

Supporting Information

Deracemizing Organocatalyzed Michael Addition Reactions of 2-(Arylthio)cyclobutanones with β -Nitrostyrenes

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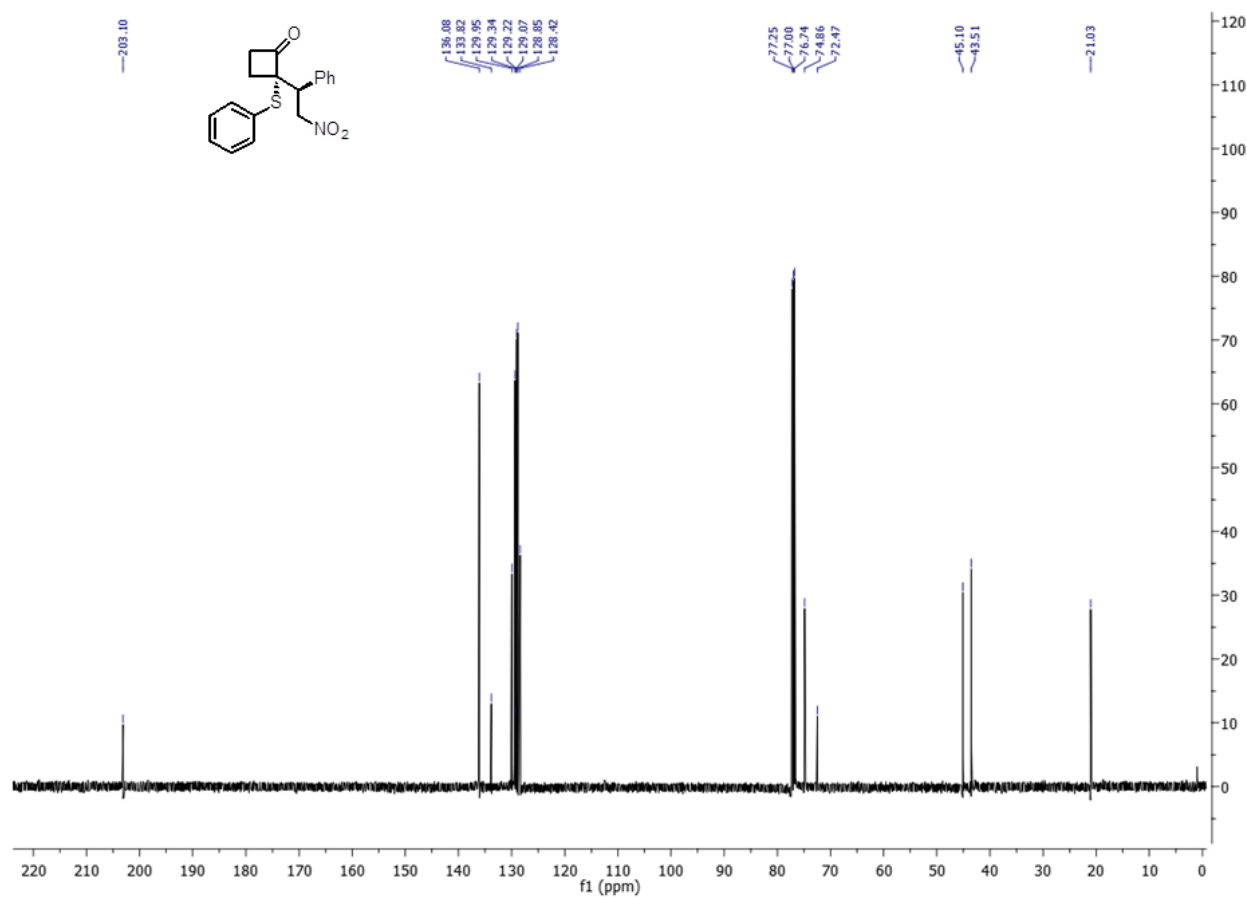
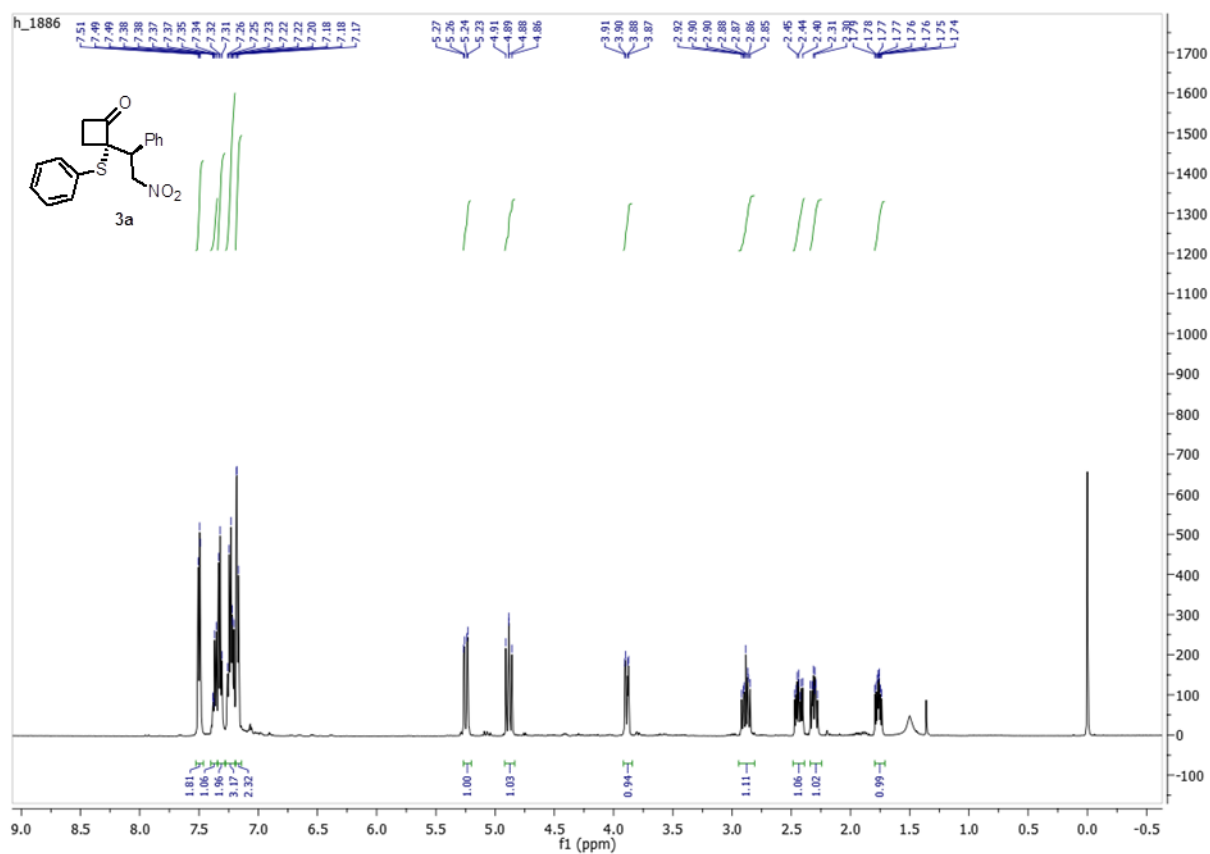
Materials and Methods

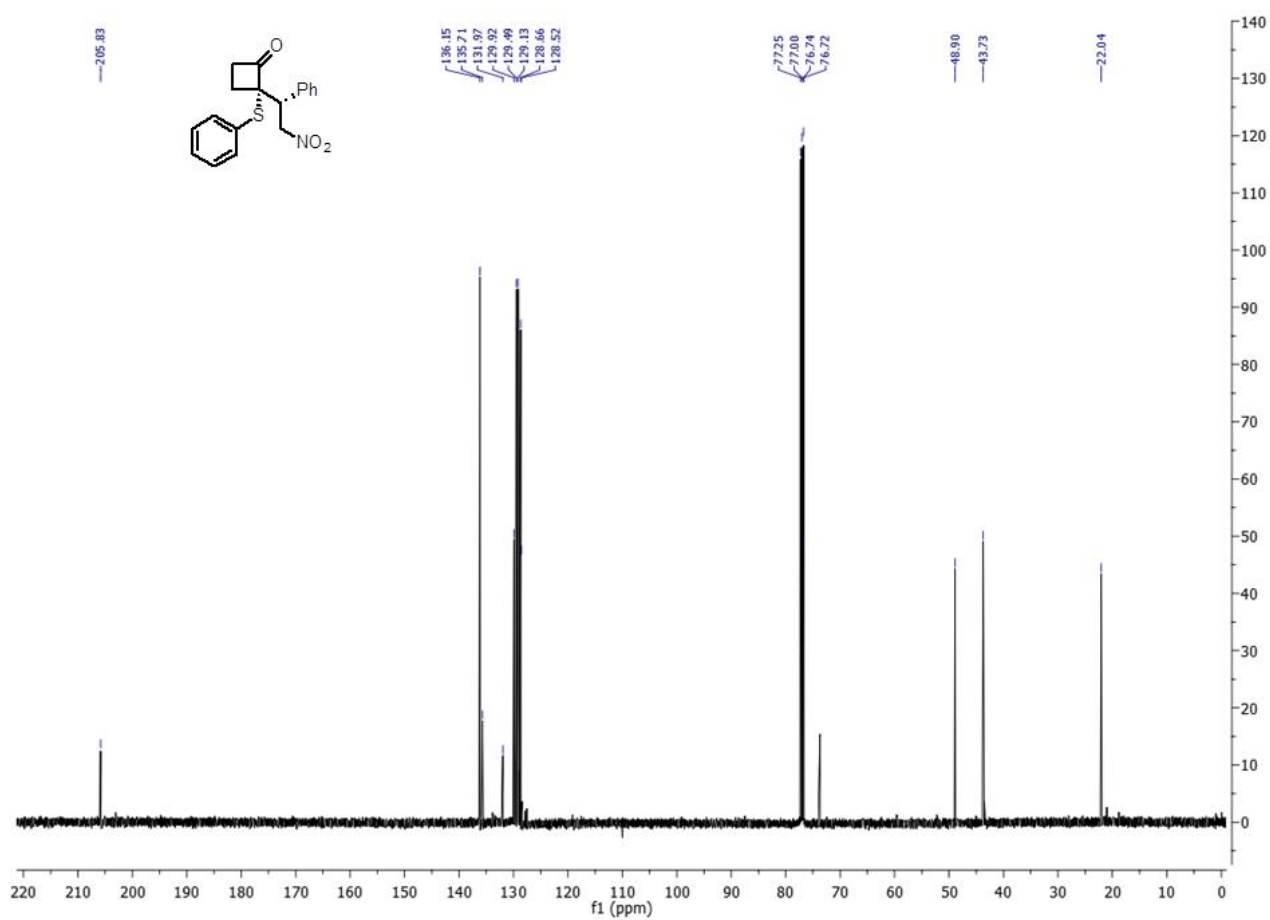
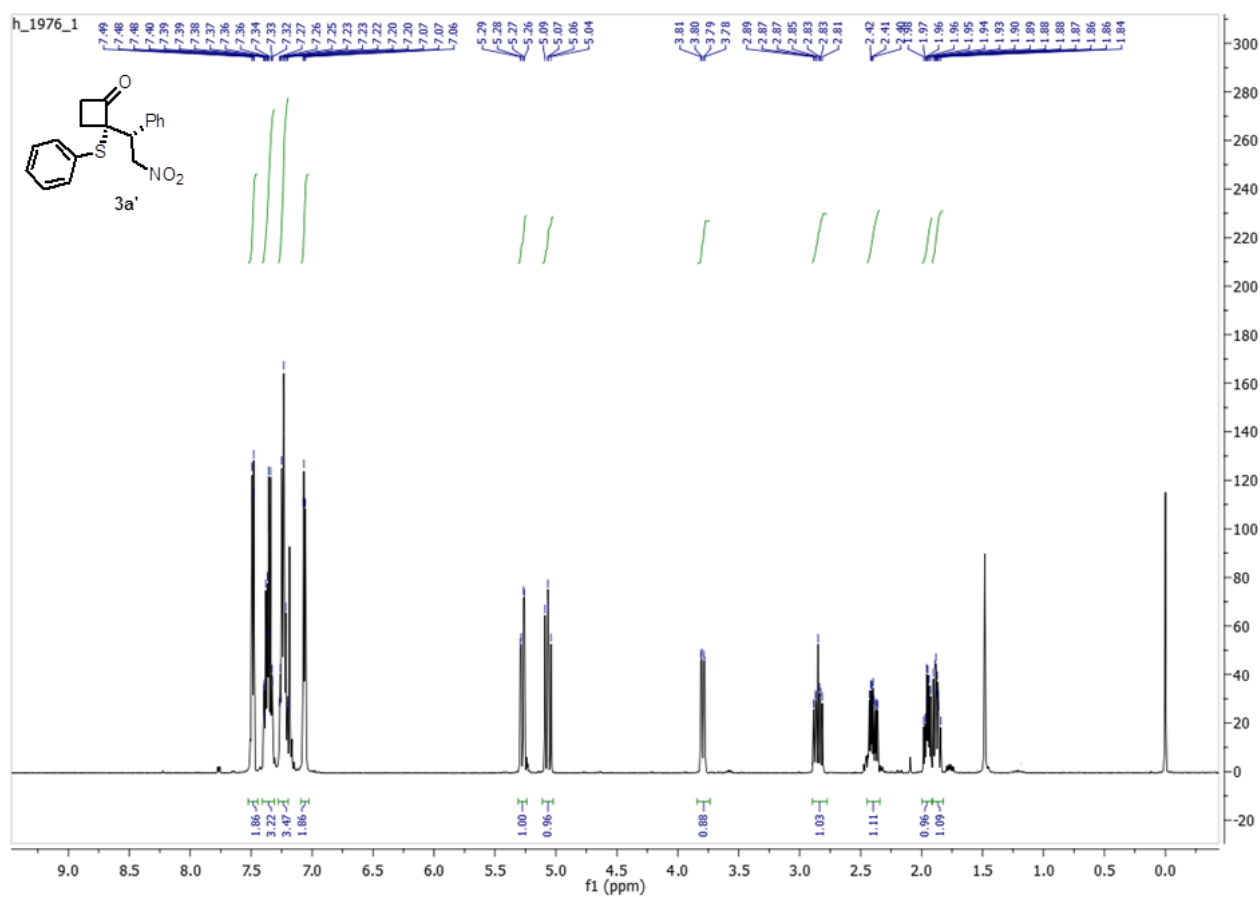
Unless stated otherwise, reaction were performed at ambient temperature (25°C). Commercially available reagents were used as received unless otherwise noted. Diphenyldisulfide, *p*-nitrophenyldisulfide, cyclobutanone **1a**, cyclopentanone **3a**, cyclohexanones **3b-e**, and ketones **5a-c** were purchased from Aldrich. Catalysts **I-VII** were purchased from Aldrich or Alfa-Aesar and used as received. ¹H NMR spectra were recorded on 400 and 500 MHz Varian spectrometers at 27°C using CDCl₃, DMF-*d*₇ or DMSO-*d*₆ as solvent. ¹³C NMR were recorded at 100 and 125 MHz at 27°C using CDCl₃, DMF-*d*₇ or DMSO-*d*₆ as solvent. Chemical shifts (δ) are given in ppm. Coupling constants (*J*) are reported in Hz. Infrared spectra were recorded on a FT-IR Bruker Equinox-55 spectrophotometer and are reported in wavenumbers. Low Mass spectra analysis were recorded on an Agilent-HP GC-MS (E.I. 70eV). High resolution mass spectra (HRMS) were obtained using a Bruker High Resolution Mass Spectrometer in fast atom bombardment (FAB+) ionization mode or acquired using an Bruker micrOTOF-Q II 10027.

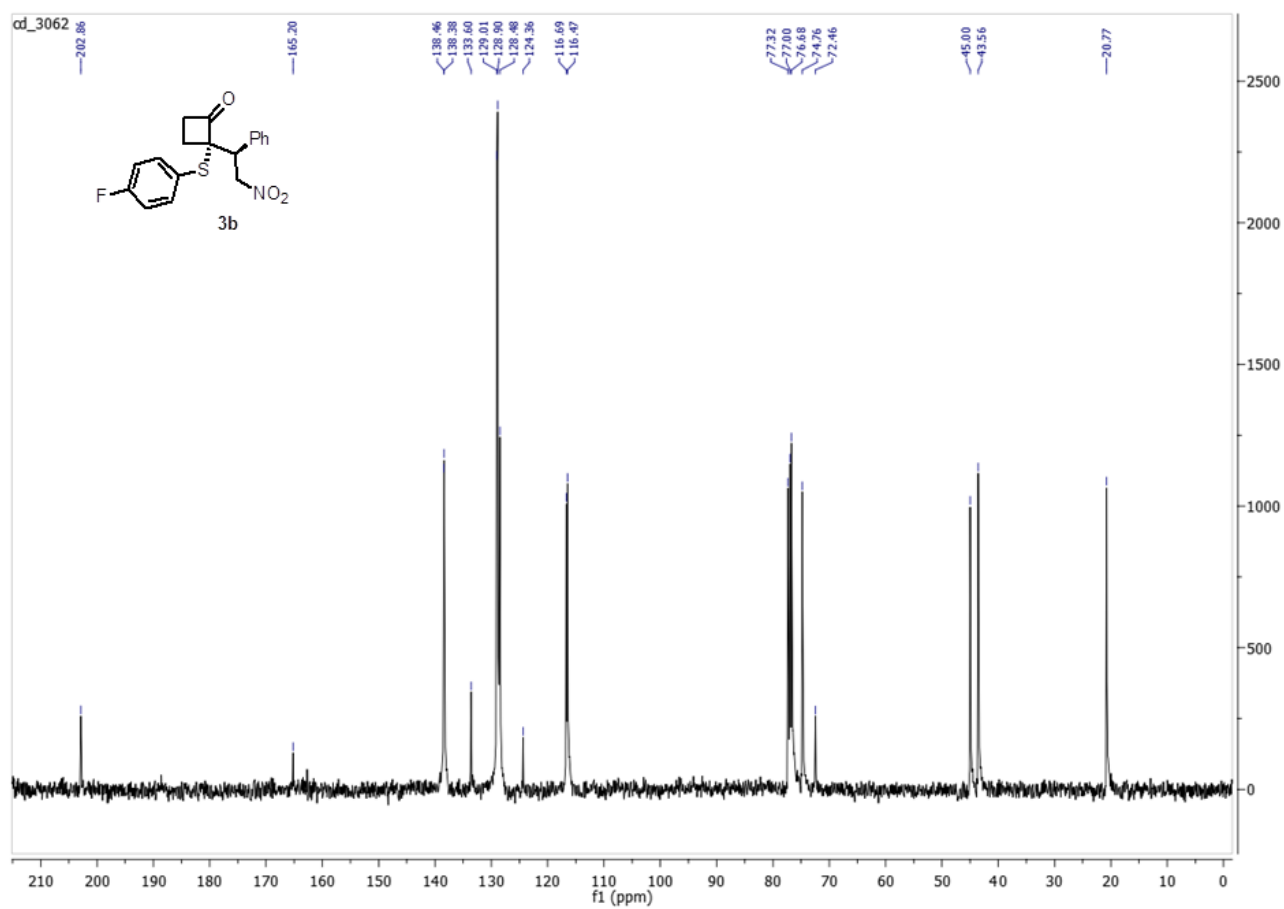
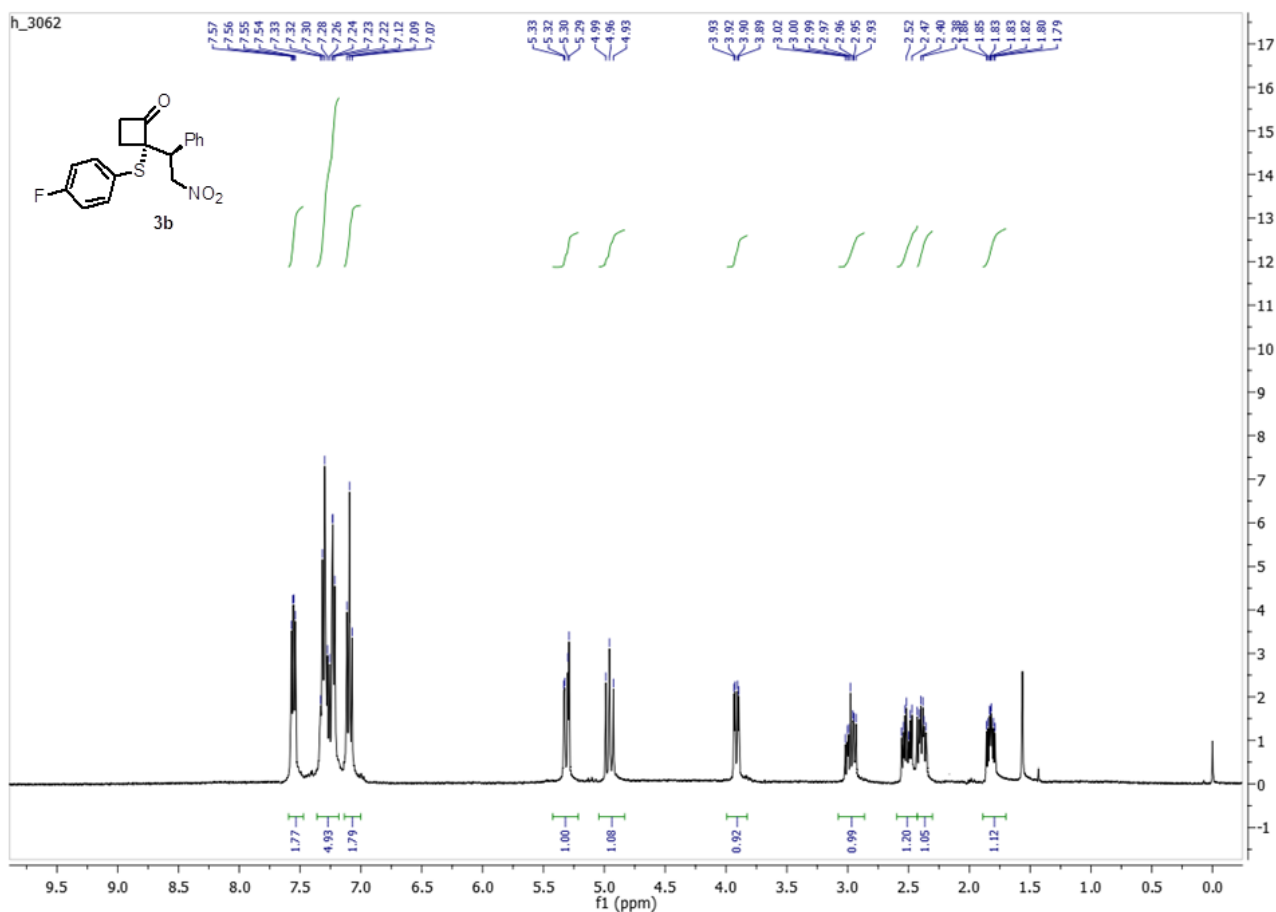
HPLC analysis were obtained from Hitachi-LaChrome 7100-UV/7400-Pump integrated system and using chiral HPLC columns OJ, OD-H, AD-H and Phenomenex-Lux.

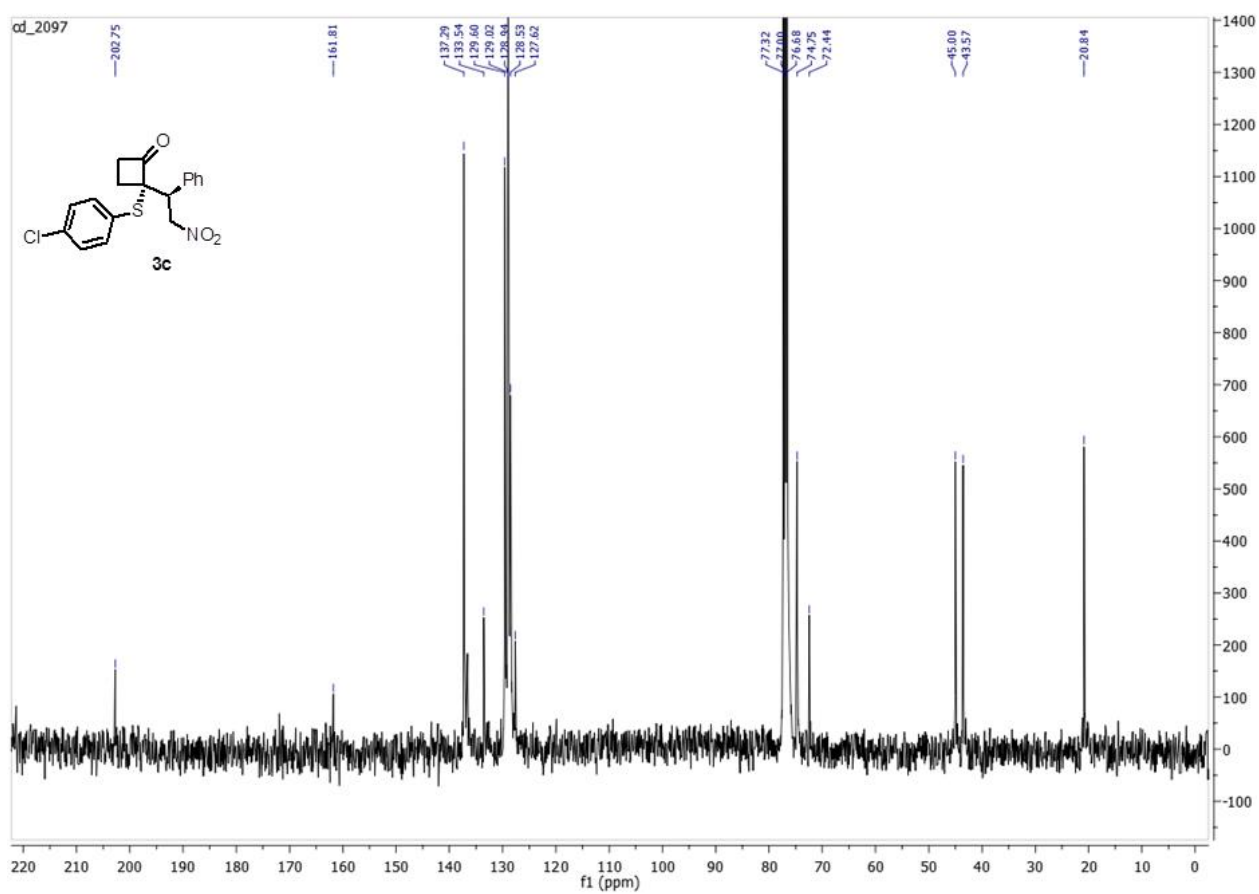
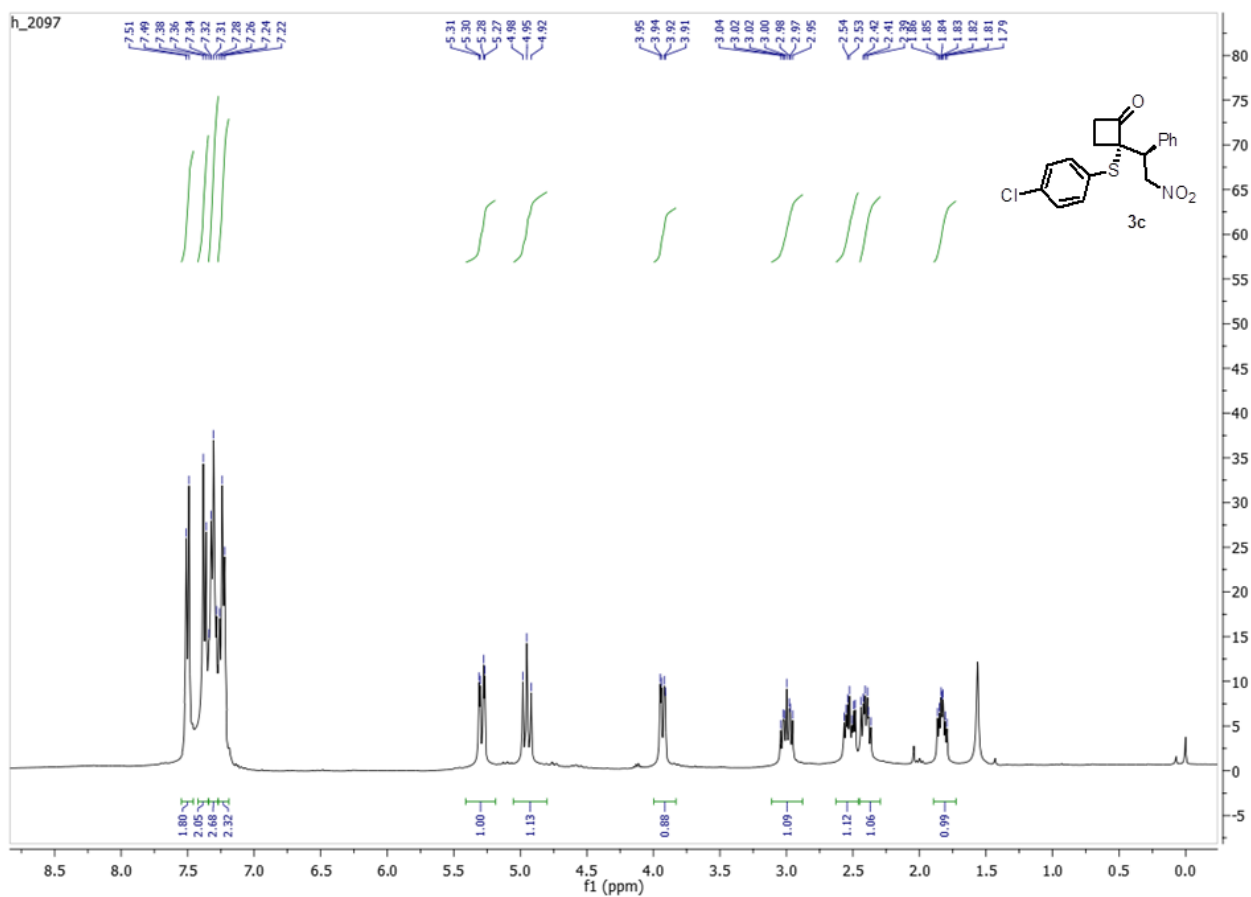
Analytical thin layer chromatography was performed using 0.25 mm Aldrich silica gel 60-F plates. Flash chromatography was performed using Merk 70-200 mesh silica gel. Yields refer to chromatography and spectroscopically pure materials.

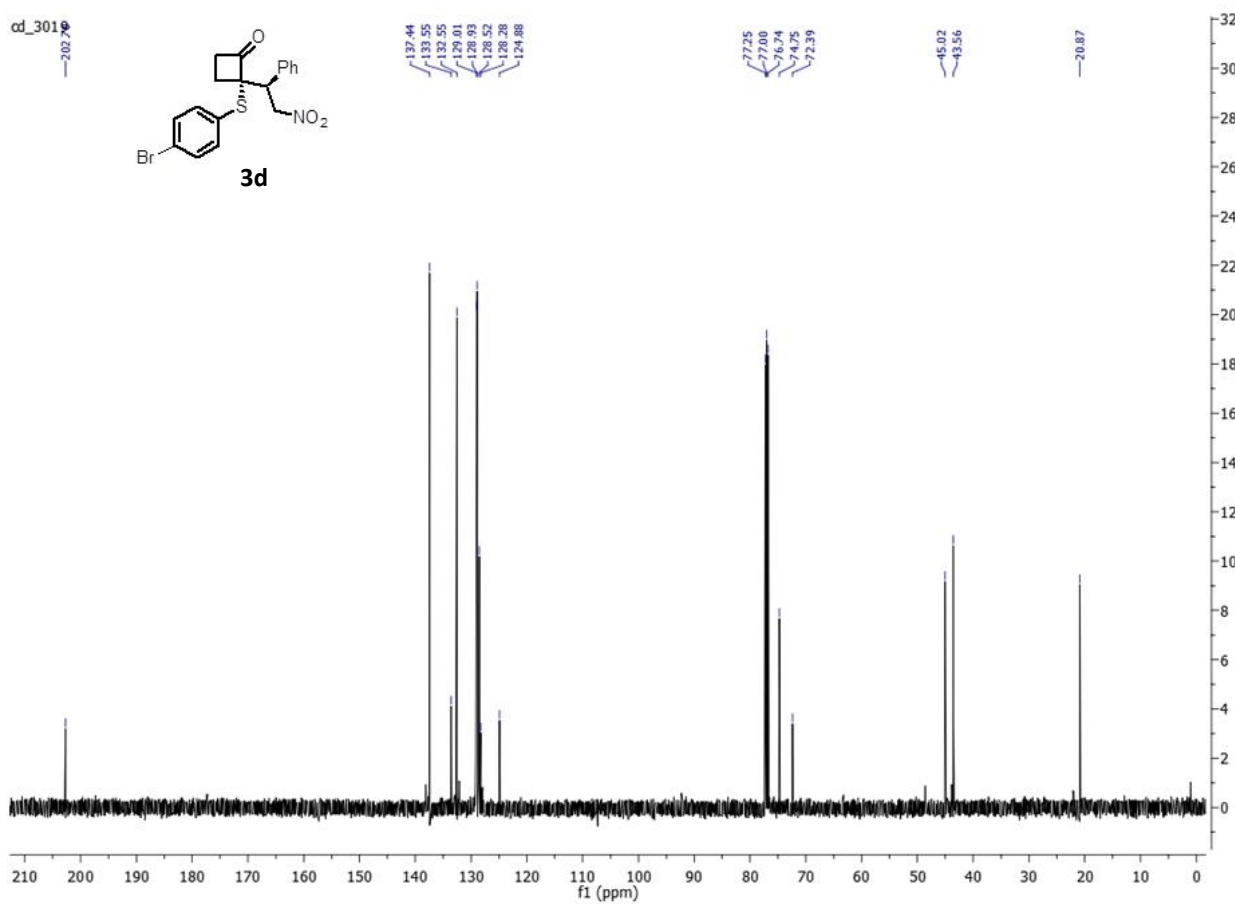
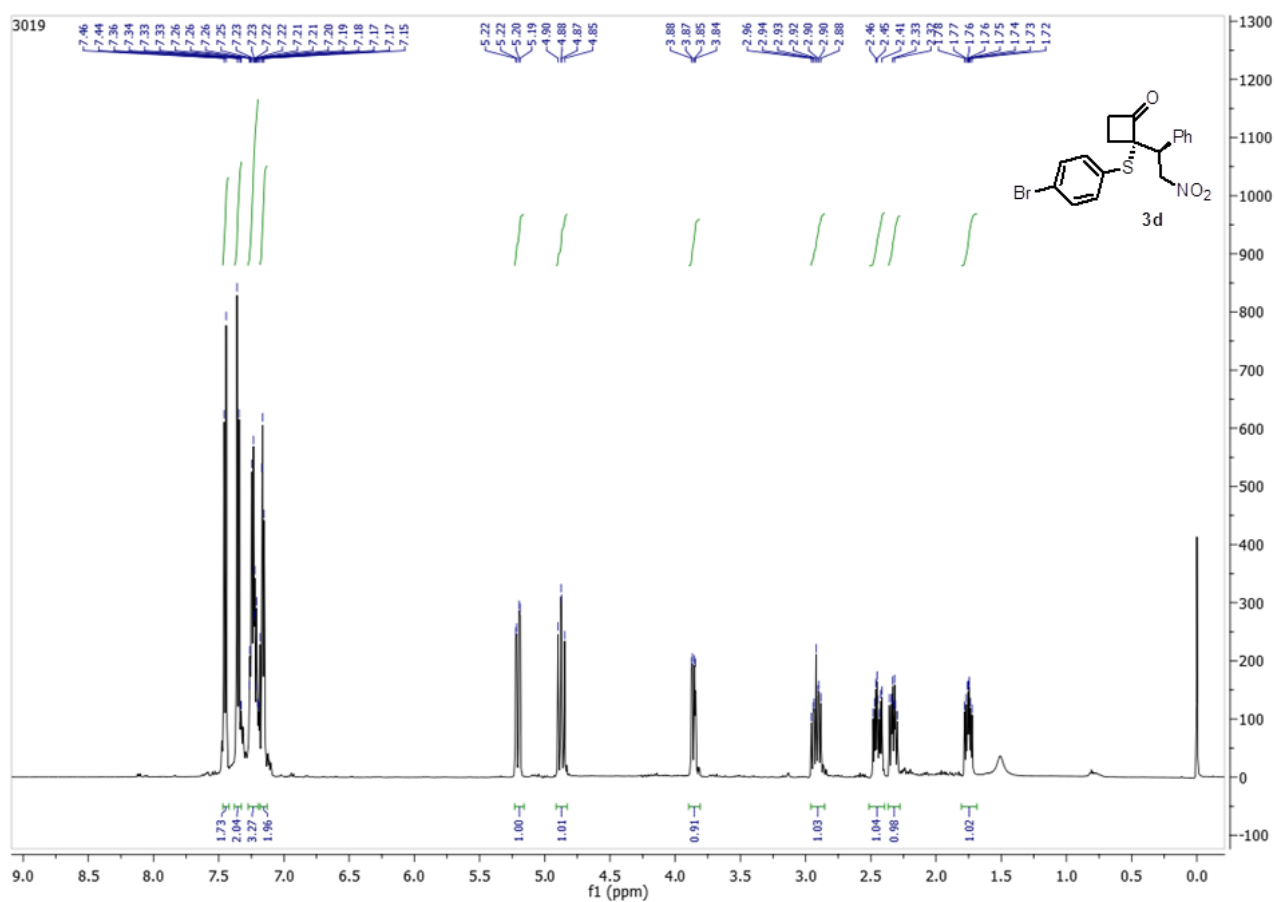
^1H and ^{13}C NMR of compounds 3a-3g

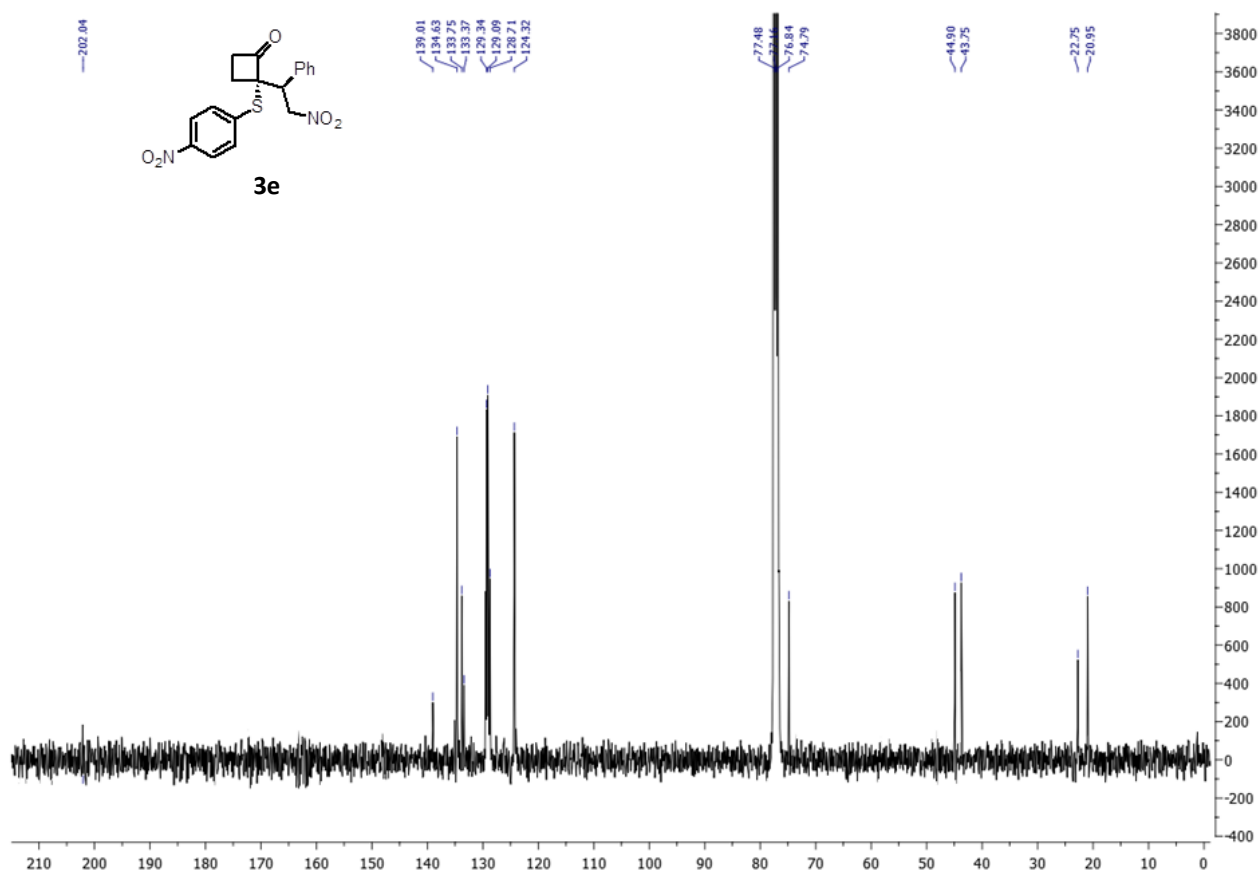
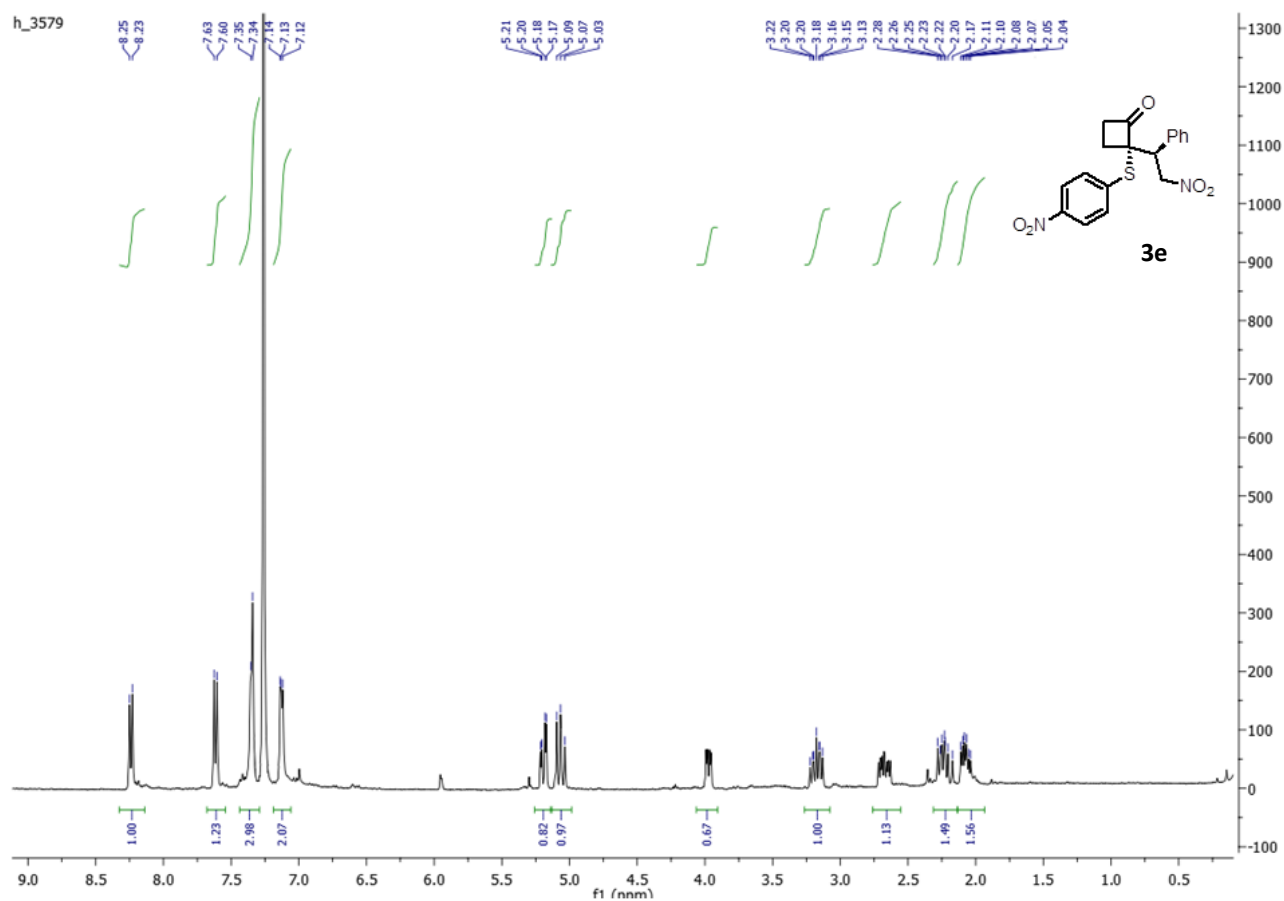


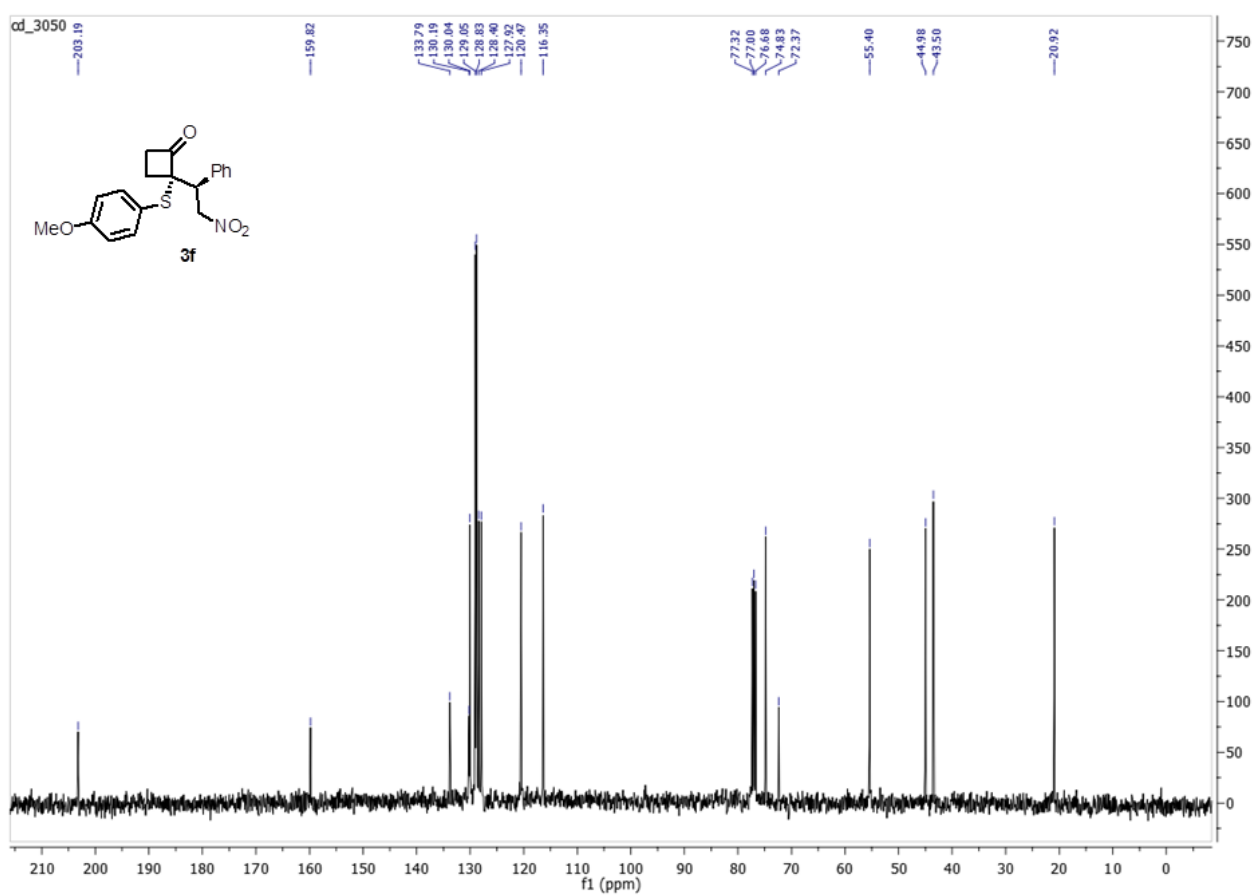
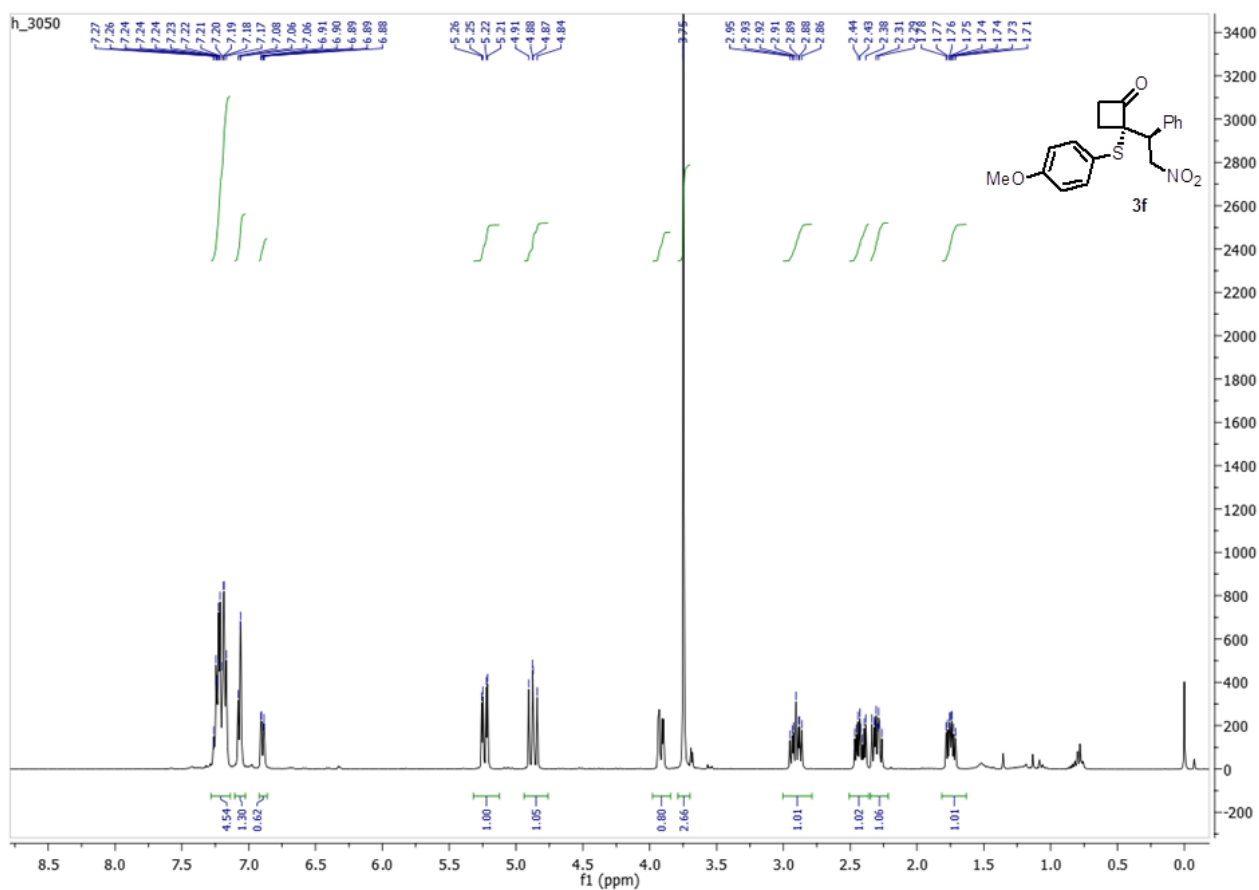


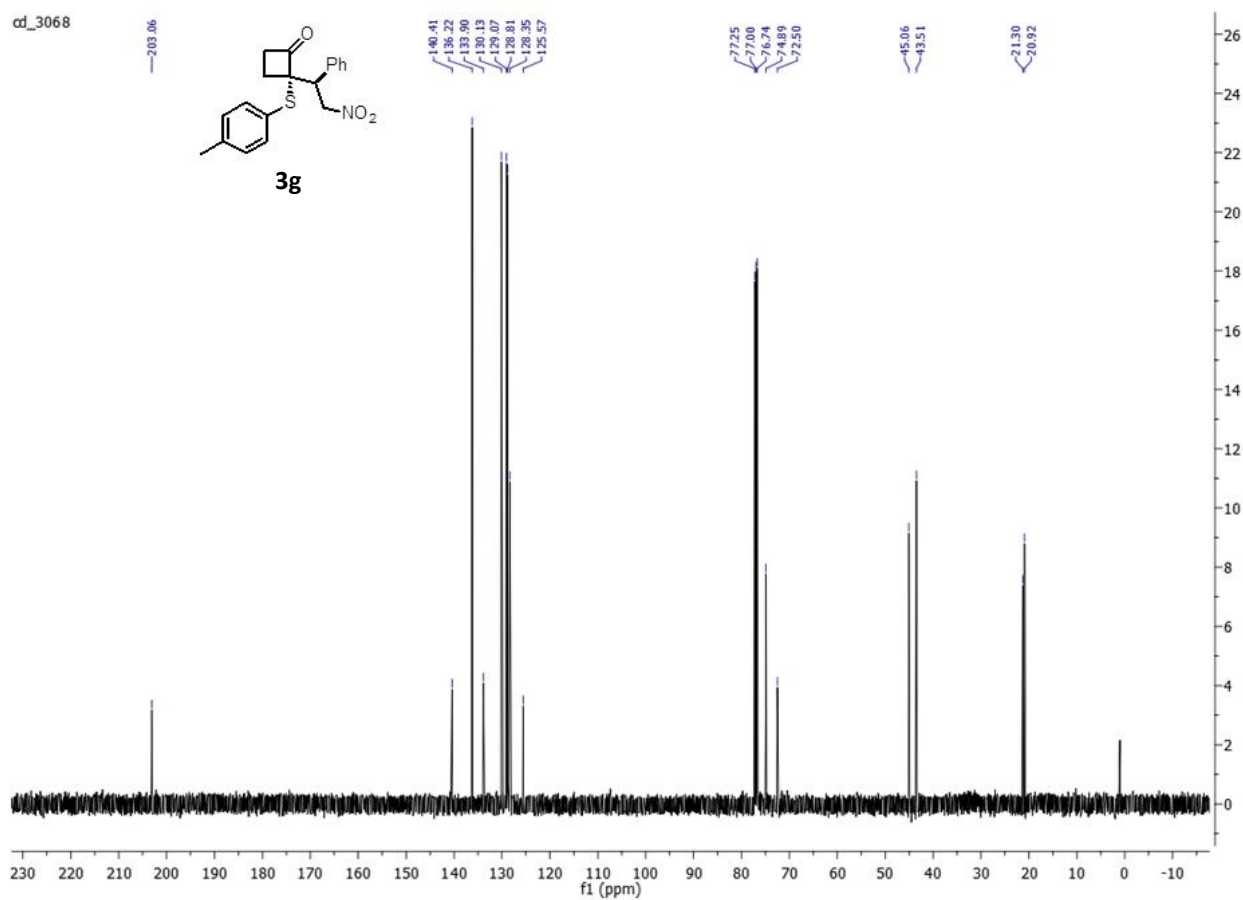
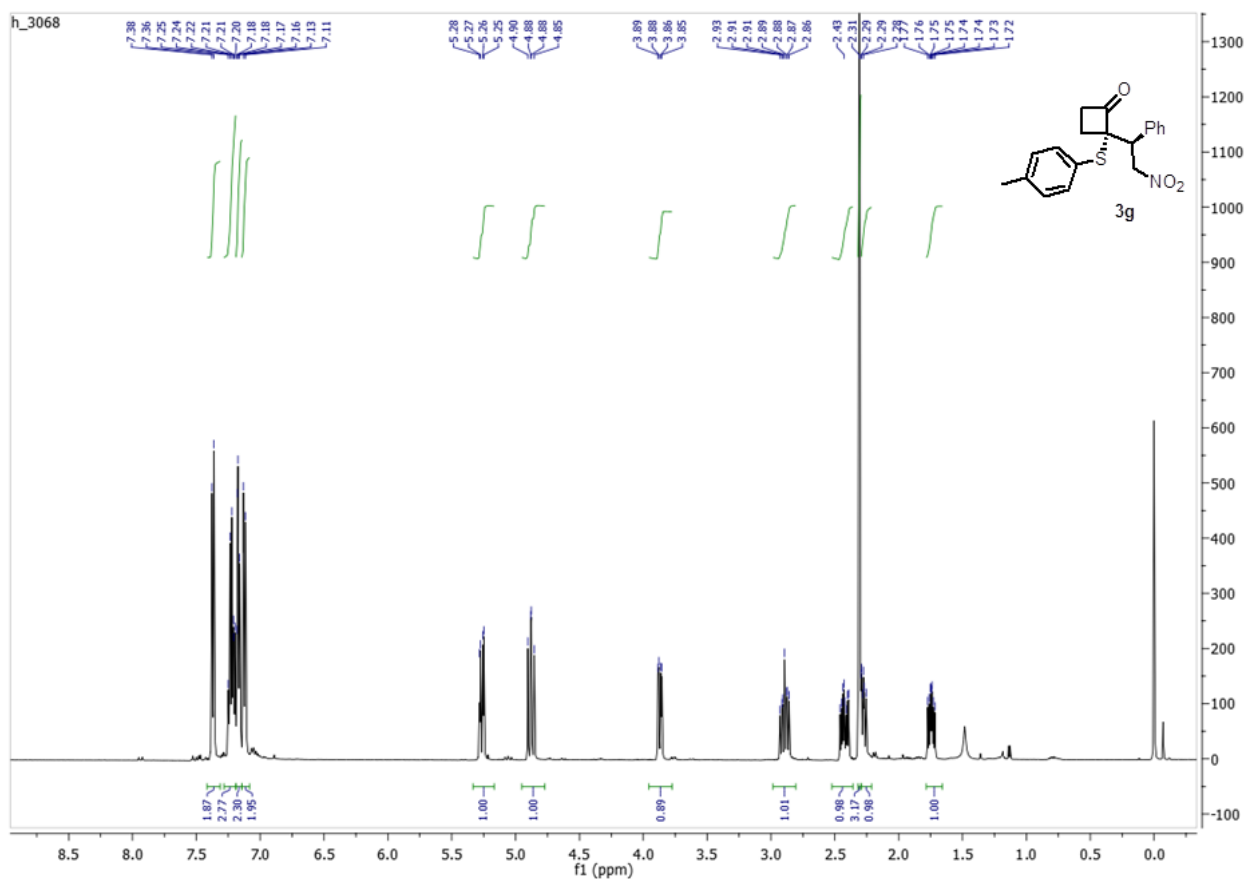




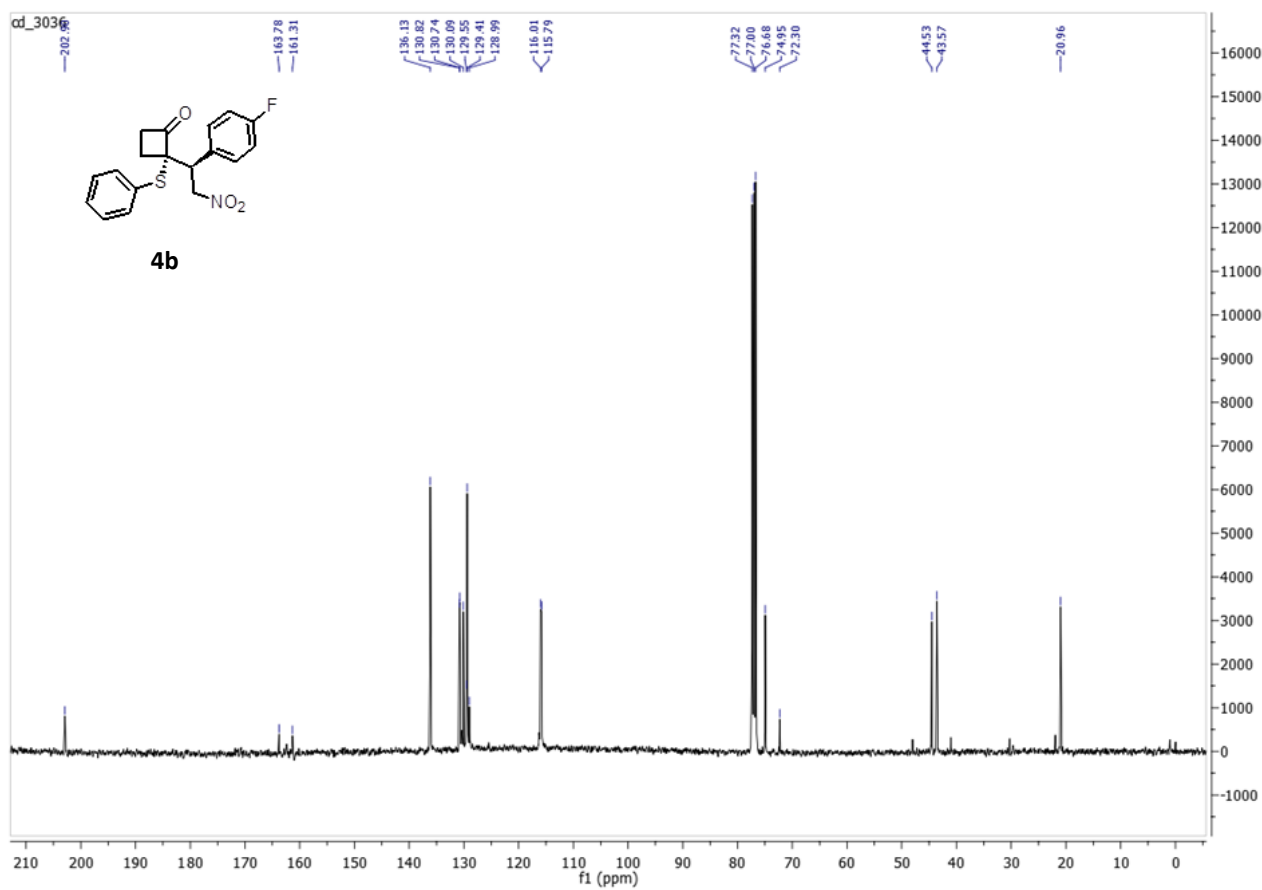
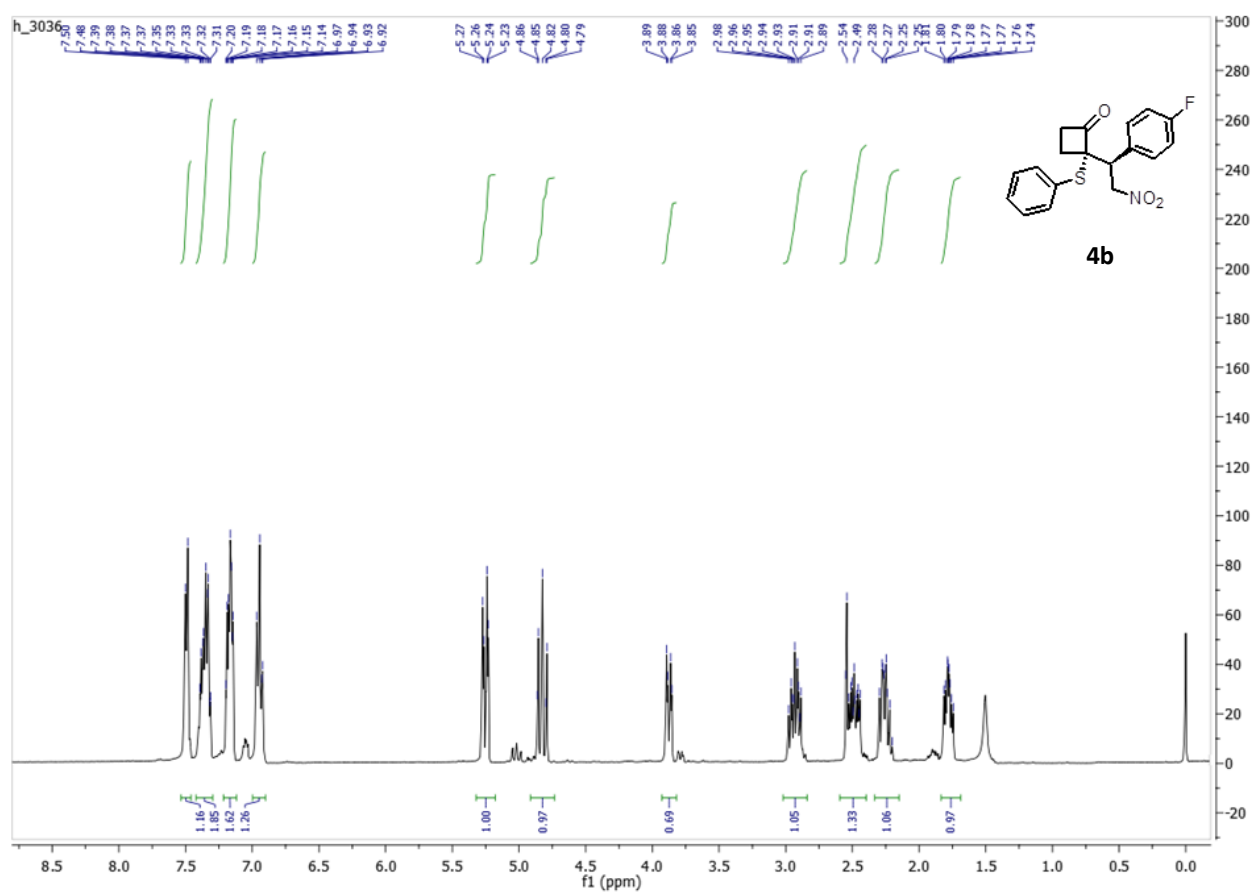


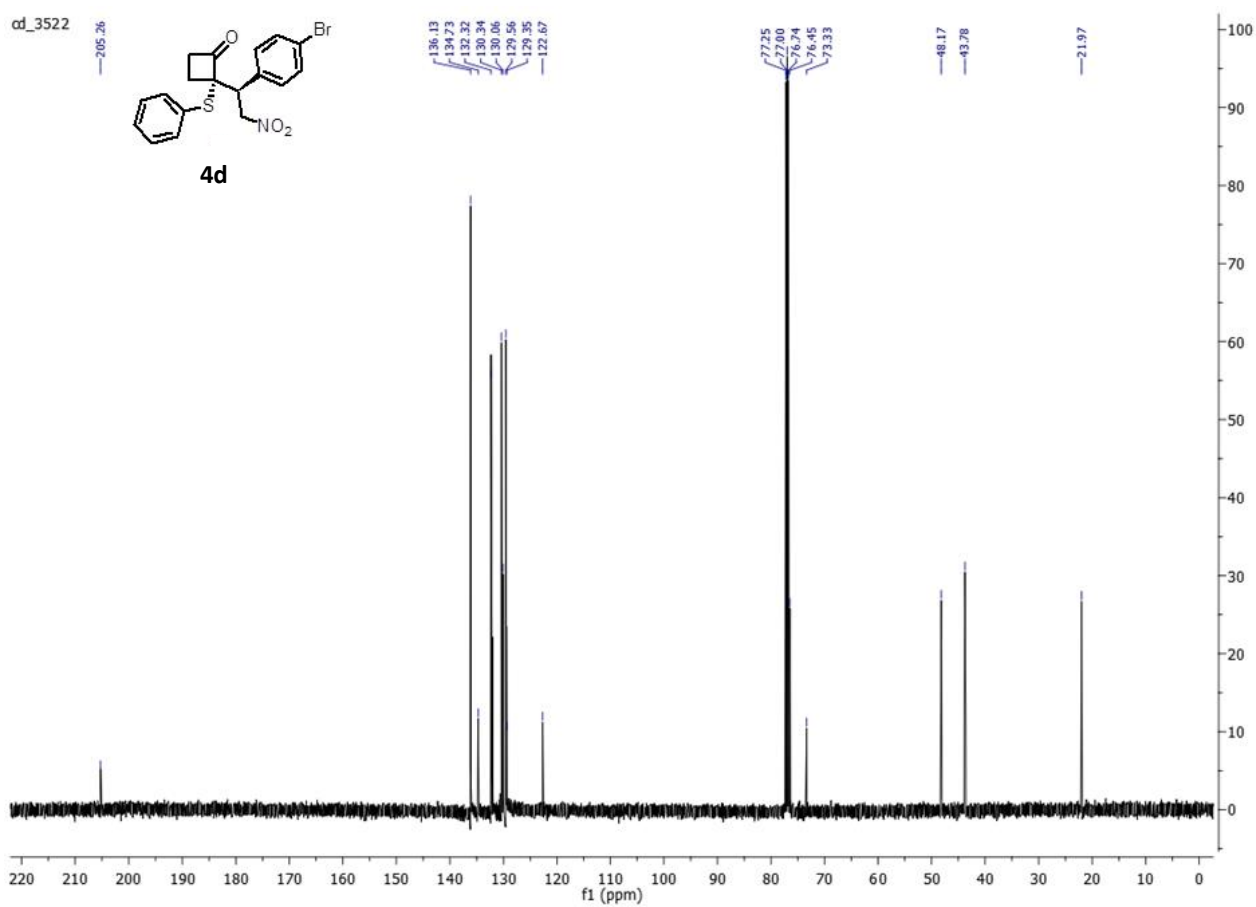
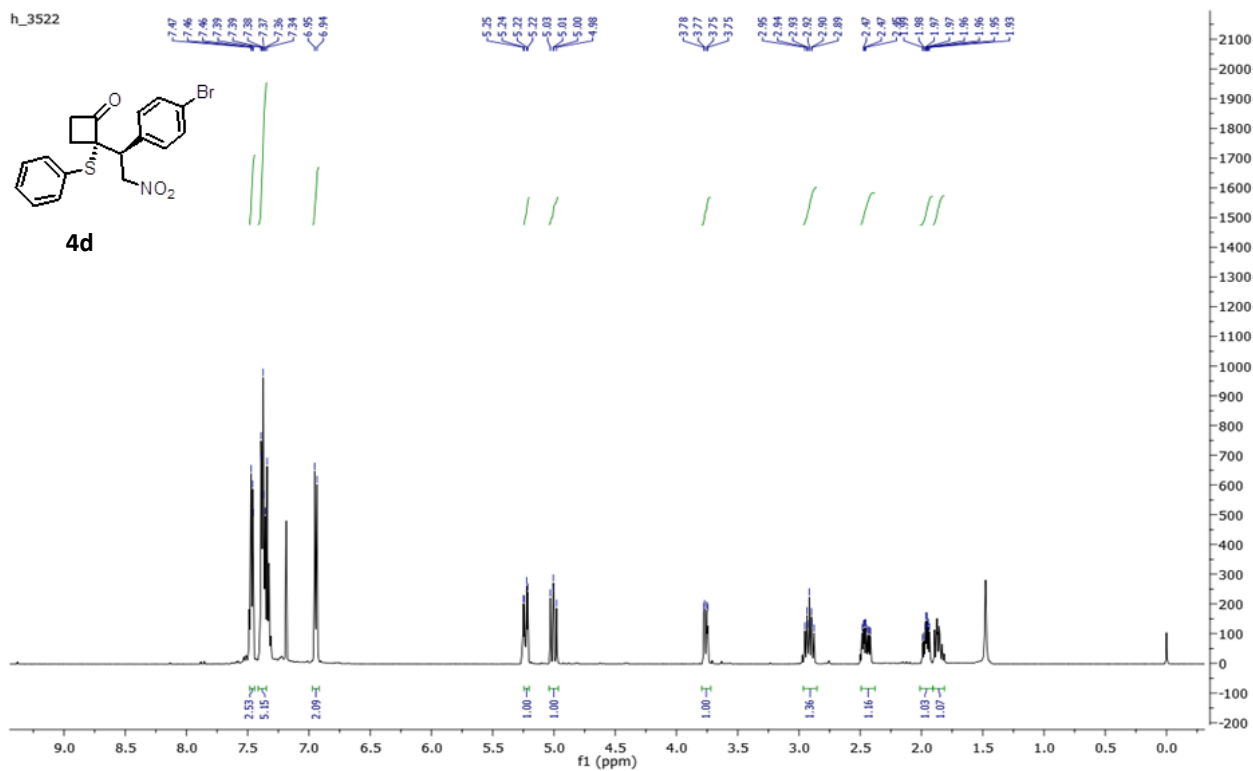


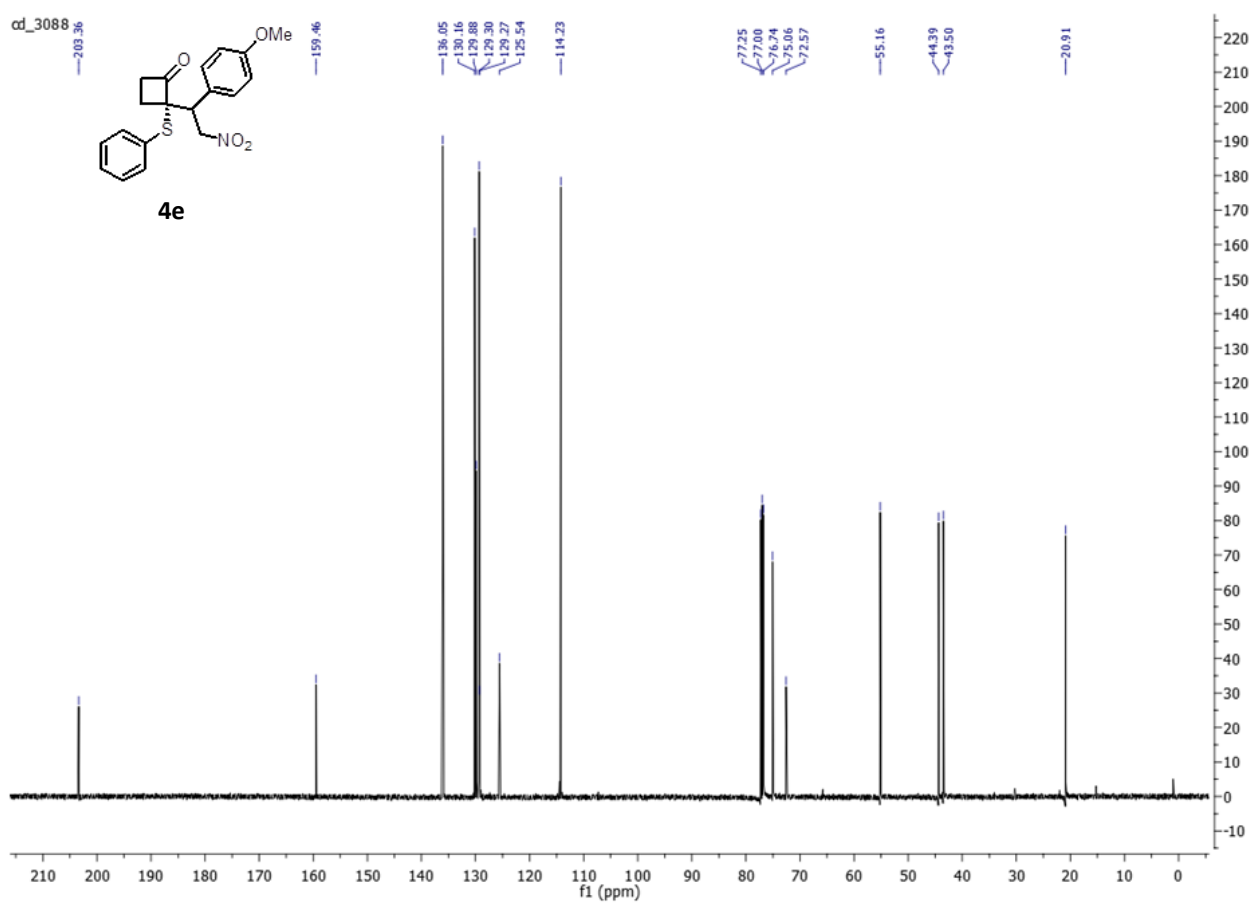
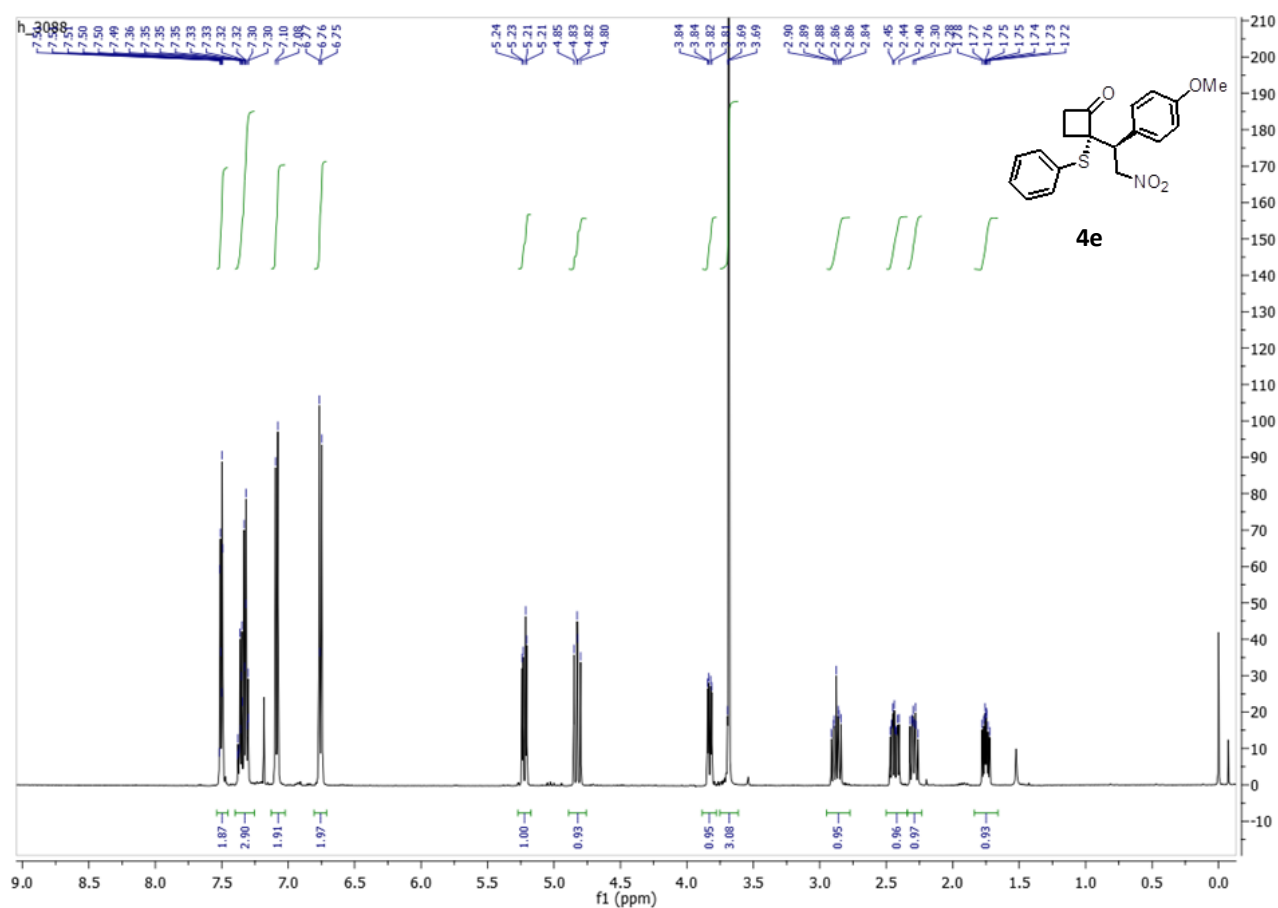


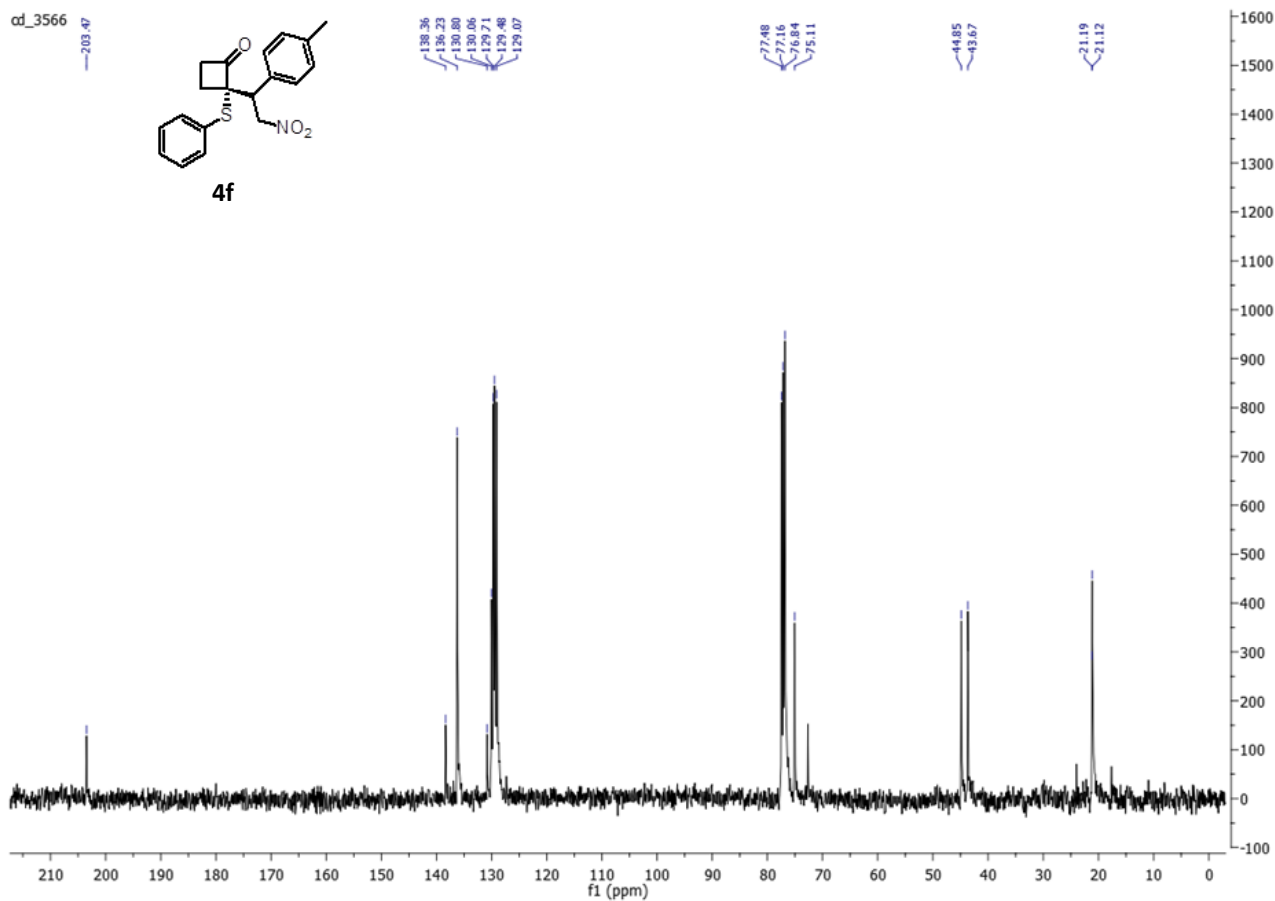
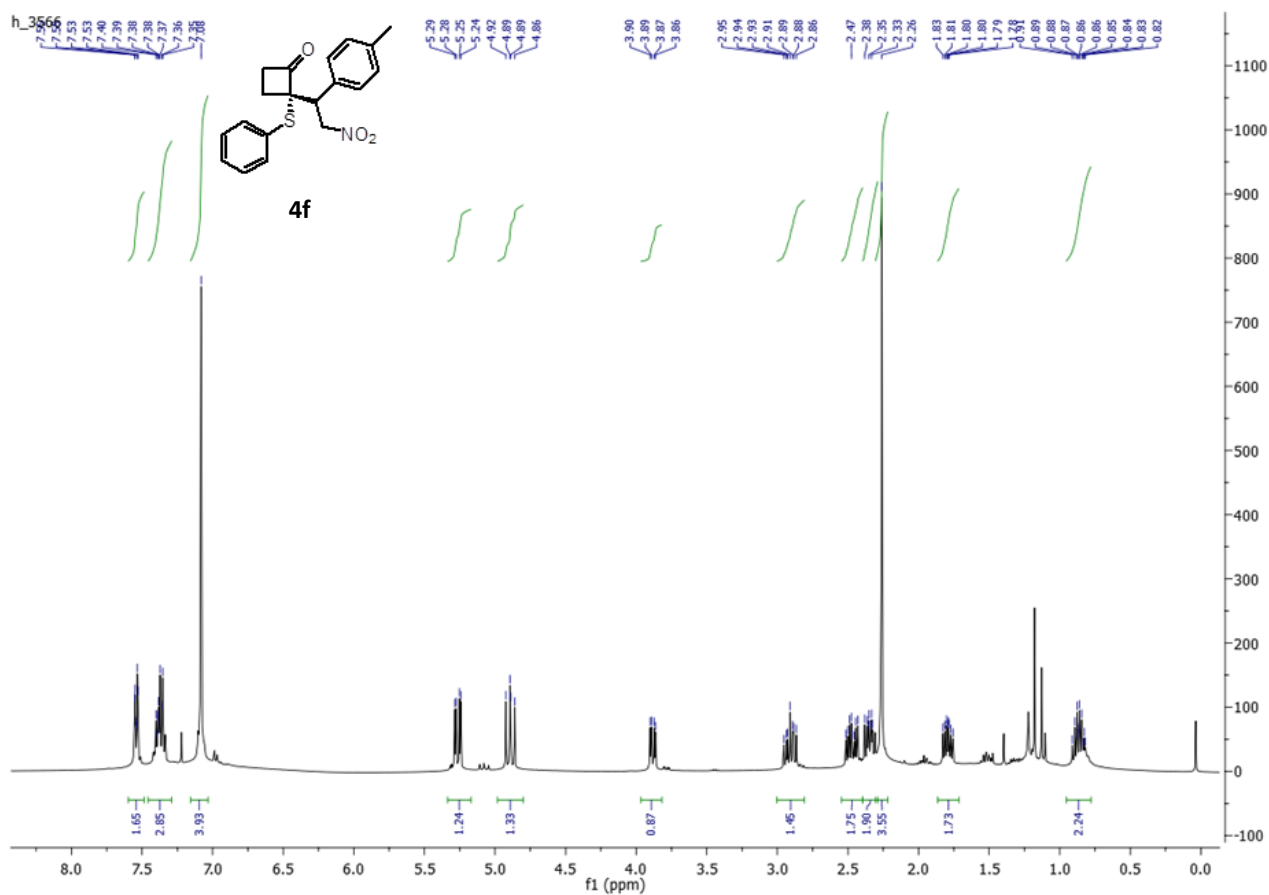


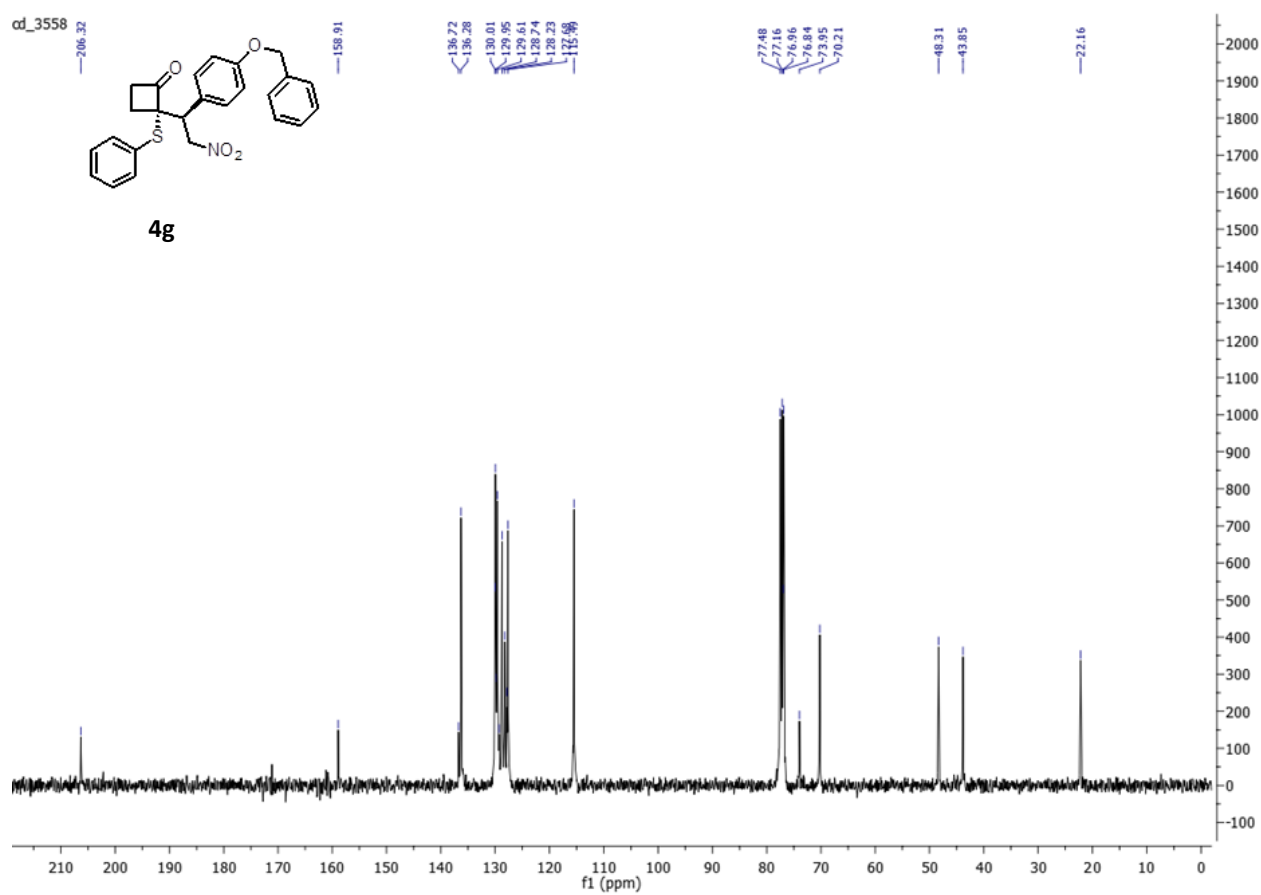
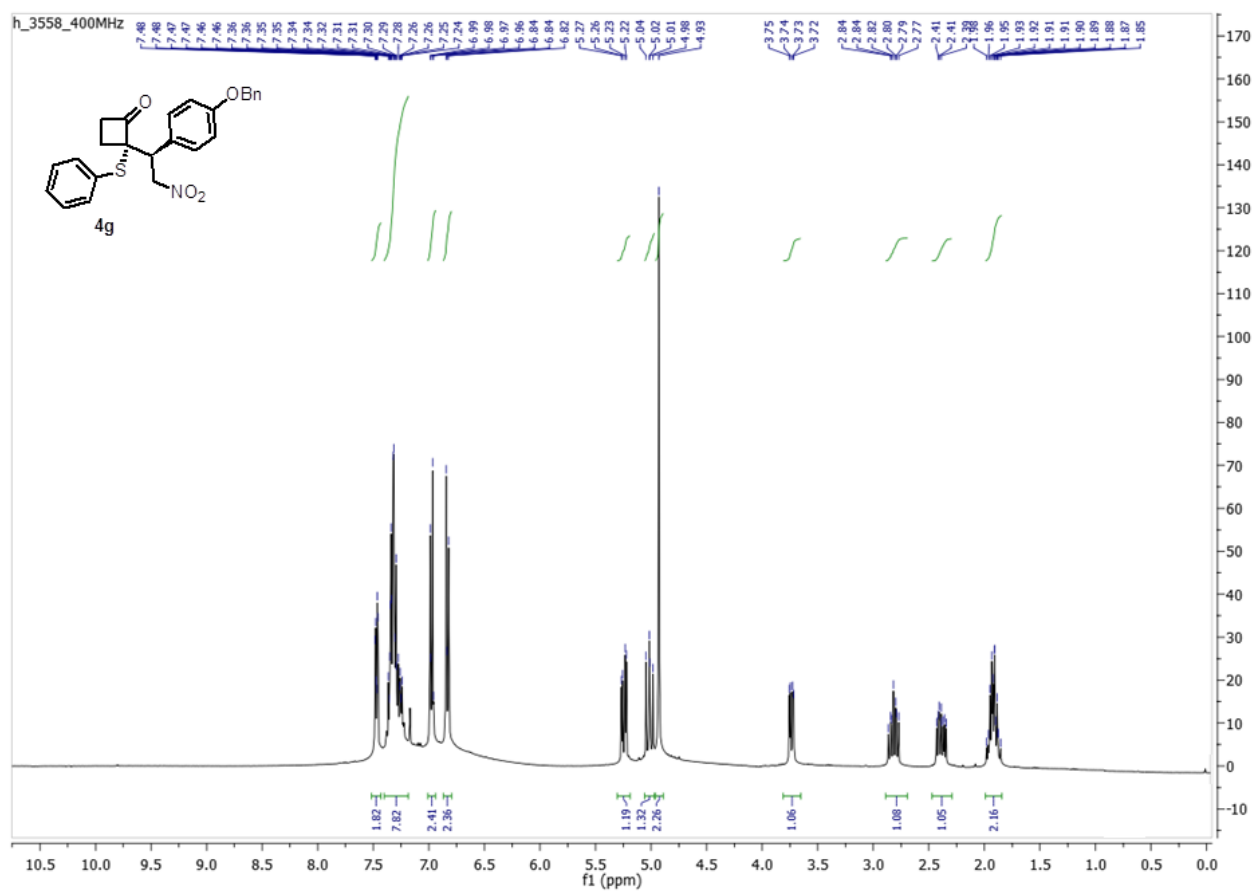
¹H and ¹³C NMR of compounds 4a-4k

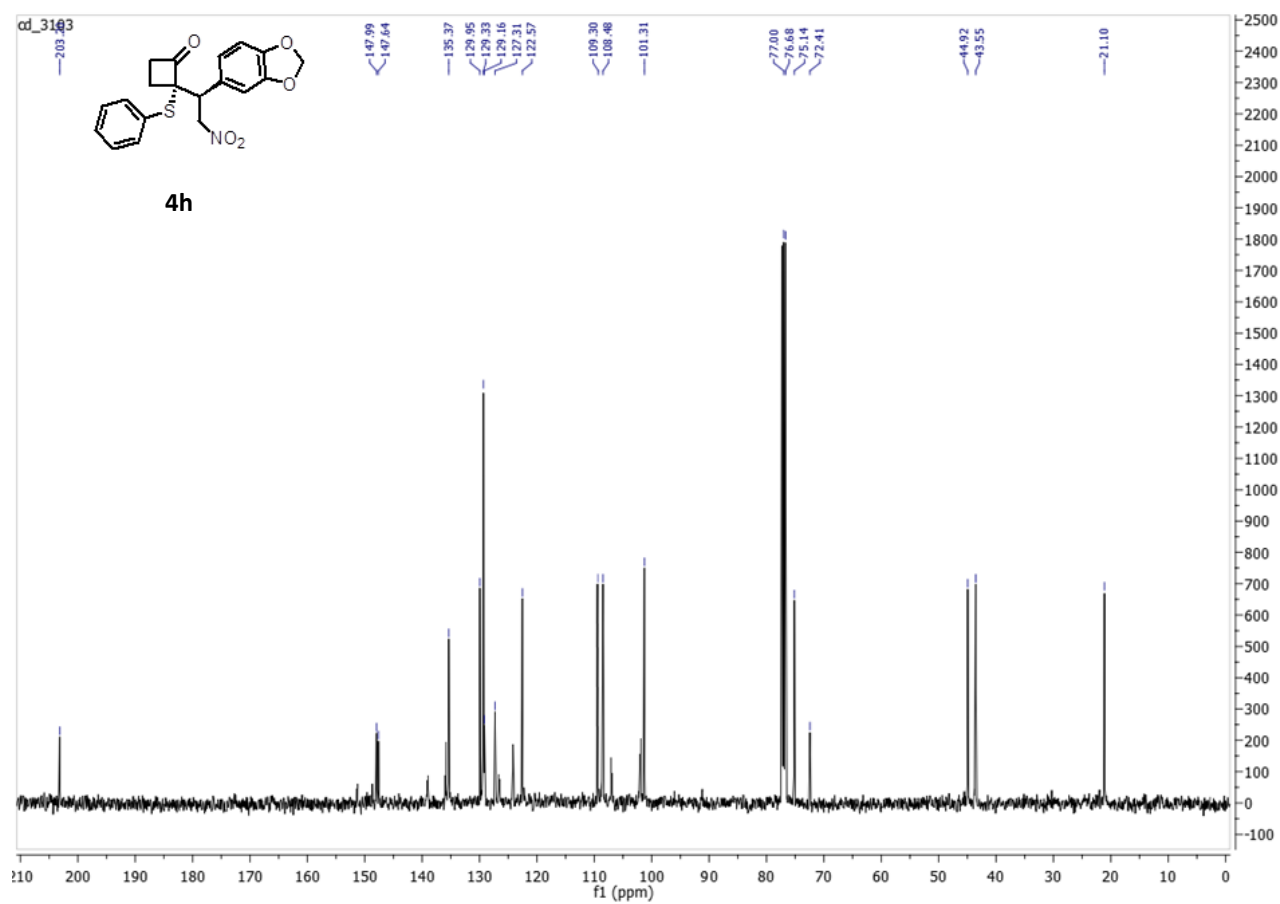
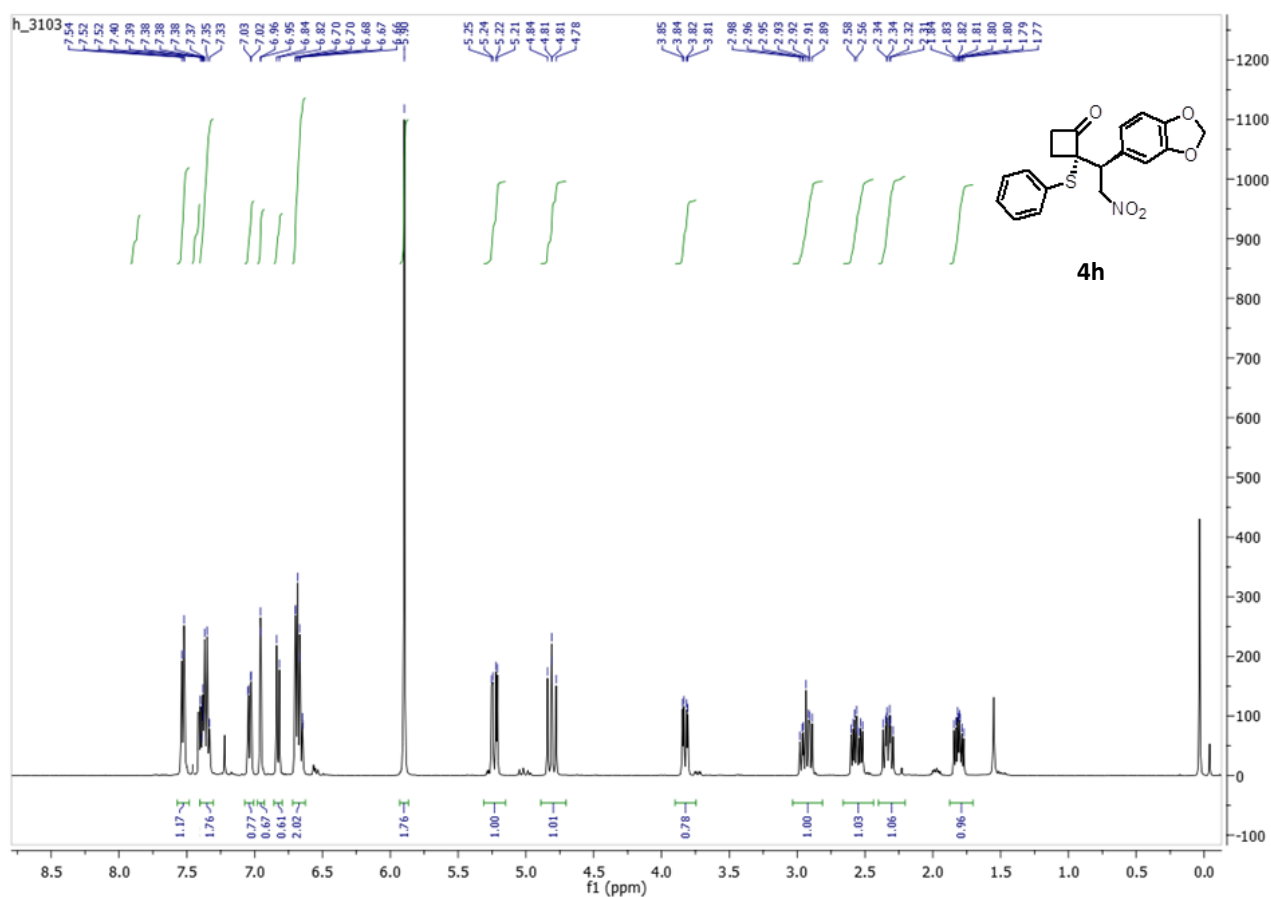


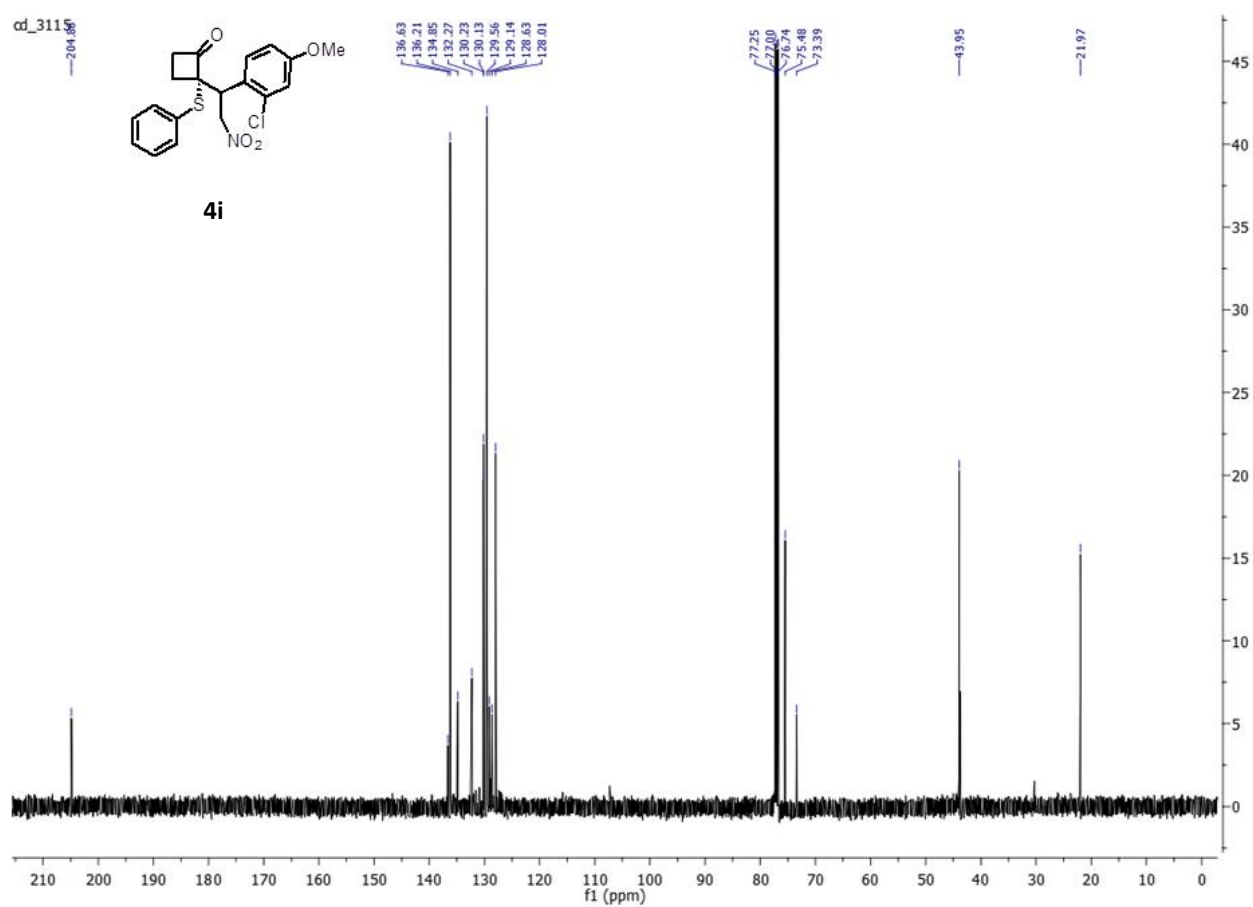
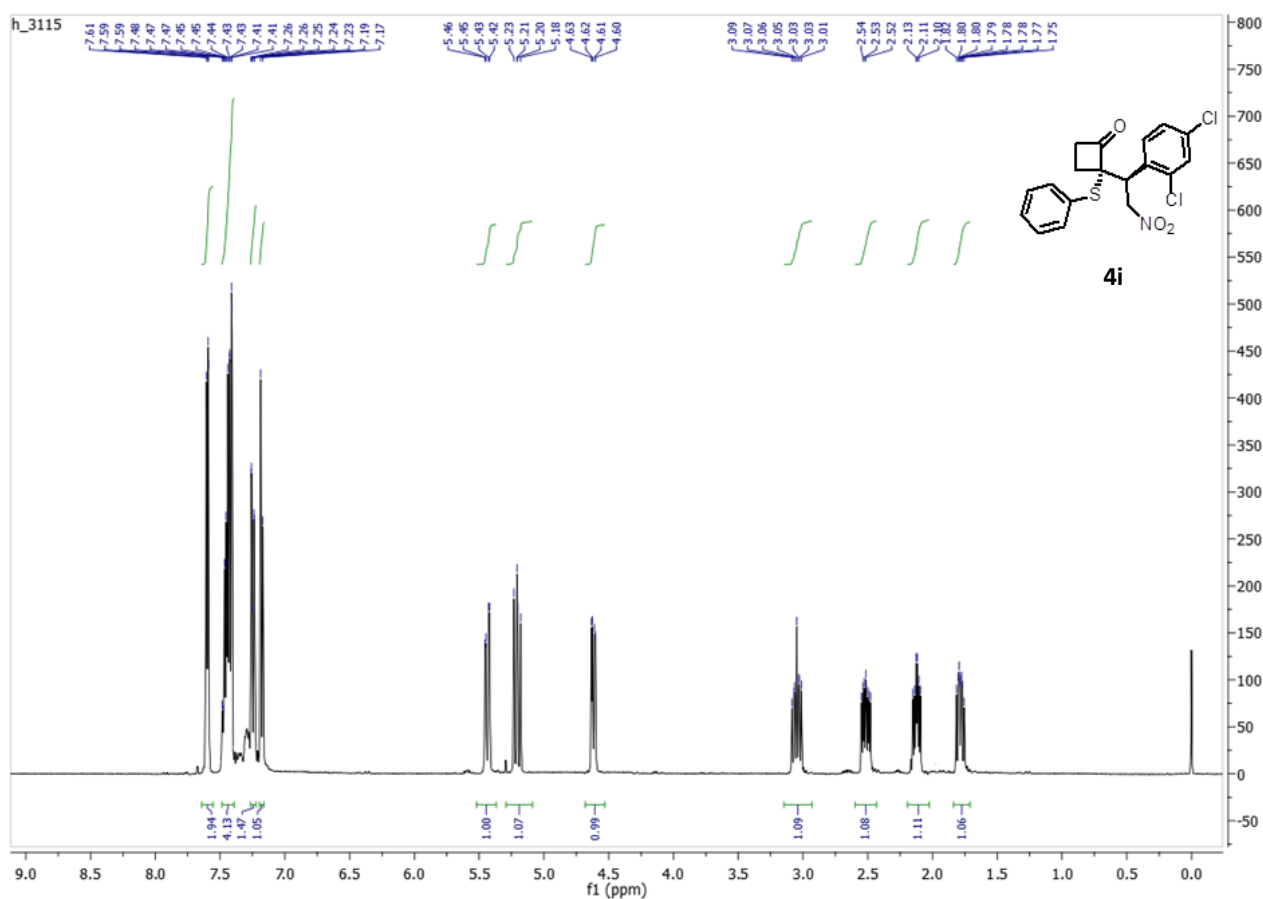


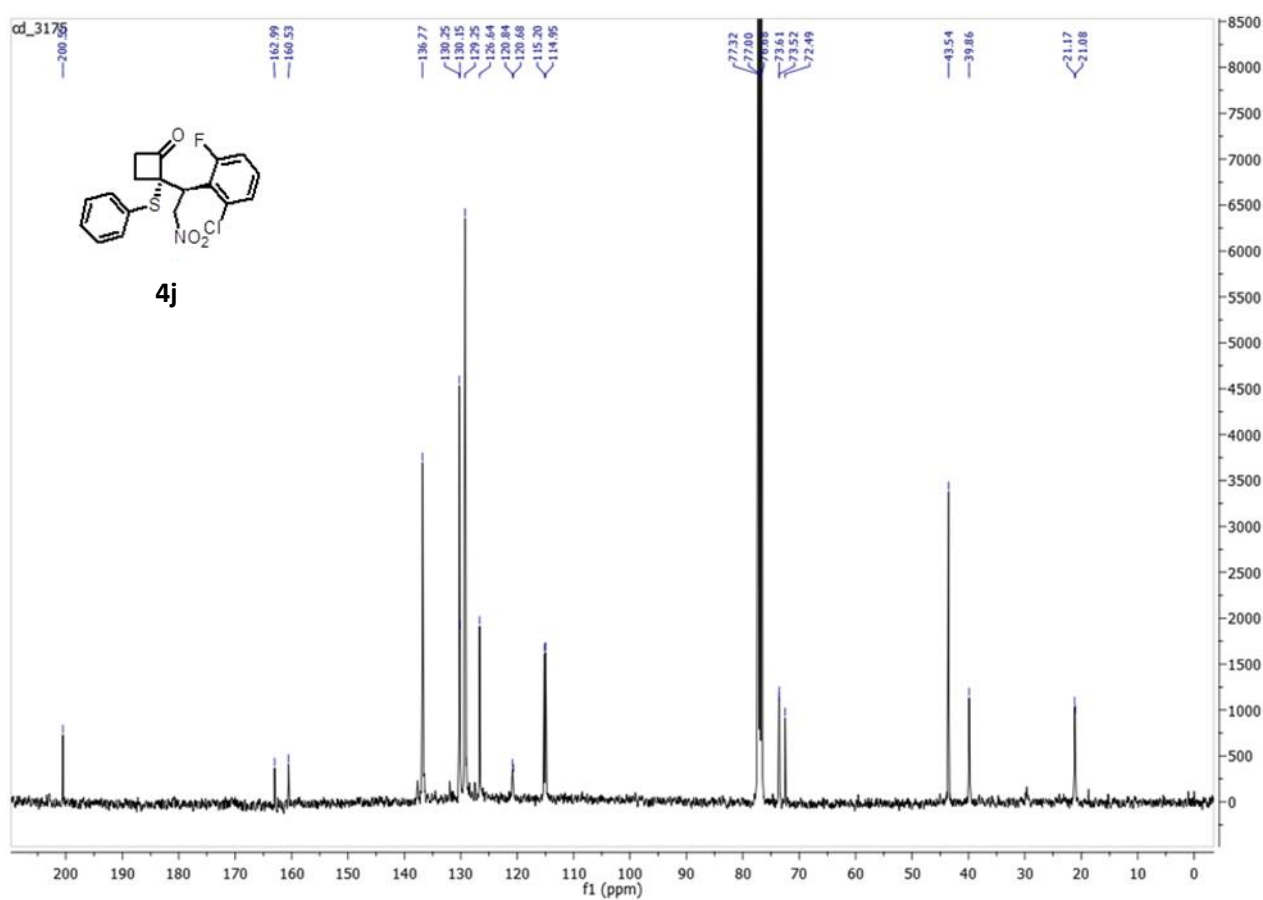
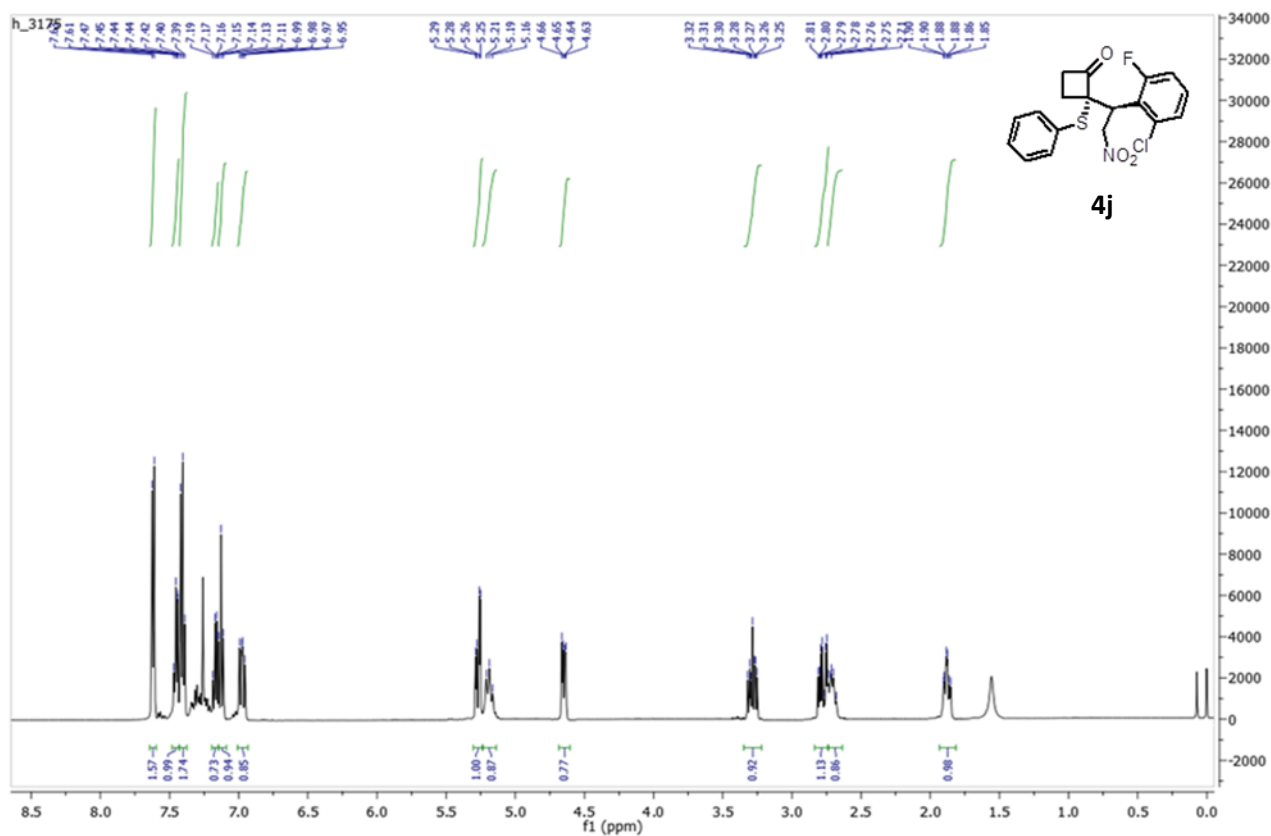


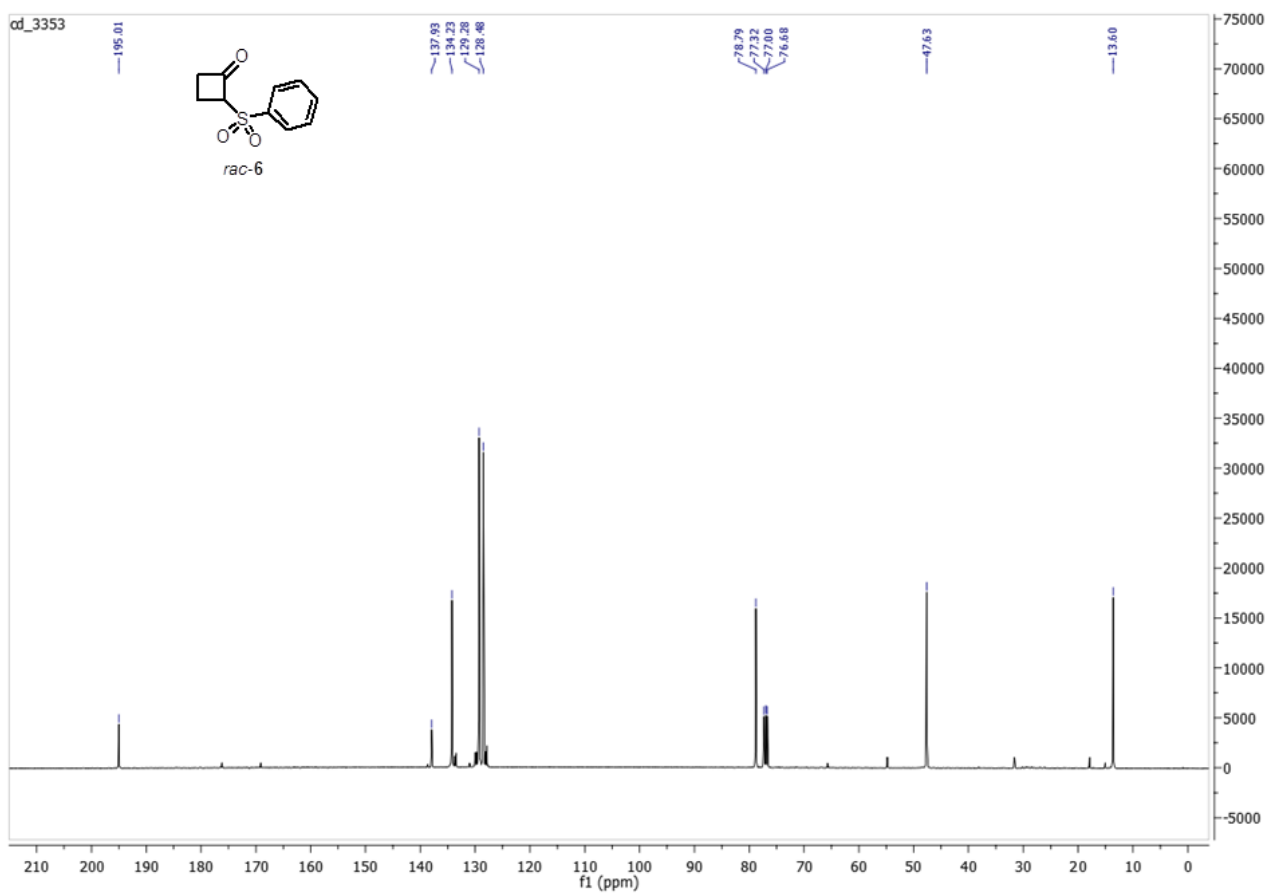
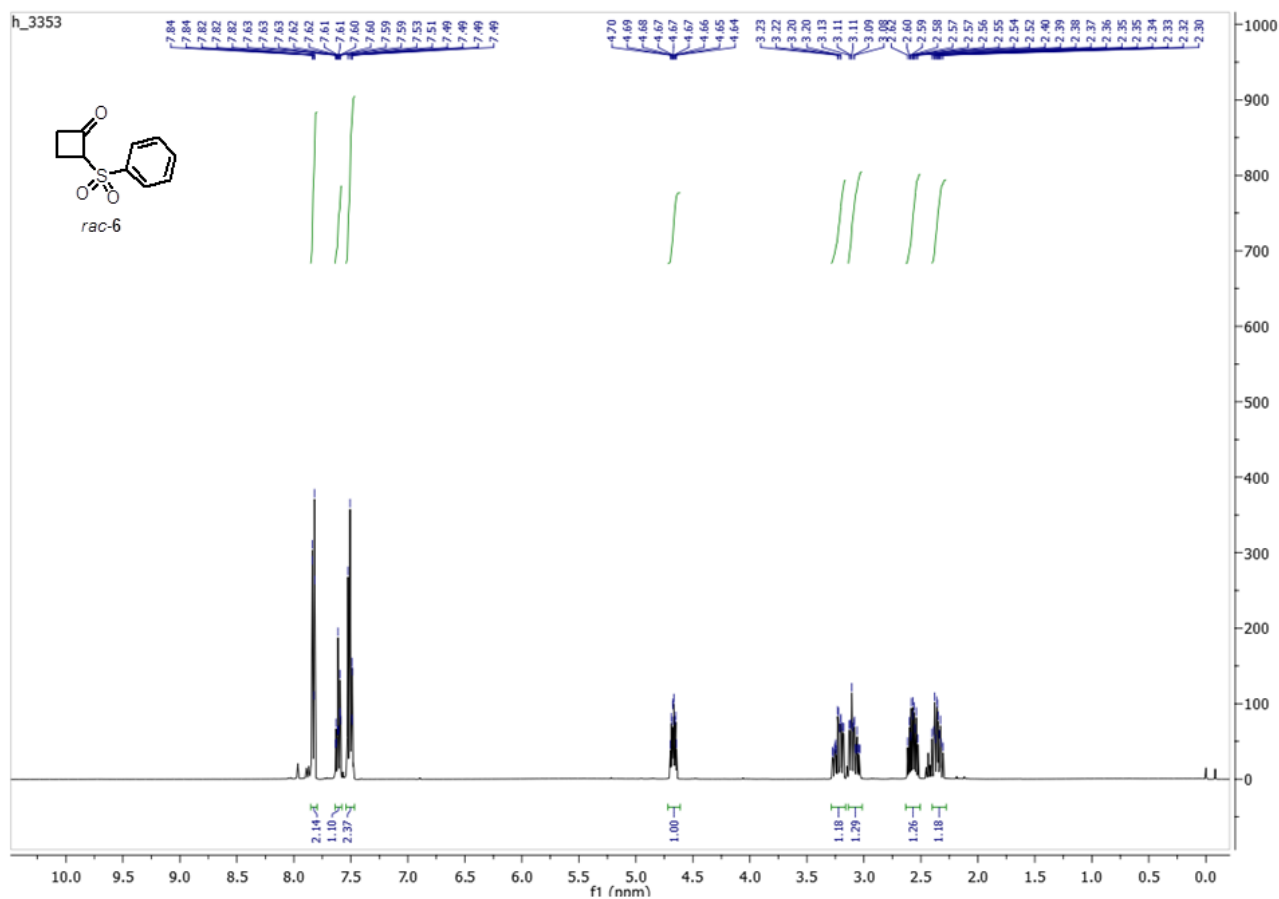


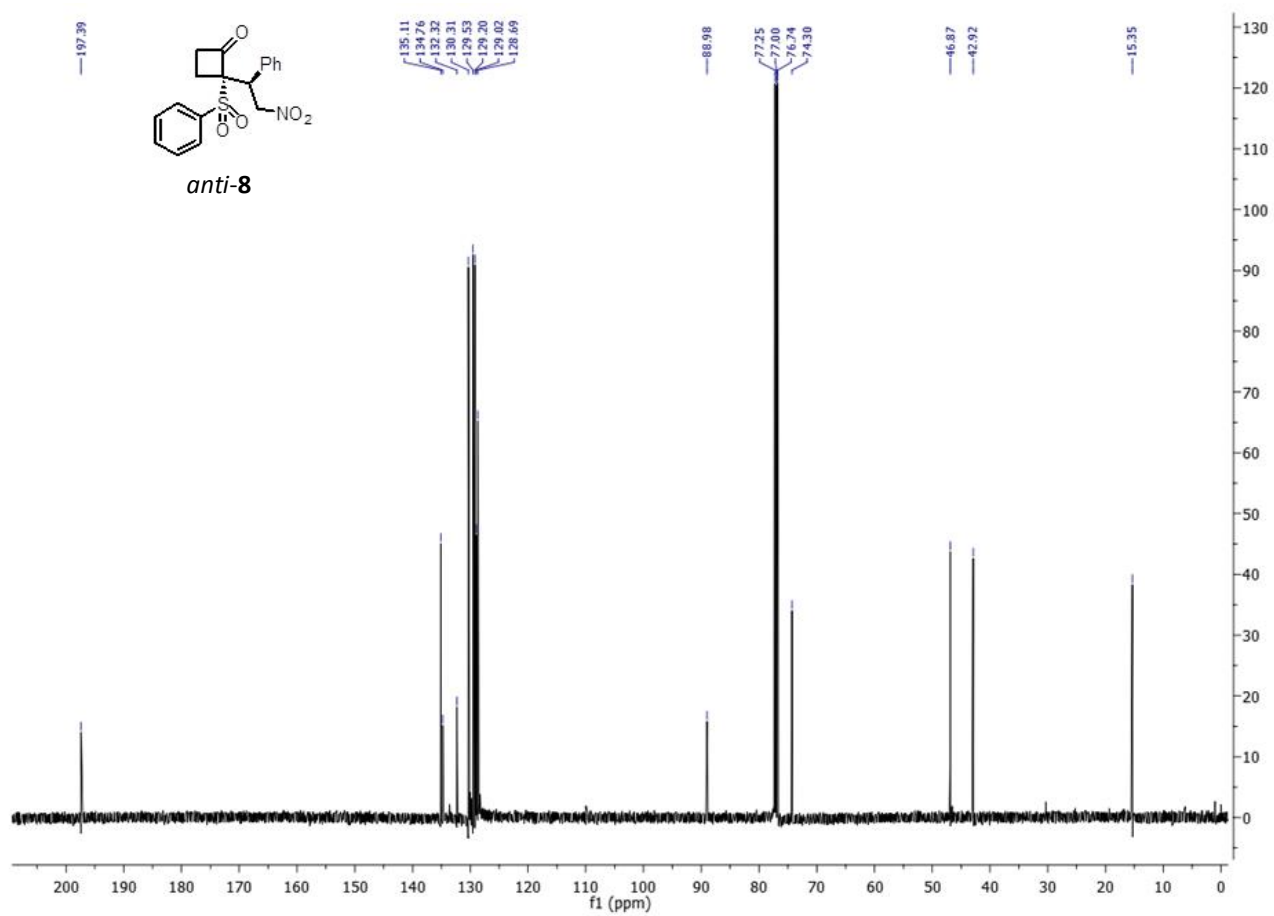
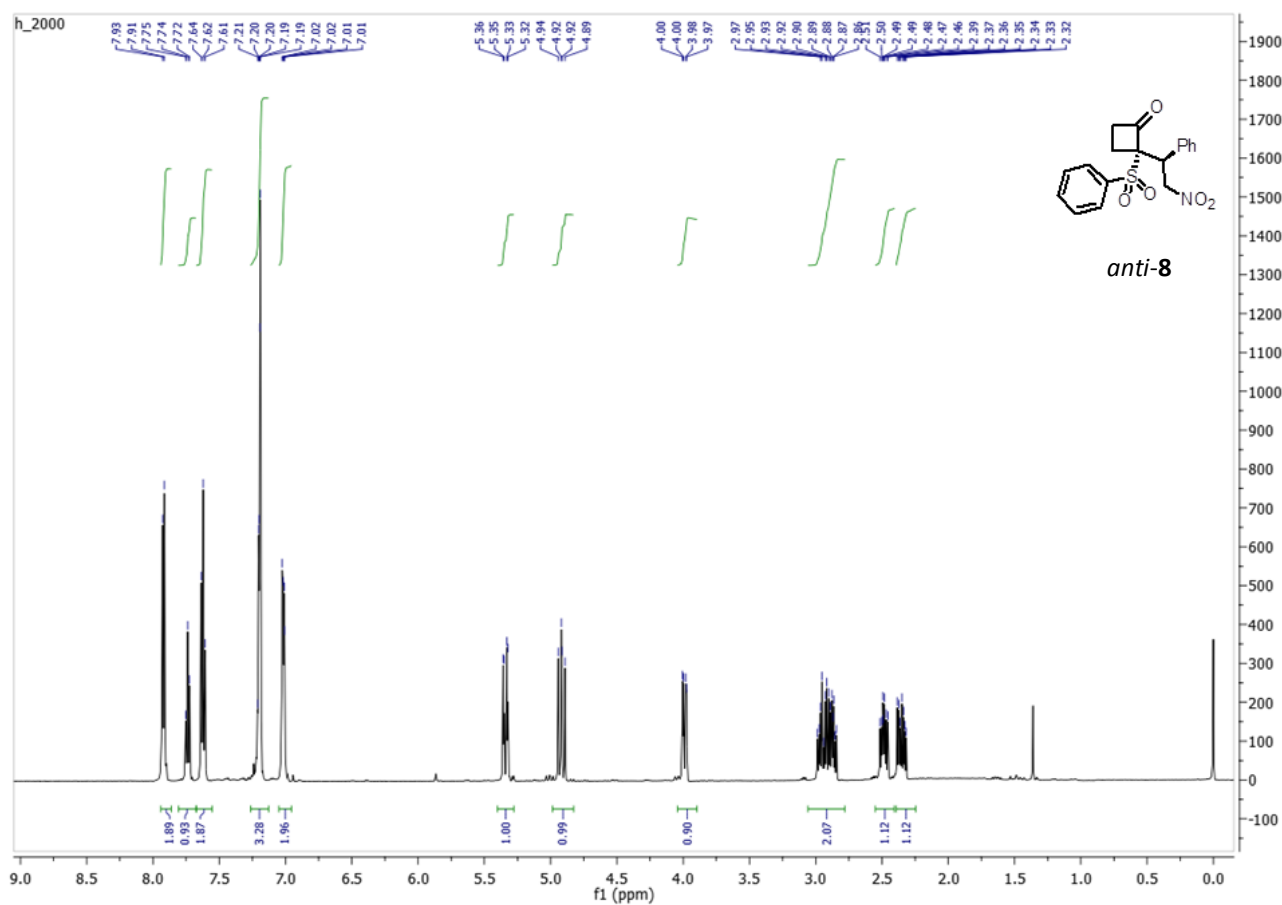


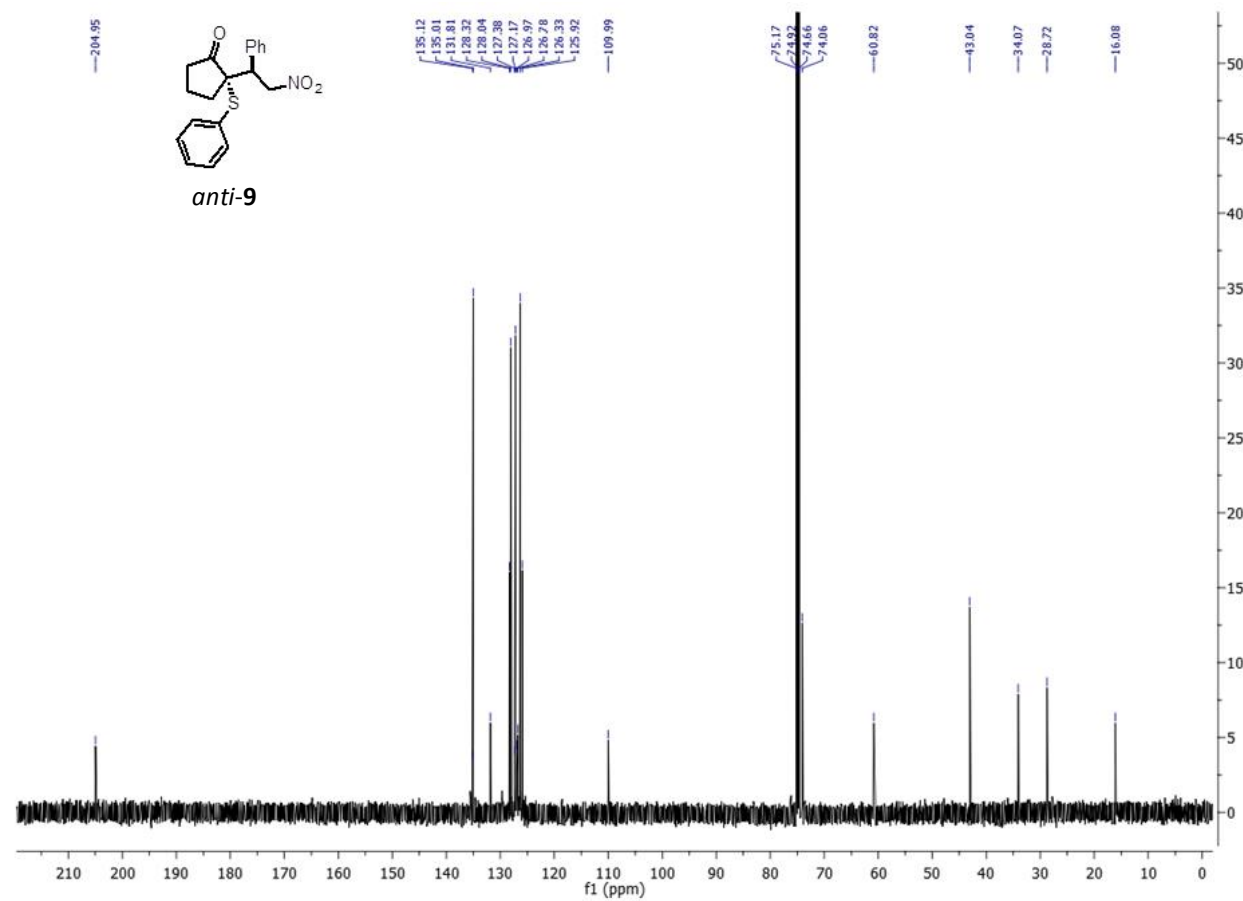
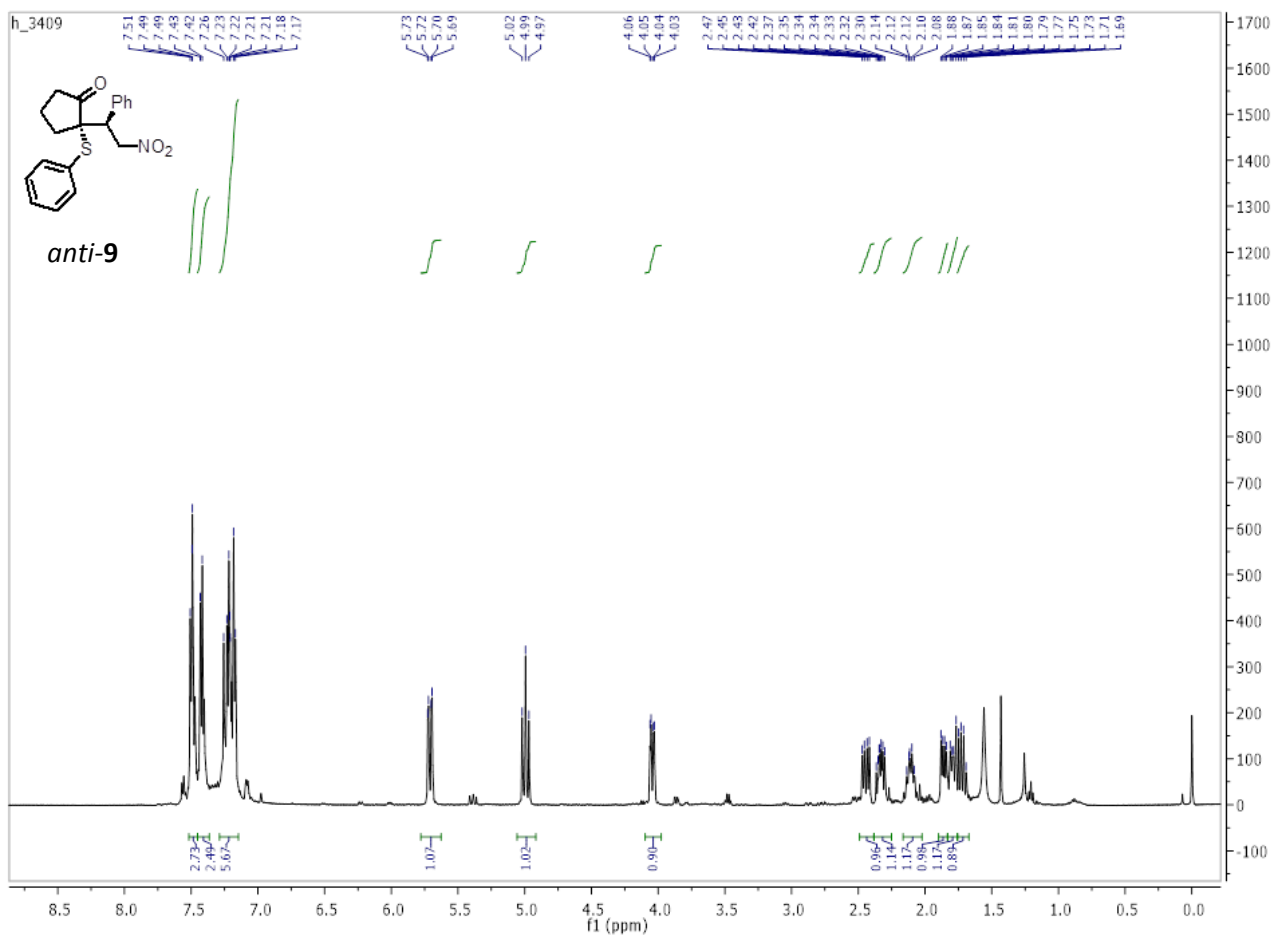


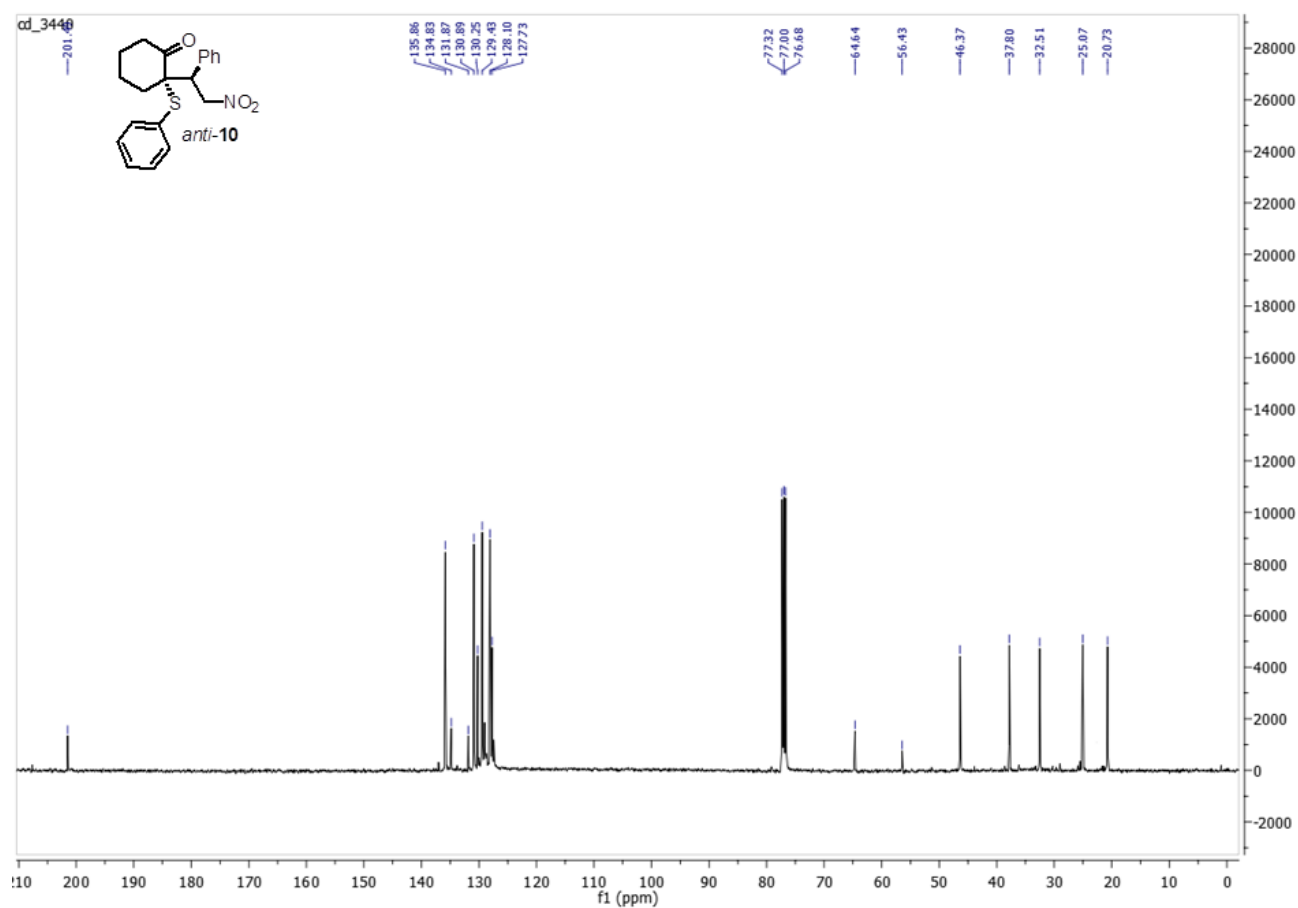
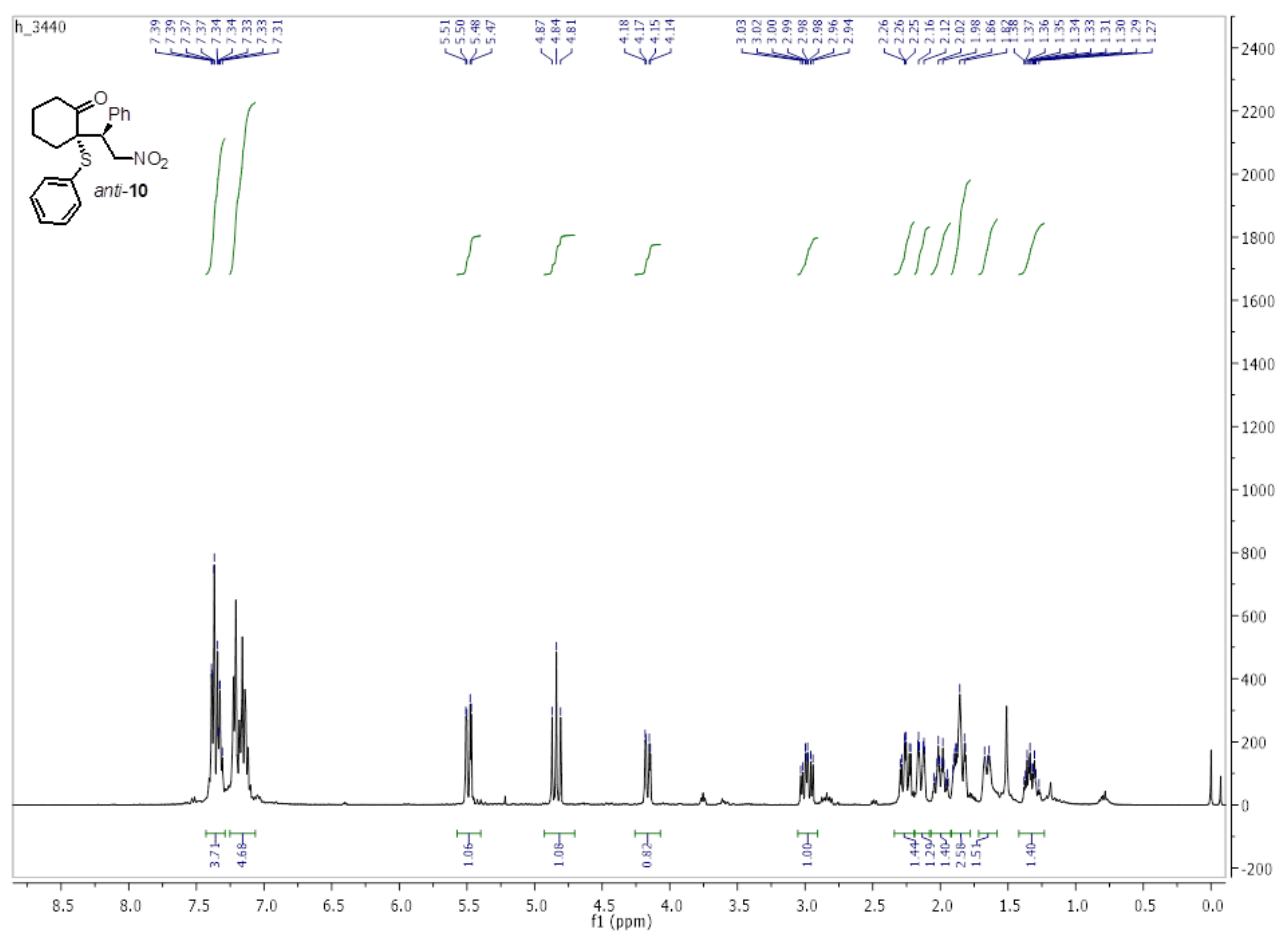








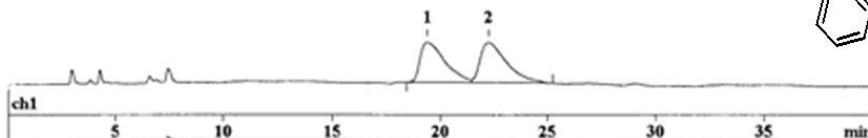
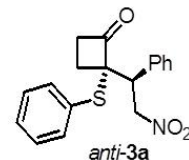




HPLC analysis of compounds *anti*-3a-3g, *anti*-4a-4j, *anti*-9, *anti*-10

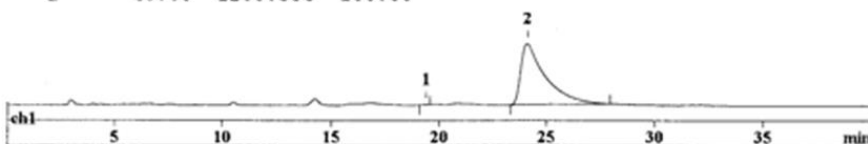
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 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %	Name
1	19.39	986.099	47.59	
2	22.23	1085.912	52.41	
2	40.00	2072.010	100.00	

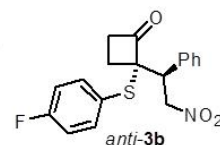


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

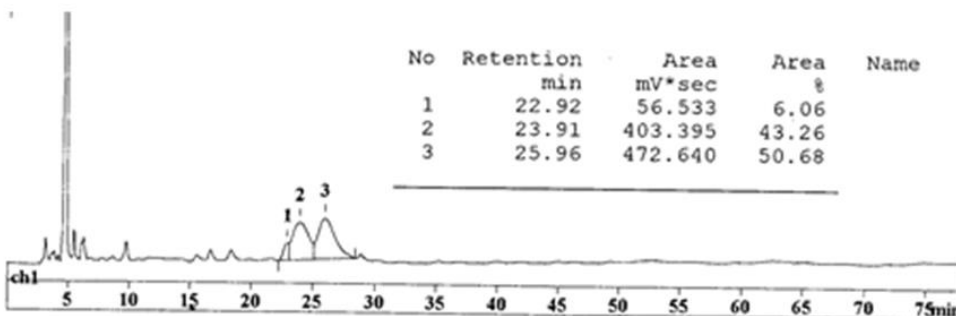
No	Retention min	Area mV*sec	Area %	Name
1	19.39	2.170	0.18	
2	24.09	1206.187	99.82	
2	40.00	1208.356	100.00	



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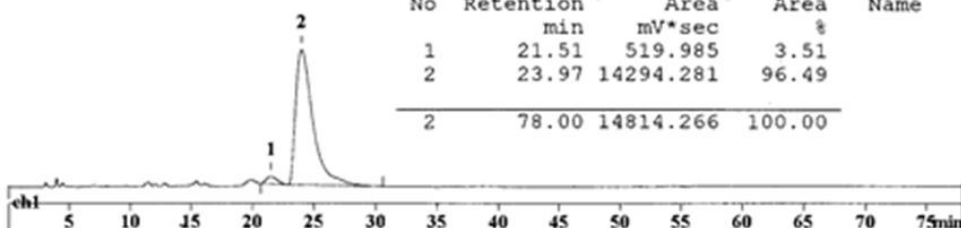


No	Retention min	Area mV*sec	Area %	Name
1	22.92	56.533	6.06	
2	23.91	403.395	43.26	
3	25.96	472.640	50.68	

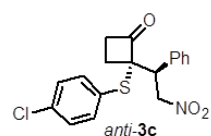


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

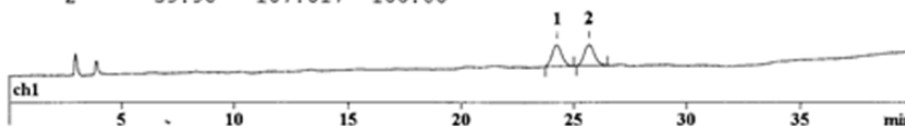
No	Retention min	Area mV*sec	Area %	Name
1	21.51	519.985	3.51	
2	23.97	14294.281	96.49	
2	78.00	14814.266	100.00	



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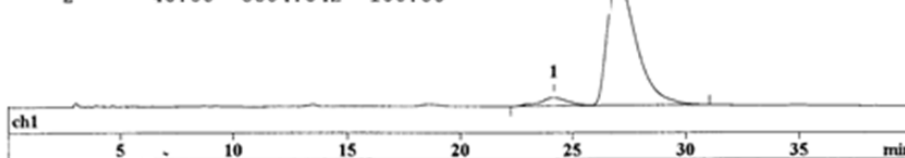


No	Retention min	Area mV*sec	Area %	Name
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2	25.68	54.496	50.92	
2	39.98	107.017	100.00	

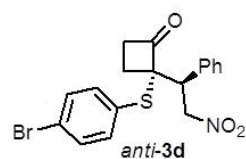


Quantitation method: Absolute concentration
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 Normalization: 100.00

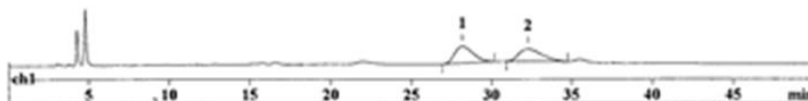
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1	24.15	431.729	6.54	
2	27.01	6173.113	93.46	
2	40.00	6604.842	100.00	



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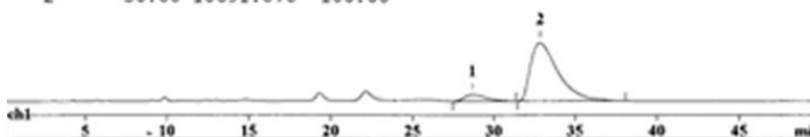


No	Retention min	Area mV*sec	Area %	Name
1	28.15	1559.619	52.02	
2	32.28	1438.726	47.98	
2	50.00	2998.345	100.00	



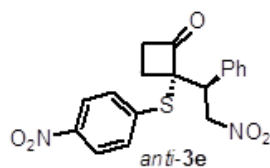
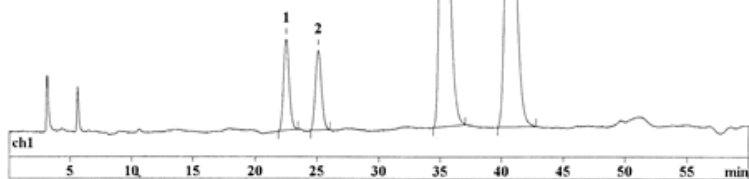
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	28.65	1536.582	8.22	
2	32.83	17155.288	91.78	
2	50.00	18691.870	100.00	



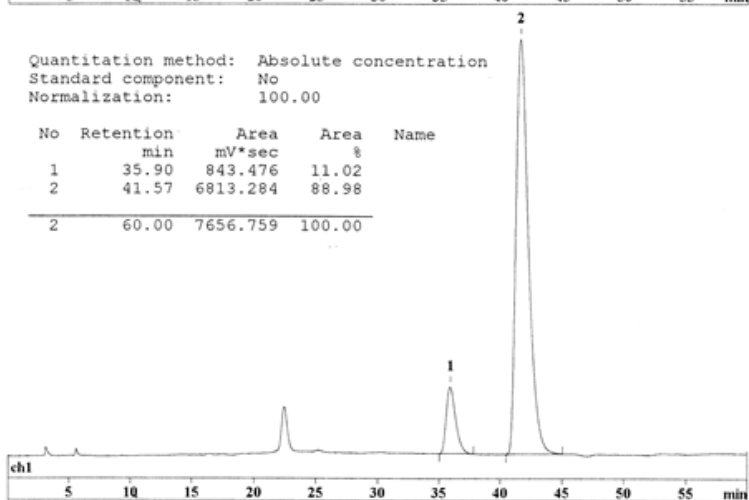
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1	22.47	151.967	6.25	
2	25.08	143.648	5.91	
3	35.24	1062.909	43.70	
4	40.64	1073.871	44.15	
4	60.00	2432.395	100.00	

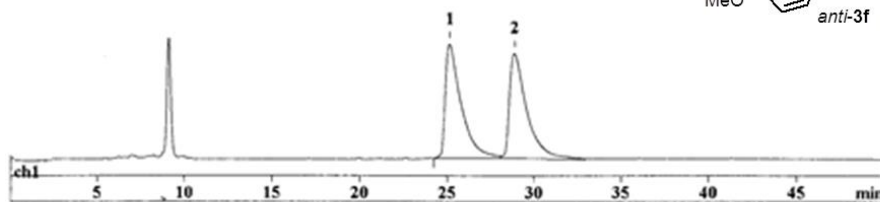
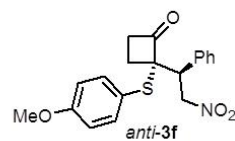


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	35.90	843.476	11.02	
2	41.57	6813.284	88.98	
2	60.00	7656.759	100.00	

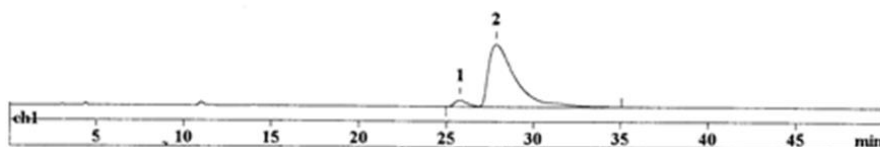


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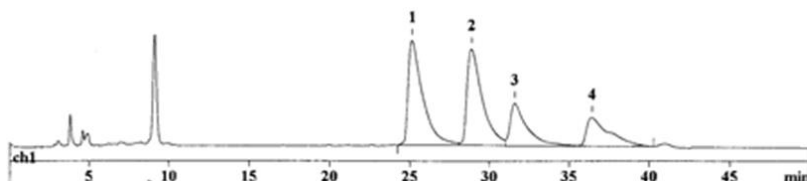
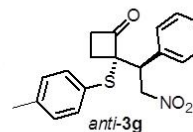


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	25.75	742.224	4.60	
2	27.82	15396.158	95.40	
2	50.00	16138.382	100.00	

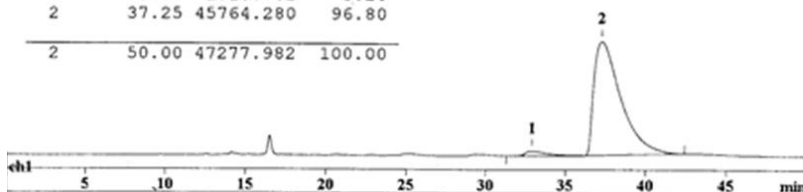


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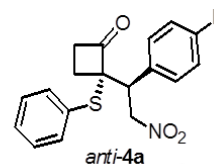


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	32.88	1513.702	3.20	
2	37.25	45764.280	96.80	
2	50.00	47277.982	100.00	

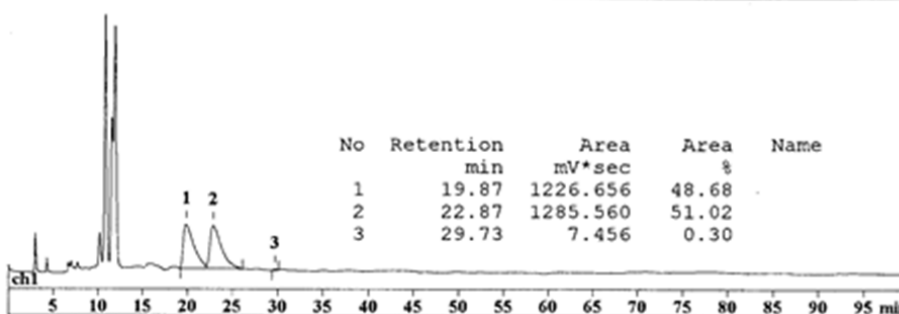
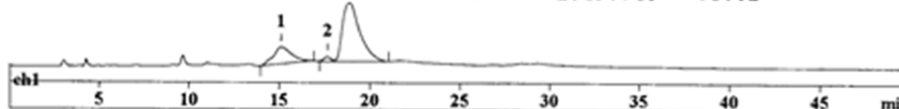


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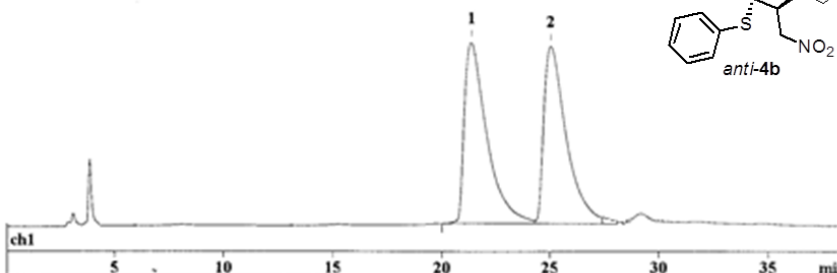
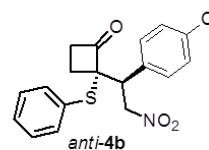
Quantitation method: Absolute concentration
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 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	15.08	409.634	22.77	
2	17.63	39.917	2.22	
3	18.85	1349.745	75.02	



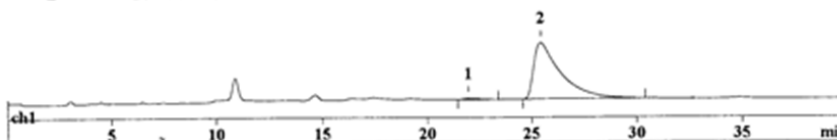
No	Retention min	Area mV*sec	Area %	Name
1	19.87	1226.656	48.68	
2	22.87	1285.560	51.02	
3	29.73	7.456	0.30	

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 Temperature: 20.0 °C
 Pressure: 0.0 bar



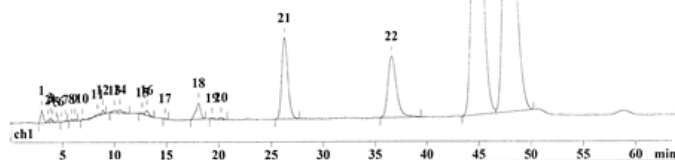
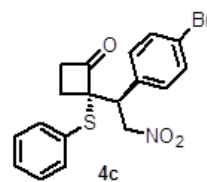
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	21.93	38.778	1.43	
2	25.41	2675.961	98.57	
2	40.00	2714.740	100.00	



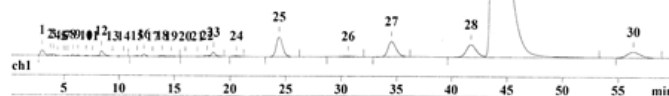
ELUENT: AD-H iso10 esa90
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %	Name
21	26.28	1230.114	5.75	
22	36.58	1312.775	6.14	
23	44.85	9048.262	42.29	
24	47.82	9274.968	43.35	



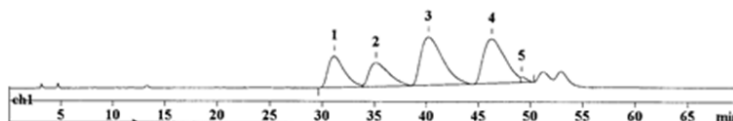
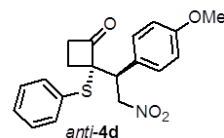
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
28	41.76	4369.783	2.39	
29	43.98	163850.486	89.57	
30	56.34	2549.419	1.39	



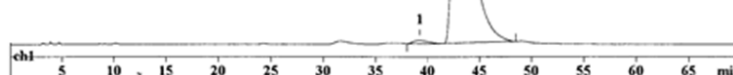
ELUENT: cipShOME_rac phenomex Lux 2:98 IPA/Hex
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %	Name
1	31.10	2321.959	16.66	
2	35.10	2177.142	15.62	
3	40.17	4918.372	35.29	
4	46.25	4360.847	31.29	



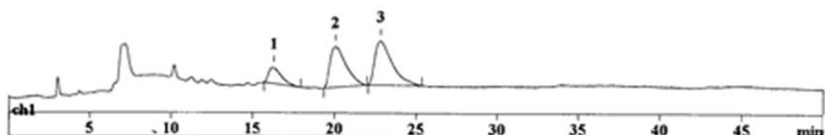
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	39.23	710.719	1.20	
2	43.07	58373.934	98.80	
2	70.00	59084.653	100.00	



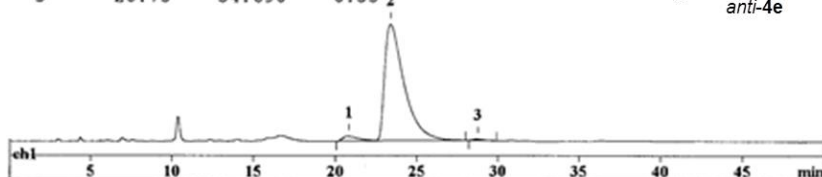
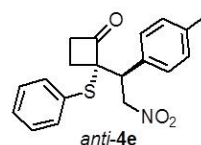
ELUENT: phenomenex iso5-esa95 1 ml/min
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %	Name
1	16.26	76.948	12.71	
2	20.01	243.438	40.20	
3	22.80	285.136	47.09	



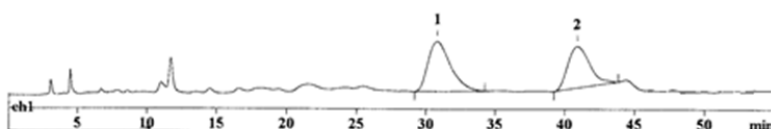
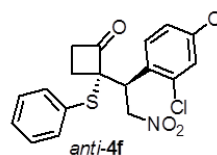
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	20.80	224.286	3.53	
2	23.38	6097.834	95.93	
3	28.75	34.690	0.55	



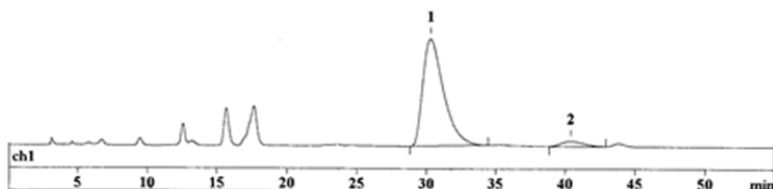
ELUENT: ci Cl2Ph rac phenomenex Lux_97:3 Hex/IPA
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %	Name
1	30.79	2242.599	55.48	
2	40.86	1799.641	44.52	
2	55.00	4042.241	100.00	



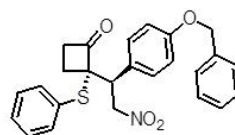
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	30.23	10595.896	95.15	
2	40.38	539.633	4.85	
2	55.00	11135.529	100.00	

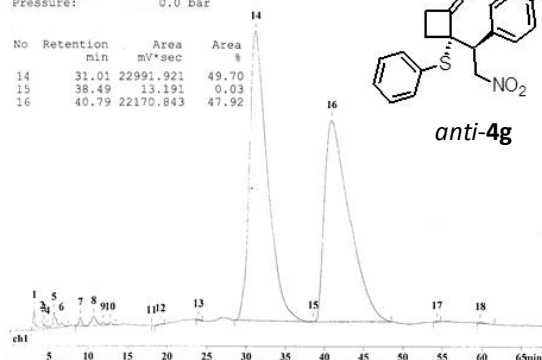


ELUENT: OJ 25/75 iso/esa
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %
14	31.01	22991.921	49.70
15	38.49	13.191	0.03
16	40.79	22170.843	47.92

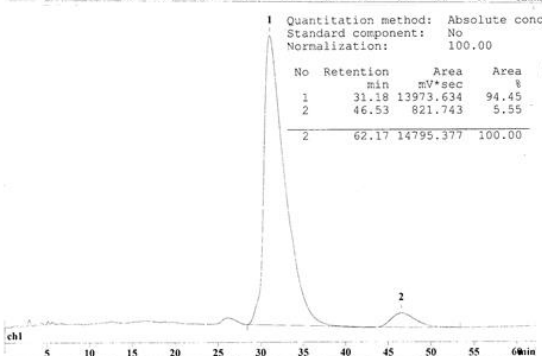


anti-4g



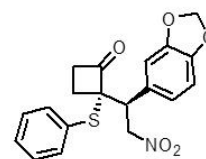
Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	31.18	13973.634	94.45	
2	46.53	821.743	5.55	
2	62.17	14795.377	100.00	

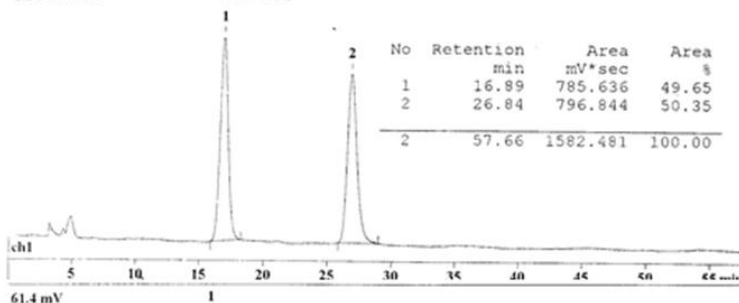


ELUENT: AD-H IPA/Hex 2:98
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

No	Retention min	Area mV*sec	Area %
1	16.89	785.636	49.65
2	26.84	796.844	50.35
2	57.66	1582.481	100.00



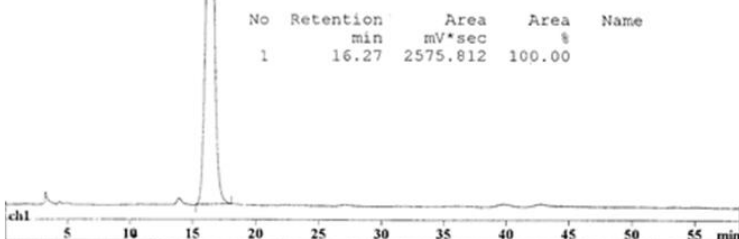
anti-4h



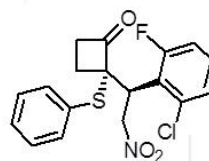
61.4 mV

Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

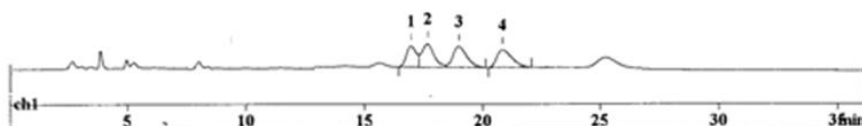
No	Retention min	Area mV*sec	Area %	Name
1	16.27	2575.812	100.00	



ELUENT: ci_ClFPh_rac OJ_95:5 Hex/IPA
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

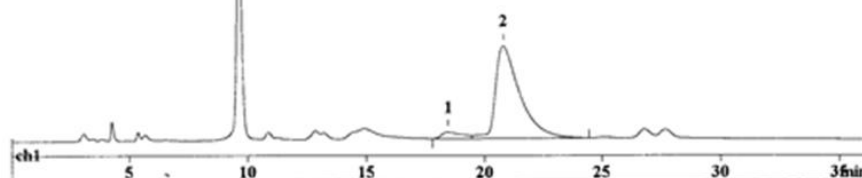


anti-4J

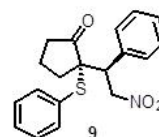


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

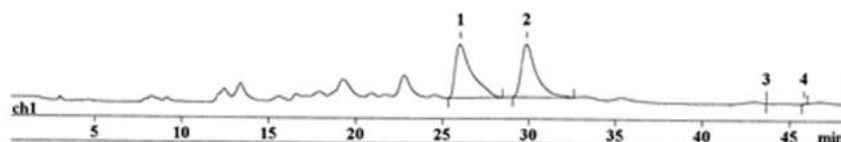
No	Retention min	Area mV*sec	Area %	Name
1	18.44	251.632	5.47	
2	20.78	4345.770	94.53	
2	36.20	4597.402	100.00	



ELUENT: AD-H iso 5/hex95 1mL/min
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar

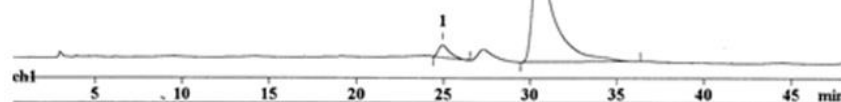


No	Retention min	Area mV*sec	Area %	Name
1	25.99	759.690	52.57	
2	29.86	683.705	47.31	
3	43.65	0.001	0.00	
4	45.80	1.738	0.12	

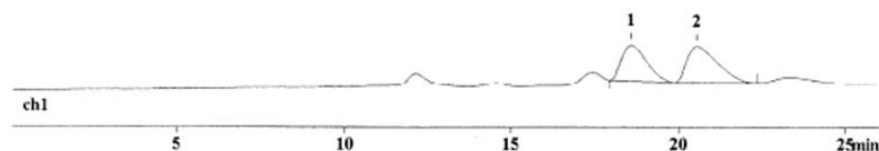
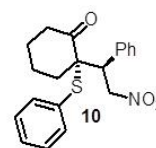


Quantitation method: Absolute concentration
 Standard component: No
 Normalization: 100.00

No	Retention min	Area mV*sec	Area %	Name
1	24.94	155.365	5.55	
2	30.50	2643.870	94.45	
2	48.11	2799.234	100.00	

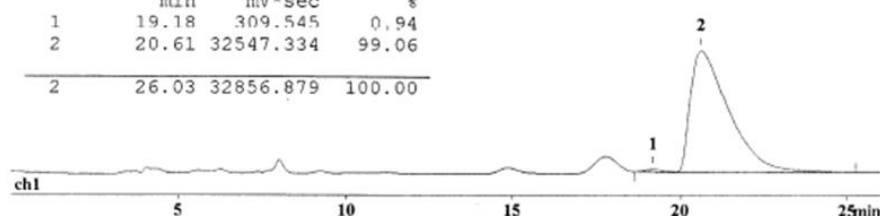


ELUENT: AD-H iso5 esa95
 Flow: 1000 µl/min
 Velocity: 0.00 mm/s
 Temperature: 20.0 °C
 Pressure: 0.0 bar



Quantitation method: Absolute concentration

No	Retention min	Area mV*sec	Area %	Name
1	19.18	309.545	0.94	
2	20.61	32547.334	99.06	
2	26.03	32856.879	100.00	



X-Ray analysis of compound 8

X-ray diffraction data were collected using a Kappa X8 APPEX II Bruker diffractometer with graphite-monochromated MoK α radiation ($\lambda = 0.71073$ Å). Crystals were mounted on a CryoLoop (Hampton Research) with Paratone-N (Hampton Research) as cryo-protectant and then flash-frozen in a nitrogen gas stream at 100 K. The temperature of the crystal was maintained at the selected value (100 K) by means of a 700 series Cryostream cooling device to within an accuracy of ± 1 K. The data were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods using SHELXS-97¹ and refined against F^2 by full-matrix least-squares techniques using SHELXL-97² with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a

- 1) G. M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution, University of Göttingen, Göttingen, Germany, **1997**.
- 2) G. M. Sheldrick, SHELXL-97, Program for the refinement of crystal structures from diffraction data, University of Göttingen, Göttingen, Germany, **1997**.

riding model with isotropic thermal parameters. All calculations were performed by using the Crystal Structure crystallographic software package WINGX.³

The absolute configuration was determined for compound **8** by refining the Flack parameter⁴ using a large number of Friedel pairs.

An ORTEP drawing of the molecule is shown in Figure S1. The crystal data collection and refinement parameters are given in Table S1.

CCDC 1442520 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk/Community/Requestastructure>.

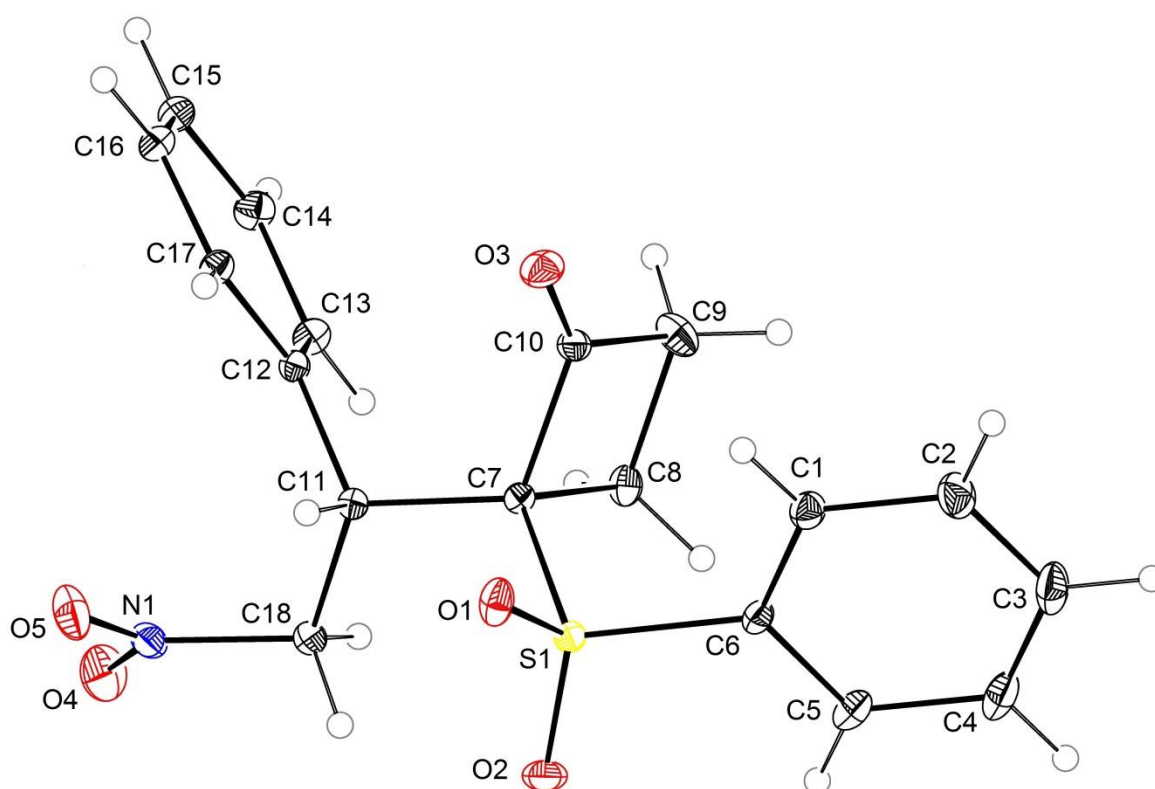


Fig. S1. ORTEP drawing for the crystal structure of compound **8**. Ellipsoids are drawn at the 30% probability level

3) L. J. Farrugia, *J. Appl. Cryst.*, **1999**, 32, 837.

4) H. D. Flack, *Acta Cryst.*, **1983**, A39, 876.

Table S1. Crystallographic data and structure refinement details for **8**.

Compound	8
Empirical Formula	C ₁₈ H ₁₇ NO ₅ S
M_r	359.38
Crystal size, mm ³	0.32 × 0.30 × 0.30
Crystal system	orthorhombic
Space group	$P 2_1 2_1 2_1$
a, Å	8.2474(5)
b, Å	11.1326(7)
c, Å	18.0136(11)
α , °	90
β , °	90
γ , °	90
Cell volume, Å ³	1653.92(18)
Z ; Z'	4 ; 1
T, K	100(1)
F ₀₀₀	752
μ , mm ⁻¹	0.225
θ range, °	2.151 - 36.853
Reflection collected	35 872
Reflections unique	8 255
R _{int}	0.0230
GOF	1.075
Refl. obs. ($I > 2\sigma(I)$)	7 739
Parameters ; Restraints	226 ; 0
wR ₂ (all data)	0.0797
R value ($I > 2\sigma(I)$)	0.0290
Flack parameter	0.049(11)
Largest diff. peak and hole (e ⁻ ·Å ⁻³)	-0.242 ; 0.329

