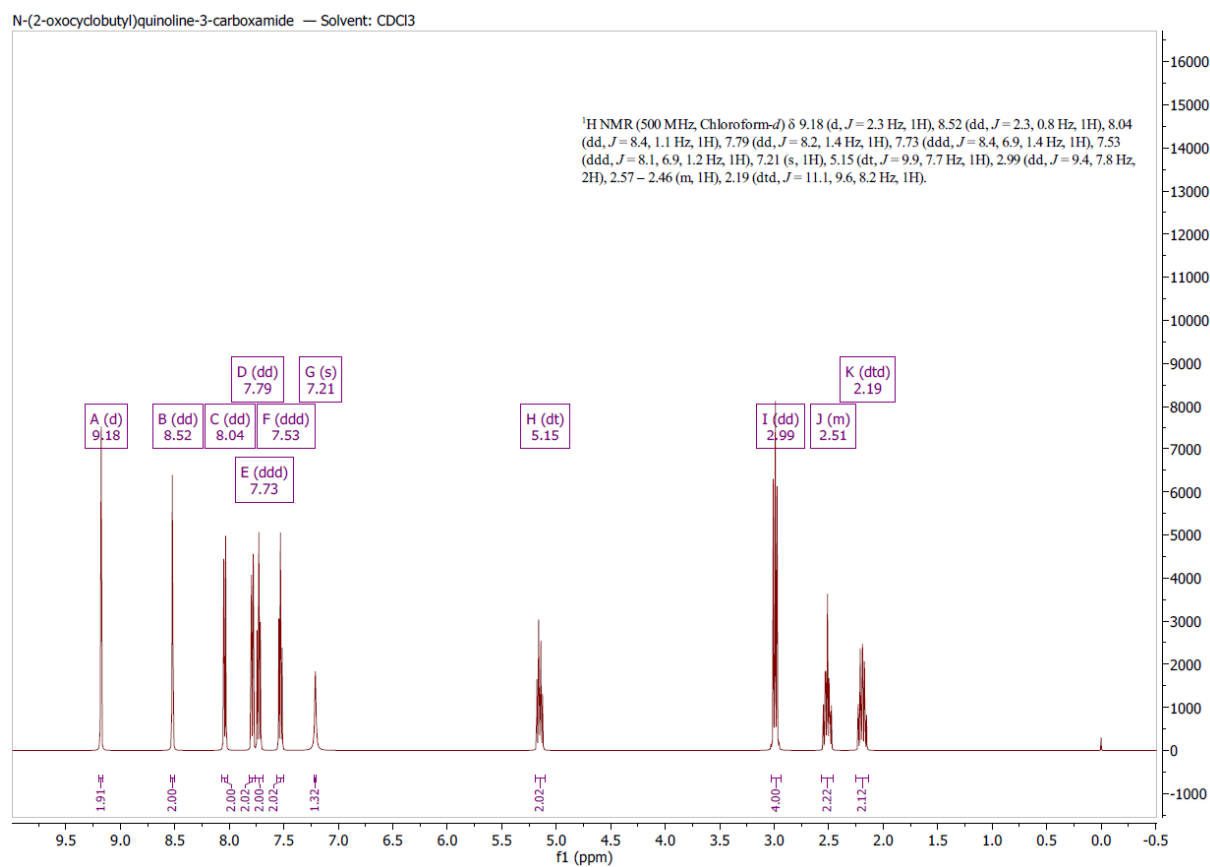
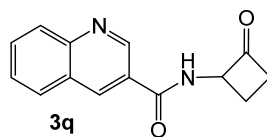


Figure S33. ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)quinoline-3-carboxamide (**3q**).

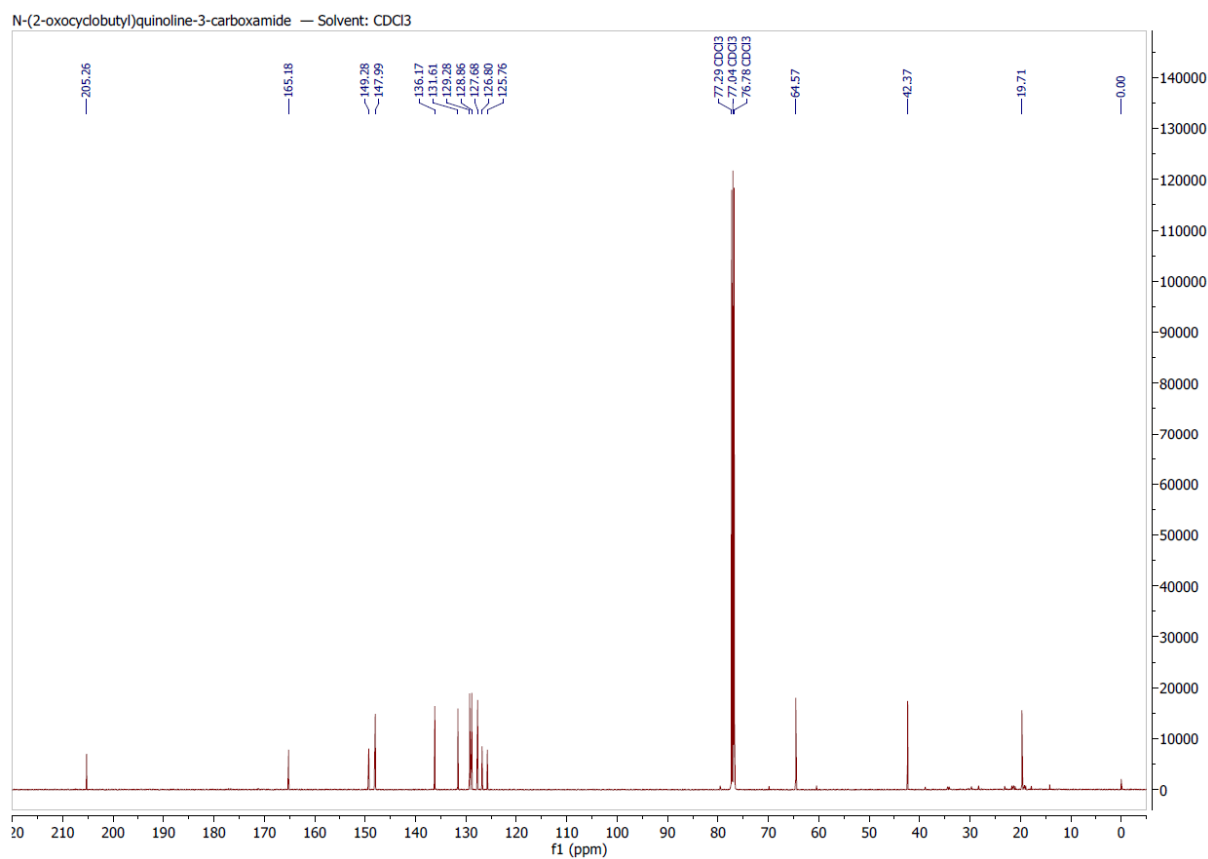
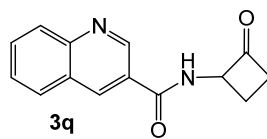
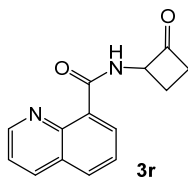


Figure S34. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)quinoline-3-carboxamide (**3q**).



N-(2-oxocyclobutyl)quinoline-8-carboxamide — Solvent: CDCl₃

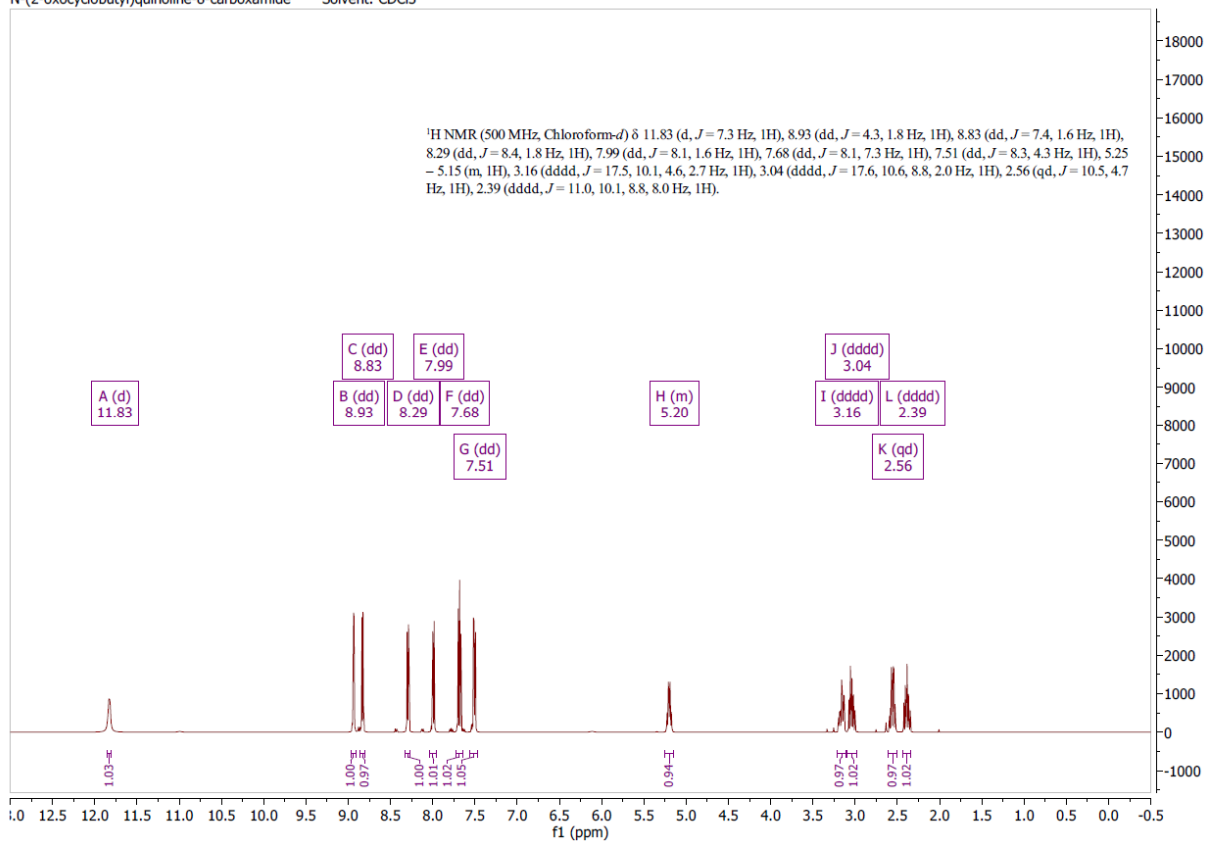


Figure S35. ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)quinoline-8-carboxamide (**3r**).

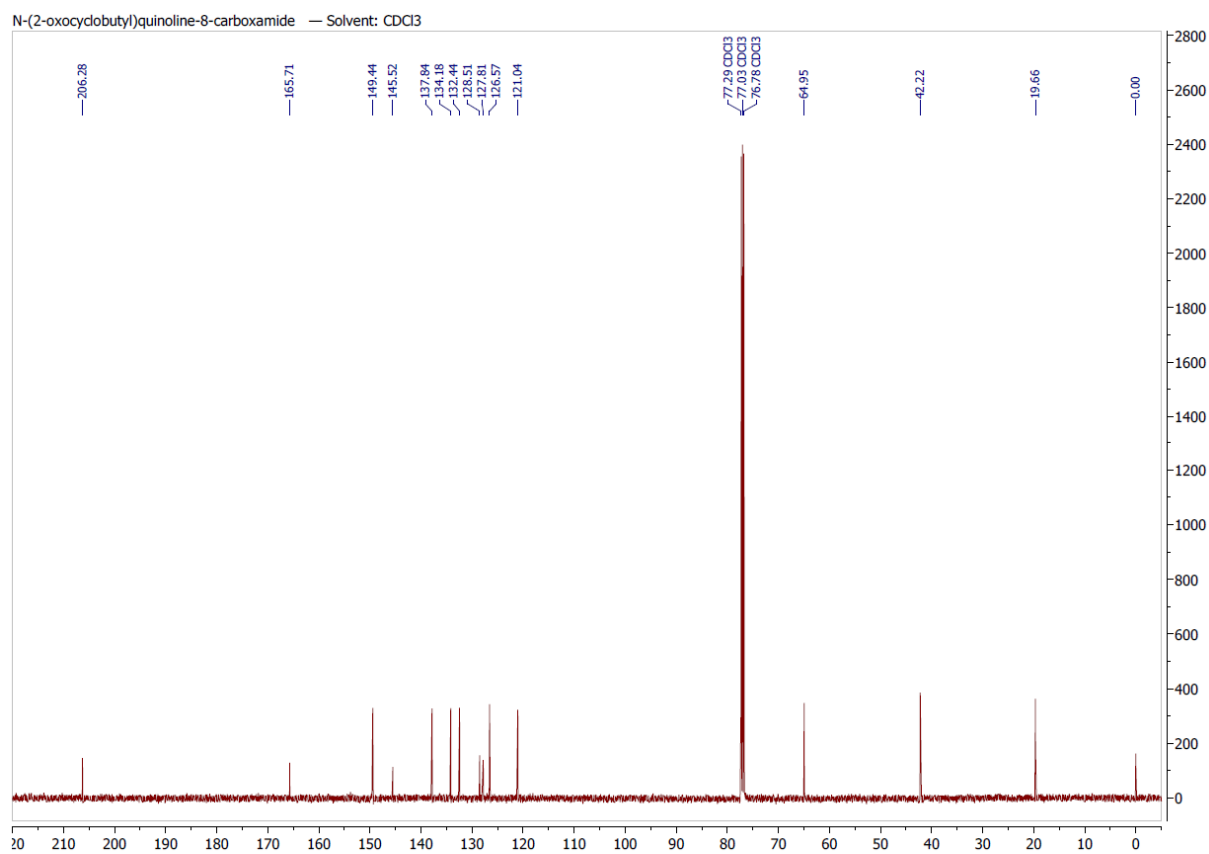
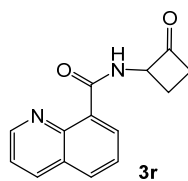


Figure S36. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)quinoline-8-carboxamide (**3r**).

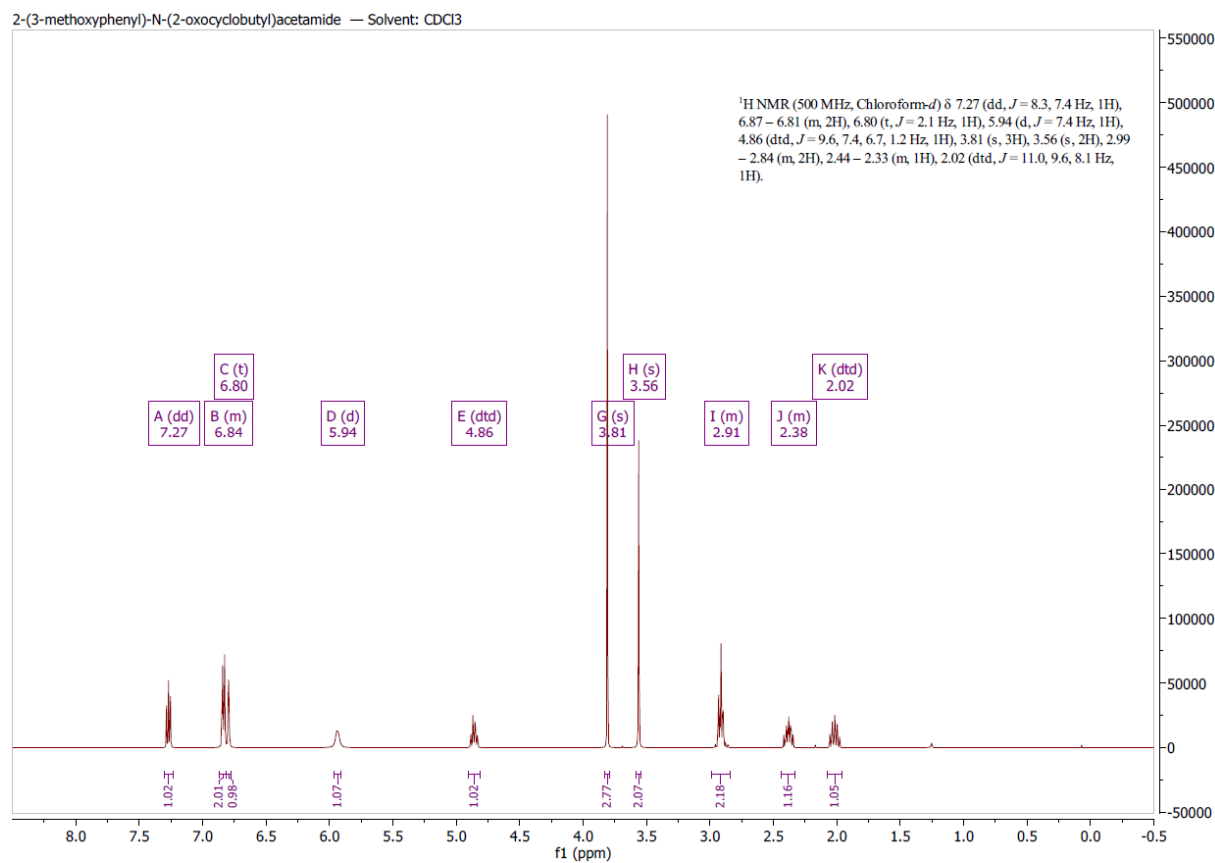
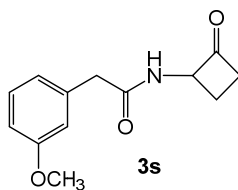


Figure S37. ¹H NMR (500 MHz CDCl₃) of 2-(3-methoxyphenyl)-N-(2-oxocyclobutyl)acetamide (**3s**).

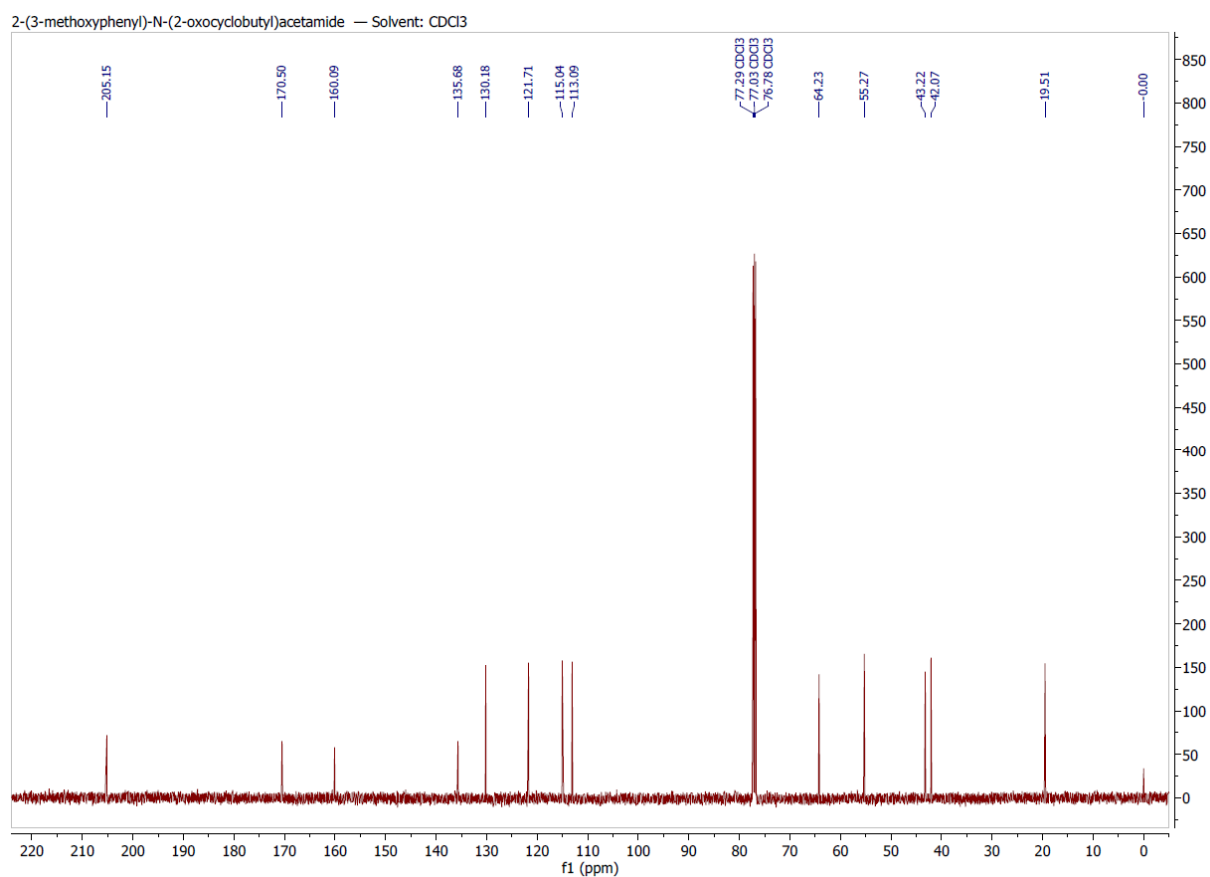
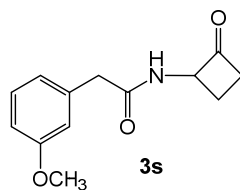


Figure S38. ¹³C NMR (126 MHz, CDCl₃) of 2-(3-methoxyphenyl)-N-(2-oxocyclobutyl)acetamide (**3s**).

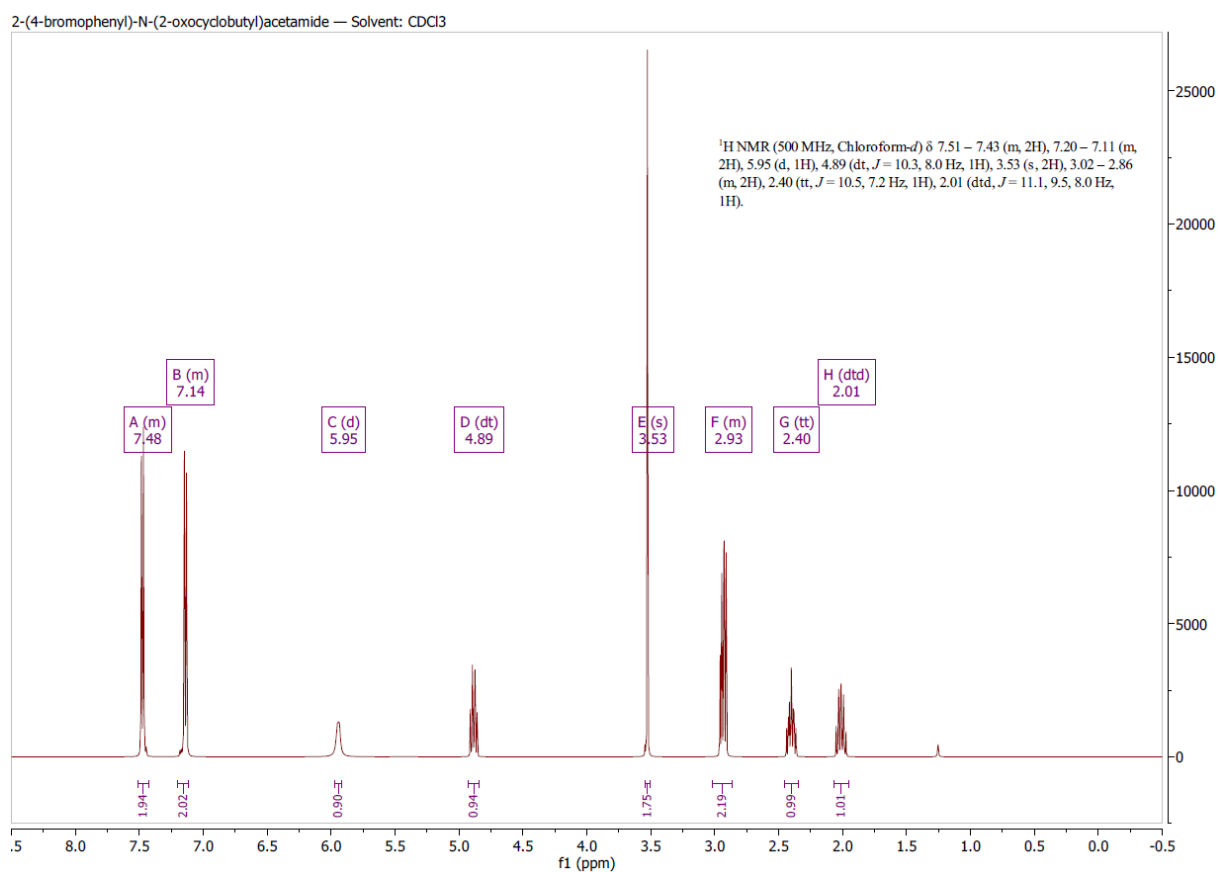
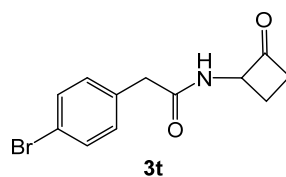


Figure S39. ¹H NMR (500 MHz CDCl₃) of 2-(4-bromophenyl)-*N*-(2-oxocyclobutyl)acetamide (**3t**).

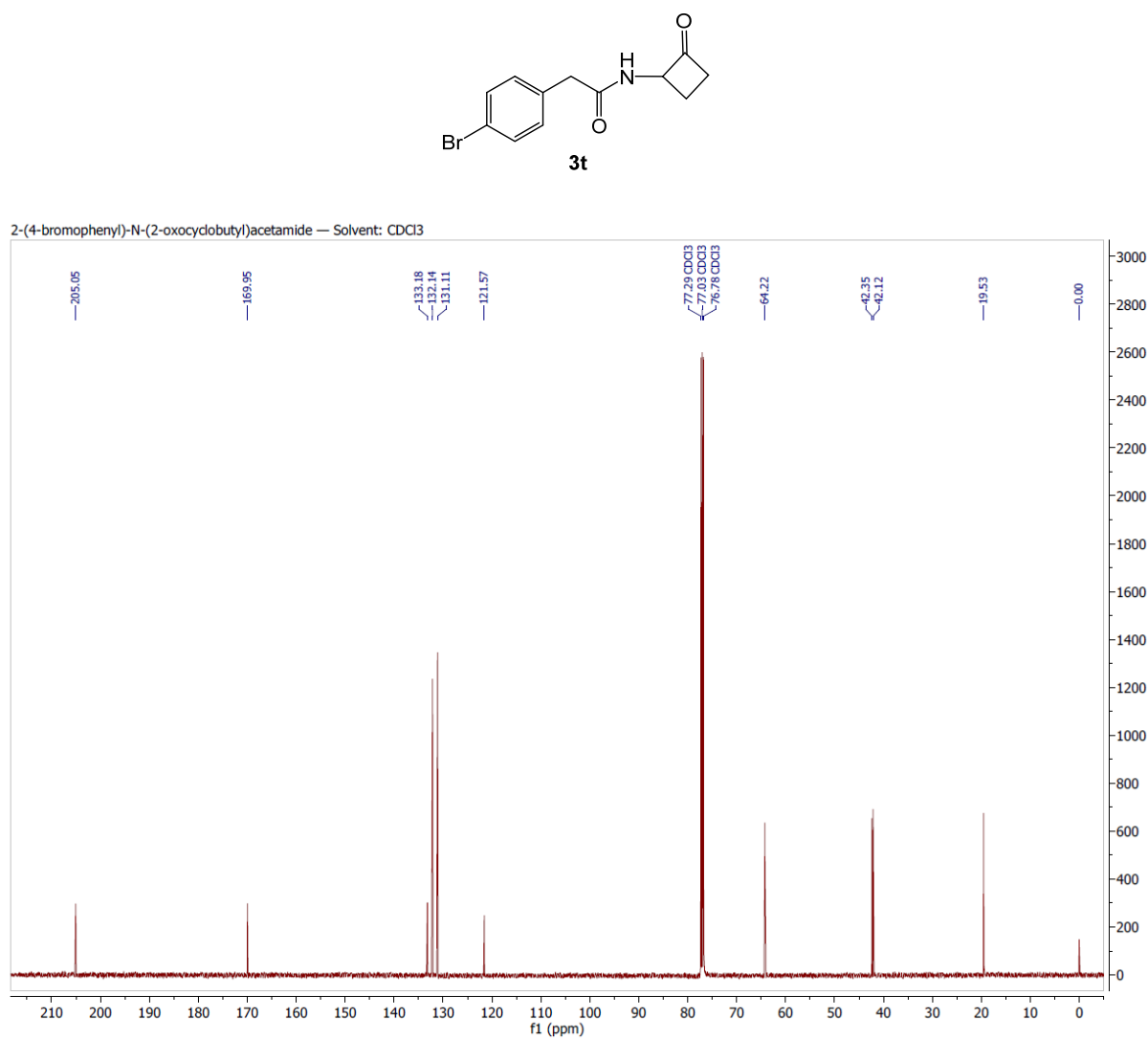


Figure S40. ¹³C NMR (126 MHz, CDCl₃) of 2-(4-bromophenyl)-N-(2-oxocyclobutyl)acetamide (**3t**).

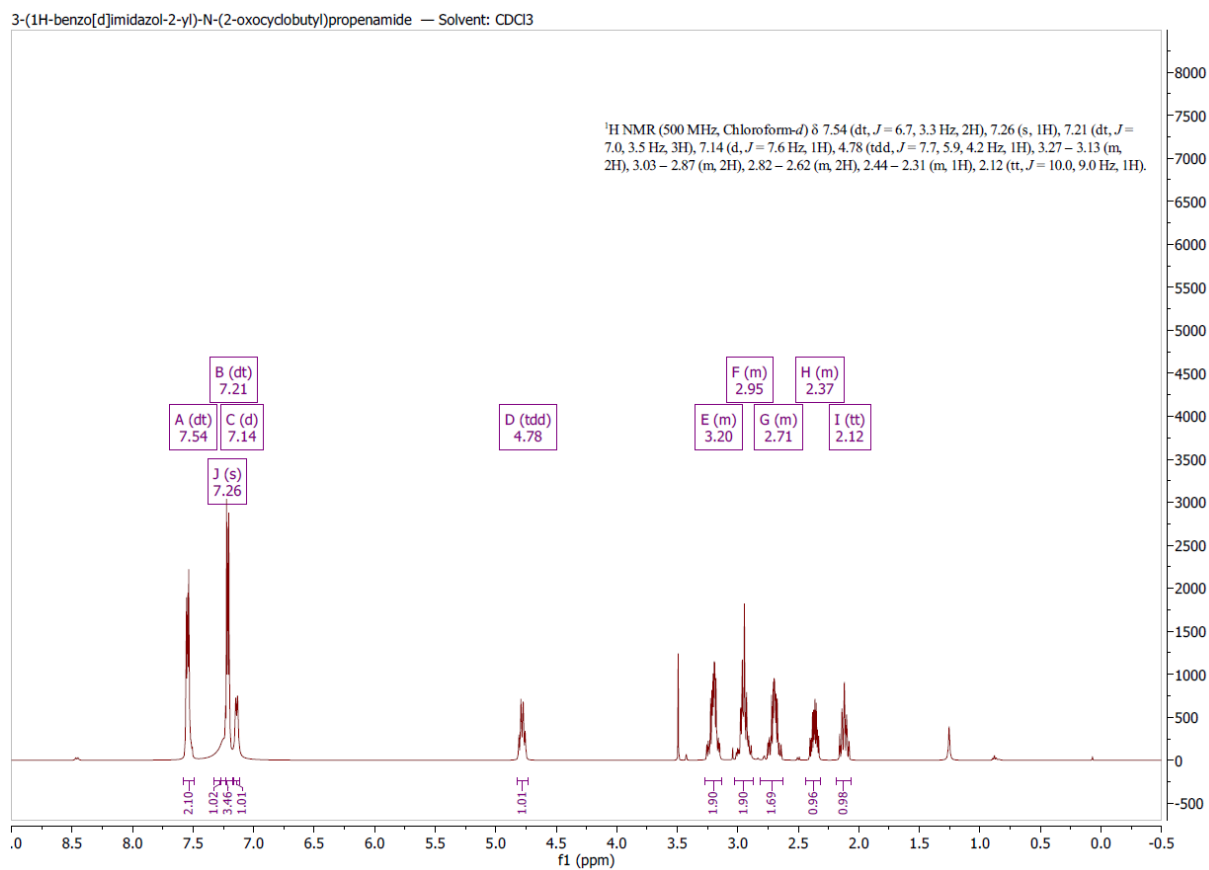
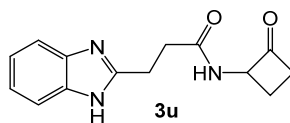


Figure S41. ¹H NMR (500 MHz CDCl₃) of 3-(1*H*-benzo[*d*]imidazol-2-yl)-*N*-(2-oxocyclobutyl)propenamide (**3u**).

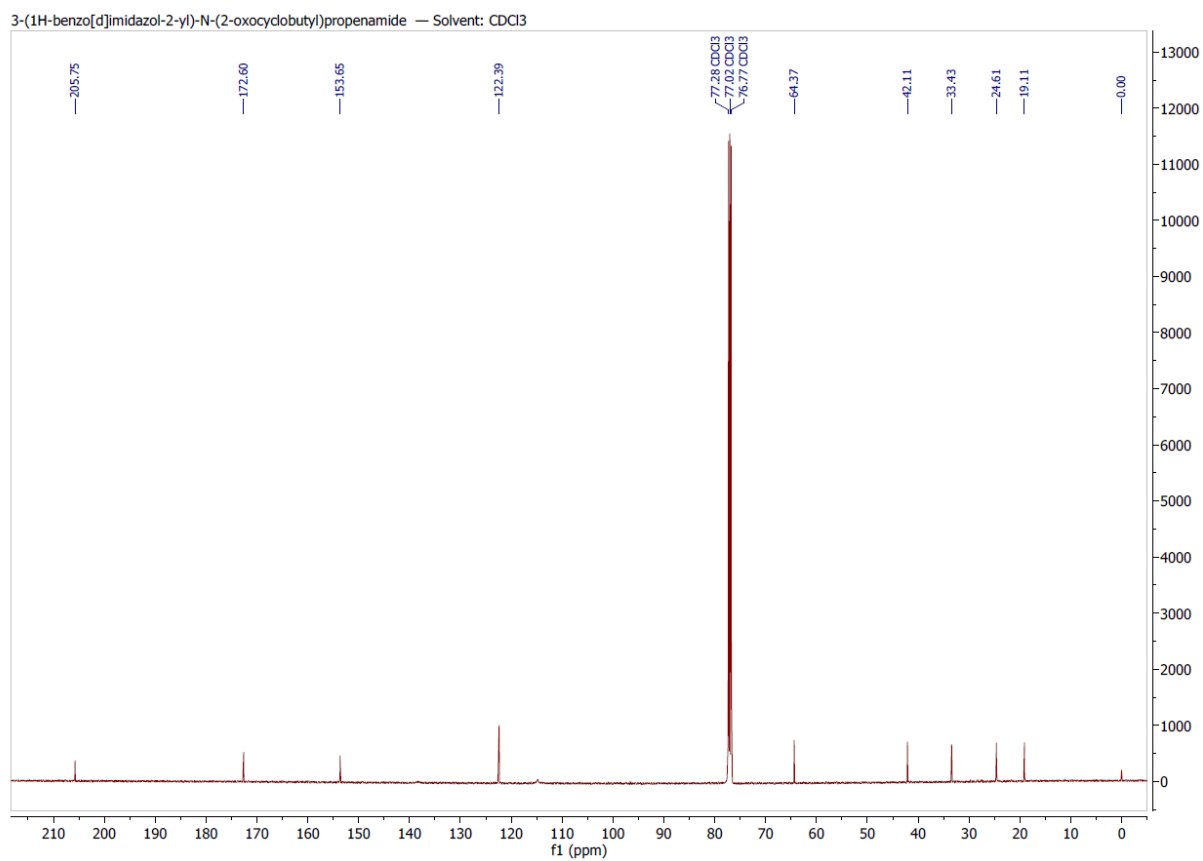
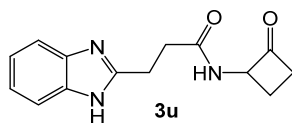


Figure S42. ¹³C NMR (126 MHz, CDCl₃) of 3-(1*H*-benzo[*d*]imidazol-2-yl)-*N*-(2-oxocyclobutyl)propanamide (**3u**).

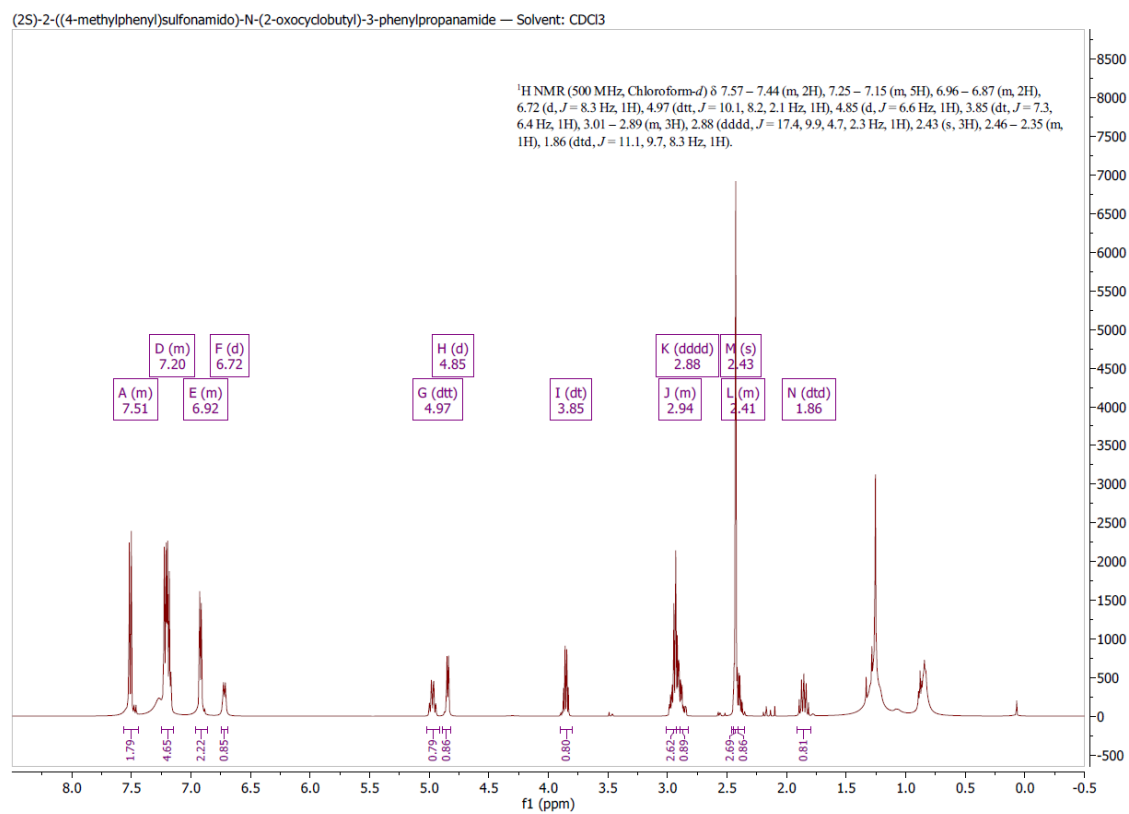
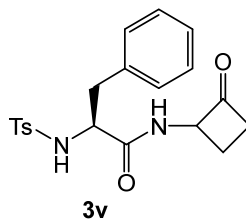


Figure S43. ¹H NMR (500 MHz CDCl₃) of (2S)-2-((4-methylphenyl)sulfonamido)-N-(2-oxocyclobutyl)-3-phenylpropanamide (**3v**).

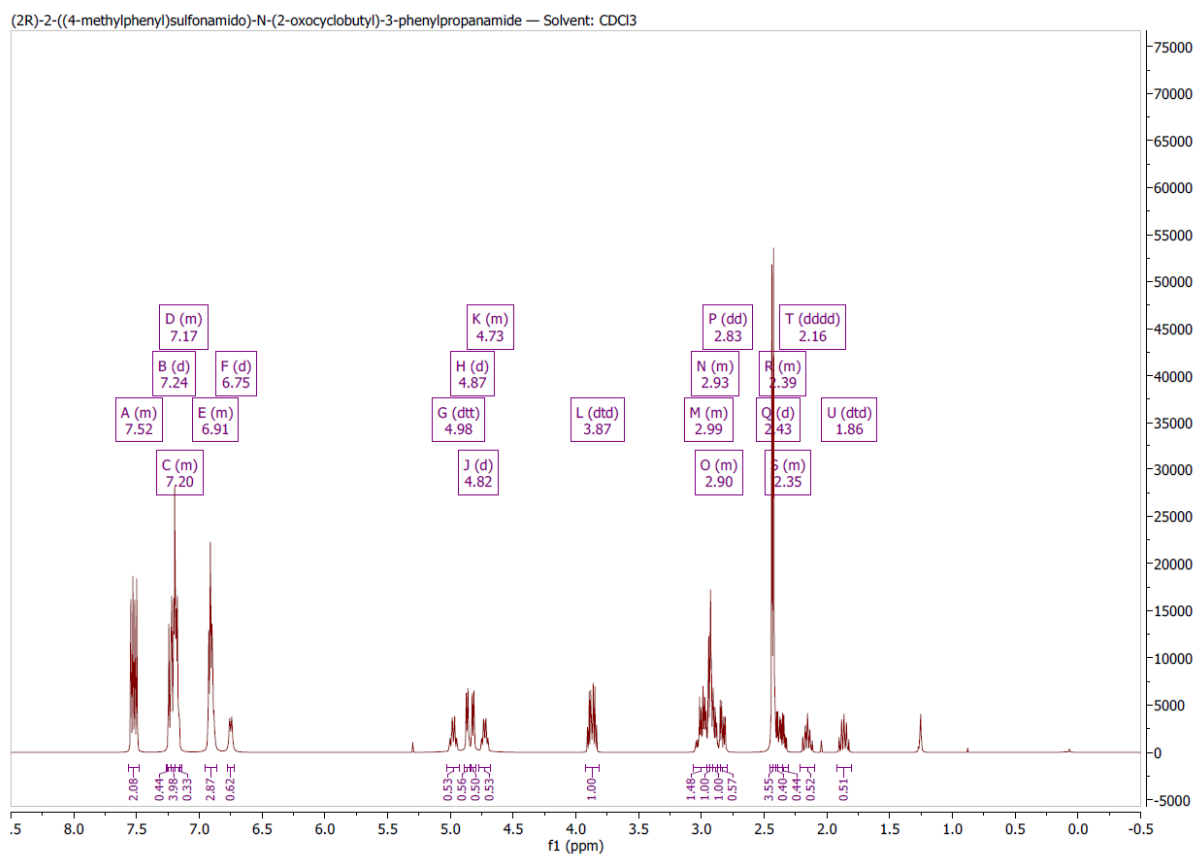
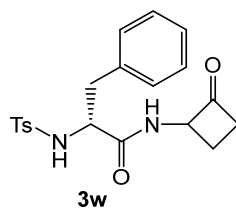


Figure S44. ¹H NMR (500 MHz CDCl₃) of (2R)-2-((4-methylphenyl)sulfonamido)-N-(2-oxocyclobutyl)-3-phenylpropanamide (**3w**).

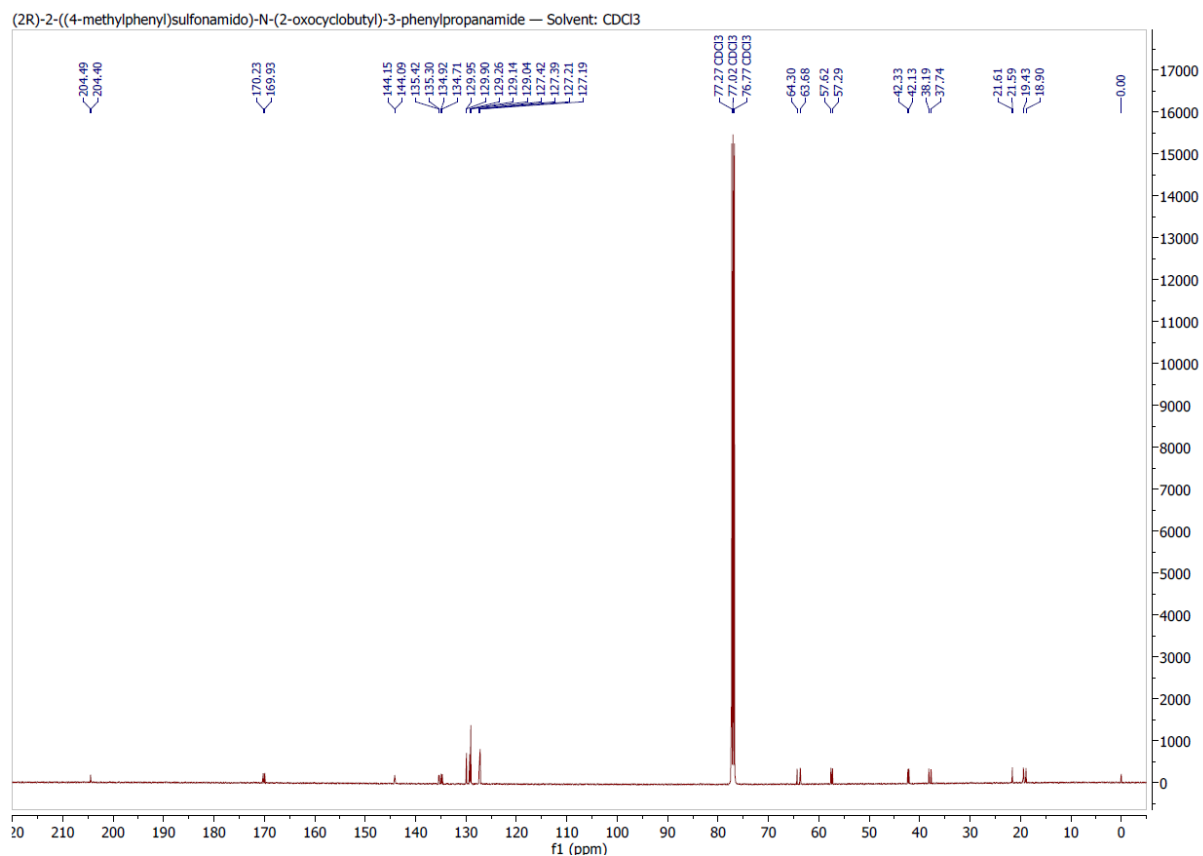
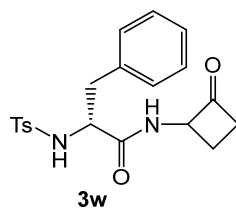


Figure S45. ¹³C NMR (126 MHz, CDCl₃) of (2R)-2-((4-methylphenyl)sulfonamido)-N-(2-oxocyclobutyl)-3-phenylpropanamide (**3w**).

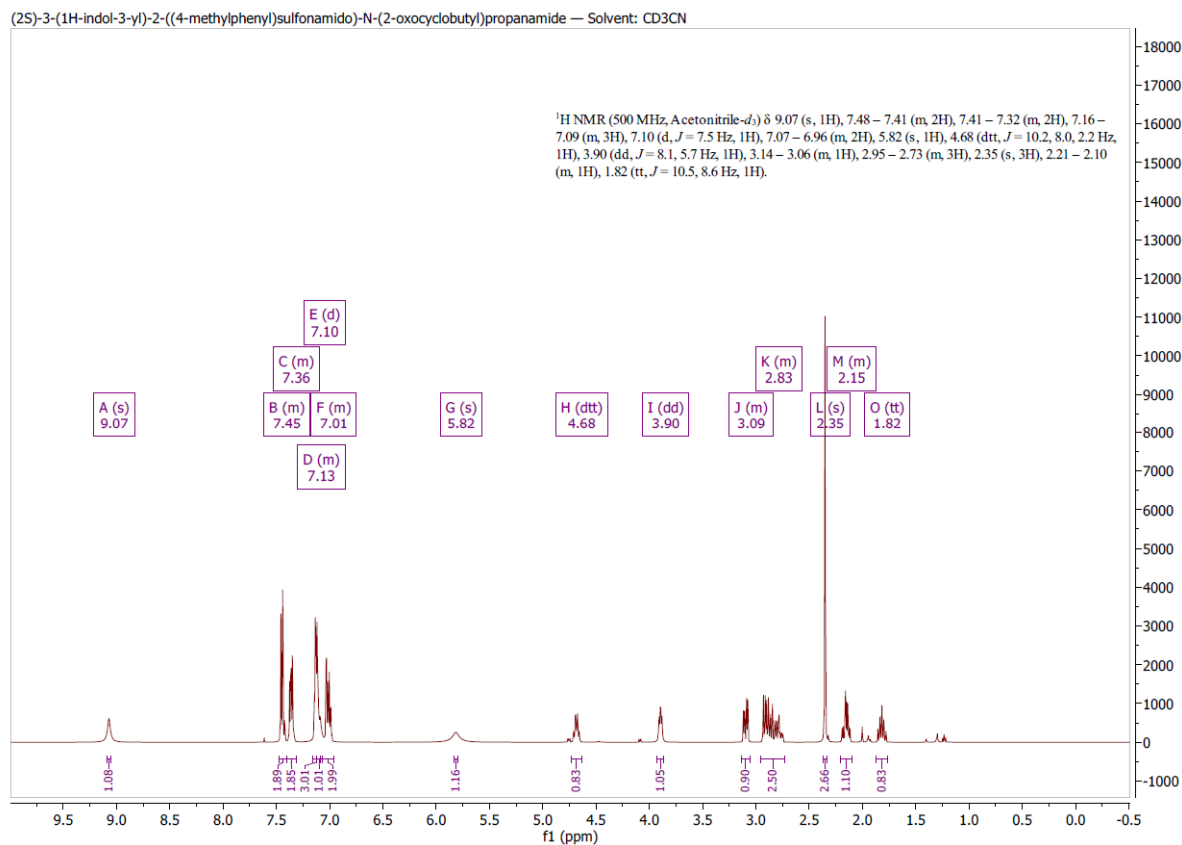
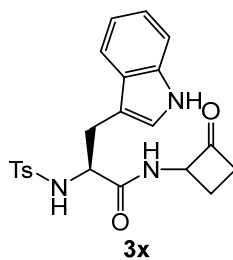


Figure S46. ¹H NMR (500 MHz CDCl₃) of (2S)-3-(1H-indol-3-yl)-2-((4-methylphenyl)sulfonamido)-N-(2-oxocyclobutyl)propanamide (**3x**).

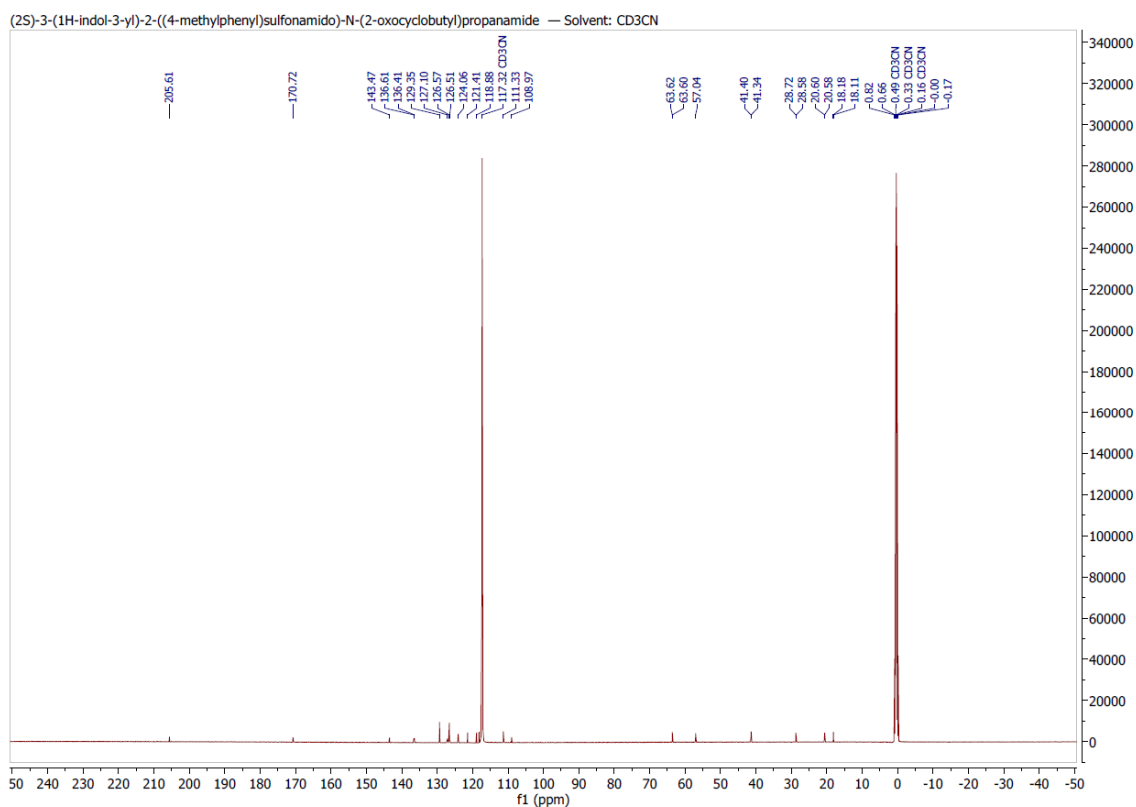
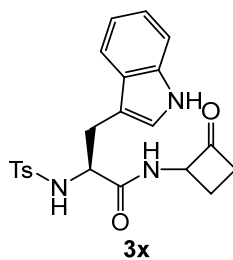


Figure S47. ¹³C NMR (126 MHz, CDCl₃) of (2*S*)-3-(1*H*-indol-3-yl)-2-((4-methylphenyl)sulfonamido)-*N*-(2-oxocyclobutyl)propanamide (**3x**).

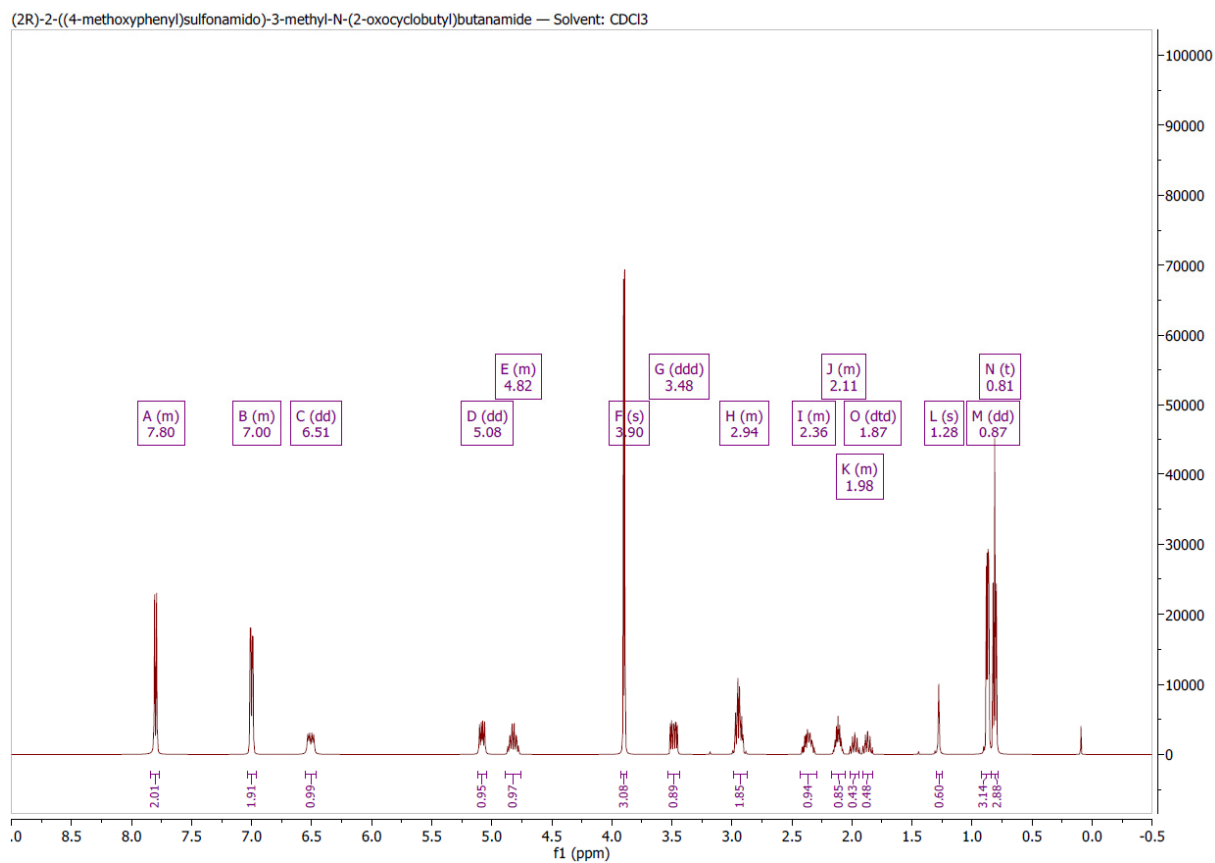
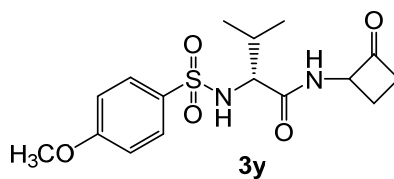


Figure S48. ¹H NMR (500 MHz CDCl₃) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).

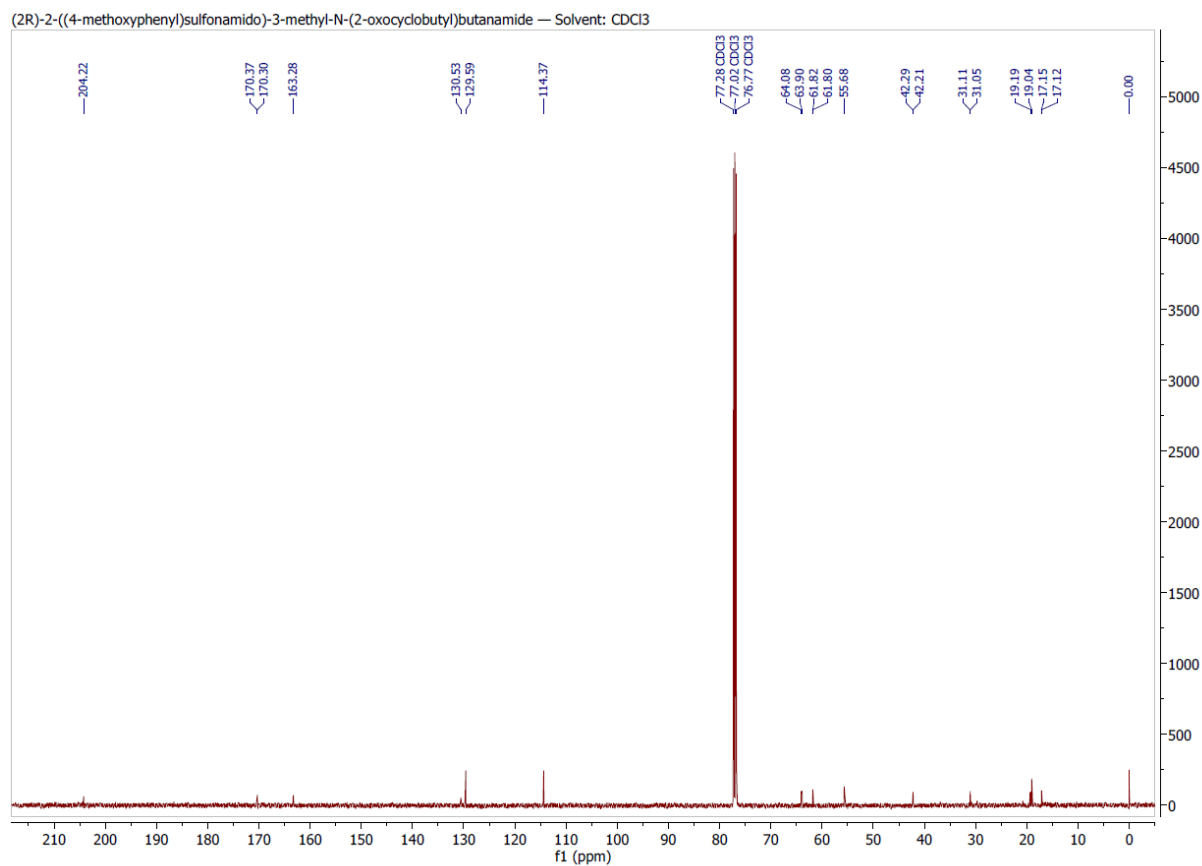
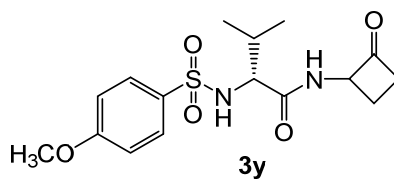


Figure S49. ¹³C NMR (126 MHz, CDCl₃) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).

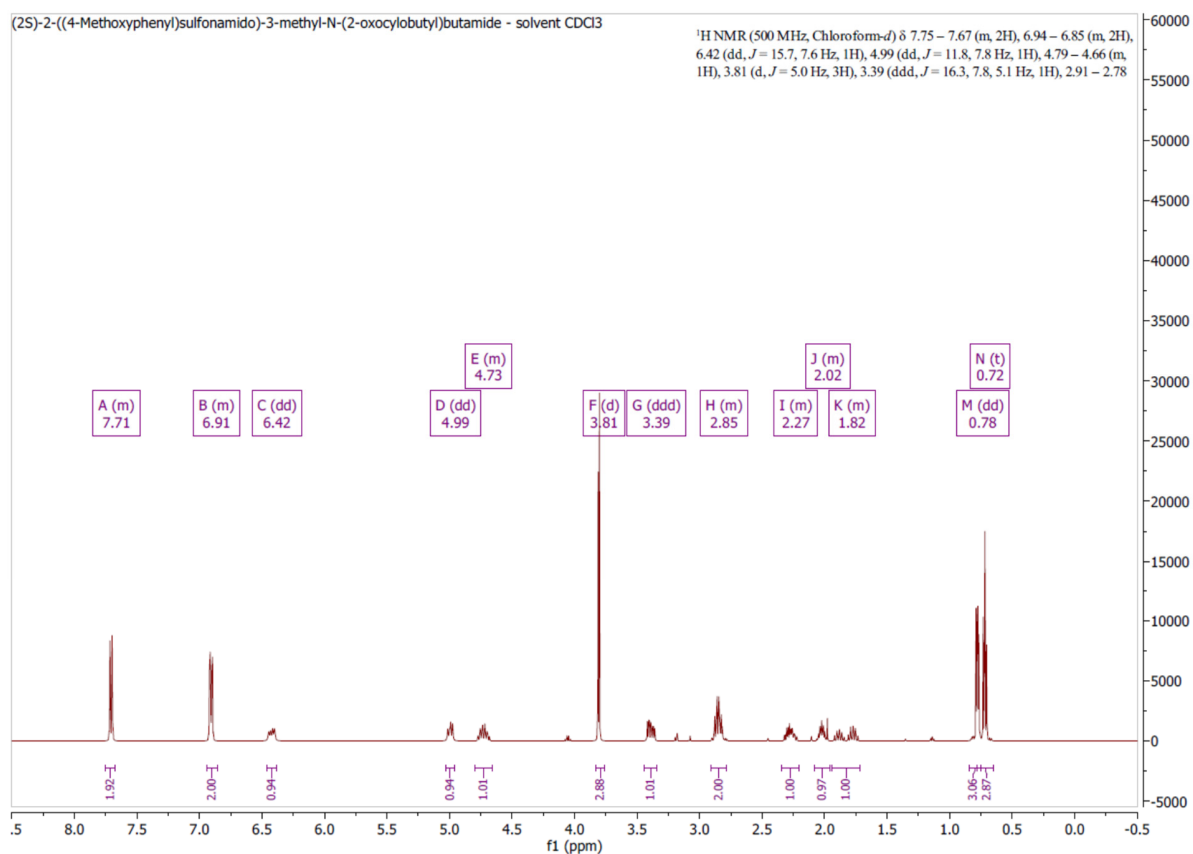
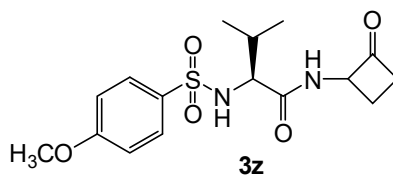


Figure S50. ¹H NMR (500 MHz CDCl₃) of (2S)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3z**).

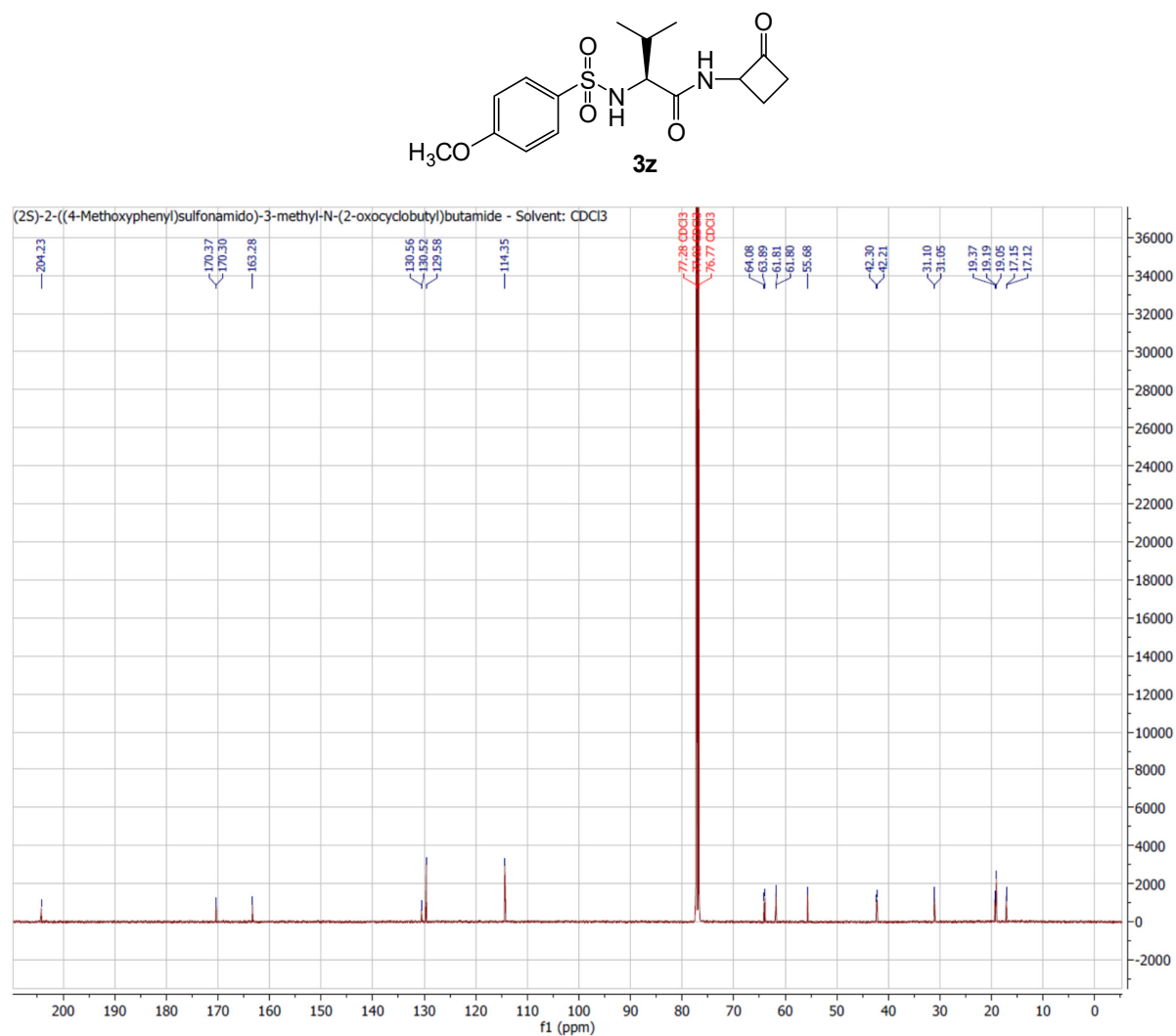


Figure S51. ¹³C NMR (126 MHz, CDCl₃) of (2S)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3z**).

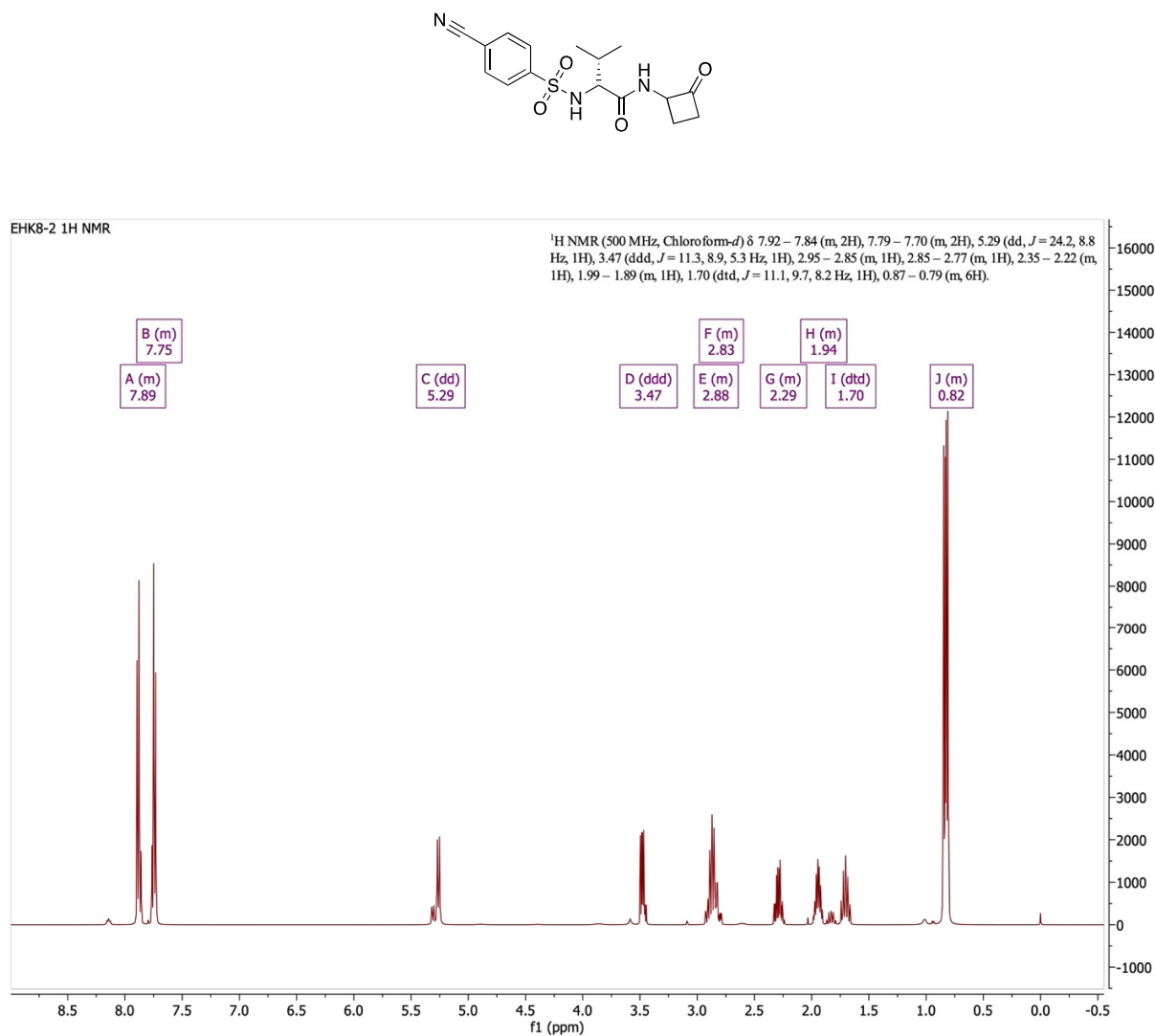


Figure S52. ¹H NMR (500 MHz CDCl₃) of (2R)-2-((4-cyanophenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3aa**).

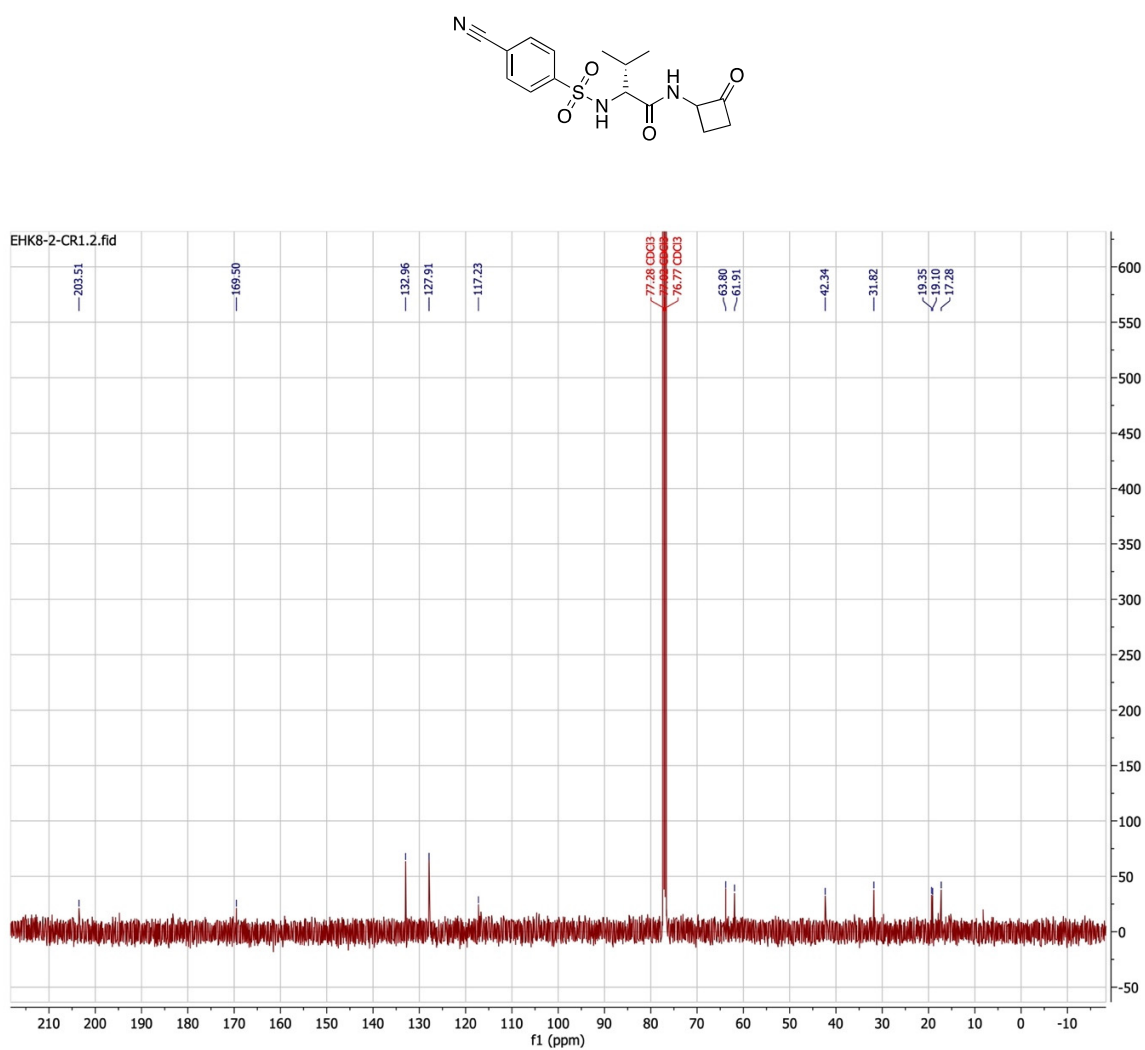


Figure S53. ¹³C NMR (126 MHz, CDCl₃) of (2R)-2-((4-cyanophenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3aa**).

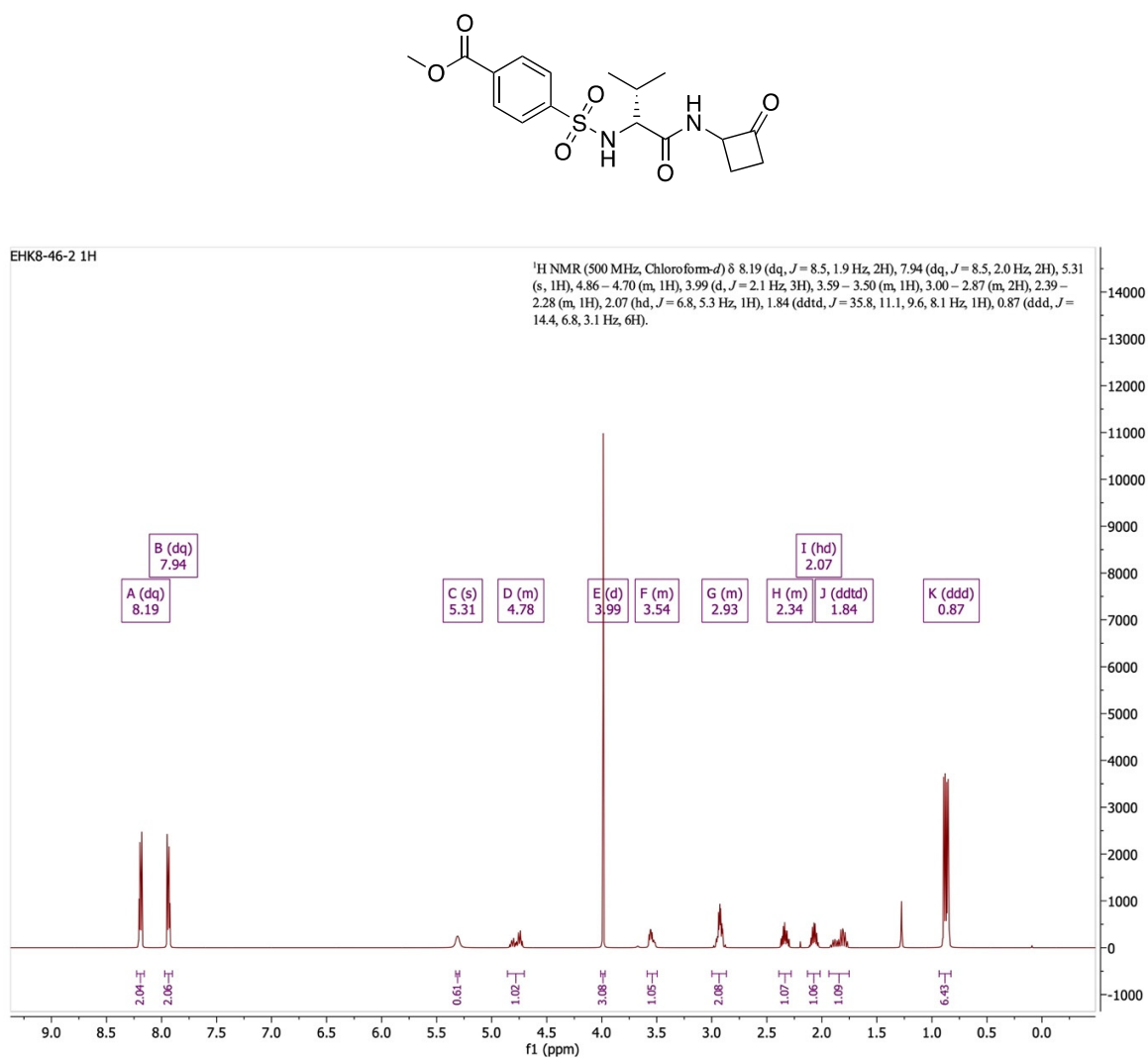


Figure S54. ¹H NMR (500 MHz CDCl₃) of methyl 4-(N-((2R)-3-methyl-1-oxo-1-((2-oxocyclobutyl)amino)butan-2-yl)sulfamoyl)benzoate (**3ab**).

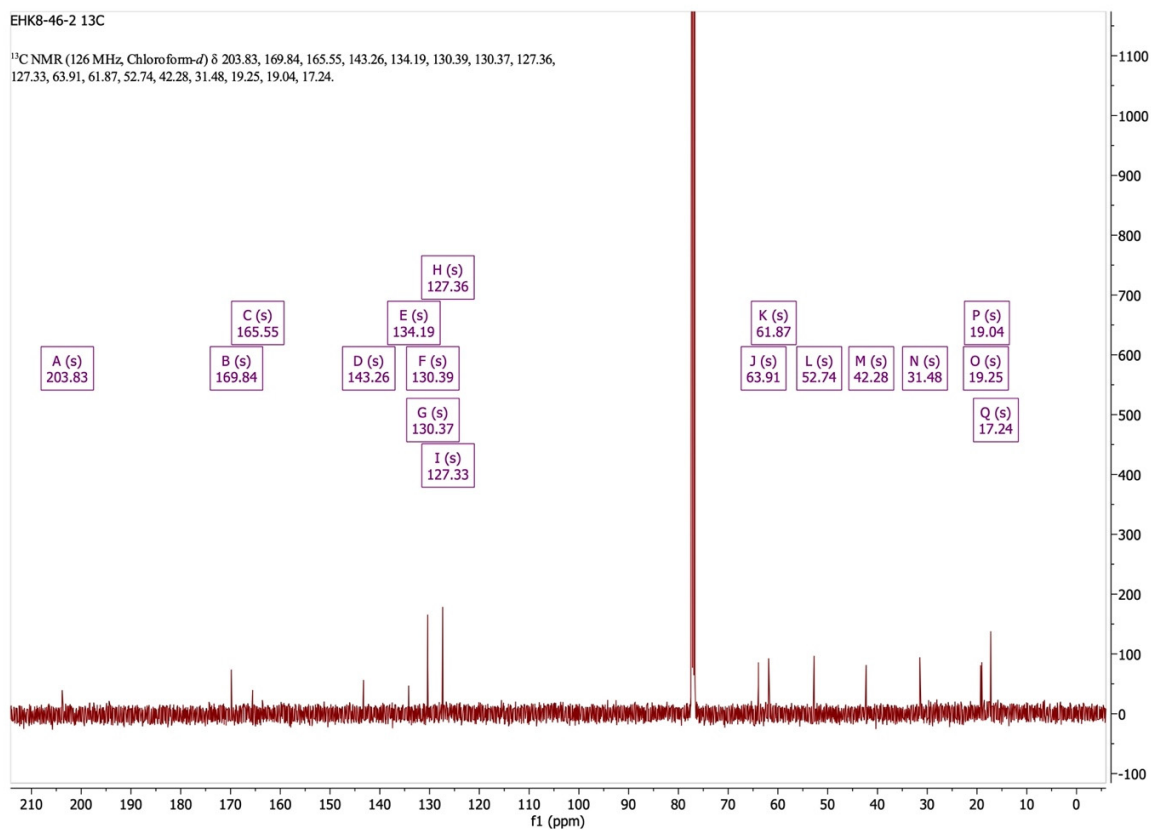
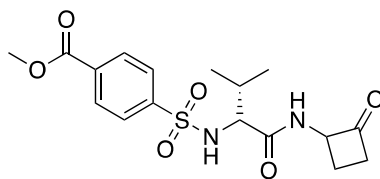
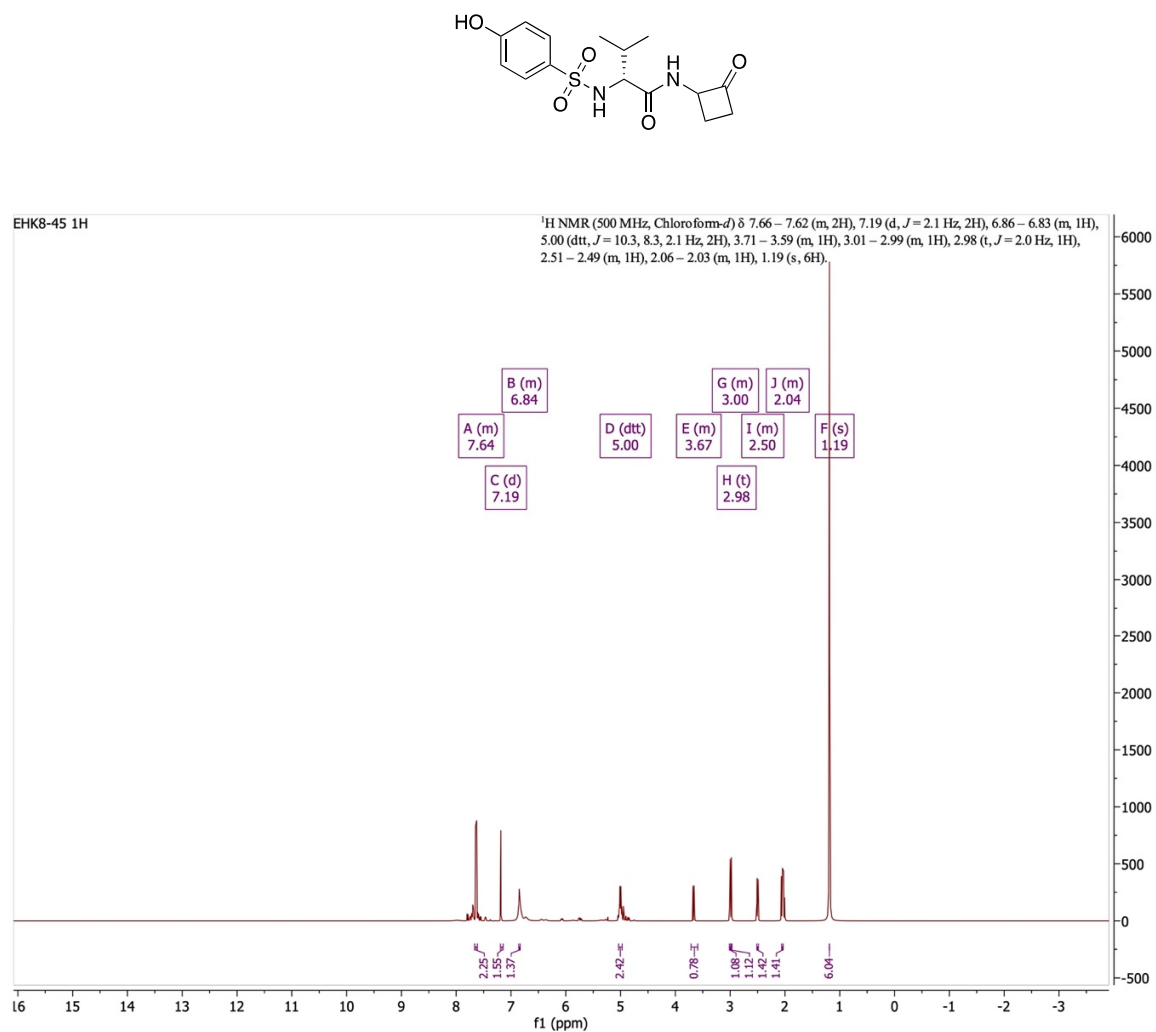


Figure S55. ¹³C NMR (126 MHz, CDCl₃) of methyl 4-(N-((2R)-3-methyl-1-oxo-1-((2-oxocyclobutyl)amino)butan-2-yl)sulfamoyl)benzoate (**3ab**).



Fig, S56. ¹H NMR (500 MHz CDCl₃) of (2R)-2-((4-hydroxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3ac**).

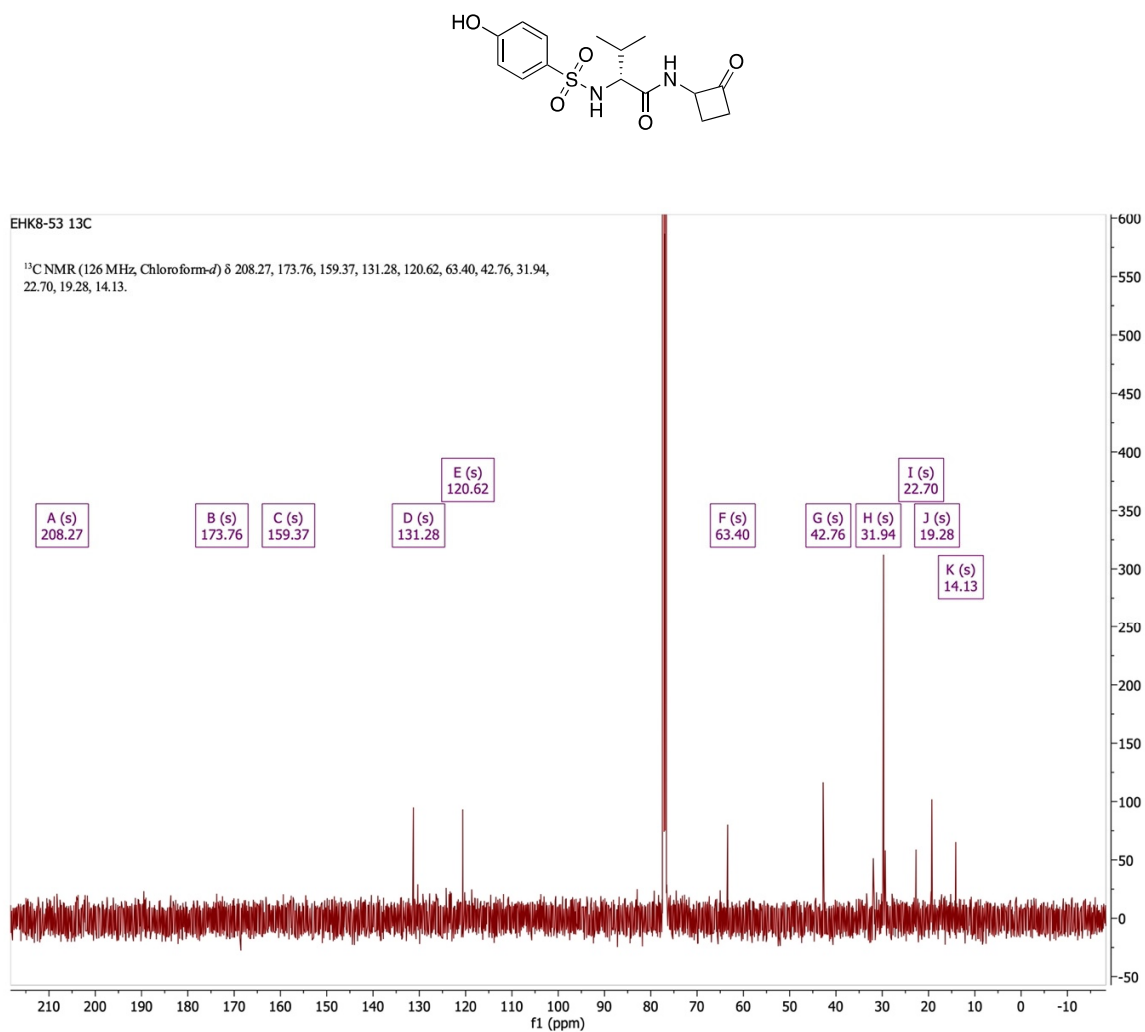


Figure S57. ¹³C NMR (126 MHz, CDCl₃) of (2R)-2-((4-hydroxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3ac**).

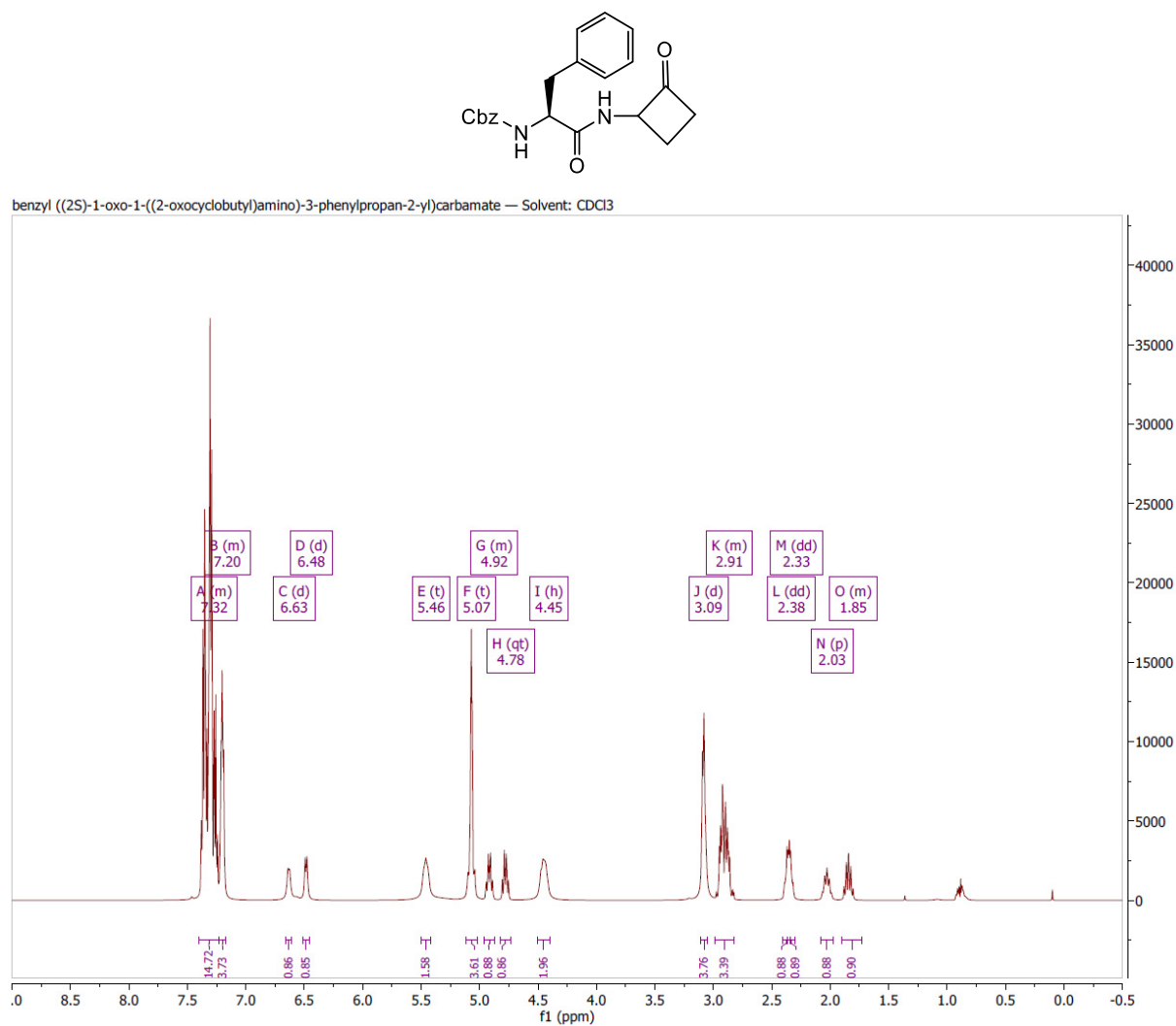


Figure S58. ¹H NMR (500 MHz CDCl₃) of benzyl ((2S)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (**3ad**).

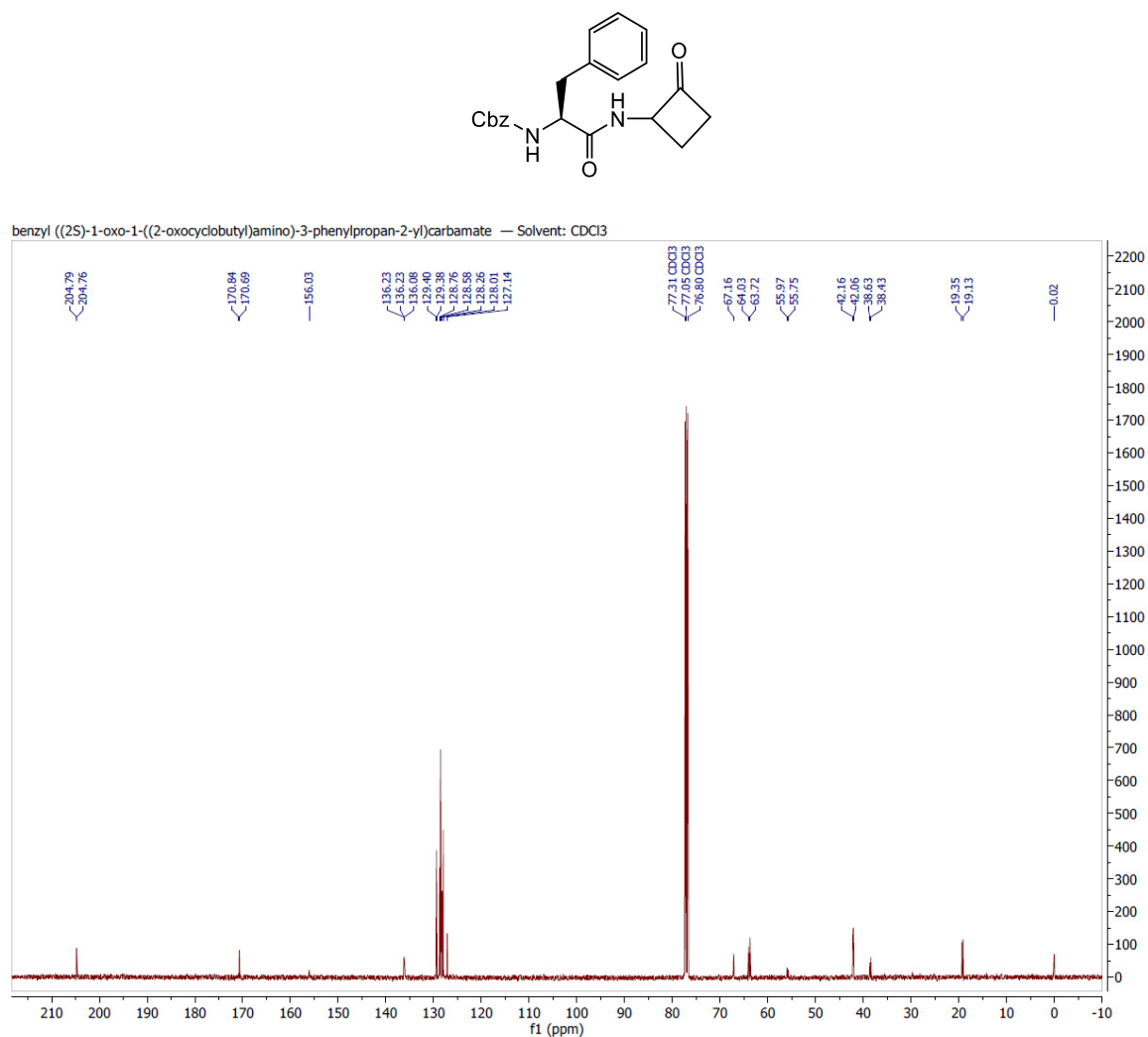


Figure S59. ¹³C NMR (126 MHz, CDCl₃) of benzyl ((2S)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (3ad).

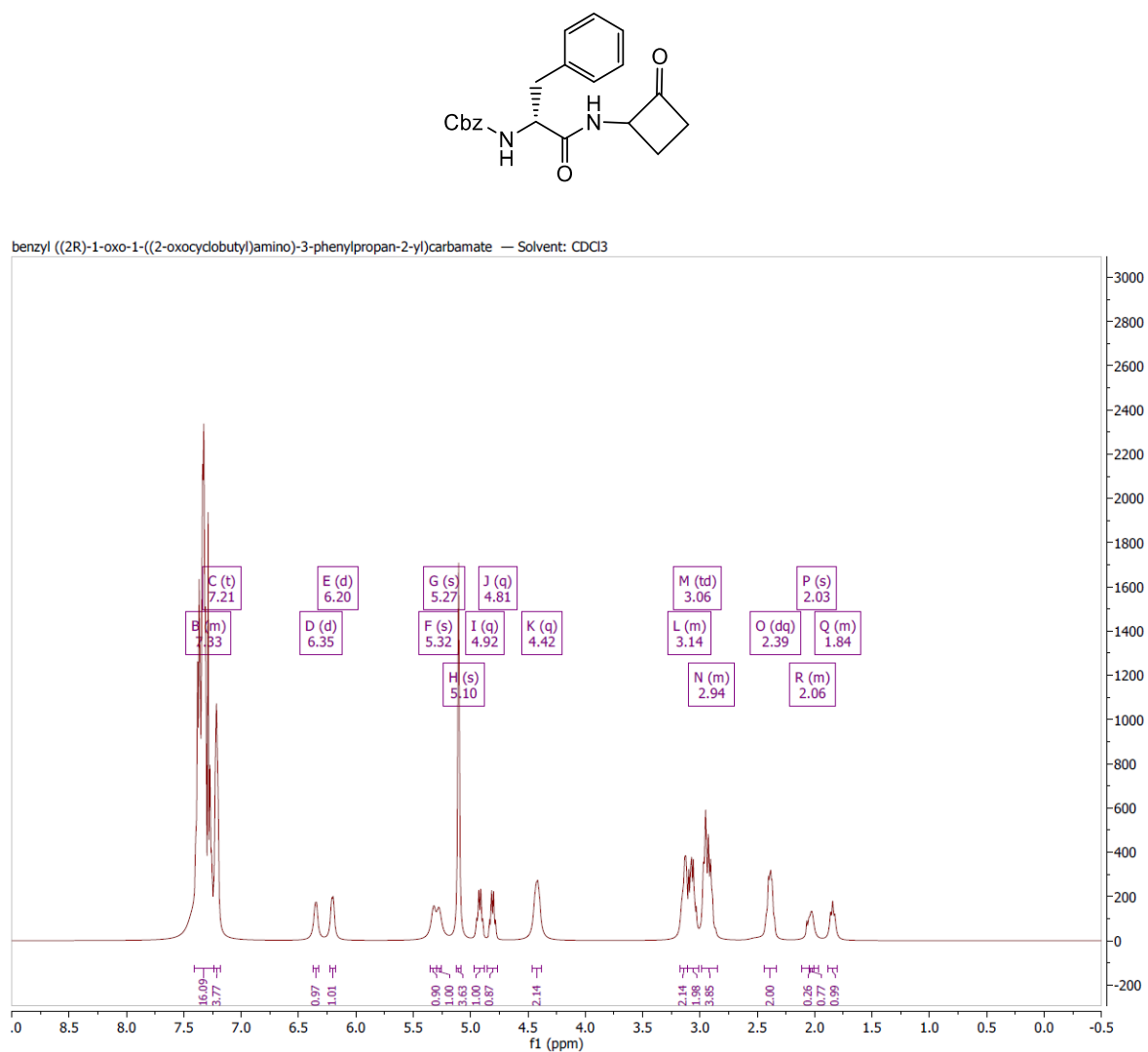


Figure S60. ¹H NMR (500 MHz CDCl₃) of benzyl ((2R)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (**3ae**).

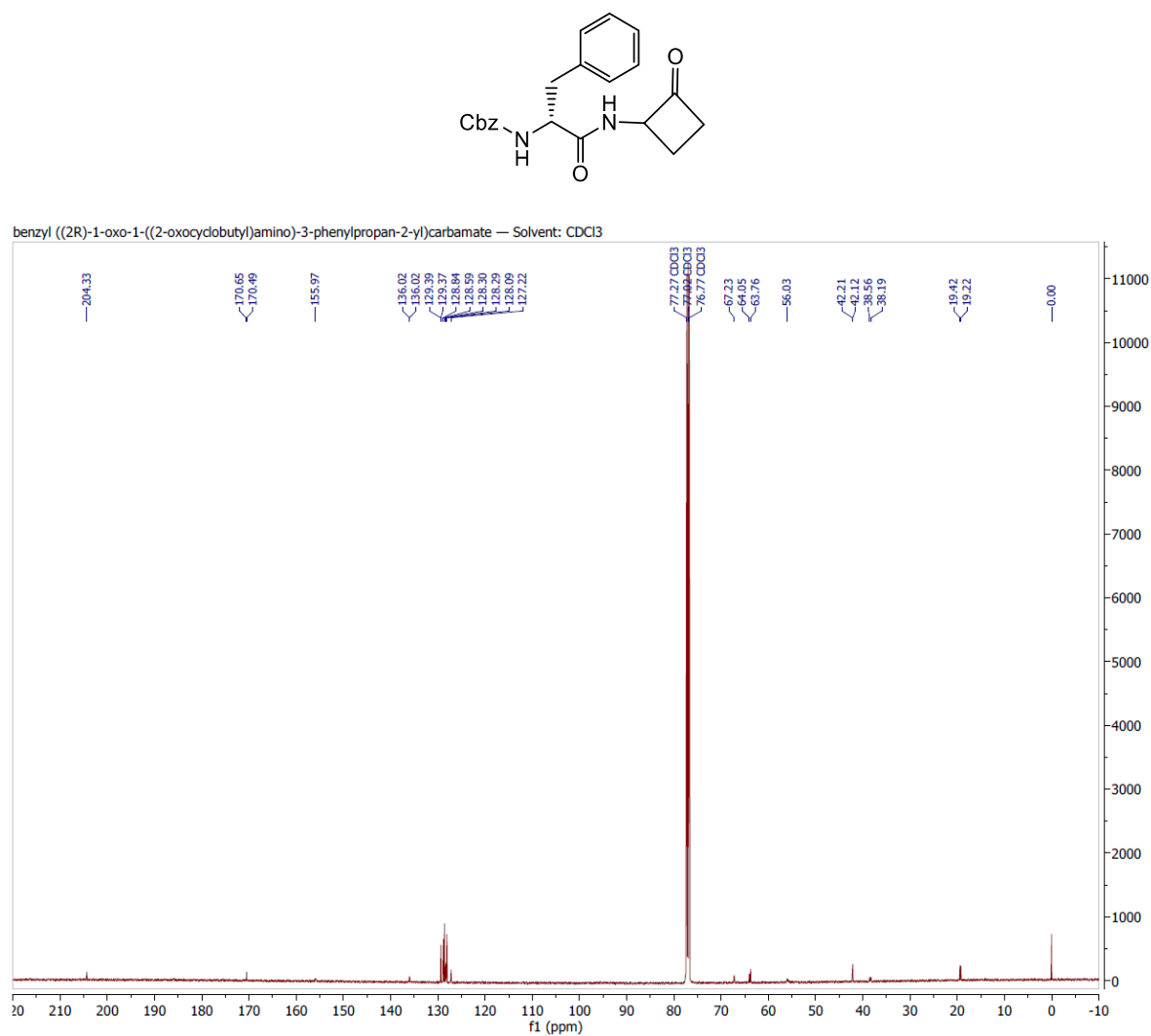


Figure S61. ¹³C NMR (126 MHz, CDCl₃) of benzyl ((2R)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (**3ae**).

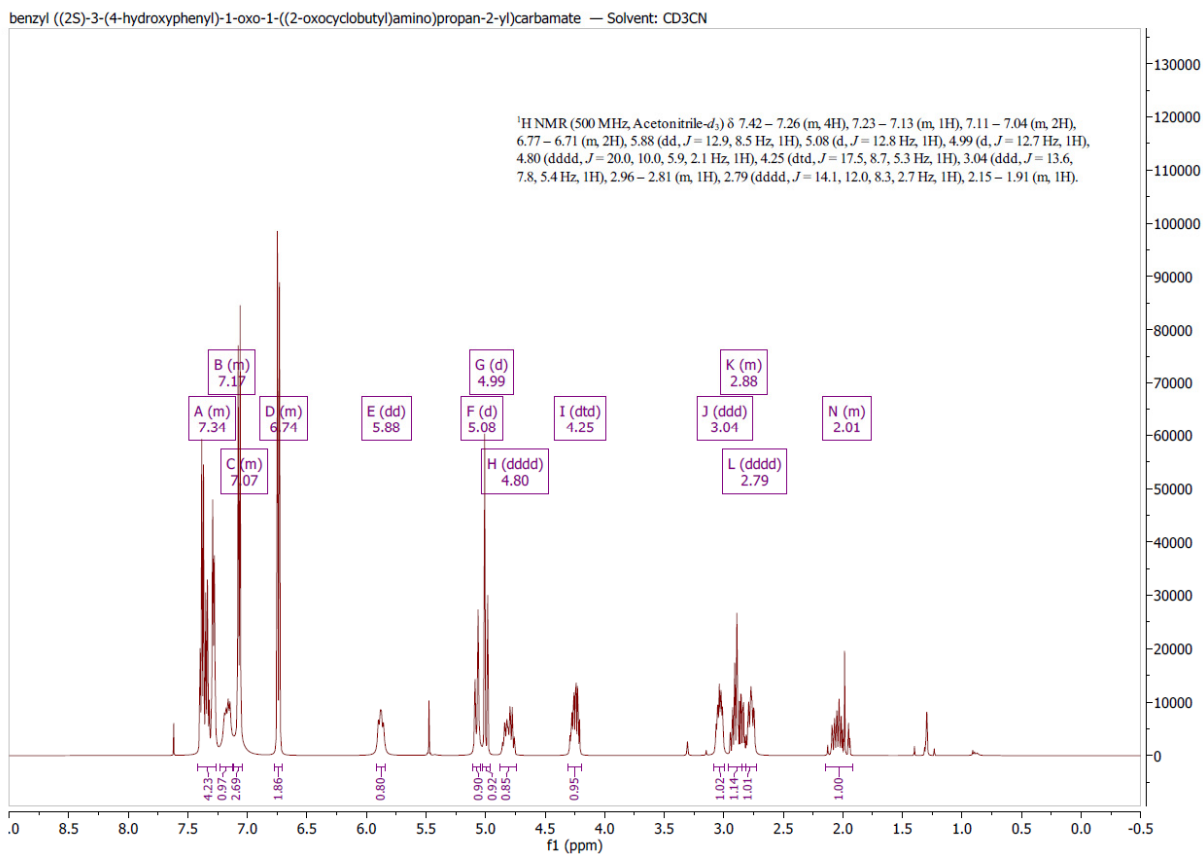
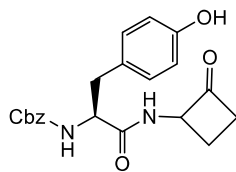


Figure S62. ¹H NMR (500 MHz CDCl₃) of benzyl ((2S)-3-(4-hydroxyphenyl)-1-oxo-1-((2-oxocyclobutyl)amino)propan-2-yl)carbamate (**3af**).

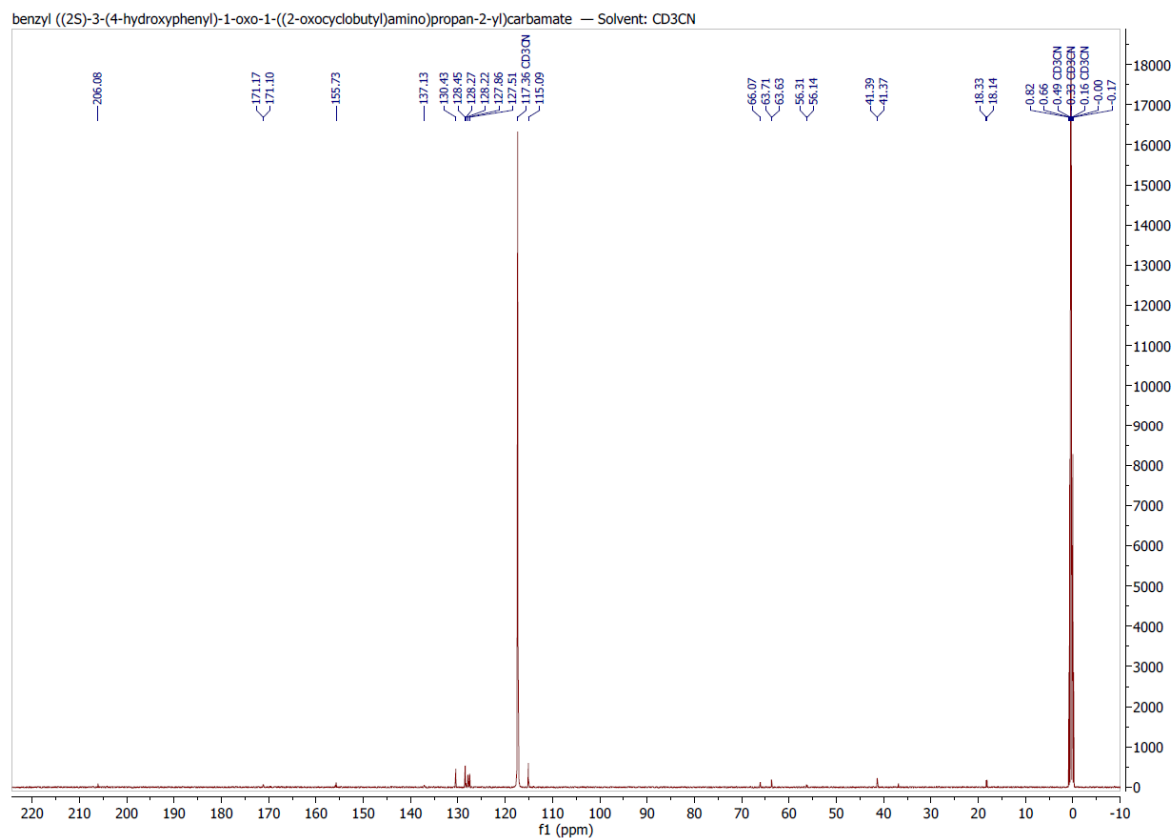
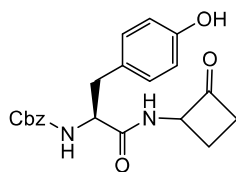


Figure S63. ¹³C NMR (126 MHz, CDCl₃) of benzyl ((2S)-3-(4-hydroxyphenyl)-1-oxo-1-((2-oxocyclobutyl)amino)propan-2-yl)carbamate (**3af**).

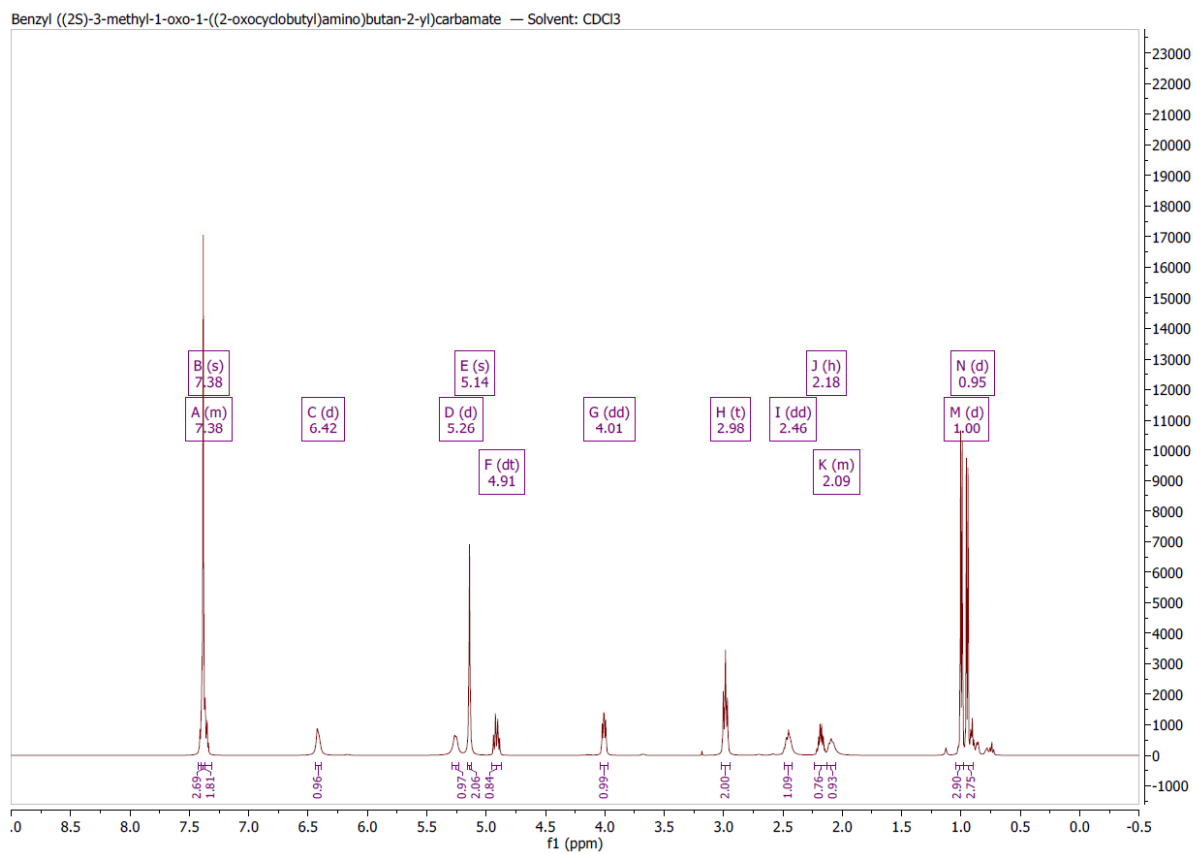
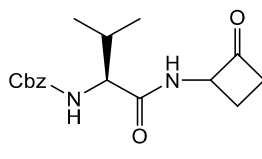


Figure S64. ¹H NMR (500 MHz CDCl₃) of benzyl ((2S)-3-methyl-1-oxo-1-((2-oxocyclobutyl)amino)butan-2-yl)carbamate (**3ag**).

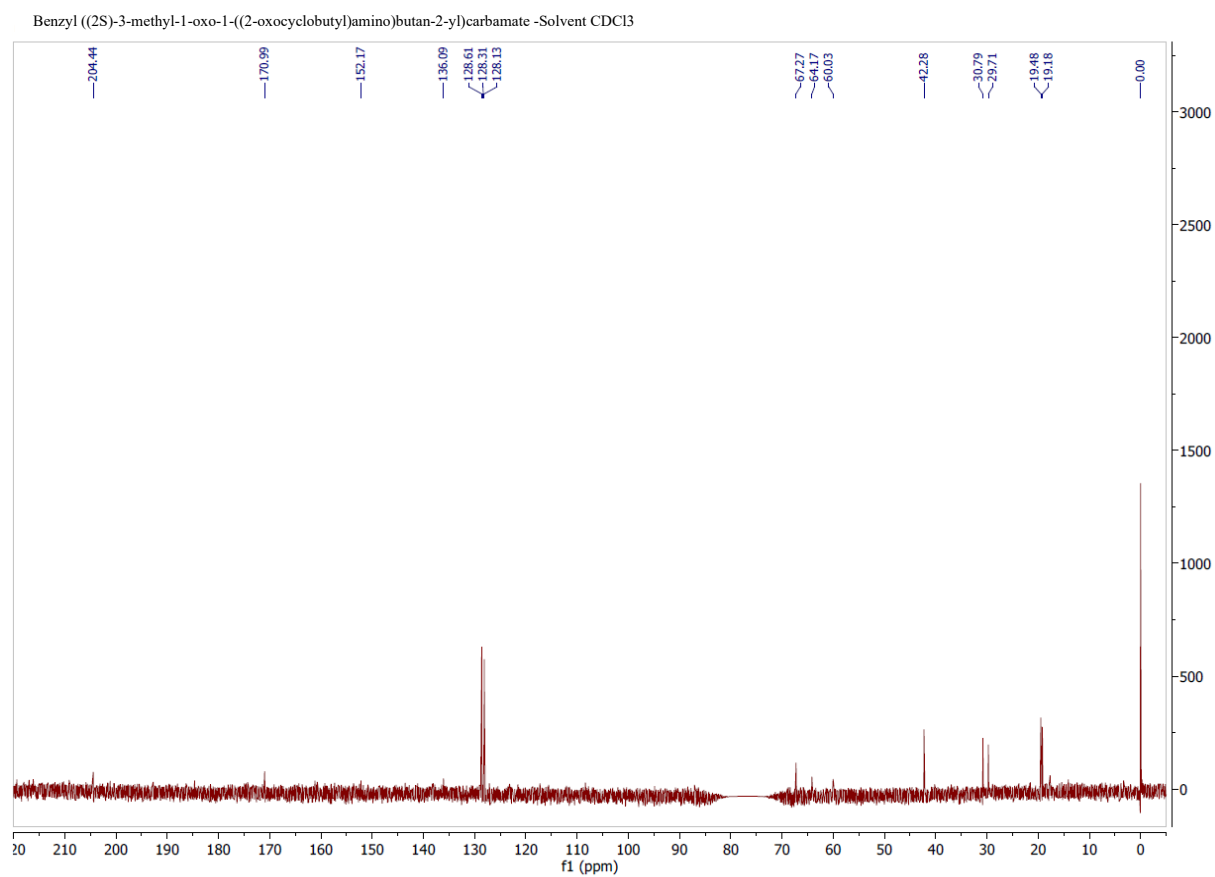
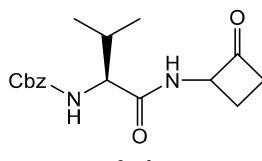


Figure S65. ¹³C NMR (126 MHz, CDCl₃) of benzyl ((2*S*)-3-methyl-1-oxo-1-((2-oxocyclobutyl)amino)butan-2-yl)carbamate (**3ag**).

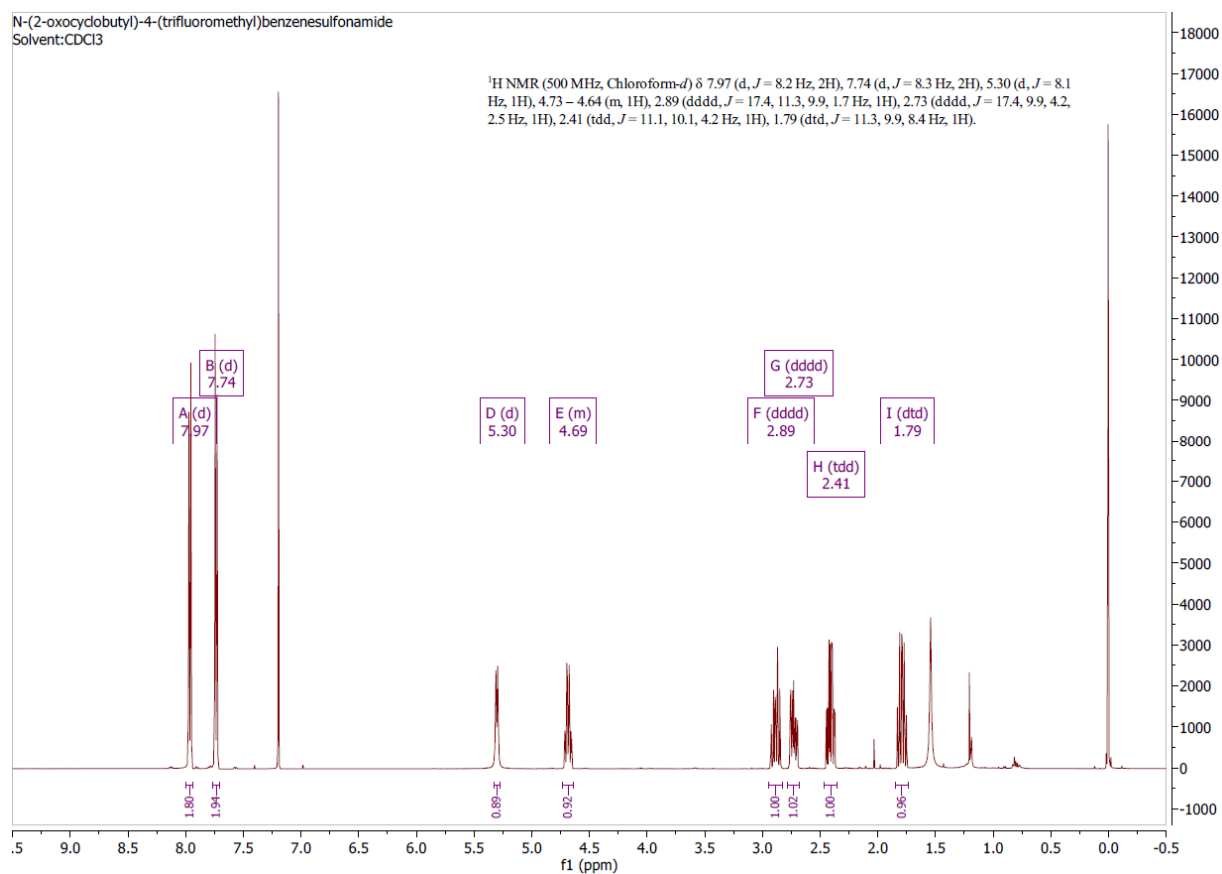
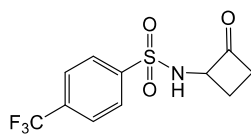


Figure S66. ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)-4-(trifluoromethyl)benzenesulfonamide (**3ah**).

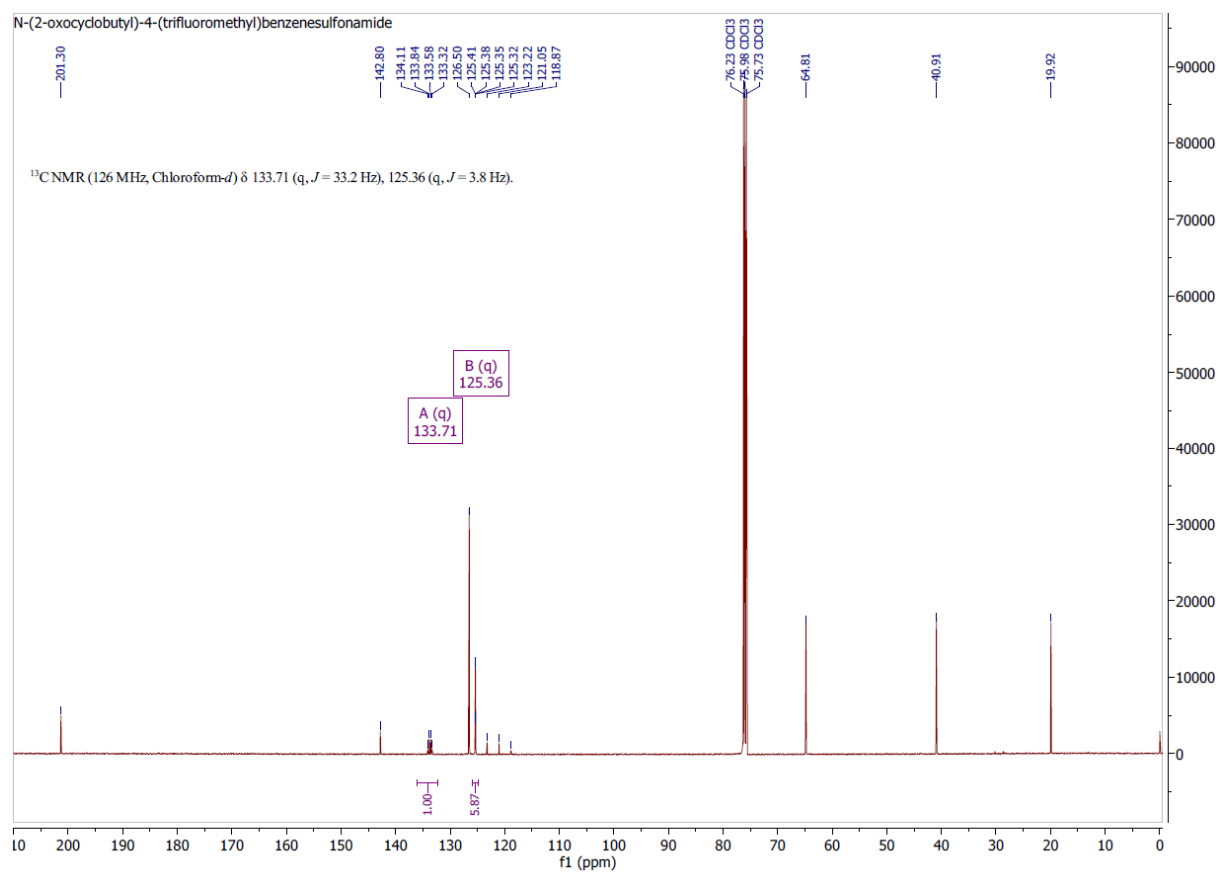
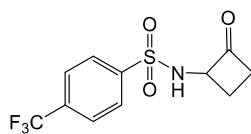


Figure S67. ^{13}C NMR (126 MHz, CDCl_3) of *N*-(2-oxocyclobutyl)-4-(trifluoromethyl)benzenesulfonamide (**3ah**).

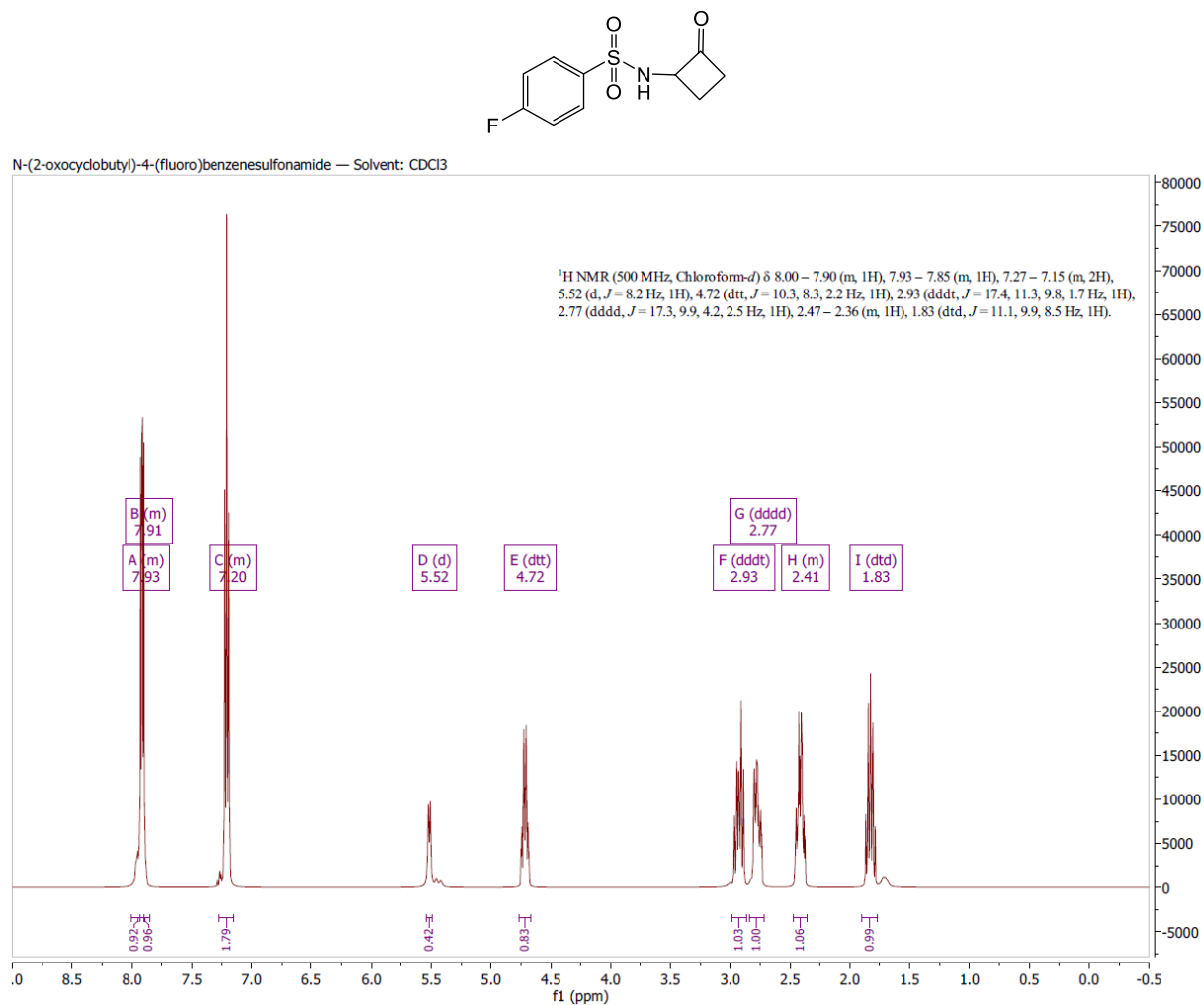


Figure S68. ¹H NMR (500 MHz CDCl₃) of *N*-(2-oxocyclobutyl)-4-(fluoro)benzenesulfonamide (**3aj**).

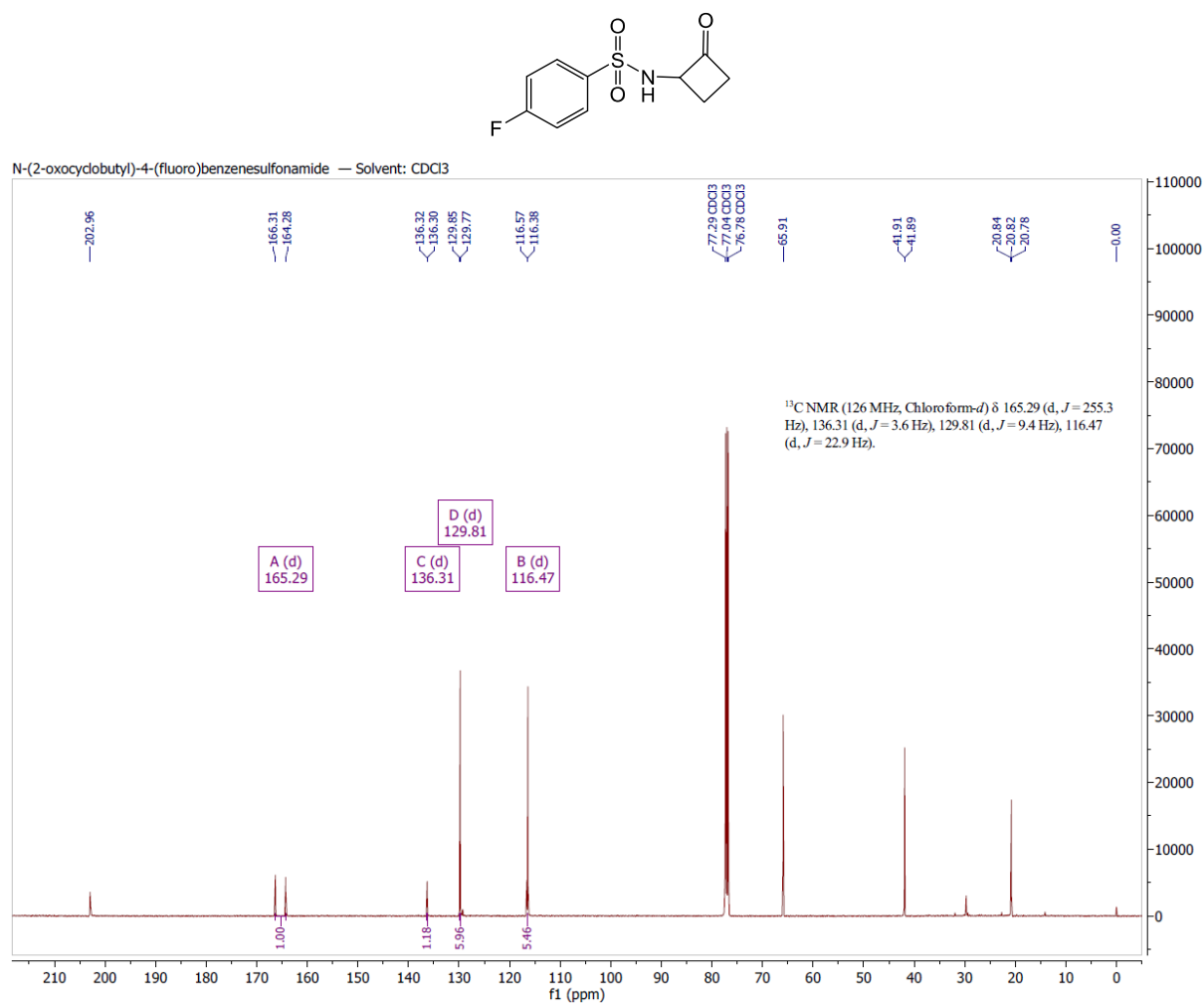
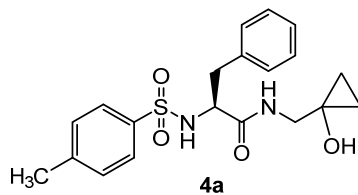


Figure S69. ¹³C NMR (126 MHz, CDCl₃) of *N*-(2-oxocyclobutyl)-4-(fluoro)benzenesulfonamide (**3aj**).



(S)-N-((1-hydroxycyclopropyl)methyl)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide — Solvent: CDCl₃

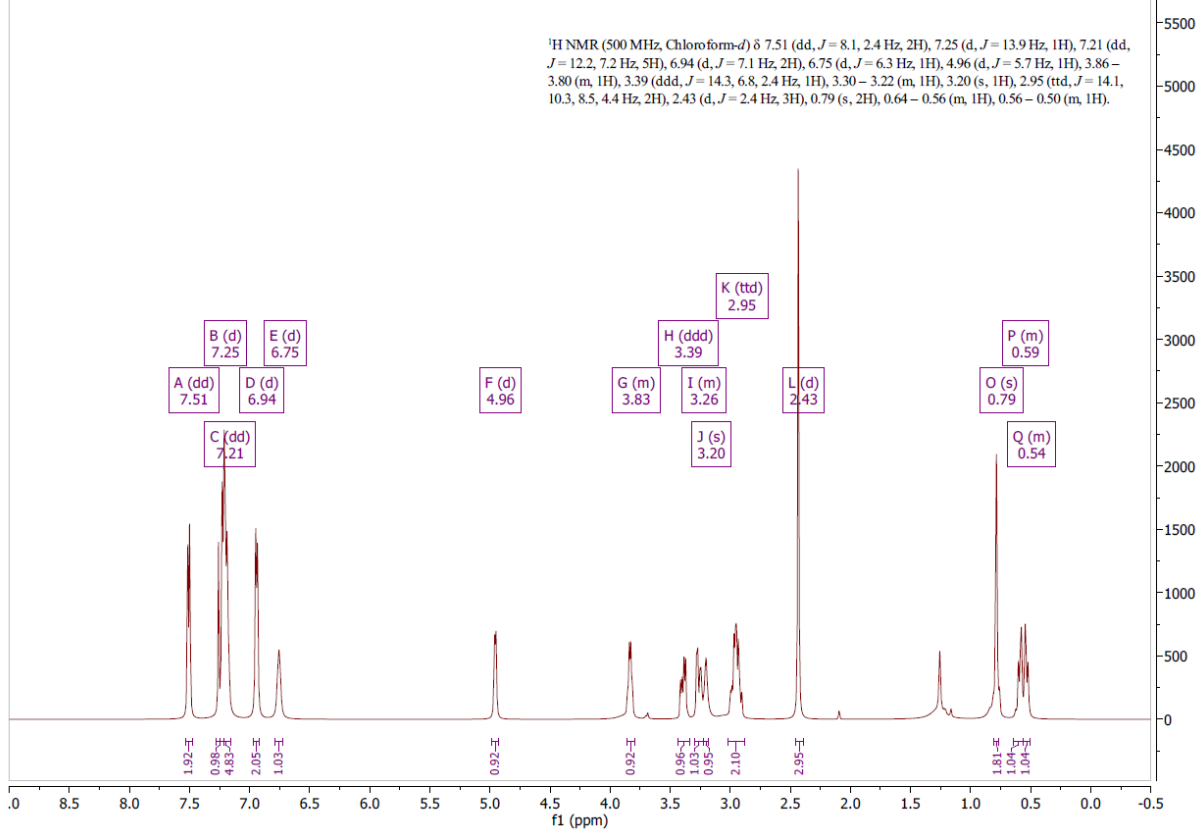


Figure S70. ¹H NMR (500 MHz CDCl₃) of (S)-N-((1-hydroxycyclopropyl)methyl)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**4a**).

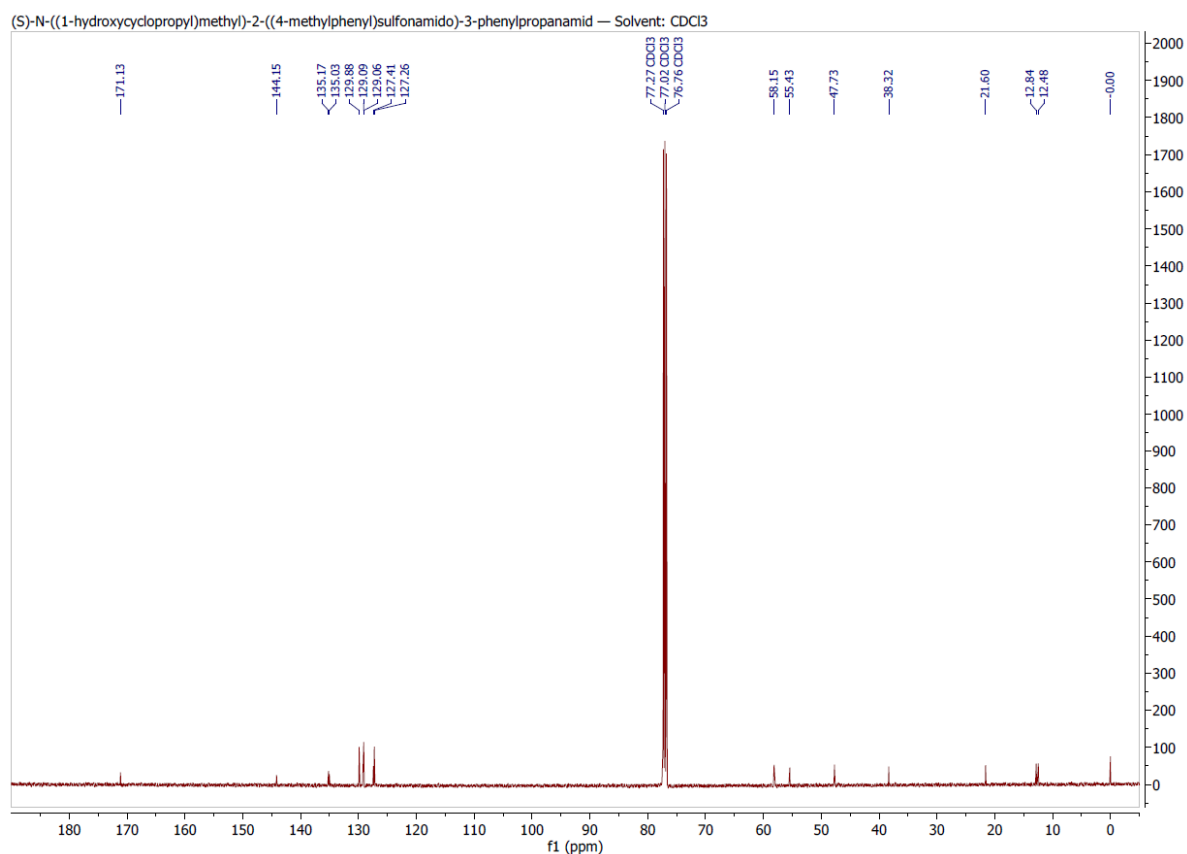
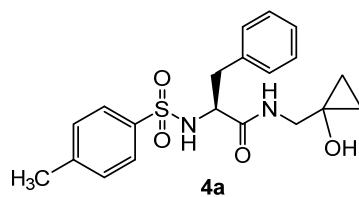


Figure S71. ¹³C NMR (126 MHz, CDCl₃) of (S)-N-((1-hydroxycyclopropyl)methyl)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**4a**).

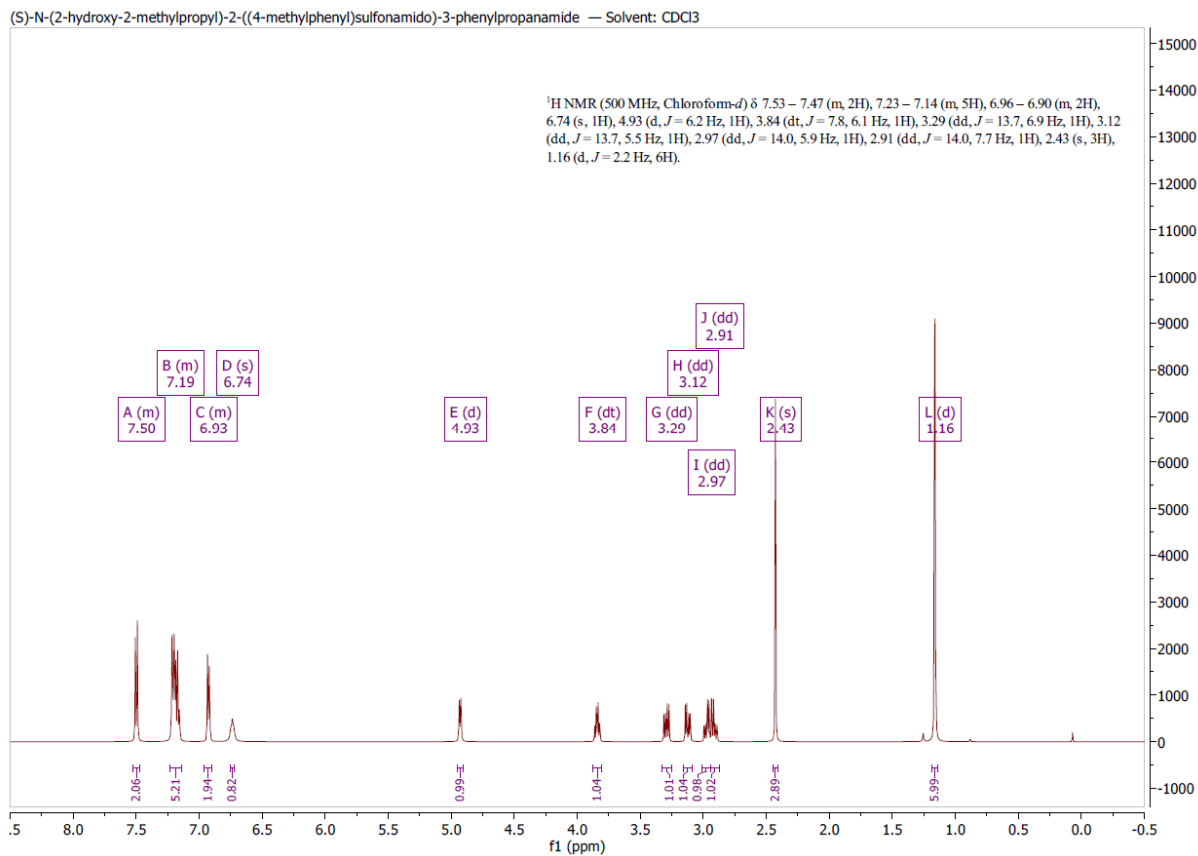
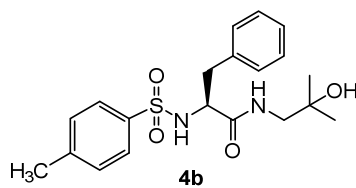


Figure S72. ¹H NMR (500 MHz CDCl₃) of (S)-N-(2-hydroxy-2-methylpropyl)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**4b**).

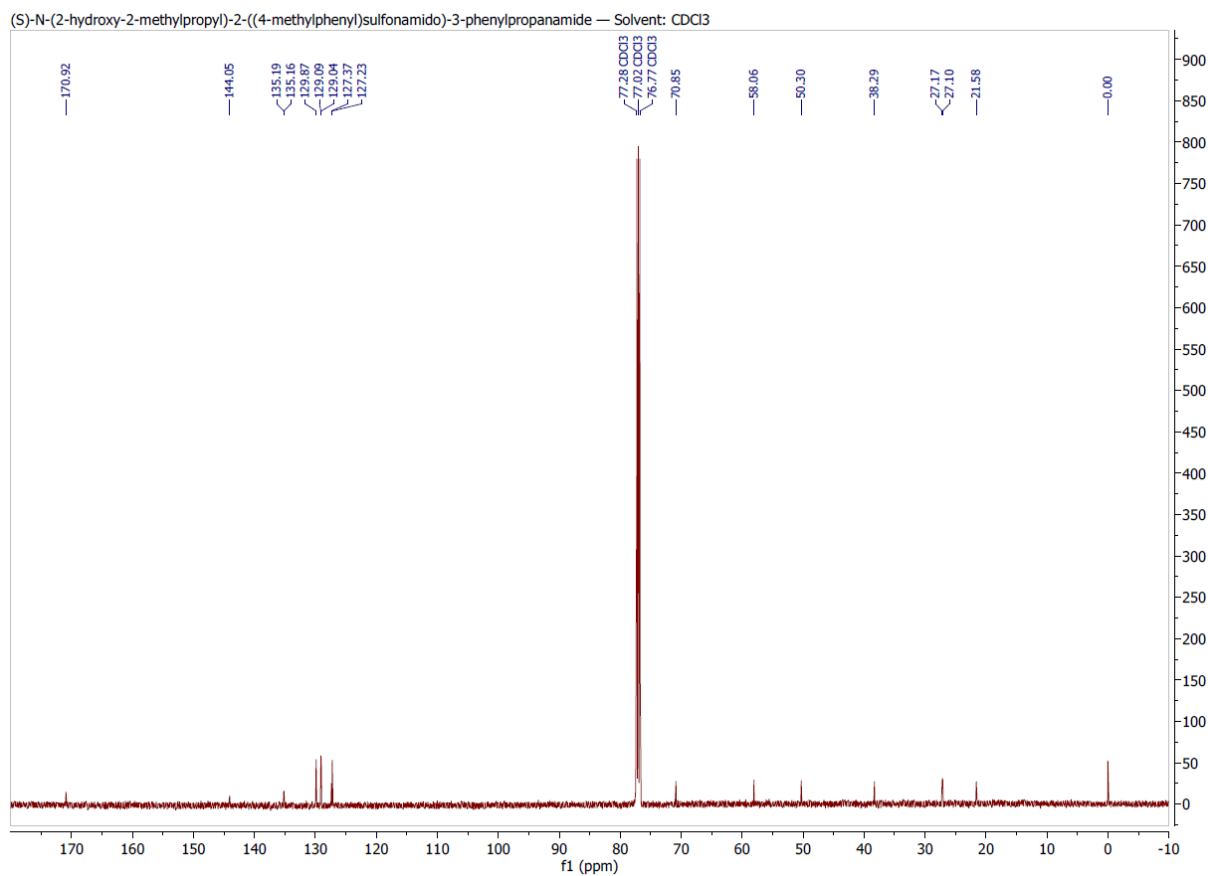
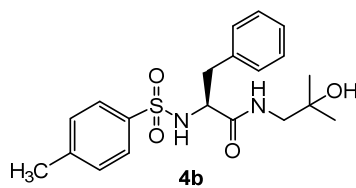


Figure S73. ¹³C NMR (126 MHz, CDCl₃) of (S)-N-(2-hydroxy-2-methylpropyl)-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**4b**).

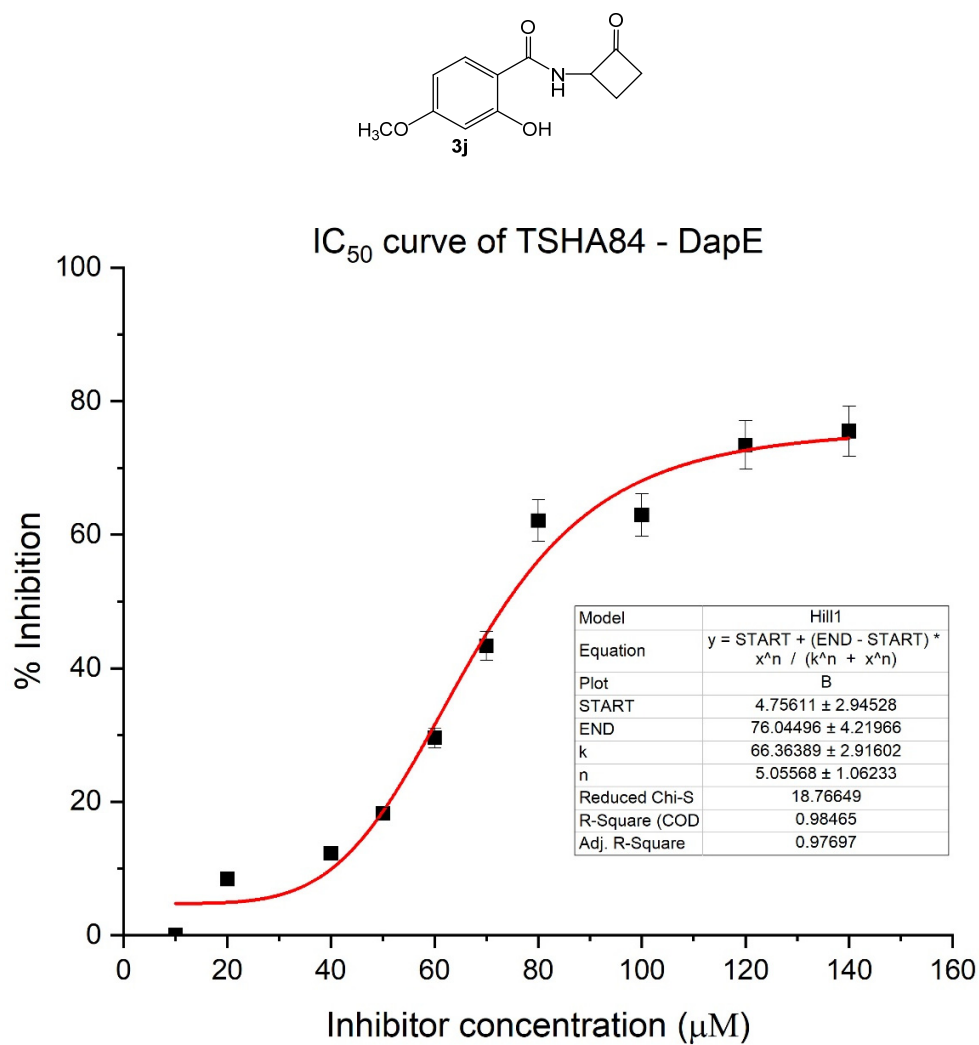


Figure S74. IC_{50} plot of 2-hydroxy-4-methoxy-*N*-(2-oxocyclobutyl)benzamide (**3j**).

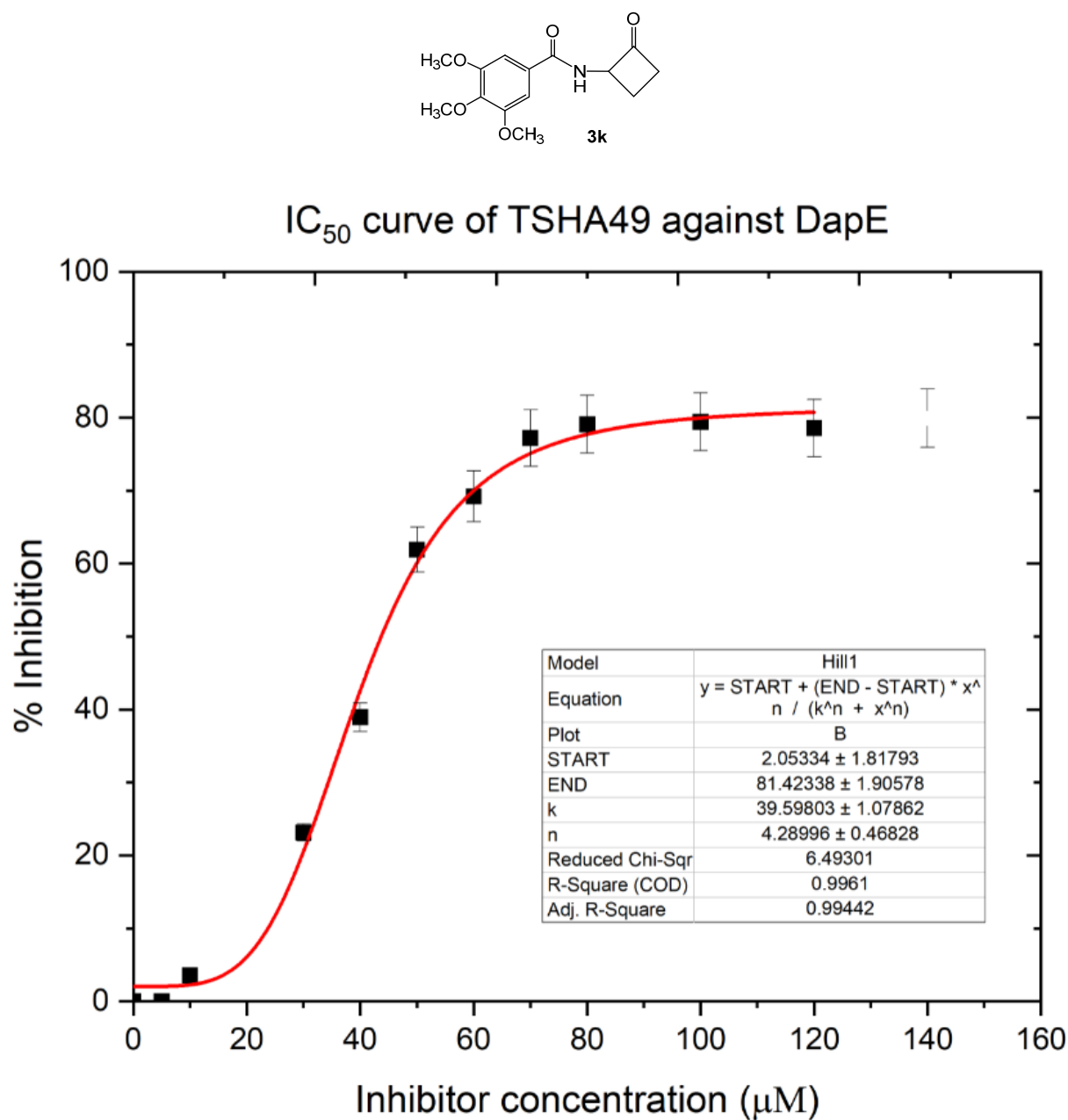


Figure S75. IC₅₀ plot of 3,4,5-trimethoxy-*N*-(2-oxocyclobutyl)benzamide (**3k**).

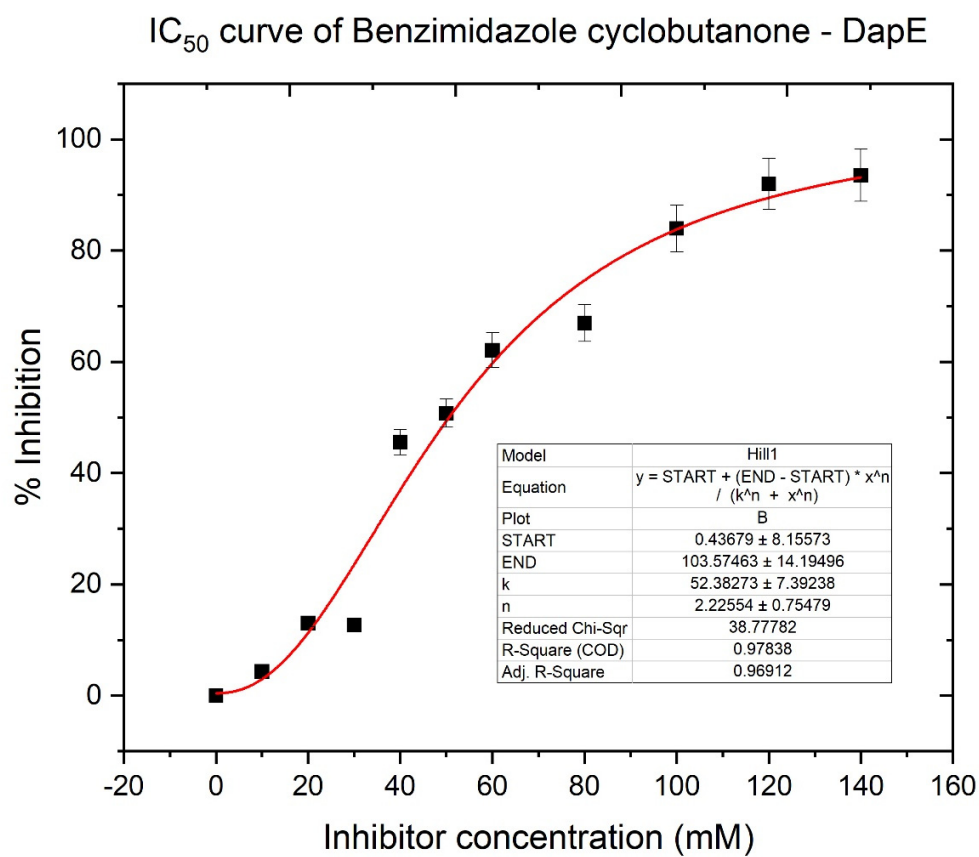
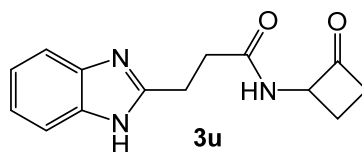


Figure S76. IC₅₀ plot of 3-(1*H*-benzo[*d*]imidazol-2-yl)-*N*-(2-oxocyclobutyl)propanamide (**3u**).

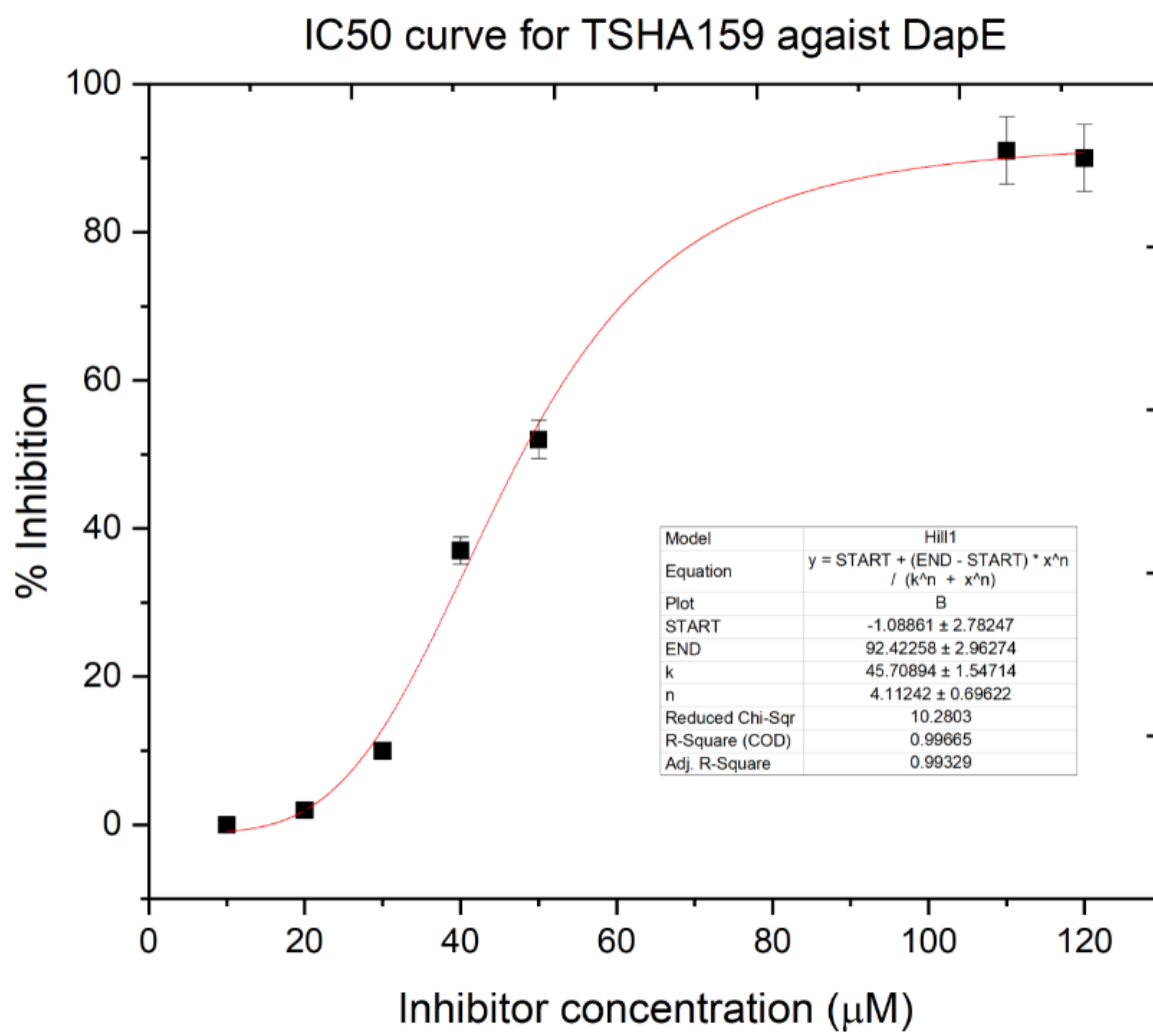
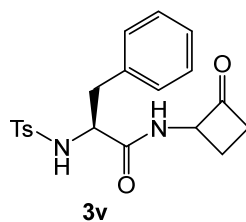


Figure S77. IC₅₀ plot of (2*S*)-2-((4-methylphenyl)sulfonamido)-*N*-(2-oxocyclobutyl)-3-phenylpropanamide (**3v**).

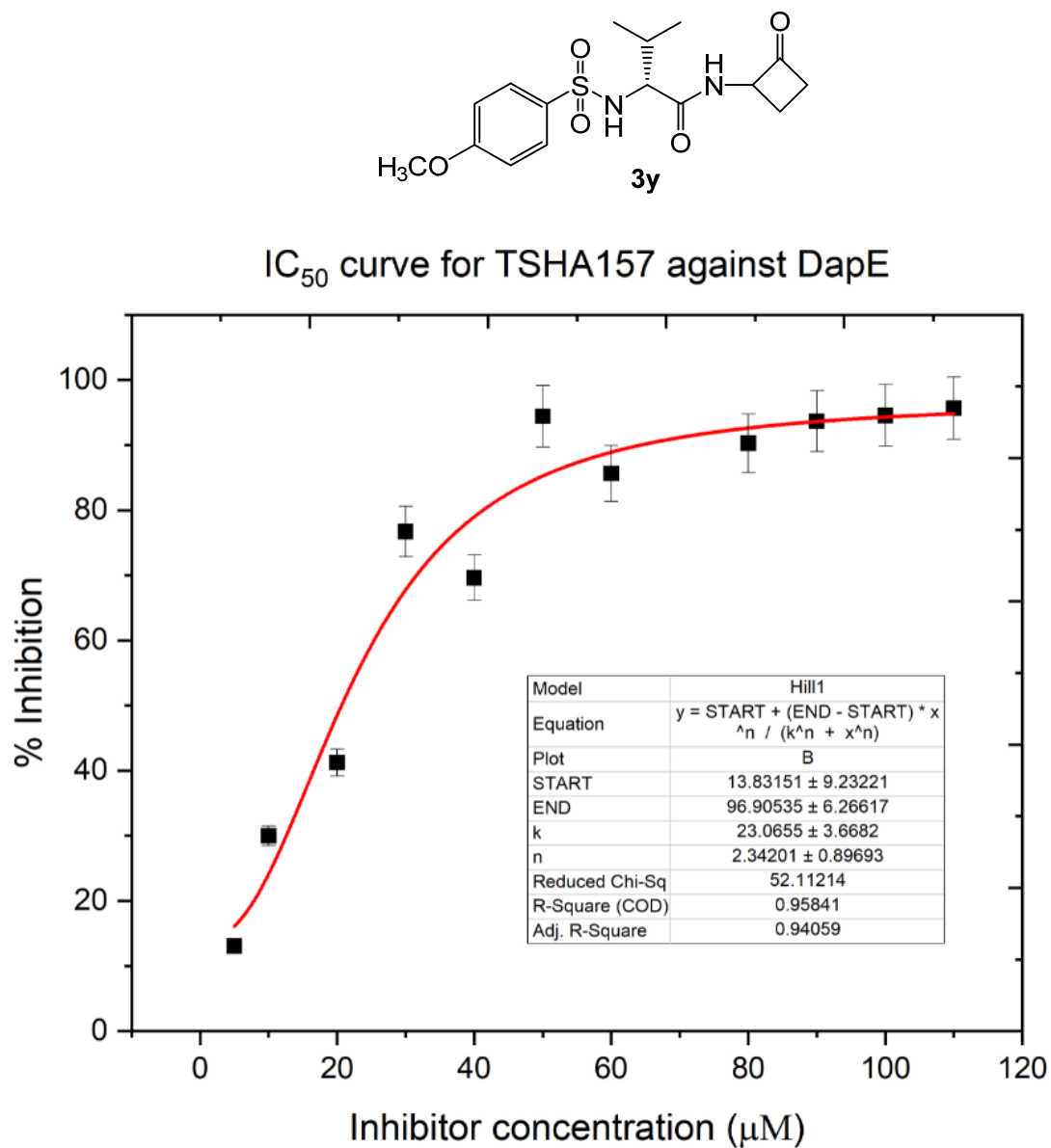


Figure S78. IC₅₀ plot of (2*R*)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-*N*-(2-oxocyclobutyl)butanamide (**3y**).

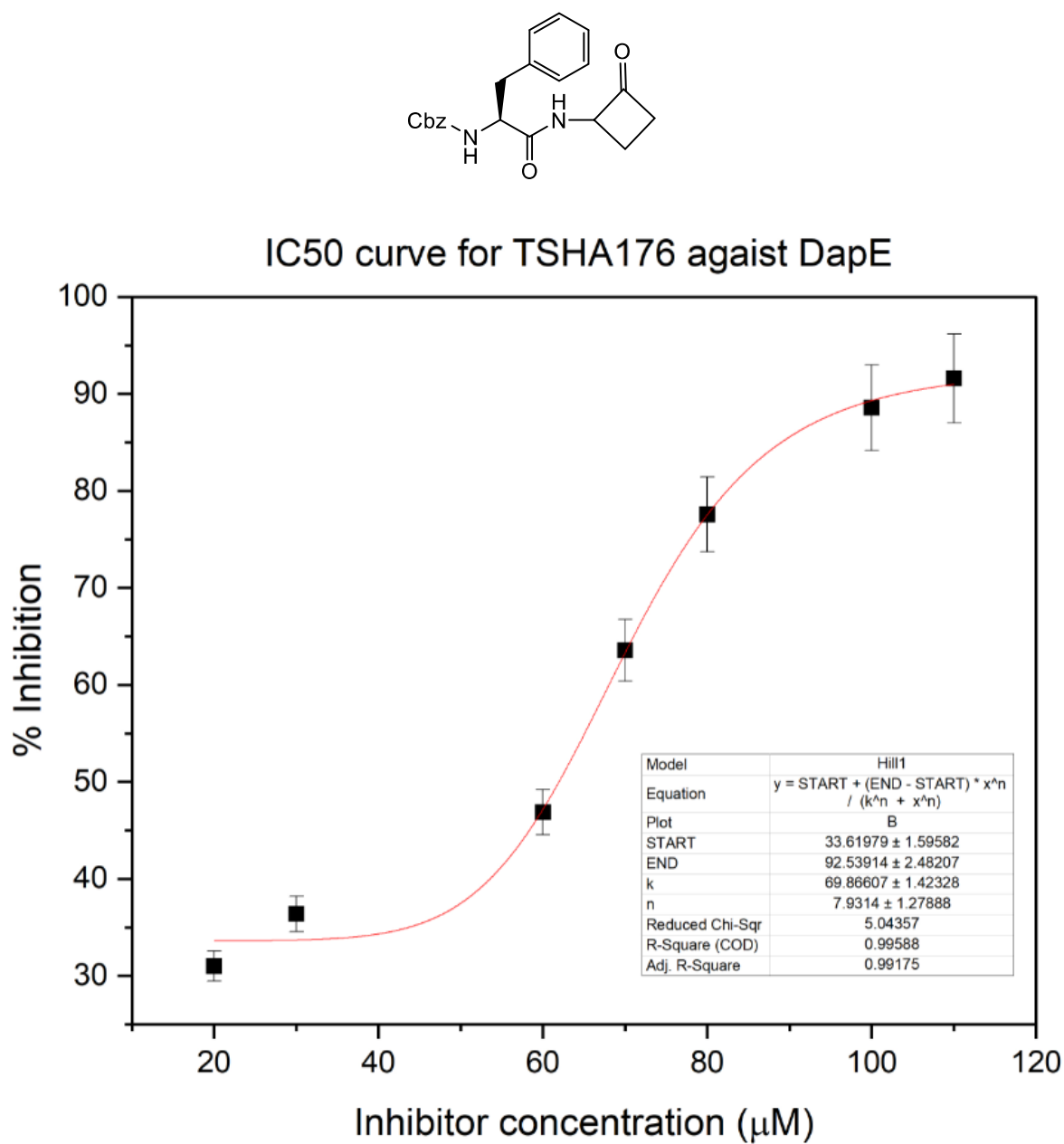


Figure S79. IC₅₀ plot of benzyl ((2*R*)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (**3ad**).

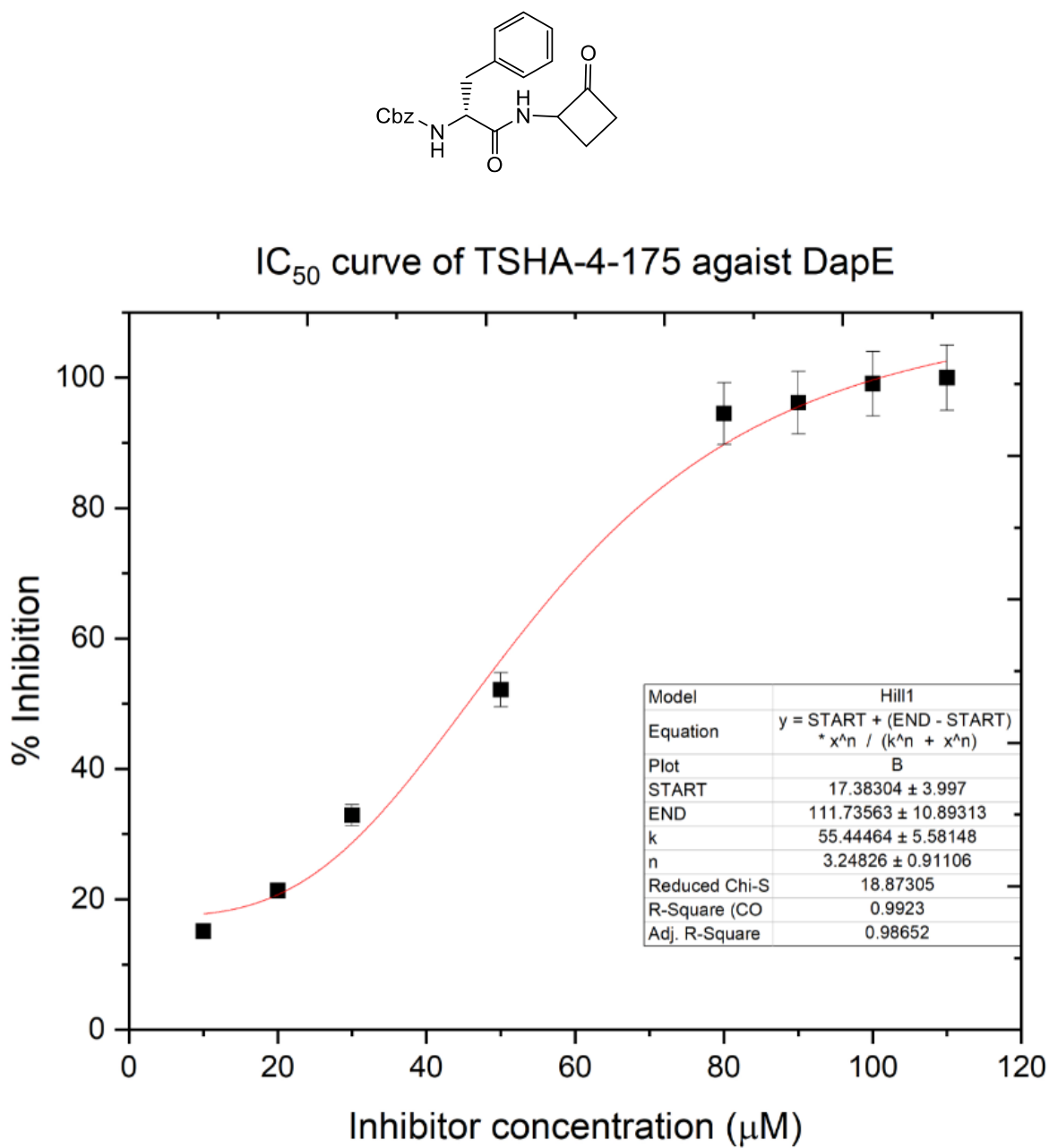


Figure S80. IC_{50} plot of benzyl ((2*R*)-1-oxo-1-((2-oxocyclobutyl)amino)-3-phenylpropan-2-yl)carbamate (**3ae**).

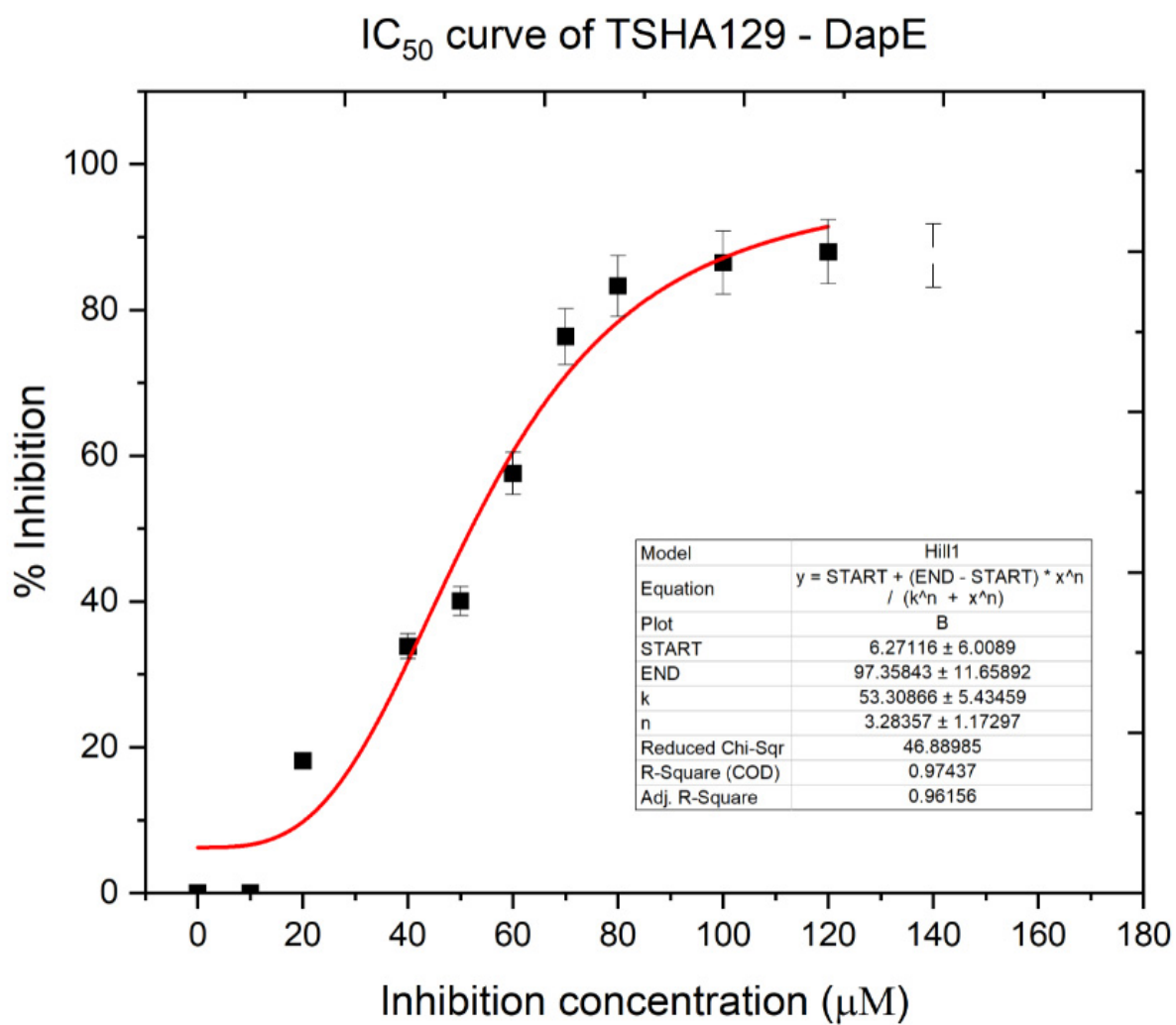
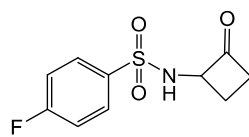


Figure S81. IC₅₀ plot of *N*-(2-oxocyclobutyl)-4-(fluoro)benzenesulfonamide (**3ah**).

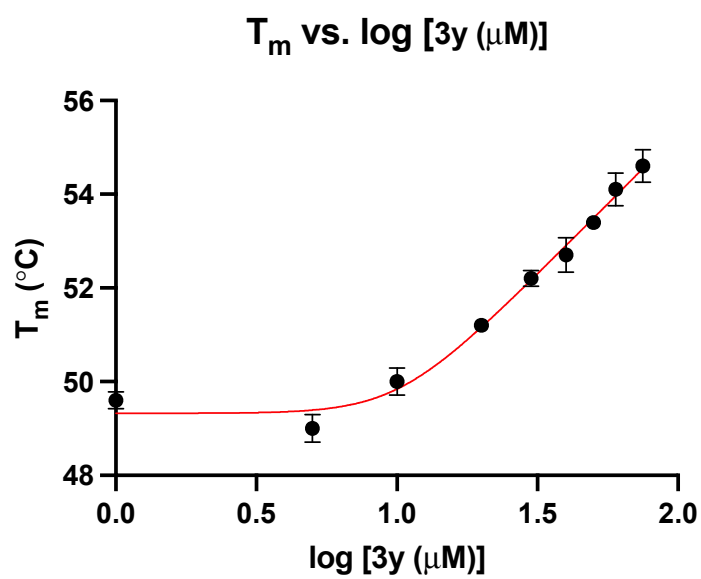


Figure S82. Thermal Shift Assay Graph of T_m vs. $\log [3y (\mu M)]$.

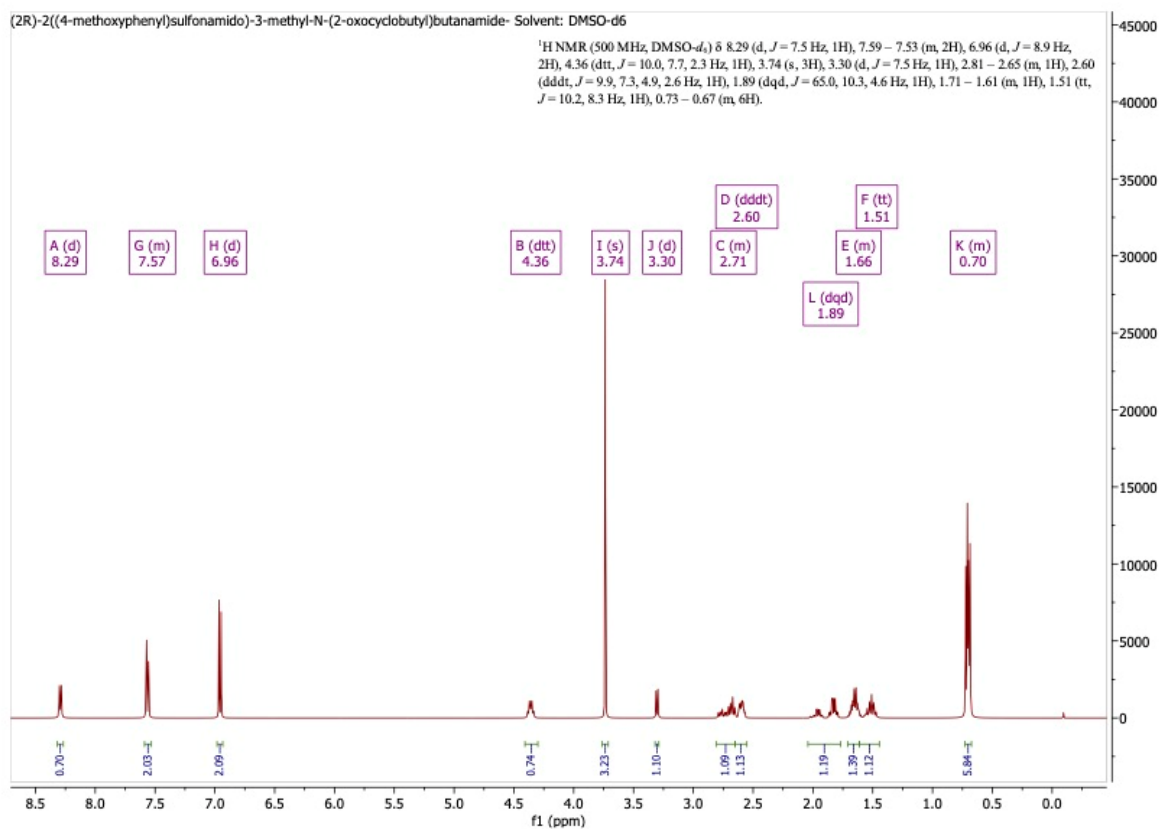


Figure S83. ¹H NMR (500 MHz DMSO-d₆) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).

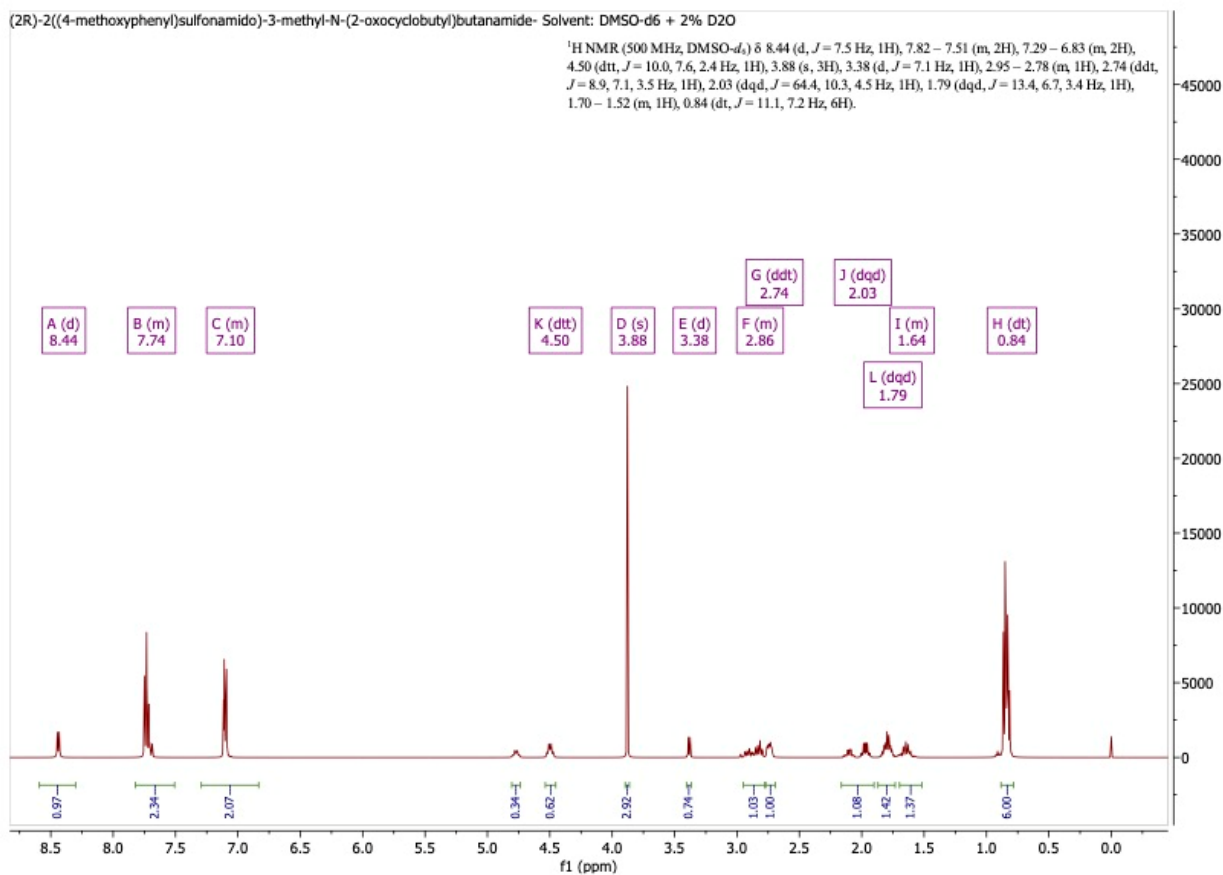


Figure S84. ¹H NMR (500 MHz DMSO-d₆ + 2% D₂O) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (3y).

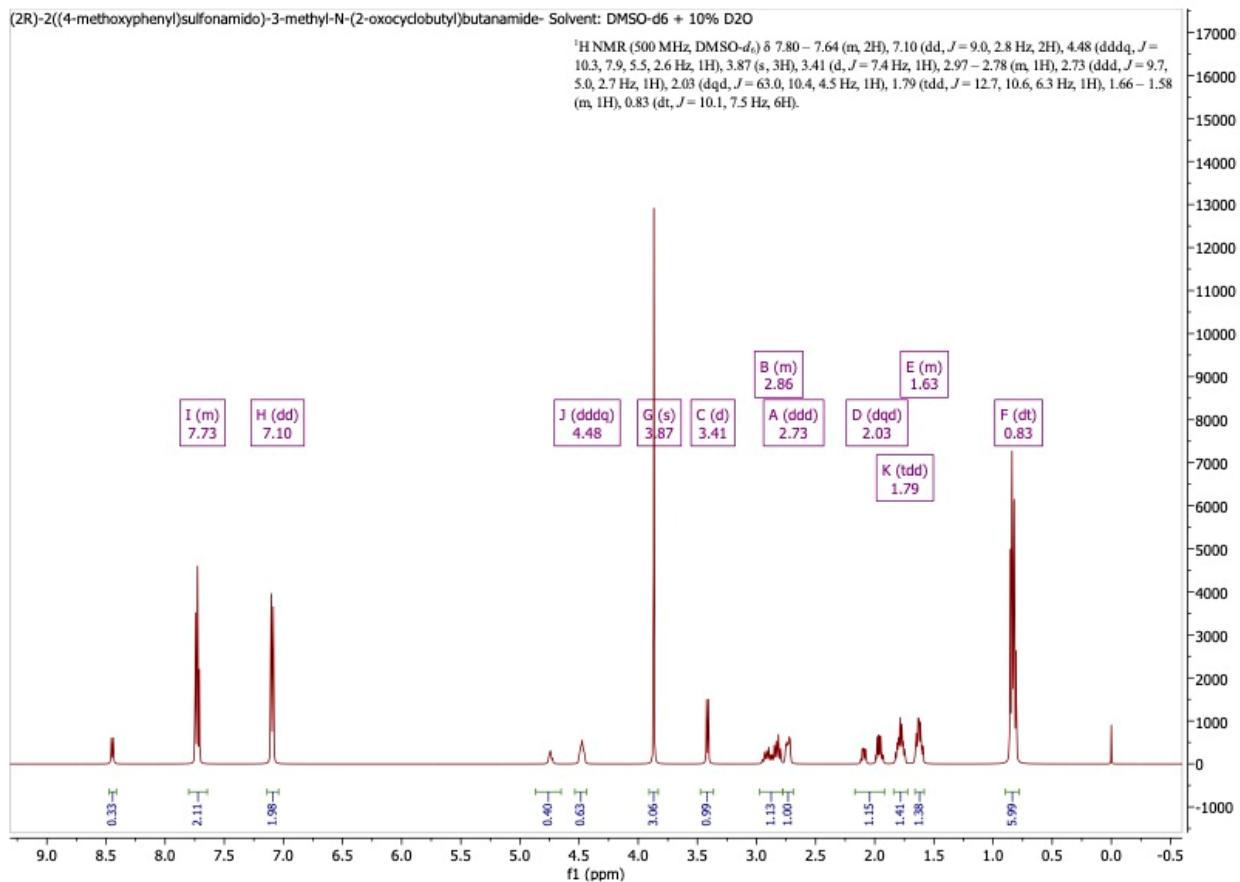


Figure S85. ¹H NMR (500 MHz DMSO-d₆ + 10% D₂O) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).

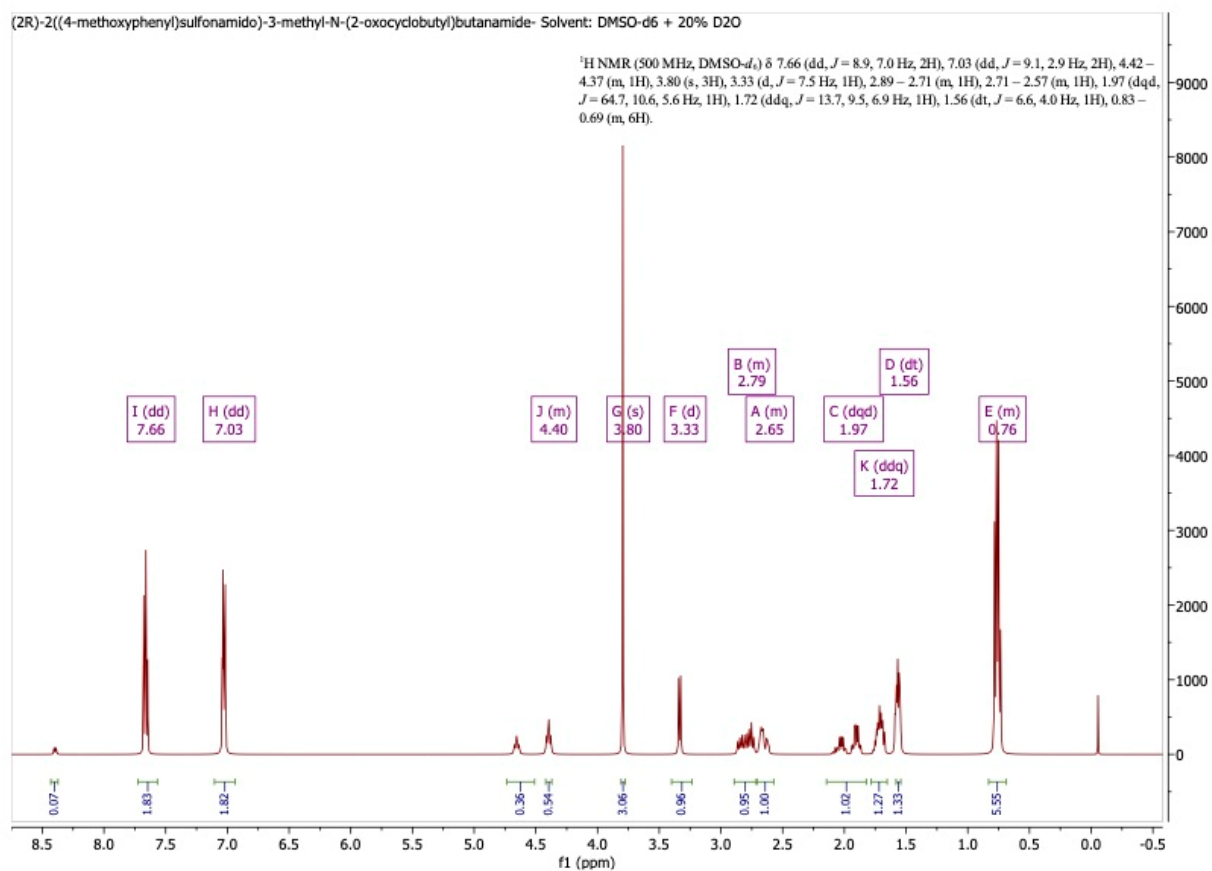


Figure S86. ¹H NMR (500 MHz DMSO-d₆ + 20% D₂O) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).

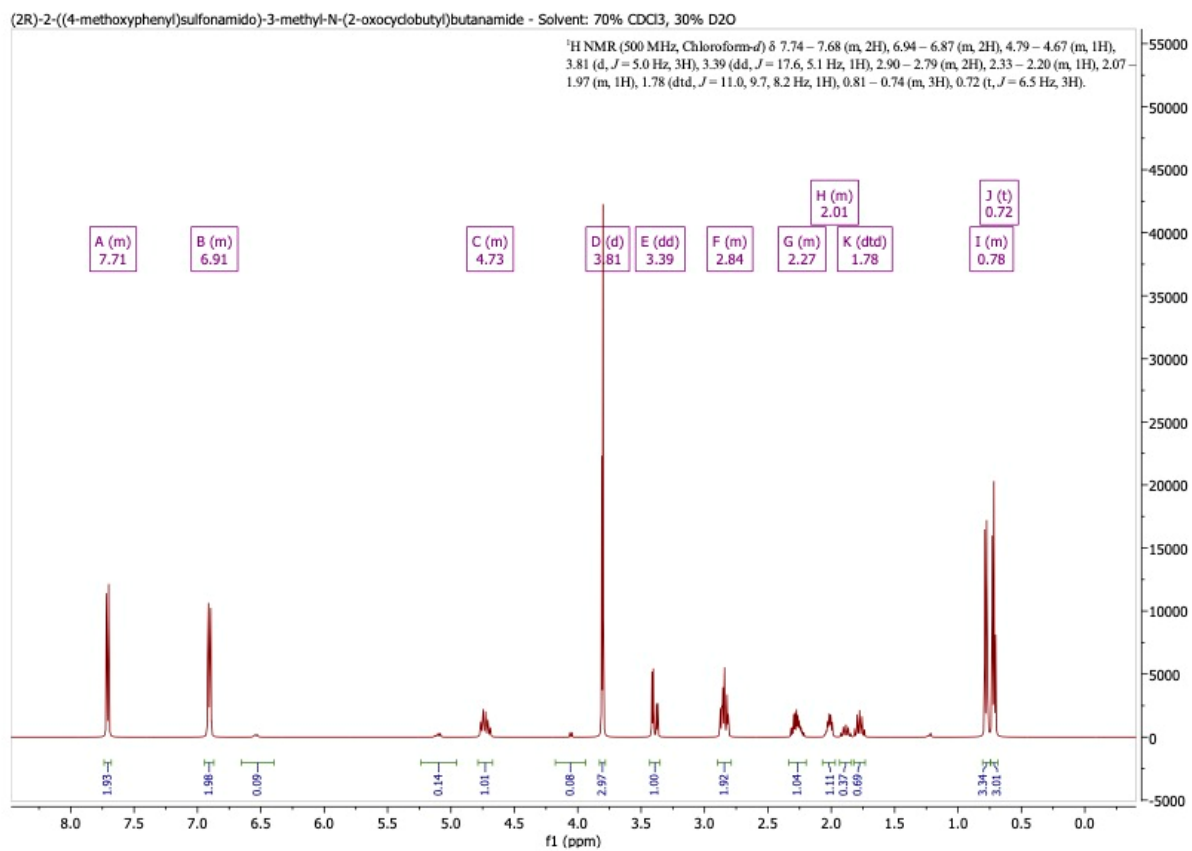


Figure S87. ¹H NMR (500 MHz CDCl₃ + 30% D₂O) of (2R)-2-((4-methoxyphenyl)sulfonamido)-3-methyl-N-(2-oxocyclobutyl)butanamide (**3y**).