This journal is © The Royal Society of Chemistry 2012

Supplementary Information

Protonation and [4+2] Cycloaddition of Enals and Unmodified Chalcones *via* N-Heterocyclic Carbene/Acid Catalysis: Toward Substrate-Independent Reaction Controls

Zhenqian Fu,[a] Hui Sun,[b] Shaojin Chen,[a] Bhoopendra Tiwari,[a] Guohui Li*[b] and Yonggui Robin Chi*[a]

[a] *Division of Chemistry & Biological Chemistry, School of Physical & Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore*

[b] *State key Laboratory of Molecular Reaction Dynamics, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Rd. Dalian, P. R. China 116023*

robinchi@ntu.edu.sg, ghli@dicp.ac.cn

Table of Contents

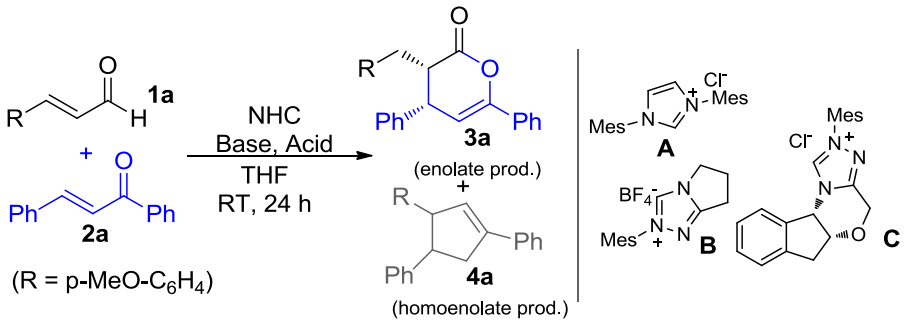
I	General information
II	Initial studies on reaction condition optimization General procedure for the catalytic synthesis of products **3** Stereochemistry determination by X-ray crystallographic analysis
III	Characterizations of products
IV	^{1}H, ^{13}C NMR and HPLC spectra

I. General Information.

Commercially available materials purchased from Alfa Aesar or Sigma-Aldrich were used as received, except aldehydes that were purified *via* distillation or column chromatography prior to use. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker (400 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^{1}H 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 (^{13}C NMR) spectra were recorded on a Bruker (100 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). The determination of enantiomeric excess 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: $[\alpha]^{rt}_{D}$ (*c* is in gm 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 or potassium permanganate stain.

II Summary of initial studies on reaction condition optimization

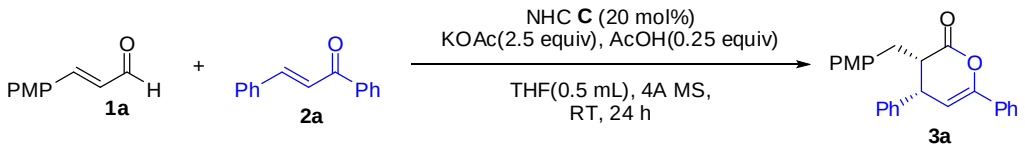
Table S1.



Entry[a]	Condition	**3a**+**4a** (%)[b]	**3a**:**4a**[c]	**3a** d.r.(ee) [d]
1	**A**, DBU	85	<1:99	-
2	**A**, DBU, HOAc	81	1:13	-
3	**A**, KOAc	20	1.5:1	
4	**A**, KOAc, HOAc	9	1.8:1	
5	**A,** K_2CO_3	>95	1:13	-
6	**A,** K_2CO_3, HOAc	>95	1: 1.7	-
7	**A**, DABCO	81	1: 4.3	-
8	**A**, DABCO,HOAc	16	1.2 : 1	-
9	**A**, KOAc	20	1.5 :1	-
10	**A**, KOAc, HOAc	9	1.8 :1	-
11	**A**, K_3PO_4,	>95	1:8	-
12	**A**, K_3PO_4, HOAc	51	1.3 :1	
13	**B**, K_3PO_4, HOAc	>95	9:1	1.7:1
14	**C**, K_3PO_4, HOAc	>95	5.6 :1	20:1
15	**C**, Et_3N	78	1.6 : 1	8:1
16	**C**, Et_3N, HOAc	73	6:1	20:1
17	**C**, NMM	44	6.5 :1	20:1
18	**C**, NMM, HOAc	37	10.9 :1	20:1
19	**C**, DIEA	63	2.5 :1	8:1
20	**C**, DIEA, HOAc	52	7.8 :1	20:1
21	**C**, DMAP	54	2.1 :1	9:1
22	**C**, DMAP, HOAc	23	12 :1	14:1
23	**C**, KOAc	78	5.2:1	20:1
24	**C**, KOAc, HOAc	71	10.5:1	20:1
25[e]	**C**, KOAc, HOAc	75	10.2:1	20:1
26[e] [f]	**C**, KOAc, HOAc	81	10:1	20:1
27[e],[f] [g]	**C, KOAc, HOAc**	**>95(86)**[h]	**10:1**	**20:1(>98%)**

[a] **1a** (0.50 mmol), **2a** (0.25 mmol), base (and acid), THF (1.0 mL), N_2. [b] Combined yield of **3a** and **4a** based on **2a**; estimated *via* ^{1}H NMR analysis of crude reaction mixture. [c] Ratio of **3a** and **4a**, estimated *via* ^{1}H NMR analysis of crude reaction mixture. [d] d.r. and ee of **3a**, estimated *via* ^{1}H NMR and chiral phase HPLC analysis respectively. Absolute configuration of the major diastereomer of **3a** was determined *via* x-ray structure of its analog **3c** (Table 2). [e] 20 mol% **C**, [f] 250% mol KOAc, 25% HOAc, 4 A MS. [g] 0.5M THF. [h] Isolated yield of **3a** (single diastereomer)

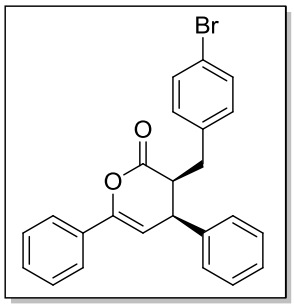
General procedure for the synthesis of 3:

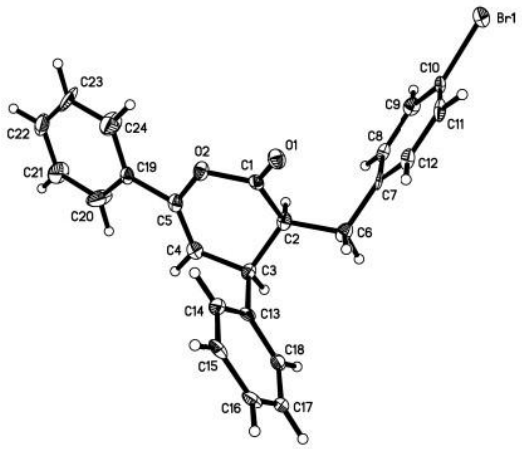


A dry 10 mL Schlenk tube equipped with a stir magnetic bar was successively charged with enal **1a** (81 mg, 0.5 mmol), chalcone **2a** (52 mg, 0.25 mmol), NHC pre-catalyst **C** (18.4 mg, 0.05 mmol), KOAc (61.4 mg, 0.625 mmol) and 4Å MS (100 mg). The tube was closed with a septum, evacuated, and refilled with nitrogen. To this mixture was added freshly distilled THF (0.5 mL), followed by AcOH (7.2 µL, 0.0625 mmol). The reaction mixture was stirred at RT for 24 h. After complete consumption of **2a**, as indicated by TLC and crude ^{1}H NMR analysis, the solvent was removed under reduced pressure. The resulting residue was purified *via* column chromatography on silica gel with hexanes/ethyl acetate (10:1) as eluent to afford product **3a** as a white solid in 86% yield (79.6 mg), 20:1 dr and 99% ee.

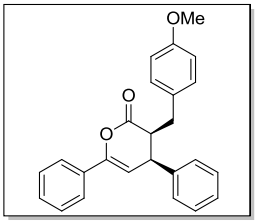
Note: The corresponding racemic products for chiral HPLC method development were prepared using the above method in presence of catalyst **B**. In most cases, this use of catalyst **B** gave products with lower dr than the use of chiral catalyst **C**.

Determination of absolute and relative configuration *via* X-ray crystallographic analysis:
Good quality crystal of **3c** (colorless flaky crystal) was obtained by vaporization of a hexane/ethyl acetate solution of compound **3c**. CCDC 870337 contains the supplementary crystallographic data.

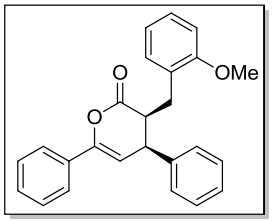




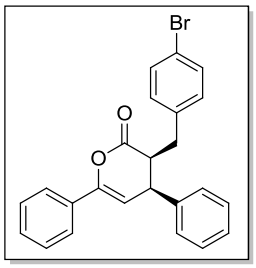
III. Characterizations of Products.



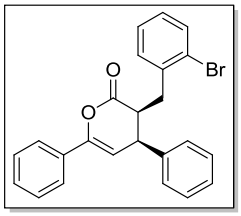
(3*S*,4*S*)-3-(4-Methoxybenzyl)-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3a): White solid, 80 mg; $[\alpha]_D^{23}$ (c 1.13, CH_2Cl_2) = +251.8; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.38 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.21 (dd, *J* = 14.4, 5.2 Hz, 1H), 3.33 (ddd, *J* = 9.2, 7.2, 5.2 Hz, 1H), 3.66 (t, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 6.02 (d, *J* = 6.8 Hz, 1H), 6.84–6.87 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 7.09–7.11 (m, 2H), 7.25–7.40 (m, 6H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.3, 158.3, 150.0, 137.9, 132.2, 130.6, 130.0, 129.2, 129.0, 128.6, 128.5, 127.8, 124.7, 114.0, 105.2, 55.3, 45.8, 40.8, 31.5; HRMS(ESI) calcd for $C_{25}H_{23}O_3(M+H)^+$: 371.1647, Found: 371.1640; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.9:0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 169.3 min, t_r (minor) = 147.3 min.



(3*S*,4*S*)-3-(2-Methoxybenzyl)-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3b) : White solid, 82 mg; $[\alpha]_D^{23}$ (*c* 1.72, CH_2Cl_2) = +234.3; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.50 (dd, *J* = 14.4, 8.4 Hz, 1H), 3.19 (dd, *J* = 14.4, 5.6 Hz, 1H), 3.55–3.57 (m, 1H), 3.65 (t, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 6.03 (d, *J* = 6.8 Hz, 1H), 6.84–6.88 (m, 2H), 6.98 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.14–7.16 (m, 2H), 7.20–7.39 (m, 7H), 7.64–7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7, 157.7, 149.8, 138.4, 132.4, 131.7, 129.1, 128.9, 128.5, 128.5, 127.9, 127.7, 126.8, 124.6, 120.3, 110.1, 105.4, 55.2, 43.4, 41.3, 28.4; HRMS(ESI) calcd for $C_{25}H_{23}O_3(M+H)^+$: 371.1647, Found: 371.1649; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel IA, 99.9:0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 83.0 min, t_r (minor) = 77.3 min.

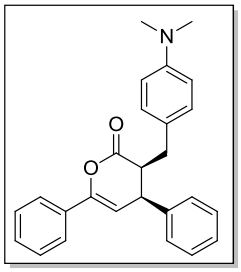


(3*S*,4*S*)-3-(4-Bromobenzyl)-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3c): White solid, 76 mg; $[\alpha]_D^{23}$ (*c* 1.96, CH_2Cl_2) = +237.2; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.42 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.18 (dd, *J* = 14.8, 5.6 Hz, 1H), 3.34 (ddd, *J* = 8.8, 6.8, 5.6 Hz, 1H), 3.65 (t, *J* = 6.8 Hz, 1H), 6.03 (d, *J* = 6.8 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.07–7.10 (m, 2H), 7.29–7.44 (m, 8H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.9, 150.0, 137.7, 137.6, 132.0, 131.6, 130.8, 129.3, 129.1, 128.6, 128.4, 128.0, 124.7, 120.4, 105.0, 45.5, 41.0, 32.0; HRMS(ESI) calcd for $C_{24}H_{20}O_2Br(M+H)^+$: 419.0647, Found: 419.0642; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OJ-H, 92:8 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 98.0 min, t_r (minor) = 79.0 min.

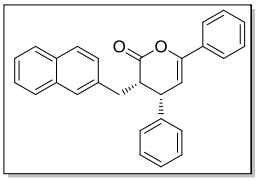


(3*S*,4*S*)-3-(2-Bromobenzyl)-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3d): White solid, 86 mg; $[\alpha]_D^{23}$ (*c* 0.78, CH_2Cl_2) = +204.3; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.74 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.08 (dd, *J* = 14.4, 7.2 Hz, 1H), 3.48–3.53 (m, 1H), 3.82 (t, *J* = 6.8 Hz, 1H), 6.06 (d, *J* = 6.8 Hz, 1H), 7.07–7.11

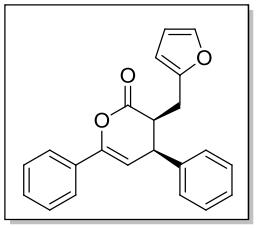
(m, 1H), 7.20–7.24 (m, 4H), 7.31–7.39 (m, 6H), 7.53 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 150.0, 138.4, 138.0, 132.8, 132.4, 132.1, 129.2, 129.1, 128.6, 128.4, 127.9, 127.3, 124.7, 104.9, 44.0, 42.1, 33.8; HRMS(ESI) calcd for $C_{24}H_{20}O_2Br(M+H)^+$: 419.0647, Found: 419.0645; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.9:0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 45.7 min, t_r (minor) = 58.3 min.



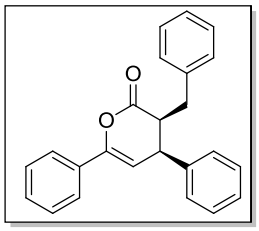
(3*S*,4*S*)-3-(4-(Dimethylamino)benzyl)-4,6-diphenyl-3,4-dihydro-*2H*-pyran-2-one (3e): yellow oil, 77 mg; $[\alpha]_D^{23}$ (c 1.2, CH_2Cl_2) = +193.1; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.33 (dd, *J* = 14.8, 9.6 Hz, 1H), 2.93 (s, 6H), 3.20 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.31 (ddd, *J* = 9.6, 6.8, 4.8 Hz, 1H), 3.67 (t, *J* = 6.8 Hz, 1H), 6.02 (d, *J* = 6.8 Hz, 1H), 6.70 (dd, *J* = 6.8, 2.0 Hz, 2H), 6.99 (d, *J* = 2.0 Hz, 2H), 7.10–7.13 (m, 2H), 7.24–7.39 (m, 6H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.5, 149.9, 149.4, 138.0, 132.3, 129.7, 129.1, 128.9, 128.6, 127.7, 126.3, 124.7, 112.9, 105.5, 46.0, 40.8, 40.6, 31.2; HRMS(ESI) calcd for $C_{26}H_{26}NO_2(M+H)^+$: 384.1964, Found: 384.1967; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OJ-H, 95:5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 353.3 min, t_r (minor) = 294.0 min.



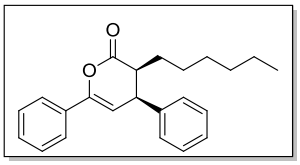
(3*S*,4*S*)-3-(Naphthalen-2-ylmethyl)-4,6-diphenyl-3,4-dihydro-*2H*-pyran-2-one (3f): White solid, 82 mg; $[\alpha]_D^{23}$ (*c* 1.64, CH_2Cl_2) = +252.2; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.61 (dd, *J* = 14.4, 9.2 Hz, 1H), 3.44–3.52 (m, 2H), 3.66 (t, *J* = 6.8 Hz, 1H), 6.02 (d, *J* = 6.8 Hz, 1H), 7.09–7.11 (m, 2H), 7.25–7.40 (m, 7H), 7.45–7.49 (m, 2H), 7.53 (s, 1H), 7.65–7.67 (m, 2H), 7.76–7.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.2, 150.0, 137.8, 136.0, 133.5, 132.3, 123.2, 129.2, 129.0, 128.6, 128.5, 128.3, 127.9, 127.7, 127.6, 127.5, 127.2, 126.2, 125.6, 124.7, 105.2, 45.6, 40.8, 32.5; HRMS(ESI) calcd for $C_{28}H_{23}O_2(M+H)^+$: 391.1698, Found: 391.1699; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OJ-H, 92:8 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 241.2 min, t_r (minor) = 150.1 min.



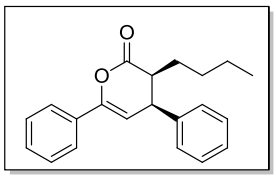
(3*S*,4*S*)-3-(Furan-2-ylmethyl)-4,6-diphenyl-3,4-dihydro-*2H*-pyran-2-one (3g) : yellow oil, 56 mg; $[\alpha]_D^{23}$ (*c* 0.95, CH_2Cl_2) = +263.4; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.48 (dd, *J* = 16.0, 9.6 Hz, 1H), 3.23 (dd, *J* = 16.0, 4.8 Hz, 1H), 3.46–3.50 (m, 1H), 3.76 (t, *J* = 6.8 Hz, 1H), 6.04 (d, *J* = 3.2 Hz, 1H), 6.07 (d, *J* = 6.8 Hz, 1H), 6.33 (dd, *J* = 2.8, 1.6 Hz, 1H), 7.13–7.15 (m, 2H), 7.27–7.42 (m, 7H), 7.66–7.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 152.5, 150.3, 141.5, 137.4, 132.1, 129.2, 129.0, 128.6, 128.5, 127.9, 124.7, 110.4, 107.1, 105.0, 43.3, 40.8, 25.2; HRMS(ESI) calcd for $C_{22}H_{19}O_3(M+H)^+$: 331.1334, Found: 331.1337; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.5:0.5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 38.8 min, t_r (minor) = 34.6 min.



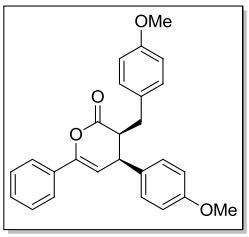
(3*S*,4*S*)-3-Benzyl-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3h): White solid, 75 mg; $[\alpha]_D^{23}$ (*c* 1.5, CH_2Cl_2) = +237.5; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.44 (dd, *J* = 14.8, 9.6 Hz, 1H), 3.29 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.39 (ddd, *J* = 9.2, 7.2, 5.2 Hz, 1H), 3.66 (t, *J* = 6.8 Hz, 1H), 6.03 (d, *J* = 6.8 Hz, 1H), 7.09–7.14 (m, 4H), 7.24–7.40 (m, 9H), 7.64–7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.2, 150.0, 138.7, 137.8, 132.2, 129.2, 129.0, 128.9, 128.6, 128.5, 127.8, 126.6, 124.7, 105.2, 45.7, 40.8, 32.3; HRMS(ESI) calcd for $C_{24}H_{21}O_2(M+H)^+$: 341.1542, Found: 341.1539; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.9: 0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 69.7 min, t_r (minor) = 87.9 min.



(3*S*,4*S*)-3-Hexyl-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3i): White solid, 69 mg; $[\alpha]_D^{23}$ (*c* 1.61, CH_2Cl_2) = +206.3; ¹H NMR (400 MHz, $CDCl_3$) δ = 0.86 (t, *J* = 6.8 Hz, 3H), 1.18–1.29 (m, 9H), 1.38–1.73 (m, 1H), 2.93 (dd, *J* = 14.0, 6.8 Hz, 1H), 3.82 (t, *J* = 6.8 Hz, 1H), 6.07 (d, *J* = 6.8 Hz, 1H), 7.16–7.18 (m, 2H), 7.26–7.41 (m, 6H), 7.66–7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.6, 150.2, 138.1, 132.3, 129.1, 128.9, 128.6, 128.2, 127.7, 124.7, 104.8, 44.3, 41.5, 31.6, 29.1, 27.3, 26.5, 22.6, 14.1; HRMS(ESI) calcd for $C_{23}H_{27}O_2(M+H)^+$: 335.2011, Found: 335.2010; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.9:0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 36.7 min, t_r (minor) = 67.4 min.

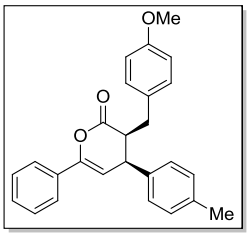


(3*S*,4*S*)-3-Butyl-4,6-diphenyl-3,4-dihydro-2*H*-pyran-2-one (3j): White solid, 59 mg; $[\alpha]_D^{23}$ (*c* 2.07, CH_2Cl_2) = +225.1; ¹H NMR (400 MHz, $CDCl_3$) δ = 0.87 (t, *J* = 7.2 Hz, 3H), 1.25–1.44 (m, 5H), 1.71–1.74 (m, 1H), 2.93 (dd, *J* = 14.0, 6.8 Hz, 1H), 3.83 (t, *J* = 6.8 Hz, 1H), 6.07 (d, *J* = 6.8 Hz, 1H), 7.16–7.18 (m, 2H), 7.27–7.42 (m, 6H), 7.67–7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.6, 150.2, 132.3, 129.1, 128.9, 128.5, 128.2, 127.7, 124.7, 104.8, 44.3, 41.5, 29.5, 26.2, 22.5, 13.9; HRMS(ESI) calcd for $C_{21}H_{23}O_2(M+H)^+$: 307.1698, Found: 307.1702; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.9:0.1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 35.6 min, t_r (minor) = 56.7 min.

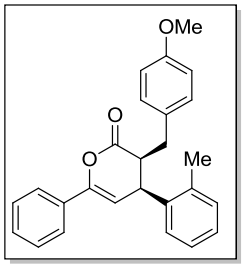


(3*S*,4*S*)-3-(4-Methoxybenzyl)-4-(4-methoxyphenyl)-6-phenyl-3,4-dihydro-2*H*-pyran-2-one (3k): yellow oil, 78 mg; $[\alpha]_D^{23}$ (*c* 2.25, CH_2Cl_2) = +225.2; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.39 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.21 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.30 (ddd, *J* = 9.2, 6.8, 5.2 Hz, 1H), 3.61 (t, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 3.81 (s, 3H), 6.01 (d, *J* = 6.8 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 4H), 6.99–7.06 (m, 4H), 7.34–7.40 (m, 3H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.4, 159.2, 158.2, 149.8, 132.3, 130.6, 130.0, 129.7, 129.5, 129.1, 128.5, 124.6, 114.3, 113.9, 105.6, 55.3, 46.0, 39.9, 31.4; HRMS(ESI) calcd for $C_{26}H_{25}O_4(M+H)^+$: 401.1753, Found: 401.1755; >98% ee (*3S*,

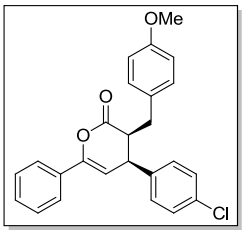
4S)- isomer as determined by HPLC (Chiralcel IA, 99.5:0.5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 176.7 min, t_r (minor) = 321.1 min.



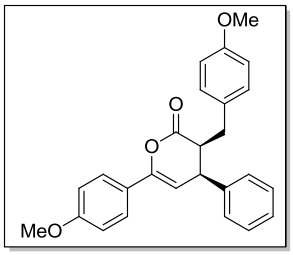
(3*S*,4*S*)-3-(4-Methoxybenzyl)-6-phenyl-4-(p-tolyl)-3,4-dihydro-*2H*-pyran-2-one (3l): White solid, 80 mg; $[\alpha]_D^{23}$ (*c* 1.51, CH_2Cl_2) = +247.4; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.34 (s, 3H), 2.39 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.20 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.30 (ddd, *J* = 9.2, 7.2, 5.2 Hz, 1H), 3.62 (t, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 6.01 (d, *J* = 6.8 Hz, 1H), 6.83–6.87 (m, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.34–7.40 (m, 3H), 7.63–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.4, 158.2, 149.8, 137.5, 134.7, 132.2, 130.7, 130.0, 129.6, 129.1, 128.5, 128.3, 124.6, 113.9, 105.5, 55.3, 45.9, 40.3, 31.4, 21.1; HRMS(ESI) calcd for $C_{26}H_{25}O_3(M+H)^+$: 385.1804, Found: 385.1801; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD-H, 99:1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 47.2 min, t_r (minor) = 63.8 min.



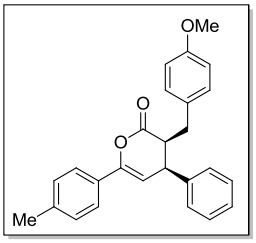
(3*S*,4*S*)-3-(4-Methoxybenzyl)-6-phenyl-4-(o-tolyl)-3,4-dihydro-*2H*-pyran-2-one(3m):White solid, 47 mg; $[\alpha]_D^{23}$ (*c* 1.22, CH_2Cl_2) = +223.0; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.05 (s, 3H), 2.53 (dd, *J* = 13.2, 8.0 Hz, 1H), 3.26–3.36 (m, 2H), 3.78 (s, 3H), 3.93 (t, *J* = 6.8 Hz, 1H), 5.92 (d, *J* = 6.8 Hz, 1H), 6.77–6.80 (m, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.11–7.20 (m, 4H), 7.32–7.38 (m, 3H), 7.60–7.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.9, 158.3, 149.4, 137.0, 135.9, 132.4, 130.8, 130.4, 129.8, 129.0, 128.5, 127.3, 127.1, 124.6, 114.0, 104.3, 55.3, 44.6, 35.7, 31.5, 19.6; HRMS(ESI) calcd for $C_{26}H_{25}O_3(M+H)^+$: 385.1804, Found: 385.1805; >98% ee (*3S*, *4S*)-isomer as determined by HPLC (Chiralcel IA, 98:2 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 53.4 min, t_r (minor) = 35.0 min.



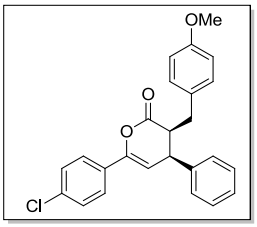
(3*S*,4*S*)-4-(4-Chlorophenyl)-3-(4-methoxybenzyl)-6-phenyl-3,4-dihydro-*2H*-pyran-2-one (3n): White solid, 67 mg; $[\alpha]_D^{23}$ (*c* 1.25, CH_2Cl_2) = +267.2; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.35 (dd, *J* = 14.8, 9.6 Hz, 1H), 3.23 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.34 (ddd, *J* = 9.6, 6.8, 5.2 Hz, 1H), 3.64 (t, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 5.99 (d, *J* = 6.8 Hz, 1H), 6.84–6.87 (m, 2H), 7.00–7.04 (m, 4H), 7.27–7.30 (m, 2H), 7.36–7.40 (m, 3H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 158.3, 150.3, 136.4, 133.7, 132.0, 130.2, 129.9, 129.8, 129.3, 129.1, 128.6, 124.7, 114.0, 104.7, 55.3, 45.5, 40.0, 31.4; HRMS(ESI) calcd for $C_{25}H_{22}O_3Cl(M+H)^+$: 405.1257, Found: 405.1262; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99:1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 59.6 min, t_r (minor) = 81.5 min.



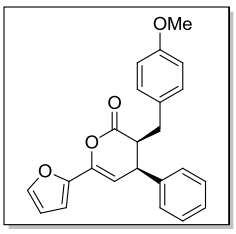
(3*S*,4*S*)-3-(4-Methoxybenzyl)-6-(4-methoxyphenyl)-4-phenyl-3,4-dihydro-*2H*-pyran-2-one (3o): White solid, 70 mg; $[\alpha]_D^{23}$ (c 0.51, CH_2Cl_2) = +203.6; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.37 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.19 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.31 (ddd, *J* = 9.2, 6.8, 5.2 Hz, 1H), 3.63 (t, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 3.82 (s, 3H), 5.88 (d, *J* = 6.8 Hz, 1H), 6.83–6.90 (m, 4H), 7.02–7.10 (m, 4H), 7.25–7.33 (m, 3H), 7.58 (dd, *J* = 6.8, 2.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.5, 160.4, 158.2, 149.8, 138.2, 130.6, 130.0, 129.4, 128.9, 128.5, 127.7, 126.1, 124.8, 114.3, 113.9, 103.4, 55.4, 55.3, 45.9, 40.7, 31.5; HRMS(ESI) calcd for $C_{26}H_{25}O_4(M+H)^+$: 401.1753, Found: 401.1758; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.5:0.5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 117.1 min, t_r (minor) = 188.5 min.



(3*S*,4*S*)-3-(4-Methoxybenzyl)-4-phenyl-6-(p-tolyl)-3,4-dihydro-*2H*-pyran-2-one (3p): White solid, 70 mg; $[\alpha]_D^{23}$ (*c* 1.14, CH_2Cl_2) = +211.2; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.34–2.40 (m, 4H), 3.20 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.32 (ddd, *J* = 9.2, 6.8, 5.2 Hz, 1H), 3.64 (t, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 5.97 (d, *J* = 6.8 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.28–7.34 (m, 3H), 7.54 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.4, 158.3, 150.1, 139.2, 138.1, 130.6, 130.0, 129.4, 129.2, 128.9, 128.5, 127.8, 124.6, 113.9, 104.3, 55.3, 45.9, 40.7, 31.5, 21.3; HRMS(ESI) calcd for $C_{26}H_{25}O_3(M+H)^+$: 385.1804, Found: 385.1805; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel IA, 98:2 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 114.2 min, t_r (minor) = 68.5 min.

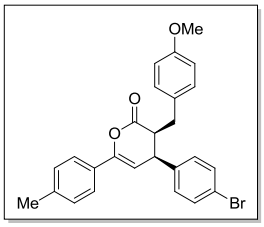


(3*S*,4*S*)-6-(4-Chlorophenyl)-3-(4-methoxybenzyl)-4-phenyl-3,4-dihydro-*2H*-pyran-2-one (3q): White solid, 76 mg (75% yield); $[\alpha]_D^{23}$ (*c* 1.45, CH_2Cl_2) = +212.0; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.38 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.20 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.32 (ddd, *J* = 9.6, 7.2, 5.2 Hz, 1H), 3.66 (t, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 6.01 (d, *J* = 6.8 Hz, 1H), 6.85 (dd, *J* = 11.2, 2.8 Hz, 2H), 7.02–7.09 (m, 4H), 7.27–7.36 (m, 5H), 7.56–7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 158.3, 149.1, 137.7, 135.1, 130.7, 130.4, 130.0, 129.0, 128.8, 128.4, 127.9, 126.0, 114.0, 105.7, 55.3, 45.8, 40.8, 31.4; HRMS(ESI) calcd for $C_{25}H_{22}O_3Cl(M+H)^+$: 405.1257, Found: 405.1253; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel IA, 99:1 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 168.6 min, t_r (minor) = 76.2 min.



(3*S*,4*S*)-6-(Furan-2-yl)-3-(4-methoxybenzyl)-4-phenyl-3,4-dihydro-*2H*-pyran-2-one (3r): White solid, 53 mg; $[\alpha]_D^{23}$ (c 1.1, CH_2Cl_2) = +178.8; ¹H NMR (400 MHz, $CDCl_3$) δ = 2.37 (dd, *J* = 14.8, 9.2 Hz, 1H), 3.19 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.33 (ddd, *J* = 9.2, 6.8, 5.2 Hz, 1H), 3.63 (t, *J* = 6.8 Hz, 1H), 3.81 (s,

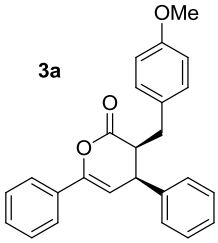
3H), 5.88 (d, *J* = 6.8 Hz, 1H), 6.83–6.85 (m, 2H), 7.01–7.04 (m, 3H), 7.09 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.27–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.8, 158.3, 145.9, 137.8, 135.8, 130.4, 130.0, 129.0, 128.4, 127.9, 127.6, 125.8, 124.8, 114.0, 104.3, 55.3, 45.9, 40.8, 31.5; HRMS(ESI) calcd for $C_{23}H_{21}O_4(M+H)^+$: 361.1440, Found: 361.1429; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel OD, 99.5:0.5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 82.1 min, t_r (minor) = 98.5 min.

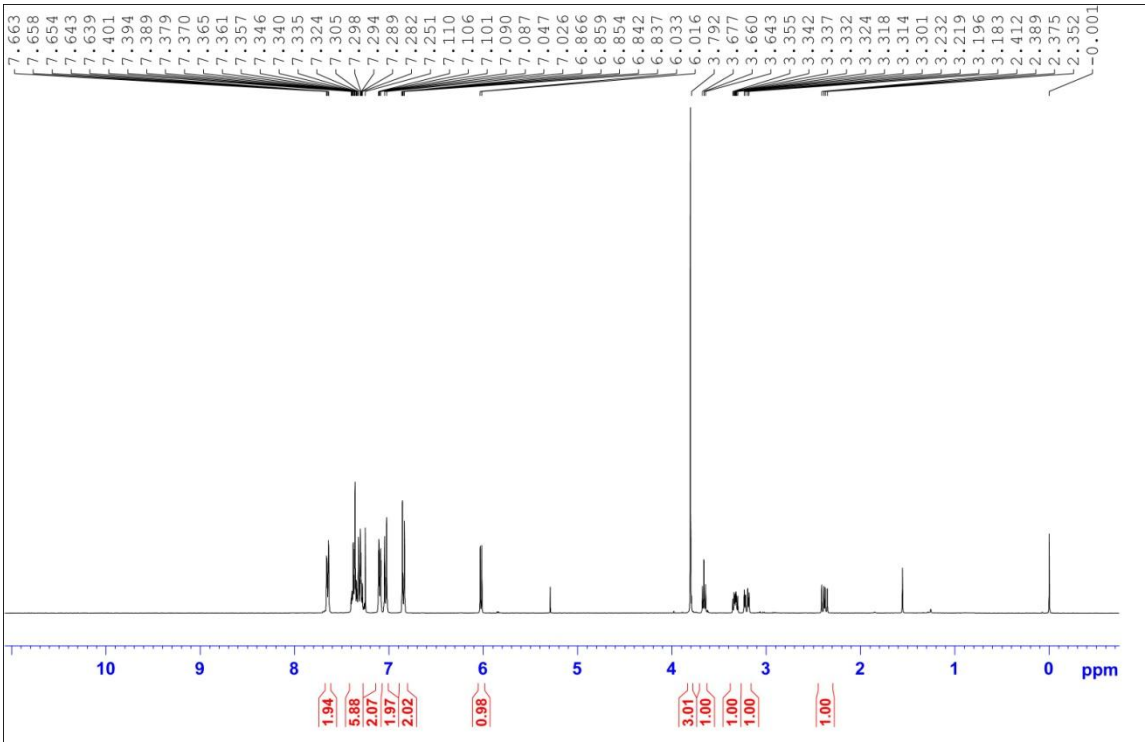


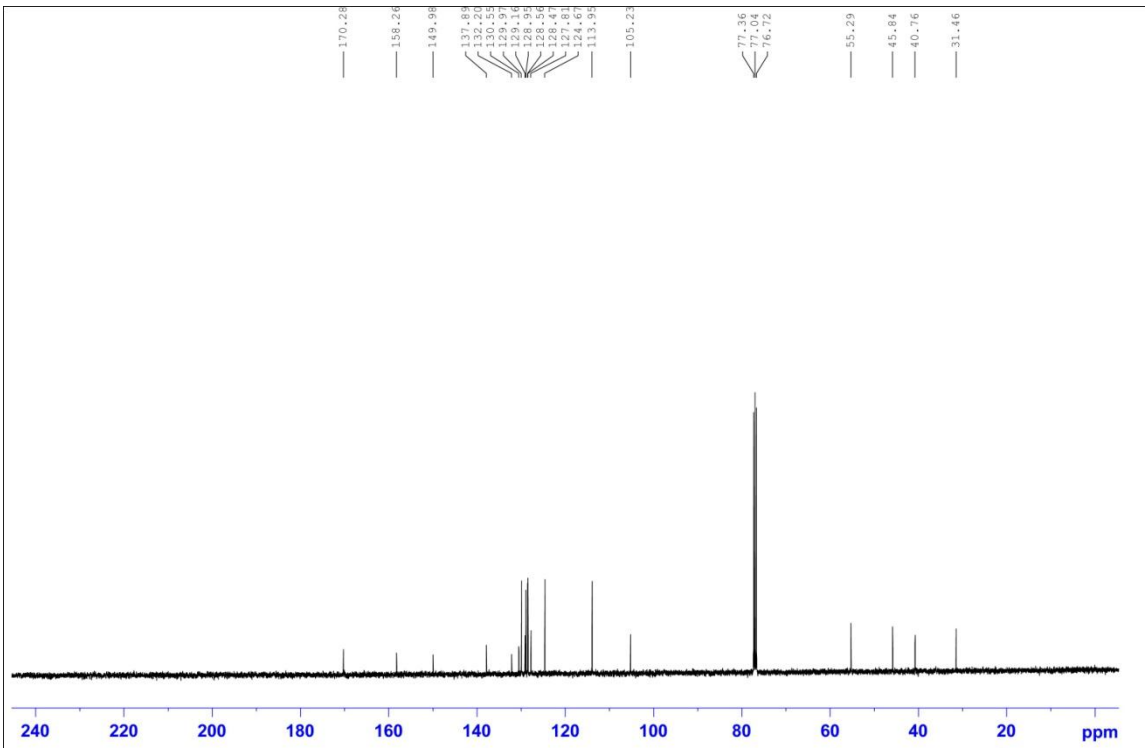
(3*S*,4*S*)-4-(4-Bromophenyl)-3-(4-methoxybenzyl)-6-(p-tolyl)-3,4-dihydro-*2H*-pyran-2-one (3s): White solid, 81 mg; $[\alpha]_D^{23}$ (*c* 1.85, CH_2Cl_2) = +218.9; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.31–2.39 (m, 4H), 3.22 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.33 (ddd, *J* = 9.2, 6.8, 5.2 Hz, 1H), 3.61 (t, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 5.93 (d, *J* = 6.8 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.95 (dd, *J* = 6.8, 1.6 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.44 (dd, *J* = 6.8, 1.6 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 158.4, 150.4, 139.4, 137.1, 132.0, 130.2, 130.1, 129.9, 129.3, 129.2, 124.6, 121.7, 114.0, 103.7, 55.3, 45.5, 40.1, 31.4, 21.3; HRMS(ESI) calcd for $C_{26}H_{24}O_3Br(M+H)^+$: 463.0909, Found: 463.0910; >98% ee (*3S*, *4S*)- isomer as determined by HPLC (Chiralcel IA, 95:5 hexanes/i-PrOH, 0.7 mL/min), t_r (major) = 67.7 min, t_r (minor) = 37.2 min.

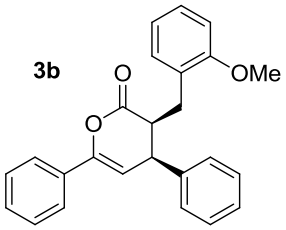
IV. ^{1}H and ^{13}C NMR spectra of the products:

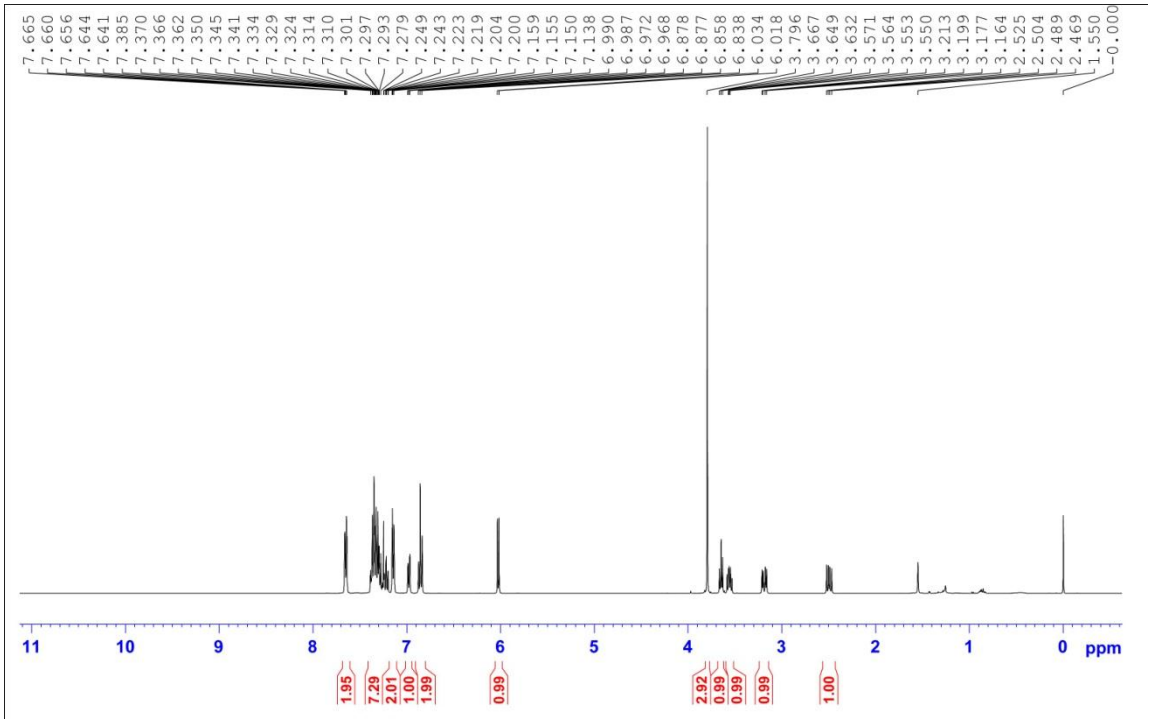
3a

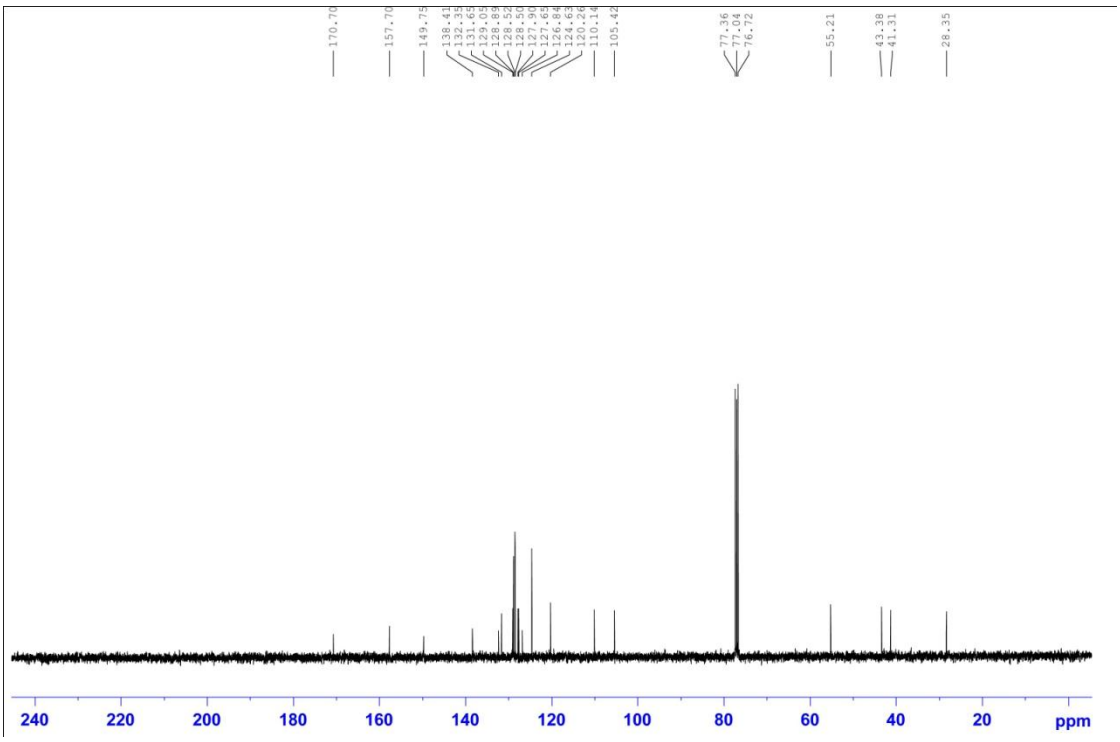




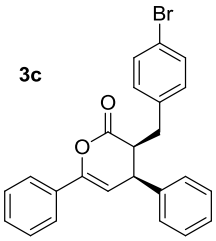


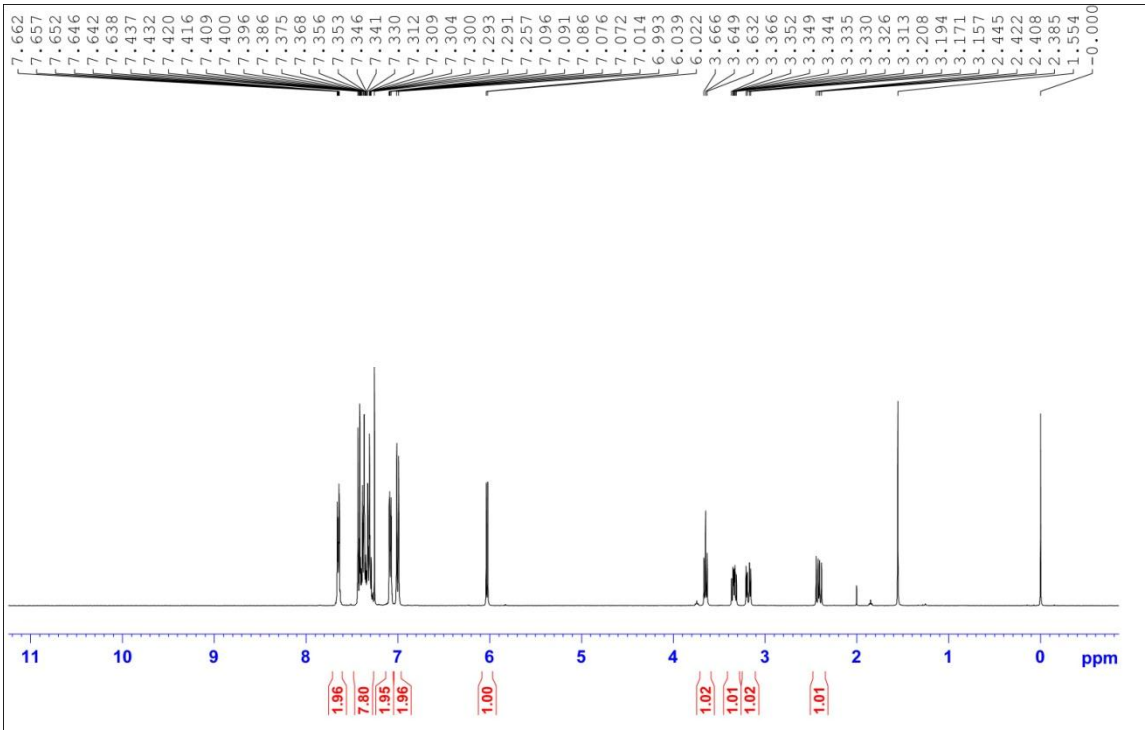

3b
O
OMe
O

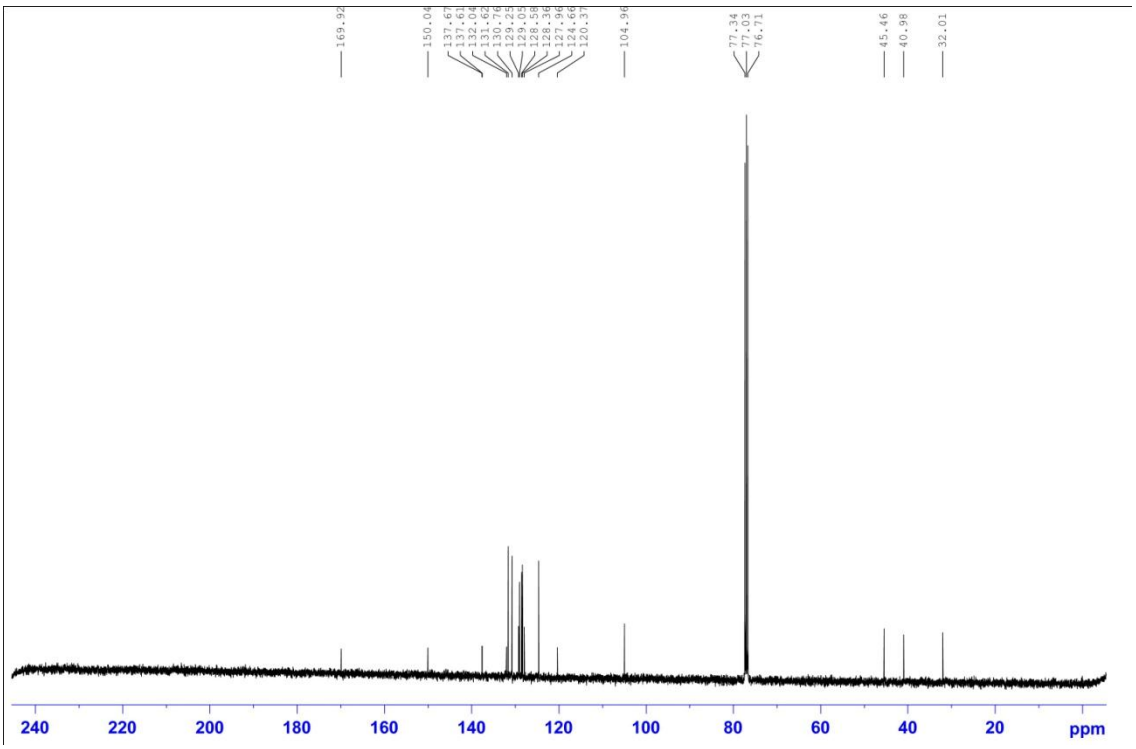

7.665 7.660 7.656 7.644 7.641 7.385 7.370 7.366 7.362 7.350 7.345 7.341 7.334 7.329 7.324 7.314 7.310 7.301 7.297 7.293 7.279 7.249 7.243 7.223 7.219 7.204 7.200 7.159 7.155 7.150 7.138 6.990 6.987 6.972 6.968 6.878 6.877 6.858 6.838 6.034 6.018 3.796 3.667 3.649 3.632 3.571 3.564 3.553 3.550 3.213 3.199 3.177 3.164 2.525 2.504 2.489 2.469 1.550 -0.000
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.95 7.29 2.01 1.00 1.99 0.99 2.92 0.99 0.99 0.99 1.00


170.70 157.70 149.75 138.41 132.35 131.65 129.05 128.89 128.52 128.50 127.90 127.69 126.84 124.63 120.26 110.14 105.42 77.36 77.04 76.72 55.21 43.38 41.31 28.35
240 220 200 180 160 140 120 100 80 60 40 20 ppm

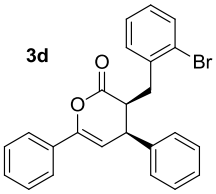
3c

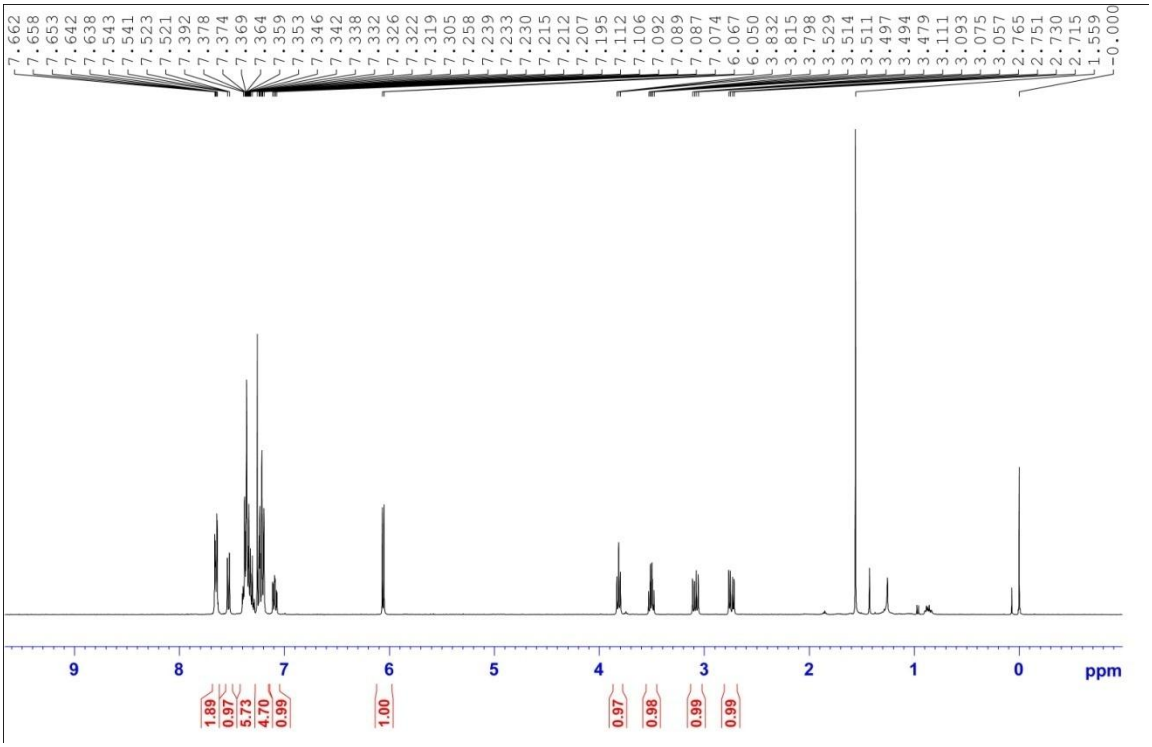

Br
O
O

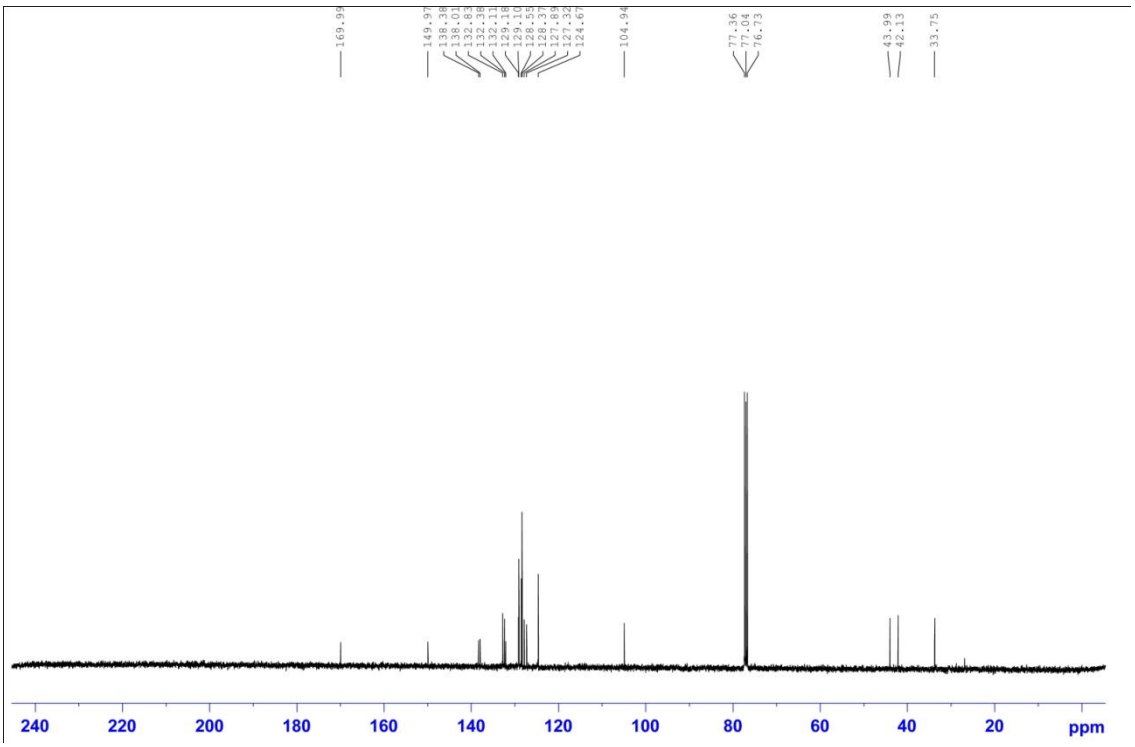

7.662
7.657
7.652
7.646
7.642
7.638
7.437
7.432
7.420
7.416
7.409
7.400
7.396
7.386
7.375
7.368
7.356
7.353
7.346
7.341
7.330
7.312
7.309
7.304
7.300
7.293
7.291
7.257
7.096
7.091
7.086
7.076
7.072
7.014
6.993
6.039
6.022
3.666
3.649
3.632
3.366
3.352
3.349
3.344
3.335
3.330
3.326
3.313
3.208
3.194
3.171
3.157
2.445
2.422
2.408
2.385
1.554
0.000
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.96
7.80
1.95
1.96
1.00
1.02
1.01
1.02
1.01


169.92
150.04
137.67
137.61
132.04
131.64
130.76
129.25
129.05
128.58
128.36
127.96
124.66
120.37
104.96
77.34
77.03
76.71
45.46
40.98
32.01
240
220
200
180
160
140
120
100
80
60
40
20
ppm

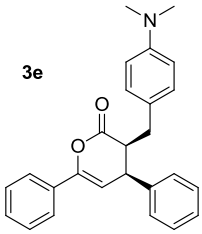
3d

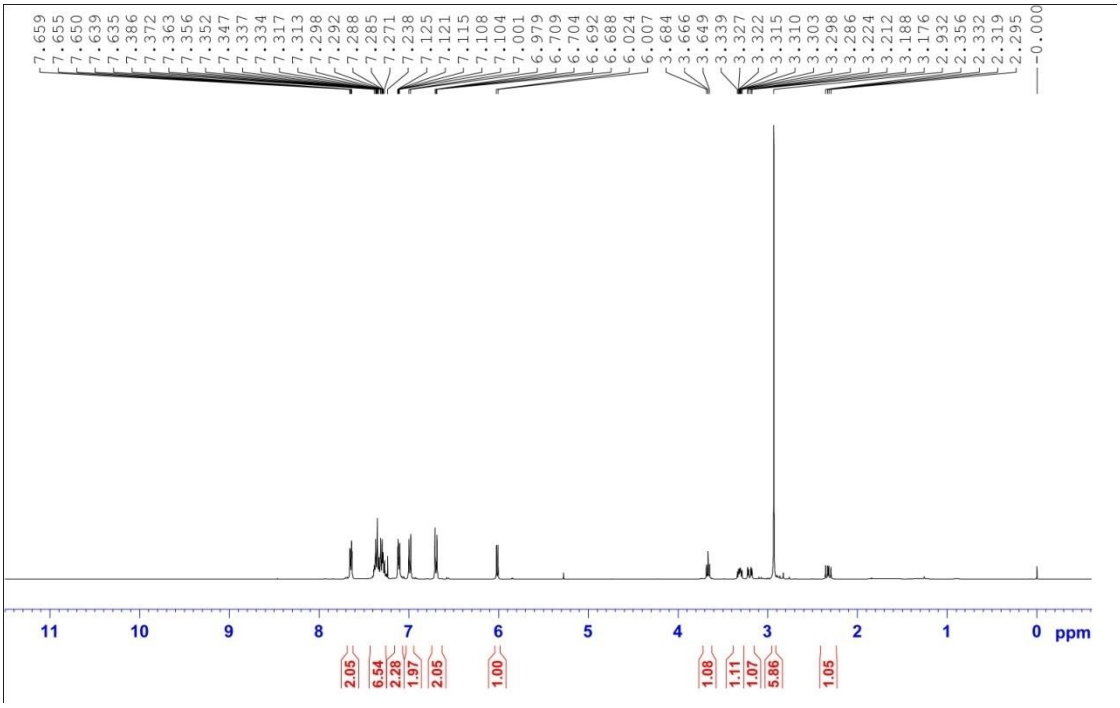

O
O
Br

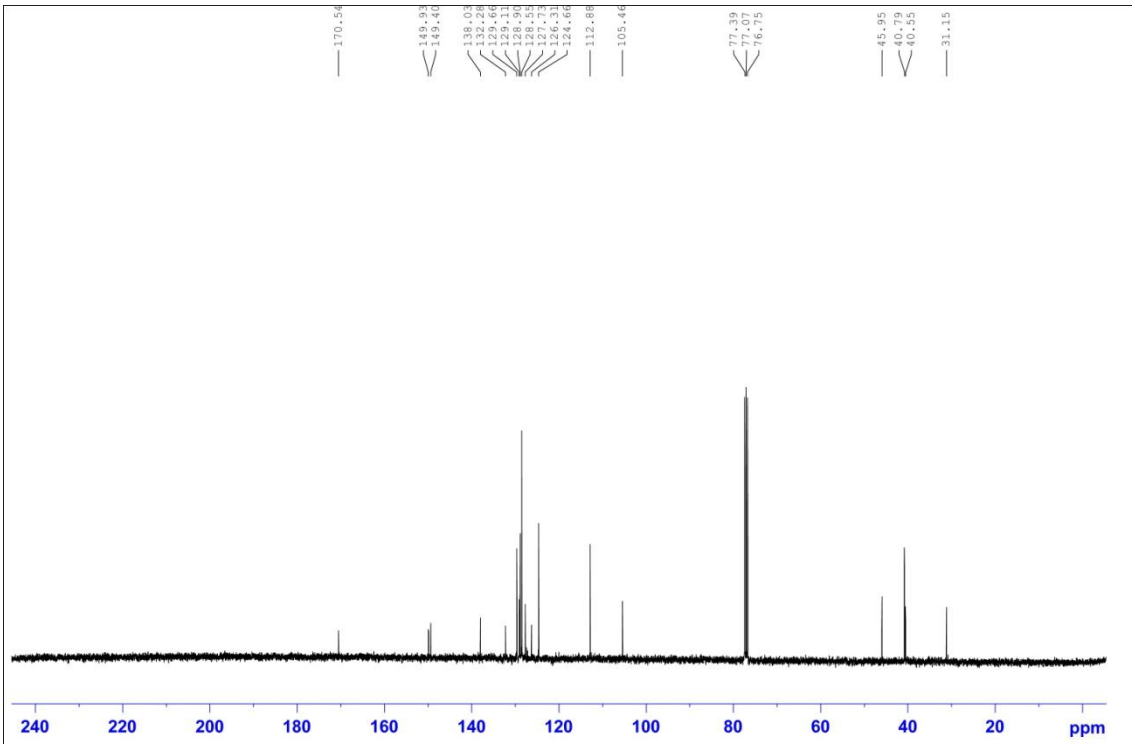

7.662
7.658
7.653
7.642
7.638
7.543
7.541
7.523
7.521
7.392
7.378
7.374
7.369
7.364
7.359
7.353
7.346
7.342
7.338
7.332
7.326
7.322
7.319
7.305
7.258
7.239
7.233
7.230
7.215
7.212
7.207
7.195
7.112
7.106
7.092
7.089
7.087
7.074
6.067
6.050
3.832
3.815
3.798
3.529
3.514
3.511
3.497
3.494
3.479
3.111
3.093
3.075
3.057
2.765
2.751
2.730
2.715
1.559
-0.000
9
8
7
6
5
4
3
2
1
0
ppm
1.89
0.97
5.73
4.70
0.99
1.00
0.97
0.98
0.99
0.99

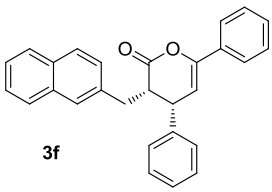

169.99
149.97
138.36
138.01
132.83
132.38
132.11
129.18
129.10
128.55
128.37
128.39
127.32
124.67
104.94
77.36
77.04
76.73
43.99
42.13
33.75
240
220
200
180
160
140
120
100
80
60
40
20
ppm

3e

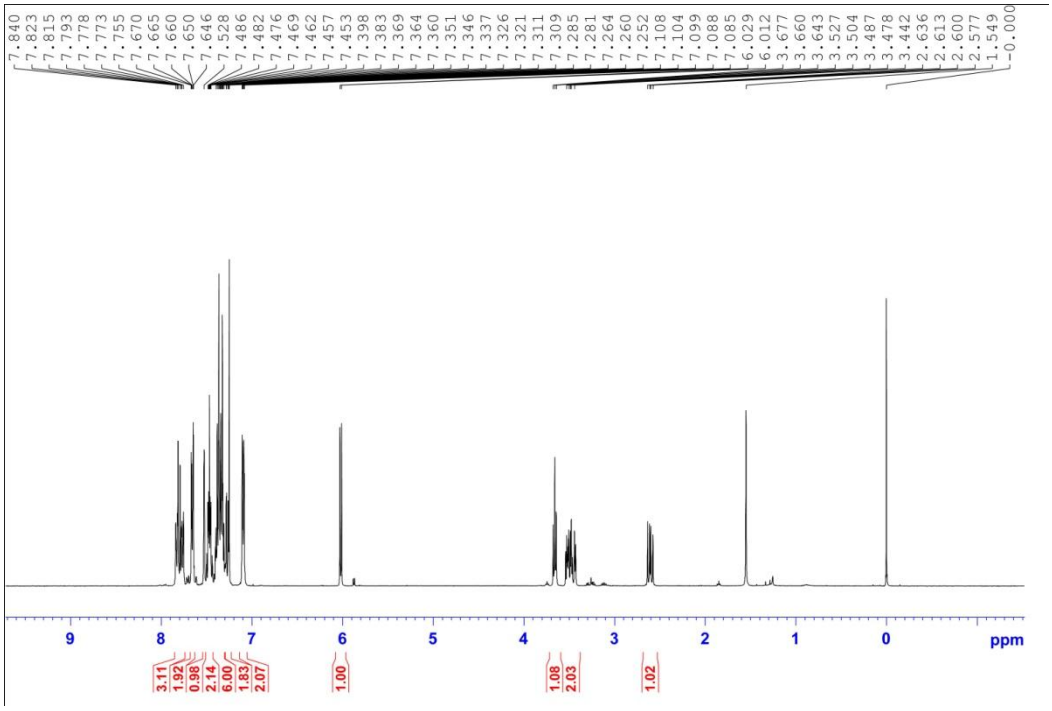


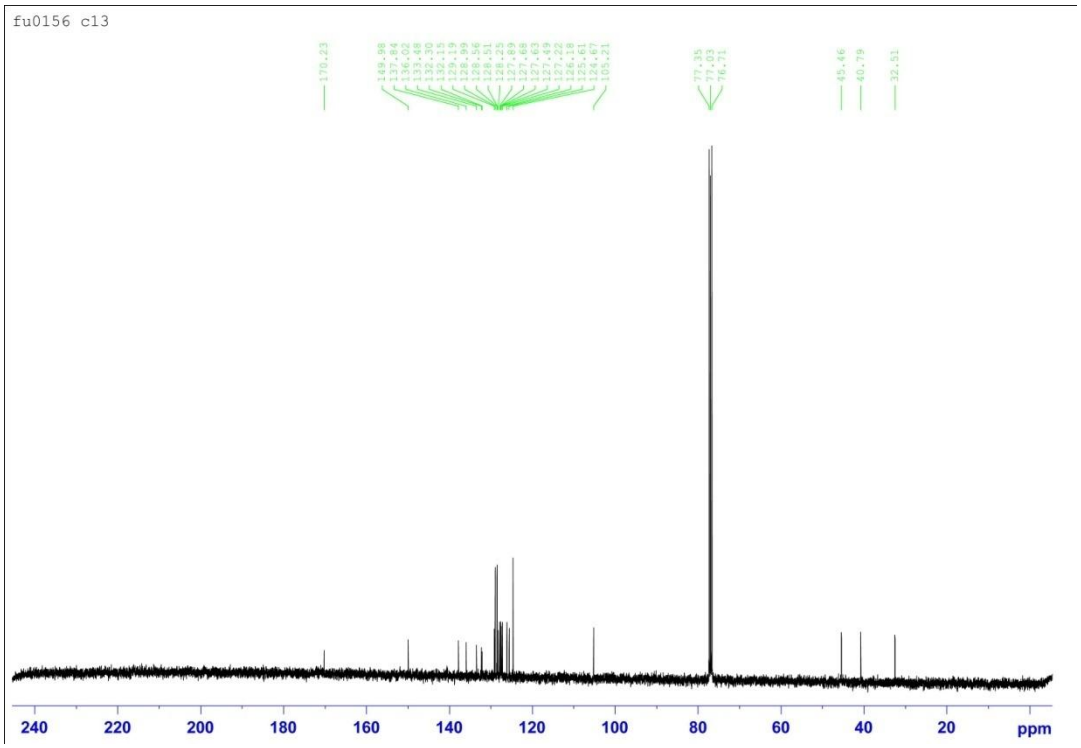

7.659 7.655 7.650 7.639 7.635 7.386 7.372 7.363 7.356 7.352 7.347 7.337 7.334 7.317 7.313 7.298 7.292 7.288 7.285 7.271 7.238 7.125 7.121 7.115 7.108 7.104 7.001 6.979 6.709 6.704 6.692 6.688 6.024 6.007 3.684 3.666 3.649 3.339 3.327 3.322 3.315 3.310 3.303 3.298 3.286 3.224 3.212 3.188 3.176 2.932 2.356 2.332 2.319 2.295 -0.000
11 10 9 8 7 6 5 4 3 2 1 0 ppm
2.05 6.54 2.28 1.97 2.05 1.00 1.08 1.11 1.07 5.86 1.05

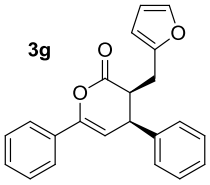

170.54
149.93 149.40
138.03 132.28 129.66 129.11 128.90 128.55 127.73 126.31 124.66
112.88
105.46
77.39 77.07 76.75
45.95 40.79 40.55
31.15
240 220 200 180 160 140 120 100 80 60 40 20 ppm

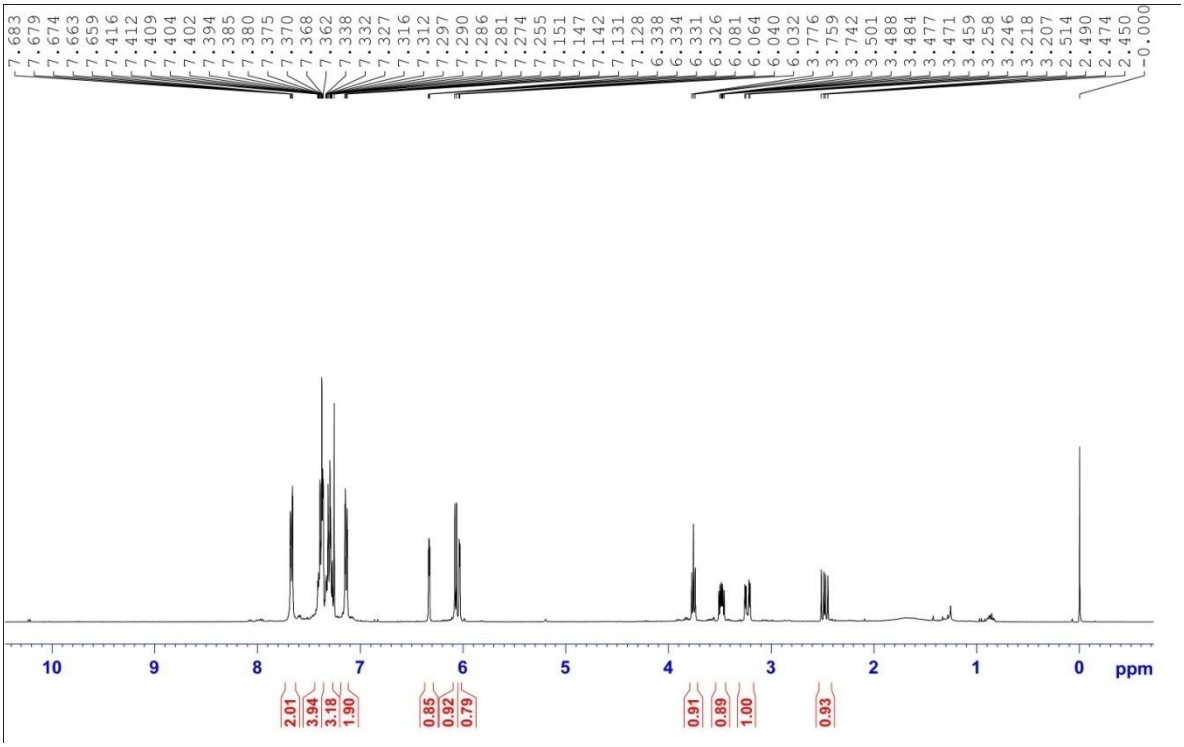


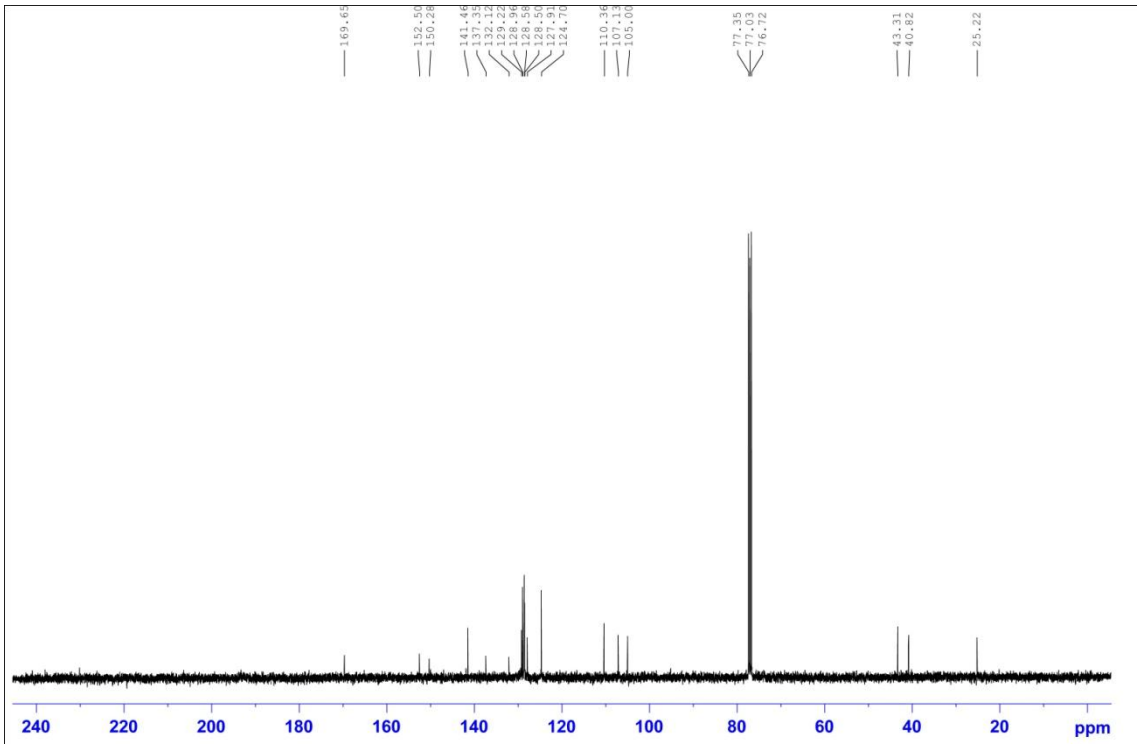
3f


7.840 7.823 7.815 7.793 7.778 7.773 7.755 7.670 7.665 7.660 7.650 7.646 7.528 7.486 7.482 7.476 7.469 7.462 7.457 7.453 7.398 7.383 7.369 7.364 7.360 7.351 7.346 7.337 7.326 7.321 7.311 7.309 7.285 7.281 7.264 7.260 7.252 7.108 7.104 7.099 7.088 7.085 6.029 6.012 3.677 3.660 3.643 3.527 3.504 3.487 3.478 3.442 2.636 2.613 2.600 2.577 1.549 -0.000
9 8 7 6 5 4 3 2 1 0 ppm
3.11 1.92 0.98 2.14 6.00 1.83 2.07 1.00 1.08 2.03 1.02

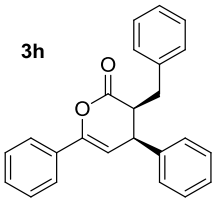

fu0156 c13
170.23
149.98 137.84 136.02 133.48 132.30 132.15 129.19 128.99 128.56 128.51 128.21 127.89 127.68 127.63 127.49 127.22 126.18 125.61 124.67 105.21
77.35 77.03 76.71
45.46 40.79 32.51
240 220 200 180 160 140 120 100 80 60 40 20 ppm

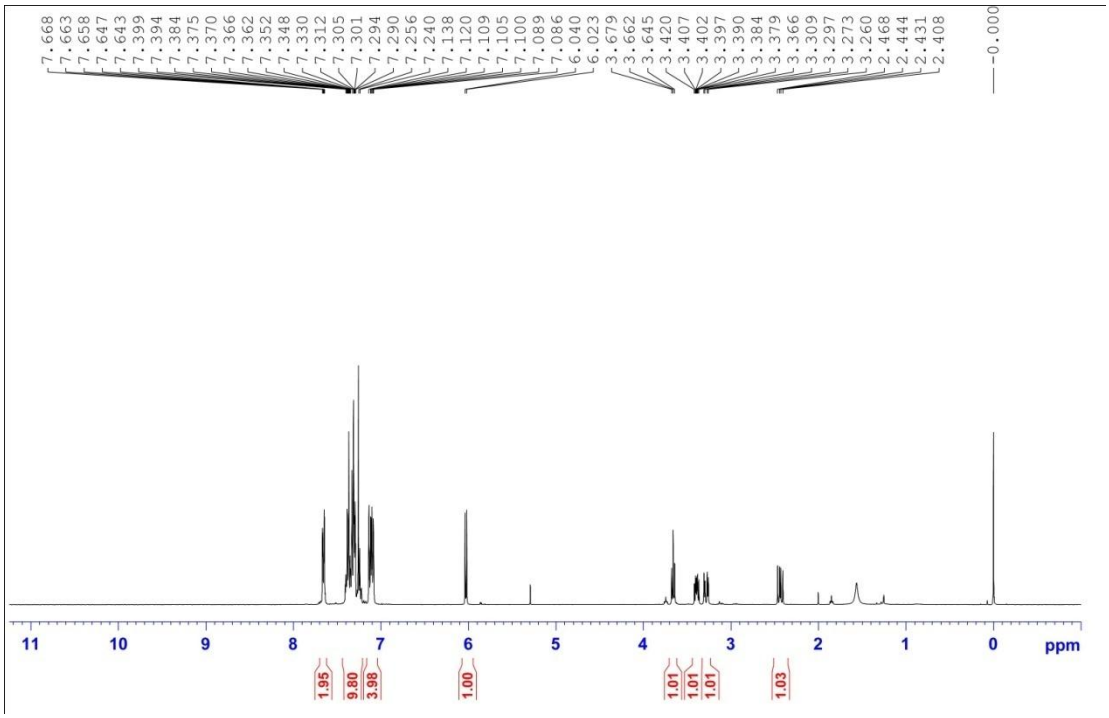

3g
O
O
O

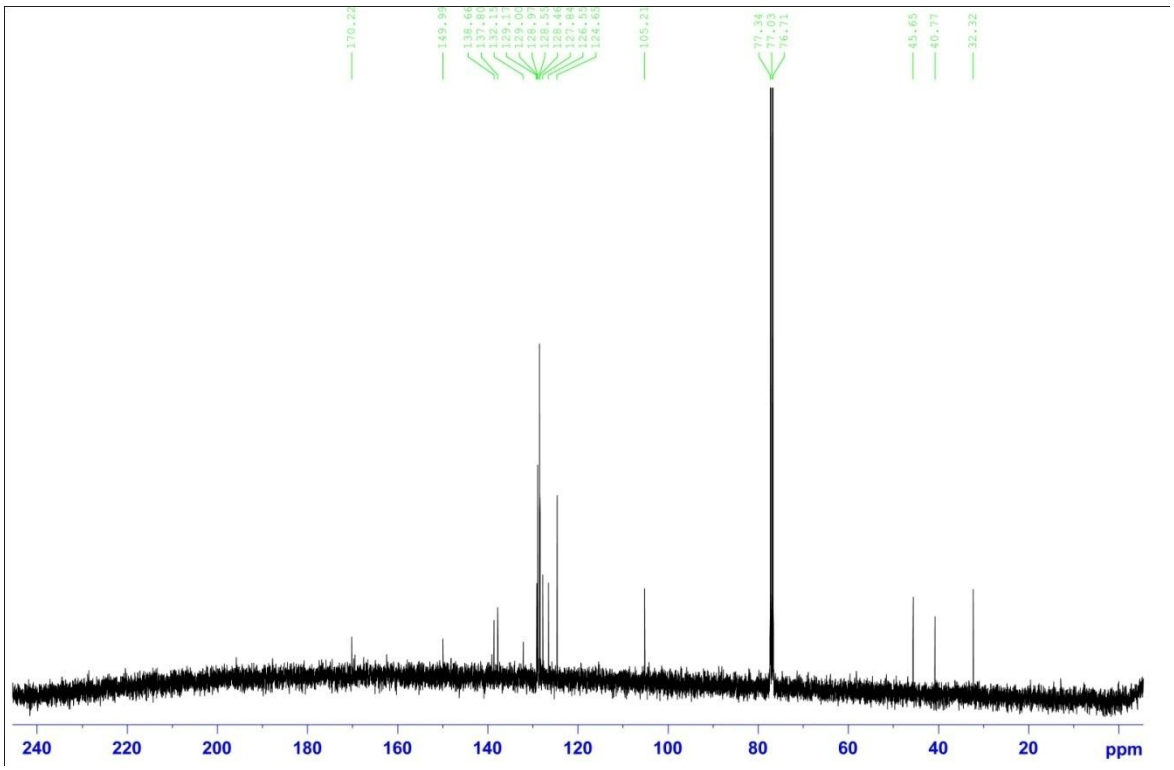

7.683
7.679
7.674
7.663
7.659
7.416
7.412
7.409
7.404
7.402
7.394
7.385
7.380
7.375
7.370
7.368
7.362
7.338
7.332
7.327
7.316
7.312
7.297
7.290
7.286
7.281
7.274
7.255
7.151
7.147
7.142
7.131
7.128
6.338
6.334
6.331
6.326
6.081
6.064
6.040
6.032
3.776
3.759
3.742
3.501
3.488
3.484
3.477
3.471
3.459
3.258
3.246
3.218
3.207
2.514
2.490
2.474
2.450
0.000
10
9
8
7
6
5
4
3
2
1
0
ppm
2.01
3.94
3.18
1.90
0.85
0.92
0.79
0.91
0.89
1.00
0.93


169.65
152.50
150.28
141.46
137.35
132.22
129.22
128.96
128.58
128.50
127.91
124.70
110.36
107.13
105.00
77.35
77.03
76.72
43.31
40.82
25.22
240
220
200
180
160
140
120
100
80
60
40
20
ppm

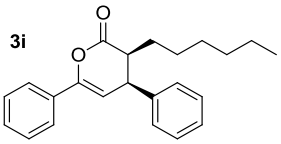
3h

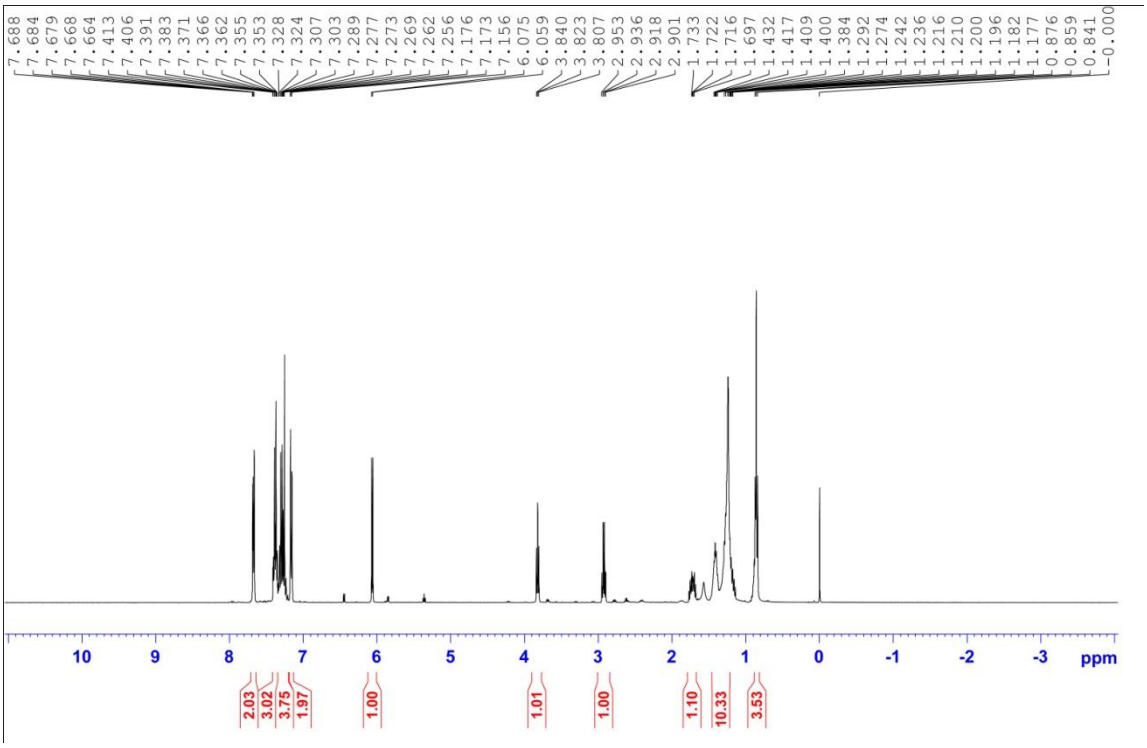


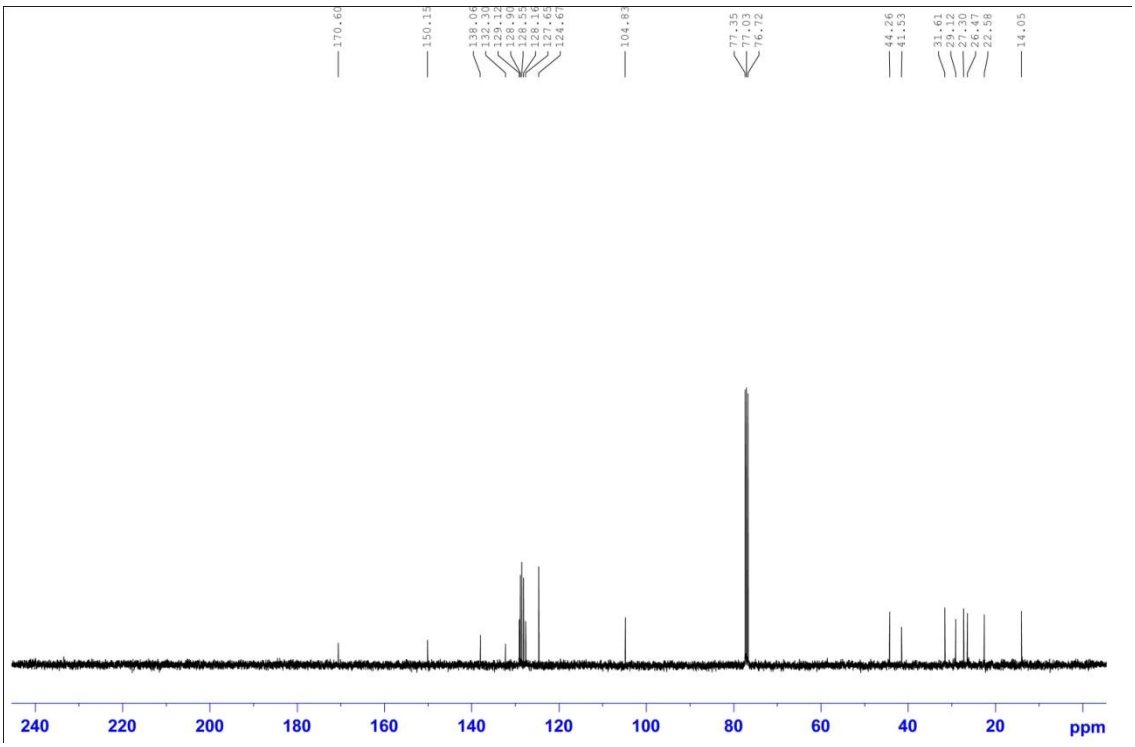

7.668
7.663
7.658
7.647
7.643
7.399
7.394
7.384
7.375
7.370
7.366
7.362
7.352
7.348
7.330
7.312
7.305
7.301
7.294
7.290
7.256
7.240
7.138
7.120
7.109
7.105
7.100
7.089
7.086
6.040
6.023
3.679
3.662
3.645
3.420
3.407
3.402
3.397
3.390
3.384
3.379
3.366
3.309
3.297
3.273
3.260
2.468
2.444
2.431
2.408
-0.000
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.95
9.80
3.98
1.00
1.01
1.01
1.01
1.03


170.22
149.99
138.66
137.80
132.15
129.17
129.00
128.97
128.55
128.46
127.84
126.52
124.63
105.21
77.34
77.03
76.71
45.65
40.77
32.32
240
220
200
180
160
140
120
100
80
60
40
20
ppm

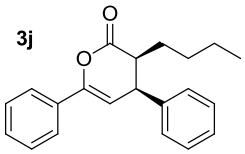
3i

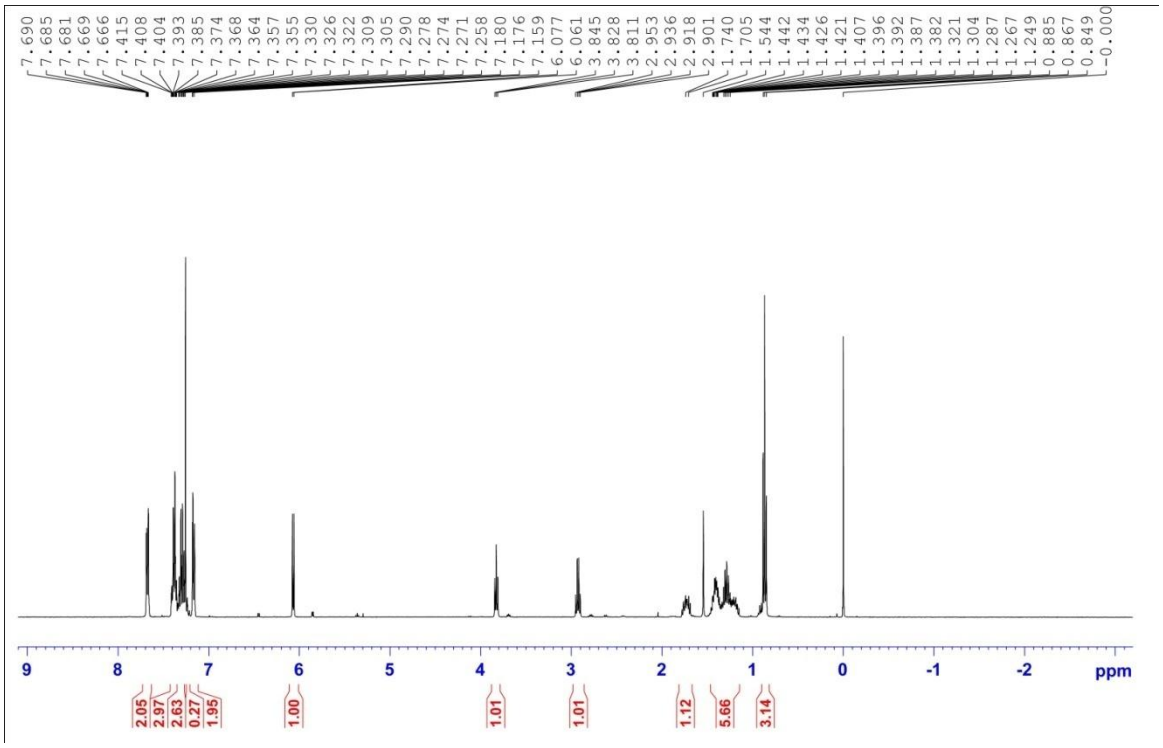


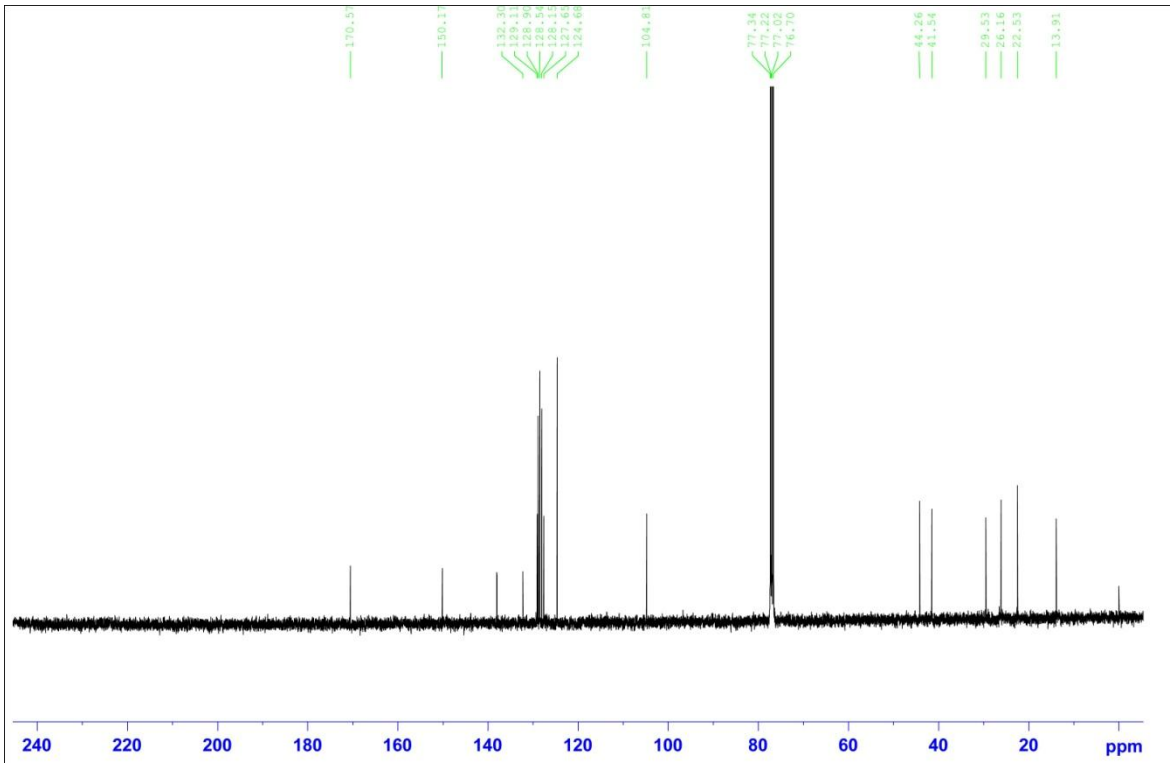

7.688 7.684 7.679 7.668 7.664 7.413 7.406 7.391 7.383 7.371 7.366 7.362 7.355 7.353 7.328 7.324 7.307 7.303 7.289 7.277 7.273 7.269 7.262 7.256 7.176 7.173 7.156 6.075 6.059 3.840 3.823 3.807 2.953 2.936 2.918 2.901 1.733 1.722 1.716 1.697 1.432 1.417 1.409 1.400 1.384 1.292 1.274 1.242 1.236 1.216 1.210 1.200 1.196 1.182 1.177 0.876 0.859 0.841 0.000
10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 ppm
2.03 3.02 3.75 1.97 1.00 1.01 1.00 1.10 10.33 3.53


170.60
150.15
138.06
132.00
129.32
128.90
128.55
128.16
127.65
124.67
104.83
77.35
77.03
76.72
44.26
41.53
31.61
29.12
27.30
26.47
22.58
14.05
240 220 200 180 160 140 120 100 80 60 40 20 ppm

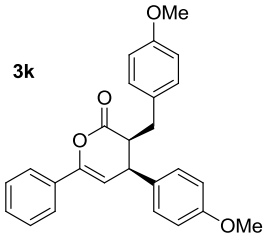
3j

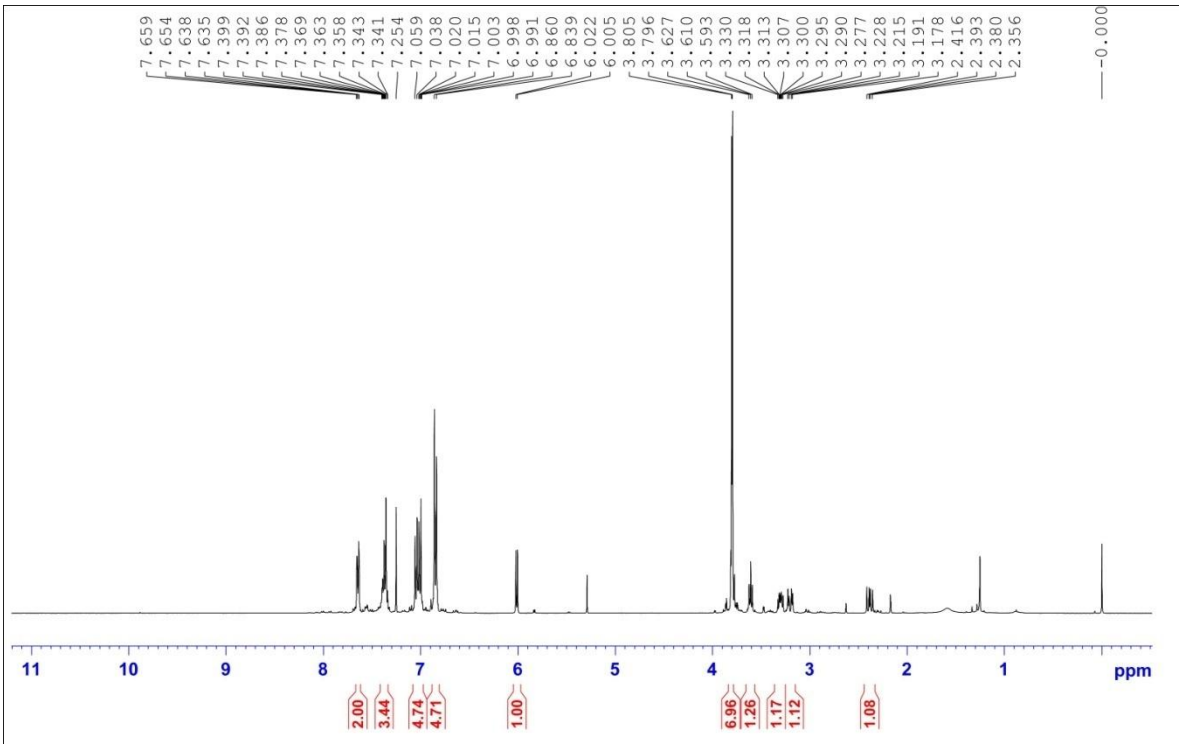


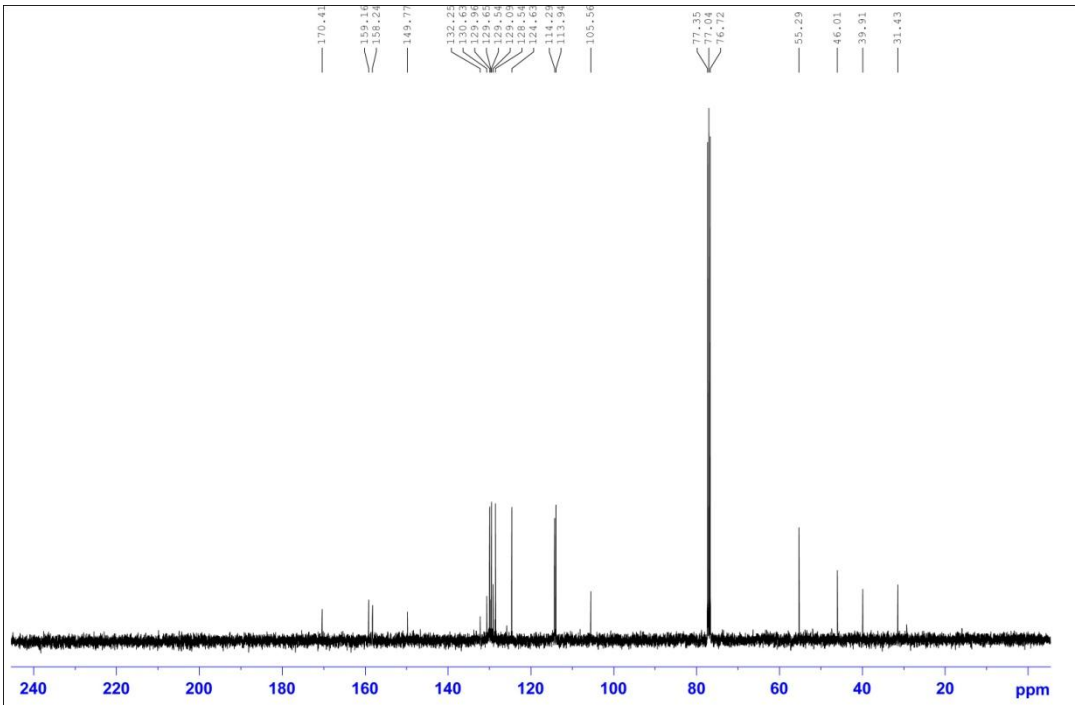

7.690 7.685 7.681 7.669 7.666 7.415 7.408 7.404 7.393 7.385 7.374 7.368 7.364 7.357 7.355 7.330 7.326 7.322 7.309 7.305 7.290 7.278 7.274 7.271 7.258 7.180 7.176 7.159 6.077 6.061 3.845 3.828 3.811 2.953 2.936 2.918 2.901 1.740 1.705 1.544 1.442 1.434 1.426 1.421 1.407 1.396 1.392 1.387 1.382 1.321 1.304 1.287 1.267 1.249 0.885 0.867 0.849 0.000
9 8 7 6 5 4 3 2 1 0 -1 -2 ppm
2.05 2.97 2.63 0.27 1.95 1.00 1.01 1.01 1.12 5.66 3.14


170.57
150.17
132.38 129.11 128.96 128.54 128.15 127.63 124.68
104.83
77.34 77.22 77.02 76.70
44.26 41.54
29.53 26.16 22.53
13.91
240 220 200 180 160 140 120 100 80 60 40 20 ppm

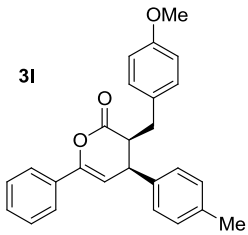
3k

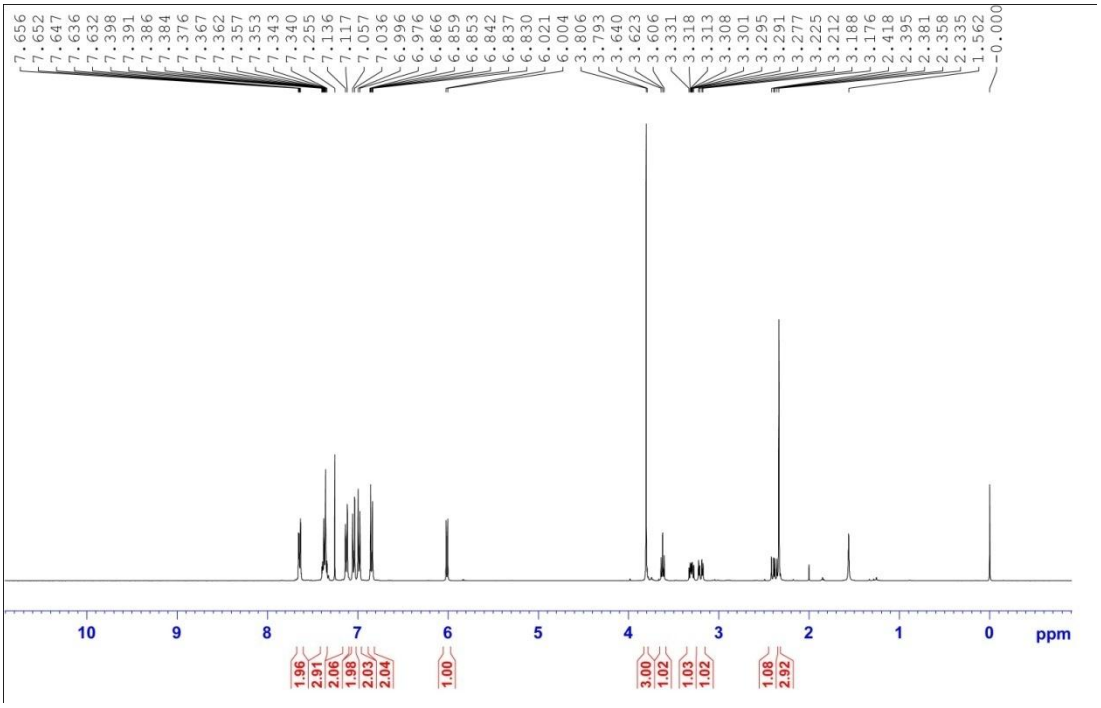

OMe
O
O
OMe

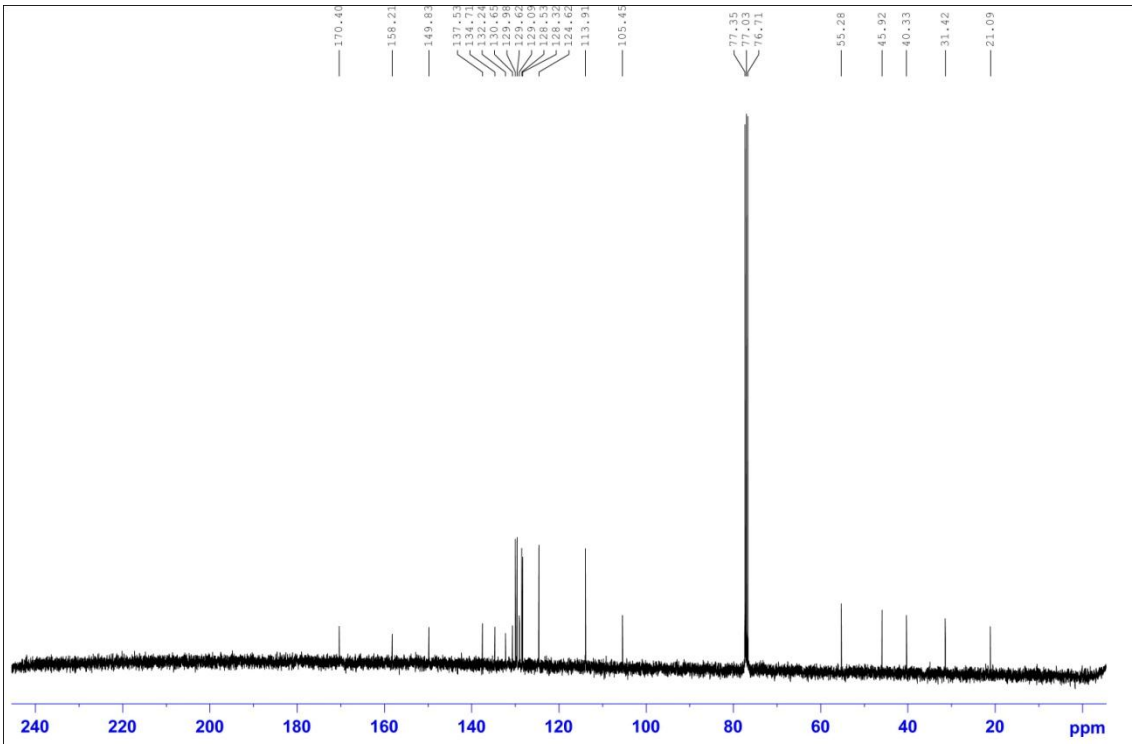

7.659
7.654
7.638
7.635
7.399
7.392
7.386
7.378
7.369
7.363
7.358
7.343
7.341
7.254
7.059
7.038
7.020
7.015
7.003
6.998
6.991
6.860
6.839
6.022
6.005
3.805
3.796
3.627
3.610
3.593
3.330
3.318
3.313
3.307
3.300
3.295
3.290
3.277
3.228
3.215
3.191
3.178
2.416
2.393
2.380
2.356
-0.000
11
10
9
8
7
6
5
4
3
2
1
ppm
2.00
3.44
4.74
4.71
1.00
6.96
1.26
1.17
1.12
1.08


170.41
159.16
158.24
149.77
132.25
130.63
129.96
129.65
129.54
129.09
128.54
124.63
114.29
113.94
105.56
77.35
77.04
76.72
55.29
46.01
39.91
31.43
240
220
200
180
160
140
120
100
80
60
40
20
ppm

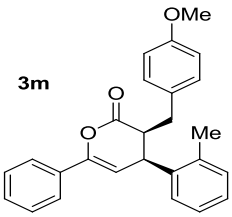
3l

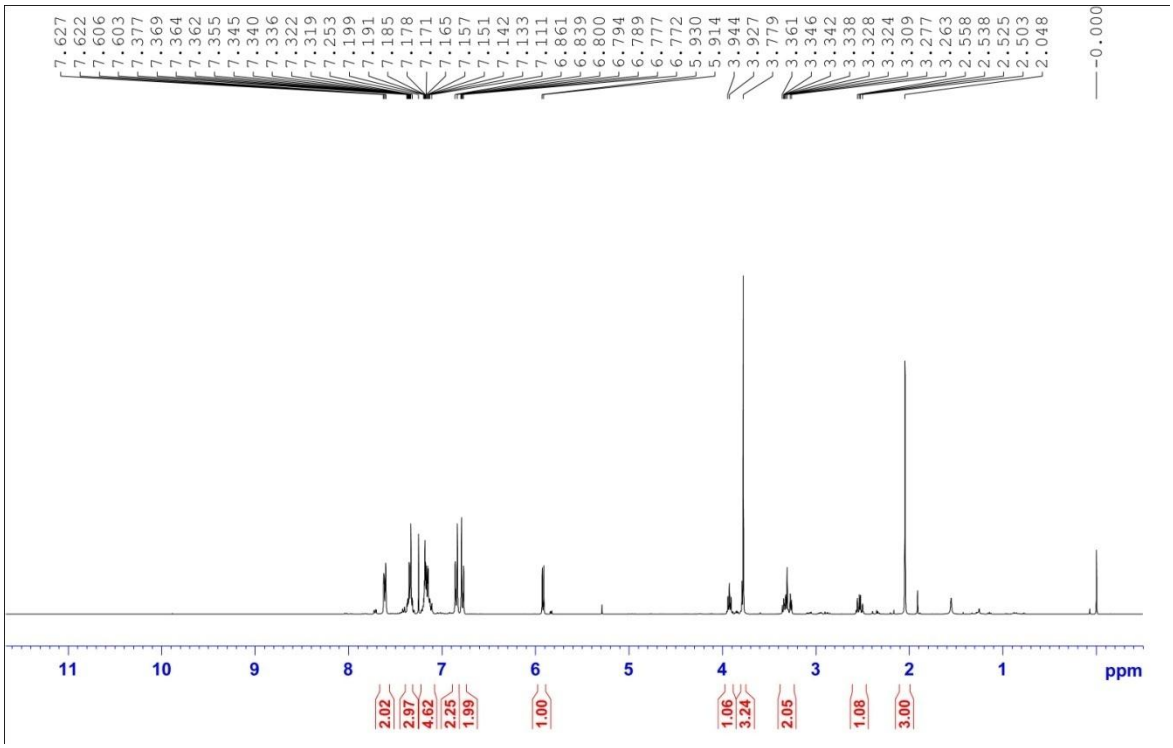

OMe
O
O
Me

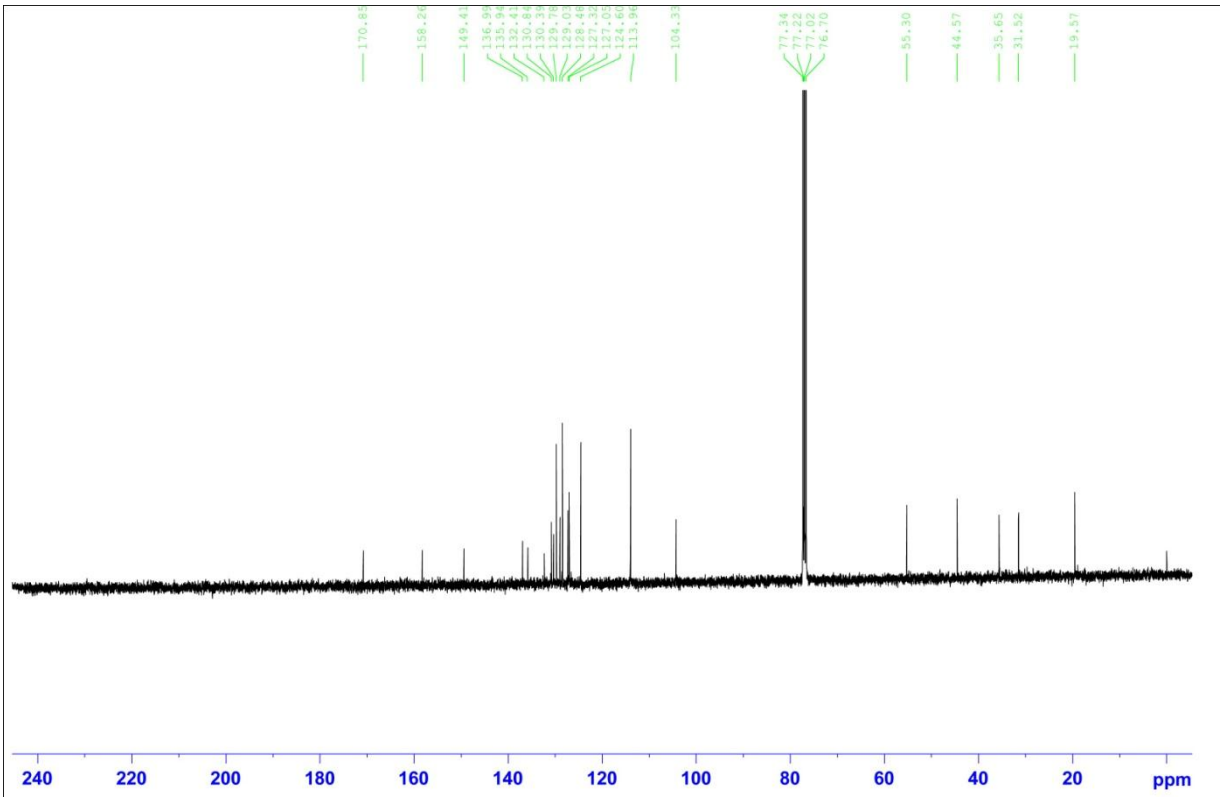

7.656
7.652
7.647
7.636
7.632
7.398
7.391
7.386
7.384
7.376
7.367
7.362
7.357
7.353
7.343
7.340
7.255
7.136
7.117
7.057
7.036
6.996
6.976
6.866
6.859
6.853
6.842
6.837
6.830
6.021
6.004
3.806
3.793
3.640
3.623
3.606
3.331
3.318
3.313
3.308
3.301
3.295
3.291
3.277
3.225
3.212
3.188
3.176
2.418
2.395
2.381
2.358
2.335
1.562
-0.000
10
9
8
7
6
5
4
3
2
1
0
ppm
1.96
2.91
2.06
1.98
2.03
2.04
1.00
3.00
1.02
1.03
1.02
1.08
2.92

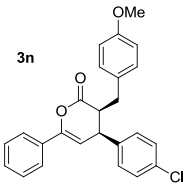

170.40
158.21
149.83
137.53
134.71
132.24
130.65
129.98
129.62
129.09
128.53
128.32
124.62
113.91
105.45
77.35
77.03
76.71
55.28
45.92
40.33
31.42
21.09
240
220
200
180
160
140
120
100
80
60
40
20
ppm

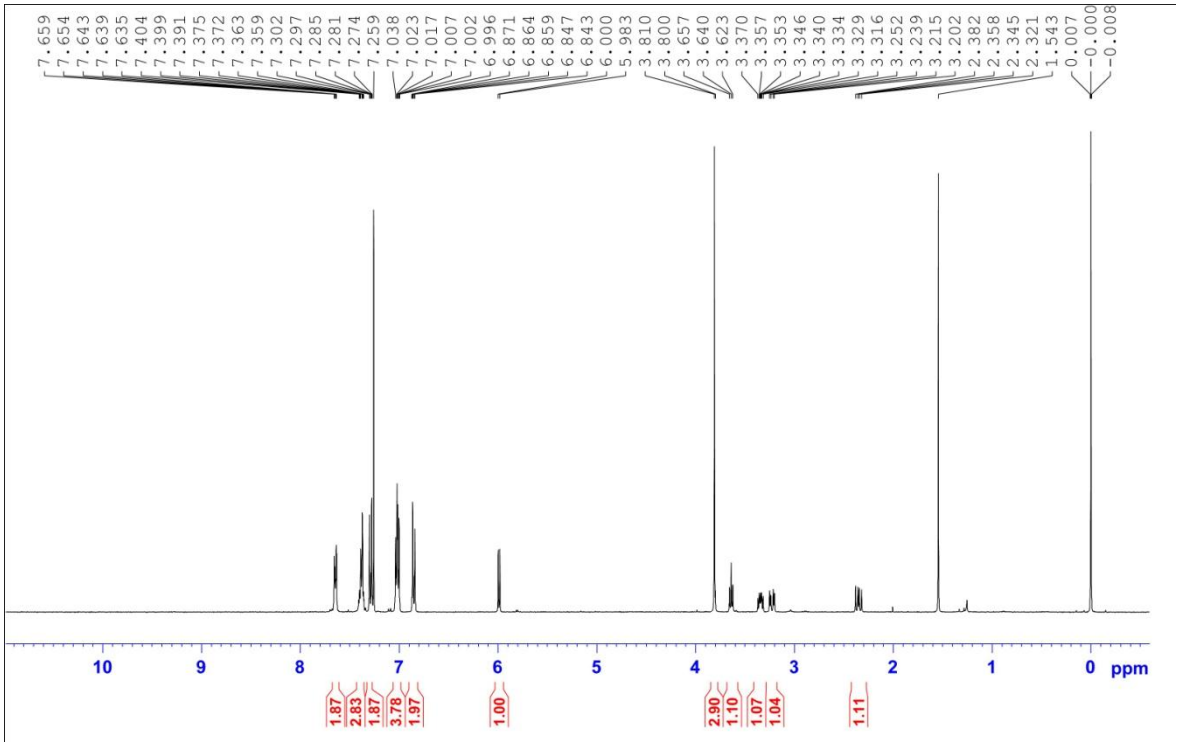
3m

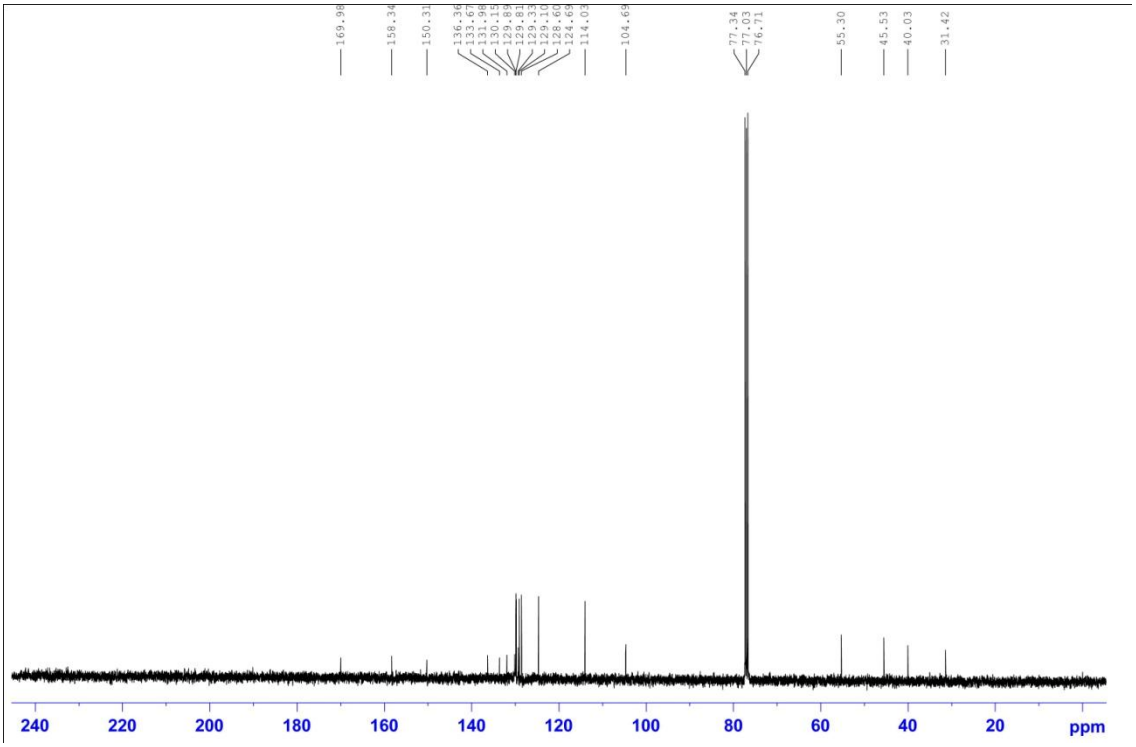

OMe
O
O
Me


7.627
7.622
7.606
7.603
7.377
7.369
7.364
7.362
7.355
7.345
7.340
7.336
7.322
7.319
7.253
7.199
7.191
7.185
7.178
7.171
7.165
7.157
7.151
7.142
7.133
7.111
6.861
6.839
6.800
6.794
6.789
6.777
6.772
5.930
5.914
3.944
3.927
3.779
3.361
3.346
3.342
3.338
3.328
3.324
3.309
3.277
3.263
2.558
2.538
2.525
2.503
2.048
0.000
11
10
9
8
7
6
5
4
3
2
1
ppm
2.02
2.97
4.62
2.25
1.99
1.00
1.06
3.24
2.05
1.08
3.00

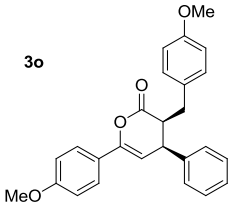

170.85
158.26
149.41
136.98
135.94
132.41
130.84
130.39
129.78
129.03
128.48
127.32
127.05
124.60
113.96
104.33
77.34
77.22
77.02
76.70
55.30
44.57
35.65
31.52
19.57
240
220
200
180
160
140
120
100
80
60
40
20
ppm

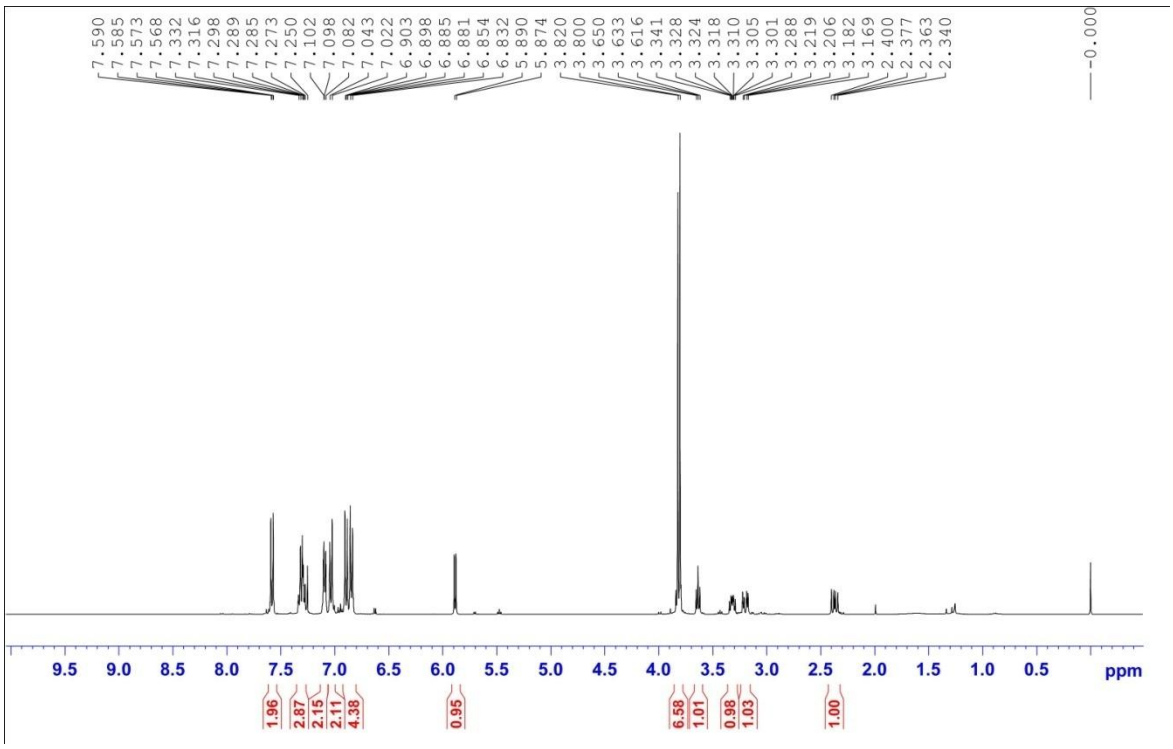

3n
OMe
O
O
Cl

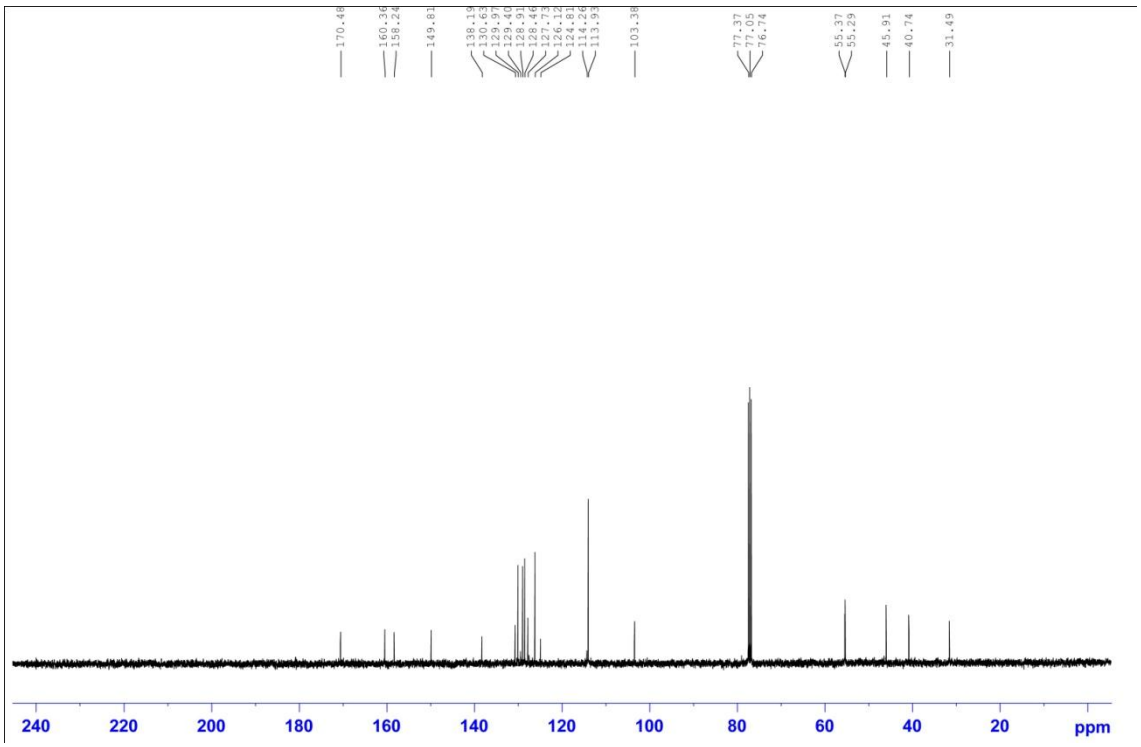

7.659 7.654 7.643 7.639 7.635 7.404 7.399 7.391 7.375 7.372 7.363 7.359 7.302 7.297 7.285 7.281 7.274 7.259 7.038 7.023 7.017 7.007 7.002 6.996 6.871 6.864 6.859 6.847 6.843 6.000 5.983 3.810 3.800 3.657 3.640 3.623 3.370 3.357 3.353 3.346 3.340 3.334 3.329 3.316 3.252 3.239 3.215 3.202 2.382 2.358 2.345 2.321 1.543 0.007 -0.000 -0.008
10 9 8 7 6 5 4 3 2 1 0 ppm
1.87 2.83 1.87 3.78 1.97 1.00 2.90 1.10 1.07 1.04 1.11


169.98 158.34 150.31 136.36 133.67 131.98 130.15 129.89 129.81 129.33 129.10 128.60 124.69 114.03 104.68 77.34 77.03 76.71 55.30 45.53 40.03 31.42
240 220 200 180 160 140 120 100 80 60 40 20 ppm

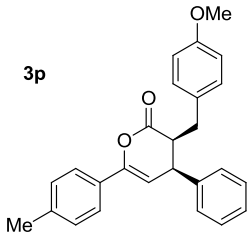
3o

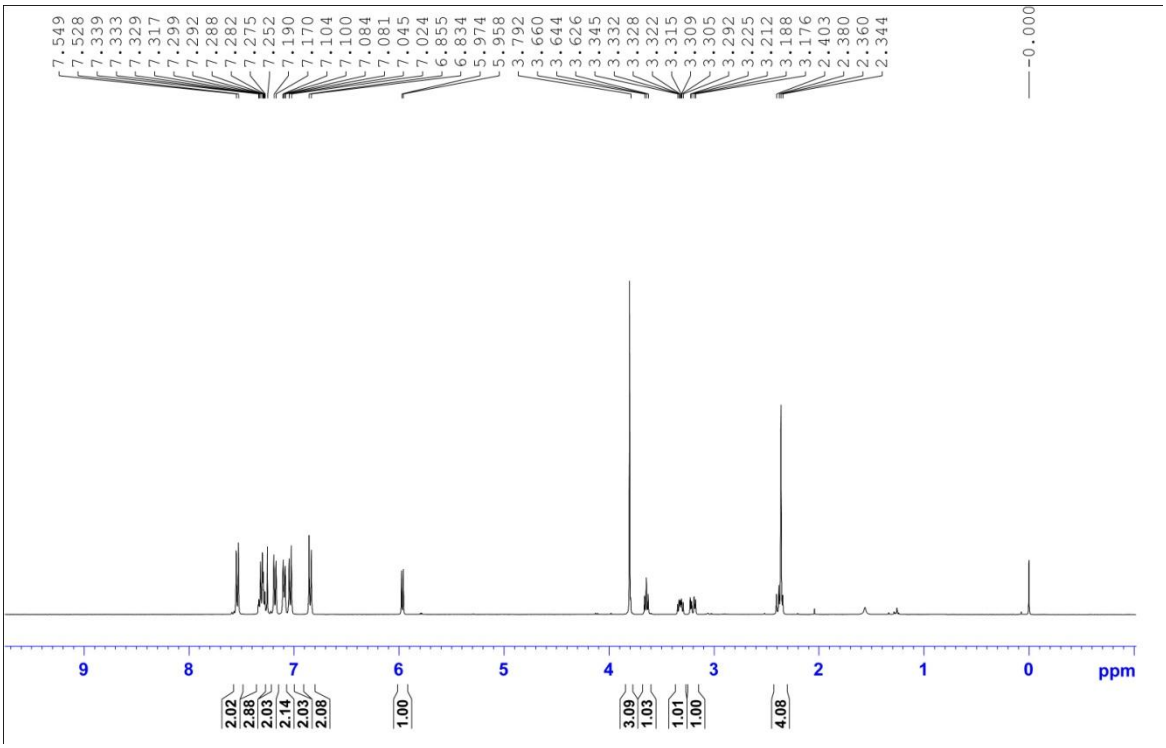

OMe
O
O
MeO

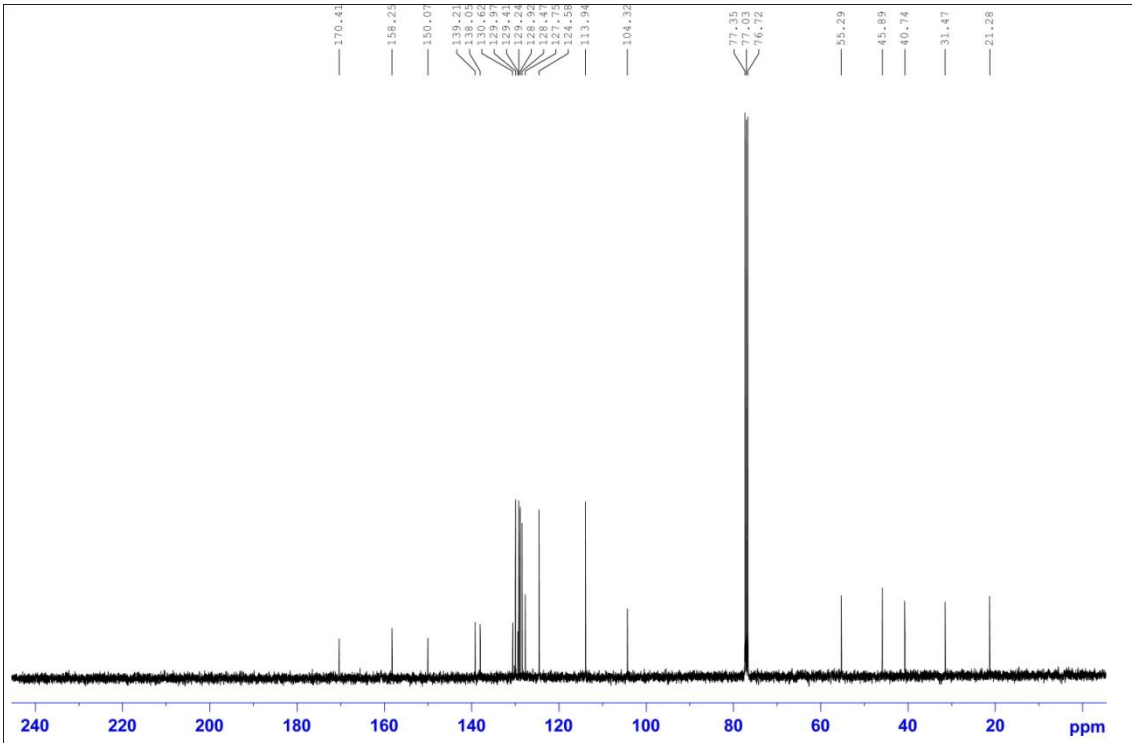

7.590
7.585
7.573
7.568
7.332
7.316
7.298
7.289
7.285
7.273
7.250
7.102
7.098
7.082
7.043
7.022
6.903
6.898
6.885
6.881
6.854
6.832
5.890
5.874
3.820
3.800
3.650
3.633
3.616
3.341
3.328
3.324
3.318
3.310
3.305
3.301
3.288
3.219
3.206
3.182
3.169
2.400
2.377
2.363
2.340
-0.000
9.5 9.0 8.5 8.0 7.5 7.0 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 ppm
1.96
2.87
2.15
2.11
4.38
0.95
6.58
1.01
0.98
1.03
1.00


170.48
160.36
158.24
149.81
138.19
130.63
129.97
129.40
128.91
128.46
127.79
127.22
124.81
114.26
113.93
103.38
77.37
77.05
76.74
55.37
55.29
45.91
40.74
31.49
240 220 200 180 160 140 120 100 80 60 40 20 ppm

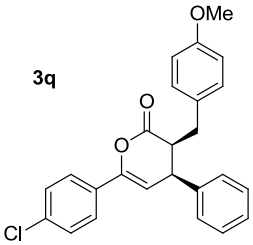
3p

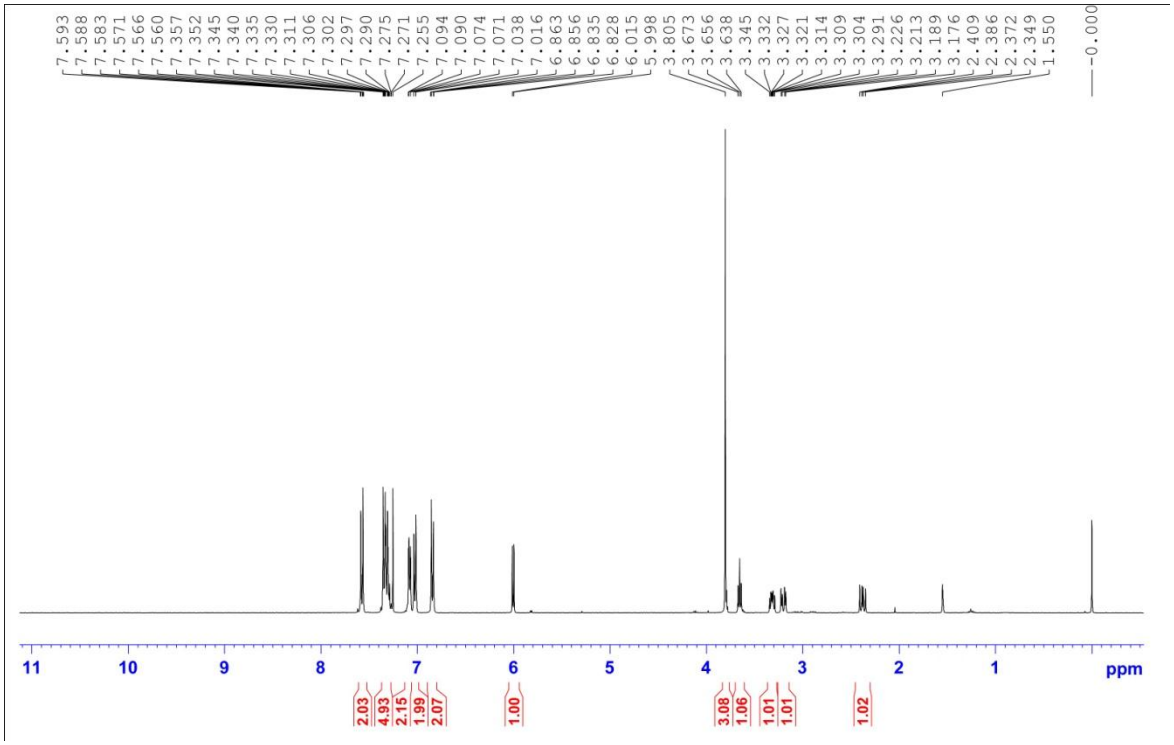

OMe
O
O
Me

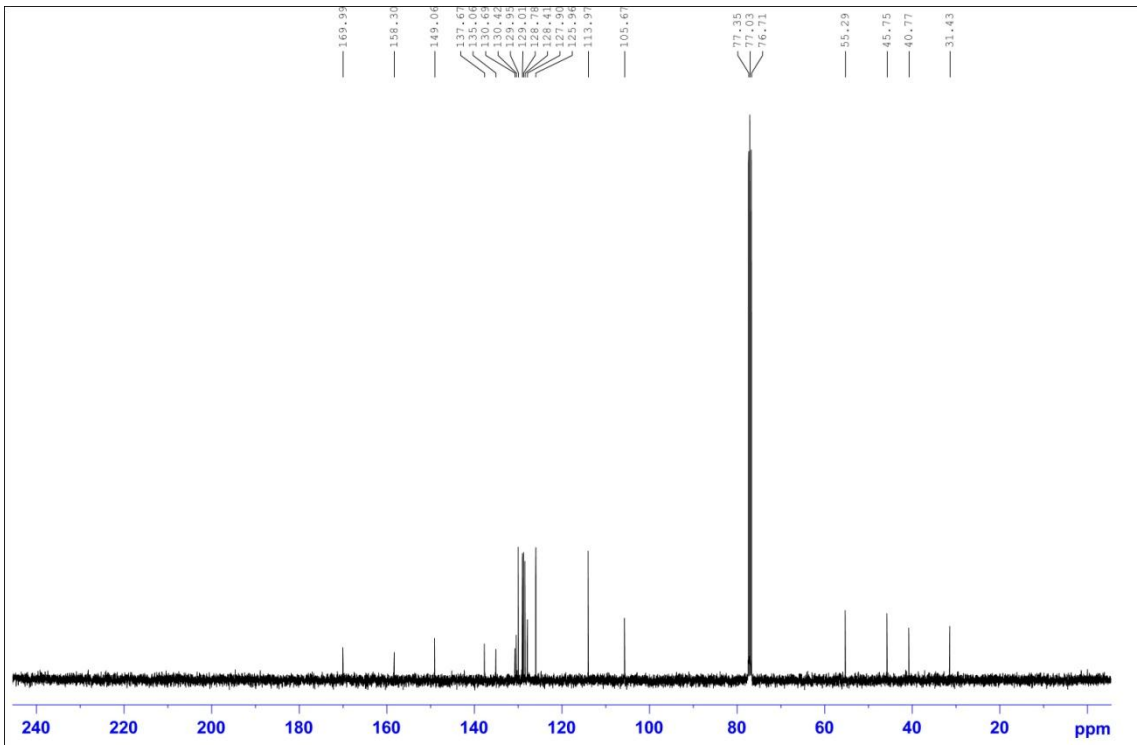

7.549
7.528
7.339
7.333
7.329
7.317
7.299
7.292
7.288
7.282
7.275
7.252
7.190
7.170
7.104
7.100
7.084
7.081
7.045
7.024
6.855
6.834
5.974
5.958
3.792
3.660
3.644
3.626
3.345
3.332
3.328
3.322
3.315
3.309
3.305
3.292
3.225
3.212
3.188
3.176
2.403
2.380
2.360
2.344
-0.000
9
8
7
6
5
4
3
2
1
0
ppm
2.02
2.88
2.03
2.14
2.03
2.08
1.00
3.09
1.03
1.01
1.00
4.08


170.41
158.25
150.07
139.21
138.05
130.62
129.97
129.41
129.24
128.92
128.47
127.75
124.58
113.94
104.32
77.35
77.03
76.72
55.29
45.89
40.74
31.47
21.28
240
220
200
180
160
140
120
100
80
60
40
20
ppm

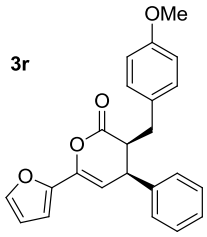
3q

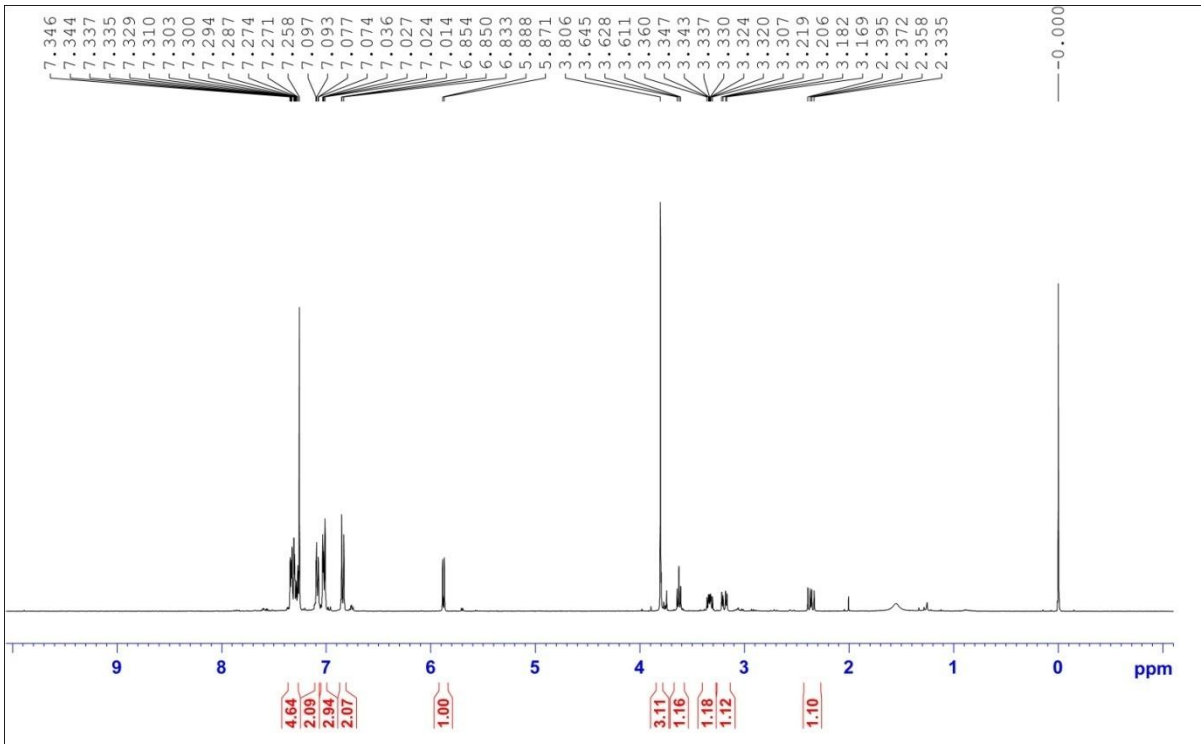

OMe
O
O
Cl

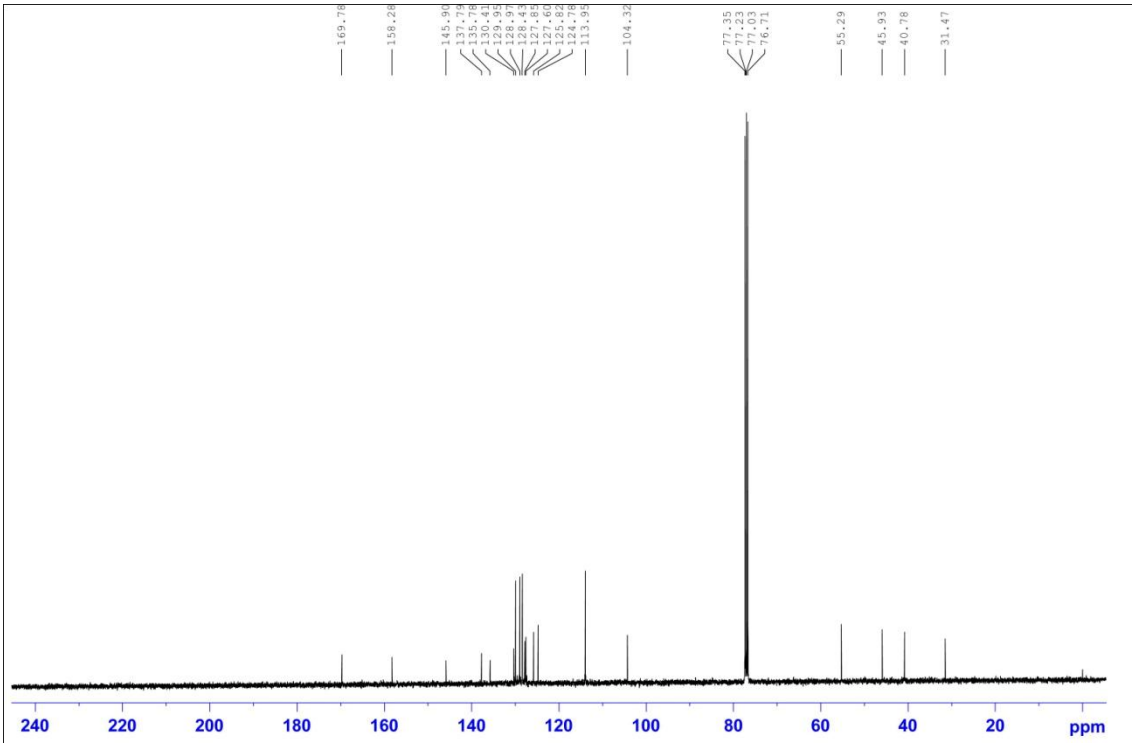

7.593 7.588 7.583 7.571 7.566 7.560 7.357 7.352 7.345 7.340 7.335 7.330 7.311 7.306 7.302 7.297 7.290 7.275 7.271 7.255 7.094 7.090 7.074 7.071 7.038 7.016 6.863 6.856 6.835 6.828 6.015 5.998 3.805 3.673 3.656 3.638 3.345 3.332 3.327 3.321 3.314 3.309 3.304 3.291 3.226 3.213 3.189 3.176 2.409 2.386 2.372 2.349 1.550 -0.000
11 10 9 8 7 6 5 4 3 2 1 ppm
2.03 4.93 2.15 1.99 2.07 1.00 3.08 1.06 1.01 1.01 1.02

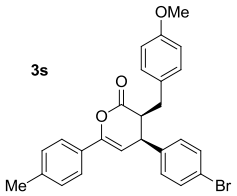

169.99 158.30 149.06 137.67 135.06 130.69 130.42 129.95 129.01 128.78 128.41 127.90 125.96 113.97 105.67 77.35 77.03 76.71 55.29 45.75 40.77 31.43
240 220 200 180 160 140 120 100 80 60 40 20 ppm

3r

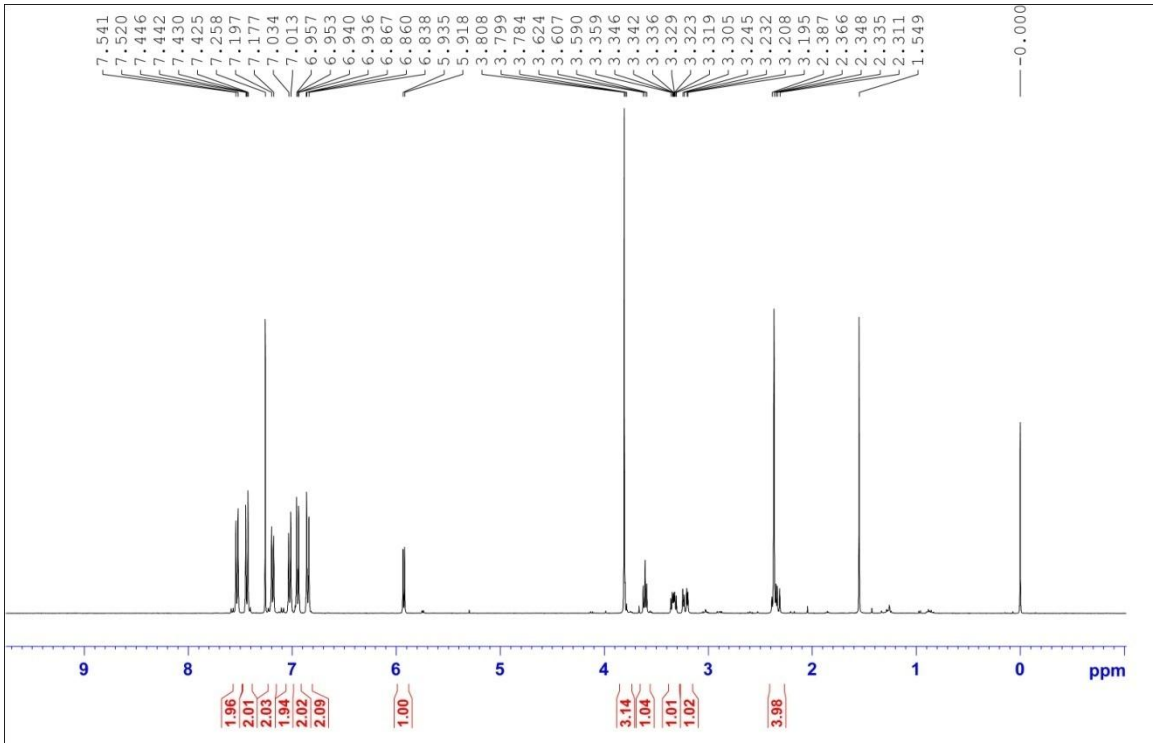

OMe
O
O
O

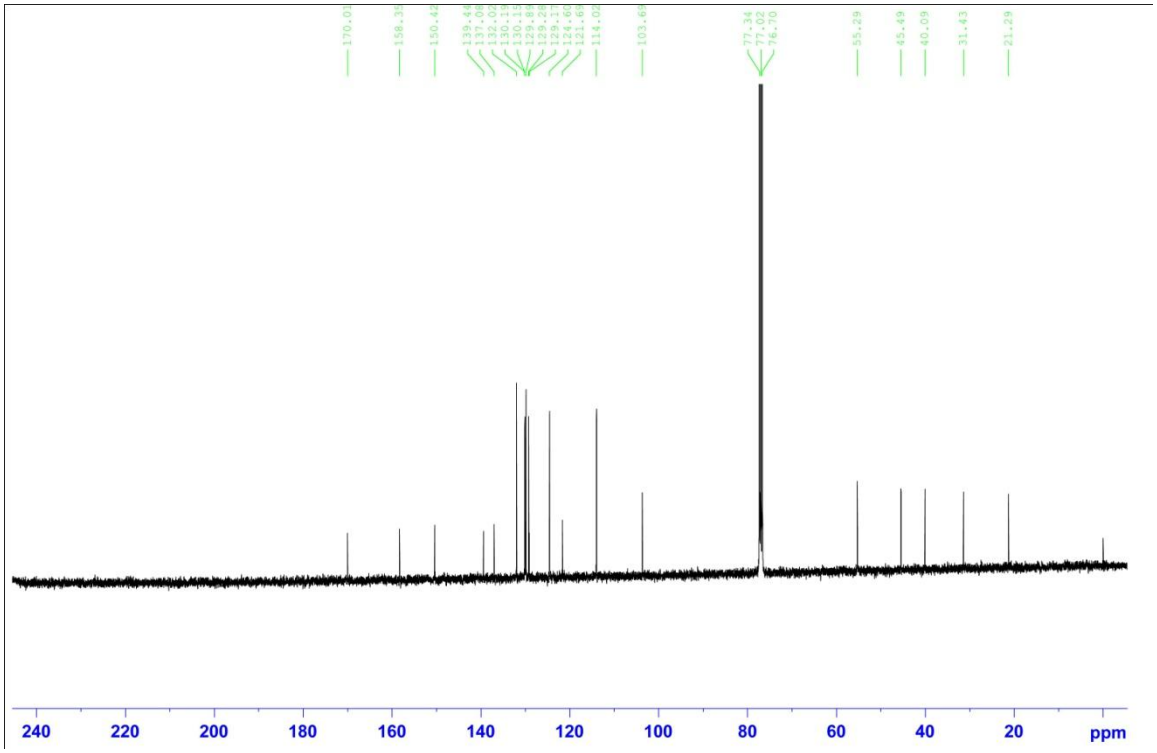

7.346
7.344
7.337
7.335
7.329
7.310
7.303
7.300
7.294
7.287
7.274
7.271
7.258
7.097
7.093
7.077
7.074
7.036
7.027
7.024
7.014
6.854
6.850
6.833
5.888
5.871
3.806
3.645
3.628
3.611
3.360
3.347
3.343
3.337
3.330
3.324
3.320
3.307
3.219
3.206
3.182
3.169
2.395
2.372
2.358
2.335
-0.000
9
8
7
6
5
4
3
2
1
0
ppm
4.64
2.09
2.94
2.07
1.00
3.11
1.16
1.18
1.12
1.10


169.78
158.28
145.90
137.79
135.78
130.41
129.95
128.97
128.43
127.85
127.60
125.82
124.78
113.95
104.32
77.35
77.23
77.03
76.71
55.29
45.93
40.78
31.47
240
220
200
180
160
140
120
100
80
60
40
20
ppm


OMe
O
O
Me
Br

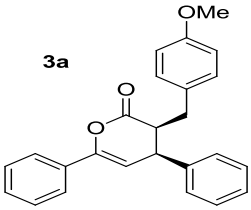
3s

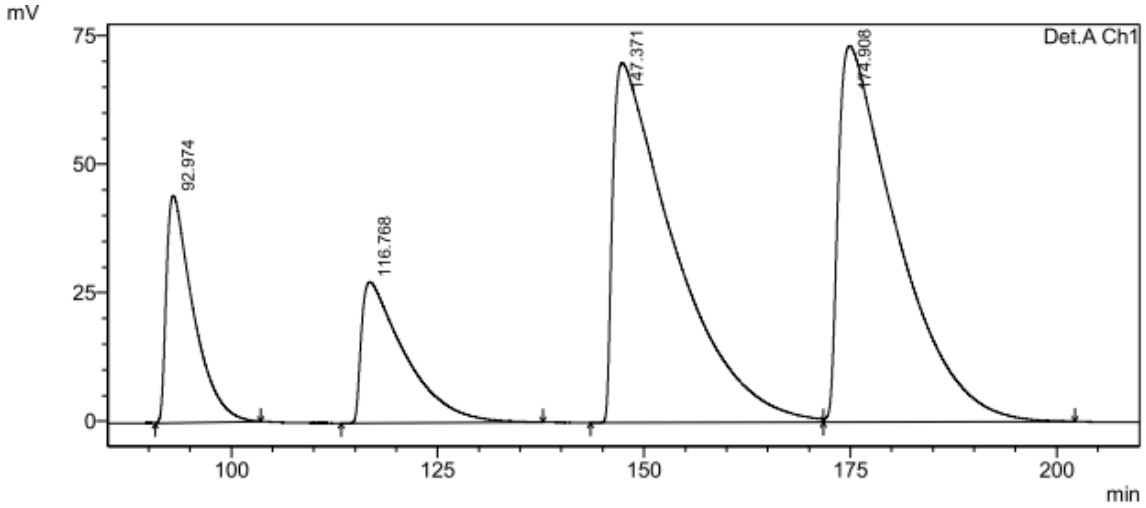

7.541
7.520
7.446
7.442
7.430
7.425
7.258
7.197
7.177
7.034
7.013
6.957
6.953
6.940
6.936
6.867
6.860
6.838
5.935
5.918
3.808
3.799
3.784
3.624
3.607
3.590
3.359
3.346
3.342
3.336
3.329
3.323
3.319
3.305
3.245
3.232
3.208
3.195
2.387
2.366
2.348
2.335
2.311
1.549
-0.000
9
8
7
6
5
4
3
2
1
0
ppm
1.96
2.01
2.03
1.94
2.02
2.09
1.00
3.14
1.04
1.01
1.02
3.98


170.01
158.35
150.42
139.44
137.06
132.02
130.19
130.15
129.89
129.28
129.17
124.60
121.69
114.02
103.69
77.34
77.02
76.70
55.29
45.49
40.09
31.43
21.29
240
220
200
180
160
140
120
100
80
60
40
20
ppm

HPLC spectra of the products.

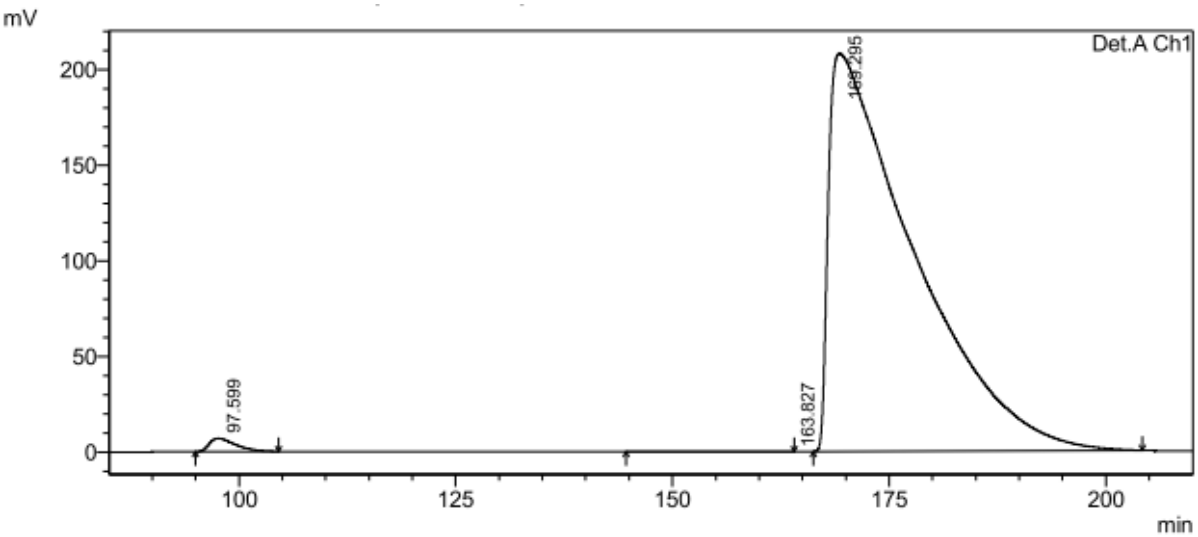
3a





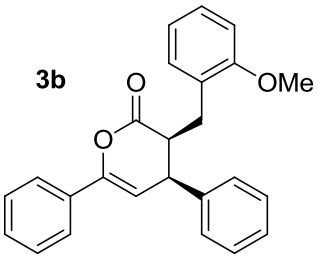
UV Detector Ch1 254nm

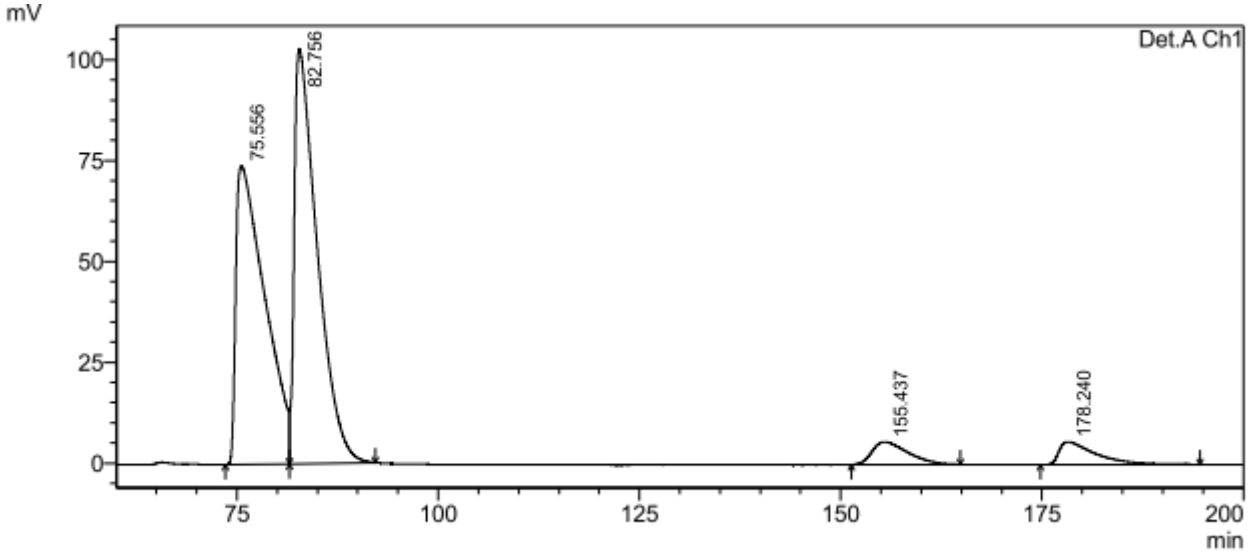
Peak#	Ret. Time	Area	Height	Area %	Height %
1	92.974	10016331	44210	10.783	20.577
2	116.768	10073399	27425	10.845	12.765
3	147.371	36307061	69998	39.087	32.581
4	174.908	36490028	73214	39.284	34.077
Total		92886819	214847	100.000	100.000



UV Detector Ch1 254nm

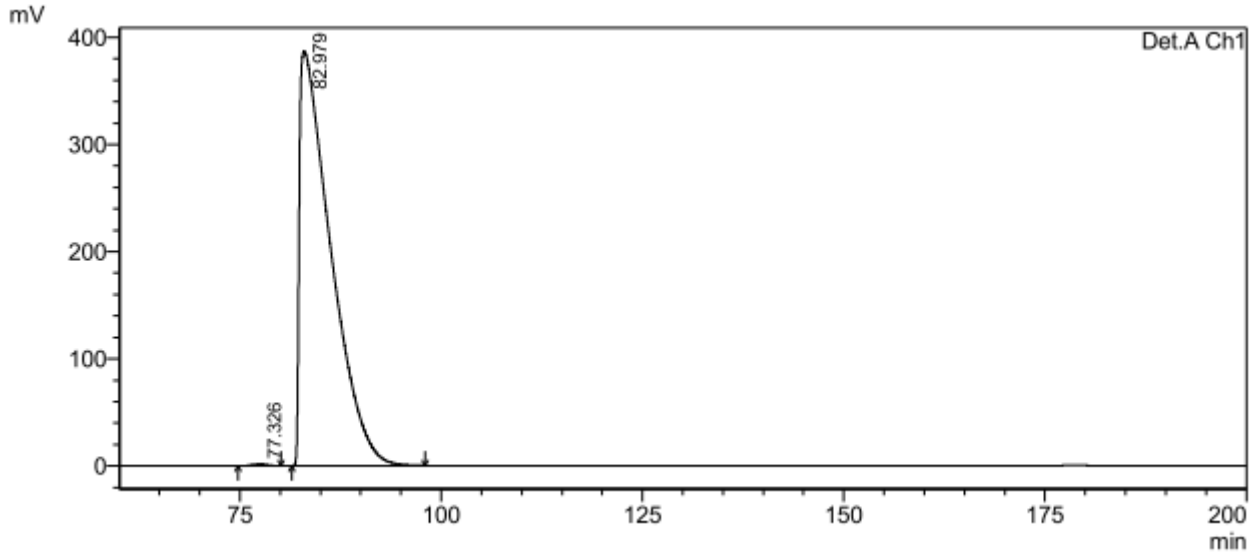
Peak#	Ret. Time	Area	Height	Area %	Height %
1	97.599	1485169	7011	1.037	3.257
2	163.827	-100713	13	-0.070	0.006
3	169.295	141802526	208219	99.033	96.737
Total		143186982	215243	100.000	100.000





UV Detector Ch1 254nm

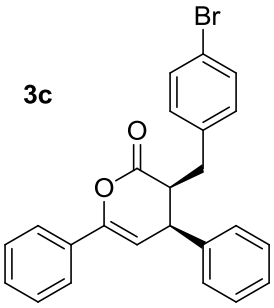
Peak#	Ret. Time	Area	Height	Area %	Height %
1	75.556	18561290	73954	43.658	39.341
2	82.756	20413004	102725	48.013	54.646
3	155.437	1747326	5642	4.110	3.002
4	178.240	1793642	5661	4.219	3.011
Total		42515262	187982	100.000	100.000

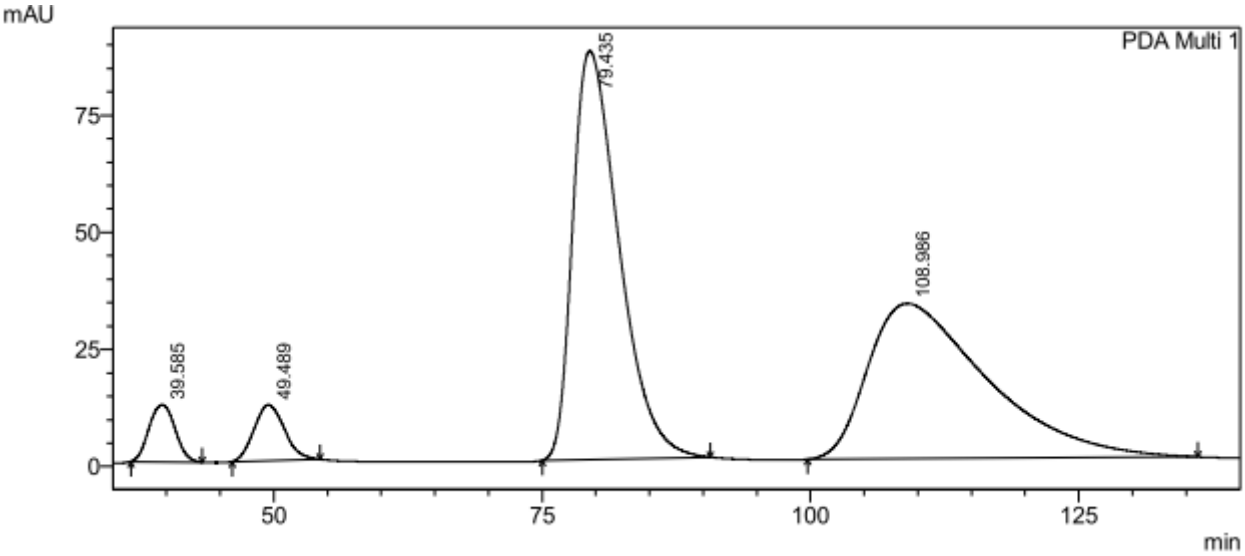


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	77.326	225962	1754	0.216	0.451
2	82.979	104496950	387058	99.784	99.549
Total		104722912	388813	100.000	100.000

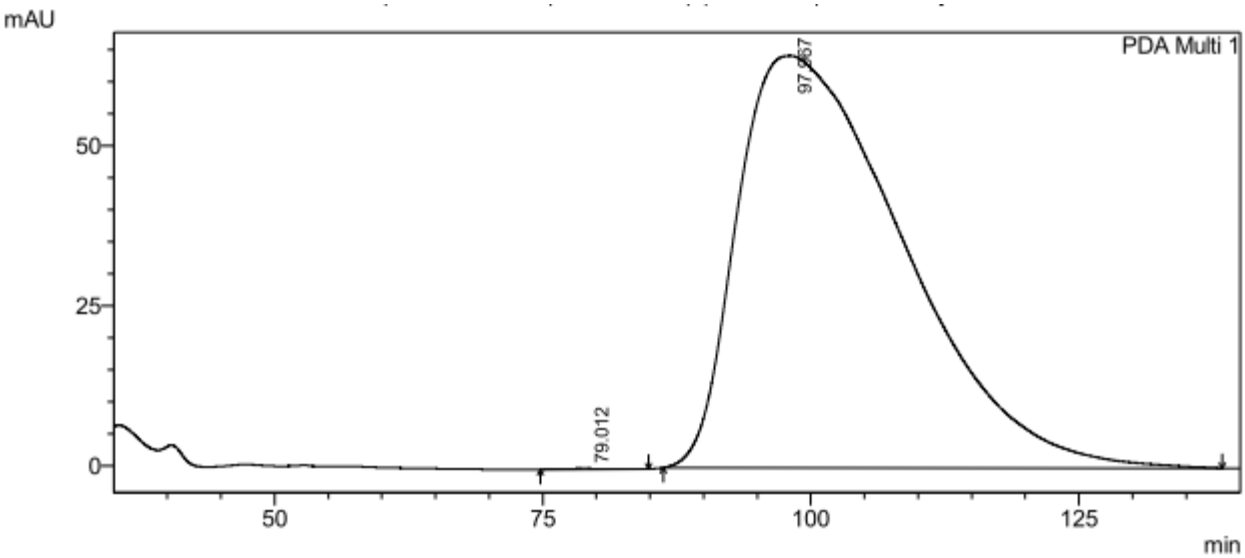
3c





PDA Ch1 254nm 4nm

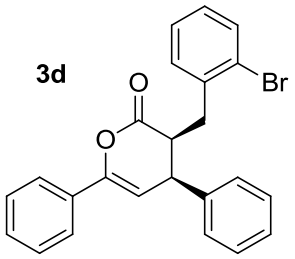
Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.585	2059055	12162	3.668	8.422
2	49.489	2351636	11933	4.189	8.263
3	79.435	26116953	87187	46.525	60.375
4	108.986	25607506	33128	45.618	22.940
Total		56135151	144409	100.000	100.000

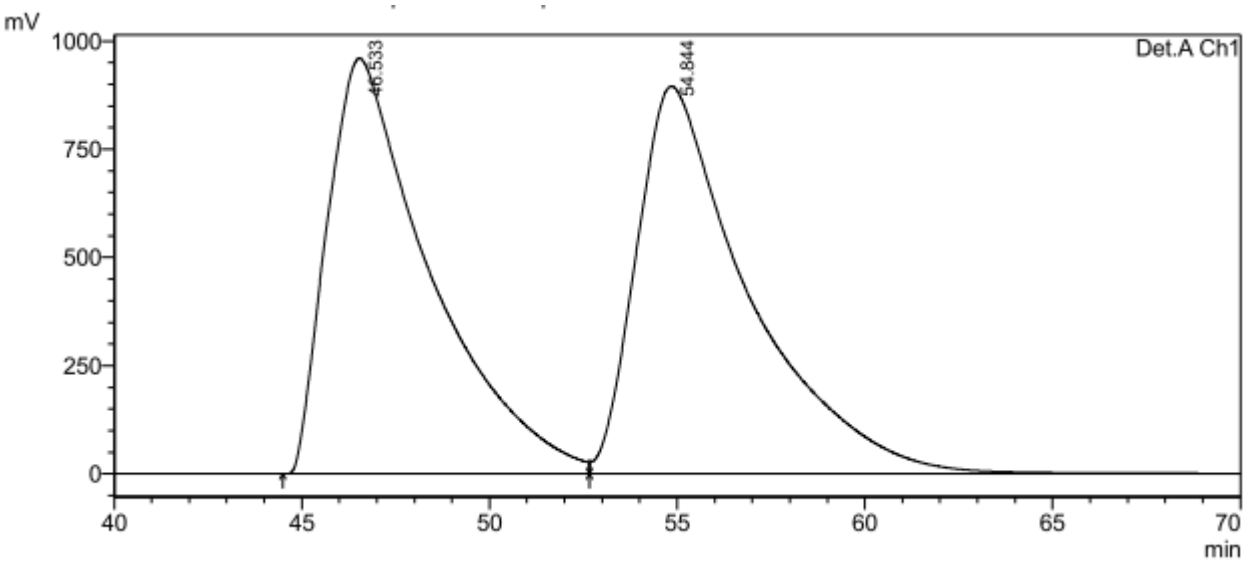


PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	79.012	16467	98	0.024	0.152
2	97.967	69361607	64357	99.976	99.848
Total		69378074	64455	100.000	100.000

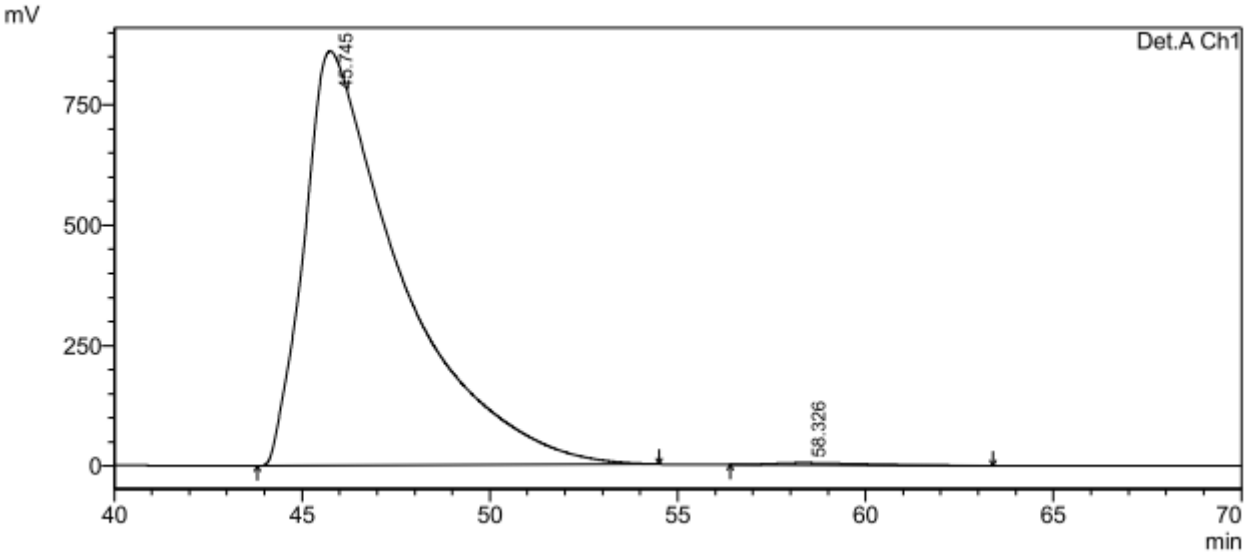
3d





UV Detector Ch1 254nm

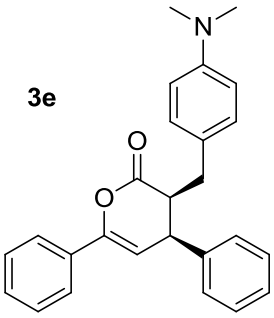
Peak#	Ret. Time	Area	Height	Area %	Height %
1	46.533	182865601	960141	49.566	51.752
2	54.844	186068078	895123	50.434	48.248
Total		368933679	1855264	100.000	100.000

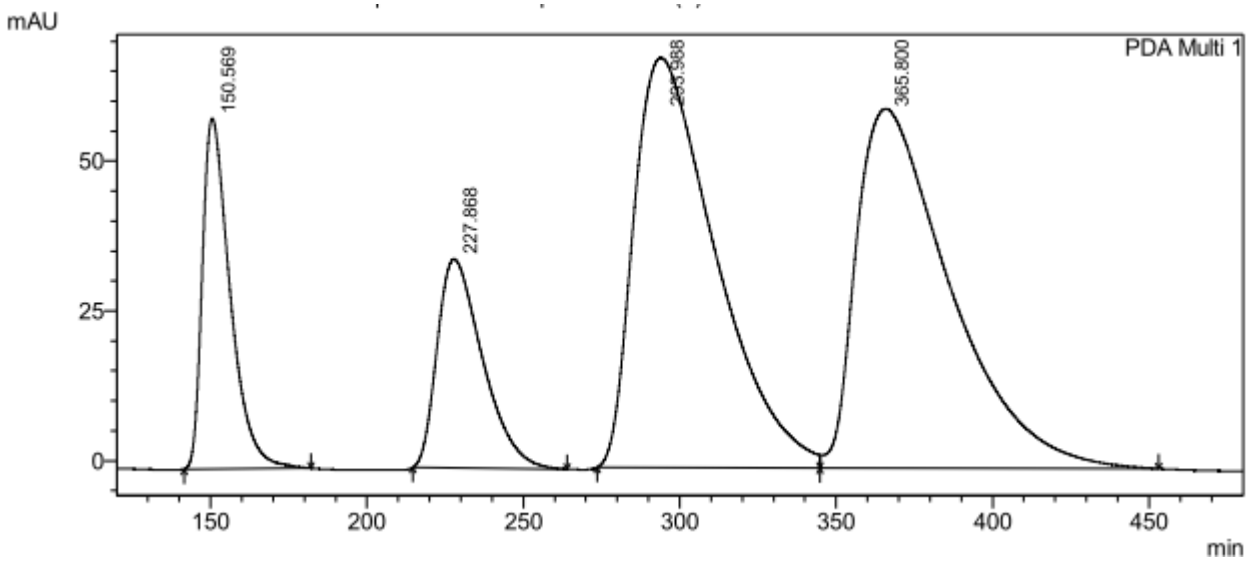


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.745	154121370	861313	99.572	99.496
2	58.326	662036	4360	0.428	0.504
Total		154783406	865673	100.000	100.000

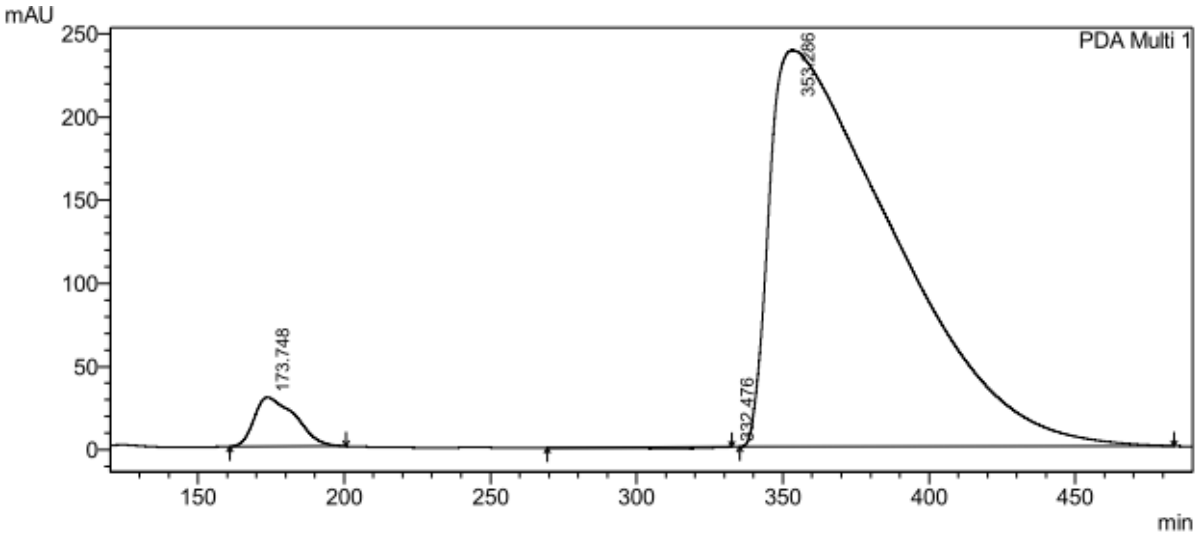
3e





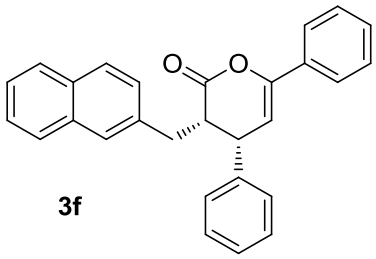
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	150.569	36137510	58504	11.260	26.388
2	227.868	35187896	34900	10.964	15.741
3	293.988	124216803	68372	38.705	30.838
4	365.800	125390372	59935	39.071	27.033
Total		320932582	221711	100.000	100.000

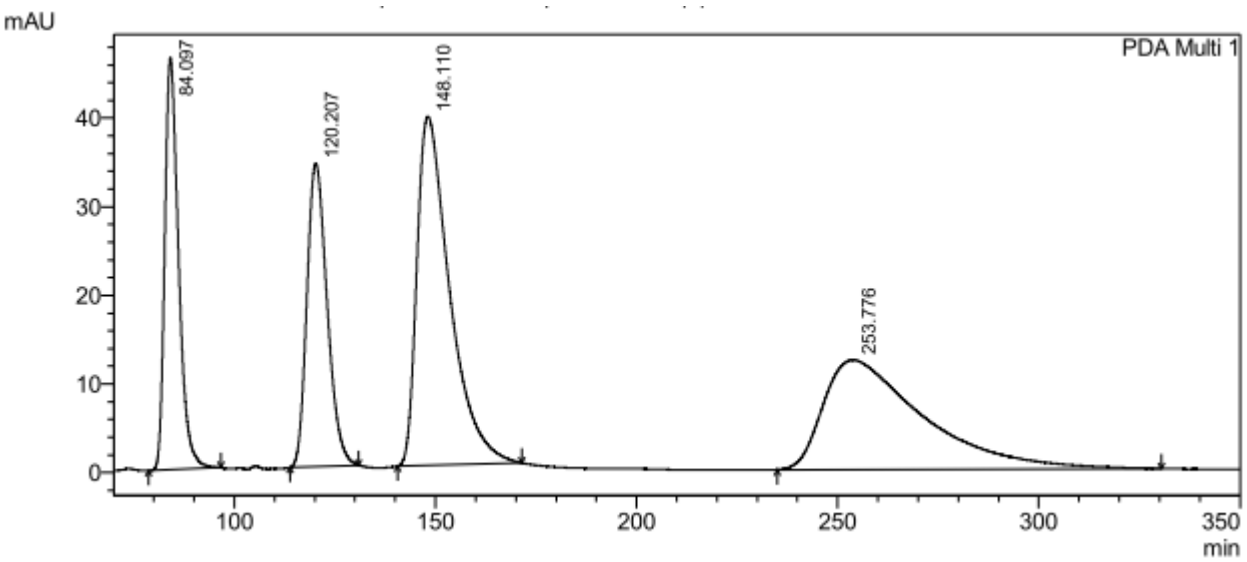


PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	173.748	28799926	29506	3.926	11.013
2	332.476	-1014517	1	-0.138	0.000
3	353.286	705741133	238416	96.212	88.987
Total		733526542	267923	100.000	100.000

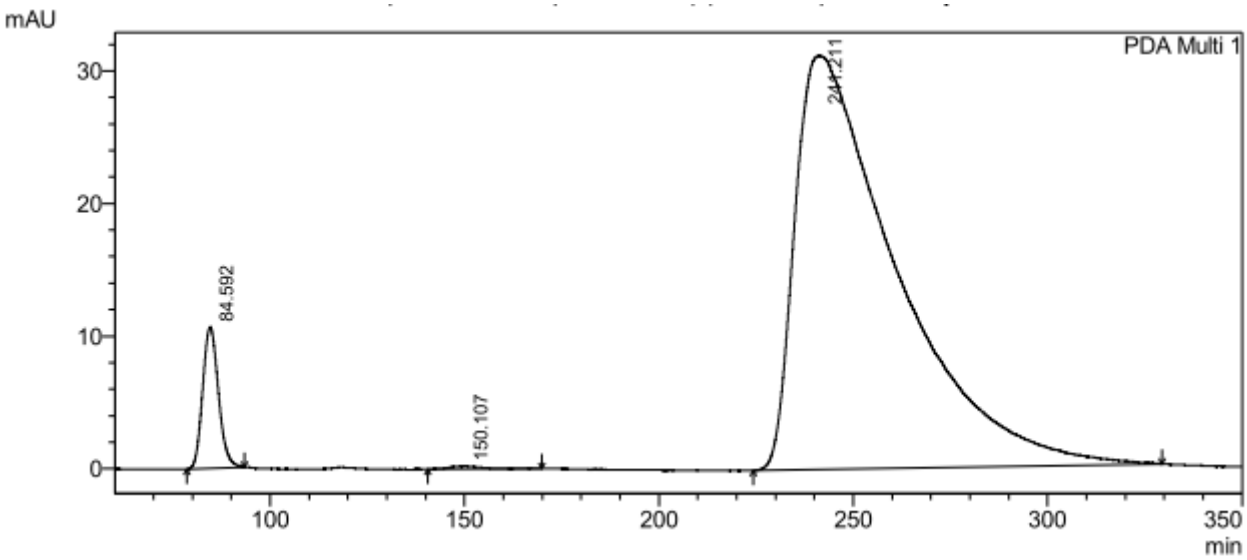


3f



PDA Ch1 254nm 4nm

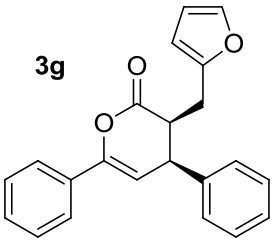
Peak#	Ret. Time	Area	Height	Area %	Height %
1	84.097	11079995	46466	16.628	35.090
2	120.207	11959969	34235	17.949	25.853
3	148.110	22329494	39361	33.511	29.725
4	253.776	21263163	12357	31.911	9.332
Total		66632622	132419	100.000	100.000

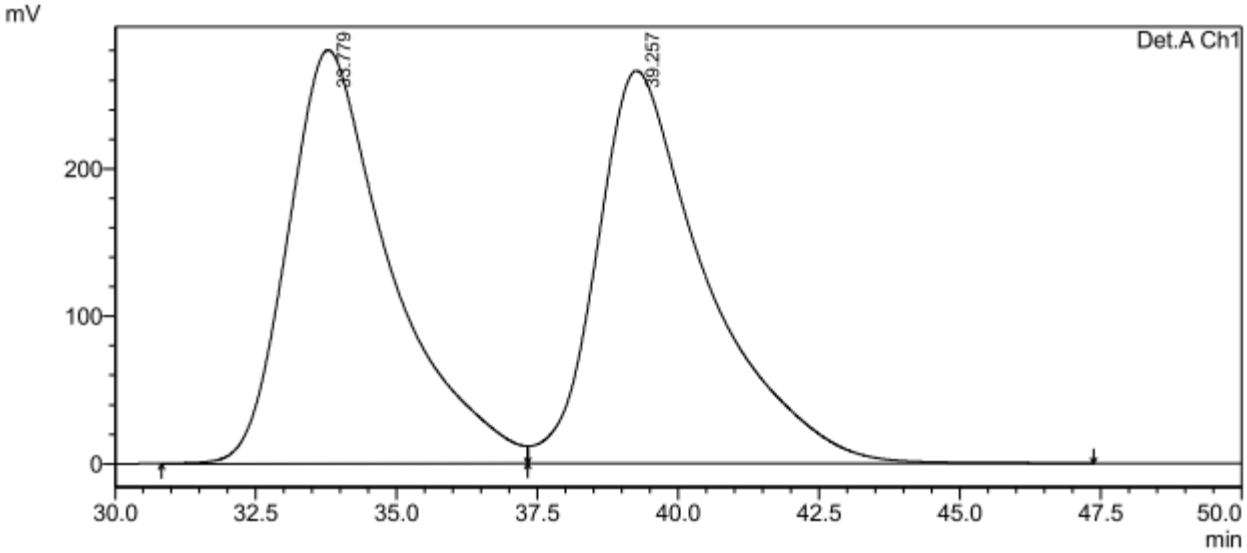


PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	84.592	3009563	10645	5.036	25.309
2	150.107	123071	216	0.206	0.514
3	241.211	56631135	31199	94.758	74.177
Total		59763769	42061	100.000	100.000

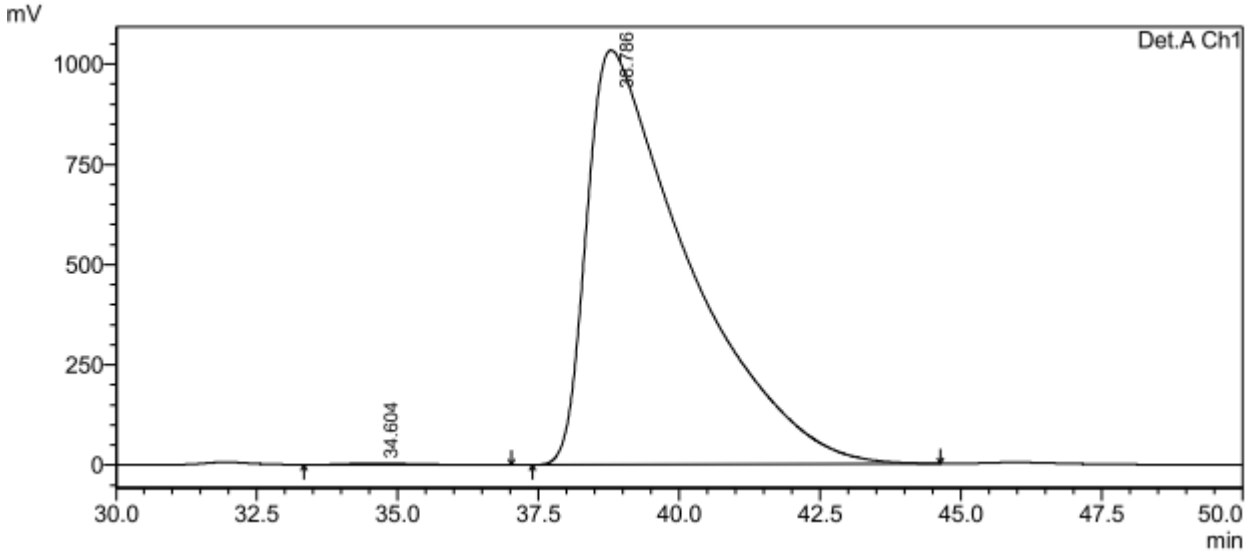
3g





UV Detector Ch1 254nm

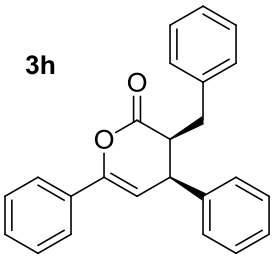
Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.779	35612940	280333	49.670	51.284
2	39.257	36085740	266297	50.330	48.716
Total		71698680	546630	100.000	100.000

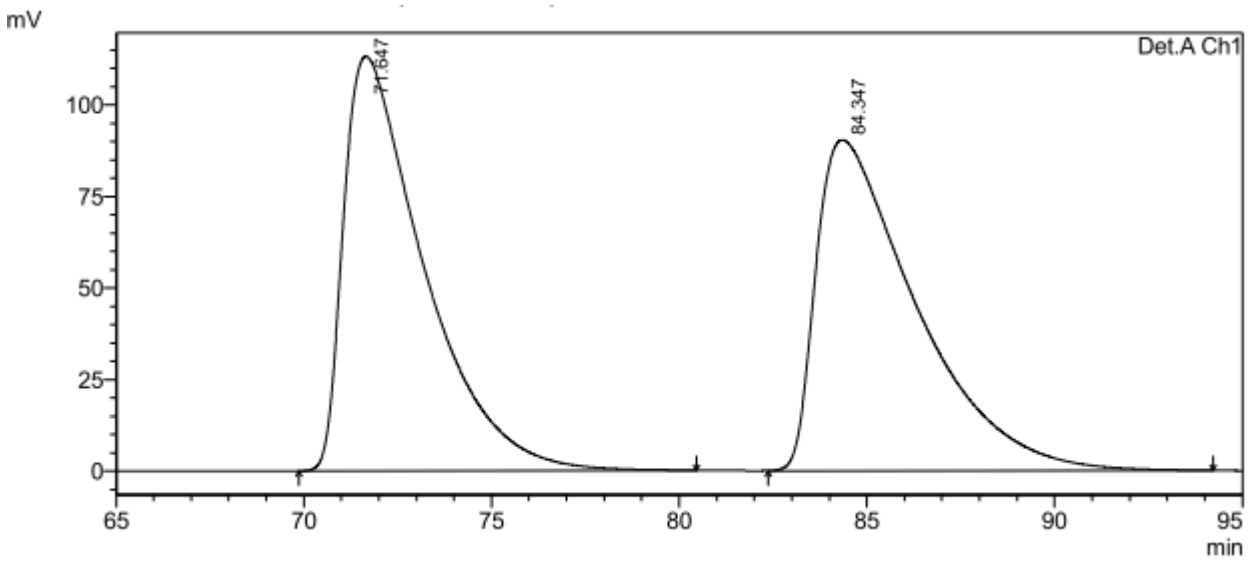


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.604	316535	3834	0.244	0.370
2	38.786	129478491	1033854	99.756	99.630
Total		129795027	1037689	100.000	100.000

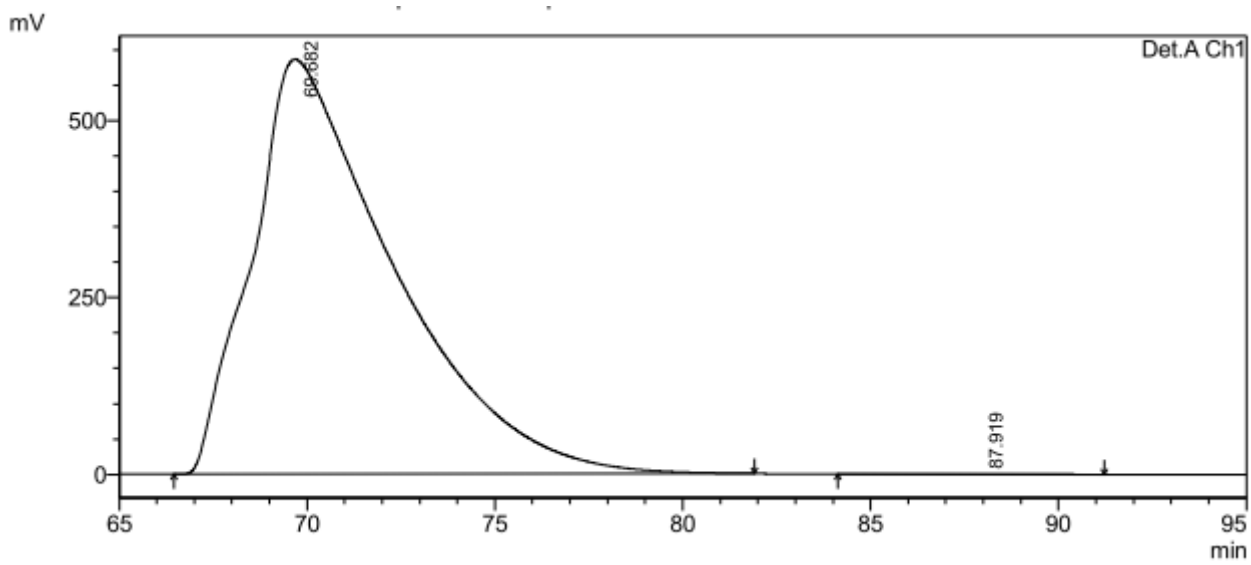
3h





UV Detector Ch1 254nm

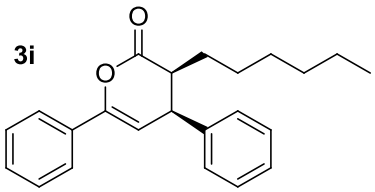
Peak#	Ret. Time	Area	Height	Area %	Height %
1	71.647	16850445	113317	50.105	55.628
2	84.347	16779574	90386	49.895	44.372
Total		33630019	203704	100.000	100.000

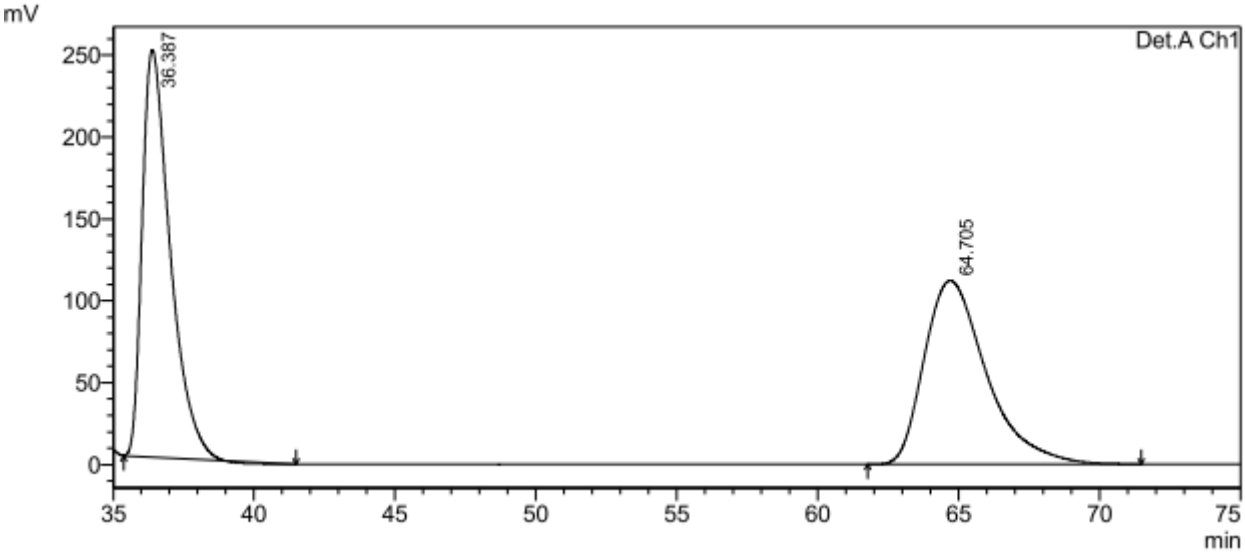


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	69.682	153515878	585745	99.968	99.944
2	87.919	48647	326	0.032	0.056
Total		153564525	586071	100.000	100.000

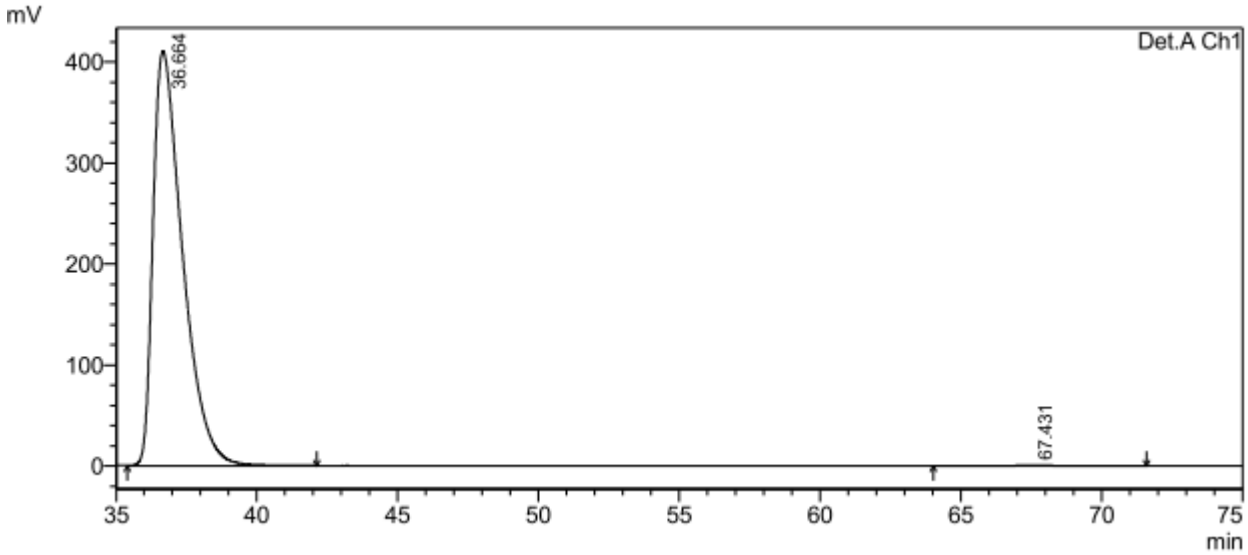
3i





UV Detector Ch1 254nm

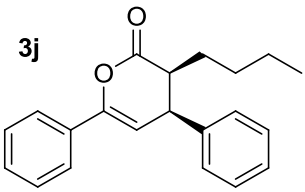
Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.387	17141110	248547	49.837	68.891
2	64.705	17253140	112238	50.163	31.109
Total		34394250	360785	100.000	100.000

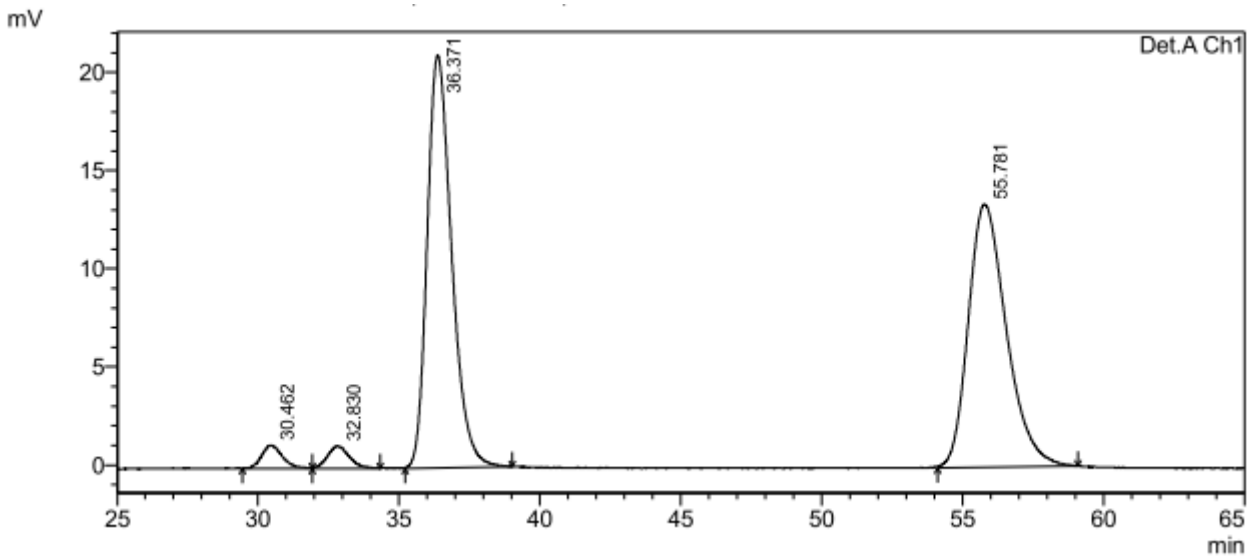


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.664	29935448	410440	99.769	99.865
2	67.431	69370	553	0.231	0.135
Total		30004818	410993	100.000	100.000

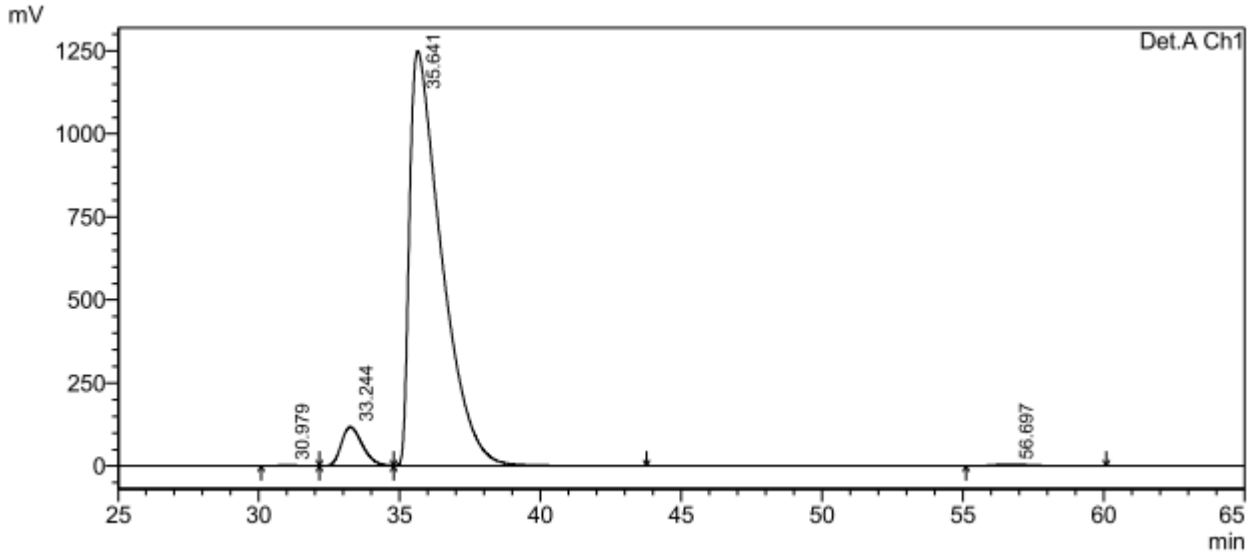
3j





UV Detector Ch1 254nm

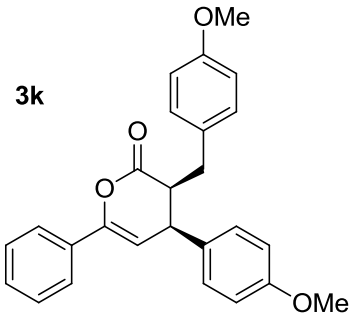
Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.462	60055	1170	2.263	3.184
2	32.830	61189	1137	2.306	3.097
3	36.371	1269137	21021	47.824	57.234
4	55.781	1263365	13400	47.607	36.485
Total		2653746	36728	100.000	100.000

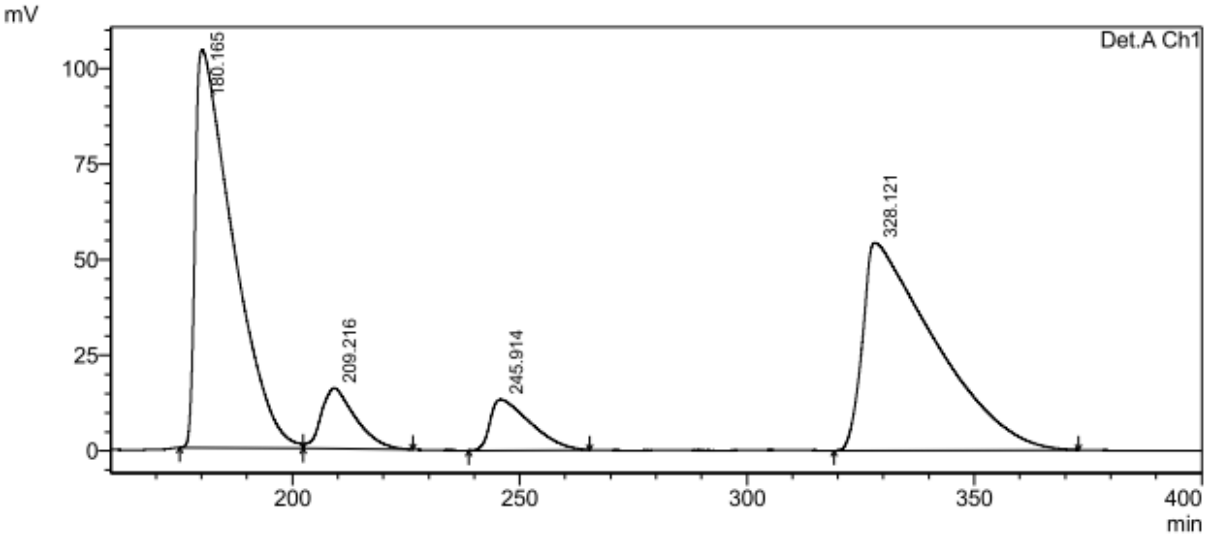


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.979	140412	2891	0.133	0.210
2	33.244	6206291	117854	5.876	8.574
3	35.641	98768961	1248911	93.514	90.855
4	56.697	504327	4966	0.477	0.361
Total		105619992	1374622	100.000	100.000

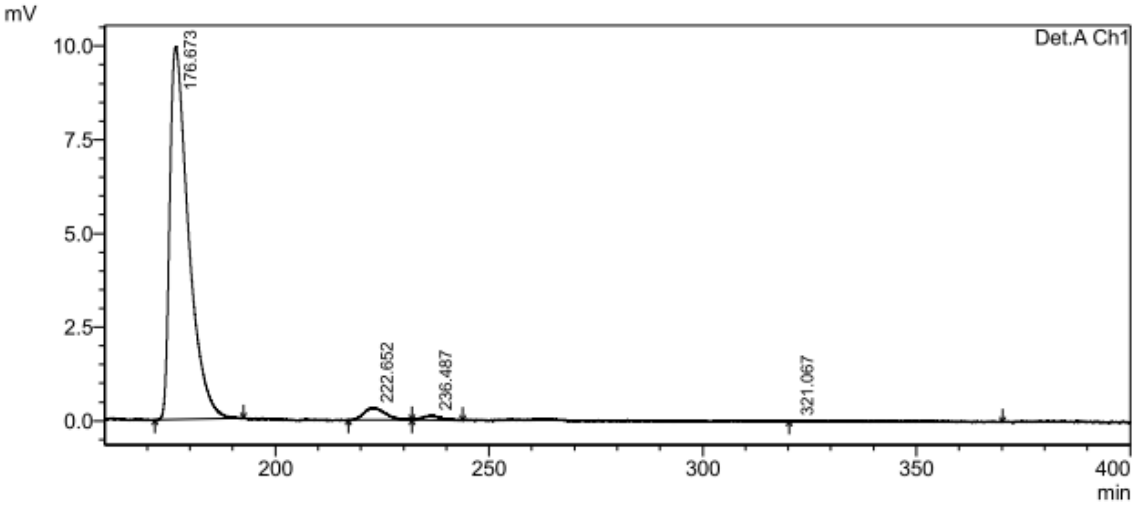
3k





UV Detector Ch1 254nm

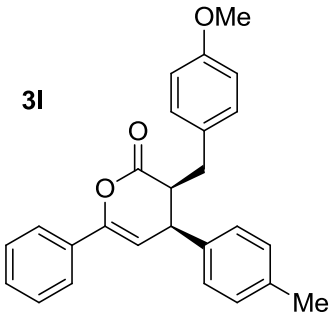
Peak#	Ret. Time	Area	Height	Area %	Height %
1	180.165	59893153	104003	43.911	55.491
2	209.216	8334304	15907	6.110	8.487
3	245.914	8098981	13266	5.938	7.078
4	328.121	60069576	54246	44.041	28.943
Total		136396014	187423	100.000	100.000

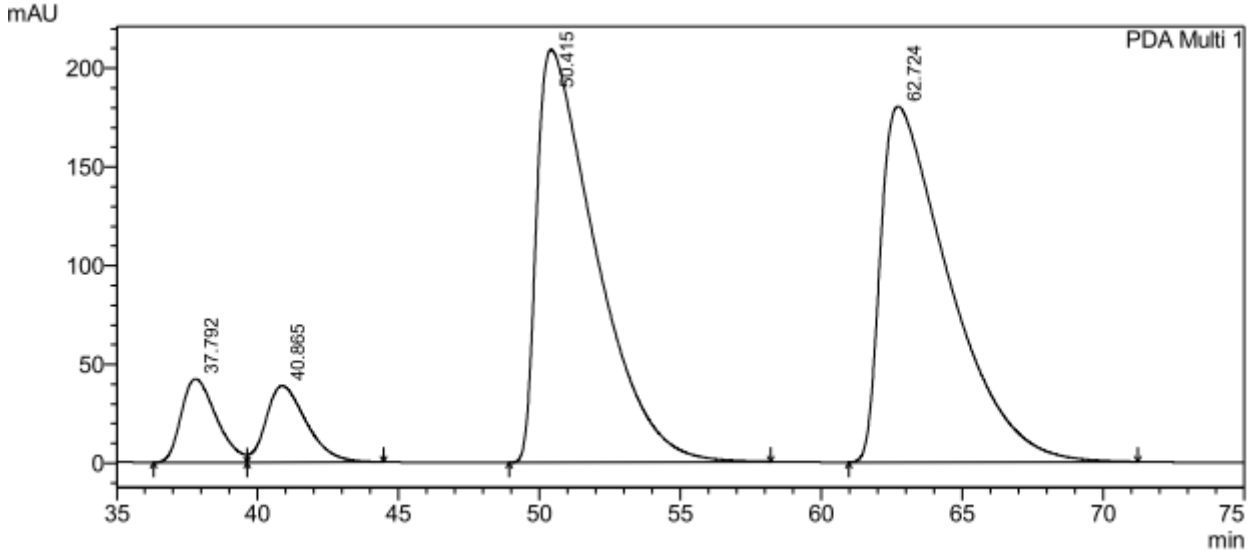


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	176.673	3035165	9949	95.332	95.411
2	222.652	114173	335	3.586	3.213
3	236.487	33814	127	1.062	1.219
4	321.067	647	16	0.020	0.157
Total		3183800	10427	100.000	100.000

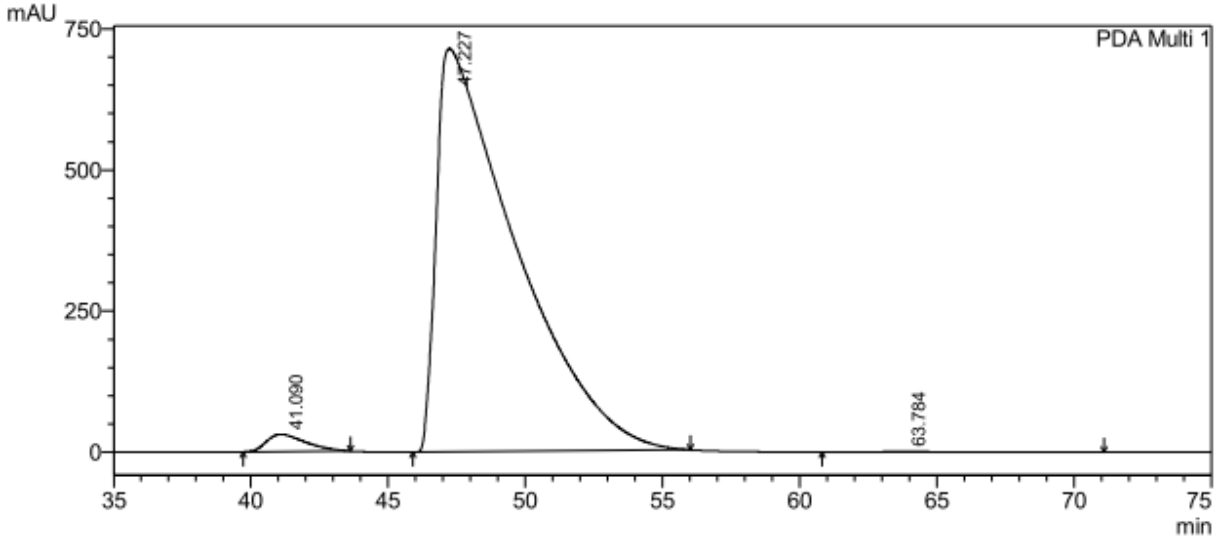
3l





PDA Ch1 254nm 4nm

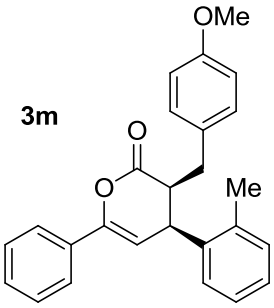
Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.792	3685224	42307	5.374	8.997
2	40.865	3841829	38683	5.603	8.226
3	50.415	30495024	209039	44.471	44.455
4	62.724	30550499	180199	44.552	38.322
Total		68572577	470228	100.000	100.000

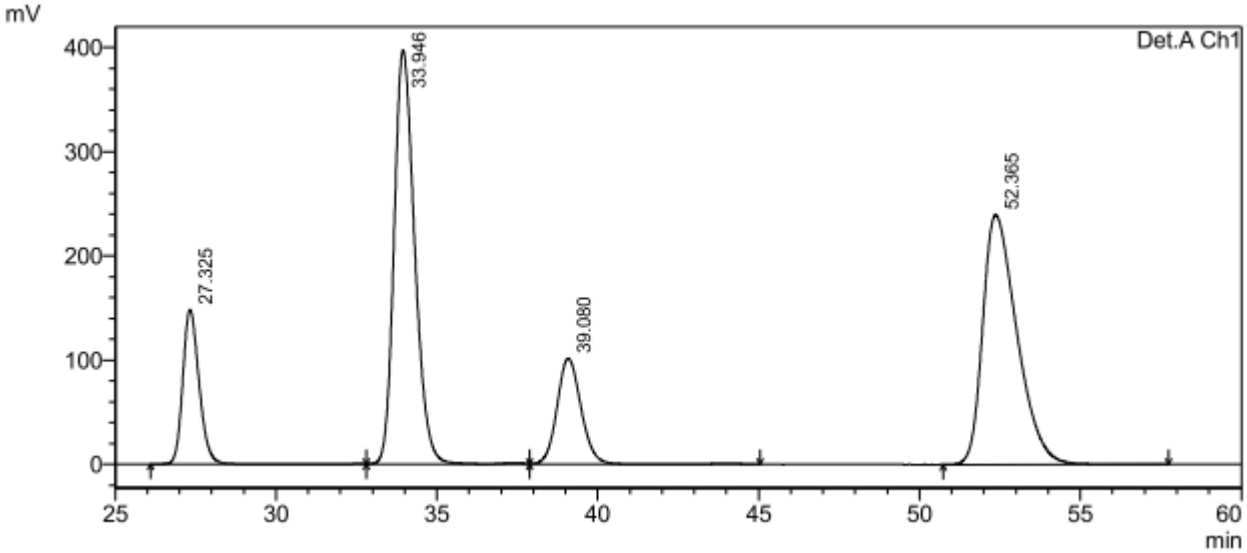


PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.090	3043982	30529	2.069	4.093
2	47.227	143926786	714566	97.840	95.792
3	63.784	132844	864	0.090	0.116
Total		147103612	745959	100.000	100.000

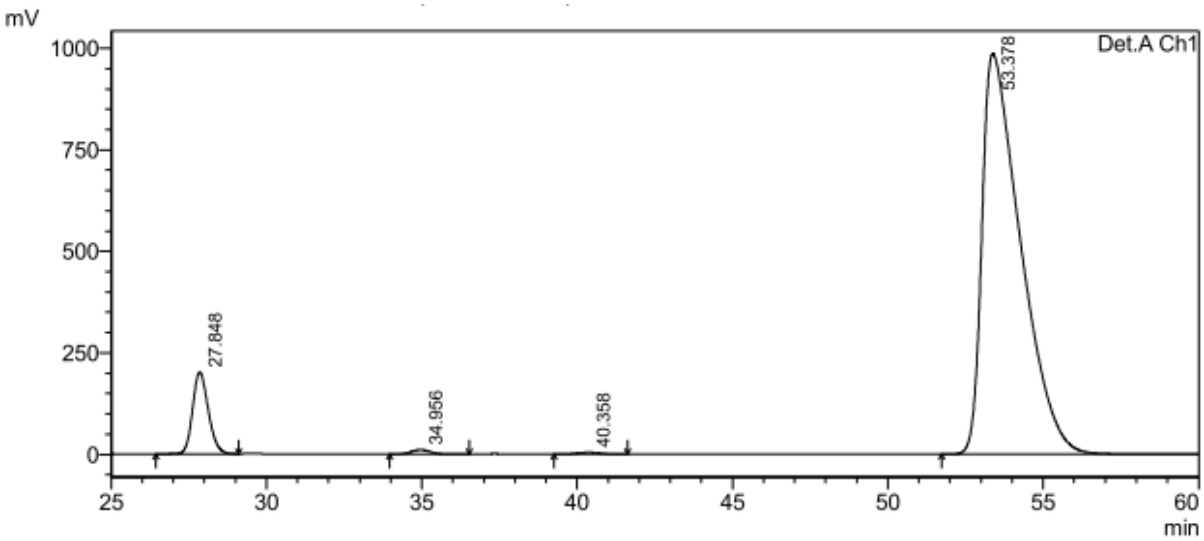
3m





UV Detector Ch1 254nm

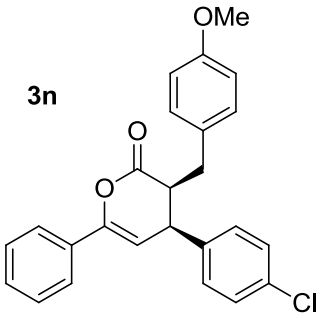
Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.325	5304017	148695	11.508	16.751
2	33.946	17761215	397484	38.538	44.777
3	39.080	5313206	101872	11.528	11.476
4	52.365	17709538	239648	38.426	26.997
Total		46087975	887700	100.000	100.000

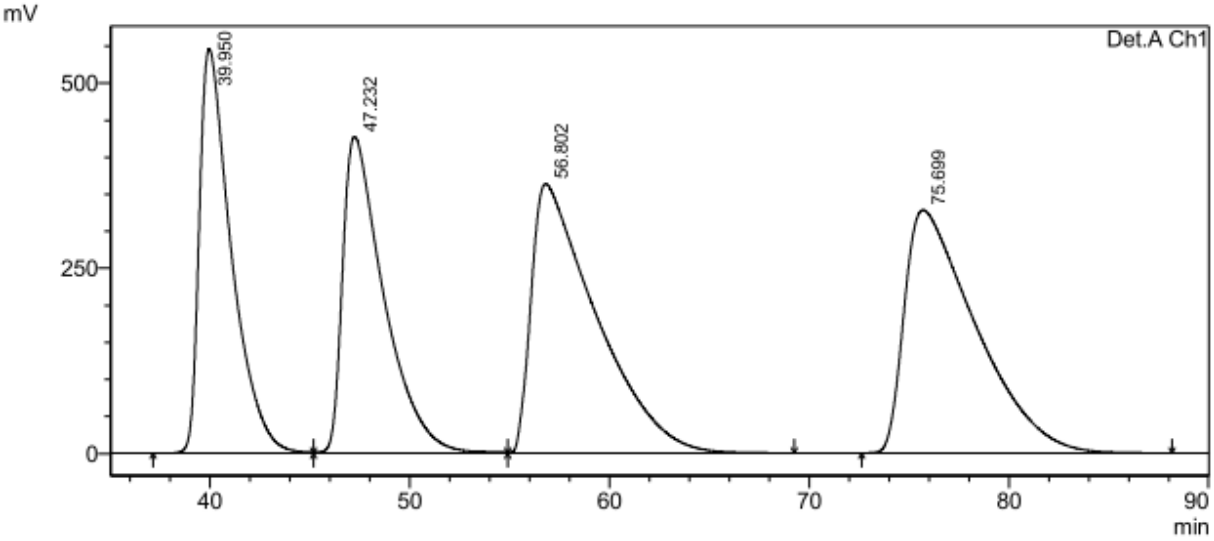


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.848	7153406	201789	7.681	16.750
2	34.956	497766	11181	0.535	0.928
3	40.358	251351	4692	0.270	0.389
4	53.378	85224078	987047	91.514	81.932
Total		93126602	1204708	100.000	100.000

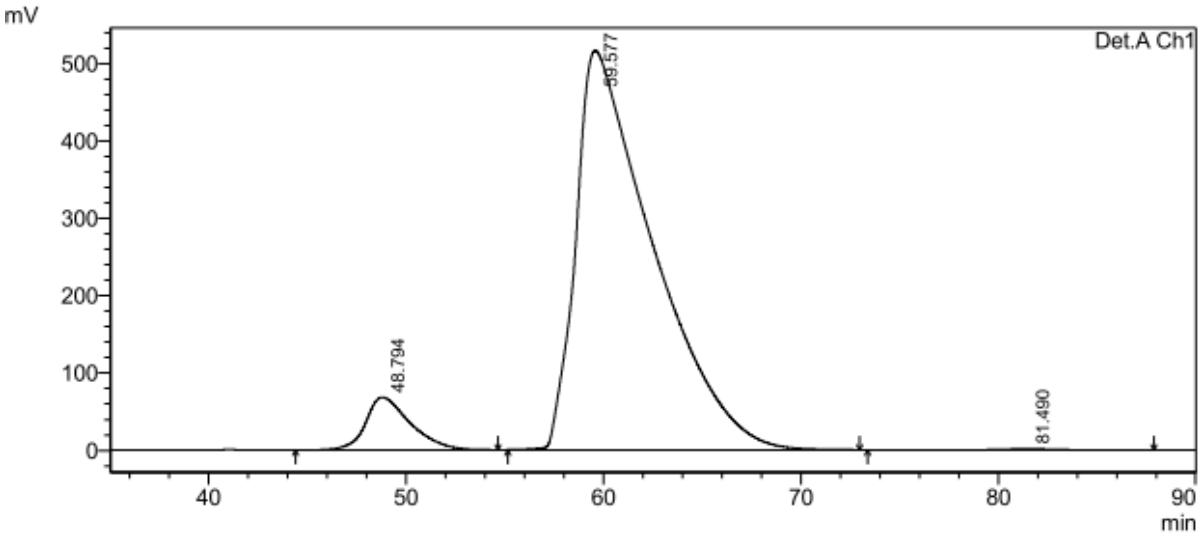
3n





UV Detector Ch1 254nm

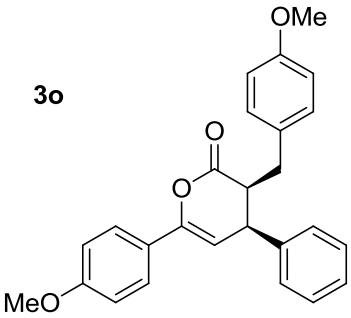
Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.950	60996251	546209	21.305	32.785
2	47.232	61384730	427809	21.440	25.678
3	56.802	82122744	363759	28.684	21.834
4	75.699	81799909	328255	28.571	19.703
Total		286303633	1666032	100.000	100.000

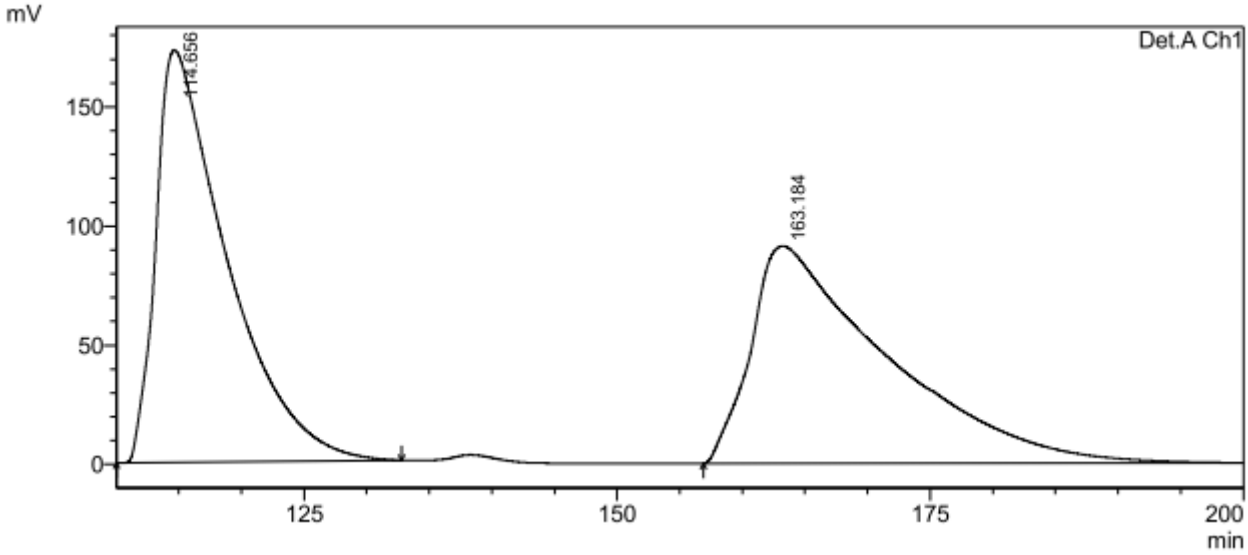


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	48.794	10761407	68292	7.132	11.646
2	59.577	139875839	516624	92.697	88.099
3	81.490	258518	1499	0.171	0.256
Total		150895763	586415	100.000	100.000

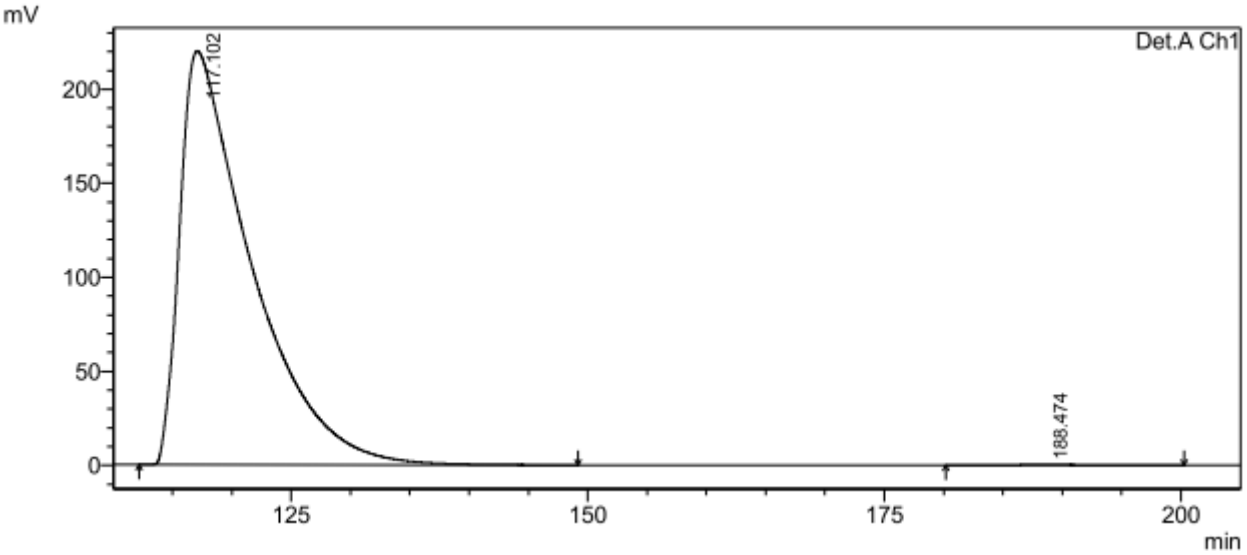
3o





UV Detector Ch1 254nm

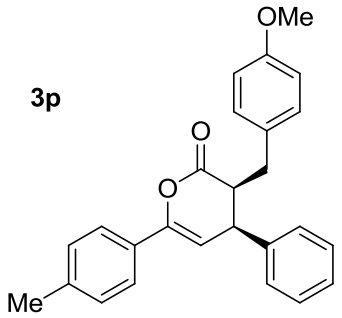
Peak#	Ret. Time	Area	Height	Area %	Height %
1	114.656	68070330	172834	49.697	65.460
2	163.184	68901580	91196	50.303	34.540
Total		136971910	264030	100.000	100.000

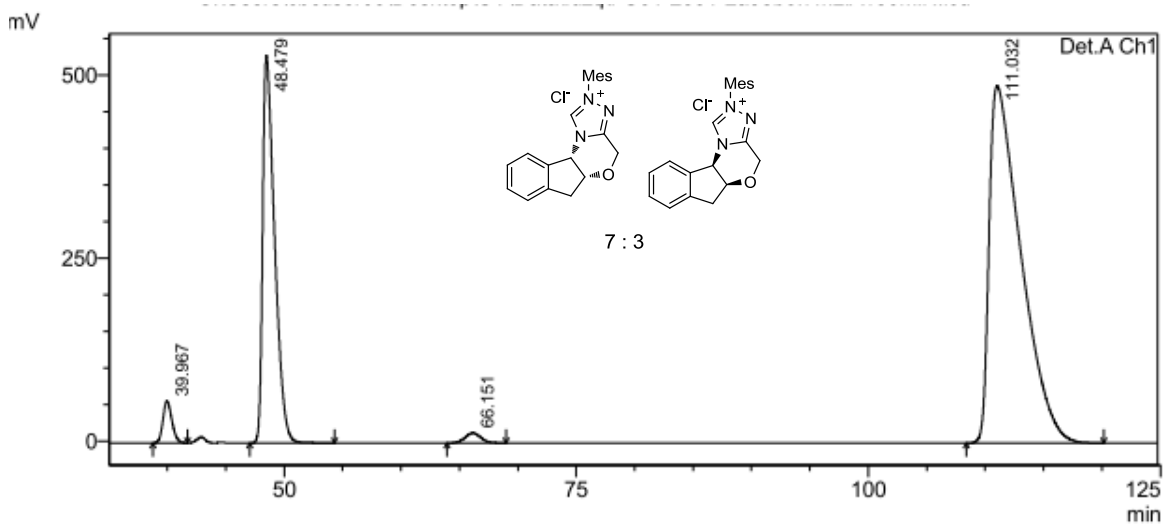


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	117.102	92411642	219968	99.805	99.819
2	188.474	180238	400	0.195	0.181
Total		92591880	220367	100.000	100.000

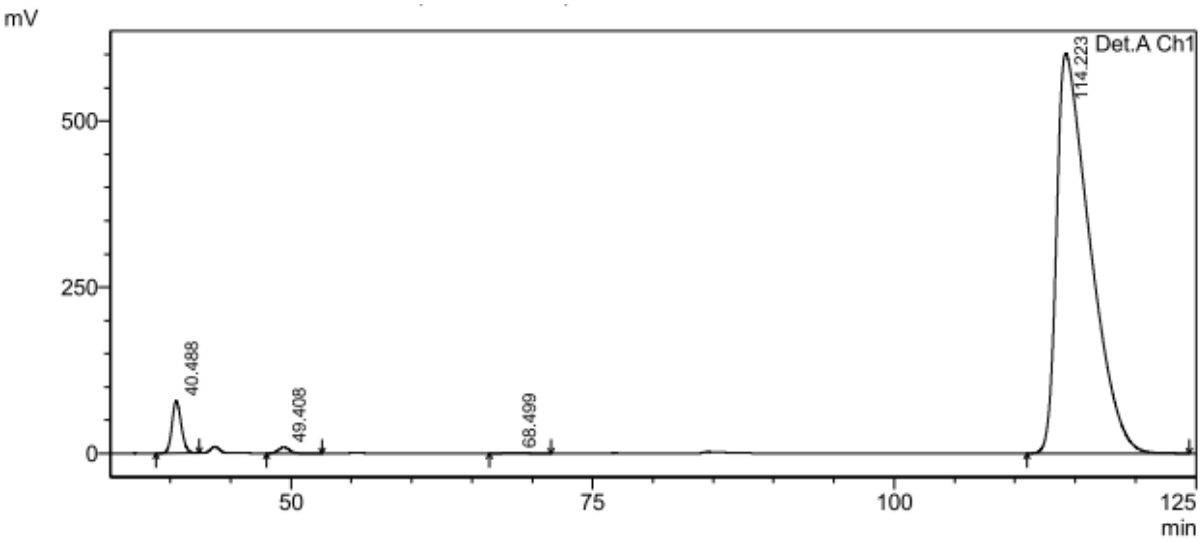
3p





UV Detector Ch1 254nm

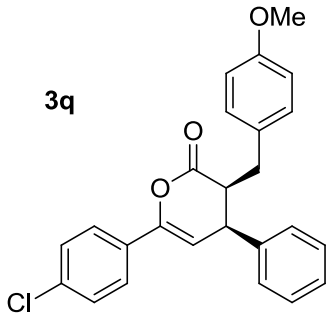
Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.967	3060985	57383	2.277	5.269
2	48.479	37710060	529565	28.046	48.630
3	66.151	1290742	13621	0.960	1.251
4	111.032	92394332	488402	68.717	44.850
Total		134456119	1088971	100.000	100.000

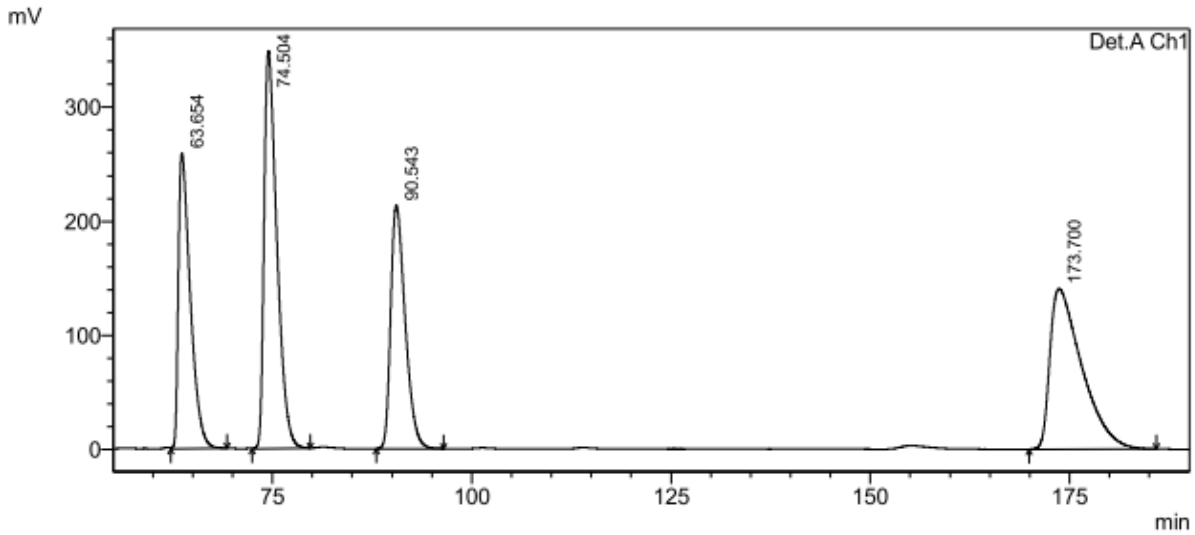


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.488	4234013	78664	3.518	11.398
2	49.408	582565	9204	0.484	1.334
3	68.499	112518	905	0.093	0.131
4	114.223	115431446	601403	95.905	87.138
Total		120360542	690177	100.000	100.000

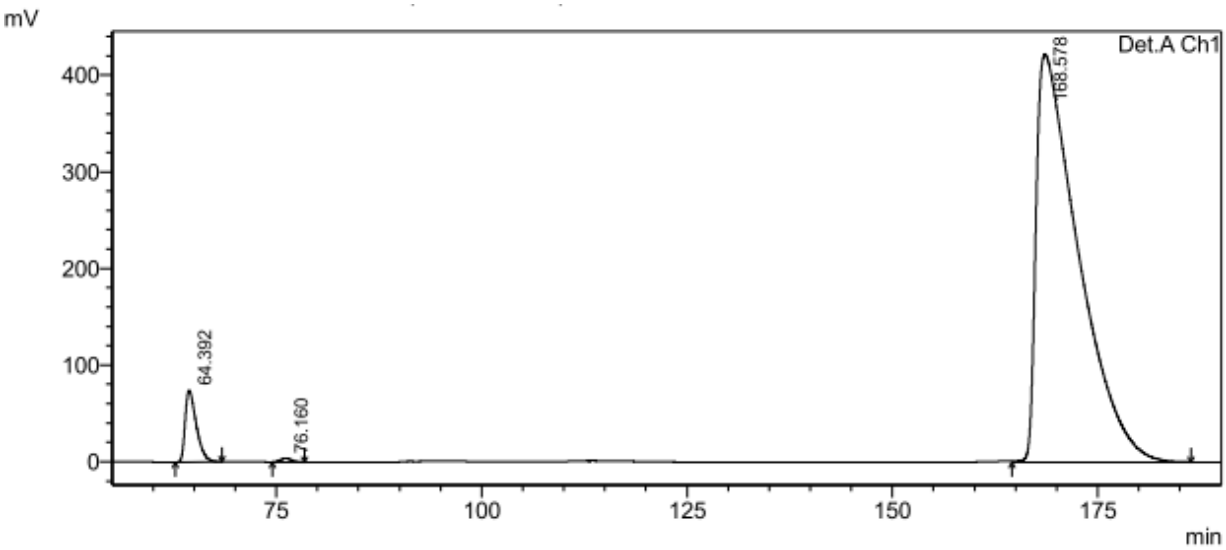
3q





UV Detector Ch1 254nm

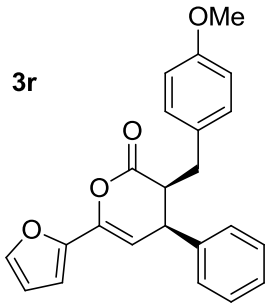
Peak#	Ret. Time	Area	Height	Area %	Height %
1	63.654	26949024	259120	20.420	26.954
2	74.504	38870364	348233	29.453	36.223
3	90.543	26996745	213379	20.456	22.196
4	173.700	39158832	140617	29.671	14.627
Total		131974965	961349	100.000	100.000

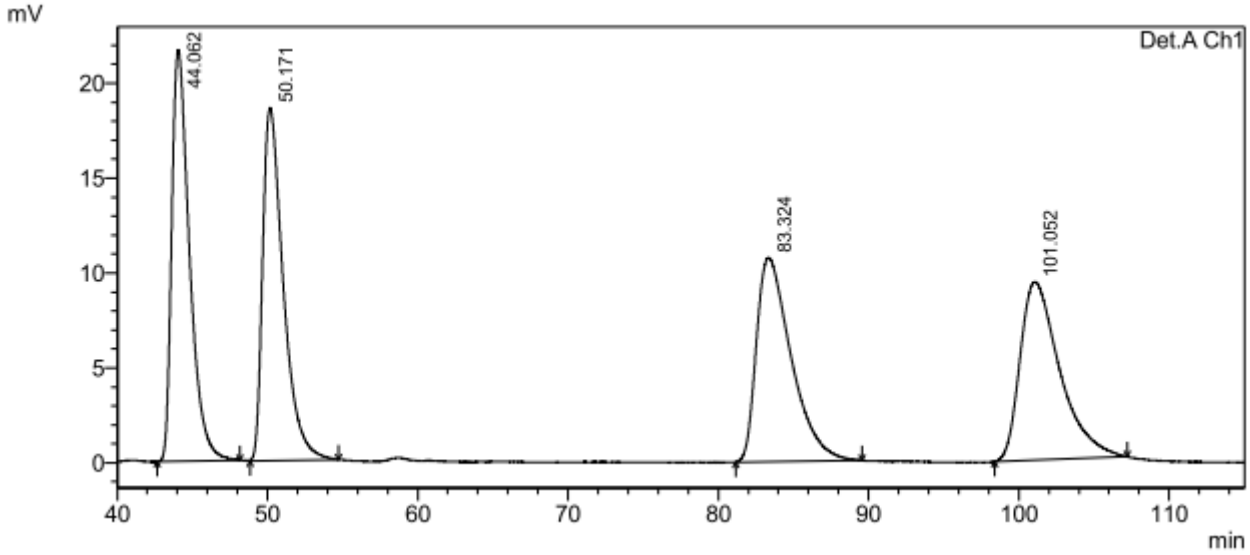


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	64.392	7053045	74355	4.452	14.869
2	76.160	362383	3706	0.229	0.741
3	168.578	151025683	421999	95.320	84.390
Total		158441111	500061	100.000	100.000

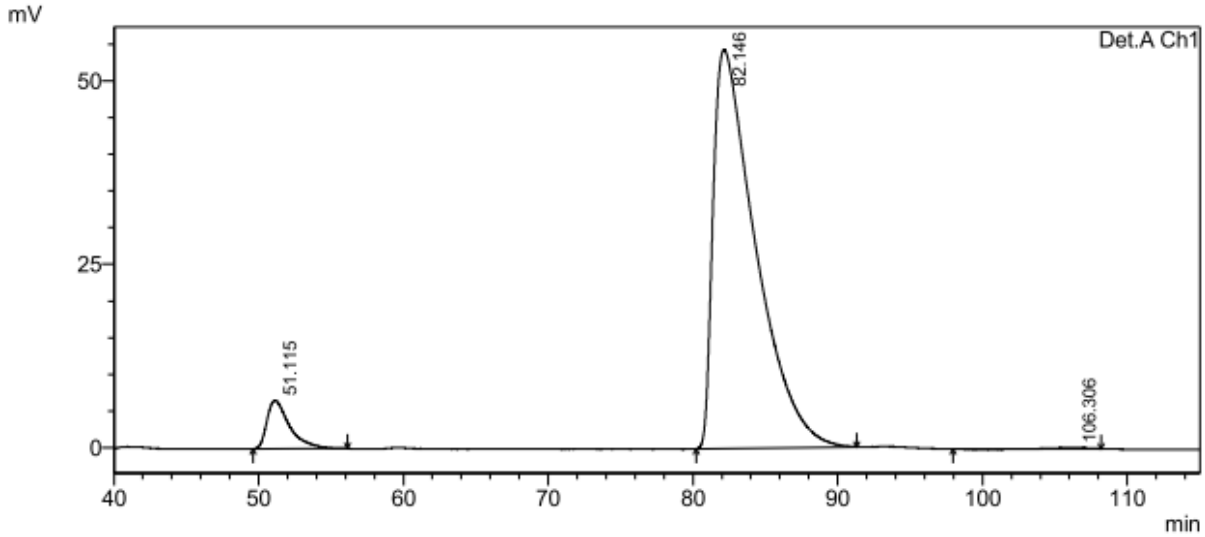
3r





UV Detector Ch1 254nm

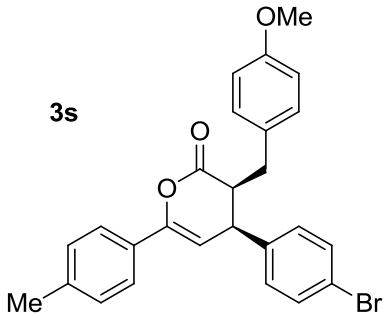
Peak#	Ret. Time	Area	Height	Area %	Height %
1	44.062	1786620	21670	25.436	35.871
2	50.171	1770039	18580	25.200	30.755
3	83.324	1733993	10762	24.687	17.814
4	101.052	1733212	9400	24.676	15.560
Total		7023865	60412	100.000	100.000

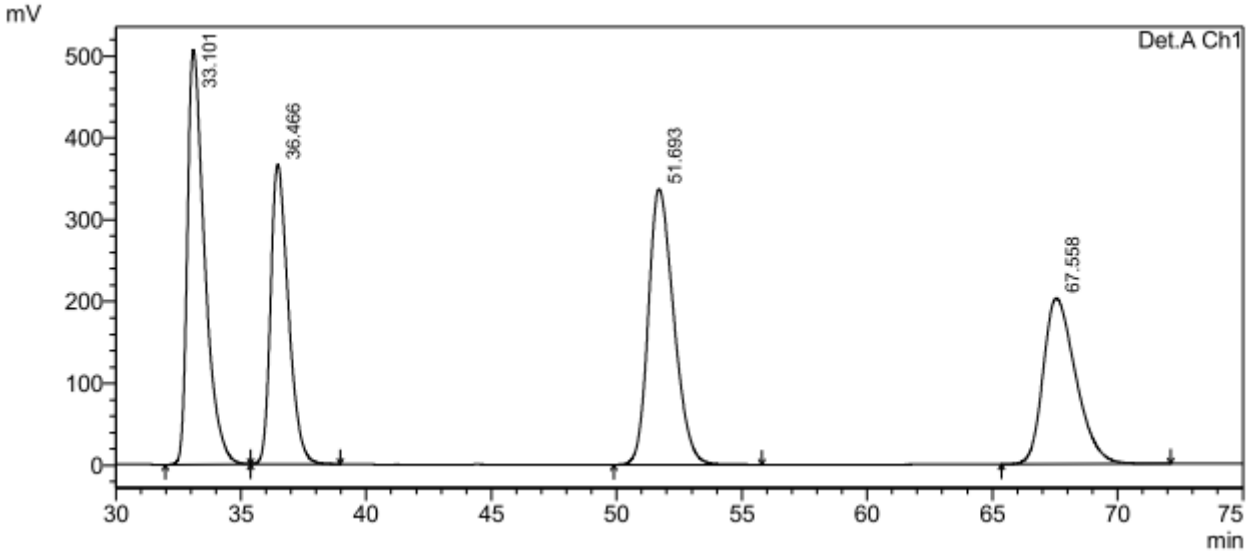


UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	51.115	723181	6617	6.131	10.826
2	82.146	11061056	54366	93.781	88.945
3	106.306	10321	140	0.088	0.229
Total		11794557	61123	100.000	100.000

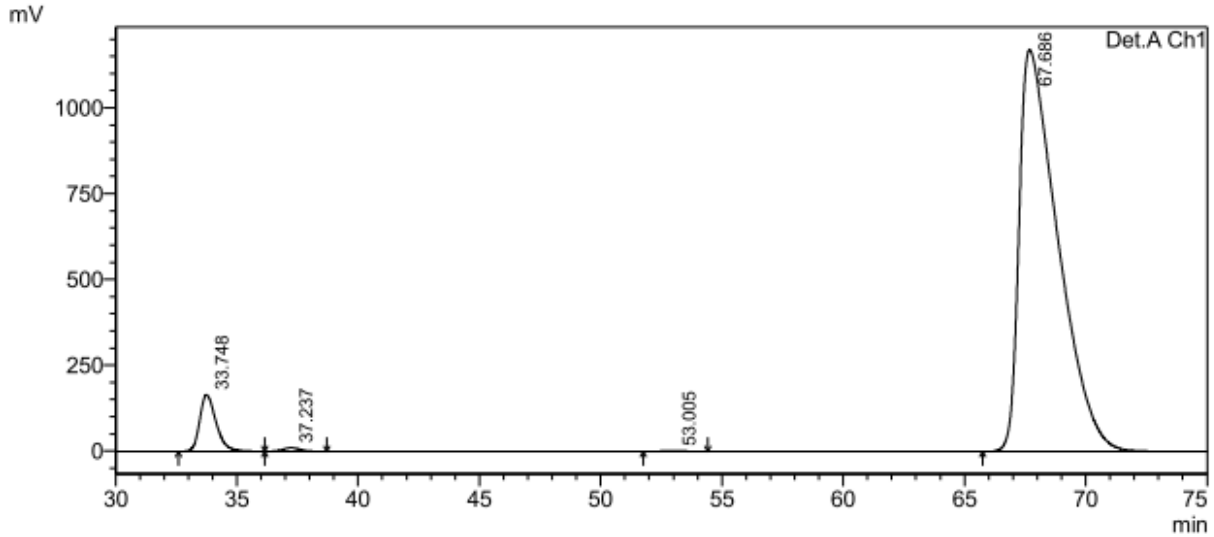
3s





UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.101	24288572	506612	28.742	35.850
2	36.466	18052242	366534	21.362	25.938
3	51.693	23777385	337132	28.137	23.857
4	67.558	18386407	202859	21.758	14.355
Total		84504606	1413136	100.000	100.000



UV Detector Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.748	7751428	164880	5.597	12.223
2	37.237	510597	10200	0.369	0.756
3	53.005	154129	2229	0.111	0.165
4	67.686	130087588	1171616	93.924	86.856
Total		138503742	1348925	100.000	100.000