Supporting Information (52 pages)

Enantiospecific 6π – Photocyclization of Atropisomeric α-substitued Acrylanilides In the Soild-State. Role of Crystalline Confinement on Enantiospecificity.

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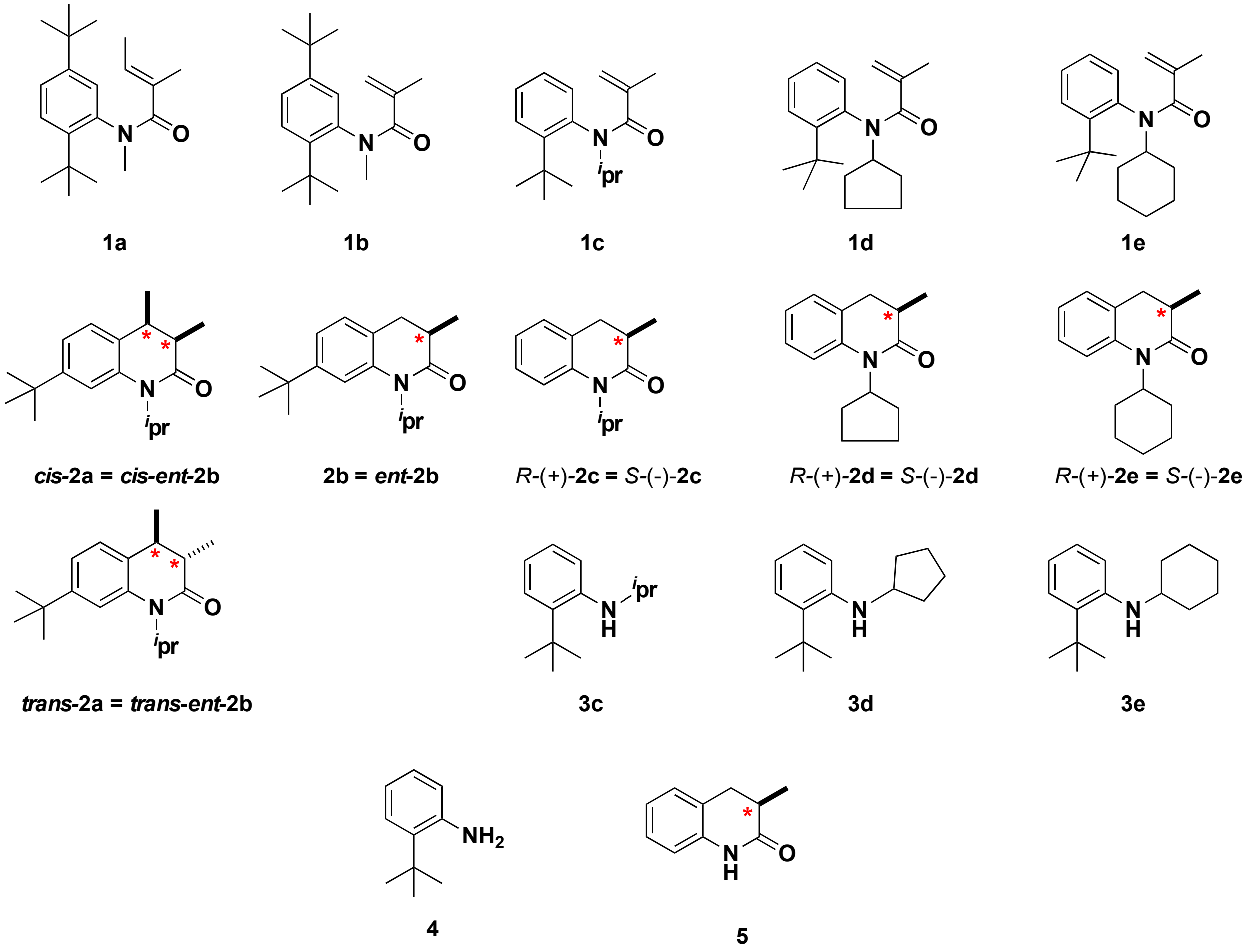
1) General methods

All commercially obtained reagents/solvents were used as received; chemicals were purchased from Alfa Aesar®, Sigma – Aldrich®, Across®, TCI® America, Mallinckrodt®, and Oakwood Products®, and were used as received without further purification. Unless stated otherwise, reactions were conducted in oven-dried glassware under an atmosphere of nitrogen using anhydrous solvents. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 400 MHz and 100 MHz spectrometers respectively. Data for ^{1}H NMR spectra are reported relative to deuterated solvent signals, and are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. Coupling constants (J) were reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: br (broad), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and ABq (AB quartet). Data for ^{13}C NMR spectra are reported in terms of chemical shift. Electro spray Ionization Spectra(High Resolution Mass Spectrometry) were recorded on a Bruker – Daltronics® BioTof mass spectrometer in positive (ESI+) ion mode. HPLC analyses were performed on Waters® HPLC equipped with 2525 pump. Waters® 2767 sample manager was used for automated sample injection. All HPLC injections were monitored using a Waters® 2487 dual wavelength absorbance detector at 254, and 270 nm. Analytical and semi-preparative injections were perfomed on chiral stationary phase using various columns*. Masslynx software version 4.1 was used to analyse/process the HPLC injections. Igor Pro® Software version 6.0 was used to process the chromatographic data. When necessary, the reactants and photoproducts were purified by chromatography: CombiFlash and/or on silica gel (Sorbent Technologies®, silica gel standard grade: Porosity 60 Å, Particle size: 230 x 400 mesh, Surface area: 500 – 600 m^{2}/g, Bulk density: 0.4 g/mL, pH range: 6.5 – 7.5). *The Retention Factor (Rf) values were recorded using a 20 % EtOAc-Hexanes as mobile phase (unless indicated) and on SORBENT TECHNOLOGIES® Silica Gel TLC plates (200 μm thickness w/ UV*$_{254}$*)*. Optical activity values were recorded on JASCO® DIP – 370 digital polarimeter. CD spectra were recorded on JASCO® - 710 digital CD spectrometer.

* Regis® PIRKLE COVALENT (R,R) WHELK–O1 10/100 FEC columns: 25cm X 4.6 mm column for analytical injections,
and 25 cm x 10.0 mm for semi-preparative injections

* CHIRALPAK® AD-H: 25cm X 4.6 mm column for analytical injections, and 25 cm x 10.0 mm for semi-preparative injections

* CHIRALPAK ® IC: 25cm X 4.6 mm column for analytical injections, and 25 cm x 10.0 mm for semi-preparative injections



1a **1b** **1c** **1d** **1e**

***cis*-2a = *cis*-*ent*-2b** **2b = *ent*-2b** *R*-(+)-**2c** = *S*-(-)-**2c** *R*-(+)-**2d** = *S*-(-)-**2d** *R*-(+)-**2e** = *S*-(-)-**2e**

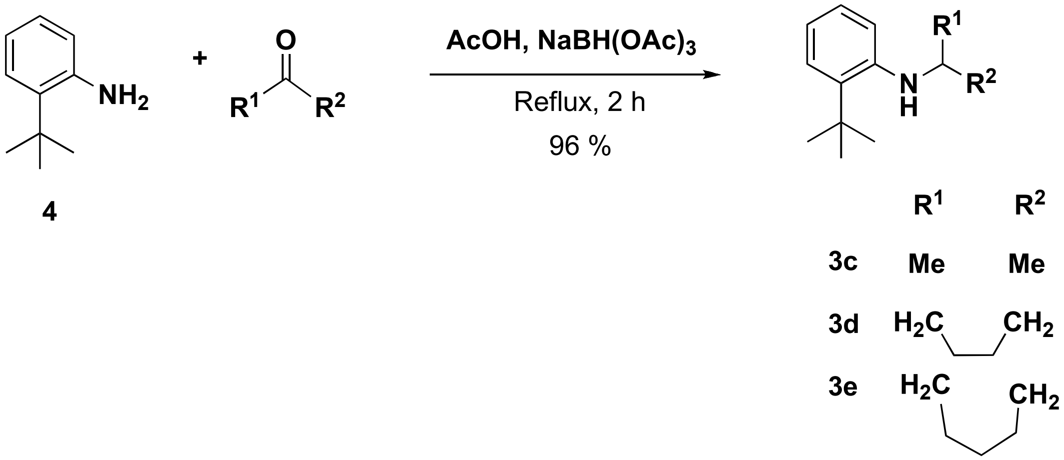
***trans*-2a = *trans*-*ent*-2b** **3c** **3d** **3e**

4 **5**

Chart S1: Starting Materials (amines, acrylanilides and/or molecularly chiral compounds) and related photoproducts.

Note: Substrate **1a,b** and their corresponding photoproducts **2a,b** were previously reported.[1,2]

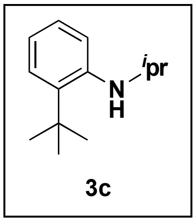
2) Synthesis and characterization of amines **3c-e**



Scheme S1: Synthesis of N-alkyl-2-tert-butylaniline **3c-e**

Commercially available *o-tert*-butyl aniline **4** (1 equi., 1g, 6.7mmol), 1.1 equi. of AcOH, and 2 equi. of $NaBH(OAc)_3$ were mixed in 8 mL of ketone (acetone, cyclopentanone, and cyclohexanone). The new reaction mixture was allowed to reflux with stirring. After 2 h, the excess of ketone solvent was removed by roto-evaporation under reduced pressure. The residue was then washed with 3x20 mL saturated $NaHCO_3$ solution. The expected aniline **3** was extracted with EtOAc, and the combined organic fraction was then dried over *anhy.* Na_2SO_4, filtered, and concentrated to obtain the expected N-alkyl aniline **3** (98 % conversion for all of the substrates). The expected compound(s) may be used in a subsequent reaction without further purification. **3c-e** were purified by flash chromatograph over silica gel using Combiflash®: 12 g silica; flow rate: 22 mL/min, mobile phase: 2 – 5% EtOAc : Hexanes

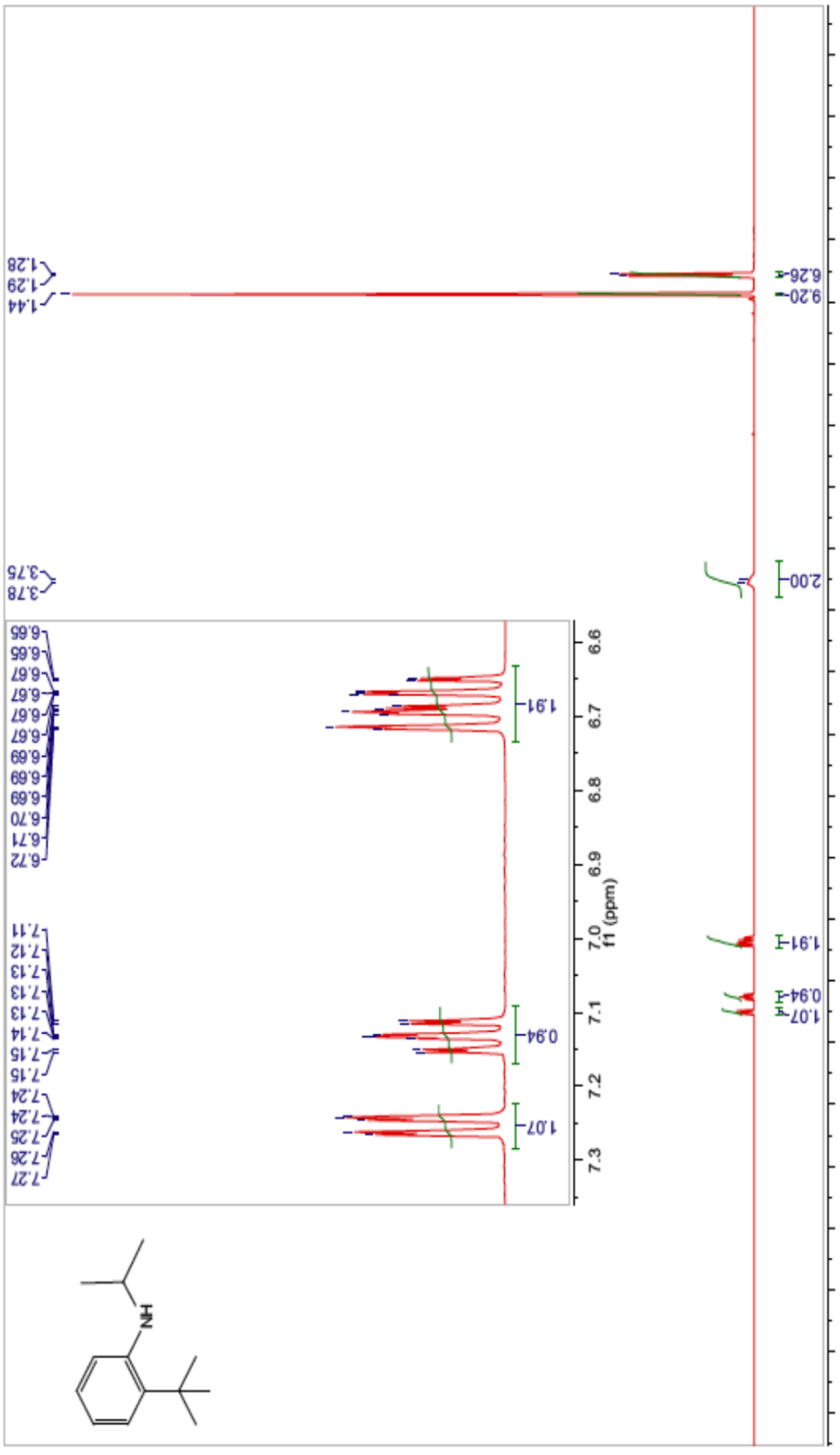
Characterization 3c:



3c

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm)

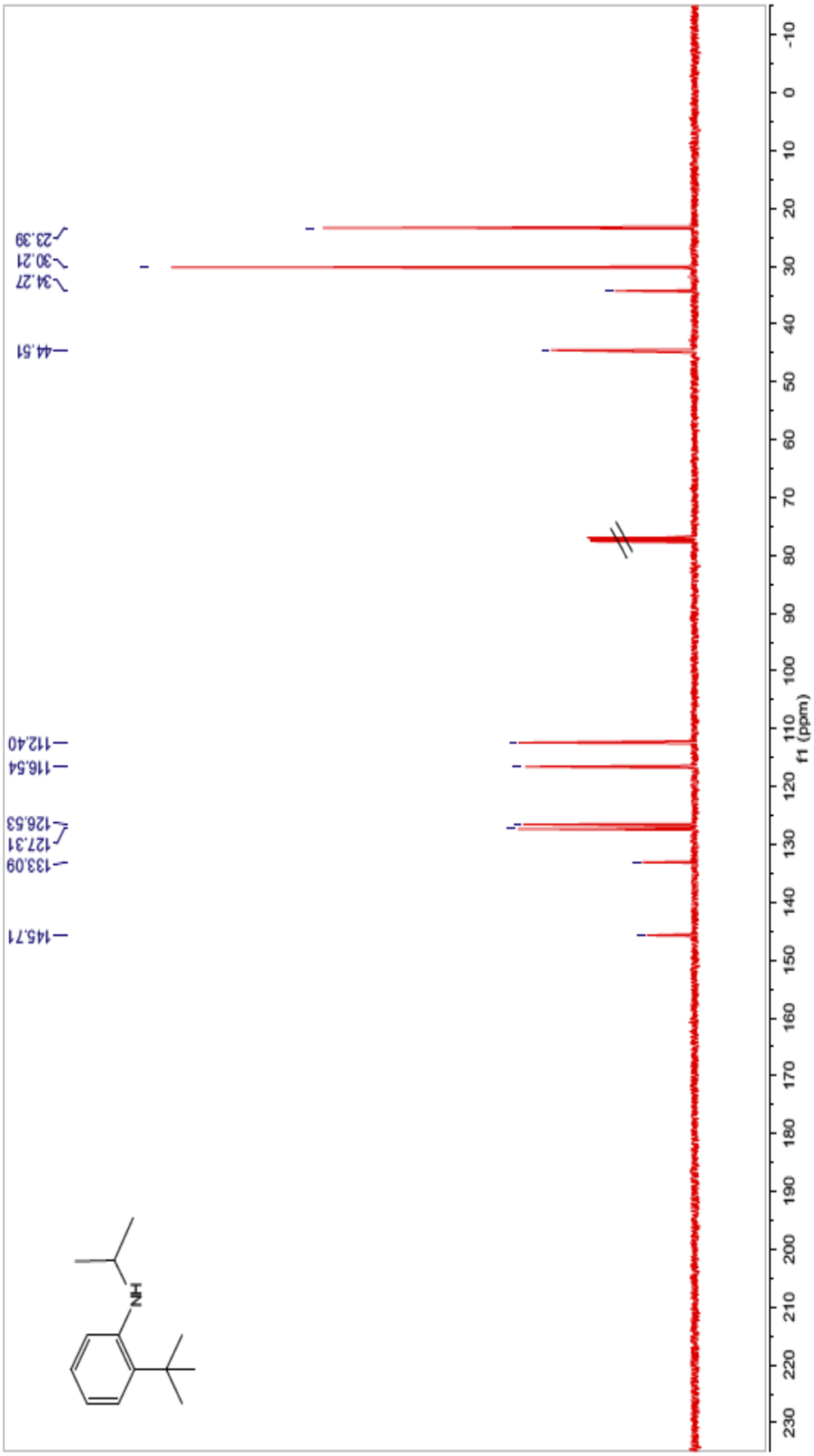
7.28 – 7.22 (dd, *J* = 8, 4 Hz, 1H), 7.16 – 7.08 (m, 1H), 6.74 – 6.6 (m, 2H), 4.0 – 3.6 (br m, 2H), 1.4 (s, 9H), 1.3 – 1.27 (d, *J* = 4Hz, 6H).



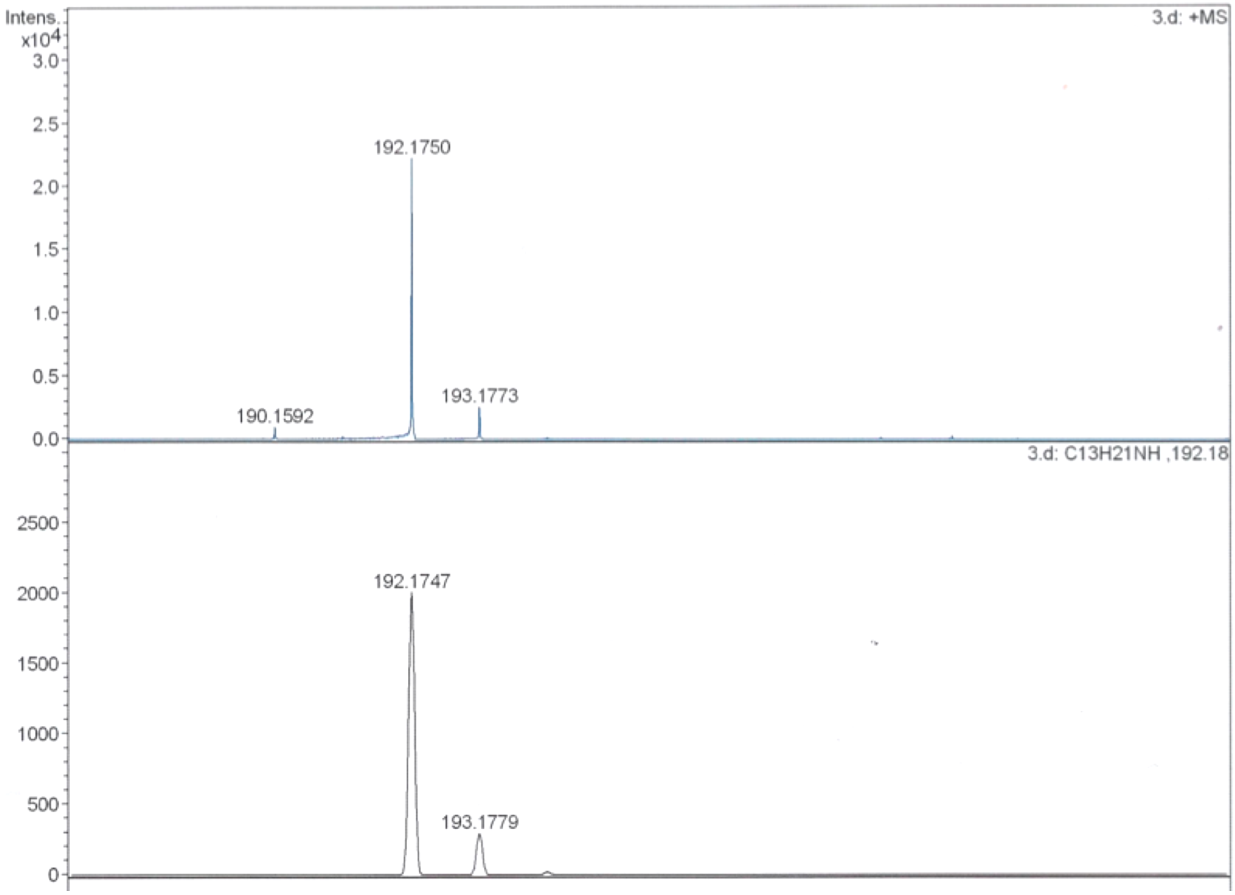
NH
1.28
1.29
1.44
3.75
3.78
6.65
6.66
6.67
6.67
6.67
6.67
6.69
6.69
6.69
6.70
6.71
6.72
7.11
7.12
7.13
7.13
7.13
7.14
7.15
7.15
7.24
7.24
7.25
7.26
7.27
6.26
9.20
2.00
1.91
0.94
1.07
f1 (ppm)

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

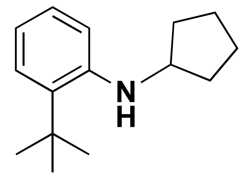
145.71, 133.09, 127.31, 126.53, 116.54, 112.4, 44.51, 34.27, 30.21, 23.39



HRMS ($M+H^+$): Observed: 192.1750; Calculated: 192.1747; Δm = 1.6 ppm



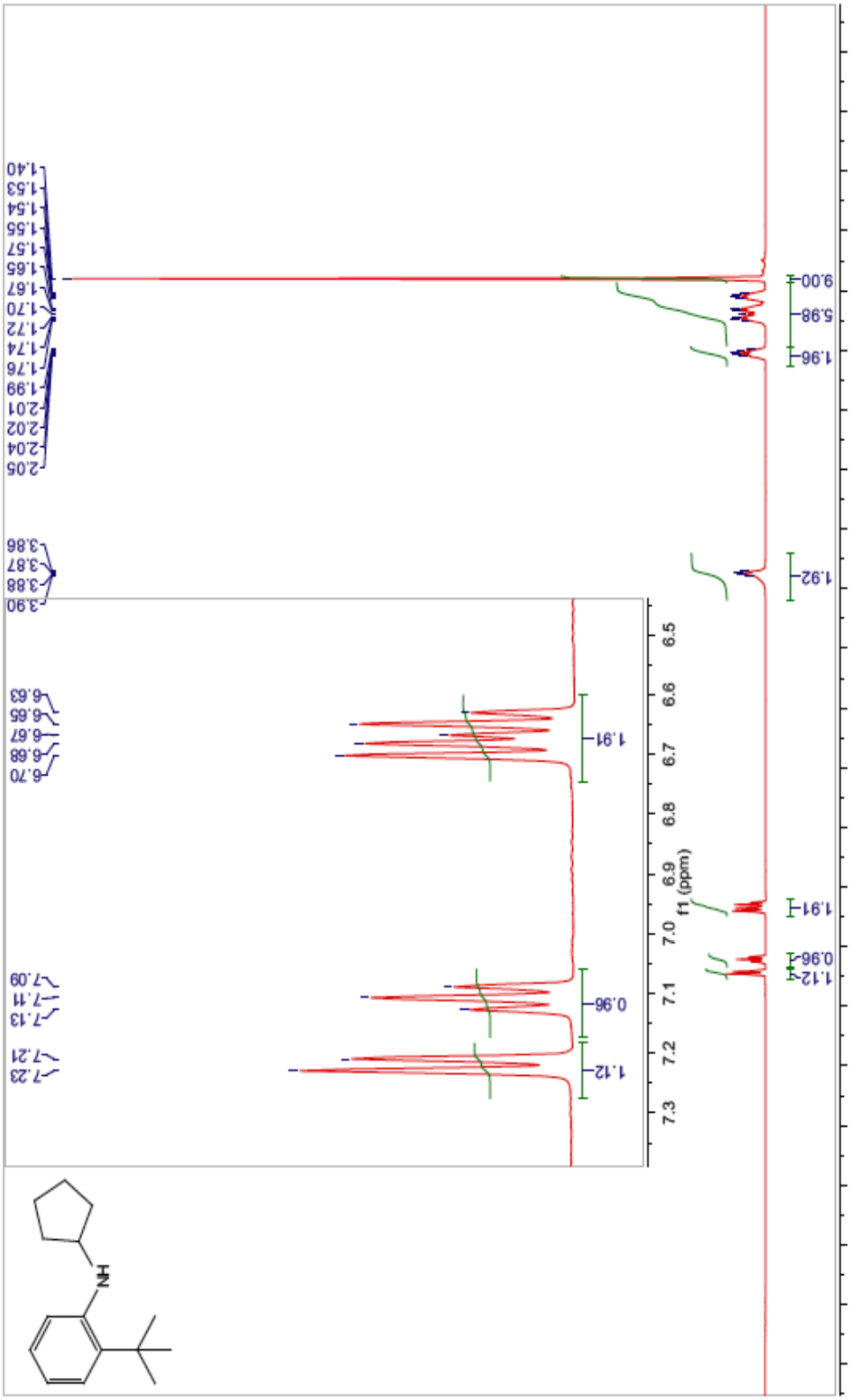
Characterization 3d:



3d

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm)

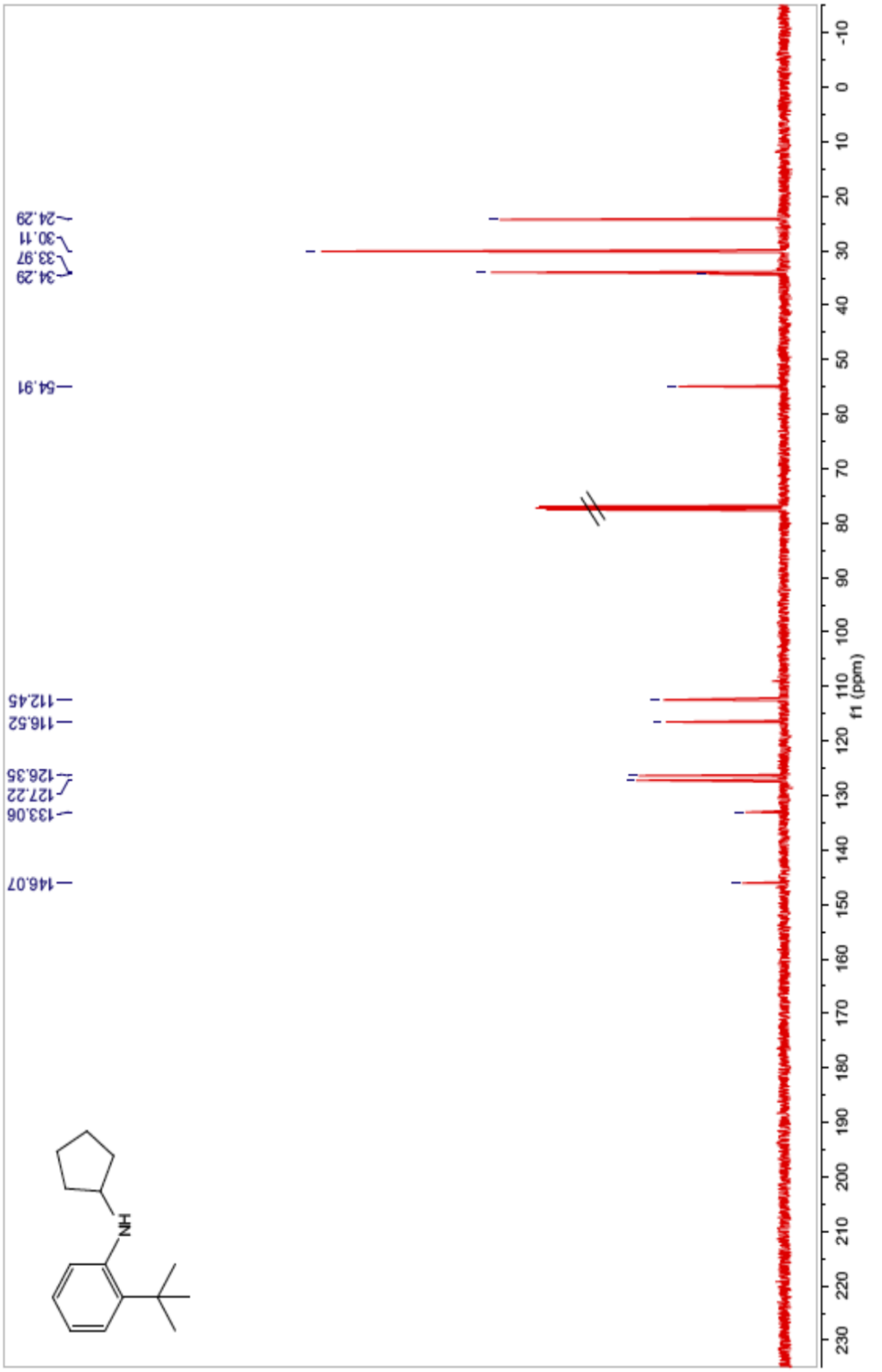
7.25 – 7.18 (d, *J* = 8Hz, 1H), 7.14 – 7.08 (t, *J* = 16, 8Hz, 1H), 6.73 – 6.59 (m, 2H), 4.0 – 3.85 (br m, 2H), 2.07 – 1.50 (m, 8H), 1.40 (s, 9H)



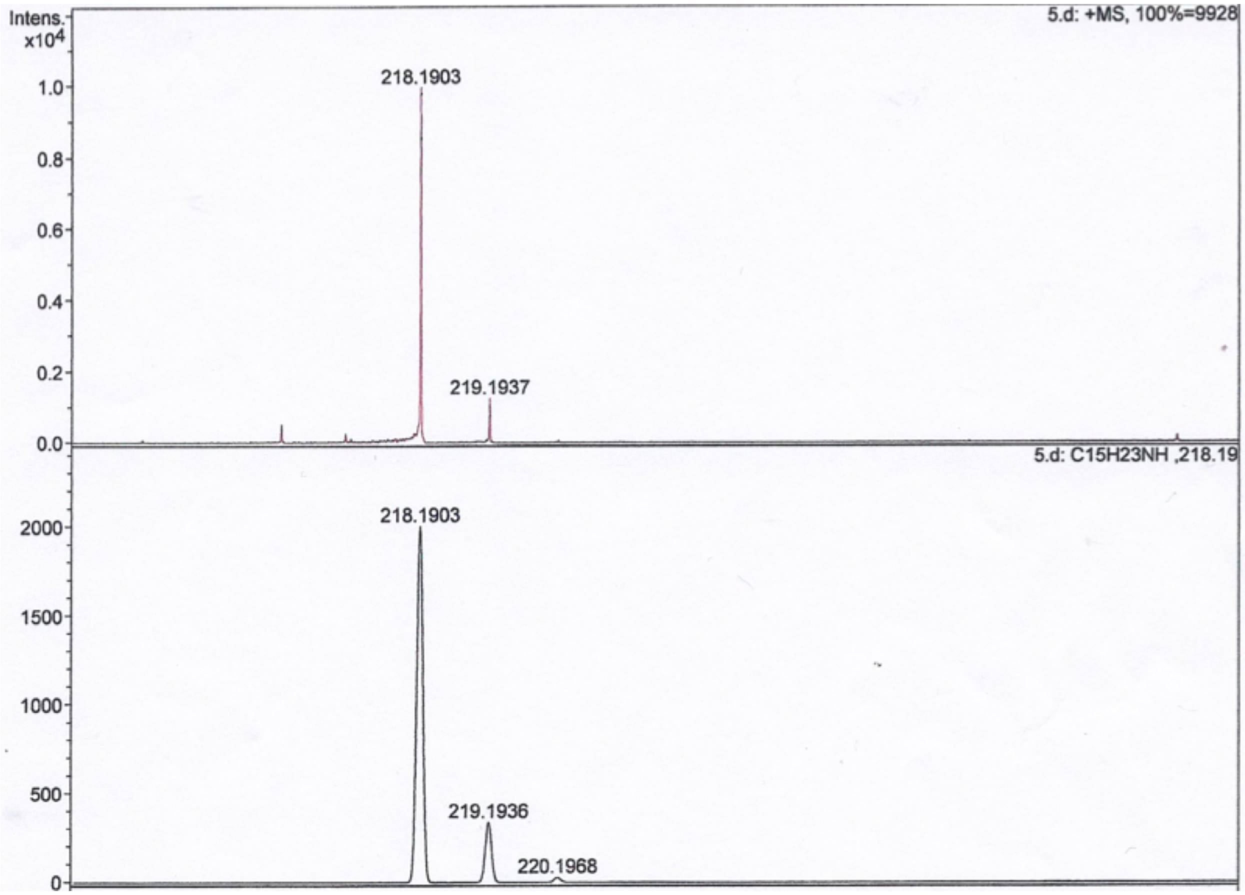
1.40
1.53
1.54
1.56
1.57
1.66
1.67
1.70
1.72
1.74
1.76
1.99
2.01
2.02
2.04
2.05
3.86
3.87
3.88
3.90
6.63
6.65
6.67
6.68
6.70
7.09
7.11
7.13
7.21
7.23
9.00
5.98
1.96
1.92
1.91
0.96
1.12
1.91
0.96
1.12
NH
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

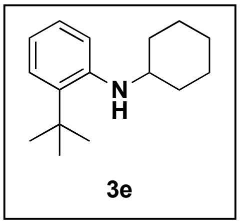
146.07, 133.06, 127.22, 126.35, 116.52, 112.45, 54.91, 34.29, 33.97, 30.11, 24.29



HRMS (M+H$^+$): Observed: 218.1903, Calculated: 218.1903, Δm = 0 ppm



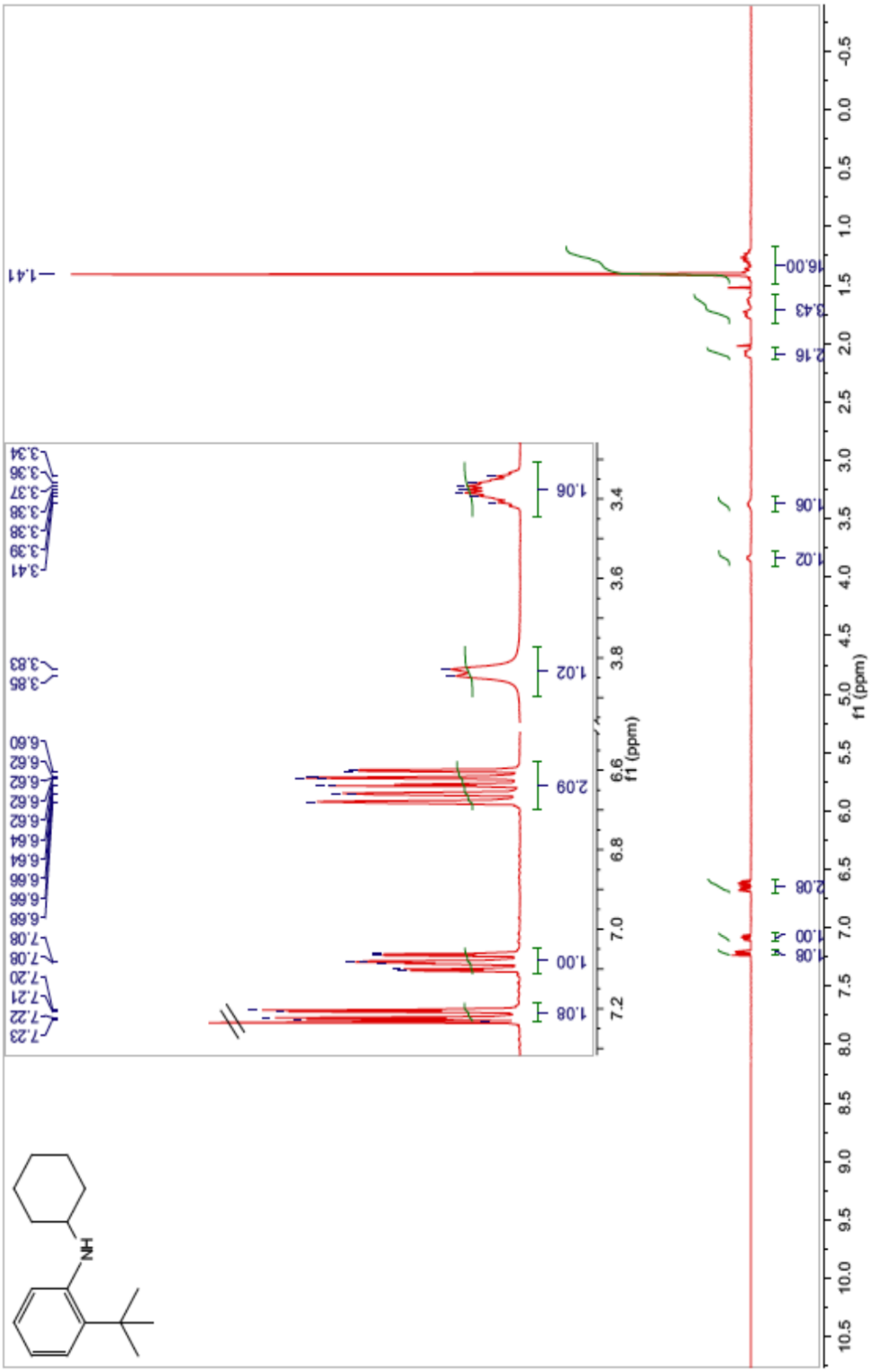
Characterization 3e:



3e

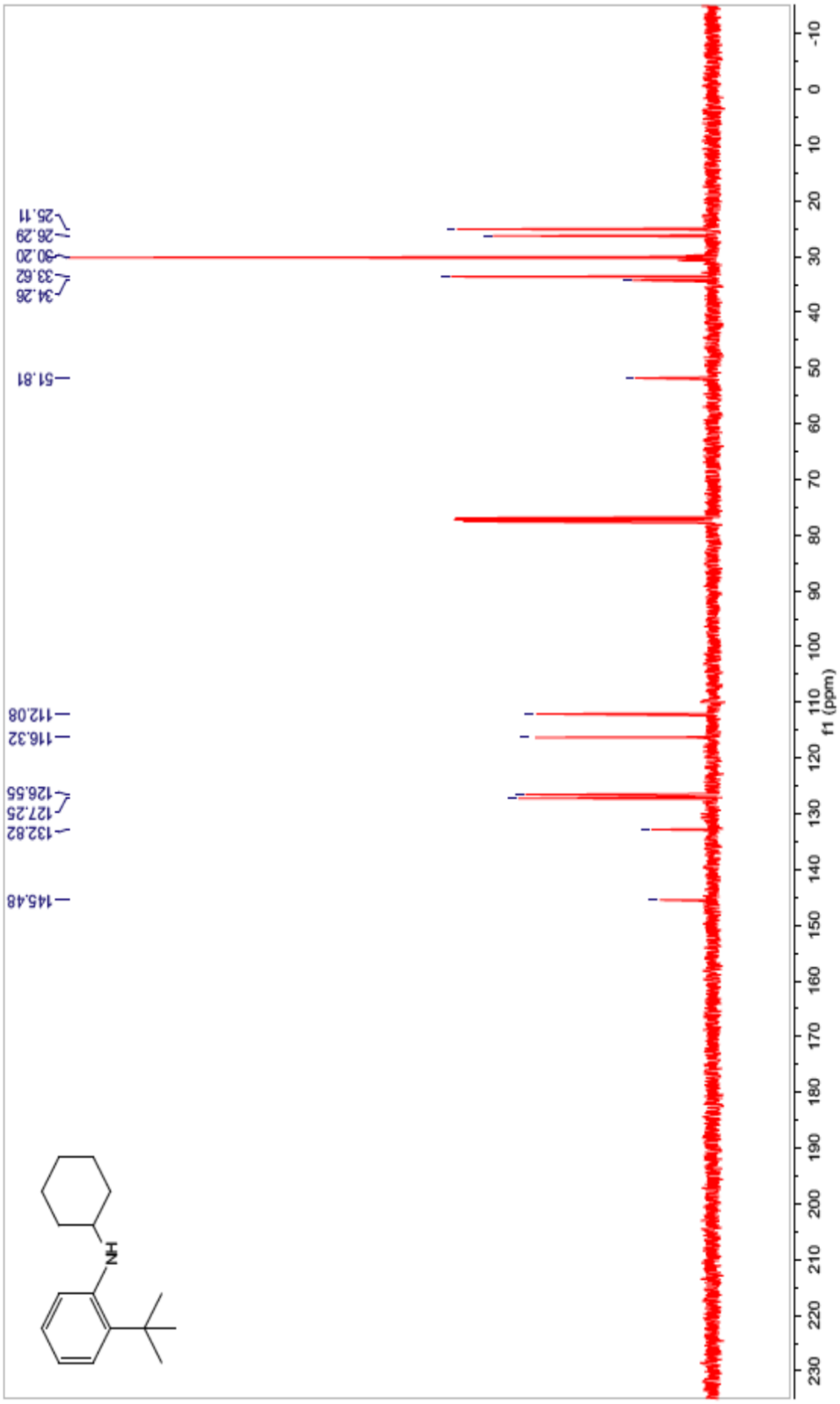
^{1}H NMR (400 MHz, CDCl$_3$, δ ppm)

7.24 – 7.19 (dd, *J* = 8, 4Hz, 1H), 7.11 – 7.04 (m, 1H), 6.7 – 6.58 (m, 2H), 3.9 – 3.75 (d, 1H), 3.45 – 3.32 (m, 1H), 2.2 – 1.1 (m, 19H)

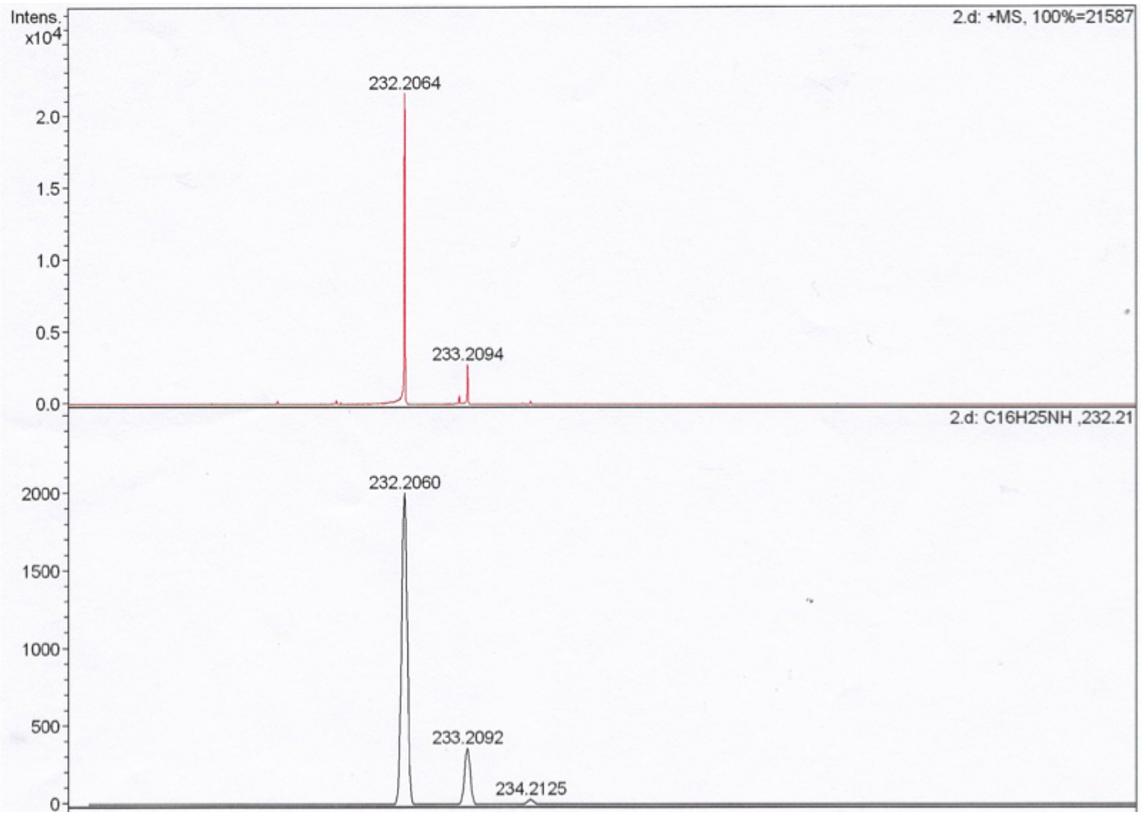

NH
1.41
16.00
3.43
2.16
1.06
1.02
2.08
1.00
1.06
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
f1 (ppm)
3.34
3.36
3.37
3.38
3.38
3.39
3.41
3.83
3.85
6.60
6.62
6.62
6.62
6.62
6.64
6.64
6.66
6.66
6.68
7.08
7.08
7.20
7.21
7.22
7.23
1.06
1.02
2.09
1.00
1.08
3.4
3.6
3.8
6.6
6.8
7.0
7.2
f1 (ppm)

^{13}C NMR (100 MHz $CDCl_3$, δ ppm)

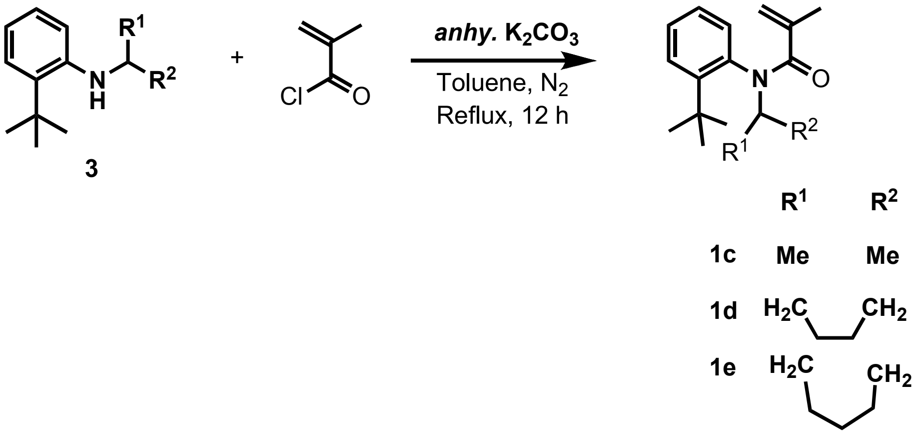
145.48, 132.82, 127.25, 126.55, 116.32, 112.08, 51.81, 34.26, 33.62, 30.20, 26.29, 25.11



HRMS ($M+Na^+$): Observed: 232.2064; Calculated: 232.2060, Δm = 1.7 ppm



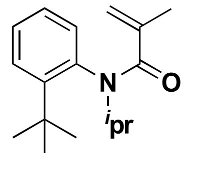
3) Synthesis and characterization of anilides **1c-e**



Scheme S2: Synthesis of acrylanilides **1c-e**

Acrylanilide **1** was prepared using procedures reported in literature.[3] In a typical reaction, freshly synthesized aniline **3** (1 equi.) was dissolved in 20 mL of toluene. The aniline solution was then stirred and purged with N_2 gas; *anhy.* K_2CO_3 (1.2 equi.) and methacryloyl chloride (1.5 equi.) were respectively and slowly added to the solution with continuous stirring. The new solution was allowed to reflux (100 °C) overnight (12 h). After, the reaction was quenched with 10 – 20 mL of DI water followed by extraction of the organic layer with EtOAc (2 x 20 mL). The organic layer was then dried over *anhy.* Na_2SO_4 and concentrated by roto-evaporation. The expected anilide was finally purified by chromatography (using CombiFlash®): 12 g silica; flow rate: 22 mL/min, mobile phase: 15% EtOAc : Hexanes.

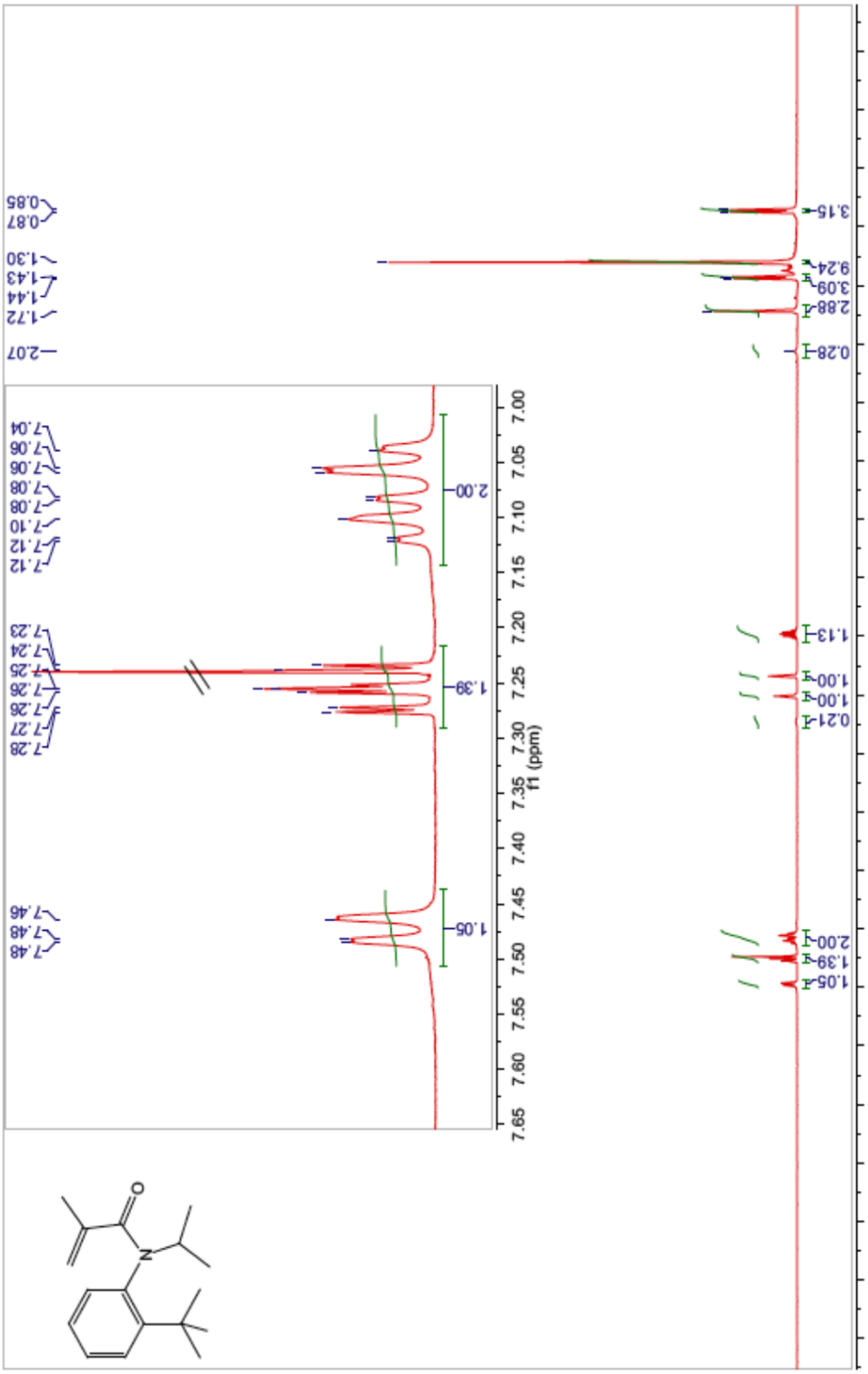
Characterization 1c:



1c

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm)

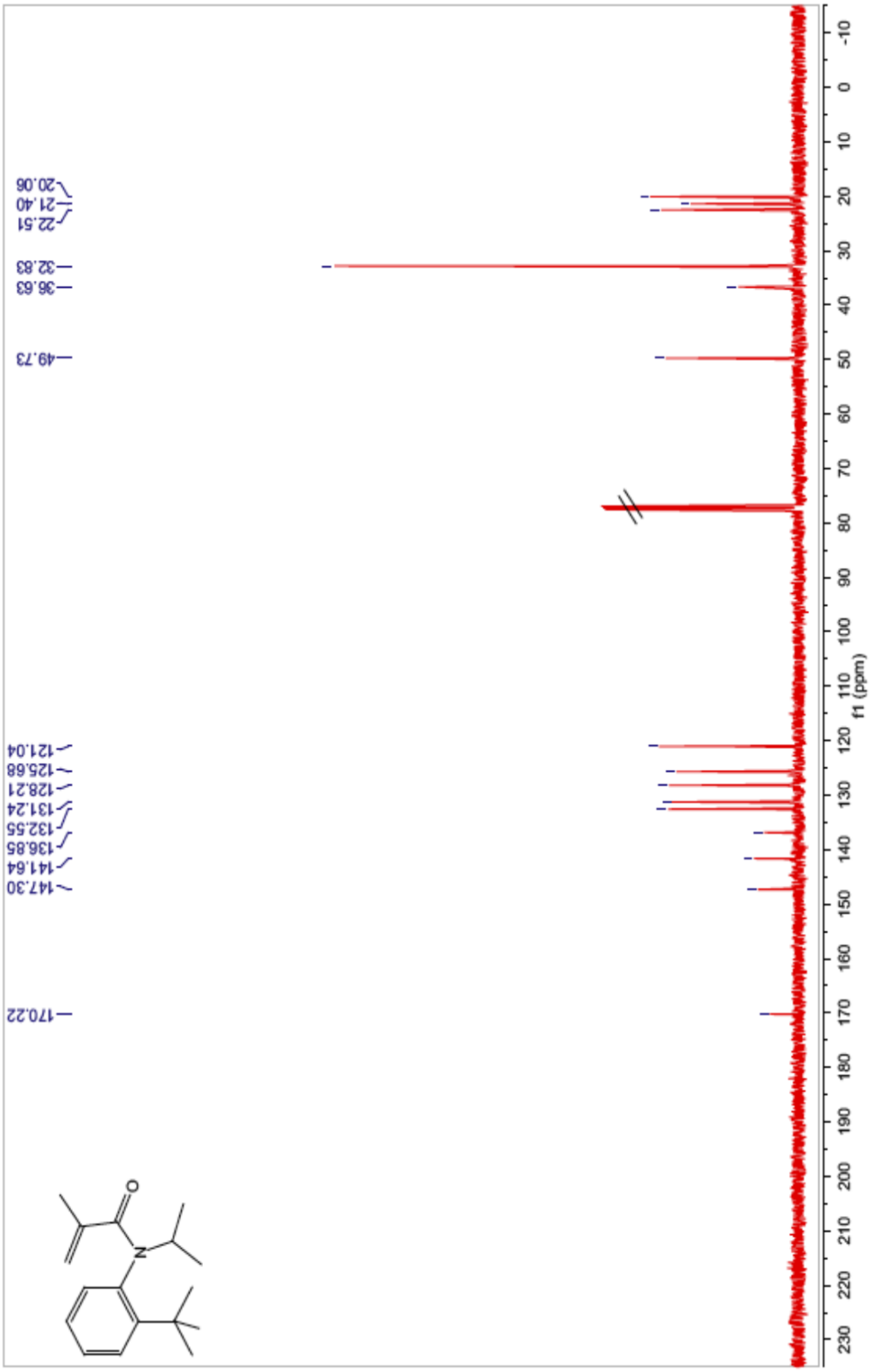
7.55 – 7.42 (d, J = 8Hz, 1H), 7.30 – 7.20 (m, 1H), 7.15 – 7.0 (m, 2H), 5.24 – 4.84 (Olefinic H, minor & major conformers, 2H), 4.55 – 4.40 (m, N-CH, 1H), 2.07 & 1.72 (acryl-CH_3, minor & major conformers, s, 3H), 1.45 – 1.4 (^{i}pr-CH_3, d, J = 4Hz, 3H), 1.30 (^{t}Bu-CH_3, s, 9H), 0.9 – 0.84 (^{i}pr-CH_3, d, J = 8Hz, 3H)



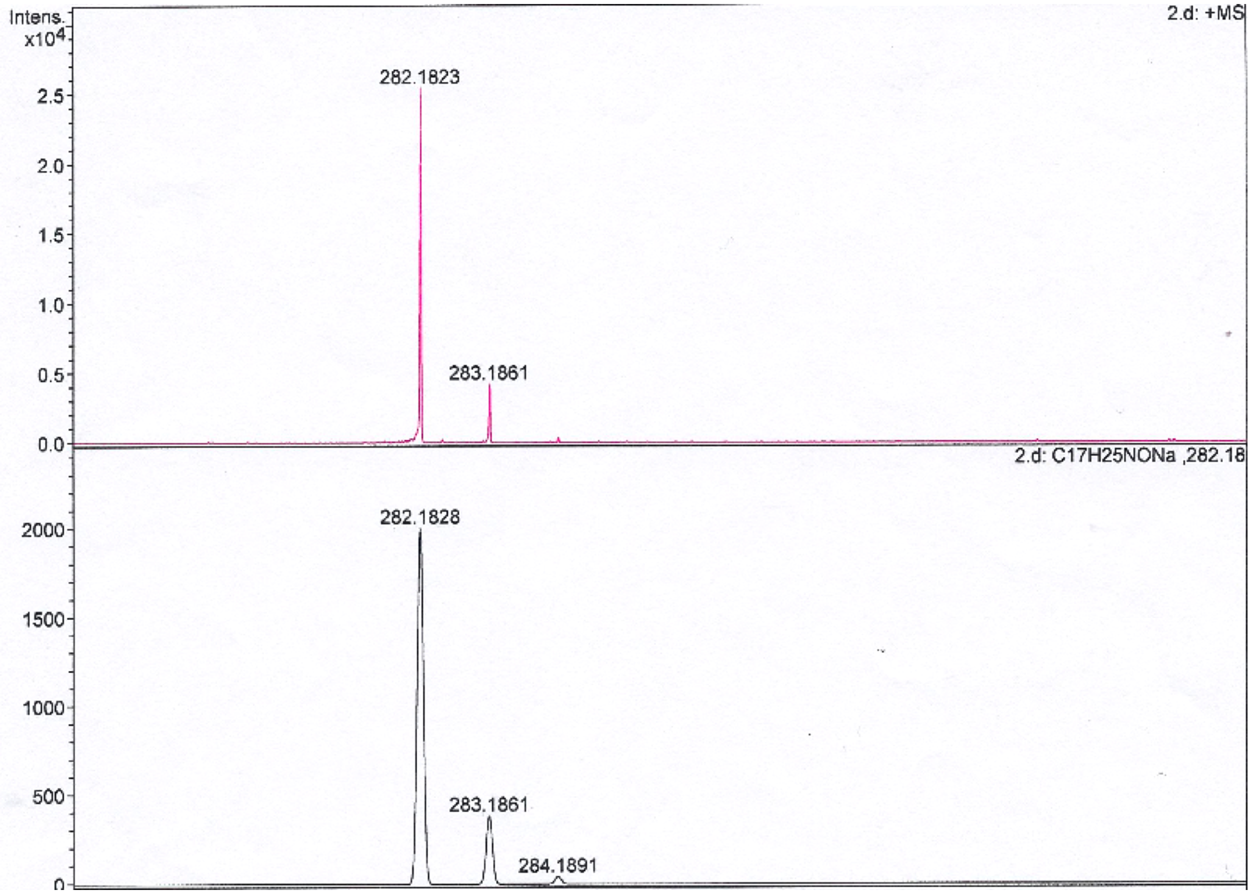
0.85
0.87
1.30
1.43
1.44
1.72
2.07
7.04
7.06
7.06
7.08
7.08
7.10
7.12
7.12
7.23
7.24
7.25
7.26
7.26
7.26
7.27
7.28
7.46
7.48
7.48
2.00
1.39
1.05
3.15
9.24
3.09
2.88
0.28
1.13
1.00
1.00
0.21
2.00
1.39
1.05
f1 (ppm)
O
N

^{13}C NMR (100 MHz, CDCl$_3$, δ ppm)

170.22, 147.30, 141.64, 136.85, 132.55, 131.24, 128.21, 125.68, 121.04, 49.73, 36.63, 32.83, 22.51, 21.40, 20.06



HRMS ($M+Na^+$): Observed: 282.1823, Calculated: 282.1828, Δm = 1.8 ppm



Polarimetry:

$1c:[\alpha]_D^{27} = +120.0^o$ (c = 0.03% in $CHCl_3$)

$ent-1c:[\alpha]_D^{27} = -126.7^o$ (c = 0.03% in $CHCl_3$)

HPLC Conditions:

Column: (R,R) WHELK–01 for analysis and AD-H for separation;

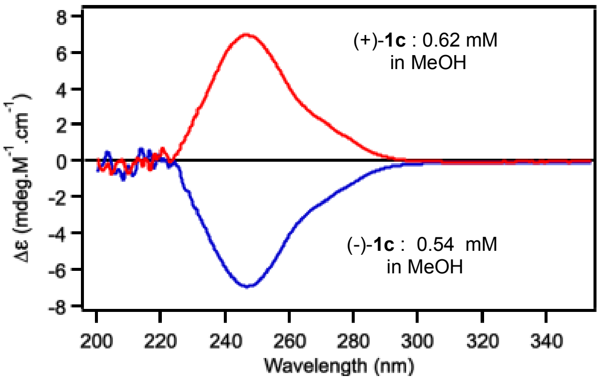
Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2

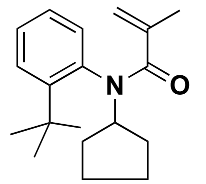
Flow rate: 1 mL/min (Analysis), and 2.5 mL/min (separation)

Retention time (min): (+)-**1c:** ~31.3, (-)-**1c:** ~43.8

CD Spectroscopy:



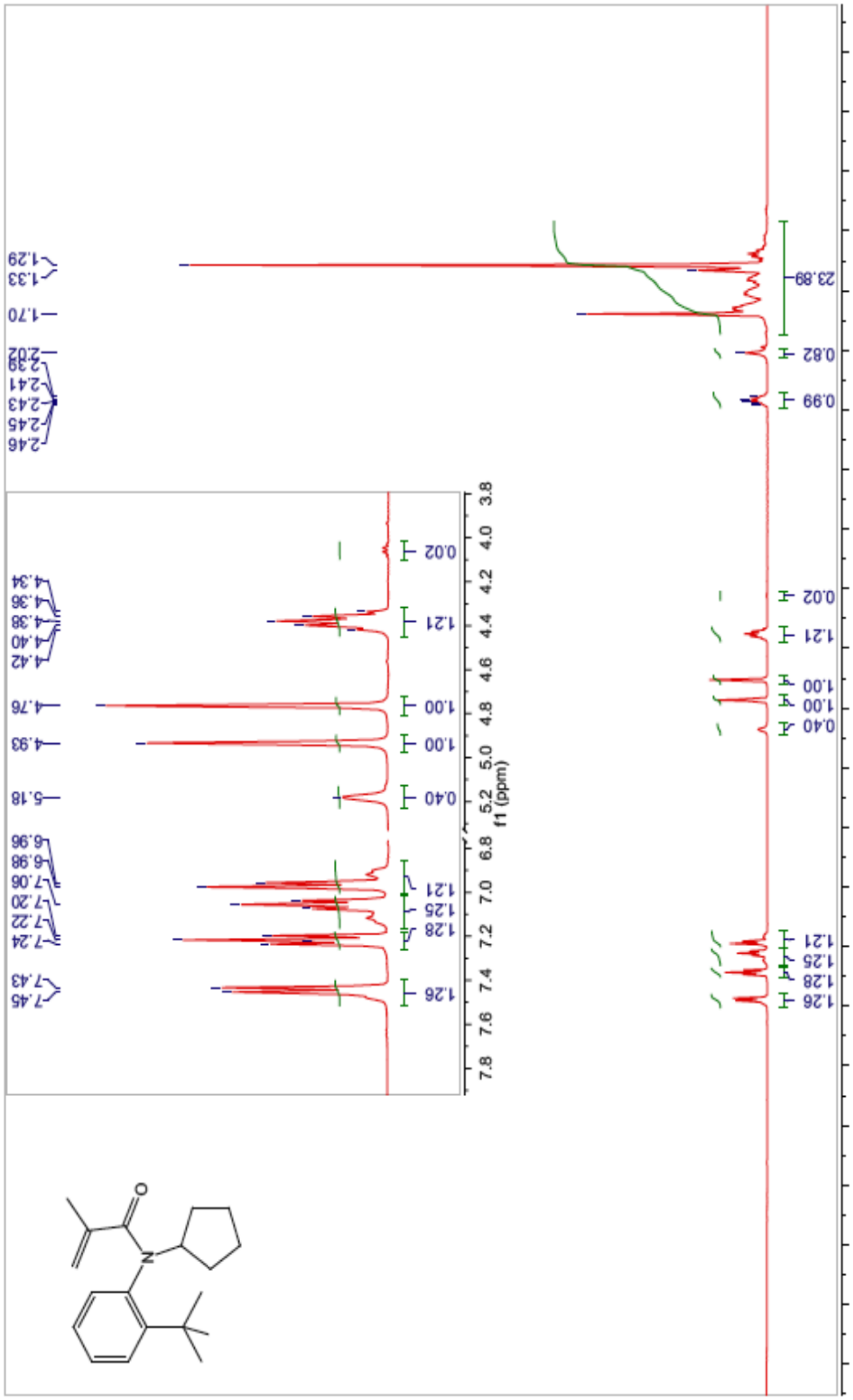
Characterization 1d:



1d

^1H NMR (400 MHz, $CDCl_3$, δ ppm)

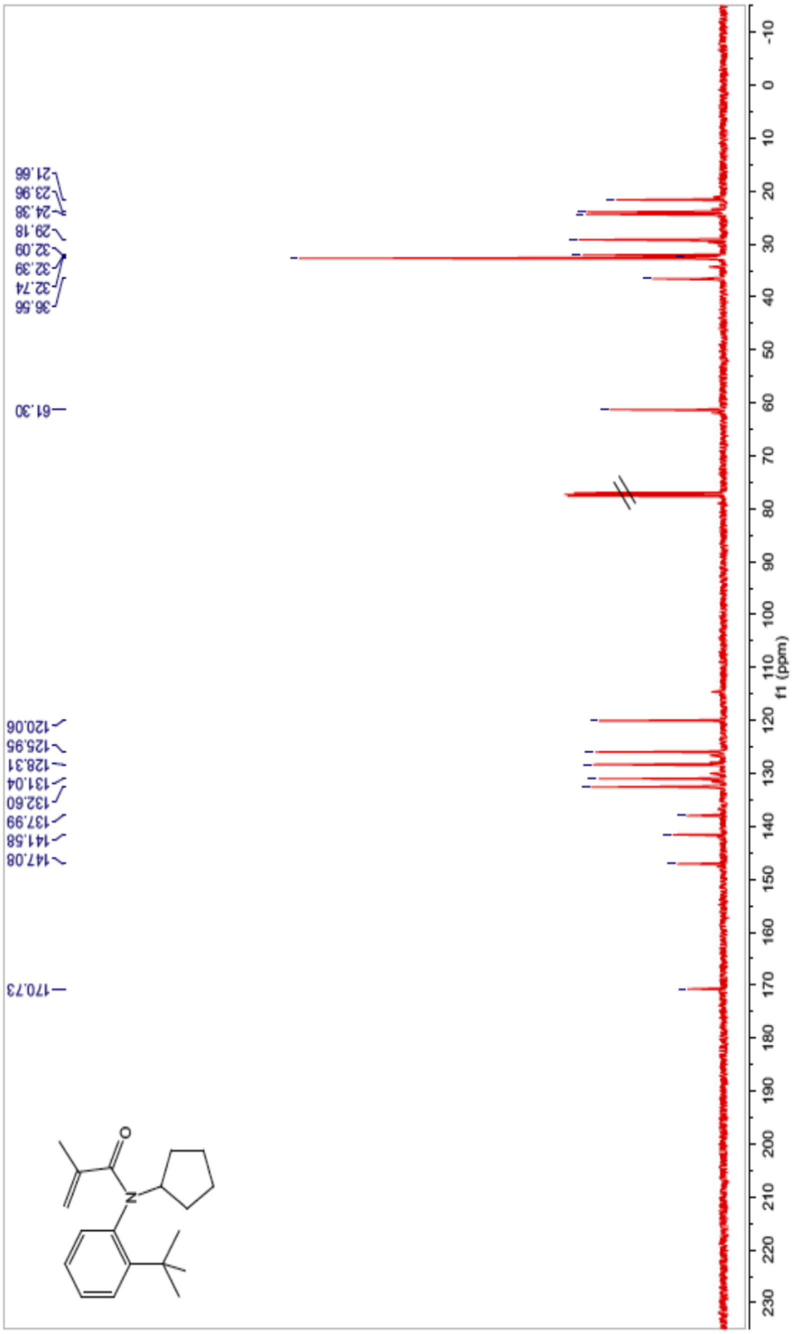
7.52 – 6.9 (Ar, major and minor conformers, 4H), 5.18- 4.75 (olefinic H, major and minor conformers, 2H), 4.45 – 4.0 (m, N-C$\underline{H}$, major and minor conformers, 1H), 2.5 – 1.0 (cyclopentyl-$\underline{CH_2}$, ^{t}Bu-$\underline{CH_3}$, acryl-$\underline{CH_3}$, major and minor conformers, 20H).



7.45
7.43
7.24
7.22
7.20
7.06
6.98
6.96
5.18
4.93
4.76
4.42
4.40
4.38
4.36
4.34
2.46
2.45
2.43
2.41
2.39
2.02
1.70
1.33
1.29
1.26
1.28
1.25
1.21
0.40
1.00
1.00
1.21
0.02
0.99
0.82
23.89
f1 (ppm)

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

170.73, 147.08, 141.58, 137.99, 132.60, 131.04, 128.31, 125.95, 120.06, 61.30, 36.56, 32.74, 32.39, 32.09, 29.18, 24.38, 23.96, 21.66



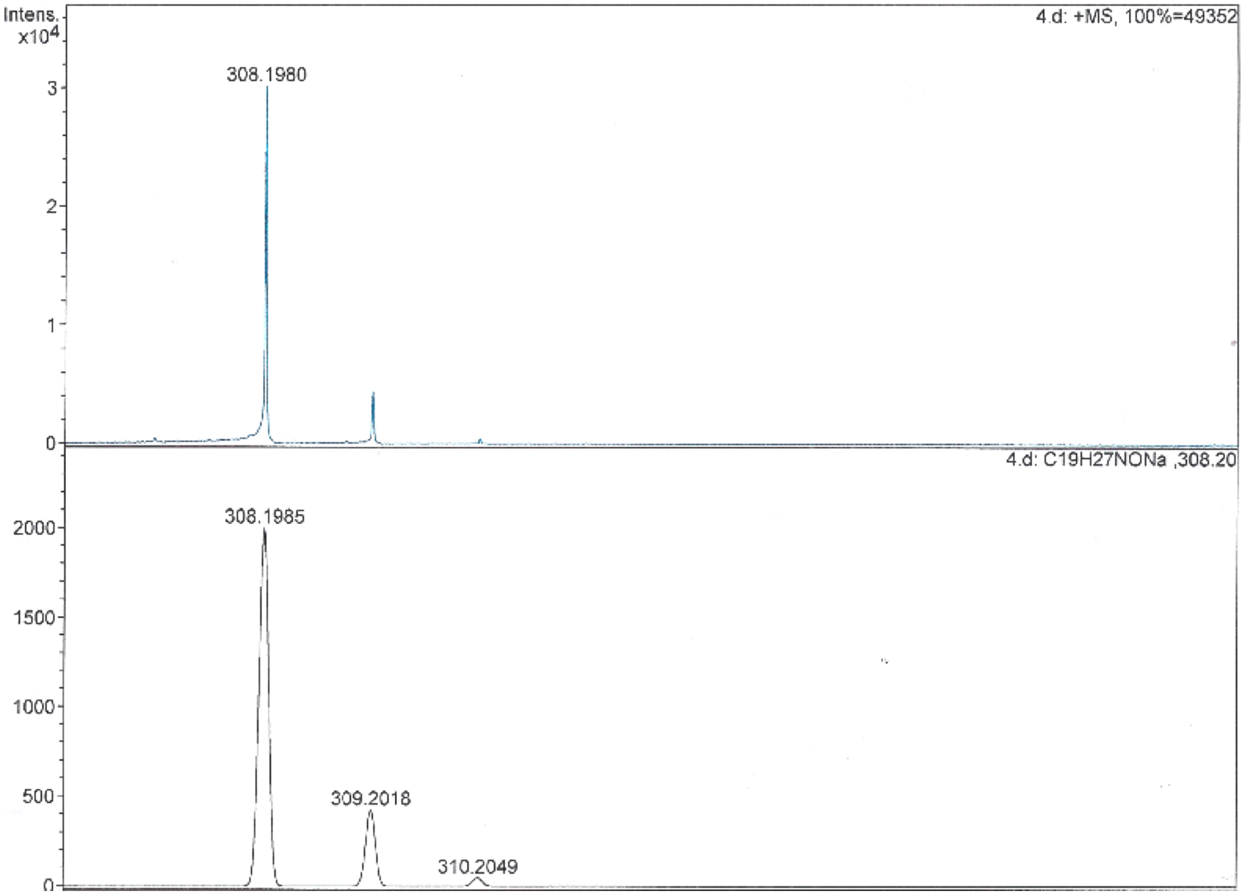
Note: The *t*-butyl carbons is shown for both major and minor conformers C(-CH_3^*)

Polarimetry:

$1d : [\alpha]_D^{27} = +80.0^o$ (c = 0.04% in CHCl$_3$)

$ent-1d : [\alpha]_D^{27} = -82.5^o$ (c = 0.04% in CHCl$_3$)

HRMS (M+Na$^+$): Observed: 308.1980, Calculated: 308.1985, Δm = 1.6 ppm



HPLC Conditions:

Column: (R,R) WHELK–01 for analysis and AD-H for separation;

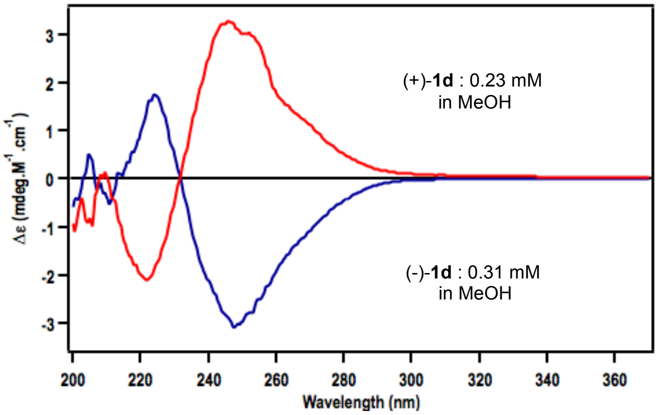
Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2;

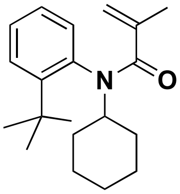
Flow rate: 1 mL/min (Analysis), and 2.5 mL/min (separation)

Retention time (min): (+)-**1d:** ~47.6, (-)-**1d:** ~67.7

CD Spectroscopy



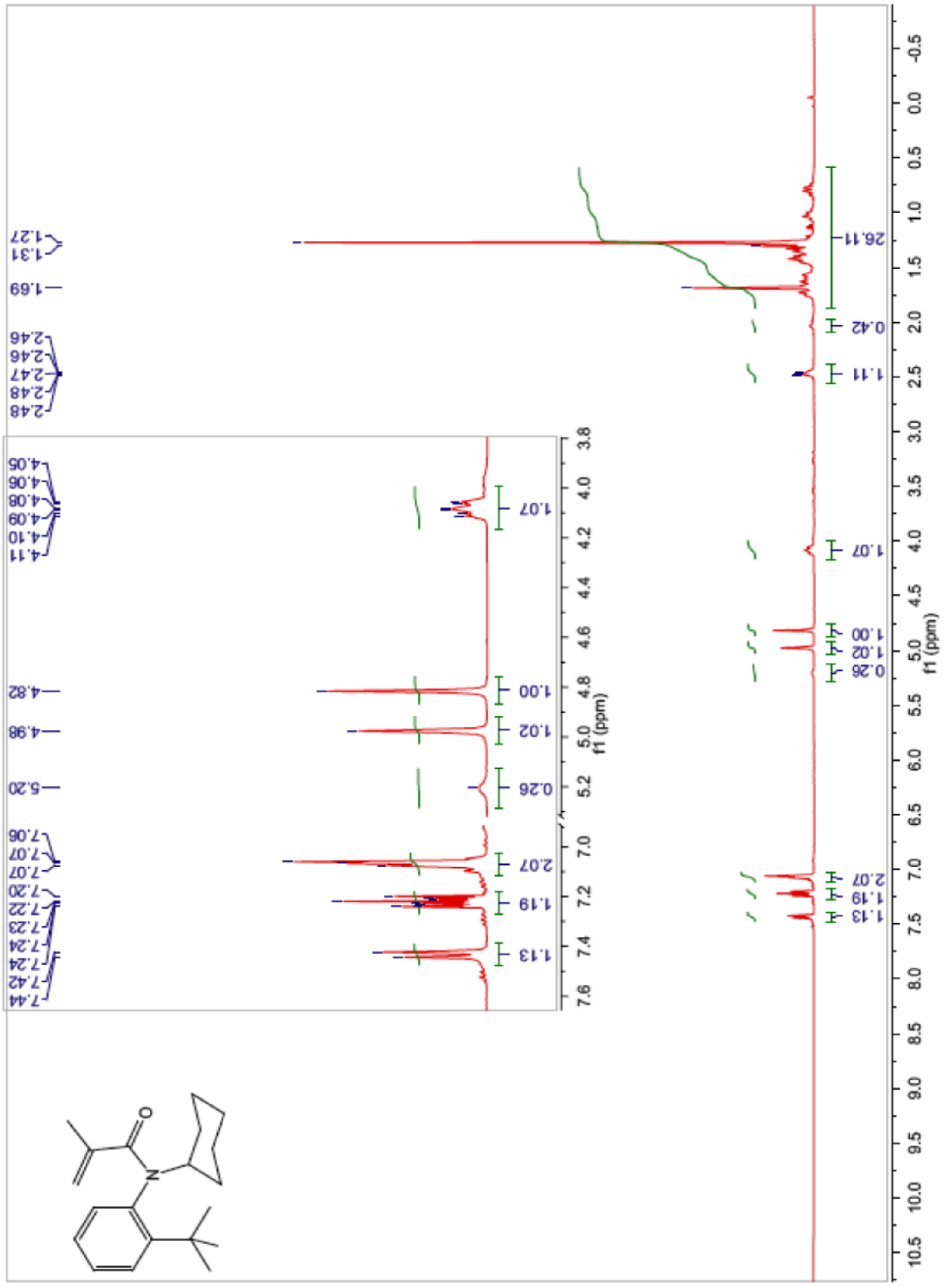
Characterization 1e:



1e

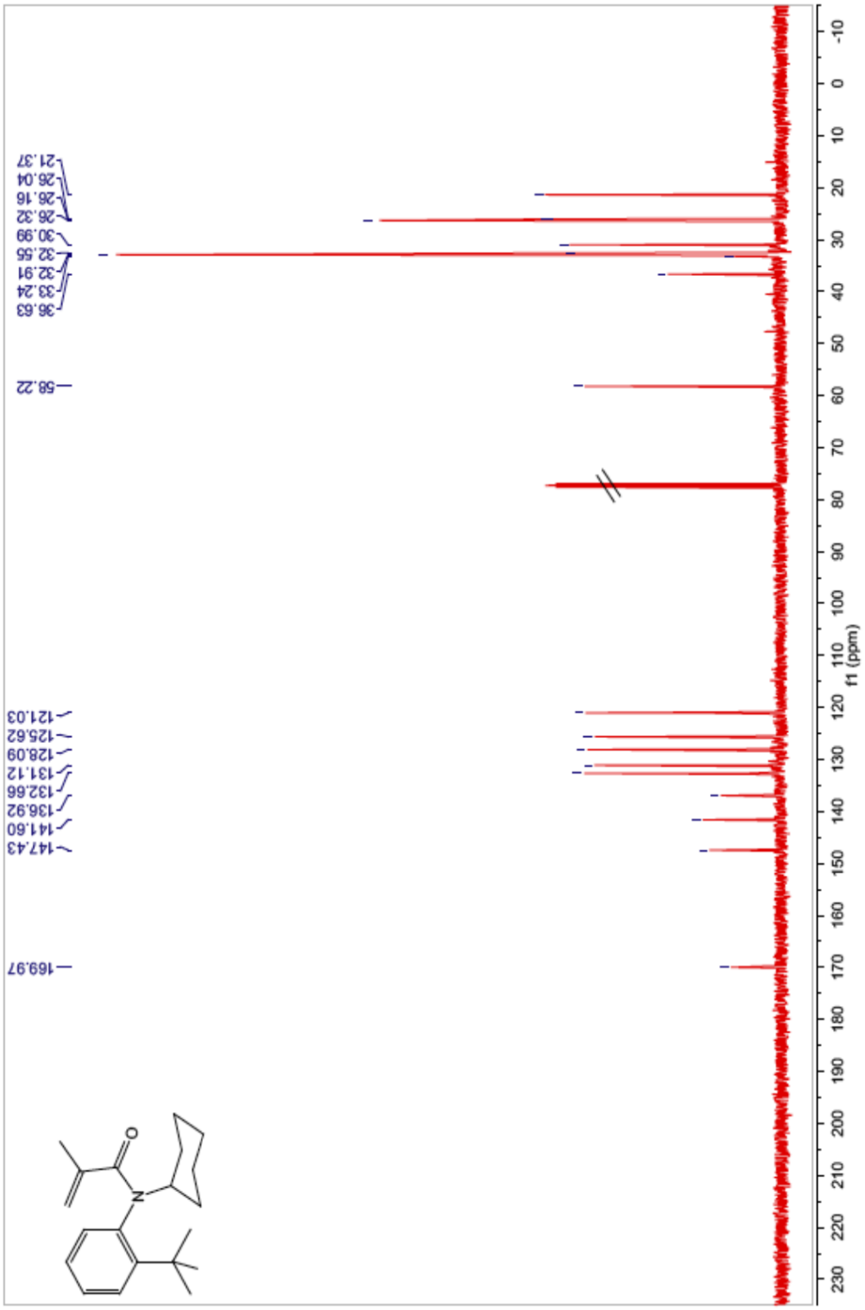
^{1}H NMR (400 MHz, CDCl$_3$, δ ppm)

7.5 – 7.0 (Ar, major and minor conformers, 4H), 5.25 – 4.82 (Olefinic H, minor and minor conformers, 2H), 4.15 – 3.9 (m, N-C<u>H</u>, major and minor conformers, 1H), 2.6 – 0.6 (cyclohexyl-$\underline{CH_2}$, ^{t}Bu-$\underline{CH_3}$, acryl-$\underline{CH_3}$, major and minor conformers, 22H)


1.27
1.31
1.69
2.46
2.46
2.47
2.48
2.48
4.05
4.06
4.08
4.09
4.10
4.11
4.82
4.98
5.20
7.06
7.07
7.07
7.20
7.22
7.23
7.24
7.24
7.42
7.44
26.11
0.42
1.11
1.07
1.00
1.02
0.26
2.07
1.19
1.13
f1 (ppm)
O
N

^{13}C NMR (100 MHz, CDCl$_3$, δ ppm)

169.97, 147.43, 141.6, 136.92, 132.66, 131.12, 128.09, 125.62, 121.03, 58.22, 36.63, 33.24, 32.91, 32.55, 30.99, 26.32, 26.16, 26.04, 21.37



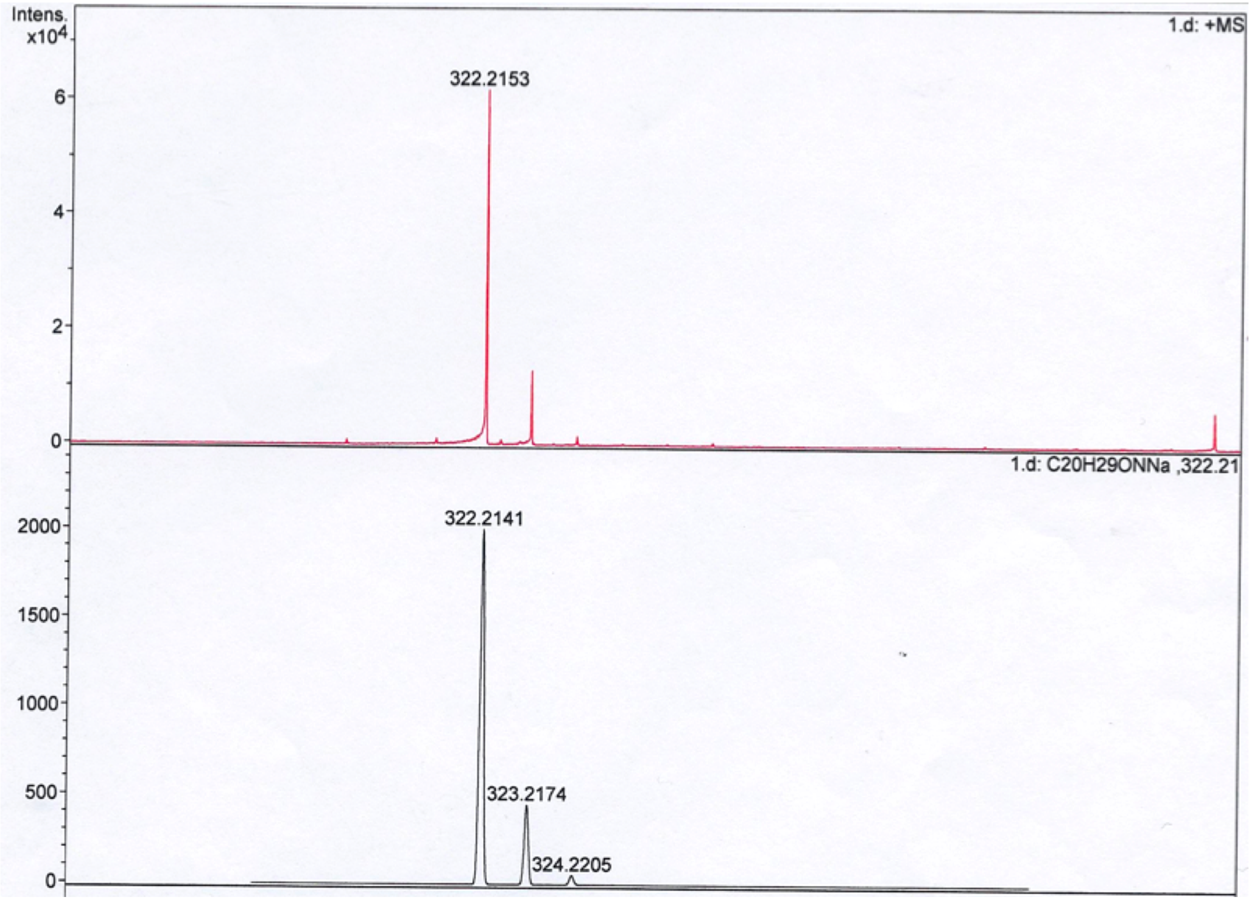
Note: The *t*-butyl carbons is shown for both major and minor conformers C (-CH_3^*)

Polarimetry:

$1e:[\alpha]_D^{27} = +163.5^o$ (c = 0.052% in $CHCl_3$)

$ent-1e:[\alpha]_D^{27} = -164.7^o$($c$ = 0.051% in $CHCl_3$)

HRMS ($M+Na^+$): Observed: 322.2153, Calculated: 322.2141, Δm = 3.7 ppm



HPLC Conditions:

Column: CHIRALPAK® IC for analysis and AD-H for separation;

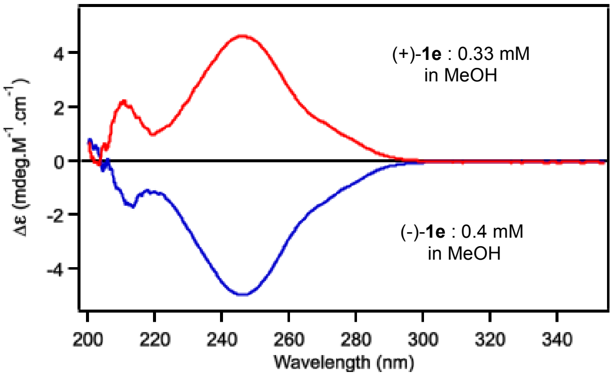
Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2;

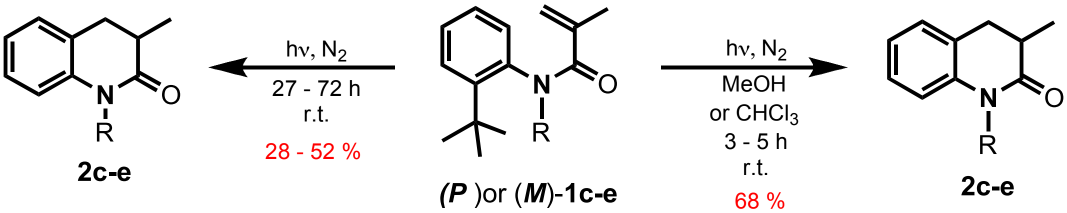
Flow rate: 1 mL/min (Analysis), and 2.5 mL/min (separation)

Retention time (min): (+)-**1e:** ~28.00, (-)-**1e:** ~32.47

CD Spectroscopy



4) Photo-irradiation procedures and characterization of quinolinones photoproducts **2c-d**



Scheme S3: Solvent-free reaction absolute conversion: R = ^{i}pr, time = 70 h

Reaction in MeOH: R = cyclopentyl, time = 5 h (based on recovered starting material)

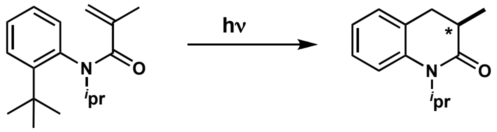
4.1) Solvent-free reaction

Optically pure isomers of **1c-e** were separated (using HPLC) and recrystallized inside a 13 mm pyrex test tube. The test tube was mounted on a merry-go-around, and was then exposed to a medium pressure Hg lamp at room temperature (26 ± 2 °C) for 27 – 72 h. During the course of the reaction, the conversion of the crystals to the corresponding product was perceptible by the formation of a brownish glue-like substance. After, the crystals and brownish substance was dissolved in a minimum of $CHCl_3$, and chromatographed to obtain the expected photoproduct.

Note: *The amount of isolated photoproduct(s) depends on the quality of the crystals, the irradiation time, and the temperature of the reaction environment.*

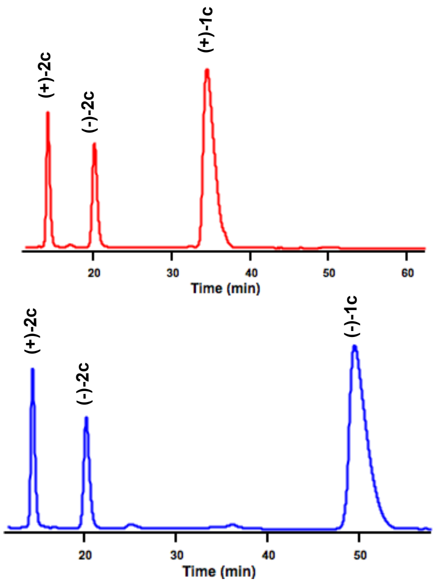
4.2) Photoreaction in Solution (MeOH, $CHCl_3$)

Optically pure isomers of **1c-e** were separated (using HPLC) and dissolved in MeOH/$CHCl_3$ (1mg/mL). The solutions were deaerated with N_2 gas, and was irradiated with a medium pressure Hg lamp at room temperature (26 ± 2 ^{o}C) for 3 – 5 h. After, the solvent was either removed by purging air through the solution for HPLC analysis (on chiral stationary phase) or chromatographed in order to isolate the expected photoproduct(s).



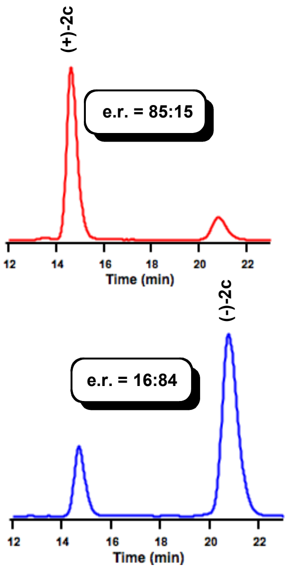
P or *M* **1c** (+/-)-**2c**

Reaction in MeOH @ RT for 3 h
Pyrex cut-off

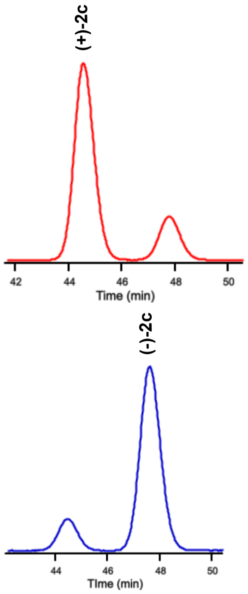


HPLC Analysis Conditions
Column: WHELK-RRWO1
Mobile phase: 98:2 Hex-IPA
Flow: 1 mL/min

Solvent-free reaction @ RT for 27 h, Pyrex cut-off



HPLC Analysis Conditions
Column: WHELK-RRWO1
Mobile phase: 98:2 Hex-IPA
Flow: 1 mL/min

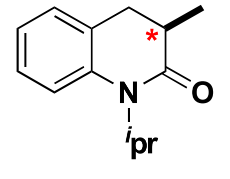


HPLC Analysis Conditions
Column: CHIRALPAK-IC
Mobile phase: 99:1 Hex-IPA
Flow: 0.5 mL/min

Note: *The enantiomers of* ***2c*** *were injected in two different chiral stationary phases viz. WHELK-RRWO1 and CHIRALPAK IC to verify the enantiomeric ratios.*

4.3) Characterization of quinolinone photoproducts **2c-e**

Characterization of *R*-(+)-**2c** = *S*-(-)-**2c:**



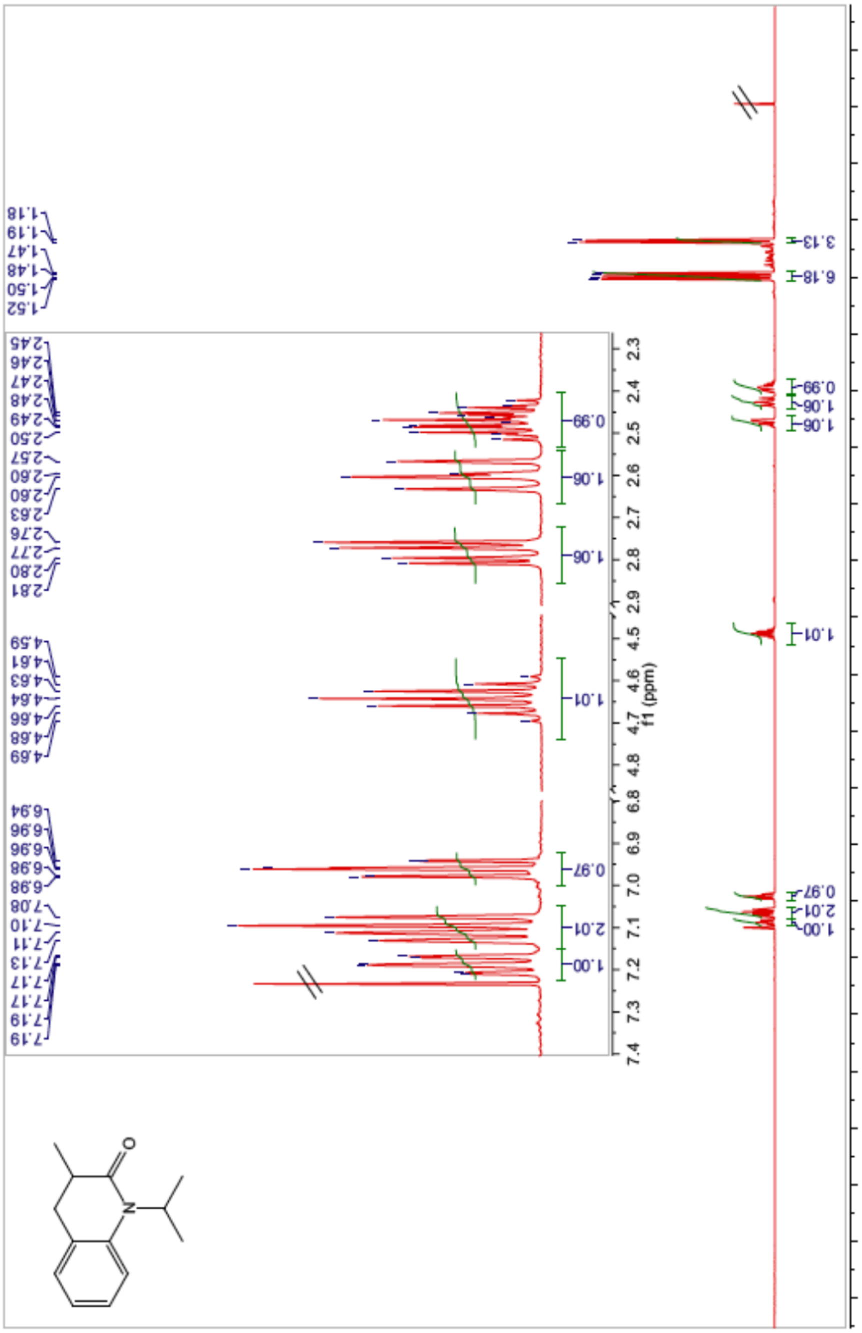
R-(+)-**2c** = *S*-(-)-**2c**

Purification Conditions:

Combiflash®: 12 g silica; flow rate: 20 mL/min; Mobile phase: 6 % EtOAc: Hexanes

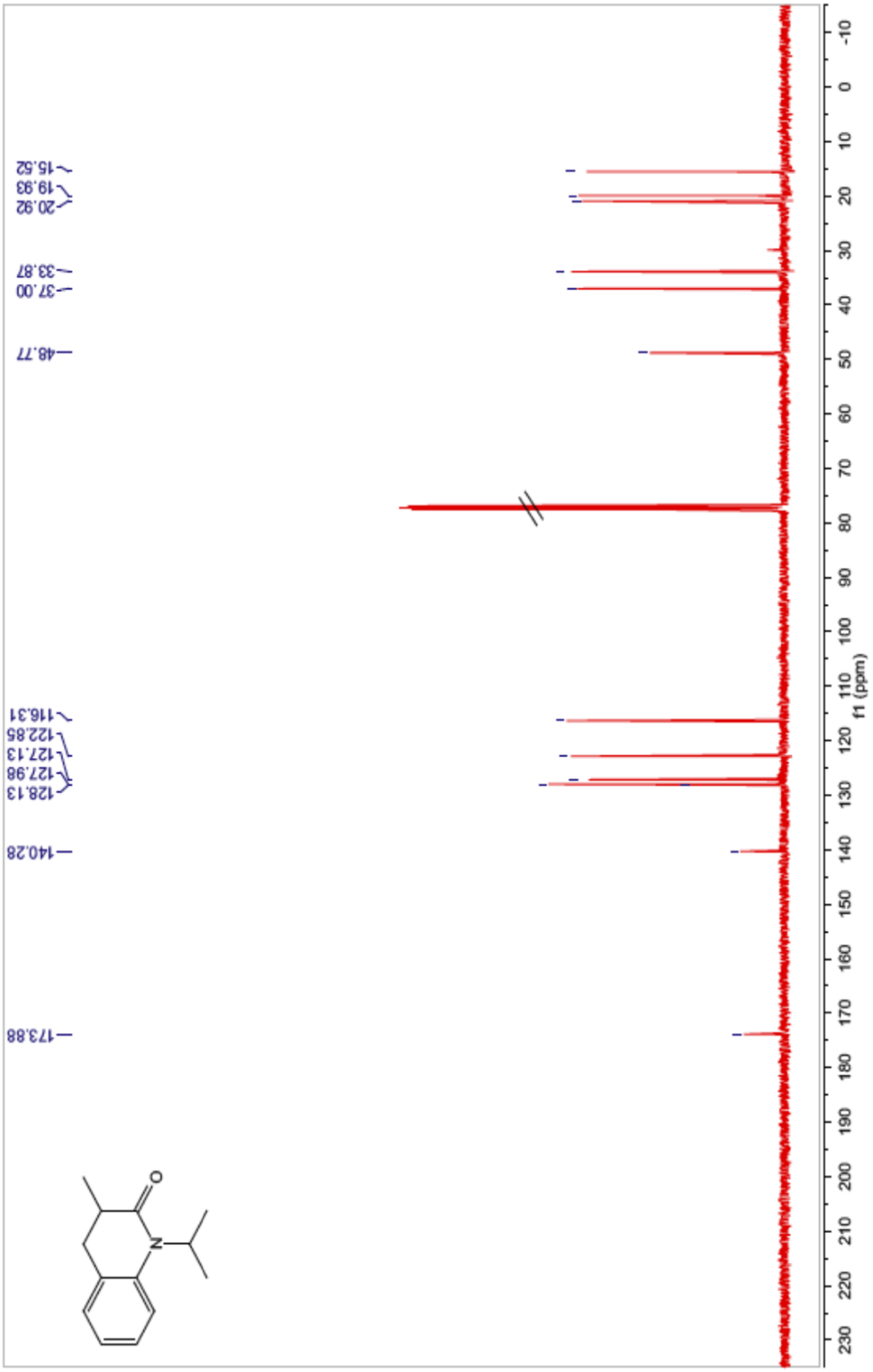
^{1}H NMR (400 MHz, CDCl$_3$, δ ppm)

7.21 – 7.14 (t, *J* = 16, 8 Hz, 1H), 7.15 – 7.05 (m, 2H), 7.0 – 6.92 (t, *J* = 16, 8 Hz, 1H), 4.71 – 4.57 (m, 1H), 2.85 – 2.74 (dd, *J* = 16, 4Hz, 1H), 2.65 – 2.55 (m, 1H), 2.54 – 2.4 (m, 1H), 1.53 – 1.46 (dd, 6H), 1.2 – 1.17 (d, *J* = 4 Hz, 3H)

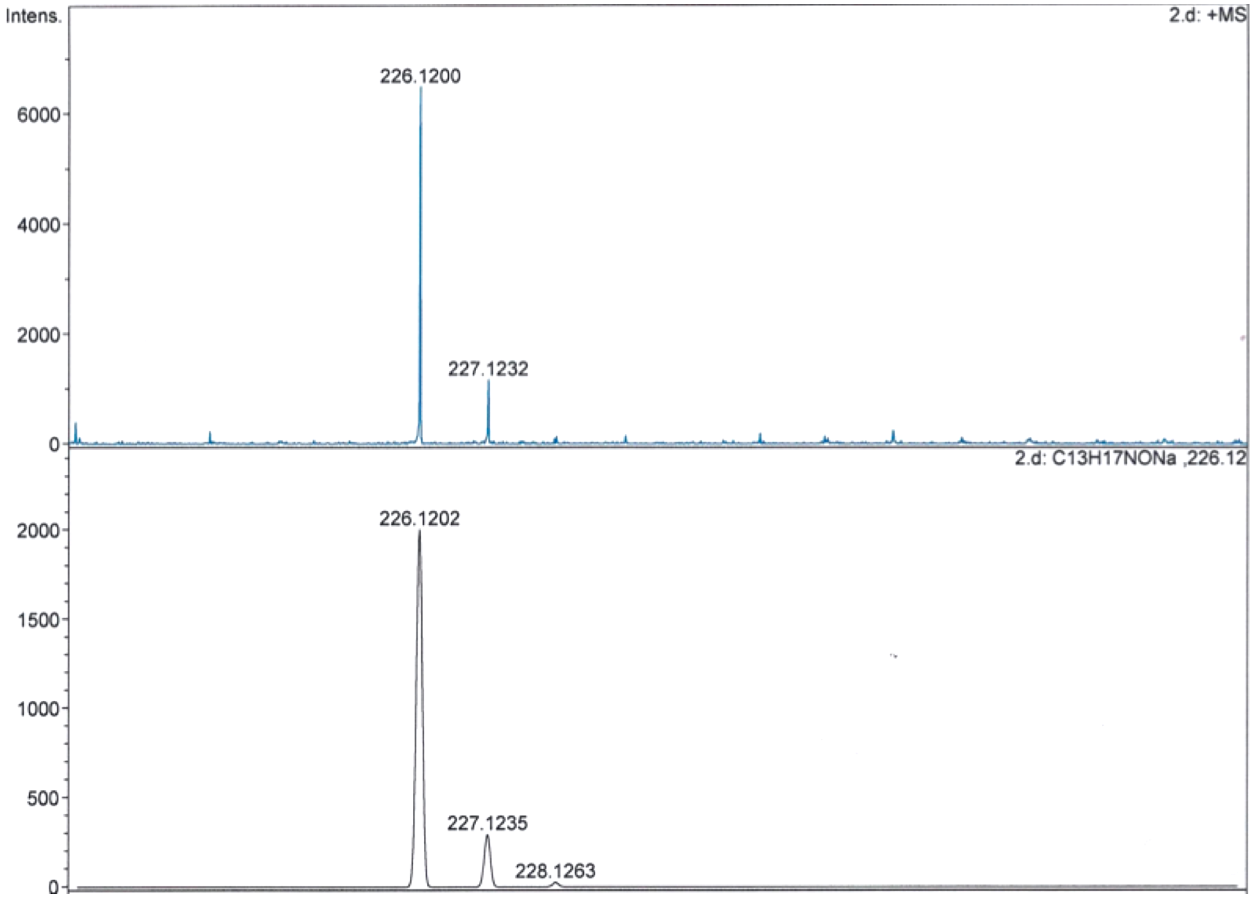

1.18
1.19
1.47
1.48
1.50
1.52
2.45
2.46
2.47
2.48
2.49
2.50
2.57
2.60
2.60
2.63
2.76
2.77
2.80
2.81
4.59
4.61
4.63
4.64
4.66
4.68
4.69
6.94
6.96
6.96
6.98
6.98
7.08
7.10
7.11
7.13
7.17
7.17
7.19
7.19
0.99
1.06
1.06
1.01
0.97
2.01
1.00
3.13
6.18
f1 (ppm)
N
O

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

173.88, 140.28, 128.13, 127.98, 127.13, 122.85, 116.31, 48.77, 37.00, 33.87, 20.92, 19.93, 15.52



HRMS (M+Na$^+$): Observed: 226.1200, Calculated: 226.1202, Δm = 0.9 ppm



Polarimetry:

$2c : [\alpha]_D^{26} = +73.9^o$ **(*c* = 0.046% in CHCl$_3$)**

$ent - 2c : [\alpha]_D^{26} = -78.7^o$ **(*c* = 0.047% in CHCl$_3$)**

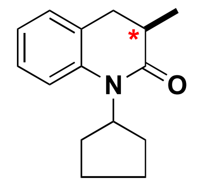
HPLC Analysis Conditions:

Column: (R,R) WHELK–01; Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2; Flow rate: 1 mL/min

Retention time (min): *R*-(+)-**2c:** ~14.1**,** *S*-(-)-**2c:** ~19.8

Characterization of *R*-(+)-2d = *S*-(-)-2d:



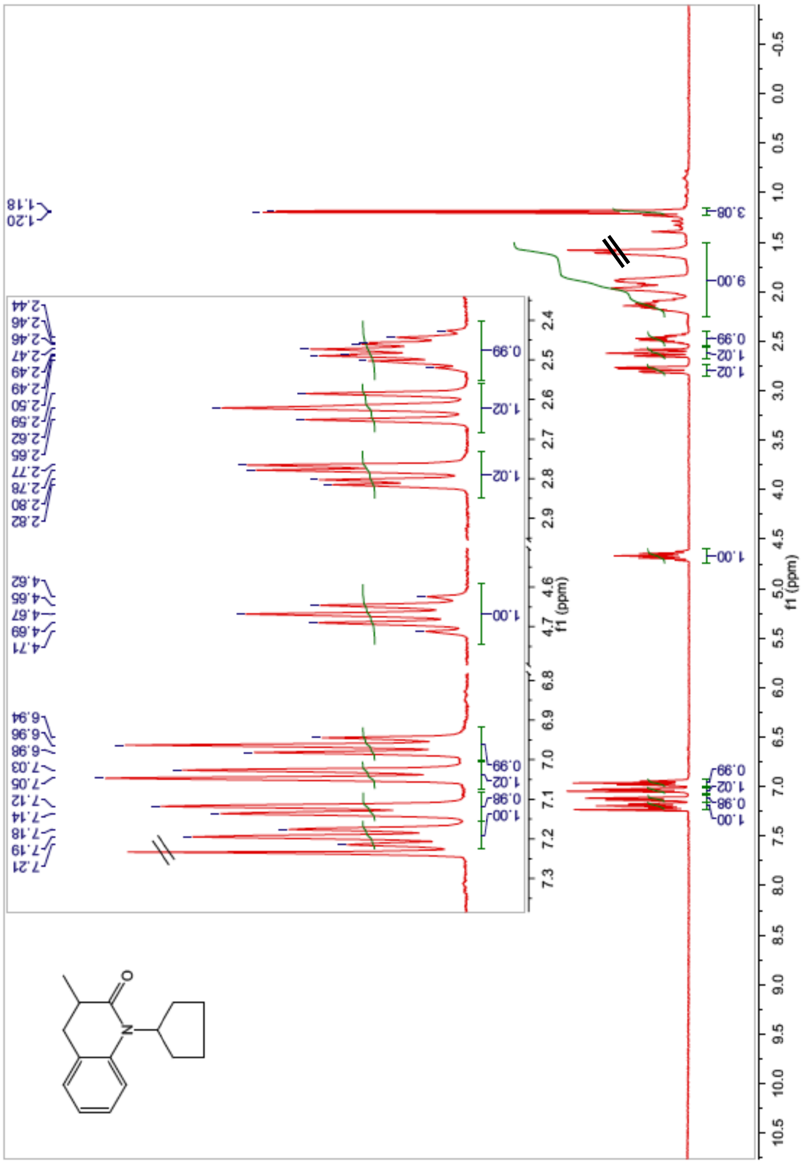
R-(+)-**2d** = *S*-(-)-**2d**

Purification Conditions:

Combiflash®: 12 g silica; flow rate: 20 mL/min; Mobile phase: 12 % EtOAc: Hexanes

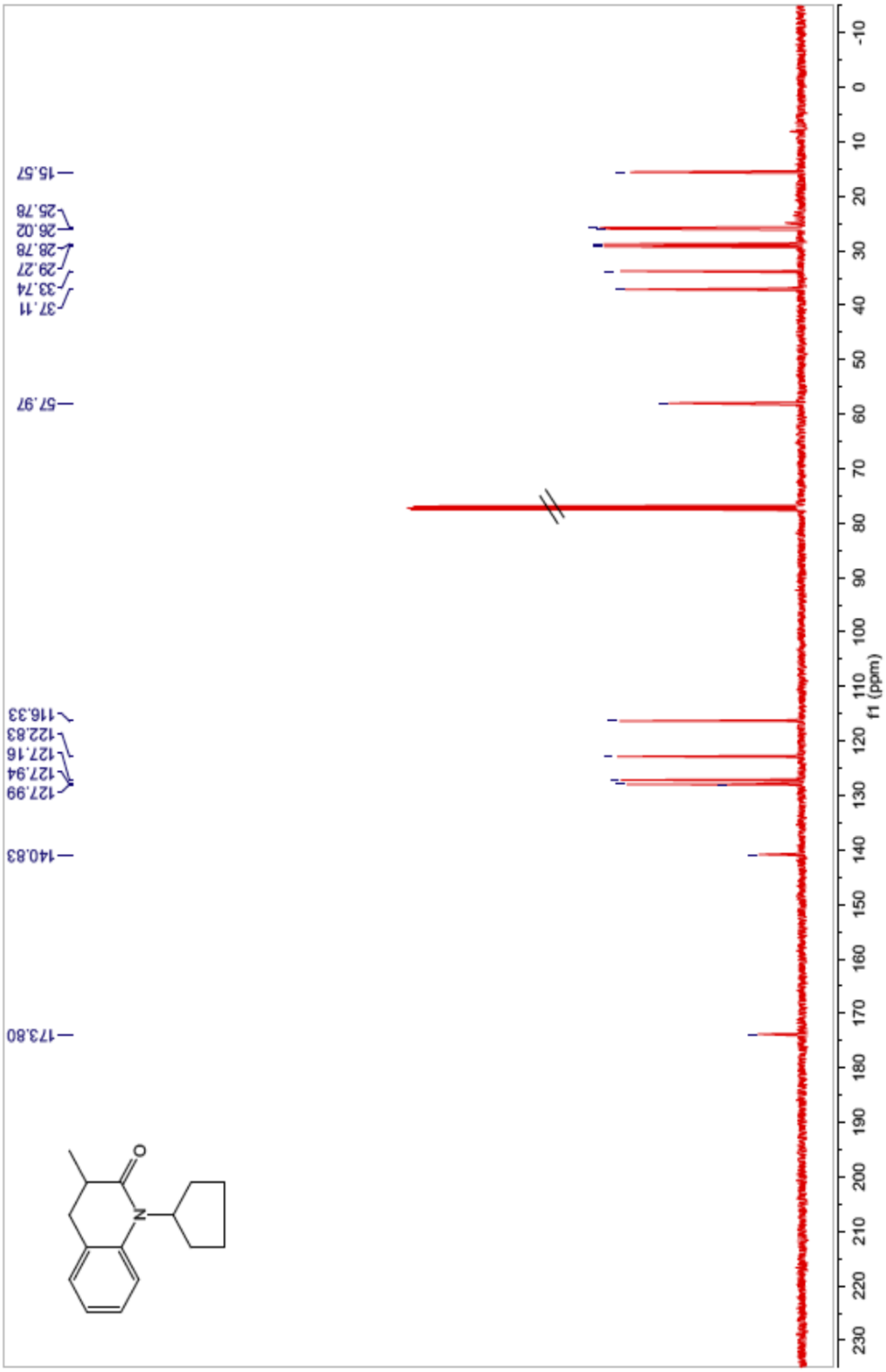
^{1}H NMR (400 MHz, CDCl$_3$, δ ppm)

7.21 – 7.15 (t, *J* = 8, 4Hz, 1H), 7.15 – 7.09 (d, *J* = 8Hz, 1H), 7.08 – 7.01 (d, 8Hz, 1H), 7.0 – 6.93 (t, *J* = 16, 8Hz, 1H), 4.73 – 4.56 (m, 1H), 2.85 – 2.74 (dd, *J* = 16, 8Hz, 1H), 2.68 – 2.55 (t, 1H), 2.54 – 2.4 (m, 1H), 2.3 – 1.5 (m, 8H), 1.22–1.16 (d, *J* = 8Hz, 3H)

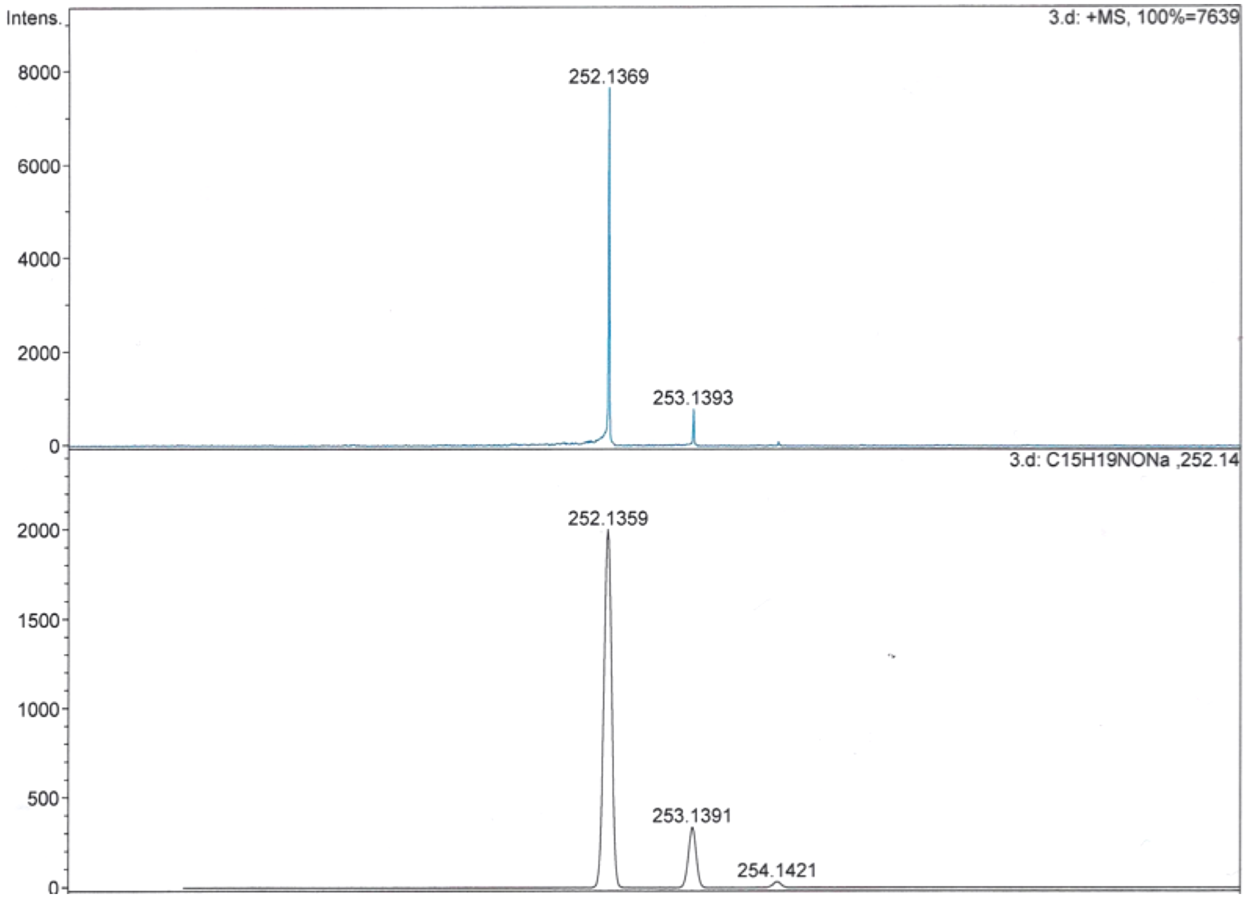


^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

173.80, 140.83, 127.99, 127.94, 127.16, 122.83, 116.33, 57.97, 37.11, 33.74, 29.27, 28.78, 26.02, 25.78, 15.57



HRMS (M+Na$^+$): Observed: 252.1369, Calculated: 252.1359, Δm = 4 ppm



Polarimetry:

$2d : [\alpha]_D^{24} = +51.2^o$ **(*c* = 0.098% in CHCl$_3$)**

$ent - 2d : [\alpha]_D^{24} = -54.0^o$ **(*c* = 0.1% in CHCl$_3$)**

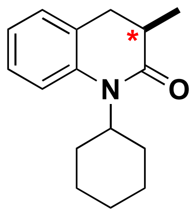
HPLC Analysis Conditions:

Column: (R,R) WHELK–01; Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2; Flow rate: 1 mL/min

Retention time (min): ***R*-(+)-2d:** ~14.8**, *S*-(-)-2d:** ~20.00

Characterization of *R*-(+)-2e = *S*-(-)-2e:



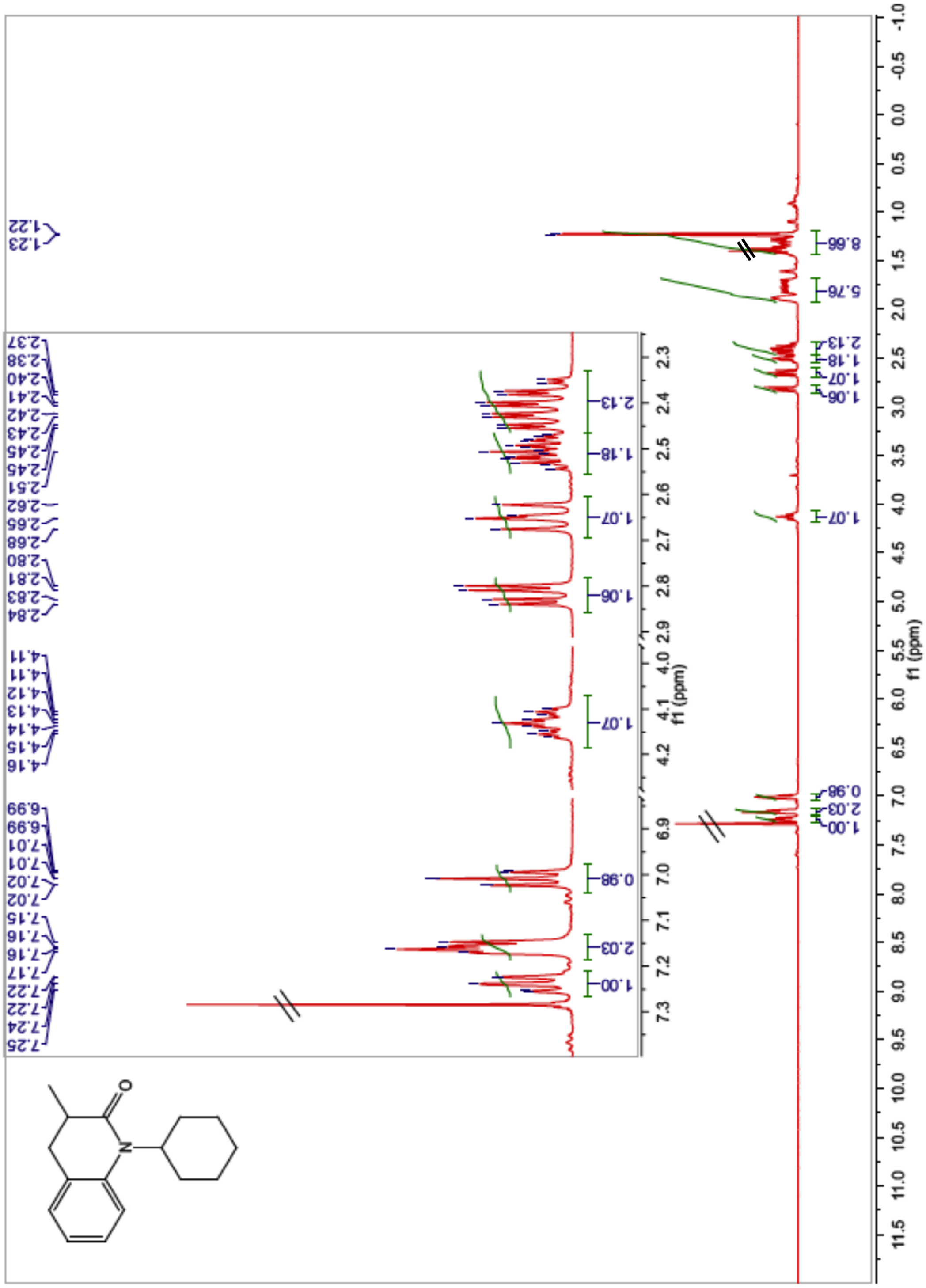
R-(+)-**2e** = *S*-(-)-**2e**

Purification Conditions:

Combiflash$^{\circledR}$: 12 g silica; flow rate: 20 mL/min; Mobile phase: 9 % EtOAc: Hexanes

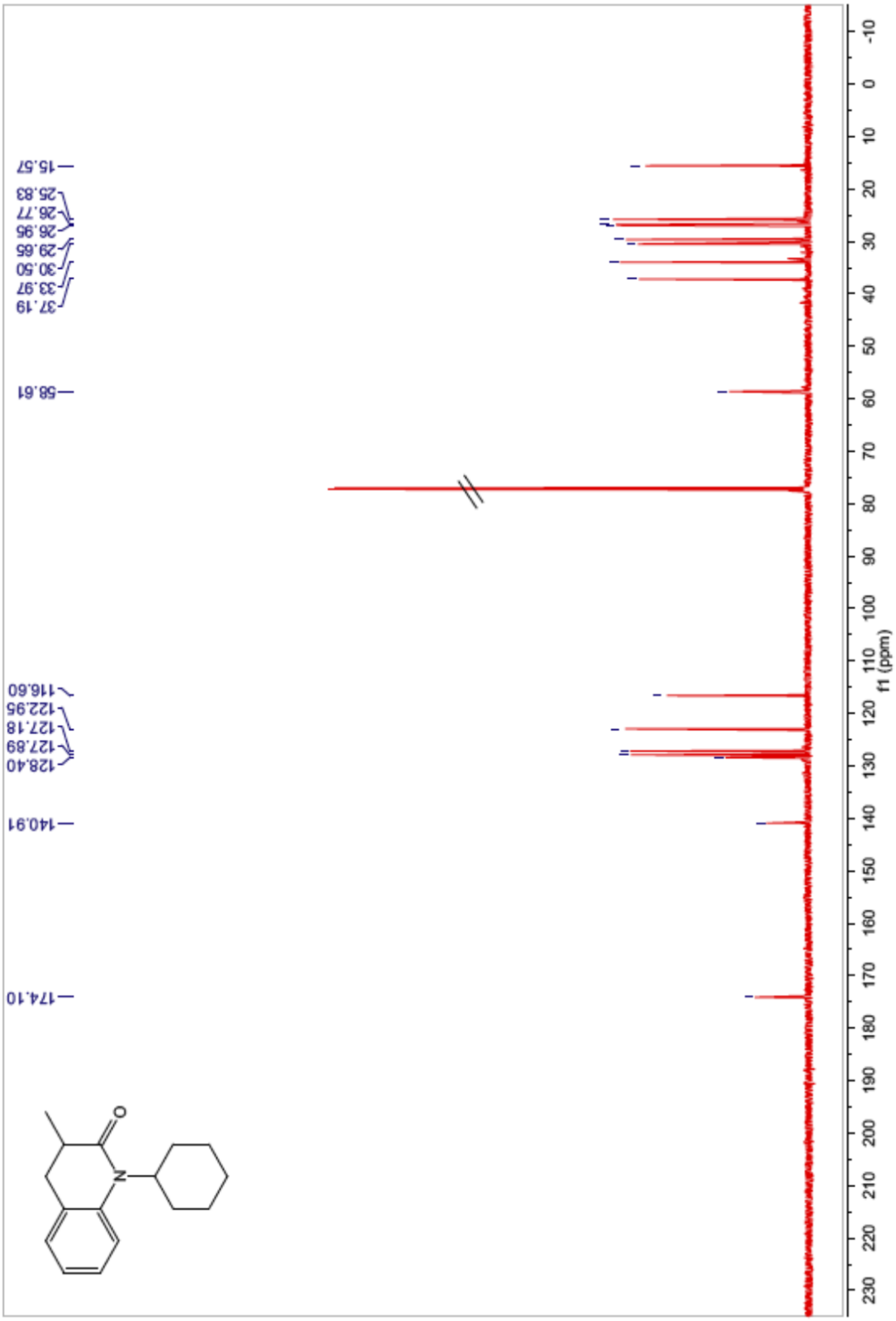
^{1}H NMR (400 MHz, CDCl$_3$, δ ppm)

7.25 – 7.2 (t, 1H), 7.2 – 7.12 (m, 2H), 7.04 – 6.95 (t, 1H), 4.18 – 4.05 (m, 1H), 2.85 – 2.76 (dd, *J* = 12, 4Hz, 1H), 2.7 – 2.6 (t, 1H), 2.55 – 2.45 (m, 1H), 2.45 – 2.31 (m, 2H), 2.0 – 1.2 (m, 11H)

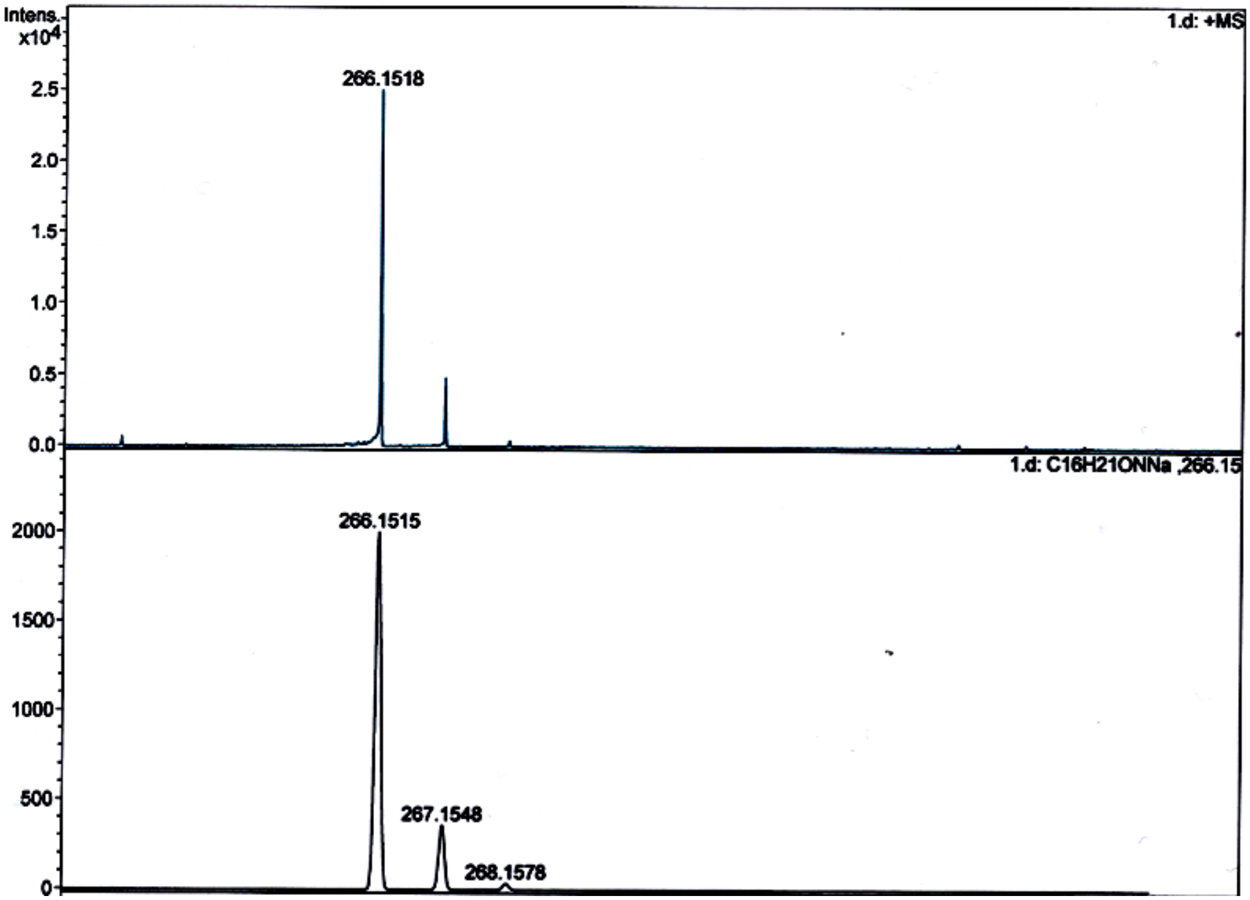

1.22
1.23
2.37
2.38
2.40
2.41
2.42
2.43
2.45
2.45
2.51
2.62
2.65
2.68
2.80
2.81
2.83
2.84
4.11
4.11
4.12
4.13
4.14
4.15
4.16
6.99
6.99
7.01
7.01
7.02
7.02
7.15
7.16
7.16
7.17
7.22
7.22
7.24
7.25
8.66
5.76
2.13
1.18
1.07
1.06
1.07
0.98
2.03
1.00
N
O
f1 (ppm)

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm)

174.10, 140.91, 128.40, 127.89, 127.18, 122.95, 116.60, 58.61, 37.19, 33.97, 30.50, 29.65, 26.95, 26.77, 25.83, 15.57



HRMS ($M+Na^+$): Observed: 266.1518, Calculated: 266.1515, Δm = 1.1 ppm



Polarimetry:

$2e : [\alpha]_D^{27} = +60.0^o$ **(*c* = 0.02% in $CHCl_3$)**

$ent-2e : [\alpha]_D^{28} = -72.0^o$ **(*c* = 0.025% in $CHCl_3$)**

HPLC Analysis Conditions:

Column: CHIRALPAK® IC; Abs. detector: 254 nm and 270 nm

Mobile phase: Hexanes:IPA = 98:2; Flow rate: 1 mL/min

Retention time (min): ***R*-(+)-2e:** ~11.35**, *S*-(-)-2e:** ~12.82

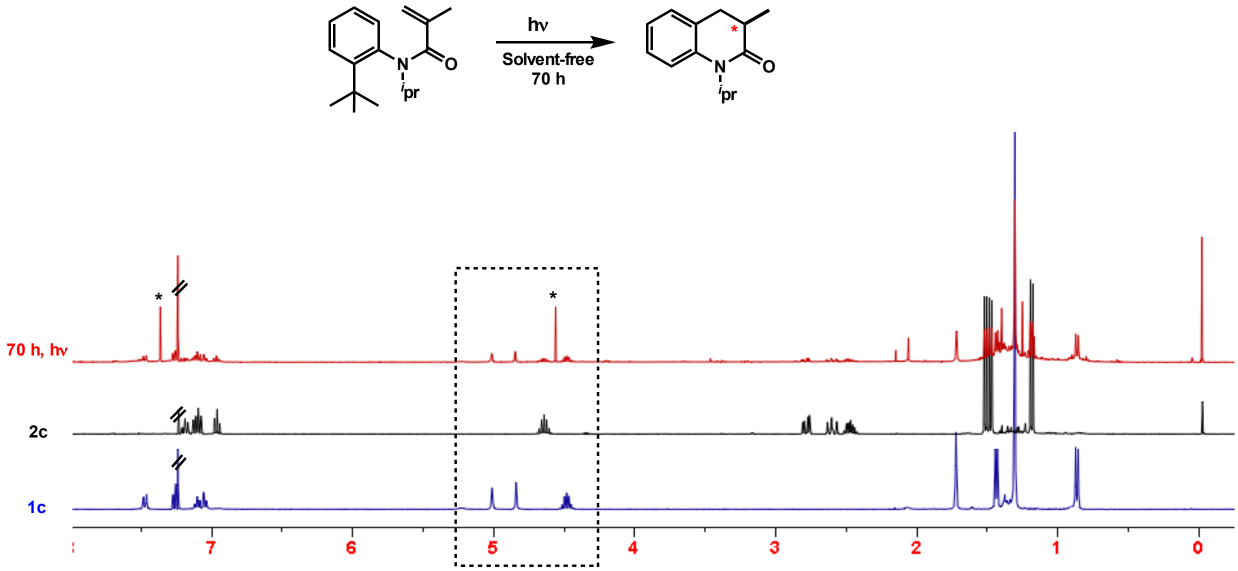
5) Absolute Photoconversion by ^{1}H NMR

Substrate **1c** was recrystallized in a 13 mm pyrex tube and irradiated (450 W medium pressure Hg lamp) for 70 h at room temperature. The sample was then dissolved in 1 mL of $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy with α,α'-dichloro-*p*-xylene, as an internal standard.

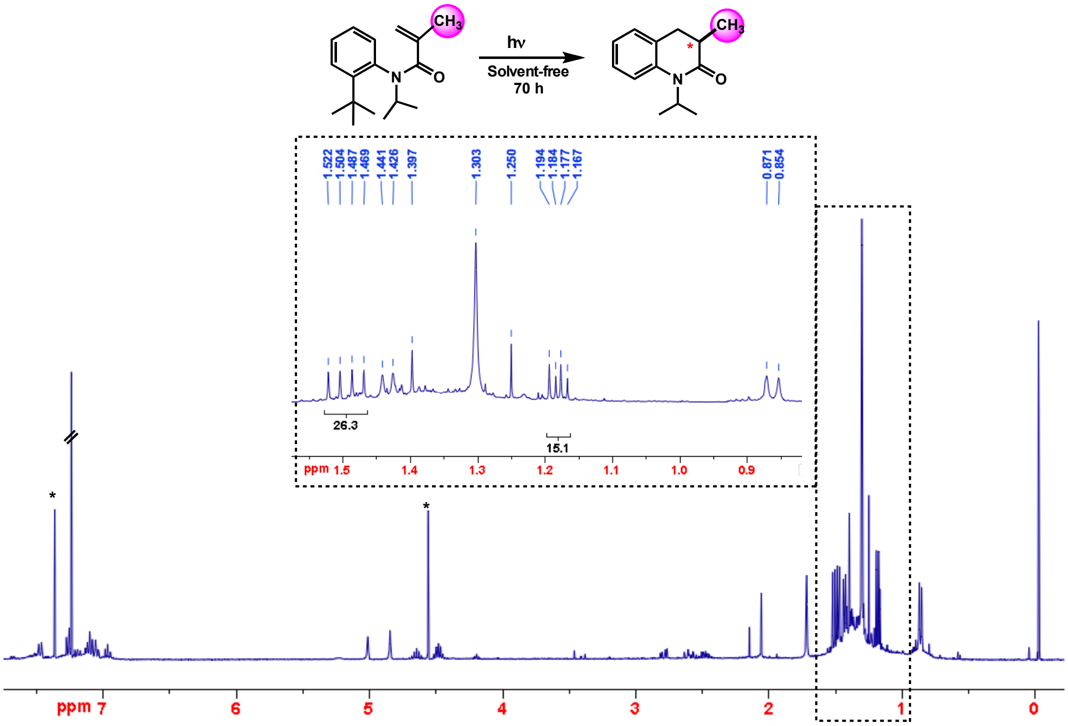
The number of moles of analyte (product or starting material) in the NMR aliquot is given by the following equation:[4,5]

$$mol_a = mol_i \times \left(\frac{Integral(analyte)}{Integral(Int\,Std.)}\right) \times \frac{N_i}{N_a}$$

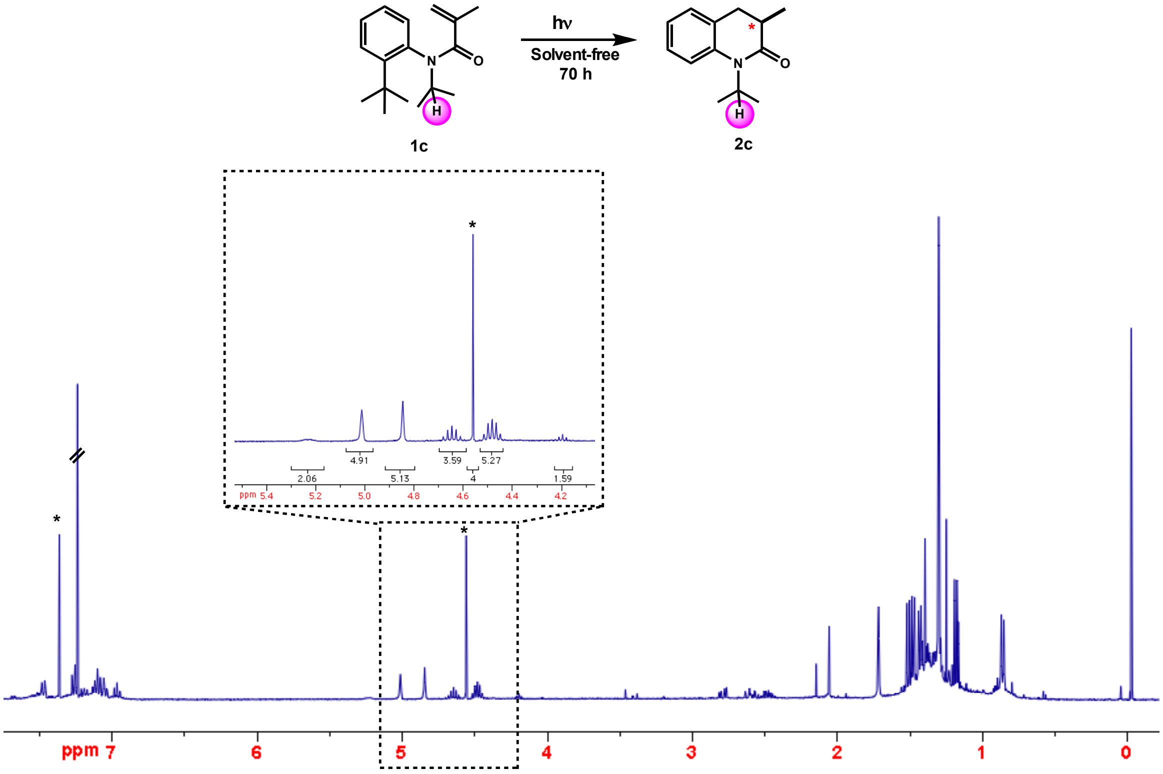
Where N_a and N_i are the number of nuclei giving rise to the relevant analyte and standard signals respectively.



* = Intenal Standard



* = Intenal Standard



* = Intenal Standard

1c initial mass is 8.5 mg.

1c concentration in 1 mL of $CDCl_3$ is 3.93×10^{-2} M (3.93×10^{-5} mol)

Internal Standard concentration in 1 mL of $CDCl_3$ is 3.37×10^{-3} M (3.37×10^{-6} mol)

$$mol_{2c} = 3.37 \times 10^{-6} \times \left(\frac{3.59}{4}\right) \times \frac{4}{1} = 1.21 \times 10^{-5}\, mol$$

$$mol_{1c} = 3.37 \times 10^{-6} \times \left(\frac{6.77}{4}\right) \times \frac{4}{1} = 2.31 \times 10^{-5}\, mol$$

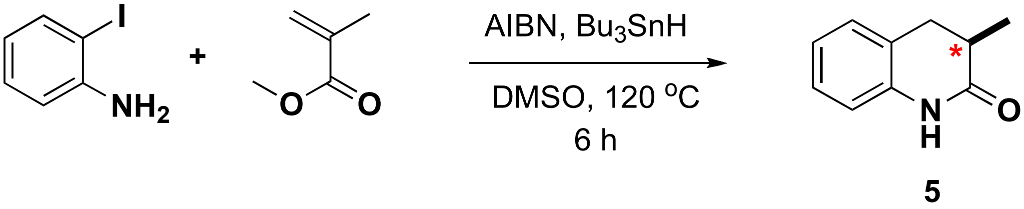
$Mass_{2c}$ = 2.46 mg

$Mass_{1c}$ = 6 mg

Absolute Conversion is 52 %

Mass Balance = 89.6%

6) Synthesis and characterization of quinolinone **5**

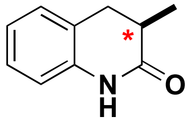


Scheme S4: Synthesis of quinolinone **5**

Synthesis of **5** was performed by synthetic procedure as detailed by by Zhou *and* co-workers.[6]

In a typical reaction, 2-iodoaniline (1 equi., 1 g, 4.57 mmol) was dissolved in 15 mL of DMSO. To the reaction mixture, methyl methacrylate (4 equi., 1.95 mL, 18.26 mmol), AIBN (4 equi., 3 g, 18.26 mmol), and Bu_3SnH (1.5 equi., 1.82 mL, 6.85 mmol) were slowly added. The mixture was heated at 140 °C with stirring. After 6 h, the reaction mixture was cooled to room temperature and quenched with 15 mL of DI water. The organic phase was extracted with 3 x 15 mL of EtOAc; the combined organic fraction was washed with brine solution and dried over *anhy.* Na_2SO_4. The expected product crude **5** was concentrated by roto-evaporation and purified by flash chromatography using Combiflash®: 12 g silica (RediSep Column); flow rate: 22 mL/min; Mobile phase: 28 % EtOAc: Hexanes.

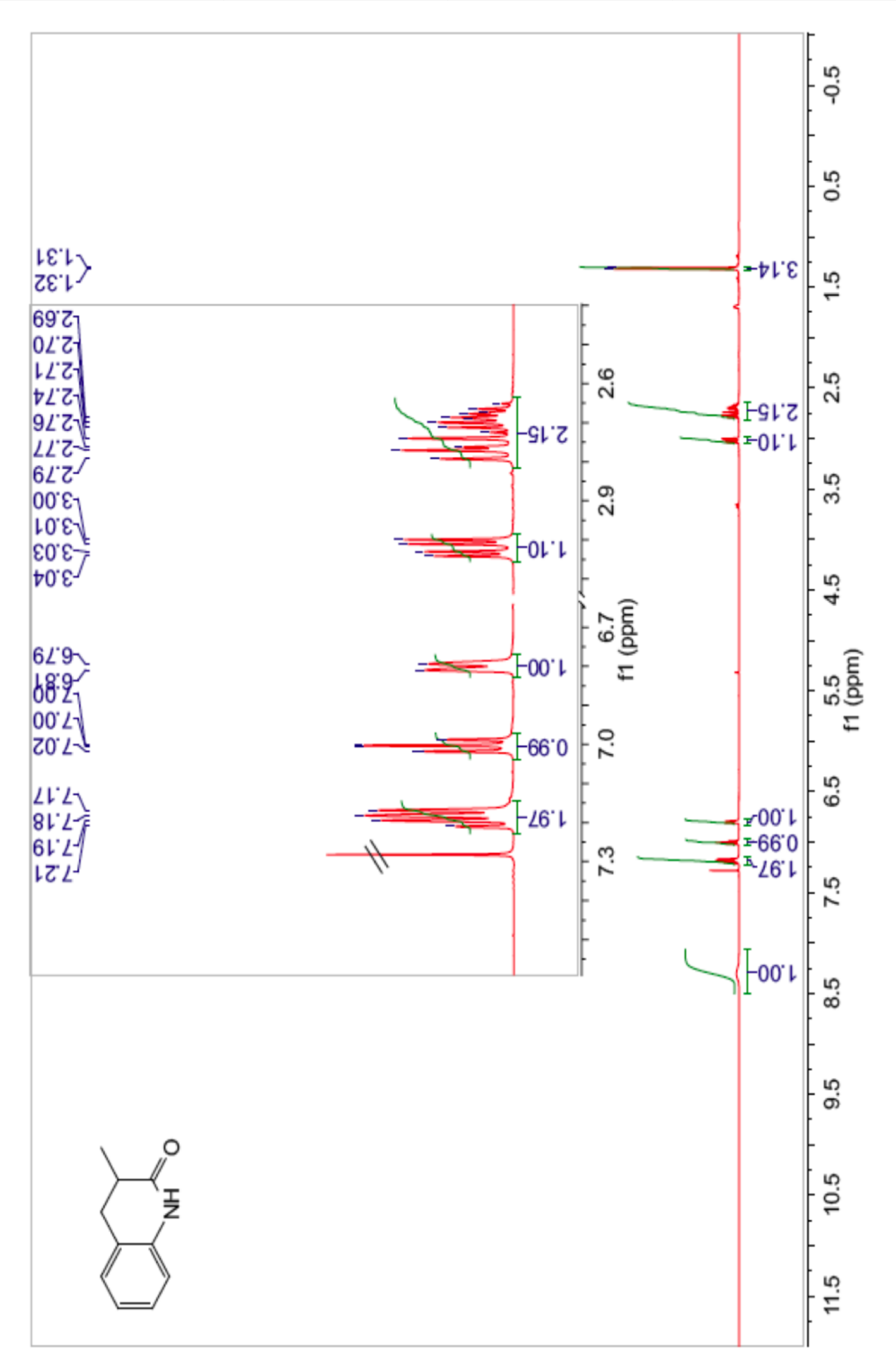
Characterization of 5:



5

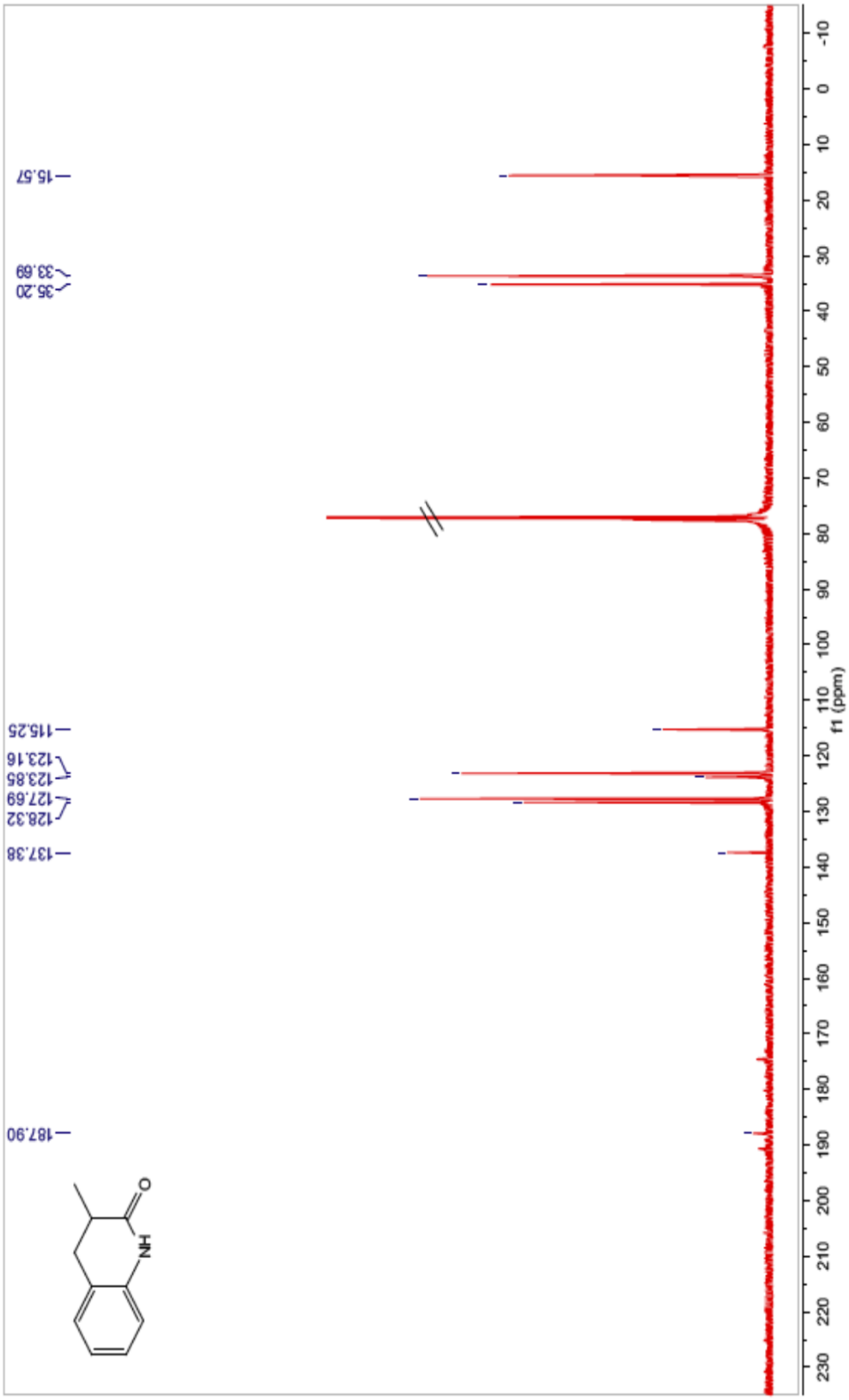
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm)

8.5 – 8.1 (br s, 1H), 7.22 – 7.15 (m, 2H), 7.03 – 6.98 (t, *J* = 8Hz, 1H), 6.83 – 6.77 (d, *J* = 8 Hz, 1H), 3.05 – 2.98 (dd, *J* = 12, 4 Hz, 1H), 2.8 – 2.63 (m, 2H), 1.35 – 1.3 (d, *J* = 4 Hz, 3H)



^{13}C NMR (100 MHz, CDCl$_3$, δ ppm)

187.90, 137.38, 128.32, 127.69, 123.85, 123.16, 115.25, 35.20, 33.69, 15.57

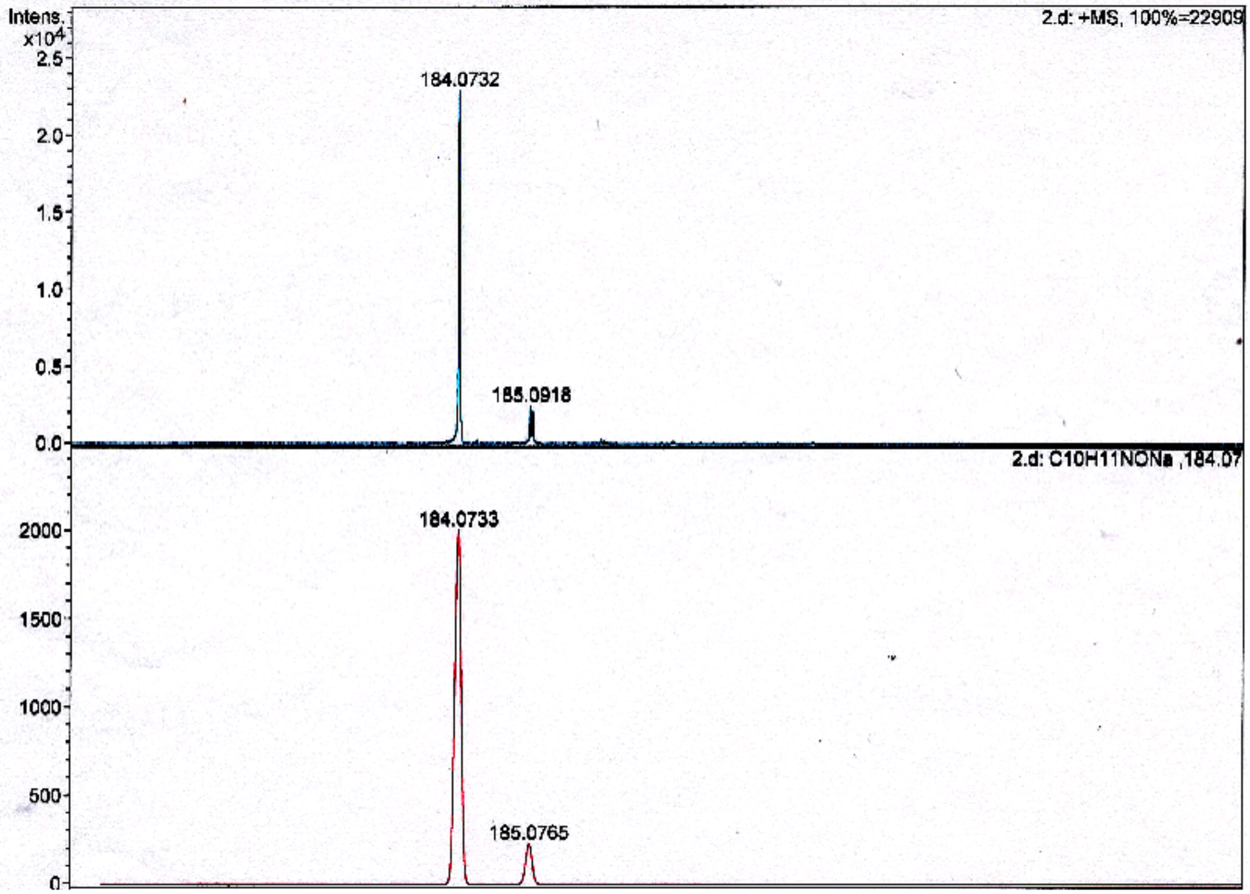


Polarimetry:

***R*-(+)-5:** $[\alpha]_D^{28}$ = +54.2 ° (*c* = 0.12% in $CHCl_3$)

***S*-(-)-5:** $[\alpha]_D^{28}$ = -49.5 ° (*c* = 0.11% in $CHCl_3$)

HRMS (M+Na$^+$): Observed: 184.0732; Calculated: 184.0733; Δm = 0.5 ppm



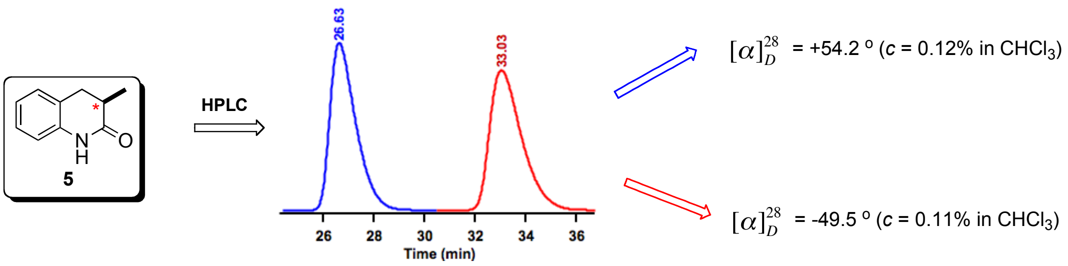
HPLC Analysis Conditions:

Column: (R,R) WHELK–01; Abs. detector: 254 nm and 270 nm

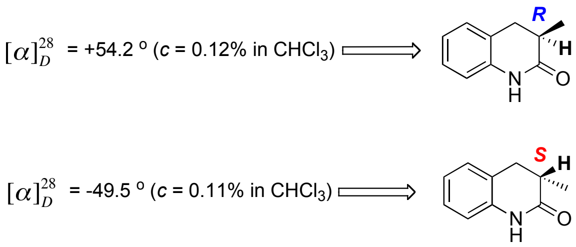
Mobile phase: Hexanes:IPA = 98:2;

Flow rate: 1 mL/min for analysis and 4 mL/min for separation

Retention time (min): ***R*-(+)-5:** ~26.6**,** ***S*-(-)-5:** ~33.03



The enantiomers of NH-Quinolinone **5** was separated by HPLC. The sign of the optical rotation of the individual enantiomers was compared with reported values in literature to ascertain the absolute configuration of 5.[7]

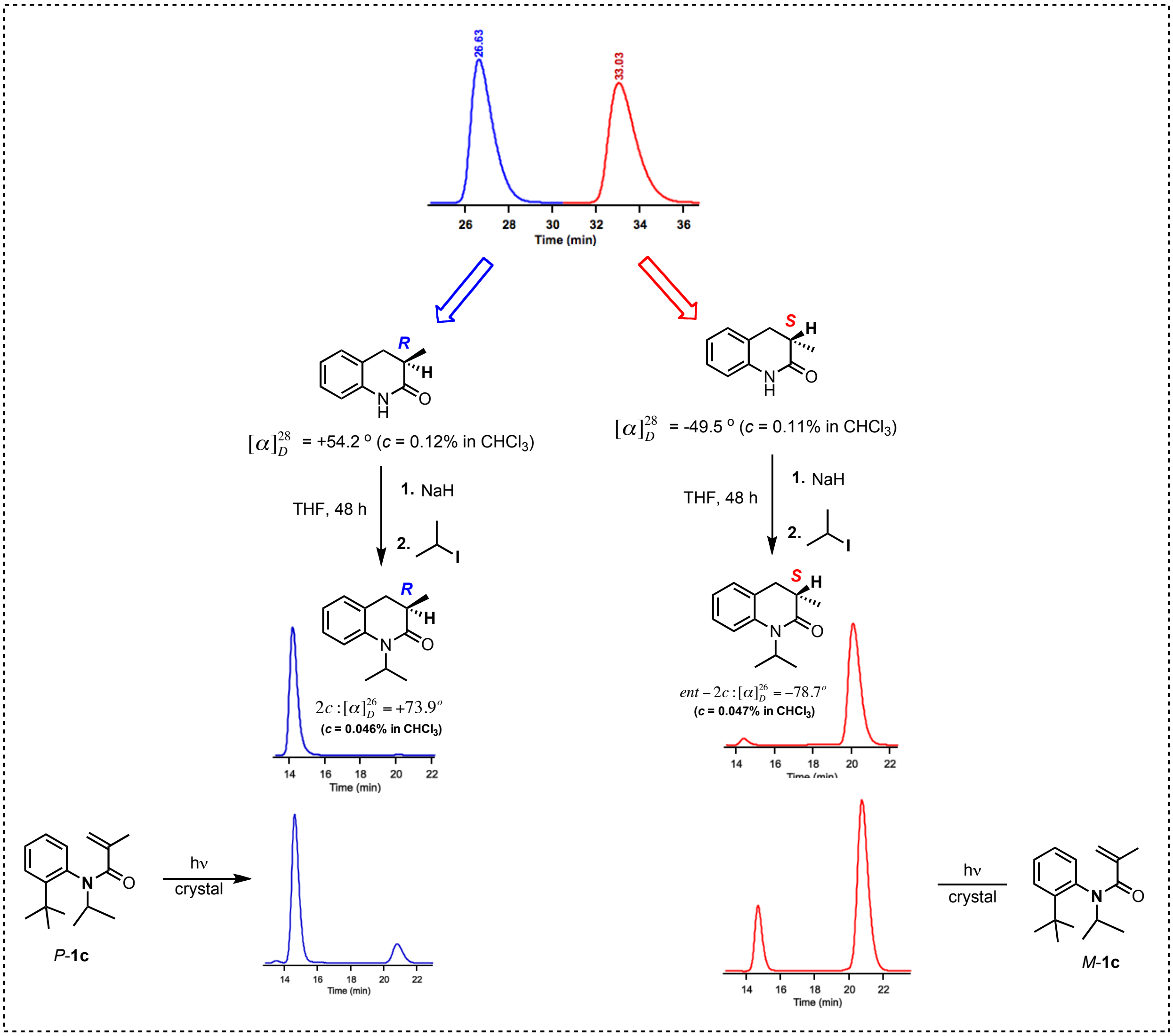


Scheme S5: Independent study to decipher the absolute configuration of enantiomeric photoproduct(s)

Photoproduct **2c-e** were independently synthesized according to reported procedures[8] using optically pure enantiomers of **5** that were separated by HPLC.

R-**2c** or *S*-**2c:** Optically pure enantiomers of **5** were dissolved in a minimum of dry THF. 3 equiv. of NaH was added to the solution followed by addition of 2-iodopropane. The reaction was followed by TLC for 48 h. After, the reaction was quenched and the corresponding optically pure isomer of **2c** was isolated with EtOAc and purified by chromatography: 15 % EtOAc:Hexanes on 25x25 cm^2 TLC plate.

The retention time of the individual enantiomer of **2c** was matched with the photoproducts obtained upon irradiation of optically pure crystals to ascertain the absolute configuration from crystal irradiation.

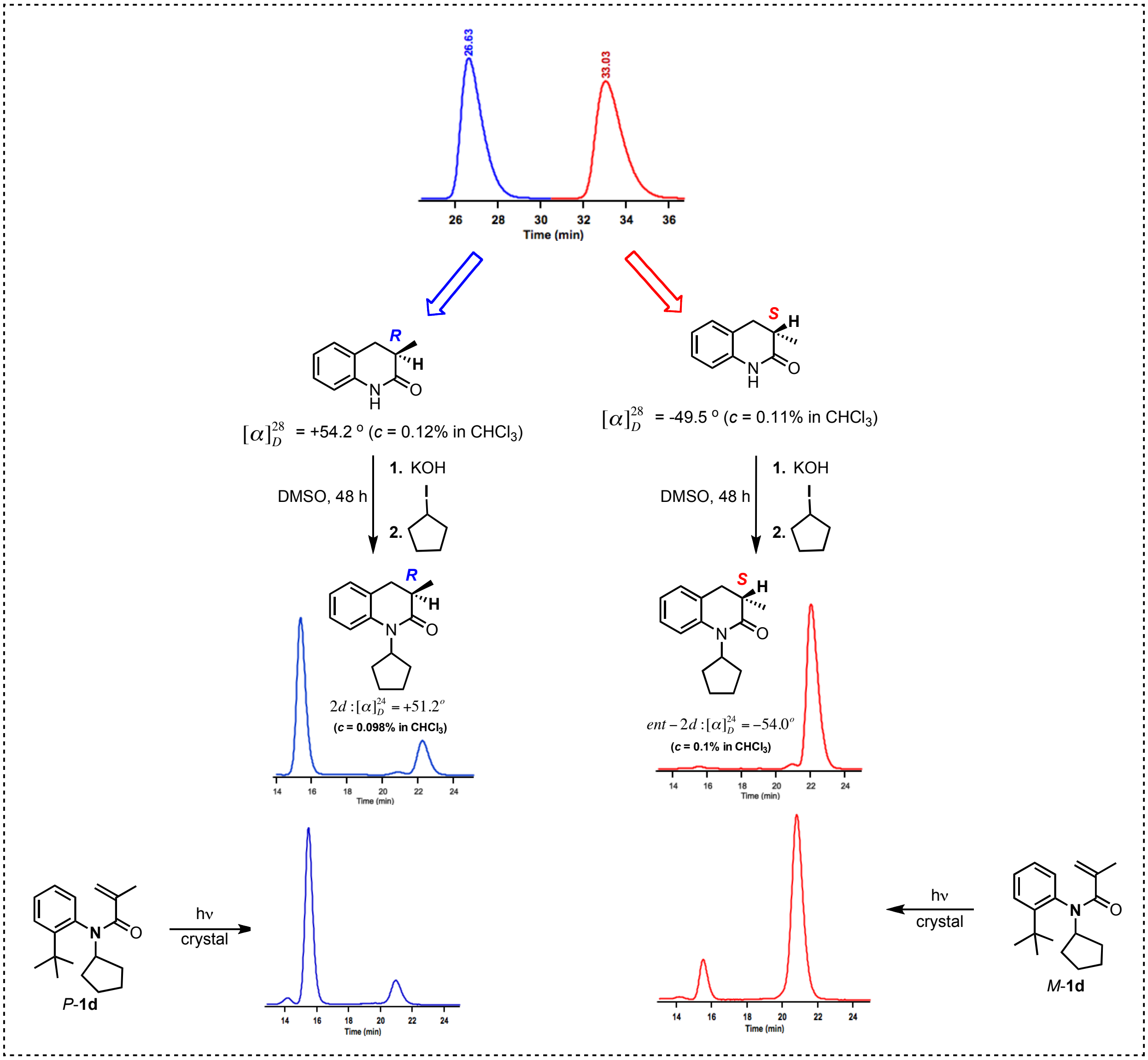


Scheme S5: Independent synthesis of enantiomers of **2c** followed by polarimetry and assignment of absolute configuration

The HPLC retention time of the optically pure isomer with known absolute configuration was matched with HPLC retention times of the photoproducts obtained upon irradiation of optically pure crystals of **1c** (*P*-**1c** or *M*-**1c**)

R-**2d** or *S*-**2d:** Optically pure enantiomers of **5** were dissolved in a minimum of DMSO. 2 pellets of KOH were added to the solution followed by addition of iodocyclopentane; The solution was heated at 48 °C; the reaction was monitored by TLC for 48 h. After, the reaction was quenched and the expected optically pure isomers of **2d** were isolated with diethyl ether and purified by chromatography: 15 % EtOAc:Hexanes on 25x25 cm TLC plate.

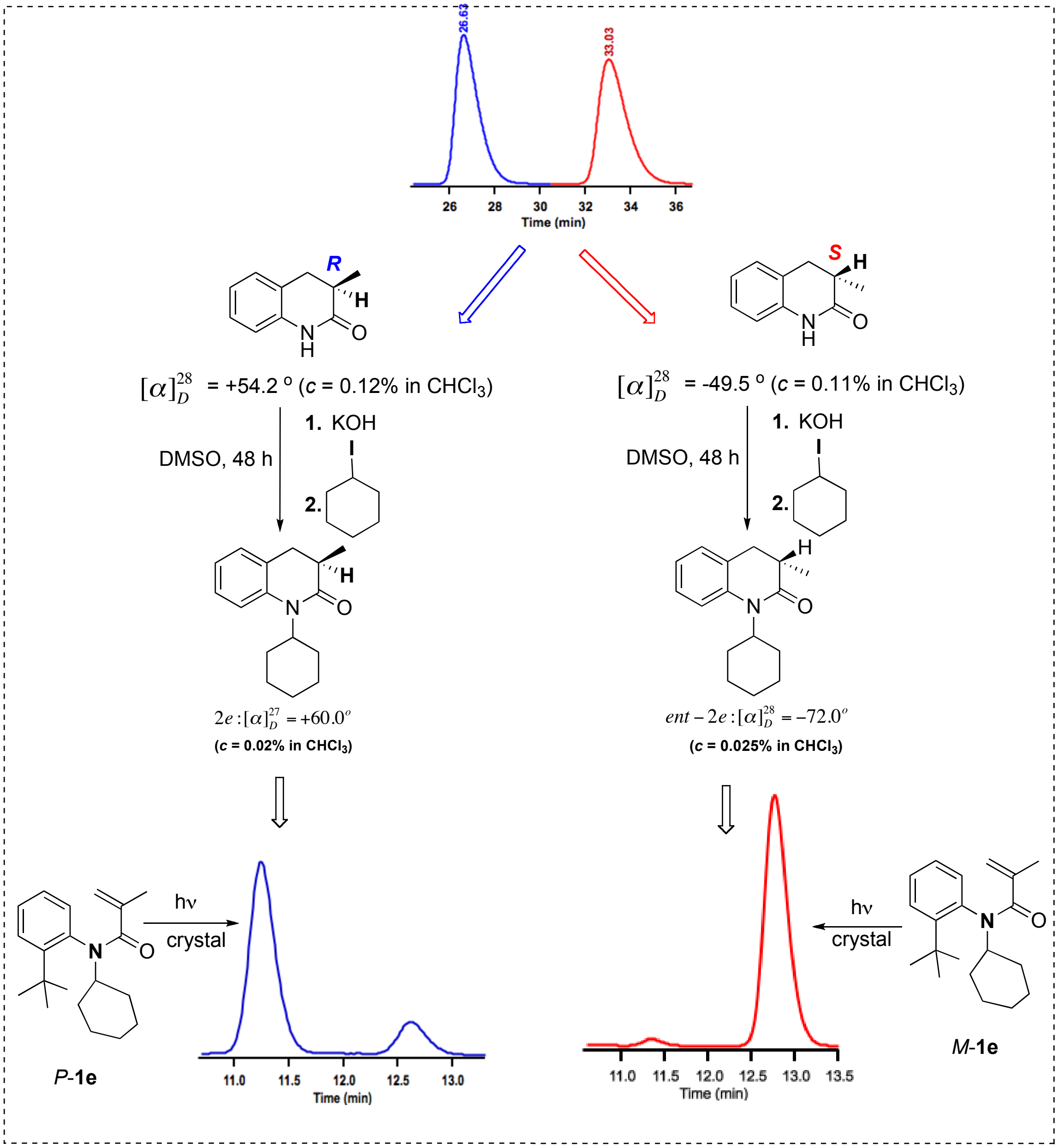
The retention time of the individual enantiomer of **2d** was matched with the photoproducts obtained upon irradiation of optically pure crystals to ascertain the absolute configuration from crystal irradiation.



Scheme S6: Independent synthesis of enantiomers of **2d** followed by polarimetry and assignment of absolute configuration

R-**2e** or *S*-**2e:** Optically pure enantiomers of **5** were separately dissolved in a minimum of DMSO. 2 pellets of KOH were added to the solution followed by addition of iodocyclohexane; the solution was heated at 48°C. The reaction was monitored by TLC for 48 h. After, the reaction was quenched and the expected optically pure isomers of **2e** were isolated with diethyl ether and purified by chromatography: 15 % EtOAc:Hexanes on 25x25 cm^2 TLC plate.

The retention time of the individual enantiomer of **2e** was matched with the photoproducts obtained upon irradiation of optically pure crystals to ascertain the absolute configuration from crystal irradiation.



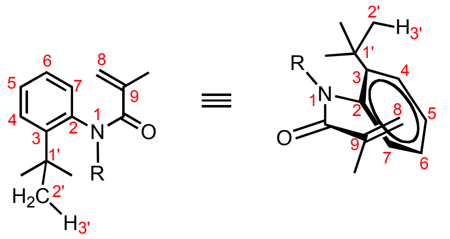
Scheme S7: Independent synthesis of enantiomers of **2e** followed by polarimetry and assignment of absolute configuration

7) X-Ray Crystallography Parameters

Structure determination: Single crystal X-ray diffraction data of compound 1c was collected on a SIEMENS diffractometer with a 1K CCD area detector (graphite-monochromated Mo Kα-radiation). The structures were solved by direct methods and refined on *F*2 using the SHELXTL V6.14 package (after absorption corrections with SADABS).
Single crystal X-ray diffraction data sets of 1d, M-1e and P-1e were collected on a Bruker Apex Duo diffractometer with a Apex 2 CCD area detector. Cu radiation was used for all 3 data sets. The structures were process with Apex 2 v2010.9-1 software package (SAINT v. 7.68A, XSHELL v. 6.3.1). Direct method was used to solve the structures after multi-scan absorption corrections. Details of all four data collections and refinements are given in the table below.

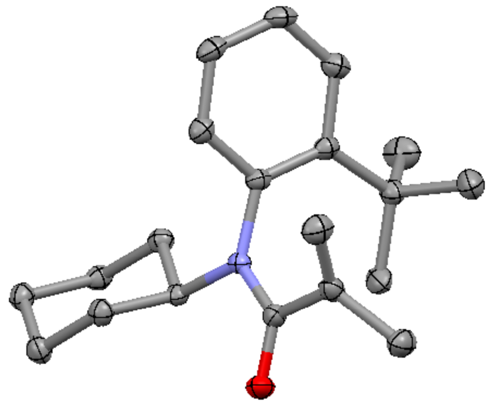
	1c	1d	M-1e	P-1e
Formula	$C_{17}H_{25}NO$	$C_{19}H_{27}NO$	$C_{20}H_{29}NO$	$C_{20}H_{29}NO$
FW	259.38	285.42	299.44	299.44
cryst. size [mm]	.22 x .40 x .58	.06 x .09 x .011	.09 x .13 x .16	.09 x .13 x .16
cryst. system	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic
Space Group, Z	C_c, 4	$P2_1/c$, 4	$P2_12_12_1$, 4	$P2_12_12_1$, 4
a [Å]	8.7219(13)	11.2894(3)	8.7688(10)	8.7698(5)
b [Å]	14.862(2)	8.7386(2)	11.3647(14)	11.3683(7)
c [Å]	12.6513(18)	17.1678(4)	17.512(2)	17.5191(10)
α [Å]	90	90	90	90
ß [Å]	99.836(4)	105.623(1)	90	90
γ [Å]	90	90	90	90
V [Å^3]	1615.8(4)	1631.09(7)	1745.2(4)	1746.61(18)
ρ_{calc} [g/cm^3]	1.066	1.162	1.140	1.139
μ [cm^{-1}]	0.065	0.540	.526	.525
F(000)	568	624	656	656
no of measured refl.	6999	21695	13484	11331
no of indep. refl.	3366	2899	3004	3080
no of refl. ($I \geq 2\sigma$)	2910	2788	2953	3033
Resolution [Å]	.78	.83	.84	.84
R1/wR2 ($I \geq 2\sigma$)[a] [%]	4.16/11.34	3.60/9.11	2.61/7.01	2.53/6.51
R1/wR2 (all data) [%]	4.97/12.15	3.71/9.20	2.66/7.05	2.59/6.56

[a]] $R1 = \Sigma||F_O| - |F_C|| / \Sigma|F_O|$, $wR2 = \{[\Sigma[(F_O)^2 - (F_C)^2]^2] / [\Sigma w(F_o^2)^2]\}^{1/2}$ for $F_o^2 > 2\sigma(F_o^2)$, $w = [\sigma^2(F_O)^2 + (AP)^2 + BP]^{-1}$ where $P = [(F_O)^2 + 2(F_C)^2] / 3$; Compound 1c: A (B) = 0.0782 (0.1202), 1d: A (B) = 0.0437 (0.6553), M-1e: A (B) = 0.0466 (0.2206), P-1e: A (B) = 0.0323 (0.2778)



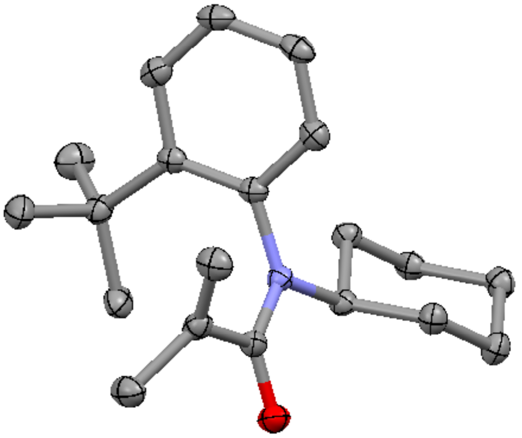
Compounds	R	*d*[C$_8$ – C$_3$] (Å)	*d*[C$_8$ – C$_7$] (Å)	*d*[C$_8$ – H$_{3'}$] (Å)
P-**1e**	cyH	3.630	3.362	2.856
M-**1e**	cyH	3.628	3.359	2.860
1d	cyP	3.983	3.338	2.994
1c	^{i}pr	3.502	3.328	2.766

X-ray crystal structure of *P*-**1e** (Hydrogen not shown for clarity).



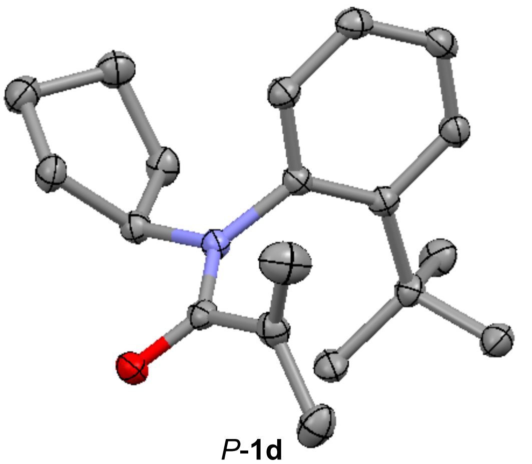
***P*-1e**

X-ray crystal structure of *M*-**1e** (Hydrogen not shown for clarity).

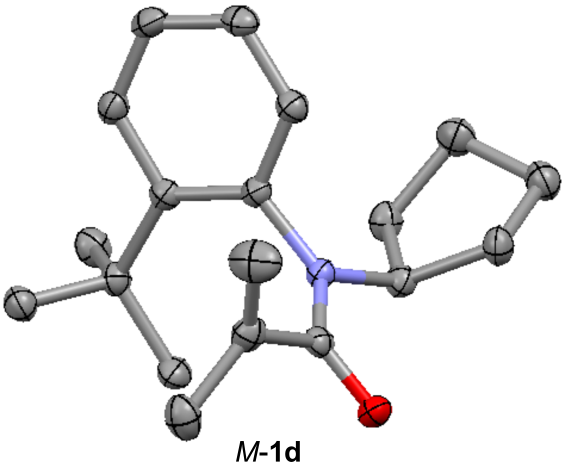


***M*-1e**

X-ray crystal structure of **1d** (both *P* and *M* isomers shown; Hydrogen not shown for clarity).

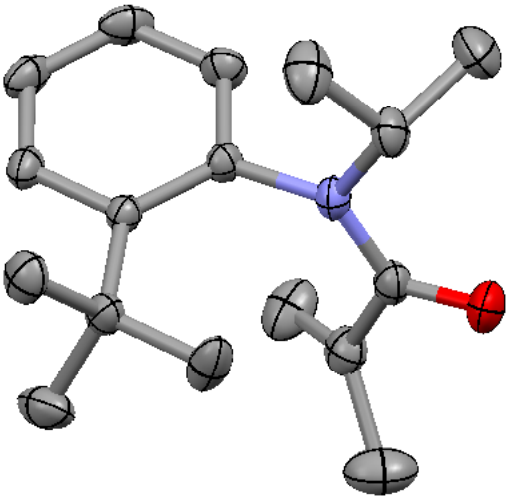


***P*-1d**

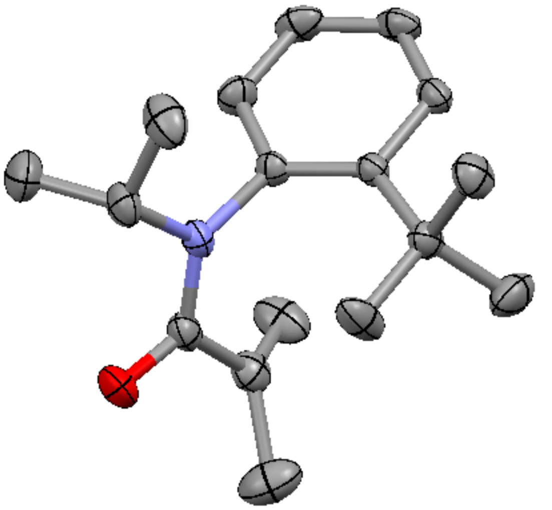


***M*-1d**

X-ray crystal structure of **1c** (both *P* and *M* isomers shown; Hydrogen not shown for clarity).



***P*-1c**



***M*-1c**

8) Reference:

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