Supporting Information

Organocatalytic Asymmetric Cascade 1,6-Addition/Hemiketalization/ retro-Henry Reaction of ortho-Hydroxyphenylsubstituted *p*-QMs with α-Nitroketones

Jing Zhou, Li-Juan Bai, Guo-Juan Liang, Qi-Gui Xu, Li-Ping Zhou, Hui Zhou*

Chongqing Research Center for Pharmaceutical Engineering, Chongqing Key Laboratory of Biochemistry and Molecular Pharmacology, School of pharmacy, Chongqing Medical University, Chongqing 400016, China

E-mail: zhoujing045@cqmu.edu.cn.

Table of Contents

1. General Methods

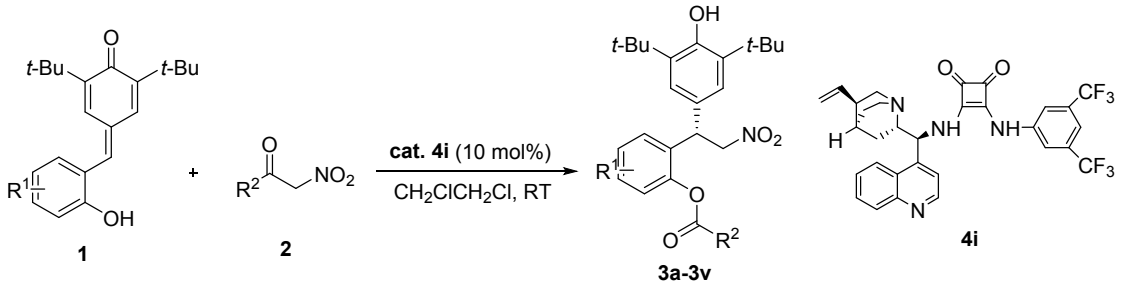
Various functional groups substituted ortho-hydroxyphenylsubstituted *p*-QMs **1** were prepared according to literature method[1]. A series of α-nitroketones **2** were prepared according to literature method[2]. Racemic products were obtained from corresponding substrates catalyzed by Et_3N or DBU at room temperature. Commercial grade solvents were dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997). ^1H NMR spectra were recorded on commercial instruments (600 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were collected on commercial instruments (150 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). Reactions were monitored by TLC and visualized with ultraviolet light. Mass spectra were recorded on Xevo G2-S QTof tandem mass spectrometer. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. The enantiomeric excess (ee) of the products were determined by HPLC using Daicel Chiralpak (OD-H) columns.

References

1. K. Zhao, Y. Zhi, T. Shu, A. Valkonen, K. Rissanen, D. Enders. *Angew. Chem. Int. Ed.* **2016**, *55*, 12104-12108.

2. Y.-Y. Liu,Y.-R. Mo, X.-D. Dong, L. Chen, L.Ye, X.-Y. Li, Z.-G. Zhao, X.F. Li. *Tetrahedron* **2019**, *75*, 2466-2471.

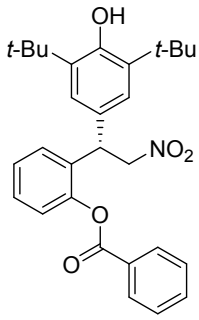
2. Experimental procedure for products 3



A solution of ortho-hydroxyphenylsubstituted *p*-QMs **1** (0.2 mmol, 1 equiv), α-nitroketones **2** (0.3 mmol, 1.5 equiv) and catalyst **4i** (0.02 mmol, 10 mol%) in CH_2ClCH_2Cl (2.0 mL) was stirred at room temperature for the time indicated in Table 3 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent PE:EtOAc = 30:1) to afford pure products **3**.

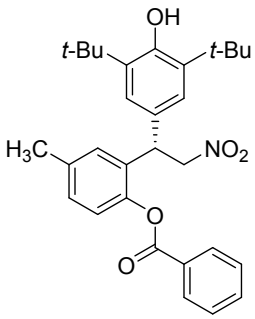
3. Characterization Data and HPLC Conditions of Products 3

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl benzoate (3a)



Light yellow solid; 84% yield; mp 132.3-133.3 °C; 97% ee; $[\alpha]_D^{20}$= +3.3 (c 1.4, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 13.31 min (major) and 6.20 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.28 (s, 18H), 4.89-4.93 (m, 1H), 5.00-5.03 (m, 1H), 5.09-5.11 (m, 2H), 6.87 (s, 2H), 7.21-7.36 (m, 4H), 7.51 (t, *J* = 7.56 Hz, 2H), 7.65 (t, *J* = 7.44 Hz, 1H), 8.14 (d, *J* = 9.42 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.0, 78.6, 123.5, 124.2, 126.3, 127.5, 128.4, 128.5, 128.7, 129.1, 130.1, 132.0, 133.8, 136.1, 148.7, 153.0, 164.3. HRMS (ESI-TOF) Calcd. for $C_{29}H_{33}NNaO_5$[M+Na]$^+$: 498.2256; Found: 498.2252.

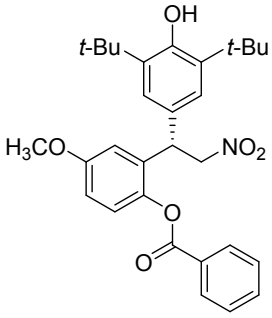
(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methylphenyl benzoate (3b)



Light yellow solid; 75% yield; mp 157.3-158.3 °C; 97% ee; $[\alpha]_D^{20}$= +17.8 (c 1.3, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 21.46 min (major) and 8.88 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 2.37

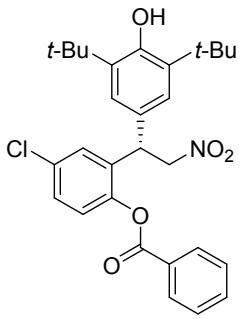
(s, 3H), 4.88-4.92 (m, 1H), 4.97-5.08 (m, 3H), 6.88 (s, 2H), 7.08 (m, 2H), 7.26 (s, 1H), 7.50 (t, *J* = 7.80 Hz, 2H), 7.64 (t, *J* = 7.44 Hz, 1H), 8.13 (d, *J* = 7.26 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.2, 30.0, 34.3, 43.0, 78.7, 123.2, 124.2, 128.1, 128.7, 129.0, 129.2, 130.2, 146.4, 153.0, 164.6. HRMS (ESI-TOF) Calcd. for $C_{30}H_{35}NNaO_5[M+Na]^+$: 512.2413; Found: 512.2409.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl benzoate (3c)



Light yellow solid; 71% yield; mp 180.3-181.2 °C; 84% ee; $[\alpha]_D^{20}$= +46.7 (c 1.8, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 6.64 min (major) and 14.39 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 3.81 (s, 3H), 4.87-4.91 (m, 1H), 4.96-4.99 (m, 1H), 5.03-5.06 (m, 1H), 5.09 (s, 1H), 6.85-6.91 (m, 3H), 7.12 (m, 1H), 7.26 (s, 1H), 7.49-7.53 (m, 3H), 8.14 (d, *J* = 7.14 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 29.4, 29.5, 30.1, 34.3, 35.9, 43.2, 55.6, 78.6, 112.7, 113.8, 117.1, 124.2, 128.3, 133.1, 133.7, 136.2, 142.1, 150.4, 152.7, 153.1, 157.5, 164.8. HRMS (ESI-TOF) Calcd. for $C_{30}H_{35}NNaO_6[M+Na]^+$: 528.2362; Found: 528.2360.

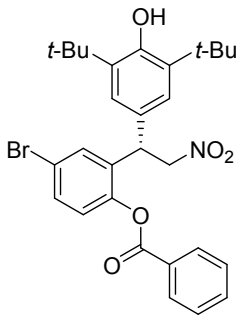
(S)-4-chloro-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl benzoate (3d)



Light yellow solid; 78% yield; mp 151.2-152.2 °C; 96% ee; $[\alpha]_D^{20}$= +24.7 (c 1.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 20.39 min (major) and 6.22 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 4.88-4.92 (m, 1H), 4.95-4.99 (m, 1H), 5.05-5.08 (m, 1H), 5.12 (s, 1H), 6.86 (s, 2H), 7.16 (d, *J* = 8.46 Hz, 1H), 7.26-7.31 (m, 2H), 7.51 (t, *J* = 7.74 Hz, 2H), 7.66 (d, *J* = 7.44 Hz, 1H), 8.13 (d, *J* = 7.14 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.3, 42.9, 78.3, 124.1, 124.9, 127.8, 128.5, 128.7, 128.8, 130.2, 147.2, 153.3,

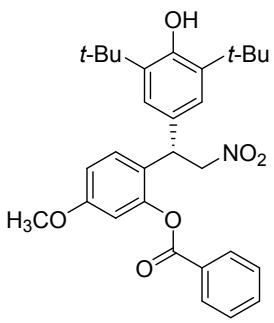
164.2. HRMS (ESI-TOF) Calcd. for $C_{29}H_{32}ClNNaO_5[M+Na]^+$: 532.1867; Found: 532.1860.

(S)-4-bromo-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl benzoate (3e)



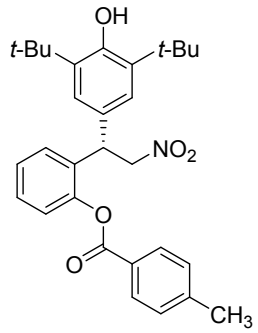
Light yellow solid; 75% yield; mp 162.5-163.5 °C; 82% ee; $[\alpha]_D^{20}$= +4.2 (c 1.6, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 6.72 min (major) and 14.73 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.22 (s, 18H), 4.81-4.84 (m, 1H), 4.88-4.91 (m, 1H), 4.99 (t, *J* = 8.04 Hz, 1H), 5.05 (s, 1H), 6.78 (s, 2H), 7.03 (d, *J* = 8.34 Hz, 1H), 7.38 (m, 2H), 7.44 (t, *J* = 7.86 Hz, 2H), 7.58 (t, *J* = 7.50 Hz, 1H), 8.06 (d, *J* = 7.26 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.3, 42.9, 78.4, 119.5, 124.1, 125.3, 127.8, 128.7, 128.8, 130.2, 131.5, 147.7, 153.3, 164.1. HRMS (ESI-TOF) Calcd. for $C_{29}H_{32}BrNNaO_5[M+Na]^+$: 576.1362; Found: 576.1357.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-5-methoxyphenyl benzoate (3f)



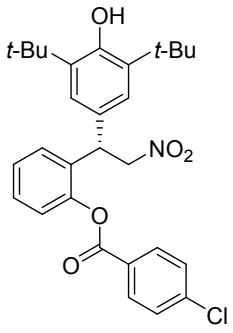
Red solid; 74% yield; mp 176.1-177.1 °C; 74% ee; $[\alpha]_D^{20}$= +34.4 (c 1.9, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 27.11 min (major) and 6.69 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 3.79 (s, 3H), 4.87-4.90 (m, 1H), 4.94-5.02 (m, 2H), 5.08 (s, 1H), 6.77-6.88 (m, 3H), 7.22 (m, 2H), 7.52 (t, *J* = 7.56 Hz, 2H), 7.65 (t, *J* = 7.32 Hz, 1H), 8.14 (d, *J* = 7.92 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 29.0, 33.2, 41.5, 54.5, 77.8, 108.1, 111.4, 123.0, 123.1, 127.1, 132.8, 135.1, 148.4, 151.9, 158.4, 163.3. HRMS (ESI-TOF) Calcd. for $C_{30}H_{35}NNaO_6[M+Na]^+$: 528.2362; Found: 528.2361.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-methylbenzoate (3g)

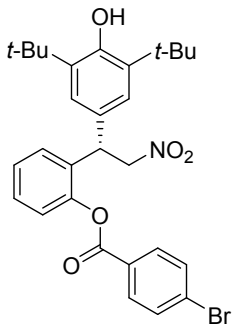


White solid; 78% yield; mp 144.8-145.8 °C; 98% ee; $[\alpha]_D^{20}$= +22.3 (c 1.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 12.83 min (major) and 6.45 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 2.45 (s, 3H), 4.89-4.93 (m, 1H), 4.98-5.01 (m, 1H), 5.08-5.11 (m, 2H), 6.88 (s, 2H), 7.20 (d, *J* = 8.46 Hz, 1H), 7.26-7.33 (m, 5H), 8.03 (d, *J* = 8.10 Hz, 2H), 7.66 (d, *J* = 7.44 Hz, 1H), 8.13 (d, *J* = 7.14 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.8, 30.0, 34.3, 43.0, 78.7, 123.6, 124.2, 126.3, 126.4, 127.6, 128.4, 128.6, 129.4, 130.2, 132.1, 136.1, 144.7, 148.7, 153.0, 164.4. HRMS (ESI-TOF) Calcd. for $C_{30}H_{35}NNaO_5[M+Na]^+$: 512.2413; Found: 512.2408.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-chlorobenzoate (3h)



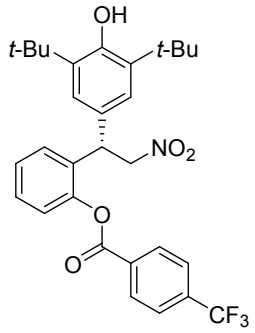
Light yellow solid; 70% yield; mp 142.7-143.7 °C; 99% ee; $[\alpha]_D^{20}$= +2.1 (c 1.4, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 22.28 min (major) and 7.66 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 4.88-4.91 (m, 1H), 4.97-5.01 (m, 1H), 5.06-5.09 (m, 2H), 6.85 (s, 2H), 7.20 (d, *J* = 8.34 Hz, 1H), 7.26-7.30 (m, 3H), 7.49 (d, *J* = 8.58 Hz, 2H), 8.06 (d, *J* = 8.58 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.0, 78.7, 123.5, 124.2, 126.5, 127.5, 127.6, 128.5, 129.1, 131.5, 132.0, 136.2, 140.4, 148.5, 153.0, 163.5. HRMS (ESI-TOF) Calcd. for $C_{29}H_{36}ClN_2O_5[M+NH_4]^+$: 527.2313; Found: 527.2307.



(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-bromobenzoate (3i)

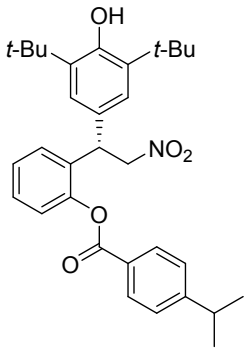
Light yellow solid; 92% yield; mp 149.5-150.5 °C; 85% ee; $[\alpha]_D^{20}$= +23.2 (c 1.4, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 21.56 min (major) and 6.80 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.29 (s, 18H), 4.88-4.91 (m, 1H), 4.97-5.01 (m, 1H), 5.06-5.09 (m, 2H), 6.84 (s, 2H), 7.19 (d, *J* = 8.46 Hz, 1H), 7.26-7.36 (m, 3H), 7.65 (d, *J* = 8.58 Hz, 2H), 7.98 (d, *J* = 8.52 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.0, 78.7, 123.5, 124.2, 126.5, 127.6, 128.0, 128.4, 128.5, 129.1, 131.6, 132.0, 136.2, 148.5, 153.0, 163.6. HRMS (ESI-TOF) Calcd. for $C_{29}H_{32}BrNNaO_5[M+Na]^+$: 576.1362; Found: 576.1353.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-(trifluoromethyl)benzoate (3j)



Yellow solid; 78% yield; mp 79.3-80.3 °C; 95% ee; $[\alpha]_D^{20}$= -5.5 (c 1.7, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 27.15 min (major) and 6.78 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.26 (s, 18H), 4.87-4.91 (m, 1H), 4.99-5.02 (m, 1H), 5.07-5.10 (m, 2H), 6.82 (s, 2H), 7.21 (m, 1H), 7.30-7.33 (m, 1H), 7.38 (m, 2H), 7.77 (d, *J* = 8.22 Hz, 2H), 8.23 (d, *J* = 8.16 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.1, 78.7, 122.6, 123.5, 124.2, 124.4, 125.7, 125.8, 126.7, 127.6, 128.4, 128.6, 130.5, 131.9, 132.4, 135.1, 136.2, 148.5, 153.1, 163.1. HRMS (ESI-TOF) Calcd. for $C_{30}H_{32}F_3NNaO_5[M+Na]^+$: 566.2130; Found: 566.2127.

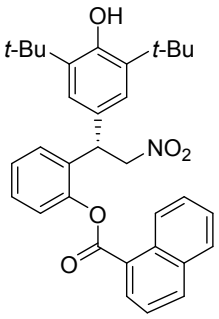
(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-isopropylbenzoate (3k)



Yellow solid; 75% yield; mp 102.2-103.2 °C; 97% ee; $[\alpha]_D^{20}$= -6.2 (c 1.4, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 12.31 min (major) and 6.06 min (minor).

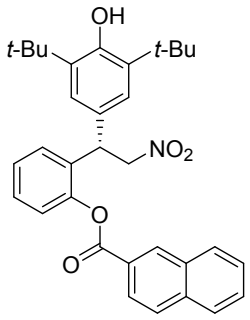
^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.27 (s, 18H), 1.29 (s, 3H), 1.30 (s, 3H), 2.98-3.03 (m, 1H), 4.89-4.92 (m, 1H), 4.99-5.02 (m, 1H), 5.07-5.10 (m, 2H), 6.86 (s, 2H), 7.19 (d, *J* = 8.70 Hz, 1H), 7.25-7.27 (m, 1H), 7.34 (m, 4H), 8.05 (d, *J* = 8.28 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 23.7, 29.7, 34.2, 34.4, 43.1, 78.7, 123.7, 124.3, 126.2, 126.7, 126.9, 127.5, 128.4, 128.6, 130.4, 132.1, 136.1, 148.8, 153.0, 155.4, 164.3. HRMS (ESI-TOF) Calcd. for $C_{32}H_{39}NNaO_5$[M+Na]$^+$: 540.2726; Found: 540.2720.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 1-naphthoate (3l)



Yellow solid; 81% yield; mp 100.4-101.4 °C; 92% ee; $[\alpha]_D^{20}$= -11.6 (c 1.5, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 16.63 min (major) and 8.49 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.22 (s, 18H), 4.89-4.93 (m, 1H), 5.02-5.05 (m, 2H), 5.15-5.17 (m, 1H), 6.87 (s, 2H), 7.28-7.33 (m, 2H), 7.39 (m, 2H), 7.60 (m, 3H), 7.91 (d, *J* = 8.04 Hz, 1H), 8.12 (d, *J* = 8.16 Hz, 1H), 8.48 (d, *J* = 7.26 Hz, 1H), 8.90 (d, *J* = 8.58 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.1, 78.7, 123.7, 124.3, 124.5, 125.1, 125.8, 126.4, 126.5, 127.7, 128.3, 128.5, 128.6, 131.3, 131.8, 136.1, 148.8, 153.0, 164.8. HRMS (ESI-TOF) Calcd. for $C_{33}H_{35}NNaO_5$[M+Na]$^+$: 548.2413; Found: 548.2413.

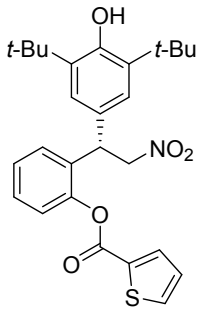
(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 2-naphthoate (3m)



Light yellow solid; 90% yield; mp 145.0-146.0 °C; 94% ee; $[\alpha]_D^{20}$= +19.5 (c 1.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 22.13 min (major) and 7.87 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.24 (s, 18H), 4.91-4.95 (m, 1H), 5.02-5.07 (m, 1H), 5.16-5.18 (m, 2H), 6.89 (s, 2H), 7.25-7.36 (m, 4H), 7.58 (m, 2H), 7.91-7.93 (m, 2H), 7.99 (d, *J* = 8.04 Hz, 1H), 8.12 (m, 1H), 8.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.9, 30.0, 34.2, 43.0, 78.7, 123.6, 124.2, 125.3, 126.3, 126.4, 126.9, 127.7, 127.8, 128.5, 128.7, 129.5, 135.9,

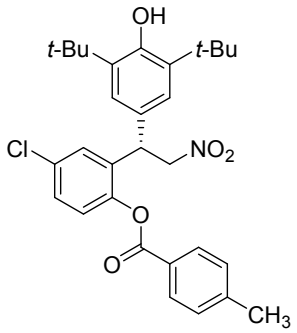
136.1, 148.8, 153.0, 164.6. HRMS (ESI-TOF) Calcd. for $C_{33}H_{35}NNaO_5[M+Na]^+$: 548.2413; Found: 548.2407.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl thiophene-2-carboxylate (3n)



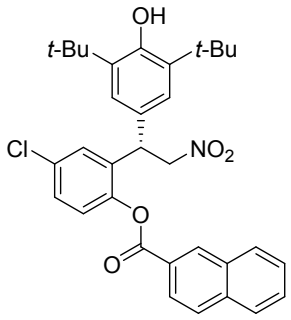
Light yellow solid; 79% yield; mp 108.7-109.6 °C; 98% ee; $[\alpha]_D^{20}$= -6.8 (c 1.4, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 12.76 min (major) and 6.41 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.30 (s, 18H), 4.91-4.95 (m, 1H), 5.00-5.03 (m, 1H), 5.09-5.13 (m, 2H), 6.89 (s, 2H), 7.16 (t, *J* = 3.84 Hz, 1H), 7.23-7.33 (m, 4H), 7.66 (d, *J* = 4.92 Hz, 1H), 7.91 (d, *J* = 2.82 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.1, 34.3, 43.1, 78.6, 123.5, 124.3, 126.5, 127.7, 128.2, 128.4, 128.5, 132.1, 132.4, 133.7, 134.8, 148.3, 153.0, 159.7. HRMS (ESI-TOF) Calcd. for $C_{27}H_{31}NNaO_5S[M+Na]^+$: 504.1821; Found: 504.1816.

(S)-4-chloro-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-methylbenzoate (3o)



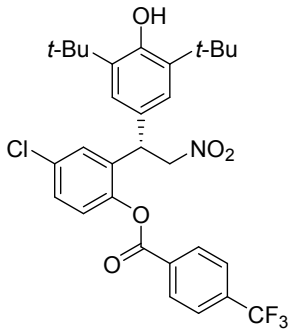
Yellow solid; 86% yield; mp 125.2-126.2 °C; 98% ee; $[\alpha]_D^{20}$= +48.8 (c 1.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 33.29 min (major) and 10.03 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.23 (s, 18H), 2.38 (s, 3H), 4.81-4.90 (m, 2H), 4.98 (t, *J* = 7.98 Hz, 1H), 5.04 (s, 1H), 6.79 (s, 2H), 7.08 (d, *J* = 8.52 Hz, 1H), 7.18-7.23 (m, 4H), 7.95 (d, *J* = 8.16 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.8, 30.0, 34.3, 42.9, 78.3, 124.1, 125.0, 126.0, 127.8, 127.9, 128.5, 129.5, 130.3, 131.6, 134.0, 136.4, 145.0, 147.2, 153.2, 164.3. HRMS (ESI-TOF) Calcd. for $C_{30}H_{34}ClNNaO_5[M+Na]^+$: 546.2023; Found: 546.2020.

(S)-4-chloro-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 2-naphthoate (3p)



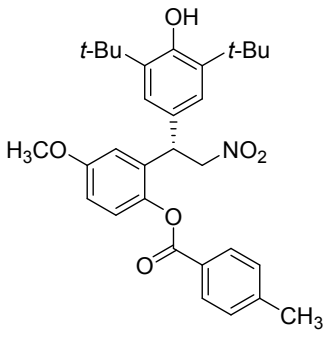
Light yellow solid; 89% yield; mp 169.8-170.8 °C; >99% ee; $[\alpha]_D^{20}$= +0.83 (c 1.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 30.50 min (major) and 10.57 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.18 (s, 18H), 4.82-4.86 (m, 1H), 4.91-4.94 (m, 1H), 5.03-5.07 (m, 2H), 6.81 (s, 2H), 7.14 (m, 1H), 7.24-7.26 (m, 2H), 7.50 (m, 2H), 7.84-7.92 (m, 3H), 8.03 (m, 1H), 8.65 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.3, 43.0, 78.4, 124.1, 125.0, 125.3, 125.9, 127.0, 127.8, 128.0, 128.6, 128.7, 128.9, 129.6, 131.8, 132.1, 136.4, 147.3, 153.3, 164.4. HRMS (ESI-TOF) Calcd. for $C_{33}H_{34}ClNNaO_5[M+Na]^+$: 582.2023; Found: 582.2019.

(S)-4-chloro-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)phenyl 4-(trifluoromethyl)benzoate (3q)



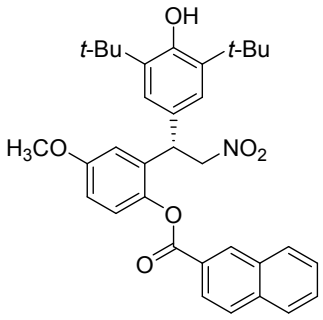
White solid; 84% yield; mp 113.7-114.7 °C; 96% ee; $[\alpha]_D^{20}$= -32.8 (c 1.3, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 27.21 min (major) and 8.93 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.27 (s, 18H), 4.87-4.90 (m, 1H), 4.94-4.98 (m, 1H), 5.04 (t, *J* = 8.04 Hz, 1H), 5.12 (s, 1H), 6.81 (s, 2H), 7.16 (d, *J* = 8.52 Hz, 1H), 7.32-7.33 (m, 2H), 7.77 (d, *J* = 8.28 Hz, 2H), 8.22 (d, *J* = 8.16 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.0, 78.4, 122.5, 124.0, 124.4, 124.8, 125.8, 127.6, 127.9, 128.6, 130.5, 132.0, 132.1, 133.9, 135.3, 136.4, 146.9, 153.3, 162.9. HRMS (ESI-TOF) Calcd. for $C_{30}H_{31}ClF_3NNaO_5[M+Na]^+$: 600.1741; Found: 600.1723.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl 4-methylbenzoate (3r)

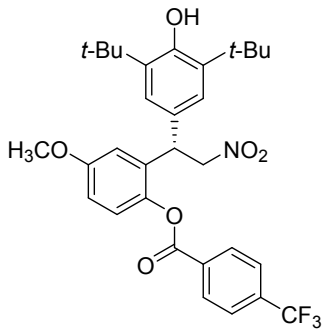


White solid; 80% yield; mp 129.1-130.1 °C; 83% ee; $[\alpha]_D^{20}$= +0.82 (c 2.2, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 20.74 min (major) and 9.66 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.30 (s, 18H), 2.45 (s, 3H), 3.80 (s, 3H), 4.87-4.91 (m, 1H), 4.94-4.98 (m, 1H), 5.04 (t, *J* = 8.04 Hz, 1H), 5.08 (s, 1H), 6.83-6.85 (m, 2H), 6.90 (s, 2H), 7.12 (d, *J* = 8.64 Hz, 1H), 7.29 (d, *J* = 7.98 Hz, 2H), 8.03 (d, *J* = 8.16 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.7, 30.1, 34.2, 43.1, 55.6, 78.6, 112.6, 113.8, 124.2, 126.4, 128.4, 129.4, 133.1, 136.1, 142.1, 144.6, 153.1, 157.4, 164.8. HRMS (ESI-TOF) Calcd. for $C_{31}H_{37}NNaO_6$[M+Na]$^+$: 542.2519; Found: 542.2514.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl 2-naphthoate (3s)



White solid; 82% yield; mp 161.4-162.4 °C; 98% ee; $[\alpha]_D^{20}$= +18.7 (c 1.5, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 6.32 min (major) and 17.16 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.26 (s, 18H), 3.82 (s, 3H), 4.89-4.93 (m, 1H), 4.99-5.01 (m, 1H), 5.03-5.12 (m, 2H), 6.87-6.91 (m, 4H), 7.19 (d, *J* = 8.58 Hz, 1H), 7.57 (m, 2H), 7.91-7.94 (m, 3H), 8.12 (m, 1H), 8.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.2, 55.6, 78.7, 112.7, 113.9, 124.2, 126.4, 127.8, 128.5, 129.6, 135.9, 136.2, 142.2, 153.1, 157.5, 165.0. HRMS (ESI-TOF) Calcd. for $C_{34}H_{37}NNaO_6$[M+Na]$^+$: 578.2519; Found: 578.2518.

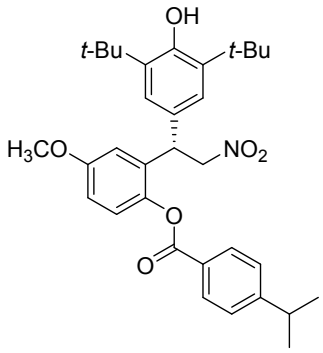


(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl 4-(trifluoromethyl)benzoate (3t)

Yellow solid; 72% yield; mp 161.1-162.1 °C; 98% ee; $[\alpha]_D^{20}$= +13.3 (c 1.0, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0

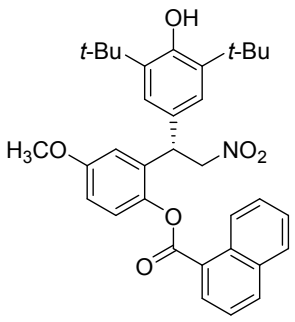
mL/min, UV detection at 254 nm, retention time: 28.74 min (major) and 9.23 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.27 (s, 18H), 3.82 (s, 3H), 4.85-4.89 (m, 1H), 4.95-5.03 (m, 2H), 5.09 (s, 1H), 6.84-6.88 (m, 4H), 7.13 (m, 1H), 7.76 (d, *J* = 8.22 Hz, 2H), 8.23 (d, *J* = 8.10 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 432, 55.6, 78.7, 112.7, 113.8, 122.6, 124.1, 124.4, 125.7, 128.1, 130.5, 153.1, 157.7, 163.5. HRMS (ESI-TOF) Calcd. for $C_{31}H_{34}F_3NNaO_6$[M+Na]$^+$: 596.2236; Found: 596.2233.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl 4-isopropylbenzoate (3u)



Light yellow solid; 79% yield; mp 141.9-142.9 °C; 95% ee; $[\alpha]_D^{20}$= -20.3 (c 1.6, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 28.52 min (major) and 9.20 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.28 (s, 24H), 2.98-3.02 (m, 1H), 3.80 (s, 3H), 4.87-4.90 (m, 1H), 4.96-4.99 (m, 1H), 5.04 (t, *J* = 7.98 Hz, 1H), 5.08 (s, 1H), 6.84-6.88 (m, 4H), 7.10 (d, *J* = 9.48 Hz, 1H), 7.34 (d, *J* = 7.80 Hz, 2H), 8.05 (d, *J* = 7.80 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 23.7, 30.0, 34.2, 34.4, 43.2, 55.6, 78.6, 112.6, 113.7, 124.2, 126.7, 126.8, 128.3, 130.3, 136.1, 142.1, 153.0, 155.3, 157.4, 164.7. HRMS (ESI-TOF) Calcd. for $C_{33}H_{41}NNaO_6$[M+Na]$^+$: 570.2832; Found: 570.2829.

(S)-2-(1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-nitroethyl)-4-methoxyphenyl 1-naphthoate (3v)

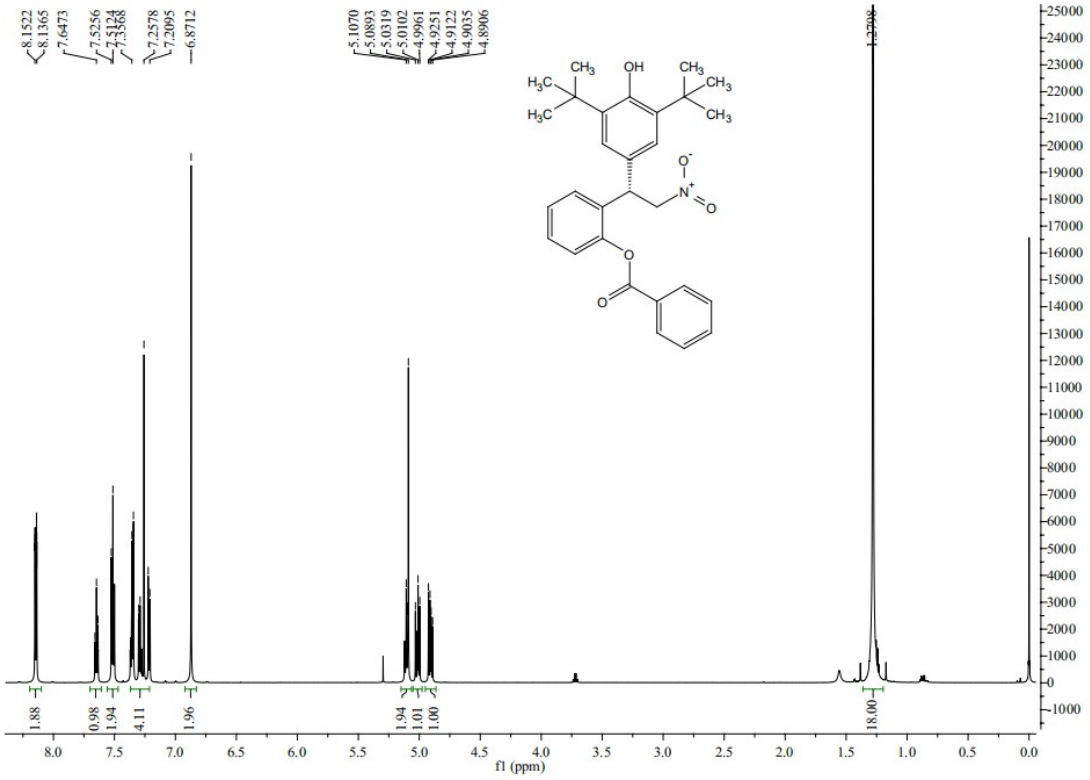


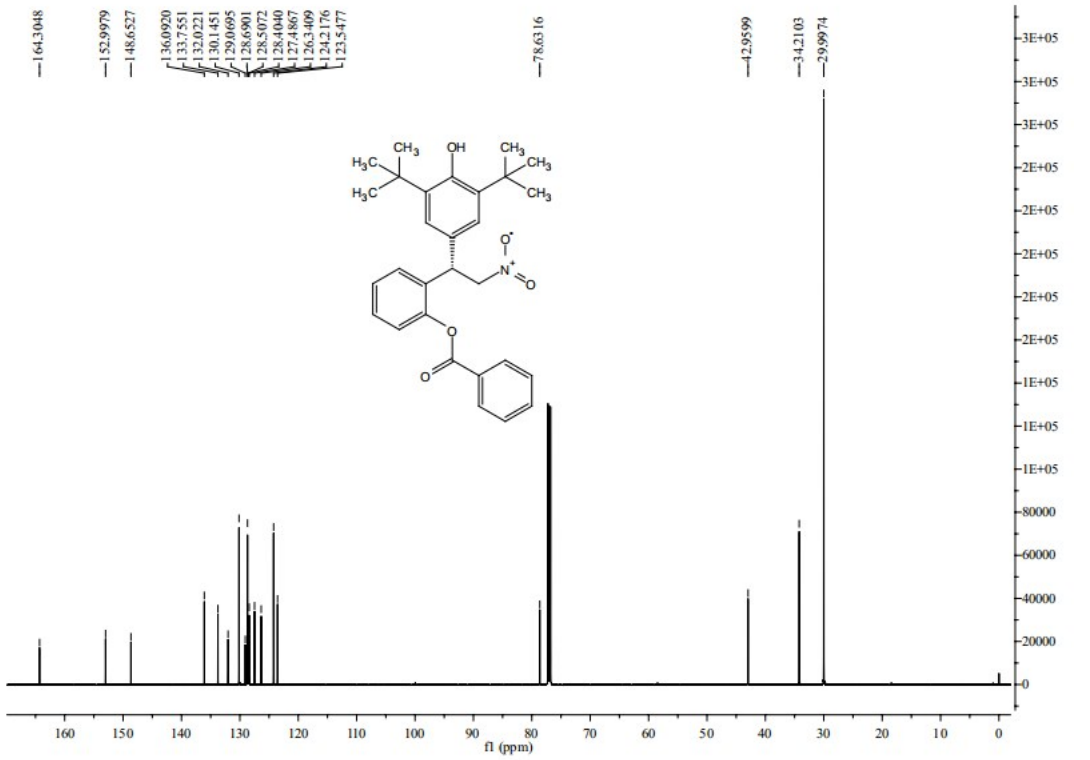
Yellow solid; 77% yield; mp 124.4-125.4 °C; 97% ee; $[\alpha]_D^{20}$= +5.4 (c 1.9, CH_2Cl_2); HPLC conditions: Chiralcel OD-H column, Hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, UV detection at 254 nm, retention time: 13.24 min (major) and 6.20 min (minor). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.23 (s, 18H), 3.82 (s, 3H), 4.87-4.91 (m, 1H), 4.98-5.02 (m, 2H), 5.04-5.10 (m, 1H), 6.88-6.91 (m, 4H), 7.20 (d, *J* = 8.40 Hz, 1H), 7.53 (m, 3H), 7.90 (d, *J* = 7.50 Hz, 1H), 8.10 (d, *J* = 8.22 Hz, 1H), 8.47 (d, *J* = 7.26 Hz, 1H), 8.91 (d,

J = 8.70 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.0, 34.2, 43.2, 55.6, 78.6, 112.7, 113.9, 124.2, 124.3, 124.5, 125.2, 125.8, 126.4, 128.2, 136.1, 142.3, 153.0, 157.5, 165.3. HRMS (ESI-TOF) Calcd. for $C_{34}H_{37}NNaO_6[M+Na]^+$: 578.2519; Found: 578.2520.

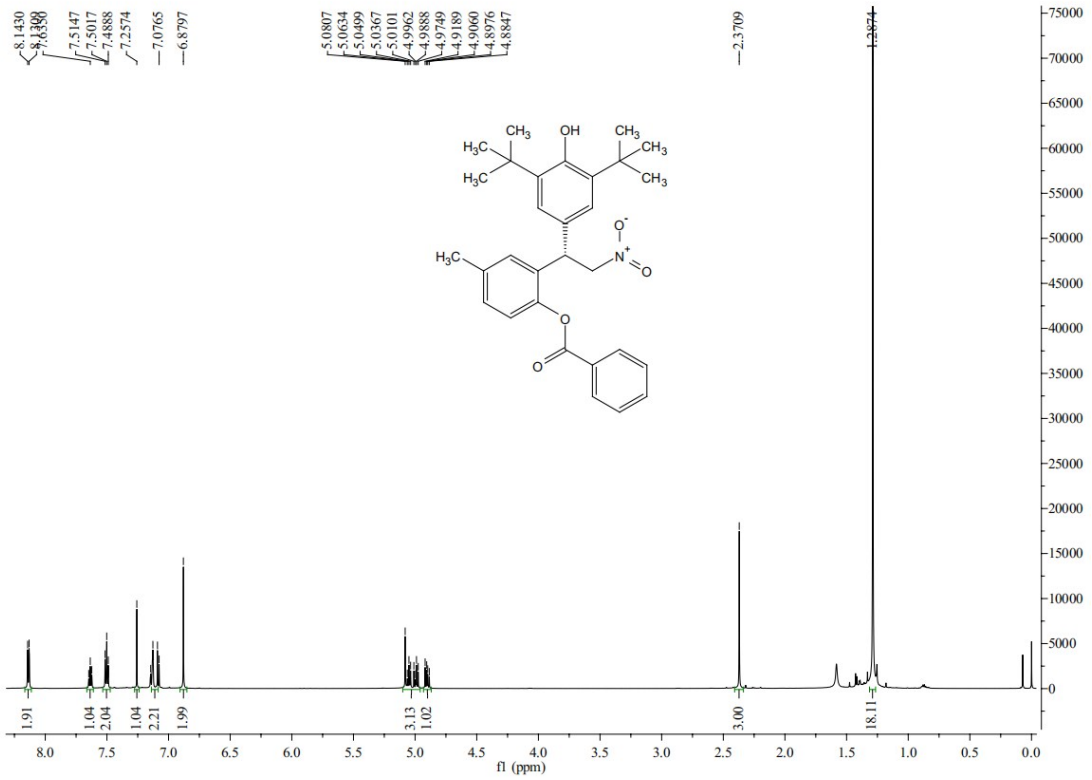
4. NMR Spectra

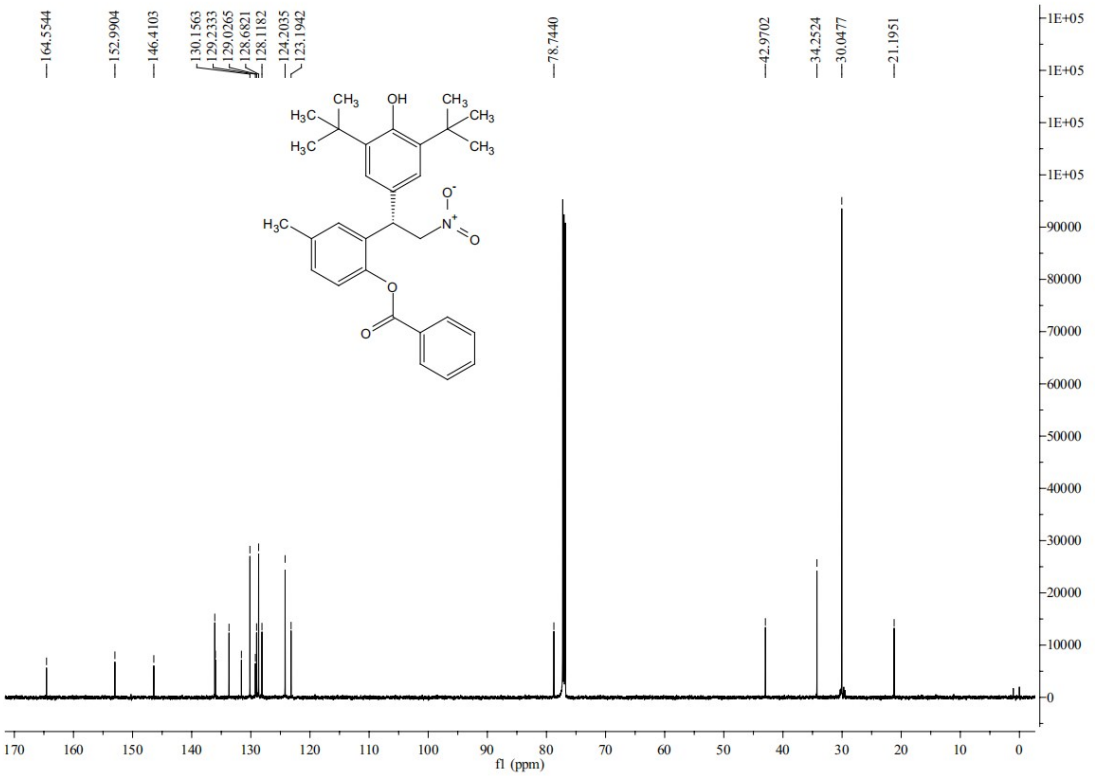
^{1}H and ^{13}C NMR of **3a**



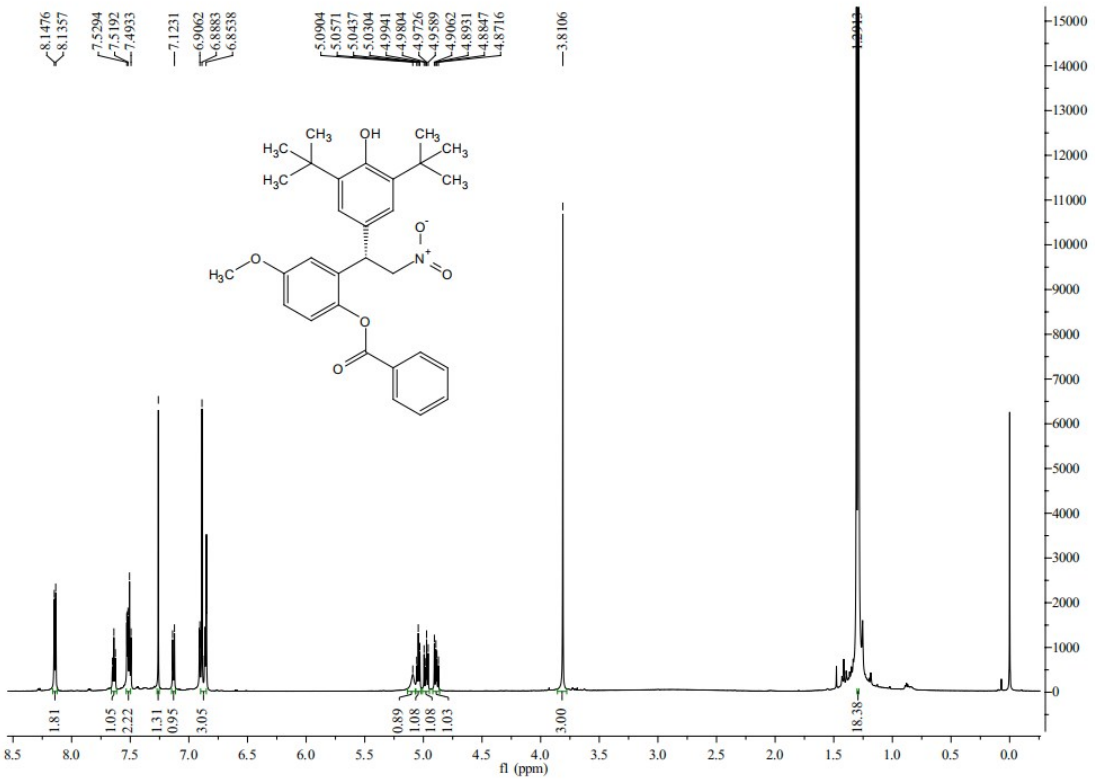


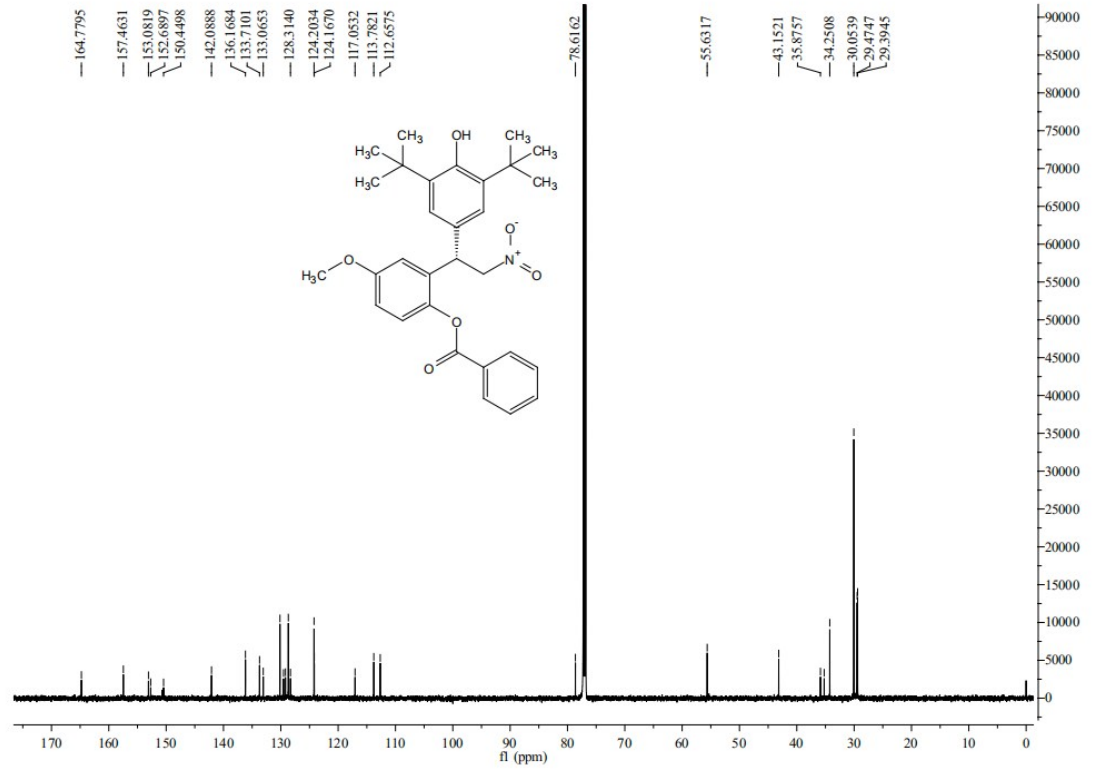
^{1}H and ^{13}C NMR of **3b**



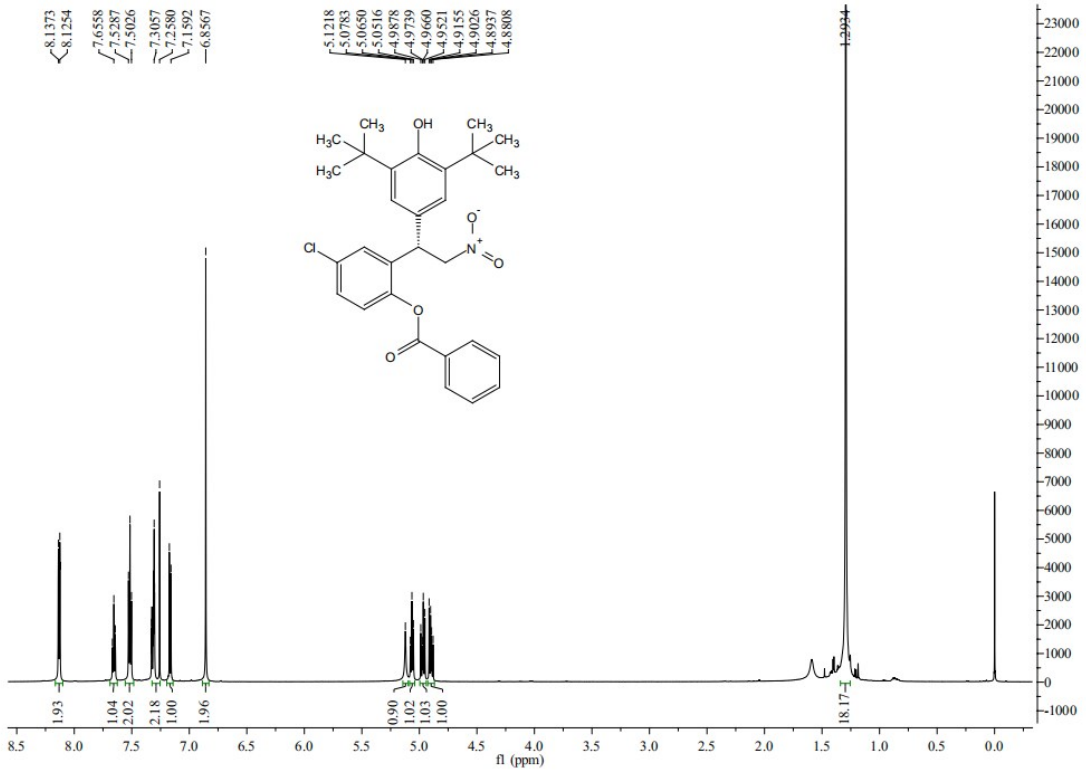


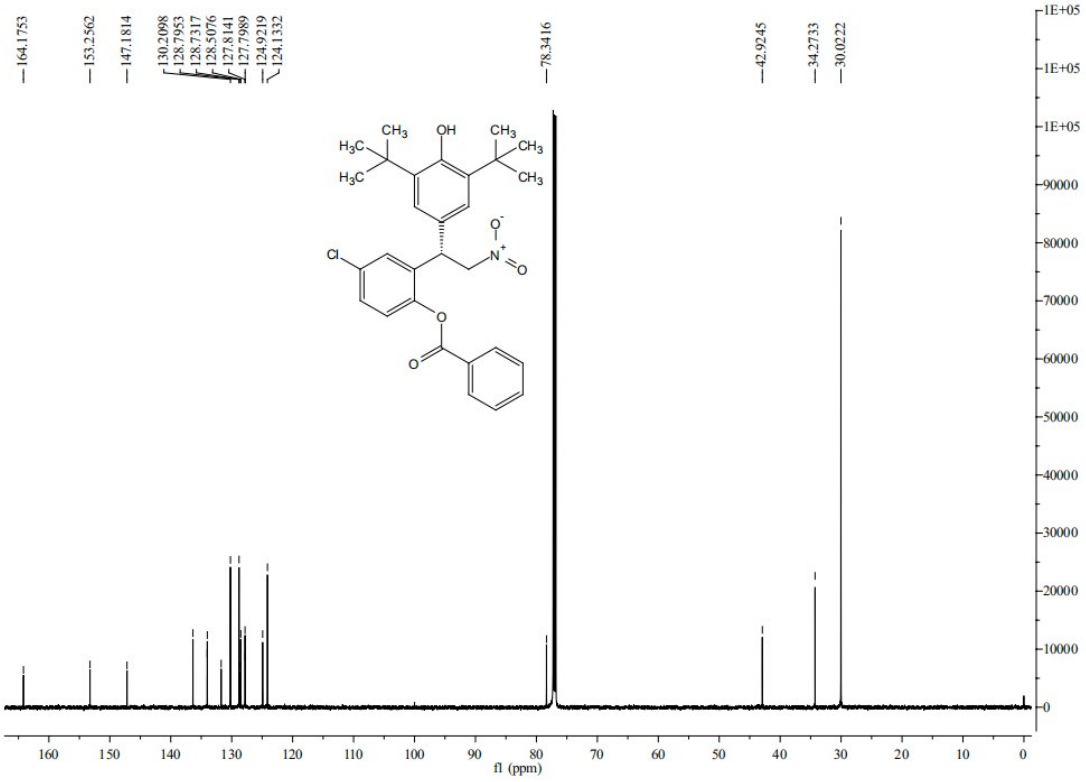
^{1}H and ^{13}C NMR of **3c**



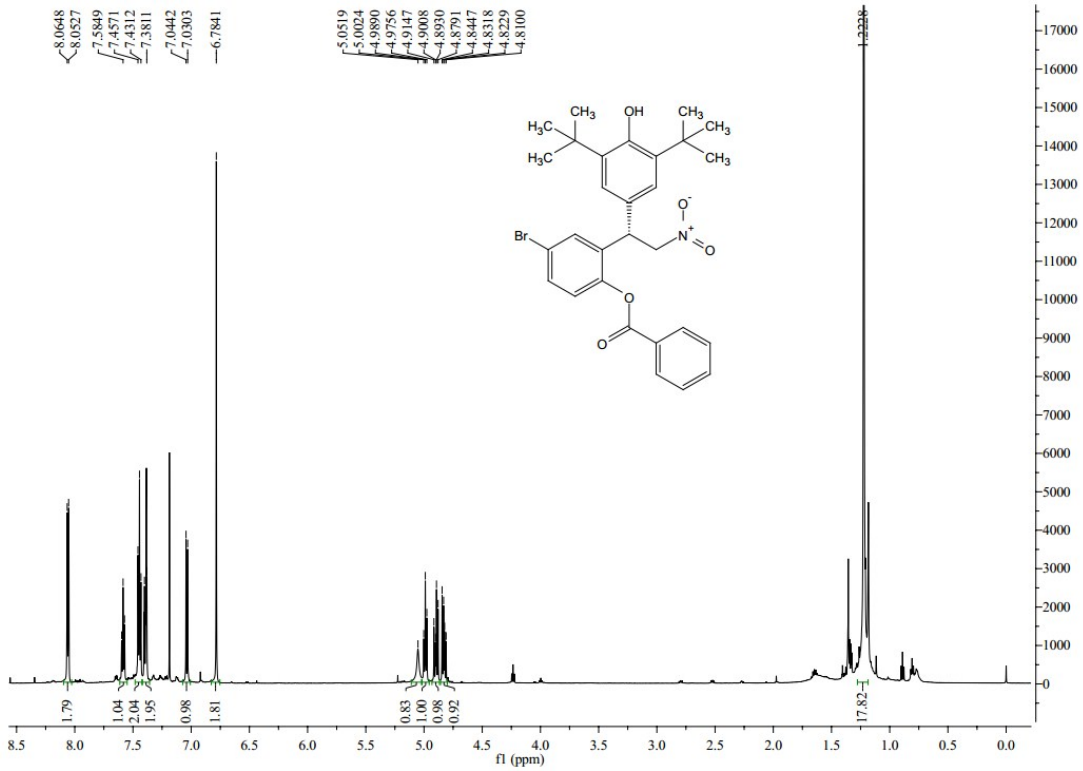


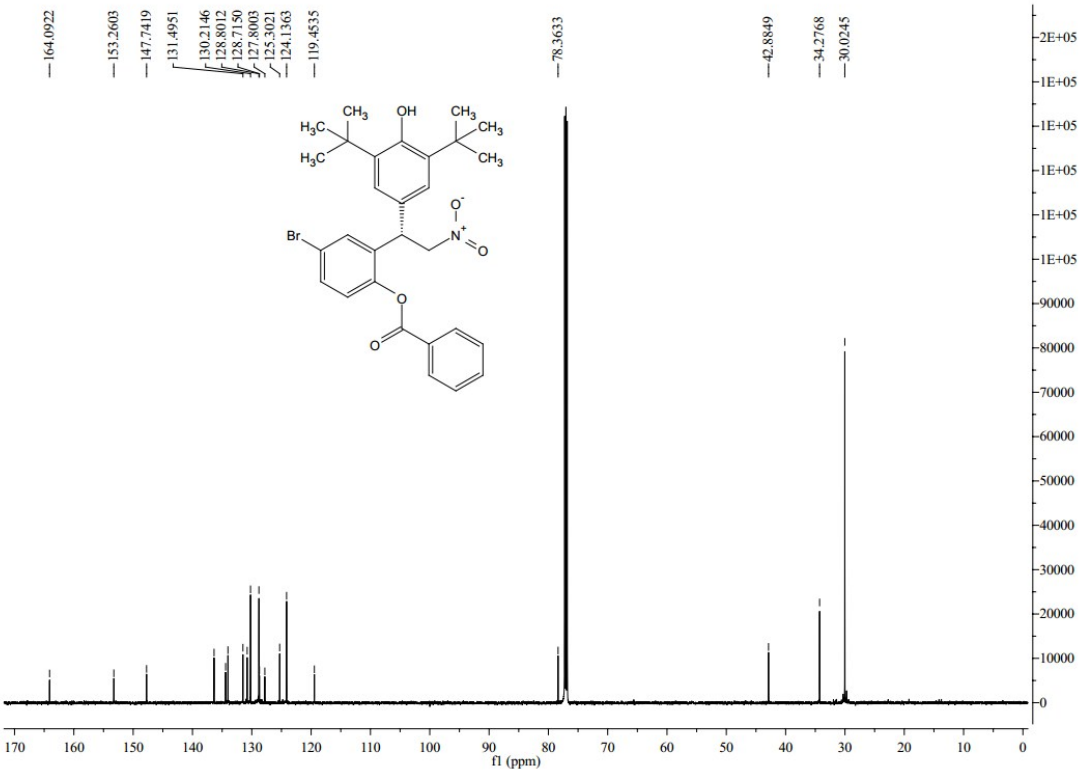
^{1}H and ^{13}C NMR of **3d**



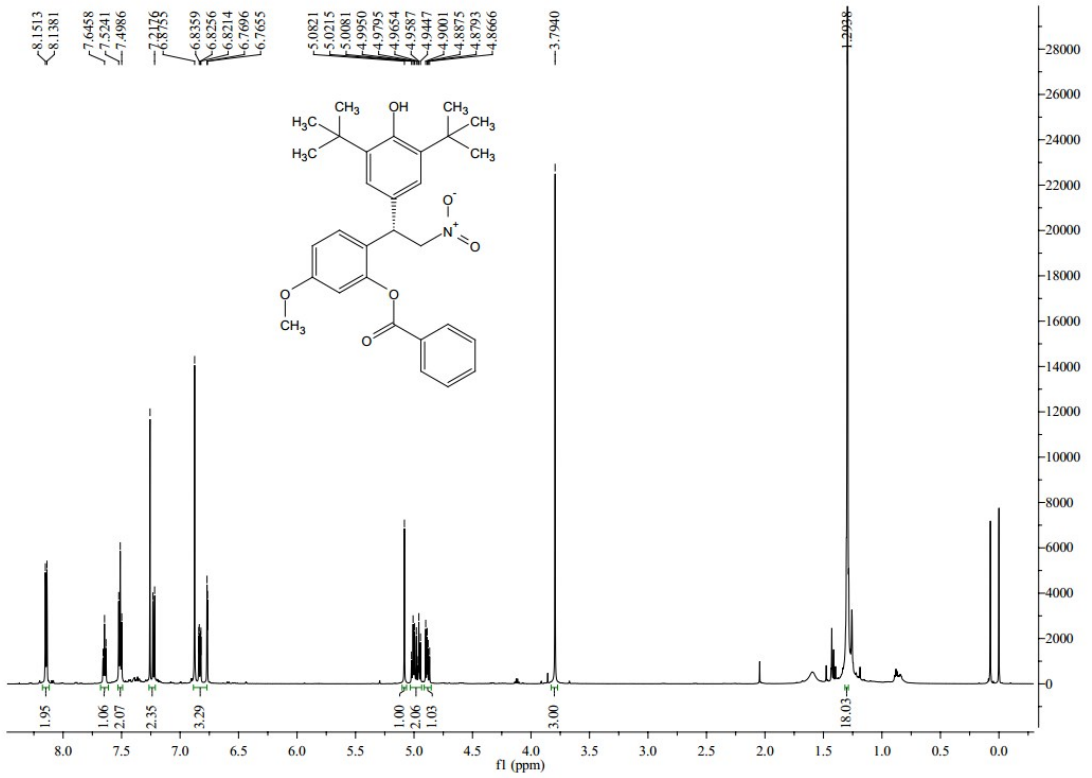


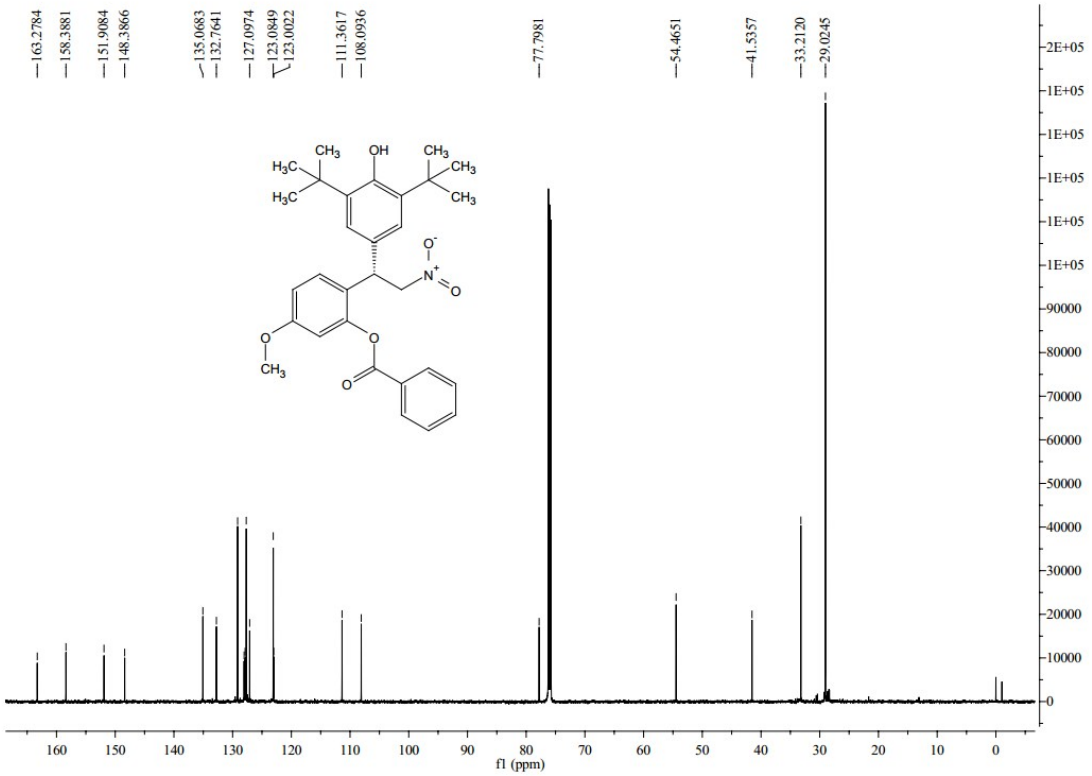
^{1}H and ^{13}C NMR of **3e**



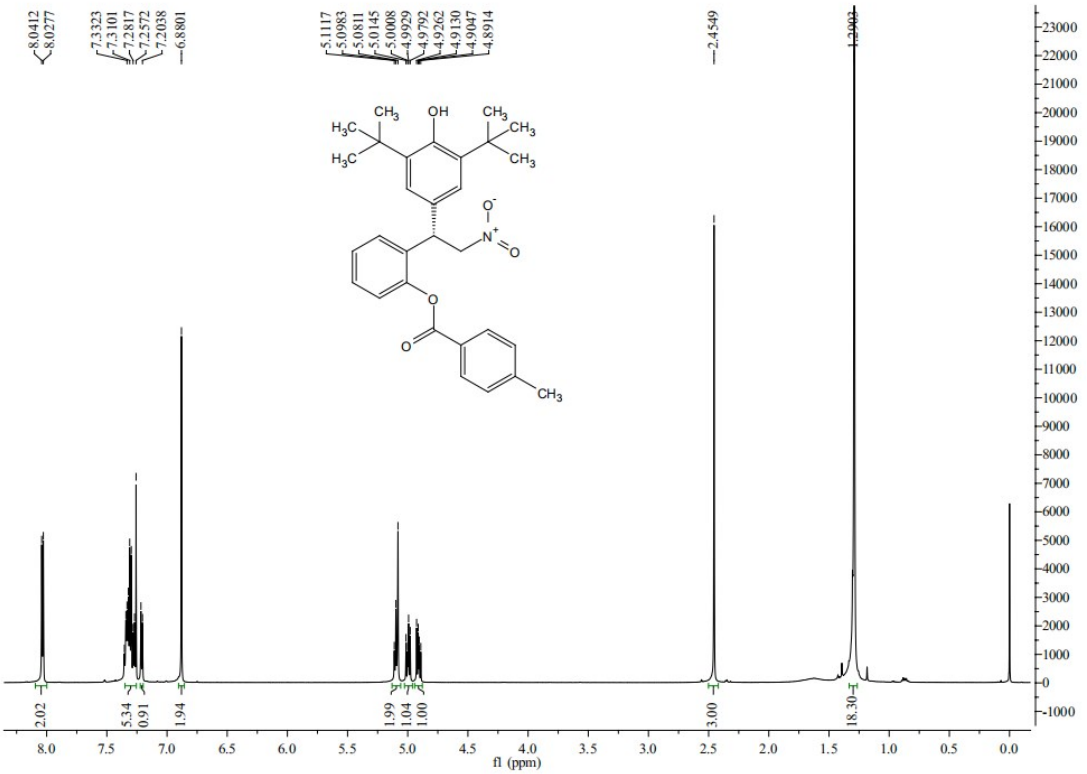


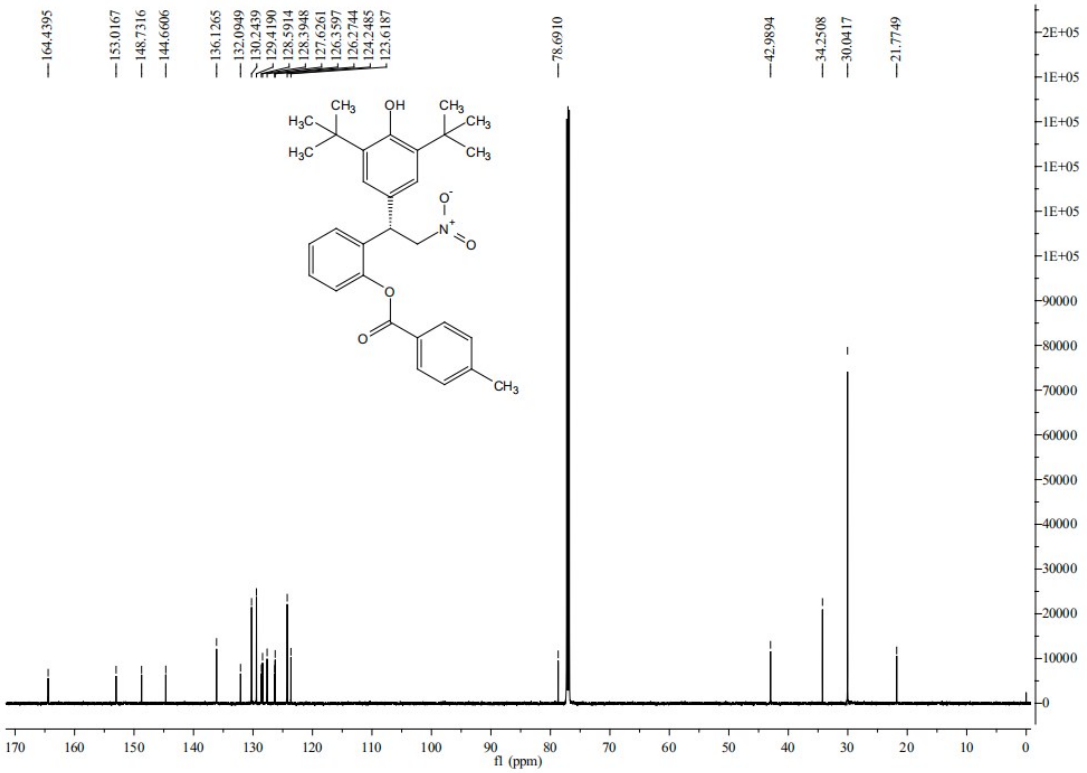
^{1}H and ^{13}C NMR of **3f**



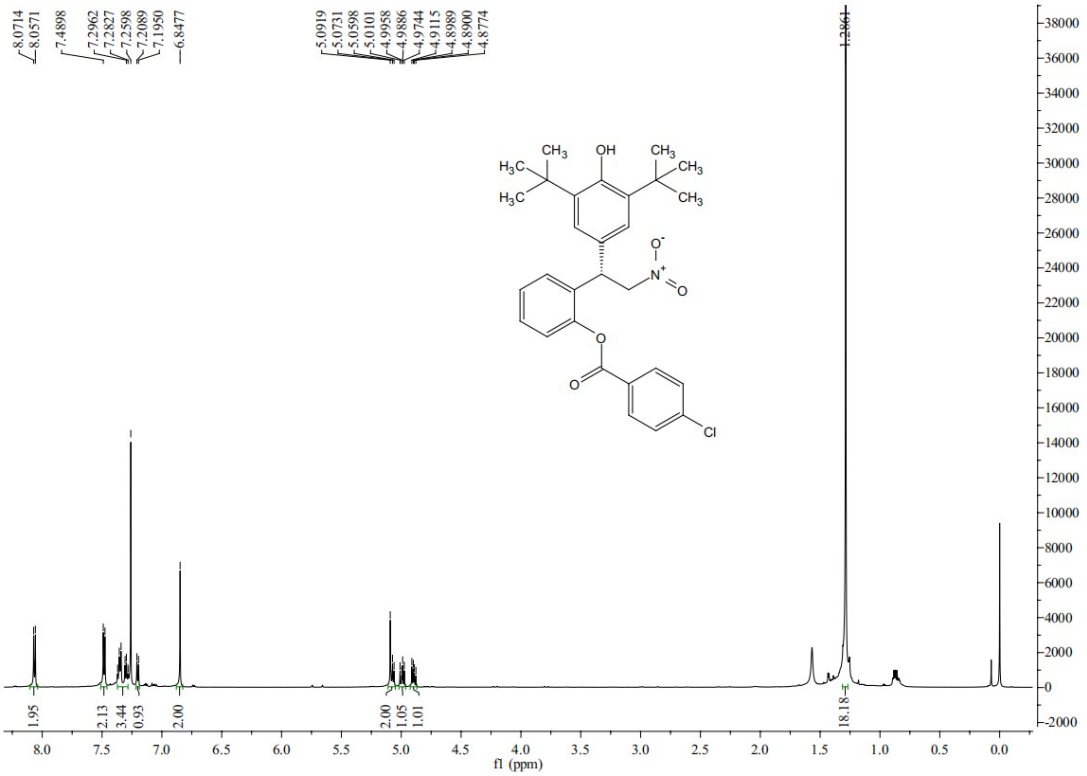


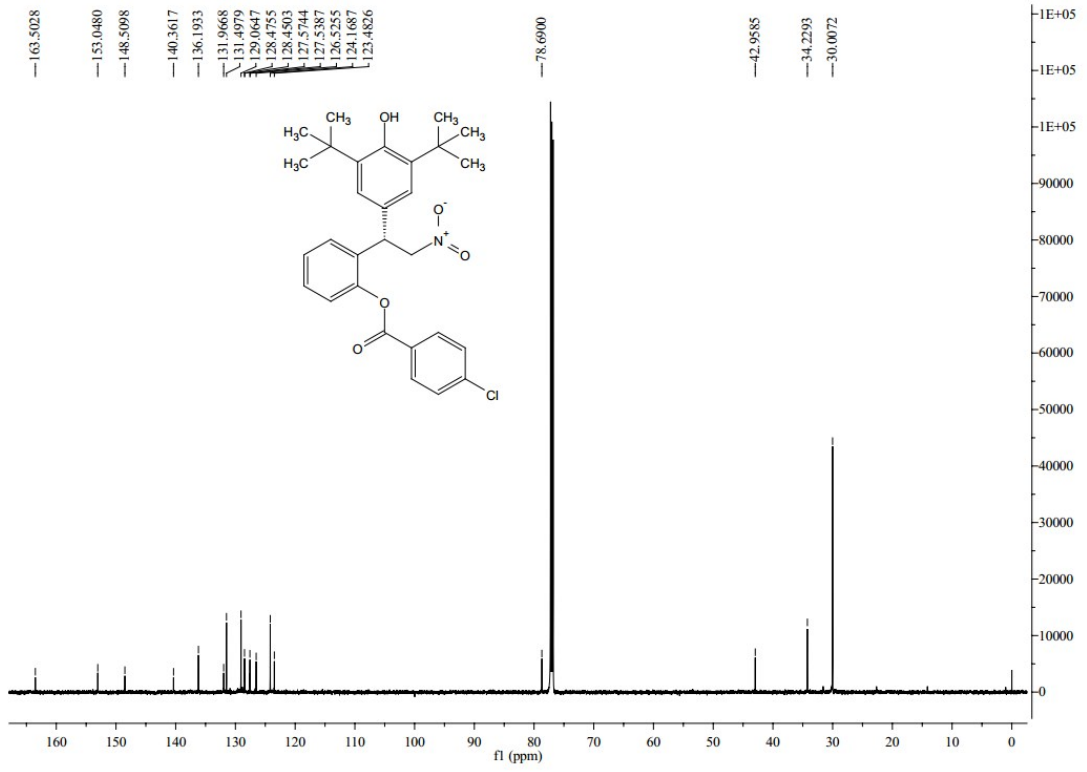
^{1}H and ^{13}C NMR of **3g**



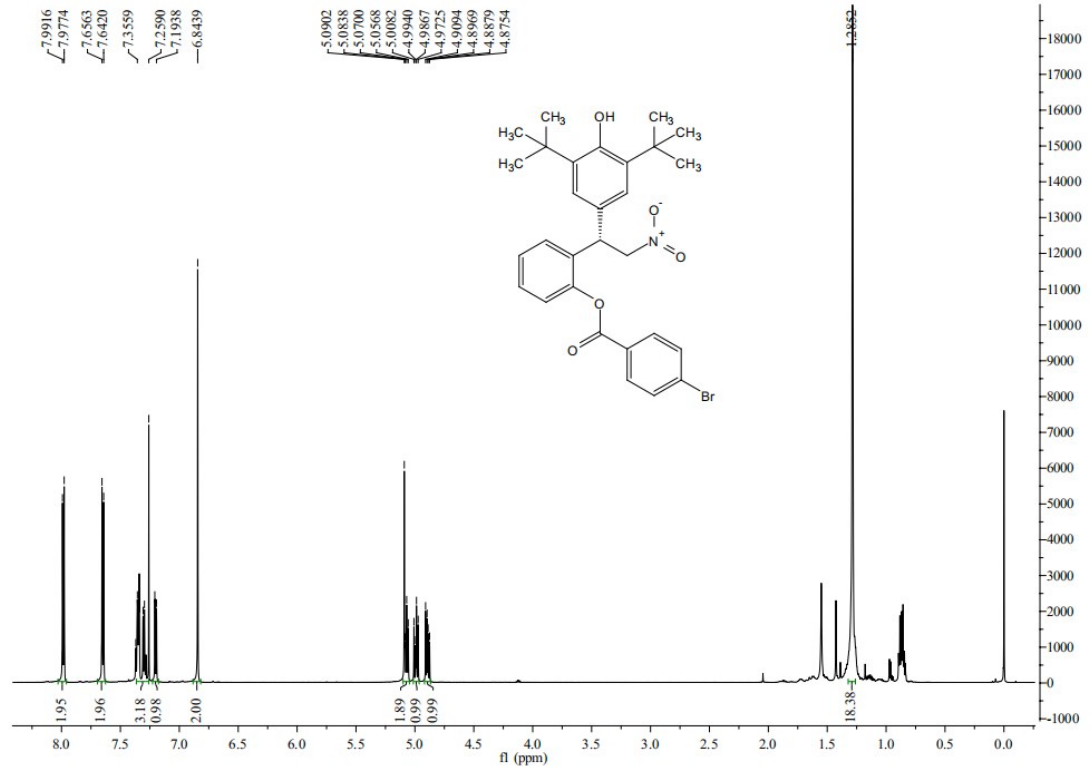


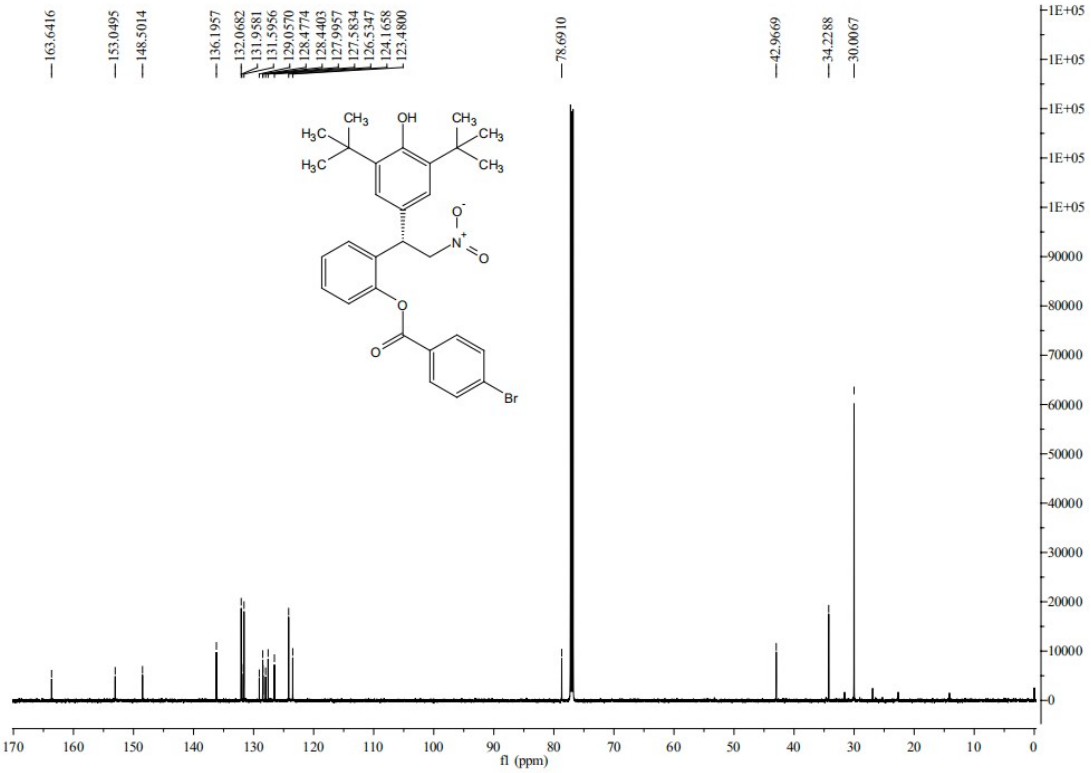
^{1}H and ^{13}C NMR of **3h**



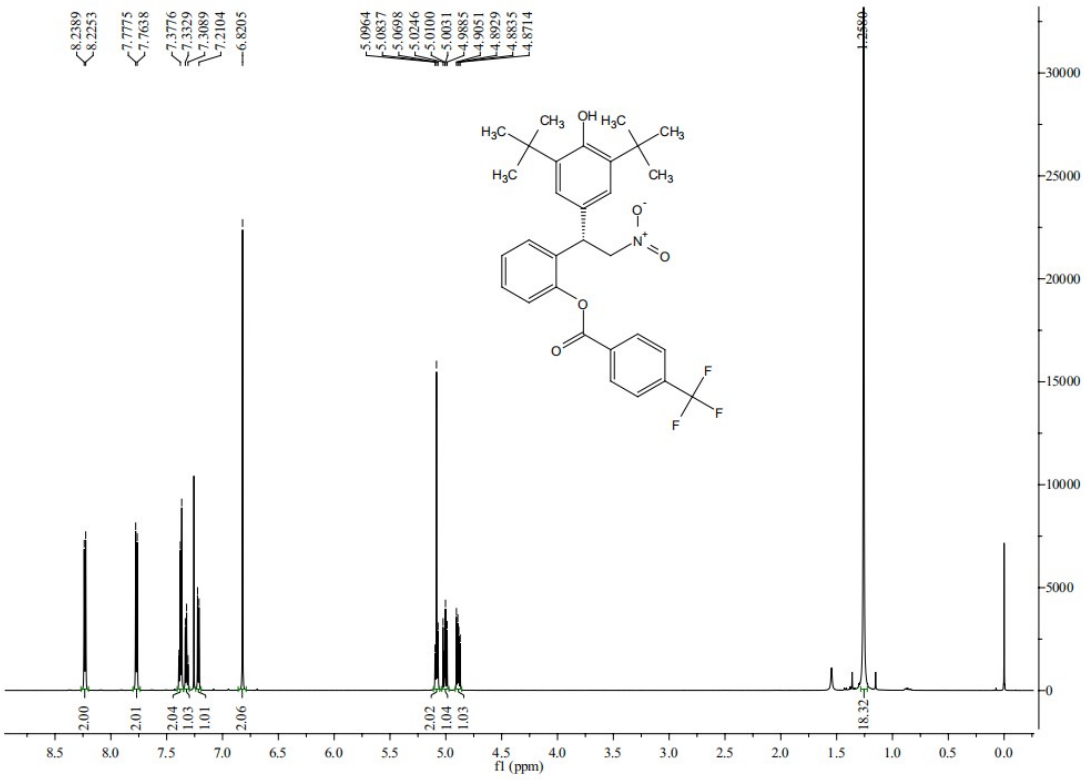


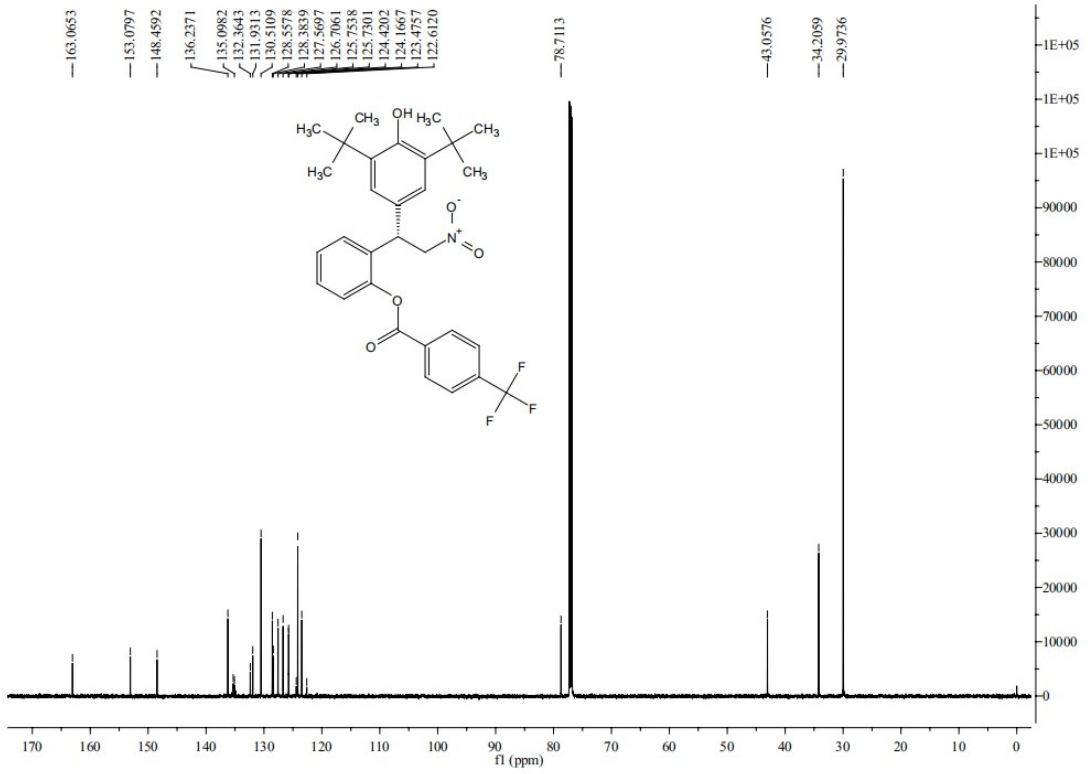
^{1}H and ^{13}C NMR of **3i**



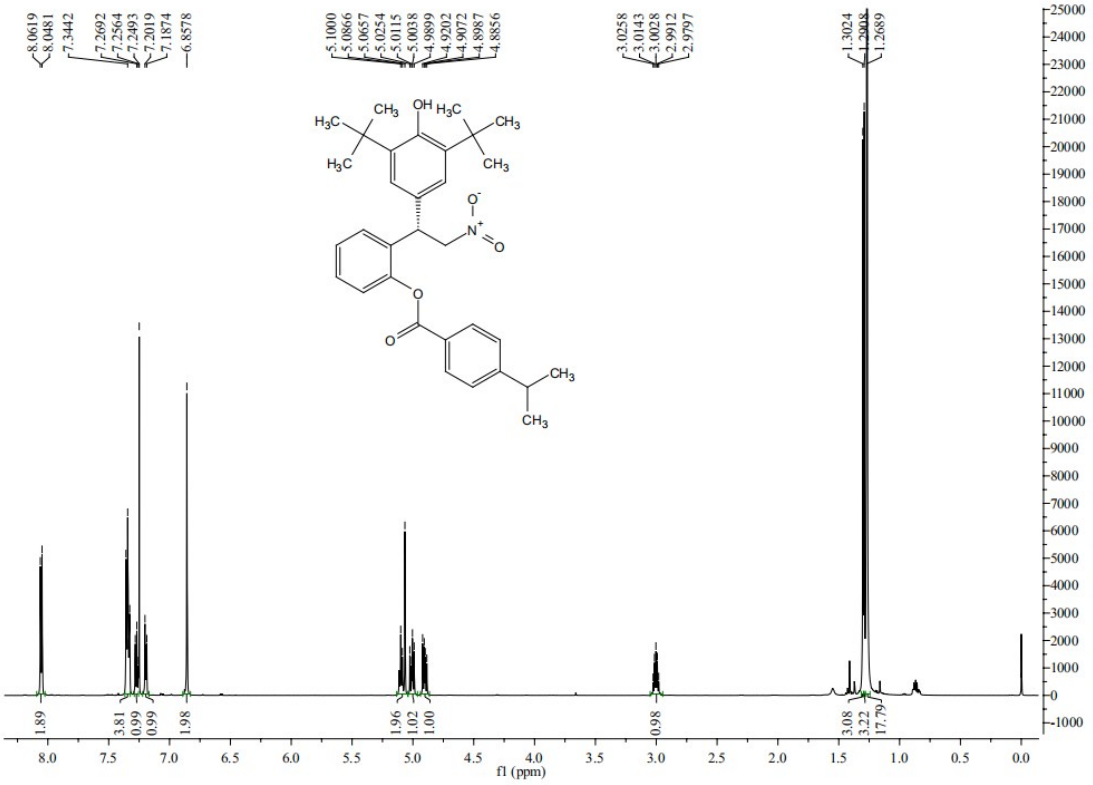


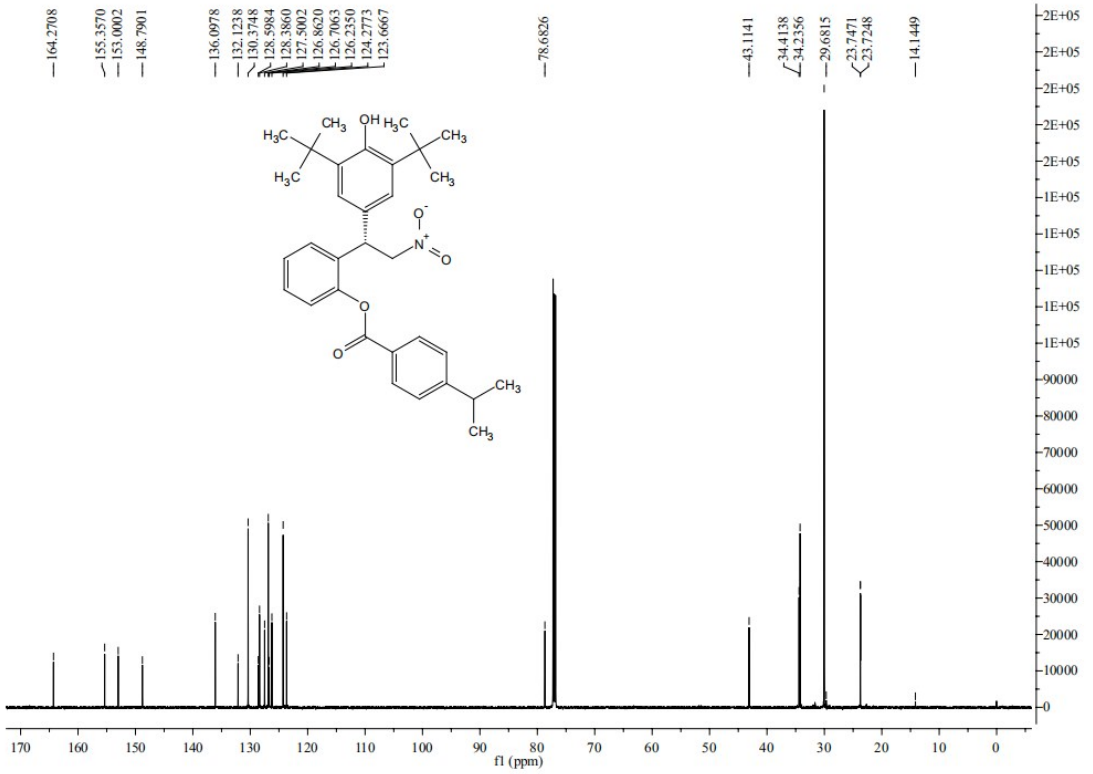
^{1}H and ^{13}C NMR of **3j**



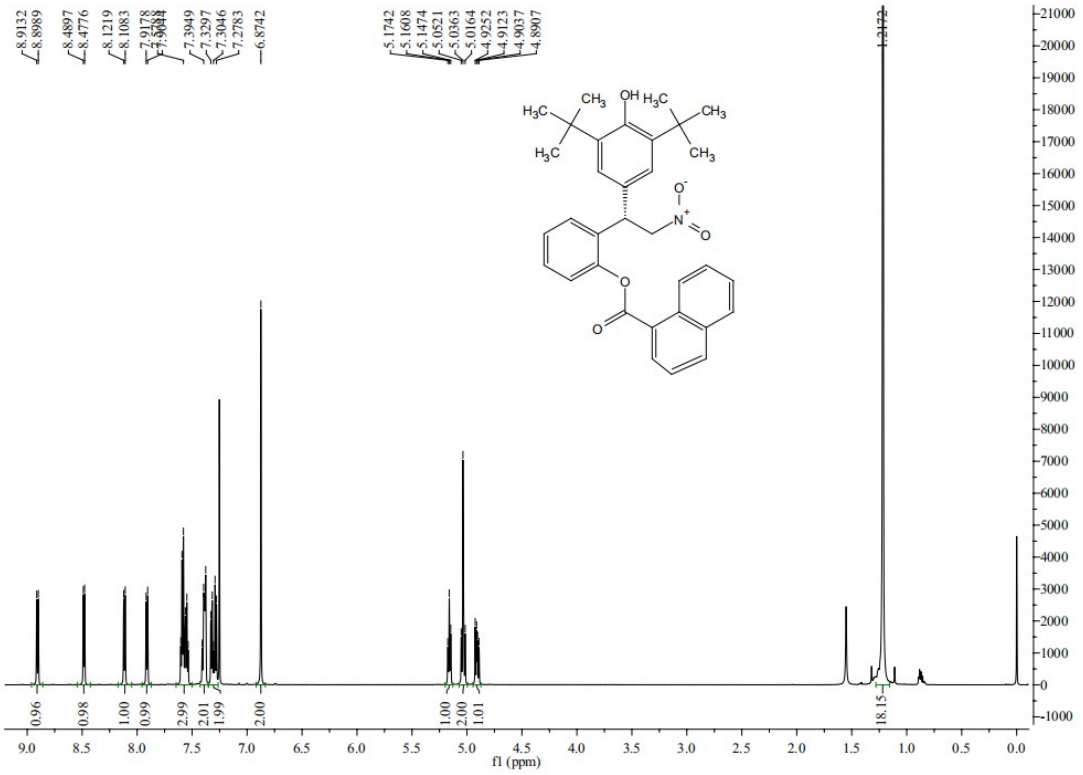


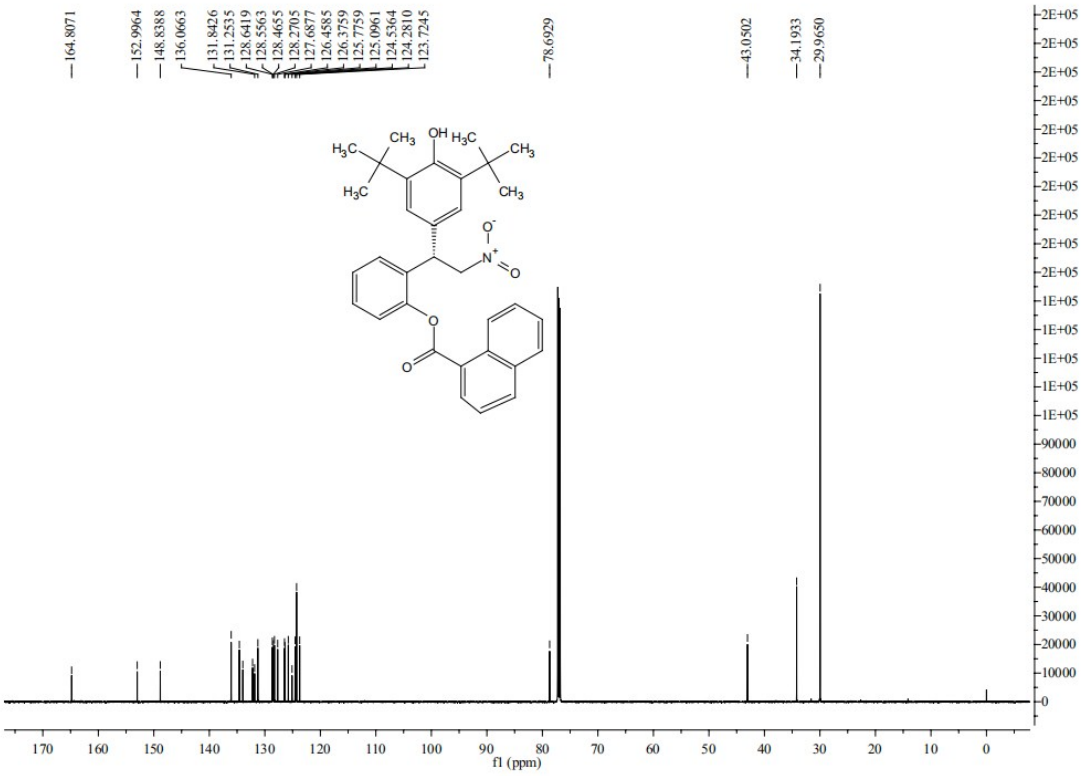
^{1}H and ^{13}C NMR of **3k**



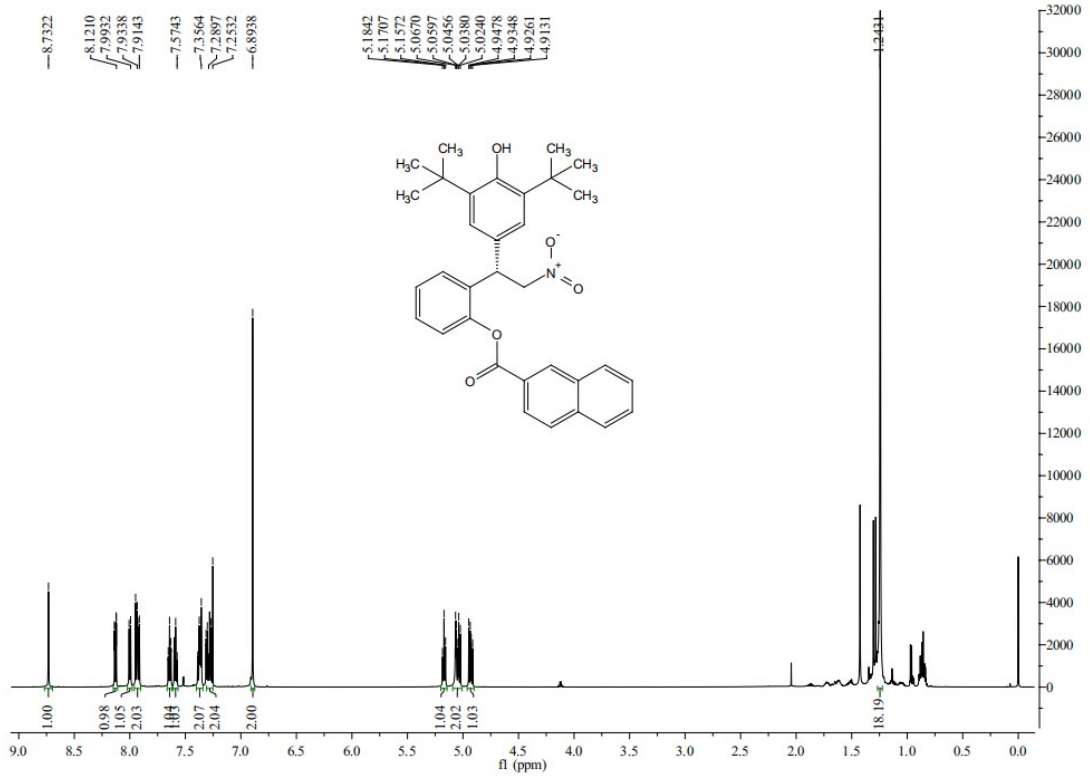


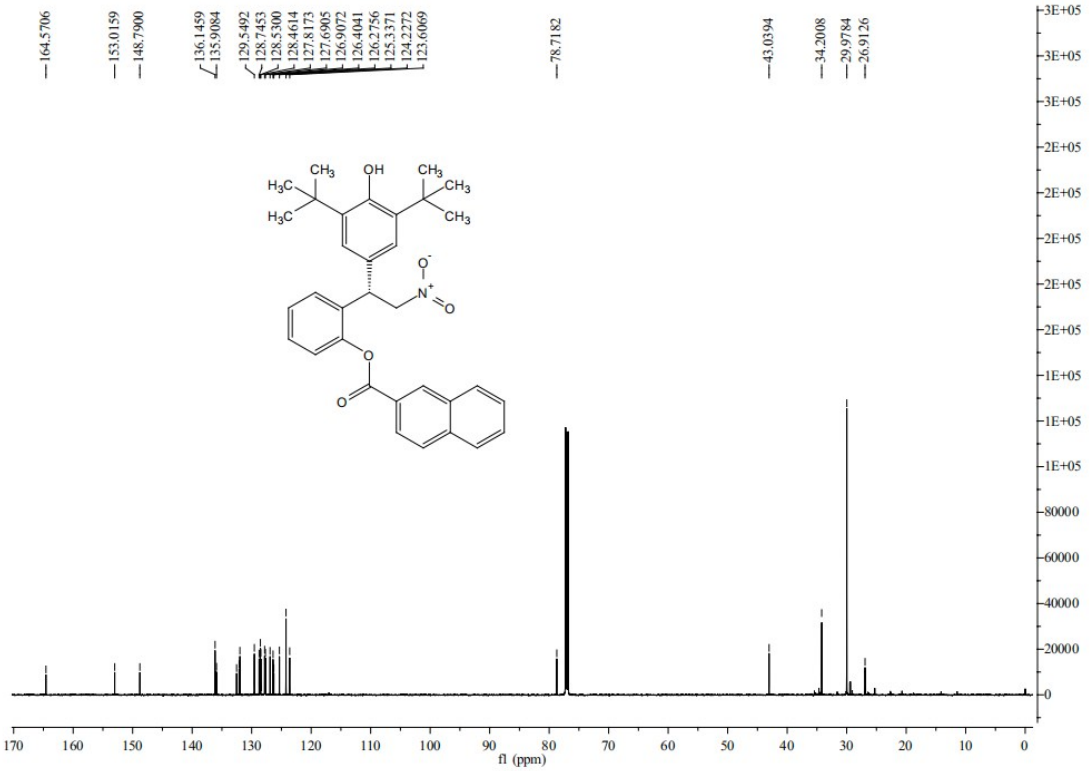
^{1}H and ^{13}C NMR of **3l**



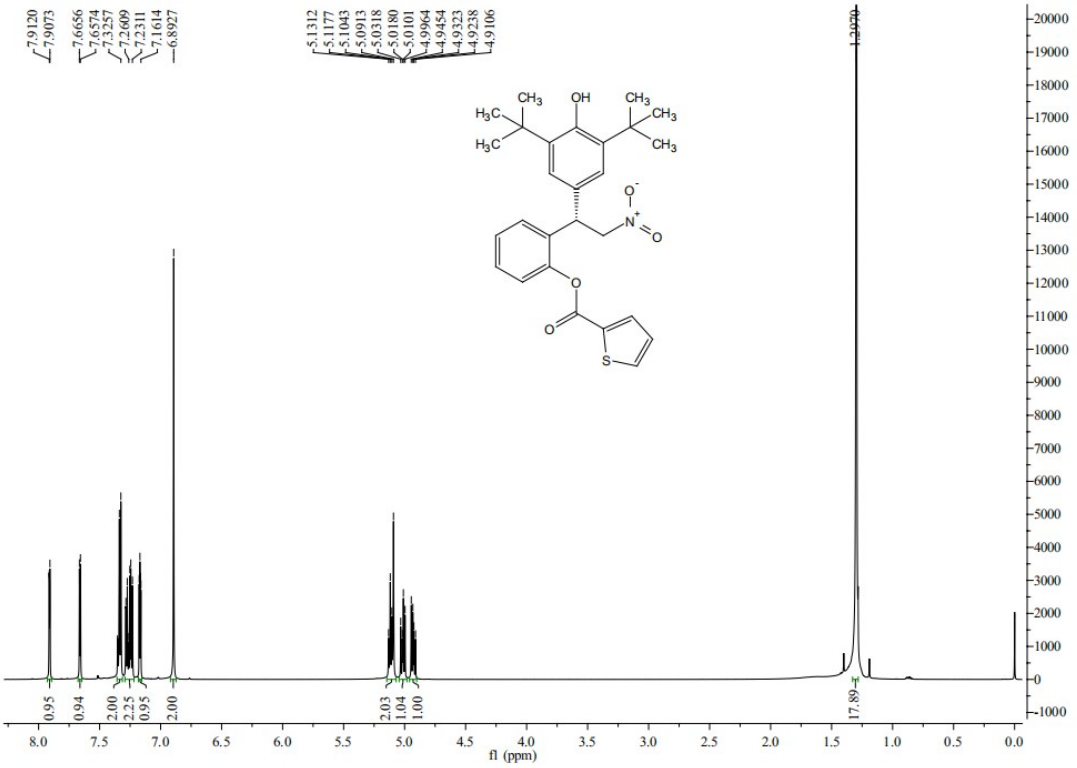


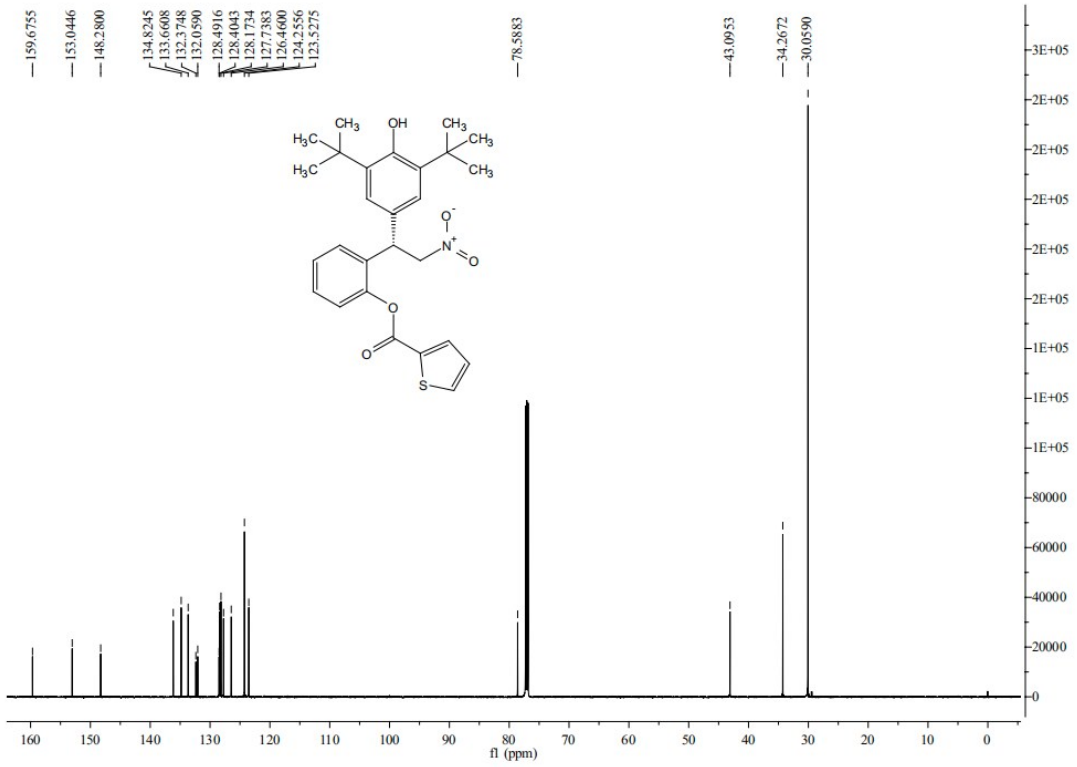
^{1}H and ^{13}C NMR of **3m**



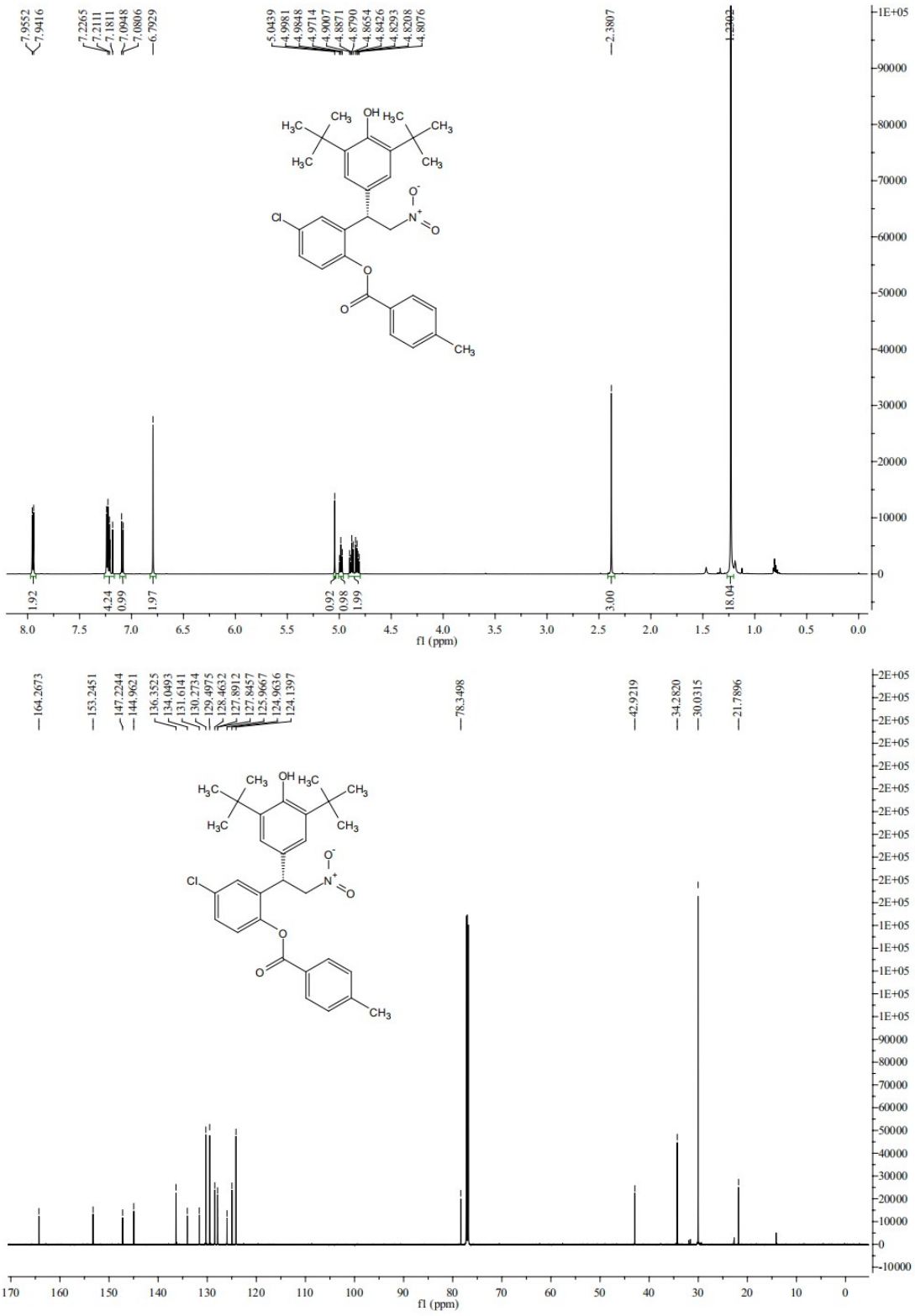


^{1}H and ^{13}C NMR of **3n**

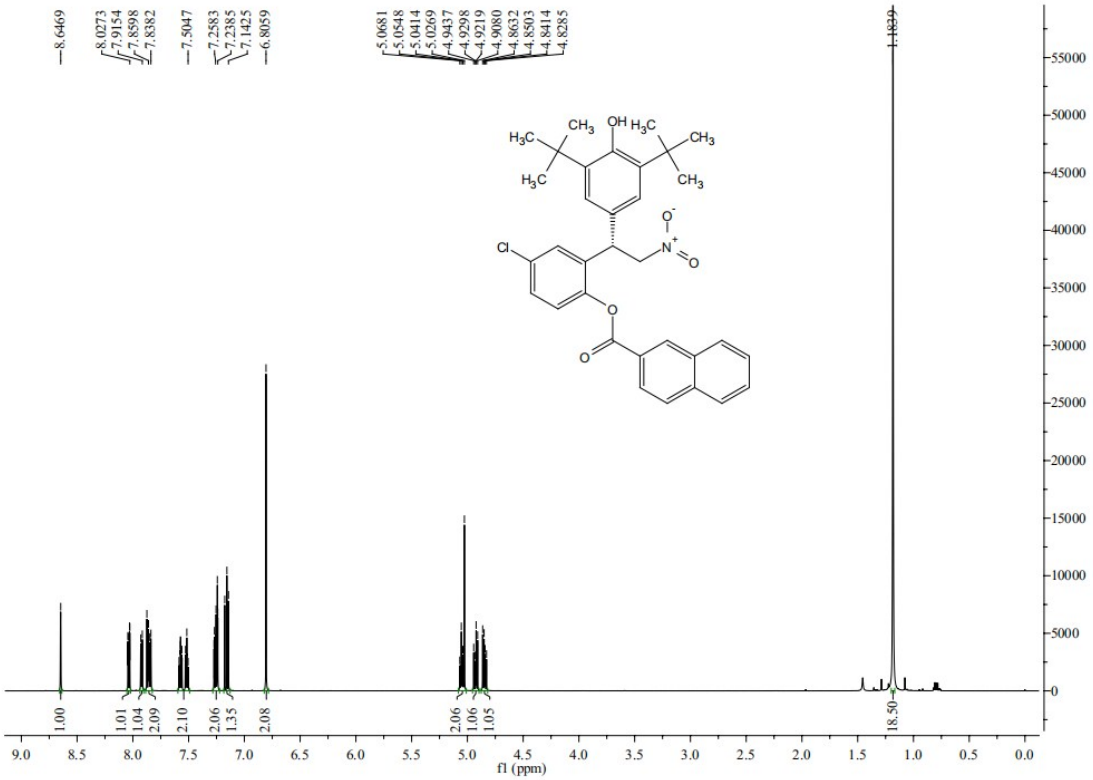


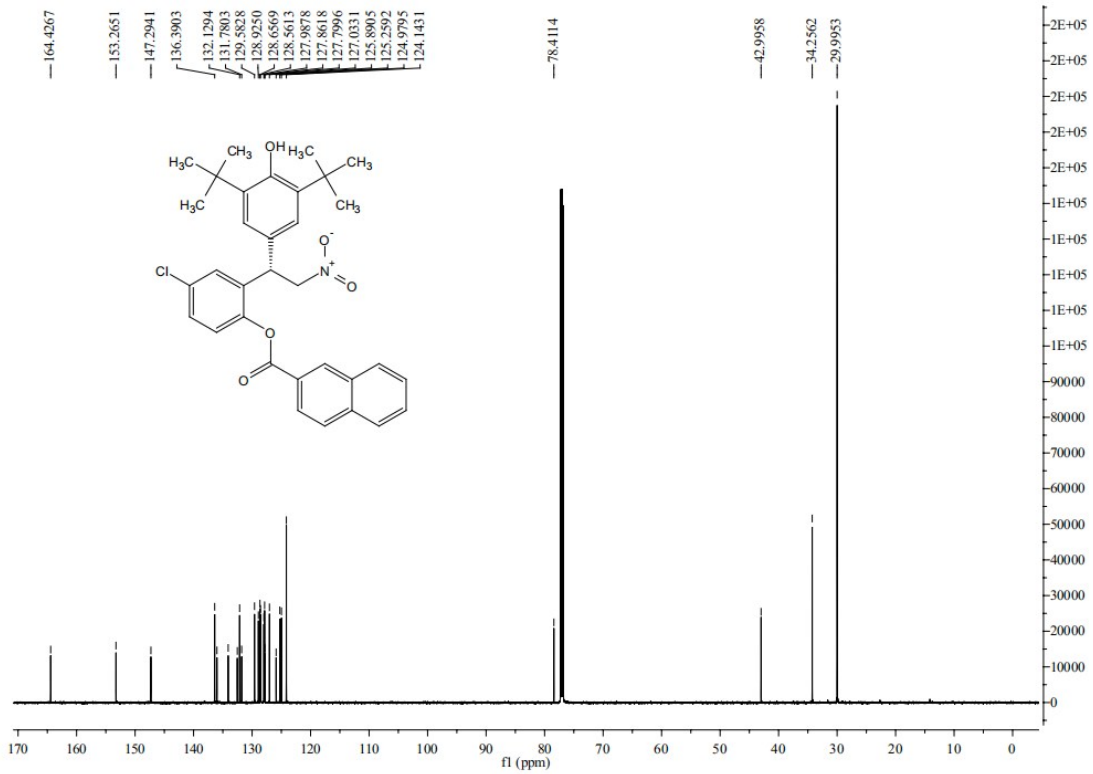


^{1}H and ^{13}C NMR of **3o**

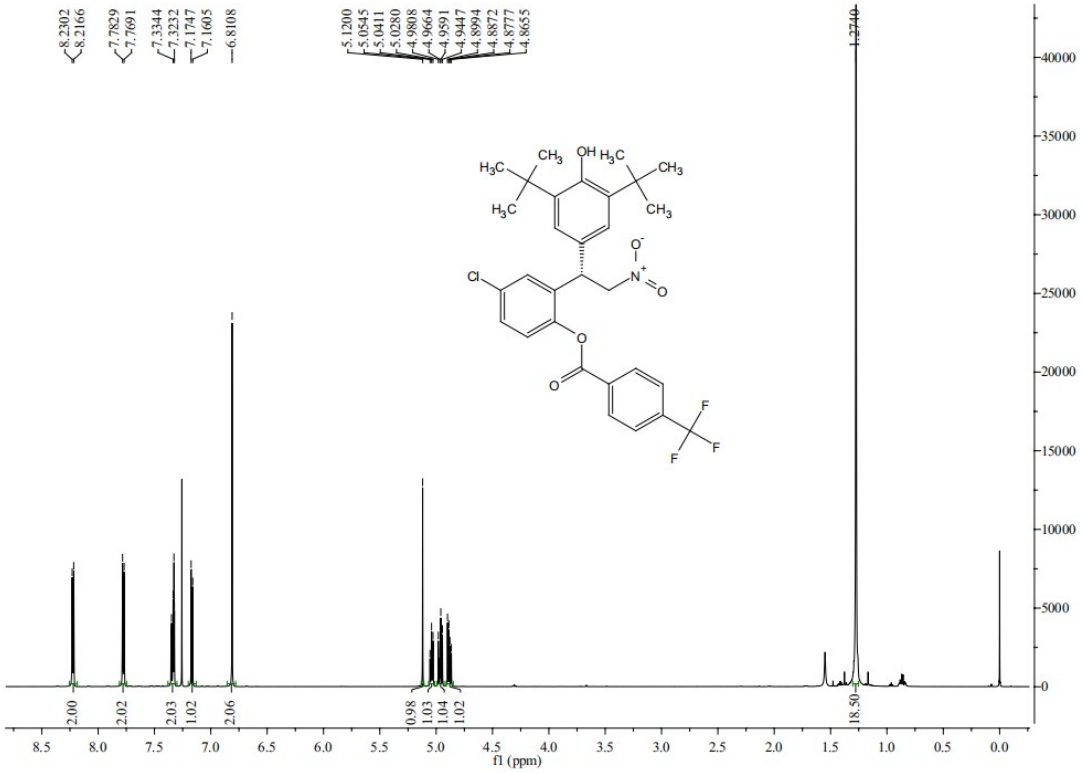


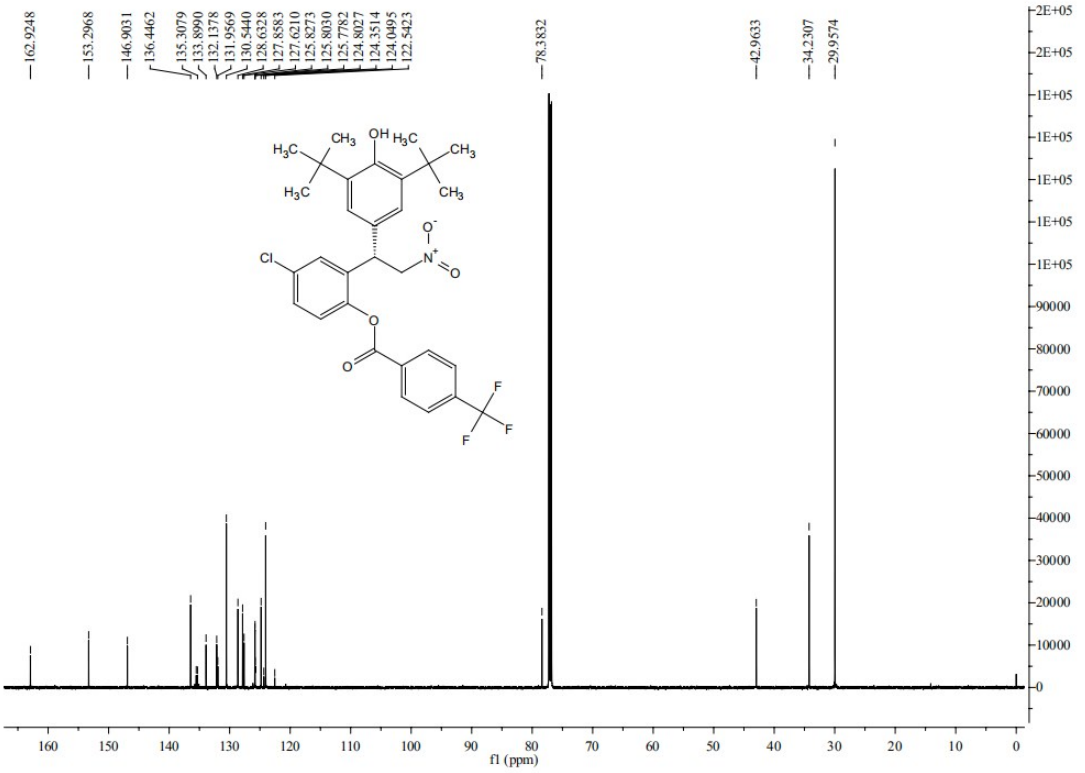
^{1}H and ^{13}C NMR of **3p**



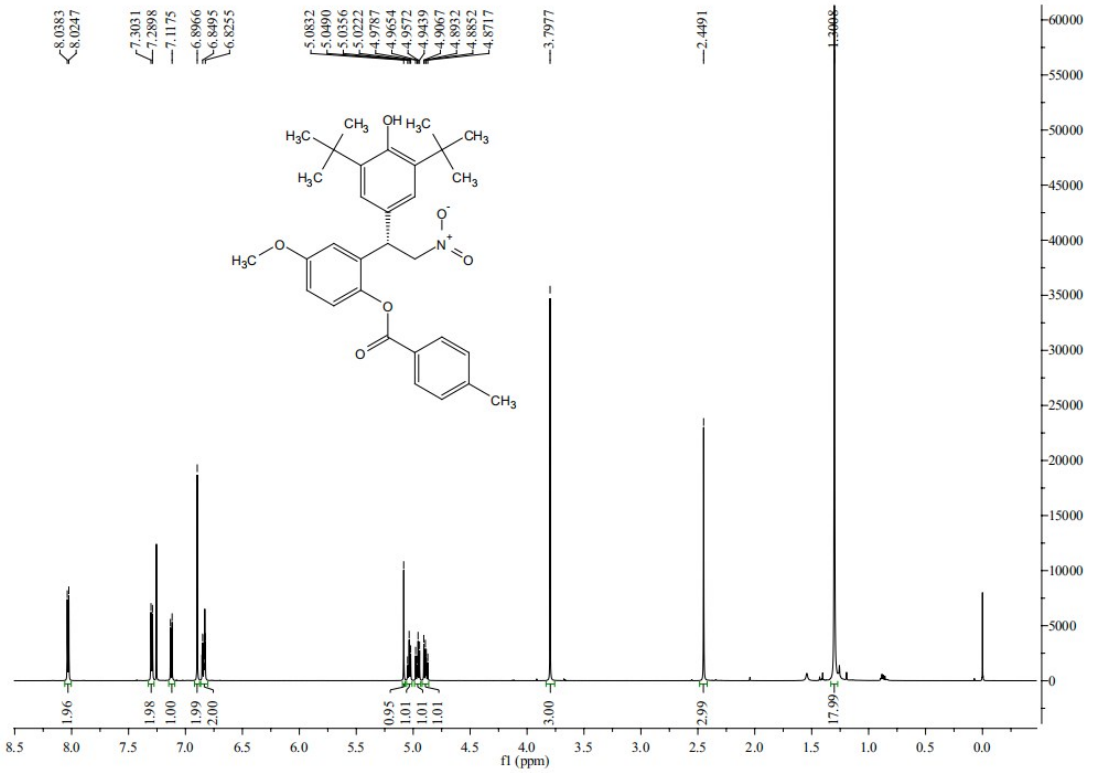


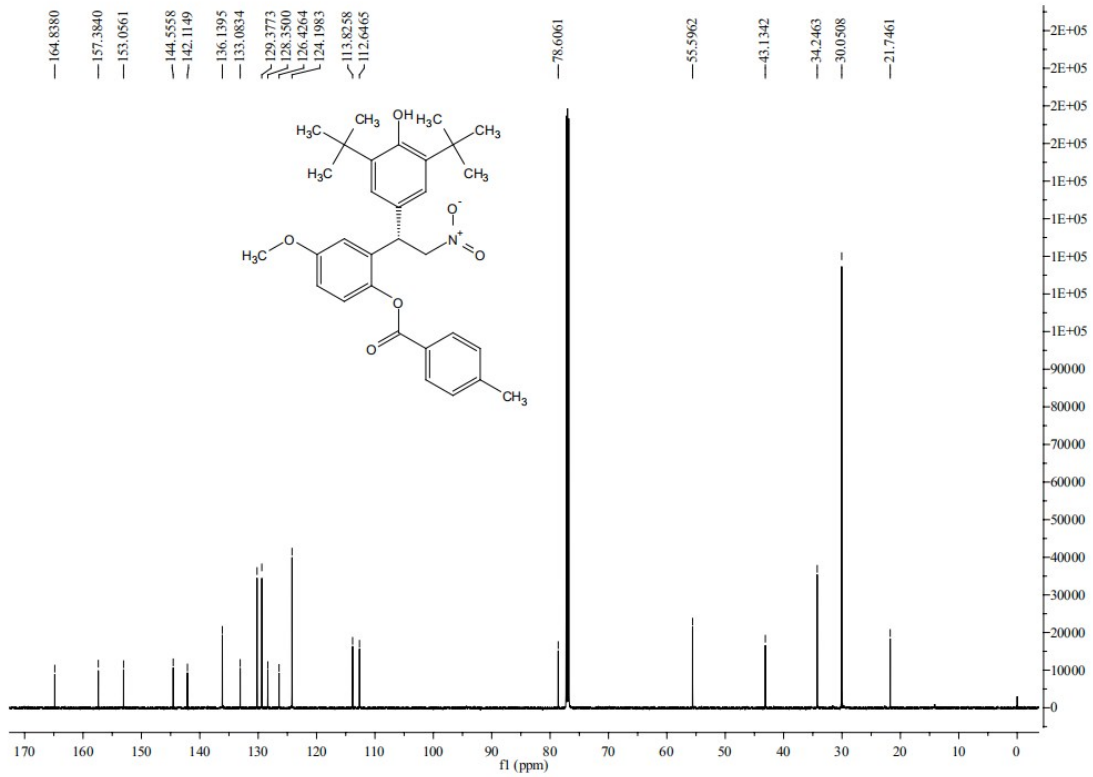
^{1}H and ^{13}C NMR of **3q**



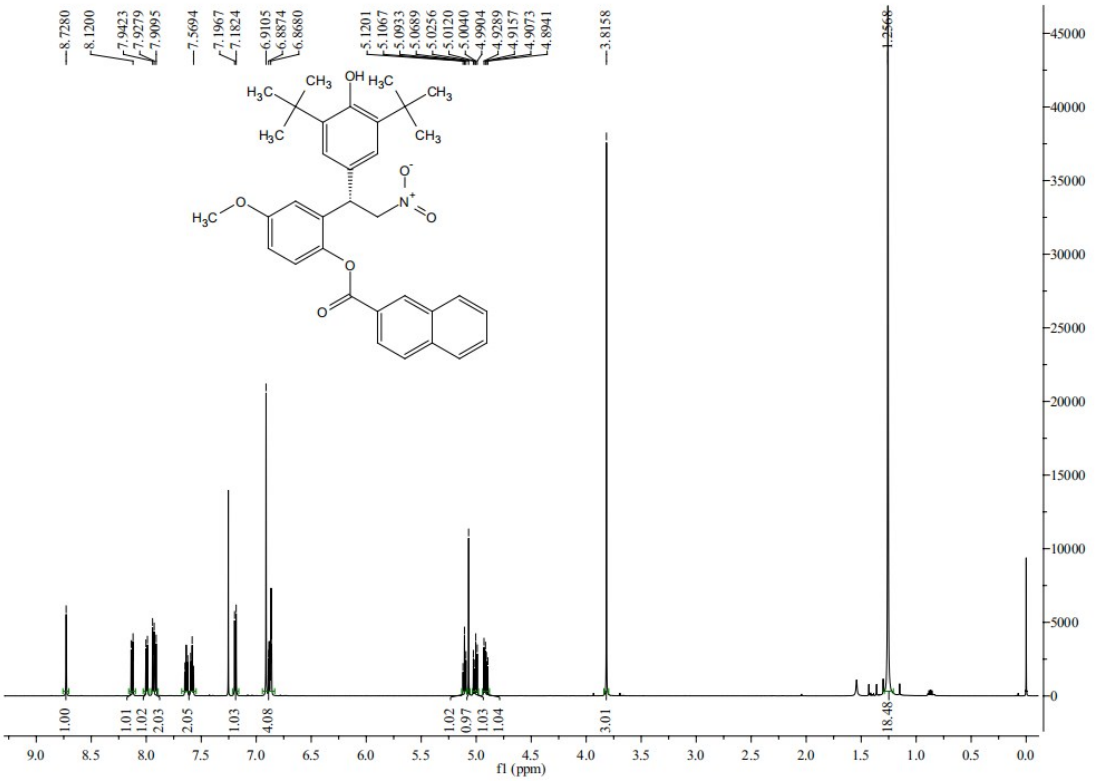


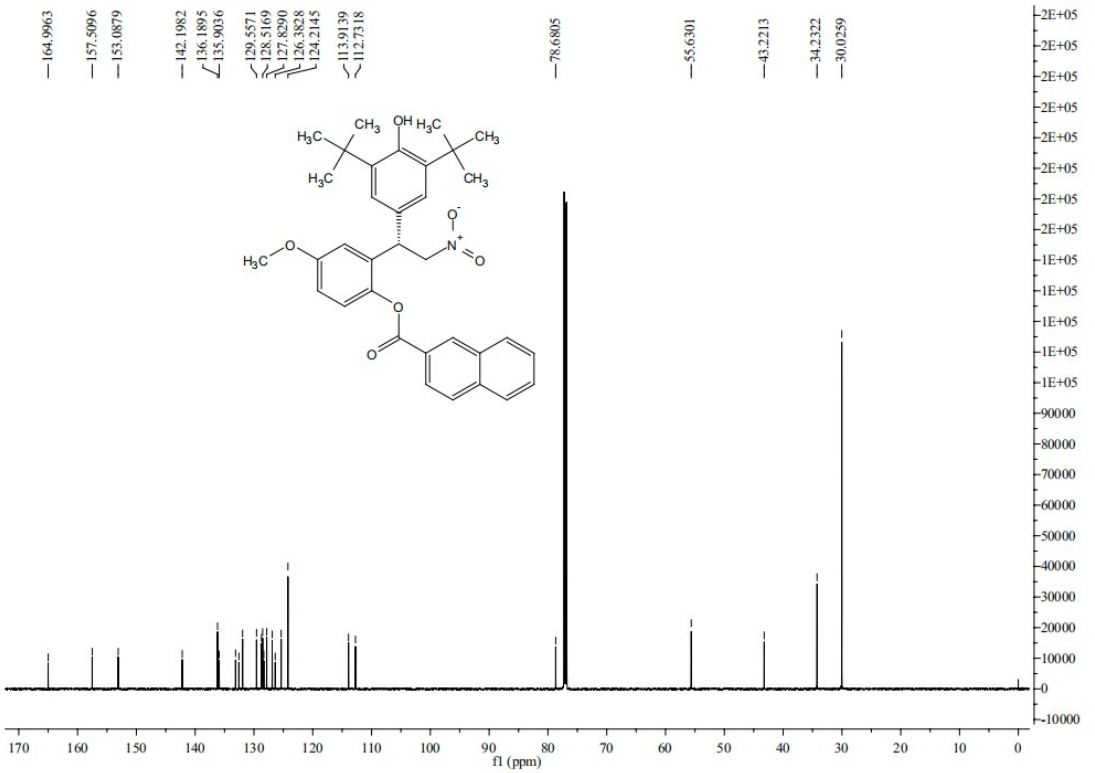
^{1}H and ^{13}C NMR of **3r**



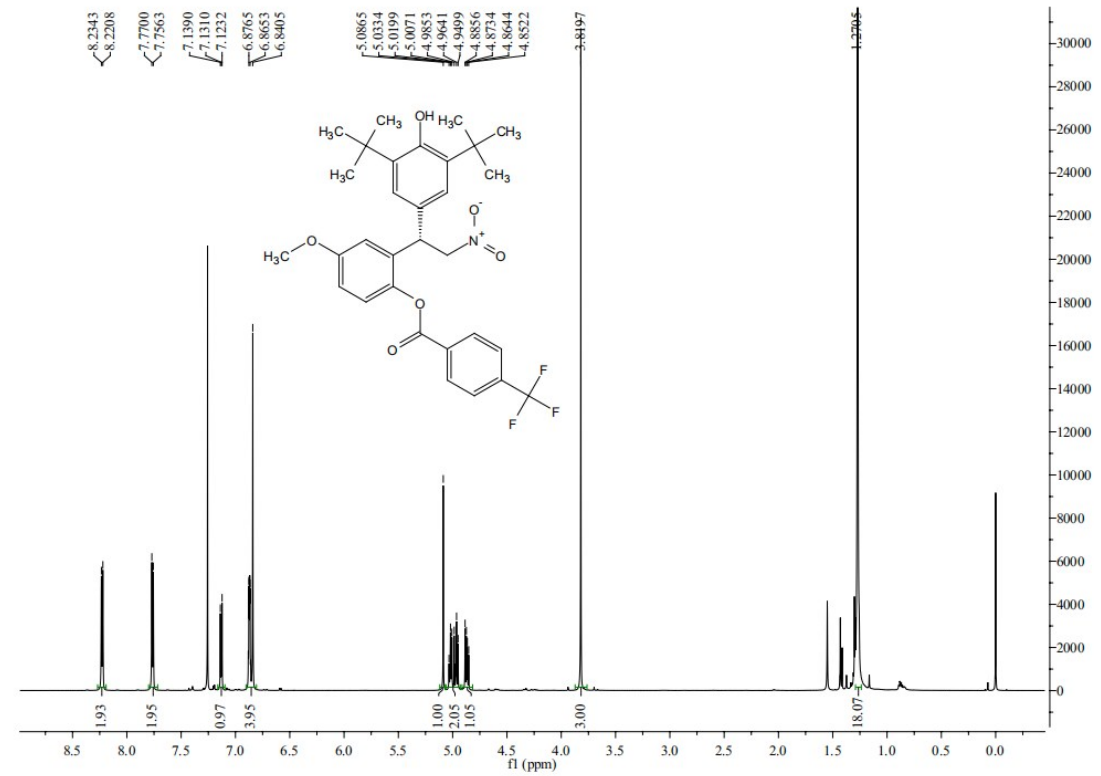


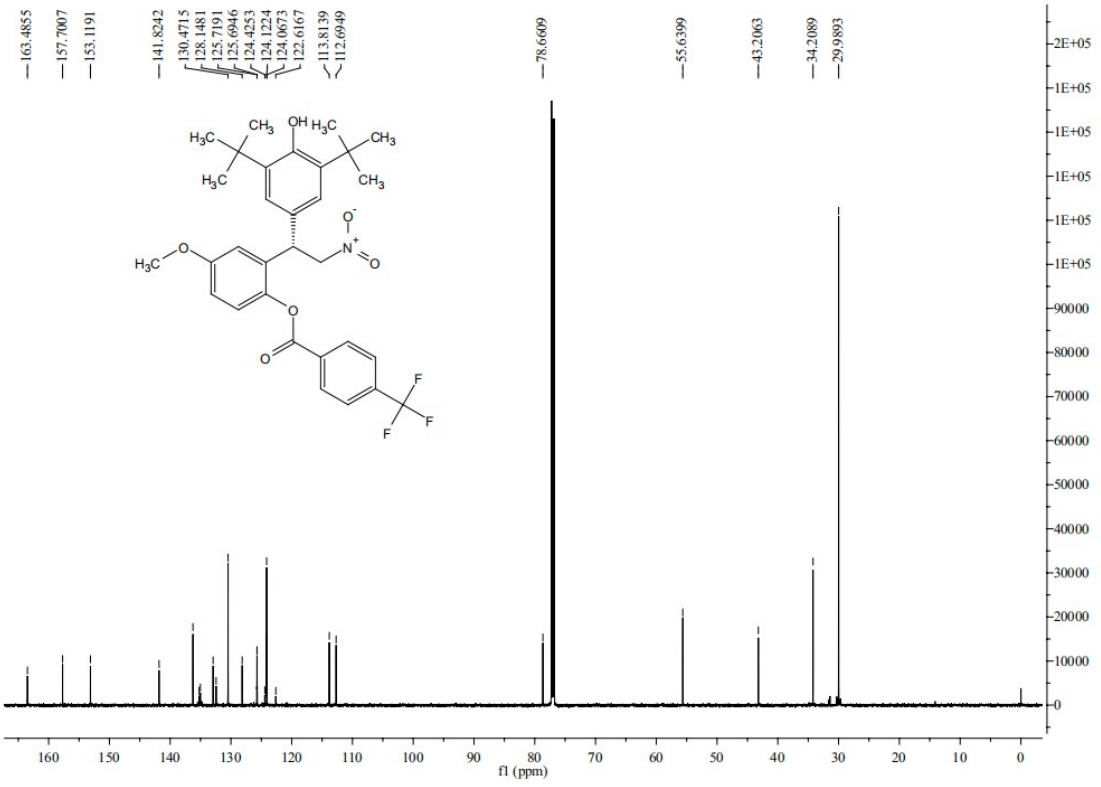
^{1}H and ^{13}C NMR of **3s**



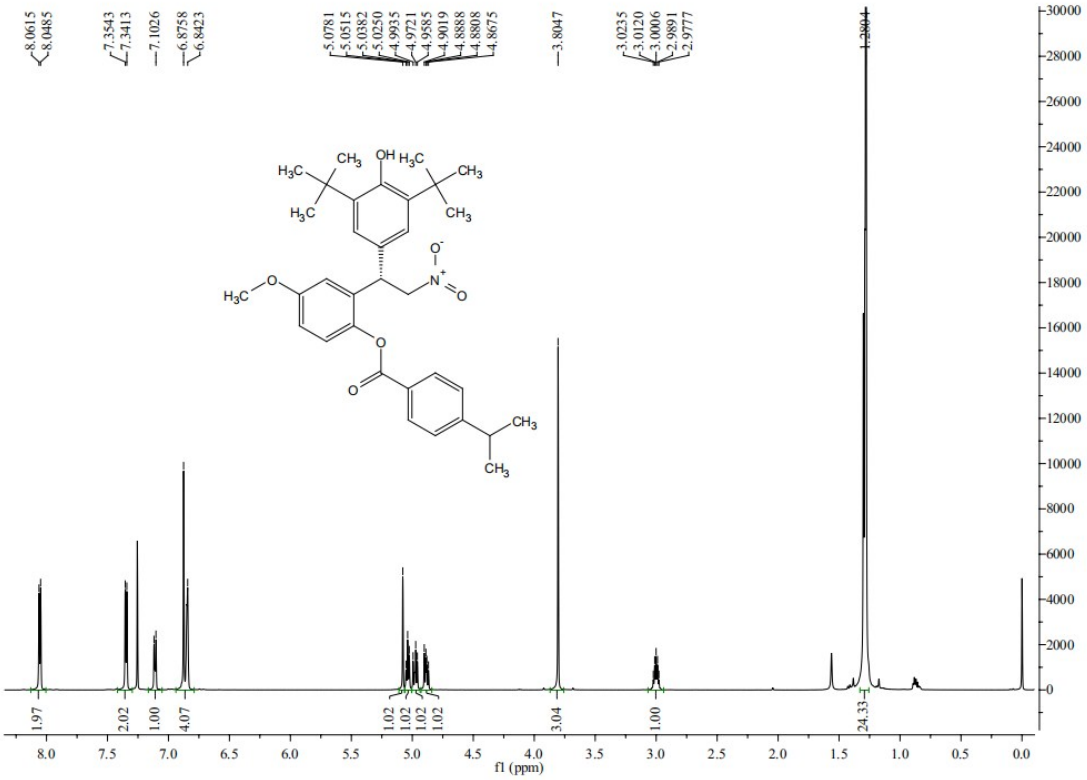


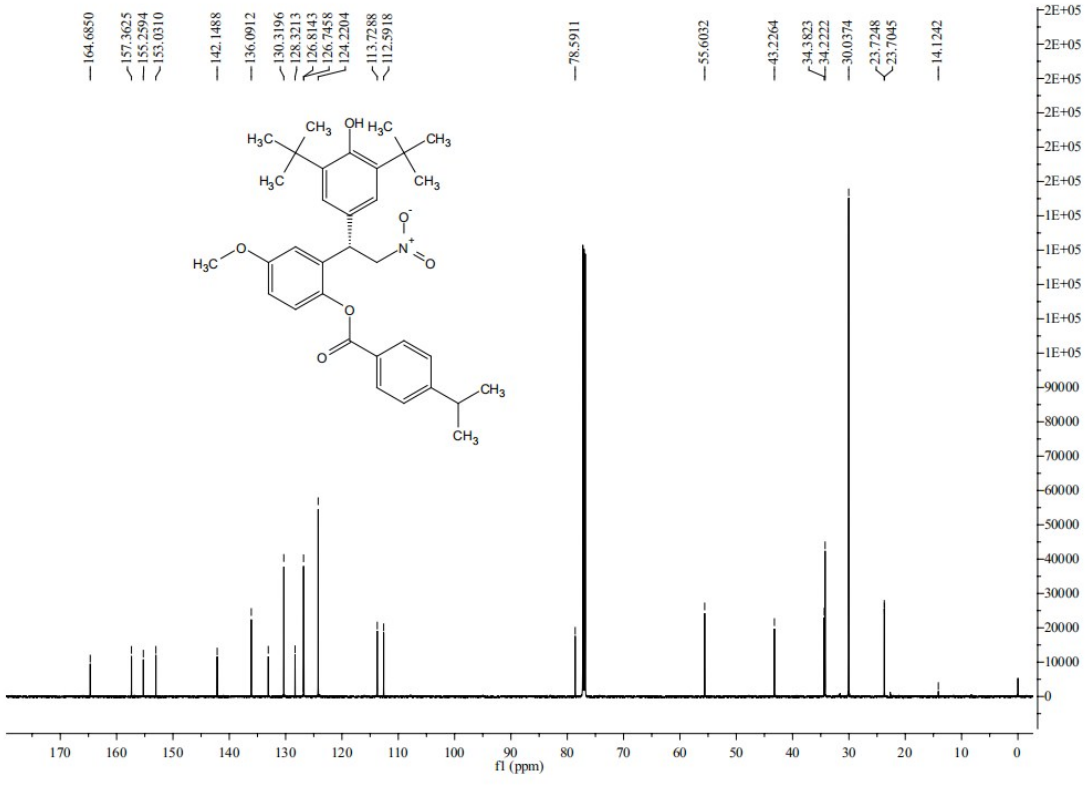
^{1}H and ^{13}C NMR of **3t**



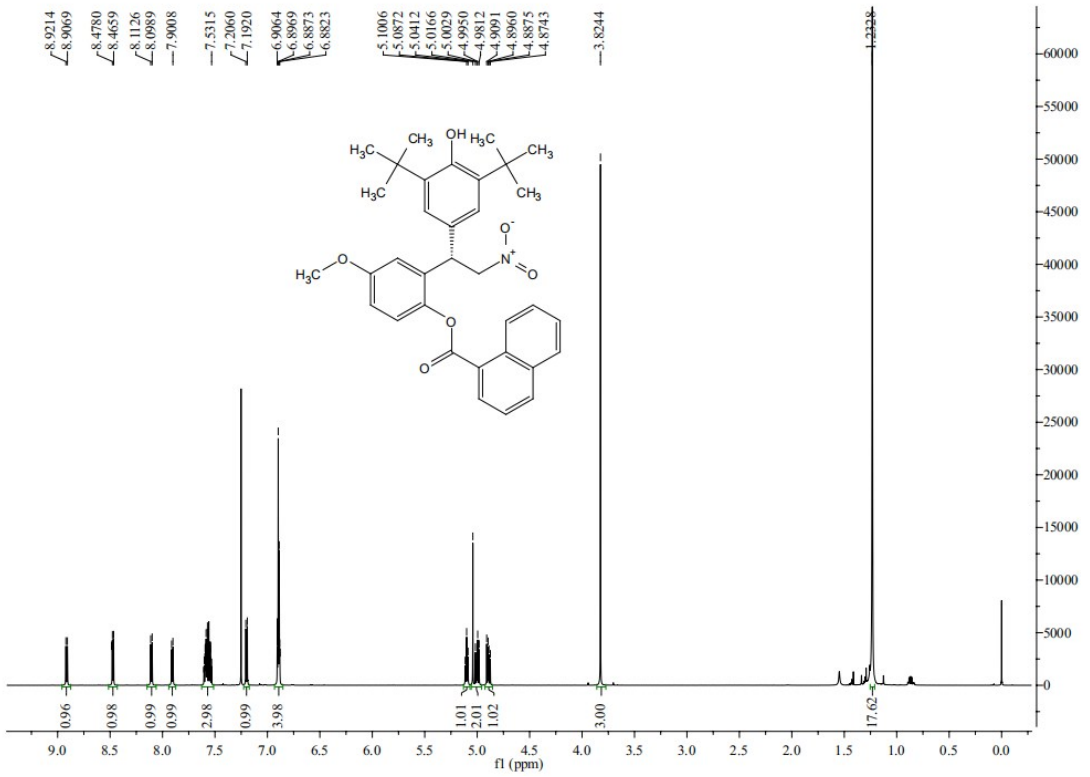


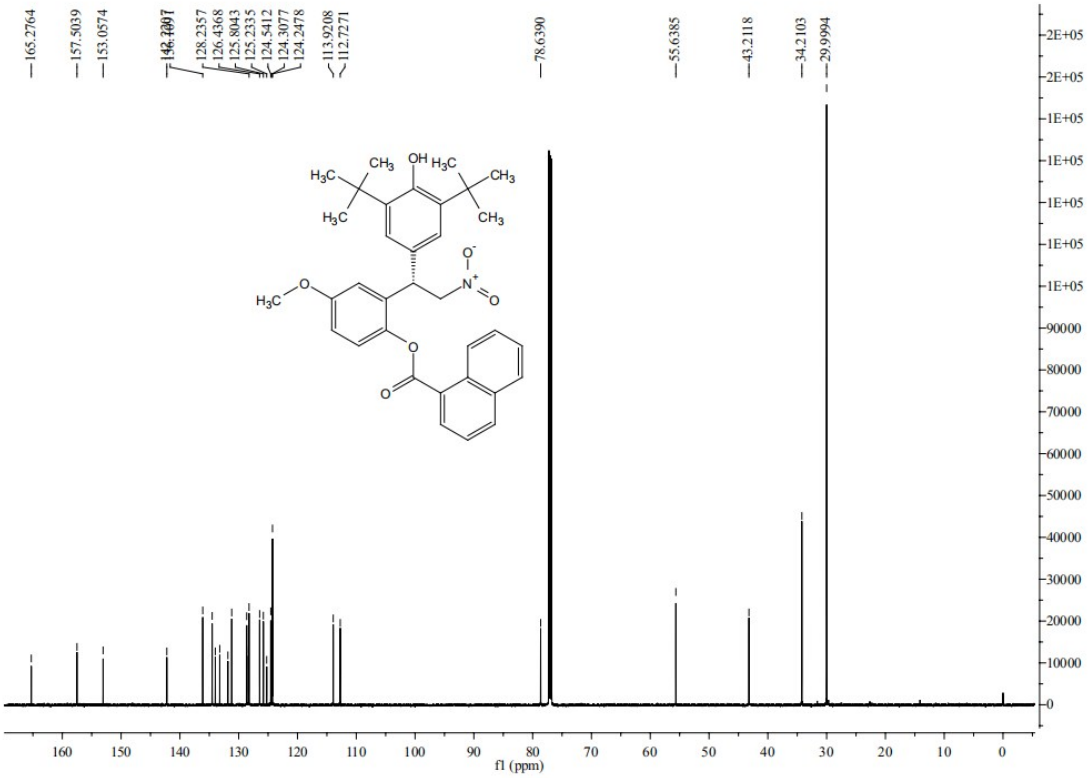
^{1}H and ^{13}C NMR of **3u**





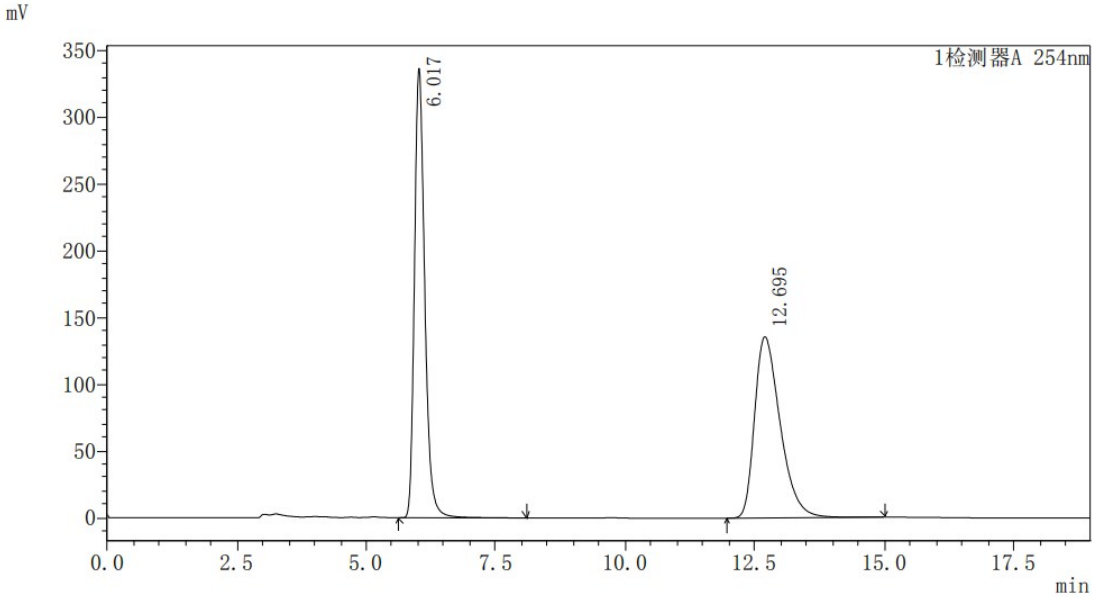
^{1}H and ^{13}C NMR of **3v**



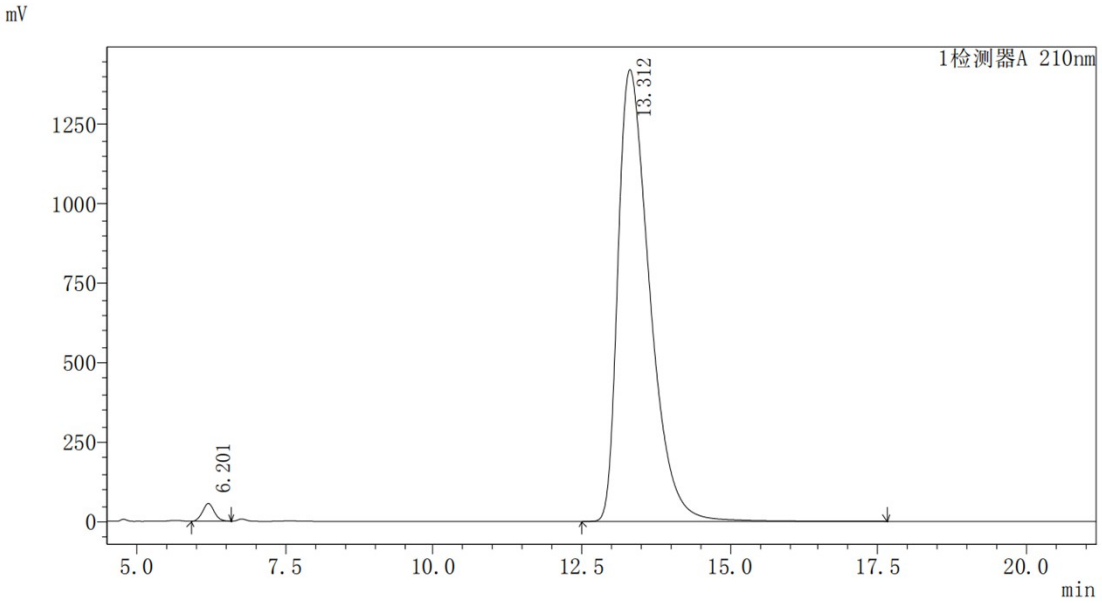


5. HPLC Spectra

HPLC of **3a**

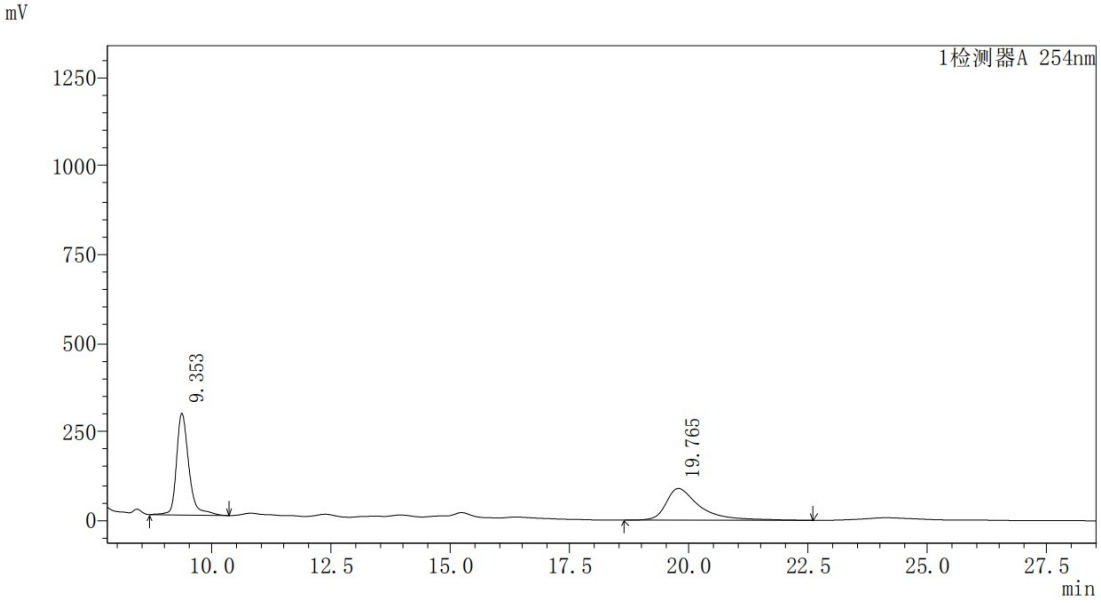


Peak number	Retention time	Area	Height	Concentration
1	6.017	4656838	336559	49.955
2	12.695	4665176	135689	50.045

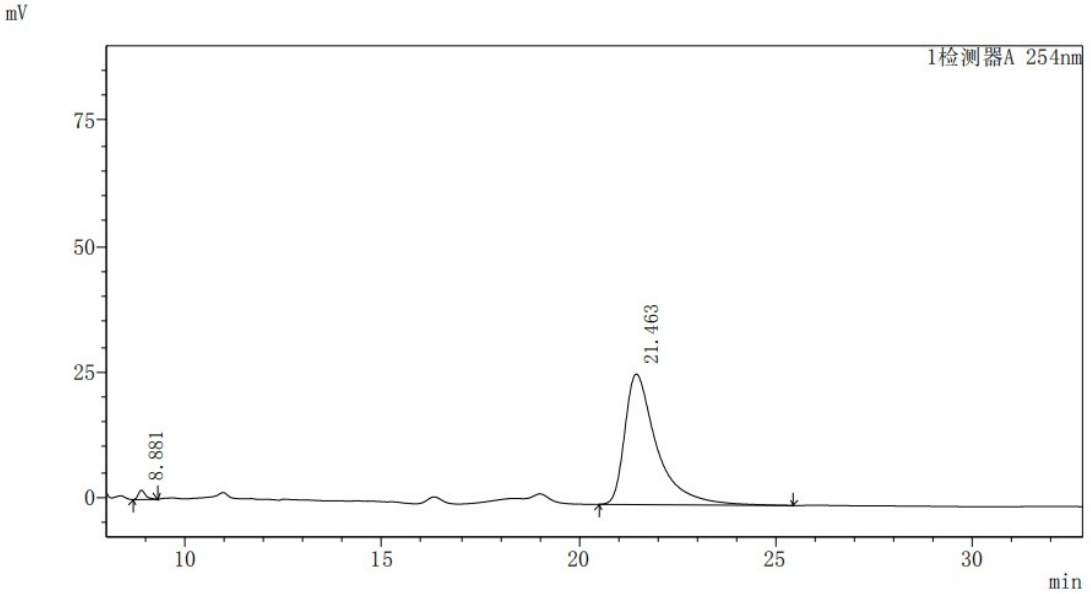


Peak number	Retention time	Area	Height	Concentration
1	6.201	769488	56016	1.439
2	13.312	52693689	1421938	98.561

HPLC of **3b**

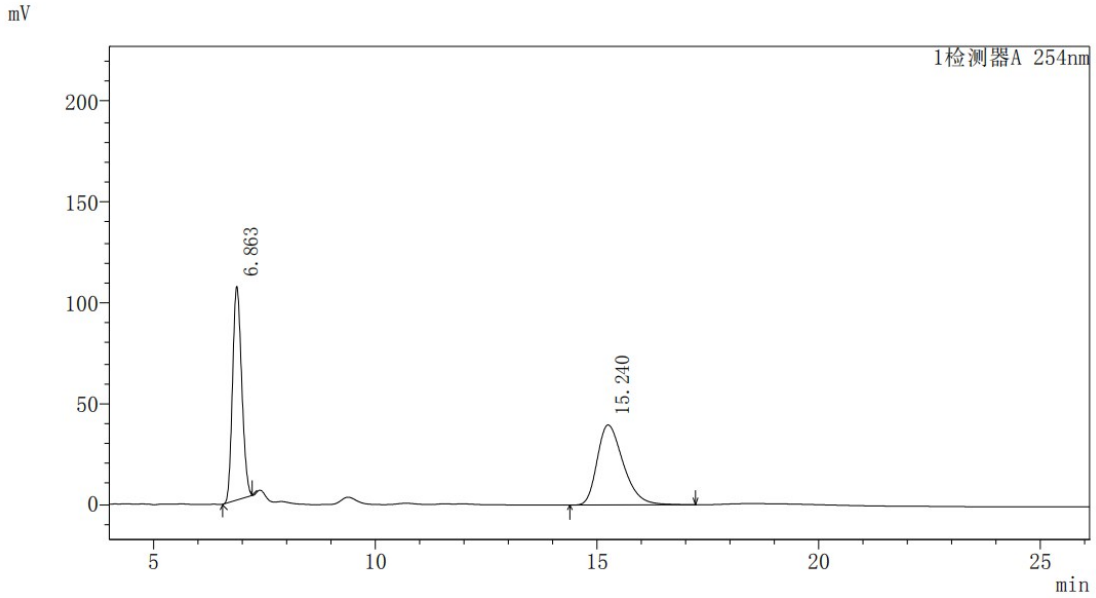


Peak number	Retention time	Area	Height	Concentration
1	9.353	5175024	287311	53.901
2	19.765	4425923	89751	46.099

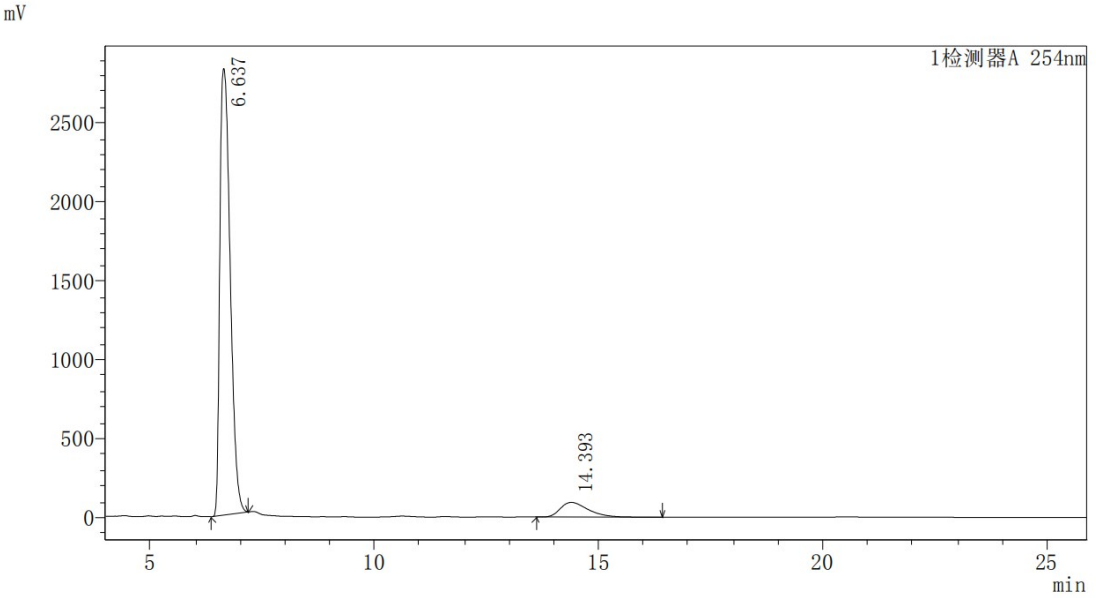


Peak number	Retention time	Area	Height	Concentration
1	8.881	23577	1856	1.575
2	21.463	1473122	25997	98.425

HPLC of **3c**

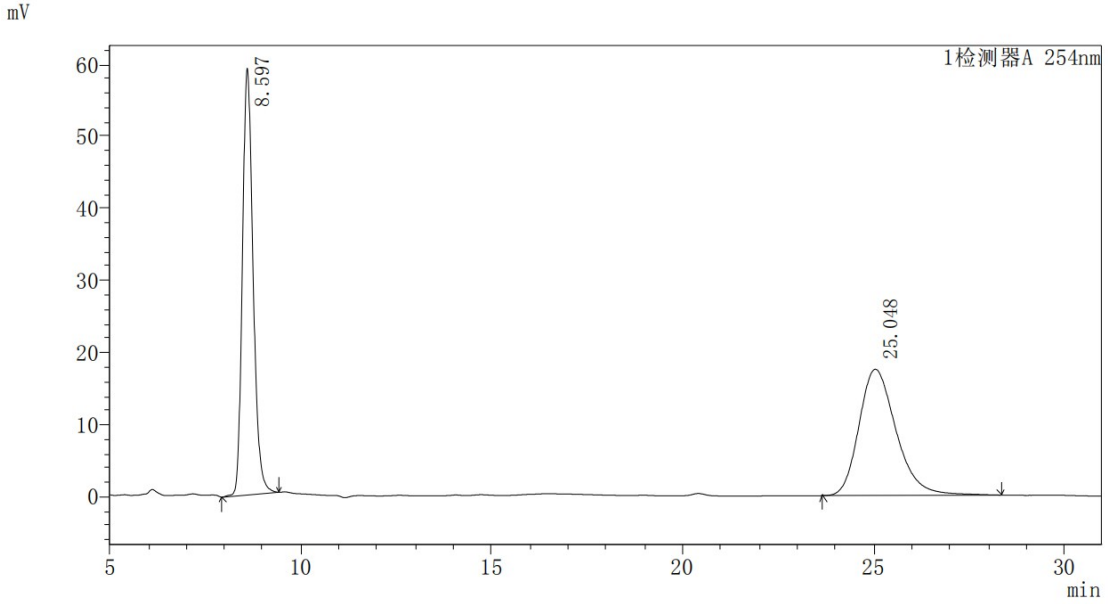


Peak number	Retention time	Area	Height	Concentration
1	6.863	1530858	106280	48.374
2	15.240	1633801	39865	51.626

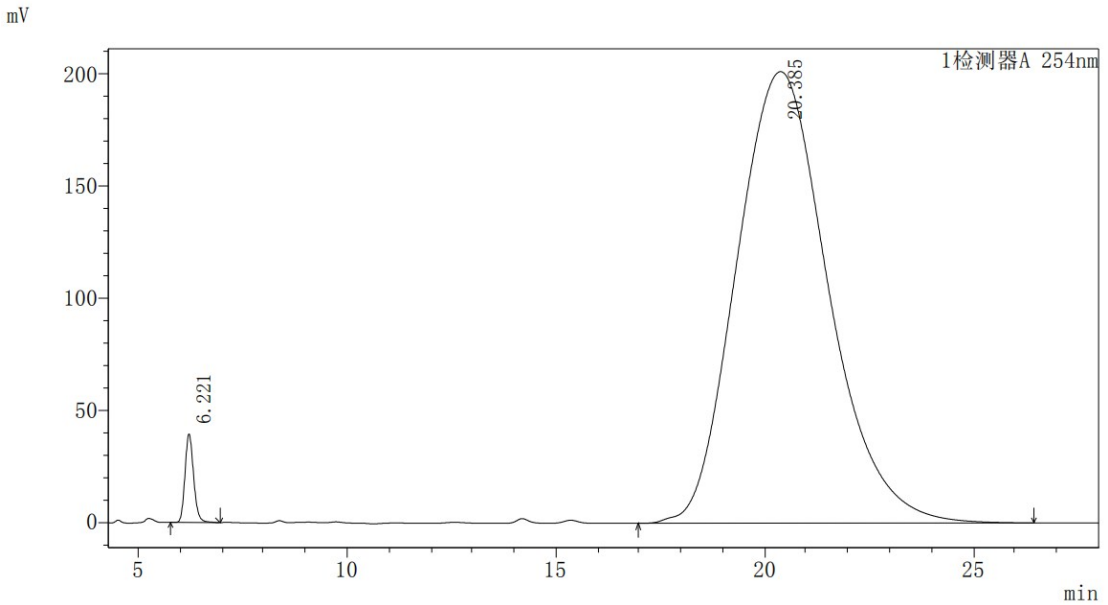


Peak number	Retention time	Area	Height	Concentration
1	6.637	45526971	2832039	91.852
2	14.393	4038632	93396	8.148

HPLC of **3d**

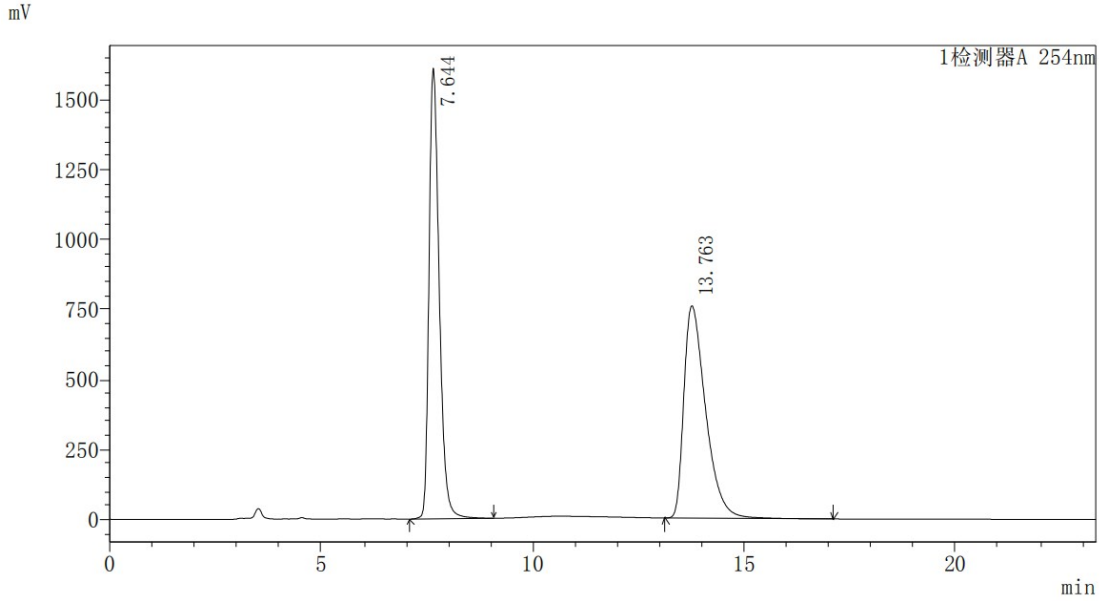


Peak number	Retention time	Area	Height	Concentration
1	8.597	1154034	59232	49.330
2	25.048	1185363	17518	50.670

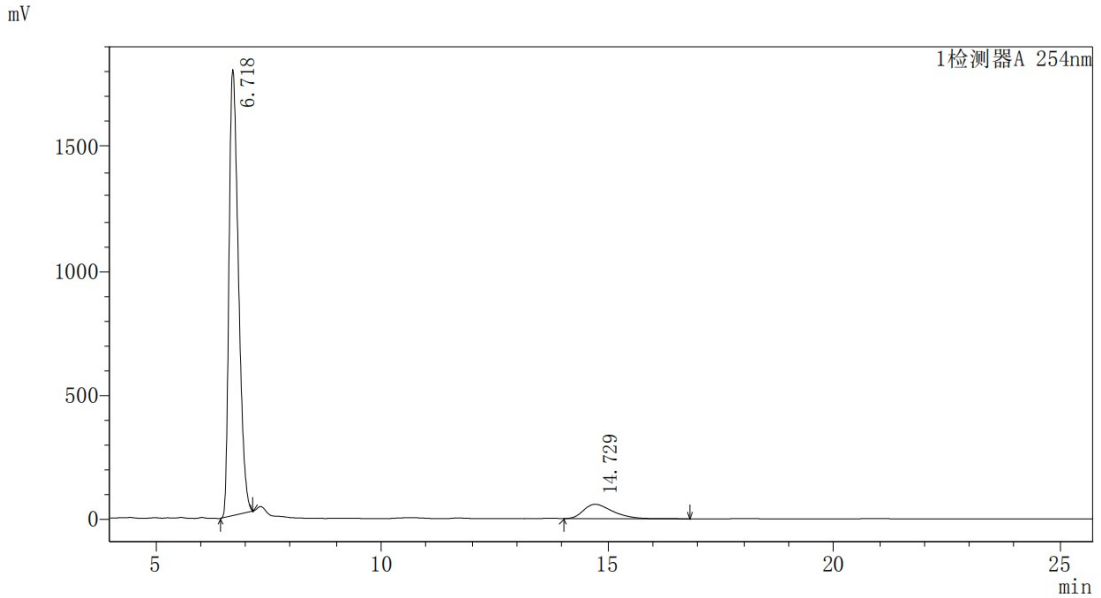


Peak number	Retention time	Area	Height	Concentration
1	6.221	569554	39534	1.820
2	20.385	30727547	201664	98.180

HPLC of **3e**

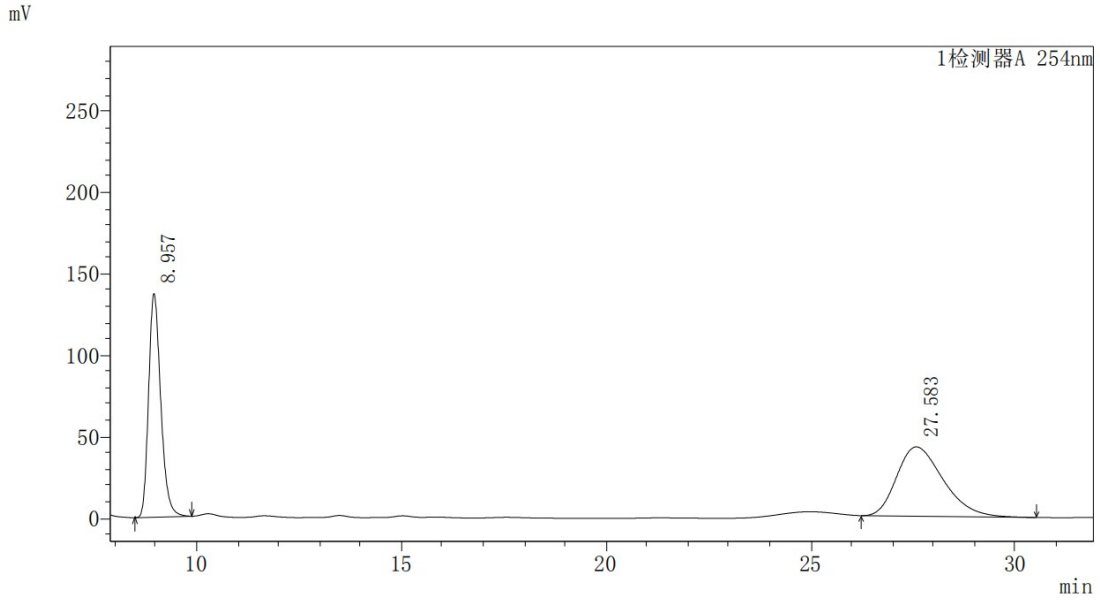


Peak number	Retention time	Area	Height	Concentration
1	7.644	27097131	1610336	49.904
2	13.763	27201640	759217	50.096

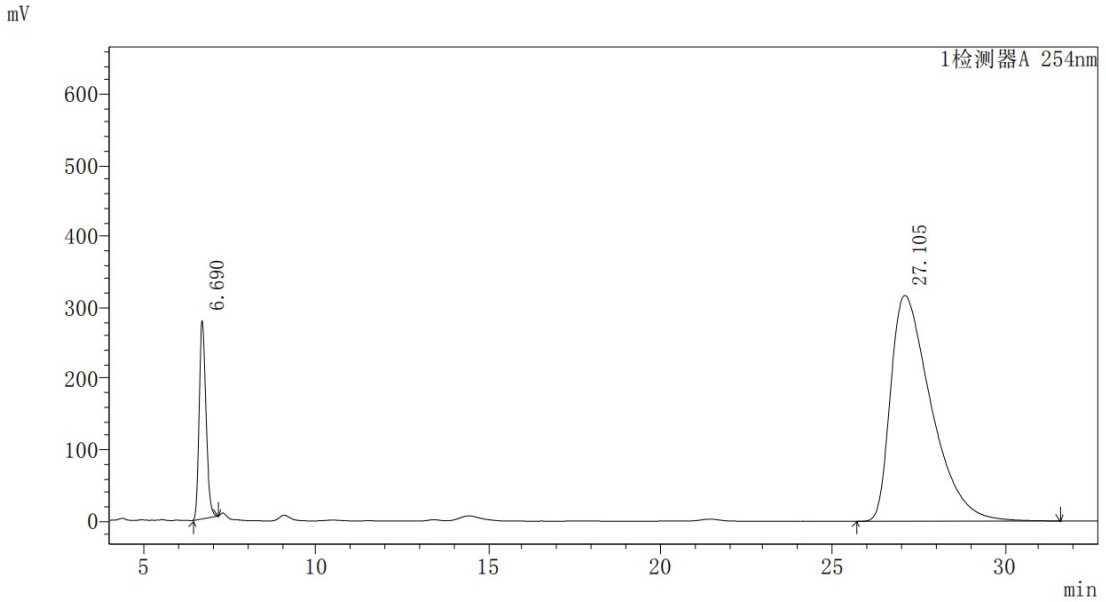


Peak number	Retention time	Area	Height	Concentration
1	6.718	26154237	1798632	90.975
2	14.729	2594501	57818	9.025

HPLC of **3f**

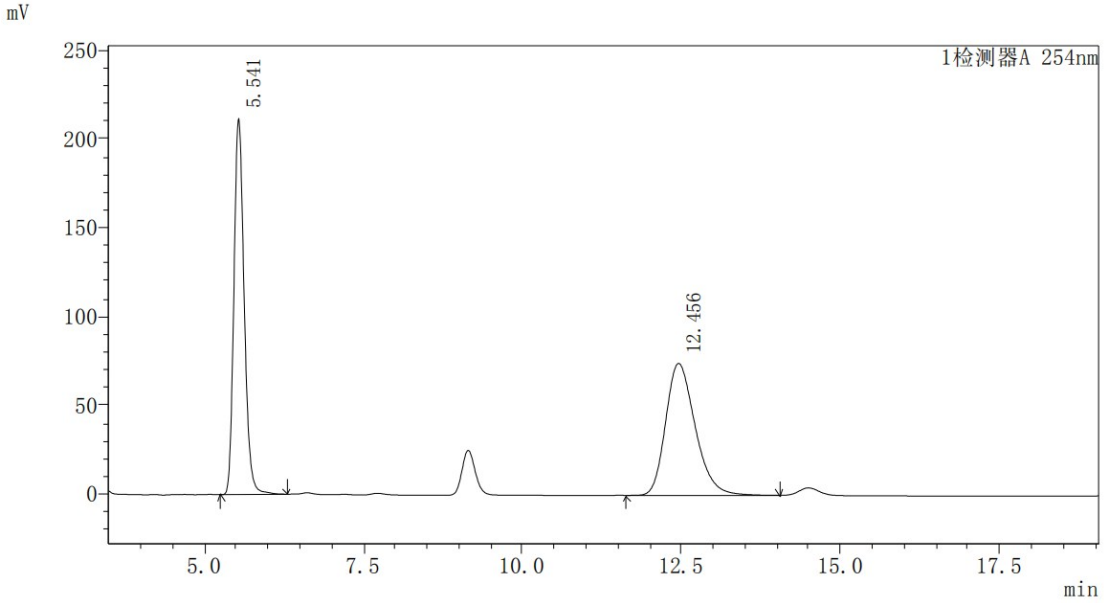


Peak number	Retention time	Area	Height	Concentration
1	8.957	2839030	137471	45.775
2	27.583	3363121	42611	54.225

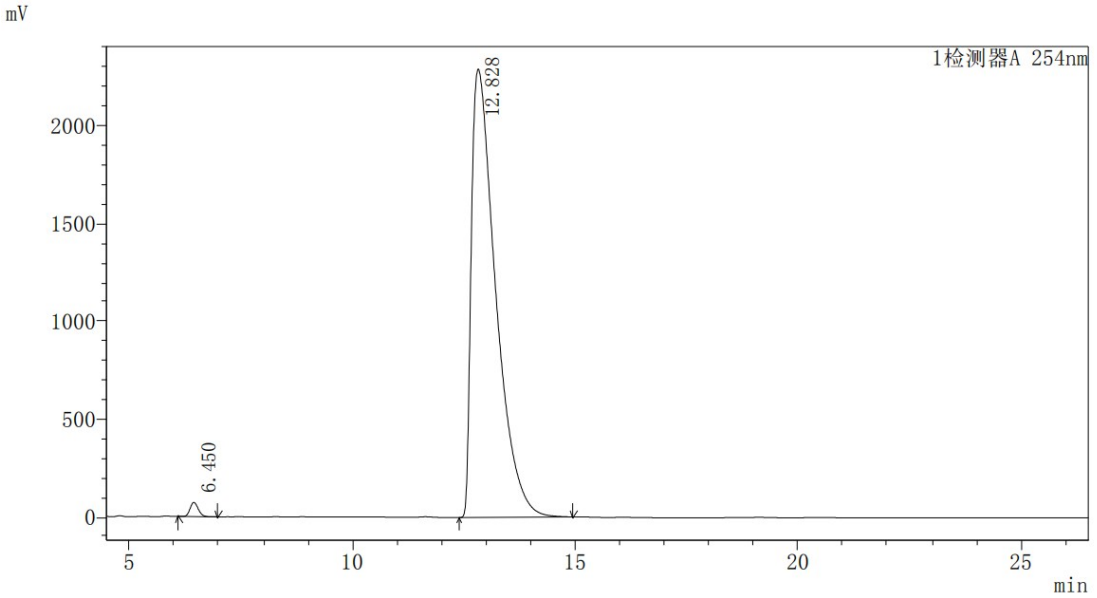


Peak number	Retention time	Area	Height	Concentration
1	6.690	3848846	278706	12.901
2	27.105	25984395	317253	87.099

HPLC of **3g**

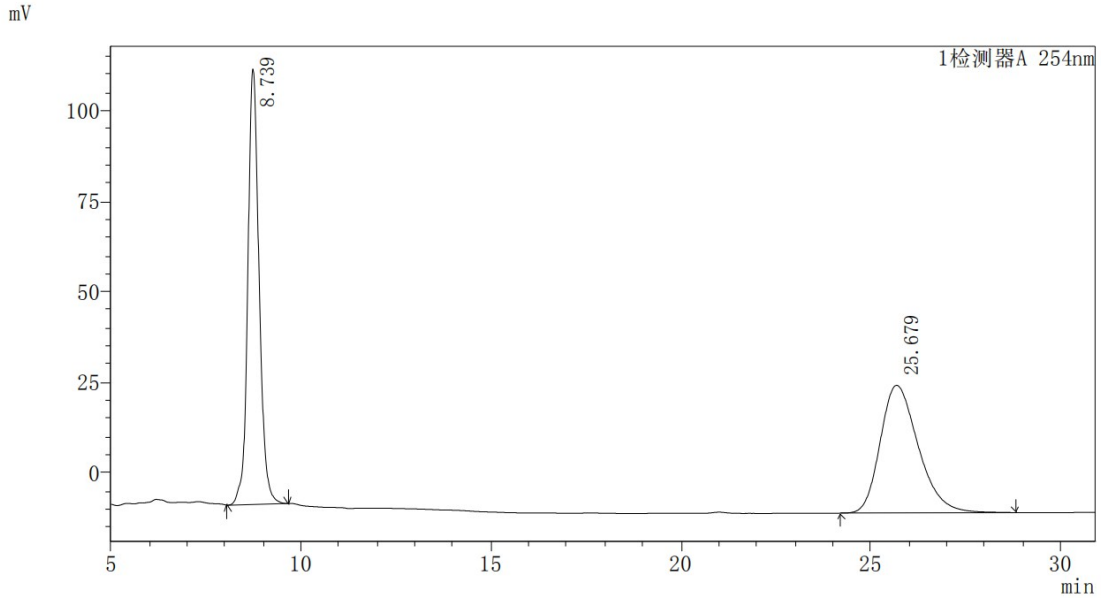


Peak number	Retention time	Area	Height	Concentration
1	5.541	2377777	211824	49.757
2	12.456	2401037	74328	50.243

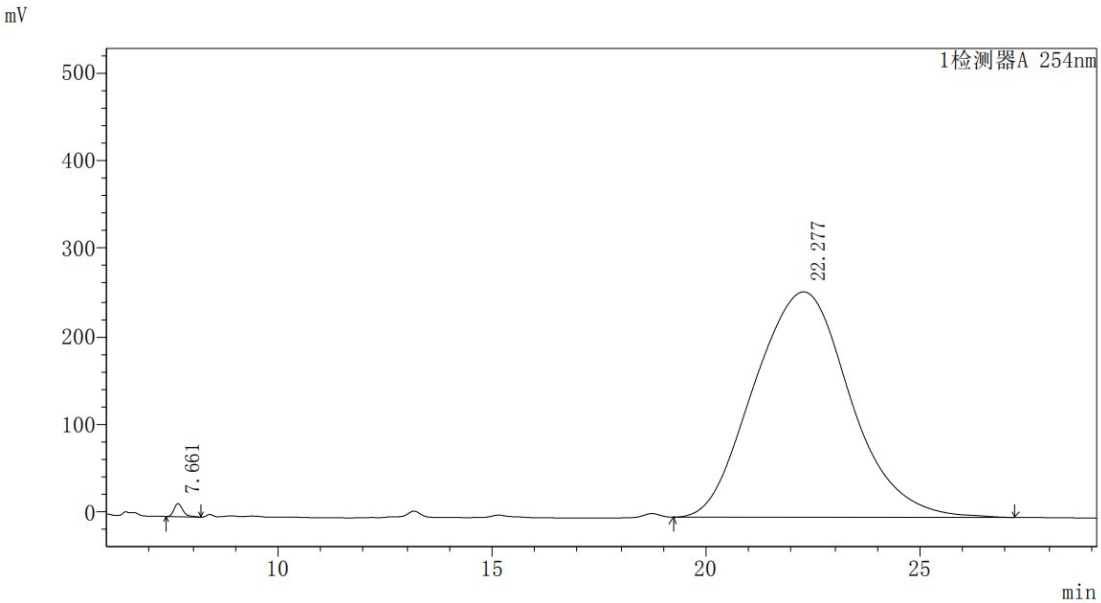


Peak number	Retention time	Area	Height	Concentration
1	6.450	927723	72790	1.059
2	12.828	86680934	2293231	98.941

HPLC of **3h**

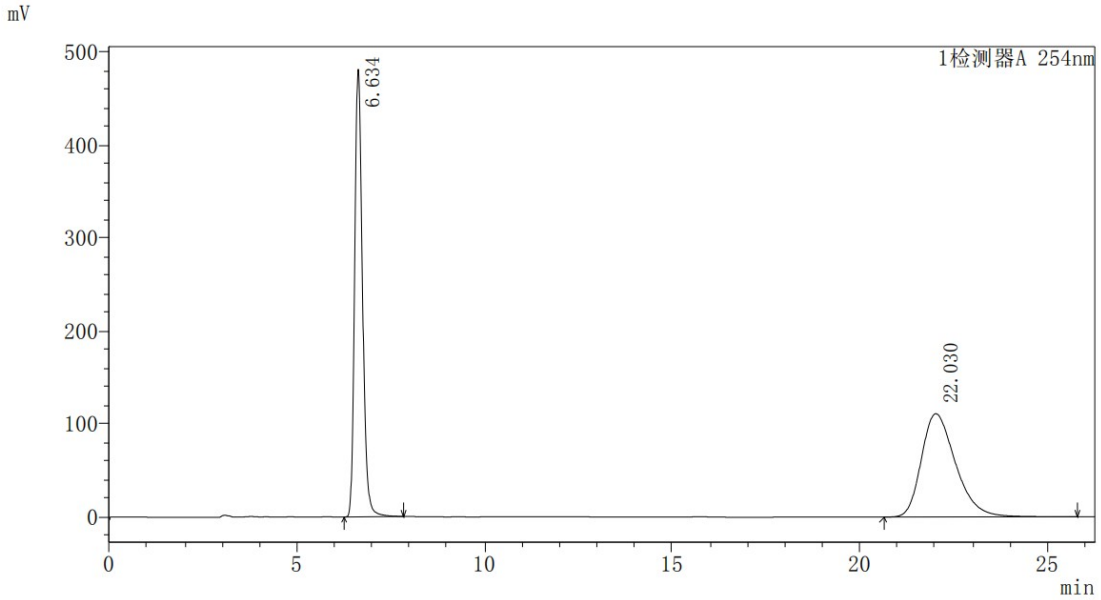


Peak number	Retention time	Area	Height	Concentration
1	8.739	2485468	120304	50.301
2	25.679	2455766	35256	49.699

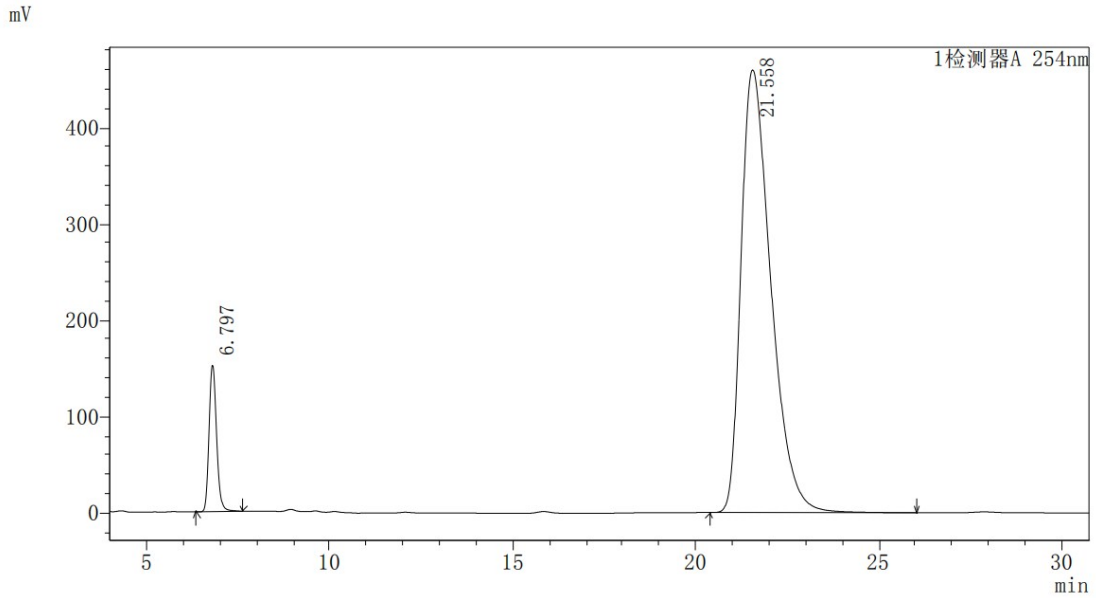


Peak number	Retention time	Area	Height	Concentration
1	7.661	217614	14839	0.539
2	22.277	40121368	256174	99.461

HPLC of **3i**

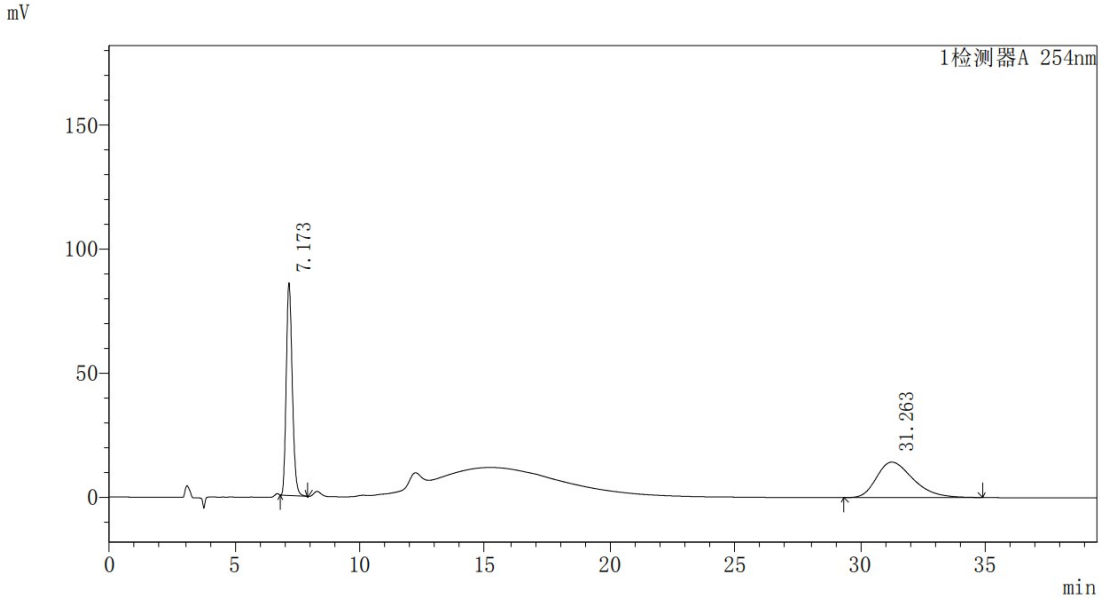


Peak number	Retention time	Area	Height	Concentration
1	6.634	6989367	481697	49.793
2	22.030	7047550	111175	50.207

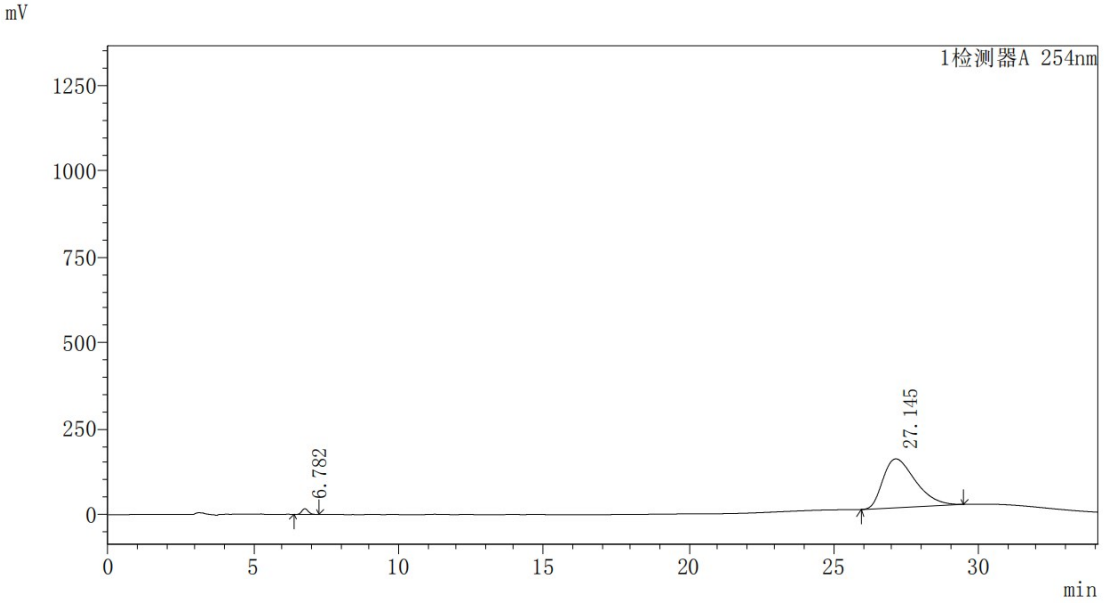


Peak number	Retention time	Area	Height	Concentration
1	6.797	2178708	152019	7.724
2	21.558	26029701	459616	92.276

HPLC of **3j**

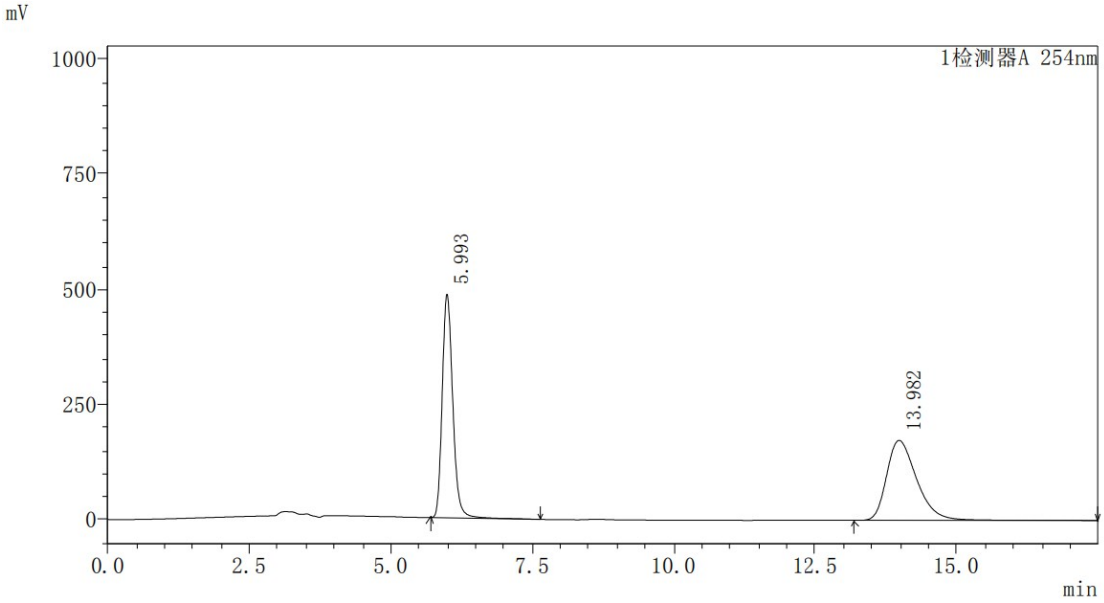


Peak number	Retention time	Area	Height	Concentration
1	7.173	1439043	85817	49.691
2	31.263	1456912	14316	50.309

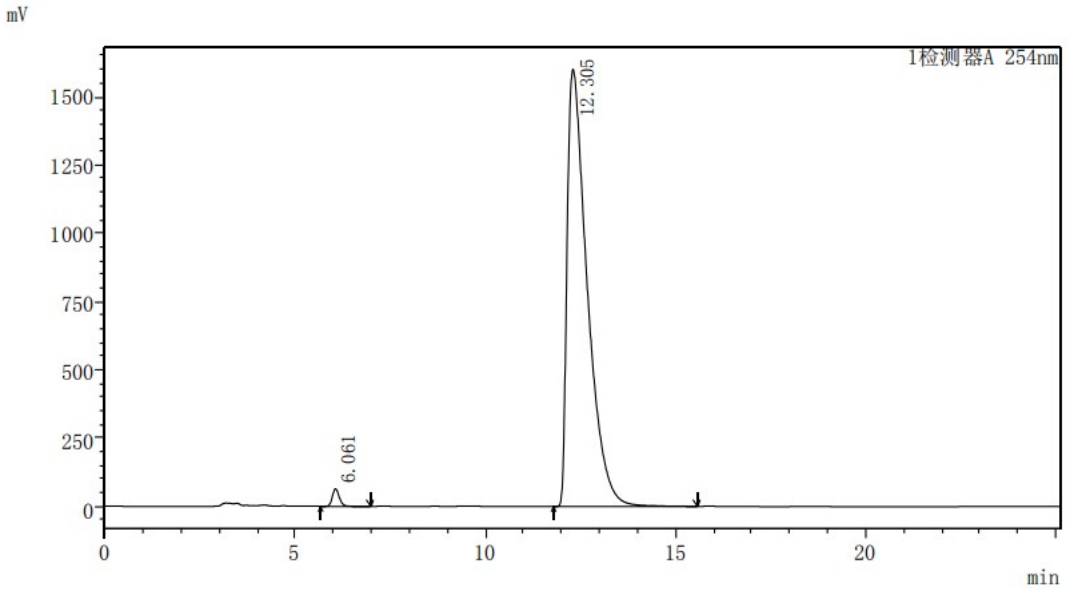


Peak number	Retention time	Area	Height	Concentration
1	6.782	267554	17072	2.345
2	27.145	11140408	142603	97.655

HPLC of **3k**

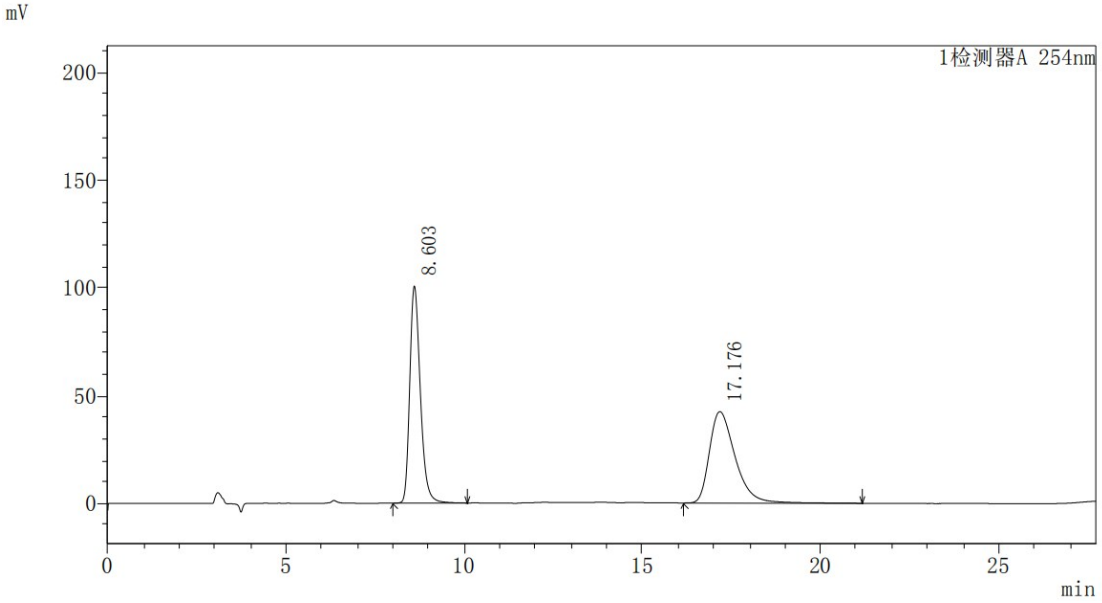


Peak number	Retention time	Area	Height	Concentration
1	5.993	6320078	485196	49.643
2	13.982	6411057	173617	50.357

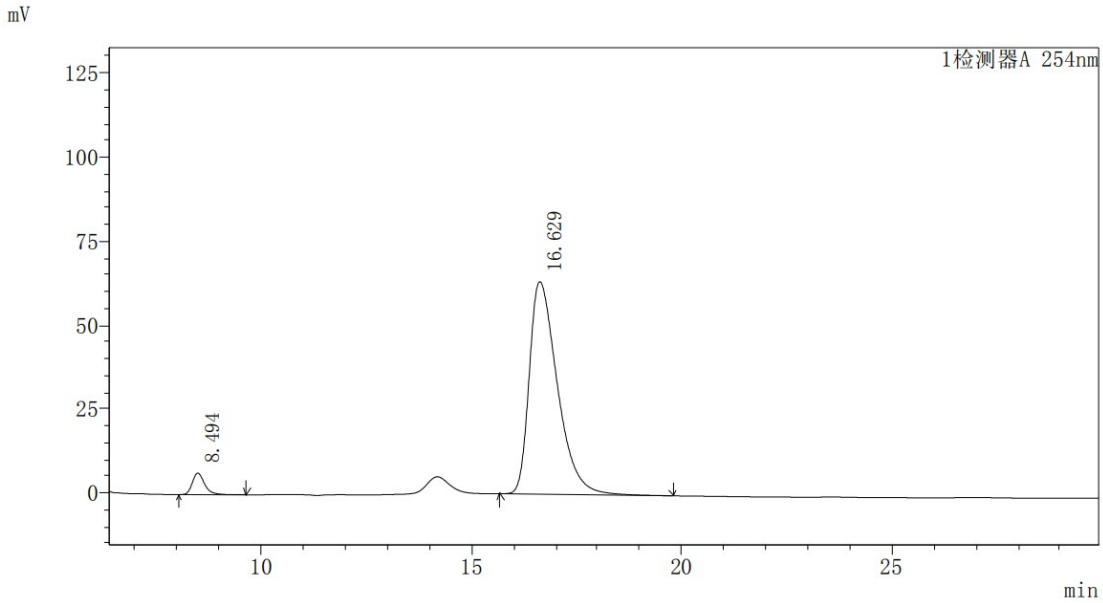


Peak number	Retention time	Area	Height	Concentration
1	6.061	821356	64440	1.377
2	12.305	58811927	1601220	98.623

HPLC of **3l**

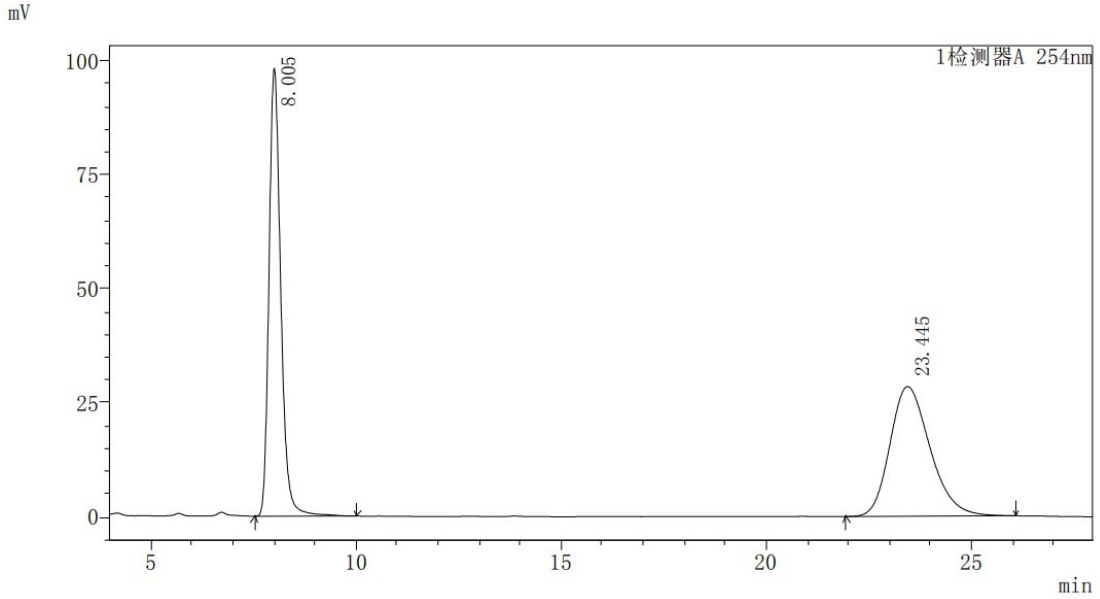


Peak number	Retention time	Area	Height	Concentration
1	8.603	2073685	100769	49.405
2	17.176	2123606	42444	50.595

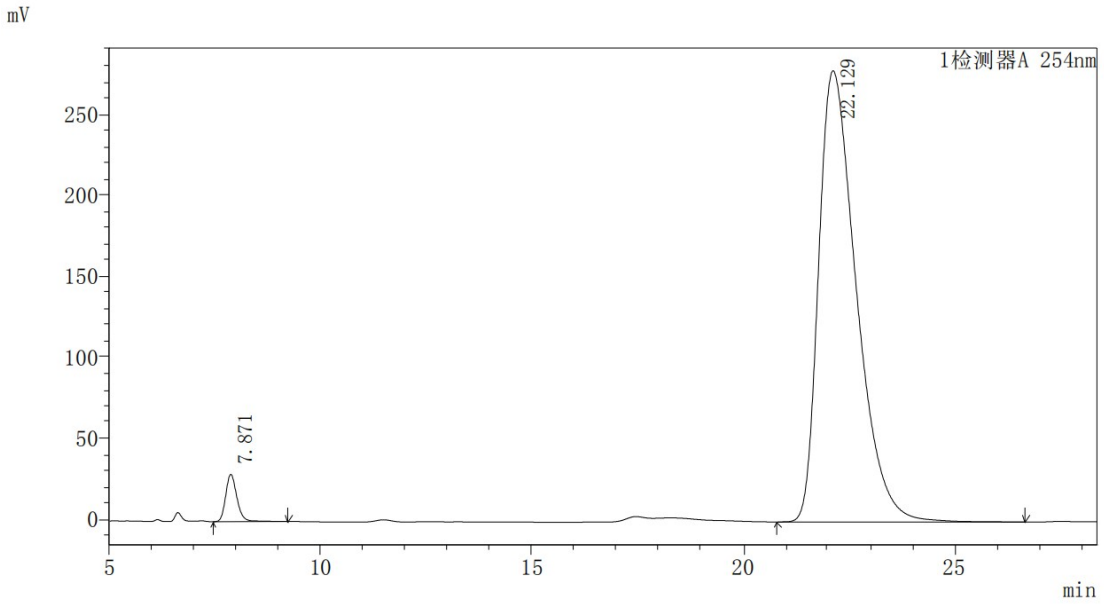


Peak number	Retention time	Area	Height	Concentration
1	8.494	129794	6410	4.216
2	16.629	2948783	63306	95.784

HPLC of **3m**

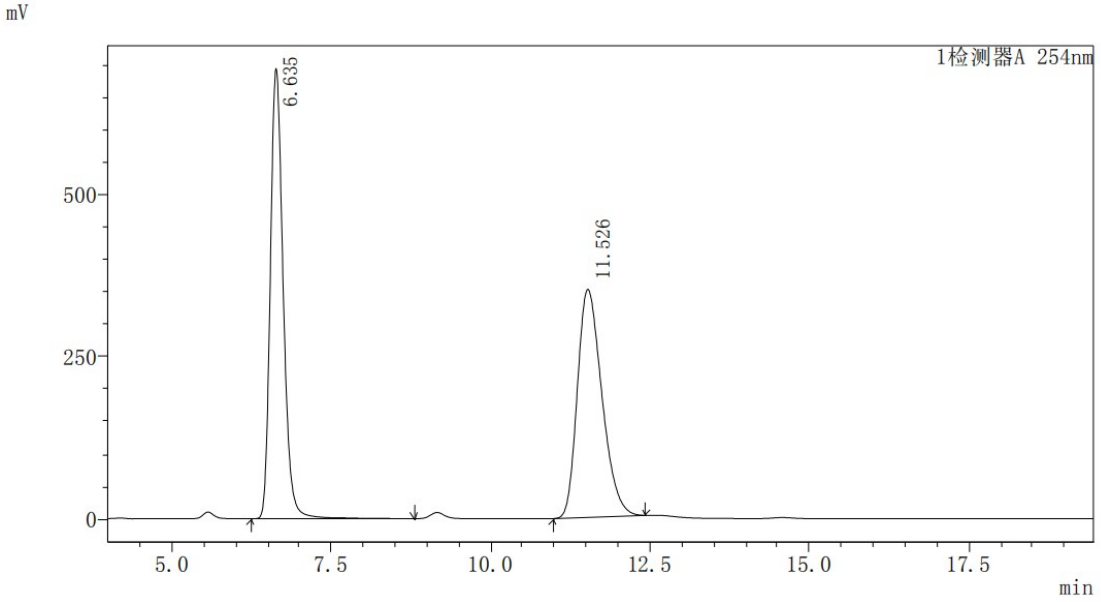


Peak number	Retention time	Area	Height	Concentration
1	8.005	1957152	98276	50.298
2	23.445	1933993	28448	49.702

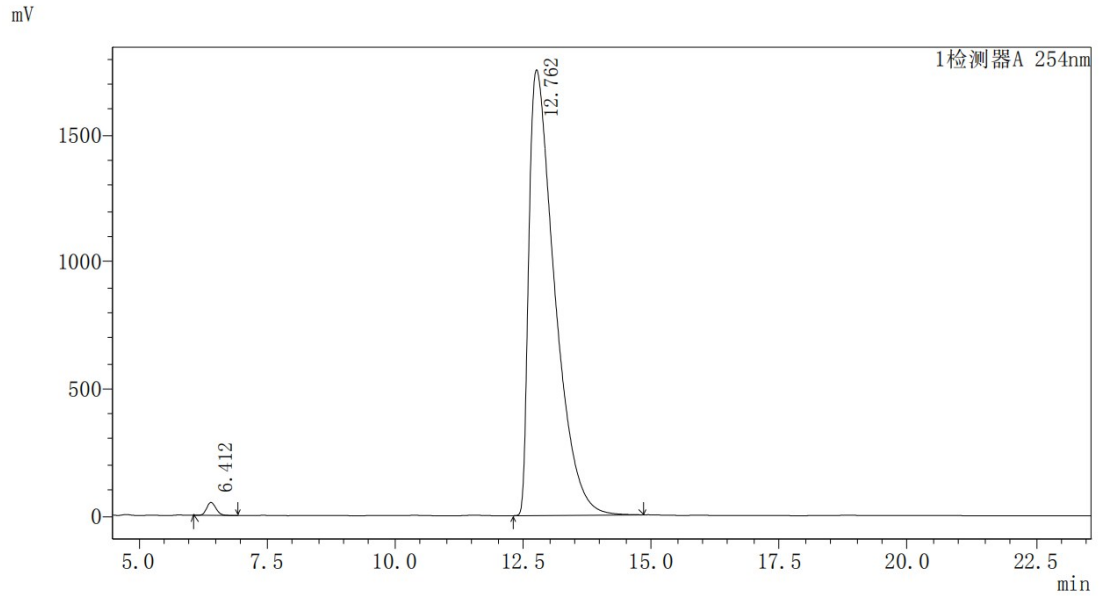


Peak number	Retention time	Area	Height	Concentration
1	7.871	540181	29239	3.044
2	22.129	17208381	278450	96.956

HPLC of **3n**

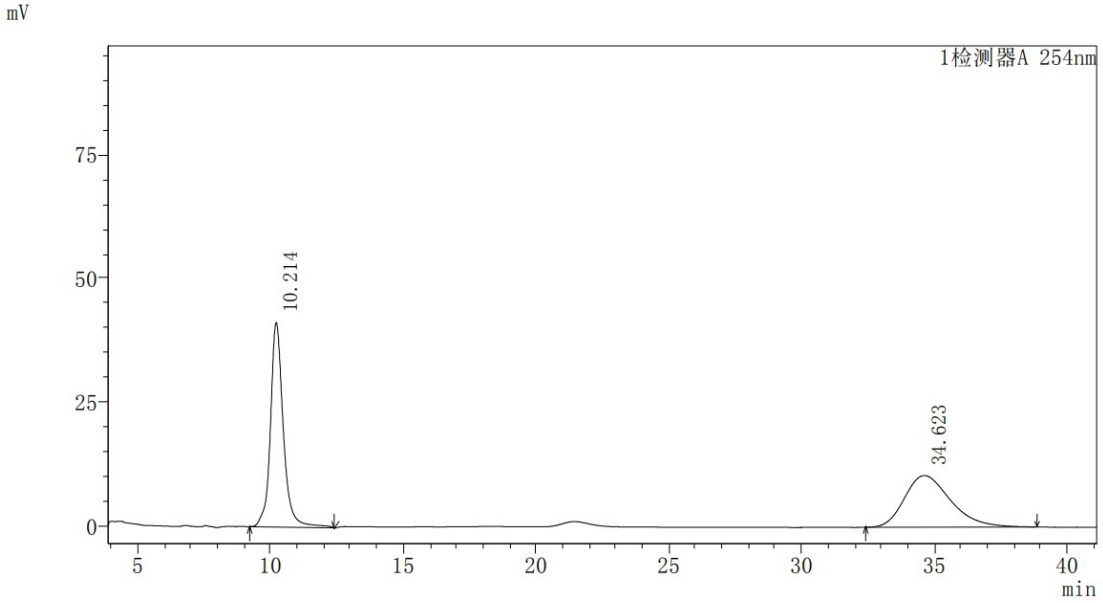


Peak number	Retention time	Area	Height	Concentration
1	6.635	9723314	694180	50.770
2	11.526	9428544	351673	49.230

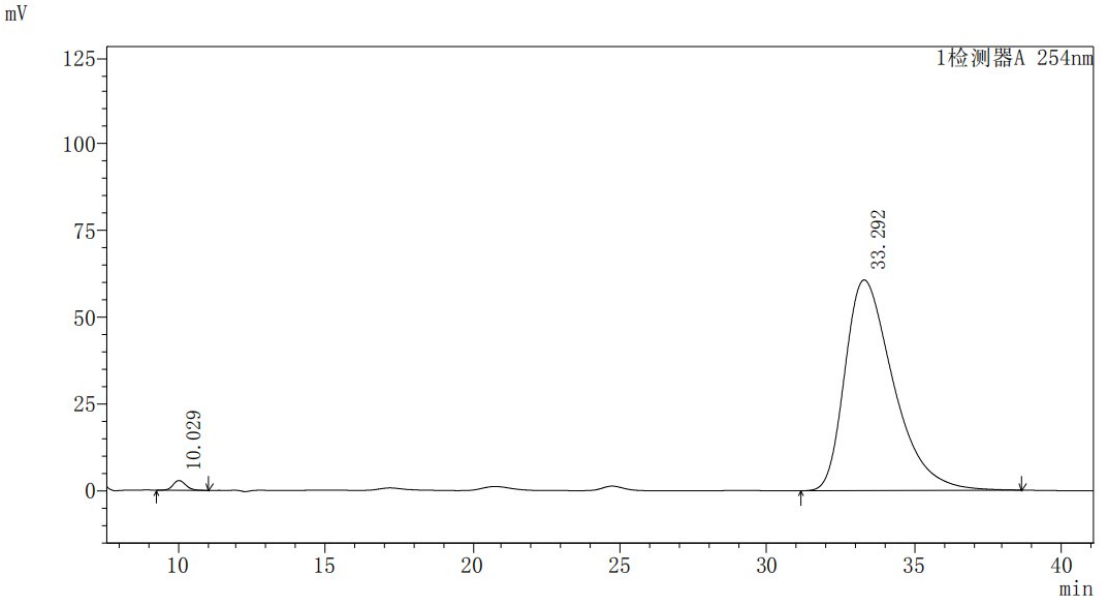


Peak number	Retention time	Area	Height	Concentration
1	6.412	648466	51137	1.046
2	12.762	61358749	1755565	98.954

HPLC of **3o**

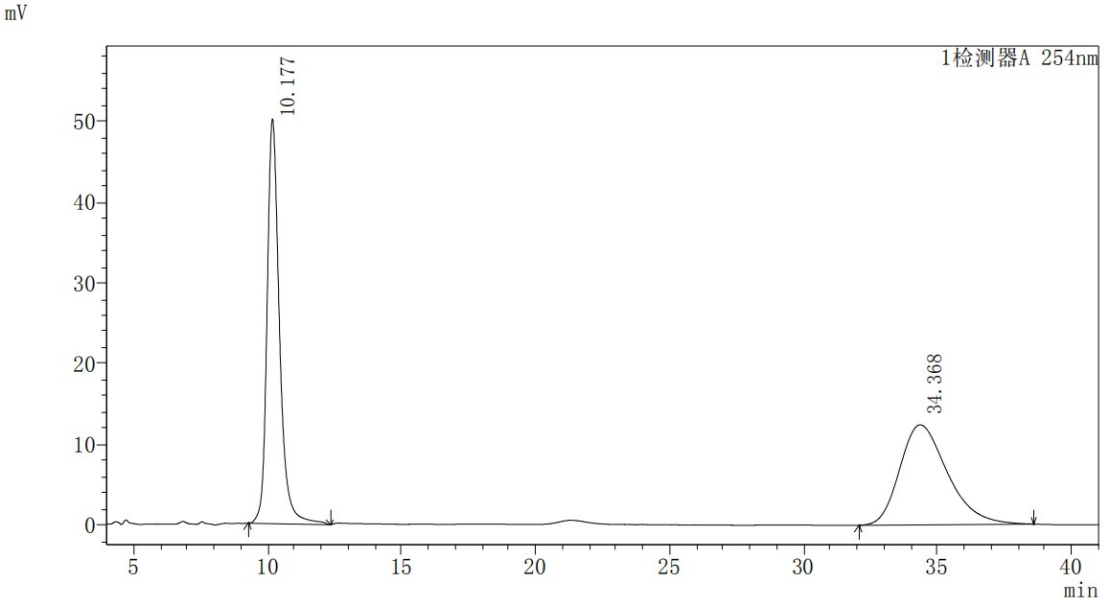


Peak number	Retention time	Area	Height	Concentration
1	10.214	1389647	41237	52.424
2	34.623	1261143	10428	47.576

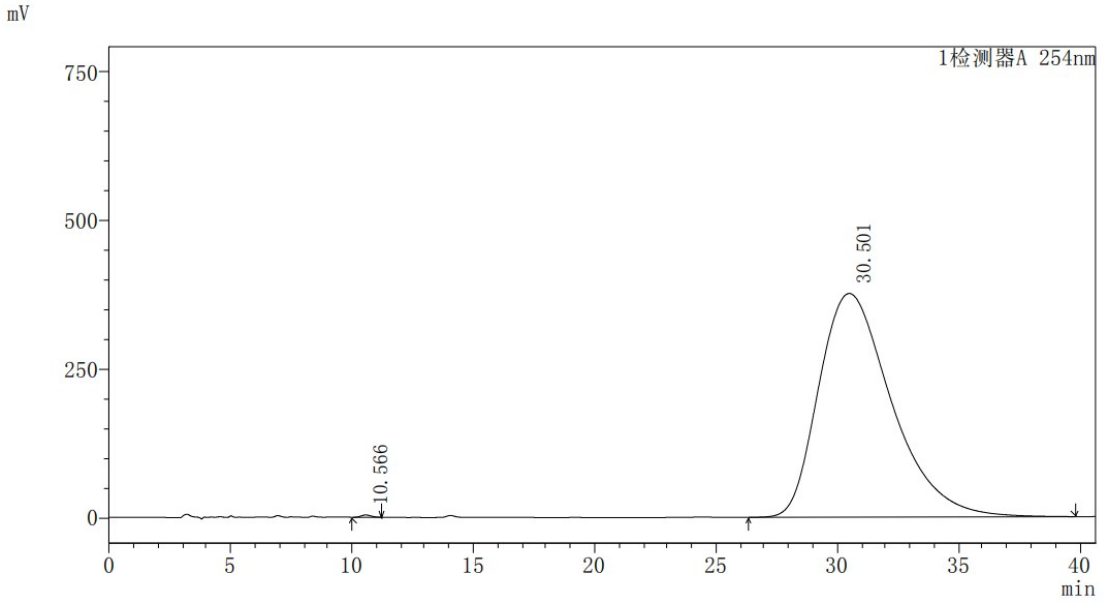


Peak number	Retention time	Area	Height	Concentration
1	10.029	87194	2846	1.236
2	33.292	6965793	60850	98.764

HPLC of **3p**

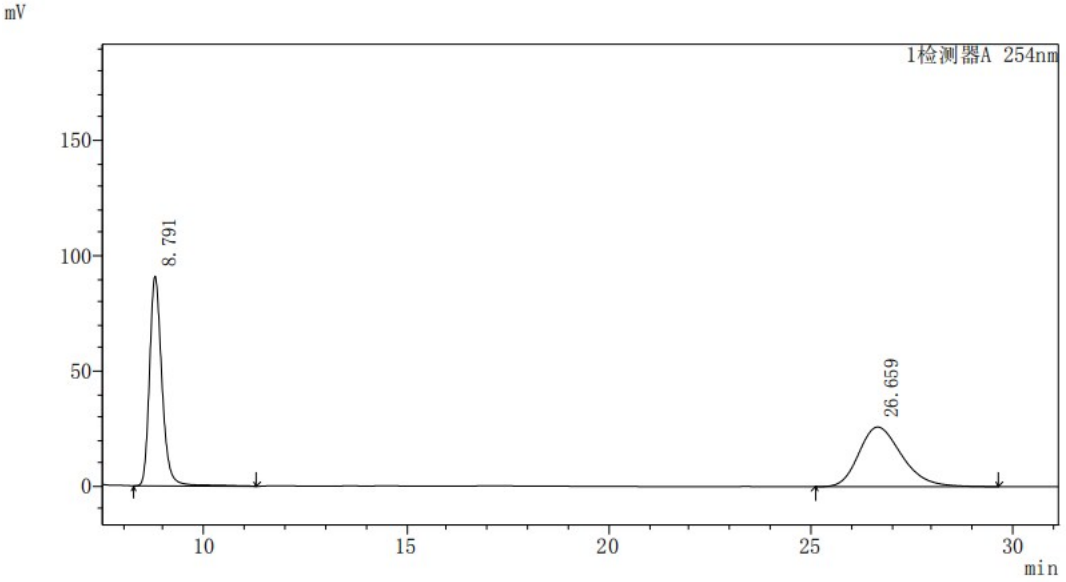


Peak number	Retention time	Area	Height	Concentration
1	10.177	1611250	50131	51.241
2	34.368	1533234	12375	48.759

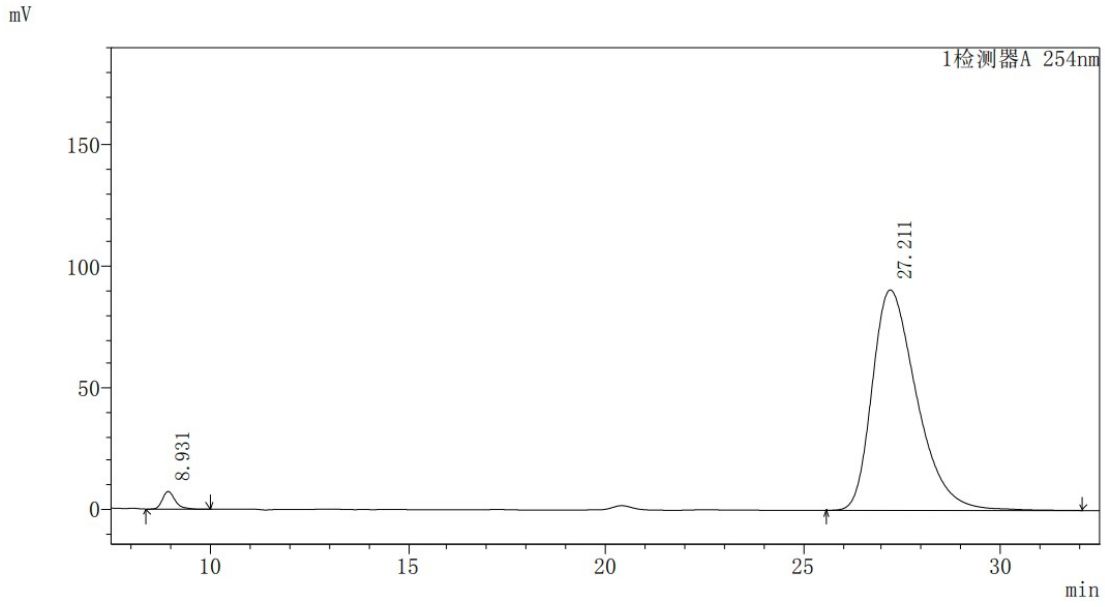


Peak number	Retention time	Area	Height	Concentration
1	10.566	111000	3888	0.141
2	30.501	78781371	377041	99.859

HPLC of **3q**

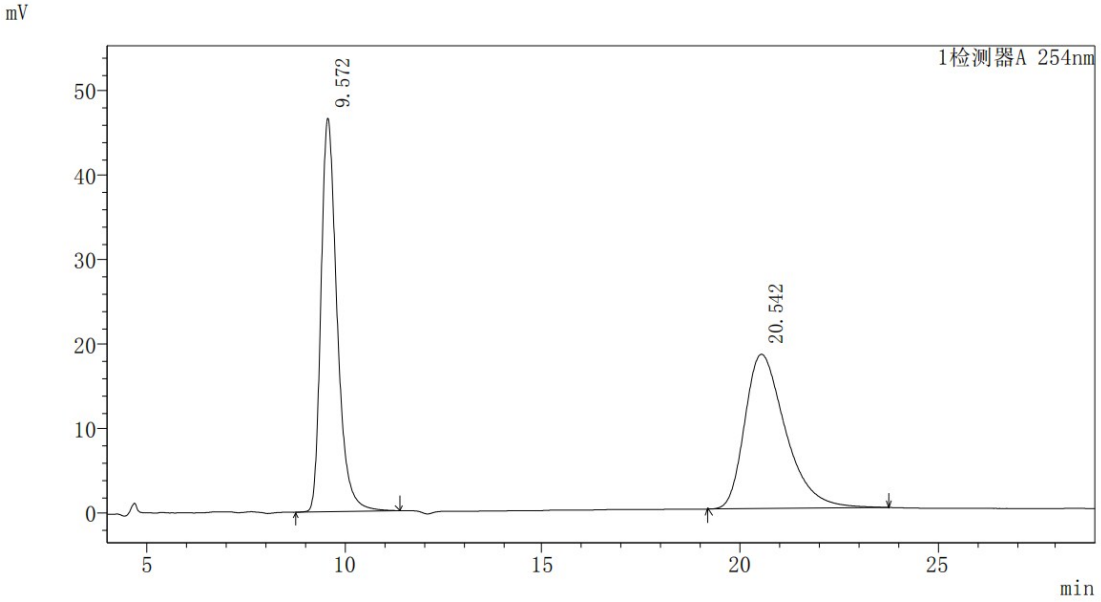


Peak number	Retention time	Area	Height	Concentration
1	8.791	1948785	90906	50.453
2	26.659	1913779	25898	49.547

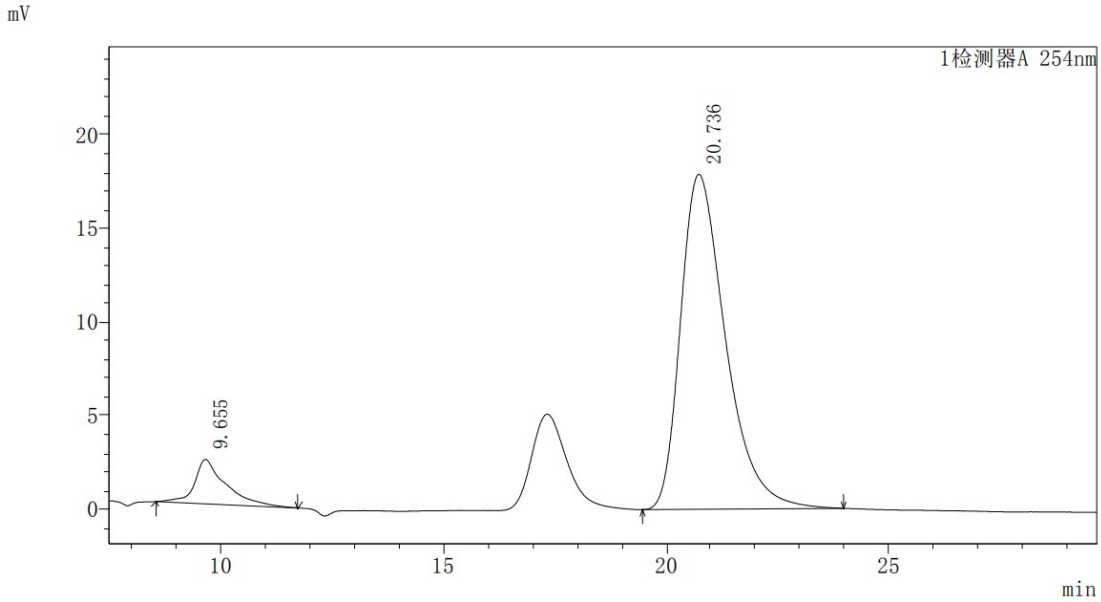


Peak number	Retention time	Area	Height	Concentration
1	8.931	163391	7285	2.241
2	27.211	7127978	90837	97.759

HPLC of **3r**

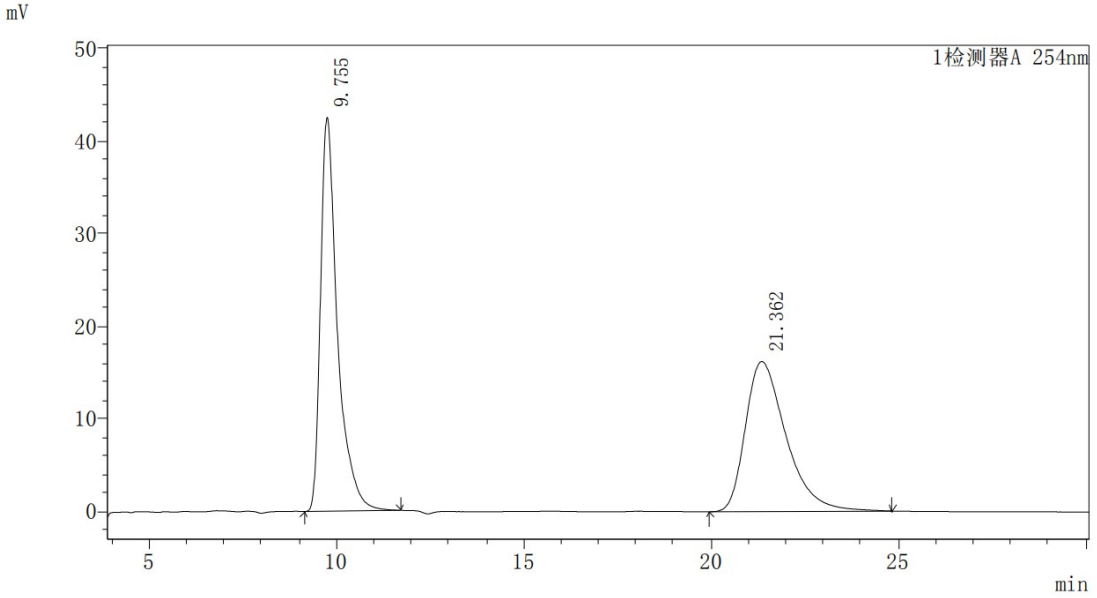


Peak number	Retention time	Area	Height	Concentration
1	9.572	1317103	46560	50.122
2	20.542	1310691	18264	49.878

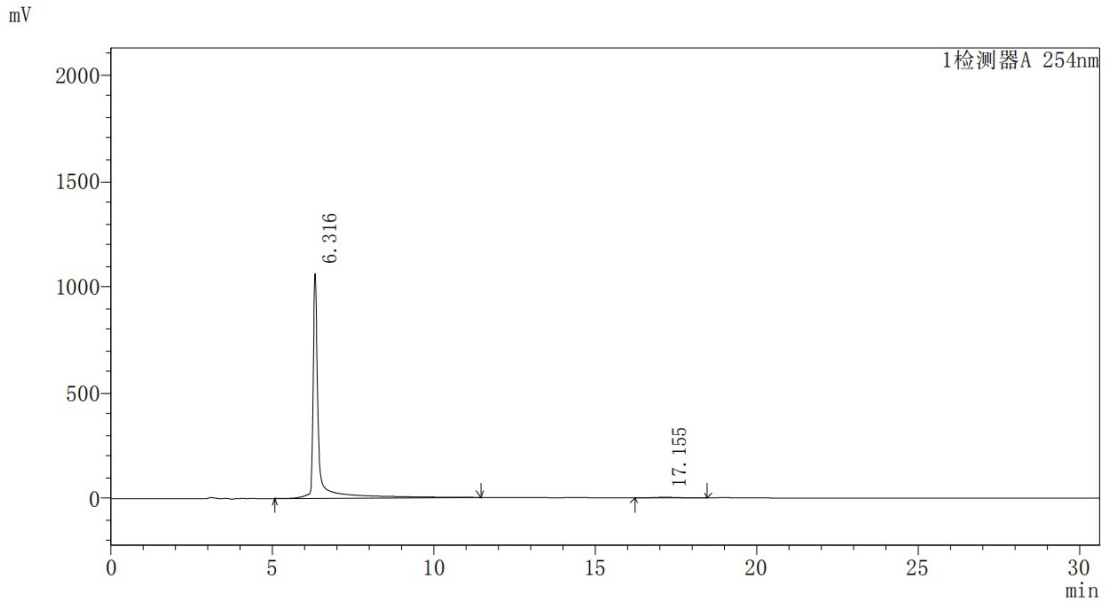


Peak number	Retention time	Area	Height	Concentration
1	9.655	115993	2372	8.440
2	20.736	1258258	17889	91.560

HPLC of **3s**

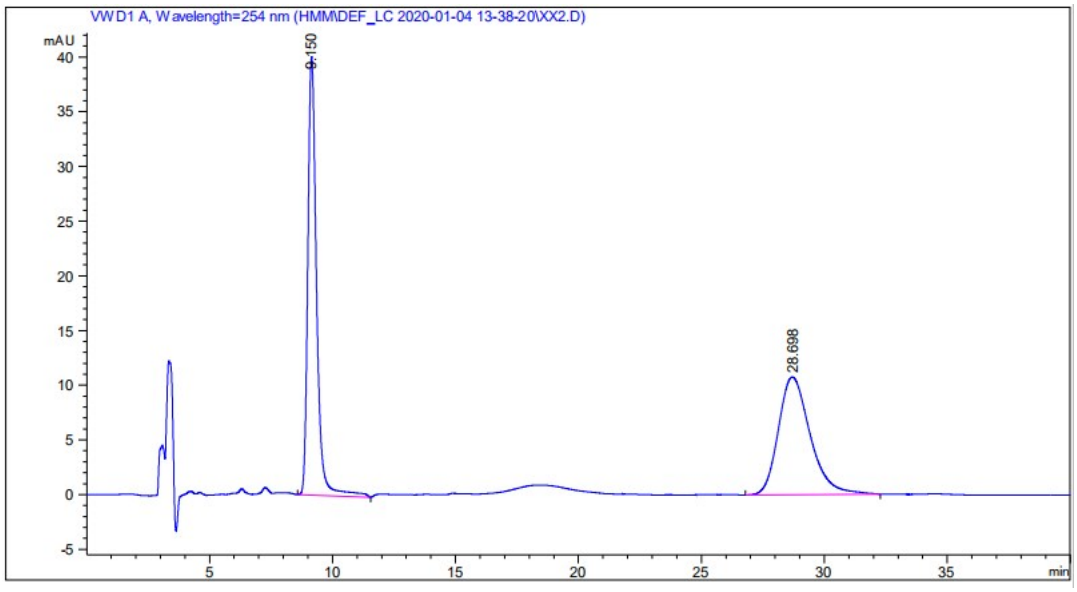


Peak number	Retention time	Area	Height	Concentration
1	9.755	1341469	42603	52.256
2	21.362	1225660	16221	47.744

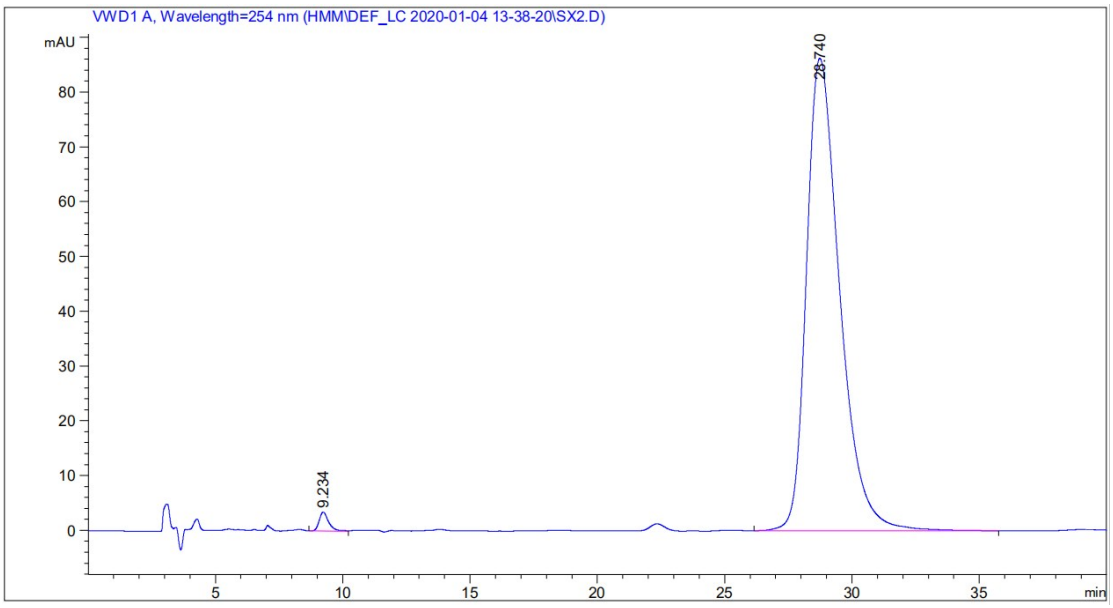


Peak number	Retention time	Area	Height	Concentration
1	6.316	12882714	1062128	98.847
2	17.155	150260	3029	1.153

HPLC of **3t**

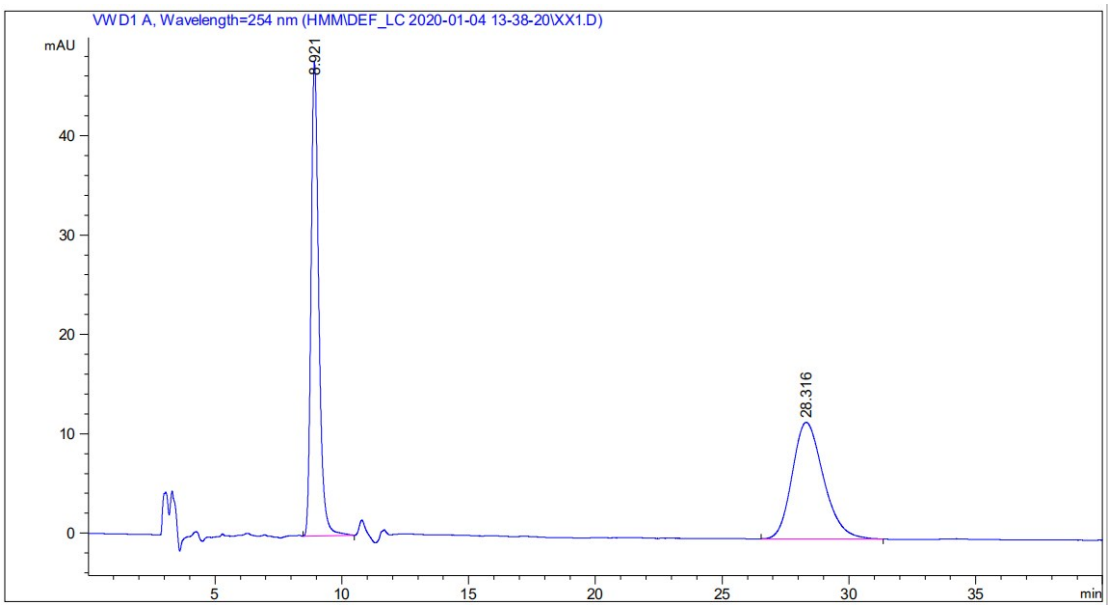


Peak number	Retention time	Area	Height	Concentration
1	9.150	987.74744	40.10510	50.5046
2	28.698	968.01160	10.76063	49.4954

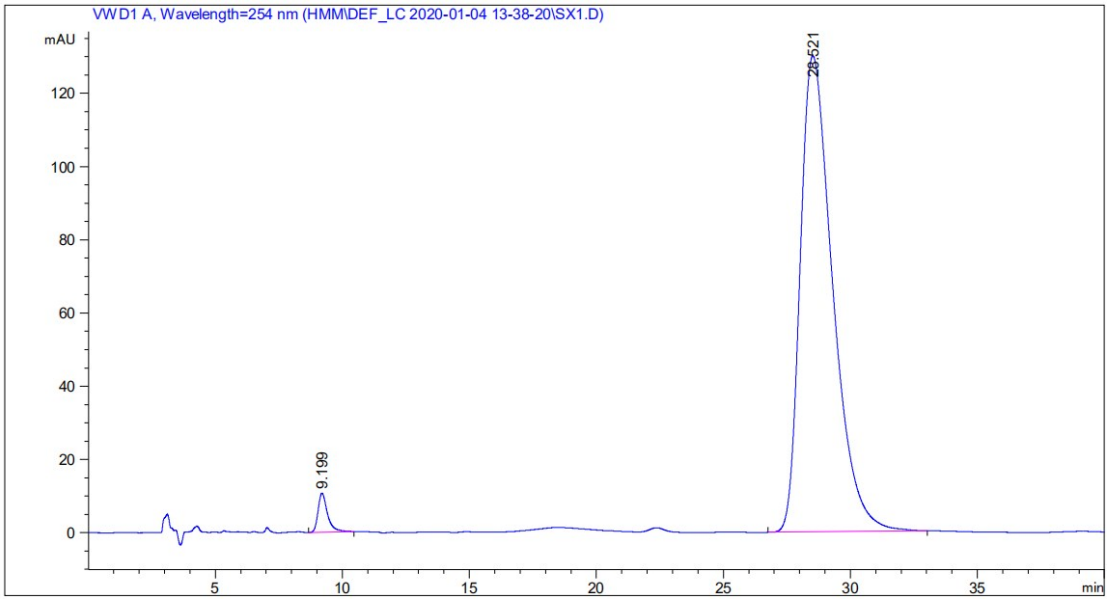


Peak number	Retention time	Area	Height	Concentration
1	9.234	93.00634	3.48894	1.1746
2	28.740	7825.25000	86.23691	98.8254

HPLC of **3u**

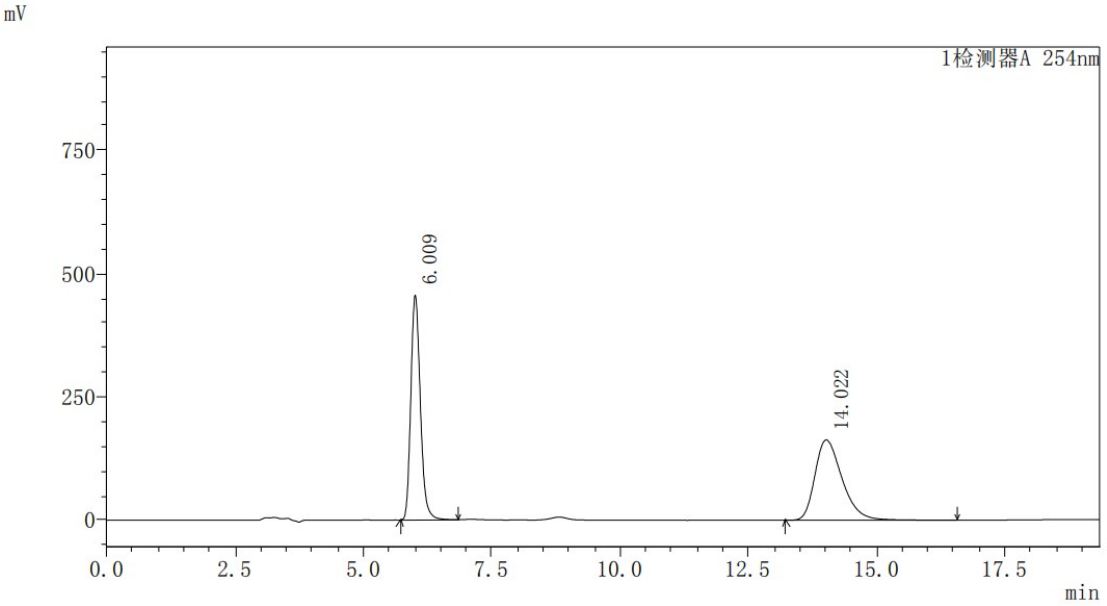


Peak number	Retention time	Area	Height	Concentration
1	8.921	1018.19214	47.75332	50.2806
2	28.316	1006.82758	11.73070	49.7194

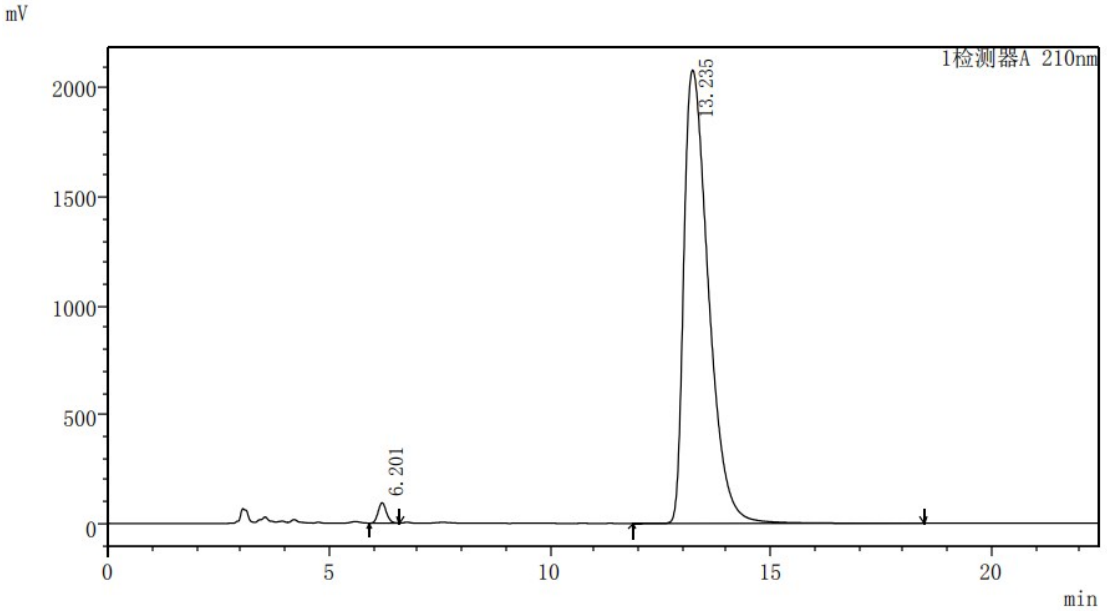


Peak number	Retention time	Area	Height	Concentration
1	9.199	274.79477	10.66090	2.3247
2	28.521	1.15460e4	130.01424	97.6753

HPLC of **3v**



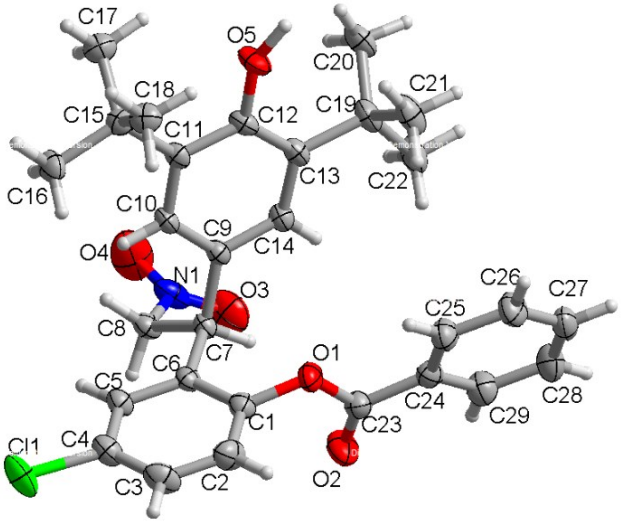
Peak number	Retention time	Area	Height	Concentration
1	6.009	5889572	455921	49.541
2	14.022	5998697	162836	50.459

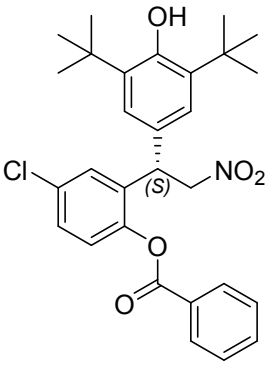


Peak number	Retention time	Area	Height	Concentration
1	6.201	1228522	93715	1.501
2	13.235	80631076	2082892	98.499

6. Single-Crystal X-ray Crystallography of Product 3d

Single-Crystal X-ray Crystallography of Product **3a (CDCC number:1950729)**





Bond precision:	C-C = 0.0055 A		Wavelength=1.54184
Cell:	a=9.6244(3)	b=9.8943(3)	c=14.3864(5)
	alpha=90	beta=94.360(3)	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	1366.01(8)	1366.00(8)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C29 H32 Cl N O5	C29 H32 Cl N O5
Sum formula	C29 H32 Cl N O5	C29 H32 Cl N O5
Mr	510.01	510.00
Dx,g cm-3	1.240	1.240
Z	2	2
Mu (mm-1)	1.546	1.546
F000	540.0	540.0
F000’	542.27	
h,k,lmax	11,11,17	11,11,17
Nref	4893[2601]	4633

Tmin,Tmax	0.805,0.857	0.832,1.000
Tmin’	0.805	

Correction method= # Reported T Limits: Tmin=0.832 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 1.78/0.95	Theta(max)= 67.070
R(reflections)= 0.0467(4182)	wR2(reflections)= 0.1350(4633)
S = 1.048	Npar= 332