# Catalytic Asymmetric [3+3] Annulation of Cyclopropanes with Mercaptoacetaldehyde

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## Supporting Information

CONTENTS:

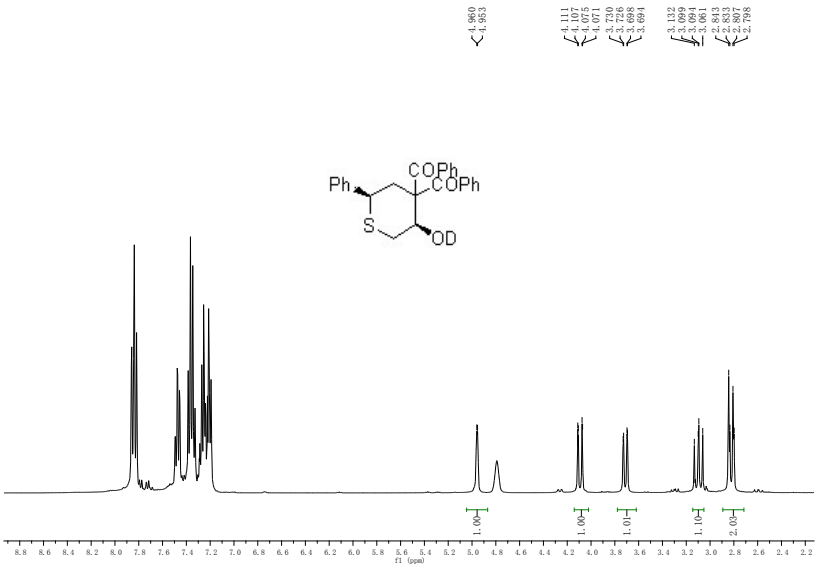
## (1) General Remarks

$^1$H NMR spectra were recorded on commercial instruments (400 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 (100 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). The enantiomeric excesses (ee) were determined by HPLC analysis on commercial chiral columns. Optical rotations were reported as follows: $[a]^T_D$ ($c$ = g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (ESI Source). All reagents and solvents were obtained from commercial suppliers and used without further purification except as indicated below. All catalytic reactions were run in dried glassware. Solvent was distilled over $CaH_2$.

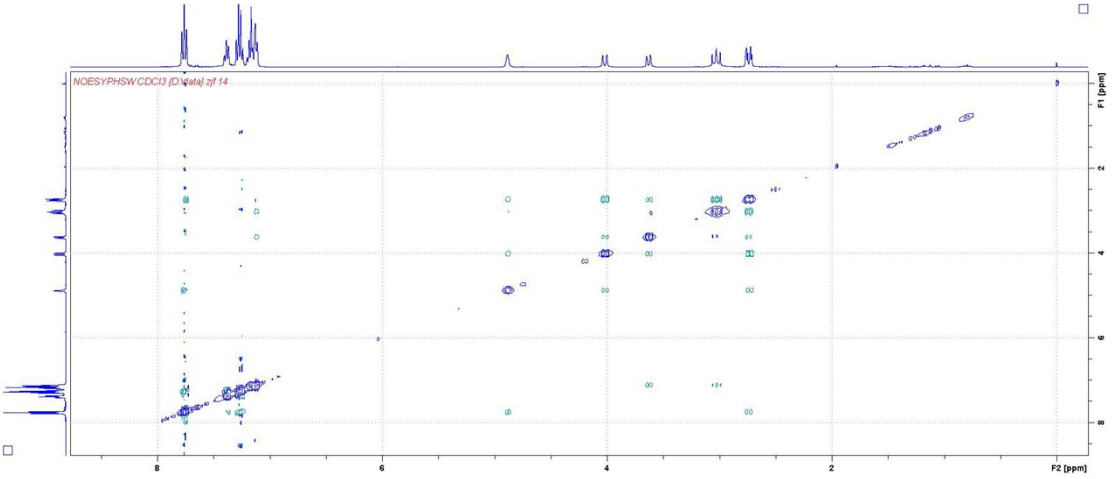
## (2) General procedure for the catalytic asymmetric [3+3] annulation

Mercaptoacetaldehyde **2** (0.05 mmol), chiral *N,N'*-dioxide L-PiPr$_3$ (10 mol%), Sc(OTf)$_3$ (10 mol%) and 4 Å M.S. (20 mg) were added in a dry reaction tube. Then, TCE (1.0 mL) was added in $N_2$ atmosphere. The mixture was stirred at 30 °C for 30 min, then **1** (0.25 mmol) was added at 50 °C, and the reaction mixture was allowed stirred at 50 °C for 24 hours. The mixture was purified by column chromatography on silica gel (petroleum ether:ethyl acetate = 10:1) to afford the desired product **3**. The yield of **3** was calculated according to the amount of 2.

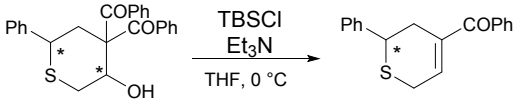
## (3) Determination of the relative configuration of 3a



NOESY of **3a**:



## (4) Synthetic transformation of [3+3] annulation adduct




**3a**
97% *ee*
*93:7* d.r.

**4** (*R*)
71% yield
97% *ee*

The corresponding adduct **3a** (30.2 mg) was dissolved in THF (1.0 mL), the mixture was cooled to 0 °C, then $Et_3N$ (1.0 equiv) and TBSCl (1.1 equiv) were added in the mixture. After that, the reaction was allowed to warm to 25 °C and stirred for 8 hours (monitored by TLC). The resulting mixture was quenched with an aqueous solution of $NaHCO_3$ and extracted with DCM. The combined organic layers were dried over $Na_2SO_4$ and evaporated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 30/1) to afford the desired product **4**.

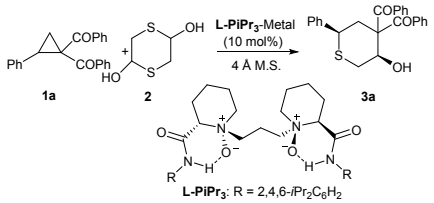
## (5) Methods for the preparation of cyclopropyl ketones 1

Cyclopropyl ketones **1a**–**1k** were prepared according to the methods reported in the literature.[1] A solution of bromine (1.0 mL, 20 mmol) in $CH_3CN$ (5.0 mL) was slowly added to a solution of dimethyl sulfide (5.4 mL, 70 mmol) in $CH_3CN$ (30 mL) kept at 0 °C to give a yellow precipitate. The corresponding styrene derivative (30 mmol) was then added .The solution was stirred for 30 min at the same temperature and then brought to room temperature and diethyl ether (30 mL) was added to it to give a white precipitate, which was filtered and washed with diethyl ether to give the corresponding bromosulfonium bromide in 62% yield. Potassium carbonate (30 mmol) was added to a solution

containing the corresponding bromosulfonium bromide (10 mmol) in DCM:H2O (1:1) mixture (40 mL). The corresponding dibenzoylmethane compound (12 mmol) was added to it and the reaction mixture was stirred over night at room temperature. The DCM layer was then separated and the aqueous layer was washed three times with dichloromethane (20 mL) and added to the organic layer. The combined organic layer was dried over anhydrous sodium sulfate and then evaporated. The residue was then purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20/1) to give the corresponding cyclopropanes in 65% yield.

## (6) Optimization of the conditions

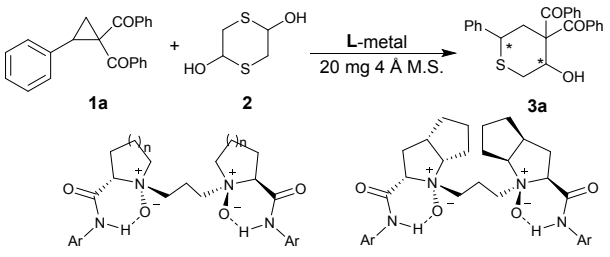
### Screening of the metal salts




| Entry[a] | Metal | Ligand | Yield[b] (%) | ee[c] (%) | dr[c] |
|---|---|---|---|---|---|
| 1 | $Sc(OTf)_3$ | **L-PiPr$_3$** | 23 | 97 | 95:5 |
| 2 | $Y(OTf)_3$ | **L-PiPr$_3$** | nr | - | - |
| 3 | $Yb(OTf)_3$ | **L-PiPr$_3$** | nr | - | - |
| 4 | $Mg(OTf)_2$ | **L-PiPr$_3$** | nr | - | - |
| 5 | $Ni(OTf)_2$ | **L-PiPr$_3$** | nr | - | - |
| 6 | $Gd(OTf)_3$ | **L-PiPr$_3$** | nr | - | - |

[a]Unless otherwise noted, the reactions were performed with **L**-metal (1:1, 10 mol%), **1a** (0.1 mmol), **2** (0.05 mmol), 4 Å M.S. (20 mg) in DCM (1.0 mL) at 30 °C for 24 h without extrusion of air. [b]Isolated yields. [c]Determined by chiral HPLC analysis.

### Screening of the ligands



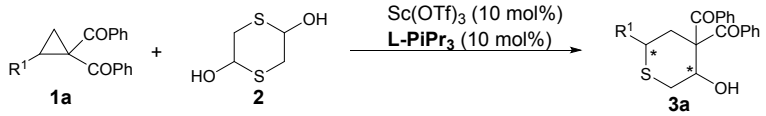

**L-PiPr$_2$**: Ar = 2,6-*i*-$Pr_2C_6H_3$, n = 2
**L-PiEt$_2$**: Ar = 2,6-$Et_2C_6H_3$, n = 2
**L-PiPr$_3$**: Ar = 2,4,6-*i*-$Pr_3C_6H_2$, n = 2
**L-PrPr$_2$**: Ar = 2,6-*i*-$Pr_2C_6H_3$, n = 1
**L-PrEt$_2$**: Ar = 2,6-$Et_2C_6H_3$, n = 1

**L-RaPr$_2$**: Ar = 2,6-*i*-$Pr_2C_6H_3$

| Entry[a] | Metal | Ligand | Yield[b] (%) | ee[c] (%) | dr[c] |
|---|---|---|---|---|---|
| 1 | $Sc(OTf)_3$ | **L-PiPr$_2$** | 33 | 89 | 96:4 |
| 2 | $Sc(OTf)_3$ | **L-PiEt$_2$** | 30 | 89 | 95:5 |
| 3 | $Sc(OTf)_3$ | **L-PiPr$_3$** | 23 | 97 | 95:5 |
| 4 | $Sc(OTf)_3$ | **L-PrPr$_2$** | 27 | 81 | 95:5 |
| 5 | $Sc(OTf)_3$ | **L-PrEt$_2$** | 18 | 51 | 95:5 |
| 6 | $Sc(OTf)_3$ | **L-RaPr$_2$** | 23 | 81 | 97:3 |

[a]Unless otherwise noted, the reactions were performed with **L**-$Sc(OTf)_3$ (1:1, 10 mol%), **1a** (0.1 mmol), **2** (0.05 mmol), 4 Å M.S. (20 mg) in DCM (1.0 mL) at 30 °C for 24 h without extrusion of air. [b]Isolated yields. [c]Determined by chiral HPLC analysis.

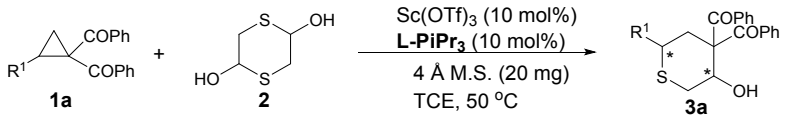
**Screening of solvents and additives**




| Entry[a] | Solvent | Additive | Yield[b] (%) | ee[c] (%) | dr[c] |
|---|---|---|---|---|---|
| 1 | DCM | 4 Å M.S. (20 mg) | 23 | 97 | 95:5 |
| 2 | DCM | none | 6 | 93 | >95:5 |
| 3 | DCM | LiCl (0.10 mmol) | 9 | 93 | >95:5 |
| 4 | DCM | LiCl (0.10 mmol), 4 Å MS (20 mg) | 14 | 95 | >95:5 |
| 5 | $CHCl_3$ | 4 Å MS (20 mg) | 17 | 99 | 94:6 |
| 6 | DCE | 4 Å MS (20 mg) | 11 | 89 | 94:6 |
| 7 | TCE | 4 Å MS (20 mg) | 18 | 99 | 94:6 |
| 8 | THF | 4 Å MS (20 mg) | 9 | 97 | 95:5 |
| 9 | Ethyl acetate | 4 Å MS (20 mg) | trace | - | - |
| 10 | MeOH | 4 Å MS (20 mg) | 6 | 99 | 98:2 |

[a]Unless otherwise noted, the reactions were performed with **L-PiPr$_3$**-$Sc(OTf)_3$ (1:1, 10 mol%), **1a** (0.1 mmol), **2** (0.05 mmol) in solvent at 30 °C for 24 h without extrusion of air. [b]Isolated yields. [c]Determined by chiral HPLC analysis.

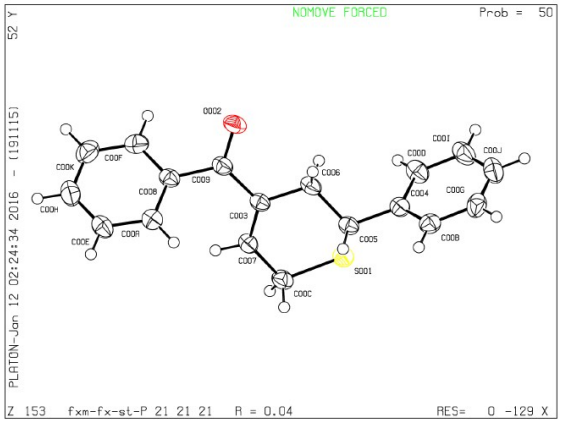
**Screening of the 1a:2 ratio**



| Entry[a] | **1a**:**2** | Yield[b] (%) | ee[c] (%) | dr[d] |
|---|---|---|---|---|
| 1 | 8:1 | 65 | 97 | 95:5 |
| 2 | 6:1 | 75 | 97 | 95:5 |
| 3 | 5:1 | 75 | 97 | 95:5 (12.5:1)[e] |
| 4 | 4.6:1 | 72 | 97 | 95:5 |
| 5 | 4:1 | 68 | 97 | 95:5 |

[a]Unless otherwise noted, the reactions were performed with **L-PiPr$_3$**-Sc(OTf)$_3$ (1:1, 10 mol%), 4 Å M.S. (20 mg) in TCE (1.0 mL) at 50 °C for 24 h without extrusion of air. [b]Isolated yields according to the amount of **2**. [c,d]Determined by chiral HPLC analysis. [e]Determined by NMR analysis.

## (7) Crystal data of compound 4



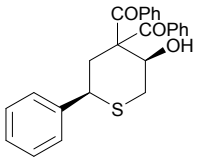

Data block: Displacement ellipsoids are drawn at 50% probability level

Table 1 Crystal data and structure refinement for fxm-fx-st-bts.

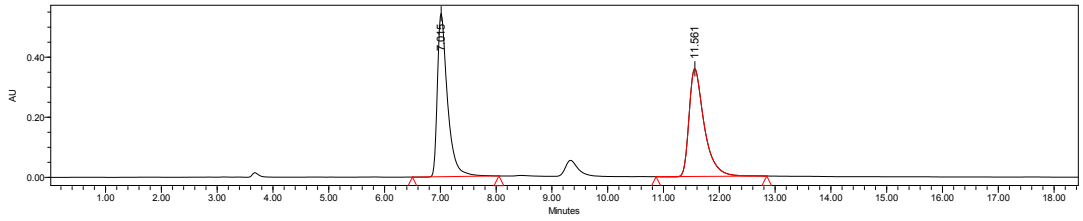
| | |
|---|---|
| Identification code | fxm-fx-st-bts |
| Empirical formula | $C_{18}H_{16}OS$ |
| Formula weight | 280.37 |
| Temperature/K | 207(70) |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 5.7389(4) |
| b/Å | 11.4338(8) |
| c/Å | 22.2456(18) |

| | |
|---|---|
| α /° | 90 |
| β /° | 90 |
| γ /° | 90 |
| Volume/Å$^3$ | 1459.70(19) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.276 |
| μ /mm$^{-1}$ | 0.214 |
| F(000) | 592.0 |
| Crystal size/mm$^3$ | 0.8 × 0.7 × 0.6 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 7.128 to 52.744 |
| Index ranges | -6 ≤ h ≤ 7, -14 ≤ k ≤ 14, -27 ≤ l ≤ 25 |
| Reflections collected | 8673 |
| Independent reflections | 2969 [$R_{int}$ = 0.0504, $R_{sigma}$ = 0.0500] |
| Data/restraints/parameters | 2969/0/181 |
| Goodness-of-fit on F$^2$ | 1.054 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0432, $wR_2$ = 0.1019 |
| Final R indexes [all data] | $R_1$ = 0.0467, $wR_2$ = 0.1068 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.17/-0.30 |
| Flack parameter | -0.01(7) |

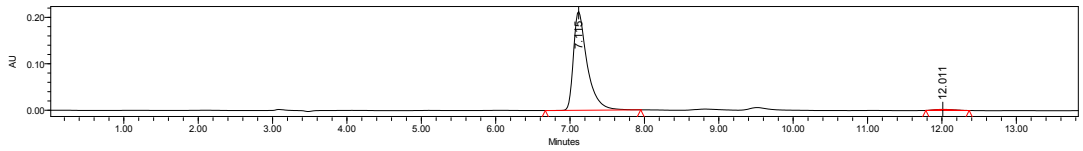
## (8) HPLC conditions[2] for the products



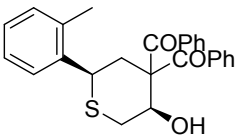

**((2*R*,5*R*)5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3a)**; 30.1 mg, 75% yield; colorless oil; 97% ee, 12.5:1 dr; $[\alpha]_D^{19}$ = +314.08 (*c* = 0.966, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.12 min, $t_{R(minor)}$ = 12.01 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.86–7.21 (m, 15H), 4.98–4.95 (dd, *J* = 2.8 Hz, 10.4 Hz, 1H), 4.11–4.07 (dd, *J* = 1.6 Hz, 14.4 Hz, 1H), 3.73–3.69 (dd, *J* = 1.6 Hz, 12.8 Hz, 1H), 3.13–3.06 (m, 2H), 2.84–2.80 (dd, *J* = 4.0 Hz, 14.4 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ = 200.21, 197.44, 140.86, 136.93, 136.64, 133.49, 132.88, 128.93, 128.76, 128.74, 128.72, 128.65,127.83, 127.19, 69.48, 65.54, 42.02, 36.88, 35.33; ESI-HRMS: calcd for **$C_{25}H_{22}NaO_3S^+$** ([M+Na$^+$]) 425.1182; found 425.1187.



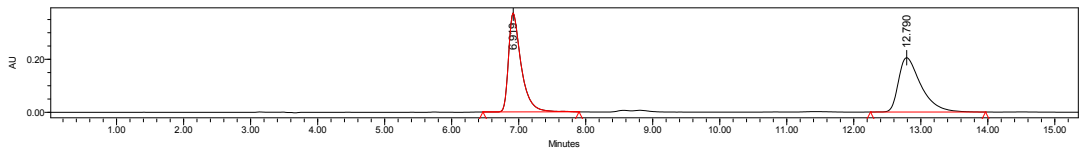

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.015 | 50.38 |
| 2 | 11.561 | 49.62 |



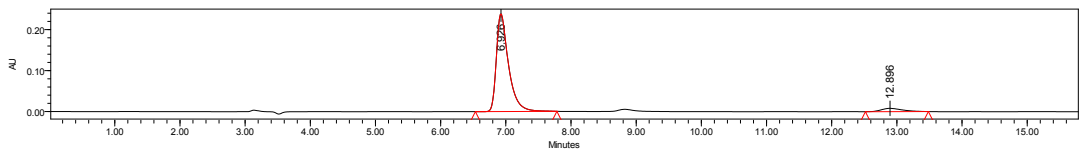

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.115 | 98.53 |
| 2 | 12.011 | 1.47 |



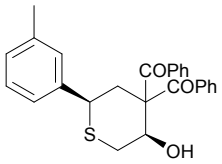

**((2*R*,5*R*)-5-hydroxy-2-(*o*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3b)**; 33.4 mg, 80% yield; colorless oil; 89% ee, >19:1 dr; $[\alpha]_D^{20}$ = +224.09 (*c* = 1.100, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.93 min, $t_{R(minor)}$ = 12.89 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.4, 4.4 Hz, 4H), 7.48 (dd, *J* = 12.4, 5.2 Hz, 3H), 7.35 (dd, *J* = 17.1, 8.0 Hz, 4H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 1H), 4.98 (dd, *J* = 10.8, 2.7 Hz, 1H), 4.09 (dd, *J* = 14.3, 1.1 Hz, 1H), 3.87 (d, *J* = 11.9 Hz, 1H), 3.23–2.98 (m, 2H), 2.90–2.69 (m, 2H), 1.89 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.28, 197.50, 139.00, 137.02, 136.61, 135.17, 133.62, 132.89, 130.52, 128.98, 128.85, 128.76, 128.64, 127.53, 126.64, 126.47, 69.72, 65.61, 37.81, 36.77, 35.26, 18.66; ESI-HRMS: calcd for $\mathbf{C_{26}H_{24}NaO_3S^+}$ ([M+Na$^+$]) 439.1338; found 439.1337.



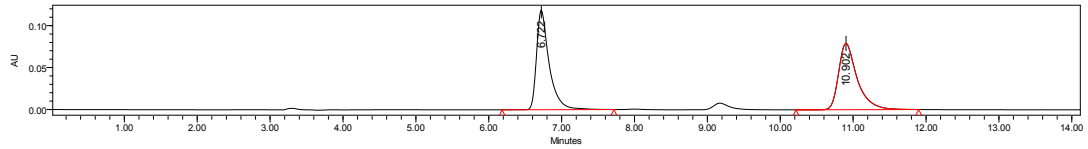

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.919 | 50.49 |
| 2 | 12.790 | 49.51 |



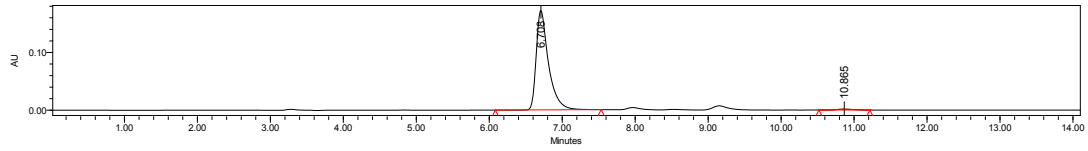
| | Retention Time | % Area |
|---|---|---|
| 1 | 6.926 | 94.51 |
| 2 | 12.890 | 5.49 |



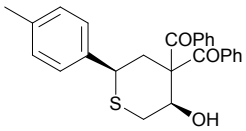

**((2*R*,5*R*)-5-hydroxy-2-(*m*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3c)**; 31.6 mg, 76% yield; colorless oil; 97% ee, 16.7:1 dr; $[\alpha]_D^{20}$ = +166.14 (*c* = 0.632, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.71 min, $t_{R(minor)}$ = 10.86 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.76 (m, 4H), 7.39 (m, 2H), 7.28 (m, 4H), 7.07 (m, 1H), 6.94 (dd, *J* = 20.1, 7.1 Hz, 3H), 4.88 (d, *J* = 8.6 Hz, 1H), 4.02 (d, *J* = 14.2 Hz, 1H), 3.60 (d, *J* = 12.7 Hz, 1H), 3.11–2.93 (m, 2H), 2.74 (d, *J* = 14.5 Hz, 2H), 2.21 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.20, 197.52, 140.75, 138.50, 136.92, 136.62, 133.48, 132.90, 128.93, 128.75, 128.67, 128.64, 128.62, 127.87, 124.28, 69.45, 65.57, 41.93, 36.73, 35.37, 21.37; ESI-HRMS: calcd for $\mathbf{C_{26}H_{24}NaO_3S^+}$ ([M+Na$^+$]) 439.1338; found 439.1334.



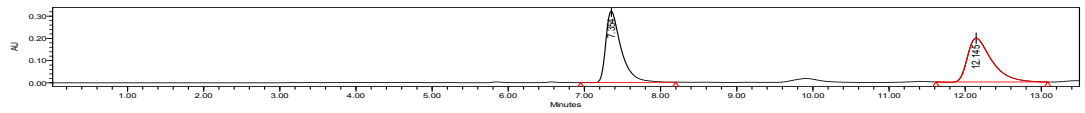

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.722 | 50.53 |
| 2 | 10.902 | 49.47 |



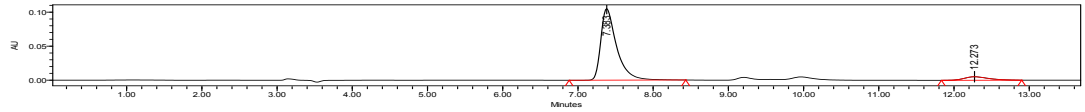

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.708 | 98.85 |
| 2 | 10.865 | 1.15 |



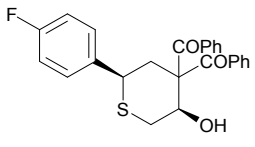

**((2*R*,5*R*)-5-hydroxy-2-(*p*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3d)**; 30.0 mg, 72% yield; colorless oil; 86% ee, 16.7:1 dr; $[\alpha]_D^{21}$ = +157.42 (*c* = 0.599, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.38 min, $t_{R(minor)}$ =12.27 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.80 (m, 4H), 7.47 (m, 2H), 7.39–7.31 (m, 4H), 7.15–7.05 (m, 4H), 4.95 (dd, *J* = 10.6, 2.6 Hz, 1H), 4.09 (dd, *J* = 14.3, 1.6 Hz, 1H), 3.68 (dd, *J* = 12.9, 1.4 Hz, 1H), 3.09 (m, 2H), 2.81 (dd, *J* = 14.3, 3.9 Hz, 2H), 2.29 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.24, 197.47, 137.88, 137.64, 136.92, 136.62, 133.48, 132.89, 129.42, 128.92, 128.75, 128.72, 128.66, 127.07, 69.49, 65.56, 41.66, 36.86, 35.37, 21.08; ESI-HRMS: calcd for $\mathbf{C_{26}H_{24}NaO_3S^+}$ ([M+Na$^+$]) 439.1338; found 439.1336.



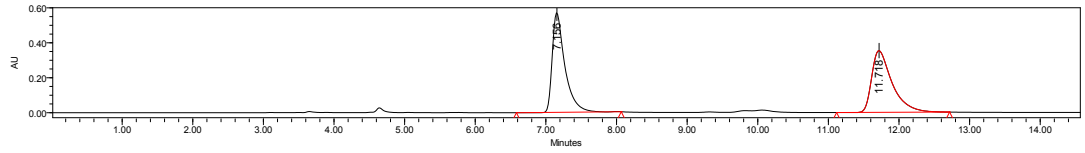

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.354 | 50.60 |
| 2 | 12.145 | 49.40 |



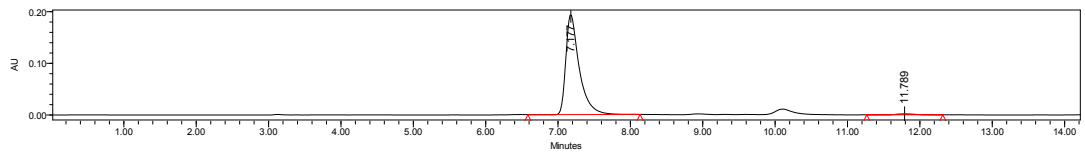

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.383 | 93.03 |
| 2 | 12.273 | 6.97 |



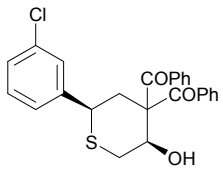

**((2*R*,5*R*)-2-(4-fluorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3e)**; 23.5 mg, 56% yield; a colorless oil; 97% ee, 14.3:1 dr; $[\alpha]_D^{19}$= +274.56 (*c* = 0.471, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.18 min, $t_{R(minor)}$ = 11.79 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.80 (m, 4H), 7.52–7.45 (m, 2H), 7.36 (m, 4H), 7.20–7.12 (m, 2H), 7.01–6.91 (m, 2H), 4.96 (dd, *J* = 10.6, 2.8 Hz, 1H), 4.08 (dd, *J* = 14.4, 1.8 Hz, 1H), 3.70 (dd, *J* = 13.0, 1.7 Hz, 1H), 3.11–2.98 (m, 2H), 2.87–2.71 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.09, 197.40, 163.38, 160.93, 136.85, 136.68, 136.65, 136.59, 133.55, 132.95, 128.95, 128.84, 128.76, 128.70, 128.66, 115.74, 115.52, 69.44, 65.48, 41.21, 37.03, 35.29; ESI-HRMS: calcd for **$C_{25}H_{21}FNaO_3S^+$** ([M+Na$^+$]) 443.1088; found 443.1091.



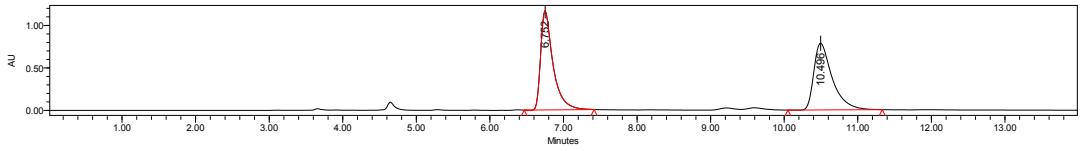

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.156 | 49.98 |
| 2 | 11.718 | 50.02 |



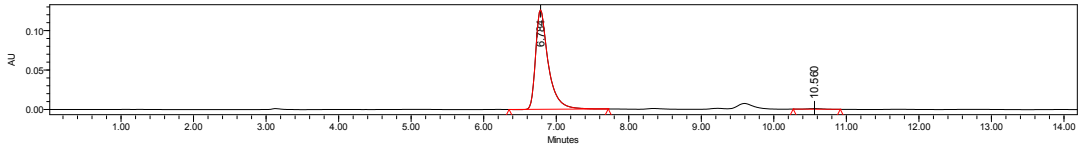

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.177 | 98.89 |
| 2 | 11.789 | 1.11 |



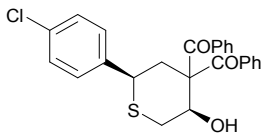

**((2*R*,5*R*)-2-(3-chlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3f)**; 27.1 mg, 62% yield; a colorless oil; 98% ee, 11.1:1 dr; $[\alpha]_D^{19}$ = +234.18 (*c* = 0.542, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.78 min, $t_{R(minor)}$ = 10.56 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 4H), 7.49 (m, 2H), 7.37 (m, 4H), 7.23–7.14 (m, 3H), 7.12–7.04 (m, 1H), 4.97 (s, 1H), 4.08 (dd, *J* = 14.3, 1.4 Hz, 1H), 3.69 (dd, *J* = 12.8, 1.3 Hz, 1H), 3.05 (dd, *J* = 15.1, 13.1 Hz, 2H), 2.88–2.73 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 199.99, 197.35, 142.77, 136.80, 136.51, 134.54, 133.61, 132.97, 130.01, 128.99, 128.77, 128.72, 128.66, 128.05, 127.47, 125.43, 69.31, 65.47, 41.52, 36.65, 35.27; ESI-HRMS: calcd for $\mathbf{C_{25}H_{21}Cl^{34.9689}NaO_3S^+}$ ([M+Na$^+$]) 459.0792, found 459.0795; calcd for $\mathbf{C_{25}H_{21}Cl^{36.9659}NaO_3S^+}$ ([M+Na$^+$]) 461.0763, found 461.0758.



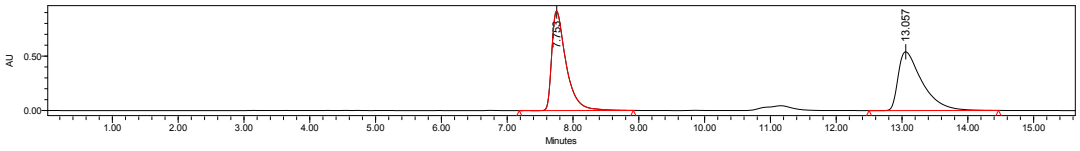

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.752 | 49.93 |
| 2 | 10.496 | 50.07 |



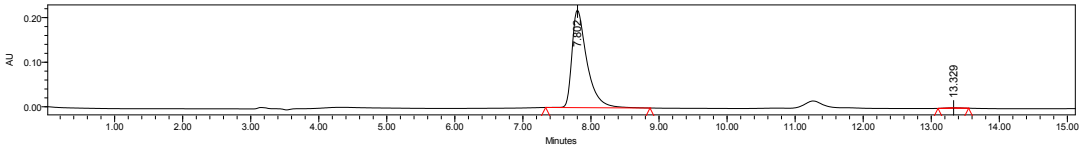

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.784 | 99.36 |
| 2 | 10.560 | 0.64 |



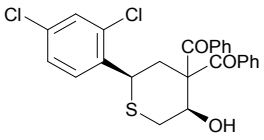

**((2*R*,5*R*)-2-(4-chlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3g)**; 22.3 mg,51% yield; colorless oil; 99% ee, 14.3:1 dr; $[\alpha]_D^{21}$ = +264.12 (*c* = 0.446, in $CH_2Cl_2$); (HPLCDAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.80 min, $t_{R(minor)}$ = 13.33 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.88–7.79 (m, 4H), 7.49 (m, 2H), 7.36 (m, 4H), 7.23 (m, 2H), 7.13 (m, 2H), 4.97 (dd, *J* = 10.4, 2.6 Hz, 1H),4.08 (dd, *J* = 14.3, 1.6 Hz, 1H), 3.69 (dd, *J* = 12.8, 1.2 Hz, 1H), 3.05 (dd, *J* = 19.5, 8.7 Hz, 2H), 2.86–2.73 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ = 172.88, 147.72, 147.45, 132.94, 120.15, 108.15, 106.83, 101.11, 83.06, 72.77, 27.86; ESI-HRMS: $\mathbf{C_{25}H_{21}Cl^{34.9689}NaO_3S^+}$ ([M+Na$^+$])459.0792, found 459.0794; calcd for $\mathbf{C_{25}H_{21}Cl^{36.9659}NaO_3S^+}$ ([M+Na$^+$]) 461.0763, found 461.0765.



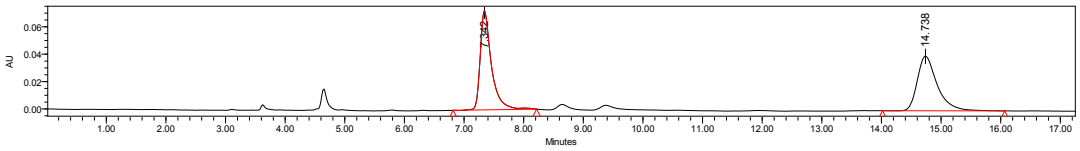

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.753 | 50.27 |
| 2 | 13.057 | 49.73 |



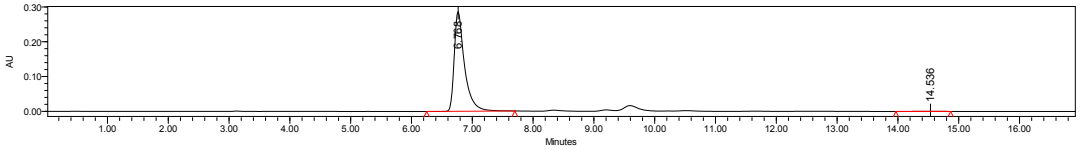

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.802 | 99.53 |
| 2 | 13.329 | 0.47 |




**((2*R*,5*R*)-2-(2,4-dichlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3h)**; 29.7 mg, 63% yield; colorless oil; 99% ee, 14.3:1 dr; $[\alpha]_D^{12}$ = +308.14 (*c* = 0.594, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.77 min, $t_{R(minor)}$ = 14.54 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90–7.80 (m, 4H), 7.53–7.45 (m, 2H), 7.41–7.33 (m, 4H), 7.20 (m, 2H), 7.08 (m, 1H), 4.97 (dd, *J* = 10.5, 2.8 Hz, 1H), 4.07 (dd, *J* = 14.4, 1.8 Hz, 1H), 3.69 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.05 (m, 2H), 2.87–2.75 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 199.99, 197.35, 142.78, 136.81, 136.51, 134.54, 133.61, 132.97, 130.01, 128.99, 128.77, 128.72, 128.67, 128.05, 127.47, 125.43, 69.32, 65.47, 41.52, 36.65, 35.27; ESI-HRMS: calcd for $\mathbf{C_{25}H_{20}Cl_2^{34.9689}NaO_3S^+}$ ([M+Na$^+$]) 493.0402, found 493.0407; calcd for $\mathbf{C_{25}H_{20}Cl^{34.9689}Cl^{36.9659}NaO_3S^+}$ ([M+Na$^+$]) 495.0373, found 495.0381.

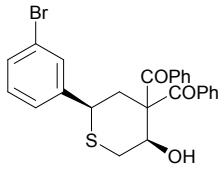



| | Retention Time | % Area |
|---|---|---|
| 1 | 7.342 | 50.70 |
| 2 | 14.738 | 49.30 |

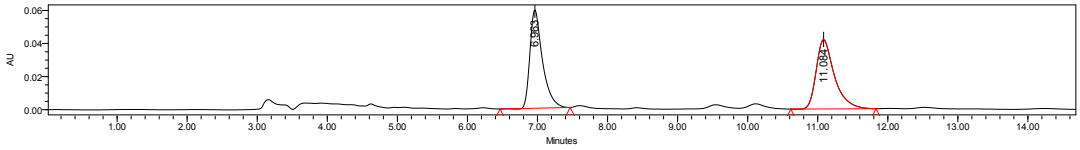



| | Retention Time | % Area |
|---|---|---|

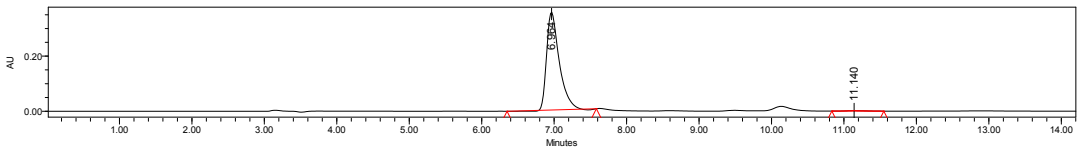
| | | |
|---|---|---|
| 1 | 6.768 | 99.90 |
| 2 | 14.536 | 0.10 |



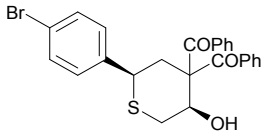

**((2*R*,5*R*)-2-(3-bromophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3i)**; 24.0 mg, 50% yield; colorless oil; 98% ee, 12.5:1 dr; $[\alpha]_D^{19}$ = +198.68 (*c* = 0.481, in $CH_2Cl_2$); (HPLCDAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.96 min, $t_{R(minor)}$ = 11.14 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.79 (m, 4H), 7.48 (m, 2H), 7.42–7.33 (m, 6H), 7.19–7.10 (m, 2H), 4.97 (dd, *J* = 10.5, 2.8 Hz, 1H), 4.07 (dd, *J* = 14.4, 1.7 Hz, 1H), 3.68 (dd, *J* = 12.9, 1.8 Hz, 1H), 3.04 (m, 2H), 2.87–2.74 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 199.97, 197.36, 143.06, 136.82, 136.53, 133.60, 132.95, 130.98, 130.36, 130.29, 128.99, 128.76, 128.72, 128.66, 125.90, 122.71, 69.33, 65.46, 41.48, 36.64, 35.27; ESI-HRMS: calcd for $\mathbf{C_{25}H_{21}Br^{78.9183}NaO_3S^+}$ ([M+Na$^+$]) 503.0287, found 503.0290; calcd for $\mathbf{C_{25}H_{21}Br^{80.9163}NaO_3S^+}$ ([M+Na$^+$]) 505.0267, found 505.0263.




| | Retention Time | % Area |
|---|---|---|
| 1 | 6.963 | 49.52 |
| 2 | 11.084 | 50.48 |

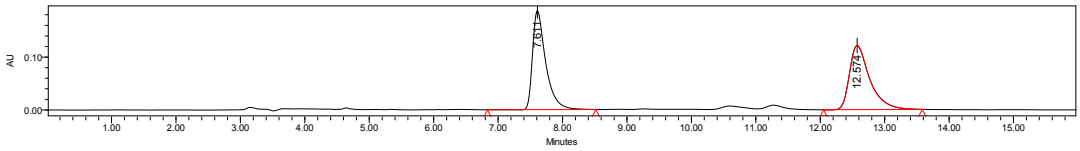



| | Retention Time | % Area |
|---|---|---|
| 1 | 6.964 | 99.35 |
| 2 | 11.140 | 0.65 |

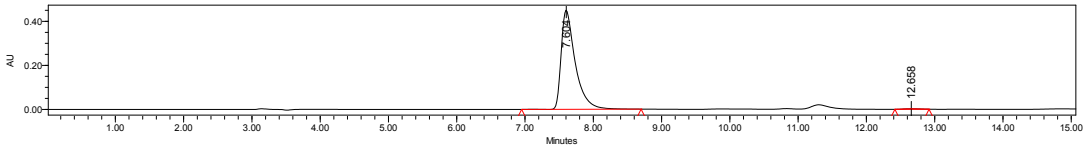



**((2*R*,5*R*)-2-(4-bromophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3j)**; 28.9 mg, 60% yield; colorless oil; 99% ee, 12.5:1 dr; $[\alpha]_D^{19}$ = +265.87 (*c* = 0.578, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.60 min, $t_{R(minor)}$ = 12.66 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.78 (m, 4H), 7.48 (m, 2H), 7.41–7.32 (m, 6H), 7.12–7.03 (m, 2H), 4.97 (dd, *J* = 10.5, 2.7 Hz, 1H), 4.06 (dd, *J* = 14.3, 1.7 Hz, 1H), 3.67 (dd, *J* = 12.9, 1.6 Hz, 1H), 3.03 (m, 2H), 2.80 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.05, 197.34, 139.87, 136.82, 136.56, 133.57, 132.97, 131.88, 128.97, 128.90, 128.77, 128.68, 128.66, 121.68, 69.38, 65.47, 41.39, 36.78, 35.25; ESI-HRMS: calcd for

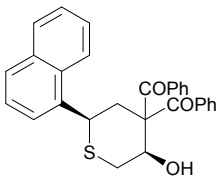
$C_{25}H_{21}Br^{78.9183}NaO_3S^+$ ([M+Na$^+$]) 503.0287, found 503.0286; calcd for $C_{25}H_{21}Br^{80.9163}NaO_3S^+$ ([M+Na$^+$]) 505.0267, found 505.0269.



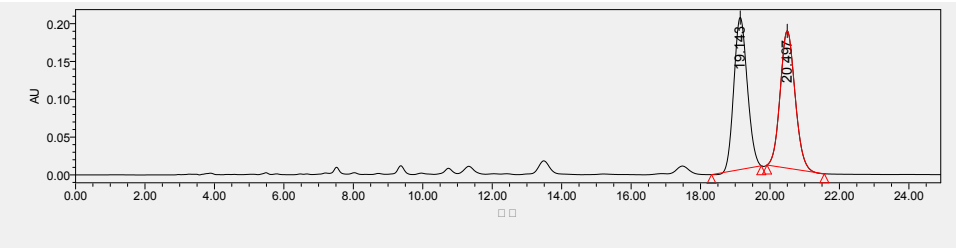

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.611 | 50.14 |
| 2 | 12.574 | 49.86 |



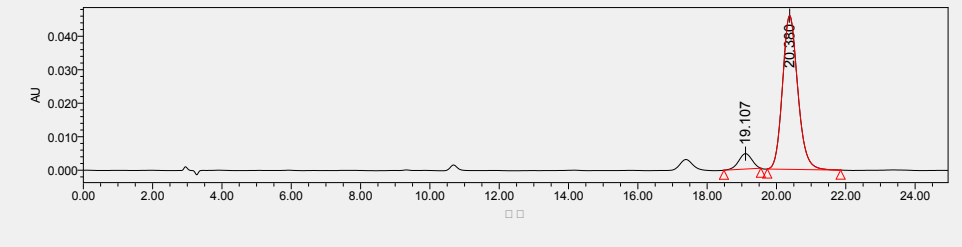

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.604 | 99.48 |
| 2 | 12.658 | 0.52 |



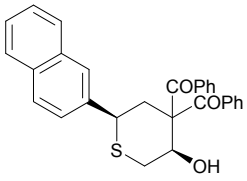

**((2*R*,5*R*)-5-hydroxy-2-(naphthalen-1-yl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3k)**; 17.2 mg, 38% yield; colorless oil ; 84% ee, 7.8:1 dr; $[\alpha]_D^{21}$ = +244.25 (*c* = 0.344, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IA), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 19.11 min, $t_{R(minor)}$ = 20.38 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (m, 4H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.65 (m, 2H), 7.44–7.26 (m, 9H), 7.07 (m, 1H), 4.99 (dd, *J* = 10.8, 2.9 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.15 (dd, *J* = 14.4, 1.3 Hz, 1H), 3.17–3.03 (m, 2H), 2.99–2.79 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ = 199.08, 196.47, 135.92, 135.62, 135.50, 132.71, 132.68, 129.24, 128.04, 128.00, 127.91, 127.72, 127.61, 127.27, 125.10, 124.58, 124.47, 123.19, 121.02, 68.80, 64.77, 36.43, 35.29, 34.31; ESI-HRMS: calcd for $C_{26}H_{24}NaO_3S^+$ ([M+Na$^+$]) 475.1338; found 475.1341.



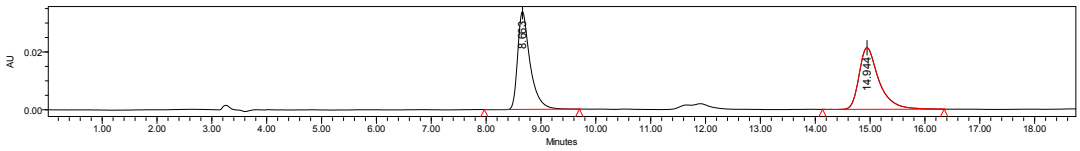

| | Retention Time | % Area |
|---|---|---|
| 1 | 19.143 | 50.14 |
| 2 | 20.497 | 49.86 |



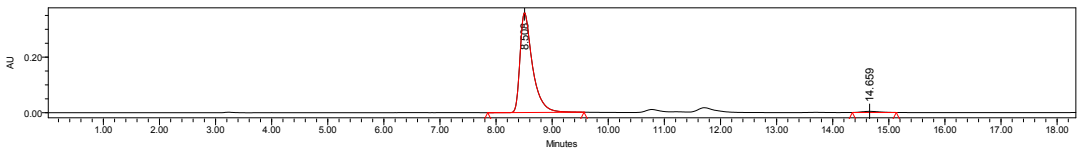

| | Retention Time | % Area |
|---|---|---|
| 1 | 19.107 | 8.06 |
| 2 | 20.380 | 91.94 |



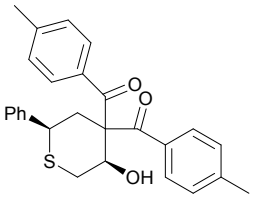

**((2*R*,5*R*)-5-hydroxy-2-(naphthalen-2-yl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3l)**; 33.4 mg, 74% yield; colorless oil; 96% ee, 16.7:1 dr; $[\alpha]_D^{19}$ = +212.01 (*c* = 0.669, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 8.51 min, $t_{R(minor)}$ = 14.66 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.86 (m, 4H), 7.74 (m, 3H), 7.70 (s, 1H), 7.49–7.42 (m, 4H), 7.37 (m, 4H), 7.33–7.28 (m, 2H), 5.01 (dd, *J* = 10.5, 2.6 Hz, 1H), 4.15 (d, *J* = 14.3 Hz, 1H), 3.89 (d, *J* = 12.7 Hz, 1H), 3.28–3.13 (m, 2H), 2.97–2.82 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.21, 197.52, 138.16, 136.91, 136.62, 133.55, 133.29, 132.95, 132.87, 128.96, 128.78, 128.76, 128.70, 128.49, 127.87, 127.62, 126.35, 126.17, 125.86, 125.43, 69.50, 65.65, 42.10, 36.76, 35.44; ESI-HRMS: calcd for **$C_{29}H_{24}NaO_3S^+$** ([M+$Na^+$]) 475.1338; found 475.1331.




| | Retention Time | % Area |
|---|---|---|
| 1 | 8.663 | 49.79 |
| 2 | 14.944 | 50.21 |

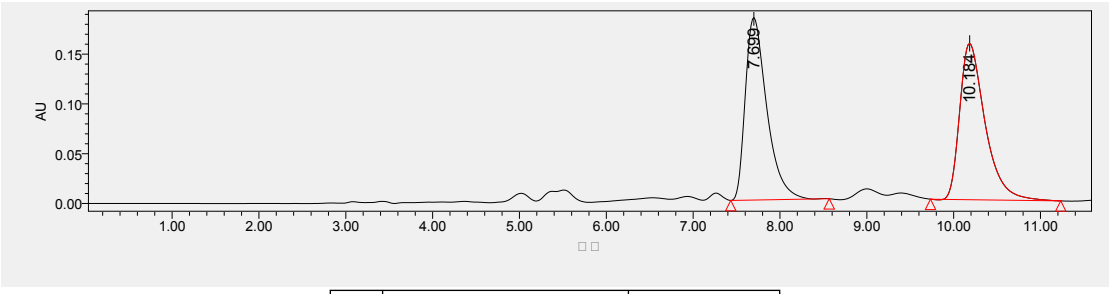



| | Retention Time | % Area |
|---|---|---|
| 1 | 8.508 | 98.46 |
| 2 | 14.659 | 1.54 |

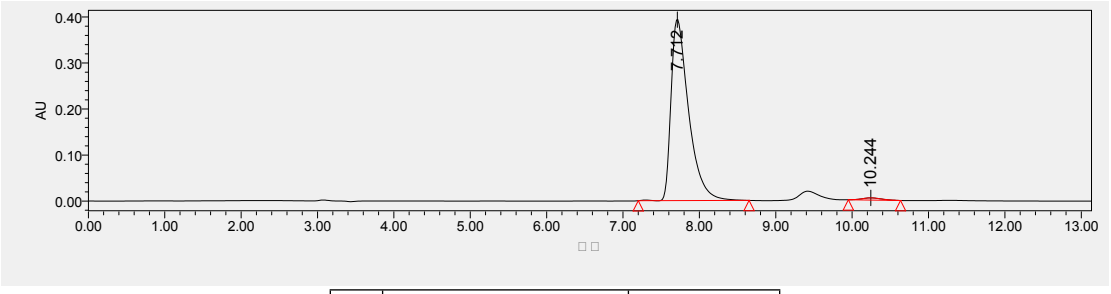



**((2*R*,5*R*)-5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis(p-tolylmethanone) (3m)**; 22.4 mg, 52% yield; colorless oil; 97% ee, 14.3:1 dr; $[\alpha]_D^{21}$ = +197.32 (*c* = 0.448, in $CH_2Cl_2$); (HPLCDAICEL CHIRALCEL IB),

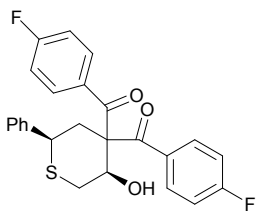
*n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 7.71 min, $t_{R(minor)}$ = 10.24 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.76 (m, 4H), 7.31–7.27 (m, 1H), 7.25–7.05 (m, 8H), 4.95 (dd, *J* = 10.6, 2.5 Hz, 1H), 4.14 (d, *J* = 14.2 Hz, 1H), 3.74 (d, *J* = 12.5 Hz, 1H), 3.12 (dd, *J* = 16.4, 12.8 Hz, 2H), 2.87–2.74 (m, 2H), 2.32 (s,3H), 2.30 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 199.80, 197.03, 144.53, 143.91, 140.99, 134.10, 133.89, 129.59, 129.46, 129.00, 128.94, 128.73, 127.79, 127.29, 68.96, 65.79, 41.91, 36.87, 35.46, 21.59; ESI-HRMS: calcd for **$C_{27}H_{26}NaO_3S^+$** ([M+Na$^+$]) 453.1495, found 453.1494.



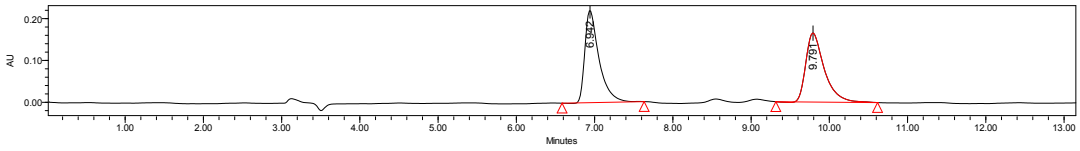

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.699 | 49.71 |
| 2 | 10.184 | 50.29 |



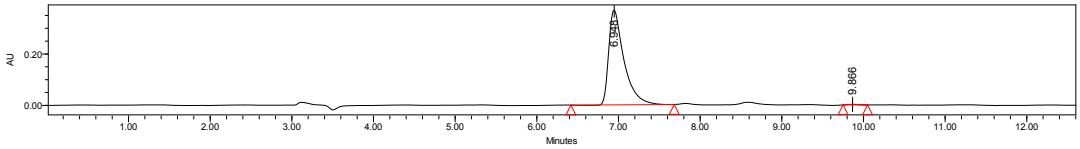

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.712 | 98.74 |
| 2 | 10.244 | 1.26 |



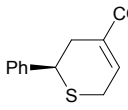

**((2*R*,5*R*)-5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis((4-fluorophenyl)methanone) (3n)**; 24.6 mg, 56% yield; colorless oil; 99% ee, 16.7:1 dr; $[\alpha]_D^{21}$= +230.35 (*c* = 0.491, in $CH_2Cl_2$); (HPLC DAICEL CHIRALCEL IB), *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(major)}$ = 6.95 min, $t_{R(minor)}$ = 9.87 min; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.96–7.85 (m, 4H), 7.37–7.26 (m, 3H), 7.22 (m, 2H), 7.08–6.98 (m, 4H), 4.94 (dd, *J* = 10.8, 2.9 Hz, 1H), 4.11 (dd, *J* = 14.3, 1.7 Hz, 1H), 3.68 (dd, *J* = 13.0, 1.6 Hz, 1H), 3.18–3.05 (m, 2H), 2.88–2.74 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 198.48, 195.73, 167.06, 166.80, 164.50, 164.26, 157.53, 140.64, 132.92, 132.54, 131.77, 131.68, 131.55, 131.46, 128.84, 127.97, 127.17, 116.36, 116.14, 115.93, 69.16, 65.70, 41.95, 36.97, 35.38; ESI-HRMS: calcd for **$C_{25}H_{20}F_2NaO_3S^+$** ([M+Na$^+$]) 461.0993, found 461.0993.



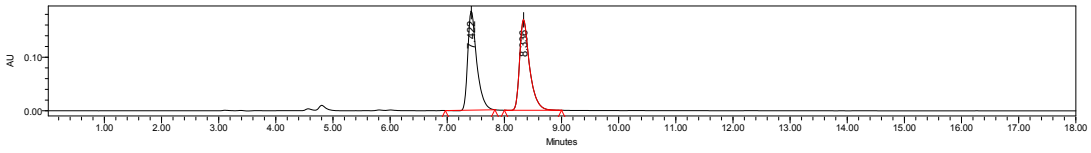

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.942 | 50.61 |
| 2 | 9.791 | 49.39 |



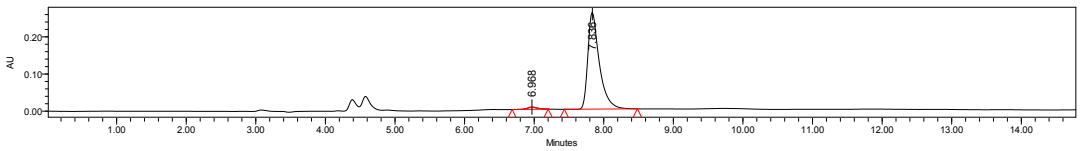

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.948 | 99.59 |
| 2 | 9.866 | 0.41 |




**(*R*)-phenyl(2-phenyl-3,6-dihydro-2*H*-thiopyran-4-yl)methanone (4)**; white solid, mp. 84-87 °C; 71% yield, 96% ee. $[\alpha]_D^{22}$ = +73.69 (*c* = 0.398, in $CH_2Cl_2$). HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{R(minor)}$ = 6.97 min, $t_{R(major)}$ = 7.84 min. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.66–7.57 (m, 2H), 7.49–7.44 (m, 1H), 7.43–7.29 (m, 5H), 7.28–7.15 (m, 2H), 6.67 (m, 1H), 3.98 (d, *J* = 10.2 Hz, 1H), 3.64 (d, *J* = 21.9 Hz, 1H), 3.26 (m, 1H), 3.16–3.04 (m, 1H), 2.89–2.73 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 197.54, 141.30, 139.66, 138.54, 138.04, 131.91, 129.37, 128.74, 128.28, 127.63, 127.49, 42.88, 32.14, 28.34. ESI-HRMS: calcd $C_{18}H_{16}NaOS^+$ ($[M+Na]^+$) 303.0814, found 303.0812.



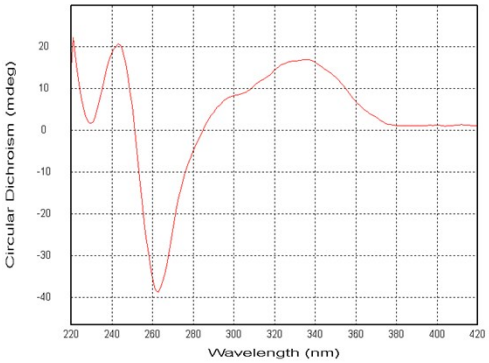

| | Retention Time | % Area |
|---|---|---|
| 1 | 7.422 | 49.65 |
| 2 | 8.336 | 50.35 |



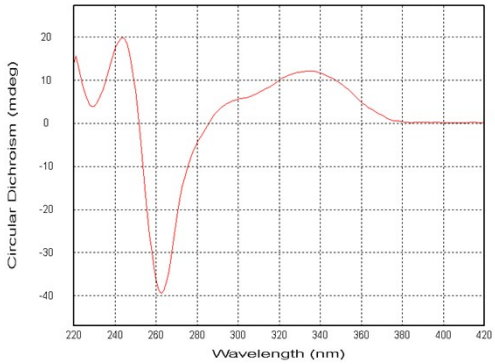

| | Retention Time | % Area |
|---|---|---|
| 1 | 6.968 | 1.95 |
| 2 | 7.836 | 98.05 |

## (9) Circular dichroism spectrum for the products

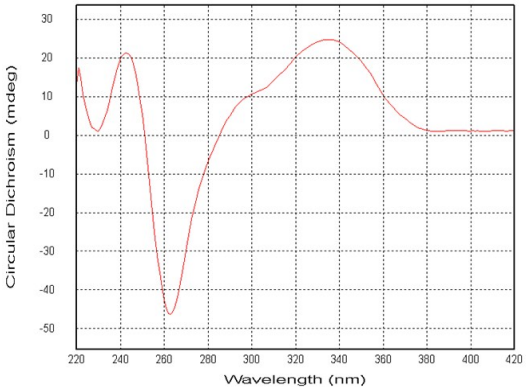
### 3a:




### 3c:

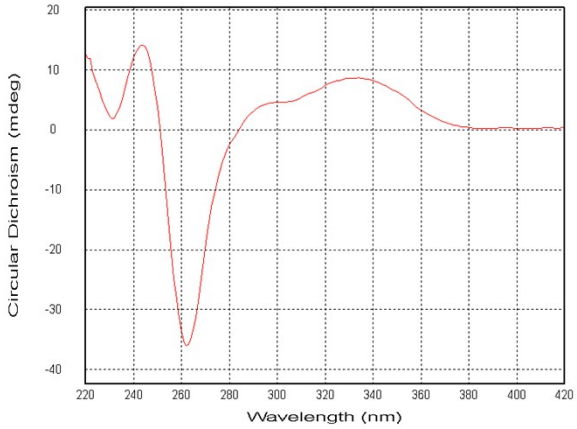



### 3d:

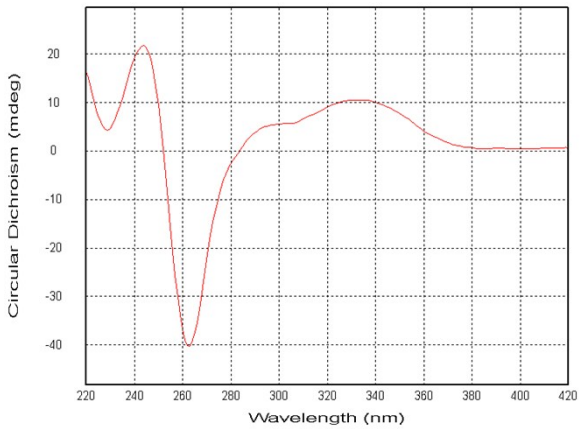


**3e:**

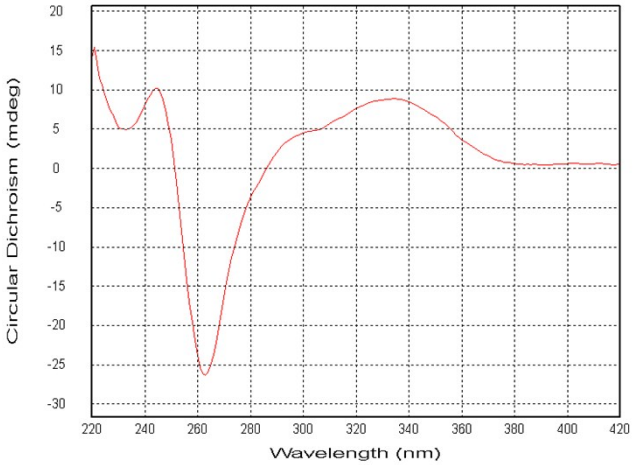
**3g:**


Circular Dichroism (mdeg)
20
10
0
-10
-20
-30
-40
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

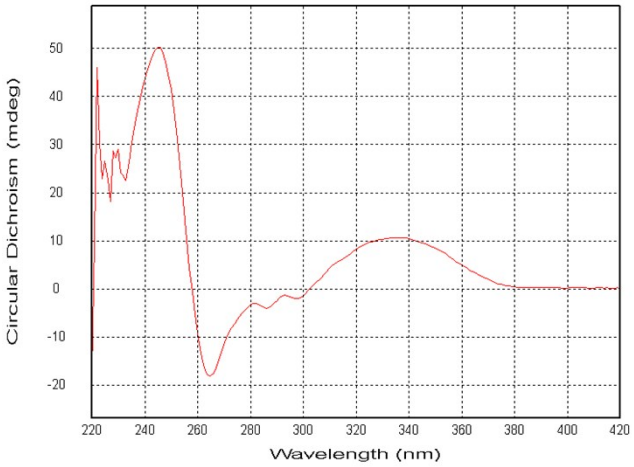
**3i:**


Circular Dichroism (mdeg)
20
10
0
-10
-20
-30
-40
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

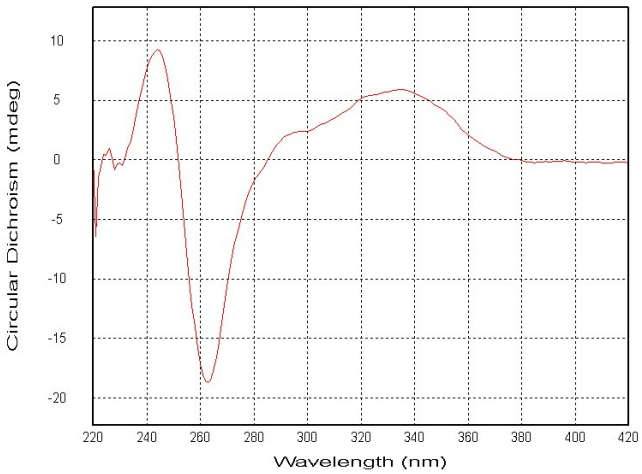
**3j:**


Circular Dichroism (mdeg)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

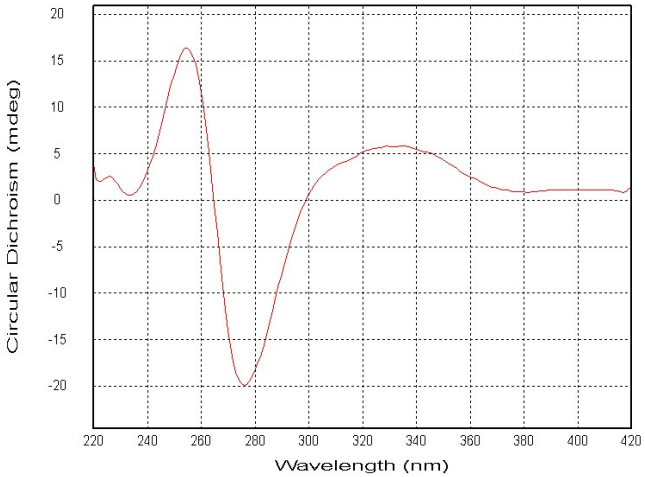
**3k:**


Circular Dichroism (mdeg)
50
40
30
20
10
0
-10
-20
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

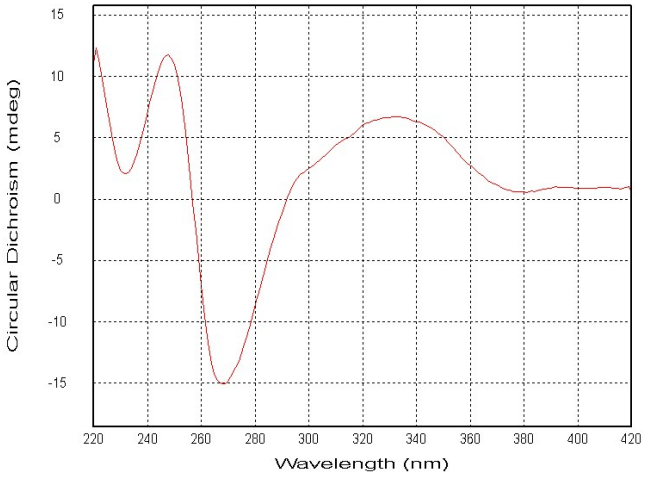
**3l:**


Circular Dichroism (mdeg)
10
5
0
-5
-10
-15
-20
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

**3m:**

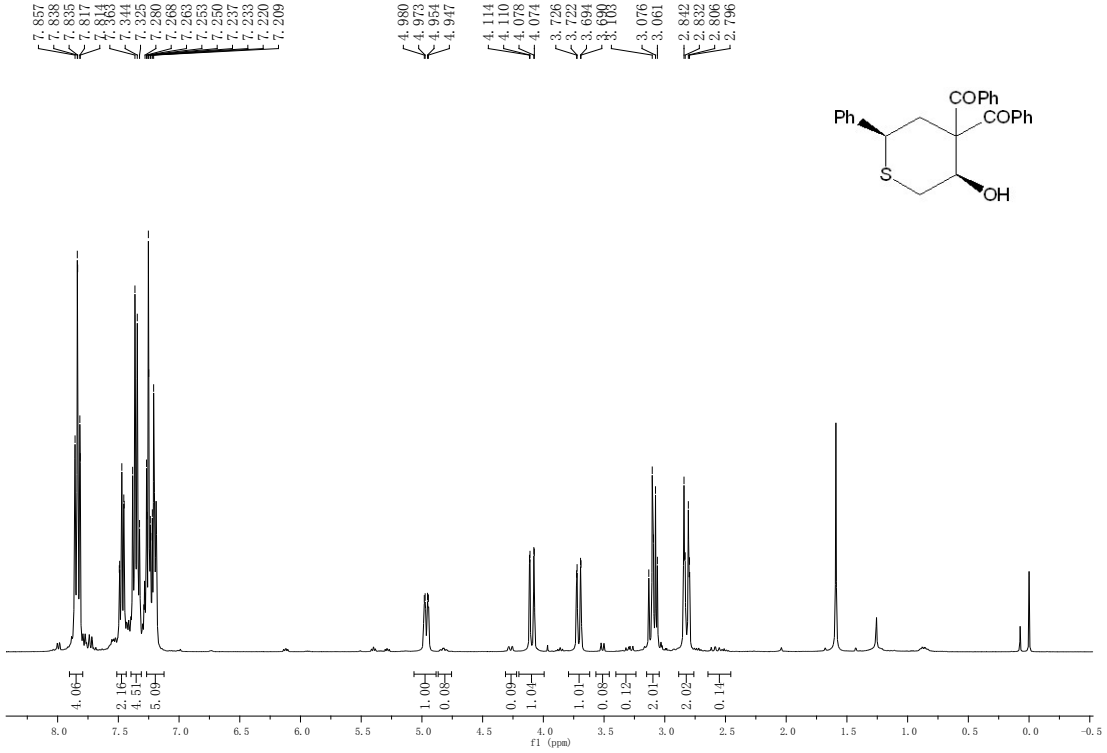

Circular Dichroism (mdeg)
20
15
10
5
0
-5
-10
-15
-20
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

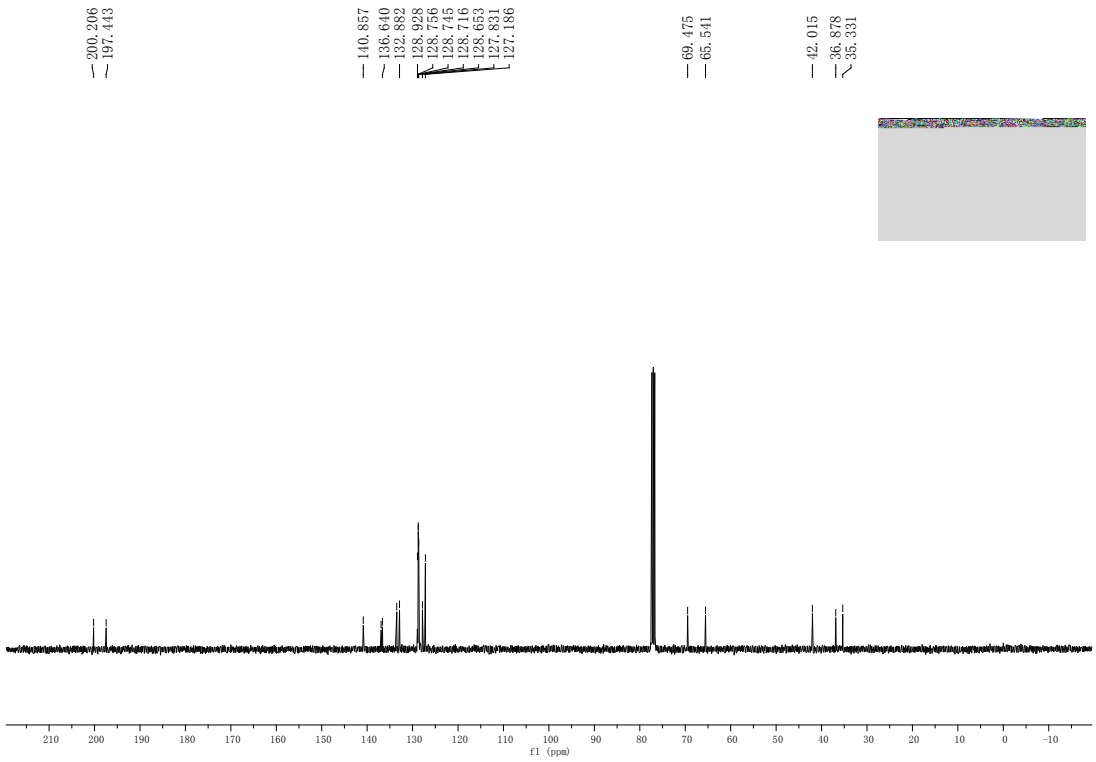
**3n:**


Circular Dichroism (mdeg)
15
10
5
0
-5
-10
-15
220
240
260
280
300
320
340
360
380
400
420
Wavelength (nm)

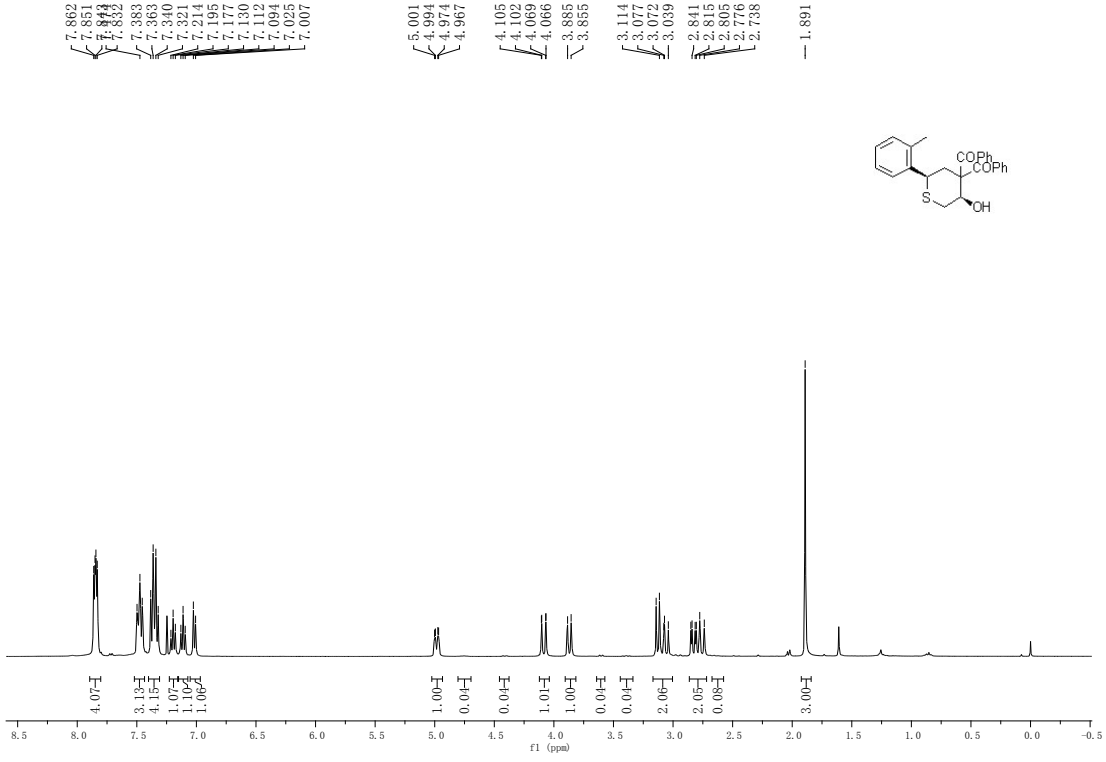
## (10) Copies of NMR spectra for products

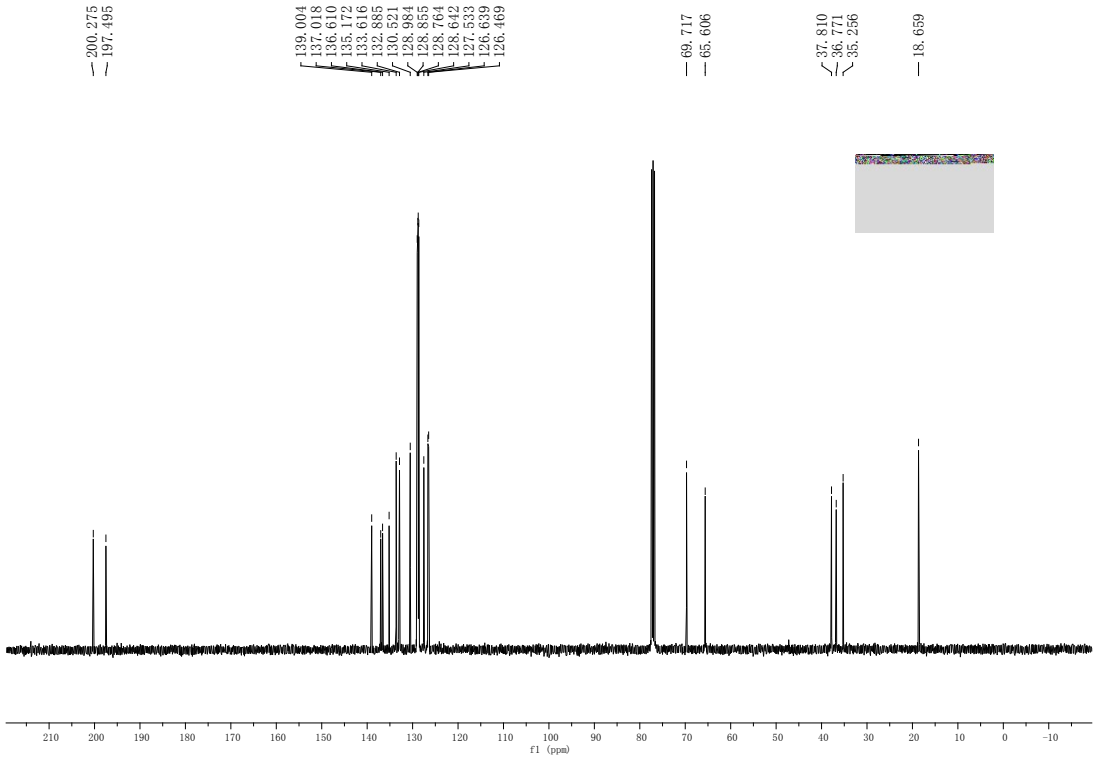
**((2*R*,5*R*)5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3a)**



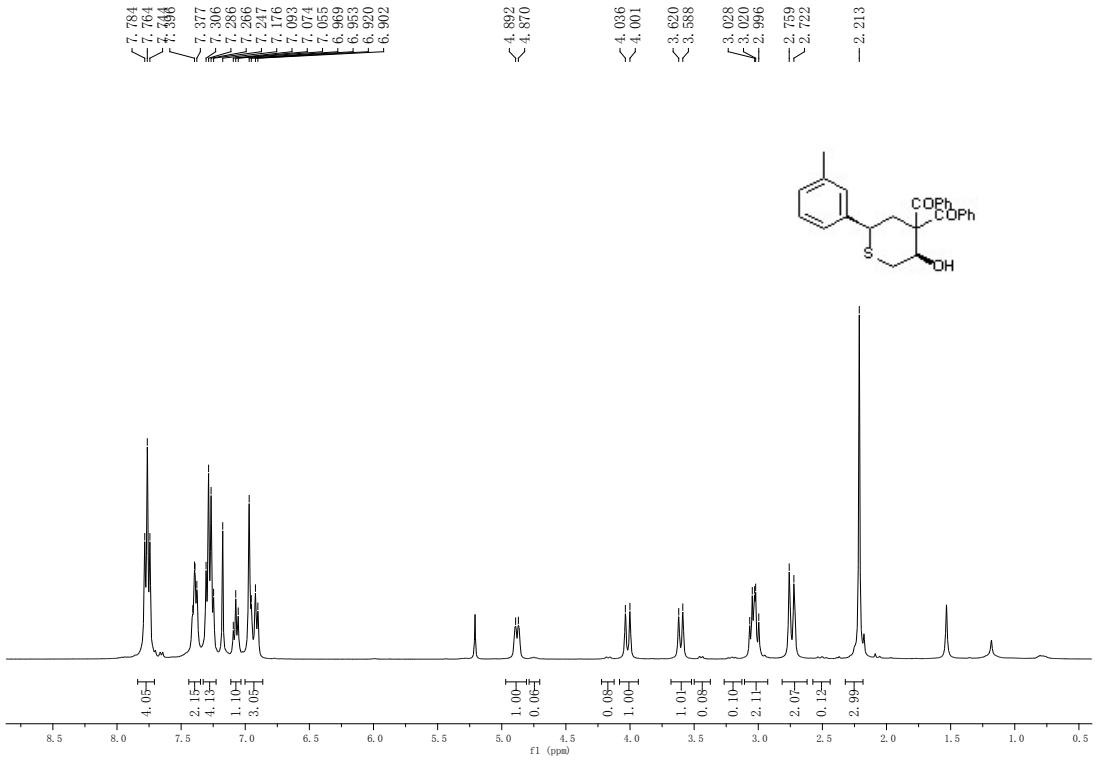


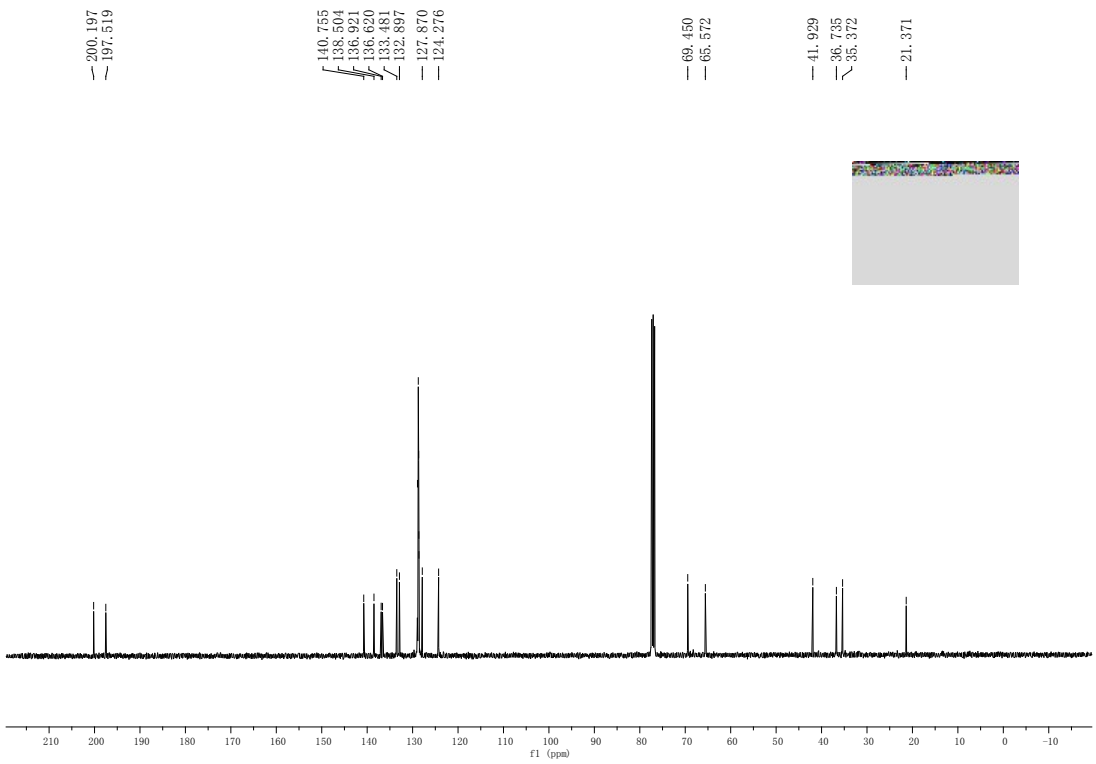

**((2*R*,5*R*)-5-hydroxy-2-(*o*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3b)**



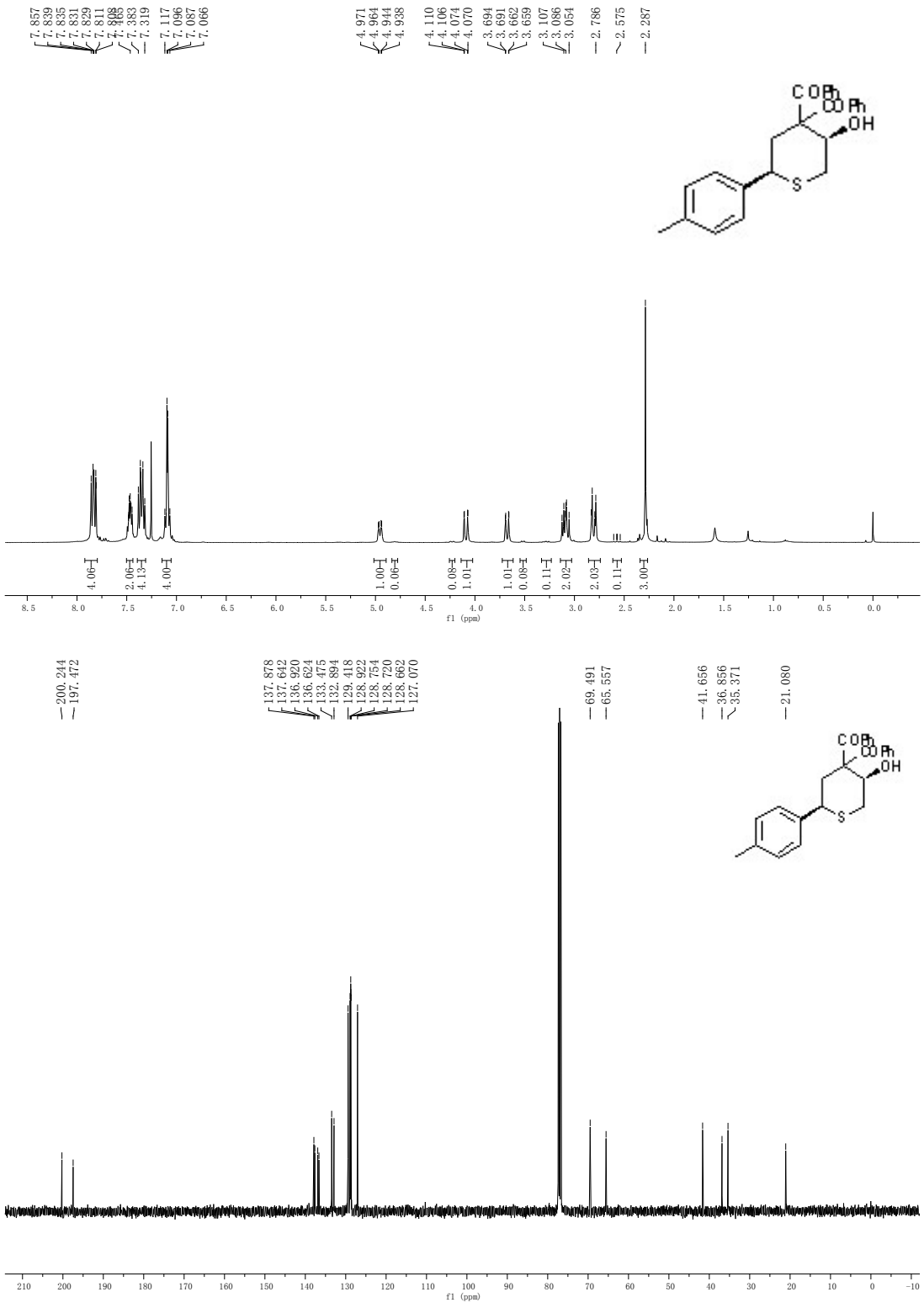



**((2*R*,5*R*)-5-hydroxy-2-(*m*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3c)**

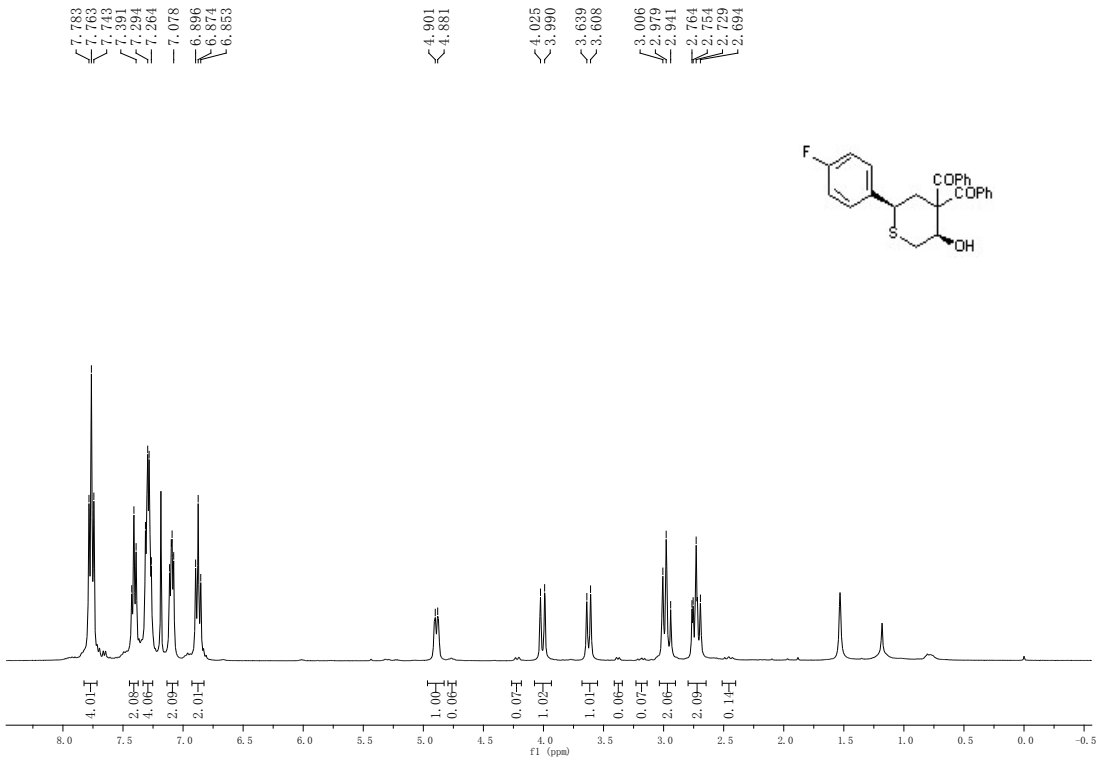


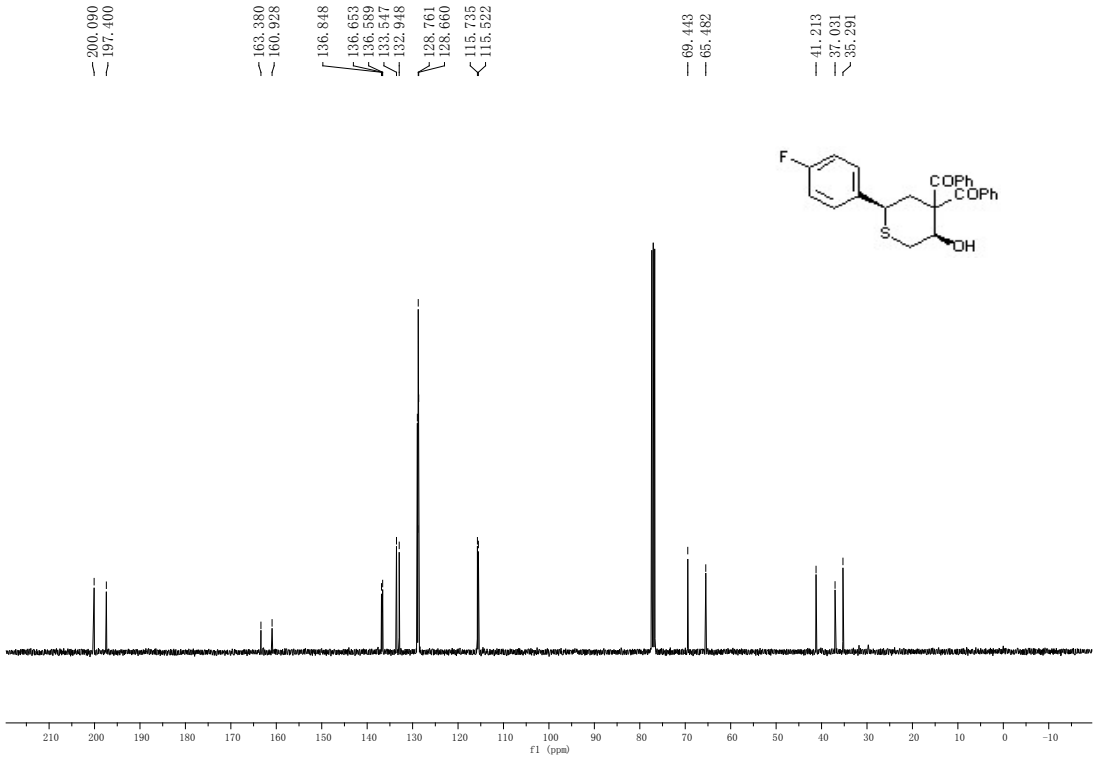

200.197
197.519
140.755
138.504
136.921
136.620
133.481
132.897
127.870
124.276
69.450
65.572
41.929
36.735
35.372
21.371
f1 (ppm)

**((2*R*,5*R*)-5-hydroxy-2-(*p*-tolyl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3d)**

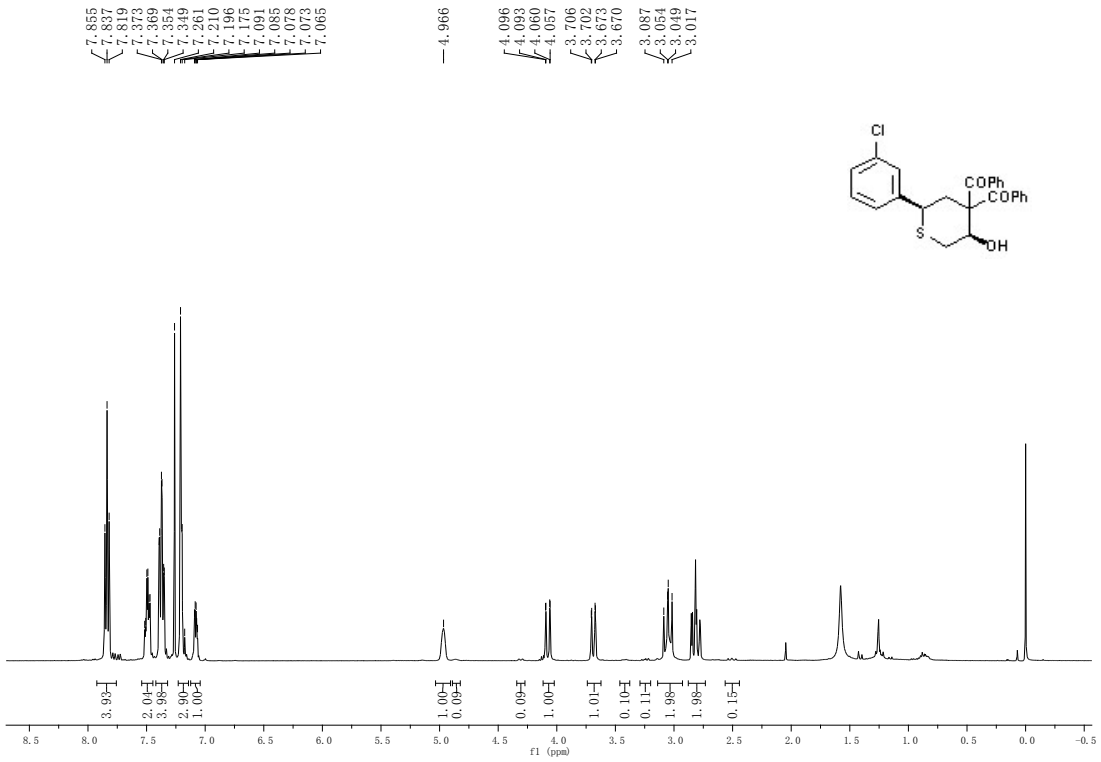


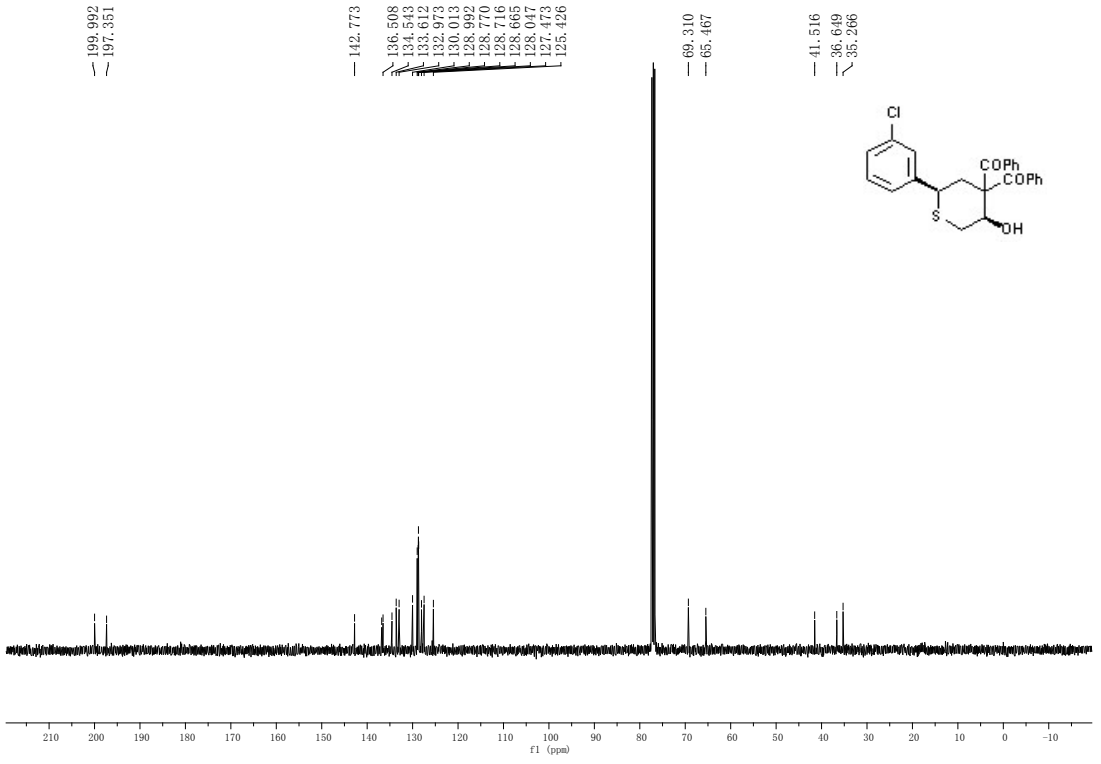
**((2*R*,5*R*)-2-(4-fluorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3e)**



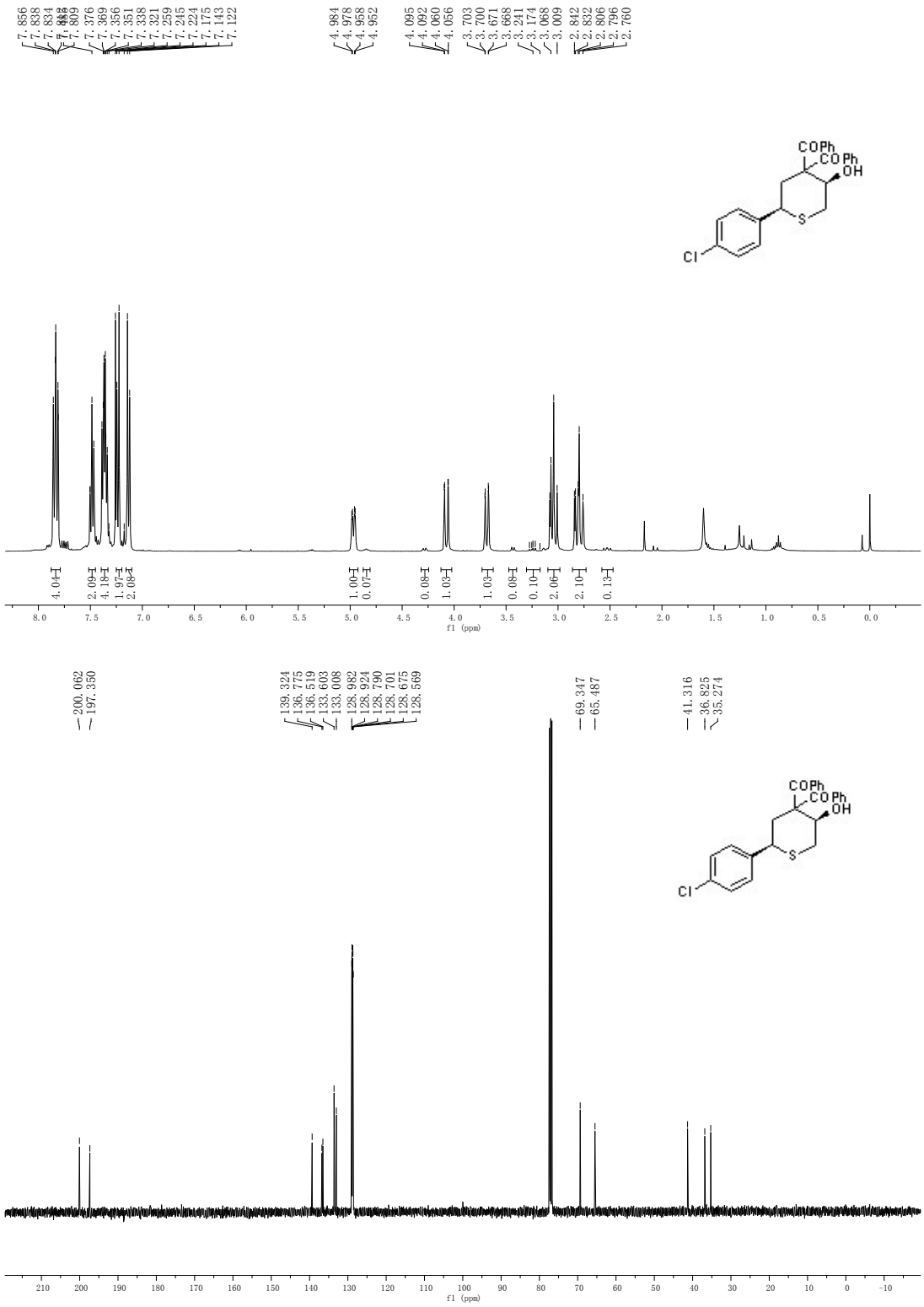



**((2*R*,5*R*)-2-(3-chlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3f)**

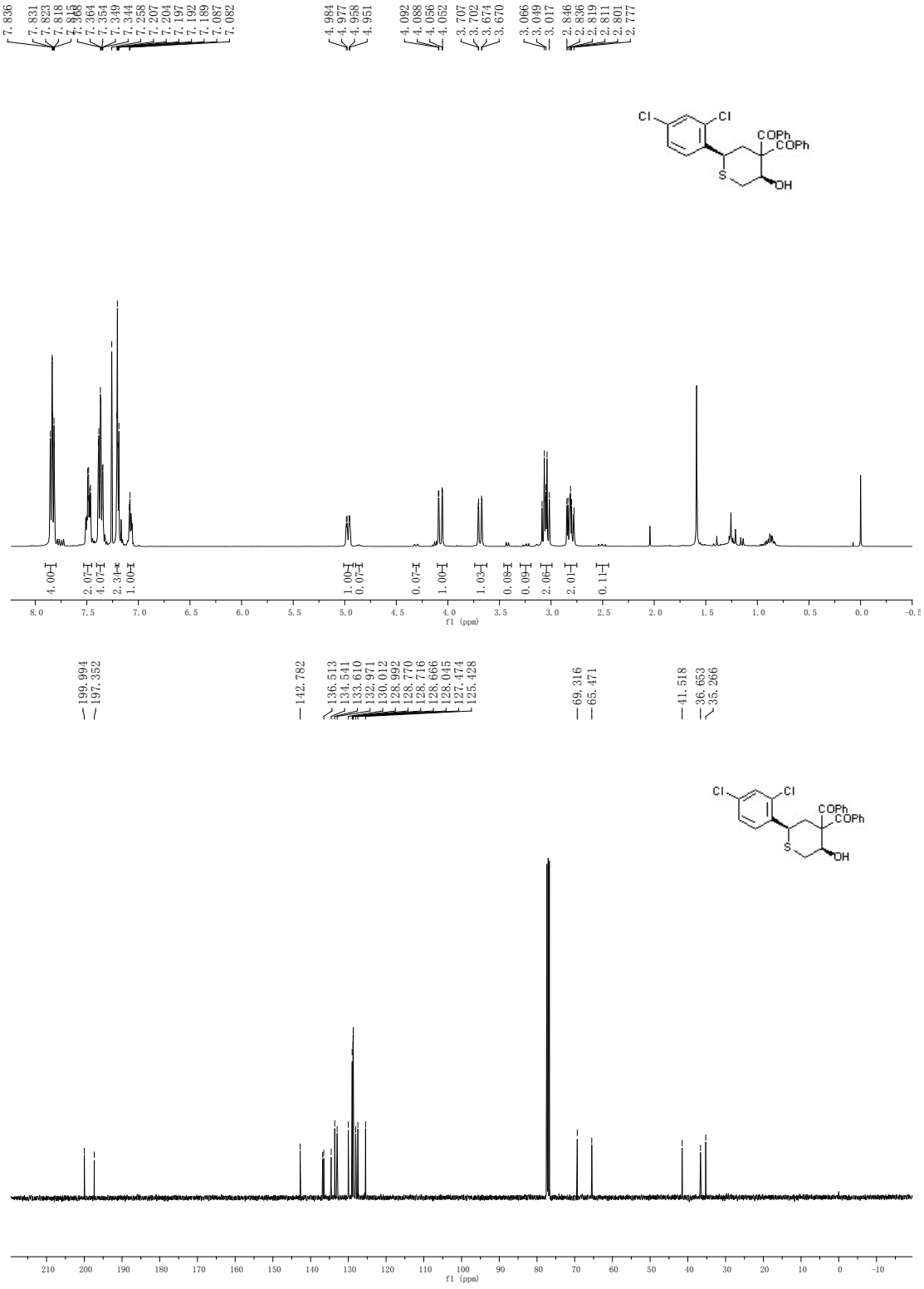


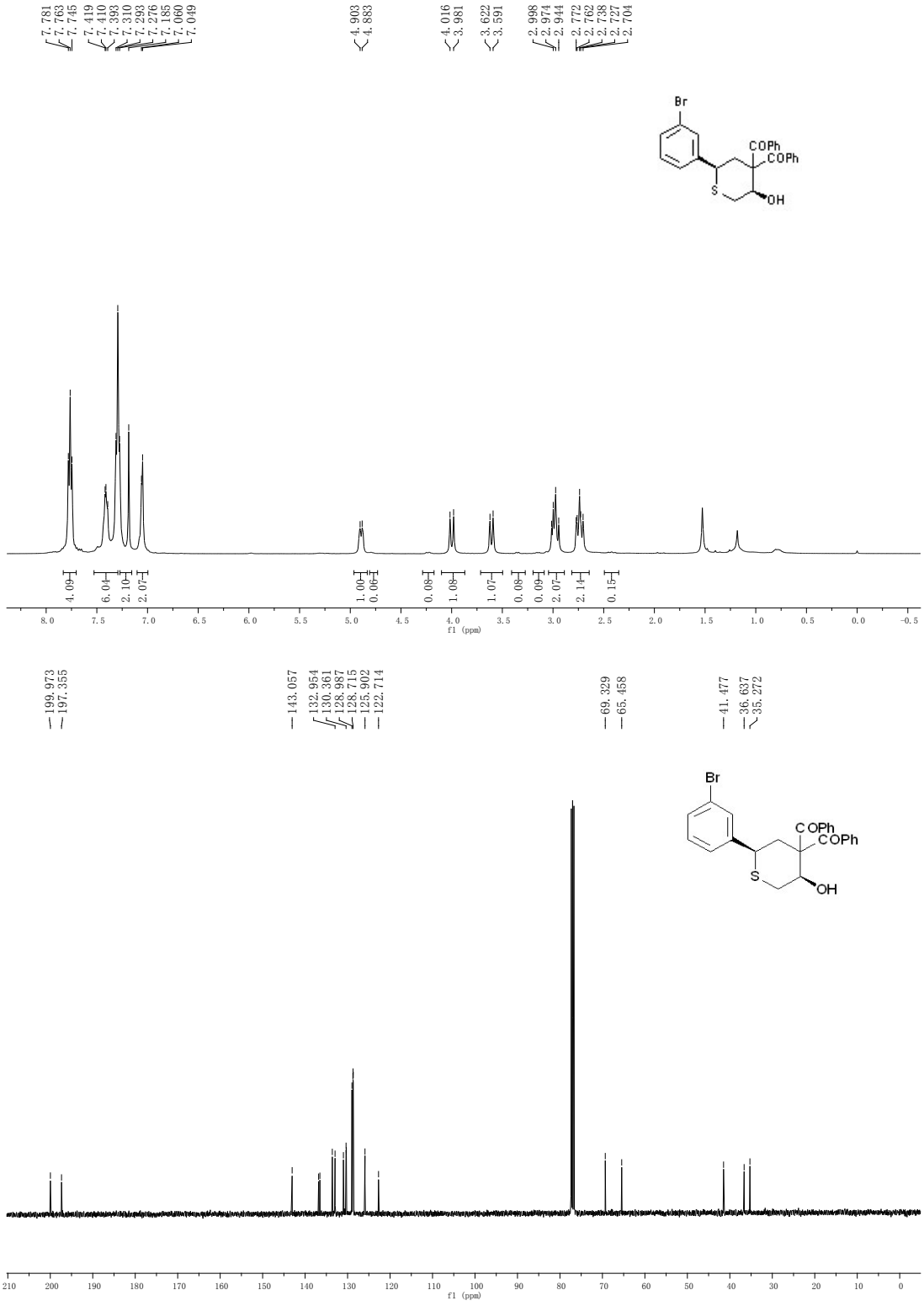
**((2*R*,5*R*)-2-(4-chlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3g)**



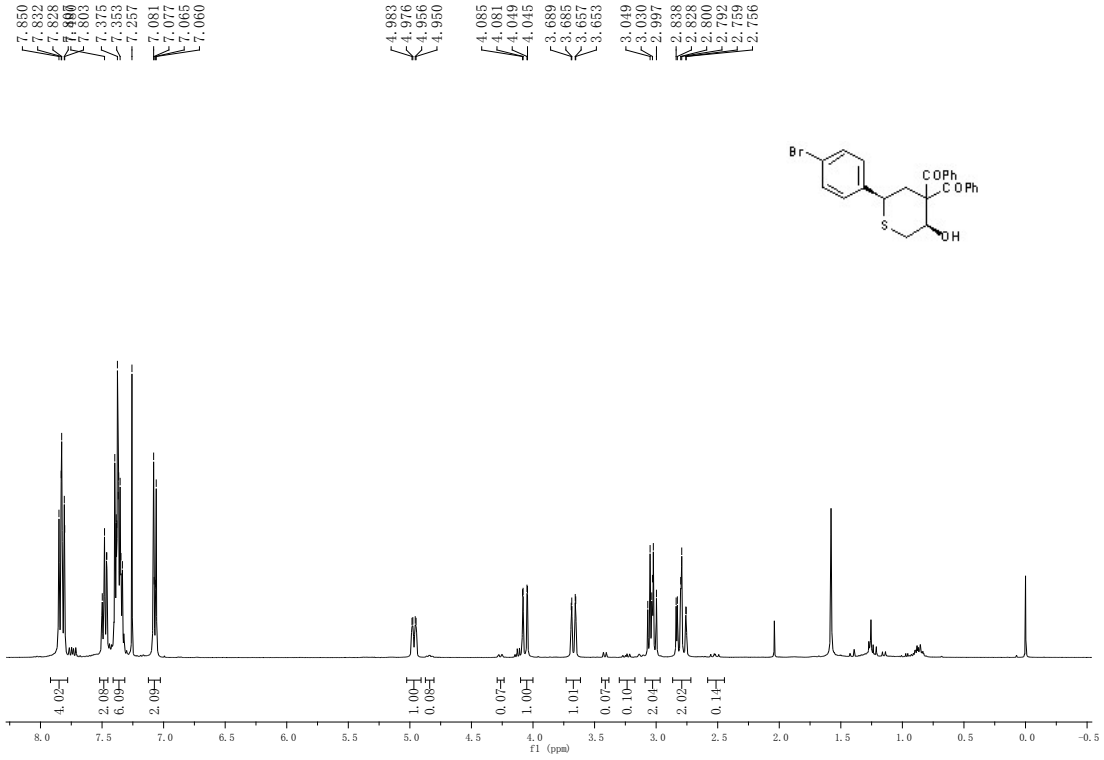
**((2*R*,5*R*)-2-(2,4-dichlorophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3h)**

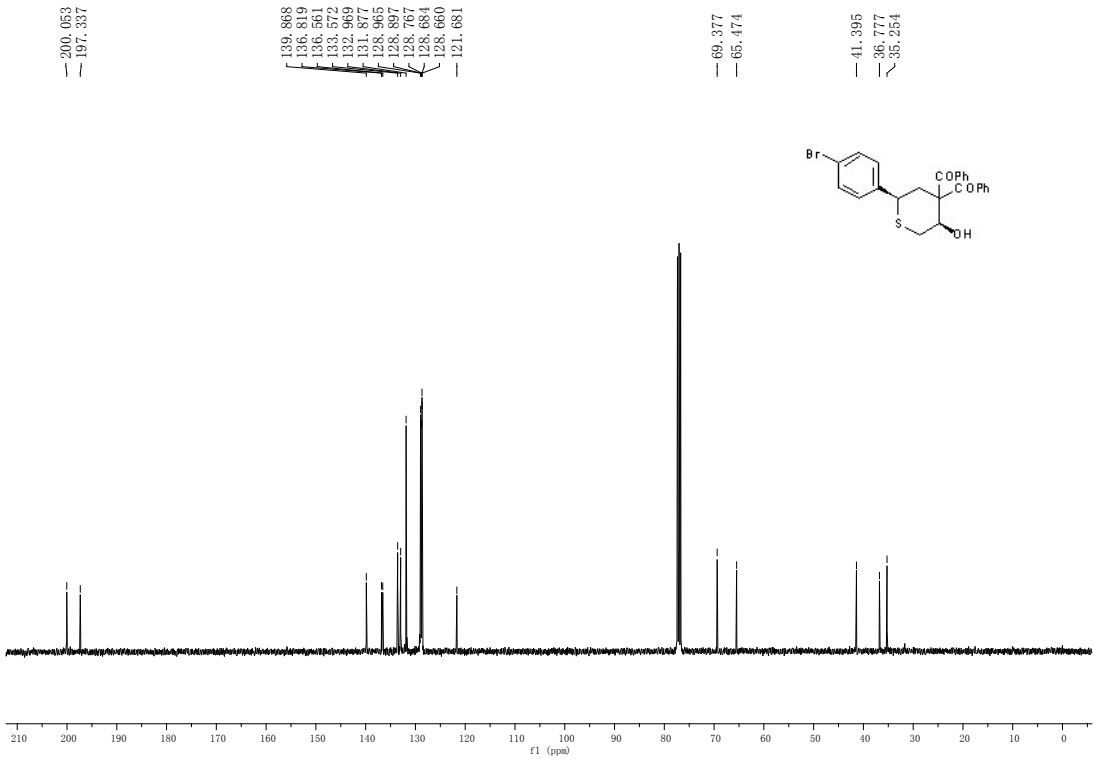


**((2*R*,5*R*)-2-(3-bromophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3i)**

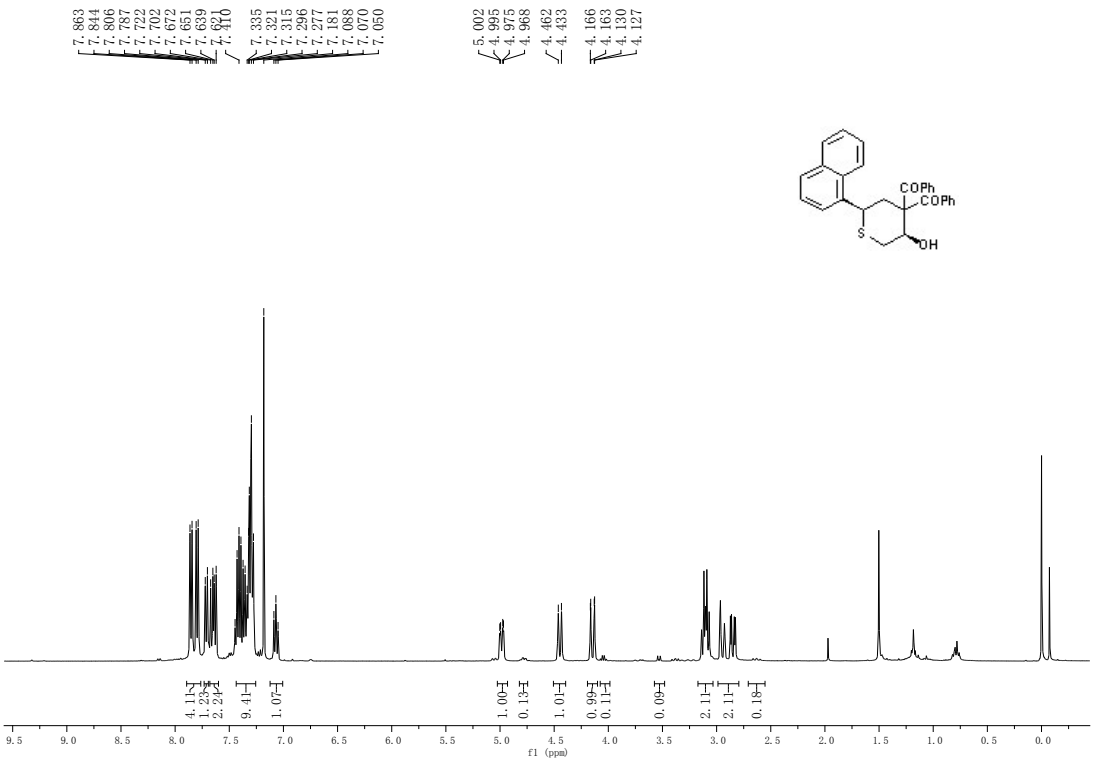


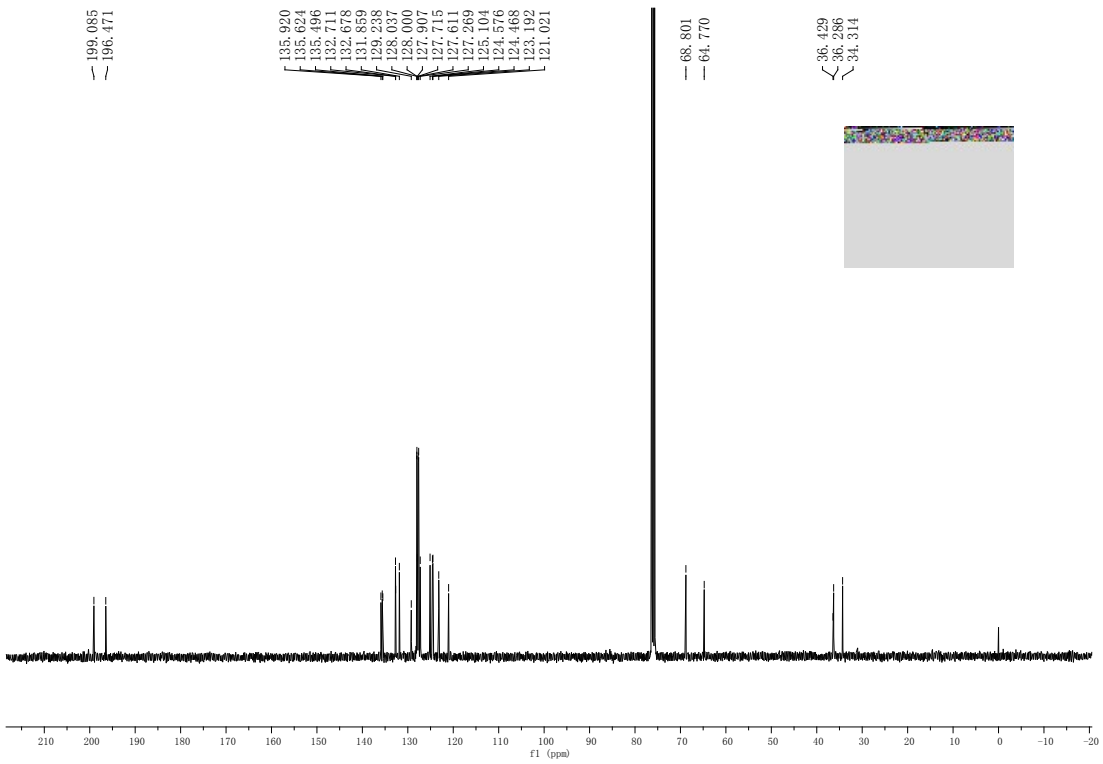
**((2*R*,5*R*)-2-(4-bromophenyl)-5-hydroxytetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3j)**



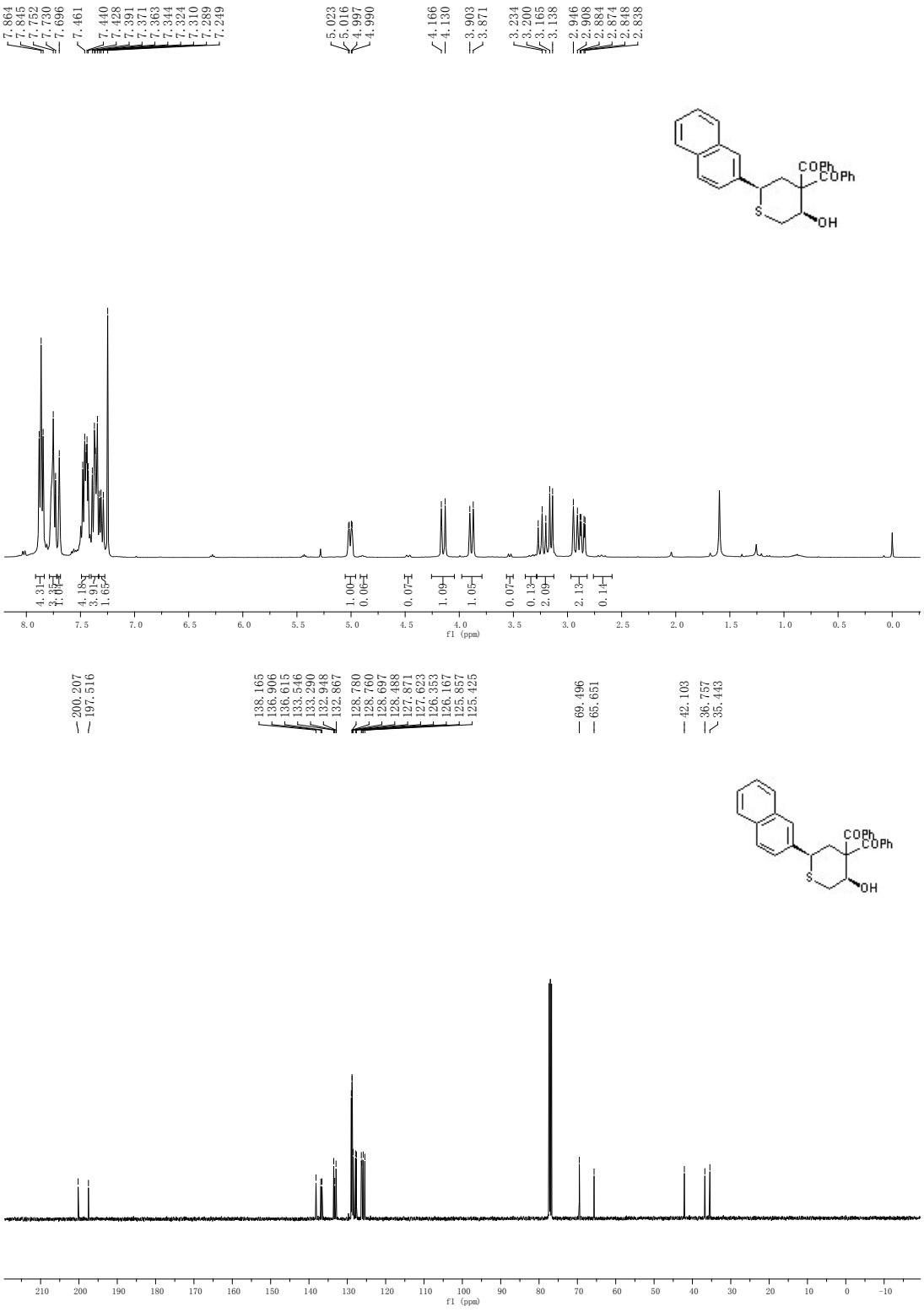



**((2*R*,5*R*)-5-hydroxy-2-(naphthalen-1-yl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3k)**

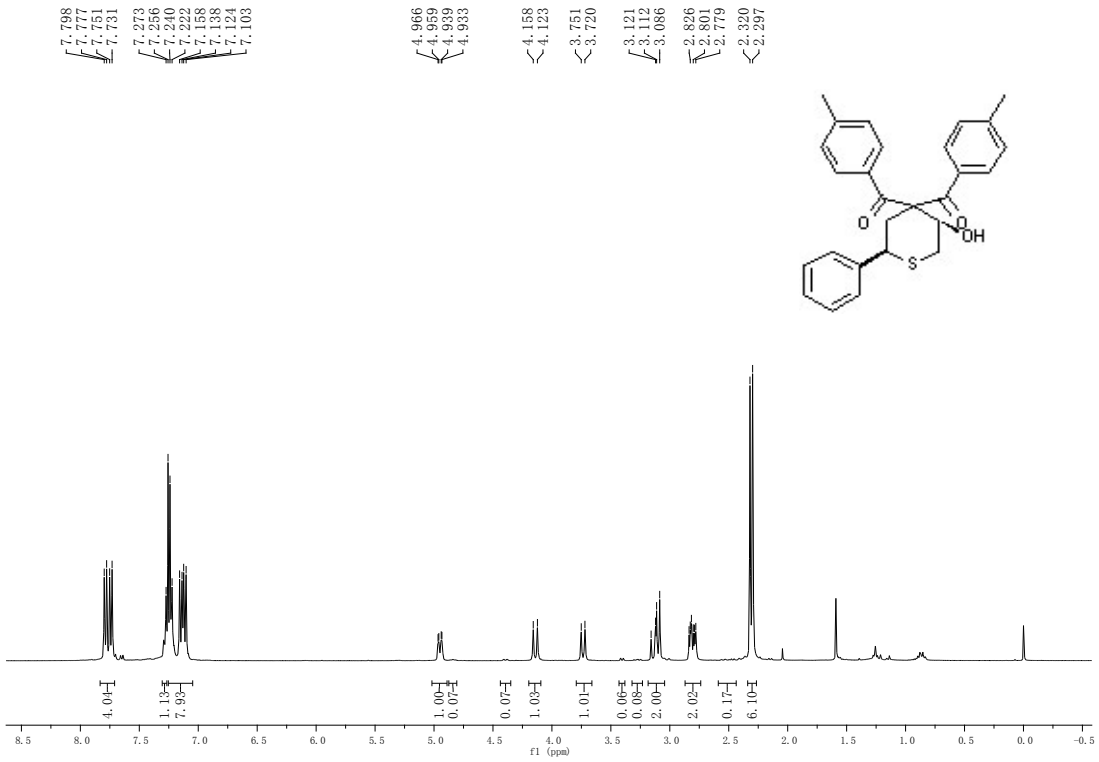


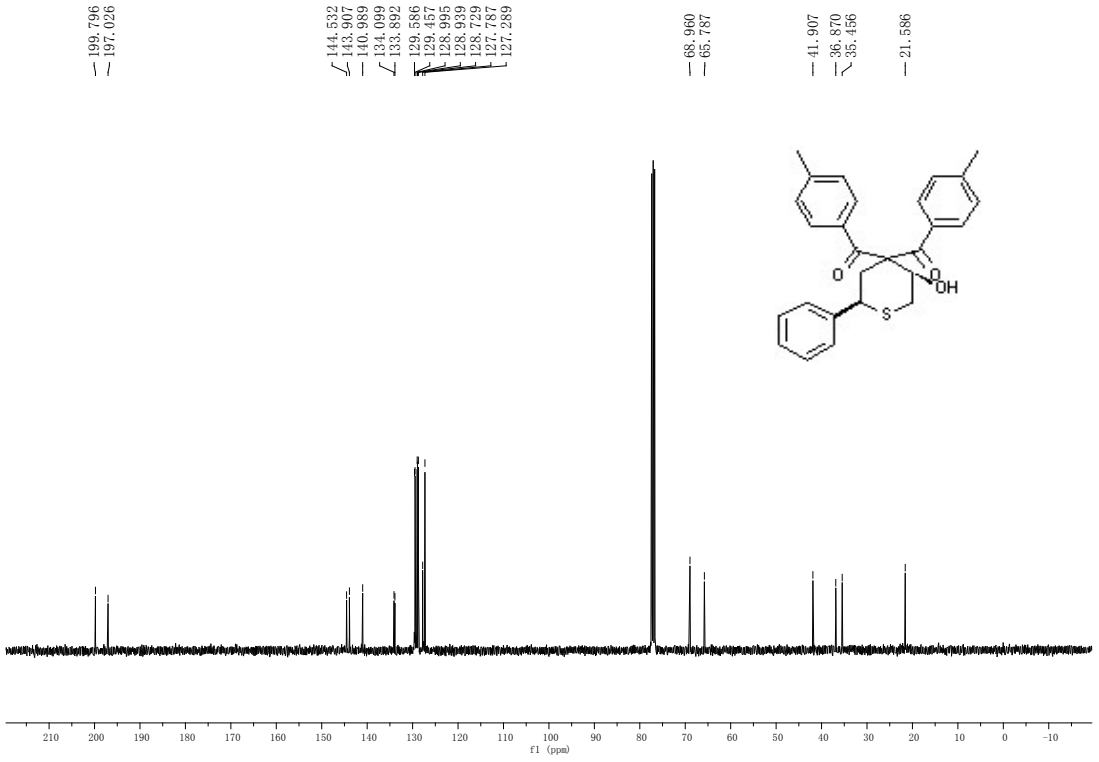

199.085
196.471
135.920
135.624
135.496
132.711
132.678
131.859
129.238
128.037
128.000
127.907
127.715
127.611
127.269
125.104
124.576
124.468
123.192
121.021
68.801
64.770
36.429
36.286
34.314
f1 (ppm)

**((2*R*,5*R*)-5-hydroxy-2-(naphthalen-2-yl)tetrahydro-2*H*-thiopyran-4,4-diyl)bis(phenylmethanone) (3l)**

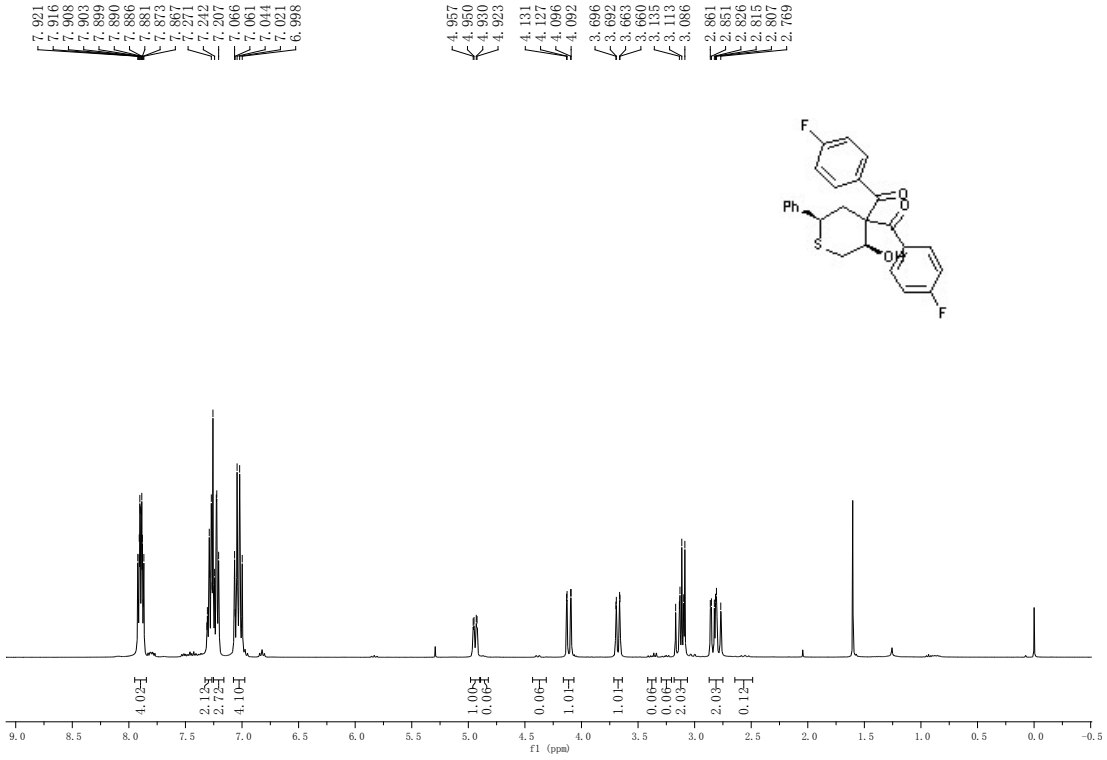


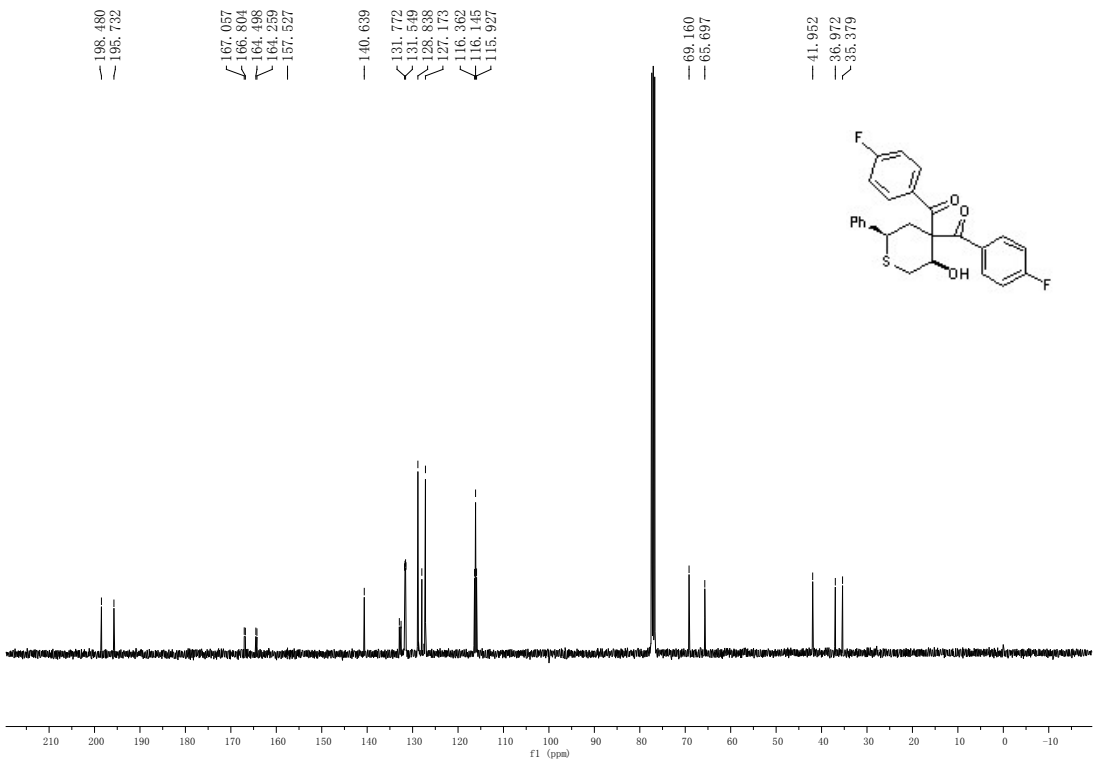
**((2*R*,5*R*)-5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis(p-tolylmethanone) (3m)**



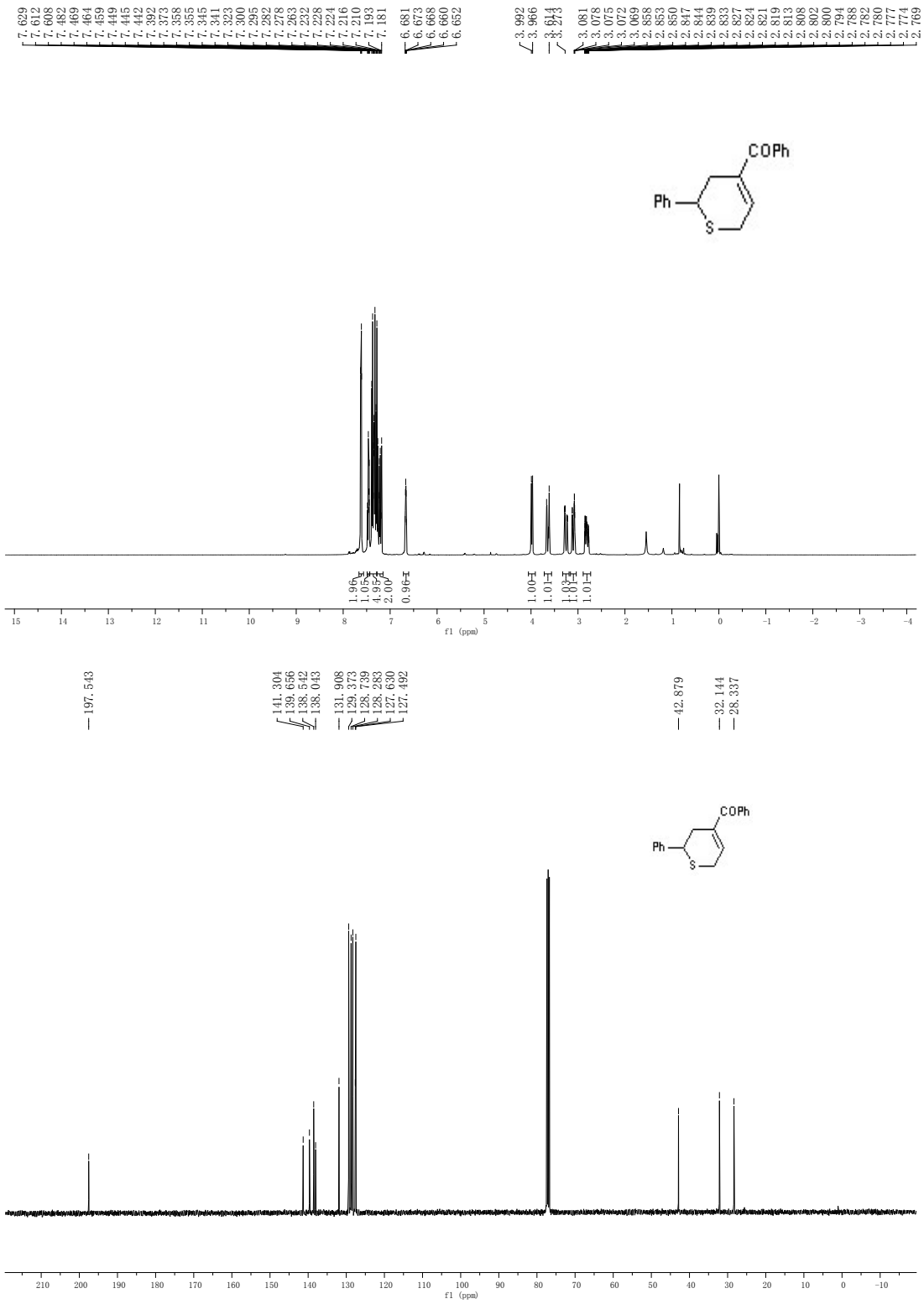



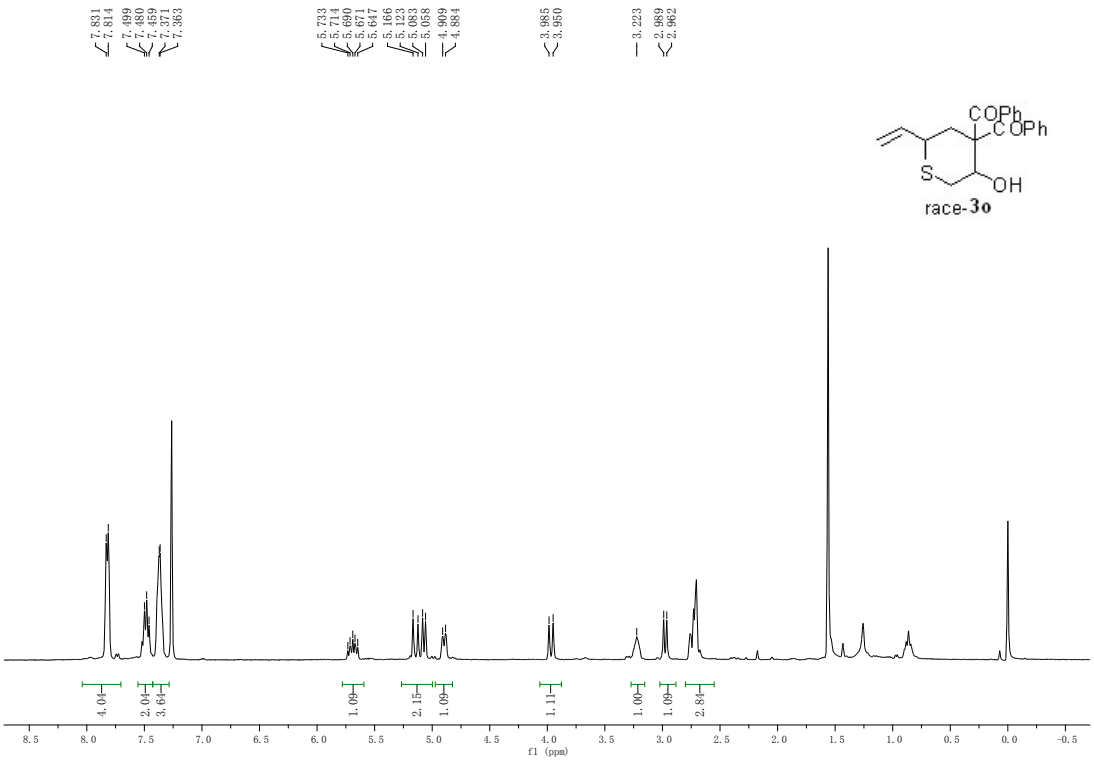
**((2*R*,5*R*)-5-hydroxy-2-phenyltetrahydro-2*H*-thiopyran-4,4-diyl)bis((4-fluorophenyl)methanone) (3n)**



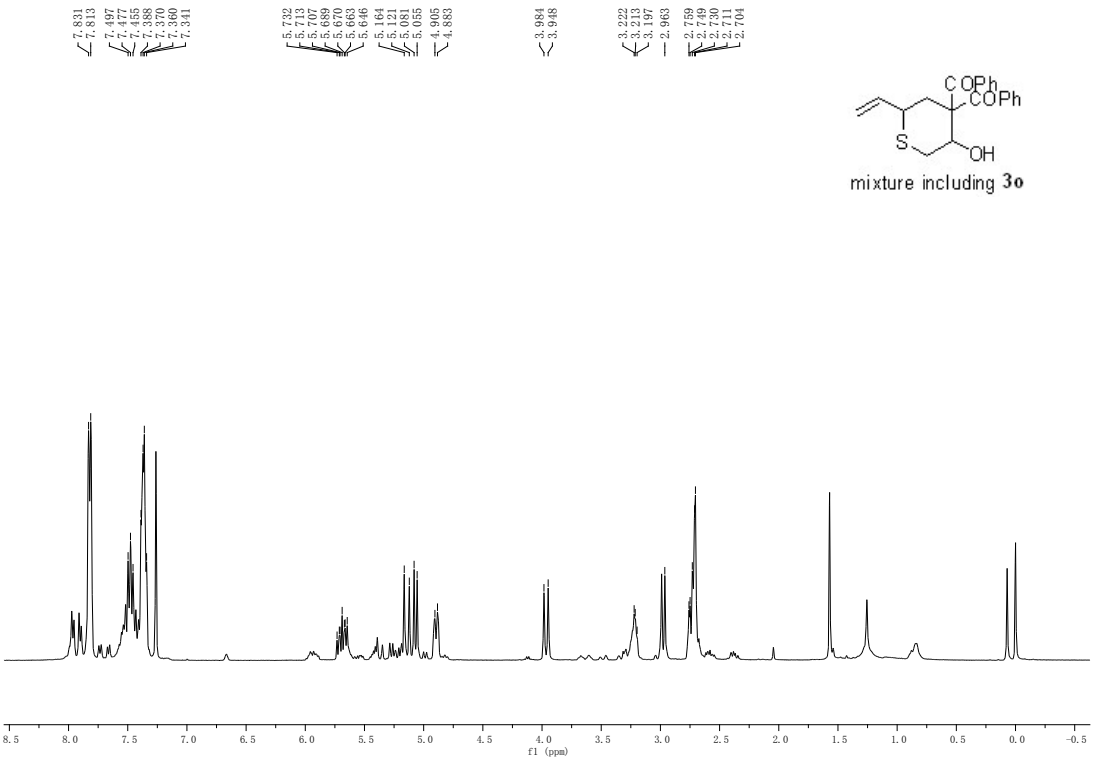



**(*R*)-phenyl(2-phenyl-3,6-dihydro-2*H*-thiopyran-4-yl)methanone (4)**






race-**3o**




mixture including **3o**

## (11) References

[1] Y. Xia, X. H. Liu, H. F. Zheng, L. L. Lin and X. M. Feng, *Angew. Chem. Int. Ed*., 2015, **54**, 227.

[2] HPLC spectrums only showed enantioselectivities of the corresponding products, and dr values were determined by NMR analysis.