

ChemistrySelect

Supporting Information

Unnatural Lysines with Reduced Sidechain *N*-Basicity: Synthesis of *N*-trifluoroethyl Substituted Lysine and Homologs

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Supporting Information

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(n = 2, 26.1-27.1 min).....S29

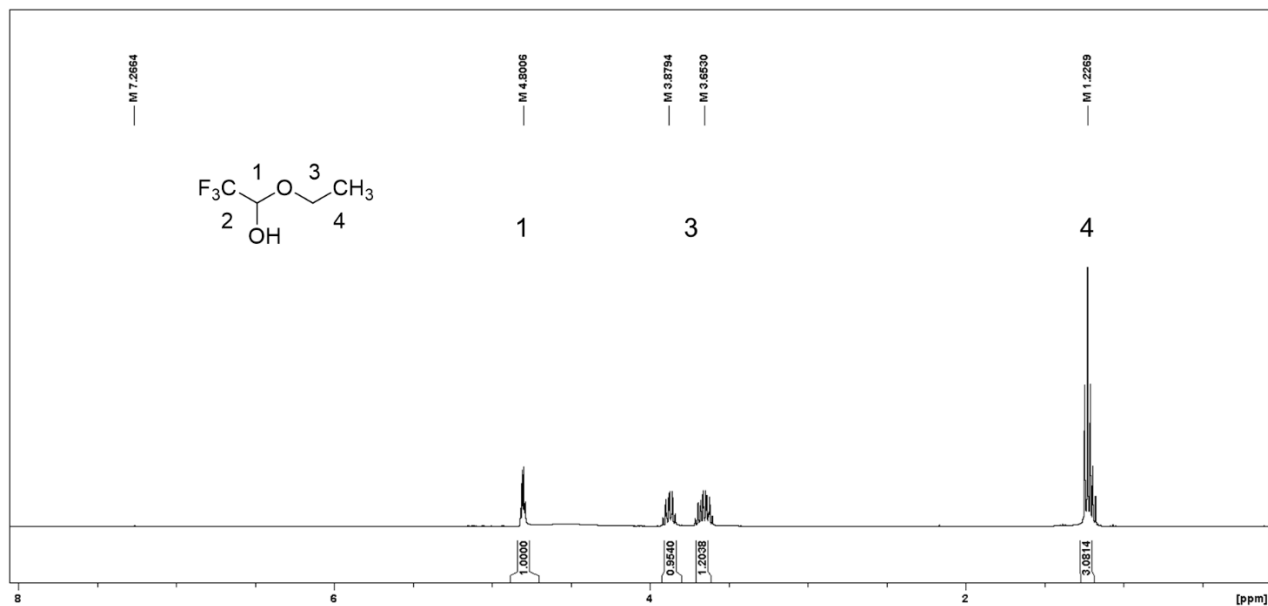


Figure S1. Trifluoroacetaldehyde ethyl hemiacetal (^1H , pulse prog. *zg30*, CDCl_3 , 400 MHz, residual internal std. CHCl_3 (δ 7.26)).

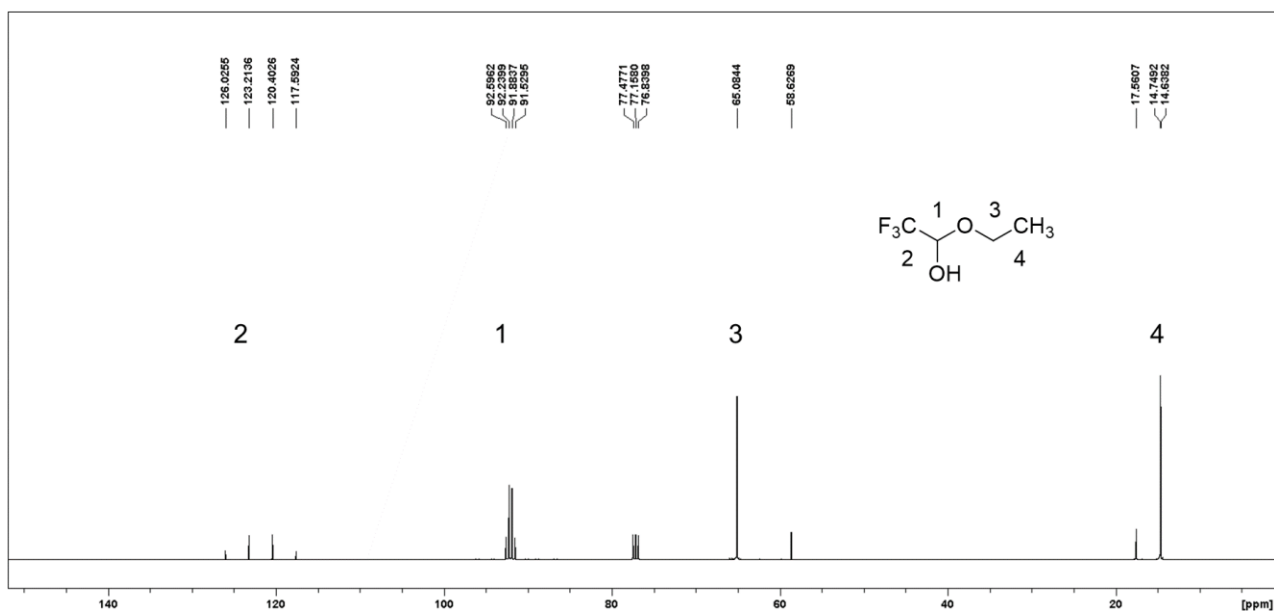


Figure S2. Trifluoroacetaldehyde ethyl hemiacetal (^{13}C , pulse prog. *zgpg30*, CDCl_3 , 400 MHz, residual internal std. CDCl_3 (δ 77.48, 77.16, 76.84), residual EtOH (δ 58.63, 17.56)).

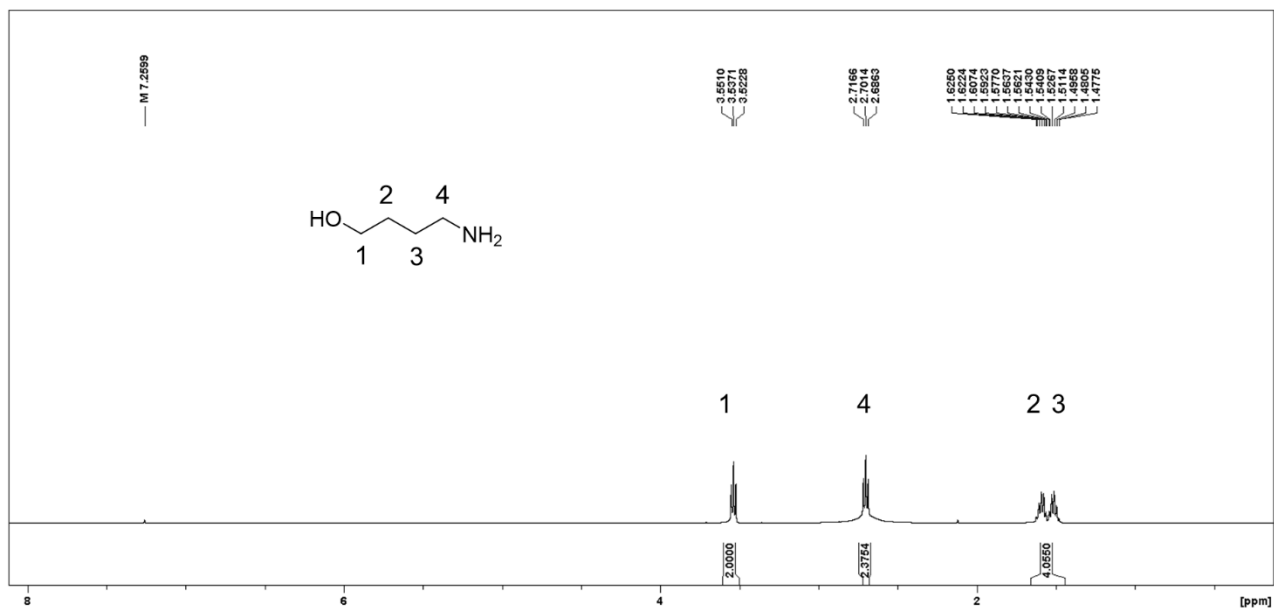


Figure S3. 4-Amino-butan-1-ol (**1**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26)).

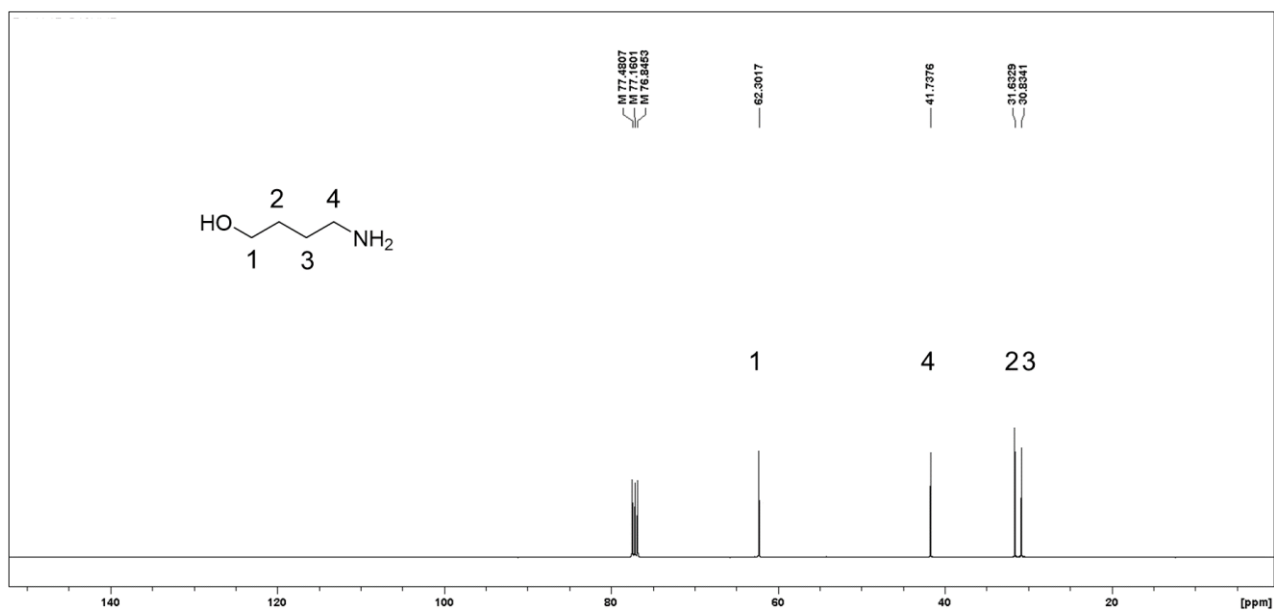


Figure S4. 4-Amino-butan-1-ol (**1**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.48, 77.16, 76.84)).

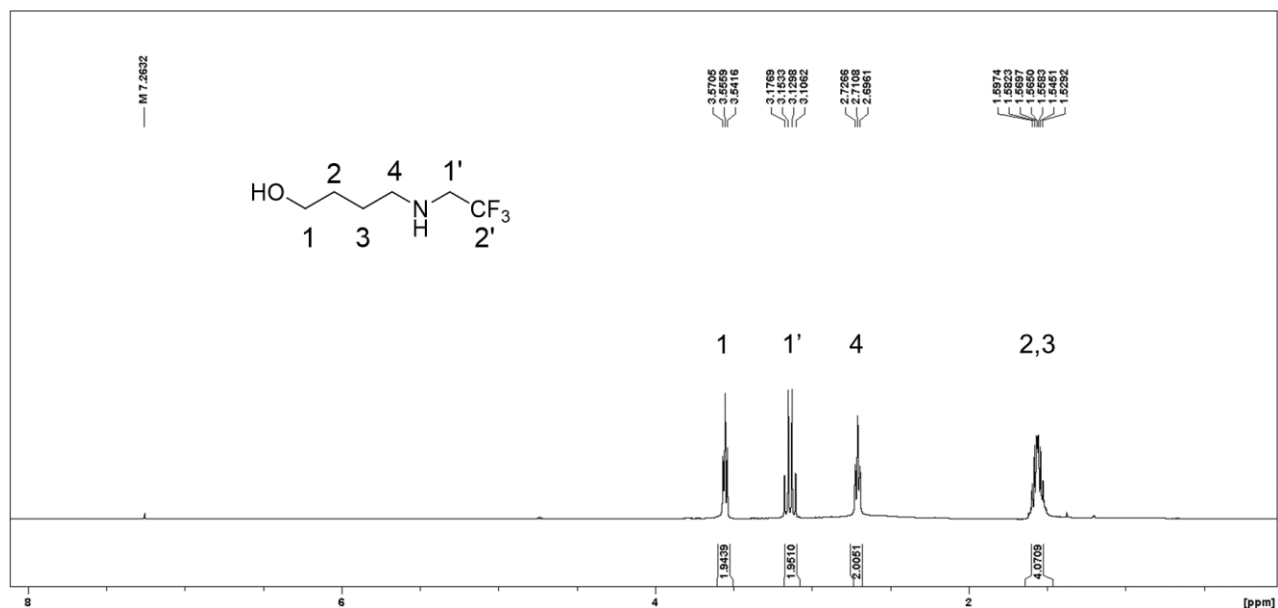


Figure S5. 4-((2,2,2-Trifluoroethyl)amino)butan-1-ol (**2**) (¹H, pulse prog. zg30, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26)).

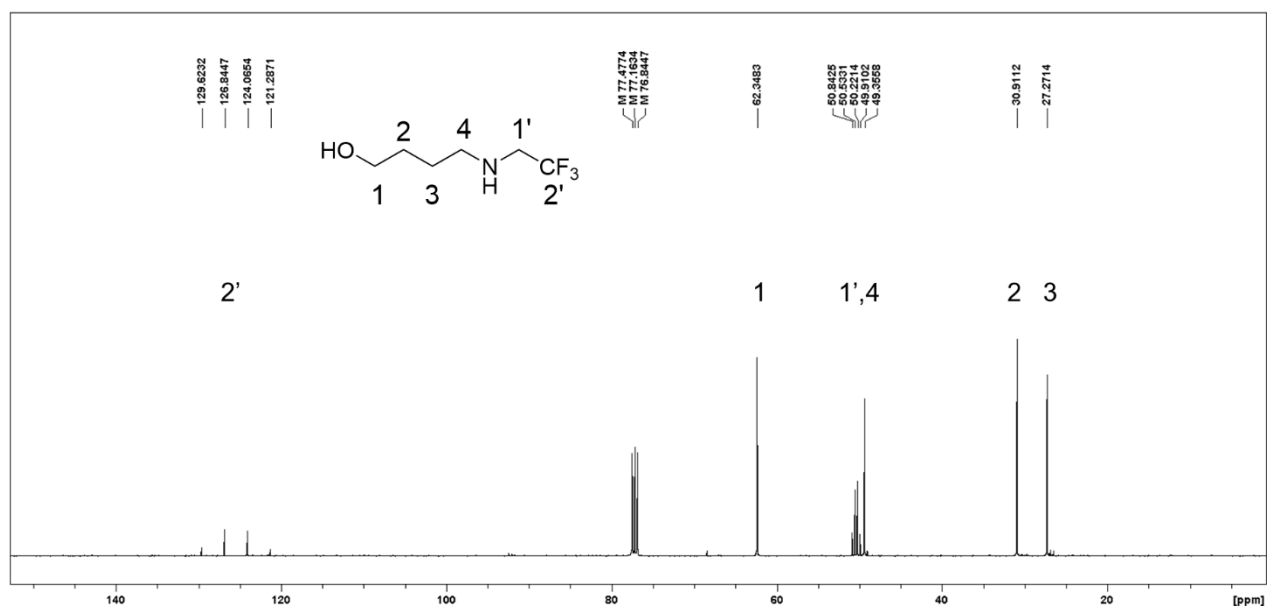


Figure S6. 4-((2,2,2-Trifluoroethyl)amino)butan-1-ol (**2**) (¹³C, pulse prog. zgpg30, CDCl₃, 400 MHz, residual internal CDCl₃ (δ 77.48, 77.16, 76.84))

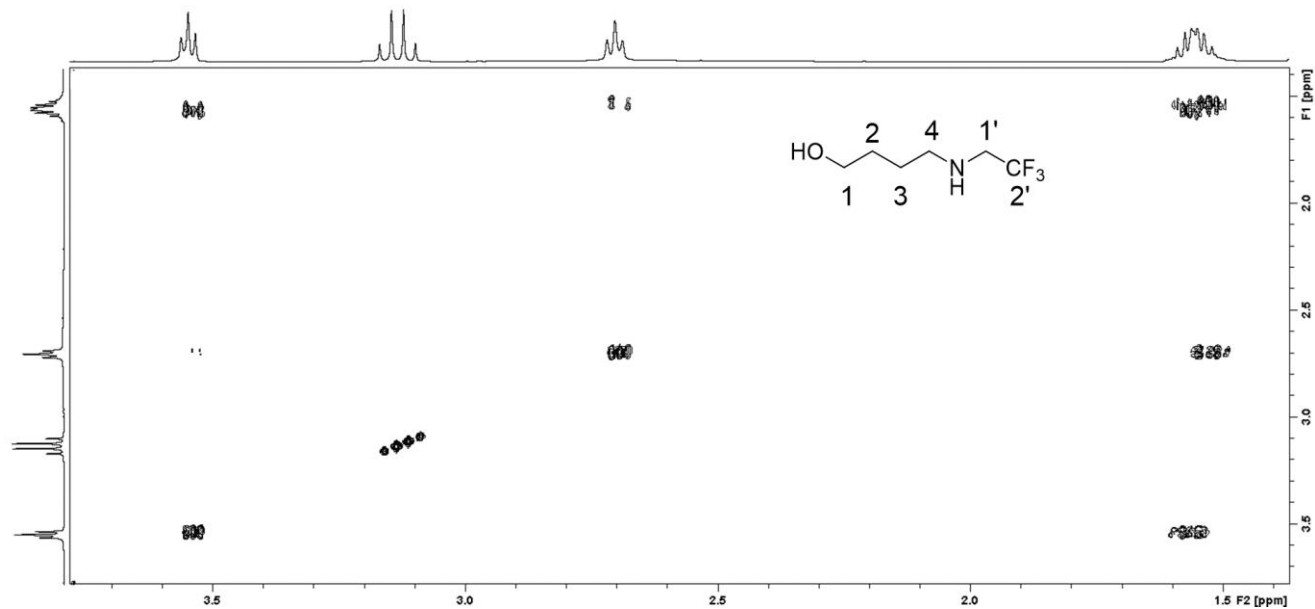


Figure S7. 4-((2,2,2-Trifluoroethyl)amino)butan-1-ol (**2**) (COSY, pulse prog. *cosygpppqf*, CDCl₃, 400 MHz).

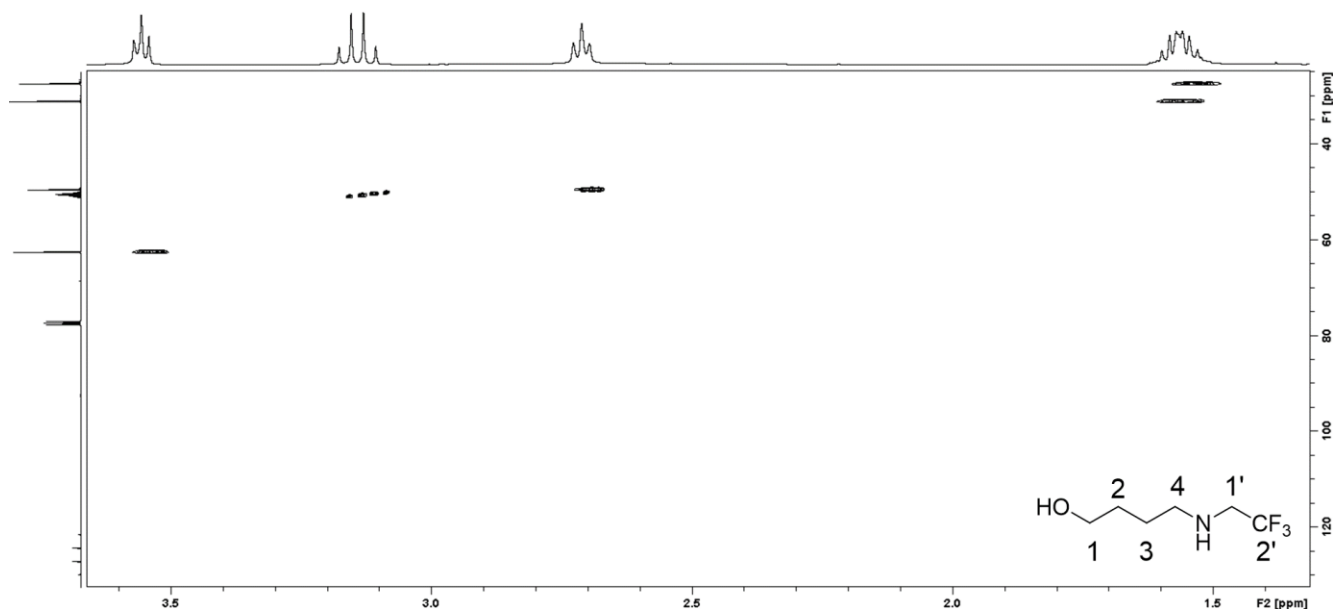


Figure S8. 4-((2,2,2-Trifluoroethyl)amino)butan-1-ol (**2**) (HSQC, pulse prog. *hsqctgpsi2*, CDCl₃, 400 MHz)

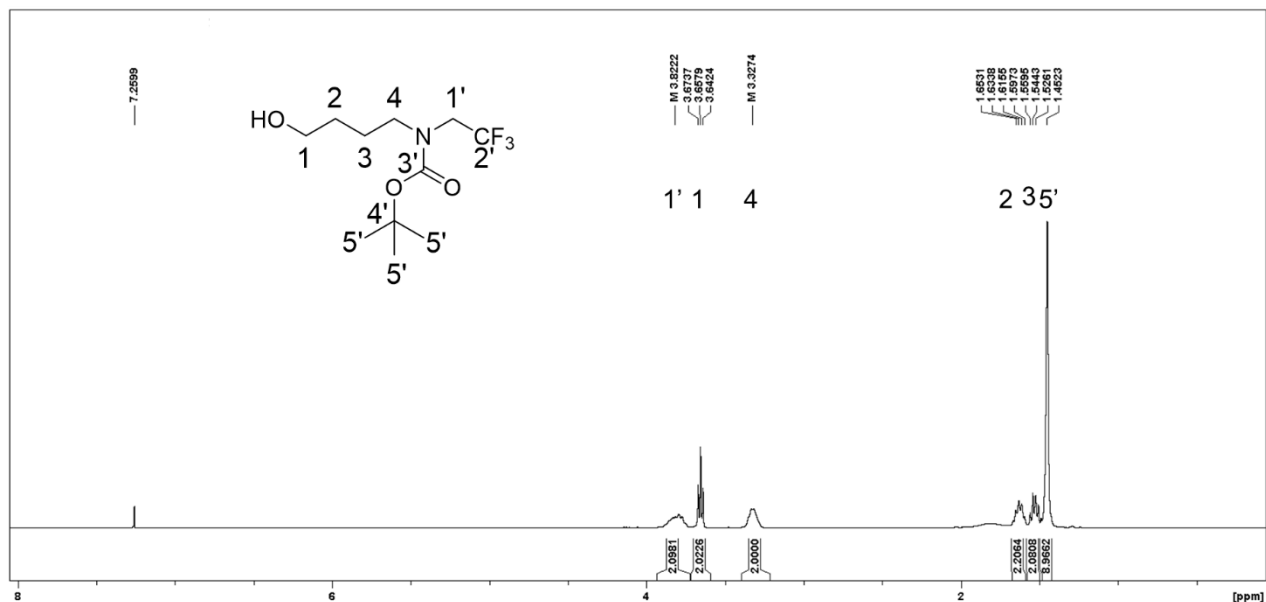


Figure S9. 4-(Boc(2,2,2-trifluoroethyl)amino)butan-1-ol (**3**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

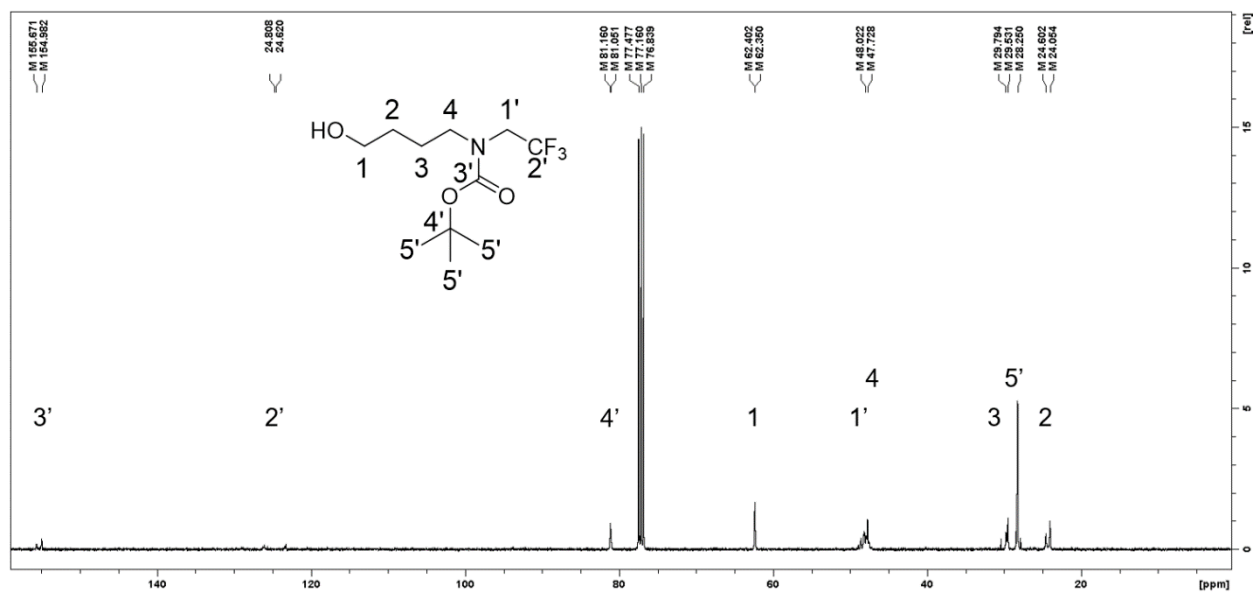


Figure S10. 4-(Boc(2,2,2-trifluoroethyl)amino)butan-1-ol (**3**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.48, 77.16, 76.84))

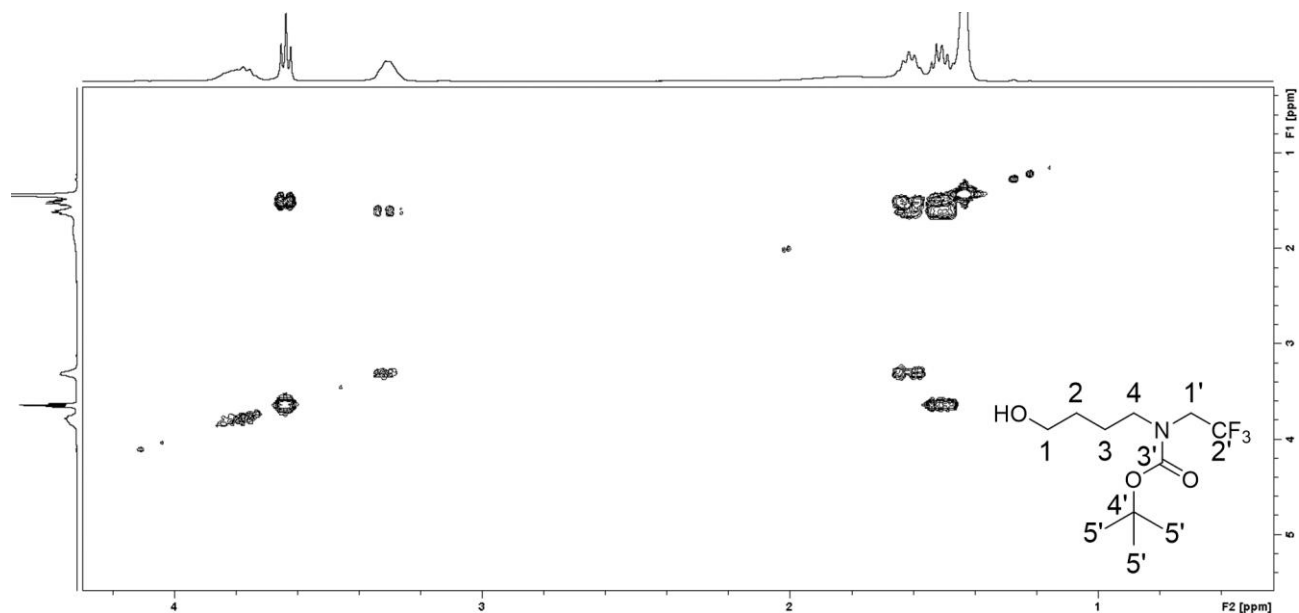


Figure S11. 4-(Boc(2,2,2-trifluoroethyl)amino)butan-1-ol (**3**) (COSY, pulse prog. cosyppppqf, CDCl₃, 400 MHz)

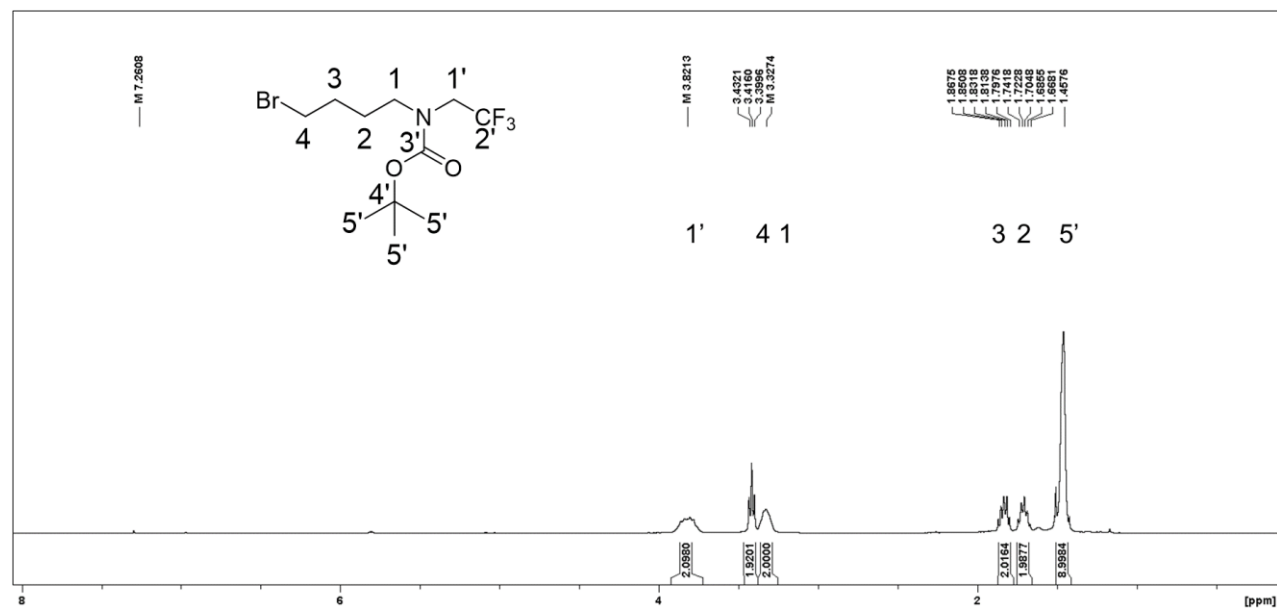


Figure S12. 4-Bromo-N-boc-N-(2,2,2-trifluoroethyl)butan-1-amine (**4**) (¹H, pulse prog. zg30, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

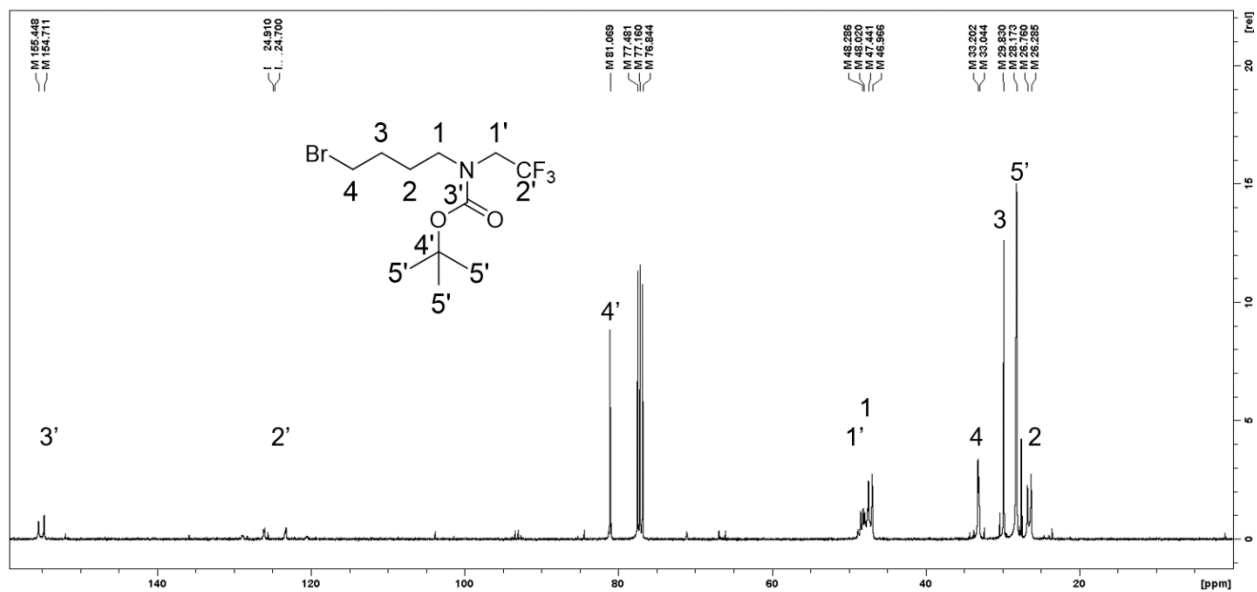


Figure S13. 4-Bromo-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)butan-1-amine (**4**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.48, 77.16, 76.84))

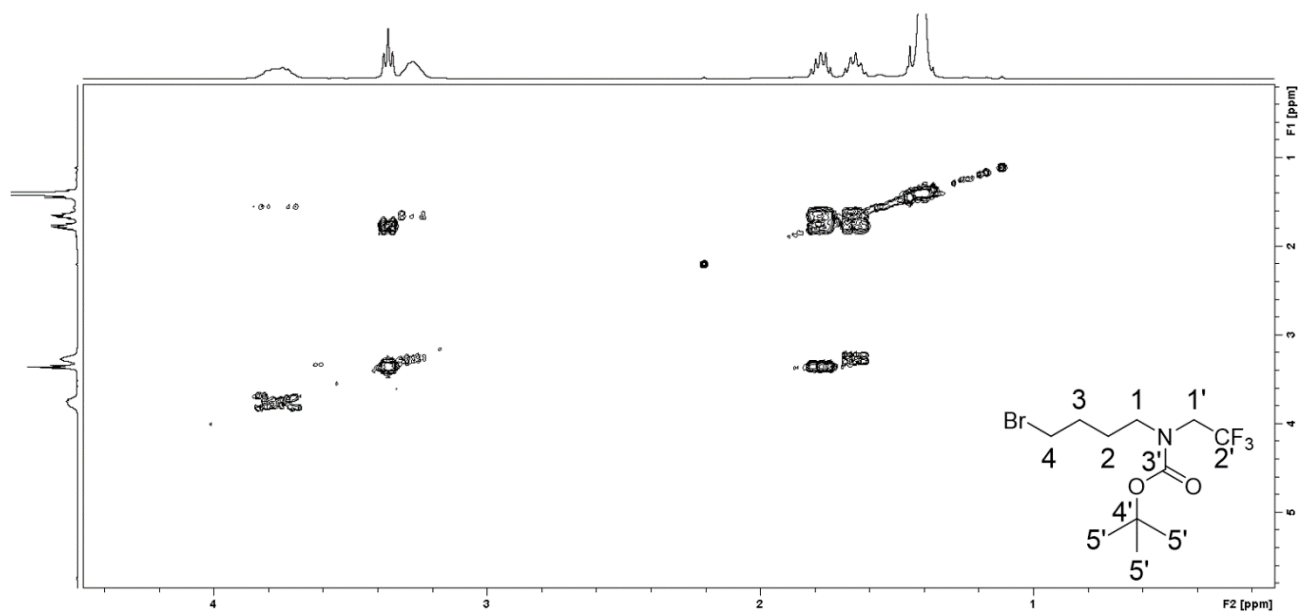


Figure S14. 4-Bromo-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)butan-1-amine (**4**) (COSY, pulse prog. *cosyppppqf*, CDCl₃, 400 MHz)

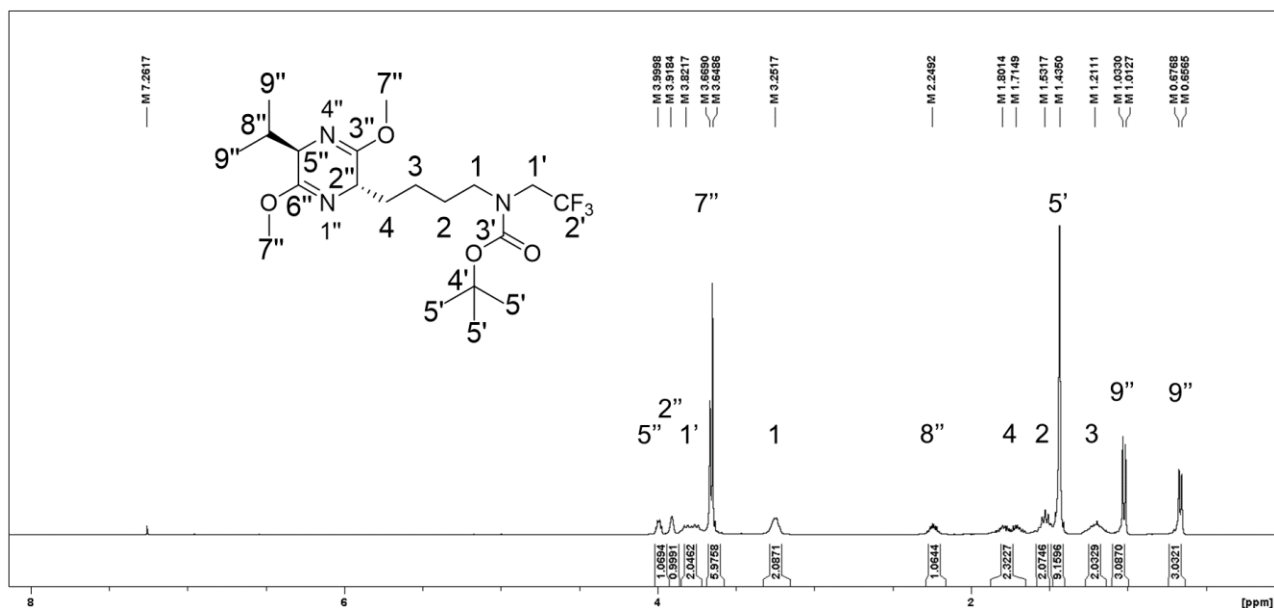


Figure S15. 4-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*tert*-butyl-*N*-(2,2,2-trifluoroethyl)butan-1-amine (**5**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

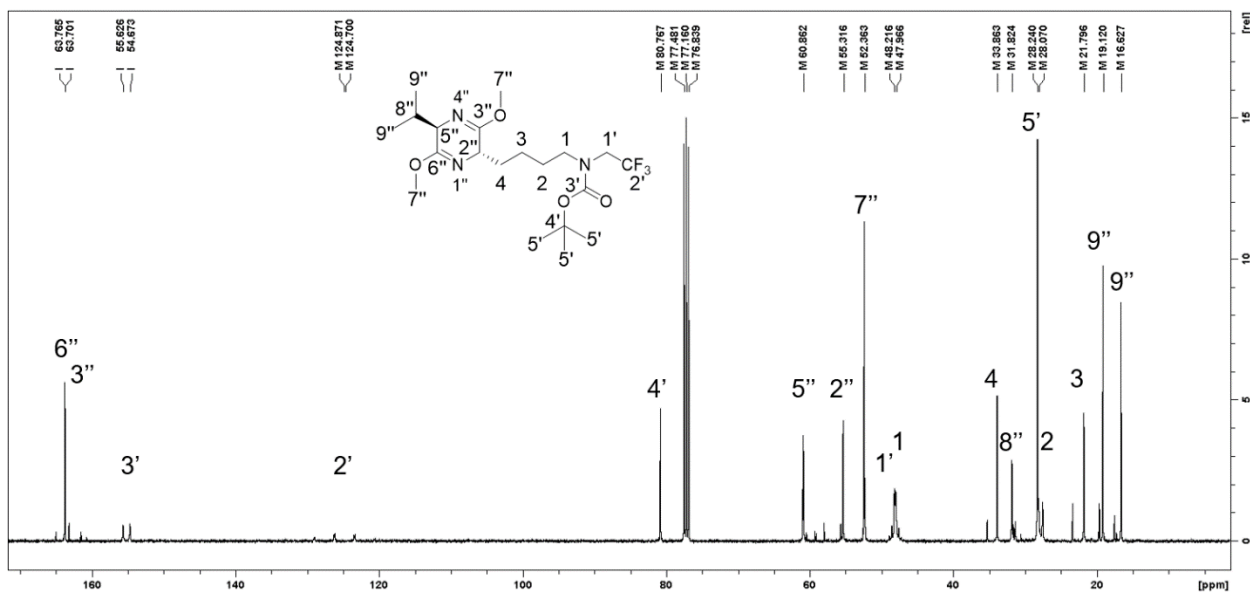


Figure S16. 4-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*tert*-butyl-*N*-(2,2,2-trifluoroethyl)butan-1-amine (**5**) (¹³C, pulse prog. *zpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.48, 77.16, 76.84))

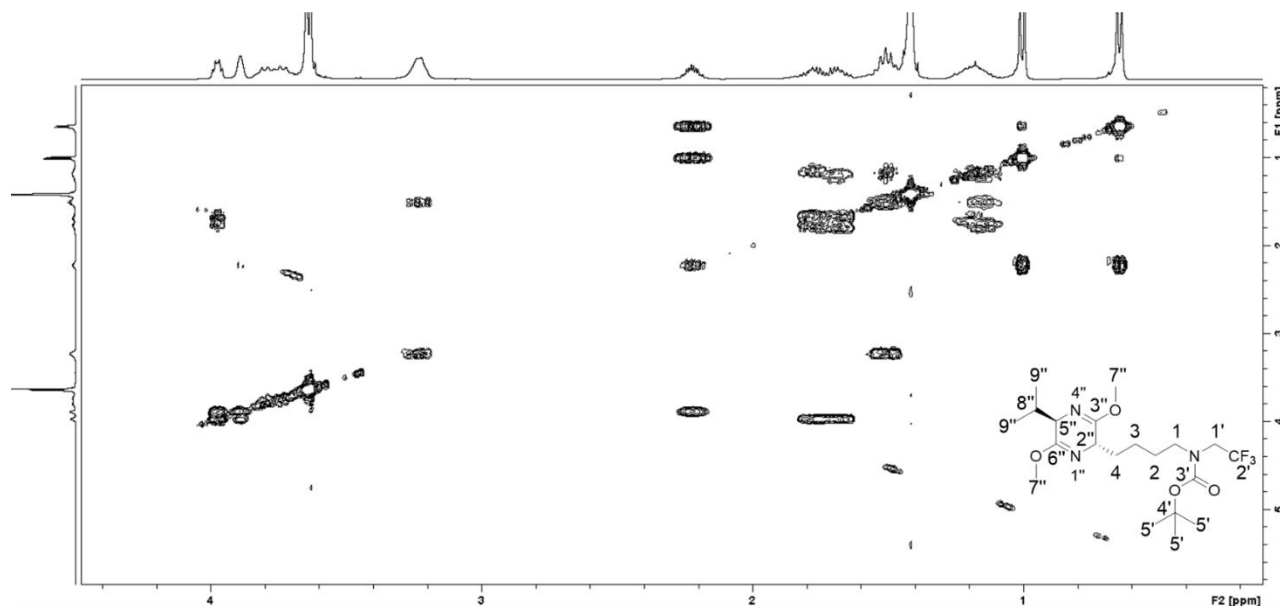


Figure S17. 4-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)butan-1-amine (**5**) (COSY, pulse prog. cosypppqf, CDCl₃, 400 MHz)

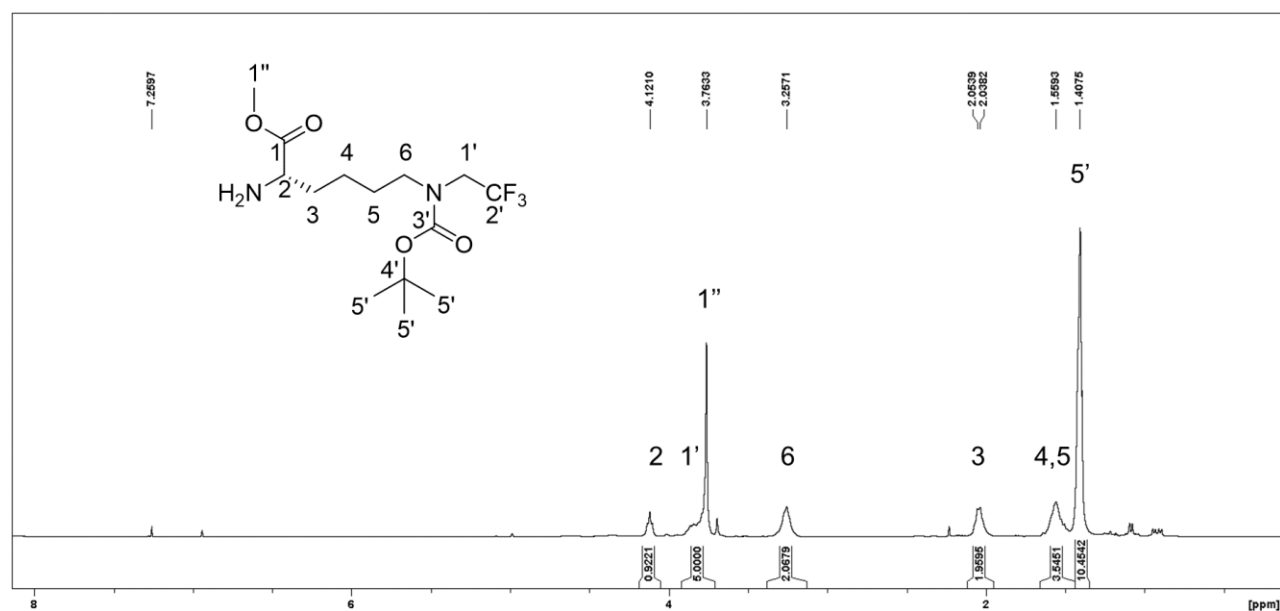


Figure S18. Methyl *N*^ε-*boc*-*N*^ε-(2,2,2-trifluoroethyl)-*L*-lysinate (**6**) (¹H, pulse prog. zg30, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

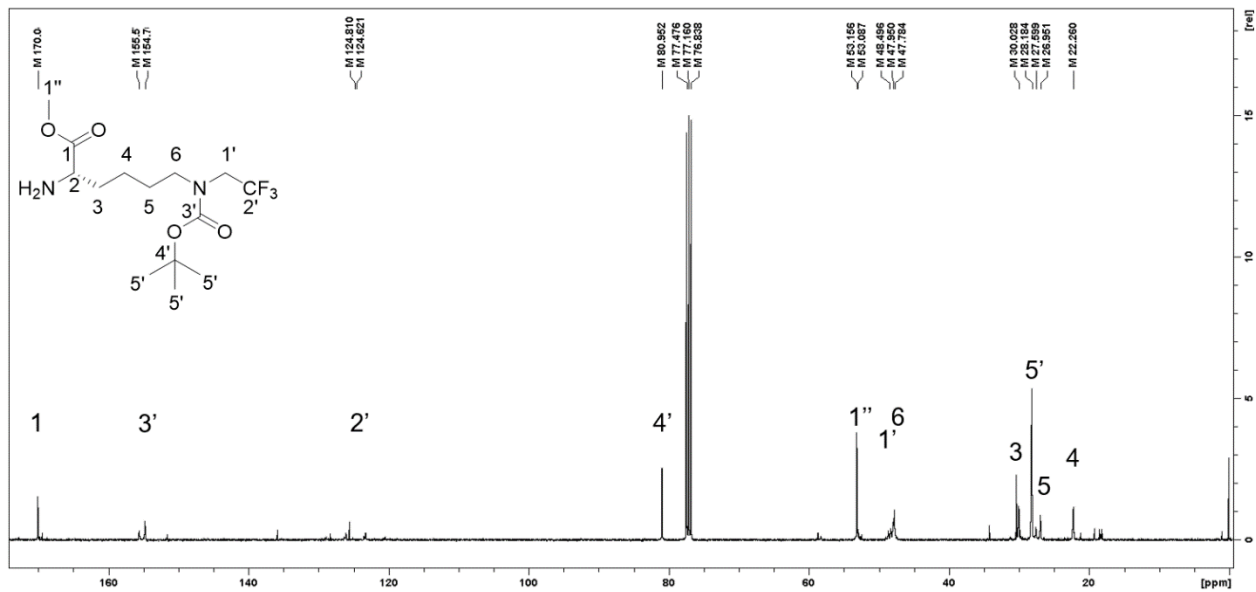


Figure S19. Methyl *N*^E-*boc*-*N*^E-(2,2,2-trifluoroethyl)-*L*-lysinate (**6**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.48, 77.16, 76.84))

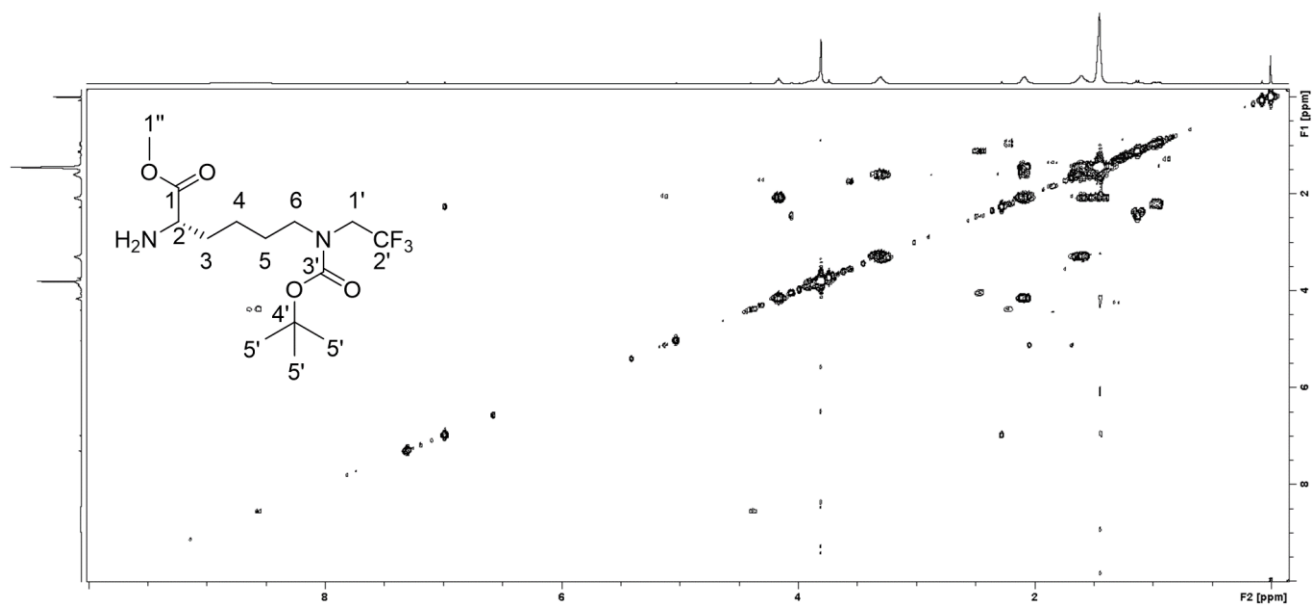


Figure S20. Methyl *N*^E-*boc*-*N*^E-(2,2,2-trifluoroethyl)-*L*-lysinate (**6**) (COSY, pulse prog. *cosygpppqf*, CDCl₃, 400 MHz)

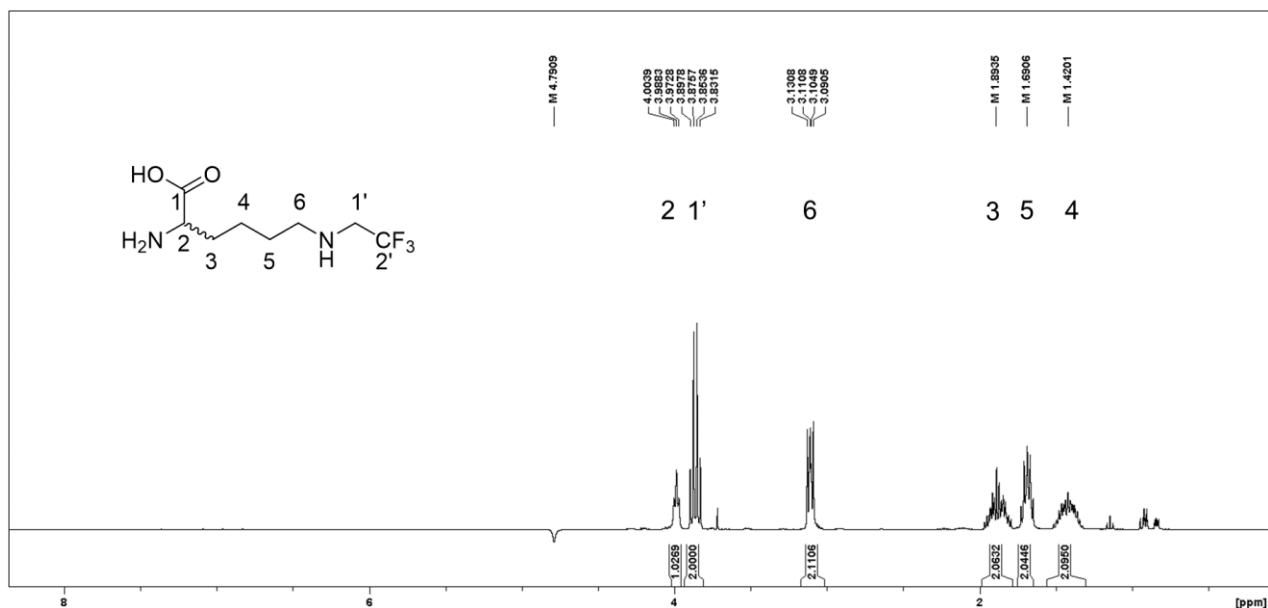


Figure S21. *N*^ε-(2,2,2-Trifluoroethyl)-*D,L*-lysine (7) (¹H, pulse prog. *noesygppld*, 90% H₂O/10% D₂O, 400 MHz, internal std. H₂O (δ 4.79))

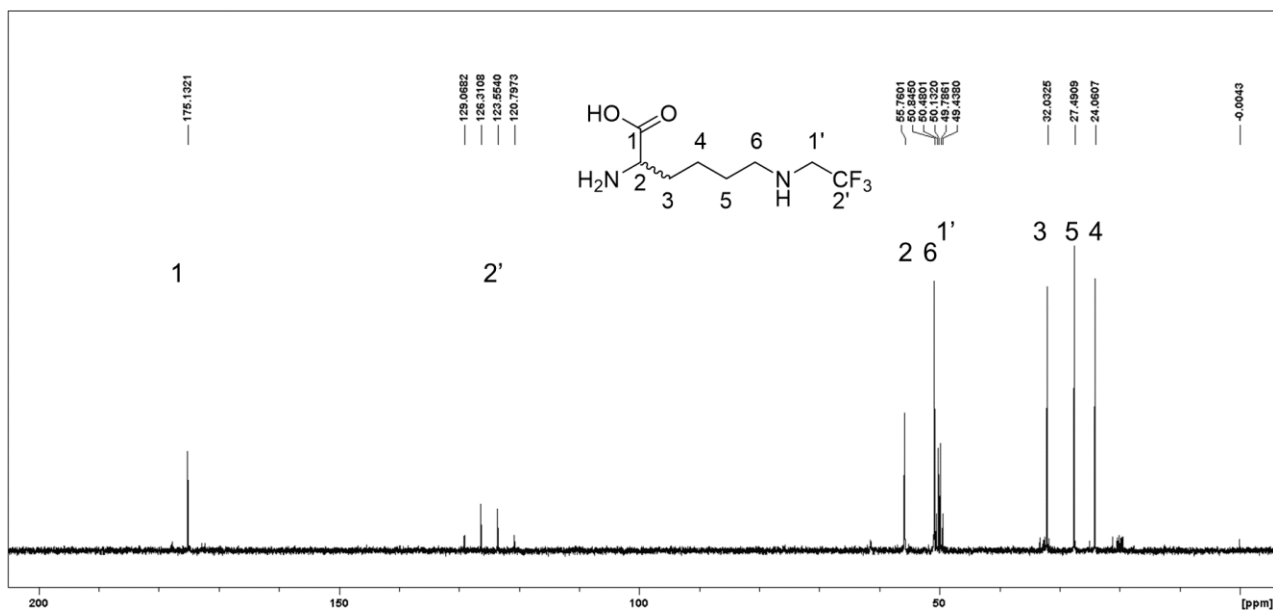


Figure S22. *N*^ε-(2,2,2-Trifluoroethyl)-*D,L*-lysine (7) (¹³C, pulse prog. *zgpg30*, 90% H₂O/10% D₂O, 400 MHz, residual internal std. DSS (δ 0.0))

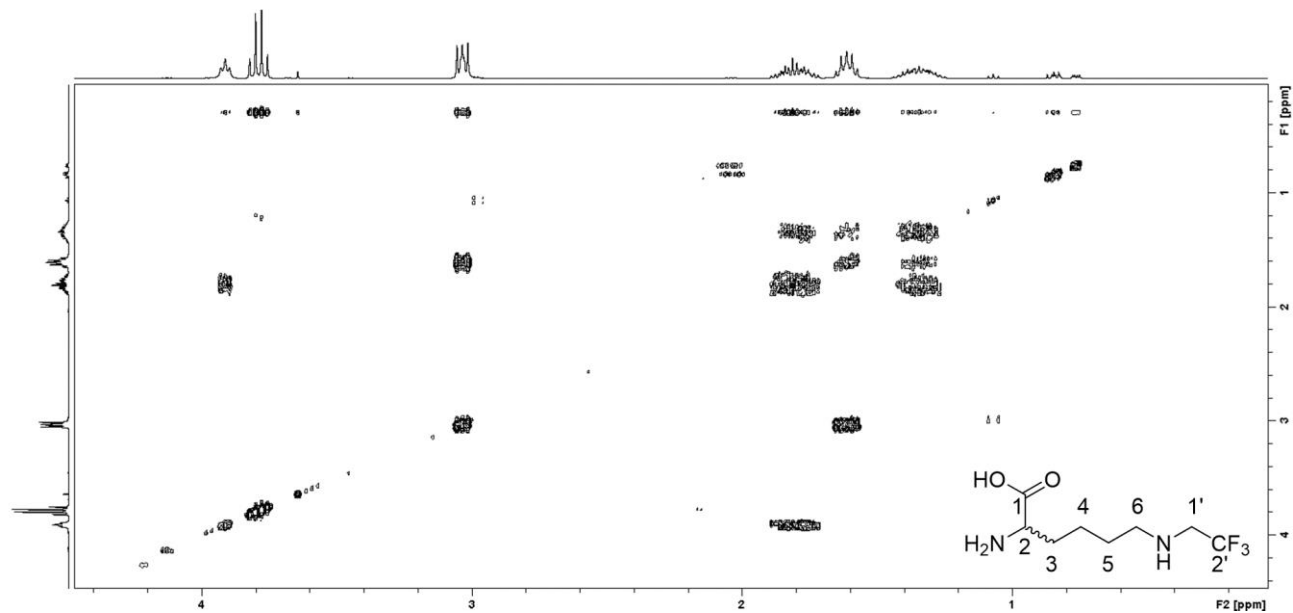


Figure S23. *N*^ε-(2,2,2-Trifluoroethyl)-*D,L*-lysine (7) (COSY, pulse prog. *cosygpppqf*, 90% H₂O/10% D₂O, 400 MHz)

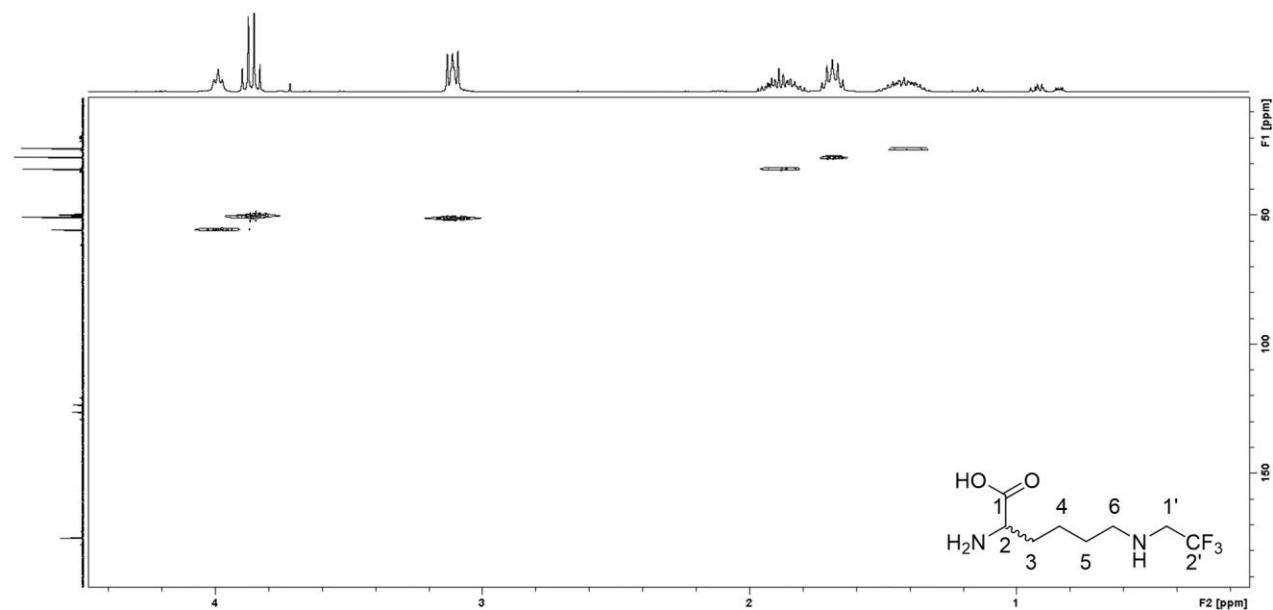


Figure S24. *N*^ε-(2,2,2-Trifluoroethyl)-*D,L*-lysine (7) (HSQC, pulse prog. *hsqcetgpsi2*, 90% H₂O/10% D₂O, 400 MHz)

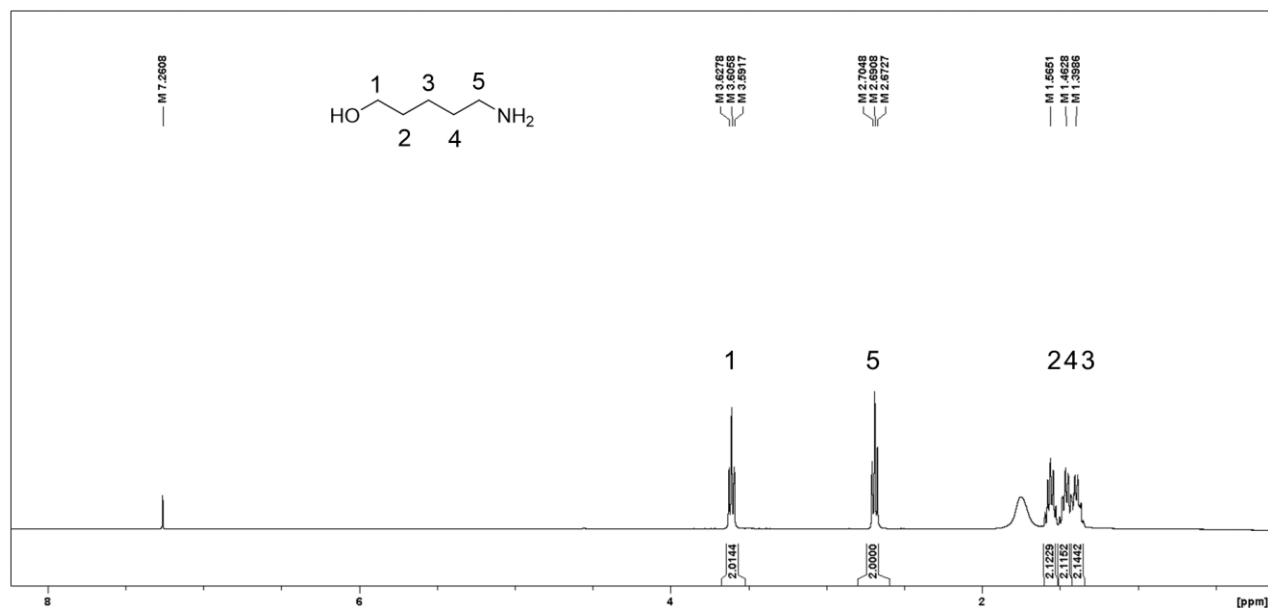


Figure S25. 5-Amino-pentan-1-ol (**1**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

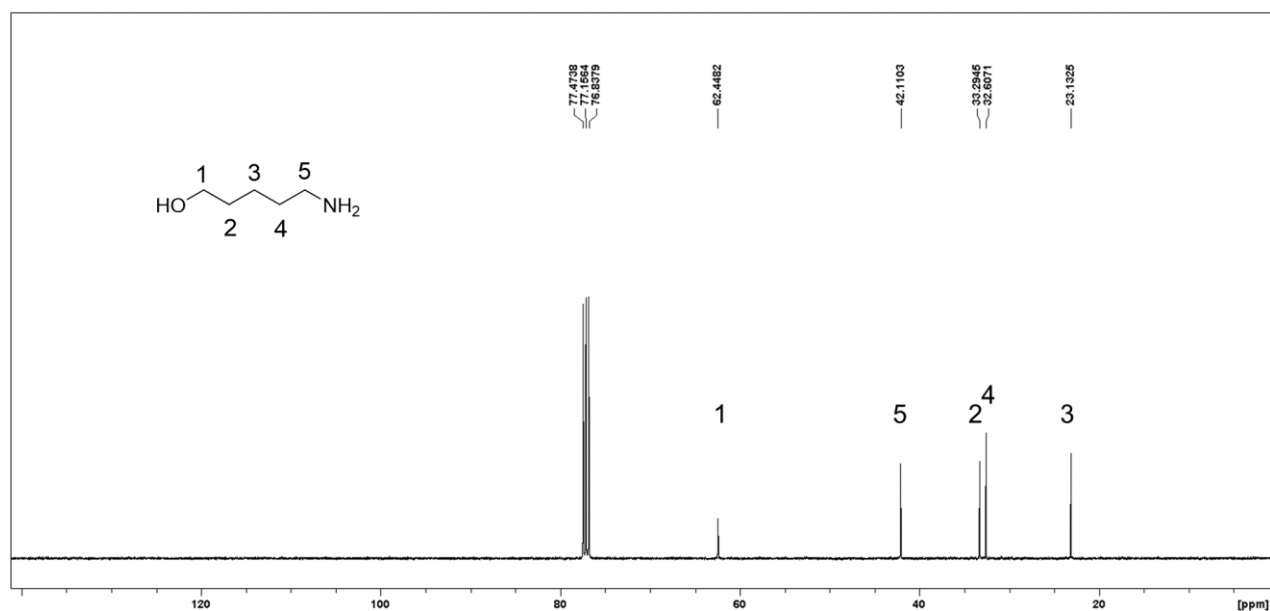


Figure S26. 5-Amino-pentan-1-ol (**1**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.47, 77.16, 76.84))

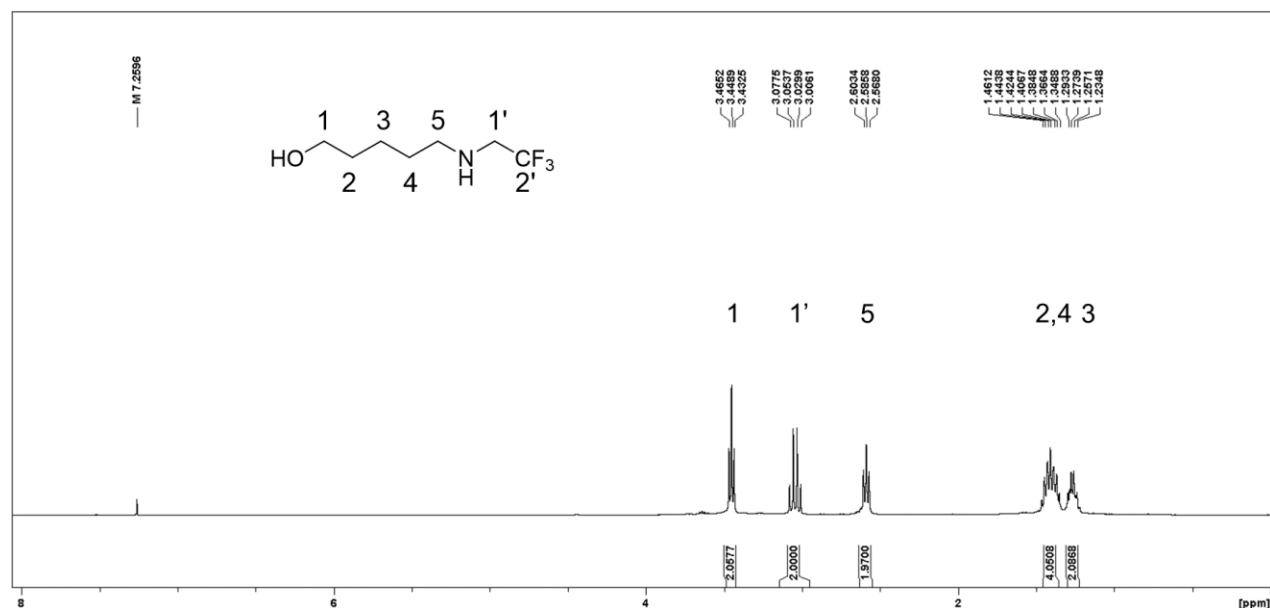


Figure S27. 5-((2,2,2-Trifluoroethyl)amino)pentan-1-ol (**2**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

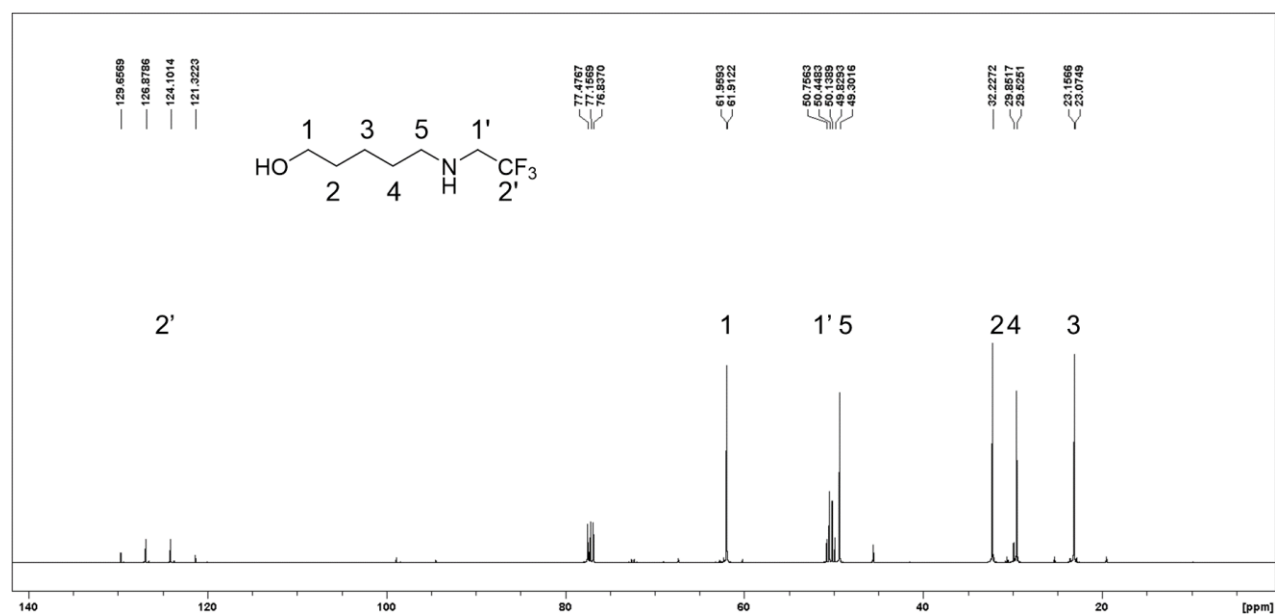


Figure S28. 5-((2,2,2-Trifluoroethyl)amino)pentan-1-ol (**2**) (¹³C, pulse prog. *zgpg30*, CDCl₃, 400 MHz, residual internal std. CDCl₃ (δ 77.47, 77.16, 76.84))

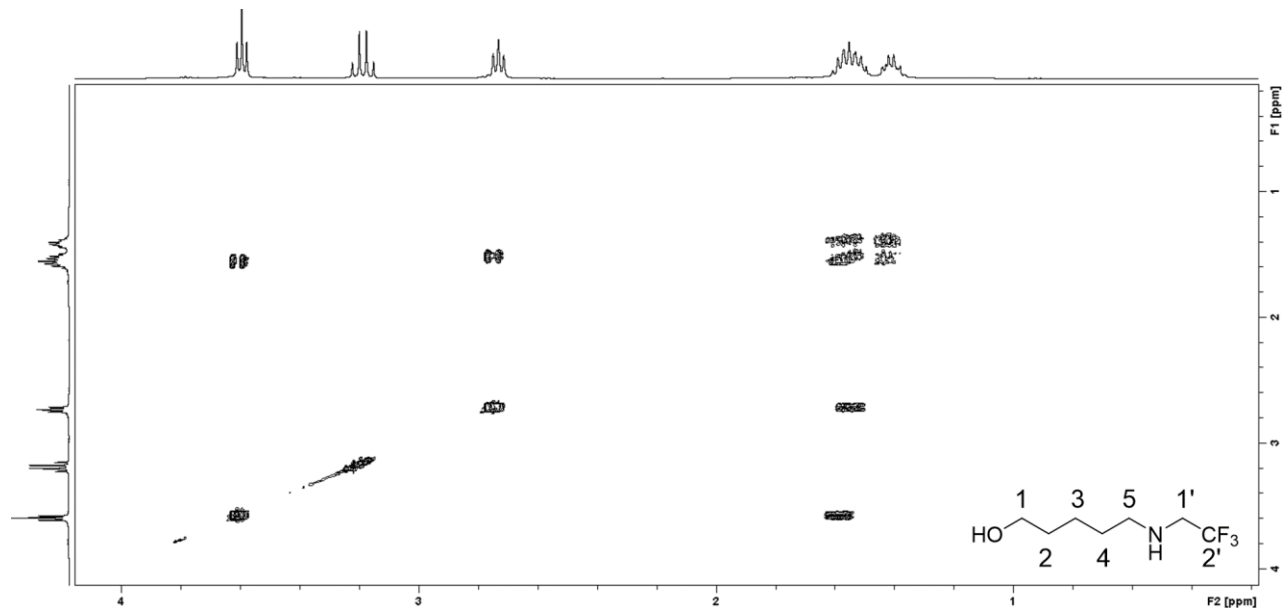


Figure S29. 5-((2,2,2-Trifluoroethyl)amino)pentan-1-ol (**2**) (COSY, pulse prog. *cosygpppqf*, CDCl₃, 400 MHz)

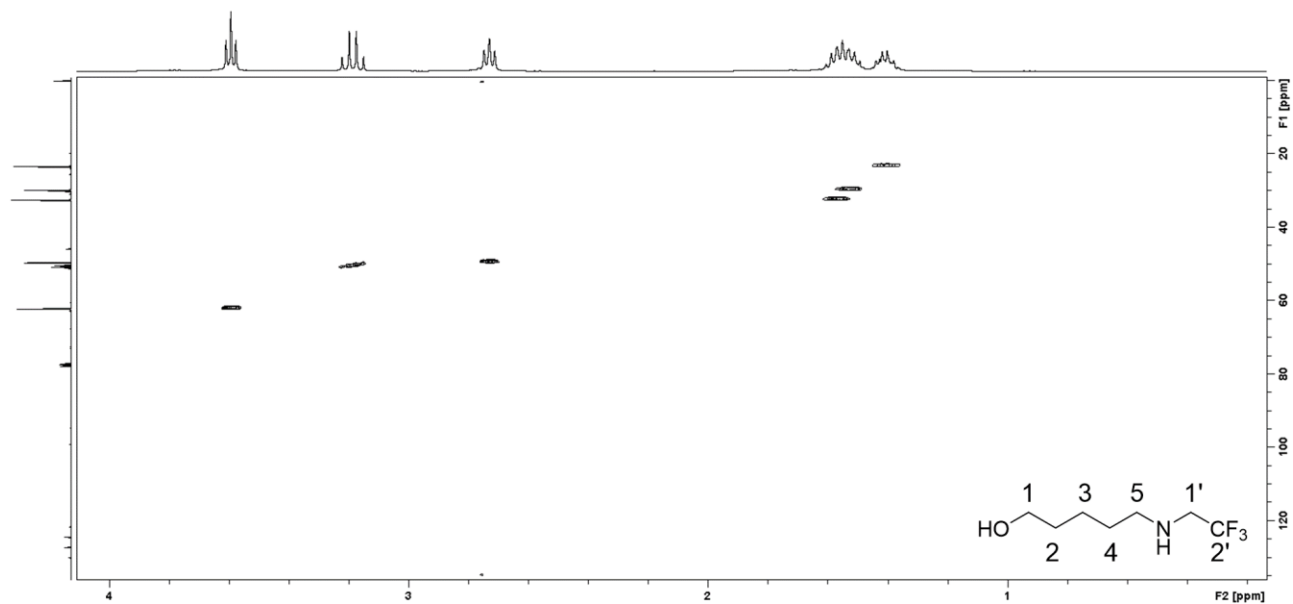


Figure S30. 5-((2,2,2-Trifluoroethyl)amino)pentan-1-ol (**2**) (HSQC, pulse prog. *hsqcetgpsi2*, CDCl₃, 400 MHz)

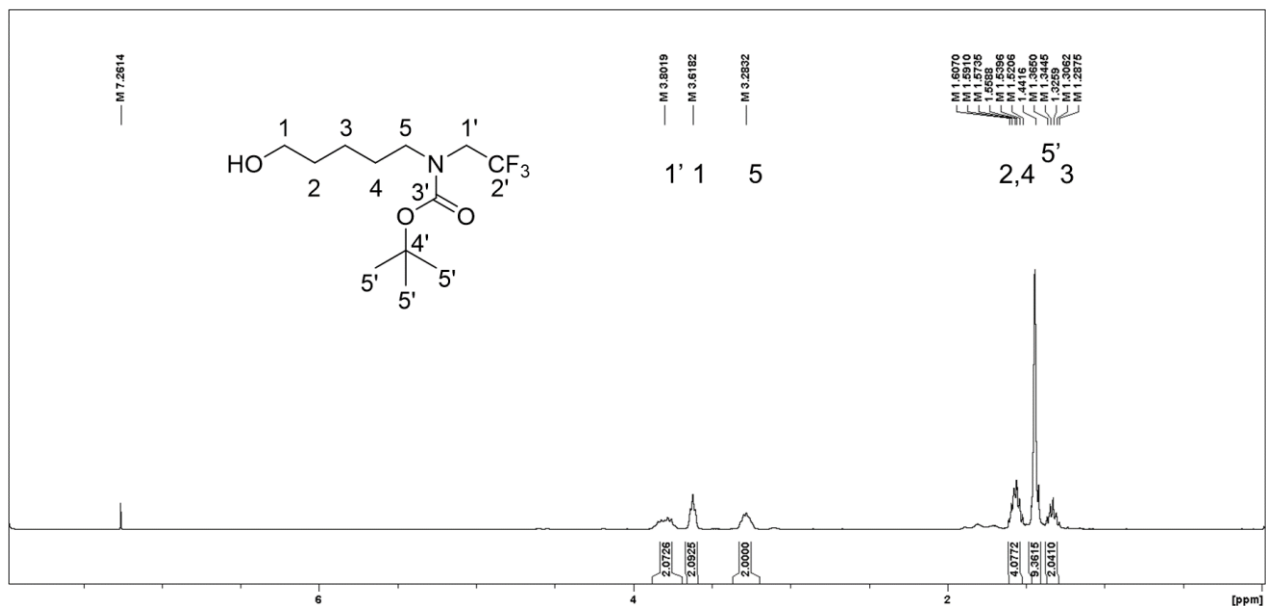


Figure S31. 5-(Boc(2,2,2-trifluoroethyl)amino)pentan-1-ol (**3**) (^1H , pulse prog. *zg30*, CDCl_3 , 400 MHz, residual internal std. CHCl_3 (δ 7.26))

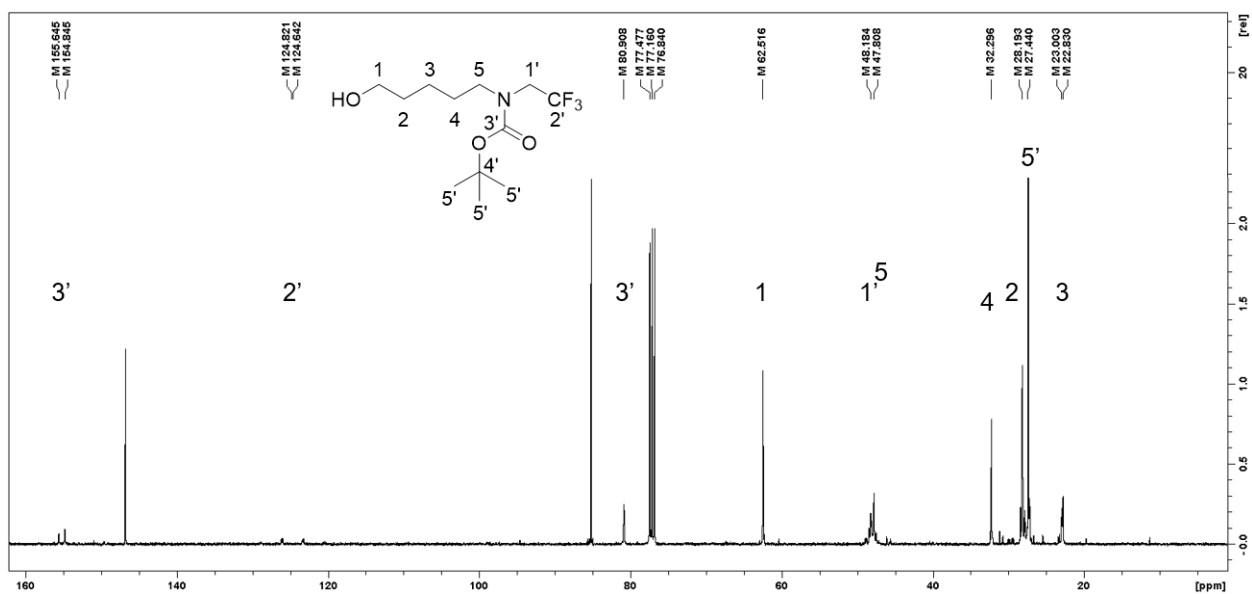


Figure S32. 5-(Boc(2,2,2-trifluoroethyl)amino)pentan-1-ol (**3**) (^{13}C , pulse prog. *zgpg30*, CDCl_3 , 400 MHz, residual internal std. CDCl_3 (δ 77.47, 77.16, 76.84))

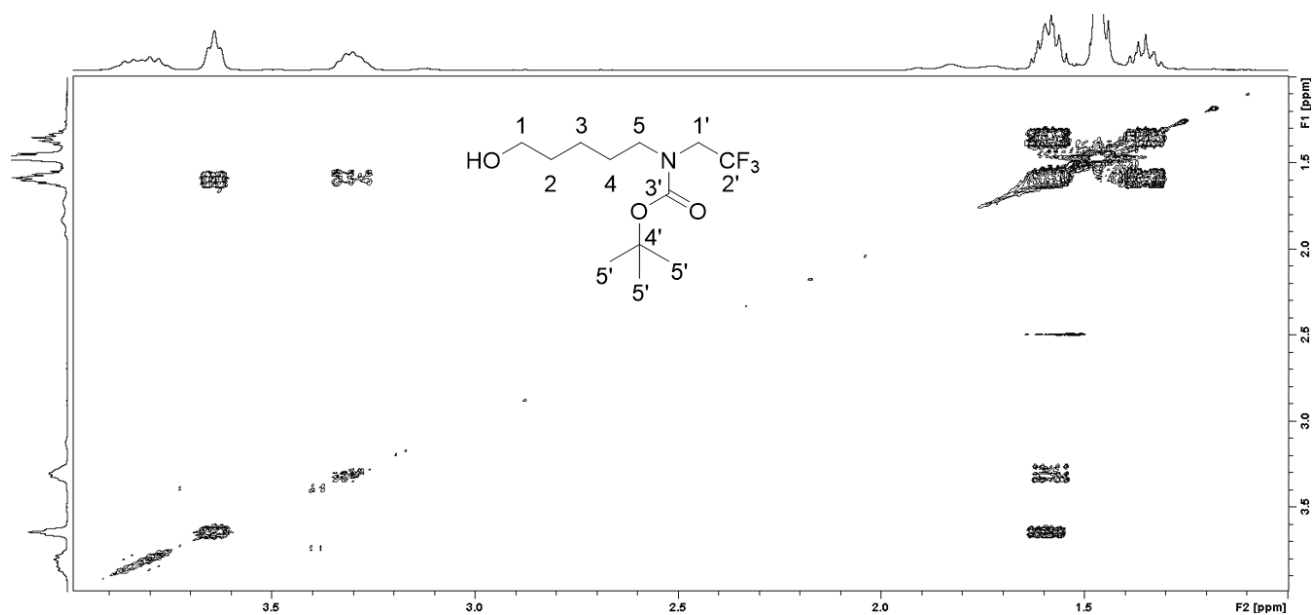


Figure S33. 5-(Boc(2,2,2-trifluoroethyl)amino)pentan-1-ol (**3**) (COSY, pulse prog. *cosygpppqf*, CDCl₃, 400 MHz)

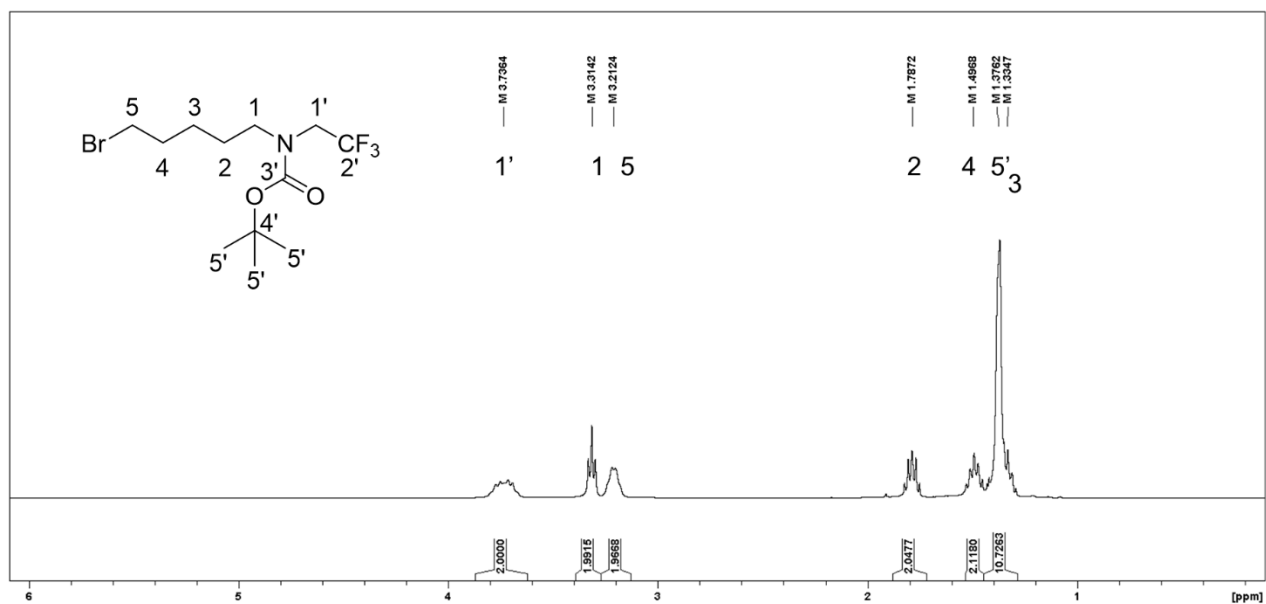


Figure S34. 5-Bromo-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**4**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

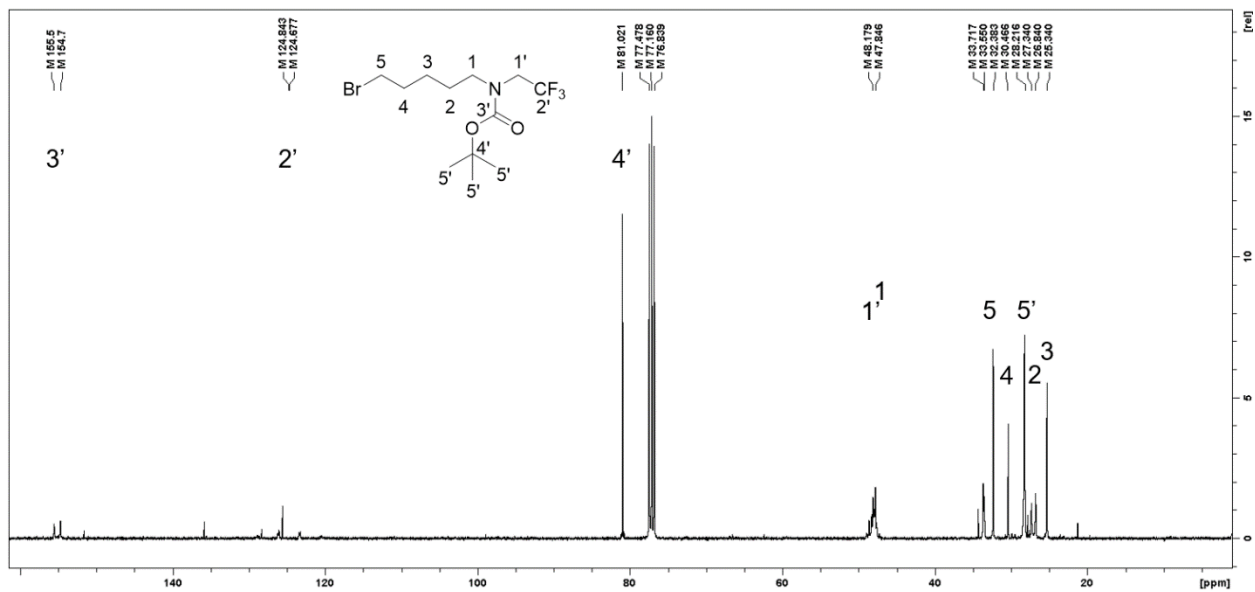


Figure S35. 5-Bromo-*N*-*tert*-butyloxycarbonyl-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**4**) (^{13}C , pulse prog. *zgpg30*, CDCl_3 , 400 MHz, residual internal std. CDCl_3 (δ 77.47, 77.16, 76.84))

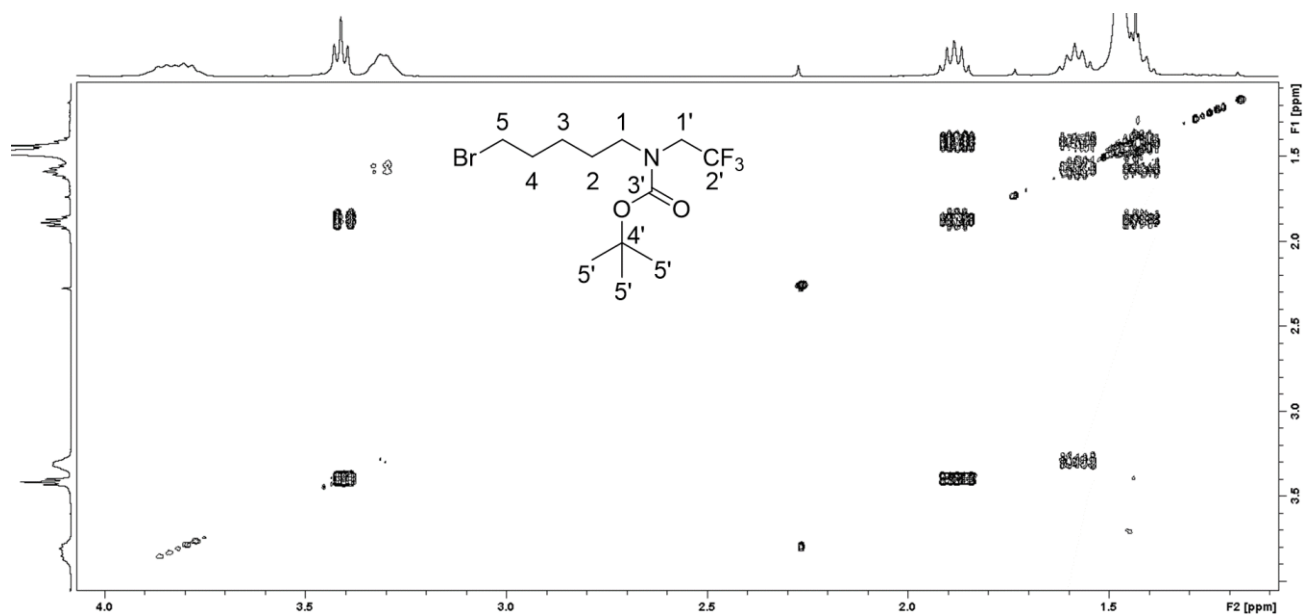


Figure S36. 5-Bromo-*N*-*tert*-butyloxycarbonyl-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**4**) (COSY, pulse prog. *cosygpppqf*, CDCl_3 , 400 MHz)

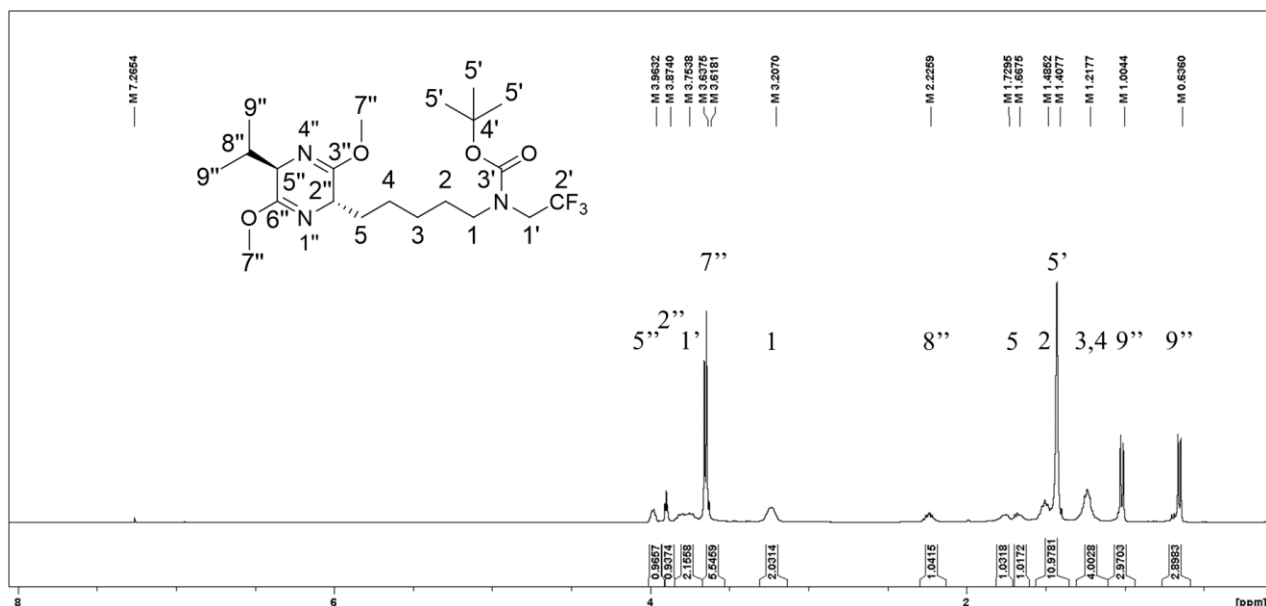


Figure S37. 5-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**5**) (^1H , pulse prog. *zg30*, CDCl_3 , 400 MHz, residual internal std. CHCl_3 (δ 7.26))

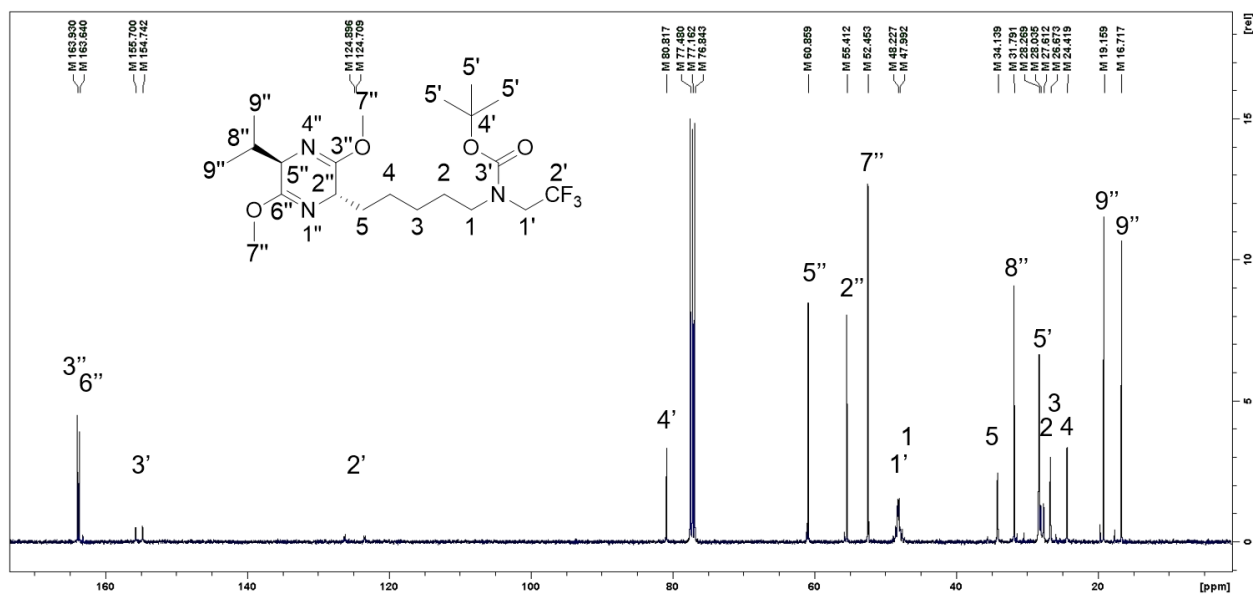


Figure S38. 5-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*boc*-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**5**) (^{13}C , pulse prog. *zgpg30*, CDCl_3 , 400 MHz, residual internal std. CDCl_3 (δ 77.47, 77.16, 76.84))

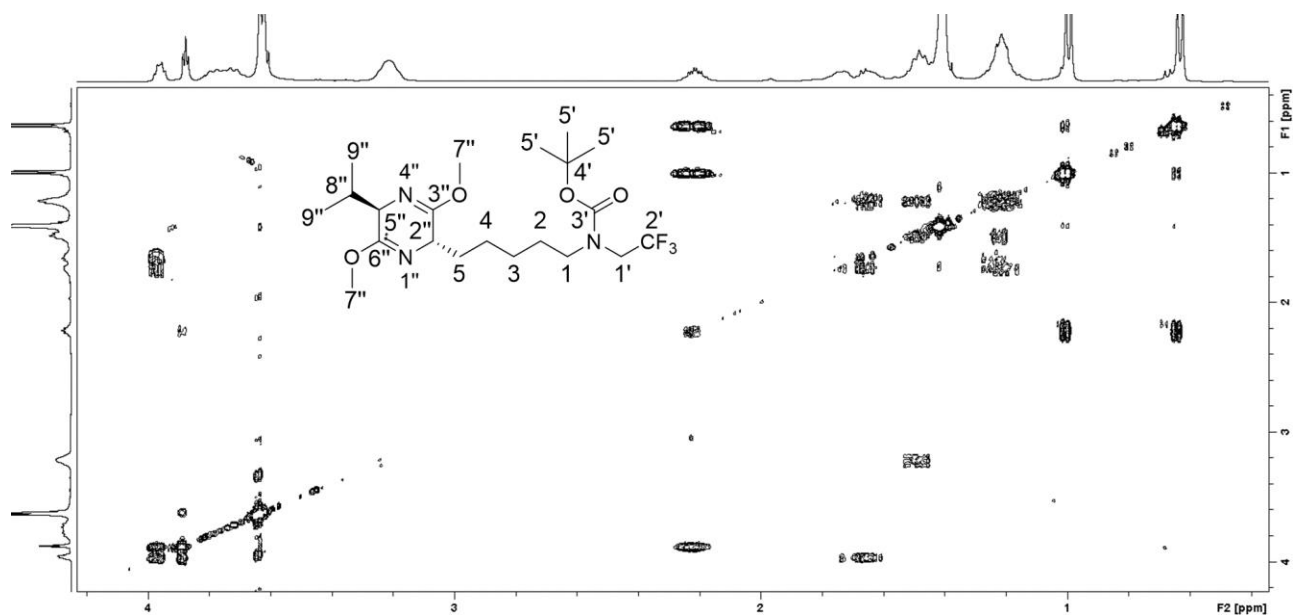


Figure S39. 5-((2*R*,5*S*)-5-Isopropyl-3,6-dimethoxy-2,5-dihydropyrazin-2-yl)-*N*-*tert*-butyl-*N*-(2,2,2-trifluoroethyl)pentan-1-amine (**5**) (COSY, pulse prog. *cosygpppqf*, CDCl₃, 400 MHz)

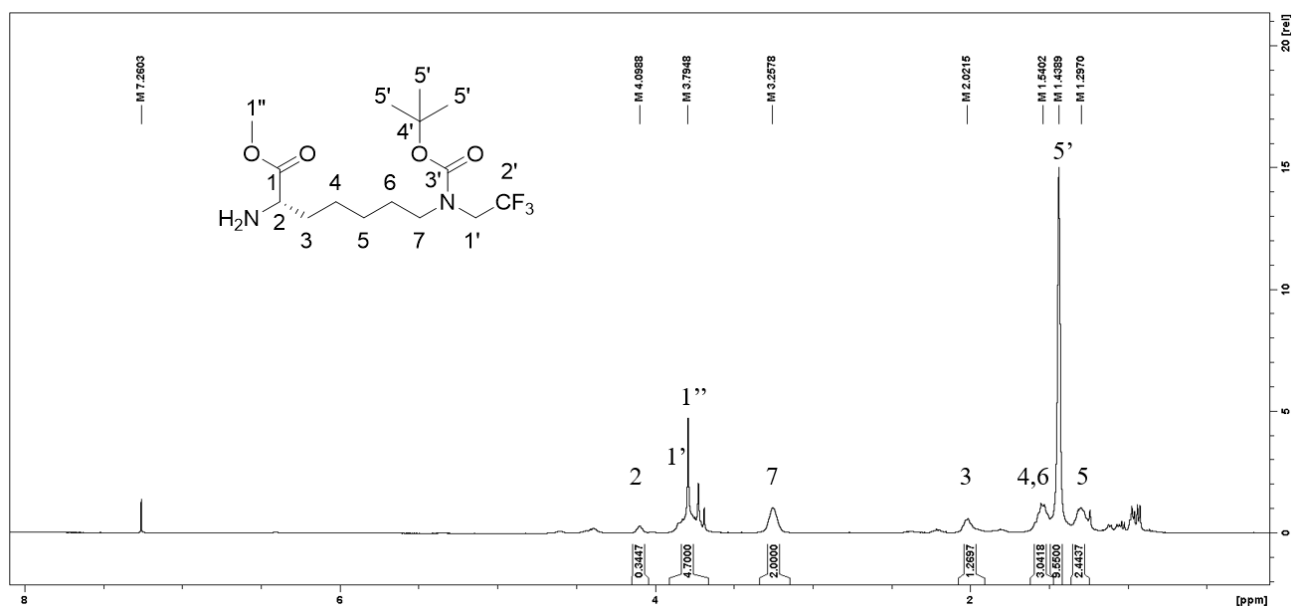


Figure S40. Methyl *N*^ε-*tert*-*N*^ε-(2,2,2-trifluoroethyl)-*L*-homolysinate (**6**) (¹H, pulse prog. *zg30*, CDCl₃, 400 MHz, residual internal std. CHCl₃ (δ 7.26))

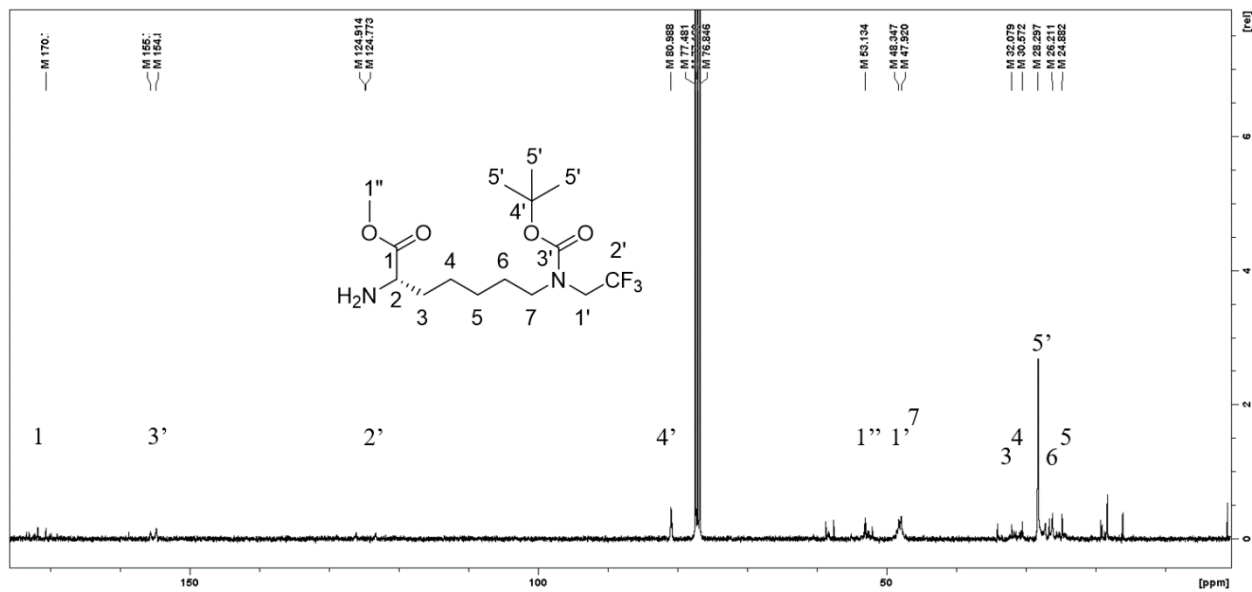


Figure S41. Methyl *N*^{boc}-*N*^(2,2,2-trifluoroethyl)-*L*-homolysinate (**6**) (^{13}C , pulse prog. *zgpg30*, CDCl_3 , 400 MHz, residual internal std. CDCl_3 (δ 77.47, 77.16, 76.84))

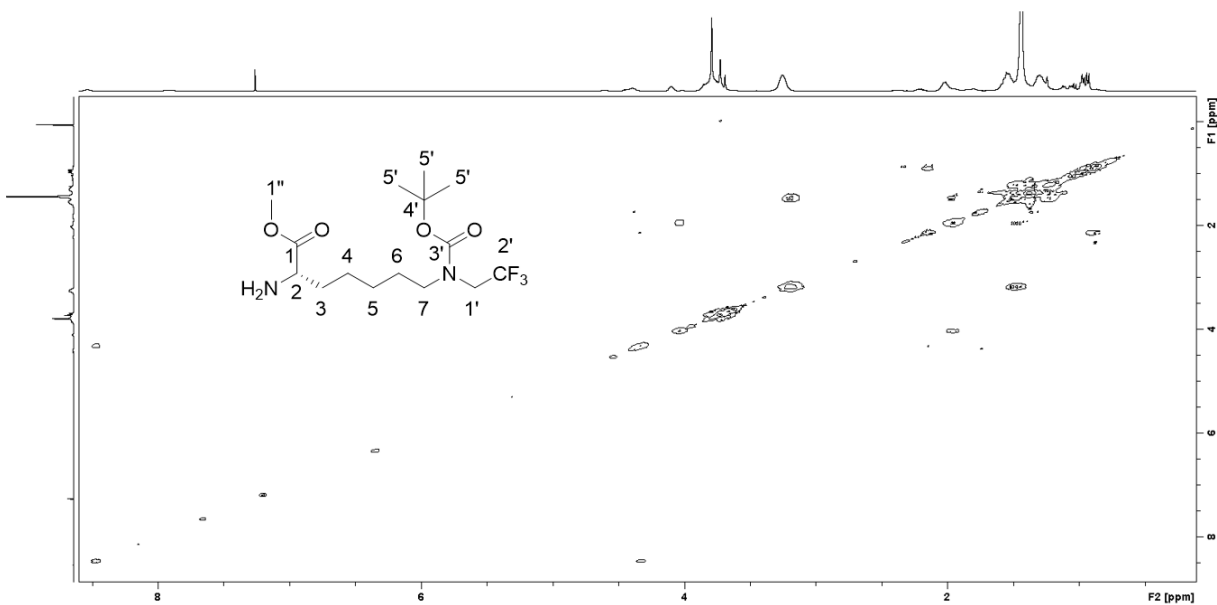


Figure S42. Methyl *N*^{boc}-*N*^(2,2,2-trifluoroethyl)-*L*-homolysinate (**6**) (COSY, pulse prog. *cosygpppqf*, CDCl_3 , 400 MHz)

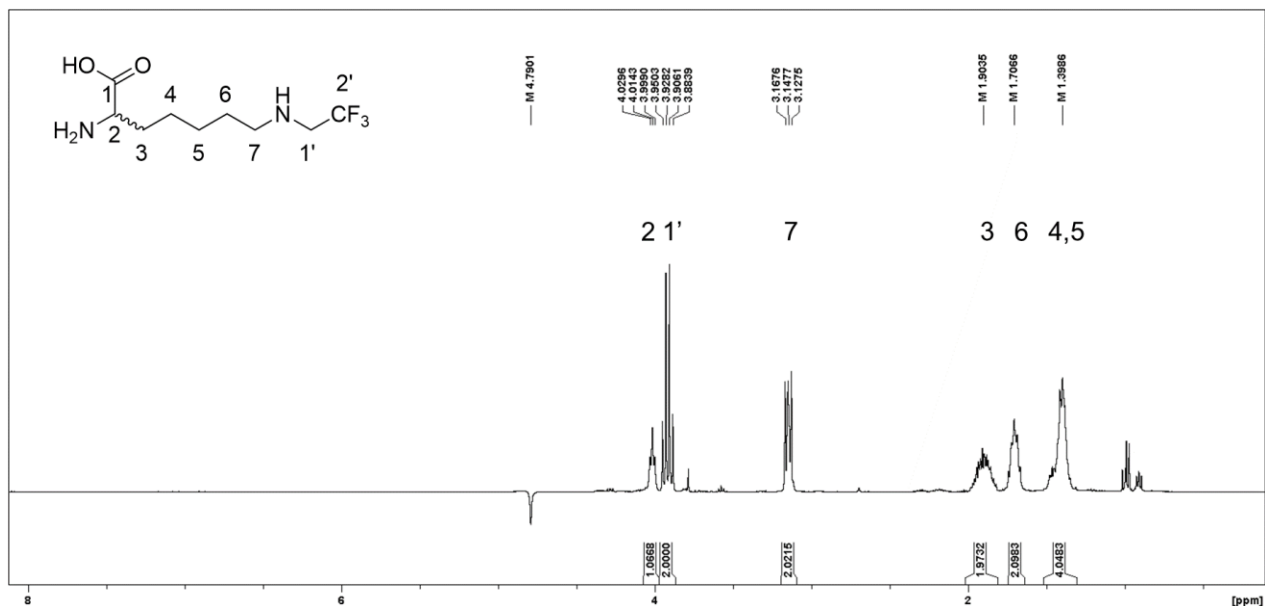


Figure S43. *N* ϵ -(2,2,2-Trifluoroethyl)-*D,L*-homolysine (7) (^1H , pulse prog. *noesygppr1d*, 90% $\text{H}_2\text{O}/10\%$ D_2O , 400 MHz, internal std. H_2O (δ 4.79))

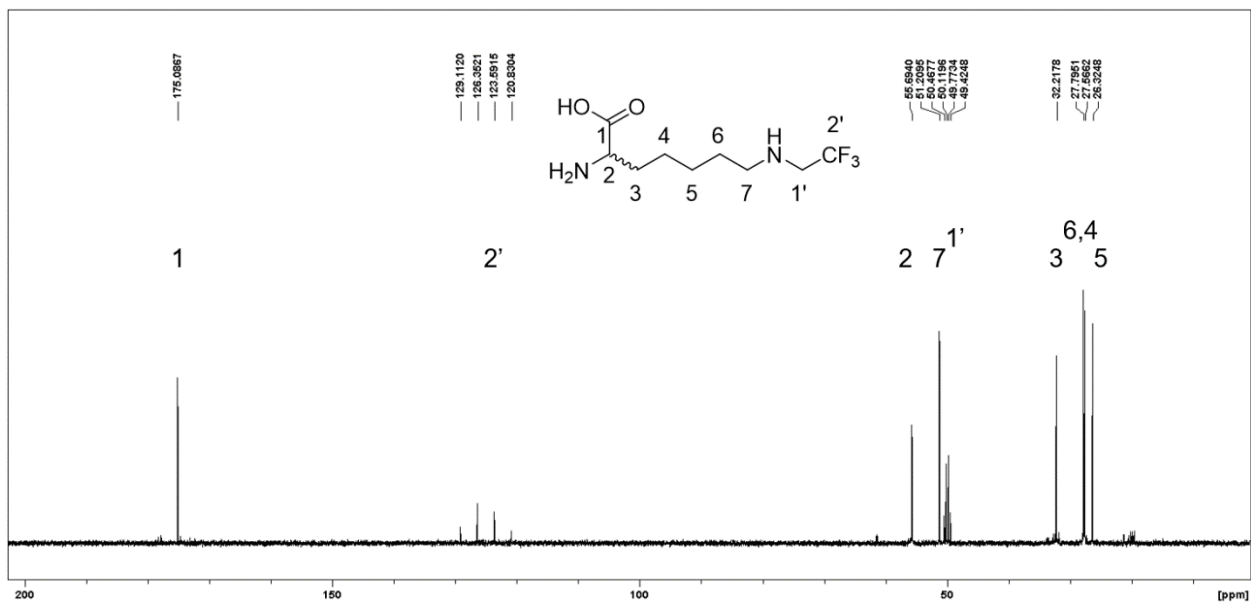


Figure S44. *N* ϵ -(2,2,2-Trifluoroethyl)-*D,L*-homolysine (7) (^{13}C , pulse prog. *zgpg30*, 90% $\text{H}_2\text{O}/10\%$ D_2O , 400 MHz, internal std. DSS(δ 0.0))

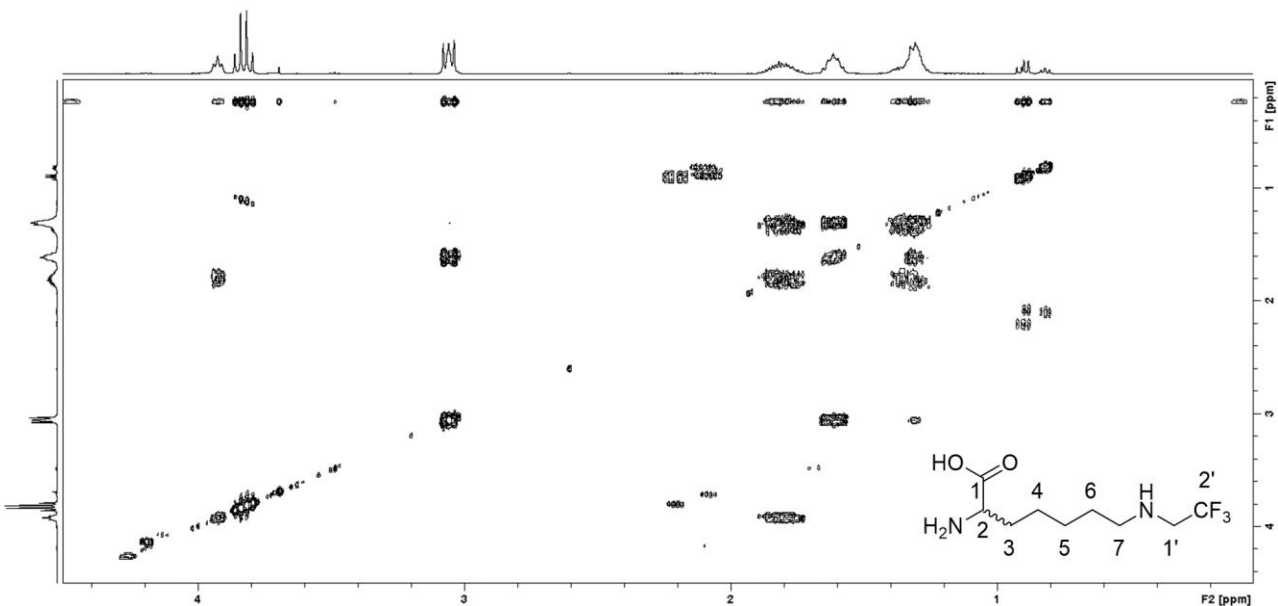


Figure S45. *N* ϵ -(2,2,2-Trifluoroethyl)-*D,L*-homolysine (**7**) (COSY, pulse prog. *cosygpppqf*, 90% $\text{H}_2\text{O}/10\%$ D_2O , 400 MHz)

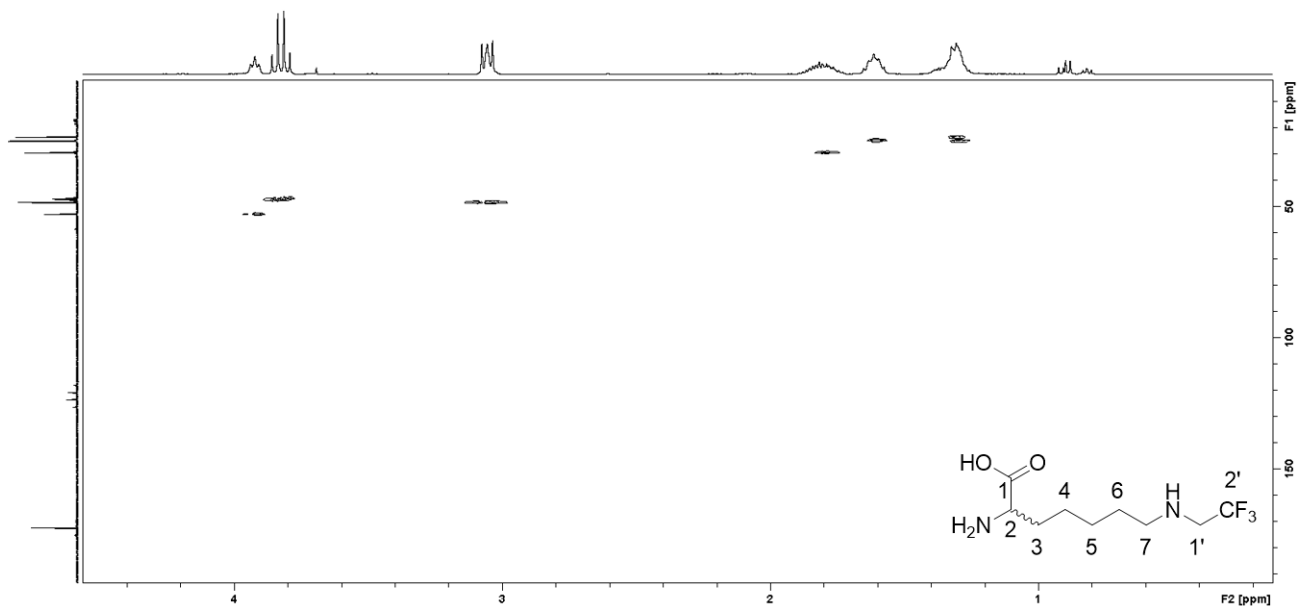


Figure S46. *N* ϵ -(2,2,2-Trifluoroethyl)-*D,L*-homolysine (**7**) (HSQC, pulse prog. *hsqcetgpsi2*, 90% $\text{H}_2\text{O}/10\%$ D_2O , 400 MHz)

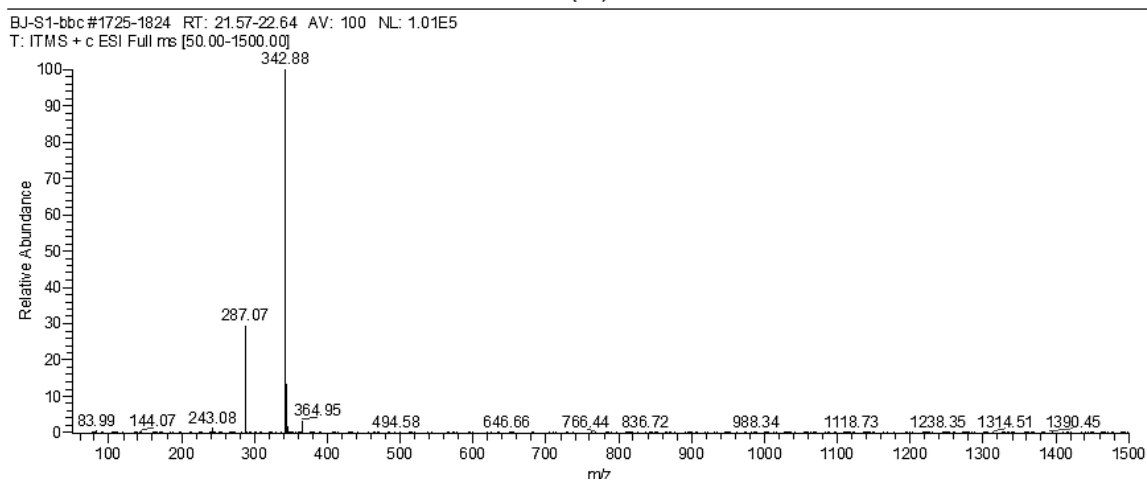
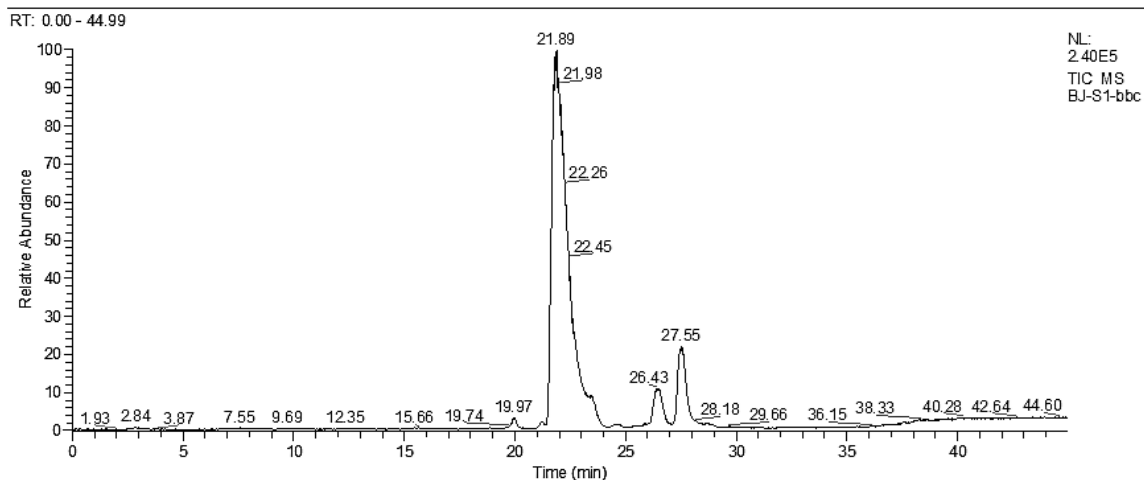


Figure S47. LCMS trace and MS spectrum of methyl N^{ϵ} -*boc*- N^{ϵ} -(2,2,2-trifluoroethyl)-*L*-lysinate.

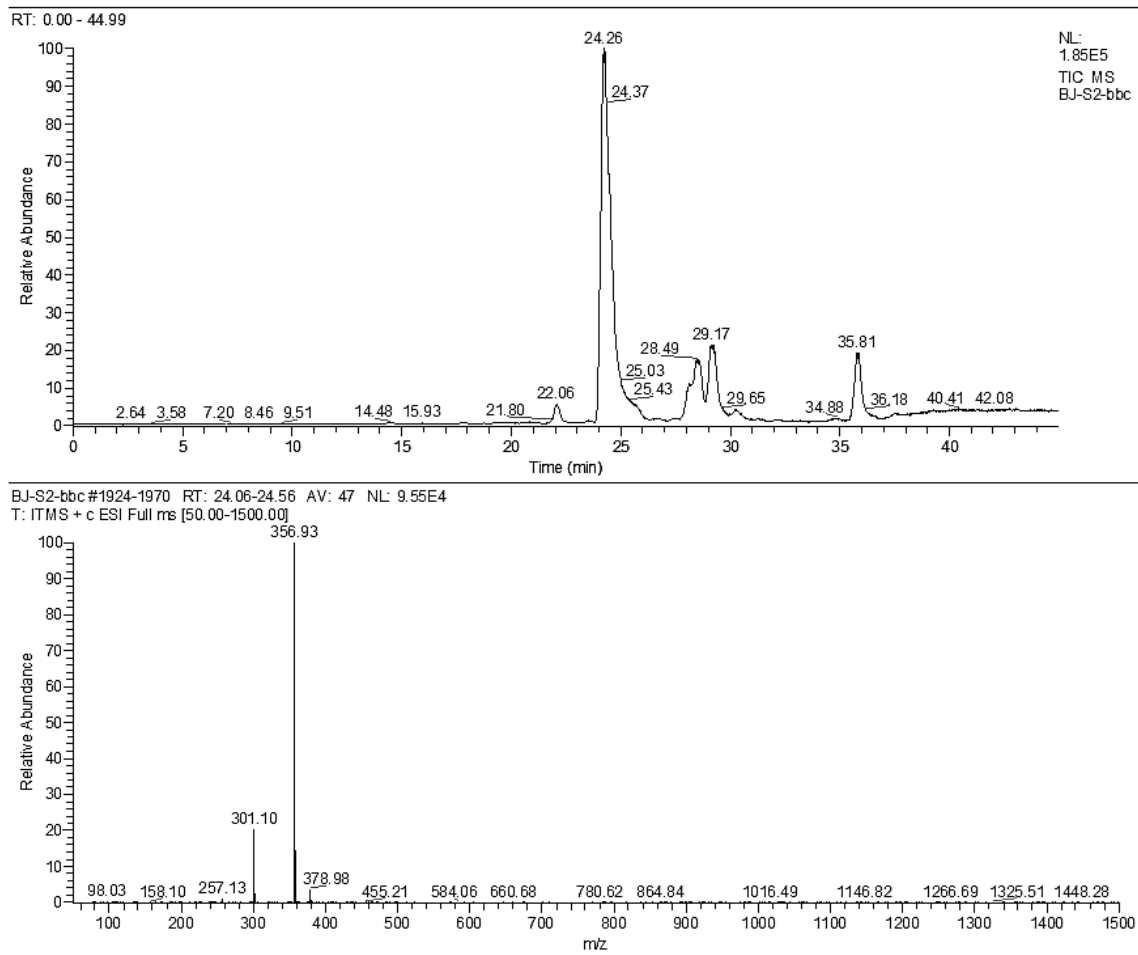


Figure S48. LCMS trace and MS spectrum of methyl N^ϵ -(2,2,2-trifluoroethyl)-*L*-homolysinate.

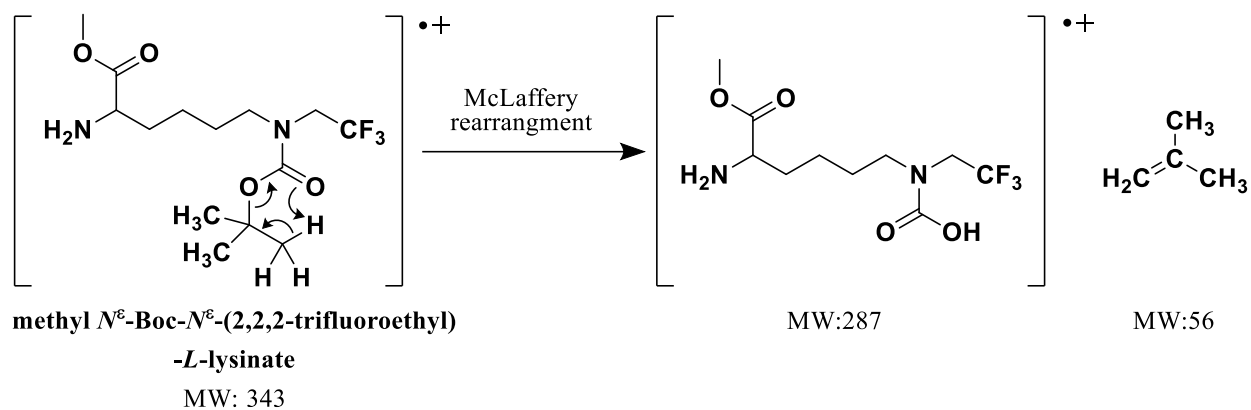


Figure S49. Boc fragmentation pattern observed in LCMS data for methyl N^ϵ -Boc- N^ϵ -(2,2,2-trifluoroethyl)-*L*-lysinate.

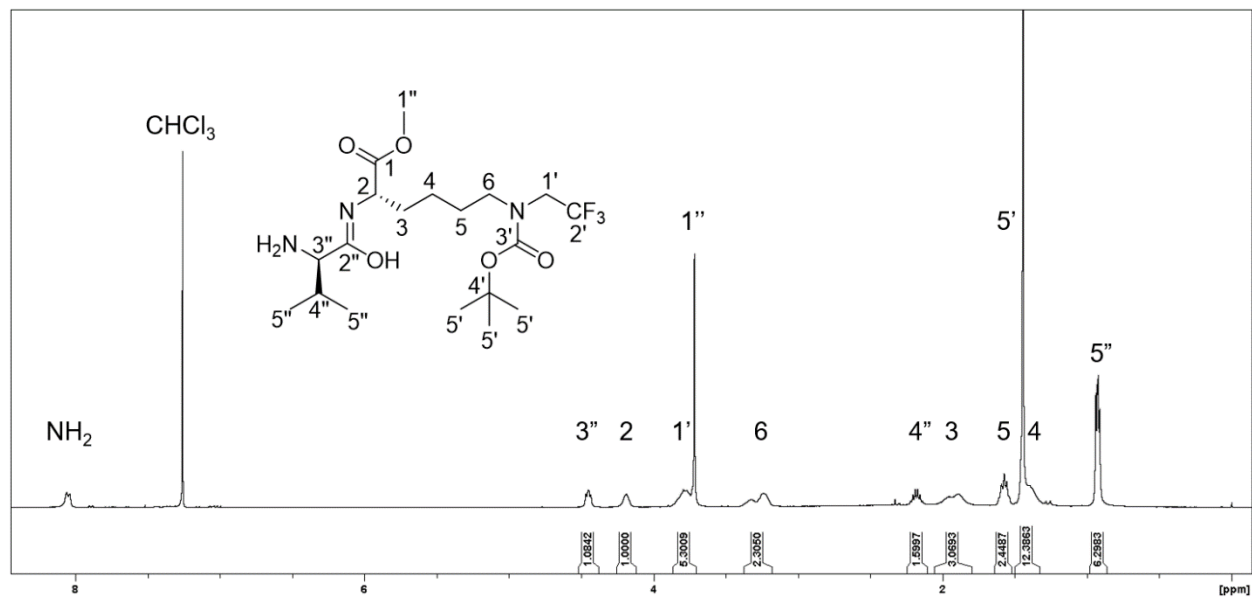


Figure S50. ^1H NMR of the of the Partially Cleaved Impurity from the Separation of **6** ($n = 2$, 26.1-27.1 min)

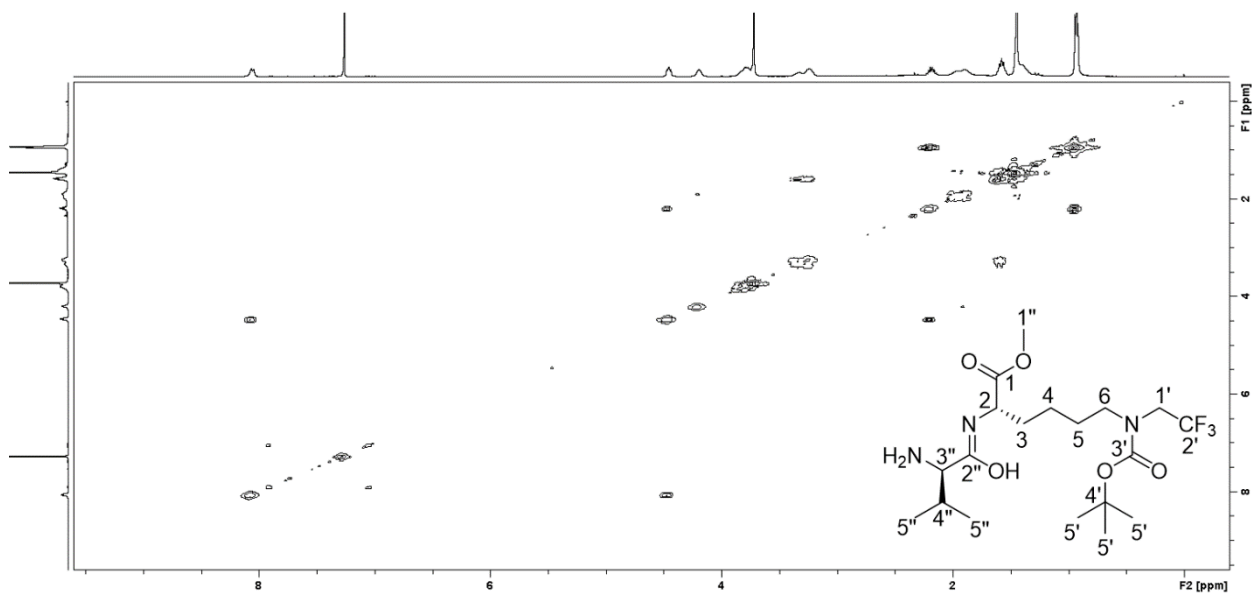


Figure S51. COSY of the of the Partially Cleaved Impurity from the Separation of **6** ($n = 2$, 26.1-27.1 min)