

Electronic supplementary information

Transaminase catalysis for enantiopure saturated heterocycles as potential drug scaffolds

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Table S1. GC methods and retention times for analysis of the transamination reactions by chiral GC.

Substrate	Temperature program	Retention times [min]		
		Ketone 57	(S)-amide (S)-55*	(R)-amide (R)-55*
57a	160-170 °C, 0.8 °C/min	1.82	7.03	7.26
57b	160-175 °C, 0.8 °C/min	3.92	16.25	16.46
57c	160-170 °C, 0.8 °C/min	1.62	5.67	5.97
57d	160-170 °C, 0.8 °C/min	1.89	7.03	7.40
57e	160-190 °C, 0.8 °C/min; 190 °C, 7.5 min	12.40	37.51	38.75
57g	180-210 °C, 0.8 °C/min	10.61	31.37	32.10

*Enantiomers of the amines **57a-g** were separated after derivatization with Ac₂O as their acetamides **55*a-g**

Table S2. Conditions for varying IPA content and substrate concentration in transamination of ketone **57a**.

Entry	Substrate concentration	Varying IPA content			Fixed IPA content		
		IPA amount	IPA equivalent	V/V%	IPA amount	IPA equivalent	V/V%
	[mM]	[μL]	[-]	[%]	[μL]	[-]	[%]
1	10	82	100	8		305	
2	25	205	100	21		122	
3	50	410	100	41	250	61	25
4	75	450	73	45		41	
5	100	450	55	45		31	

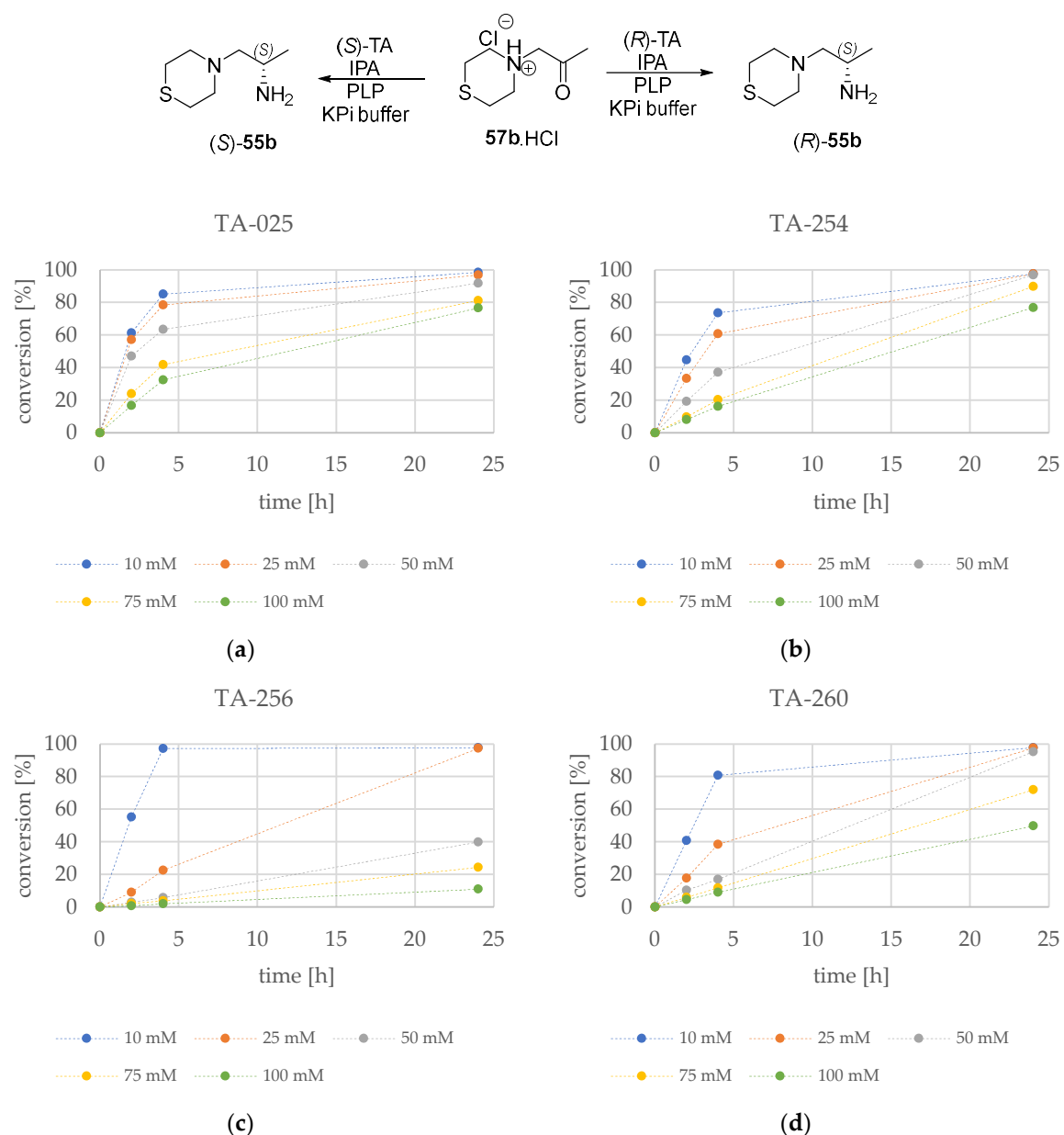


Figure S1. Effect of substrate concentration on transamination of **57b.HCl** with four TAs: **a)** (R)-TA-025, **b)** (S)-TA-254, **c)** (S)-TA-256 and **d)** (S)-TA-260. Reaction conditions: 10-100 mM **57b**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

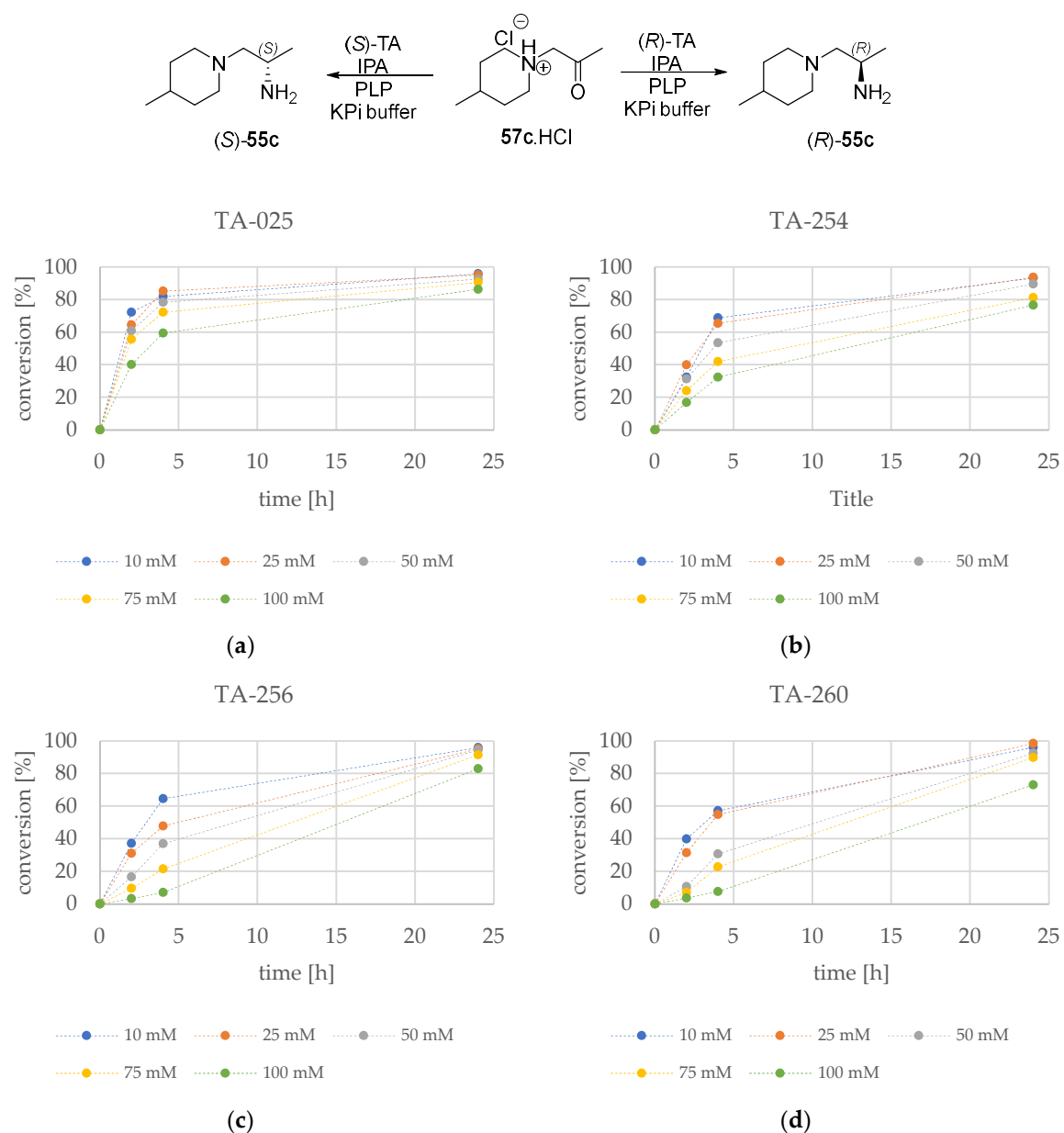


Figure S2. Effect of substrate concentration on transamination of **57c.HCl** with four TAs with **a)** (R)-TA-025, **b)** (S)-TA-254, **c)** (S)-TA-256 and **d)** (S)-TA-260. Reaction conditions: 10-100 mM **57c**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

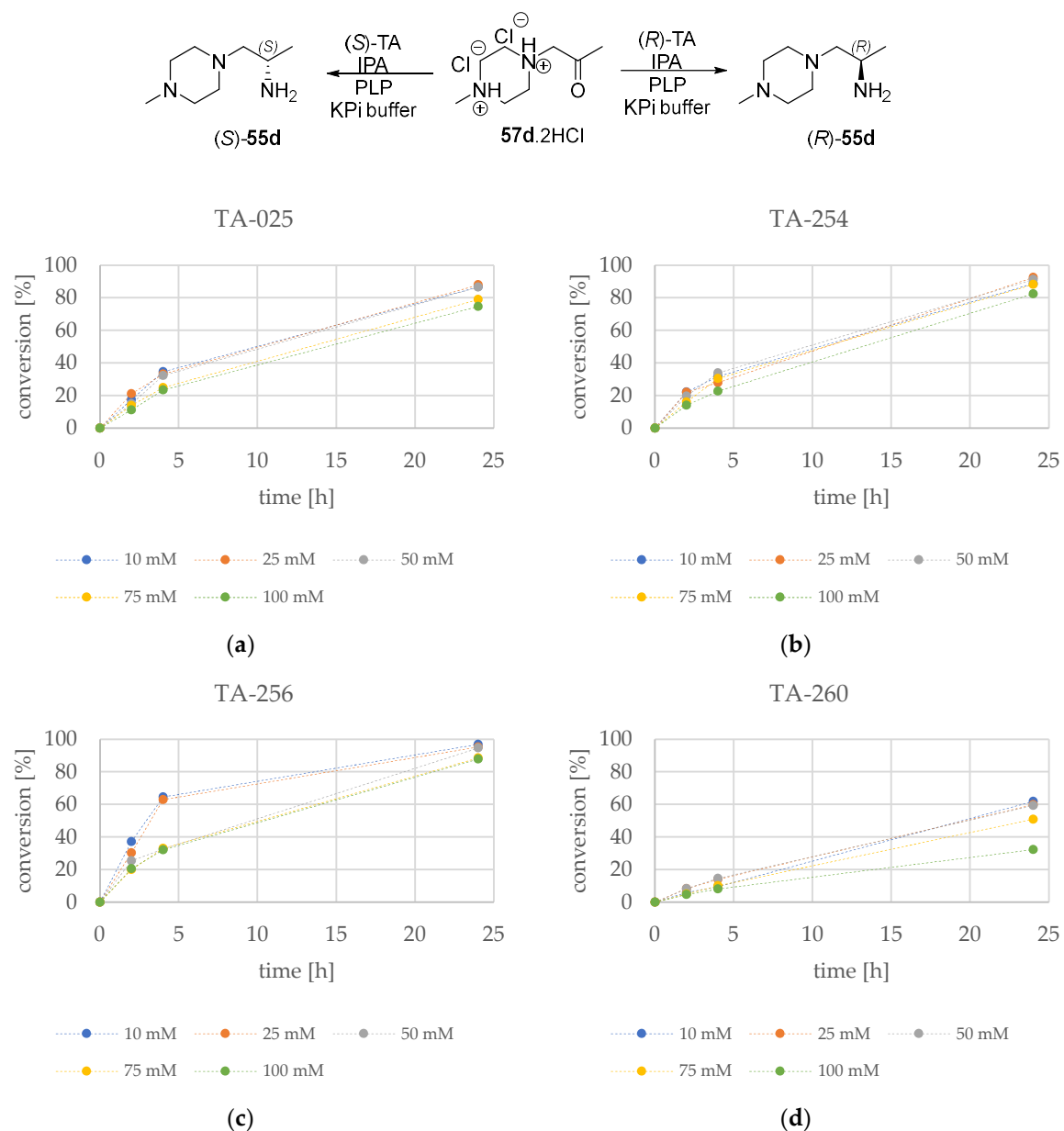


Figure S3. Effect of substrate concentration on transamination of **57d.2HCl** with four TAs with **a)** (R)-TA-025, **b)** (S)-TA-254, **c)** (S)-TA-256 and **d)** (S)-TA-260. Reaction conditions: 10-100 mM **57d**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

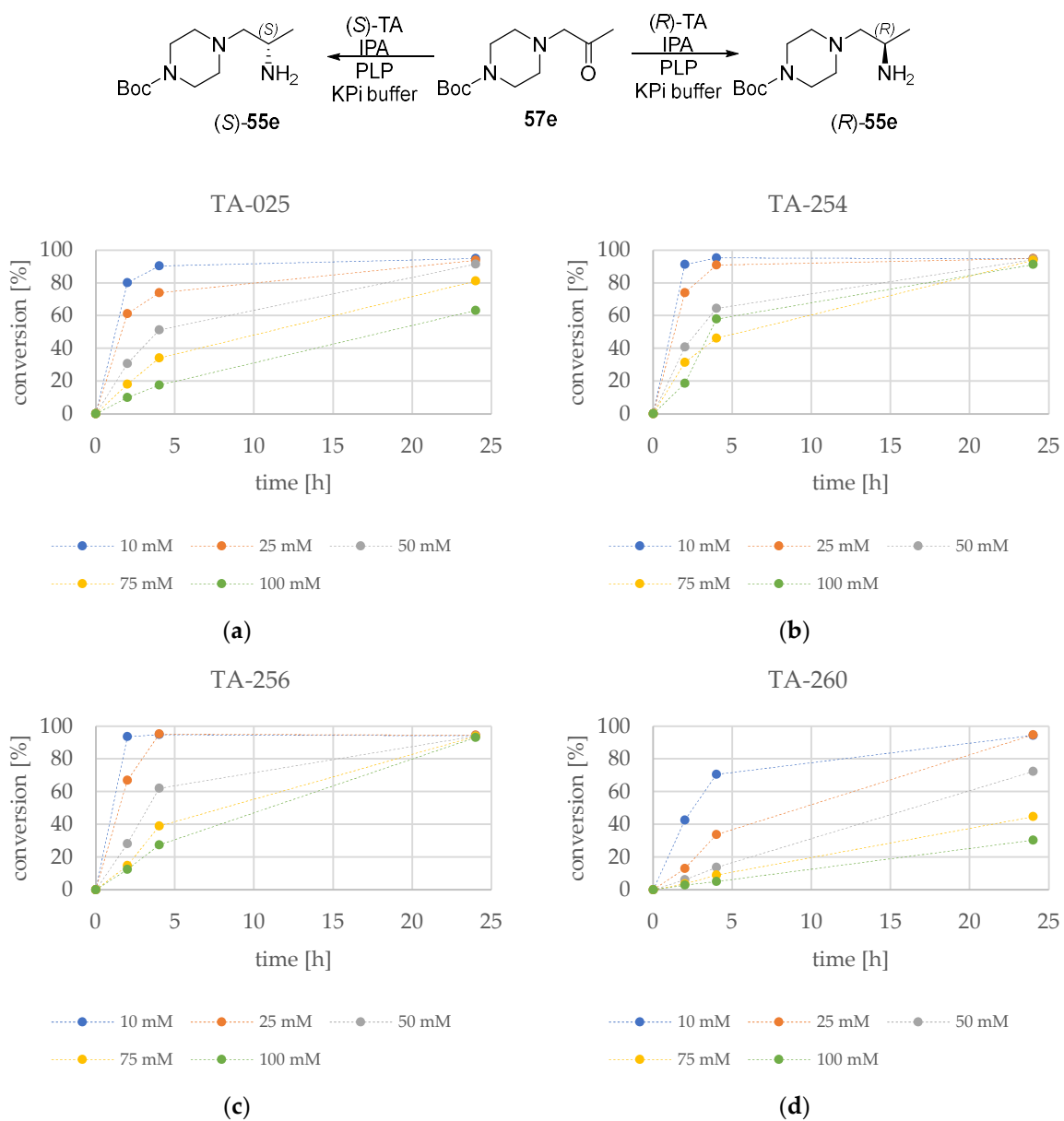


Figure S4. Effect of substrate concentration on transamination of **57e** with four TAs with **a)** (R)-TA-025, **b)** (S)-TA-254, **c)** (S)-TA-256 and **d)** (S)-TA-260. Reaction conditions: 10-100 mM **57e**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

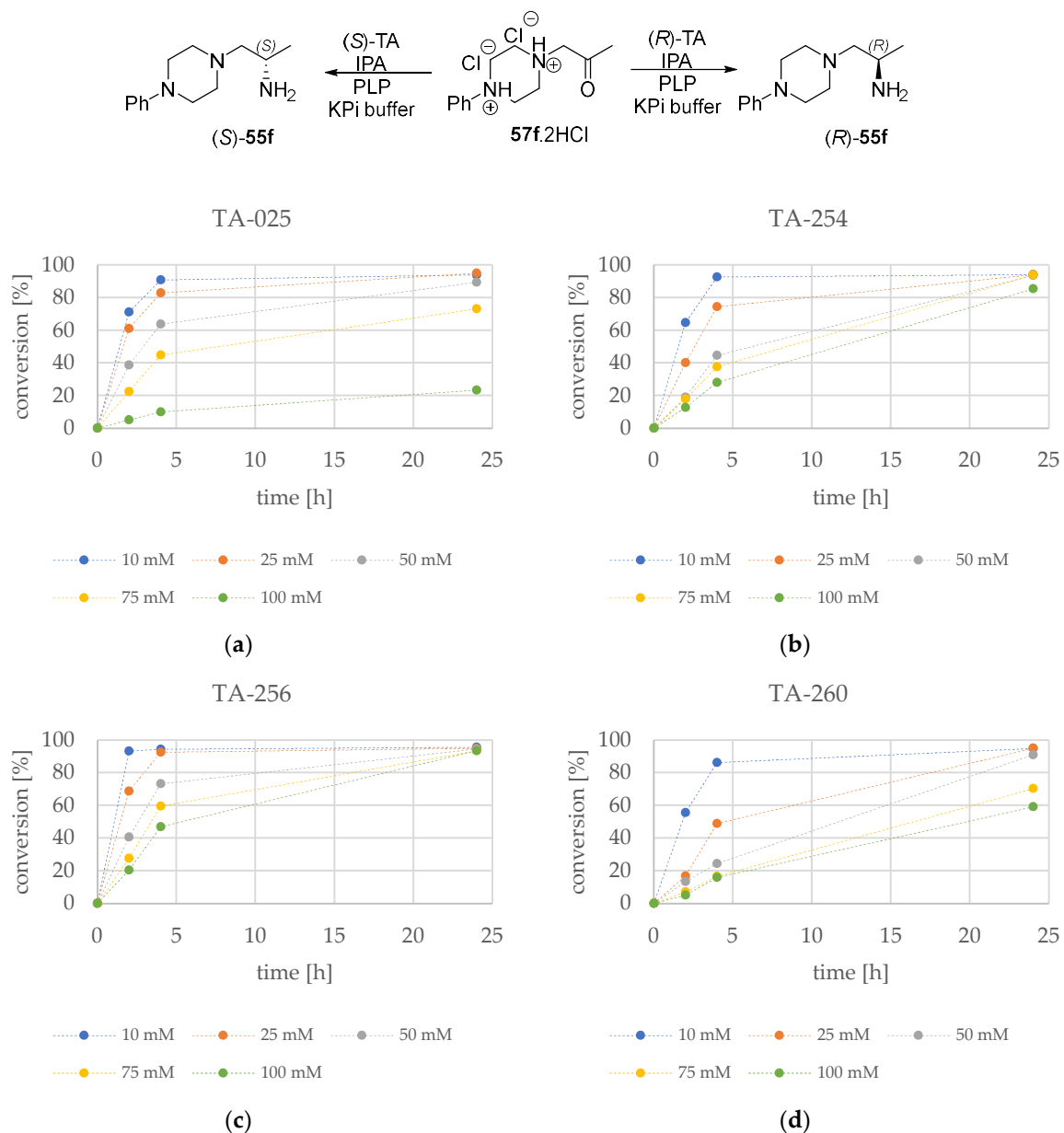


Figure S5. Effect of substrate concentration on transamination of **57f.2HCl** with four TAs with **a)** (*R*)-TA-025, **b)** (*S*)-TA-254, **c)** (*S*)-TA-256 and **d)** (*S*)-TA-260. Reaction conditions: 10-100 mM **57f**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

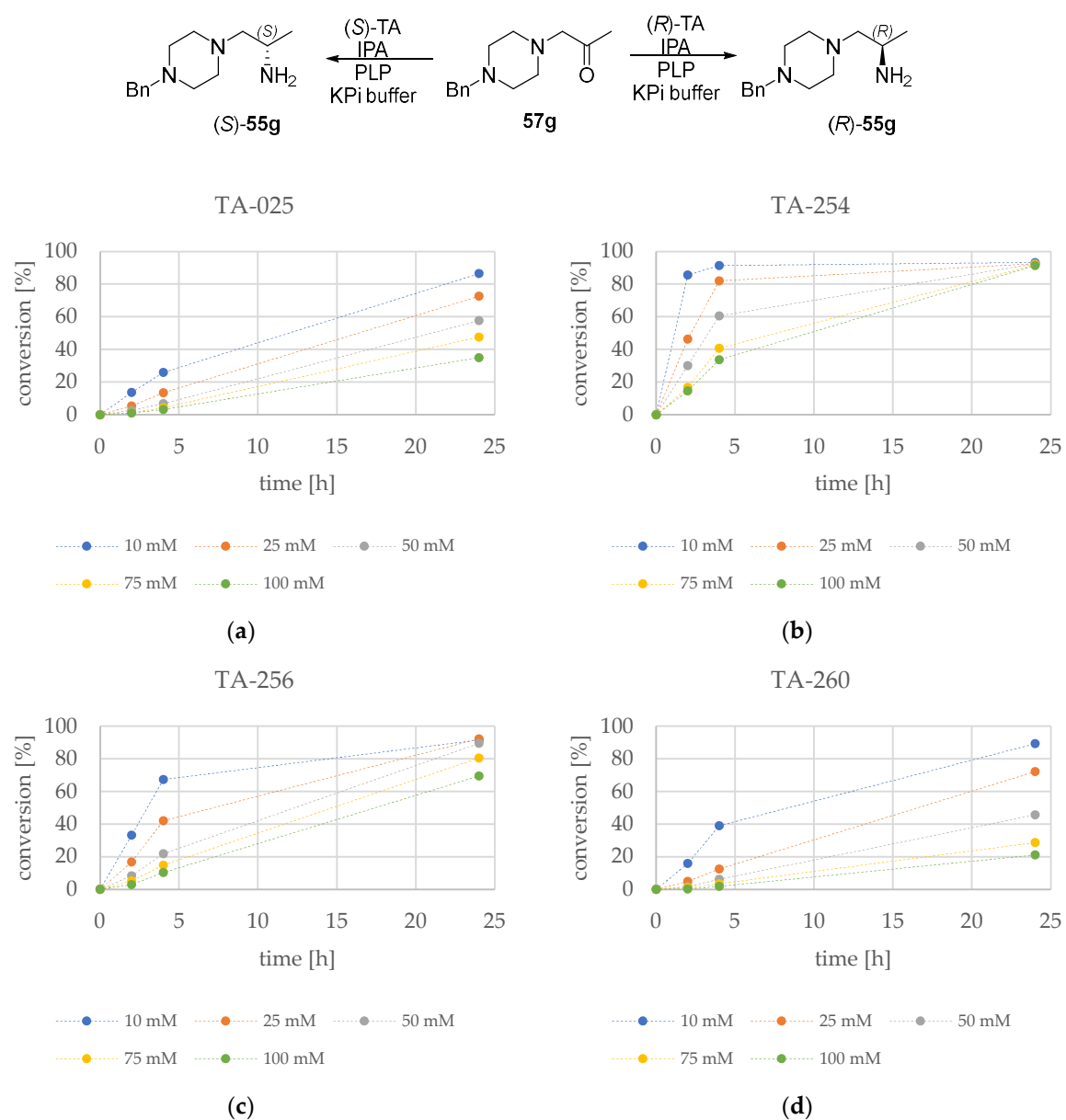


Figure S6. Effect of substrate concentration on transamination of **57g** with four TAs with **a)** (R)-TA-025, **b)** (S)-TA-254, **c)** (S)-TA-256 and **d)** (S)-TA-260. Reaction conditions: 10-100 mM **57g**, 25 V/V% IPA; 2 mg lyophilized TA biocatalyst, 1 mM PLP, KPi buffer (100 mM, pH 7.5), total volume 1 mL.

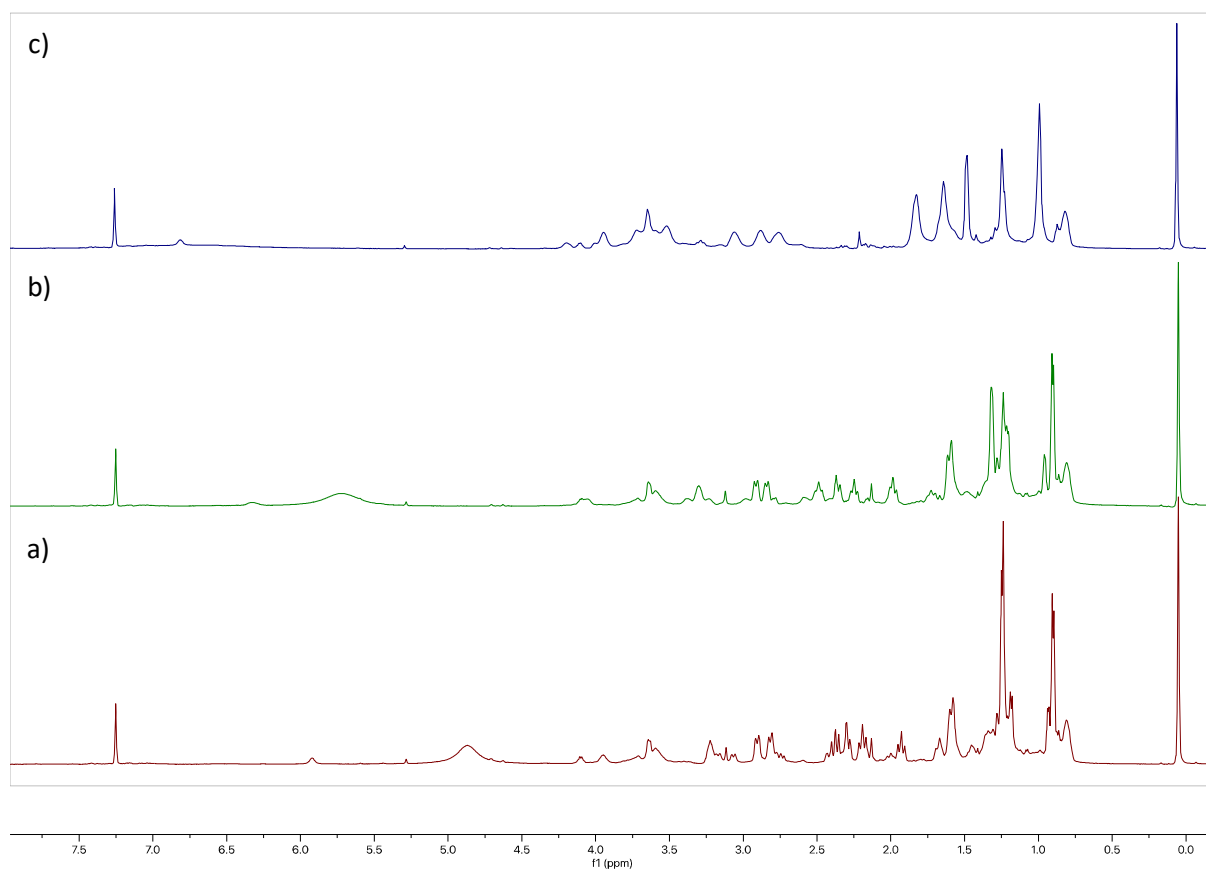


Figure S7. ^1H NMR spectra of (S)-55c a) without TFA, with b) 10% TFA, c) 50% TFA.

GC chromatograms of the starting materials and the products of the TA-catalyzed stereoselective biotransformations

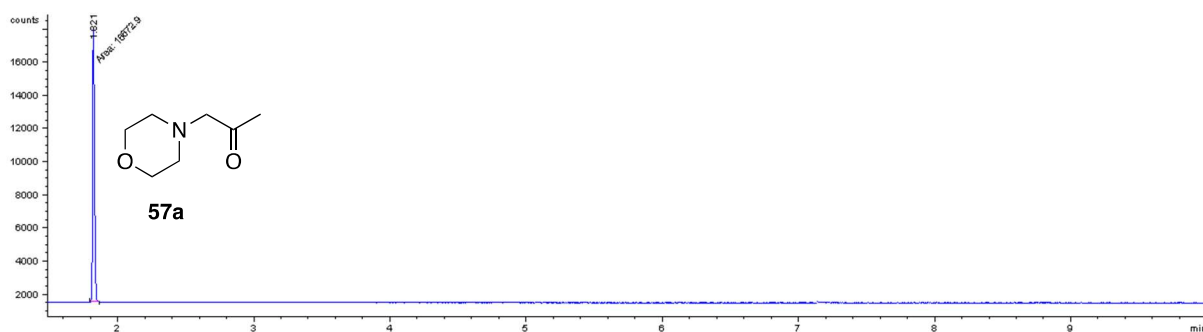


Figure S8. GC chromatogram of 1-morpholinopropane-2-one (**57a**)

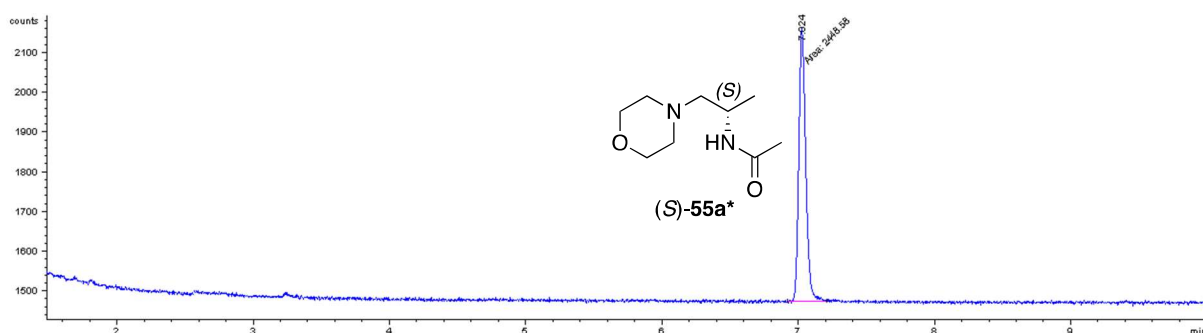


Figure S9. GC chromatogram of acetamide ((*S*)-**55*a**) of (*S*)-1-morpholinopropane-2-amine ((*S*)-**55a**) after derivatization with Ac₂O.

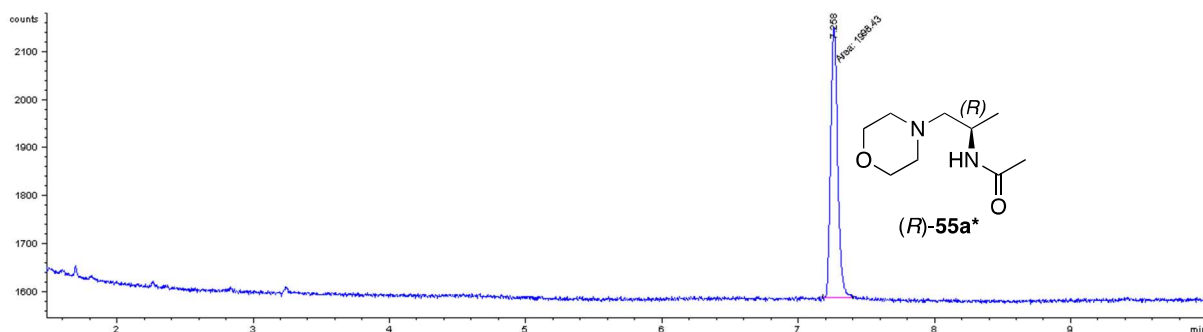


Figure S10. GC chromatogram of acetamide ((*R*)-**55*a**) of (*R*)-1-morpholinopropane-2-amine ((*R*)-**55a**) after derivatization with Ac₂O.

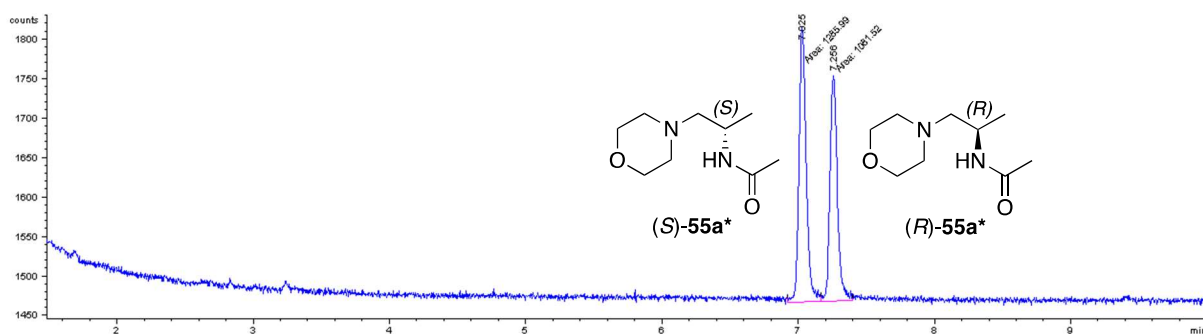


Figure S11. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*a**) from a mixture of (*S*)- and (*R*)-1-morpholinopropane-2-amine ((*S*)- and (*R*)-**55a**) after derivatization with Ac₂O.

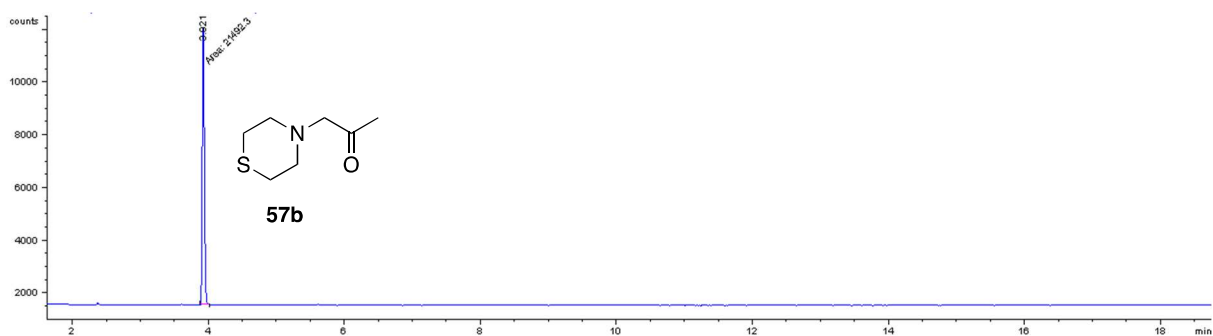


Figure S12. GC chromatogram of 1-thiomorpholinopropane-2-one (**57b**)

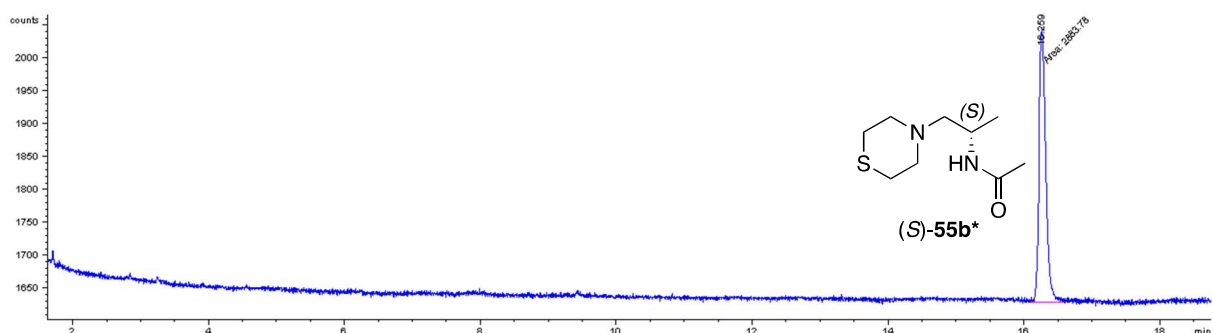


Figure S13. GC chromatogram of acetamide ((*S*)-**55*b**) of (*S*)-1-thiomorpholinopropane-2-amine ((*S*)-**55b**) after derivatization with Ac₂O.

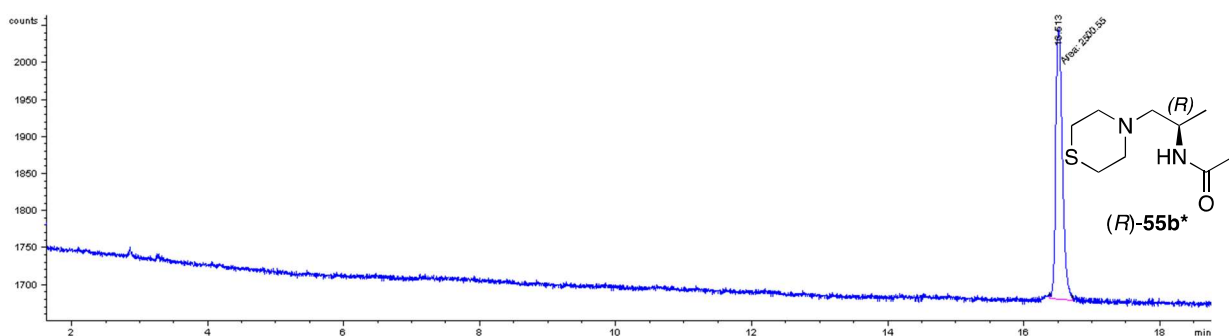


Figure S14. GC chromatogram of acetamide ((*R*)-**55*b**) of (*R*)-1-thiomorpholinopropane-2-amine ((*R*)-**55b**) after derivatization with Ac₂O.

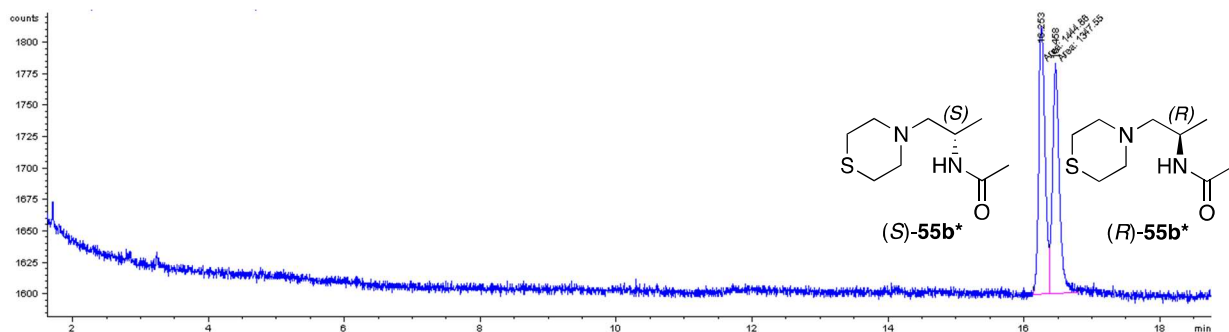


Figure S15. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*b**) from a mixture of (*S*)- and (*R*)-1-thiomorpholinopropane-2-amine ((*S*)- and (*R*)-**55b**) after derivatization with Ac₂O.

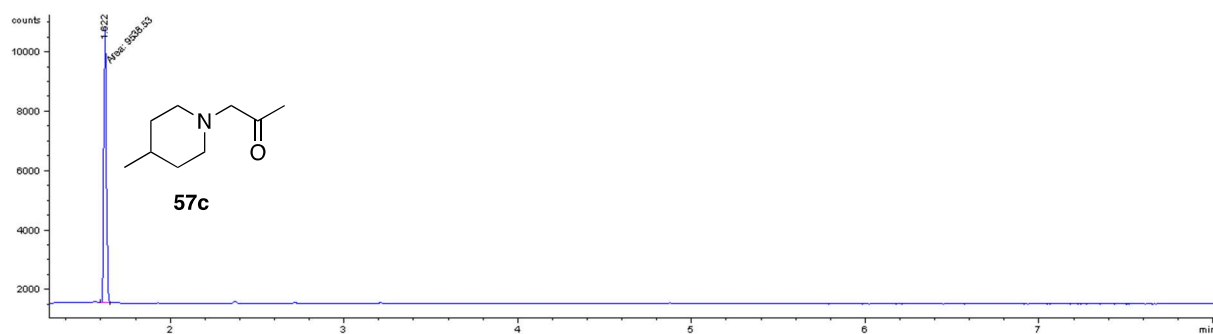


Figure S16. GC chromatogram of 1-(4-methylpiperidin-1-yl)propan-2-one (**57c**)

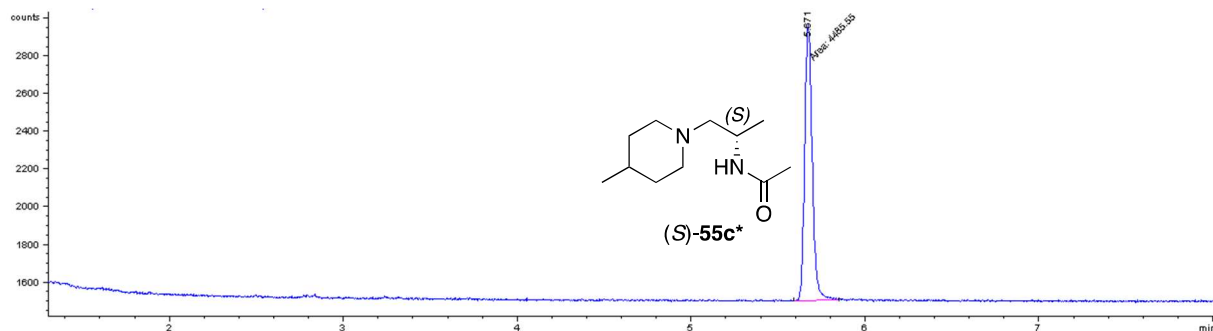


Figure S17. GC chromatogram of acetamide ((*S*)-**55*c**) of (*S*)-1-(4-methylpiperidin-1-yl)propan-2-amine ((*S*)-**55c**) after derivatization with Ac₂O.

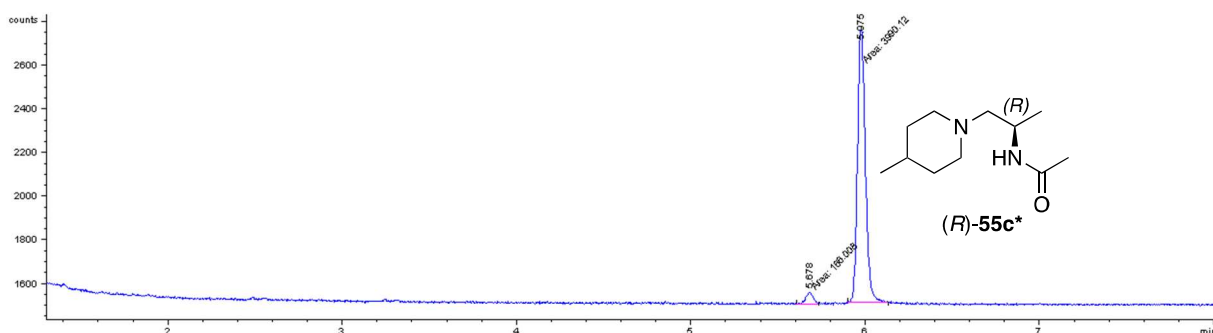


Figure S18. GC chromatogram of acetamide ((*R*)-**55*c**) of (*R*)-1-(4-methylpiperidin-1-yl)propan-2-amine ((*R*)-**55c**) after derivatization with Ac₂O.

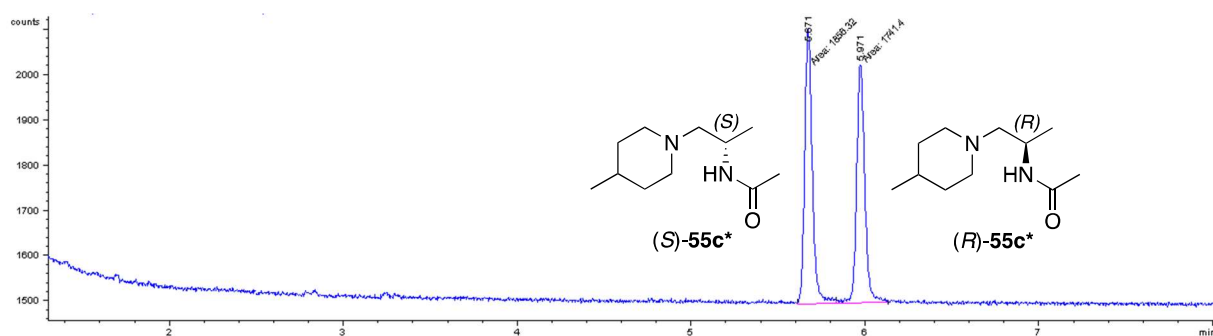


Figure S19. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*c**) from a mixture of (*S*)- and (*R*)-1-(4-methylpiperidin-1-yl)propan-2-amine ((*S*)- and (*R*)-**55c**) after derivatization with Ac₂O.

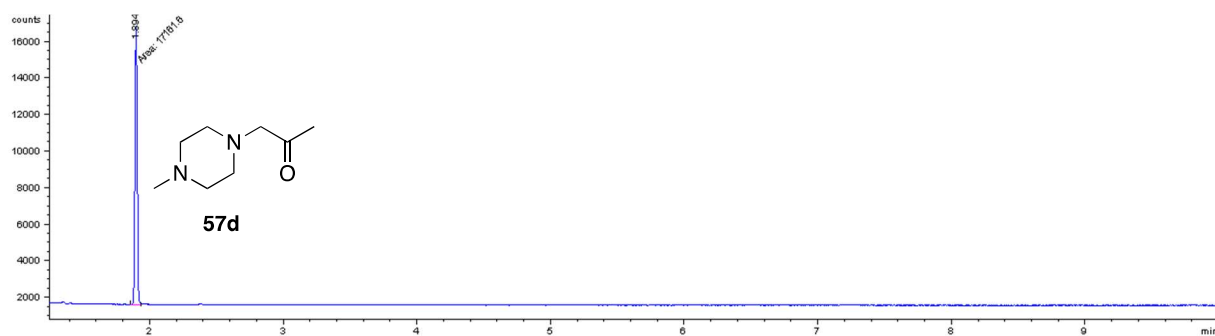


Figure S20. GC chromatogram of 1-(4-methylpiperazin-1-yl)propan-2-one (**57d**)

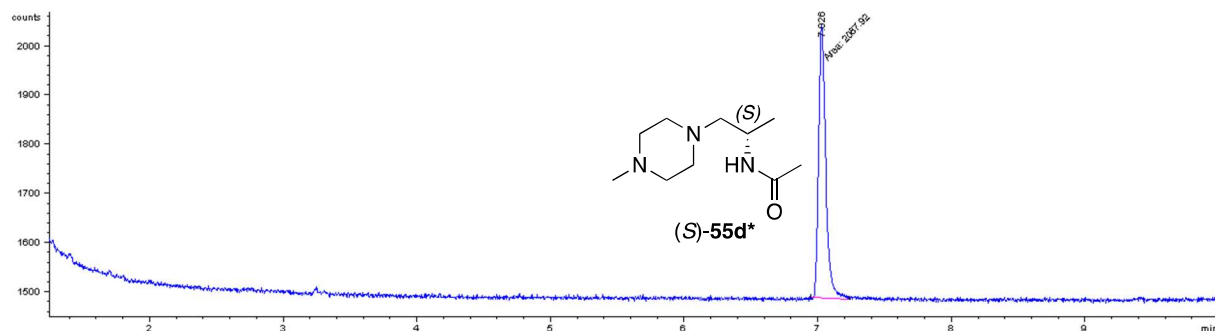


Figure S21. GC chromatogram of acetamide ((*S*)-**55*d**) of (*S*)-1-(4-methylpiperazin-1-yl)propan-2-amine ((*S*)-**55d**) after derivatization with Ac₂O.

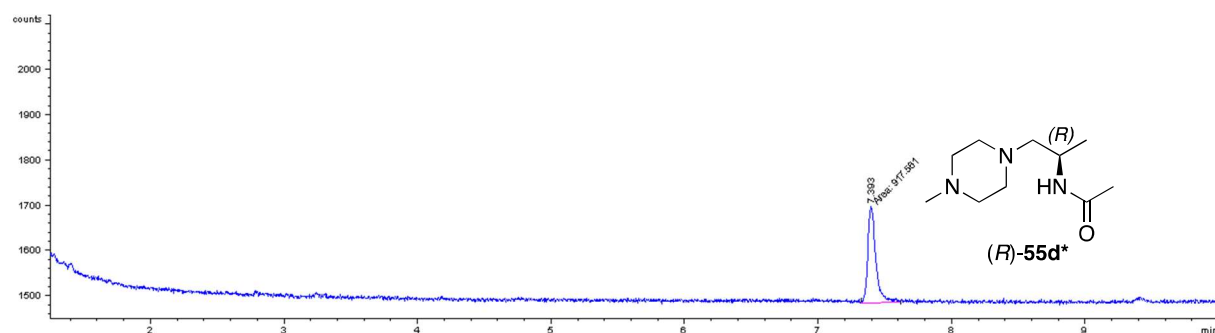


Figure S22. GC chromatogram of acetamide ((*R*)-**55*d**) of (*R*)-1-(4-methylpiperazin-1-yl)propan-2-amine ((*R*)-**55d**) after derivatization with Ac₂O.

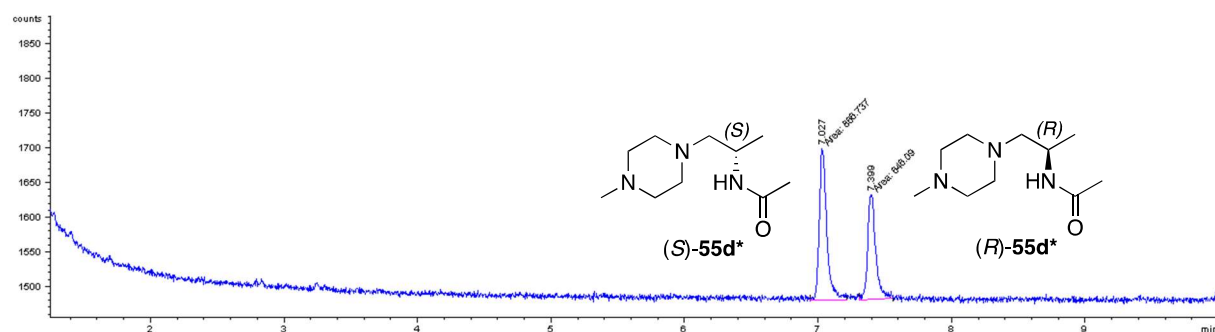


Figure S23. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*d**) from a mixture of (*S*)- and (*R*)-1-(4-methylpiperazin-1-yl)propan-2-amine ((*S*)- and (*R*)-**55d**) after derivatization with Ac₂O.

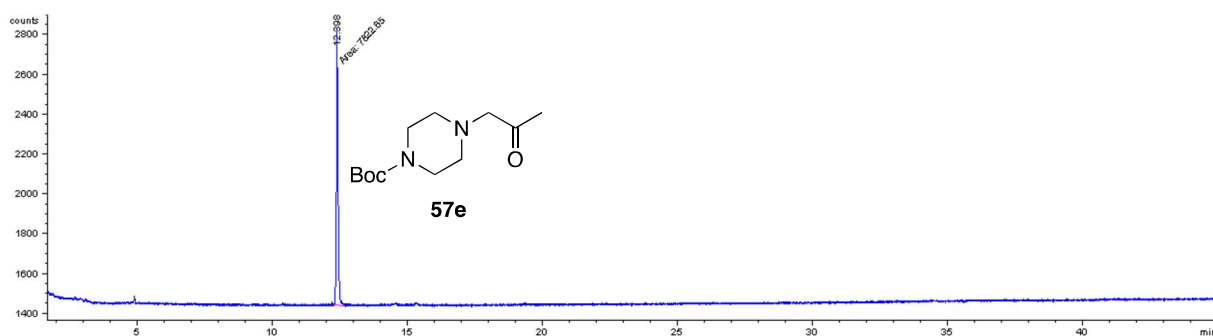


Figure S24. GC chromatogram of *tert*-butyl 4-(2-oxopropyl)piperazine-1-carboxylate (**57e**)

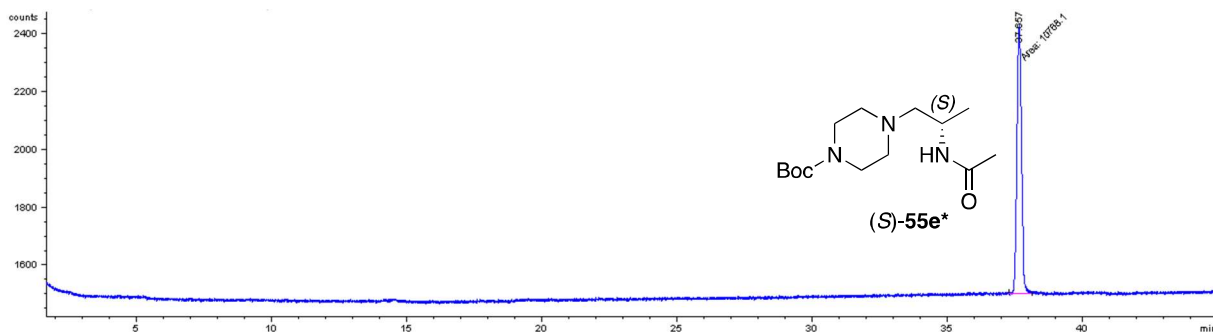


Figure S25. GC chromatogram of acetamide ((*S*)-**55*e**) of *tert*-butyl (*S*)-4-(2-aminopropyl)piperazine-1-carboxylate ((*S*)-**55e**) after derivatization with Ac₂O.

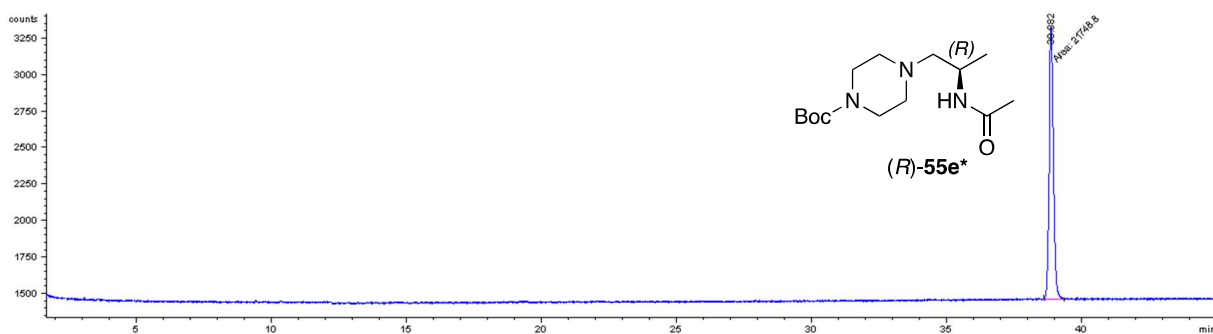


Figure S26. GC chromatogram of acetamide ((*R*)-**55*e**) of *tert*-butyl (*R*)-4-(2-aminopropyl)piperazine-1-carboxylate ((*R*)-**55e**) after derivatization with Ac₂O.

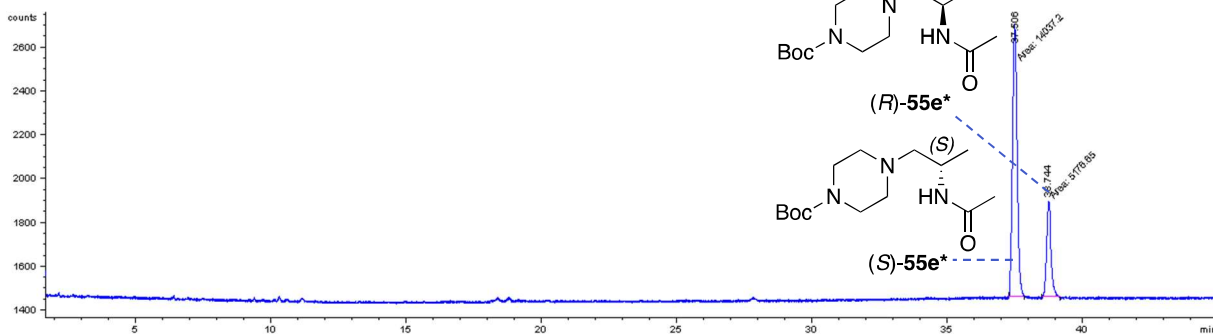


Figure S27. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*e**) from a mixture of *tert*-butyl (*S*)-4-(2-aminopropyl)piperazine-1-carboxylate and *tert*-butyl (*R*)-4-(2-aminopropyl)piperazine-1-carboxylate ((*S*)- and (*R*)-**55e**) after derivatization with Ac₂O.

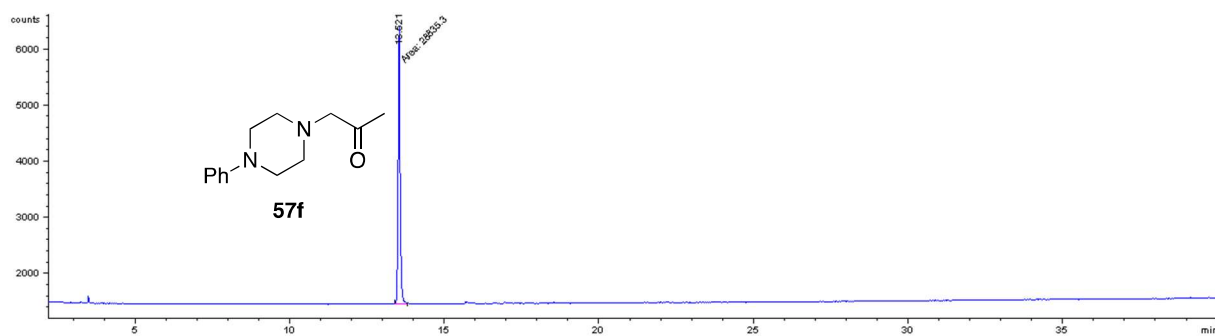


Figure S28. GC chromatogram of 1-(4-phenylpiperazin-1-yl)propan-2-one (**57f**)

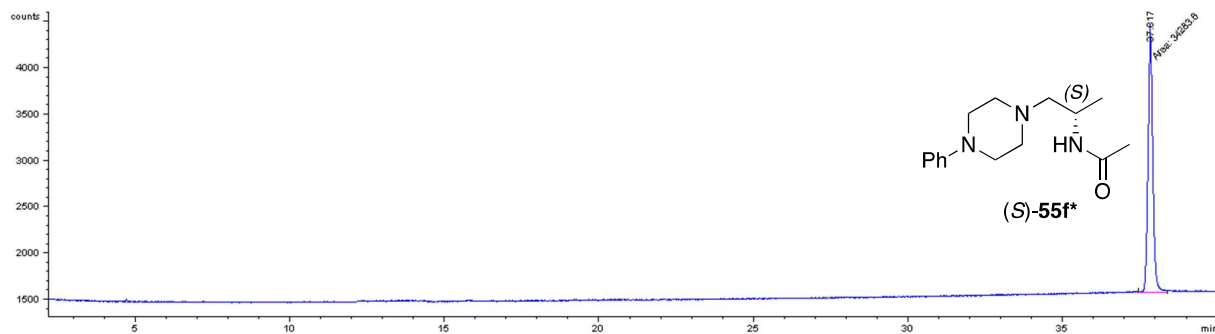


Figure S29. GC chromatogram of acetamide ((*S*)-**55*f**) of (*S*)-1-(4-phenylpiperazin-1-yl)propan-2-amine ((*S*)-**55f**) after derivatization with Ac₂O.

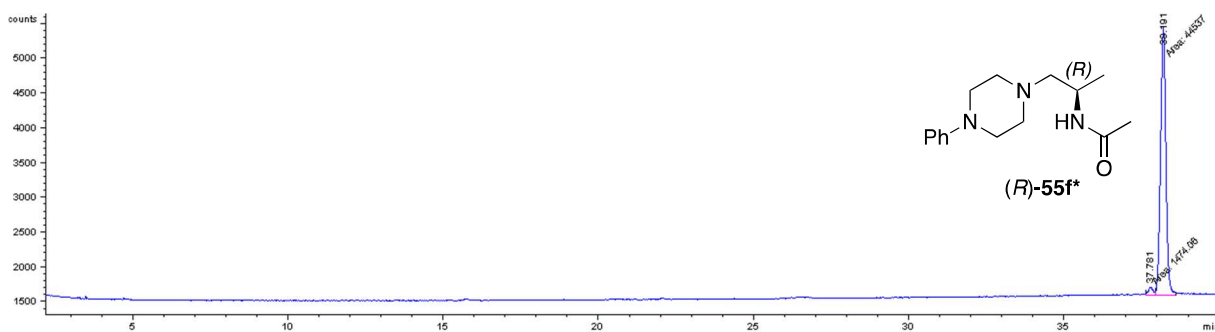


Figure S30. GC chromatogram of acetamide ((*R*)-**55*f**) of (*R*)-1-(4-phenylpiperazin-1-yl)propan-2-amine ((*R*)-**55f**) after derivatization with Ac₂O.

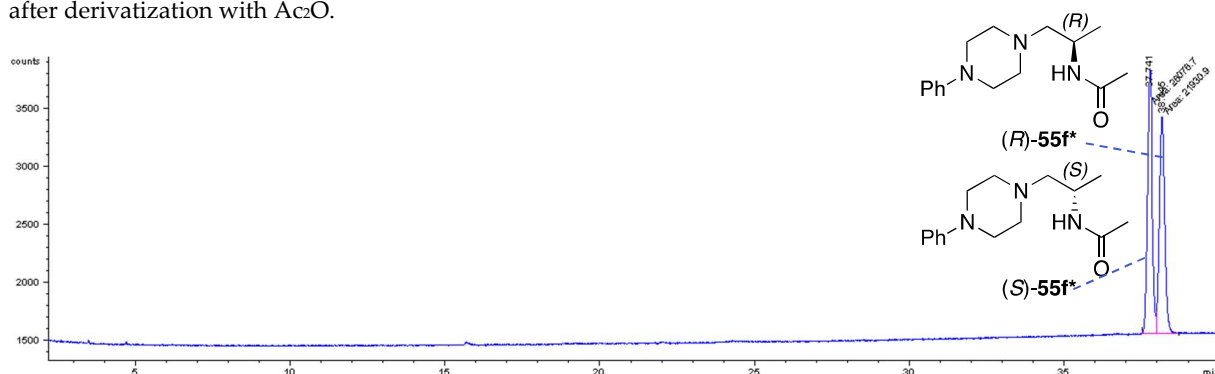


Figure S31. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*f**) from a mixture of (*S*)- and (*R*)-1-(4-phenylpiperazin-1-yl)propan-2-amine ((*S*)- and (*R*)-**55f**) after derivatization with Ac₂O.

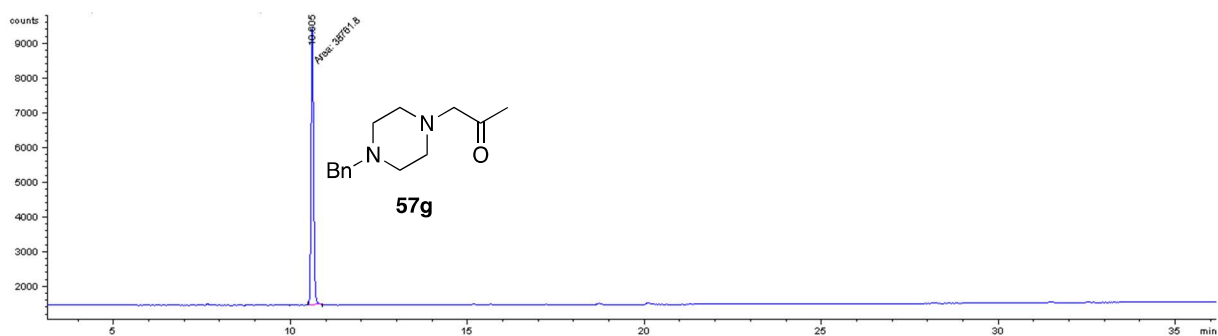


Figure S32. GC chromatogram of 1-(4-benzylpiperazin-1-yl)propan-2-one (**57g**)

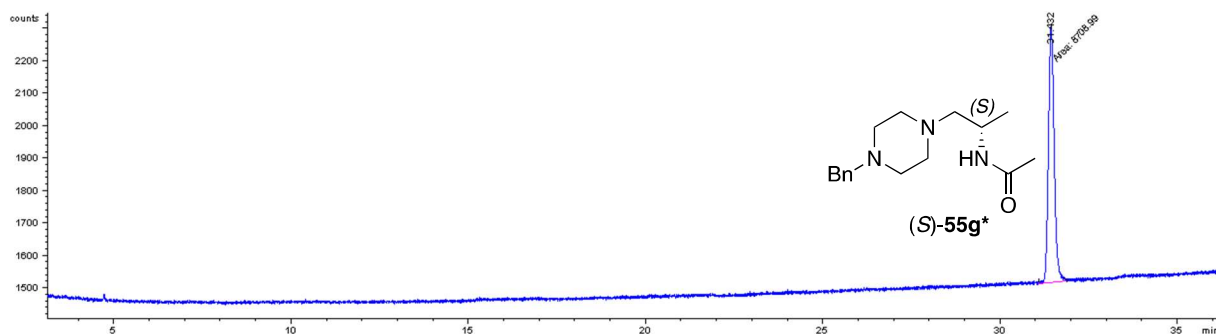


Figure S33. GC chromatogram of acetamide ((*S*)-**55*g**) of (*S*)-1-(4-benzylpiperazin-1-yl)propan-2-amine ((*S*)-**55g**) after derivatization with Ac₂O.

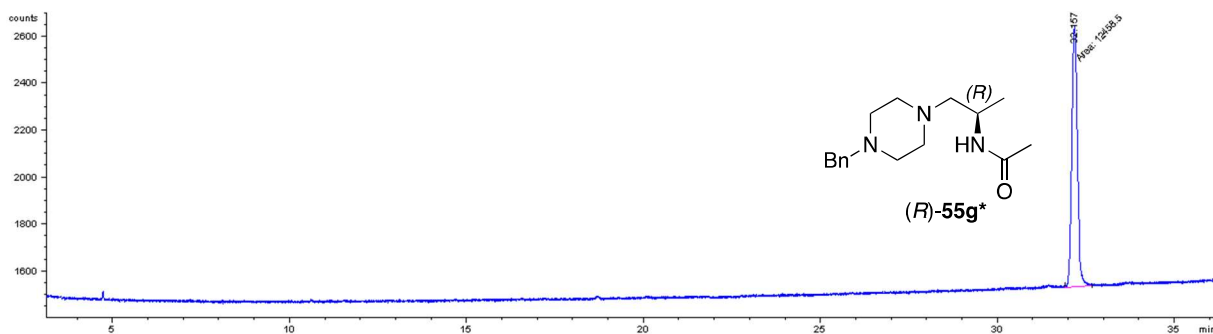


Figure S34. GC chromatogram of acetamide ((*R*)-**55*g**) of (*R*)-1-(4-benzylpiperazin-1-yl)propan-2-amine ((*R*)-**55g**) after derivatization with Ac₂O.

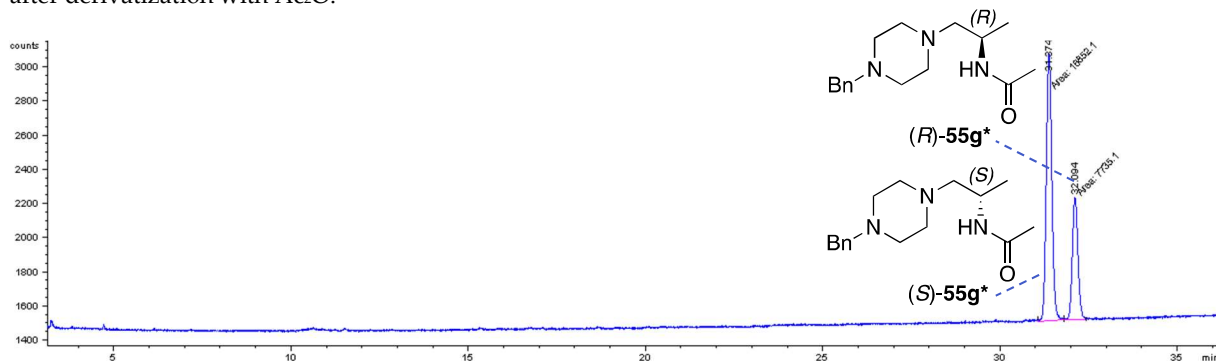


Figure S35. GC chromatogram of acetamides ((*S*)- and (*R*)-**55*g**) from a mixture of (*S*)- and (*R*)-1-(4-benzylpiperazin-1-yl)propan-2-amine ((*S*)- and (*R*)-**55g**) after derivatization with Ac₂O.

NMR spectra of compounds



Figure S36. ¹H-NMR spectrum of *tert*-butyl 4-(2-oxopropyl)piperazine-1-carboxylate (57e).

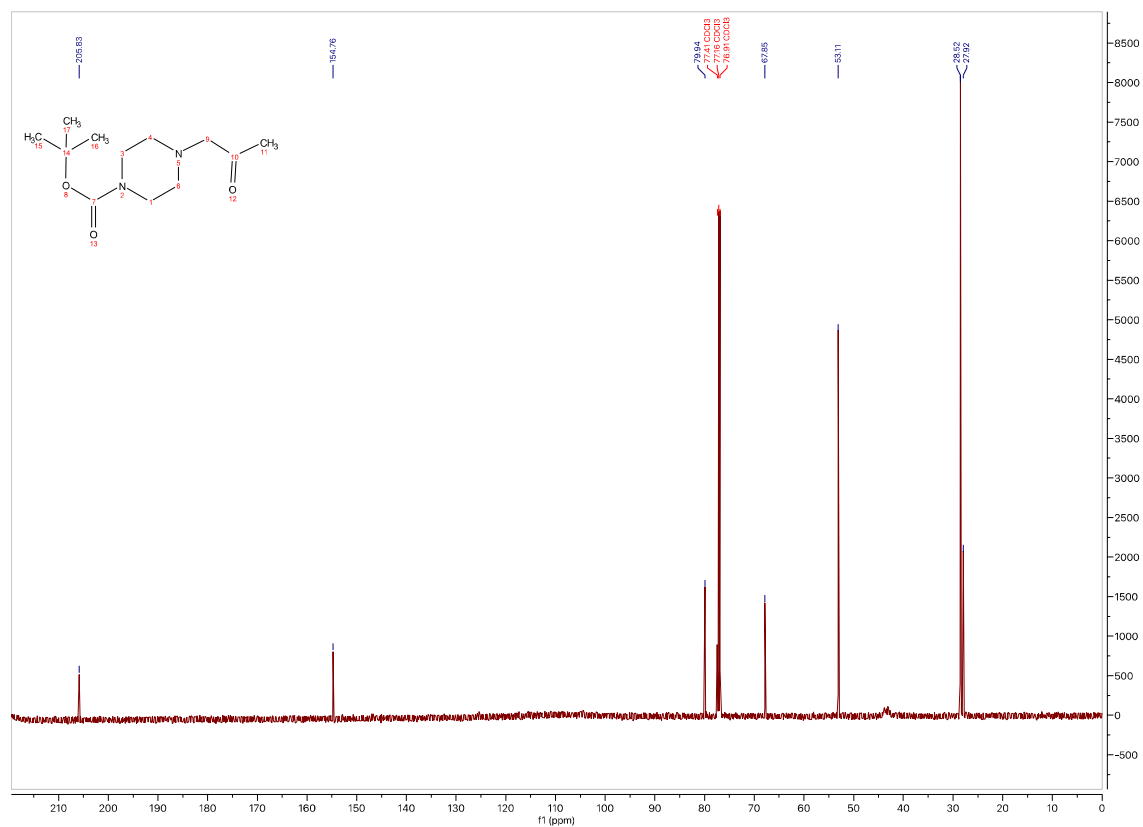


Figure S37. ¹³C-NMR spectrum of *tert*-butyl 4-(2-oxopropyl)piperazine-1-carboxylate (57e)

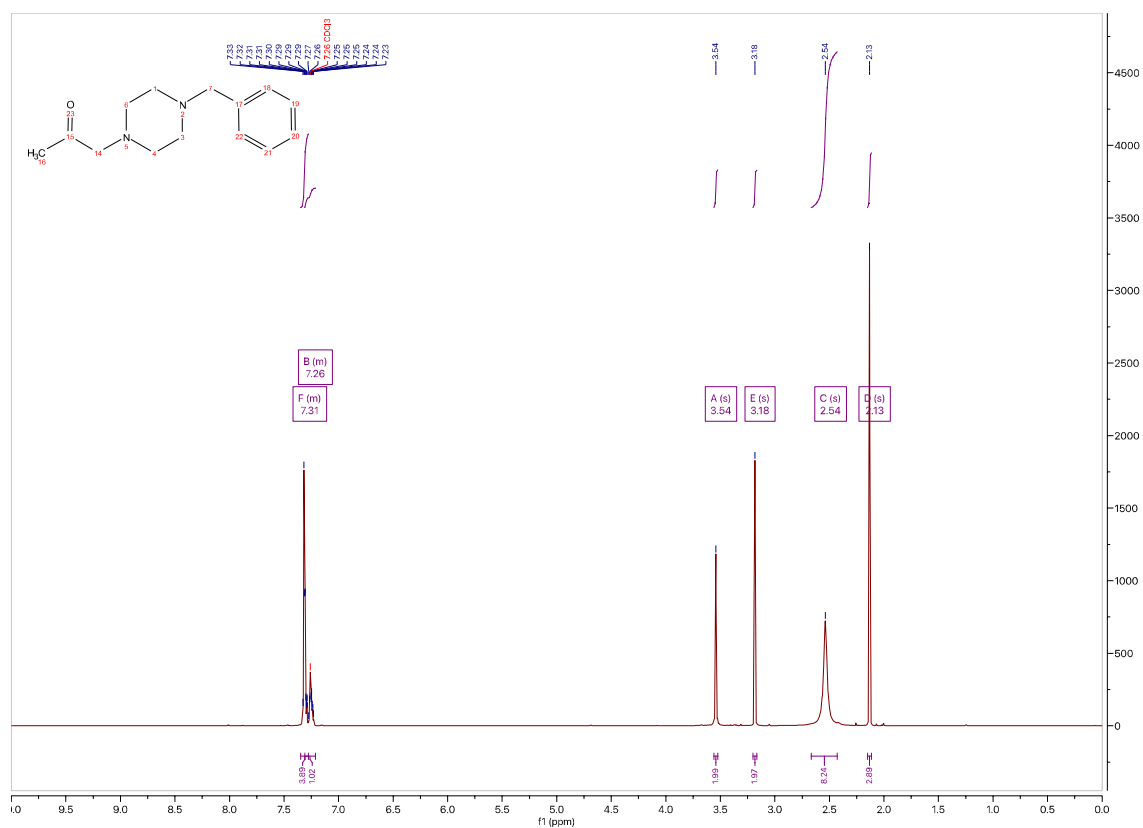


Figure S38. ¹H-NMR spectrum of 1-(4-benzylpiperazin-1-yl)propan-2-one (57g).

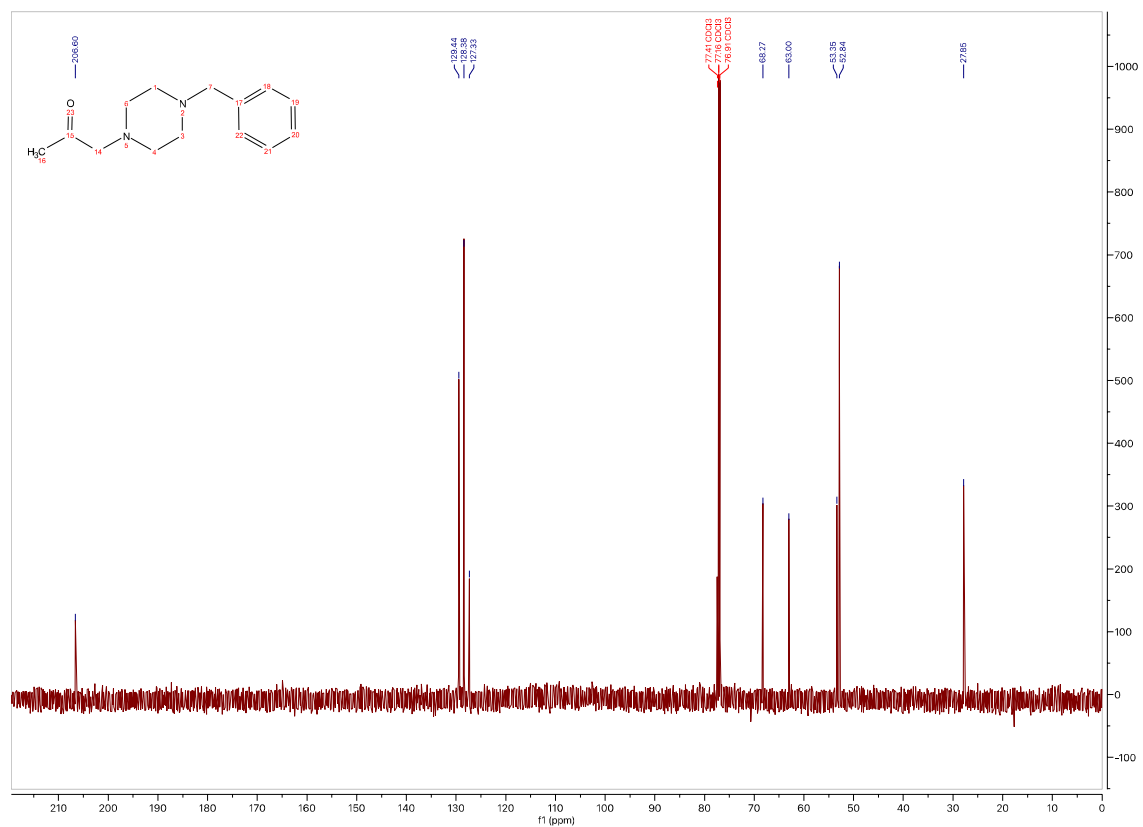


Figure S39. ¹³C-NMR spectrum of 1-(4-benzylpiperazin-1-yl)propan-2-one (57g).

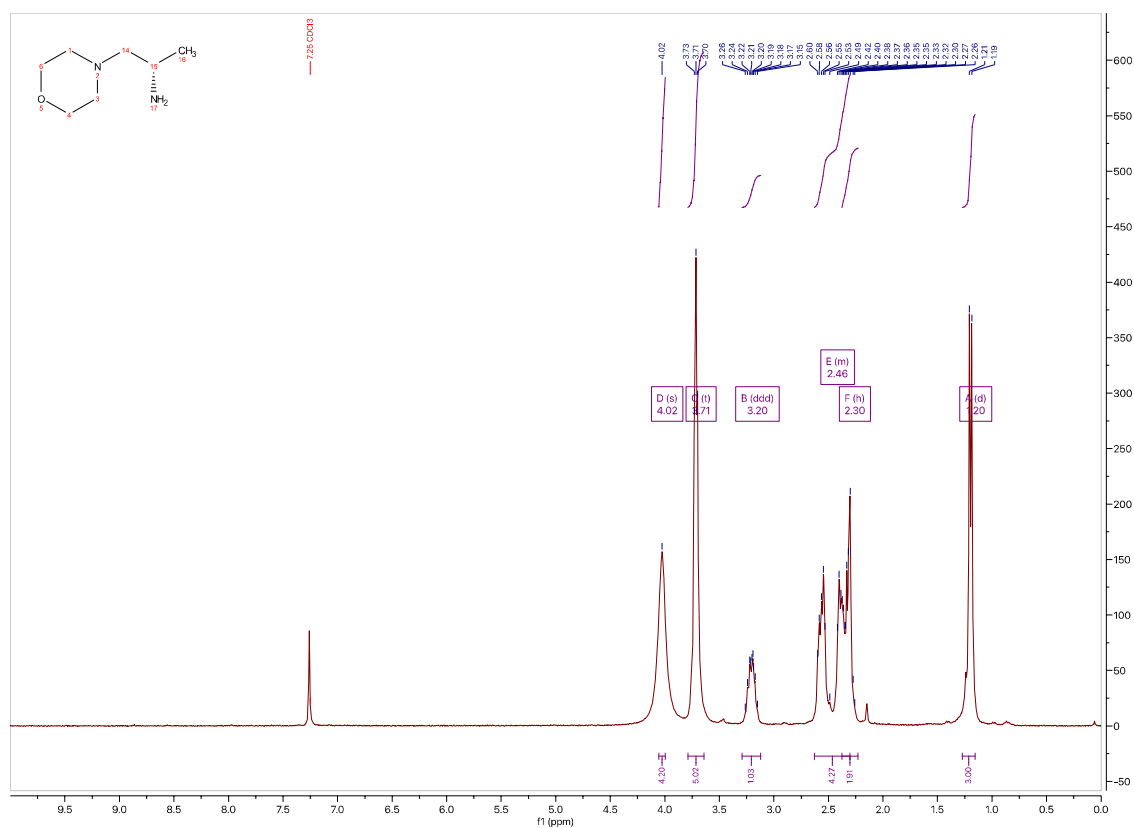


Figure S40. ¹H-NMR spectrum of (S)-1-morpholinopropan-2-amine [(S)-55a].

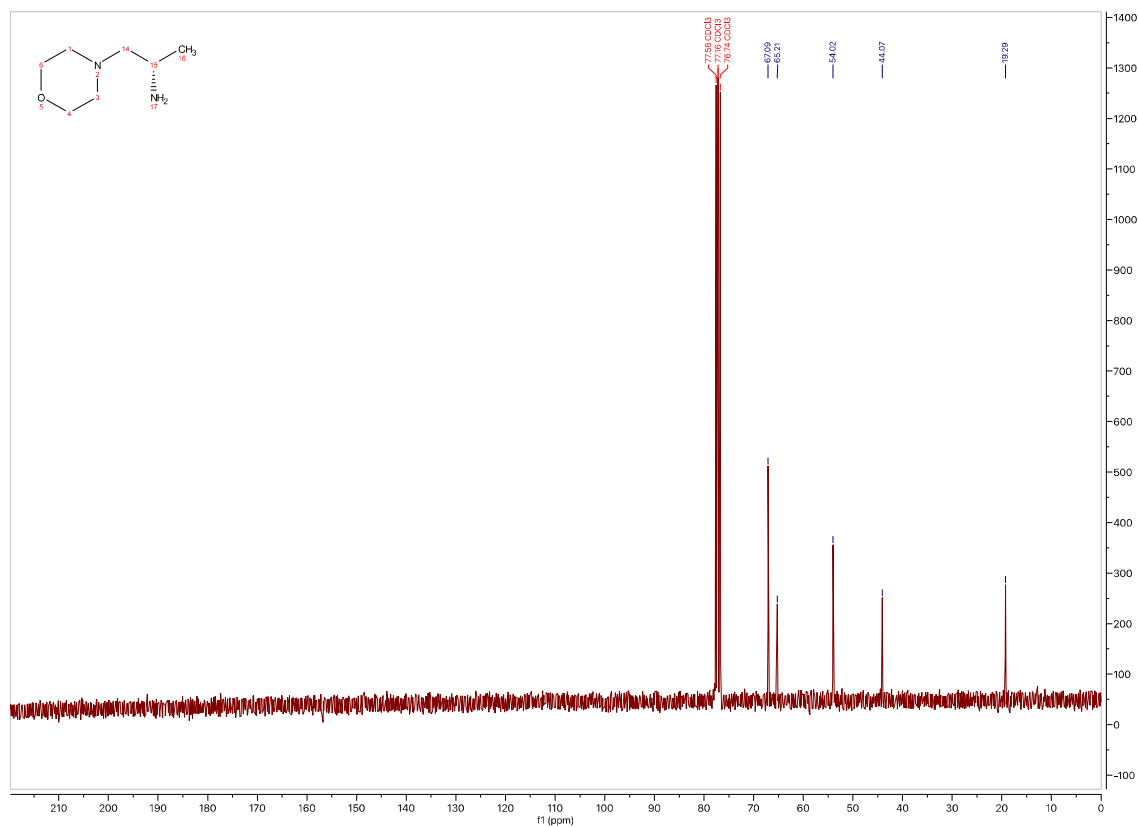


Figure S41. ¹³C-NMR spectrum of (S)-1-morpholinopropan-2-amine [(S)-55a].

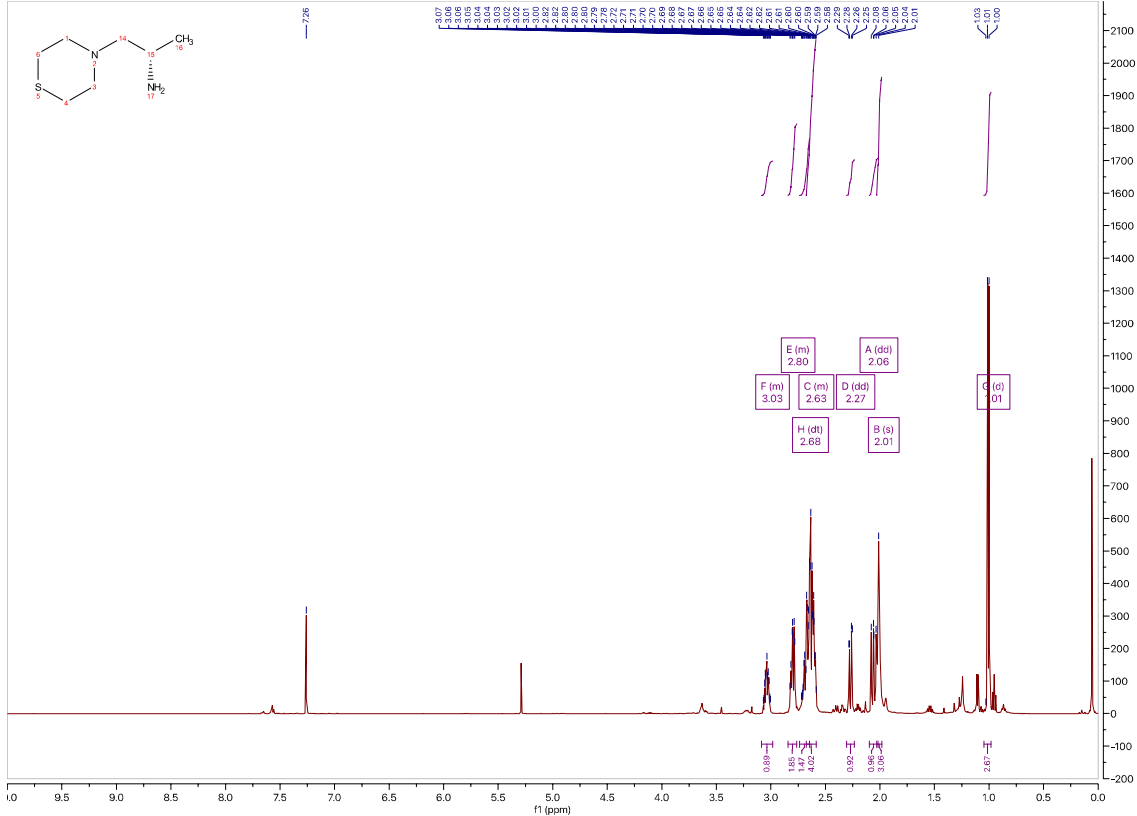


Figure S42. ^1H -NMR spectrum of (S)-1-thiomorpholinopropan-2-amine [(S)-**55b**].

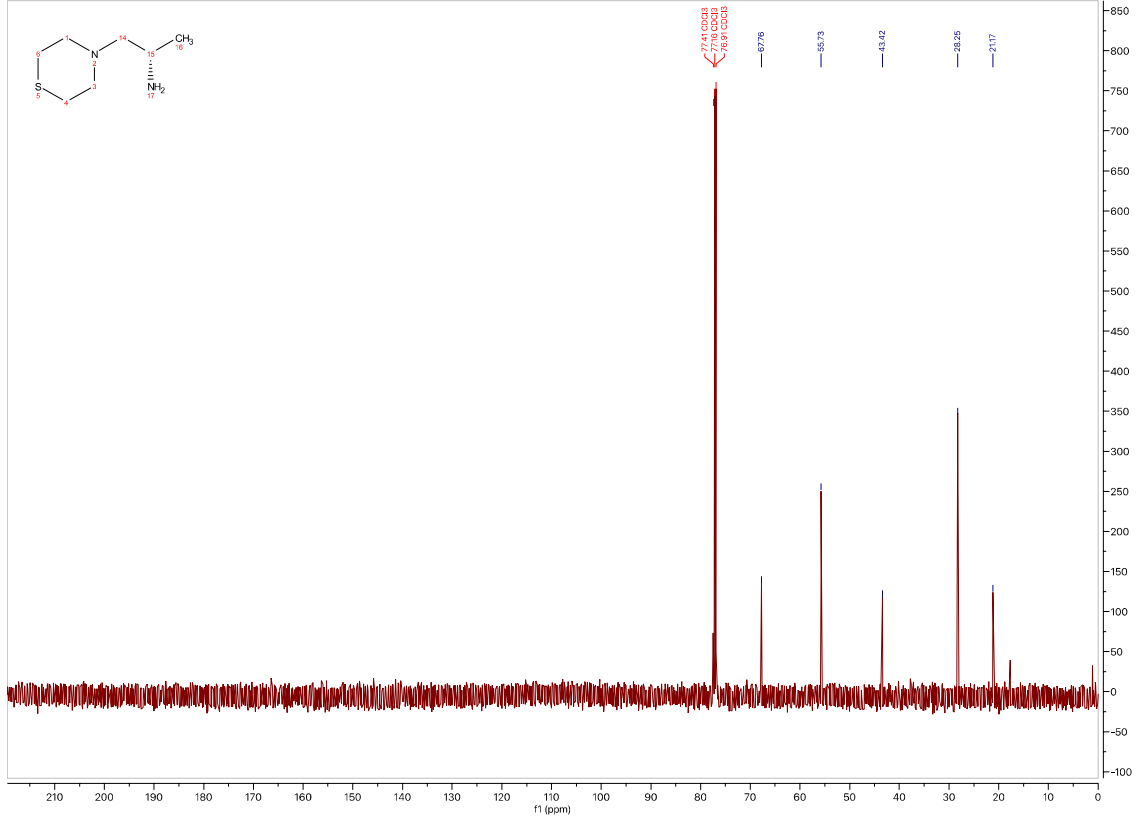


Figure S43. ^{13}C -NMR spectrum of (S)-1-thiomorpholinopropan-2-amine [(S)-**55b**].

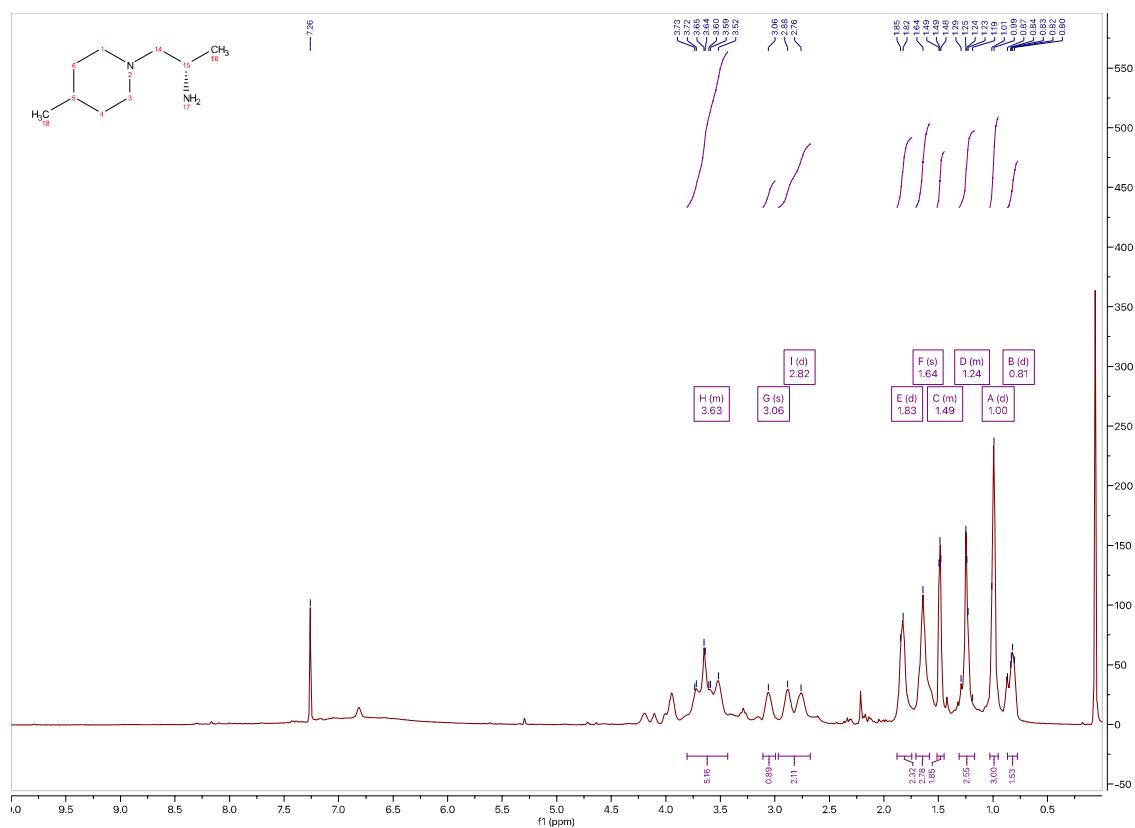


Figure S44. ¹H-NMR spectrum of (S)-1-(4-methylpiperidin-1-yl)propan-2-amine [(S)-55c].

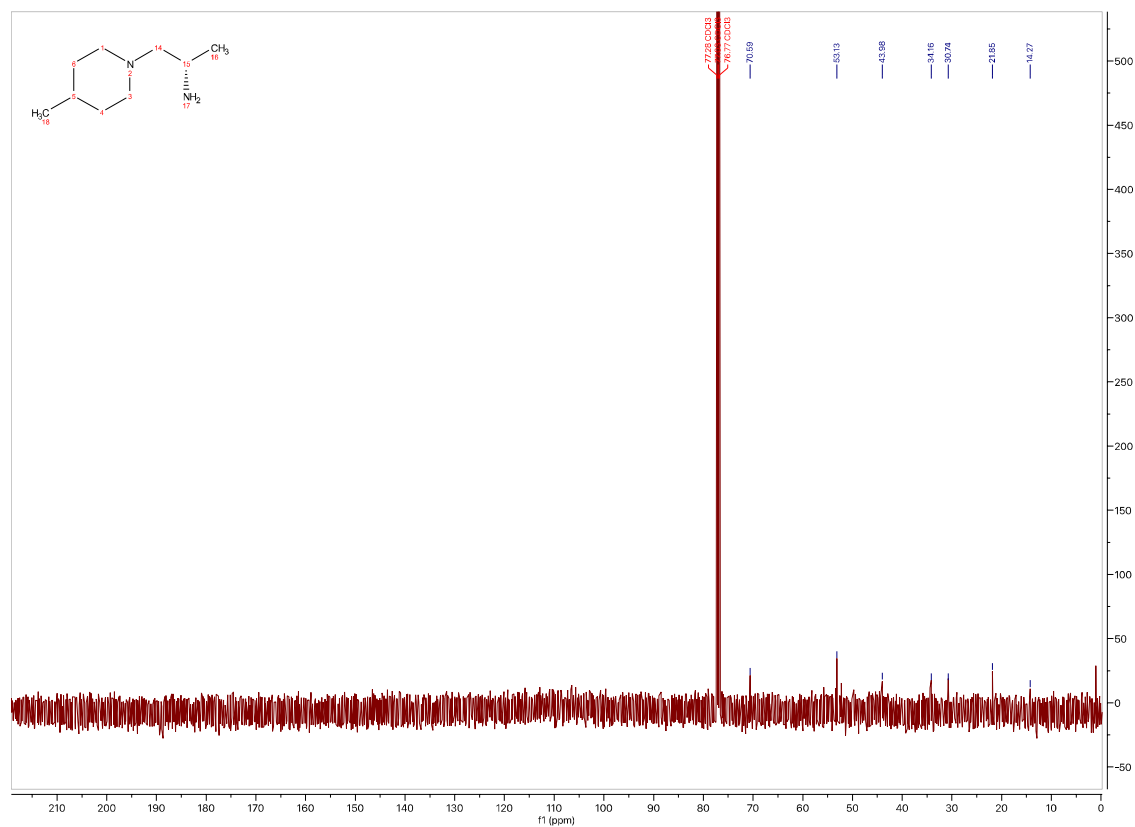


Figure S45. ¹³C-NMR spectrum of (S)-1-(4-methylpiperidin-1-yl)propan-2-amine [(S)-55c].

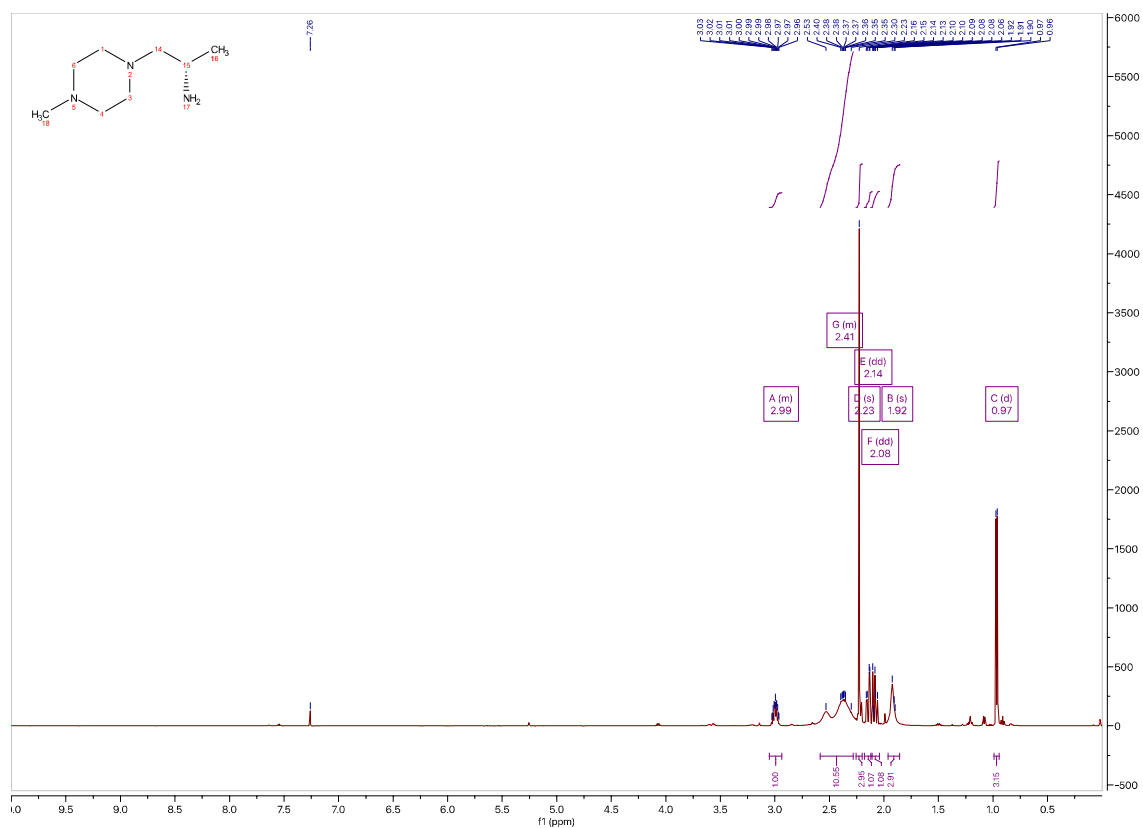


Figure S46. ^1H -NMR spectrum of (S)-1-(4-methylpiperazin-1-yl)propan-2-amine [(S)-55d].

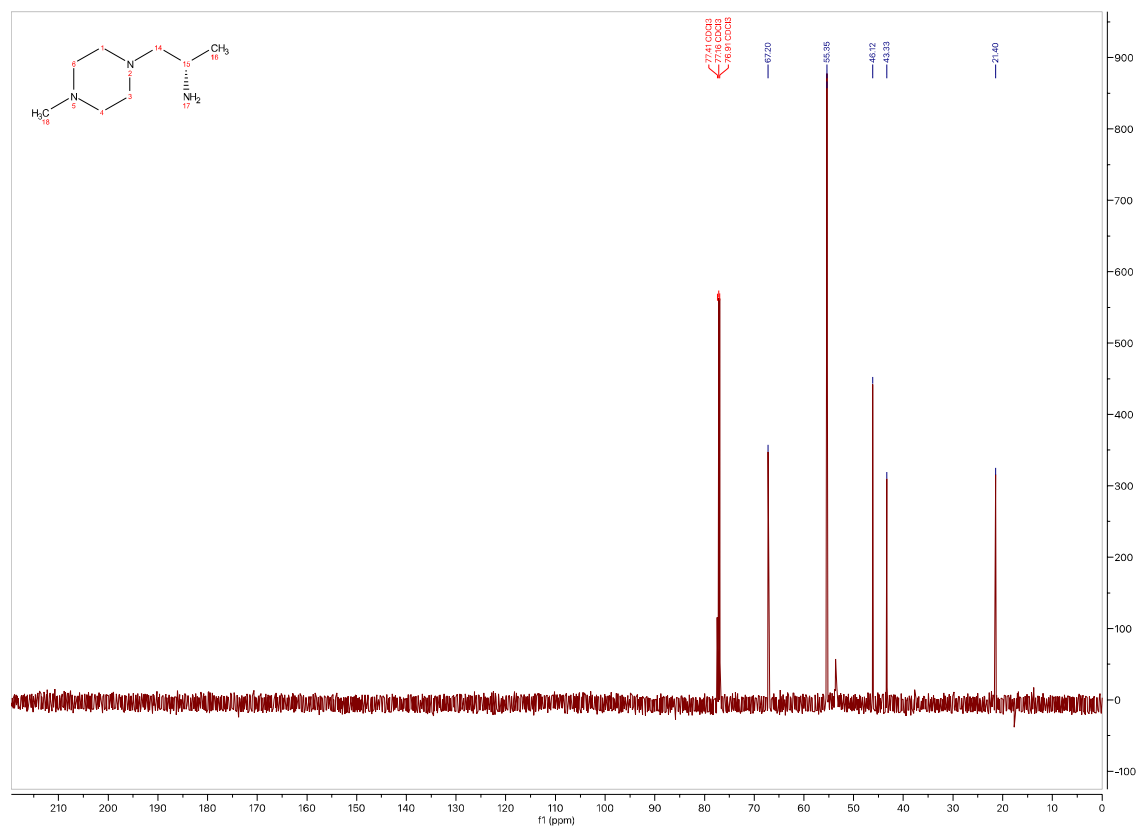


Figure S47. ^{13}C -NMR spectrum of (S)-1-(4-methylpiperazin-1-yl)propan-2-amine [(S)-55d].

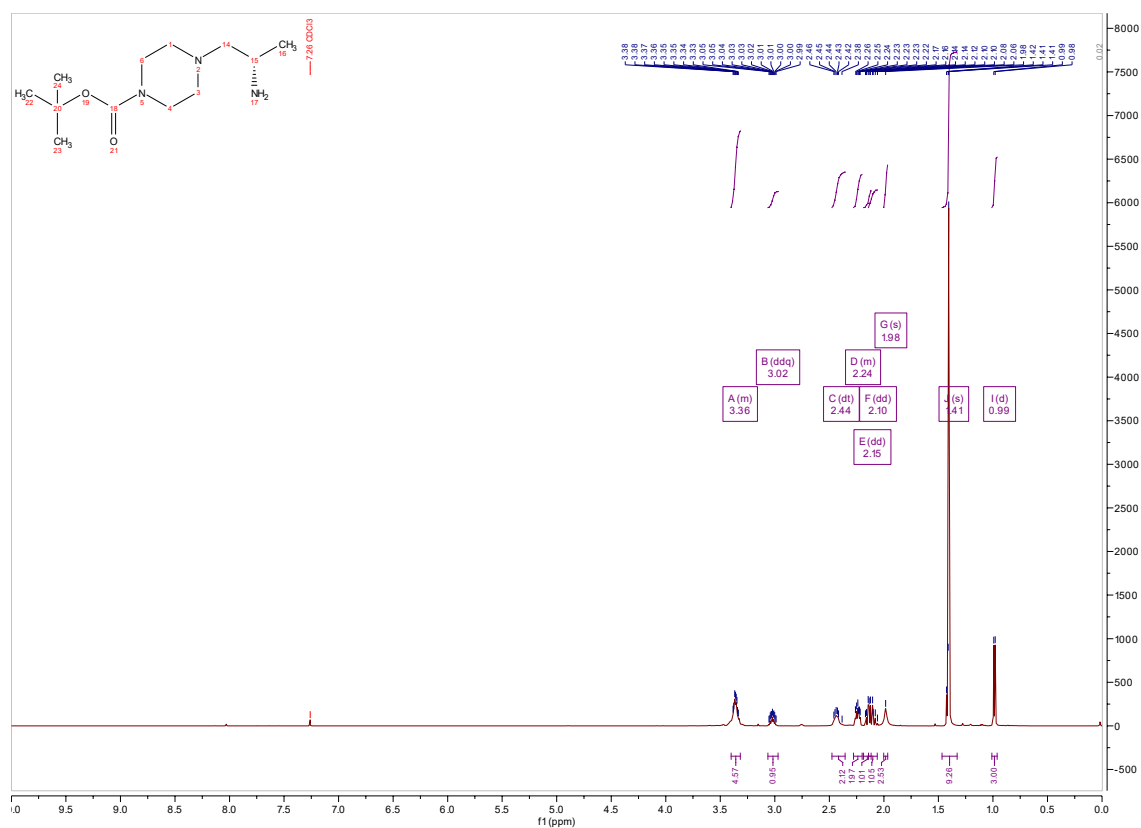


Figure S48. ¹H-NMR spectrum of *tert*-butyl (S)-4-(2-aminopropyl)piperazine-1-carboxylate [(S)-55e].

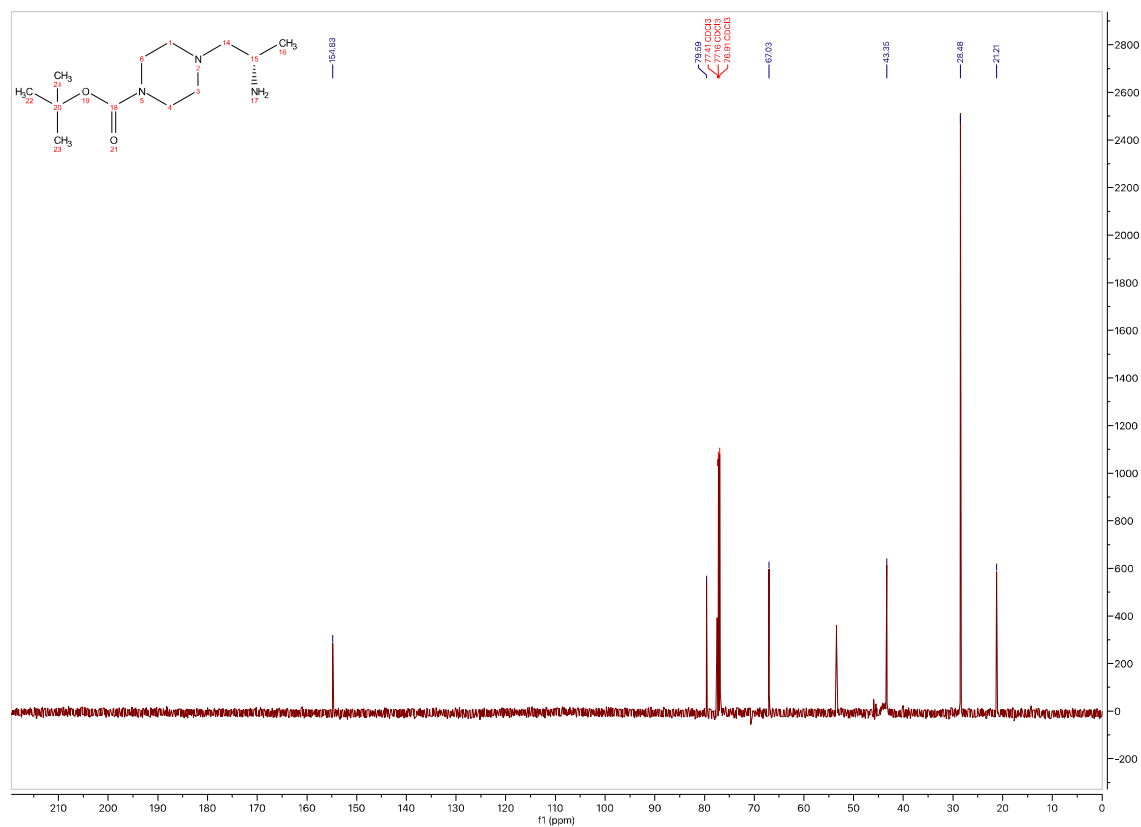


Figure S49. ¹³C-NMR spectrum of *tert*-butyl (S)-4-(2-aminopropyl)piperazine-1-carboxylate [(S)-55e].

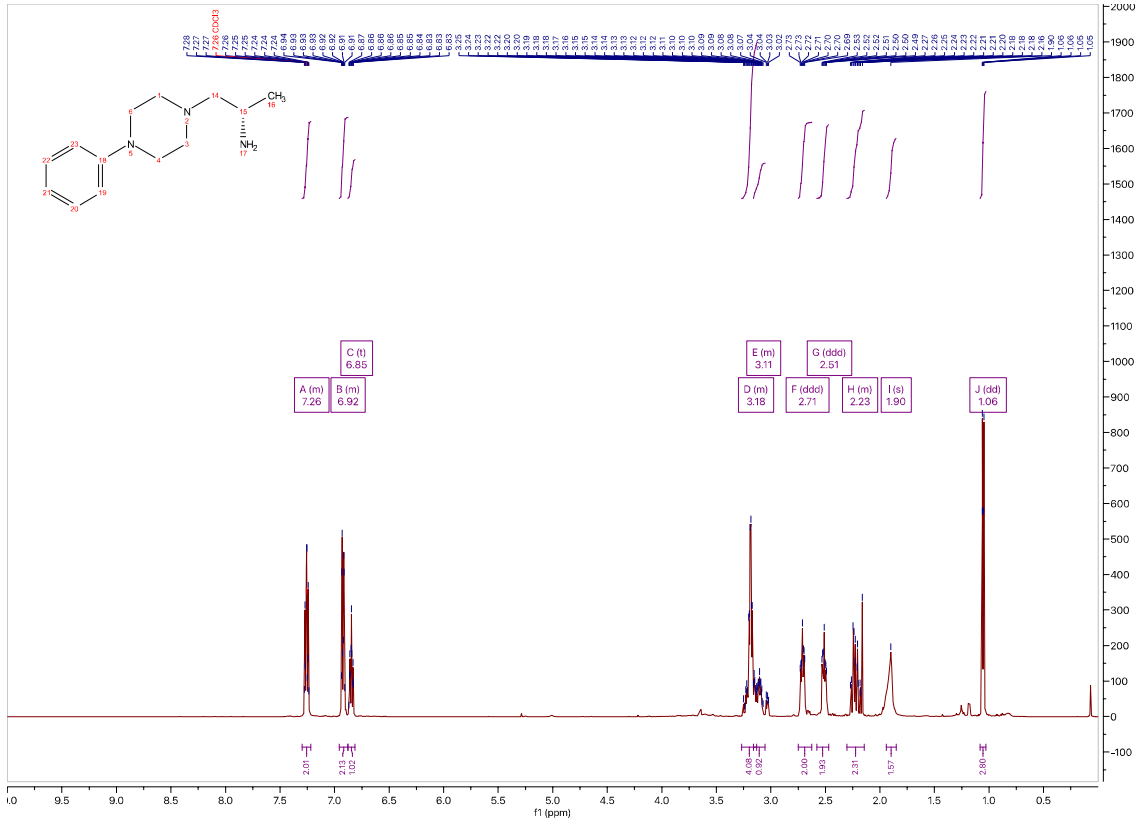


Figure S50. ^1H -NMR spectrum of (S)-1-(4-phenylpiperazin-1-yl)propan-2-amine [(S)-55f].

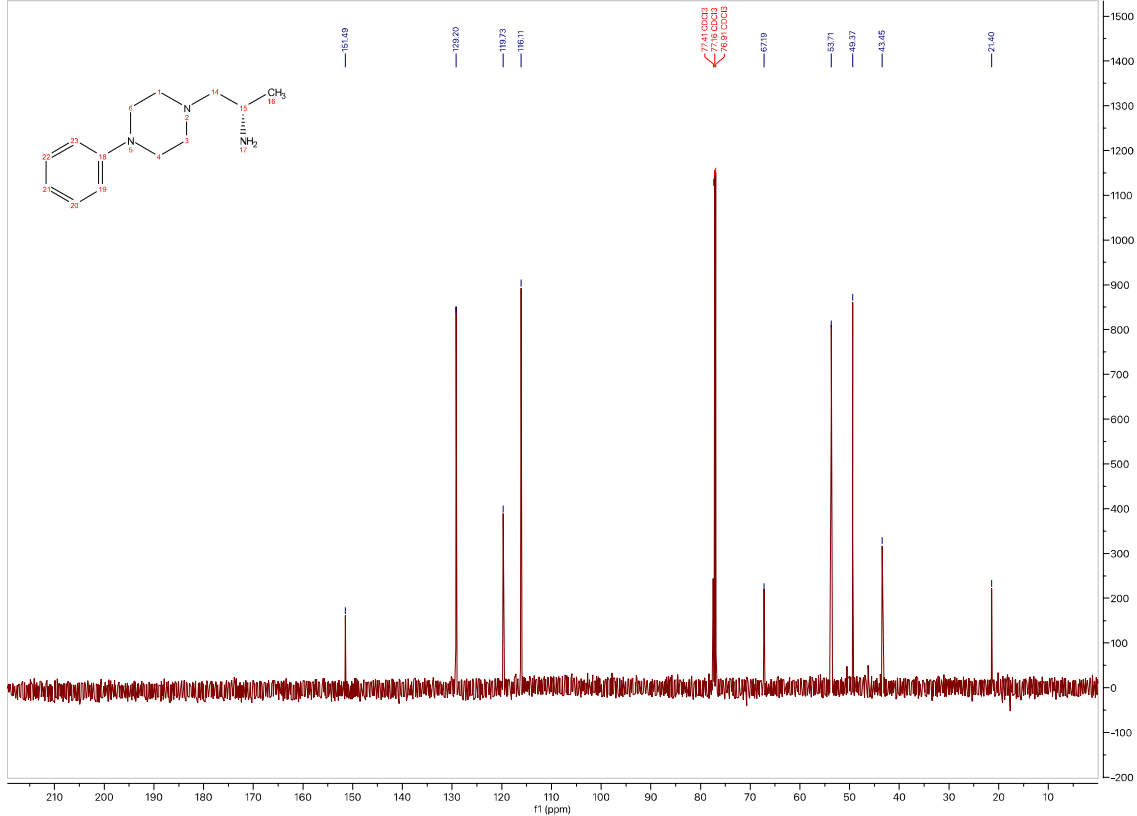


Figure S51. ^{13}C -NMR spectrum of (S)-1-(4-phenylpiperazin-1-yl)propan-2-amine [(S)-55f].

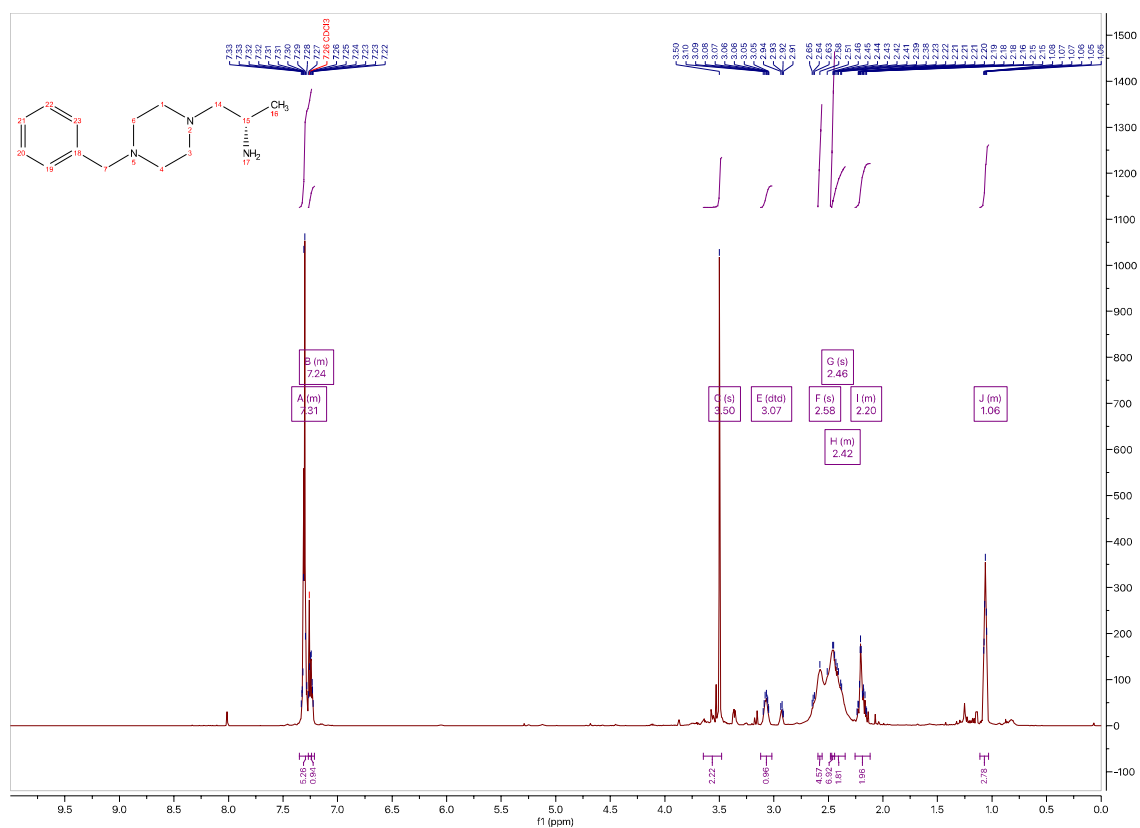


Figure S52. ^1H -NMR spectrum of (*S*)-1-(4-benzylpiperazin-1-yl)propan-2-amine [(*S*)-55g].

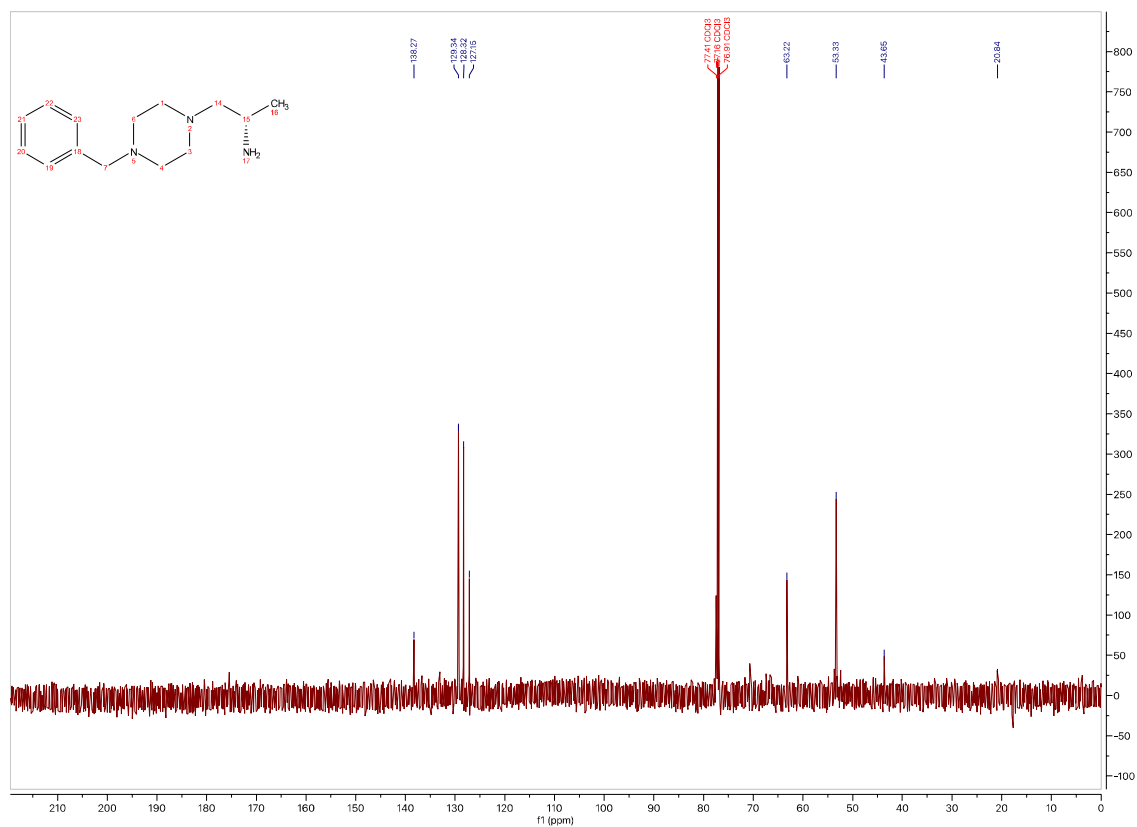


Figure S53. ^{13}C -NMR spectrum of (*S*)-1-(4-benzylpiperazin-1-yl)propan-2-amine [(*S*)-55g].