Electronic Supplementary Material (ESI) for ChemComm.

Supporting information

Copper-catalyzed asymmetric 1,6-conjugate addition of in situ generated *para*-quinone methides with β-ketoesters

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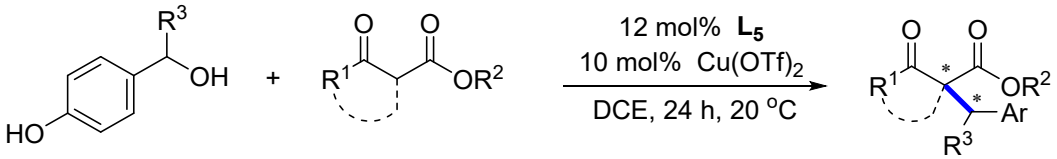
1. General Information

All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. ^{1}H NMR spectra were recorded on Bruker (400 MHz), Bruker AVANCE III (500 MHz) or Bruker ASCEND (600 MHz) in $CDCl_3$ using residual solvent signals as the internal standard ($CDCl_3$ δ = 7.26 ppm). ^{13}C NMR spectra were recorded at 101 MHz (Bruker), 126 MHz (Bruker AVANCE III) or 151 MHz (Bruker ASCEND) in $CDCl_3$ using solvent signals as the internal standard ($CDCl_3$ δ = 77.16 ppm). High-resolution electrospray ionization mass spectra (HR-ESI-MS) were recorded on an Agilent 6545 Q-TOF LCMS spectrometer equipped with an ESI source and controlled by using MassHunter software. Melting points (m.p.) were obtained using a Büchi B-545 apparatus and uncorrected. Chiral HPLC analyses were performed using JASCO LC-2000 Plus and Agilent 1260 chromatography. Chiralpak IA, IB, IC, ID and AD-H columns were purchased from Daicel Chemical Industries (Shanghai, China). Optical rotations were measured on a Rudolph Autopol IV polarimeter. Column chromatography and flash chromatography experiments were conducted using silica gel GF254 (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC experiments were carried out on glass-backed silica plates. The 4-hydroxybenzyl alcohol **1**[1] and β-indanone ester **2a**-**2g** and **2i**[2], **2h**[3], **2o**[4] were prepared according to the reported literature procedures.

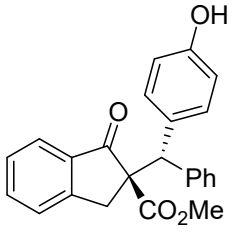
2. General procedure for the synthesis of 3



1 **2** **3** Ar=4-OHPh

An oven-dried Schlenk flask was charged with $Cu(OTf)_2$ (0.01 mmol), ligand $\mathbf{L_5}$ (0.012 mmol), DCE (1.5 mL) and a stir bar. The reaction mixture was stirred at room temperature for 1h. Then β-ketoesters **2** (0.12 mmol) was added, the reaction solution was stirred for 30 min, and then 4-hydroxybenzyl alcohol **1** (0.1 mmol) was added to react at 20 °C for 24 h. After completion, the mixture was concentrated in vacuum. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate/petroleum ether (1:4) to afford the producs **3**.

3. Characterization data of product 3



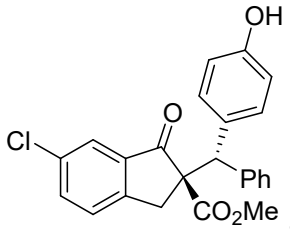
3a: major diastereomer

Methyl (R)-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 85% as a white solid, mp: 63-65 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.50 (qd, *J* = 7.1, 1.2 Hz, 1H), 7.38 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.29 – 7.28 (m, 2H), 7.25 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.05 (d, *J* = 4.3 Hz, 2H), 6.91 – 6.87 (m, 2H), 6.53 – 6.48 (m, 2H), 5.62 (s, 1H), 5.51 (s, 1H), 4.24 (d, *J* = 17.5 Hz, 1H), 3.57 (d, *J* = 17.1 Hz, 1H), 3.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 201.67, 169.88, 154.51,

154.17, 141.71, 135.57, 134.57, 131.55, 131.12, 128.57, 128.52, 127.59, 126.53, 126.13, 124.67, 114.98, 66.67, 53.58, 53.08, 33.57. $[\alpha]_D^{30}$ = -230.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID column at 254 nm (n-hexane/*i*-PrOH = 80/20), 1.0 mL/min; Major enantiomer: t_R = 16.3 min, 25.4 min; minor enantiomer: t_R = 15.5 mim, 29.8 min; 2.6:1 dr, 93/97% ee. HRMS (ESI) calcd for $C_{24}H_{20}O_4Na$ *m/z* $[M+Na]^+$: 395.1254, found: 395.1258.



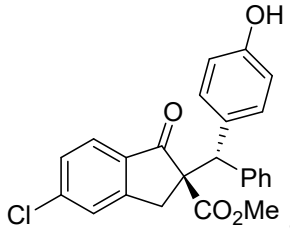
3b: major diastereomer

Methyl (R)-6-chloro-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 79% as a white solid, mp: 84-86 °C.

^1H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.36 – 7.29 (m, 3H), 7.27 – 7.23 (m, 3H), 6.92 – 6.84 (m, 2H), 6.58 – 6.48 (m, 2H), 5.49 (s, 1H), 5.25 (s, 1H), 4.20 (d, *J* = 17.1 Hz, 1H), 3.52 (d, *J*= 17.1 Hz, 1H), 3.50 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 200.3, 169.5, 154.5, 152.2, 141.4, 136.0, 135.5, 133.9, 131.5, 131.1, 128.6, 128.5, 127.3, 126.6, 124.3, 115.1, 67.2, 53.6, 53.2, 33.2. $[\alpha]_D^{30}$ = -314.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA and IB column respectively and at 254 nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 8.1 min, 9.2 min; minor enantiomer: t_R = 7.9 min, 15.6 min. 2.7:1 dr, 90/93% ee. HRMS (ESI) calcd for $C_{24}H_{19}ClO_4Na$ *m/z* $[M+Na]^+$: 429.0864, found:429.0871.

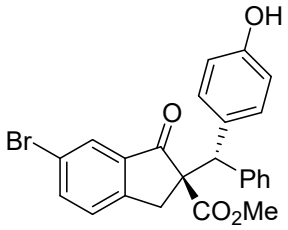


3c: major diastereomer

Methyl (R)-5-chloro-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 83% as a white solid, mp: 79-83 °C.

^1H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.35 – 7.31 (m, 2H), 7.28 – 7.23 (m, 4H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.57 – 6.50 (m, 2H), 5.49 (s, 1H), 5.15 (s, 1H), 4.22 (d, *J* = 17.3 Hz, 1H), 3.54 (d, *J* = 17.1 Hz, 1H), 3.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.08, 169.52, 155.44, 154.42, 142.16, 141.43, 133.05, 131.53, 131.09, 128.58, 128.51, 128.47, 126.62, 126.35, 125.69, 115.06, 66.79, 53.55, 53.17, 33.29. $[\alpha]_D^{30}$ = -283.00(c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA and IC column respectively and at 254 nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 6.9 min, 8.2 min; minor enantiomer: t_R = 11.0 min, 15.3 min. 3:1 dr, 93/93% ee. HRMS (ESI) calcd for $C_{24}H_{19}ClO_4Na$ *m/z* $[M+Na]^+$: 429.0864, found: 429.0871.

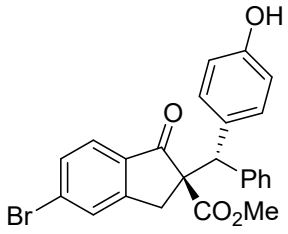


3d: major diastereomer

Methyl (R)-6-bromo-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 74% as a yellow solid, mp: 85-88 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 1.9 Hz, 1H), 7.60 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.28 – 7.23 (m, 4H), 6.91 – 6.85 (m, 2H), 6.56 – 6.51 (m, 2H), 5.49 (s, 1H), 5.20 (s, 1H), 4.18 (d, *J* = 17.1 Hz, 1H), 3.50 (d, *J* = 17.1 Hz, 1H), 3.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.2, 169.4, 154.4, 152.6, 141.4, 138.2, 136.4, 131.5, 131.1, 128.6, 128.5, 127.7, 127.4, 126.6, 121.7, 115.1, 67.1, 53.6, 53.2, 33.2. $[\alpha]_D^{30}$ = -318.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254 nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 8.2 min, 17.6 min; minor enantiomer: t_R = 8.0 min, 16.9 min. 2.2:1 dr, 91/91% ee. HRMS (ESI) calcd for $C_{24}H_{19}BrO_4Na$ *m/z* $[M+Na]^+$: 473.0359, found: 473.0367.

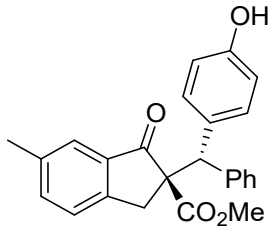


3e: major diastereomer

Methyl (R)-5-bromo-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 71% as a yellow solid, mp: 102-104 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 – 7.55 (m, 1H), 7.52 (d, J = 8.2 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.35 – 7.31 (m, 2H), 7.27 – 7.23 (m, 3H), 6.91 – 6.83 (m, 2H), 6.56 – 6.50 (m, 2H), 5.49 (s, 1H), 5.19 (s, 1H), 4.22 (d, J = 17.1 Hz, 1H), 3.54 (d, J = 17.2 Hz, 1H), 3.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.30, 169.45, 155.53, 154.43, 141.42, 133.43, 131.52, 131.33, 131.13, 131.09, 129.45, 128.58, 128.47, 126.62, 125.74, 115.07, 66.73, 53.53, 53.17, 33.23. $[\alpha]_D^{30}$ = -223.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA and IC column respectively and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 7.1 min, 8.4 min; minor enantiomer: t_R = 10.8 min, 14.5 min. 2.2:1 dr, 98/>99% ee. HRMS (ESI) calcd for $C_{24}H_{19}BrO_4Na$ *m/z* $[M+Na]^+$: 473.0359, found:473.0364.

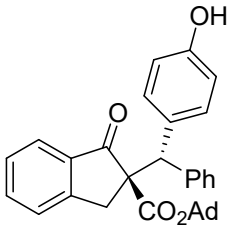


3f: major diastereomer

Methyl (R)-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-6-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 84% as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 1H), 7.35 – 7.30 (m, 3H), 7.29 – 7.22 (m, 4H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.52 (d, *J* = 8.3 Hz, 2H), 5.50 (s, 1H), 5.31 (s, 1H), 4.17 (d, *J* = 17.0 Hz, 1H), 3.50 (d, *J* = 16.8 Hz, 1H), 3.47 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 201.52, 169.93, 154.33, 151.58, 141.80, 137.54, 136.90, 134.75, 131.78, 131.13, 128.59, 128.49, 126.49, 125.77, 124.52, 114.97, 67.00, 53.50, 53.01, 33.19, 20.98. $[\alpha]_D^{30}$ = -289.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID and IA column respectively and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 8.4 min, 15.6 min; minor enantiomer: t_R = 9.2 min, 20.5 min. 2.6:1 dr, >99/84% ee. HRMS (ESI) calcd for $C_{25}H_{22}O_4Na$ *m/z* $[M+Na]^+$: 409.1410, found: 409.1419.

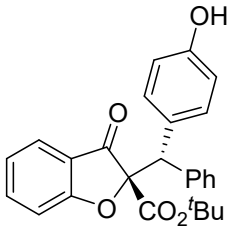


3g: major diastereomer

(3S,5S,7S)-Adamantan-1-yl (R)-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 72% as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.47 (dt, *J* = 7.4, 1.2 Hz, 1H), 7.37 – 7.30 (m, 5H), 7.28 – 7.23 (m, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.52 (d, *J* = 8.2 Hz, 2H), 5.47 (s, 1H), 5.45 (s, 1H), 4.15 (d, *J* = 16.6 Hz, 1H), 3.45 (d, *J* = 16.7 Hz, 1H), 2.01 (p, *J* = 3.2 Hz, 3H), 1.83 – 1.79 (m, 3H), 1.69 – 1.64 (m, 3H), 1.51 (q, *J* = 12.2, 11.6 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.07, 167.57, 154.42, 154.26, 142.28, 135.27, 134.66, 132.09, 131.06, 128.86, 128.42, 127.36, 126.37, 126.03, 124.51, 114.96, 82.25, 67.78, 53.55, 40.41, 36.01, 33.65, 30.70. $[\alpha]_D^{30}$ = -160.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254 nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 6.6 min, 12.9 min; minor enantiomer: t_R = 6.7 min, 16.2 min. 7.3:1 dr, 99/98% ee. HRMS (ESI) calcd for $C_{33}H_{32}O_4Na$ *m/z* $[M+Na]^+$: 515.2193, found: 515.2198.



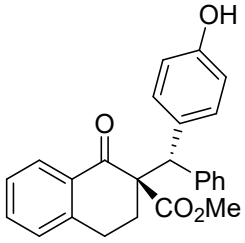
3h: major diastereomer

Tert-butyl (S)-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-3-oxo-2,3-dihydrobenzofuran -2-carboxylate

Yield 87% as a yellow solid, mp: 77-81°C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.61 (m, 2H), 7.56 – 7.50 (m, 2H), 7.39 – 7.32 (m, 2H), 7.24 – 7.20 (m, 1H), 7.12 – 7.07 (m, 2H), 6.99 – 6.91 (m, 2H), 6.53 – 6.47 (m, 2H), 5.11 (s, 1H), 4.97 (s, 1H), 1.18 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.61, 172.66, 163.60, 154.49, 140.54, 138.39, 130.99, 129.64, 128.68, 128.56, 126.80, 124.58, 122.30, 119.59, 114.84, 113.11, 94.76, 83.82, 54.96, 27.31. $[\alpha]_D^{30}$ = -187.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak AD-H column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 0.8 mL/min; Major enantiomer: t_R = 6.4min, 8.7min; minor enantiomer: t_R = 10.8 min, 11.8 min. 2.8:1 dr, 93/78% ee. HRMS (ESI) calcd

for $C_{26}H_{24}O_5$ *m/z* $[M-H]^-$: 415.1551, found: 415.1557.

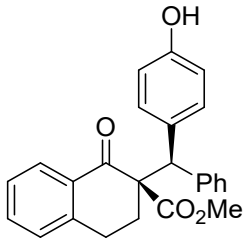


3i: major diastereomer

Methyl (R)-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-1,2,3,4-tetrahydronaphthalene -2-carboxylate

Yield 60% as a black solid, mp: 58-63°C.

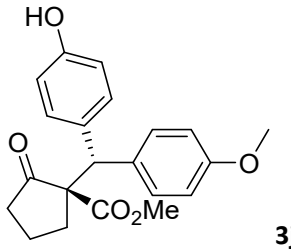
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.25 (s, 1H), 7.89 (d, *J* = 1.5 Hz, 1H), 7.42 – 7.36 (m, 4H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.22 (m, 3H), 7.19 – 7.16 (m, 1H), 6.64 – 6.59 (m, 2H), 4.98 (s, 1H), 3.34 (s, 3H), 2.98 – 2.95 (m, 1H), 2.73 – 2.69 (m, 1H), 2.22 (tt, *J* = 13.6, 12.5, 5.3 Hz, 2H). ^{13}C NMR (151 MHz, DMSO) δ 193.28, 170.45, 156.19, 143.38, 141.30, 134.21, 132.48, 131.75, 131.08, 130.53, 129.43, 128.37, 127.92, 127.21, 126.95, 115.07, 62.63, 60.22, 52.61, 26.12, 14.56. $[\alpha]_D^{30}$ = 84.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 1 mL/min; Major enantiomer: t_R = 8.8 min, 10.8 min; minor enantiomer: t_R = 7.3 min, 9.9 min. 1.2:1 dr, 80/84% ee. HRMS (ESI) calcd for $C_{25}H_{21}O_4$ *m/z* $[M-H]^-$: 385.1445, found: 385.1449.



3i: minor diastereomer

methyl (R)-2-((R)-(4-hydroxyphenyl)(phenyl)methyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.87 (d, *J* = 1.5 Hz, 1H), 7.52 (td, *J* = 7.4, 1.5 Hz, 2H), 7.30 – 7.25 (m, 4H), 7.22 – 7.19 (m, 3H), 7.16 – 7.11 (m, 1H), 6.68 – 6.64 (m, 2H), 4.96 (s, 1H), 3.33 (s, 3H), 3.12 – 2.99 (m, 2H), 2.94 – 2.91 (m, 1H), 2.69 – 2.64 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 193.36, 170.56, 156.50, 143.38, 141.73, 134.21, 132.42, 131.85, 131.08, 130.77, 130.62, 129.43, 128.22, 127.89, 126.54, 115.19, 62.63, 60.22, 52.61, 26.16, 21.23.

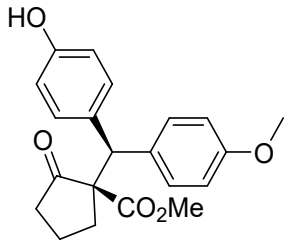


3j: major diastereomer

Methyl (R)-1-((R)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-2-oxocyclopentane-1-carboxylate

Yield 96% as a yellow oil.

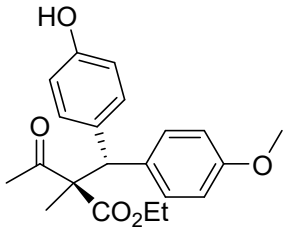
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.33 (s, 1H), 6.83 (d, *J* = 1.2 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.66 (d, *J* = 8.6 Hz, 2H), 6.62 (d, J = 8.6 Hz, 2H), 4.89 (s, 1H), 3.72 (s, 3H), 3.37 (s, 3H), 2.83 – 2.79 (m, 1H), 2.28 – 2.22 (m, 2H), 1.69 – 1.59 (m, 2H), 1.50 – 1.46 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 212.90, 168.92, 157.48, 155.92, 133.44, 130.76, 130.49, 129.65, 114.90, 113.57, 65.79, 54.90, 53.03, 52.35, 37.95, 28.89, 19.22. $[\alpha]_D^{30}$ = -45.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak AD-H column and at 254 nm (n-hexane/*i*-PrOH = 95/5), 0.8 mL/min; Major enantiomer: t_R = 49.6 min, 88.4 min; minor enantiomer: t_R = 56.7 min, 75.7 min. 1.1:1 dr, 89/93% ee. HRMS (ESI) calcd for $C_{21}H_{21}O_5$ *m/z* [M-H]$^-$: 353.1394, found: 353.1398.



3j: minor diastereomer

methyl (R)-1-((S)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-2-oxocyclopentane-1-carboxylate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.13 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 1.3 Hz, 2H), 4.88 (s, 1H), 3.69 (s, 3H), 3.38 (s, 3H), 2.90 – 2.83 (m, 1H), 2.21 – 2.11 (m, 2H), 1.78 – 1.69 (m, 2H), 1.56 – 1.50 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 212.90, 168.90, 157.48, 155.64, 132.54, 131.43, 130.79, 129.67, 115.02, 113.46, 65.85, 54.93, 53.03, 52.35, 37.95, 29.04, 19.20.

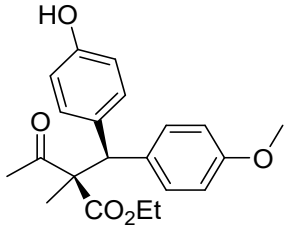


3k: major diastereomer

Ethyl 2-((R)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-2-methyl-3-oxobutanoate

Yield 63% as a yellow oil.

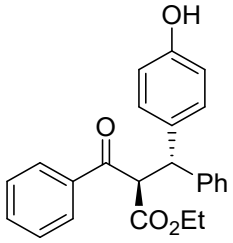
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.30 (s, 1H), 7.20 (d, *J* = 2.0 Hz, 2H), 7.08 (d, *J* = 2.6 Hz, 2H), 6.81 (d, *J* = 2.2 Hz, 2H), 6.64 (d, *J* = 1.7 Hz, 2H), 4.96 (s, 1H), 3.99 – 3.93 (m, 2H), 3.70 (s, 3H), 2.02 (s, 3H), 1.41 (s, 3H), 1.03 – 1.02 (m, 3H). ^{13}C NMR (126 MHz, DMSO) δ 204.64, 171.53, 158.04, 156.19, 133.89, 131.90, 131.21, 131.09, 115.26, 113.80, 65.06, 61.55, 55.39, 52.55, 27.27, 18.27, 14.03. $[\alpha]_D^{30}$ = 6.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IC column and at 254 nm (n-hexane/*i*-PrOH = 95/5), 0.8 mL/min; Major enantiomer: t_R = 30.5 min, 41.5 min; minor enantiomer: t_R = 33.8 min, 38.0 min. 1.1:1 dr, 82/79% ee. HRMS (ESI) calcd for $C_{21}H_{23}O_5$ *m/z* [M-H]$^-$: 355.1551, found: 355.1559.



3k: minor diastereomer

Ethyl (R)-2-((S)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-2-methyl-3-oxobutanoate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 7.22 (d, *J* = 2.0 Hz, 2H), 7.10 (d, *J* = 2.6 Hz, 2H), 6.80 (d, *J* = 2.1 Hz, 2H), 6.62 (d, *J* = 1.7 Hz, 2H), 4.96 (s, 1H), 4.04 – 3.97 (m, 2H), 3.70 (s, 3H), 2.02 (s, 3H), 1.42 (s, 3H), 1.03 – 0.97 (m, 3H). ^{13}C NMR (126 MHz, DMSO) δ 204.64, 171.46, 158.07, 156.26, 133.34, 131.31, 131.27, 131.03, 115.10, 113.67, 65.08, 61.55, 55.39, 52.48, 27.25, 18.18, 14.03.

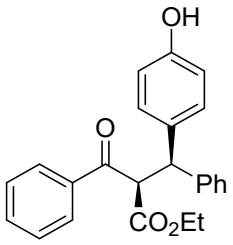


3l: major diastereomer

Methyl (2R,3S)-2-benzoyl-3-(4-hydroxyphenyl)-3-phenylpropanoate

Yield 83% as a white solid, mp: 69-72°C.

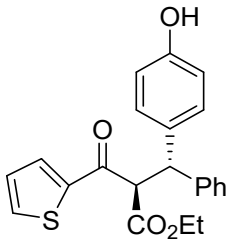
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.23 (s, 1H), 8.09 (dd, *J* = 2.9, 1.4 Hz, 2H), 7.53 – 7.50 (m, 3H), 7.41 – 7.36 (m, 2H), 7.34 – 7.30 (m, 2H), 7.15 – 7.10 (m, 2H), 7.05 – 6.99 (m, 1H), 6.71 – 6.62 (m, 2H), 5.84 (d, *J* = 2.8 Hz, 1H), 4.75 (d, *J* = 2.1 Hz, 1H), 3.87 – 3.82 (m, 2H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO) δ 193.61, 167.99, 156.39, 143.32, 136.46, 134.34, 132.84, 129.65, 129.26, 129.08, 128.71, 128.47, 126.47, 115.46, 61.21, 58.34, 50.60, 14.06. $[\alpha]_D^{30}$ = 10.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IC column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 1.0 mL/min; Major enantiomer: t_R = 5.9 min, 14.7 min; minor enantiomer: t_R = 7.3 min, 11.8 min. 1.1:1 dr, 76/82% ee. HRMS (ESI) calcd for $C_{24}H_{21}O_4$ *m/z* [M-H]$^-$: 373.1445, found: 373.1442.



3l: minor diastereomer

Ethyl (2R,3R)-2-benzoyl-3-(4-hydroxyphenyl)-3-phenylpropanoate

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.12 (s, 1H), 8.11 (dd, *J* = 2.9, 1.2 Hz, 2H), 7.68 – 7.63 (m, 2H), 7.55 – 7.53 (m, 3H), 7.29 – 7.24 (m, 2H), 7.22 – 7.18 (m, 2H), 7.18 – 7.15 (m, 1H), 6.54 – 6.48 (m, 2H), 5.86 (d, *J* = 2.8 Hz, 1H), 4.77 (d, *J* = 2.1 Hz, 1H), 3.82 – 3.73 (m, 2H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO) δ 193.74, 167.97, 156.09, 143.57, 136.36, 134.37, 133.05, 129.28, 129.25, 129.21, 128.65, 127.91, 126.76, 115.42, 61.17, 58.05, 50.69, 13.99.

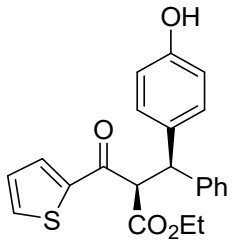


3m: major diastereomer

Ethyl (2R,3S)-3-(4-hydroxyphenyl)-3-phenyl-2-(thiophene-2-carbonyl)propanoate

Yield 89% as a yellow oil.

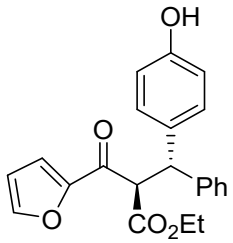
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.17 (s, 1H), 8.42 – 8.39 (m, 2H), 7.53 – 7.50 (m, 2H), 7.34 – 7.32 (m, 2H), 7.28 (d, *J* = 0.9 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.54 – 6.52 (m, 2H), 5.69 (d, *J* = 1.2 Hz, 1H), 4.72 (d, *J* = 3.1 Hz, 1H), 3.86 – 3.81 (m, 2H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 186.47, 167.86, 156.16, 143.82, 143.29, 137.09, 135.96, 132.75, 129.55, 129.16, 128.67, 128.36, 126.77, 115.49, 61.23, 59.04, 50.54, 14.02. $[\alpha]_D^{30}$ = 7.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IC column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 1.0 mL/min; Major enantiomer: t_R = 7.5 min, 20.5 min; minor enantiomer: t_R = 9.6 min, 18.1 min. 1.3:1 dr, 82/89% ee. HRMS (ESI) calcd for $C_{22}H_{19}O_4S$ *m/z* [M-H]$^-$: 379.1011, found: 379.1010.



3m: minor diastereomer

Ethyl (2R,3R)-3-(4-hydroxyphenyl)-3-phenyl-2-(thiophene-2-carbonyl)propanoate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 8.09 – 7.98 (m, 2H), 7.42 – 7.38 (m, 2H), 7.31 – 7.29 (m, 2H), 7.28 (d, *J* = 4.6 Hz, 1H), 7.19 – 7.11 (m, 3H), 6.69 – 6.64 (m, 2H), 5.71 (d, *J* = 1.3 Hz, 1H), 4.74 (d, *J* = 3.1 Hz, 1H), 3.93 – 3.86 (m, 2H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 186.35, 167.86, 156.40, 143.68, 143.22, 137.06, 135.87, 132.82, 129.39, 129.16, 128.73, 127.98, 126.59, 115.44, 61.28, 59.24, 50.43, 14.10.

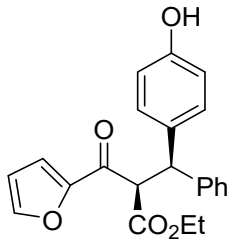


3n: major diastereomer

Ethyl (2R,3S)-2-(furan-2-carbonyl)-3-(4-hydroxyphenyl)-3-phenylpropanoate

Yield 75% as a yellow solid, mp: 62-66°C.

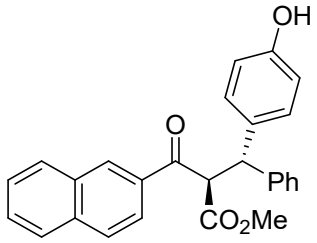
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.18 (s, 1H), 8.02 – 7.98 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.32 – 7.24 (m, 4H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 4.6 Hz, 1H), 6.52 (d, *J* = 8.5 Hz, 2H), 5.49 (s, 1H), 4.71 (d, *J* = 3.6 Hz, 1H), 3.91 – 3.77 (m, 2H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 181.17, 167.78, 156.21, 151.79, 149.66, 143.31, 132.52, 129.19, 128.68, 128.26, 126.76, 122.20, 115.48, 113.30, 61.21, 58.59, 50.32, 14.06. $[\alpha]_D^{30}$ = 43.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IC column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 1.0 mL/min; Major enantiomer: t_R = 16.5 min, 20.0 min; minor enantiomer: t_R = 10.8 min, 24.5 min. 1.2:1 dr, 85/85% ee. HRMS (ESI) calcd for $C_{22}H_{19}O_5$ *m/z* [M-H]$^-$: 363.1238, found: 363.1240.



3n: minor diastereomer

Ethyl (2R,3R)-2-(furan-2-carbonyl)-3-(4-hydroxyphenyl)-3-phenylpropanoate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 7.94 – 7.89 (m, 2H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 1.5 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.74 (d, *J* = 4.3 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 2H), 5.47 (s, 1H), 4.69 (d, *J* = 3.7 Hz, 1H), 3.91 – 3.86 (m, 2H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 181.27, 167.78, 156.39, 151.70, 149.66, 143.02, 132.82, 129.44, 128.73, 128.02, 126.65, 122.20, 115.45, 113.30, 61.26, 58.41, 50.21, 14.13.

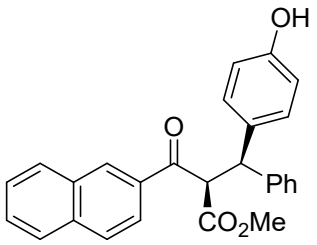


3o: major diastereomer

Methyl (2R,3S)-2-(2-naphthoyl)-3-(4-hydroxyphenyl)-3-phenylpropanoate

Yield 50% as a yellow oil.

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.33 (s, 1H), 9.02 (s, 1H), 8.18 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 6.4 Hz, 2H), 7.95 (d, *J* = 1.7 Hz, 1H), 7.73 – 7.69 (m, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.35 – 7.26 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 6.08 (d, J = 5.1 Hz, 1H), 4.85 (d, J = 4.7 Hz, 1H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 193.82, 168.58, 156.40, 143.34, 135.72, 133.74, 132.58, 132.00, 130.29, 129.65, 129.50, 129.22, 128.70, 128.30, 128.03, 127.62, 126.79, 126.52, 124.21, 115.56, 57.45, 52.71, 50.88. $[\alpha]_D^{30}$ = 8.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IC column and at 254 nm (n-hexane/*i*-PrOH = 80/20), 1.0 mL/min; Major enantiomer: t_R = 6.7 min, 17.0 min; minor enantiomer: t_R = 7.8 min, 14.1 min. 1.1:1 dr, 68/86% ee. HRMS (ESI) calcd for $C_{27}H_{21}O_4$ *m/z* $[M-H]^-$: 409.1445, found: 409.1442.

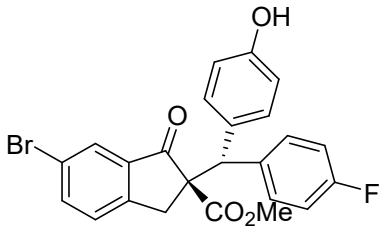


3o: minor diastereomer

Methyl (2R,3R)-2-(2-naphthoyl)-3-(4-hydroxyphenyl)-3-phenylpropanoate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 1H), 9.02 (s, 1H), 8.20 (d, *J* = 2.5 Hz, 1H), 7.98 – 7.96 (m, 2H), 7.95 – 7.93 (m, 1H), 7.69 – 7.64 (m, 2H), 7.59 – 7.55 (m, 2H), 7.26 – 7.21 (m, 2H), 7.10 (t, *J* = 7.6 Hz, 2H), 7.00 – 6.96 (m, 1H), 6.52 – 6.44 (m, 2H), 6.11 (d, *J* = 5.1 Hz, 1H), 4.82 (d, *J* = 4.7 Hz, 1H), 3.38 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 193.65, 168.58, 156.10, 143.53, 135.70, 133.66, 132.80, 132.58, 131.93, 130.29, 129.65, 129.22, 128.89, 128.76, 128.30, 128.14, 127.62, 126.79, 124.23,

115.45, 57.83, 52.66, 50.79.

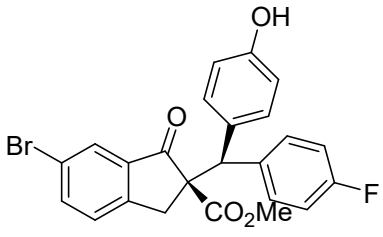


3p: major diastereomer

Methyl (R)-6-bromo-2-((R)-(4-fluorophenyl)(4-hydroxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 93% as a yellow solid, mp: 62-66 °C.

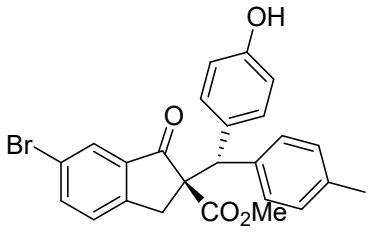
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 1.9 Hz, 1H), 7.61 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.25 – 7.20 (m, 2H), 7.05 – 6.99 (m, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.55 (d, *J* = 8.7 Hz, 2H), 5.46 (s, 1H), 5.39 (s, 1H), 4.15 (d, *J* = 17.0 Hz, 1H), 3.51 (s, 3H), 3.47 (d, *J* = 17.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.90, 169.30, 161.5(d, *J* = 245.6 Hz), 154.60, 152.45, 138.31, 137.20(d, J = 3.6 Hz), 136.30, 131.13, 130.95, 130.00 (d, *J* = 8.0 Hz), 127.66, 127.46, 121.78, 115.50(d, *J* = 21.1 Hz) 115.17, 67.10, 53.25, 52.87, 33.05. ^{19}F NMR (565 MHz, DMSO) δ -116.47. $[\alpha]_D^{30}$ = -257.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 8.4 min, 10.1 min; minor enantiomer: t_R = 8.2 min, 14.3 min. 1.9:1 dr, 86/91% ee. HRMS (ESI) calcd for $C_{24}H_{18}BrFO_4Na$ *m/z* $[M+Na]^+$: 491.0265, found:491.0267.



3p: minor diastereomer

Methyl (R)-6-bromo-2-((S)-(4-fluorophenyl)(4-hydroxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-Indene-2-carboxylate

^{1}H NMR (600 MHz, DMSO-d6) δ 9.38 (s, 1H), 7.79 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.72 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.08 – 7.05 (m, 2H), 7.05 – 7.01 (m, 2H), 6.95 – 6.90 (m, 2H), 6.76 – 6.70 (m, 2H), 5.24 (s, 1H), 4.03 (d, *J* = 7.0 Hz, 1H), 3.52 (d, *J* = 17.8 Hz, 1H), 3.46 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 199.83, 169.27, 161.18(d, *J* = 243.9 Hz), 156.42, 153.05, 138.80, 136.56(d, *J* = 3.0 Hz), 136.45, 131.86(d, *J* = 8.0 Hz), 131.35, 129.95, 129.15, 126.80, 121.57, 115.78, 115.33(d, *J* = 21.0 Hz), 66.74, 53.42, 33.52, 21.21.



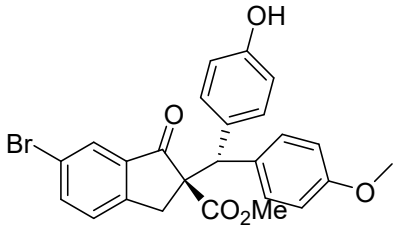
3q: major diastereomer

Methyl (R)-6-bromo-2-((S)-(4-hydroxyphenyl)(p-tolyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 52% as a brown oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.77 (m, 1H), 7.60 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.27 (d, *J* = 8.2 Hz,

1H), 7.13 (d, *J* = 1.2 Hz, 4H), 6.92 – 6.85 (m, 2H), 6.57 – 6.49 (m, 2H), 5.44 (s, 1H), 5.04 (s, 1H), 4.17 (d, *J* = 17.1 Hz, 1H), 3.51 (s, 3H), 3.49 (d, *J* = 17.0 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.18, 169.45, 154.32, 152.61, 138.28, 138.15, 136.46, 136.14, 131.76, 131.05, 129.24, 128.36, 127.65, 127.38, 121.65, 115.02, 67.15, 53.23, 53.17, 33.20, 21.00. $[\alpha]_D^{30}$ = -239.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 7.4 min, 12.9 min. 1.8:1 dr, 93% ee, --. HRMS (ESI) calcd for $C_{25}H_{21}BrO_4Na$ m/z $[M+Na]^+$: 487.0515, found: 487.0521.

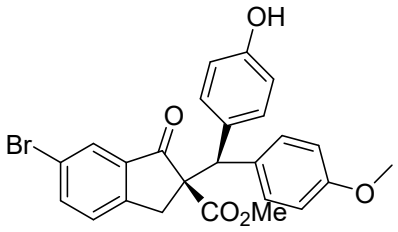


3r: major diastereomer

Methyl (R)-6-bromo-2-((R)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 71% as a yellow solid, mp: 72-76 °C.

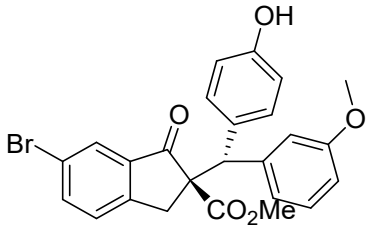
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.21 (s, 1H), 7.78 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.71 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.17 – 7.12 (m, 2H), 6.89 – 6.85 (m, 2H), 6.78 – 6.72 (m, 2H), 6.50 – 6.41 (m, 2H), 5.19 (s, 1H), 4.05 (d, *J* = 17.6 Hz, 1H), 3.74 (s, 3H), 3.53 (d, *J* = 17.6 Hz, 1H), 3.43 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 204.58, 174.09, 162.81, 161.06, 157.97, 141.26, 138.62, 135.74, 134.91, 134.63, 126.22, 120.02, 118.96, 84.37, 84.15, 83.93, 71.66, 60.16, 58.06, 57.50, 38.14. $[\alpha]_D^{30}$ = -275.00 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 10.9 min, 14.0 min; minor enantiomer: t_R = 9.4 min, 15.3 min. 1.2:1 dr, 77/82% ee. HRMS (ESI) calcd for $C_{25}H_{21}BrO_5Na$ *m/z* $[M+Na]^+$: 503.0465, found: 503.0464.



3r: minor diastereomer

Methyl (R)-6-bromo-2-((S)-(4-hydroxyphenyl)(4-methoxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.47 (s, 1H), 7.78 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.72 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.07 – 7.02 (m, 2H), 6.93 – 6.88 (m, 2H), 6.75 – 6.69 (m, 2H), 6.68 – 6.63 (m, 2H), 5.20 (s, 1H), 4.06 (d, *J* = 7.4 Hz, 1H), 3.58 (s, 2H), 3.52 (d, *J* = 17.7 Hz, 1H), 3.44 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 199.80, 169.31, 158.14, 156.32, 153.19, 138.71, 136.51, 132.26, 131.83, 131.05, 129.86, 129.16, 126.81, 121.52, 115.70, 113.86, 67.08, 55.29, 53.35, 33.45, 21.21.

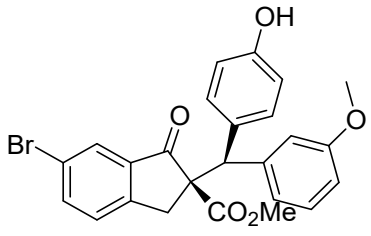


3s: major diastereomer

Methyl (R)-6-bromo-2-((R)-(4-hydroxyphenyl)(3-methoxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 89% as a white solid, mp: 78-84°C.

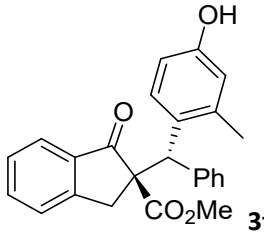
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 1.9 Hz, 1H), 7.60 (dt, *J* = 8.1, 1.7 Hz, 1H), 7.28 – 7.22 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.86 – 6.83 (m, 1H), 6.79 (ddd, *J* = 6.6, 2.2, 1.0 Hz, 2H), 6.56 – 6.51 (m, 2H), 5.45 (s, 1H), 5.30 (s, 1H), 4.16 (d, *J* = 17.1 Hz, 1H), 3.78 (d, *J* = 0.9 Hz, 3H), 3.52 (s, 3H), 3.48 (d, *J* = 17.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.15, 169.37, 159.64, 154.49, 152.67, 143.01, 138.23, 136.36, 131.27, 131.03, 129.51, 127.65, 127.41, 121.69, 120.74, 115.08, 114.70, 111.81, 67.09, 55.17, 53.58, 53.23, 33.25. $[\alpha]_D^{30}$ = -191.38 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak IA column and at 254nm (n-hexane/*i*-PrOH = 85/15), 1.0 mL/min; Major enantiomer: t_R = 8.9 min, 28.4 min; minor enantiomer: t_R = 8.9 min, 21.6 min. 1.3:1 dr, 90/90% ee. HRMS (ESI) calcd for $C_{25}H_{21}BrO_5Na$ *m/z* $[M+Na]^+$: 503.0465, found: 503.0465.



3s: minor diastereomer

Methyl (R)-6-bromo-2-((S)-(4-hydroxyphenyl)(3-methoxyphenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.79 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.09 – 7.05 (m, 2H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.75 – 6.70 (m, 2H), 6.61 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.57 – 6.54 (m, 1H), 6.52 (t, *J* = 2.1 Hz, 1H), 5.22 (s, 1H), 4.02 (d, *J* = 17.6 Hz, 1H), 3.56 (s, 3H), 3.52 (d, *J* = 17.6 Hz,1H), 3.45 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 199.78, 169.28, 159.13, 156.46, 153.14, 141.99, 138.74, 136.57, 131.27, 130.01, 129.58, 129.19, 126.82, 122.16, 121.55, 116.16, 115.73, 112.02, 66.93, 55.22, 53.41, 53.30, 33.71.



3t: major diastereomer

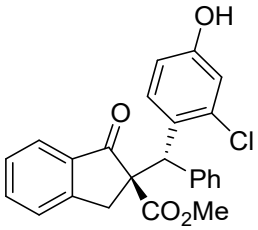
methyl (R)-2-((S)-(4-hydroxy-2-methylphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 86% as a white oil.

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.08 (s, 1H), 7.66 (td, *J* = 7.4, 1.2 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.17 (s, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.95 (m, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 6.47 (d, *J* = 2.6 Hz, 1H), 6.23 (dd, *J* = 8.5, 2.7 Hz, 1H), 5.50 (s, 1H), 4.05 (d, *J* = 7.1 Hz, 1H), 4.03 (d, *J* = 7.1 Hz, 1H), 3.57 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (151 MHz, DMSO) δ 200.47, 170.84, 155.90, 153.75, 142.38, 138.22, 136.04, 135.22, 130.20, 129.06, 128.68, 128.42, 128.26, 127.07, 126.67, 124.27, 117.77, 112.94, 66.03, 53.43, 47.95, 35.02, 20.66. $[\alpha]_D^{30}$ = -11.5 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID column and at 254nm (n-hexane/*i*-PrOH = 90/10), 1.0 mL/min; Major enantiomer: t_R = 12.9 min, 13.6 min; minor enantiomer: t_R = 22.6 min, 31.4 min. 4:1 dr, 94/92% ee.

HRMS (ESI) calcd for $C_{25}H_{22}O_4Na$ *m/z* $[M+Na]^+$: 409.141, found: 409.1416.

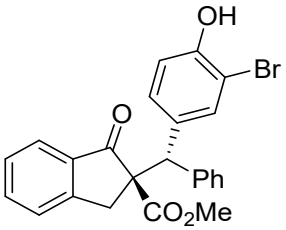


3u: major diastereomer

methyl (R)-2-((R)-(2-chloro-4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 84% as a yellow oil.

^{1}H NMR (600 MHz, DMSO-d_6) δ 9.74 (s, 1H), 7.67 (td, *J* = 7.4, 1.2 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.53 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.40 – 7.37 (m, 1H), 7.28 – 7.24 (m, 2H), 7.20 – 7.16 (m, 3H), 7.06 (d, *J* = 8.7 Hz, 1H), 6.74 (d, *J* = 2.6 Hz, 1H), 6.44 (dd, *J* = 8.7, 2.6 Hz, 1H), 5.73 (s, 1H), 4.04 (d, *J* = 7.1 Hz, 1H), 3.83 (d, *J* = 9.1 Hz, 1H), 3.59 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 200.04, 170.75, 157.06, 153.29, 140.81, 136.11, 135.44, 134.64, 130.29, 129.28, 128.72, 128.45, 128.39, 127.17, 127.00, 124.34, 116.72, 114.61, 65.74, 53.51, 48.56, 35.53. $[\alpha]_D^{30}$ = -5.7 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID column and at 254nm (n-hexane/*i*-PrOH = 90/10), 1.0 mL/min; Major enantiomer: t_R = 16.0 min, 20.9 min; minor enantiomer: t_R = 9.6 min, 10.6 min. 4:1 dr, 94/92% ee. HRMS (ESI) calcd for $C_{24}H_{19}ClO_4Na$ *m/z* $[M+Na]^+$: 429.0875, found: 429.0871.

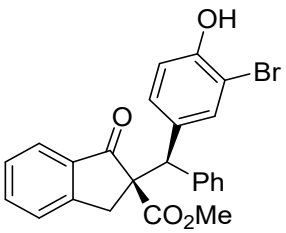


3v: major diastereomer

Methyl (R)-2-((S)-(3-bromo-4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate

Yield 79% as a yellow oil.

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.07 (s, 1H), 7.67 – 7.61 (m, 3H), 7.36 – 7.32 (m, 2H), 7.28 (d, *J* = 7.4 Hz, 2H), 7.17 – 7.12 (m, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 7.02 – 6.99 (m, 1H), 6.80 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 5.28 (s, 1H), 4.14 (d, *J* = 17.5 Hz, 1H), 3.57 (d, *J* = 17.5 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 200.92, 169.57, 154.23, 153.11, 141.67, 136.43, 134.28, 132.03, 130.38, 130.02, 129.03, 128.85, 127.05, 126.95, 126.58, 124.51, 116.31, 109.17, 66.04, 53.28, 52.88, 33.88. $[\alpha]_D^{30}$ = -10.5 (c = 1.0 in CH_3OH). The enantiomers were analyzed by HPLC using Daicel Chiralpak ID column and at 254nm (n-hexane/*i*-PrOH = 90/10), 1.0 mL/min; Major enantiomer: t_R = 15.4 min, 27.8 min; minor enantiomer: t_R = 12.9 min, 32.3 min. 4:1 dr, 94/92% ee. HRMS (ESI) calcd for $C_{24}H_{19}BrO_4Na$ *m/z* $[M+Na]^+$: 473.0359, found: 473.0361.



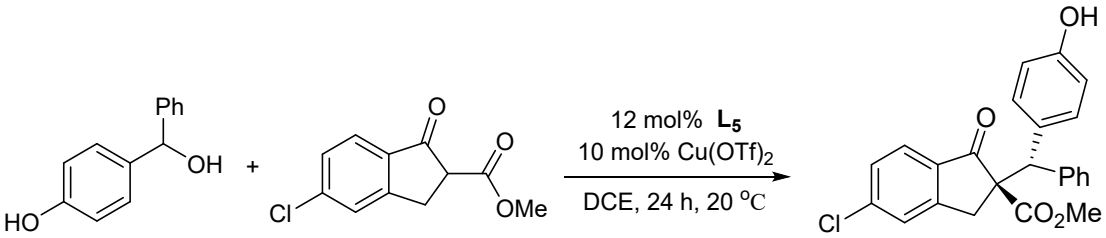
3v: minor diastereomer

Methyl (R)-2-((R)-(3-bromo-4-hydroxyphenyl)(phenyl)methyl)-1-oxo-2,3-dihydro-1H-indene-

2-carboxylate

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.22 (s, 1H), 7.59 – 7.55 (m, 3H), 7.44 (d, *J* = 2.1 Hz, 1H), 7.38 (d, *J* = 7.4 Hz, 2H), 7.27 – 7.24 (m, 2H), 7.22 – 7.18 (m, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 5.28 (s, 1H), 4.04 (d, *J* = 7.1 Hz, 1H), 3.59 (d, *J* = 9.8 Hz, 1H), 3.47 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 200.61, 169.64, 154.07, 153.21, 139.94, 136.31, 134.44, 133.86, 133.29, 130.97, 128.53, 128.45, 127.41, 127.20, 127.17, 124.86, 116.45, 109.67, 66.08, 53.38, 52.83, 33.73.

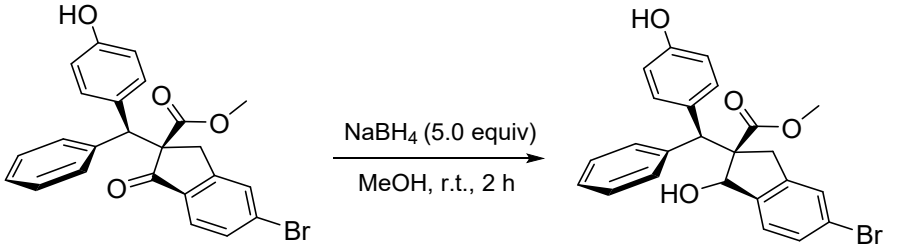
4. Gram-Scale Synthesis



1a (0.5g, 2.5mmol) **2c** (0.672g, 3mmol) **3c** (82% yield, 2.4:1 dr, 90/90% ee)

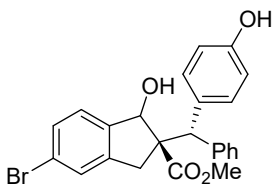
An oven-dried Schlenk flask was charged with $Cu(OTf)_2$ (0.09g, 0.25 mmol), ligand **L_5** (0.1275g 0.3 mmol), DCE (37.5 mL) and a stir bar. The reaction mixture was stirred at room temperature for 1h. Then β-ketoesters **2c** (0.672g, 3 mmol) was added, the reaction solution was stirred for 30 min, and then 4-hydroxybenzyl alcohol **1a** (0.5g, 2.5 mmol) was added to react at 20 °C for 24 h. After completion, the mixture was dried and concentrated. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate/petroleum ether (1:4) to afford the producs **3c** (82%yield, 0.83g).

5. Synthesis of Compound 4



3e (>99% ee, >99:1 dr) **4** (94% yield, 93% ee,>99:1 dr)

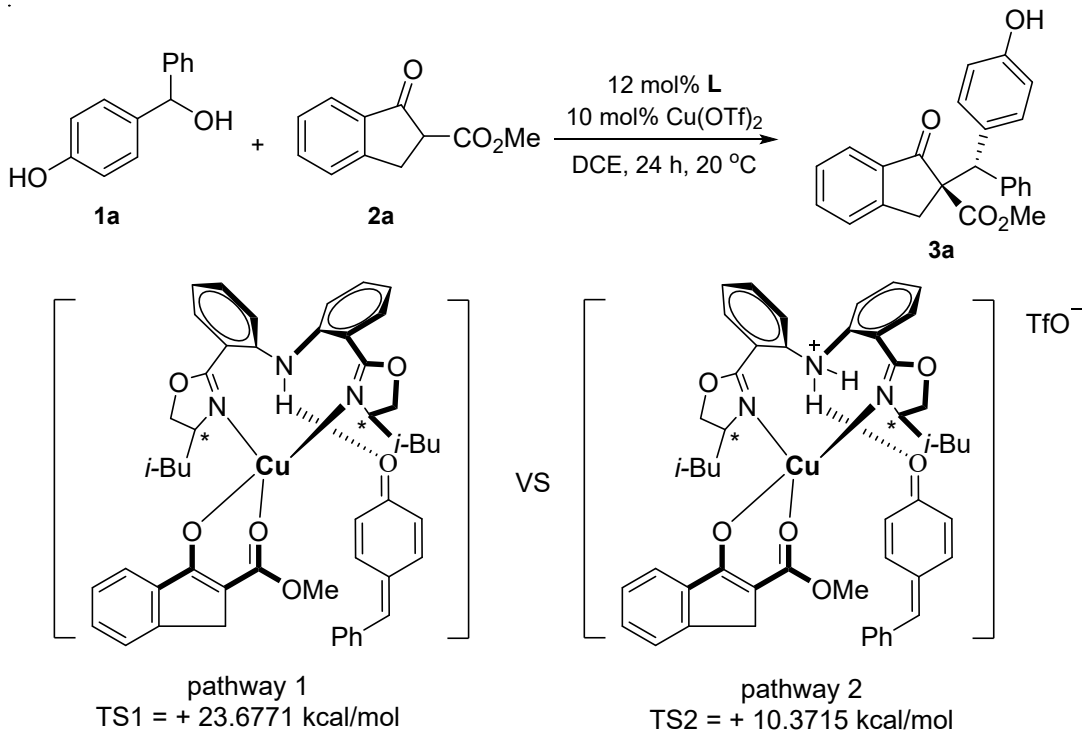
To a solution of compound **3e** (225 mg, 0.5 mmol) in methanol (50 mL) was added $NaBH_4$ (95 mg, 2.5 mmol) in portions. The reaction mixture was then stirred at rt for 2 hours. After completion, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate (3 × 50 mL). The combined organic solvents were concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 6/1) to afford a colorless soild **4**.



Methyl(2R)-5-bromo-1-hydroxy-2-((S)-(4-hydroxyphenyl)(phenyl)methyl)-2,3-dihydro-1H-indene-2-carboxylate (4)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.43 (m, 2H), 7.31 (m, 2H), 7.27 (d, J = 1.8 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.19 – 7.13 (m, 4H), 6.63 – 6.57 (m, 2H), 5.44 (s, 1H), 4.95 (s, 1H), 3.58 (d, J = 16.1 Hz, 1H), 3.41 (s, 3H), 3.26 (d, J = 16.1 Hz, 1H), 2.07 (s, 1H), 1.29 (t, J = 7.1 Hz, 1H). ^{13}C NMR (151 MHz, CDCl3) δ 175.42, 154.25, 143.37, 141.95, 141.40, 132.75, 131.19, 130.00, 128.96, 128.40, 127.60, 126.59, 125.63, 122.46, 114.68, 78.85, 64.53, 52.09, 51.50, 38.24. HRMS (ESI) calcd for $C_{24}H_{21}BrO_4$ *m/z* [M-H]$^-$: 451.0550, found: 451.0554.

6. DFT calculations



Discussion: The molecular structure of **1a**, **2a**, **3a** and the catalysts involved in the reaction were optimized by Gaussian 09W software and semi-empirical PM6 method. The preliminary conclusions reached are as follows:

(1) Two envisaged pathways (TS1 and TS2) is thermodynamically feasible and belongs to exothermic reactions (the heat of reaction is -10.15 kcal/mol) ;

(2) The designed pathway 1, the transition state energy barrier TS1 without proton participation was to be 23.6771 kcal/mol (with the reactant **1a** + **2a** as the zero point); the presumed pathway 2, the transition state energy barrier with proton participation TS2 = 10.3715 kcal/mol (with the reactant **1a + 2a** as the zero point);

(3) Comparing the kinetic energy barrier of the two pathways, because TS2 < TS1, it is speculated that pathway 2 is more conducive to the progression of the reaction.

7. References

[1] (*a*) K. M. Fisher and Y. Bolshan, *J. Org. Chem.*, 2015, **80**, 12676; (*b*) M. Lanzi, J. Merad, D. V. Boyarskaya, G. Maestri, C. Allain and G. Masson, *Org. Lett.*, 2018, **20**, 5247.

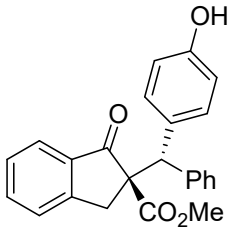
[2] M. Huang, S. Duan, X. Ma, B. Cai, D. Wu, Y. Li, L. Li, H. Zhang and X. Yang, *Medchemcomm*, 2019,

10, 1027.

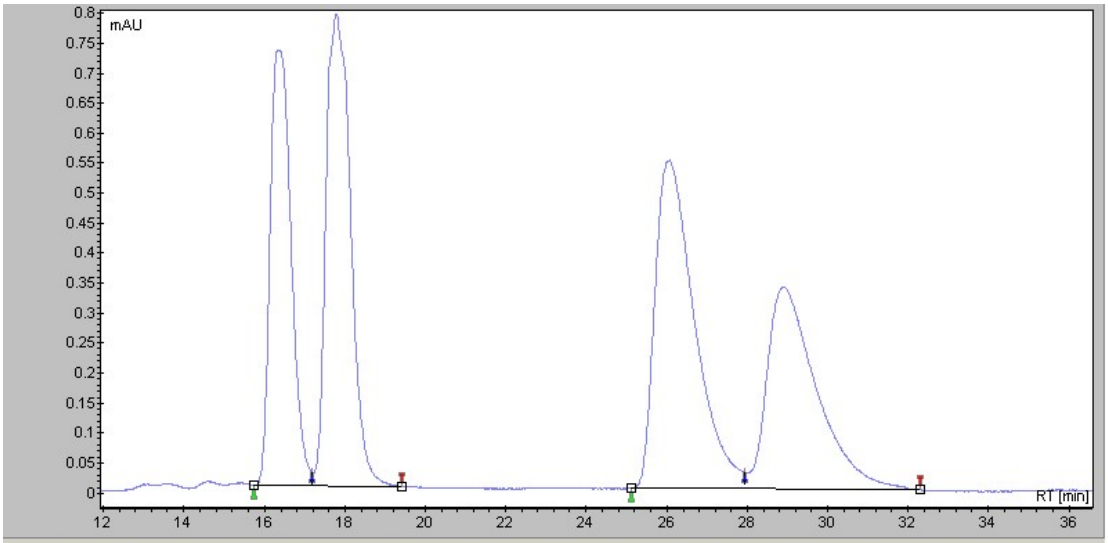
[3] W. Liu, S. Z. Ali, S. E. Ammann and M. C. White, *J. Am. Chem. Soc.,* 2018, **140**, 10658.

[4] C.T. Chen, N. C. Maity, R. Agarwal, C. F. Lai, Y. Y. Liao and W. R. Yu, *J. Org. Chem.,* 2020, **85**, 6408.

8. HPLC chromatograms



3a



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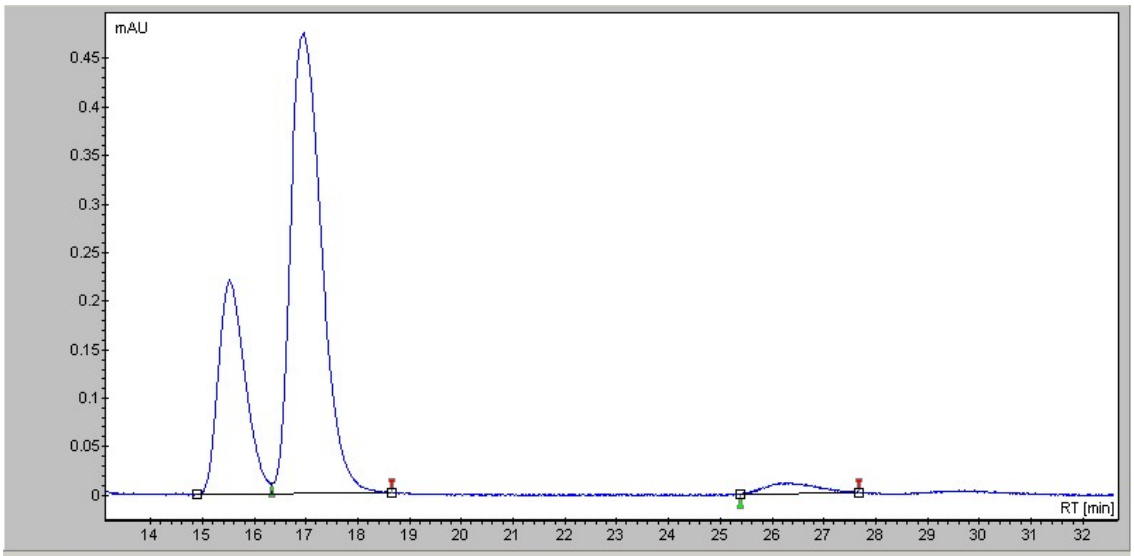
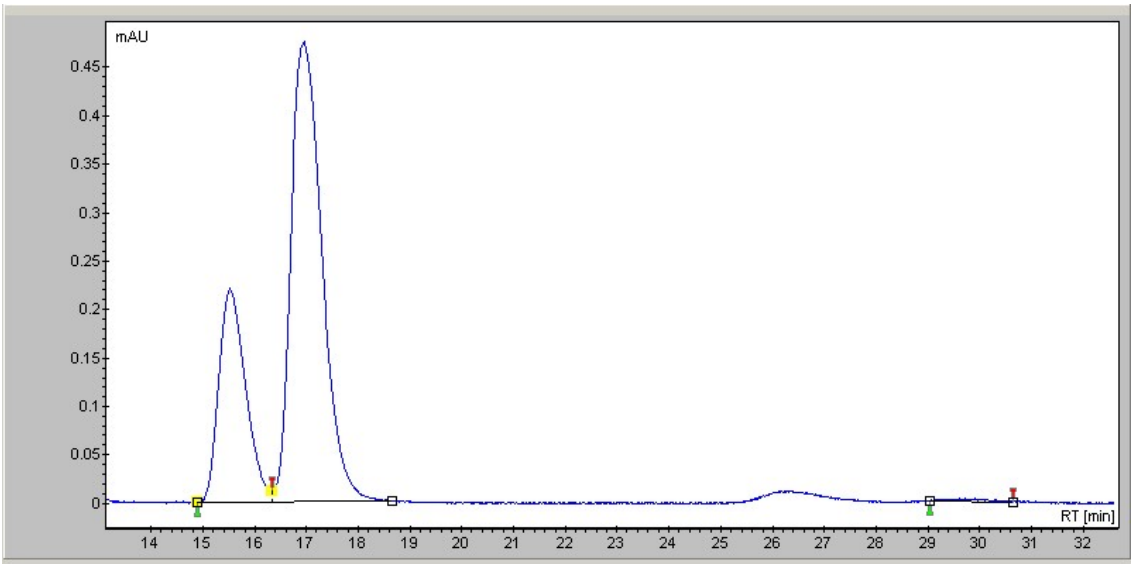
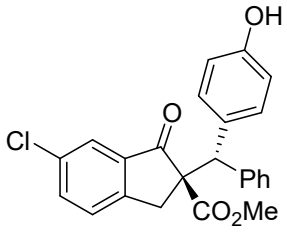
1	UNKNOWN	15.747	16.345	17.176	0.000	20.96	0.7	0.4	20.957
2	UNKNOWN	17.176	17.783	19.412	0.000	26.56	0.8	0.6	26.557
3	UNKNOWN	25.106	26.042	27.936	0.000	29.65	0.5	0.6	29.652
4	UNKNOWN	27.936	28.906	32.302	0.000	22.83	0.3	0.5	22.834



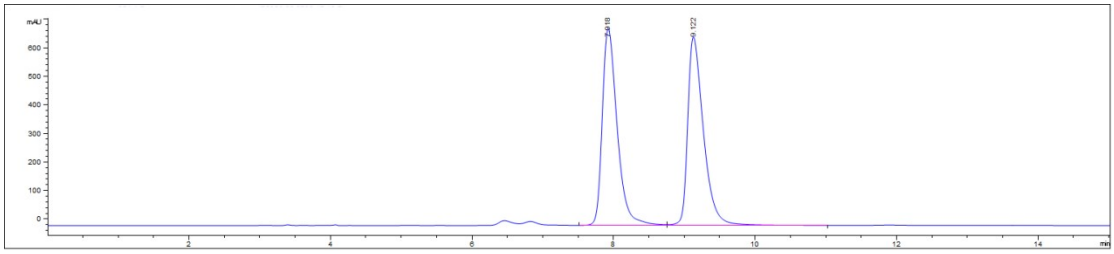
#	Name	Start [Min]	Time [Min]	End [Min]	Ret. time Offset	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	16.338	16.959	18.654	0.000	96.52	0.5	0.3	96.518
2	UNKNOWN	25.386	26.265	27.676	0.000	3.48	0.0	0.0	3.482
Total						100.00	0.5	0.3	100.000



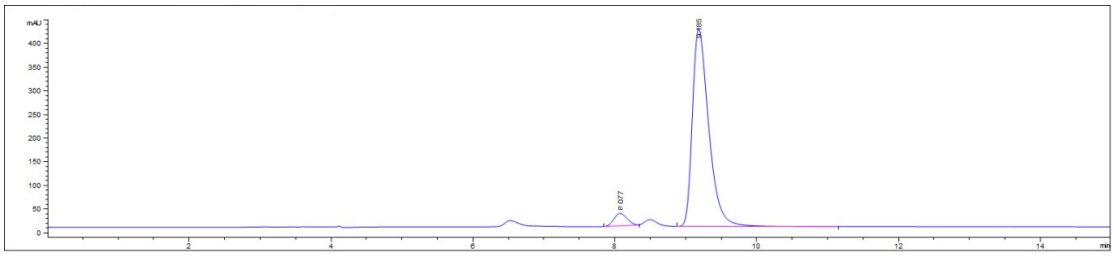
#	Name	Start [Min]	Time [Min]	End [Min]	Ret. time Offset	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	14.893	15.519	16.338	0.000	98.66	0.2	0.1	98.663
2	UNKNOWN	29.039	29.771	30.647	0.000	1.34	0.0	0.0	1.337



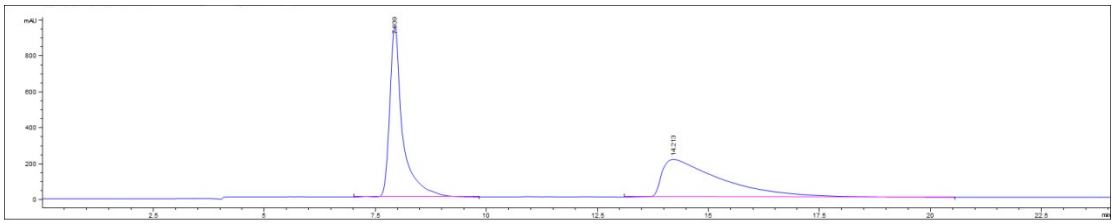
3b



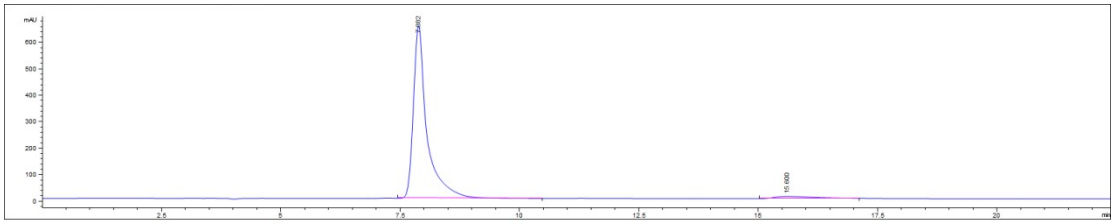
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.918	10115.6	691.1	0.2228	0.618	49.790	BV
2	9.122	10200.8	661.6	0.2339	0.53	50.210	VB



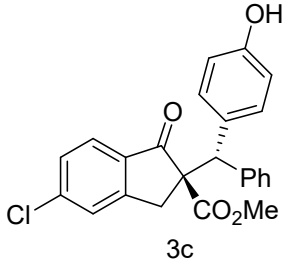
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.077	363.4	27.1	0.2235	0.844	5.109	MM
2	9.185	6749.6	417.8	0.2465	0.578	94.891	VB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.754	13496	705.6	0.2751	0.545	49.804	BB
2	13.666	13602.1	163.2	1.1401	0.231	50.196	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.882	12921.9	653.7	0.2846	0.556	96.707	BB
2	15.6	440	7.5	0.9716	0.438	3.293	MM



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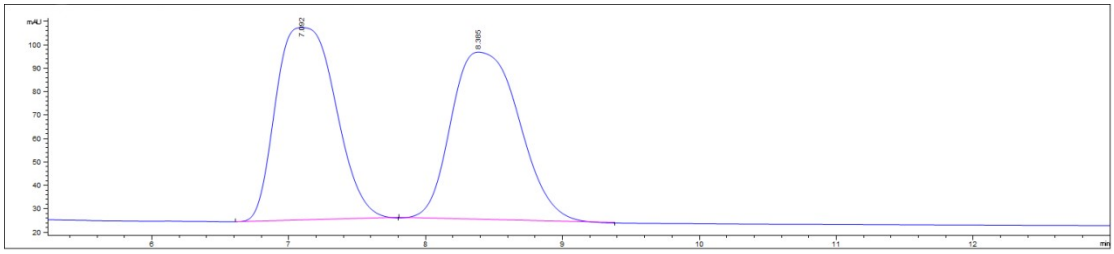
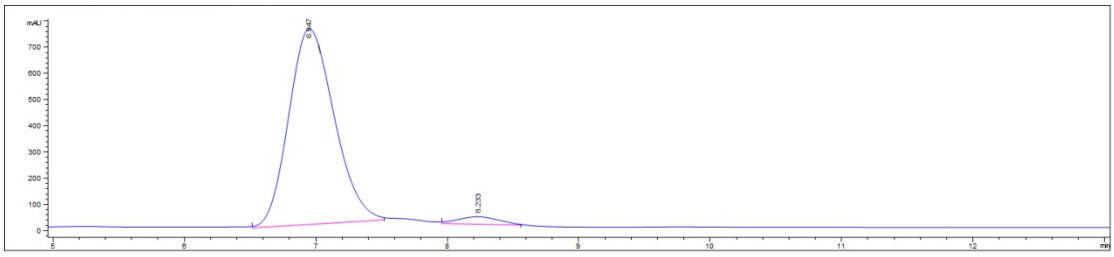
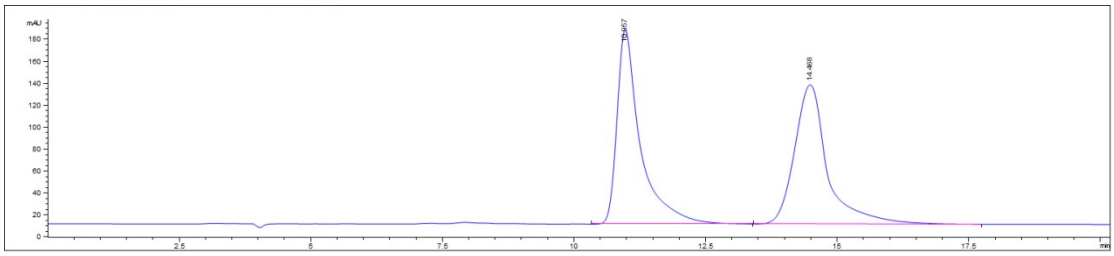


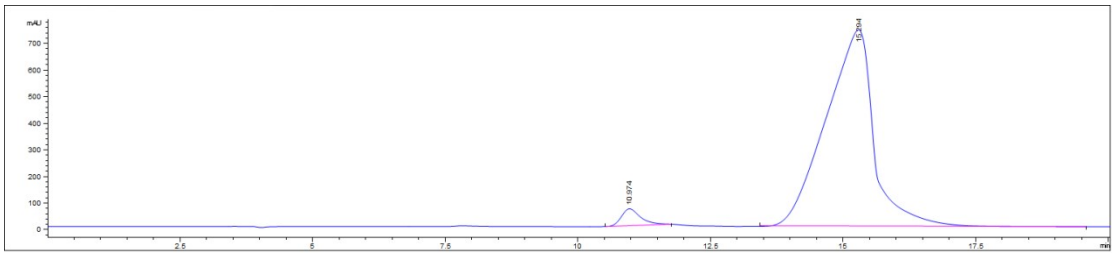
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.092	2484.8	82	0.4916	0.736	50.128	BB
2	8.385	2472.1	71.4	0.5578	0.658	49.872	BB



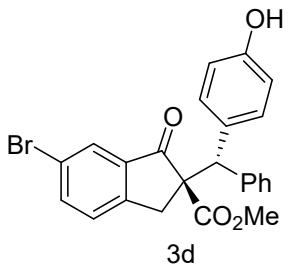
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.947	17910.4	746	0.4001	0.814	96.537	MM
2	8.233	642.4	29.2	0.3666	0.817	3.463	MM



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.957	5459.3	177.4	0.4409	0.488	49.763	BB
2	14.468	5511.3	126.9	0.6506	0.798	50.237	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.974	1693.2	64.8	0.4355	0.697	3.494	MM
2	15.294	46773.6	741.1	0.8983	1.838	96.506	BB



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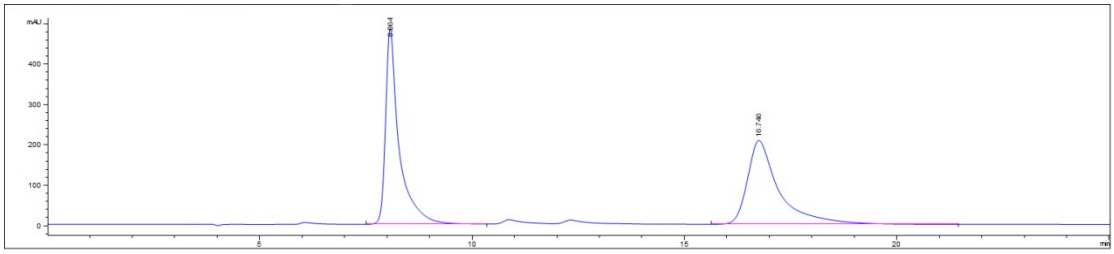
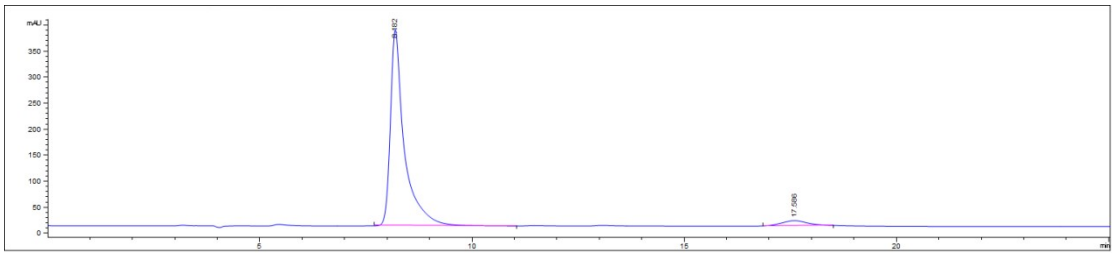
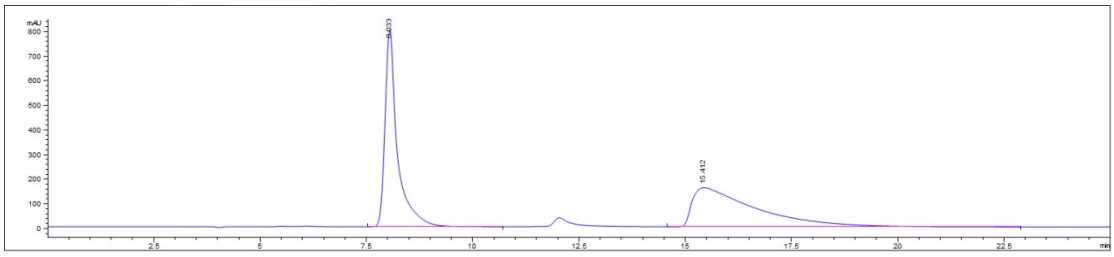


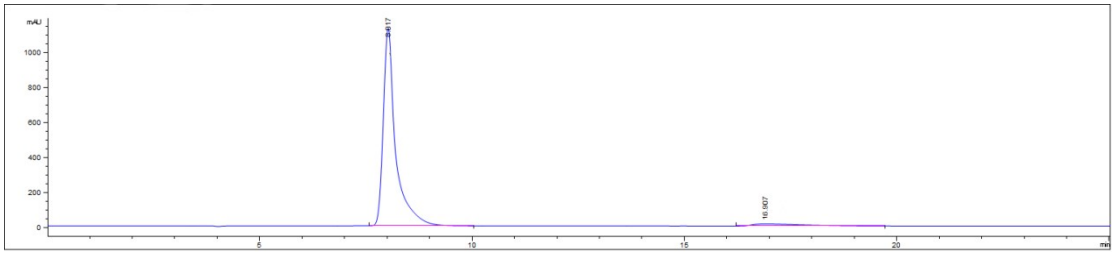
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.064	10743.4	485.5	0.3142	0.463	50.086	BB
2	16.746	10706.7	207.4	0.7422	0.514	49.914	BB



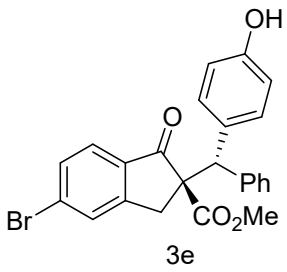
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.182	8642.6	377.5	0.3251	0.482	95.292	BB
2	17.586	427	9.8	0.7258	0.922	4.708	MM



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.033	16204.7	802.1	0.2917	0.551	49.583	BB
2	15.412	16477.5	159.6	1.3867	0.205	50.417	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.017	23004.4	1130.8	0.3391	0.616	95.641	MM
2	16.907	1048.5	12.4	1.4104	0.318	4.359	MM



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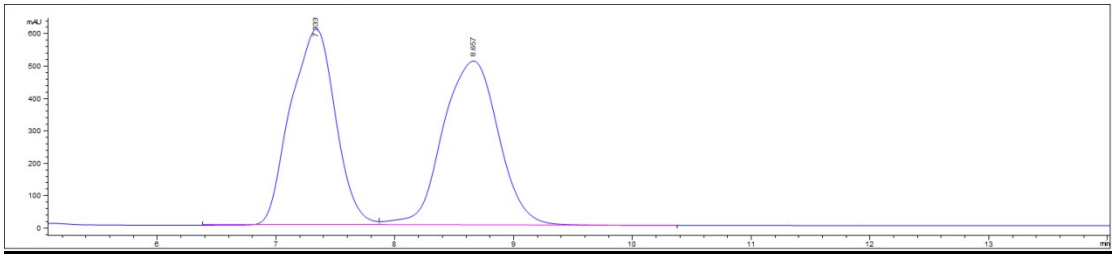
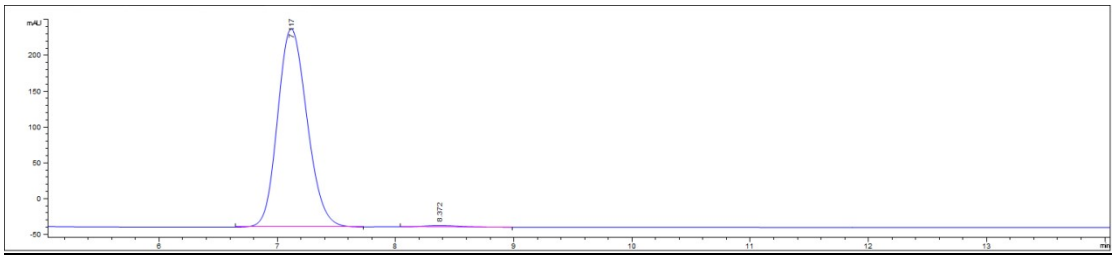
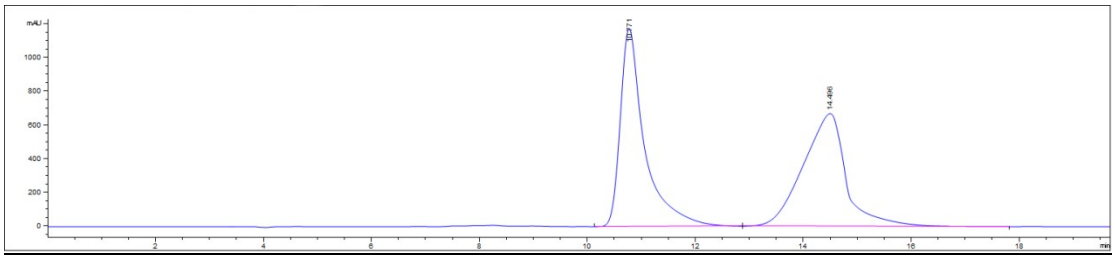


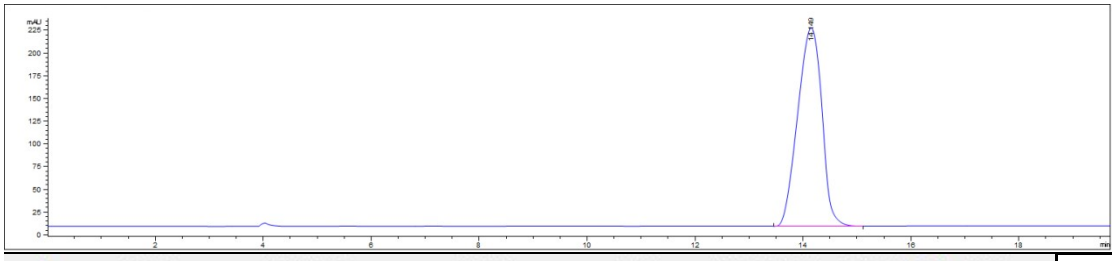
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.333	16004.4	608.4	0.3789	1.249	49.044	BV
2	8.657	16628.3	509.5	0.5267	1.16	50.956	VB



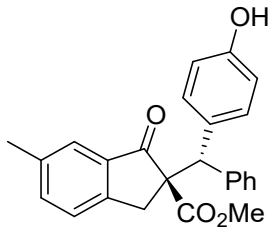
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.117	4773.8	276.2	0.2716	0.818	99.197	BB
2	8.372	38.6	1.9	0.3102	0.75	0.803	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.771	36509.2	1170.9	0.4498	0.517	49.804	BB
2	14.496	36796.5	666.2	0.8464	1.467	50.196	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	14.149	6759.6	217.9	0.51	1.214	100.000	BB



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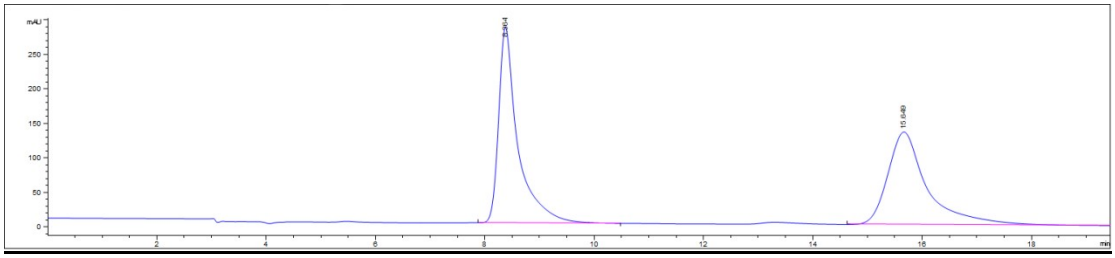
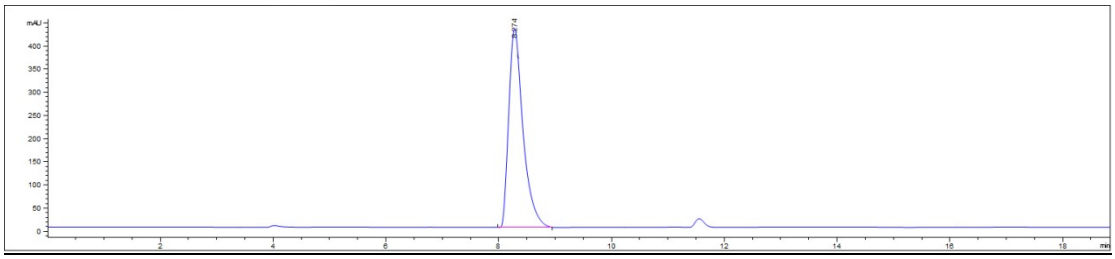
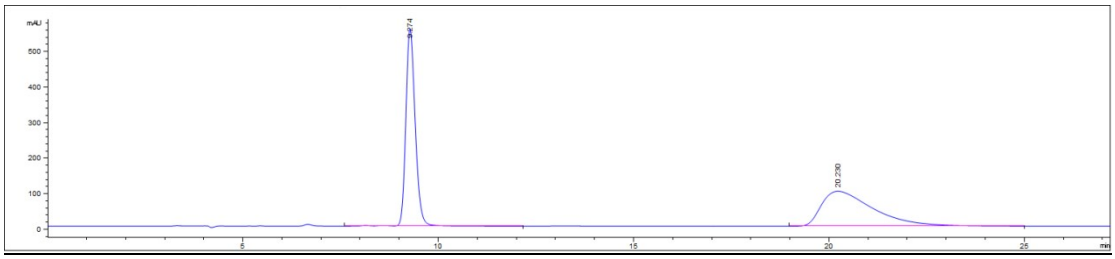


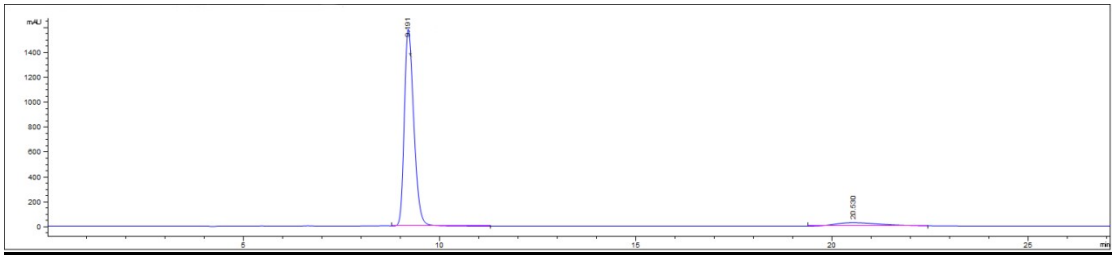
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.364	6910.3	282.6	0.3473	0.491	50.486	BB
2	15.649	6777.3	134.1	0.7337	0.618	49.514	BBA



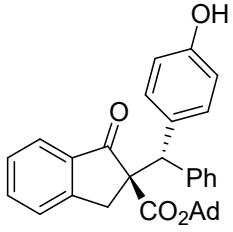
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.274	7546.2	428.1	0.2938	0.657	100.000	MM



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.274	9302.7	554.1	0.2563	0.777	50.590	VB R
2	20.23	9085.9	98.2	1.3852	0.431	49.410	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.191	26819.9	1588.5	0.2814	0.693	91.809	MM
2	20.53	2392.8	27.7	1.4399	0.572	8.191	MM



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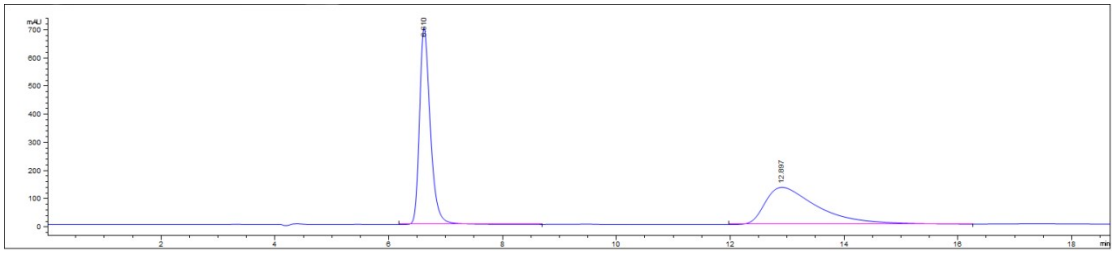
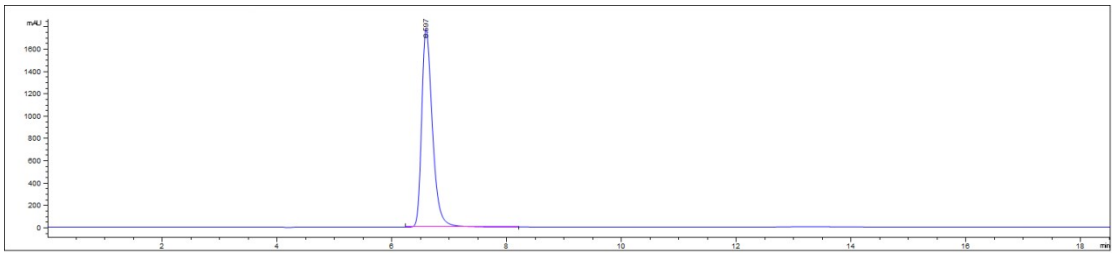
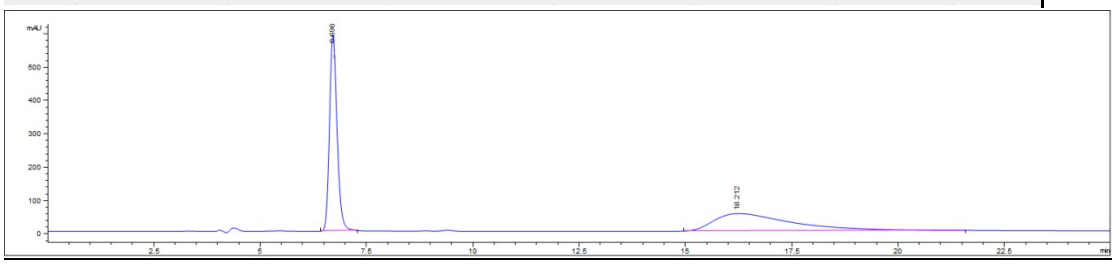


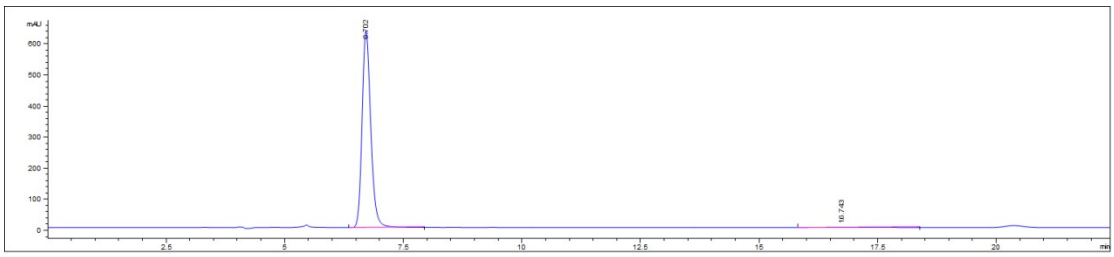
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.61	9216.2	697.1	0.2002	0.672	52.179	BB
2	12.897	8446.3	131.6	0.9609	0.436	47.821	BB



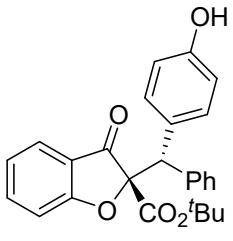
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.597	23153.7	1773.7	0.1983	0.638	100.000	BB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.696	7326.6	589.9	0.207	0.794	51.610	MM
2	16.212	6869.6	52.3	2.188	0.41	48.390	MM



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.702	8098.3	634.9	0.1948	0.765	99.198	BB
2	16.743	65.5	7.2E-1	1.5062	0.673	0.802	MM



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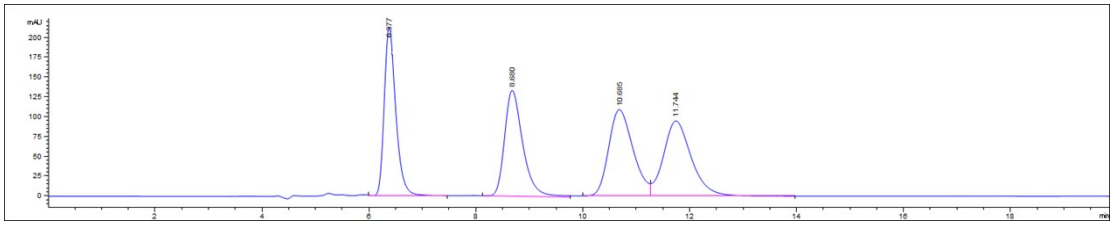
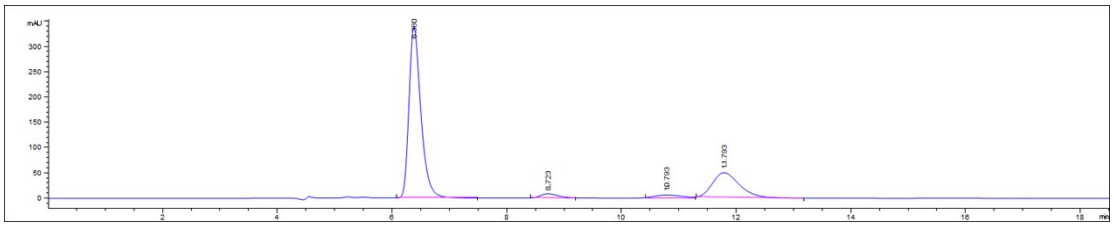
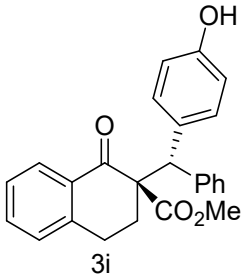


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.377	3246.7	213.3	0.2536	0.708	24.341	MM
2	8.68	3206.7	134.2	0.3981	0.694	24.041	MM
3	10.685	3456.2	109.2	0.4873	0.741	25.911	BV
4	11.744	3428.8	94.8	0.5462	0.763	25.706	VB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.38	4858.2	336.3	0.2185	0.66	70.838	BB
2	8.723	185	8.4	0.3649	0.708	2.697	MM
3	10.793	199.9	5.9	0.5646	0.743	2.915	MM
4	11.793	1615.1	48.8	0.5512	0.704	23.550	MM



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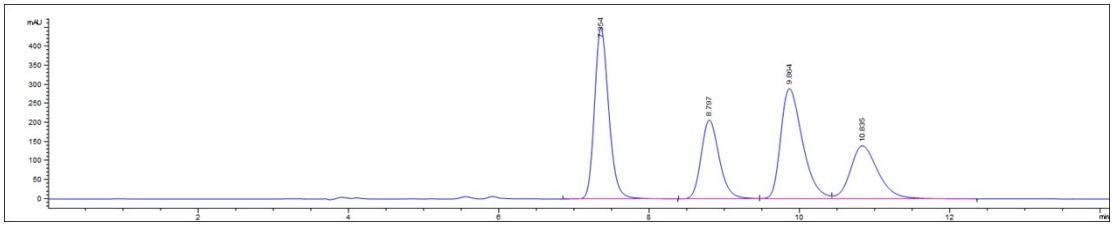
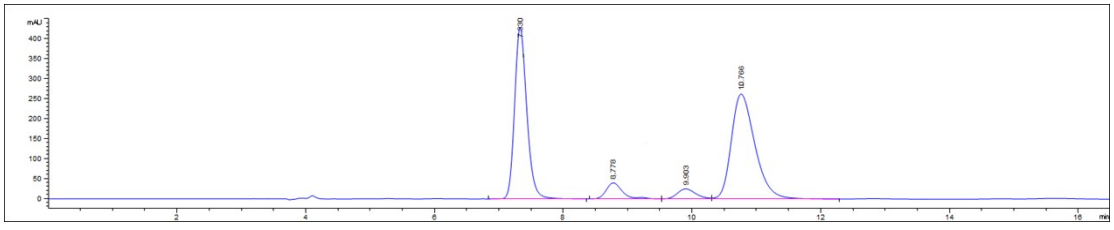
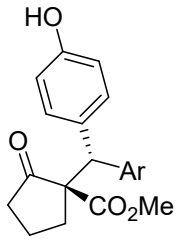


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.354	5934.1	450.8	0.2036	0.769	31.446	BB
2	8.797	3486	207.7	0.2578	0.772	18.473	BV
3	9.864	5869.7	290.7	0.3095	0.628	31.104	VV
4	10.835	3581.2	139.8	0.3909	0.725	18.977	VB



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.33	5689.5	430.8	0.2201	0.788	41.702	MM
2	8.778	728.2	40.5	0.2999	0.739	5.337	MF
3	9.903	504.2	25.3	0.3318	0.795	3.696	MF
4	10.766	6721.3	263.9	0.4244	0.691	49.265	FM



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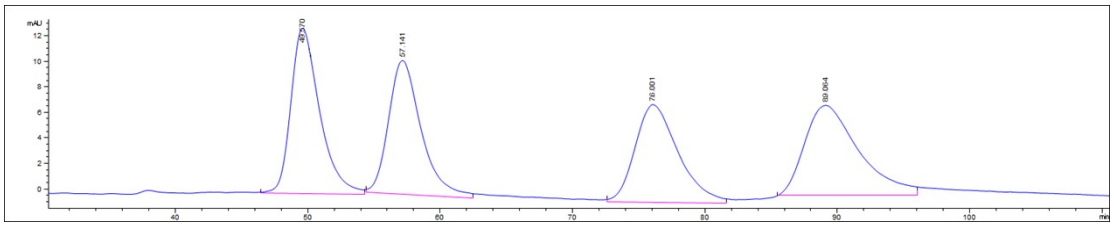
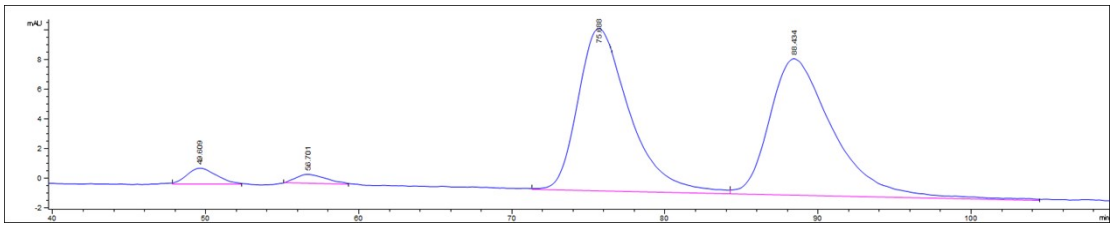
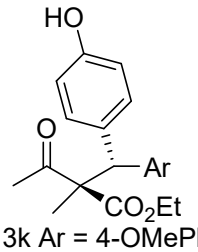


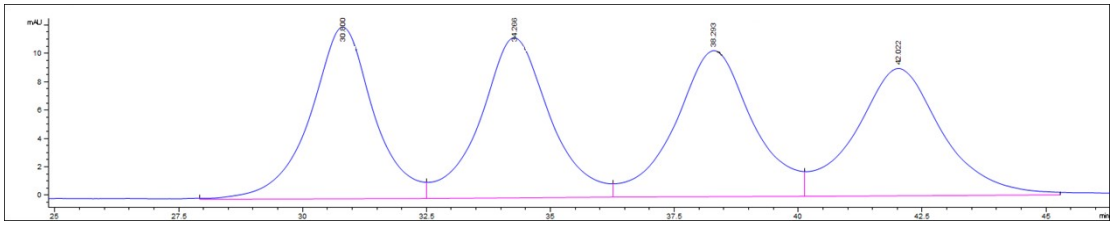
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	49.57	1971	13	2.5303	0.664	26.215	MM
2	57.141	1798.3	10.5	2.861	0.745	23.917	MM
3	76.001	1742	7.7	3.7803	0.681	23.169	MM
4	89.064	2007.5	7	4.7474	0.616	26.700	MM



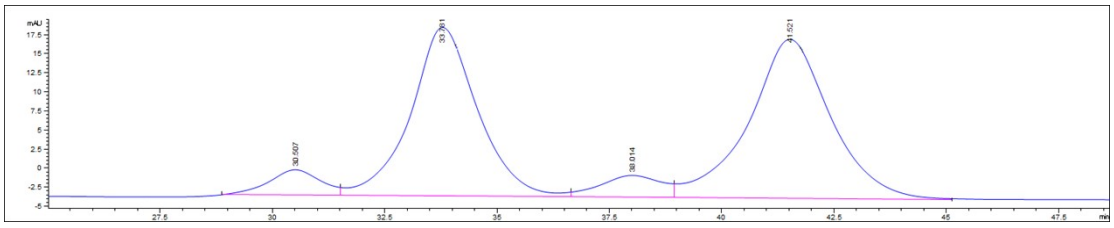
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	49.609	153.7	1.1	2.3207	0.763	2.785	MM
2	56.701	91.3	6.4E-1	2.3939	0.65	1.654	MM
3	75.688	2573.7	11	3.9097	0.658	46.621	MF
4	88.434	2701.7	9.2	4.8729	0.593	48.940	FM



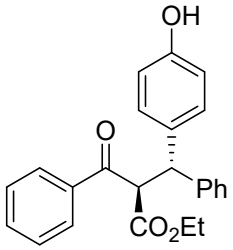
3k Ar = 4-OMePh



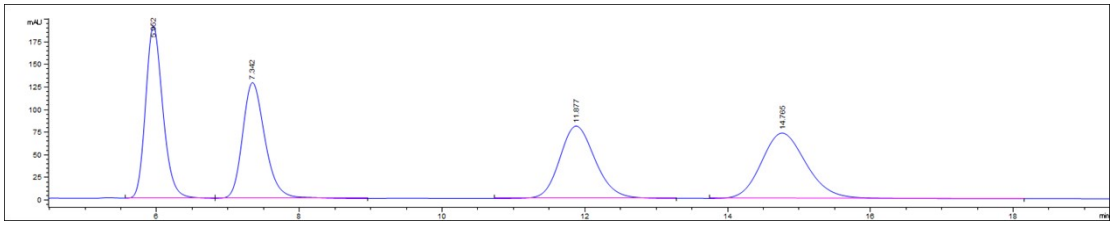
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	30.8	1089	12.1	1.4955	1.033	24.542	MF
2	34.266	1109.5	11.3	1.6327	0.927	25.004	MF
3	38.293	1132.7	10.3	1.8261	0.972	25.529	MF
4	42.022	1105.9	9	2.0449	0.952	24.925	FM



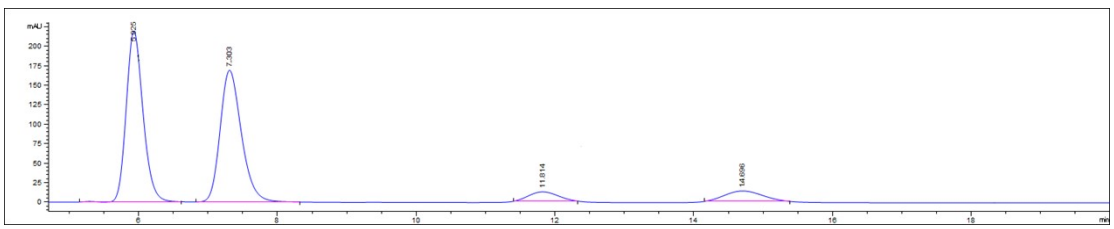
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	30.507	264.1	3.3	1.3321	1.037	4.806	MF
2	33.781	2302.6	22	1.7413	0	41.909	MF
3	38.014	273.9	2.9	1.5836	1.08	4.986	MF
4	41.521	2653.7	20.8	2.1263	0.989	48.299	FM



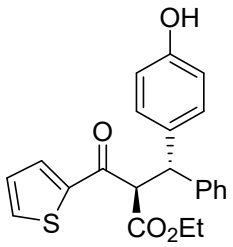
3l



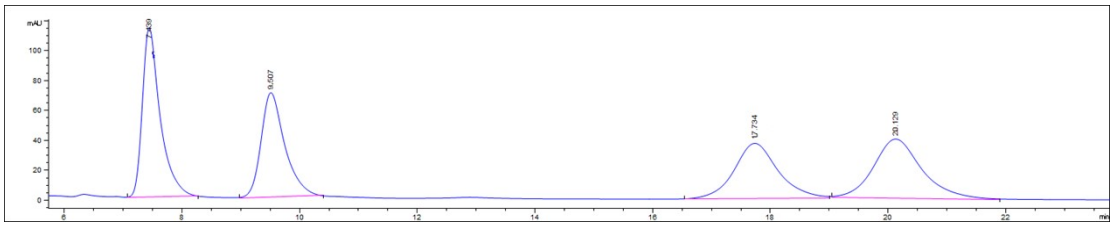
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.952	3177.5	189.3	0.2579	0.783	26.794	BB
2	7.342	2780.4	127.2	0.335	0.748	23.445	BB
3	11.877	2749.3	79.5	0.5333	0.824	23.184	BB
4	14.765	3151.8	71.9	0.6753	0.816	26.577	BB



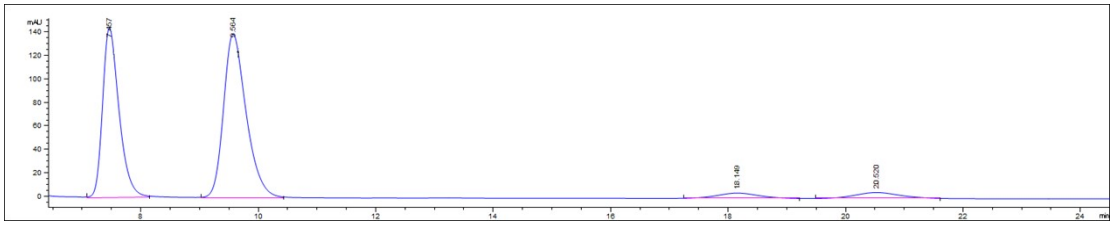
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.925	3720.8	219.8	0.2821	0.819	45.192	MM
2	7.303	3634.4	169.4	0.3576	0.76	44.142	MM
3	11.814	362.4	12.2	0.4932	0.861	4.401	MM
4	14.696	515.8	13.6	0.6342	0.882	6.265	MM



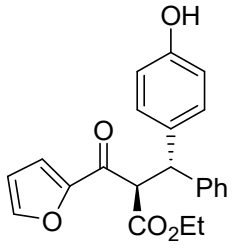
3m



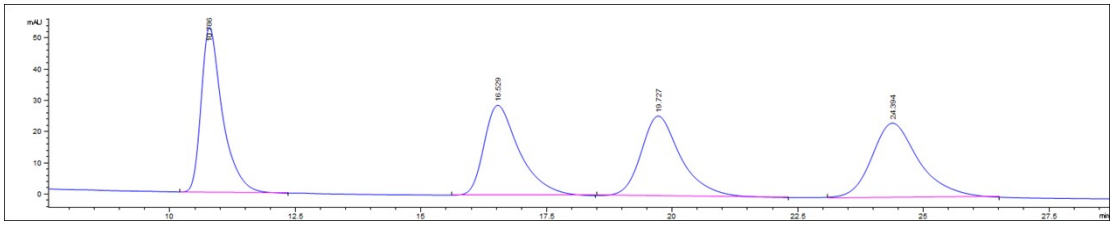
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.439	2382.5	113	0.3513	0.607	27.733	MM
2	9.507	1970.9	69.9	0.4696	0.697	22.942	MM
3	17.734	1930.4	36.9	0.8723	0.87	22.470	MM
4	20.129	2307	39.7	0.9685	0.802	26.855	MM



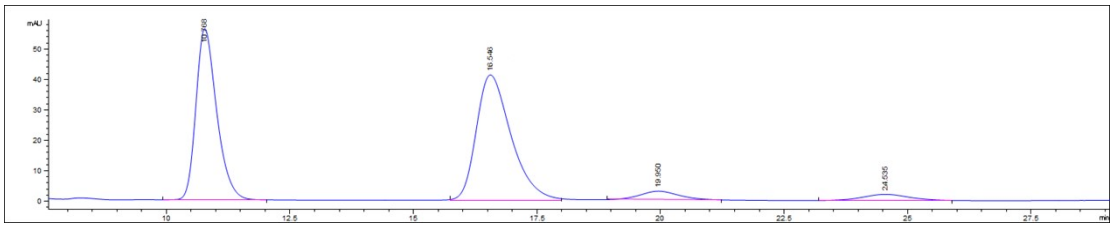
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.457	2857.1	145.8	0.3265	0.683	39.837	MM
2	9.564	3811.1	140.8	0.4512	0.708	53.139	MM
3	18.149	226.3	4.6	0.8275	0.9	3.155	MM
4	20.52	277.4	5.1	0.9002	0.889	3.868	MM



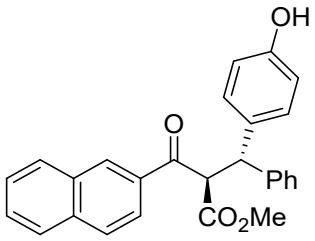
3n



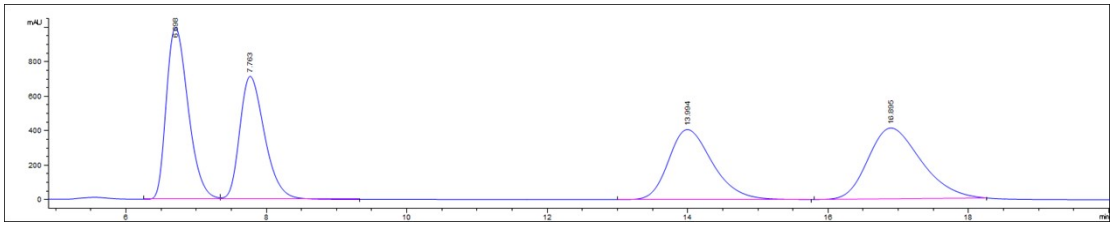
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.786	1563.5	52.9	0.4385	0.597	26.217	BB
2	16.529	1417.8	28.9	0.737	0.588	23.773	BB
3	19.727	1423.3	25.7	0.826	0.709	23.867	BB
4	24.394	1559.1	23.8	1.0897	0.773	26.143	MM



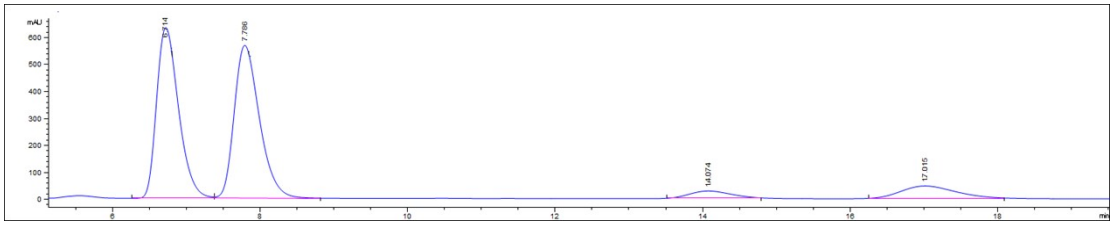
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.768	1648.1	56.4	0.4449	0.699	41.362	BB
2	16.546	2037.4	41.4	0.82	0.663	51.133	MM
3	19.95	162	2.9	0.9438	0.866	4.064	MM
4	24.535	137.1	2.1	1.111	0.964	3.441	MM



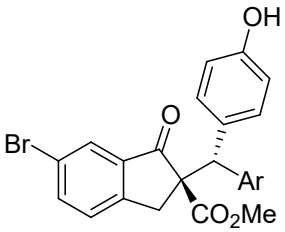
3o



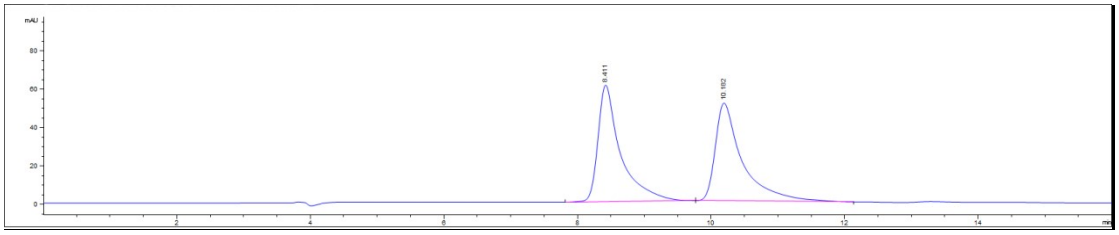
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.698	21650	999.1	0.3388	0.678	27.387	VV
2	7.763	17658	715.1	0.3821	0.679	22.338	VB
3	13.994	17706.5	406.9	0.6656	0.716	22.399	BB
4	16.895	22036.2	414.8	0.8853	0.743	27.876	MM



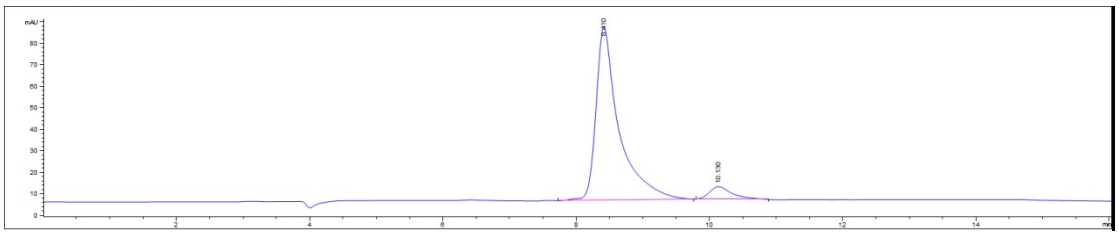
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.714	13171.3	635.7	0.3453	0.696	43.335	MF
2	7.786	13680.5	570.8	0.3994	0.691	45.010	FM
3	14.074	1058.5	27.2	0.6497	0.795	3.483	MM
4	17.015	2483.9	47.2	0.8771	0.762	8.172	MM



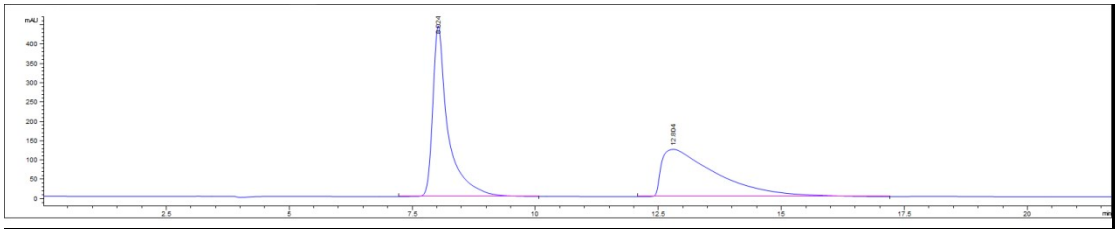
3p Ar = 4-FPh



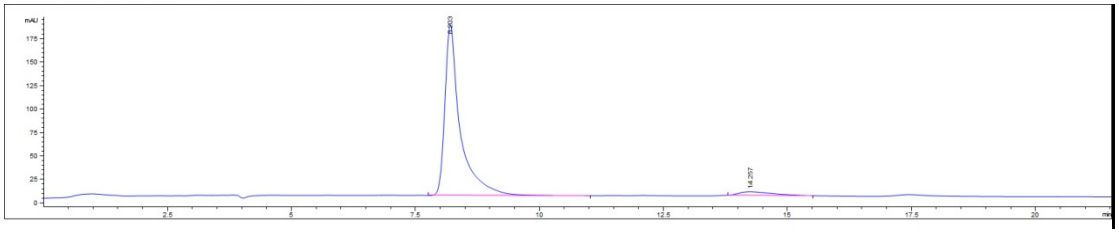
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.411	1423.4	60.5	0.3325	0.473	49.936	BB
2	10.182	1427	50.7	0.3984	0.43	50.064	BB



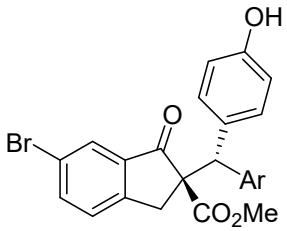
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.41	1925.5	80.1	0.3406	0.477	93.253	BB
2	10.13	139.3	5.8	0.3987	0.624	6.747	MM



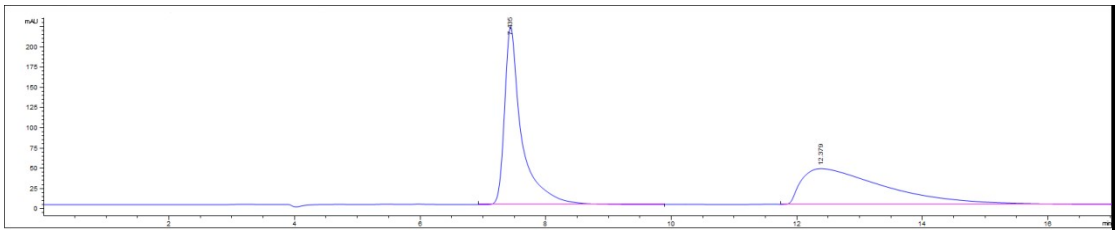
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.024	9586.2	443.1	0.3084	0.491	50.114	BB
2	12.804	9542.4	122.8	1.0828	0.242	49.886	BB



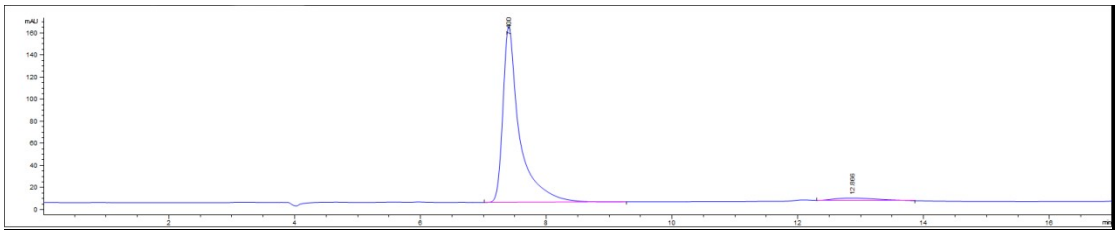
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.203	3904.3	181.1	0.3056	0.483	95.480	BB
2	14.257	184.8	3.8	0.8004	0.453	4.520	MM



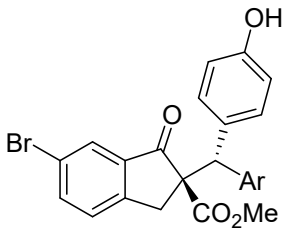
3q Ar = 4-MePh



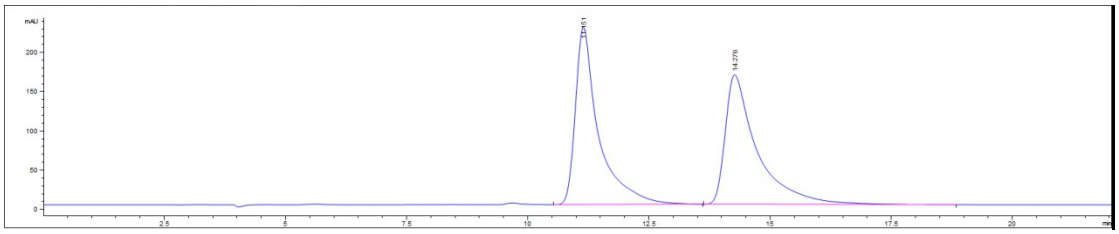
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.435	4149.8	219.2	0.2689	0.485	50.418	BB
2	12.379	4081	44.1	1.3745	0.28	49.582	BB



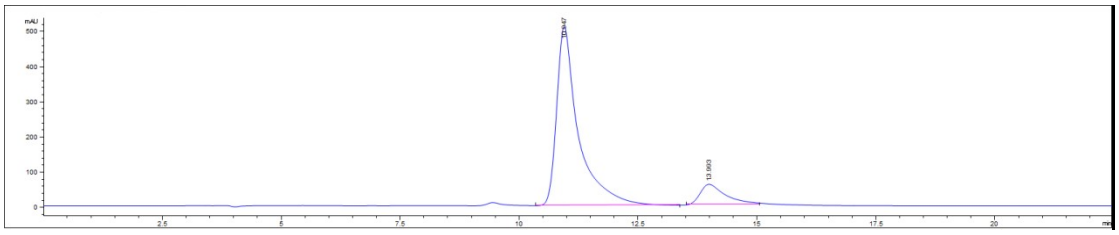
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	7.4	2913.9	158.9	0.2599	0.484	96.473	BB
2	12.866	106.5	2.2	0.8115	0.611	3.527	MM



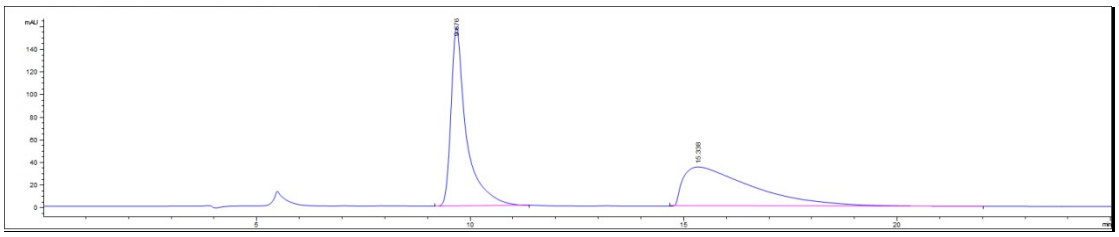
3r Ar = 4-OMePh



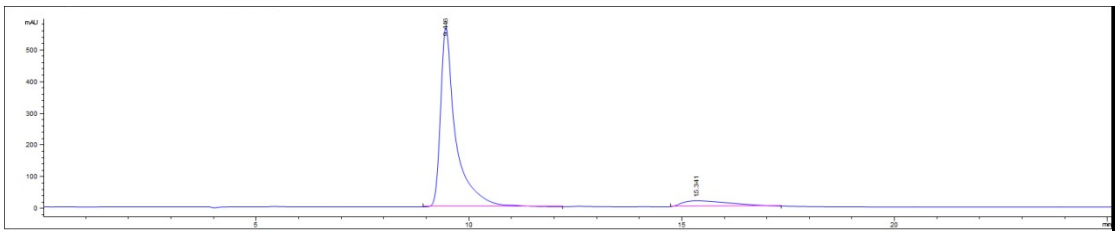
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	11.151	7549.5	226.3	0.4733	0.472	49.897	BB
2	14.276	7580.5	165.2	0.6432	0.38	50.103	BB



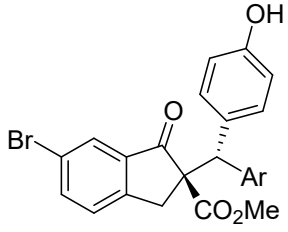
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	10.947	16244.9	507.6	0.4554	0.476	88.379	BB
2	13.993	2136.1	57.5	0.6192	0.503	11.621	MM



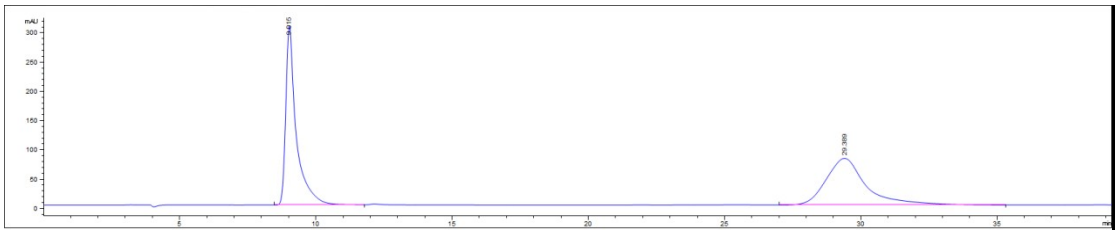
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.676	3948.5	157.5	0.3584	0.499	49.977	BB
2	15.338	3952.1	34.7	1.6341	0.25	50.023	BB



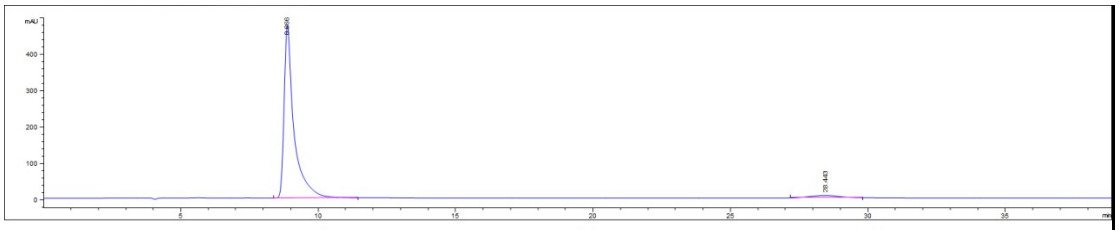
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.446	14093	563.9	0.3556	0.474	90.762	BB
2	15.341	1434.4	18.1	1.3211	0.413	9.238	MM



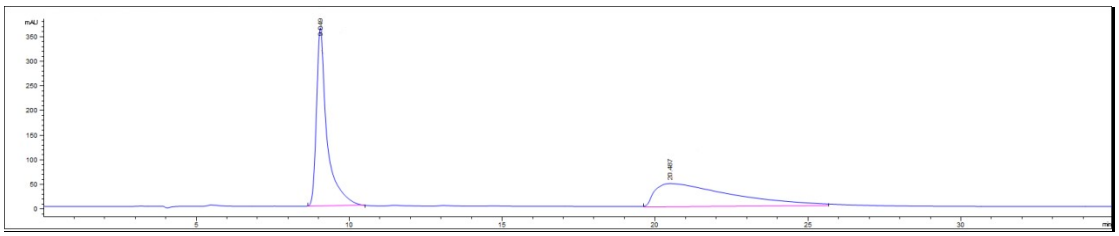
3s Ar = 3-OMePh



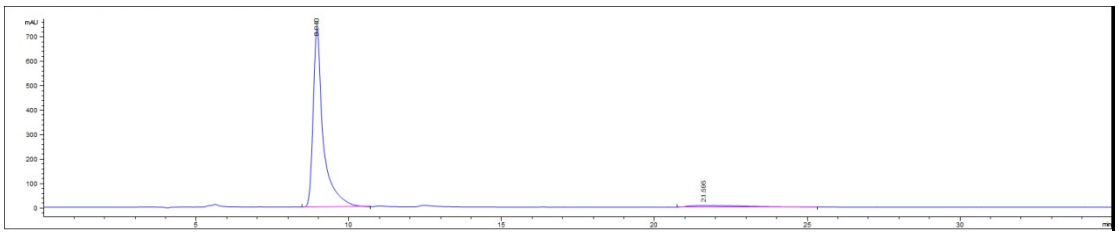
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.015	8185.2	304.4	0.3817	0.464	50.183	BB
2	29.389	8125.6	79.5	1.5227	0.769	49.817	BB



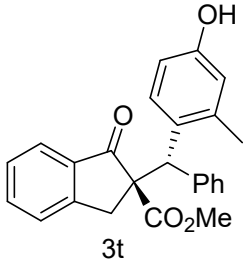
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.866	11775.4	470.7	0.3538	0.446	94.812	BB
2	28.443	644.3	7.5	1.2408	0.85	5.188	BB



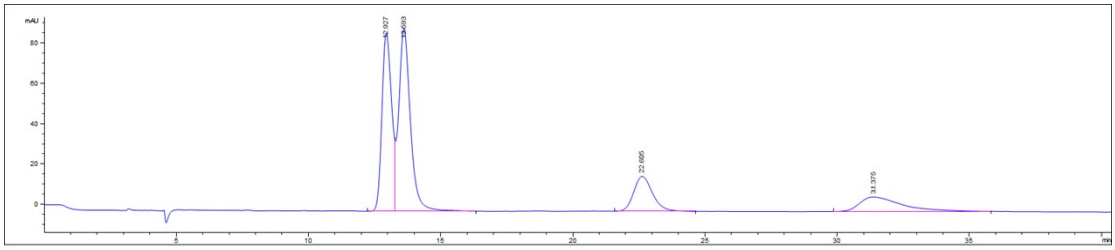
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.049	8681.2	362.1	0.3996	0.563	50.495	MM
2	20.487	8511	48.2	2.9432	0.239	49.505	MM



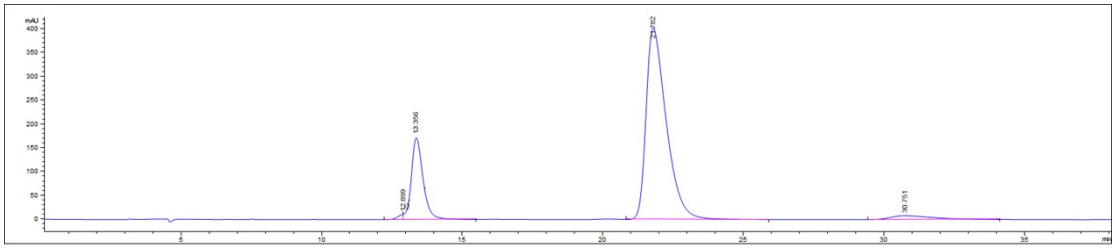
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.94	16849.2	732.8	0.3322	0.552	95.088	BB
2	21.595	870.4	6.8	2.145	0.341	4.912	MM



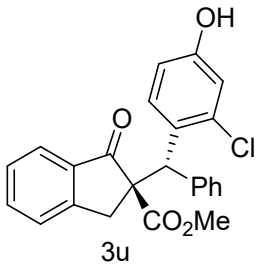
3t



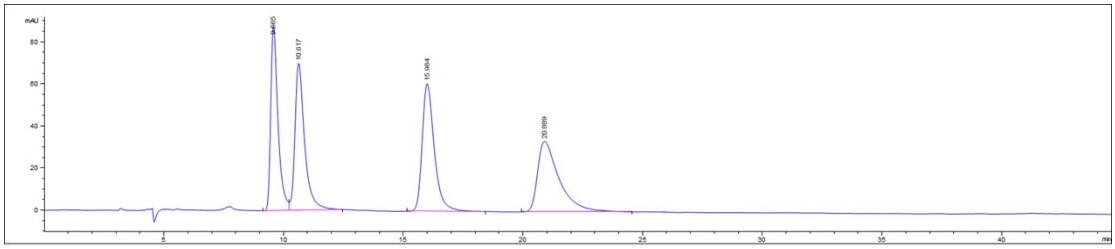
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.927	2288.2	88.6	0.3953	0.789	33.302	BV
2	13.593	2779.8	91.2	0.4537	0.715	40.458	VB
3	22.605	862.1	17.3	0.7339	0.78	12.547	BB
4	31.375	940.8	7.6	2.0665	0.469	13.693	MM



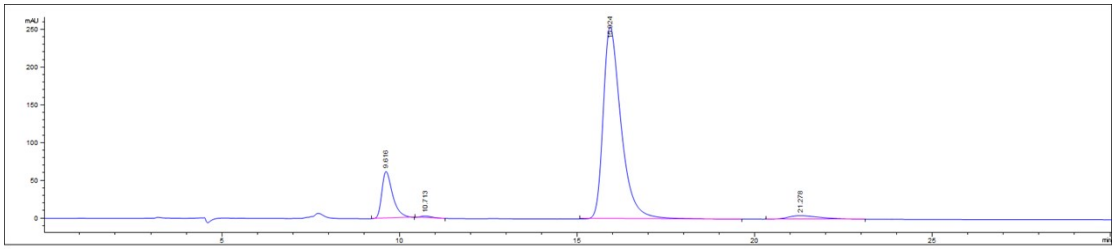
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.899	153.4	11.1	0.2299	0	0.585	MF
2	13.356	5008.3	172.9	0.4828	0.718	19.100	FM
3	21.782	20200.9	404.6	0.7505	0.513	77.041	BB
4	30.751	858.4	8	1.2584	0.495	3.274	BB



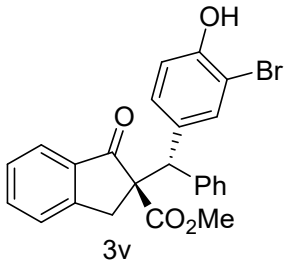
3u



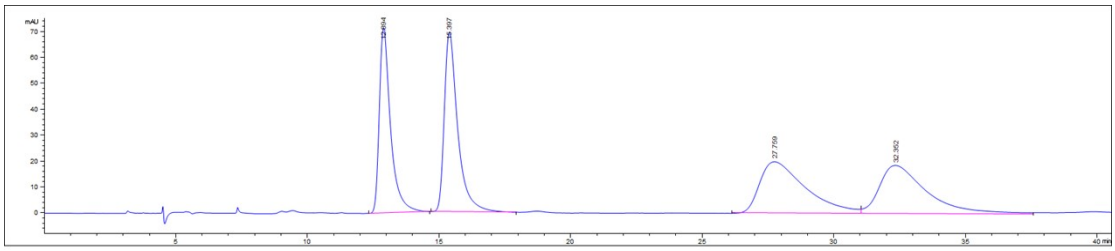
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.565	1851.7	87.4	0.3172	0.573	23.048	BV
2	10.617	1959.5	69.7	0.4161	0.578	24.389	VB
3	15.984	2129.3	60.5	0.5328	0.657	26.504	BB
4	20.889	2093.6	33.4	0.8864	0.448	26.059	BB



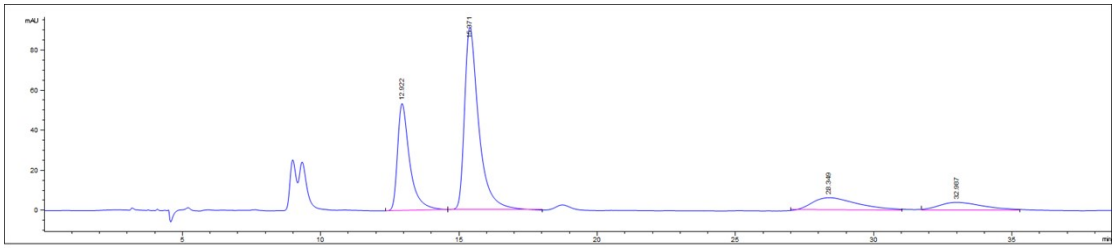
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	9.616	1317.3	61.7	0.3229	0.598	12.451	BB
2	10.713	49.2	2.2	0.3464	0.615	0.465	BB
3	15.924	8920.7	254.3	0.5273	0.589	84.319	BB
4	21.278	292.5	4.7	0.7466	0.593	2.765	BB



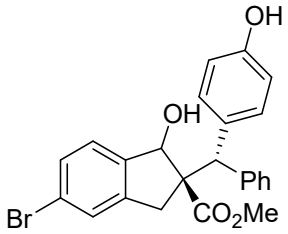
3v



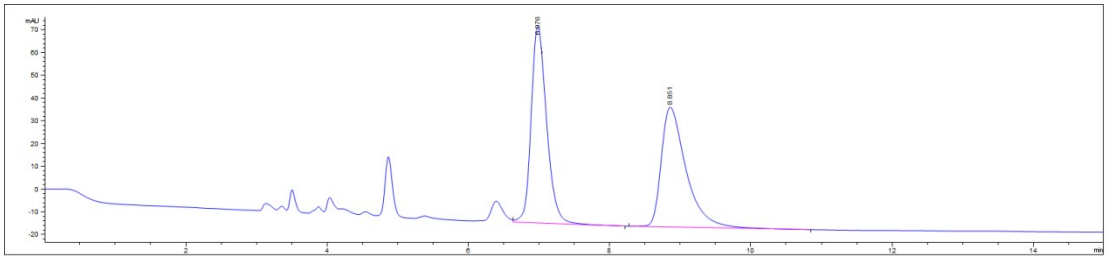
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.894	2125.1	71.4	0.4431	0.551	22.862	BB
2	15.397	2458.4	69.3	0.5258	0.555	26.448	BB
3	27.759	2396.1	19.9	2.0088	0	25.778	MF
4	32.352	2315.7	18.6	2.0792	0.493	24.913	FM



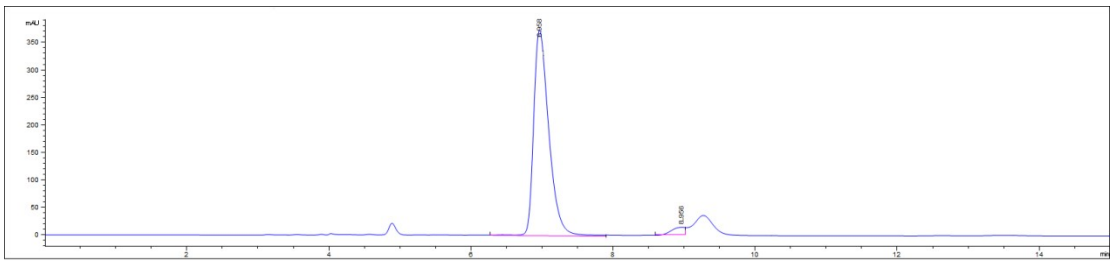
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.922	1633.1	53.4	0.4526	0.549	26.860	BB
2	15.371	3261.8	91.2	0.5332	0.545	53.646	BB
3	28.349	710.2	6.2	1.924	0.525	11.681	MM
4	32.987	475	4.1	1.9462	0.665	7.813	MM



4

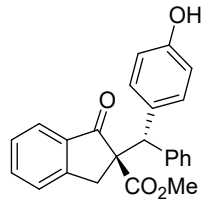


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.976	1314	86	0.2546	0.729	50.638	FM
2	8.851	1280.9	52.4	0.3671	0.525	49.362	BB

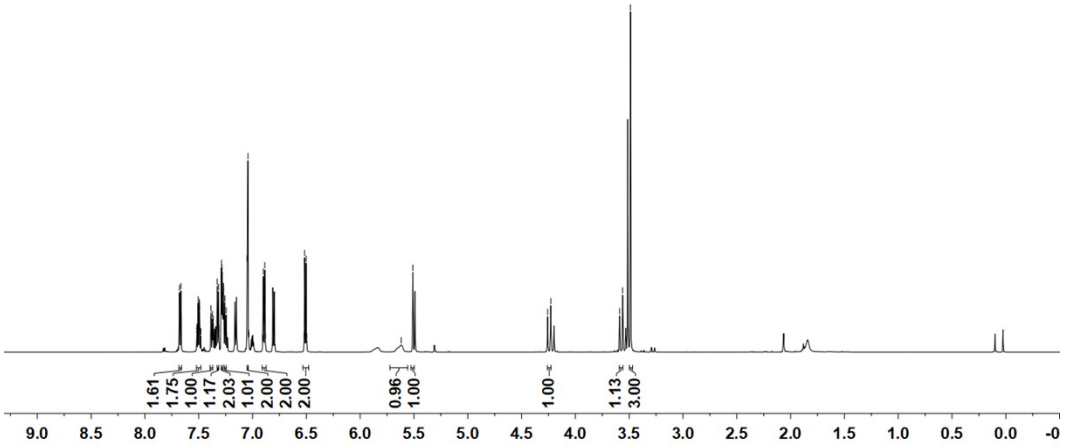


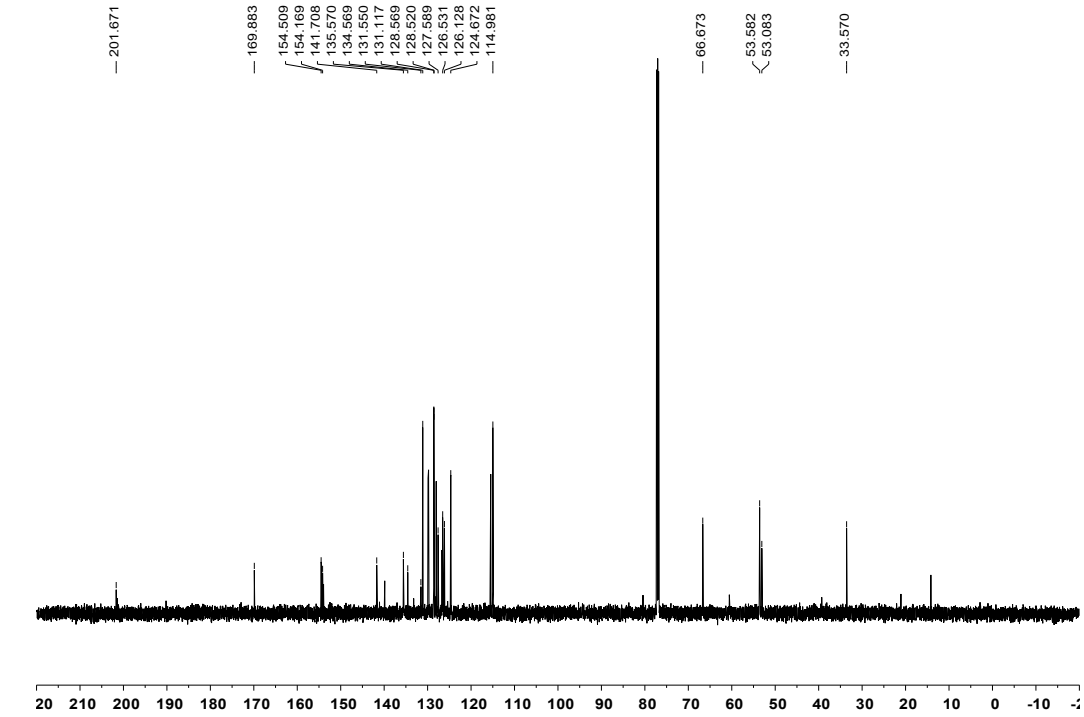
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.958	5639.9	375.9	0.25	0.606	96.622	MM
2	8.956	197.2	14.7	0.2239	2.694	3.378	MF

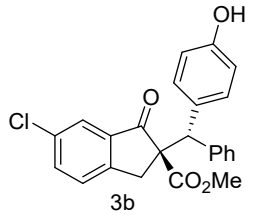
9. ^{1}H-NMR and ^{13}C-NMR spectra



3a
major diastereomer

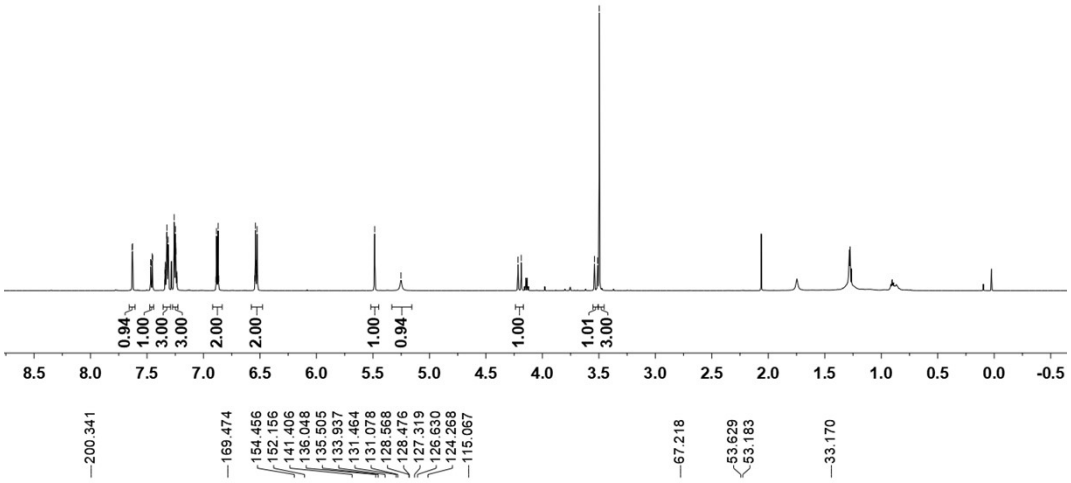


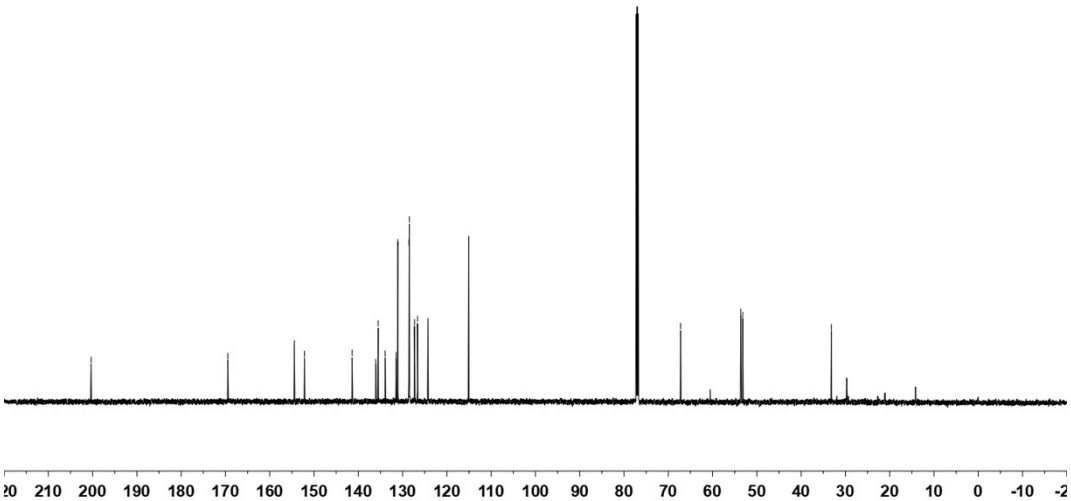


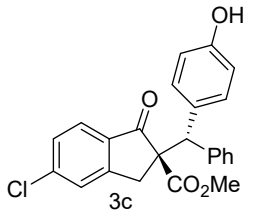


3b

major diastereomer

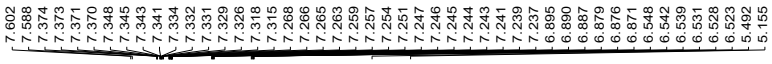


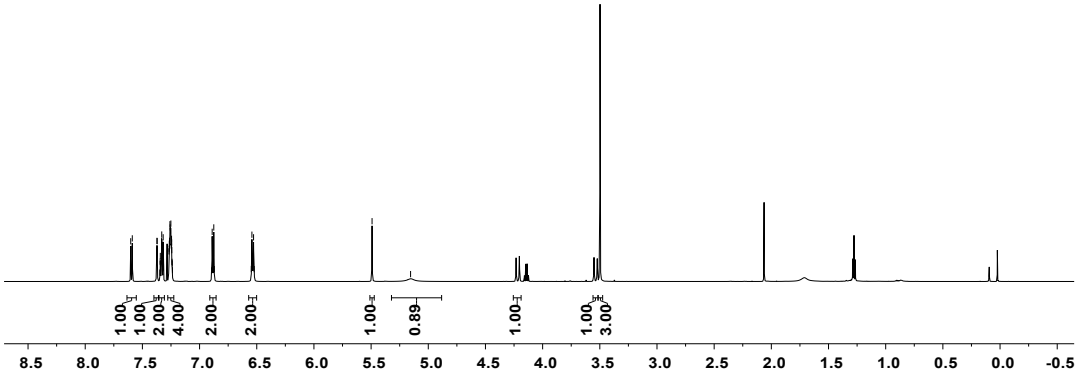


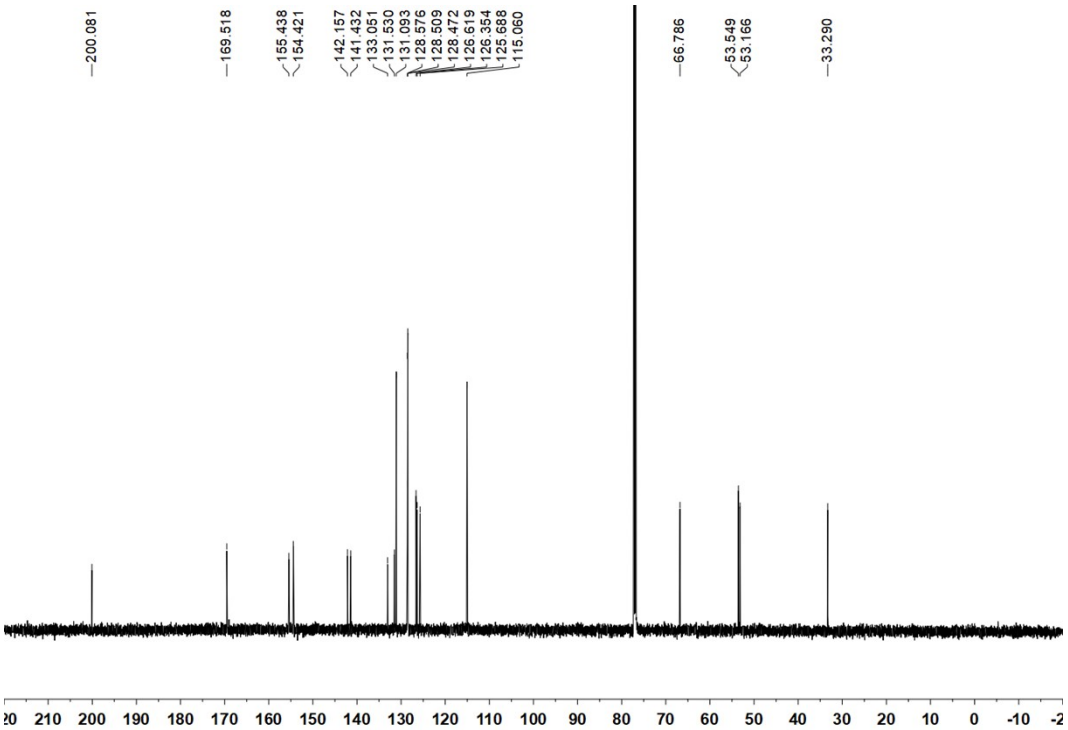


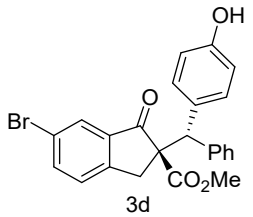
3c

major diastereomer



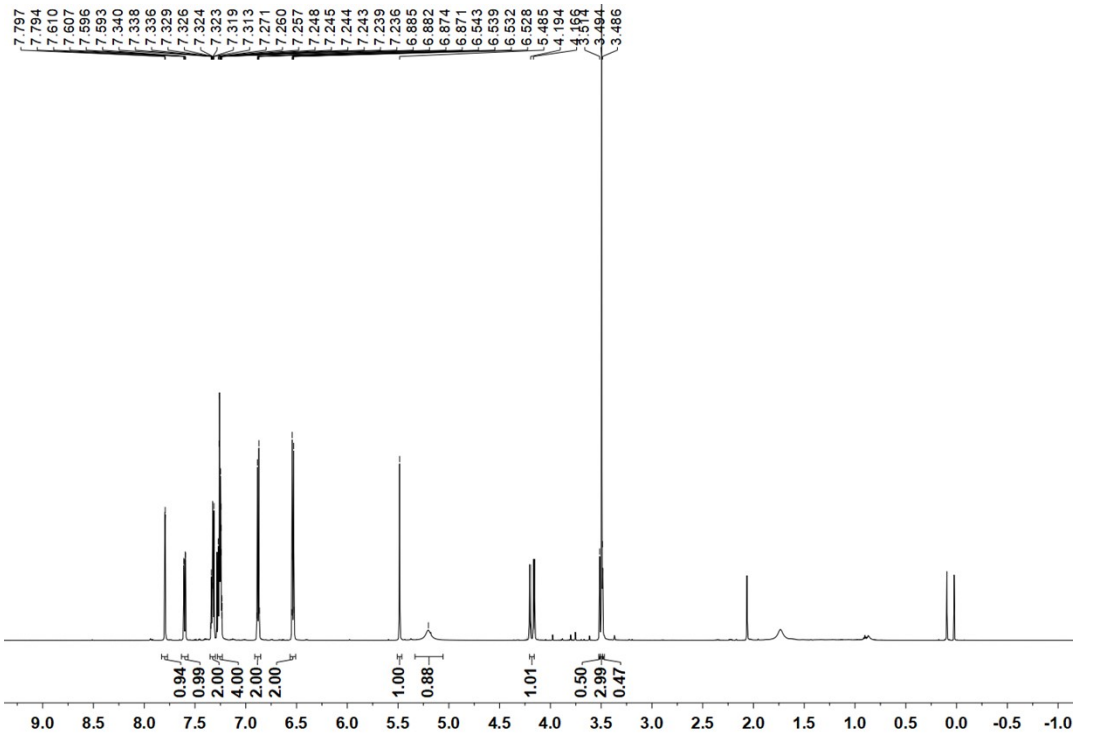


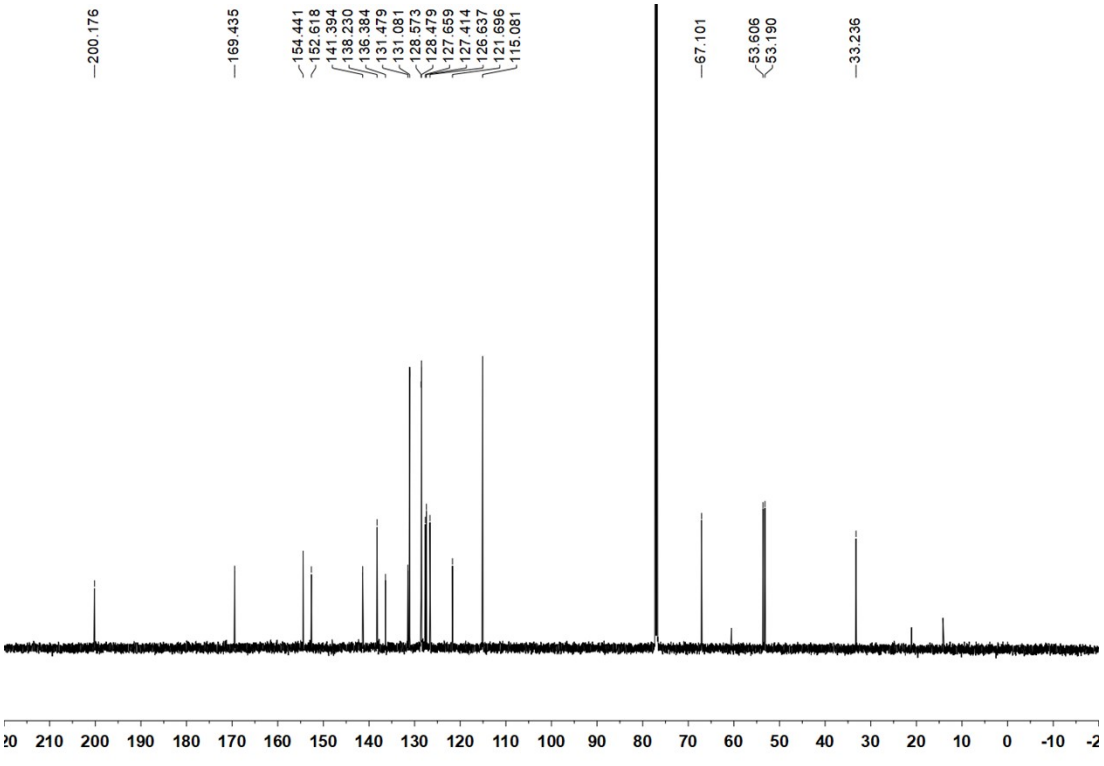


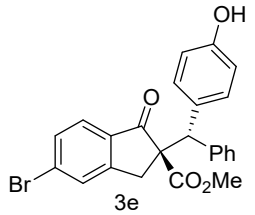


3d

major diastereomer

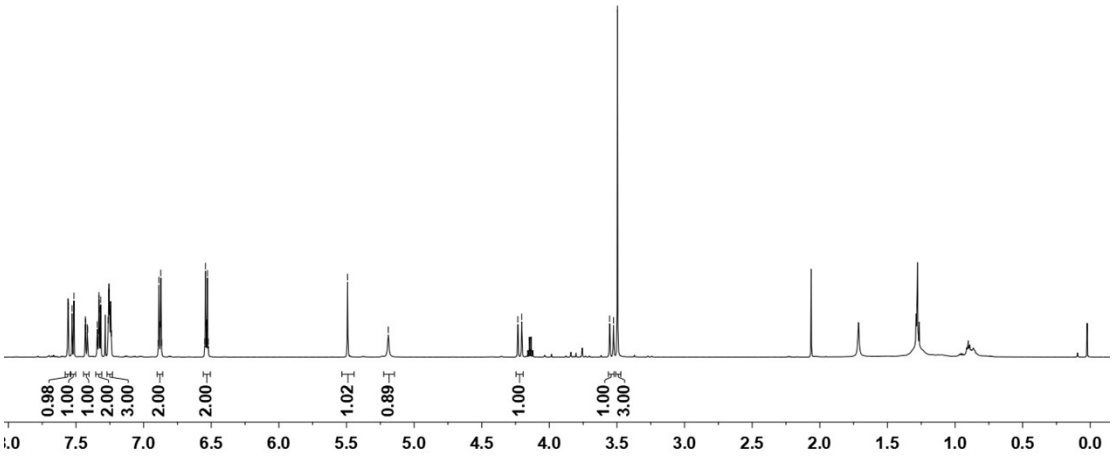


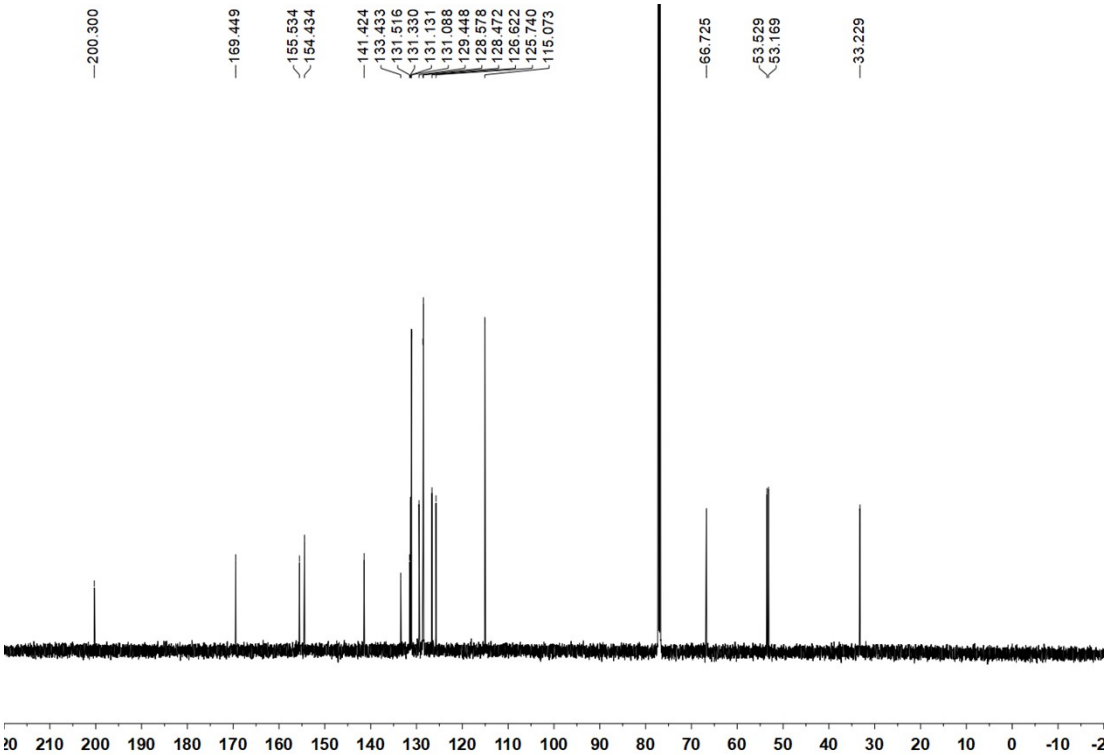


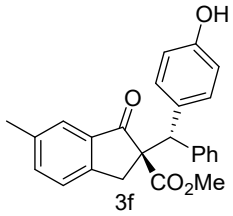


3e

major diastereomer

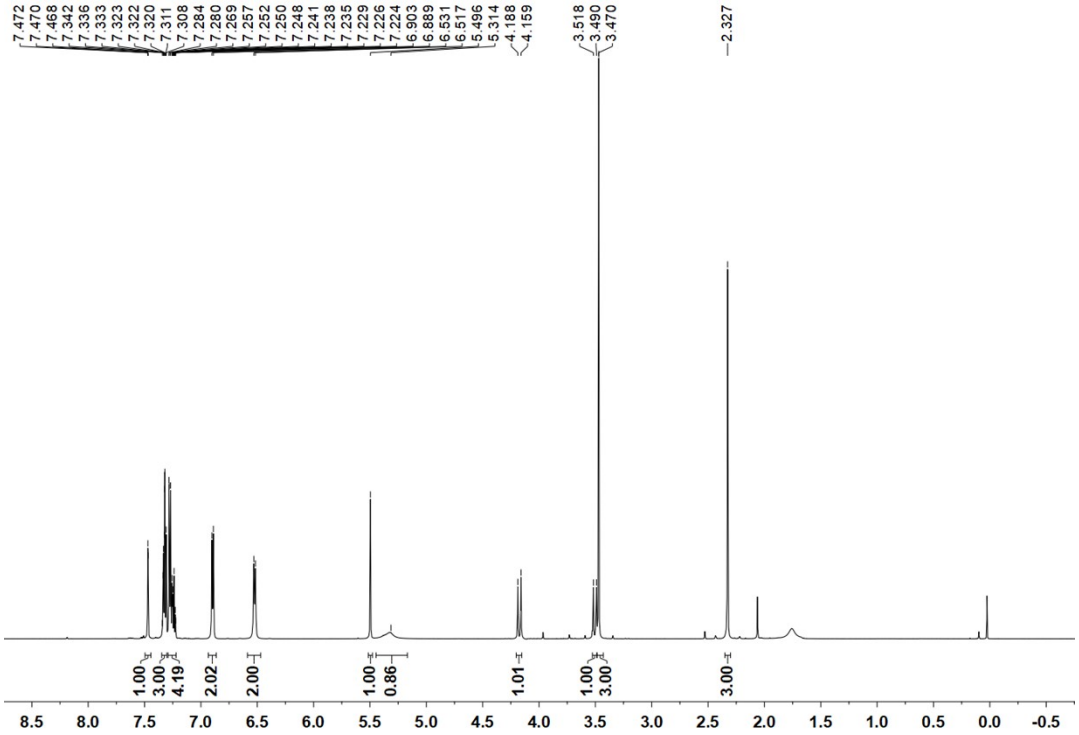


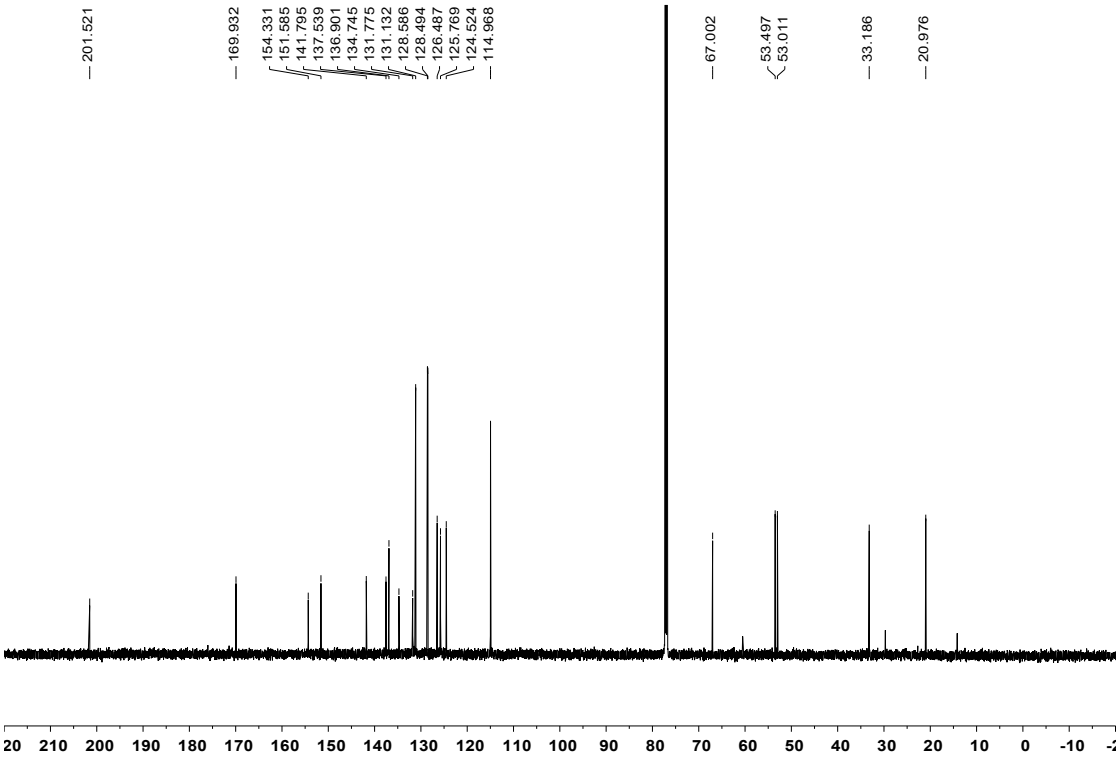


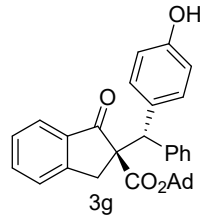


3f

major diastereomer

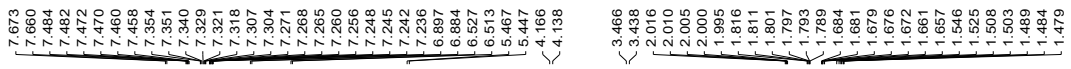


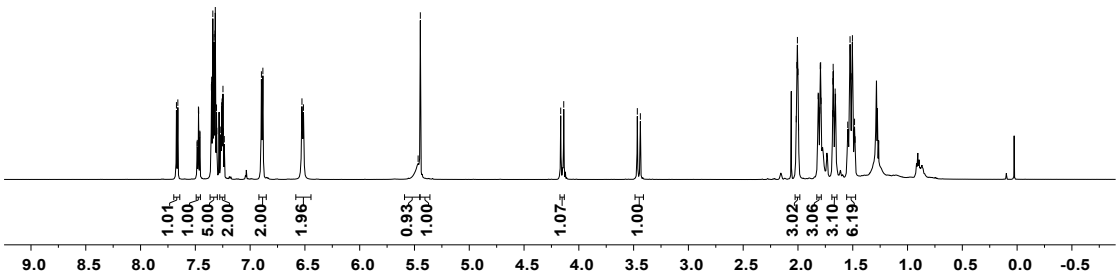


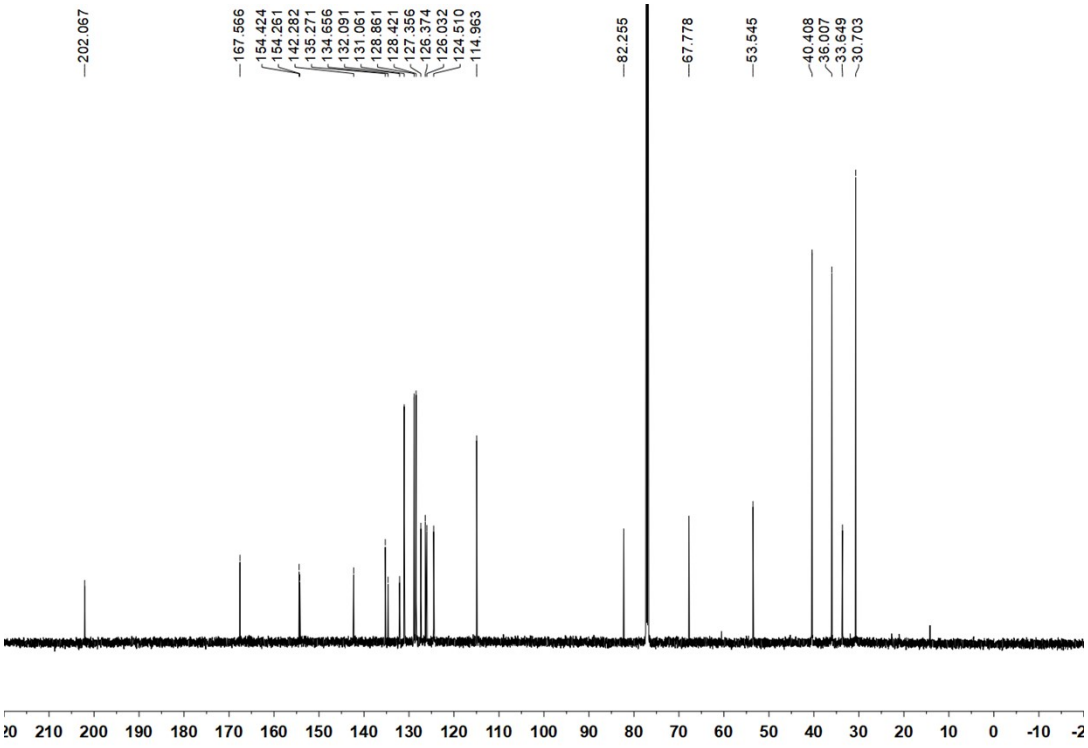


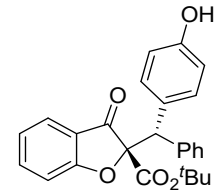
3g

major diastereomer

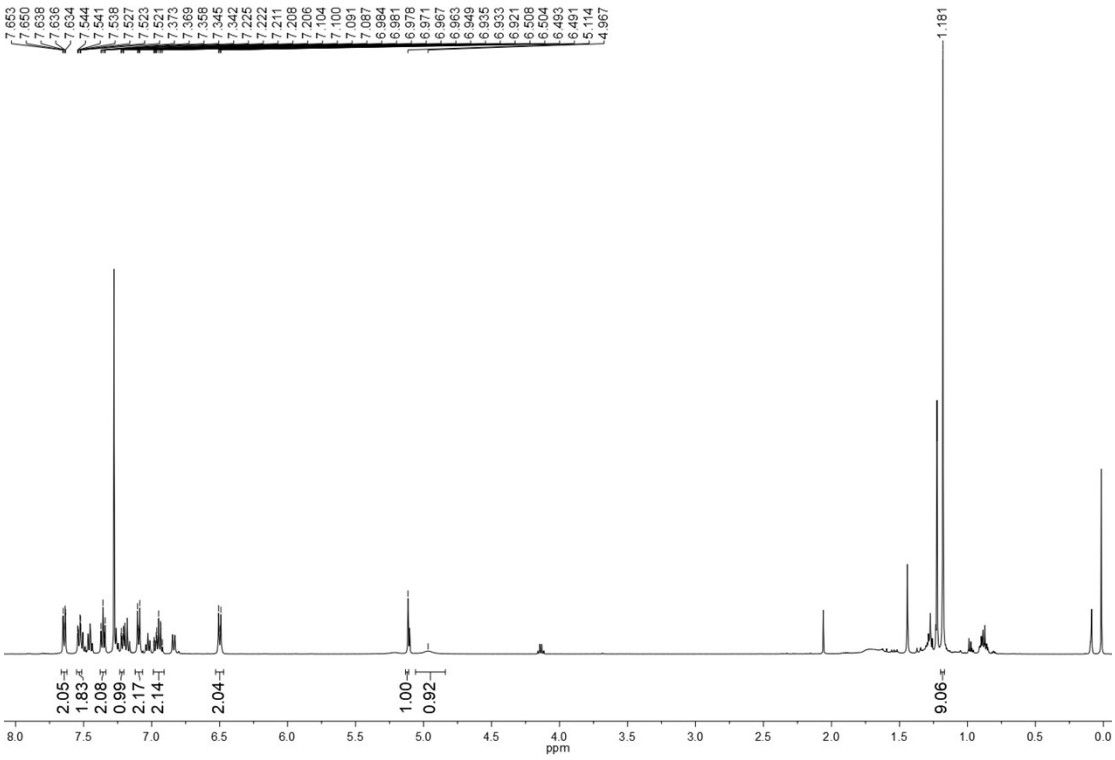


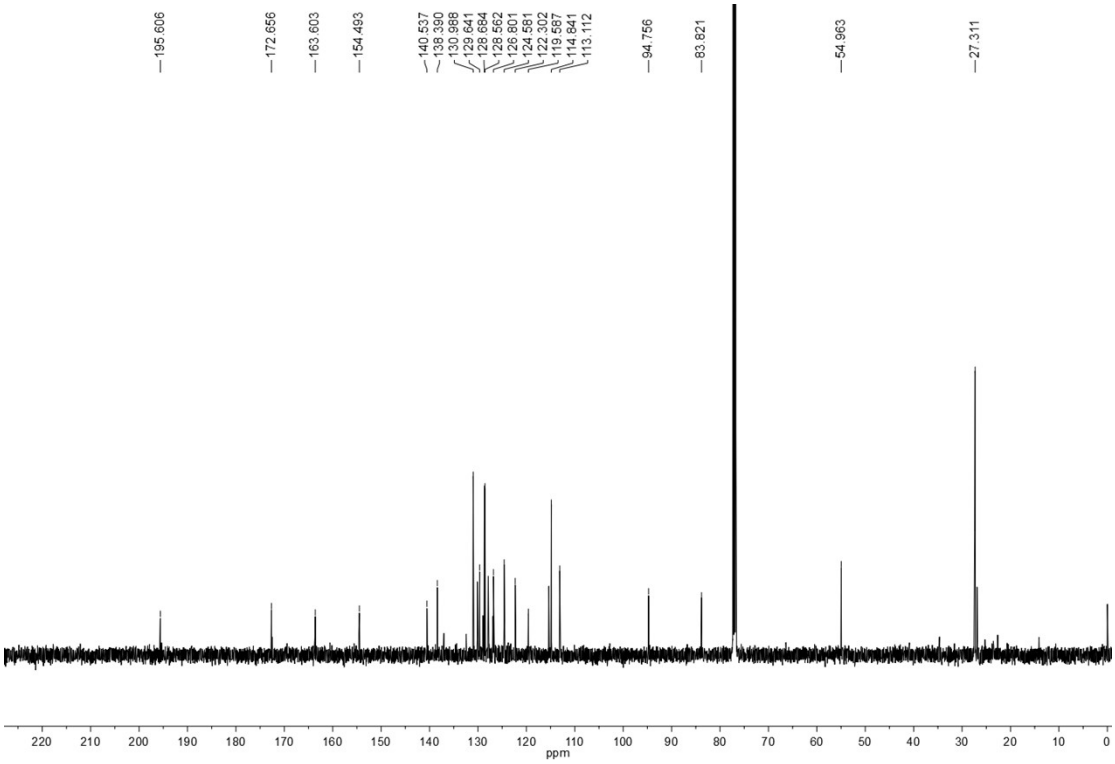


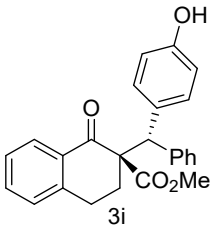




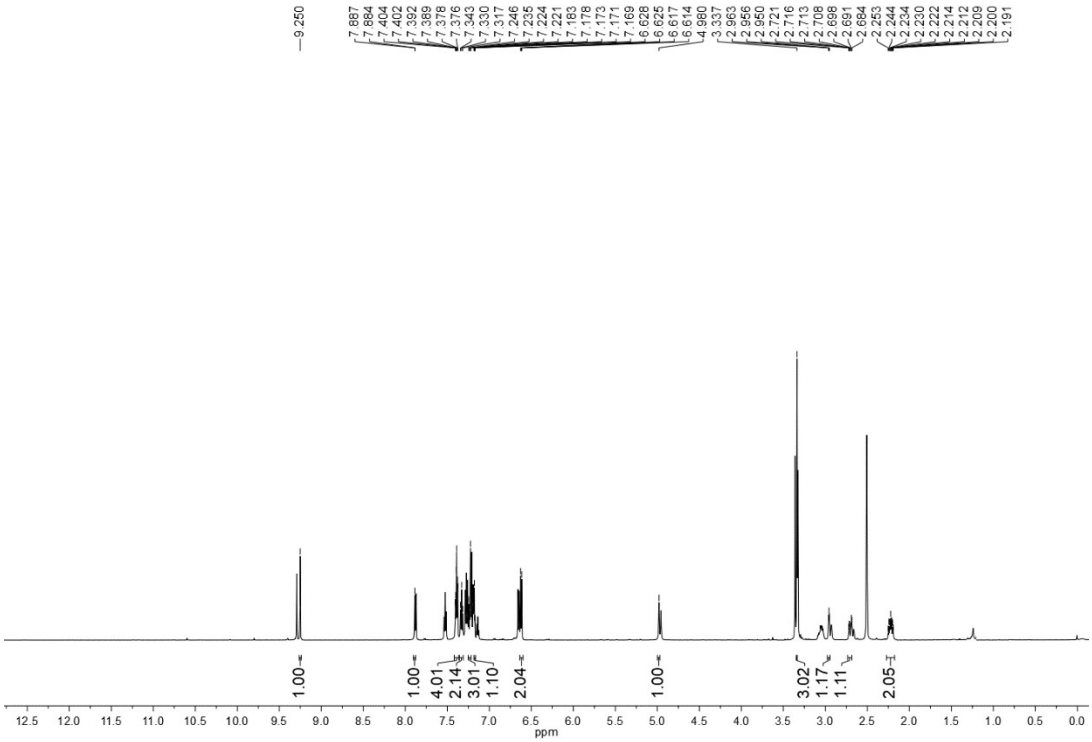
3h
major diastereomer

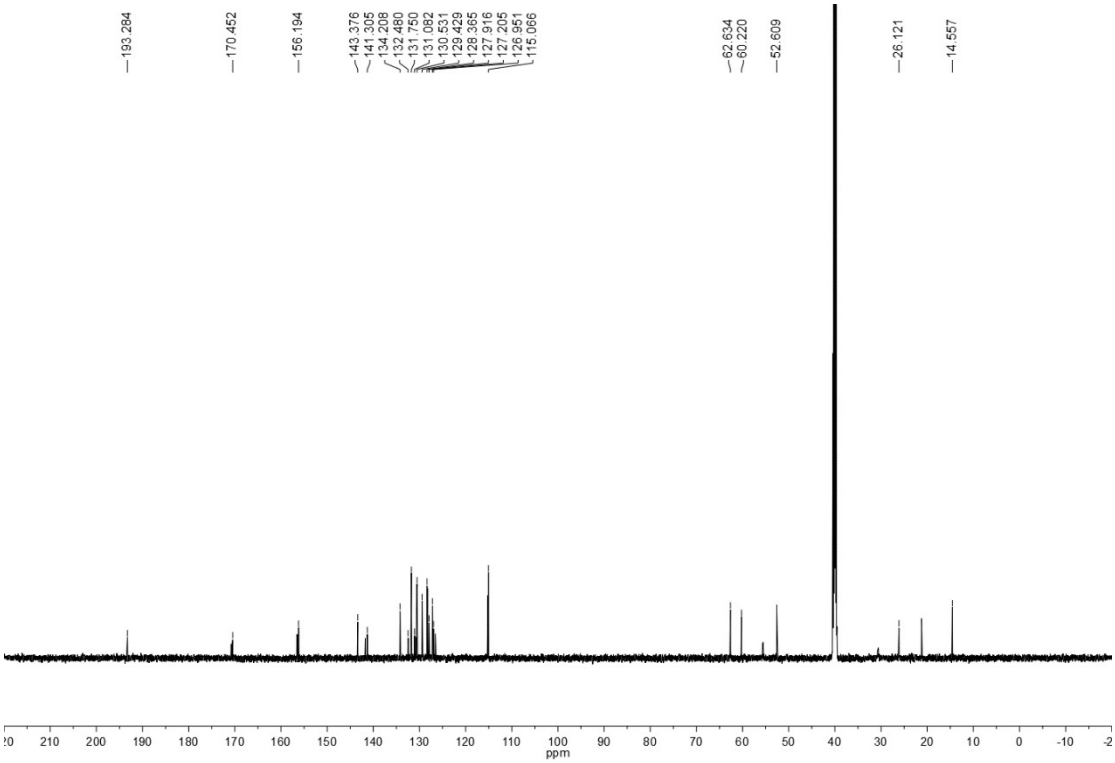


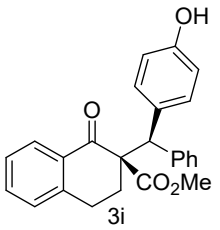




3i
major diastereomer

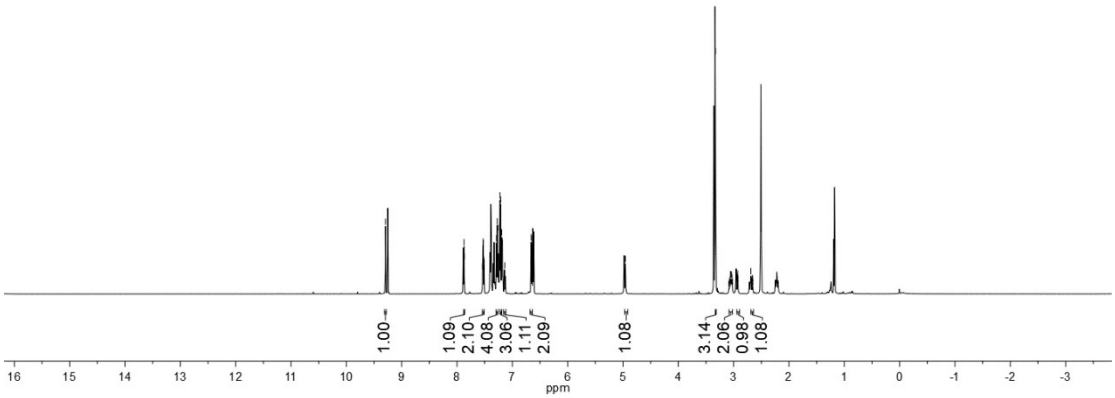


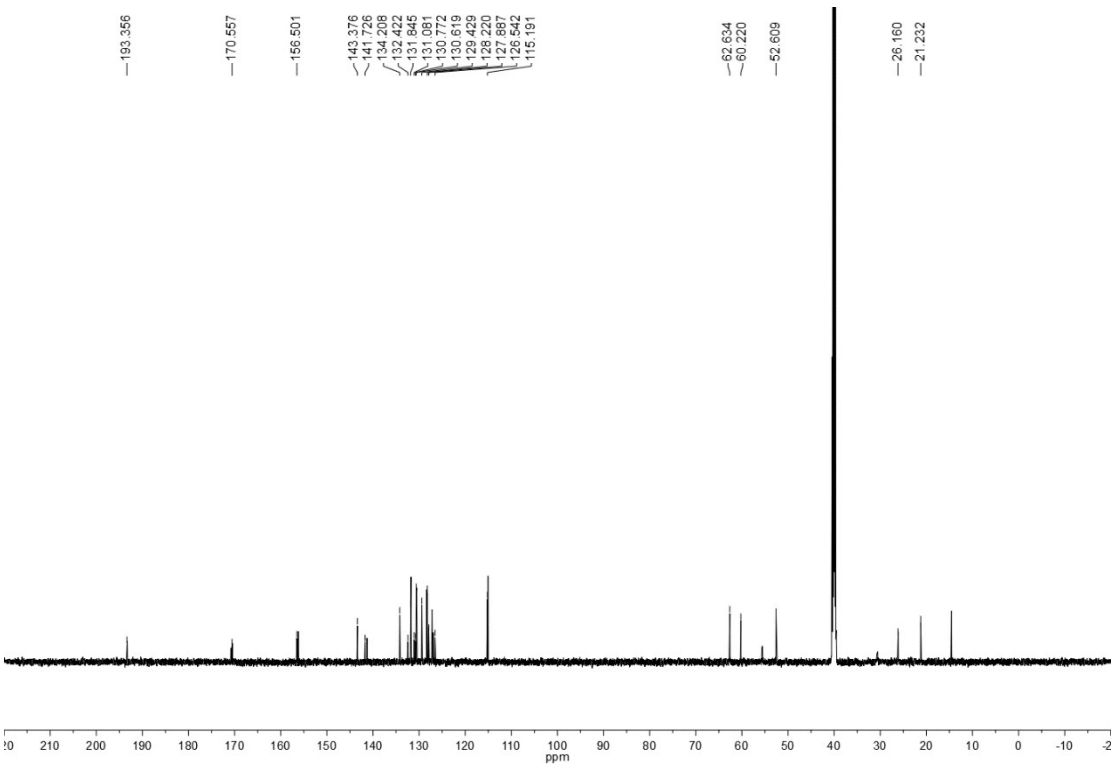


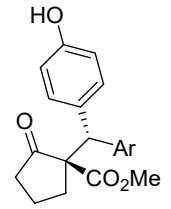


3i

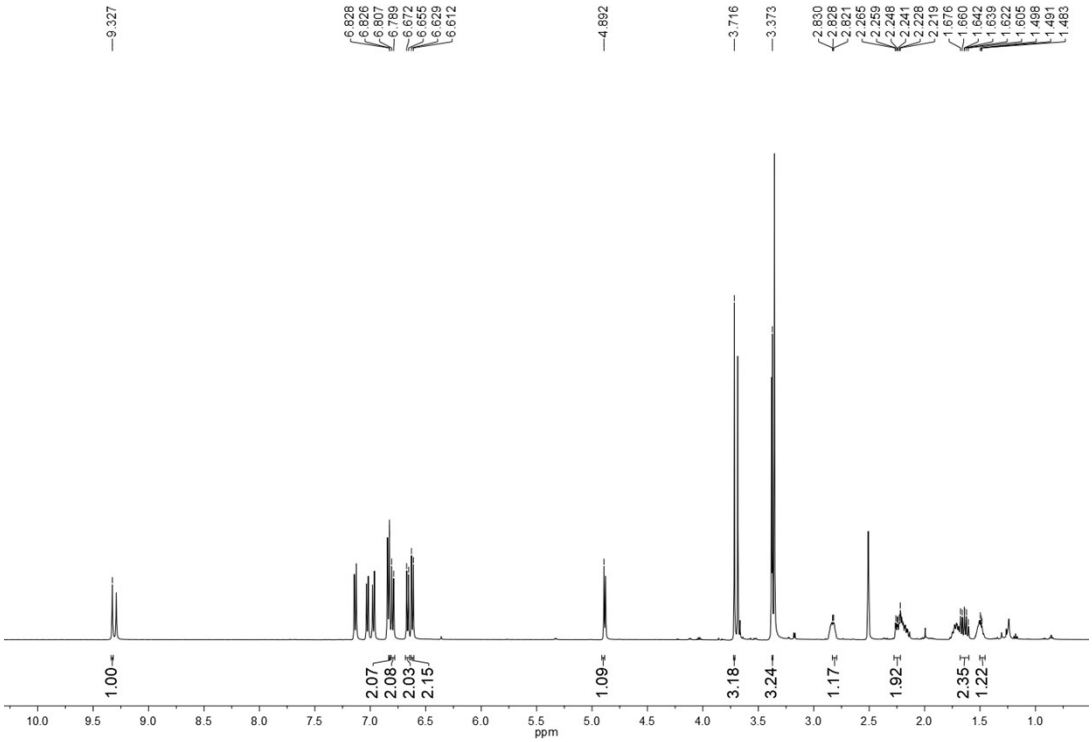
minor diastereomer

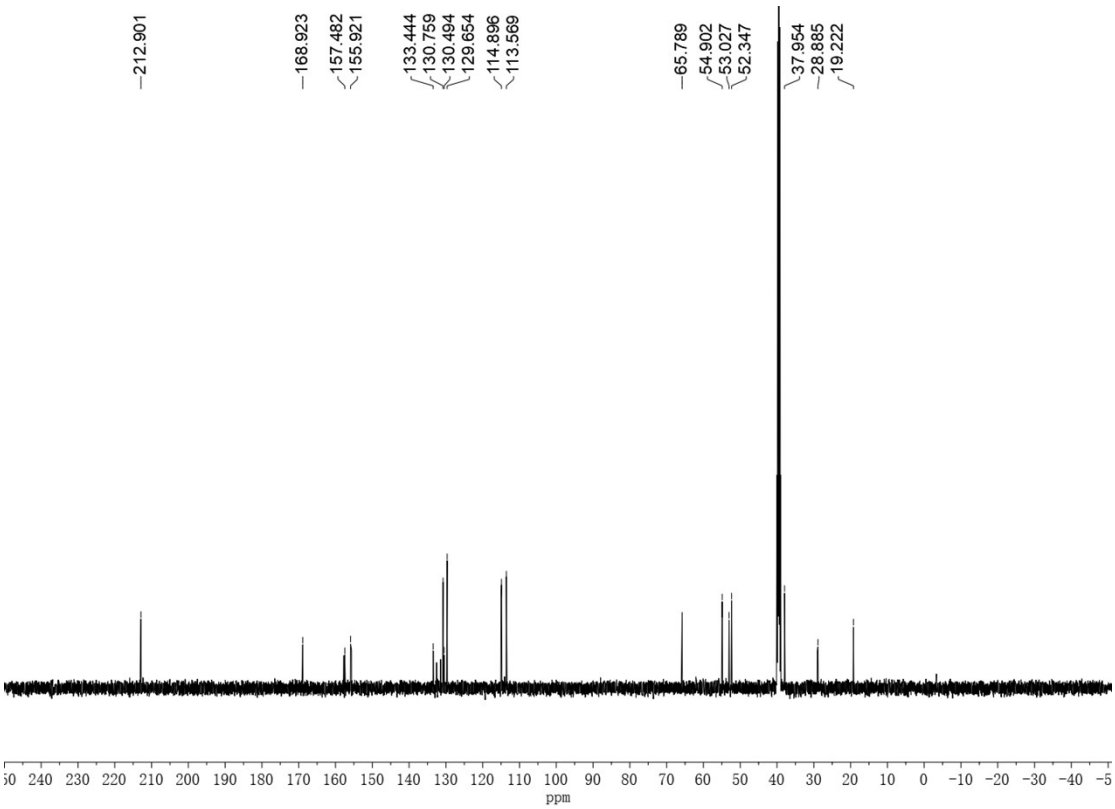


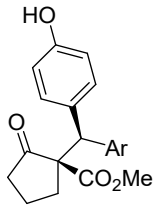




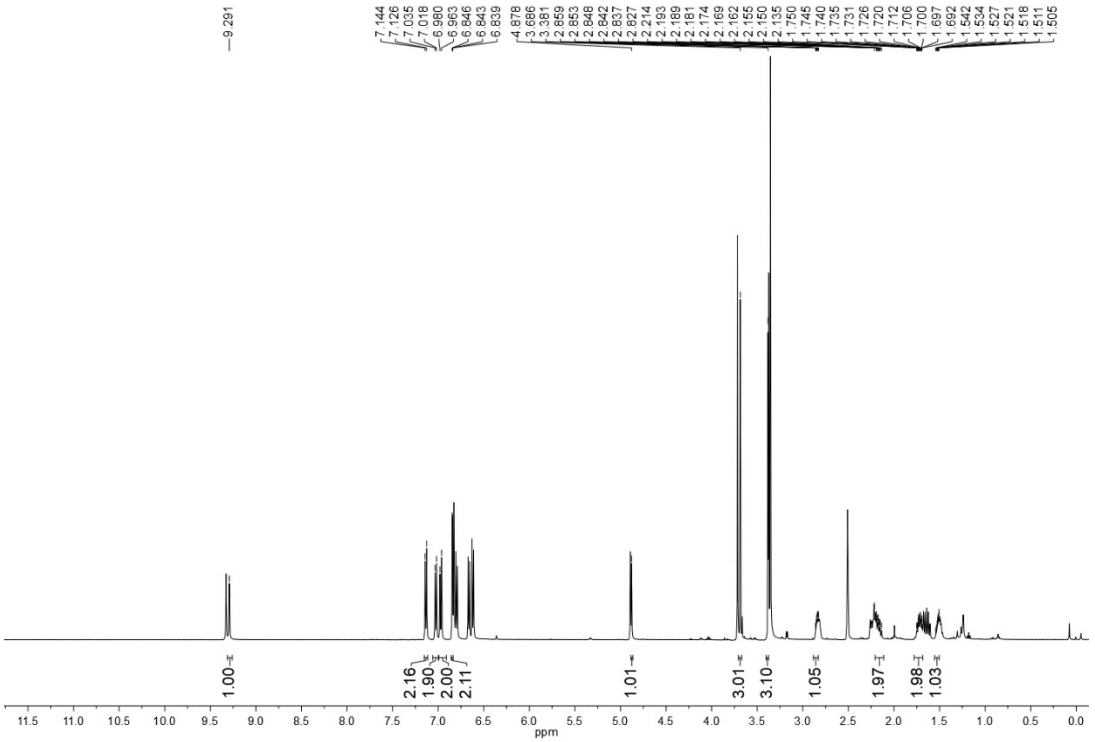
3j: Ar = 4-OMePh
major diastereomer

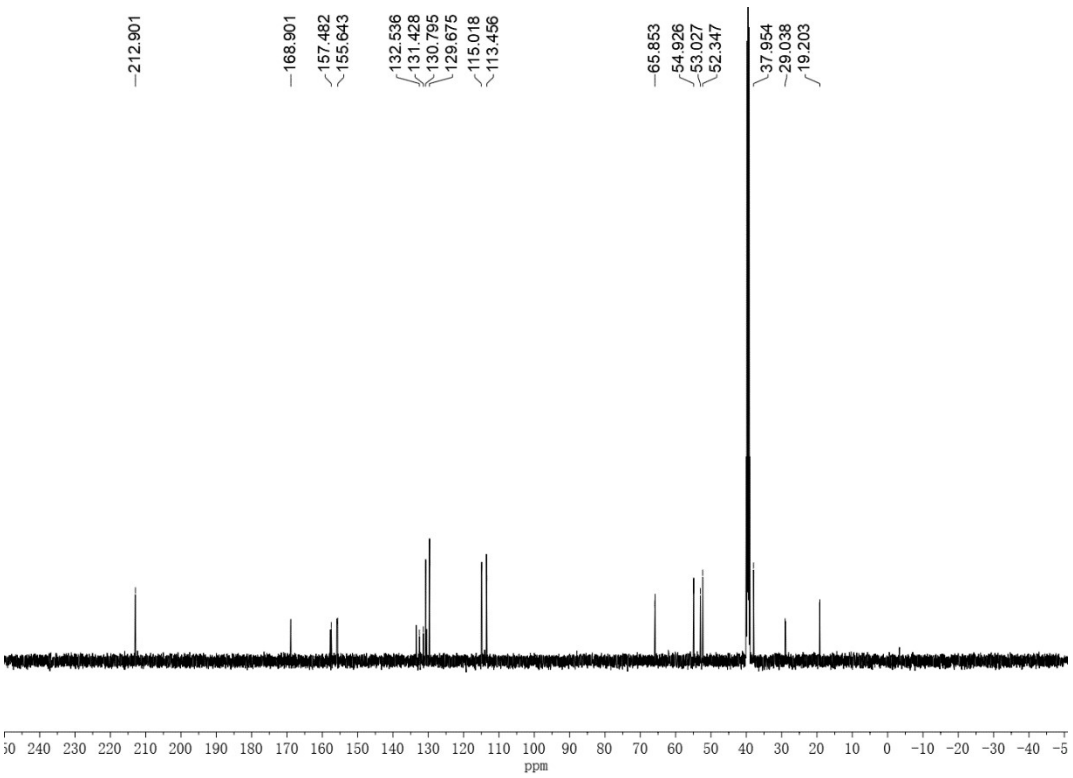


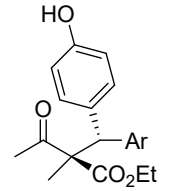




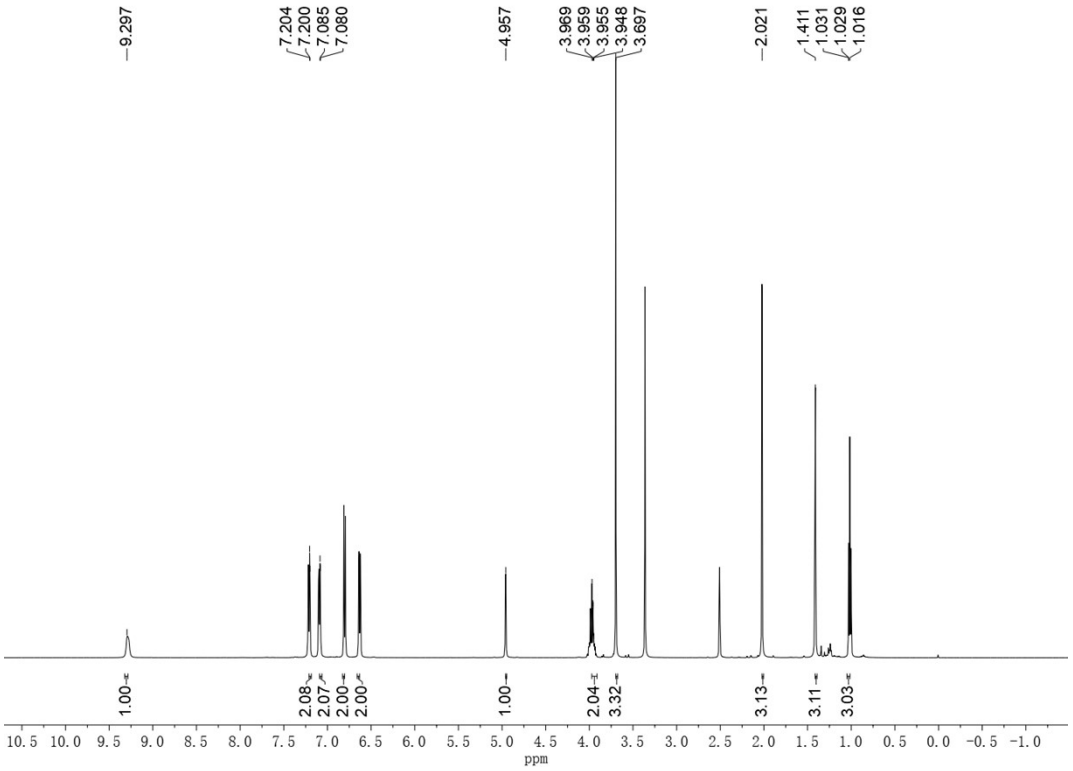
3j: Ar = 4-OMePh
minor diastereomer

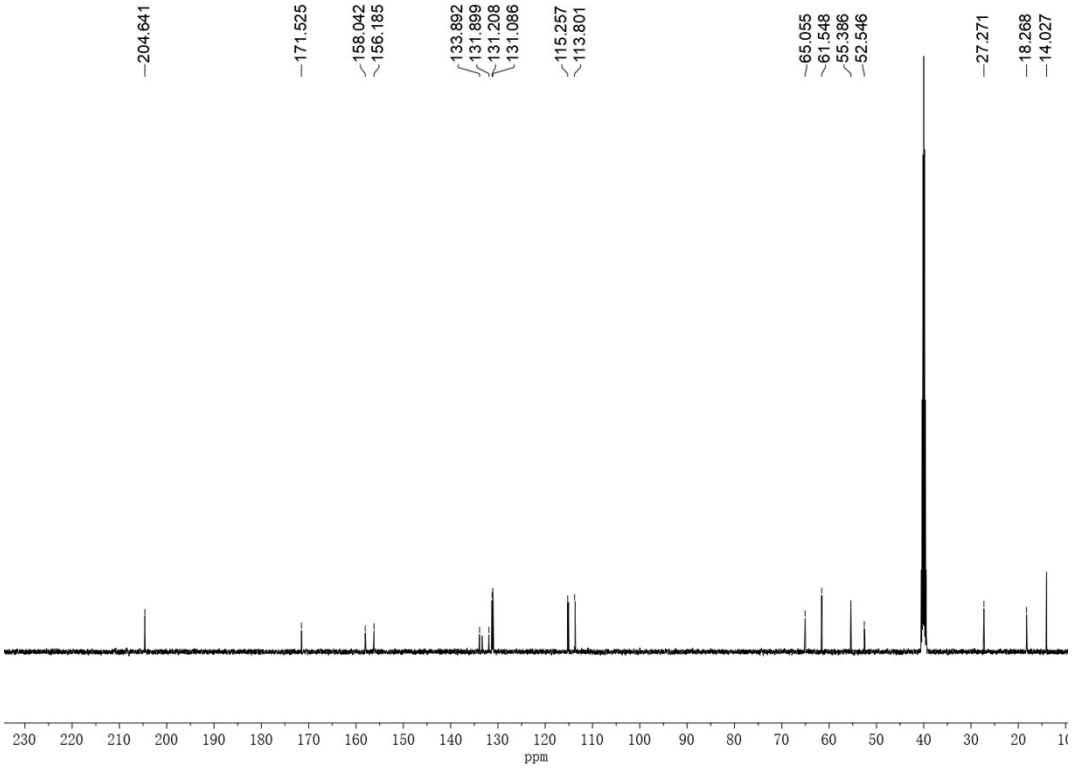


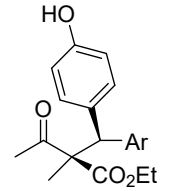




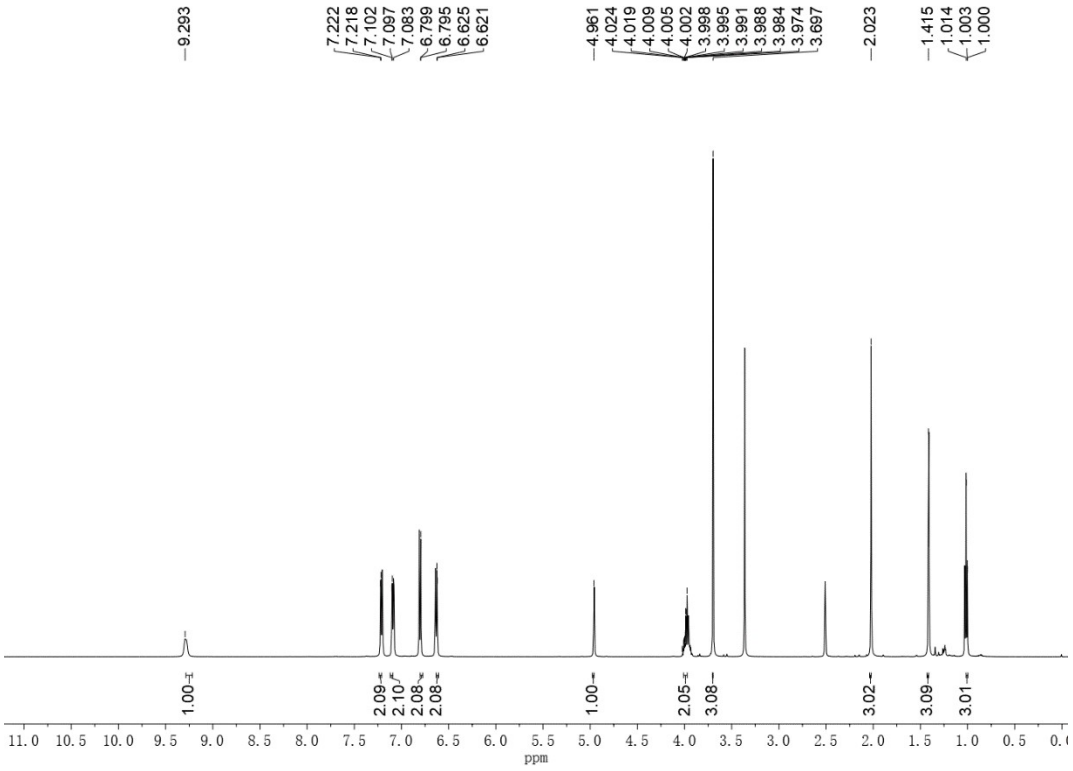
3k: Ar = 4-OMePh
major diastereomer

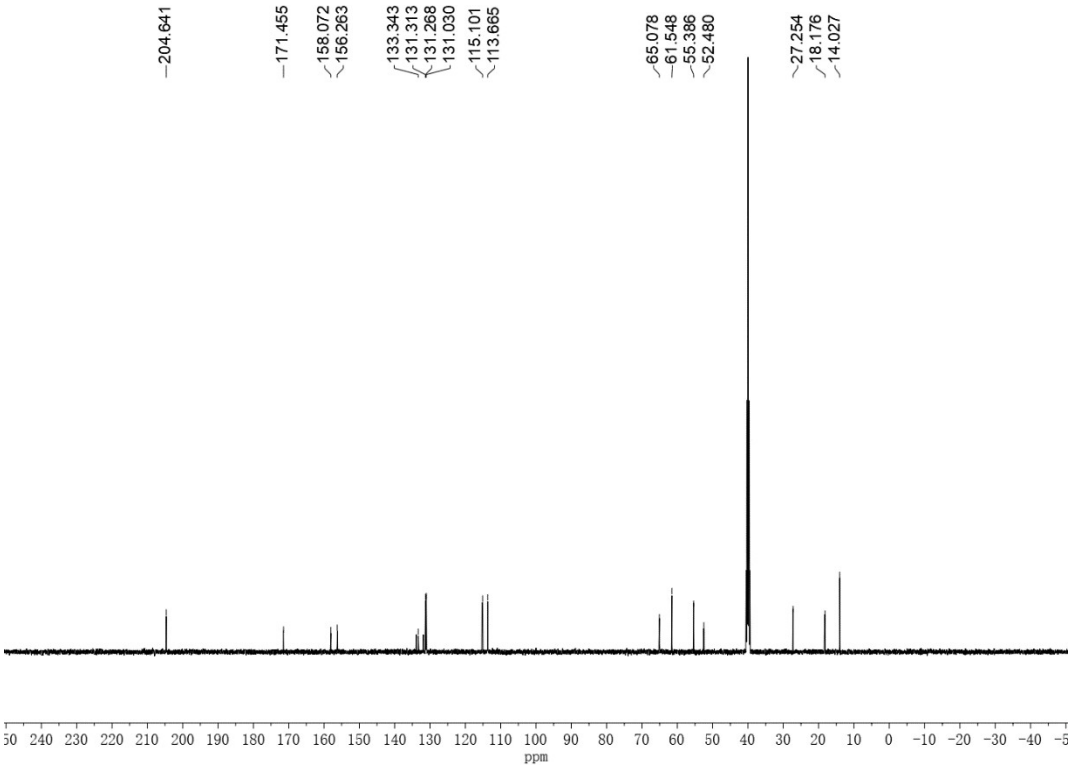


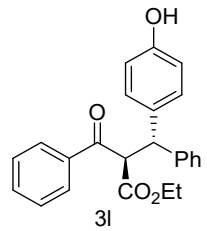




3k: Ar = 4-OMePh
minor diastereomer

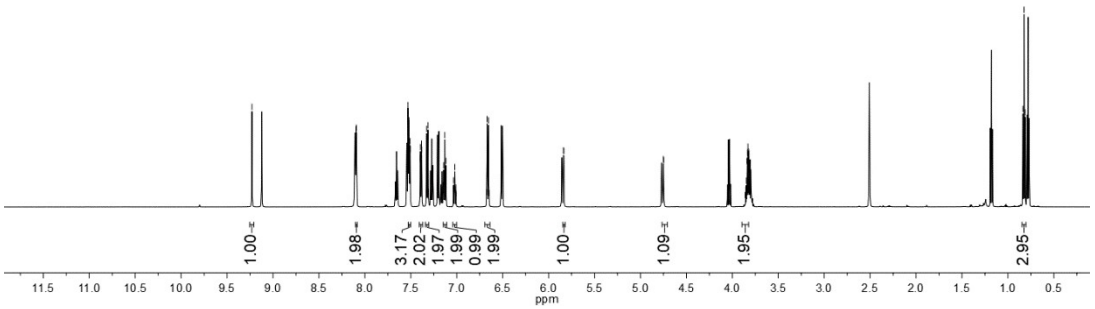


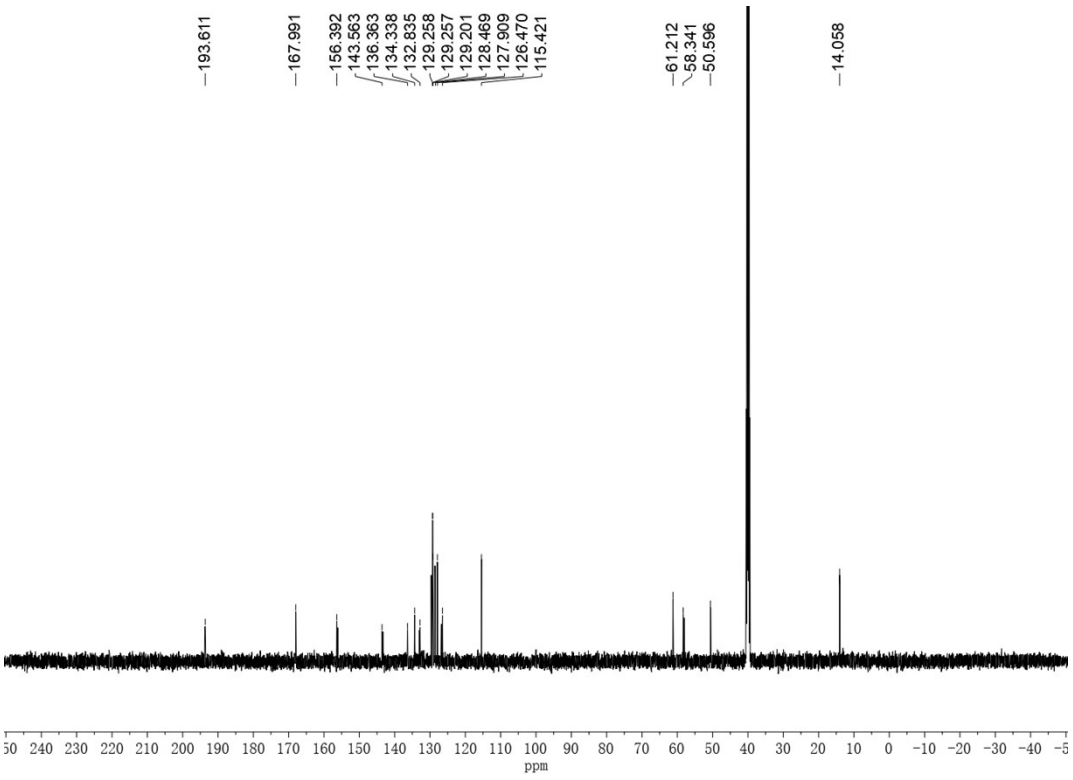


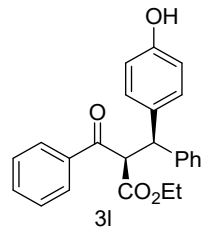


3l

major diastereomer

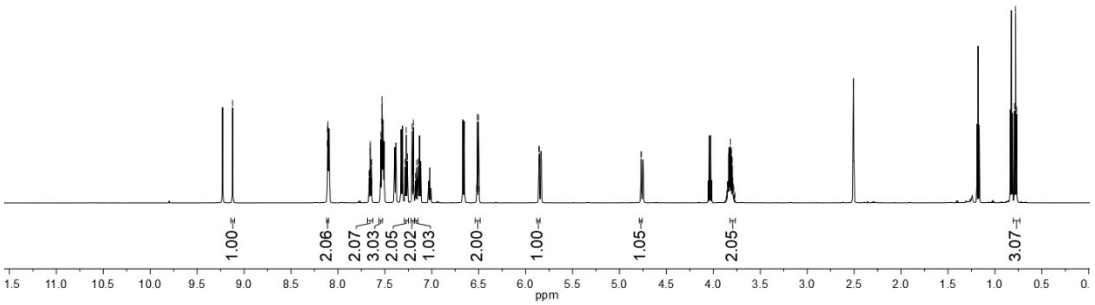


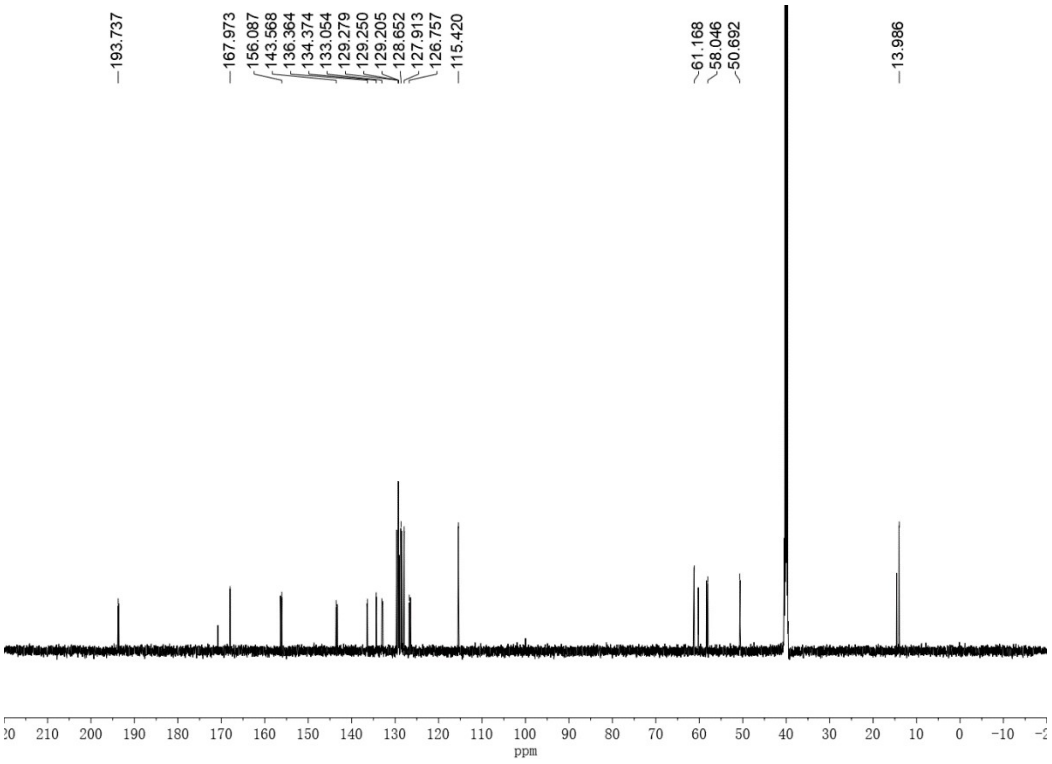


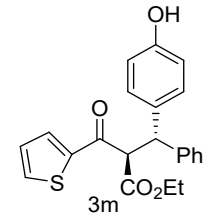


3l

minor diastereomer

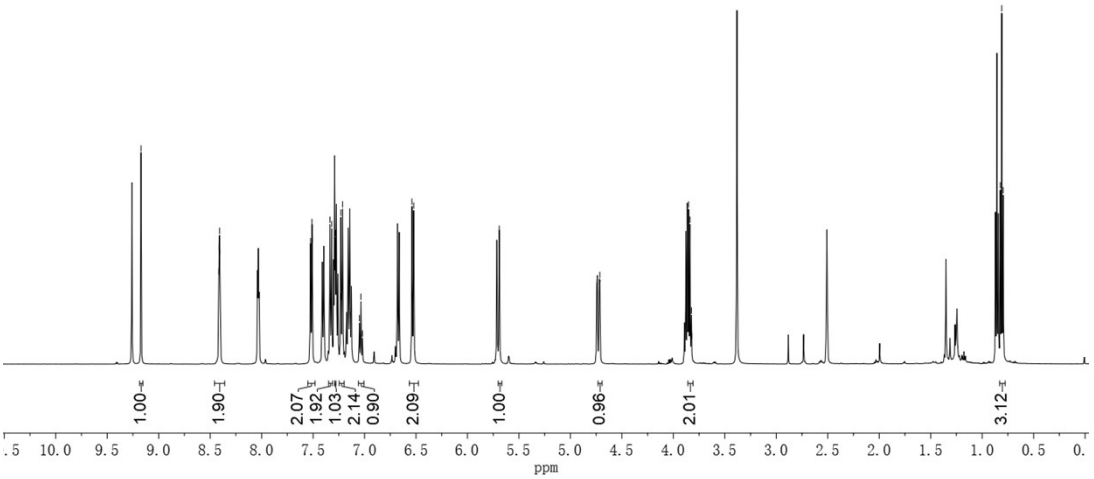


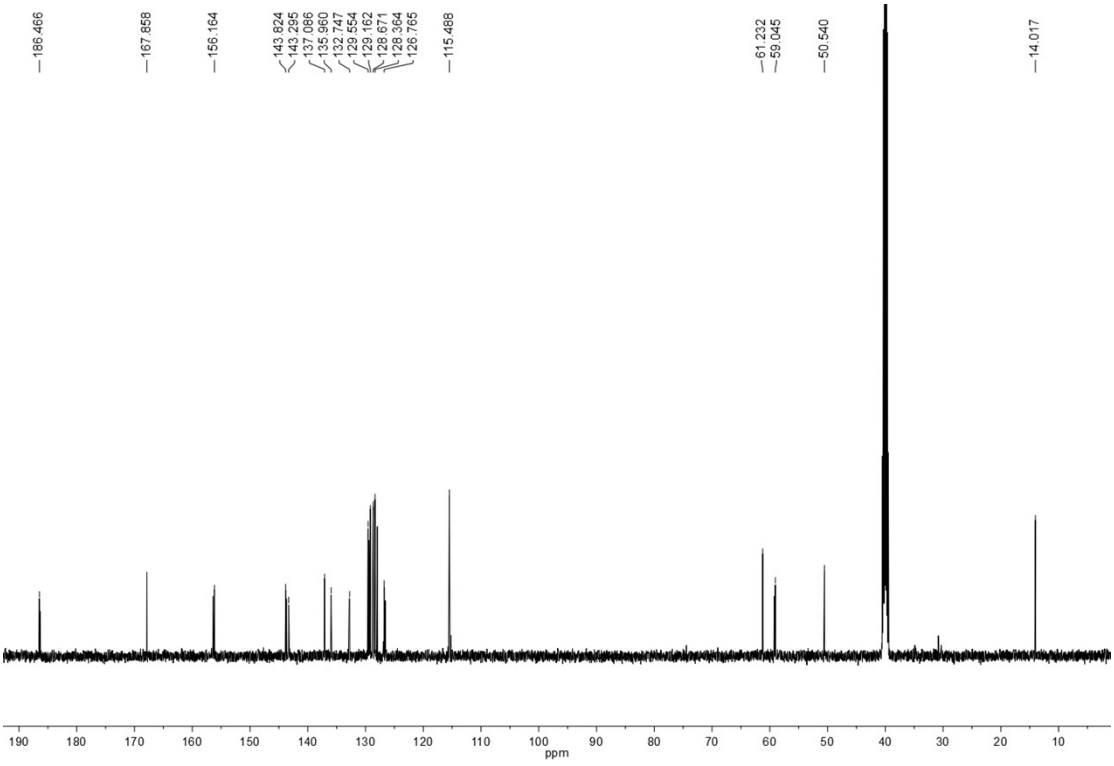


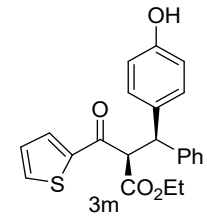


3m

major diastereomer

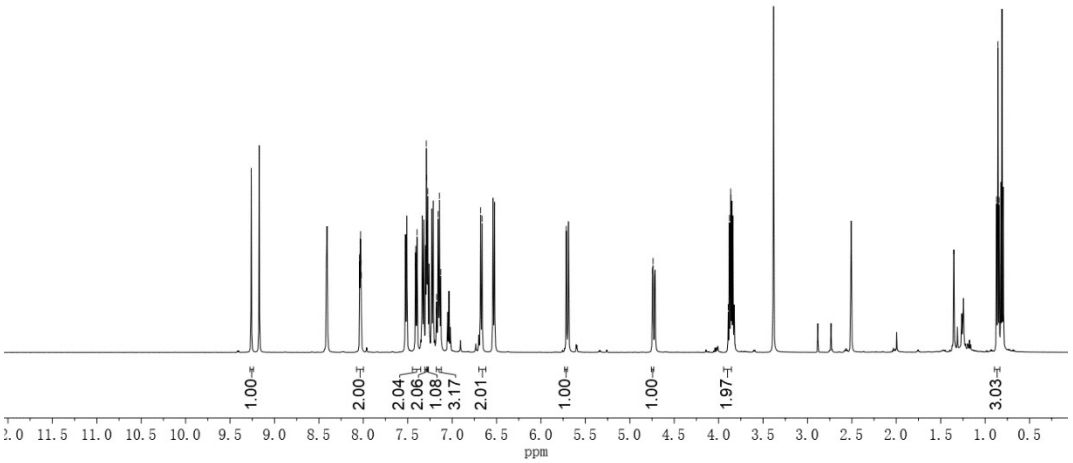


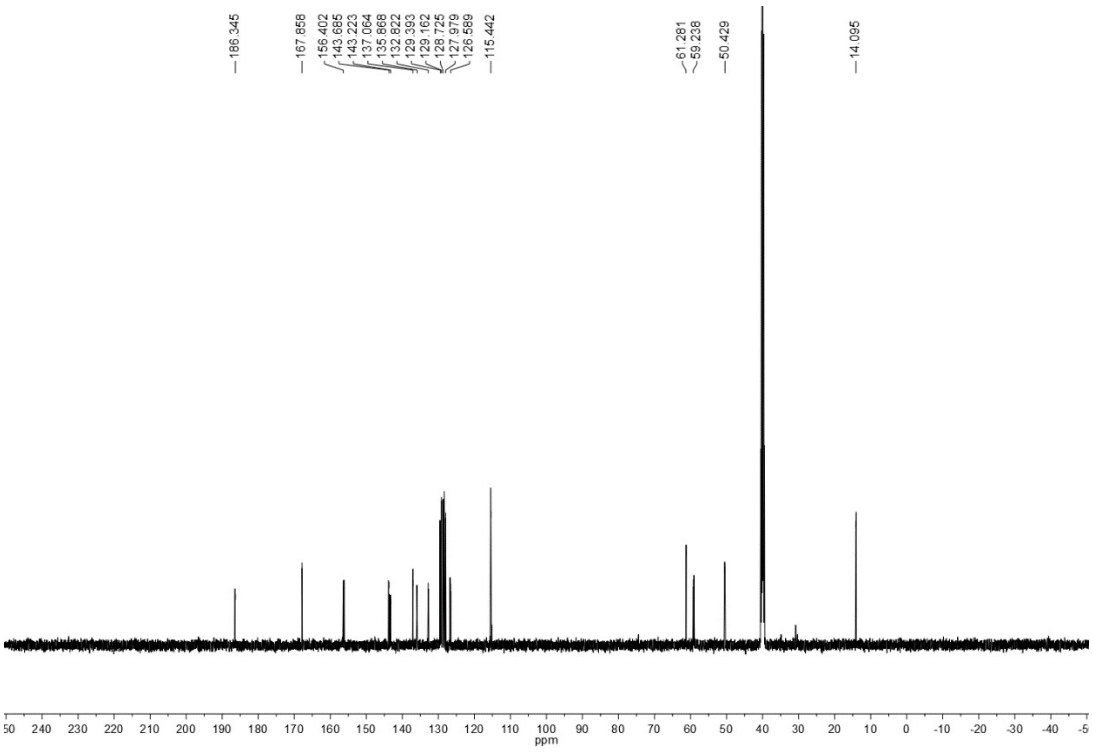


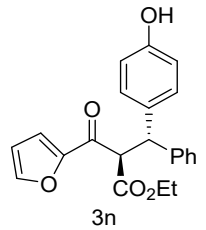


3m

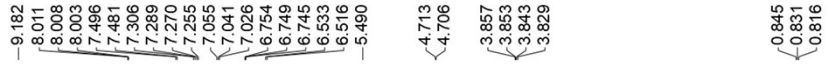
minor diastereomer

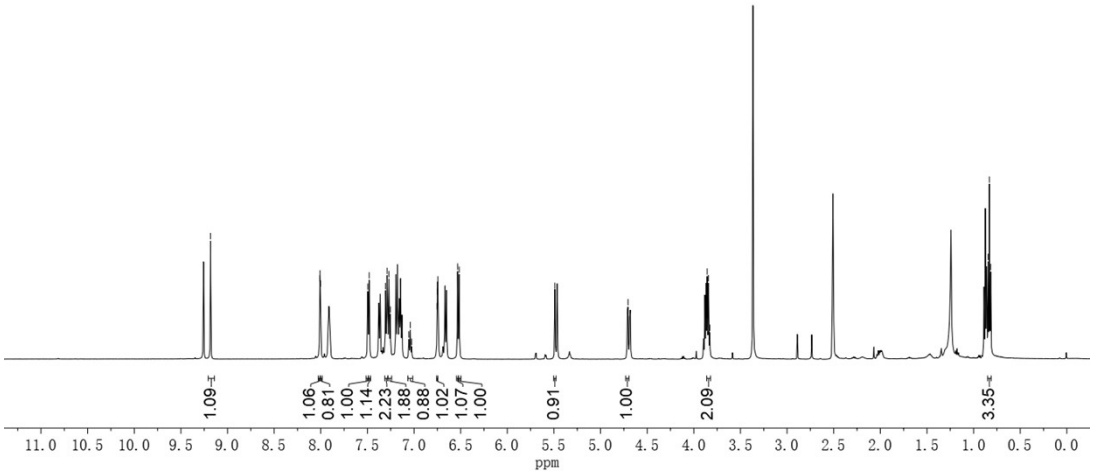


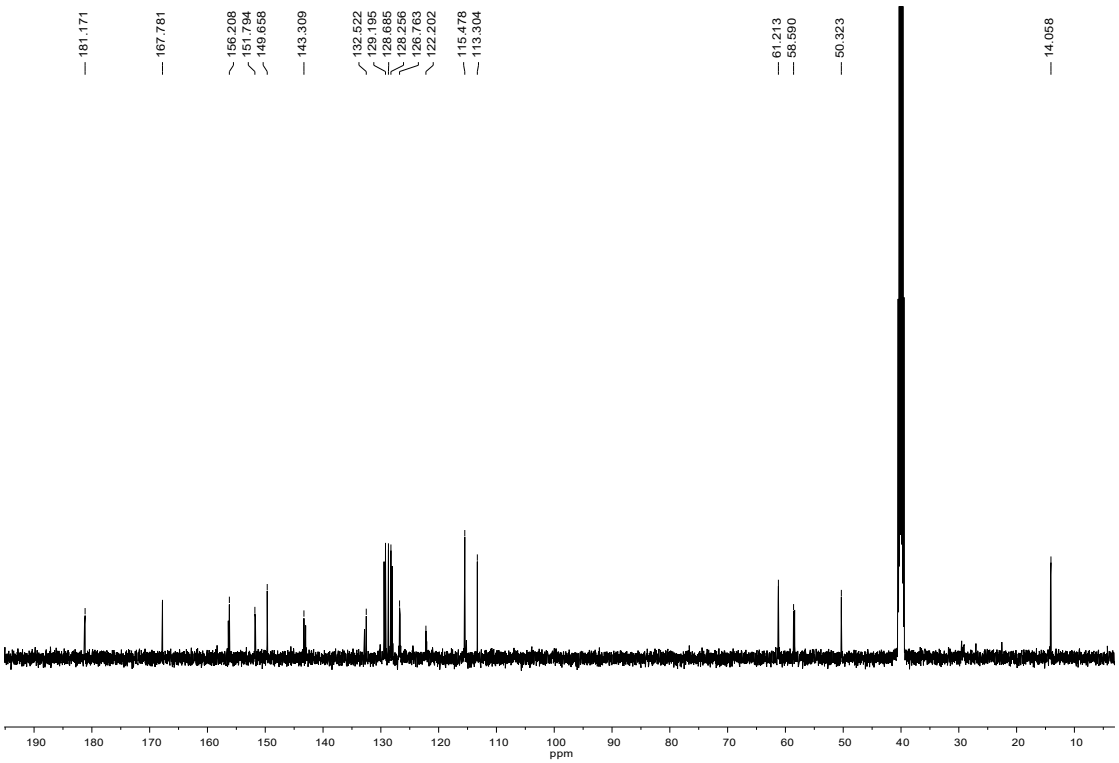


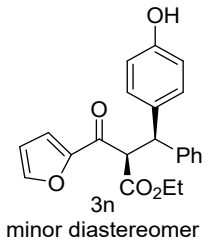


3n
major diastereomer

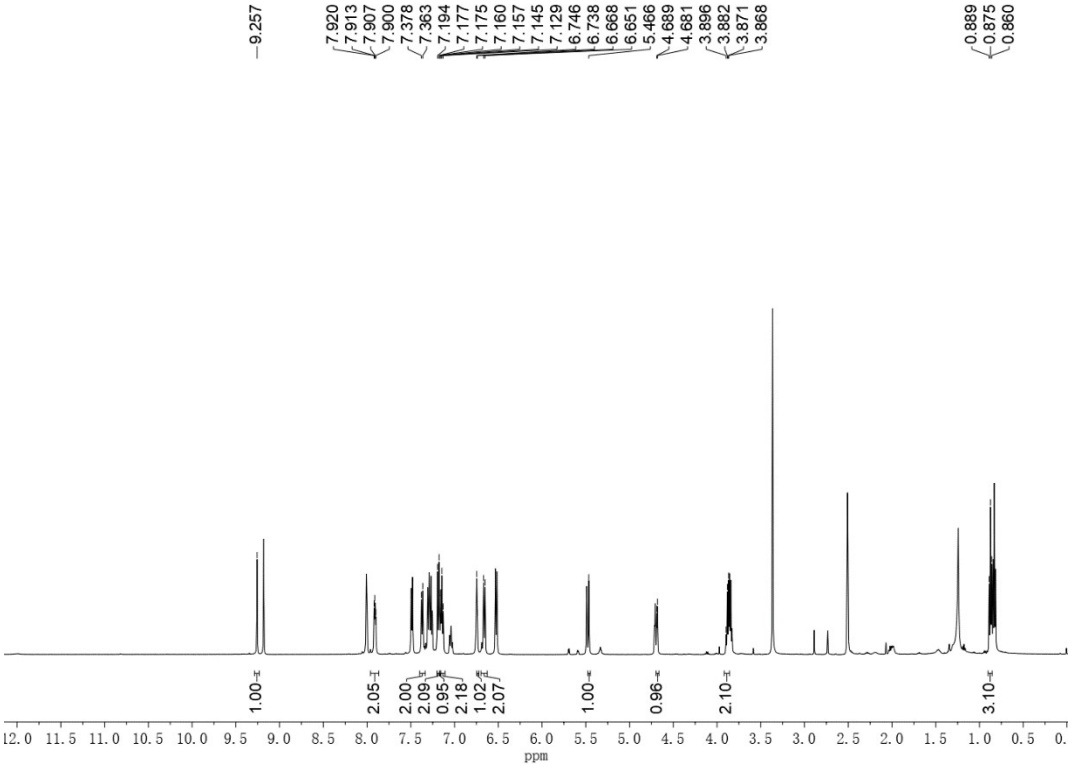


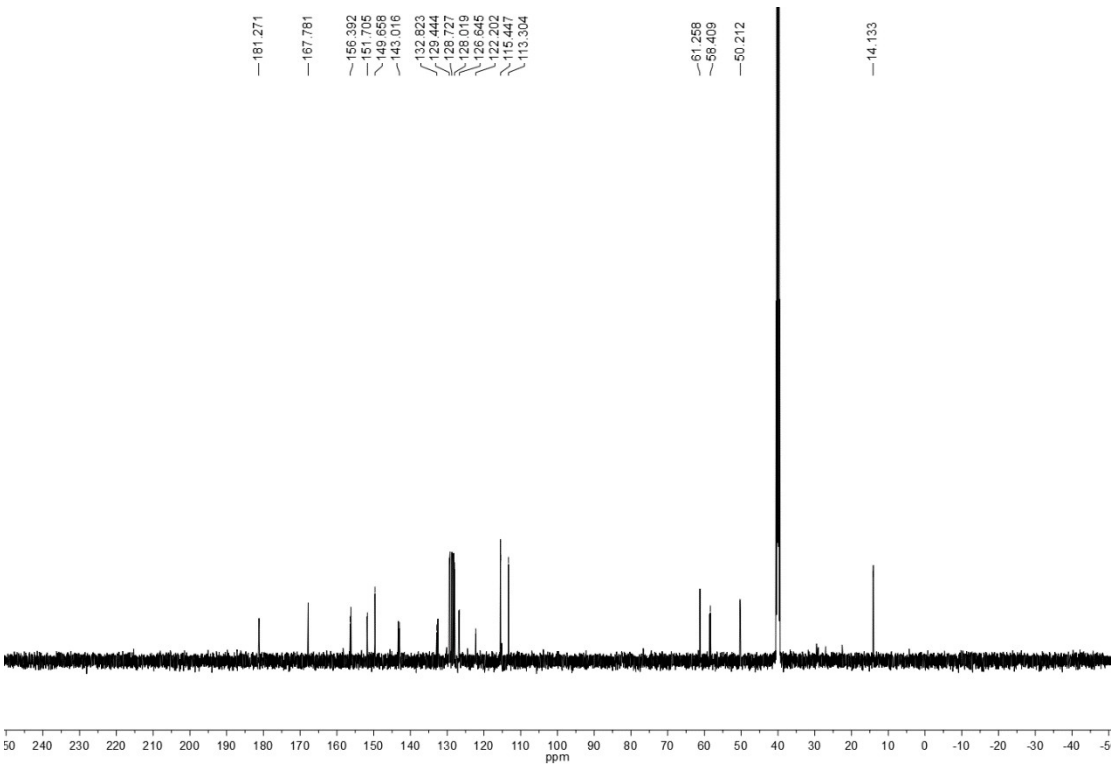


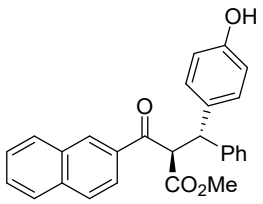




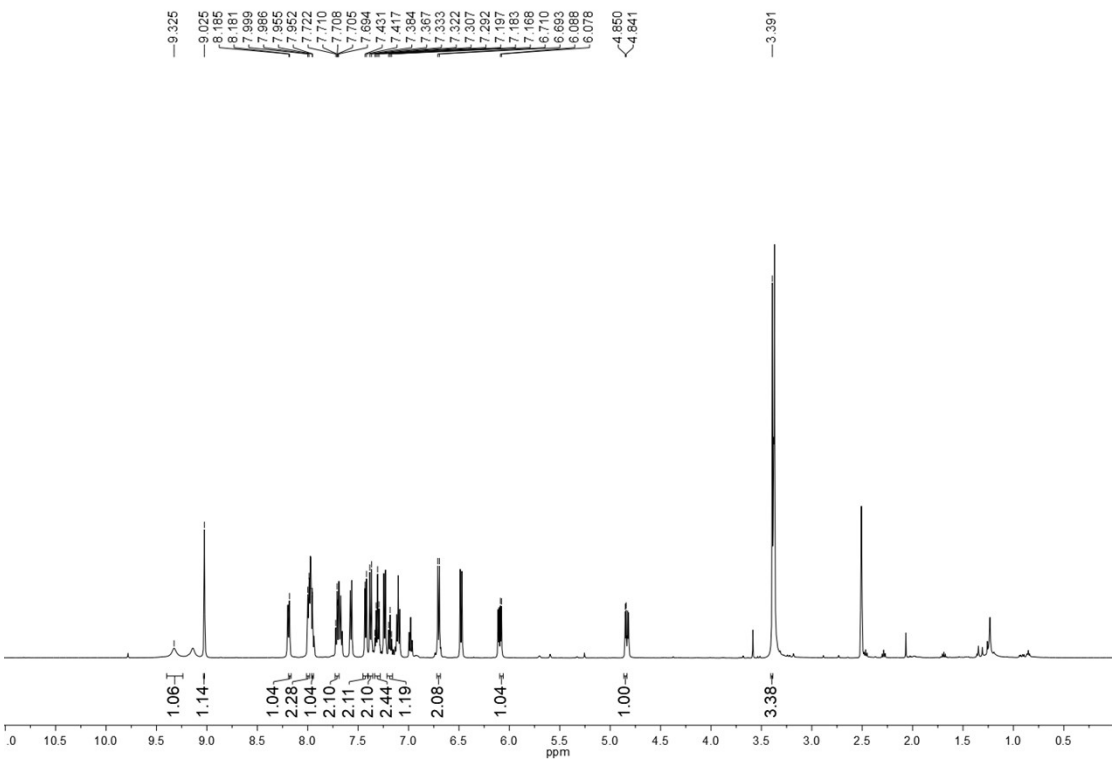
minor diastereomer

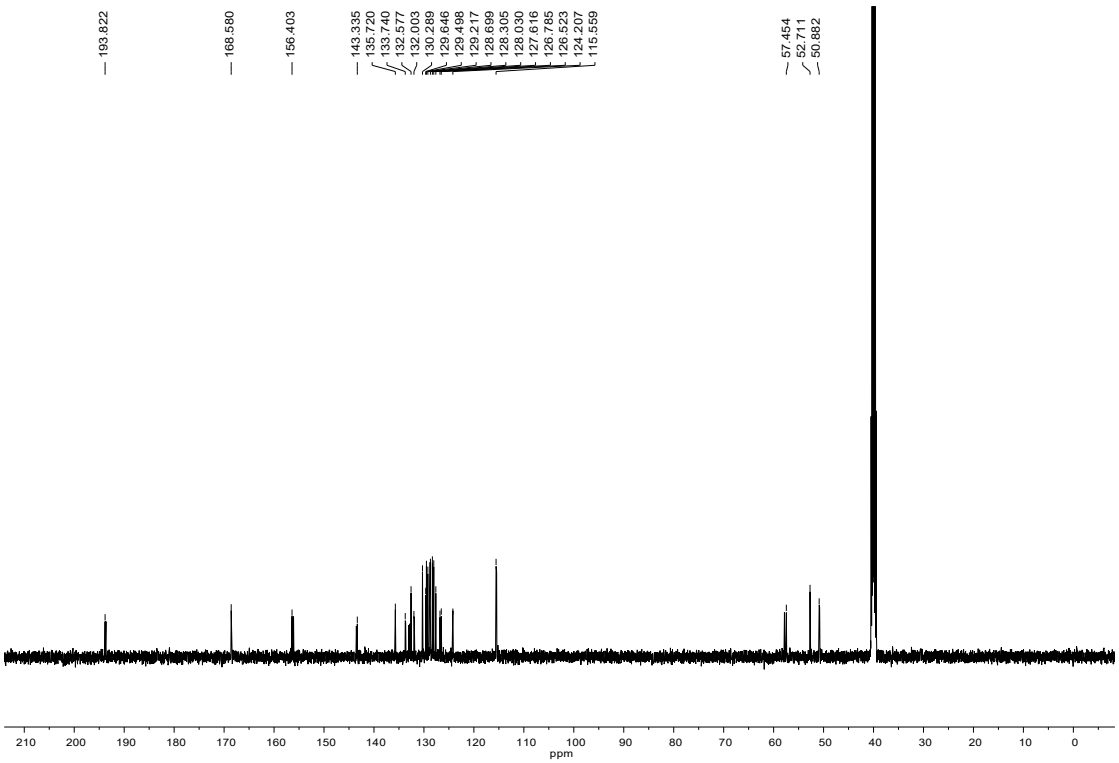


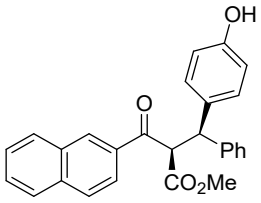




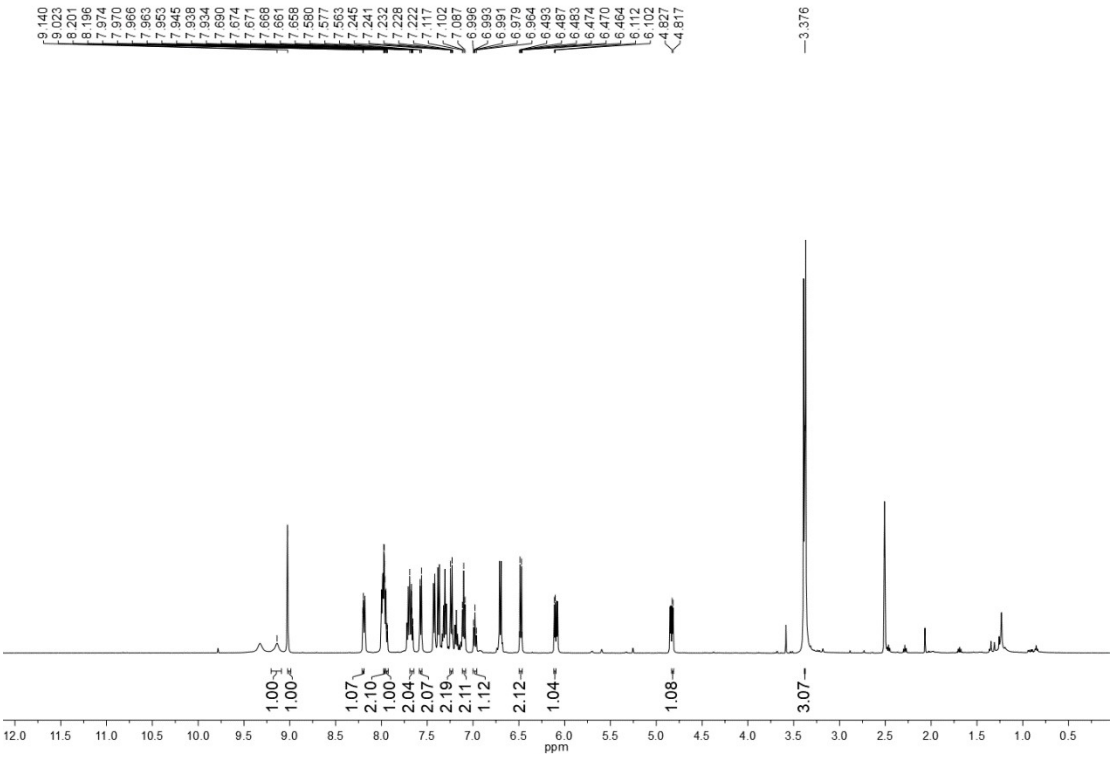
3o
major diastereomer

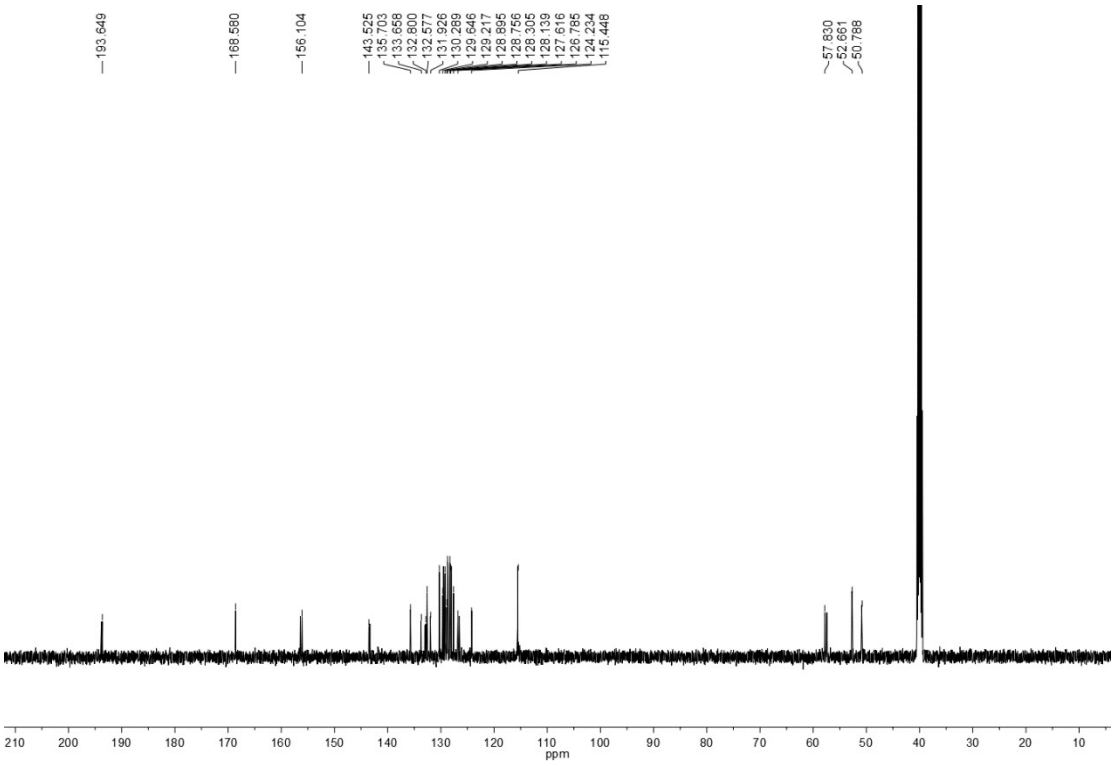


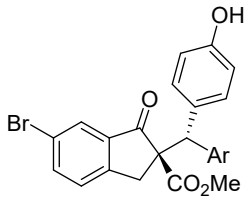




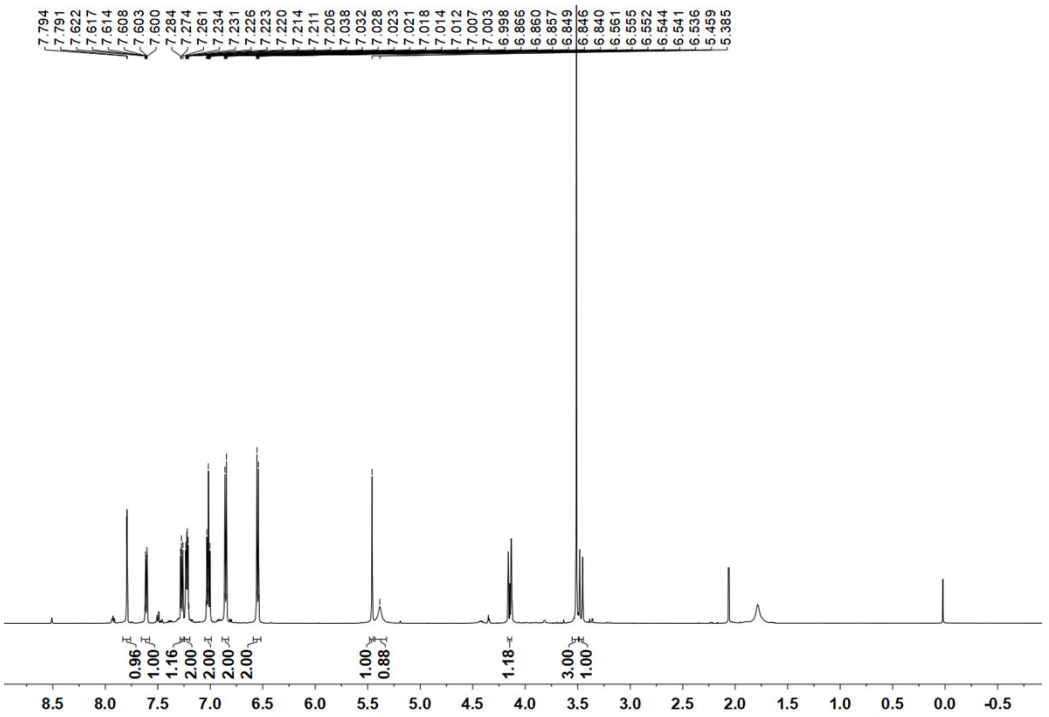
3o
minor diastereomer

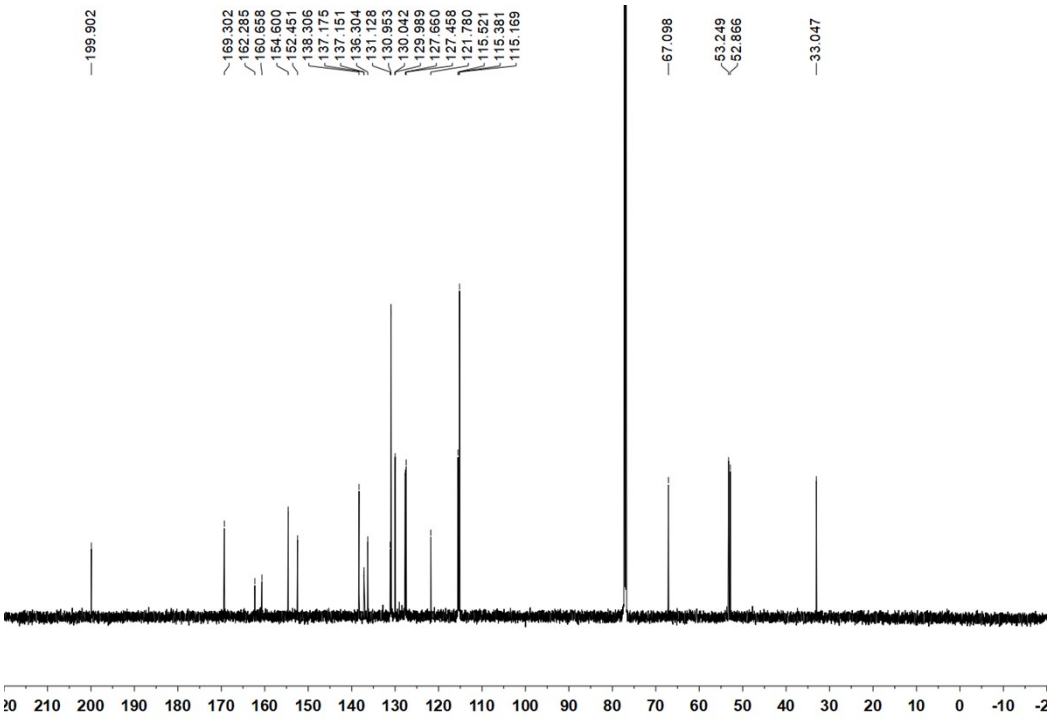


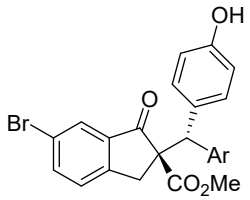

193.649
168.580
156.104
143.525
135.703
133.658
132.800
132.577
131.926
130.289
129.646
129.217
128.895
128.756
128.305
128.139
127.616
126.785
124.234
115.448
57.830
52.661
50.788
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



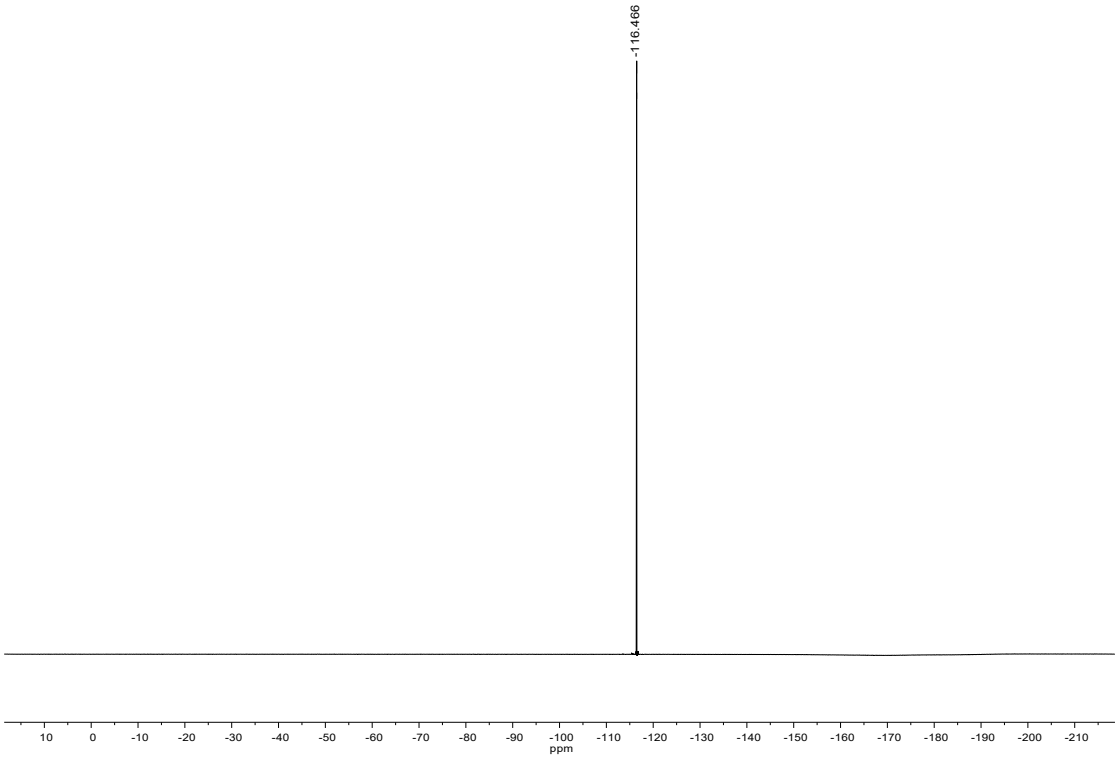
3p: Ar = 4-FPh
major diastereomer

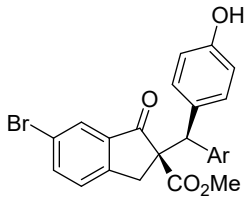




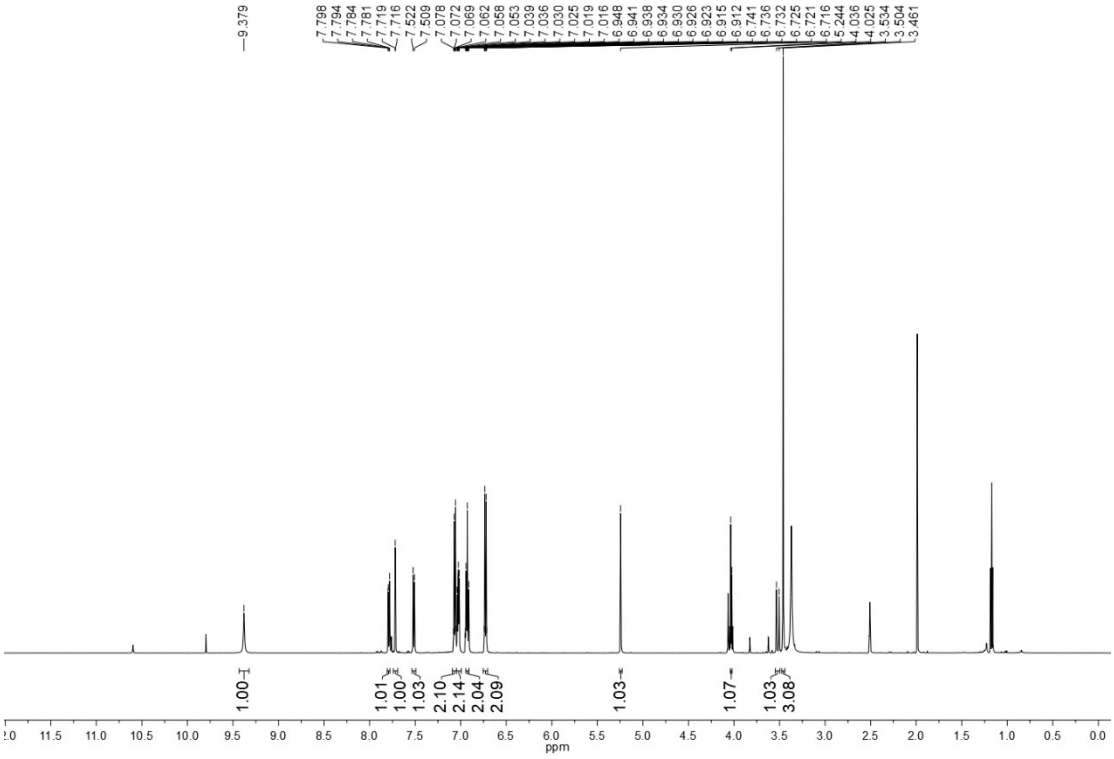


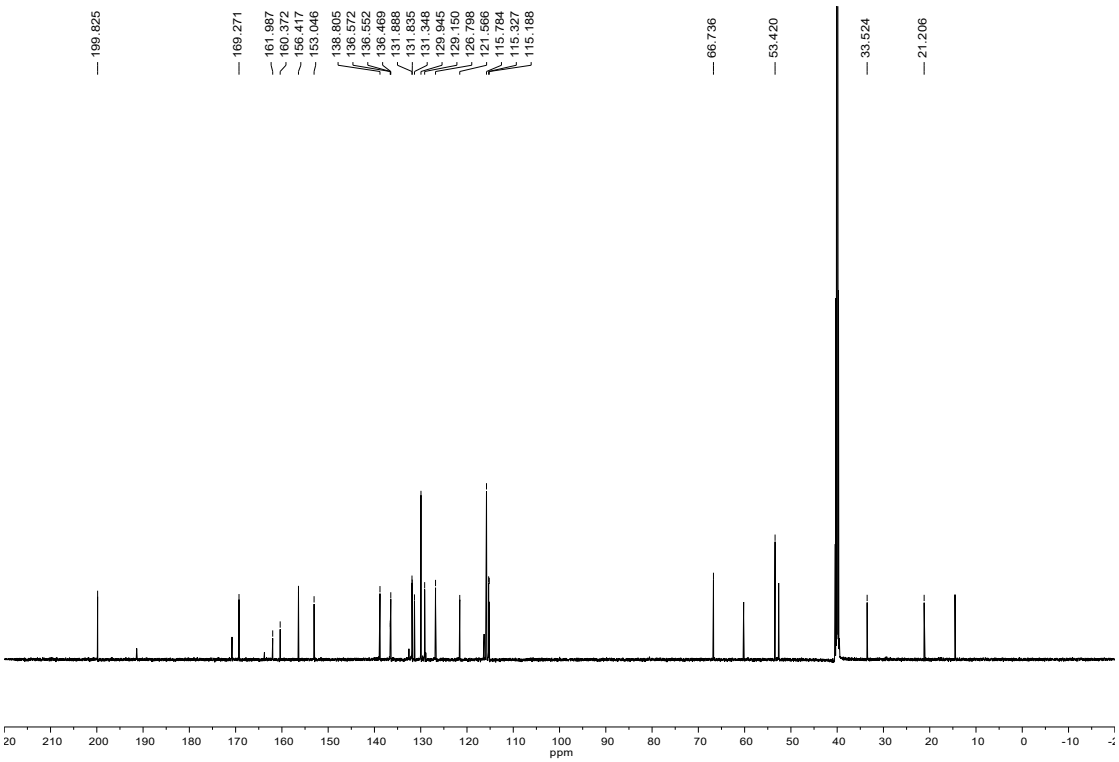
3p: Ar = 4-FPh
major diastereomer





3p: Ar = 4-FPh
minor diastereomer




199.825
169.271
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136.572
136.552
136.469
131.888
131.835
131.348
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66.736
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33.524
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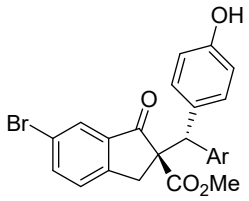
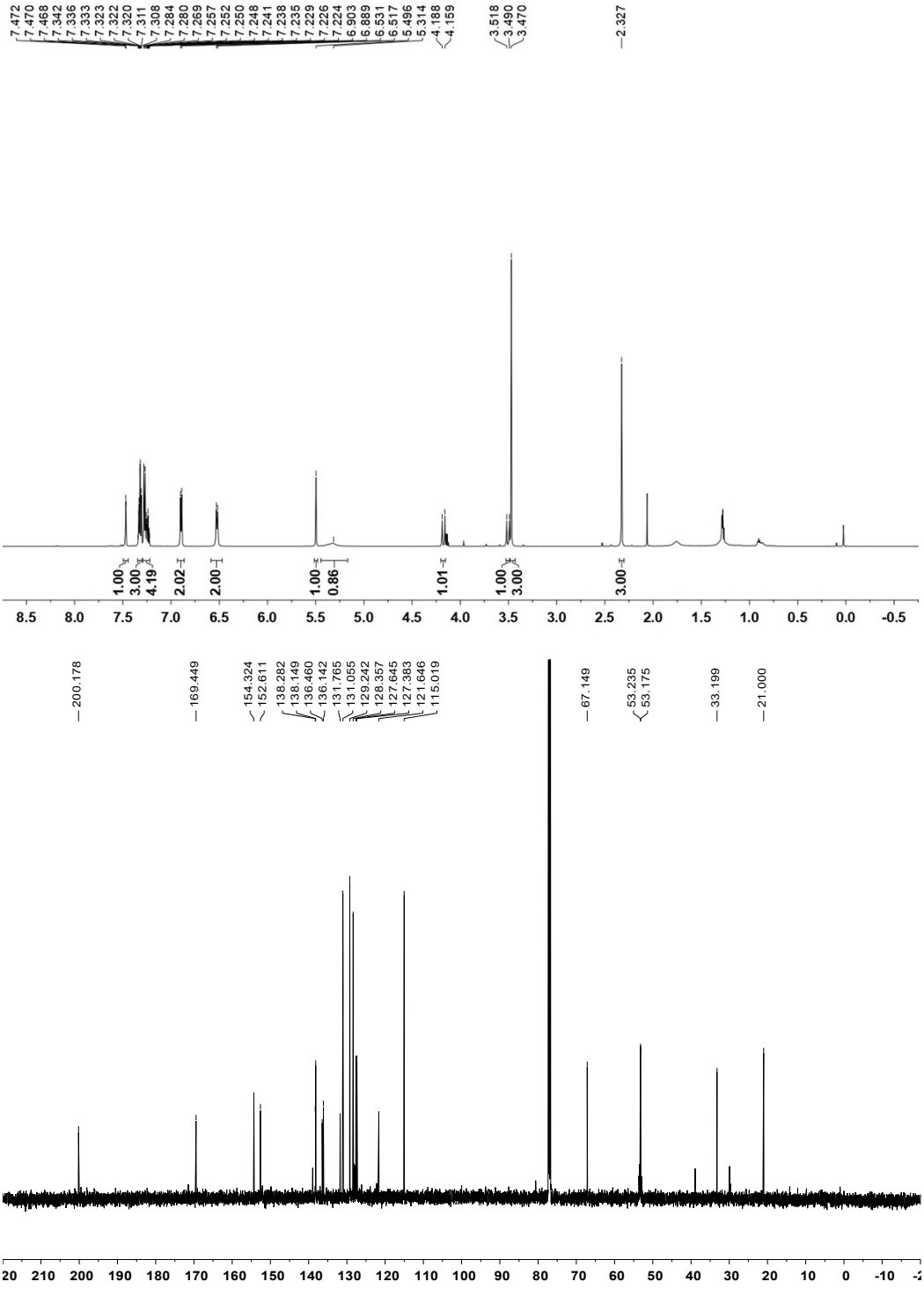
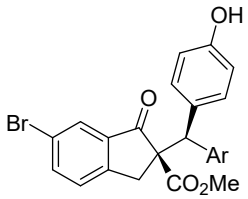
ppm

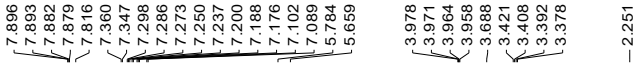


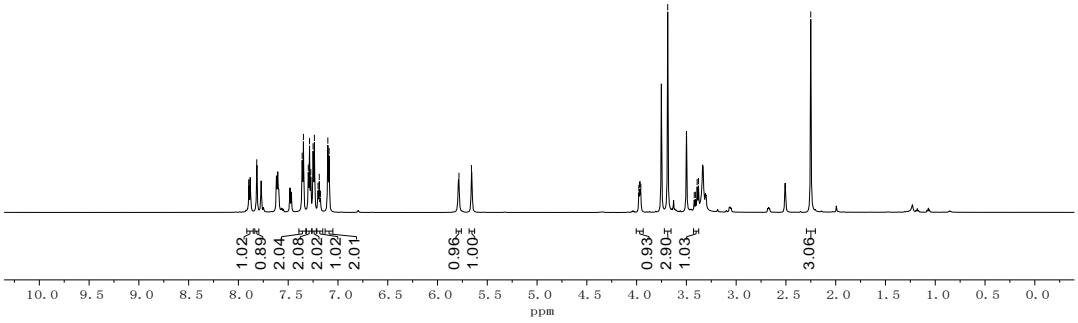
3q: Ar = 4-MePh
major diastereomer

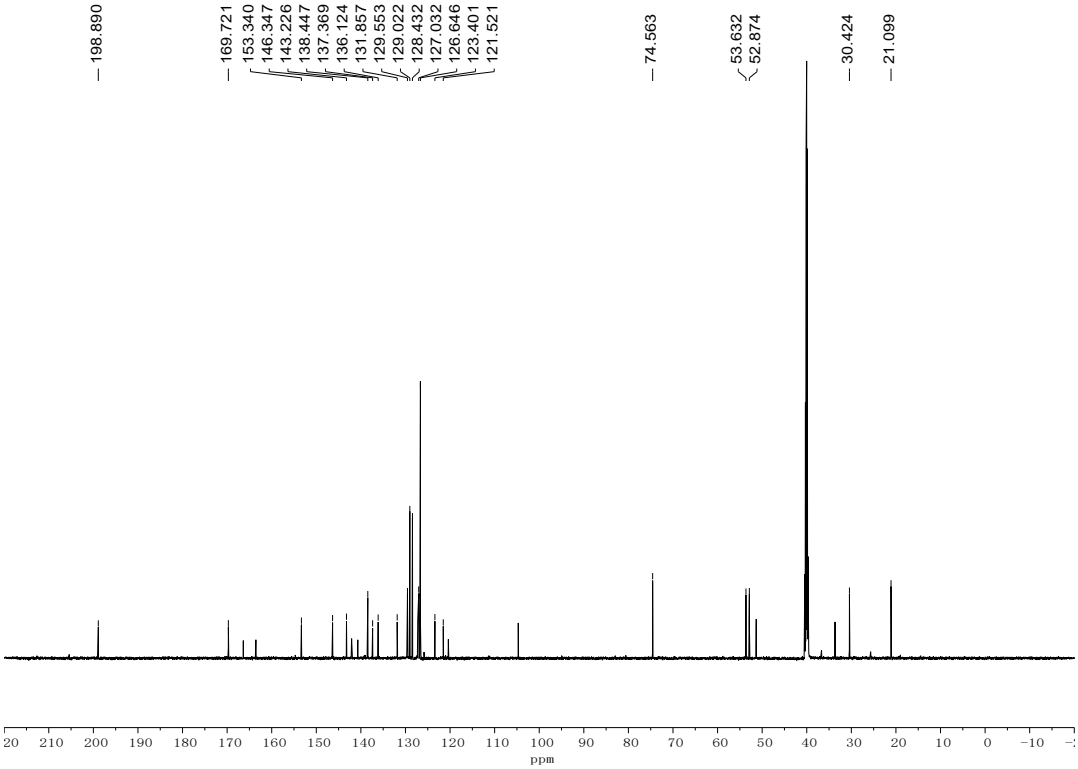


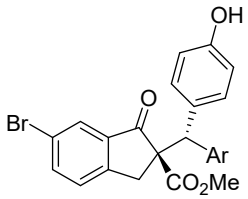


3q: Ar = 4-MePh
minor diastereomer

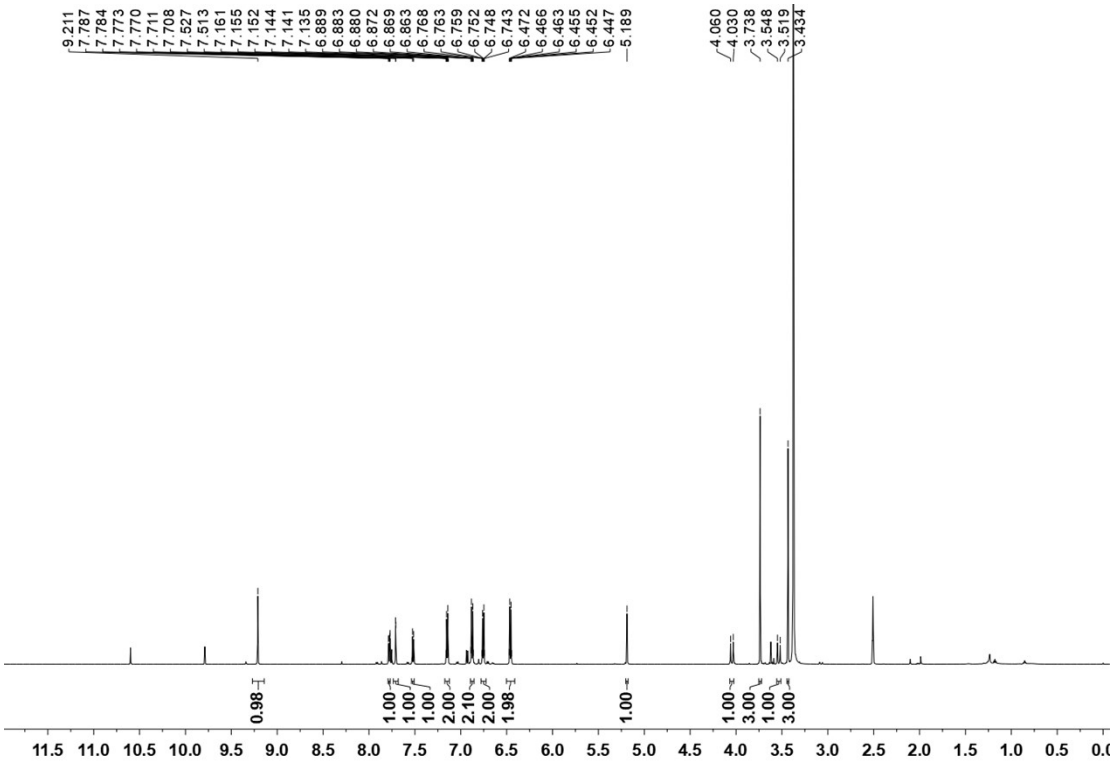


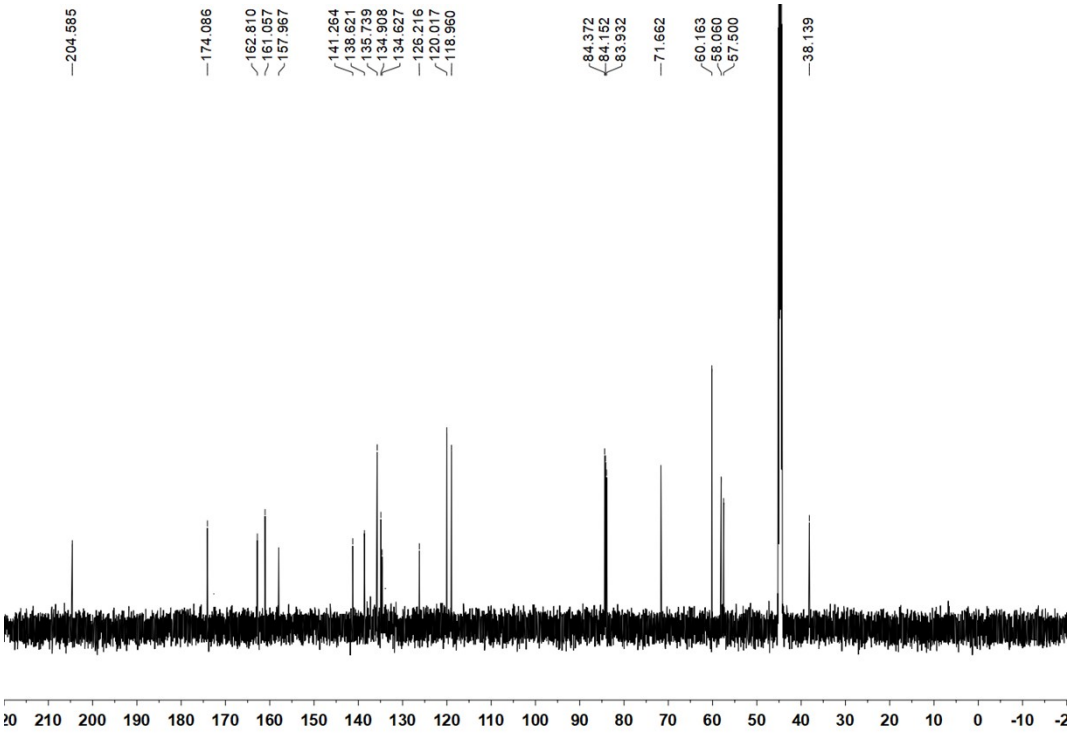


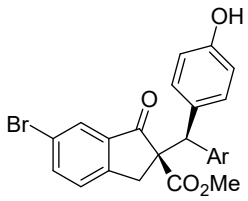




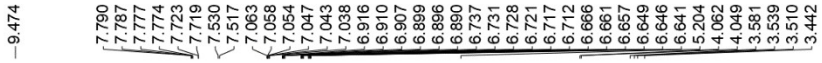
3r: Ar = 4-OMePh
major diastereomer

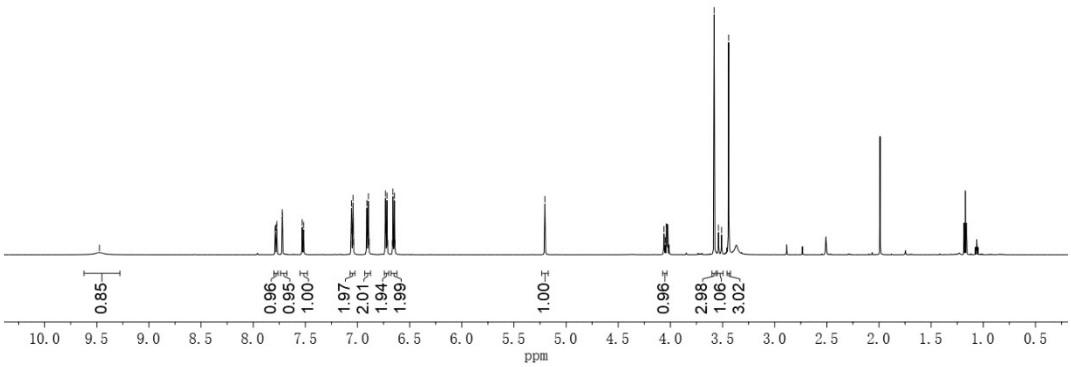


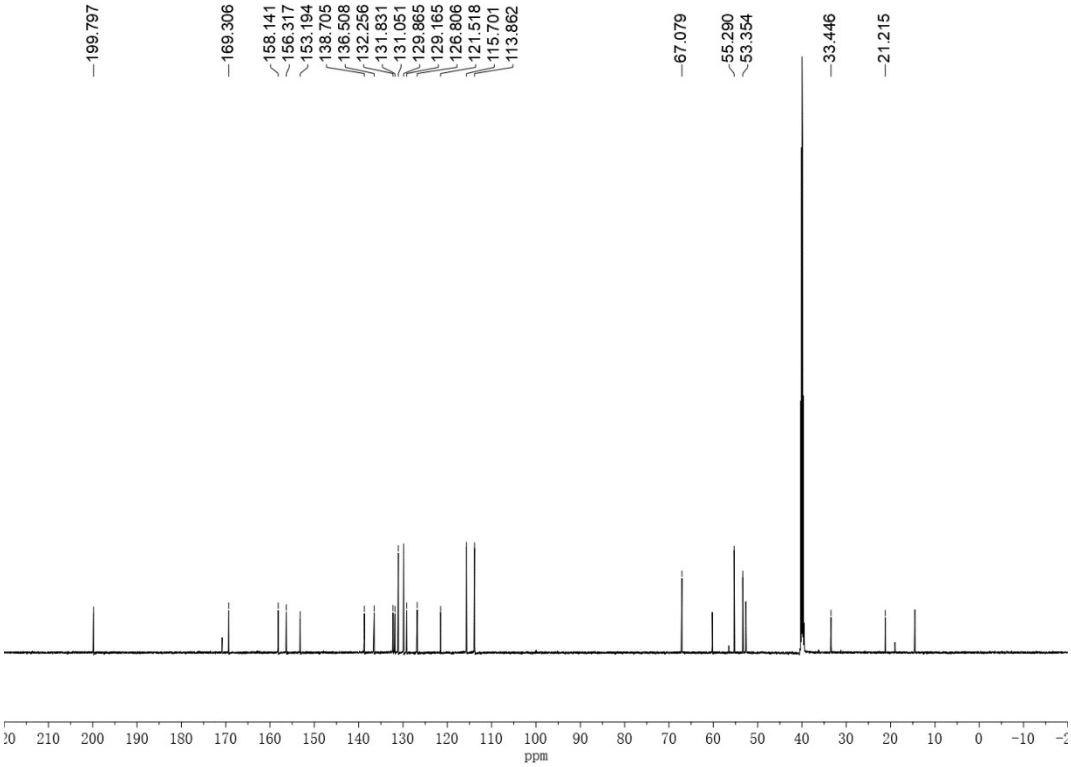


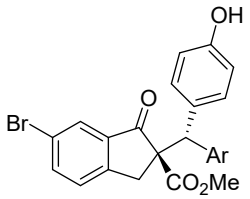


3r: Ar = 4-OMePh
minor diastereomer

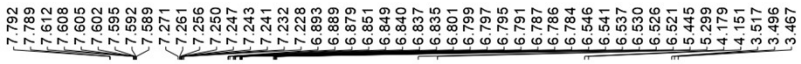


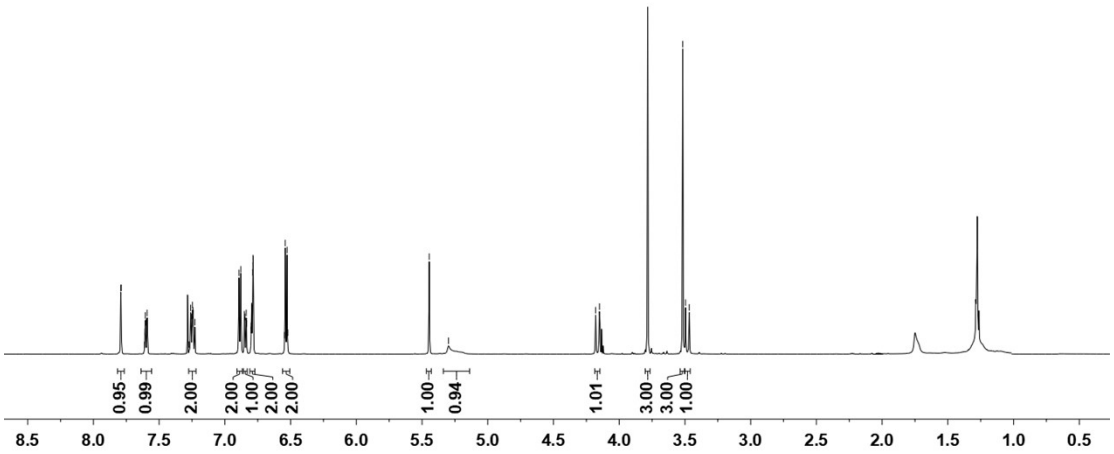


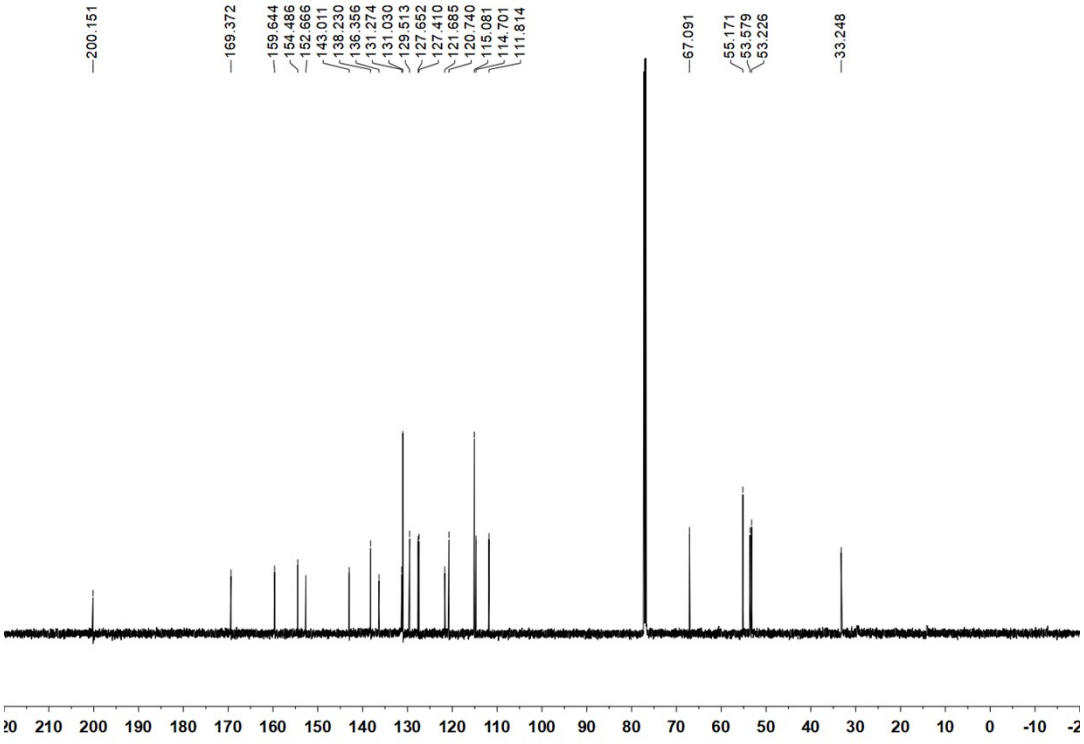


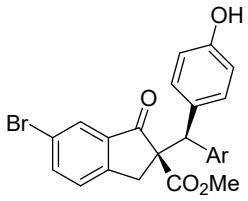


3s: Ar = 3-OMePh
major diastereomer

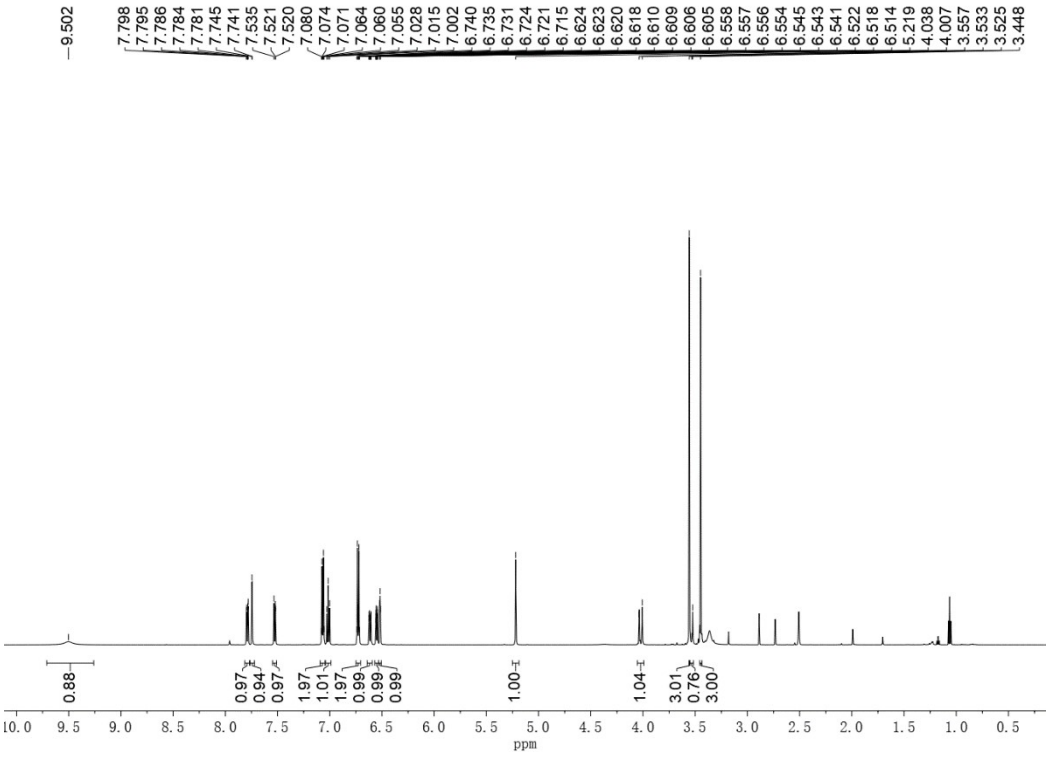


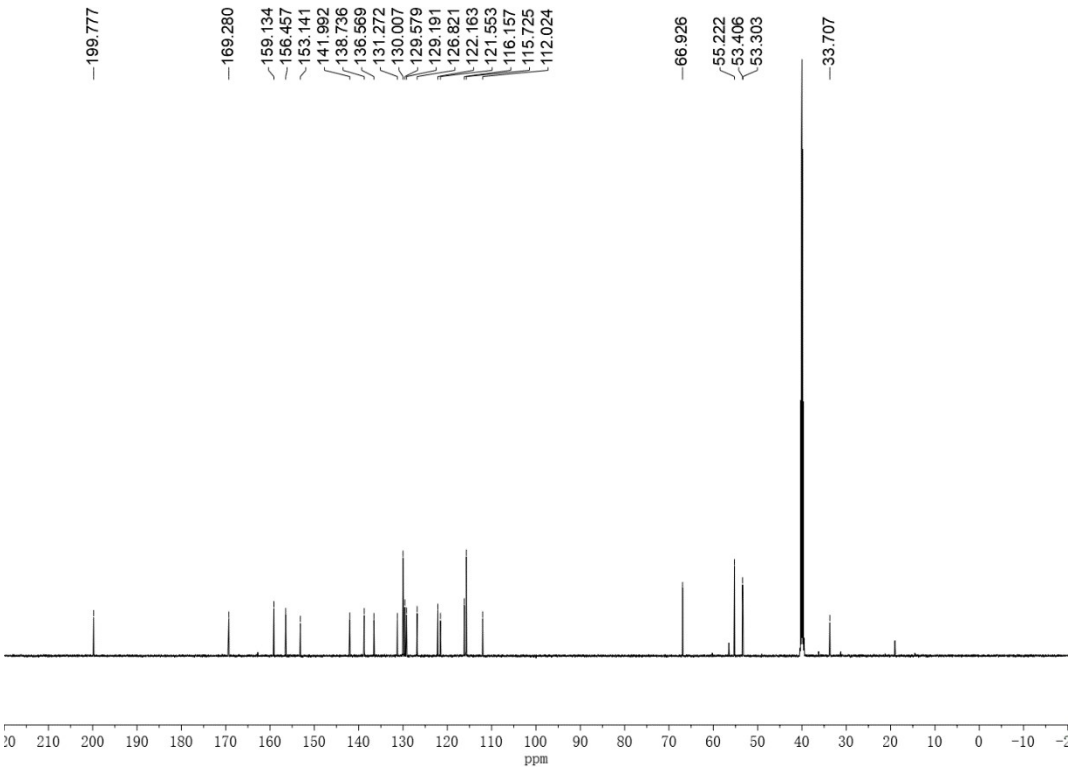


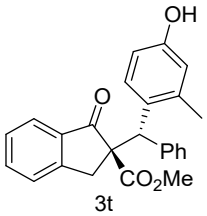




3s: Ar = 3-OMePh
minor diastereomer

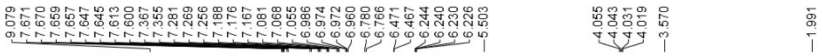


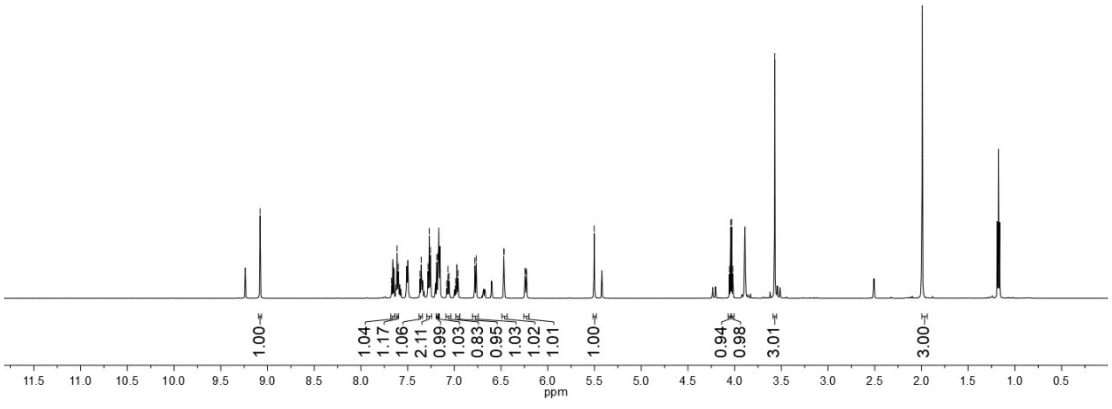


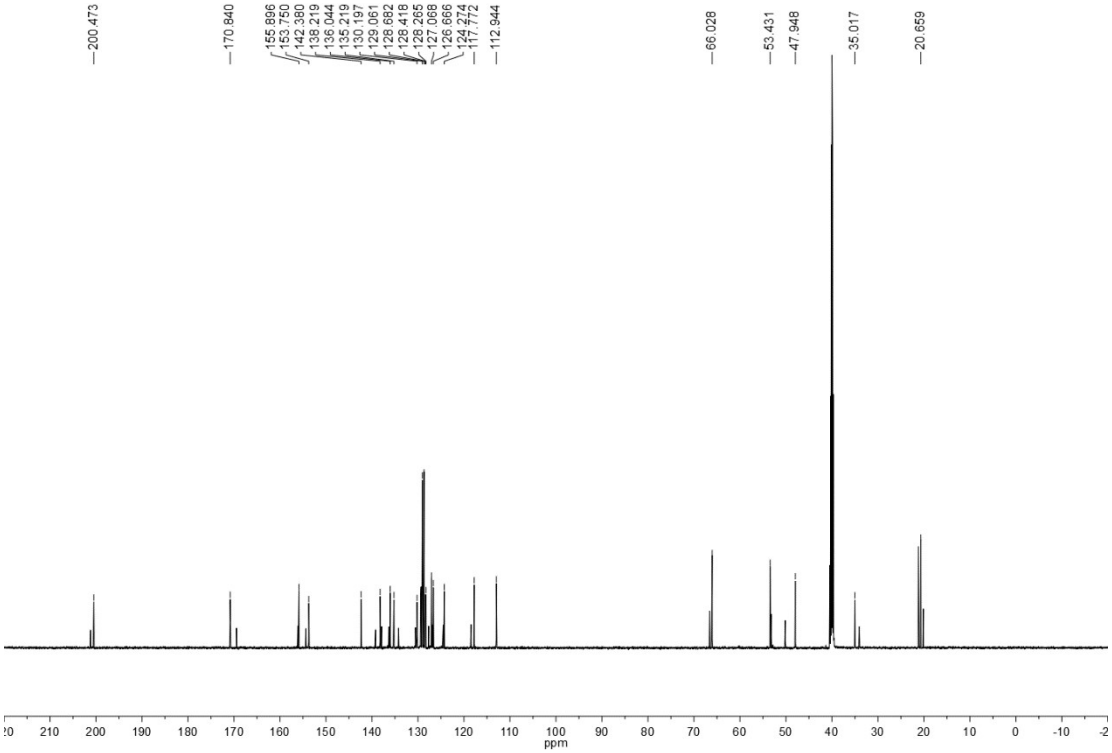


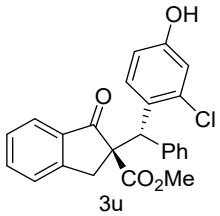
3t

major diastereomer

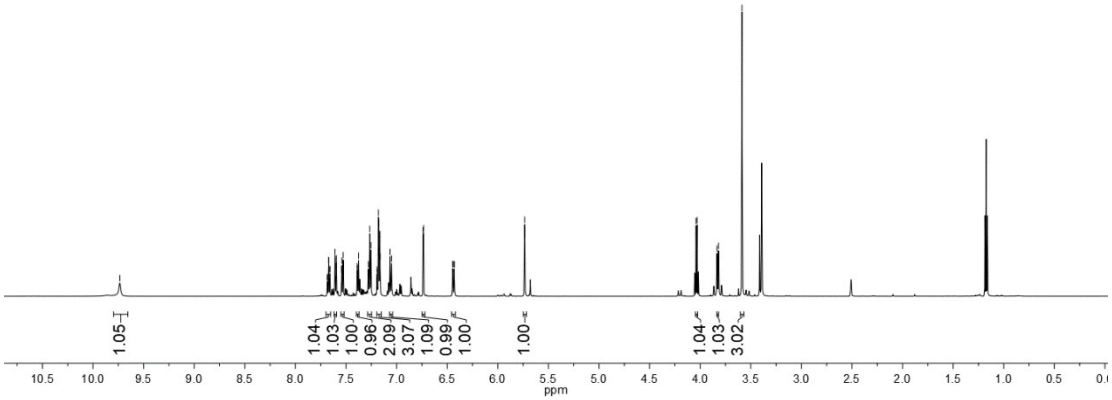


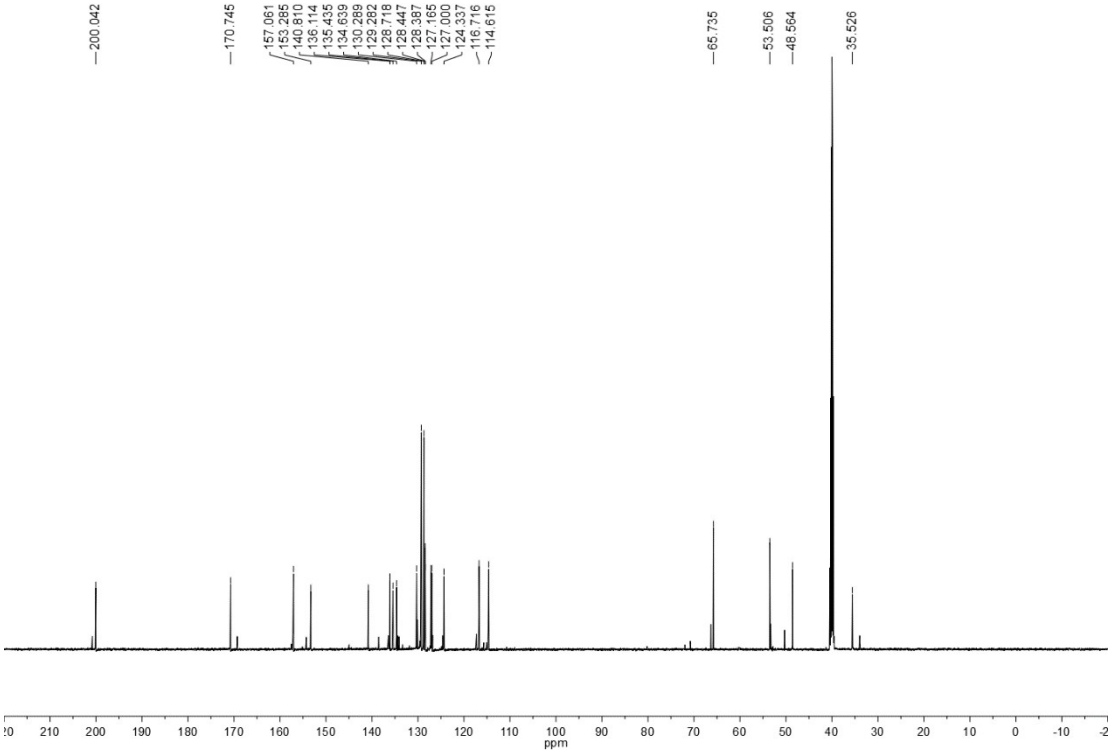


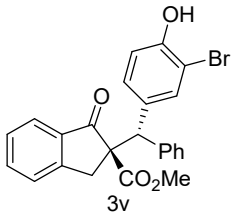




3u
major diastereomer

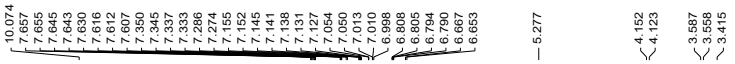


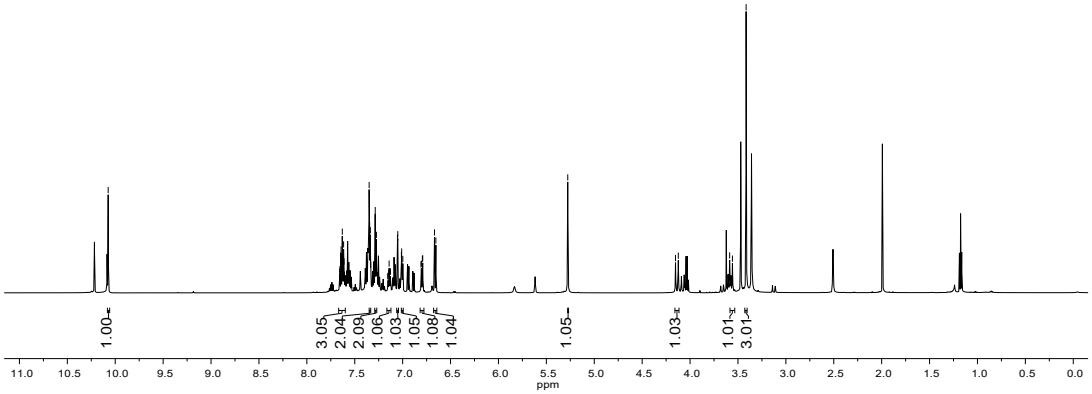


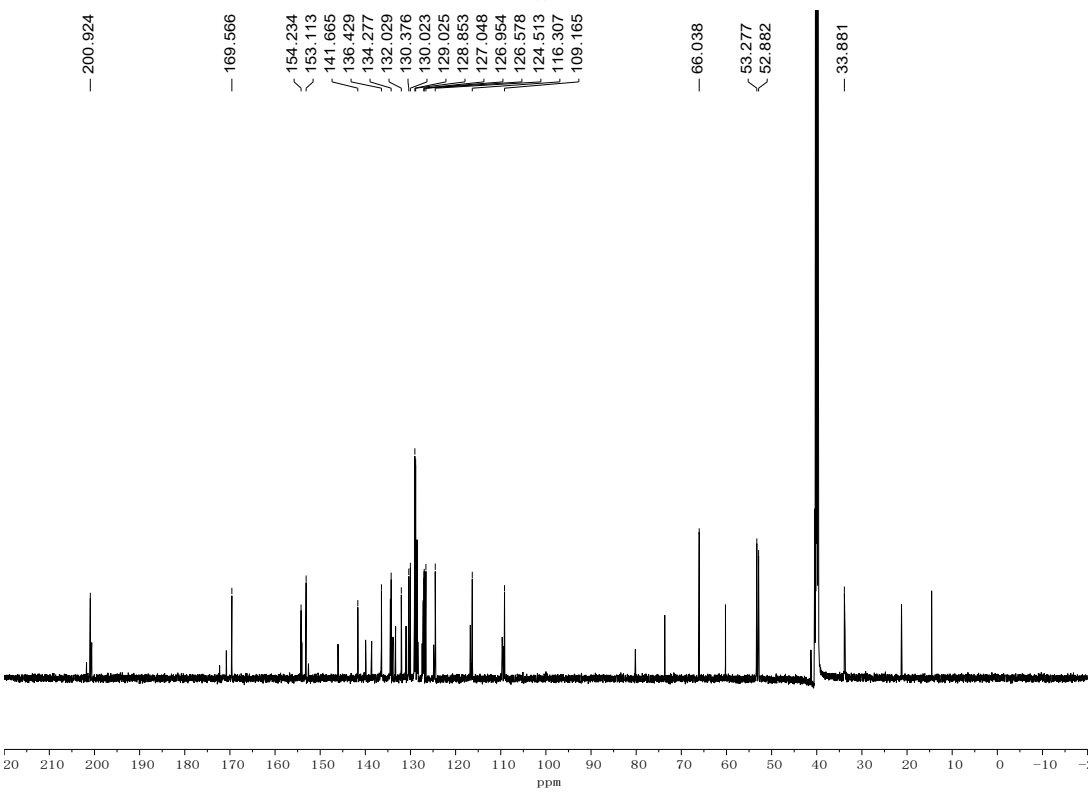


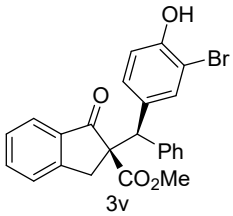
3v

major diastereomer



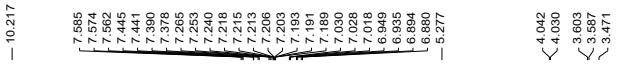


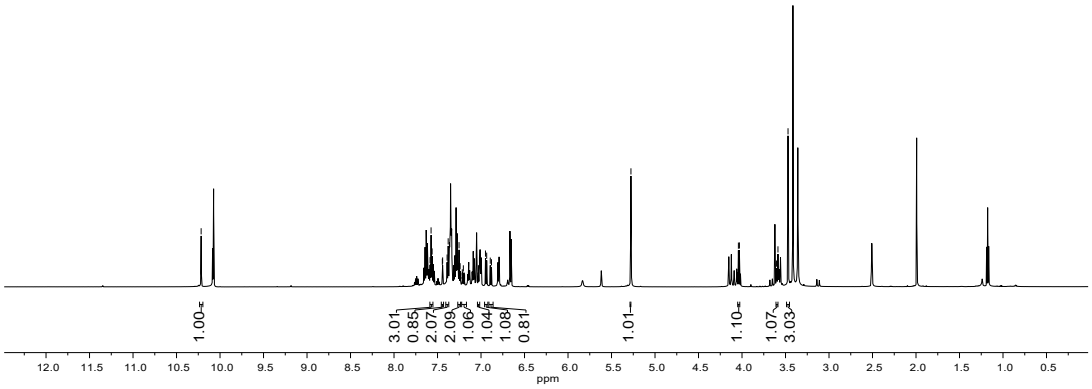


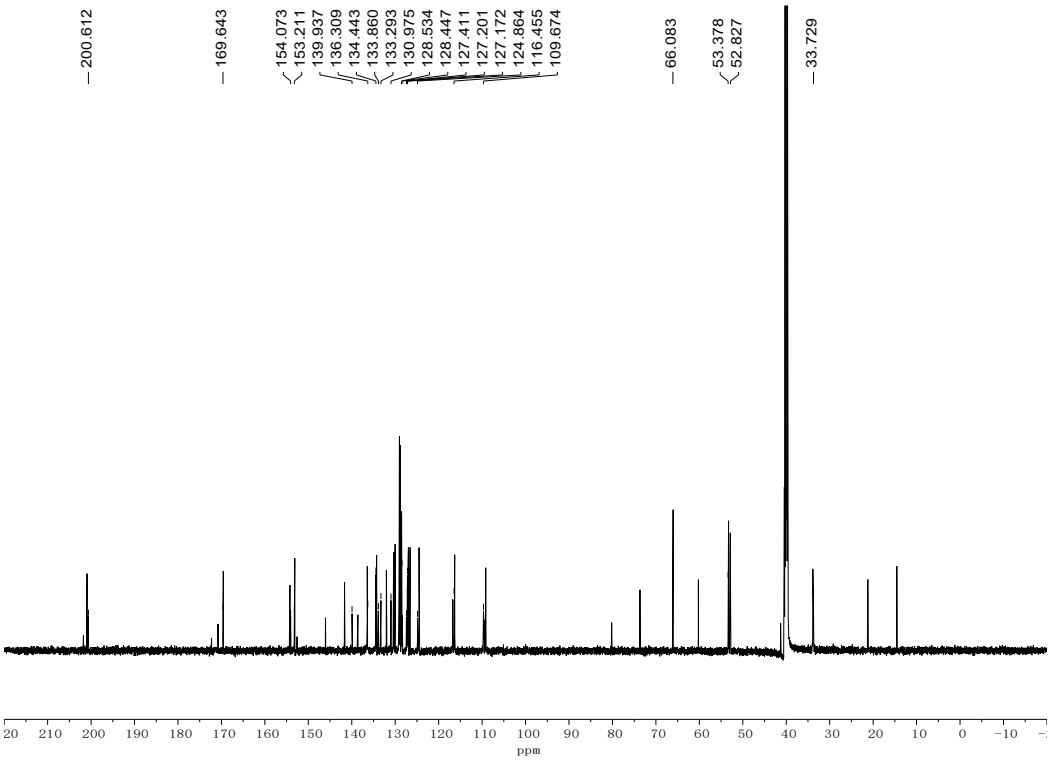


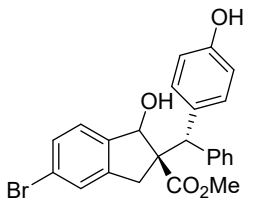
3v

minor diastereomer








OH
OH
Ph
Br
CO2Me

4


7.447
7.444
7.435
7.433
7.431
7.321
7.317
7.308
7.298
7.295
7.271
7.268
7.236
7.234
7.232
7.225
7.222
7.219
7.212
7.210
7.208
7.181
7.177
7.170
7.166
7.163
7.150
7.138
7.135
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6.612
6.608
6.601
6.597
6.592
5.444
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3.410
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3.248
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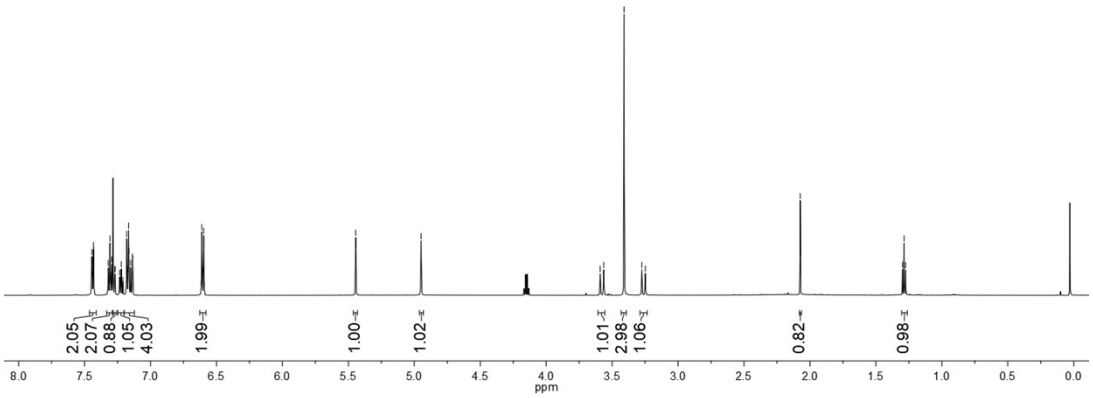
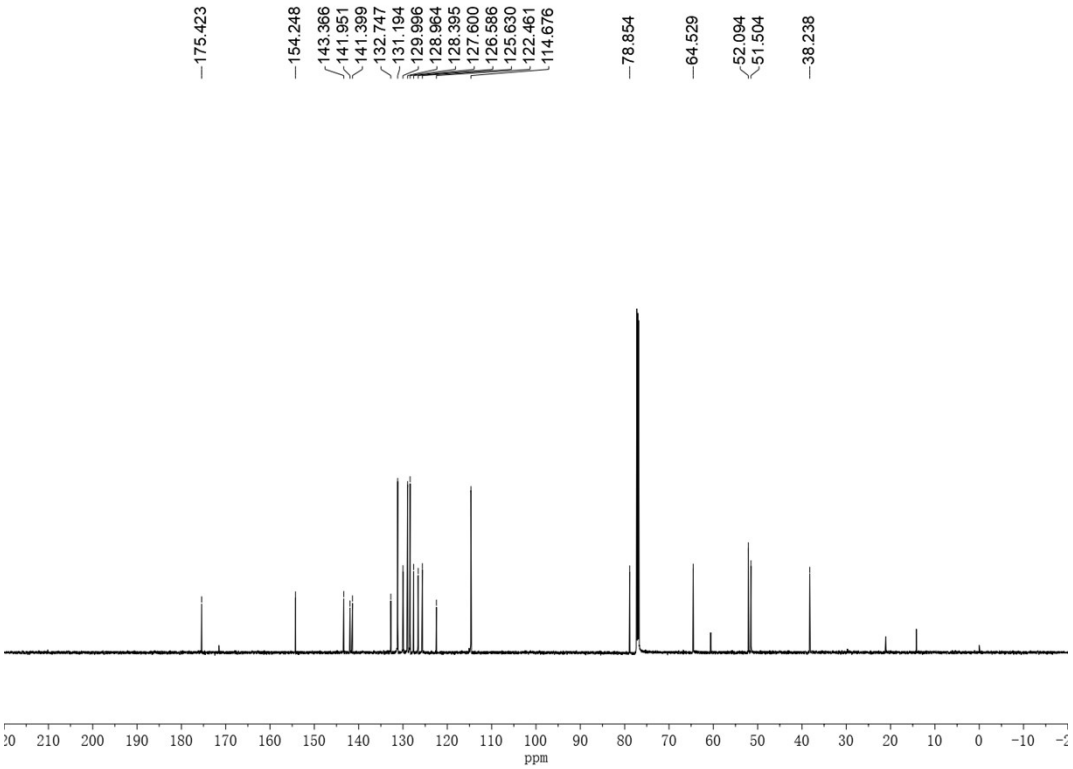
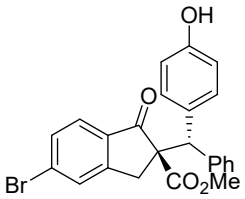
1.298
1.286
1.275


2.05
2.07
0.88
1.05
4.03
1.99
1.00
1.02
1.01
2.98
1.06
0.82
0.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

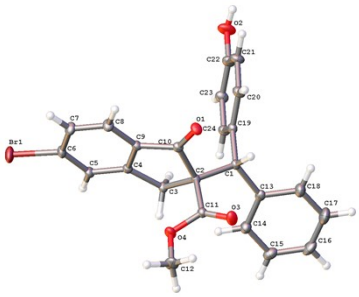

175.423
154.248
143.366
141.951
141.399
132.747
131.194
129.996
128.964
128.395
127.600
126.586
125.630
122.461
114.676
78.854
64.529
52.094
51.504
38.238
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
ppm

10. Crystal data and structure refinement for the enantiopure major diastereomer of 3e and minor diastereomer of 3c.

Crystals of enantiopure major diastereomer of **3e** suitable for X-ray analysis were obtained from crystallization in a
solution of CH_2Cl_2 and MeOH.



3e

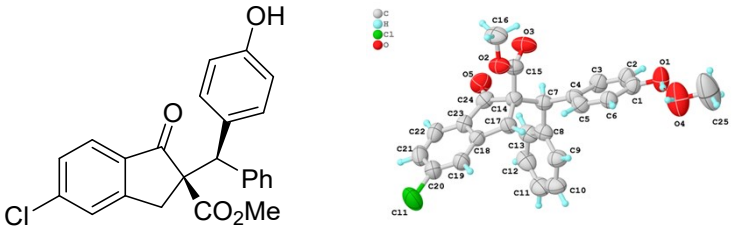


(ellipsoid contour at 50% probability level)

CCDC	2132066	
Empirical formula	C_{24} H_{19} Br O_4	
Formula weight	451.30	
Temperature	193.01 K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 6.76460(10) Å	α= 90°.
	b = 16.0325(3) Å	β= 90°.
	c = 19.2455(3) Å	γ = 90°.
Volume	2087.24(6) $Å^3$	
Z	4	
Density (calculated)	1.436 Mg/m^3	
Absorption coefficient	1.986 mm^{-1}	
F(000)	920	
Crystal size	0.05 x 0.03 x 0.03 mm^3	
Theta range for data collection	3.121 to 54.909°.	
Index ranges	-8<=h<=6, -19<=k<=19, -23<=l<=23	
Reflections collected	22356	
Independent reflections	3955 [R(int) = 0.0415]	
Completeness to theta = 53.594°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.5097	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3955 / 0 / 264	
Goodness-of-fit on F^2	1.072	

Final R indices [I>2sigma(I)]	R1 = 0.0249, wR2 = 0.0632
R indices (all data)	R1 = 0.0255, wR2 = 0.0638
Absolute structure parameter	0.046(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.223 and -0.661 e.Å^{-3}

Crystals of enantiopure minor diastereomer of **3c** suitable for X-ray analysis were obtained from crystallization in a solution of CH_2Cl_2 and MeOH.



(ellipsoid contour at 50% probability level)

CCDC	2165881
Empirical formula	$C_{25}H_{22}ClO_5$
Formula weight	437.87
Temperature/K	173.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.1420(11)
b/Å	11.4280(15)
c/Å	22.2670(19)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2326.3(5)
Z	4
ρ_{calc}g/cm^3	1.250
μ/mm^{-1}	1.723
F(000)	916.0
Crystal size/mm^3	0.12 × 0.11 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	10.46 to 158.42
Index ranges	-10 ≤ h ≤ 11, -13 ≤ k ≤ 14, -27 ≤ l ≤ 22
Reflections collected	20073
Independent reflections	4711 [R_{int} = 0.1189, R_{sigma} = 0.0858]
Data/restraints/parameters	4711/0/284
Goodness-of-fit on F^2	0.978
Final R indexes [I>=2σ (I)]	R_1 = 0.0690, wR_2 = 0.1787
Final R indexes [all data]	R_1 = 0.0985, wR_2 = 0.2080
Largest diff. peak/hole / e Å^{-3}	0.26/-0.30
Flack parameter	0.080(17)