Aerobic C-H Amination of Tetrahydrocarbazole Derivatives via Photochemically Generated Hydroperoxides

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General Information

Except when indicated otherwise, all reagents and solvents were purchased from commercial sources and used as received. All reactions and work-up procedures were conducted under air except where noted otherwise. Flash column chromatography was performed using either Merck Silica Gel 60 (40-63 μm) or Sigma Aldrich activated, neutral, Brockmann I aluminium oxide. TLC was performed on Macherey-Nagel Polygram Sil G/UV_{254} or Macherey-Nagel Polygram Alox N/UV_{254} thin layer plates and visualised by UV-light and $KMnO_4$ solution. NMR spectra were recorded on a Bruker AV500, AV400 or DPX 300 MHz spectrometers. The chemical shifts are reported in ppm downfield of internal standard tetramethylsilane for ^{1}H NMR and ^{13}C NMR. Chemical shifts are designated using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet. Peaks were assigned based on ^{13}C-DEPT- or 2D NMR spectra. High resolution mass spectra were recorded with a Bruker APEX III FTICR-MS or a Finnigan SSQ 7000 quadrupole MS or a Finnigan MAT 95 double focusing sector field MS instrument. Infrared spectra were measured with a PerkinElmer Spectrum 100 FT-IR spectrometer on a diamond ATR unit.

Abbreviations

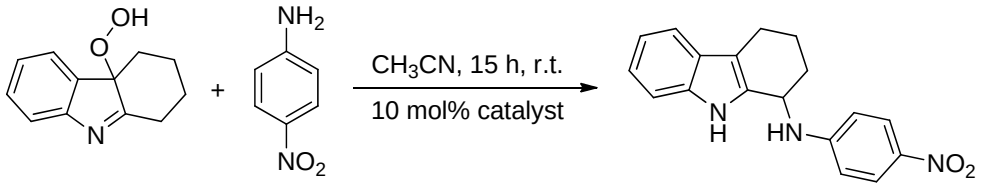
AcOH	Acetic acid
DMSO	Dimethyl sulfoxide
MeOH	Methanol
MsOH	Methanesulfonic acid
PTSA	*p*-Toluenesulfonic acid
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran

Optimization of reaction conditions

All reactions were run until full conversion of the starting hydroperoxide **3** was achieved, according to thin layer chromatography or ^{1}H-NMR analysis of the crude reaction mixture.

Screening of Catalysts:

To optimize the yield of the desired coupling product, different catalysts were tested in CH_3CN at room temperature. TFA was found to be the most suitable catalyst for our coupling reaction.



3 (1.0 eq) (1.0 eq) **4**

Supplementary Table S1: Screening of catalysts

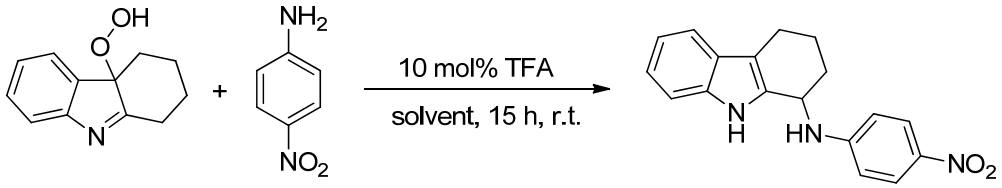
Entry	Catalyst	Remaining aniline (%)	Product 4 (%, NMR Yield)
1	$FeCl_3$	93	7
2	$FeBr_3$	100	0
3	$K_4Fe(CN)_6$	100	0
4	$Fe(OTf)_3$	90	10
5	$Yb(OTf)_3$	90	10
6	$Sc(OTf)_3$	92	8
7	$Fe(NO_3)_3.9H_2O$	91	9
8	TFA	86	14
9	PTSA	95	5
10	MsOH	100	0

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), CH_3CN (10 ml), catalyst (0.049 mmol).

$FeCl_2$, iron acetate, $Fe(C_2H_5)_2BF_4$, iron acetylacetonate, $FePO_4$, Mohrs salt, cyclopentadienyliron dicarboxyl iodide, $FeBr_2$, and $FeCl_3.6H_2O$ were also tried, but they gave inferior results.

Screening of Solvents:

After the selection of catalyst, the coupling reaction was performed in different solvents. Methanol was found to be superior to all the tested solvents which afforded the coupling product in 76% yield in just 4h.



3 (1.0 eq) (1.0 eq) **4**

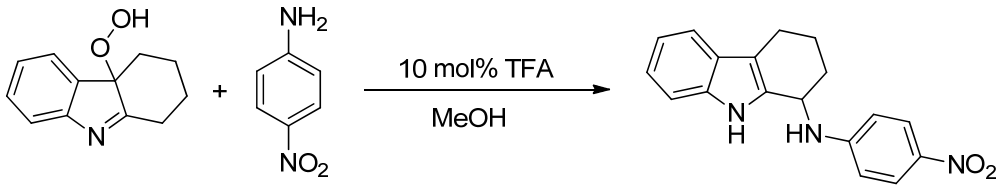
Supplementary Table S2: Screening of solvents

Entry	Solvent	Remaining aniline (%)	Product 4 (%, NMRYield)
1	**CH_3CN**	**86**	**14**
2	**DMSO**	**34**	**66(4h)**
3	**DMF**	**56**	**44(4h)**
4	**Toluene**	**77**	**23**
5	**$CHCl_3$**	**83**	**17**
6	**EtOAc**	**35**	**65**
7	**MeOH**	**25**	**75 (4h)**

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), solvent (10 ml), TFA (0.049 mmol).

Screening of Temperatures:

After performing the reaction at different temperatures, room temperature was found to be optimal for the reaction.



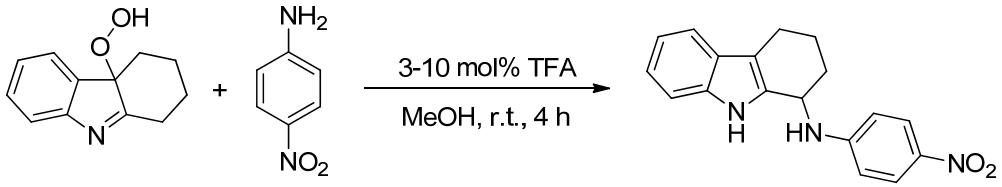
3 (1.0 eq) (1.0 eq) **4**

Supplementary Table S3: Screening of temperature

Entry	Temp.	Time (h)	Remaining aniline (%)	Product 4 (%, NMRYield)
1	**r.t.**	**4**	**25**	**75**
2	**40°C**	**3**	**30**	**70**
3	**0°C**	**15**	**35**	**65**
4	**-40°C**	**15**	**80**	**20**

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), MeOH (10 ml), TFA (0.049 mmol).

Screening of catalyst loading:



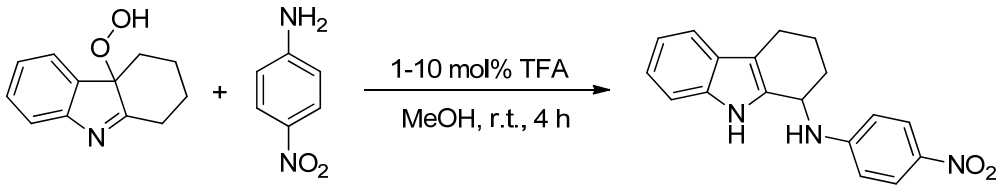
3 (1.0 eq) (1.0 eq) **4**

Supplementary Table S4: Screening of catalyst loading

Entry	Catalyst (mol%)	Remaining aniline (%)	Product 4 (%, NMRYield)
1	**3**	**40**	**60**
2	**5**	**12**	**66**
3	**10**	**24**	**76**
4	**20**	**30**	**70**

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), MeOH (10 ml), TFA (3-20 mol%).

Screening of catalyst loading at higher concentration:



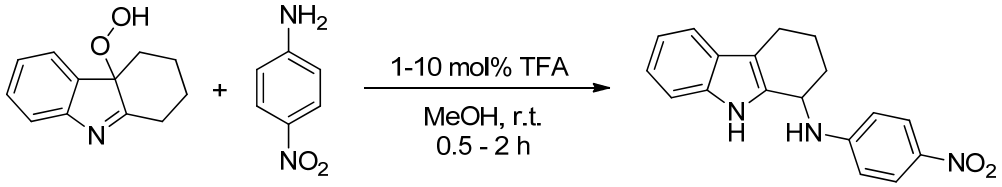
3 (1.0 eq) (1.0 eq) **4**

Supplementary Table S5: Screening of catalyst loading at higher concentration

Entry	Cat. (mol%)	Remaining aniline (%)	Product 4 (%, NMRYield)
1	**10**	**14**	**86**
2	**5**	**33**	**67**
3	**3**	**34**	**66**
4	**1**	**35**	**65**

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), MeOH (0.5 ml), TFA (3-20 mol%).

Optimization of reaction time at higher substrate concentration:



3 (1.0 eq) (1.0 eq) **4**

Supplementary Table S6: Optimization of time at higher substrate concentration

Entry	time	Remaining aniline (%)	Product 4 (%, NMRYield)
1	**2 h**	**13**	**87**
2	**1h**	**35**	**65**
3	**30 min**	**37**	**63**

Conditions: **3** (0.49 mmol), *p*-nitroaniline (0.49 mmol), MeOH (0.5 ml), TFA (0.049 mmol).

Synthetic procedures

Synthesis of starting materials

The different tetrahydrocarbazole and indol derivatives were synthesized by Fischer Indole Synthesis using standard procedures.[1,2]

General procedure for the synthesis of hydroperoxides:[3]

The desired substrate (1 g) was dissolved in toluene (100 ml). To this solution was added rose bengal (2 mg). The resultant reaction mixture was irradiated with a 23 watt lamp under an atmosphere of O_2. The progress of the reaction was controlled by ^{1}HNMR. After full conversion of the substrate, the precipitated solid was filtered to afford the desired product in quantitative yields. All hydroperoxides looked pink because of the presence of rose bengal.

General procedures, reaction of hydroperoxides with N-H nucleophiles

Method A (MeOH/TFA)

The hydroperoxide (0.49 mmol, 1.0 equiv.) was dissolved in methanol (0.5 ml). To this reaction mixture was added the desired nucleophile (0.49 mmol, 1.0 equiv.) followed by the addition of TFA (3.7 µL, 0.049 mmol, 0.1 equiv.). After 2-4 h, the solvent was reduced to dryness and the resulting solid was purified by column chromatography or by recrystallization.

Method B (AcOH)

The hydroperoxide (0.49 mmol, 1.0 equiv.) was dissolved in acetic acid (0.5 ml). To this reaction mixture was added the desired nucleophile (0.49 mmol, 1.0 equiv.). After 2-4 h, the solvent was reduced to dryness and the resulting solid was purified by column chromatography or by recrystallization.

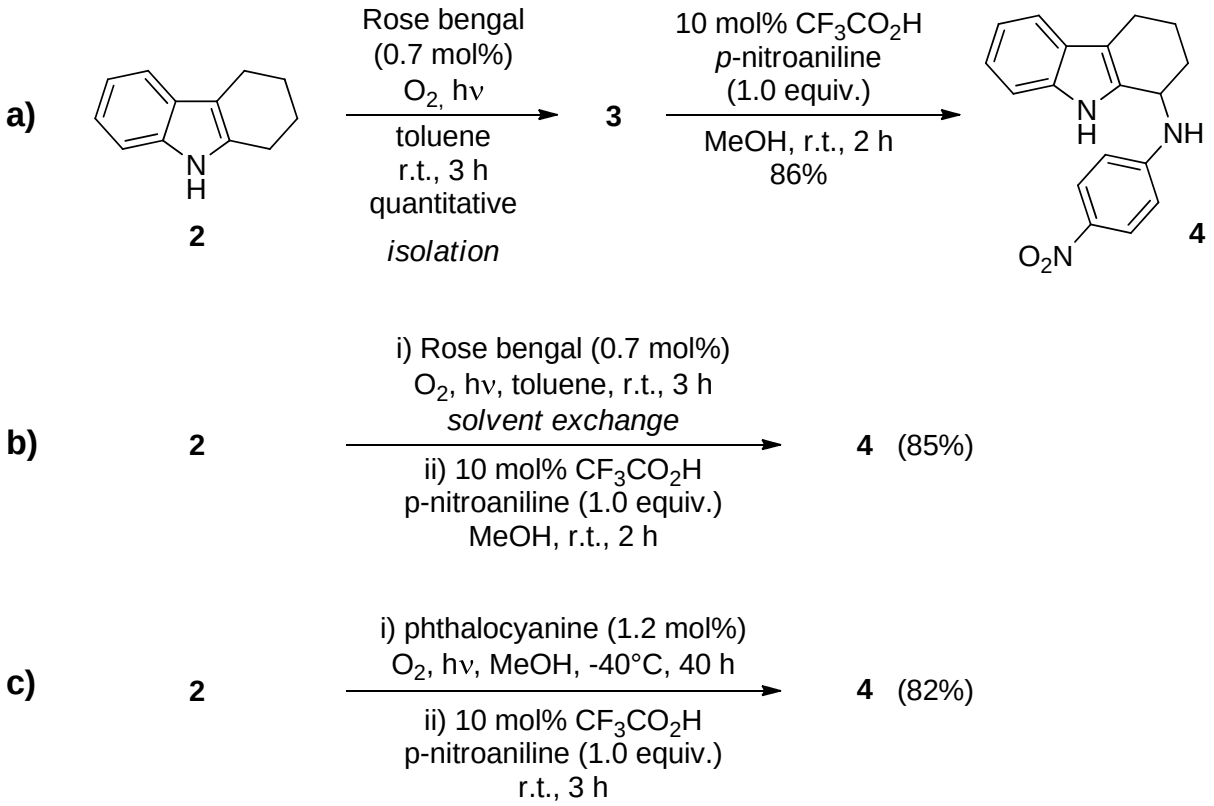
Comparison of two-step and one-pot methods

Two-step method: The hydroperoxide **3** is synthesized in toluene as described above and employed in the coupling step as isolated compound. Using this procedure, a yield of 86% over two steps was achieved for the coupling of tetrahydrocarbazole **2** and *p*-nitroaniline (Supplementary Figure S1a).

One-pot method with exchange of solvent: after synthesis of the peroxide **3** in toluene according to the procedure described above, toluene is removed under vacuum and the resulting mixture is directly employed in the next step. Using this procedure, a yield of 85% over two steps was achieved for the coupling of tetrahydrocarbazole **2** and *p*-nitroaniline (Supplementary Figure S1b).

One-pot method without change of solvent:

The indole derivative (0.49 mmol) was dissolved in methanol (10 ml). To this solution was added phthalocyanine (2 mg). The resultant reaction mixture was irradiated with a 500 watt lamp under an atmosphere of oxygen for 40 hours at -40°C. The progress of the reaction was controlled by 1H NMR. After full conversion of the substrate, aniline (1.0 equiv.) and TFA (10 mol%) was added and the mixture was stirred at ambient temperature. After 3 hours, the solvent was reduced to dryness and the resulting solid was purified by column chromatography or by recrystallization. Using this procedure, a yield of 82% was achieved for the coupling of tetrahydrocarbazole **2** and *p*-nitroaniline (Supplementary Figure S1c).



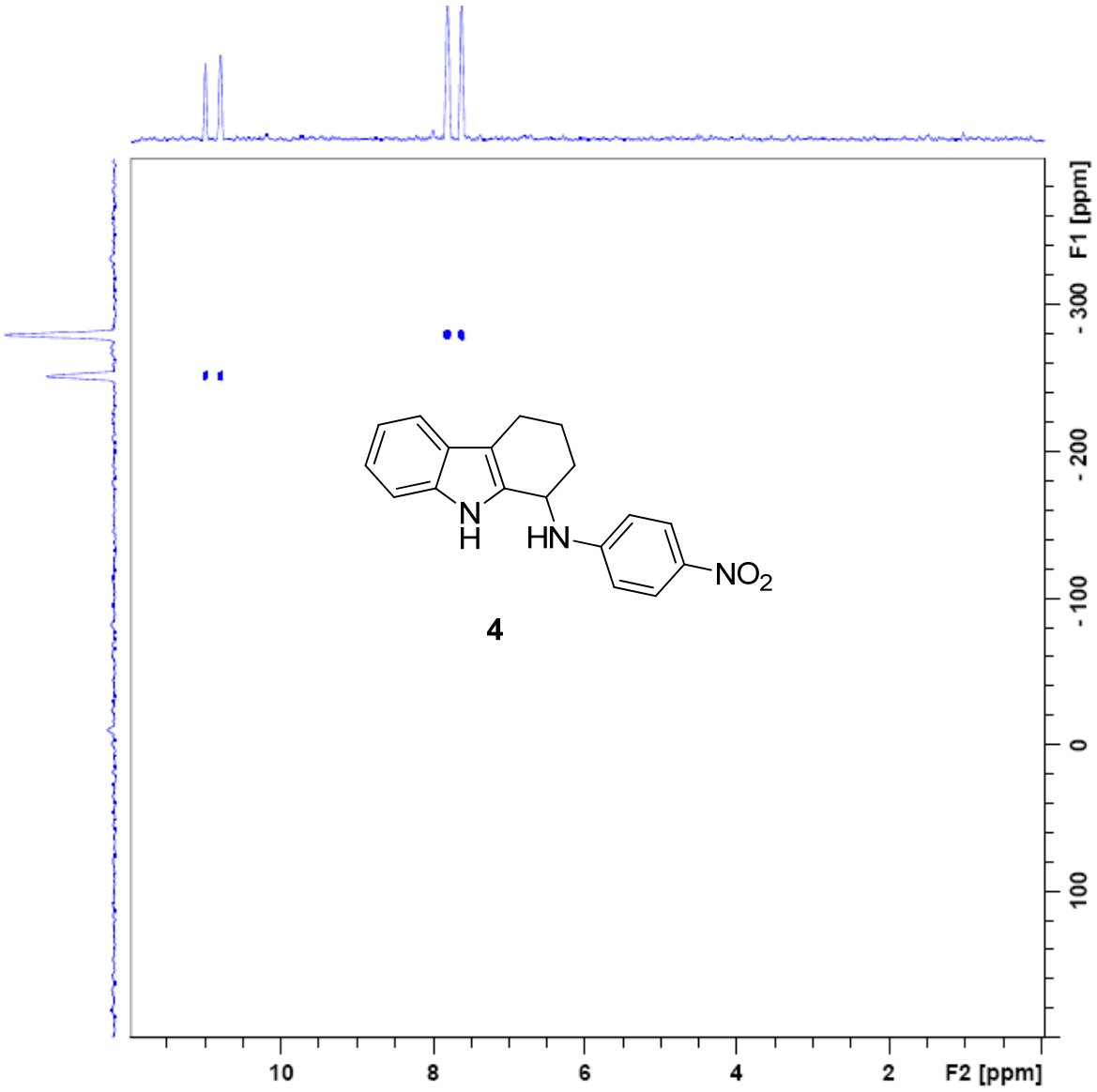
Supplementary Figure S1 Investigation of the reaction sequence. a), Two-step protocol with isolation of intermediate hydroperoxide **3**. **b)**, One-pot, two-step protocol exchanging the solvent without isolation of hydroperoxide **3**. **c)**, One-pot, two-step protocol in methanol without need to exchange the solvent.

Structure determination of the coupling products

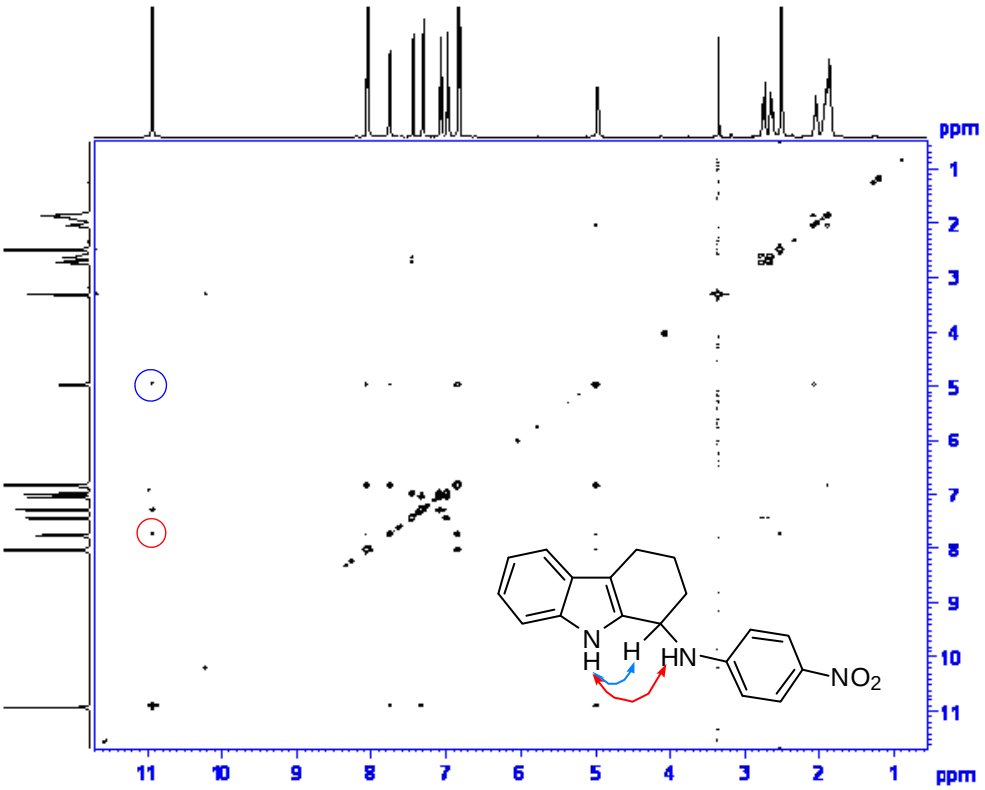
Position of the new C-N bond

To determine the structure of the coupling products and unambiguously distinguish it from all the other possible isomers, a detailed NMR analysis of product **4** was performed.

With the help of ^{15}N-HMBC, it was possible to assign the hydrogen atoms directly connected to nitrogen (Supplementary Figure S2). The correct regioisomer was confirmed by Nuclear Overhauser effect spectroscopy (NOESY), which showed the long range coupling of indolic N-H with the aniline N-H and methyne C-H (Supplementary Figure S3).



Supplementary Figure S2: ^{15}N-HMBC of 4 in DMSO (to determine the *N*-bound hydrogen atoms)

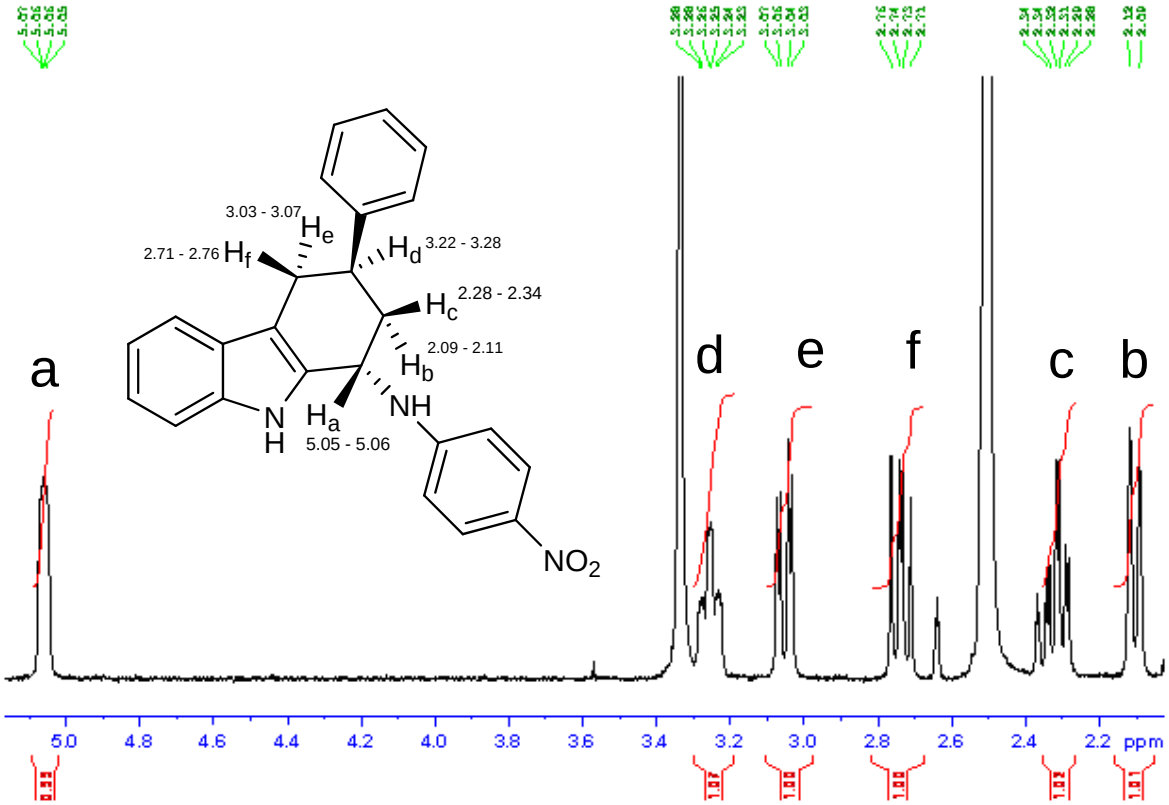


Supplementary Figure S3: NOESY of 4 in DMSO (to determine the position of the new C-N bond)

Additionally, the structures of several products were determined by X-ray crystallography, giving consistent results (see below).

Relative configuration of the diastereomers of 15 and 16

The reaction of phenyl substituted tetrahydrocarbazole hydroperoxide with *p*-nitroaniline led to the formation of two diastereomers with a ratio of 85:15. It was possible to isolate the major diastereomer by column chromatography. The configuration of the major diastereomer was determined by assigning all protons by H,H-COSY, HMBC and HSQC and determining the coupling constants between H_a- H_b/H_c and H_d- H_b/H_c and H_d-H_e/H_f (Supplementary Figure S4 and Supplementary Table S7).



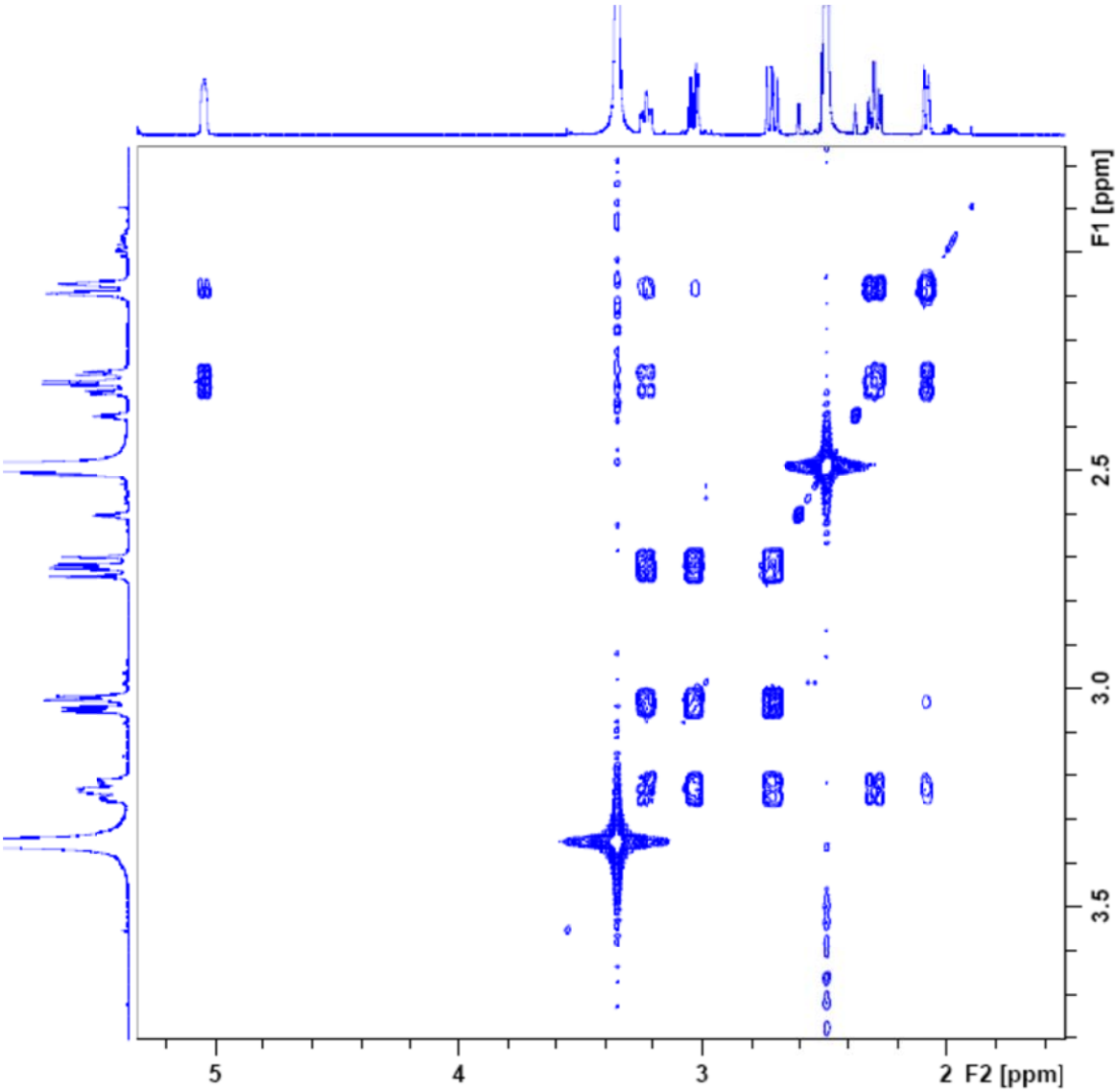
Supplementary Figure S4: ^{1}H NMR in DMSO of the major diastereomer of 15

Supplementary Table S7: Chemical shifts and coupling constants for the major diastereomer of 15.

Entry	Proton	Chemical shift (ppm)	Multiplicity	Coupling constant (*J, Hz*)
1	b	2.09-2.11	d	13.4
2	c	2.28-2.34	td	13.1, 4.2
3	f	2.71-2.76	dd	15.4, 11.4
4	e	3.03-3.07	dd	15.5, 4.7
5	d	3.22-3.28	tdd	13.9, 4.9, 2.9
6	a	5.05	m	<6

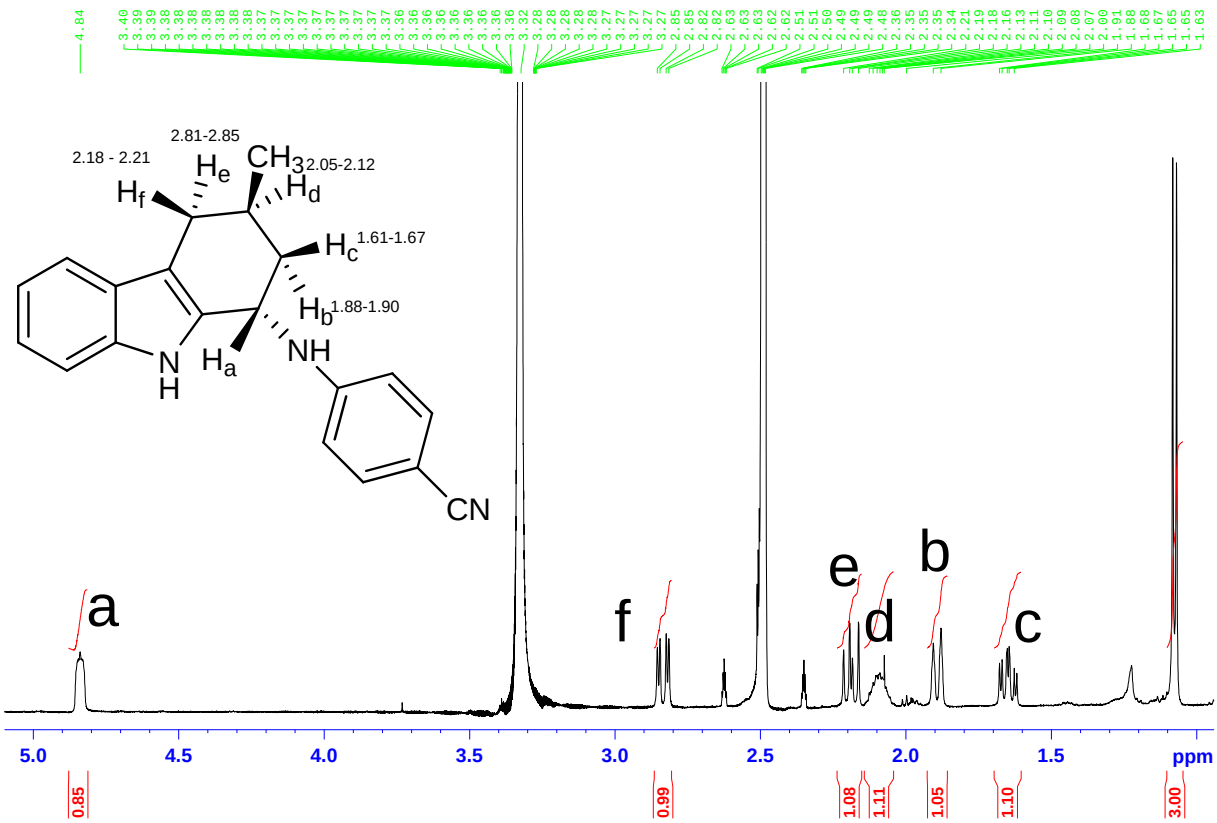
Proton H_b shows a broad doublet at 2.09-2.11 ppm with the coupling constant value of 13.4 Hz (geminal coupling with H_c). The additional coupling of H_b with H_d and H_a can be observed in H,H-COSY spectrum (Supplementary Figure S5). H_a shows a multiplet at 5.05 ppm, however, by carefully examining the spectra it can be seen that coupling constant value is not greater than 6 Hz which proves the equatorial-axial and equatorial-equatorial relation of H_a with H_b and H_c, respectively.

The absence of an axial-axial coupling constant between H_a and H_b / H_c and the presence of an axial-axial coupling constant between H_d - H_b / H_c and H_d - H_e / H_f indicates that the aniline substituent is in an axial position and the phenyl ring in an equatorial one. Accordingly, the relationship between the phenyl and aniline substituents is *trans*.



Supplementary Figure S5: Expansion of H,H COSY in DMSO of the major diastereomer of 15

The relative configuration of the major diastereomer of **16** was determined in the same way (Supplementary Figure S6, Supplementary Table S8).



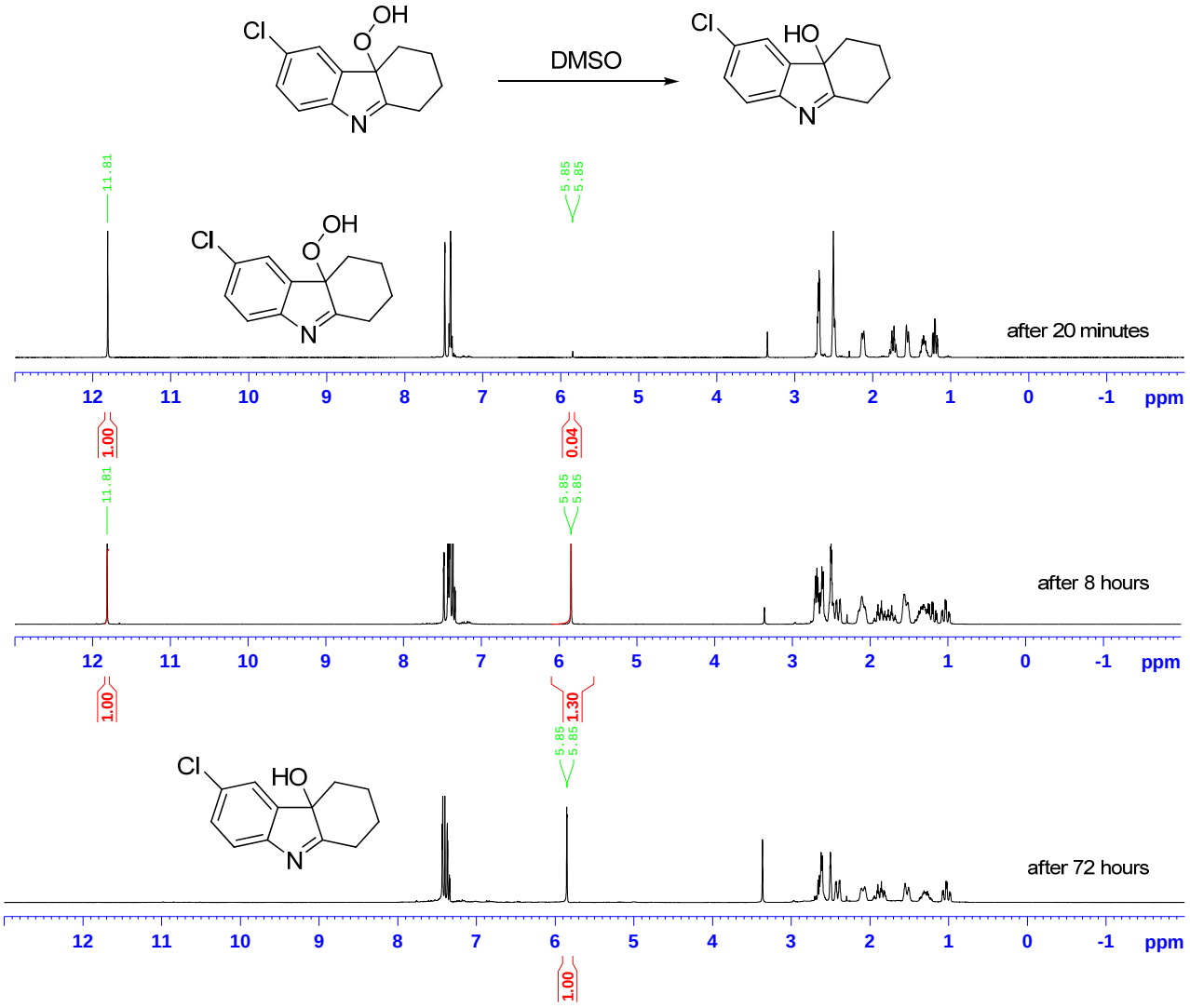
Supplementary Figure S6: Expansion of ^{1}H NMR in DMSO of the major diastereomer of 16

Supplementary Table S8: Chemical shifts and coupling constants for the major diastereomer of 16.

Entry	Proton	Chemical shift (ppm)	Multiplicity	Coupling constant (*J, Hz*)
1	c	1.61-1.67	td	13.1, 4.5
2	b	1.88-1.90	d	13.2
3	f	2.18-2.21	dd	15.4, 10.4
4	e	2.81-2.85	dd	15.2, 4.5
5	d	2.05-2.12	m	-
6	a	5.05	m	<6

Reduction of hydroperoxides to alcohols in DMSO-d_6

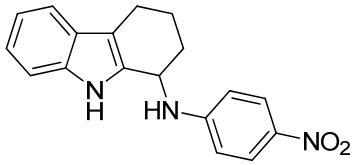
A reduction of the hydroperoxide group in **3** and its derivatives to the alcohol was observed in DMSO by measuring the ^{1}H NMR spectra at different time intervals. For example, the chloro tetrahydrocarbazole hydroperoxide was completely reduced to the corresponding alcohol after 72 hours in DMSO-d_6 (Supplementary Figure S7). This generally caused problems of obtaining clean ^{13}C-NMR spectra, since these required longer acquisition times. Alternative solvents were less suited for the characterization of the hydroperoxides, either because the solubility was too low, decomposition reactions occurred or the hydroperoxide group was not detectable.



Supplementary Figure S7 Reduction of a tetrahydrocarbazole hydroperoxide in DMSO-d_6

Characterization of the coupling products

***N*-(4-Nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (4):**



Synthesized according to Method A, R_f = 0.60 (hexane/ethy acetate 70:30).

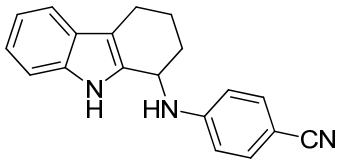
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Yellow solid, Yield: 86%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.93 (s, 1H), 8.04 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.1 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 6.83 (d, J = 8.9 Hz, 2H), 4.98-4.96 (m, 1H), 2.76-2.72 (m, 1H), 2.66-2.60 (m, 1H), 2.07-2.02 (m, 1H), 1.93-1.84 (m, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 153.6 , 136.0, 135.5, 133.0, 126.4, 126.3, 121.2, 118.2, 118.0, 111.1, 110.7, 45.6, 29.2, 20.6, 19.6 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{17}N_3O_2Na_1$ $[M+Na]^+$: 330.121296; found: 330.120960.

4-(2,3,4,9-Tetrahydro-1H-carbazol-1-ylamino)benzonitrile (5):



Synthesized according to Method B, R_f = 0.62 (hexane/ethy acetate 70:30).

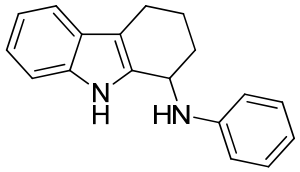
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, white solid, Yield: 80%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.89 (s, 1H), 7.48 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 6.96 (t, J = 7.2 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 4.88-4.87 (m, 1H), 2.75-2.70 (m, 1H), 2.64-2.59 (m, 1H), 2.02-1.96 (m, 1H), 1.95-1.90 (m, 1H), 1.87-1.80 (m, 2H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.2 , 136.0, 133.5, 133.3, 126.4, 121.0, 120.6, 118.1, 117.8, 111.1, 110.5, 95.4, 45.2, 28.9, 20.6, 19.6 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{19}H_{17}N_3Na_1$ $[M+Na]^+$: 310.131469; found: 310.131446

***N*-Phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (6):**



Synthesized according to Method B, R_f = 0.78 (hexane/ethy acetate 70:30).

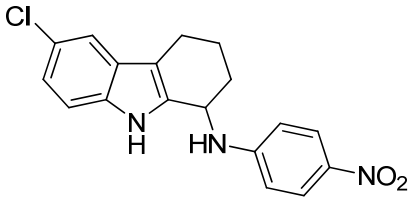
Purification: The crude product was purified via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) to afford the desired product as white solid, Yield: 60%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.84 (s, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.10 (t, J = 7.5 Hz, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.73 (d, J = 8.1 Hz, 2H), 6.54 (t, J = 7.3 Hz, 1H), 5.92 (d, J = 8.8 Hz, 1H), 4.78-4.76 (m, 1H), 2.73-2.69 (m, 1H), 2.64-2.59 (m, 1H), 2.0-1.91 (m, 2H), 1.86-1.77 (m, 2H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 147.8, 136.0, 134.8, 128.9, 126.6, 120.8, 118.0, 117.7, 15.6, 112.6, 111.0, 110.0, 45.8, 28.9, 20.8, 19.8, ppm;

HR-MS (ESIneg) m/z: M^+ calcd. for $C_{18}H_{17}N_2$ $[M-H]^-$: 261.139722; found: 261.139424

6-Chloro-*N*-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (7):



Synthesized according to Method A, R_f = 0.49 (hexane/ethy acetate 70:30).

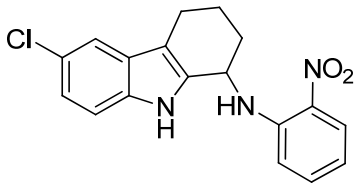
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Yellow solid, Yield: 85%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.16 (s, 1H), 8.04 (d, J = 7.5 Hz, 2H), 7.76 (d, J = 6.7 Hz, 1H), 7.41 (s, 1H), 7.30 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 7.2 Hz, 1H), 6.83 (d, J = 7.5 Hz, 2H), 4.89 (m, 1H), 2.70 (m, 1H), 2.63 (m, 1H), 2.04 (m, 1H), 1.91-1.85 (m, 3H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 153.6 , 135.7, 135.0, 134.5, 126.6, 126.3, 122.9, 121.1, 117.3, 112.6, 110.7, 45.6, 29.2, 20.4, 19.6 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{16}N_3O_2Cl_1Na_1[M+Na]^+$: 364.082326; found: 364.082303

6-Chloro-*N*-(2-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (8):



Synthesized according to Method A, R_f = 0.55 (hexane/ethy acetate 70:30).

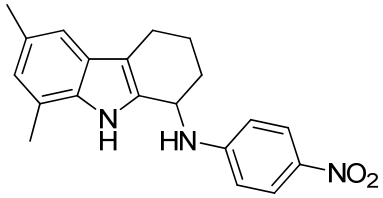
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, yellow solid, Yield: 55%;

^{1}H NMR (500 MHz, DMSO-d6): δ 11.20 (s, 1H), 8.23 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 8.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.49 (s, 1H), 7.34 (d, J = 8.6 Hz, 1H), 7.30 (d, J = 8.6 Hz, 1H), 7.08 (d, J = 8.5 Hz, 1H), 6.77 (t, J = 7.7 Hz, 1H), 5.22 (d, J = 5.7 Hz, 1H), 2.76-2.73 (m, 1H), 2.64-2.61 (m, 1H), 2.16-2.15 (m, 1H), 1.99-1.88 (m, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 144.2, 136.8, 134.8, 134.6, 131.3, 127.6, 126.3, 123.1, 121.3, 117.5, 115.8, 114.8, 112.7, 111.1, 46.2, 29.3, 20.2, 20.1 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{16}N_3O_2Cl_1Na_1[M+Na]^+$: 364.082326; found: 364.082303

6,8-Dimethyl-*N*-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (9):



Synthesized according to Method A, R_f = 0.63 (hexane/ethy acetate 70:30).

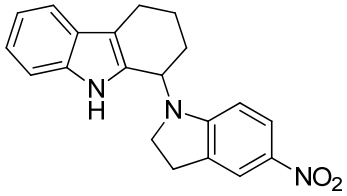
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Yellow solid, Yield: 86%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.71 (s, 1H), 8.03 (d, J = 8.6 Hz, 2H), 7.74 (d, J = 8.0 Hz, 1H), 6.90 (s, 1H), 6.81 (d, J = 8.7 Hz, 2H), 6.52 (s, 1H), 4.91-4.90 (m, 1H), 3.00 (d, J = 15.8 Hz, 1H), 2.89-2.85 (m, 1H), 2.54 (s, 3H), 2.31 (s, 3H), 1.97-1.83 (m, 4H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 153.5, 136.6, 135.5, 131.5, 129.9, 129.1, 126.3, 123.3, 121.3, 111.0, 108.8, 45.6, 28.6, 23.1, 21.3, 19.8, 19.5, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{21}N_3O_2Na_1$ $[M+Na]^+$: 358.152592; found: 358.152310

1-(5-Nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (10):



Synthesized according to Method A, R_f = 0.63 (hexane/ethy acetate 70:30).

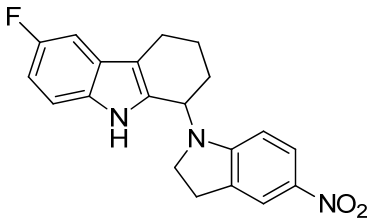
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Orange solid, Yield: 95%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.90 (s, 1H), 7.97 (dd, J = 8.9 Hz , J = 2.4 Hz, 1H), 7.86 (d, J = 2.2 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.53 (d, J = 8.9 Hz, 1H), 5.21-5.19 (m, 1H), 3.68-3.63 (q, J = 18.7 Hz , J = 9.3 Hz, 1H), 3.47-3.41 (q, J = 17.8 Hz , J = 8.8 Hz, 1H), 3.05 (t, J = 8.6 Hz, 2H), 2.70-2.64 (m, 2H), 2.09-2.02 (m, 2H), 1.91-1.85 (m, 2H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 156.5 (q), 136.3 (q), 136.2 (q), 131.5 (q), 130.7 (q), 126.6 (q), 126.4 (t), 121.1 (t), 120.1 (t), 118.3 (t), 118.0 (t), 111.6 (q), 111.1 (t), 104.0 (t), 49.9 (t), 48.8 (s), 26.3 (s), 26.1 (s), 21.9 (s), 20.4 (s) ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{19}N_3O_2Na_1$ $[M+Na]^+$: 356.136948; found: 356.137207.

6-Fluoro-1-(5-nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (11):



Synthesized according to Method A, R_f = 0.58 (hexane/ethy acetate 70:30).

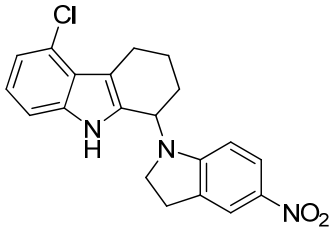
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Orange solid, Yield: 55%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.01 (s, 1H), 7.97 (dd, J = 8.9 Hz , J = 2.3 Hz, 1H), 7.87 (s, 1H), 7.25 (dd, J = 8.8 Hz, J = 4.5 Hz, 1H), 7.18 (dd, J = 9.8 Hz, J = 2.4 Hz, 1H), 6.89 (td, J = 9.2 Hz, J = 2.4 Hz, 1H), 6.53 (d, J = 8.9 Hz, 1H**),** 5.22-5.19 (m, 1H), 3.65 (q, J = 9.3Hz, 1H), 3.41 (q, J = 8.8 Hz, 1H), 3.06 (t, J = 8.7 Hz, 2H), 2.62-2.61 (m, 2H), 2.06-2.03 (m, 2H), 1.94-1.82 (m, 2H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 157.6, 156.5, 155.7, 136.4, 133.8, 132.9, 130.7, 128.8, 128.1, 126.9, 126.8, 126.4, 125.3, 120.2, 112.0, 111.9, 111.8, 109.1, 108.9, 104.0, 102.9, 102.7, 49.9, 48.7, 26.3, 25.9, 21.8, 20.3 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{18}F_1N_3O_2Na_1$ $[M+Na]^+$: 374.127526; found: 374.127686

5-Chloro-1-(5-nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (12):



Synthesized according to Method A, R_f = 0.60 (hexane/ethy acetate 70:30).

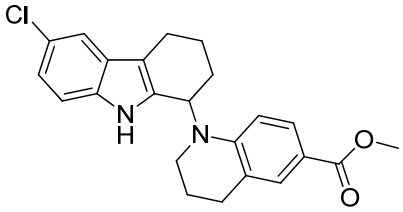
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, Orange solid, Yield: 70%;

^{1}H NMR (500 MHz, DMSO-d6): δ 11.34 (s, 1H), 7.97 (dd, J = 8.9 Hz , J = 1.8 Hz, 1H), 7.84 (s, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 6.99 (t, J = 7.7 Hz, 1H), 6.49 (d, J = 8.9 Hz, 1H**),** 5.16-5.15 (m, 1H), 3.68-3.62 (q, J = 9.2 Hz, 1H), 3.48-3.42 (q, J = 8.8 Hz, 1H), 3.05 (t, J = 8.6 Hz, 2H), 2.74-2.67 (m, 2H), 2.08-1.92 (m, 2H), 1.86-1.85 (m, 2H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 156.4, 136.0, 133.1, 132.8, 130.8, 128.6, 126.5, 121.0, 120.0, 119.4, 117.1, 115.6, 113.2, 103.7, 49.3, 49.2, 26.4, 26.2, 21.2, 20.4 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{18}N_3Cl_1O_2Na_1$ $[M+Na]^+$: 390.097970; found: 390.097825

Methyl 1-(6-chloro-2,3,4,9-tetrahydro-1H-carbazol-1-yl)-1,2,3,4-tetrahydroquinoline-6-carboxylate (13):



Synthesized according to Method A, R_f = 0.48 (hexane/ethy acetate 70:30).

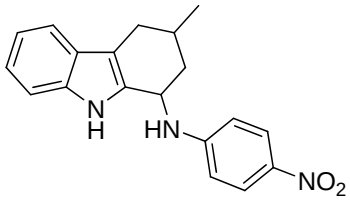
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. White solid, Yield: 55%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.07 (s, 1H), 7.63 (m (br), 1H), 7.56 (s, 1H), 7.45 (s 1H), 7.26 (d, J = 8.5 Hz, 1H), 7.03 (dd, J = 8.5 Hz, J = 1.1 Hz, 1H), 6.98 (m, br, 1H**),** 5.40 (m, br, 1H), 3.75 (s, 3H), 3.04-2.91 (m, 2H), 2.75-2.66 (m, 4H), 2.09-1.70 (m, 6H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 166.3, 134.6, 130.2, 129.0, 127.9, 122.9, 121.8, 120.7, 117.1, 115.3, 112.5, 109.7, 109.6, 51.1, 27.7, 21.8, 20.8, 20.3, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{23}H_{23}Cl_1N_2O_2Na_1$ $[M+Na]^+$: 417.134022; found: 417.134037

3-Methyl-*N*-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (14):



Synthesized according to Method A, R_f = 0.50 (hexane/ethy acetate 70:30) as a mixture of diastereomers (*trans*:*cis* 83:17) in 67% yield. The ratio of diastereomers was determined by ^{1}H-NMR analysis of the crude reaction mixture, the major diastereomer was assigned as *trans* based on comparison with product **20**.

Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Yellow solid, Yield: 67%.

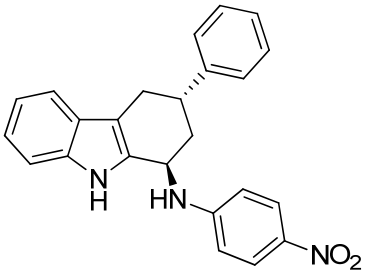
Major Diastereomer (*trans*): ^{1}H NMR (500 MHz, DMSO-d6): 10.98 (s, 1H), 8.04 (d, J = 8.7 Hz, 2H), 7.77 (d, J = 7.8, 1H), 7.45 (d, J = 7.8, 1H), 7.30 (d, J = 8.1, 1H), 7.07 (t, J = 7.4, 1H), 6.97 (t, J =.7.4 Hz, 1H), 6.81 (d, J =.8.8 Hz, 2H), 4.-94 (br, m, 1H), 2.87 (dd, J = 15.3 Hz, J = 4.5 Hz, 1H), 2.22 (dd, J = 15.3, J = 10.4, 1H), 2.3-2.10 (m, 1H), 1.93 (d, J = 13.2 Hz, 1H), 1.72 (dt, J = 13.0 Hz, J = 4.3 Hz , 1H) 1.10 (d, J = 6.6 Hz, 3H)ppm;

Minor Diastereomer (*cis*): ^{1}H NMR (500 MHz, DMSO-d6): 10.85 (s, 1H), 8.04-803 (m, 2H), 7.79 (d, J = 8.8, 1H), 7.40 (d, J = 7.7, 1H), 7.31-7.29 (m, 1H), 7.06-7.02 (m, 1H), 6.97-6.94 (m, 1H), 6.84-6.81 (m, 2H), 5.11-5.09 (br, m, 1H), 2.87-2.81 (m, 1H), 2.28-2.19 (m, 2H), 2.3-2.12-2.10 (m, 1H), 1.46-1.39 (3, 1H), 1.14 (d, J = 6.6 Hz, 3H)ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 153.2, 136.4, 135.5, 132.4, 126.3, 126.2, 121.3, 118.2, 118.0, 111.1,111.0, 45.1, 37.2, 29.2, 25.1, 21.6 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{19}H_{19}N_3O_2Na_1$ $[M+Na]^+$: 344.136948; found: 344.137078

_N_-(4-Nitrophenyl)-3-phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (15):



Synthesized according to Method A, reaction time was 12 h, R_f = 0.60 (hexane/ethy acetate 70:30).

Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, yielding a yellow solid as a mixture of diastereomers (*trans*:*cis* 91:09) in 67% yield. The ratio of diastereomers was determined by ^{1}H-NMR analysis of the crude reaction mixture. The major diastereomer could be isolated via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) in 45% yield.

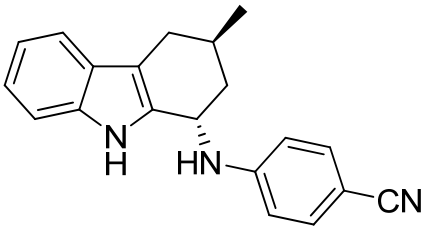
Major Diastereomer (*trans*):

^{1}H NMR (500 MHz, DMSO-d6): δ 11.08 (s, 1H), 8.03 (d J = 9.0 Hz, 2H), 7.91(d, J = 7.7, 1H), 7.48(d, J = 7.8, 1H), 7.35-7.31 (m, 5H), 7.24-7.21 (m, 1H), 7.10 (t, J =.8.1 Hz), 6.90 (t, J =.7.8 Hz), 6.84 (d, J = 9.1, 2H), 5.06-5.05 (m, 1H), 3.28-3.22 (m, 1H), 3.05 (dd, J = 15.4, J = 4.7, 1H), 2.74 (dd, J = 15.4, J = 11.3, 1H), 2.31 (dt, J = 13.0, J = 4.2, 1H), 2.10 (d, J = 13.4, 1H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 153.1, 145.9, 136.4, 135.7, 132.1, 128.4, 127.0, 126.8, 126.3, 126.2, 126.1, 121.5, 118.4, 118.1, 111.1, 111.0, 45.2, 36.34, 35.7, 29.3 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{24}H_{21}N_3O_2Na_1$ $[M+Na]^+$: 406.152595; found: 406.152717

4-(3-Methyl-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (16):



Synthesized according to Method A, R_f = 0.50 (hexane/ethy acetate 70:30).

Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, yielding a white solid as a mixture of diastereomers

(*trans*:*cis* 65:35) in 80% yield. The ratio of diastereomers was determined by ^{1}H-NMR analysis of the crude reaction mixture. The major diastereomer could be isolated via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) in 47% yield.

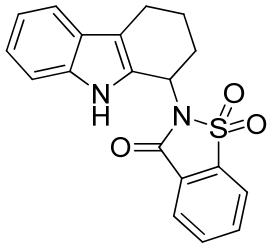
Major Diastereomer (*trans*):

^{1}H NMR (500 MHz, DMSO-d6): 10.93 (s, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 7.8, 1H), 7.27 (dt, *J* = 7.8, *J* = 0.8, 1H), 7.13 (d, *J* = 8.0, 1H), 7.06 (td, *J* = 8.1, *J* = 1.1, 1H), 6.96 (td, *J* = 7.9 Hz, *J* = 0.9, 1H), 6.79 (d, *J* =.8.9 Hz, 2H), 4.87-4.84 (m, 1H), 2.85 (dd, *J* = 15.3 Hz, *J* = 4.5 Hz, 1H), 2.21 (dd, *J* = 15.1, *J* = 10.5, 1H), 2.13-2.09 (m, 1H), 1.91 (d, *J* = 13.2 Hz, 1H), 1.67 (dt, *J* = 13.1 Hz, *J* = 4.4 Hz , 1H), 1.09 (d, *J* = 6.5 Hz, 3H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 150.9, 136.4, 133.4, 132.9, 126.2, 121.2, 120.7, 118.2, 117.9, 111.1, 110.9, 95.4, 44.7, 36.7, 29.3, 25.1, 21.6, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{19}N_3Na_1$ $[M+Na]^+$: 324.147117; found: 324.146804

1-Saccharinyl-2,3,4,9-tetrahydro-1H-carbazole (17):



Synthesized according to Method A (without TFA), R_f = 0.50 (hexane/ethy acetate 70:30).

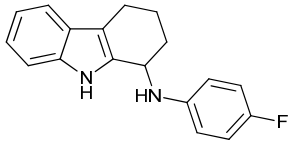
Purification: The desired product was precipitated by using a mixture of hexane/ethyl acetate. Yield: 52%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.80 (s, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 8.05 (t, *J* = 7.6 Hz, 1H), 8.00 (t, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.54 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 5.71 (t, *J* = 7.6 Hz, 1H), 2.71 (m, 2H), 2.44 (q, *J* = 8.3 Hz, 1H), 2.28-2.26 (m, 1H), 2.19-2.18 (m, 1H), 1.96-1.90 (m, 1H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 158.2 , 136.9, 136.2, 135.5, 135.0, 129.7, 126.6, 124.9, 121.2, 121.1, 118.3, 118.0, 111.7, 111.1, 47.6, 28.4, 22.2, 20.2 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{19}H_{16}N_2O_3S_1Na_1$ $[M+Na]^+$: 375.077386; found: 375.077706

***N*-(4-Fluorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (18):**



Synthesized according to Method B, R_f = 0.79 (hexane/ethy acetate 70:30).

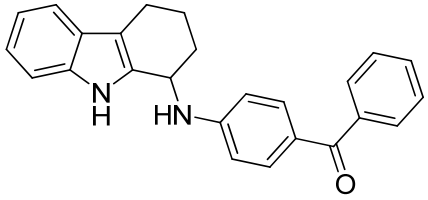
Purification: The crude product was purified via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) to afford the desired product as white solid, Yield: 65%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.83 (s, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.04 (t, J = 7.9 Hz, 1H), 6.97-6.92 (m, 3H), 6.73 (dd, J = 8.9 Hz, J = 4.6 Hz, 2H), 5.88 (d, J = 8.9 Hz, 1H), 4.74-4.71 (m, 1H), 2.73-2.68 (m, 1H), 2.64-2.59 (m, 1H), 1.98-1.93 (m, 2H), 1.86-1.77 (m, 2H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 155.0, 153.2, 144.5, 136.0, 134.8, 126.6, 120.8, 118.0, 117.7, 115.3, 115.1, 113.4, 113.3, 111.0, 110.0, 46.3, 28.8, 20.8, 19.8 ppm;

HR-MS EI (DE) m/z: M^+ calcd. for $C_{18}H_{17}N_2F_1$ $[M]^+$: 280.137580; found: 280.137313

Phenyl (4-(2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)phenyl)methanone (19):



Synthesized according to Method A, R_f = 0.62 (hexane/ethy acetate 70:30).

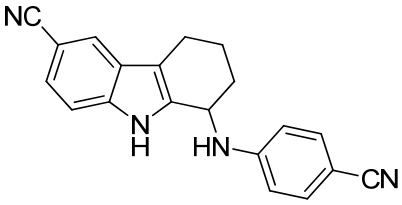
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate, white solid, Yield: 70%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.91 (s, 1H), 7.64-7.58 (m, 5H), 7.53 (t, J = 7.6 Hz, 2H), 7.43 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1 H), 7.18 (d, J= 8.3 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 6.82 (d, J = 8.8 Hz, 2H), 4.93-4.92 (m, 1H), 2.76-2.71 (m, 1H), 2.65-2.61 (m, 1H), 2.05-1.84 (m, 4H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 193.3, 152.0, 139.0, 136.1, 133.6, 132.5, 131.1, 128.8, 128.2, 126.5, 123.7, 121.0, 118.2, 117.9, 111.1, 110.5, 45.5, 29.2, 20.7, 19.7, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{25}H_{22}N_2Na_1O_1$ $[M+Na]^+$: 389.162429; found: 389.162734

1-(4-Cyanophenylamino)-2,3,4,9-tetrahydro-1H-carbazole-6-carbonitrile (20):



Synthesized according to Method B, reaction time was 12 h, R_f = 0.43 (hexane/ethy acetate 70:30).

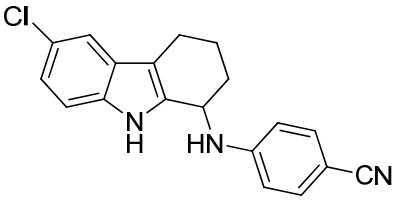
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. White solid, Yield: 50%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.56 (s, 1H), 7.99 (s, 1H), 7.49 (d, J = 8.3 Hz, 2H), 7.42 (q, J = 18.6 Hz, J = 8.4 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 2H), 4.94-4.92 (m, 1H), 2.76-2.73 (3, 1H), 2.66-2.63 (m, 1H), 2.04-1.99 (m, 1H), 1.91-1.82 (m, 3H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.2 , 137.9, 136.5, 133.5, 126.4, 123.9, 123.7, 120.9, 120.6, 112.3, 111.8, 100.1, 95.8, 45.2, 28.9, 20.3, 19.5 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{16}N_4Na_1$ $[M+Na]^+$: 335.126711; found: 335.126902

4-(6-Chloro-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (21):



Synthesized according to Method B, R_f = 0.60 (hexane/ethy acetate 70:30).

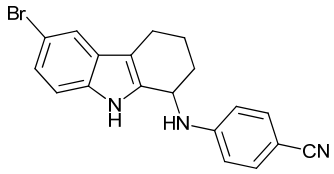
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. White solid, Yield: 88%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.12 (s, 1H), 7.48 (t, J = 8.5 Hz, 3H), 7.30 (d, J = 8.5 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.05 (dd, J = 8.5 Hz, J = 1.8Hz, 1H), 6.81 (d, J = 8.7 Hz, 2H), 4.90-4.88 (m, 1H), 2.71-2.68 (m, 1H), 2.62-2.58 (m, 1H), 2.03-1.98 (m, 1H), 1.94-1.87 (m, 1H) 1.83-1.81 (m, 2H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.2 , 135.6, 134.5, 133.4, 127.6, 122.8, 120.9, 120.6, 117.2, 112.6, 110.5, 95.6, 45.3, 29.0, 20.4, 19.7 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{19}H_{16}N_3Cl_1O_2Na_1[M+Na]^+$: 344.092495; found: 344.092205

4-(6-Bromo-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (22):



Synthesized according to Method A, reaction time was 12 h, r_f = 0.44 (EtOAc/Isohexane, 30:70).

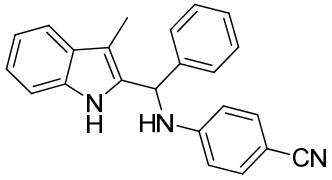
Purification: Over the course of the reaction, the precipitation of a large proportion of the desired coupling product was observed. The complete precipitation could be achieved by using a mixture of hexane/ethyl acetate. Off white solid, Yield: 80%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.14 (s, 1H), 7.61 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.16 (t, J = 8.6 Hz, 2 H), 6.81 (d, J = 8.6 Hz, 2H), 4.88-4.90 (m, 1H), 2.68-2.71 (m, 1H), 2.58-2.61 (m, 1H), 1.98-2.03 (m, 1H), 1.89-1.92 (m, 1H), 1.81-1.83 (m, 2H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.2 (q), 135.4.0 (q), 134.7 (q), 133.4 (t), 128.4 (t), 123.5 (t), 120.7 (q), 120.2 (t), 113.0 (t), 110.8 (q), 110.5 (q), 95.7 (q), 45.3 (q), 29.0 (s), 20.4 (s), 19.7 (s) ppm;

HRMS-(EI) (m/z): M+ calcd for $C_{19}H_{16}Br_1N_3Na_1$, 388.041988; found 388.041996.

4-((3-Methyl-1H-indol-2-yl)(phenyl)methylamino)benzonitrile (23):



Synthesized according to Method B, R_f = 0.45 (hexane/ethy acetate 70:30).

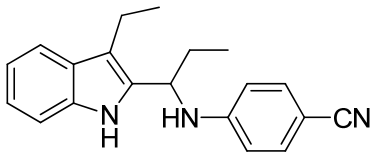
Purification: The crude product was purified via column chromatography (aluminium oxide, hexane/ethylacetate 90:10) to afford the desired product as white solid, Yield: 67%;

^{1}H NMR (500 MHz, DMSO-d6): δ 10.74 (s, 1H), 7.46-7.41 (m, 5H), 7.36 (t, J = 7.3 Hz, 2H), 7.32 (d, J = 5.0 Hz, 1H), 7.28 (d, J = 7.6 Hz, 2H), 7.02 (t, J = 7.4 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.74 (d, J = 8.1 Hz, 2H), 5.93 (d, J = 4.9 Hz, 1H), 2.24 (s, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.3, 140.7, 135.4, 134.4, 133.1, 128.6, 128.5, 127.3, 127.2, 120.9, 120.4, 118.2, 117.9, 112.9, 111.1, 106.1, 96.7, 53.8, 8.4 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{21}N_3Na_1$ $[M+Na]^+$: 360.147112; found: 360.147287

4-(1-(3-Ethyl-1H-indol-2-yl)propylamino)benzonitrile (24):



Synthesized according to Method B, R_f = 0.45 (hexane/ethy acetate 70:30).

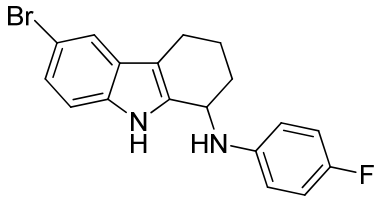
Purification: The crude product was purified via column chromatography (florisil, hexane/ethylacetate/triethylamine 90:10) to afford the desired product as white solid, Yield: 60%.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.61 (s, 1H), 7.43 (d, J = 8.11 Hz, 1H), 7.39 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.00 (t, J = 7.2 Hz, 1H), 6.93 (t, J = 7.2 Hz, 1H), 6.90 (d, J = 6.2 Hz, 1H), 6.6 (d, J = 6.7 Hz, 2H), 4.57 (q, J = 6.8 Hz, 1H), 2.80 (qd, J = 7.3 Hz , J = 3.3 Hz, 2H), 1.98 (s, J = 7.2 Hz, 1H), 1.86 (s, J = 7.2 Hz, 1H), 1.17 (t, J = 7.5 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 151.5, 135.4, 134.7, 133.1, 127.7, 120.5, 118.1, 118.0, 112.7, 112.3, 111.0, 96.0, 51.1., 28.7, 16.9, 15.7, 10.9 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{20}H_{21}N_3Na_1$ $[M+Na]^+$: 326.162768; found: 326.162661

6-Bromo-*N*-(4-fluorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (25):



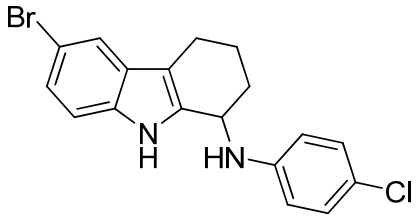
Synthesized according to Method B, reaction time was 12 h, R_f = 0.78 (hexane/ethy acetate 70:30).

Purification: The crude product was purified via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) to afford the desired product as white solid, Yield: 55%;

^{1}H NMR (500 MHz, DMSO-d6): δ 11.09 (s, 1H), 7.58 (d, J = 1.7 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 7.14 (dd, J = 8.5 Hz, J = 1.8 Hz , 1H), 6.94 (t, J = 9.8 Hz, J = 8.9 Hz, 2H), 6.72 (dd, J = 4.59 Hz, J = 8.9 Hz, 2H), 5.91 (d, J = 8.8 Hz, 1H), 4.75-4.74 (m, 1H), 2.69-2.65 (m, 1H), 2.61-2.57 (m, 1H), 2.00-1.91 (m, 2H), 1.79-1.77 (m, 3H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 155.1, 153.3, 144.4, 136.7, 134.7, 128.5, 123.2, 120.1, 115.3, 115.2, 113.5., 113.4, 113.0, 110.6, 110.0, 46.4, 28.8, 20.5, 19.8 ppm;

6-Bromo-*N*-(4-chlorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (26):



Synthesized according to Method B, reaction time was 12 h, R_f = 0.78 (hexane/ethy acetate 70:30).

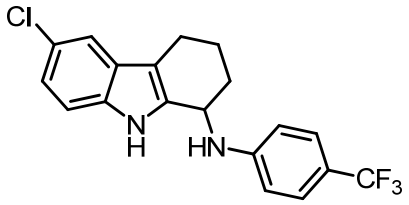
Purification: The crude product was purified via column chromatography (Aluminium oxide, hexane/ethylacetate 90:5) to afford the desired product as white solid, Yield: 70%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.11 (s, 1H), 7.59 (d, J = 1.8 Hz, 1H), 7.26 (d, J = 8.5 Hz, 1H), 7.15 (dd, J = 8.5 Hz, J = 1.9 Hz , 1H), 7.12 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 8.9 Hz, 2H), 6.23 (d, J = 8.8 Hz, 1H), 4.77-4.75 (m, 1H), 2.69-2.66 (m, 1H), 2.62-2.57 (m, 1H), 1.99-1.91 (m, 2H), 1.81-1.78 (m, 2H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 146.7, 136.3, 134.7, 128.6, 128.4, 123.2, 120.1, 118.9, 113.9, 113.0, 110.7, 110.1, 45.9, 28.8, 20.5, 19.8, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{16}Br_1Cl_1N_2$ $[M]^+$: 374.018554; found: 374.018317

6-Chloro-*N*-(4-(trifluoromethyl)phenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (27):



Synthesized according to Method B, R_f = 0.78 (hexane/ethy acetate 70:30).

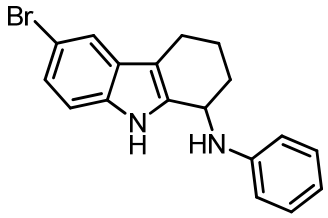
Purification: The crude product was purified via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) to afford the desired product as white solid, Yield: 68%.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.11 (s, 1H), 7.46 (d, J = 1.9 Hz, 2H), 7.40 (d, J = 8.5 Hz, 1H),7.31 (d, J = 8.5 Hz, 1H), 7.05 (dd, J = 8.5 Hz, J = 2.0 Hz , 1H), 6.83 (t, J = 8.2 Hz, 3H), 4.88-4.86 (m, 1H), 2.71-2.67 (m, 1H), 2.63-2.61 (m, 1H), 2.02-1.99 (m, 1H), 1.94-1.92 (m, 1H), 1.85-1.81 (m, 2H) ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 150.7, 136.0, 134.5, 127.7, 126.3, 126.2, 125.2 (quatret), 122.8, 120.8, 117.2, 115.1 (quatret), 112.6, 111.7, 110.4, 45.5, 28.9, 20.5, 19.7, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{19}H_{16}Cl_1F_3N_2Na_1$ $[M+Na]^+$: 387.084631; found: 387.084784

6-Bromo-*N*-phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (28):



Synthesized according to Method B, reaction time was 12 h, R_f = 0.79 (hexane/ethy acetate 70:30).

Purification: The crude product was purified via column chromatography (silica gel, hexane/ethylacetate/triethylamine 90:5:5) to afford the desired product as white solid, Yield: 60%

^{1}H NMR (500 MHz, DMSO-d6): δ 11.10 (s, 1H), 7.59 (d, J = 1.7 Hz, 1H), 7.26 (d, J=8.56 Hz, 1 H), 7.15 (dd, J= 8.51 Hz , J=1.90 Hz, 1 H), 7.10 (t, J = 7.4 Hz, 2H), 6.73 (d, J = 7.9 Hz, 2H), 6.56 (t, J = 7.3 Hz, 1H), 5.97 (d, J = 8.9 Hz, 1H), 4.79-4.77 (m, 1H), 2.70-2.66 (m, 1H), 2.62-2.57 (m, 1H), 2.02-1.93 (m, 2H), 1.85-1.77 (m, 2H), ppm;

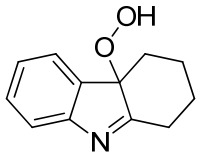
^{13}C NMR (125 MHz, DMSO-d6): δ 147.8, 136.8, 134.7, 128.5, 123.1, 120.1, 115.8, 113.0, 112.6, 110.6, 110.0, 45.9, 28.9, 20.5, 19.9, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{17}Br_1N_2Na_1$ $[M+Na]^+$: 363.046740; found: 363.046458

Characterization of hydroperoxides

Low solubility and stability (in acidic and basic solvents) are the main problems associated with these hydroperoxides. DMSO was found to be a suitable solvent for the measurement of NMR spectra. However, in DMSO these hydroperoxides are reduced to the corresponding alcohol (see above). Therefore, it was not possible to measure clean carbon spectra for some of these compounds.

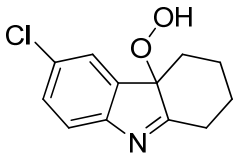
4a-Hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (3):



Synthesized according to the general procedure for the synthesis of hydroperoxides.
Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.66 (s, 1H), 7.42 (dd, J = 10.2 Hz , J = 7.5 Hz, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 7.4 Hz , 1H), 2.71-2.68 (m, 2H), 2.50-2.47 (m, 1H), 2.13(d, J = 13.5 Hz, 1H), 1.76 (ddt, J = 27.0 Hz, J = 13.5 Hz, J = 3.5 Hz, 1H), 1.55 (d, J = 13.4 Hz, 1H), 1.39-1.29 (m, 1H), 1.17 (dt, J = 14.2 Hz, J = 4.1 Hz, 1H), ppm;
^{13}C NMR (125 MHz, DMSO-d6): δ 184.1, 153.9, 138.9, 129.1, 125.0, 122.7, 119.7, 91.1, 35.3, 29.2, 27.9, 20.3, ppm;
HR-MS EI (DE) m/z: M^+ calcd. for $C_{12}H_{13}N_1O_2[M]^+$: 203.094626; found: 203.094831

6-Chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole:



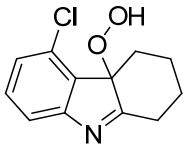
Synthesized according to the general procedure for the synthesis of hydroperoxides.
Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.80 (s, 1H), 7.48 (d, J = 1.2 Hz, 1H), 7.43-7.40 (m, 2H), 2.71-2.69 (m, 2H), 2.50-2.49 (m, 1H), 2.13(d, J = 12.0 Hz, 1H), 1.74 (qt, J = 13.5 Hz, J = 3.5 Hz, 1H), 1.55 (d, J = 13.4 Hz, 1H), 1.39-1.30 (m, 1H), 1.20 (dt, J = 14.2 Hz, J = 4.1 Hz, 1H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 185.2, 152.7, 141.1, 129.8, 129.0, 123.2, 121.0, 91.4, 35.1, 29.3, 27.9, 20.2 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{12}H_{12}N_1O_2Cl_1Na_1$ $[M+Na]^+$: 260.044876; found: 260.044990

5-Chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole



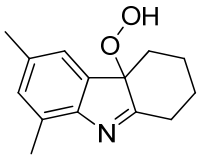
Synthesized according to general procedure for the synthesis of hydroperoxide.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.82 (s, 1H), 7.40 (t, J = 7.1 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 2.76-2.72 (m, 2H), 2.48-2.45 (m, 1H), 2.16-2.13 (m, 1H), 1.75 (qt, J = 13.5 Hz, 3.5 Hz, 1H), 1.56 (d, J = 13.4 Hz, 1H), 1.26-1.21 (m, 1H), 1.21 (dt, J = 14.2 Hz, J = 4.4 Hz, 1H), ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{12}H_{12}N_1O_2Cl_1Na_1$ $[M+Na]^+$: 260.044876; found: 260.044990

4a-Hydroperoxy-6,8-dimethyl-2,3,4,4a-tetrahydro-1H-carbazole



Synthesized according to general procedure for the synthesis of hydroperoxide.

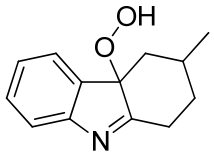
Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 10.35 (s, 1H), 6.82 (s, 1H), 6.45 (s, 1H), 2.86 (m, 2H), 2.63 (m, 2H), 2.49 (s, 3H), 2.28 (s, 3H), 1.56 (d, J = 13.2 Hz, 1H), 1.77-1.75 (m, 4H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 136.0, 132.7, 128.6, 128.3, 124.1, 121.0, 108.3, 108.2, 23.5, 23.1, 22.9, 22.4, 21.2, 19.4, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{14}H_{17}N_1O_2Na_1$ $[M+Na]^+$: 254.115174; found: 254.115345

4a-Hydroperoxy-3-methyl-2,3,4,4a-tetrahydro-1H-carbazole:



Synthesized according to the general procedure for the synthesis of hydroperoxides.

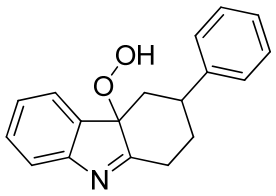
Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.77 (s, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.34 (dt, , J = 7.5 Hz, J = 1.0 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 2.76 (dt, , J = 13.2 Hz, J = 5.4 Hz 1H), 2.65-2.62 (m, 1H), 2.41(d, J = 14.4 Hz, 1H), 2.08-2.06 (m, 2H), 1.09 (dq, J = 13.4 Hz, J = 4.1 Hz, 1H), 0.94 (d, J = 14.4 Hz, 1H), 0.89 (d, J = 6.5 Hz, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 184.3, 154.0, 138.8, 129.1, 125.1, 122.6, 119.7, 91.2, 42.9, 36.1, 28.5, 26.9, 20.4, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{13}H_{15}N_1O_2Na_1$ $[M+Na]^+$: 240.099500; found: 240.099752

4a-Hydroperoxy-3-phenyl-2,3,4,4a-tetrahydro-1H-carbazole:



Synthesized according to the general procedure for the synthesis of hydroperoxides.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

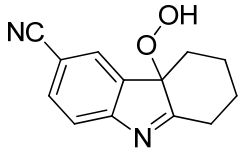
^{1}H NMR (500 MHz, DMSO-d6): δ 11.77 (s, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.34 (dt, , J = 7.5 Hz, J = 1.0 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 2.76 (dt, , J = 13.2 Hz, J = 5.4 Hz 1H), 2.65-

2.62 (m, 1H), 2.41(d, *J* = 14.4 Hz, 1H), 2.08-2.06 (m, 2H), 1.09 (dq, *J* = 13.4 Hz, *J* = 4.1 Hz, 1H), 0.94 (d, *J* = 14.4 Hz, 1H), 0.89 (d, *J* = 6.5 Hz, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 183.3, 154.1, 144.0, 138.5, 139.3, 128.4, 127.0, 126.3, 125.2, 122.9, 119.8, 91.1, 41.4, 38.1, 35.5, 28.9, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{18}H_{17}N_1O_2Na_1$ $[M+Na]^+$: 302.115151; found: 302.115128

4a-Hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole-6-carbonitrile:



Synthesized according to the general procedure for the synthesis of hydroperoxides, but using a 500 watt halogen lamp at -40°C.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.88 (s, 1H), 7.1 (s, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 2.77-2.74 (m, 2H), 2.53-2.52 (m, 1H), 2.16 (d, *J* = 11.9 Hz, 1H), 1.75 (q, *J* = 10.2 Hz, 1H), 1.57 (d, *J* = 13.0 Hz, 1H), 1.41-1.32 (m, 1H), 1.20 (dt, *J* = 14.2 Hz, *J* = 4.0 Hz, 1H), ppm;

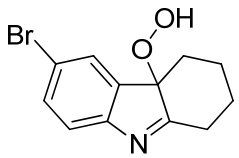
^{13}C NMR (125 MHz, DMSO-d6): δ 188.9, 157.6 140.0, 134.6, 126.5, 120.8, 119.1, 107.5, 93.3, 29.5, 27.9, 20.1 ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{13}H_{12}N_2O_2Na_1$ $[M+Na]^+$: 251.07097; found: 251.079211

6-Bromo-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole:

Synthesized according to the general procedure for the synthesis of hydroperoxides.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.



^{1}H NMR (500 MHz, DMSO-d6): δ 11.78 (s, 1H), 7.41 (dd, *J* = 8.1 Hz, *J* = 4.5 Hz , 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 9.0 Hz, 1H), 2.70-2.67 (m, 2H), 2.50-2.46 (m, 1H), 2.12 (d, *J*

= 12.2 Hz, 1H), 1.74 (q, *J* = 13.5 Hz, 1H), 1.56 (d, *J* = 13.2 Hz, 1H), 1.38-1.30 (m, 1H), 1.20 (dt, *J* = 14.2 Hz, *J* = 4.0 Hz, 1H), ppm;

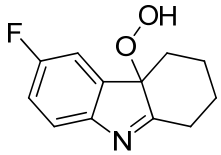
^{13}C NMR (125 MHz, DMSO-d6): δ 184.5, 184.4, 161.3, 159.4, 150.0, 141.1, 141.0, 120.6, 120.5, 115.4, 115.2, 110.9, 110.6, 91.4, 35.1, 29.2, 27.9, 20.2, ppm;

HR-MS (ESIpos) m/z: M^+ calcd. for $C_{12}H_{12}Br_1N_1O_2Na_1$ $[M+Na]^+$: 303.994376; found: 303.994445

6-Fluoro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole:

Synthesized according to the general procedure for the synthesis of hydroperoxides.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.



^{1}H NMR (500 MHz, DMSO-d6): δ 11.81 (s, 1H), 7.61 (s , 1H), 7.54 (d, *J* = 8.10 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 2.69 (dd, *J* = 8.7 Hz, *J* = 3.7 Hz, 2H), 2.50-2.48 (m, 1H), 2.12 (d, *J* = 12.3 Hz, 1H), 1.74 (q, *J* = 13.5 Hz, 1H), 1.55 (d, *J* = 13.1 Hz, 1H), 1.36-1.32 (m, 1H), 1.21 (dt, *J* = 14.2 Hz, *J* = 3.8 Hz, 1H), ppm;

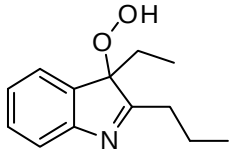
^{13}C NMR (125 MHz, DMSO-d6): δ 185.0, 153.0, 141.4, 131.9, 125.9, 121.5, 118.1, 91.4, 35.1, 29.2, 27.8, 20.2, ppm;

HR-MS EI(DE) m/z: M^+ calcd. for $C_{12}H_{12}F_1N_1O_2$ [M]: 221.08507; found: 221.085092

3-Ethyl-3-hydroperoxy-2-propyl-3H-indole:

Synthesized according to the general procedure for the synthesis of hydroperoxides but using a 500 watt halogen lamp at -40°C.

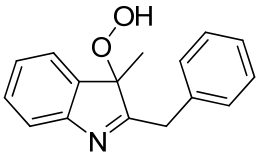
Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.



^{1}H NMR (500 MHz, DMSO-d6): δ 11.60 (s, 1H), 7.38-7.35 (m, 2H), 7.33 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.20 (td, *J* = 7.3 Hz, *J* = 0.90 Hz, 1H), 2.60 (dt, *J* = 17.9 Hz, *J* = 7.3 Hz, 1H), 2.40 (dt, *J* = 18.0 Hz, *J* = 7.4 Hz, 1H), 1.94-1.89 (m, 1H), 1.80-1.70 (m, 3H), ppm;

HR-MS (CI(DE)) m/z: M^+ calcd. for $C_{16}H_{15}N_1O_2Na_1$ $[M+H]^+$: 220.133752; found: 220.133523

2-Benzyl-3-hydroperoxy-3-methyl-3H-indole:



Synthesized according to the general procedure for the synthesis of hydroperoxides but using 500 watt halogen lamp at -40°C.

Purification: The crude product was purified by simple filtration as pink solid in quantitative yield.

^{1}H NMR (500 MHz, DMSO-d6): δ 11.81 (s, 1H), 7.42 (d, J = 7.1 Hz, 1H), 7.36-7.30 (m, 6H), 7.26-7.19 (m, 2H), 3.94 (q, J = 16.0 Hz, 2H), 3.04 (s, 3H), ppm;

^{13}C NMR (125 MHz, DMSO-d6): δ 184.7, 153.2, 138.6, 136.6, 129.7, 129.3, 128.1, 126.3, 125.5, 122.5, 119.8, 92.7, 34.4, 19.0 ppm;

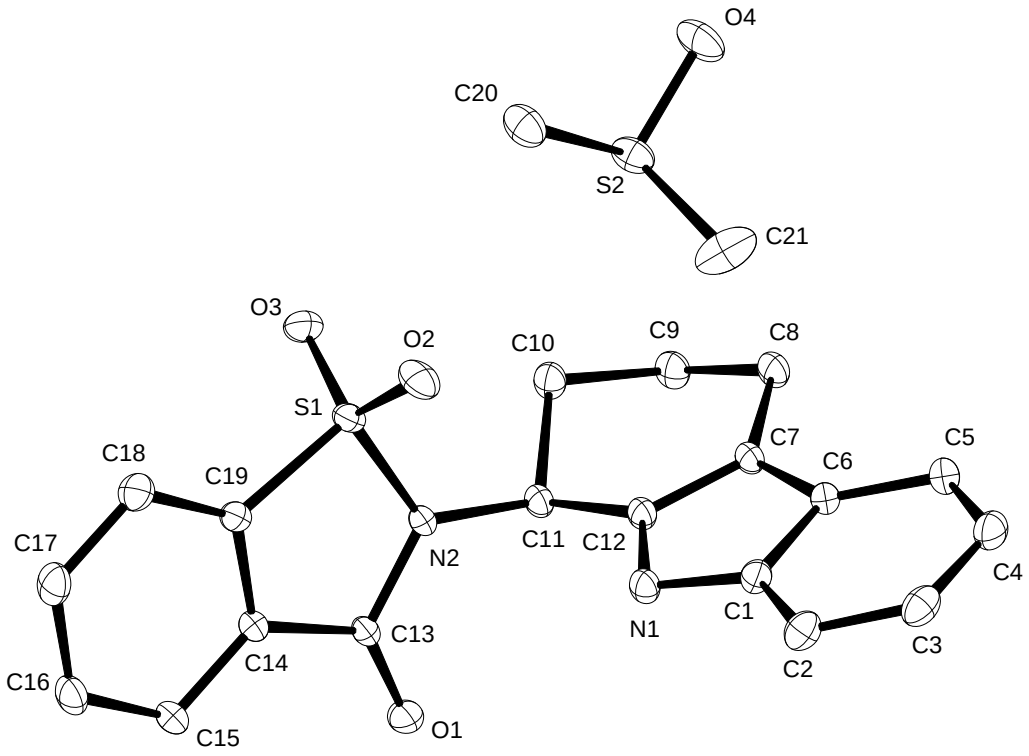
HR-MS (ESIpos) m/z: M^+ calcd. for $C_{16}H_{15}N_1O_2Na_1$ $[M+Na]^+$: 276.099501; found: 276.099676

X-ray Data

1-Saccharinyl-2,3,4,9-tetrahydro-1H-carbazole (17)

Crystallized from DMSO-d_6.

CCDC reference number	914987	
Empirical formula	$C_{19}H_{16}N_2O_3S \cdot C_2H_6SO$	
Color	colourless	
Formula weight	430.53 g · mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	MONOCLINIC	
Space group	**$P2_1/n$, (no. 14)**	
Unit cell dimensions	a = 11.338(2) Å	α= 90°.
	b = 7.9222(17) Å	β= 94.389(4)°.
	c = 22.498(5) Å	γ = 90°.
Volume	2014.9(7) $Å^3$	
Z	4	
Density (calculated)	1.419 Mg · m^{-3}	
Absorption coefficient	0.295 mm^{-1}	
F(000)	904 e	
Crystal size	0.260 x 0.203 x 0.061 mm^3	
θ range for data collection	1.82 to 35.06°.	
Index ranges	$-18 \le h \le 18$, $-12 \le k \le 12$, $-36 \le l \le 36$	
Reflections collected	70025	
Independent reflections	8855 [R_{int} = 0.0296]	
Reflections with I>2σ(I)	7748	
Completeness to θ = 27.50°	100.0 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.99 and 0.96	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8855 / 0 / 268	
Goodness-of-fit on F^2	1.101	
Final R indices [I>2σ(I)]	R_1 = 0.0434	wR^2 = 0.1124
R indices (all data)	R_1 = 0.0513	wR^2 = 0.1176
Largest diff. peak and hole	1.230 and -0.678 e · $Å^{-3}$	



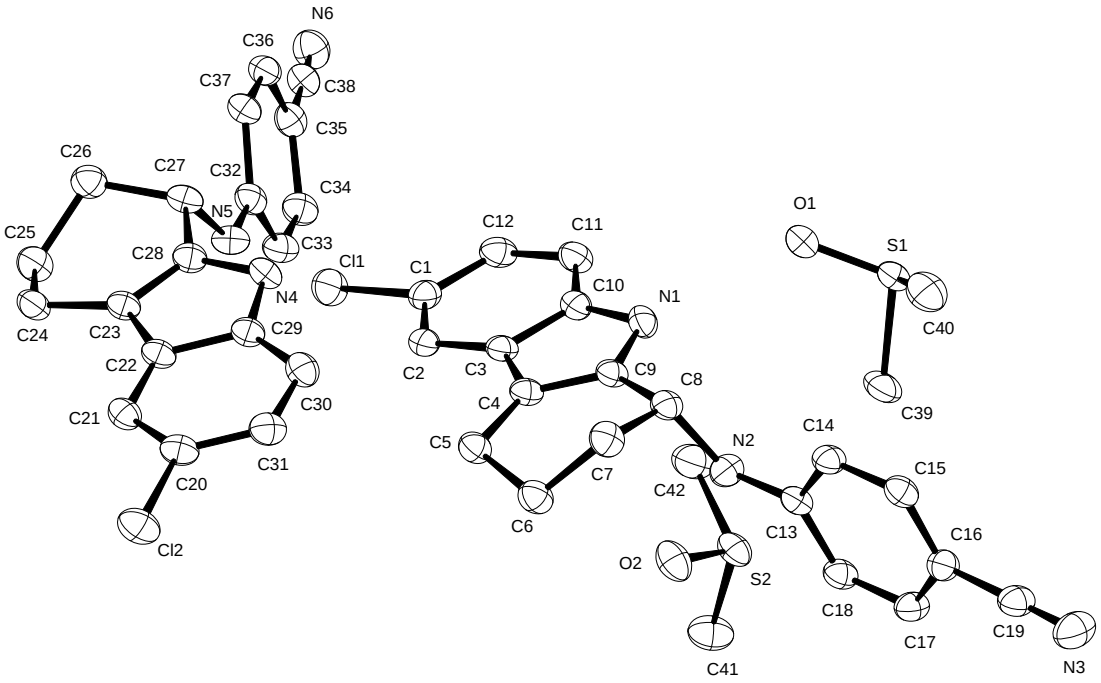
Supplementary Figure S8 X-ray structure of 1-saccharinyl-2,3,4,9-tetrahydro-1H-carbazole (17)

4-(6-Chloro-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (21)

Crystallized from DMSO-d_6.

CCDC reference number	914988	
Empirical formula	$C_{21}H_{22}ClN_3OS$	
Color	colourless	
Formula weight	399.93 g · mol^{-1}	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	TRICLINIC	
Space group	**P$\bar{1}$, (no. 2)**	
Unit cell dimensions	a = 10.3396(3) Å	α= 83.171(2)°
	b = 11.1324(3) Å	β= 75.762(2)°
	c = 18.1230(5) Å	γ = 89.106(2)°
Volume	2007.42(10) Å^3	
Z	4	
Density (calculated)	1.323 Mg · m^{-3}	
Absorption coefficient	2.777 mm^{-1}	
F(000)	840 e	

Crystal size	0.33 x 0.30 x 0.08 mm^3	
θ range for data collection	2.53 to 64.60°	
Index ranges	$-10 \le h \le 11$, $-12 \le k \le 13$, $-21 \le l \le 21$	
Reflections collected	41515	
Independent reflections	6514 [$R_{int} = 0.0823$]	
Reflections with $I>2\sigma(I)$	5028	
Completeness to θ = 64.60°	96.5 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.87 and 0.60	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6514 / 0 / 491	
Goodness-of-fit on F^2	1.024	
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0414$	$wR^2 = 0.0946$
R indices (all data)	$R_1 = 0.0622$	$wR^2 = 0.1051$
Largest diff. peak and hole	0.238 and -0.368 e · $Å^{-3}$	

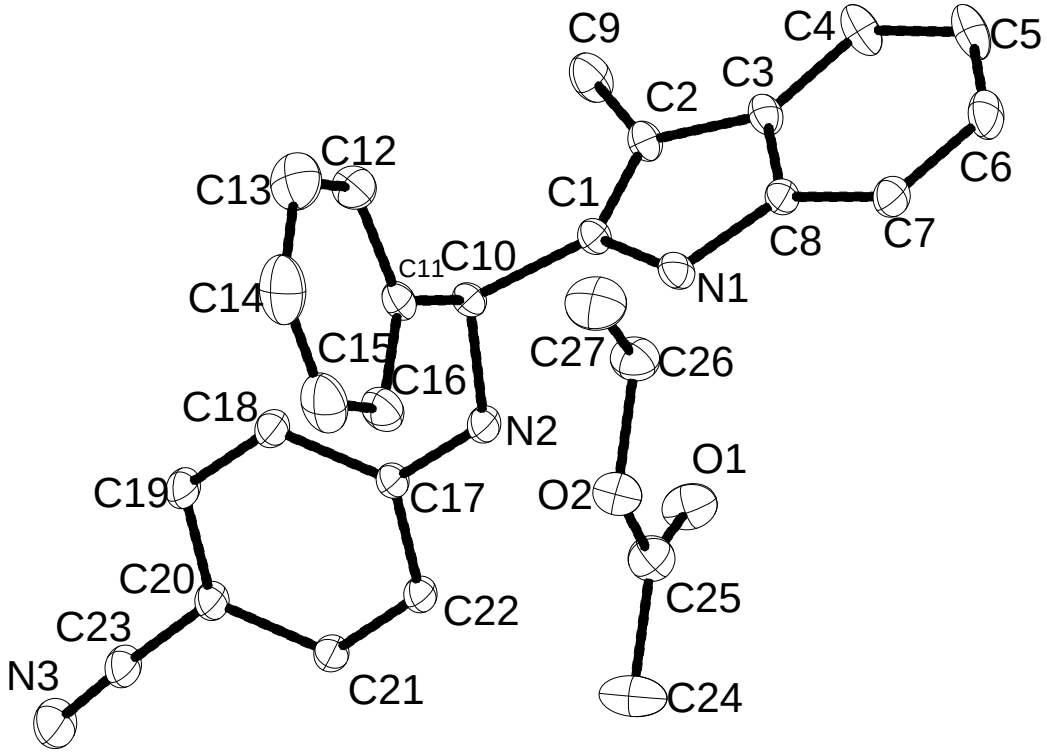


Supplementary Figure S9 X-ray structure of 4-(6-chloro-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (21)

4-((3-Methyl-1H-indol-2-yl)(phenyl)methylamino)benzonitrile (23)

Crystallized from EtOAc/pentane.

CCDC reference number	915539	
Empirical formula	$C_{25}\ H_{23}\ N_3\ O$	
Color	colourless	
Formula weight	381.46 g · mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	MONOCLINIC	
Space group	p 2_1/c, (no. 14)	
Unit cell dimensions	a = 13.8860(15) Å	α= 90°.
	b = 9.6705(10) Å	β= 99.869(2)°.
	c = 15.6885(16) Å	γ = 90°.
Volume	2075.5(4) $Å^3$	
Z	4	
Density (calculated)	1.221 Mg · m^{-3}	
Absorption coefficient	0.076 mm^{-1}	
F(000)	808 e	
Crystal size	0.22 x 0.15 x 0.07 mm^3	
θ range for data collection	2.48 to 34.34°.	
Index ranges	-22 ≤ h ≤ 22, -15≤ k ≤ 15, -24≤ l ≤ 24	
Reflections collected	70526	
Independent reflections	8678 [R_{int} = 0.0410]	
Reflections with I>2σ(I)	6665	
Completeness to θ = 34.34°	99.9 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.99572 and 0.98700	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8678 / 0 / 291	
Goodness-of-fit on F^2	1.028	
Final R indices [I>2σ(I)]	R_1 = 0.0462	w R^2 = 0.1233
R indices (all data)	R_1 = 0.0659	w R^2 = 0.1384
Largest diff. peak and hole	0.512 and -0.323 e · $Å^{-3}$	



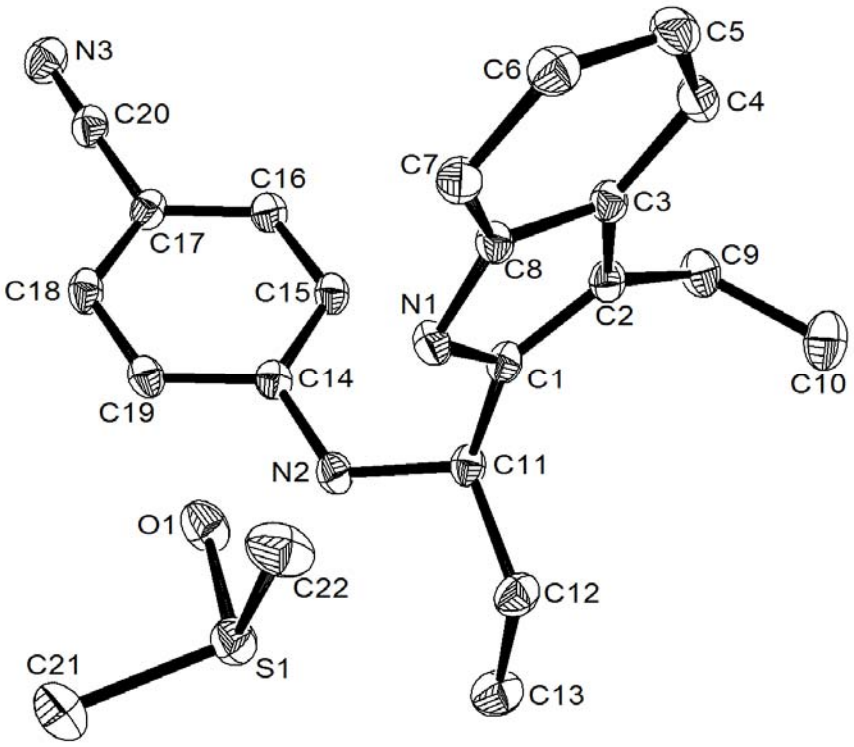
Supplementary Figure S10: X-ray structure of 4-((3-methyl-1H-indol-2-yl)(phenyl)methylamino)benzonitrile (23)

4-(1-(3-Ethyl-1H-indol-2-yl)propylamino)benzonitrile (24)

Crystallized from DMSO-d_6.

CCDC reference number	915538	
Identification code	7982	
Empirical formula	$C_{22}\ H_{27}\ N_3\ O\ S$	
Color	pale yellow	
Formula weight	381.52 g · mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	**$P2_1/n$, (no. 14)**	
Unit cell dimensions	a = 17.059(2) Å	α= 90°.
	b = 7.2199(9) Å	β= 99.489(2)°.
	c = 17.196(2) Å	γ = 90°.
Volume	2089.0(4) $Å^3$	

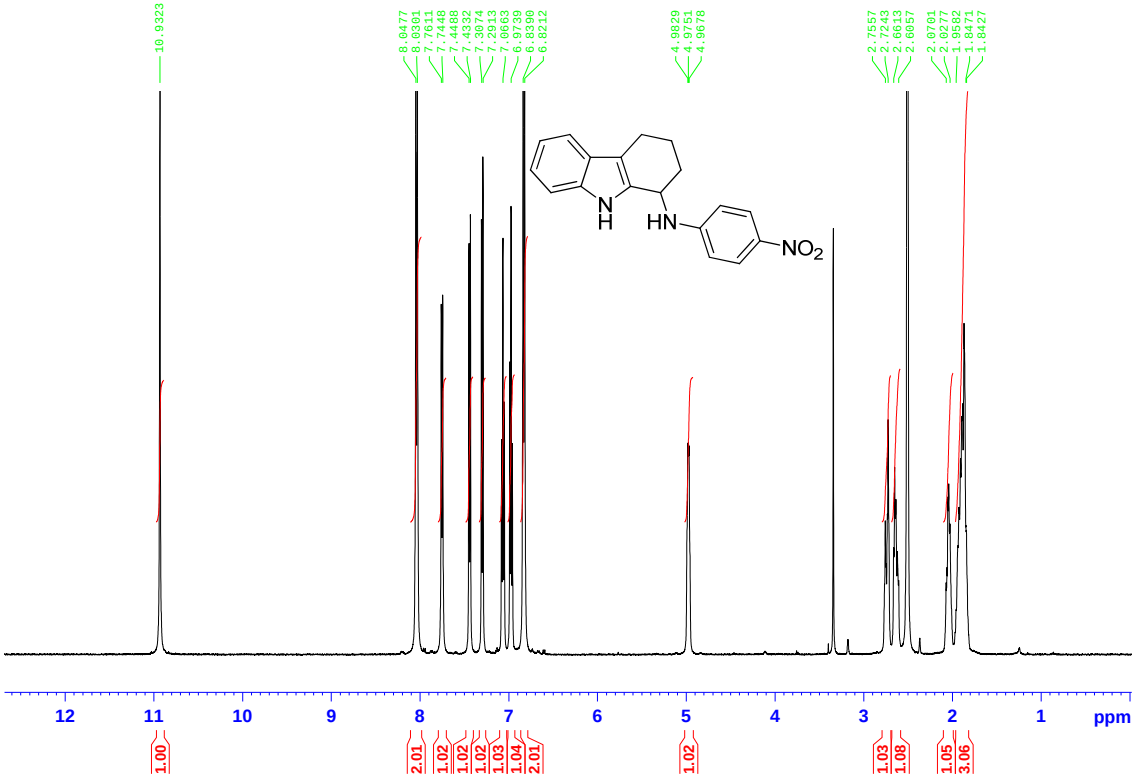
Z	4	
Density (calculated)	1.213 Mg · m^{-3}	
Absorption coefficient	0.171 mm^{-1}	
F(000)	816 e	
Crystal size	0.30 x 0.05 x 0.03 mm^3	
θ range for data collection	2.402 to 30.744°.	
Index ranges	$-24 \le h \le 24$, $-10 \le k \le 10$, $-24 \le l \le 24$	
Reflections collected	43886	
Independent reflections	6489 [R_{int} = 0.0845]	
Reflections with I>2σ(I)	4506	
Completeness to θ = 25.242°	99.9 %	
Absorption correction	Gaussian	
Max. and min. transmission	1.00 and 0.99	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6489 / 0 / 256	
Goodness-of-fit on F^2	1.011	
Final R indices [I>2σ(I)]	R_1 = 0.0491	wR^2 = 0.1164
R indices (all data)	R_1 = 0.0851	wR^2 = 0.1354
Largest diff. peak and hole	0.550 and -0.473 e · $Å^{-3}$	



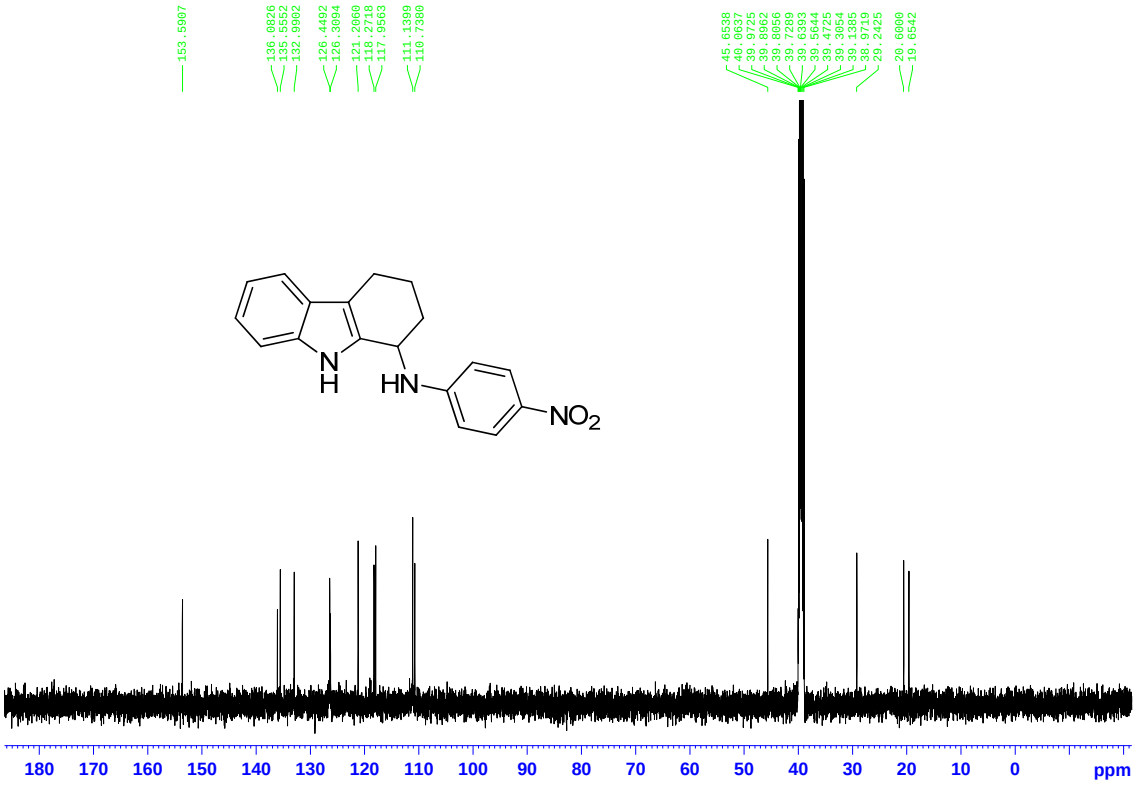
Supplementary Figure S11 X-ray structure of 4-(1-(3-ethyl-1H-indol-2-yl)propylamino)benzonitrile (24)

Copies of the NMR spectra

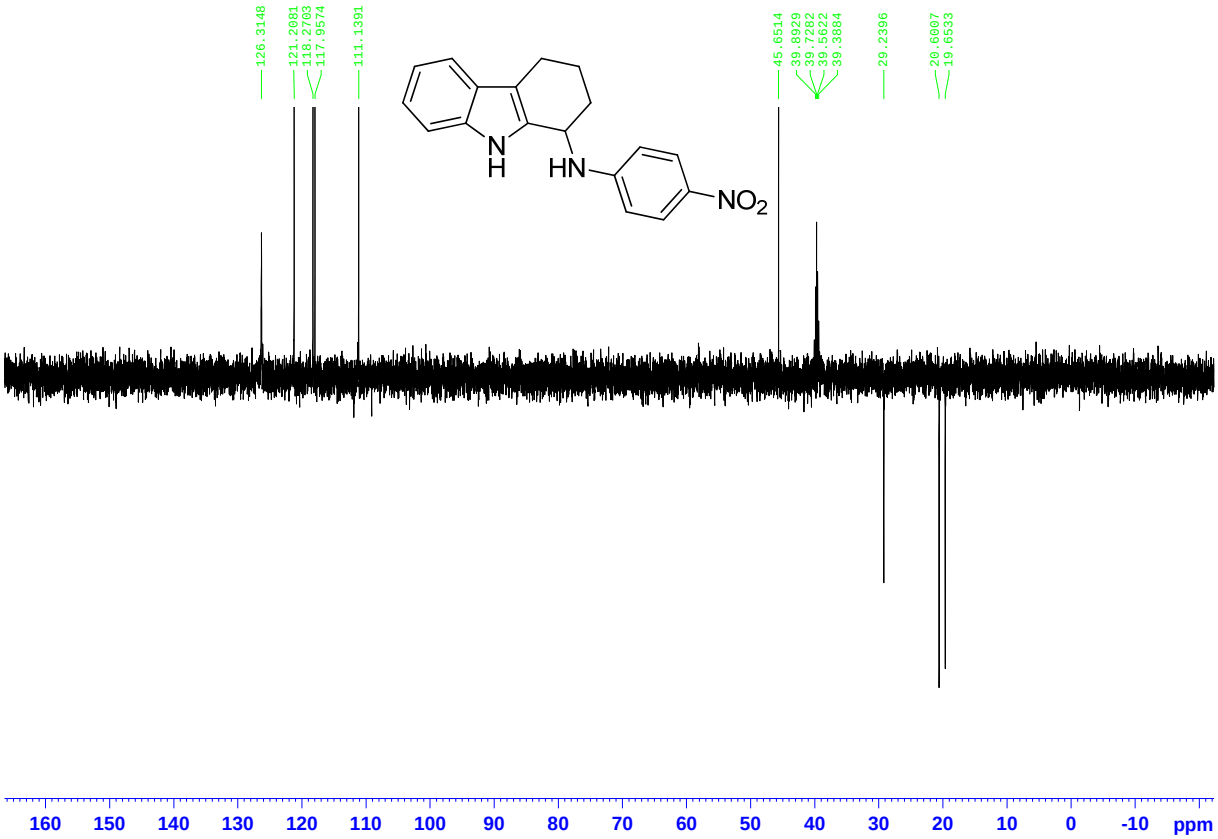
N-(4-Nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (4)



Supplementary Figure S12: ^{1}H NMR in DMSO of 4

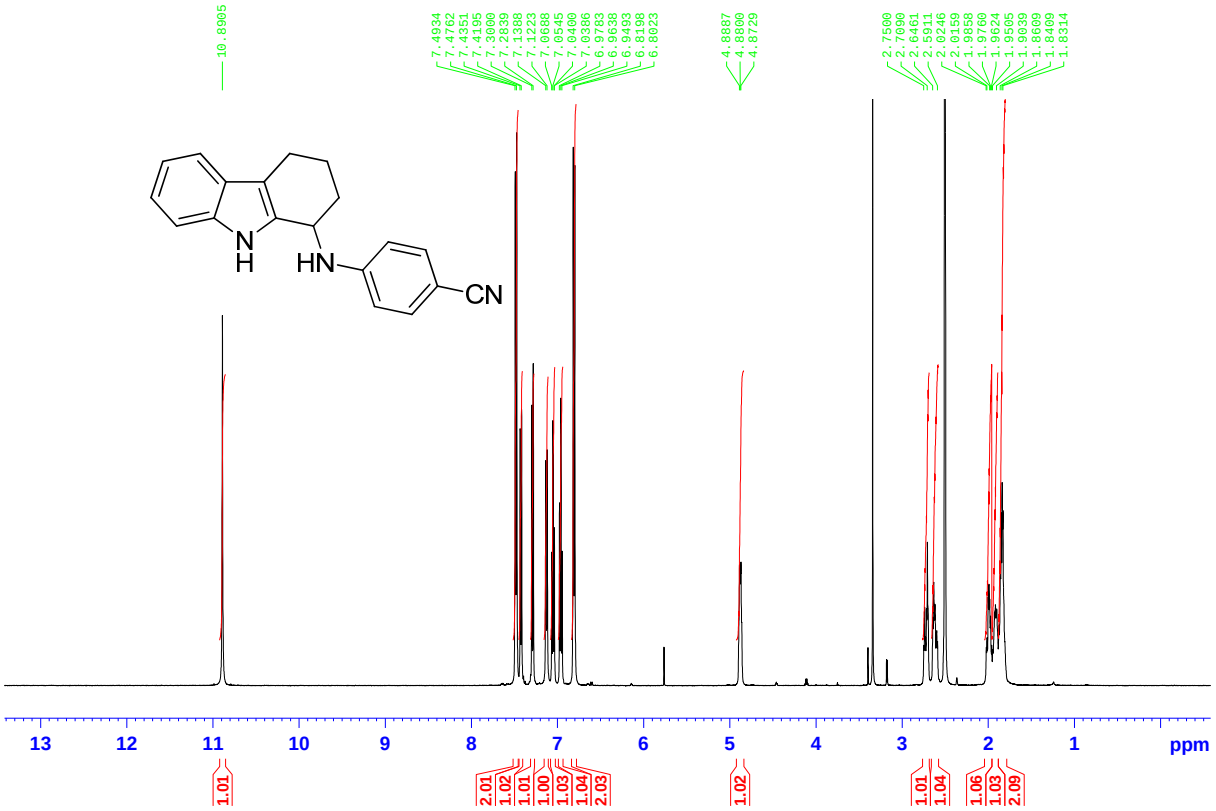


Supplementary Figure S13: ^{13}C NMR in DMSO of 4

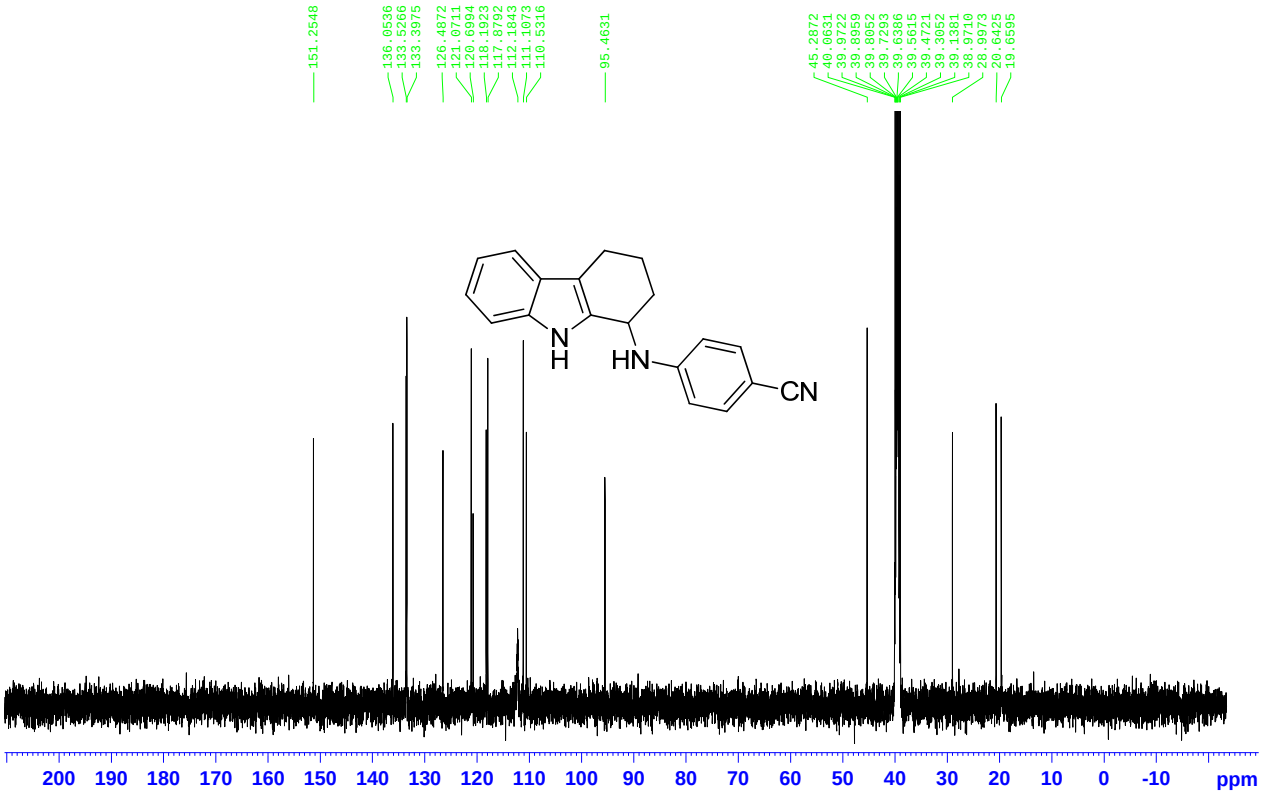


Supplementary Figure S14: dept 135 NMR in DMSO of 4

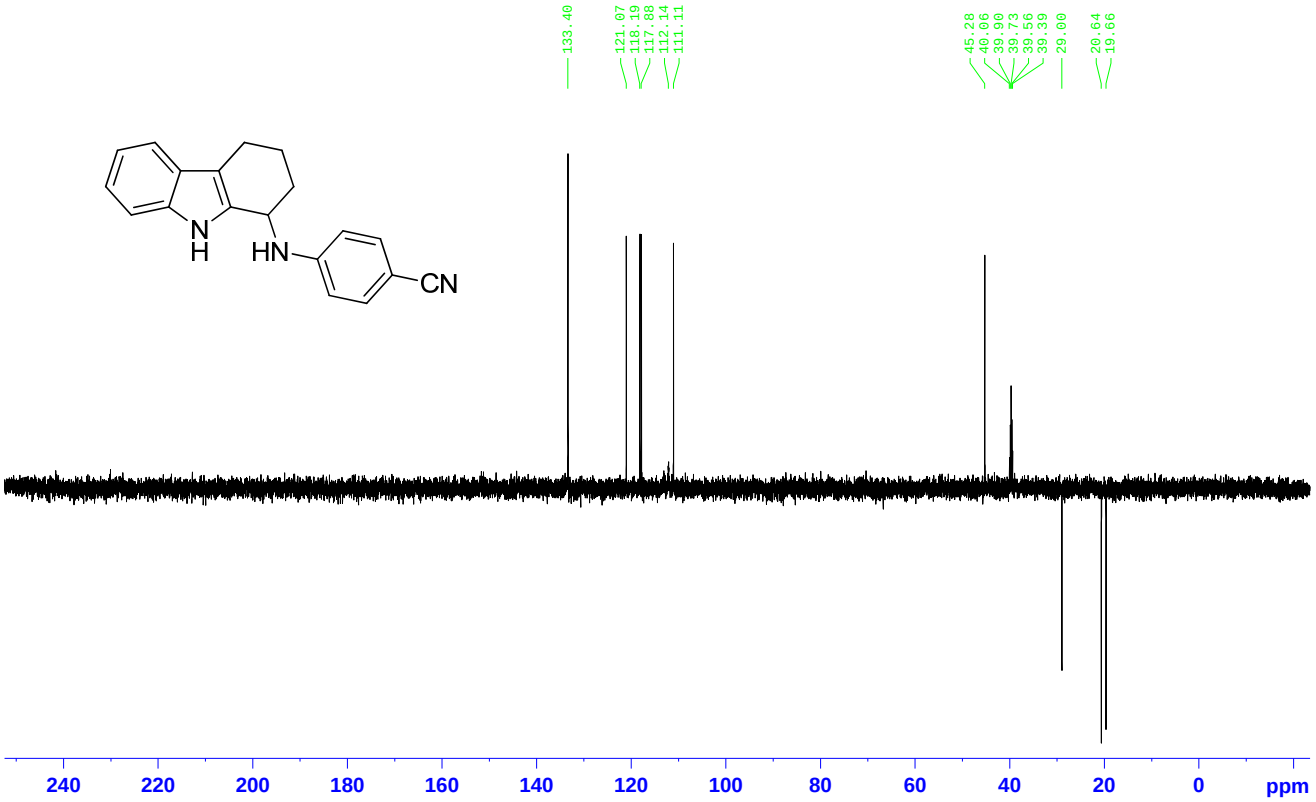
4-(2,3,4,9-Tetrahydro-1H-carbazol-1-ylamino)benzonitrile (5)



Supplementary Figure S15: ^{1}H NMR in DMSO of 5

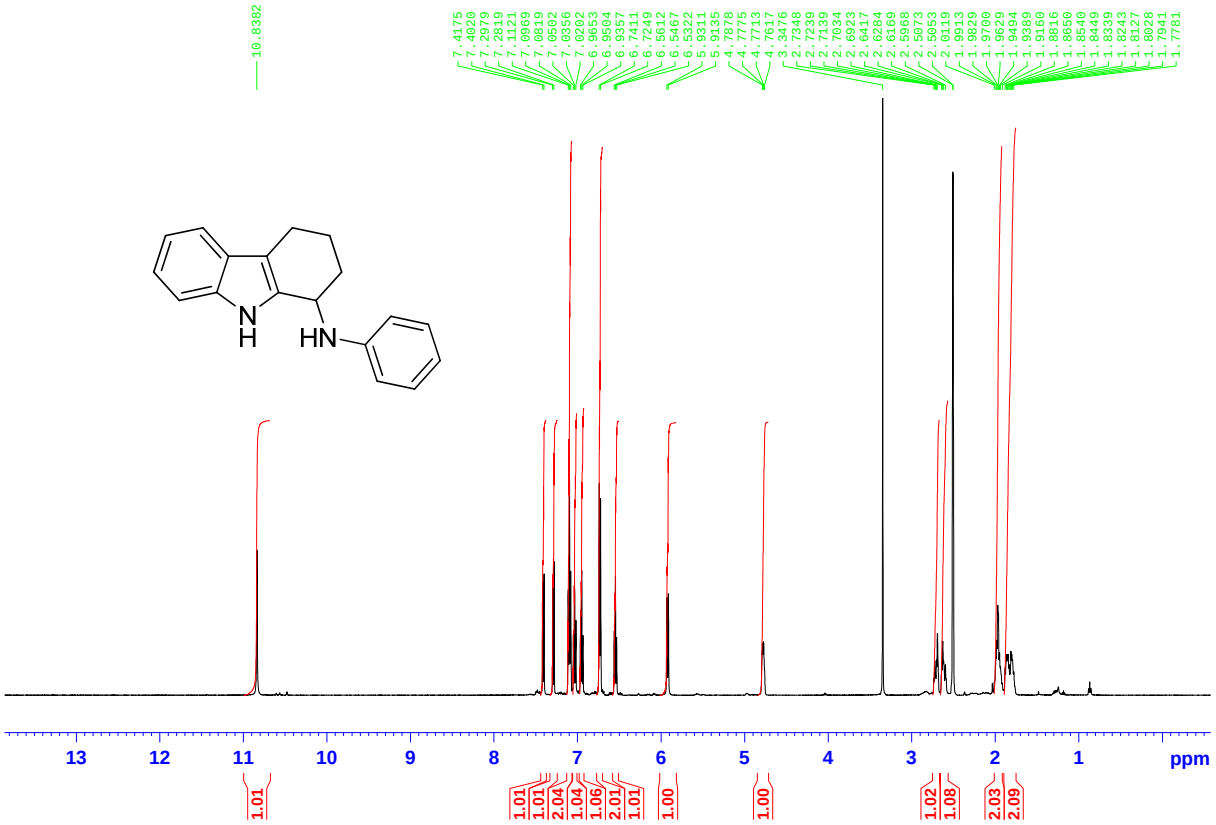


Supplementary Figure S16: ^{13}C NMR in DMSO of 5



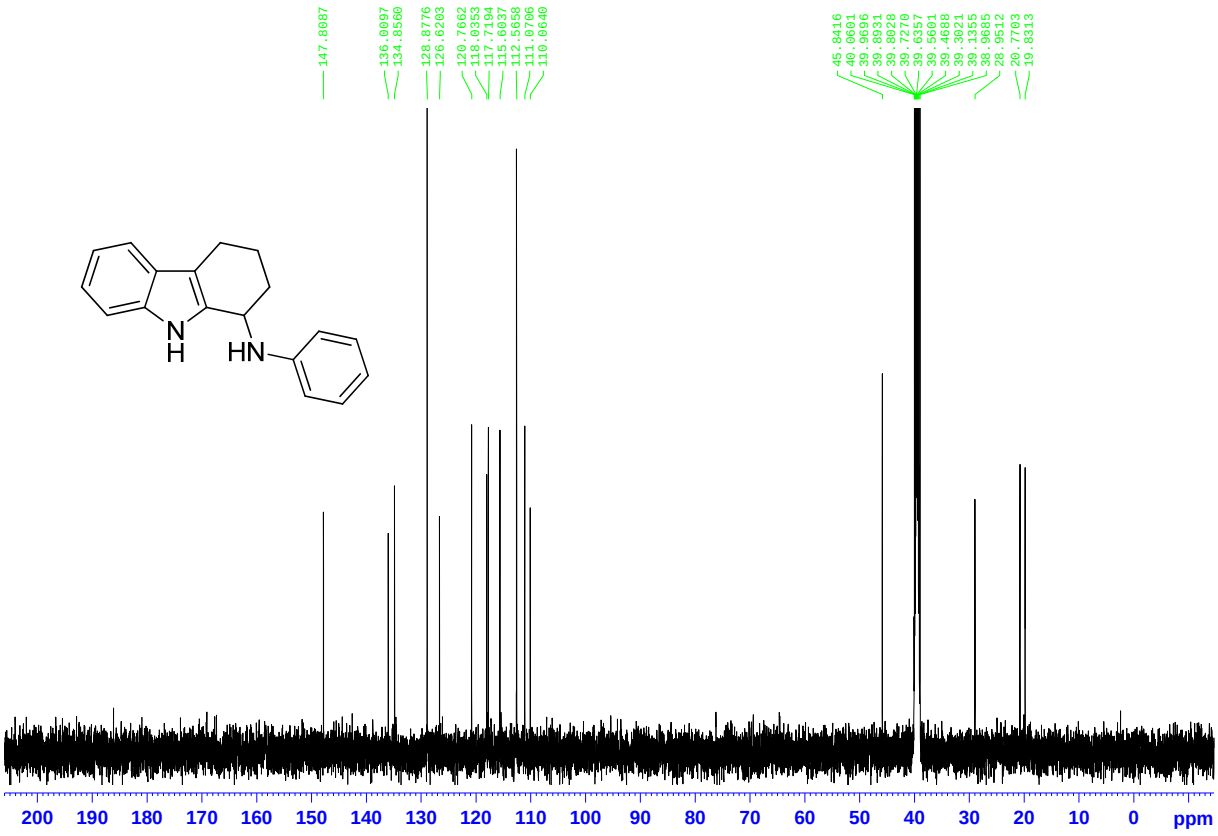
Supplementary Figure S17: dept 135 NMR in DMSO of 5

N-Phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (6)

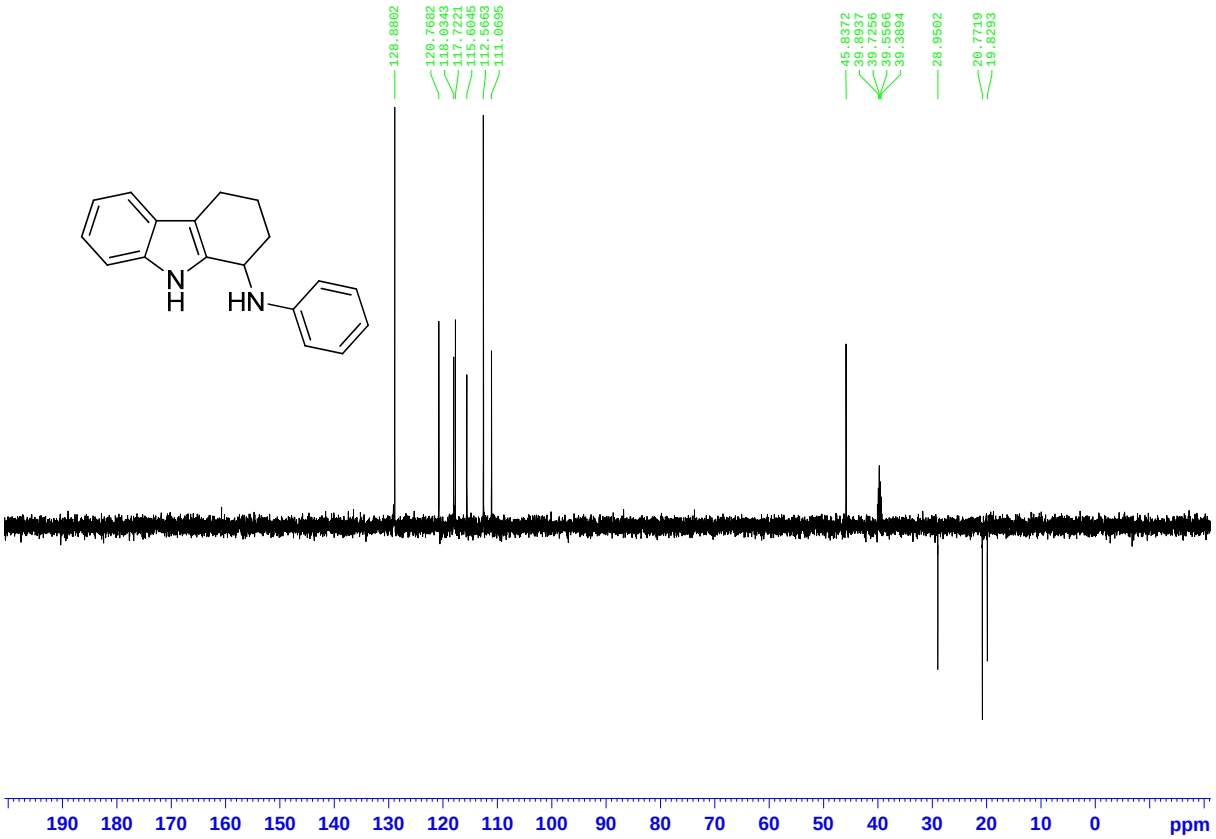


Supplementary Figure S18: ^{1}H NMR in DMSO of 6

-

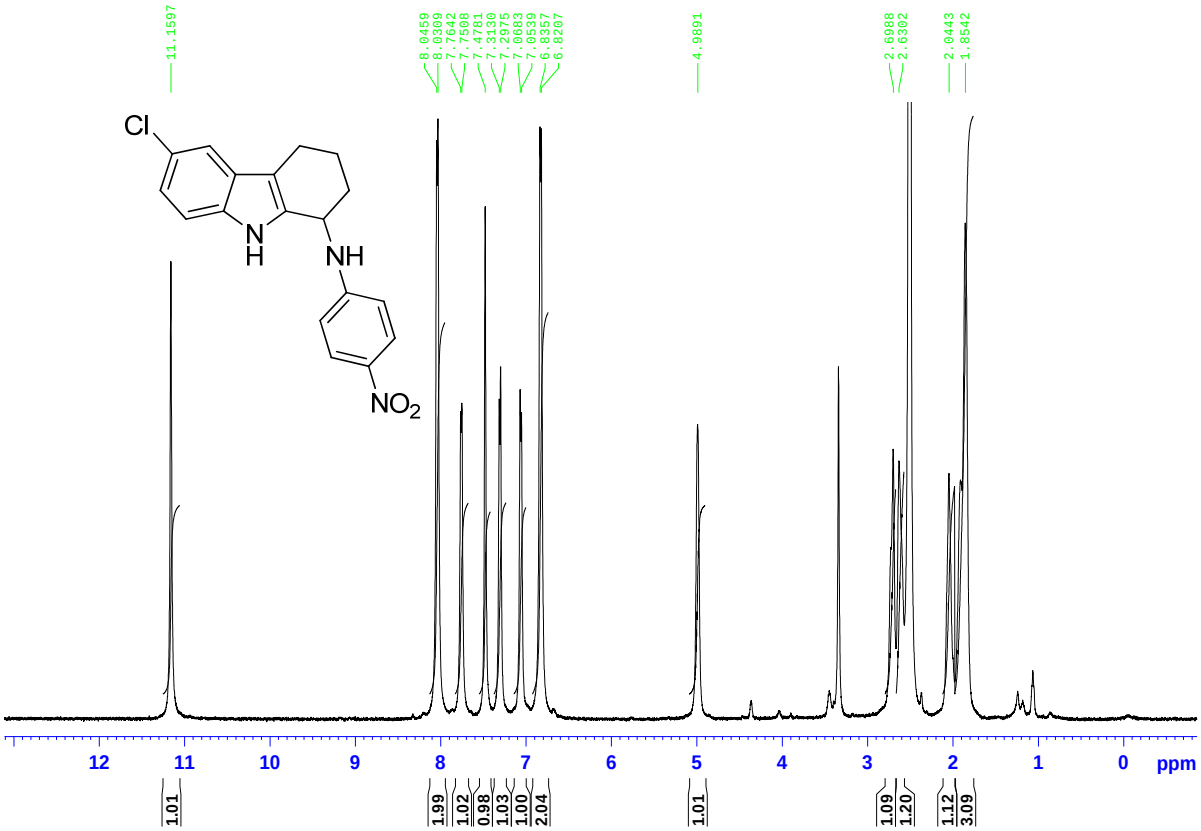


Supplementary Figure S19: ^{13}C NMR in DMSO of 6

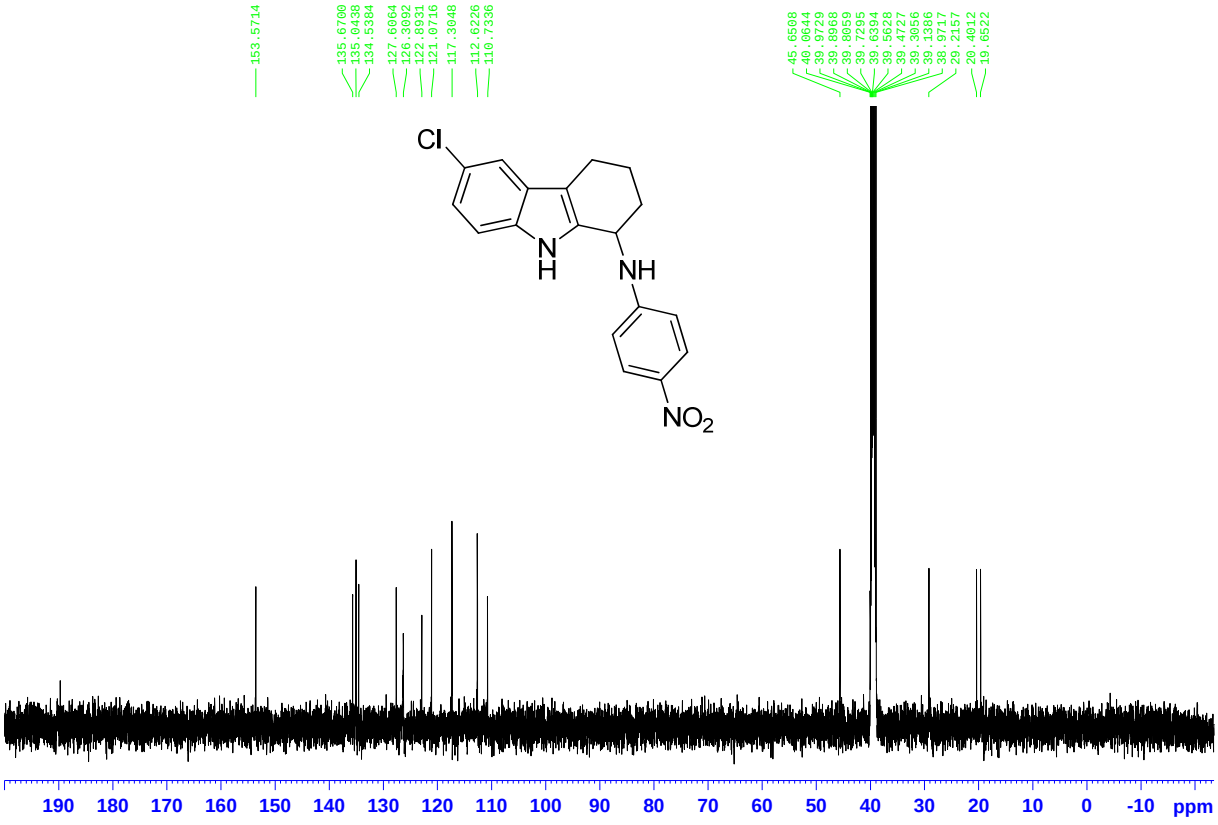


Supplementary Figure S20: dept 135 NMR of 6

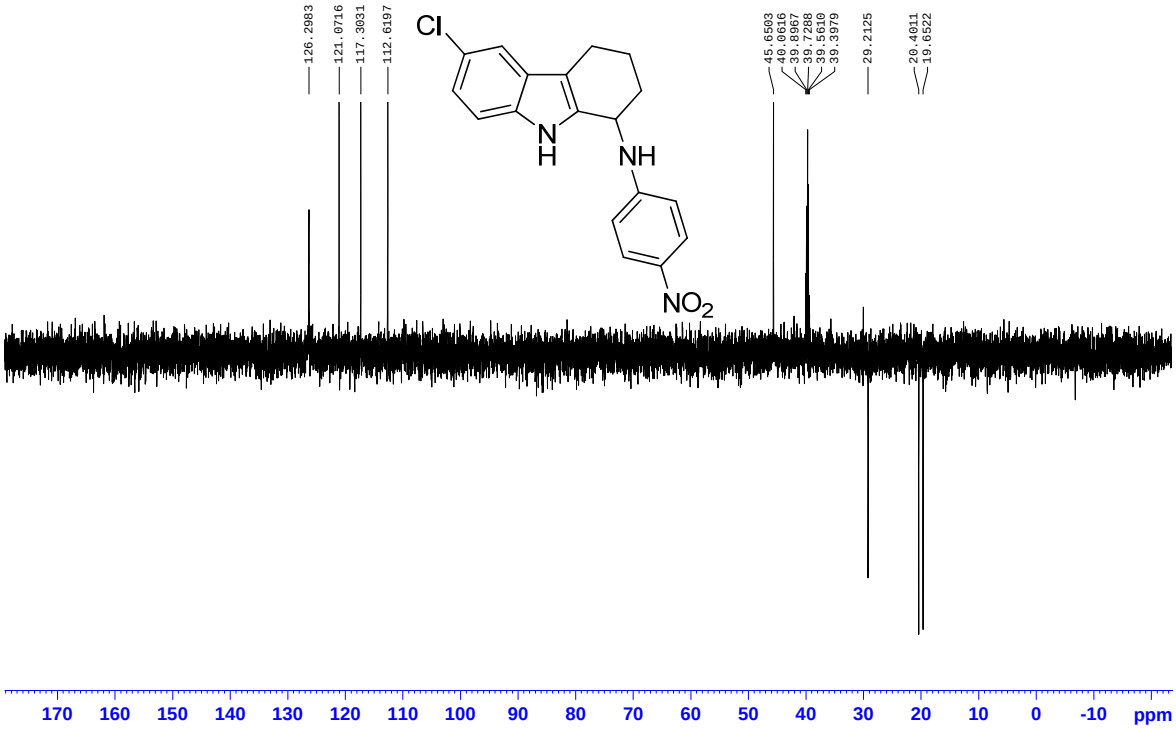
6-Chloro-*N*-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (7):



Supplementary Figure S21: ^{1}H NMR in DMSO of 7

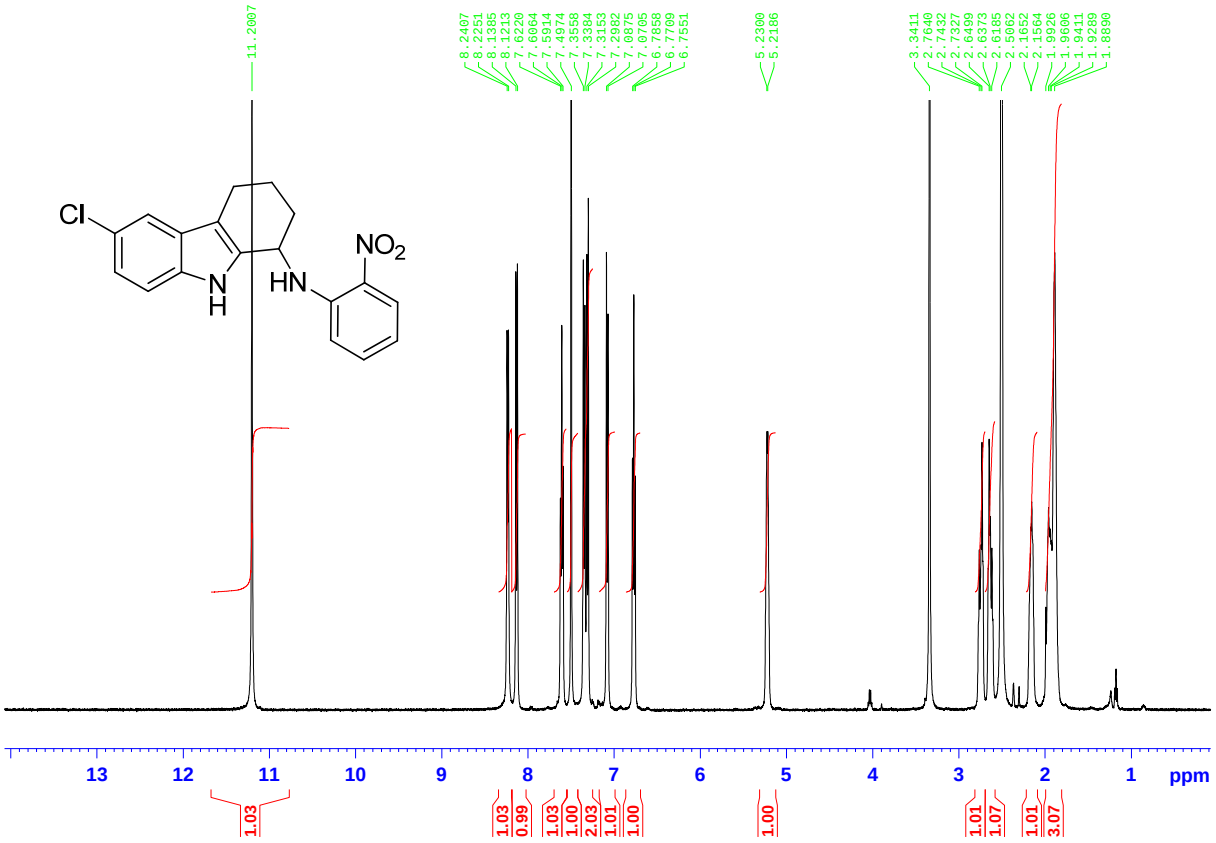


Supplementary Figure S22: ^{13}C NMR in DMSO of 7

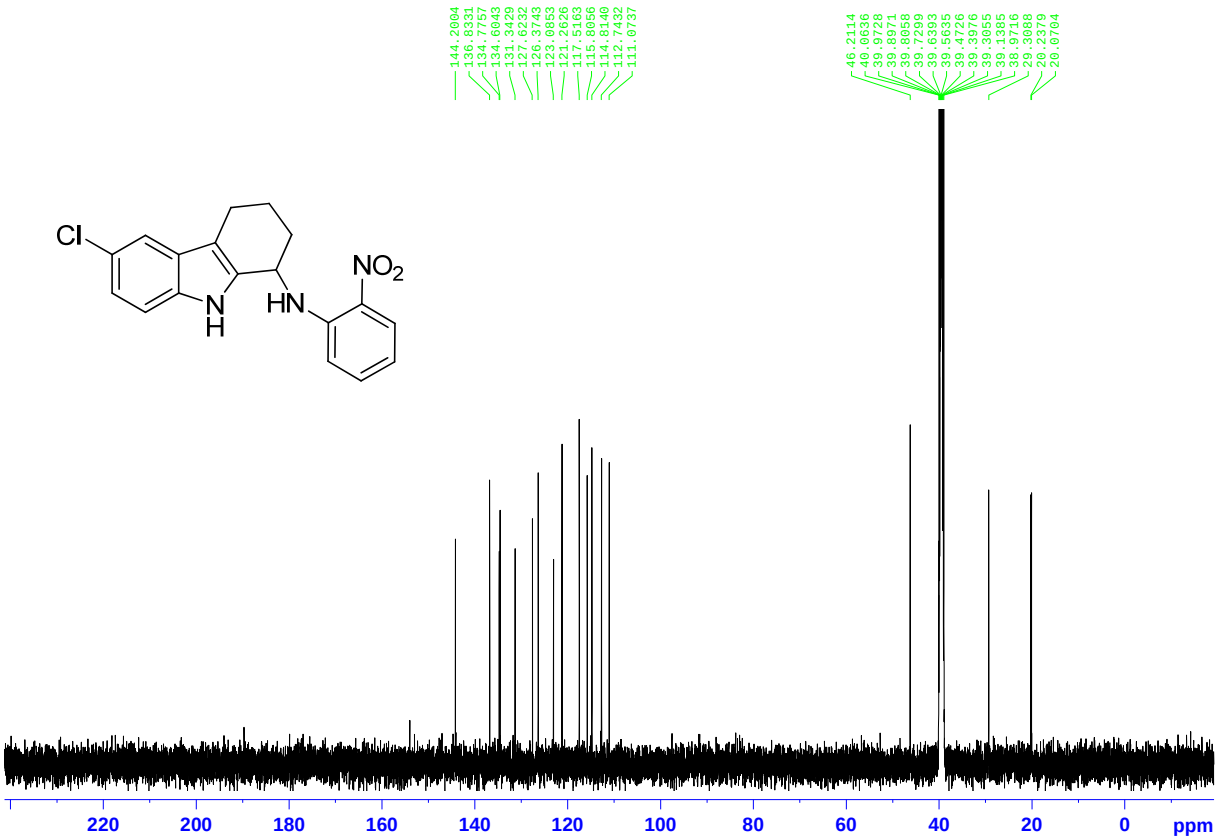


Supplementary Figure S23: dept 135 NMR in DMSO of 7

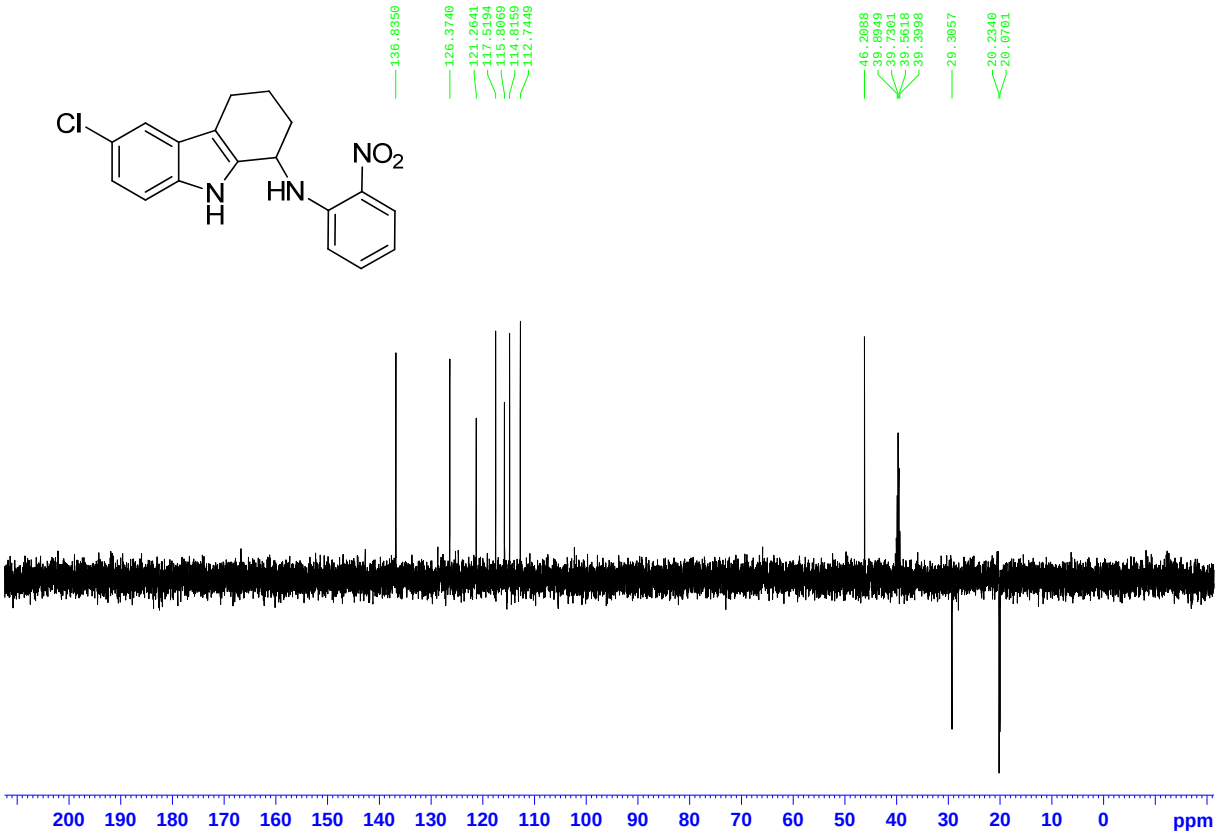
6-Chloro-*N*-(2-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (8)



Supplementary Figure S24: ^{1}H NMR in DMSO of 8

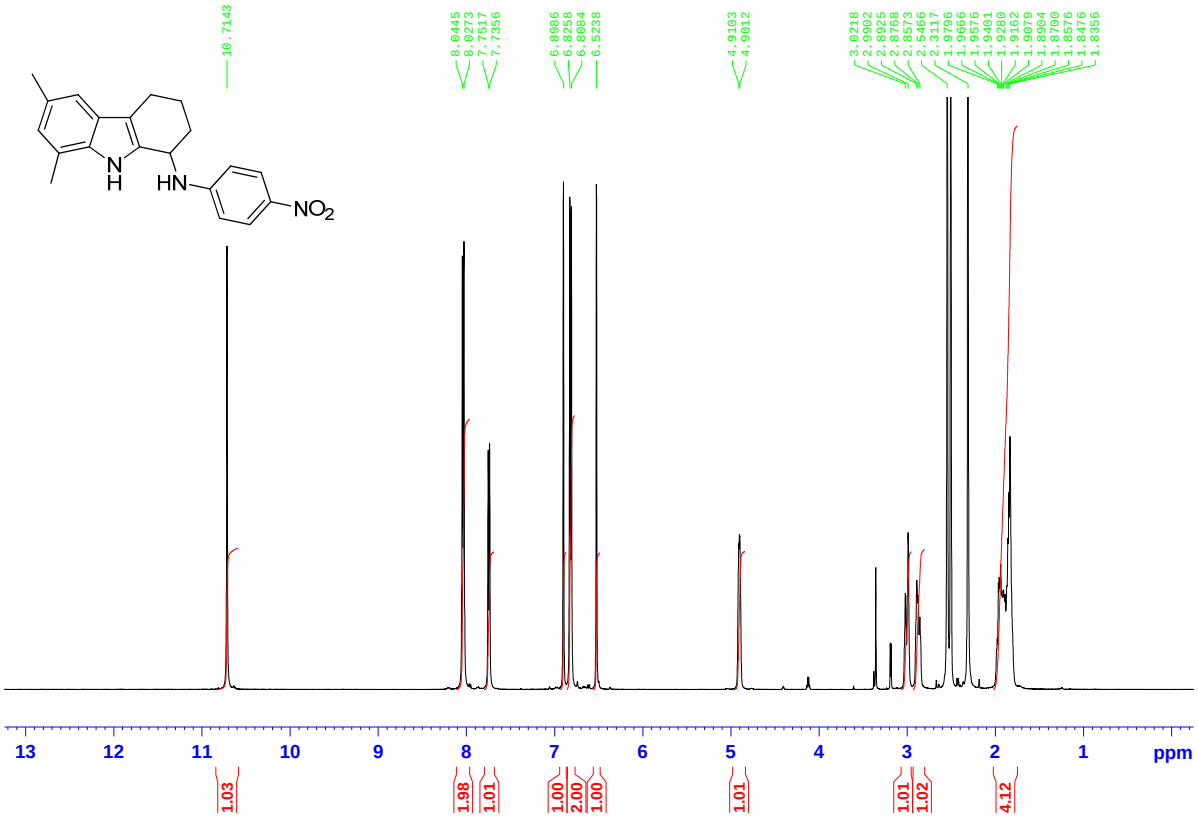


Supplementary Figure S25: ^{13}C NMR in DMSO of 8

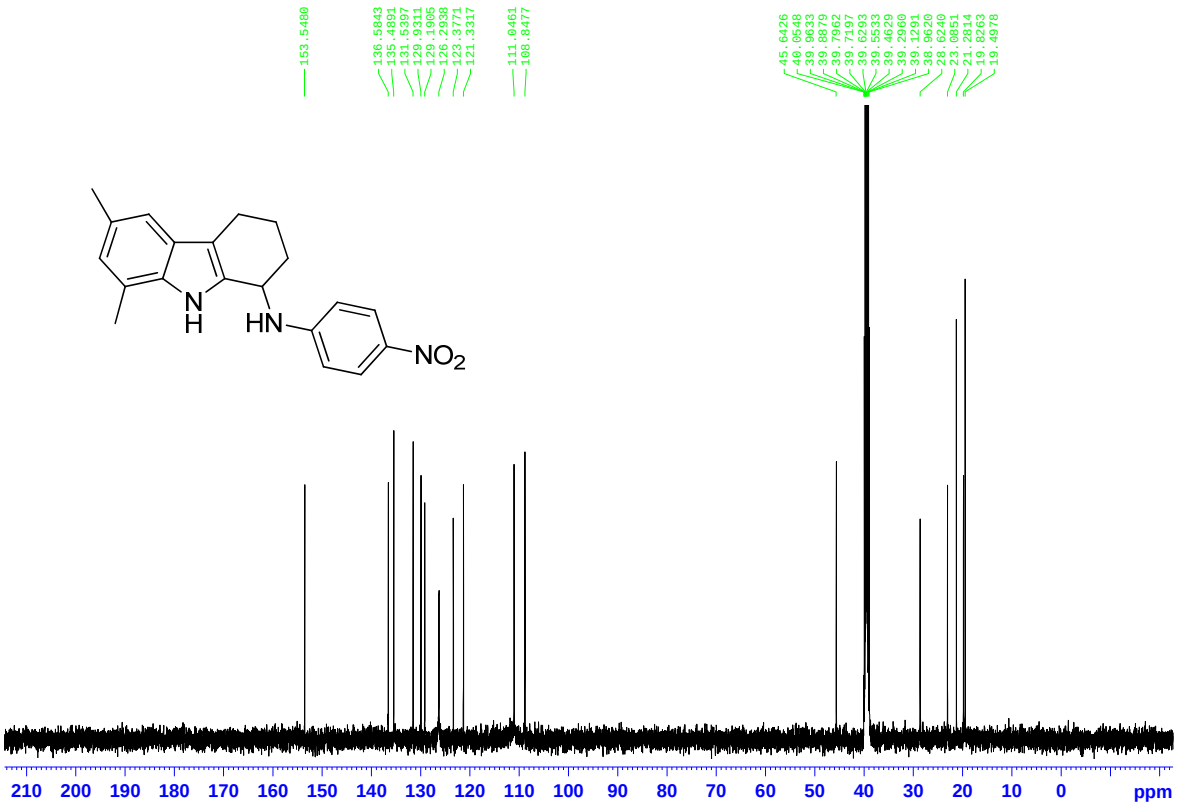


Supplementary Figure S26: dept 135 NMR of 8

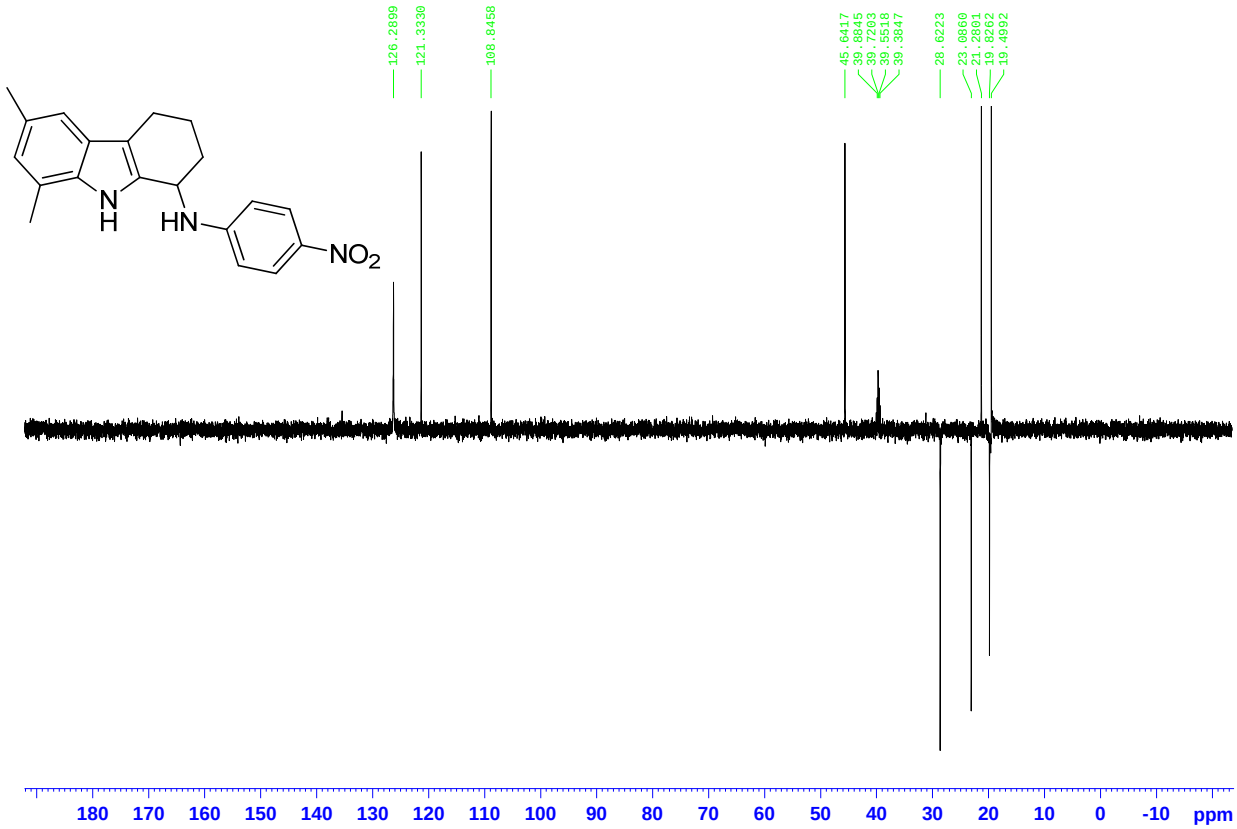
6,8-Dimethyl-*N*-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (9)



Supplementary Figure S27: ^{1}H NMR in DMSO of 9

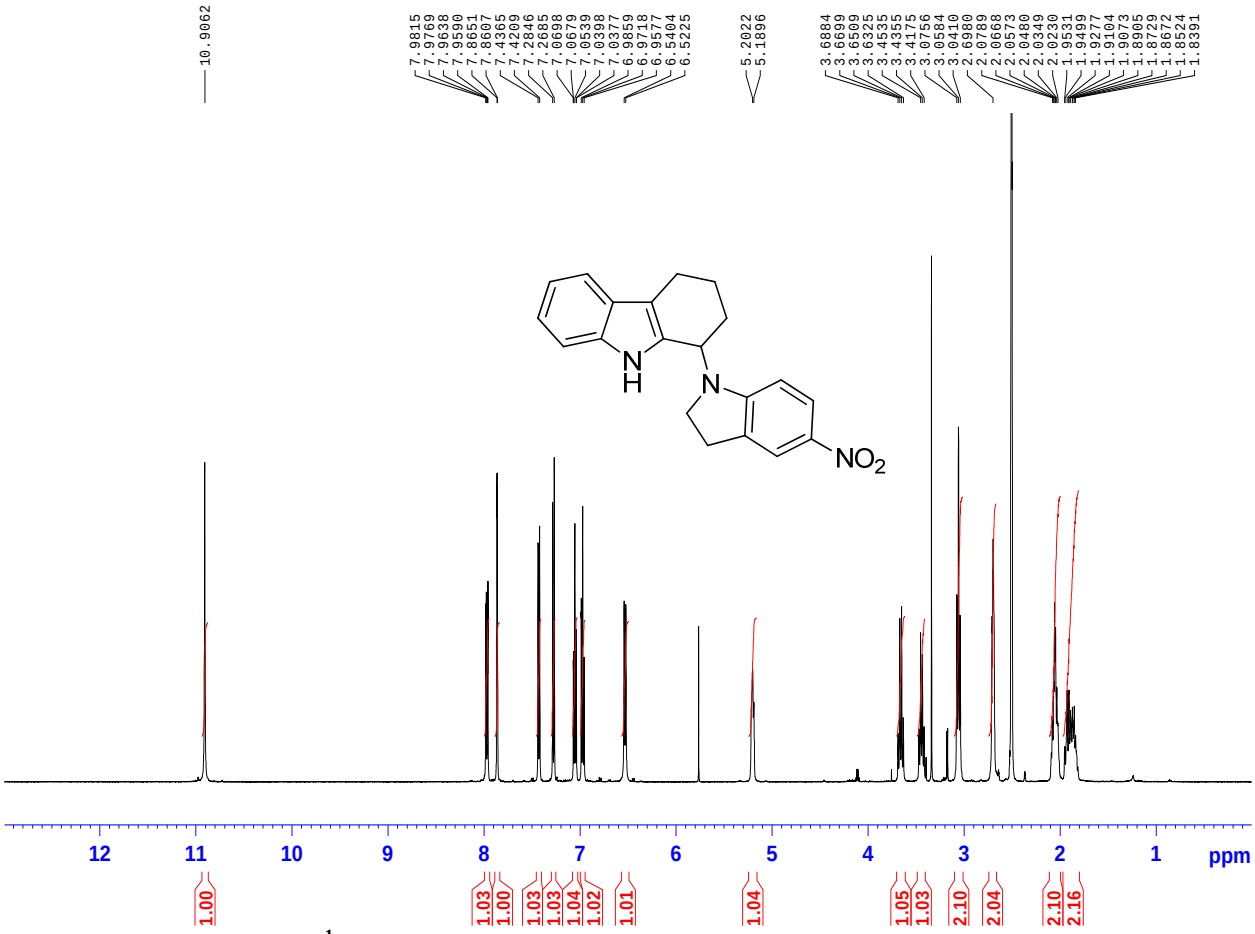


Supplementary Figure S28: ^{13}C NMR in DMSO of 9

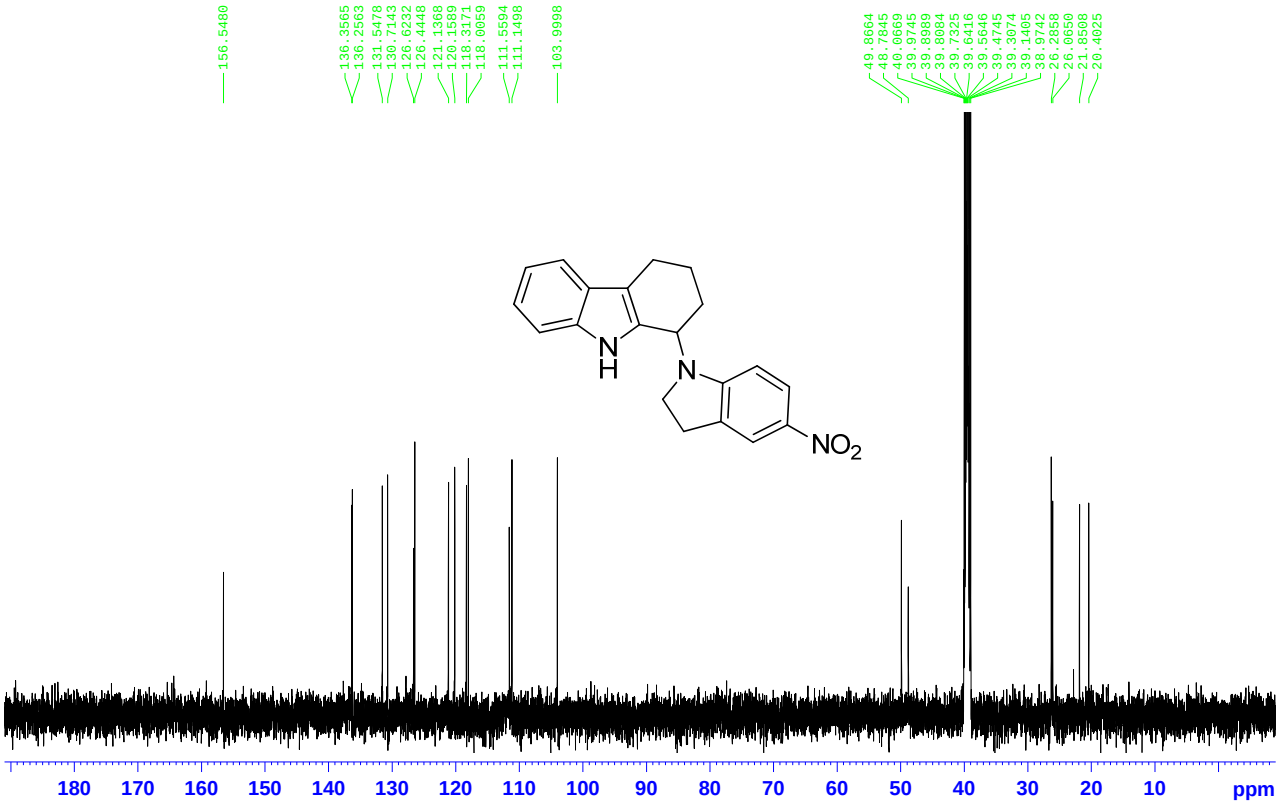


Supplementary Figure S29: dept 135 NMR of 9

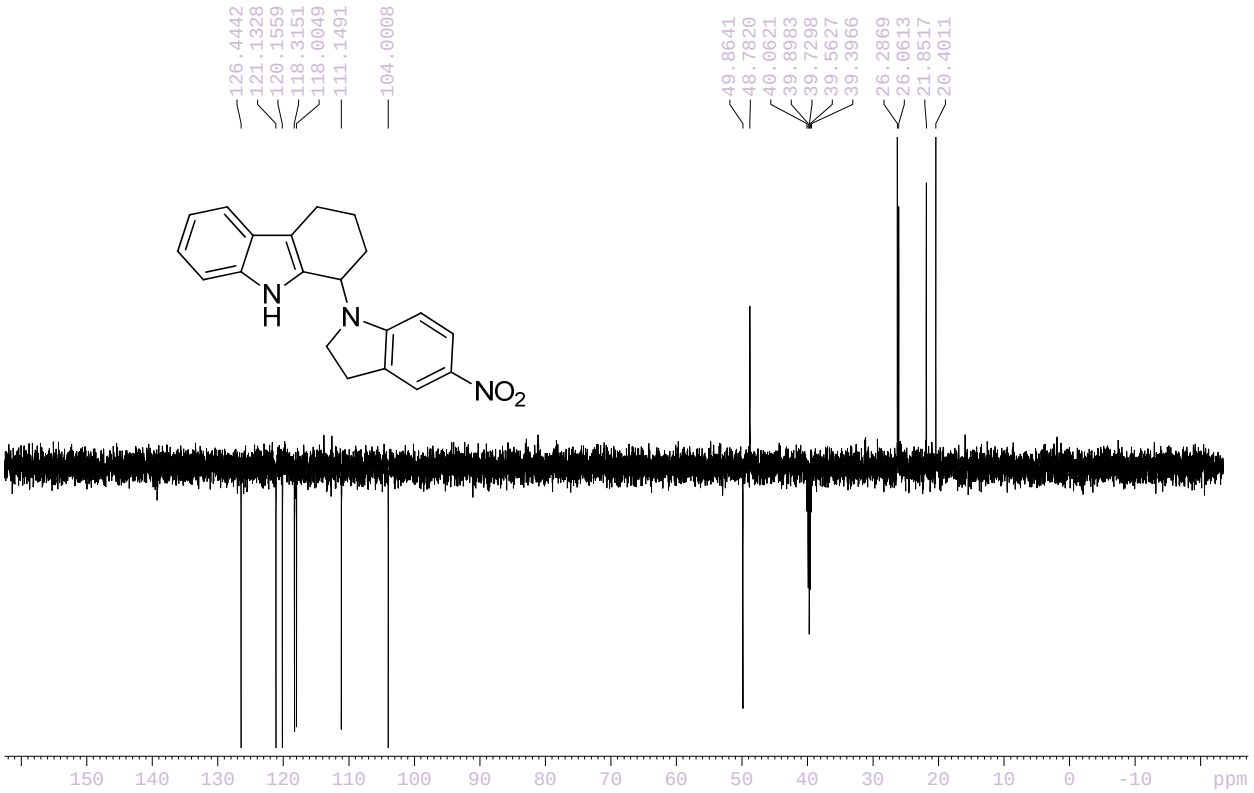
1-(5-Nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (10)



Supplementary Figure S30: ^{1}H NMR in DMSO of 10

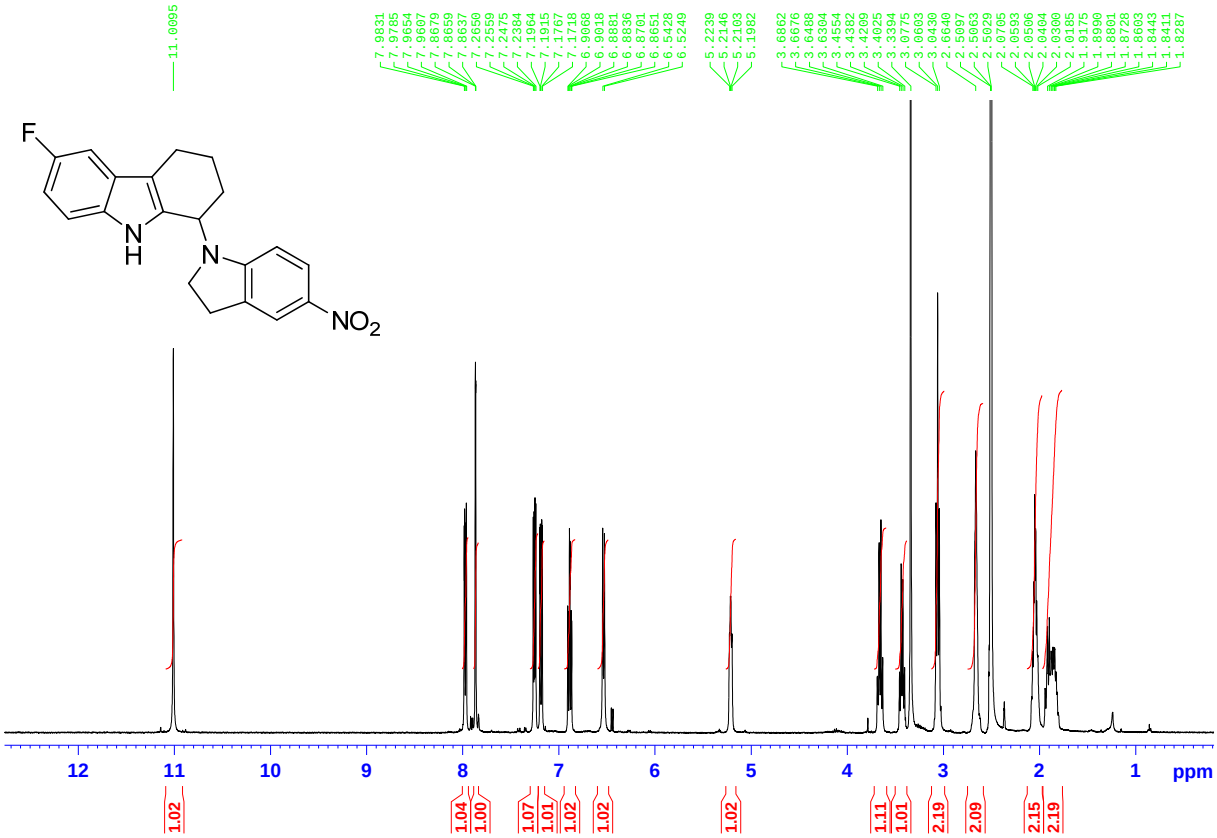


Supplementary Figure S31: ^{13}C NMR in DMSO of 10

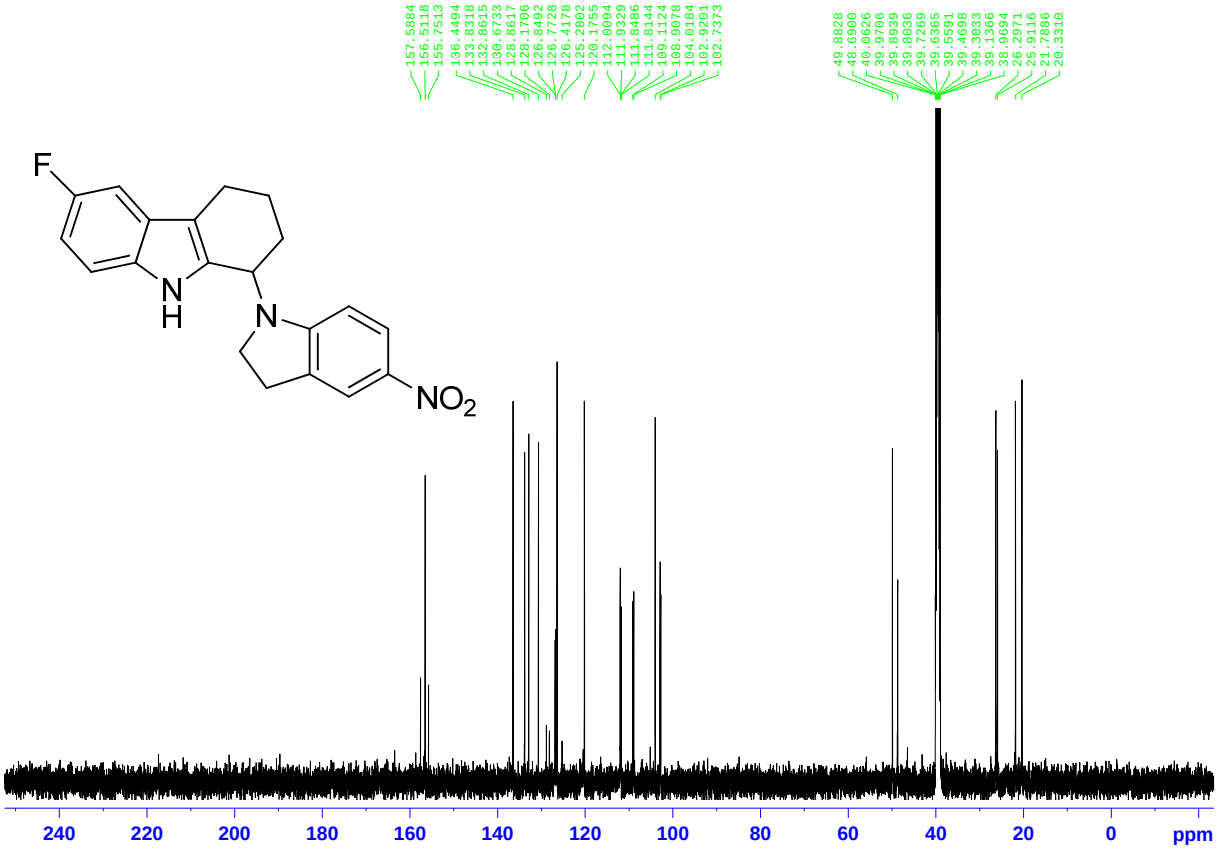


Supplementary Figure S32: dept 135 NMR in DMSO of 10

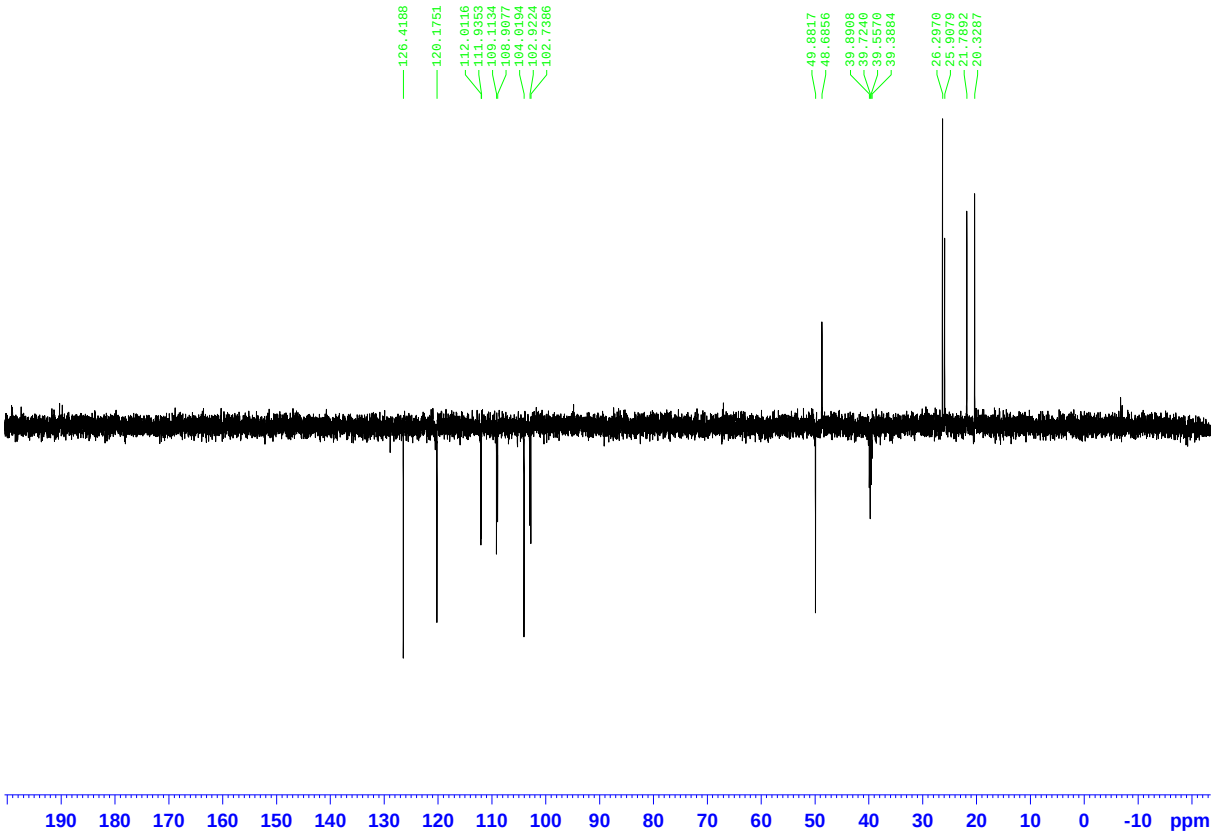
6-Fluoro-1-(5-nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (11)



Supplementary Figure S33: ^{1}H NMR in DMSO of 11

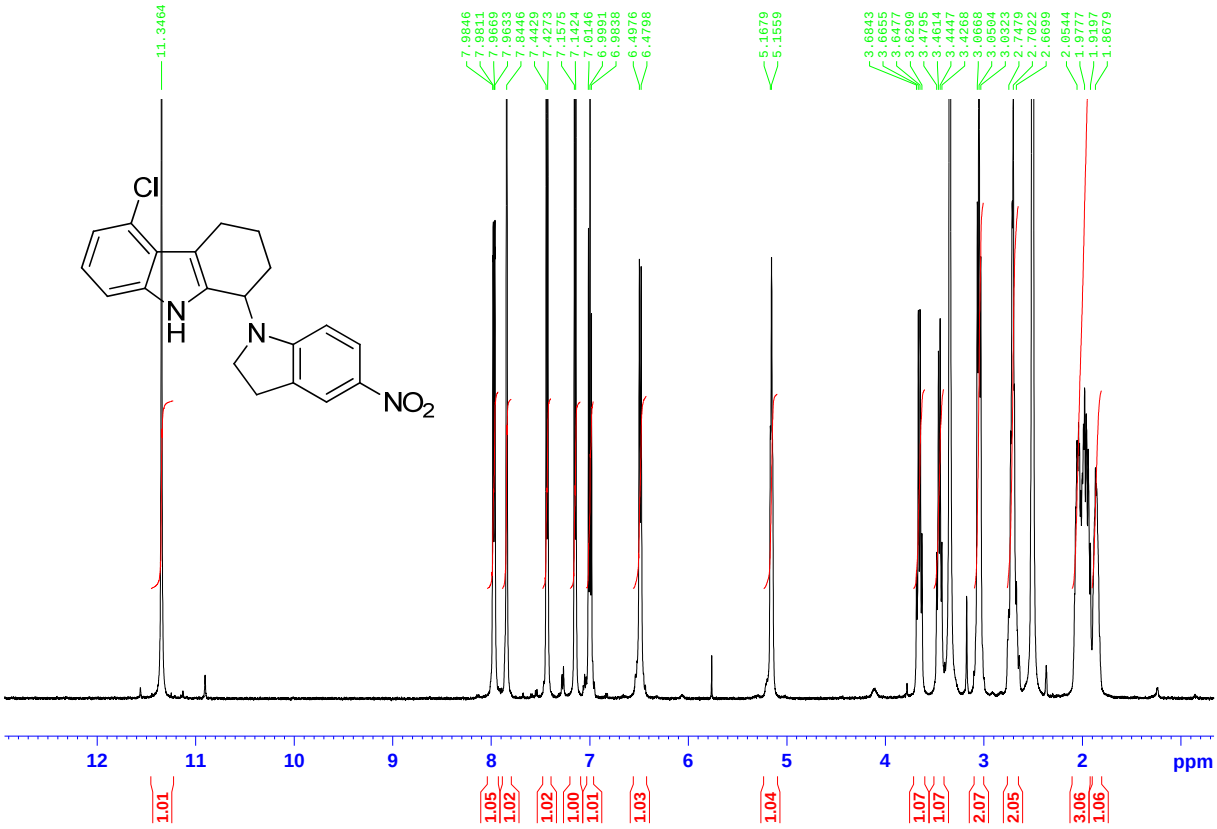


Supplementary Figure S34: ^{13}C NMR in DMSO of 11

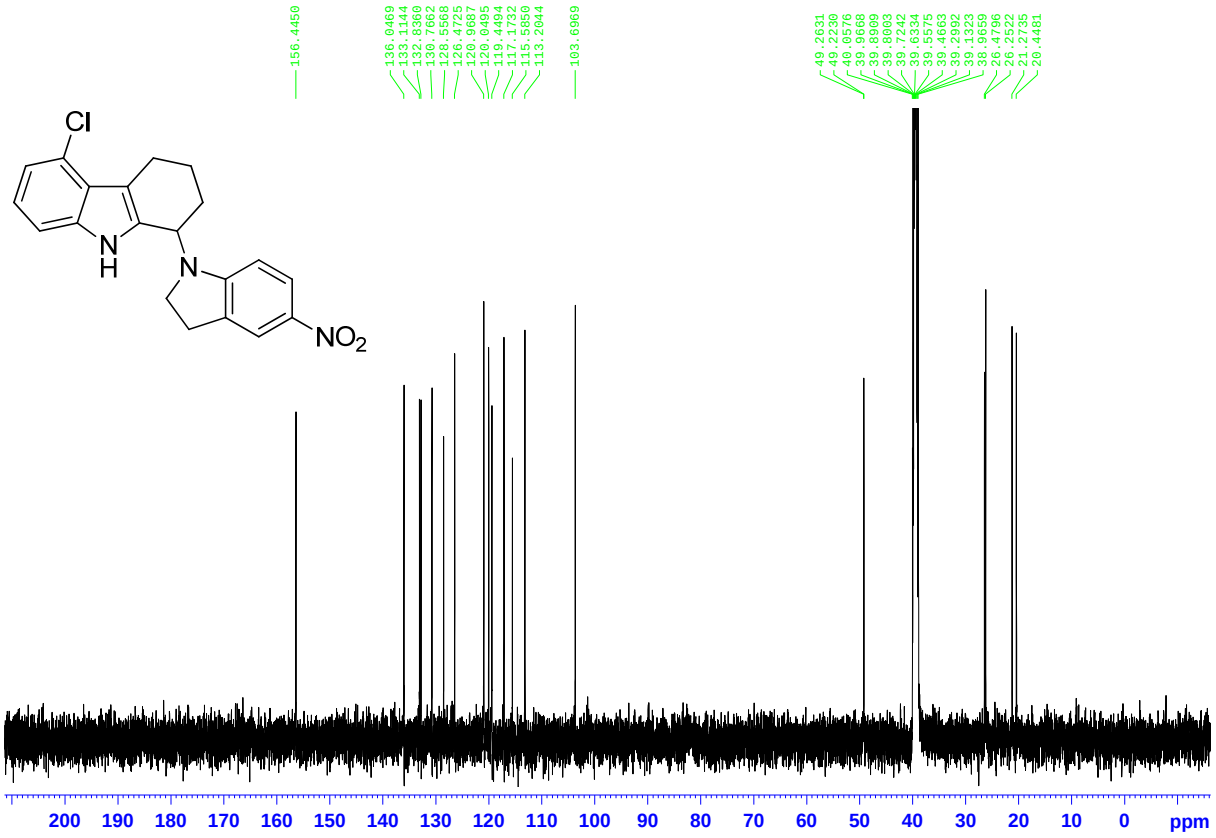


Supplementary Figure S35: dept 135 NMR in DMSO of 11

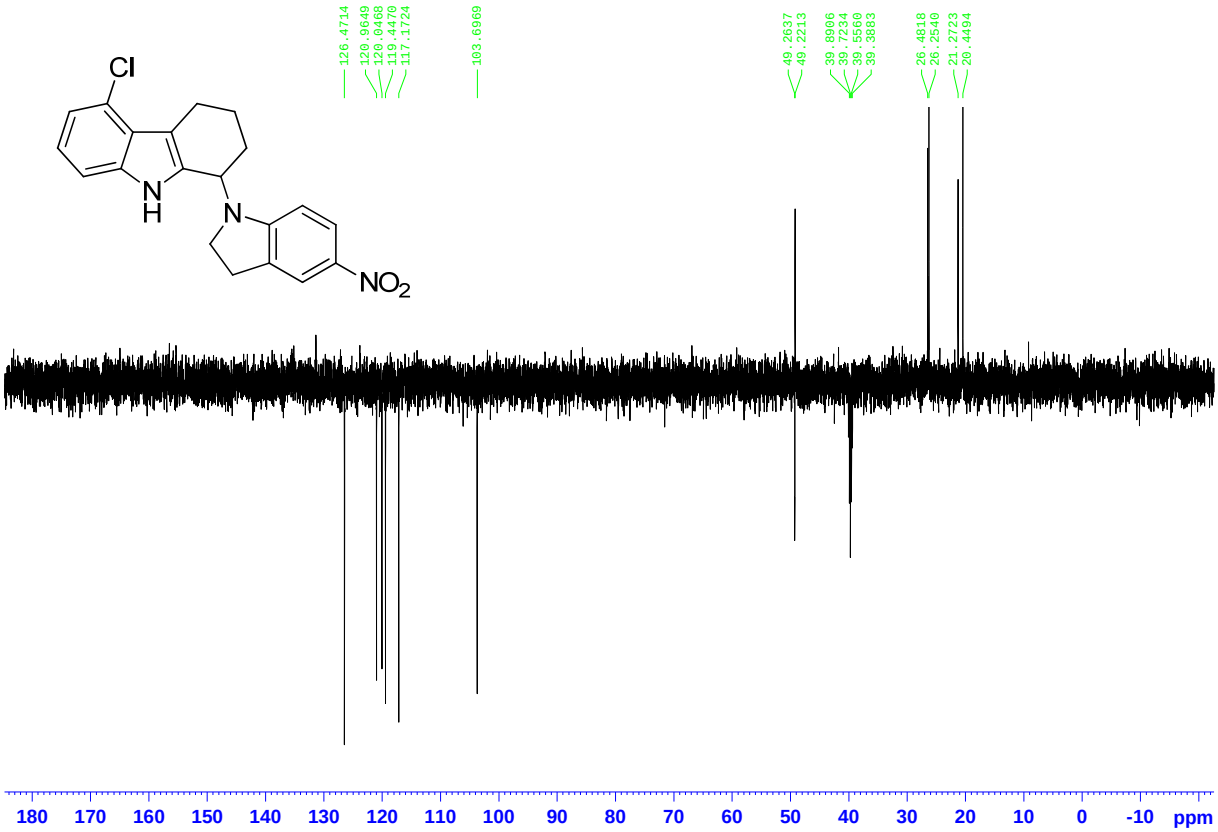
5-Chloro-1-(5-nitroindolin-1-yl)-2,3,4,9-tetrahydro-1H-carbazole (12)



Supplementary Figure S36: ^{1}H NMR in DMSO of 12

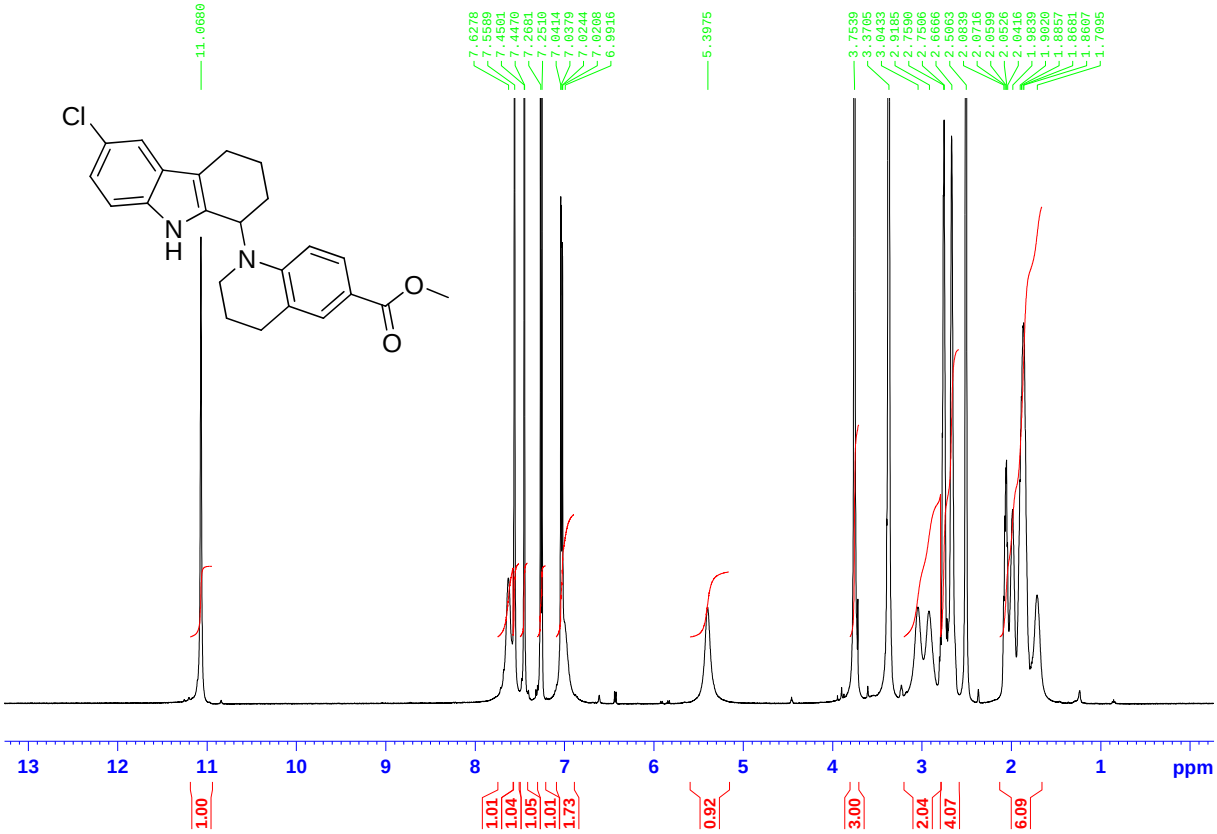


Supplementary Figure S37: ^{13}C NMR in DMSO of 12

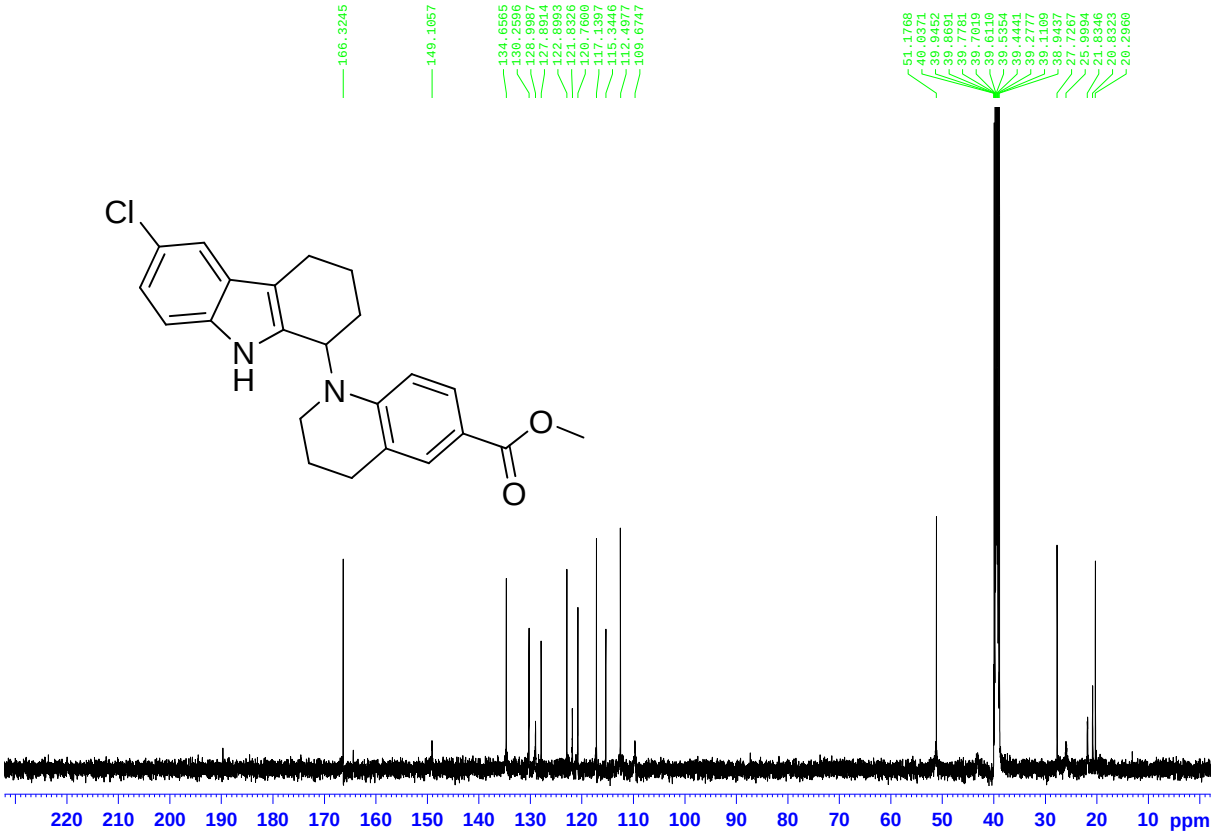


Supplementary Figure S38: dept 135 NMR in DMSO of 12

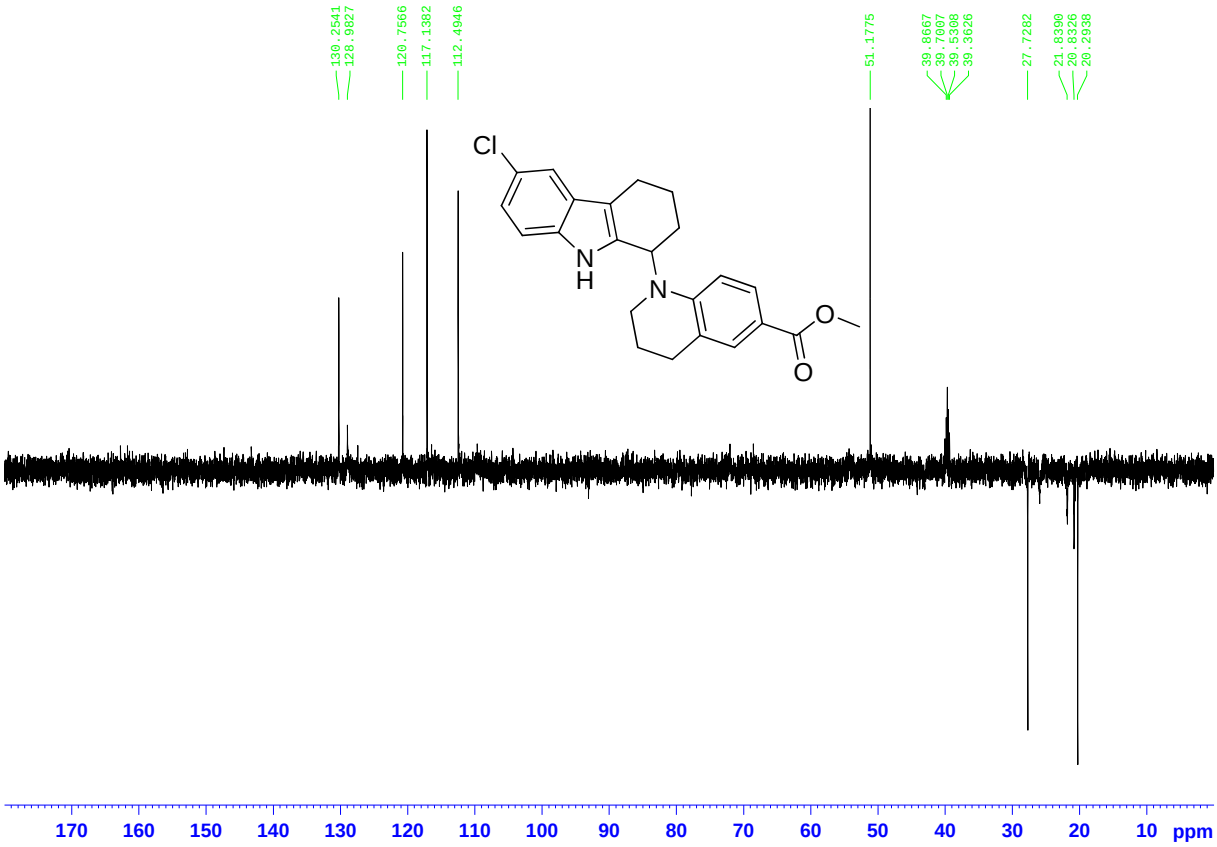
Methyl 1-(6-chloro-2,3,4,9-tetrahydro-1H-carbazol-1-yl)-1,2,3,4-tetrahydroquinoline-6-carboxylate (13)



Supplementary Figure S39: 1H NMR in DMSO of 13

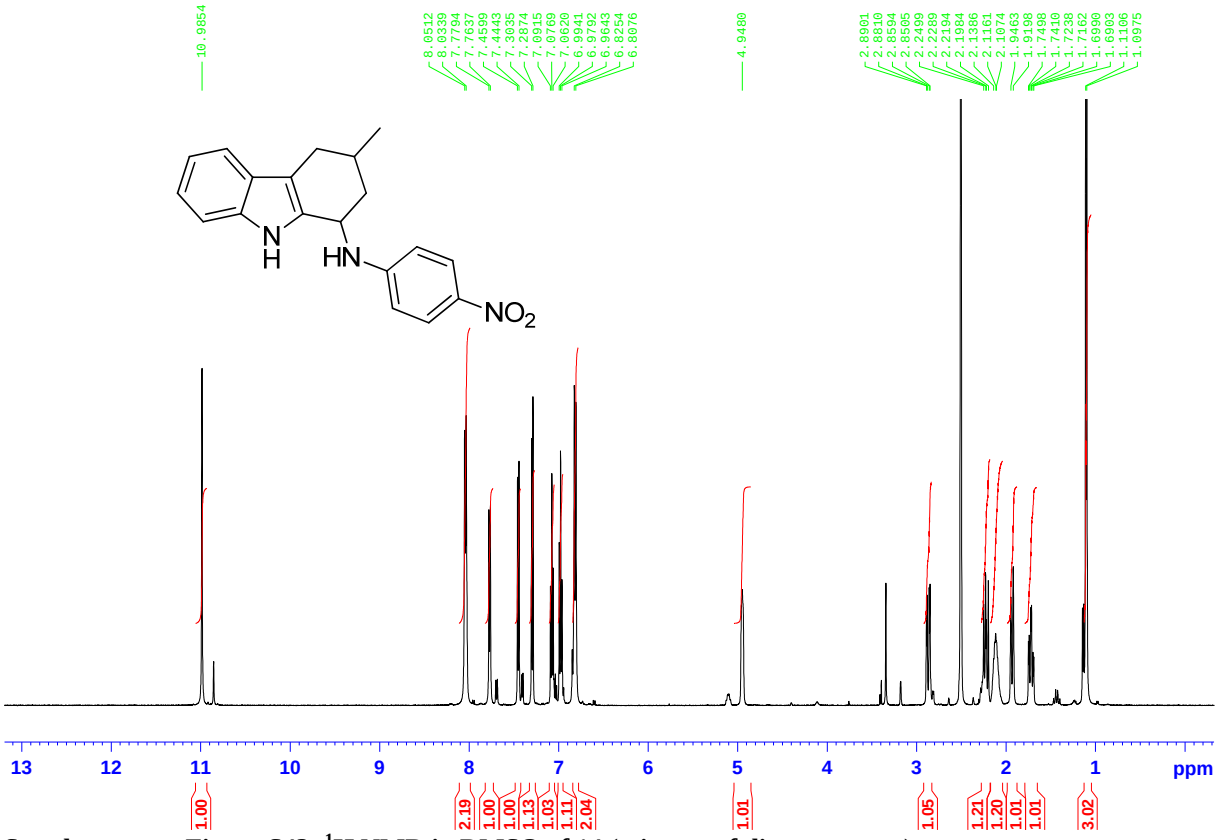


Supplementary Figure S40: ^{13}C NMR in DMSO of 13

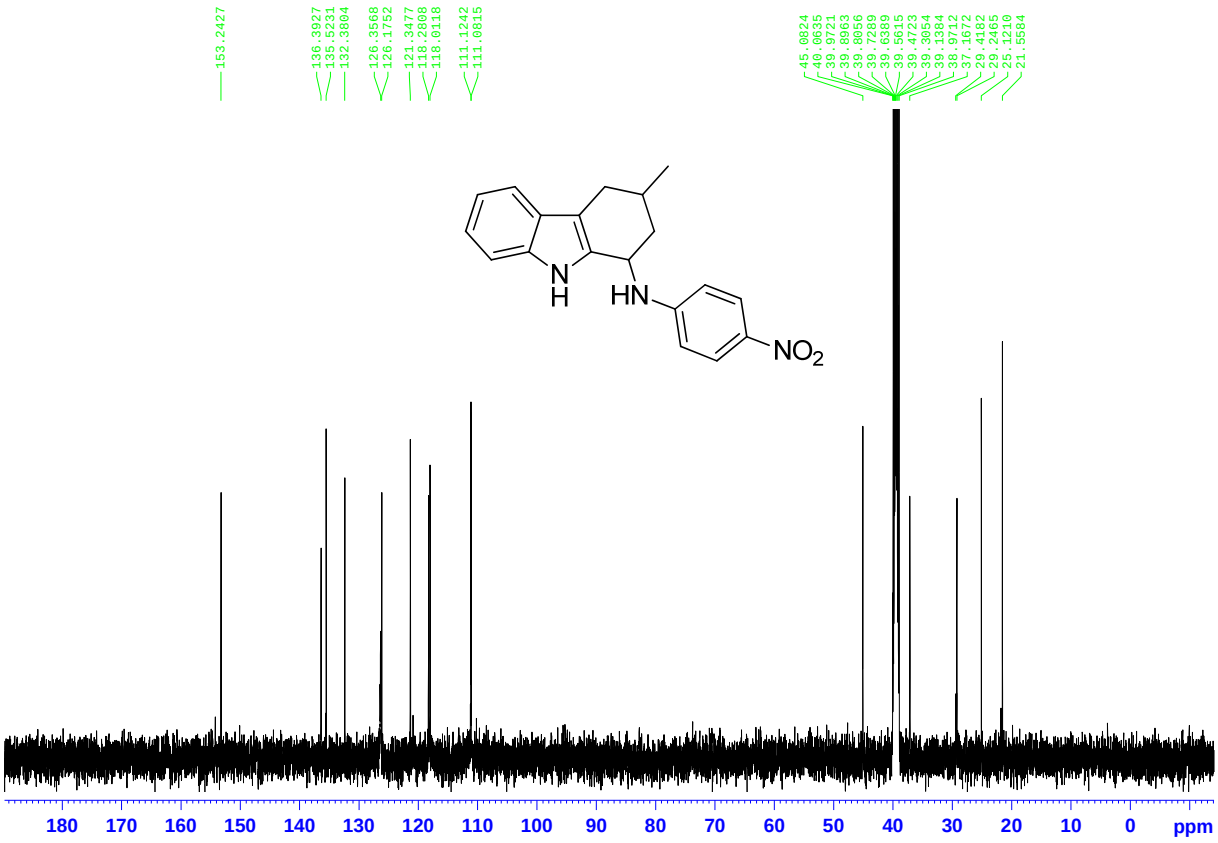


Supplementary Figure S41: dept 135 NMR of 13

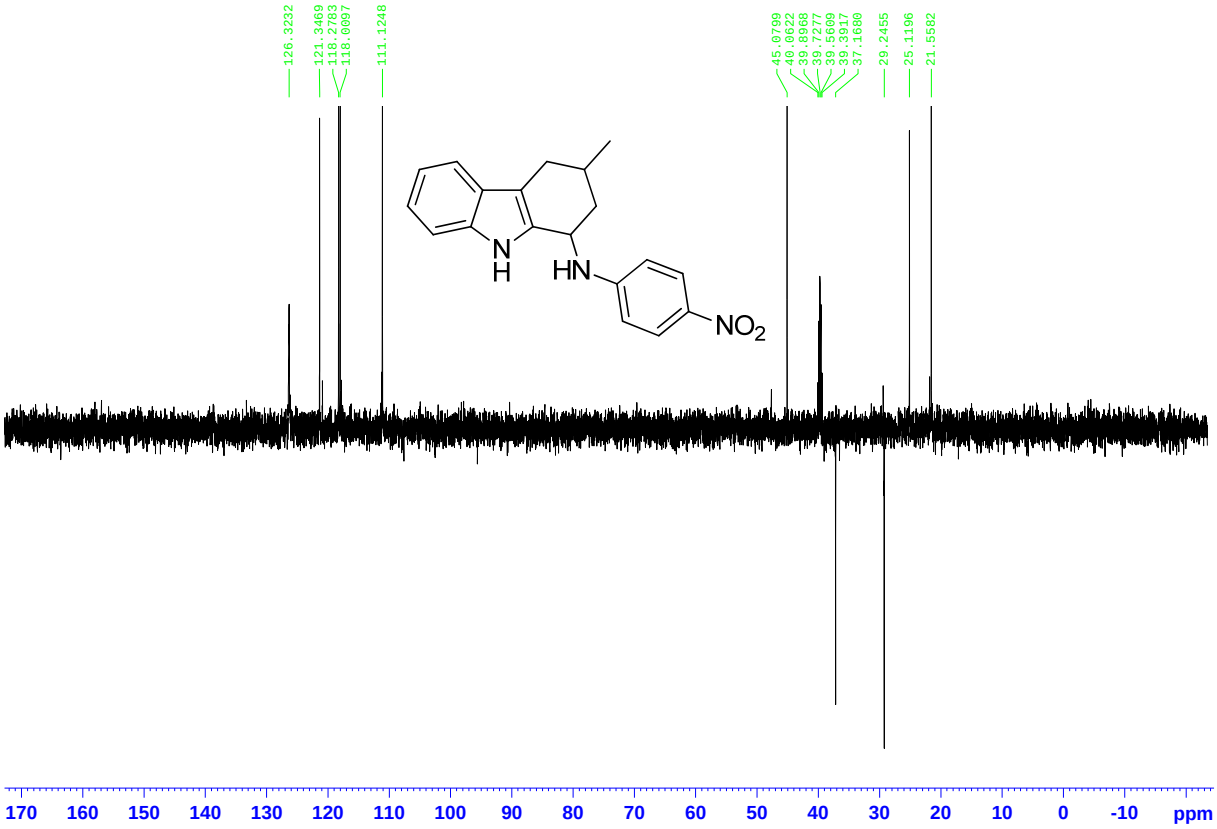
3-Methyl-N-(4-nitrophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (14)



Supplementary Figure S42: ^{1}H NMR in DMSO of 14 (mixture of diastereomers)

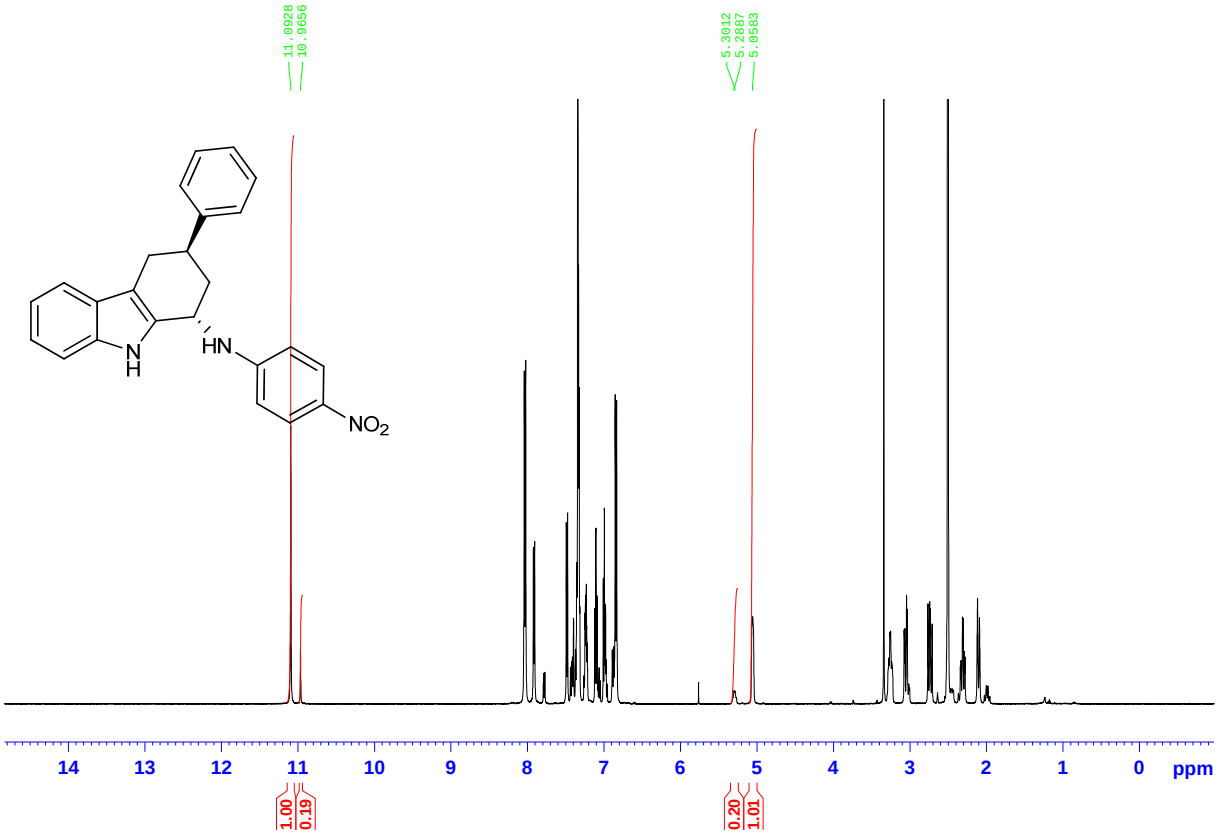


Supplementary Figure S43: ^{13}C NMR in DMSO of 14 (mixture of diastereomers)

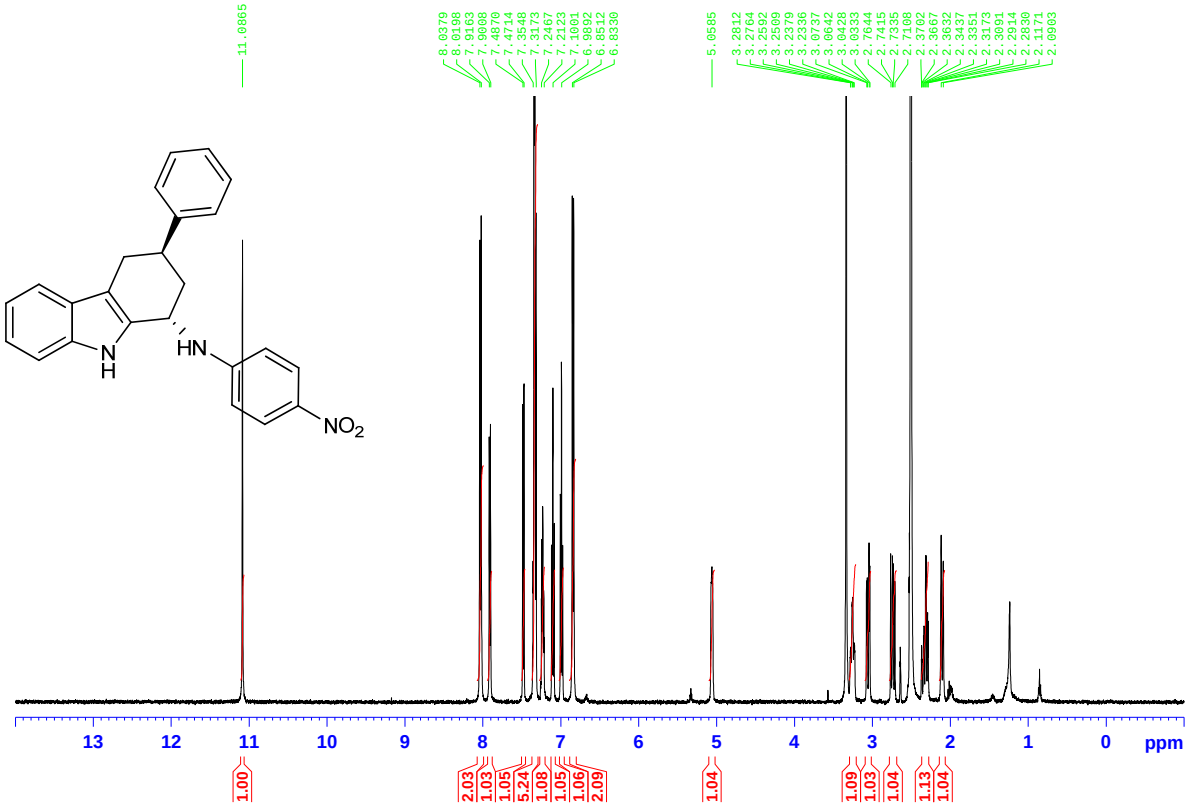


Supplementary Figure S44: dept 135 NMR of 14 (mixture of diastereomers)

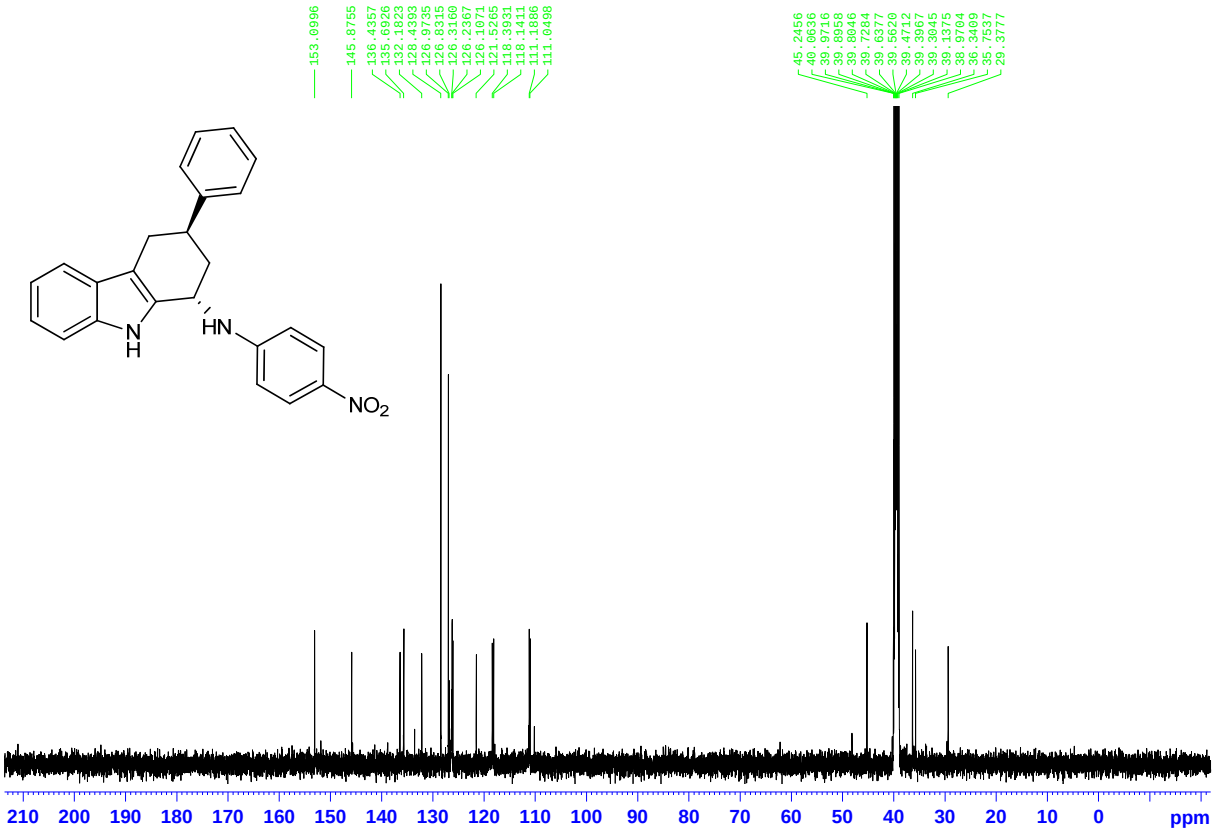
N-(4-Nitrophenyl)-3-phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (15)



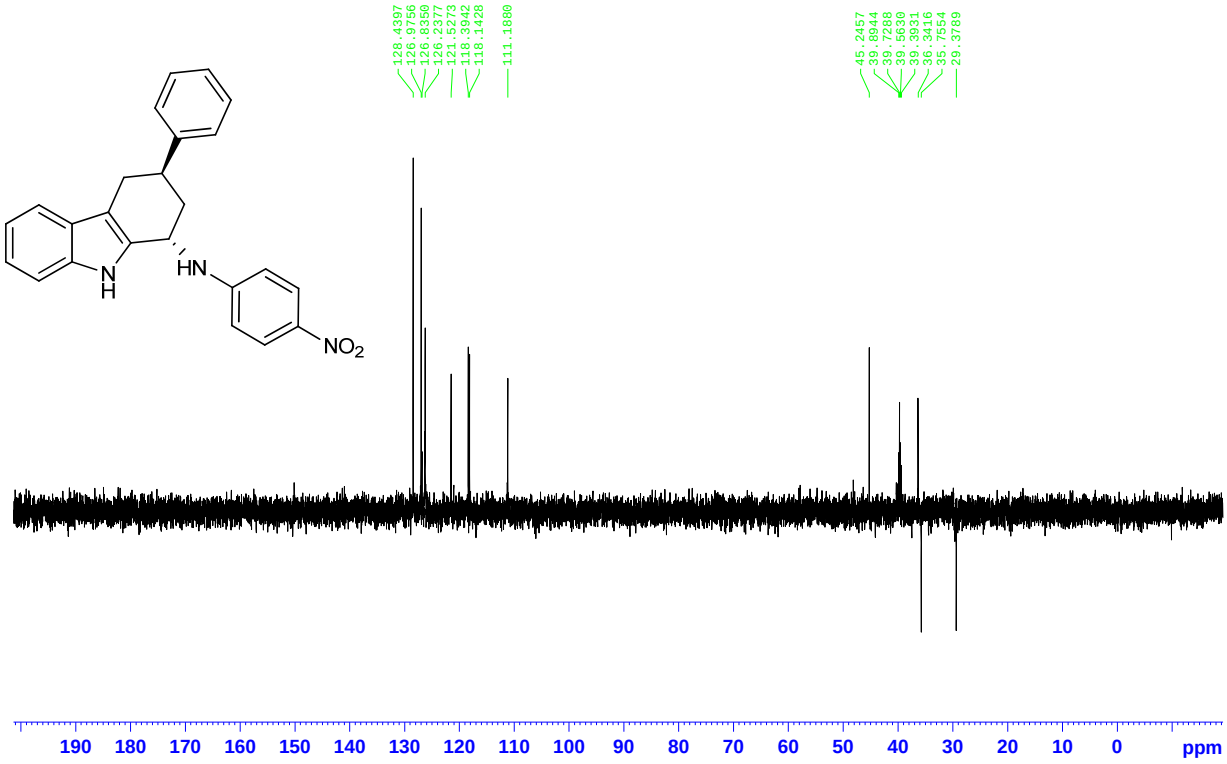
Supplementary Figure S45: ^{1}H NMR in DMSO of 15 (mixture of diastereomers)



Supplementary Figure S46: ^{1}H NMR in DMSO of 15 (major diastereomer)

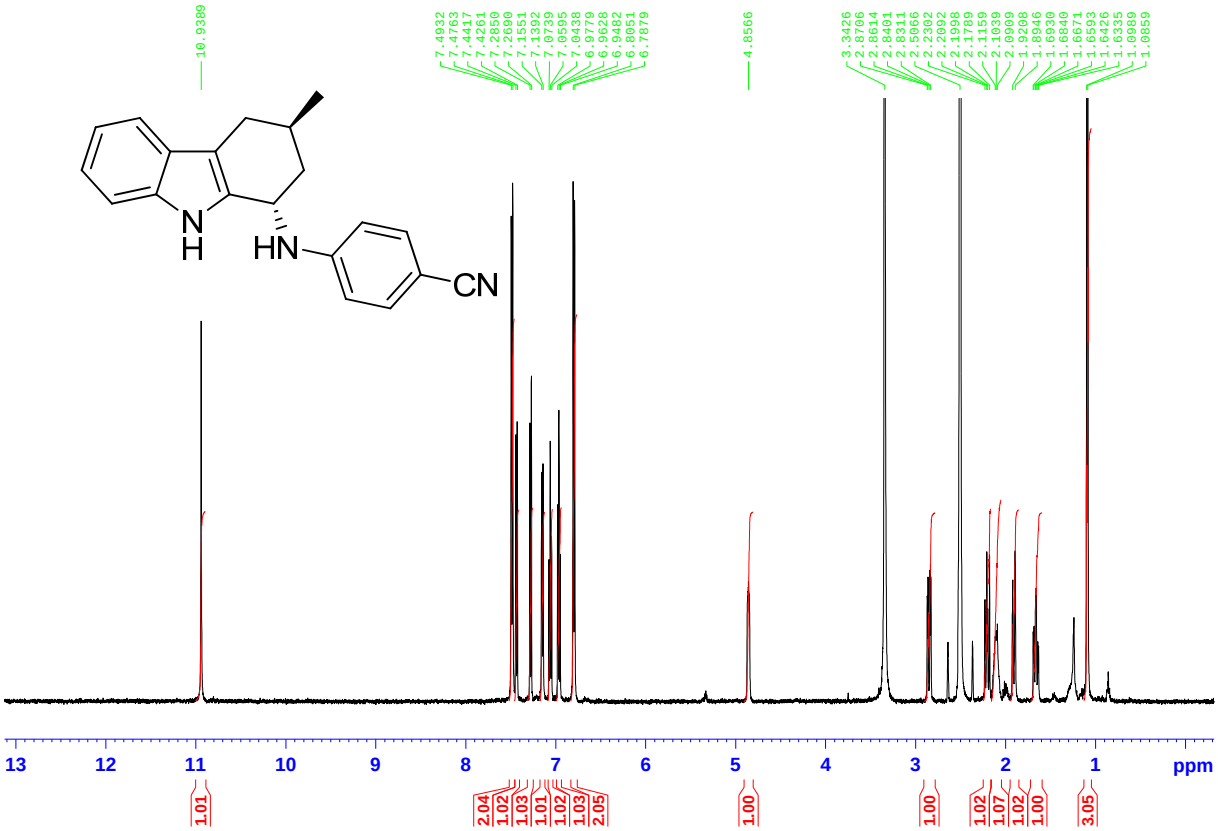


Supplementary Figure S47: ^{13}C NMR in DMSO of 15 (major diastereomer)

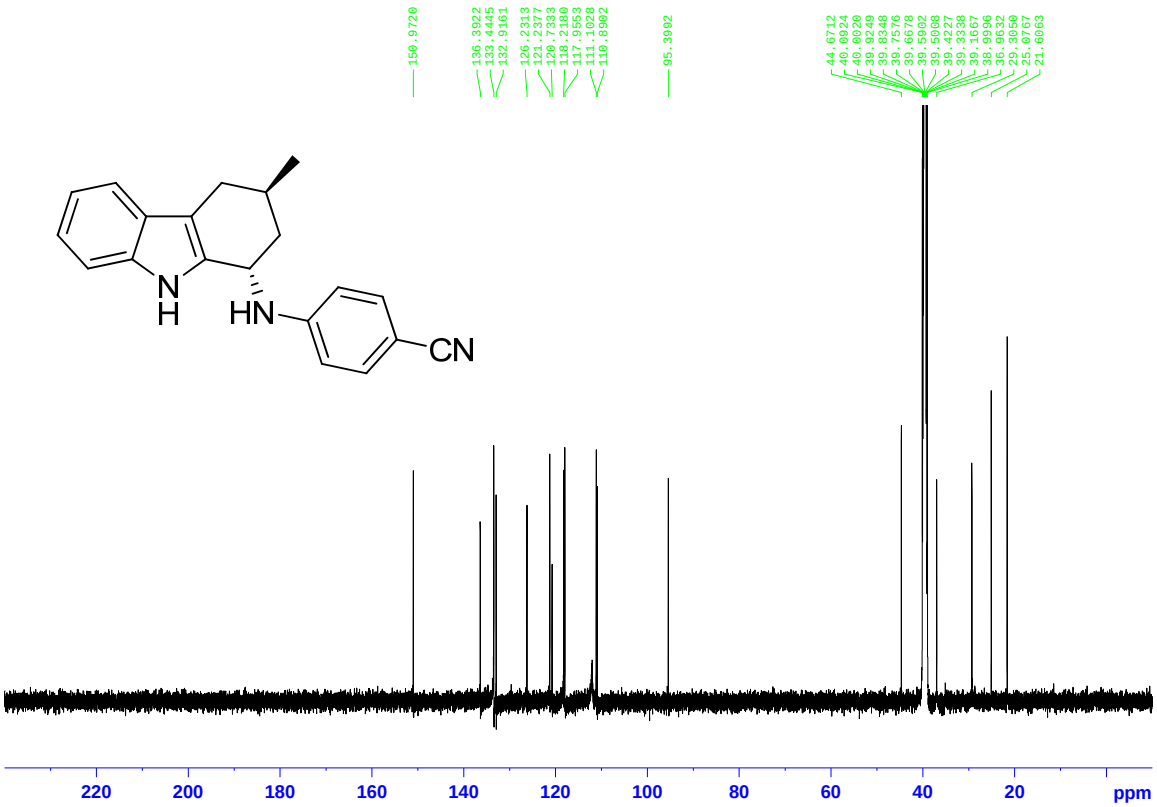


Supplementary Figure S48: dept 135 NMR in DMSO of 15 (major diastereomer)

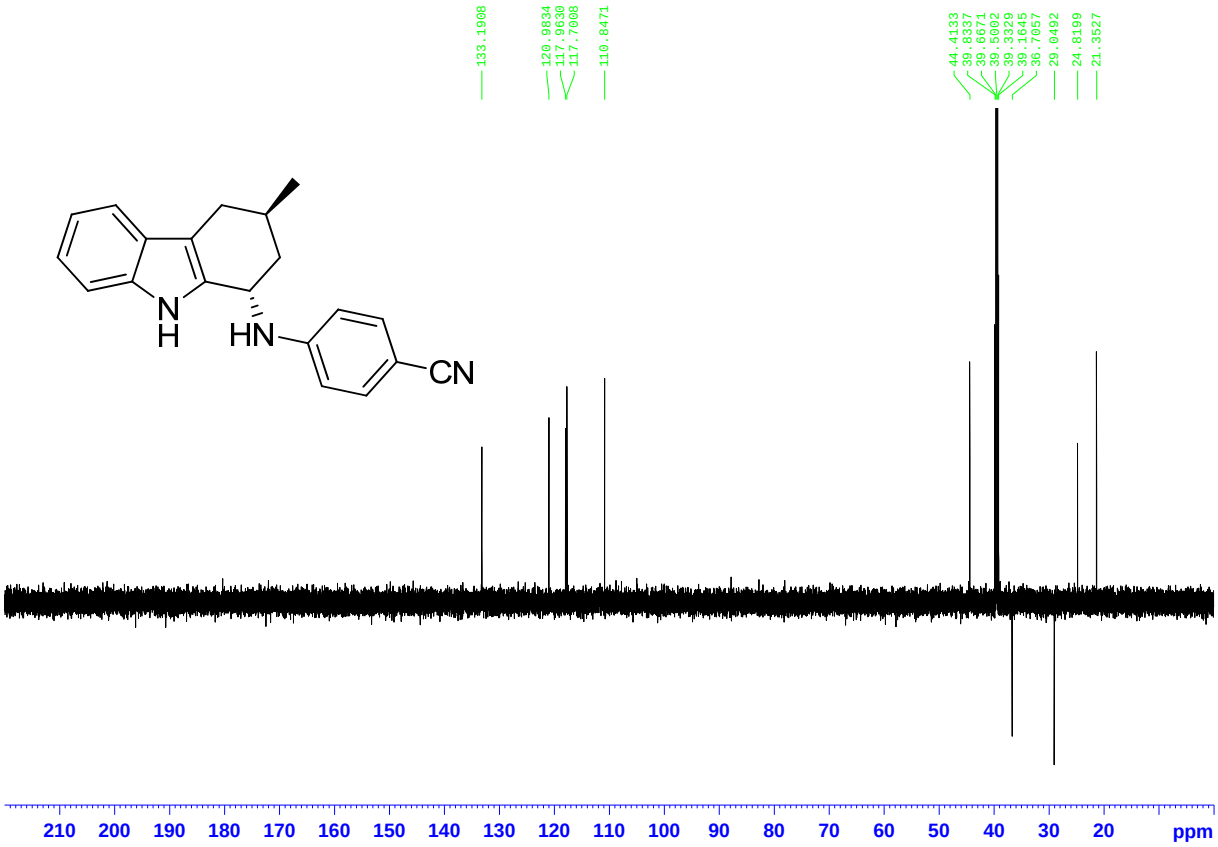
4-(-3-Methyl-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (16)



Supplementary Figure S49: ^{1}H NMR in DMSO of 16

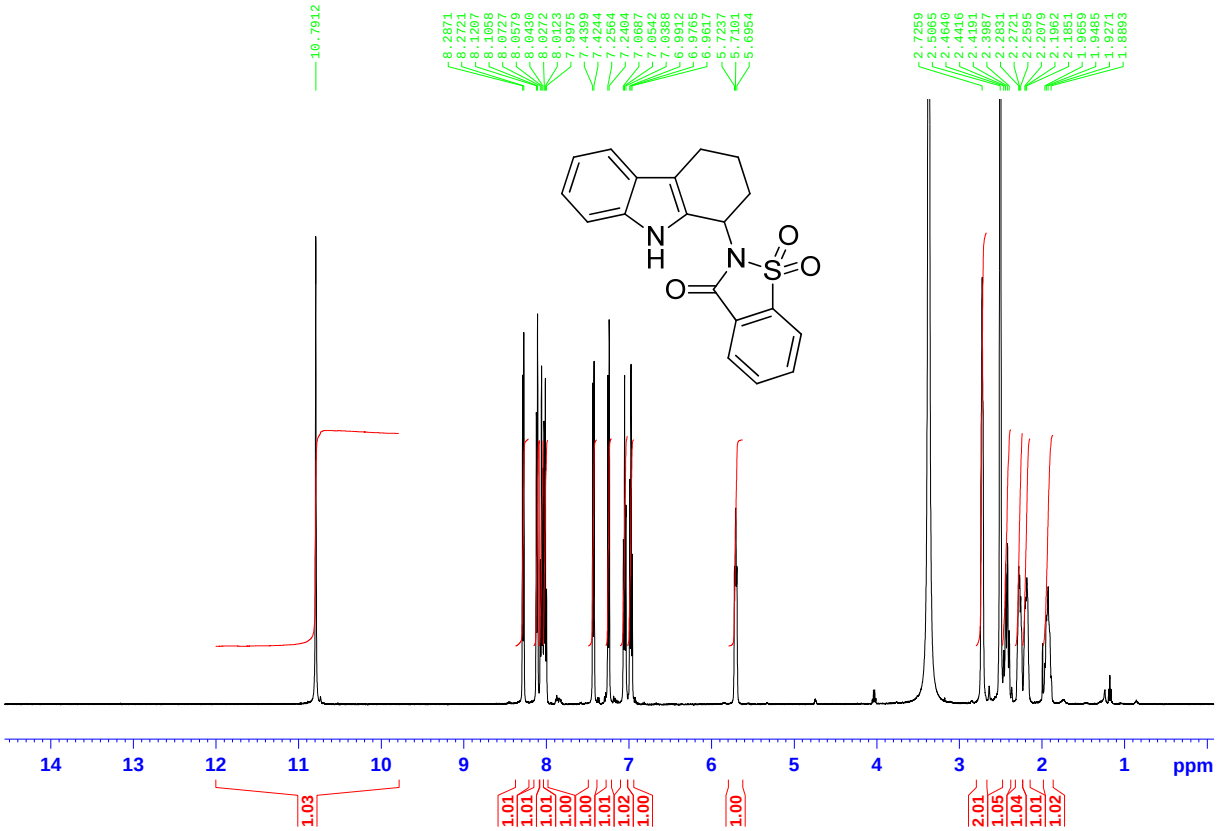


Supplementary Figure S50: ^{13}C NMR in DMSO of 16

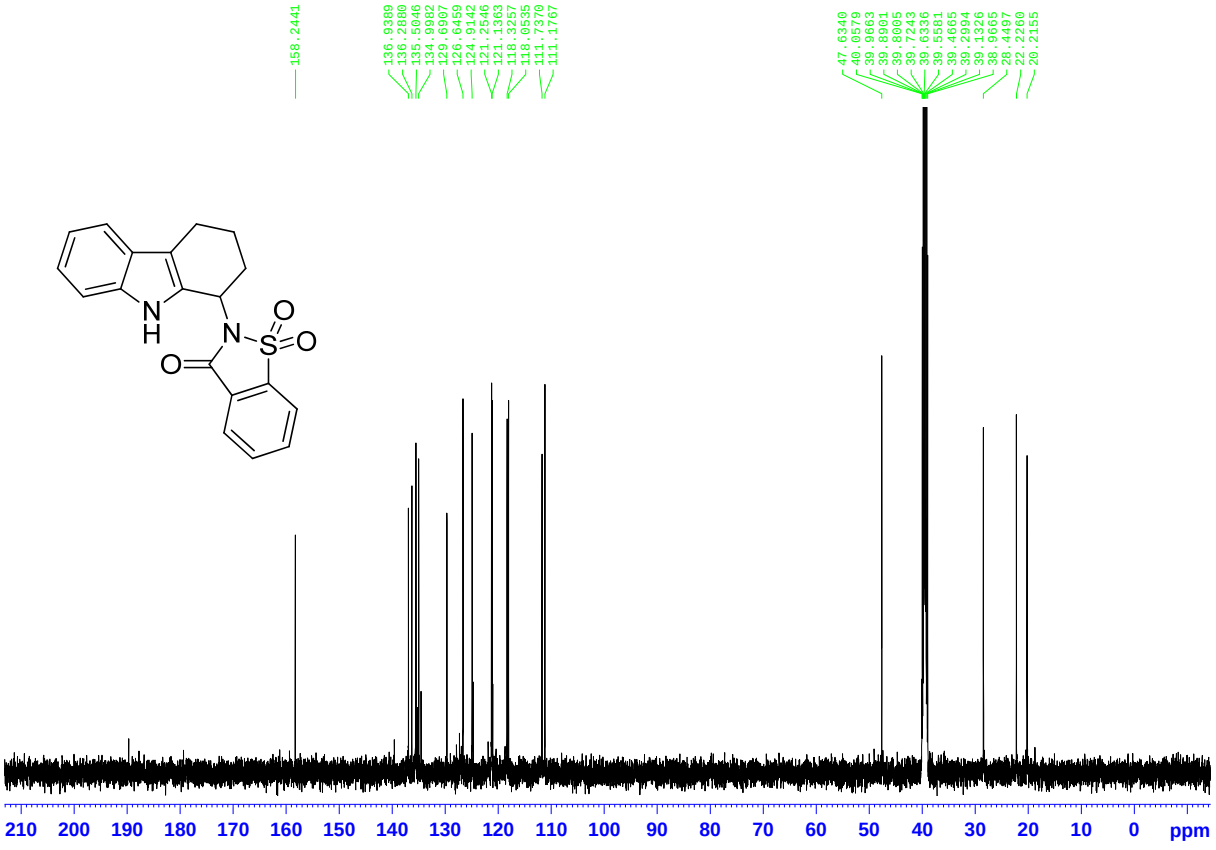


Supplementary Figure S51: dept 135 NMR in DMSO of 16

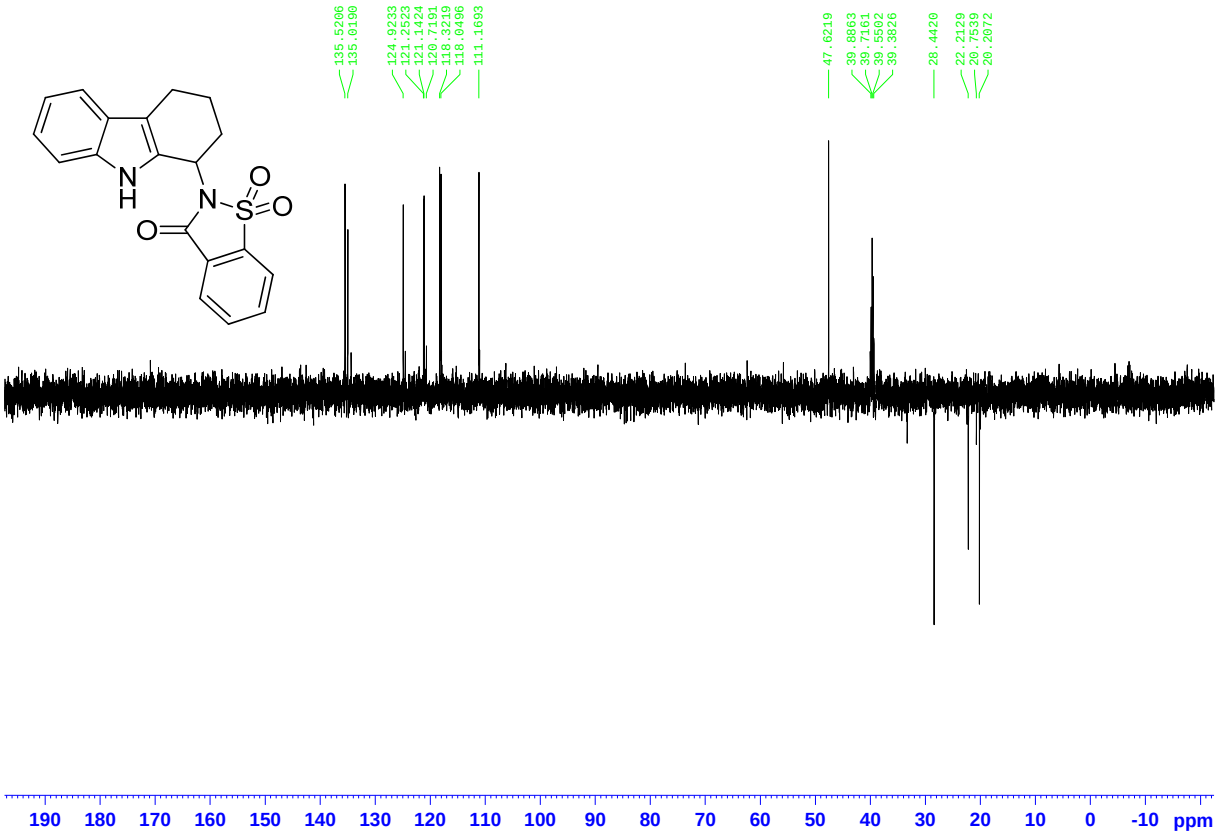
1-Saccharinyl-2,3,4,9-tetrahydro-1H-carbazole (17)



Supplementary Figure S52: ^{1}H NMR in DMSO of 17

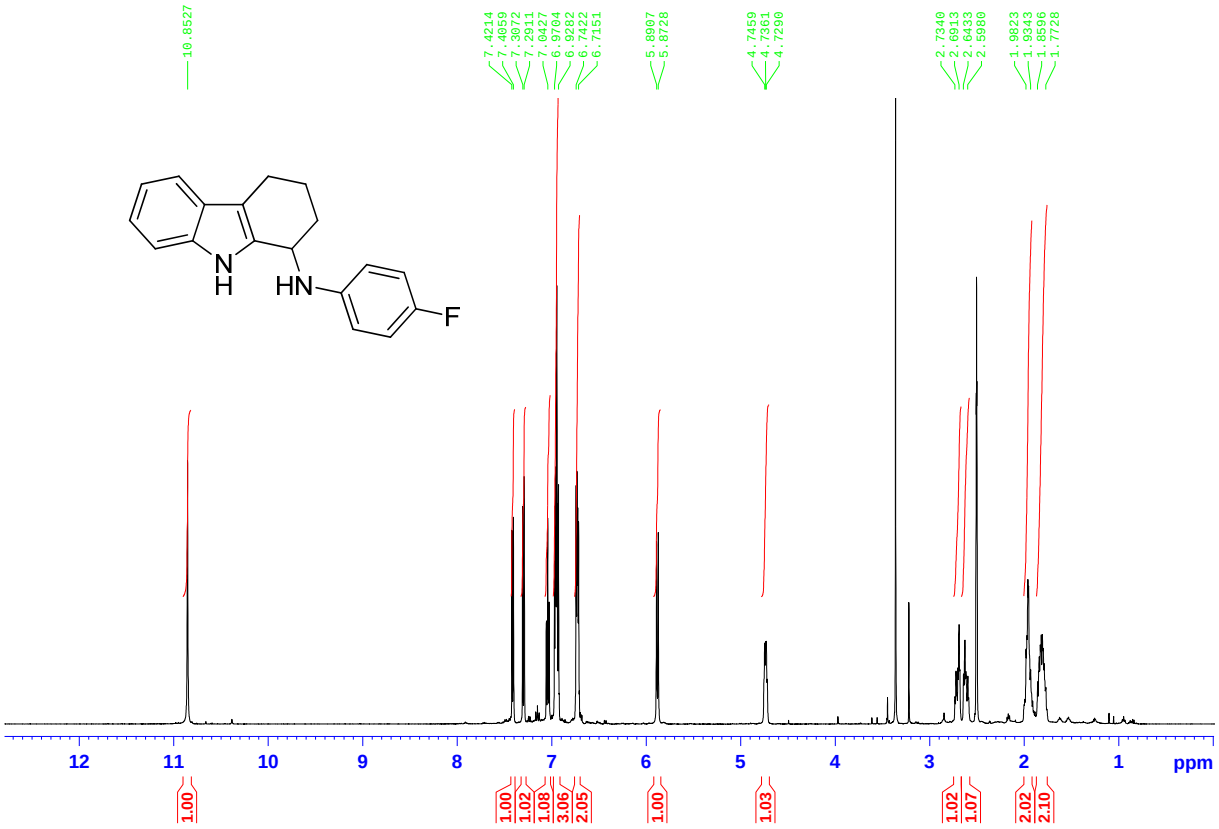


Supplementary Figure S53:^{13}C NMR in DMSO of 17

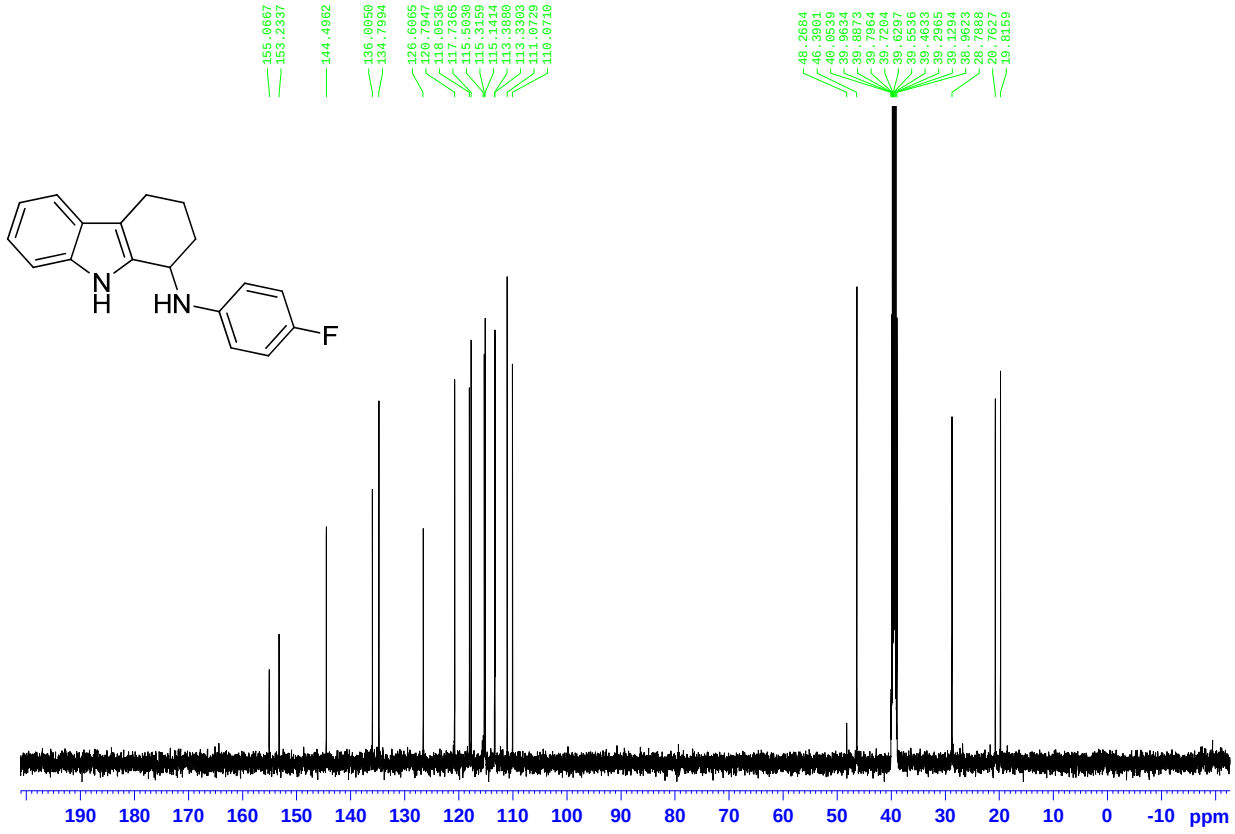


Supplementary Figure S54: dept 135 NMR of 17

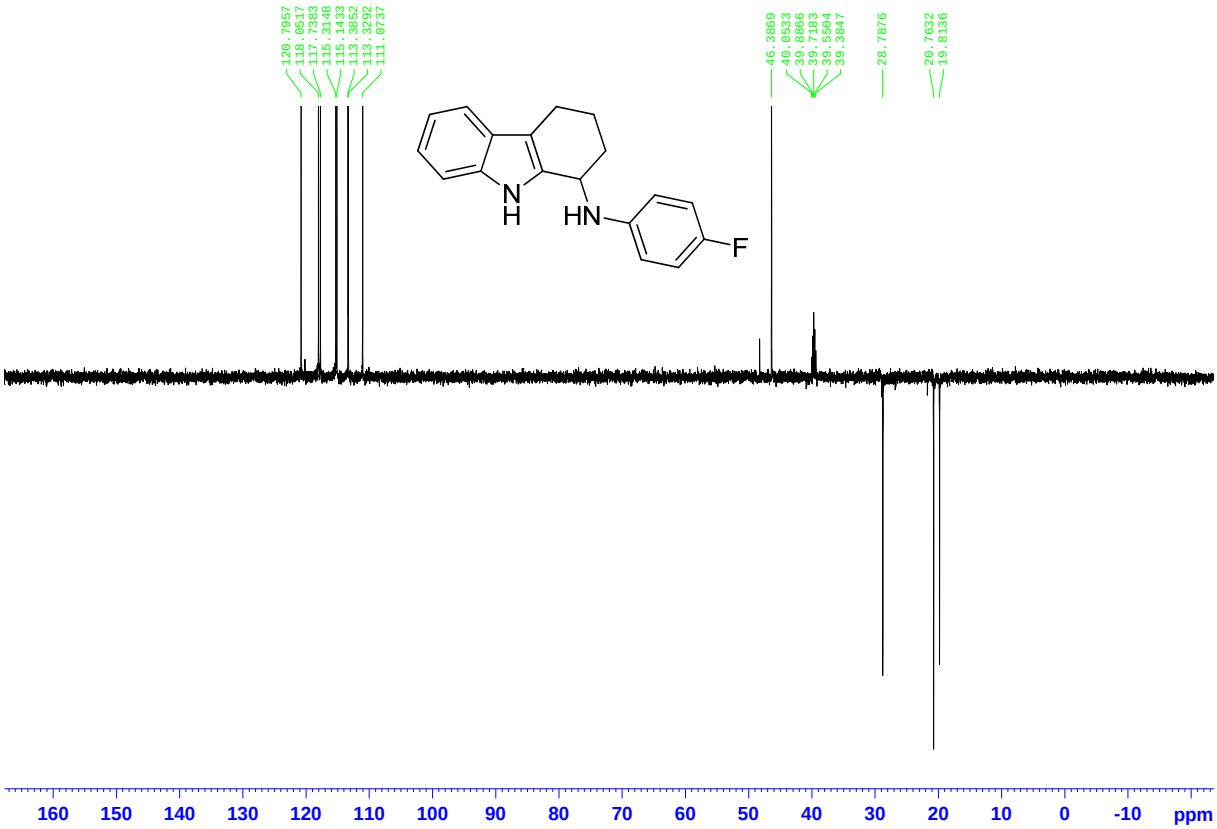
N-(4-Fluorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (18)



Supplementary Figure S55: ^{1}H NMR in DMSO of 18

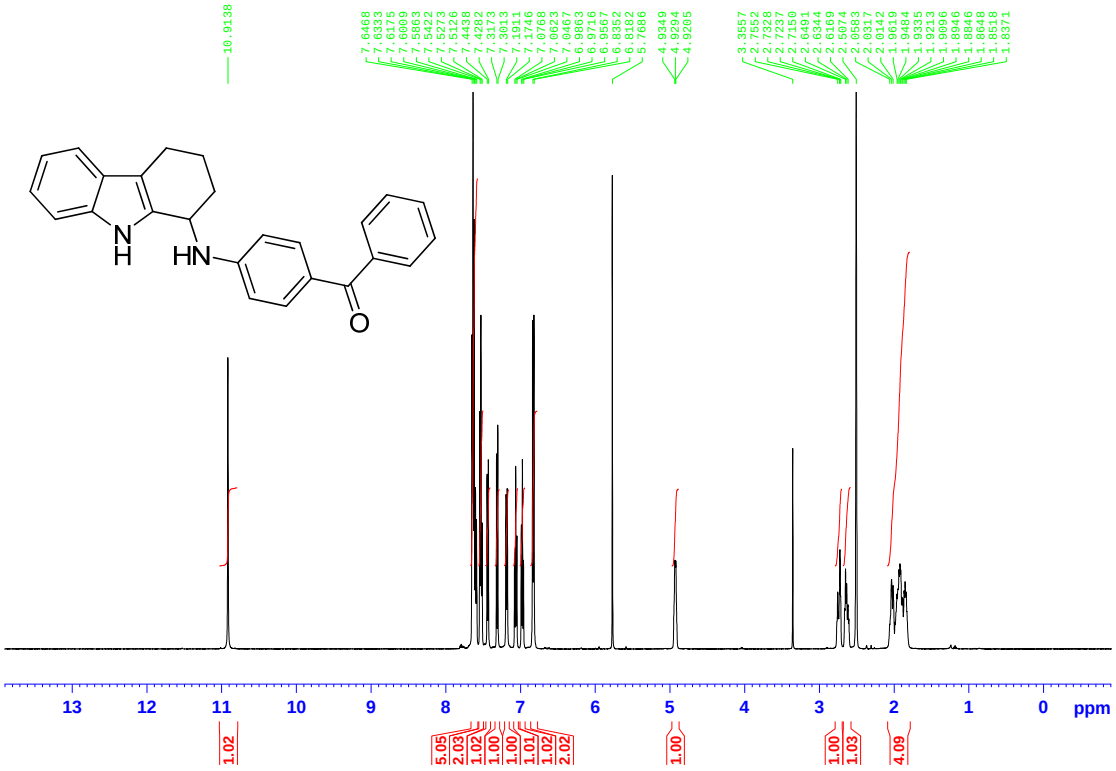


Supplementary Figure S56: ^{13}C NMR in DMSO of 18

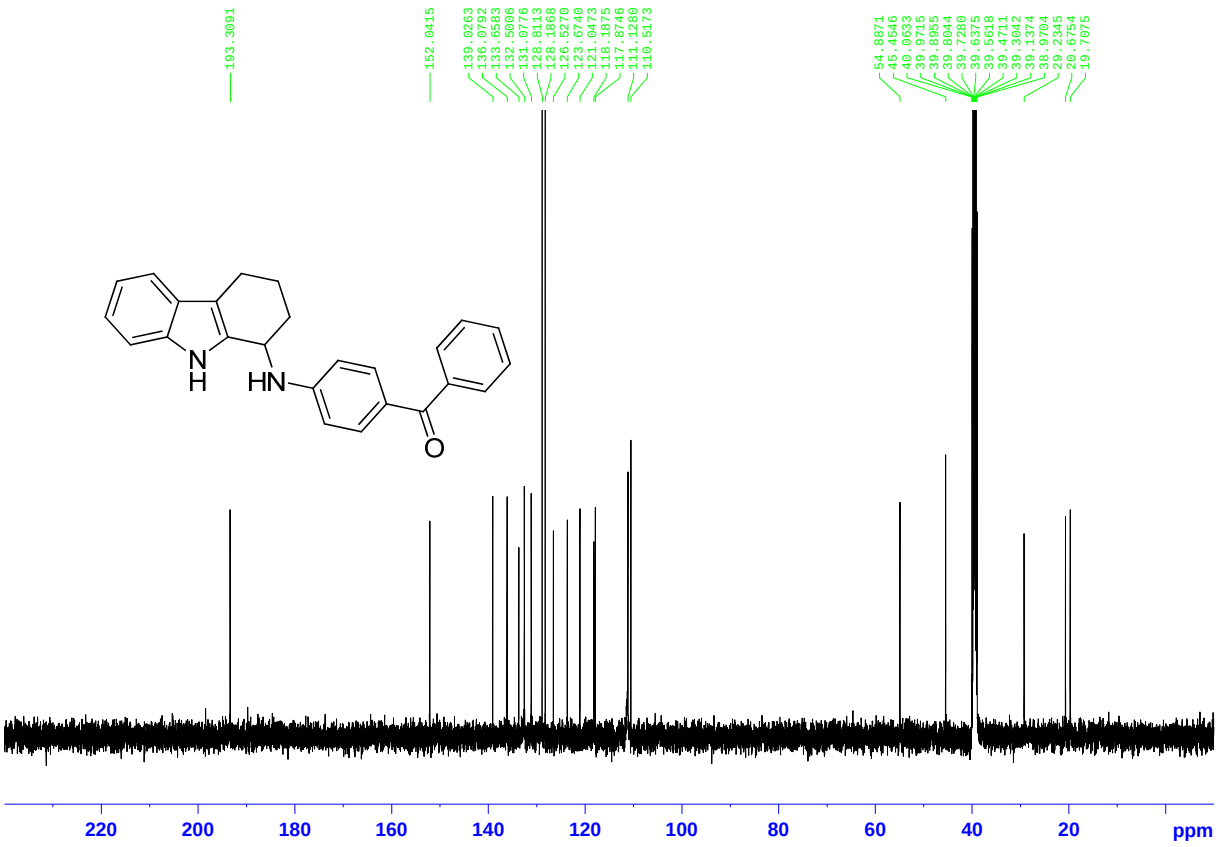


Supplementary Figure S57: dept 135 NMR of 18

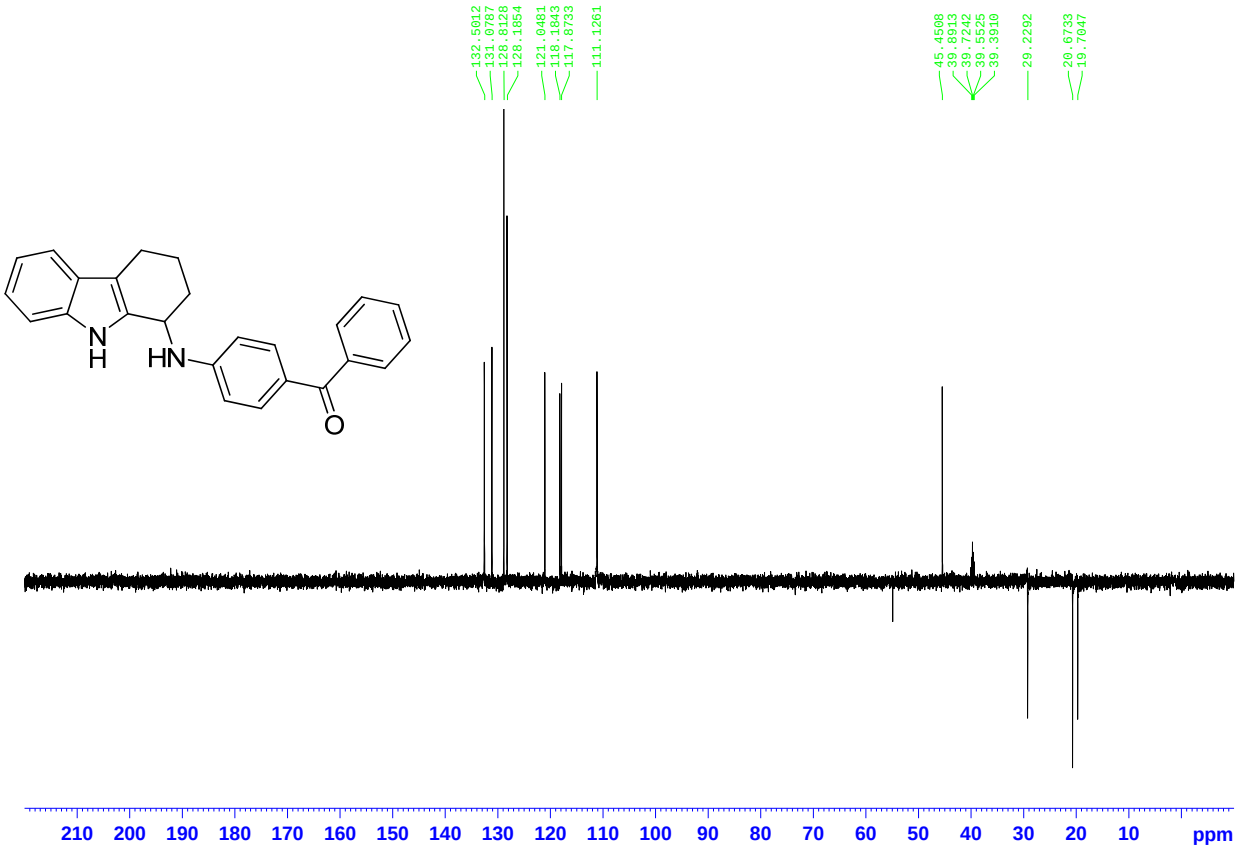
Phenyl(4-(2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)phenyl)methanone (19)



Supplementary Figure S58: ^{1}H NMR in DMSO of 19

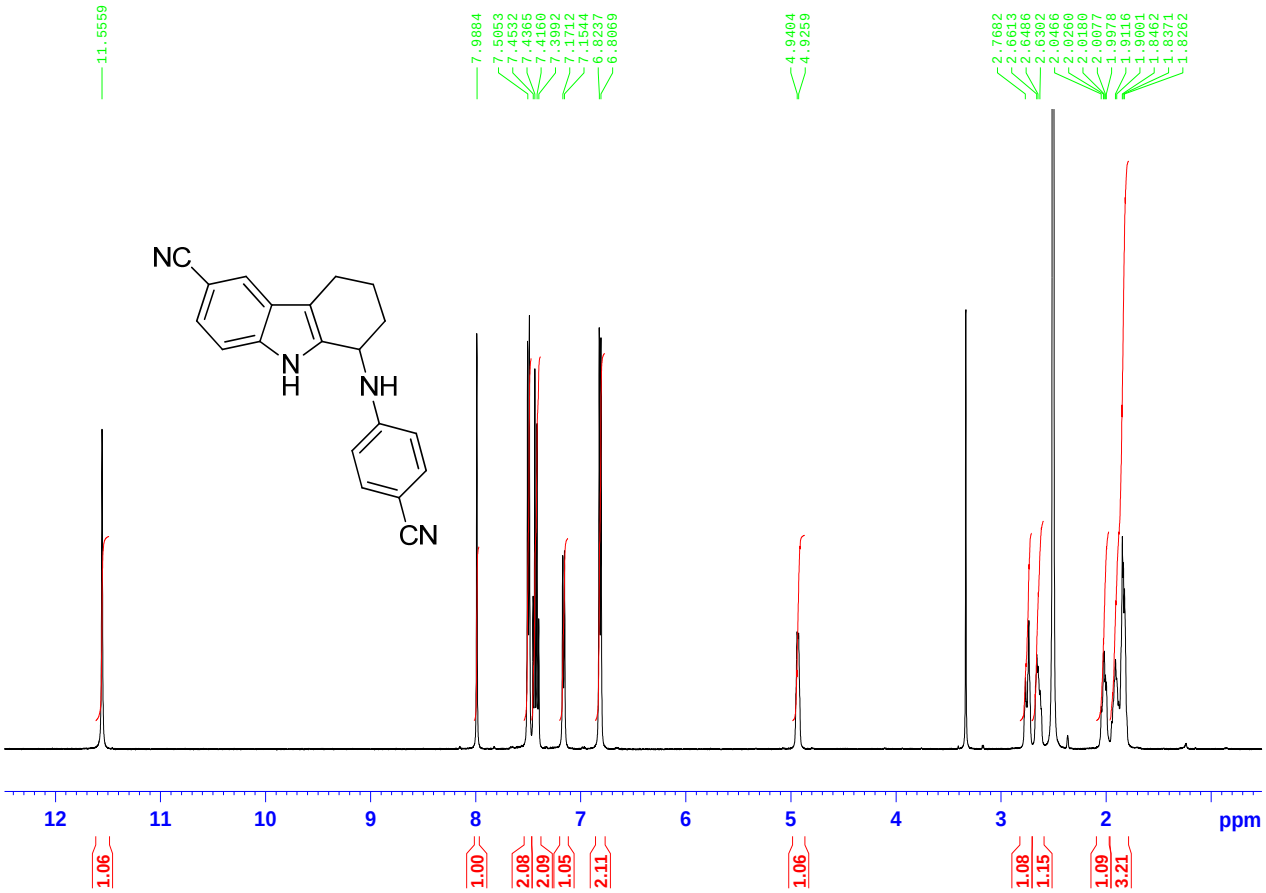


Supplementary Figure S59: ^{13}C NMR in DMSO of 19

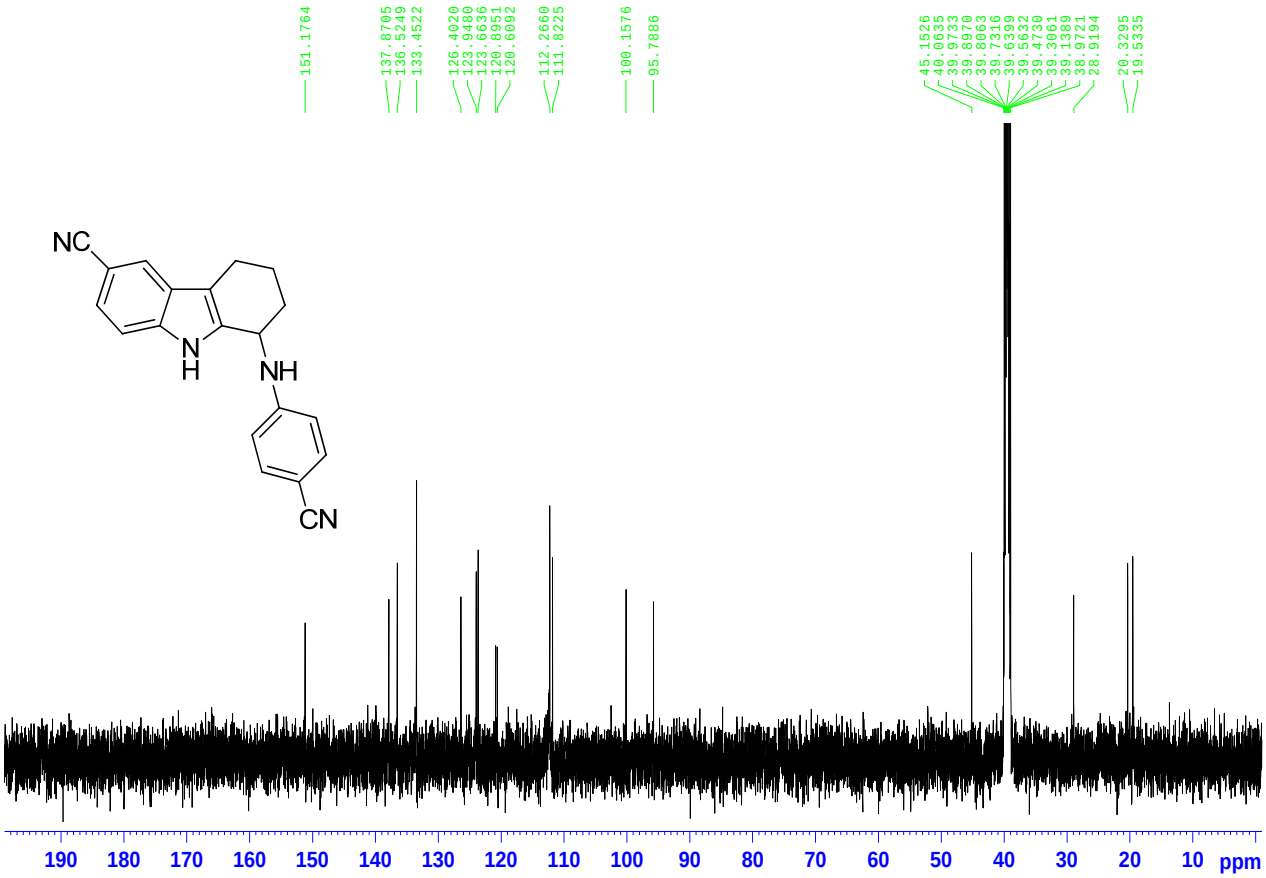


Supplementary Figure S60: dept 135 NMR of 19

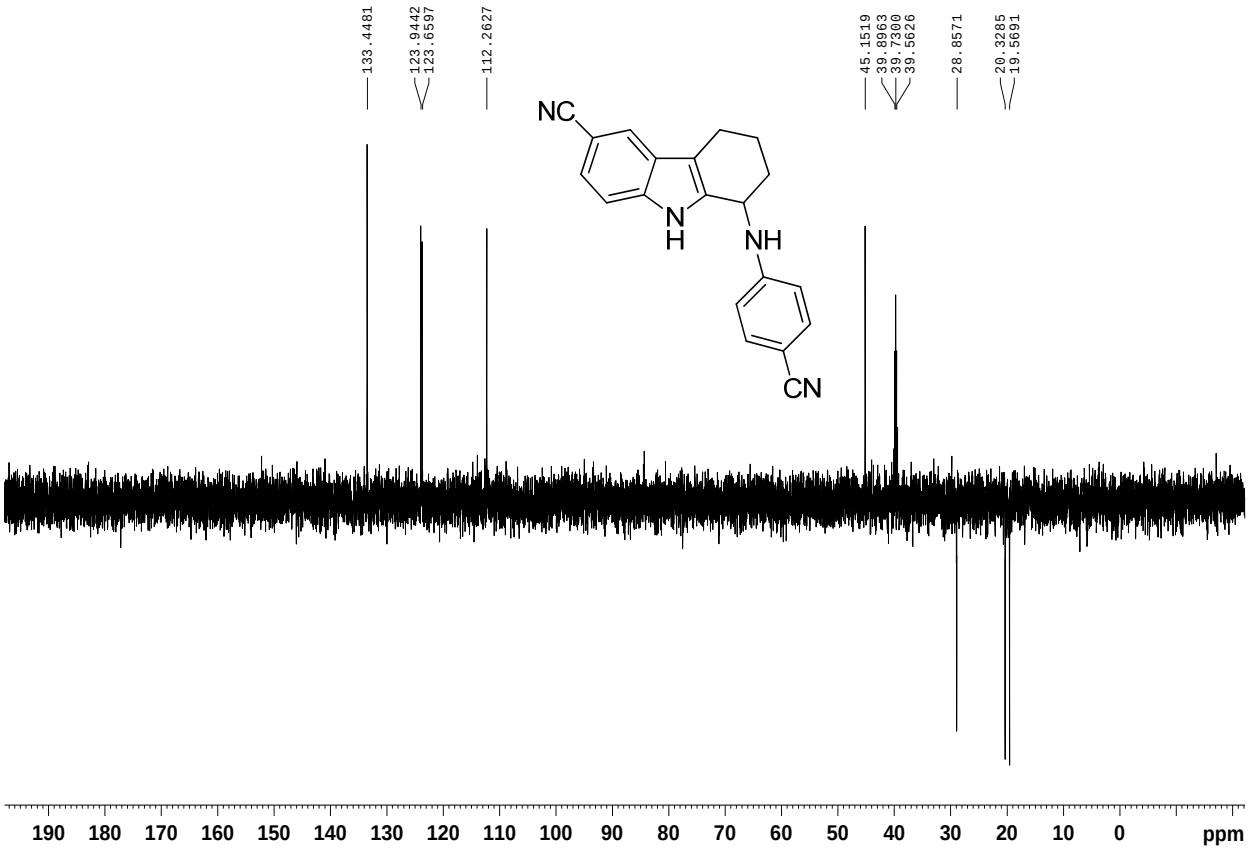
1-(4-Cyanophenylamino)-2,3,4,9-tetrahydro-1H-carbazole-6-carbonitrile (20)



Supplementary Figure S61: ^{1}H NMR in DMSO of 20

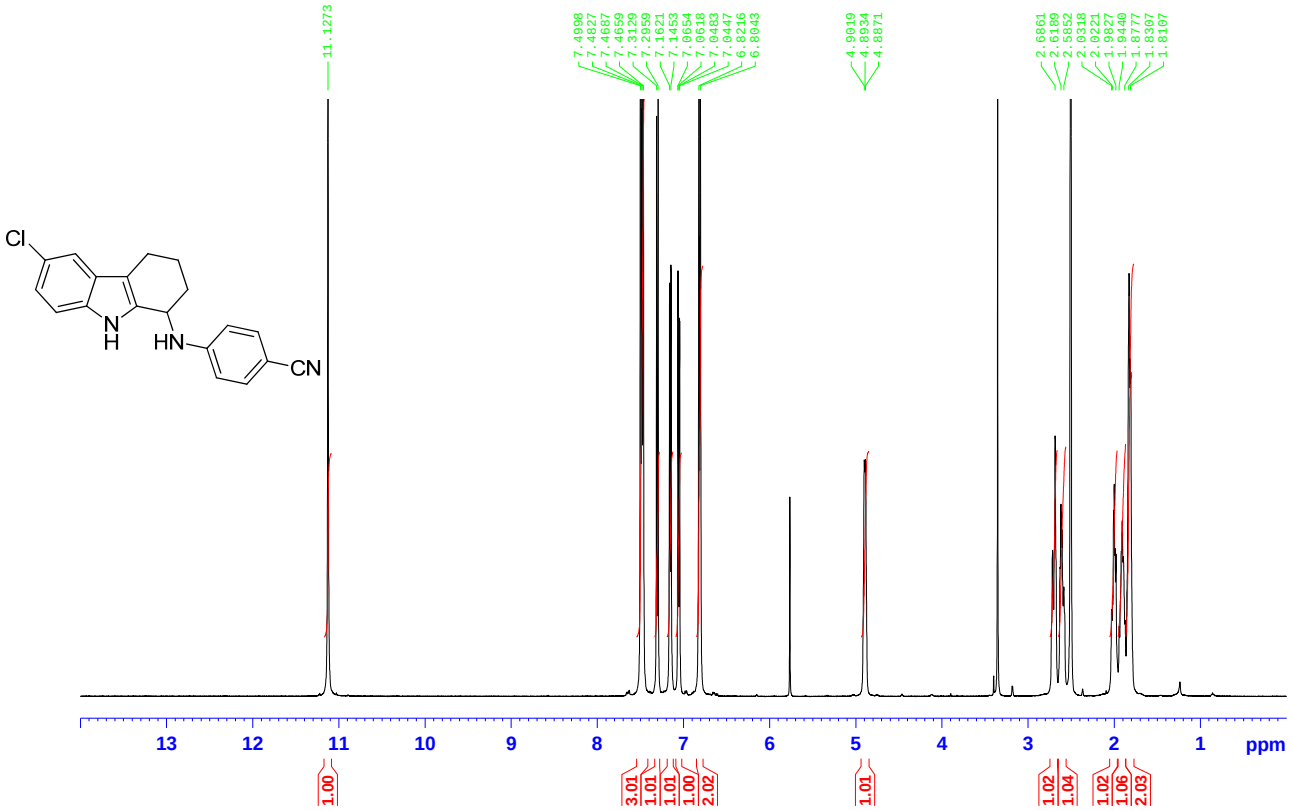


Supplementary Figure S62: ^{13}C NMR in DMSO of 20

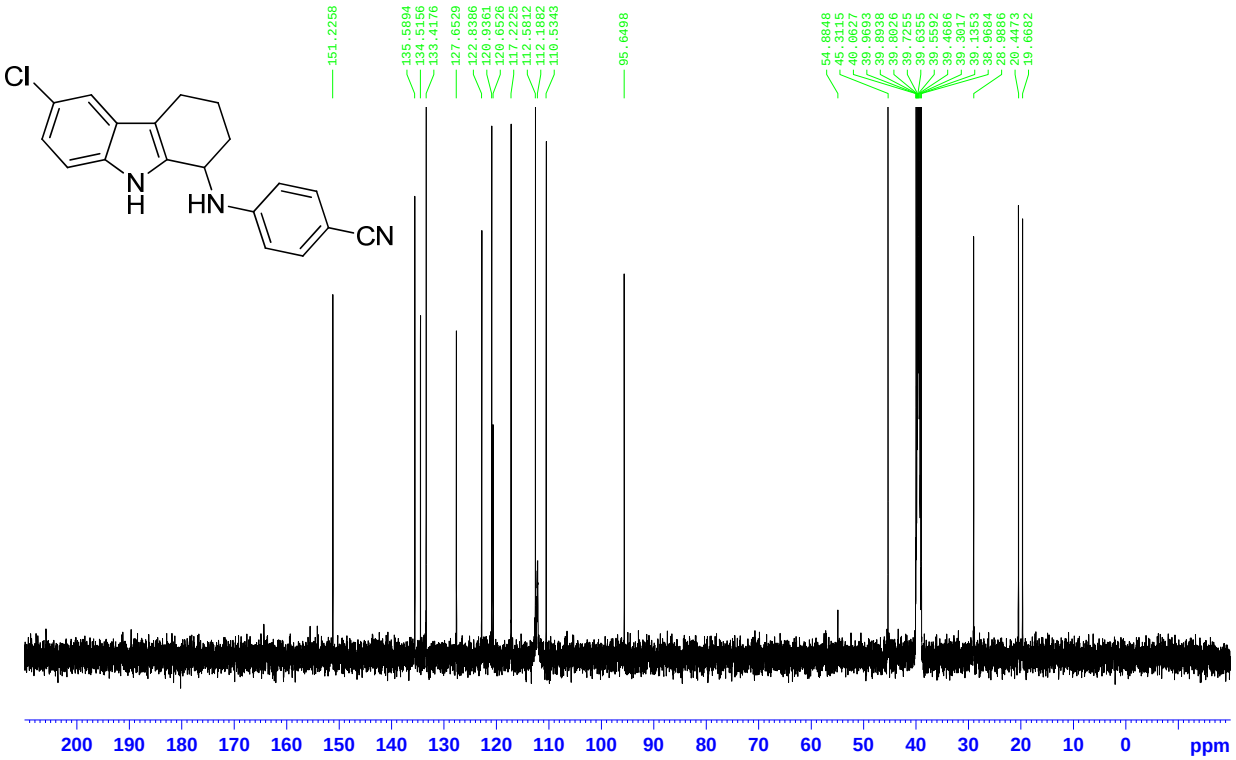


Supplementary Figure S63: dept 135 NMR in DMSO of 20

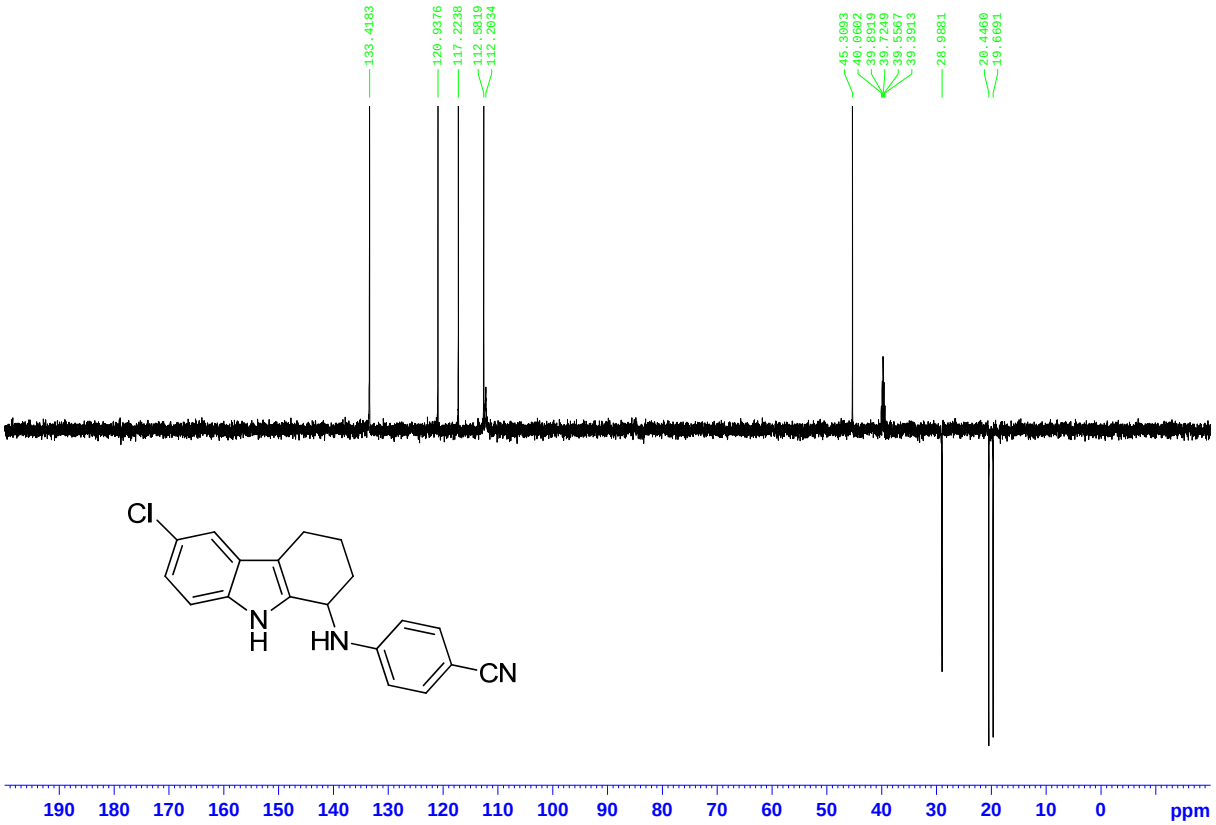
4-(6-Chloro-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (21)



Supplementary Figure S64: ^{1}H NMR in DMSO of 21

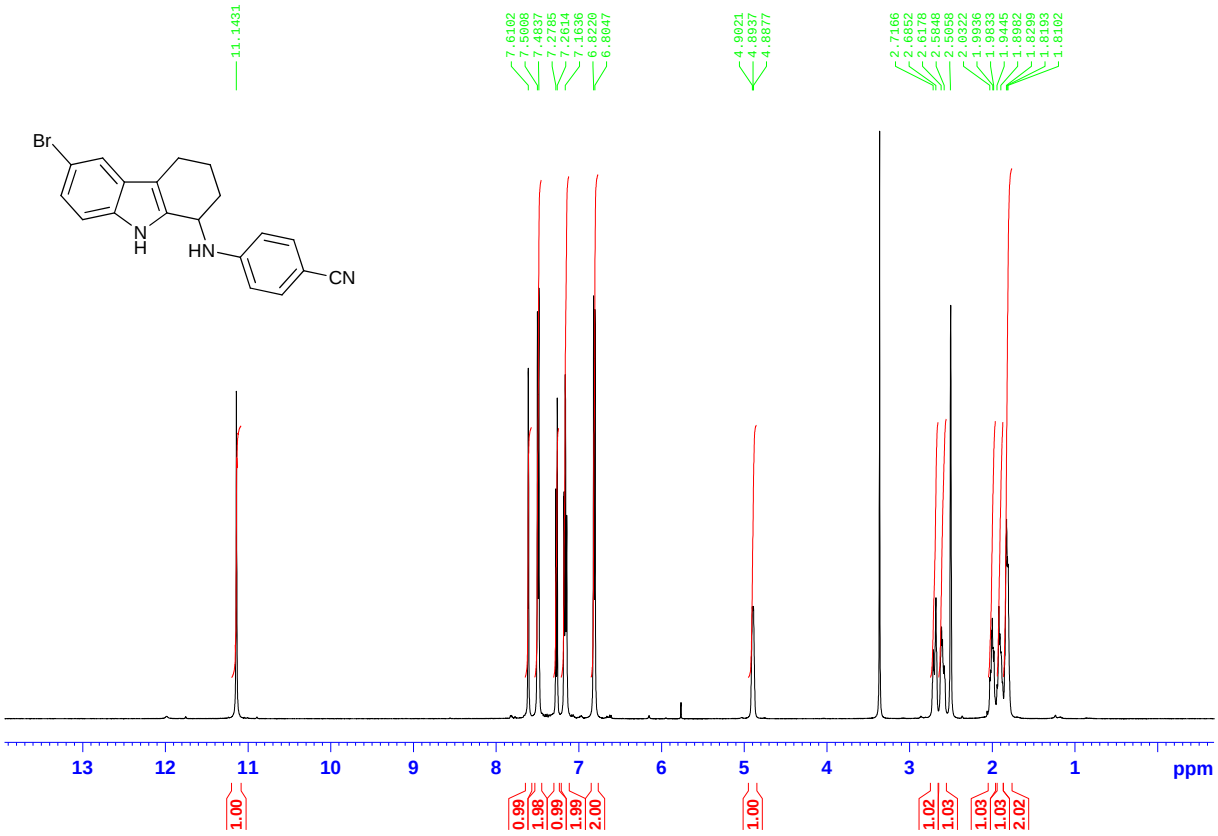


Supplementary Figure S65: ^{13}C NMR in DMSO of 21

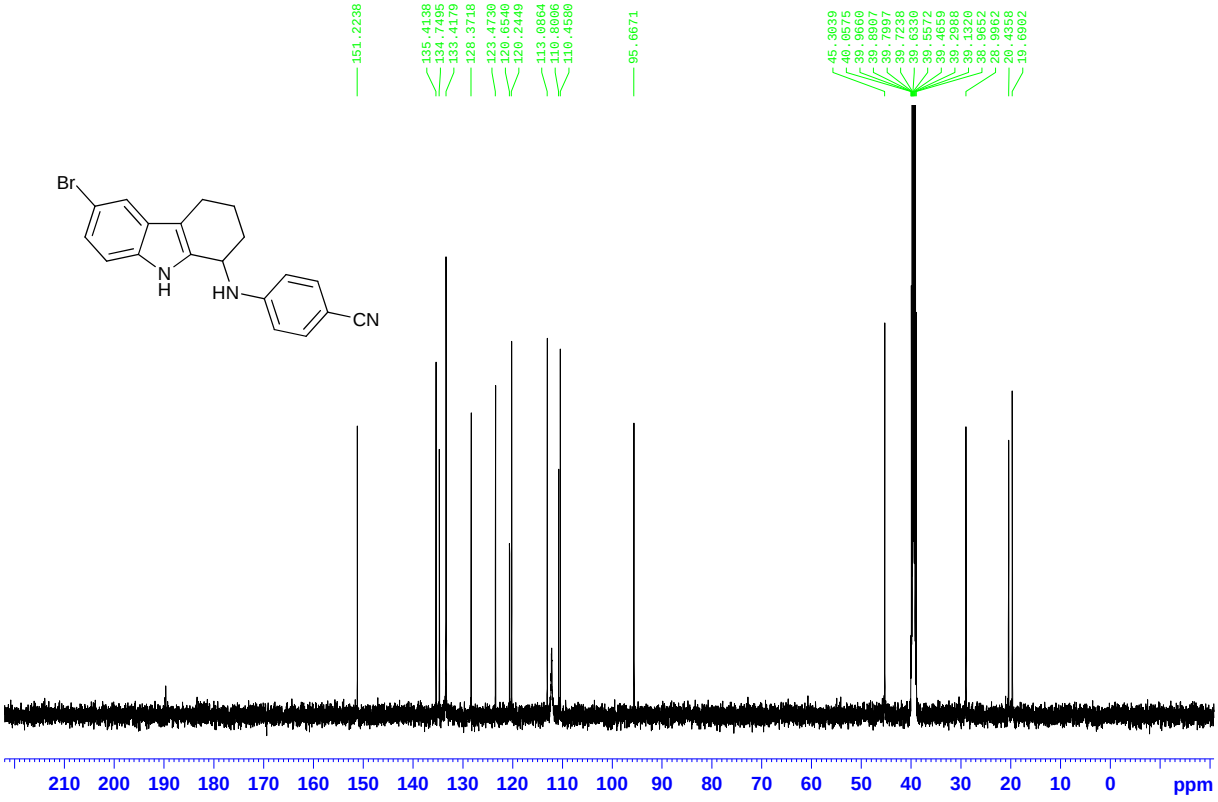


Supplementary Figure S66: dept 135 NMR of 21

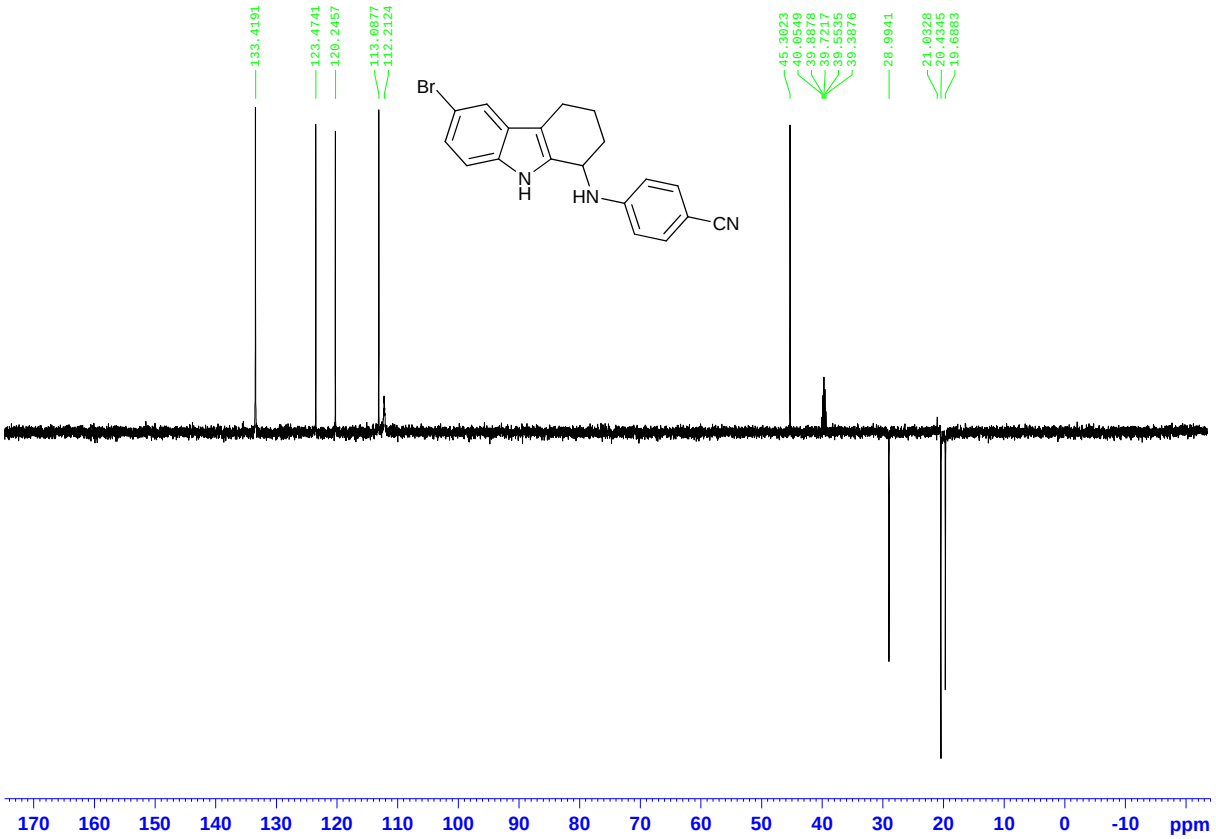
4-(6-Bromo-2,3,4,9-tetrahydro-1H-carbazol-1-ylamino)benzonitrile (22)



Supplementary Figure S67: ^{1}H NMR in DMSO of 22

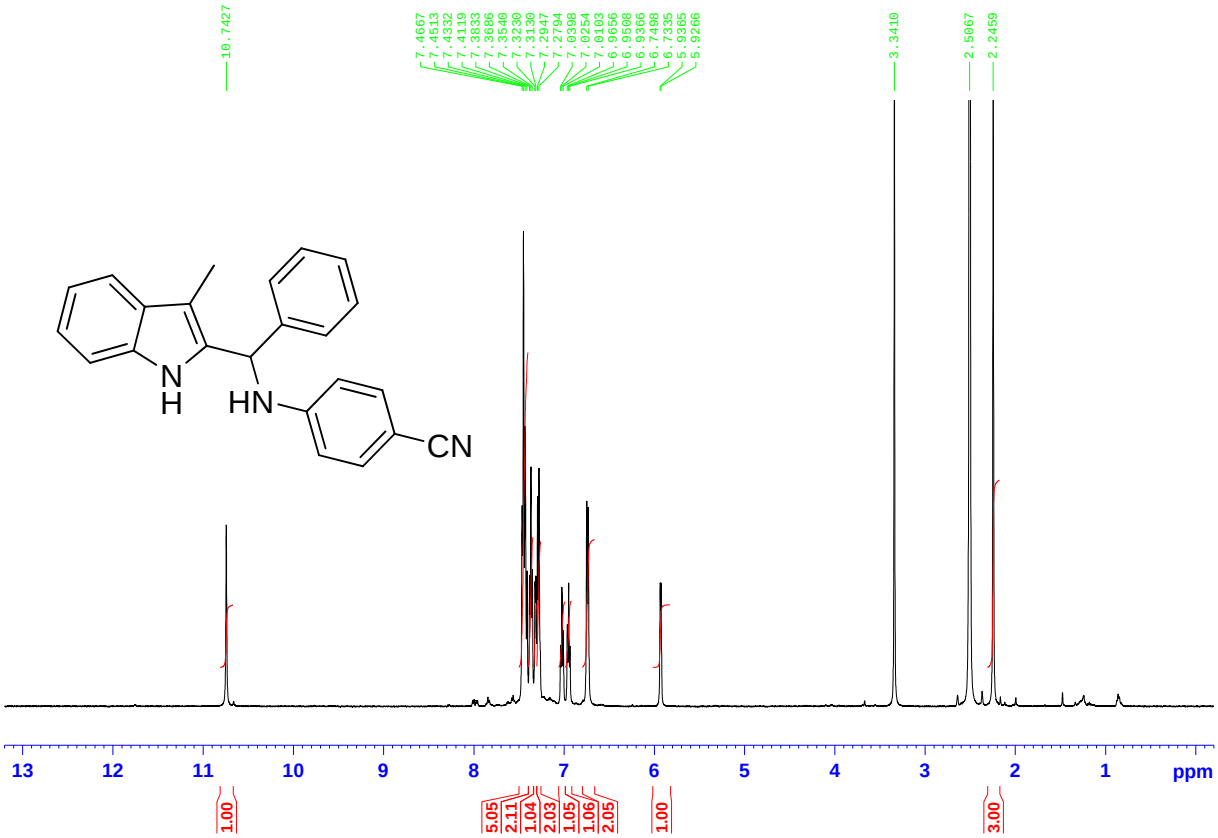


Supplementary Figure S68: ^{13}C NMR in DMSO of 22

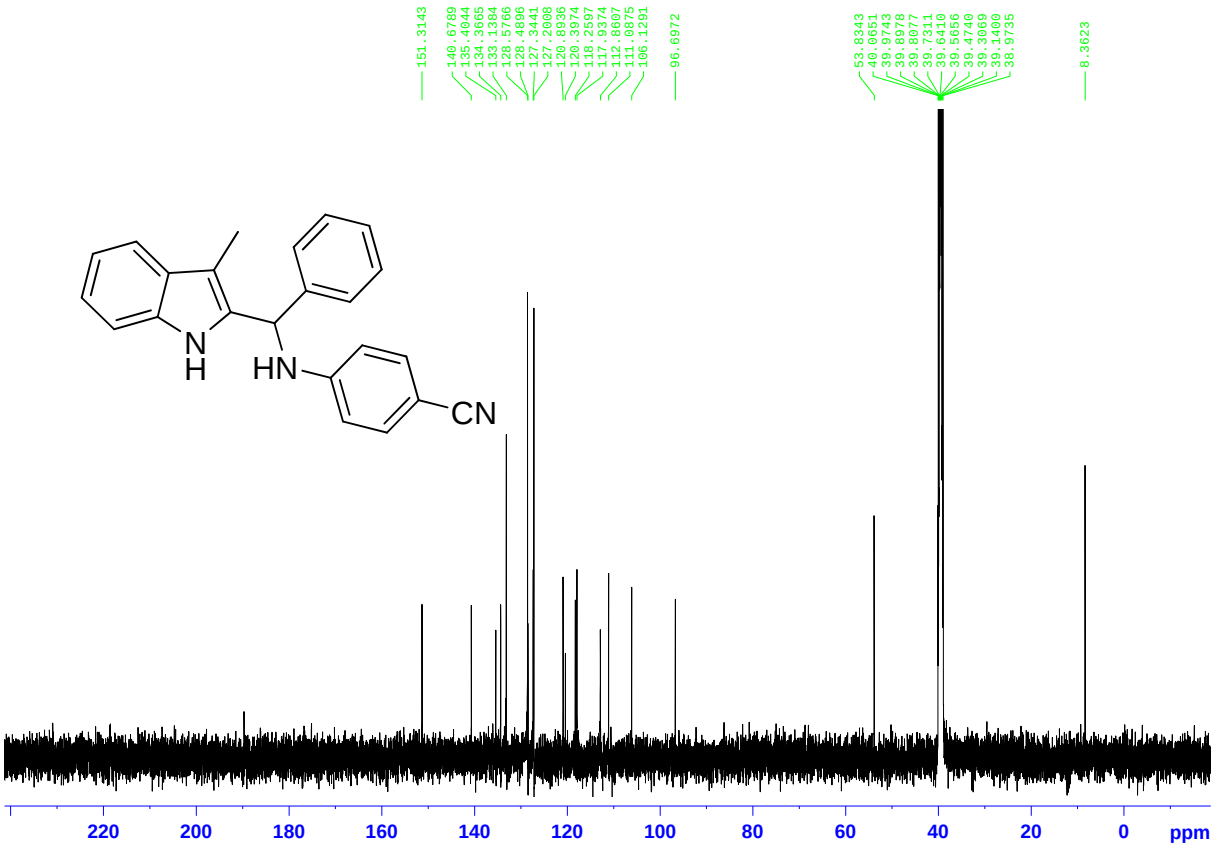


Supplementary Figure S69: dept 135 NMR of 22

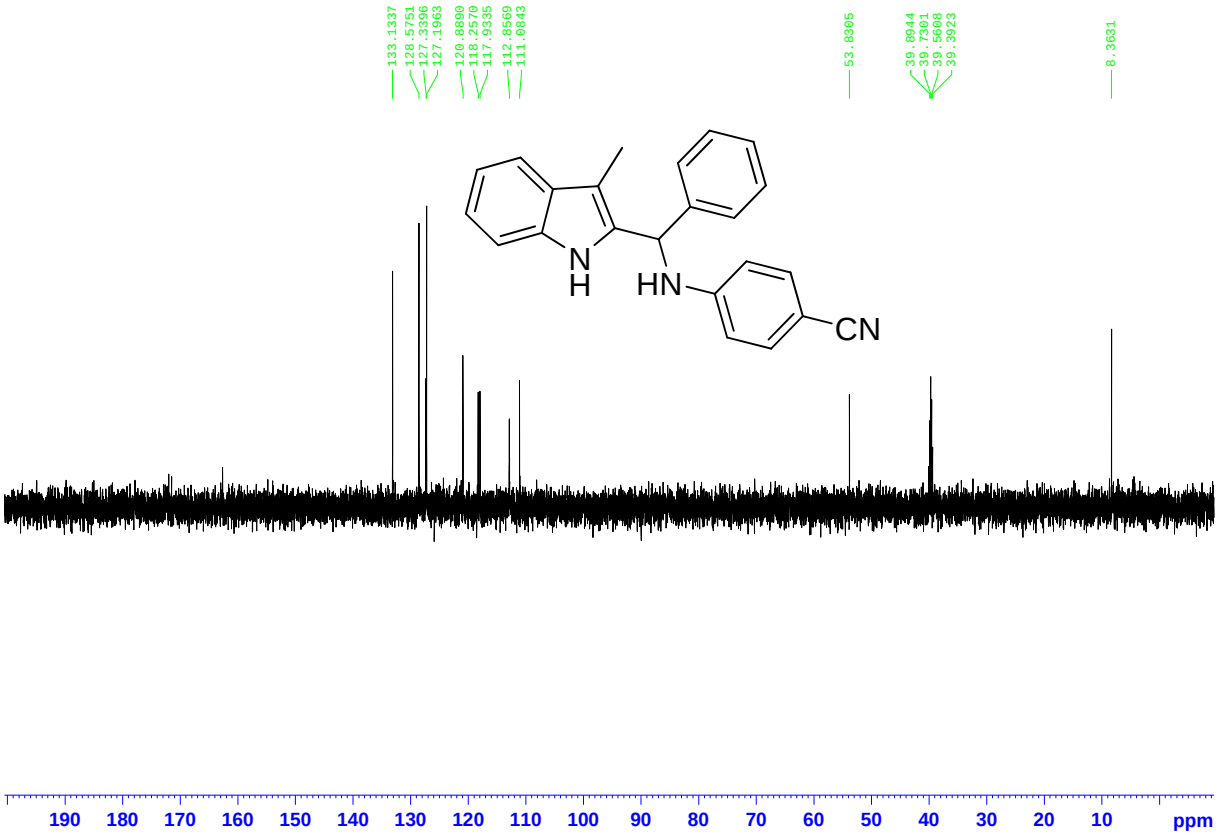
4-((3-Methyl-1H-indol-2-yl)(phenyl)methylamino)benzonitrile (23)



Supplementary Figure S70: ^{1}H NMR in DMSO of 26

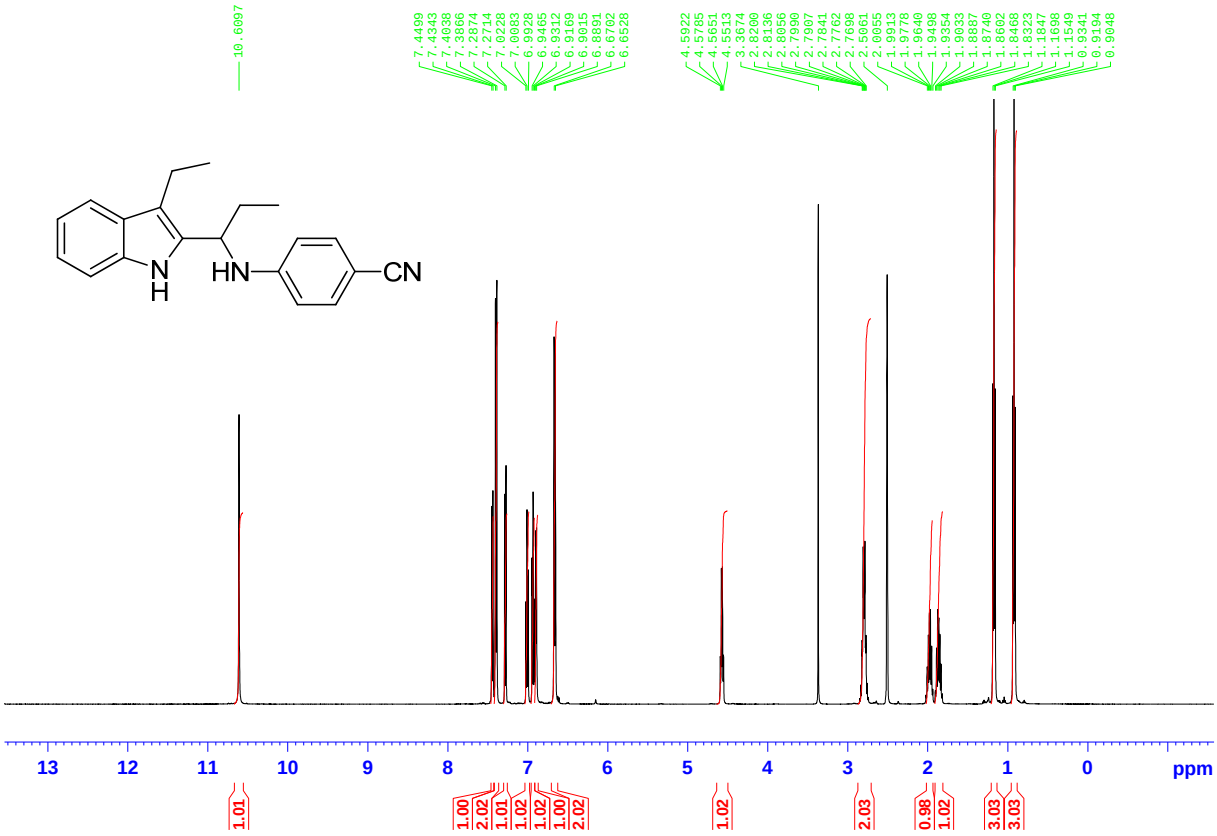


Supplementary Figure S71: ^{13}C NMR in DMSO of 26

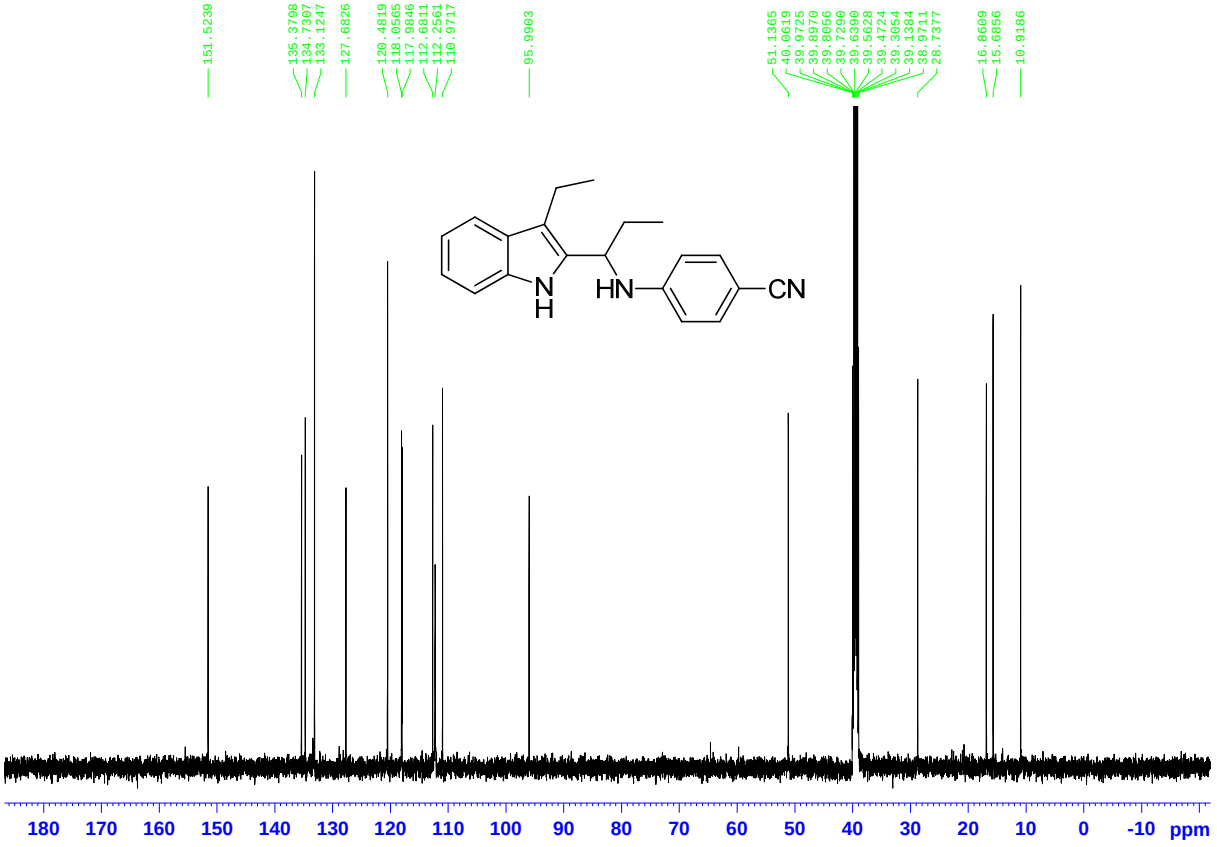


Supplementary Figure S72: dept 135 NMR in DMSO of 26

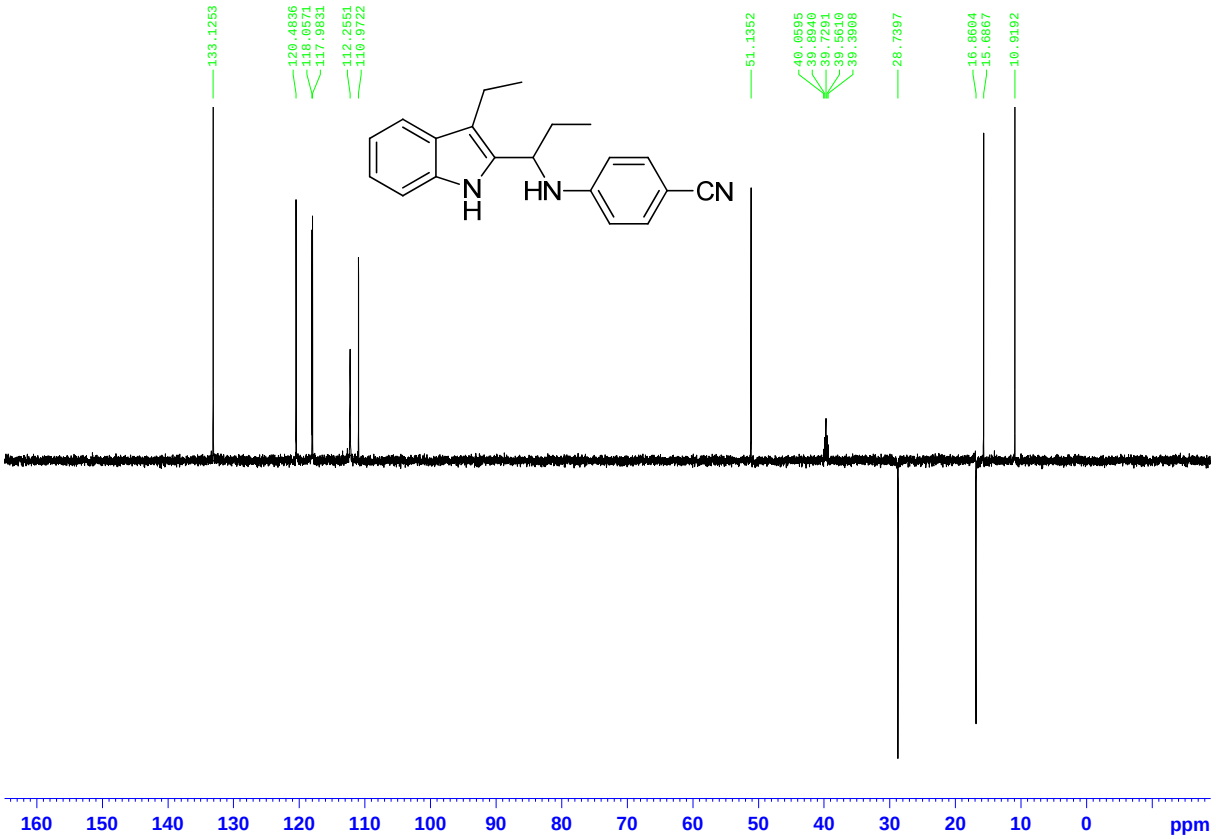
4-(1-(3-Ethyl-1H-indol-2-yl)propylamino)benzonitrile (24)



Supplementary Figure S73: ^{1}H NMR in DMSO of 27

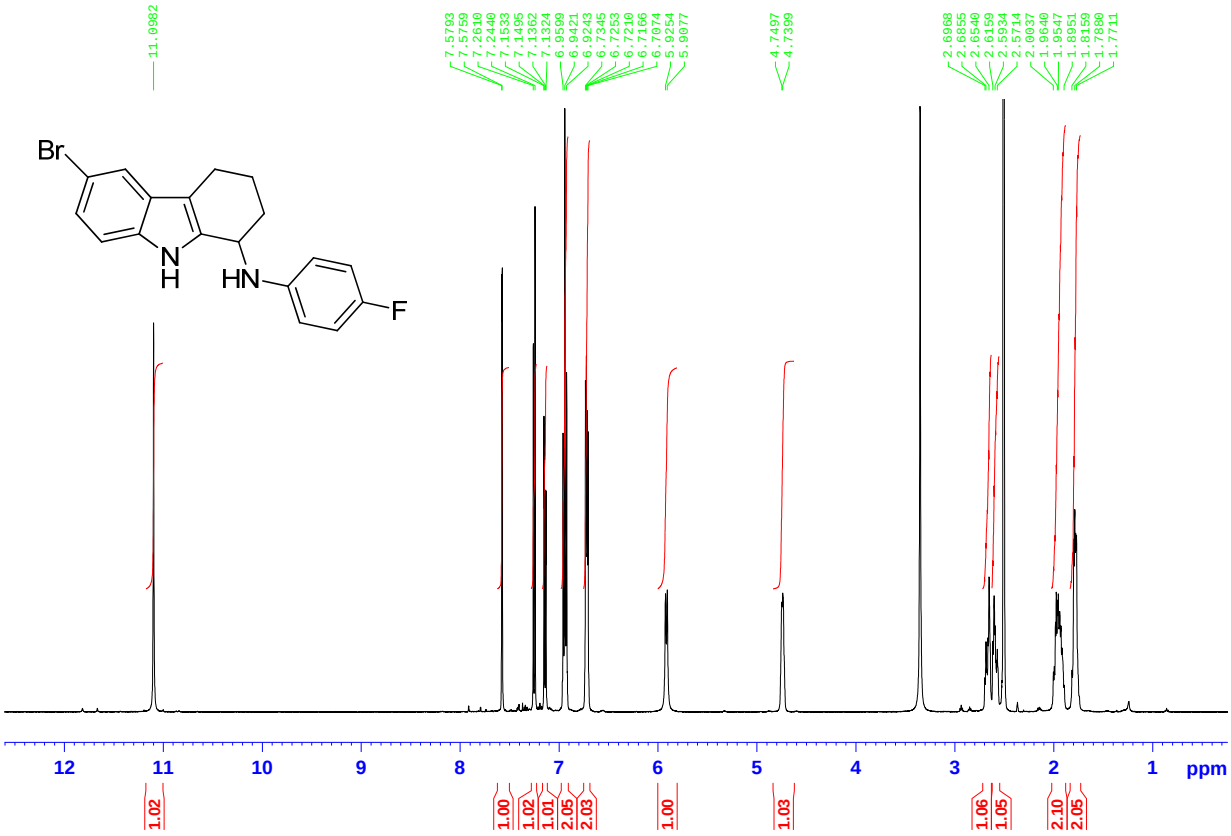


Supplementary Figure S74: ^{13}C NMR in DMSO of 27

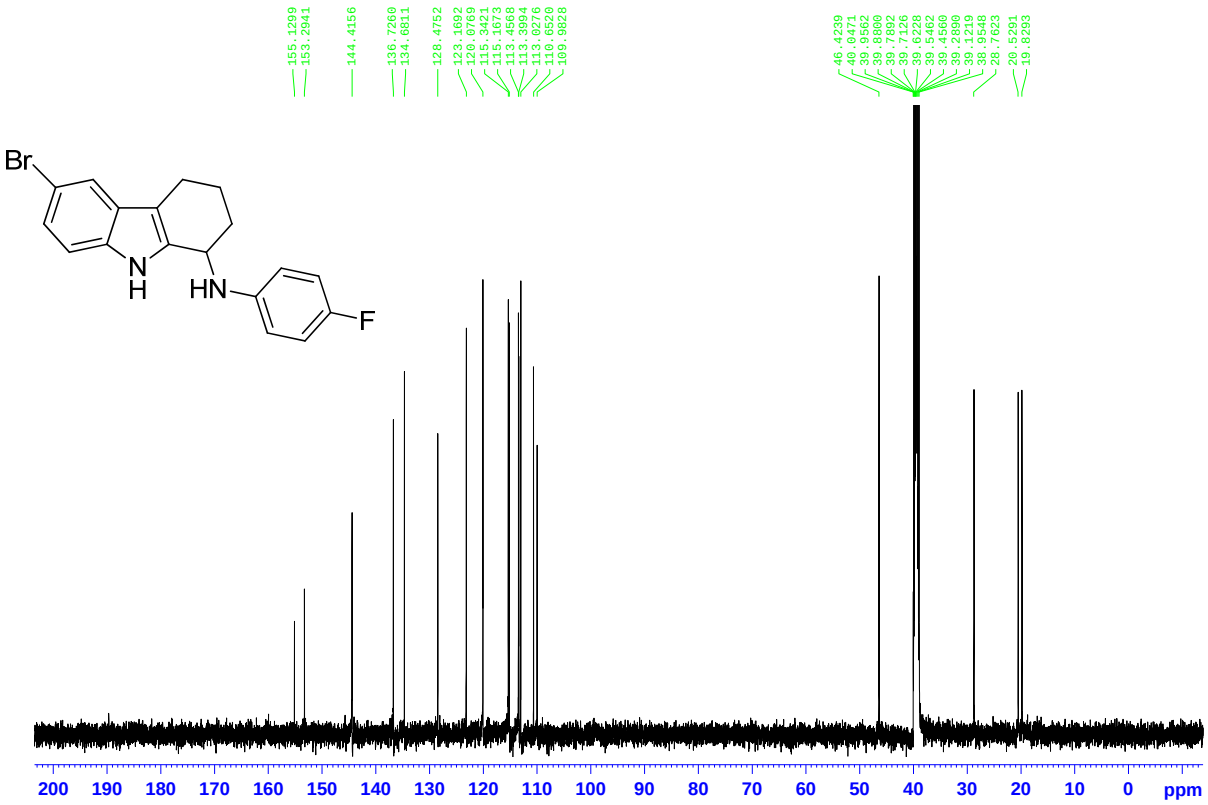


Supplementary FigureS 75: dept 135 NMR in DMSO of 27

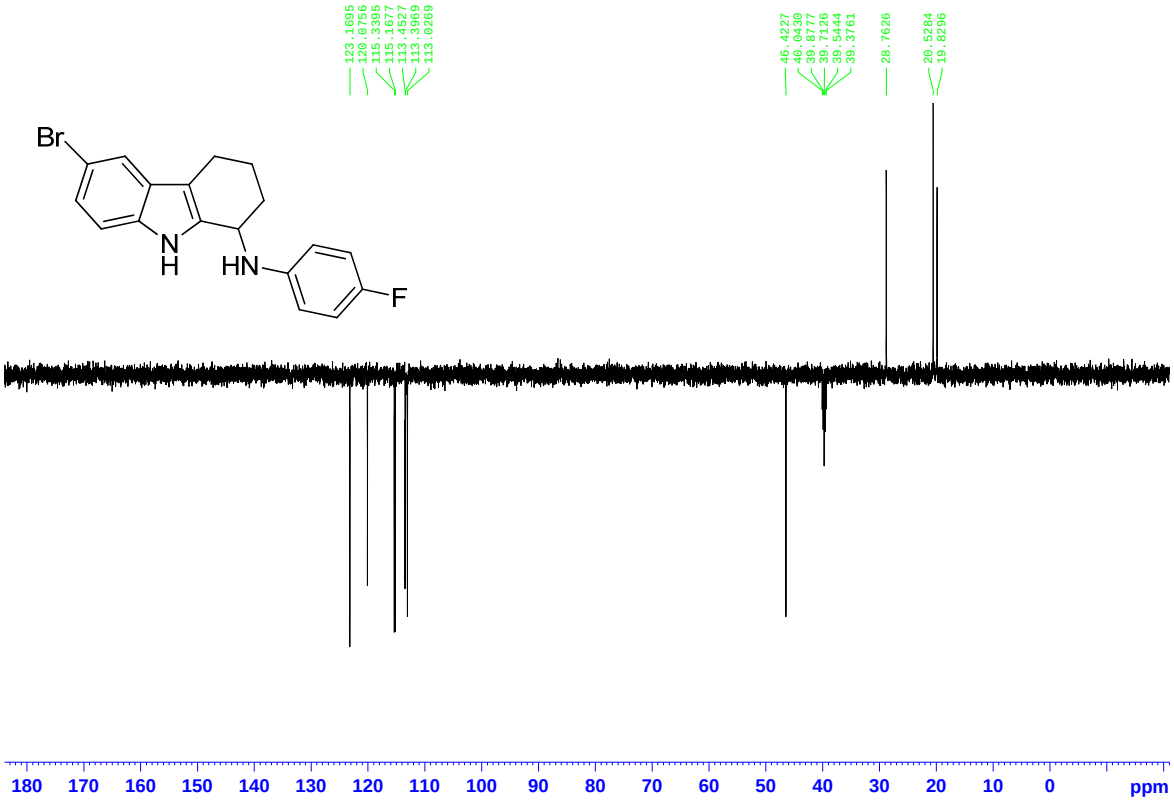
6-Bromo-*N*-(4-fluorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (25)



Supplementary Figure S76: ^{1}H NMR in DMSO of 25

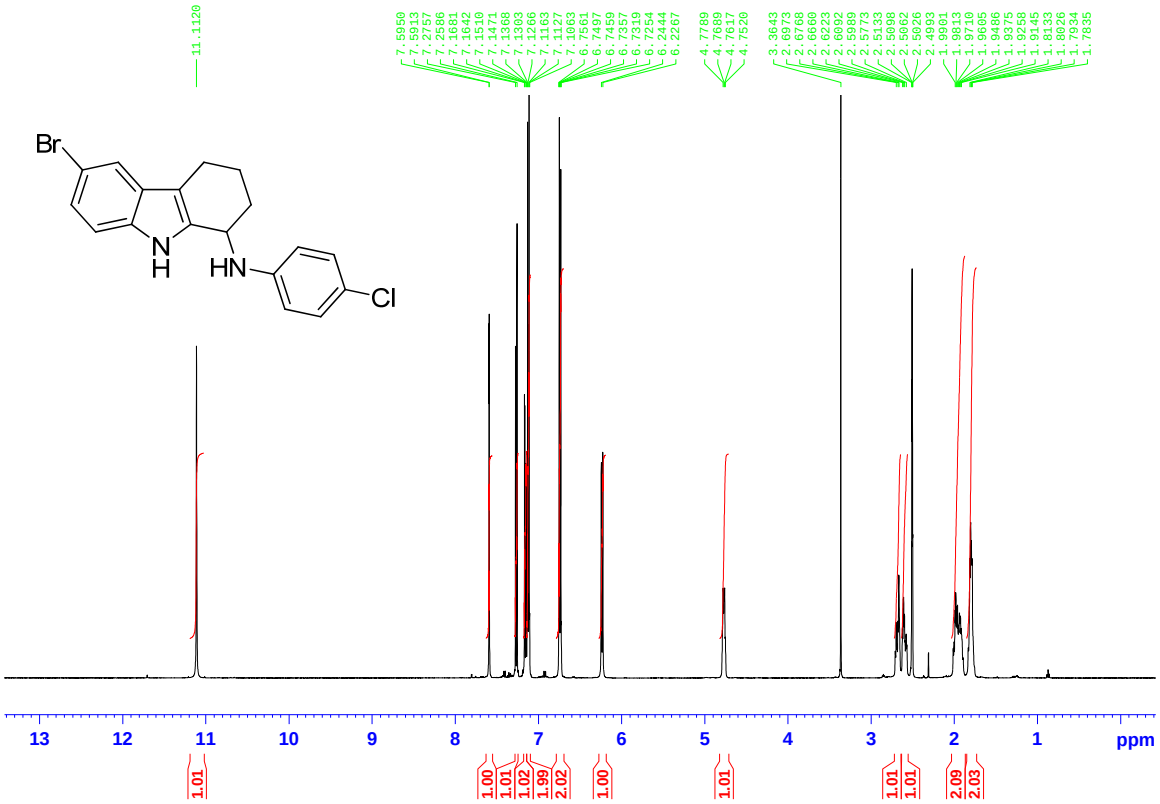


Supplementary Figure S77: ^{13}C NMR in DMSO of 25

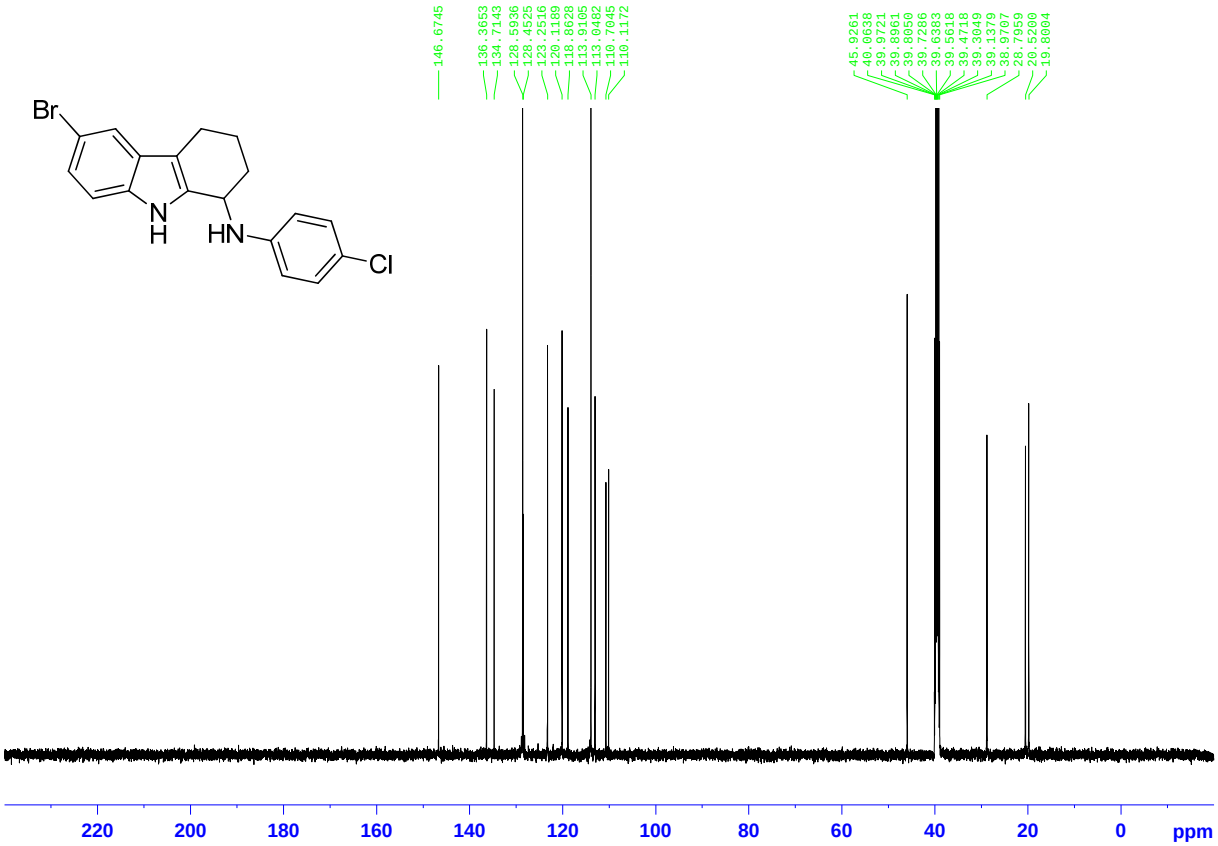


Supplementary Figure S78: dept 135 NMR in DMSO of 25

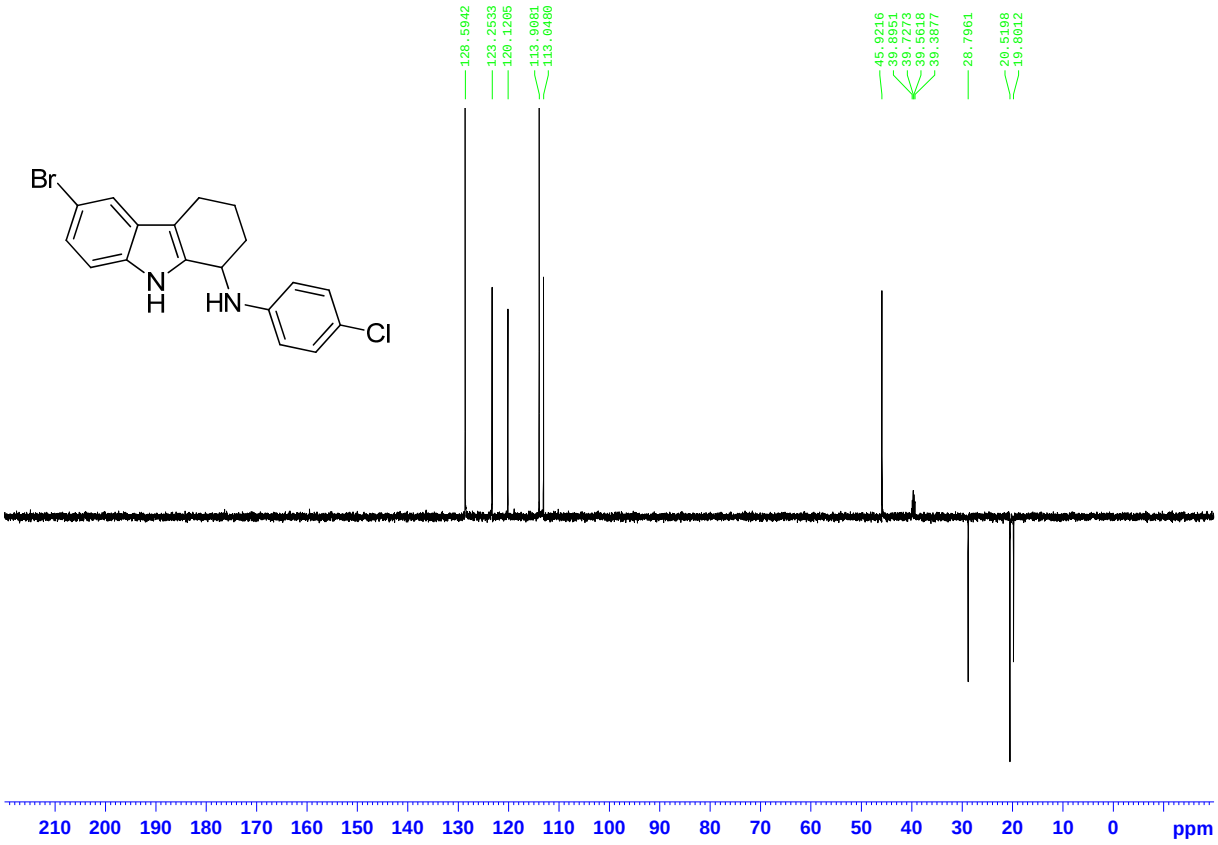
6-Bromo-*N*-(4-chlorophenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (26)



Supplementary Figure S79: ^{1}H NMR in DMSO of 26

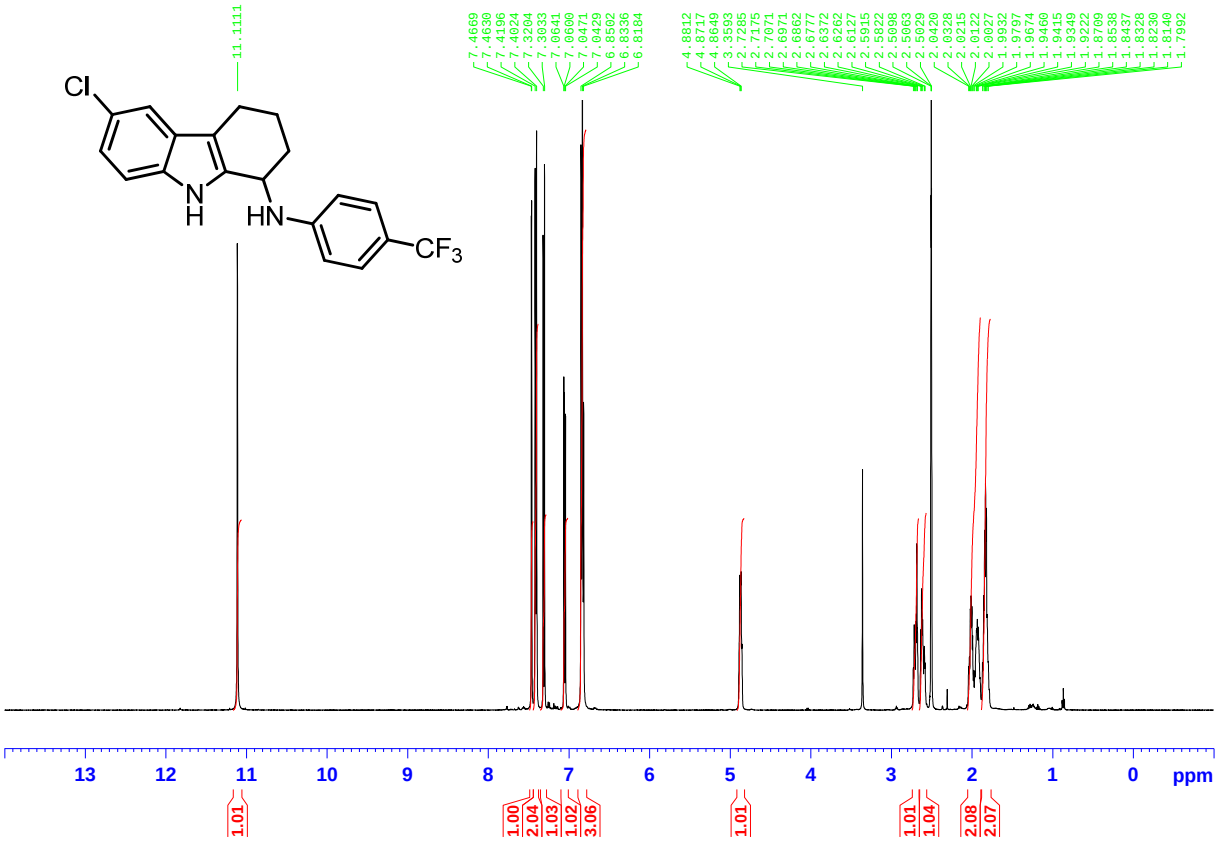


Supplementary Figure S80: ^{13}C NMR in DMSO of 26

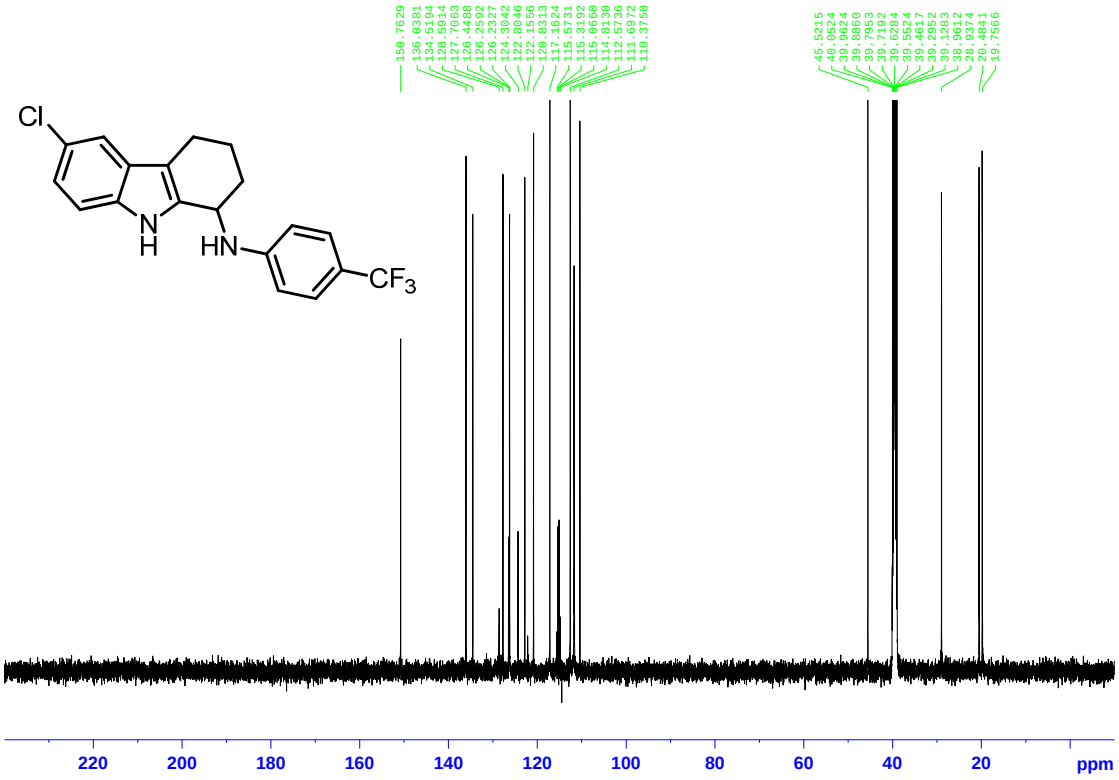


Supplementary Figure S81: dept 135 NMR in DMSO of 26

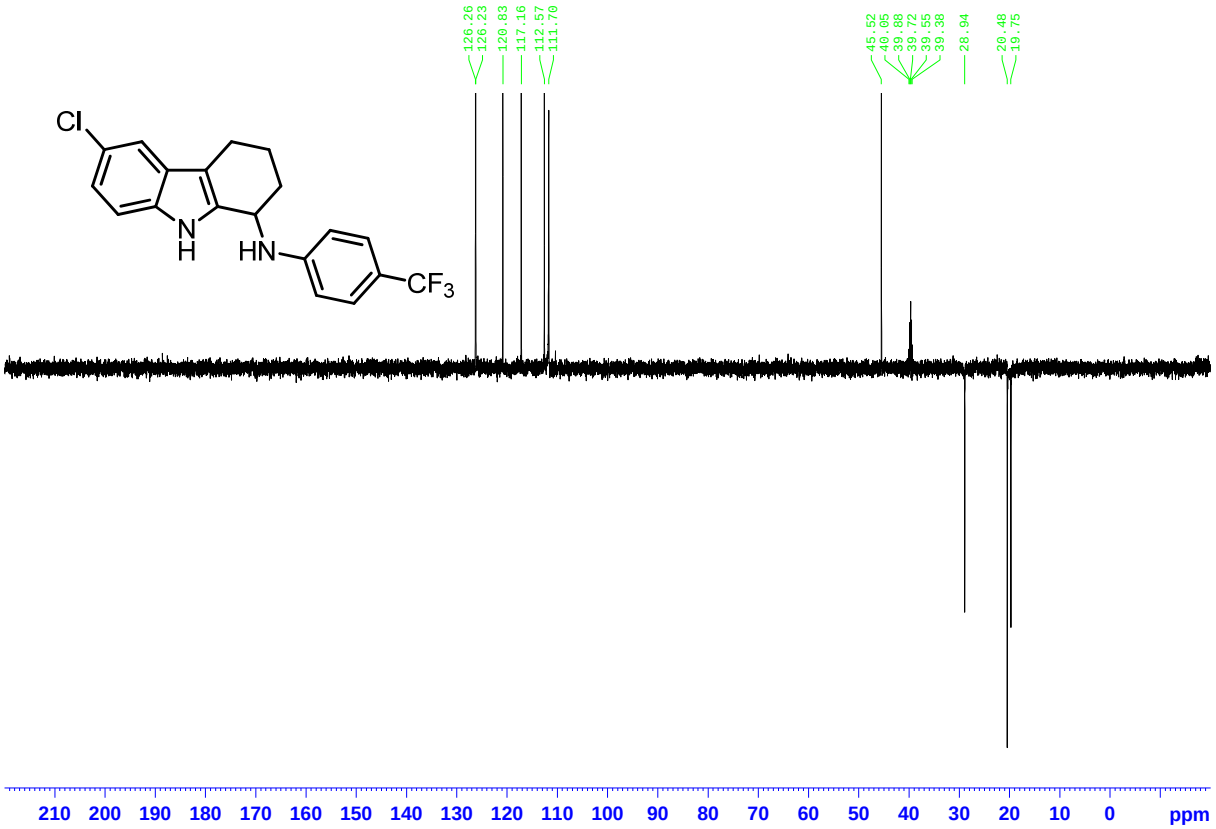
6-Chloro-*N*-(4-(trifluoromethyl)phenyl)-2,3,4,9-tetrahydro-1H-carbazol-1-amine (27)



Supplementary Figure S82: ^{1}H NMR in DMSO of 27

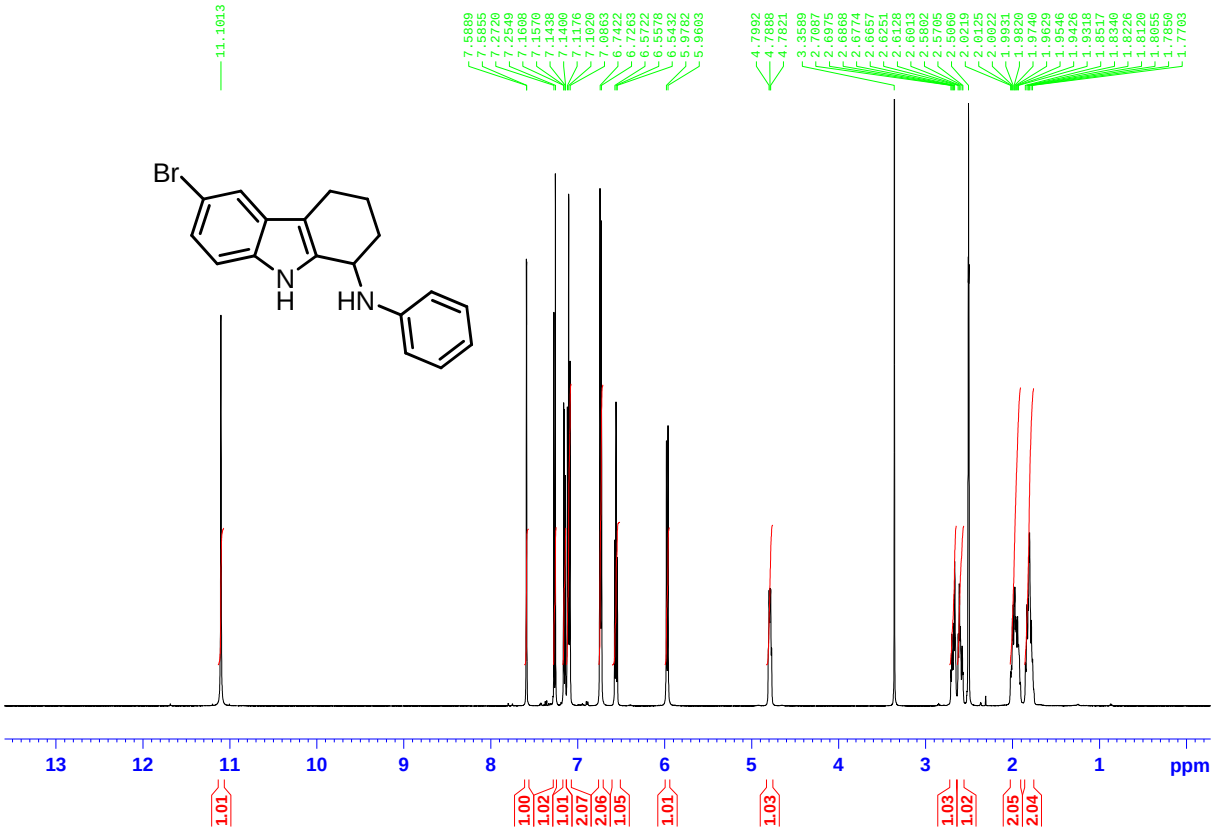


Supplementary Figure S83: ^{13}C NMR in DMSO of 27

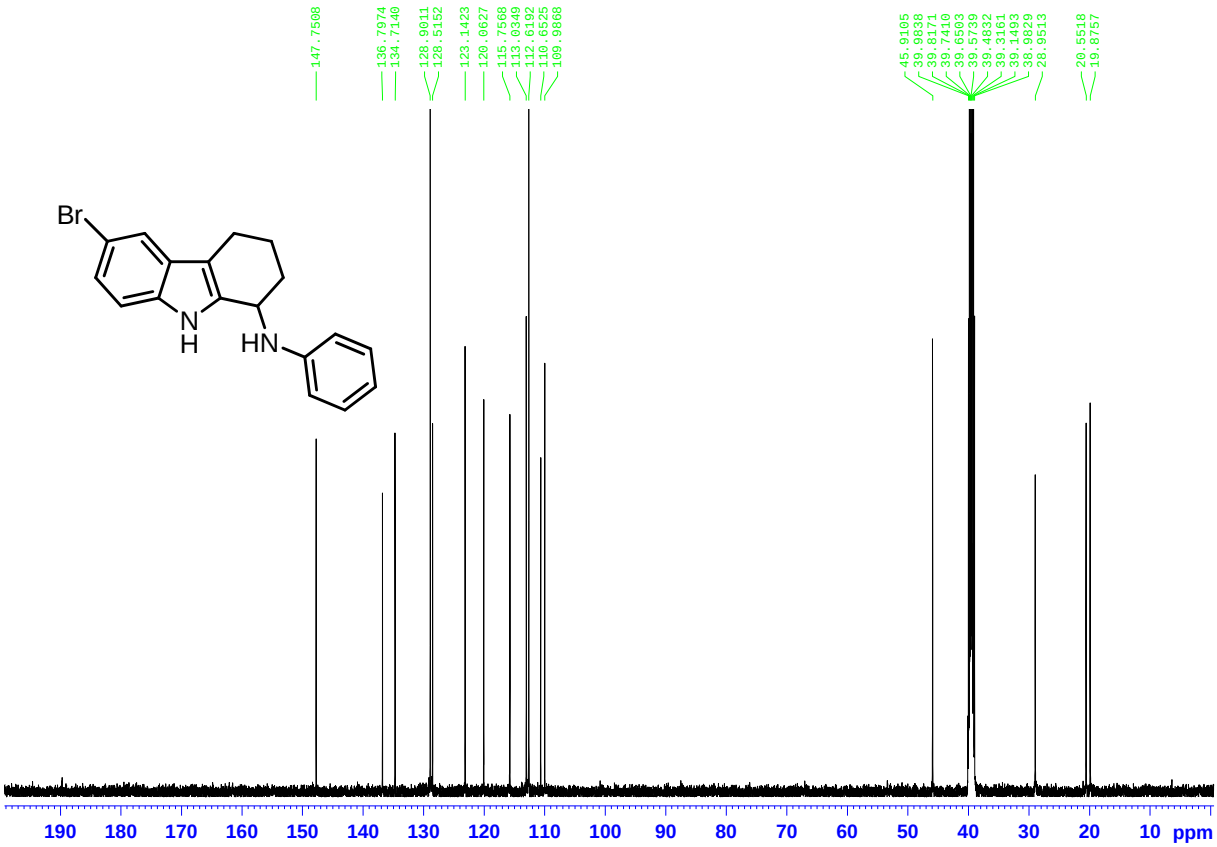


Supplementary Figure S84: dept 135 NMR in DMSO of 27

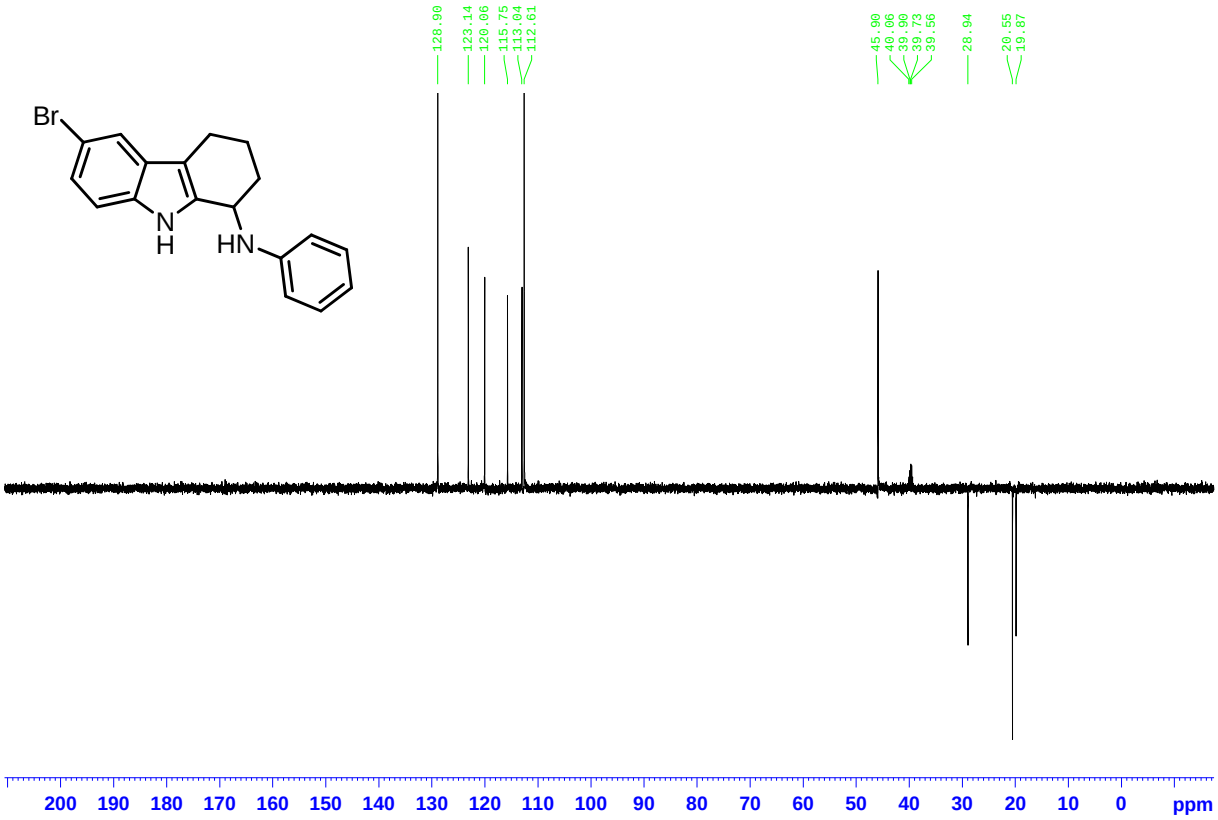
6-Bromo-*N*-phenyl-2,3,4,9-tetrahydro-1H-carbazol-1-amine (28)



Supplementary Figure S85: ^{1}H NMR in DMSO of 28

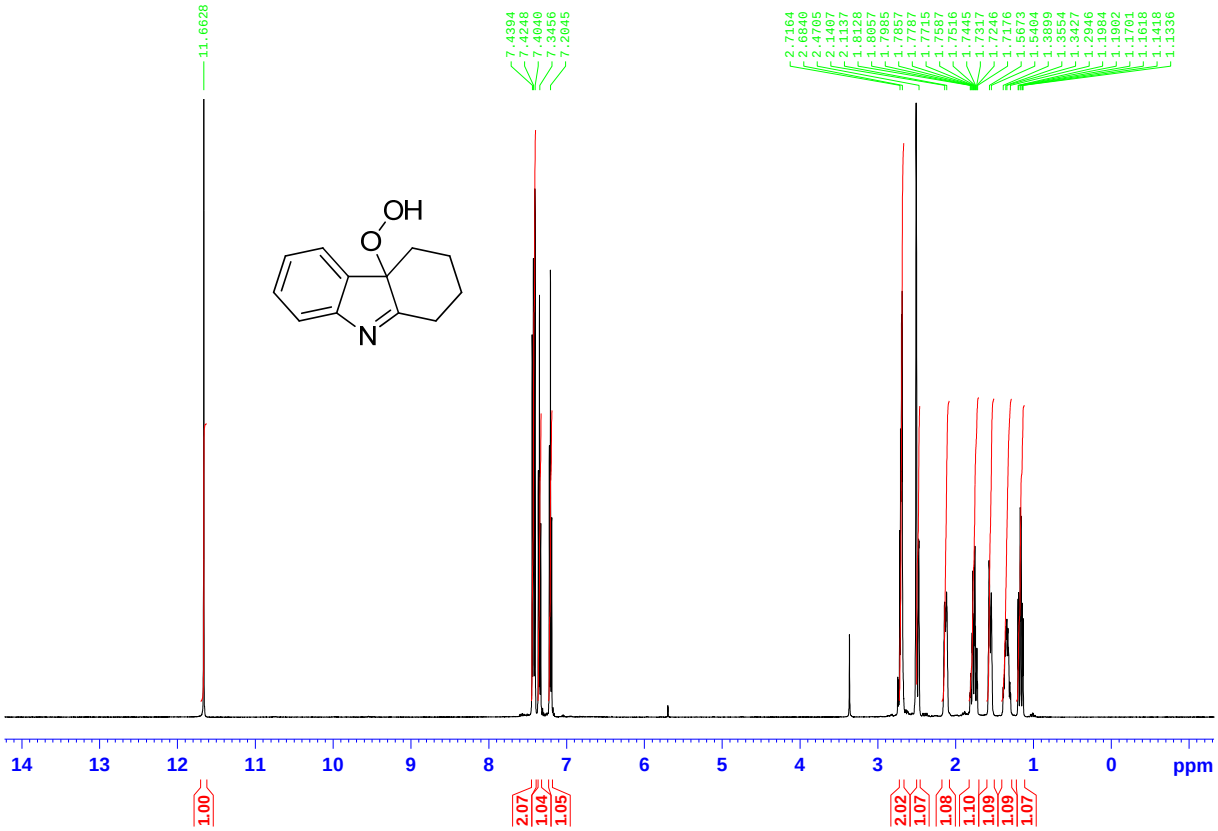


Supplementary Figure S86: ^{13}C NMR in DMSO of 28

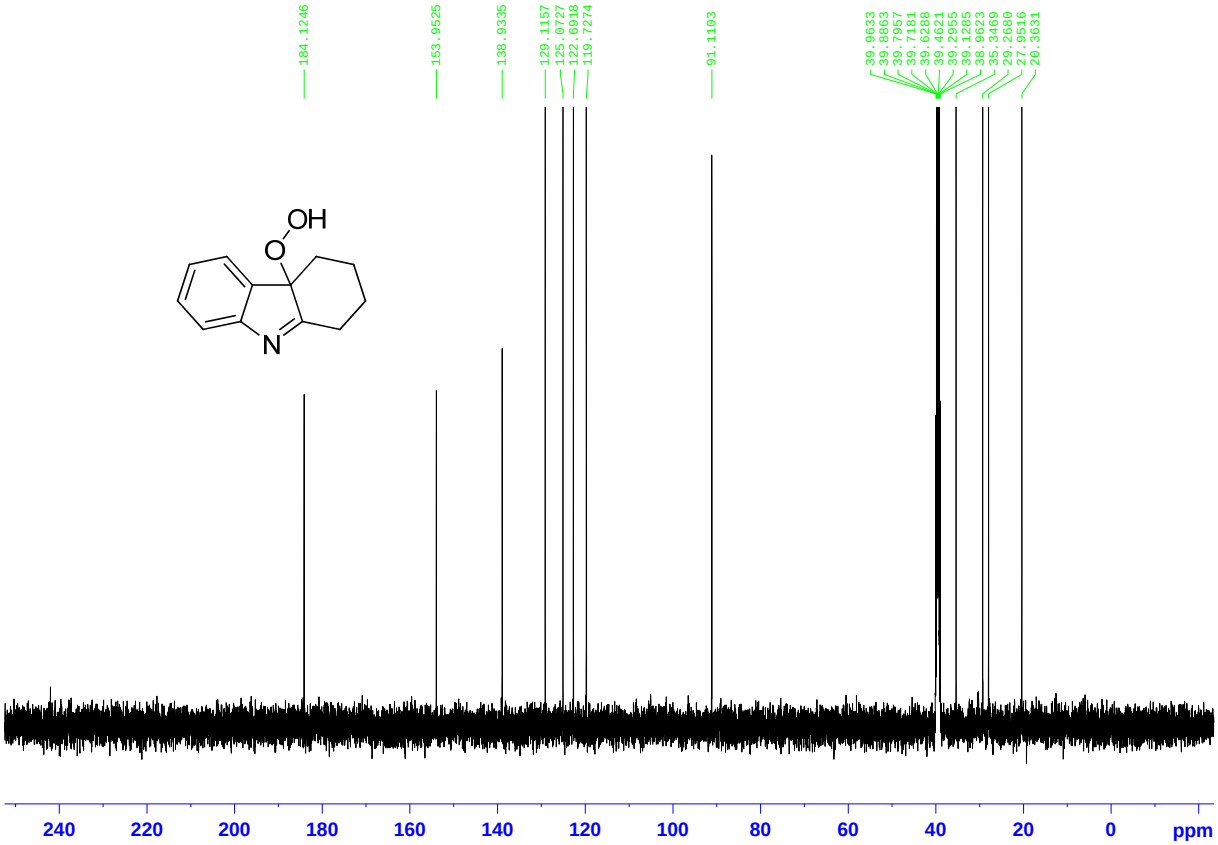


Supplementary Figure S87: dept 135 NMR in DMSO of 28

4a-Hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (3)

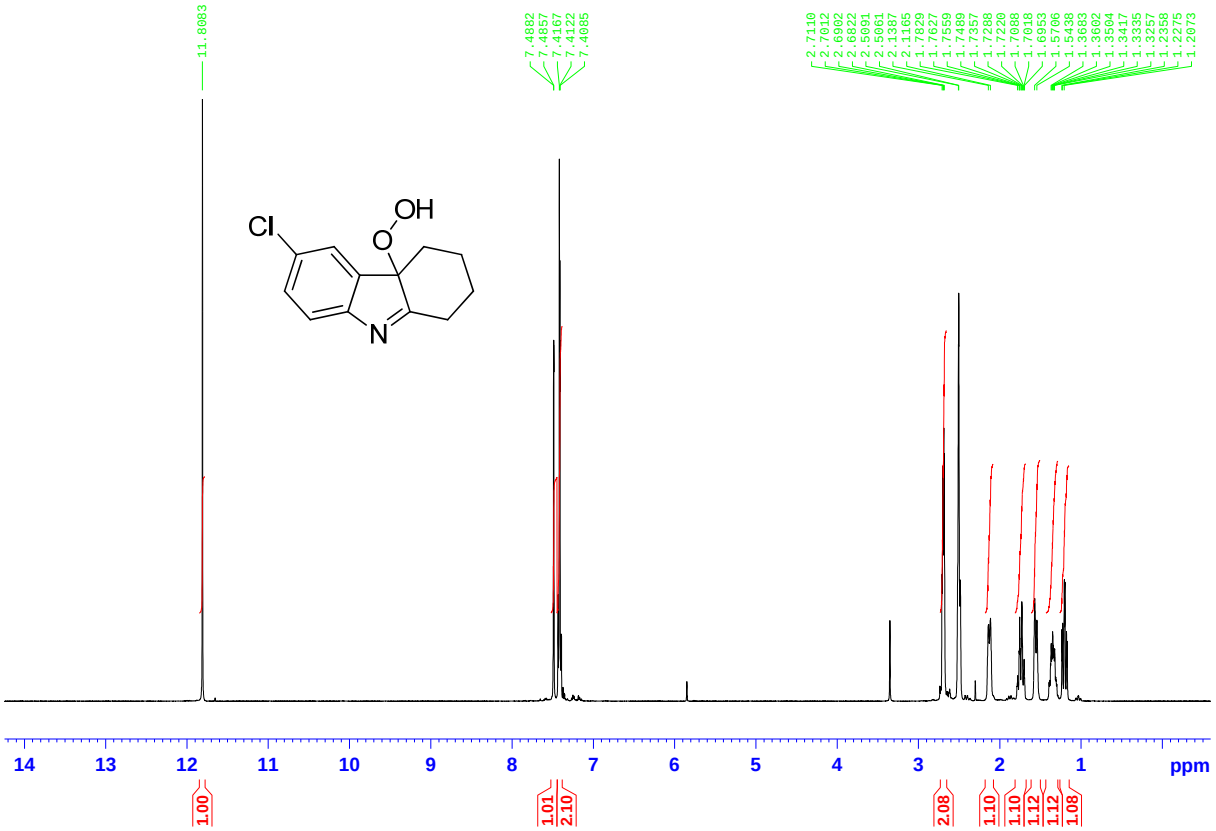


Supplementary Figure S88: ^{1}H NMR in DMSO of 3

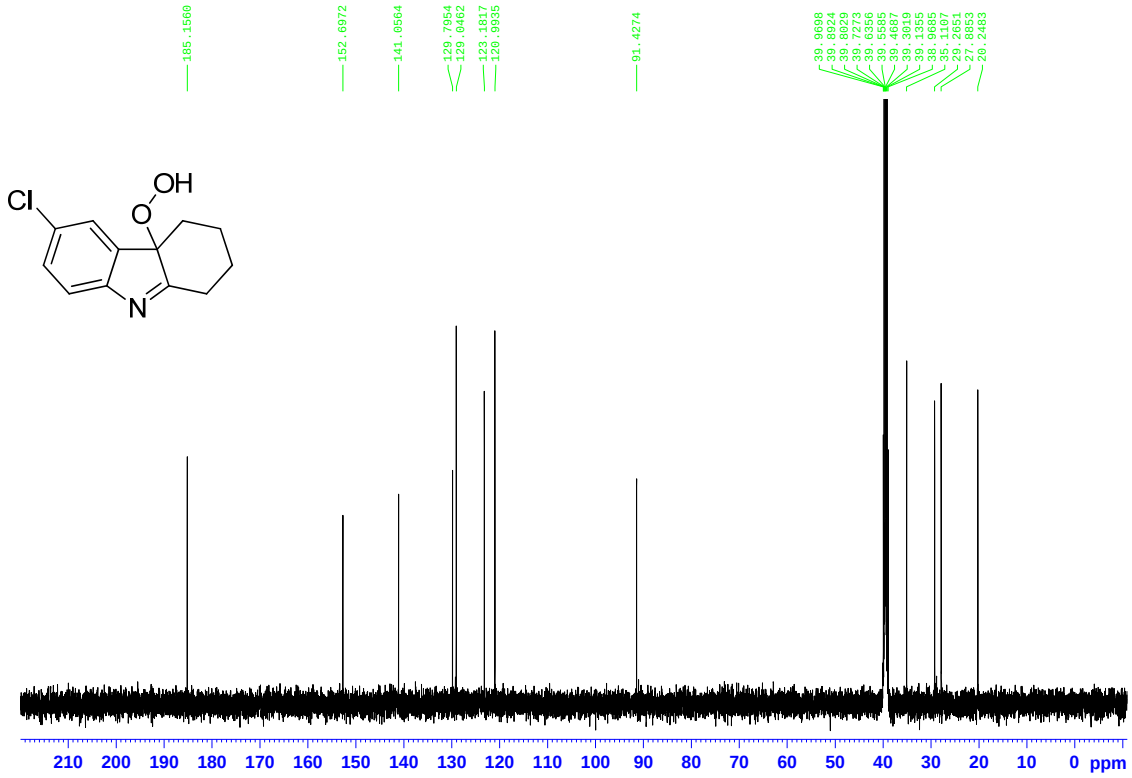


Supplementary Figure S89: ^{13}C NMR in DMSO of 3

6-Chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

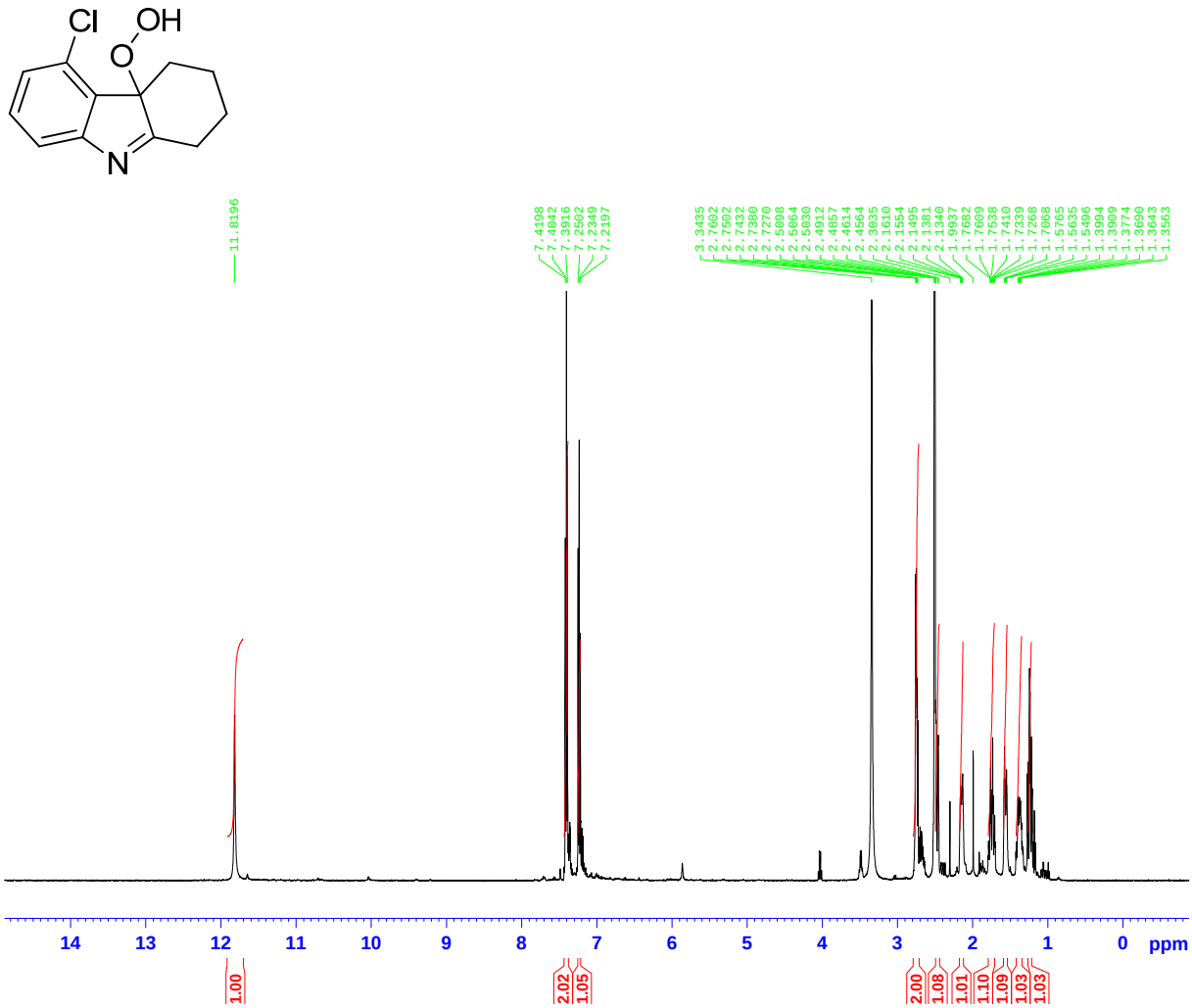


Supplementary Figure S90: ^{1}H NMR in DMSO of 6-chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole



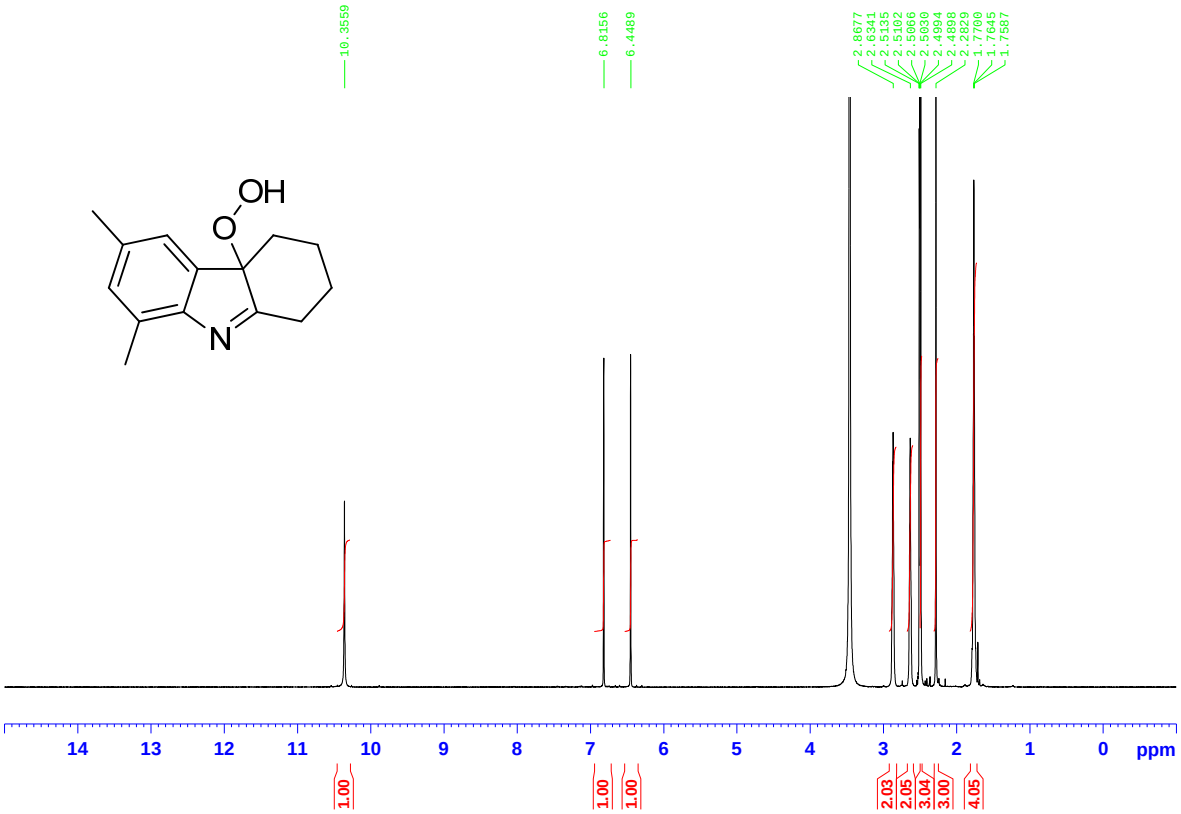
Supplementary Figure S91: ^{13}C NMR in DMSO of 6-chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (short NMR without DEPT due to slow decomposition)

5-Chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

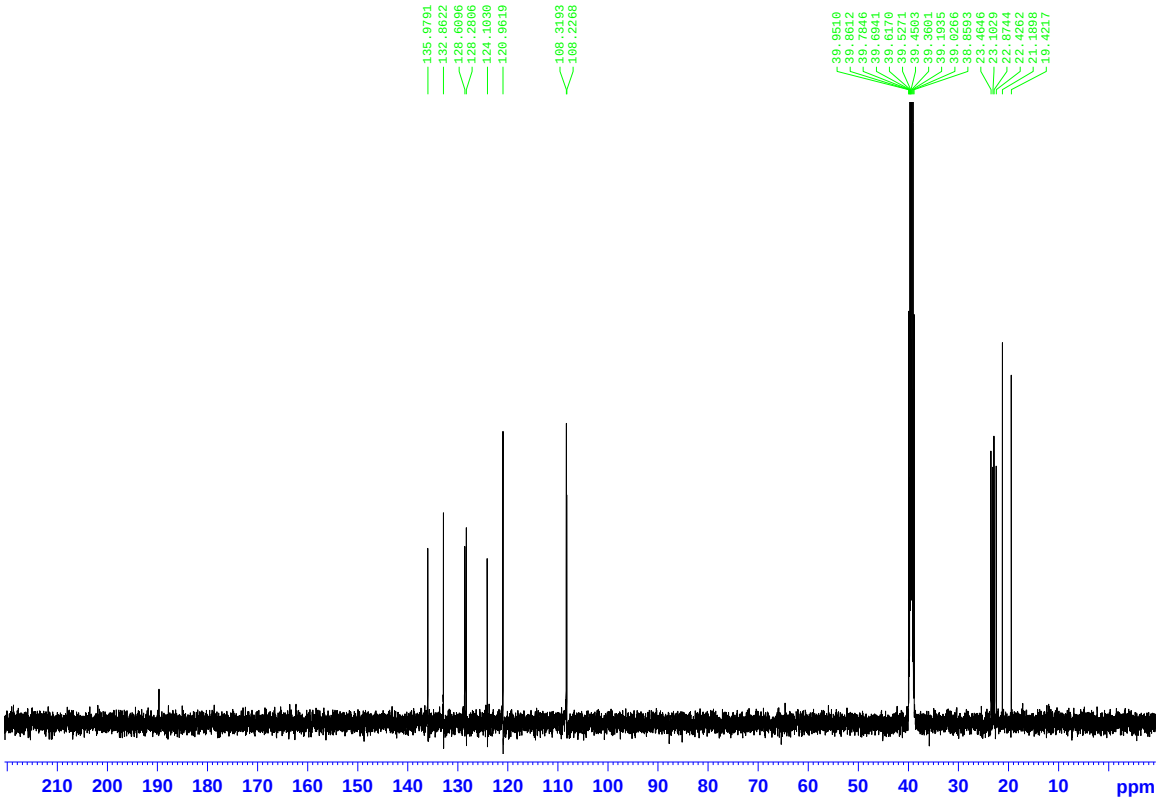


Supplementary Figure S92: ^{1}H NMR in DMSO of 5-chloro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (relative fast decomposition in DMSO)

4a-Hydroperoxy-6,8-dimethyl-2,3,4,4a-tetrahydro-1H-carbazole

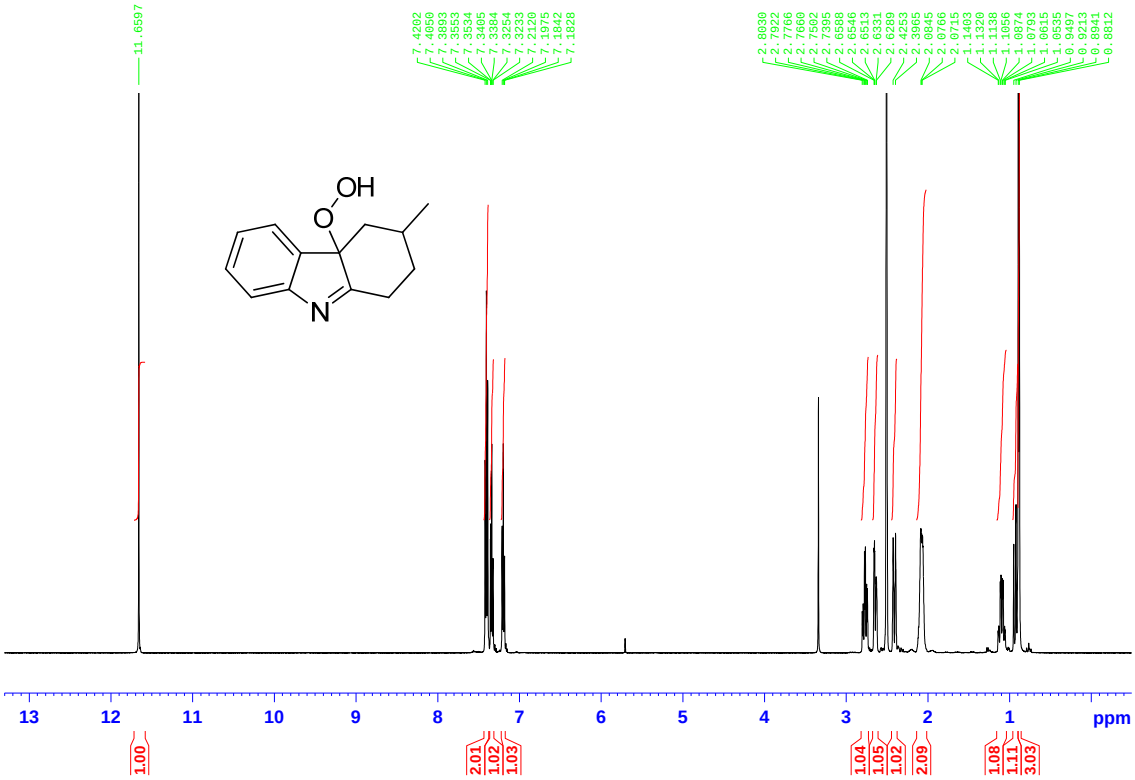


Supplementary Figure S93: ^{1}H NMR in DMSO of 4a-hydroperoxy-6,8-dimethyl-2,3,4,4a-tetrahydro-1H-carbazole

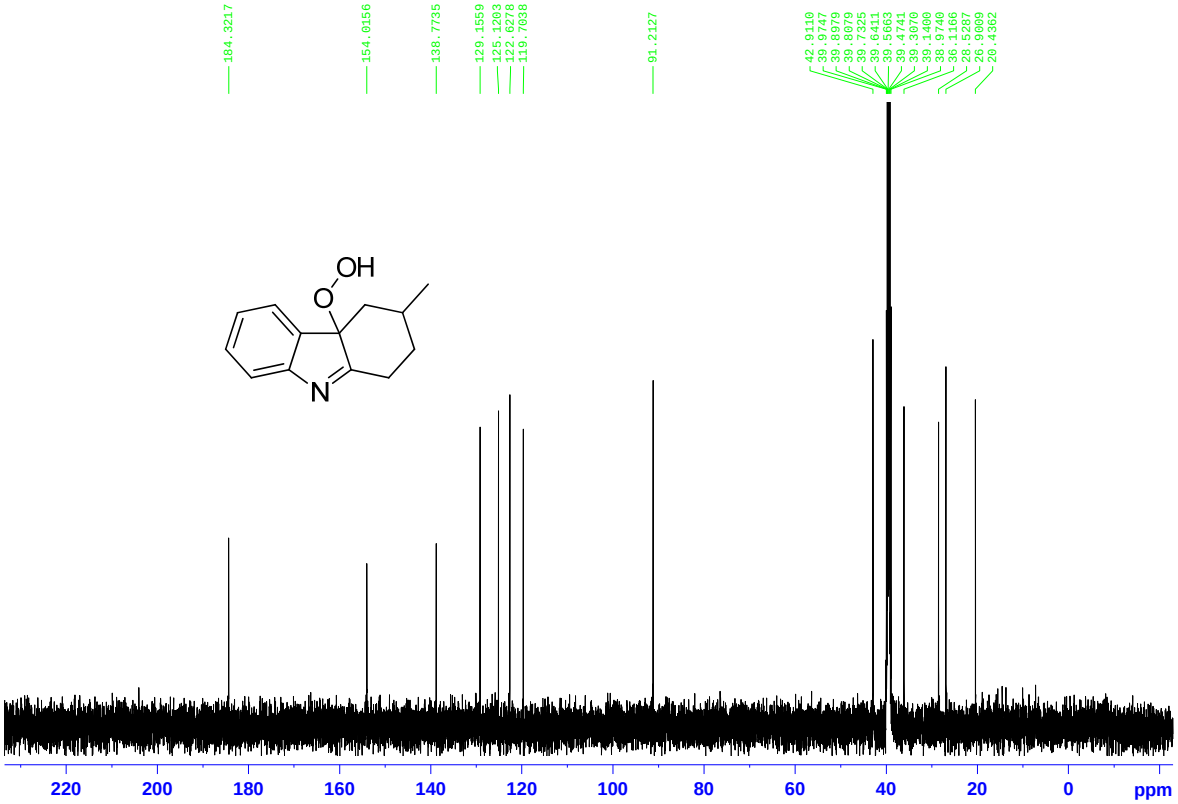


Supplementary Figure S94: ^{13}C NMR in DMSO of 4a-hydroperoxy-6,8-dimethyl-2,3,4,4a-tetrahydro-1H-carbazole

4a-Hydroperoxy-3-methyl-2,3,4,4a-tetrahydro-1H-carbazole

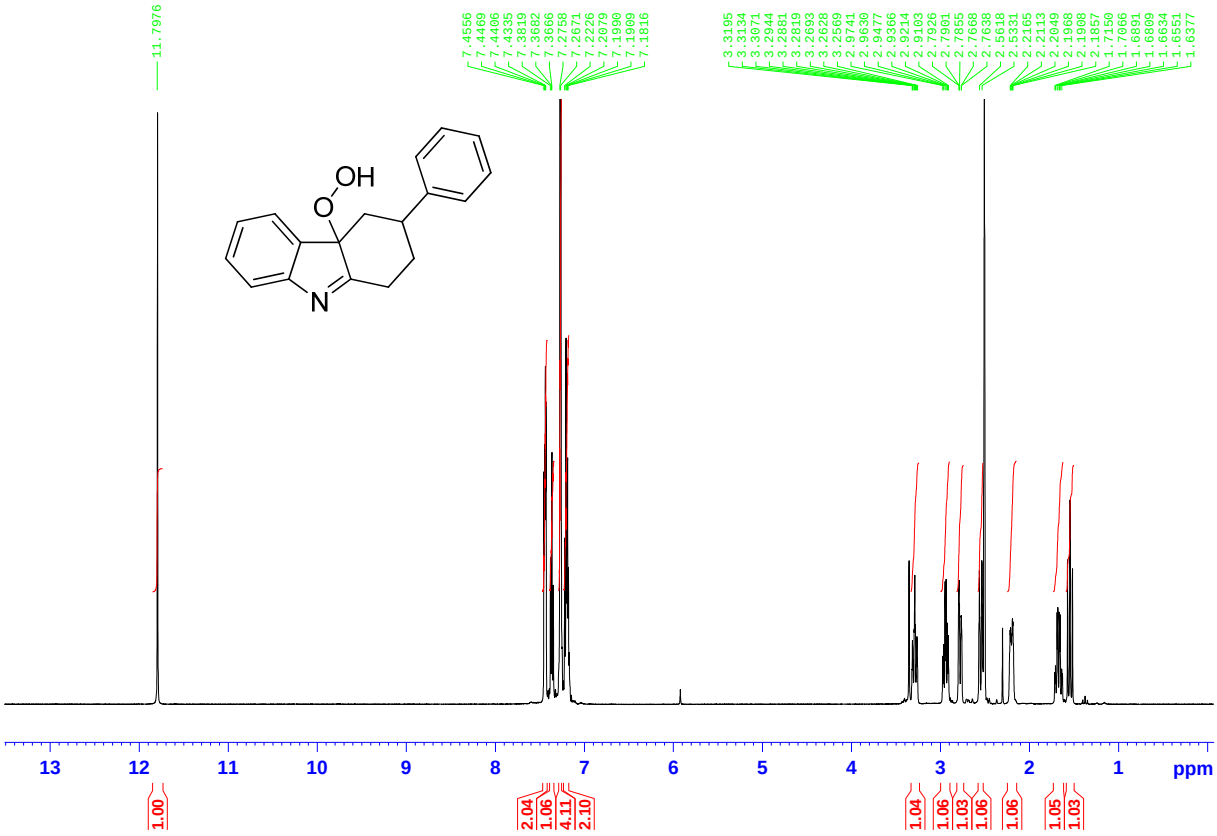


Supplementary Figure S95: ^{1}H NMR in DMSO of 4a-hydroperoxy-3-methyl-2,3,4,4a-tetrahydro-1H-carbazole

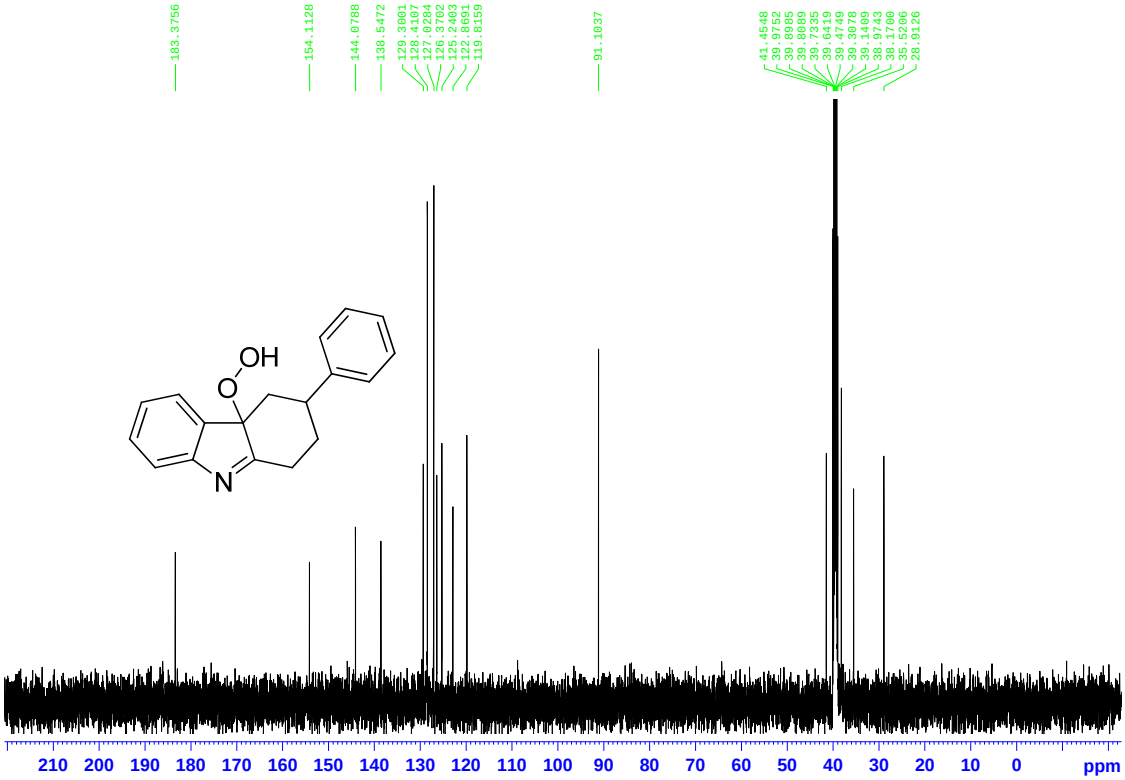


Supplementary Figure S96: ^{13}C NMR in DMSO of 4a-hydroperoxy-3-methyl-2,3,4,4a-tetrahydro-1H-carbazole (short NMR without DEPT due to slow decomposition)

4a-Hydroperoxy-3-phenyl-2,3,4,4a-tetrahydro-1H-carbazole

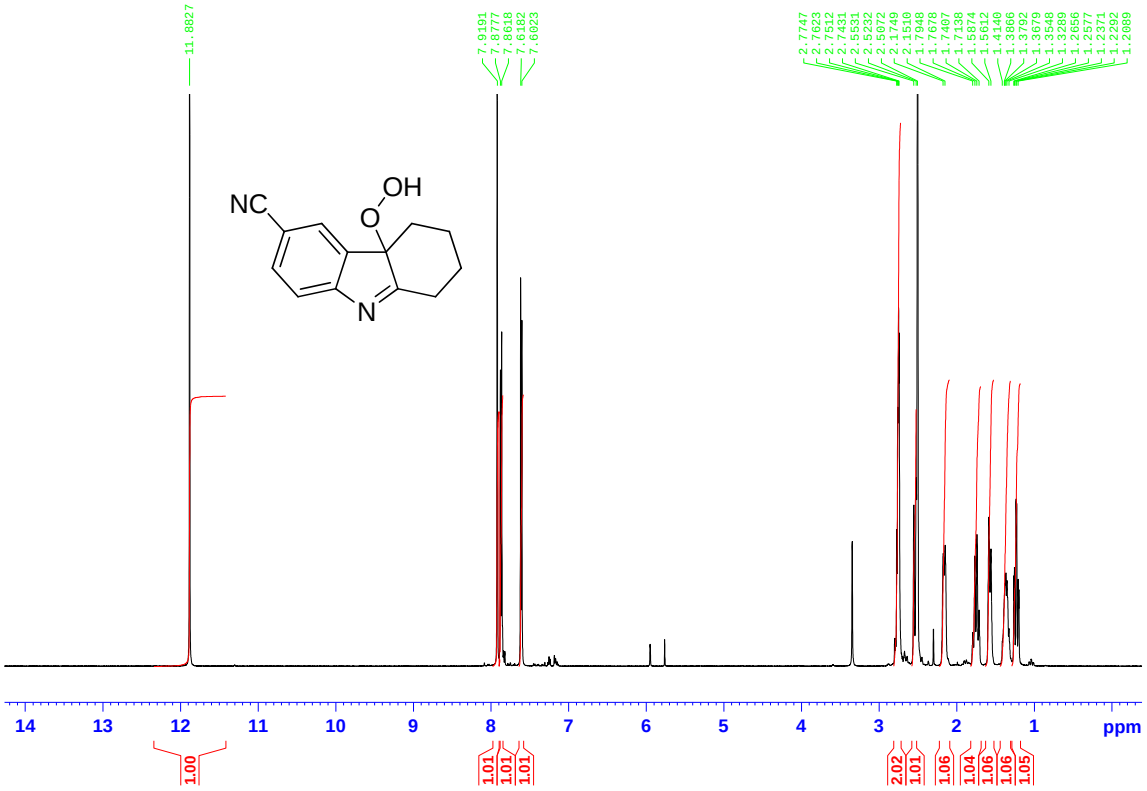


Supplementary Figure S97: ^{1}H NMR in DMSO of 4a-hydroperoxy-3-phenyl-2,3,4,4a-tetrahydro-1H-carbazole

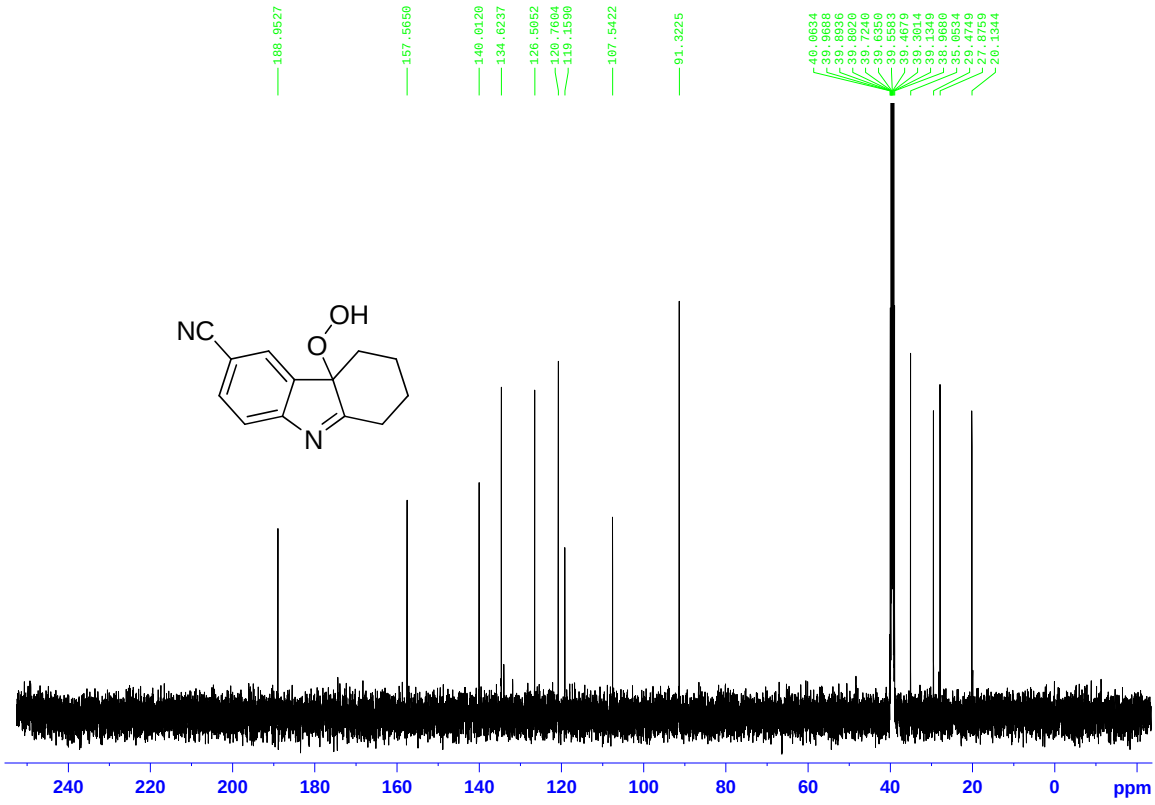


Supplementary Figure S98: ^{13}C NMR in DMSO of 4a-hydroperoxy-3-phenyl-2,3,4,4a-tetrahydro-1H-carbazole (short NMR without DEPT due to slow decomposition)

4a-Hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole-6-carbonitrile

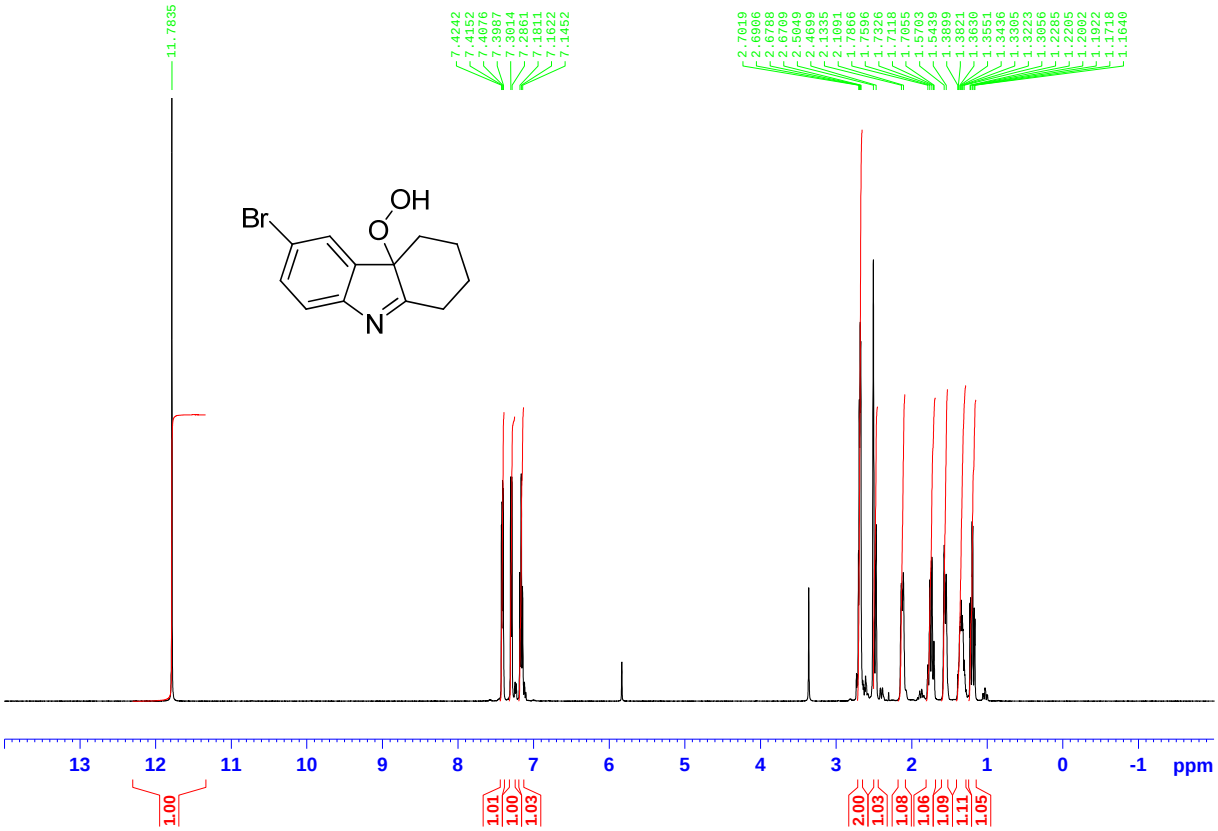


Supplementary Figure S99: ^{1}H NMR in DMSO of 4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole-6-carbonitrile

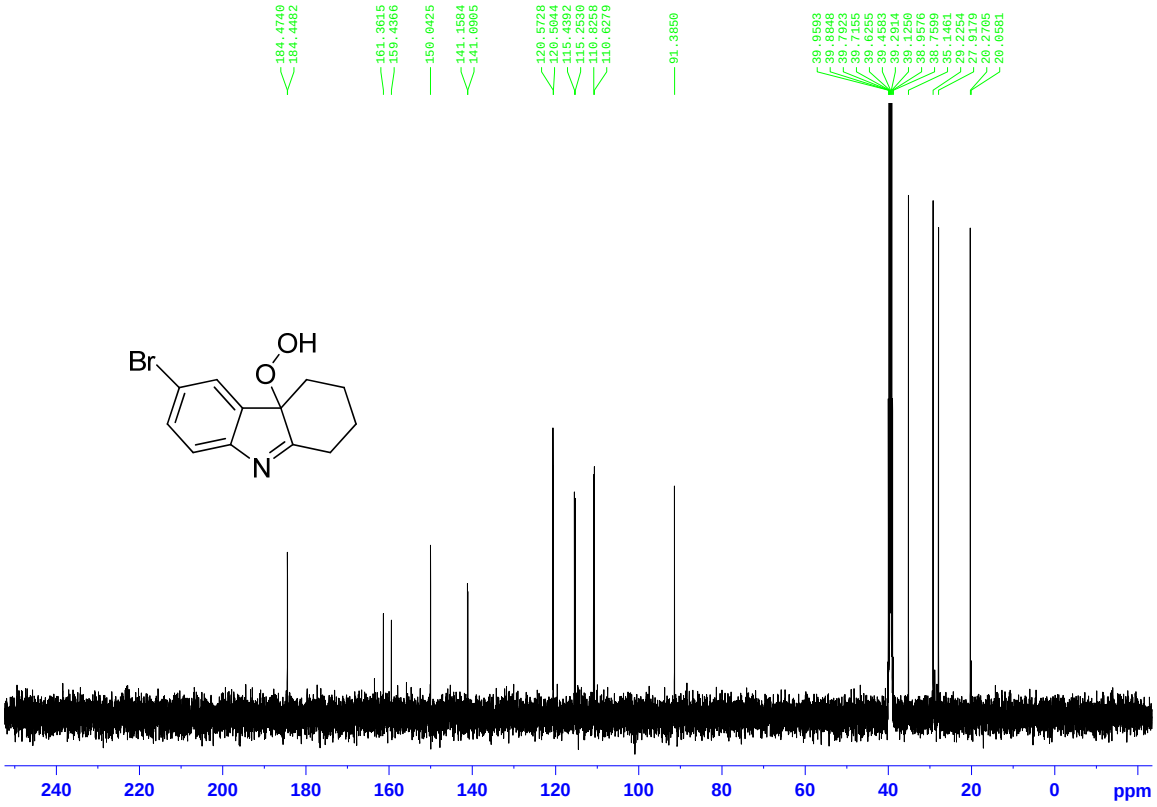


Supplementary Figure S100: ^{13}C NMR in DMSO of 4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole-6-carbonitrile (short NMR without DEPT due to slow decomposition)

6-Bromo-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

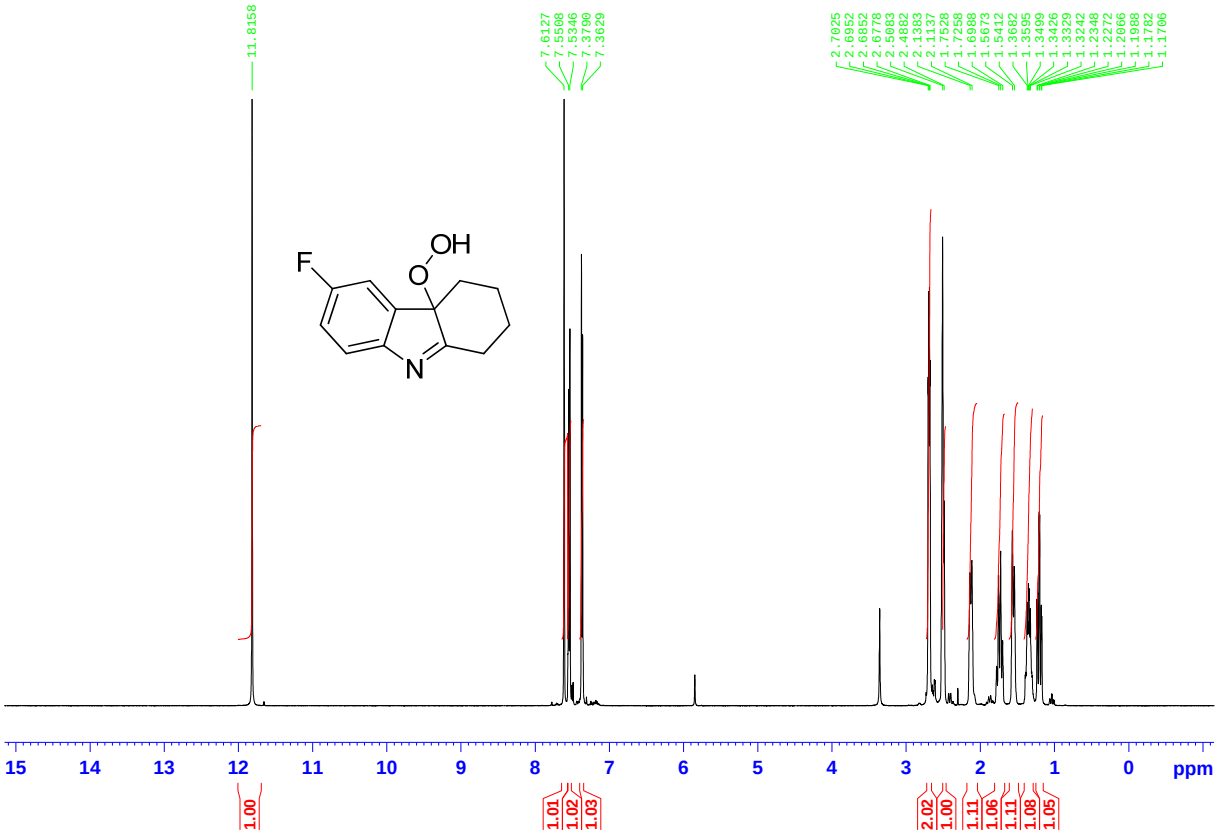


Supplementary Figure S101: ^{1}H NMR in DMSO of 6-bromo-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

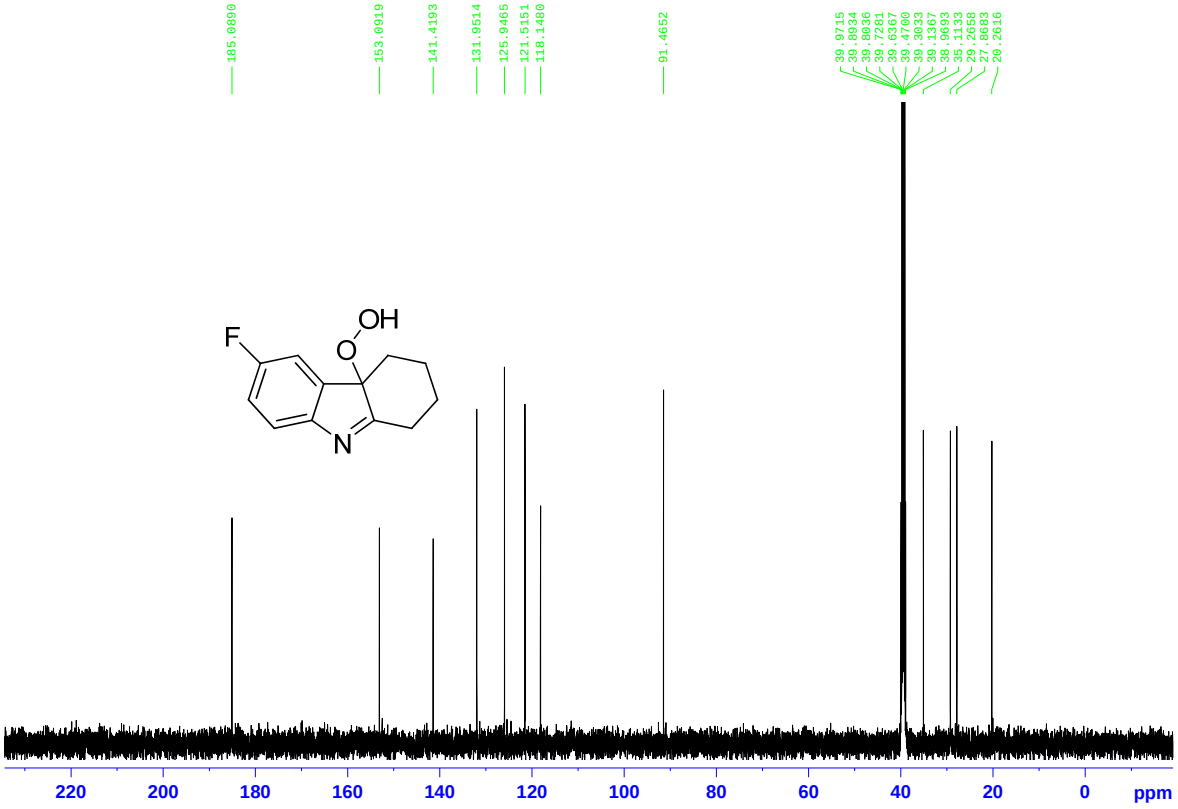


Supplementary FigureS 102: ^{13}C NMR in DMSO of 6-bromo-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (short NMR without DEPT due to slow decomposition)

6-Fluoro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

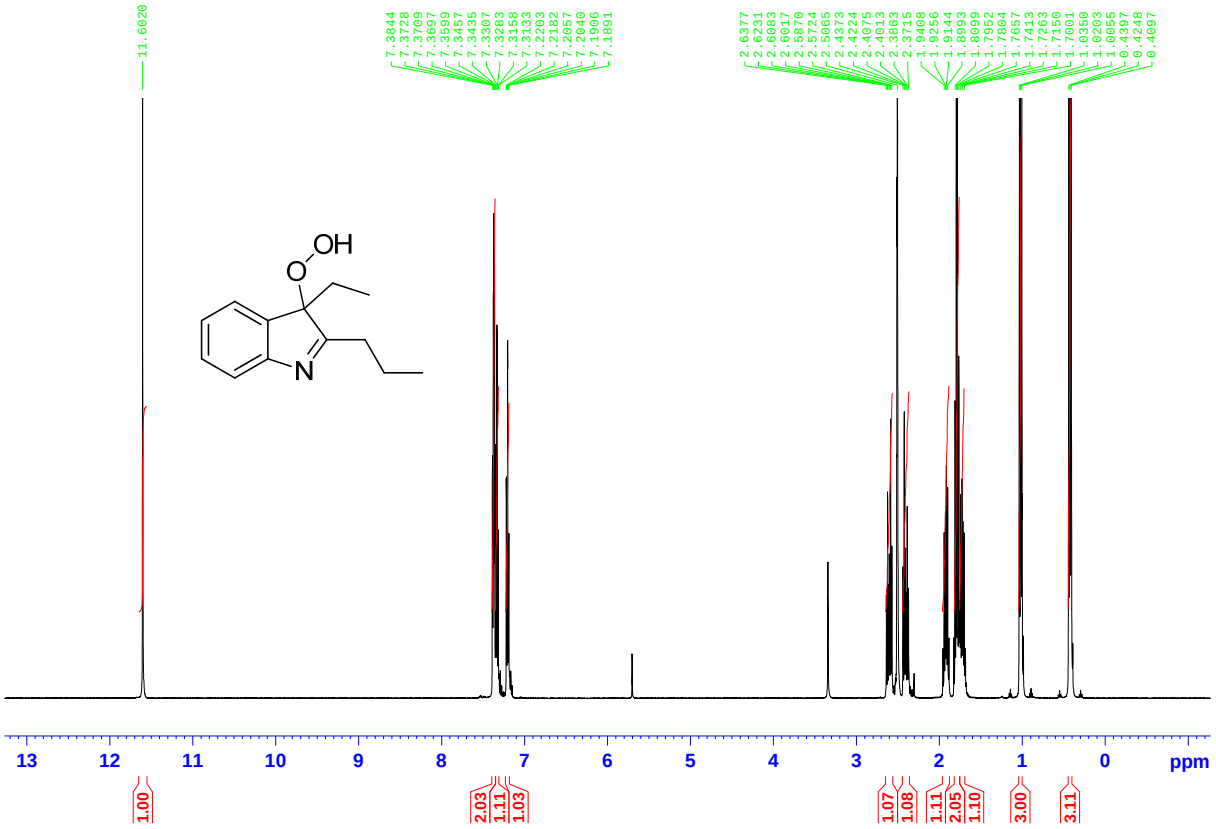


Supplementary Figure S103: ^{1}H NMR in DMSO of 6-fluoro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole

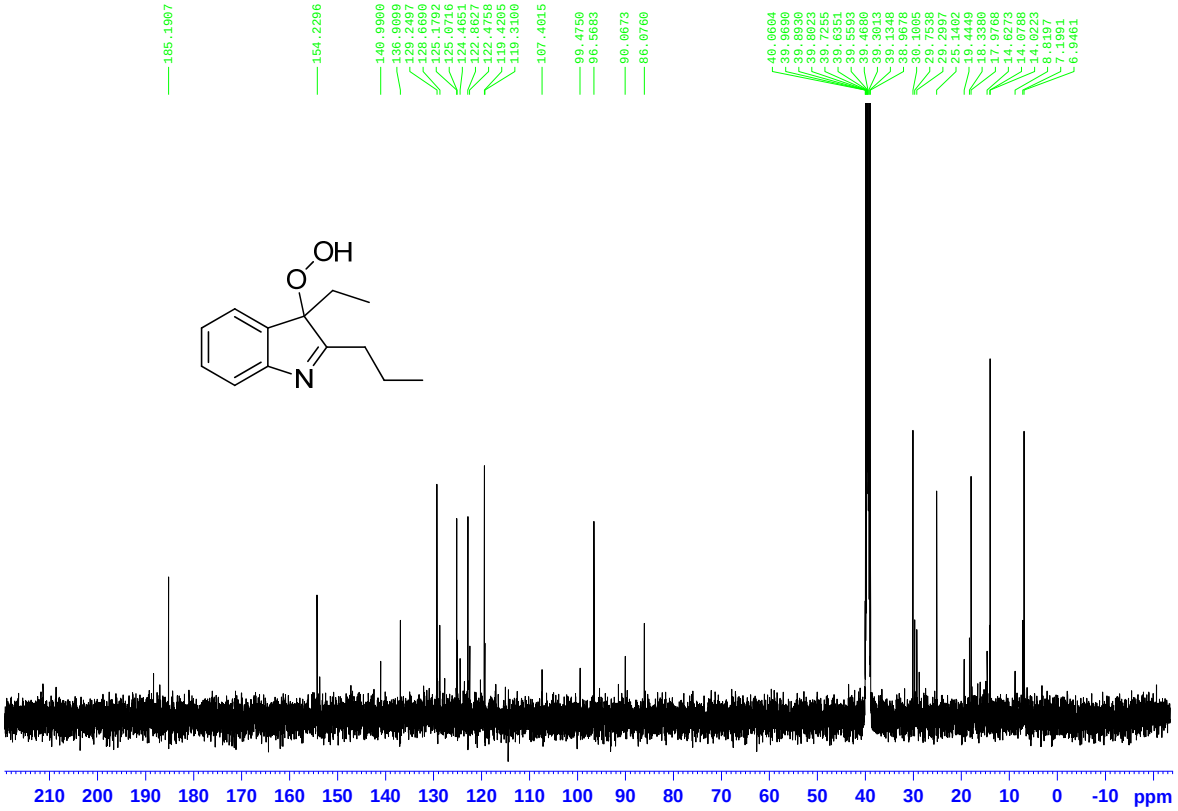


Supplementary Figure S104: ^{13}C NMR in DMSO of 6-fluoro-4a-hydroperoxy-2,3,4,4a-tetrahydro-1H-carbazole (short NMR without DEPT due to slow decomposition)

3-Ethyl-3-hydroperoxy-2-propyl-3H-indole

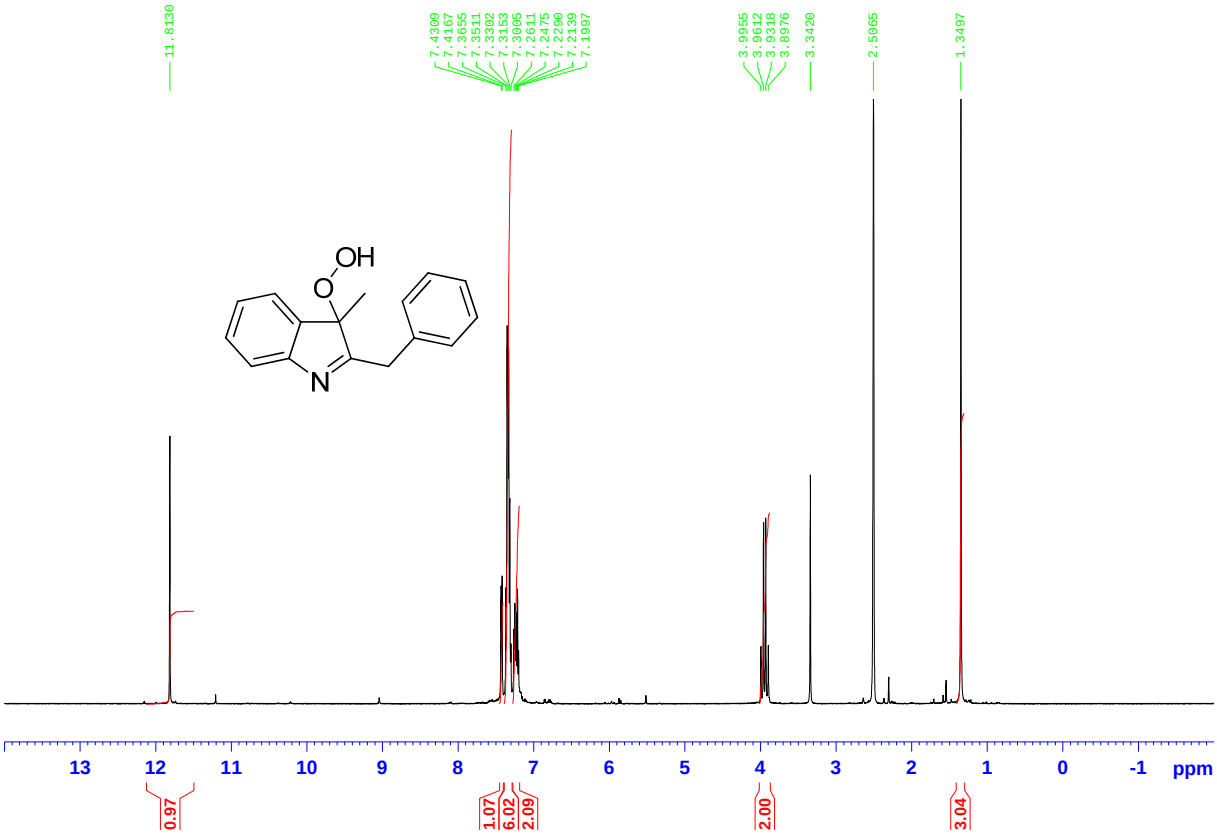


Supplementary Figure S105: ^{1}H NMR in DMSO of 3-ethyl-3-hydroperoxy-2-propyl-3H-indole

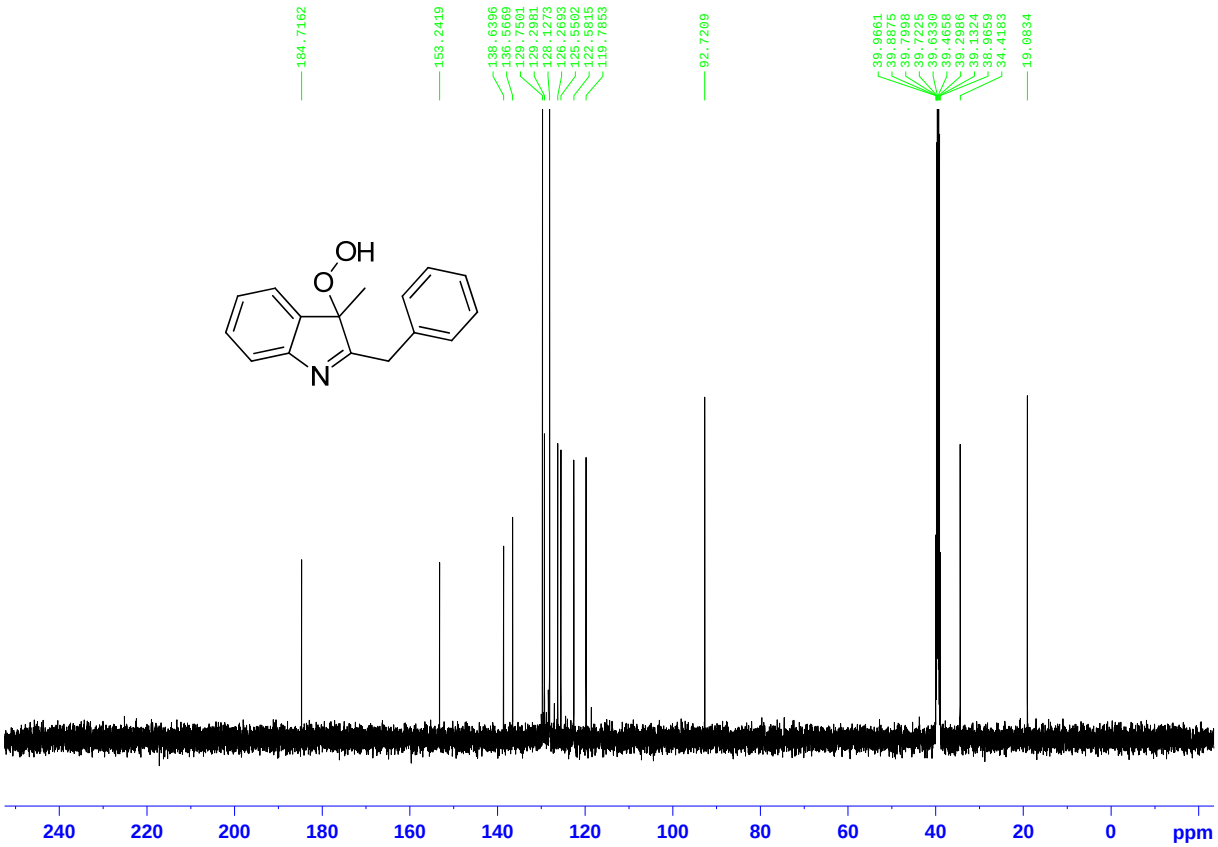


Supplementary Figure S106: ^{13}C NMR in DMSO of 3-ethyl-3-hydroperoxy-2-propyl-3H-indole (short NMR without DEPT due to slow decomposition)

2-Benzyl-3-hydroperoxy-3-methyl-3H-indole



Supplementary Figure S107: ^{1}H NMR in DMSO of 2-benzyl-3-hydroperoxy-3-methyl-3H-indole



Supplementary Figure S108: ^{13}C NMR in DMSO of 2-benzyl-3-hydroperoxy-3-methyl-3H-indole (short NMR without DEPT due to slow decomposition)

Supplementary References

1 Varma, P. P., Sherigara, B. S., Mahadevan, K. M. & Hulikal, V. Efficient and Straightforward Synthesis of Tetrahydrocarbazoles and 2,3-Dimethyl Indoles Catalyzed by CAN. *Synthetic Communications* 39, 158-165, (2008).

2 Stadlbauer, W., Van Dang, H. & Berger, B. S. Synthesis and reactions of 4-hydroxy-8,9,10,11-tetrahydropyrido[3,2,1-jk]carbazol-6-ones. *Journal of Heterocyclic Chemistry* 47, 807-824, (2010).

3 Mateo, C. A., Urrutia, A., Rodríguez, J. G., Fonseca, I. & Cano, F. H. Photooxygenation of 1,2,3,4-Tetrahydrocarbazole: Synthesis of Spiro[cyclopentane-1,2‘-indolin-3‘-one]. *J. Org. Chem.* 61, 810-812, (1996).