

Supporting Information

Enantioselective Activation of Stable Carboxylate Esters as Enolate Equivalents *via* N-Heterocyclic Carbene Catalysts

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I. General Information: Commercially available materials purchased from Alfa Aesar or Aldrich was used as received. CH₂Cl₂ was distilled from CaH₂ and stored over 4 Å molecular sieves. THF was distilled from Na and used directly. α , β -unsaturated imine **2** was synthesized from the reported method.^[1] Proton nuclear magnetic resonance (¹H NMR; 400 MHz) spectra were recorded on a Bruker Avance 400 spectrometer or a JEOL ECA400 (400 MHz) spectrometer in CDCl₃ [using TMS (for ¹H, δ = 0.00) as internal standard]. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ 7.26, singlet). ¹H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (¹³C NMR, 100 MHz) spectra on a Bruker Avance 400 spectrometer in CDCl₃ [using CDCl₃ (for ¹³C, δ = 77.23) as internal standard]. High-resolution mass spectra were obtained with a Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). Flash chromatography was performed using Merck silica gel 60 with distilled solvents. The determination of er was performed *via* chiral HPLC analysis using Shimadzu LC-20AD HPLC workstation. X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffractionmeter. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Jasco P-1030 polarimeter and are reported as follows: $[\alpha]_D^{25}$ (c in g per 100 mL solvent). Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

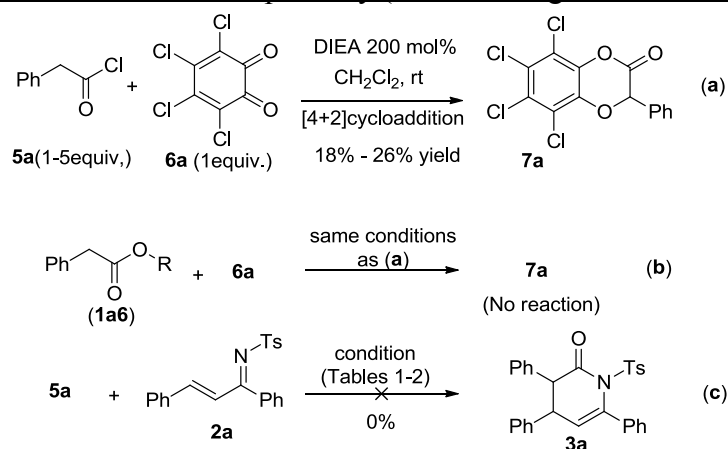
II. General Procedures:

a) Synthesis of carboxylic acid esters (1): A literature method^[2] with simple modifications was used. A solution of the corresponding carboxylic acid (15 mmol) in 10 mL of thionyl chloride was heated to reflux for 2 h. Thionyl chloride was then removed *via* vacuum. The remaining residue was diluted with 20 mL CH₂Cl₂, followed by a dropwise addition of a solution of Et₃N (45 mmol) and 4-Nitrophenol (22.5 mmol) in 10 mL of CH₂Cl₂ at 0 °C. The mixture was allowed to warm to rt and stirred overnight. When the reaction was completed as indicated by TLC analysis, the mixture was washed with saturated aqueous NaHCO₃. The aqueous layers were extracted with CH₂Cl₂ (20 mL × 3). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated. The residue was subjected to SiO₂ flash column chromatography to obtain the ester products. Esters **1b** and **1e** were characterized *via* ¹H and ¹³C NMR; other esters are known compounds.

b) NHC-catalyzed reactions of esters and unsaturated imines (Tables 1-4): To a 10 mL of two-necked oven-dried flask was added ester **1** (0.15 mmol, 1.5 equiv), α, β-unsaturated imine **2** (0.1 mmol), chiral triazolium salt **C** (0.03 mmol) and Me₄NCl (0.1 mmol). The flask was then evacuated and refilled with dry Argon. Anhydrous CH₂Cl₂ (0.5 mL) was added, followed by an injection of DIEA (0.5 mmol). The mixture was stirred at rt for 24 h. Solvent was removed under reduced pressure, and the residue was purified *via* column chromatography on silica gel with hexane/ethyl acetate as eluent to afford the desired product. Racemic products were synthesized *via* similar procedure using achiral triazolium salt **A** (0.03 mmol).

c) Experiments suggesting the absence of ketene intermediates: To a 10 mL of two-necked oven-dried flask was added ester **1a6** or acetyl chloride **5a** (0.5 mmol, 5.0 equiv.) and tetrachloro-*o*-quinone **6a** (0.1 mmol). The flask was then evacuated and refilled with dry Argon. Anhydrous CH₂Cl₂ (1.0 mL) was added and followed by an injection of DIEA (0.2 mmol, 2.0 equiv.). The mixture was stirred at rt for 24 h. The yields for the formation of the 4+2 cycloaddition product **7a** were estimated *via* ¹H NMR analysis of crude reaction mixture. Isolated yield of **7a** was 17% when 1.0 equiv. acetyl chloride **5a** was used under otherwise identical (non-optimized) conditions.

Evidence suggesting a direct ester activation pathway (not involving ketene intermediates):

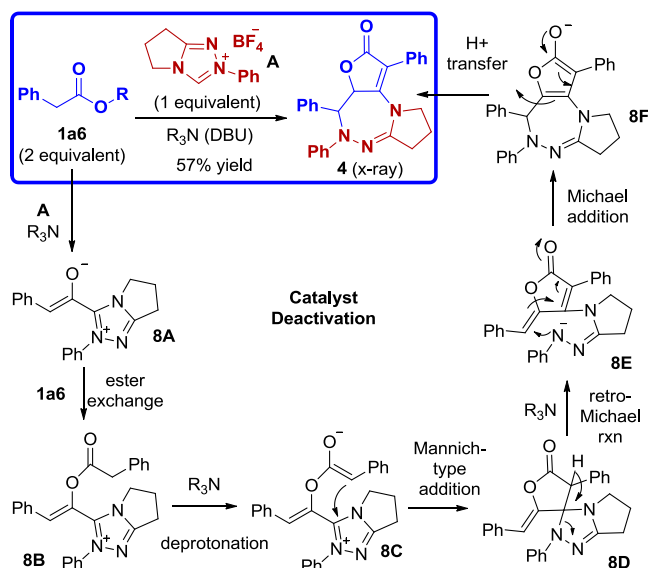


Mechanistically, the enolate key intermediate (**III**, Scheme 1b) is likely formed through deprotonation of a NHC-bounded activated ester intermediate (**II**, Scheme 1b). We postulated that intermediate **II** (Scheme 1b) is formed through a direct displacement *via* a nucleophilic addition of NHC to ester substrate

I. Although an alternative pathway involving a ketene intermediate cannot be completely ruled out, our studies suggest the absence of such an intermediate (Scheme 2). For example, phenyl acetyl chloride **5a** could form a ketene intermediate that subsequently underwent a cycloaddition with tetrachloro-*o*-quinone (**6a**) to give **7a** in 18-26% yield under unoptimized conditions (eq. a). Replacing **5a** with our ester substrate **1a6** under this and a number of other conditions did not lead to any formation of **7a**, suggesting the absence of a ketene intermediate using the ester substrates (eq. b). In addition, the use of acetyl chlorides (e.g. **5a**) in our reactions did not lead to product **3a**, indicating that the mono-substituted ketene intermediate generated from **5a** was not suitable for our NHC-catalyzed reactions (eq. c).

d) Catalyst deactivation: Independent experiment for the synthesis of **4**: To a 10 mL of two-necked oven-dried flask was added ester **1** (0.2 mmol, 1.5 equiv) and achiral triazolium salt **A** (0.1 mmol). The flask was then evacuated and refilled with dry Argon. Anhydrous THF (1.0 mL) was added, followed by an injection of DBU (0.4 mmol). The mixture was stirred at rt for 24 h. Solvent was removed under reduced pressure, and the residue was purified *via* column chromatography on silica gel with hexane/ethyl acetate as eluent to afford the desired product as a colorless solid in 57% yield. Good quality crystal (for X-ray) was obtained *via* vaporization of an acetone solution. ¹H NMR (400 MHz, CDCl₃) δ 1.92-1.96 (2H, m), 2.75-2.90 (2H, m), 3.04-3.10 (1H, m), 3.33-3.39 (1H, m), 5.19 (1H, d, *J* = 2.8 Hz), 5.97 (1H, d, *J* = 2.6 Hz), 6.67 (2H, broad s), 6.92 (1H, t, *J* = 13.9 Hz, 7.02 Hz), 7.20-7.33 (12H, m); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 32.3, 52.4, 66.2, 102.8, 115.0, 120.7, 126.6, 127.7, 127.8, 128.4, 128.7, 129.0, 130.1, 130.2, 133.8, 135.4, 147.6, 155.4, 172.5; HRMS (ESI): calculated for [C₂₇H₂₄N₃O₂]⁺: *m/z* = 422.1790, found: *m/z* = 422.1788.

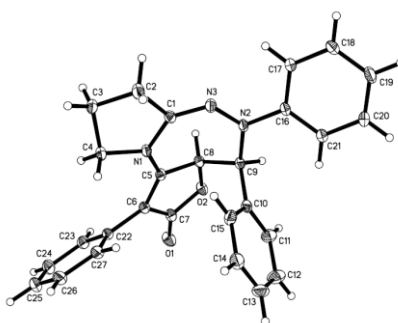
Catalyst deactivation and the proposed pathway:



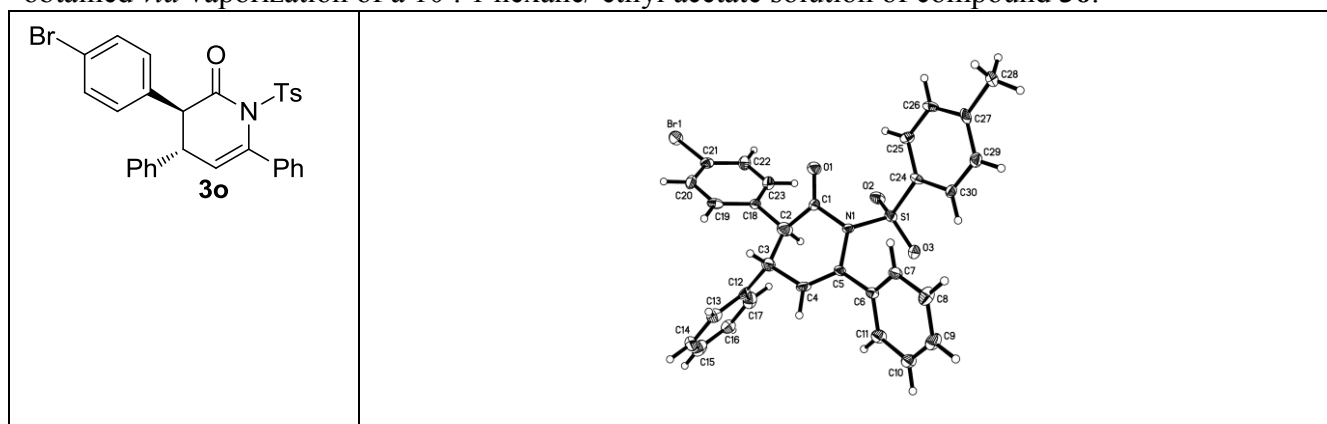
One catalyst deactivation pathway was observed during the reaction optimizations, which further confirmed the involvement of NHC in the catalytic activation of esters to generate enolate intermediates. Two equivalents of the ester substrate (**1a6**) reacted with one equivalent of NHC catalyst **A** to give **4** as a stable adduct. The formation of **4** was observable but minimal (< 5%) when DIEA was used as the base, but became significant when stronger organic bases (e.g., DBU) were used. An independent reaction starting with ester **1a6**, NHC pre-catalyst **A** and DBU as the base gave **4** in 57% isolated yield. A

postulated pathway rationalizing the catalyst deactivation is briefed in Scheme 3. The key steps likely involve an ester exchange between NHC-bounded enolate **8A** and substrate **1a6** (or its activated form) to give **8B**. Intermediate **8B** then undergoes a few transformations to eventually end up as adduct **4** (Scheme 3). Subjection of **4** to the reaction condition did not lead to any detectable formation of catalyst **A**, suggesting an irreversible catalyst deactivation process. When chiral NHC pre-catalysts (Table 2, **B-D**) were used with DIEA as the base, this particular catalyst deactivation was nearly undetectable, as indicated by TLC and crude ^1H NMR analysis. The fact that 20-30 mol% NHC catalysts are necessary (Tables 2-4) suggests that other non-confirmed pathways for NHC deactivations are present.

e) x-ray structure of 4:



h) Determination of absolute configuration via x-ray analysis: Absolute configuration of the lactam products was determined via x-ray structure analysis of **3o**. The crystal (colorless flaky crystal) was obtained via vaporization of a 10 : 1 hexane/ ethyl acetate solution of compound **3o**.

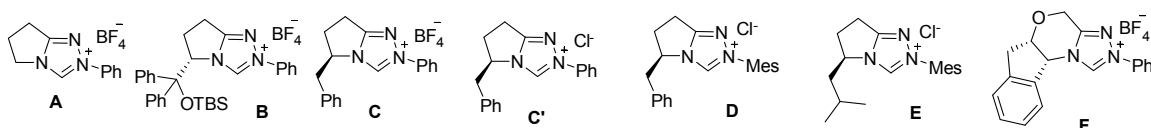
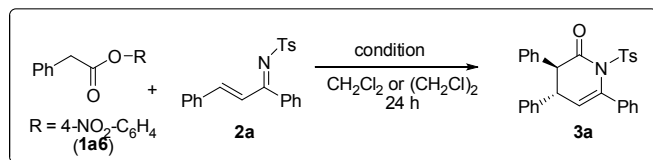


[1] R. N. Ram, A. A. Khan, *Synthetic Commun* **2001**, 31, 841-846.

[2] C. Ramamurthy, V. Nagaswami, *Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1972-1999)*, **1982**, 1625 – 1632.

III: Condition Optimization: Screening of NHC catalysts, bases, solvents, and additives (selected results)

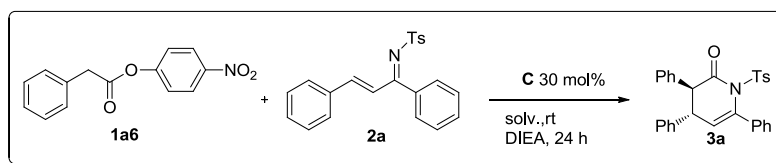
a). Screening of NHC catalysts ^[a]



Entry	NHC (mol%)	Base/Solvent	Additive ^[f]	Temp (°C)	Yield(%) ^[b]	dr ^[c]	er ^[d]
1	-	DIEA / $(\text{CH}_2\text{Cl})_2$	-	70	<5	-	-
2	-	TEA / $(\text{CH}_2\text{Cl})_2$	-	70	<5	-	-
3	-	DBU / $(\text{CH}_2\text{Cl})_2$	-	rt	54	>20 : 1	-
4	A (50)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	81	10 : 1	-
5	A (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	83 ^[g]	11 : 1	-
6	A (10)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	39	8 : 1	-
7	A (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	40	81	13 : 1	-
8	A (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	rt	61 ^[g]	7 : 1	-
9	A (30)	DBU/ $(\text{CH}_2\text{Cl})_2$	-	rt	72	>20 : 1	-
10	B (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	14	-	-
11	C (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	72 ^[g]	12 : 1	87:13
12	C (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	40	78	16 : 1	90 : 10
13	C (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	rt	59 ^[g]	12 : 1	92 : 8
14	C (20)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	rt	47	10 : 1	92 : 8
15	C (30)	DIEA/ CH_2Cl_2	-	rt	59	12 : 1	94 : 6
16	C (30)	DIEA/THF	-	rt	<5	-	-
17	C' (30)	DIEA/ CH_2Cl_2	-	rt	75	>20 : 1	94 : 6
18	D (30)	DIEA ^[e] / CH_2Cl_2	-	rt	78 ^[g]	10 : 1	84 : 16
19	E (30)	DIEA ^[e] / CH_2Cl_2	-	rt	60	14 : 1	78 : 22
20	F (30)	DIEA/ $(\text{CH}_2\text{Cl})_2$	-	70	16	-	-
21	C (30)	DIEA / CH_2Cl_2	Me_4NCl	rt	87 ^[g]	13 : 1	94 : 6
22	C (30)	DIEA ^[e] / CH_2Cl_2	Me_4NCl	0	89 ^[g]	16 : 1	96 : 4

[a] conditions: **1a**, 0.15 mmol; **2a**, 0.10 mmol; Base, 200 mol %; solvent, 0.5 mL; under Ar. [b] Yield (of two diastereomers) estimated *via* ^1H NMR analysis of crude reaction mixture. [c] Determined *via* ^1H NMR analysis of crude reaction mixture. [d] er of trans-**3a**, as determined *via* chiral HPLC. [e] 10 equiv of DIEA was used. [f] 1 equiv of additive was used. [g] isolated yield (as in manuscript Tables 1-2). DIEA = Ethyldiisopropylamine; TEA = Triethylamine; DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene.

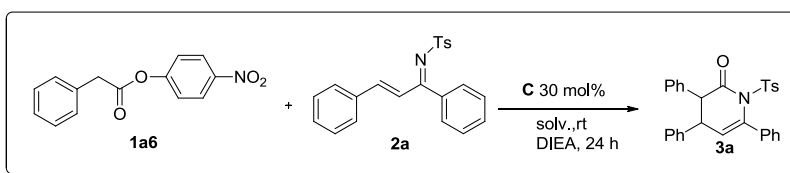
b). Solvent Screening ^[a]



Entry	Solvent	Yield (%) ^[b]	dr ^[c]	er ^[d]
1	CH ₂ Cl ₂	59	12 : 1	92 : 8
2	(CH ₂ Cl) ₂	52	>20 : 1	91 : 9
3	THF	Trace	-	-
4	EtOAc	Trace	-	-
5	CDCl ₃	37	4 : 1	93 : 7
6	(CHCl ₂) ₂	Trace	-	-
7	C ₂ H ₅ Br	Trace	-	-
8	Chlorobenzene	Trace	-	-
9 ^[e]	DIEA	N. R.	-	-

[a] Conditions: **1a**, 0.15 mmol; **2**, 0.1 mmol; **C**, 30 mol %; DIEA 2 equiv; solvent, 0.5 mL. All reactions were carried out under Ar. [b] Yield (of two diastereomers) estimated *via* ¹H NMR analysis of crude reaction mixture. [c] Determined *via* ¹H NMR analysis of crude reaction mixture. [d] er of *trans*-**3a**, as determined *via* chiral HPLC. [e] DIEA as solvent.

c). Additive screening ^[a]

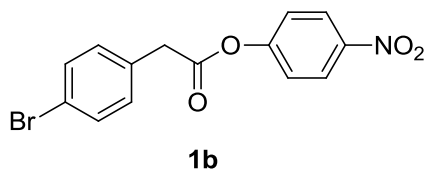


Entry	Solvent	Additives	Yield (%) ^[b]	Dr ^[c]	er ^[d]
1	(CH ₂ Cl) ₂	Et ₄ NCl	71	16 : 1	88 : 12
2	(CH ₂ Cl) ₂	Et ₄ NBr	85	>20 : 1	89 : 11
3	(CH ₂ Cl) ₂	Me ₄ NCl	87	>20 : 1	92 : 8
4	(CH ₂ Cl) ₂	Bu ₄ NAc	26	10 : 1	78 : 22
5	(CH ₂ Cl) ₂	Bu ₄ NCl	54	10 : 1	90 : 10
6	(CH ₂ Cl) ₂	Bu ₄ NI	73	7 : 1	92 : 8
7	(CH ₂ Cl) ₂	Bu ₄ NBr	78	10 : 1	89 : 11
8	CH ₂ Cl ₂	Me ₄ NCl	84	15 : 1	94 : 6
9 ^[e]	CH ₂ Cl ₂	Me ₄ NCl	67	>20 : 1	95 : 5

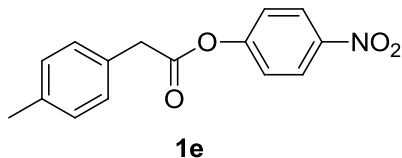
[a] Conditions: **2**, 0.15 mmol; **1a**, 0.1 mmol; **C**, 30 mol %; DIEA 2 equiv; solvent, 0.5 mL. All reactions were carried out under Ar. [b] Isolated yield (of major diastereomer) [c] Determined *via* ¹H NMR analysis of crude reaction mixture. [d] er of *trans*-**3a**, as determined *via* chiral HPLC. [e] at 0 °C.

IV. Characterization of substrates and products:

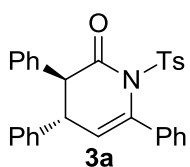
4-Nitrophenyl 2-(4-bromophenyl)acetate (1b): $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.85 (2H, s), 7.24-7.26 (4H, m), 7.52 (2H, d, $J = 8.4$ Hz), 8.26 (2H, d, $J = 9.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 40.7, 121.8, 122.3, 125.2, 131.0, 131.6, 132.0, 145.4, 155.2, 168.5; **HRMS** (ESI): calculated for $[\text{C}_{14}\text{H}_{11}\text{NO}_4\text{Br}]^+$: $m/z = 335.9871$, found: $m/z = 335.9862$.



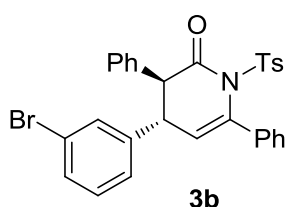
4-Nitrophenyl 2-(*p*-tolyl)acetate (1e): $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.36 (3H, s), 3.85 (2H, s), 7.19 (2H, d, $J = 6.4$ Hz), 7.23-7.26 (4H, m), 8.24 (2H, d, $J = 4.0$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 21.1, 40.9, 122.3, 125.1, 129.1, 129.6, 137.4, 145.3, 155.4, 169.2; **HRMS** (ESI): calculated for $[\text{C}_{15}\text{H}_{14}\text{NO}_4]^+$: $m/z = 272.0923$, found: $m/z = 272.0924$.



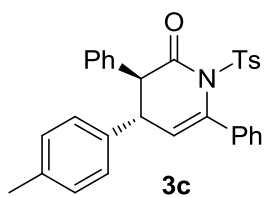
(3*S*, 4*S*)-3, 4, 6-Triphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3a): This compound was synthesized with 1000 mol% of DIEA at 0 °C in CH_2Cl_2 for 24 h. 89% yield; 16 : 1 dr; colorless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.45 (3H, s), 3.90 (1H, d, $J = 10.5$ Hz), 4.03 (1H, dd, $J = 10.5$ Hz, $J = 4.1$ Hz), 6.01 (1H, d, $J = 4.6$ Hz), 6.80-6.83 (2H, m), 7.03-7.05 (2H, m), 7.12-7.19 (5H, m), 7.27 (2H, d, $J = 8.2$ Hz), 7.36-7.43 (5H, m), 7.84 (2H, d, $J = 8.2$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 21.7, 45.1, 59.0, 122.7, 126.0, 127.1, 127.3, 127.8, 128.4, 128.5, 128.6, 128.7, 129.1, 129.5, 136.4, 137.0, 139.8, 140.1, 145.0, 173.0; **HRMS** (ESI): calculated for $[\text{C}_{30}\text{H}_{26}\text{NO}_3\text{S}]^+$: $m/z = 480.1633$, found: $m/z = 480.1636$; **Optical rotation:** $[\alpha]_D^{20}$: 59 (c 2.3, CHCl_3); **HPLC** analysis: 96 : 4 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.5 mL/min), R_t (major) = 20.4 min, R_t (minor) = 30.2 min.



(3*S*, 4*S*)-4-(3-Bromophenyl)-3, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3b): 87% yield; 14 : 1 dr; colorless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.46 (3H, s), 3.86 (1H, d, $J = 10.8$ Hz), 4.00 (1H, dd, $J = 10.8$ Hz, $J = 4.0$ Hz), 5.95 (1H, d, $J = 4.4$ Hz), 6.82-6.84 (2H, m), 6.95 (1H, d, $J = 7.6$ Hz), 7.03 (1H, t, $J = 8.0$ Hz), 7.16-7.17 (3H, m), 7.23-7.39 (4H, m), 7.41-7.43 (5H, m), 7.82 (2H, d, $J = 8.4$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 21.7, 44.8, 58.8, 121.5, 122.7, 126.1, 126.6, 127.6, 128.5, 128.6, 128.7, 129.1, 129.5, 130.2, 130.4, 130.7, 136.0, 136.3, 136.9, 140.7, 142.2, 145.2, 172.6; **HRMS** (ESI): calculated for $[\text{C}_{30}\text{H}_{25}\text{NO}_3\text{SBr}]^+$: $m/z = 558.0739$, found: $m/z = 558.0735$; **Optical rotation:** $[\alpha]_D^{20}$: 42 (c 3.7, CHCl_3); **HPLC** analysis: 93 : 7 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 14.6 min, R_t (minor) = 24.9 min.

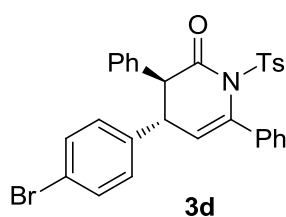


(3*S*, 4*S*)-3, 6-Diphenyl-4-(*p*-tolyl)-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3c): 84% yield; 16 : 1 dr; colorless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.24 (3H, s), 2.46 (3H, s), 3.89 (1H, d, $J = 10.4$ Hz), 4.00 (1H, dd, $J = 10.4$ Hz, $J = 4.0$ Hz), 5.99 (1H, d, $J = 4.4$ Hz), 6.82-6.84 (2H, m), 6.93 (2H, d, $J = 8.0$ Hz), 6.97 (2H, d, $J = 8.0$ Hz), 7.12-7.14 (3H, m), 7.27 (2H, d, $J = 5.6$ Hz), 7.36-7.43 (5H, m), 7.83 (2H, d, $J = 8.4$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 21.0, 21.7, 44.6, 58.9, 114.6, 123.0, 126.0, 127.3, 127.6, 128.4, 128.7, 129.0, 129.3, 129.5, 136.4, 136.5, 136.7, 136.8, 137.1, 139.9, 144.9, 173.1; **HRMS** (ESI): calculated for $[\text{C}_{31}\text{H}_{28}\text{NO}_3\text{S}]^+$: $m/z = 494.1790$, found: $m/z = 494.1790$; **Optical**



rotation: $[\alpha]_D^{20}$: 41 (c 3.6, CHCl₃); **HPLC** analysis: 93 : 7 er (Chiralcel OD-H, 20 : 80 ⁱPrOH /Hexane, 0.75 mL/min), R_t (major) = 14.2 min, R_t (minor) = 19.5 min.

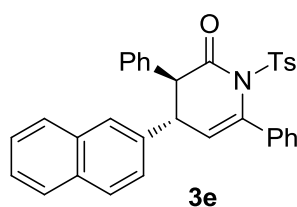
(3*S*, 4*S*)-4-(4-Bromophenyl)-3, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3d): 88% yield; 11 :



1 dr; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.46 (3H, s), 3.86 (1H, d, *J* = 10.4 Hz), 4.01 (1H, dd, *J* = 10.4 Hz, *J* = 4.4 Hz), 5.94 (1H, d, *J* = 4.4 Hz), 6.82-6.84 (2H, m), 6.92 (2H, d, *J* = 8.4 Hz), 7.15-7.17 (3H, m), 7.29 (2H, d, *J* = 8.8 Hz), 7.36-7.42 (5H, m), 7.81 (2H, d, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 44.6, 58.7, 121.1, 121.9, 126.1, 127.6, 128.5, 128.6, 128.7, 129.1, 129.4, 129.5, 131.8, 136.1, 136.3, 136.9, 138.9, 140.6, 145.1, 172.7; **HRMS**

(ESI): calculated for [C₃₀H₂₅NO₃SBr]⁺: *m/z* = 558.0739, found: *m/z* = 558.0734; **Optical rotation:** $[\alpha]_D^{20}$: 56 (c 3.6, CHCl₃); **HPLC** analysis: 93 : 7 er (Chiralcel OD-H, 20 : 80 ⁱPrOH /Hexane, 0.5 mL/min), R_t (major) = 25.7 min, R_t (minor) = 41.8 min.

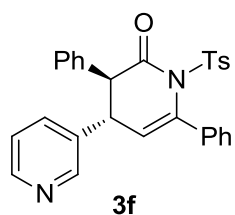
(3*S*, 4*S*)-4-(Naphthalen-2-yl)-3, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3e): 88%



yield; >20 : 1 dr; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.39 (3H, s), 4.08 (1H, d, *J* = 9.6 Hz), 4.21 (1H, dd, *J* = 9.6 Hz, *J* = 4.4 Hz), 6.09 (1H, d, *J* = 4.8 Hz), 6.90-6.92 (2H, m), 7.11-7.13 (5H, m), 7.19 (1H, d, *J* = 8.8 Hz), 7.38-7.48 (7H, m), 7.52 (1H, s), 7.66-7.69 (2H, m), 73.74-7.78 (3H, m); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 44.8, 58.2, 122.2, 125.6, 125.9, 126.0, 126.2, 126.5, 127.4, 127.5, 127.7, 128.4, 128.5, 128.6, 129.0, 129.4, 132.4, 133.3,

136.2, 136.3, 137.1, 137.2, 140.3, 144.9, 172.8; **HRMS** (ESI): calculated for [C₃₄H₂₈NO₃S]⁺: *m/z* = 530.1790, found: *m/z* = 530.1800; **Optical rotation:** $[\alpha]_D^{20}$: 71 (c 2.8, CHCl₃); **HPLC** analysis: 93 : 7 er (Chiralcel AD-H, 20 : 80 ⁱPrOH /Hexane, 0.75 mL/min), R_t (major) = 74.7 min, R_t (minor) = 215.3 min.

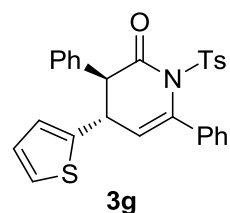
(3'*S*, 4'*S*)-3',6'-Diphenyl-1'-tosyl-3', 4'-dihydro-[3, 4'-bipyridin]-2'(1'*H*)-one (3f): 84% yield; 13 : 1 dr;



colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.47 (3H, s), 3.87 (1H, d, *J* = 11.4 Hz), 4.08 (1H, dd, *J* = 11.0 Hz, *J* = 4.6 Hz), 5.97 (1H, d, *J* = 4.1 Hz), 6.80-6.82 (2H, m), 7.11-7.16 (4H, m), 7.29 (2H, d, *J* = 8.2 Hz), 7.37-7.42 (6H, m), 7.84 (2H, d, *J* = 8.7 Hz), 8.28 (1H, d, *J* = 2.3 Hz), 8.40 (1H, dd, *J* = 4.6 Hz, *J* = 1.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 42.9, 58.9, 121.2, 123.5, 126.1, 127.7, 128.5, 128.6, 128.7, 128.8, 129.1, 129.5, 135.2, 135.6, 135.7, 136.2, 136.6, 140.98, 145.2, 148.5, 149.4, 172.5; **HRMS** (ESI): calculated for [C₂₉H₂₅N₂O₃S]⁺: *m/z* = 481.1586, found: *m/z* =

481.1589; **Optical rotation:** $[\alpha]_D^{20}$: 32 (c 3.7, CHCl₃); **HPLC** analysis: 94 : 6 er (Chiralcel OD-H, 20 : 80 ⁱPrOH/Hexane, 0.75 mL/min), R_t (major) = 35.5 min, R_t (minor) = 79.8 min.

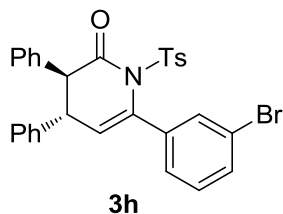
(3*S*, 4*S*)-3, 6-Diphenyl-4-(thiophen-2-yl)-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3g): 92% yield; 13 :



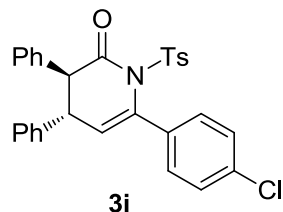
1 dr; light yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 2.43 (3H, s), 3.95 (1H, d, *J* = 8.7 Hz), 4.28 (1H, dd, *J* = 9.2 Hz, *J* = 5.0 Hz), 6.03 (1H, d, *J* = 5.0 Hz), 6.68 (1H, d, *J* = 3.7 Hz), 6.79 (1H, dd, *J* = 5.5 Hz, *J* = 3.2 Hz), 6.92-6.95 (2H, m), 7.11 (1H, d, *J* = 5.5 Hz), 7.18-7.25 (5H, m), 7.36-7.44 (4H, m), 7.75 (2H, d, *J* = 8.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 40.4, 59.2, 121.4, 124.6, 125.4, 126.1, 126.9, 127.6, 128.5, 128.6, 128.7, 129.1, 129.4, 136.2, 136.2, 136.9, 140.5, 143.1, 145.0, 172.3; **HRMS**

(ESI): calculated for $[C_{28}H_{24}NO_3S_2]^+$: $m/z = 486.1198$, found: $m/z = 486.1194$; **Optical rotation**: $[\alpha]_D^{20}$: 27 (c 3.0, $CHCl_3$); **HPLC** analysis: 86 : 14 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 15.8 min, R_t (minor) = 22.1 min.

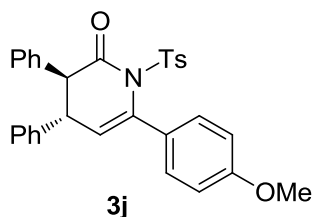
(3*S*, 4*S*)-6-(3-Bromophenyl)-3, 4-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3h): 85% yield; >20 : 1 dr; colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.89 (1H, d, $J = 10.8$ Hz), 4.07 (1H, dd, $J = 10.8$ Hz, $J = 4.0$ Hz), 6.03 (1H, d, $J = 4.0$ Hz), 6.84-6.87 (2H, m), 7.03 (2H, d, $J = 7.6$ Hz), 7.14-7.20 (6H, m), 7.24-7.31 (3H, m), 7.38-7.42 (2H, m), 7.49 (1H, d, $J = 8.4$ Hz), 7.84 (2H, d, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 45.2, 59.0, 122.4, 124.1, 124.9, 127.2, 127.4, 127.7, 128.4, 128.7, 128.8, 128.9, 129.3, 129.4, 130.1, 131.5, 136.2, 136.2, 138.7, 138.9, 139.6, 145.2, 173.0; **HRMS** (ESI): calculated for $[C_{30}H_{25}NO_3SBr]^+$: $m/z = 558.0739$, found: $m/z = 558.0745$; **Optical rotation**: $[\alpha]_D^{20}$: 12 (c 3.4, $CHCl_3$); **HPLC** analysis: 94 : 6 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 11.6 min, R_t (minor) = 22.2 min.



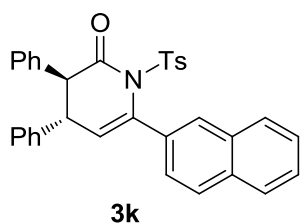
(3*S*, 4*S*)-6-(4-Chlorophenyl)-3, 4-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3i): 85% yield; 15 : 1 dr; colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.89 (1H, d, $J = 10.8$ Hz), 4.01 (1H, dd, $J = 10.8$ Hz, $J = 4.0$ Hz), 6.00 (1H, d, $J = 4.4$ Hz), 6.78-6.80 (2H, m), 7.02 (2H, d, $J = 7.6$ Hz), 7.11-7.19 (6H, m), 7.28 (2H, d, $J = 8.0$ Hz), 7.32-7.38 (4H, m), 7.84 (2H, d, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 45.0, 58.7, 123.1, 127.2, 127.3, 127.4, 127.7, 128.4, 128.6, 129.2, 129.4, 134.3, 135.6, 136.2, 139.1, 139.6, 145.2, 172.8; **HRMS** (ESI): calculated for $[C_{30}H_{25}NO_3SCl]^+$: $m/z = 514.1244$, found: $m/z = 514.1250$; **Optical rotation**: $[\alpha]_D^{20}$: 47 (c 3.5, $CHCl_3$); **HPLC** analysis: 94 : 6 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 12.0 min, R_t (minor) = 26.5 min.



(3*S*, 4*S*)-6-(4-Methoxyphenyl)-3, 4-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3j): 94% yield; >20 : 1 dr; colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.85 (3H, s), 3.88 (1H, d, $J = 10.5$ Hz), 4.00 (1H, dd, $J = 10.8$ Hz, $J = 4.3$ Hz), 5.93 (1H, d, $J = 4.3$ Hz), 6.78-6.80 (2H, m), 6.89 (2H, d, $J = 8.8$ Hz), 7.04 (2H, d, $J = 8.0$ Hz), 7.11-7.17 (6H, m), 7.26-7.29 (2H, m), 7.35 (2H, d, $J = 8.8$ Hz), 7.85 (2H, d, $J = 8.3$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 45.3, 55.6, 59.3, 114.0, 121.6, 127.3, 127.5, 128.0, 128.6, 128.8, 129.0, 129.2, 129.3, 129.7, 136.7, 140.0, 140.2, 145.2, 160.0, 173.4; **HRMS** (ESI): calculated for $[C_{31}H_{28}NO_4S]^+$: $m/z = 510.1739$, found: $m/z = 510.1730$; **Optical rotation**: $[\alpha]_D^{20}$: 30 (c 3.2, $CHCl_3$); **HPLC** analysis: 93 : 7 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 13.5 min, R_t (minor) = 27.4 min.

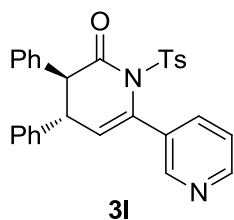


(3*S*, 4*S*)-6-(Naphthalen-2-yl)-3, 4-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3k): 83% yield; 15 : 1 dr; colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.94 (1H, d, $J = 10.8$ Hz), 4.11 (1H, dd, $J = 10.5$ Hz, $J = 4.0$ Hz), 6.14 (1H, d, $J = 4.3$ Hz), 6.84-6.88 (2H, m), 7.06 (2H, d, $J = 7.8$ Hz), 7.12-7.20 (6H, m), 7.23 (2H, d, $J = 7.0$ Hz), 7.48-7.52 (2H, m), 7.55 (1H, dd, $J = 8.5$ Hz, $J = 1.8$ Hz), 7.69-7.73 (1H, m), 7.79 (1H, s), 7.82-7.87 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 45.3, 59.2, 123.5, 124.1, 124.8, 126.4, 126.5, 127.1, 127.4, 127.8, 128.1, 128.3, 128.4,

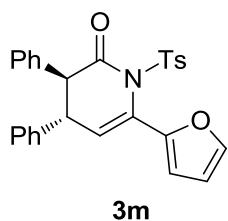


128.6, 128.8, 129.1, 129.5, 132.9, 133.3, 134.3, 136.4, 139.9, 140.1, 145.0, 173.3; **HRMS** (ESI): calculated for $[C_{34}H_{28}NO_3S]^+$: $m/z = 530.1790$, found: $m/z = 530.1790$; $[\alpha]_D^{20}$: 42 (c 3.8, $CHCl_3$); **HPLC** analysis: 94 : 6 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 13.1 min, R_t (minor) = 26.4 min.

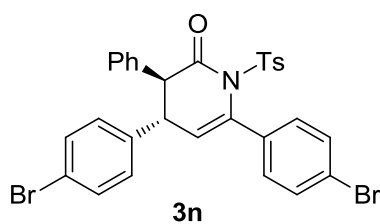
(4S, 5S)-4, 5-Diphenyl-1-tosyl-4, 5-dihydro-[2, 3'-bipyridin]-6(1H)-one (3l): 86% yield; >20 : 1 dr; colorless oil; **1H NMR** (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.93 (1H, d, $J = 10.3$ Hz), 4.06 (1H, dd, $J = 10.3$ Hz, $J = 4.3$ Hz), 6.05 (1H, d, $J = 4.5$ Hz), 6.83-6.85 (2H, m), 7.04 (2H, d, $J = 7.8$ Hz), 7.13-7.20 (6H, m), 7.29 (2H, d, $J = 8.3$ Hz), 7.33 (1H, dd, $J = 7.8$ Hz, $J = 5.0$ Hz), 7.76 (1H, dt, $J = 8.0$ Hz, $J = 2.0$ Hz), 7.81 (2H, d, $J = 8.3$ Hz), 8.61 (1H, dd, $J = 4.8$ Hz, $J = 1.5$ Hz), 8.64 (1H, d, $J = 2.0$ Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 21.7, 45.0, 58.6, 123.2, 124.3, 127.3, 127.5, 127.7, 128.5, 128.6, 128.7, 129.3, 133.2, 133.6, 136.0, 137.3, 139.4, 145.4, 146.9, 149.4, 172.5; **HRMS** (ESI): calculated for $[C_{29}H_{25}N_2O_3S]^+$: $m/z = 481.1586$, found: $m/z = 481.1588$; **Optical rotation**: $[\alpha]_D^{20}$: 25 (c 3.6, $CHCl_3$); **HPLC** analysis: 91 : 9 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 25.6 min, R_t (minor) = 43.0 min.



(3S, 4S)-6-(Furan-2-yl)-3, 4-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1H)-one (3m): 94% yield; 13 : 1 dr; colorless oil; **1H NMR** (400 MHz, $CDCl_3$) δ 2.47 (3H, s), 3.86 (1H, d, $J = 10.8$ Hz), 3.98 (1H, dd, $J = 10.8$ Hz, $J = 4.0$ Hz), 6.23 (1H, d, $J = 4.0$ Hz), 6.48 (1H, dd, $J = 3.2$ Hz, $J = 2.0$ Hz), 6.55 (1H, d, $J = 3.6$ Hz), 6.71-6.74 (2H, m), 7.02 (2H, d, $J = 8.0$ Hz), 7.08-7.18 (6H, m), 7.32 (2H, d, $J = 8.0$ Hz), 7.43 (1H, d, $J = 1.2$ Hz), 7.99 (2H, d, $J = 8.3$ Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 21.7, 44.8, 58.9, 108.0, 111.6, 121.2, 127.2, 127.3, 127.8, 128.3, 128.6, 128.8, 129.2, 129.5, 130.7, 136.2, 136.5, 139.6, 142.0, 145.1, 149.2, 172.4; **HRMS** (ESI): calculated for $[C_{28}H_{24}NO_4S]^+$: $m/z = 470.1426$, found: $m/z = 470.1436$; **Optical rotation**: $[\alpha]_D^{20}$: 47 (c 3.5, $CHCl_3$); **HPLC** analysis: 88 : 12 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 21.0 min, R_t (minor) = 24.6 min.



(3S, 4S)-4, 6-Bis(4-bromophenyl)-3-phenyl-1-tosyl-3, 4-dihydropyridin-2(1H)-one (3n): 84% yield; 15 : 1 dr; colorless solid; **1H NMR** (400 MHz, $CDCl_3$) δ 2.46 (3H, s), 3.85 (1H, d, $J = 10.3$ Hz), 3.98 (1H, dd, $J = 10.3$ Hz, $J = 4.3$ Hz), 5.94 (1H, d, $J = 4.3$ Hz), 6.79-6.81 (2H, m), 6.90 (2H, d, $J = 8.3$ Hz), 7.14-7.17 (3H, m), 7.28 (6H, d, $J = 8.3$ Hz), 7.49 (2H, d, $J = 8.5$ Hz), 7.81 (2H, d, $J = 8.5$ Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 21.7, 44.4, 58.4, 121.1, 122.3, 122.6, 127.5, 127.6, 128.5, 128.6, 129.2, 129.4, 131.6, 131.8, 135.8, 135.9, 136.0, 138.6, 139.6, 145.4, 172.4; **HRMS** (ESI): calculated for $[C_{30}H_{24}NO_3SBr_2]^+$: $m/z = 635.9844$, found: $m/z = 635.9842$; **Optical rotation**: $[\alpha]_D^{20}$: 57 (c 4.3, $CHCl_3$); **HPLC** analysis: 94 : 6 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 16.1 min, R_t (minor) = 39.1 min.



(3*S*, 4*S*)-3-(4-Bromophenyl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3o): 77% yield; >20 : 1 dr; colorless solid; ¹H NMR (400 MHz, CD₂Cl₂) δ 2.48 (3H, s), 3.88 (1H, d, *J* = 12 Hz), 3.94 (1H, dd, *J* = 12.0 Hz, *J* = 3.6 Hz), 6.03 (1H, d, *J* = 3.6 Hz), 6.57 (2H, d, *J* = 4.8 Hz), 7.02 (2H, d, *J* = 6 Hz), 7.15-7.23 (3H, m), 7.25 (2H, d, *J* = 4.4 Hz), 7.33-7.47 (7H, m), 7.82 (2H, d, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CD₂Cl₂) δ 21.5, 44.8, 58.1, 121.2, 123.3, 125.9, 127.3, 127.8, 128.4, 128.5, 128.7, 129.2, 139.3, 130.7, 131.3, 135.6, 136.4, 137.2, 139.6, 140.0, 145.6, 172.5; **HRMS** (ESI): calculated for [C₃₀H₂₅NO₃SBr]⁺: *m/z* = 558.0739, found: *m/z* = 558.0742; **Optical rotation**: [α]_D²⁰: 54 (c 1.1, CHCl₃); **HPLC** analysis: >99 : 1 er (Chiralcel AD-H, 20 : 80 ⁱPrOH/Hexane, 0.75 mL/min), *R*_t (major) = 68.1 min, *R*_t (minor) = 100.1 min.

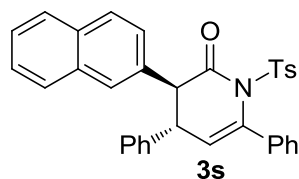
(3*S*, 4*S*)-3-(4-Chlorophenyl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3p): This compound was synthesized with 200 mol% of DIEA at 60°C in 1, 2-Dichloroethane for 24 hours. No Me₄NCl was used. 70% yield; >20 : 1 dr; colorless solid; ¹H NMR (400 MHz, CDCl₃) δ 2.47 (3H, s), 3.86 (1H, d, *J* = 11.6 Hz), 3.99 (1H, dd, *J* = 11.6 Hz, *J* = 3.6 Hz), 6.01 (1H, d, *J* = 3.6 Hz), 6.71 (2H, d, *J* = 6.4 Hz), 7.00 (2H, d, *J* = 8.0 Hz), 7.08-7.15 (2H, m), 7.16-7.20 (3H, m), 7.29 (2H, d, *J* = 8.0 Hz), 7.35-7.42 (5H, m), 7.84 (2H, d, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 45.2, 58.5, 123.0, 126.0, 127.3, 127.7, 128.4, 128.6, 128.7, 129.1, 129.5, 130.2, 133.2, 134.8, 136.3, 136.8, 139.5, 140.1, 145.2, 172.8; **HRMS** (ESI): calculated for [C₃₀H₂₅NO₃SCl]⁺: *m/z* = 514.1244, found: *m/z* = 514.1238; **Optical rotation**: [α]_D²⁰: 57 (c 1.1, CHCl₃); **HPLC** analysis: > 99 : 1 er (Chiralcel OD-H, 20 : 80 ⁱPrOH/Hexane, 0.5 mL/min), *R*_t (major) = 20.3 min, *R*_t (minor) = 24.7 min.

(3*S*, 4*S*)-3-(4-Methoxyphenyl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3q): 52% yield; 15 : 1 dr; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.45 (3H, s), 3.70 (3H, s), 3.84 (1H, d, *J* = 10.6 Hz), 3.99 (1H, dd, *J* = 11.0 Hz, *J* = 4.1 Hz), 6.00 (1H, d, *J* = 4.1 Hz), 6.66 (2H, d, *J* = 9.2 Hz), 6.73 (2H, d, *J* = 9.2 Hz), 7.04 (2H, d, *J* = 7.8 Hz), 7.14-7.20 (3H, m), 7.27 (2H, d, *J* = 8.7 Hz), 7.36-7.43 (5H, m), 7.84 (2H, d, *J* = 8.7 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 45.2, 55.1, 58.2, 113.8, 123.0, 126.0, 127.1, 127.8, 128.4, 128.5, 128.6, 129.0, 129.5, 129.8, 136.4, 137.1, 139.9, 140.0, 145.0, 158.6, 173.4; **HRMS** (ESI): calculated for [C₃₁H₂₈NO₄S]⁺: *m/z* = 510.1739, found: *m/z* = 510.1745; **Optical rotation**: [α]_D²⁰: 39 (c 1.3, CHCl₃); **HPLC** analysis: 93 : 7 er (Chiralcel OD-H, 20 : 80 ⁱPrOH/Hexane, 0.75 mL/min), *R*_t (major) = 19.1 min, *R*_t (minor) = 29.7 min.

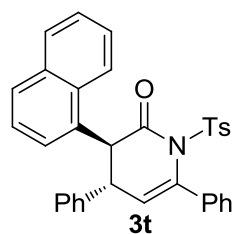
(3*S*, 4*S*)-4, 6-Diphenyl-3-(*p*-tolyl)-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3r): 77 % yield; >20 : 1 dr; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 2.22 (3H, s), 2.45 (3H, s), 3.87 (1H, d, *J* = 10.5 Hz), 4.02 (1H, dd, *J* = 11.5 Hz, *J* = 4.1 Hz), 5.99 (1H, d, *J* = 4.1 Hz), 6.71 (2H, d, *J* = 8.2 Hz), 6.93 (2H, d, *J* = 8.2 Hz), 7.05-7.07 (2H, m), 7.14-7.18 (3H, m), 7.25-7.27 (2H, m), 7.36-7.44 (5H, m), 7.83 (2H, d, *J* = 8.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 21.7, 45.0, 58.5, 122.8, 126.0, 127.1, 127.8, 128.4, 128.5, 128.6, 129.0, 129.1, 129.5, 133.3, 136.4, 137.0, 137.1, 140.0, 145.0, 173.2; **HRMS** (ESI): calculated for [C₃₁H₂₈NO₃S]⁺: *m/z* = 494.1790, found: *m/z* = 494.1792; **Optical rotation**: [α]_D²⁰: 43 (c 2.9, CHCl₃); **HPLC** analysis: 97 : 3 er (Chiralcel AD-H, 20 : 80 ⁱPrOH/Hexane, 0.75 mL/min), *R*_t (major)

= 41.9 min, R_t (minor) = 187.3 min.

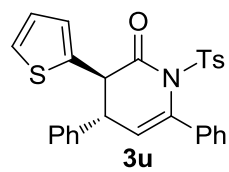
(3*S*, 4*S*)-3-(Naphthalen-2-yl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3s): 74% yield; 14 : 1 dr; colorless solid; ^1H NMR (400 MHz, CDCl_3) δ 2.48 (3H, s), 4.08 (1H, d, J = 10.8 Hz), 4.15 (1H, dd, J = 10.4 Hz, J = 4.4 Hz), 6.04 (1H, d, J = 4.0 Hz), 6.95 (1H, d, J = 8.4 Hz), 7.06-7.15 (5H, m), 7.25 (1H, s), 7.29 (2H, d, J = 8.4 Hz), 7.36-7.41 (5H, m), 7.43-7.47 (2H, m), 7.57-7.59 (1H, m), 7.64 (1H, d, J = 8.8 Hz), 7.70-7.72 (1H, m), 7.86 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 45.0, 59.0, 122.9, 125.9, 126.0, 126.1, 127.2, 127.6, 127.7, 127.8, 128.3, 128.5, 128.6, 128.7, 129.2, 129.6, 132.5, 133.1, 133.8, 136.4, 137.1, 139.8, 140.1, 145.1, 173.1; **HRMS** (ESI): calculated for $[\text{C}_{34}\text{H}_{28}\text{NO}_3\text{S}]^+$: m/z = 530.1790, found: m/z = 530.1793; **Optical rotation**: $[\alpha]_D^{20}$: -34 (c 2.8, CHCl_3); **HPLC** analysis: 89 : 11 er (Chiralcel AS-H, 20 : 80 i PrOH/Hexane, 0.5 mL/min), R_t (major) = 119.6 min, R_t (minor) = 65.2 min.



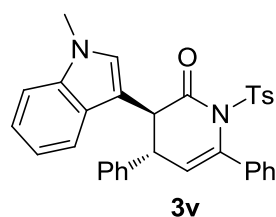
(3*S*, 4*S*)-3-(Naphthalen-1-yl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3t): 64% yield; 10 : 1 dr; colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 2.48 (3H, s), 4.40 (1H, dd, J = 10.4 Hz, J = 4.4 Hz), 4.59 (1H, d, J = 9.6 Hz), 6.01 (1H, d, J = 4.4 Hz), 6.97-7.00 (3H, m), 7.07-7.11 (3H, m), 7.18 (1H, t, J = 7.2 Hz), 7.25-7.27 (3H, m), 7.32-7.50 (7H, m), 7.65 (2H, d, J = 8.4 Hz), 7.77 (1H, d, J = 8.0 Hz), 7.84 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 44.0, 56.7, 122.8, 123.5, 125.0, 125.4, 126.0, 126.1, 127.1, 127.4, 127.6, 128.4, 128.5, 128.6, 129.1, 129.2, 129.7, 131.0, 132.4, 134.0, 136.2, 137.2, 140.0, 140.2, 145.0, 172.6; **HRMS** (ESI): calculated for $[\text{C}_{34}\text{H}_{28}\text{NO}_3\text{S}]^+$: m/z = 530.1790, found: m/z = 530.1792; **Optical rotation**: $[\alpha]_D^{20}$: 12 (c 2.3, CHCl_3); **HPLC** analysis: 80 : 20 er (Chiralcel OD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 16.7 min, R_t (minor) = 61.7 min.



(3*R*, 4*S*)-4, 6-Diphenyl-3-(thiophen-2-yl)-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3u): This compound was synthesized with 200 mol% of DIEA at 60°C in 1, 2-Dichloroethane for 24 hours. No Me_4NCl was used. 83% yield; 6 : 1 dr; light yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 2.42 (3H, s), 4.01 (1H, dd, J = 7.3 Hz, J = 5.9 Hz), 4.30 (1H, d, J = 7.3 Hz), 6.01 (1H, d, J = 5.5 Hz), 6.74 (1H, d, J = 3.2 Hz), 6.81 (1H, dd, J = 5.0 Hz, J = 3.7 Hz), 7.10 (1H, d, J = 5.0 Hz), 7.18-7.28 (7H, m), 7.37-7.44 (5H, m), 7.75 (2H, d, J = 8.2 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 44.9, 53.6, 120.9, 125.2, 126.1, 126.5, 127.0, 127.4, 127.6, 128.4, 128.5, 128.8, 129.0, 129.4, 136.0, 137.1, 138.0, 139.2, 140.8, 145.0, 171.0; **HRMS** (ESI): calculated for $[\text{C}_{28}\text{H}_{24}\text{NO}_3\text{S}_2]^+$: m/z = 486.1198, found: m/z = 486.1199; **Optical rotation**: $[\alpha]_D^{20}$: 21 (c 2.7, CHCl_3); **HPLC** analysis: 81 : 19 er (Chiralcel AD-H, 20 : 80 i PrOH/Hexane, 0.75 mL/min), R_t (major) = 51.2 min, R_t (minor) = 76.6 min.

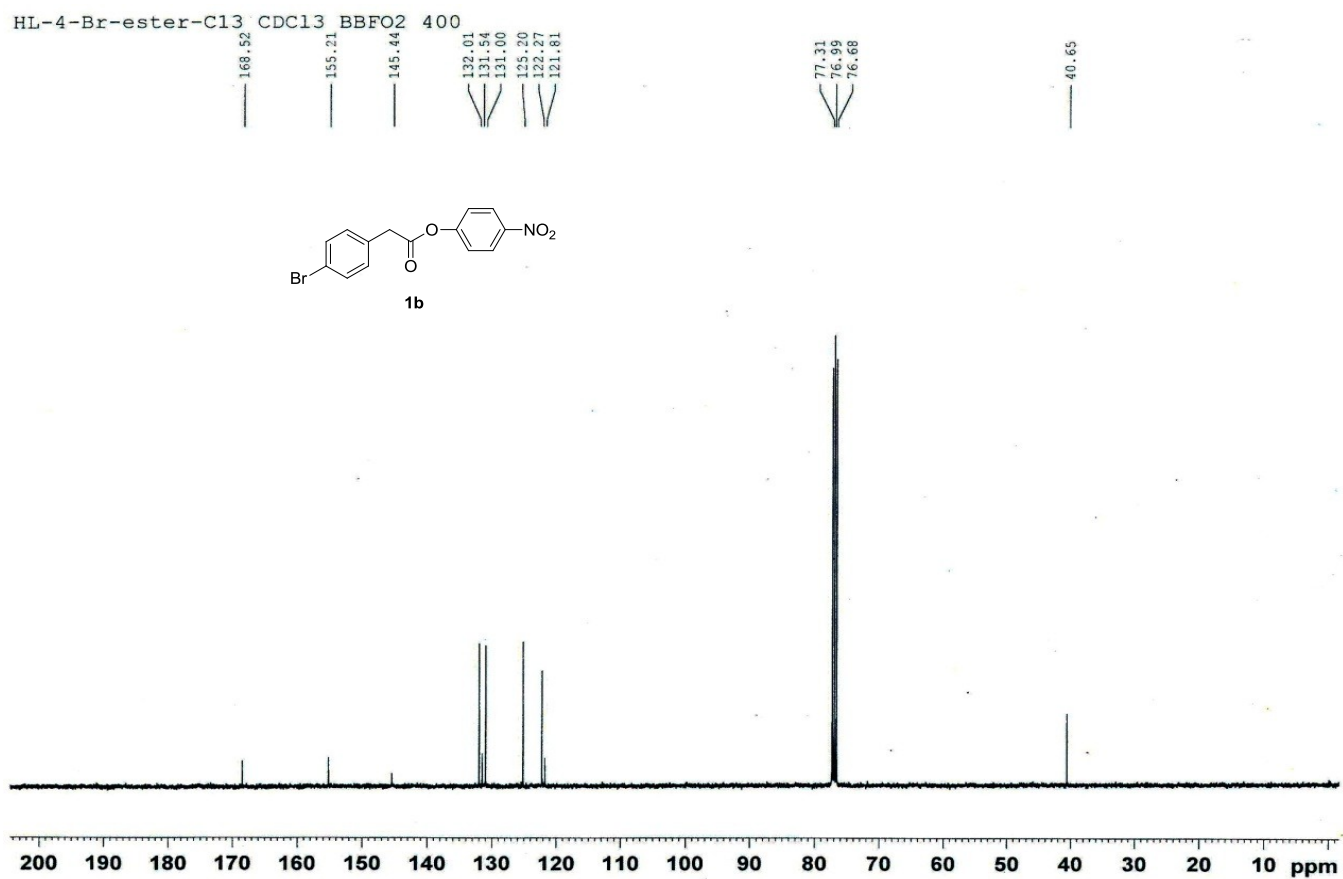
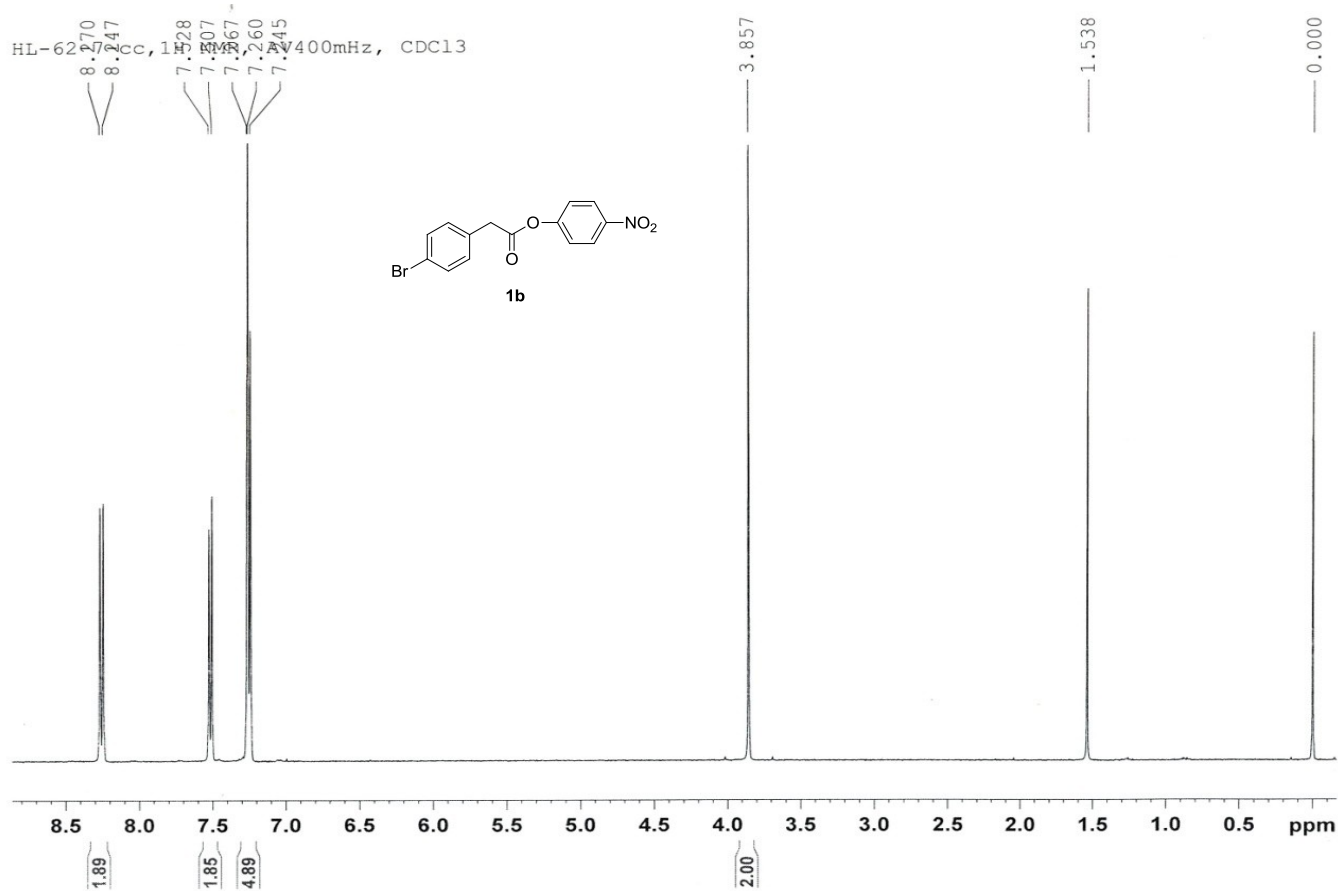


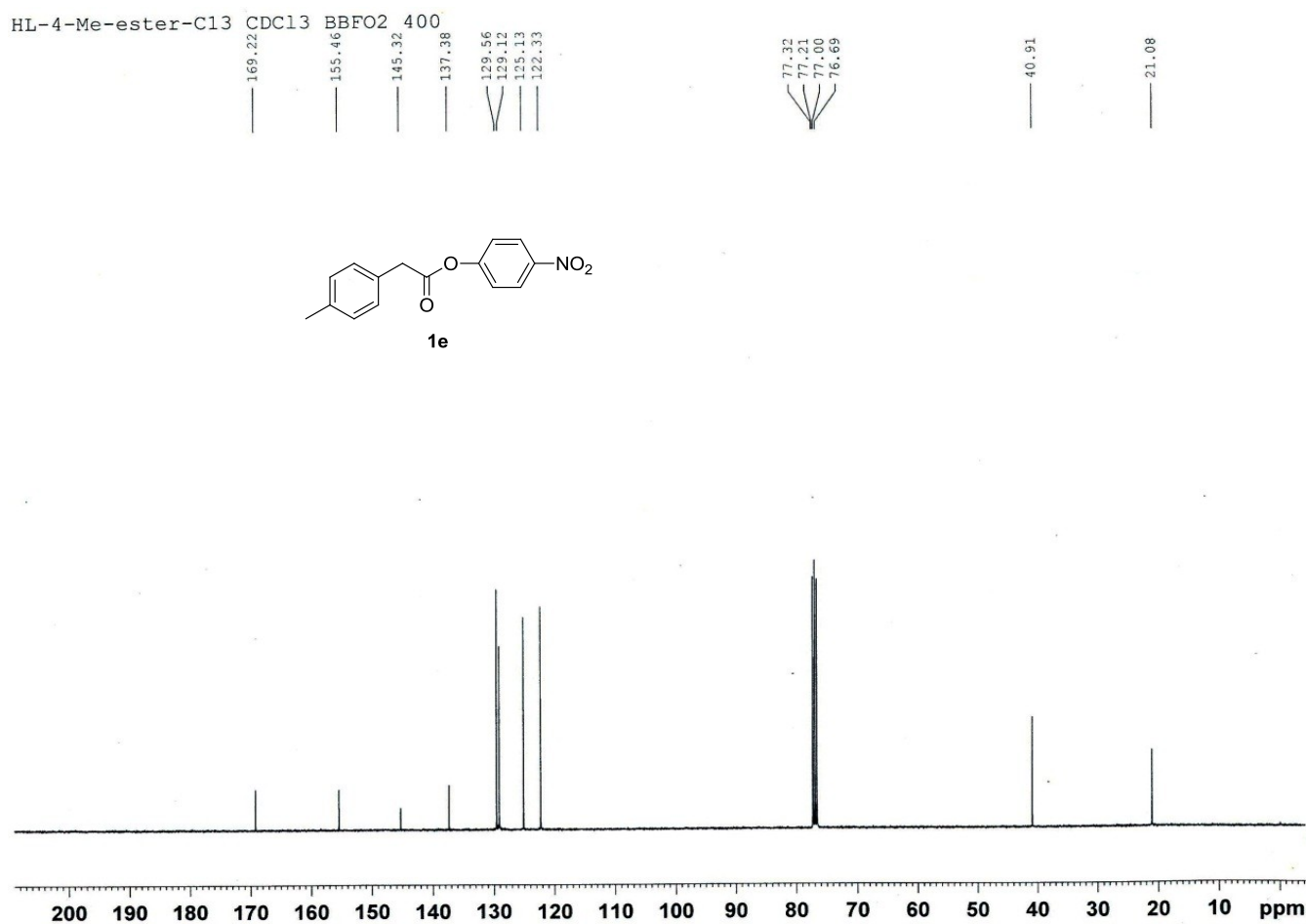
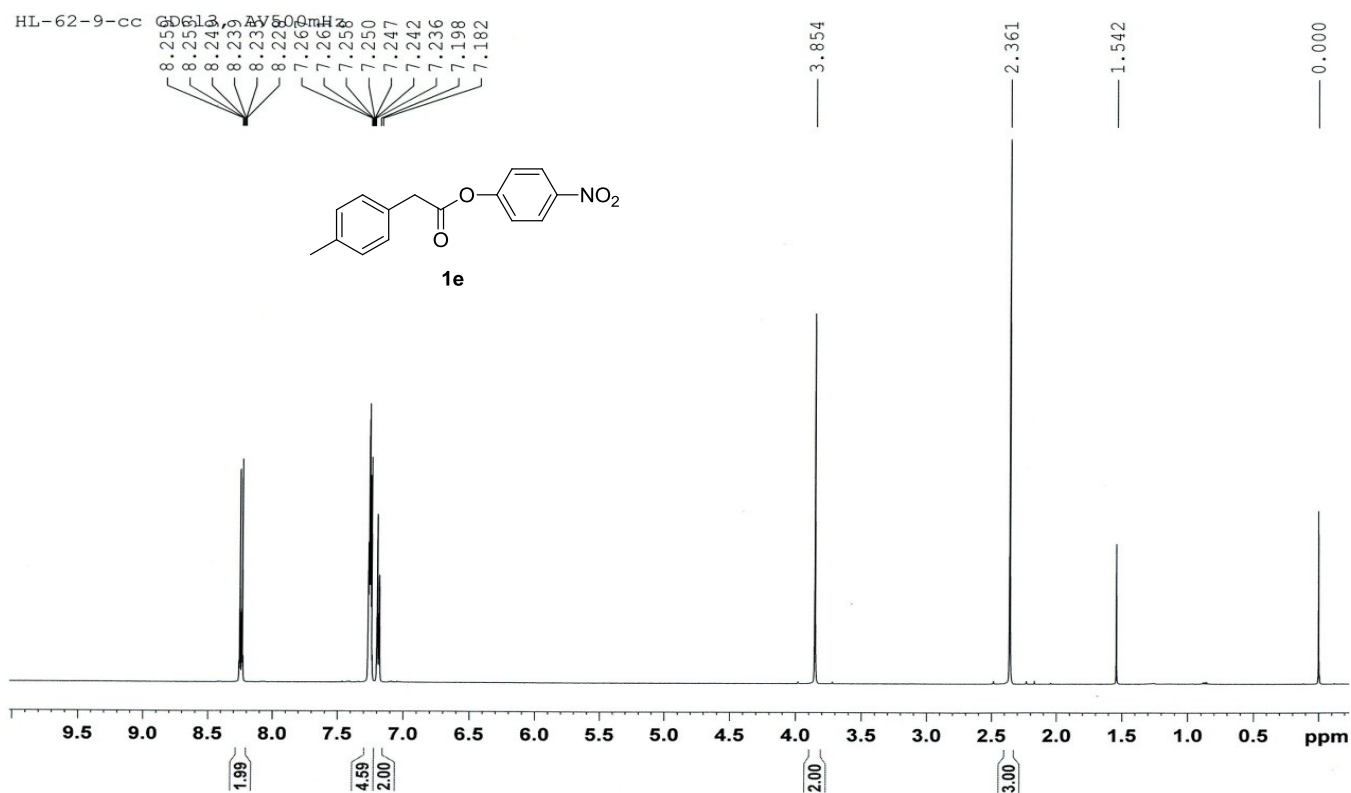
(3*S*, 4*S*)-3-(1-Methyl-1*H*-indol-3-yl)-4, 6-diphenyl-1-tosyl-3, 4-dihydropyridin-2(1*H*)-one (3v): 51% yield; >20 : 1 dr; light yellow oil; ^1H NMR (400 MHz, CDCl_3) δ 2.47 (3H, s), 3.53 (3H, s), 4.15 (1H, d, J = 9.6 Hz), 4.20 (1H, dd, J = 9.6 Hz, J = 4.3 Hz), 6.05 (1H, d, J = 4.4 Hz), 6.55 (1H, s), 6.89-7.03 (4H, m), 7.11-7.18 (5H, m), 7.26 (2H, d, J = 8.1 Hz), 7.37-7.41 (3H, m), 7.49-7.51 (2H, m), 7.87 (2H, d, J = 8.2 Hz);

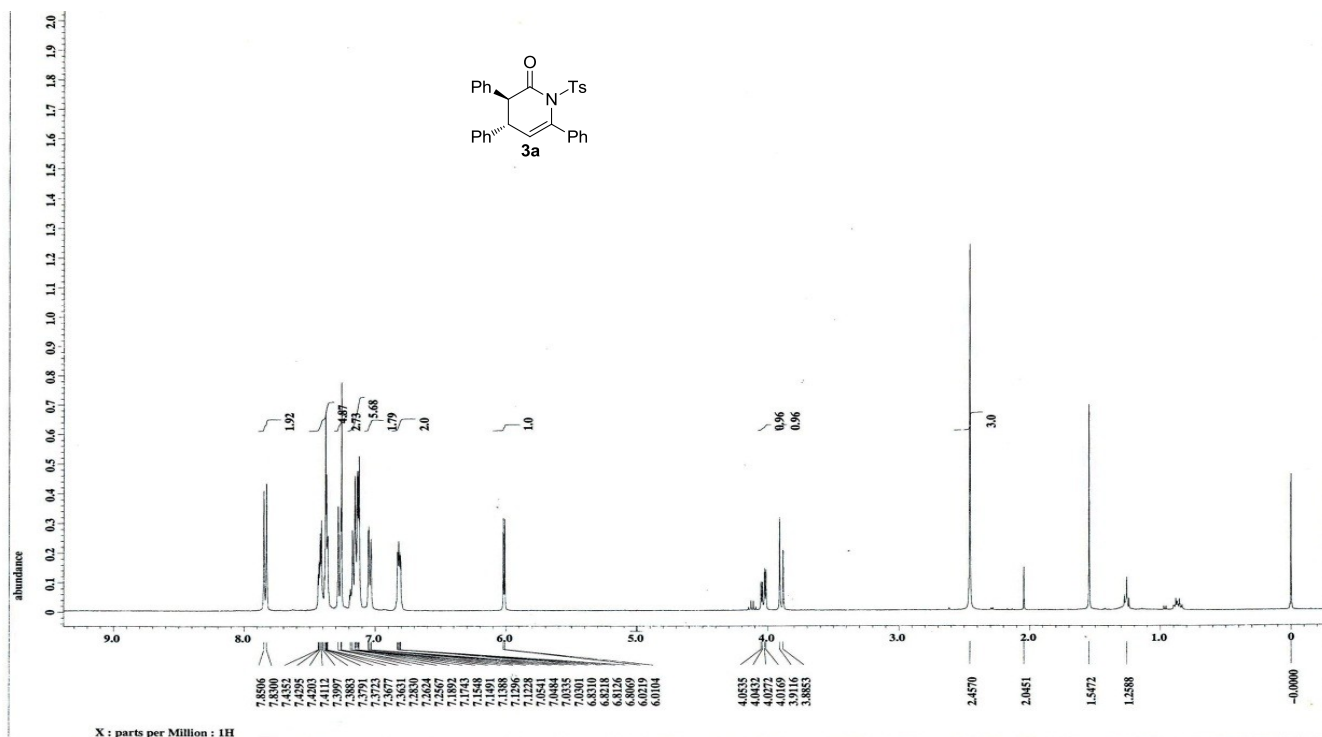


¹³C NMR (100 MHz, CDCl₃) δ 21.7, 32.5, 43.5, 51.0, 109.0, 109.4, 119.0, 119.2, 121.6, 122.5, 125.8, 126.2, 126.9, 127.5, 127.9, 128.3, 128.4, 128.5, 129.1, 129.7, 136.4, 137.0, 137.6, 140.3, 140.5, 144.9, 172.1; **HRMS** (ESI): calculated for [C₃₃H₂₉N₂O₃S]⁺: m/z = 533.1899, found: m/z = 533.1903; **Optical rotation**: [α]_D²⁰: 10 (c 2.7, CHCl₃); **HPLC** analysis: 80 : 20 er (Chiralcel AD-H, 20 : 80 *i*PrOH/Hexane, 0.75 mL/min), R_t (major) = 70.9 min, R_t (minor) = 173.8 min.

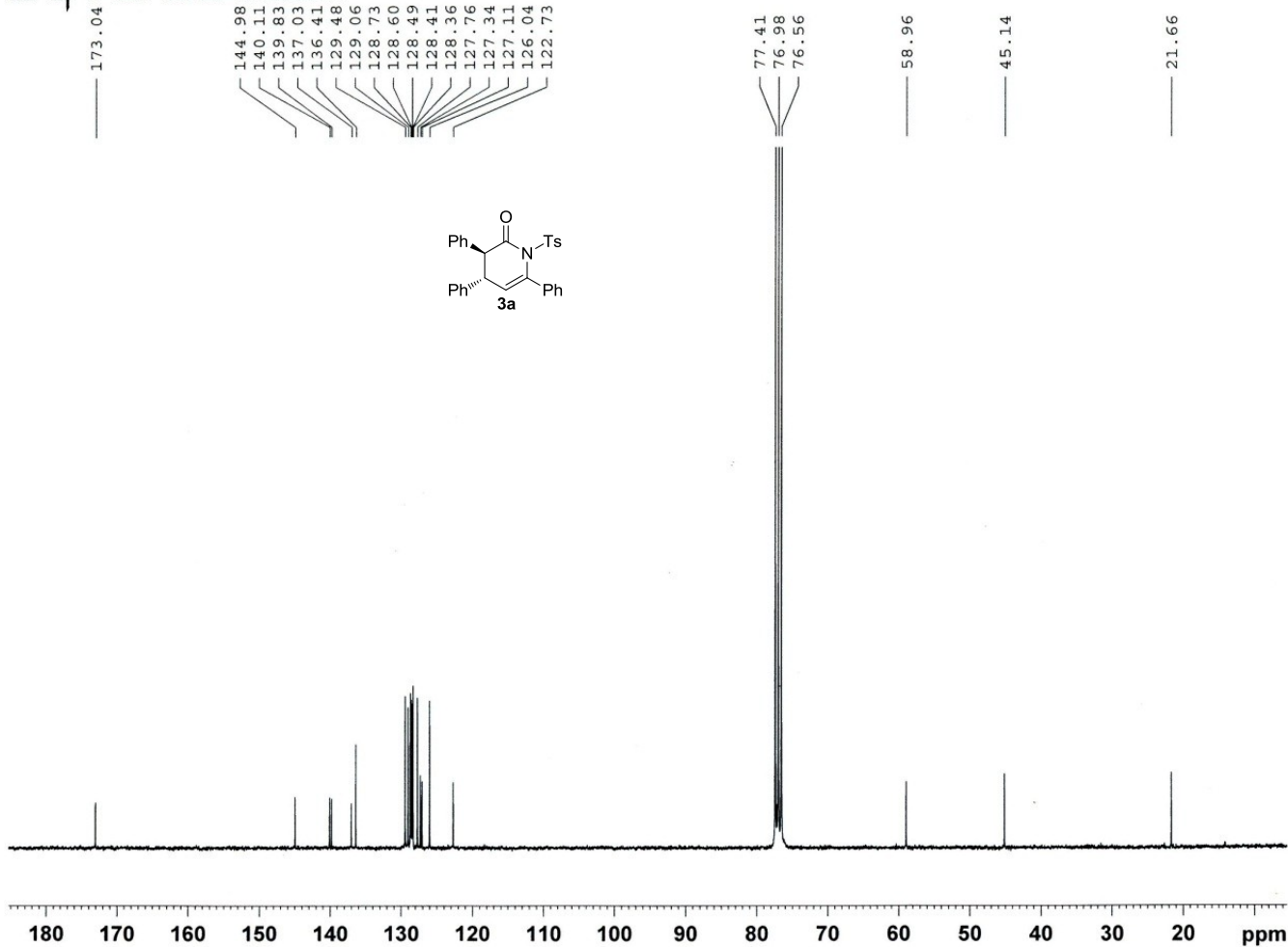
V: NMR and HPLC Spectra

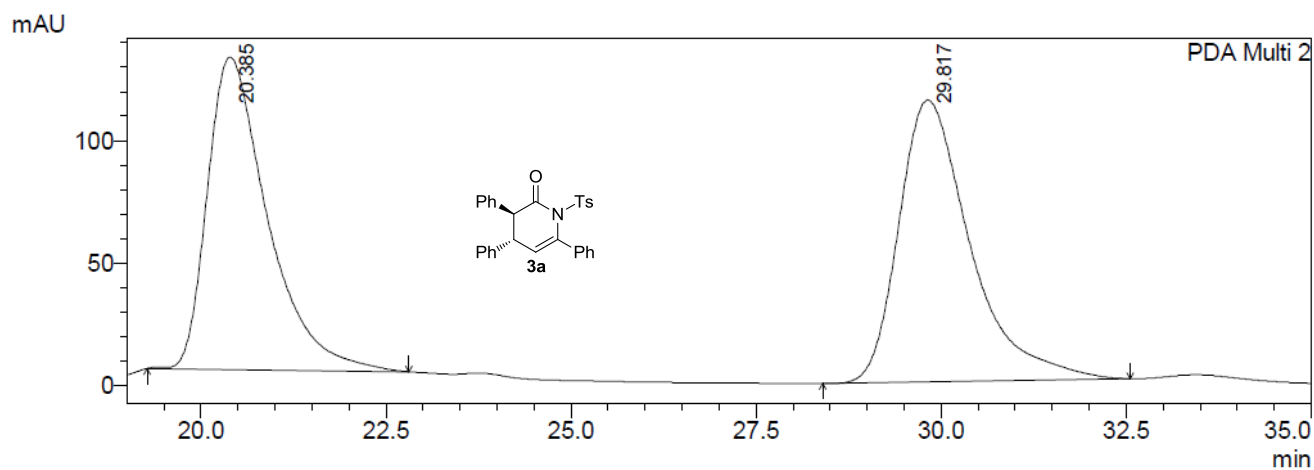






HL-64-1-C13 CDC13 AV300mHz

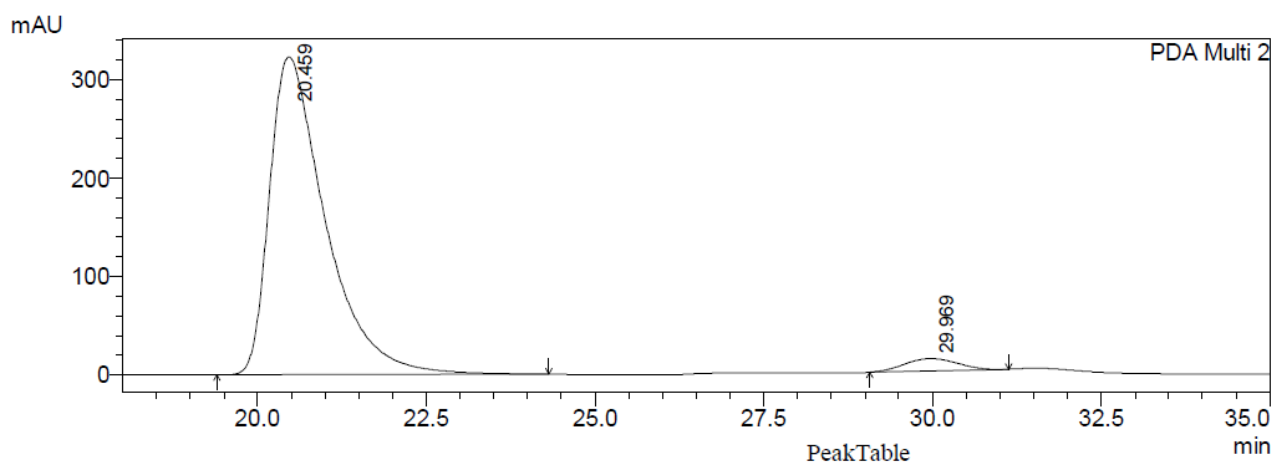




PeakTable

PDA Ch2 220nm 4nm

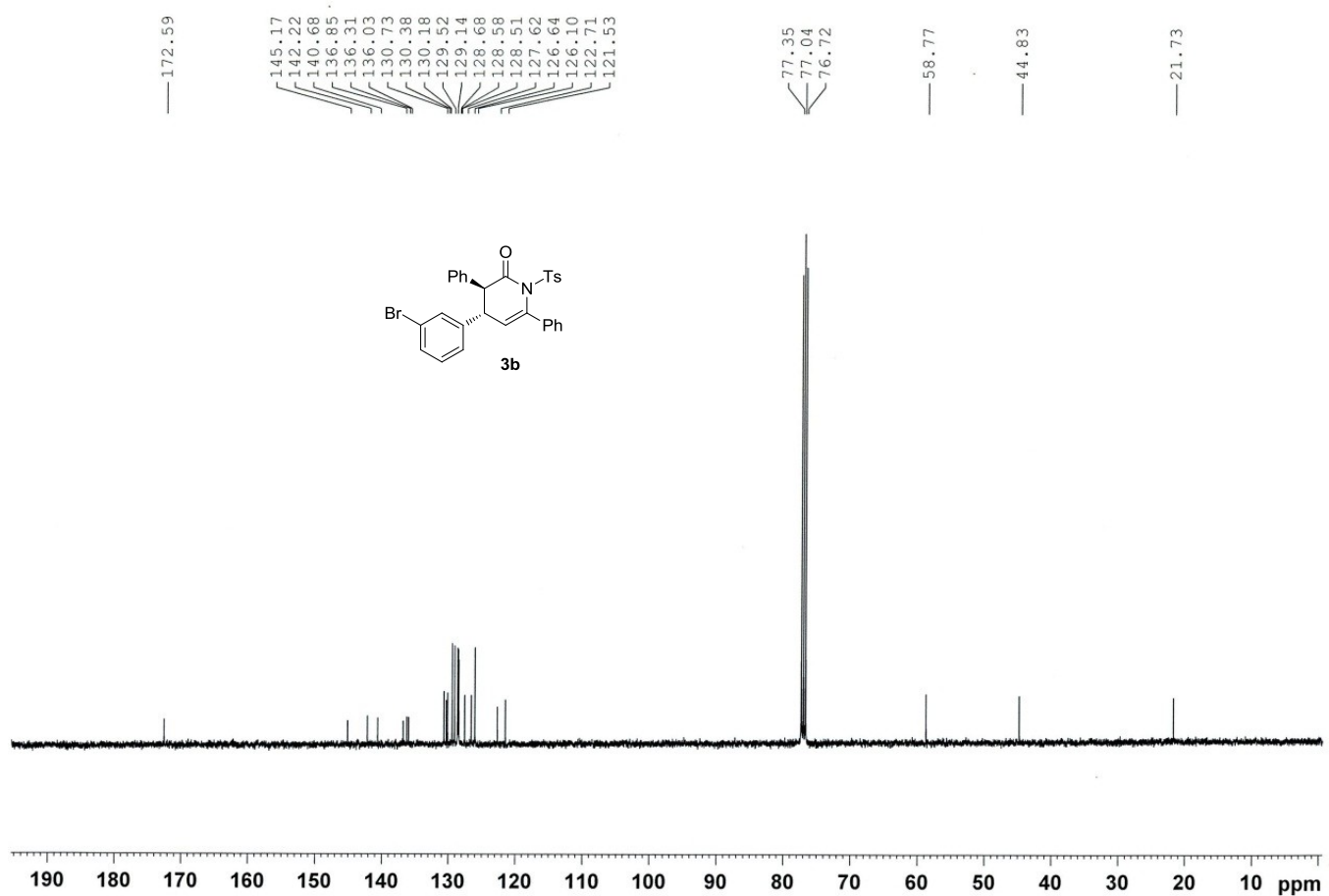
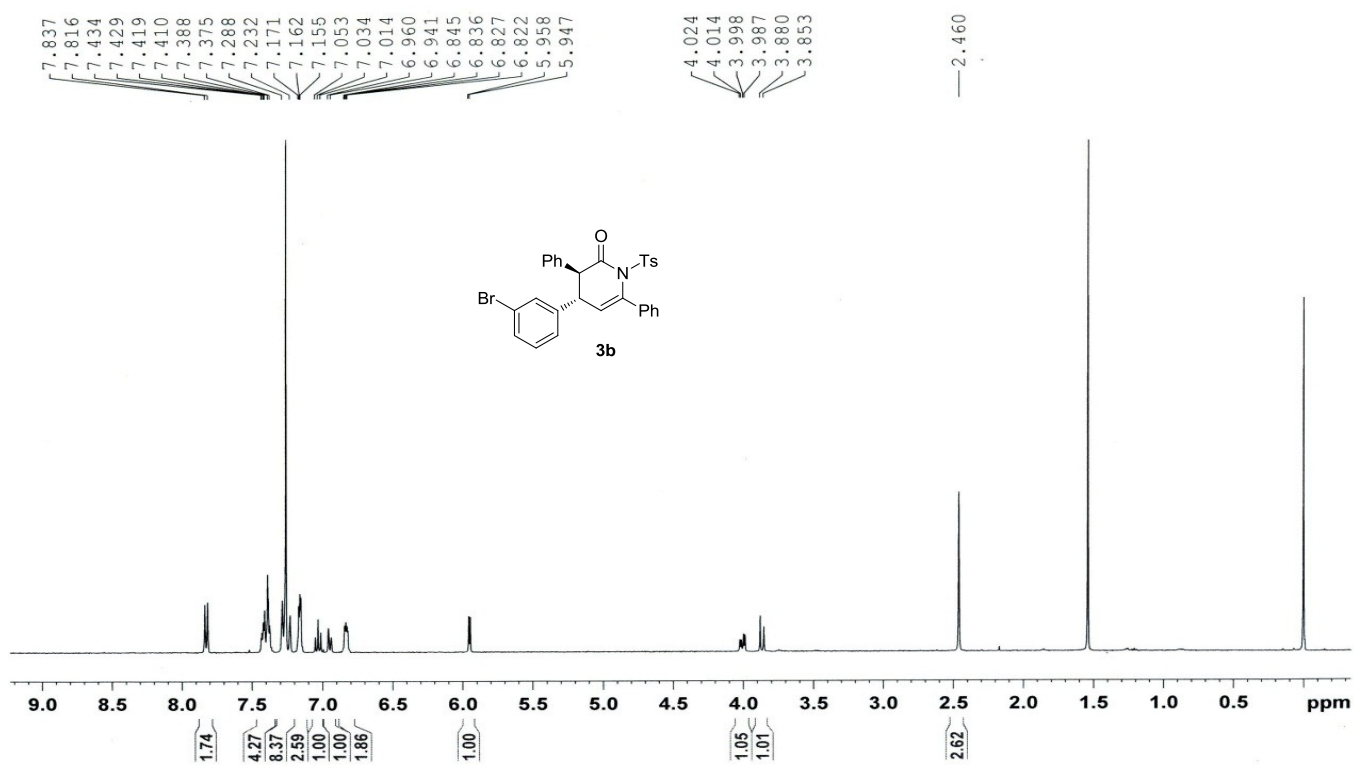
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.385	7227446	127551	48.292	52.572
2	29.817	7738622	115070	51.708	47.428
Total		14966068	242621	100.000	100.000

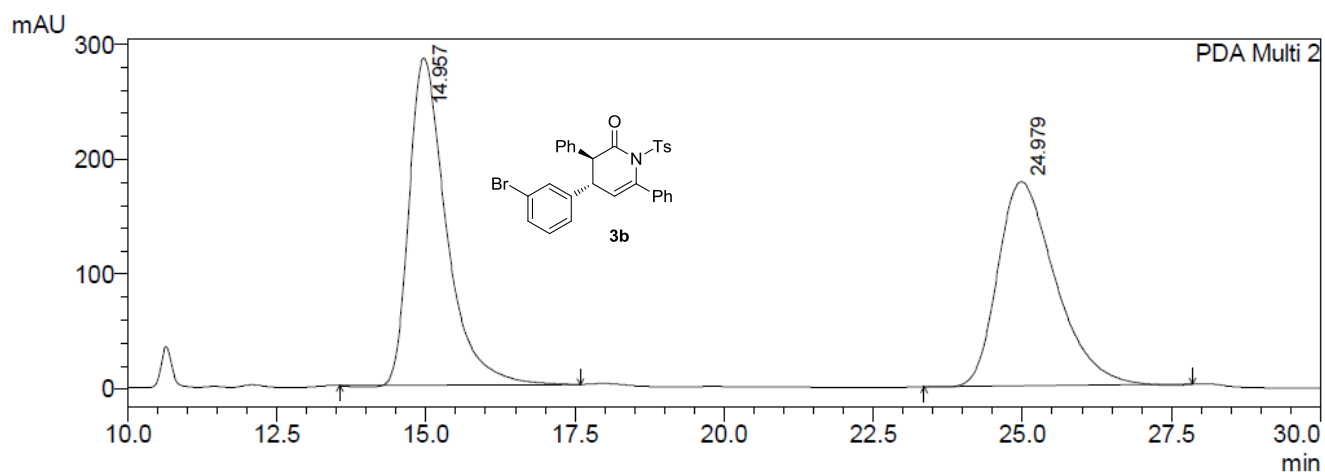


PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.459	18650780	323289	96.468	96.219
2	29.969	682878	12704	3.532	3.781
Total		19333658	335993	100.000	100.000

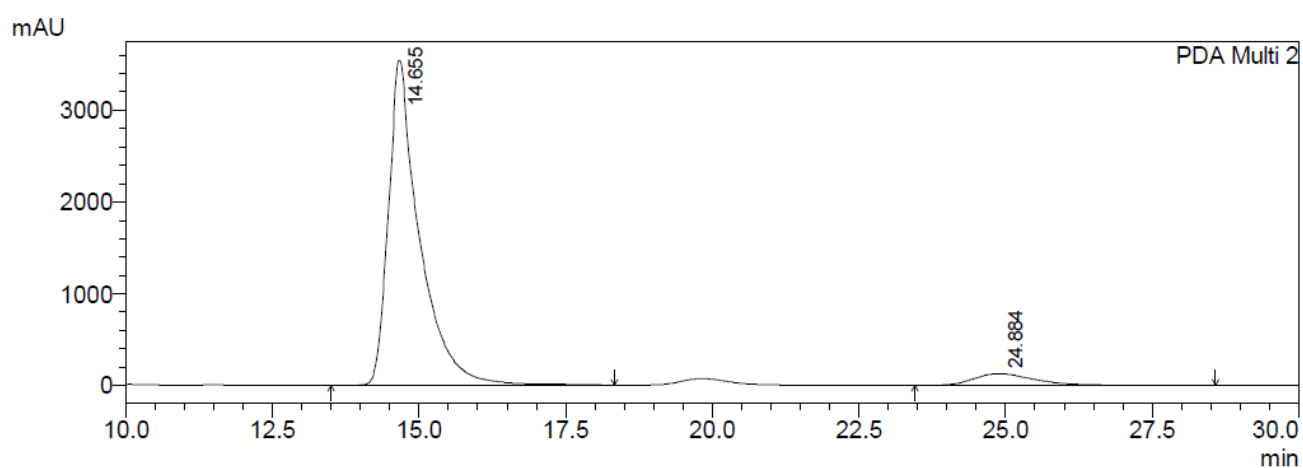




PeakTable

PDA Ch2 220nm 4nm

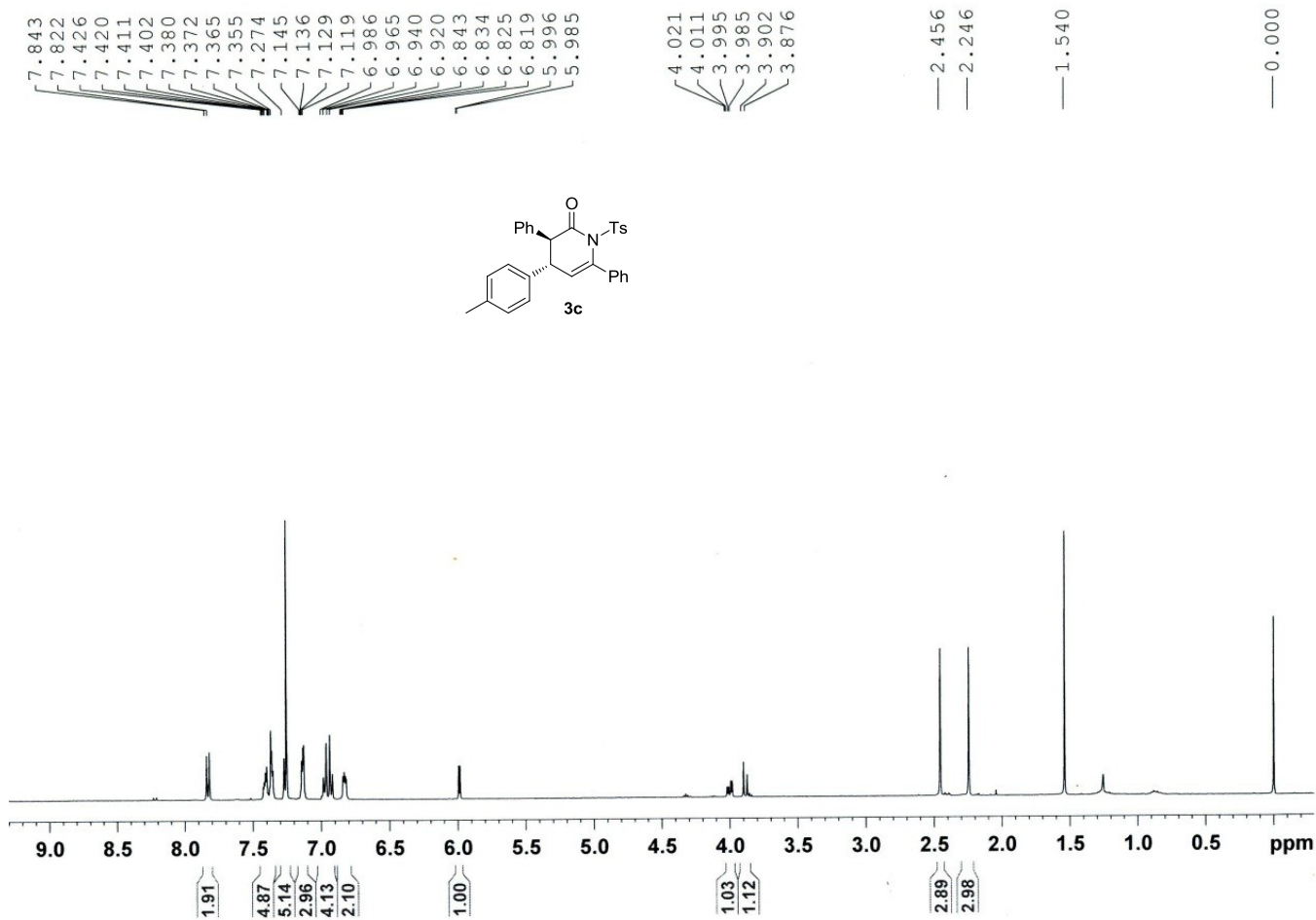
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.957	12380313	285087	50.930	61.582
2	24.979	11928124	177852	49.070	38.418
Total		24308437	462939	100.000	100.000



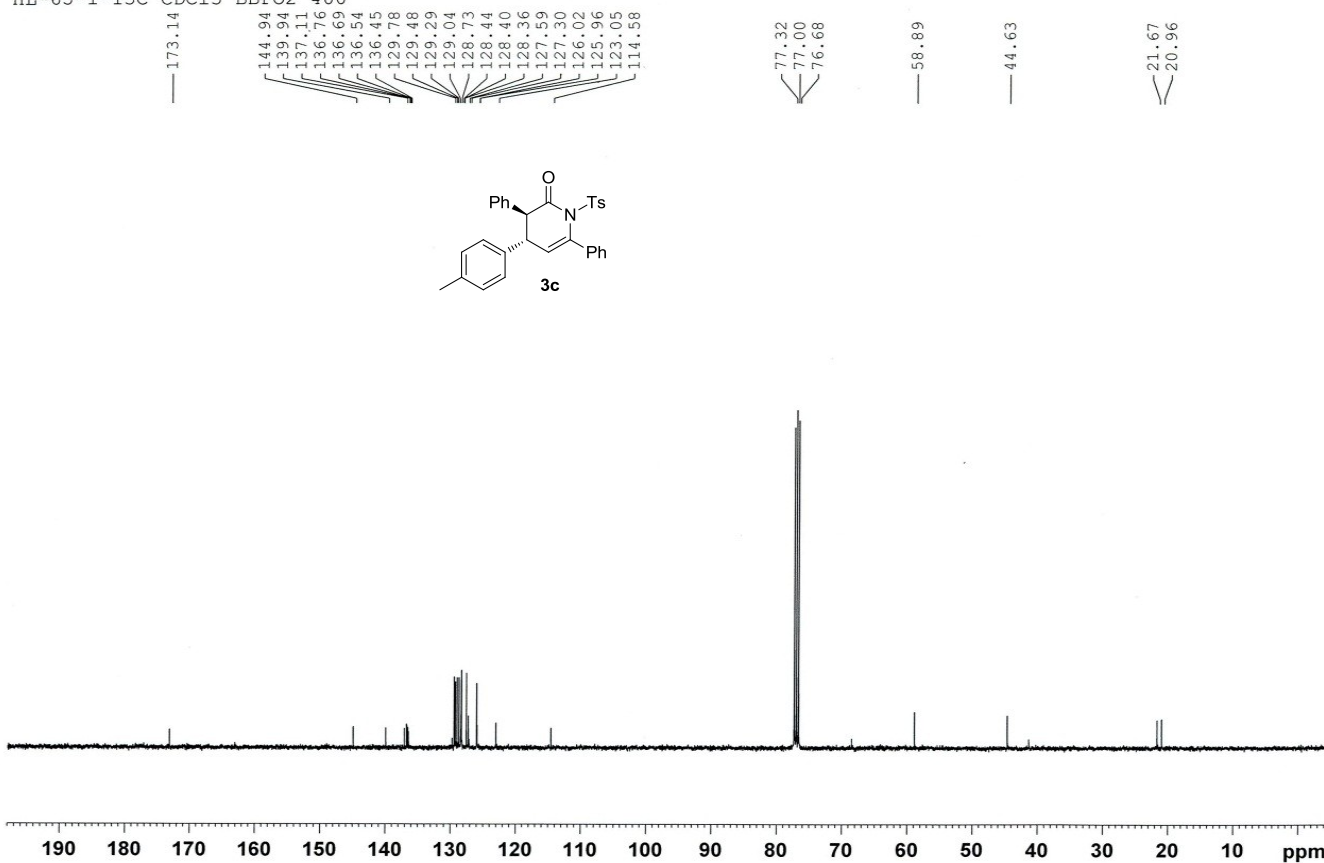
PeakTable

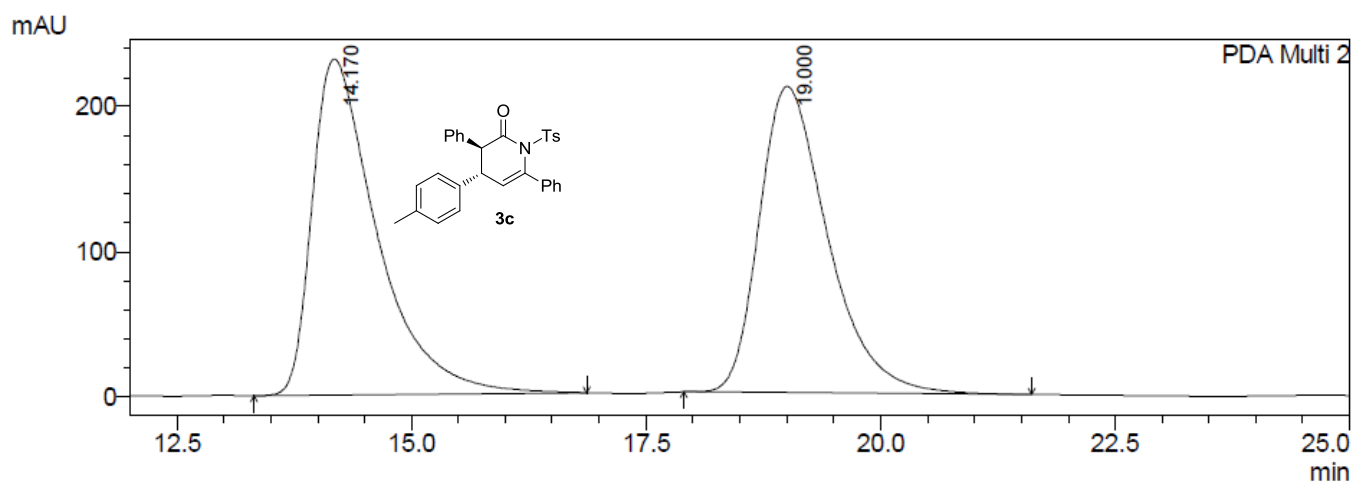
PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.655	130768093	3540766	93.413	96.549
2	24.884	9220814	126551	6.587	3.451
Total		139988907	3667317	100.000	100.000



HL-65-1-13C CDCl₃ BBFO2 400

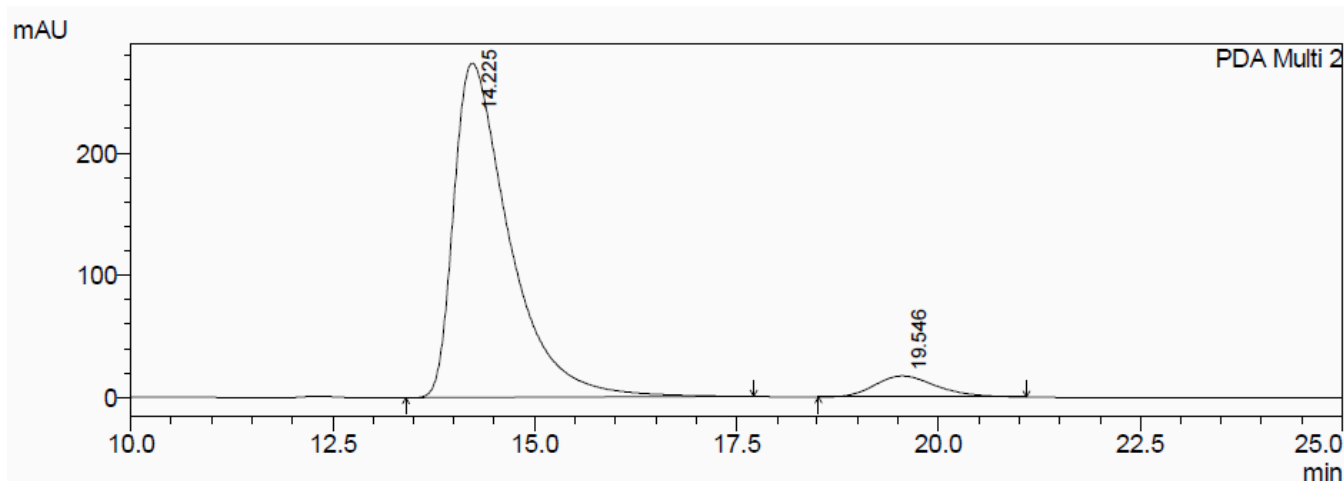




PeakTable

PDA Ch2 220nm 4mm

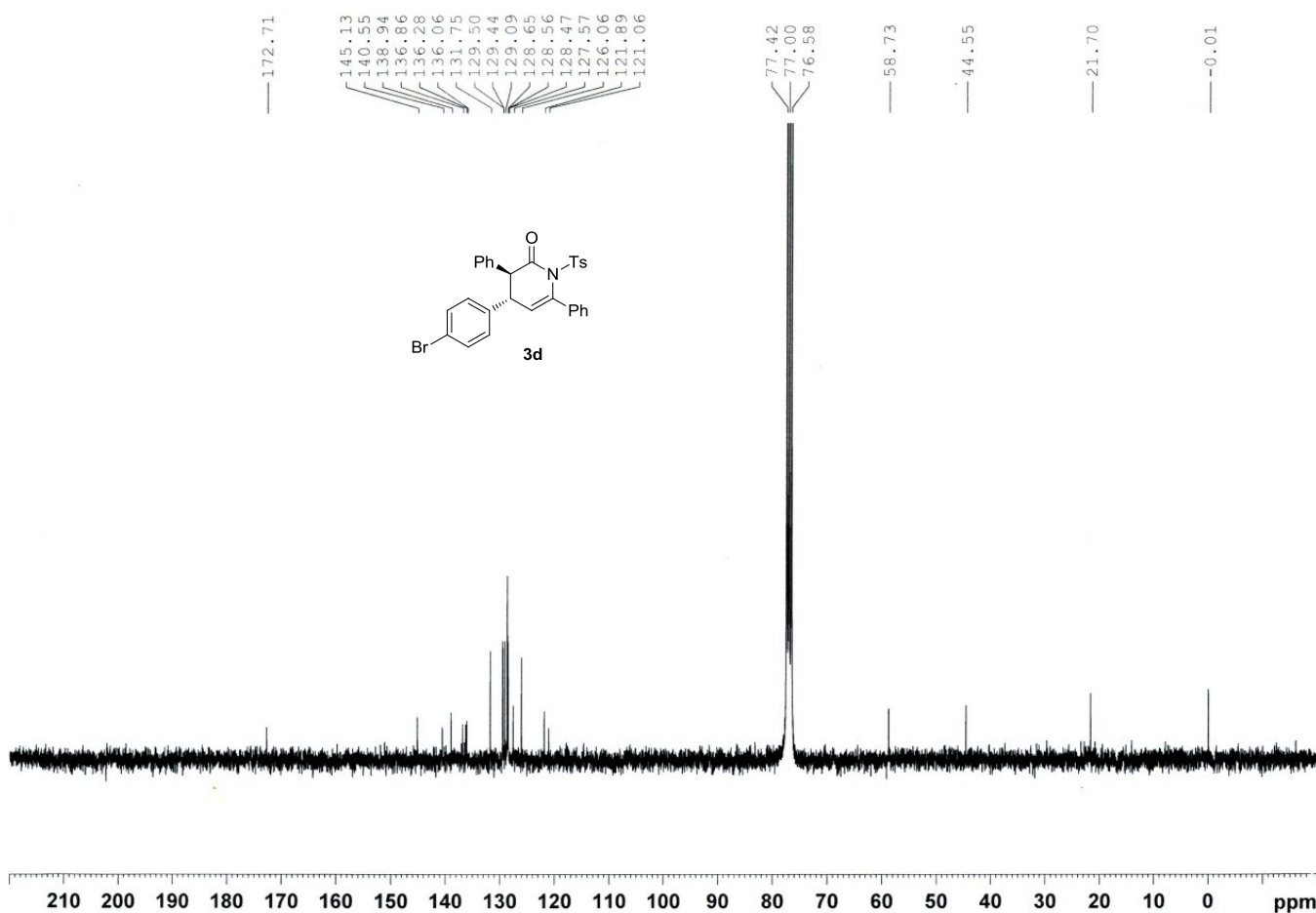
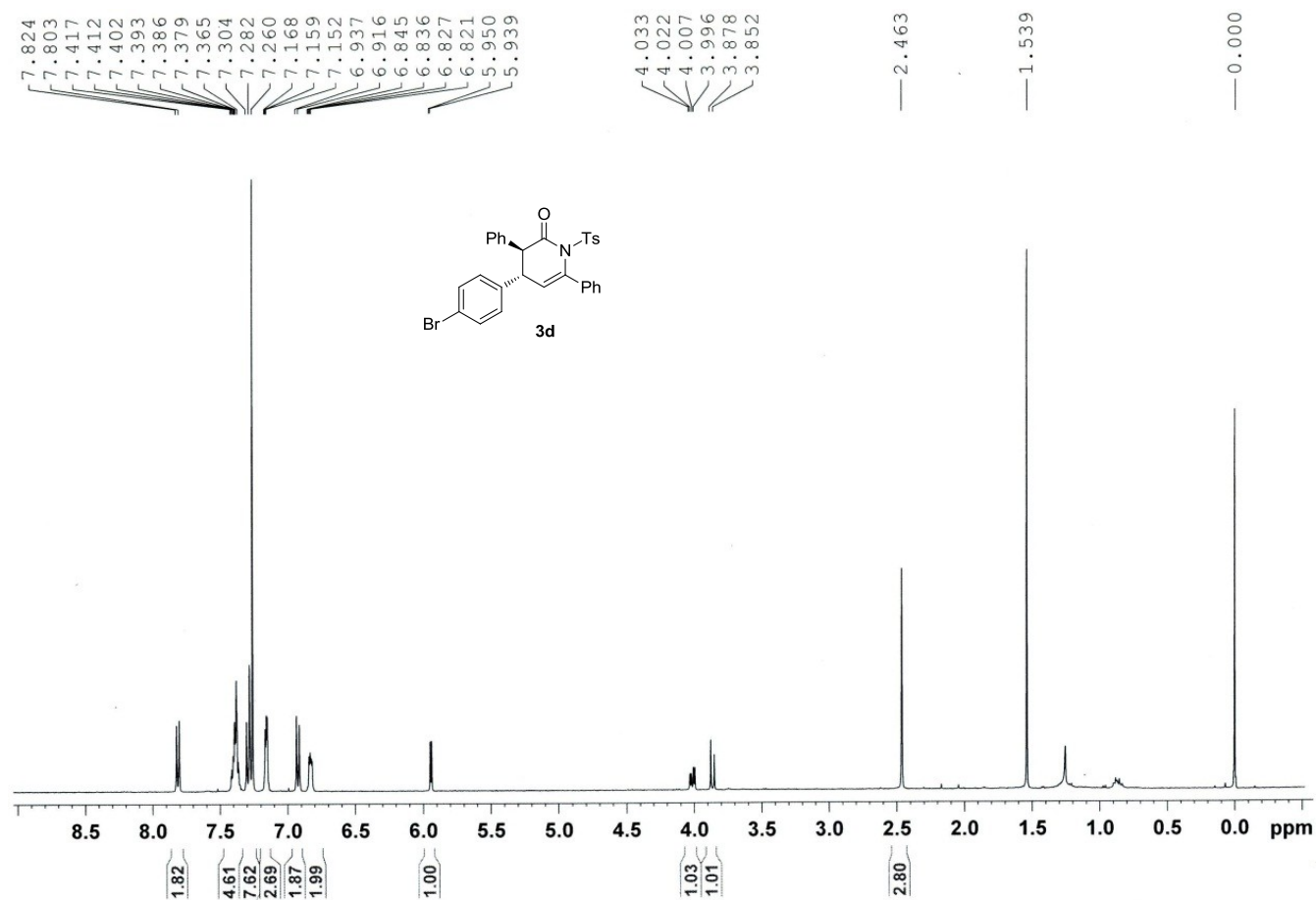
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.170	11151441	231435	50.924	52.334
2	19.000	10746756	210790	49.076	47.666
Total		21898198	442225	100.000	100.000

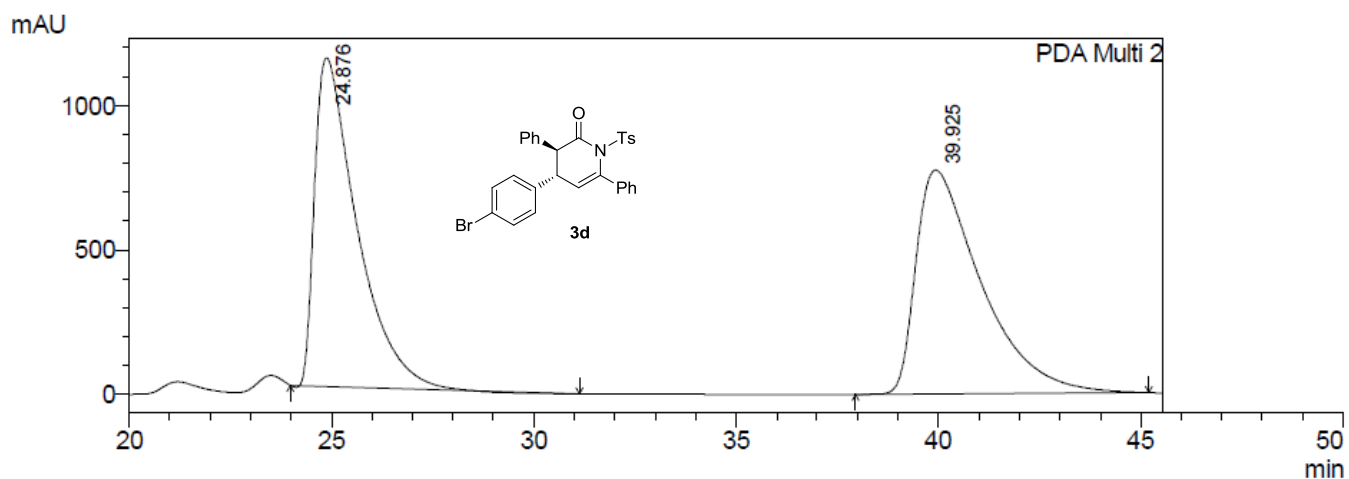


PeakTable

PDA Ch2 220nm 4mm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.225	13115193	273799	93.464	94.087
2	19.546	917163	17207	6.536	5.913
Total		14032356	291006	100.000	100.000

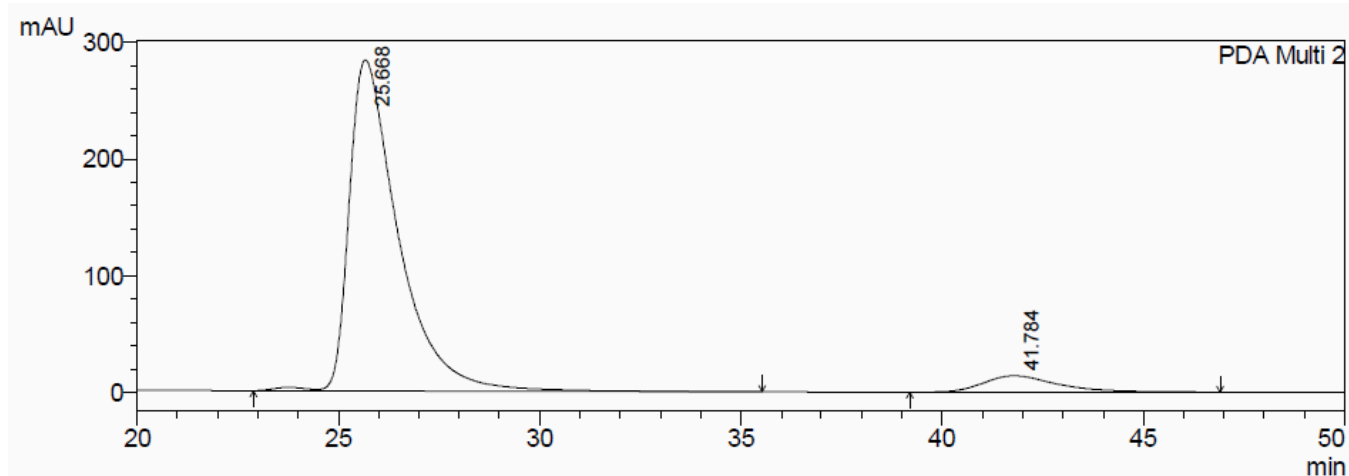




PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.876	82326599	1136277	48.751	59.511
2	39.925	86546272	773070	51.249	40.489
Total		168872871	1909346	100.000	100.000

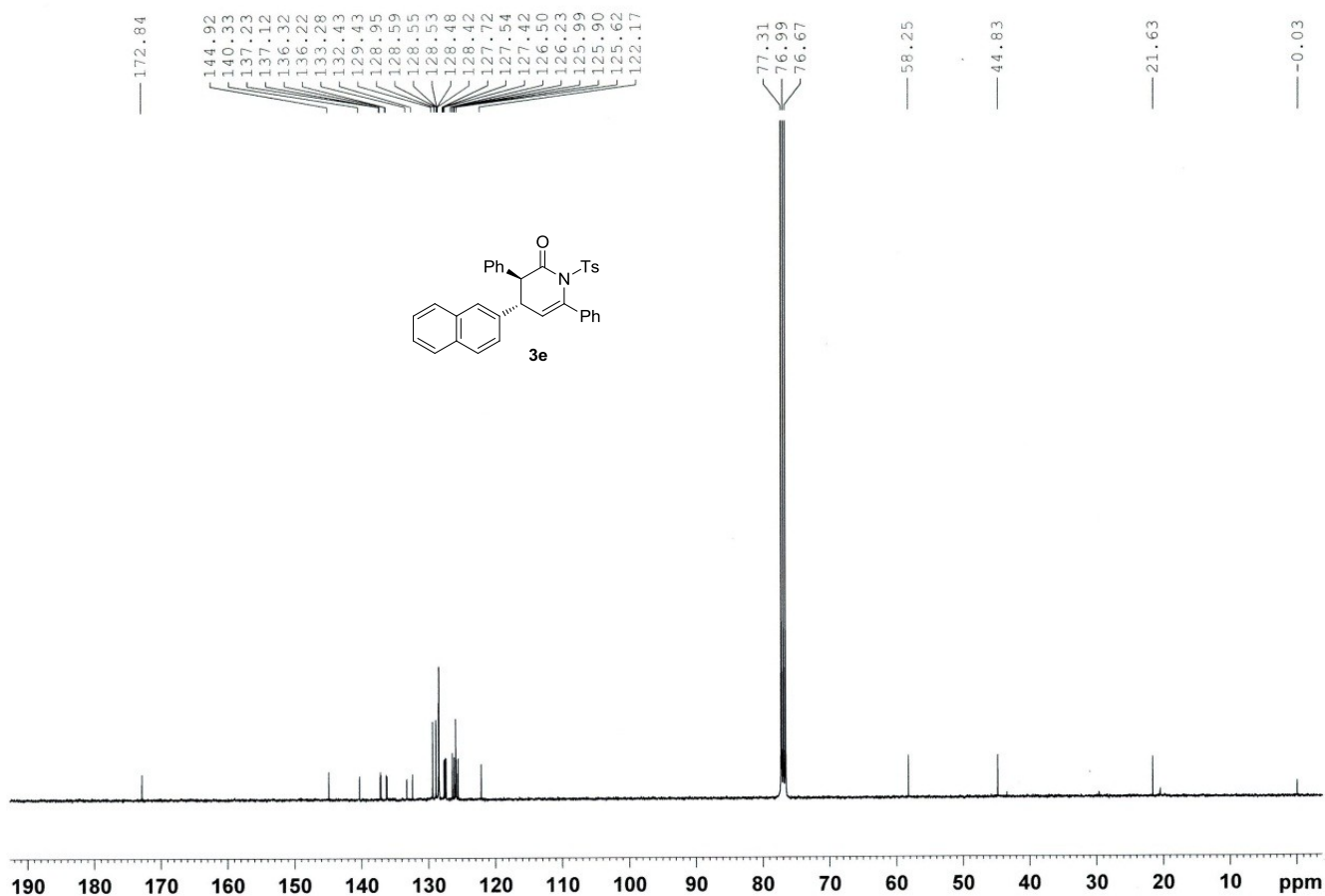
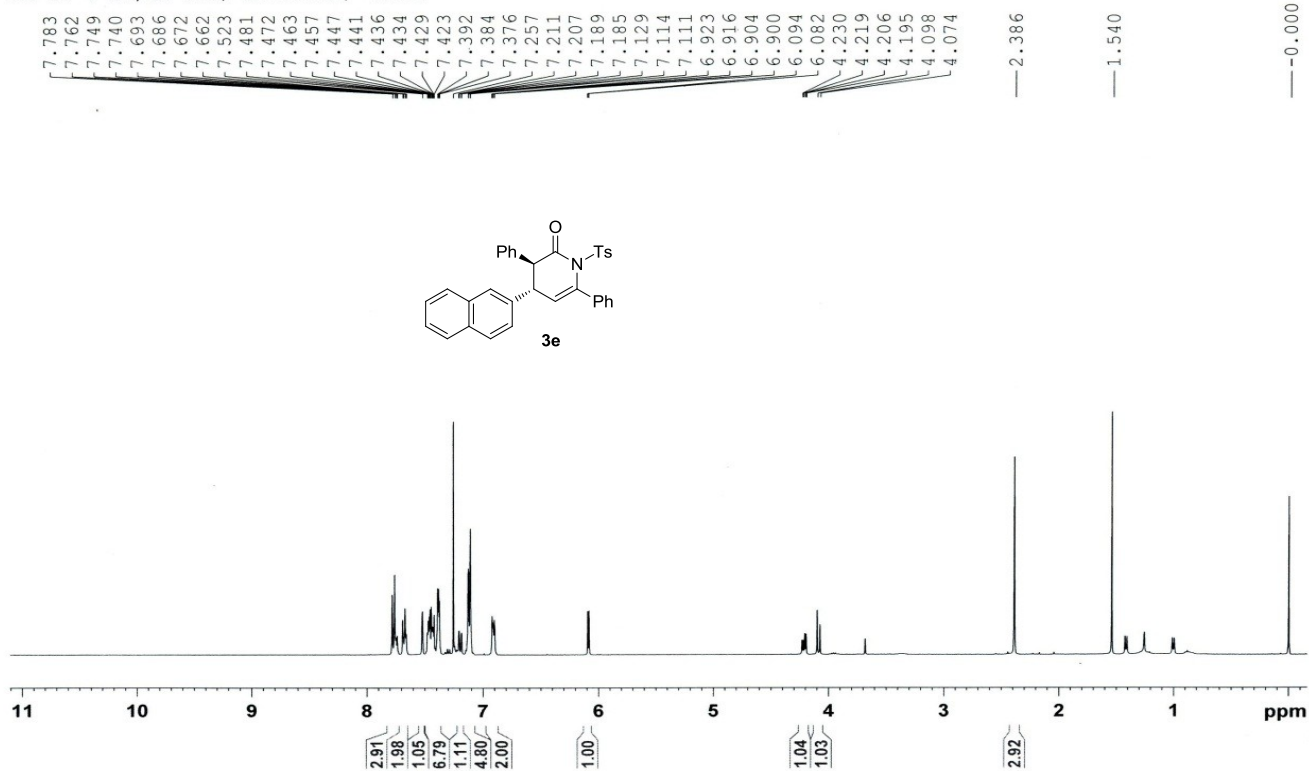


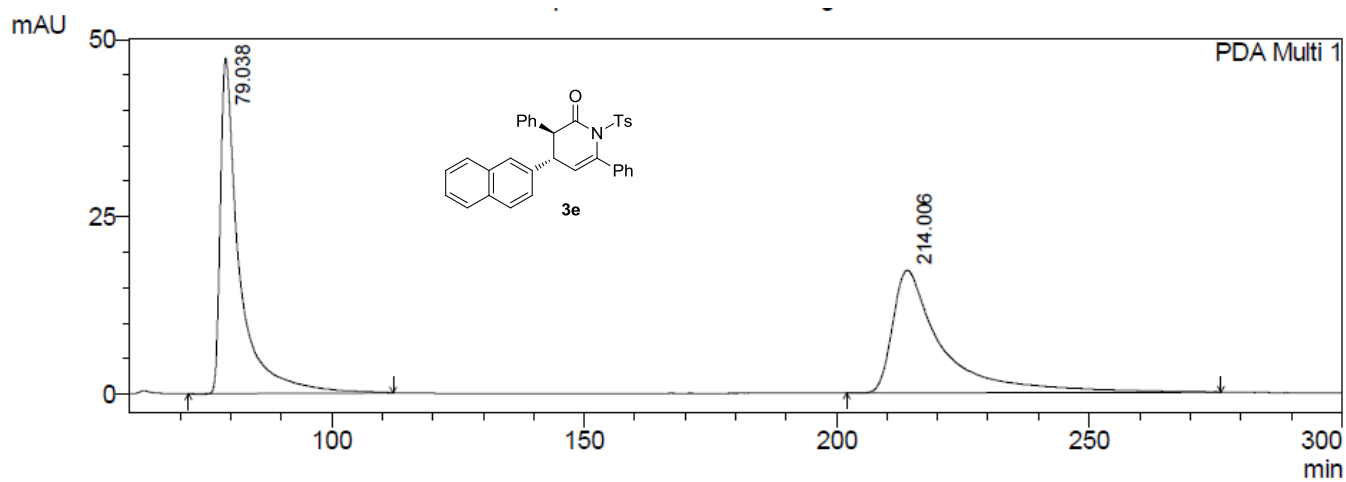
PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.668	24137605	283895	93.176	95.364
2	41.784	1767690	13800	6.824	4.636
Total		25905295	297695	100.000	100.000

HL-65-4-cc, 1H NMR, AV400MHz, CDCl3

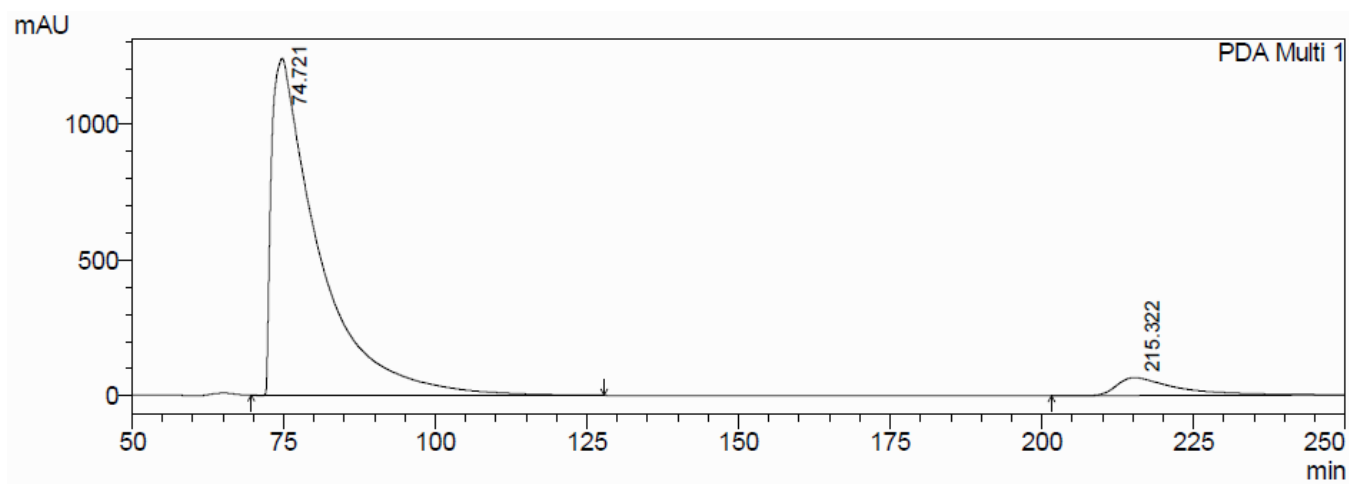




PeakTable

PDA Ch1 254nm 4nm

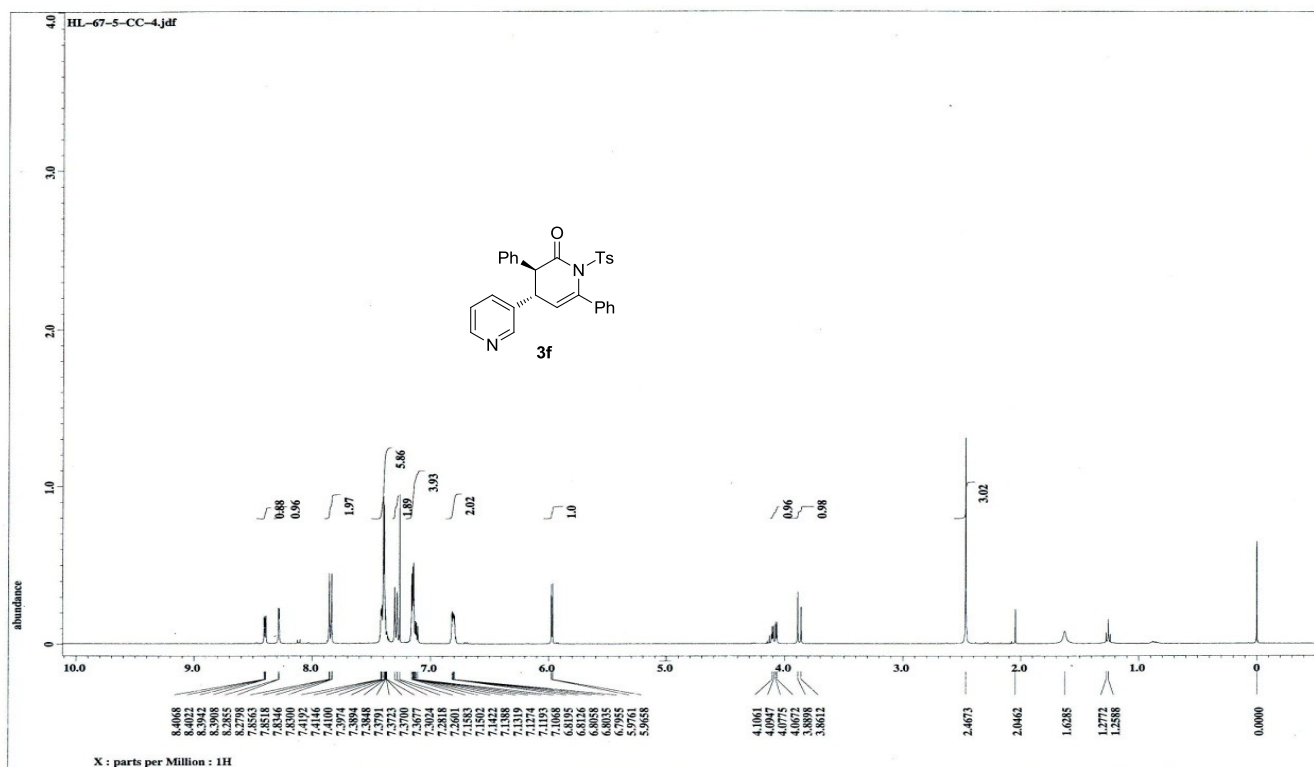
Peak#	Ret. Time	Area	Height	Area %	Height %
1	79.038	12427044	47317	51.172	73.222
2	214.006	11857661	17304	48.828	26.778
Total		24284705	64621	100.000	100.000



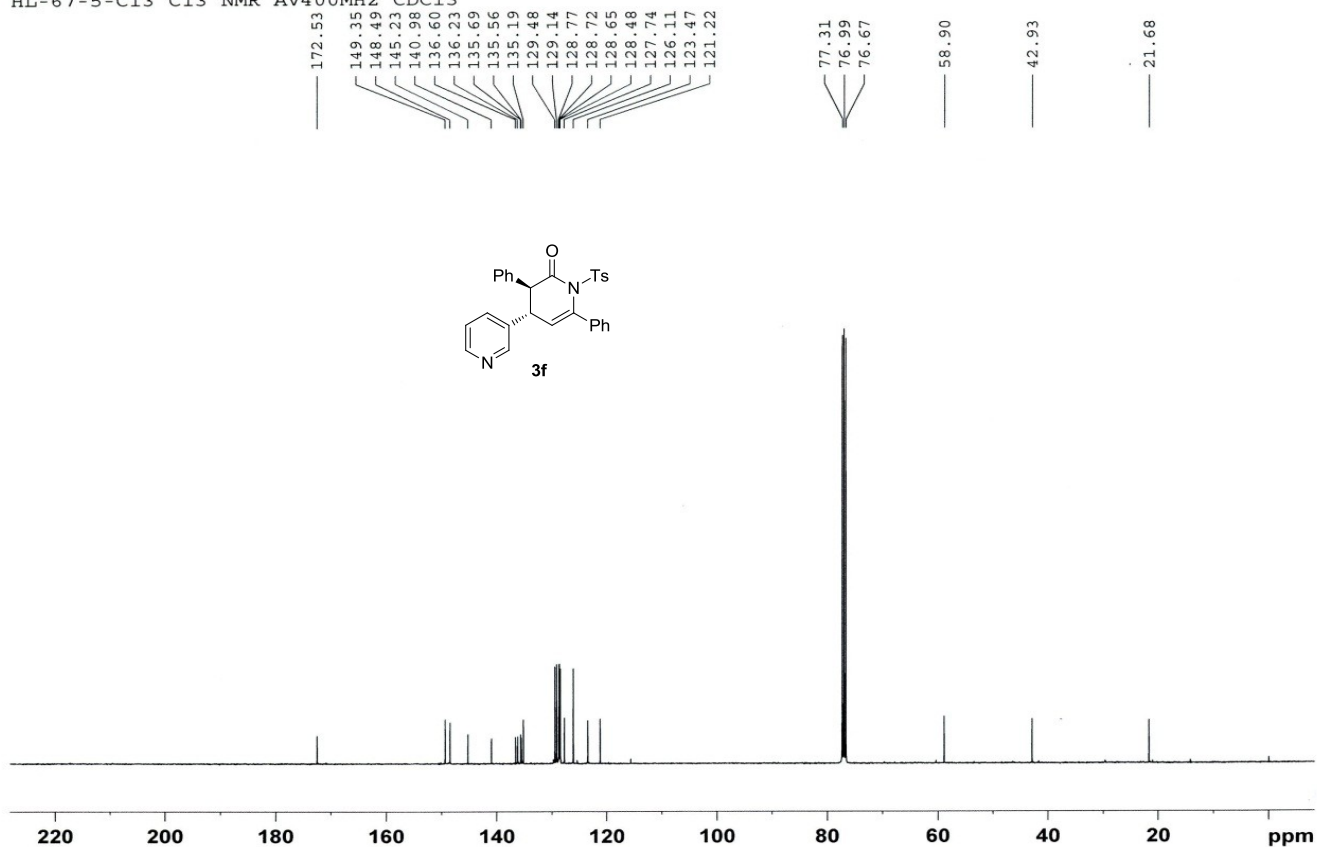
PeakTable

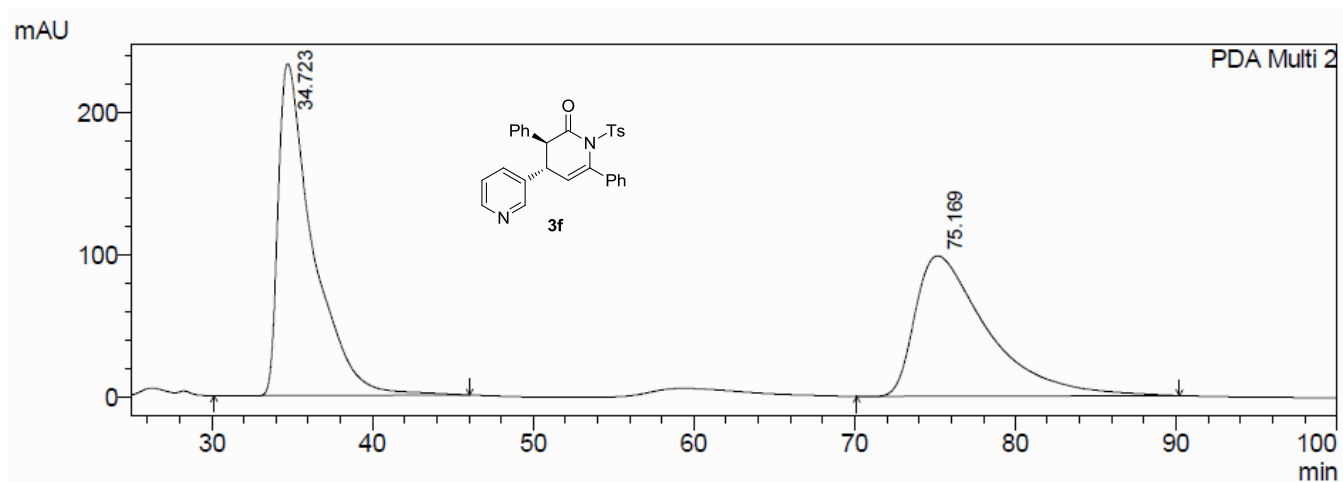
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	74.721	670611255	1239966	93.437	94.921
2	215.322	47105913	66349	6.563	5.079
Total		717717168	1306315	100.000	100.000

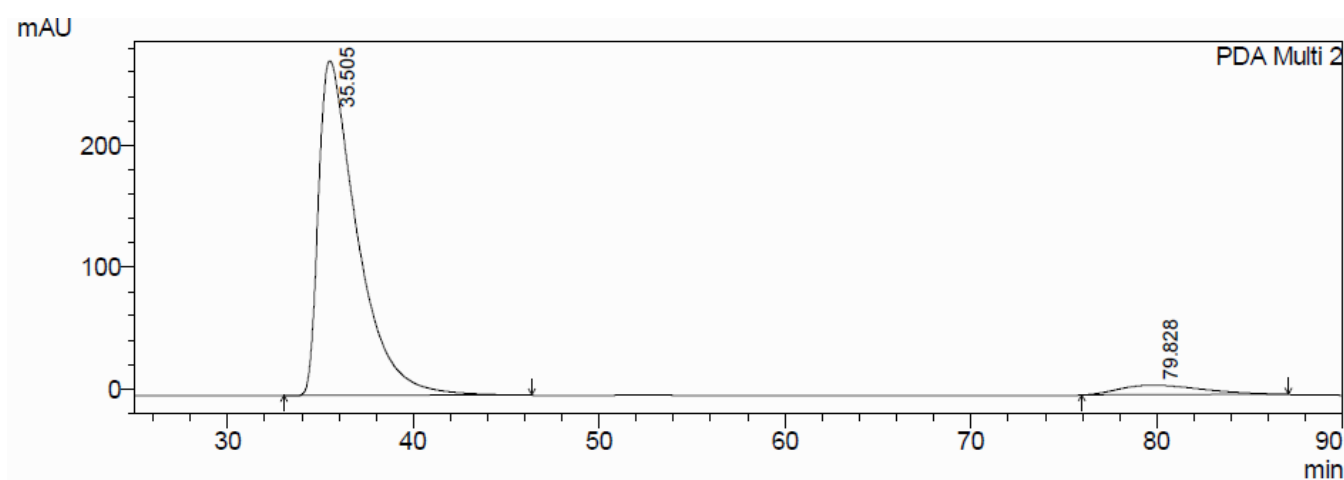


HL-67-5-C13 C13 NMR AV400MHZ CDC13

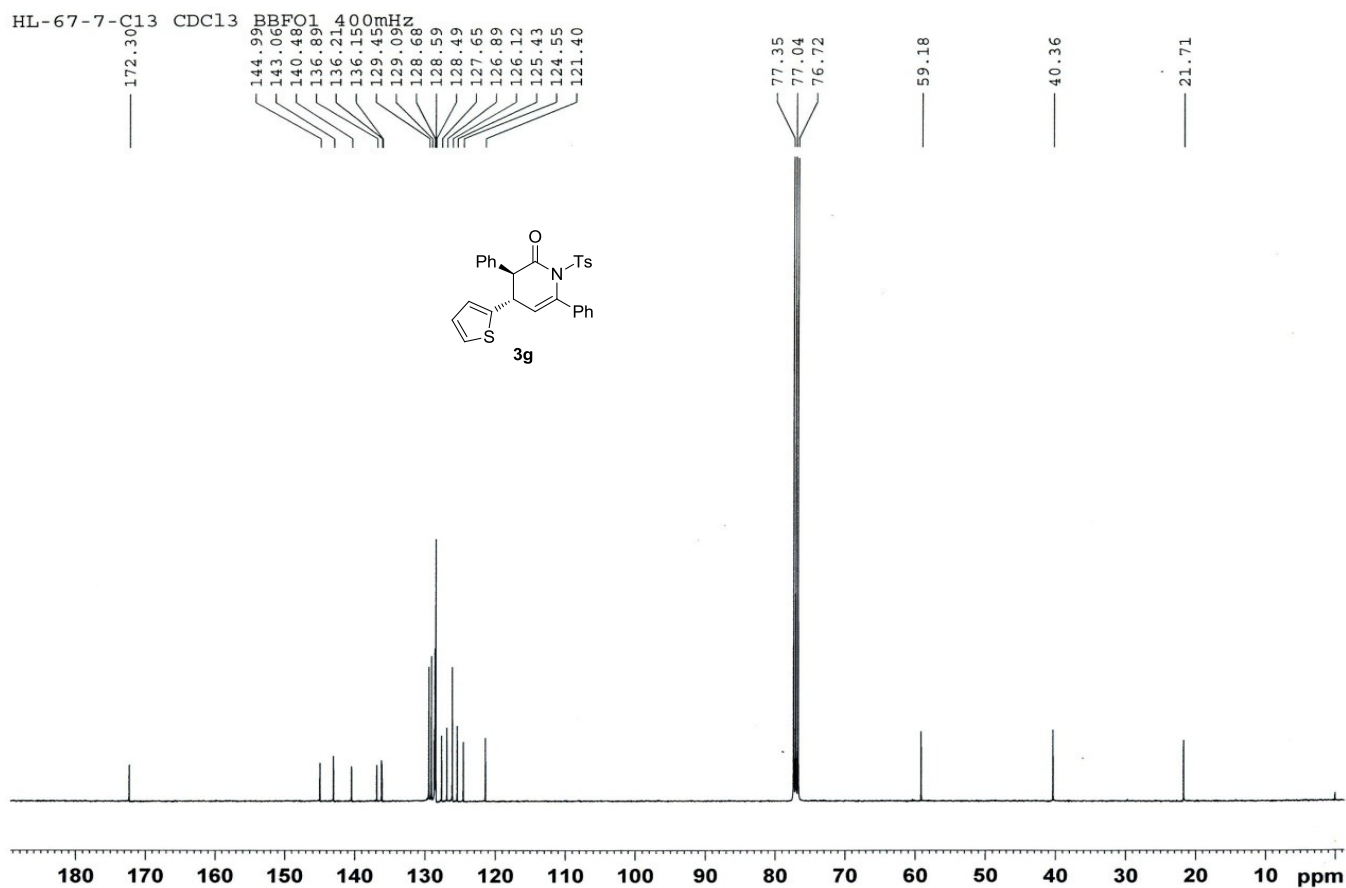
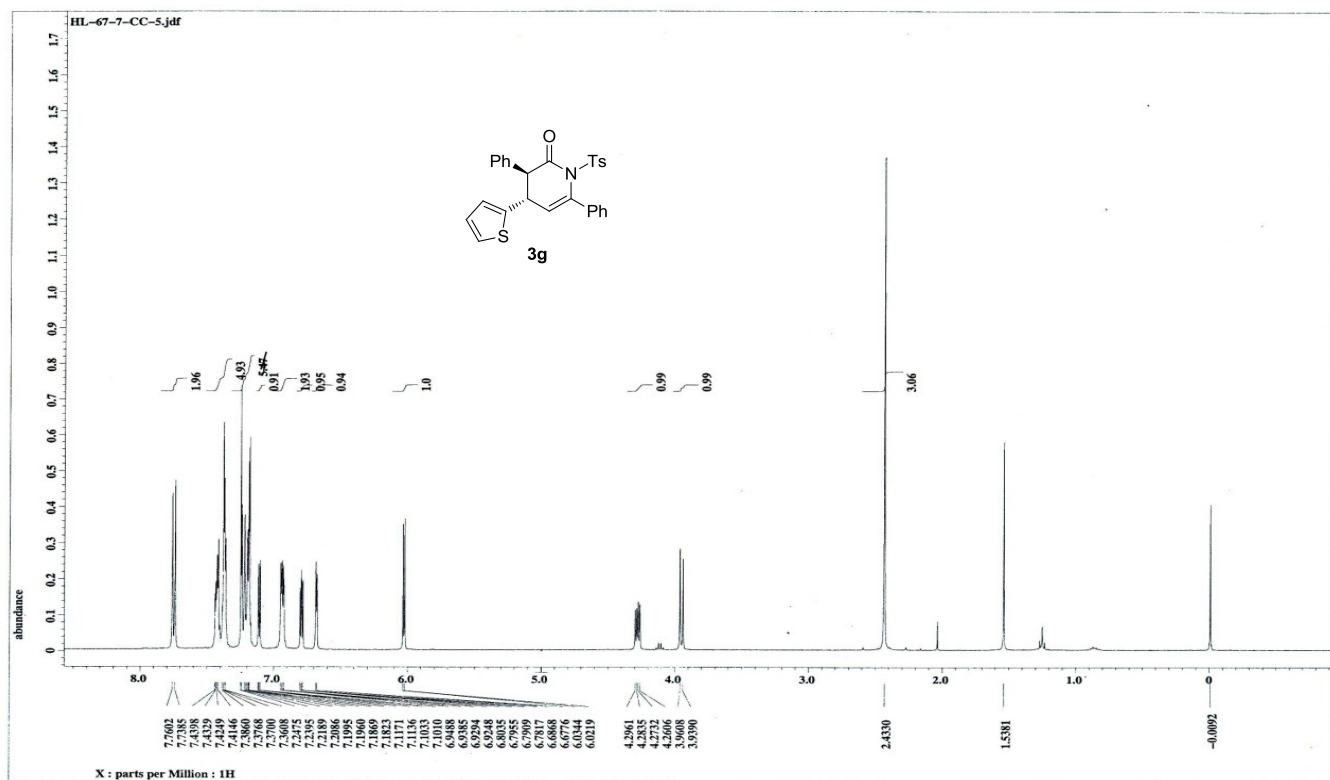


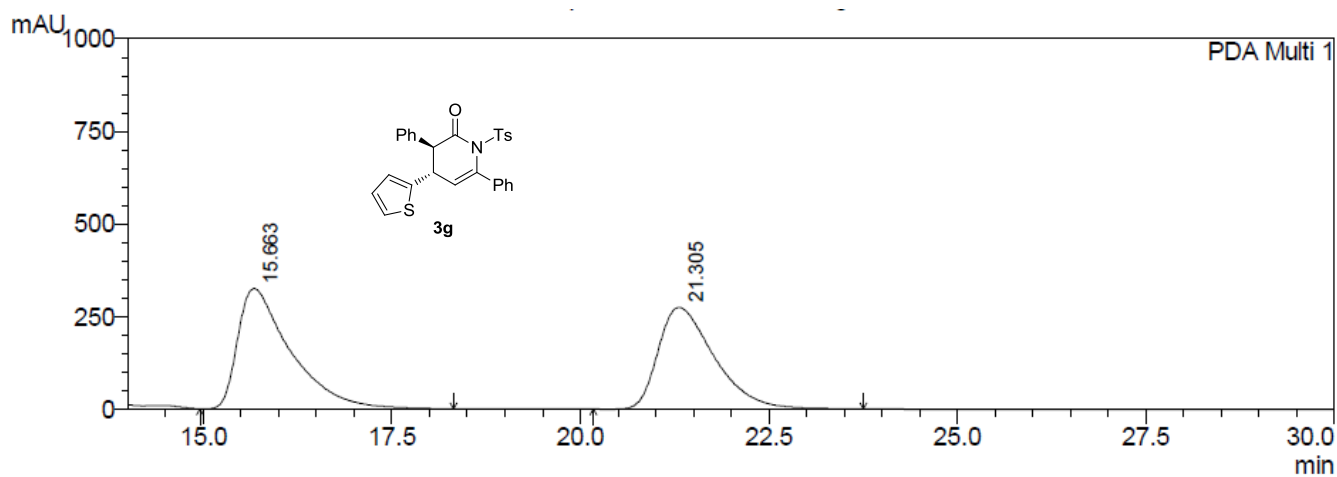


PeakTable					
PDA Ch2 220nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.723	34981063	233408	53.029	70.296
2	75.169	30985308	98628	46.971	29.704
Total		65966370	332036	100.000	100.000



PeakTable					
PDA Ch2 220nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.505	39770003	274687	94.152	97.177
2	79.828	2470011	7980	5.848	2.823
Total		42240014	282666	100.000	100.000

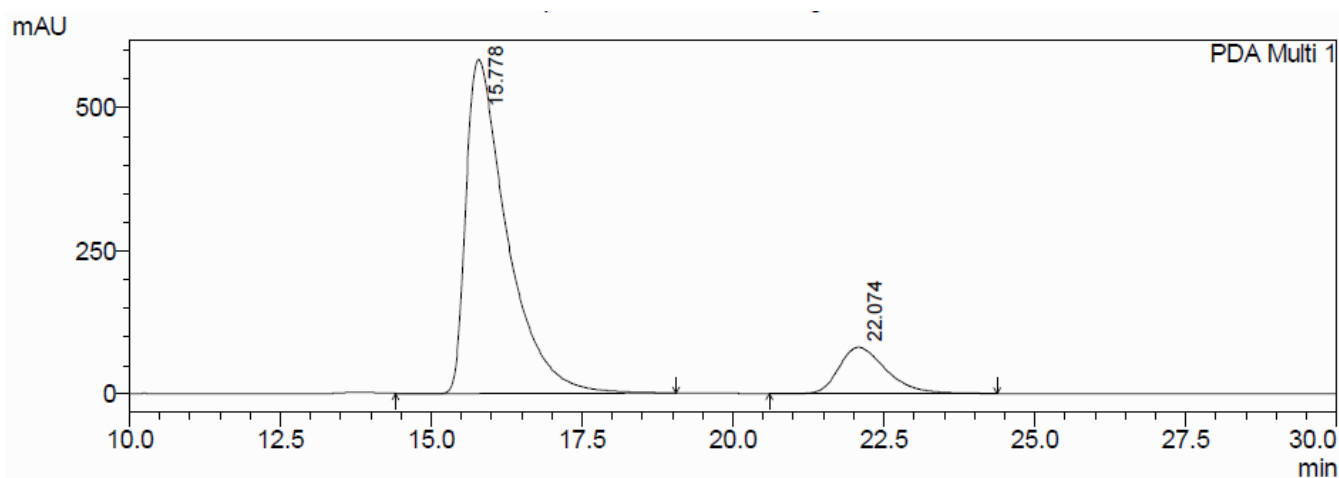




PeakTable

PDA Ch1 254nm 4nm

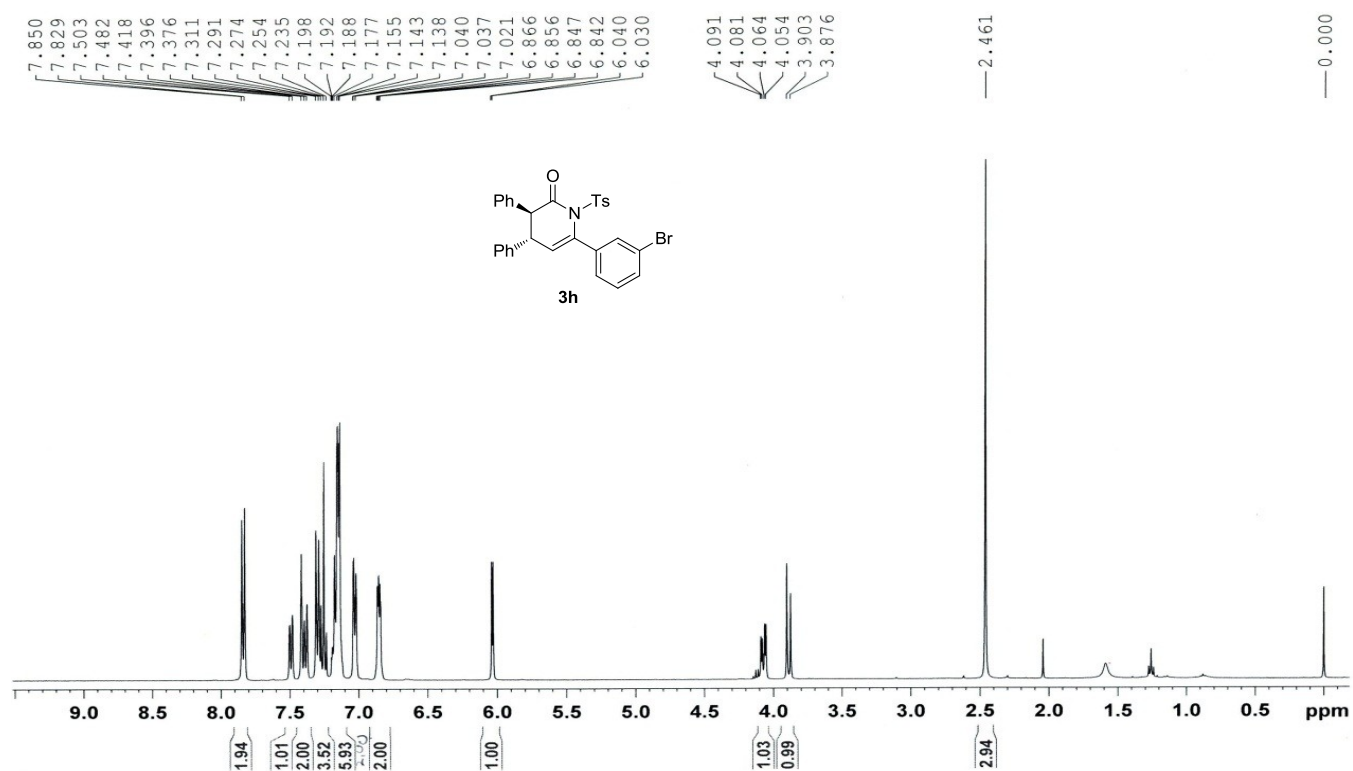
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.663	15847905	324083	52.779	54.193
2	21.305	14179199	273933	47.221	45.807
Total		30027104	598016	100.000	100.000



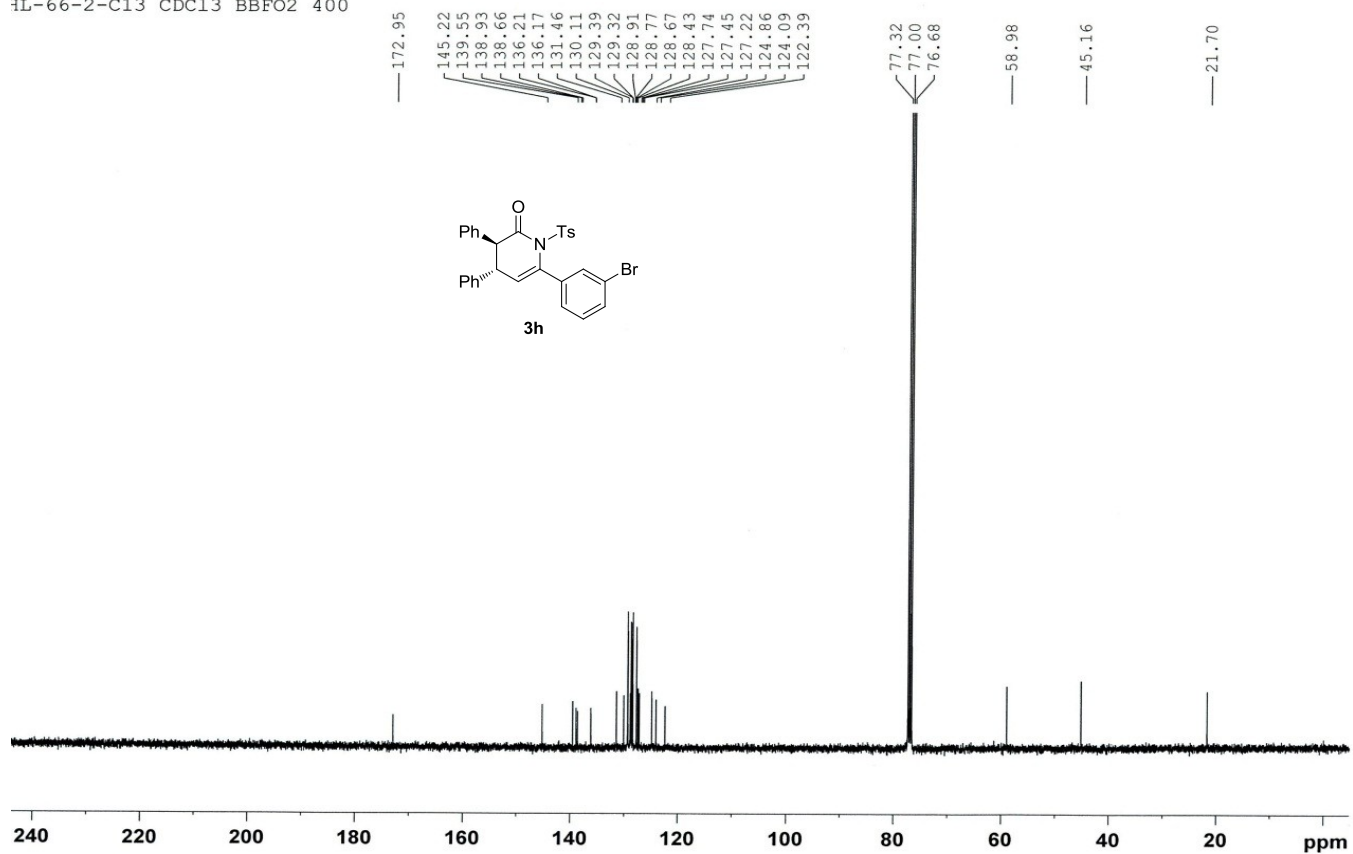
PeakTable

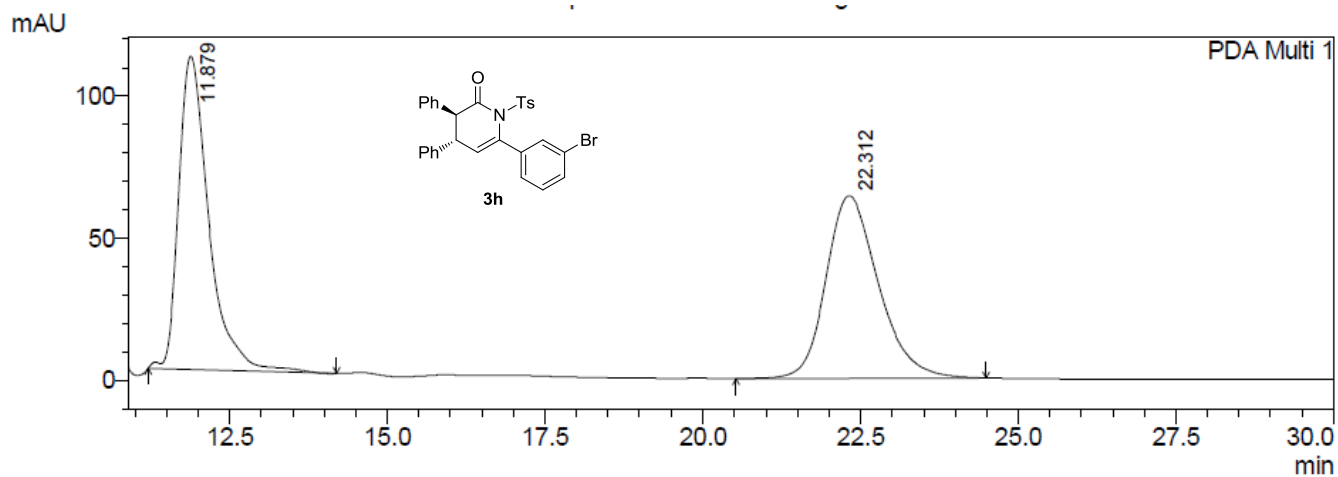
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.778	27547739	583344	86.239	87.839
2	22.074	4395639	80760	13.761	12.161
Total		31943378	664104	100.000	100.000



HL-66-2-C13 CDC13 BBFO2 400

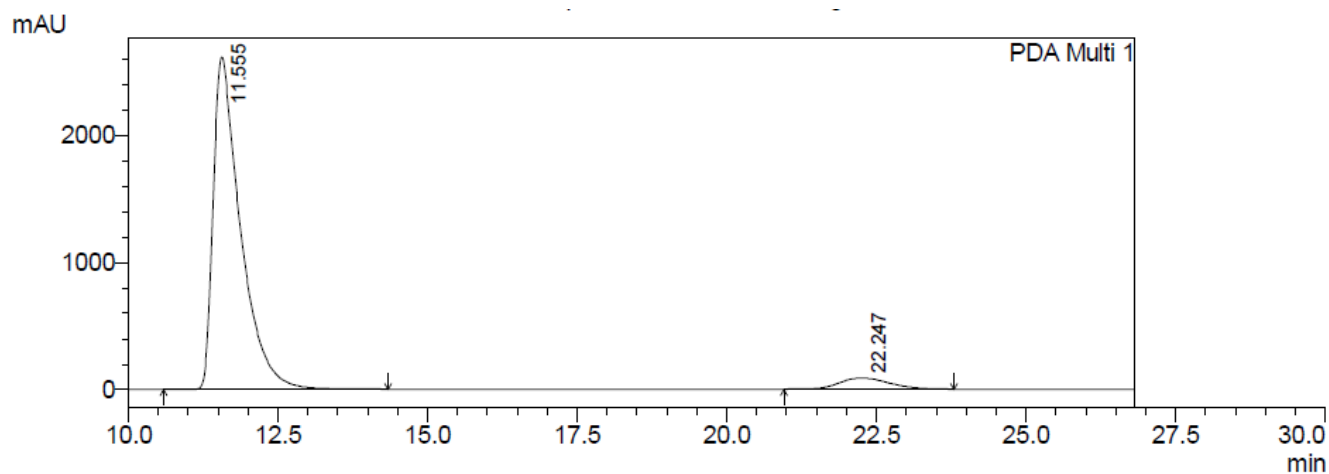




PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.879	3644101	110339	49.573	63.202
2	22.312	3706950	64243	50.427	36.798
Total		7351051	174582	100.000	100.000

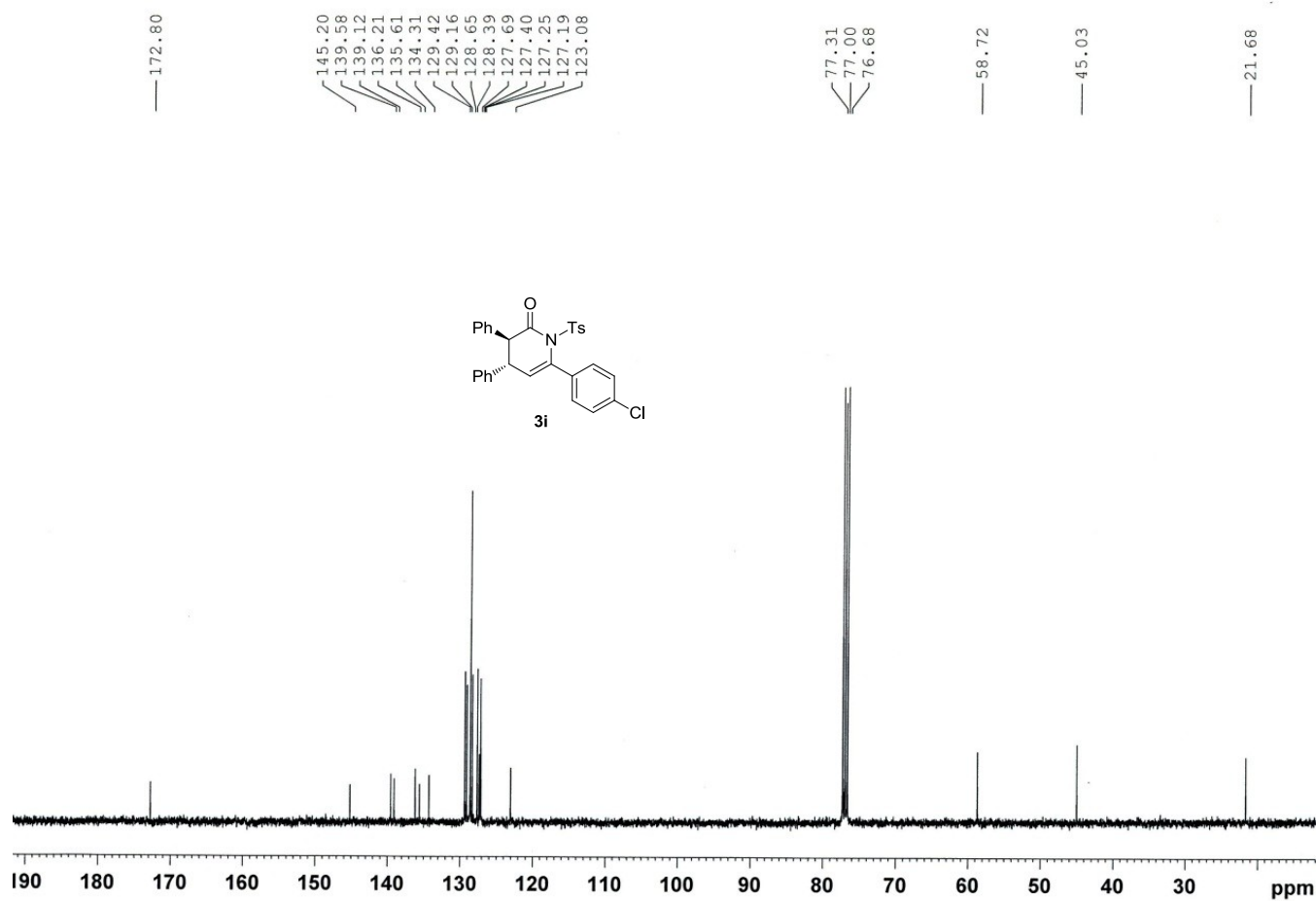
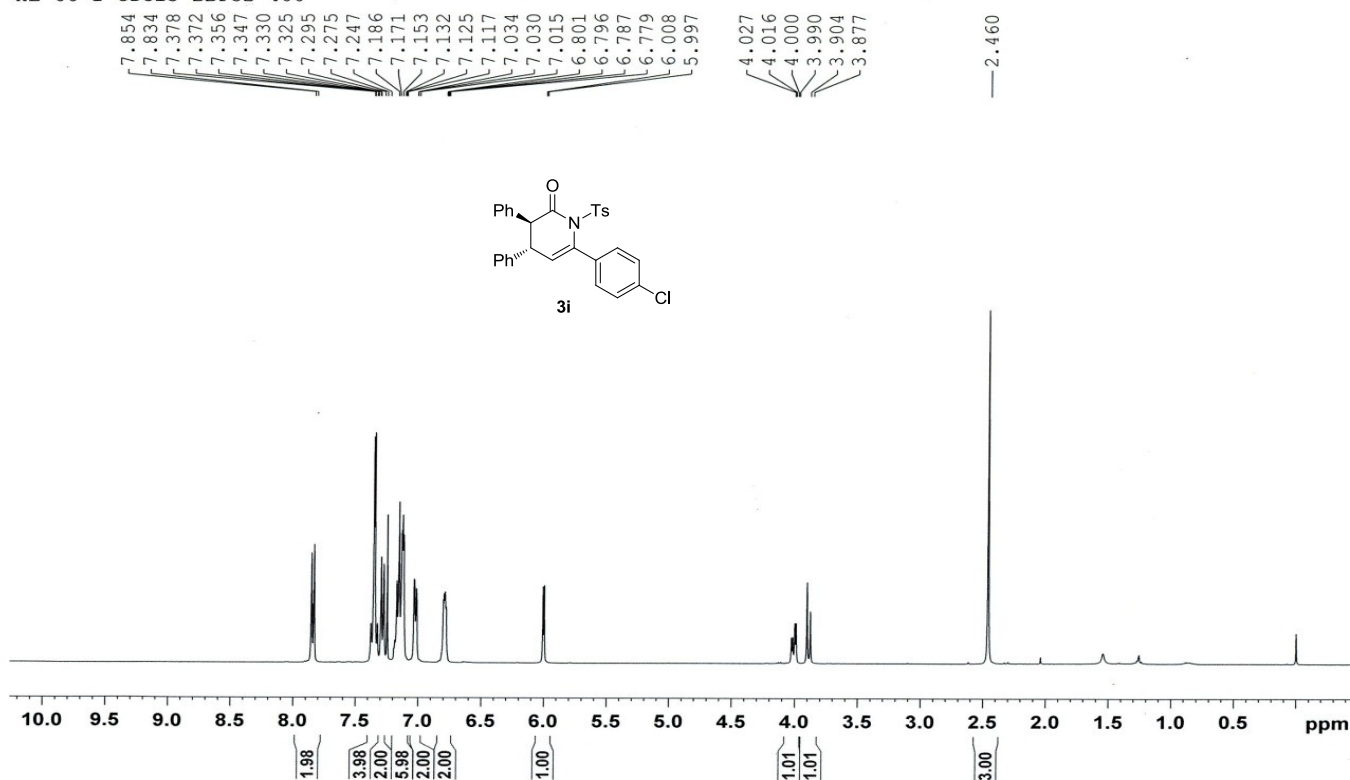


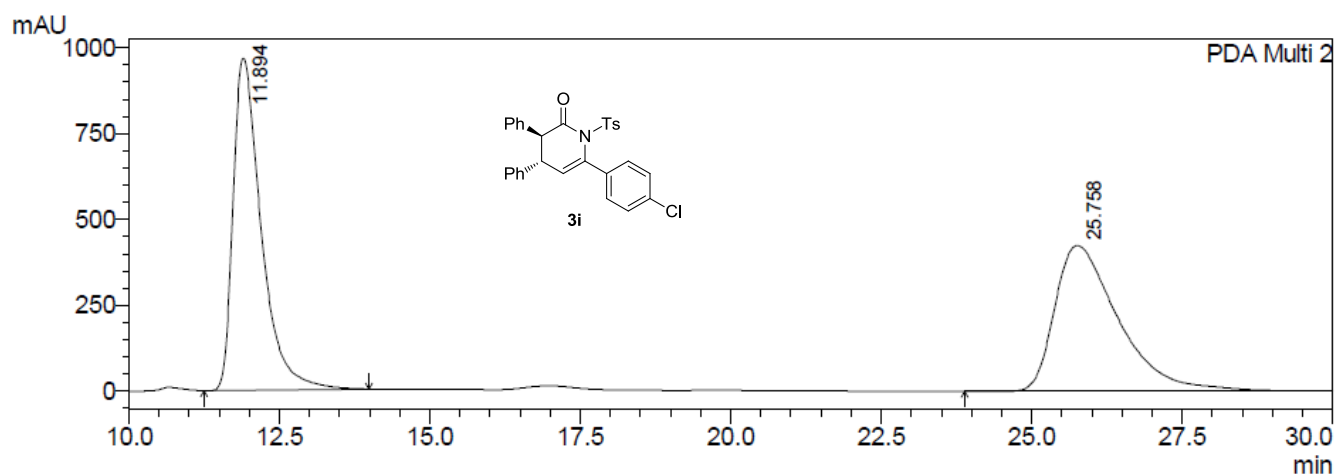
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.555	82953461	2615666	93.984	96.660
2	22.247	5309597	90377	6.016	3.340
Total		88263058	2706043	100.000	100.000

HL-66-1 CDC13 BBFO2 400

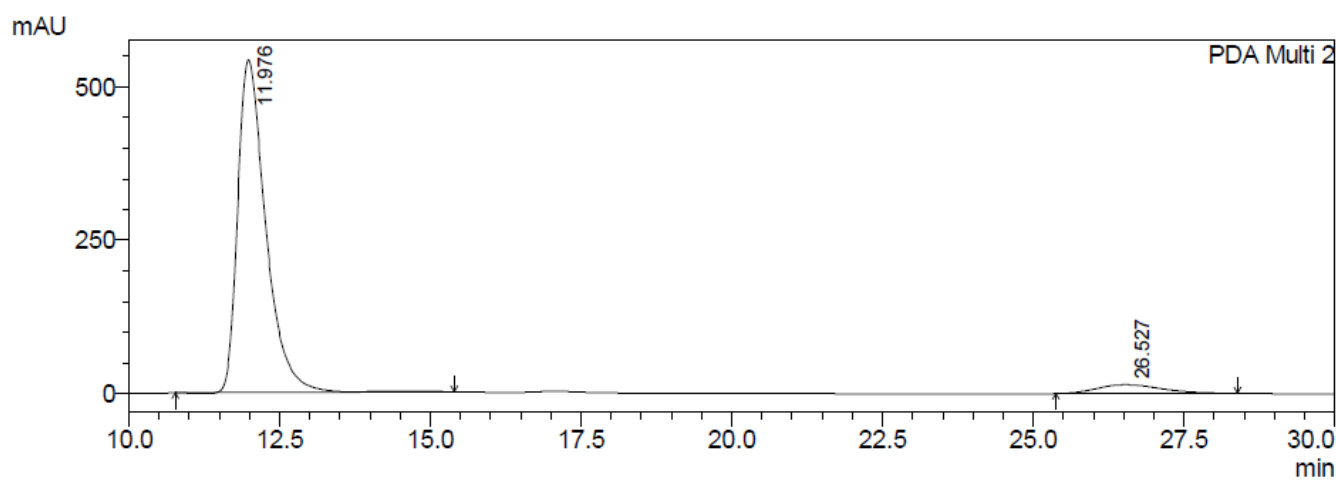




PeakTable

PDA Ch2 220nm 4mm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.894	31368288	965180	50.160	69.504
2	25.758	31168327	423496	49.840	30.496
Total		62536614	1388676	100.000	100.000

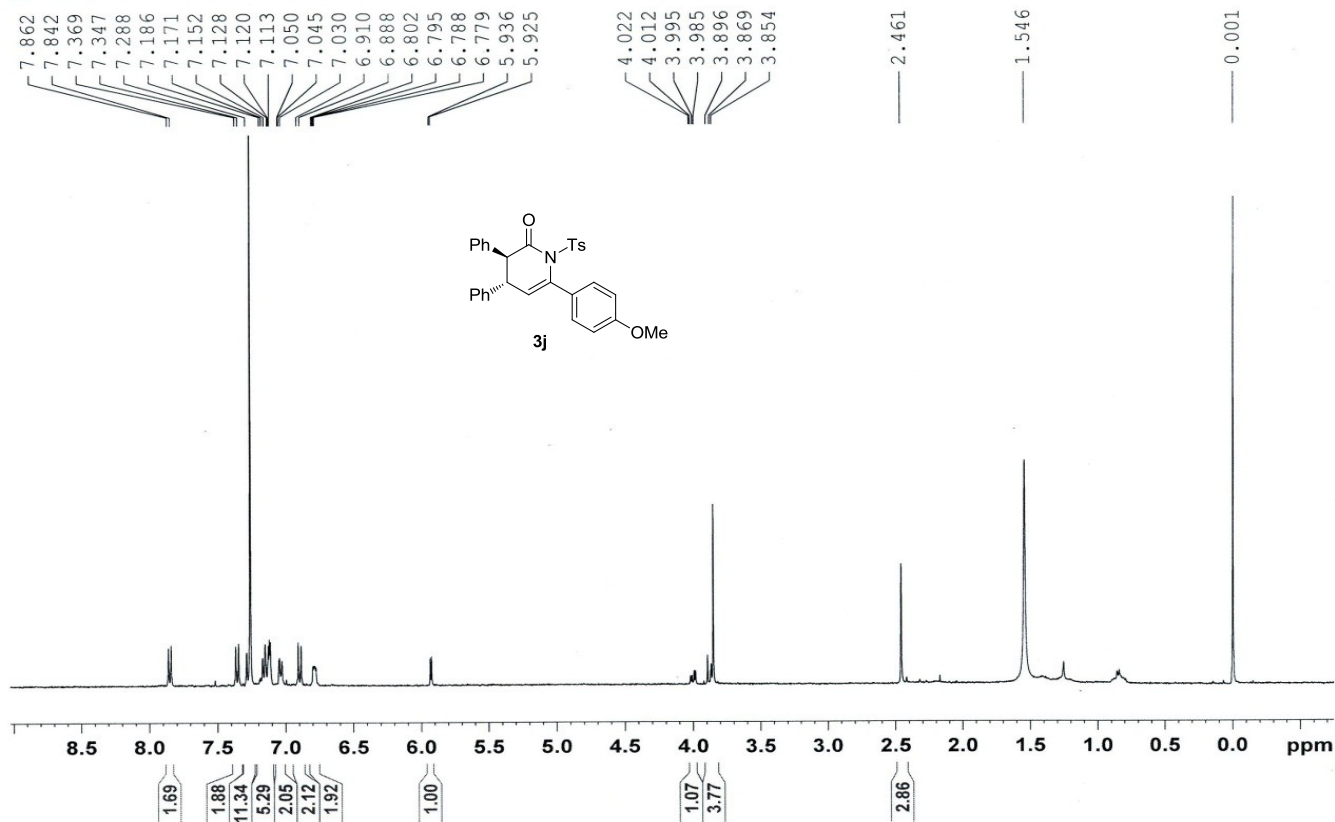


PeakTable

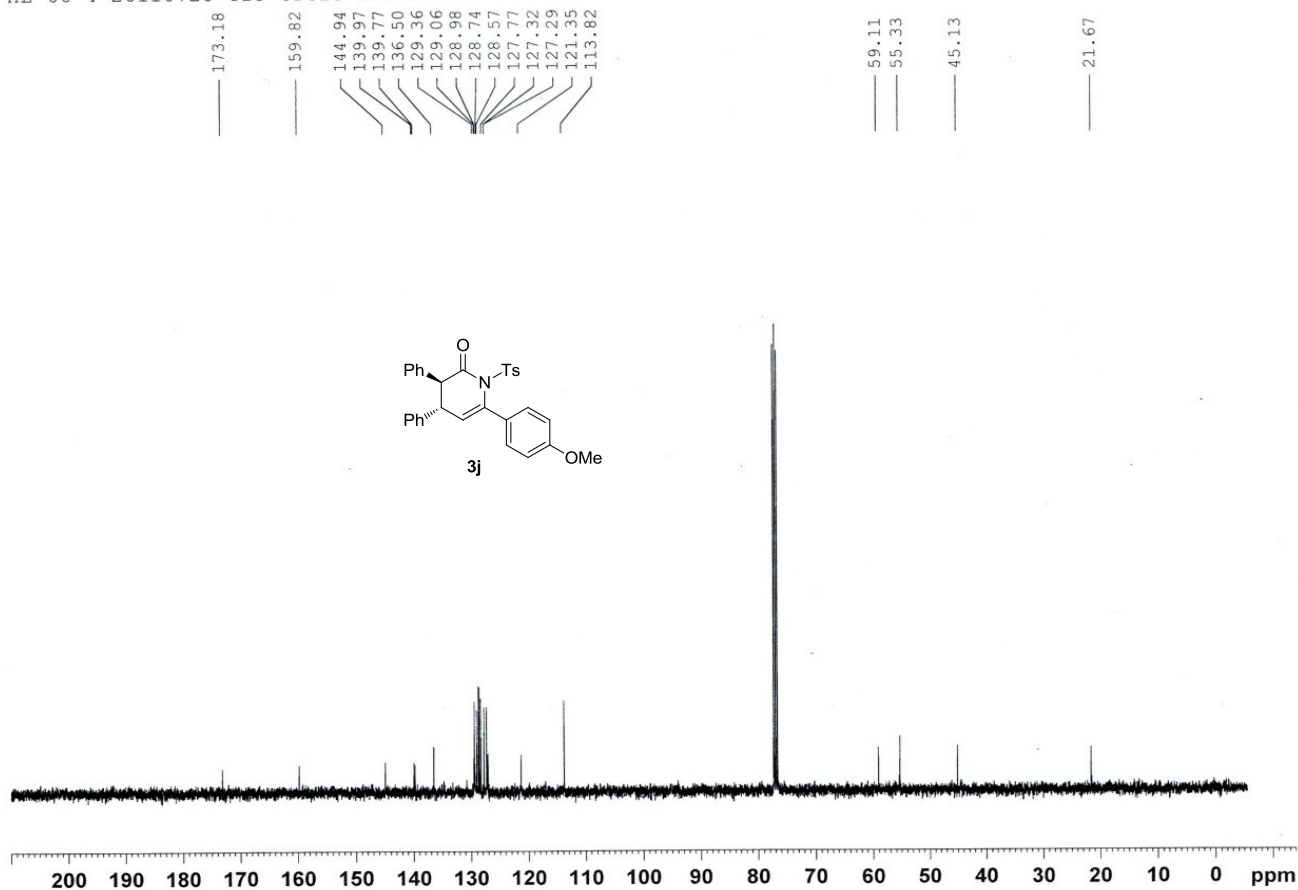
PDA Ch2 220nm 4mm

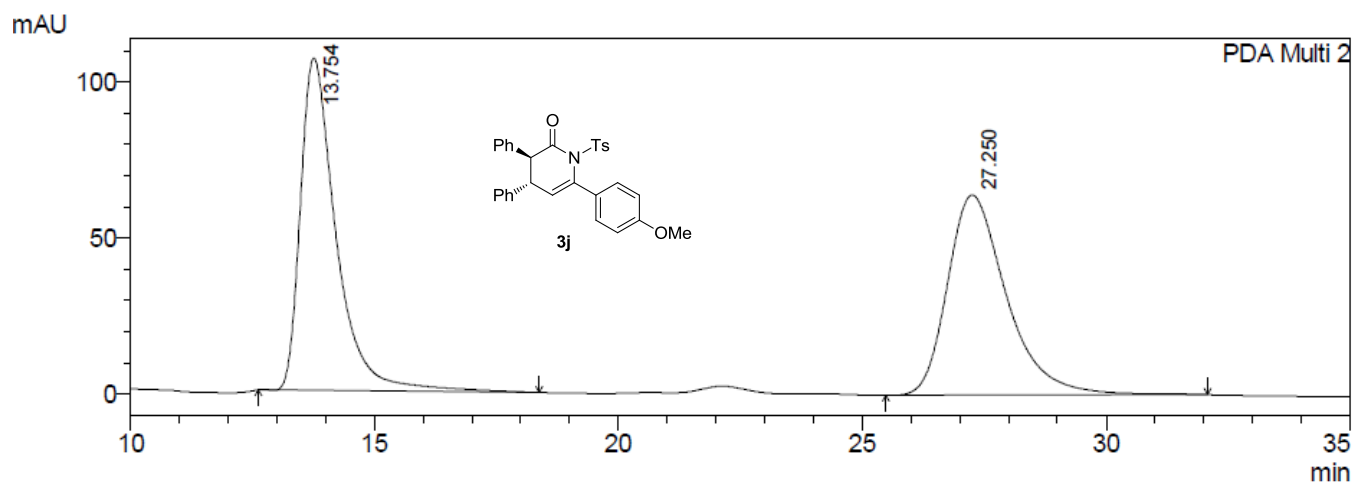
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.976	17584708	542355	94.320	97.409
2	26.527	1059058	14426	5.680	2.591
Total		18643767	556781	100.000	100.000

HL-66-5-20110728-3 CDCl₃ BBFO2 400



HL-66-4-20110728-C13 CDCl₃ BBFO2 400

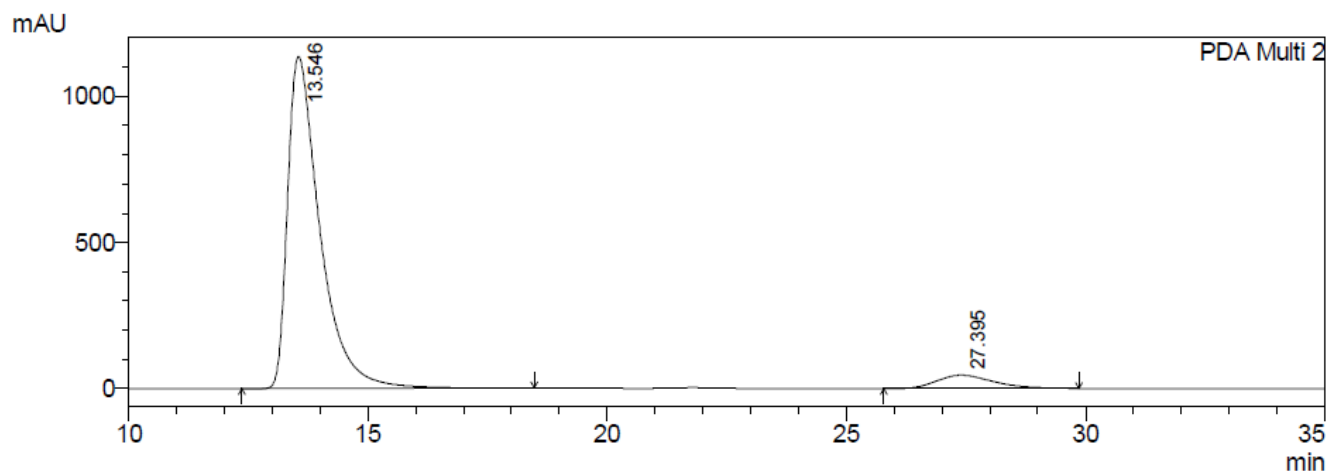




PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.754	5440389	106574	50.083	62.425
2	27.250	5422389	64148	49.917	37.575
Total		10862778	170721	100.000	100.000

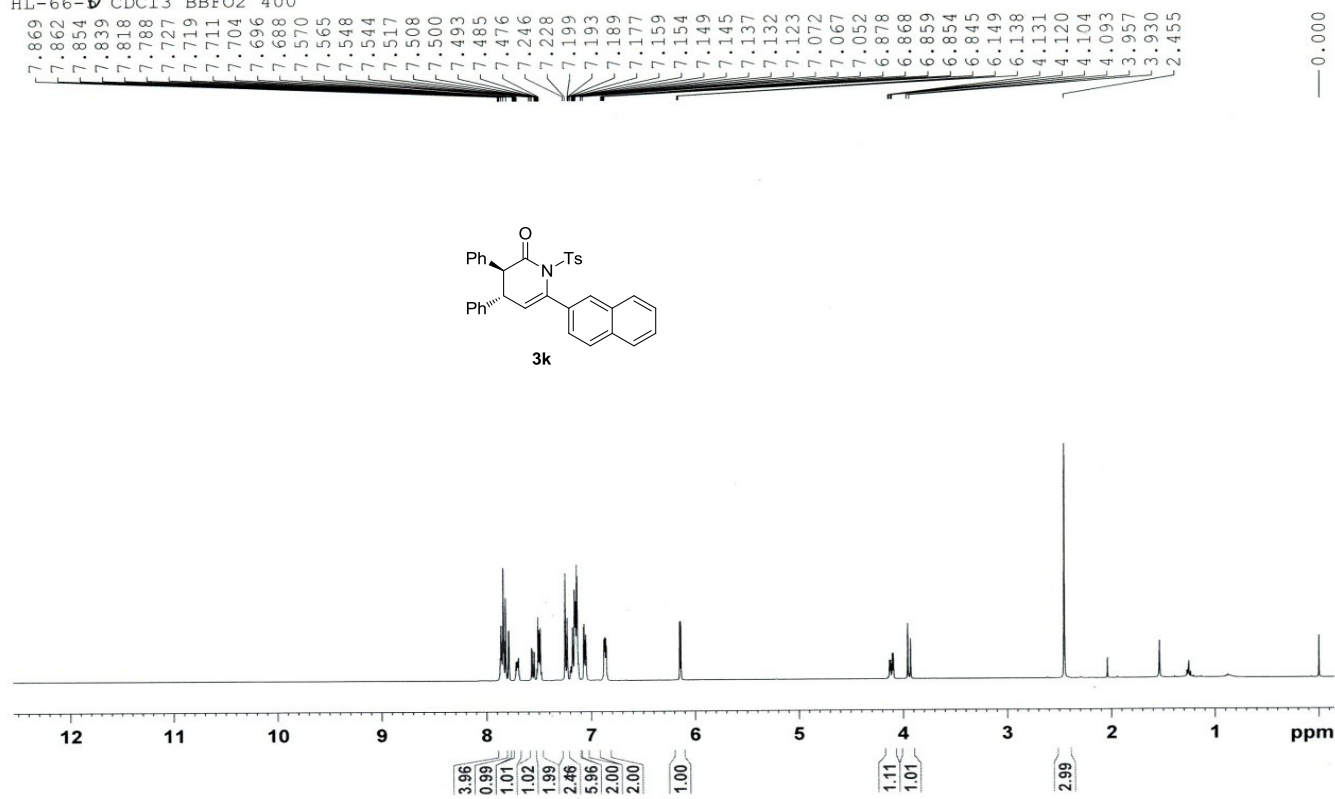


PeakTable

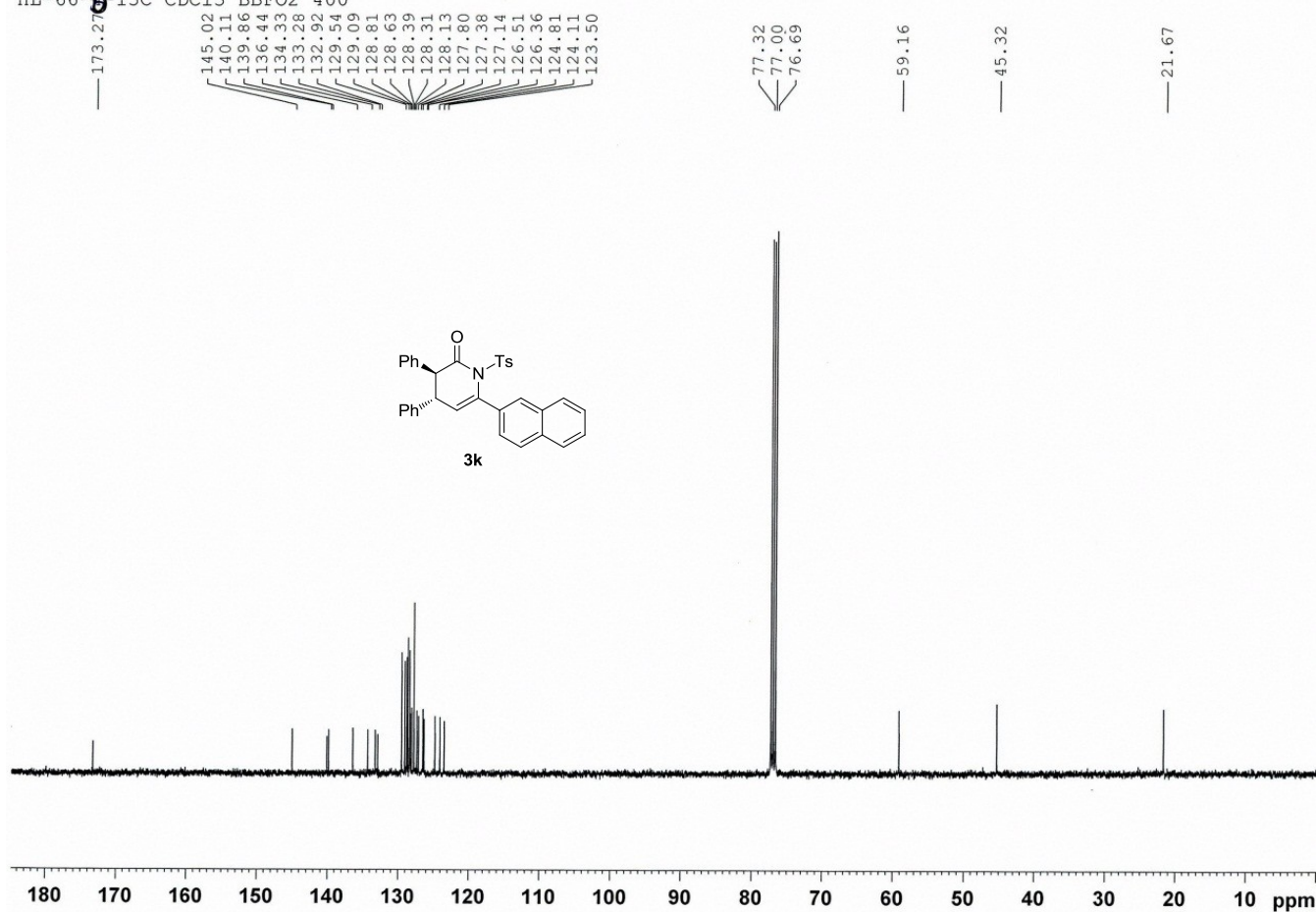
PDA Ch2 220nm 4nm

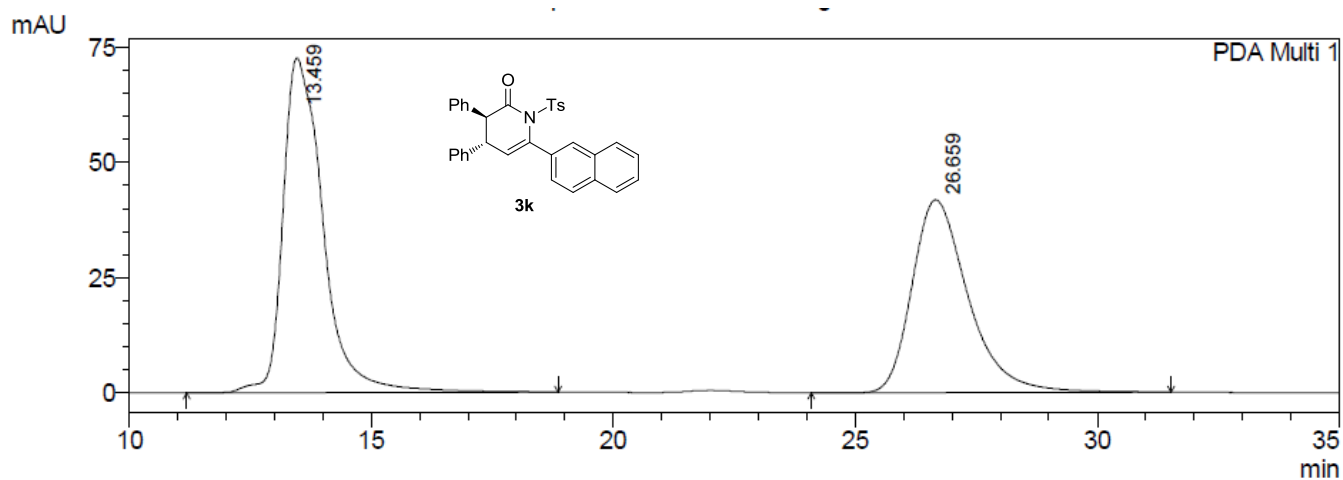
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.546	53403392	1134442	93.430	96.134
2	27.395	3755044	45625	6.570	3.866
Total		57158437	1180067	100.000	100.000

HL-66-6 CDC13 BBFO2 400

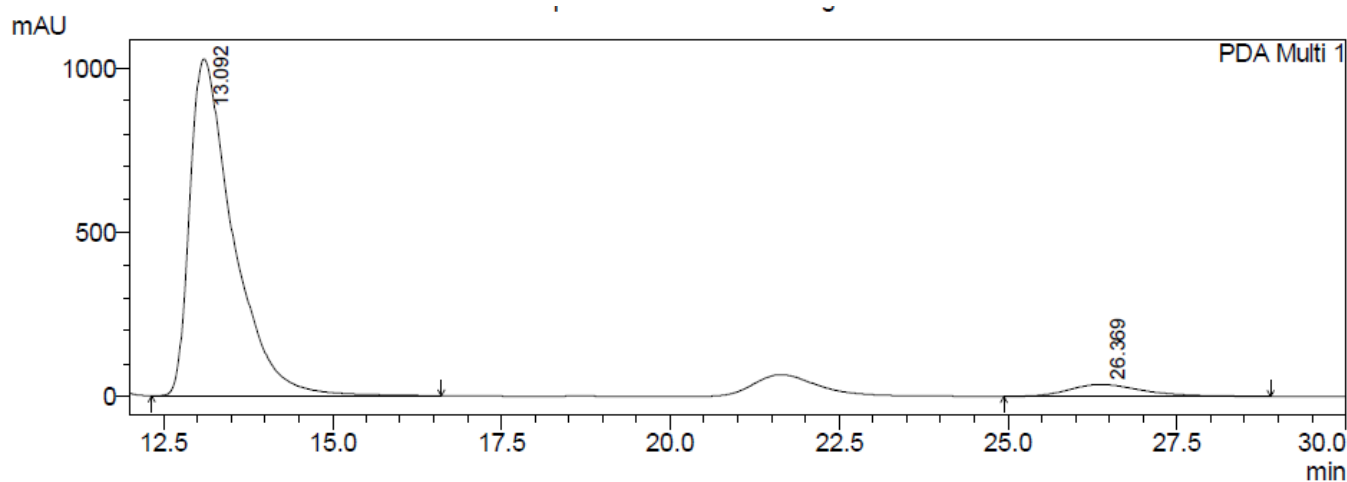


HL-66-6-13C CDC13 BBFO2 400



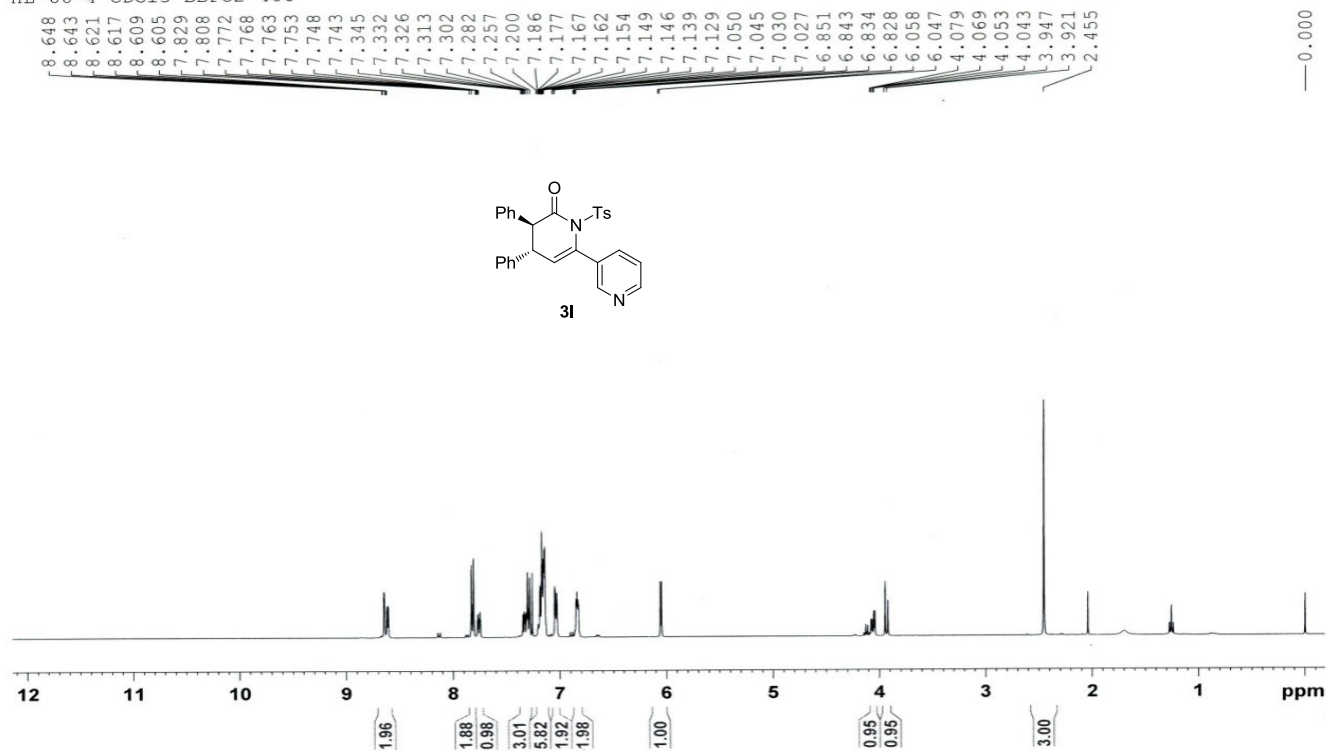


PeakTable					
PDA Ch1 254nm 4nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.459	4179450	72555	55.274	63.469
2	26.659	3381833	41761	44.726	36.531
Total		7561283	114316	100.000	100.000

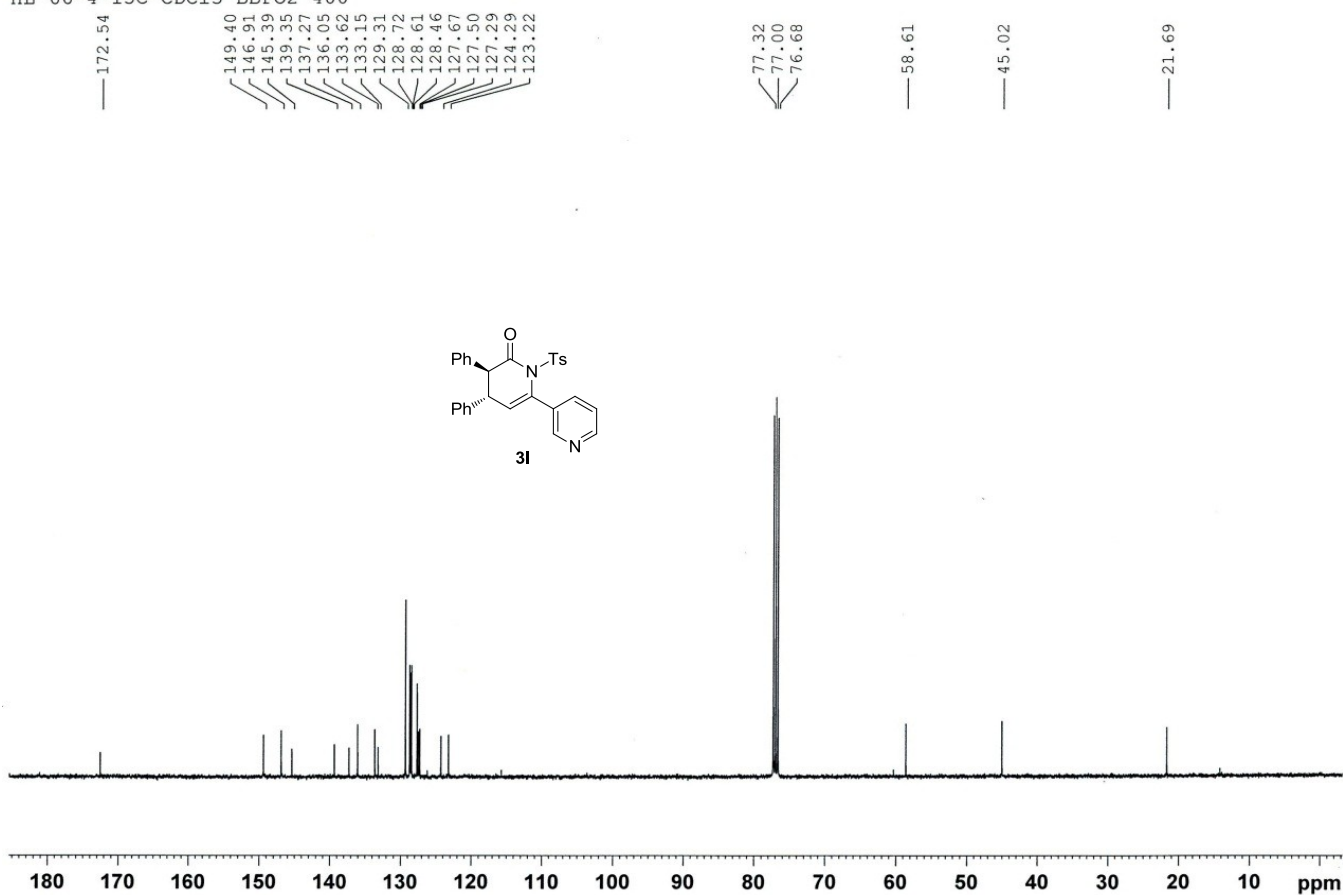


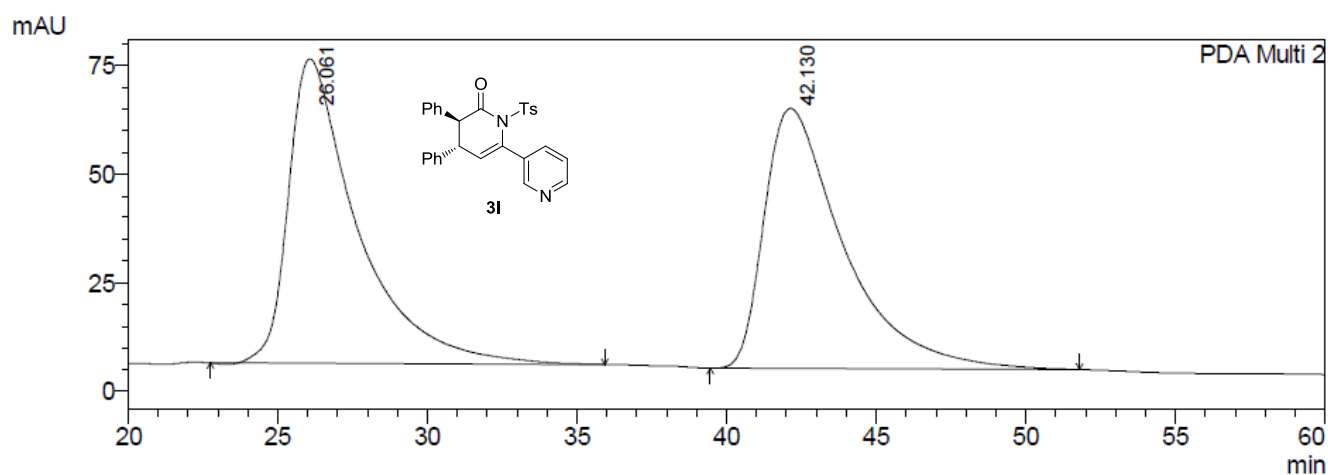
PeakTable					
PDA Ch1 254nm 4nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.092	45748364	1025325	94.310	96.605
2	26.369	2760027	36035	5.690	3.395
Total		48508391	1061360	100.000	100.000

HL-66-4 CDC13 BBFO2 400



HL-66-4-13C CDC13 BBFO2 400

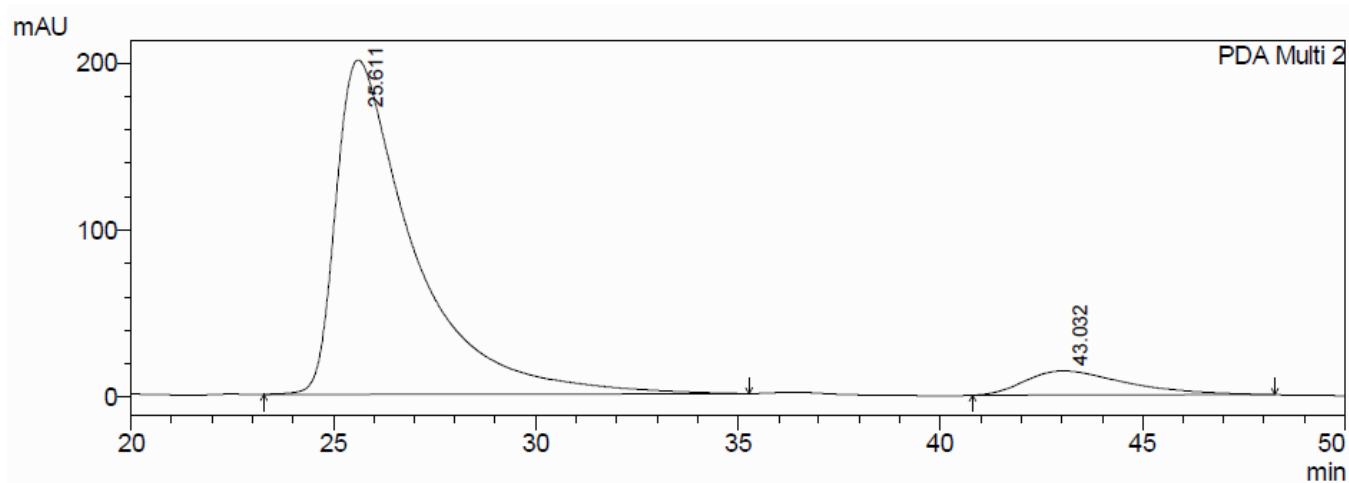




PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.061	11259761	70157	50.407	53.941
2	42.130	11077728	59904	49.593	46.059
Total		22337488	130060	100.000	100.000

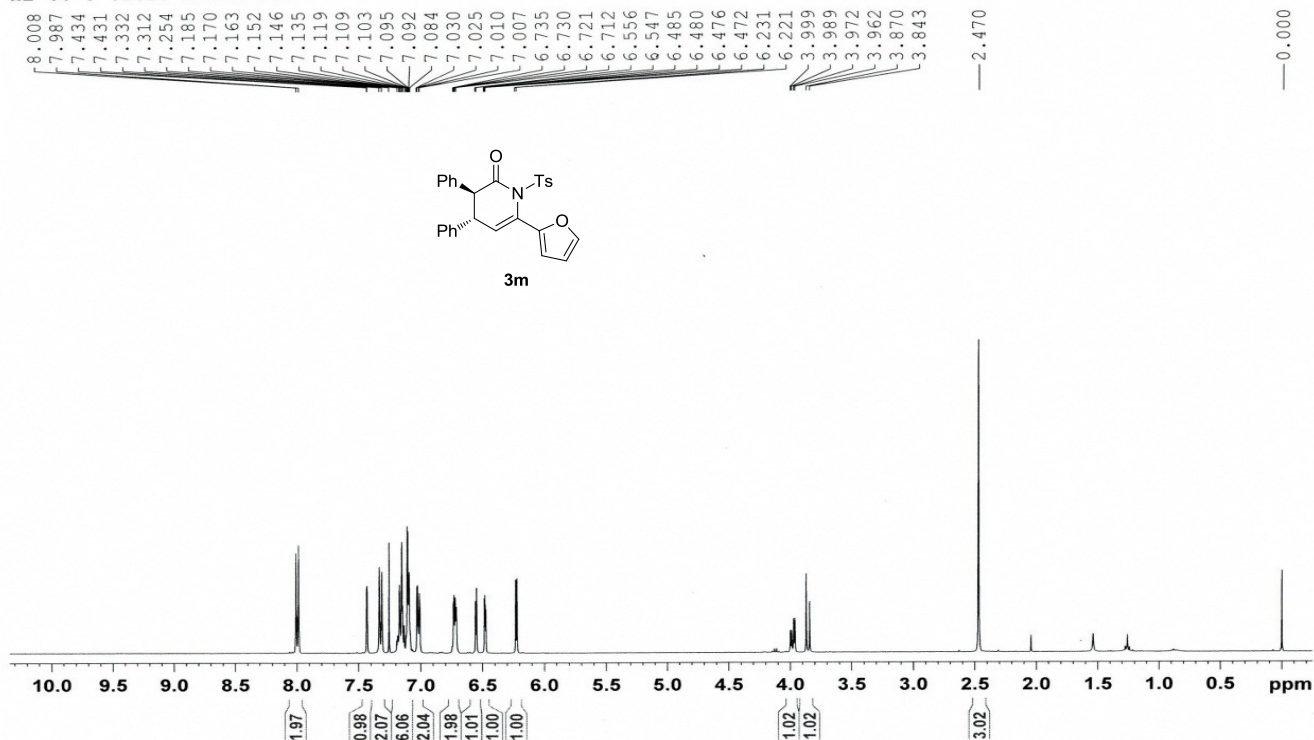


PeakTable

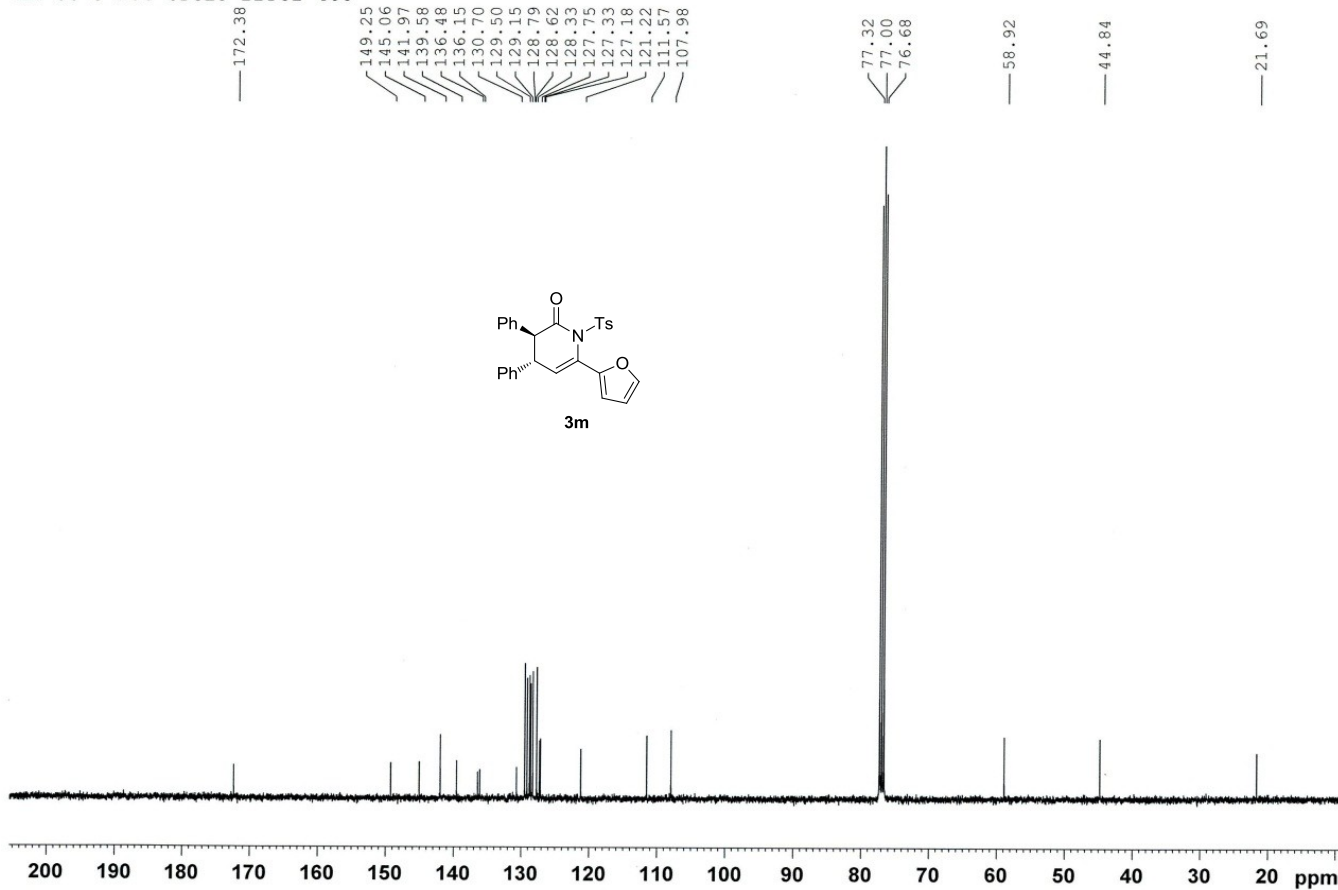
PDA Ch2 220nm 4nm

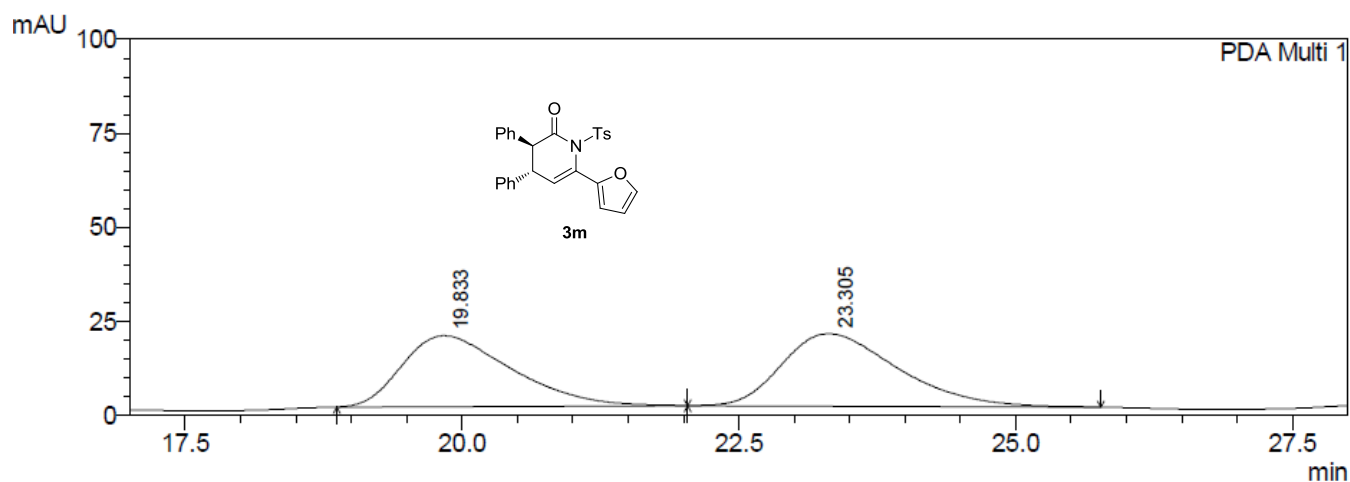
Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.611	26739548	199719	91.390	93.290
2	43.032	2519079	14364	8.610	6.710
Total		29258627	214083	100.000	100.000

HL-66-3 CDCl₃ BBFO2 400

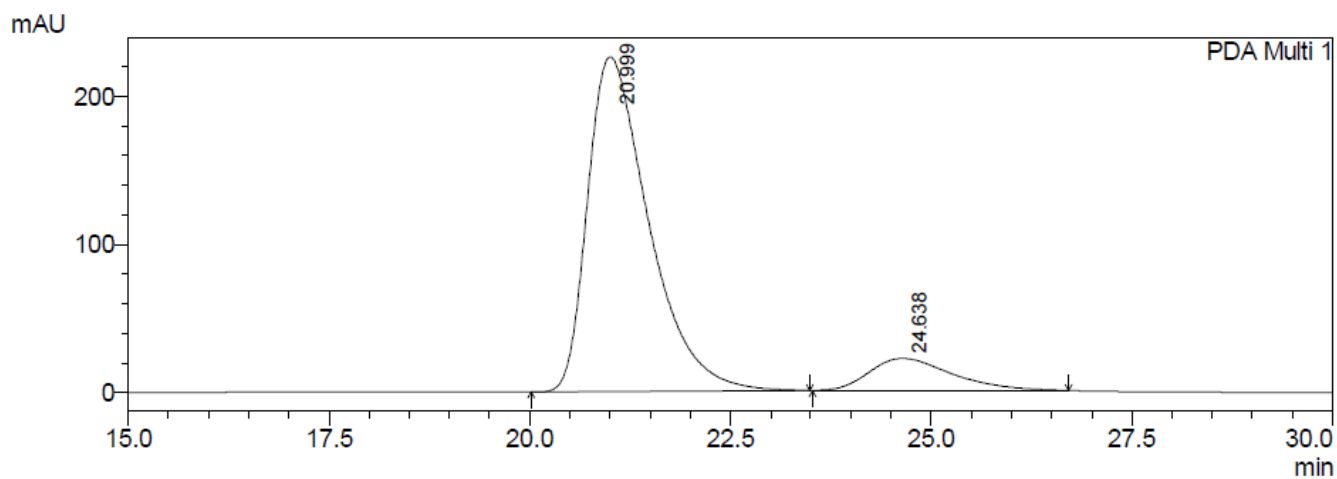


HL-66-3-13C CDCl₃ BBFO2 400





PeakTable					
PDA Ch1 254nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.833	1287024	18781	47.928	49.423
2	23.305	1398300	19219	52.072	50.577
Total		2685324	38001	100.000	100.000



PeakTable					
PDA Ch1 254nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.999	11992687	226138	88.492	91.228
2	24.638	1559528	21744	11.508	8.772
Total		13552214	247882	100.000	100.000

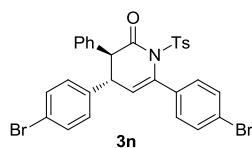
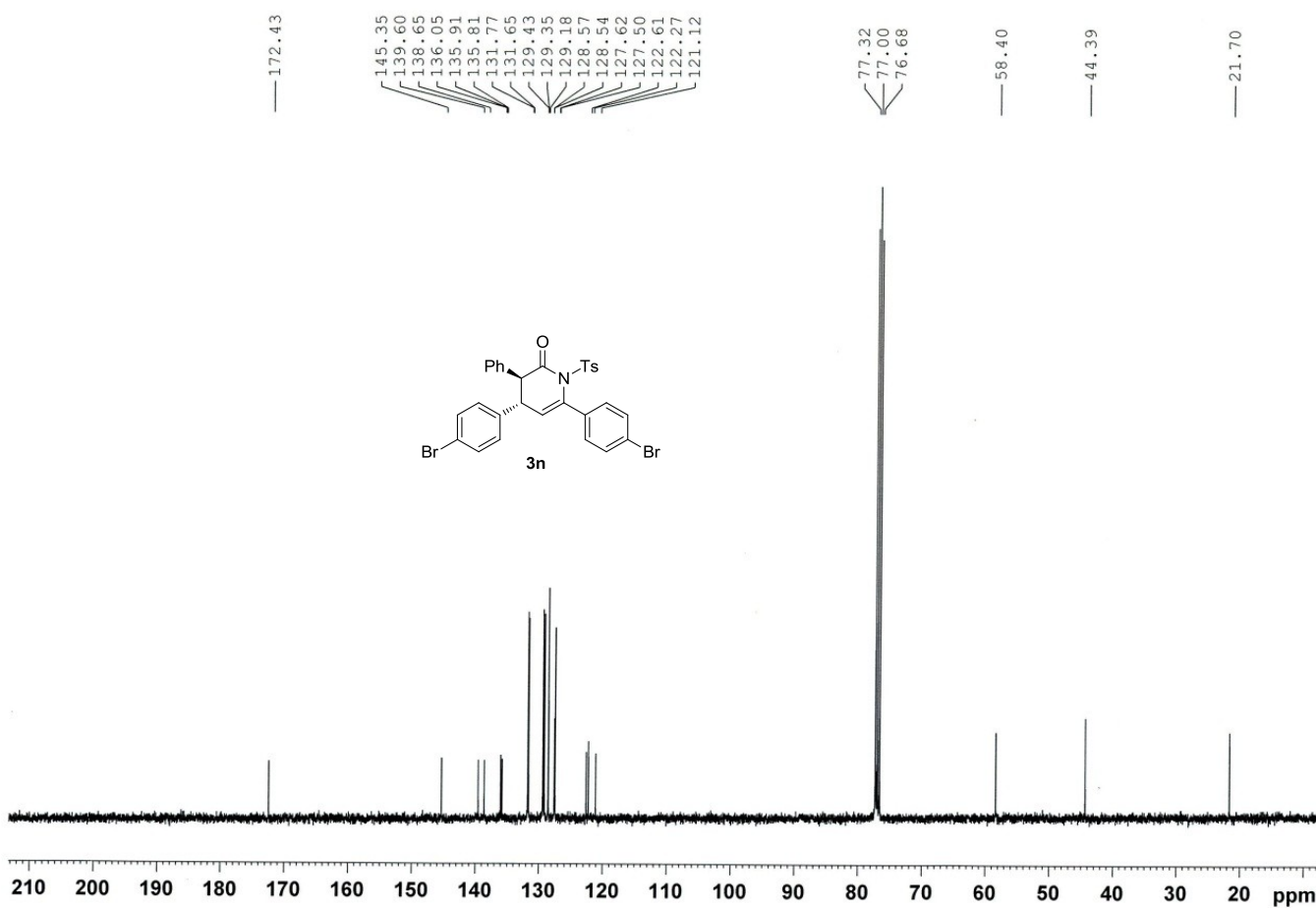
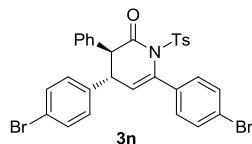
HL-66-7 CDC13

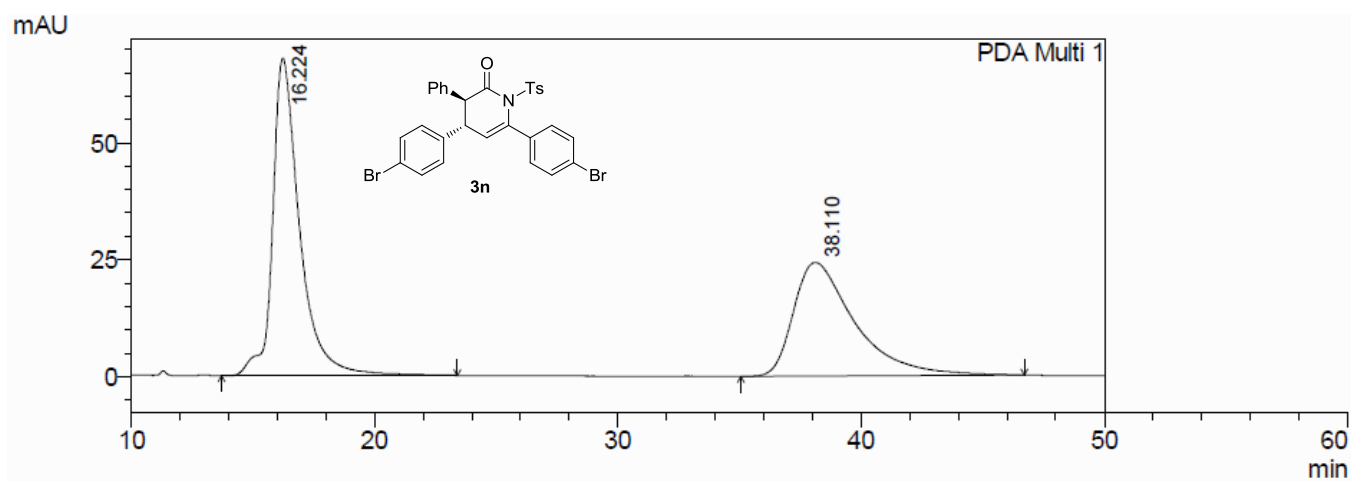
7.822, 7.806, 7.504, 7.500, 7.489, 7.484, 7.479, 7.295, 7.274, 7.251, 7.168, 7.159, 7.152, 7.143, 6.911, 6.890, 6.810, 6.804, 6.798, 6.795, 6.786, 5.947, 5.936, 3.996, 3.985, 3.970, 3.960, 3.869, 3.844, —2.466, —0.001

1.98, 2.01, 5.91, 3.00, 2.01, 2.00, 1.00, 1.01, 1.02, 13.00

ppm

3n

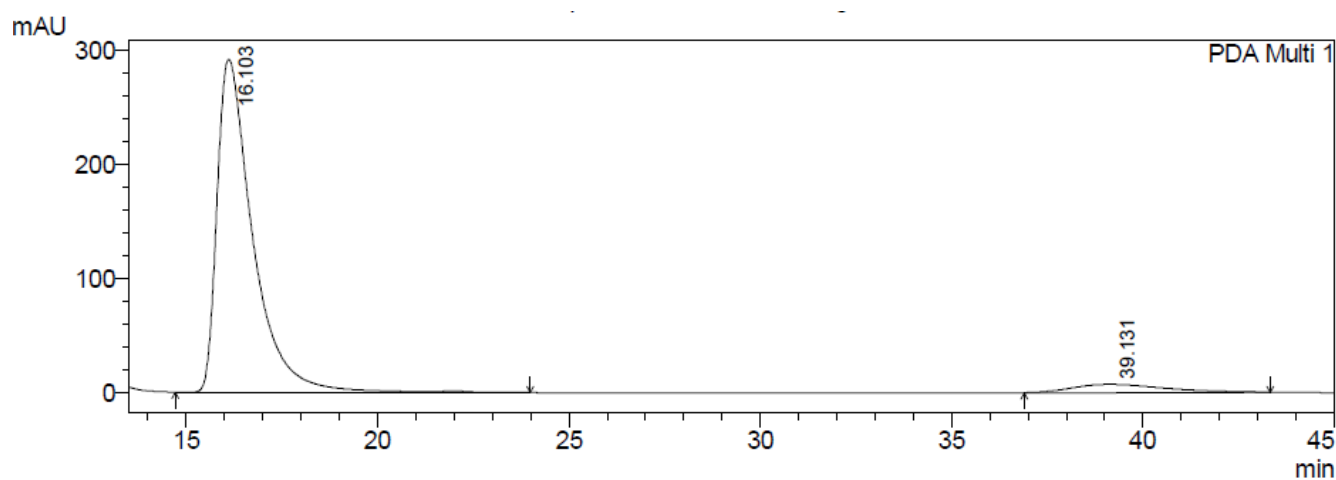
BrC1=CC=C(C=C1)[C@H]2C(=O)N(C3=CC=C(C=C3)S(=O)(=O)C4=CC=CC=C4)C=C[C@@H]2C5=CC=C(C=C5)Br



PeakTable

PDA Ch1 254nm 4mm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.224	5242393	67900	55.256	73.659
2	38.110	4245152	24281	44.744	26.341
Total		9487545	92182	100.000	100.000

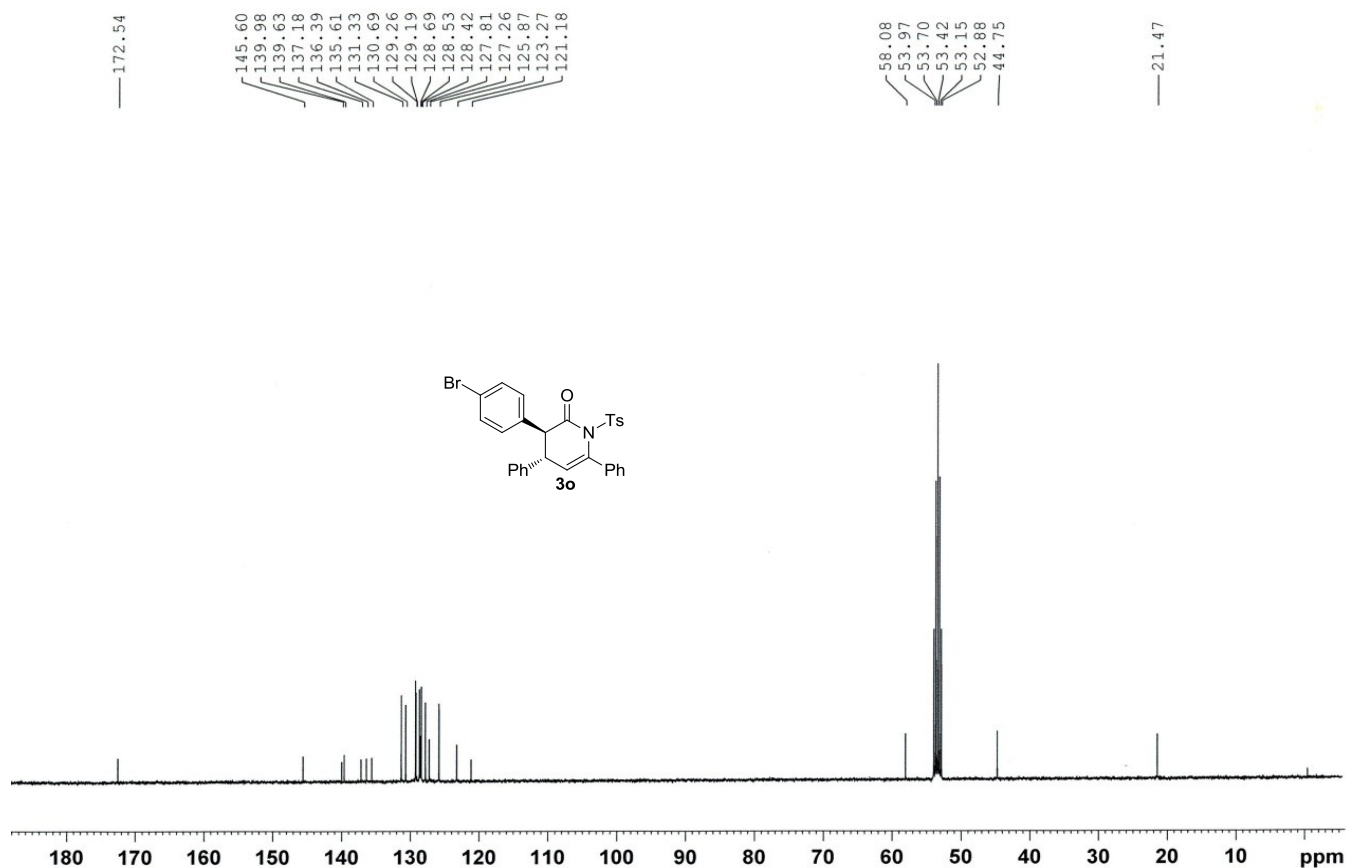
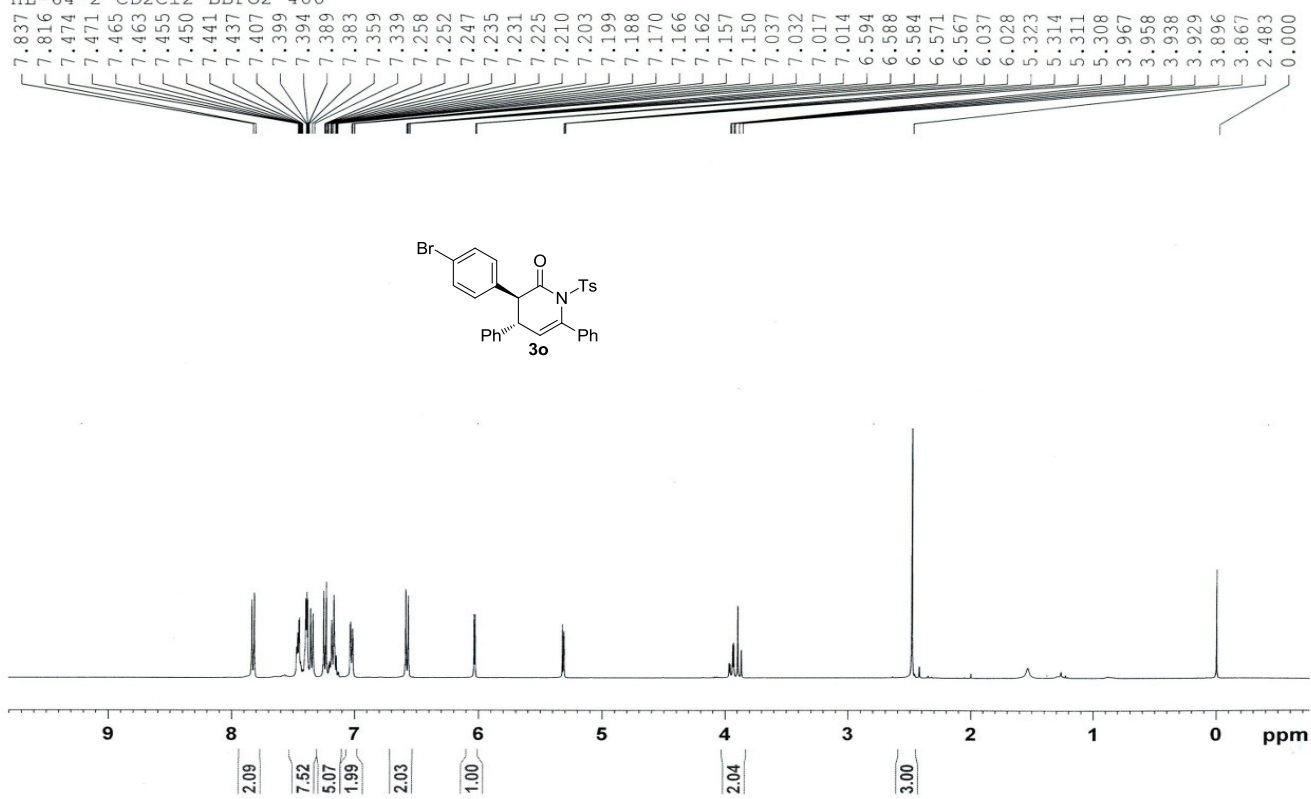


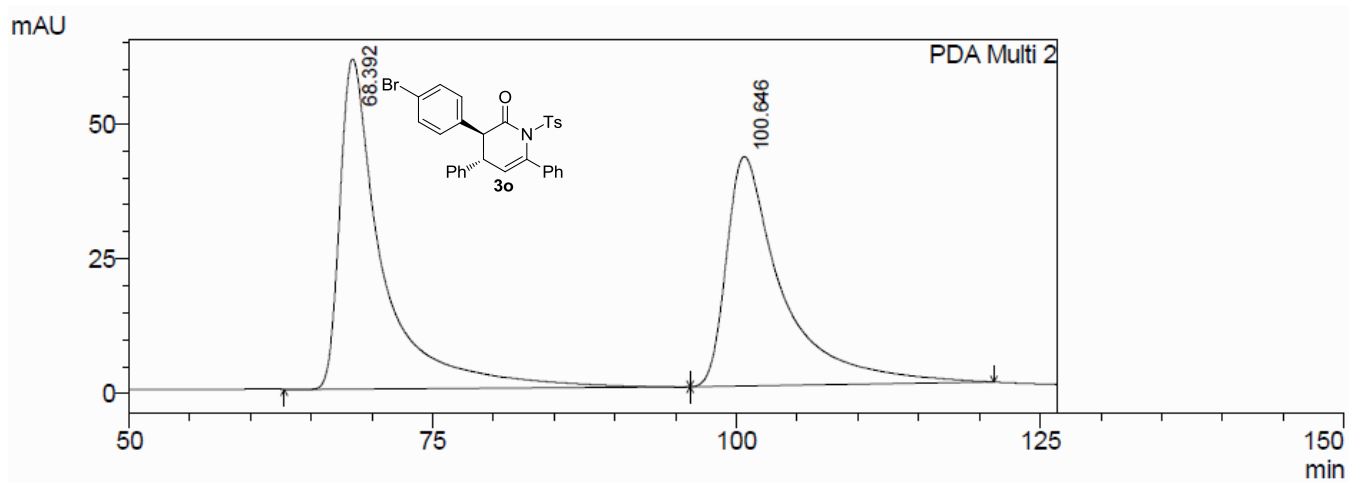
PeakTable

PDA Ch1 254nm 4mm

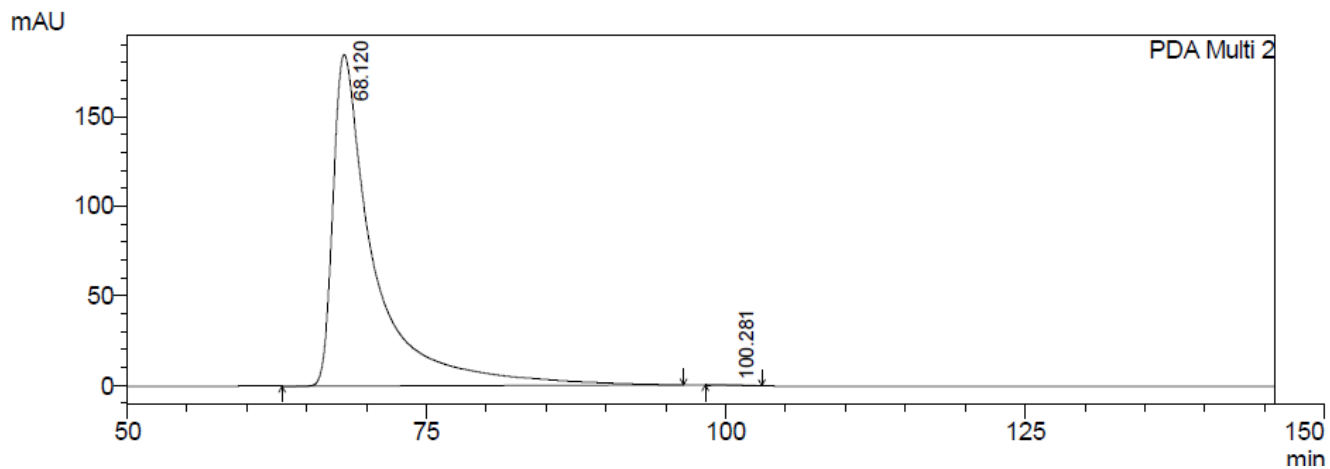
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.103	19031581	291891	93.939	97.584
2	39.131	1227996	7226	6.061	2.416
Total		20259577	299117	100.000	100.000

HL-64-2 CD2Cl2 BBFO2 400

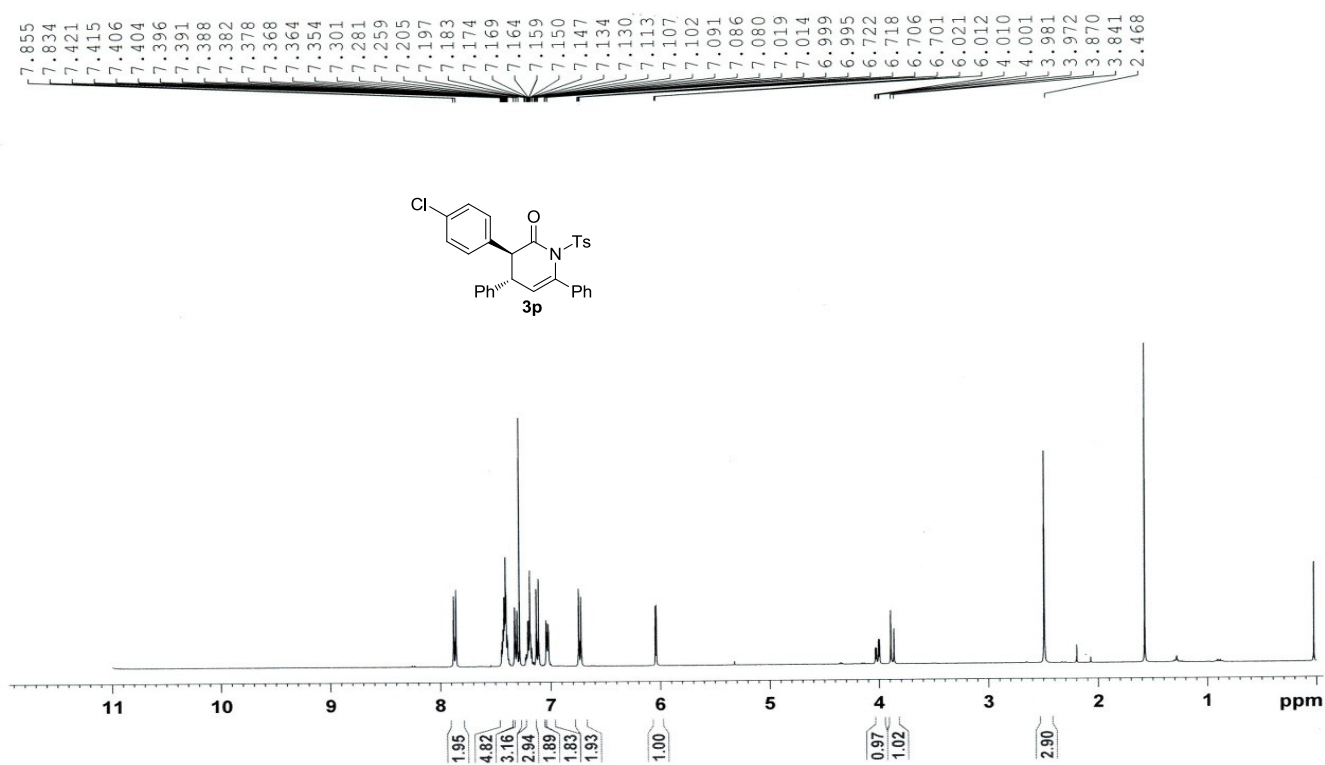




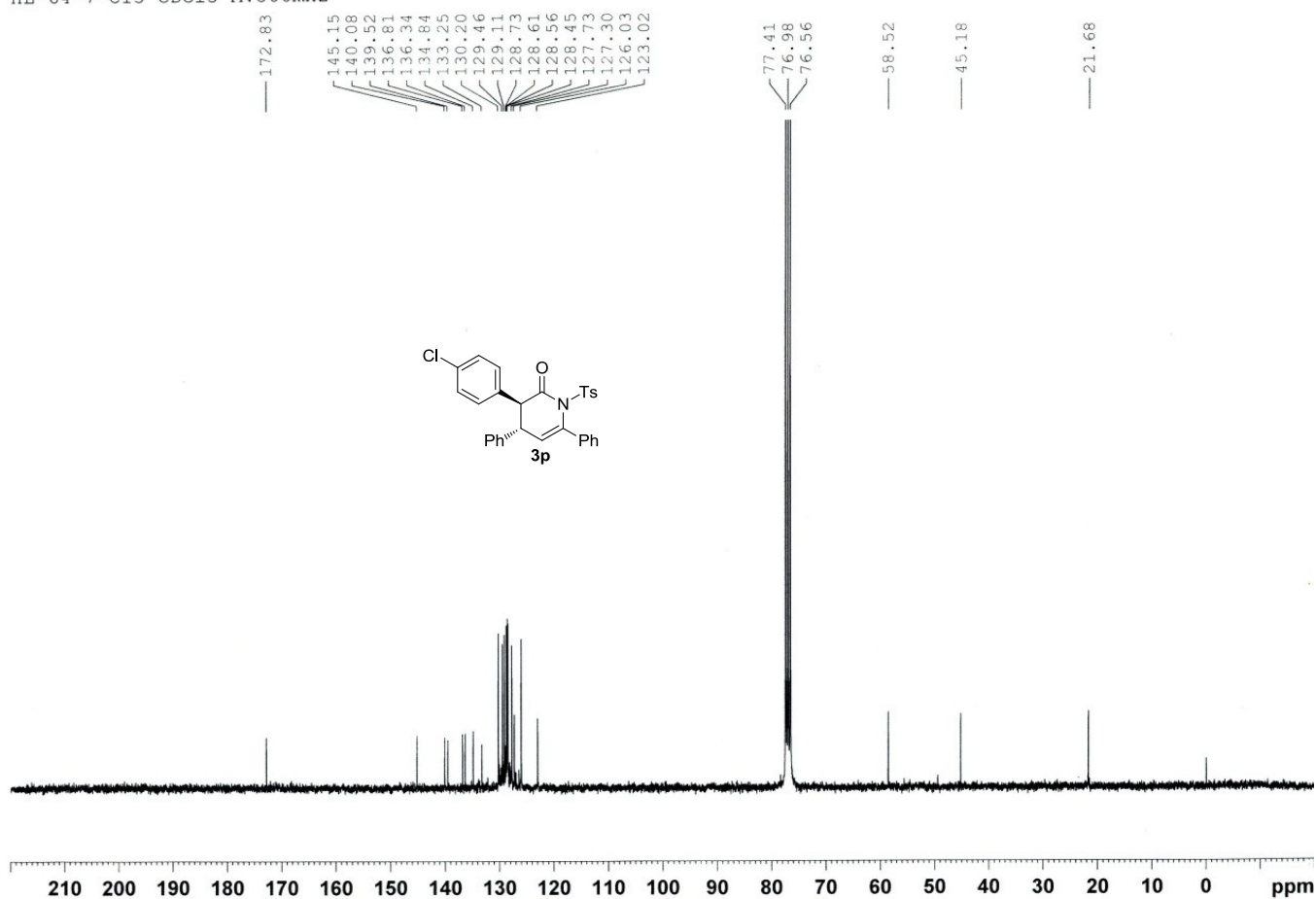
PeakTable

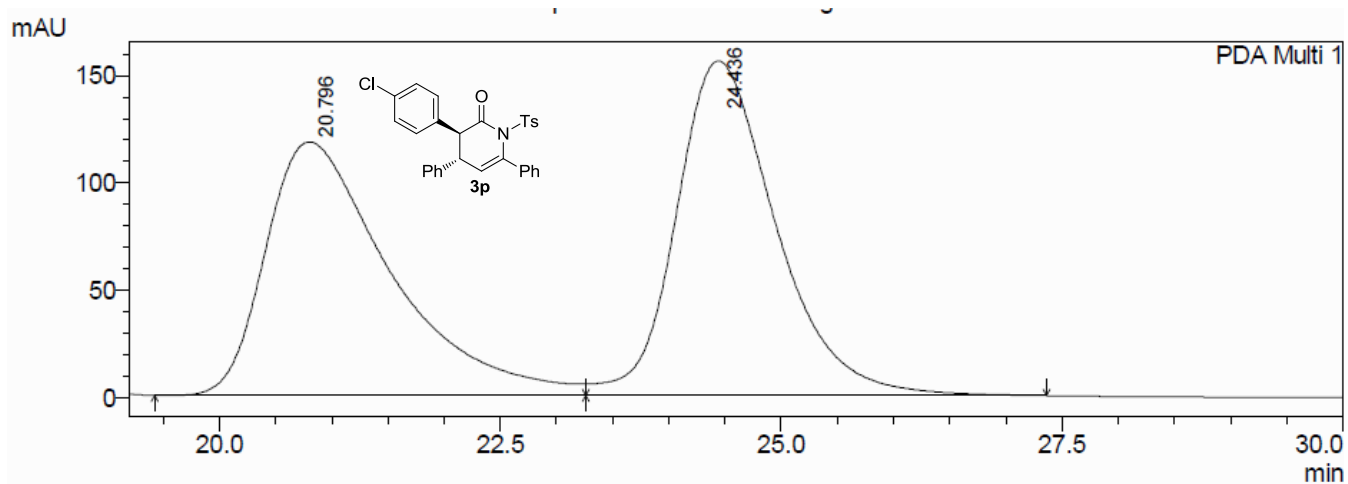


PeakTable

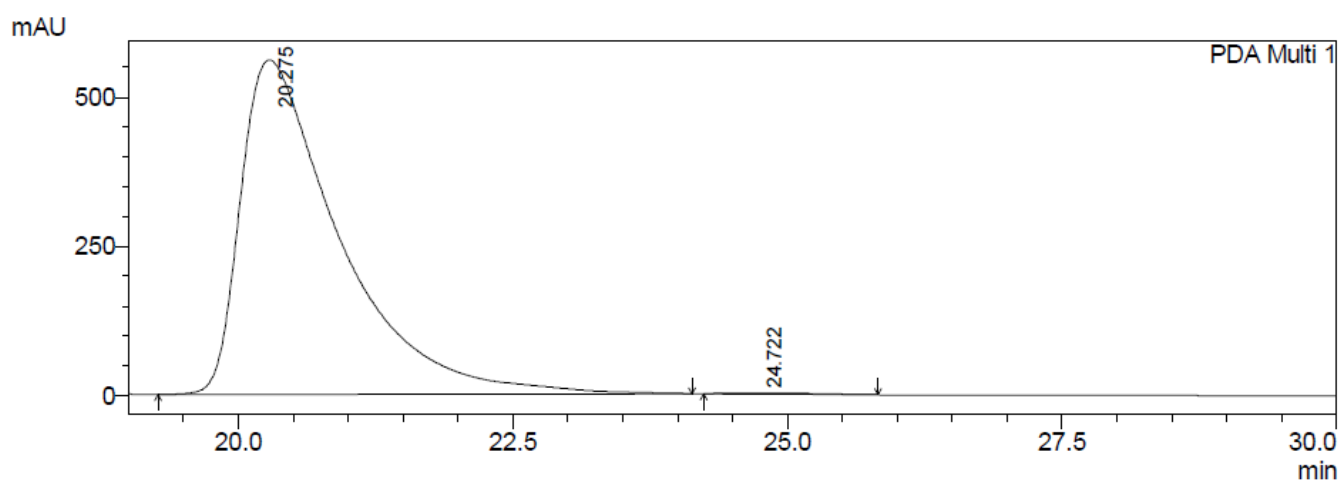


HL-64-7-C13 CDC13 AV300MHz

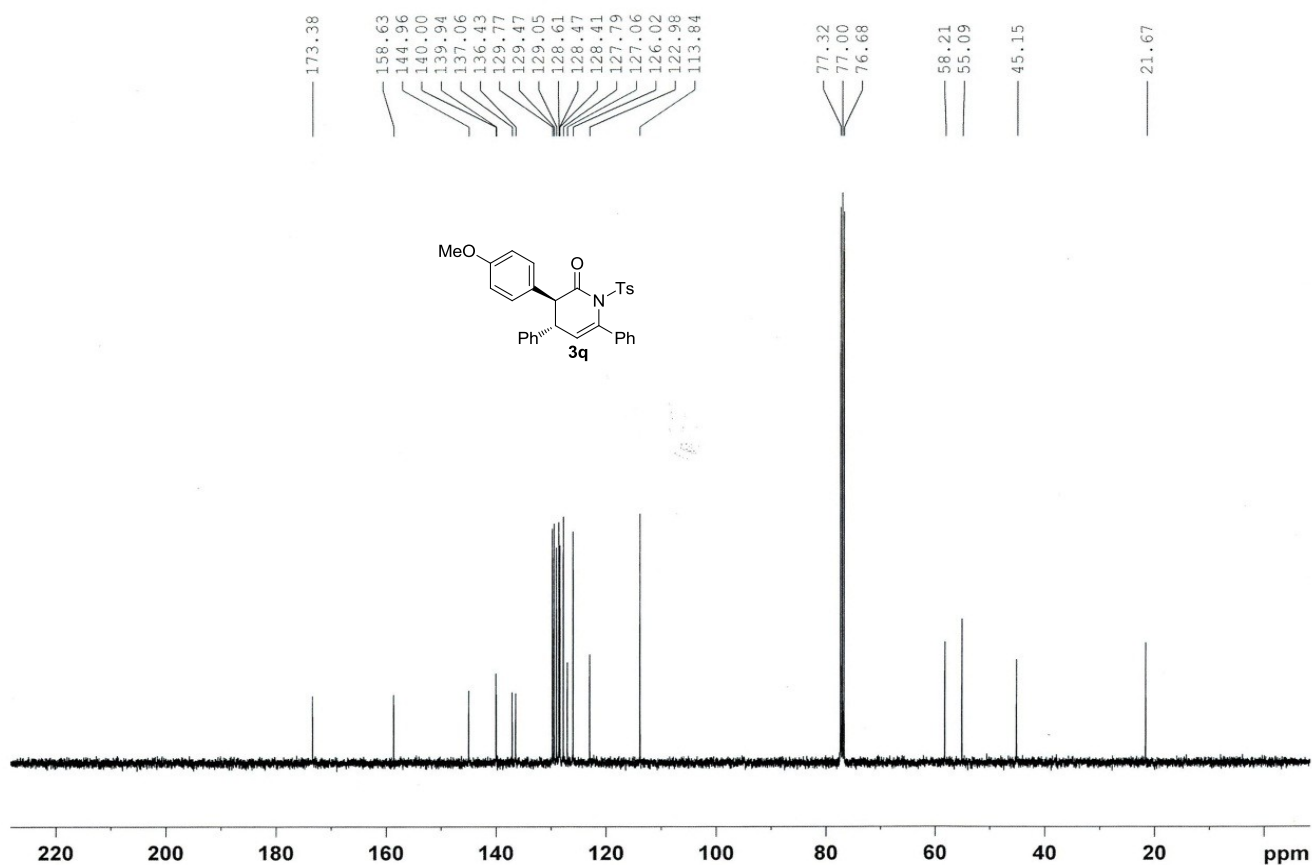
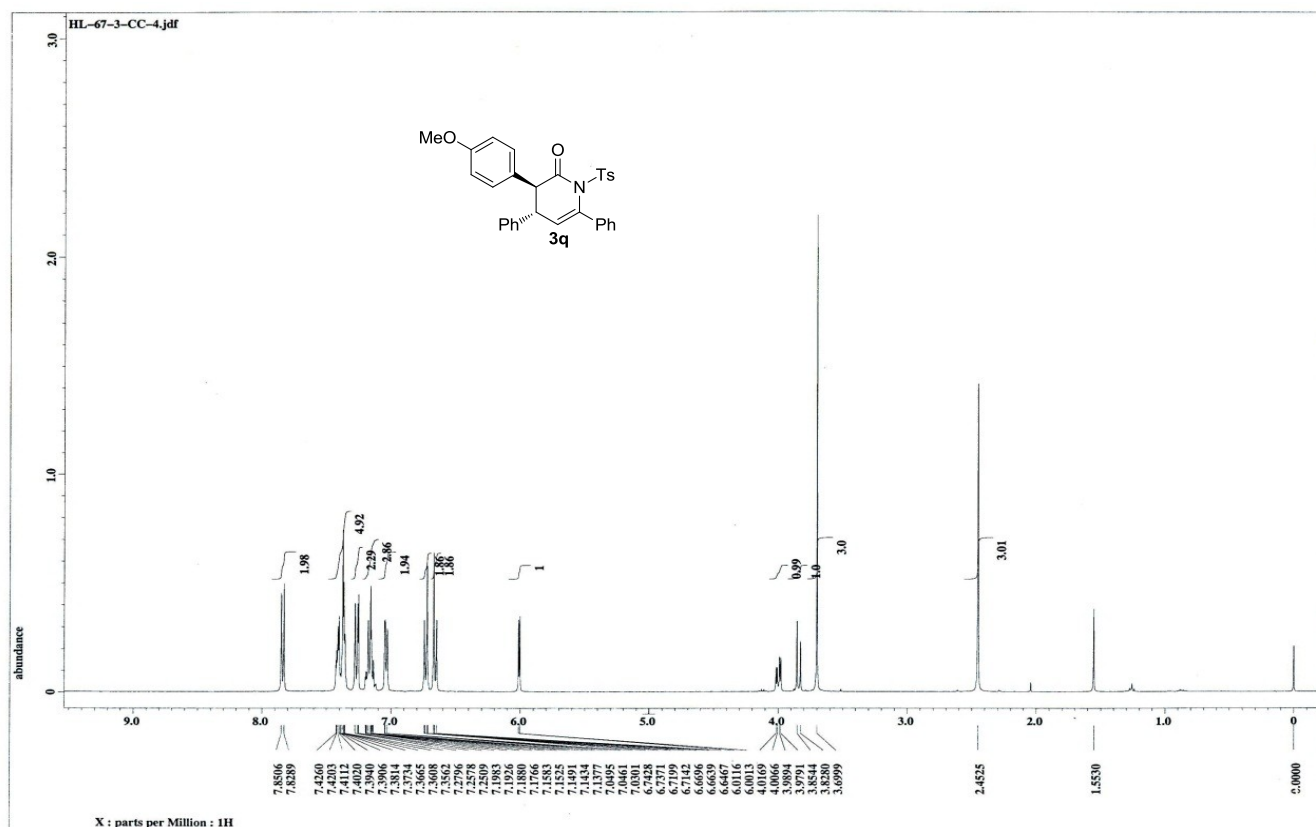


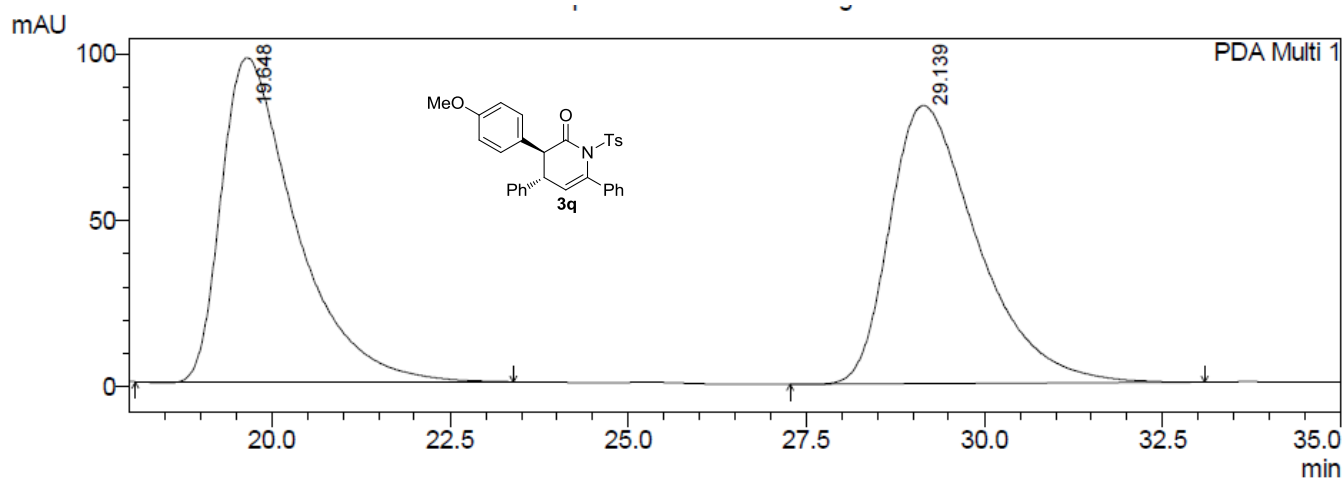


PeakTable					
PDA Ch1 254nm 4nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.796	9184346	118056	48.769	43.111
2	24.436	9648155	155788	51.231	56.889
Total		18832501	273844	100.000	100.000



PeakTable					
PDA Ch1 254nm 4nm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.275	35206542	560326	99.718	99.683
2	24.722	99656	1784	0.282	0.317
Total		35306197	562111	100.000	100.000

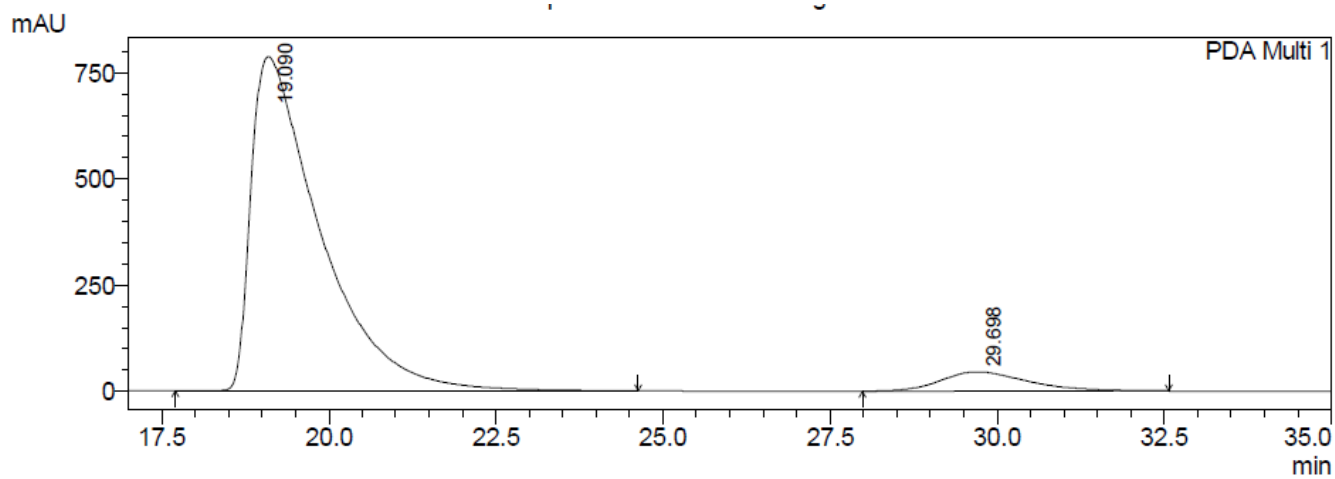




PeakTable

PDA Ch1 254nm 4nm

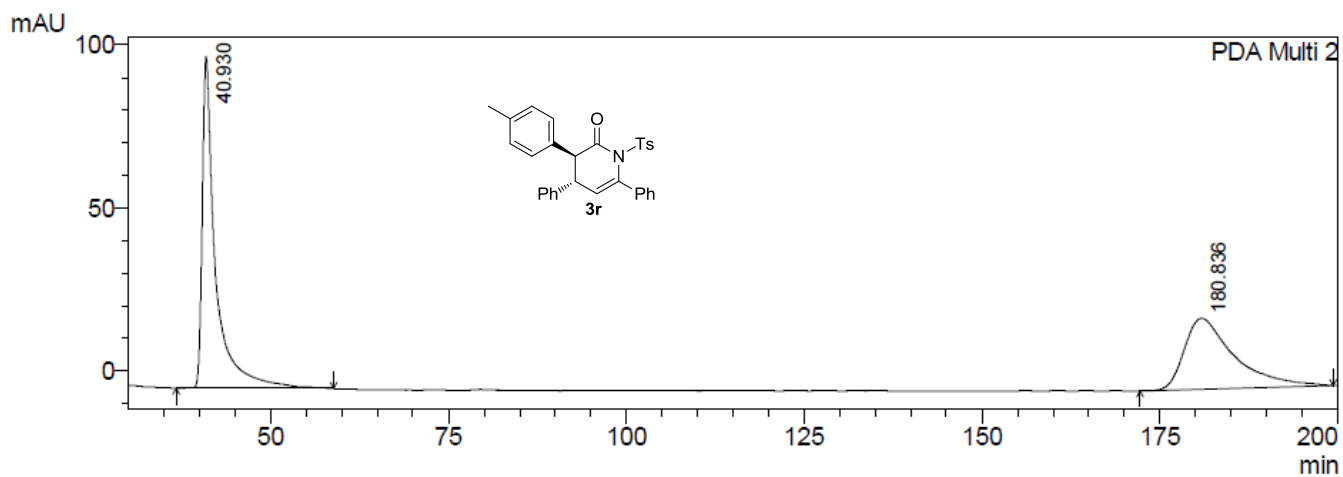
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.648	7077077	97189	49.573	53.825
2	29.139	7199019	83376	50.427	46.175
Total		14276096	180565	100.000	100.000



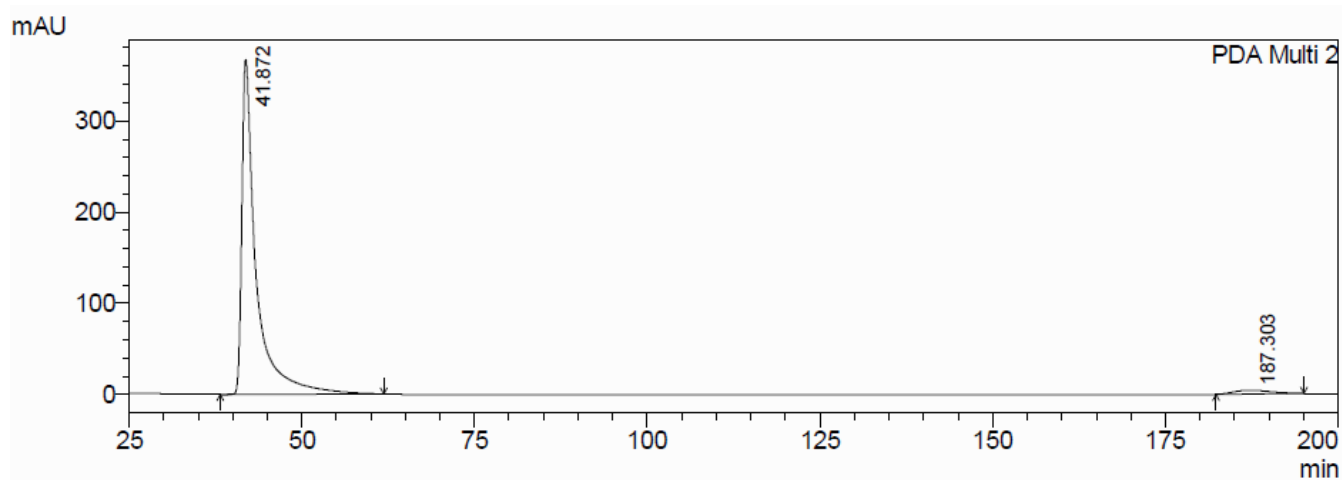
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.090	56579971	787126	93.145	94.526
2	29.698	4164283	45582	6.855	5.474
Total		60744253	832708	100.000	100.000

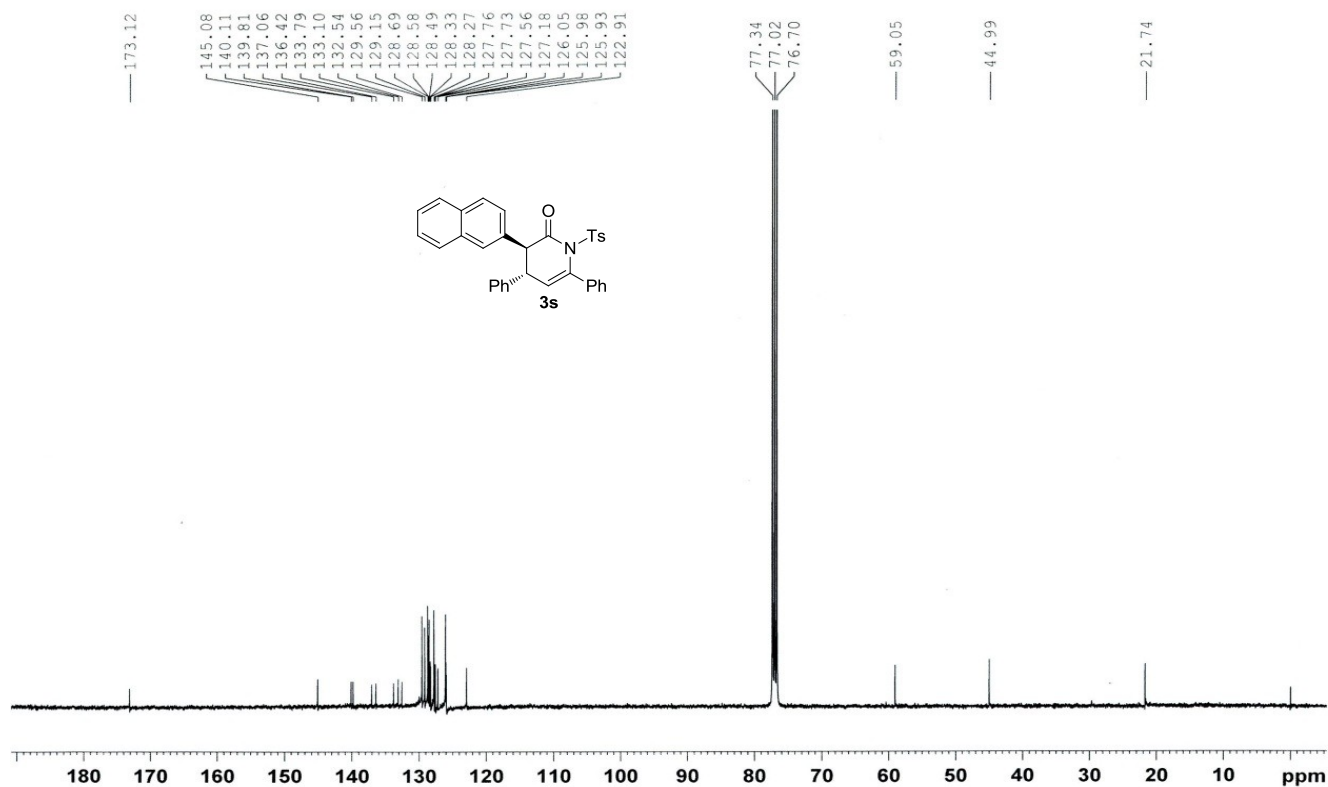
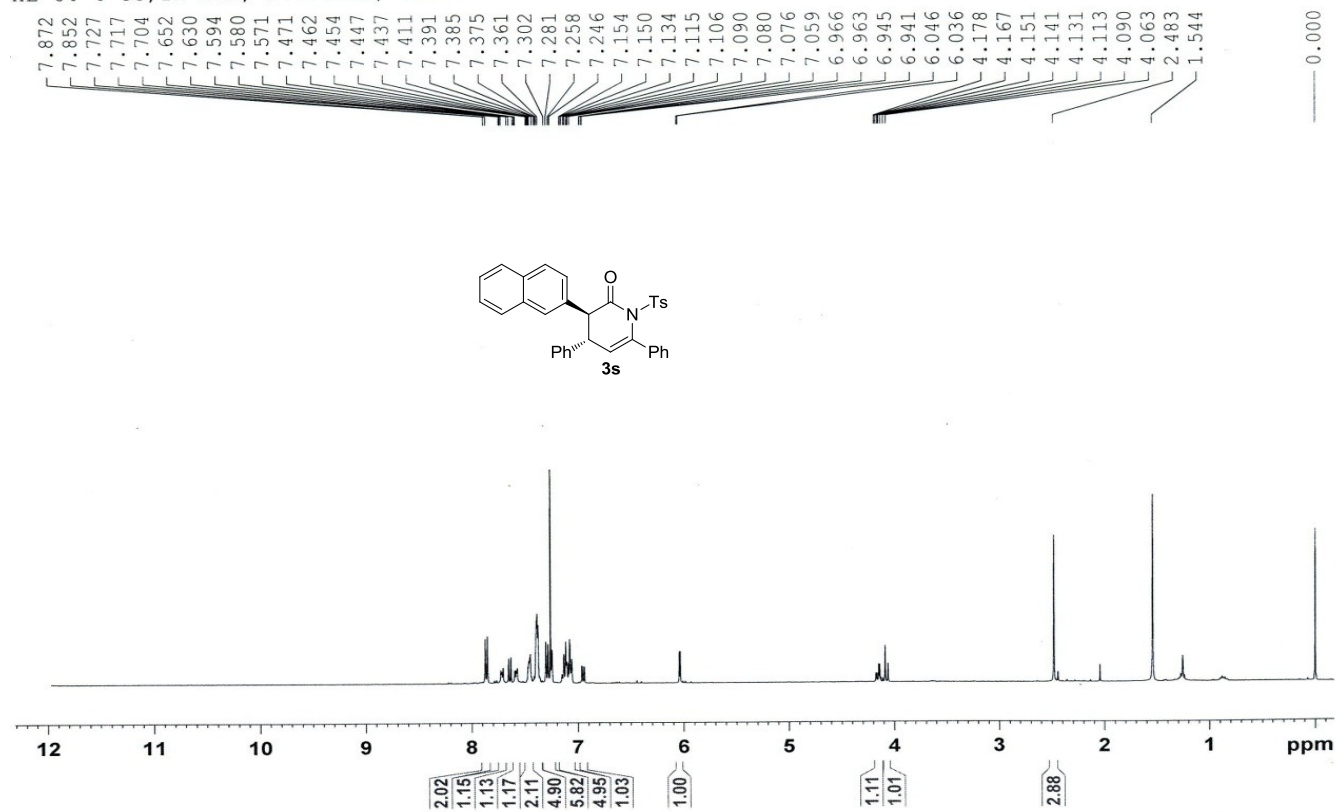


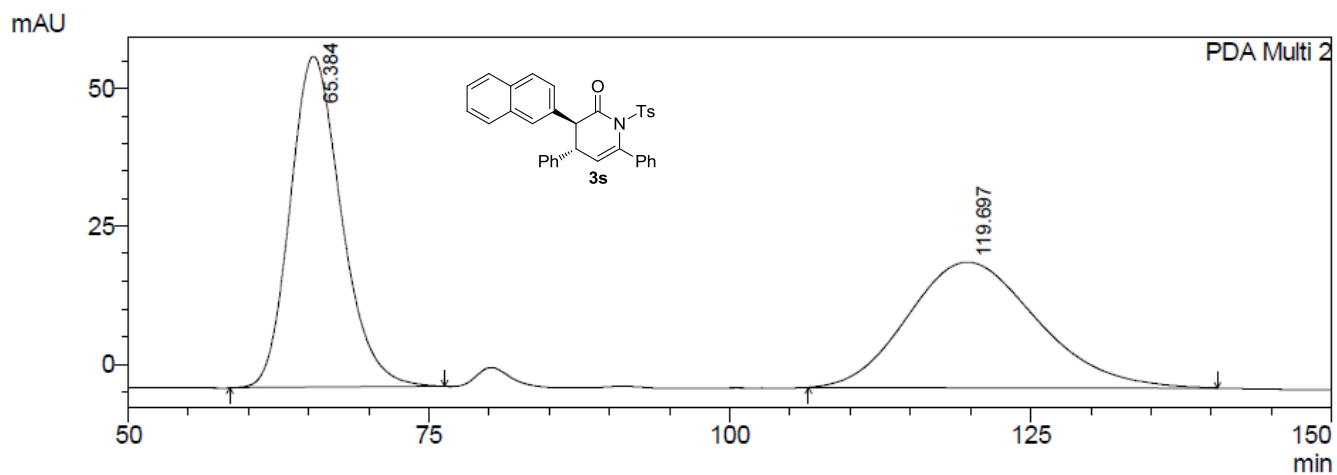
PeakTable					
PDA Ch2 220nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.930	13260425	101866	55.720	82.436
2	180.836	10538043	21703	44.280	17.564
Total		23798468	123569	100.000	100.000



PeakTable					
PDA Ch2 220nm 4mm					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.872	52495426	366818	97.116	98.882
2	187.303	1558752	4149	2.884	1.118
Total		54054178	370967	100.000	100.000

HL-64-4-cc, 1H NMR, AV400MHz, CDCl3

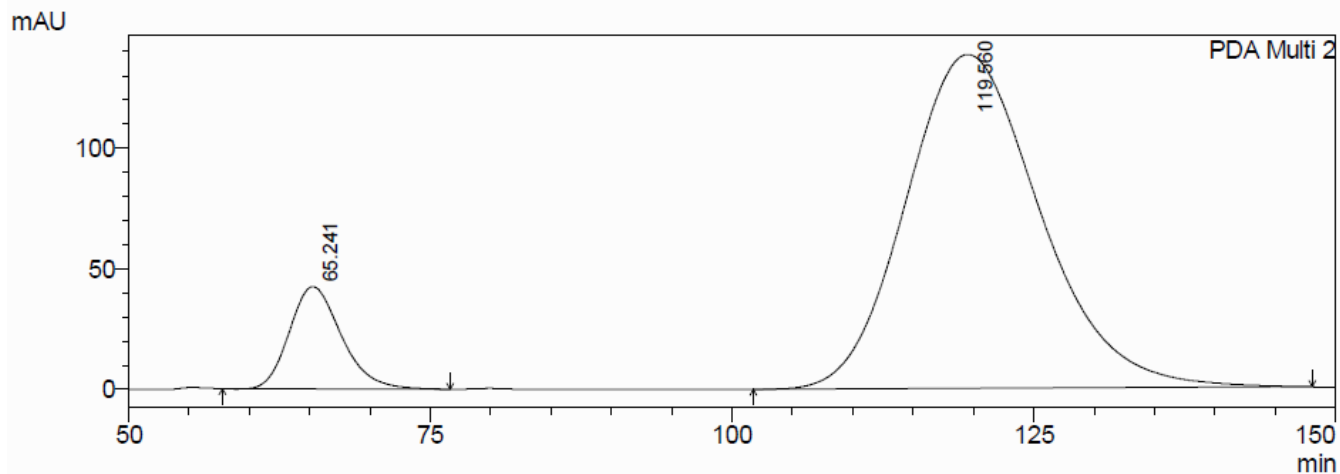




PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	65.384	17744042	59908	50.993	72.515
2	119.697	17053062	22707	49.007	27.485
Total		34797104	82615	100.000	100.000

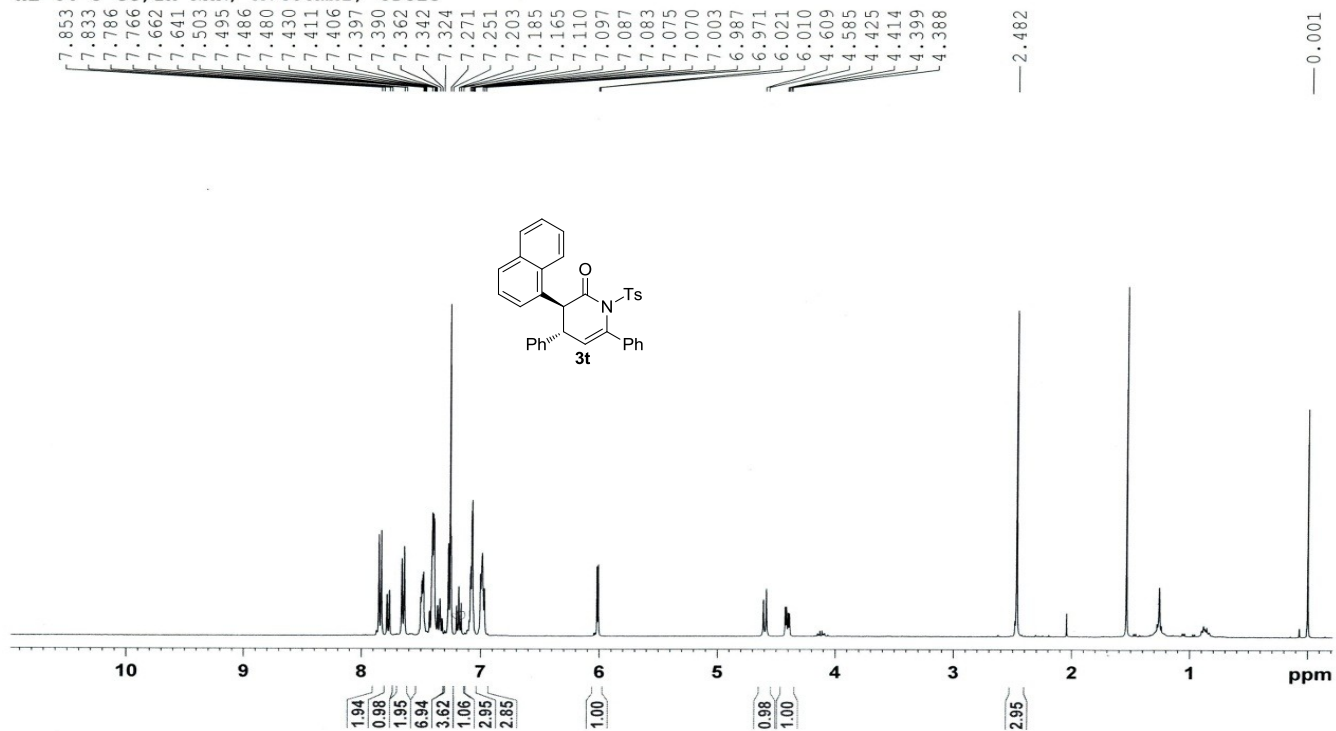


PeakTable

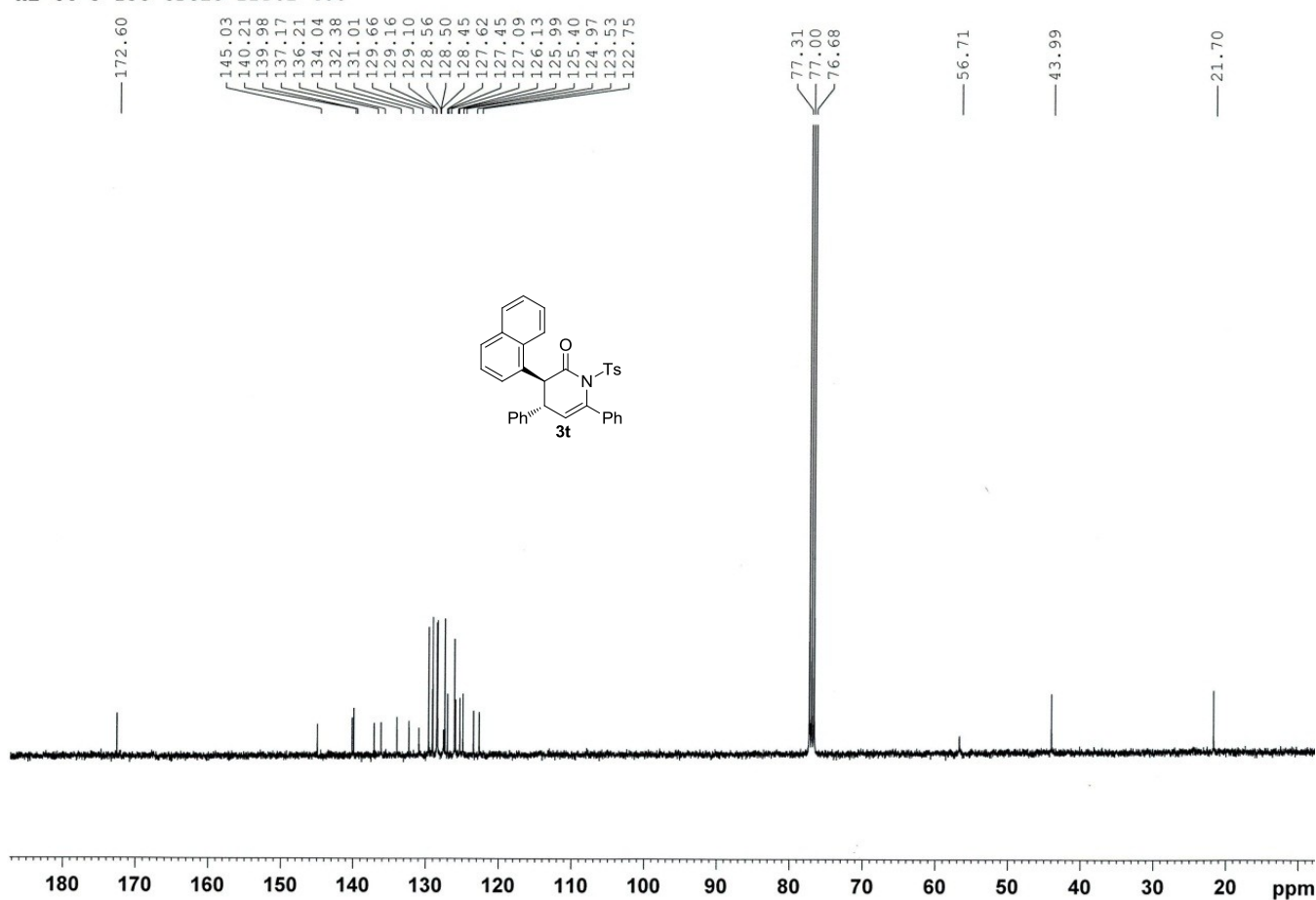
PDA Ch2 220nm 4nm

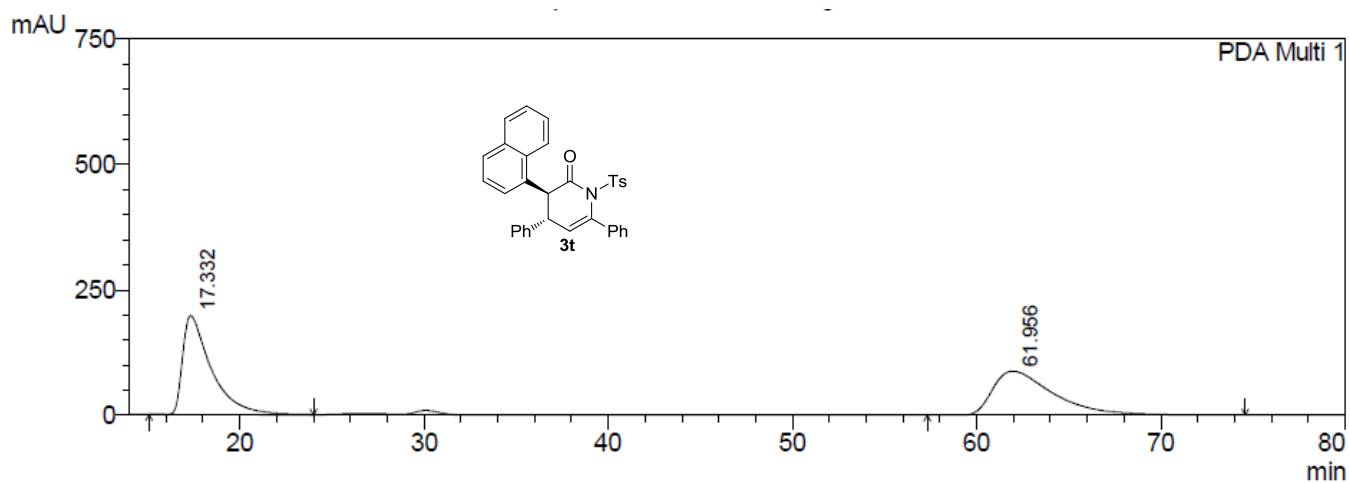
Peak#	Ret. Time	Area	Height	Area %	Height %
1	65.241	12674506	42336	10.565	23.422
2	119.560	107294540	138418	89.435	76.578
Total		119969047	180755	100.000	100.000

HL-64-3-cc, 1H NMR, AV400MHz, CDCl3



HL-64-3-13C CDCl3 BBFO2 400

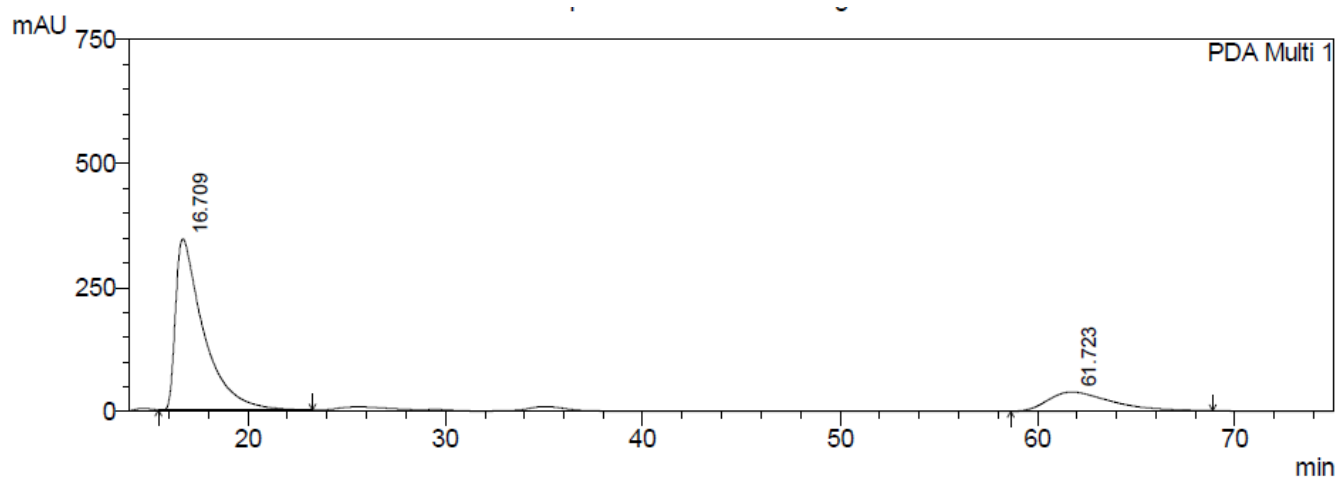




PeakTable

PDA Ch1 254nm 4nm

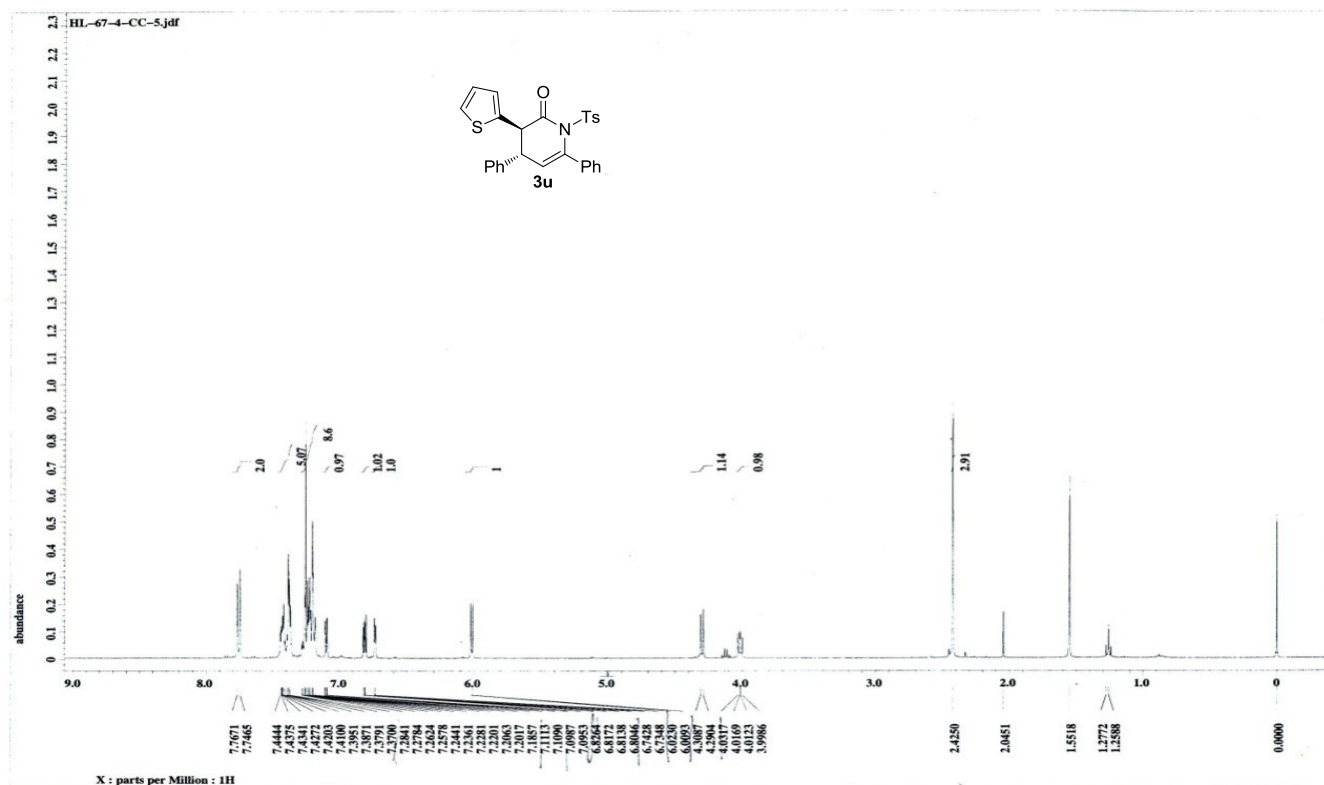
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.332	21395566	196885	50.360	68.784
2	61.956	21089960	89353	49.640	31.216
Total		42485526	286238	100.000	100.000



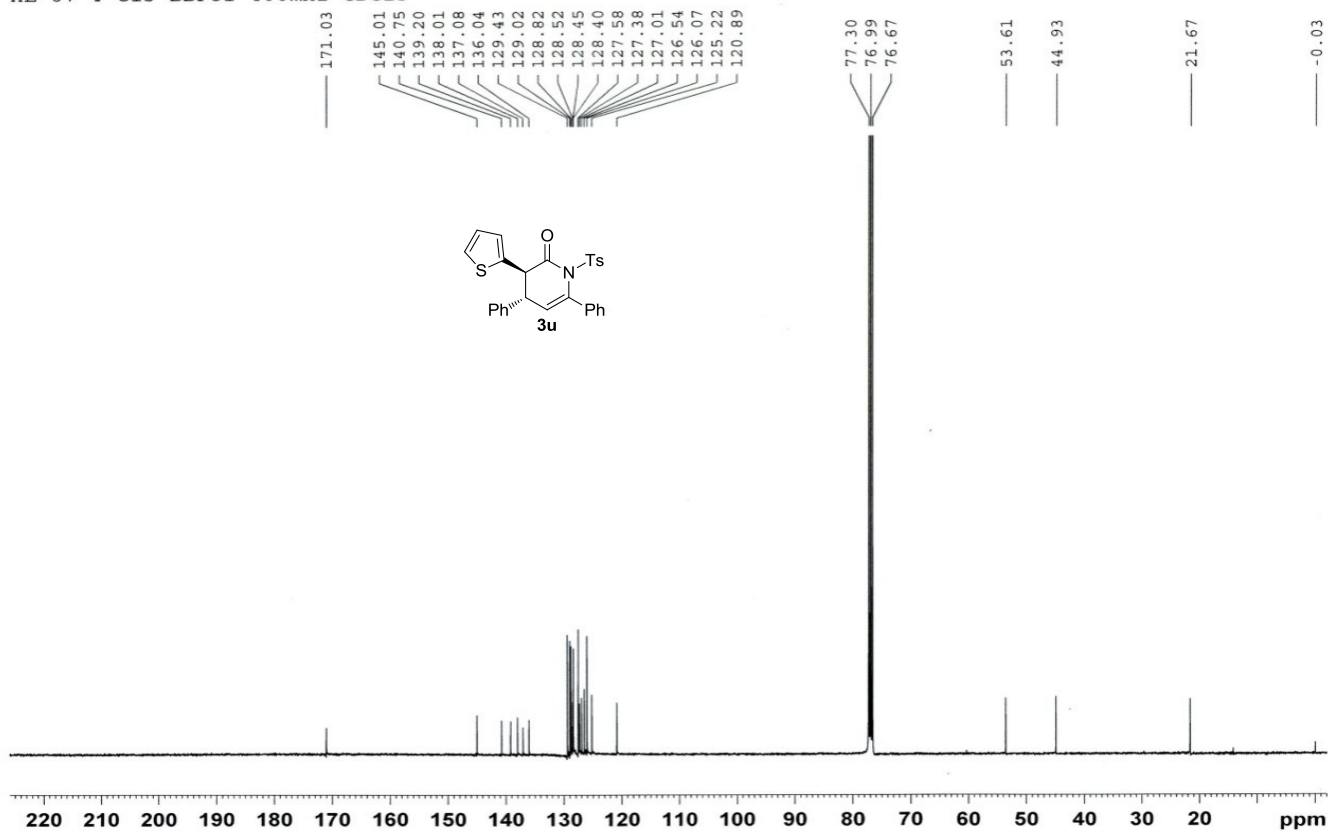
PeakTable

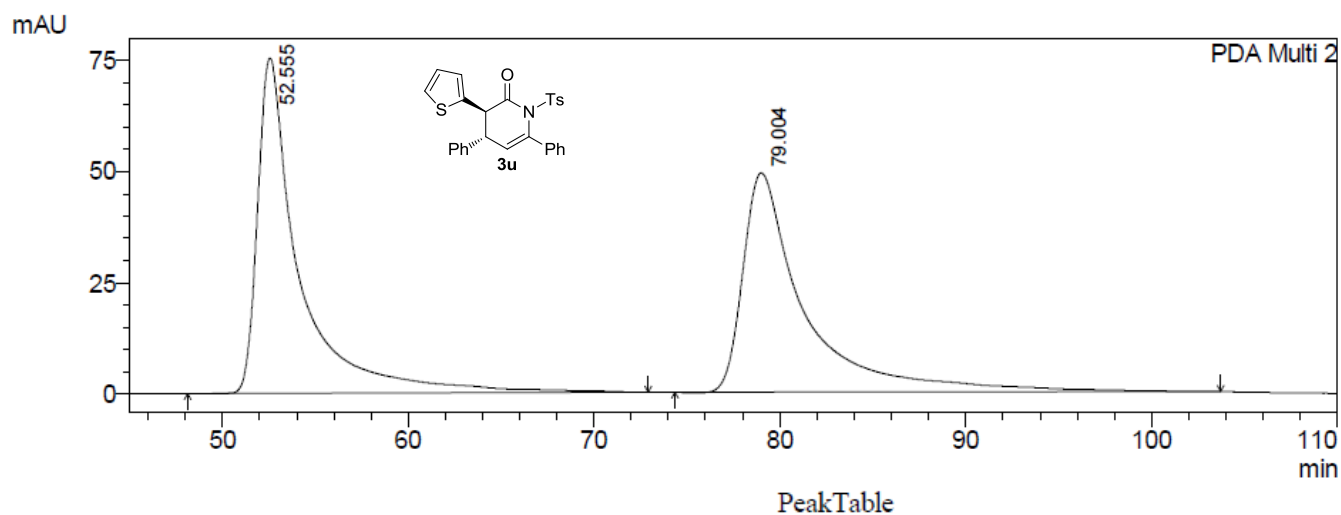
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.709	34191485	344779	79.672	89.914
2	61.723	8723710	38676	20.328	10.086
Total		42915196	383455	100.000	100.000



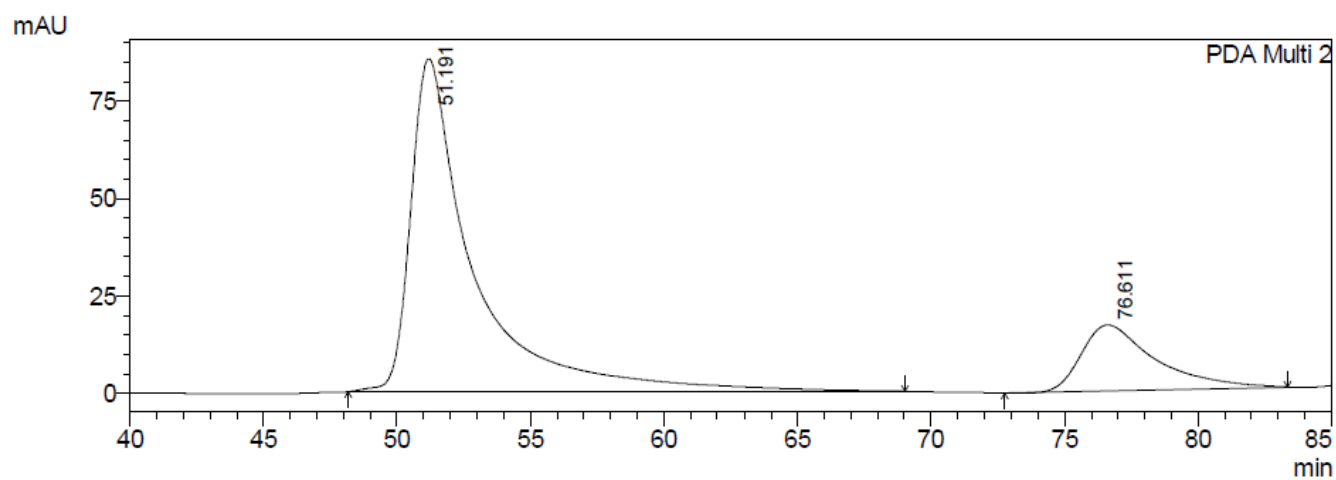
HL-67-4-C13 BBF01 400MHz CDCl3





PDA Ch2 220nm 4mm

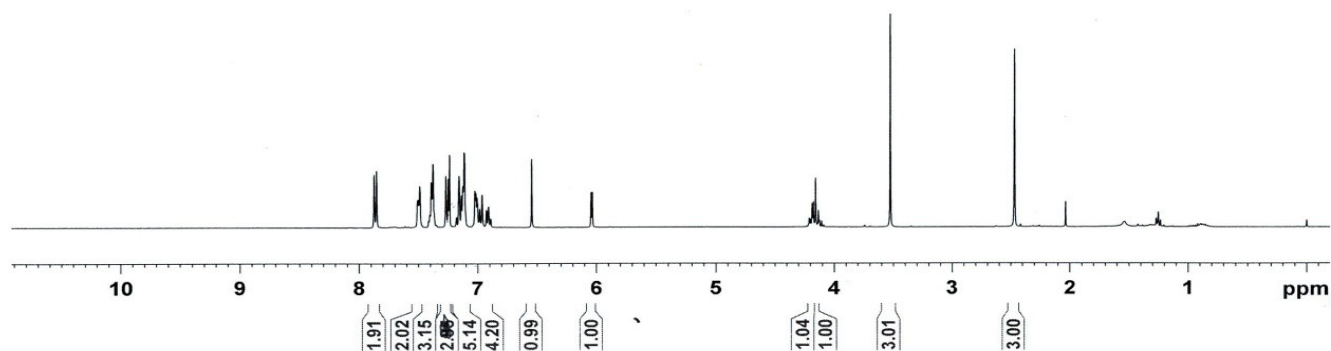
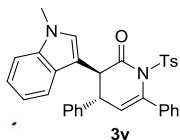
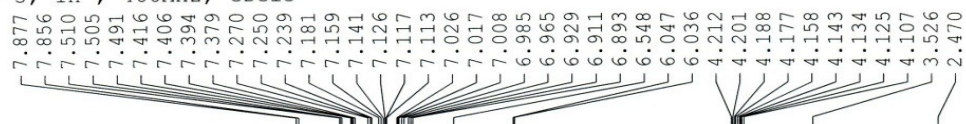
Peak#	Ret. Time	Area	Height	Area %	Height %
1	52.555	11867822	75372	50.927	60.464
2	79.004	11435803	49284	49.073	39.536
Total		23303625	124657	100.000	100.000



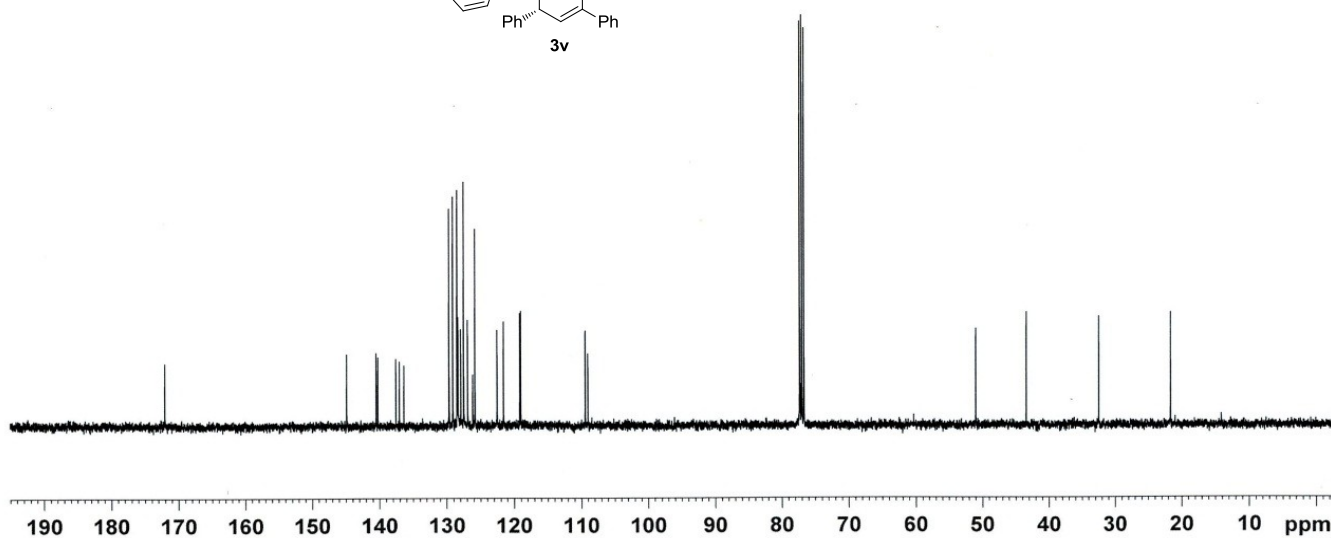
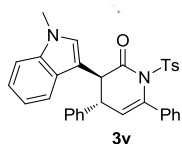
PDA Ch2 220nm 4mm

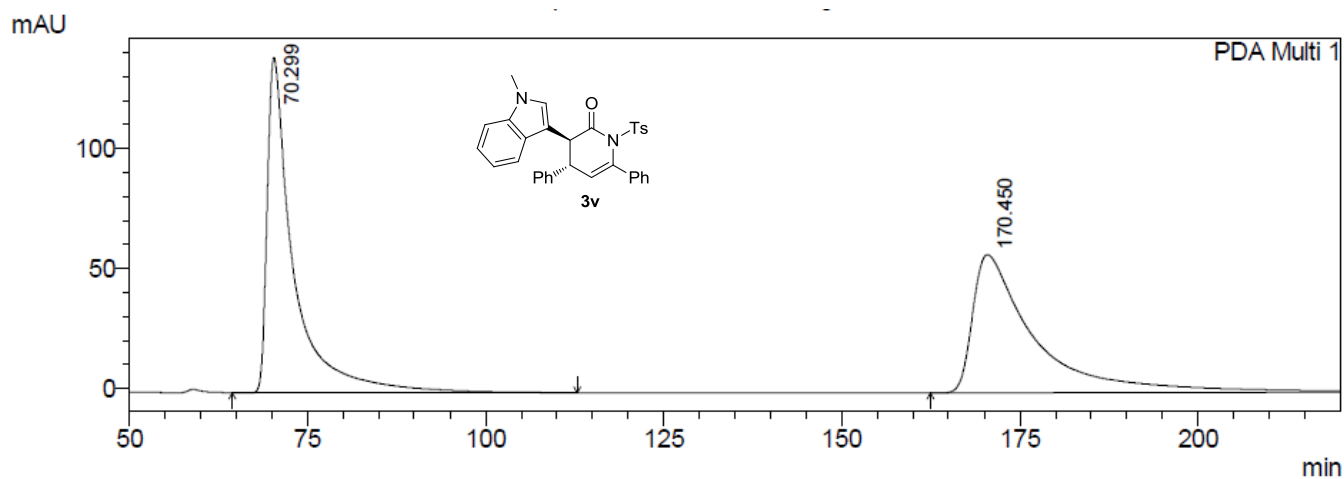
Peak#	Ret. Time	Area	Height	Area %	Height %
1	51.191	13927560	85358	81.163	83.498
2	76.611	3232369	16870	18.837	16.502
Total		17159929	102227	100.000	100.000

HL-91-5, ¹H, 400MHz, CDCl₃



HL-91-5-C13, ¹H, 400MHz, CDCl₃

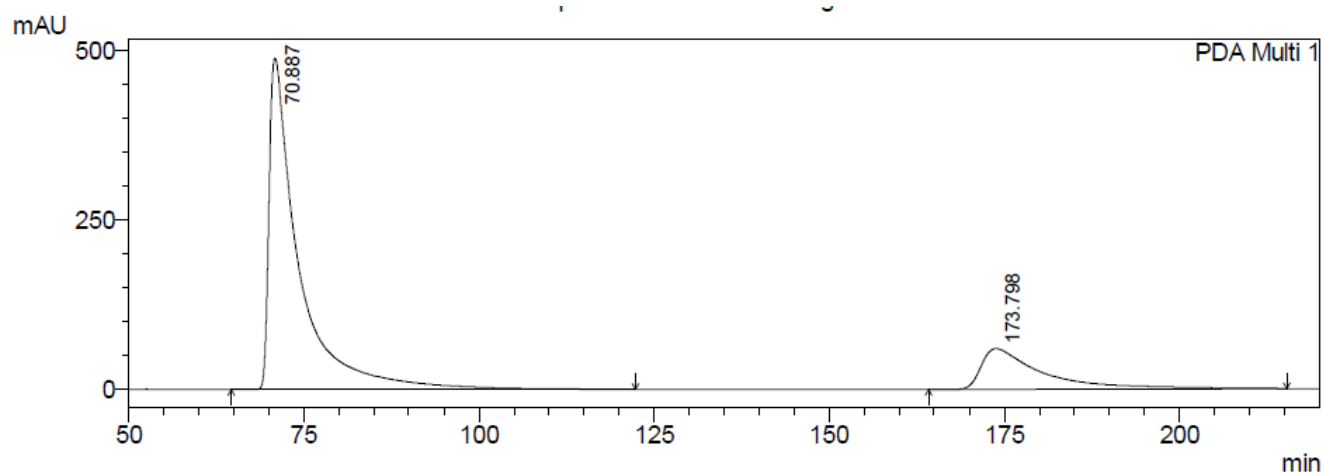




PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	70.299	36201081	140041	50.115	70.806
2	170.450	36034245	57741	49.885	29.194
Total		72235326	197782	100.000	100.000



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	70.887	143535404	488196	79.854	89.077
2	173.798	36211364	59864	20.146	10.923
Total		179746768	548060	100.000	100.000

