Enantiopure Isothiourea@Carbon-Based Support: Stacking Interactions for Recycling a Lewis Base in Asymmetric Catalysis

Yu-Chao Yuan,[a,b,1] Mariam Abd El Sater,[a,c] Mohamed Mellah,[a] Nada Jaber,[c] Olivier R. P. David,[b]* Emmanuelle Schulz[a]*

[a]*Université Paris Saclay, CNRS, Institut de Chimie Moléculaire et des Matériaux d'Orsay, 91405 Orsay, France, emmanuelle.schulz@universite-paris-saclay.fr*
[b]*Institut Lavoisier, UMR 8180, Université de Versailles Saint-Quentin-en-Yvelines, Université Paris Saclay, 45 avenue des Etats-Unis, 78035 Versailles, France, olivier.david@uvsq.fr*
[c]*Laboratoire de Chimie Médicinale et des Produits Naturels, Université Libanaise, Faculté des Sciences (I) and PRASE-EDST, Hadath, Beyrouth, Lebanon.*

Supporting Information

Contents

[1] *Jiangsu Key Laboratory of New Drug Research and Clinical Pharmacy, School of Pharmacy, Xuzhou Medical University, 221004 Xuzhou, China*

1. General Information.

Unless otherwise noted, all reactions were performed in oven-dried Schlenk tubes with Schlenk line connected to dry argon. All reagents were obtained commercially and used without further purification. Solvents were dried by distillation under argon from the followings: tetrahydrofuran and diethyl ether (sodium/benzophenone); toluene (calcium hydride); dichloromethane (calcium hydride). K_2CO_3, Cs_2CO_3, and KO*t*Bu were dried by heating at 110 °C for 12 h, left to cool under argon before using. Organic extracts were, in general, dried over anhydrous magnesium sulfate ($MgSO_4$). Precursors purchased from Sigma-Aldrich, Acros, TCI, Alfa Aesar and Fluorochem. Commercial reduced graphene oxide was purchased from Graphenea.

NMR spectrum: ^1H and ^{13}C spectra are recorded on AM 250, AV 300 or AV 360 Bruker spectrometers, operating at 250, 300 or 360 MHz for ^1H NMR, ^{19}F NMR and 75 or 90 MHz for ^{13}C NMR. Chemical shifts are reported in ppm (δ) relative with the solvent signal as reference. Chemical shifts are reported downfield from $CDCl_3$ (δ: 7.26 ppm), CD_3OD (δ: 3.31 ppm) or $(CD_3)_2SO$ (δ: 2.50 ppm) for ^1H NMR. Chemical shifts of ^{13}C NMR are reported in the scale relative to the solvent of $CDCl_3$ (δ: 77.0 ppm), CD_3OD (δ: 49.0 ppm) or $(CD_3)_2SO$ (δ: 39.5 ppm) used as an internal reference. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration.

Mass spectroscopy: Mass spectra were recorded on MicroTOF-Qq Bruker spectrometer by electrospray ionization (ESI) or QTOF 6540 Agilent spectrometer by atmospheric pressure photoionization (APPI).

Infrared spectra: IR spectra (in cm^{-1}) were recorded on a FTIR spectrometer (Perkin-Elmer spectrum one, NaCl pellets or Bruker Vertex 70 ATR Pike Germanium).

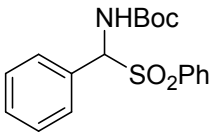
High Performance Liquid Chromatography: HPLC analysis was performed using a JASCO pump-PU 2089 associated to an UV detector (UV 100) from TSP, using Daicel Chiralpak AD-H and Chiralcel OD-H columns. Supercritical fluid chromatography (SFC) separation was performed with Investigator SFC System (Waters) equipped with a photodiode array UV detector. Data are reported as follows: column type, temperature, eluent, flow rate, pressure in column, retention time.

Spectropolarimeter: Optical rotations were measured on an Anton Paar's MCP 150 polarimeter and reported as follows: $[\alpha]^T_D$ (concentration (g/100 mL), solvent).

Chromatography: Flash column chromatography was performed using silica gel Merck (0.04–0.063μm).

2. Preparation of *pyr*-hyperBTM.

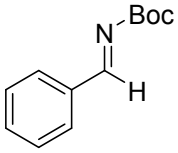
tert-Butyl (phenyl(phenylsulfonyl)methyl)carbamate



1a

Following the method described by List et al.:[1] to a stirred solution of *tert*-butyl carbamate (7.03 g, 60 mmol) in THF (26 mL) in a 250 mL three neck round bottom flask equipped with an overhead stirrer was added water (53 mL), sodium benzenesulfinate (10.0 g, 61 mmol), benzaldehyde (6.2 mL, 61 mmol) and formic acid (13 mL, 343 mmol). The reaction mixture was stirred for 24 h at rt. The resulting precipitate was filtered and washed with water (25 mL) followed by hexane/CH_2Cl_2 (91/9) (2 × 25 mL). Stirring the combined liquors from filtration and the water wash for a further 24 h provided a second, smaller quantity of solid. The combined solids were dried in an oven at 90 °C until a constant weight, giving sulfone (±)-**1a** as a white solid (14.35 g, 69%); ^{1}H NMR (300 MHz, d_6-DMSO) δ = 7.93-7.90 (m, 2H), 7.75-7.56 (m, 6H), 7.45-7.40 (m, 3H), 6.03 (d, J = 10.8 Hz, 1H), 1.22 (s, 9H) ppm. The spectral data match those previously reported.[1]

tert-Butyl benzylidenecarbamate

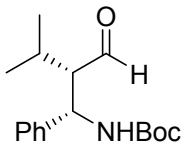


1b

A 500 mL, two-necked, round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and a reflux condenser capped with an inlet adaptor connected to an argon-vacuum manifold, was charged with anhydrous potassium carbonate (33.17 g, 240 mmol, 6.0 equiv.). The solid was placed under vacuum (0.5 mmHg) and flame-dried. The flask was purged with argon and anhydrous tetrahydrofuran (250 mL) was added via cannula under argon at 25 °C. Then, the septum was removed and compound **1a** (13.90 g, 40 mmol, 1.0 equiv.) was added into the flask. The septum was exchanged for a glass stopper, and the resulting suspension was heated to reflux at 80-85 °C (oil bath temp) with vigorous stirring under argon. After 15 h, the reaction was cooled to 25 °C and the solid is filtered off through alternating layers of Celite (1 cm thick)/Na_2SO_4(1 cm thick)/Celite (1 cm thick) using a Büchner funnel (diameter 100 mm), and washed with anhydrous tetrahydrofuran (50 mL). The filtrate is concentrated at 30 °C (water bath temperature) by rotary evaporation (20 mmHg) and dried under vacuum (0.5

mmHg) to give the corresponding *N*-Boc-imine **1b** as colorless oil (8.21 g, 99%); ^{1}H NMR (300 MHz, d_6-acetone) δ = 8.79 (s, 1H), 7.97-7.94 (m, 2H), 7.64-7.61 (m, 1H), 7.58-7.53 (m, 2H), 1.54 (s, 9H) ppm. The spectral data match those previously reported.[1]

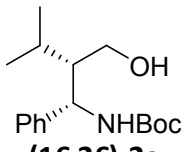
tert-Butyl ((1*S*,2*S*)-2-formyl-3-methyl-1-phenylbutyl)carbamate



(1*S*,2*S*)-2

Following the method described by List et al.:[1] to a stirred solution of imine **1b** (8.21 g, 40 mmol) in CH_3CN (350 mL) in a flame dried 1 L three neck round bottom flask equipped with an overhead stirrer under argon was added isovaleraldehyde (8.6 mL, 80 mmol). The resulting solution was cooled to 0 °C in an ice/brine bath. (*L*)- proline (921 mg, 8 mmol) was added and the reaction mixture was stirred for 14 h at 0 °C before warming to rt. Water (110 mL), Et_2O (70 mL) and brine (15 mL) was added and the organic layer was separated. The aqueous layer was extracted with Et_2O (2 × 30 mL). The organic extracts were combined, dried ($MgSO_4$), filtered and concentrated in *vacuo*. Trituration of the resulting solid with hexane (2 × 40 mL) gave aldehyde (1*S*,2*S*)-**2** (>99:1 dr) as a white solid (6.27 g, 54%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.49 (d, *J* = 4.2 Hz, 1H), 7.36-7.22 (m, 5H), 5.17-5.01 (m, 2H), 2.52-2.46 (m, 1H), 2.16-2.03 (m, 1H), 1.40 (s, 9H), 1.14 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H) ppm; Chiral HPLC Chiralcel OD-H (2% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(1*R*,2*R*): 8.19 min, t_R(1*S*,2*S*): 9.43 min, 99% ee. The spectral data match those previously reported.[1]

tert-Butyl ((1*S*,2*S*)-2-(hydroxymethyl)-3-methyl-1-phenylbutyl)carbamate

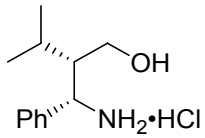


(1*S*,2*S*)-2a

Following a slightly modified method from that described by Smith et al.:[2] to a slurry of aldehyde (1*S*,2*S*)-**2** (6.27 g, 21.5 mmol) in methanol (125 mL) at 2 °C in a 500 mL three neck round bottom flask equipped with an overhead stirrer, was added $NaBH_4$ (1.25 g, 33 mmol) portion wise over 30 min and the reaction mixture was left to stir for 1 h at rt. Saturated aqueous $NaHCO_3$ was added (8 mL) drop wise over 10 min forming a white precipitate. The methanol was removed in *vacuo* and water (80 mL) and CH_2Cl_2 (60 mL) were added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic

extracts were combined, dried ($MgSO_4$), filtered and concentrated in *vacuo* and dried for 2 h at 2 mbar to give alcohol (1*S*,2*S*)-**2a** as a white solid (6.27 g, 99%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.38-7.23 (m, 5H), 5.50 (d, *J* = 9.3 Hz, 1H), 5.03 (s, br, 1H), 3.70-3.66 (m, 1H), 3.51 (dd, *J* = 11.4, 8.7 Hz, 1H), 1.87-1.71 (m, 3H), 1.42 (s, 9H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H) ppm. The spectral data match those previously reported.[2]

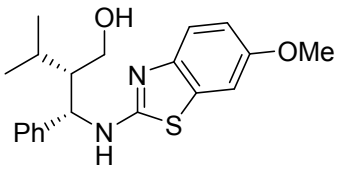
(*S*)-2-((*S*)-Amino(phenyl)methyl)-3-methylbutan-1-ol hydrochloride



(1*S*,2*S*)-2b

To a slurry of alcohol (1*S*,2*S*)-**2a** (6.27 g, 21.5 mmol) in dioxane (20 mL) was added 4M HCl in dioxane (26.5 mL, 106 mmol) drop wise over 30 min and the reaction mixture was left to stir for 12 h at rt. 15 mL of dioxane was removed in vacuo and the solution cooled to 15 °C to precipitate a white solid. Et_2O (10 mL) was added and the precipitate was filtered, washed with Et_2O (2 × 20 mL) and the resulting white solid dried (15 mbar, 45 °C) for 2 h to give amino alcohol (1*S*,2*S*)-**2b** as a white solid (4.39 g, 89%); ^{1}H NMR (300 MHz, d_4-methanol) δ = 7.55-7.40 (m, 5H), 4.58 (d, *J* = 4.2 Hz, 1H), 3.76 (ddd, *J* = 10.8, 4.8, 0.9 Hz, 1H), 3.49 (dd, *J* = 10.5, 9.6 Hz, 1H), 2.08-2.00 (m, 1H), 1.60-1.48 (m, 1H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H) ppm. The spectral data match those previously reported.[2]

(*S*)-2-((*S*)-((6-Methoxybenzo[*d*]thiazol-2-yl)amino)(phenyl)methyl)-3-methylbutan-1-ol

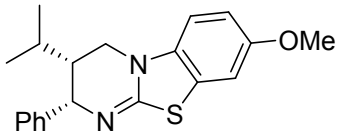


(1*S*,2*S*)-2c

Following a procedure outlined by Smith,[3] 2-chloro-6-methoxybenzo[*d*]thiazole (3.3 g, 16.7 mmol, 1 equiv.) was added to a solution of (*S*)-2-((*S*)-amino(phenyl)methyl)-3-methylbutan-1-ol hydrochloride **2b** (4.0 g, 17.5 mmol, 1.05 equiv.), and *i*-Pr_2NEt (11 mL, 66.8 mmol, 4 equiv.) in *o*-dichlorobenzene (8 mL, 2.0 M). The resulting pale-yellow suspension was heated at reflux until completion. The resulting mixture was cooled to rt, H_2O (12 mL) was added and the aqueous phase extracted with CH_2Cl_2 (3 × 15 mL). The combined organic fractions were washed with brine, dried ($MgSO_4$), and concentrated in *vacuo* to afford the crude product which was purified by column chromatography (CH_2Cl_2: EtOAc = 5:1) to afford the amino

alcohol product (1*S*,2S)-**2c** as a brown solid (4.37 g, 73% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.46-7.26 (m, 6H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 9.0, 2.7 Hz, 1H), 5.01 (d, *J* = 4.5 Hz, 1H), 3.83-3.78 (m, 4H), 3.62 (t, *J* = 10.2 Hz, 1H), 2.12-2.04 (m, 1H), 1.80-1.73 (m, 1H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H) ppm.

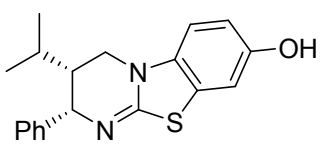
(2*S*,3*R*)-3-Isopropyl-8-methoxy-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine



(2*S*,3*R*)-3

To a slurry of the crude amino alcohol (1*S*,2S)-**2c** (4.35 g, 12.2 mmol, 1 equiv.) in anhydrous CH_2Cl_2 (61 mL, 0.2 M) was added Et_3N (6.78 mL, 48.8 mmol, 4 equiv.) and the reaction mixture was cooled to 0 °C. Methanesulfonyl chloride (1.22 mL, 15.8 mmol, 1.3 equiv.) was added and the reaction mixture was stirred at rt for 4 h. Once complete consumption of the amino alcohol was observed (about 4 h), *i*-PrOH (4.7 mL, 5 equiv.) was added and the reaction was heated at reflux for 24 h. The reaction was quenched with 1 M aq. NaOH (16 mL) and the biphasic mixture stirred vigorously for 30 min. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic fractions washed with brine (50 mL), dried ($MgSO_4$) and concentrated in *vacuo* to afford the crude product which was purified by column chromatography (CH_2Cl_2: EtOAc = 5:1) to afford an off white solid that was recrystallised from 50% EtOAc in Hexane to give (2*S*,3*R*)-3-isopropyl-8-methoxy-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine **3** as a colourless solid (3.3 g, 80%); $[\alpha]^{20}_D$ +308.0 (c 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.33-7.19 (m, 5H), 6.94 (d, *J* = 2.4 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 1H), 4.90 (d, *J* = 3.9 Hz, 1H), 3.86-3.80 (m, 4H), 3.33 (dd, *J* = 11.4, 11.4 Hz, 1H), 2.00-1.90 (m, 1H), 1.37-1.25 (m, 1H), 1.13 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (90 MHz, $CDCl_3$): δ = 158.4, 140.8, 134.9, 128.0, 127.1, 124.1, 111.5, 108.2, 107.8, 61.1, 56.0, 42.0, 40.8, 26.9, 22.0, 20.0 ppm; HRMS (ESI) calcd. for $[M+H]^+$ $C_{20}H_{23}N_2OS$, 339.1526, found 339.1527 (0.3 ppm).

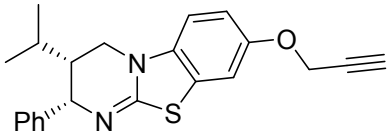
(2*S*,3*R*)-3-Isopropyl-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidin-8-ol



(2*S*,3*R*)-3a

BBr_3 (42 mL, 42 mmol, 1 M in CH_2Cl_2, 6 equiv.) was added dropwise to a solution of (2*S*,3*R*)-3-isopropyl-8-methoxy-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine **3** (2.37 g, 7 mmol, 1 equiv.) in CH_2Cl_2 (47 mL) at 0 °C. The solution was stirred at 0 °C for 2 h then warmed to rt and stirred for 16 h. The reaction was carefully quenched with MeOH (50 mL). Then saturated $NaHCO_3$ was added until pH reached *ca.* 8. CH_2Cl_2 (50 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated in *vacuo* to afford (2*S*,3*R*)-3-isopropyl-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidin-8-ol **3a** as a colourless solid (1.69 g, 74%). ^{1}H NMR (360 MHz, d_6-DMSO) δ = 9.27 (s, 1H), 7.32 (dd, *J* = 7.9, 6.8 Hz, 2H), 7.26-7.19 (m, 3H), 6.93 (d, *J* = 2.5 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.65 (dd, *J* = 8.6, 2.5 Hz, 1H), 4.76 (d, *J* = 4.3 Hz, 1H), 3.90-3.85 (m, 1H), 3.32-3.26 (m, 1H), 1.91-1.83 (m, 1H), 1.19-1.10 (m, 1H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (90 MHz, d_6-DMSO): δ = 157.1, 153.1, 142.1, 133.8, 128.6, 128.2, 127.2, 122.8, 113.2, 109.6, 109.3, 60.8, 42.1, 27.0, 22.4, 19.9 ppm; HRMS (ESI) calcd. for $[M+H]^+$ $C_{19}H_{21}N_2OS$, 325.1369, found 325.1371 (0.5 ppm).

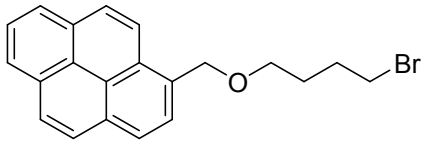
(2*S*,3*R*)-3-Isopropyl-2-phenyl-8-(prop-2-yn-1-yloxy)-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine 11



(2*S*,3*R*)-4

KO*t*Bu (1.42 g, 12.74 mmol, 2.6 equiv.) was added to a solution of (2*S*,3*R*)-3-isopropyl-2-phenyl-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidin-8-ol **3a** (1.59 g, 4.9 mmol, 1 equiv.) in THF/DMSO (1:1, 36 mL) at 0 °C, and the reaction mixture was stirred for 2 h. Propargyl bromide (0.8 mL, 7.35 mmol, 80% in toluene, 1.5 equiv.) was added and the reaction mixture was allowed to warm to rt (ca. 2 h) and quenched with brine (30 mL). The aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic fractions were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether: EtOAc = 1:1) to afford (2*S*,3*R*)-3-isopropyl-2-phenyl-8-(prop-2-yn-1-yloxy)-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine **4** as a brown solid (1.02 g, 57%); ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.32-7.17 (m, 5H), 7.01 (d, *J* = 2.5 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 4.89 (dd, *J* = 4.5, 1.5 Hz, 1H), 4.65 (d, *J* = 2.5 Hz, 2H), 3.81 (ddd, *J* = 11.5, 5.2, 1.8 Hz, 1H), 3.31 (t, *J* = 11.5 Hz, 1H), 2.53 (t, *J* = 2.5 Hz, 1H), 1.97-1.85 (m, 1H), 1.32–1.23 (m, 1H), 1.11 (d, *J* = 6.2 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H) ppm. The spectral data match those previously reported.[3]

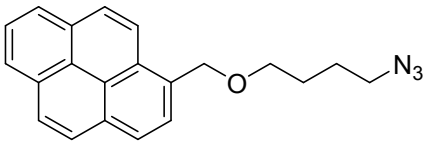
1-((4-Bromobutoxy)methyl)pyrene



6

NaH (8.0 g, 200 mmol, 20 equiv.) was added to a solution of 1-pyrenemethanol (2.32 g, 10 mmol, 1 equiv.) in 100 mL dry THF under N_2 atmosphere at room temperature. The mixture was stirred for 0.5 h. Then 1,4-dibromobutane (2.16 g, 100 mmol, 10 equiv.) was added and stirred for 48 h. The solvent was removed by vacuum evaporation, and water was carefully added to the reaction mixture to quench the unreacted NaH. The solution was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layer was washed with 5% aqueous HCl (100 mL), 10% aqueous Na_2CO_3 (100 mL) and finally with water, and then was dried over anhydrous $MgSO_4$. The organic phase was concentrated and purified by silica gel column chromatography (petroleum ether: EtOAc = 10:1) to afford **6** as a white solid (3.29 g, 89 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 9.3 Hz, 1H), 8.22-8.14 (m, 4H), 8.06-8.00 (m, 4H), 5.20 (s, 2H), 3.62 (t, *J* = 6.0 Hz, 2H), 3.41 (t, *J* = 6.6 Hz, 2H), 2.03-1.94 (m, 2H), 1.85-1.76 (m, 2H) ppm. The spectral data match those previously reported.[4]

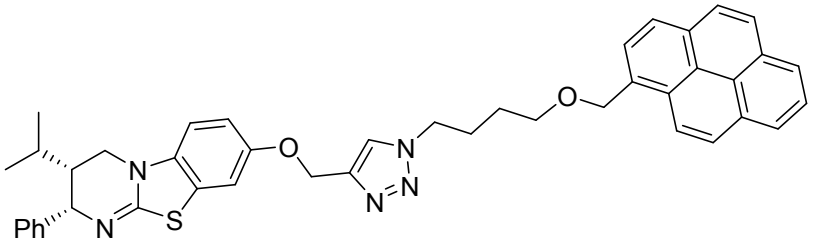
1-((4-Azidobutoxy)methyl)pyrene



7

The 1-((4-bromobutoxy)methyl)pyrene **6** (3.28 g, 9 mmol, 1 equiv.) was dissolved in 30 mL DMF. Sodium azide (641 mg, 10 mmol, 1.1 equiv.) was then added and the reaction mixture was stirred at rt under argon atmosphere. The reaction mixture was monitored by TLC and when complete, the DMF was removed under high vacuum. The crude compound was purified by flash chromatography on silica gel (petroleum ether: EtOAc = 10:1) to obtain the desired product **7** as a white solid (2.95 g, 99 %);. ^{1}H NMR (360 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 9.0 Hz, 1H), 8.20 (ddd, *J* = 7.6, 7.6, 1.1 Hz, 2H), 8.16 (s, 1H), 8.14 (d, *J* = 1.1 Hz, 1H), 8.06 (s, 2H), 8.02 (dd, *J* = 7.6, 7.6 Hz, 2H), 5.19 (s, 2H), 3.61 (t, *J* = 6.1 Hz, 2H), 3.26 (t, *J* = 6.1 Hz, 2H), 1.74-1.70 (m, 4H) ppm; ^{13}C{^{1}H} NMR (90 MHz, $CDCl_3$): δ = 131.5, 131.3, 130.9, 129.3, 127.7, 127.4, 126.9, 125.3, 125.0, 124.8, 124.5, 123.4, 71.6, 69.7, 51.3, 27.1, 25.9 ppm. HRMS (ESI) calcd. for $[M+Na]^+$ $C_{21}H_{19}N_3ONa$ 352.1420, found 352.1412 (2.4 ppm).

(2*S*,3*R*)-3-isopropyl-2-phenyl-8-((1-(4-(pyren-1-ylmethoxy)butyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine



(2*S*,3*R*)-*pyr*-hyperBTM

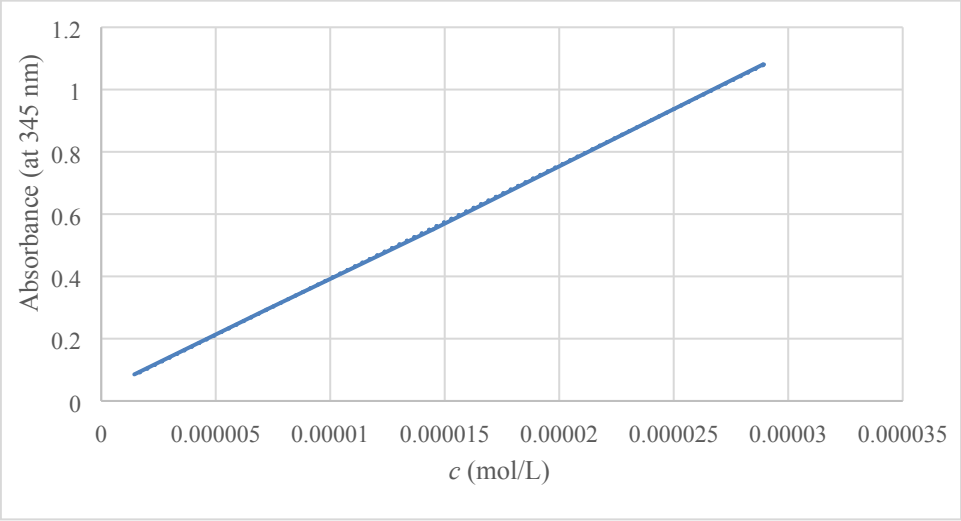
Under argon, a dry schlenk was charged with (2*S*,3*R*)-3-isopropyl-2-phenyl-8-(prop-2-yn-1-yloxy)-3,4-dihydro-2*H*-benzo[4,5]thiazolo[3,2-*a*]pyrimidine **4** (980 mg, 2.7 mmol, 1 equiv.), 1-((4-azidobutoxy)methyl)pyrene **7** (978 mg, 2.97 mmol, 1.1 equiv.), CuI (25.7 mg, 5 mol%), degassed THF (25 ml) and a stirring bar. Anhydrous DIPEA was added (1.56 ml, 9.45 mmol, 3.5 equiv.) and the reaction mixture was stirred at 40° C for 16 h. After removing the solvent under reduced pressure, followed by a trituration in Et_2O, the resulting solid was recovered after filtration. The mixture was then diluted in DCM (10 mL) and washed with an EDTA solution (0.05 M). After drying the combined organic phases on $MgSO_4$, filtration and solvent evaporation, the final pure product (2*S*,3*R*)-***pyr*-hyperBTM** was obtained as a yellow solid (1.0 g, 54%). $[\alpha]^{20}_D$ +105.0 (c 1.0 in $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 9.0 Hz, 1H), 8.20-8.12 (m, 4H), 8.06-7.98 (m, 4H), 7.37 (s, 1H), 7.34-7.21 (m, 5H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.82 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 5.18 (s, 2H), 5.03 (s, 2H), 4.91 (d, *J* = 4.3 Hz, 1H), 4.29 (t, *J* = 7.2 Hz, 2H), 3.81-3.76 (m, 1H), 3.63 (t, *J* = 6.1 Hz, 2H), 3.31 (t, *J* = 11.5 Hz, 1H), 2.04-1.86 (m, 3H), 1.70-1.62 (m, 2H), 1.34-1.25 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (90 MHz, $CDCl_3$): δ = 158.6, 153.9, 143.7, 140.6, 135.2, 131.4, 131.2, 130.8, 129.4, 128.4, 128.0, 127.8, 127.5, 127.4, 127.2, 127.1, 126.1, 125.3, 124.9, 124.7, 124.5, 123.4, 122.8, 112.6, 109.5, 107.9, 71.7, 69.4, 62.8, 61.0, 50.1, 42.0, 40.8, 27.4, 26.9, 26.6, 22.0, 20.0 ppm. HRMS (ESI) calcd. for $[M+H]^+$ $C_{43}H_{42}N_5O_2S$ 692.3054, found 692.3029 (3.6 ppm).

3. General procedure for the immobilization of *pyr*-hyperBTM onto rGO

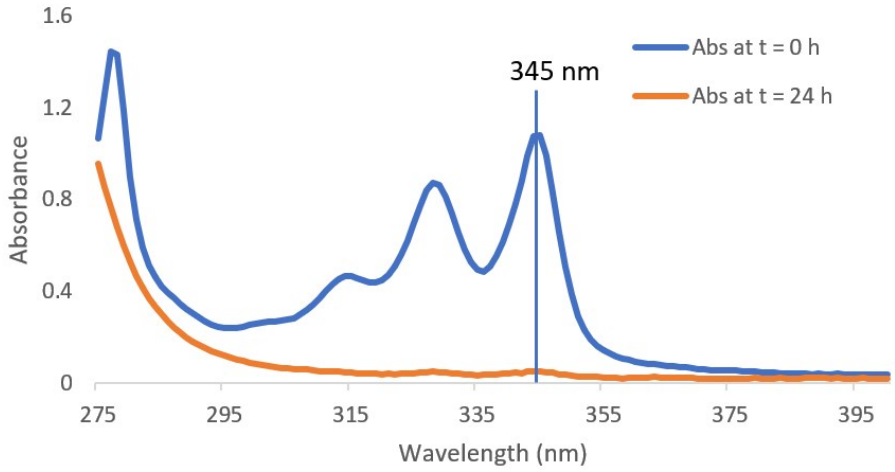
A glass vial with a screw cap septum top was charged with 80 mg of reduced graphene oxide (rGO) and 3.2 mL of anhydrous DCM. The suspension was immersed in an ultrasound bath for 1 hour, then the ***pyr*-hyperBTM** (20 mg) was added, and the mixture was sonicated for another 5 minutes. After stirring for 24 hours at room temperature under air, the agitation was stopped and 10 µL were taken from the supernatant solution, diluted in 20 mL of DCM and then subjected to UV-Vis detection. The supported catalyst was recovered by filtration and centrifugation and then washed with DCM (20 mL). Residual solvent was removed under reduced pressure without heating.

The immobilization was confirmed by UV-Vis analysis, and the exact amount of immobilized catalyst was determined by UV-Vis. Furthermore, the mass of the obtained solid was equal to the sum of the mass of rGO and the mass of the introduced catalyst.

The UV-visible analysis was performed using an UV-Vis spectrum scanning method (200-500 nm). A calibration line (A= *f c*) has been drawn by measuring the absorbances (A) of diverse solutions with different concentrations (*c*) at the λmax (345 nm).



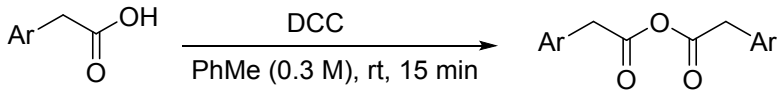
UV-Vis Calibration curve Abs= *f* [*pyr*-hyperBTM]



UV-Visible spectra of ***pyr*-hyperBTM** solution before and after immobilization

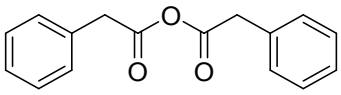
4. Preparation of substrates.

4.1 General Procedure: *Synthesis of Anhydrides*



To a solution of the appropriate carboxylic acid (1 eq) in toluene (0.3 M), DCC (0.50-0.55 eq) was added and the solution stirred at room temperature for 15 min. The suspension was filtered through Celite®, which was washed with extra toluene, and the filtrate was concentrated *in vacuo* to give the crude product, which was used without further purification.

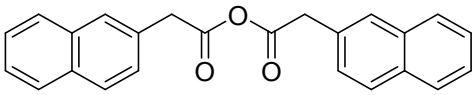
2-Phenylacetic anhydride 8a



8a

Following General Procedure 4.1, *N*,*N*'-Dicyclohexylcarbodiimide (DCC) (1.03 g, 5 mmol, 0.5 equiv.) was added to a solution of phenylacetic acid (1.36g, 10 mmol, 1 equiv.) in toluene (0.3 M, 34 mL) at rt to give product **8a** as a white solid (1.26 g, >99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.36-7.29 (m, 6H), 7.24-7.19 (m, 4H), 3.72 (s, 4H) ppm. The spectral data match those previously reported.[5]

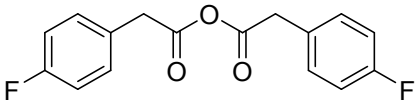
2-(Naphthalen-2-yl)acetic anhydride 8b



8b

Following General Procedure 4.1, *N*,*N*'-Dicyclohexylcarbodiimide (DCC) (2.06 g, 10 mmol, 0.5 equiv.) was added to a solution of 2-naphthylacetic acid (3.72 g, 20 mmol, 1 equiv.) in toluene (0.3 M, 67 mL) at rt to give product **8b** as a white solid (1.4 g, 40%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82-7.79 (m, 2H), 7.72-7.70 (m, 4H), 7.63 (s, 2H), 7.50-7.46 (m, 4H), 7.27 (dd, *J* = 8.4, 1.8 Hz, 2H), 3.88 (s, 4H) ppm. The spectral data match those previously reported.[5]

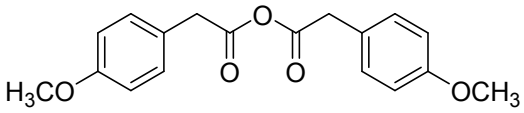
2-(4-Fluorophenyl)acetic anhydride 8c



8c

Following General Procedure 4.1, *N*,*N*'-Dicyclohexylcarbodiimide (DCC) (1.03g, 5 mmol, 0.5 equiv.) was added to a solution of 4-fluorophenylacetic acid (1.54 g, 10 mmol, 1 equiv.) in toluene (0.3 M, 34 mL) at rt to give product **8c** as a white solid (1.50 g, >99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.21-7.14 (m, 4H), 7.05-6.97 (m, 4H), 3.70 (s, 4H) ppm; ^{19}F{^{1}H} NMR (235 MHz, $CDCl_3$): δ = -114.56 ppm. The spectral data match those previously reported.[5]

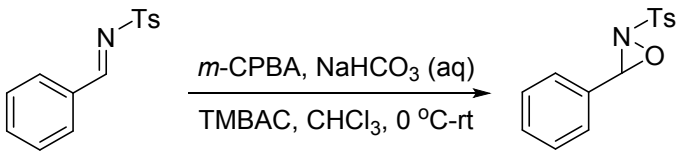
2-(4-Methoxyhenyl)acetic anhydride 8d



8d

Following General Procedure 4.1, *N*,*N*'-Dicyclohexylcarbodiimide (DCC) (1.03 g, 5 mmol, 0.5 equiv.) was added to a solution of 4-methoxyhenylacetic acid (1.66 g, 10 mmol, 1 equiv.) in toluene (0.3 M, 34 mL) at rt to give product **8d** as a white solid (1.57 g, >99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.12 (d, *J* = 8.7 Hz, 4H), 6.85 (d, *J* = 8.7 Hz, 4H), 3.80 (s, 6H), 3.66 (s, 4H) ppm. The spectral data match those previously reported.[5]

4.2 General Procedure 2: *Synthesis of N-Sulfonyl Oxaziridine*

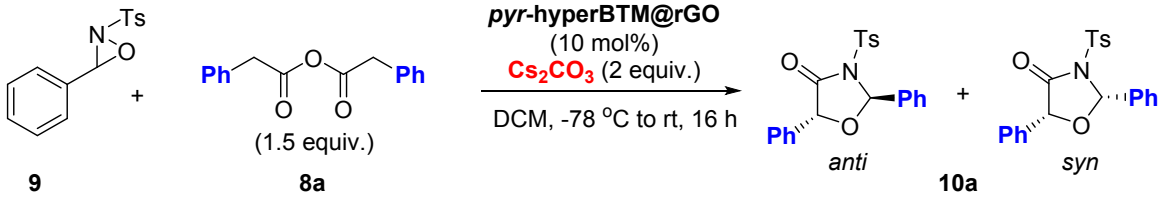


To a solution of saturated aqueous sodium bicarbonate (10 mL, 1 M) and benzyltrimethylammonium chloride (102 mg, 0.55 mmol, 0.11 eq), the appropriate *N*-sulfonyl imine (1.3 g, 5 mmol, 1 eq) was added as a solution in $CHCl_3$ (5 mL, 1 M). The mixture was cooled to 0 °C and a solution of *m*-CPBA (1.28 g, 5.5 mmol, 1.1 eq) in $CHCl_3$ (11 mL, 0.5 M) was added dropwise at 0 °C and stirred for 1 h. The organic layer was separated, washed with water, 10% sodium sulphite solution, water and brine before drying ($MgSO_4$) and concentrating in vacuo, keeping the bath temperature below 40 °C. The crude oxaziridine was recrystallised from a small amount of ethyl acetate and petrol ether without heating (60% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.93 (d, *J* = 8.5 Hz, 2H), 7.46-7.40 (m, 7H), 5.45 (s, 1H), 2.50 (s, 3H) ppm. The spectral data match those previously reported.[5]

5. Recycling tests for screening reaction conditions

The appropriate oxaziridine **9** (1 equiv) and ***pyr*-hyperBTM@rGO** (10 mol%) were added to a solution of the 2-phenylacetic anhydride **8a** (1.5 equiv) and base (2 equiv) in CH_2Cl_2 (0.2 M) at -78 °C. The reaction mixture was stirred at -78 °C then warmed slowly to room temperature over 24h. The ***pyr*-hyperBTM@rGO** was filtered off, washed with the appropriate solvent (3 x 3 mL). The recovered catalyst was dried under vacuum for 2-3 h and the dried catalyst was directly used in the next recycling run. The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (petroleum ether:EtOAc=10:1) to afford the desired product **10a**.

Table S1. Recycling tests with ***pyr*-hyperBTM@rGO** and Cs_2CO_3 as a base.

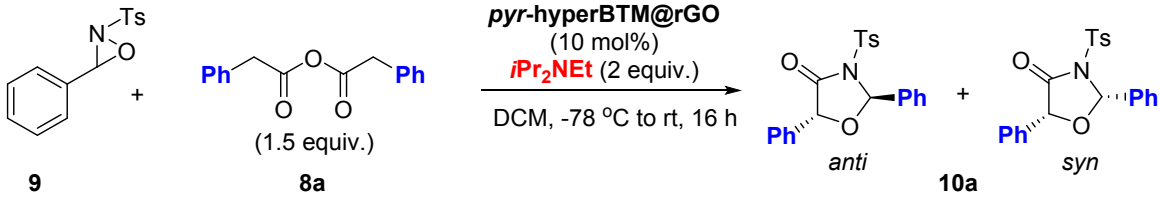


9 **8a** **10a**

	Work-up washing	Yield[a]	d.r.$_{anti/syn}$[b]	ee$_{anti/syn}$[b]
1st attempt	**DCM**			
Without additional base With 2 eq Cs_2CO_3	1st run	64	69 / 31	87 / 81
	2nd run	20	88 / 12	87 / -6
	3rd run	< 5	-	-
2nd attempt	**H_2O + acetone**			
	1st run	81	67 / 33	85 / 90
	2nd run	40	74 / 26	67 / 92
	3rd run[c]	23	67 / 33	54 / 75

[a]isolated yield of *anti*-**10a** + *syn*-**10a**. [b]determined by HPLC analysis. [c]before the 3rd run, ***pyr*-hyperBTM@rGO** was stirred at 60 °C for 30 min in 2 mL toluene, toluene was removed and the catalyst dried under vacuum))

Table S2. Recycling tests with ***pyr*-hyperBTM@rGO** and *i*Pr_2NEt as a base.



9 **8a** **10a**

	Work-up washing	Yield[a]	d.r.$_{anti/syn}$[b]	ee$_{anti/syn}$[b]
1st attempt	**acetone**			
	1st run	76	64 / 36	92 / 93
	2nd run	47	67 / 33	73 / 89
	3rd run	55	60 / 40	90 / 92
2nd attempt	**DCM**			
	1st run	75	59 / 41	88 / 92
	2nd run	65	56 / 44	89 / 88
	3rd run	60	50 / 50	93 / 85

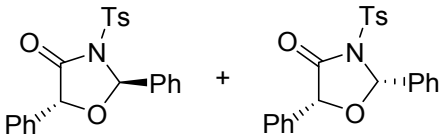
[a]isolated yield of *anti*-**10a** + *syn*-**10a**. [b]determined by HPLC analysis

6. General procedure for the asymmetric reaction recycling

General procedure for the asymmetric organocatalytic formation of oxazolidin-4-ones:

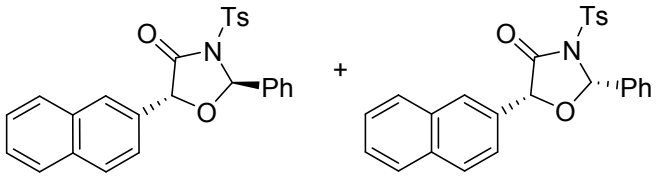
The appropriate oxaziridine **9** (1 equiv) and ***pyr*-hyperBTM@rGO** (10 mol%) were added to a solution of the appropriate homoanhydride (1.5 equiv) and cesium carbonate (2 equiv) in CH_2Cl_2 (0.2 M) at -78 ^oC. The reaction mixture was stirred at -78 ^oC then warmed slowly to room temperature over 24h. The ***pyr*-hyperBTM@rGO** was filtered off, washed with CH_2Cl_2 (3 x 3 mL). The recovered catalyst was dried under vacuum for 2-3 h and the dried catalyst was directly used in the next recycling run. The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (petroleum ether: EtOAc = 10:1) to afford the desired products **10a-10d**.

7. Characterization data of products 10a-10d.



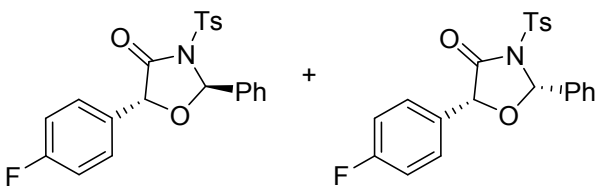
10a

(2*R*,5*R*)-2,5-Diphenyl-3-tosyloxazolidin-4-one (*anti*-10a) and (2*S*,5*R*)-2,5-diphenyl-3-tosyloxazolidin-4-one (*syn*-10a): White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59-7.34 (m, 12H), 7.20-7.15 (m, 2H), 6.73 (s, 1H, *anti*-**10a**), 6.59 (s, 1H, *syn*-**10a**), 5.44 (s, 1H, *anti*-**10a**), 5.40 (s, 1H, *syn*-**10a**), 2.40 (s, 3H, *anti*-**10a**), 2.38 (s, 3H, *syn*-**10a**), ppm; ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 168.8 (*anti*-**10a**), 168.6 (*syn*-**10a**), 145.7 (*anti*-**10a**), 145.6 (*syn*-**10a**), 136.6 (*anti*-**10a**), 136.4 (*syn*-**10a**), 135.1 (*syn*-**10a**), 134.8 (*anti*-**10a**), 134.4 (*anti*-**10a**), 134.0 (*syn*-**10a**), 130.4 (*syn*-**10a**), 130.2 (*anti*-**10a**), 129.5, 129.2, 128.9, 128.8, 128.63, 128.56, 128.4, 128.3, 128.2, 127.5, 126.5 (*anti*-**10a**), 126.4 (*syn*-**10a**), 91.3 (*anti*-**10a**), 90.9 (*syn*-**10a**), 79.0 (*syn*-**10a**), 78.7 (*anti*-**10a**), 21.8 ppm. The spectral data match those previously reported.[5]



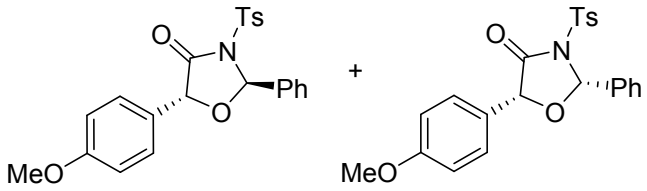
10b

(2*R*,5*R*)-5-(Naphthalen-2-yl)-2-phenyl-3-tosyloxazolidin-4-one (*anti*-10b) and (2*S*,5*R*)-5-(naphthalen-2-yl)-2-phenyl-3-tosyloxazolidin-4-one (*syn*-10b): White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87-7.75 (m, 4H), 7.60-7.39 (m, 10H), 7.19-7.14 (m, 2H), 6.79 (s, 1H, *anti*-**10b**), 6.66 (s, 1H, *syn*-**10b**), 5.61 (s, 1H, *anti*-**10b**), 5.57 (s, 1H, *syn*-**10b**), 2.38 (s, 3H, *anti*-**10b**), 2.37 (s, 3H, *syn*-**10b**) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 168.8 (*anti*-**10b**), 168.6 (*syn*-**10b**), 145.8, 145.6, 136.7 (*anti*-**10b**), 136.5 (*syn*-**10b**), 135.1 (*syn*-**10b**), 134.8 (*anti*-**10b**), 133.6, 133.5, 133.1 (*anti*-**10b**), 133.0 (*syn*-**10b**), 131.7 (*syn*-**10b**), 131.5 (*anti*-**10b**), 130.5, 130.3, 129.6, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.5, 126.8, 126.6, 126.5, 126.1, 125.8, 123.7 (*anti*-**10b**), 123.6 (*syn*-**10b**), 91.4 (*syn*-**10b**), 91.0 (*anti*-**10b**), 79.1, 78.8 (*anti*-**10b**), 21.8 ppm. The spectral data match those previously reported.[5]



10c

(2*R*,5*R*)-5-(4-Fluorophenyl)-2-phenyl-3-tosyloxazolidin-4-one (*anti*-10c) and (2*S*,5*R*)-5-(4-fluorophenyl)-2-phenyl-3-tosyloxazolidin-4-one (*syn*-10c): White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.33 (m, 9H), 7.20-7.15 (m, 2H), 7.09-7.01 (m, 2H), 6.71 (s, 1H, *anti*-**10c**), 6.58 (s, 1H, *syn*-**10c**), 5.41 (s, 1H, *anti*-**10c**), 5.37 (s, 1H, *syn*-**10c**), 2.41 (s, 3H, *anti*-**10c**), 2.38 (s, 3H, *syn*-**10c**) ppm; ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 168.6 (*anti*-**10c**), 168.5 (*syn*-**10c**), 164.9 (*anti*-**10c**), 164.7 (*syn*-**10c**), 161.6, 161.5, 145.9 (*anti*-**10c**), 145.7 (*syn*-**10c**), 136.5 (*anti*-**10c**), 136.3 (*syn*-**10c**), 135.0 (*syn*-**10c**), 134.7 (*anti*-**10c**), 130.5 (*syn*-**10c**), 130.3 (*anti*-**10c**), 129.9, 129.6, 128.8, 128.6, 128.5, 128.3, 128.24, 128.19, 127.4, 116.1, 115.8, 115.5, 91.2 (*anti*-**10c**), 90.9 (*syn*-**10c**), 78.4 (*syn*-**10c**), 78.1 (*anti*-**10c**), 21.8 ppm; ^{19}F{^{1}H} NMR (235 MHz, CDCl3):δ= –112.2 (*anti*-**10c**), -112.8 (*syn*-**10c**). The spectral data match those previously reported.[5]



10d

(2*R*,5*R*)-5-(4-Methoxyphenyl)-2-phenyl-3-tosyloxazolidin-4-one and (*anti*-10d) (2*S*,5*R*)-5-(4-methoxyphenyl)-2-phenyl-3-tosyloxazolidin-4-one (*syn*-10d): Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47-7.26 (m, 7H), 7.22-7.14 (m, 2H), 7.11-7.05 (m, 2H), 6.81-6.76 (m, 2H), 6.58 (d, *J* = 1.2 Hz, 1H, *anti*-**10d**), 6.45 (d, *J* = 1.2 Hz, 1H, *syn*-**10d**), 5.27 (s, 1H, *anti*-**10d**), 5.24 (s, 1H, *syn*-**10d**), 3.70 (s, 3H, *anti*-**10d**), 3.68 (s, 3H, *syn*-**10d**), 2.31 (s, 3H, *anti*-**10d**), 2.29 (s, 3H, *syn*-**10d**), ppm; ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 169.1 (*anti*-**10d**), 169.0 (*syn*-**10d**), 160.4, 160.2, 145.7 (*anti*-**10d**), 145.6 (*syn*-**10d**), 136.7 (*anti*-**10d**), 136.4 (*syn*-**10d**), 135.2 (*syn*-**10d**), 134.9 (*anti*-**10d**), 130.4 (*syn*-**10d**), 130.2 (*anti*-**10d**), 129.6, 128.8, 128.6, 128.43, 128.39, 128.27, 128.1, 127.5, 126.6 (*anti*-**10d**), 126.2 (*syn*-**10d**), 114.4 (*anti*-**10d**), 114.2 (*syn*-**10d**), 91.1 (*anti*-**10d**), 90.8 (*syn*-**10d**), 79.0 (*syn*-**10d**), 78.6 (*anti*-**10d**), 55.4, 21.8 ppm. The spectral data match those previously reported.[5]

8. References.

[1] J. W. Yang, S. C. Pan, B. List, *Org. Synth.*, **2009**, *86*, 11.

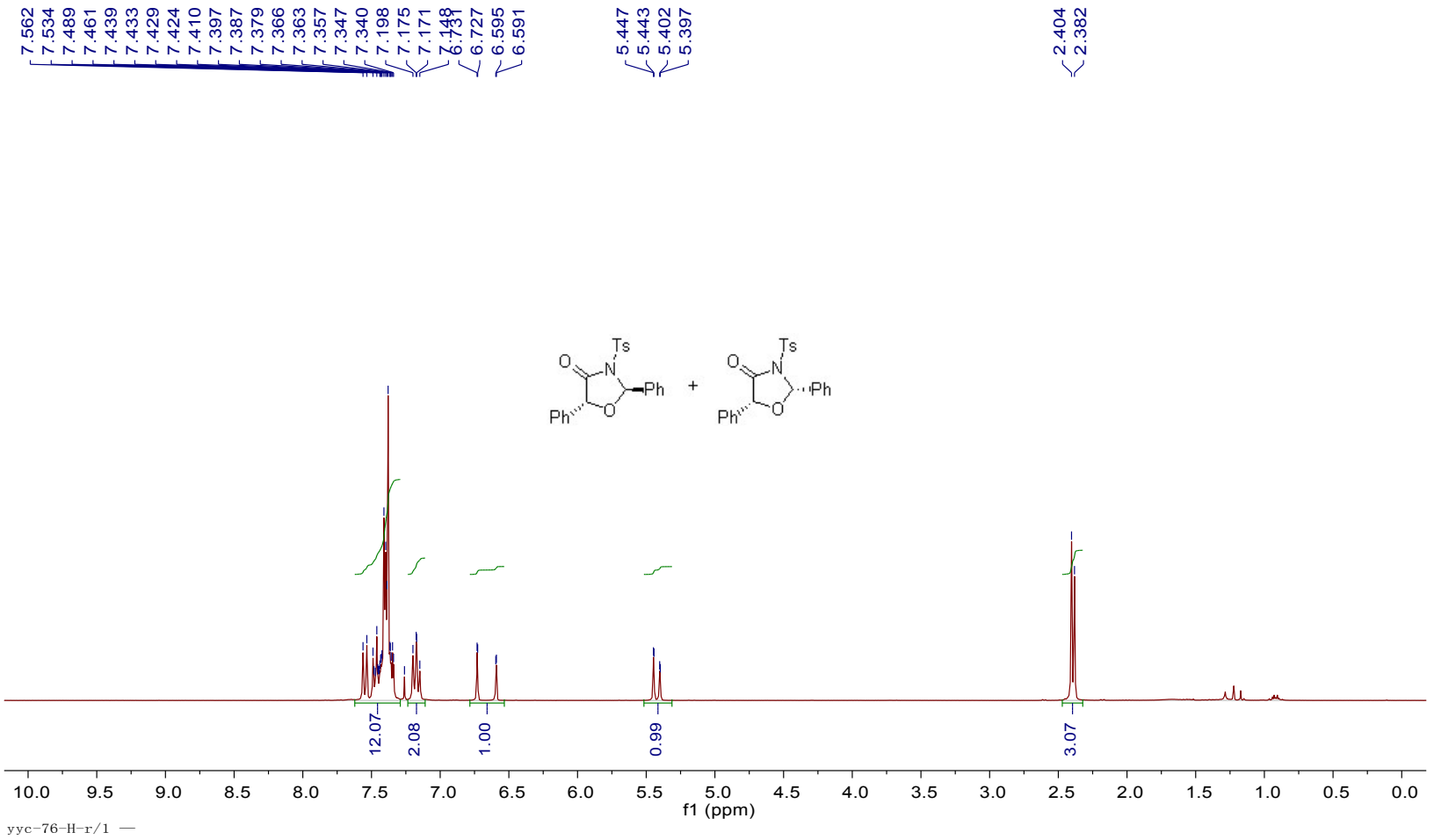
[2] C. Joannesse, C. P. Johnston, C. Concellon, C. Simal, D. Philp, A. D. Smith, *Angew. Chem. Int. Ed.*, **2009**, *48*, 8914.

[3] D. S. B. Daniels, S. R. Smith, T. Lebl, P. Shapland, A. D. Smith, *Synthesis* **2015**, *47*, 34.

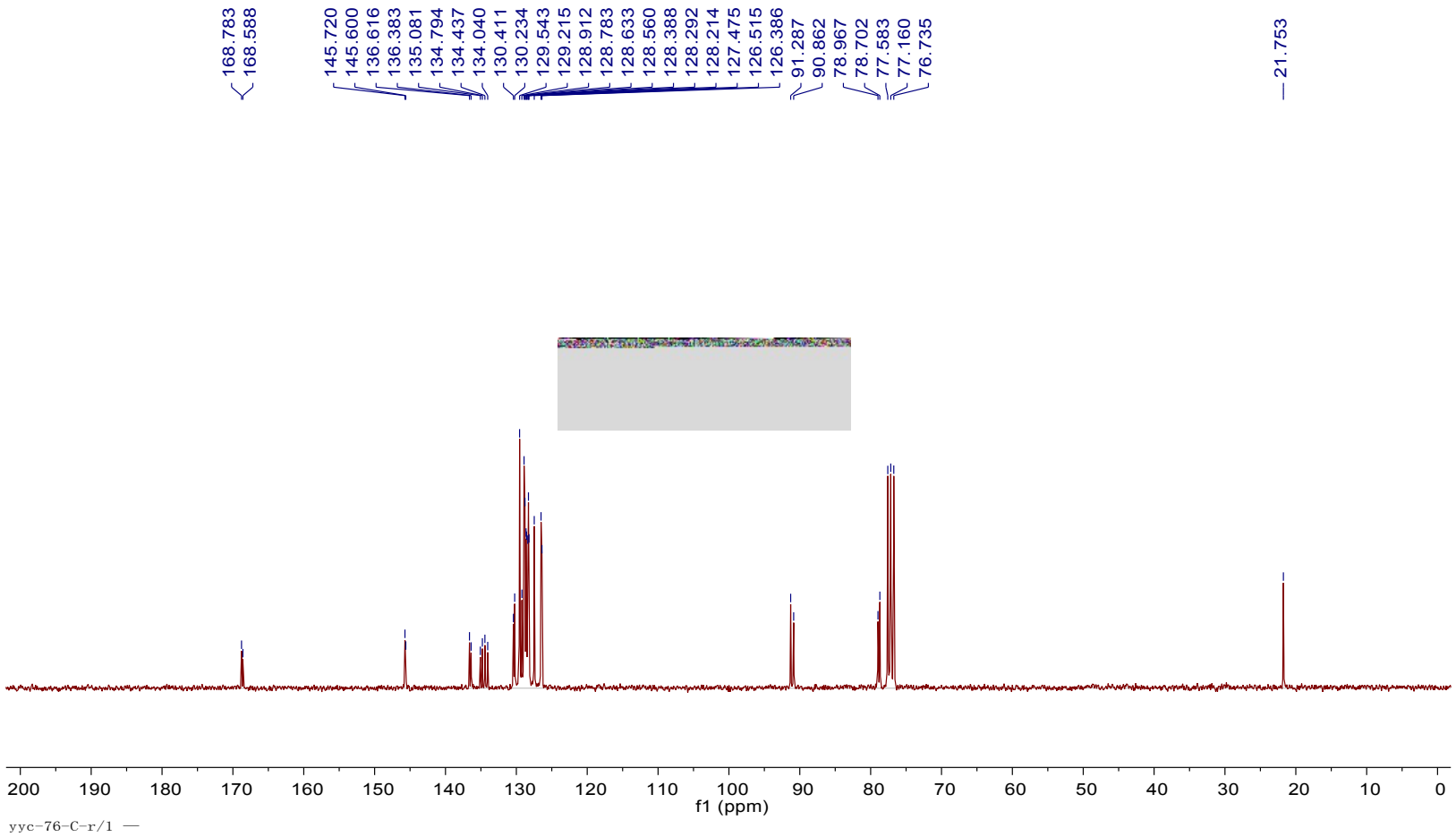
[4] Y.-L. Chu, C.-C. Cheng, Y.-P. Chen, Y.-C. Yen, F.-C. Chang, *J. Mater. Chem.*, **2012**, *22*, 9285.

[5] S. R. Smith, C. Fallan, J. E. Taylor, R. McLennan, D. S. B. Daniels, L. C. Morrill, A. M. Z. Slawin and A. D. Smith, *Chem. Eur. J.*, **2015**, *21*, 10530.

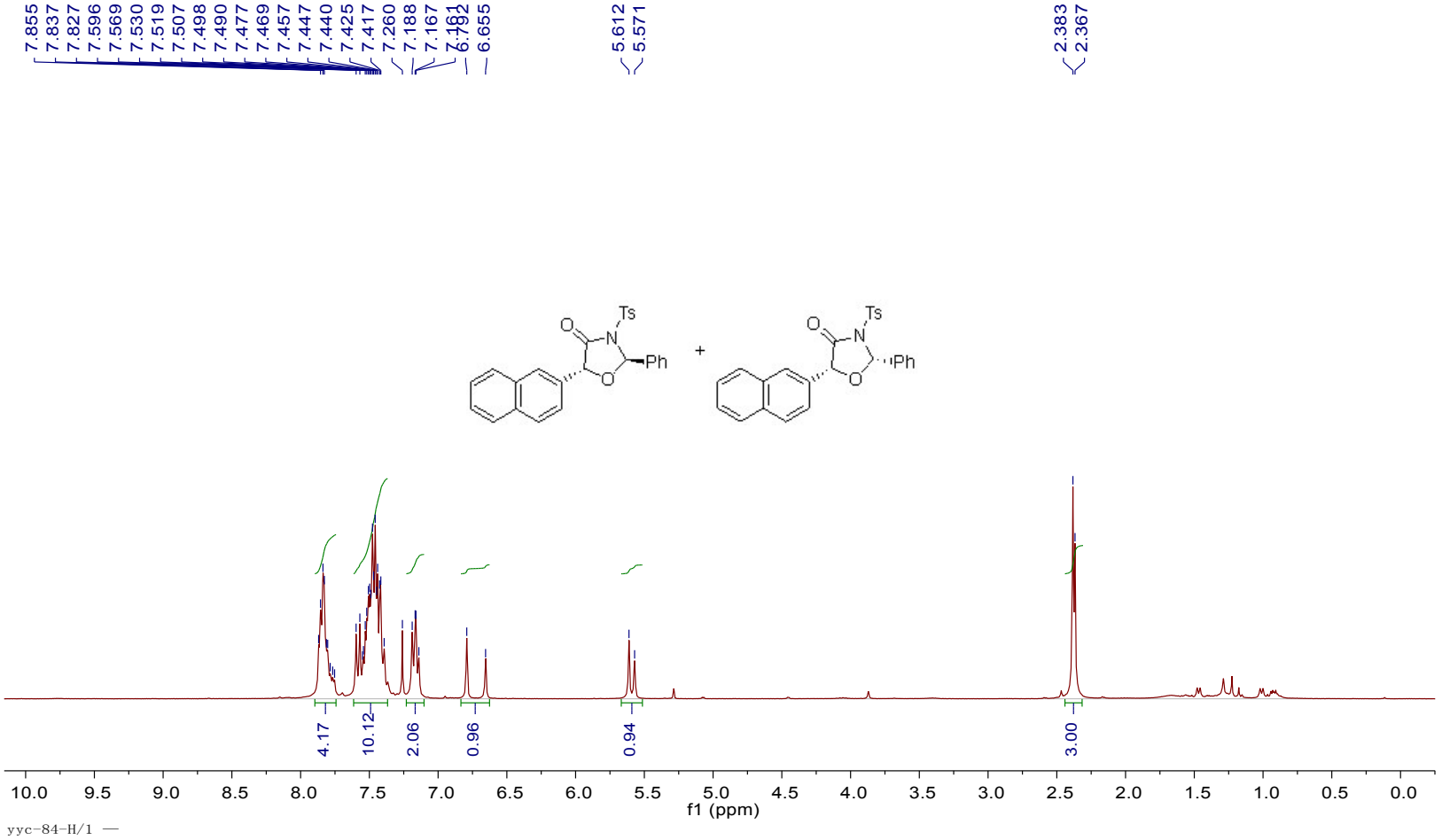
9. NMR spectra of products 10a-10d and *pyr*-hyperBTM



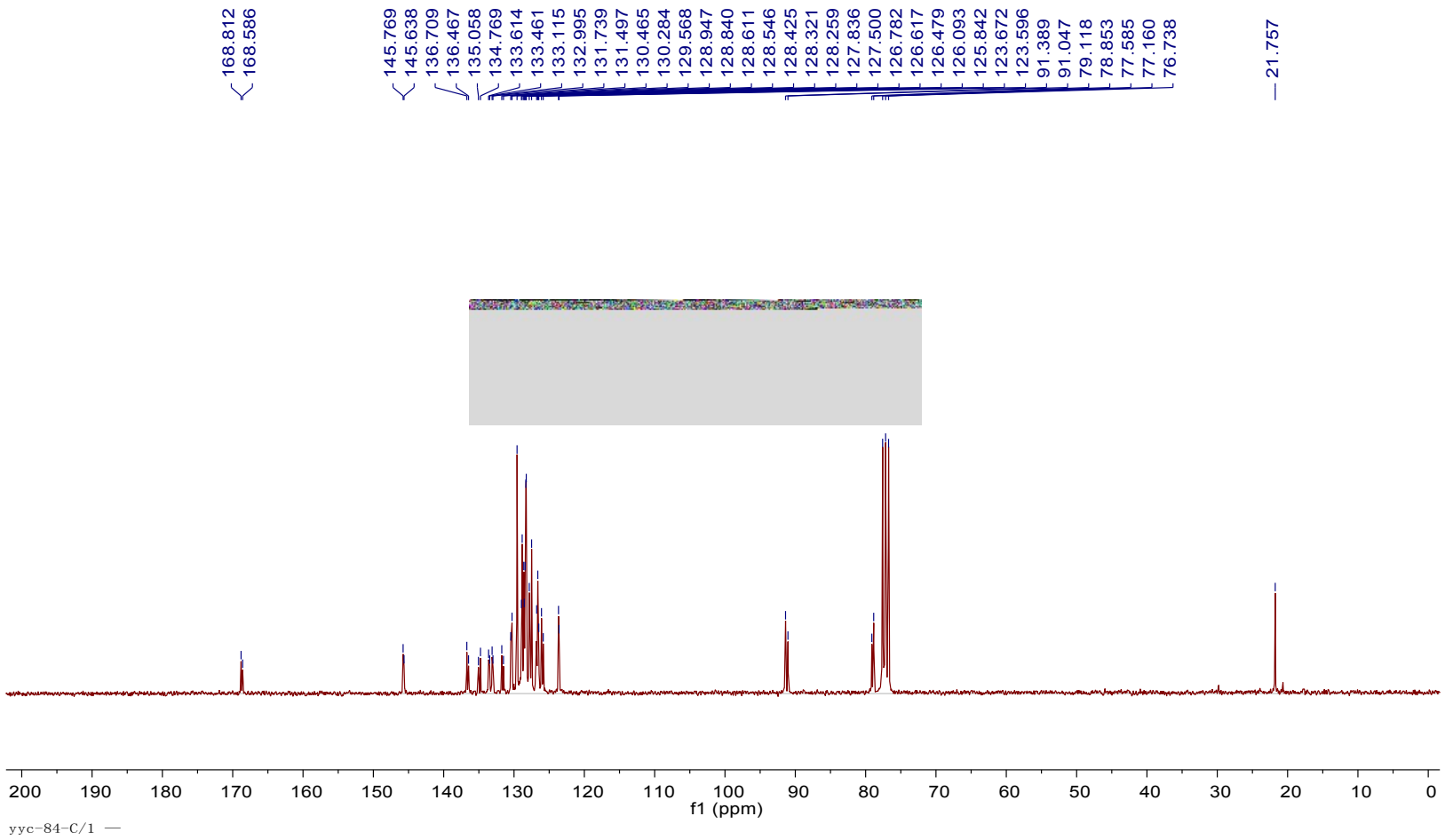
^{1}H NMR spectrum of **10a**



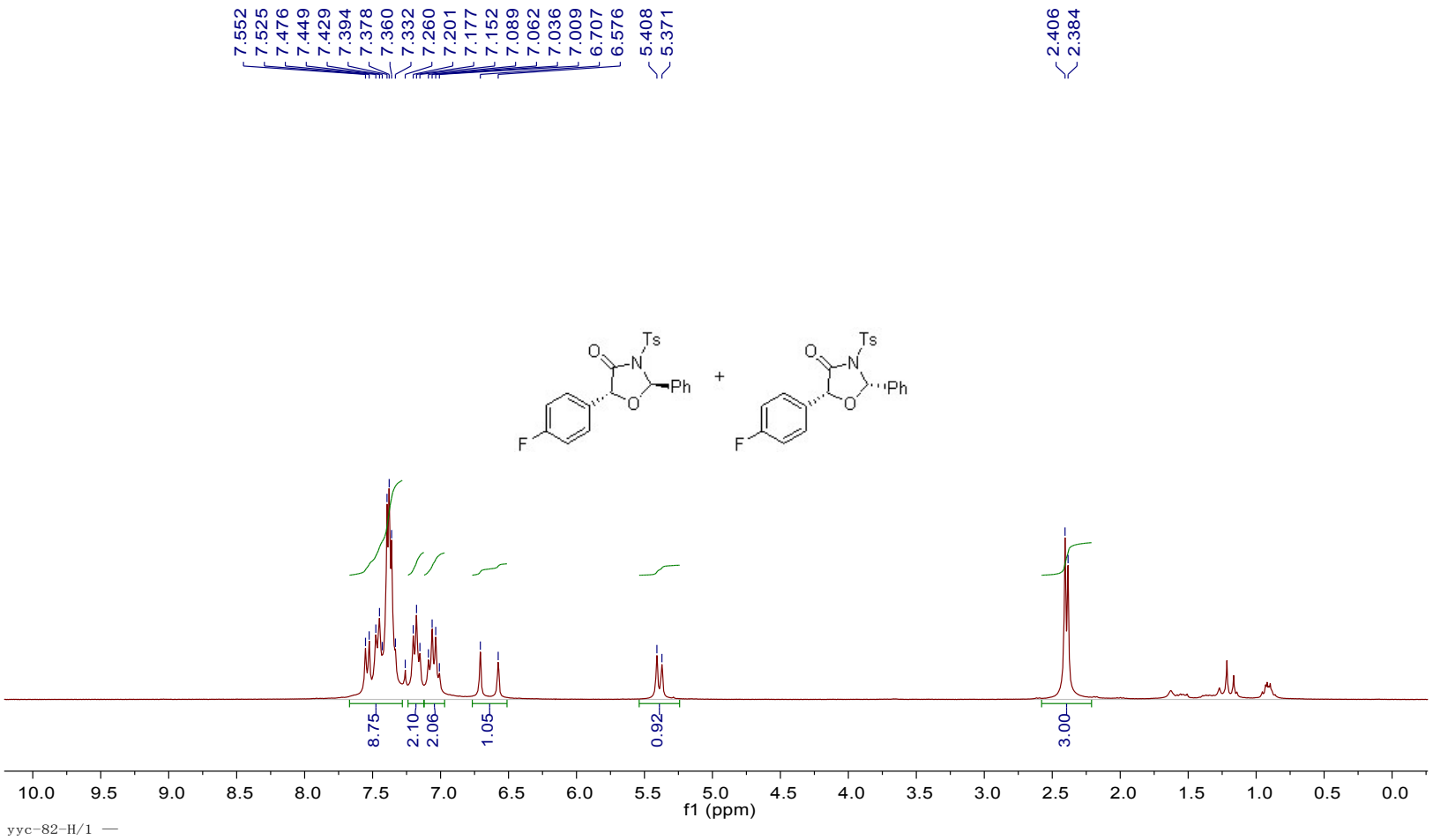
$^{13}C\{^{1}H\}$ NMR spectrum of **10a**



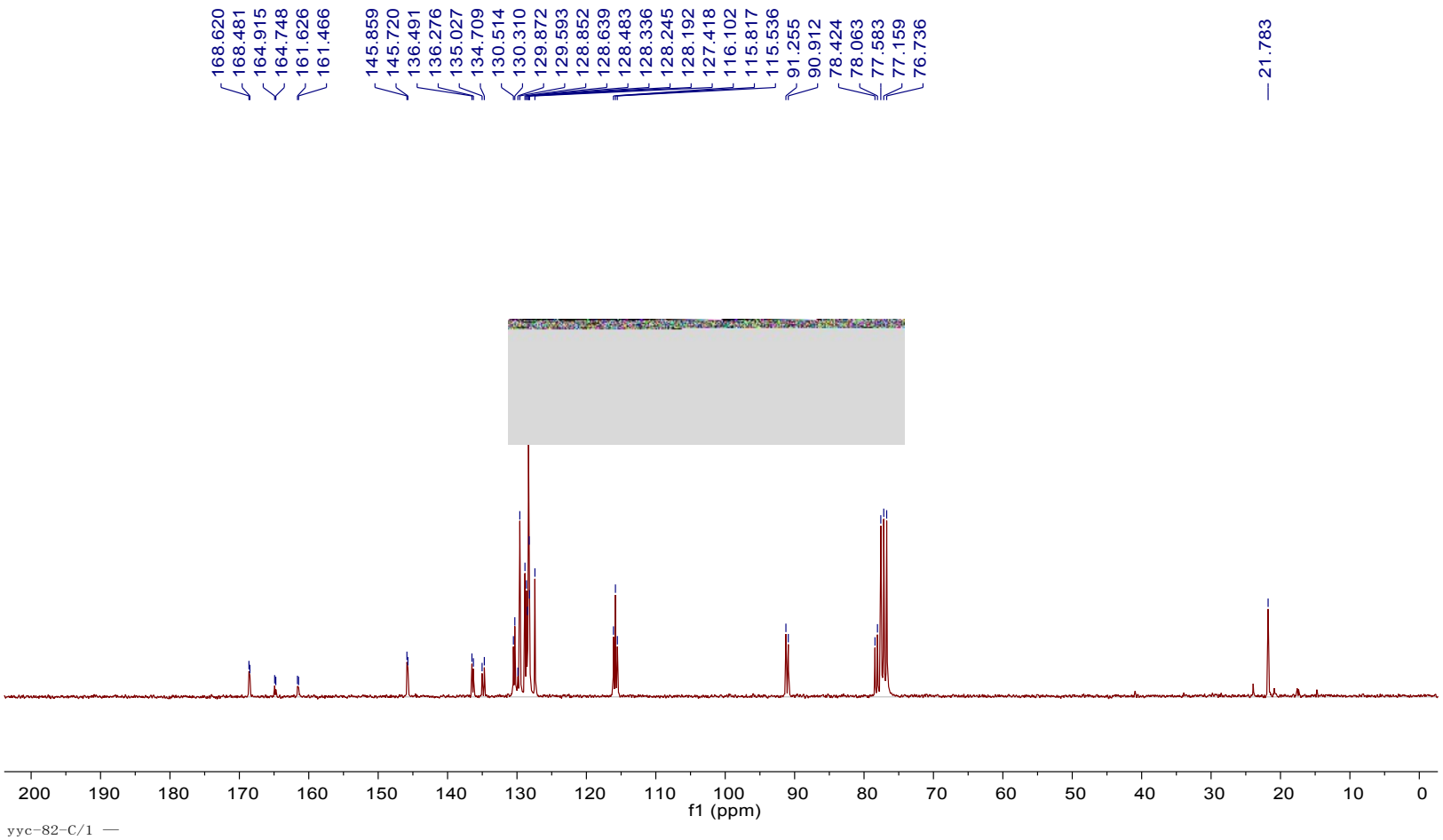
^{1}H NMR spectrum of **10b**



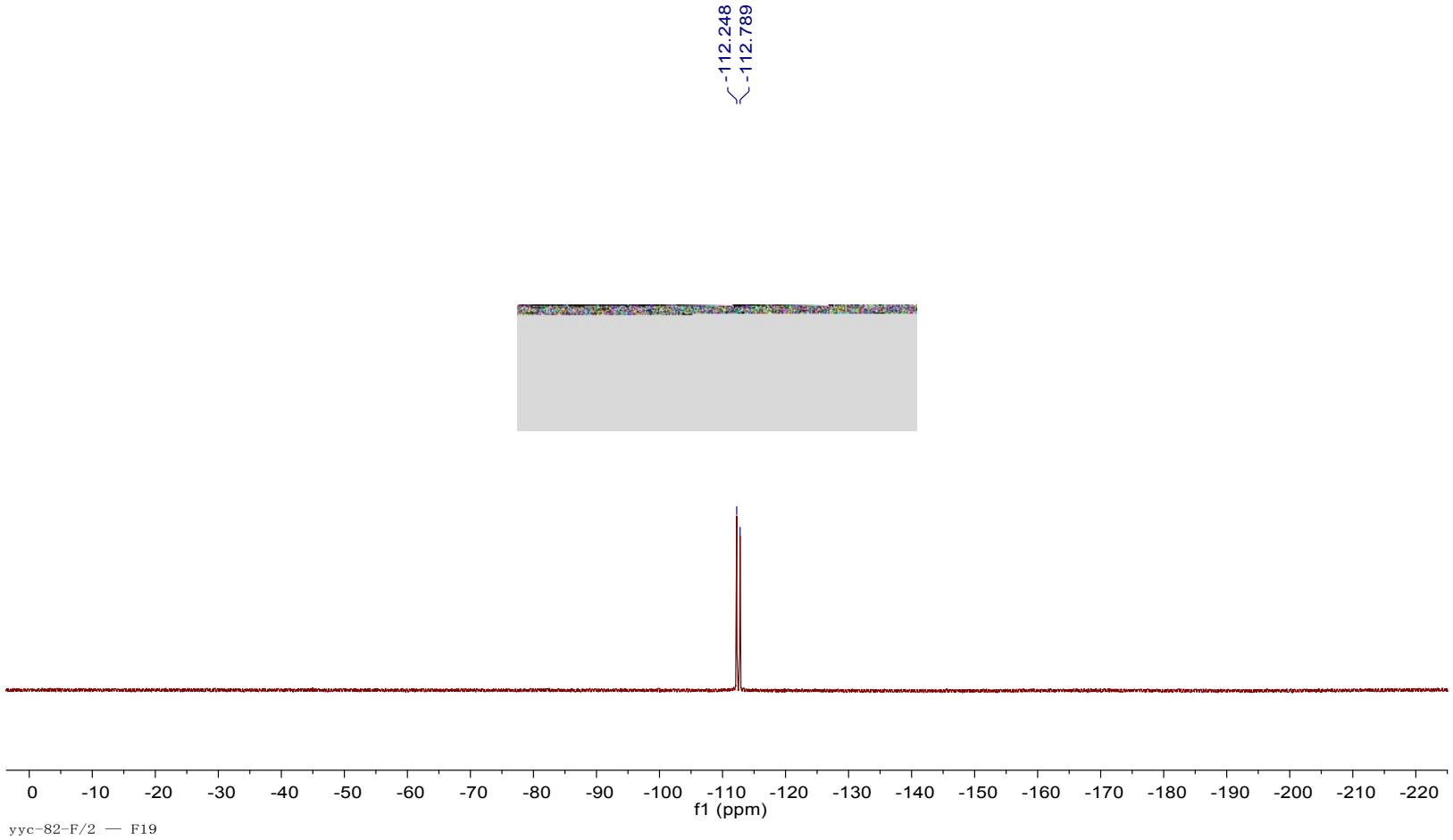
$^{13}C\{^{1}H\}$ NMR spectrum of **10b**



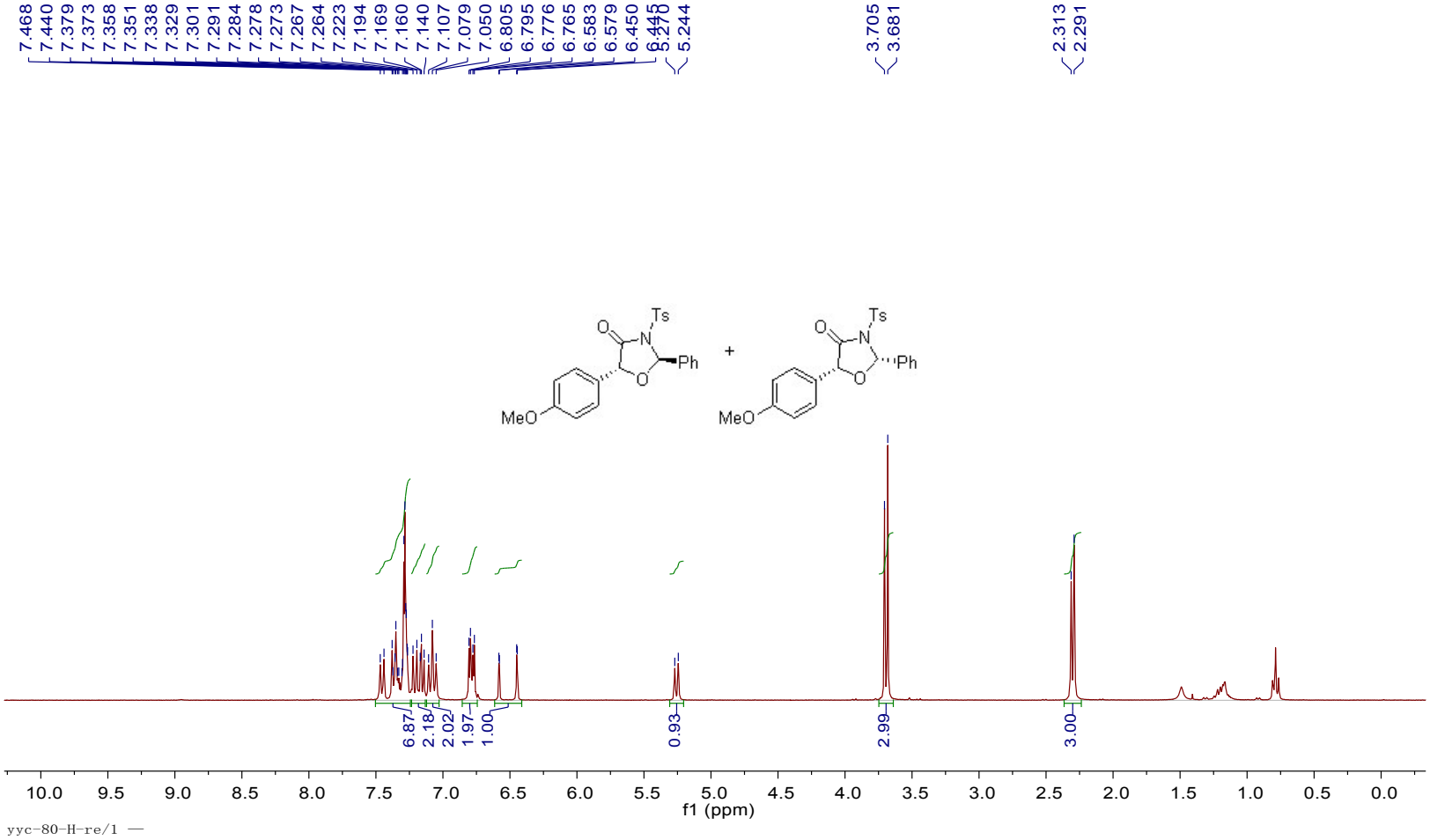
^{1}H NMR spectrum of **10c**



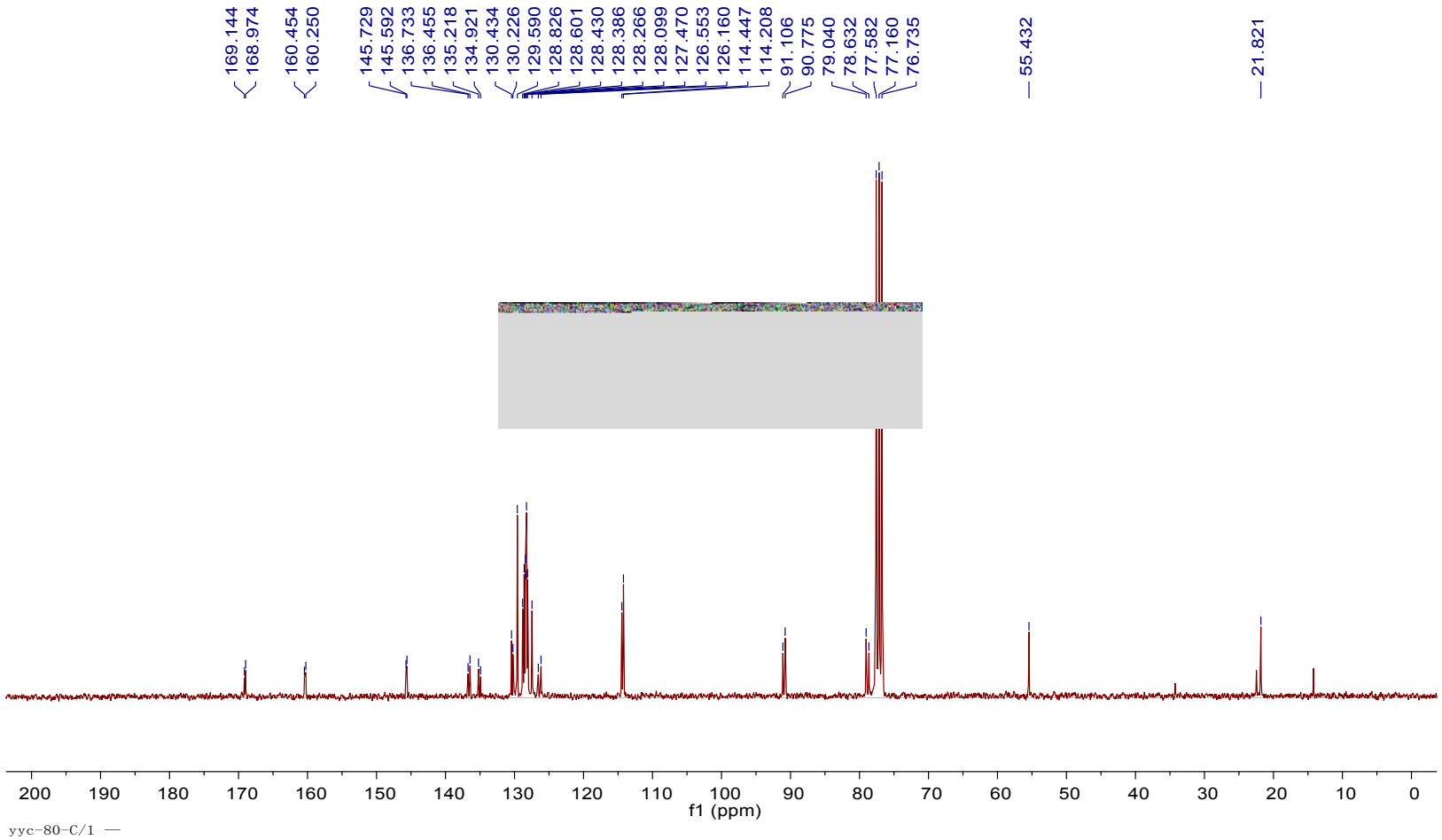
$^{13}C\{^{1}H\}$ NMR spectrum of **10c**



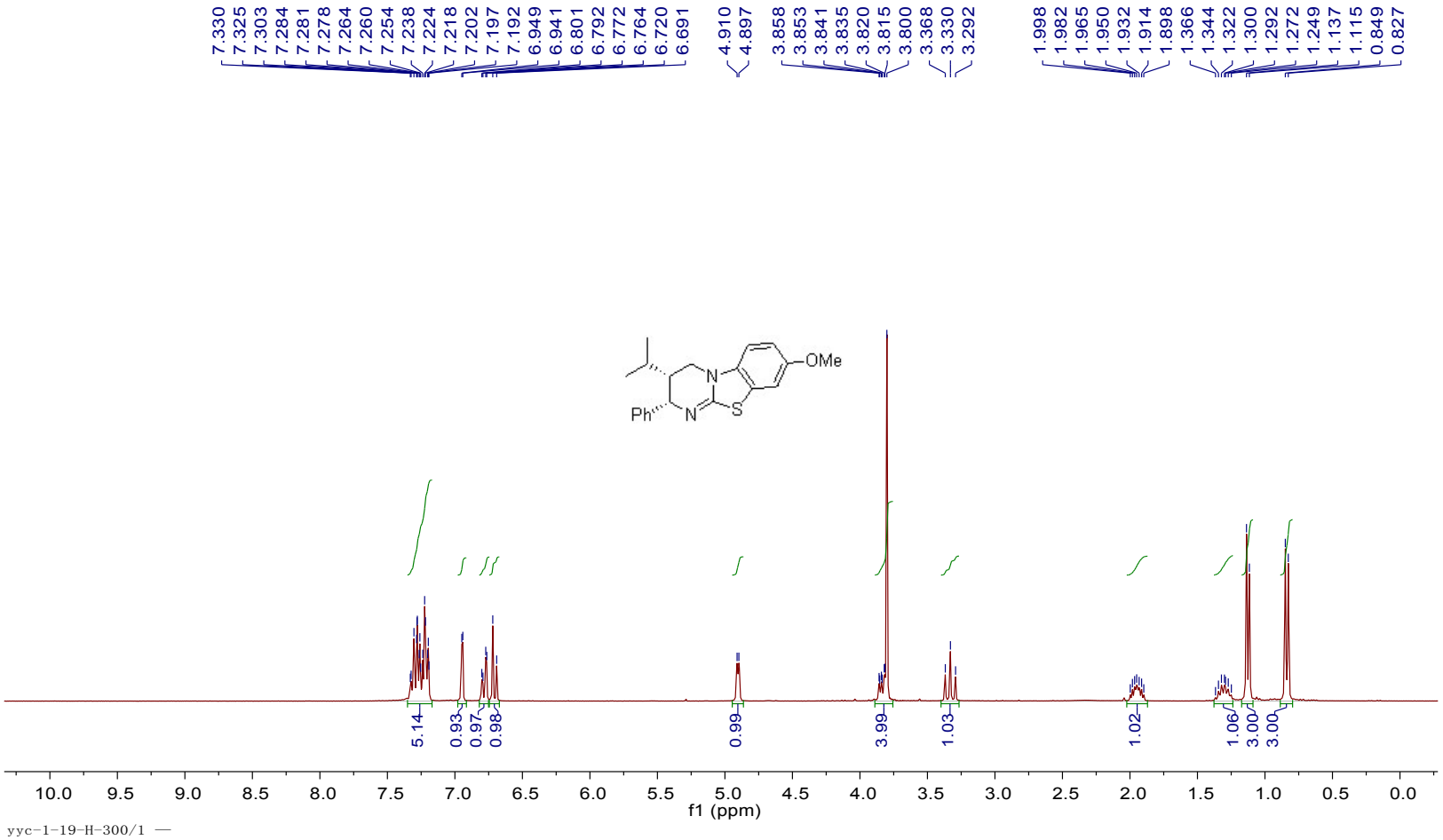
$^{19}F\{^{1}H\}$ NMR spectrum of **10c**



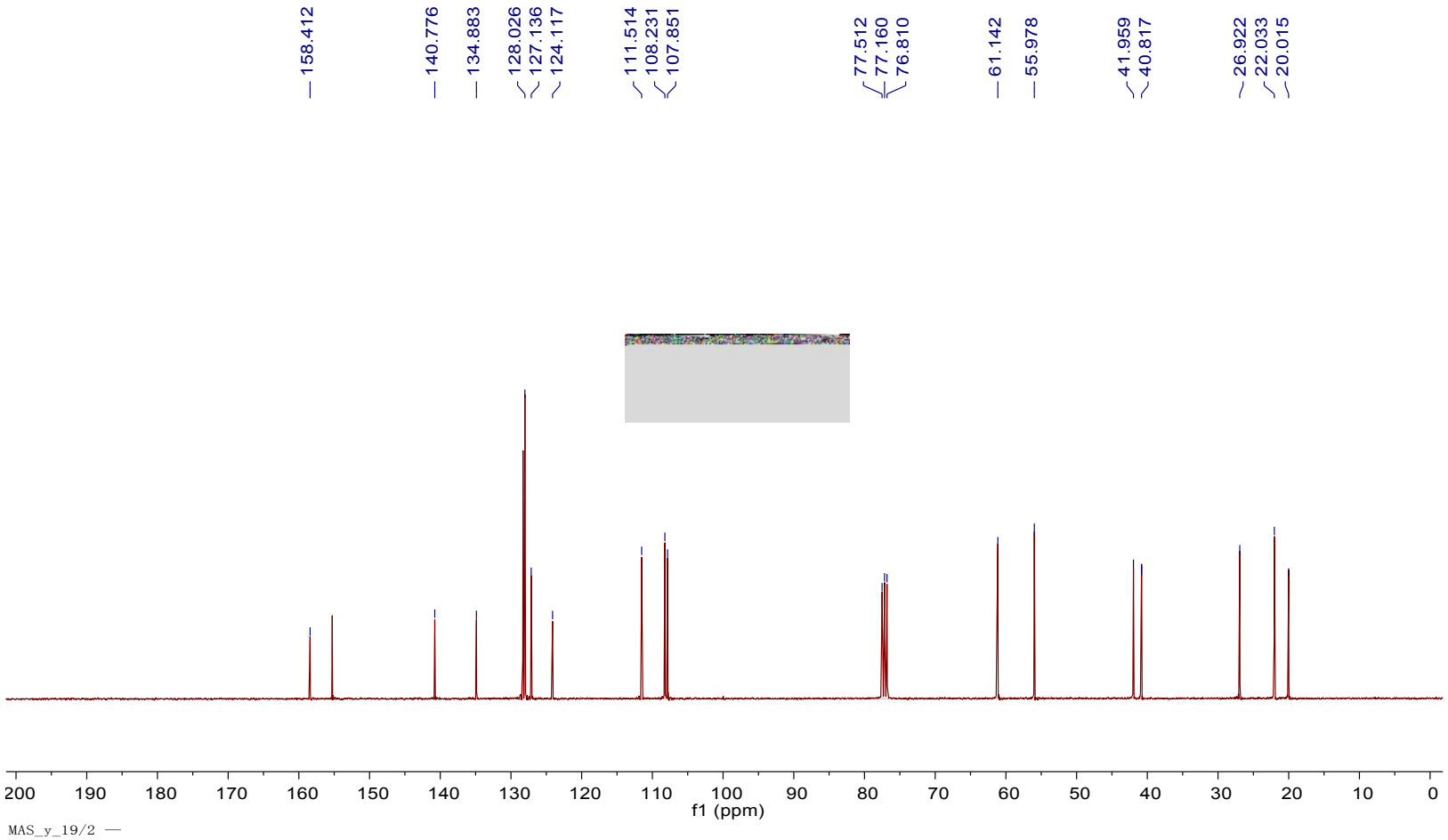
^{1}H NMR spectrum of **10d**



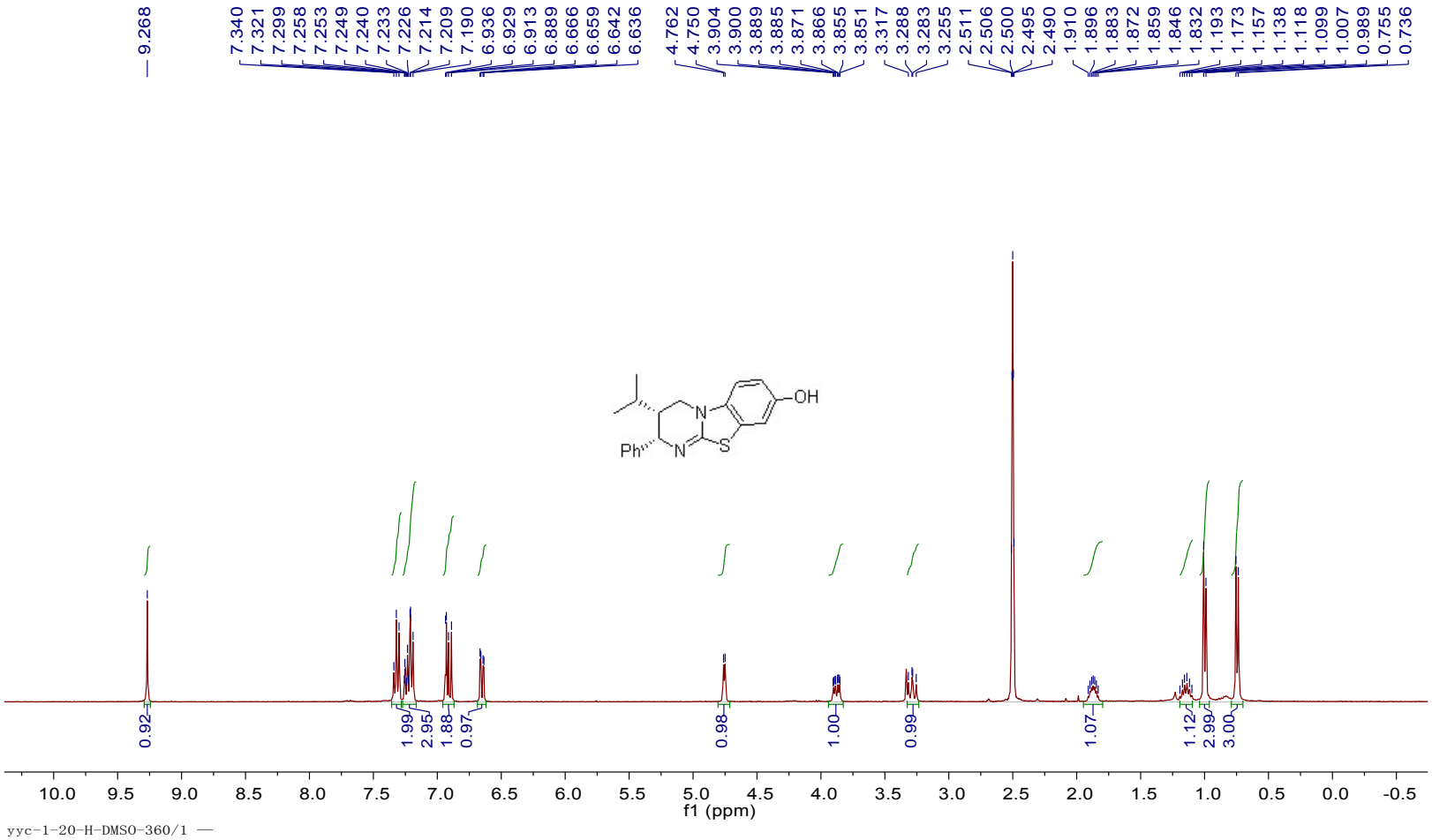
$^{13}C\{^{1}H\}$ NMR spectrum of **10d**



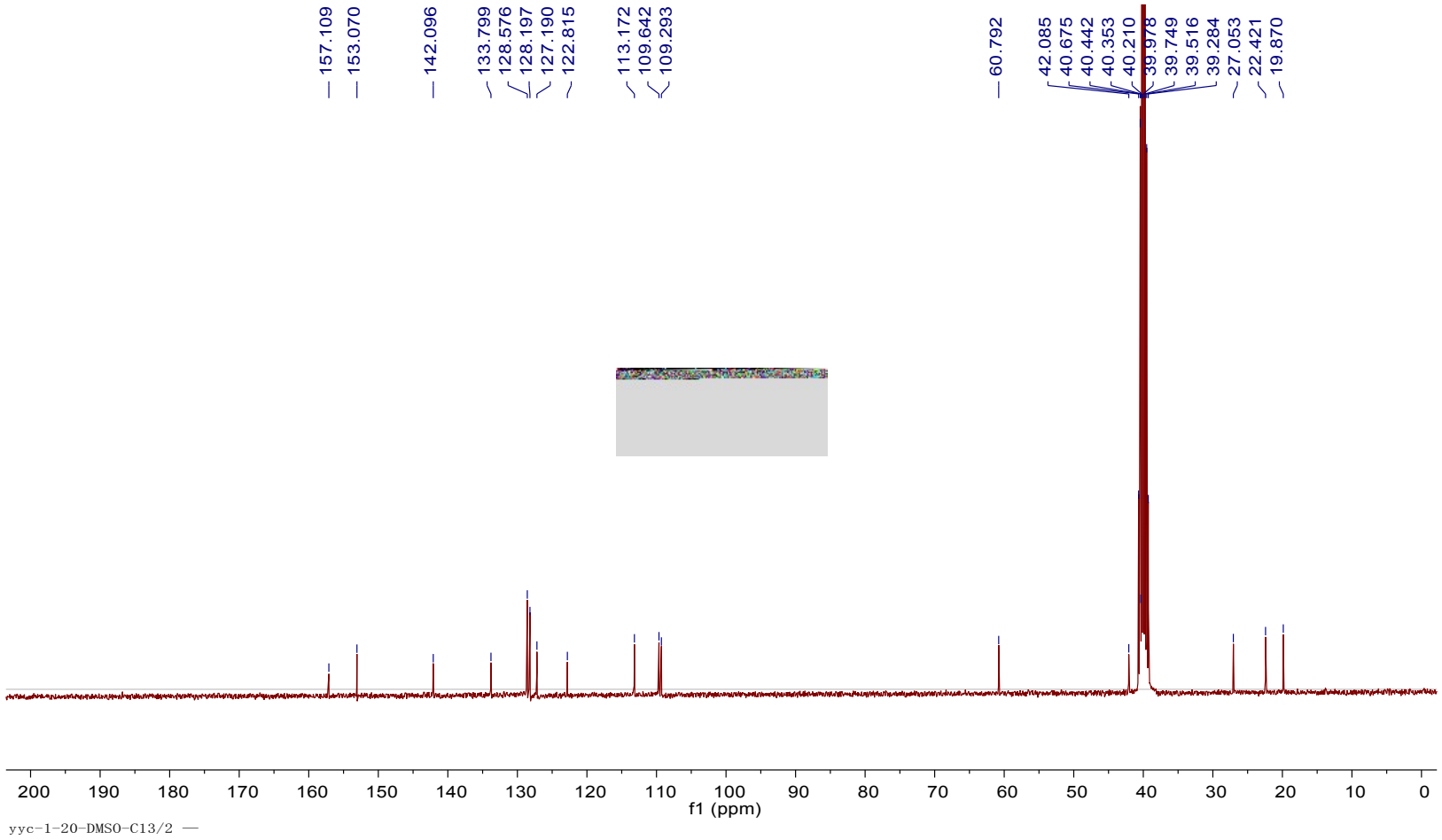
^{1}H NMR spectrum of **(2*S*,3*R*)-3**



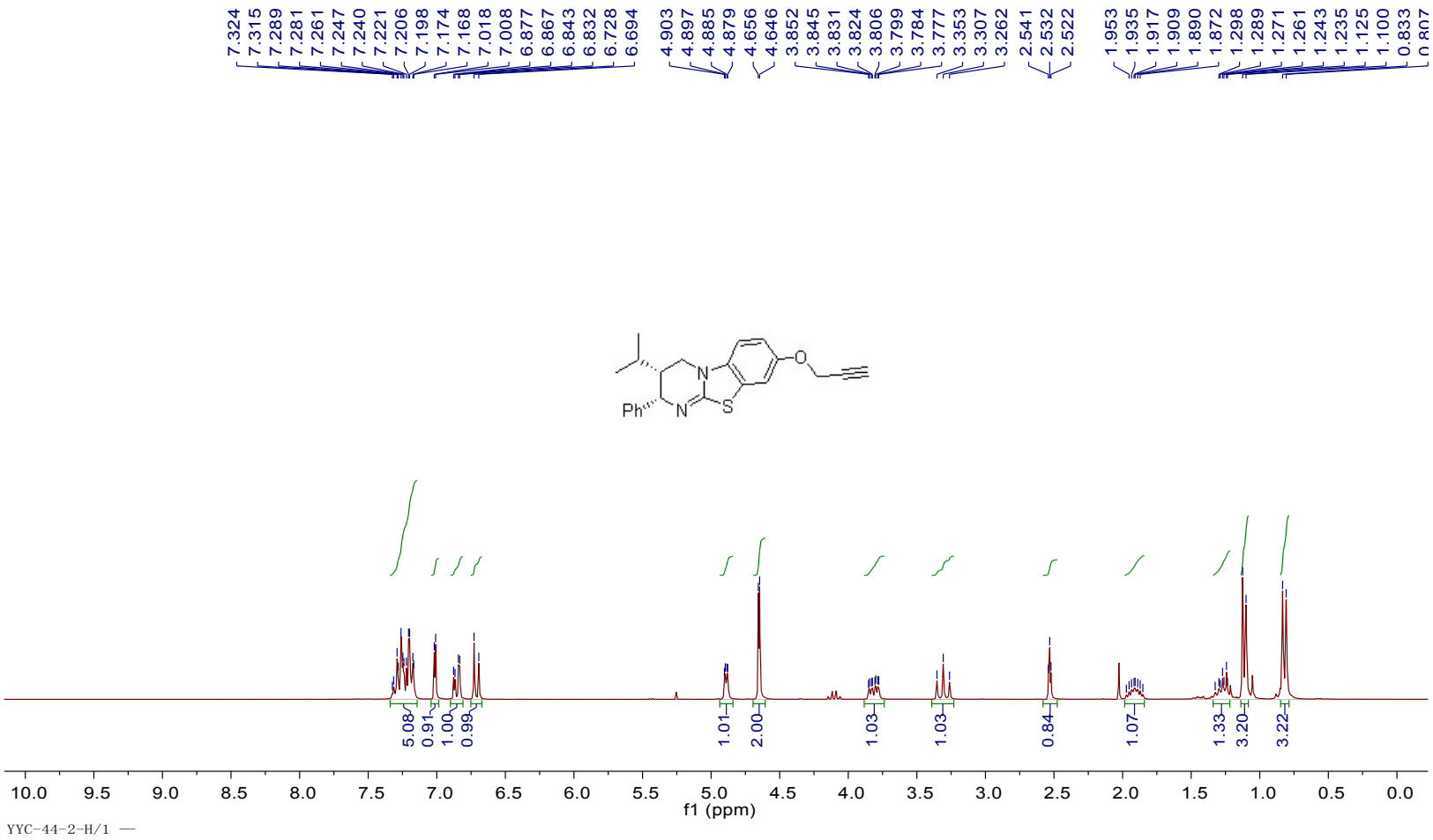
$^{13}C\{^{1}H\}$ NMR spectrum of **(2*S*,3*R*)-3**



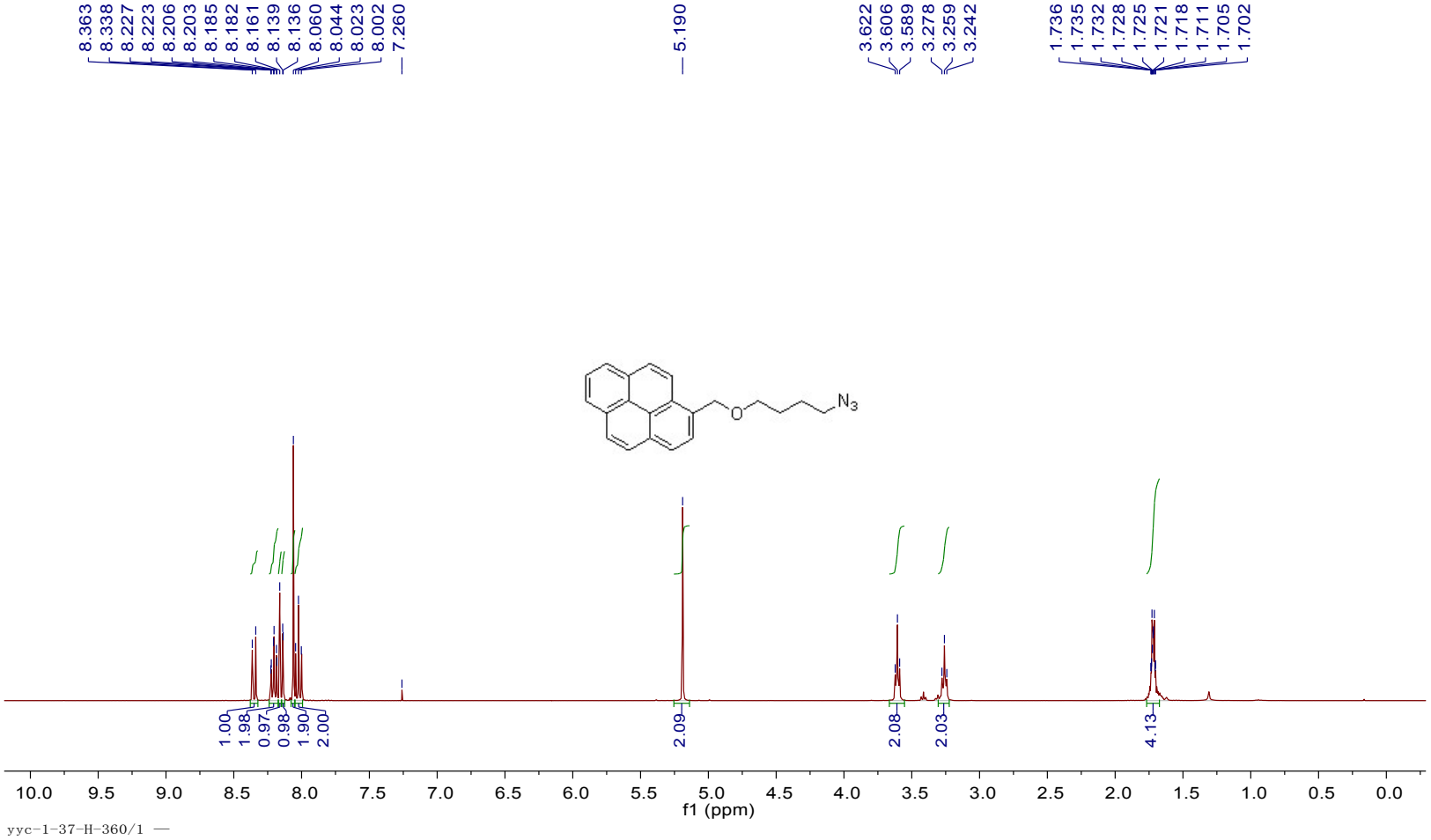
^{1}H NMR spectrum of **(2*S*,3*R*)-3a**



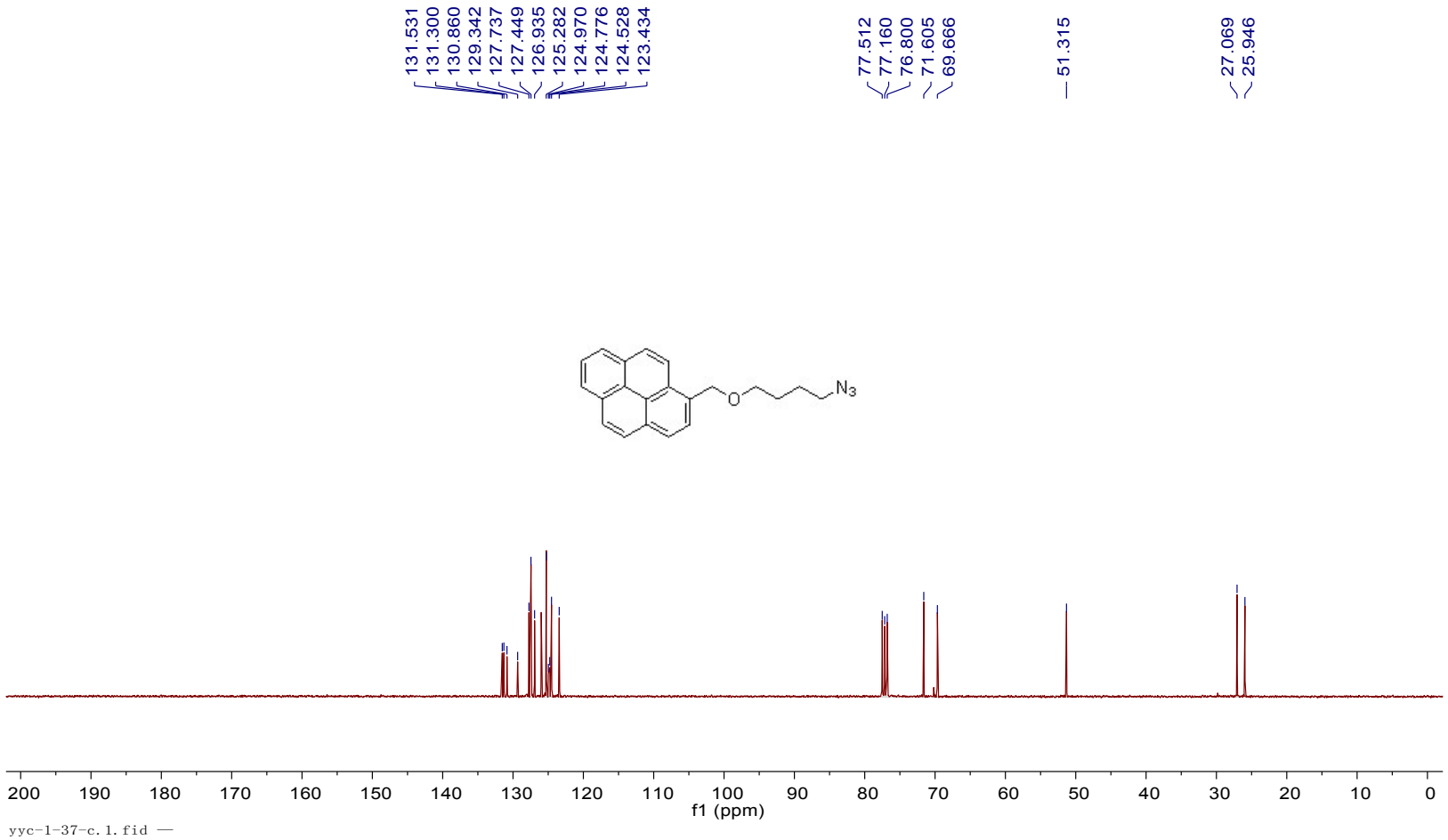
$^{13}C\{^{1}H\}$ NMR spectrum of **(2*S*,3*R*)-3a**



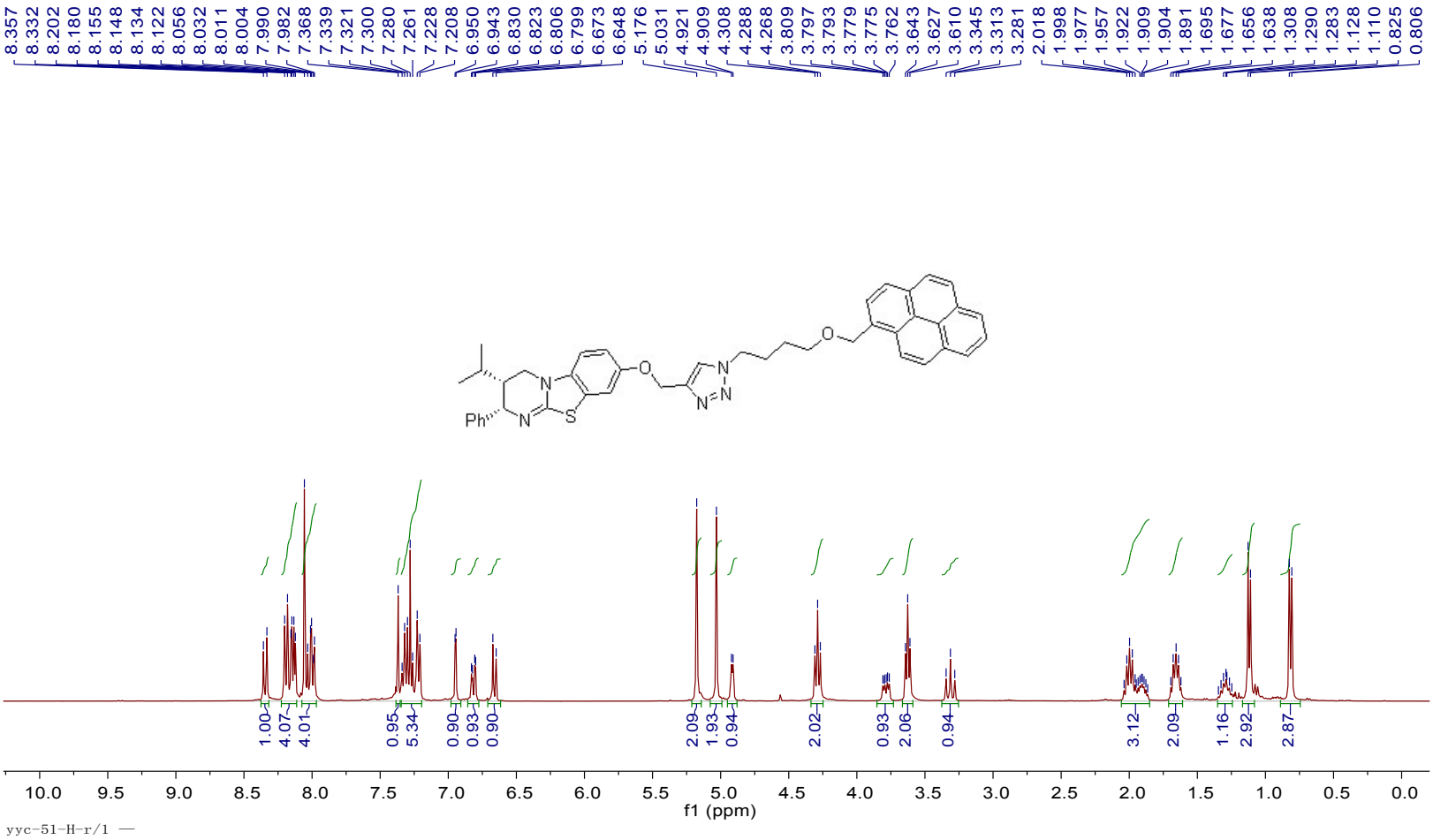
^{1}H NMR spectrum of **(2*S*,3*R*)-4**



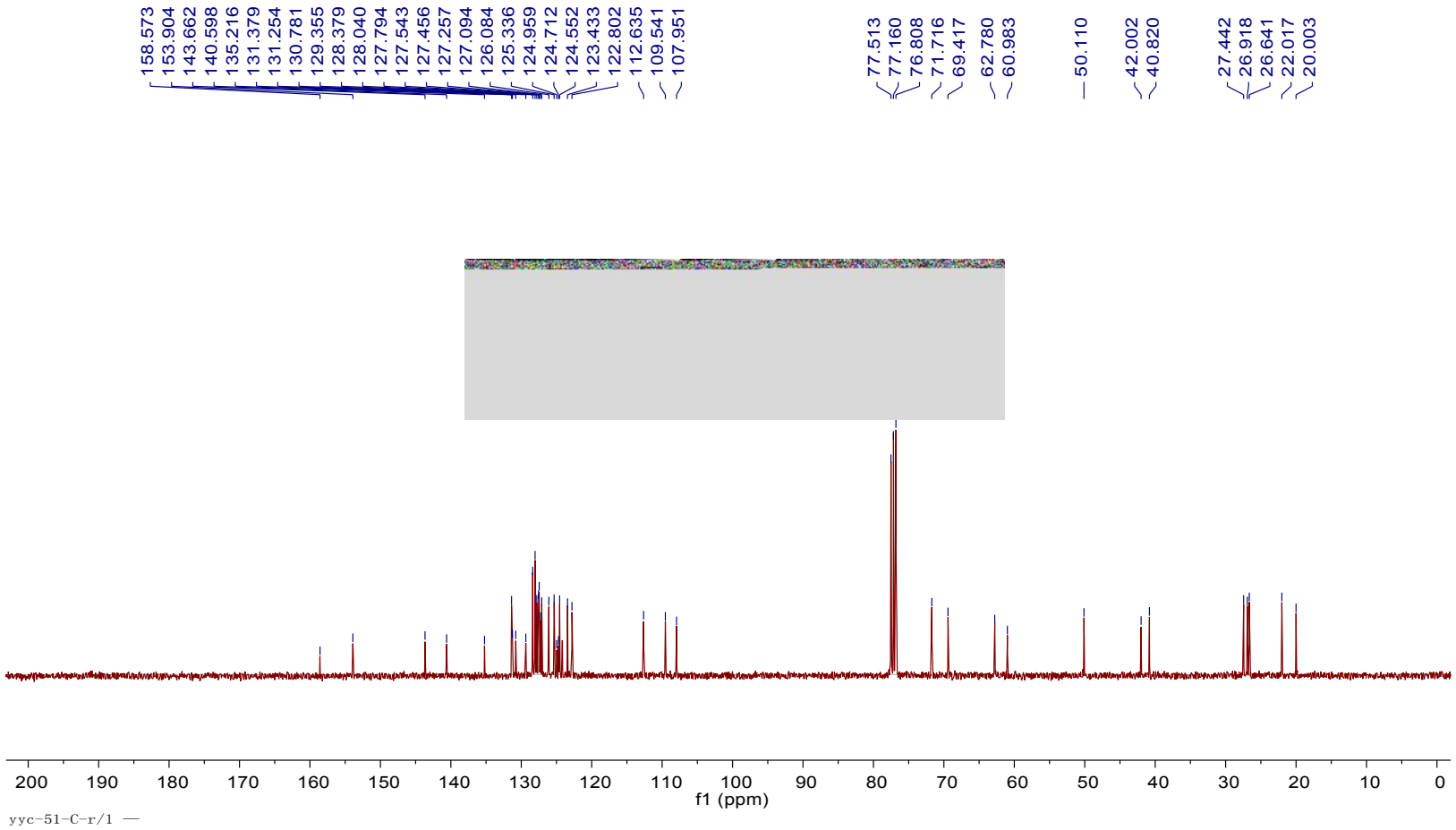
^{1}H NMR spectrum of **7**



$^{13}C\{^{1}H\}$ NMR spectrum of **7**

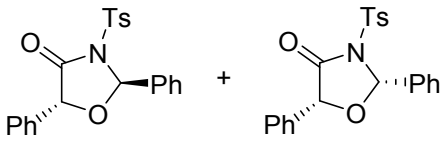


^{1}H NMR spectrum of **(2*S*,3*R*)-*pyr*-hyperBTM**



$^{13}C\{^{1}H\}$ NMR spectrum of **(2*S*,3*R*)- *pyr*-hyperBTM**

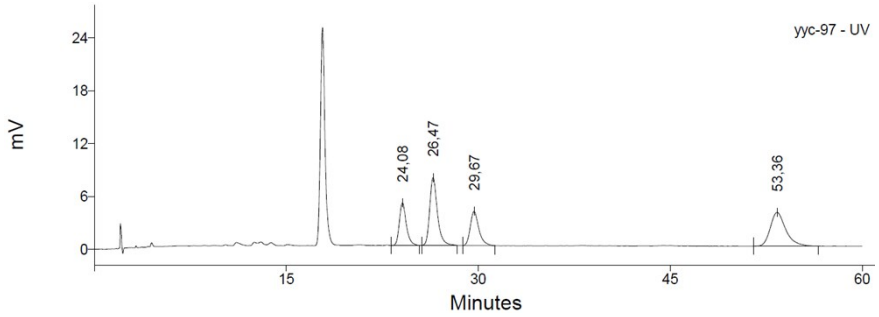
10. HPLC Traces



10a

Data for the anti diastereoisomer: Chiral HPLC analysis, Chiralcel AD-H (95:5 hexane:IPA, flow rate 1.5 mL min^{-1}, 211 nm, 39 °C) t_R (2*R*,5*R*): 26.9 min, t_R (2*S*,5*S*): 53.9 min, 96% ee.

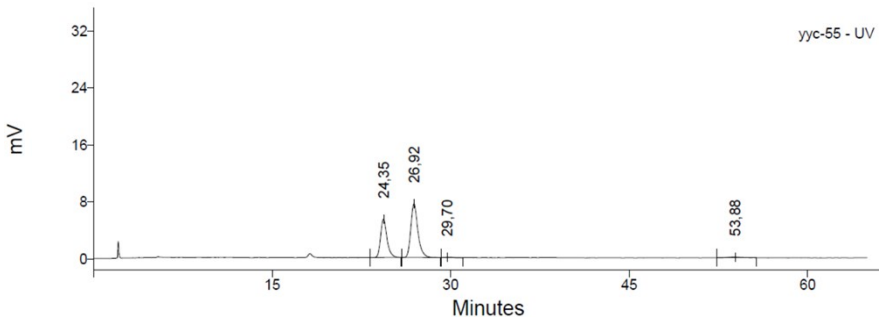
Data for the syn diastereoisomer: Chiral HPLC analysis, Chiralcel AD-H (95:5 hexane:IPA, flow rate 1.5 mL min^{-1}, 211 nm, 39 °C) t_R (2*S*,5*R*): 24.3 min, t_R (2*R*,5*S*): 29.7 min, 98% ee.



Informations :
AD-H- hex/IPA: 95/5 - 1.5 ml/min - 211nm 39°C

Résultats d'intégration

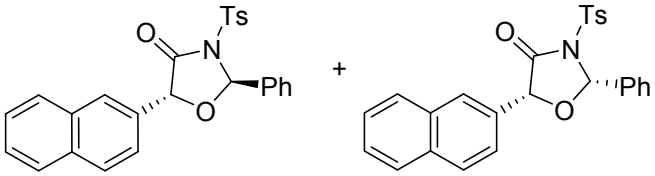
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (USP, EP)	Plateaux (EP)
1		24,08	181,54	**18,17**	1,29	10241,33
2		26,47	320,43	**32,06**	1,32	10354,41
3		29,67	179,24	**17,94**	1,32	10369,27
4		53,36	318,12	**31,83**	1,34	10340,54
SOMME			**999,34**	**100,00**		



Informations :
AD-H- hex/IPA: 95/5 - 1.5 ml/min - 211nm 39°C

Résultats d'intégration

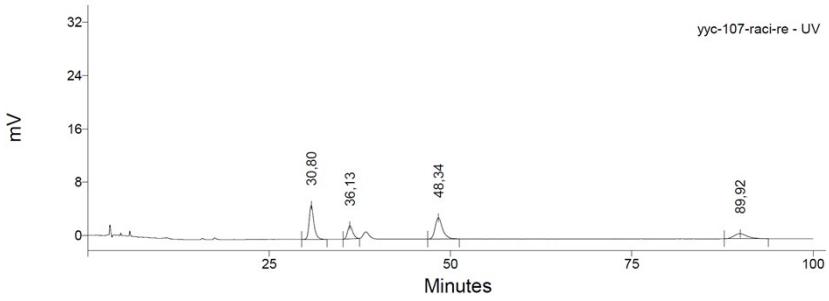
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (USP, EP)	Plateaux (EP)
1		24,35	201,78	**38,56**	1,30	10571,21
2		26,92	312,21	**59,67**	1,30	10738,02
3		29,70	2,40	**0,46**	#	9278,77
4		53,88	6,83	**1,31**	1,16	12541,96
SOMME			**523,21**	**100,00**		



10b

Data for the anti diastereoisomer: Chiral HPLC analysis, Chiralcel AD-H (90:10 hexane:IPA, flow rate 1.0 mL min-1, 211 nm, 40 °C) t_R (2*R*,5*R*): 36.0 min, t_R (2*S*,5*S*): 89.7 min, 86% ee.

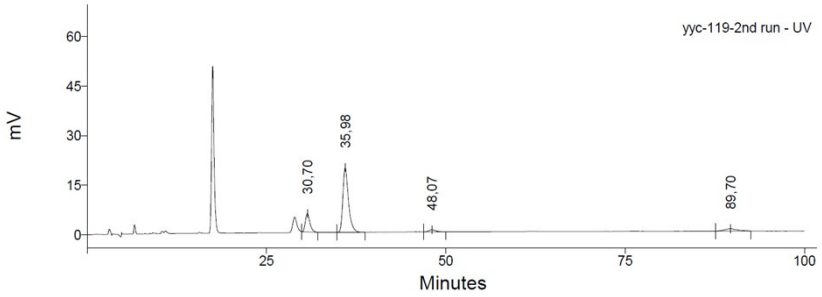
Data for the syn diastereoisomer: Chiral HPLC analysis, Chiralcel AD-H (90:10 hexane:IPA, flow rate 1.0 mL min-1, 211 nm, 40 °C) t_R (2*S*,5*R*): 30.7 min, t_R (2*R*,5*S*): 48.1 min, 69% ee.



Informations :
AD-H - hex/IPA: 90/10 - 1.0 mL/min - 211 nm 40°C

Résultats d'intégration

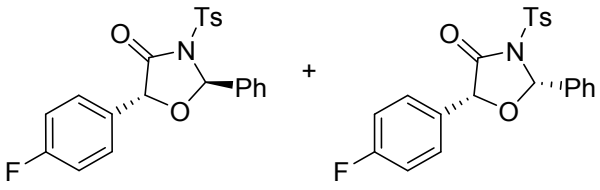
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (USP, EP)	Plateaux (EP)
1		30,80	228,85	**35,27**	1,31	11992,30
2		36,13	95,55	**14,73**	1,34	12844,34
3		48,34	225,88	**34,81**	1,33	12063,38
4		89,92	98,59	**15,19**	1,33	12260,32
SOMME			**648,87**	**100,00**		



Informations :
AD-H - hex/IPA: 90/10 - 1.0 ml/min - 211 nm 40°C

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (USP, EP)	Plateaux (EP)
1		30,70	244,88	**17,13**	1,27	12220,91
2		35,98	1057,95	**74,01**	1,42	11344,14
3		48,07	44,64	**3,12**	1,40	11825,84
4		89,70	82,02	**5,74**	1,28	12168,98
SOMME			**1429,49**	**100,00**		



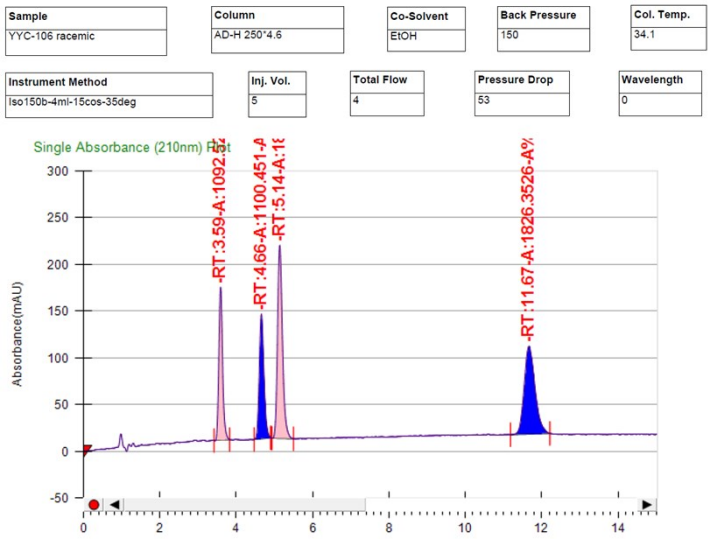
10c

SFC Analysis: CHIRALPAK® AD-H, 35 °C, 5% MeOH, 4.0 mL min^{-1}, 150 bar, retention times:

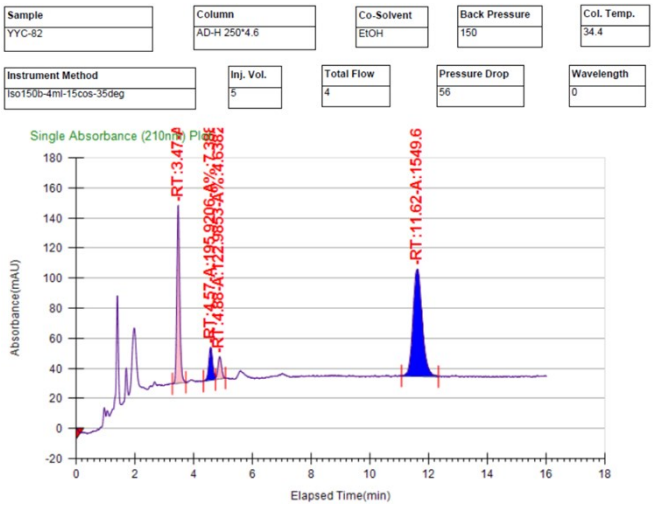
Data for the anti diastereoisomer: t_R (2*S*,5*S*): 4.9 min, t_R (2*R*,5*R*): 11.6 min, 85% ee.

Data for the syn diastereoisomer: t_R (2*S*,5*R*): 4.6 min, t_R (2*R*,5*S*): 3.5 min, 60% ee.

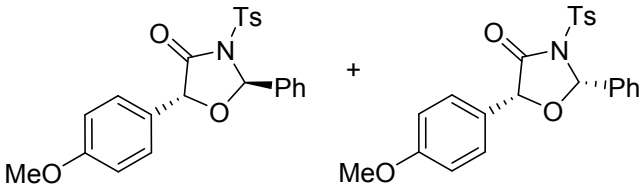
The *anti*/*syn* attribution is made according to the NMR which indicates the main diastereoisomer. The attribution of the configurations is made by analogy with the data of ref 5.



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	18.6805	1092.5212	3.59 min	163.5718
2	Peak2	18.816	1100.451	4.66 min	133.4745
3	Peak3	31.2756	1829.1474	5.14 min	206.6156
4	Peak4	31.2279	1826.3526	11.67 min	94.1105



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	29.5278	782.9463	3.47 min	118.1412
2	Peak2	7.3889	195.9206	4.57 min	21.7665
3	Peak3	4.6382	122.9853	4.88 min	14.6723
4	Peak4	58.445	1549.6999	11.62 min	71.3037



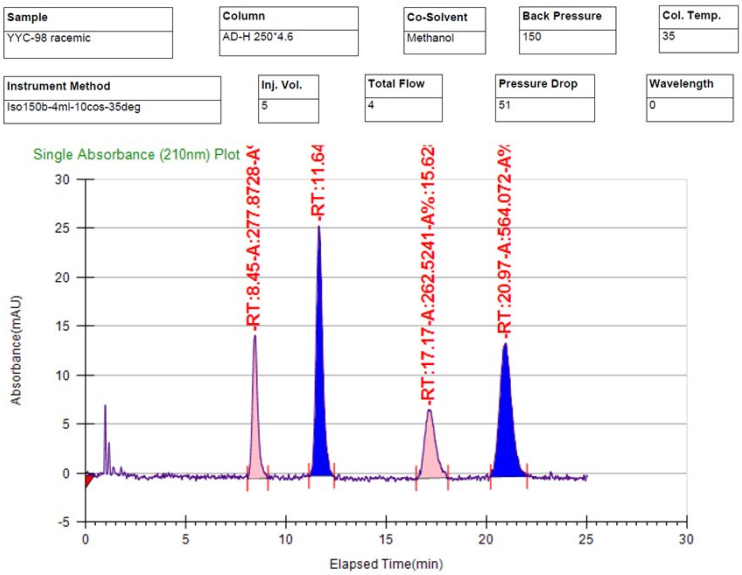
10d

SFC Analysis: [CHIRALPAK® AD-H, 35 °C, 5% MeOH, 4.0 mL min^{-1}, 150 bar, retention times:

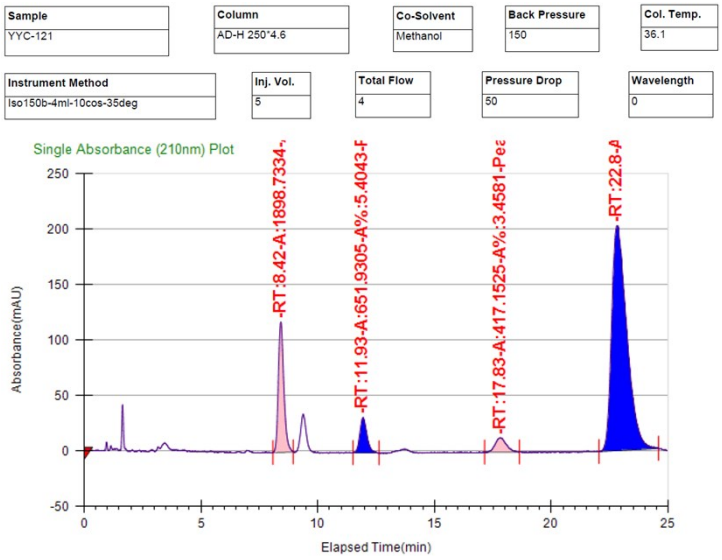
Data for the anti diastereoisomer: t_R (2*R*,5*R*): 22.8 min, t_R (2*S*,5*S*): 11.9 min, 87% ee.

Data for the syn diastereoisomer: t_R (2*S*,5*R*): 8.4 min, t_R (2*R*,5*S*): 17.8 min, 64% ee.

The *anti*/*syn* attribution is made according to the NMR which indicates the main diastereoisomer. The attribution of the configurations is made by analogy with the data of ref 5.



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	16.5418	277.8728	8.45 min	14.6069
2	Peak2	34.2508	575.3513	11.64 min	25.525
3	Peak3	15.6281	262.5241	17.17 min	6.9836
4	Peak4	33.5793	564.072	20.97 min	13.6293



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	15.74	1898.7334	8.42 min	117.5466
2	Peak2	5.4043	651.9305	11.93 min	31.4974
3	Peak3	3.4581	417.1525	17.83 min	12.8126
4	Peak4	75.3976	9095.3156	22.8 min	202.6987