Supporting Information

Ammonium zincates as catalysts for the microwave-enhanced synthesis of symmetric piperazines by regioselective opening of aziridines

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Index

General considerations

All chemicals and solvents were commercially available and used as received except where specified. ^{1}H NMR analyses were performed with 400 MHz spectrometers at room temperature. The coupling constants (*J*) are expressed in hertz (Hz), and the chemical shifts (δ) in ppm. Catalytic tests were analysed by ^{1}H NMR spectroscopy. Low resolution MS spectra were acquired with instruments equipped with ESI/ion trap sources. High resolution MS spectra were acquired on a Q-ToF SYNAPT G2-Si HDMS 8K instrument (Waters) equipped with a ZsprayTM ESI source (Waters). The values are expressed as mass−charge ratio and the relative intensities of the most significant peaks are shown in brackets. Elemental analyses were recorded in the analytical laboratories of Università degli Studi di Milano. Catalytic experiments under microwave heating were carried out in a 300 W Personal Chemistry "Emrys creator" single-mode microwave synthesizer at 2450 MHz. Aziridines, except for commercially available **1r**, were synthesized according to published procedures: **1b**, **1e**, **1f**, and **1n**;[1] **1a**, **1c and 1l**;[2] **1d**;[3] **1m**;[4] **1o**;[5] **1p**;[6] and **1s**.[7]

[1] D. Carminati, E. Gallo, C. Damiano, A. Caselli, D. Intrieri, *Eur. J. Inorg. Chem.* **2018**, *2018*, 5258–5262.

[2] G. Bresciani, M. Bortoluzzi, G. Pampaloni, F. Marchetti, *Org. Biomol. Chem* **2021**, *19*, 4152.

[3] P. Sonzini, N. Berthet, C. Damiano, V. Dufaud, E. Gallo, *J. Catal.* **2022**, *414*, 143–154.

[4] F. Sebest, L. Casarrubios, H. S. Rzepa, A. J. P. White, S. Díez-González, *Green Chem.* **2018**, *20*, 4023–4035.

[5] M. Sengoden, M. North, A. C. Whitwood, *ChemSusChem* **2019**, *12*, 3296–3303.

[6] M. Prieschl, D. Cantillo, C. O. Kappe, *J. Flow Chem.* **2021**, *11*, 117–125.

[7] A. K. Ravn, M. B. T. Vilstrup, P. Noerby, D. U. Nielsen, K. Daasbjerg, T. Skrydstrup, *J. Am. Chem. Soc.* **2019**, *141*, 11821–11826.

Synthesis of the zincate salts:

All the zincate salts were synthesized according to the procedure already reported by us.[8]

$[TBA]_2[ZnCl_4]$. To a solution of tetrabutylammonium chloride in ethanol (6.00 mmol, 1.67 g in 15 mL) was slowly added a solution of zinc(II) chloride in ethanol (3.00 mmol, 0.408 g in 15 mL). After stirring for 1 h at 40°C, the solution was concentrated under reduced pressure and the residue dissolved in the minimum amount of methanol and cooled at -20°C overnight. The precipitated product was filtered and was obtained as a white solid. Yield: 1.31 g (63%). The product was fully characterized by ESI-MS and elemental analysis.

HRMS-ESI(+): calculated for $C_{16}H_{36}N$ 242.2848, found 242.2850 (100%, TBA^+).

HRMS-ESI(-): calculated for $ZnCl_3^-$ 168.8357, found 168.8357 (100%, $ZnCl_3^-$).

Elemental analysis calculated for $[C_{32}H_{72}Cl_4ZnN_2]$ C, 55.53; H, 10.49; N, 4.05; found C, 54.89; H, 9.92; N, 3.58. Despite several different preparations, we never succeeded in having a better Elemental analysis for this compound. This can be due to the fact, as also shown by the HRMS-ESI(-) spectra, that the anion $[ZnCl_3]^-$ is the most stable amongst all the salts synthesized and an equilibria with **$[TBA][ZnCl_3]$** exists (a ratio $[TBA]_2[ZnCl_4]/[TBA][ZnCl_3]$ = 5:1 would explain the observed elemental analysis). Another possibility is the formation of partially hydrated form, due to the high hydrophilicity of the starting $ZnCl_2$ and TBACl.

$[TBA]_2[ZnBr_4]$. To a solution of tetrabutylammonium bromide in ethanol (6.00 mmol, 1.93 g in 15 mL) was slowly added a solution of zinc(II) bromide in ethanol (3.00 mmol, 0.675 g in 15 mL). After stirring for 1 h at 40°C, the solution was concentrated in vacuum and the residue dissolved in the minimum amount of methanol and cooled at -20°C overnight. The precipitated product was filtered and was obtained as a white solid. Yield: 1.86 g (71%). The product was fully characterized by ESI-MS and elemental analysis.

HRMS-ESI(+): calculated for $C_{16}H_{36}N$ 242.2848, found 242.2850 (100%, TBA^+).

HRMS-ESI(-): calculated for $ZnBr_3^-$ 300.6843, found 300.6842 (100%, $ZnBr_3^-$).

Elemental analysis calculated for $[C_{32}H_{72}Br_4ZnN_2]$ C, 44.18; H, 8.34; N, 3.22; found C, 44.60; H, 8.60; N, 3.35.

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[8] N. Panza, M. Alberti, C. Damiano, A. Caselli, *Front. Catal.* **2022**, *2*, 991270.

[TBA]$_2$[ZnI$_4$]. To a solution of tetrabutylammonium iodide in ethanol (9.20 mmol, 3.40 g in 15 mL) was slowly added a solution of zinc(II) iodide in methanol (4.60 mmol, 1.47 g in 5 mL). After stirring for 1 h at 40°C, the solution was filtered and concentrated to a third of the volume and cooled at -20°C overnight. The product was obtained as a pale-yellow solid. Yield: 4.28 g (88%). The product was fully characterized by ESI-MS and elemental analysis.

HRMS-ESI(+): calculated for $C_{16}H_{36}N$ 242.2848, found 242.2850 (100%, TBA^+).

HRMS-ESI(-): only I^-, NaI_2^- and I_3^- where found (see Supplementary Figure 4)

Elemental analysis calculated for [$C_{32}H_{72}I_4ZnN_2$] C, 27.91; H, 5.27; N, 2.03; found C, 27.92; H, 5.23; N, 1.92.

[TMA]$_2$[ZnI$_4$]. To a solution of tetramethylammonium iodide in methanol (2.0 mmol, 402.1 mg in 5 mL) was slowly added a solution of zinc(II) iodide in ethanol (1.0 mmol, 319.2 mg in 5 mL). After stirring for 1 h at 40°C, the solution was filtered and concentrated to a third of the volume and cooled at -20°C overnight. The product was obtained as a pale-yellow solid. Yield 685.2 mg (95%). The product was characterized by elemental analysis.

Elemental analysis calculated for [$C_8H_{24}I_4ZnN_2$] C, 13.32; H, 3.35; N, 3.88; found C, 13.72; H, 3.23; N, 3.92.

High-resolution mass spectroscopy analysis:

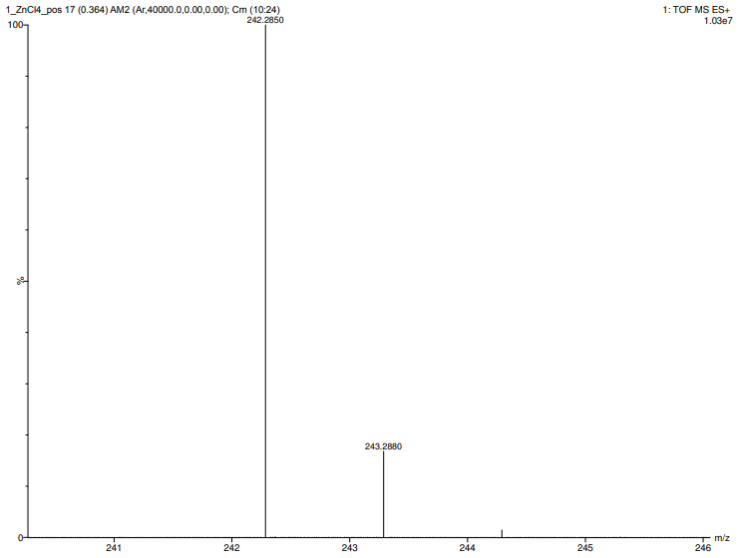


Figure S1. HRMS spectra (ESI positive mode) of **$[TBA]_2[ZnCl_4]$** (40-600 m/z range). The peak at 242.2850 m/z (100%) is assigned to TBA^+ (calculated 242.2848).

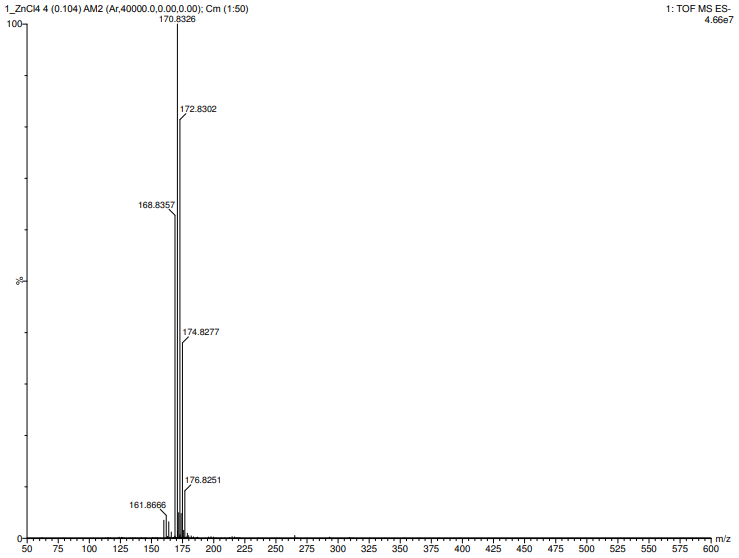


Figure S2. HRMS spectra (ESI negative mode) of **$[TBA]_2[ZnCl_4]$** (50-600 m/z range). The peak at 168.8357 m/z (100%) is assigned to $[ZnCl_3]^-$ (calculated 168.8357).

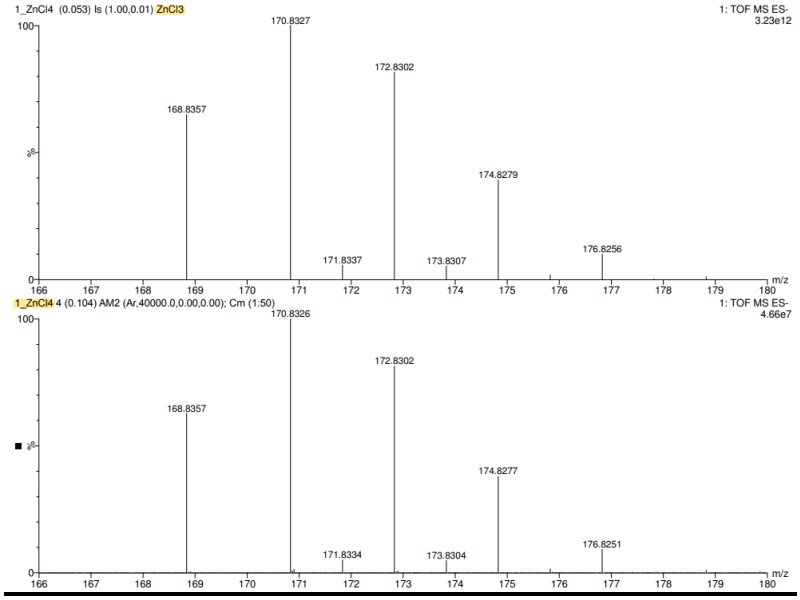


Figure S3. Comparison between the found spectra (lower line) and the isotope model (upper line) for the ion $[ZnCl_3]^-$.

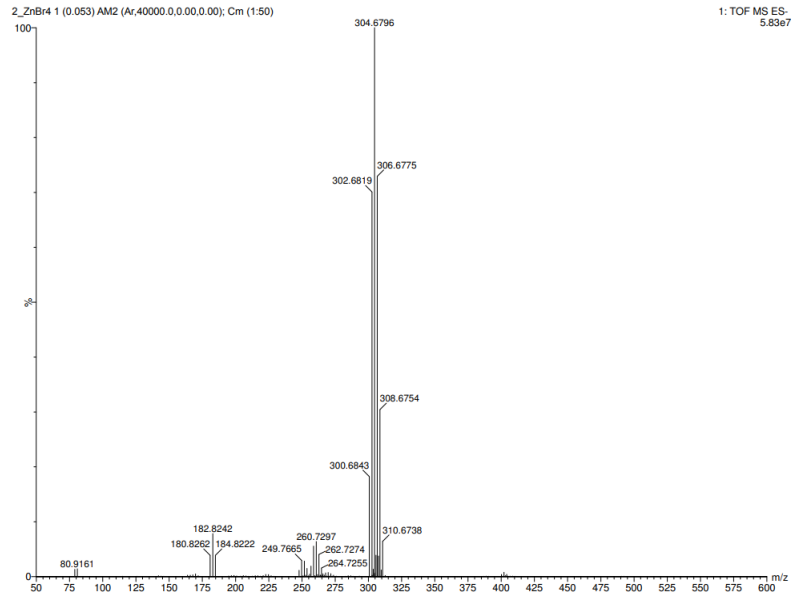


Figure S4. HRMS spectra (ESI negative mode) of **$[TBA]_2[ZnBr_4]$** (50-400 m/z range). The peak at 300.6843 m/z (100%) is assigned to $[ZnBr_3]^-$ (calculated 300.6842). The comparison between the found spectra (lower line) and the isotope model is reported below.

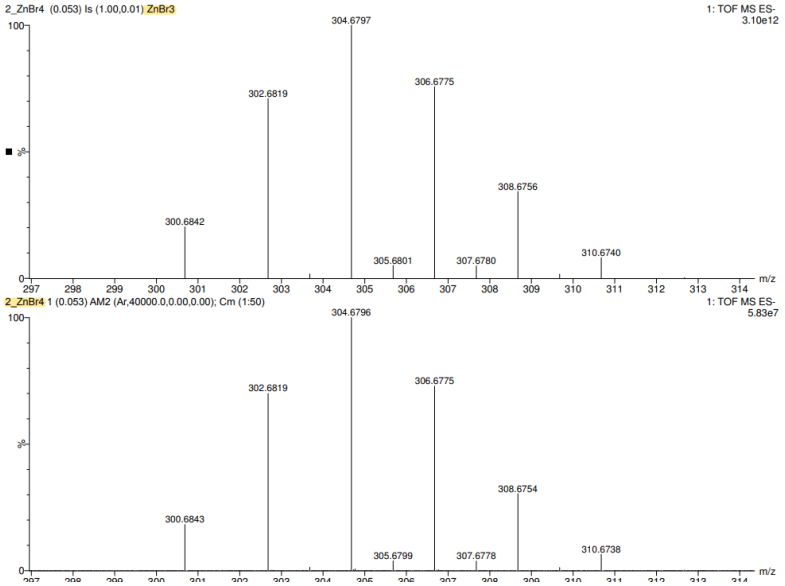


Figure S5. Comparison between the found spectra (lower line) and the isotope model (upper line) for the ion $[ZnBr_3]^-$.

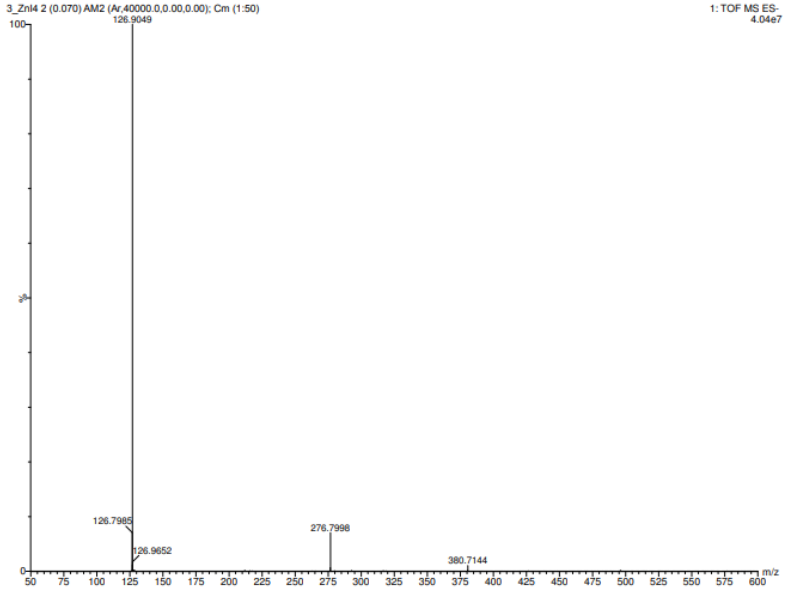
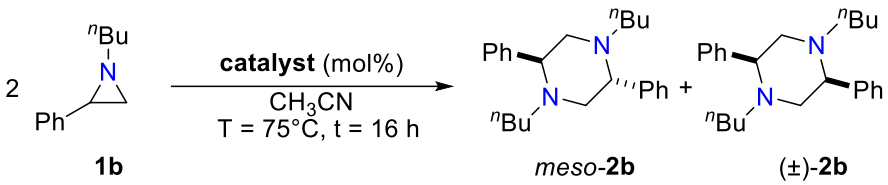


Figure S6. HRMS spectra (ESI negative mode) of **$[TBA]_2[ZnI_4]$** (50-600 m/z range). The peak at 126.9049 m/z is attributed to I^-, 276.7998 is attributed to NaI_2^- and 380.7144 is I_3^-.

Optimization of the reaction conditions

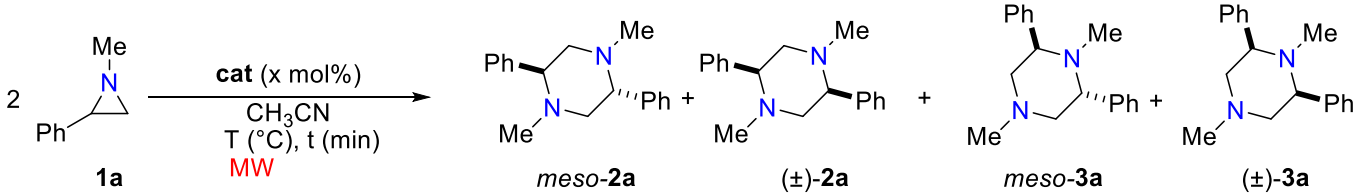
Table S1: Synthesis of symmetric piperazines *meso*-**2b** and (±)-**2b** (*meso*-1,4-dibutyl-2,5-diphenylpiperazine and (±)-1,4-dibutyl-2,5-diphenylpiperazine, respectively) catalyzed by ammonium zincates, **[TBA]$_2$[ZnX$_4$]**.[a]



Entry	Catalyst	Cat. loading (mol %)	**1b**/CH_3CN (mmol/ml)	Con.[b] **1b**%	Sel.[c] **2b**%	TOF[d] (h^{-1})
1	**[TBA]$_2$[ZnCl$_4$]**	2.5	1.0/1.0	30	30	0.75
2	**[TBA]$_2$[ZnBr$_4$]**	2.5	1.0/1.0	47	59	1.17
3	**[TBA]$_2$[ZnI$_4$]**	2.5	1.0/1.0	91	80	2.3
4	**[TBA]$_2$[ZnI$_4$]**	5	1.0/1.0	94	75	1.1
5	**[TBA]$_2$[ZnI$_4$]**	2.5	0.5/5.0	60	94	1.5
6	**[TBA]$_2$[ZnI$_4$]**	5	0.5/5.0	75	97	0.9
7	**ZnCl$_2$**	2.5	1.0/1.0	99	-	2.5
8	**ZnBr$_2$**	2.5	1.0/1.0	90	31	2.3
9	**ZnI$_2$**	2.5	1.0/1.0	99	45	2.5
10	**TBACl**	5	1.0/1.0	26	-	0.7
11	**TBAB**	5	1.0/1.0	41	46	1.0
12	**TBAI**	5	1.0/1.0	43	76	1.1
13	**none**		1.0/1.0	35	45	-

[a]Reaction conditions: 1-butyl-2-phenyl aziridine, **1b**, and catalyst in CH_3CN at T = 75°C, t = 16 h. [b]Conversion determined by GC using DMT as IS [c]Selectivity determined by ^{1}H NMR using DMT as IS. Selectivity reported as the sum of *meso*-**2b** and (±)-**2b**, obtained as 1:1 mixture. [d]Turnover frequency ($mol_{\mathbf{1a}(converted)} \cdot mol_{cat}^{-1} \cdot$ reaction $time^{-1}$).

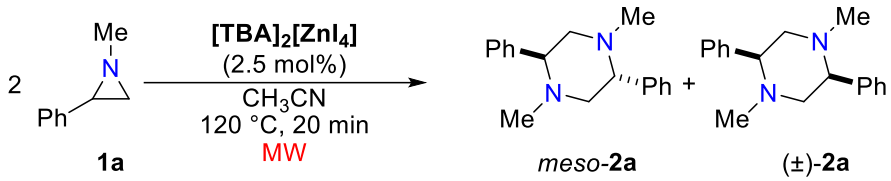
Table S2: Optimization of the synthesis of symmetric piperazines *meso*-**2a** and (±)-**2a** (*meso*-1,4-dimethyl-2,5-diphenylpiperazine and (±)-1,4-dimethyl-2,5-diphenylpiperazine, respectively) under microwave heating.[a]



Entry	Catalyst	Cat. loading (mol %)	T (°C)	T (min)	Con.[b] **1a**%	Sel.[c] **2a**%	TOF[d] (h^{-1})
1	**$[TBA]_2[ZnI_4]$**	2.5	100	20	68	81	81.6
2	**$[TBA]_2[ZnI_4]$**	2.5	120	5	68	85	326.4
3	**$[TBA]_2[ZnI_4]$**	2.5	120	10	78	88	187.2
4	**$[TBA]_2[ZnI_4]$**	2.5	120	20	96	94	115.2
5	**$[TBA]_2[ZnI_4]$**	2.5	120	60	>99	77	40.0
6	**$[TBA]_2[ZnBr_4]$**	2.5	120	20	>99	75	120.0
7	**$[TBA]_2[ZnI_4]$**	1	120	20	>99	82	300.0
8	**$[TBA]_2[ZnBr_4]$**	1	120	20	98	81	294.0
9	**$[TBA]_2[ZnI_4]$**	0.1	120	20	**92**	**97**	**2760.0**
10	**$[TBA]_2[ZnBr_4]$**	0.1	120	20	87	82	2610.0
11	**ZnI_2**	2.5	120	20	96	70	115.2
12	**ZnI_2**	1	120	20	94	79	282.0
13	**ZnI_2**	0.1	120	20	63	76	1890.0
14	**TBAI**	5	120	20	99	84	59.4
15	**TBAI**	1	120	20	96	73	288.0
16	**TBAI**	0.2	120	20	92	83	1380.0
17	**TBAI**	0.1	120	20	69	55	2070.0
18	**TBAB**	0.2	120	20	85	81	1275.0
19	**$[TMA]_2[ZnI_4]$**	2.5	120	20	95	80	114.0
20	**none**	-	120	20	62	66	-

[a]Reaction conditions: 1-methyl-2-phenyl aziridine, **1a**, (1 mmol) and catalyst (x mol%) in CH_3CN (1 mL). [b]Conversion determined by GC using DMT as IS. [c]Selectivity determined by ^1H NMR using DMT as IS. Selectivity reported as the sum of *meso*-**2a** and (±)-**2a**, obtained as 1:1 mixture. [d]Turnover frequency ($mol_{\mathbf{1a}(converted)} \cdot mol_{cat}^{-1} \cdot$ reaction $time^{-1}$).

Table S3. Effect of aziridine **1a** concentration and of the scale-up and -down on the catalytic reaction[a]

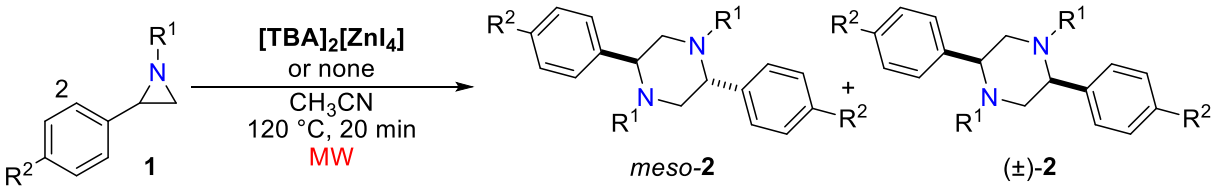


1a *meso*-**2a** (±)-**2a**

Entry	**1a** (mmol)	CH_3CN (mL)	Con.[b] **1a**%	Sel.[c] **2a**%	TOF[d] (h^{-1})
1	1.0	1.0	96	94	116.4
2	0.2	0.2	83	84	100.6
3	2.0	2.0	88	79	106.7
4	0.2	2.0	94	53	113.9
5	1.0	0.5	99	85	120.0

[a]Reaction conditions: 1-methyl-2-phenyl aziridine, **1a,** and catalyst (2.5 mol%) in CH_3CN. [b]Conversion determined by GC using DMT as IS. [c]Selectivity determined by ^{1}H NMR using DMT as IS. Selectivity reported as the sum of *meso*-**2a** and (±)-**2a**, obtained as 1:1 mixture. [d]Turnover frequency ($mol_{\mathbf{1a}(converted)} \cdot mol_{cat}^{-1} \cdot$reaction time^{-1}).

Table S4. Reaction scope, with and without catalyst[a]

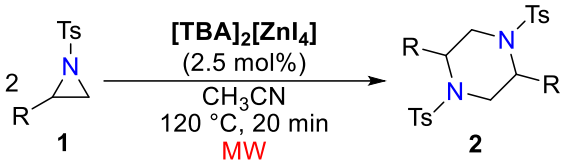


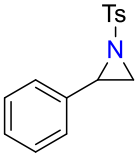
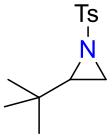
1 *meso*-**2** (±)-**2**

Entry	R^1	R^2	Piperazine	yield[b] **catal.**	yield[c] **uncatal.**
1	*n*Bu	H	**2b**	47	21
2	Me	H	**2a**	71	41
3	H	H	**2c**	n.d.	n.d.
4	*s*Bu	H	**2d**	n.d	n.d.
5	CH_2Ph	H	**2e**	21	n.d.
6	CH_2CHCH_2	H	**2f**	27	n.d.
7	CH_2CH_2NHTs	H	**2g**	n.d.	n.d.
8	Me	Me	**2h**	82	44
9	Me	*t*Bu	**2i**	52	n.d.
10	Me	Br	**2l**	37	n.d.
11	Me	F	**2m**	20	n.d.
12	*n*Bu	Me	**2n**	22	n.d.
13	*n*Bu	Cl	**2o**	12	n.d.
14	*n*Bu	F	**2p**	n.d.	n.d.

[a]Reaction conditions: aziridine, **1**, (1 mmol) and catalyst (2.5 mol%) in CH_3CN (1 mL). [b]Isolated yields, reported as the sum of *meso*-**2** and (±)-**2**. In all cases, ^{1}H NMR analysis of the reaction crude revealed a 1:1 molar ratio *meso*-**2**:(±)-**2**. [c]Yield determined by ^{1}H NMR using DMT as IS, reported as the sum of *meso*-**2** and (±)-**2**, obtained as 1:1 mixture.

Table S5. Reaction scope, coupling reactions of N-tosyl aziridines[a]

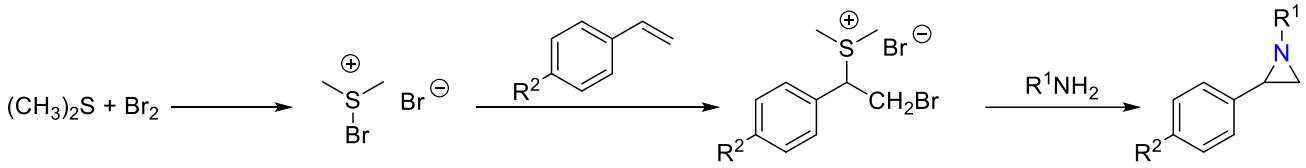


Entry	aziridine	Piperazine	yield[b]
1		**2r**	25
2		**2s**	n.d.
3		**2t**	n.d.

[a]Reaction conditions: aziridine, **1**, (1 mmol) and catalyst (2.5 mol%) in CH_3CN (1 mL). [b]Isolated yield.

Synthesis and characterization of N-alkyl aziridines 1g-1i

General procedure



Step 1: Dimethyl sulfide (14.7 mL, 200 mmol) was dissolved in dichloromethane (40 ml) and the solution was cooled to 0°C; a solution of bromine (10 mL, 200 mmol) in DCM (40 mL) was then added dropwise over 30 minutes; temperature must be maintained to 0°C during the addition. Precipitation of yellow-orange crystals of bromodimethylsulfonium bromide was noticeable since the beginning of the addition. The precipitate was then collected on a septum and washed with cold diethyl ether to remove residual bromine traces.

Step 2: Styrene (200 mmol) was added dropwise at 0°C to a solution of bromodimethylsulfonium bromide (200 mmol) in MeCN (80 mL); the mixture was allowed to react at 0°C for a different time, which depend on the nature of the styrene employed. The starting orange solution turns white or yellow during the reaction. At the end of the reaction, the brominated salt was precipitated by the addition of diethyl ether (70-100 mL); the precipitate was then collected on a septum and washed with diethyl ether and dried *in vacuo*.

Step 3: The white crystals of 1-(dimethylsulfonium)-1-aryl-2-bromoethyl bromide (1 eq, amount depending on Step 2) were suspended in water (6 mL per each gram of styrene sulphonium bromide) and a solution of the desired amine (5 eq) in water (10 M) was added dropwise. The resulting mixture was stirred overnight. Then, 20.0 mL of brine and 20.0 mL of diethyl ether were added, and the phases were separated. The aqueous phase was washed twice with 20.0 mL of diethyl ether and the combined organic phases were dried over Na_2SO_4. The solid was filtered off and the solvent was evaporated under reduced pressure. The obtained crude was purified by flash chromatography.

1-(ethyl-2-tosyl)-2-phenylaziridine, 1g

The general procedure was followed by using styrene and *N*-(2-aminoethyl)-4-methylbenzenesulfonamide. Only, in this case, due to low solubility in water of the amine, this last was directly added directly dropwise during Step 3. Work up was carried out using DCM instead of diethyl ether and the crude was purified trough column chromatography (eluent DCM:EtOAc:TEA = 5:5:0.1) to obtain a greenish oil (yield: 60%).

1g: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.67 (dd, 2H, J = 8.3, 1.5 Hz), 7.31 – 7.14 (m, 7H), 5.14 (m, 1H), 3.15 (m, 1H), 3.08 (m, 1H), 2.63 (m, 1H), 2.43 (m, 1H), 2.41 (s, 3H), 2.32 (m, 1H), 1.87 (m, 1H), 1.71 (m, 1H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 143.2, 139.5, 136.6, 129.6, 128.4, 127.1, 127.1, 126.0, 59.1, 42.9, 40.9, 37.7, 21.5. Elemental Analysis calcd. for $C_{17}H_{20}N_2O_2S$: C, 64.53; H, 6.37; N, 8.85, found: C, 64.10; H, 6.55, N, 8.51. LR-MS (ESI): m/z ($C_{17}H_{20}N_2O_2S$) calcd 316.12, found $[M+H]^+$ 317.25 (100%).

1-methyl-2-(4-methylphenyl)aziridine, 1h

The general procedure was followed by using *p*-methyl styrene and methylamine to obtain a light pink oil (yield: 97%).

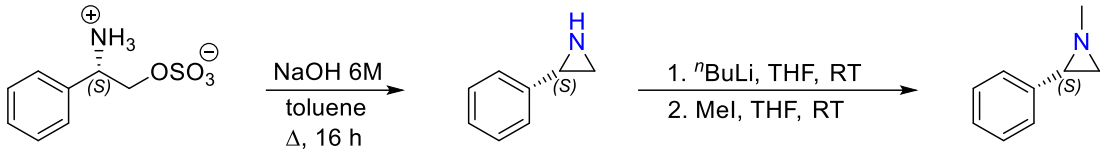
1h: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.14 (bs, 4H), 2.51 (s, 3H), 2.35 (s, 3H), 2.26 (dd, 1H, *J* = 6.5, 3.4 Hz), 1.91 (d, 1H, *J* = 3.4 Hz), 1.62 (d, 1H, *J* = 6.5 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 137.2, 136.4, 129.0, 125.9, 48.0, 42.2, 39.2, 21.1. Elemental Analysis calcd. for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.51, found: C, 81.62; H, 8.96, N, 9.42. LR-MS (ESI): m/z ($C_{10}H_{13}N$) calcd 147.10, found $[M+H]^+$ 148.21 (100%).

1-methyl-2-(4-(1',1'-dimethyl)ethylphenyl)aziridine, 1i

The general procedure was followed by using *p*-^{t}butyl styrene and methylamine to obtain a light pink oil (yield: 78%).

1i: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.36 (d, 2H, *J* = 8.3 Hz), 7.19 (d, 2H, *J* = 8.3 Hz), 2.50 (s, 3H), 2.27 (dd, 1H, *J* = 6.5, 3.4 Hz), 1.93 (dd, 1H, *J* = 3.4, 0.8 Hz), 1.63 (d,1H, *J* = 6.5 Hz), 1.33 (s, 9H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 149.8, 137.2, 125.7, 125.2, 48.0, 42.1, 39.2, 34.4, 31.4. $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40, found: C, 82.66; H, 10.01, N, 7.52. LR-MS (ESI): m/z ($C_{13}H_{19}N$) calcd 189.15, found $[M+H]^+$ 190.18 (100%).

Synthesis of enantiomerically pure (*S*)-1-methyl-2-phenylaziridine 1a



Step 1: The chiral salt was dissolved in a 6.0 molar solution of NaOH (1 ml for each 10 mg of reagent); an equal volume of toluene was then added to the mixture. The reaction was heated for 18 h under reflux conditions, leading to an orange organic phase formation; the two phases was separated, and the aqueous phase was extracted with ethyl acetate. The unified organic phase was then washed with brine, dried with $MgSO_4$, and concentrated under vacuum; the pure product was isolated by chromatographic column, using as eluent initially hexane/acetate 8:2 + TEA 1%, and hexane/acetate 3:7 after the elution of the by-product. A yellowish liquid was obtained (yield 65%).

^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.24-7.36 (m, 5H), 3.03 (dd, 1H, J = 6.3, 3.4 Hz), 2.22 (d, 1H, J = 6.3 Hz), 1.81 (s, 1H), 0.76 (bs, 1H). The collected analytical data are in agreement with those reported in literature.[9]

Step 2: 1 equivalent of N-H aziridine was dissolved in THF (20 ml for each mmol of aziridine) and a 2.0 molar solution of *n*-buthyl lithium (1 eq) in hexane was added dropwise; the mixture was allowed to react under nitrogen atmosphere for about 30 min, until a bright orange color. Once the lithiated salt is formed, 1 eq of methyl iodide was added dropwise and the reaction was left to stir for 1 h; at the end of the reaction time, the residual basicity was quenched with a saturated solution of NH_4Cl. The product was extracted with diethyl ether, dried with $MgSO_4$, concentrated under reduced pressure and then purified by chromatographic column, using as eluent a mixture hexane/ethyl acetate 9:1 + 5% TEA. A colorless liquid was obtained. (yield 30%).

^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.22-7.34 (m, 5H), 2.51 (s, 3H), 2.29 (dd, 1H, J = 6.5, 3.3 Hz), 1.93 (d, 1H, J = 3.3 Hz), 1.65 (d, 1H, J = 6.5 Hz). The collected analytical data are in agreement with those reported in literature.[8]

Optical Purity: compound injected in a chiral HPLC system (chiralpak IB, 25°C, speed flow at 0.5 ml/min) using as eluent a mixture hexane/isopropanol 9:1; only one peak was revealed, with a retention time of 11.5 minutes.

[9] P. Trinchera, B. Musio, L. Degennaro, A. Moliterni, A. Falcicchio, R. Luisi, *Org. Biomol. Chem.* **2012**, *10*, 1962–1965.

General procedure for aziridine dimerization to yield symmetric piperazines

Method A (thermal heating): The catalyst (0.025 mmol), acetonitrile (1 mL) and the substrate (1 mmol) were added in this order in a round bottom pressure tube. Each piece of glassware was previously dried in an oven at 120 °C. The reaction mixture was stirred for 16 hours at 75°C in a preheated hot bath.

Method B (microwave heating): The catalyst (0.025 mmol), acetonitrile (1 mL) and the substrate (1 mmol) were added in this order in a microwave vial. The reaction was stirred for 20 minutes – 80 minutes (according to the specific experiment) at 100 – 140 °C.

GC analysis. At the end of the reaction the reaction mixture was diluted with ethyl acetate in a 10 mL volumetric flask. 0.1 mL were taken and further diluted with ethyl acetate in a volumetric 10 mL volumetric flask to obtain a concentration of analytes in the range of 0.1-0.3 mg/mL. Before completing dilution, 0.1 mL of a solution of DMT in acetonitrile (10 mg/mL) was added as internal standard (IS), to obtain a final IS concentration of 0.1 mg/mL. **NMR yield with IS**: At the end of the reaction, the reaction mixture was diluted with ethyl acetate in a 10 mL volumetric flask. 5 mL were taken and 24.3 mg (0.125 mmol) of DMT were added as IS. The solvent was evaporated under reduced pressure, and about 750 μL of $CDCl_3$ are added for ^{1}H-NMR analysis.

Kinetic experiments

[TBA]$_2$[ZnI$_4$] (0.025 mmol), acetonitrile (1 mL) and the 1-methyl-2-phenylaziridine, **1a**, (1 mmol) were added in this order in a microwave vial. The reaction was stirred for 1 to 20 minutes (see Table S6) at 120 °C. At the end of the reaction the reaction mixture was diluted with ethyl acetate in a 10 mL volumetric flask. 0.1 mL were taken and further diluted with ethyl acetate in a volumetric 10 mL volumetric flask to obtain a concentration of analytes in the range of 0.1-0.3 mg/mL. Before completing dilution, 0.1 mL of a solution of DMT in acetonitrile (10 mg/mL) was added as internal standard (IS), to obtain a final IS concentration of 0.1 mg/mL, to determine the aziridine conversion.

Table S6. Aziridine **1a** conversion at different reaction times[a]

t (min)	Conversion (%)[b]	Unreacted 1a (mg)	1/t	1/unreacted 1a	log [1a]
1	43%	75.9183	1.00	0.013172055	4.329657762
2	52%	63.9312	0.500	0.015641815	4.157807505
3	59%	54.6079	0.333	0.018312369	4.000178561
4	63%	49.2803	0.250	0.020292084	3.897524407
5	66%	45.2846	0.200	0.022082562	3.812967019
6	68%	42.6208	0.167	0.023462722	3.752342397
8	70%	39.957	0.125	0.025026904	3.687803876
10	72%	37.2932	0.100	0.02681454	3.618811004
20	92%	10.6552	0.050	0.09385089	2.366048036

[a]Reaction conditions: aziridine, **1a**, (1 mmol) and catalyst (2.5 mol%) in CH_3CN (1 mL). [b] Conversion determined by GC using DMT as IS.

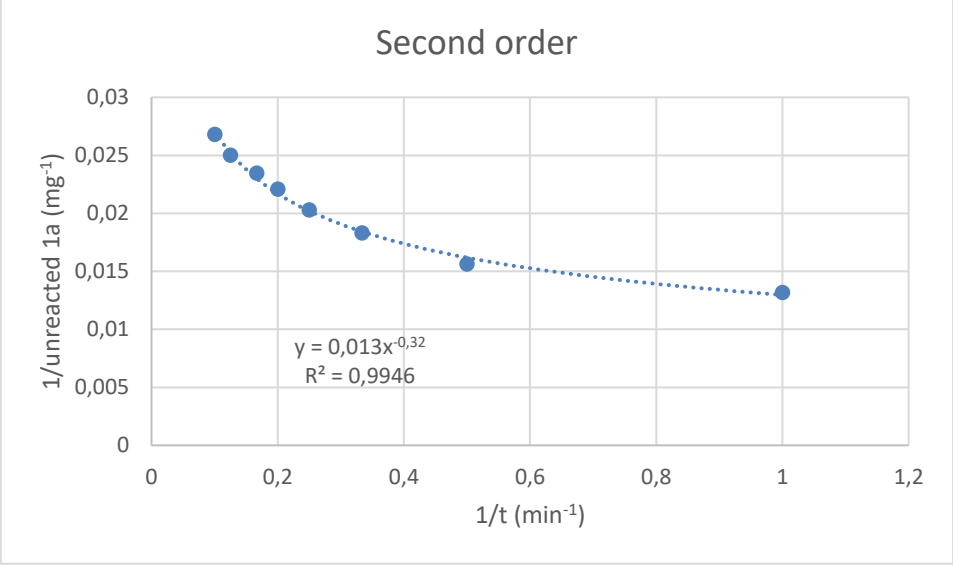


Fig S7. Pseudo-second order fit for the aziridine **1a** conversion (data at 20 min omitted).

Characterization of 1,4-dialkyl-2,5-arylpiperazines

1,4-dimethyl-2,5-phenylpiperazine, 2a

At the end of the reaction *meso*-**2a** spontaneously precipitated as a white crystalline powder and was collected by filtration (yield 44%). The solution was evaporated to dryness then separated by column chromatography, eluent gradient *n*-hexane/EtOAc/TEA from 9:0.5:0.5 to 6:3.5:0.5. (±)-**2a** was isolated as a viscous yellowish oil (yield 27). A further fraction of (±)-**2a** was also isolated, but mixed with (±)-**3a** (see below for characterization). Any attempts to separate the two compounds failed, also due to the few mg obtained. *Meso*-**3a** was instead separated as a yellowish oil (1%).

meso-**2a**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.44 (m, 4H), 7.37 (m, 4H), 7.31 (m, 2H), 3.28 (dd, 2H, *J* = 10.6, 3.0 Hz), 2.99 (dd, 2H, *J* = 11.7, 3.0 Hz), 2.40 (dd, 2H, *J* = 11.7, 10.6 Hz), 2.08 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.3, 128.5, 127.9, 127.6, 69.4, 64.2, 43.3. Elemental Analysis calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32; N, 10.52; found: C, 81.25 H, 8.58; N, 10.41. LR-MS (ESI): m/z ($C_{18}H_{22}N_2$) calcd 266.18, found $[M+H]^+$ 267.33 (100%).

(±)-**2a**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.71 (d, 4H, *J* = 8.3Hz), 7.41 (m, 4H), 7.33 (m, 2H), 3.57 (dd, 2H, *J* = 6.3, 3.9 Hz), 2.96 (dd, 2H, *J* = 11.9, 6.2 Hz), 2.68 (dd, 2H, *J* = 11.9, 3.9 Hz), 2.16 (s, 6H).^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.7, 129.4, 128.0, 127.3, 65.9, 57.9, 43.3. Elemental Analysis calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32; N, 10.52; found: C, 81.35 H, 8.45; N, 10.32. LR-MS (ESI): m/z ($C_{18}H_{22}N_2$) calcd 266.18, found $[M+H]^+$ 267.56 (100%).

1,4-dimethyl-2,6-phenylpiperazine, 3a

meso-**3a**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.62 (m, 4H), 7.37 – 7.29 (m, 6H), 3.88 (dd, *J* = 6.2, 3.8 Hz, 2H), 2.84 (dd, *J* = 11.1, 3.8, 2H), 2.64 (m, 2H), 2.28 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.1, 129.4, 128.0, 127.2, 62.8, 62.0, 46.3, 39.9. Elemental Analysis calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32 N, 10.52 found: C, 81.35; H, 8.21 N, 10.23. LR-MS (ESI): m/z ($C_{18}H_{22}N_2$) calcd 266.18, found $[M+H]^+$ 267.28 (100%). The compound was analyzed by HPLC (chiralpak IB and chiralpak OJ, 25°C, speed flow at 0.7 ml/min) using as eluent a mixture hexane/isopropanol 9:1; only one peak was revealed in all cases.

(±)-**3a**: As previously stated, this isomer was not isolated in a pure form, but it was detected in the spectra of (±)-**2a** as a minor by-product. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 3.43 (dd, 2 H, *J* = 10.7, 3.0 Hz), 2.87 (m, 2H), 2.30 (s, 3H), 2.21 (m, 2H) overlapping with one CH_3 of (±)-**2a**, 1.88 (s, 3H). 10 ArH not identified due to overlap with (±)-**2a** signals. ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 69.9 (CH), 64.1 (CH_2), 45.7 (CH_3), 41.0 (CH_3). Aromatic carbons not detected due to overlap with (±)-**2a** signals.

1,4-dibutyl-2,5-phenylpiperazine, 2b

At the end of the reaction *meso*-**2b** spontaneously precipitated as a white powder and was collected by filtration (yield 27%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 9:1. (±)-**2b** was isolated as a viscous yellowish oil (yield 20).

meso-**2b**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.45 (m, 4H), 7.36 (m, 4H), 7.30 (m, 2H), 3.42 (dd, 2H, *J* = 10.6, 2.6 Hz), 3.09 (dd, 2H, *J* = 11.6, 2.8 Hz), 2.48 (m, 2H), 2.27 (pst, 2H, *J* = 11.0 Hz), 1.92

(m, 2H), 1.41-1.29 (m, 4H), 1.25-1.02 (m, 4H), 0.95 (t, 6H, J = 7.2 Hz). ^{13}C NMR (101 MHz, 25 °C, $CDCl_3$) δ 142.9 (C), 128.4 (CH), 128.1 (CH), 127.3 (CH), 67.8 (CH), 60.9 (CH_2), 54.4 (CH_2), 28.9 (CH_2), 19.6 (CH_2), 14.0 (CH_3). Elemental Analysis calcd. for $C_{24}H_{34}N_2$: C, 82.23; H, 9.78; N, 7.99; found: C, 82.44; H, 10.01; N, 7.78. LR-MS (ESI): m/z ($C_{24}H_{34}N_2$) calcd 350.27, found $[M+H]^+$ 351.36 (100%). M.p. = 103-105 °C

(±)-**2b**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.70 (d, 4H, J =7.3 Hz), 7.44-7.19 (m, 6H), 3.70 (m, 2H,), 3.02 (dd, 2H, J = 11.8, 6.2 Hz), 2.64 (dd, 2H, J = 11.8, 3.4 Hz), 2.34 (m, 2H), 2.17 (m, 2H), 1.52-1.36 (m, 4H), 1.36-1.12 (m, 4H), 0.85 (t, 6H, J = 7.4 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.2 (C), 129.3 (CH), 128.0 (CH), 127.1 (CH), 64.5 (CH), 61.6 (CH_2), 54.9 (CH_2), 29.3 (CH_2), 20.6 (CH_2), 14.1 (CH_3). Elemental Analysis calcd. for $C_{24}H_{34}N_2$: C, 82.23; H, 9.78; N, 7.99; found: C, 81.97; H, 10.11; N, 7.67. LR-MS (ESI): m/z ($C_{24}H_{34}N_2$) calcd 350.27, found $[M+H]^+$ 351.26 (100%).

1,4-dibenzyl-2,5-phenylpiperazine, 2e

At the end of the reaction *meso*-**2e** spontaneously precipitated as a white powder and was collected by filtration (yield 13%). The solution was evaporated to dryness then separated by column chromatography, eluent gradient *n*-hexane/EtOAc/ from 9:1 to 6:4. (±)-**2e** was isolated as a yellowish powder (yield 8%).

meso-**2e**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.43 – 7.22 (m, 20H), 3.81 (d, 2H, J = 13.6 Hz), 3.50 (dd, 2H, J = 10.5, 3.0 Hz), 2.95 (dd, 2H, J = 11.6, 3.0 Hz), 2.88 (d, 2H, J = 13.5 Hz), 2.31 (dd, 2H, J = 11.7, 10.5 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.9, 138.8, 128.7, 128.5, 128.1, 127.5, 127.1, 126.7, 67.6, 60.7, 58.9. Elemental Analysis calcd. for $C_{30}H_{30}N_2$: C, 86.08; H, 7.22; N, 6.69; found: C, 85.94; H, 7.37; N, 6.56. LR-MS (ESI): m/z ($C_{30}H_{30}N_2$) calcd 418.24, found $[M+H]^+$ 419.26 (100%).

(±)-**2e**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.43 – 7.07 (m, 20H), 3.80 (d, 2H, J = 13.5 Hz), 3.50 (dd, 2H, J = 10.5, 3.1 Hz), 2.95 (dd, 2H, J = 11.7, 3.0 Hz), 2.88 (d, 2H, J = 13.5 Hz), 2.31 (pst, 2H, J = 11.1 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.9, 138.8, 132.9, 128.7, 128.5, 128.1, 127.5, 127.3, 67.6, 60.7, 58.9. Elemental Analysis calcd. for $C_{30}H_{30}N_2$: C, 86.08; H, 7.22; N, 6.69; found: C, 85.94; H, 7.37; N, 6.56. LR-MS (ESI): m/z ($C_{30}H_{30}N_2$) calcd 418.24, found $[M+H]^+$ 419.96 (100%).

1,4-diallyl-2,5-phenylpiperazine, 2f

At the end of the reaction *meso*-**2f** spontaneously precipitated as a white powder and was collected by filtration (yield 15%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 8:2. (±)-**2f** was isolated as a yellow oil (yield 12%).

meso-**2f**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.46 (d, 4H, J = 7.0 Hz), 7.37 (td, 4H, J = 7.3, 1.4 Hz), 7.32 (dt, 2H, J = 7.5, 1.4 Hz), 5.79 (dddd, 2H, J = 16.9, 10.4, 8.3, 4.8 Hz), 5.05 (dd, 2H, J = 4.8, 1.4 Hz), 5.02 (dt, 2H, J = 16.9, 3.0 Hz), 3.49 (dd, 2H, J = 10.5, 3.0 Hz), 3.23 (ddt, 2H, J = 13.8, 4.9, 1.8 Hz), 3.09 (dd, 2H, J = 11.8, 3.0 Hz), 2.53 (dd, 2H, J = 13.8, 8.3 Hz), 2.32 (dd, 2H, J = 11.7, 10.6 Hz).^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 141.6, 134.8, 128.5, 128.1, 127.5, 117.7, 67.2, 60.7, 57.6. Elemental Analysis calcd. for $C_{22}H_{26}N_2$: C, 82.97; H, 8.23; N, 8.80; found: C, 82.88; H, 8.24; N, 8.65. LR-MS (ESI): m/z ($C_{22}H_{26}N_2$) calcd 318.21, found $[M+H]^+$ 319.82 (100%).

(±)-**2f**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.74 (d, 4H, *J* = 7.0 Hz), 7.42 (t, 4H, *J* = 7.4 Hz), 7.24 (m, 2H) overlapping with signals due to polymeric materials, 5.88 (dddd, 2H, *J* = 17.3, 10.3, 7.0, 5.7 Hz), 5.20 – 5.07 (m, 6H), 3.77 (dd, 2H, *J* = 6.3, 3.8 Hz), 3.04 (d, 2H, *J* = 6.1 Hz), 2.87 (dd, 2H, *J* = 13.9, 7.0 Hz), 2.72 (dd, 2H, *J* = 12.1, 3.8 Hz). Unfortunately, any attempts to obtain this compound completely pure from traces of polymeric materials meet with failure. For that reason, no further analyses were carried out.

1,4-dimethyl-2,5-(4-methylphenyl)piperazine, 2h

At the end of the reaction *meso*-**2h** spontaneously precipitated as a white powder and was collected by filtration (yield 46%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 8:2. (±)-**2h** was isolated as a yellow oil (yield 36%).

meso-**2h**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.32 (m, 4H), 7.19 (d, 4H, *J* = 8.1 Hz), 3.27 (m, 2H), 2.97 (m, 2H,), 2.40 (m, 2H) overlapping with 2.38 (s, 6H), 2.08 (s, 6H).^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 138.2 (C), 137.3 (C), 129.2 (CH), 127.8 (CH), 69.1 (CH), 64.2 (CH_2), 43.1 (CH_3), 21.1 (CH_3). Elemental Analysis calcd. for $C_{20}H_{26}N_2$: C, 81.58; H, 8.90; N, 9.51; found: C, 81.23; H, 8.77; N, 9.41. LR-MS (ESI): m/z ($C_{20}H_{26}N_2$) calcd 294.21, found $[M+H]^+$ 295.33 (100%).

(±)-**2h**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.60 (d, 4H, *J* = 7.1 Hz), 7.22 (d, 4H, *J* = 7.1 Hz), 3.54 (m, 2H), 2.94 (m, 2H), 2.65 (m, 2H), 2.41 (s, 6H), 2.15 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 137.1 (C), 136.8 (C), 129.3 (CH), 128.7 (CH), 65.7 (CH), 58.0 (CH_2), 43.3 (CH_3), 21.2 (CH_3). Elemental Analysis calcd. for $C_{20}H_{26}N_2$: C, 81.58; H, 8.90; N, 9.51 found: C, 81.67; H, 8.57; N, 9.42. LR-MS (ESI): m/z ($C_{20}H_{26}N_2$) calcd 294.21, found $[M+H]^+$ 295.35 (100%).

1,4-dimethyl-2,5-(4-(1',1'-dimethyl)ethylphenyl)piperazine, 2i

At the end of the reaction *meso*-**2i** spontaneously precipitated as a white powder and was collected by filtration (yield 31%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 7:3. (±)-**2i** was isolated as a yellow powder (yield 21%).

meso-**2i**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.41 – 7.34 (m, 8H), 3.29 (m, 2H), 3.00 (m, 2H), 2.41 (m, 2H), 2.09 (s, 6H), 1.35 (s, 18H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 150.5, 127.5, 125.4, 69.0, 64.1, 43.2, 34.8, 31.4, one quaternary aromatic carbon was not detected. Elemental Analysis calcd. for $C_{26}H_{38}N_2$: C, 82.48; H, 10.12; N, 7.40 found: C, 82.16; H, 10.33; N, 7.21. LR-MS (ESI): m/z ($C_{26}H_{38}N_2$) calcd 378.30, found $[M+H]^+$ 379.38 (100%).

(±)-**2i**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.64 (d, 4H, *J* = 8.2 Hz), 7.42 (d, 4H, *J* = 8.3 Hz), 3.54 (dd, 2H, *J* = 5.7, 4.0 Hz), 2.95 (dd, 2H, *J* = 11.6, 5.7 Hz), 2.66 (dd, 2H, *J* = 11.6, 4.0 Hz), 2.15 (s, 6H), 1.38 (s, 18H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 150.0, 137.1, 129.1, 124.8, 65.6, 58.0, 43.3, 34.5, 31.5. Elemental Analysis calcd. for $C_{26}H_{38}N_2$: C, 82.48; H, 10.12; N, 7.40 found: C, 82.22; H, 10.01; N, 7.14. LR-MS (ESI): m/z ($C_{26}H_{38}N_2$) calcd 378.30, found $[M+H]^+$ 379.51 (100%).

1,4-dimethyl-2,5-(4-bromophenyl)piperazine, 2l

At the end of the reaction *meso*-**2l** spontaneously precipitated as a white powder and was collected by filtration (yield 20%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 6:4. (±)-**2l** was isolated as a yellow powder (yield 17%).

meso-**2l**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.50 (d, 4H, *J* = 8.3 Hz), 7.30 (d, 4H, *J* = 8.1 Hz), 3.21 (dd, 2H, *J* = 10.6, 3.0 Hz), 2.91 (dd, 2H, *J* = 11.7, 3.0 Hz), 2.30 (dd, 2H, *J* = 11.6, 10.6 Hz), 2.04 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 140.2, 131.7, 129.6, 121.3, 68.6, 63.9, 43.1. Elemental Analysis calcd. for $C_{18}H_{20}Br_2N_2$: C, 50.97; H, 4.75; N, 6.60; found: C, 51.23; H, 4.68; N, 6.45. LR-MS (ESI): m/z ($C_{18}H_{20}Br_2N_2$) calcd 424.00, found $[M+H]^+$ 425.27 (100%).

(±)-**2l**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.52 (m, 8H), 3.51 (m, 2H), 2.83 (m, 2H), 2.63 (dd, 2H, *J* = 12.0, 4.1 Hz), 2.12 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 138.9, 131.2, 131.0, 121.3, 65.0, 57.4, 43.2. Elemental Analysis calcd. for $C_{18}H_{20}Br_2N_2$: C, 50.97; H, 4.75; N, 6.60; found: C, 50.87; H, 4.63; N, 6.21. LR-MS (ESI): m/z ($C_{18}H_{20}Br_2N_2$) calcd 424.00, found $[M+H]^+$ 425.32 (100%).

1,4-dimethyl-2,5-(4-fluorophenyl)piperazine, 2m

At the end of the reaction *meso*-**2m** spontaneously precipitated as a white powder and was collected by filtration (yield 14%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 6:4. (±)-**2m** was isolated as a yellow powder (yield 6%).

meso-**2m**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.38 (dd, 4H, J = 8.0, 3.9 Hz), 7.05 (pst, 4H, *J* = 8.0 Hz), 3.23 (dd, 2H, *J* = 10.6, 3.0 Hz), 2.92 (dd, 2H, J = 11.7, 3.0 Hz), 2.32 (dd, 2H, *J* = 11.7, 10.6 Hz), 2.04 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 162.2 (*J* = 244 Hz), 136.9 (*J* = 3 Hz), 129.3 (*J* = 7 Hz), 115.3 (*J* = 21 Hz), 68.53, 64.17, 43.13 Elemental Analysis calcd. for $C_{18}H_{20}F_2N_2$: C, 71.50; H, 6.67; N, 9.26; found: C, 71.22; H, 6.79; N, 9.00. LR-MS (ESI): m/z ($C_{18}H_{20}Br_2N_2$) calcd 302.16, found $[M+H]^+$ 303.44 (100%).

(±)-**2m**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.75 – 7.51 (m, 4H), 7.07 (pst, 4H, *J* = 8.8 Hz), 3.54 (m, 2H), 2.86 (dd, 2H, *J* = 11.9, 6.2 Hz), 2.64 (dd, 2H, *J* = 11.9, 3.9 Hz), 2.12 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 162.1 (*J* = 244 Hz), 135.7, 130.7 (*J* = 8 Hz), 114.8 (*J* = 21 Hz), 65.0, 57.7, 43.1. Elemental Analysis calcd. for $C_{18}H_{20}F_2N_2$: C, 71.50; H, 6.67; N, 9.26; found: C, 71.48; H, 6.59; N, 8.92. LR-MS (ESI): m/z ($C_{18}H_{20}Br_2N_2$) calcd 302.16, found $[M+H]^+$ 303.39 (100%).

1,4-dibutyl-2,5-(4-methylphenyl)piperazine, 2n

At the end of the reaction *meso*-**2n** spontaneously precipitated as a white powder and was collected by filtration (yield 15%). The solution was evaporated to dryness then separated by column chromatography, eluent *n*-hexane/EtOAc = 8:2. (±)-**2n** was isolated as a yellow oil (yield 7%).

meso-**2n**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.34 (d, 4H, *J* = 8.0 Hz), 7.18 (d, 4H, *J* = 8.0 Hz), 3.39 (dd, 2H, *J* = 10.6, 3.0 Hz), 3.07 (dd, 2H, *J* = 11.5, 3.0 Hz), 2.50 (m, 2H), 2.39 (s, 6H), 2.26 (pst, 2H, *J* = 11.1 Hz), 1.93 (m, 2H), 1.44 – 1.30 (m, 4H), 1.35 – 0.94 (m, 4H), 0.79 (t, 6H, *J* = 7.3 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 139.2, 136.9, 129.1, 127.9, 67.5, 61.0, 54.4, 28.3, 21.2, 20.5, 14.0. Elemental Analysis calcd. for $C_{26}H_{38}N_2$: C, 82.48; H, 10.12; N, 7.40; found: C, 82.11; H, 9.99; N, 7.32. LR-MS (ESI): m/z ($C_{26}H_{38}N_2$) calcd 378.30, found $[M+H]^+$ 379.44 (100%).

(±)-**2n**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.60 (d, 4H, *J* = 7.8 Hz), 7.20 (d, 4H, *J* = 7.8 Hz), 3.66 (dd, 2H, *J* = 6.4, 3.8 Hz), 2.99 (dd, 2H, *J* = 11.8, 6.3 Hz), 2.62 (dd, 2H, *J* = 12.0, 3.8 Hz), 2.57 – 2.48 (m, 2H), 2.39 (s, 6H), 2.18 – 2.11 (m, 2H), 1.68 – 1.63 (m, 4H), 1.32 – 1.20 (m, 4H), 0.85 (t, *J* = 7.3

Hz, 6H). The purity of the recovered product was not sufficient for Elemental Analysis. LR-MS (ESI): m/z ($C_{26}H_{38}N_2$) calcd 378.30, found $[M+H]^+$ 379.42 (100%).

1,4-dibutyl-2,5-(4-chlorophenyl)piperazine, 2o

At the end of the reaction *meso*-**2o** spontaneously precipitated as a white powder and was collected by filtration (yield 8%). The solution was evaporated to dryness then separated by column chromatography, eluent gradient *n*-hexane/EtOAc from 9:1 to 5:5. (±)-**2o** was isolated as a yellow oil (yield 4%).

meso-**2o**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.39 – 7.30 (m, 8H), 3.37 (dd, 2H, *J* = 10.6, 3.1 Hz), 3.02 (dd, 2H, *J* = 11.6, 3.1 Hz), 2.43 (m, 2H), 2.18 (pst, 2H, *J* = 11.1 Hz), 1.90 (m, 2H), 1.42 – 1.26 (m, 4H), 1.25 – 1.00 (m, 4H), 0.79 (t, 6H, *J* = 7.3 Hz). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 140.6, 133.0, 129.3, 128.6, 67.0, 60.7, 54.4, 28.3, 20.5, 14.0. Elemental Analysis calcd. for $C_{24}H_{32}Cl_2N_2$: C, 71.50; H, 6.67; N, 9.26; found: C, 71.48; H, 6.59; N, 8.92. LR-MS (ESI): m/z ($C_{24}H_{32}Cl_2N_2$) calcd 418.19, found $[M+H]^+$ 419.30 (100%).

(±)-**2o**: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.60 (m, 4H), 7.37 (m, 4H), 3.67 (m, 2H), 2.92 (m, 2H), 2.62 (m, 2H), 2.40 – 2.00 (m, 4H), 1.58 – 1.43 (m, 4H), 1.34 – 1.20 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 6H). The purity of the recovered product was not sufficient for other analyses.

1,4-ditosylpiperazine, 2r

At the end of the reaction **2r** spontaneously precipitated as a white powder and was collected by filtration (yield 25%).

2r: ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$) δ 7.62 (d, 4H, *J* = 8.3 Hz), 7.35 (d, 4H, *J* = 8.2 Hz), 3.10 (s, 8H), 2.47 (s, 6H). ^{13}C NMR (101 MHz, 25°C, $CDCl_3$) δ 144.2, 132.2, 129.9, 127.7, 45.5, 21.5. Elemental Analysis calcd. for $C_{18}H_{22}N_2O_4S_2$: C, 54.80; H, 5.62; N, 7.10; found: C, 55.01; H, 5.25; N, 6.92. LR-MS (ESI): m/z ($C_{18}H_{20}Br_2N_2$) calcd 394.10, found $[M+Na]^+$ 417.38 (100%).

^{1}H and ^{13}C NMR spectra of isolated compounds

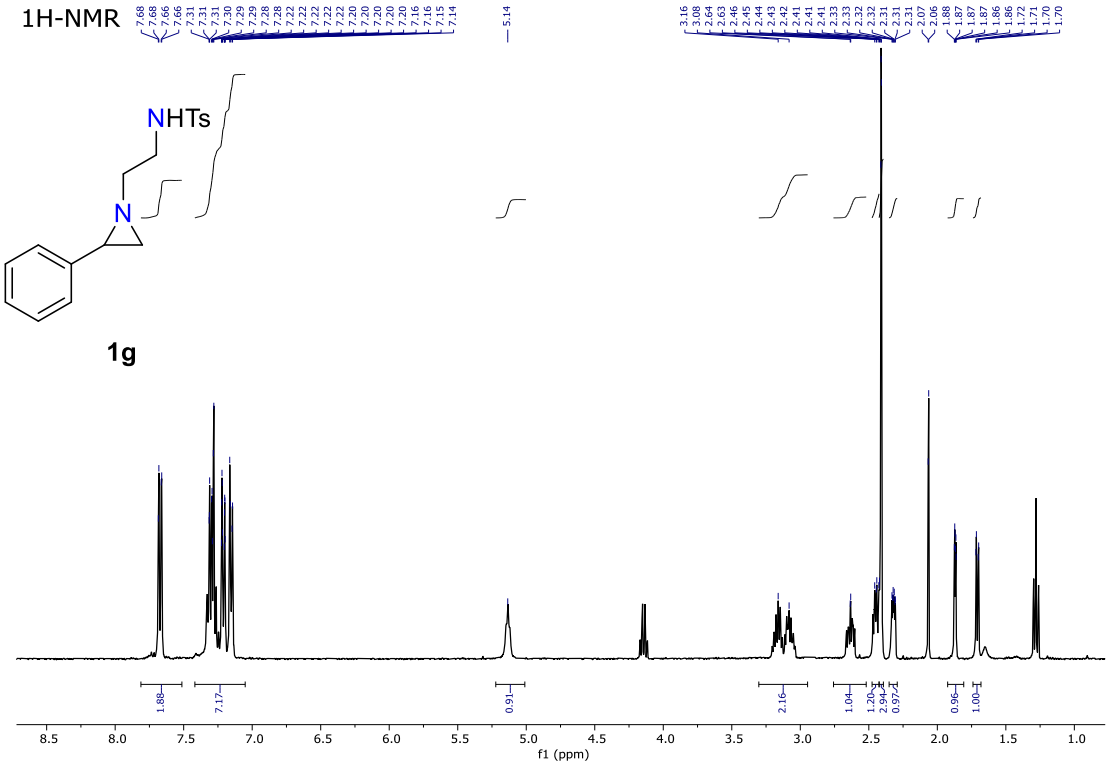


Figure S8: ^{1}H NMR of isolated compound **1g** in $CDCl_3$

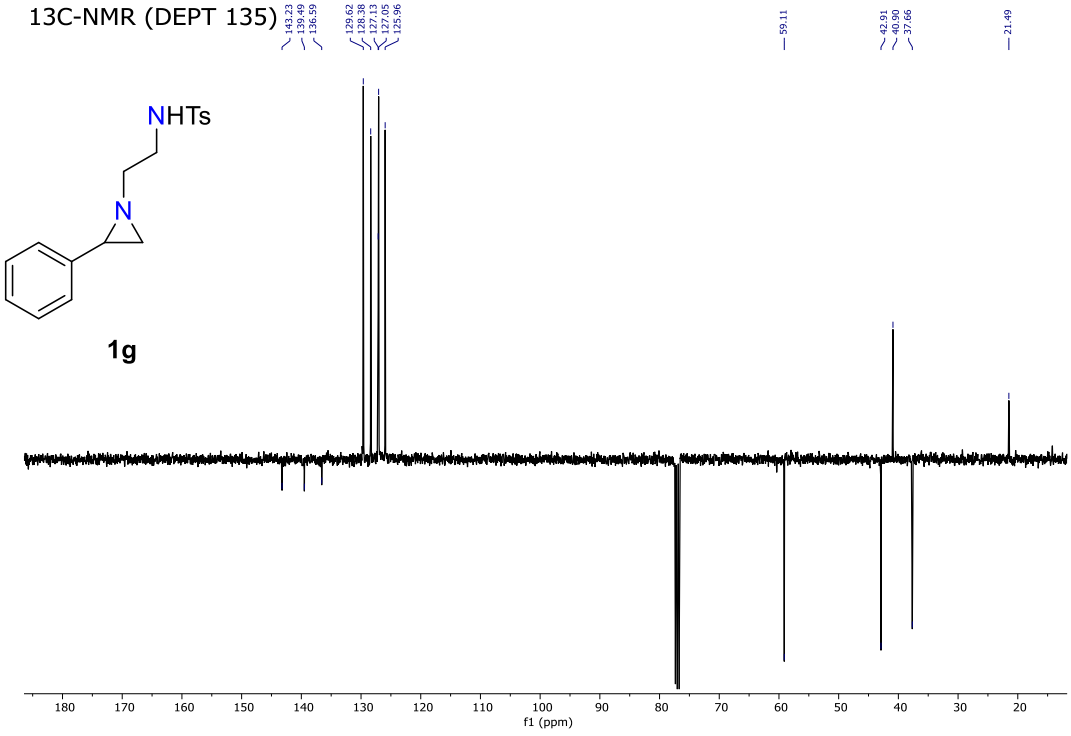


Figure S9: ^{13}C NMR of isolated compound **1g** in $CDCl_3$

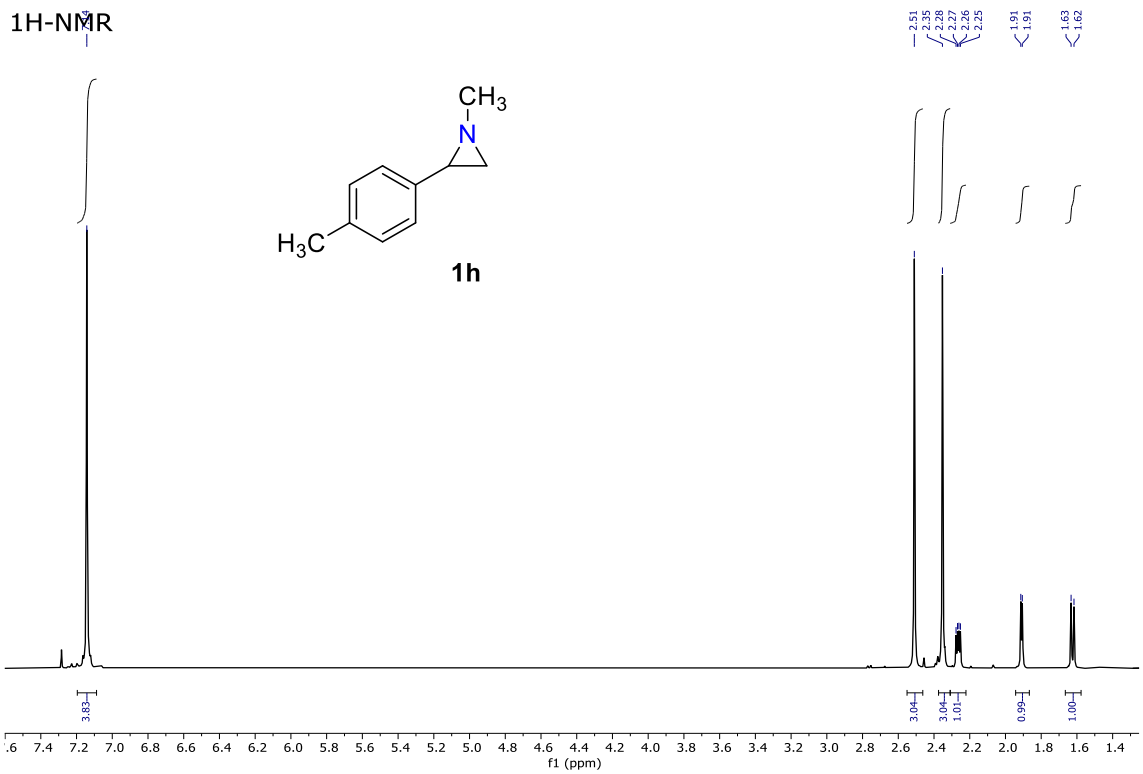


Figure S10: ^{1}H NMR of isolated compound **1h** in $CDCl_3$

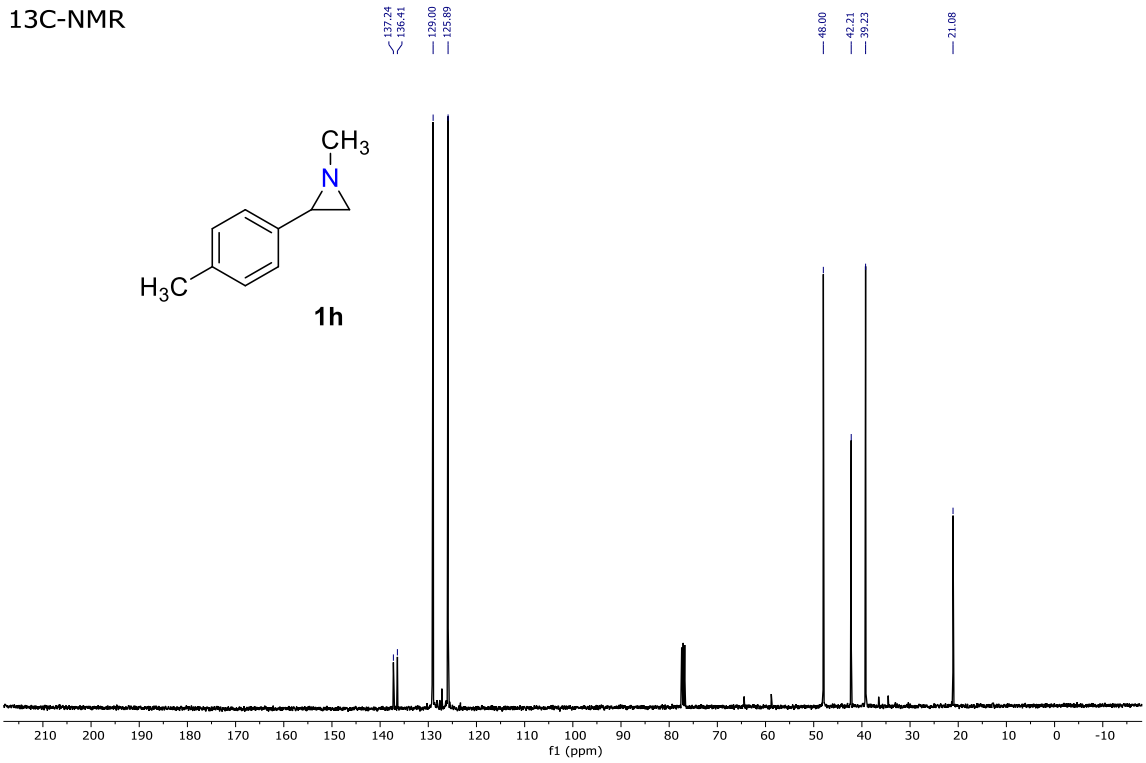


Figure S11: ^{13}C NMR of isolated compound **1h** in $CDCl_3$

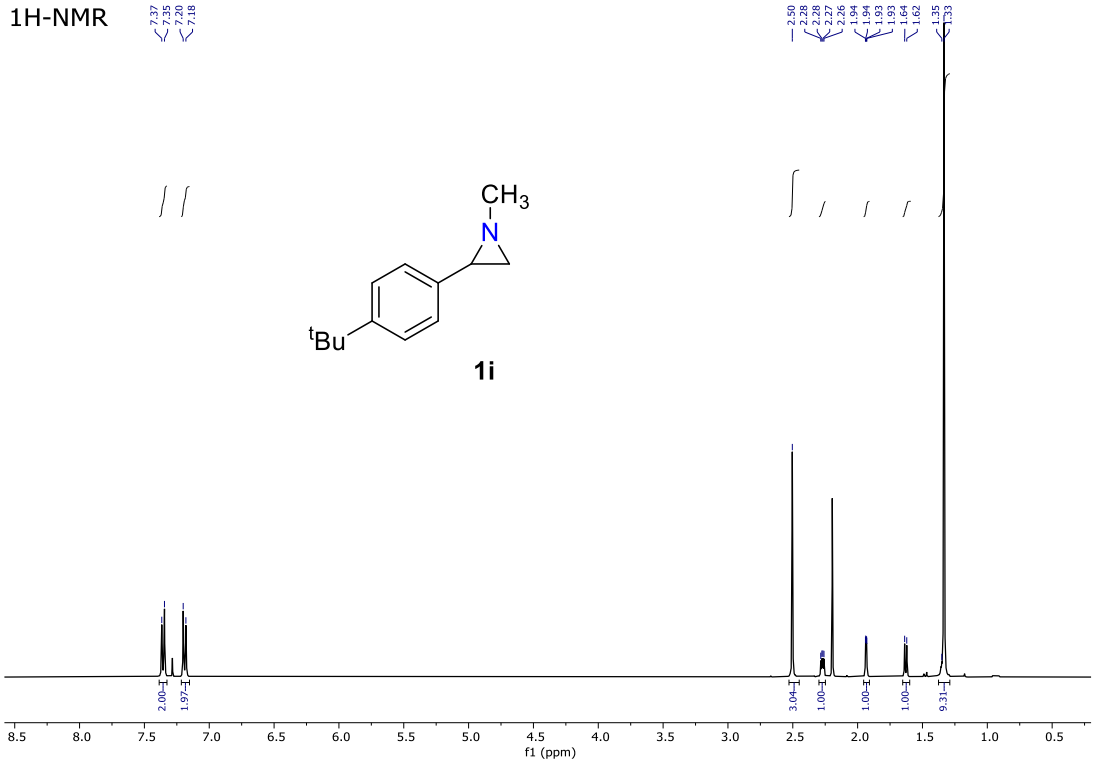


Figure S12: ^{1}H NMR of isolated compound **1i** in $CDCl_3$

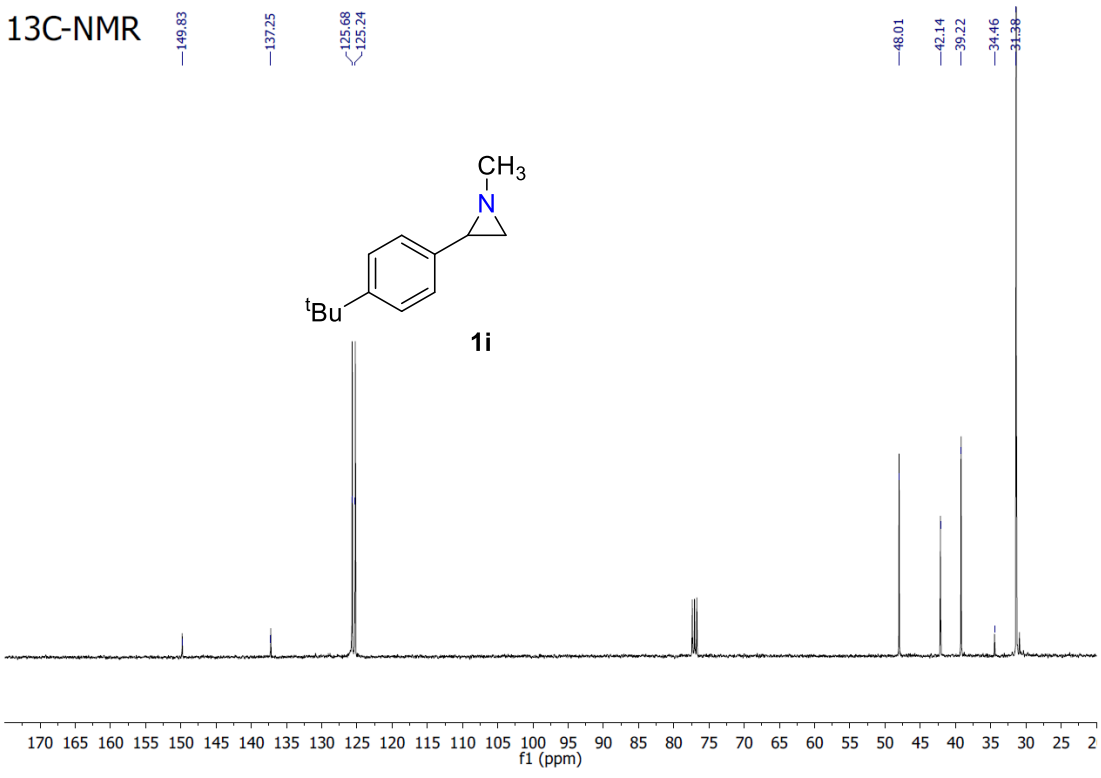


Figure S13: ^{13}C NMR of isolated compound **1i** in $CDCl_3$

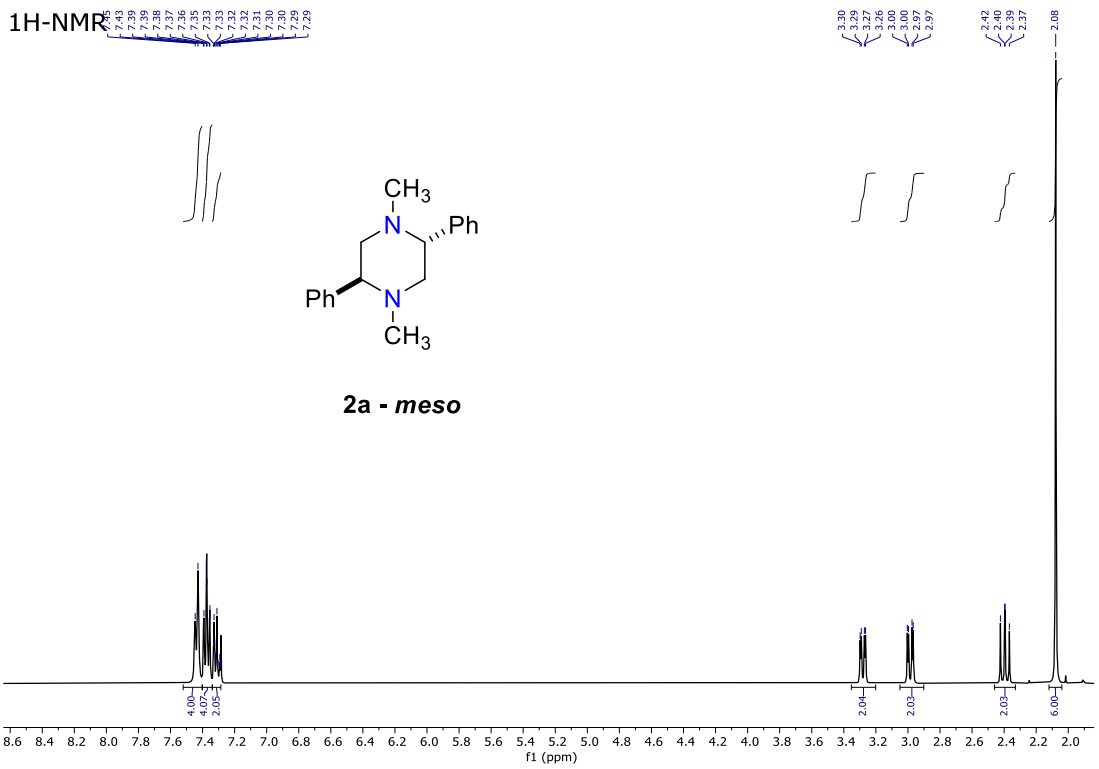


Figure S14: ^{1}H NMR of isolated compound *meso*-**2a** in $CDCl_3$

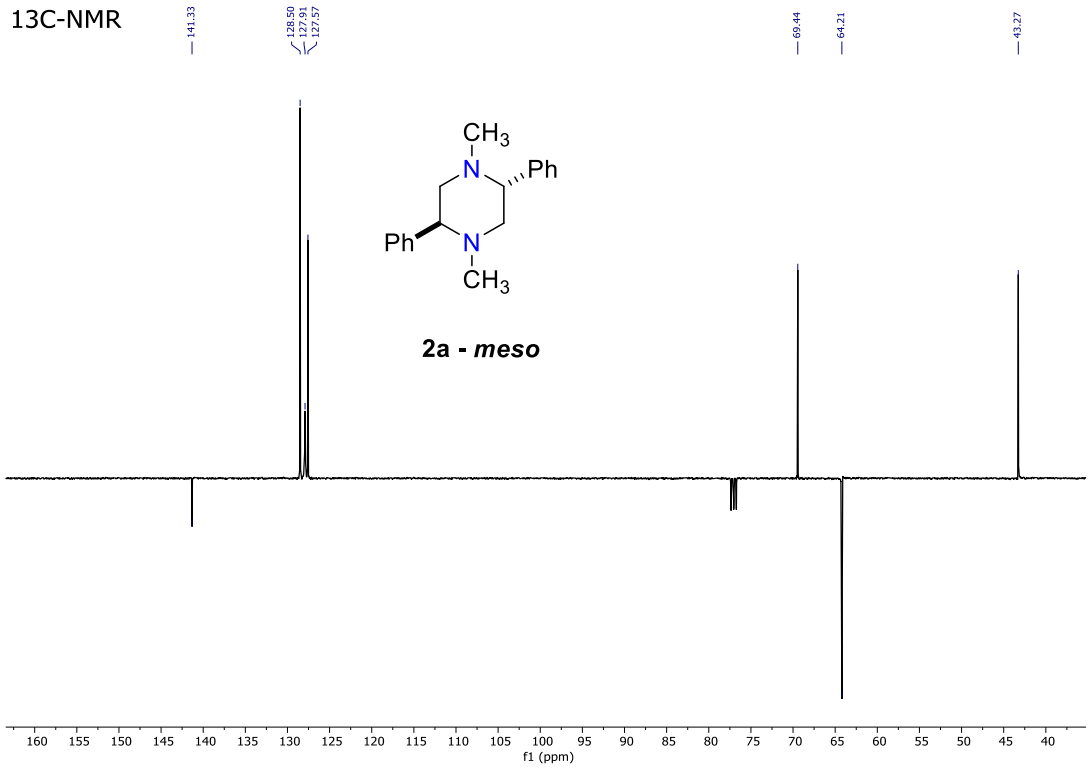


Figure S15: ^{13}C NMR of isolated compound *meso*-**2a** in $CDCl_3$

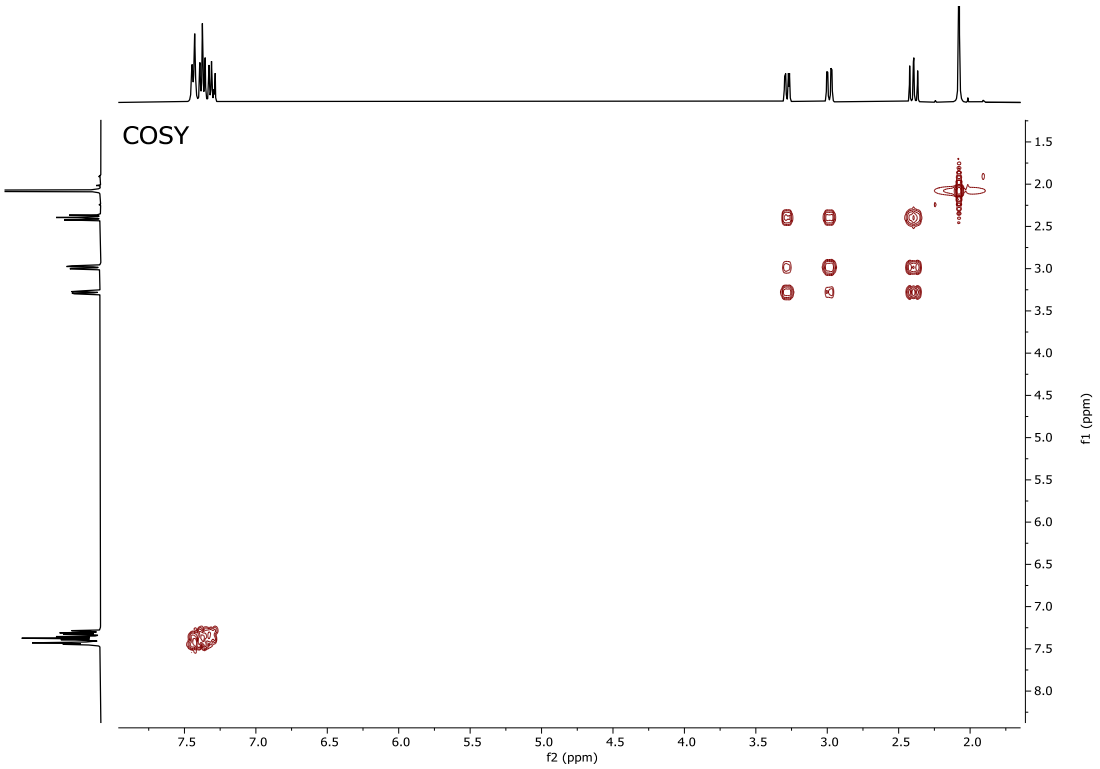


Figure S16: 2D ^{1}H COSY NMR of isolated compound *meso*-**2a** in $CDCl_3$

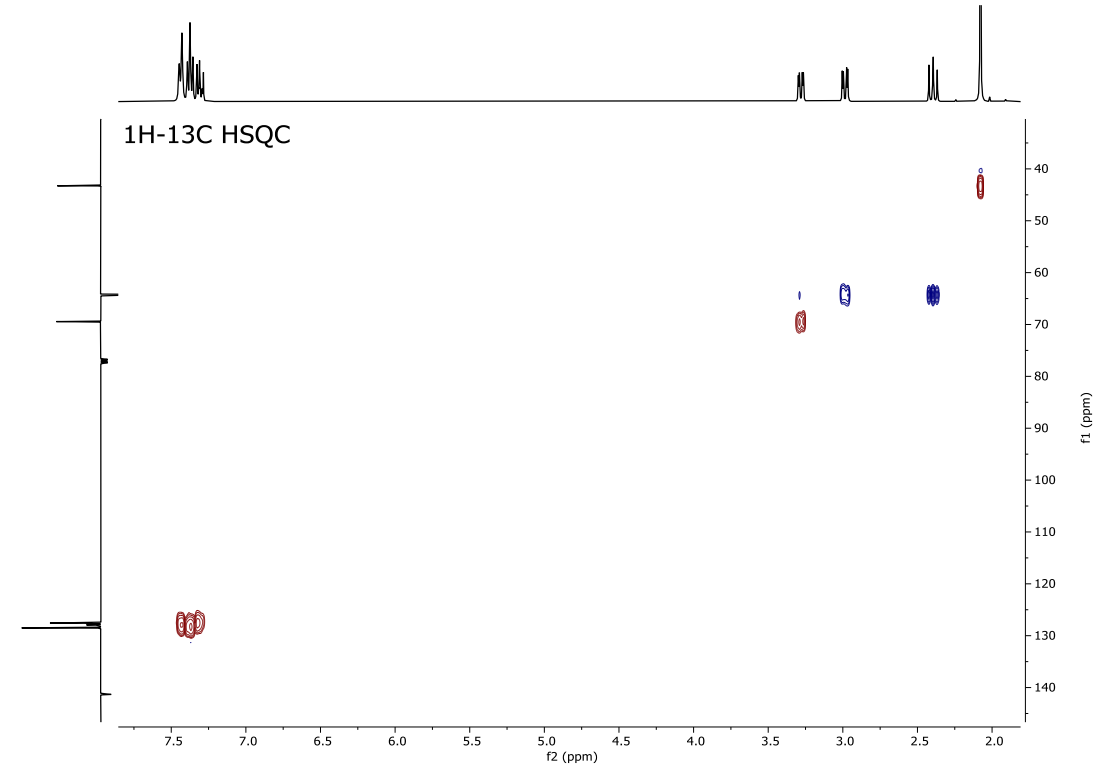


Figure S17: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2a** in $CDCl_3$

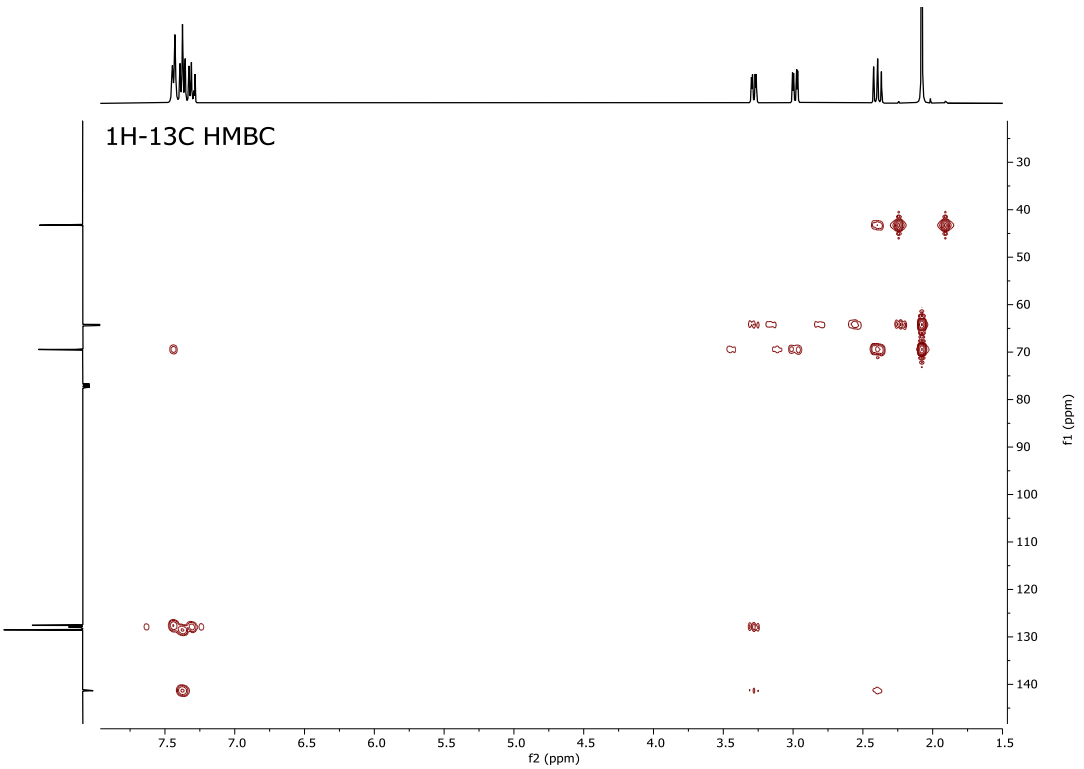


Figure S18: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2a** in $CDCl_3$

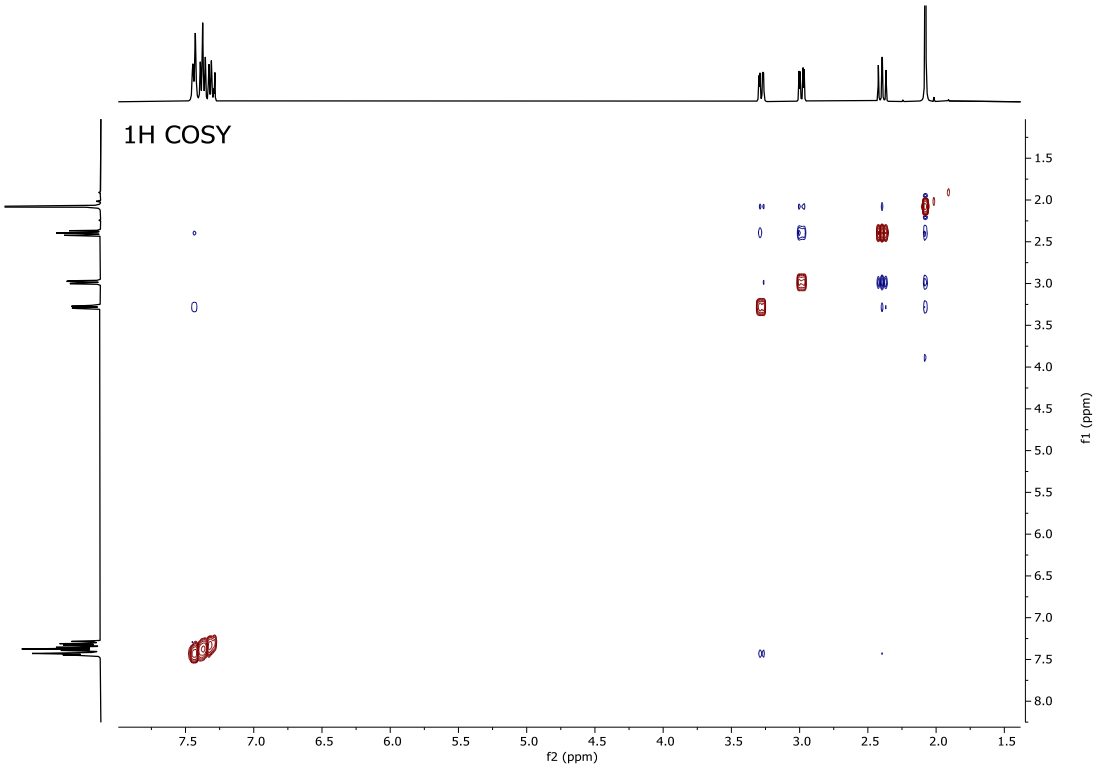


Figure S19: 2D ^{1}H COSY NMR of isolated compound *meso*-**2a** in $CDCl_3$

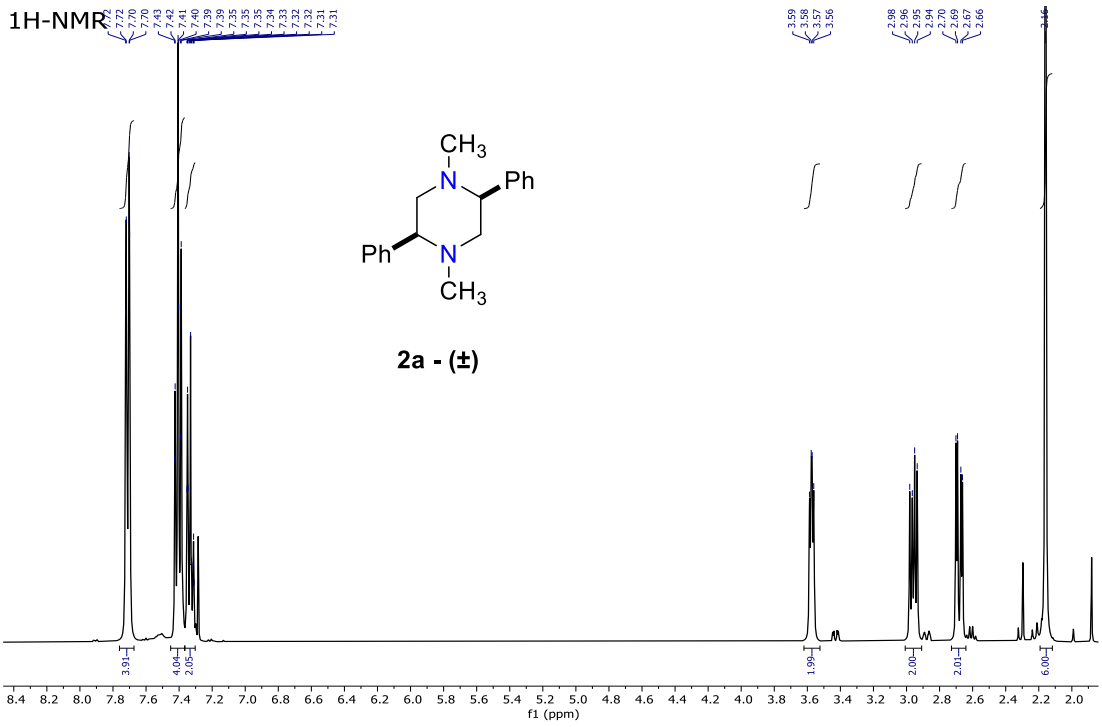


Figure S20: ^{1}H NMR of isolated compound (±)-**2a** in $CDCl_3$

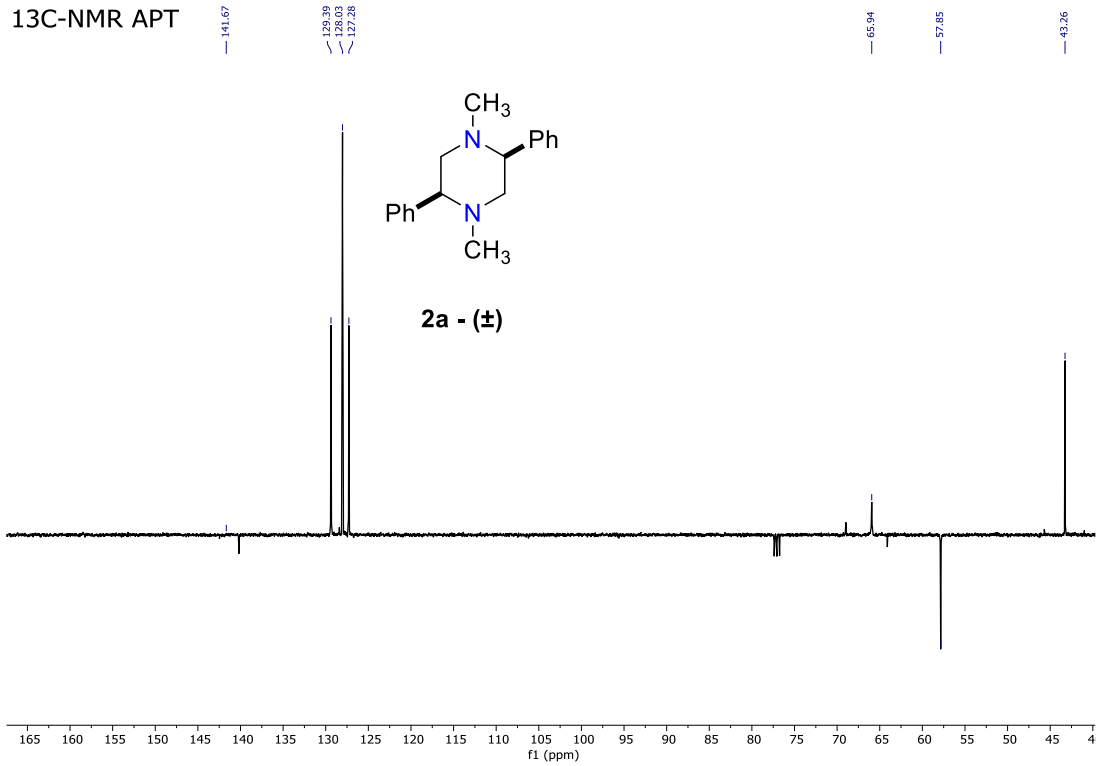


Figure S21: ^{13}C NMR of isolated compound (±)-**2a** in $CDCl_3$

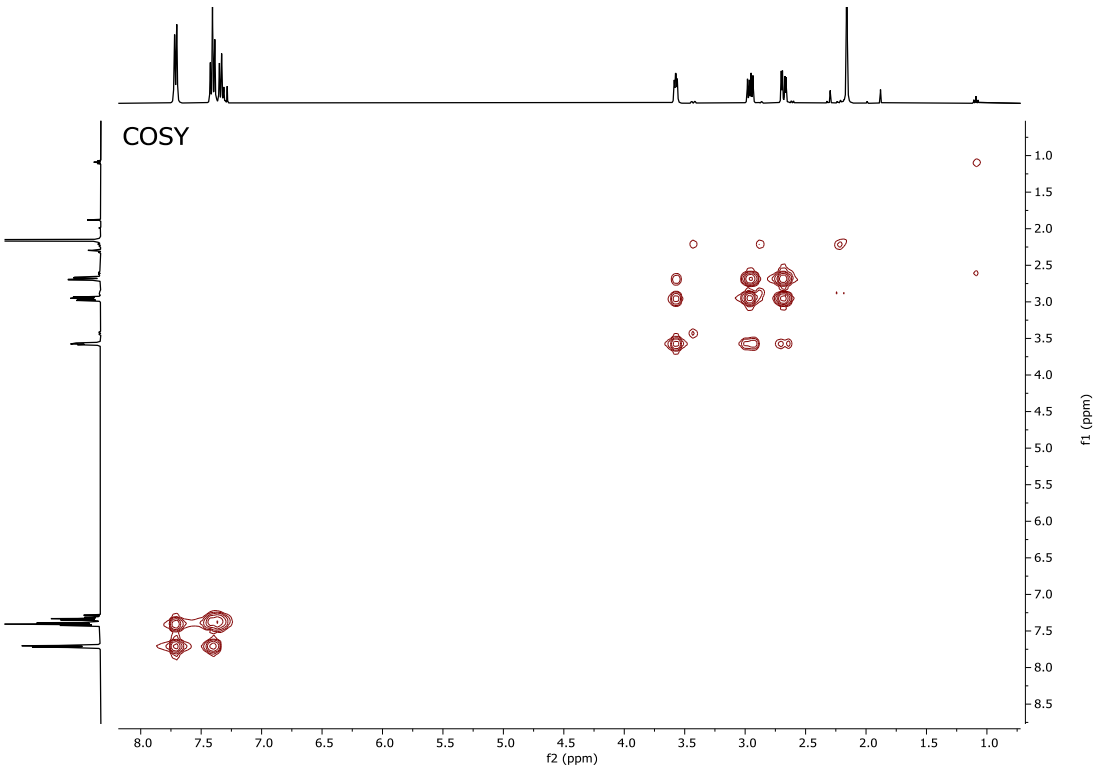


Figure S22: 2D ^{1}H COSY NMR of isolated compound (±)-**2a** in $CDCl_3$

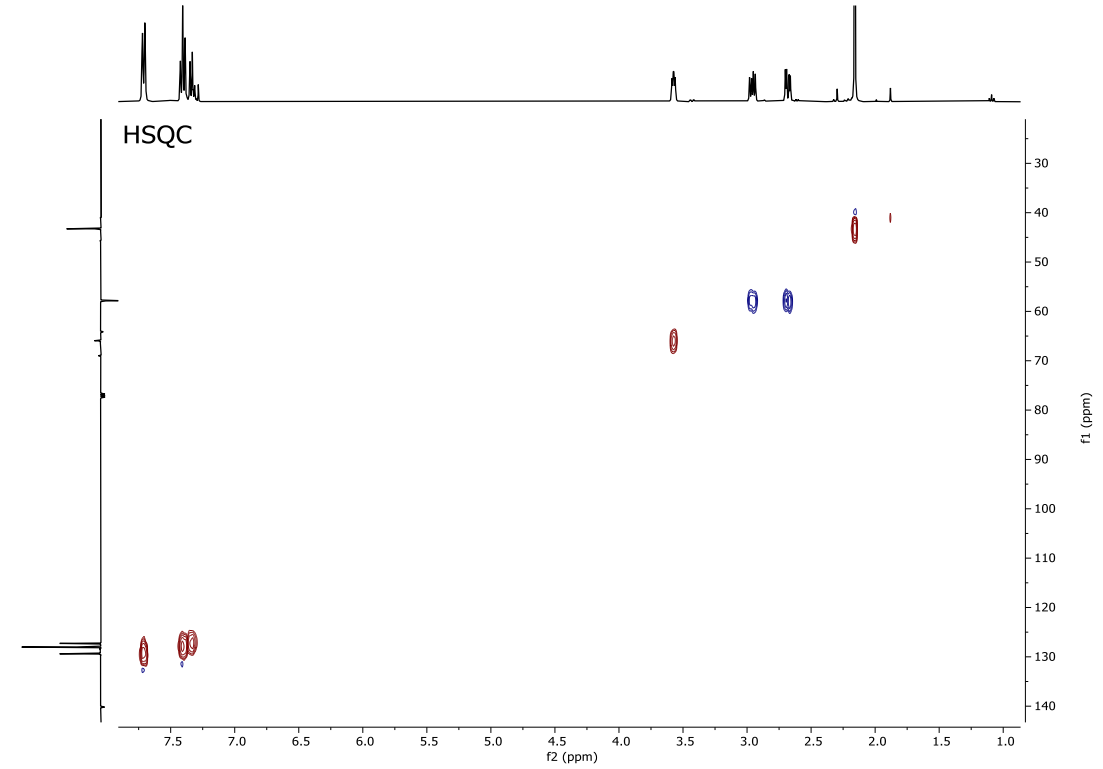


Figure S23: 2D ^{1}H-^{13}C HSQC NMR of isolated compound (±)-**2a** in $CDCl_3$

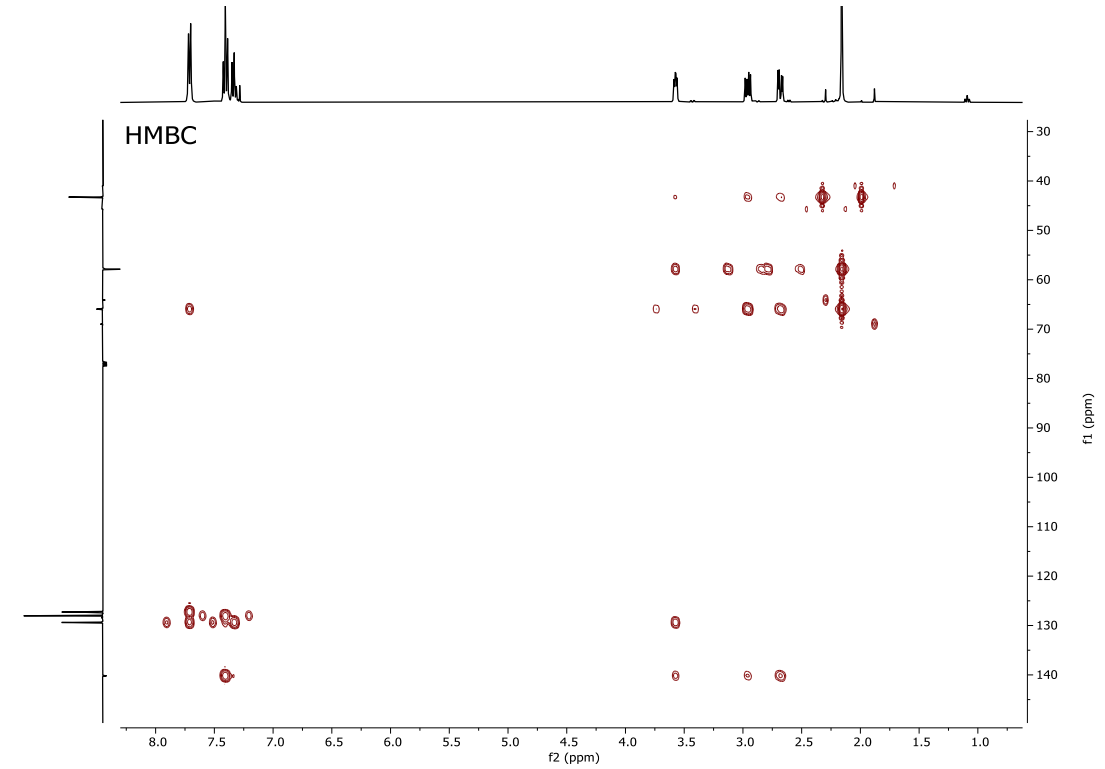


Figure S24: 2D ^{1}H-^{13}C HMBC NMR of isolated compound (±)-**2a** in $CDCl_3$

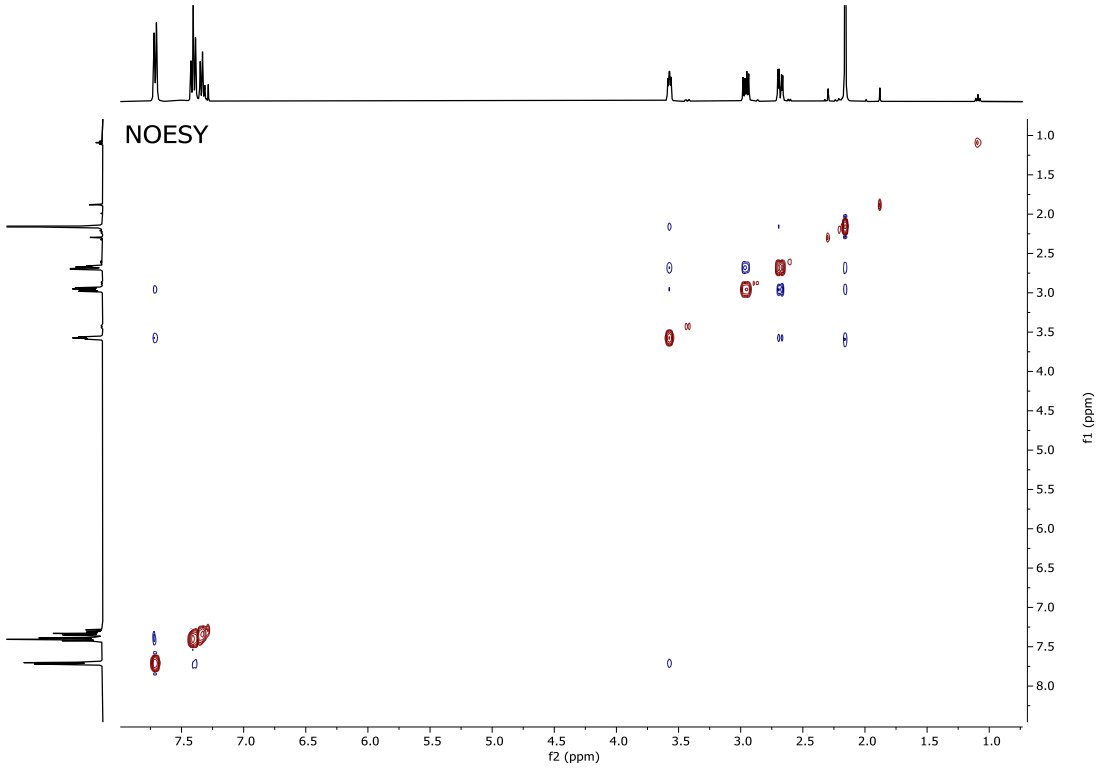


Figure S25: 2D ^{1}H COSY NMR of isolated compound (±)-**2a** in $CDCl_3$

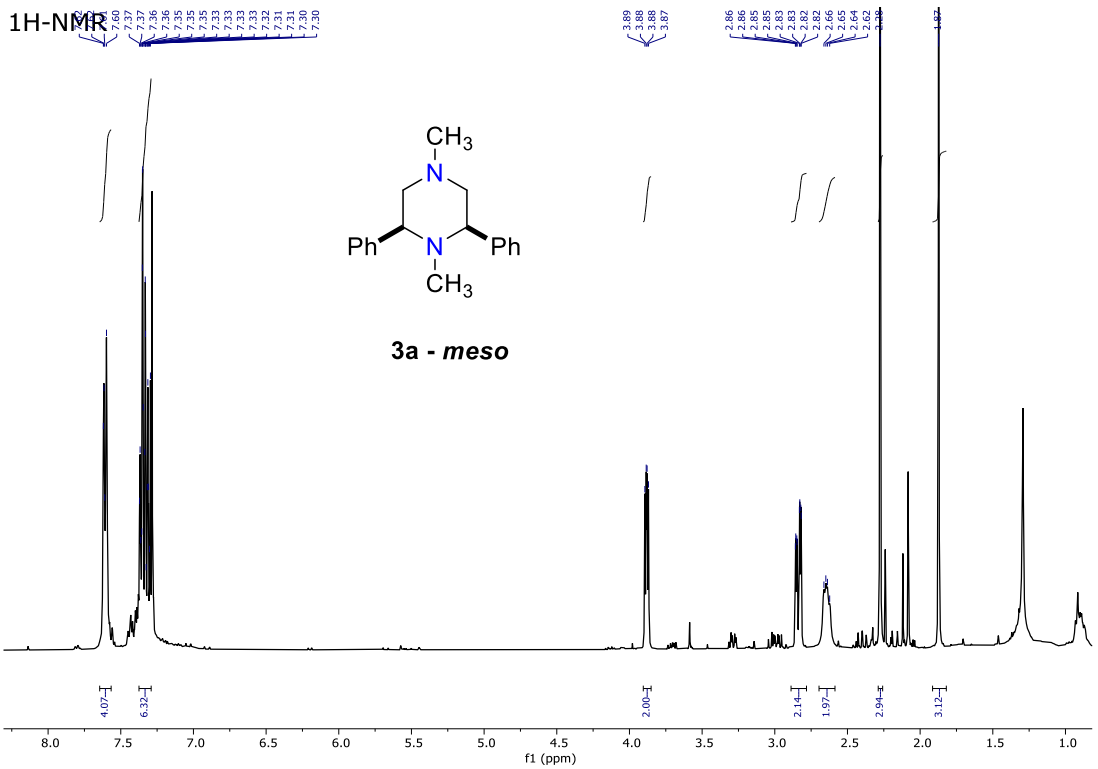


Figure S26: ^{1}H NMR of isolated compound *meso*-**3a** in $CDCl_3$

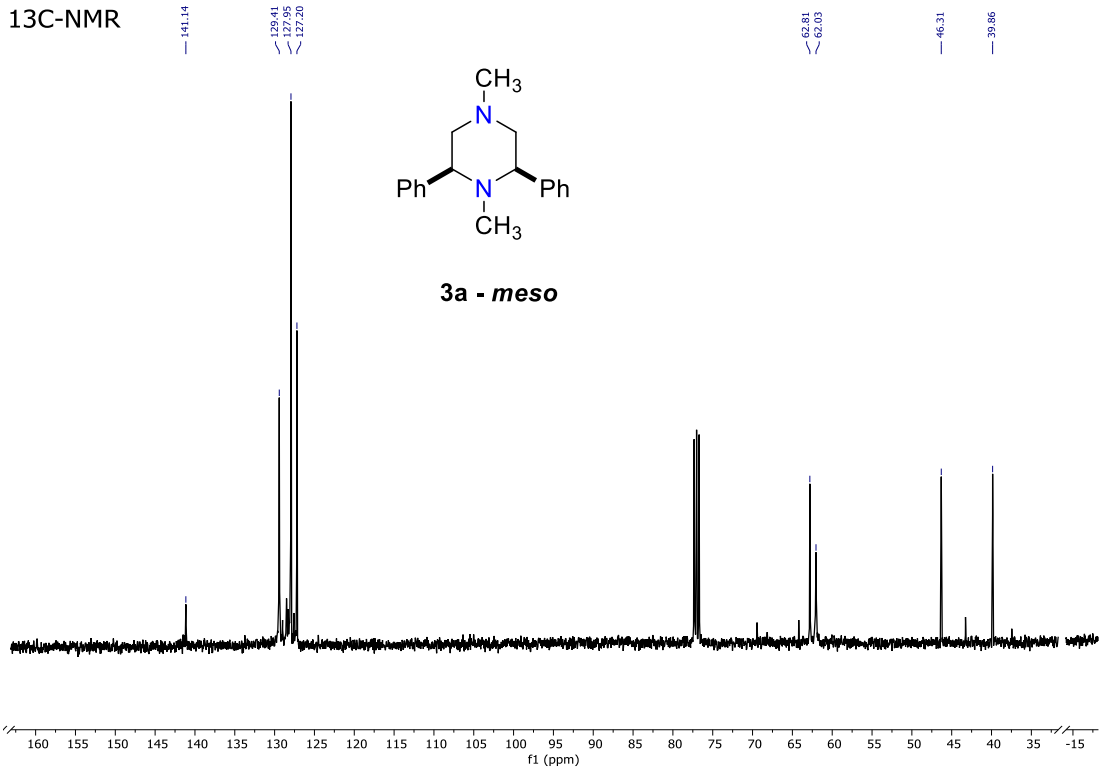


Figure S27: ^{13}C NMR of isolated compound *meso*-**3a** in $CDCl_3$

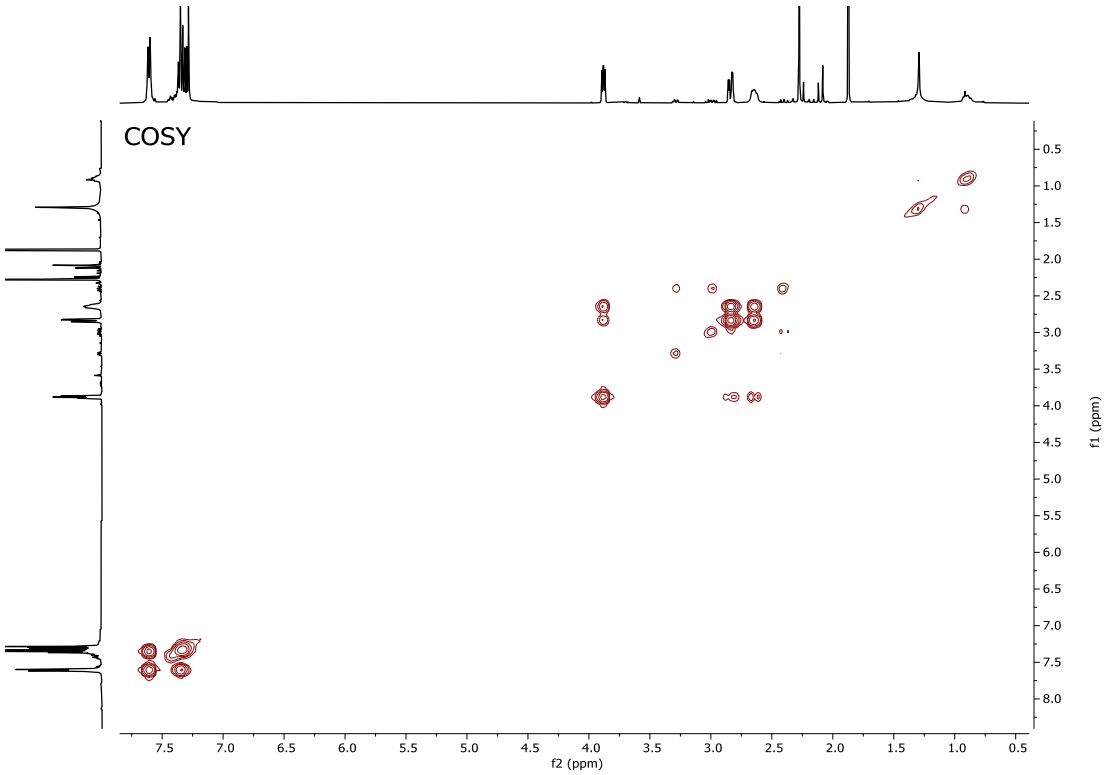


Figure S28: 2D ^{1}H COSY NMR of isolated compound *meso*-**3a** in $CDCl_3$

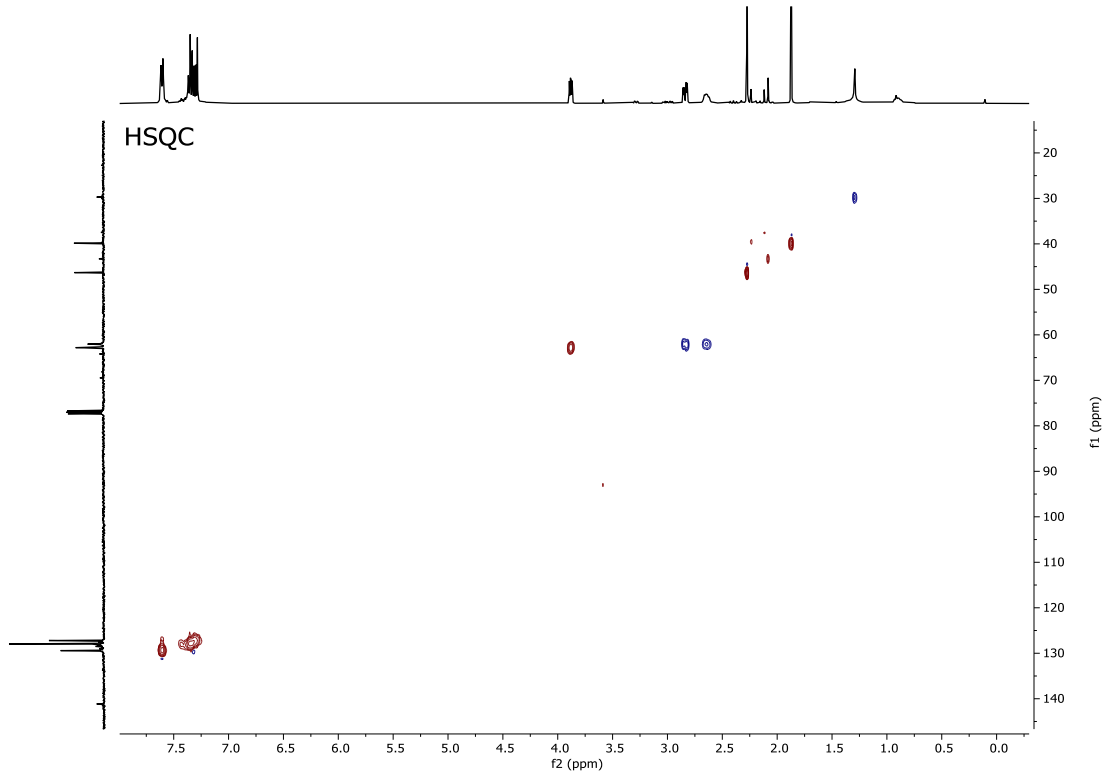


Figure S29: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**3a** in $CDCl_3$

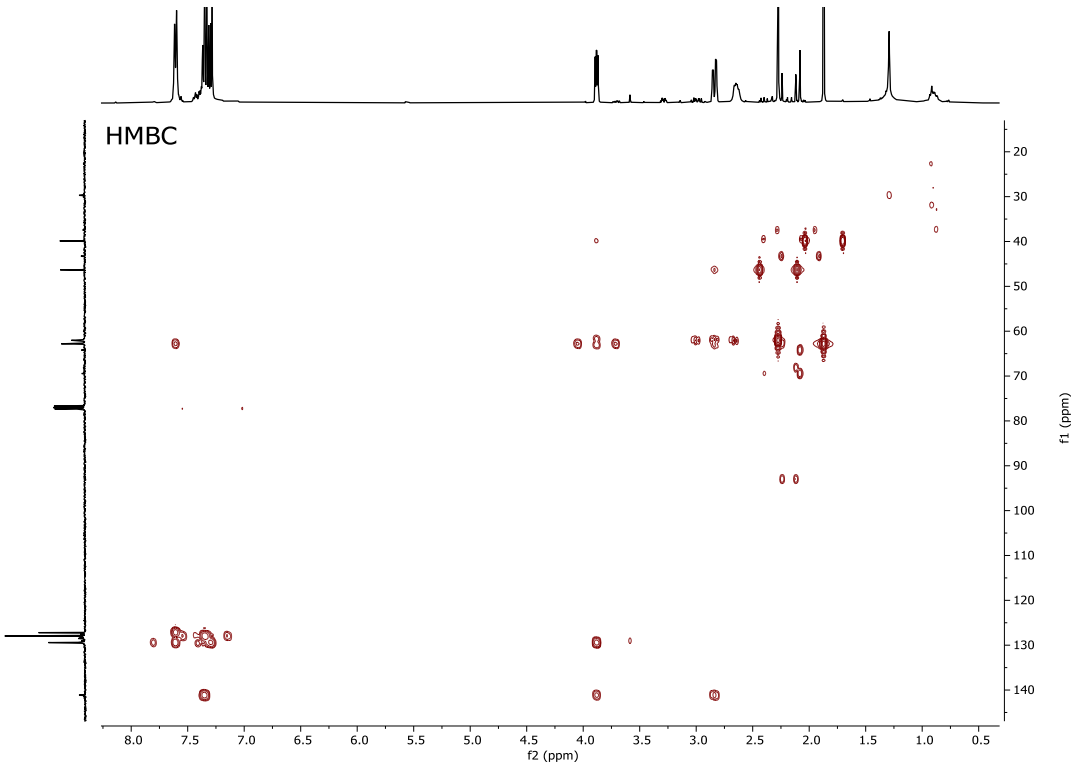


Figure S30: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**3a** in $CDCl_3$

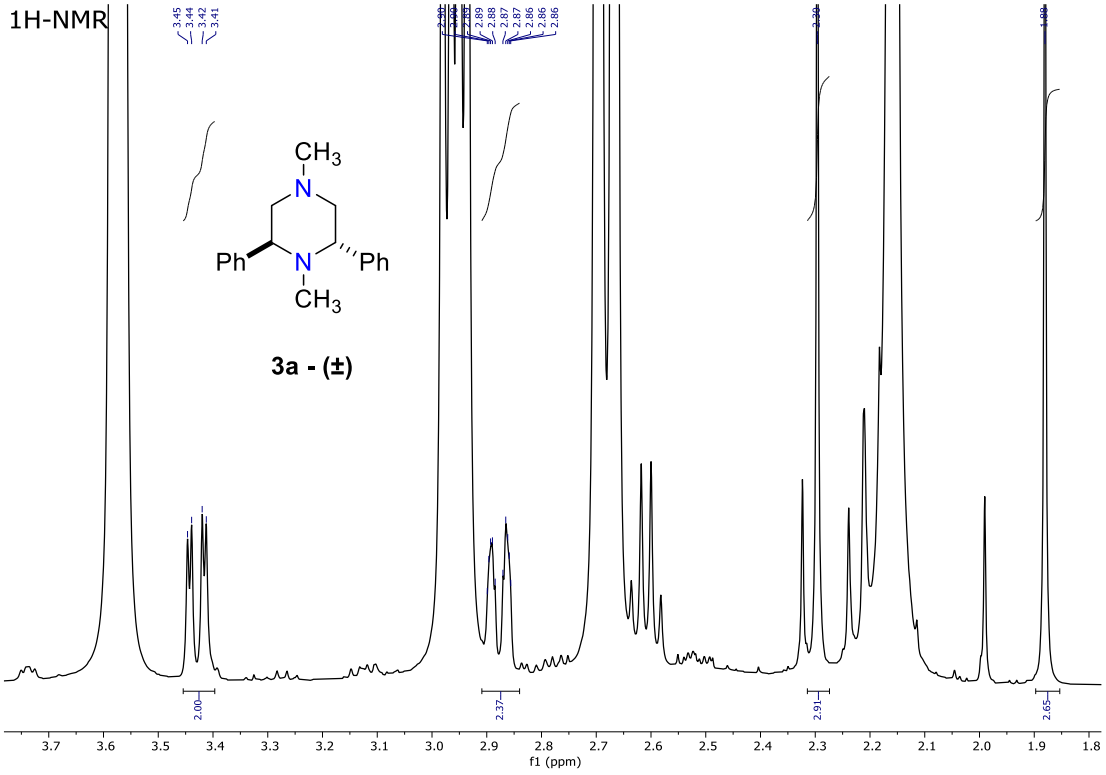


Figure S31: ^{1}H NMR of compound (±)-**3a**, isolated together with (±)-**2a**, in $CDCl_3$

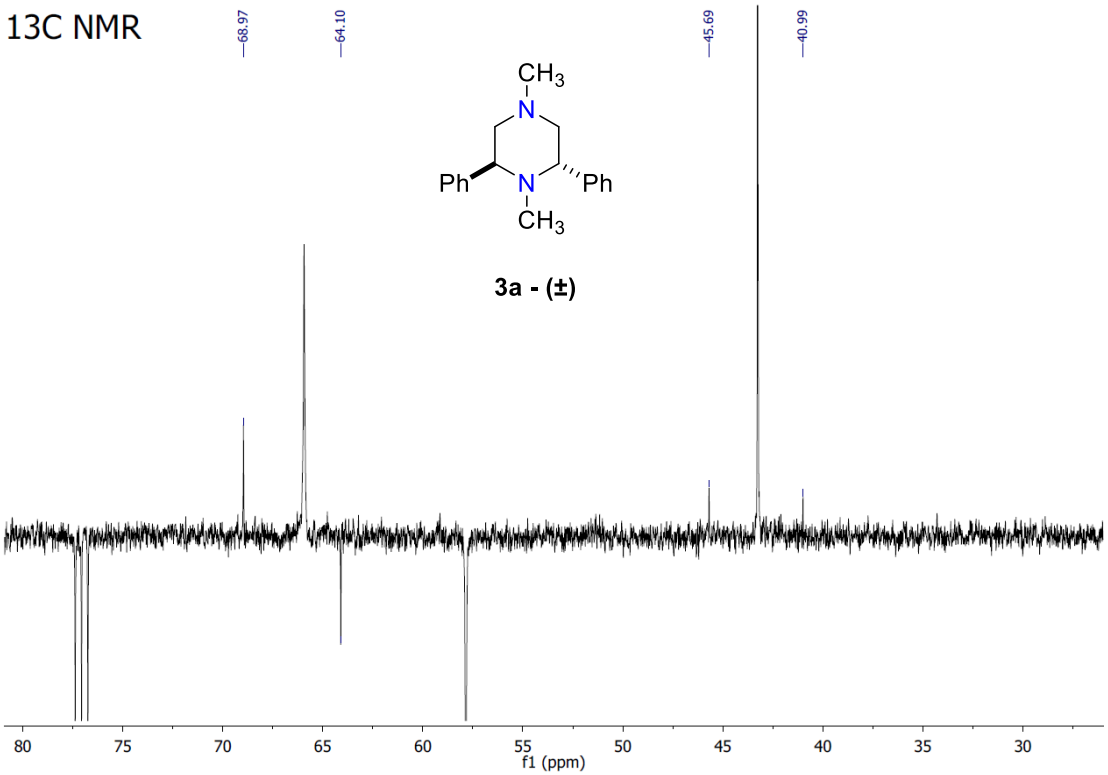


Figure S32: ^{13}C NMR of compound (±)-**3a**, isolated together with (±)-**2a**, in $CDCl_3$

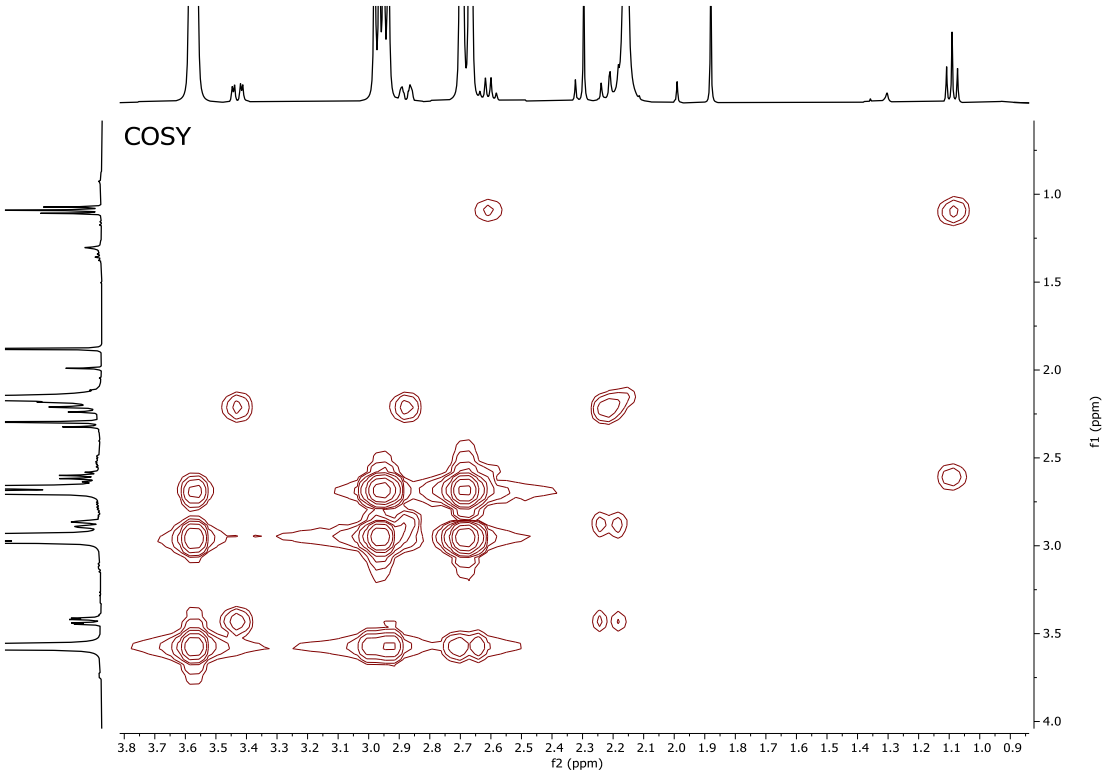


Figure S33: 2D ^{1}H COSY NMR of compound (±)-**3a**, isolated together with (±)-**2a**, in $CDCl_3$

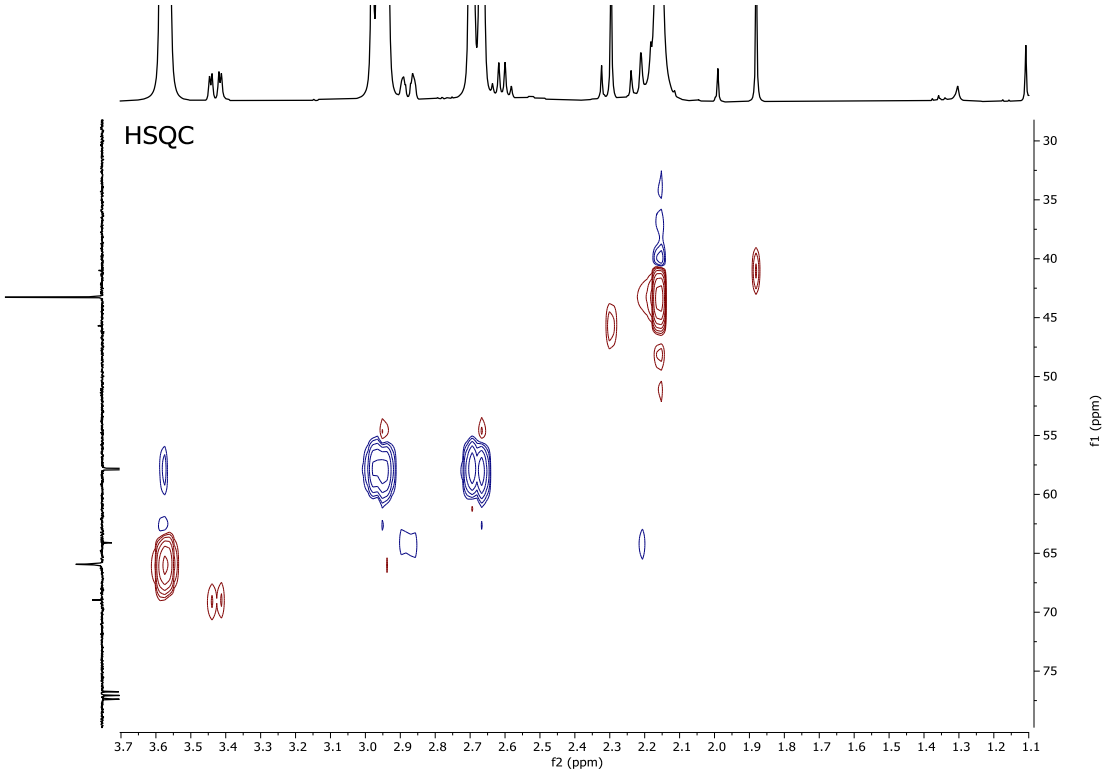


Figure S34: 2D ^{1}H-^{13}C HSQC NMR of compound (±)-**3a**, isolated together with (±)-**2a**, in $CDCl_3$

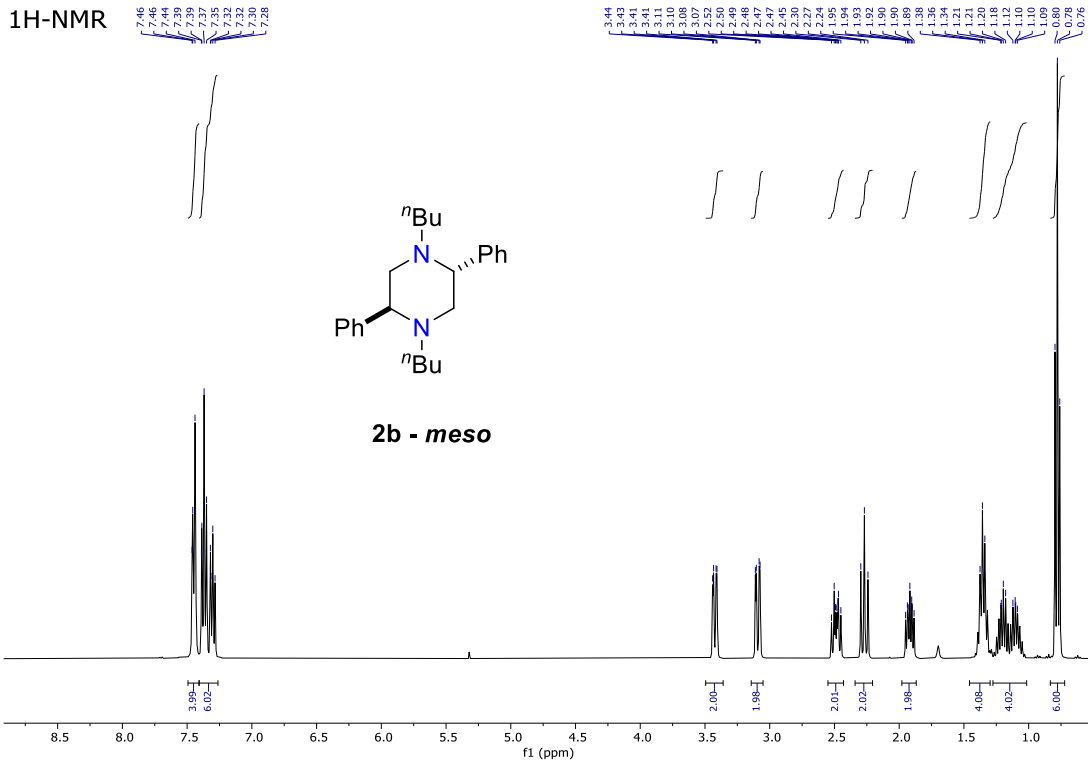


Figure S35: ^{1}H NMR of isolated compound *meso*-**2b** in $CDCl_3$

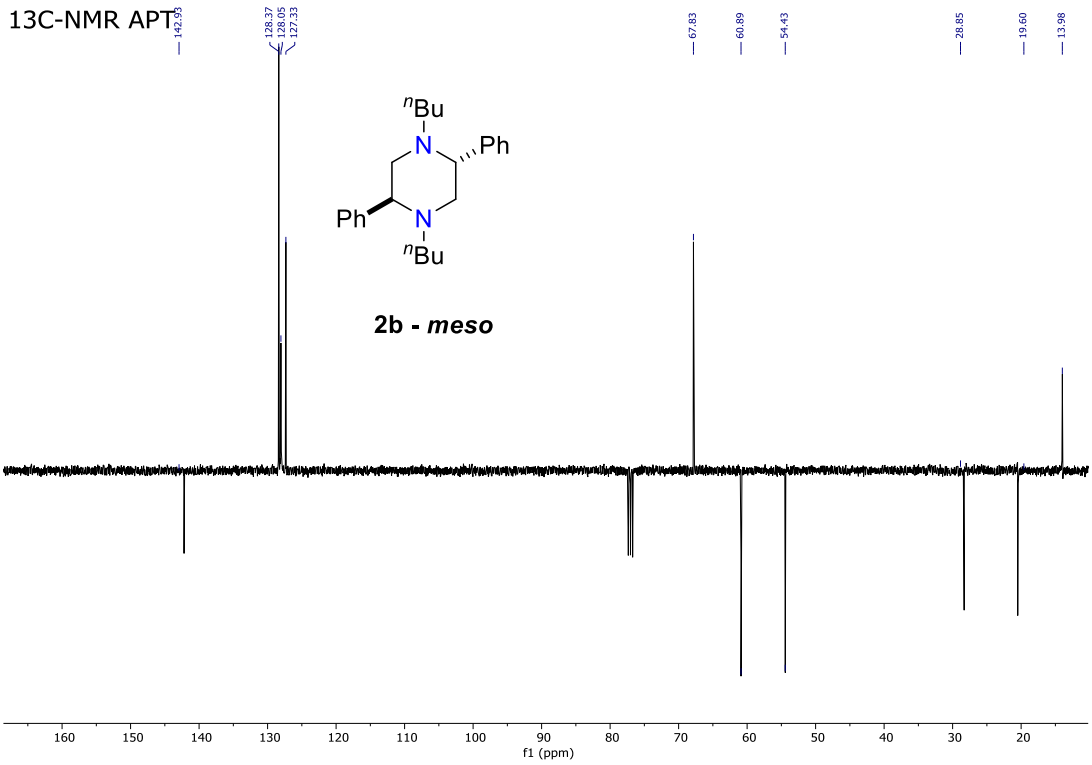


Figure S36: ^{13}C NMR of isolated compound *meso*-**2b** in $CDCl_3$

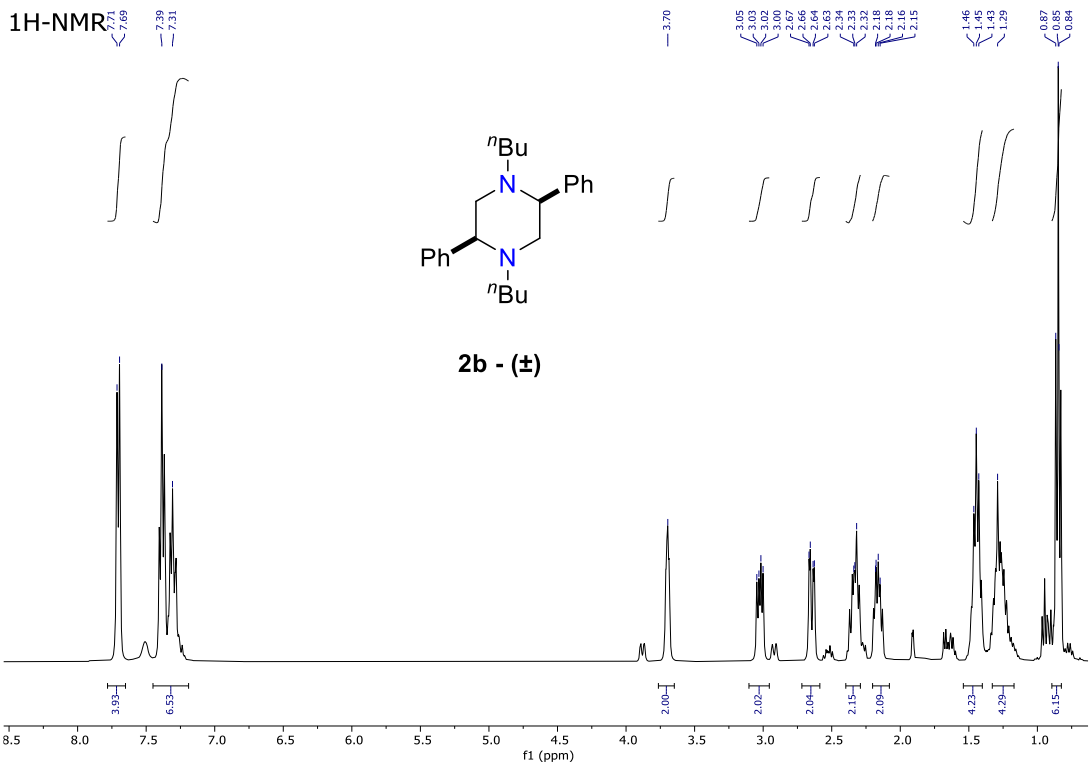


Figure S37: ^{1}H NMR of isolated compound (±)-**2b** in $CDCl_3$

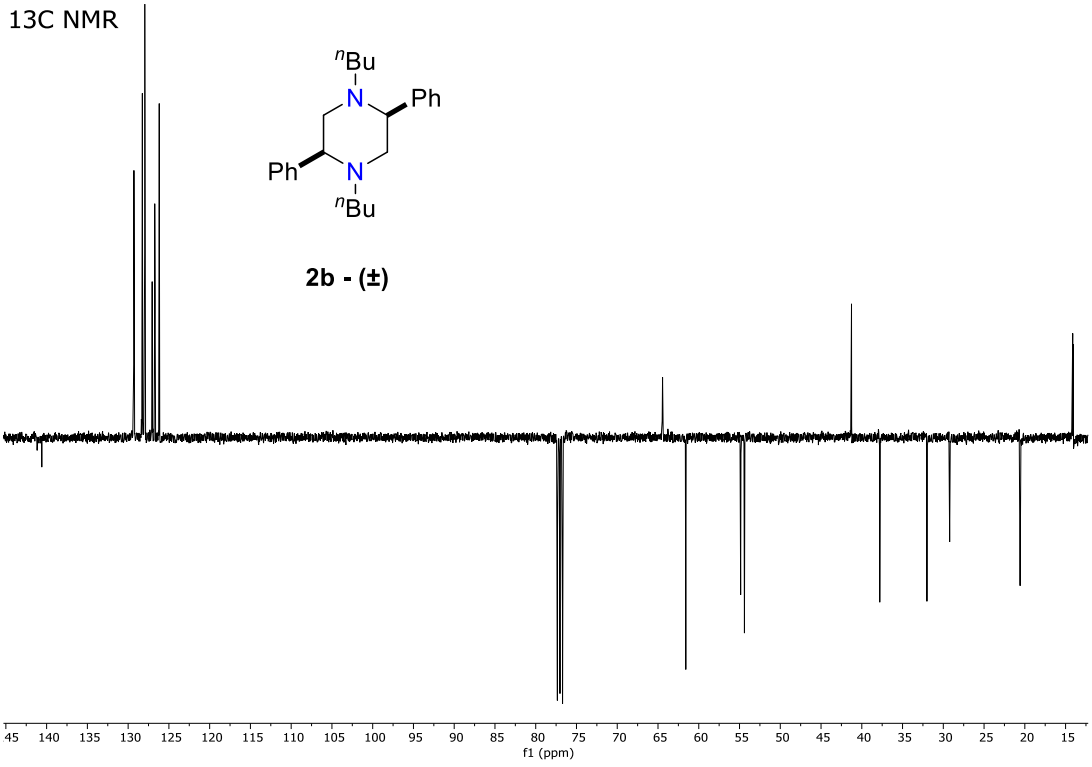


Figure S38: ^{13}C NMR of isolated compound (±)-**2b** in $CDCl_3$

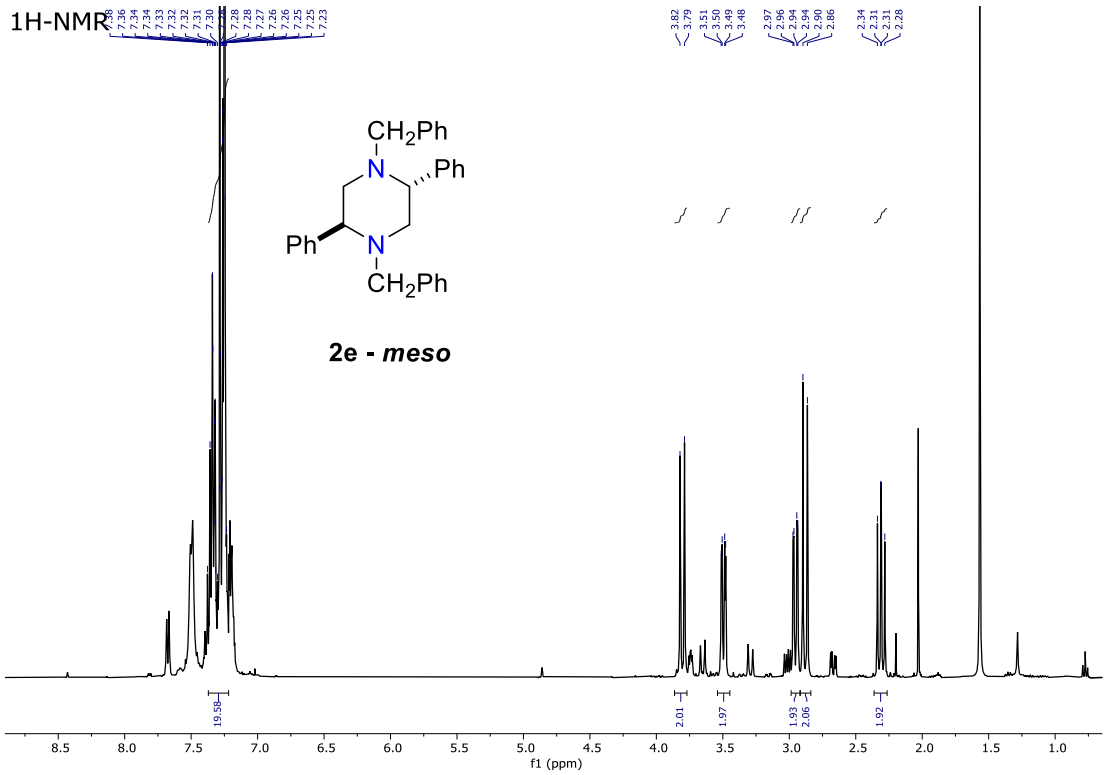


Figure S39: ^{1}H NMR of isolated compound *meso*-**2e** in $CDCl_3$

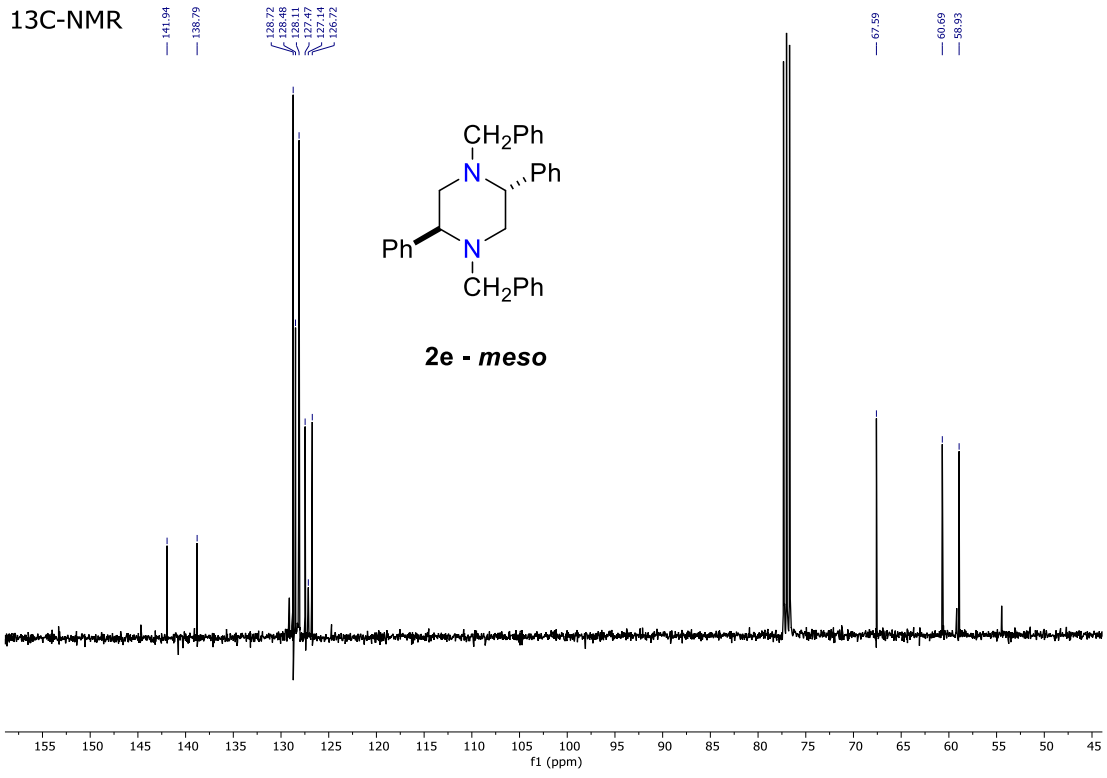


Figure S40: ^{13}C NMR of isolated compound *meso*-**2e** in $CDCl_3$

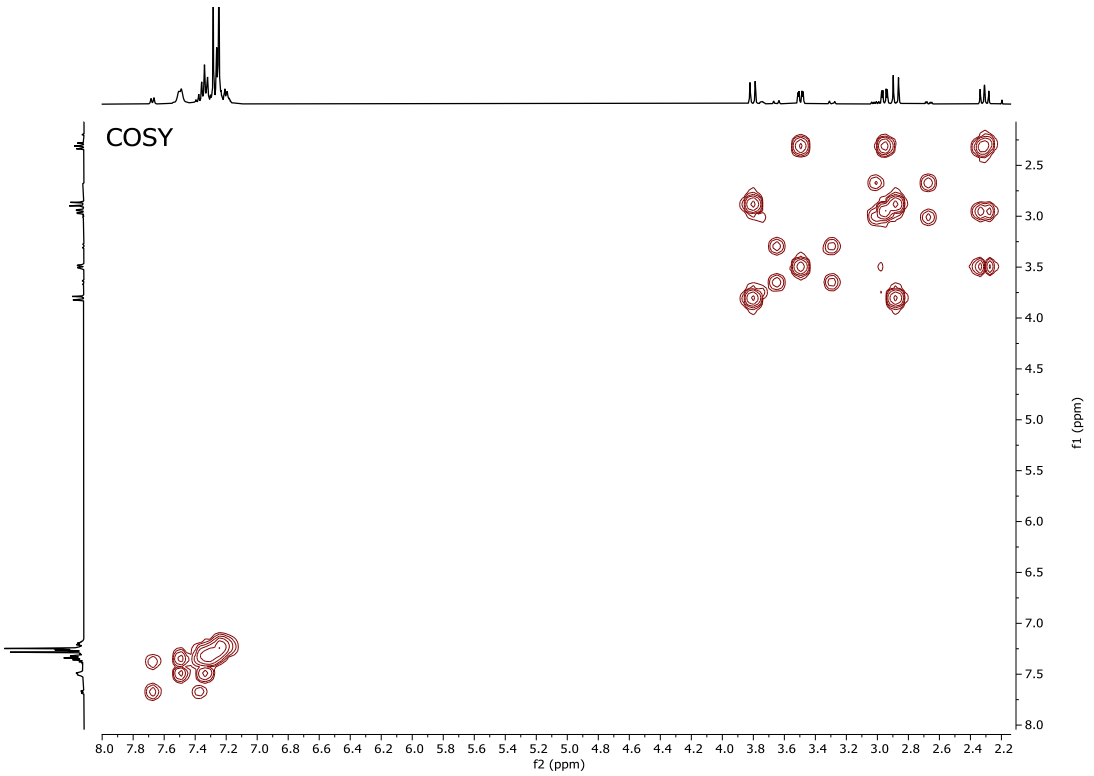


Figure S41: 2D ^{1}H COSY NMR of isolated compound *meso*-**2e** in $CDCl_3$

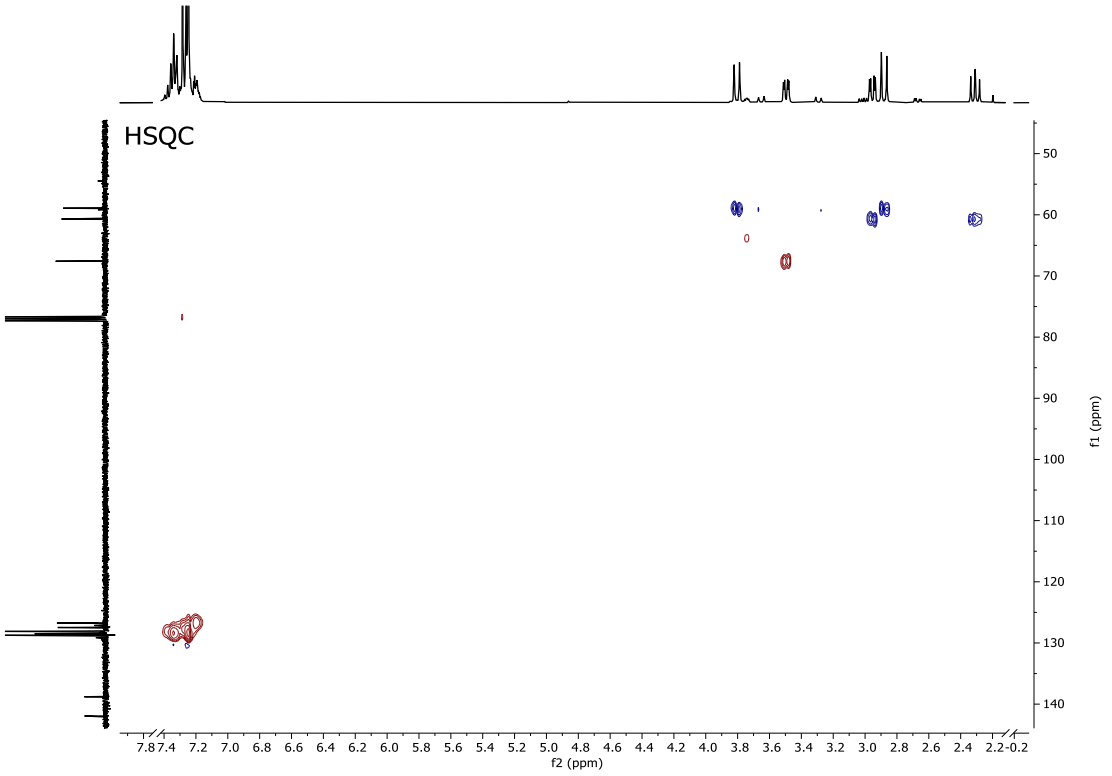


Figure S42: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2e** in $CDCl_3$

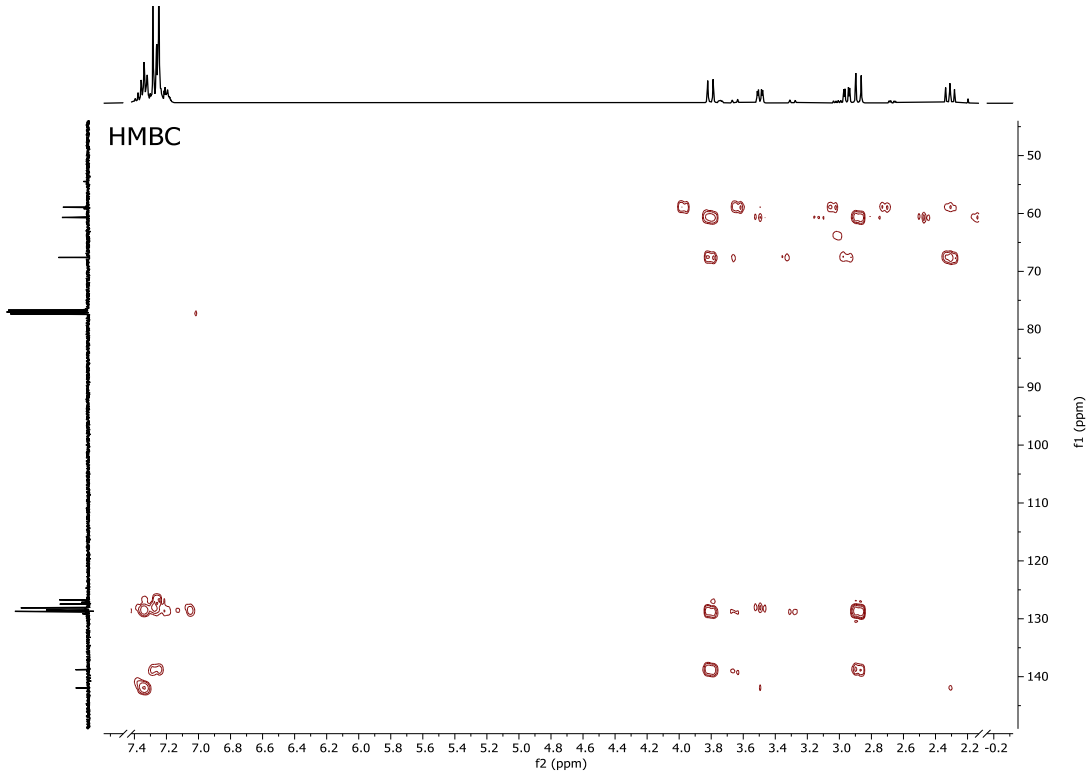


Figure S43: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2e** in $CDCl_3$

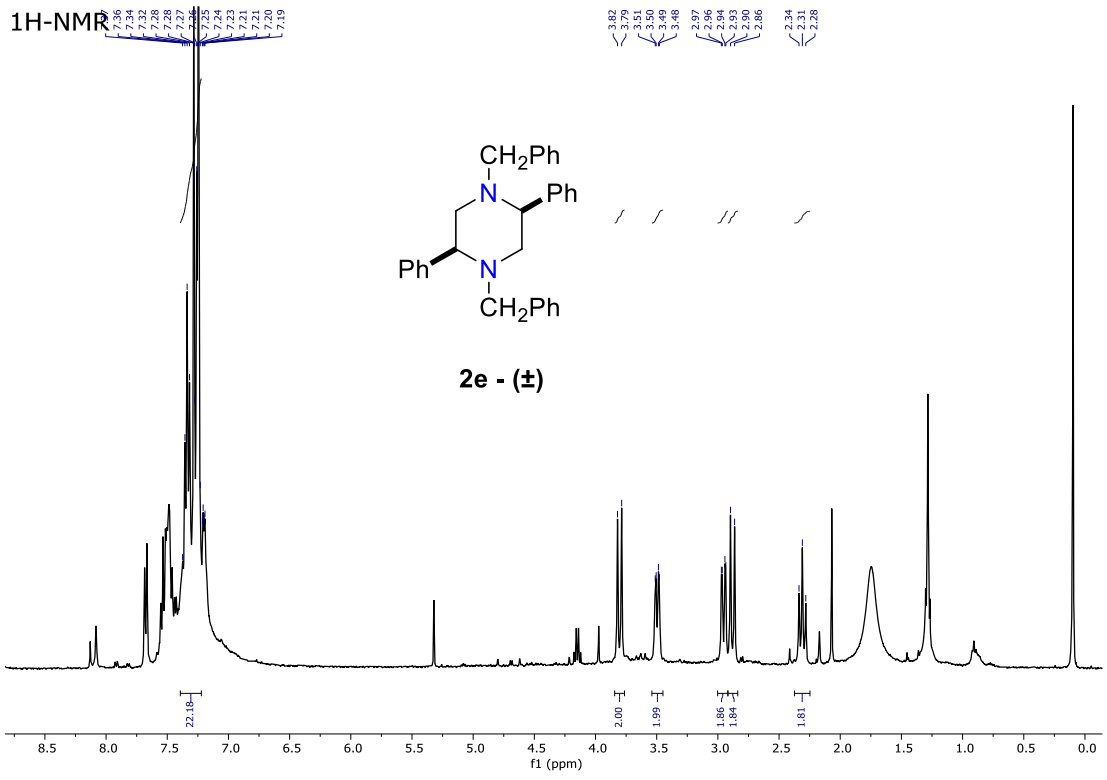


Figure S44: ^{1}H NMR of isolated compound (±)-**2e** in $CDCl_3$

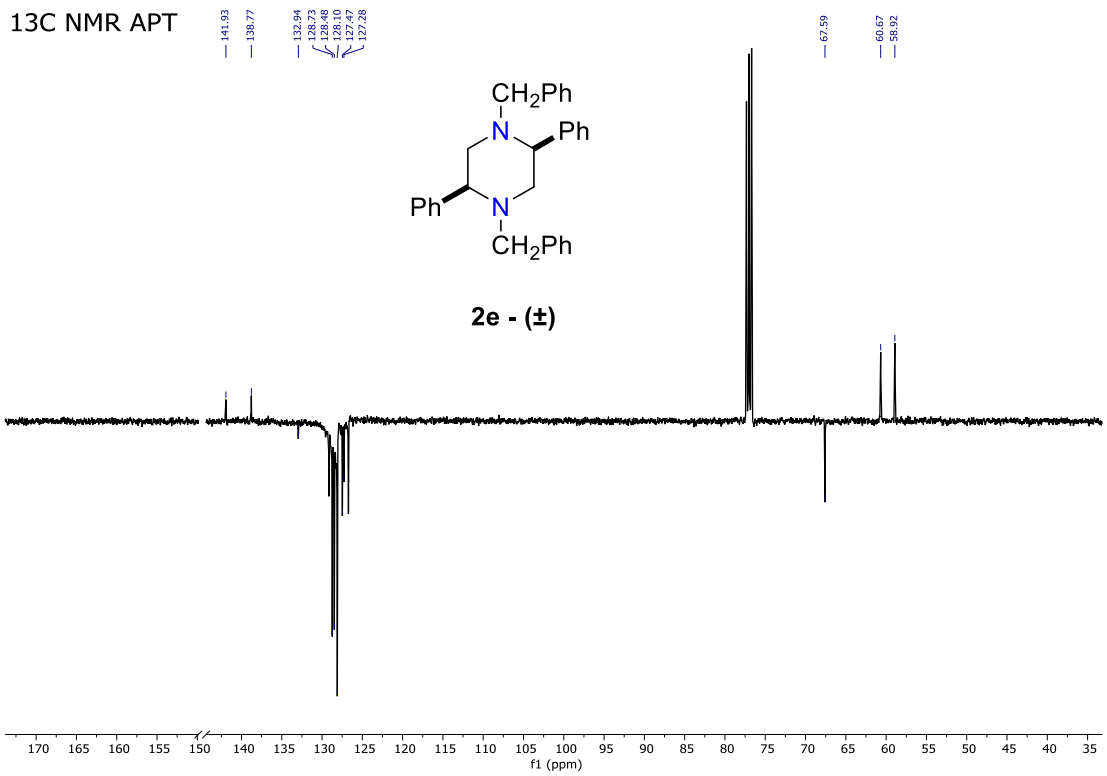


Figure S45: ^{13}C NMR of isolated compound (±)-**2e** in $CDCl_3$

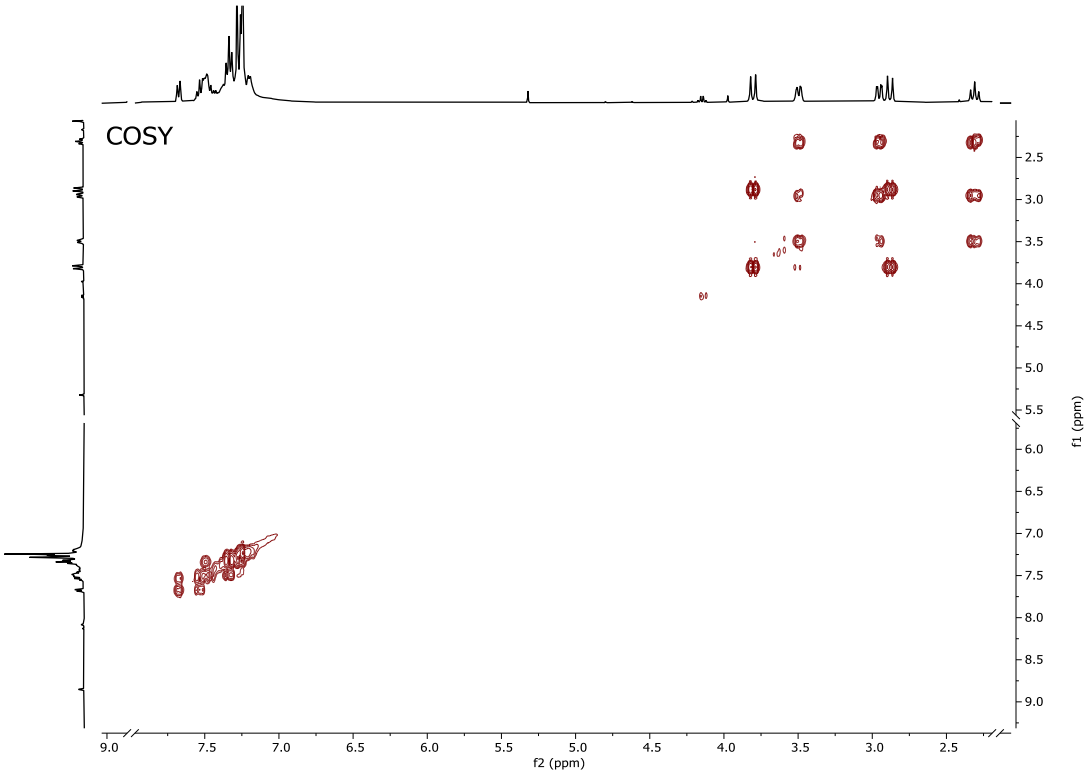


Figure S46: 2D ^{1}H COSY NMR of isolated compound (±)-**2e** in $CDCl_3$

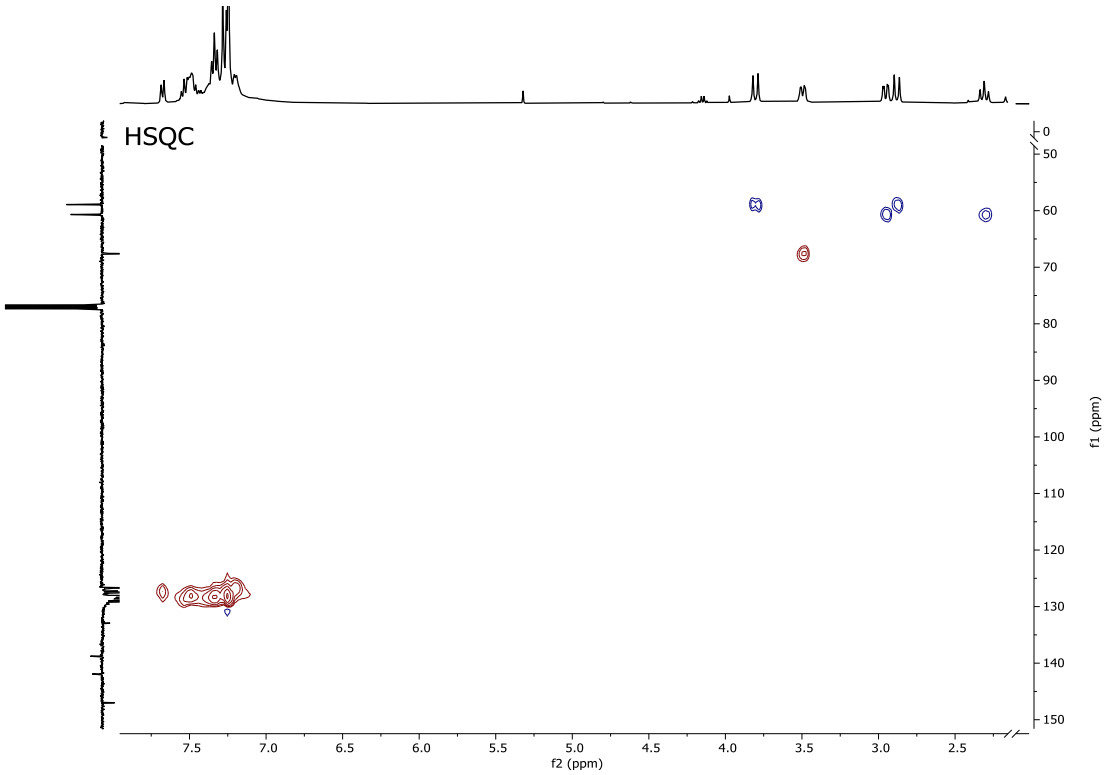


Figure S47: 2D ^{1}H-^{13}C HSQC NMR of isolated compound (±)-**2e** in $CDCl_3$

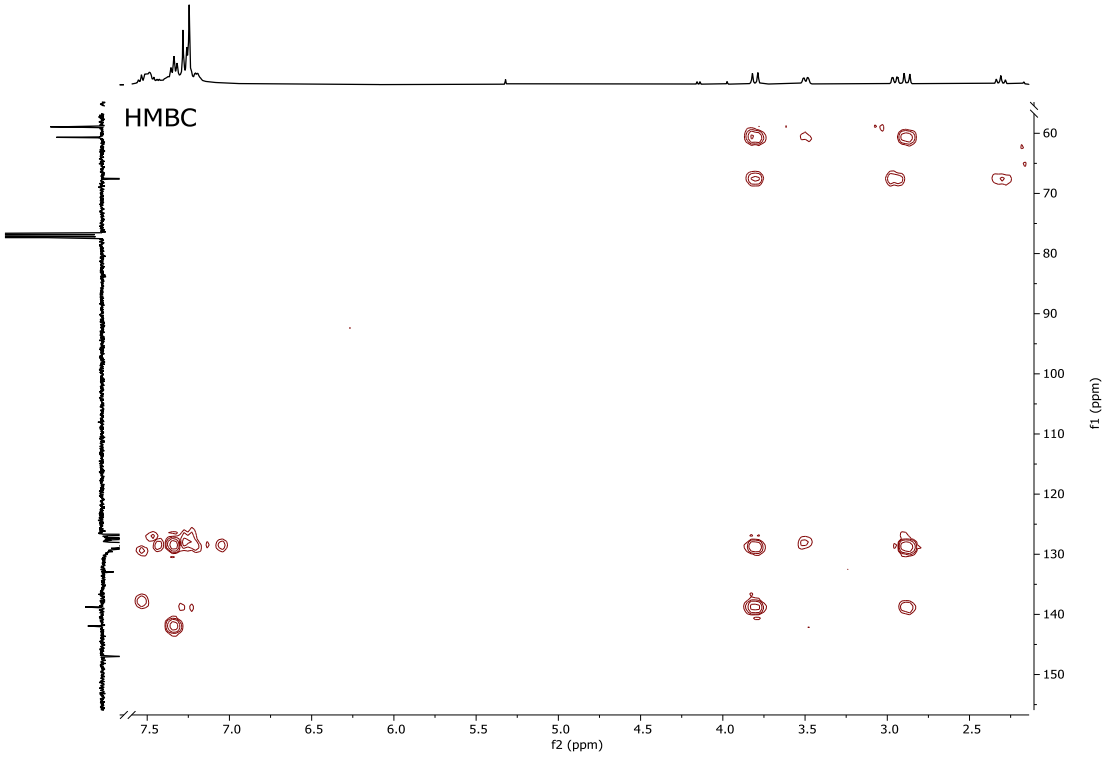


Figure S48: 2D ^{1}H-^{13}C HMBC NMR of isolated compound (±)-**2e** in $CDCl_3$

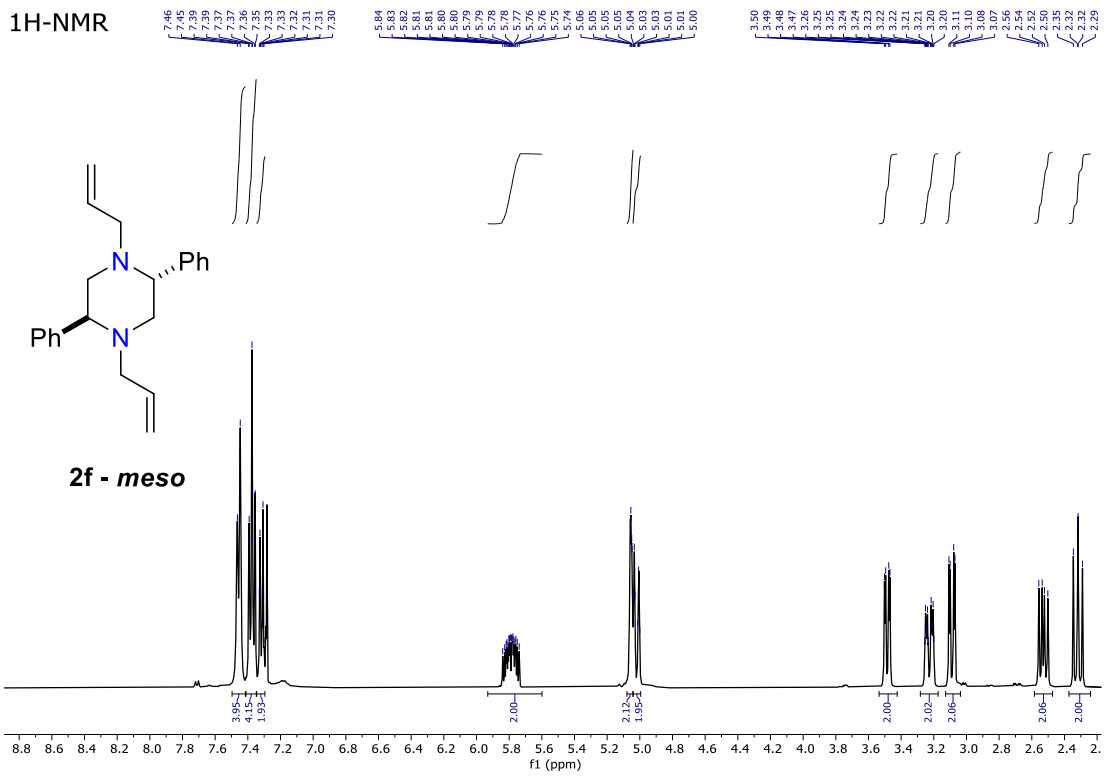


Figure S49: ^{1}H NMR of isolated compound *meso*-**2f** in $CDCl_3$

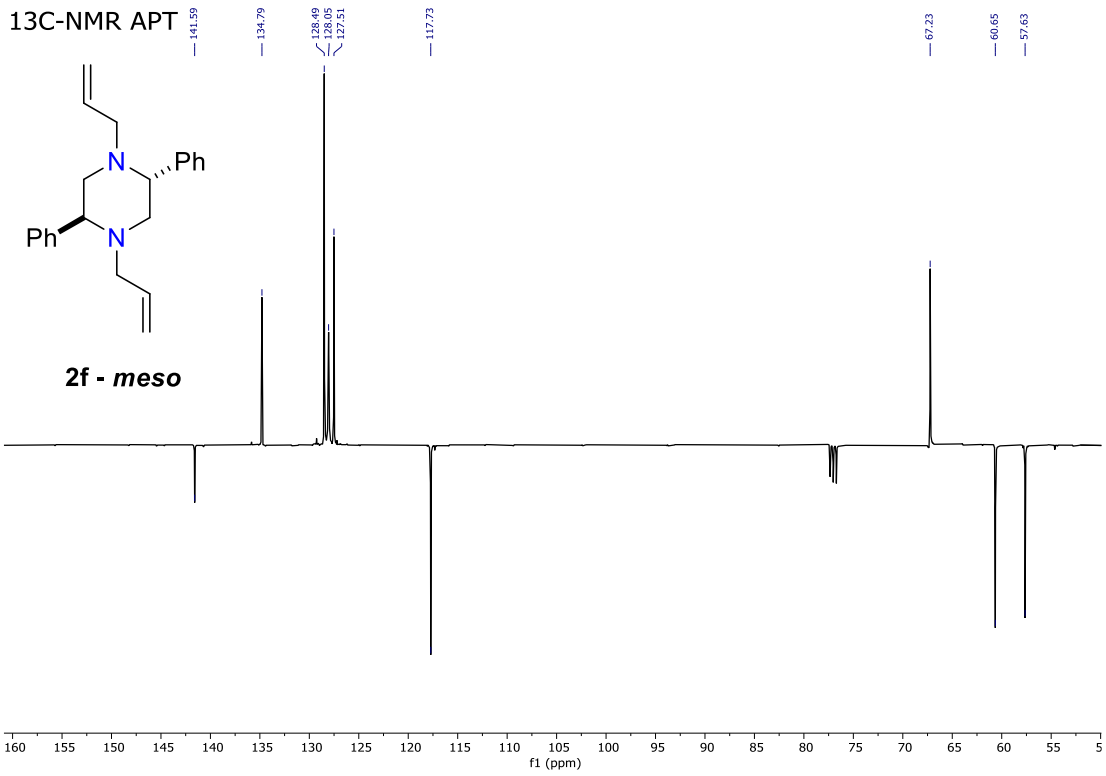


Figure S50: ^{13}C NMR of isolated compound *meso*-**2f** in $CDCl_3$

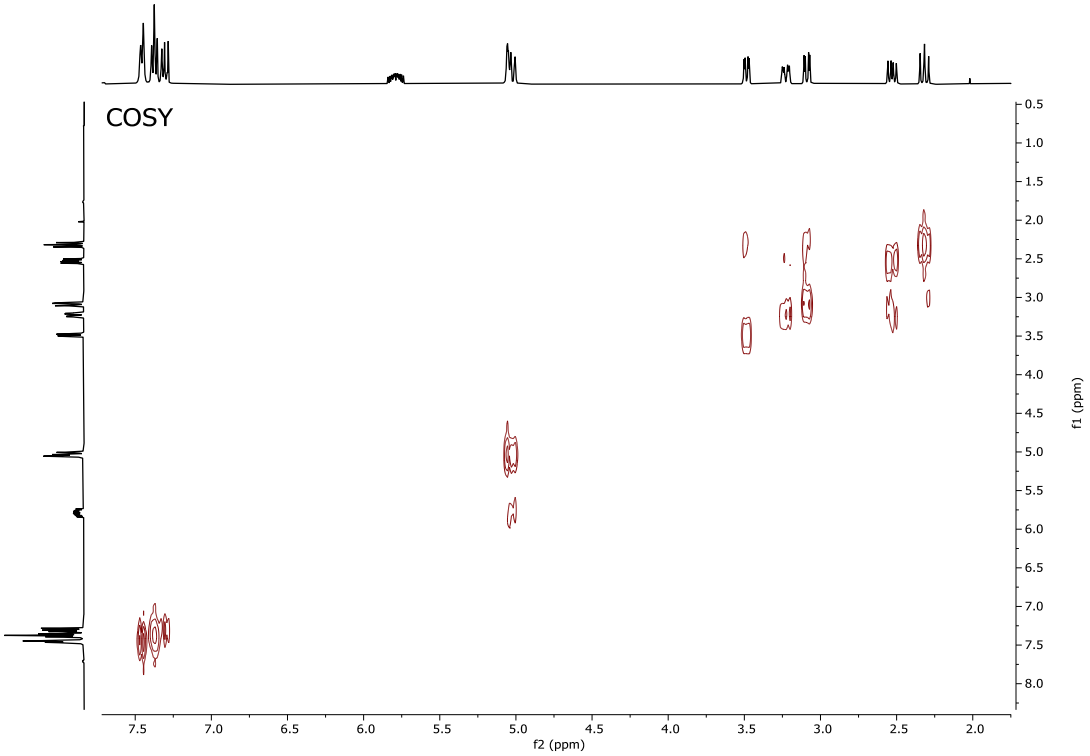


Figure S51: 2D ^{1}H COSY NMR of isolated compound *meso*-**2f** in $CDCl_3$

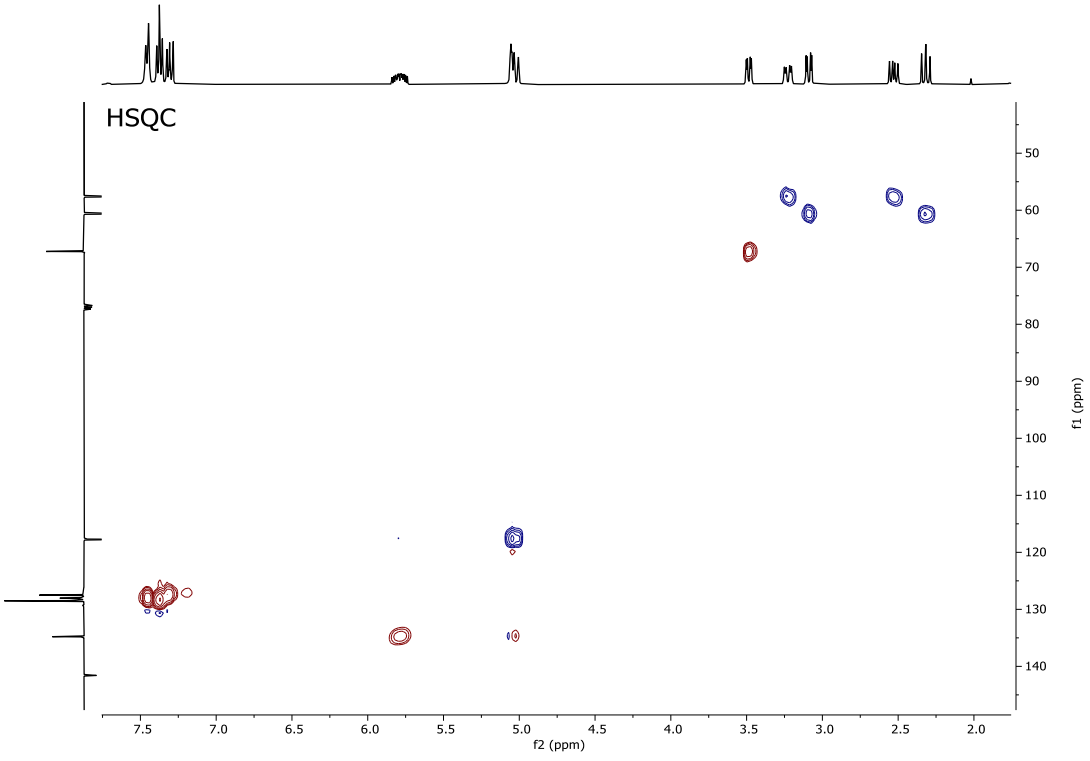


Figure S52: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2f** in $CDCl_3$

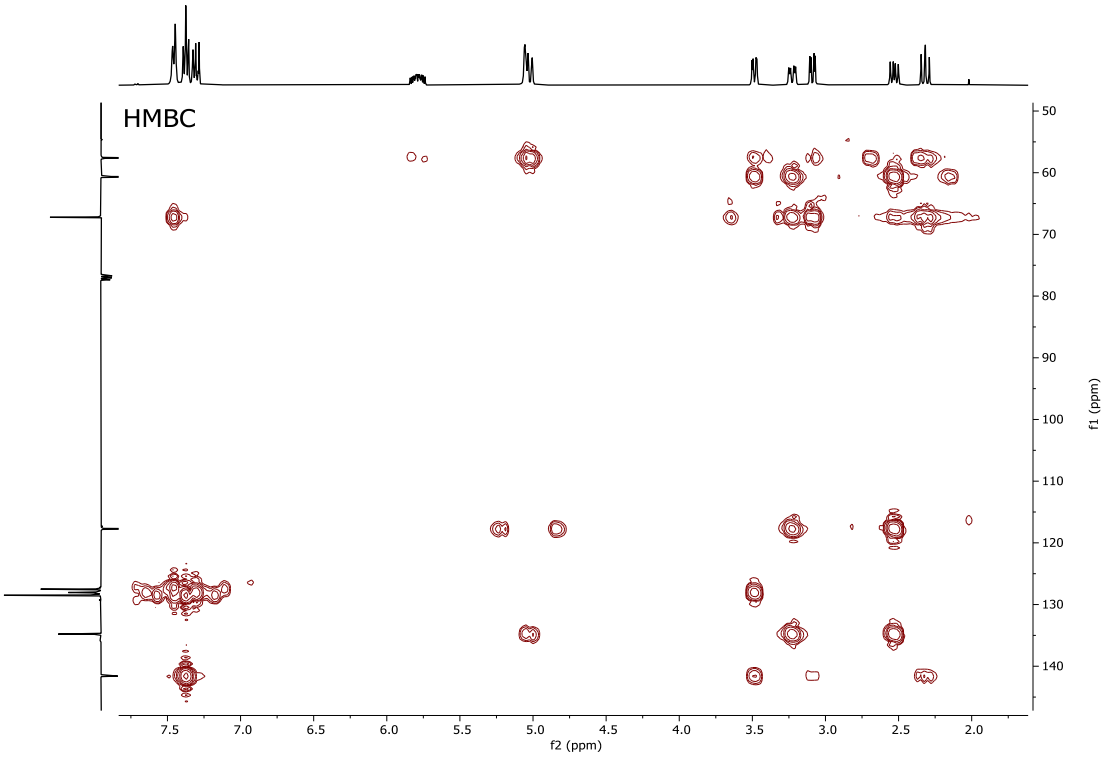


Figure S53: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2f** in $CDCl_3$

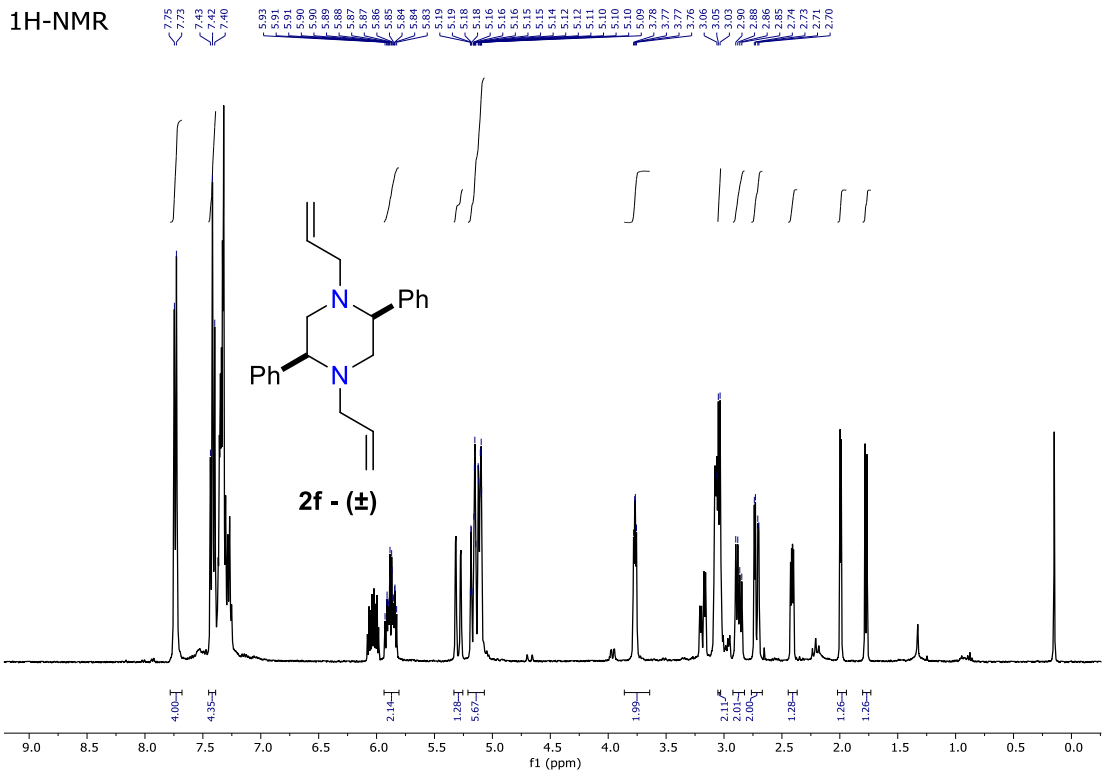


Figure S54: ^{1}H NMR of isolated compound (±)-**2f** in $CDCl_3$

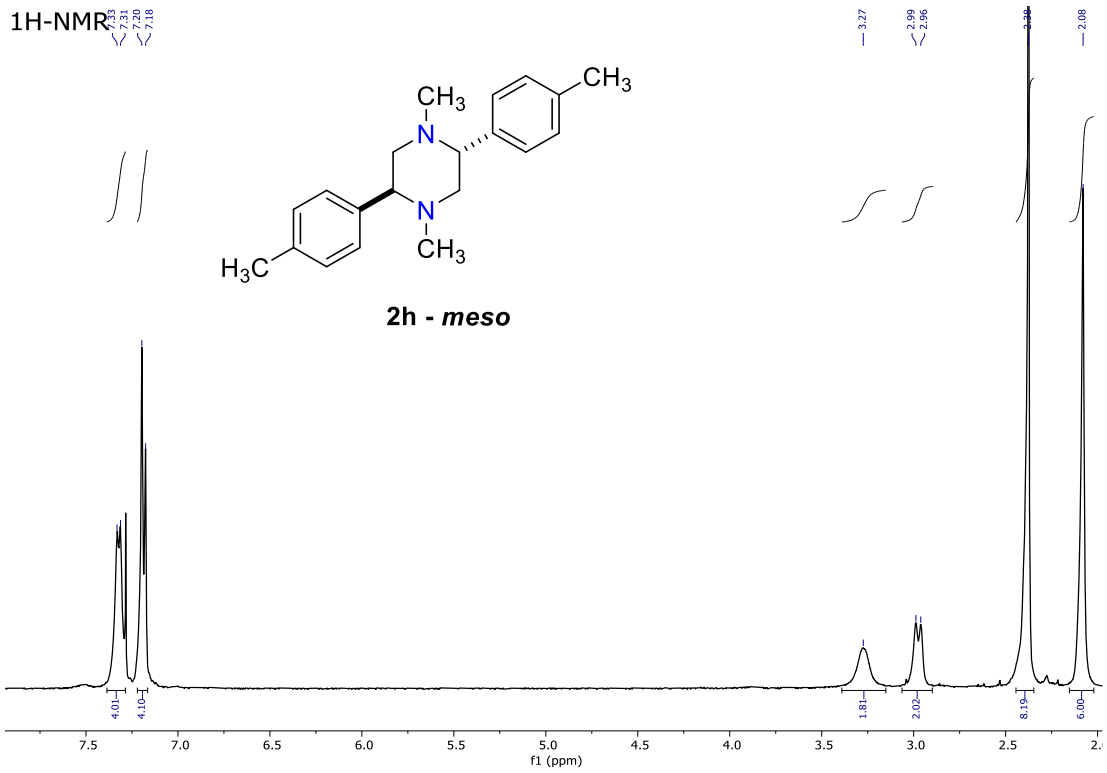


Figure S55: ^{1}H NMR of isolated compound *meso*-**2h** in $CDCl_3$

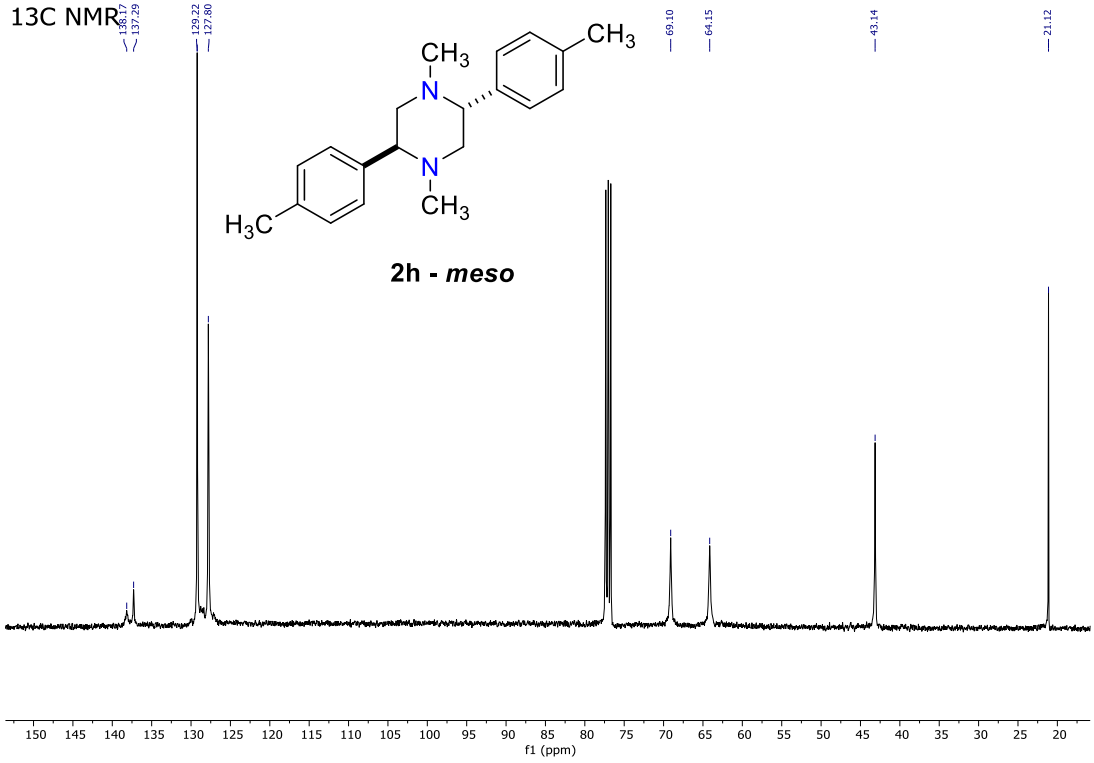


Figure S56: ^{13}C NMR of isolated compound *meso*-**2h** in $CDCl_3$

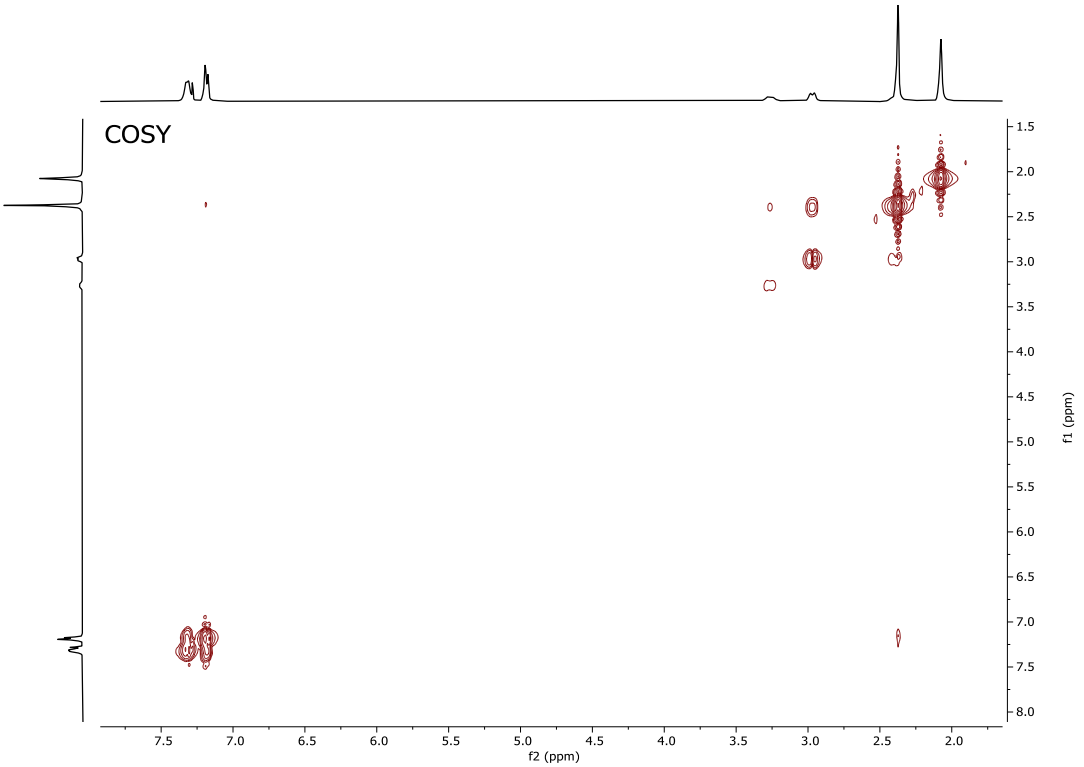


Figure S57: 2D ^{1}H COSY NMR of isolated compound *meso*-**2h** in $CDCl_3$

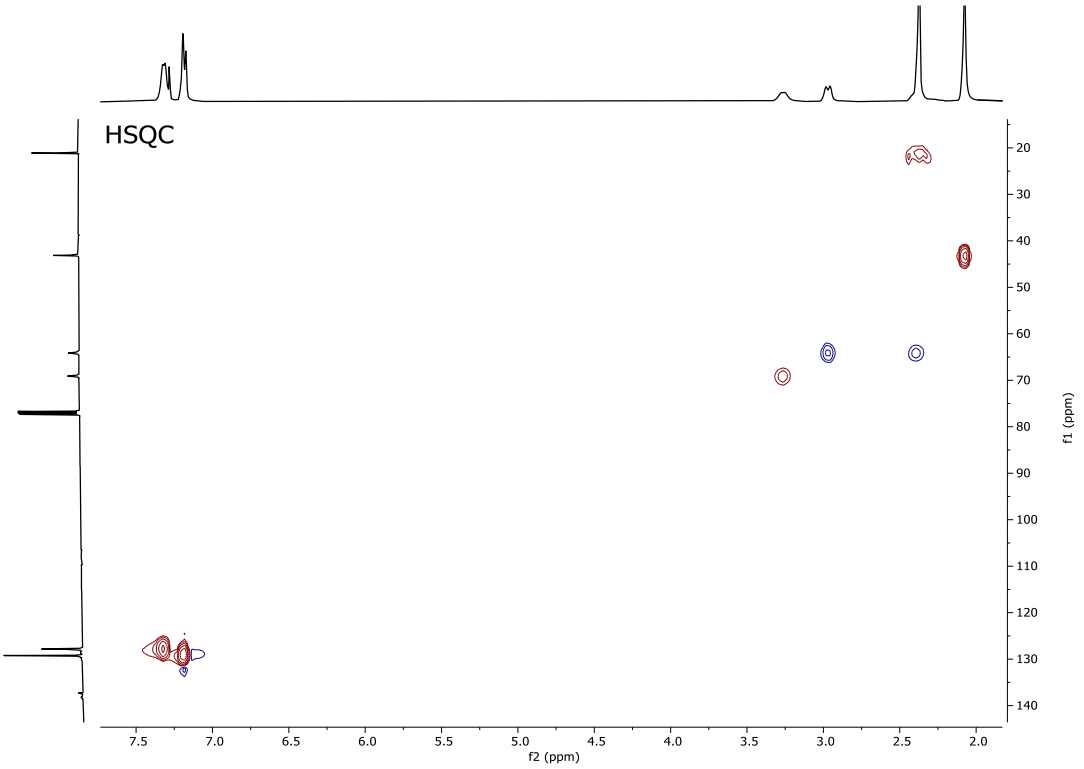


Figure S58: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2h** in $CDCl_3$

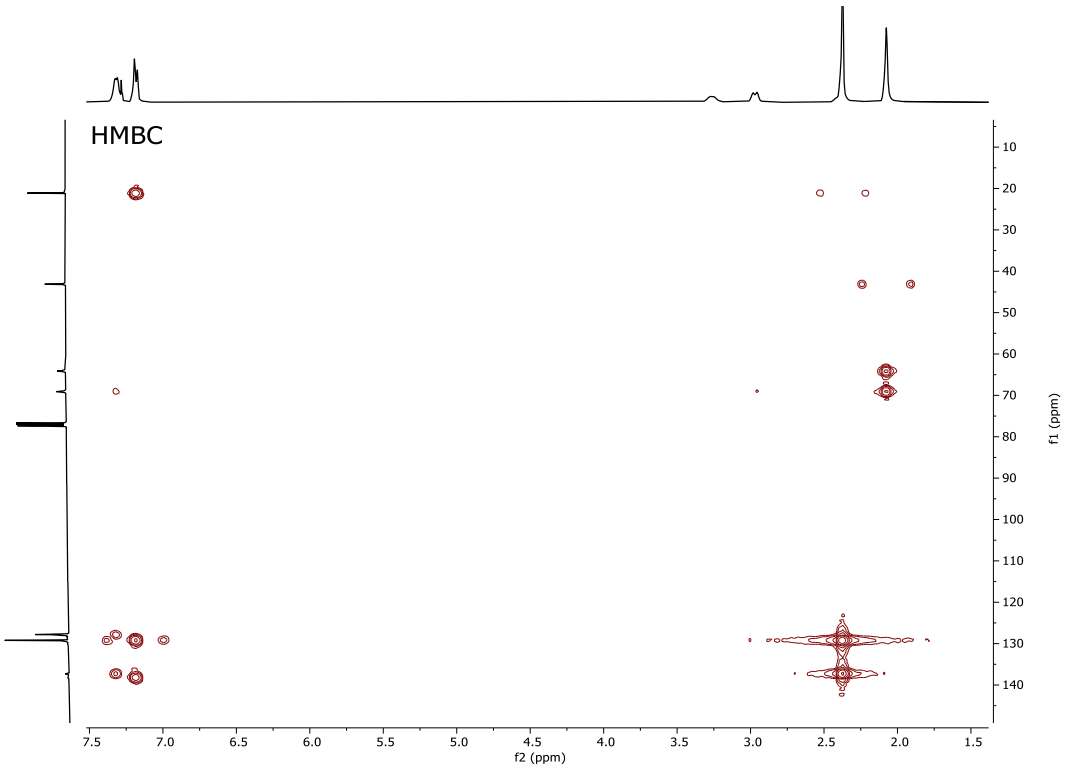


Figure S59: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2h** in $CDCl_3$

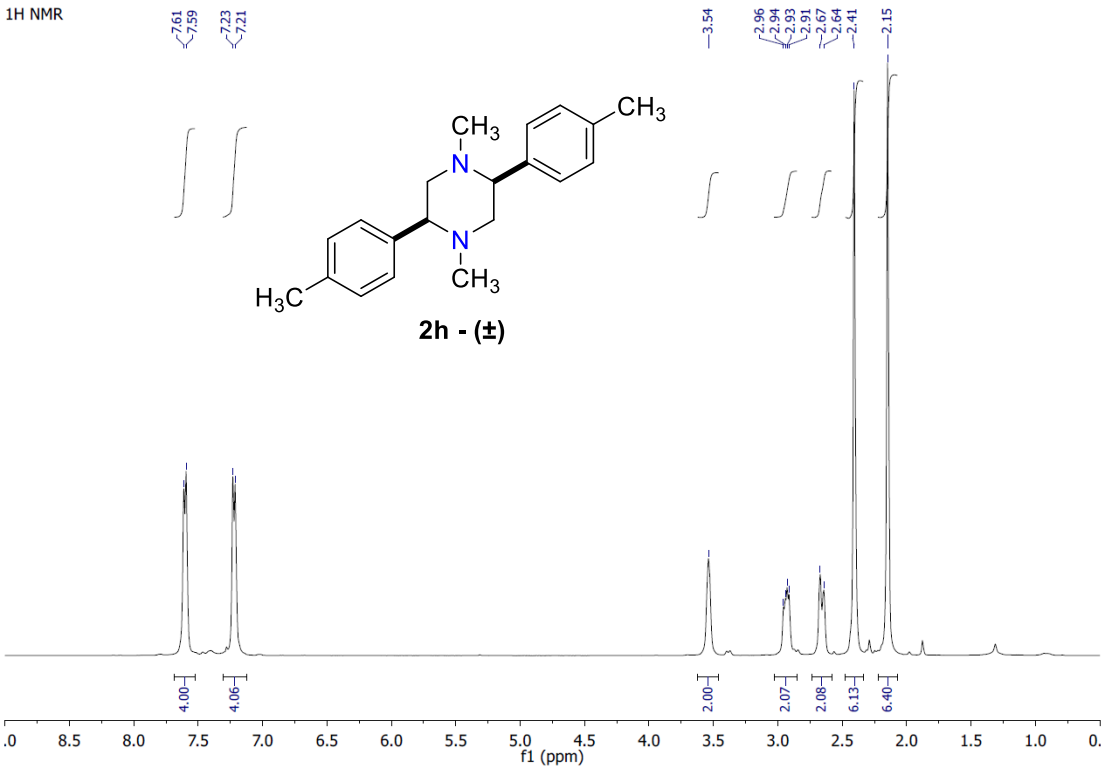


Figure S60: ^{1}H NMR of isolated compound (±)-**2h** in $CDCl_3$

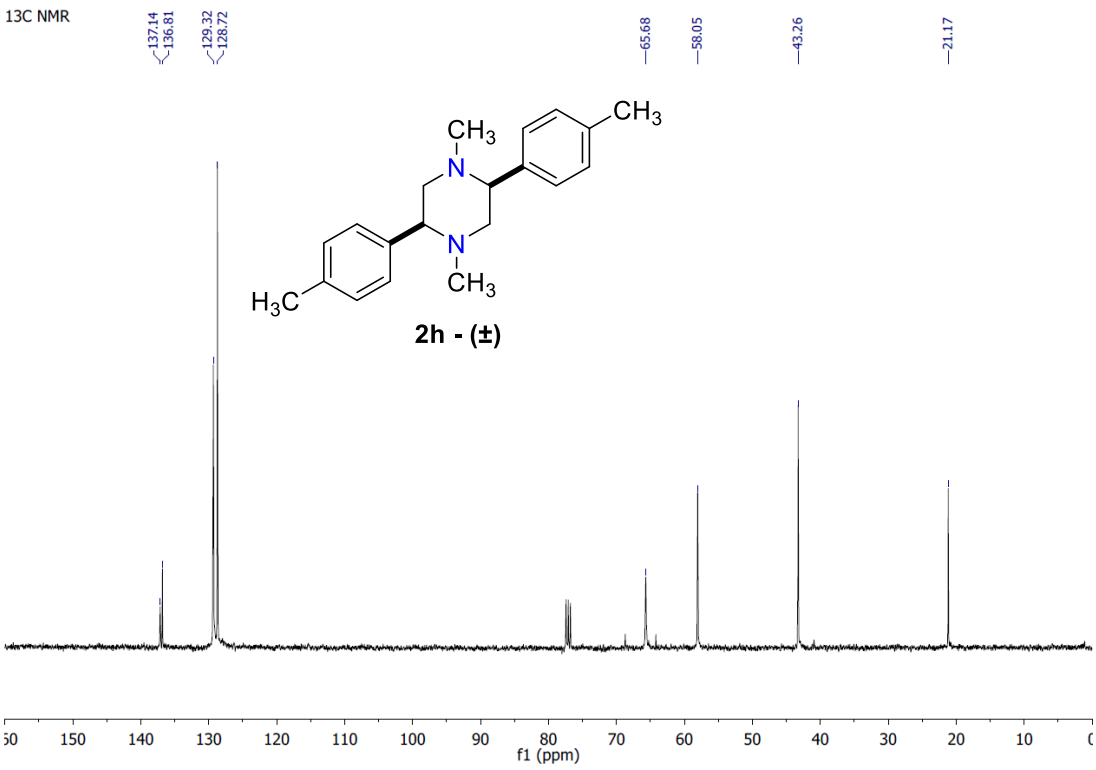


Figure S61: ^{13}C NMR of isolated compound (±)-**2h** in $CDCl_3$

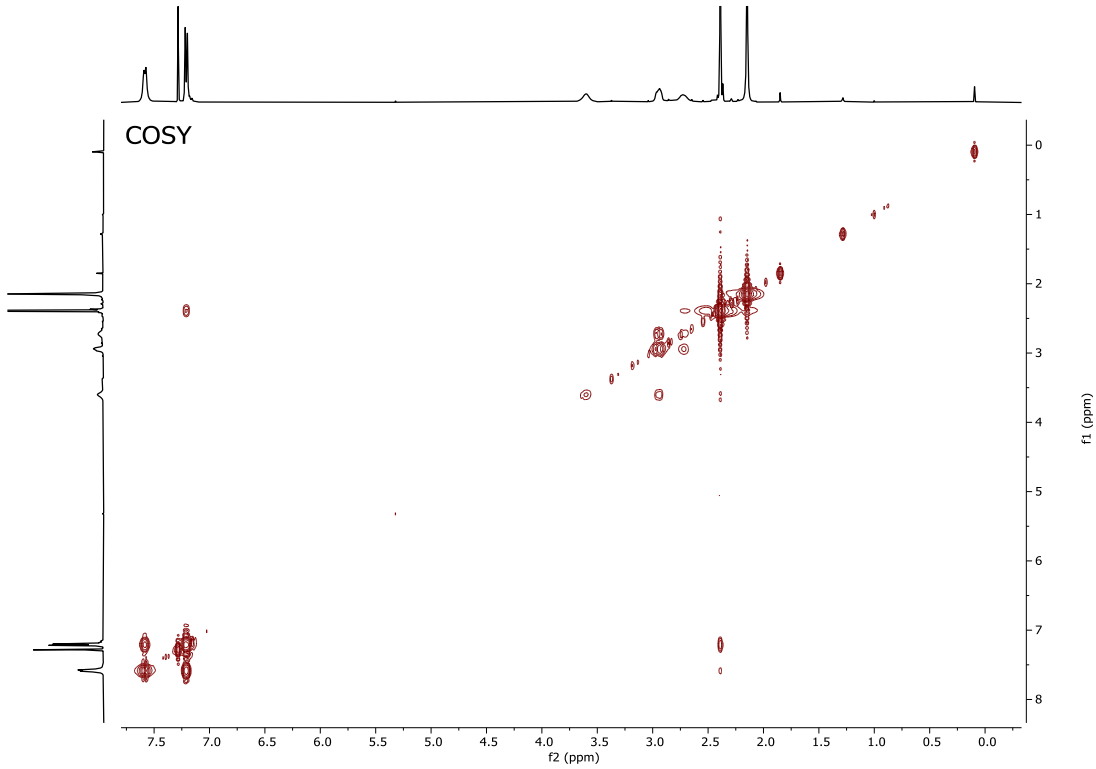


Figure S62: 2D ^{1}H COSY NMR of isolated compound (±)-**2h** in $CDCl_3$

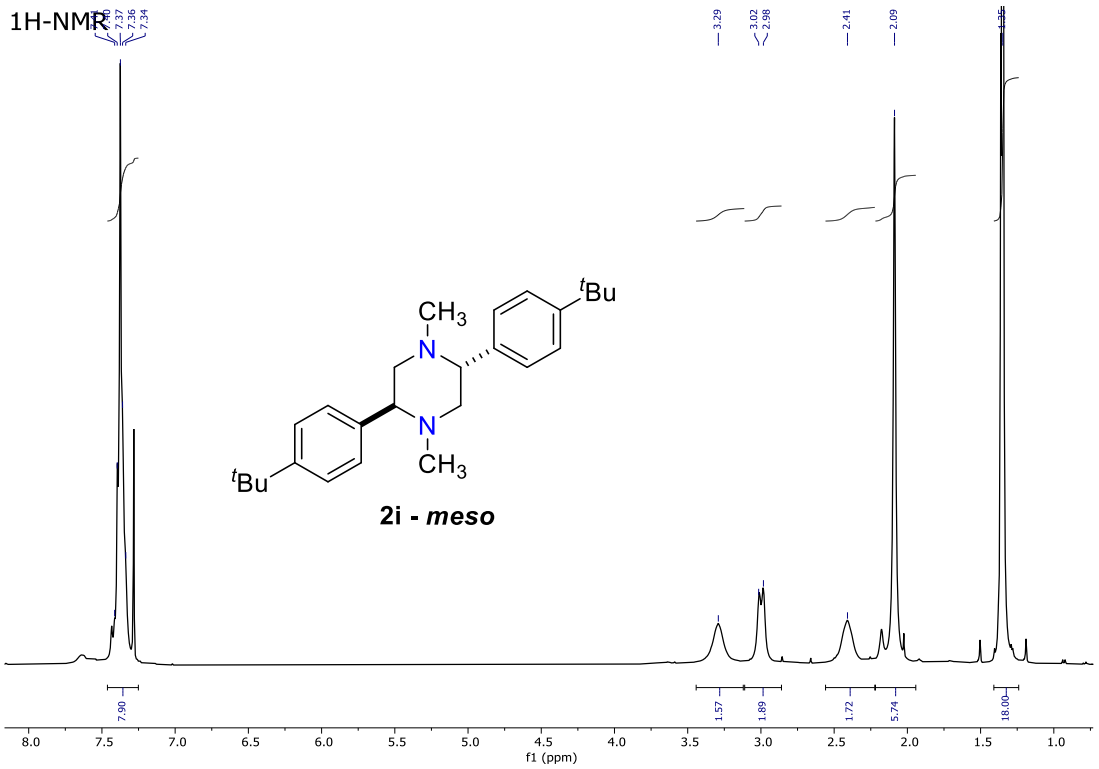


Figure S63: ^{1}H NMR of isolated compound *meso*-**2i** in $CDCl_3$

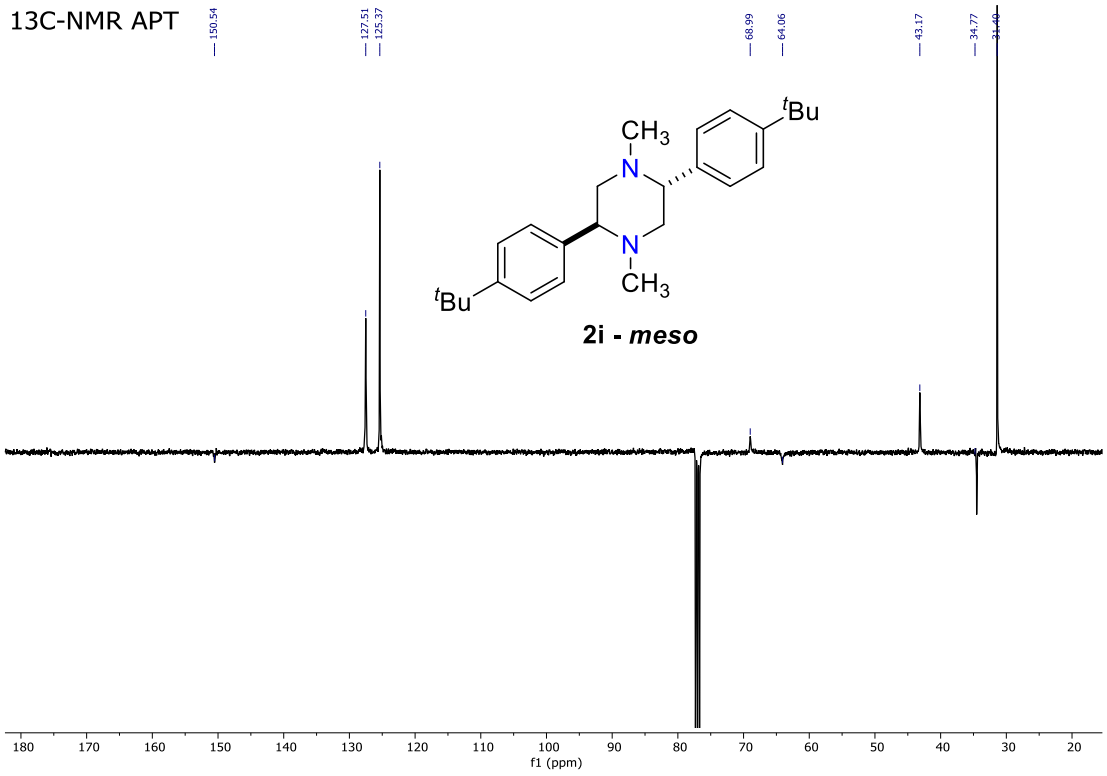


Figure S64: ^{13}C NMR of isolated compound *meso*-**2i** in $CDCl_3$

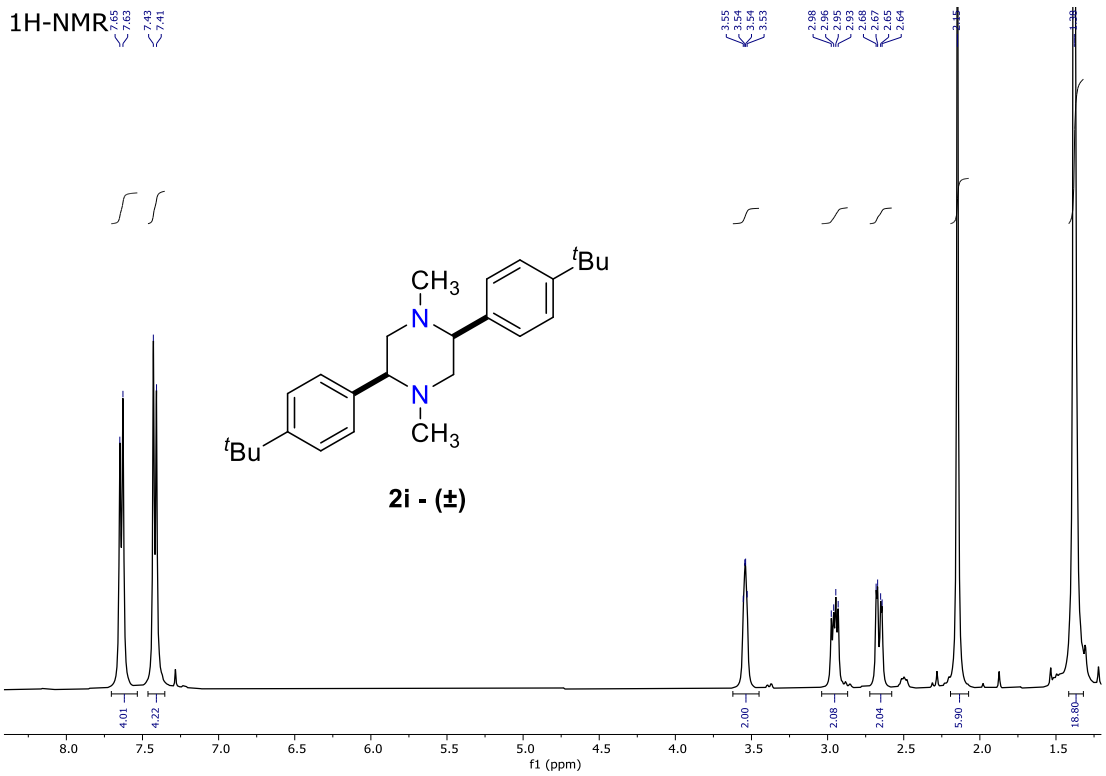


Figure S65: ^{1}H NMR of isolated compound (±)-**2i** in $CDCl_3$

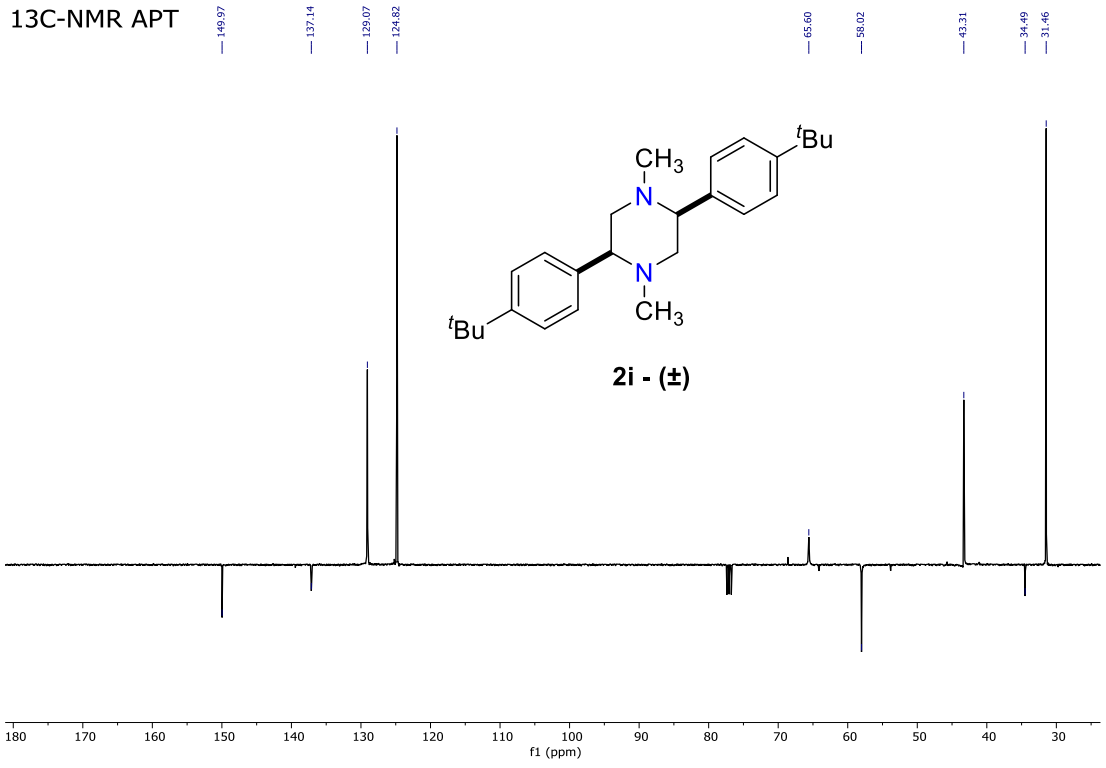


Figure S66: ^{13}C NMR of isolated compound (±)-**2i** in $CDCl_3$

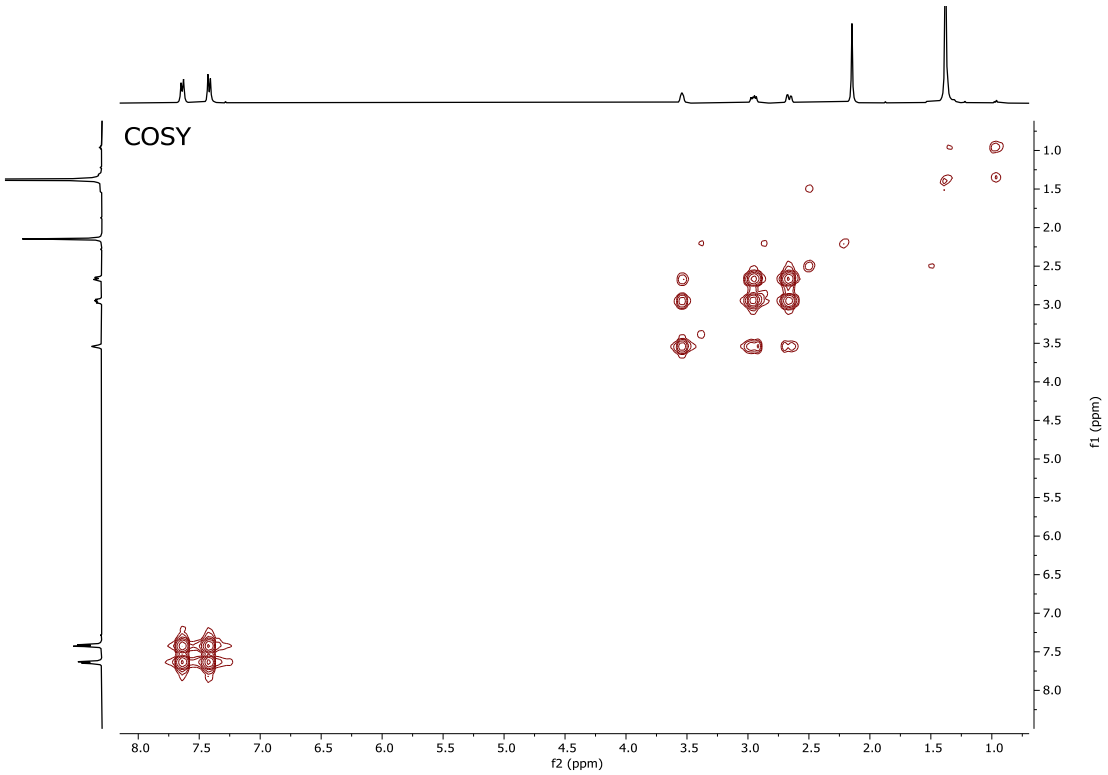


Figure S67: 2D ^{1}H COSY NMR of isolated compound (±)-**2i** in $CDCl_3$

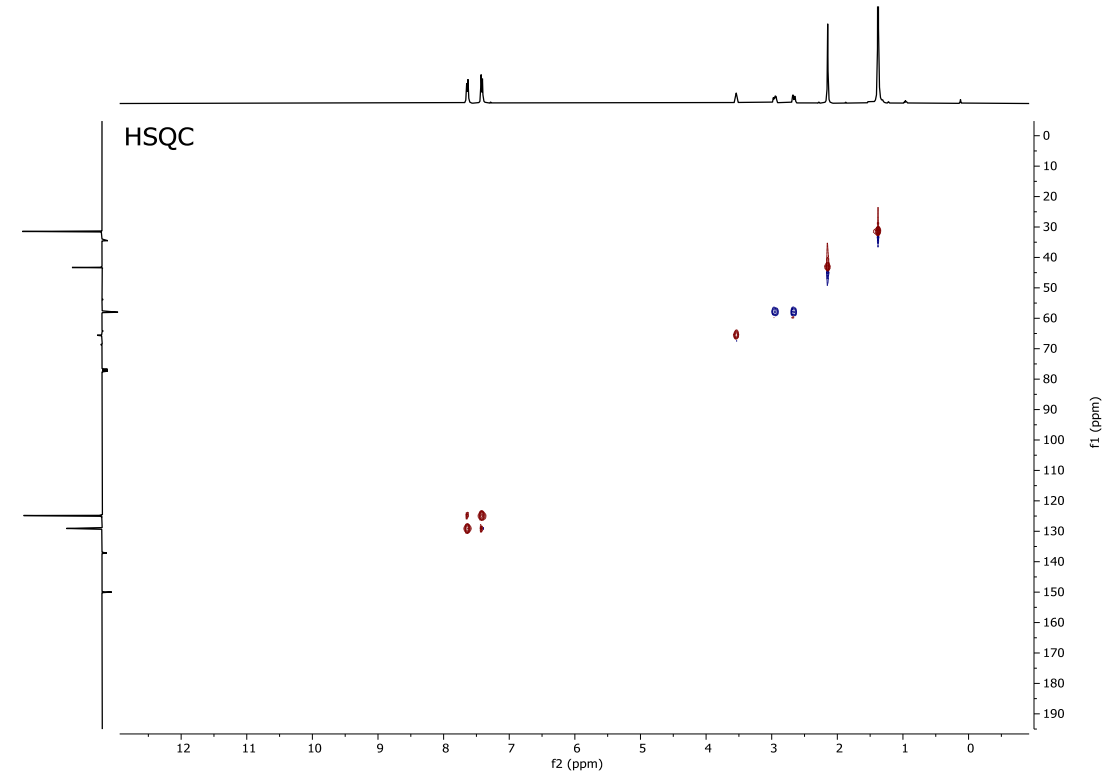


Figure S68: 2D ^{1}H-^{13}C HSQC NMR of isolated compound (±)-**2i** in $CDCl_3$

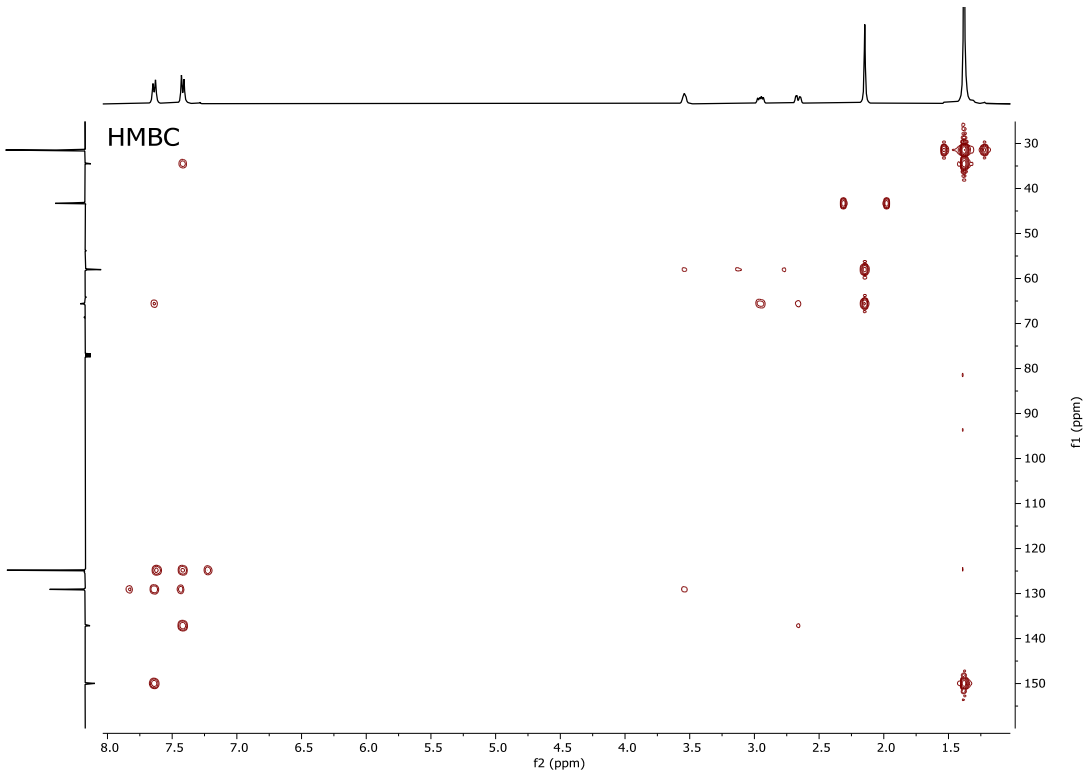


Figure S69: 2D ^{1}H-^{13}C HMBC NMR of isolated compound (±)-**2i** in $CDCl_3$

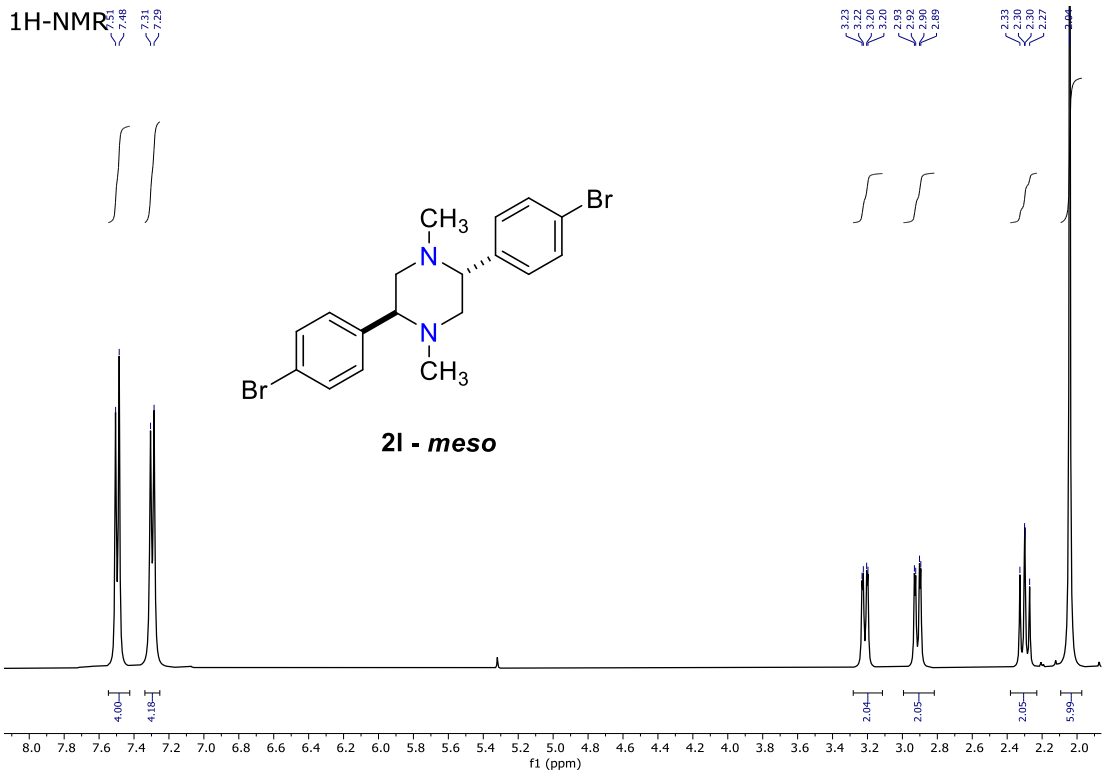


Figure S70: ^{1}H NMR of isolated compound *meso*-**2l** in $CDCl_3$

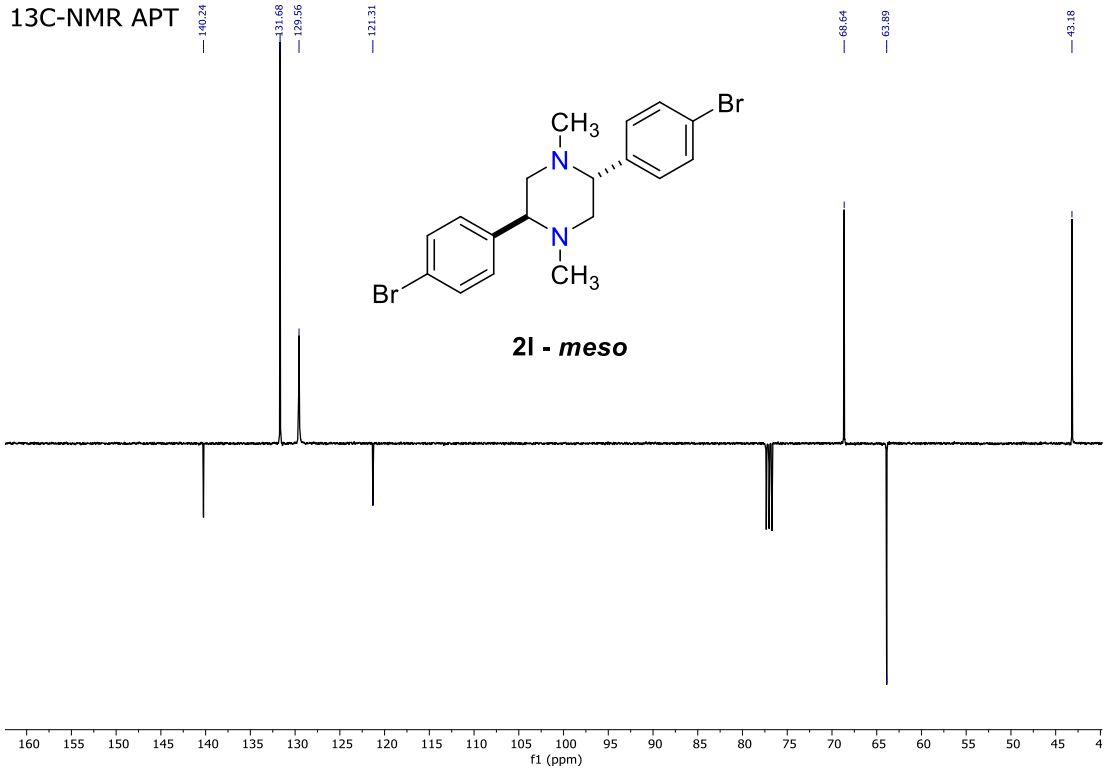


Figure S71: ^{13}C NMR of isolated compound *meso*-**2l** in $CDCl_3$

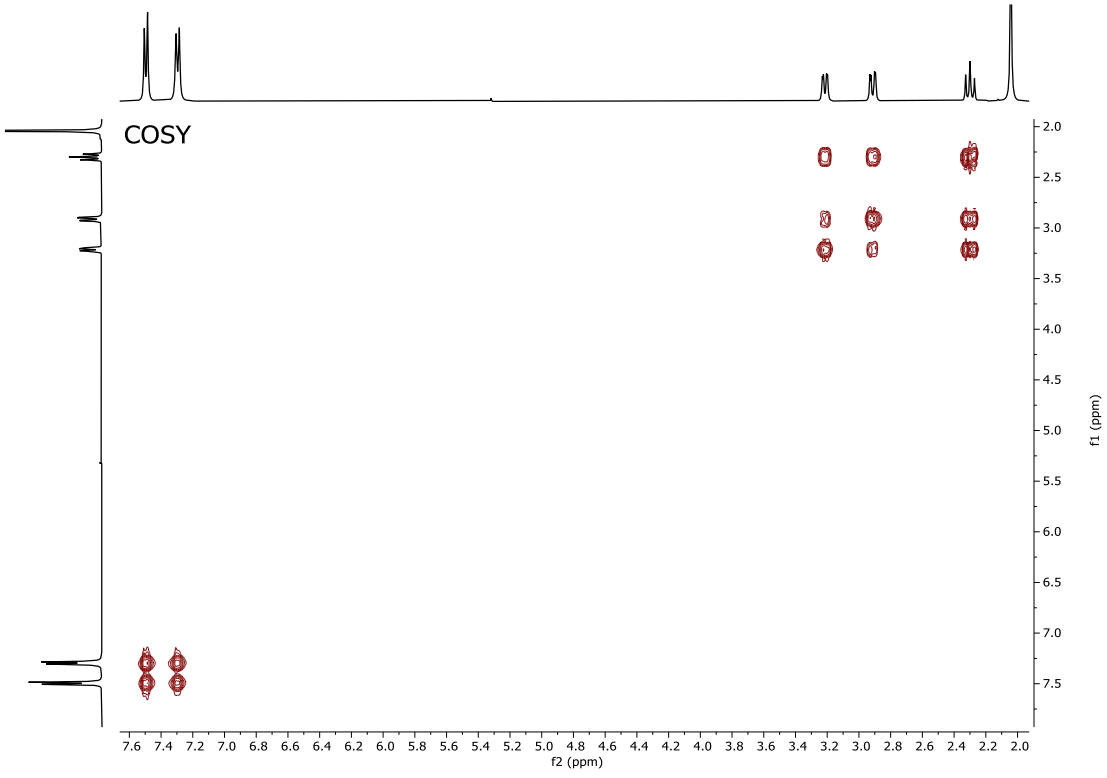


Figure S72: 2D ^{1}H COSY NMR of isolated compound *meso*-**2l** in $CDCl_3$

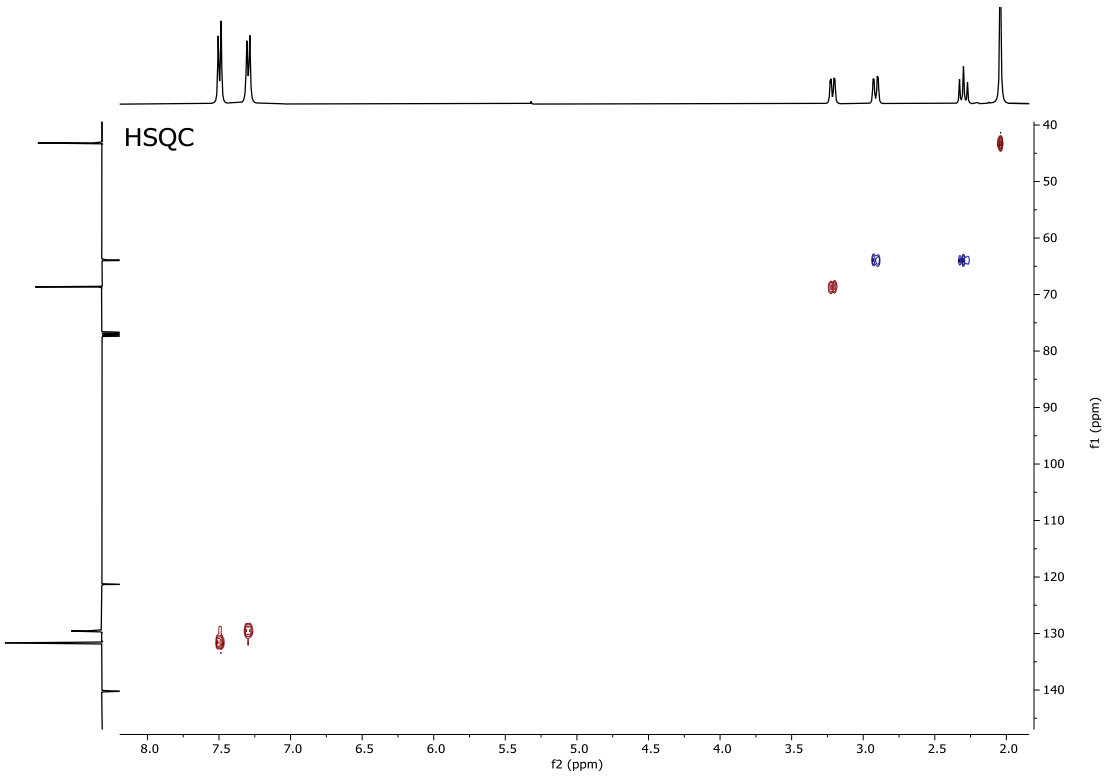


Figure S73: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2l** in $CDCl_3$

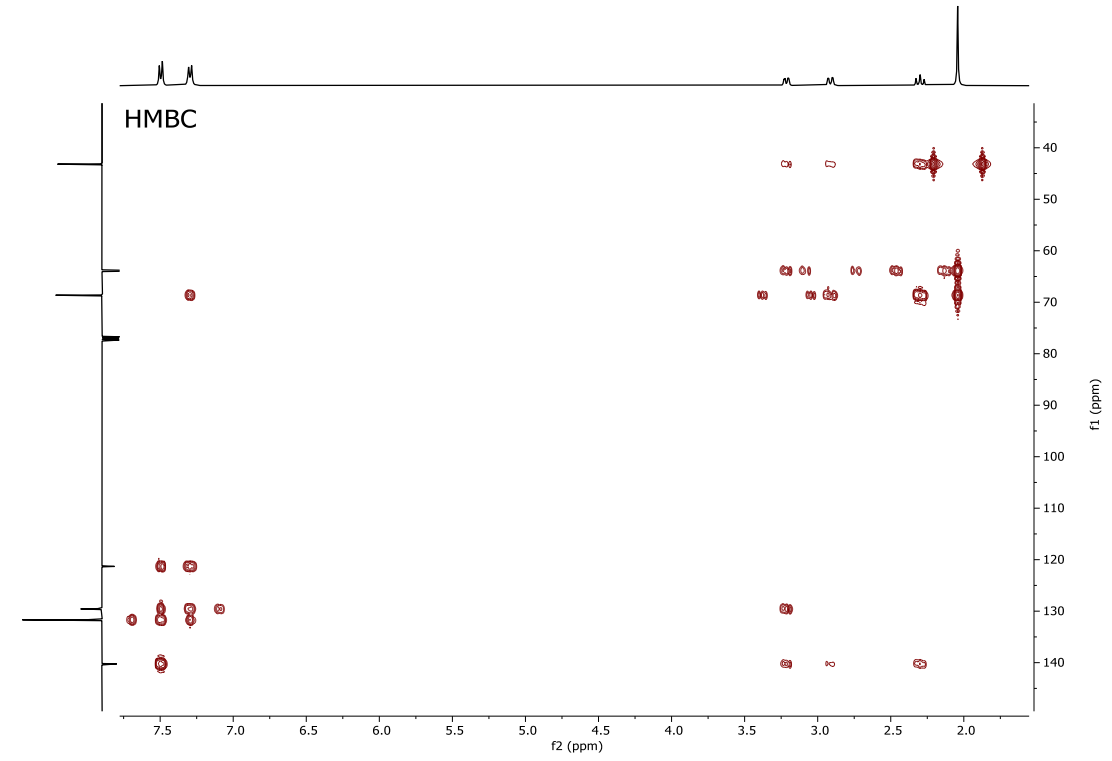


Figure S74: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2l** in $CDCl_3$

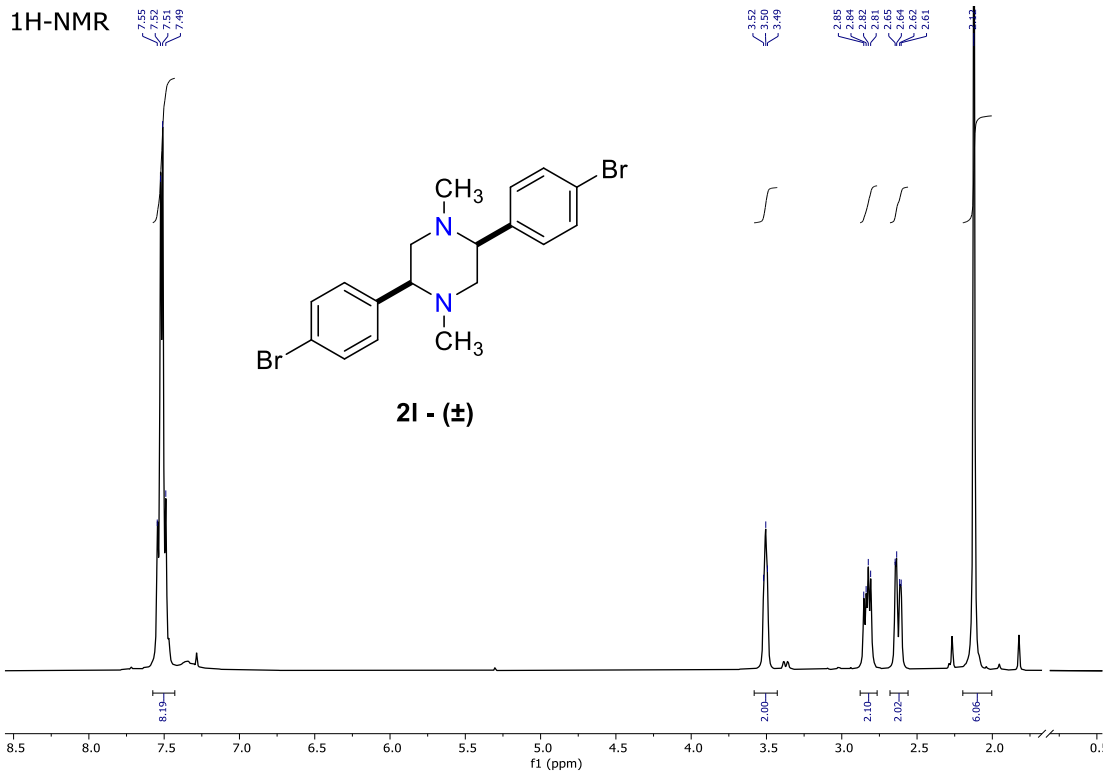


Figure S75: ^{1}H NMR of isolated compound (±)-**2l** in $CDCl_3$

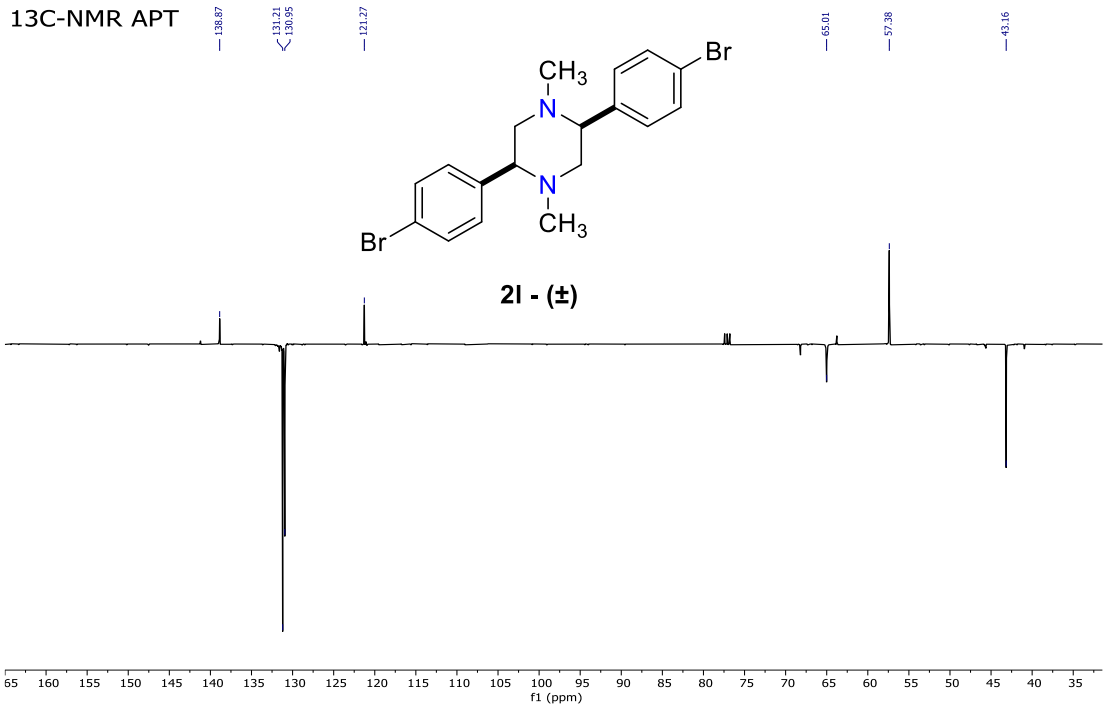


Figure S76: ^{13}C NMR of isolated compound (±)-**2l** in $CDCl_3$

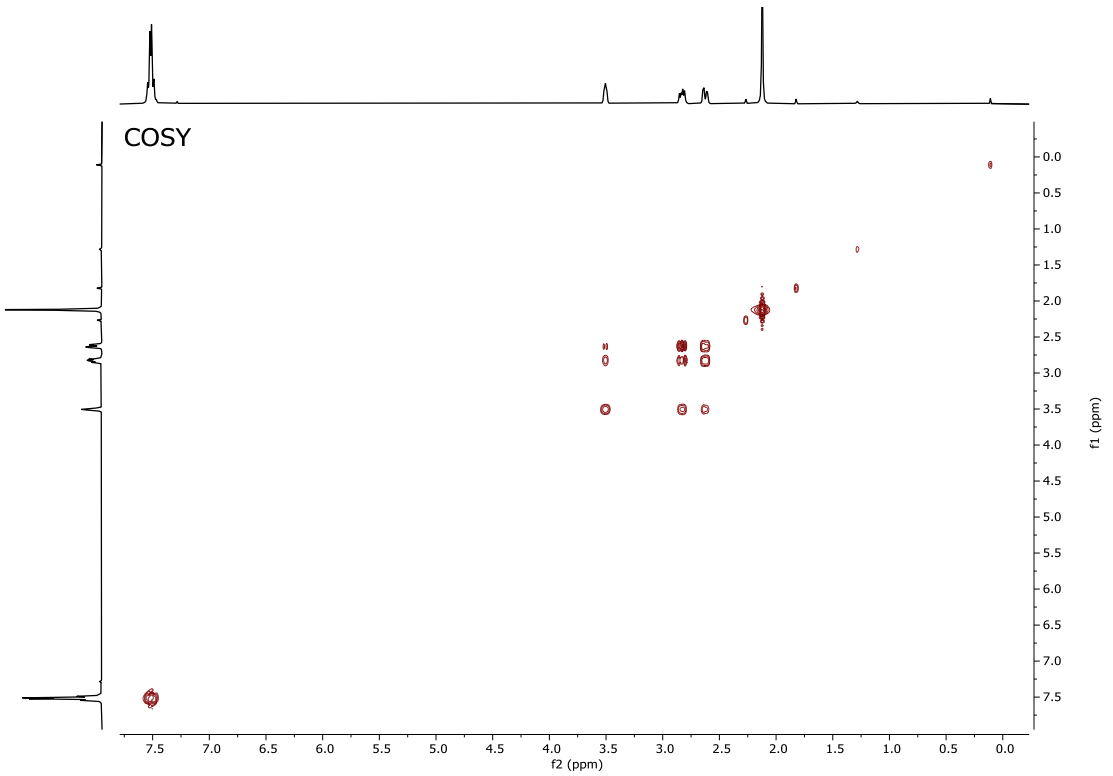


Figure S77: 2D ^{1}H COSY NMR of isolated compound (±)-**2l** in $CDCl_3$

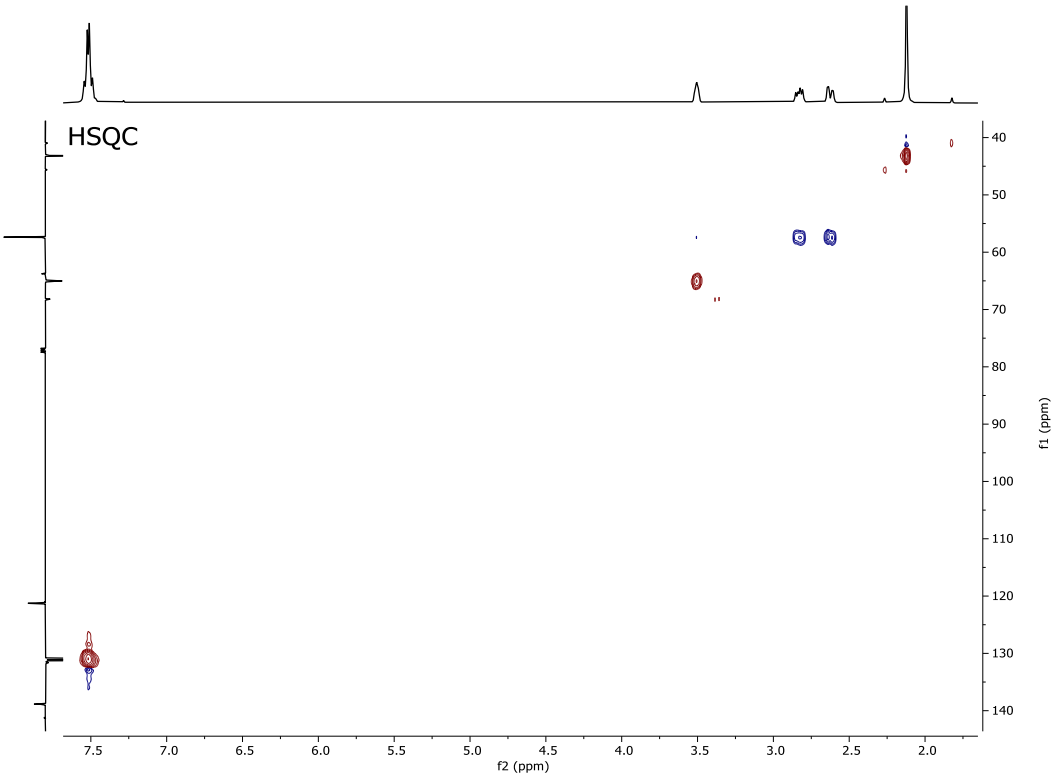


Figure S78: 2D ^{1}H-^{13}C HSQC NMR of isolated compound (±)-**2l** in $CDCl_3$

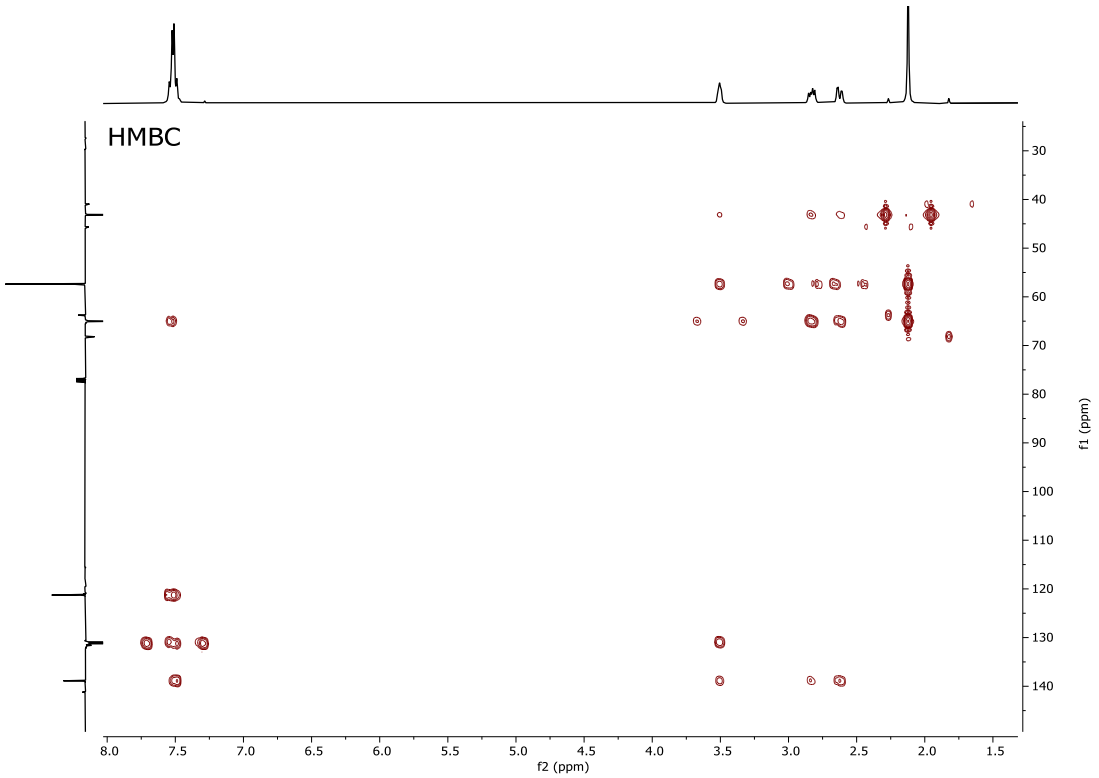


Figure S79: 2D ^{1}H-^{13}C HMBC NMR of isolated compound (±)-**2l** in $CDCl_3$

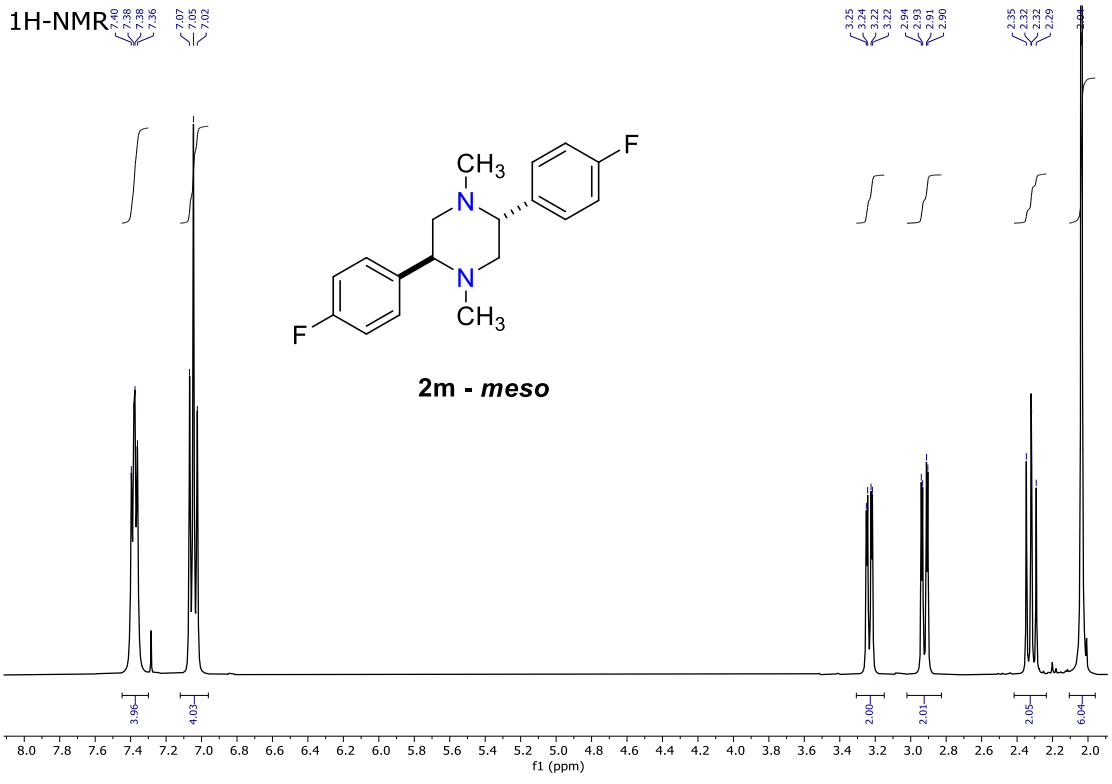


Figure S80: ^{1}H NMR of isolated compound *meso*-**2m** in $CDCl_3$

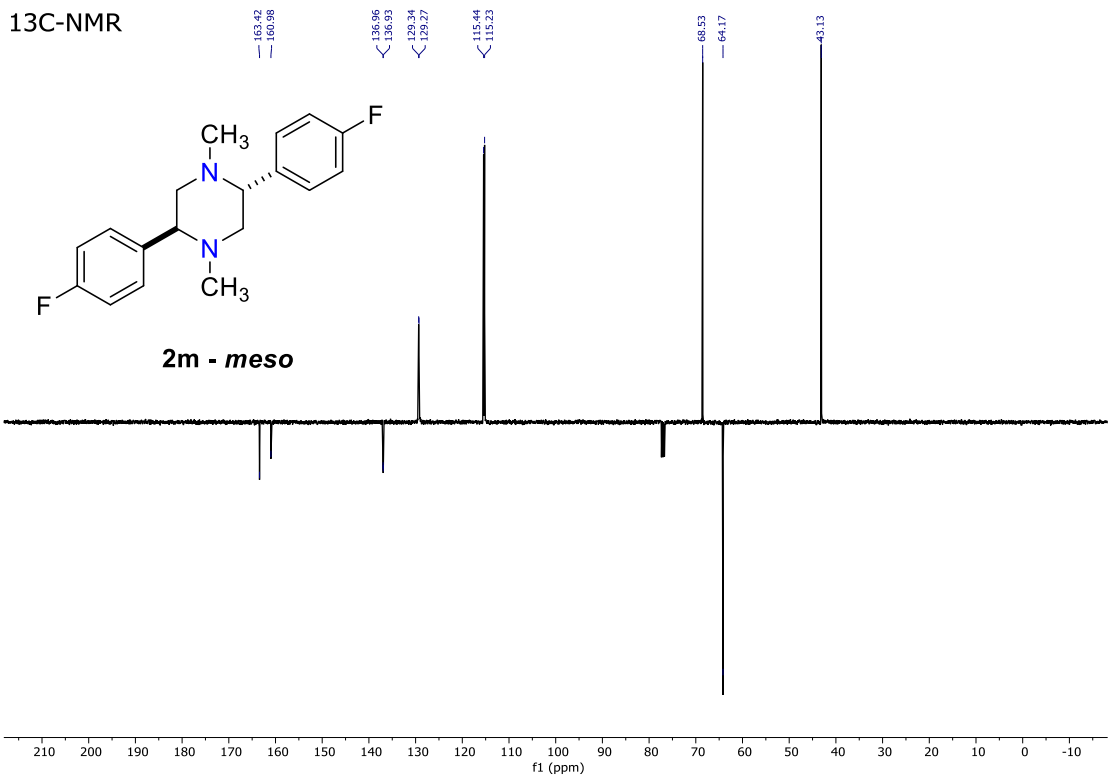


Figure S81: ^{13}C NMR of isolated compound *meso*-**2m** in $CDCl_3$

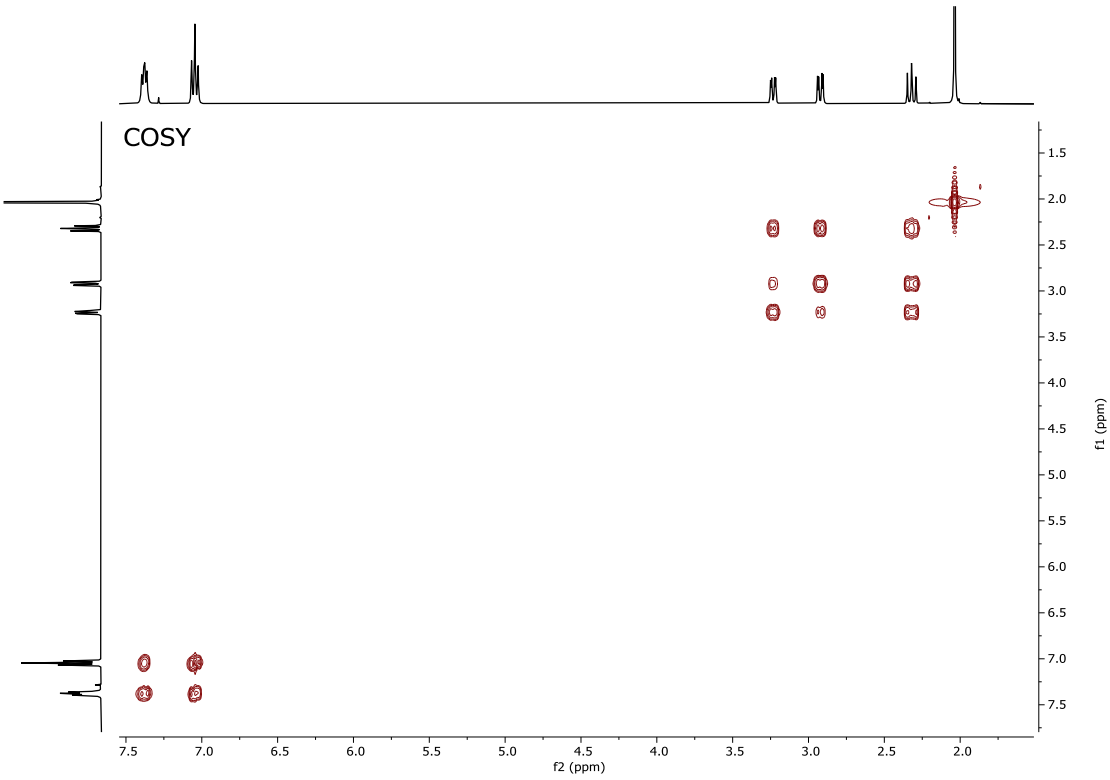


Figure S82: 2D ^{1}H COSY NMR of isolated compound *meso*-**2m** in $CDCl_3$

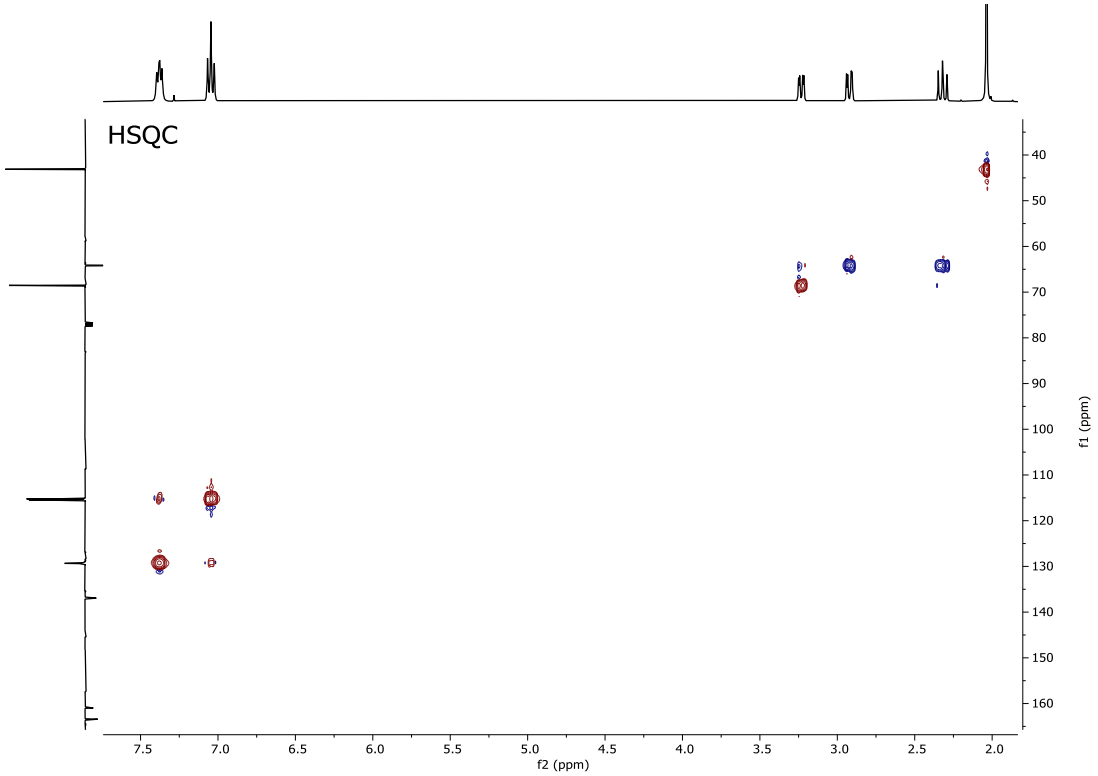


Figure S83: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2m** in $CDCl_3$

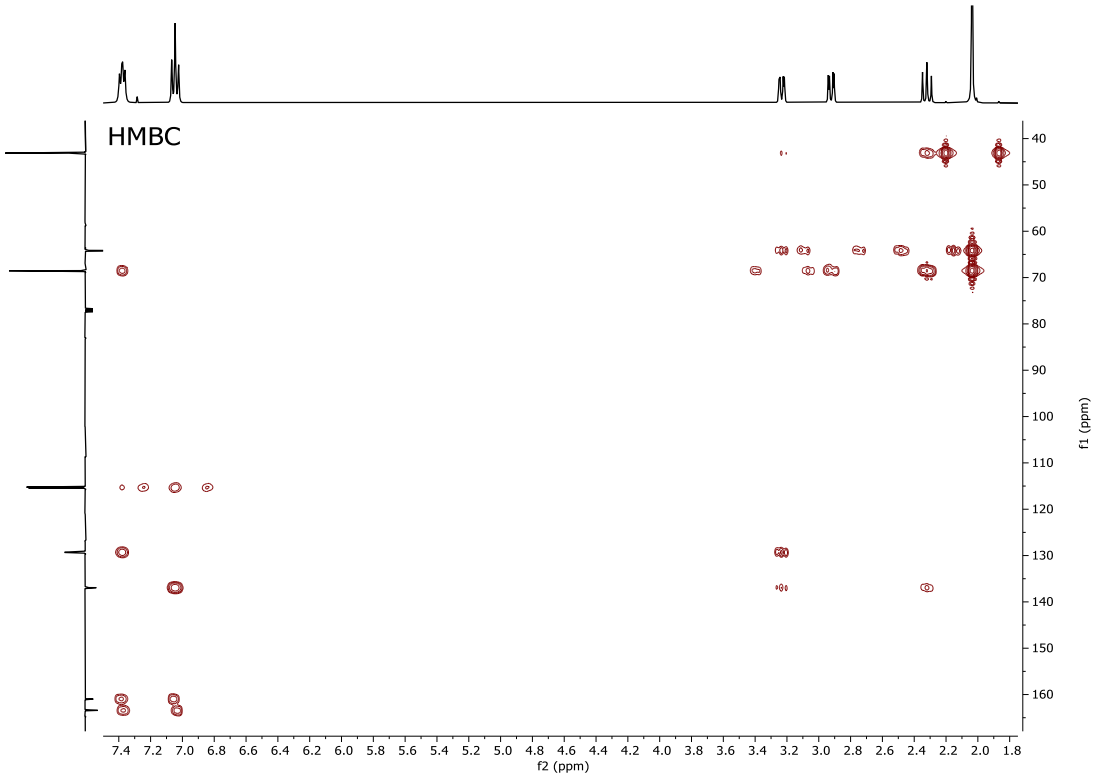


Figure S84: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2m** in $CDCl_3$

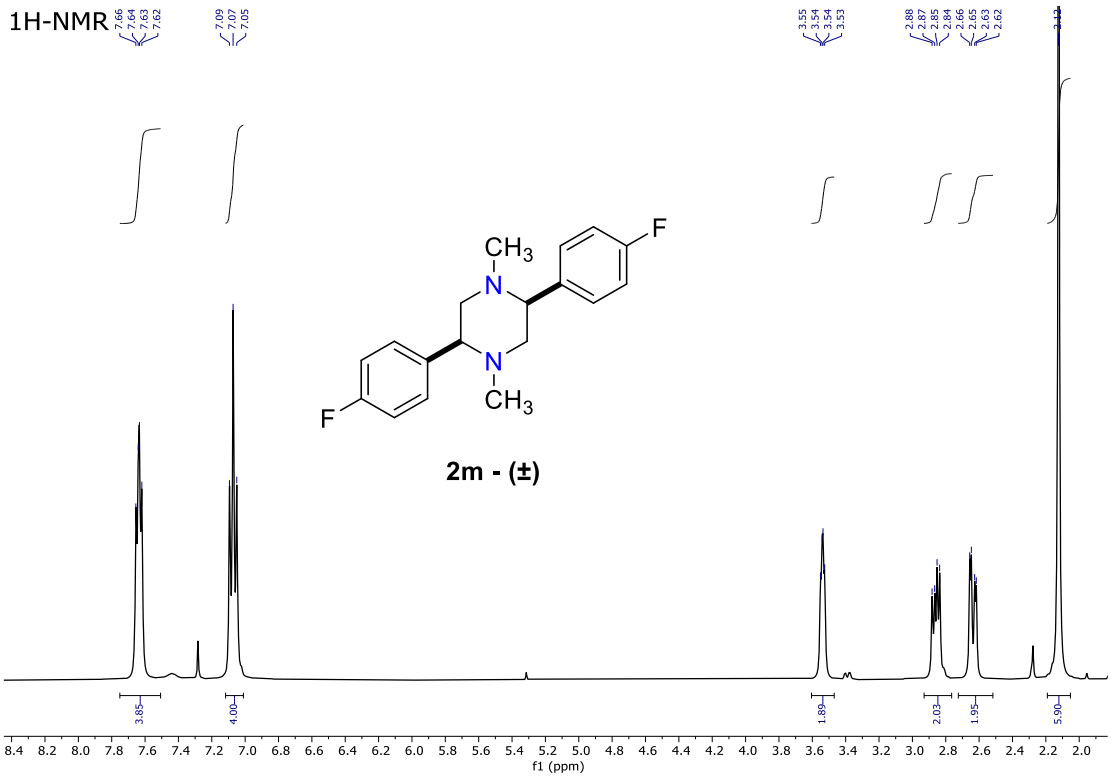


Figure S85: ^{1}H NMR of isolated compound (±)-**2m** in $CDCl_3$

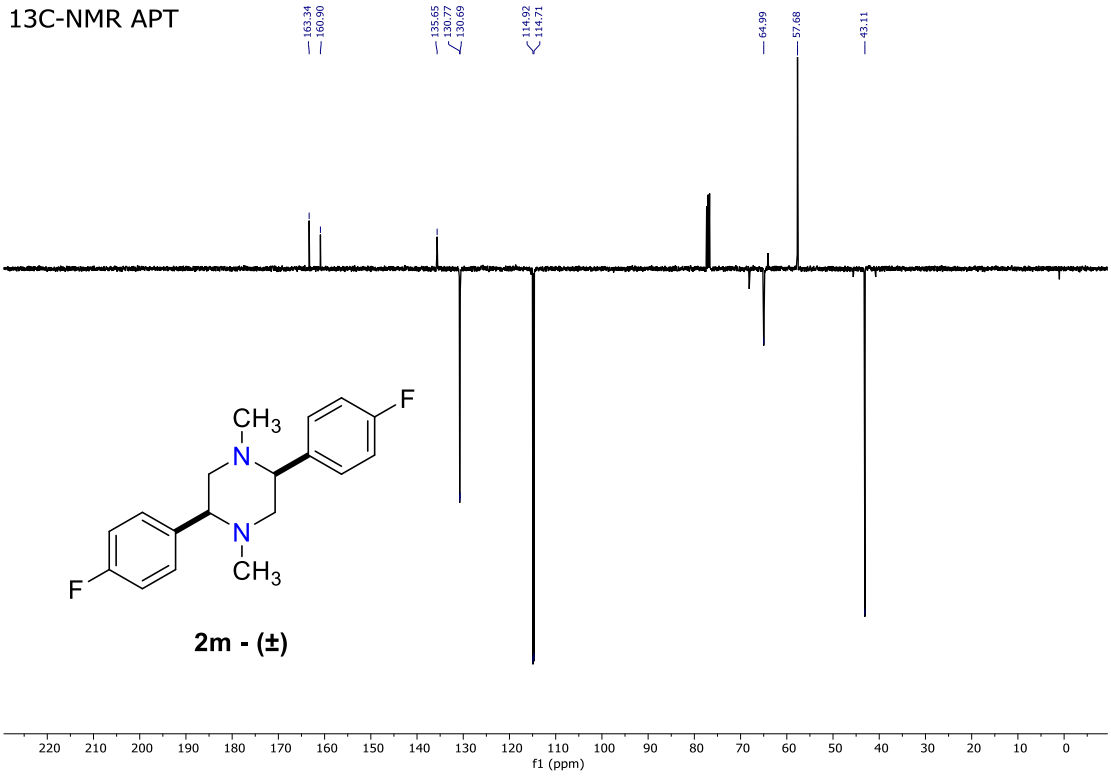


Figure S86: ^{13}C NMR of isolated compound (±)-**2m** in $CDCl_3$

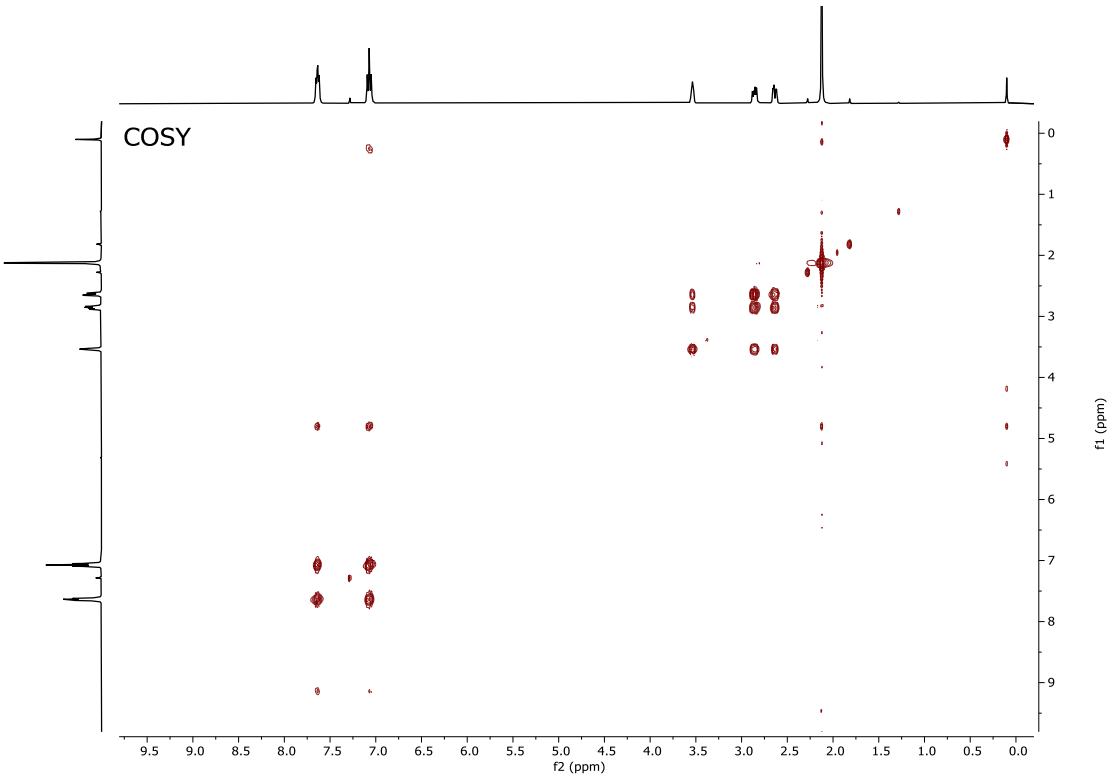


Figure S87: 2D ^{1}H COSY NMR of isolated compound (±)-**2m** in $CDCl_3$

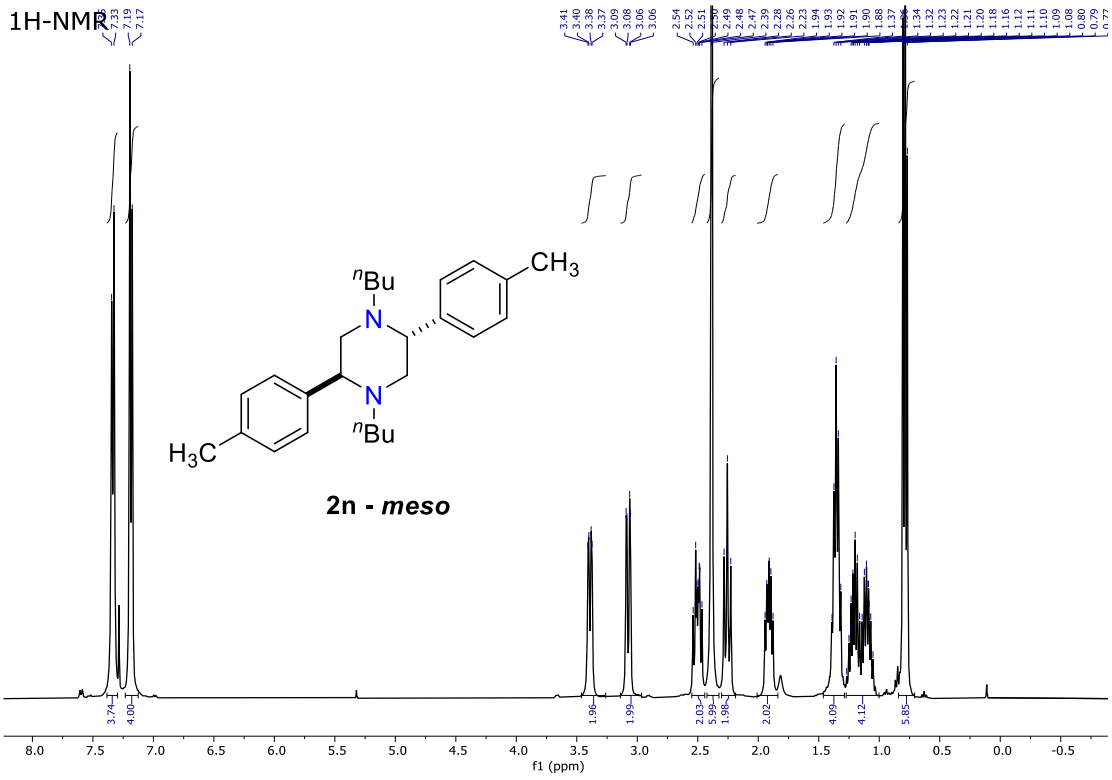


Figure S88: ^{1}H NMR of isolated compound *meso*-**2n** in $CDCl_3$

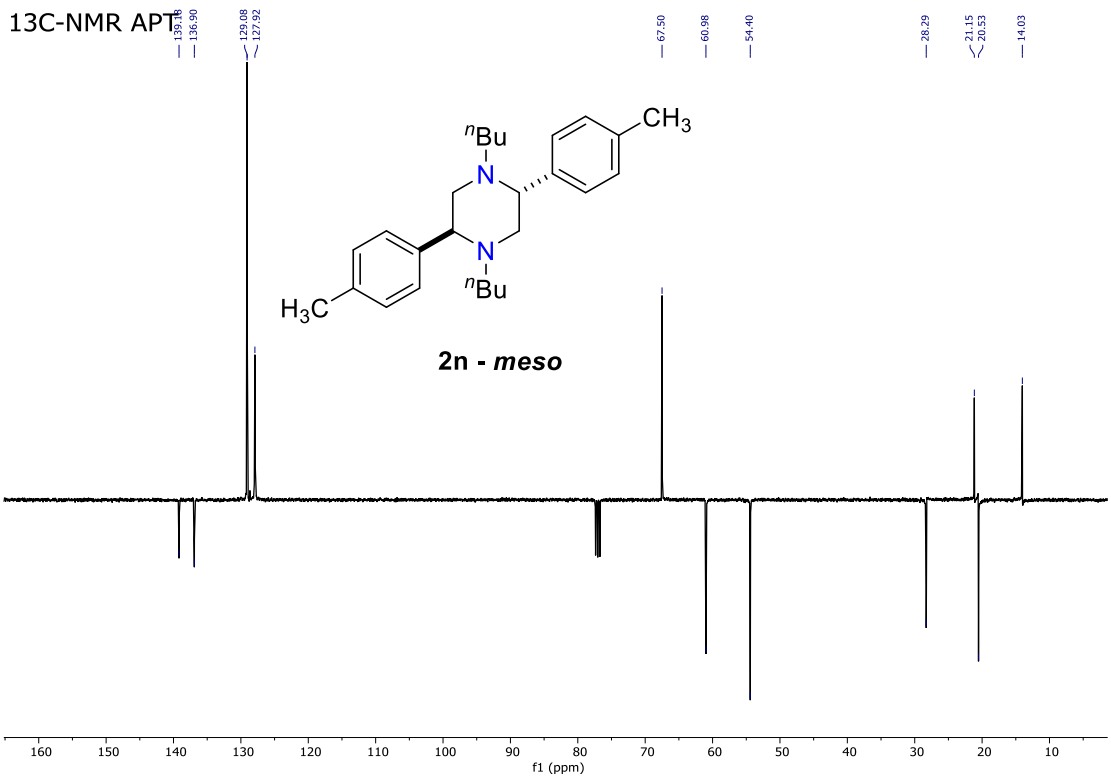


Figure S89: ^{13}C NMR of isolated compound *meso*-**2n** in $CDCl_3$

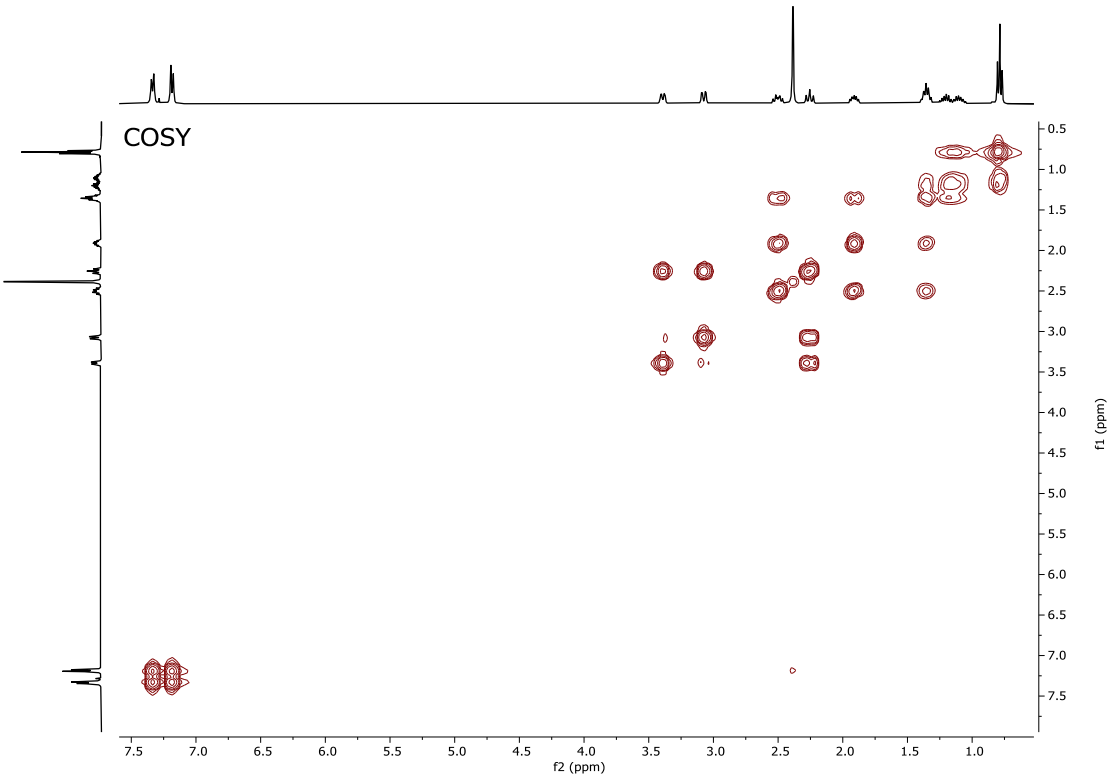


Figure S90: 2D ^{1}H COSY NMR of isolated compound *meso*-**2n** in $CDCl_3$

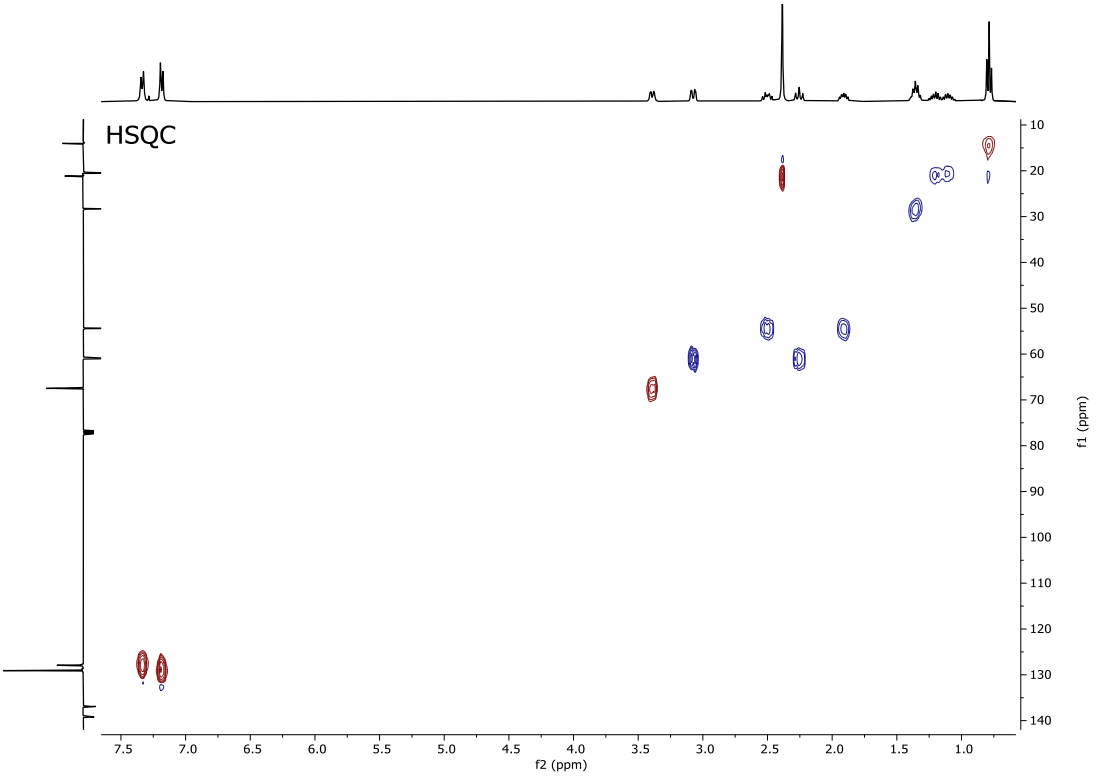


Figure S91: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2n** in $CDCl_3$

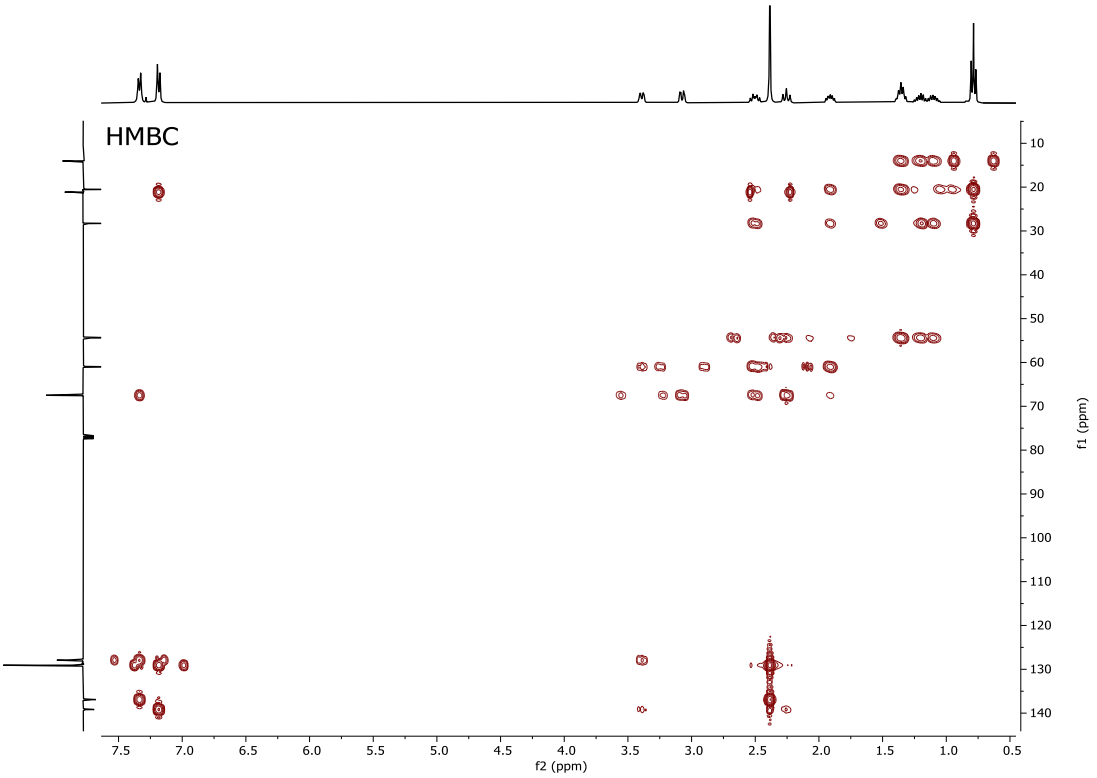


Figure S92: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2n** in $CDCl_3$

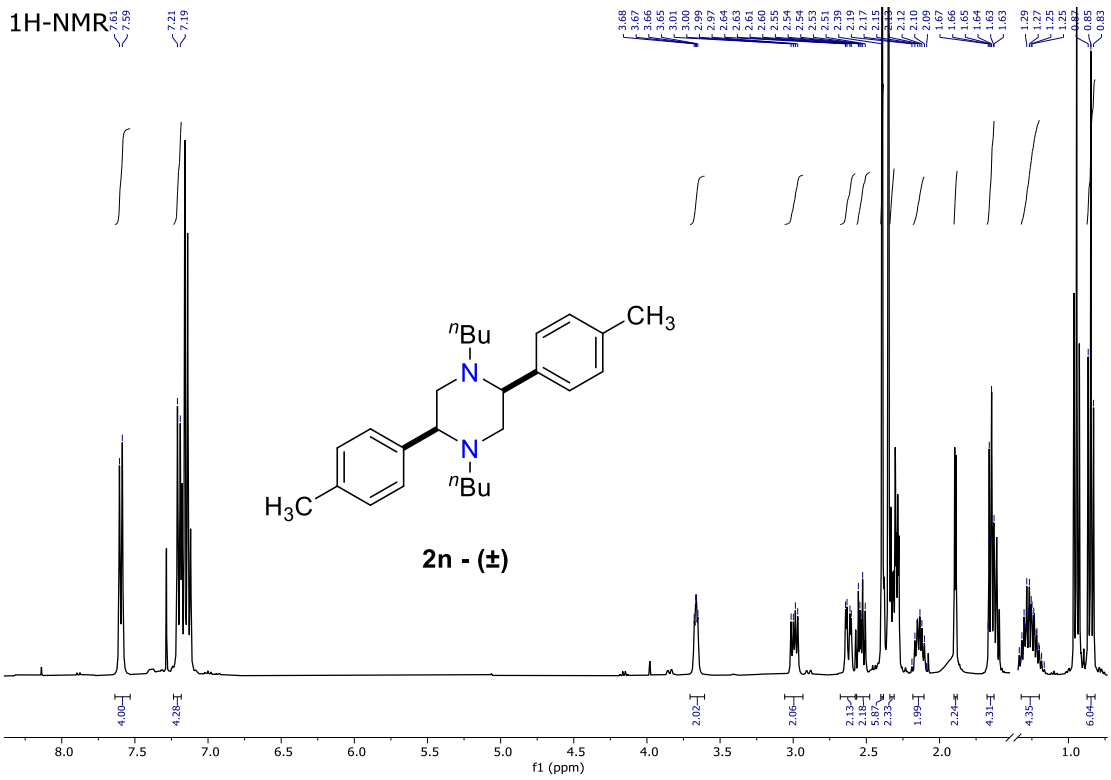


Figure S93: ^{1}H NMR of isolated compound (±)-**2n** in $CDCl_3$

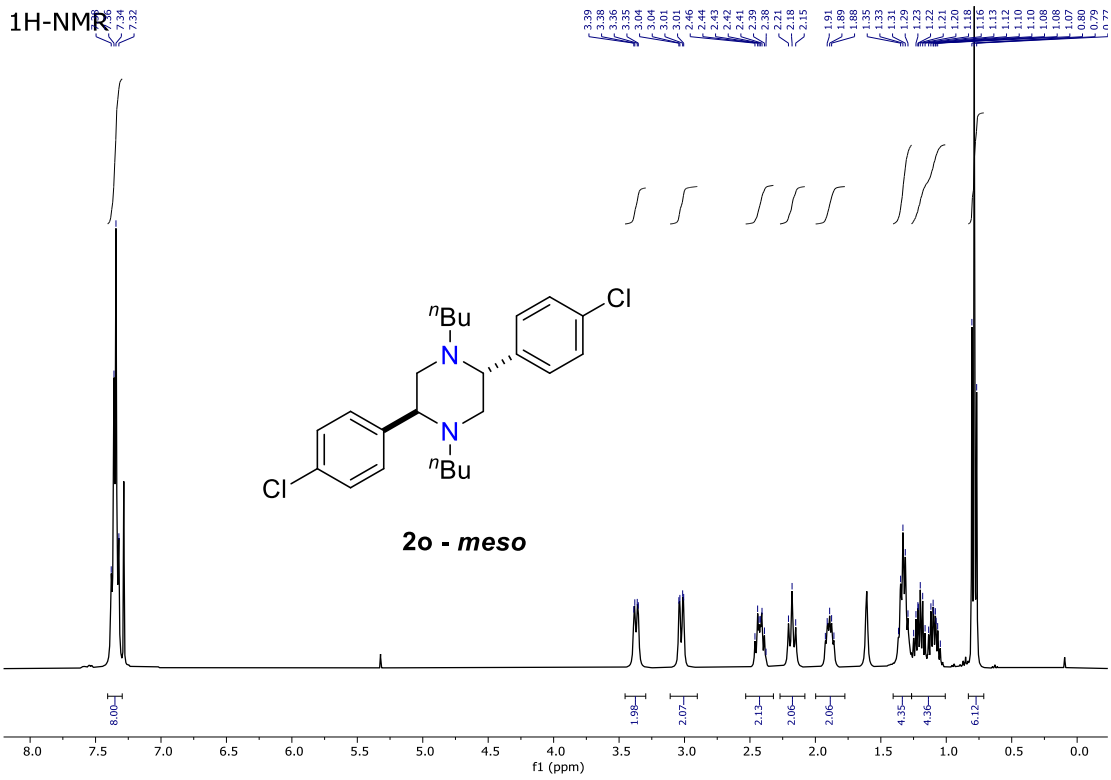


Figure S94: ^{1}H NMR of isolated compound *meso*-**2o** in $CDCl_3$

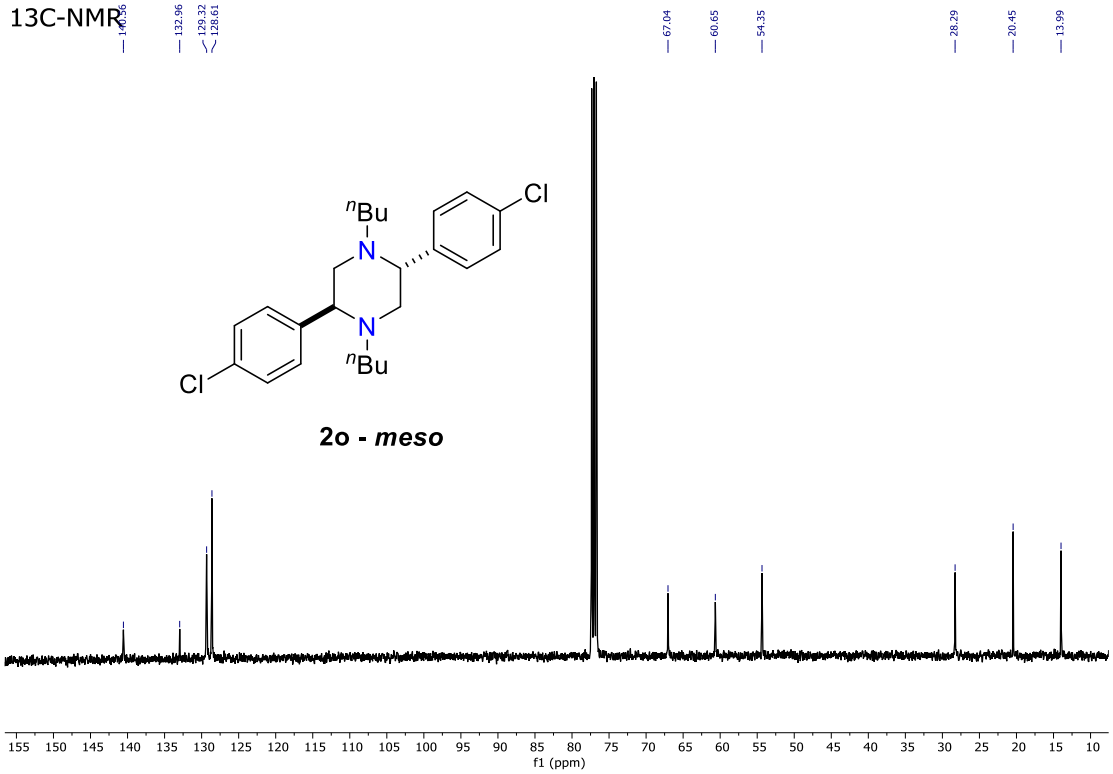


Figure S95: ^{13}C NMR of isolated compound *meso*-**2o** in $CDCl_3$

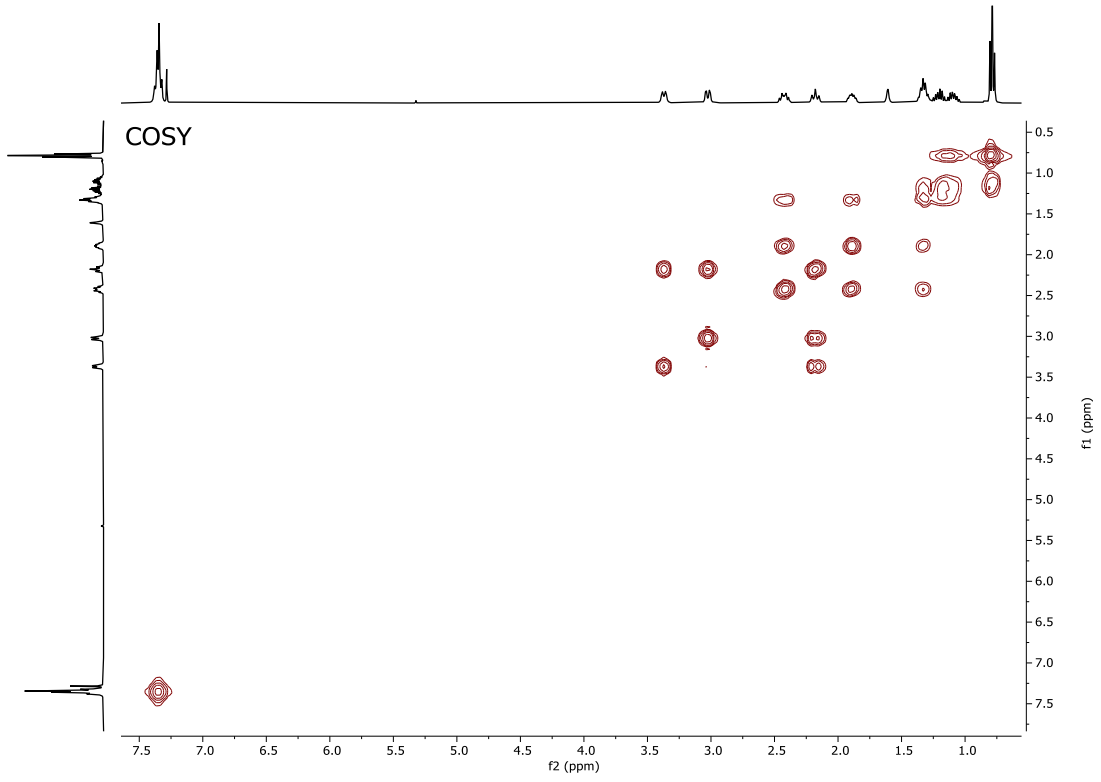


Figure S96: 2D ^{1}H COSY NMR of isolated compound *meso*-**2o** in $CDCl_3$

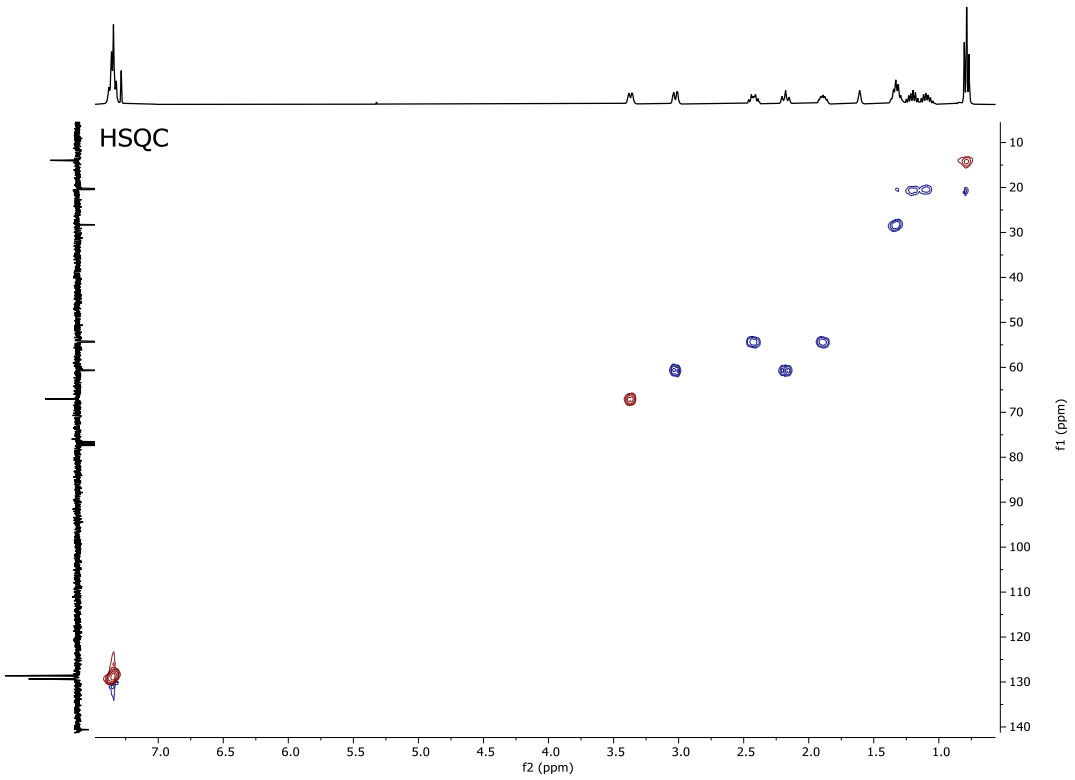


Figure S97: 2D ^{1}H-^{13}C HSQC NMR of isolated compound *meso*-**2o** in $CDCl_3$

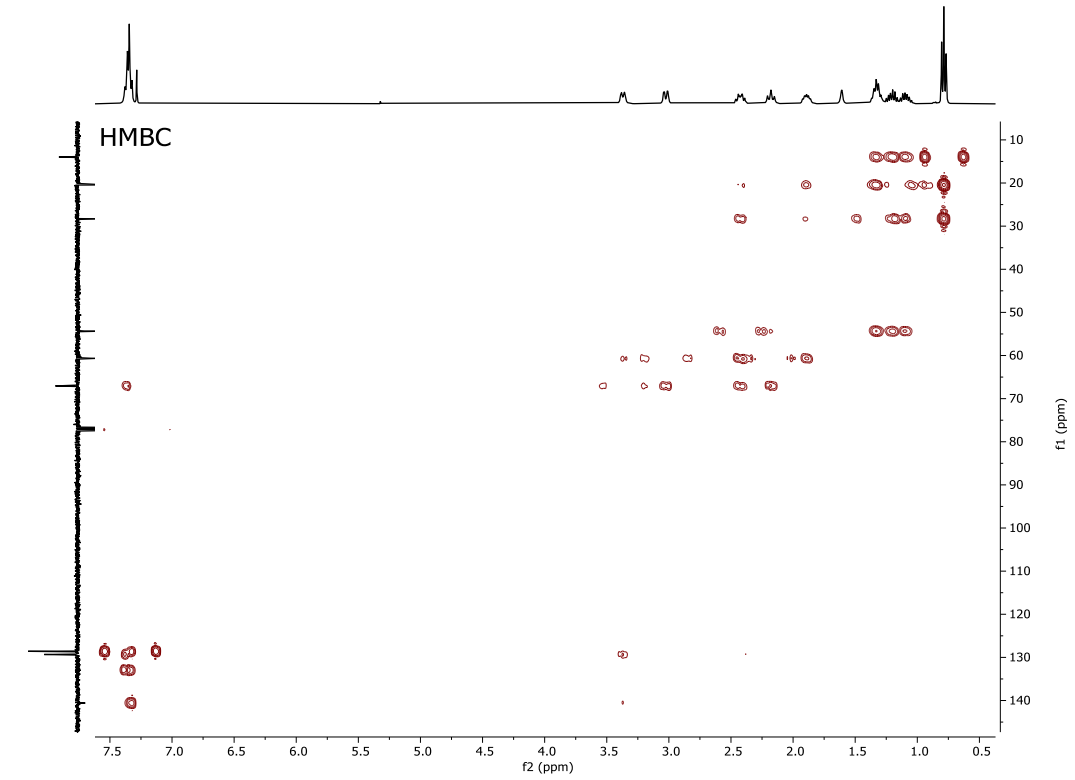


Figure S98: 2D ^{1}H-^{13}C HMBC NMR of isolated compound *meso*-**2o** in $CDCl_3$

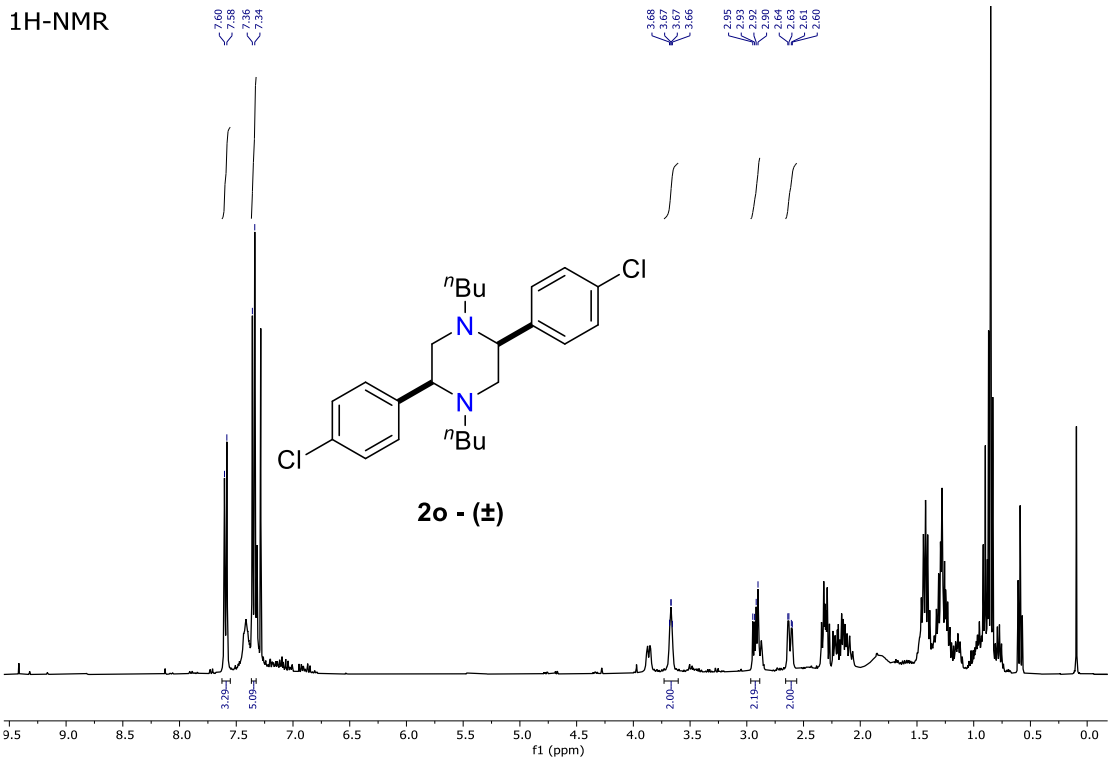


Figure S99: ^{1}H NMR of isolated compound (±)-**2o** in $CDCl_3$

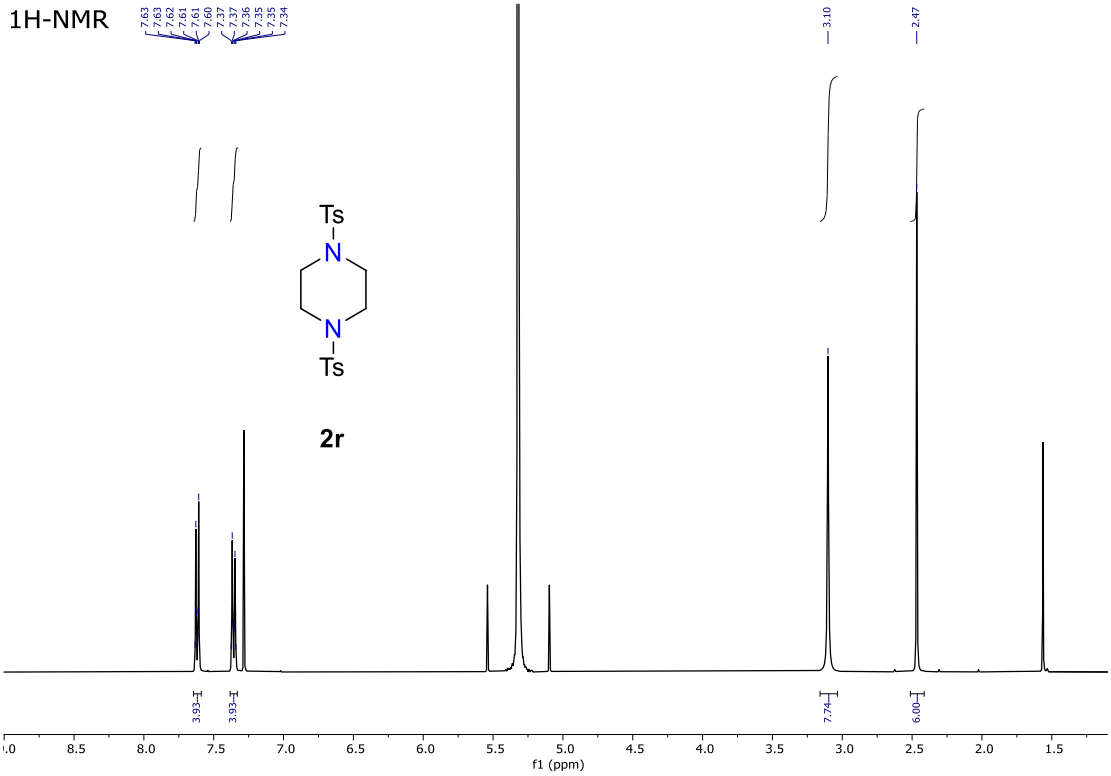


Figure S100: ^{1}H NMR of isolated compound **2r** in $CDCl_3$

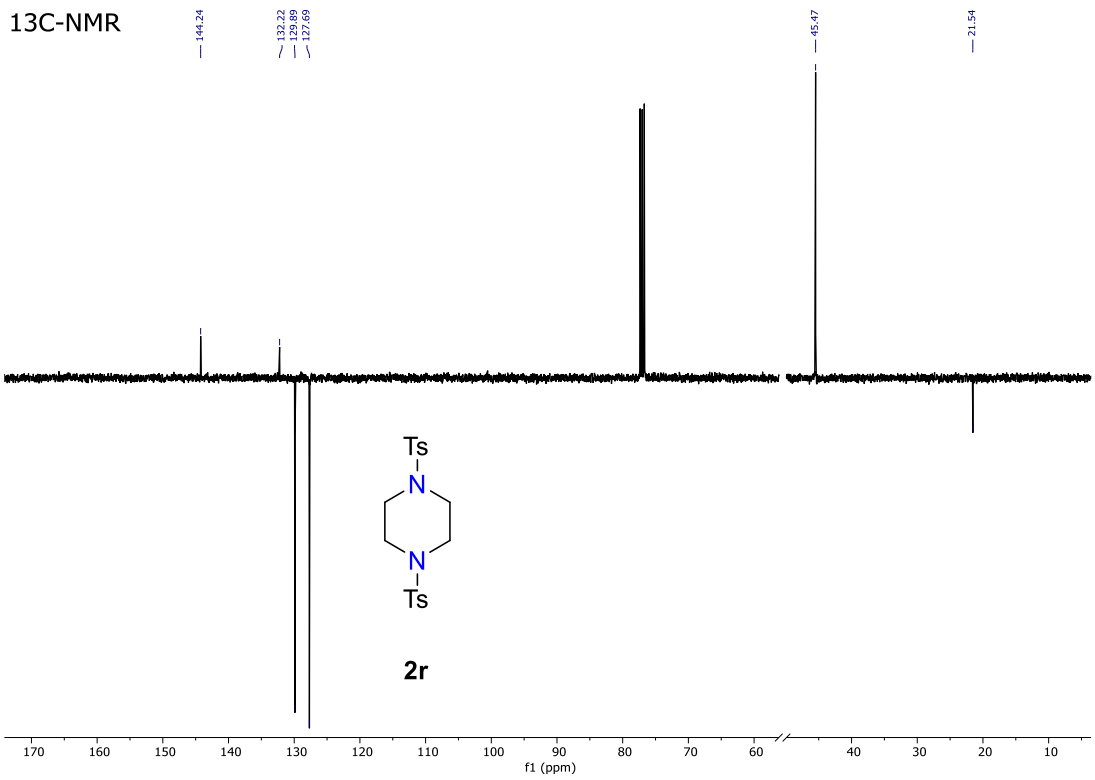


Figure S101: ^{13}C NMR of isolated compound **2r** in $CDCl_3$

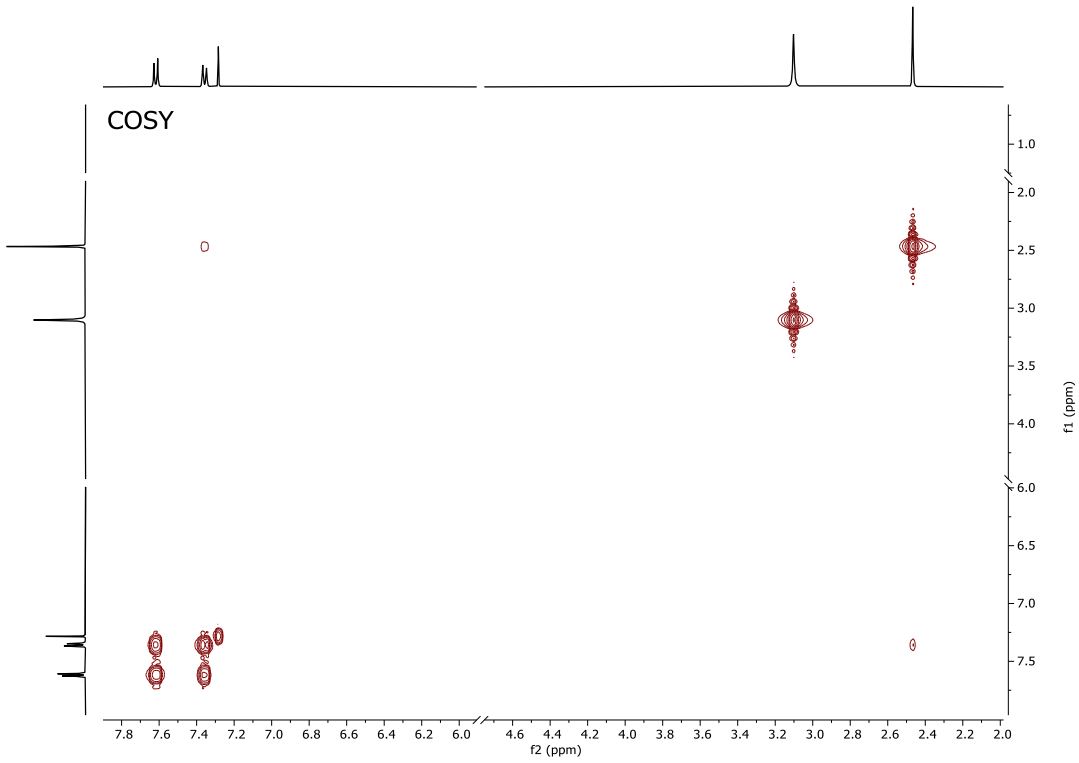


Figure S102: 2D ^{1}H COSY NMR of isolated compound **2r** in $CDCl_3$

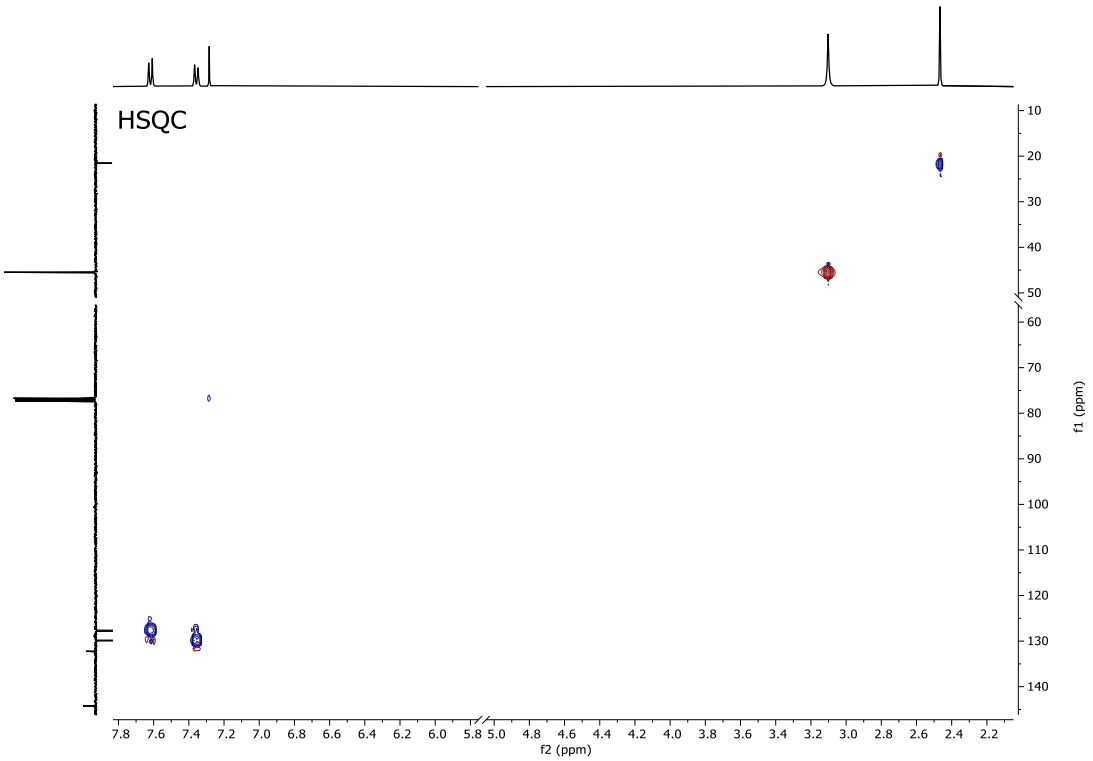


Figure S103: 2D ^{1}H-^{13}C HSQC NMR of isolated compound **2r** in $CDCl_3$

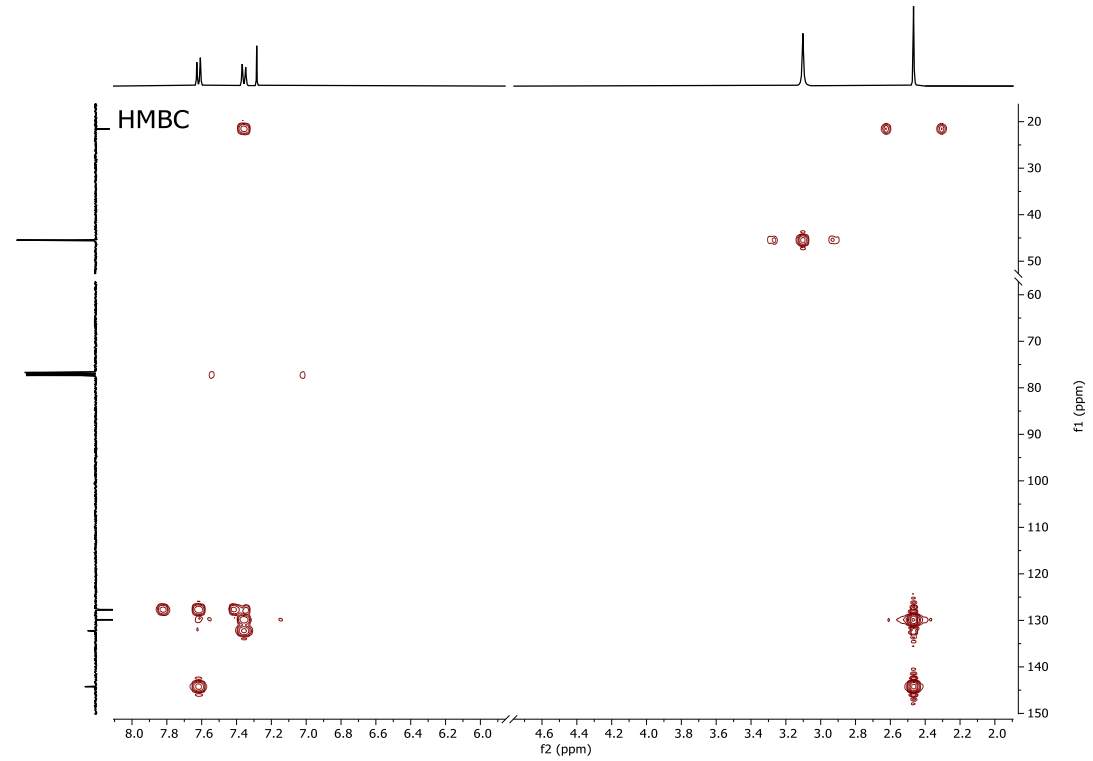


Figure S104: 2D ^{1}H-^{13}C HMBC NMR of isolated compound **2r** in $CDCl_3$