# *Supplementary information*

***Title:*** Highly Enantioselective Aldol Reaction of Acetone with $\beta$, $\gamma$-Unsaturated $\alpha$-Keto Ester Promoted by Simple Chiral Primary-tertiary Diamine Catalysts

***Author(s):*** Lin Peng, Liang-Liang Wang, Jian-Fei Bai, Li-Na Jia, Yun-Long Guo, Xi-Ya Luo, Fei-Ying Wang, Xiao-Ying Xu* and Li-Xin Wang*

## Contents

# A. General Information and Starting Materials.

**General Information.**

NMR spectra were recorded with tetramethylsilane as the internal standard. $^{1}$H NMR spectra were recorded at 300 MHz, and $^{13}$C NMR spectra were recorded at 75 MHz (Bruker Avance). Chemical shifts (δ) were reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for $^{1}$H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) for $^{13}$C NMR spectroscopy. IR spectra were recorded on a ThermoFisher Nicolet 6700 FTIR spectrometer on a KBr beamsplitter. High-resolution mass spectra were obtained with the Bruker Q TOF mass spectrometer. Optical rotations were measured at 589 nm at 20 $^{o}$C on a Polarimeter 341 optical rotation spectrometer. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. Reactions were monitored by TLC and visualized with ultraviolet light. Enantiomeric excess was determined by HPLC analysis on Chiral OD-H, chiralpak AD-H and chiralpakl AS-H column.

**Starting Materials.**

All solvents and inorganic reagents were of p.a. quality and used without purification. All the *β*, *γ*-unsaturated-*α*-keto esters were prepared following the literature procedures.[1] Unless otherwise noted, materials were obtained from commercial sources and used without purification.

# B. General Procedure for the Asymmetric Aldol Reaction.

Unless noted, the reaction was carried out as following: catalyst **1a** (20 mol %) and 3,5-dinitrobenzoic acid (20 mol %) were added to a stirred solution of *β*, *γ*-unsaturated-α-keto ester **2** (0.2 mmol) in cyclohexane (0.6 mL) at -20 $^{o}$C under an atmosphere of air. The resulting solution was stirred for 10 min prior to the addition of acetone (4.0 mmol). After stirring for the indicated reaction time at -20 $^{o}$C (monitored by TLC), the solvent was removed under vacuum, and the residue was purified by column chromatography on silica gel to yield the desired Aldol adducts.

# C. Characterization Data of the Products.

**(S)-methyl 2-hydroxy-4-oxo-2-styrylpentanoate (3a).**[2]

Prepared according to general procedure. The product was obtained in 95 % yield, white solid, $[\alpha]_D^{20}$ = -93.3 (c = 0.65 in $CHCl_3$, 94 % ee); **$^{1}$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.39-7.25 (m, 5H), 6.86 (d, *J* = 15.8 Hz, 1H), 6.16 (d, *J* = 15.8 Hz, 1H), 3.80 (s, 3H), 3.27 (d, *J* = 17.5 Hz, 1H), 2.93 (d, *J* = 17.5 Hz, 1H), 2.19 (s, 3H) ; **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.9, 174.2, 135.8, 130.7, 128.6, 128.1, 128.0, 126.7, 75.2, 53.2, 51.7, 30.6; IR (film, $cm^{-1}$): *v* = 3439, 3029, 2960, 1745, 1716, 1435, 1366, 1252, 1220, 1141; HRMS (ESI-TOF) calcd for $C_{14}H_{16}O_4Na$ ($[M+Na]^+$): 271.0941, found: 271.0947; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 13.97 (major), 21.67 min (minor).

**(S)-ethyl 2-hydroxy-4-oxo-2-styrylpentanoate (3b).**[2]

Prepared according to general procedure. The product was obtained in 91 % yield, colorless oil, $[\alpha]_D^{20}$ = - 79.7 (c = 0.80 in $CHCl_3$, 92 % ee); **$^{1}$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.38-7.21 (m, 5H), 6.86 (d, *J* = 15.8 Hz, 1H), 6.17 (d, *J* = 15.8 Hz, 1H), 4.28-4.19 (m, 2H), 4.06 (br s, 1H), 3.24 (d, *J* = 17.4 Hz, 1H), 2.91 (d, *J* = 17.4 Hz, 1H), 2.16 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.5, 173.6, 135.8, 130.4, 128.4, 128.3, 127.9, 126.6, 75.0, 62.1, 51.5, 30.5, 13.9; IR (film, $cm^{-1}$): *v* = 3497, 3026, 2982, 1735, 1365, 1256, 1214, 1140; HRMS (ESI-TOF) calcd for $C_{15}H_{18}O_4Na$ ($[M+Na]^+$): 285.1097, found: 285.1101; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 11.64 (major), 20.64 min (minor).

**(S)-isopropyl 2-hydroxy-4-oxo-2-styrylpentanoate (3c).**[2]

Prepared according to general procedure. The product was obtained in 90 % yield, colorless oil, $[\alpha]_D^{20}$ = - 81.7 (c = 0.80 in $CHCl_3$, 91 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.38-7.22 (m, 5H), 6.86 (d, *J* = 15.8 Hz, 1H), 6.16 (d, *J* = 15.8 Hz, 1H), 5.14-5.06 (m, 1H), 3.23 (d, *J* = 17.4 Hz, 1H), 2.91 (d, *J* = 17.4 Hz, 1H), 2.18 (s, 3H), 1.29-1.25 (m, 6H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.4, 173.1, 136.0, 130.5, 128.5, 127.9, 126.6, 75.1, 70.1, 51.7, 30.6, 21.6, 21.5; IR (film, $cm^{-1}$): *v* = 3495, 3059, 2981, 2936, 1728, 1449, 1375, 1258, 1218, 1158, 1106; HRMS (ESI-TOF) calcd for $C_{16}H_{20}O_4Na$ ($[M+Na]^+$): 299.1254, found: 299.1261; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 9.57 (major), 17.83 min (minor).

**(S)-butyl 2-hydroxy-4-oxo-2-styrylpentanoate (3d).**

Prepared according to general procedure. The product was obtained in 84 % yield, colorless oil, $[\alpha]_D^{20}$ = - 76.1 (c = 0.82 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.39-7.21 (m, 5H), 6.86 (d, *J* = 15.8 Hz, 1H), 6.17 (d, *J* = 15.8 Hz, 1H), 4.22-4.17 (m, 2H), 3.79 (br s, 1H), 3.25 (d, *J* = 17.4 Hz, 1H), 2.92 (d, *J* = 17.4 Hz, 1H), 2.17 (s, 3H), 1.69-1.60 (m, 2H), 1.43-1.27 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.5, 173.7, 135.9, 130.5, 128.5, 128.4, 127.9, 126.6, 75.1, 66.0, 51.6, 30.5, 30.3, 18.9, 13.5; IR (film, $cm^{-1}$): *v* = 3503, 3026, 2961, 1736, 1496, 1449, 1364, 1256, 1212, 1140; HRMS (ESI-TOF) calcd for $C_{17}H_{22}O_4Na$ ($[M+Na]^+$): 313.1410, found: 313.1425; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 10.13 (major), 18.66min (minor).

**(S)-methyl 2-(4-fluorostyryl)-2-hydroxy-4-oxopentanoate (3e).**

Prepared according to general procedure. The product was obtained in 96 % yield, white solid, $[\alpha]_D^{20}$ = - 78.6 (c = 0.54 in $CHCl_3$, 91 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.35-7.30 (m, 2H), 7.02-6.96 (m, 2H), 6.81 (d, *J* = 15.8 Hz, 1H), 6.07 (d, *J* = 15.8 Hz, 1H), 3.79 (br s, 1H), 3.79 (s, 3H), 3.25 (d, *J* = 17.5 Hz, 1H), 2.91 (d, *J* = 17.5 Hz, 1H), 2.18 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.8, 174.1, 162.5 (d, $J_{C\text{-}F}$ = 246.0 Hz), 132.0 (d, $J_{C\text{-}F}$ = 3.3 Hz), 129.5, 128.3 (d, $J_{C\text{-}F}$ =8.1 Hz), 127.8 (d, $J_{C\text{-}F}$ = 2.0 Hz), 115.5 (d, $J_{C\text{-}F}$ = 21.5 Hz), 75.1, 53.2, 51.7, 30.6; IR (film, $cm^{-1}$): *v* = 3550, 3072, 2963, 1743, 1713, 1599, 1510, 1442, 1371, 1226, 1136; HRMS (ESI-TOF) calcd for $C_{14}H_{15}FO_4Na$ ($[M+Na]^+$): 289.0847, found: 289.0853; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 10.82 (major), 9.50 min (minor).

**(S)-methyl 2-(4-chlorostyryl)-2-hydroxy-4-oxopentanoate (3f).**

Prepared according to general procedure. The product was obtained in 64 % yield, white solid, $[\alpha]_D^{20}$ = - 78.5 (c = 0.42 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.31-7.25 (m, 4H), 6.81 (d, *J* = 15.8 Hz, 1H), 6.13 (d, *J* = 15.8 Hz, 1H), 3.79 (br s, 1H), 3.79 (s, 3H), 3.25 (d, *J* = 17.5 Hz, 1H), 2.90 (d, *J* = 17.5 Hz, 1H), 2.18 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.7, 174.0, 134.4, 133.7, 129.5, 128.7, 127.9, 75.2, 53.2, 51.6, 30.6; IR (film, $cm^{-1}$): *v* = 3511, 3005, 2956, 1732, 1493, 1440, 1367, 1220, 1140; HRMS (ESI-TOF) calcd for $C_{14}H_{15}ClO_4Na$ ($[M+Na]^+$): 305.0551, found: 305.0559; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 11.34 (major), 9.60 min (minor).

**(S)-methyl 2-hydroxy-2-(4-nitrostyryl)-4-oxopentanoate (3g).**[2]

Prepared according to general procedure. The product was obtained in 85 % yield, yellow solid, $[\alpha]_D^{20}$ = - 70.0 (c = 0.84 in $CHCl_3$, 95 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 8.17 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 15.8 Hz, 1H), 6.34 (d, *J* = 15.8 Hz, 1H), 3.81 (s, 3H), 3.28 (d, *J* = 17.5 Hz, 1H), 2.92 (d, *J* = 17.5 Hz, 1H), 2.20 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.4, 173.6, 147.2, 142.3, 132.8, 128.9, 127.3, 124.0, 75.3, 53.4, 51.5, 30.6; IR (film, $cm^{-1}$): *v* = 3452, 3066, 2960, 1753, 1725, 1595, 1521, 1509, 1341, 1218, 1142; HRMS (ESI-TOF) calcd for $C_{14}H_{15}NO_6Na$ ($[M+Na]^+$): 316.0792, found: 316.0804; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 24.76 (major), 21.97 min (minor).

**(S)-methyl 2-hydroxy-2-(4-methylstyryl)-4-oxopentanoate (3h).**

Prepared according to general procedure. The product was obtained in 90 % yield, white solid, $[\alpha]_D^{20}$ = - 85.4 (c = 0.56 in $CHCl_3$, 92 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.27 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.82 (d, *J* = 15.9 Hz, 1H), 6.10 (d, *J* = 15.8 Hz, 1H), 3.79 (br s, 1H), 3.79 (s, 3H), 3.26 (d, *J* = 17.6 Hz, 1H), 2.92 (d, *J* = 17.5 Hz, 1H), 2.33 (s, 3H), 2.19 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 207.0, 174.3, 138.0, 133.1, 130.6, 129.3, 127.1, 126.6, 75.2, 53.1, 51.7, 30.7, 21.2; IR (film, $cm^{-1}$): *v* = 3446, 3027, 2951, 1747, 1706, 1430, 1389, 1360, 1258, 1197, 1148; HRMS (ESI-TOF) calcd for $C_{15}H_{18}O_4Na$ ($[M+Na]^+$): 285.1097, found: 285.1101; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 12.15 (major), 10.22 min (minor).

**(S)-methyl 2-(3-fluorostyryl)-2-hydroxy-4-oxopentanoate (3i).**

Prepared according to general procedure. The product was obtained in 99 % yield, white solid, $[\alpha]_D^{20}$ = - 87.0 (c = 0.64 in $CHCl_3$, 92 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.28-7.25 (m, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.05 (d, *J* = 2.0 Hz, 1H), 6.94 (t, *J* = 8.3 Hz, 1H), 6.83 (d, *J* = 15.8 Hz, 1H), 6.16 (d, *J* = 15.8 Hz, 1H), 3.79 (s, 1H), 3.25 (d, *J* = 17.5 Hz, 1H), 2.91 (d, *J* = 17.5 Hz, 1H), 2.18 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.7, 174.0, 162.9 (d, $J_{C\text{-}F}$ = 244.1 Hz),, 138.2 (d, $J_{C\text{-}F}$ = 7.7 Hz), 130.1, 130.0, 129.7, 129.6 (d, $J_{C\text{-}F}$ = 10.4 Hz), 122.7 (d, $J_{C\text{-}F}$ = 2.7 Hz), 114.8 (d, $J_{C\text{-}F}$ = 21.3 Hz), 113.0 (d, $J_{C\text{-}F}$ = 21.8 Hz), 75.1, 53.2, 51.7, 30.6; IR (film, $cm^{-1}$): *v* = 3438, 3035, 2960, 1742, 1716, 1161, 1579, 1429, 1365, 1229, 1141; HRMS (ESI-TOF) calcd for $C_{14}H_{15}FO_4Na$ ($[M+Na]^+$): 289.0847, found: 289.0849; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 10.65 (major), 11.83 min (minor).

**(S)-methyl 2-(3-chlorostyryl)-2-hydroxy-4-oxopentanoate (3j).**

Prepared according to general procedure. The product was obtained in 95 % yield, white solid, $[\alpha]_D^{20}$ = - 63.8 (c = 0.35 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.36 (s, 1H), 7.27 (s, 3H), 6.81 (d, *J* = 15.8 Hz, 1H), 6.17 (d, *J* = 15.8 Hz, 1H), 3.80 (br s, 1H), 3.80 (s, 3H), 3.25 (d, *J* = 17.5 Hz, 1H), 2.91 (d, *J* = 17.5 Hz, 1H), 2.19 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.6, 174.0, 137.7, 134.5, 129.8, 129.7, 129.5, 127.9, 126.4, 125.1, 75.1, 53.2, 51.6, 30.6; IR (film, $cm^{-1}$): *v* = 3430, 2994, 2953, 1746, 1713, 1593, 1563, 1437, 1393, 1363, 1261, 1206, 1145; HRMS (ESI-TOF) calcd for $C_{14}H_{15}ClO_4Na$ ($[M+Na]^+$): 305.0551, found: 305.0549; The enantiomeric excess was determined by HPLC analysis [AD-H, *i*-PrOH/hexane = 5/95, flow rate 1.0 mL/min, UV 254 nm]: 23.94 (major), 22.67 min (minor).

**(S)-methyl 2-(3-bromostyryl)-2-hydroxy-4-oxopentanoate (3k).**

Prepared according to general procedure. The product was obtained in 54 % yield, white solid, $[\alpha]_D^{20}$ = - 64.3 (c = 0.53 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.51 (s, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 3.1 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 6.15 (d, *J* = 15.8 Hz, 1H), 3.79 (s, 3H), 3.24 (d, *J* = 17.5 Hz, 1H), 2.90 (d, *J* = 17.5 Hz, 1H), 2.18 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.6, 173.9, 138.0, 130.8, 130.1, 129.7, 129.3, 125.5, 122.7, 75.1, 53.2, 51.5, 30.6; IR (film, $cm^{-1}$): *v* = 3429, 2993, 2952, 1747, 1711, 1558, 1436, 1393, 1363, 1259, 1205, 1145; HRMS (ESI-TOF) calcd for $C_{14}H_{15}BrO_4Na$ ($[M+Na]^+$): 349.0046, found: 349.0054; The enantiomeric excess was determined by HPLC analysis [AS-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 13.00 (major), 18.20 min (minor).

**(S)-ethyl 2-hydroxy-2-(3-nitrostyryl)-4-oxopentanoate (3l).**[2]
Prepared according to general procedure. The product was obtained in 98 % yield, colorless oil, $[\alpha]_D^{20}$ = - 73.9 (c = 0.98 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 8.23 (s, 1H), 8.10- 8.06 (m, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 15.8 Hz, 1H), 6.31 (d, *J* = 15.8 Hz, 1H), 4.31-4.22 (m, 2H), 3.27 (d, *J* = 17.5 Hz, 1H), 2.92 (d, *J* = 17.4Hz, 1H), 2.19 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.3, 173.2, 148.5, 137.7, 132.9, 131.6, 129.5, 128.6, 122.5, 120.9, 75.1, 62.6, 51.5, 30.6, 14.0; IR (film, $cm^{-1}$): *v* = 3496, 3079, 2990, 1731, 1525, 1352, 1221, 1152; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_6Na$ ($[M+Na]^+$): 330.0948, found: 330.0955; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 16.39 (major), 14.71 min (minor).

**(S)-methyl 2-hydroxy-2-(3-methylstyryl)-4-oxopentanoate (3m).**
Prepared according to general procedure. The product was obtained in 98 % yield, white solid, $[\alpha]_D^{20}$ = - 84.2 (c = 0.60 in $CHCl_3$, 93 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.27-7.17 (m, 3H), 7.07 (d, *J* = 6.6 Hz, 1H), 6.83 (d, *J* = 15.8 Hz, 1H), 6.15 (d, *J* = 15.8 Hz, 1H), 4.03 (br s, 1H), 3.80 (s, 3H), 3.26 (d, *J* = 17.5 Hz, 1H), 2.93 (d, *J* = 17.5 Hz, 1H), 2.34 (s, 3H), 2.19 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.8, 174.2, 138.1, 135.8, 130.8, 128.8, 128.4, 128.0, 127.3, 123.9, 75.2, 53.1, 51.7, 30.6, 21.3; IR (film, $cm^{-1}$): *v* = 3434, 3026, 2957, 1743, 1716, 1435, 1365, 1267, 1224, 1141; HRMS (ESI-TOF) calcd for $C_{15}H_{18}O_4Na$ ($[M+Na]^+$): 285.1097, found: 285.1096; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 12.87 (major), 18.80 min (minor).

**(S)-methyl 2-hydroxy-2-(3-methoxystyryl)-4-oxopentanoate (3n).**
Prepared according to general procedure. The product was obtained in 98 % yield, colorless oil, $[\alpha]_D^{20}$ = - 77.6 (c = 1.0 in $CHCl_3$, 90 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.26-7.18 (m, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.88 (s, 1H), 6.80-6.77 (m, 2H), 6.14 (d, *J* = 15.8 Hz, 1H), 3.78 (s, 3H), 3.78 (br s, 1H), 3.77 (s, 3H), 3.24 (d, *J* = 17.5 Hz, 1H), 2.91 (d, *J* = 17.5 Hz, 1H), 2.16 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.7, 174.1, 159.6, 137.2, 130.5, 129.5, 128.4, 119.2, 113.6, 111.8, 75.1, 55.1, 53.0, 51.5, 30.5; IR (film, $cm^{-1}$): *v* = 3497, 3003, 2954, 1740, 1599, 1581, 1435, 1365, 1269, 1241, 1157; HRMS (ESI-TOF) calcd for $C_{15}H_{18}O_5Na$ ($[M+Na]^+$): 301.1046, found: 301.1052; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 19.62 (major), 32.76 min (minor).

**(S)-methyl 2-(2-chlorostyryl)-2-hydroxy-4-oxopentanoate (3o).**
Prepared according to general procedure. The product was obtained in 91 % yield, colorless oil, $[\alpha]_D^{20}$ = - 64.3 (c = 0.94 in $CHCl_3$, 91 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.48-7.45 (m, 1H), 7.35-7.31 (m, 1H), 7.22-7.17 (m, 3H), 6.17 (d, *J* = 15.8 Hz, 1H), 4.05 (br s, 1H), 3.80 (s, 3H), 3.26 (d, *J* = 17.4 Hz, 1H), 2.95 (d, *J* = 17.5 Hz, 1H), 2.19 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.6, 174.0, 131.2, 129.7, 129.5, 129.0, 128.6, 127.2, 126.9, 126.8, 75.3, 53.2, 51.5, 30.6; IR (film, $cm^{-1}$): *v* = 3497, 3002, 2953, 1740, 1438, 1365, 1218, 1144; HRMS (ESI-TOF) calcd for $C_{14}H_{15}ClO_4Na$ ($[M+Na]^+$): 305.0551, found: 305.0559; The enantiomeric excess was determined by HPLC analysis [AD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 16.42 (major), 11.87 min (minor).

**(S)-methyl 2-(2-bromostyryl)-2-hydroxy-4-oxopentanoate (3p).**
Prepared according to general procedure. The product was obtained in 98 % yield, colorless oil, $[\alpha]_D^{20}$ = - 69.7 (c = 1.2 in $CHCl_3$, 91 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.52 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.26-7.21 (m, 2H), 7.12-7.07 (m, 1H), 6.12 (d, *J* = 15.7 Hz, 1H), 3.80 (br s, 1H), 3.80 (s, 3H), 3.25 (d, *J* = 17.4 Hz, 1H), 2.95 (d, *J* = 17.4 Hz, 1H), 2.18 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.6, 173.9, 135.8, 132.9, 131.4, 129.7, 129.2, 127.4, 127.1, 123.9, 75.3, 53.2, 51.5, 30.6; IR (film, $cm^{-1}$): *v* = 3500, 3003, 2953, 1740, 1467, 1437, 1365, 1250, 1218, 1144; HRMS (ESI-TOF) calcd for $C_{14}H_{15}BrO_4Na$ ($[M+Na]^+$): 349.0046, found: 349.0047; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 21.13 (major), 18.57 min (minor).

**(S)-methyl 2-hydroxy-2-(2-(naphthalen-1-yl)vinyl)-4-oxopentanoate (3q).**
Prepared according to general procedure. The product was obtained in 93 % yield, colorless oil, $[\alpha]_D^{20}$ = - 87.9 (c = 0.96 in $CHCl_3$, 96 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 8.13 (d, *J* = 8.7 Hz, 1H), 7.84-7.78 (m, 2H), 7.68 (d, *J* = 15.5 Hz, 1H), 7.58-7.43 (m, 4H), 6.23 (d, *J* = 15.5 Hz, 1H), 3.84 (s, 3H), 3.32 (d, *J* = 17.5 Hz, 1H), 3.02 (d, *J* = 17.4 Hz, 1H), 2.21 (s, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.7, 174.2, 133.6, 133.4, 131.3, 131.0, 128.4, 128.3, 128.0, 126.1, 125.8, 125.4, 123.8, 123.7, 75.4, 53.1, 51.7, 30.6; IR (film, $cm^{-1}$): *v* = 3500, 3047, 2953, 1739, 1591, 1509, 1436, 1394, 1365, 1270, 1244, 1217, 1171, 1141; HRMS (ESI-TOF) calcd for $C_{18}H_{18}O_4Na$ ($[M+Na]^+$): 321.1097, found: 321.1101; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 25.49 (major), 35.17 min (minor).

**(S)-ethyl 2-hydroxy-4-oxo-2-(2-(thiophen-2-yl)vinyl)pentanoate (3r).**
Prepared according to general procedure. The product was obtained in 40 % yield, colorless oil, $[\alpha]_D^{20}$ = - 59.9 (c = 0.48 in $CHCl_3$, 90 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.16 (d, *J* = 4.9 Hz, 1H), 7.00-6.92 (m, 3H), 6.00 (d, *J* = 15.6 Hz, 1H), 4.29-4.16 (m, 2H), 3.71 (br s, 1H), 3.21 (d, *J* = 17.5 Hz, 1H), 2.89 (d, *J* = 17.5 Hz, 1H), 2.16 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); **$^{13}$C NMR** (75 MHz, $CDCl_3$): δ = 206.5, 173.4, 140.9, 127.6, 127.4, 126.7, 124.8, 123.9, 74.7, 62.3, 51.5, 30.5, 13.9; IR (film, $cm^{-1}$): *v* = 3496, 3007, 2982, 1735, 1365, 1263, 1212, 1137; HRMS (ESI-TOF) calcd for $C_{13}H_{16}O_4SNa$ ($[M+Na]^+$): 291.0662, found: 291.0669; The enantiomeric excess was determined by HPLC analysis [OD-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 9.95 (major), 12.75 min (minor).

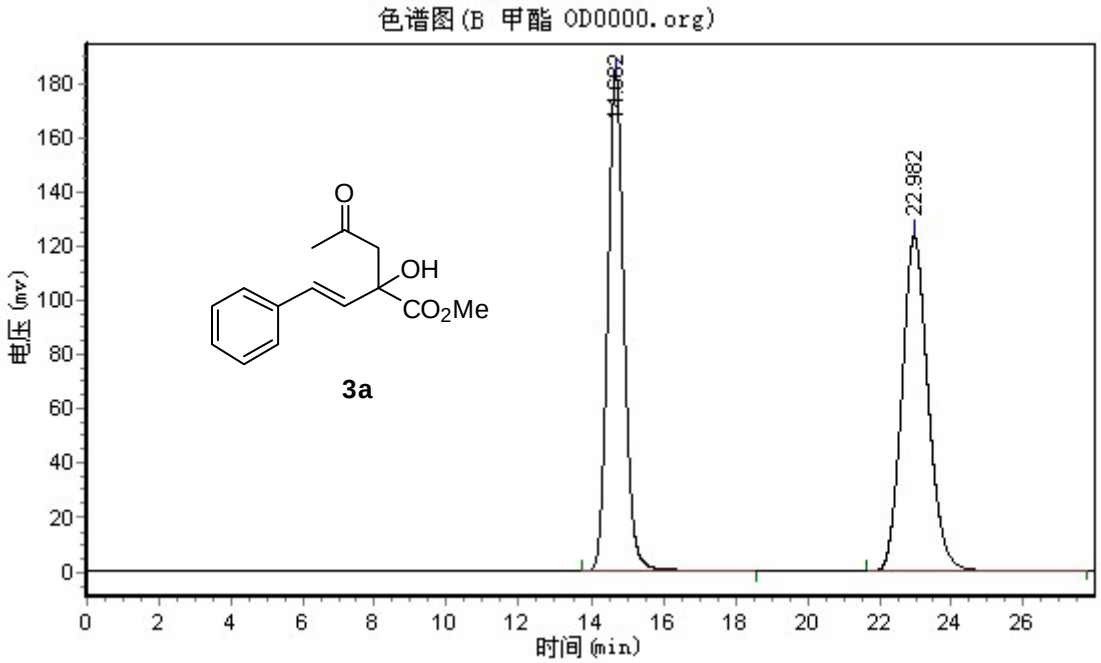
**(R)-methyl 2-hydroxy-2-((S)-2-oxocyclopentyl)-4-phenylbut-3-enoate (3t).** [3]

Prepared according to general procedure. The product was obtained in 93 % yield, white solid, $[\alpha]_D^{20}$ = - 146.4 (c = 0.34 in $CHCl_3$, 95 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.40-7.24 (m, 5H), 6.84 (d, *J* = 15.7 Hz, 1H), 6.18 (d, *J* = 15.7 Hz, 1H), 3.88 (s, 3H), 2.92-2.89 (m, 1H), 2.18-1.98 (m, 6H); The enantiomeric excess was determined by HPLC analysis [AS-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 13.15 (major), 18.08 min (minor).

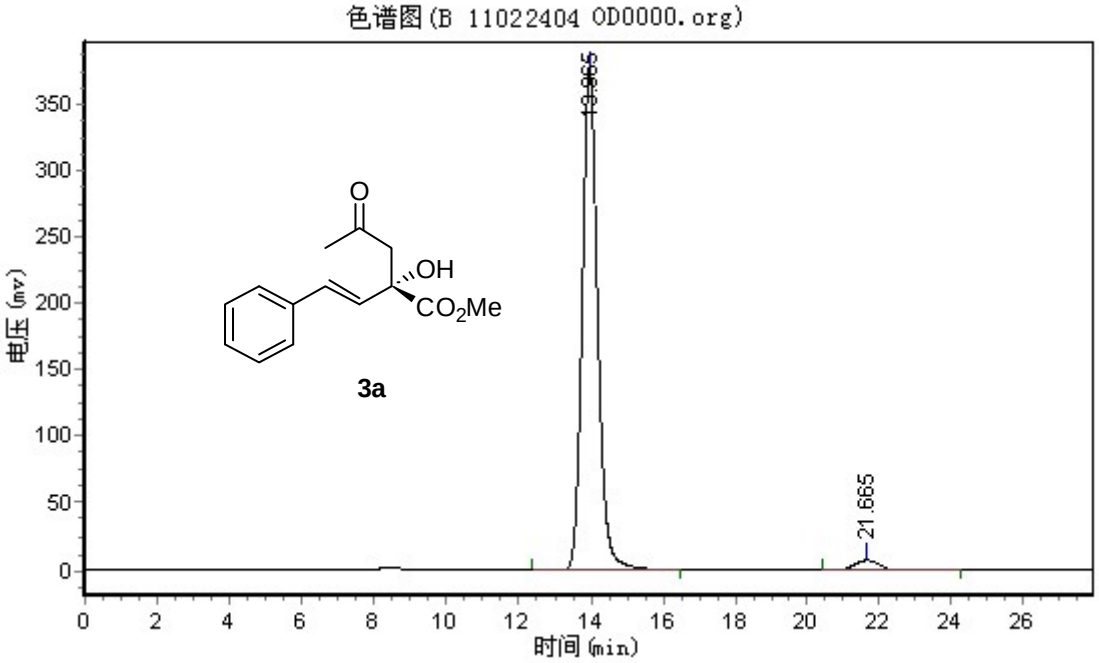
**(R)-methyl 2-hydroxy-2-((S)-4-oxotetrahydro-2H-pyran-3-yl)-4-phenylbut-3-enoate (3u).** [3]

Prepared according to general procedure. The product was obtained in 99 % yield, colorless oil, $[\alpha]_D^{20}$ = - 77.7 (c = 1.1 in $CHCl_3$, 81 % ee); **$^1$H NMR** (300 MHz $CDCl_3$) δ (ppm) 7.39-7.26 (m, 5H), 6.88 (d, *J* = 15.8 Hz, 1H), 6.05 (d, *J* = 15.8 Hz, 1H), 4.33-4.29 (m, 2H), 3.80 (s, 3H), 3.74-3.63 (m, 2H), 3.37-3.34 (m, 1H), 2.42-2.37 (m, 2H); The enantiomeric excess was determined by HPLC analysis [AS-H, *i*-PrOH/hexane = 10/90, flow rate 1.0 mL/min, UV 254 nm]: 19.30 (major), 34.57 min (minor).

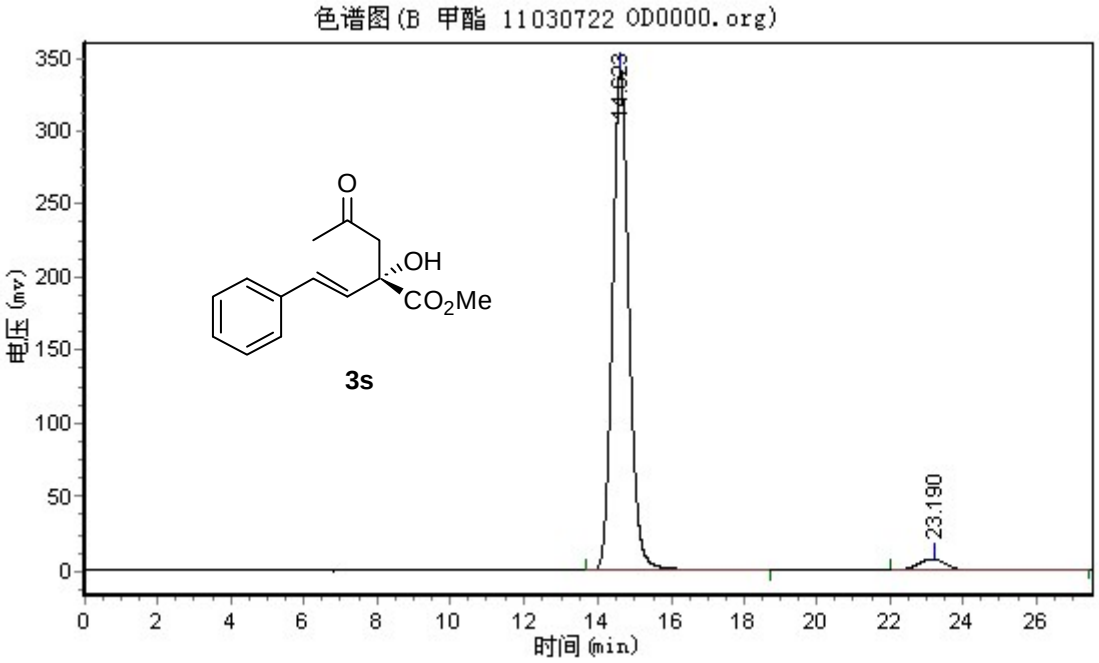
## D. HPLC Analysis of the Products.



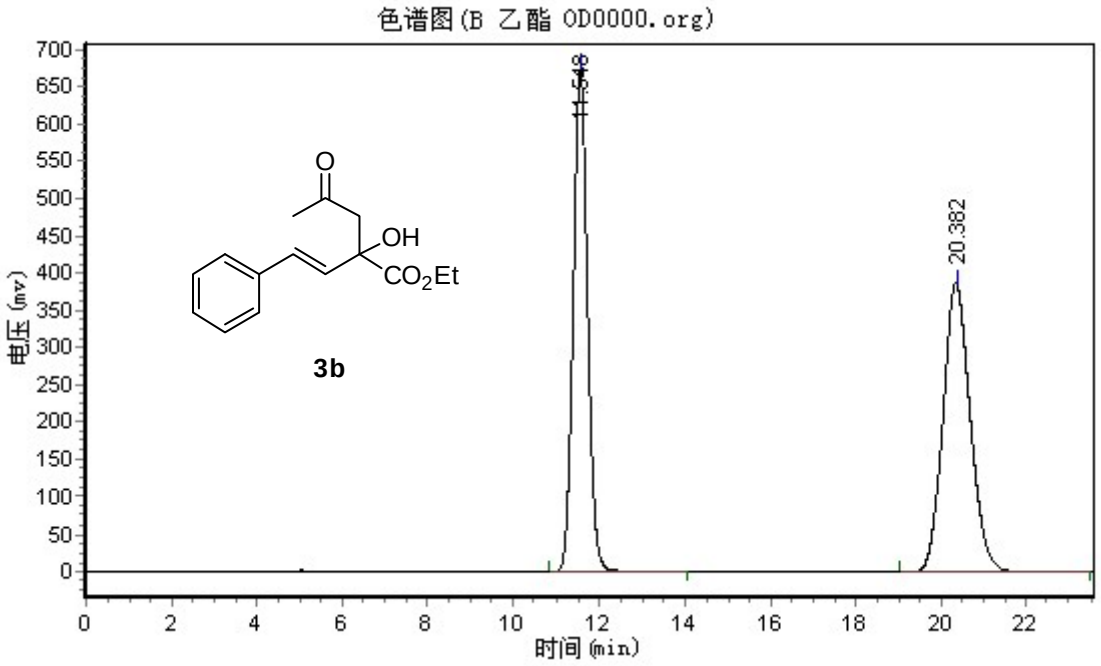

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 14.682 | 184936.328 | 5861215.000 | 48.2679 |
| 2 | 22.982 | 123298.133 | 6281881.500 | 51.7321 |



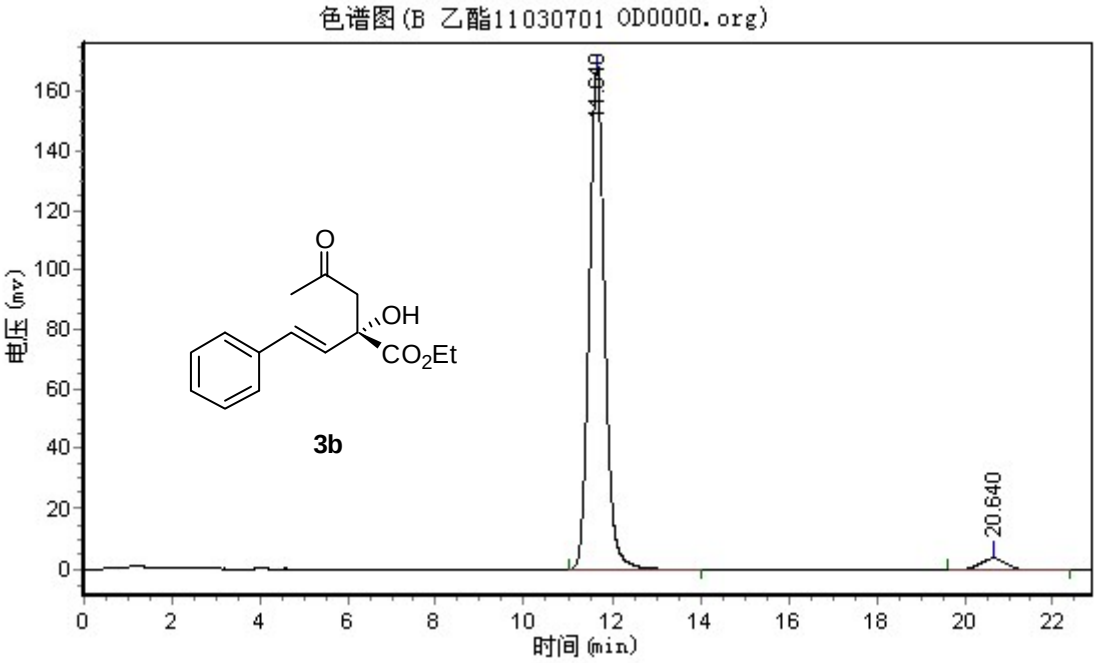

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 13.965 | 376688.046 | 11244985.000 | 96.8319 |
| 2 | 21.665 | 7686.955 | 367913.219 | 3.1681 |



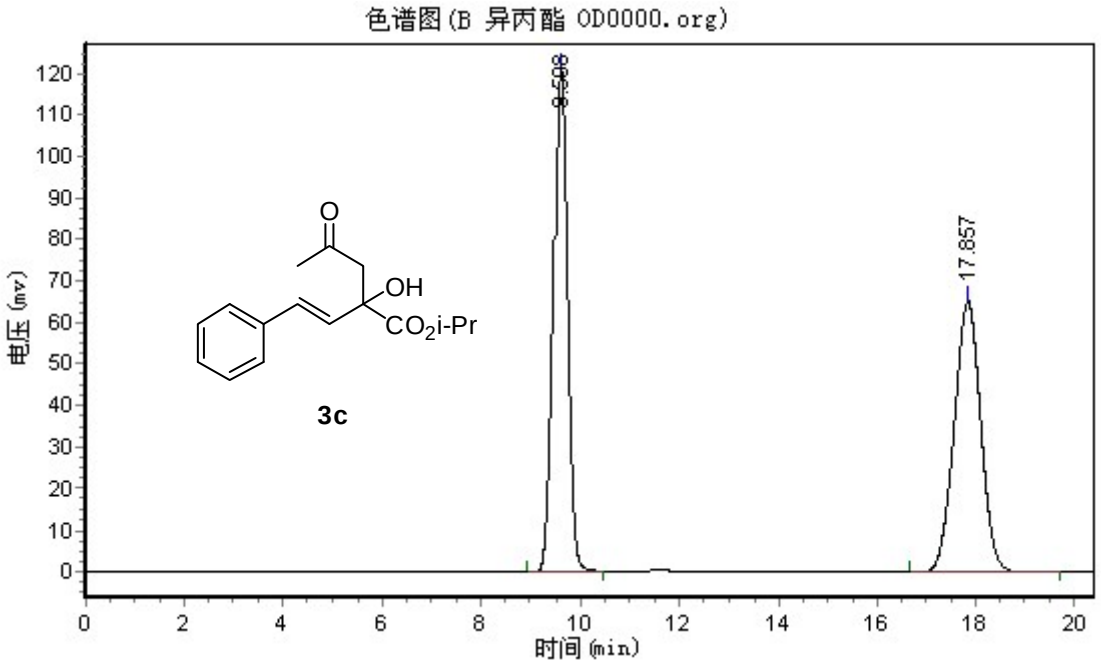

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 14.623 | 342663.875 | 10838021.000 | 96.1667 |
| 2 | 23.190 | 7912.757 | 432010.625 | 3.8333 |



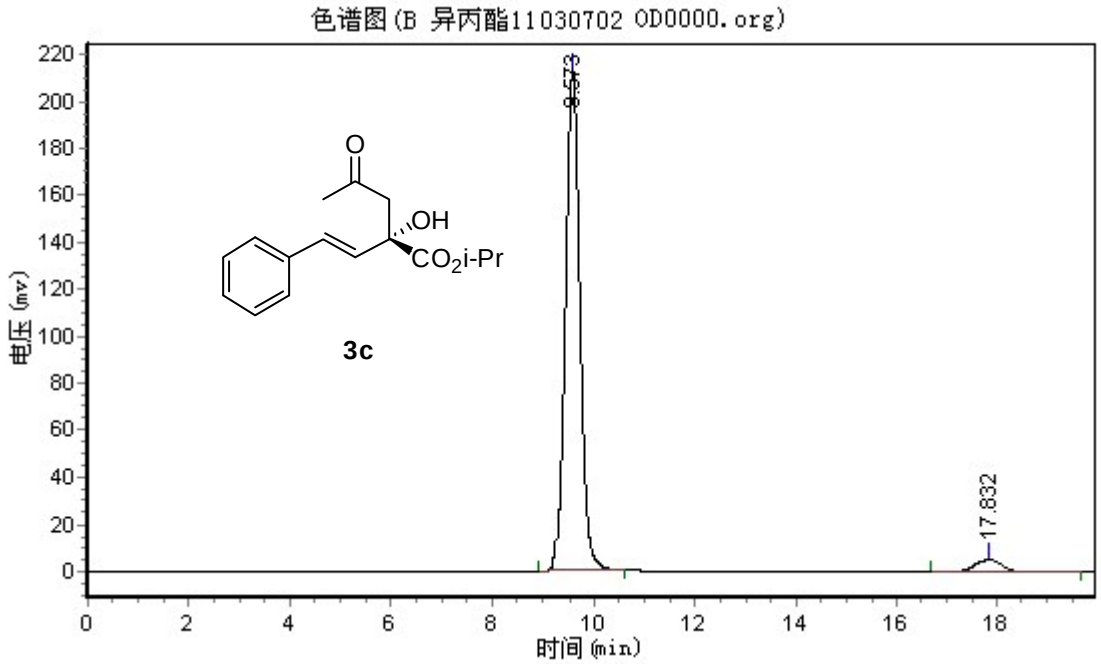

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 11.548 | 673939.125 | 15802638.000 | 48.0196 |
| 2 | 20.382 | 386916.844 | 17106108.000 | 51.9804 |



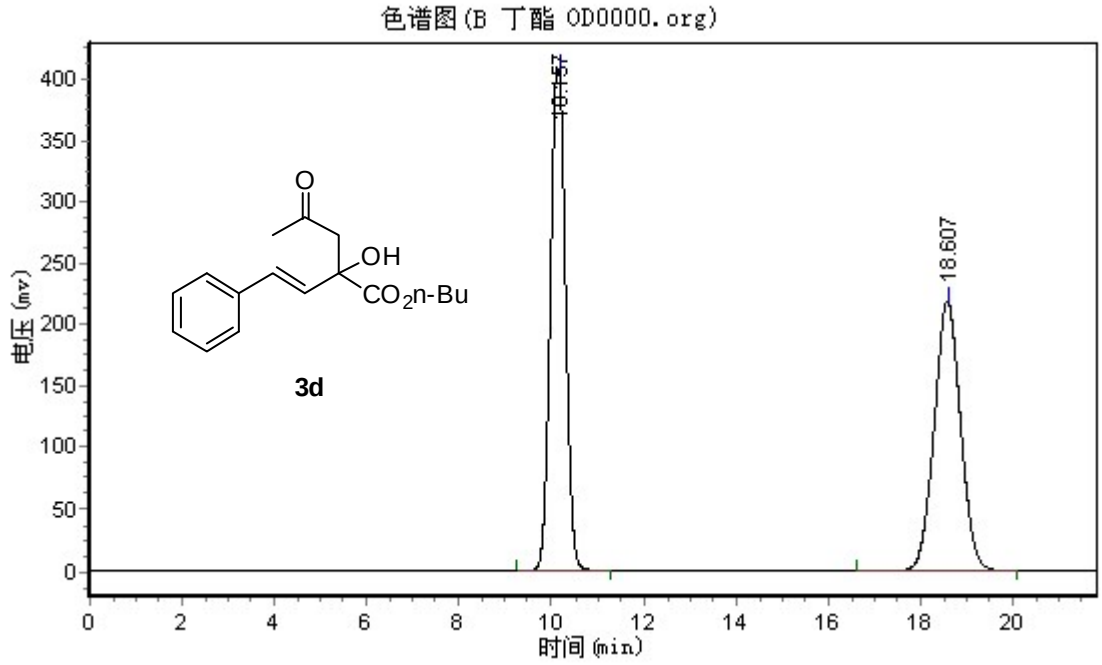

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 11.640 | 167813.000 | 4159807.750 | 95.7529 |
| 2 | 20.640 | 4073.009 | 184506.797 | 4.2471 |



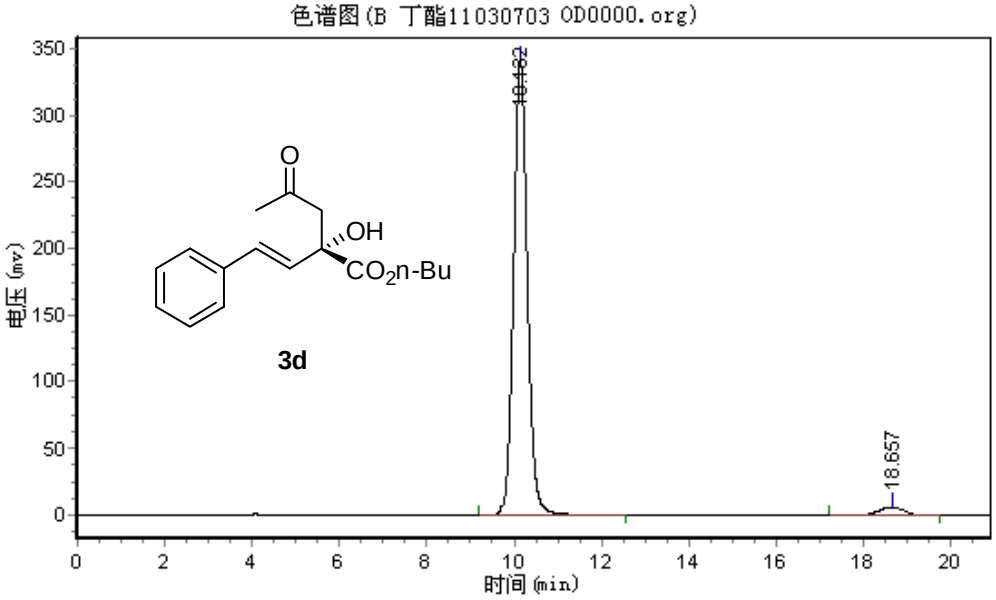

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.598 | 120889.672 | 2257006.000 | 48.1984 |
| 2 | 17.857 | 64991.262 | 2425733.500 | 51.8016 |



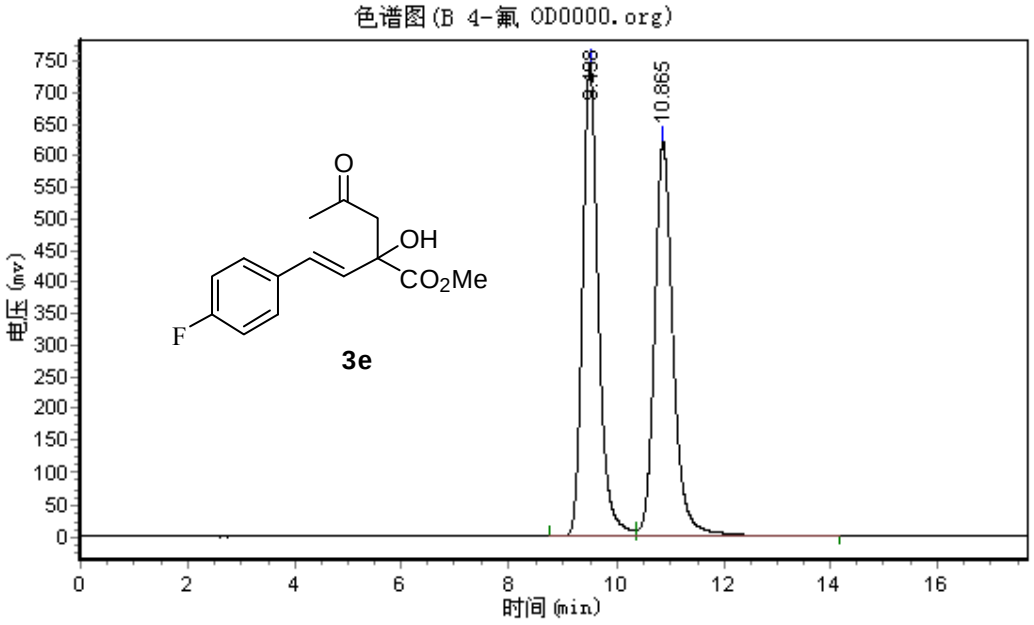

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.573 | 213384.766 | 4233699.000 | 95.2357 |
| 2 | 17.832 | 5371.611 | 211794.297 | 4.7642 |



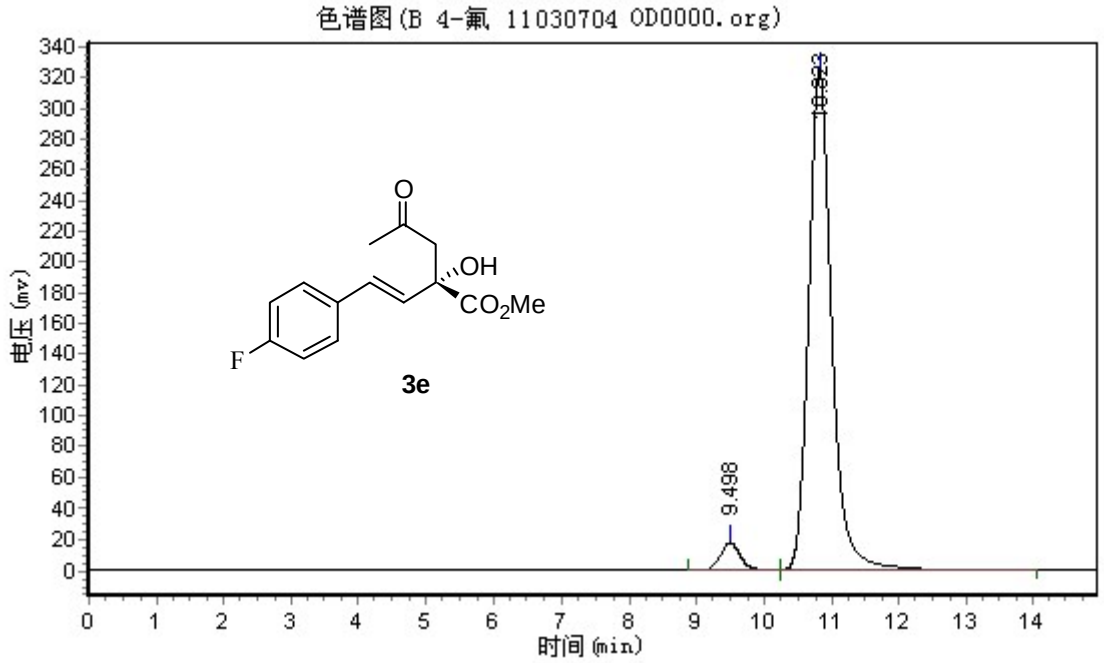

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.157 | 408586.719 | 8393552.000 | 49.1663 |
| 2 | 18.607 | 218846.719 | 8678213.000 | 50.8337 |



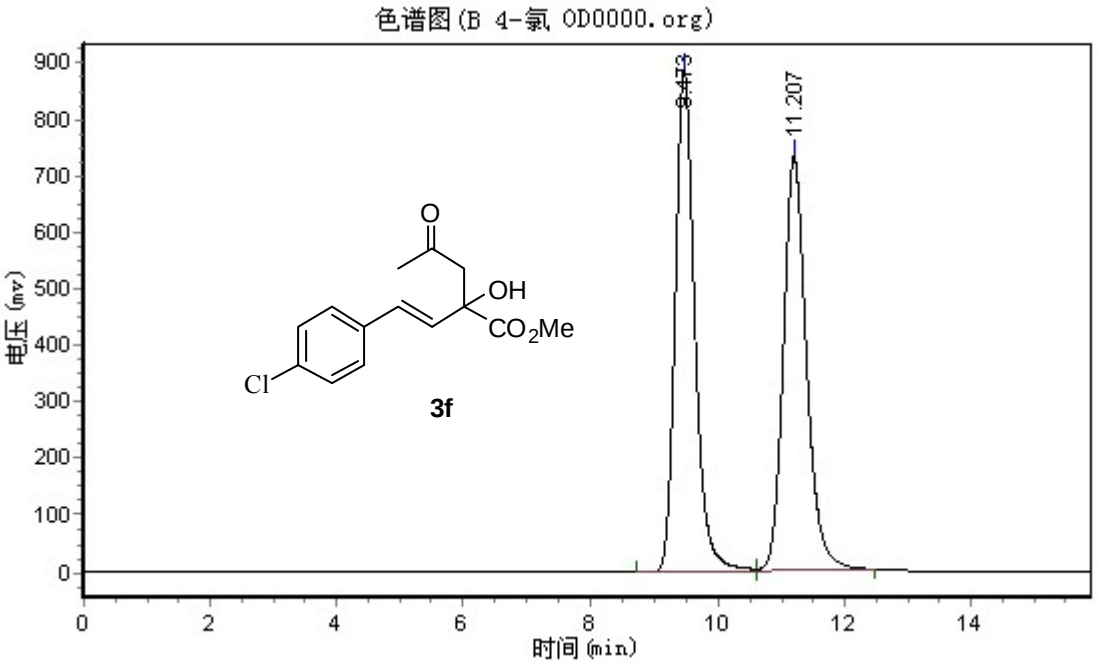

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.132 | 341505.469 | 7548435.000 | 96.4789 |
| 2 | 18.657 | 6713.639 | 275492.094 | 3.5211 |



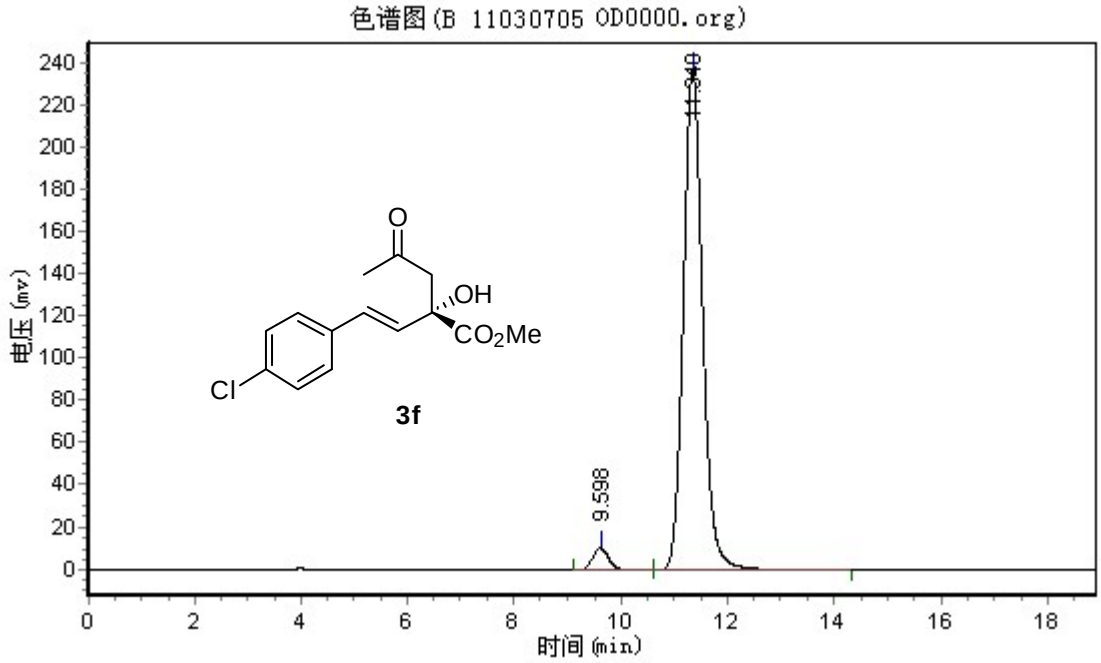

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.498 | 744611.625 | 15367721.000 | 50.3914 |
| 2 | 10.865 | 621162.313 | 15128973.000 | 49.6086 |



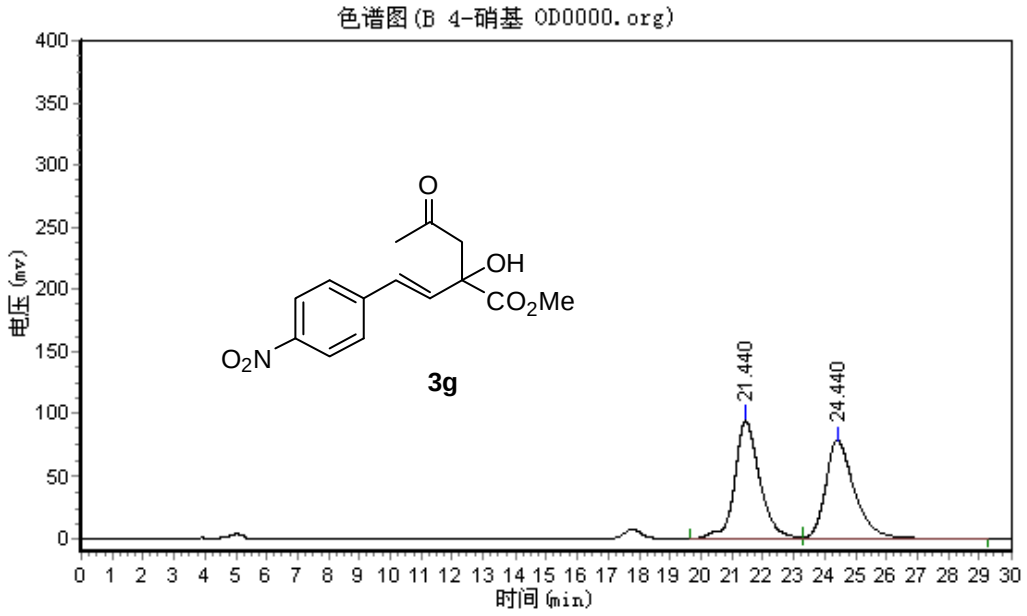

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.498 | 18216.451 | 374113.031 | 4.6223 |
| 2 | 10.823 | 325744.125 | 7719593.500 | 95.3777 |



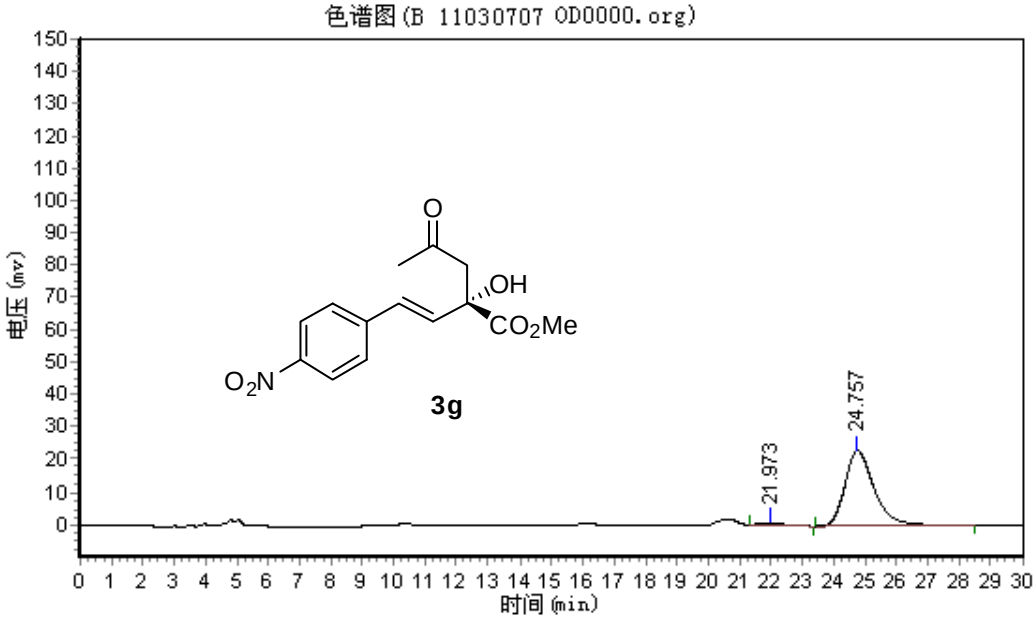

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.473 | 888632.563 | 19134014.000 | 50.3142 |
| 2 | 11.207 | 732727.688 | 18895066.000 | 49.6858 |



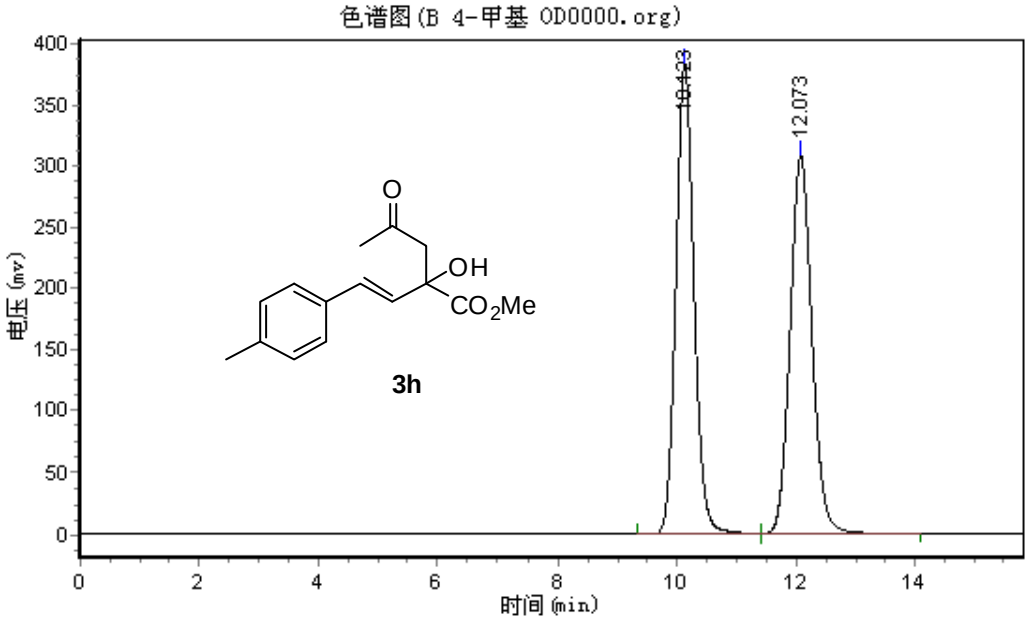

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.598 | 10444.813 | 225159.438 | 3.6332 |
| 2 | 11.340 | 236978.188 | 5972133.000 | 96.3668 |



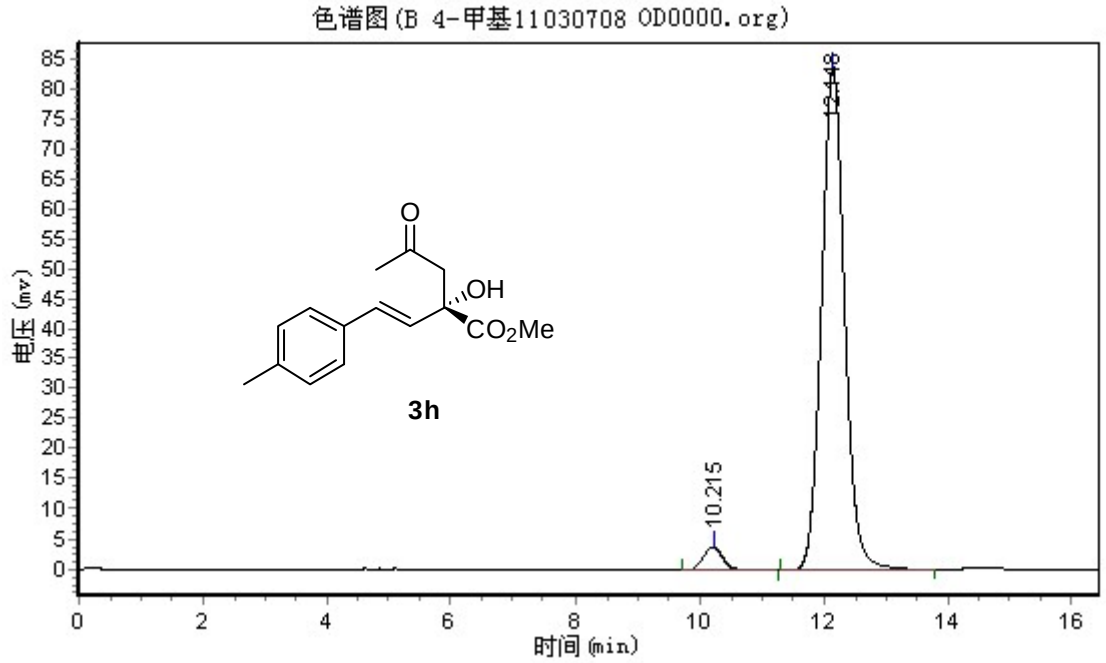

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 21.440 | 93075.813 | 5347599.000 | 50.9184 |
| 2 | 24.440 | 78682.594 | 5154690.500 | 49.0816 |



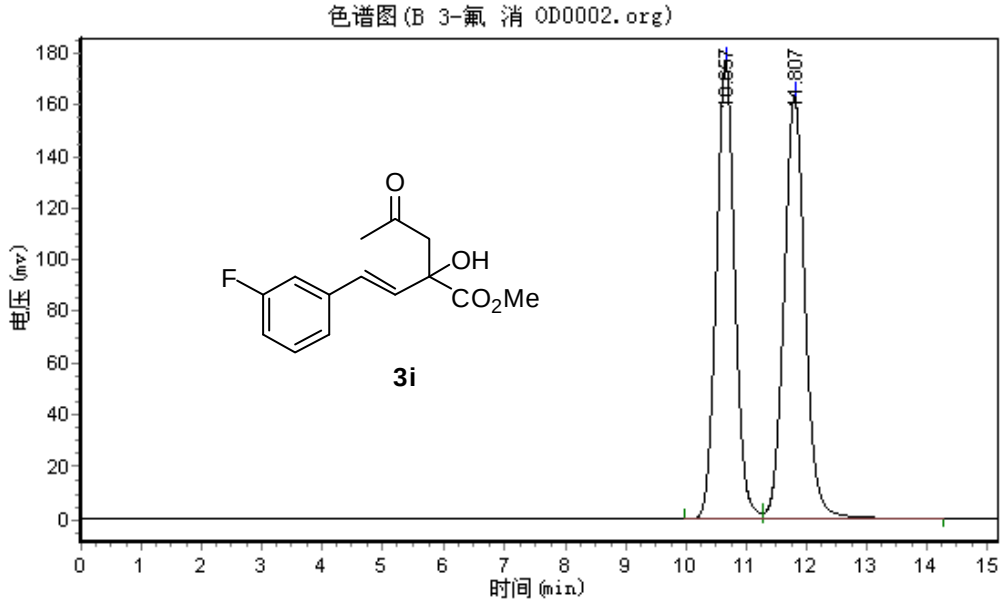

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 21.973 | 848.857 | 35962.852 | 2.3430 |
| 2 | 24.757 | 22950.367 | 1498931.500 | 97.6570 |



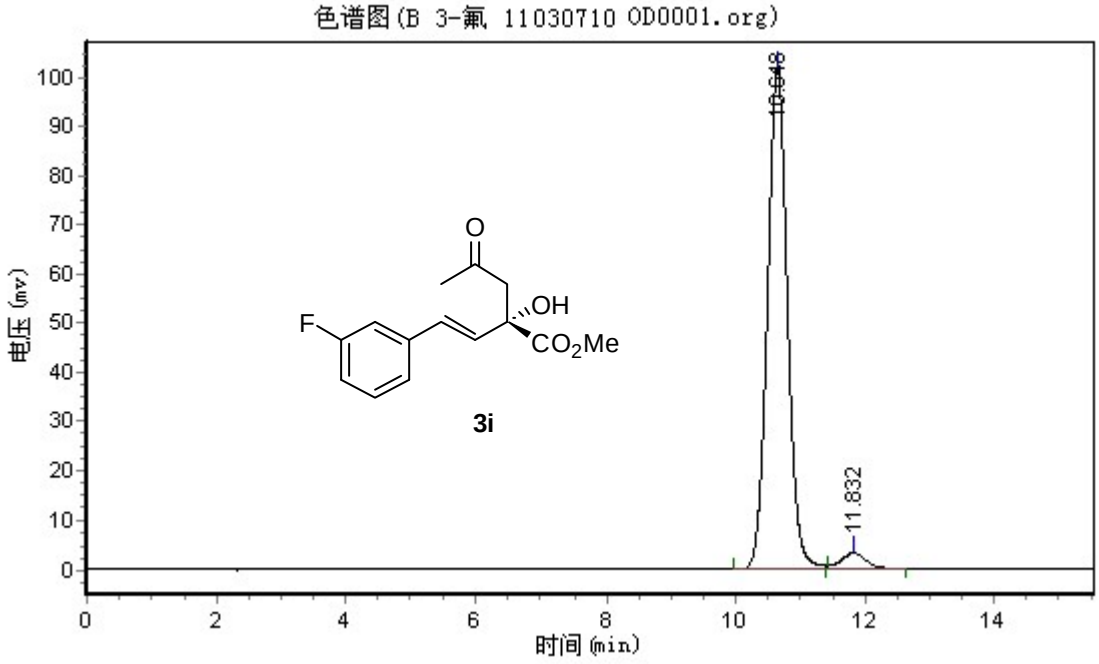

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.123 | 384107.719 | 8114047.000 | 50.6277 |
| 2 | 12.073 | 308089.688 | 7912835.500 | 49.3723 |



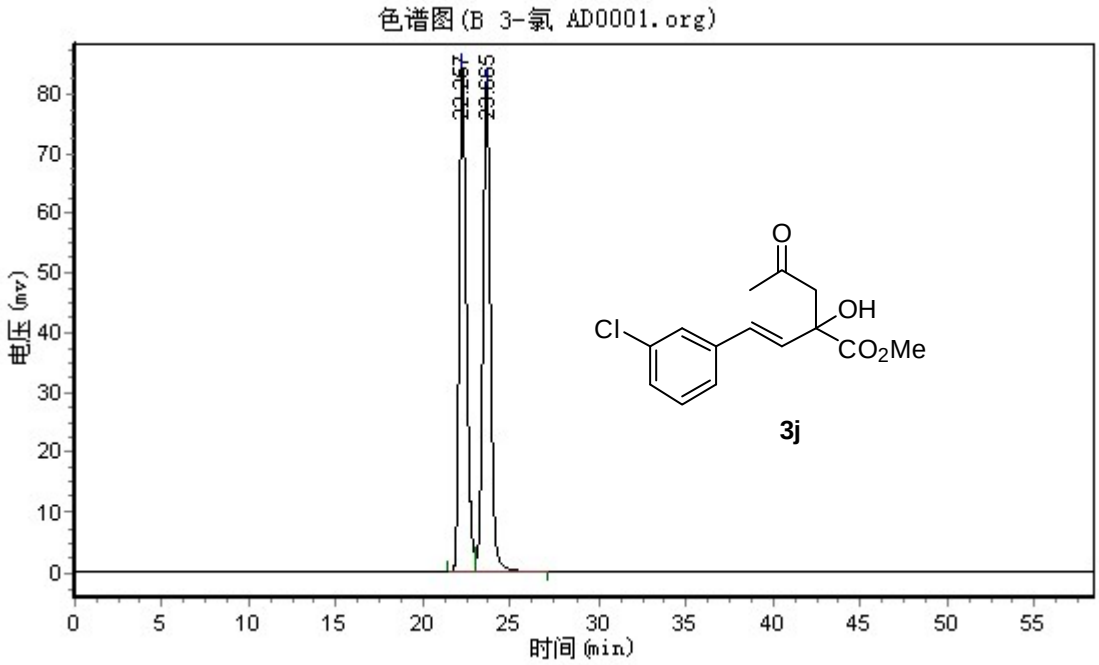

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.215 | 3966.372 | 88430.500 | 3.9281 |
| 2 | 12.148 | 83569.063 | 2162786.000 | 96.0719 |



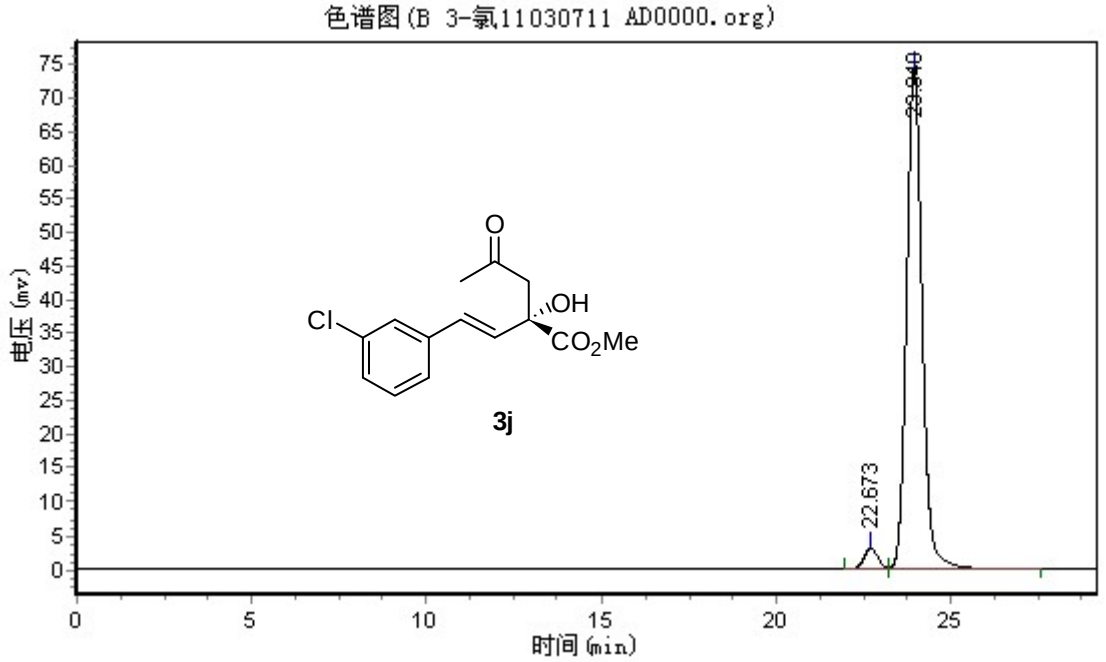

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.657 | 176577.656 | 3766840.500 | 48.7053 |
| 2 | 11.807 | 163152.422 | 3967098.000 | 51.2947 |



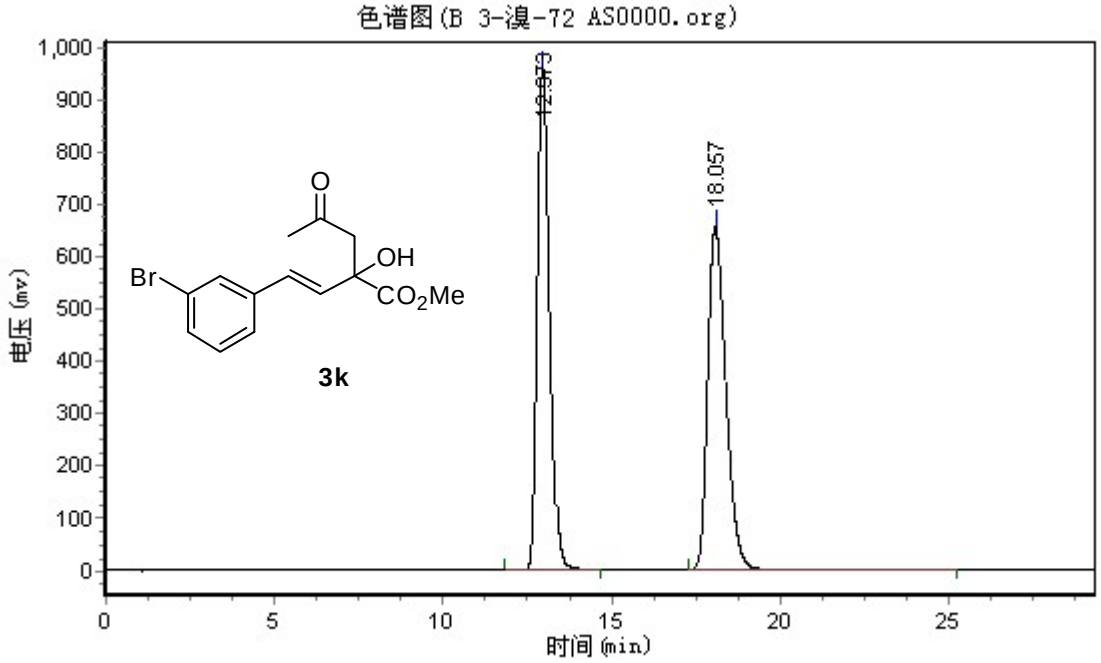

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 10.648 | 102050.688 | 2173595.250 | 96.0966 |
| 2 | 11.832 | 3256.451 | 88290.156 | 3.9034 |



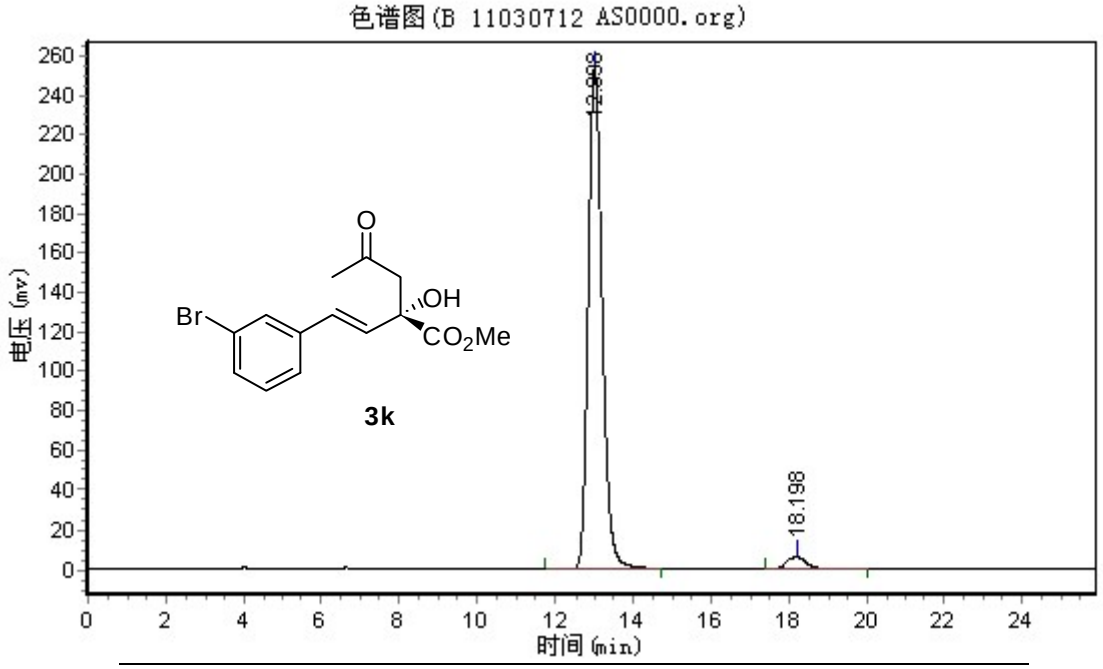

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 22.257 | 84051.805 | 2435637.750 | 49.4725 |
| 2 | 23.665 | 81053.773 | 2487573.500 | 50.5275 |



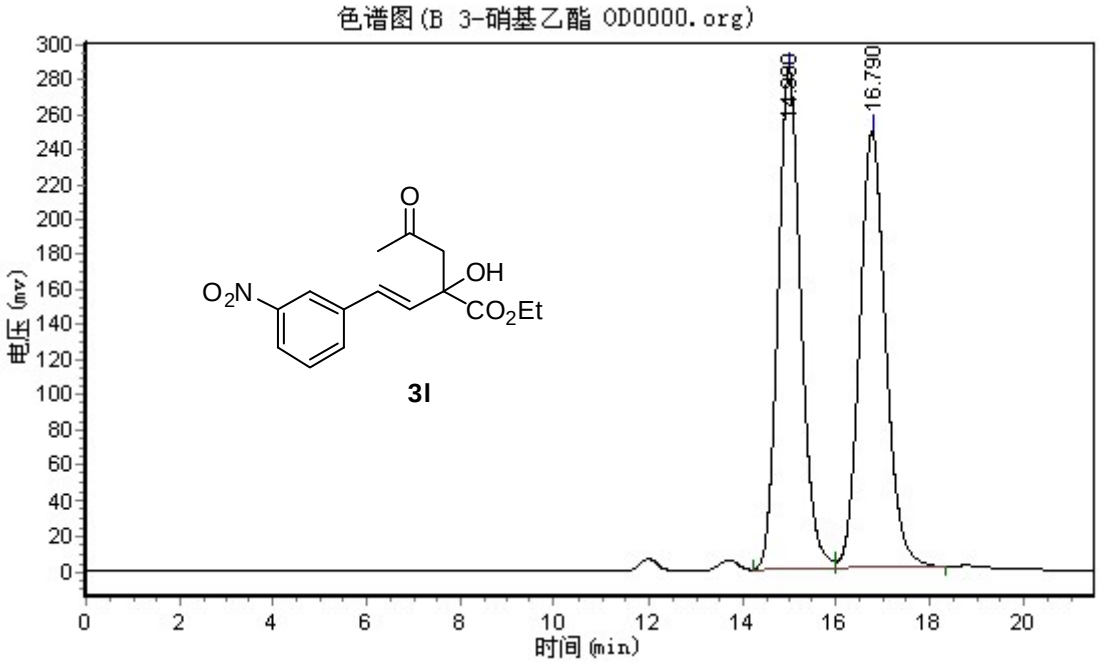

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 22.673 | 3063.675 | 87772.773 | 3.6639 |
| 2 | 23.940 | 74516.680 | 2307824.000 | 96.3361 |



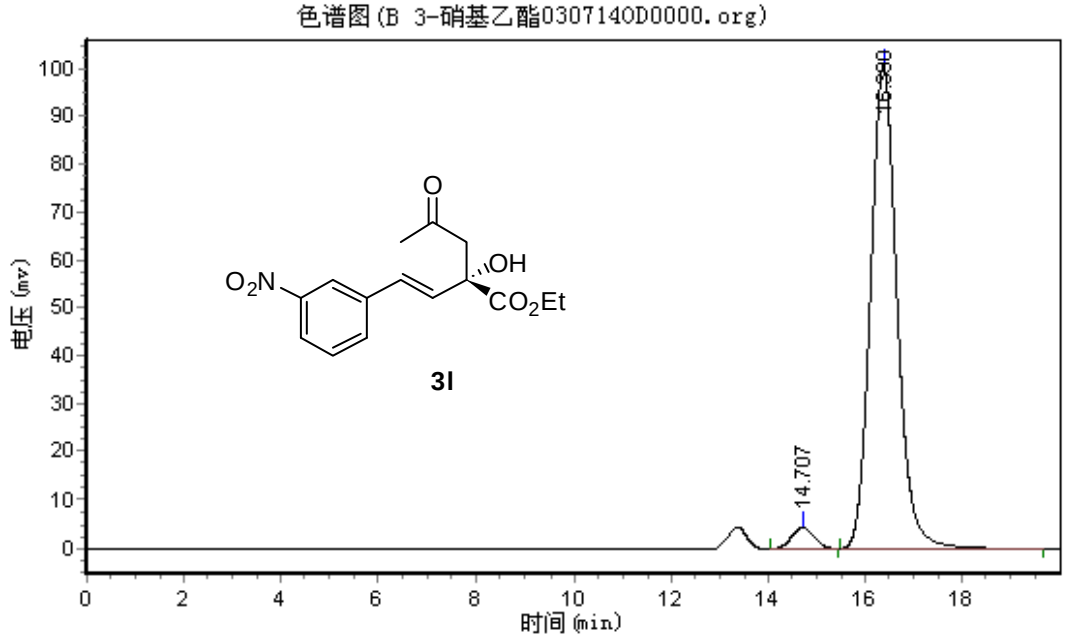

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 12.973 | 961517.875 | 23911834.000 | 49.1843 |
| 2 | 18.057 | 654855.250 | 24704988.000 | 50.8157 |



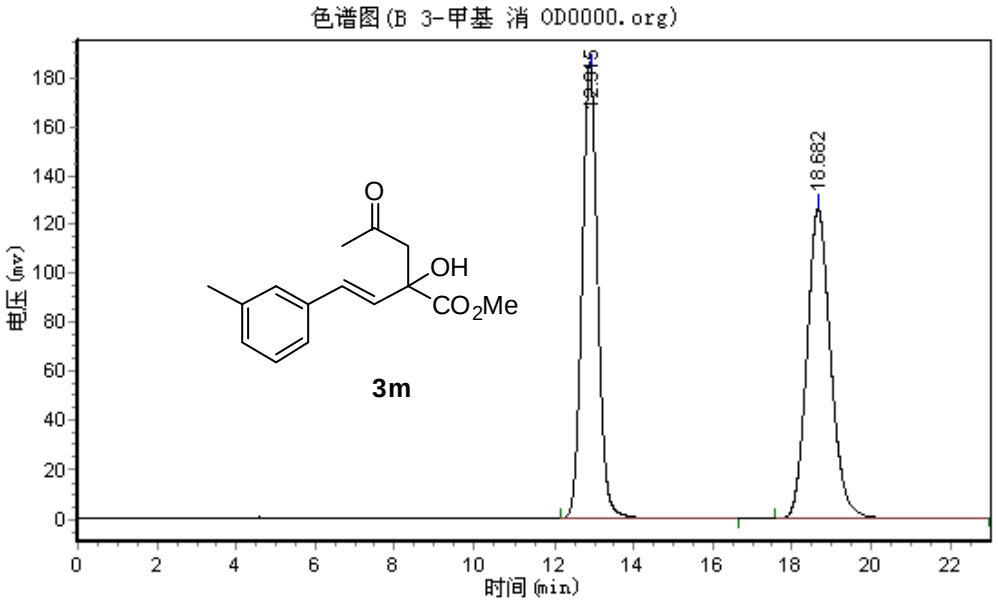

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 12.998 | 254054.578 | 6384946.000 | 96.4518 |
| 2 | 18.198 | 6340.635 | 234882.906 | 3.5482 |



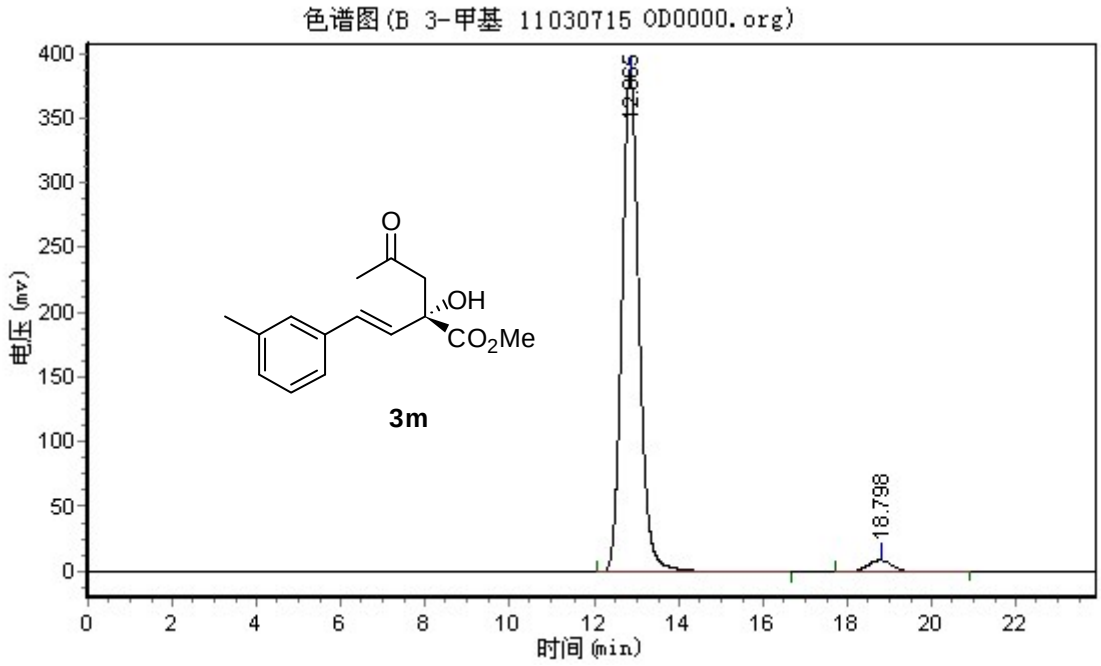

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 14.990 | 284846.250 | 9772511.000 | 49.8480 |
| 2 | 16.790 | 249930.844 | 9832127.000 | 50.1520 |



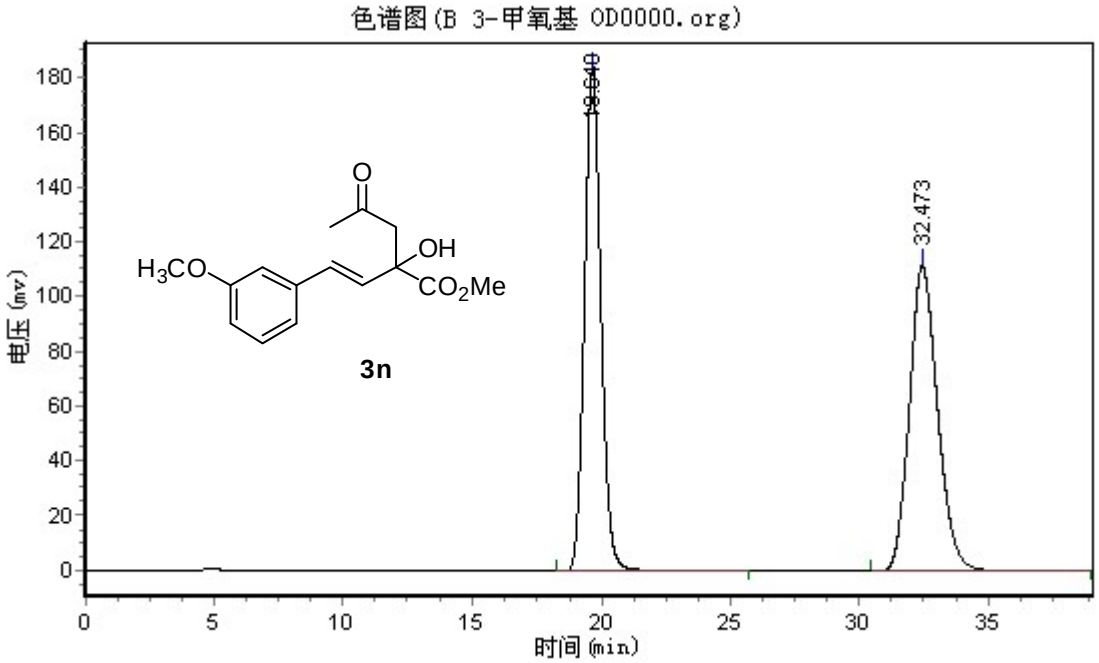

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 14.707 | 4374.605 | 143250.297 | 3.6165 |
| 2 | 16.390 | 100767.695 | 3817797.750 | 96.3835 |



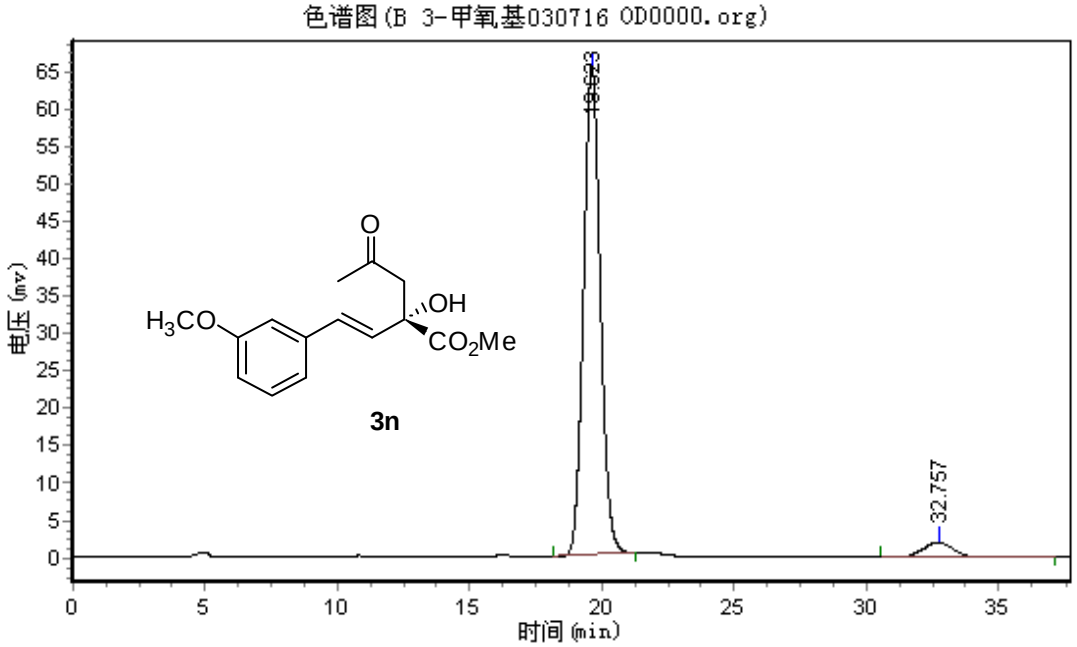

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 12.915 | 185472.484 | 5103790.500 | 49.2308 |
| 2 | 18.682 | 126373.938 | 5263267.000 | 50.7691 |



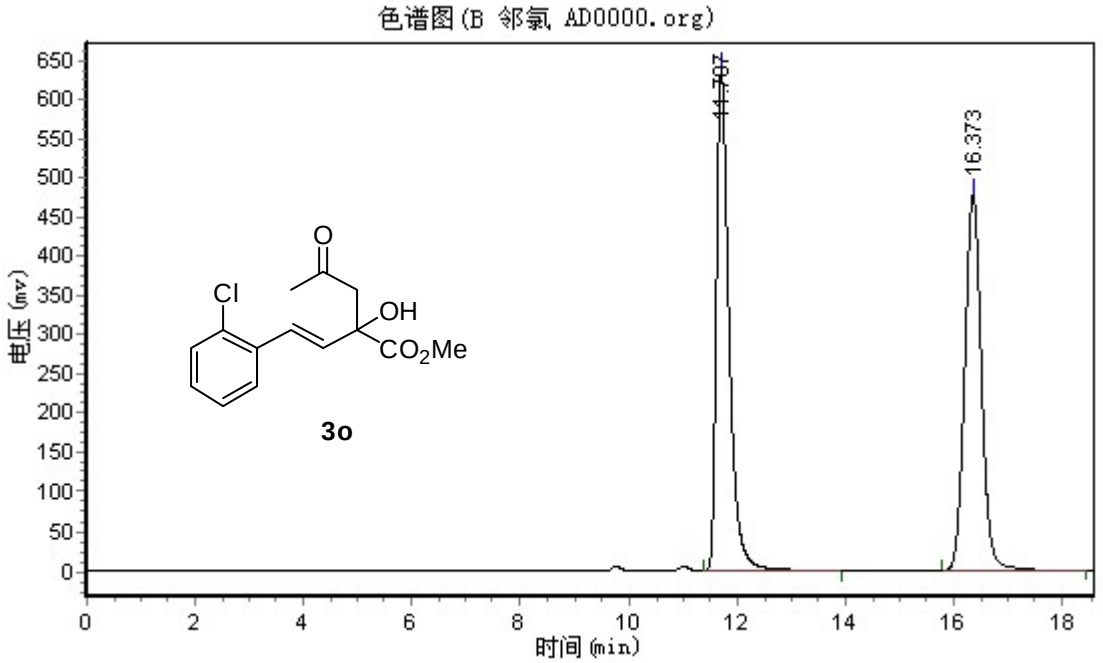

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 12.865 | 386492.938 | 11014000.000 | 96.4289 |
| 2 | 18.798 | 9288.667 | 407886.813 | 3.5711 |



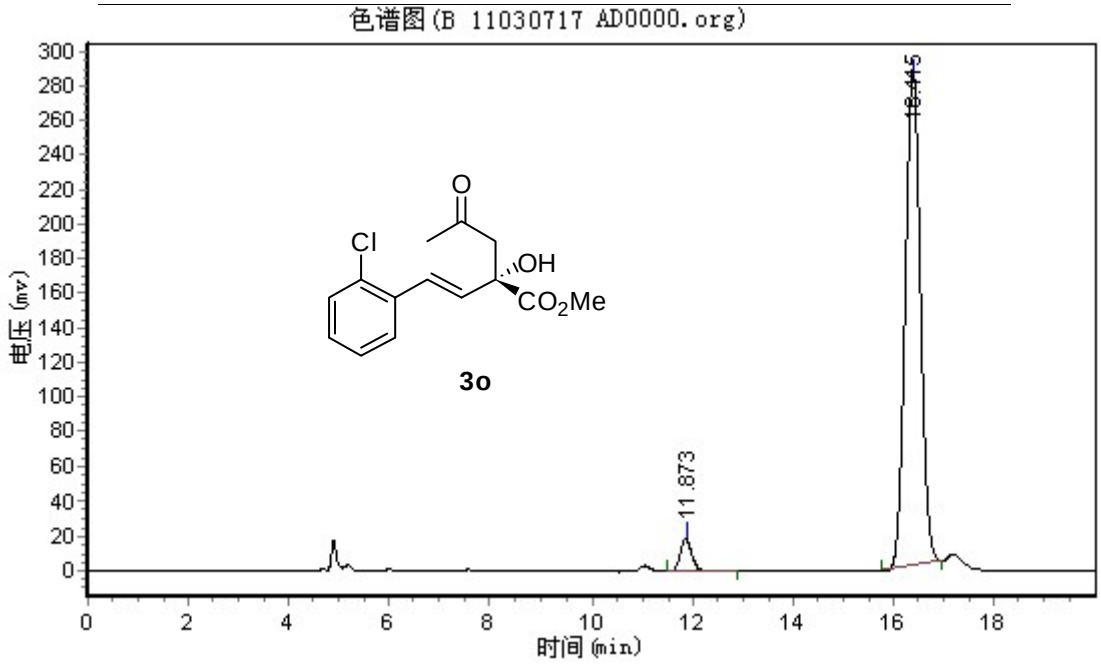

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 19.640 | 183527.141 | 8196294.500 | 49.1670 |
| 2 | 32.473 | 111311.219 | 8474027.000 | 50.8330 |



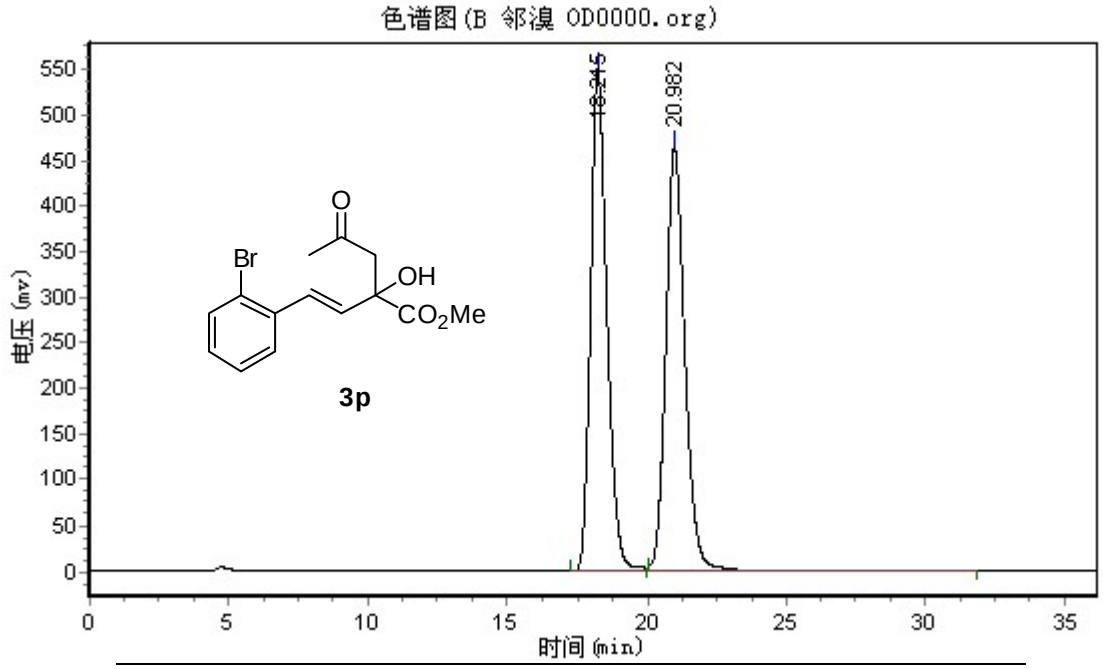

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 19.623 | 65707.422 | 2944951.750 | 94.8067 |
| 2 | 32.757 | 2048.333 | 161317.906 | 5.1933 |



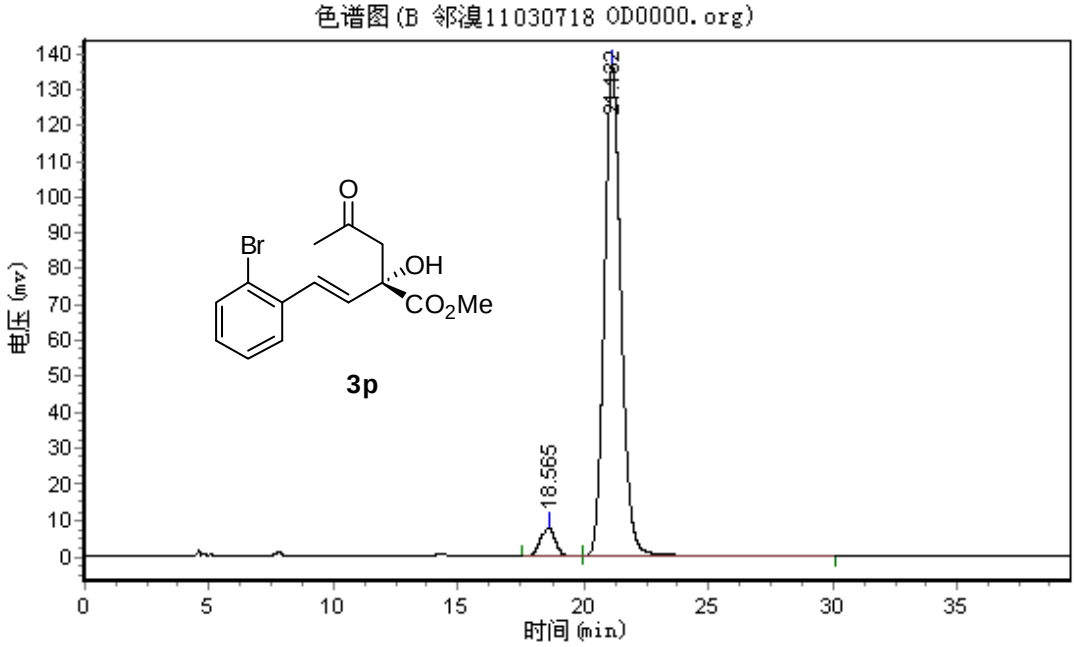

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 11.707 | 639752.313 | 10537213.000 | 50.3373 |
| 2 | 16.373 | 478400.438 | 10395985.000 | 49.6627 |



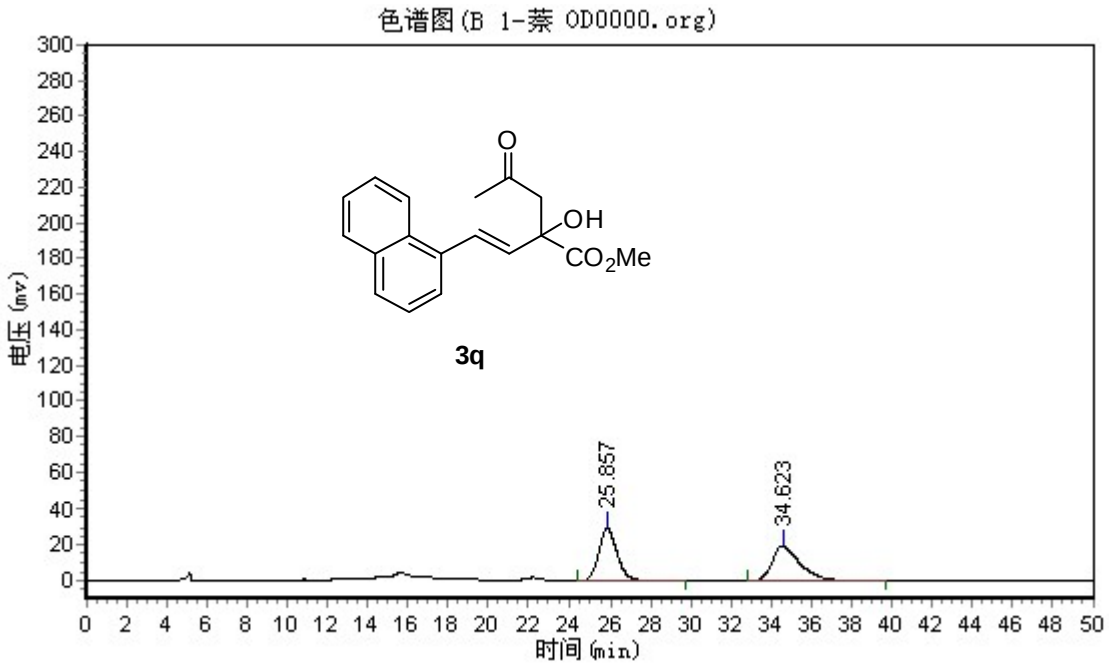

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 11.873 | 18658.529 | 294596.094 | 4.6900 |
| 2 | 16.415 | 285069.531 | 5986783.000 | 95.3100 |



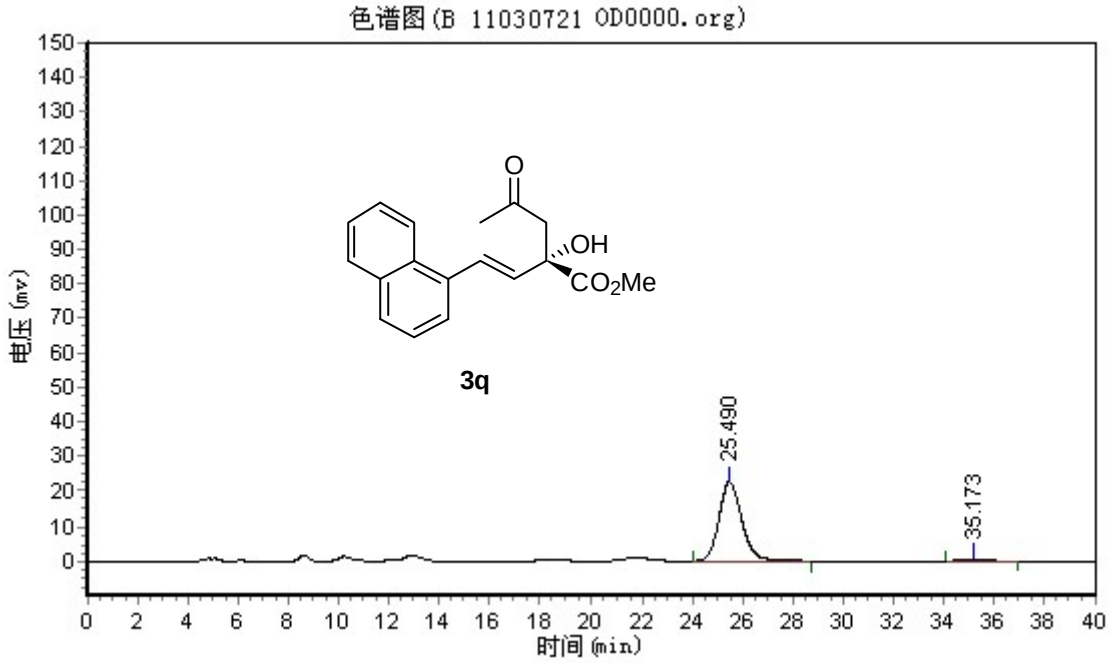

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 18.215 | 551094.688 | 22500072.000 | 50.2357 |
| 2 | 20.982 | 464572.563 | 22288968.000 | 49.7643 |



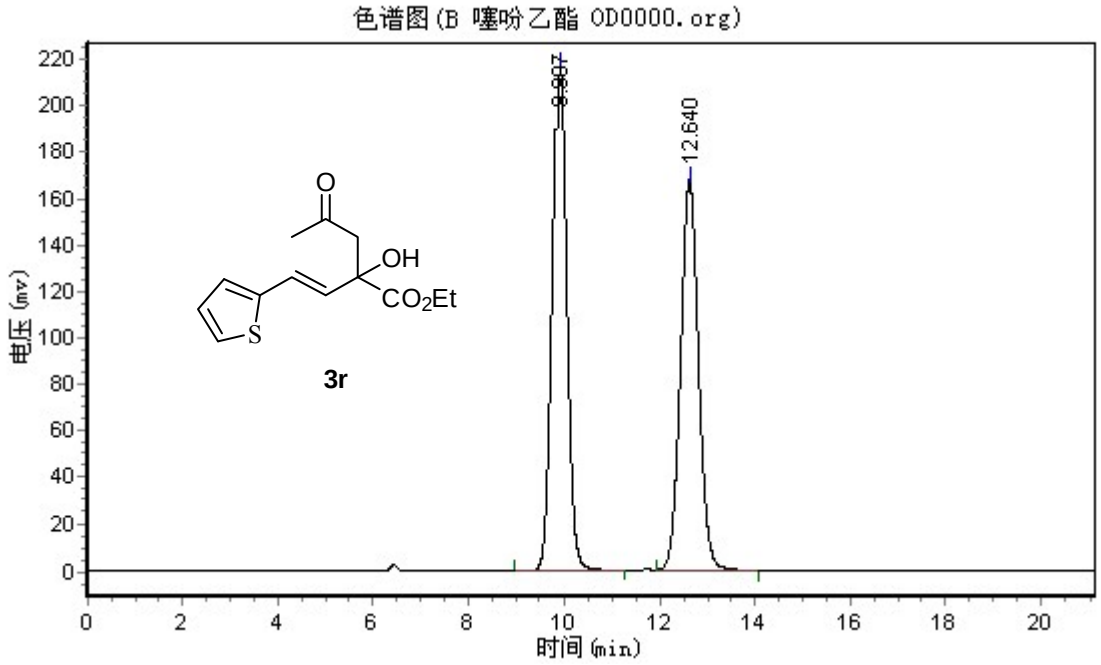

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 18.565 | 8005.803 | 319530.656 | 4.7202 |
| 2 | 21.132 | 136654.844 | 6449932.000 | 95.2798 |



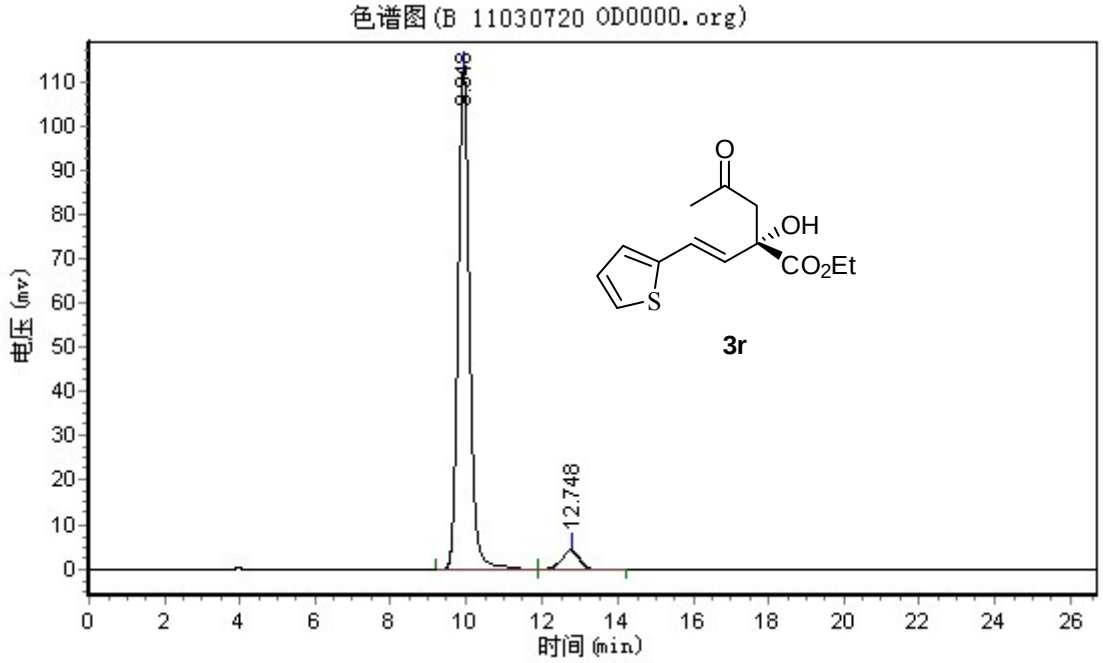

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 25.857 | 29084.516 | 1812218.000 | 49.4274 |
| 2 | 34.623 | 19340.063 | 1854206.250 | 50.5726 |



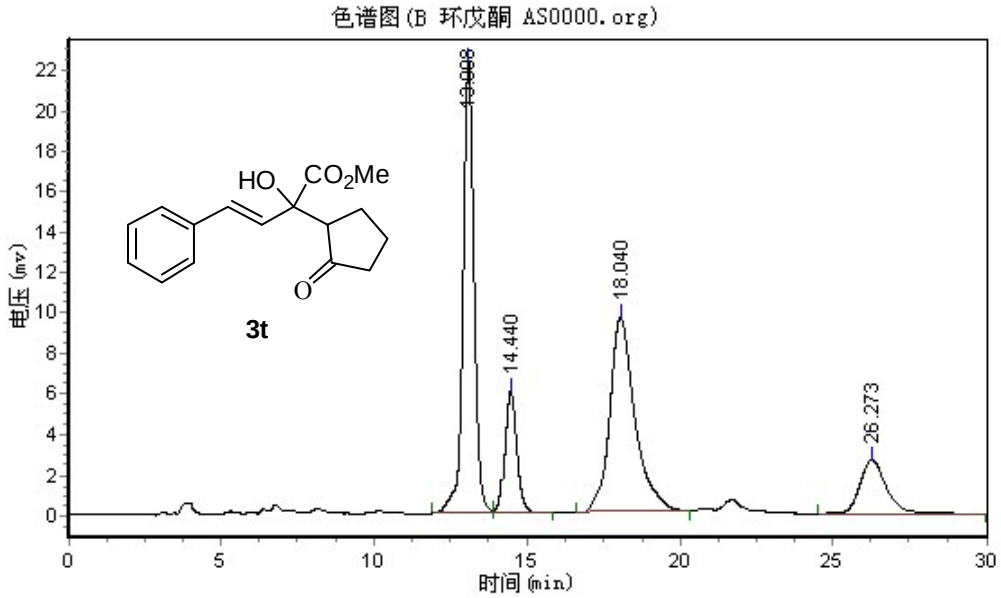

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 25.490 | 22673.736 | 1414229.250 | 98.1759 |
| 2 | 35.173 | 322.400 | 26276.600 | 1.8241 |



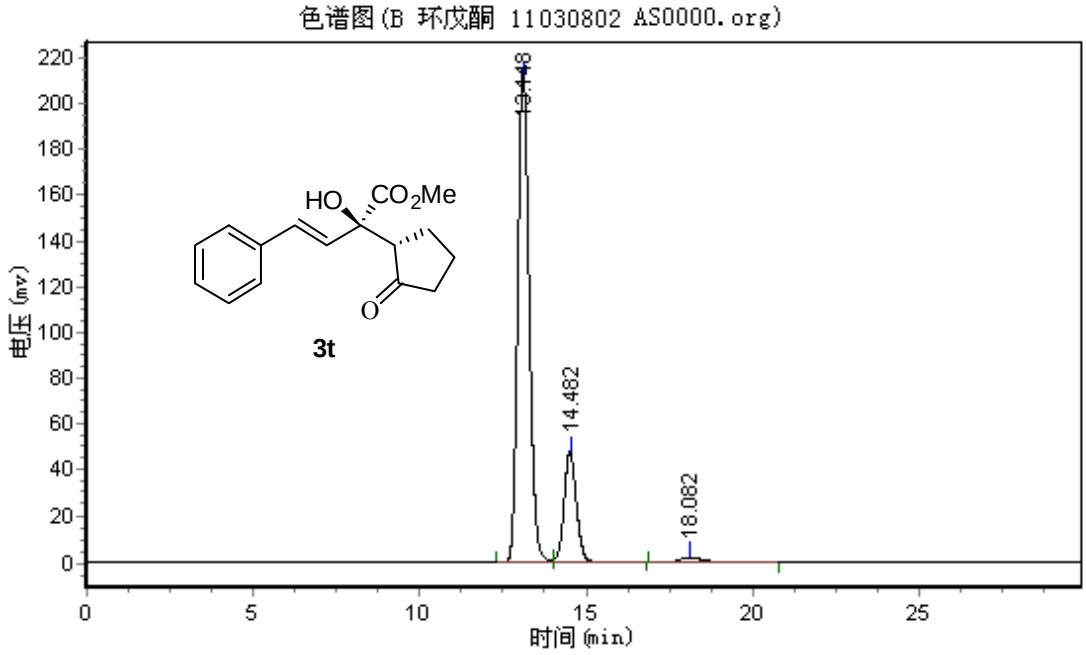

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.907 | 215933.750 | 4306556.500 | 49.2018 |
| 2 | 12.640 | 167562.078 | 4446286.500 | 50.7982 |



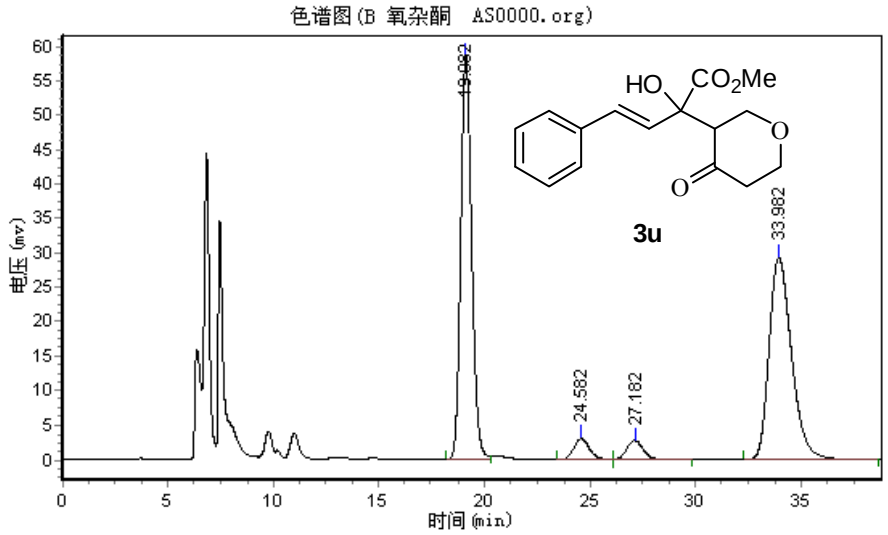

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 9.948 | 113197.180 | 2392284.250 | 94.7408 |
| 2 | 12.748 | 4345.539 | 132797.953 | 5.2592 |



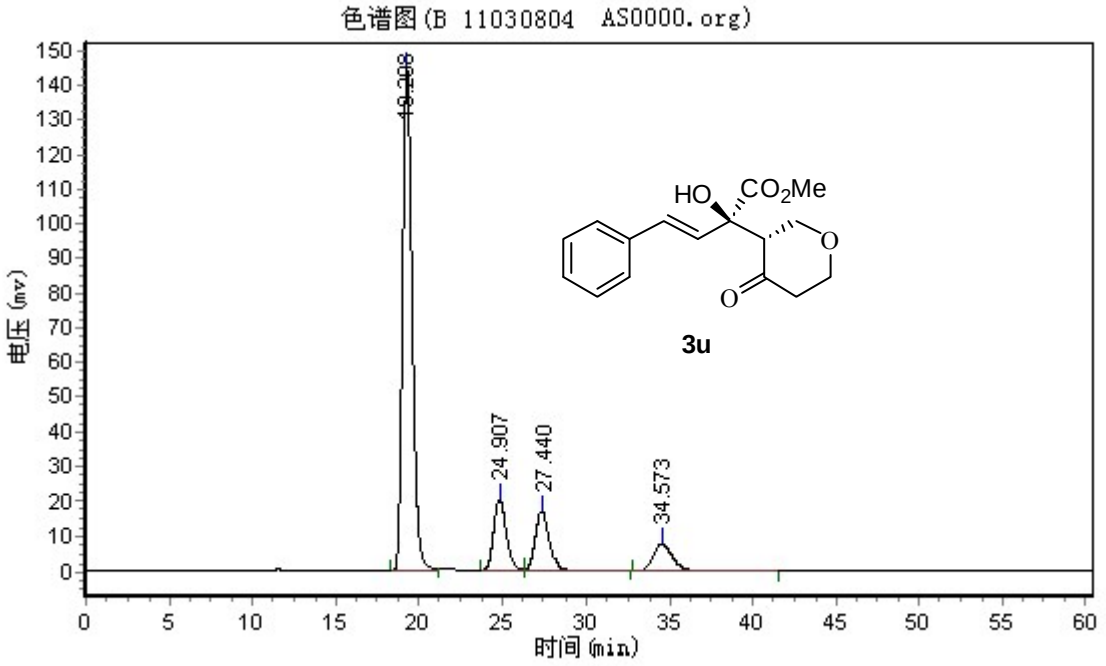

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 13.098 | 22263.852 | 560524.250 | 38.8952 |
| 2 | 14.440 | 5976.448 | 157078.781 | 10.8998 |
| 3 | 18.040 | 9645.834 | 566992.250 | 19.3441 |
| 4 | 26.273 | 2587.251 | 156517.094 | 10.8609 |




| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 13.148 | 214358.844 | 5125394.500 | 78.8220 |
| 2 | 14.482 | 47834.219 | 1251060.500 | 19.2397 |
| 3 | 18.082 | 2228.906 | 126038.602 | 1.9383 |

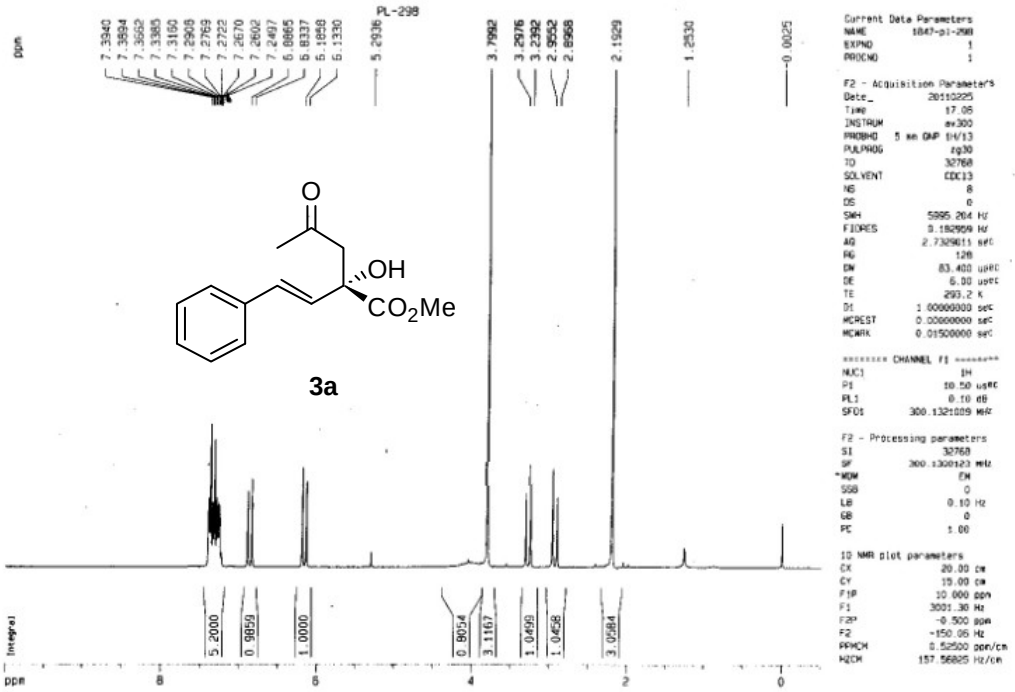


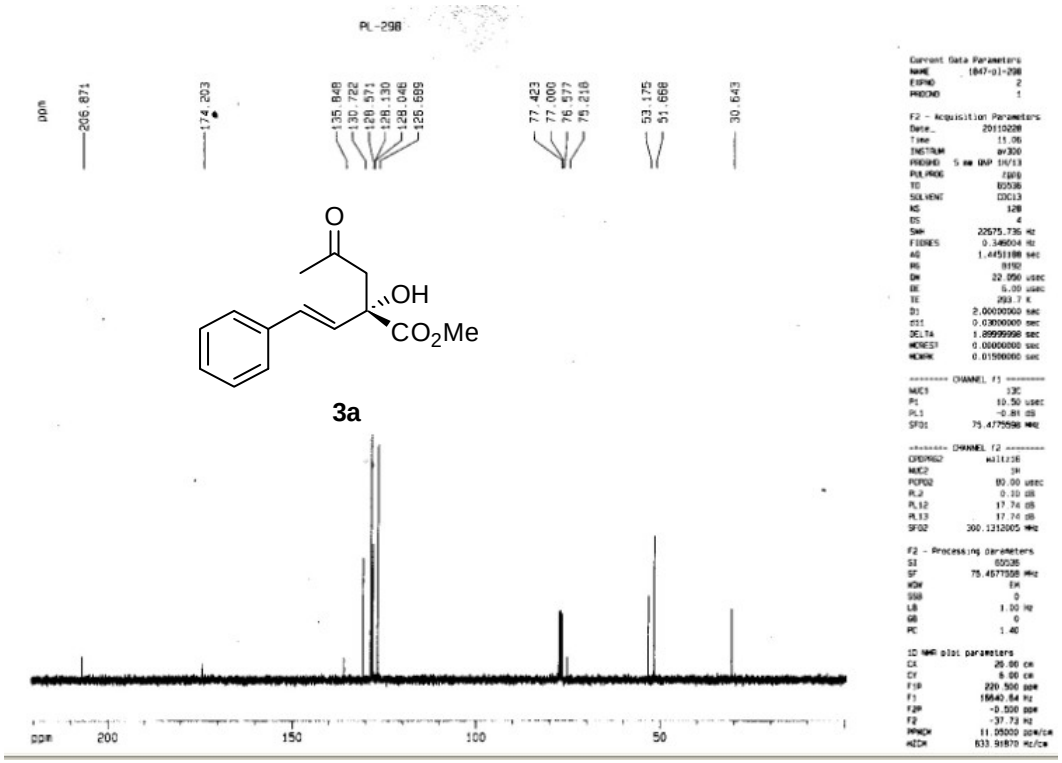

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 19.082 | 58320.047 | 2113104.250 | 46.0039 |
| 2 | 24.582 | 3009.031 | 156807.391 | 3.4138 |
| 3 | 27.182 | 2810.150 | 154150.906 | 3.3560 |
| 4 | 33.982 | 29328.684 | 2169251.250 | 47.2263 |

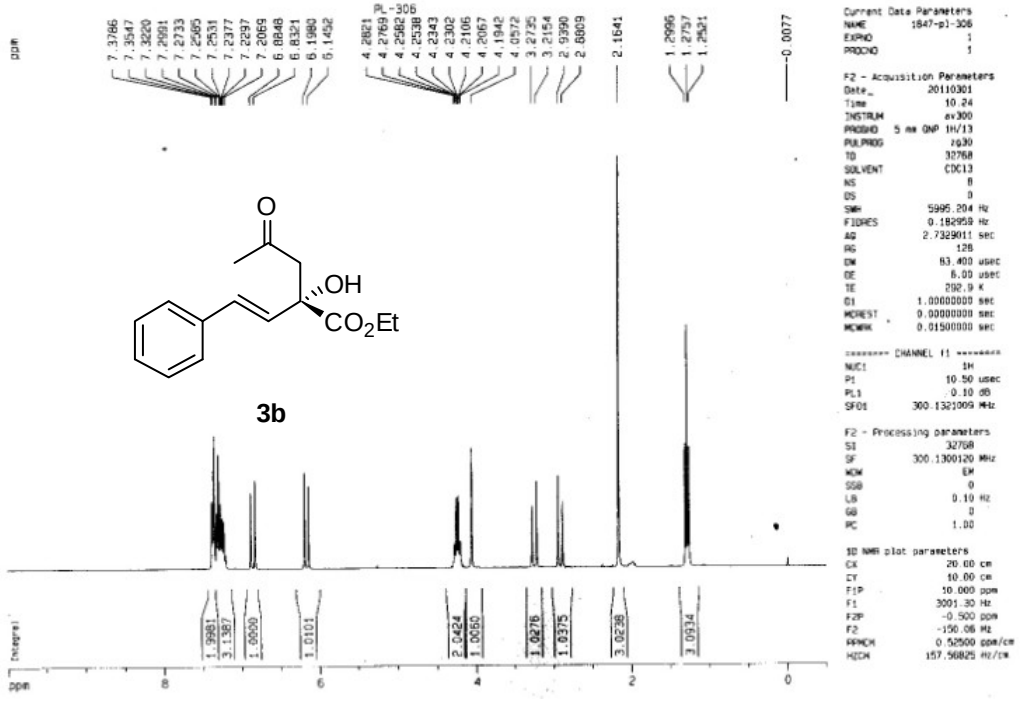


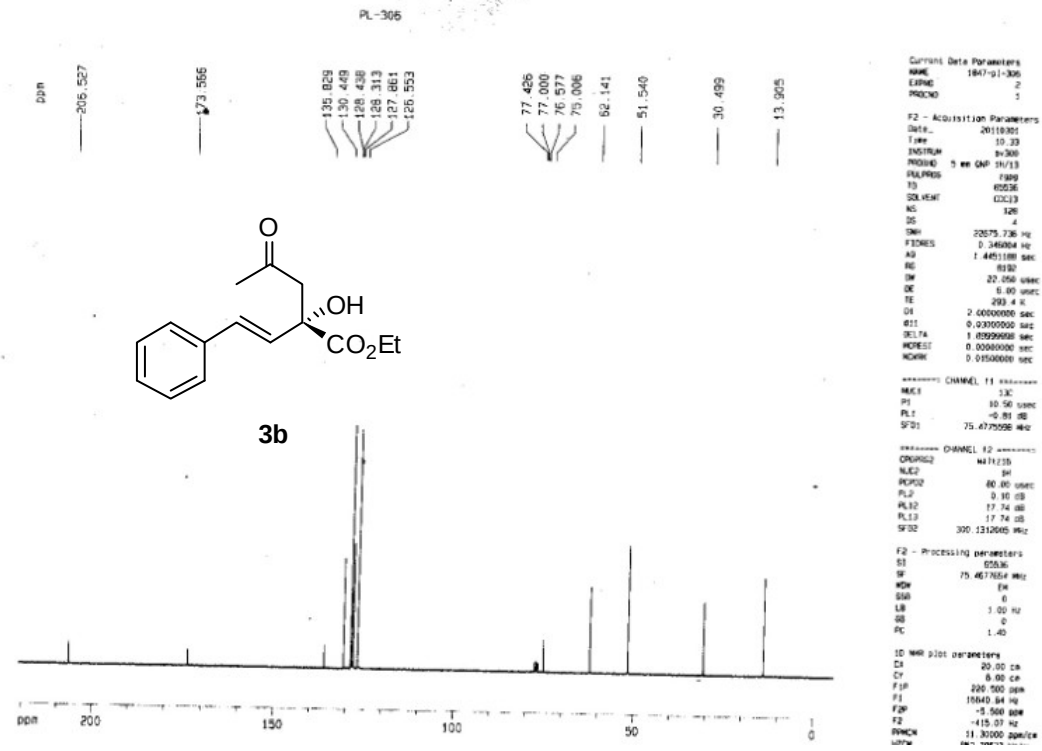

| Peak | RT (min) | Height (mV*sec) | Area (mV) | Area (%) |
|---|---|---|---|---|
| 1 | 19.298 | 144767.359 | 5845152.000 | 68.3197 |
| 2 | 24.907 | 20498.162 | 1088958.125 | 12.7280 |
| 3 | 27.440 | 17125.297 | 1006973.500 | 11.7698 |
| 4 | 34.573 | 7757.968 | 614498.125 | 7.1824 |

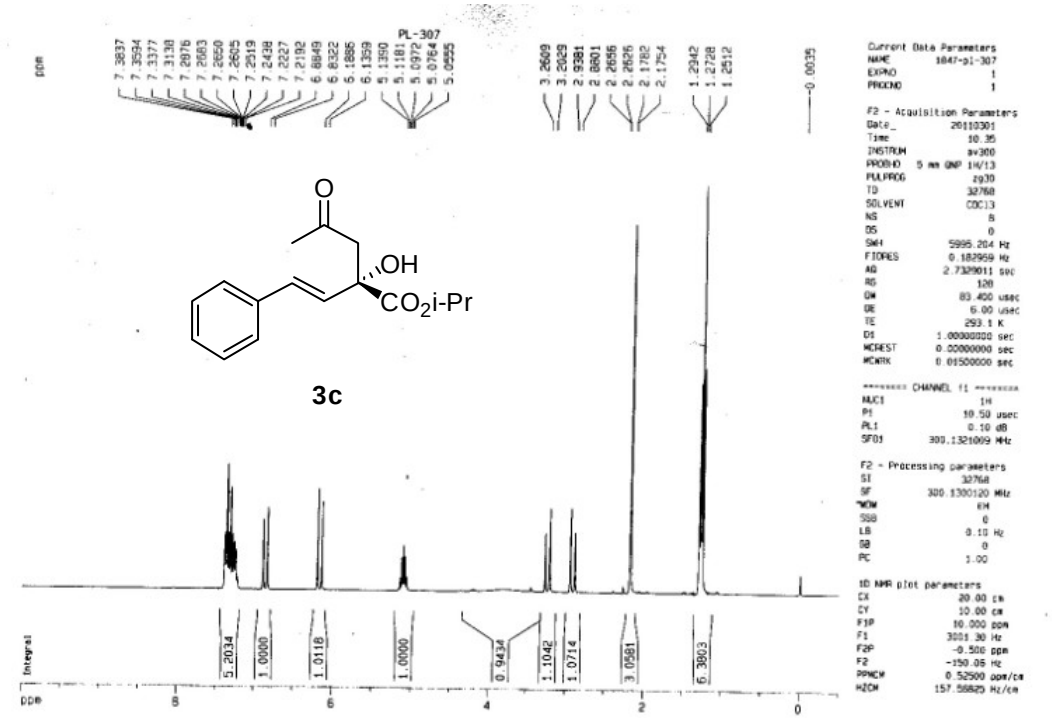
# E. NMR Analysis of the Products.



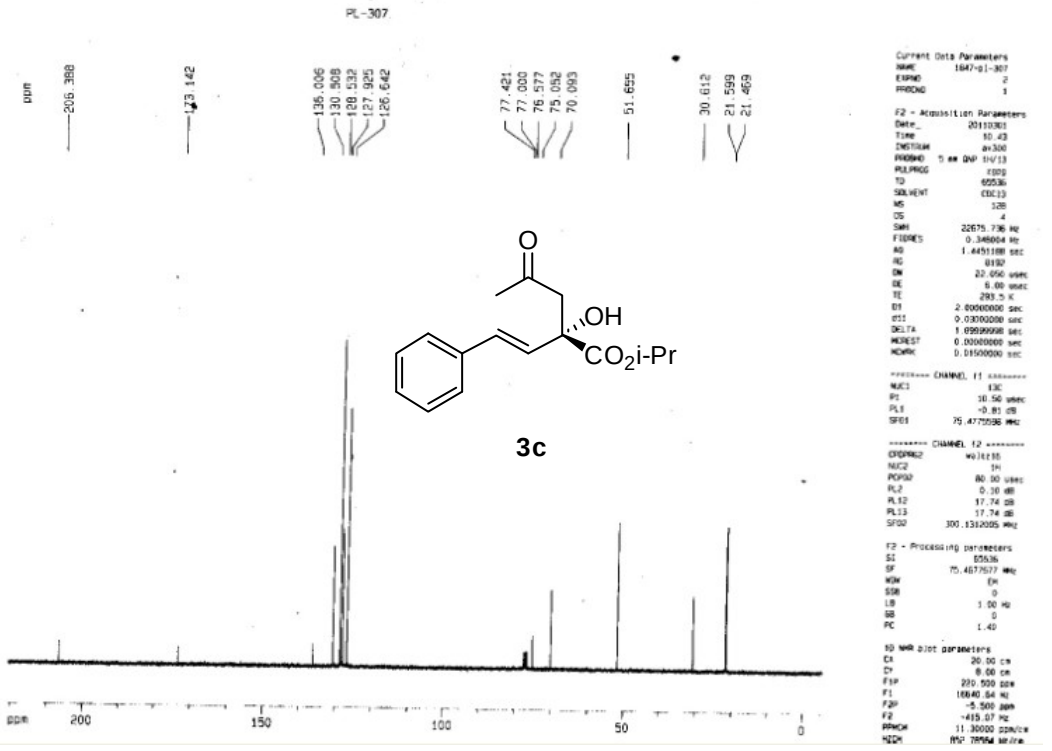




PL-306
OH
$CO_2Et$
3b

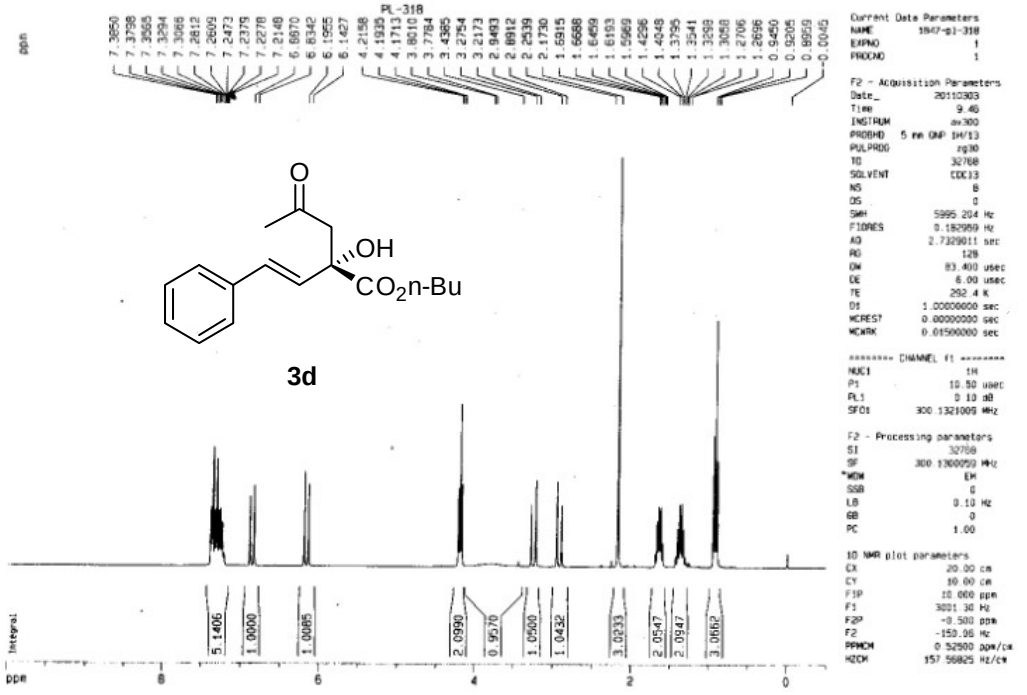

PL-306
OH
$CO_2Et$
3b

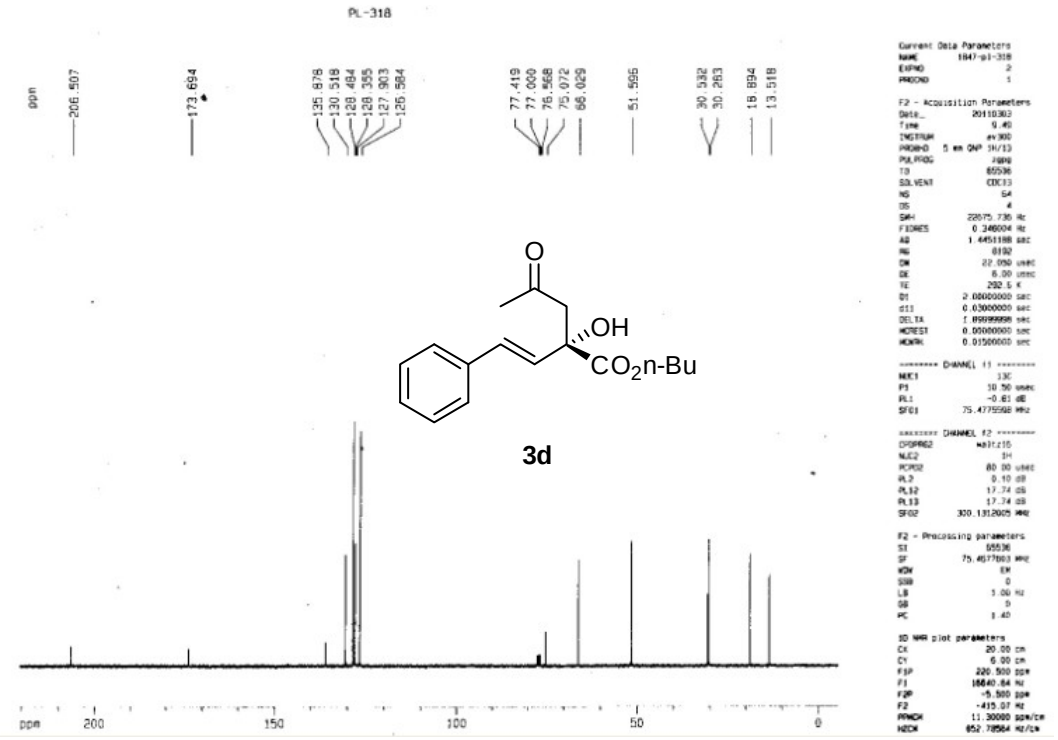


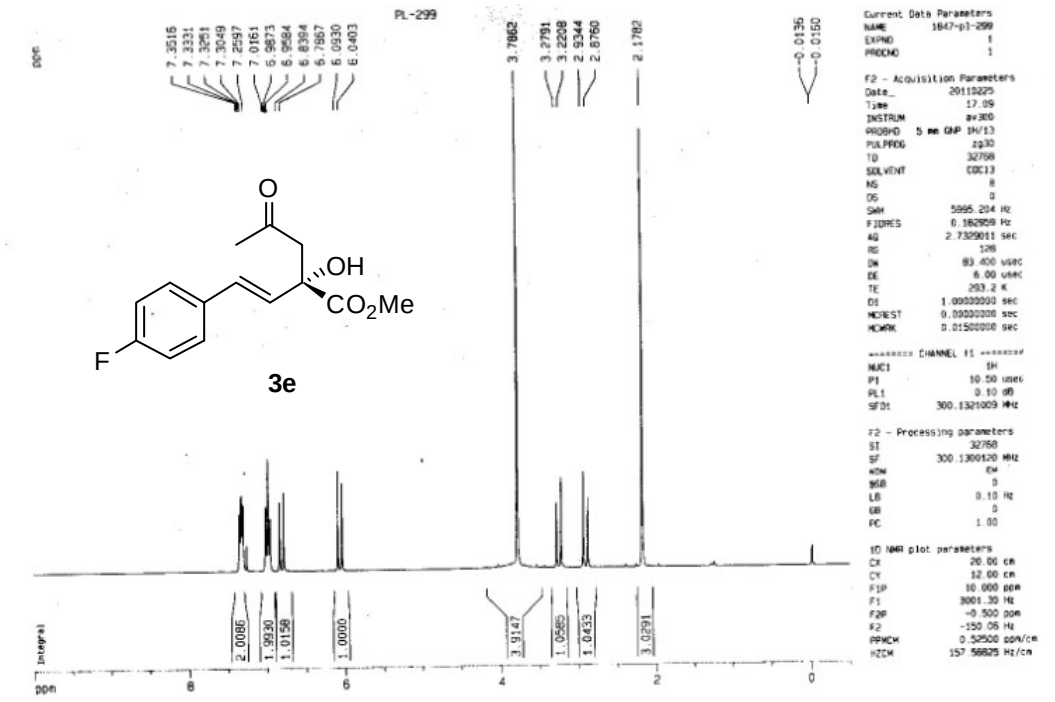

**3c**

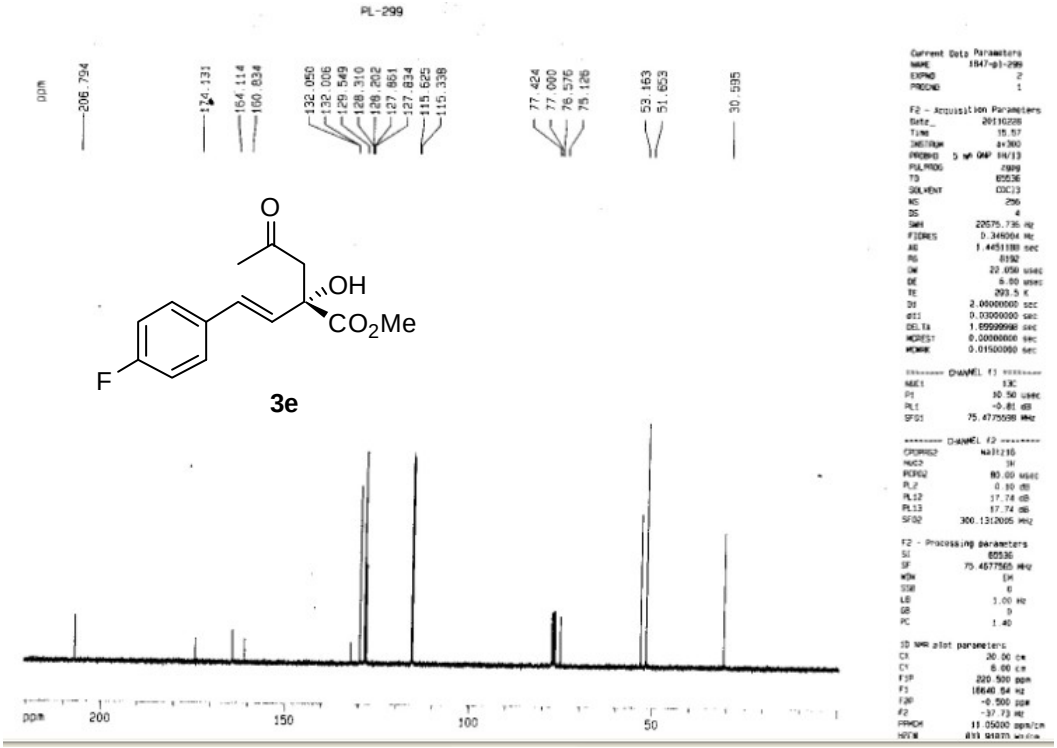


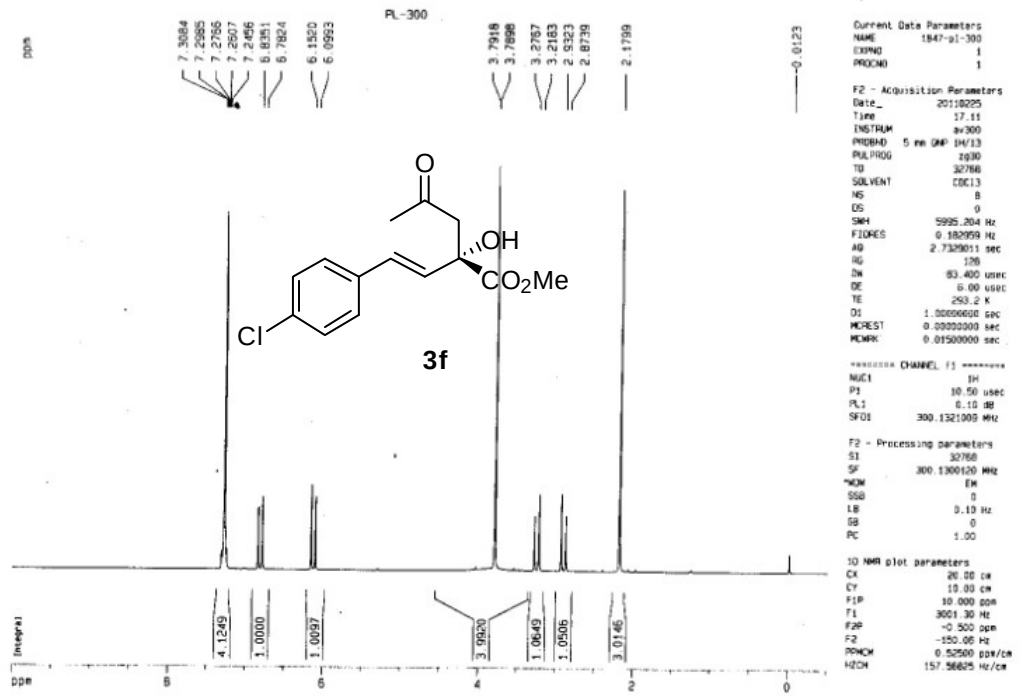

**3c**

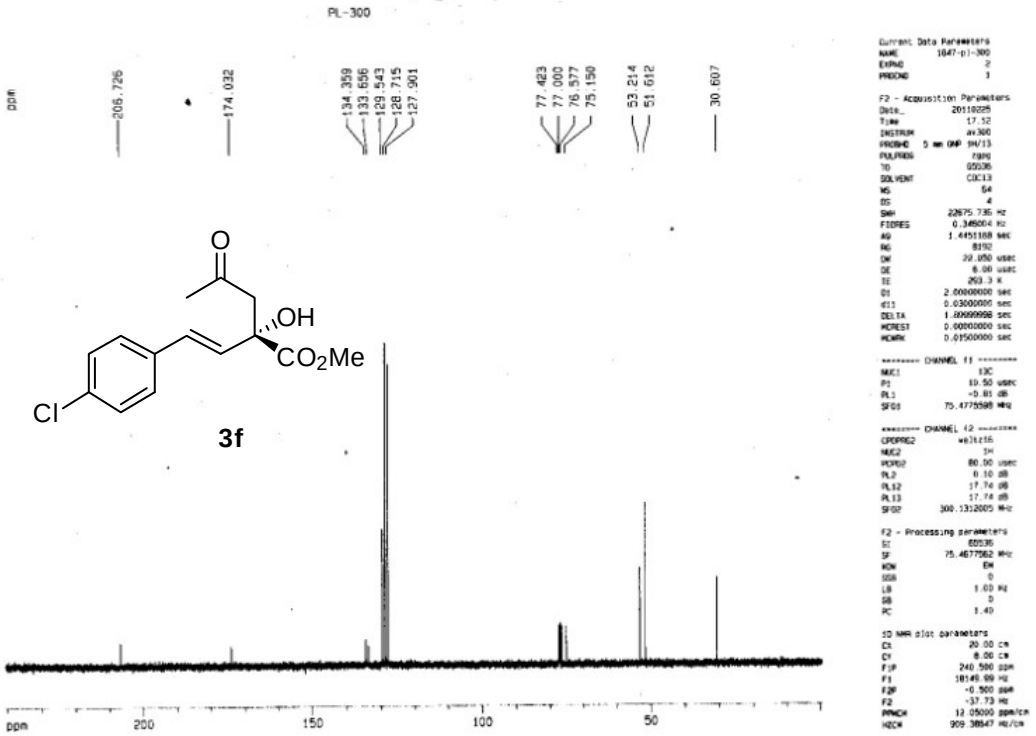


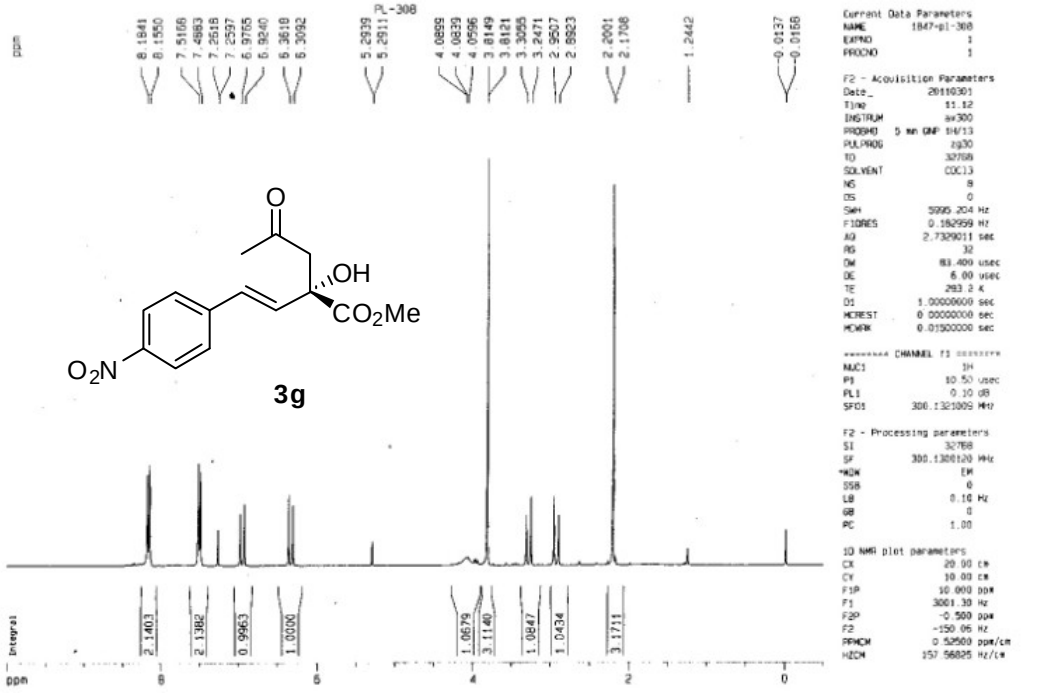



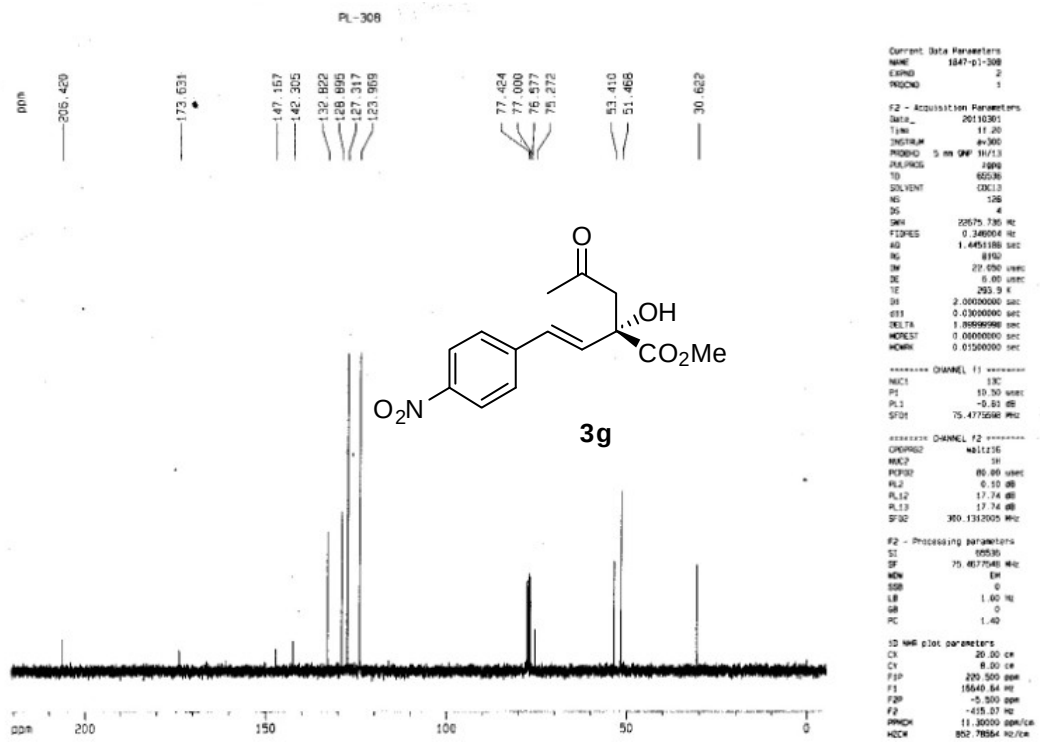


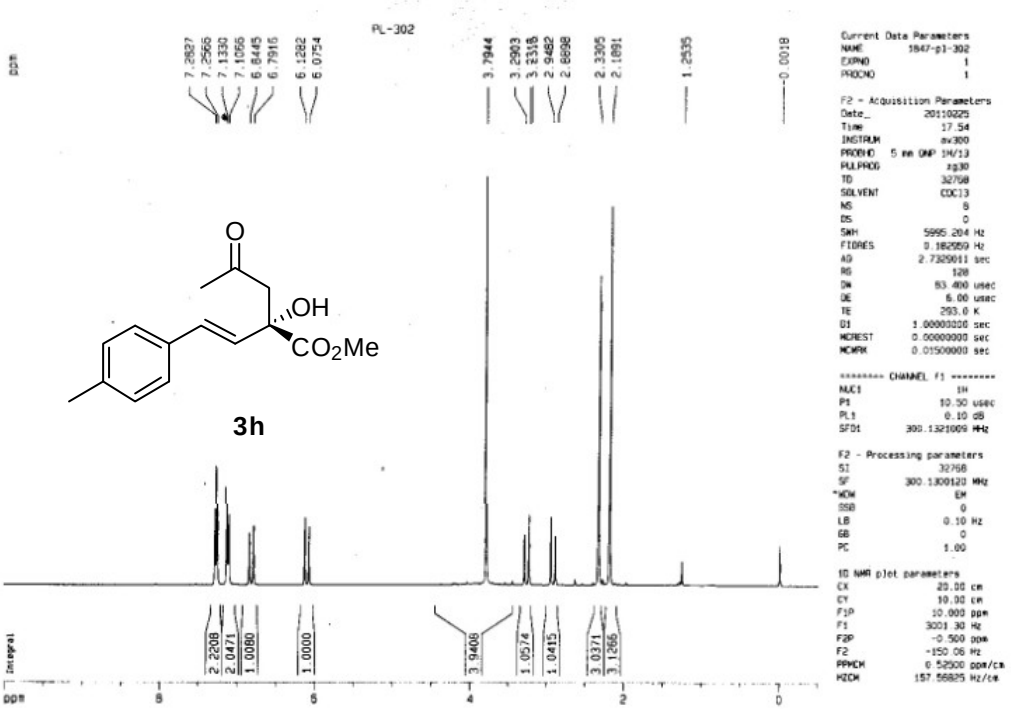



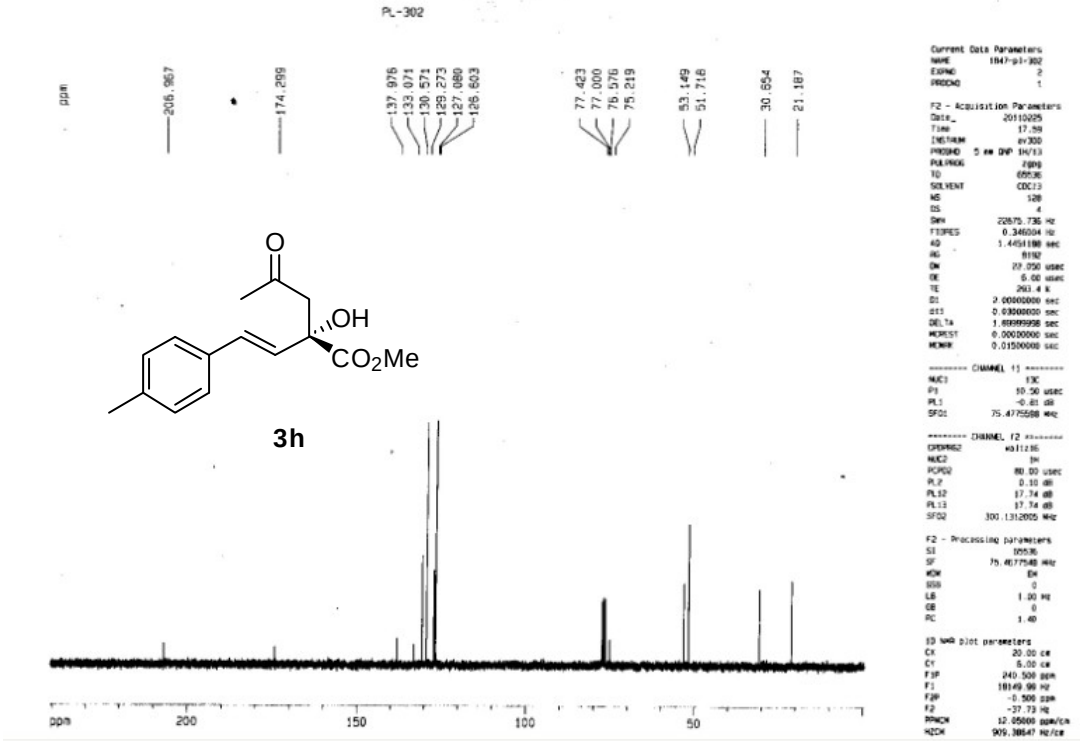


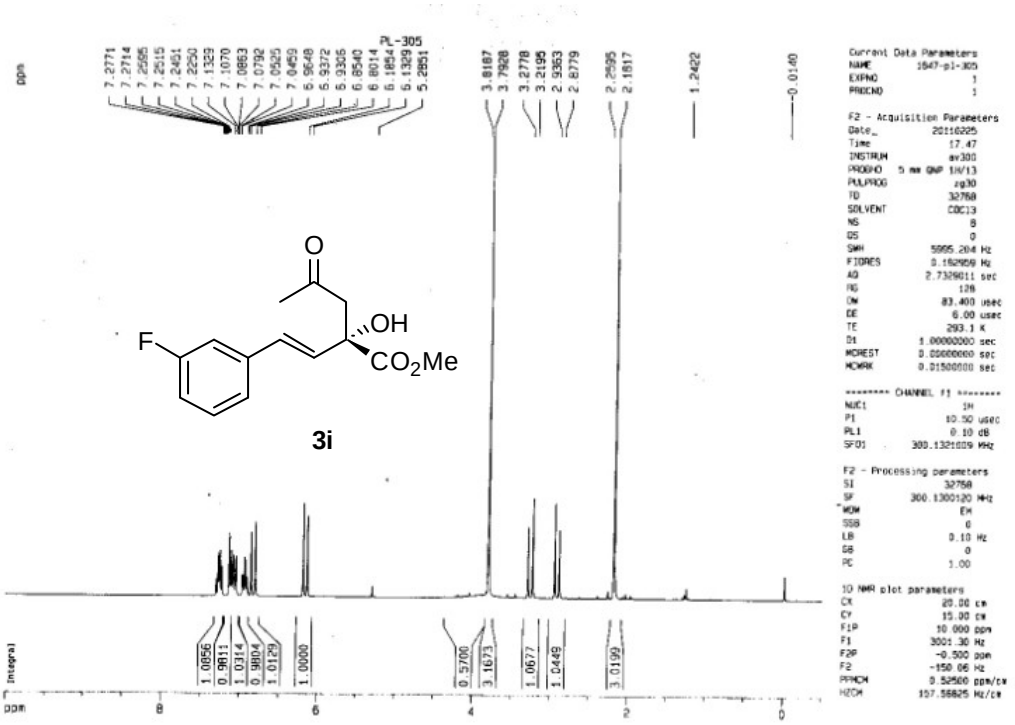



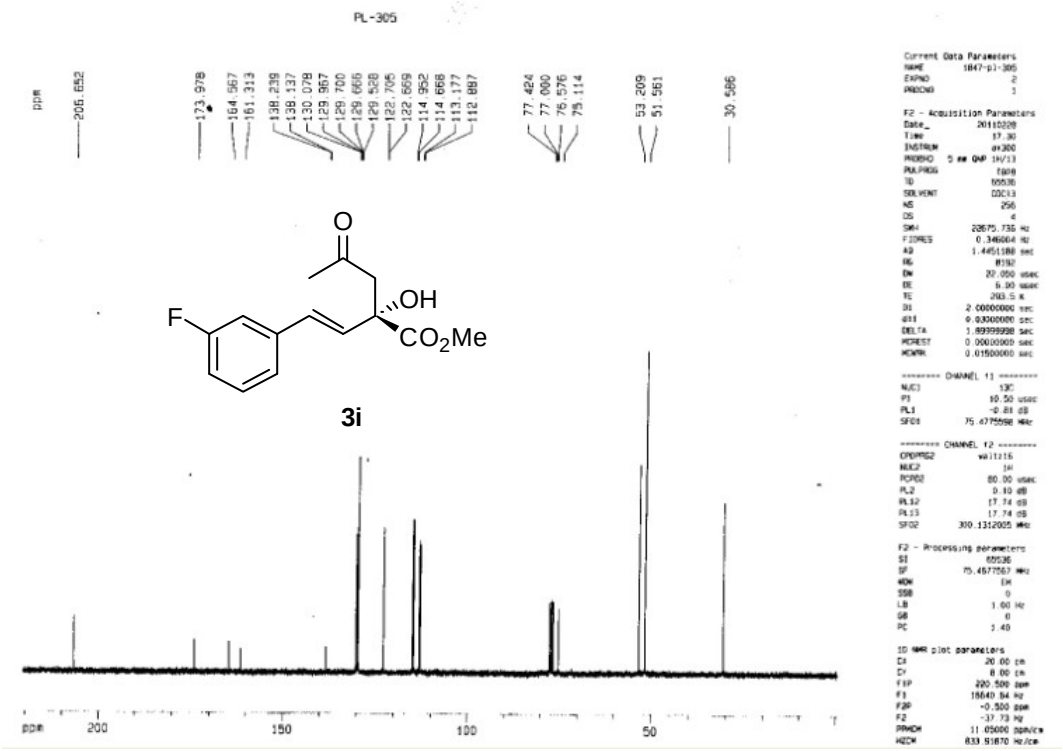


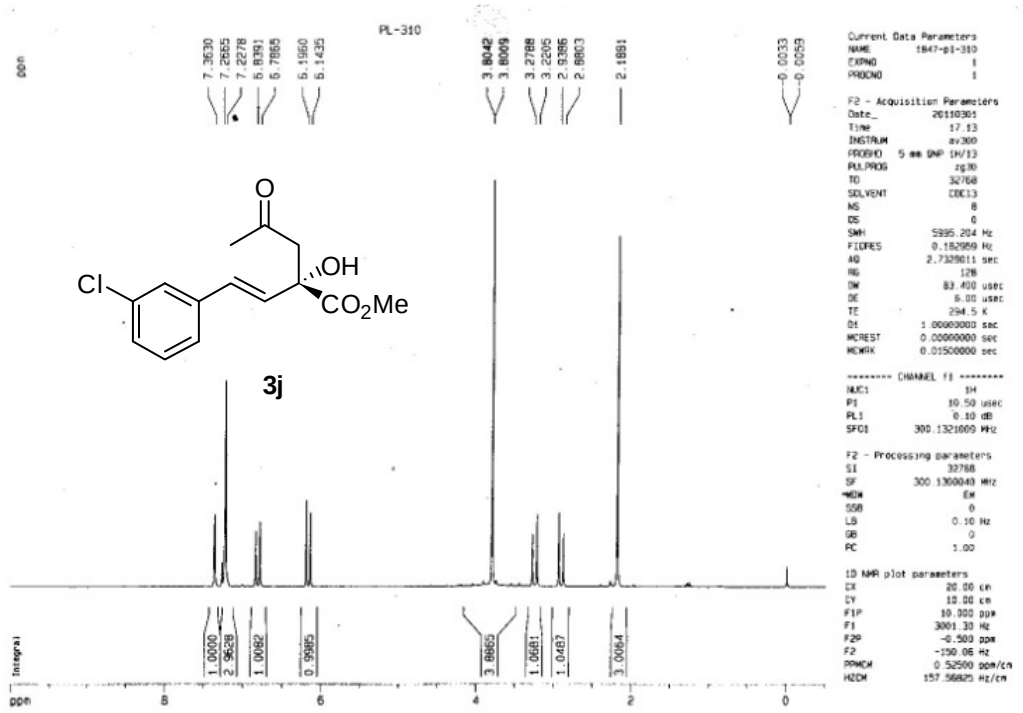



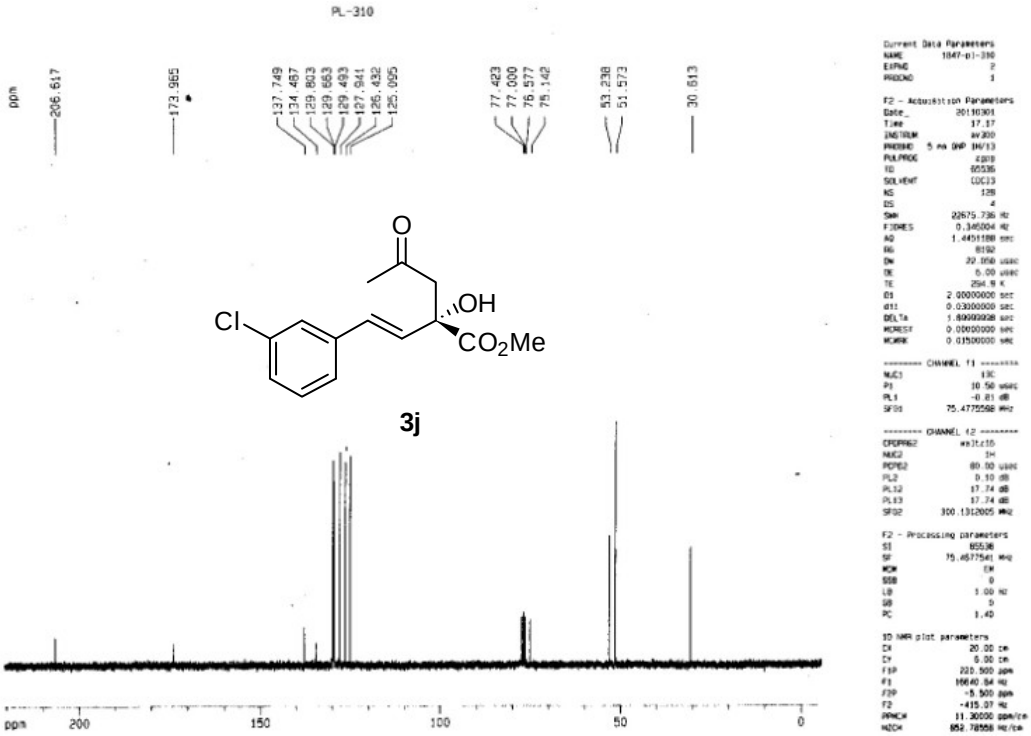


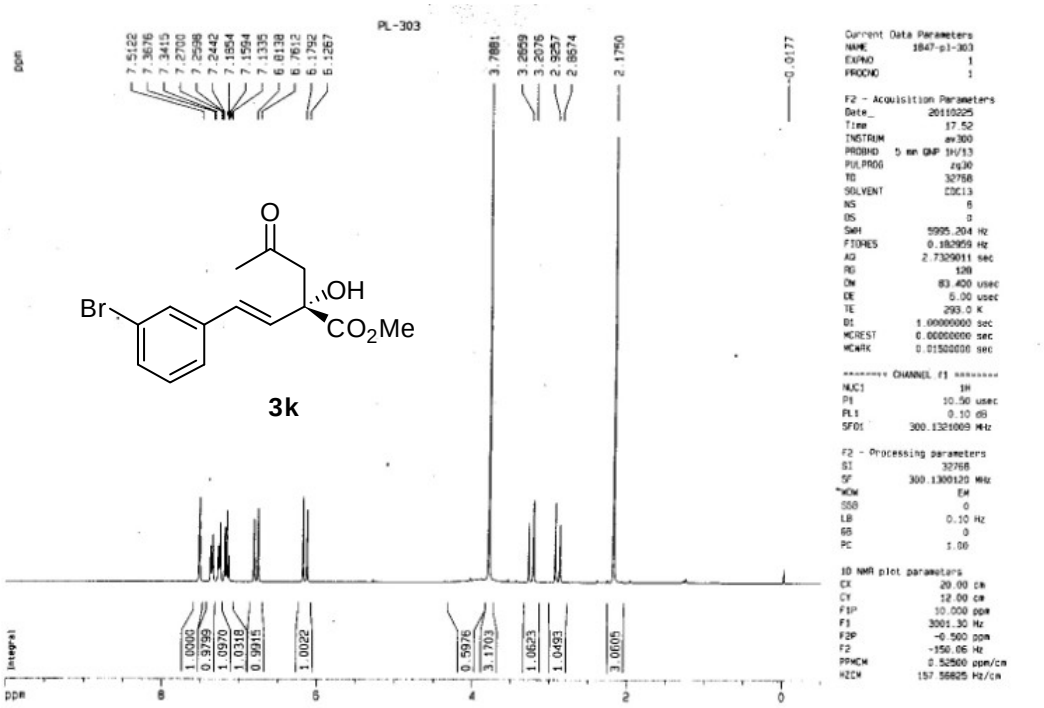



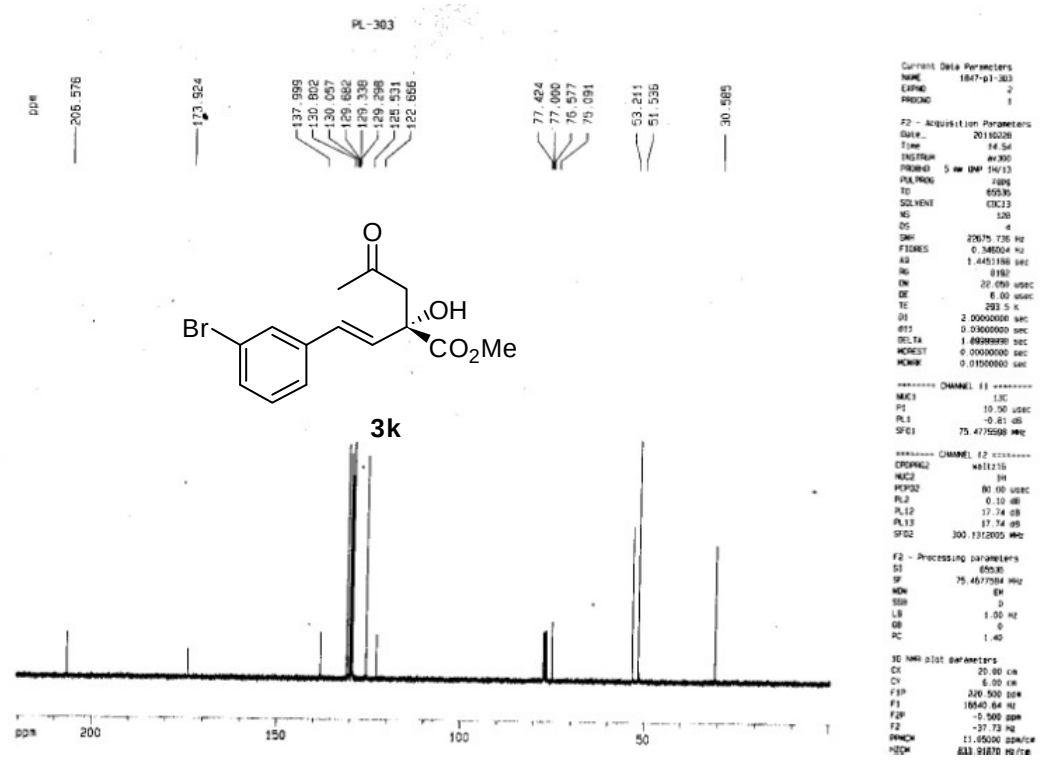


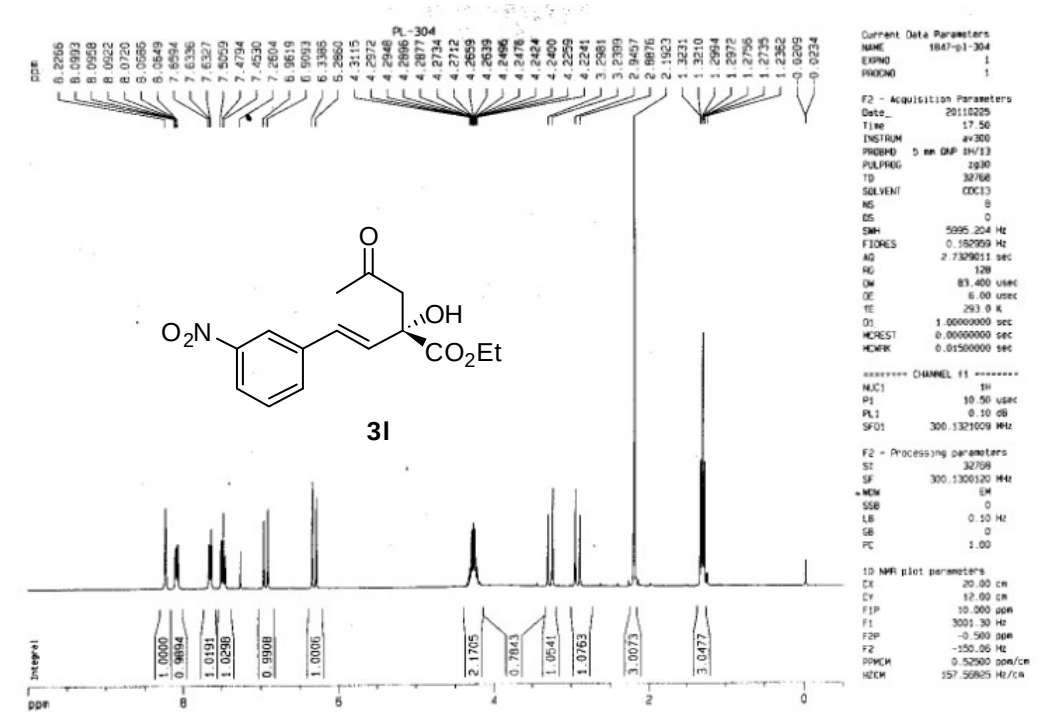



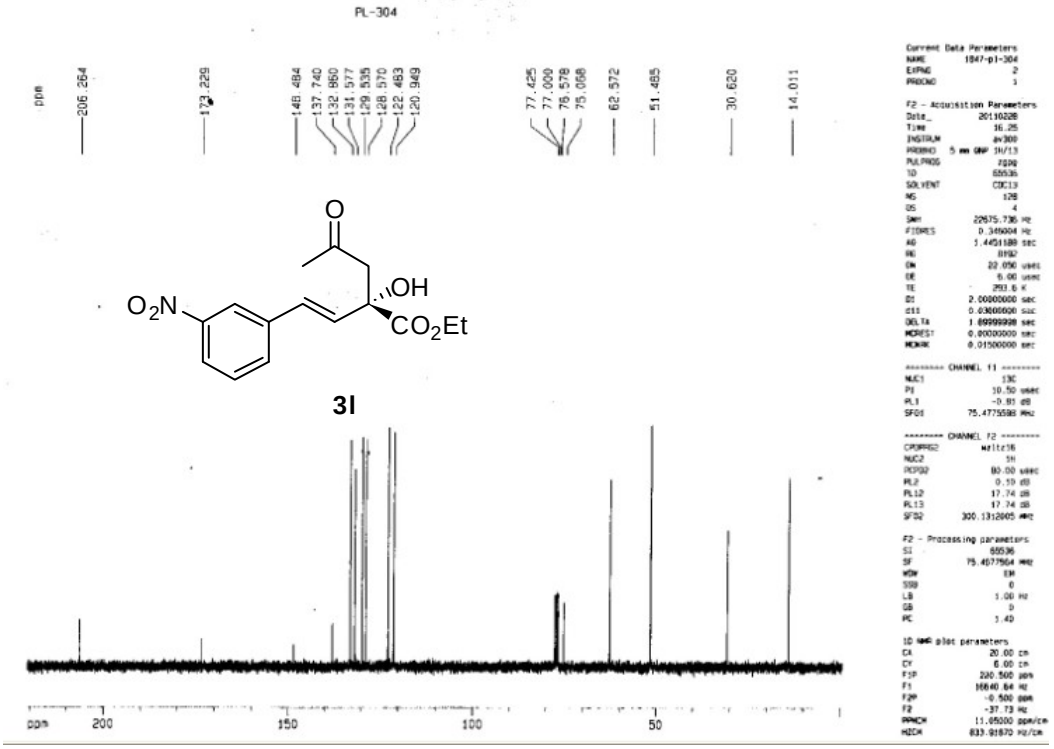


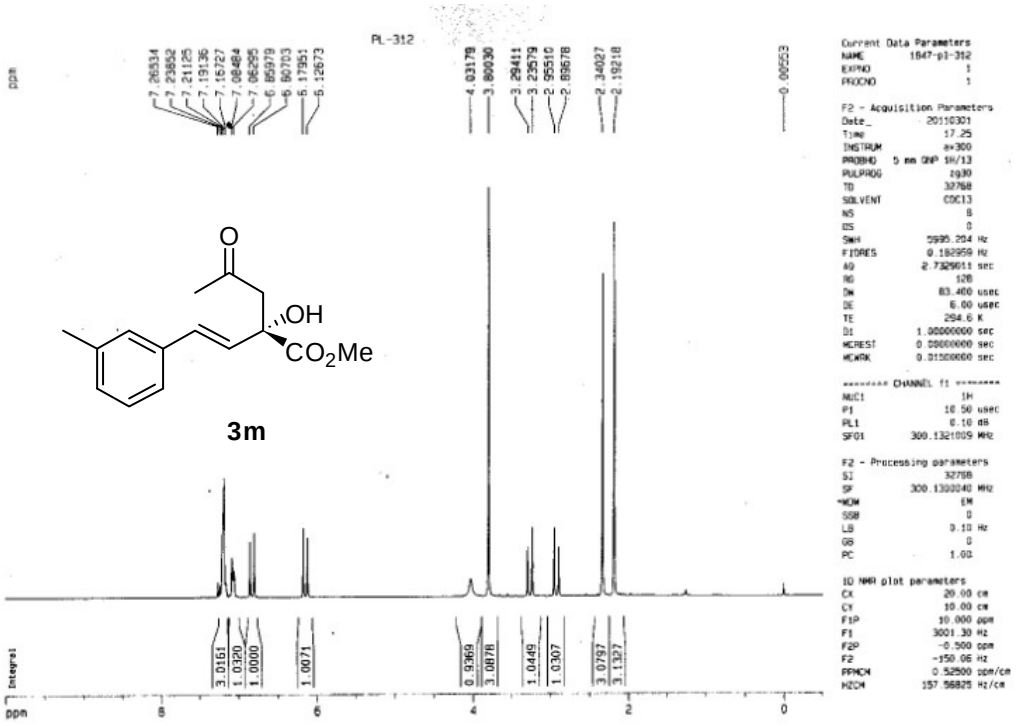





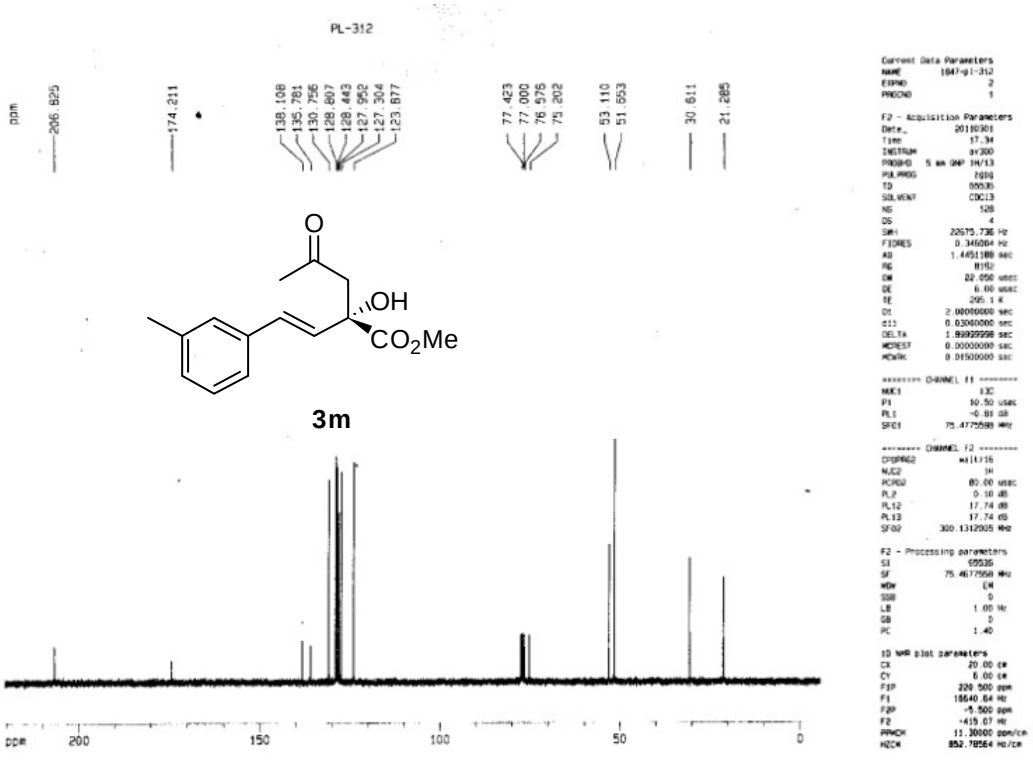





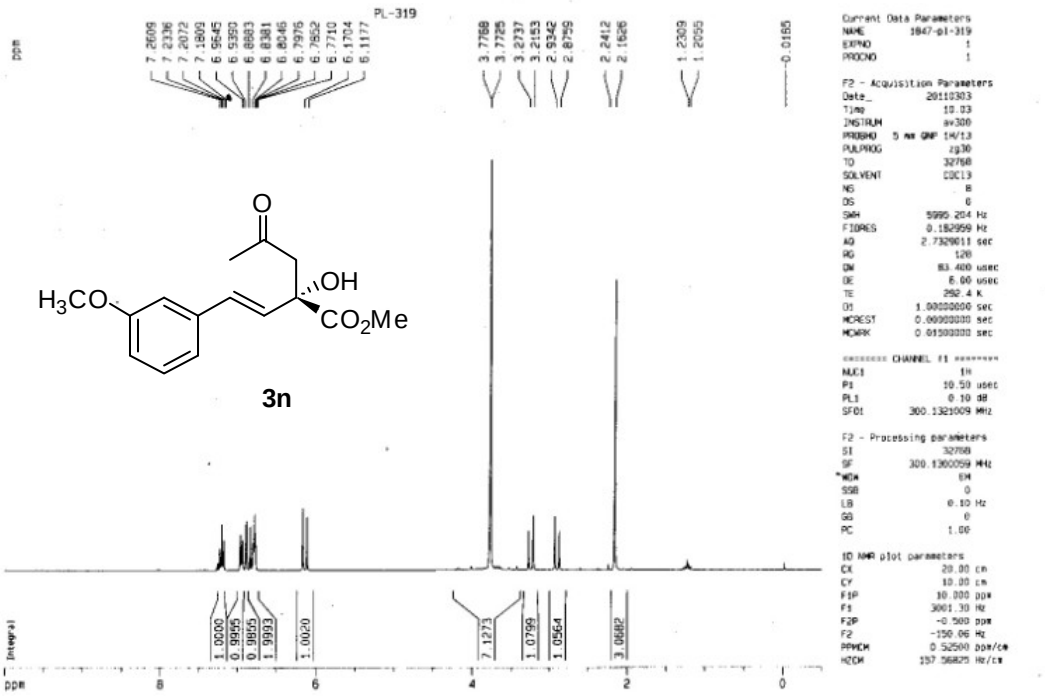



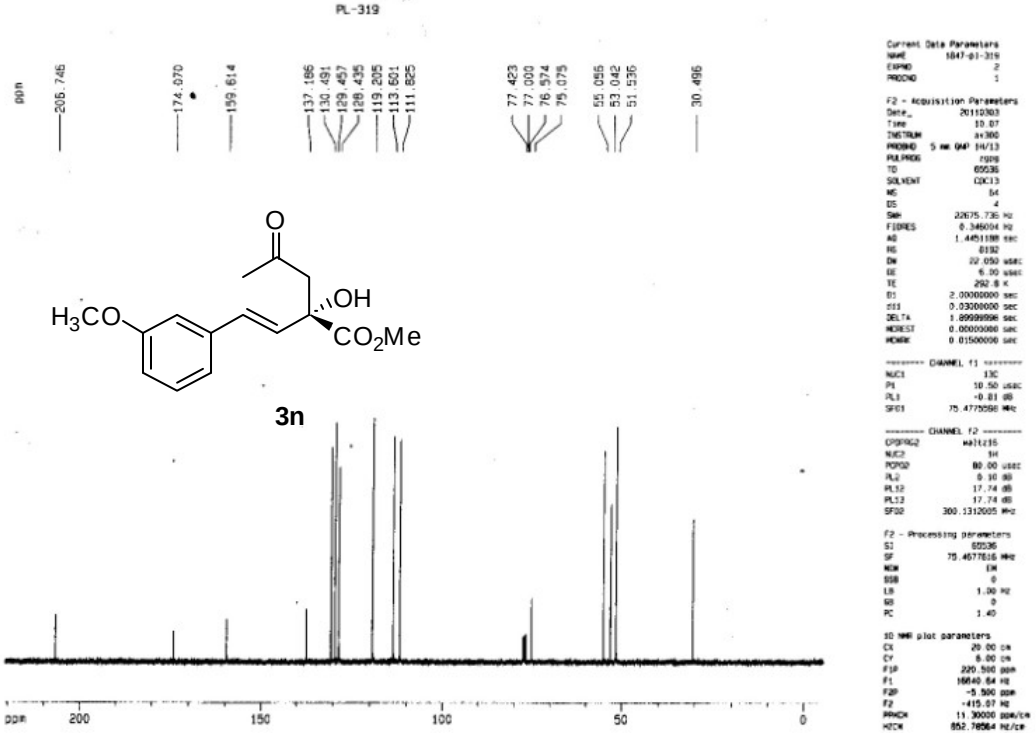


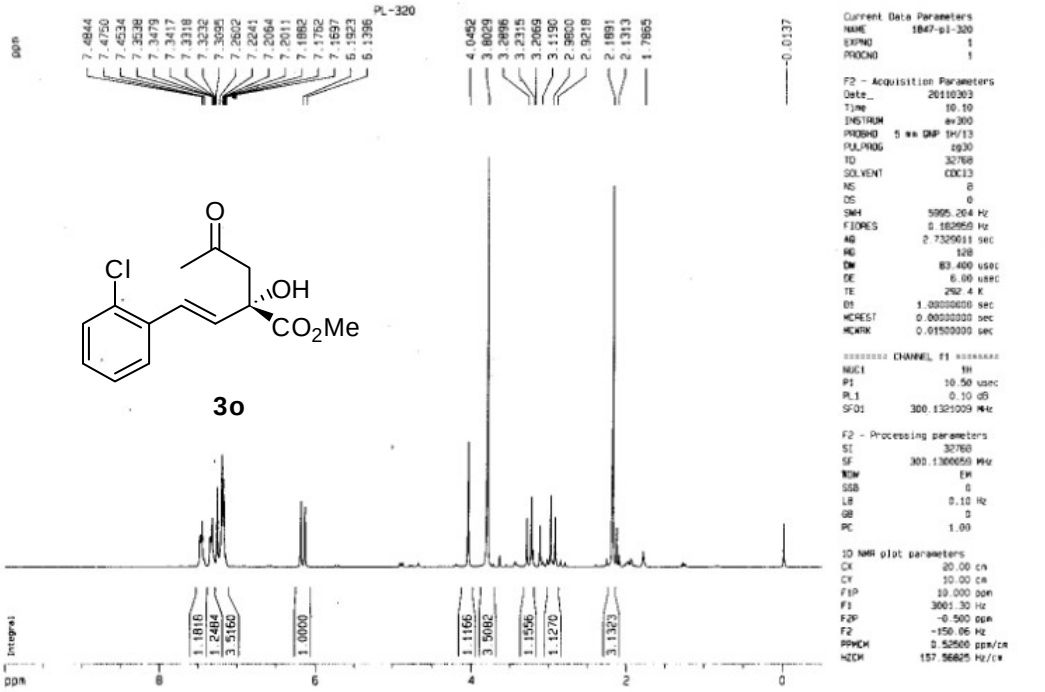

**3m**

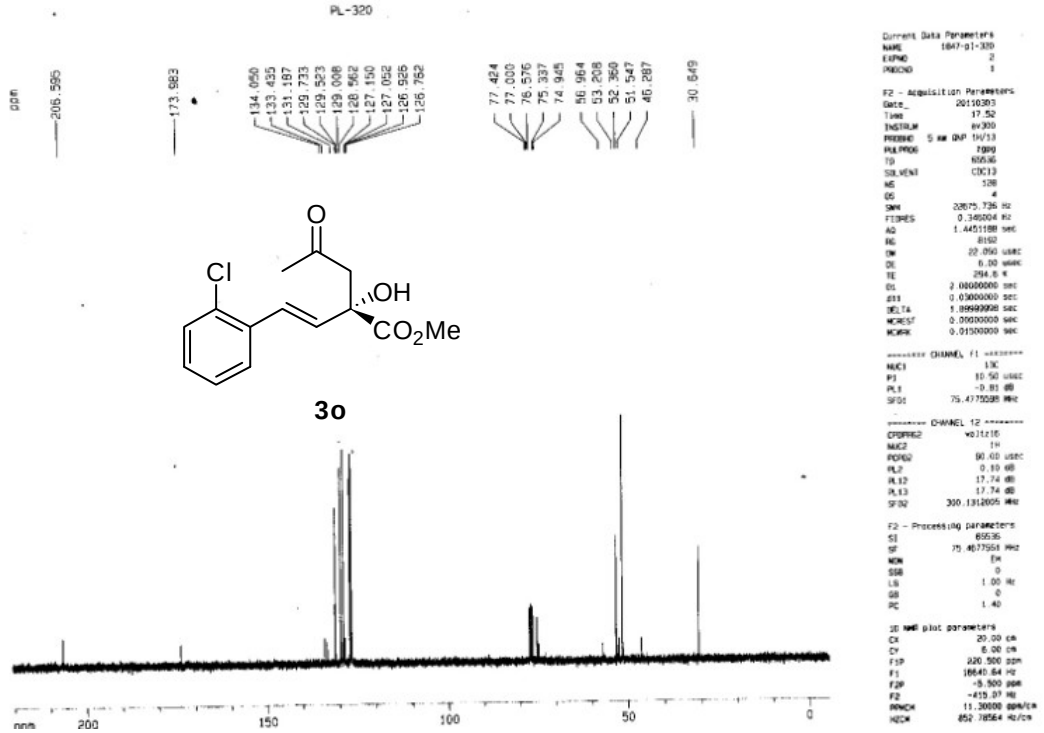


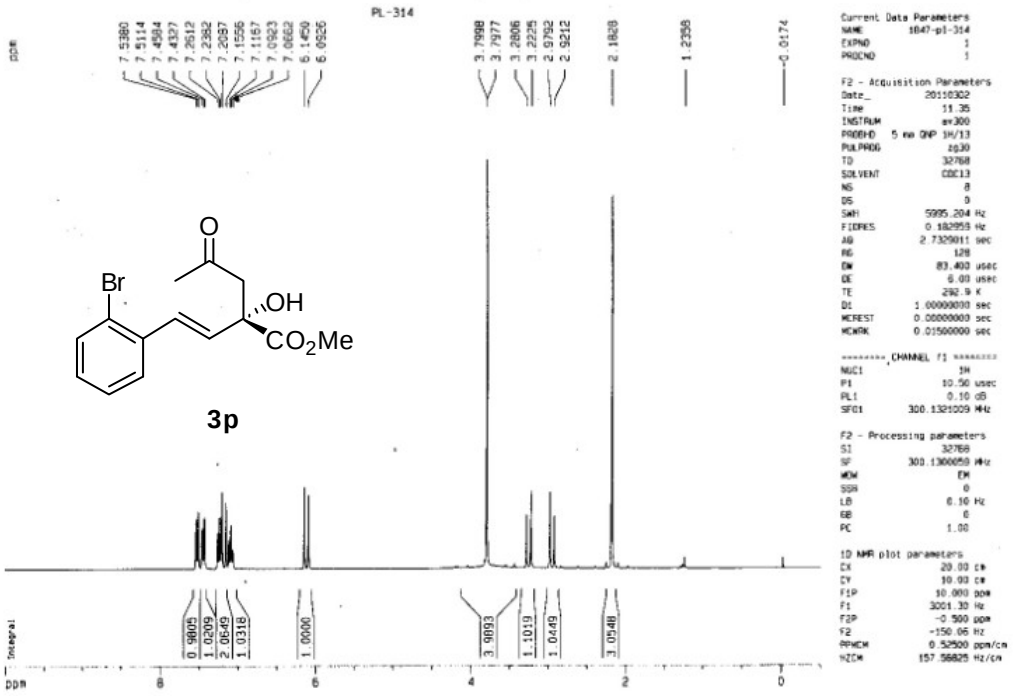

**3m**



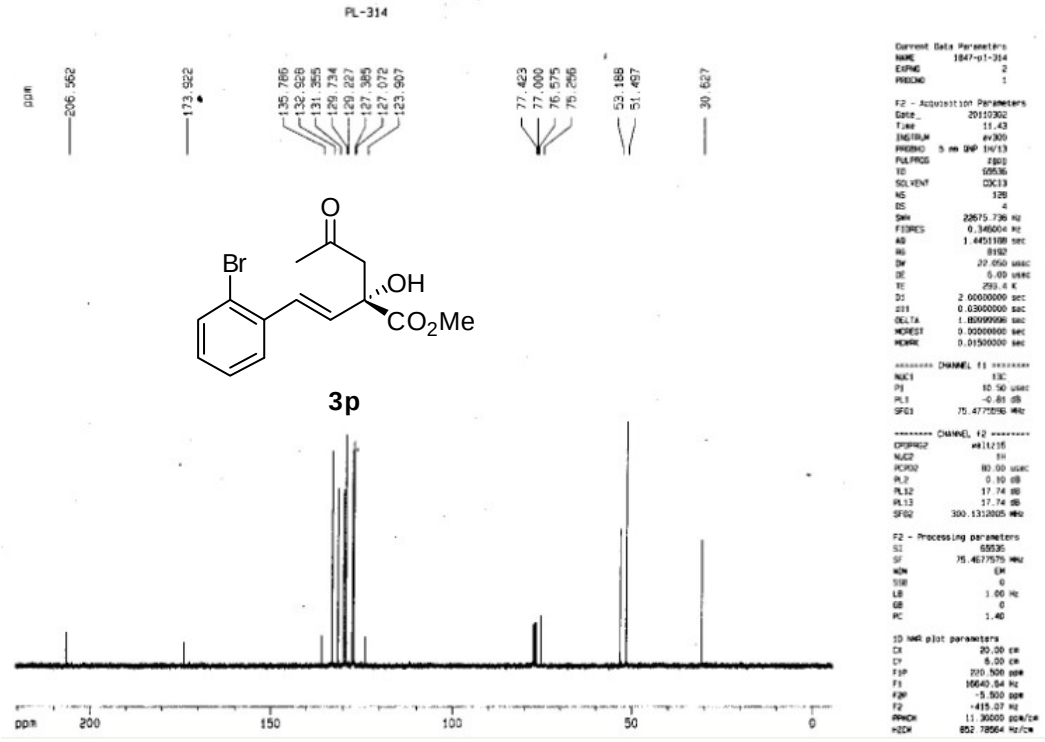





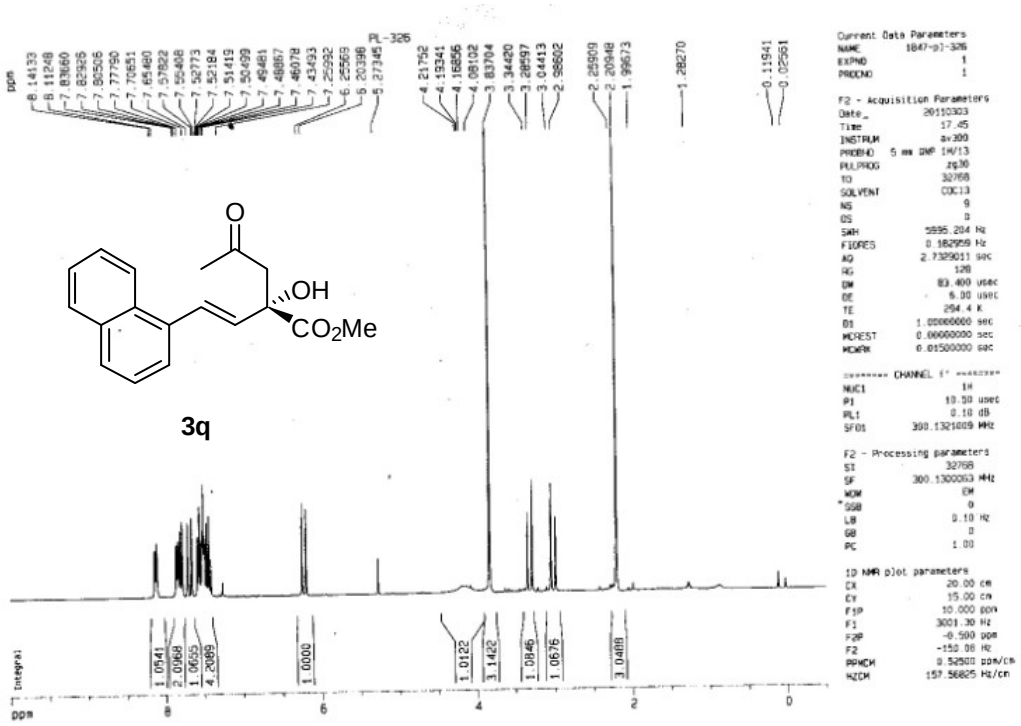



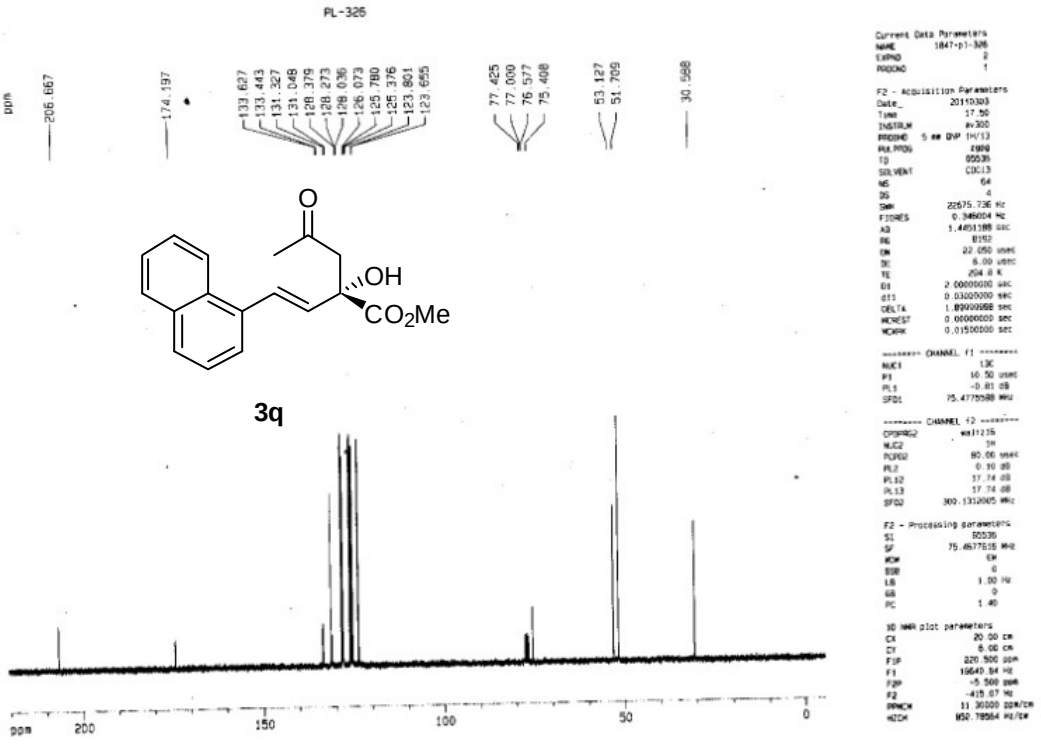


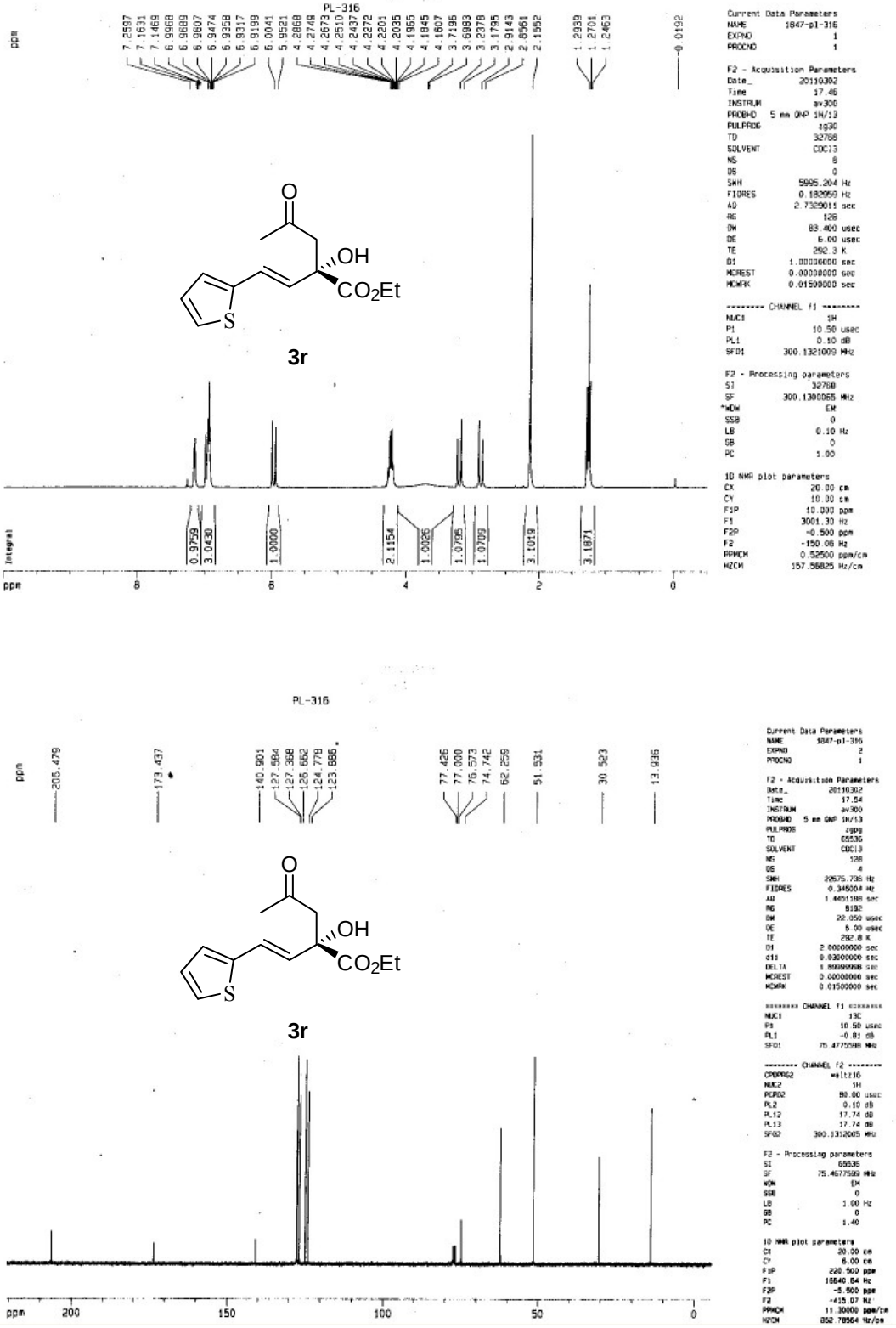

**3p**




**3p**






## F. References.

[1] Y.-C. Wu, L. Liu, H.-J. Li, D. Wang, Y.-J. Chen, *J. Org. Chem.* **2006**, *71*, 6592-6595.

[2] P.-F. Li, J.-L. Zhao, F.-B. Li, A. S. C. Chan, F. Y. Kwong, *Org. Lett.* **2010**, *12*, 5616-5619.

[3] a) C.-L. Cao, X.-L. Sun, Y.-B. Kang, Y. Tang, *Org. Lett.* **2007**, *9*, 4151-4154; b) C.-W. Zheng, Y.-Y. Wu, X.-Sh. Wang, G. Zhao, *Adv. Synth. Catal.* **2008**, *350*, 2690-2694.