Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Photo-induced 1,2-thiohydroxylation of maleimide involving disulfide and singlet oxygen

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Contents:

1. General Information and Instrumentation:

All chemicals were obtained from commercial sources and were used without further purification. The starting material **1** was synthesized according to previously described method.[1] Reactions were monitored via TLC, prepared using silica gel 60 F_{254} (0.25 mm), and were detected under UV light at 254 nm. The chromatography separation was carried out using 60−120 mesh-sized silica gel. Ethyl acetate/ hexane mixtures were used as the eluent. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in 500, and 400 MHz NMR in deuterated solvents, and the chemical shifts (δ) are given in ppm. The ^{1}H spectra were referenced to TMS (0 ppm) for $CDCl_3$; for ^{13}C $CDCl_3$ (77.16 ppm). IR spectra were recorded neat using an FT-IR spectrometer. HRMS was recorded using ESI (Q-TOF type mass analyzer) in positive modes. UV−vis experiment was performed in 1 mL quartz cuvettes with a path length equal to 1 cm. Photoluminescence was carried out in 1 mL quartz cuvettes.

2. Light Information and Reaction Setup:

Philips 4 x 5 W white LED bulbs ($\lambda_{em,max}$ = 419 nm) were used as the light source for this light-promoted reaction and no filter was used. A borosilicate 10 mL vial was used as the reaction vessel. The distance from the light source to the irradiation vessel was ∼3−5 cm. Regular fan was used to ventilate the area to maintain the room temperature (27–30 ºC). The reaction set-up for this photochemical reaction is shown below (Figure S1)

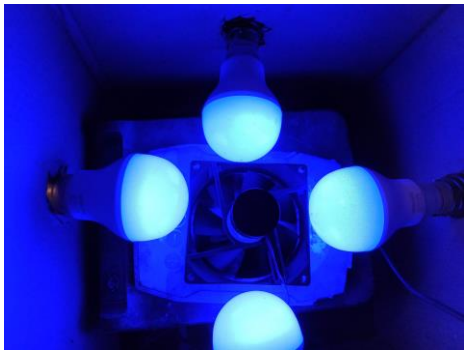
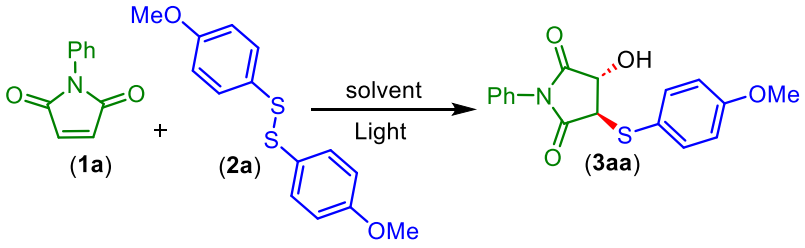


Figure S1 Photochemical Reaction Set-up.

3. Optimization of Reaction Parameters:

Table S1: Optimization of reaction conditions



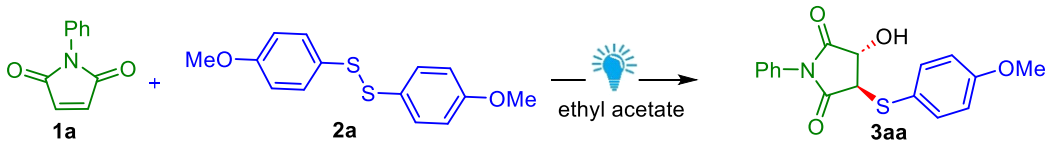
Sl. No.	Deviation from standard conditions	Yield%[b]
1.	None	86
2.	$CHCl_3$ instead of ethyl acetate	63
3.	DCE instead of ethyl acetate	60
4.	DCM instead of ethyl acetate	65
5.	TFE instead of ethyl acetate	71
6.	1,4 dioxane instead of ethyl acetate	30
7.	Toluene instead of ethyl acetate	40
8.	PhCl instead of ethyl acetate	20
9.	EtOH instead of ethyl acetate	55
10.	0.6 and 0.75 equivalents of **2a**	86 and 87
11.	No light	0
12.	Green LEDs instead of blue LEDs	0

[a]Reaction Conditions unless specified otherwise: **1a** (0.25 mmol), **2a** (0.125 mmol), solvent (2 mL) for 9 h under 5W x 4 blue LEDs ($\lambda_{em,max}$ = 419 nm) in an open air. [b]Isolated yield.

Although the yield was quite good (86%), a series of optimization studies were carried out to improve it further Initially, various solvents were screened such as $CHCl_3$, dichloroethane

(DCE), dichloromethane (DCM), tetrafluoroethanol (TFE), 1,4-dioxane, toluene, PhCl, EtOH, (entry 2–9, Table1). But there was no improvement in the yield and ethyl acetate turned out to be the best solvent. Upon increasing the loading of 1,2-*bis*(4-methoxyphenyl)disulfane (**2a**) to 0.6 and 0.75 equiv there was no further enhancement in the yield (entry 10, Table1). Also, there was no reaction in the absence of light and under green LEDs (entry 11-12, Table 1). Thus, the optimized condition found was *N*-phenylmaleimide (**1a**, 1 equiv) and 1,2-*bis*(4-methoxyphenyl)disulfane (**2a**, 0.5 equiv) in ethyl acetate under the exposure of blue light (4 x 5W, $\lambda_{em,max}$ = 419 nm) in an open air.

4. General Procedure for the Synthesis of 3aa



An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), a magnetic stir bar in ethyl acetate (2 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The progress of the reaction was monitored via TLC. After completion of the reaction, the solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the desired product **3aa** as grey solid in 86% yields (71 mg).

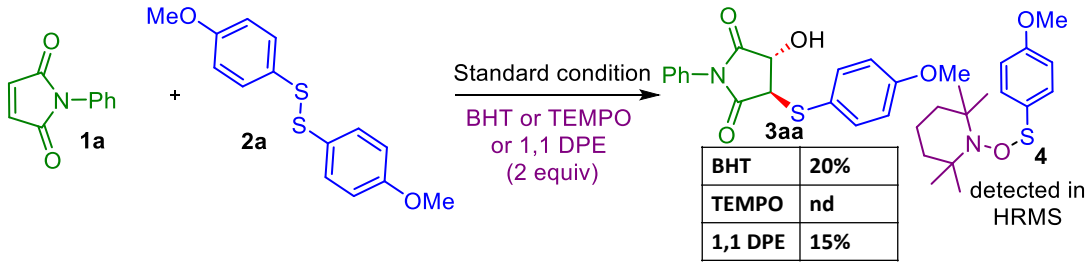
5. General Procedure for the Synthesis of 3aa in 2 mmol Scale

An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (2 mmol, 346 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (1 mmol, 278 mg), a magnetic stir bar in ethyl acetate (3 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The progress of the reaction was monitored via TLC. After completion of the reaction, the solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with

ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the desired product **3aa** as grey solid in 79% yields (519 mg).

6. Mechanistic Studies

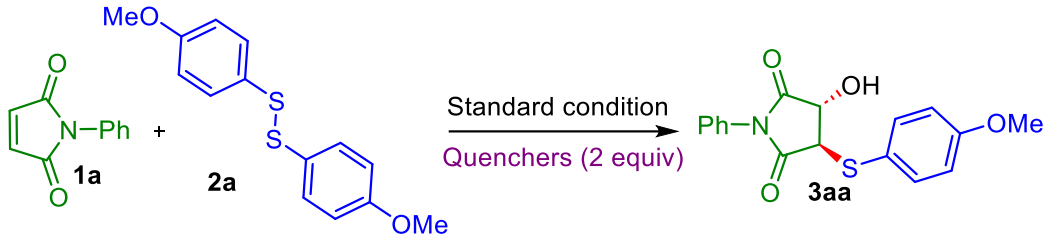
(A) Procedure for Trapping of Radicals:



BHT	**20%**
TEMPO	**nd**
1,1 DPE	**15%**

An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), BHT (2 equiv, 0.5 mmol, 110 mg) or TEMPO (2 equiv, 0.5 mmol, 78 mg) or 1,1-diphenylethylene (DPE) (2 equiv, 0.5 mmol, 90 mg) a magnetic stir bar in ethyl acetate (1.5 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the product **3aa** as grey solid in 16 mg (20% yield) for BHT, 0 mg (0% yield) for TEMPO and 12 mg (15% yield) for DPE. These results support the radical nature of the reaction.

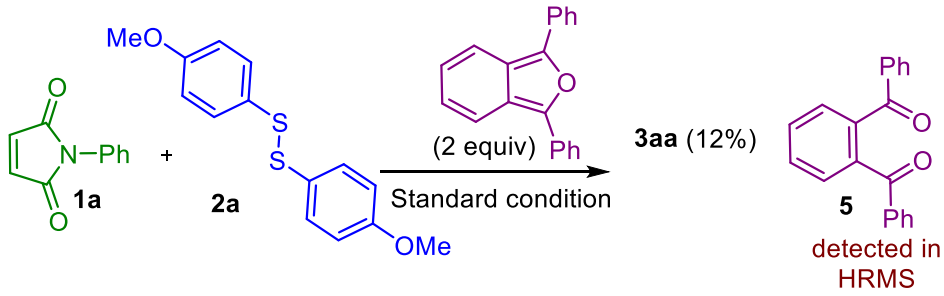
(B) Procedure for Detection of Singlet Oxygen and Superoxide:



Quencher (2 equiv)	Role	Yield%
DABCO	Singlet oxygen quencher	00
p-benzoquinone	Superoxide quencher	81%

An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), DABCO (2 equiv, 0.5 mmol, 56 mg) or *p*-benzoquinone (2 equiv, 0.5 mmol, 54 mg), a magnetic stir bar in ethyl acetate (1.5 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the product **3aa** as grey solid in 0 mg (0% yield) for DABCO and 66 mg (81% yield) for *p*-benzoquinone. The failure to obtain the product **3aa** in the presence of DABCO confirms the involvement of the singlet oxygen in the reaction and for *p*-benzoquinone, the 81% yield of **3aa** suggests noninvolvement of superoxide in the reaction.

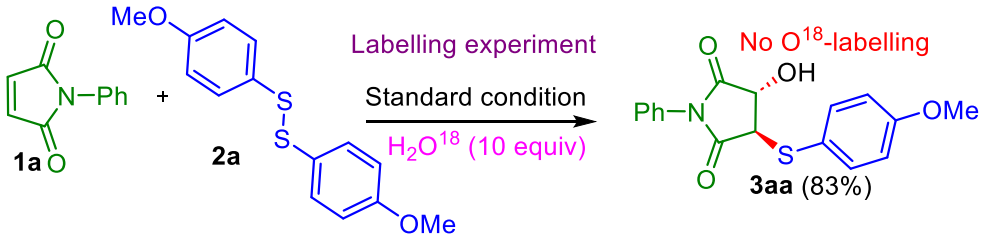
(C) Procedure for Singlet Oxygen Trapping:



An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), 1,3-diphenylisobenzofuran (2 equiv, 0.5 mmol, 135 mg) a magnetic stir bar in ethyl acetate (1.5 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the product **3aa** as grey solid in 12% yields (10 mg) and 1,2-phenylene*bis*(phenylmethanone) (**5**) was detected in HRMS analysis of the crude reaction mixture.

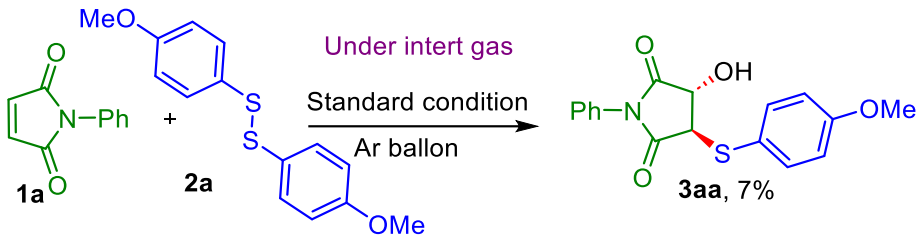
(D) Procedure for Investigation of Origin of Hydroxy Functionality

(i) H_2O^{18} Labelling Experiment:



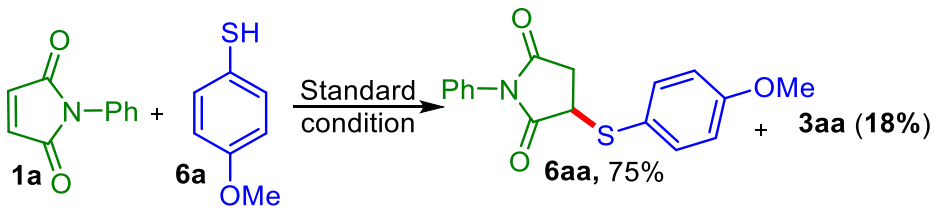
An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), H_2O^{18} (10 equiv, 2.5 mmol, 50 mg) a magnetic stir bar in ethyl acetate (1.5 mL) and was stirred at room temperature for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the product **3aa** as grey solid in 83% yields (68 mg). No H_2O^{18} labelled **3aa** was detected.

(ii) Reaction in Dry and Argon Atmosphere:



An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), a magnetic stir bar in dry ethyl acetate (1.5 mL) and was stirred at room temperature for 9 h under an argon atmosphere under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then purified over column chromatography by eluting with hexane: ethyl acetate (83:17) mixture to afford the product **3aa** in 7% yield.

(E) Reaction with 4-methoxybenzenethiol (6a) in Lieu of 1,2-*bis*(4-methoxyphenyl)disulfane (2a)



An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 4-methoxybenzenethiol (**6a)** (0.25 mmol, 35 mg), a magnetic stir bar in ethyl acetate (1.5 mL) and was stirred at room temperature in an open air for 9 h the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. The solvent was removed by rotary evaporation. The reaction mixture was then mixed with water (10 mL) and extracted with ethyl acetate (2 × 15 mL). The organic layer was dried over anhydrous sodium sulfate and was evaporated under reduced pressure. The residue so obtained was then purified over column chromatography by eluting with hexane: ethyl acetate (88:12) mixture to afford the product **6aa** in 75% yield (58 mg) and **3aa** in 18% yields (14 mg).

(F) HRMS Analysis

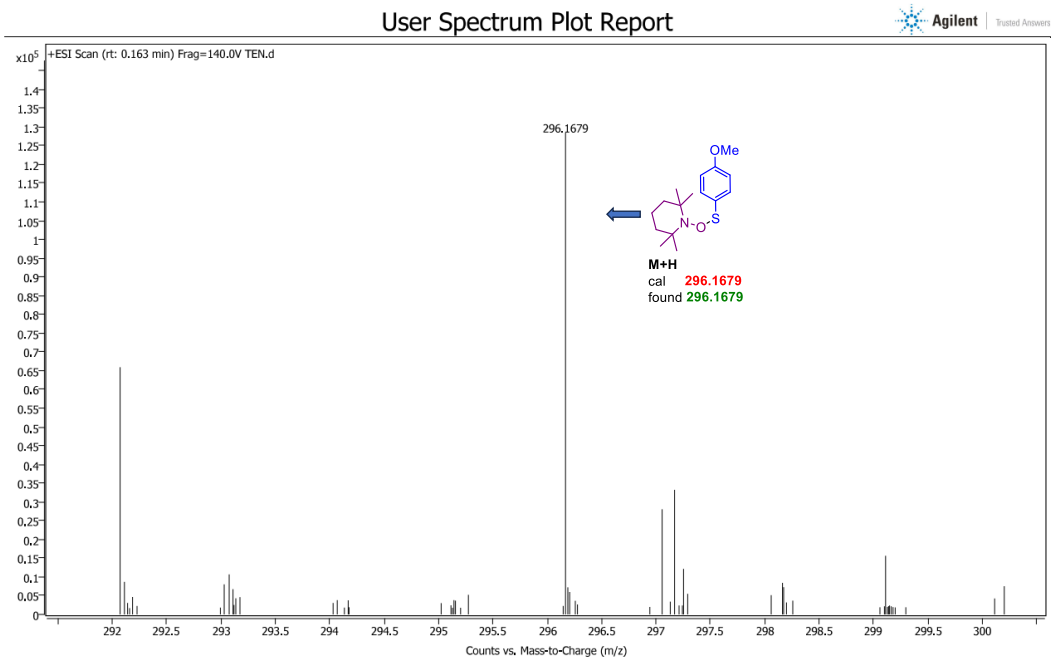


Figure S2: Detection of 4

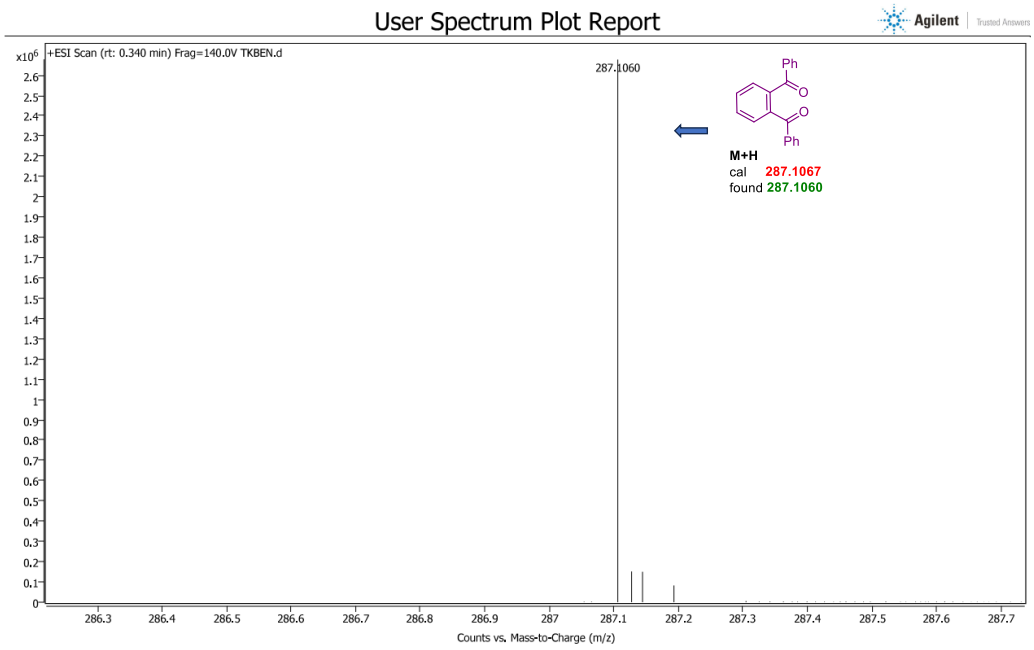


Figure S3: Detection of 5

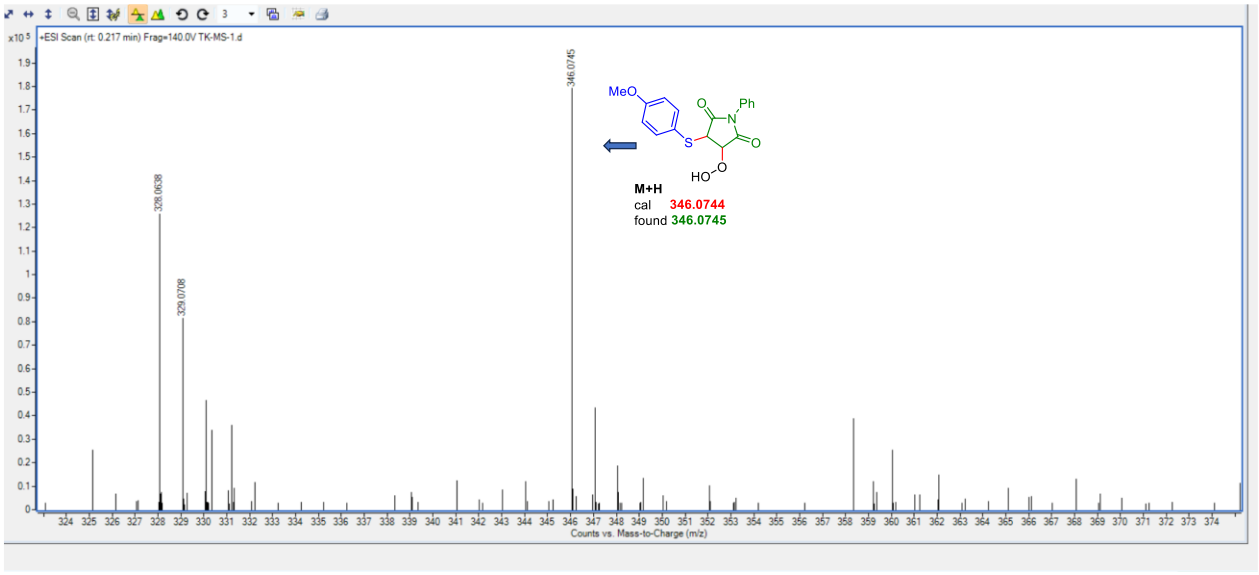


Figure S4: Detection of intermediate IV in crude reaction aliquot.

(G) Detection of H_2O_2 Release During the Reaction.

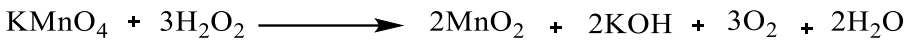
(i) H_2O_2 detection by iodometry

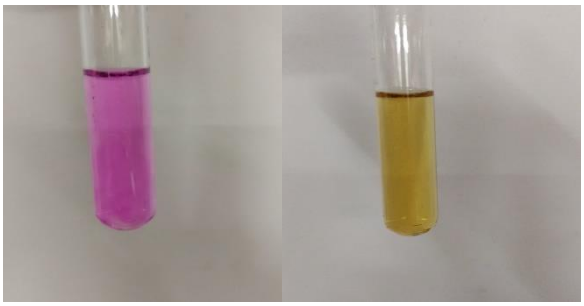
(a) (b) (c)

Figure S5: H_2O_2 detection experiment: (a) Reaction mixture after completion (b) Portion of the freshly prepared KI starch solution in 0.02 M H_2SO_4. (b) Appearance of dark blue colour due to the formation of I_2-starch complex (H_2O_2 detected).

An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), a magnetic stir bar in ethyl acetate (2 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. . In a separate test tube, KI-starch solution was prepared by adding aqueous solution of KI (0.2 mmol in 1.5 mL H_2O), 0.02 M H_2SO_4 (1 ml) and 0.5 mL of freshly prepared starch solution. To a portion of the reaction mixture, the freshly prepared KI-starch solution was added and stirred vigorously. Instantly, the aqueous solution turned to dark blue colour (Fig S5c) indicating the presence of H_2O_2.

(ii) H_2O_2 detection in a typical reaction with $KMnO_4$.



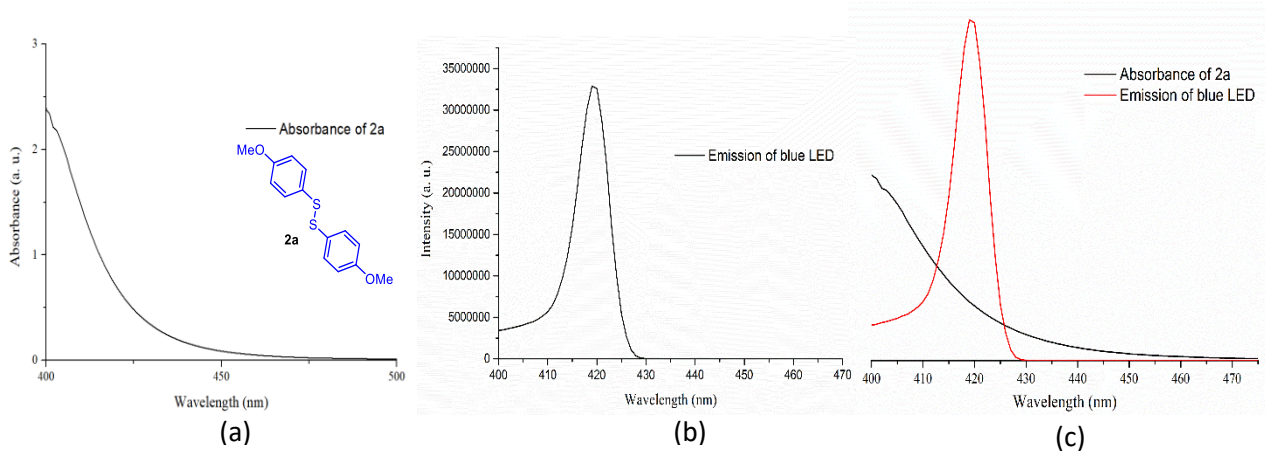


(a) (b)

Figure S6: (a) $KMnO_4$ solution (b) $KMnO_4$ solution after addition of reaction mixture.

An oven-dried 10 mL vial was charged with *N*-phenylmaleimide (**1a)** (0.25 mmol, 43 mg), 1,2-*bis*(4-methoxyphenyl)disulfane (**2a)** (0.125 mmol, 35 mg), a magnetic stir bar in ethyl acetate (2 mL) and was stirred at room temperature in an open-air for 9 h under the irradiation of 4 x 5 W blue LEDs ($\lambda_{em,max}$ = 419 nm) approximately at a distance of ~3−5 cm. . In a separate test tube, $KMnO_4$ solution was prepared by adding $KMnO_4$ (300 µM) in H_2O. A portion of the reaction mixture was added to the $KMnO_4$ solution (Fig S6a). Instantly, the aqueous solution turned to pale yellow colour (Fig S6b) indicating the presence of H_2O_2.

(H) UV- vis and Emission Spectra



FigS7: (a) UV-vis absorbance of 1,2-*bis*(4-methoxyphenyl)disulfane (2a) in Ethyl acetate at a concentration of 0.05 M at room temperature. (b) Emission spectra of blue LED. (c) spectral overlap of UV-vis absorption spectrum of 2a and emission spectra of blue LED.

The absorbance spectra of 1,2-*bis*(4-methoxyphenyl)disulfane (**2a**) has been recorded which show an absorbance in the region 400–440 nm. Also, the emission spectra of blue LED have been recorded, which has a maximum emission at 419 nm. The absorbance spectra of **2a** and the emission spectra of blue LED overlap each other as shown in Fig S7c.

7. Crystallographic Description

Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoK$_\alpha$ radiation (λ = 0.71073 Å) at 298 K for **3aa**. Cell parameters were retrieved using SMART[a] software and refined with SAINT[a] on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS.[b] The structure was solved by direct methods implemented in SHELX-2014[c] program and refined by full-matrix least-squares methods on F2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions.

a. SMART V 4.043 Software for the CCD Detector System; Siemens Analytical Instruments Division: Madison, WI, 2008.

b. SAINT Plus (v 6.14) Bruker AXS Inc., Madison, WI, 2008.

c. Sheldrick, G. M. SHELXL-2014, Program for the Refinement of Crystal Structures; University of Göttingen: Göttingen (Germany), 1997.

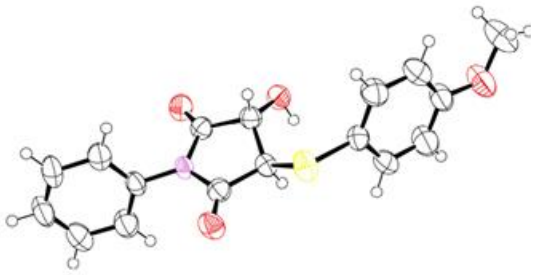


Figure S8. ORTEP diagram of **3aa** with ellipsoid probability 50%.

Table S2. **Crystal Data table for 3aa**

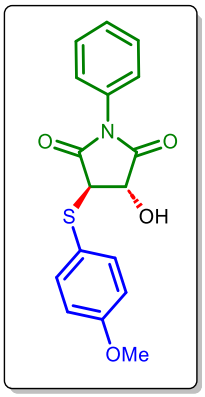
Empirical formula	$C_{17}H_{15}NO_4S$
CCDC number	2278695
Formula weight	329.36
Temperature	298 (2)
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.2038(7) Å, b = 13.8139(17) Å, c = 21.853(3) Å α= 90°, β= 90°, γ= 90°
Volume	1570.9(3) $Å^3$
Z	4
Density (calculated)	1.393 g/cm^{-3}
Absorption coefficient	0.226
F(000)	688
Theta range for data collection	1.744 to 24.991°
Index ranges	-6 < = h < = 6, -16 < = k < = 16, -25< = l < = 25
Reflections collected	37567
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2765/ 0/ 212
Goodness-of-fit on F2	0.895
Final R indices [I>2sigma(I)]	0.0594, wR2 = 0.1401
R indices (all data)	0.1223, wR2 = 0.1804

8. References:

1. R. Mandal, B. Emayavaramban, B. Sundararaju, *Org. Lett*. 2018, **20**, 2835.

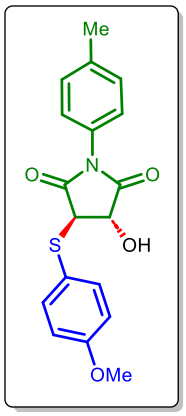
9. Spectral Data

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (3aa)



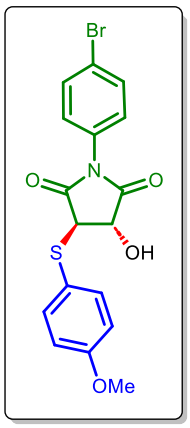
Grey solid (71 mg, 86% yield), m.p. 140–143 °C; purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.5 Hz, 2H), 7.46–7.43 (m, 2H), 7.41–7.38 (m, 1H), 7.14 (d, J = 7.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 4.62 (d, J = 4.0 Hz, 1H), 3.98 (d, J = 5.0 Hz, 1H), 3.81 (s, 3H), 3.30 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.7, 171.6, 161.2, 137.6, 131.3, 129.4, 129.2, 126.3, 120.3, 115.2, 72.9, 55.6, 53.7. IR (neat, cm^{-1}) 3155, 3054, 1599, 1489, 1452, 1328, 1258, 1049, 758, 696. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{16}NO_4S^+$ 330.0795, found 330.0796.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(p-tolyl)pyrrolidine-2,5-dione (3ba)



White solid (72 mg, 84% yield); m.p. 137–140 °C; purified over a column of silica gel (16% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 4.62–4.60 (m, 1H), 3.97 (d, J = 5.0 Hz, 1H), 3.81 (s, 3H), 3.39 (s, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.9, 171.8, 161.2, 139.4, 137.6, 130.0, 128.6, 126.1, 120.3, 115.2, 72.9, 55.6, 53.7, 21.4. IR (neat, cm^{-1}) 3388, 1699, 1591, 1493, 1395, 1245, 1178, 1024, 798, 730. HRMS (ESI) $[M + H]^+$ calcd for $C_{18}H_{18}NO_4S^+$ 344.0951, found 344.0946.

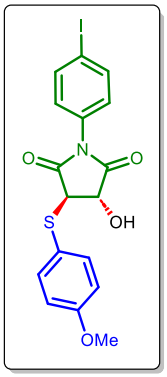
(3S,4R)-1-(4-Bromophenyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ca)



White solid (88 mg, 87% yield); m.p. 180–182 °C; purified over a column of silica gel (16% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.06 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 4.63–4.61 (m, 1H), 3.97 (d, J = 5.0 Hz, 1H), 3.81 (s, 3H), 3.15 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.3, 171.3, 161.3, 137.6, 132.6, 132.5, 130.2, 127.7, 123.1, 121.4, 120.1, 115.3, 73.0, 55.6, 53.6. IR (neat, cm^{-1}) 3389,

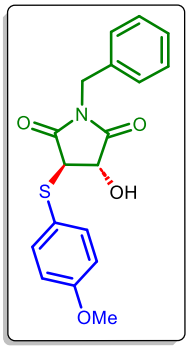
1705, 1592, 1491, 1392, 1244, 1177, 1014, 828, 767. HRMS (ESI) [M + H]$^+$ calcd for $C_{17}H_{15}BrNO_4S^+$ 407.9900, found 407.9900.

(3S,4R)-3-Hydroxy-1-(4-iodophenyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3da)



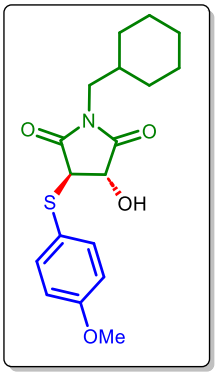
Light yellow solid (101 mg, 89% yield); m.p. 191–196°C; purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.61 (d, J = 5.2 Hz, 1H), 3.97 (d, J = 4.8 Hz, 1H), 3.81 (s, 3H), 3.40 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.2, 171.3, 161.3, 138.5, 137.6, 131.0, 127.9, 120.1, 115.3, 94.7, 73.0, 55.6, 53.6. IR (neat, cm^{-1}) 3442, 1705, 1591, 1489, 1396, 1244, 1177, 1101, 1006, 764. HRMS (ESI) [M + H]$^+$ calcd for $C_{17}H_{15}INO_4S^+$ 455.9761, found 455.9762.

(3S,4R)-1-Benzyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ea)



Brown solid (69 mg, 80% yield); m.p. 126–130 °C; purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.5 Hz, 2H), 7.27–7.26 (m, 3H), 7.20–7.18 (m, 2H), 6.73 (d, J = 9.0 Hz, 2H), 4.59 (q, J = 14.7 Hz, 2H), 4.44 (d, J = 5.0 Hz, 1H), 3.81 (d, J = 5.0 Hz, 1H), 3.77 (s, 3H), 3.46 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 175.4, 172.2, 160.9, 137.4, 135.0, 128.8, 128.7, 128.2, 120.2, 115.1, 72.7, 55.5, 53.6, 42.9. IR (neat, cm^{-1}) 3352, 1696, 1589, 1499, 1399, 1242, 1171,1082, 1023, 817. HRMS (ESI) [M + H]$^+$ calcd for $C_{18}H_{18}NO_4S^+$ 344.0951, found 344.0951.

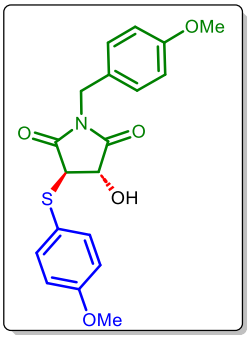
(3S,4R)-1-(Cyclohexylmethyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3fa)



Yellow liquid (68 mg, 78% yield); purified over a column of silica gel (15% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.48–4.46 (m, 1H), 3.80 (d, J = 5.5 Hz, 1H), 3.79 (s, 3H), 3.29 (dd, J = 7.3, 2.3 Hz, 2H), 3.13 (d, J = 3.0 Hz, 1H), 1.62–1.52 (m, 4H), 1.41 (d, J = 12.9 Hz, 1H), 1.31 (d, J = 11.5Hz, 1H), 1.15–1.06 (m, 3H), 0.87 – 0.79 (m, 2H); ^{13}C{^{1}H}

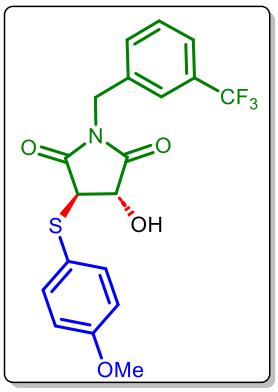
NMR (126 MHz, $CDCl_3$) δ 175.9, 172.4, 161.1, 137.7, 120.2, 115.1, 72.6, 55.5, 53.7, 45.4, 36.0, 30.6, 30.5, 26.2, 25.7, 25.6. IR (neat, cm^{-1}) 3056, 1586, 1483, 1320, 1167, 1011, 975, 692, 677. HRMS (ESI) $[M + H]^+$ calcd for $C_{18}H_{24}NO_4S^+$ 350.1421 , found 350.1422.

(3S,4R)-3-Hydroxy-1-(4-methoxybenzyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ga)



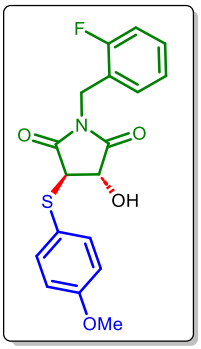
White solid (76 mg, 82% yield); m.p. 112–116 °C; purified over a column of silica gel (20% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 8.5 Hz, 2H), 7.16 (d, J = 9.0 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 6.73 (d, J = 8.5 Hz, 2H), 4.53 (q, J = 14.0 Hz, 2H), 4.41 (d, J = 4.0 Hz, 1H), 3.79 (d, J = 4.0 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.37 (s, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 175.4, 172.2, 160.9, 159.5, 137.3, 130.3, 127.3, 120.3, 115.1, 114.1, 72.8, 55.42, 55.38, 53.6, 42.4. IR (neat, cm^{-1}) 3376, 1708, 1593, 1511, 1395, 1293, 1249, 1175, 1027, 828. HRMS (ESI) $[M + H]^+$ calcd for $C_{19}H_{20}NO_5S^+$ 374.1057, found. 374.1054.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(3-(trifluoromethyl)benzyl)pyrrolidine-2,5-



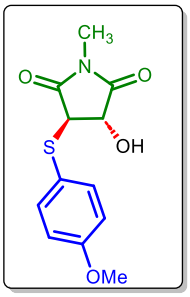
Brown solid (87 mg, 85% yield); m.p. 147–148 °C; purified over a column of silica gel (19% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 5.5 Hz, 2H), 7.42–7.39 (m, 4H), 6.74 (d, J = 9.0 Hz, 2H), 4.65 (q, J = 13.5 Hz, 2H), 4.47–4.45 (m, 1H), 3.83 (d, J = 5.0 Hz, 1H), 3.77 (s, 3H), 3.22 (s, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 175.0, 172.1, 161.1, 137.4, 135.9, 132.2, 131.3 (d, J = 32.4 Hz), 129.4, 125.7 (q, J = 21.3 Hz), 125.2 (q, J =3.6 Hz), 122.9, 120.0, 115.1, 72.7, 55.4, 53.6, 42.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6. IR (neat, cm^{-1}) 3066, 1588, 1489, 1333, 1166, 1011, 865, 677. HRMS (ESI) $[M + H]^+$ calcd for $C_{19}H_{17}F_3NO_4S^+$ 412.0825, found 412.0829.

(3S,4R)-1-(2-Fluorobenzyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ia)



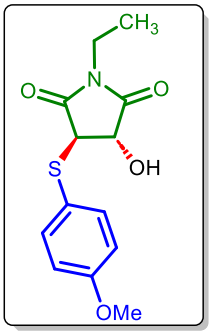
Brown liquid (75 mg, 83% yield); purified over a column of silica gel (18% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 9.0 Hz, 2H), 7.25–7.23 (m, 1H), 7.02–7.01 (m, 2H), 6.77 (d, J = 9.0 Hz, 2H), 6.70 (d, J = 1.0 Hz, 1H), 4.68 (q, J = 12.7 Hz, 2H), 4.48 (d, J = 5.0 Hz, 1H), 3.84 (d, J = 5.0 Hz, 1H), 3.79 (s, 3H), 3.39 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 175.1, 171.9, 161.0, 137.5, 135.3, 130.1 (d, J = 3.5 Hz), 130.0 (d, J = 8.2 Hz), , 124.3 (d, J = 3.7 Hz), 121.7 (d, J = 14.5 Hz), 120.2, 115.7 (d, J = 21.3 Hz), 115.1, 72.6, 55.5, 53.7, 36.7 (d, J = 4.7 Hz,). ^{19}F NMR (471 MHz, $CDCl_3$) δ -116.9. IR (neat, cm^{-1}) 3414, 1710, 1590, 1492, 1344, 1244, 1170, 1098, 830, 752. HRMS (ESI) $[M + H]^+$ calcd for $C_{18}H_{17}FNO_4S^+$ 362.0857, found 362.0856.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-methylpyrrolidine-2,5-dione (3ja)



Brown solid (57 mg, 86% yield); m.p. 93–95 °C; purified over a column of silica gel (15% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 4.47 (d, J = 4.8 Hz, 1H), 3.84 (d, J = 4.8 Hz, 1H), 3.80 (s, 3H), 3.44 (s, 1H), 2.95 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 175.8, 172.7, 161.0, 137.2, 120.5, 115.1, 72.9, 55.5, 53.8, 25.4. IR (neat, cm^{-1}) 3327, 1683, 1590, 1492, 1444, 1285, 1240, 1092, 1029, 776, 629. HRMS (ESI) $[M + H]^+$ calcd for $C_{12}H_{14}NO_4S^+$ 268.0638, found 268.0634.

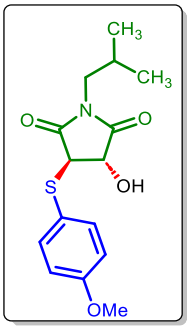
(3S,4R)-1-Ethyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ka)



Brown liquid (55 mg, 79% yield); purified over a column of silica gel (16% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.45 (d, J = 5.0 Hz, 1H), 3.81 (d, J = 5.0 Hz, 1H), 3.80 (s, 3H), 3.51 (q, J = 7.2 Hz, 2H), 3.45 (s, 1H), 1.07 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 13C NMR (126 MHz, CDCl3) δ 175.6, 172.4, 161.0, 137.3, 120.5,

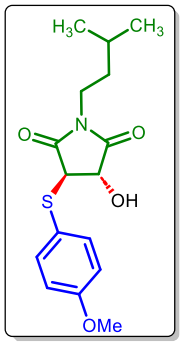
115.1, 72.9, 55.5, 53.6, 34.4, 12.9. IR (neat, cm^{-1}) 3066, 2967, 1606, 1589, 1473, 1278, 1015, 956, 745, 694. HRMS (ESI) $[M + H]^+$ calcd for $C_{13}H_{16}NO_4S^+$ 282.0795, found 282.0790.

(3S,4R)-3-Hydroxy-1-isobutyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3la)



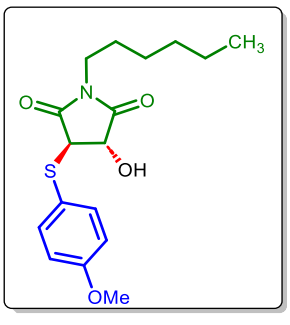
Brown solid (59 mg, 76% yield); m.p. 143–145 °C; purified over a column of silica gel (17% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 4.46 (d, J = 5.0 Hz, 1H), 3.82 (d, J = 5.0 Hz, 1H), 3.79 (s, 3H), 3.28 (s, 1H), 3.27–3.26 (m, 2H), 1.94–1.89 (m, 1H), 0.79 (d, J = 6.5 Hz, 3H), 0.73 (d, J = 6.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 176.0, 172.5, 161.1, 137.6, 120.4, 115.1, 72.6, 55.5, 53.7, 46.6, 27.1, 20.0, 19.9. IR (neat, cm^{-1}) 3120, 1567, 1484, 1446, 1335, 1226, 1098, 975, 742, 699. HRMS (ESI) $[M + H]^+$ calcd for $C_{15}H_{20}NO_4S^+$ 310.1108, found 310.1107.

(3S,4R)-3-Hydroxy-1-isopentyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ma)



Brown solid (60 mg, 74% yield); m.p. 165–169 °C; purified over a column of silica gel (16% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.46 (d, J = 4.5 Hz, 1H), 3.80 (d, J = 4.5 Hz, 1H), 3.79 (s, 3H), 3.53 (s, 1H), 3.46 (t, J = 7.5 Hz, 2H), 1.41–1.35 (m, 1H), 1.34–1.28 (m, 2H), 0.88 (d, J = 3.5 Hz, 3H), 0.87 (d, J = 3.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 175.7, 172.4, 161.0, 137.5, 120.5, 115.1, 72.9, 55.5, 53.7, 37.9, 36.3, 25.9, 22.35, 22.34. IR (neat, cm^{-1}) 3137, 1581, 1478, 1388, 1336, 1101, 976, 896, 711, 698. HRMS (ESI) $[M + H]^+$ calcd for $C_{16}H_{22}NO_4S^+$ 324.1264, found. 324.1268.

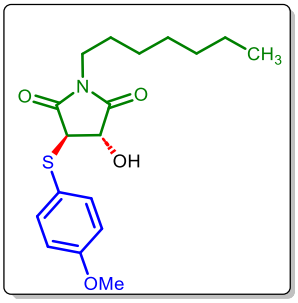
(3S,4R)-1-Hexyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3na)



Brown liquid (63 mg, 75% yield); purified over a column of silica gel (15% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.46–4.44 (m, 1H),

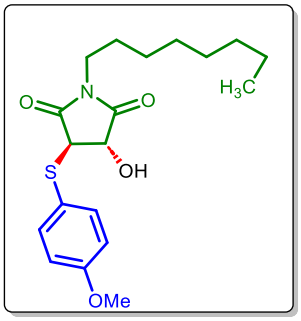
3.81–3.80 (m, 1H), 3.79 (s, 3H), 3.44 (t, *J* = 7.3 Hz, 2H), 3.19 (s, 1H), 1.47–1.40 (m, 2H), 1.27–1.20 (m, 4H), 1.17–1.12 (m, 2H), 0.87 (t, *J* = 6.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.7, 172.4, 161.1, 137.5, 120.4, 115.1, 72.8, 55.5, 53.7, 39.5, 31.4, 27.6, 26.4, 22.6, 14.1. IR (neat, cm^{-1}) 3419, 1701, 1589, 1492, 1398, 1289, 1174, 1026, 829, 632. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{24}NO_4S^+$ 338.1421, found 338.1418.

(3S,4R)-1-Heptyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3oa)



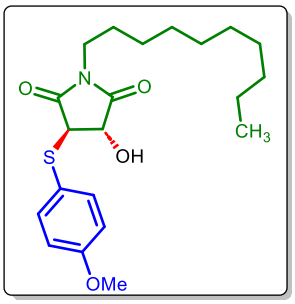
Brown liquid (75 mg, 85% yield); purified over a column of silica gel (18% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.45 (d, *J* = 2.5 Hz, 1H), 3.80 (d, *J* = 2.5 Hz, 1H), 3.79 (s, 3H), 3.44 (t, *J* = 7.5 Hz, 2H), 3.25 (s, 1H), 1.48–1.41 (m, 2H), 1.31–1.21 (m, 6H), 1.16–1.10 (m, 2H), 0.87 (t, *J* = 7.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.7, 172.4, 161.0, 137.5, 120.4, 115.1, 72.8, 55.5, 53.7, 39.5, 31.8, 28.9, 27.6, 26.7, 22.7, 14.2. IR (neat, cm^{-1}) 3157, 1581, 1485, 1454, 1236, 1087, 1044, 934, 747, 697. HRMS (ESI) $[M + H]^+$ calcd for $C_{18}H_{26}NO_4S^+$ 352.1577, found 352.1571.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-octylpyrrolidine-2,5-dione (3pa)



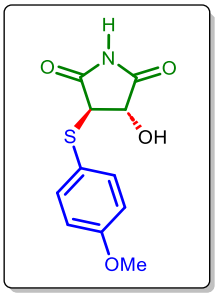
Brown liquid (81 mg, 89% yield); purified over a column of silica gel (18% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.45 (d, *J* = 3.0 Hz, 1H), 3.80 (d, *J* = 3.0 Hz, 1H), 3.79 (s, 3H), 3.44 (t, *J* = 7.3 Hz, 2H), 3.31 (s, 1H), 1.47–1.40 (m, 2H), 1.30–1.21 (m, 8H), 1.16–1.10 (m, 2H), 0.88 (t, *J* = 7.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.8, 172.5, 161.0, 137.4, 120.4, 115.1, 72.8, 55.5, 53.7, 39.5, 31.9, 29.22, 29.17, 27.6, 26.8, 22.7, 14.2. IR (neat, cm^{-1}) 3419, 1702, 1591, 1492, 1398, 1246, 1172, 1030, 830, 632. HRMS (ESI) $[M + H]^+$ calcd for $C_{19}H_{28}NO_4S^+$ 366.1734, found 366.1734.

(3S,4R)-1-Decyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3qa)



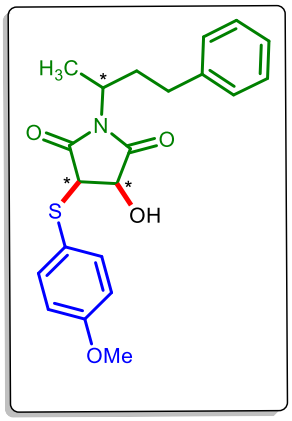
Brown liquid (76 mg, 77% yield); purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.45 (d, J = 4.4 Hz, 1H), 3.80 (d, J = 3.0 Hz, 1H), 3.78 (s, 3H), 3.44 (t, J = 7.4 Hz, 2H), 3.20 (s, 1H), 1.46–1.42 (m, 2H), 1.29–1.20 (m, 12H), 1.17–1.12 (m, 2H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 175.7, 172.4, 161.0, 137.4, 120.4, 115.1, 72.8, 55.5, 53.7, 39.5, 32.0, 29.7, 29.6, 29.4, 29.2, 27.6, 26.8, 22.8, 14.3. IR (neat, cm^{-1}) 3421, 1702, 1591, 1492, 1399, 1246, 1173, 1030, 829, 632. HRMS (ESI) $[M + H]^+$ calcd for $C_{21}H_{32}NO_4S^+$ 394.2047, found 394.2049.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ra)



Brown liquid (54 mg, 85% yield); purified over a column of silica gel (20% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.52 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 4.48 (d, J = 6.0 Hz, 1H), 3.89 (d, J = 5.5 Hz, 1H), 3.81 (s, 3H), 3.30 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 13C NMR (126 MHz, CDCl3) δ 175.1, 171.8, 161.1, 137.4, 135.3, 115.3, 73.5, 55.5, 54.9. IR (neat, cm^{-1}) 3241, 2933, 1608, 1488, 1429, 1291, 1181, 1012, 930, 759. HRMS (ESI) $[M + H]^+$ calcd for $C_{11}H_{12}NO_4S^+$ 254.0482, found 254.0483.

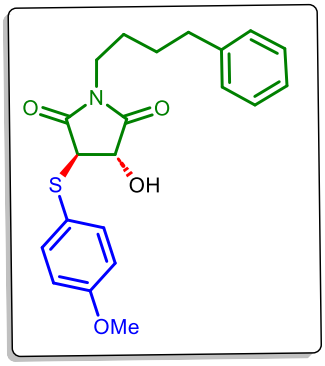
3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutan-2-yl)pyrrolidine-2,5-dione (3sa)



Light yellow solid (75 mg, 78% yield); dr 1:0.87; m.p. 100-104 °C; purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 4H), 7.25–7.23 (m, 4H), 7.19–7.14 (m, 2H), 7.07 (t, J = 8.0 Hz, 4H), 6.81 (d, J = 8.5 Hz, 4H), 4.31–4.27 (m, 2H), 4.22–4.15 (m, 2H), 3.71 (s, 3H), 3.67 (s, 3H), 3.63 (d, J = 5.5 Hz, 1H), 3.57 (d, J = 5.5 Hz, 1H), 3.26–3.23 (m, 2H),

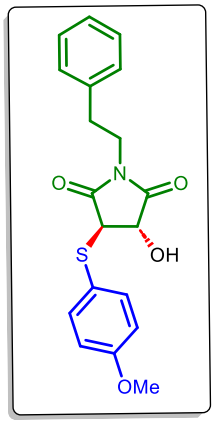
2.48–2.43 (m, 2H), 2.38 – 2.14 (m, 4H), 1.91–1.83 (m, 2H), 1.30 (d, J = 7.0 Hz, 3H), 1.27 (d, J = 7.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.87, 175.86, 172.4, 160.99, 160.97, 141.0, 140.9, 137.5, 137.4, 128.6, 128.5, 128.4, 126.22, 126.19, 120.6, 120.5, 115.07, 115.06, 72.31, 72.27, 55.44, 55.36, 53.64, 53.62, 49.2, 49.0, 33.9, 33.8, 33.2, 33.0, 18.2, 18.0. IR (neat, cm^{-1}) 3385, 1689, 1590, 1491, 1367, 1246, 1166, 1028, 826, 699. HRMS (ESI) $[M + H]^+$ calcd for $C_{21}H_{24}NO_4S^+$ 386.1421, found 386.1425.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutyl)pyrrolidine-2,5-dione (3ta)



Brown liquid (83 mg, 86% yield); purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 9.0 Hz, 2H), 7.27 (t, J = 6.8 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 7.5 Hz, 2H), 6.79 (d, J = 9.0 Hz, 2H), 4.44 (d, J = 5.5 Hz, 1H), 3.80 (d, J = 5.5 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 1H), 3.46 (t, J = 6.5 Hz, 2H), 2.56 (t, J = 7.0 Hz, 2H), 1.50–1.49 (m, 4H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.9, 172.5, 161.0, 141.8, 137.4, 128.5, 126.0, 120.3, 115.1, 72.6, 55.5, 53.7, 39.1, 35.2, 28.4, 27.1. IR (neat, cm^{-1}) 3420, 1700, 1591, 1492, 1396, 1245, 1146, 1029, 829, 740. HRMS (ESI) $[M + H]^+$ calcd for $C_{21}H_{24}NO_4S$ 386.1421 , found 386.1427.

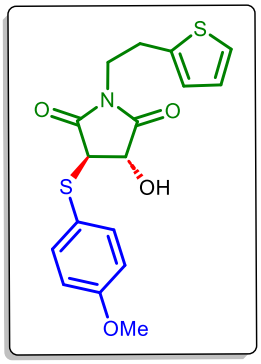
(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenethylpyrrolidine-2,5-dione (3ua)



Brown solid (80 mg, 89% yield); m.p. 153–155 °C; purified over a column of silica gel (17% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 9.0 Hz, 2H), 7.25–7.20 (m, 3H), 7.08 (d, J = 6.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 4.37 (d, J = 3.0 Hz, 1H), 3.79 (s, 3H), 3.76 (d, J = 5.5 Hz, 1H), 3.69 (t, J = 7.6 Hz, 2H), 3.33 (s, 1H), 2.83–2.73 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 175.5, 172.2, 161.1, 137.44, 137.37, 128.9, 128.7, 127.0, 120.5, 115.1, 72.6, 55.5, 53.7, 40.5, 33.5. IR (neat, cm^{-1}) 3078, 1681, 1508, 1336, 1287,

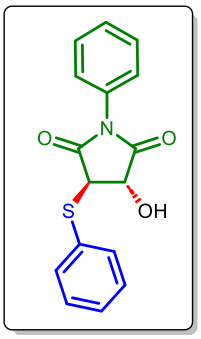
1156, 1114, 984, 835, 756, 685. HRMS (ESI) $[M + H]^+$ calcd for $C_{19}H_{20}NO_4S^+$ 358.1108, found 358.1107.

(3S,4R)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(2-(thiophen-2-yl)ethyl)pyrrolidine-2,5-dione



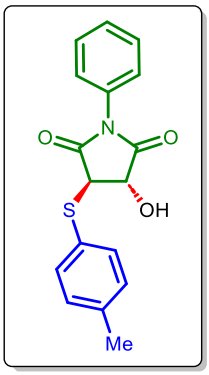
Brown solid (73 mg, 81% yield); m.p. 120–124 °C; purified over a column of silica gel (18% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.8 Hz, 2H), 7.13 (dd, J = 4.8, 1.2 Hz, 1H), 6.90–6.87 (m, 1H), 6.86 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 2.8 Hz, 1H), 4.41 (d, J = 4.0 Hz, 1H), 3.80 (s, 3H), 3.78 (d, J = 4.0 Hz, 1H), 3.72 (t, J = 7.2 Hz, 2H), 3.11 (s, 1H), 3.05–3.00 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 175.3, 172.1, 161.1, 139.3, 137.4, 127.2, 126.0, 124.5, 120.5, 115.2, 72.7, 55.5, 53.8, 40.6, 27.5. IR (neat, cm^{-1}) 3317, 2965, 1600, 1511, 1478, 1370, 1264, 964, 746, 681. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{18}NO_4S_2^+$ 364.0672, found 364.0675.

(3S,4R)-3-Hydroxy-1-phenyl-4-(phenylthio)pyrrolidine-2,5-dione (3ab)



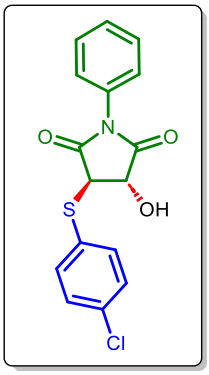
White solid (42 mg, 56% yield); m.p. 148–151 °C; purified over a column of silica gel (15% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64–7.62 (m, 3H), 7.46 (t, J = 7.5 Hz, 2H), 7.40–7.37 (m, 4H), 7.19–7.17 (m, 1H), 4.66–4.65 (m, 1H), 4.13 (d, J = 5.5 Hz, 1H), 3.30 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.6, 171.5, 134.6, 129.7, 129.5, 129.42, 129.41, 129.2, 126.3, 125.6, 119.9, 73.4, 53.3. IR (neat, cm^{-1}) 3172, 1476, 1461, 1239, 1166, 1037, 968, 637. HRMS (ESI) $[M + H]^+$ calcd for $C_{16}H_{14}NO_3S^+$ 300.0689, found 300.0710.

(3S,4R)-3-Hydroxy-1-phenyl-4-(p-tolylthio)pyrrolidine-2,5-dione (3ac)



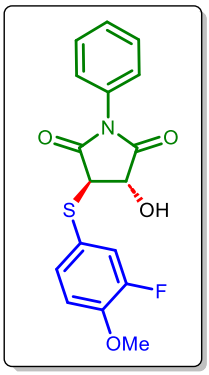
White solid (56 mg, 71% yield); m.p. 141–148 °C; purified over a column of silica gel (16% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.41 (d, J = 7.5 Hz, 1H), 7.18–7.15 (m, 4H), 4.63 (d, J = 5.0 Hz, 1H), 4.05 (d, J = 5.5 Hz, 1H), 3.36 (s, 1H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.7, 171.6, 140.1, 135.2, 131.3, 130.5, 129.4, 129.2, 126.7, 126.3, 73.1, 53.4, 21.4. IR (neat, cm^{-1}) 3372, 1676, 1351, 1320, 1208, 1026, 928, 738, 655. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{16}NO_3S^+$ 314.0845, found 314.0851.

(3R,4S)-3-((4-Chlorophenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ad)



White solid (58 mg, 70% yield); m.p. 156–159 °C; purified over a column of silica gel (19% ethyl acetate in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 2H), 7.47– .46 (m, 2H), 7.44–7.41 (m, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.2 Hz, 2H), 4.63 (d, J = 5.6 Hz, 1H), 4.12 (d, J = 5.6 Hz, 1H), 3.43 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.4, 171.3, 135.9, 135.7, 131.1, 129.8, 129.5, 129.4, 129.3, 126.2, 73.3, 53.5. IR (neat, cm^{-1}) 3072, 1676, 1651, 1369, 1158, 1028, 938, 688, 599. HRMS (ESI) $[M + H]^+$ calcd for $C_{16}H_{13}ClNO_3S^+$ 334.0305, found 334.0303.

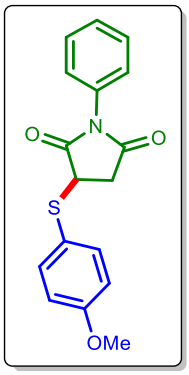
(3R,4S)-3-((3-Fluoro-4-methoxyphenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ae)



White solid (67 mg, 77% yield); m.p. 149–154 °C; purified over a column of silica gel (23% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (t, J = 7.5 Hz, 2H), 7.42–7.38 (m, 3H), 7.20 (d, J = 7.5 Hz, 2H), 6.94 (t, J = 9.0 Hz, 1H), 4.61 (d, J = 5.0 Hz, 1H), 4.03 (d, J = 5.0 Hz, 1H), 3.90 (s, 3H), 3.37 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.5, 171.4, 149.5 (d, J = 10.3 Hz), 132.2 (d, J = 3.7 Hz), 131.2, 129.5, 129.31, 129.27, 126.2, 123.1 (d, J = 18.5 Hz), 121.3 (d, J = 6.7 Hz), 113.9 (d, J = 2.3 Hz), 72.9, 56.4, 53.8. ^{19}F NMR (471

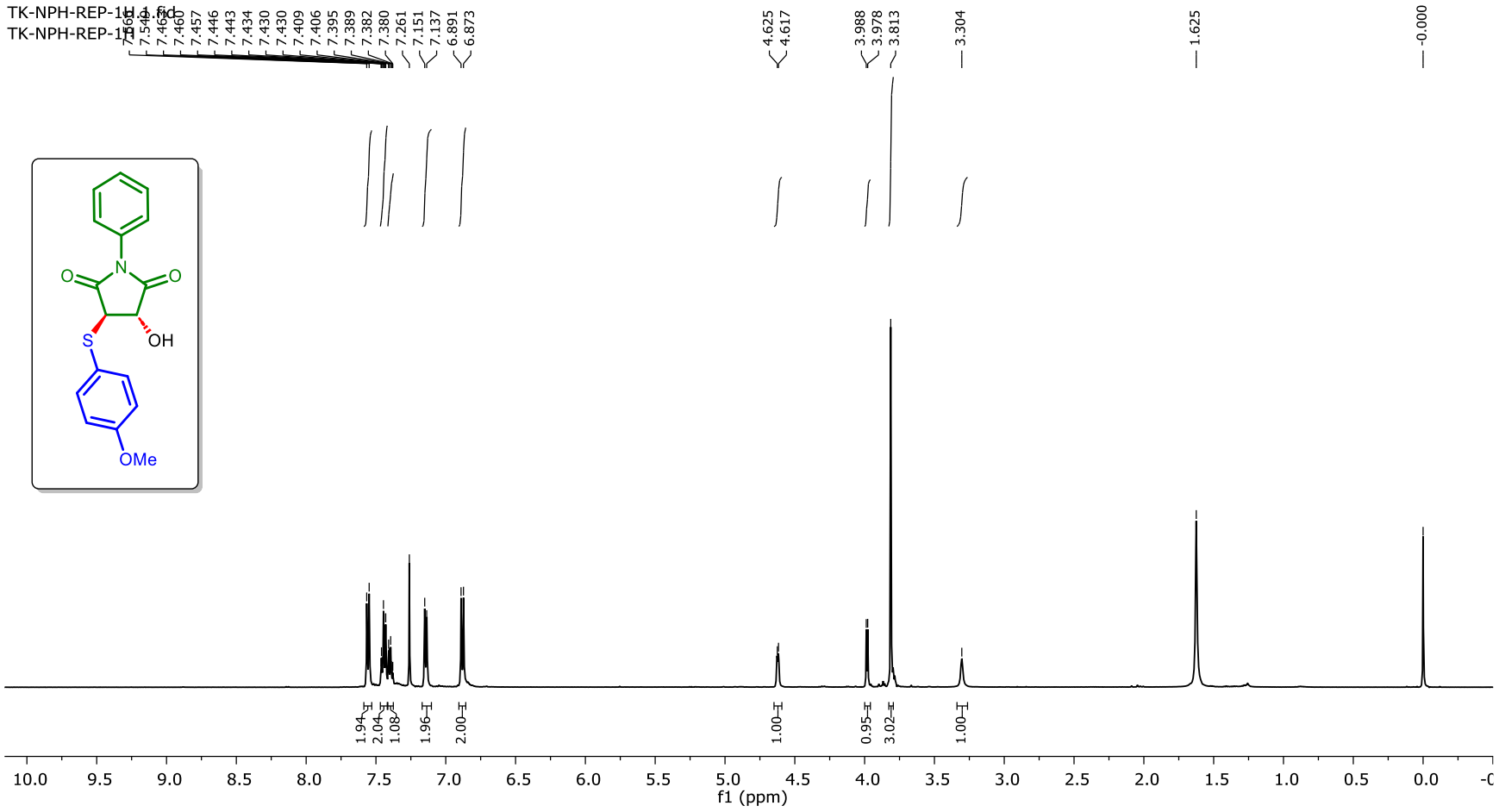
MHz, $CDCl_3$) δ -132.4. IR (neat, cm^{-1}) 3172, 1523, 1445, 1329, 1165, 1127, 858, 738, 635. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{15}FNO_4S^+$ 348.0700, found 348.0696.

3-((4-Methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (6aa)

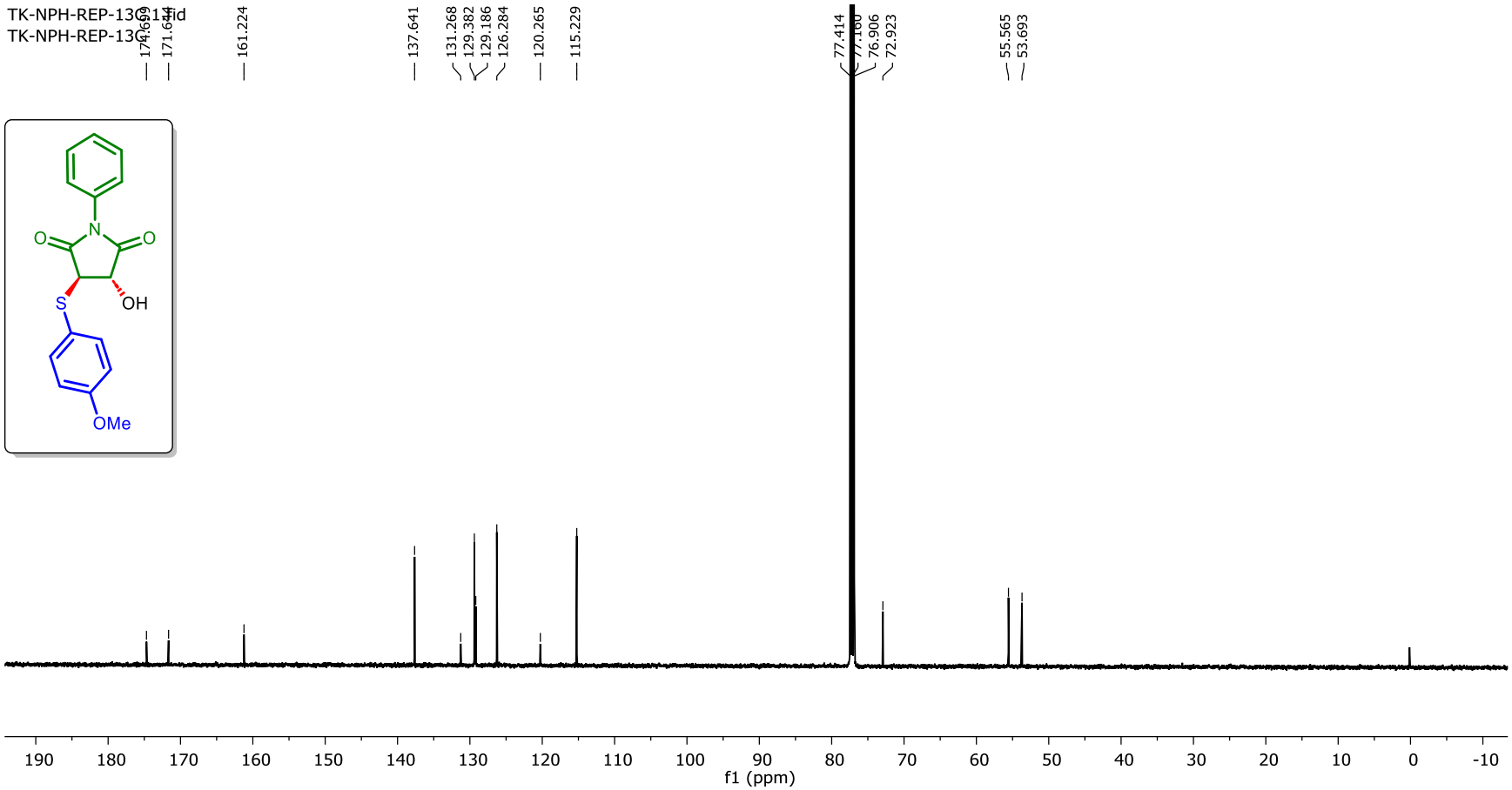


Brown liquid (58 mg, 75% yield; purified over a column of silica gel (11% ethyl acetate in hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.5 Hz, 2H), 7.44–7.41 (m, 2H), 7.37 (d, J = 7.5 Hz, 1H), 7.04 (d, J = 7.5 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 4.03 (dd, J = 9.5, 3.5 Hz, 1H), 3.81 (s, 3H), 3.31 (q, J = 9 Hz, 1H), 2.90 (dd, J = 19.0, 3.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 174.8, 173.8, 161.4, 137.9, 131.7, 129.3, 128.9, 126.5, 119.7, 115.2, 55.6, 44.7, 36.4. IR (neat, cm^{-1}) 3163, 1514, 1455, 1314, 1115, 1107, 755, 631, 601. HRMS (ESI) $[M + H]^+$ calcd for $C_{17}H_{16}NO_3S^+$ 314.0845, found 314.0844.

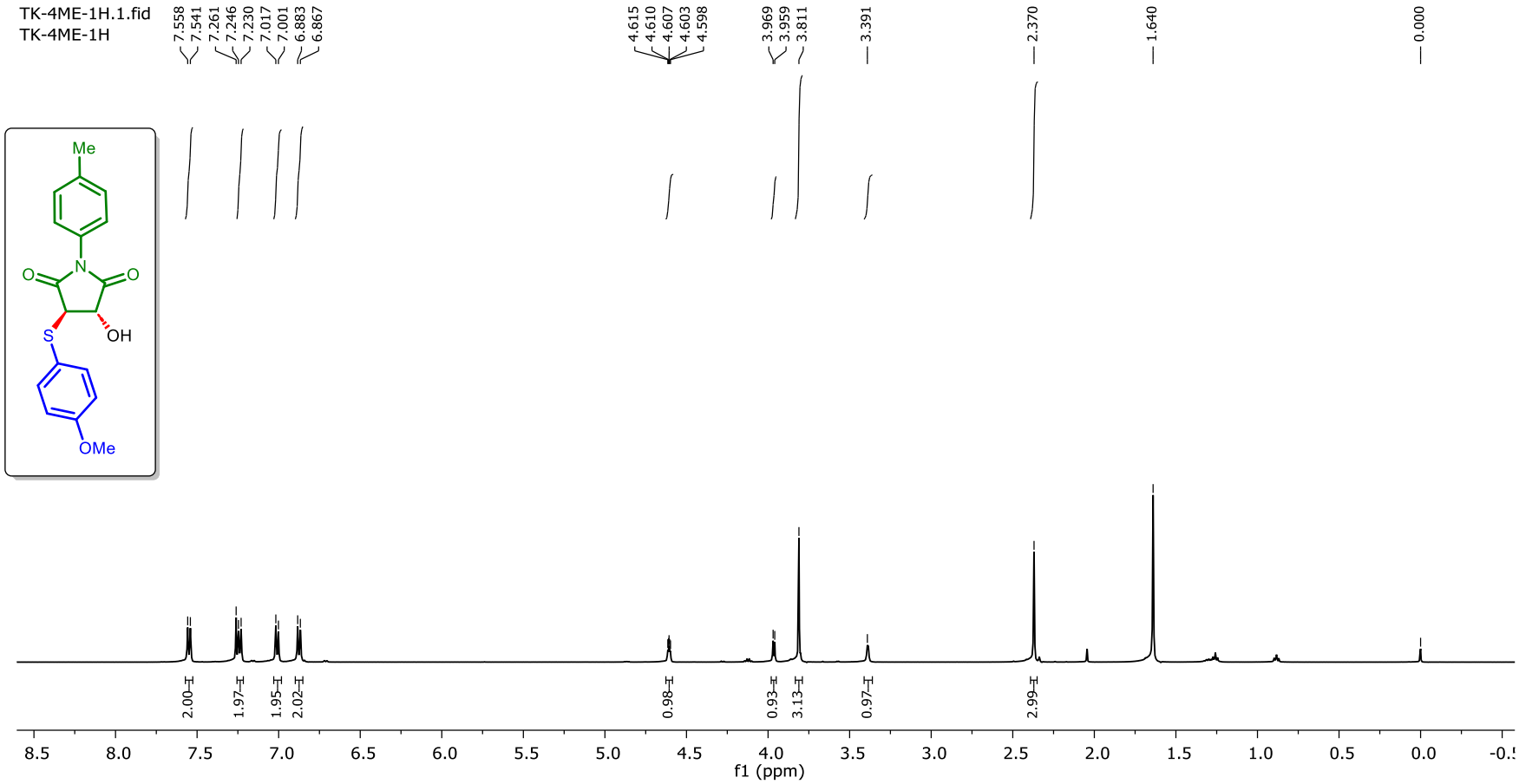
10. NMR Spectra



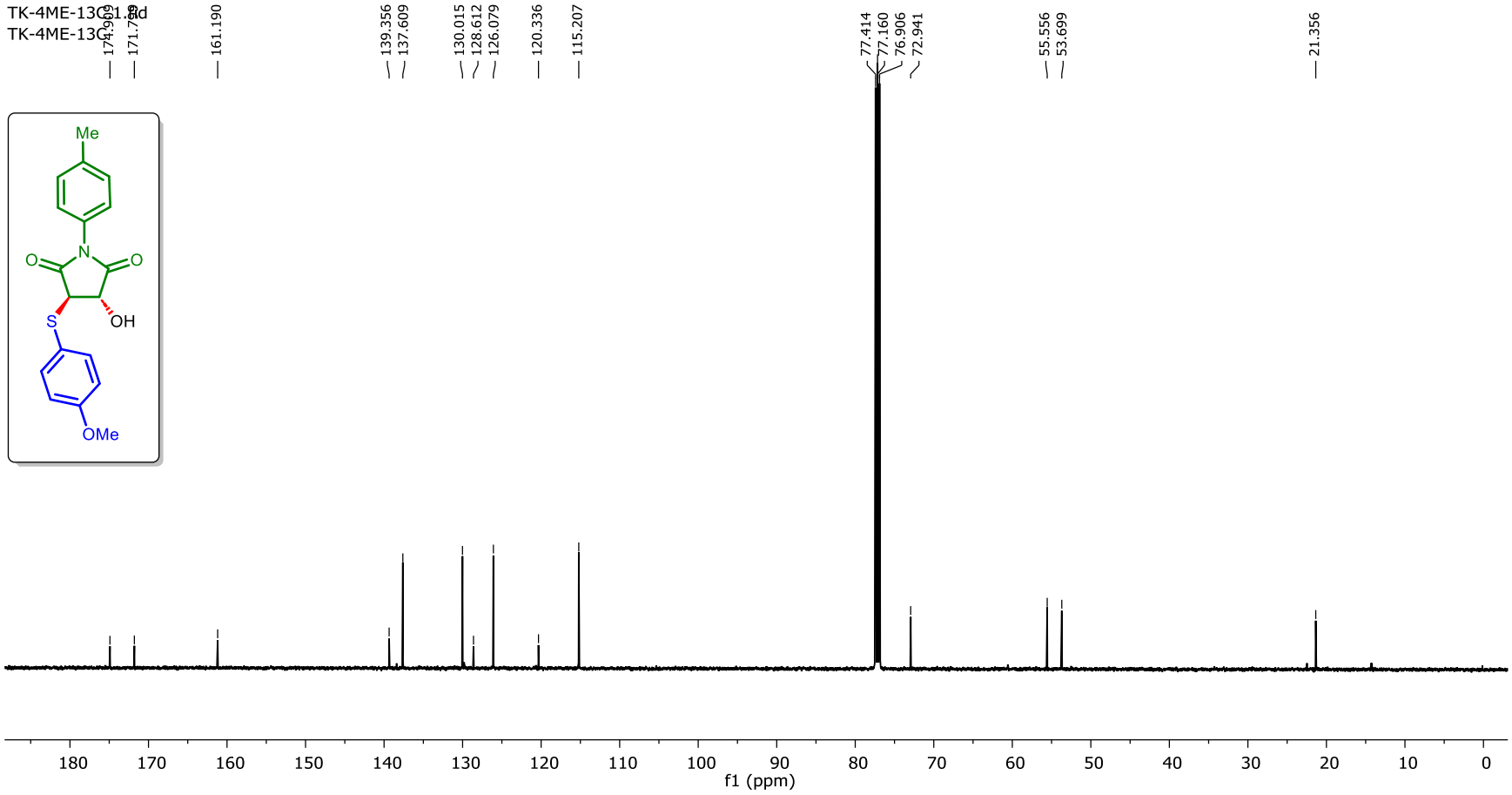
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (3aa): ^{1}H NMR ($CDCl_3$, 500 MHz)



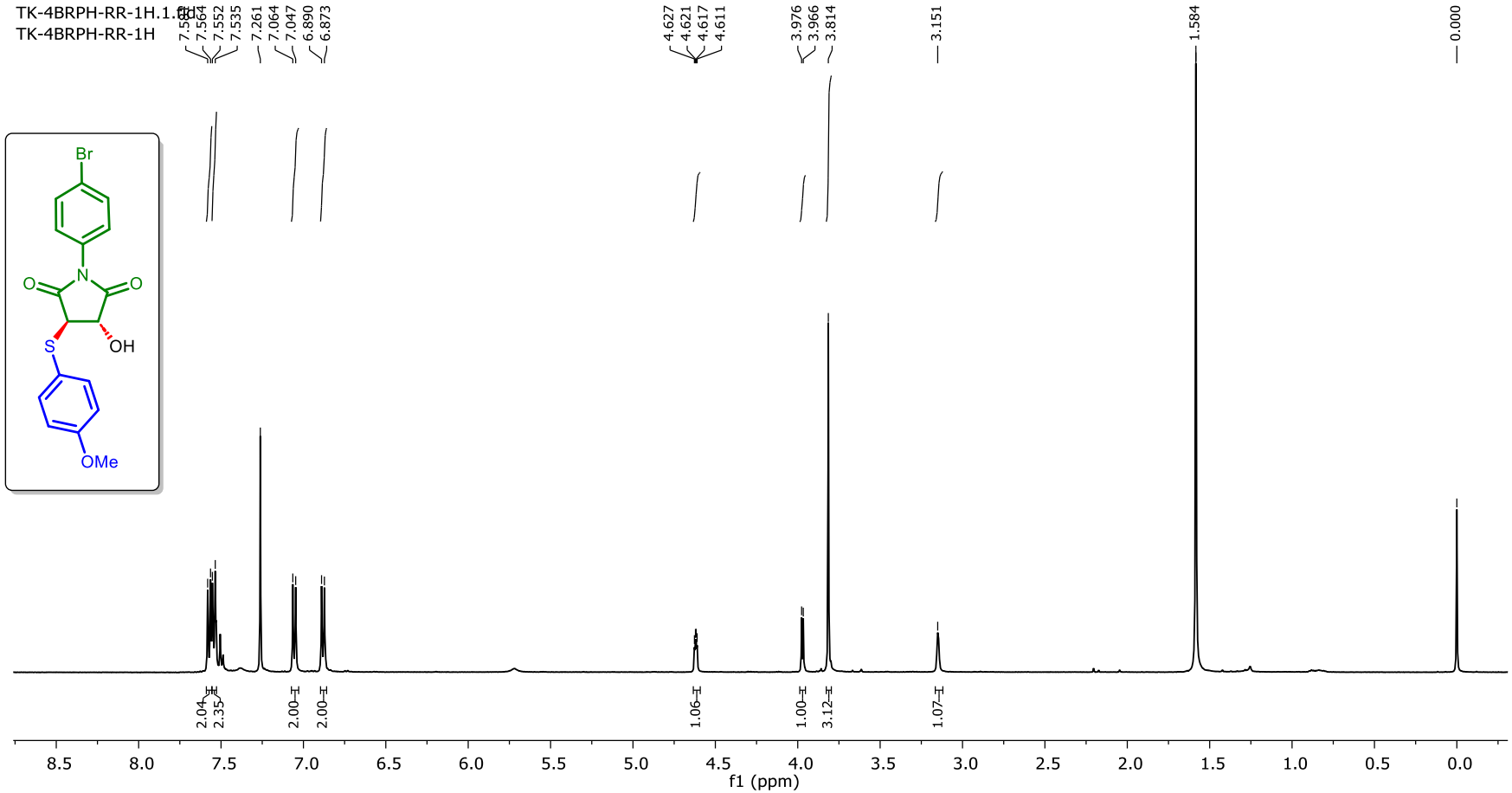
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (3aa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



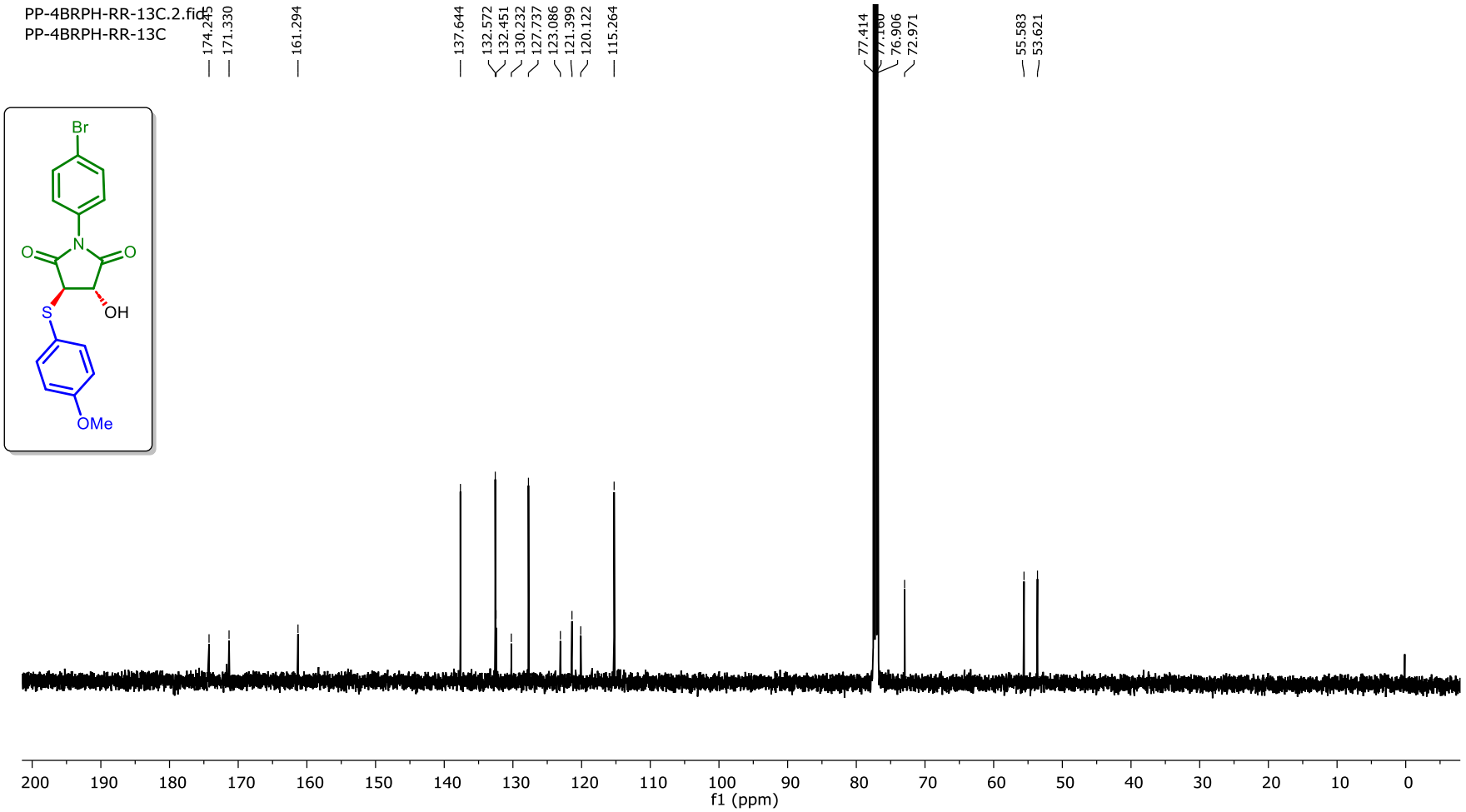
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(*p*-tolyl)pyrrolidine-2,5-dione (3ba): ^{1}H NMR ($CDCl_3$, 500 MHz)



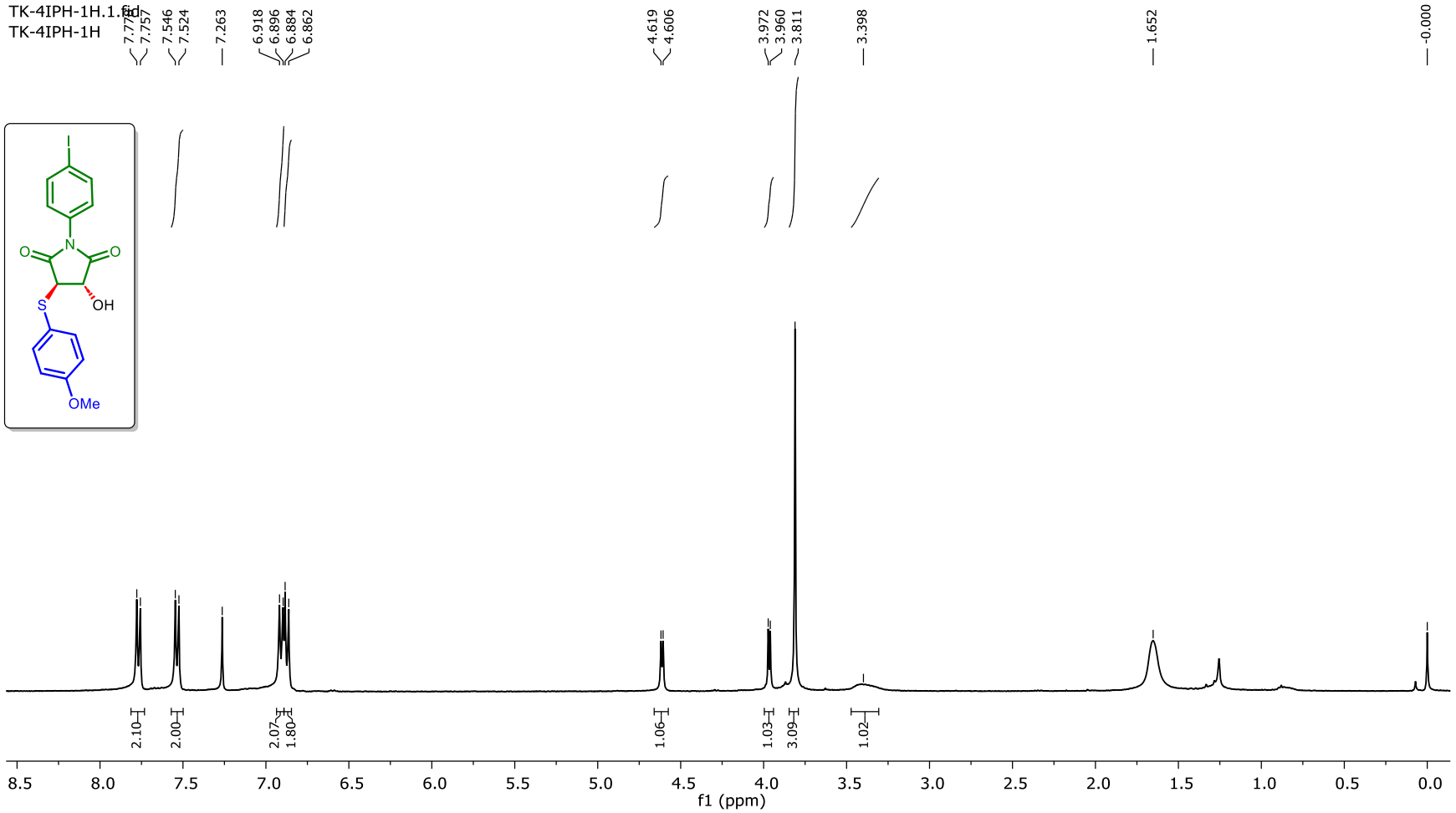
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(*p*-tolyl)pyrrolidine-2,5-dione (3ba): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



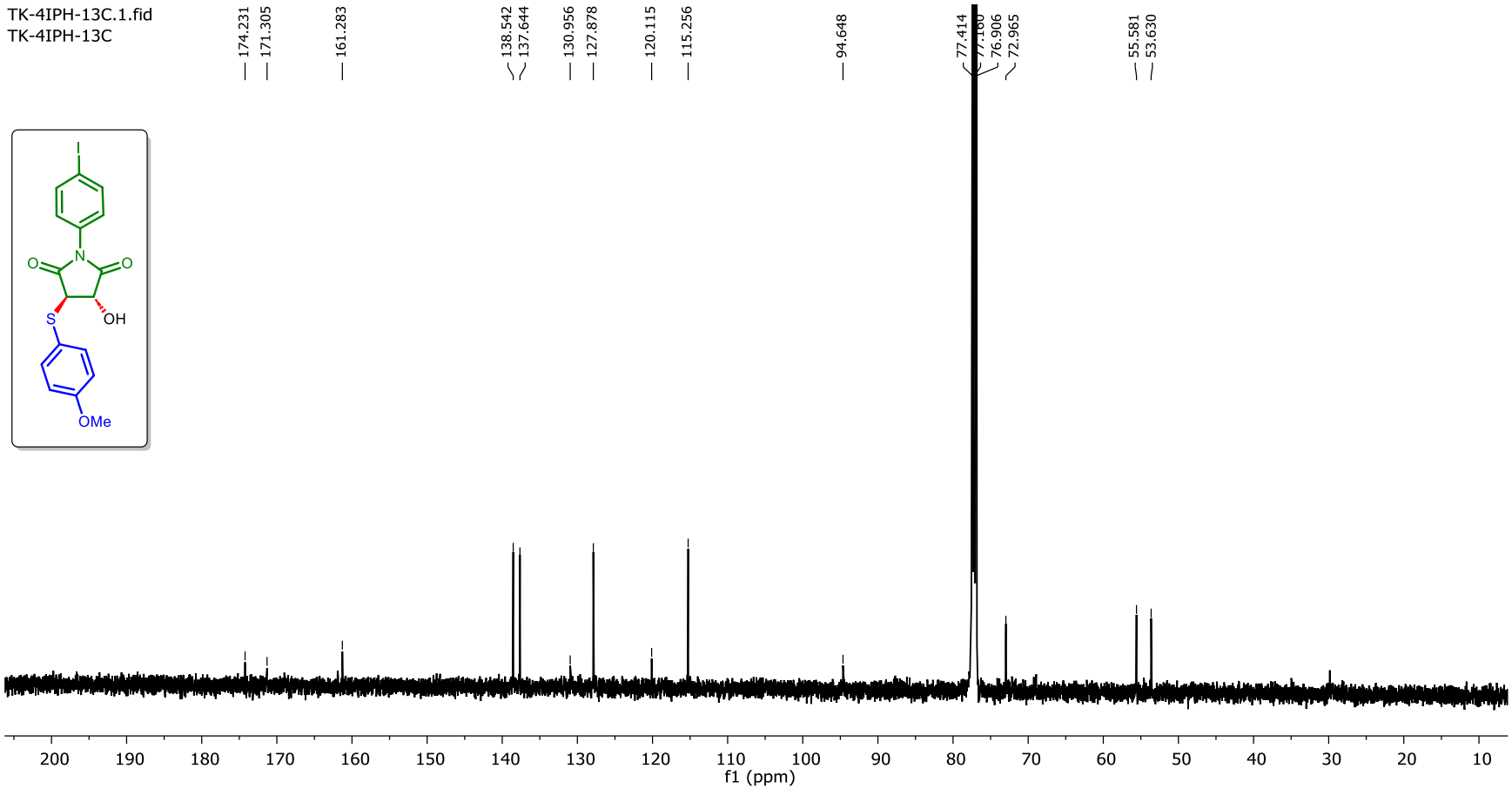
(3*S*,4*R*)-1-(4-Bromophenyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ca): ^{1}H NMR ($CDCl_3$, 500 MHz)



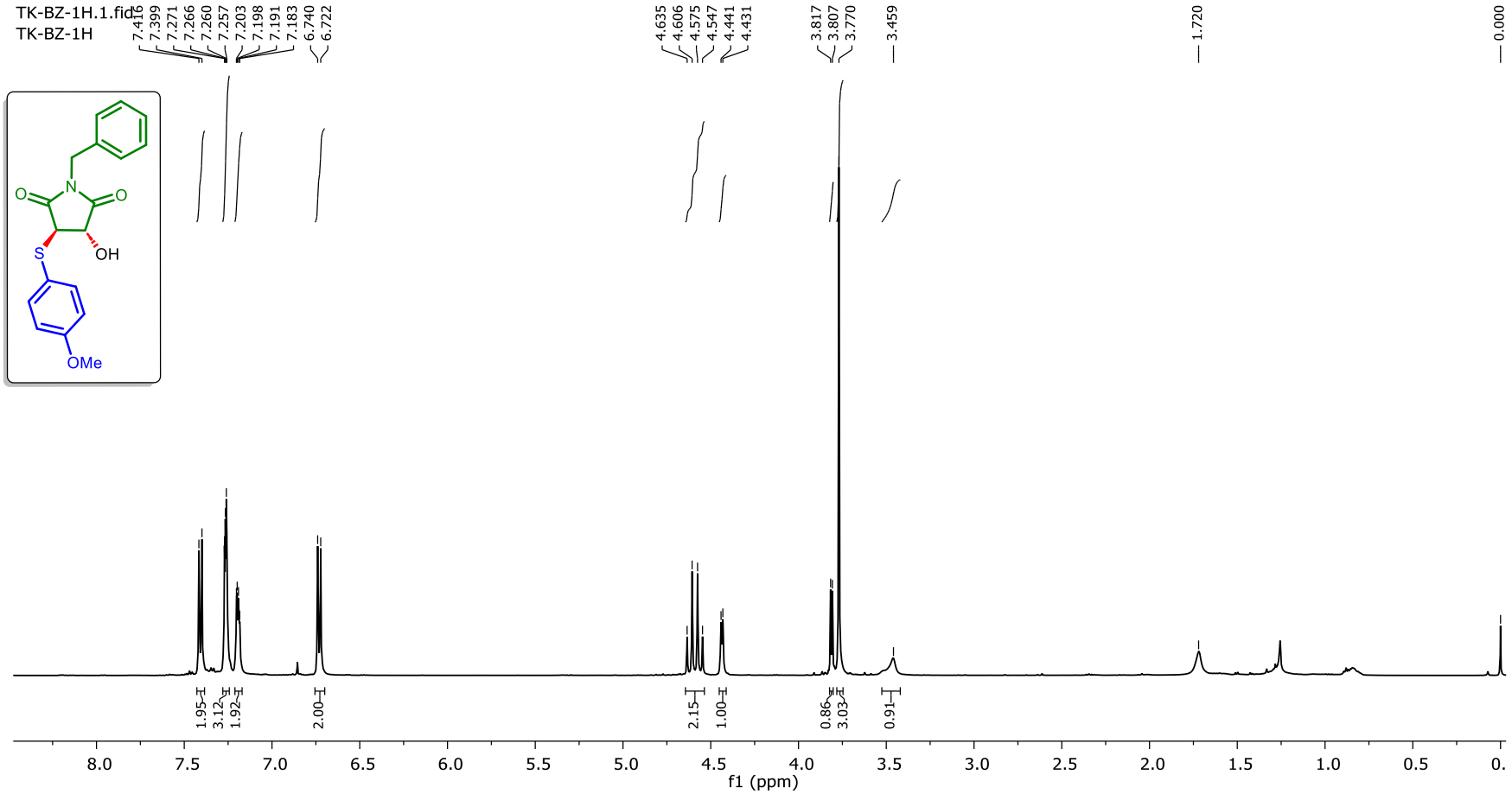
(3*S*,4*R*)-1-(4-Bromophenyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ca): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



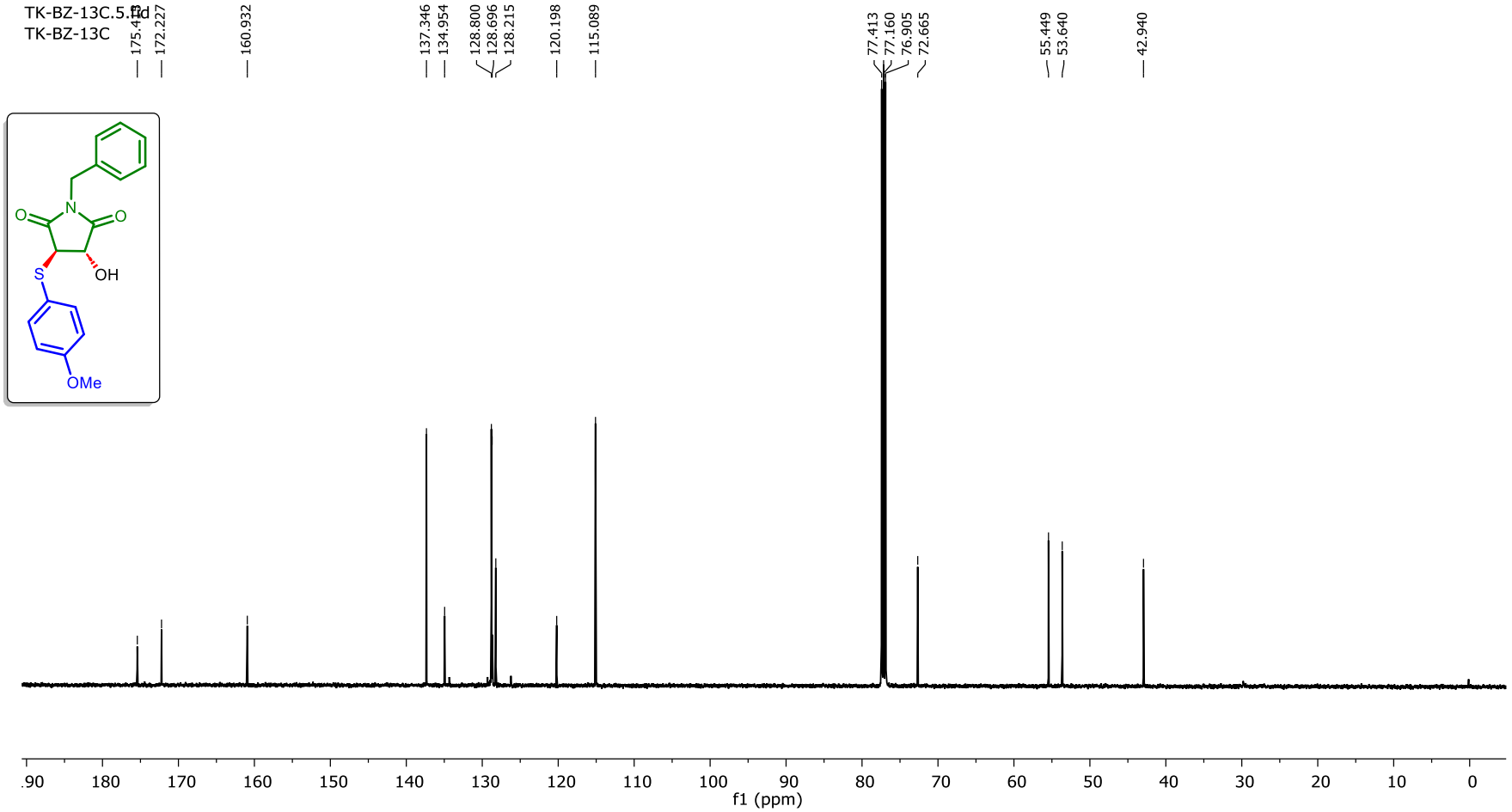
(3*S*,4*R*)-3-Hydroxy-1-(4-iodophenyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3da): ^{1}H NMR ($CDCl_3$, 400 MHz)



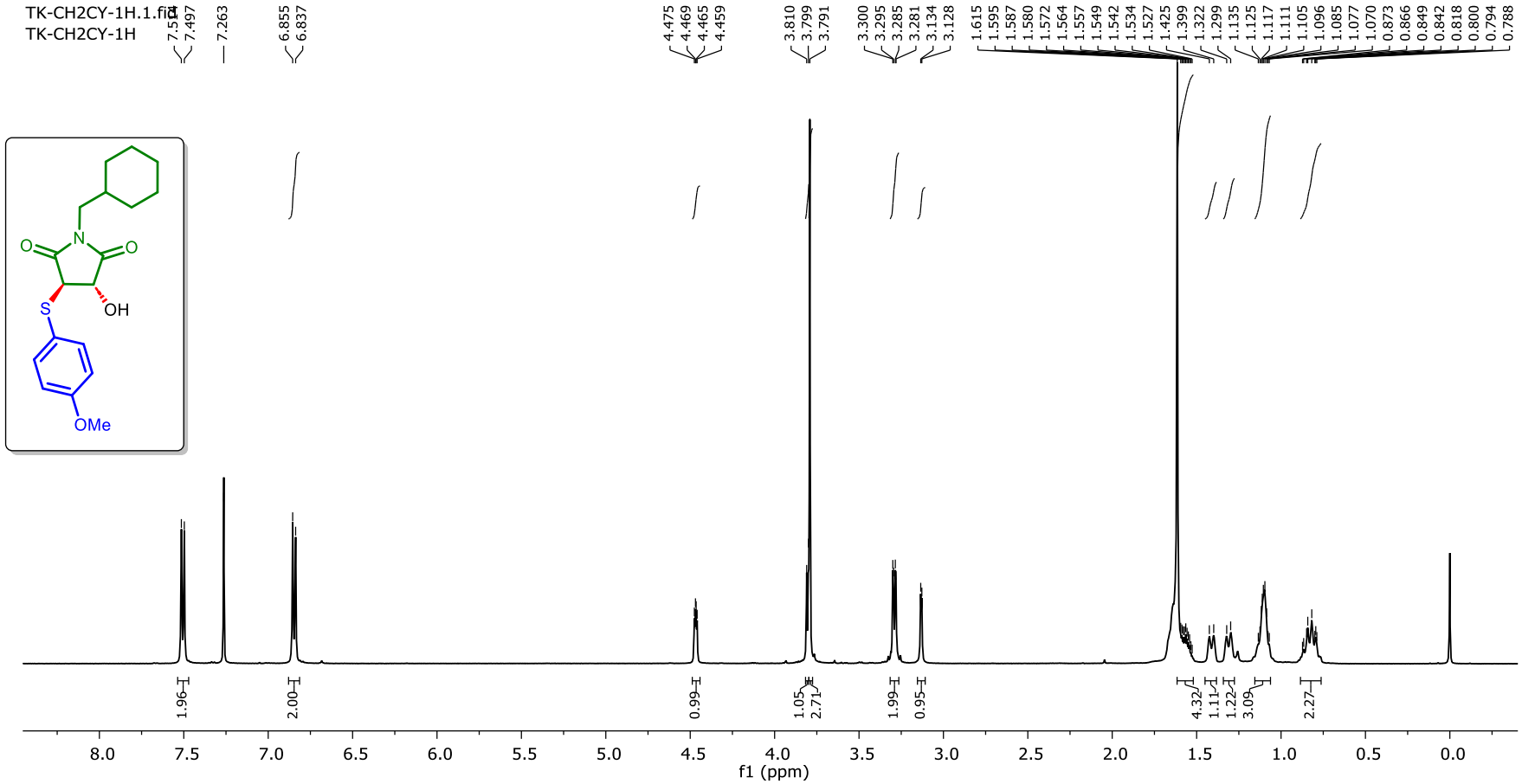
(3*S*,4*R*)-3-Hydroxy-1-(4-iodophenyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3da): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



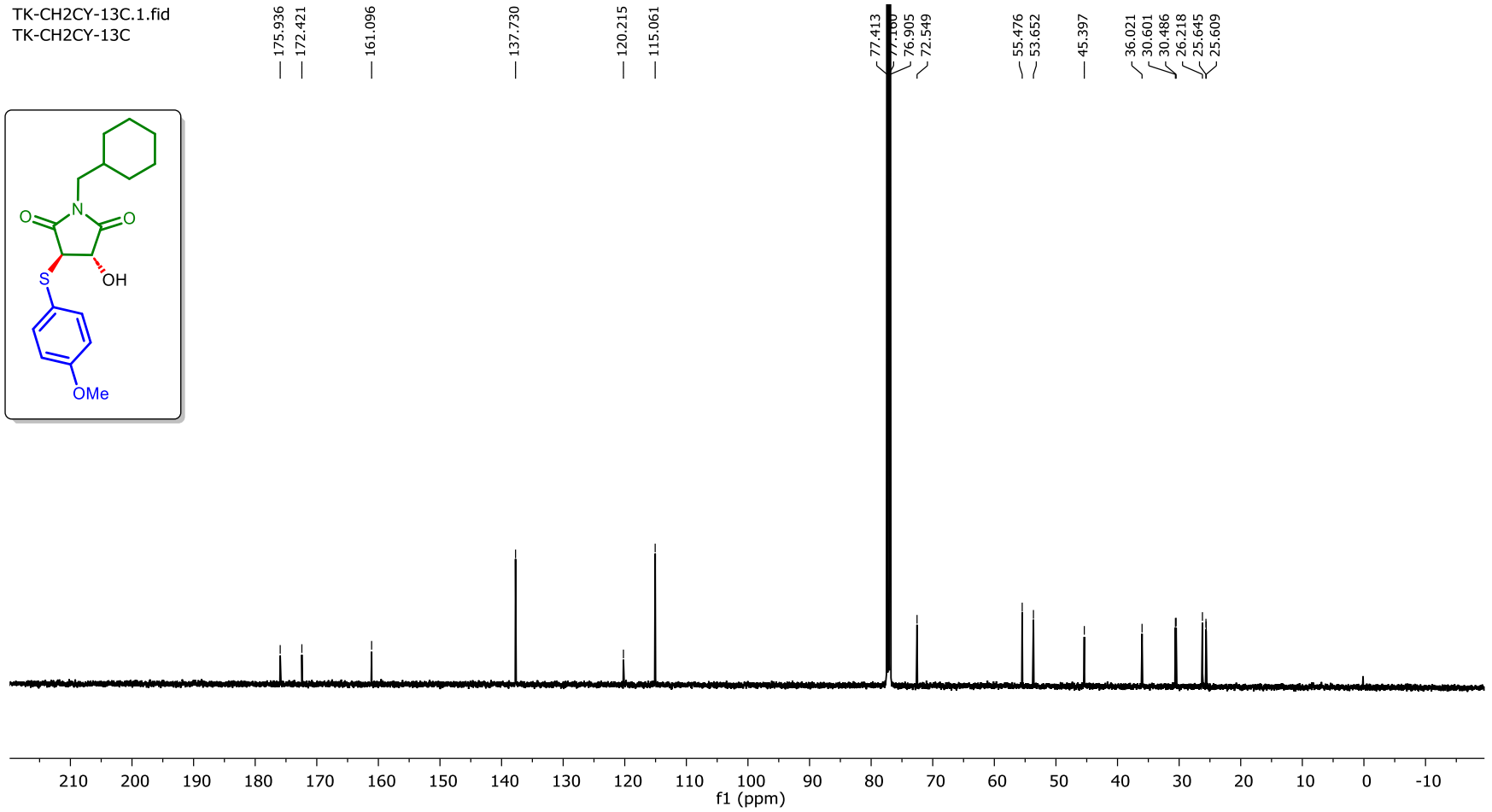
(3*S*,4*R*)-1-Benzyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ea): ^{1}H NMR ($CDCl_3$, 500 MHz)



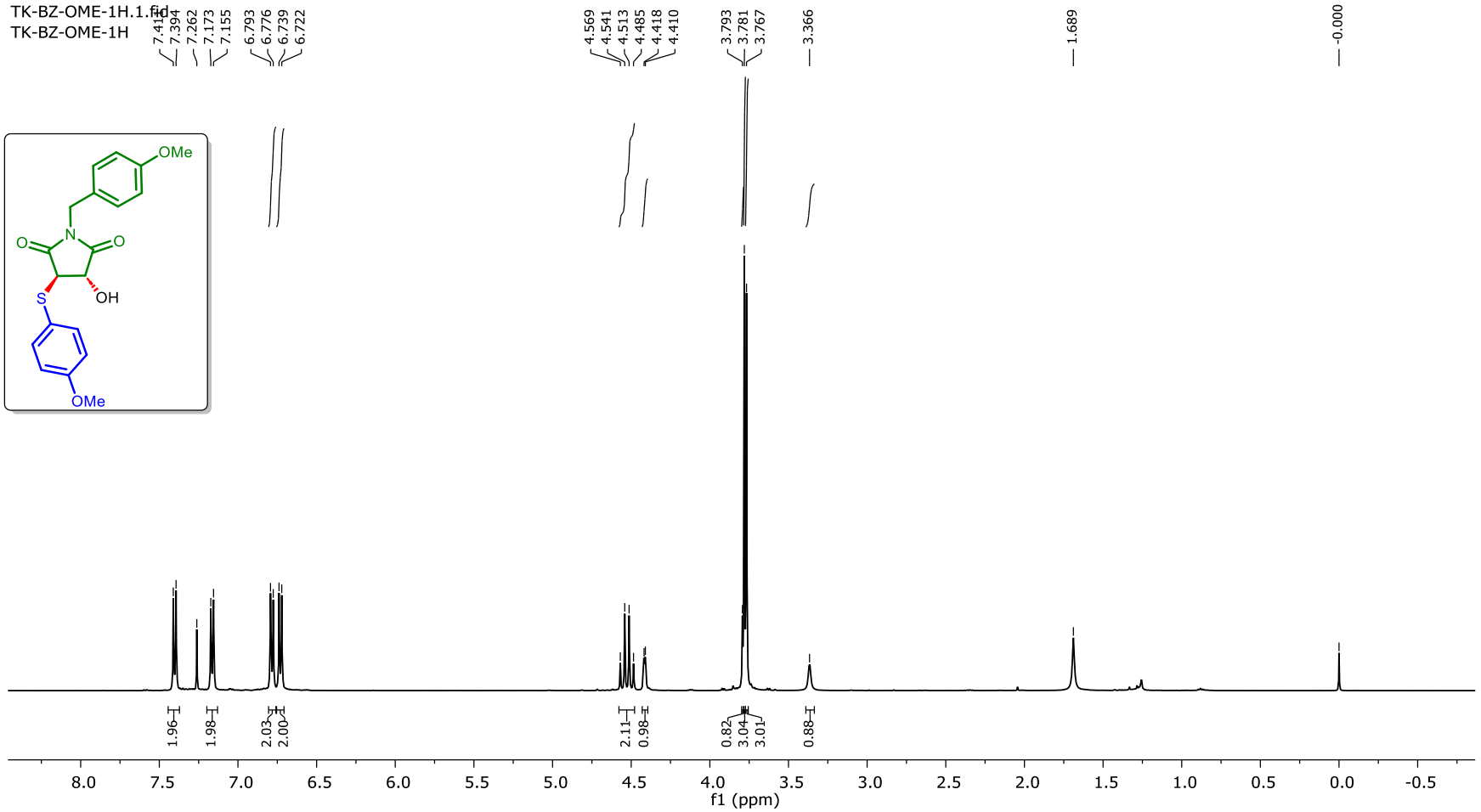
(3*S*,4*R*)-1-Benzyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ea): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



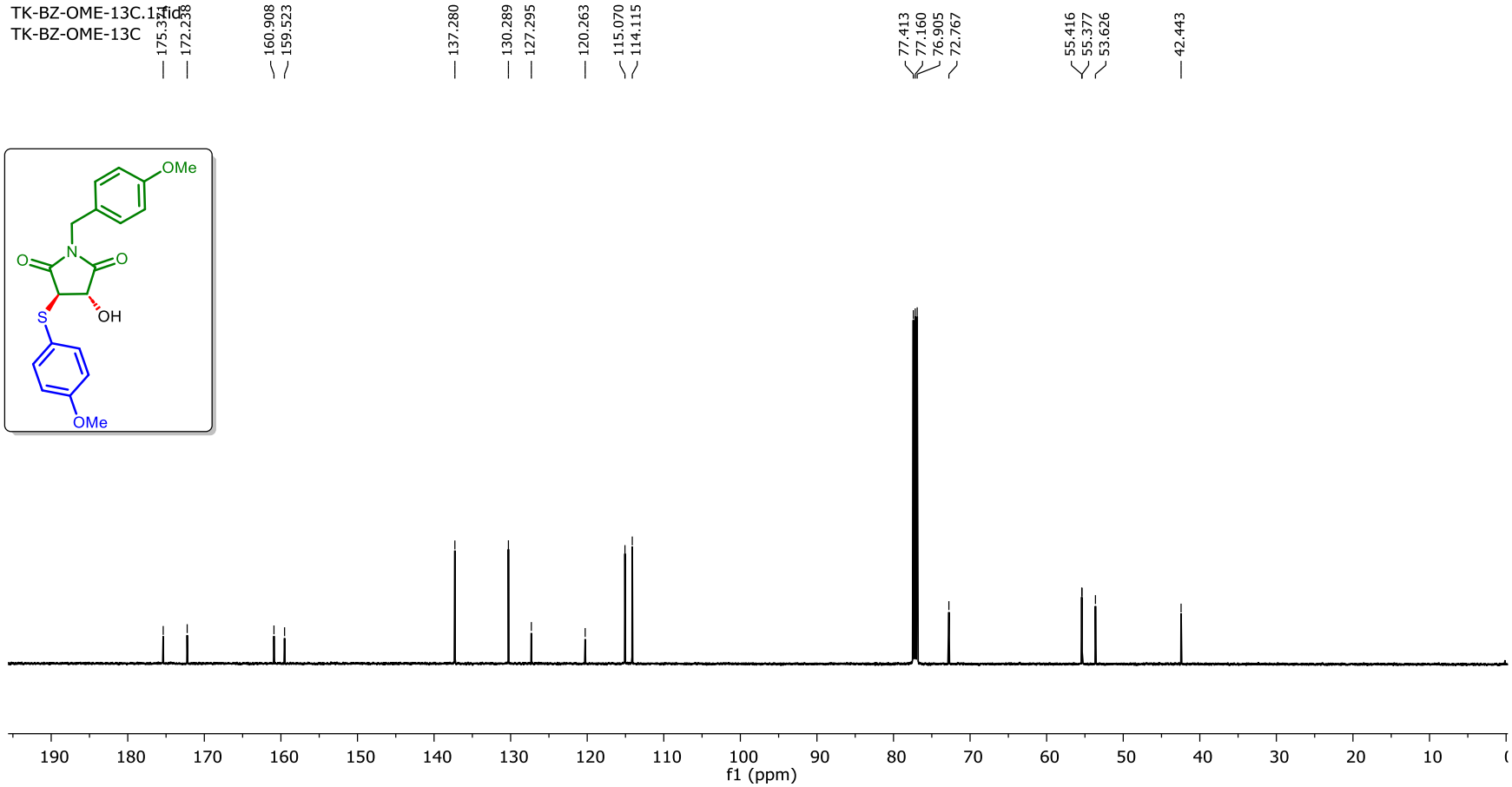
(3*S*,4*R*)-1-(Cyclohexylmethyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3fa): ^{1}H NMR ($CDCl_3$, 500 MHz)



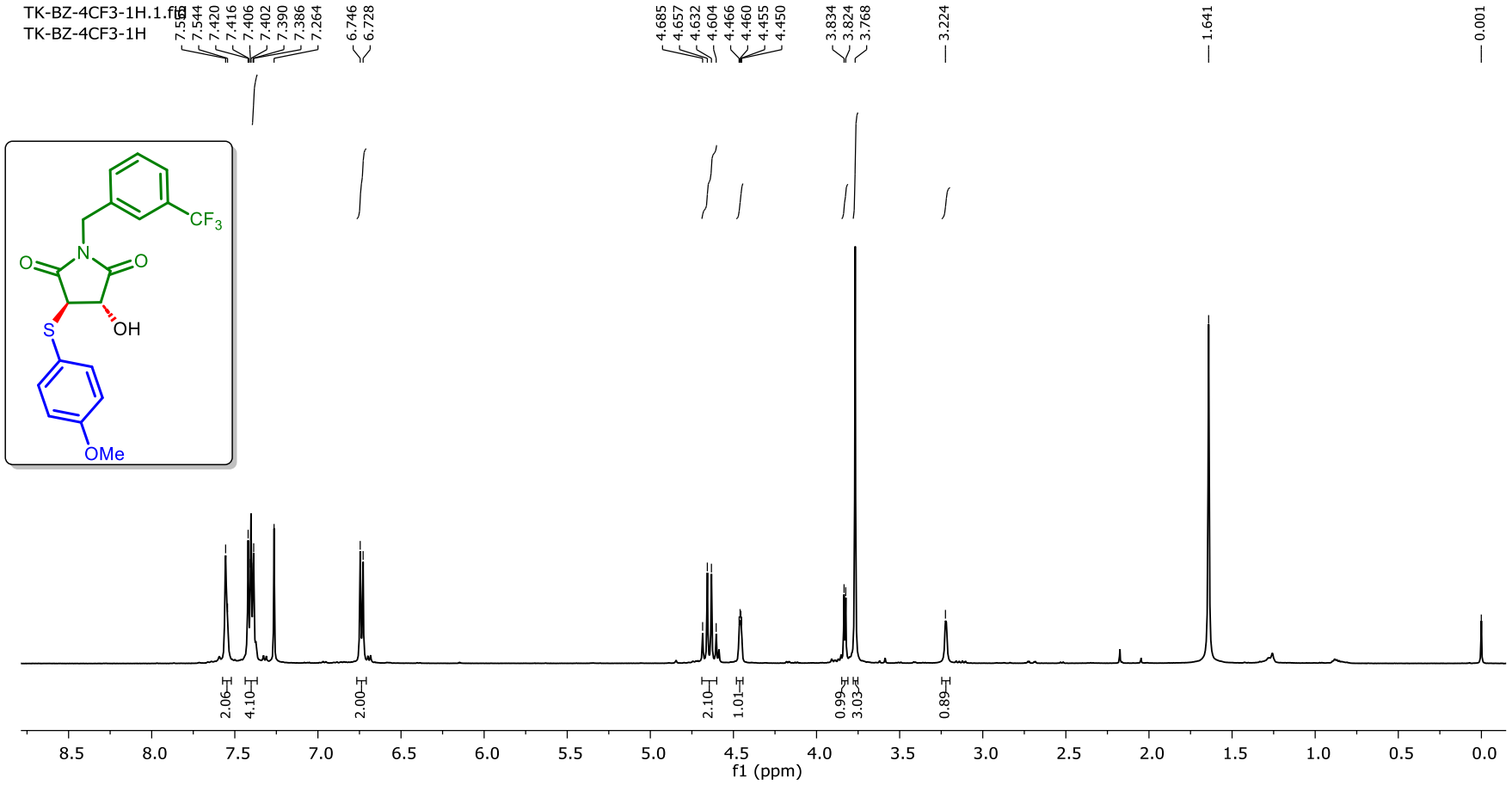
(3*S*,4*R*)-1-(Cyclohexylmethyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3fa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



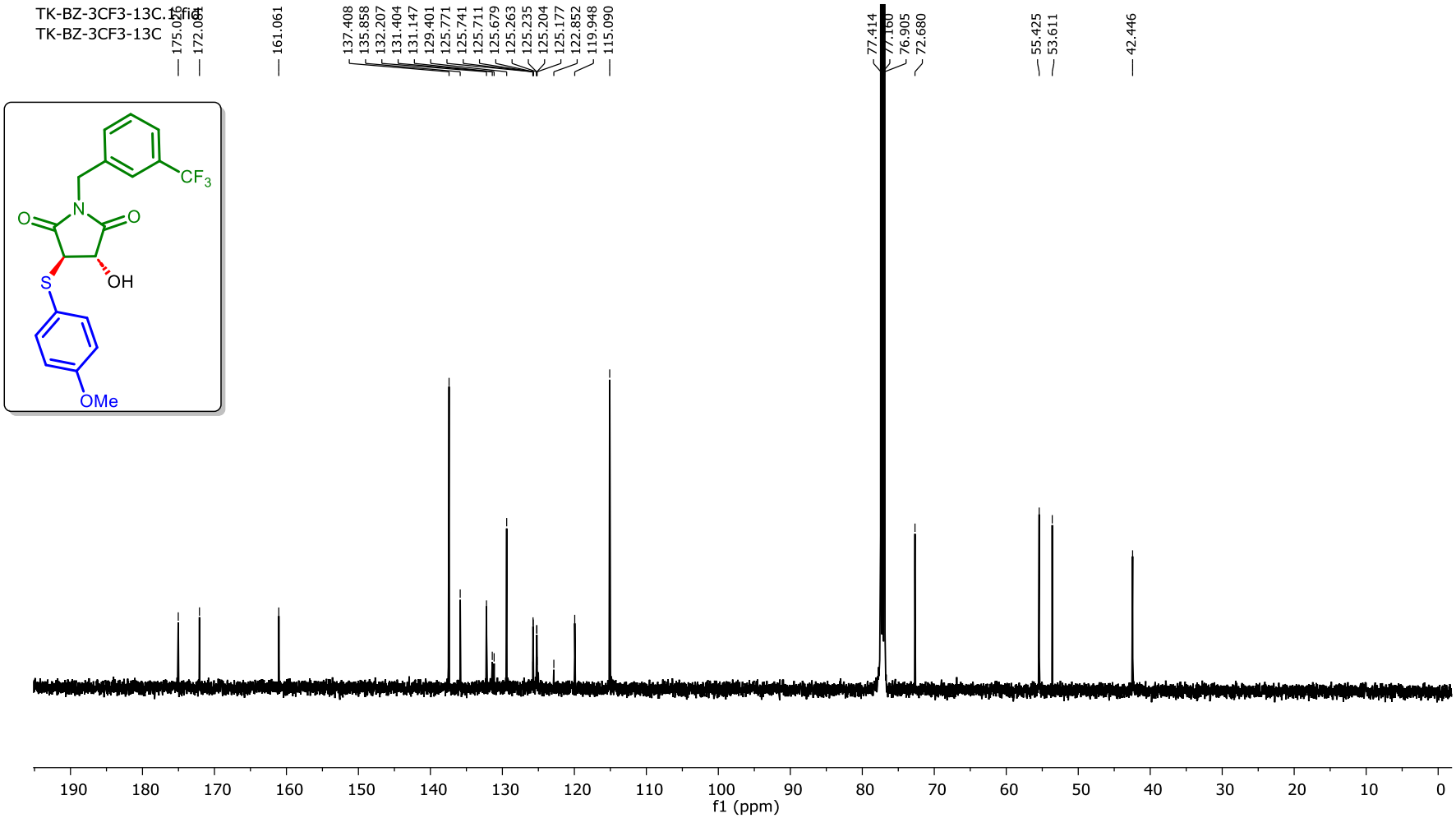
(3*S*,4*R*)-3-Hydroxy-1-(4-methoxybenzyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ga): ^{1}H NMR ($CDCl_3$, 500 MHz)



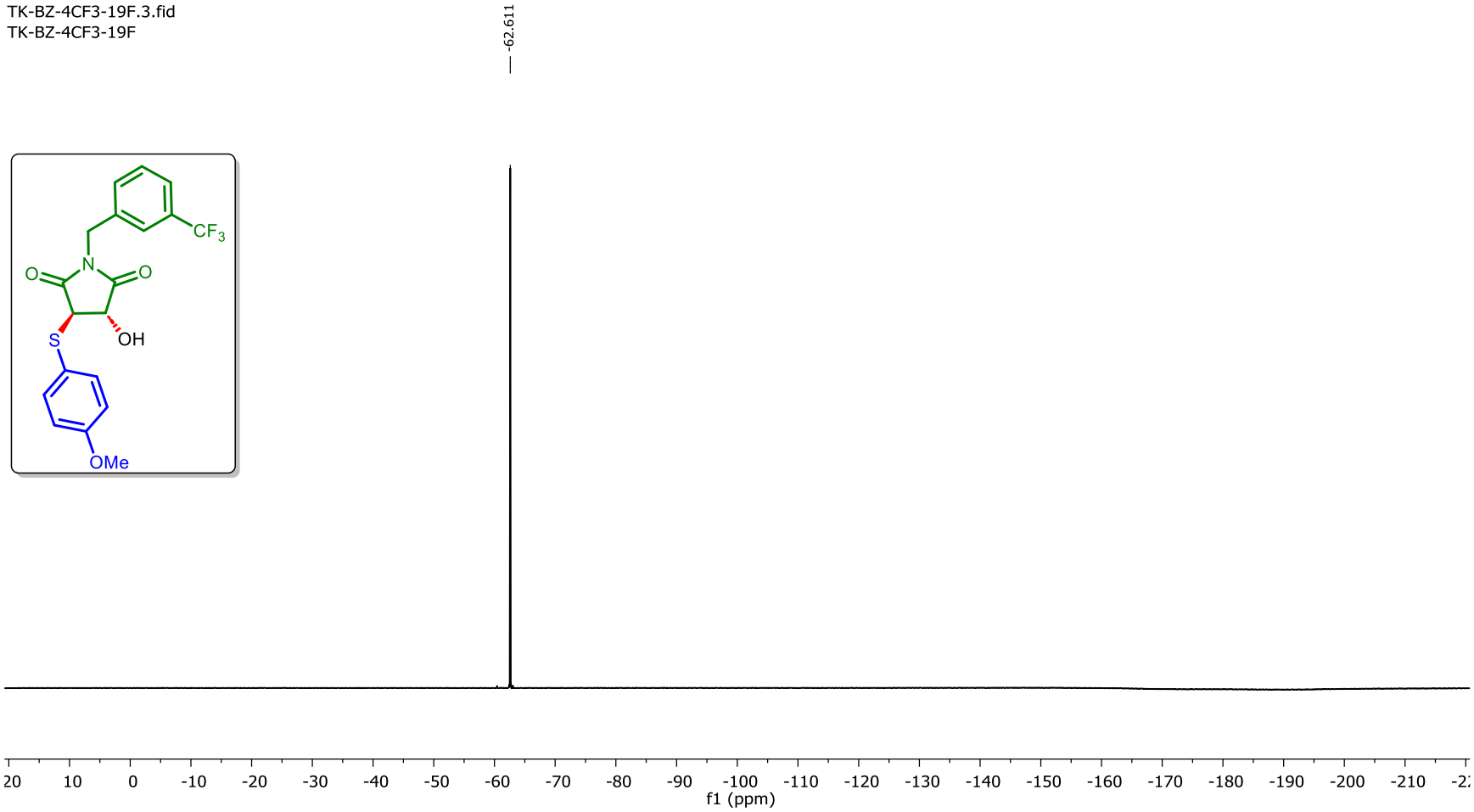
(3*S*,4*R*)-3-Hydroxy-1-(4-methoxybenzyl)-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ga): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



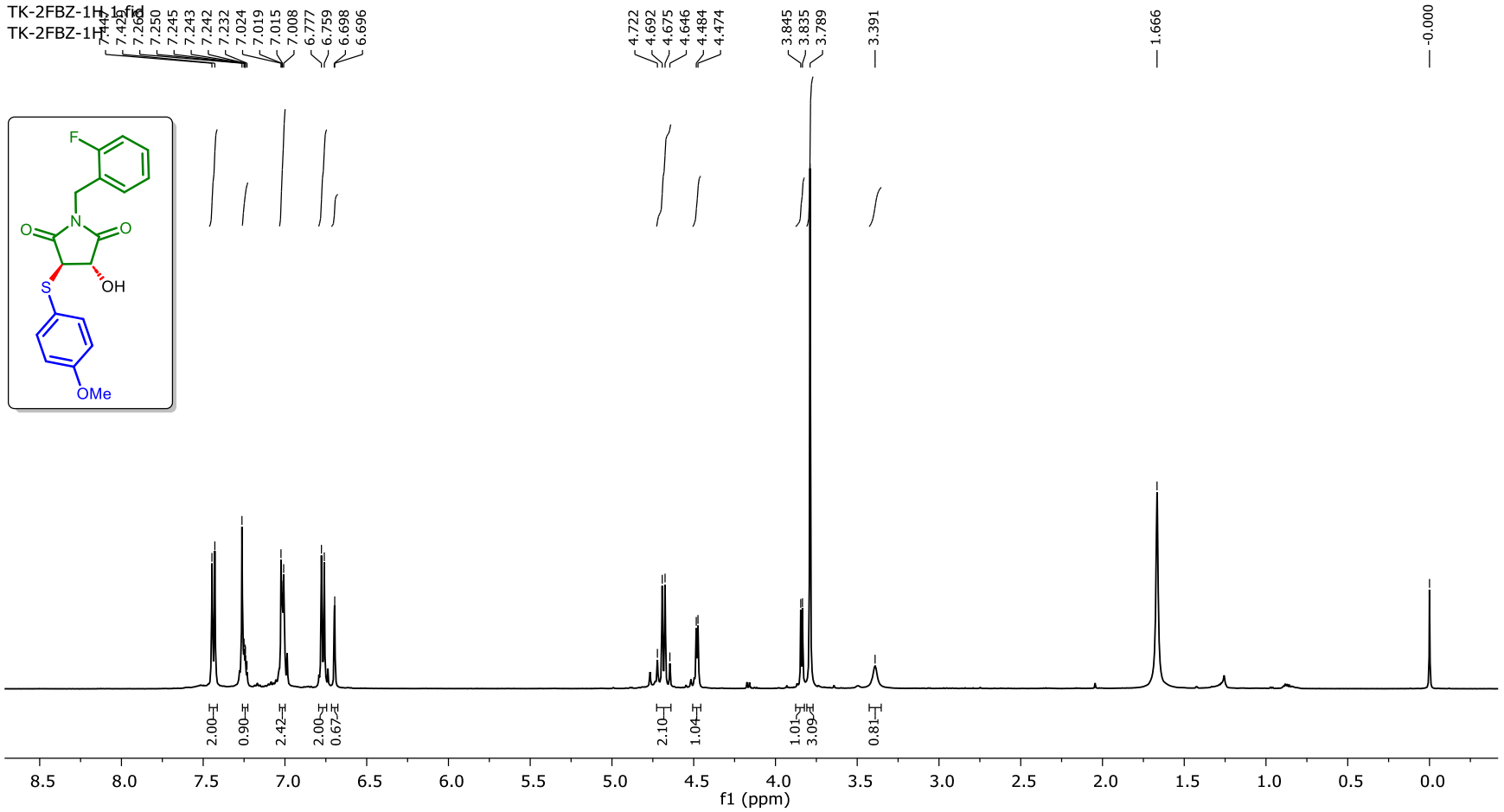
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(3-(trifluoromethyl)benzyl)pyrrolidine-2,5-dione (3ha): ^{1}H NMR ($CDCl_3$, 500 MHz)



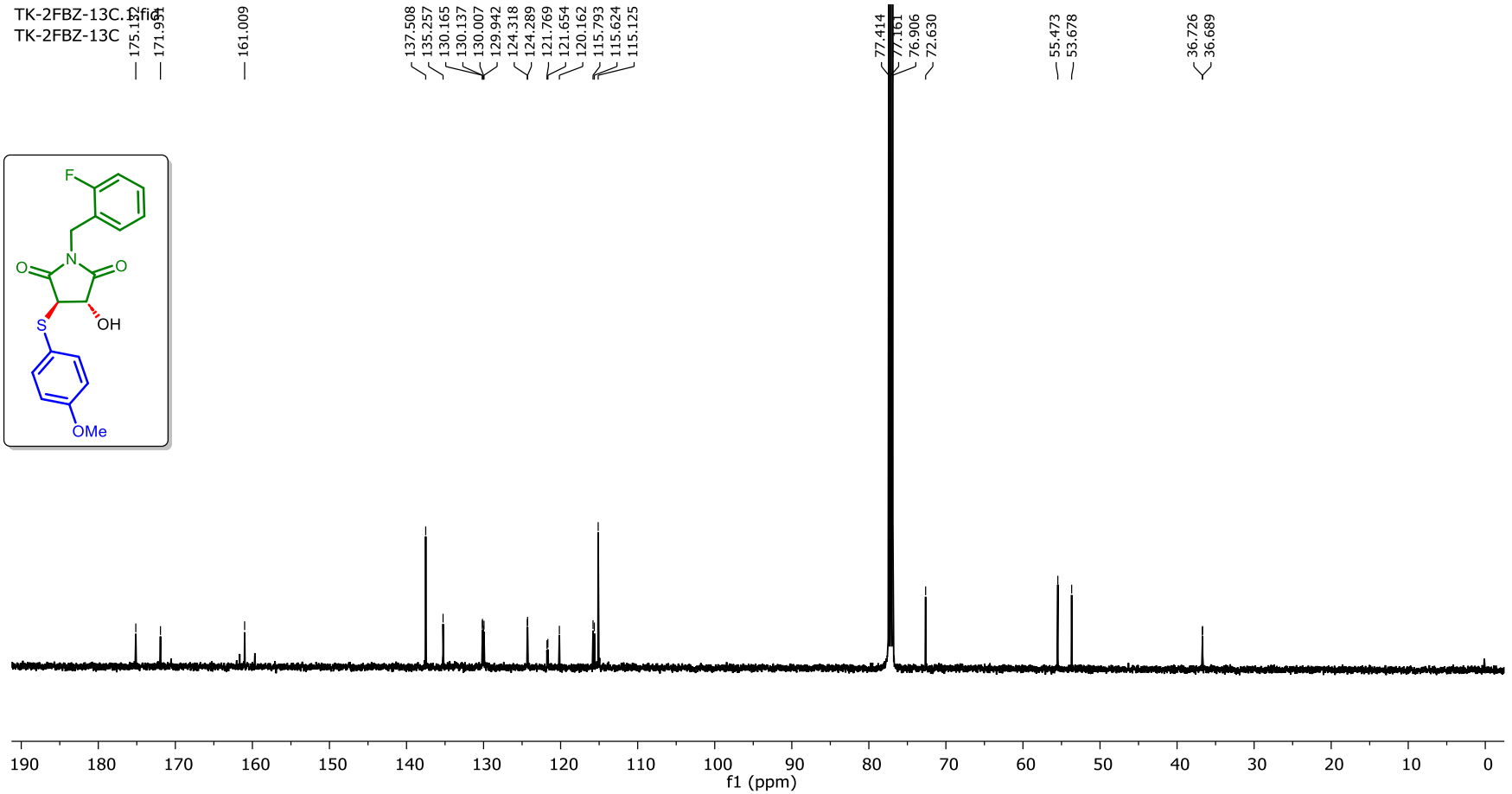
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(3-(trifluoromethyl)benzyl)pyrrolidine-2,5-dione (3ha): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



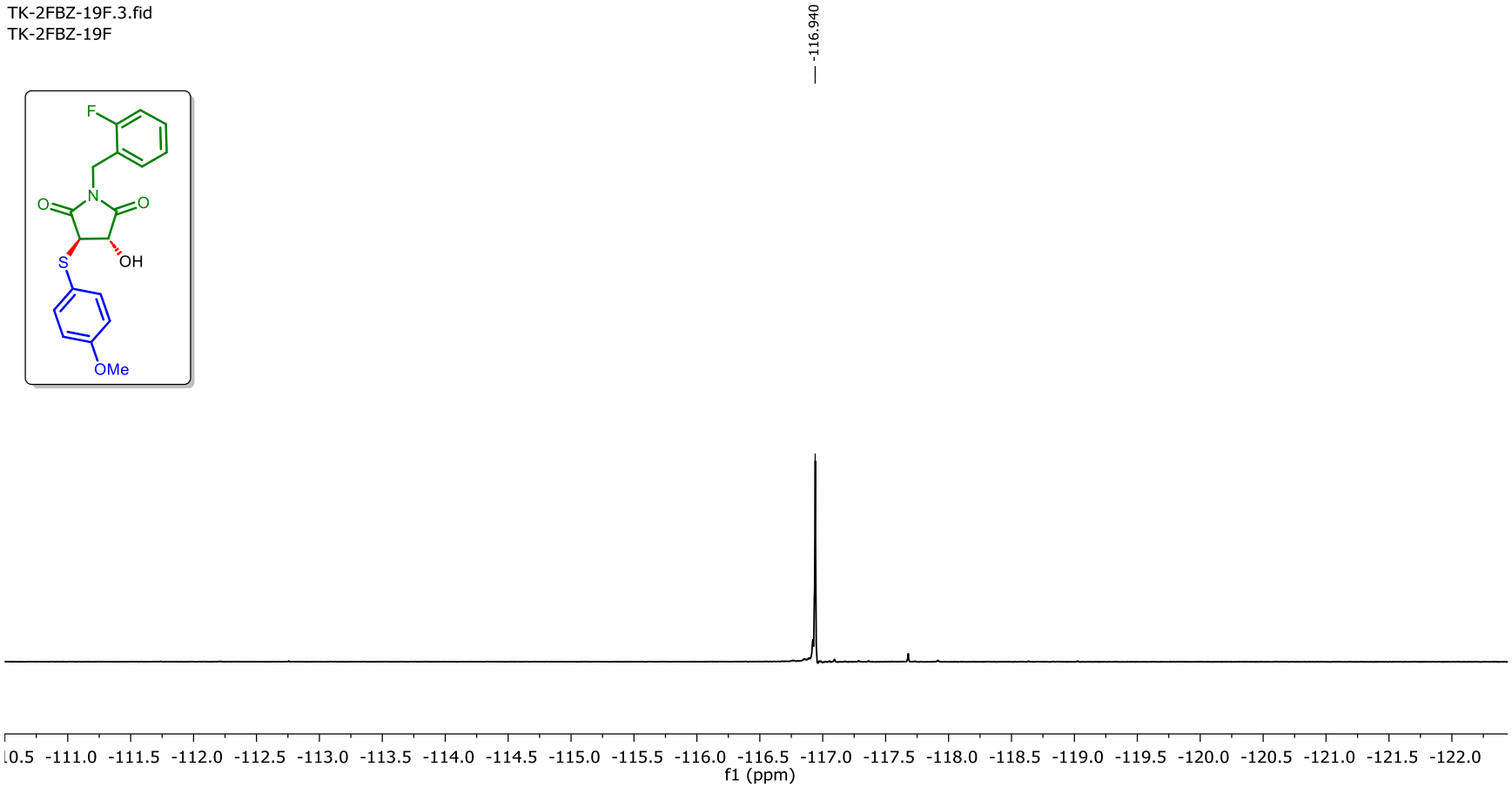
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(3-(trifluoromethyl)benzyl)pyrrolidine-2,5-dione (3ha): ^{19}FNMR ($CDCl_3$, 471 MHz)



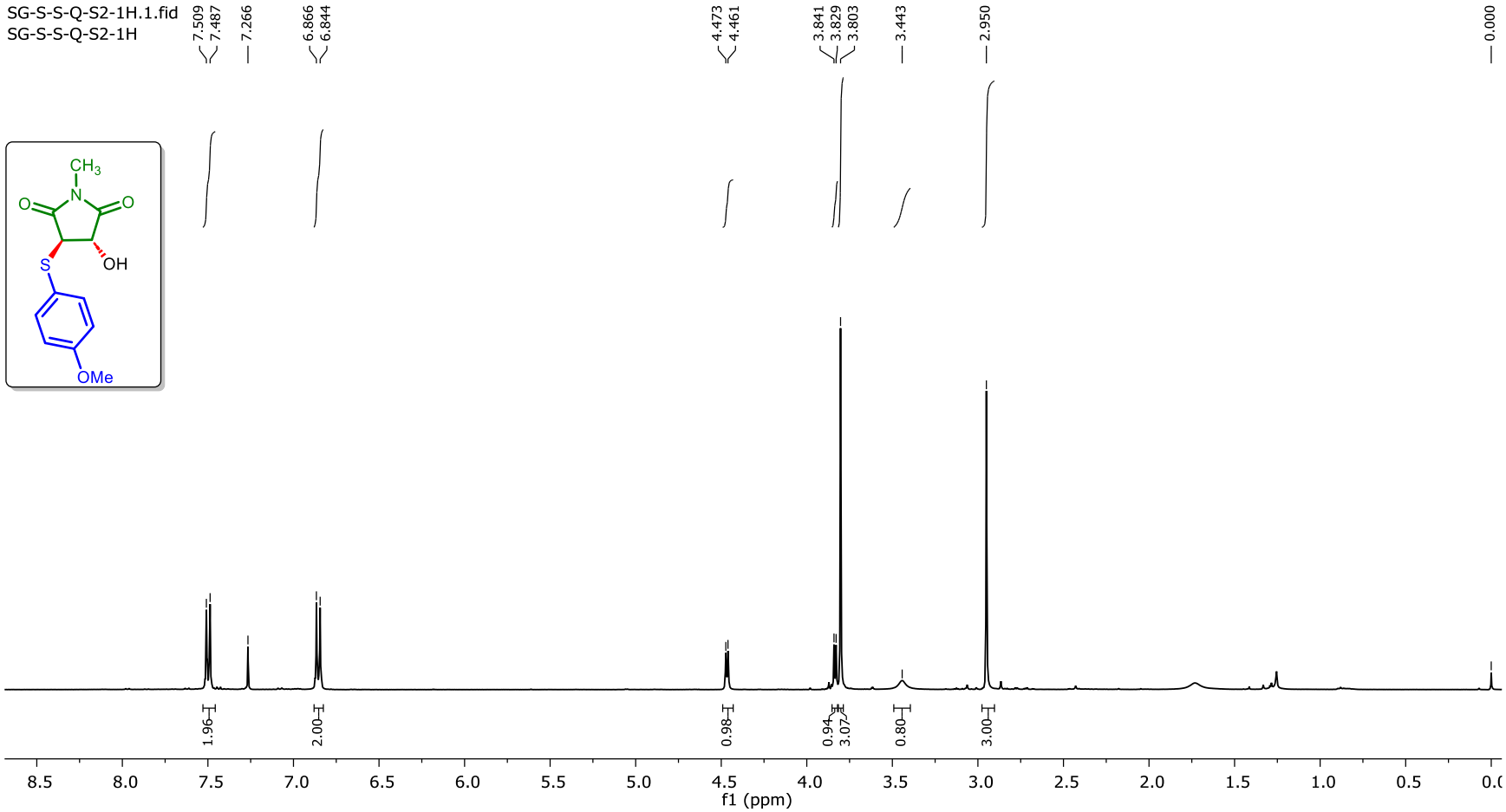
(3*S*,4*R*)-1-(2-Fluorobenzyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ia): ^{1}H NMR ($CDCl_3$, 500 MHz)



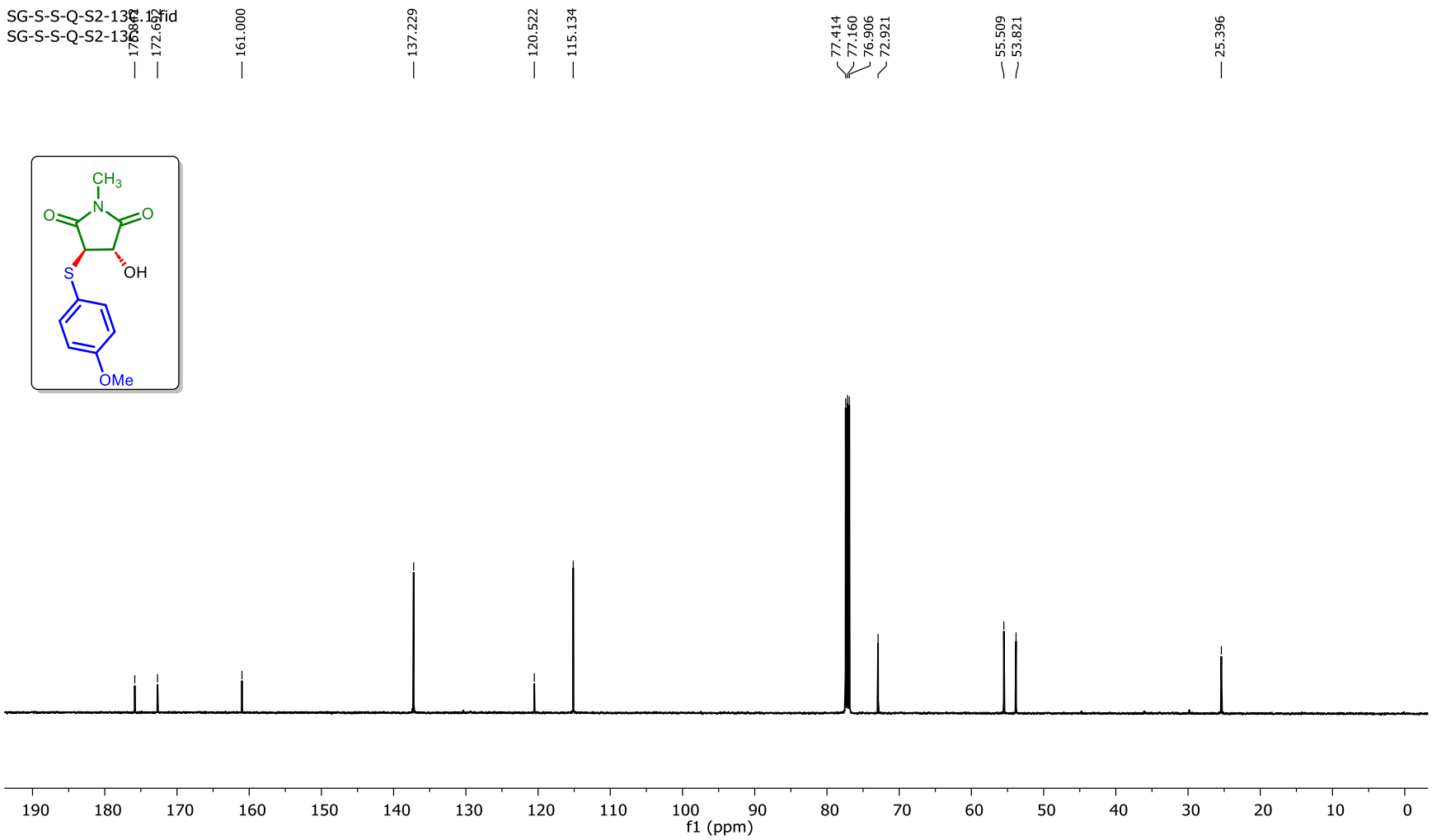
(3*S*,4*R*)-1-(2-Fluorobenzyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ia): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



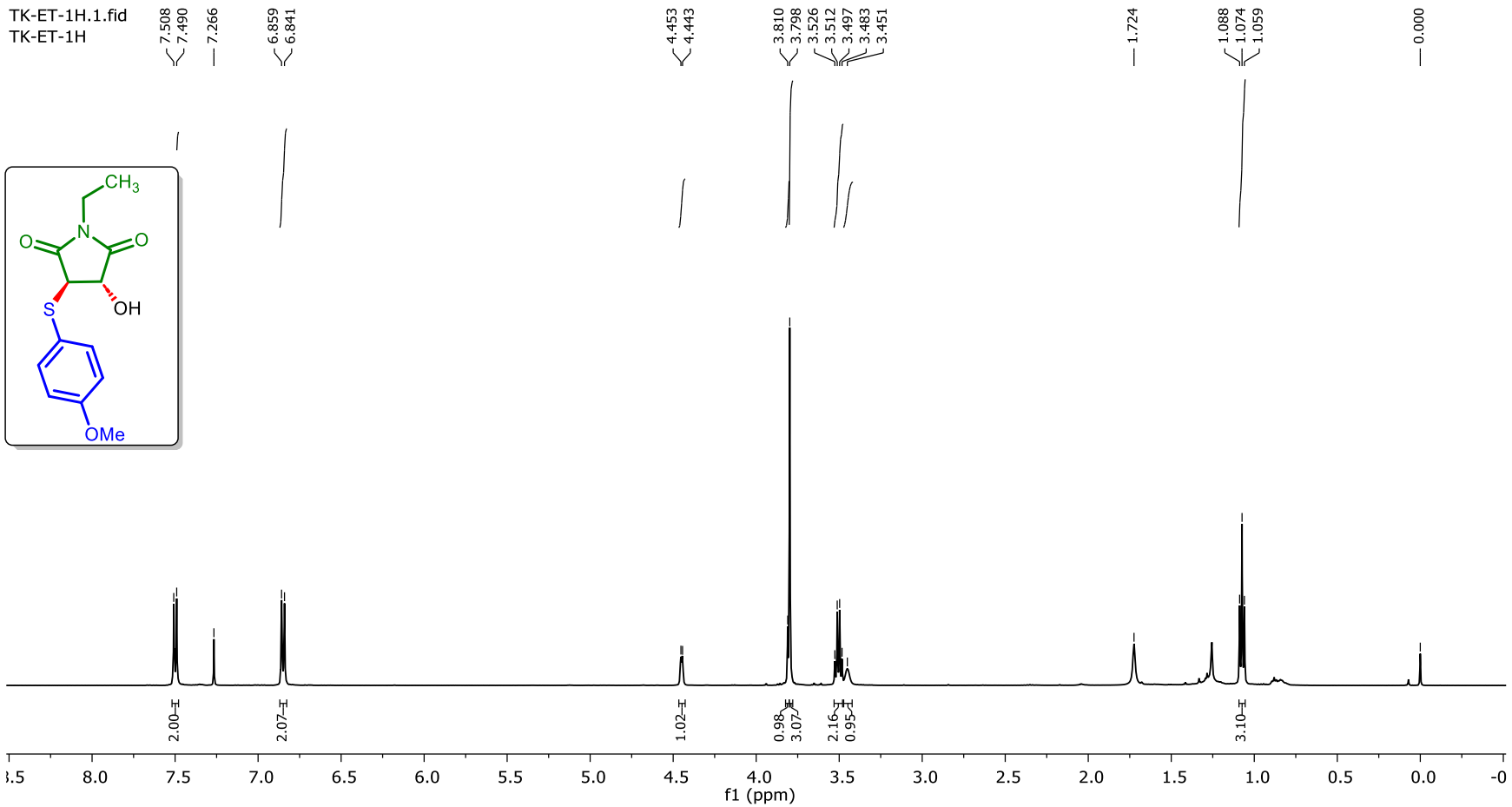
(3*S*,4*R*)-1-(2-Fluorobenzyl)-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ia): ^{19}F NMR ($CDCl_3$, 471 MHz)



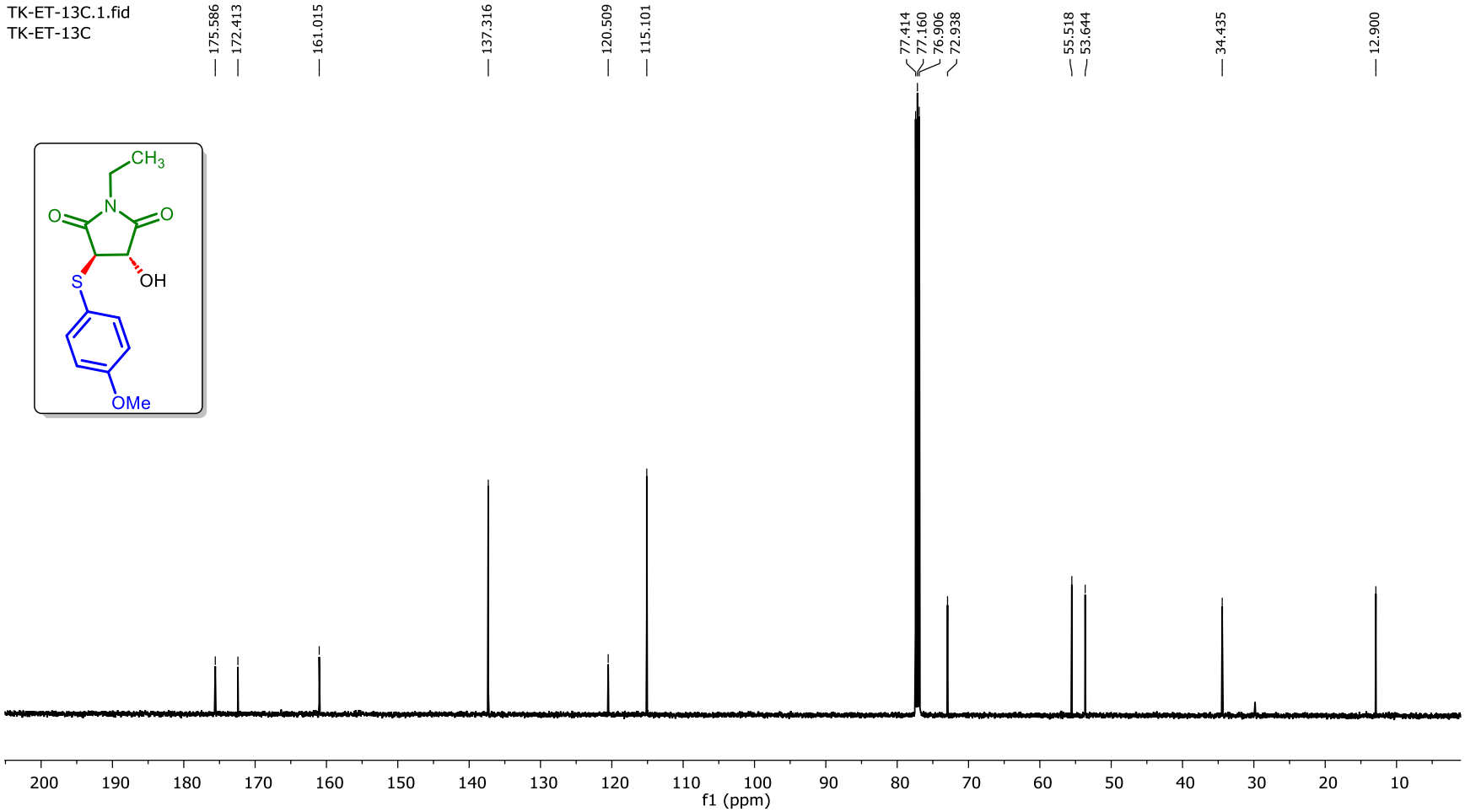
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-methylpyrrolidine-2,5-dione (3ja): ^{1}H NMR ($CDCl_3$, 400 MHz)



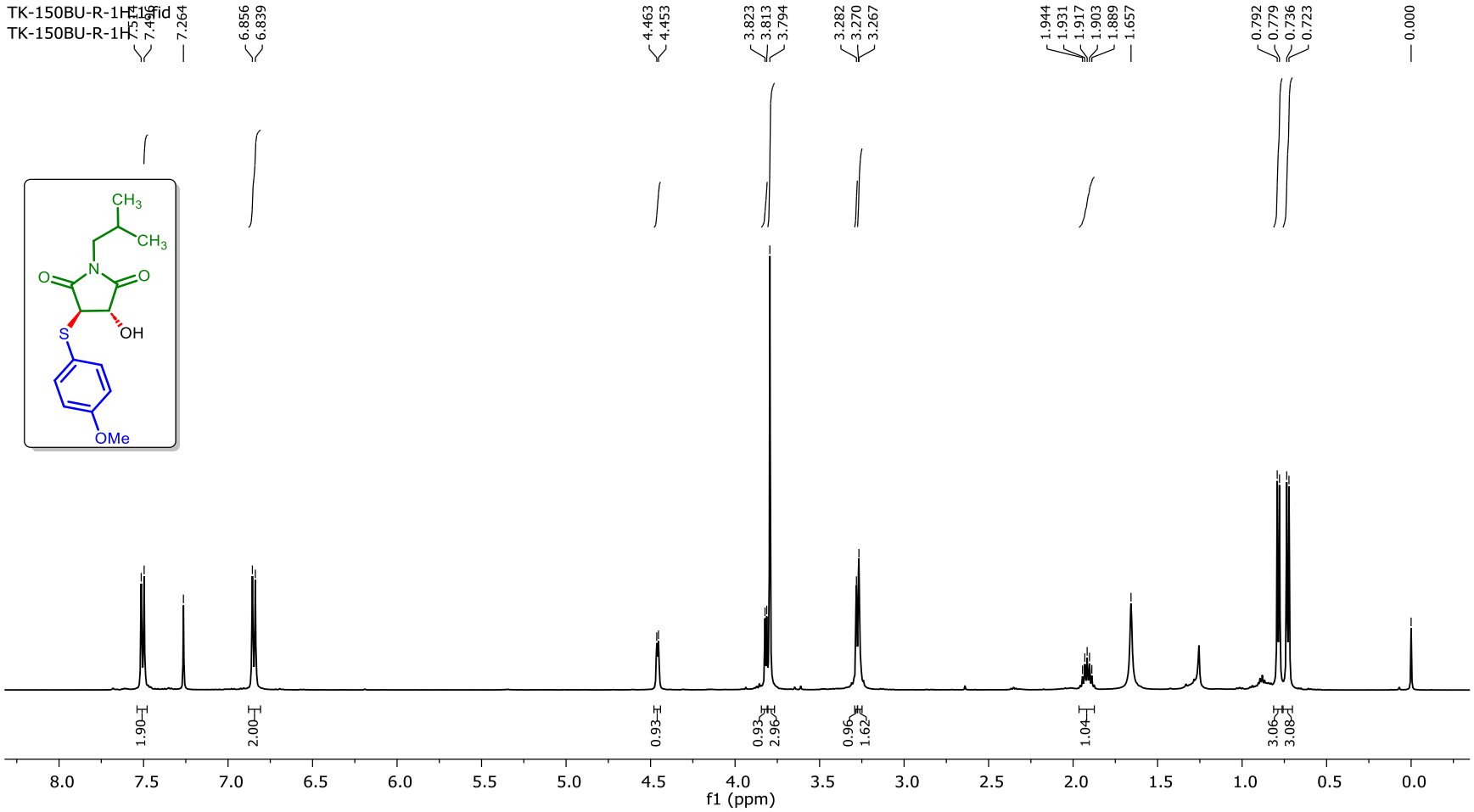
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-methylpyrrolidine-2,5-dione (3ja): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



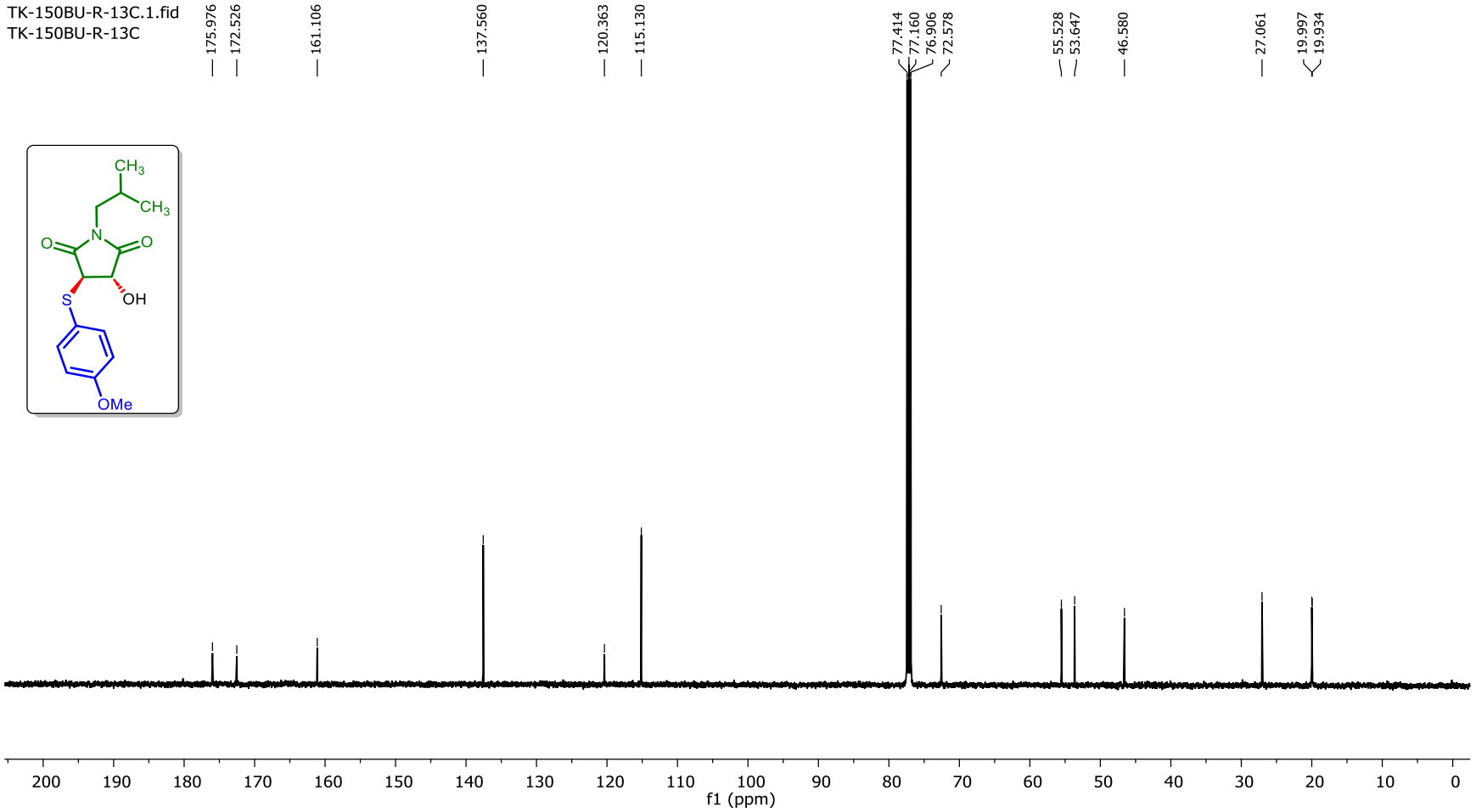
(3*S*,4*R*)-1-Ethyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ka): ^{1}H NMR ($CDCl_3$, 500 MHz)



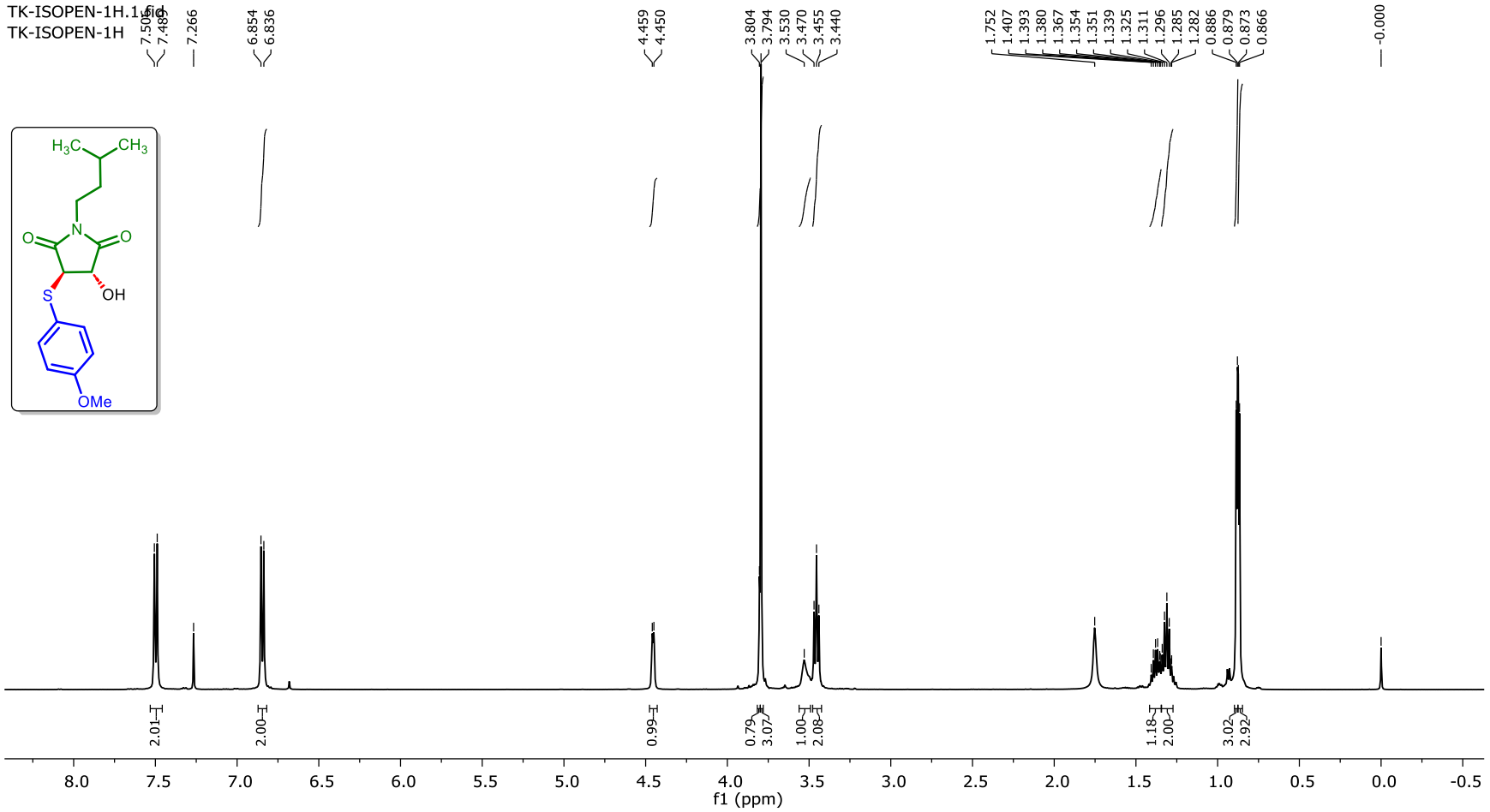
(3*S*,4*R*)-1-Ethyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ka): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



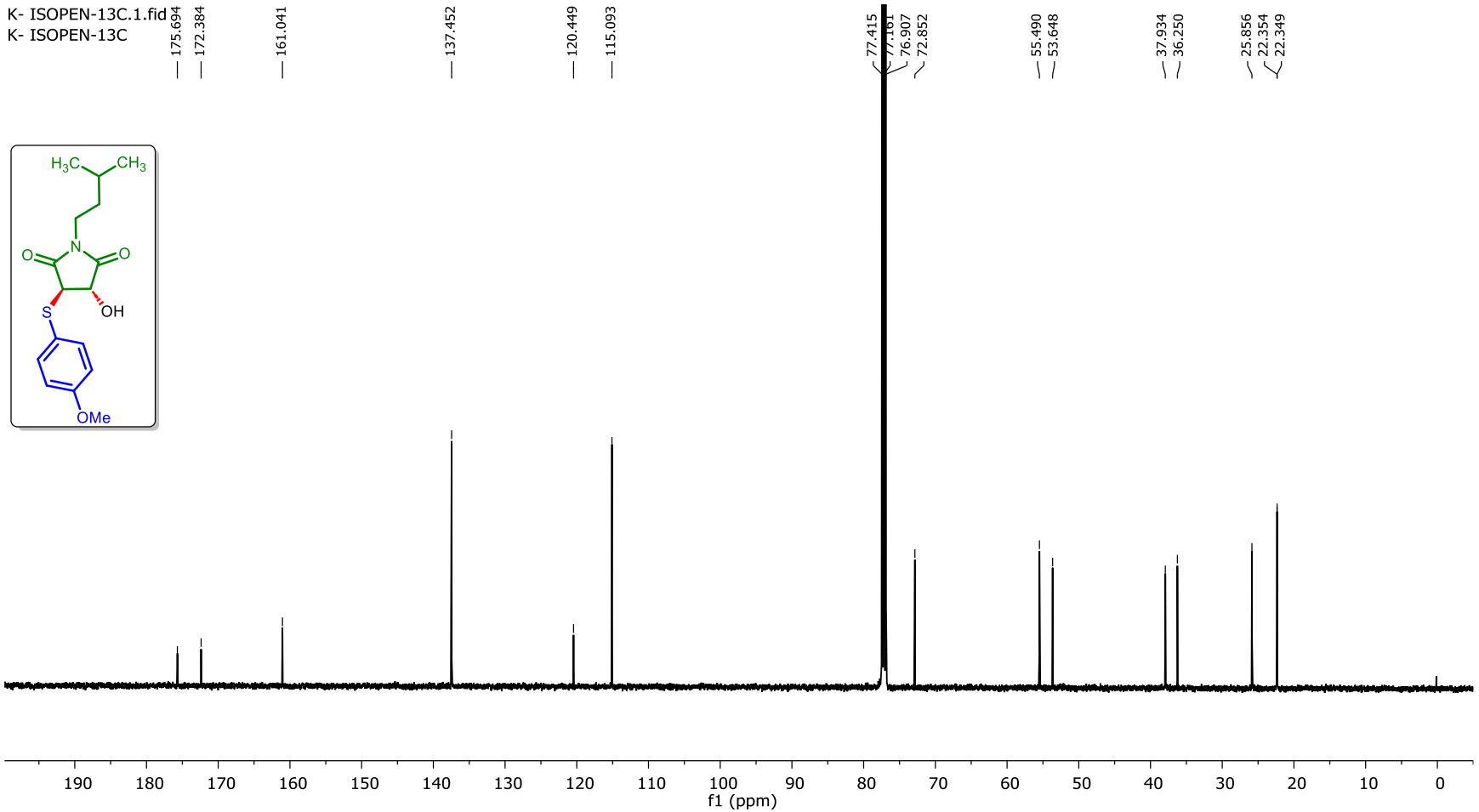
(3*S*,4*R*)-3-Hydroxy-1-isobutyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3la): ^{1}H NMR ($CDCl_3$, 500 MHz)



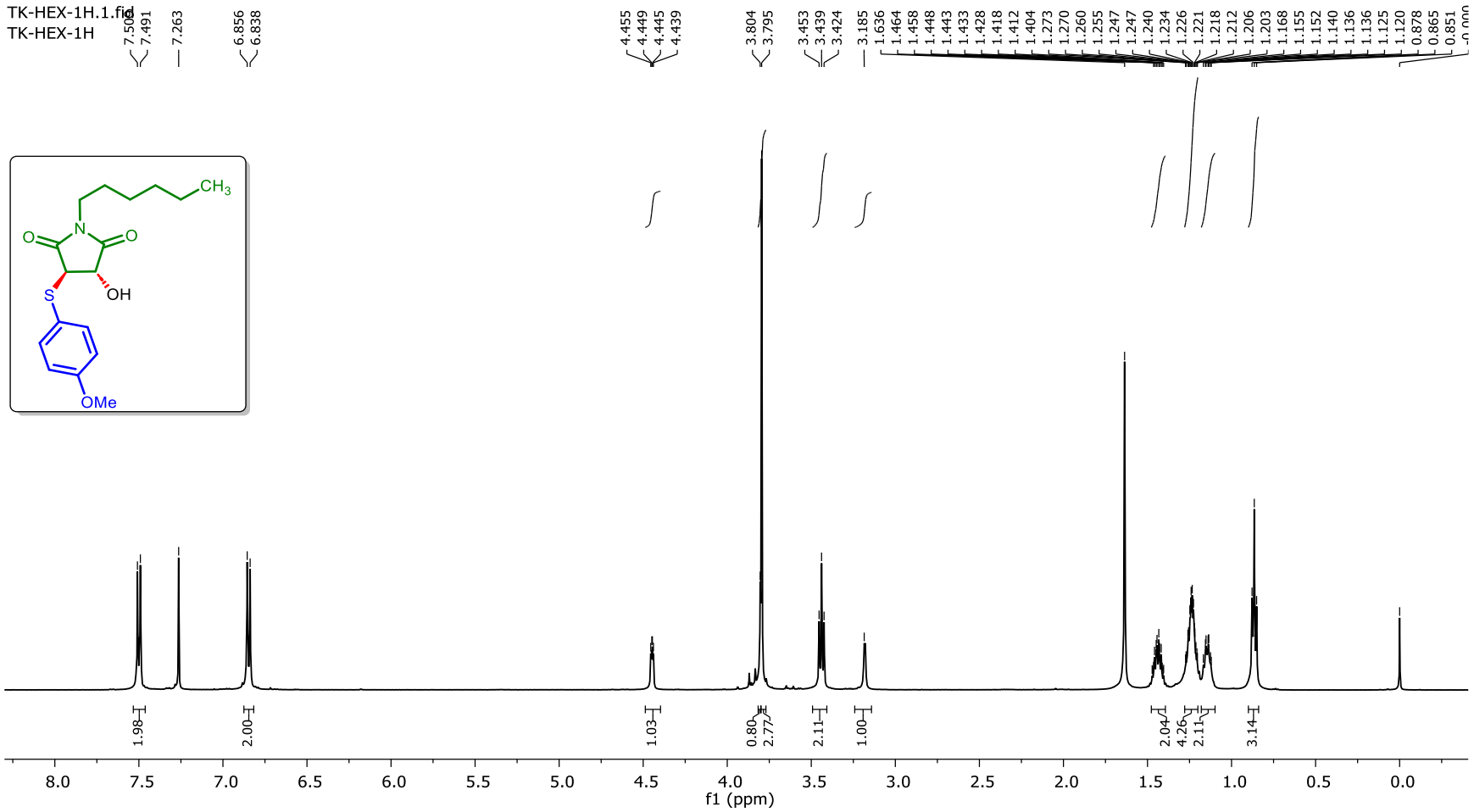
(3*S*,4*R*)-3-Hydroxy-1-isobutyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3la): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



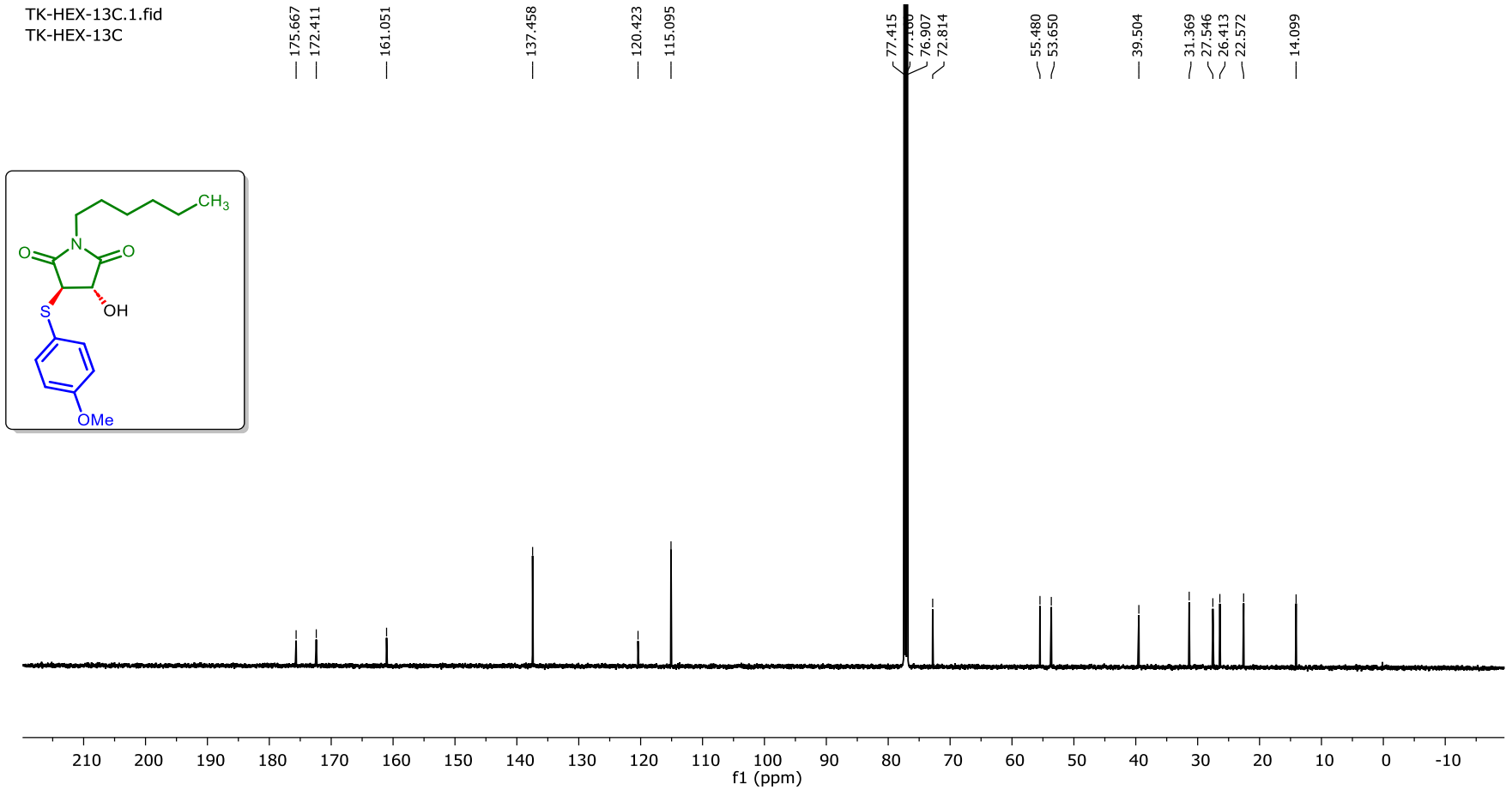
(3*S*,4*R*)-3-Hydroxy-1-isopentyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ma): ^{1}H NMR ($CDCl_3$, 500 MHz)



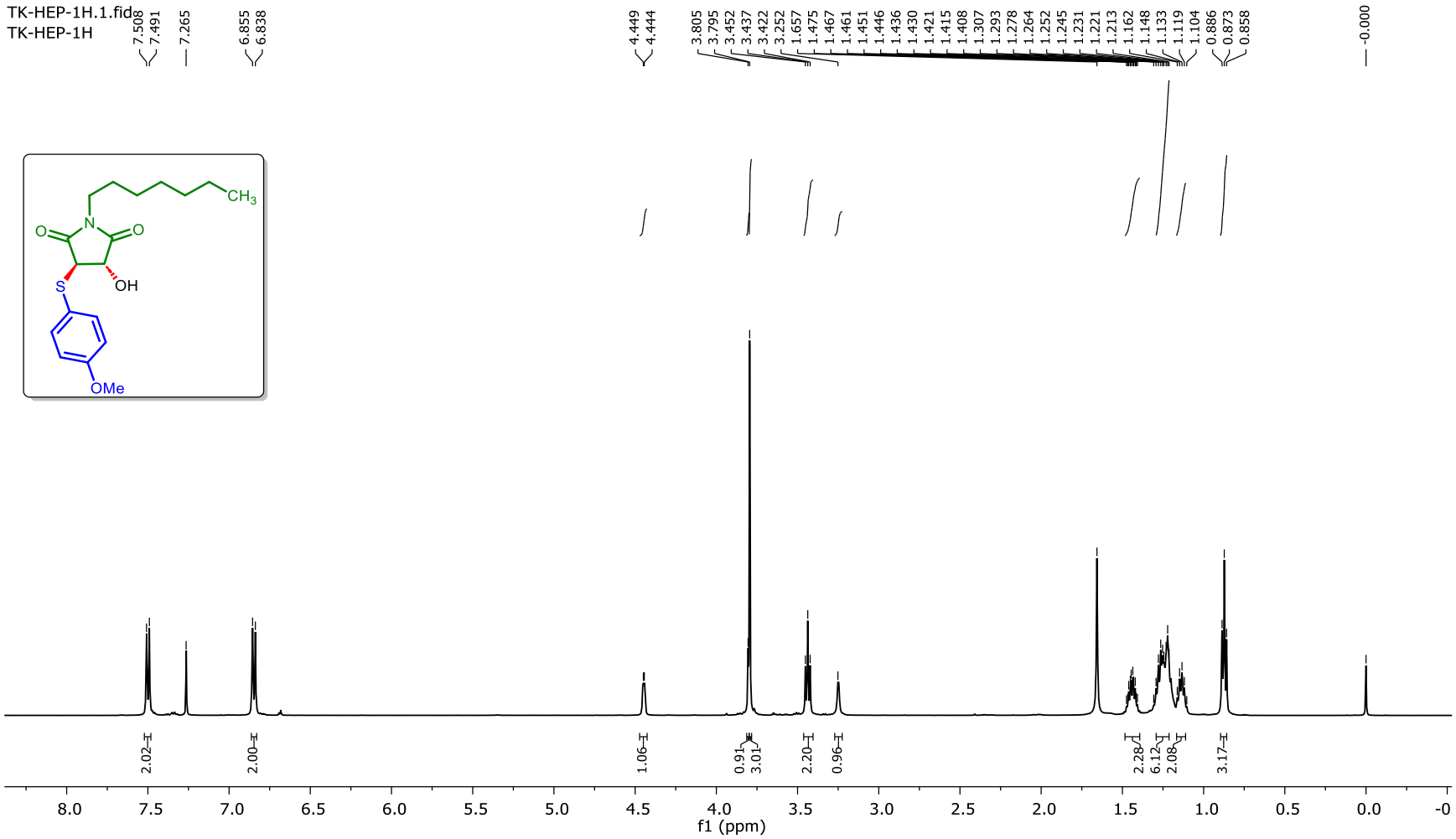
(3*S*,4*R*)-3-Hydroxy-1-isopentyl-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ma): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



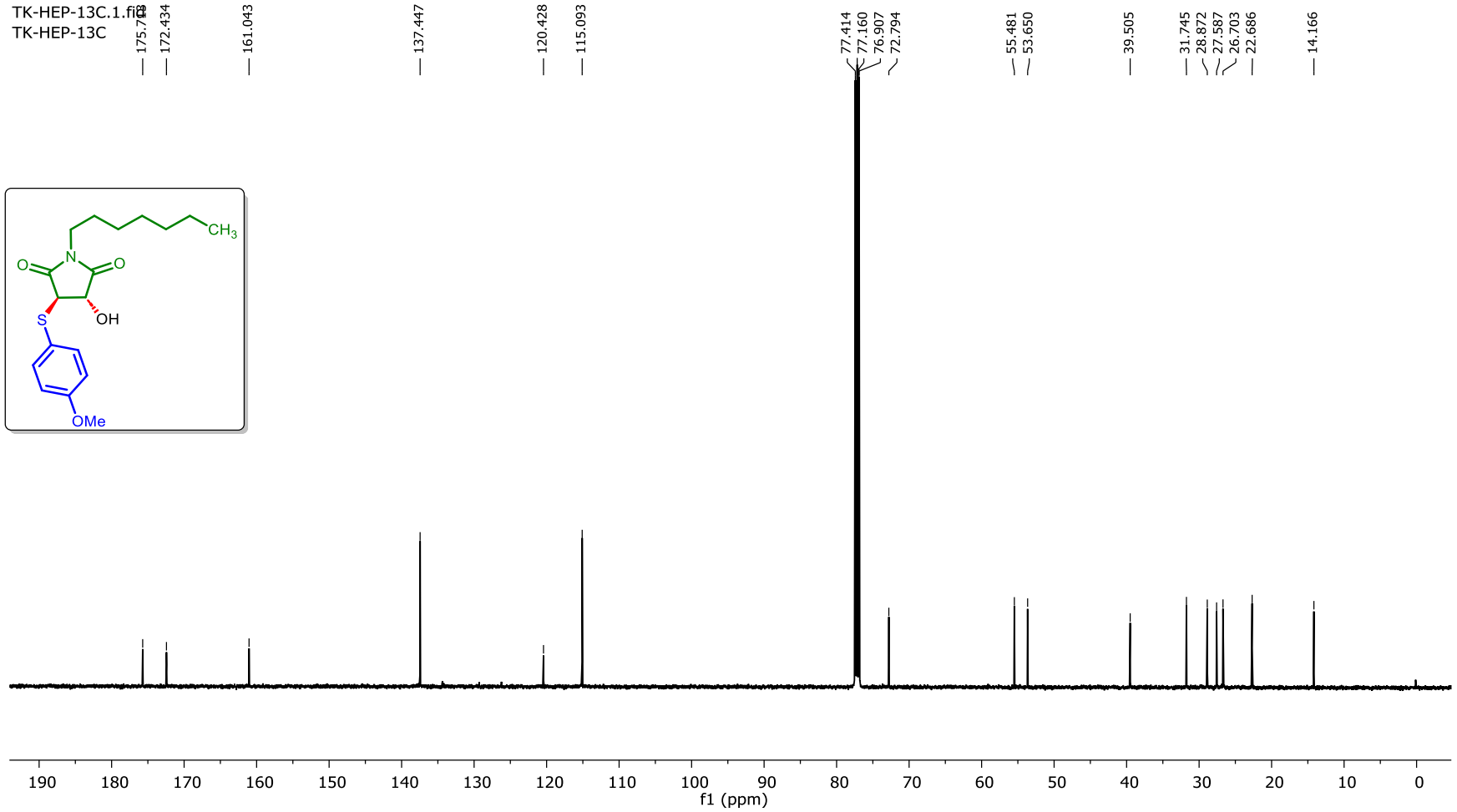
(3*S*,4*R*)-1-Hexyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3na): ^{1}H NMR ($CDCl_3$, 500 MHz)



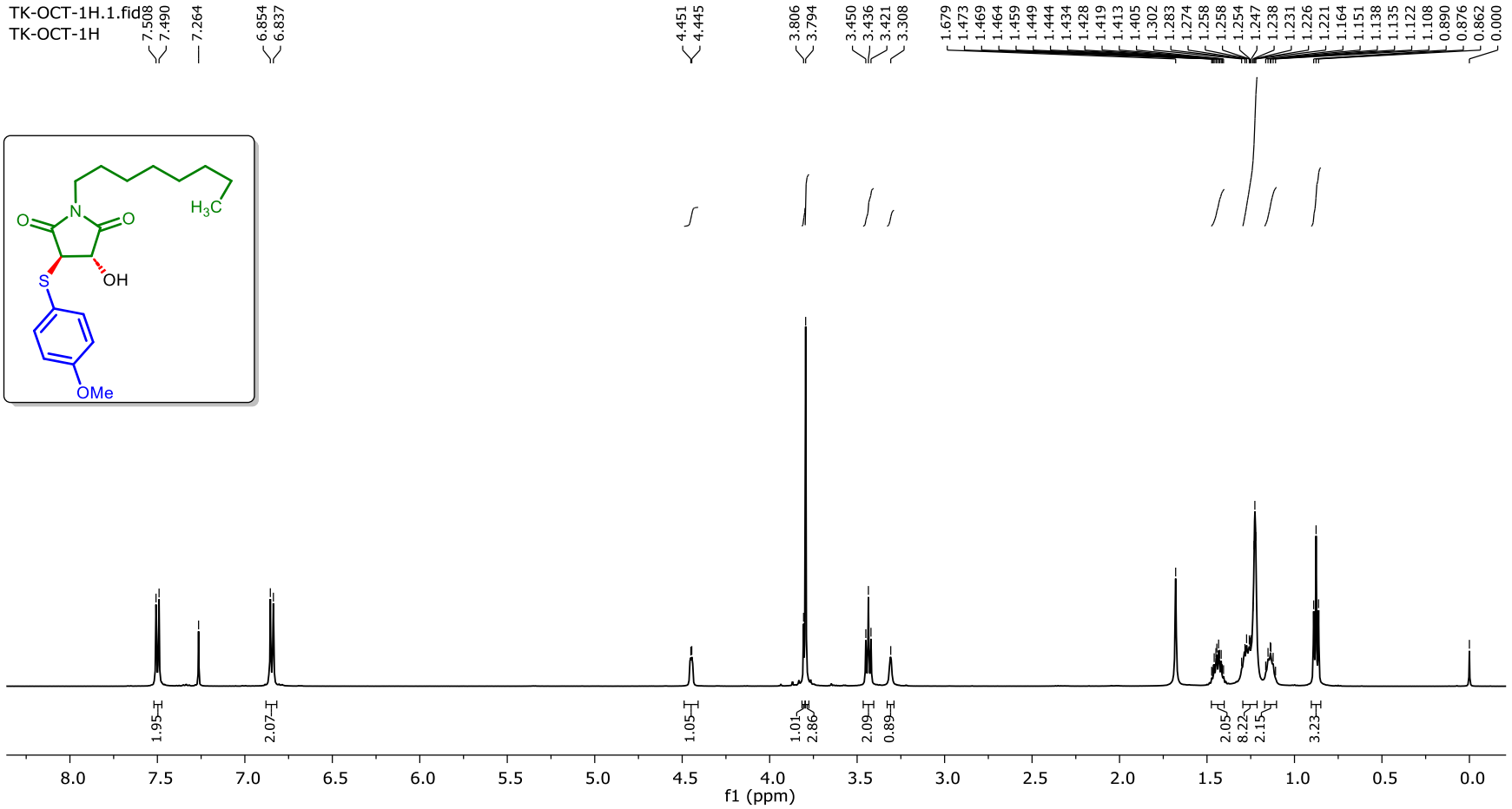
(3*S*,4*R*)-1-Hexyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3na): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



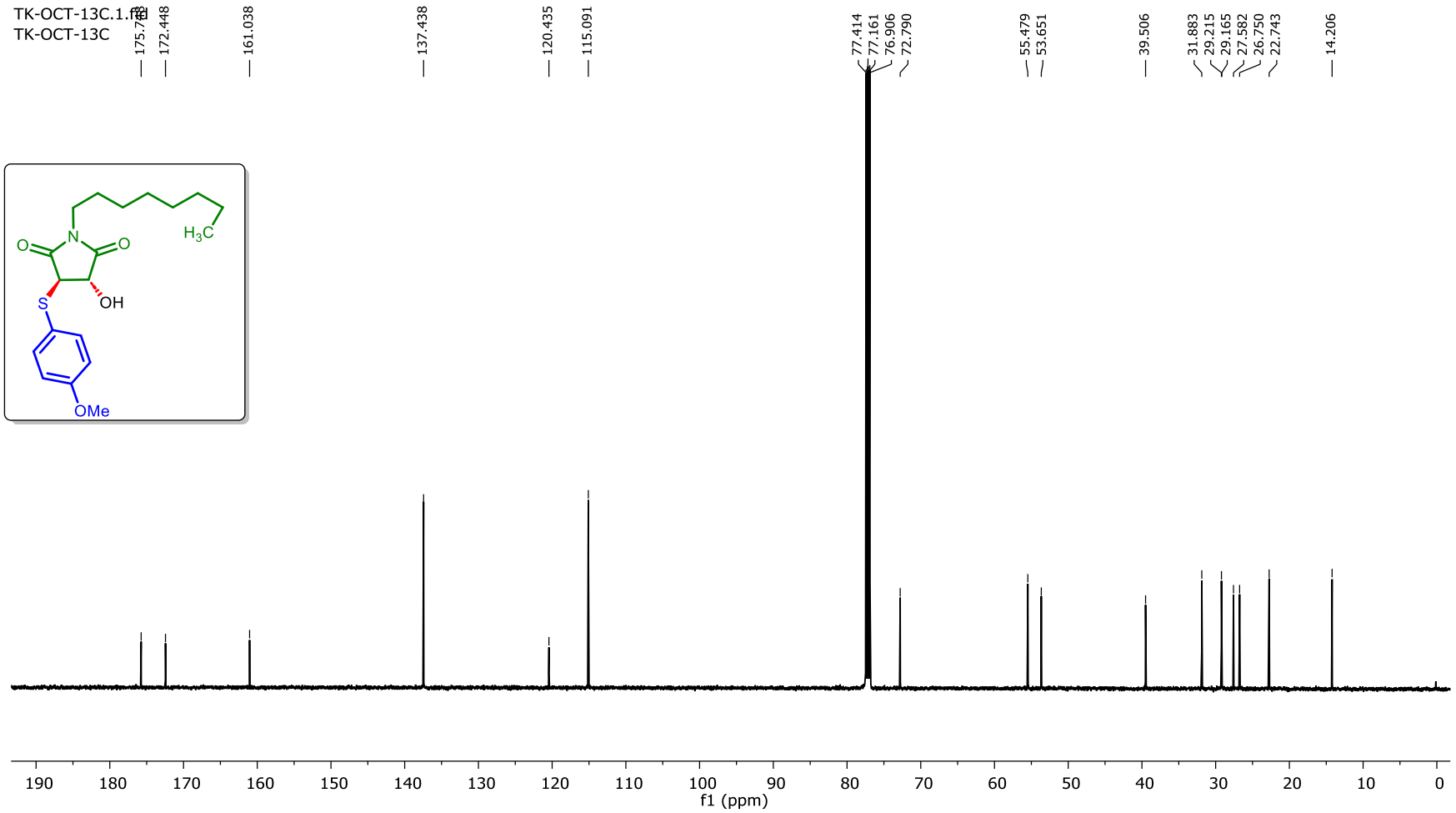
(3*S*,4*R*)-1-Heptyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3oa): ^{1}H NMR ($CDCl_3$, 500 MHz)



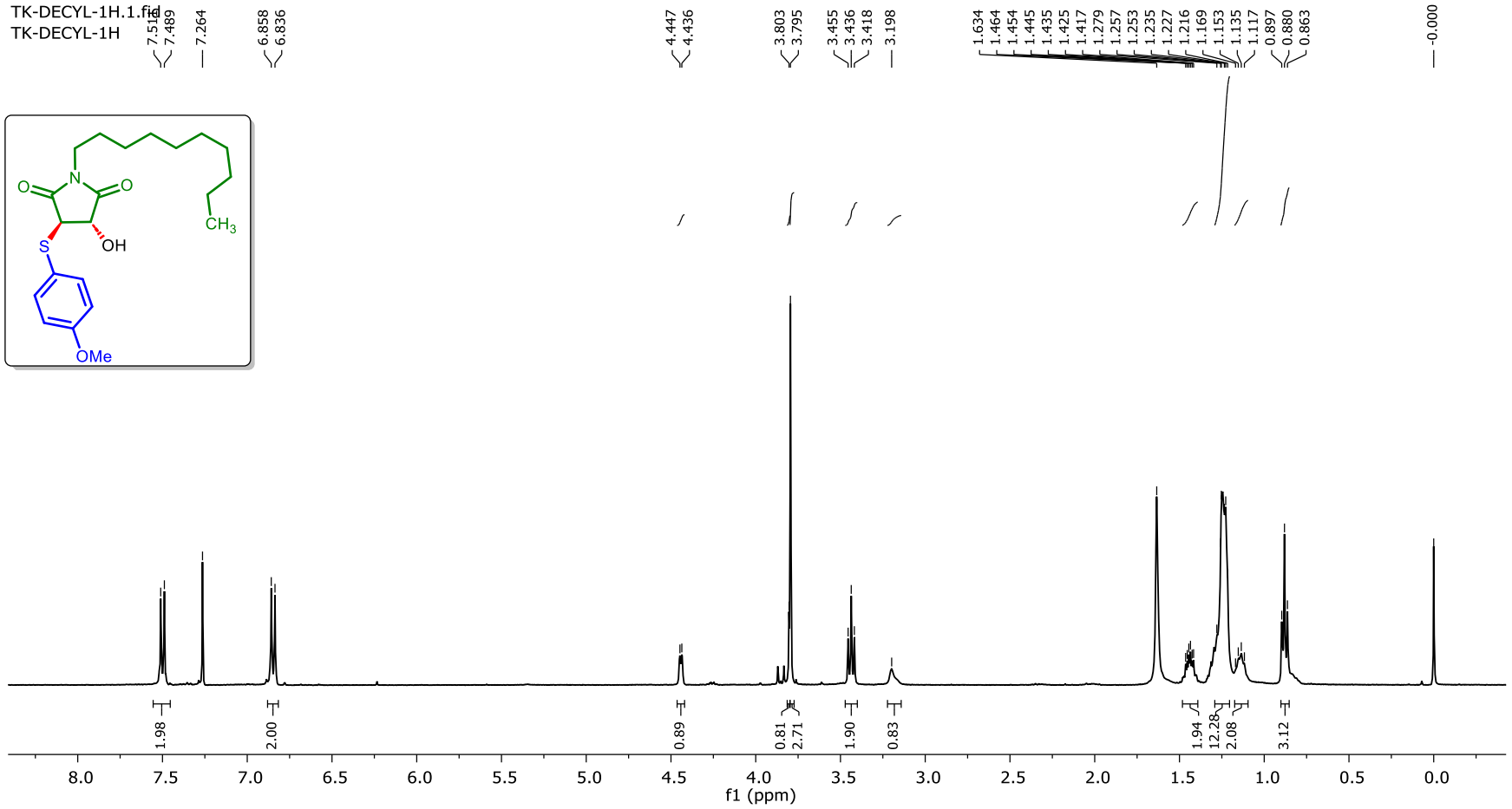
(3*S*,4*R*)-1-Heptyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3oa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



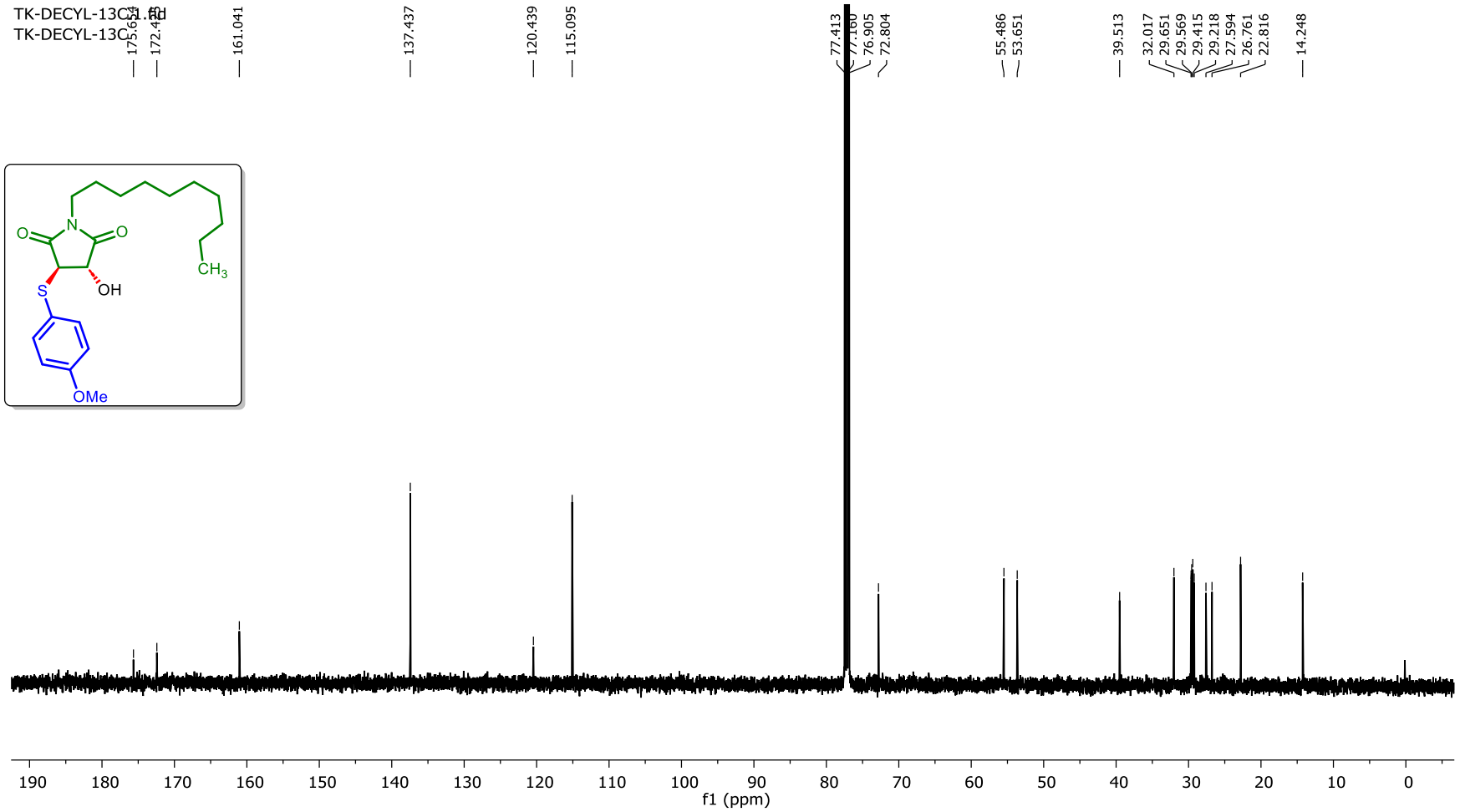
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-octylpyrrolidine-2,5-dione (3pa): ^{1}H NMR ($CDCl_3$, 500 MHz)



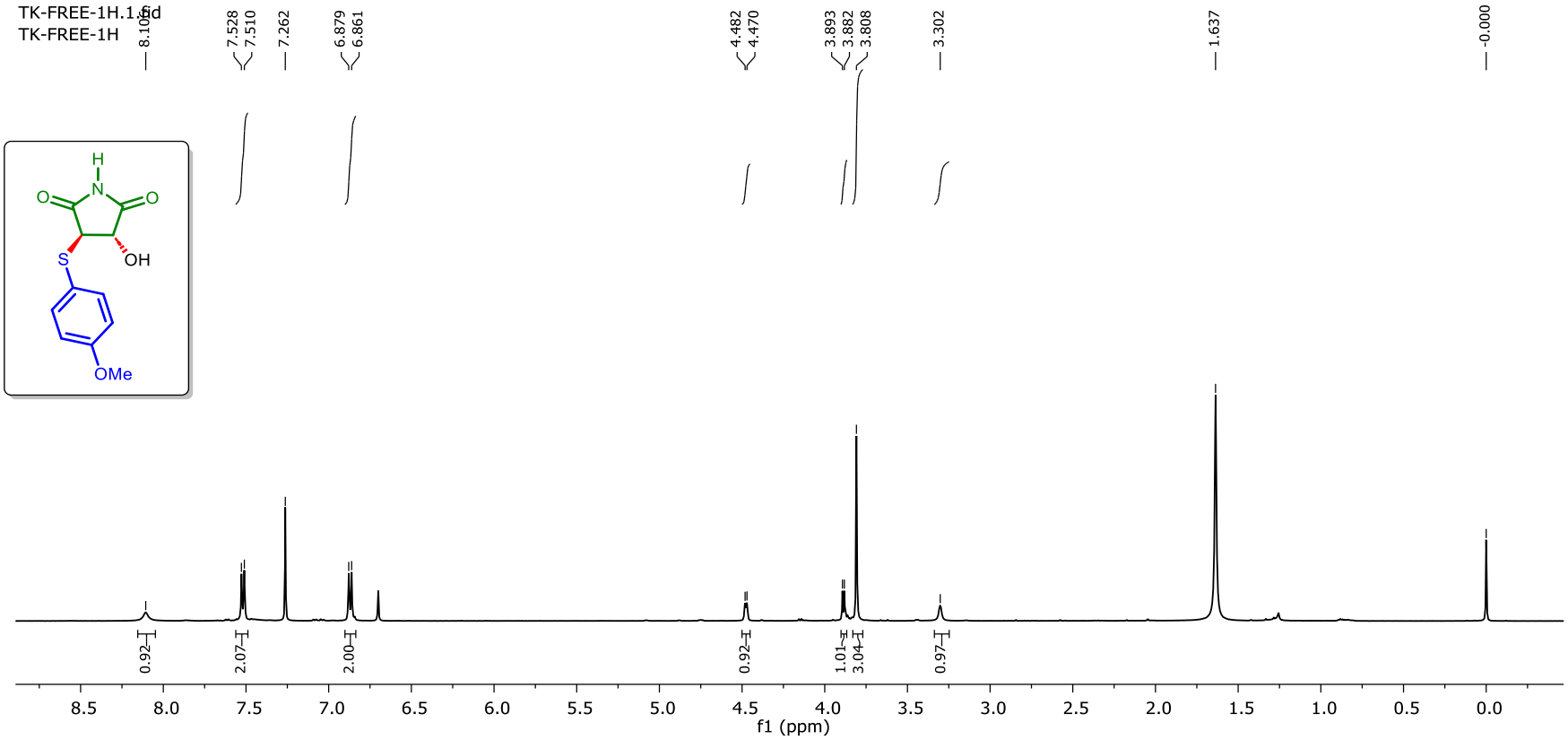
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-octylpyrrolidine-2,5-dione (3pa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



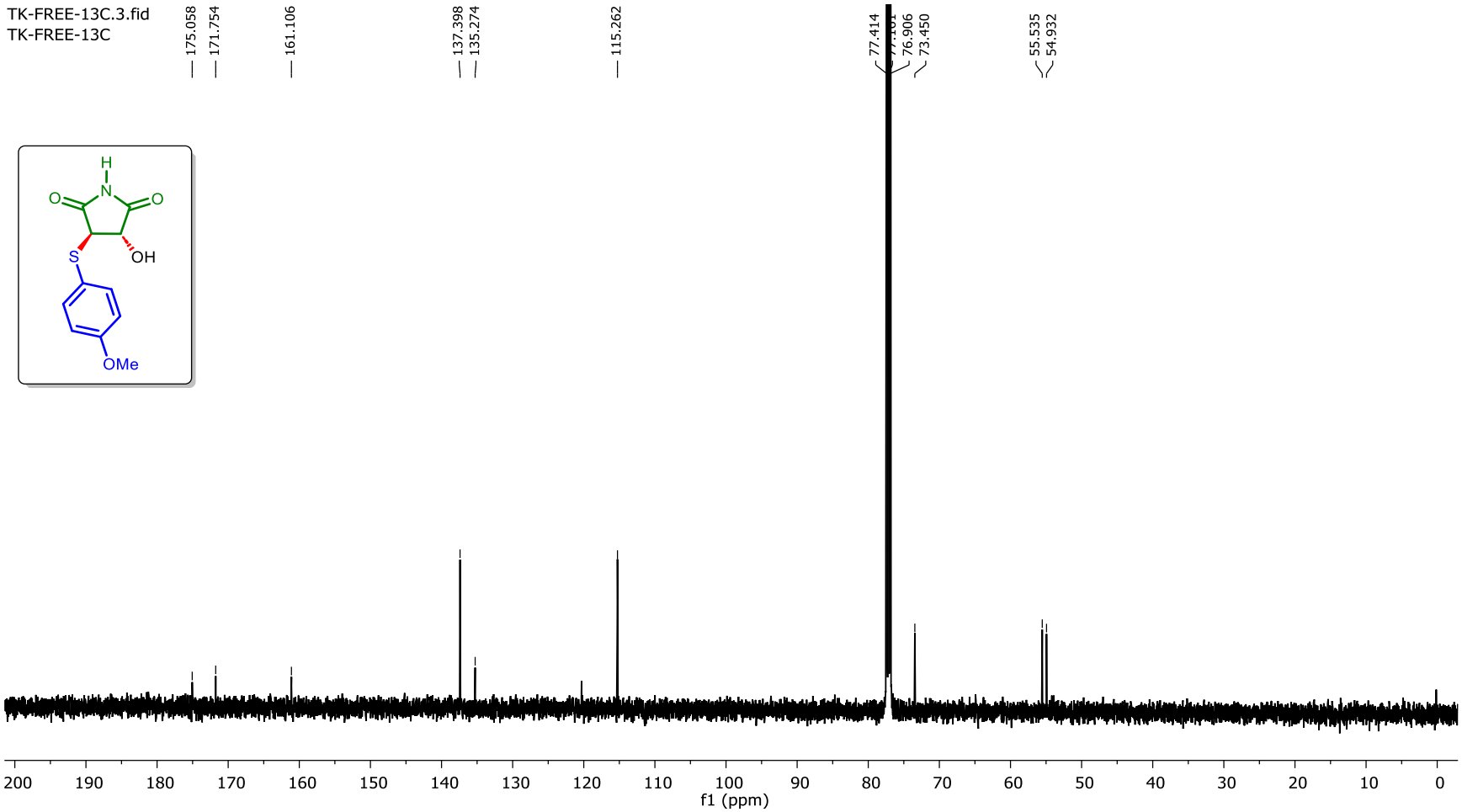
(3*S*,4*R*)-1-Decyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3qa): ^{1}H NMR ($CDCl_3$, 400 MHz)



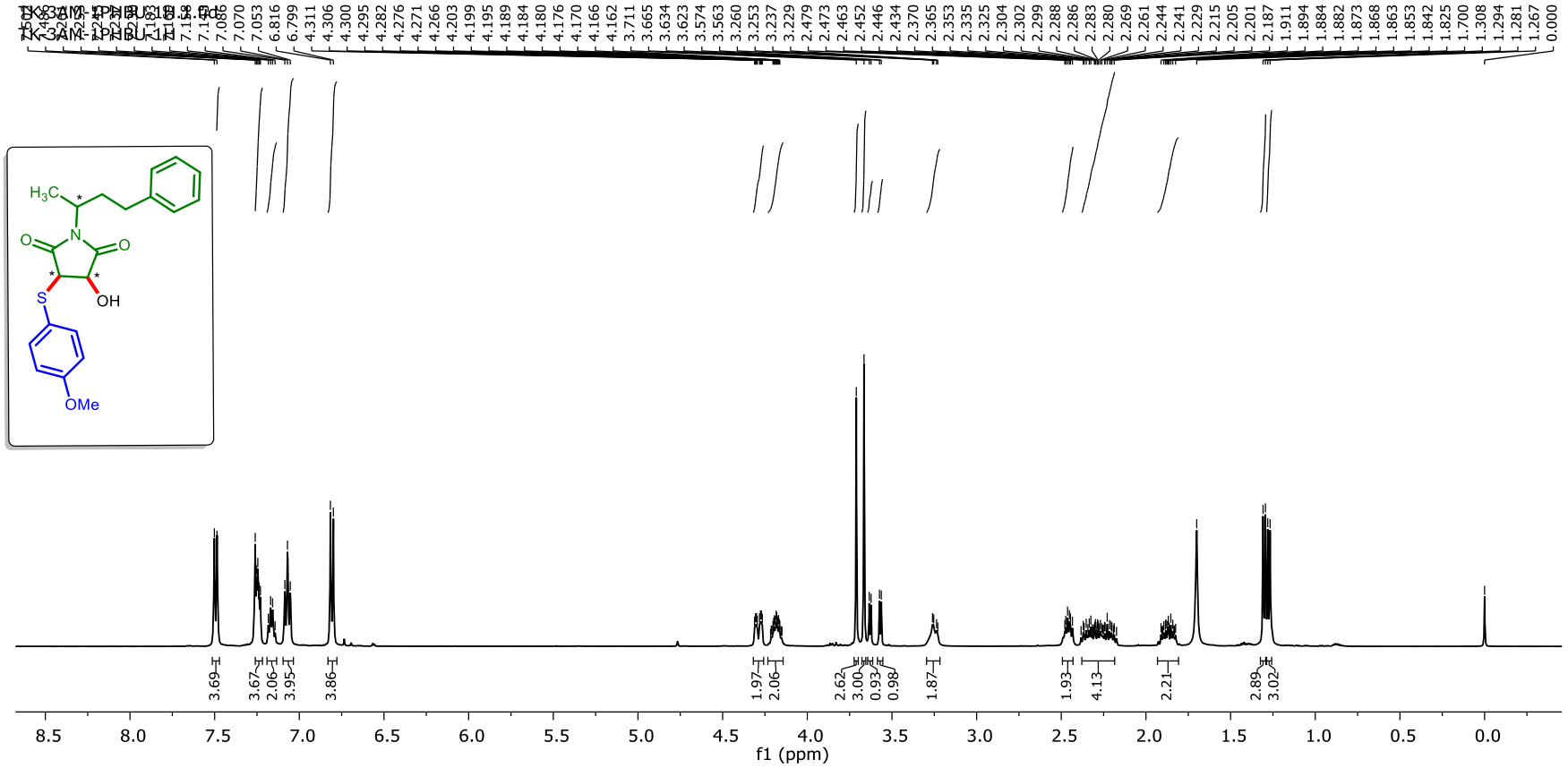
(3*S*,4*R*)-1-Decyl-3-hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3qa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



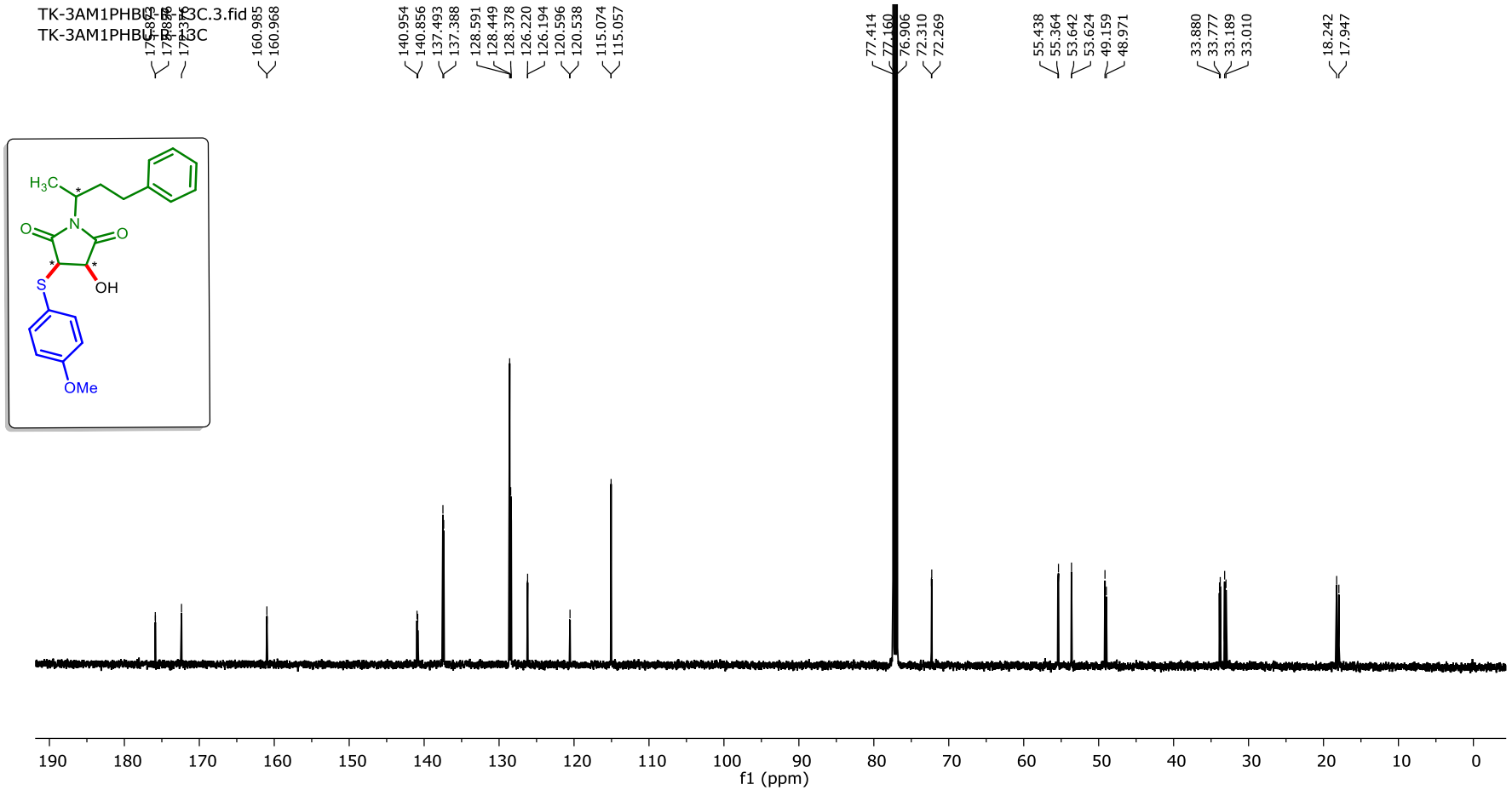
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ra): ^{1}H NMR ($CDCl_3$, 500 MHz)



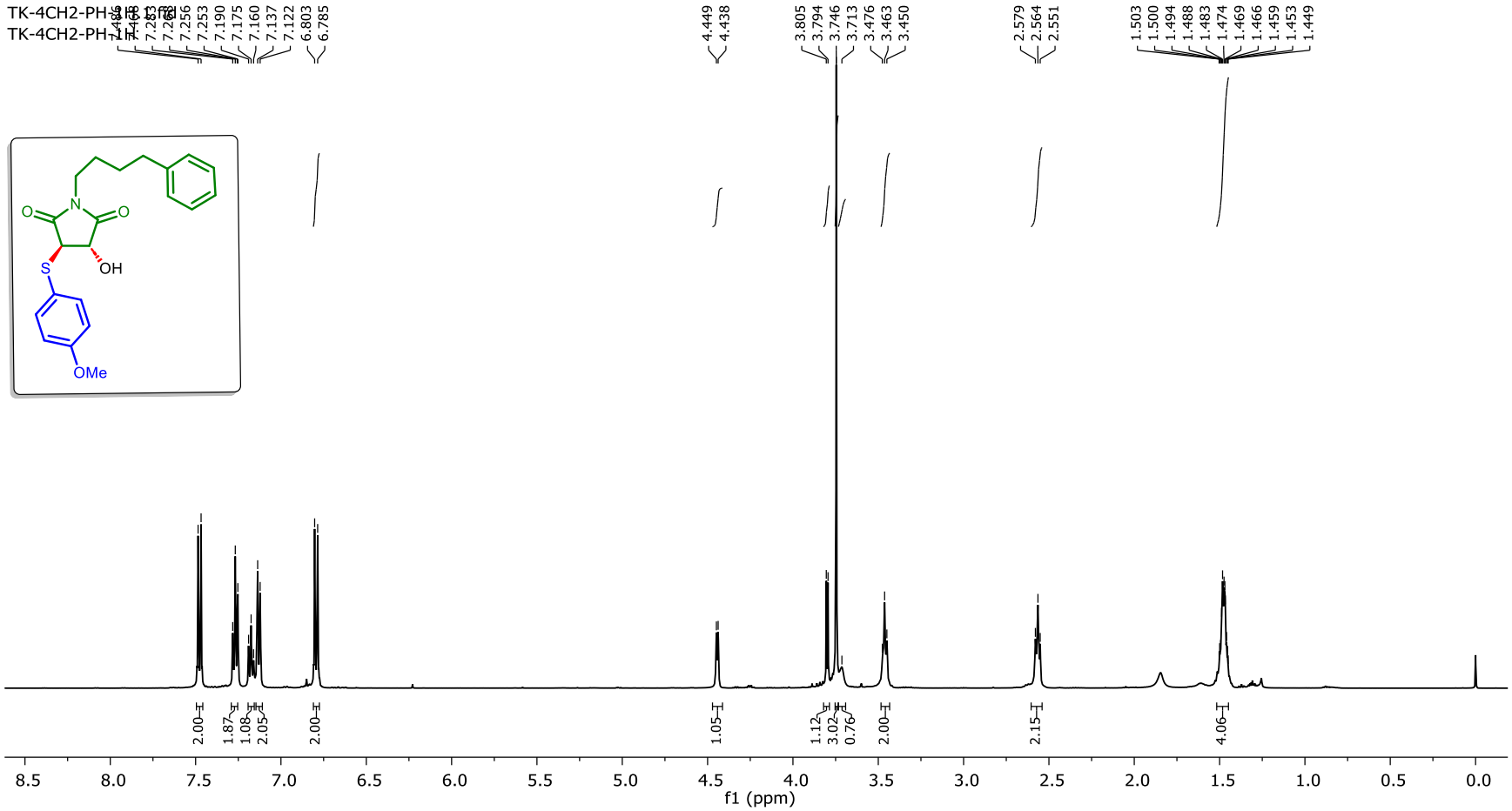
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)pyrrolidine-2,5-dione (3ra): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



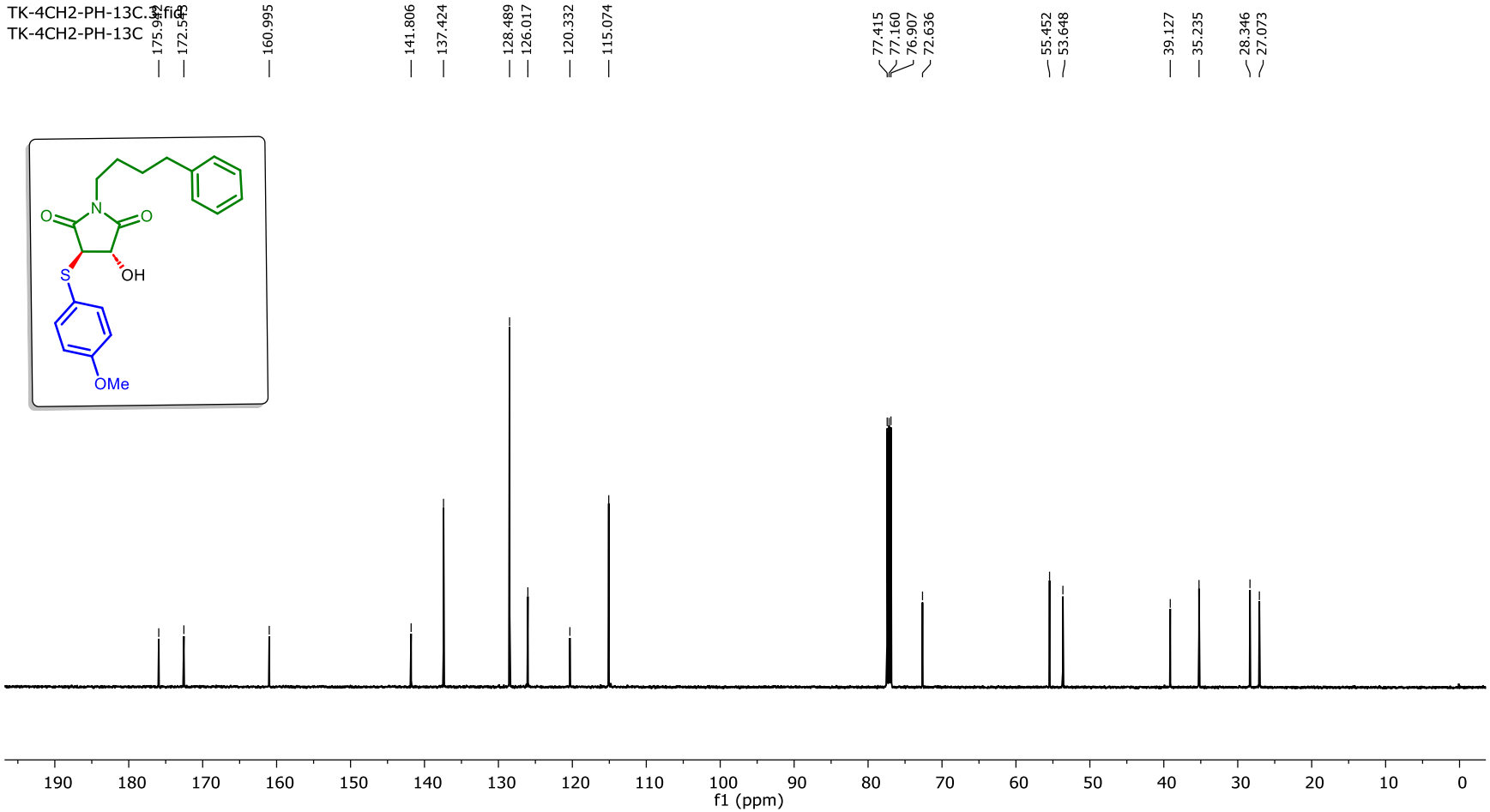
3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutan-2-yl)pyrrolidine-2,5-dione (3sa): ^{1}H NMR ($CDCl_3$, 500 MHz)



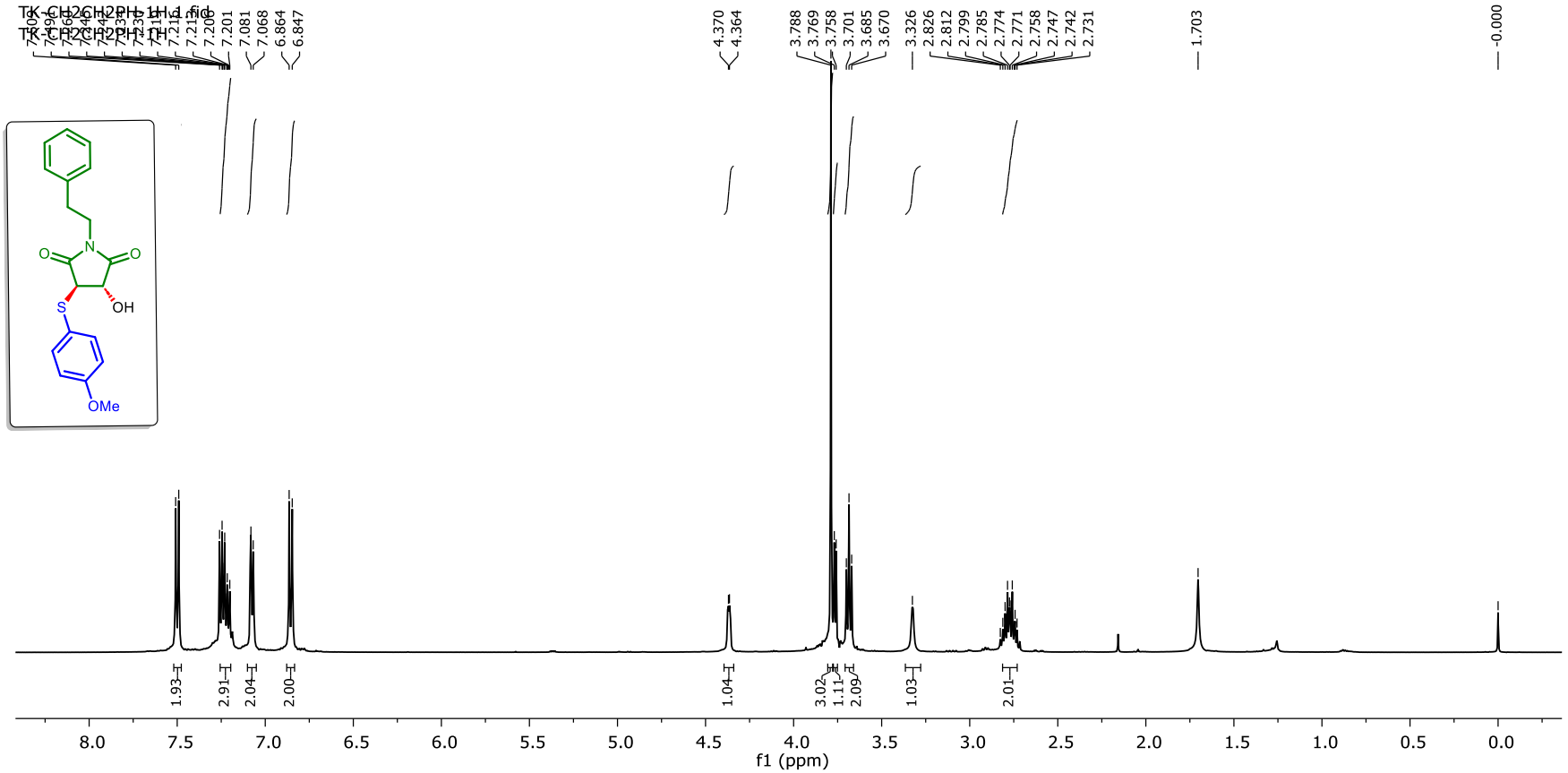
3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutan-2-yl)pyrrolidine-2,5-dione (3sa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



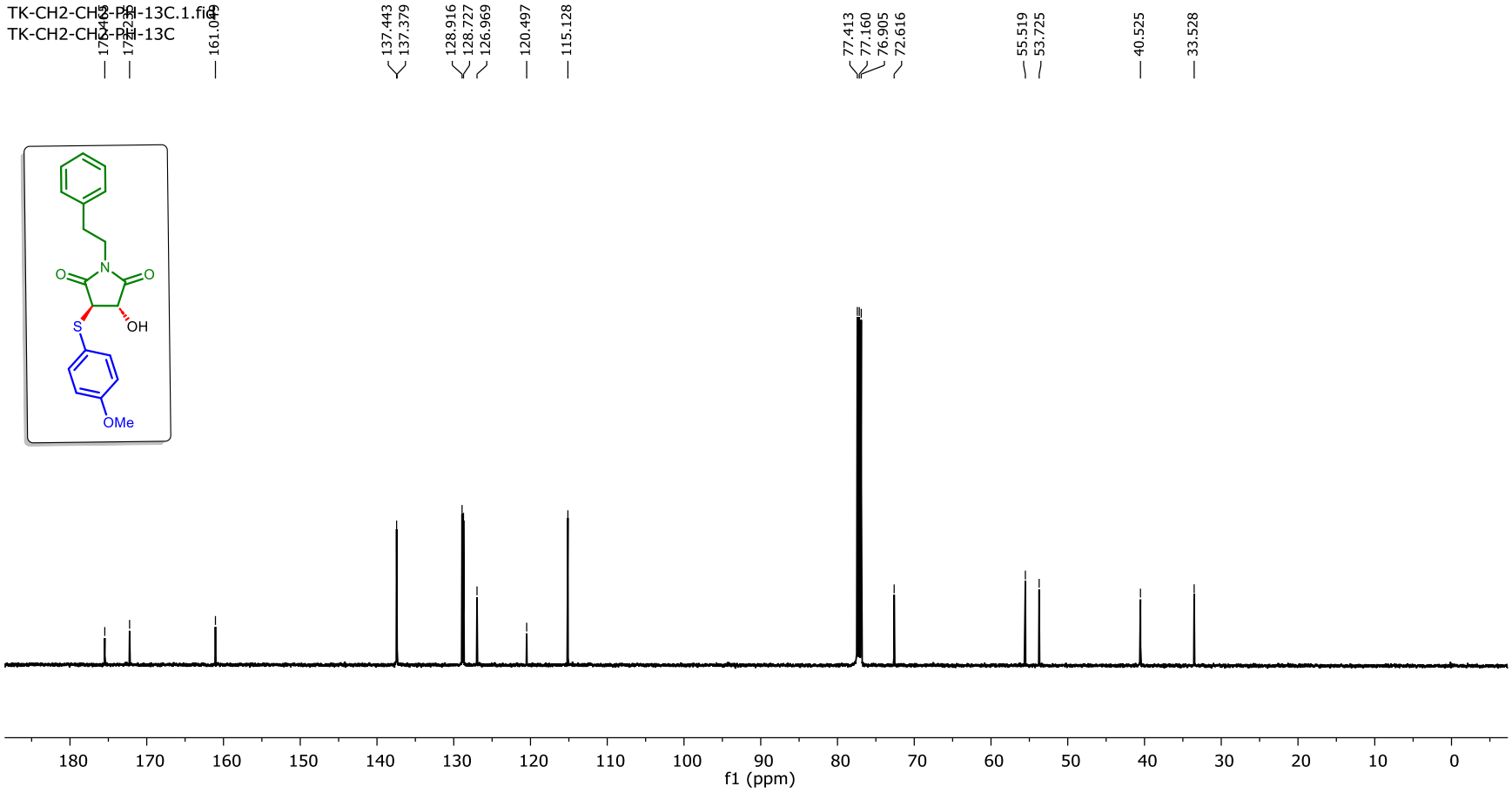
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutyl)pyrrolidine-2,5-dione (3ta): ^{1}H NMR ($CDCl_3$, 500 MHz)



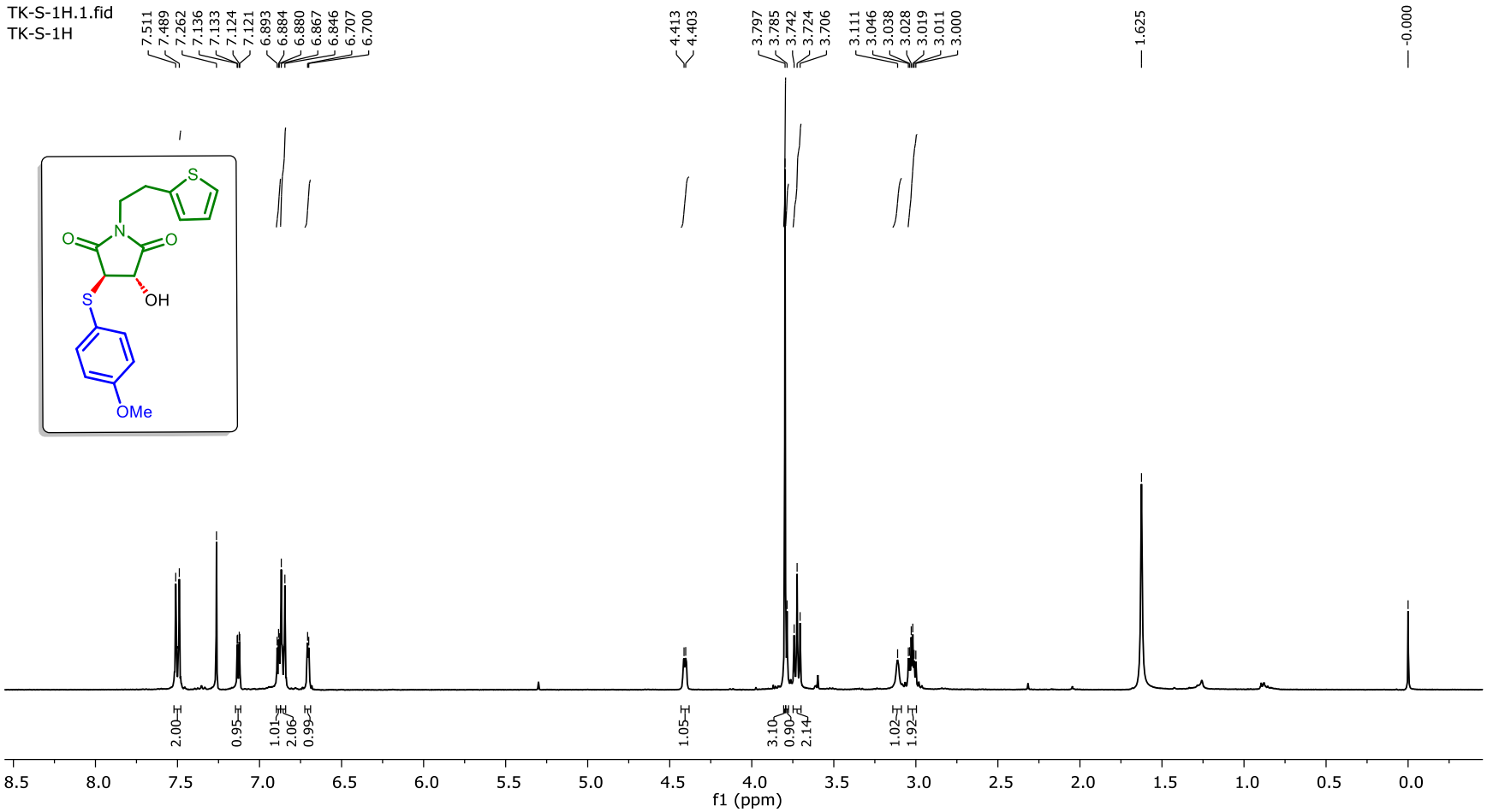
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(4-phenylbutyl)pyrrolidine-2,5-dione (3ta): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



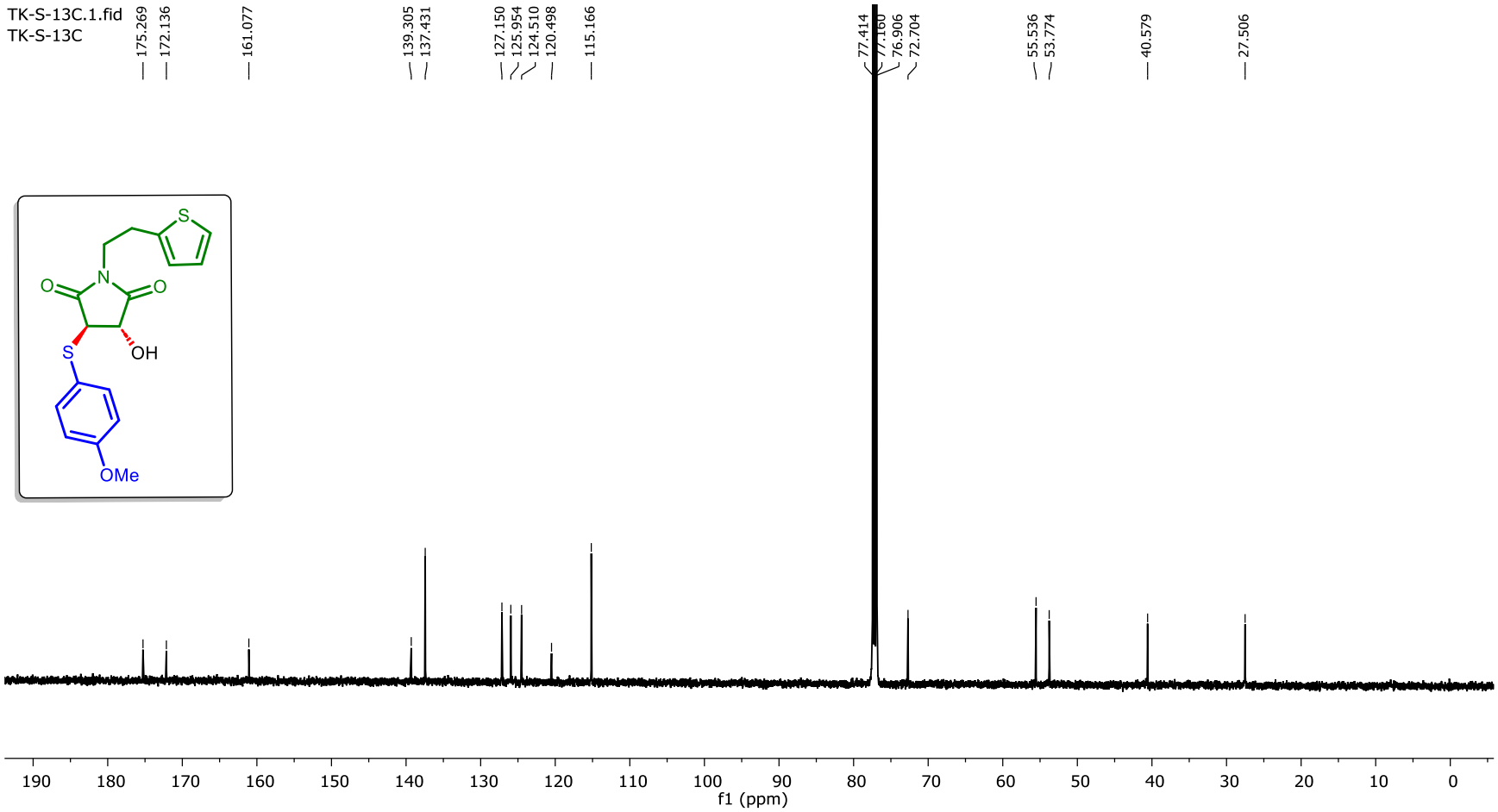
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenethylpyrrolidine-2,5-dione (3ua): ^{1}H NMR ($CDCl_3$, 500 MHz)



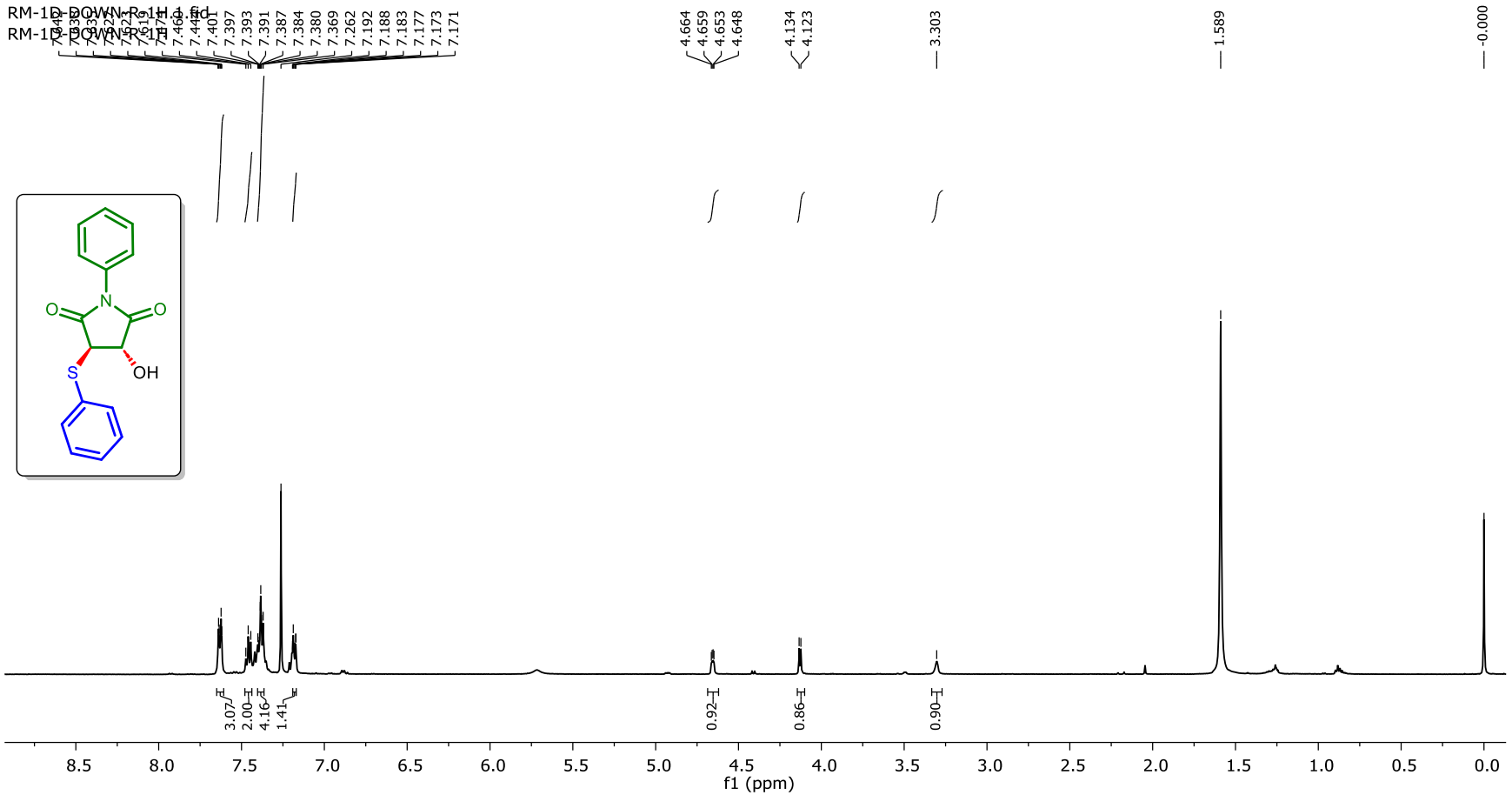
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-phenethylpyrrolidine-2,5-dione (3ua): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



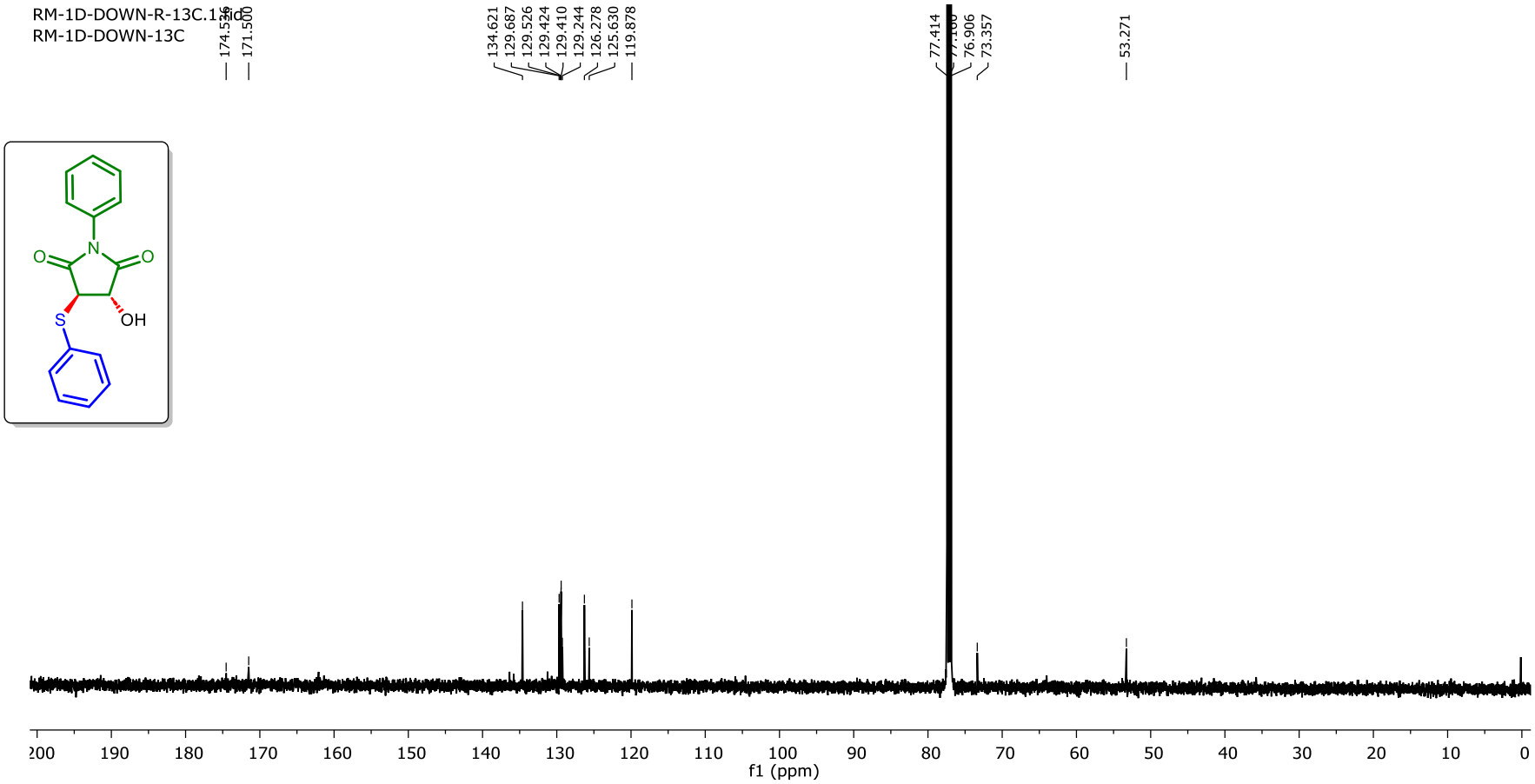
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(2-(thiophen-2-yl)ethyl)pyrrolidine-2,5-dione (3va): ^{1}H NMR ($CDCl_3$, 400 MHz)



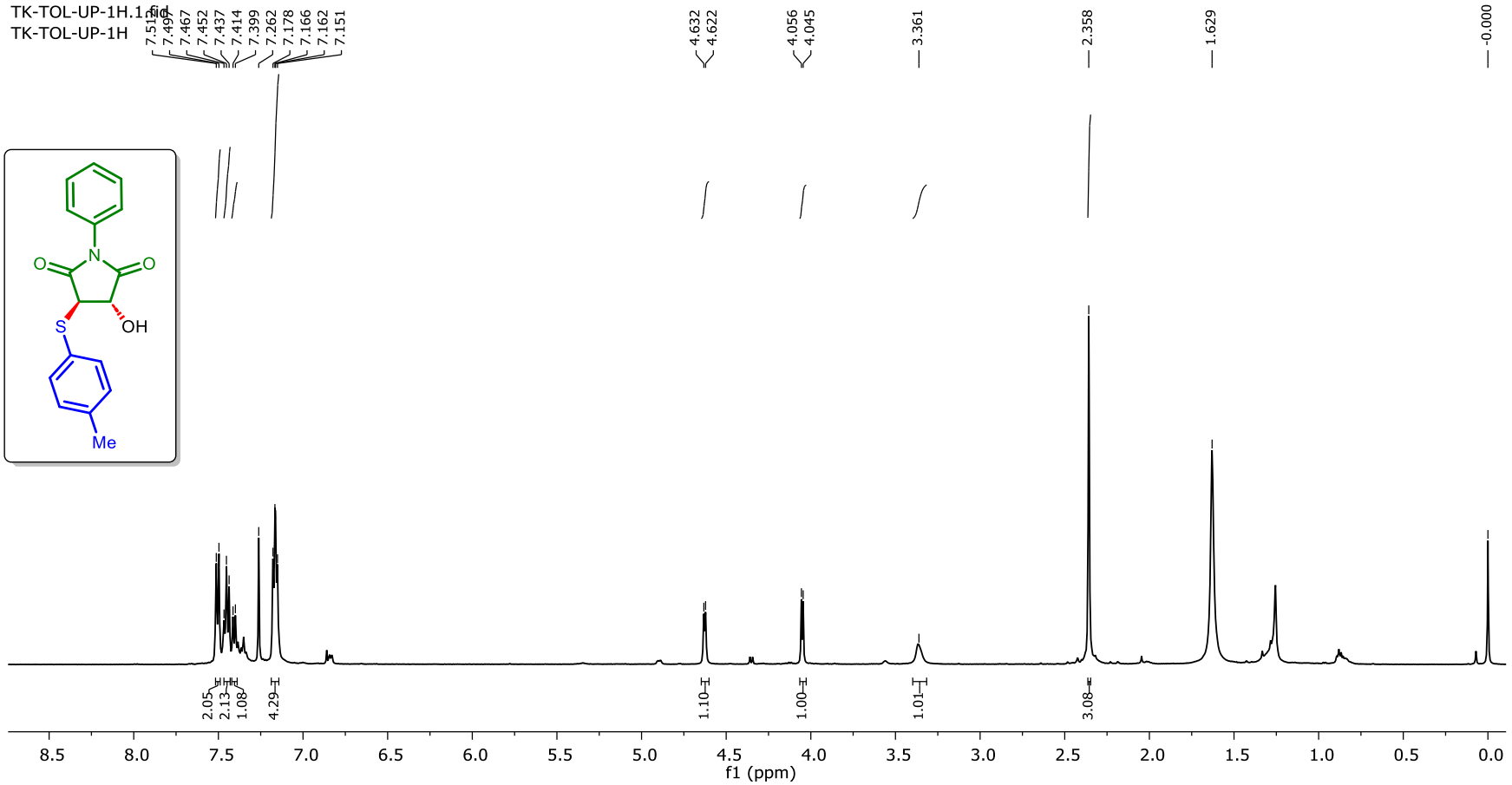
(3*S*,4*R*)-3-Hydroxy-4-((4-methoxyphenyl)thio)-1-(2-(thiophen-2-yl)ethyl)pyrrolidine-2,5-dione (3va): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



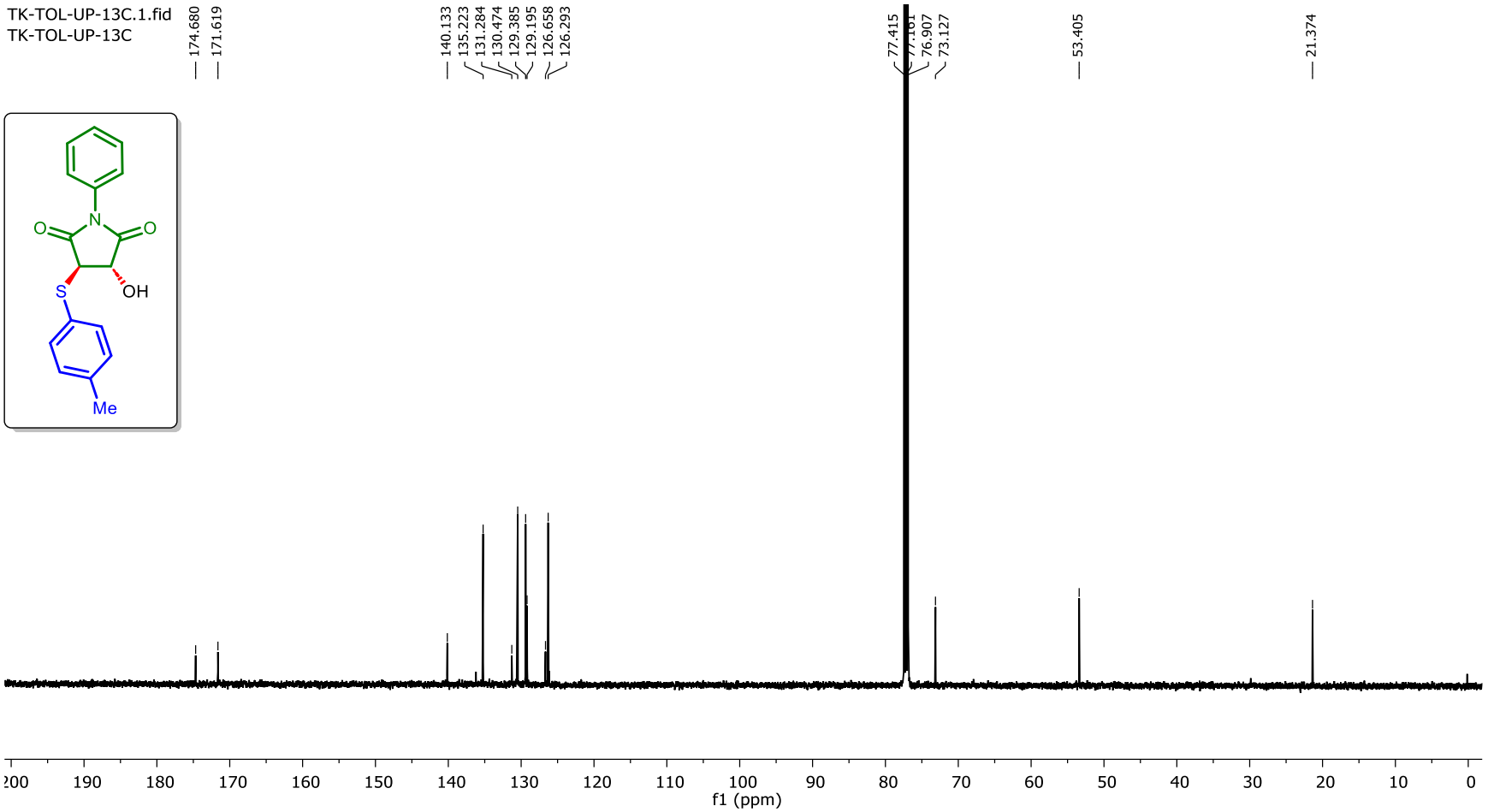
(3*S*,4*R*)-3-Hydroxy-1-phenyl-4-(phenylthio)pyrrolidine-2,5-dione (3ab): ^{1}H NMR ($CDCl_3$, 500 MHz)



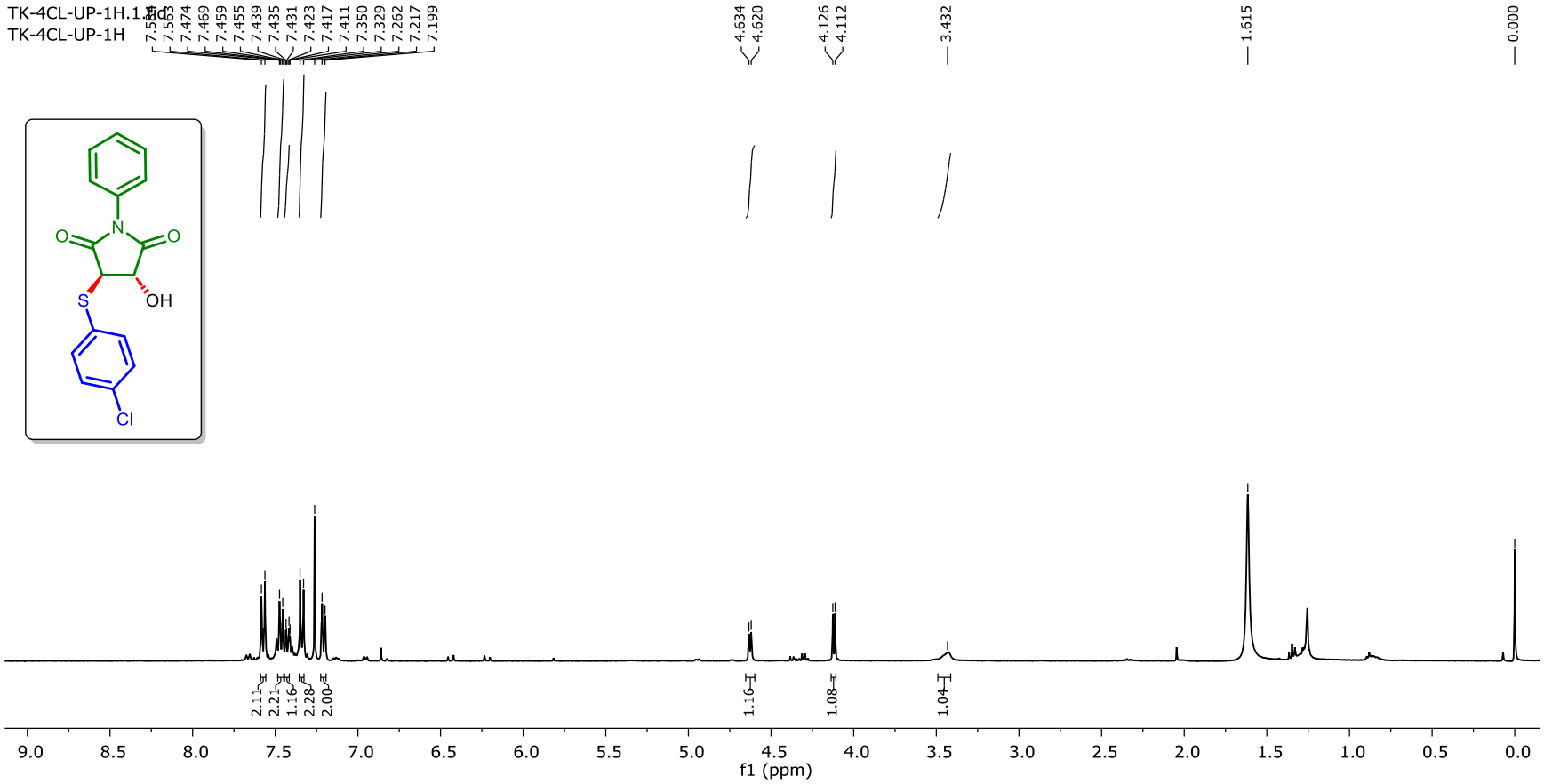
(3*S*,4*R*)-3-Hydroxy-1-phenyl-4-(phenylthio)pyrrolidine-2,5-dione (3ab): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



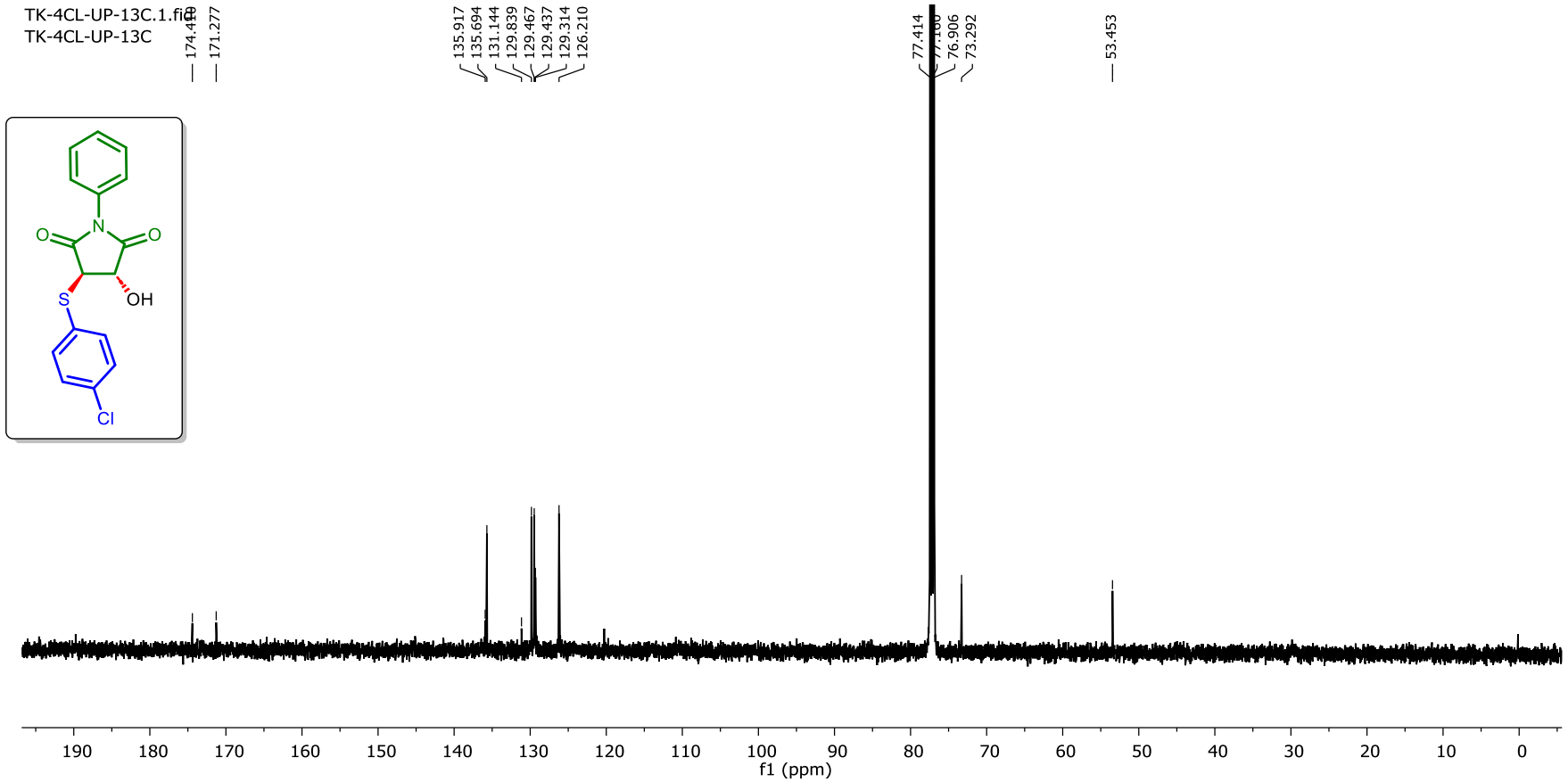
(3*S*,4*R*)-3-Hydroxy-1-phenyl-4-(*p*-tolylthio)pyrrolidine-2,5-dione (3ac): ^{1}H NMR ($CDCl_3$, 500 MHz)



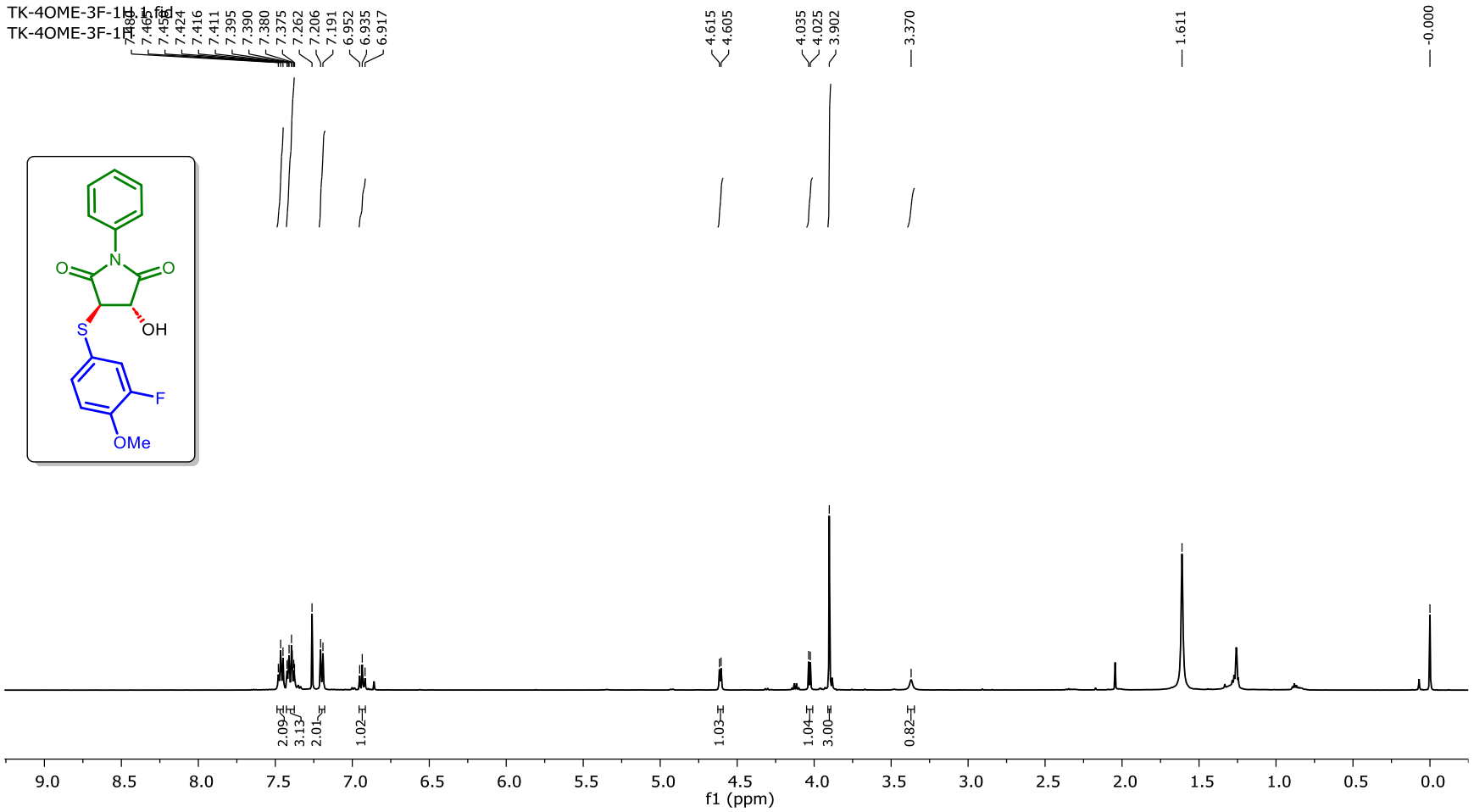
(3*S*,4*R*)-3-Hydroxy-1-phenyl-4-(*p*-tolylthio)pyrrolidine-2,5-dione (3ac): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



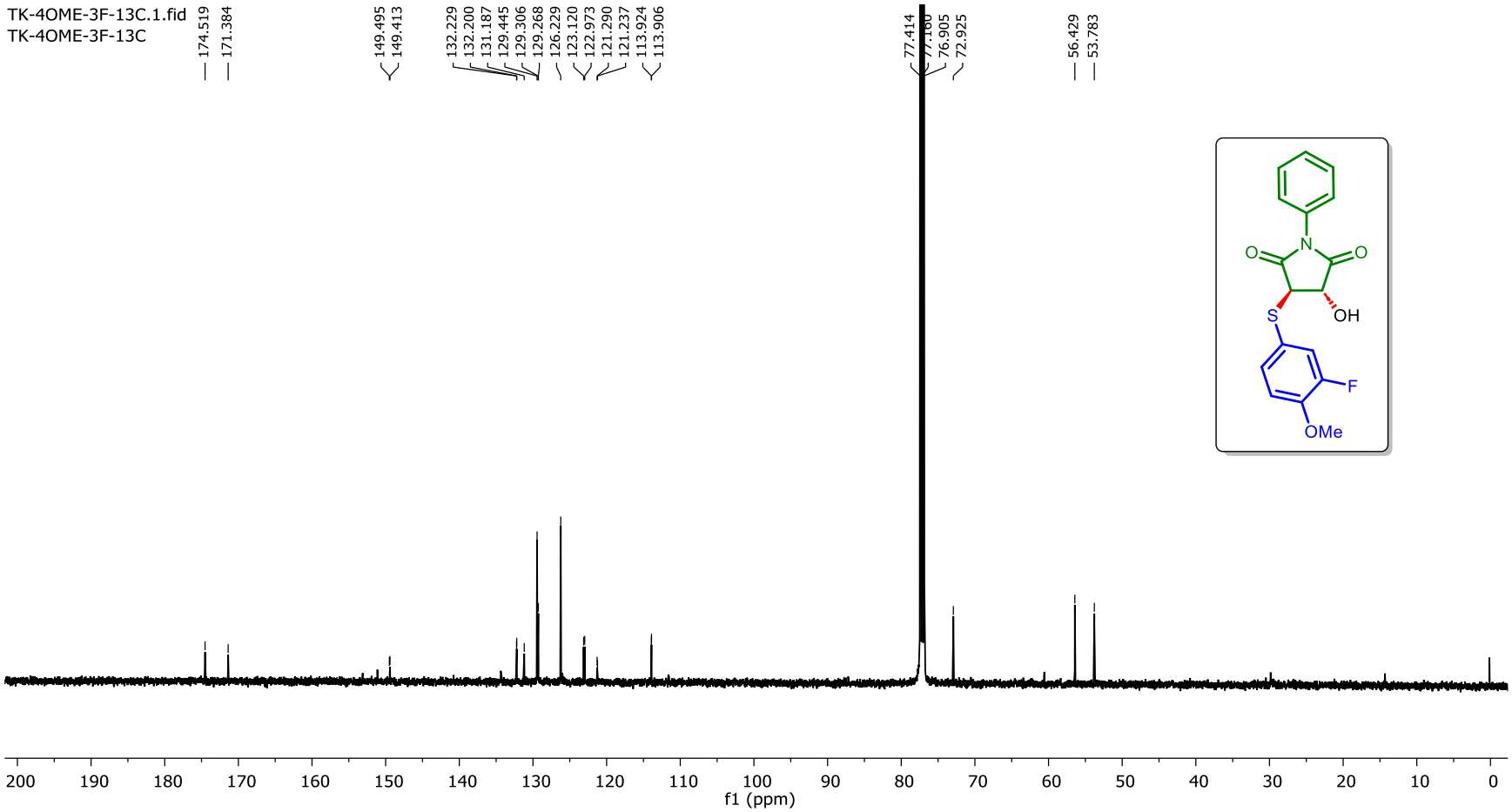
(3*R*,4*S*)-3-((4-Chlorophenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ad): ^{1}H NMR ($CDCl_3$, 400 MHz)



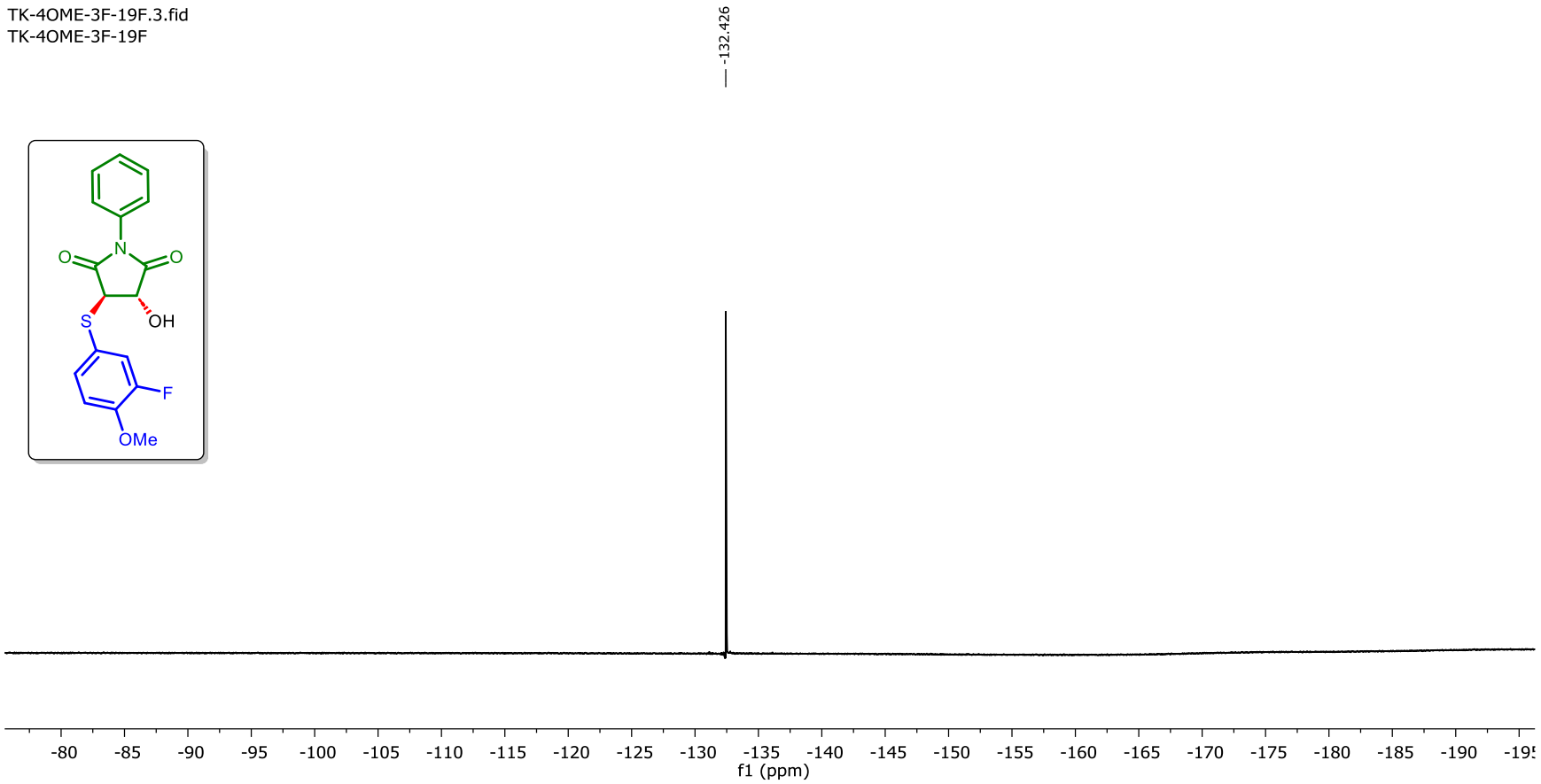
(3*R*,4*S*)-3-((4-Chlorophenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ad): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



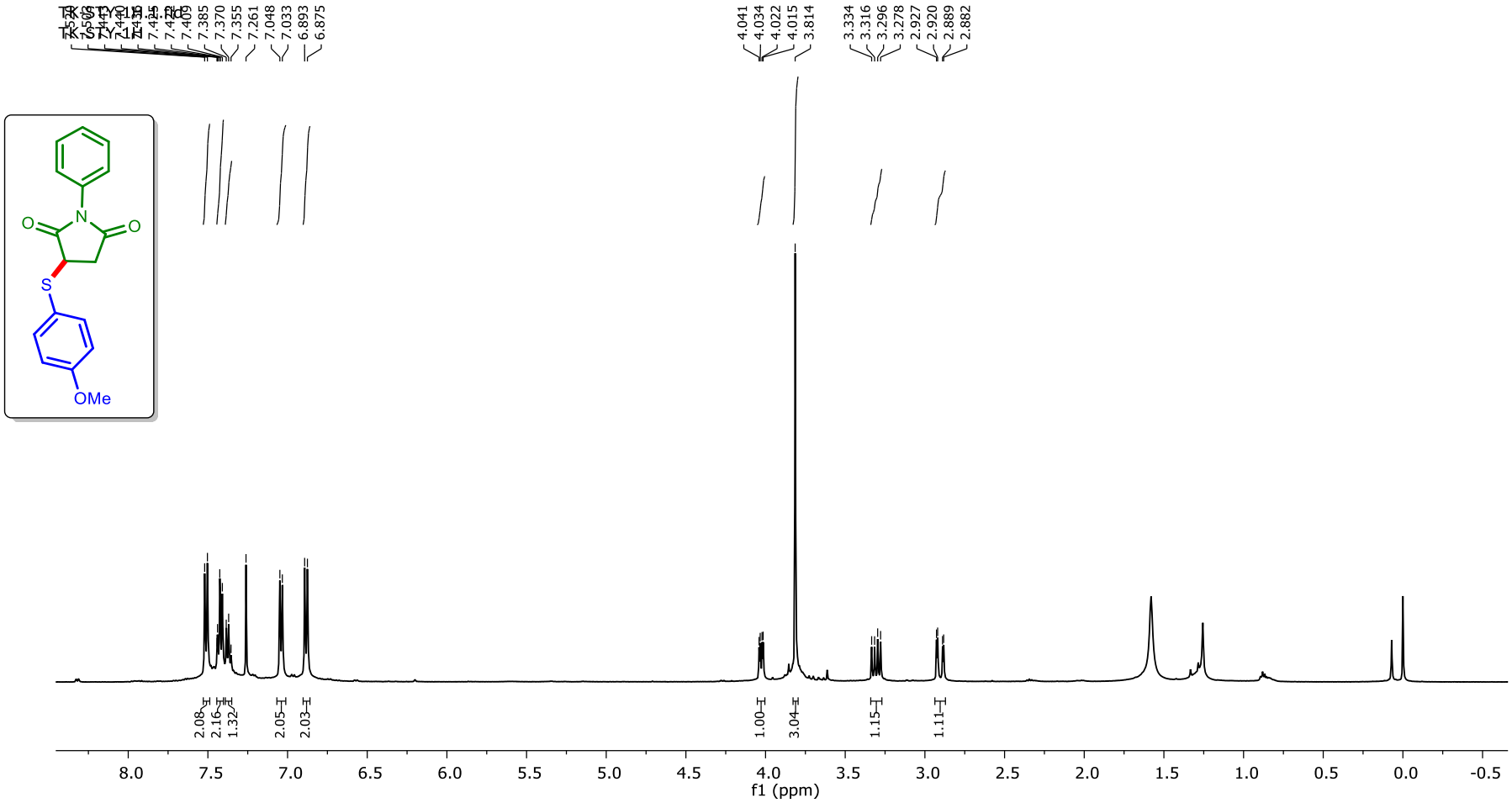
(3*R*,4*S*)-3-((3-Fluoro-4-methoxyphenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ae): ^{1}H NMR ($CDCl_3$, 500 MHz)



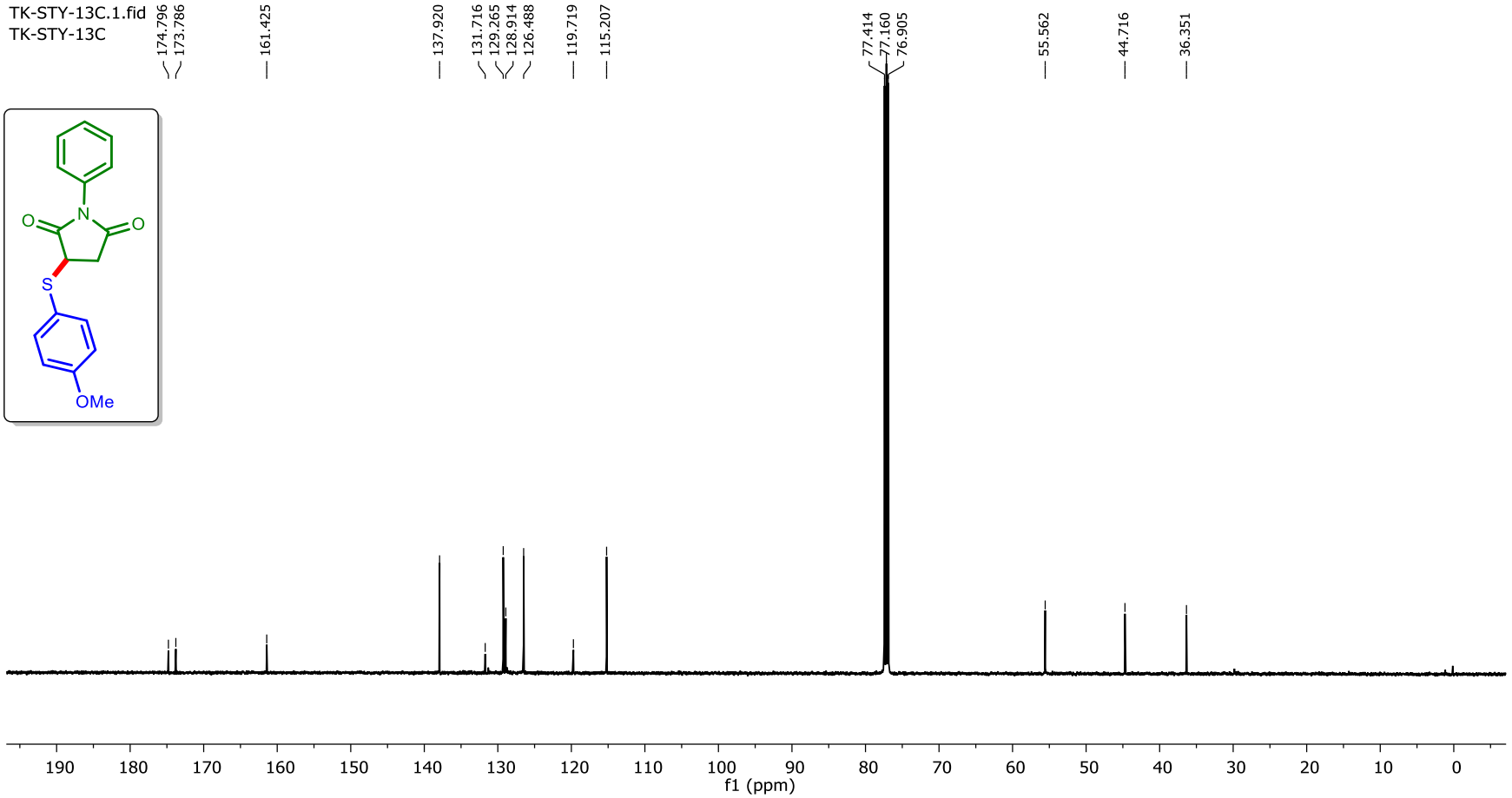
(3*R*,4*S*)-3-((3-Fluoro-4-methoxyphenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ae): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



(3*R*,4*S*)-3-((3-Fluoro-4-methoxyphenyl)thio)-4-hydroxy-1-phenylpyrrolidine-2,5-dione (3ae): ^{19}F NMR ($CDCl_3$, 471 MHz)



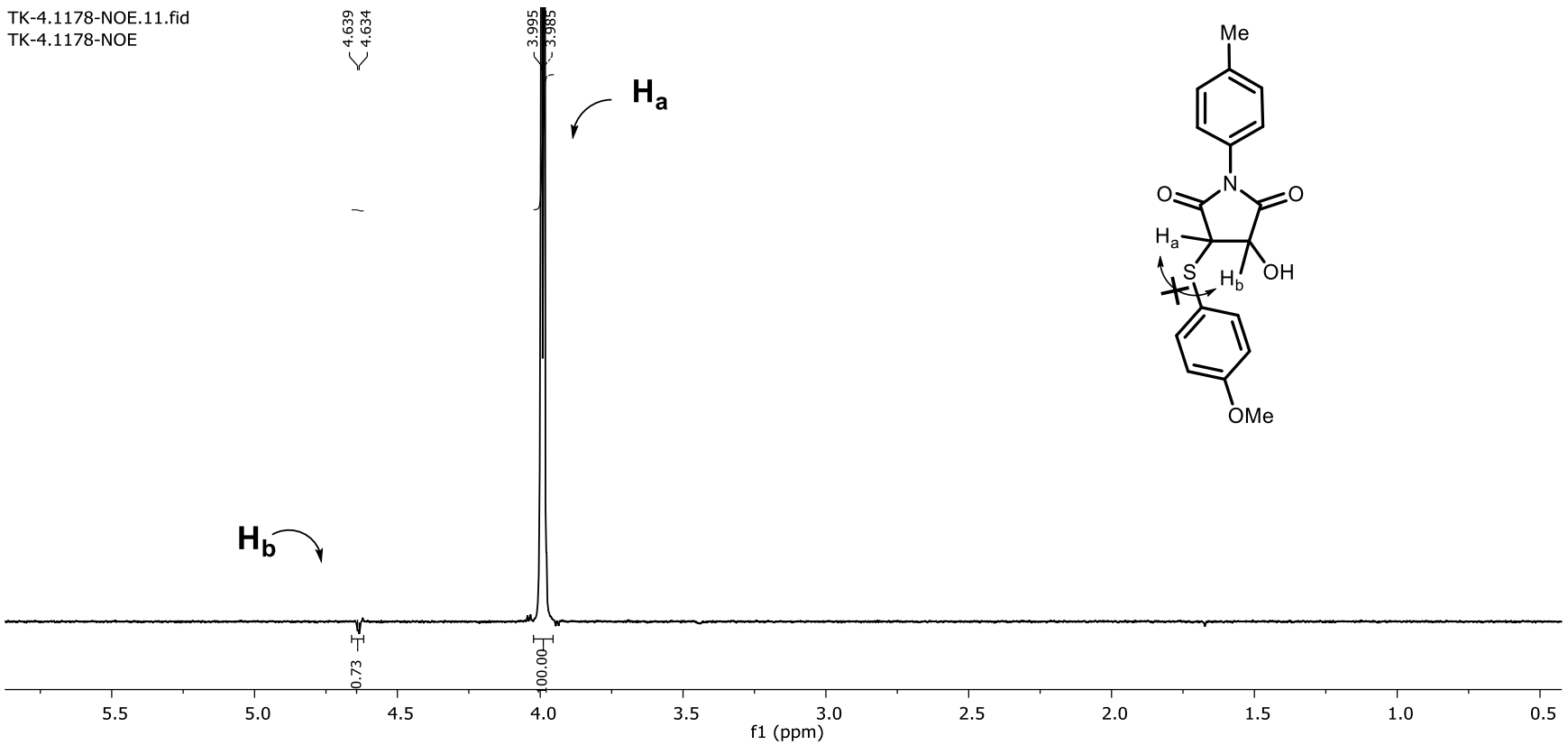
3-((4-methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (6aa): ^{1}H NMR ($CDCl_3$, 500 MHz)

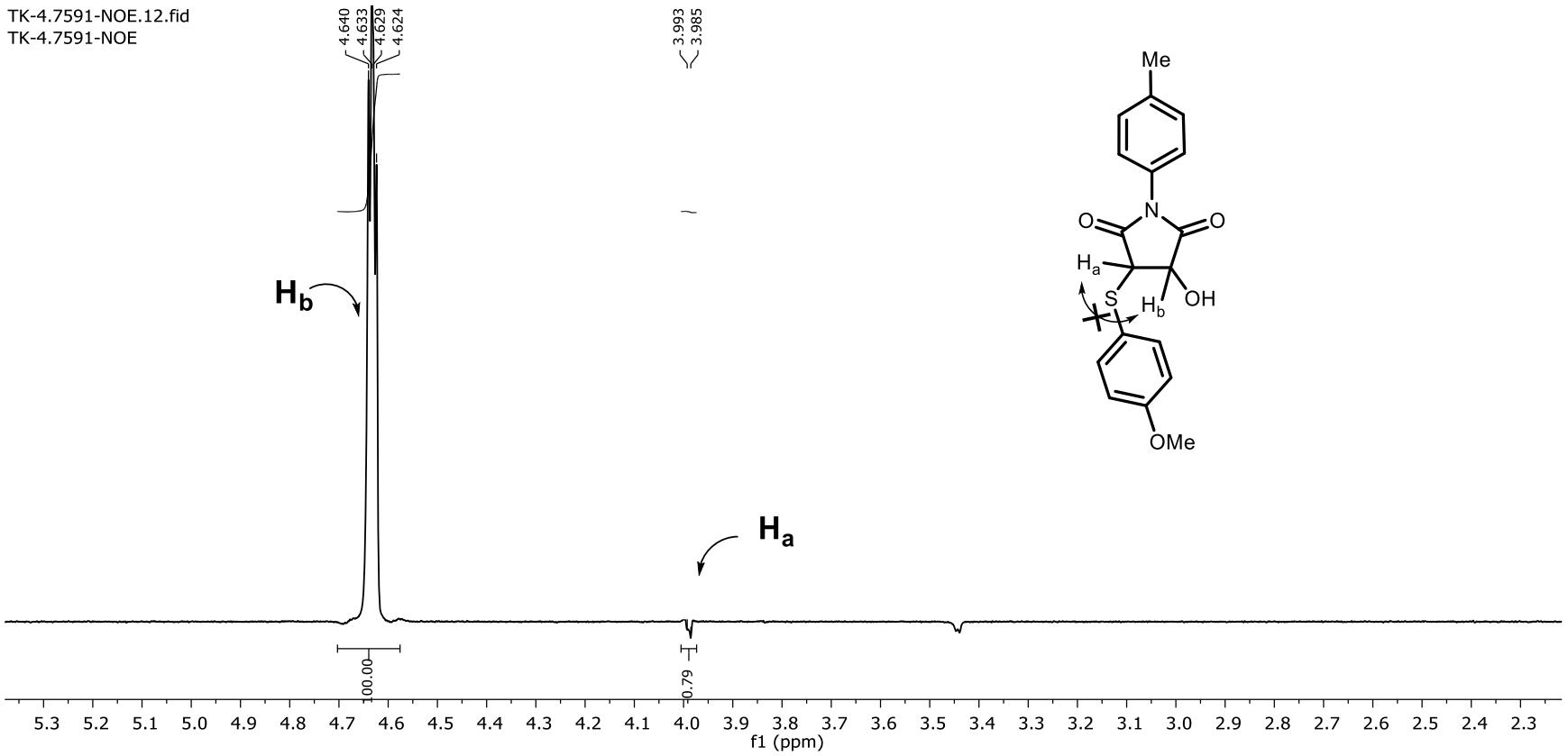


3-((4-methoxyphenyl)thio)-1-phenylpyrrolidine-2,5-dione (6aa): $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

11. NOE Experiment of 3ba

Upon irradiation of H_a, enhancement was observed in the signal corresponding to H_b (0.73% w.r.t. H_a), which indicates that H_a is in *trans* relation with H_b. Similarly, upon irradiation of H_b, enhancement was observed for H_a (0.79% w.r.t. H_b), which also indicates that H_a is in *trans* relation with H_b.


TK-4.1178-NOE.11.fid
TK-4.1178-NOE
4.639
4.634
3.995
3.985
Ha
Hb
0.73
100.00
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
Me
N
O
O
Ha
S
Hb
OH
OMe


TK-4.7591-NOE.12.fid
TK-4.7591-NOE
4.640
4.633
4.629
4.624
3.993
3.985
Hb
Ha
Me
O
N
O
Ha
S
Hb
OH
OMe
100.00
0.79
5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3
f1 (ppm)