

Supporting Information

Synthesis of 7-Halogenated Isatin Sulfonamides: Nonradioactive Counterparts of Caspase-3/-7 Inhibitor-based Potential Radiopharmaceuticals for Molecular Imaging of Apoptosis

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Table of Contents

Radio-HPLC chromatograms of [^{18}F] 39 after the radiosynthesis (Figure S1-S2)	S3
Radio-HPLC chromatograms after the [^{18}F] 39 serum stability test (Figure S3-S6)	S4
NMR spectroscopic data with signal assignments	S6
(S)-7-Iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins	S6
(S)-7-Bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins	S8
(S)-7-Chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins	S11
(S)-7-Fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins	S12
Copies of ^1H , ^{13}C , and ^{19}F NMR spectra	S14

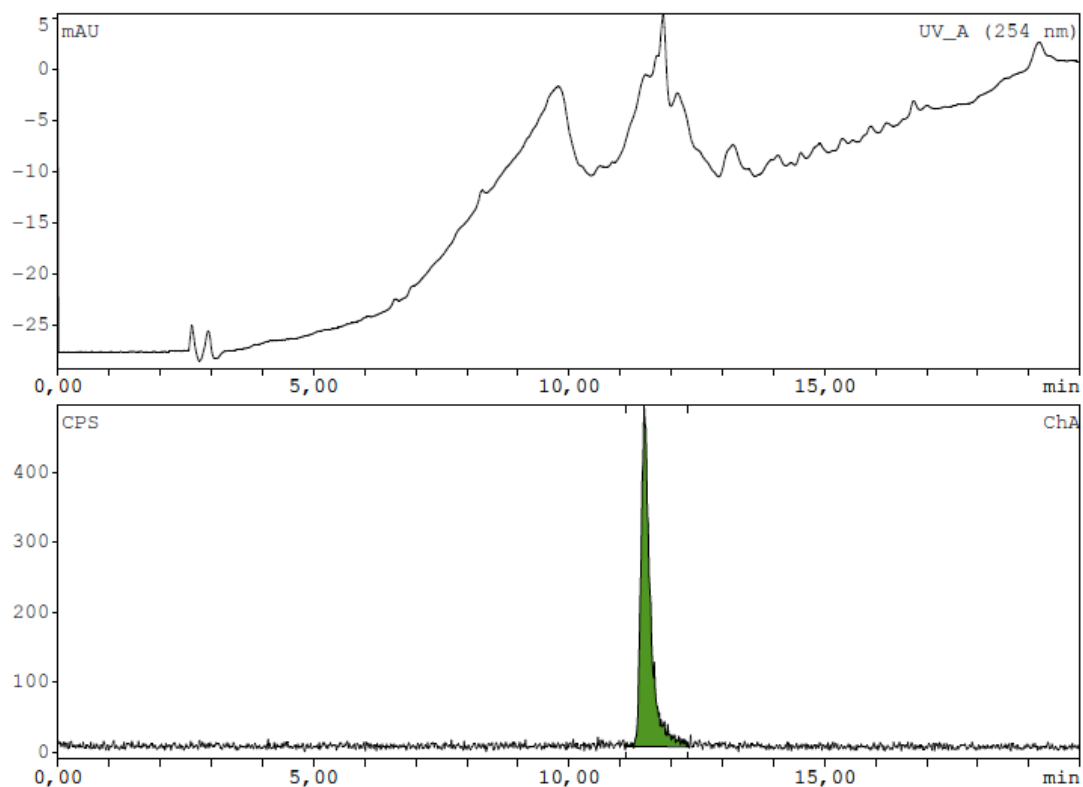


Figure S1. Radio-HPLC chromatogram with UV (top) and γ -detector (bottom) of $[^{18}\text{F}]\mathbf{39}$ after the isotopic exchange reaction.

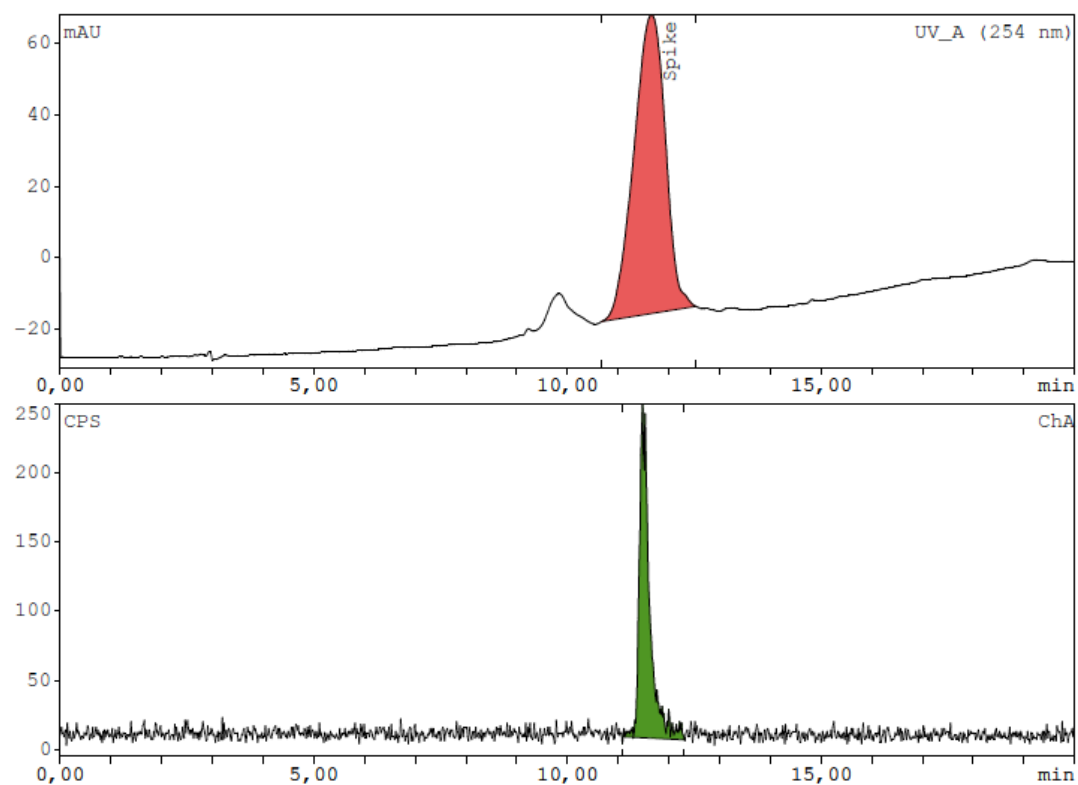


Figure S2. Radio-HPLC chromatogram with UV (top) and γ -detector (bottom) of $[^{18}\text{F}]\mathbf{39}$ spiked with the reference compound **39** after the isotopic exchange reaction.

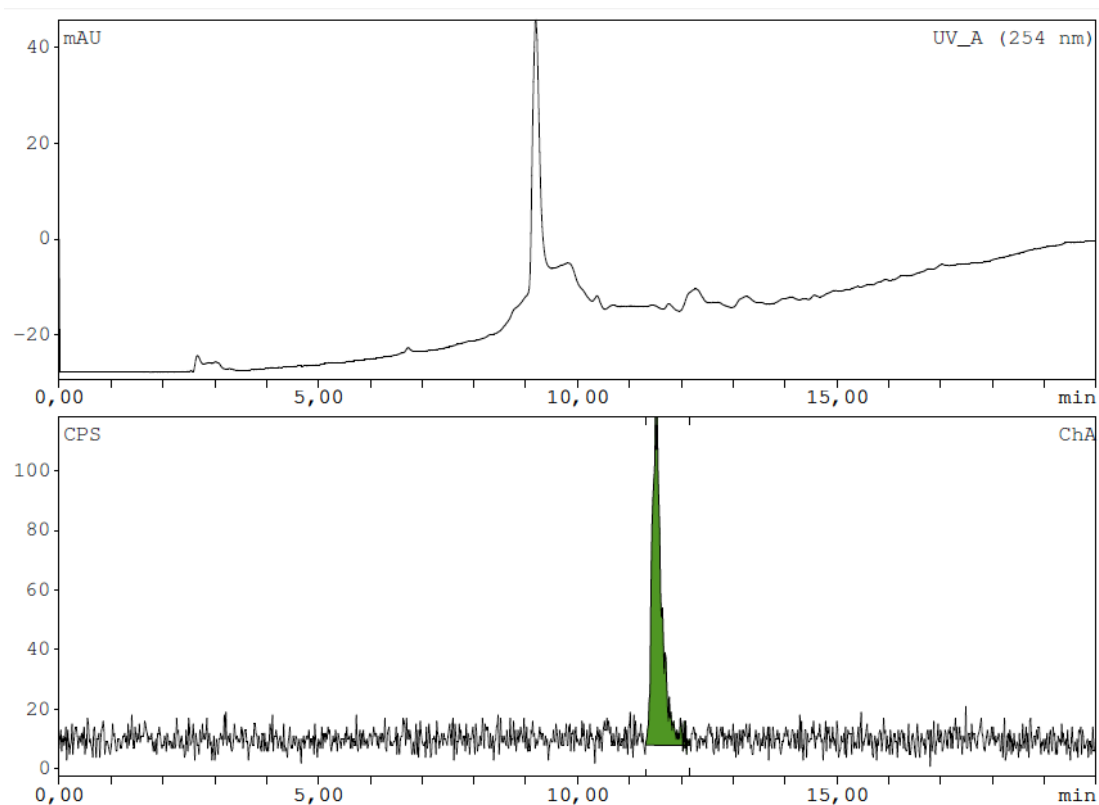


Figure S3. Radio-HPLC chromatogram of the *in vitro* stability of [^{18}F]39 after incubation in human blood serum at 37°C after 10 min.

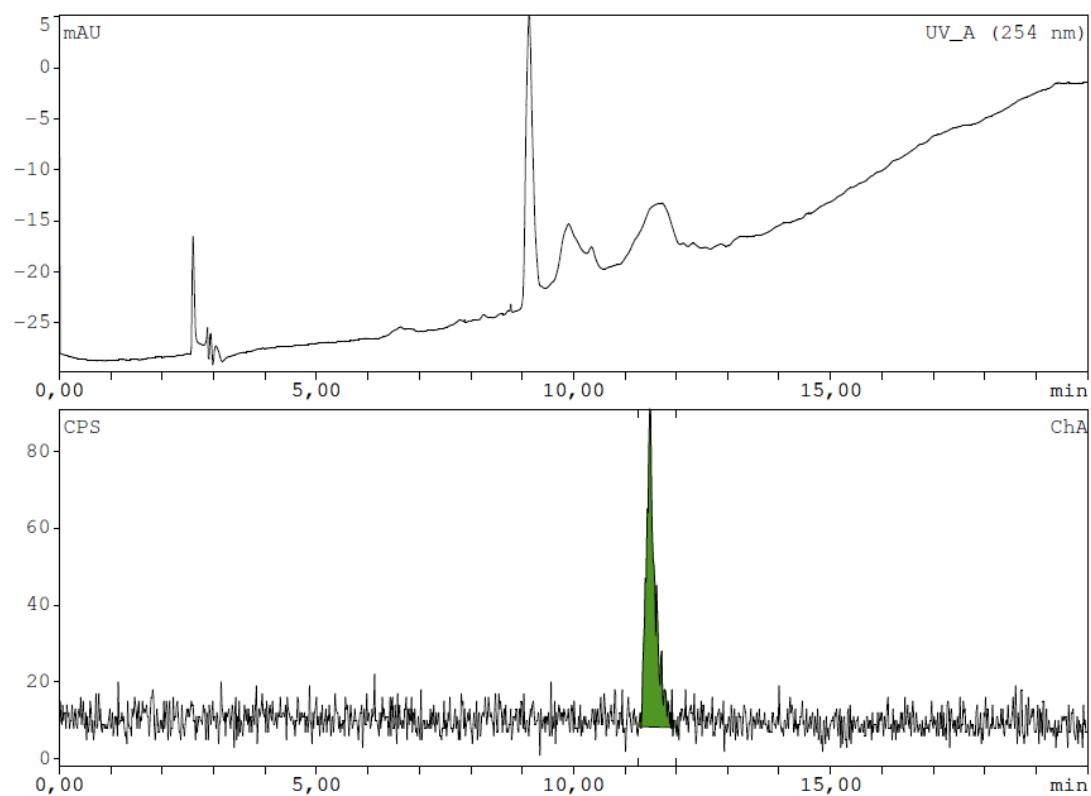


Figure S4. Radio-HPLC chromatogram of the *in vitro* stability of [^{18}F]39 after incubation in human blood serum at 37°C after 30 min.

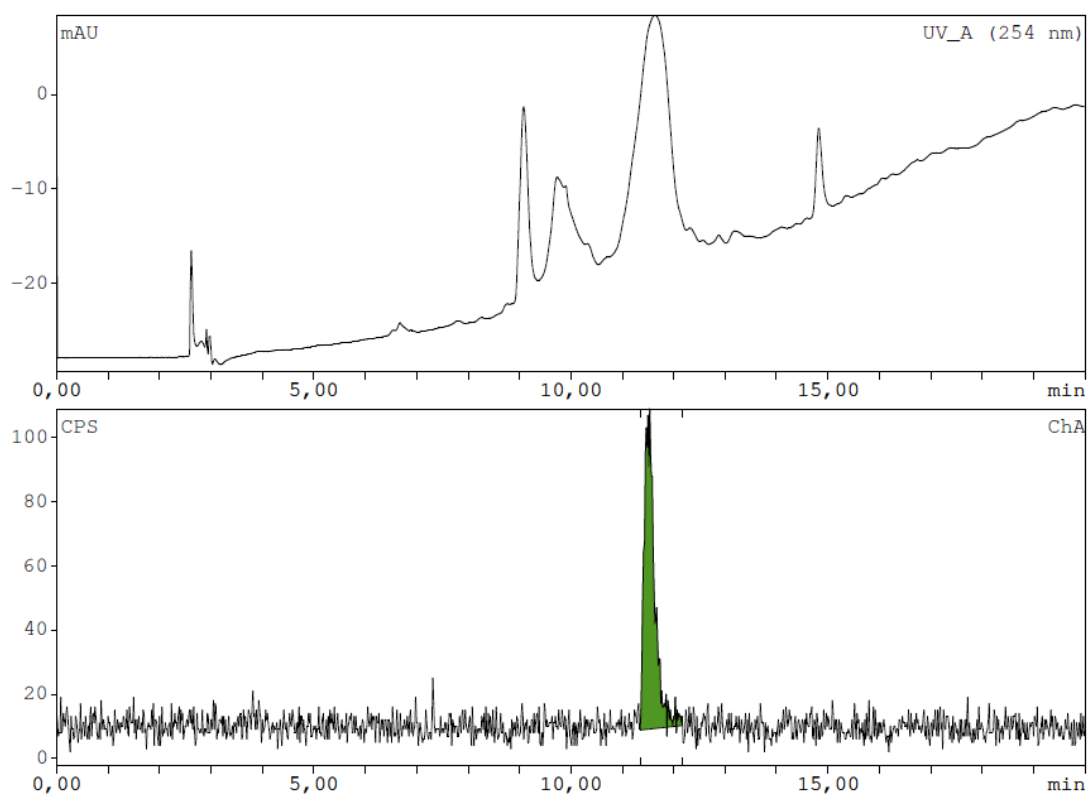


Figure S5. Radio-HPLC chromatogram of the *in vitro* stability of [^{18}F]39 after incubation in human blood serum at 37°C after 60 min.

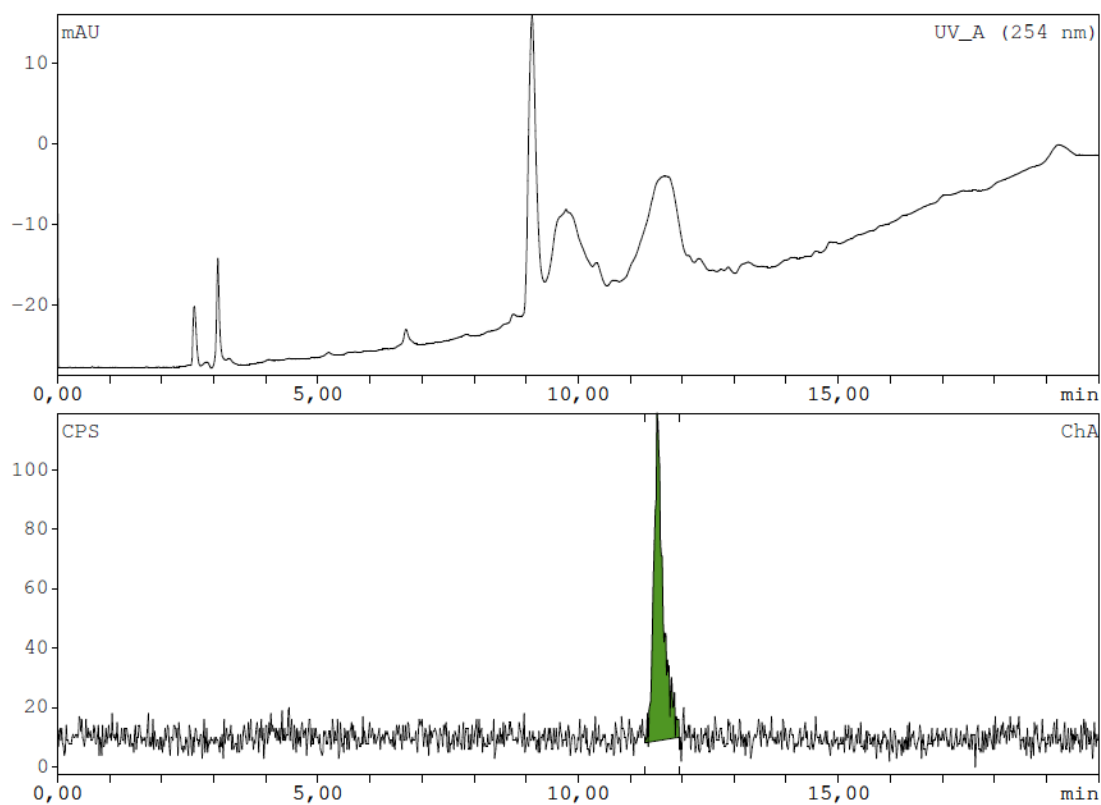
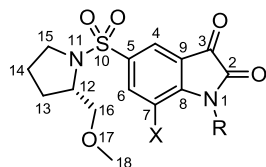


Figure S6. Radio-HPLC chromatogram of the *in vitro* stability of [^{18}F]39 after incubation in human blood serum at 37°C after 90 min.

NMR Spectroscopic Data with Signal Assignments

4.3 (S)-7-Iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins

4.3.1 (S)-7-Iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**10**)



^1H NMR (400 MHz, CDCl_3): δ = 8.50 (br s, 1H, 1-NH), 8.39 (d, $^4J_{\text{H,H}} = 1.6$ Hz, 1H, 6-CH), 8.03 (d, $^4J_{\text{H,H}} = 1.3$ Hz, 1H, 4-CH), 3.84-3.75 (m, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.47-3.38 (m, 1H, 15-CH_a), 3.40 (dd, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 3.7$ Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.20-3.12 (m, 1H, 15-CH_b), 2.00-1.84 (m, 2H, 13-CH_a, 14-CH_a), 1.80-1.64 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 182.0 (3-CO), 157.9 (2-CO), 154.0 (8-CN), 145.0 (6-CH), 136.0 (5-CSO₂), 124.1 (4-CH), 118.7 (9-CCO), 78.1 (7-Cl), 74.7 (16-CH₂), 59.4 (12-CH), 59.2 (18-CH₃), 49.3 (15-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂) ppm.

4.3.2 (S)-N-Methyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**11**)

^1H NMR (400 MHz, CDCl_3): δ = 8.47 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 7.99 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 3.84-3.75 (m, 1H, 12-CH), 3.73 (s, 3H, 19-CH₃), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.45-3.35 (m, 1H, 15-CH_a), 3.39 (dd, $^2J_{\text{H,H}} = 9.6$ Hz, $^3J_{\text{H,H}} = 3.4$ Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.21-3.10 (m, 1H, 15-CH_b), 2.00-1.83 (m, 2H, 13-CH_a, 13-CH_b), 1.80-1.65 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.2 (3-CO), 158.3 (2-CO), 153.9 (8-CN), 149.0 (6-CH), 135.7 (5-CSO₂), 123.7 (4-CH), 119.6 (9-CCO), 74.7 (16-CH₂), 72.7 (7-Cl), 59.4 (12-CH), 59.2 (18-CH₃), 49.3 (15-CH₂), 29.9 (19-CH₃), 28.8 (13-CH₂), 24.2 (14-CH₂) ppm.

4.3.3 (S)-N-Ethyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**12**)

^1H NMR (400 MHz, CDCl_3): δ = 8.42 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 7.93 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 4-CH), 4.25 (q, $^3J_{\text{H,H}} = 7.1$ Hz, 2H, 19-CH₂), 3.78-3.70 (m, 1H, 12-CH), 3.48 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.39-3.31 (m, 1H, 15-CH_a), 3.34 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 3.3$ Hz, 1H, 16-CH_b), 3.30 (s, 3H, 18-CH₃), 3.16-3.04 (m, 1H, 15-CH_b), 1.94-1.79 (m, 2H, 13-CH_a, 14-CH_a), 1.75-1.61 (m, 2H, 13-CH_b, 14-CH_b), 1.32 (t, $^3J_{\text{H,H}} = 7.1$ Hz, 3H, 20-CH₃) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.5 (3-CO), 158.3 (2-CO), 153.5 (8-CN), 149.3 (6-CH), 135.4 (5-CSO₂), 123.8 (4-CH), 120.0 (9-CCO), 74.7 (16-CH₂), 72.3 (7-Cl), 59.4 (12-CH), 59.2 (18-CH₃), 49.3 (15-CH₂), 35.9 (19-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂), 15.0 (20-CH₃) ppm.

4.3.4 (S)-N-Propyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**13**)

^1H NMR (400 MHz, CDCl_3): δ = 8.47 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 8.00 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 4-CH), 4.15 (t, $^3J_{\text{H,H}} = 7.7$ Hz, 2H, 19- CH_2), 3.80 (tt, $^3J_{\text{H,H}} = 7.3$ Hz, $^3J_{\text{H,H}} = 3.8$ Hz, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.6$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.46-3.37 (m, 1H, 15- CH_a), 3.40 (dd, $^2J_{\text{H,H}} = 9.9$ Hz, $^3J_{\text{H,H}} = 2.9$ Hz, 1H, 16- CH_b), 3.36 (s, 3H, 18- CH_3), 3.22-3.12 (m, 1H, 15- CH_b), 2.00-1.85 (m, 2H, 13- CH_a , 14- CH_a), 1.81-1.68 (m, 2H, 13- CH_b , 14- CH_b), 1.77 (sextet, $^3J_{\text{H,H}} = 7.5$ Hz, 2H, 20- CH_2), 1.01 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 3H, 21- CH_3) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.4 (3-CO), 158.4 (2-CO), 153.7 (8-CN), 149.3 (6-CH), 135.5 (5- CSO_2), 123.8 (4-CH), 119.9 (9-CCO), 74.7 (16- CH_2), 72.4 (7-Cl), 59.4 (12-CH), 59.2 (18- CH_3), 49.3 (15- CH_2), 42.0 (19- CH_2), 28.8 (13- CH_2), 24.2 (14- CH_2), 23.1 (20- CH_2), 10.5 (21- CH_3) ppm.

4.3.5 (S)-N-Butyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**14**)

^1H NMR (300 MHz, CDCl_3): δ = 8.47 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 7.99 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 4-CH), 4.19 (t, $^3J_{\text{H,H}} = 7.5$ Hz, 2H, 19- CH_2), 3.85-3.74 (m, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.46-3.34 (m, 2H, 15- CH_a , 16- CH_b), 3.36 (s, 3H, 18- CH_3), 3.22-3.10 (m, 1H, 15- CH_b), 2.01-1.83 (m, 2H, 13- CH_a , 14- CH_a), 1.83-1.65 (m, 4H, 13- CH_b , 14- CH_b , 20- CH_2), 1.44 (sextet, $^3J_{\text{H,H}} = 7.3$ Hz, 2H, 21- CH_2), 0.99 (t, $^3J_{\text{H,H}} = 7.3$ Hz, 3H, 22- CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 181.4 (3-CO), 158.4 (2-CO), 153.7 (8-CN), 149.3 (6-CH), 135.4 (5- CSO_2), 123.8 (4-CH), 119.9 (9-CCO), 74.7 (16- CH_2), 72.5 (7-Cl), 59.3 (12-CH), 59.2 (18- CH_3), 49.3 (15- CH_2), 40.5 (19- CH_2), 31.7 (20- CH_2), 28.8 (13- CH_2), 24.2 (14- CH_2), 19.6 (21- CH_2), 13.8 (22- CH_3) ppm.

4.3.6 (S)-N-(3-Fluoropropyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**15**)

^1H NMR (300 MHz, CDCl_3): δ = 8.48 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 8.00 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 4-CH), 4.62 (dt, $^2J_{\text{H,F}} = 46.9$ Hz, $^3J_{\text{H,H}} = 5.6$ Hz, 2H, 21- CH_2), 4.43 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 2H, 19- CH_2), 3.85-3.75 (m, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.47-3.34 (m, 2H, 15- CH_a , 16- CH_b), 3.37 (s, 3H, 18- CH_3), 3.23-3.11 (m, 1H, 15- CH_b), 2.31-2.11 (m, 2H, 20- CH_2), 2.00-1.84 (m, 2H, 13- CH_a , 14- CH_a), 1.84-1.65 (m, 2H, 13- CH_b , 14- CH_b) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 181.0 (3-CO), 158.6 (2-CO), 153.3 (8-CN), 149.2 (6-CH), 135.6 (5- CSO_2), 123.9 (4-CH), 120.0 (9-CCO), 81.5 (d, $^1J_{\text{C,F}} = 166.4$ Hz, 21- CH_2), 74.7 (16- CH_2), 72.6 (7-Cl), 59.4 (12-CH), 59.1 (18- CH_3), 49.3 (15- CH_2), 37.9 (d, $^3J_{\text{C,F}} = 4.6$ Hz, 19- CH_2), 30.5 (d, $^2J_{\text{C,F}} = 19.7$ Hz, 20- CH_2), 28.8 (13- CH_2), 24.2 (14- CH_2) ppm. ^{19}F NMR (282 MHz, CDCl_3): δ = -221.5 (s, 1F, 21- CH_2F) ppm.

4.3.7 (S)-N-(4-Fluorobutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**16**)

^1H NMR (300 MHz, CDCl_3): δ = 8.48 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 8.00 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 4-CH), 4.52 (dt, $^2J_{\text{H,F}} = 47.4$ Hz, $^3J_{\text{H,H}} = 5.5$ Hz, 2H, 22- CH_2), 4.26 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 2H, 19- CH_2), 3.85-3.75 (m, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.46-3.33 (m, 2H, 15- CH_a , 16- CH_b), 3.36 (s, 3H, 18- CH_3), 3.22-3.11 (m, 1H, 15- CH_b), 2.03-1.57 (m, 8H, 13- CH_2 , 14- CH_2 , 20- CH_2 , 21- CH_2) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 181.2 (3-CO), 158.4 (2-CO), 153.4 (8-CN), 149.3 (6-CH), 135.6 (5- CSO_2), 123.9 (4-CH), 119.9 (9-CCO), 83.2 (d, $^1J_{\text{C,F}} = 165.8$ Hz, 22- CH_2), 74.7 (16- CH_2), 72.5 (7-Cl), 59.4 (12-CH), 59.2 (18- CH_3), 49.3 (15- CH_2), 40.2 (19- CH_2), 28.8 (13- CH_2), 27.3 (d, $^2J_{\text{C,F}} = 20.3$ Hz, 21- CH_2), 26.0 (d, $^3J_{\text{C,F}} = 4.4$ Hz, 20- CH_2), 24.2 (14- CH_2) ppm. ^{19}F NMR (282 MHz, CDCl_3): δ = -217.9 (s, 1F, 22- CH_2F) ppm.

4.3.8 (S)-N-(4-Hydroxybutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**17**)

^1H NMR (300 MHz, CDCl_3): δ = 8.48 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 6-CH), 8.00 (d, $^4J_{\text{H,H}} = 1.9$ Hz, 1H, 4-CH), 4.26 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 2H, 19- CH_2), 3.85-3.75 (m, 1H, 12-CH), 3.73 (t, $^3J_{\text{H,H}} = 6.2$ Hz, 2H, 22- CH_2), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.47-3.34 (m, 1H, 15- CH_a), 3.39 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16- CH_b), 3.37 (s, 3H, 18- CH_3), 3.22-3.11 (m, 1H, 15- CH_b), 2.02-1.63 (m, 8H, 13- CH_2 , 14- CH_2 , 20- CH_2 , 21- CH_2) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 181.3 (3-CO), 158.5 (2-CO), 153.5 (8-CN), 149.3 (6-CH), 135.4 (5- CSO_2), 123.8 (4-CH), 120.0 (9-CCO), 74.7 (16- CH_2), 72.6 (7-Cl), 62.1 (22- CH_2), 59.4 (12-CH), 59.2 (18- CH_3), 49.3 (15- CH_2), 40.4 (19- CH_2), 29.2 (20- CH_2), 28.8 (13- CH_2), 26.4 (21- CH_2), 24.2 (14- CH_2) ppm.

4.4 (S)-7-Bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins

4.4.1 (S)-7-Bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**18**)

^1H NMR (400 MHz, CDCl_3): δ = 8.74 (s, 1H, 1-NH), 8.17 (d, $^4J_{\text{H,H}} = 1.6$ Hz, 1H, 6-CH), 7.96 (dd, $^4J_{\text{H,H}} = 1.6$ Hz, 1H, 4-CH), 3.78-3.69 (m, 1H, 12-CH), 3.49 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16- CH_a), 3.40-3.30 (m, 1H, 15- CH_a), 3.33 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16- CH_b), 3.30 (s, 3H, 18- CH_3), 3.16-3.06 (m, 1H, 15- CH_b), 1.94-1.78 (m, 2H, 13- CH_a , 14- CH_a), 1.74-1.60 (m, 2H, 13- CH_b , 14- CH_b) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.2 (3-CO), 157.9 (2-CO), 150.8 (8-CN), 139.4 (6-CH), 135.7 (5- CSO_2), 123.4 (4-CH), 118.9 (9-CCO), 106.2 (7-CBr), 74.7 (16- CH_2), 59.4 (12-CH), 59.1 (18- CH_3), 49.3 (15- CH_2), 28.8 (13- CH_2), 24.2 (14- CH_2) ppm.

4.4.2 (S)-N-Methyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**19**)

^1H NMR (400 MHz, CDCl_3): δ = 8.20 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.96 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 3.83-3.75 (m, 1H, 12-CH), 3.70 (s, 3H, 19-CH₃), 3.53 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.45-3.36 (m, 1H, 15-CH_a), 3.39 (dd, $^2J_{\text{H,H}} = 9.9$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.35 (s, 3H, 18-CH₃), 3.21-3.11 (m, 1H, 15-CH_b), 1.99-1.84 (m, 2H, 13-CH_a, 14-CH_a), 1.79-1.65 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.1 (3-CO), 158.2 (2-CO), 151.0 (8-CN), 142.2 (6-CH), 135.4 (5-CSO₂), 123.0 (4-CH), 119.9 (9-CCO), 104.5 (7-CBr), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 29.9 (19-CH₃), 28.8 (13-CH₂), 24.2 (14-CH₂) ppm.

4.4.3 (S)-N-Ethyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**20**)

^1H NMR (400 MHz, CDCl_3): δ = 8.22 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.98 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.28 (q, $^3J_{\text{H,H}} = 7.1$ Hz, 2H, 19-CH₂), 3.84-3.76 (m, 1H, 12-CH), 3.54 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.46-3.36 (m, 1H, 15-CH_a), 3.39 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.17 (dt, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 7.3$ Hz, 1H, 15-CH_b), 2.00-1.84 (m, 2H, 13-CH_a, 14-CH_a), 1.81-1.68 (m, 2H, 13-CH_b, 14-CH_b), 1.39 (t, $^3J_{\text{H,H}} = 7.1$ Hz, 3H, 20-CH₃) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.5 (3-CO), 158.1 (2-CO), 150.6 (8-CN), 142.5 (6-CH), 135.3 (5-CSO₂), 123.2 (4-CH), 120.2 (9-CCO), 103.9 (7-CBr), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 36.9 (19-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂), 14.9 (20-CH₃) ppm.

4.4.4 (S)-N-Propyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**21**)

^1H NMR (400 MHz, CDCl_3): δ = 8.22 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.99 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.15 (t, $^3J_{\text{H,H}} = 7.8$ Hz, 2H, 19-CH₂), 3.85-3.77 (m, 1H, 12-CH), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.48-3.37 (m, 1H, 15-CH_a), 3.40 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.37 (s, 3H, 18-CH₃), 3.19 (dt, $^2J_{\text{H,H}} = 9.9$ Hz, $^3J_{\text{H,H}} = 7.3$ Hz, 1H, 15-CH_b), 2.01-1.87 (m, 2H, 13-CH_a, 14-CH_a), 1.85-1.69 (m, 2H, 13-CH_b, 14-CH_b), 1.80 (sextet, $^3J_{\text{H,H}} = 7.6$ Hz, 2H, 20-CH₂), 1.01 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 3H, 21-CH₃) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 181.4 (3-CO), 158.3 (2-CO), 150.7 (8-CN), 142.5 (6-CH), 135.3 (5-CSO₂), 123.2 (4-CH), 120.2 (9-CCO), 104.0 (7-CBr), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 43.1 (19-CH₂), 28.9 (13-CH₂), 24.2 (14-CH₂), 23.0 (20-CH₂), 10.8 (21-CH₃) ppm.

4.4.5 (S)-N-Butyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**22**)

^1H NMR (400 MHz, CDCl_3): δ = 8.15 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.91 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.11 (t, $^3J_{\text{H,H}} = 7.6$ Hz, 2H, 19-CH₂), 3.78-3.70 (m, 1H, 12-CH), 3.48 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.40-3.31 (m, 1H, 15-CH_a), 3.33 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.30 (s, 3H, 18-CH₃), 3.11 (dt, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 15-

CH_b), 1.94-1.80 (m, 2H, 13-CH_a, 14-CH_a), 1.76-1.62 (m, 2H, 13-CH_b, 14-CH_b), 1.73-1.62 (m, 2H, 20-CH₂), 1.37 (sextet, $^3J_{\text{H,H}} = 7.5$ Hz, 2H, 21-CH₂), 0.92 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 3H, 22-CH₃) ppm. ^{13}C NMR (100 MHz, CDCl₃): $\delta = 181.4$ (3-CO), 158.2 (2-CO), 150.7 (8-CN), 142.5 (6-CH), 135.3 (5-CSO₂), 123.2 (4-CH), 120.3 (9-CCO), 104.0 (7-CBr), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 41.5 (19-CH₂), 31.6 (20-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂), 19.8 (21-CH₂), 13.7 (22-CH₃) ppm.

4.4.6 (S)-N-(3-Fluoropropyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**23**)

^1H NMR (400 MHz, CDCl₃): $\delta = 8.24$ (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 8.00 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.61 (dt, $^2J_{\text{H,F}} = 46.9$ Hz, $^3J_{\text{H,H}} = 5.5$ Hz, 2H, 21-CH₂), 4.41 (t, $^3J_{\text{H,H}} = 7.3$ Hz, 2H, 19-CH₂), 3.86-3.78 (m, 1H, 12-CH), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.47-3.39 (m, 1H, 15-CH_a), 3.40 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.1$ Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.19 (dt, $^2J_{\text{H,H}} = 9.1$ Hz, $^3J_{\text{H,H}} = 7.0$ Hz, 1H, 15-CH_b), 2.29-2.13 (m, 2H, 20-CH₂), 2.02-1.85 (m, 2H, 13-CH_a, 14-CH_a), 1.83-1.68 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (100 MHz, CDCl₃): $\delta = 181.0$ (3-CO), 158.4 (2-CO), 150.4 (8-CN), 142.5 (6-CH), 135.7 (5-CSO₂), 123.3 (4-CH), 120.3 (9-CCO), 104.0 (7-CBr), 81.6 (d, $^1J_{\text{C,F}} = 166.4$ Hz, 21-CH₂), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 38.9 (d, $^3J_{\text{C,F}} = 4.4$ Hz, 19-CH₂), 30.5 (d, $^2J_{\text{C,F}} = 19.7$ Hz, 20-CH₂), 28.9 (13-CH₂), 24.2 (14-CH₂) ppm. ^{19}F NMR (282 MHz, CDCl₃): $\delta = -221.5$ (s, 1F, 21-CH₂F) ppm.

4.4.7 (S)-N-(4-Fluorobutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**24**)

^1H NMR (400 MHz, CDCl₃): $\delta = 8.29$ (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 8.05 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.58 (dt, $^2J_{\text{H,F}} = 47.4$ Hz, $^3J_{\text{H,H}} = 5.7$ Hz, 2H, 22-CH₂), 4.31 (t, $^3J_{\text{H,H}} = 7.6$ Hz, 2H, 19-CH₂), 3.92-3.83 (m, 1H, 12-CH), 3.61 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.53-3.45 (m, 1H, 15-CH_a), 3.46 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.43 (s, 3H, 18-CH₃), 3.25 (dt, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 7.1$ Hz, 1H, 15-CH_b), 2.05-1.92 (m, 4H, 13-CH_a, 14-CH_a, 20-CH₂), 1.95-1.76 (m, 2H, 21-CH₂), 1.88-1.76 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (100 MHz, CDCl₃): $\delta = 181.2$ (3-CO), 158.3 (2-CO), 150.5 (8-CN), 142.5 (6-CH), 135.5 (5-CSO₂), 123.2 (4-CH), 120.3 (9-CCO), 104.0 (7-CBr), 83.2 (d, $^1J_{\text{C,F}} = 165.8$ Hz, 22-CH₂), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 41.2 (19-CH₂), 28.8 (13-CH₂), 27.5 (d, $^2J_{\text{C,F}} = 20.3$ Hz, 21-CH₂), 26.0 (d, $^3J_{\text{C,F}} = 4.2$ Hz, 20-CH₂), 24.2 (14-CH₂) ppm. ^{19}F NMR (282 MHz, CDCl₃): $\delta = -218.6$ (s, 1F, 22-CH₂F) ppm.

4.4.8 (S)-N-(4-Hydroxybutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**25**)

^1H NMR (400 MHz, CDCl₃): $\delta = 8.22$ (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.98 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.24 (t, $^3J_{\text{H,H}} = 7.6$ Hz, 2H, 19-CH₂), 3.85-3.77 (m, 1H, 12-CH), 3.72 (t, $^3J_{\text{H,H}} = 6.3$ Hz, 2H, 22-CH₂), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.48-3.37 (m, 1H, 15-CH_a),

3.40 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 16-CH_b), 3.37 (s, 3H, 18-CH₃), 3.18 (dt, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 7.2$ Hz, 1H, 15-CH_b), 1.99-1.90 (m, 2H, 13-CH_a, 14-CH_a), 1.94-1.84 (m, 2H, 21-CH₂), 1.82-1.72 (m, 2H, 13-CH_b, 14-CH_b), 1.73-1.63 (m, 2H, 20-CH₂) ppm. ^{13}C NMR (100 MHz, CDCl₃): $\delta = 181.3$ (3-CO), 158.3 (2-CO), 150.6 (8-CN), 142.5 (6-CH), 135.4 (5-CSO₂), 123.2 (4-CH), 120.3 (9-CCO), 104.0 (7-CBr), 74.7 (16-CH₂), 62.2 (22-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 41.5 (19-CH₂), 29.4 (20-CH₂), 28.9 (13-CH₂), 26.4 (21-CH₂), 24.2 (14-CH₂) ppm.

4.5 (S)-7-Chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins

4.5.1 Sodium 7-chloro-2,3-dioxoindoline-5-sulfonate (**29**)

^1H NMR (400 MHz, DMSO-*d*₆): $\delta = 11.55$ (s, 1H, 1-NH), 7.78 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 6-CH), 7.57 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 4-CH) ppm. ^{13}C NMR (100 MHz, DMSO-*d*₆): $\delta = 183.3$ (3-CO), 160.0 (2-CO), 147.8 (8-CN), 144.0 (5-CSO₂), 134.1 (6-CH), 120.0 (4-CH), 119.4 (9-CCO), 115.5 (7-CCl) ppm.

4.5.2 5,7-Dichlorosulfonyl isatin (**30**)

^1H NMR (300 MHz, DMSO-*d*₆): $\delta = 11.52$ (s, 1H, 1-NH), 7.72 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 6-CH), 7.51 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 6-CH) ppm. ^{13}C NMR (75 MHz, DMSO-*d*₆): $\delta = 183.4$ (3-CO), 160.2 (2-CO), 147.9 (8-CN), 144.2 (5-CSO₂), 134.1 (6-CH), 120.0 (4-CH), 119.6 (9-CCO), 115.7 (7-CCl) ppm.

4.5.3 (S)-7-Chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**31**)

^1H NMR (300 MHz, CD₃CN): $\delta = 9.64$ (br s, 1H, 1-NH), 8.04 (d, $^4J_{\text{H,H}} = 1.7$ Hz, 1H, 6-CH), 7.84 (d, $^4J_{\text{H,H}} = 1.7$ Hz, 1H, 4-CH), 3.80-3.66 (m, 1H, 12-CH), 3.46 (dd, $^2J_{\text{H,H}} = 9.6$ Hz, $^3J_{\text{H,H}} = 4.1$ Hz, 1H, 16-CH_a), 3.38-3.27 (m, 1H, 15-CH_a), 3.36 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 7.1$ Hz, 1H, 16-CH_b), 3.30 (s, 3H, 18-CH₃), 3.23-3.11 (m, 1H, 15-CH_b), 1.90-1.47 (m, 4H, 13-CH₂, 14-CH₂) ppm. ^{13}C NMR (75 MHz, CD₃CN): $\delta = 183.2$ (3-CO), 159.6 (2-CO), 151.6 (8-CN), 137.2 (6-CH), 134.7 (5-CSO₂), 123.1 (4-CH), 120.4 (9-CCO), 118.9 (7-CCl), 75.7 (16-CH₂), 60.4 (12-CH), 59.3 (18-CH₃), 50.3 (15-CH₂), 29.3 (13-CH₂), 24.8 (14-CH₂) ppm.

4.5.4 (S)-N-Butyl-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**32**)

^1H NMR (300 MHz, CDCl₃): $\delta = 8.03$ (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 6-CH), 7.93 (d, $^4J_{\text{H,H}} = 1.8$ Hz, 1H, 4-CH), 4.15 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 2H, 19-CH₂), 3.85-3.73 (m, 1H, 12-CH), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 4.0$ Hz, 1H, 16-CH_a), 3.48-3.34 (m, 1H, 15-CH_a), 3.43-3.35 (m, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.24-3.10 (m, 1H, 15-CH_b), 2.04-1.64 (m, 4H, 13-CH₂, 14-CH₂), 1.84-1.64 (m, 2H, 20-CH₂), 1.43 (sextet, $^3J_{\text{H,H}} = 7.3$ Hz, 2H, 21-CH₂), 0.99 (t, $^3J_{\text{H,H}} = 7.3$ Hz, 3H, 22-CH₃) ppm. ^{13}C NMR (75 MHz, CDCl₃): $\delta = 181.5$ (3-CO), 158.1 (2-CO), 149.3 (8-CN), 139.2

(6-CH), 134.9 (5-CSO₂), 122.6 (4-CH), 120.0 (9-CCO), 117.5 (7-CCl), 74.7 (16-CH₂), 59.3 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 42.0 (19-CH₂), 31.6 (20-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂), 19.8 (21-CH₂), 13.7 (22-CH₃) ppm.

4.5.5 (S)-N-(4-Fluorobutyl)-7-chloro-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatin (**33**)

¹H NMR (400 MHz, CDCl₃): δ = 8.03 (d, ⁴J_{H,H} = 1.8 Hz, 1H, 6-CH), 7.93 (d, ⁴J_{H,H} = 1.8 Hz, 1H, 4-CH), 4.51 (dt, ²J_{H,F} = 47.4 Hz, ³J_{H,H} = 5.7 Hz, 2H, 22-CH₂), 4.21 (t, ³J_{H,H} = 7.4 Hz, 2H, 19-CH₂), 3.85-3.75 (m, 1H, 12-CH), 3.54 (dd, ²J_{H,H} = 9.5 Hz, ³J_{H,H} = 4.0 Hz, 1H, 16-CH_a), 3.49-3.34 (m, 1H, 15-CH_a), 3.39 (dd, ²J_{H,H} = 9.5 Hz, ³J_{H,H} = 7.3 Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.24-3.12 (m, 1H, 15-CH_b), 2.04-1.64 (m, 8H, 13-CH₂, 14-CH₂, 20-CH₂, 21-CH₂) ppm.
¹³C NMR (100 MHz, CDCl₃): δ = 181.3 (3-CO), 158.2 (2-CO), 149.0 (8-CN), 139.2 (6-CH), 135.2 (5-CSO₂), 122.7 (4-CH), 120.1 (9-CCO), 117.5 (7-CCl), 83.3 (d, ¹J_{C,F} = 165.6 Hz, 22-CH₂), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 49.3 (15-CH₂), 41.7 (19-CH₂), 28.8 (13-CH₂), 27.5 (d, ²J_{C,F} = 20.2 Hz, 21-CH₂), 26.0 (d, ³J_{C,F} = 4.2 Hz, 20-CH₂), 24.2 (14-CH₂) ppm.
¹⁹F NMR (282 MHz, CDCl₃): δ = -219.1 (s, 1F, 22-CH₂F) ppm.

4.6 (S)-7-Fluoro-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatins

4.6.1 Sodium 7-fluoroisatin-5-sulfonate (**35**)

¹H NMR (300 MHz, DMSO-d₆): δ = 11.65 (br s, 1H, 1-NH), 7.64 (dd, ³J_{H,F} = 10.0 Hz, ⁴J_{H,H} = 1.3 Hz, 1H, 6-CH), 7.50 (d, ⁴J_{H,H} = 1.4 Hz, 1H, 4-CH) ppm. ¹³C NMR (75 MHz, DMSO-d₆): δ = 182.8 (3-CO), 159.4 (2-CO), 146.1 (d, ¹J_{C,F} = 247.4 Hz, 7-CF), 143.8 (d, ³J_{C,F} = 3.0 Hz, 5-CSO₂), 137.4 (d, ²J_{C,F} = 13.7 Hz, 8-CN), 121.4 (d, ²J_{C,F} = 18.8 Hz, 6-CH), 119.7 (d, ³J_{C,F} = 3.9 Hz, 9-CCO), 117.2 (d, ⁴J_{C,F} = 3.1 Hz, 4-CH) ppm. ¹⁹F NMR (282 MHz, DMSO-d₆): δ = -132.9 (s, 1F, 7-CF) ppm.

4.6.2 5-Chlorosulfonyl-7-fluoroisatin (**36**)

¹H NMR (300 MHz, DMSO-d₆): δ = 11.68 (s, 1H, 1-NH), 7.73 (dd, ³J_{H,F} = 9.8 Hz, ⁴J_{H,H} = 1.4 Hz, 1H, 6-CH), 7.70-7.66 (m, 1H, 4-CH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 183.0 (3-CO), 159.2 (2-CO), 146.5 (d, ¹J_{C,F} = 248.9 Hz, 7-CF), 143.5 (d, ³J_{C,F} = 3.1 Hz, 5-CSO₂), 138.1 (d, ²J_{C,F} = 13.9 Hz, 8-CN), 122.3 (d, ²J_{C,F} = 19.1 Hz, 6-CH), 119.2 (d, ³J_{C,F} = 4.0 Hz, 9-CCO), 118.0 (d, ⁴J_{C,F} = 3.3 Hz, 4-CH) ppm. ¹⁹F NMR (282 MHz, DMSO-d₆): δ = -133.0 (s, 1F, 7-CF) ppm.

4.6.3 (S)-7-Fluoro-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatin (**37**)

¹H NMR (300 MHz, DMSO-d₆): δ = 11.99 (br s, 1H, 1-NH), 8.01 (dd, ³J_{H,F} = 9.5 Hz, ⁴J_{H,H} = 1.6 Hz, 1H, 6-CH), 7.66 (d, ⁴J_{H,H} = 1.6 Hz, 1H, 4-CH), 3.81-3.68 (m, 1H, 12-CH), 3.44 (dd, ²J_{H,H} = 9.5 Hz, ³J_{H,H} = 3.9 Hz, 1H, 16-CH_a), 3.37-3.30 (m, 1H, 15-CH_a), 3.31-3.25 (m, 1H, 16-CH_b),

3.28 (s, 3H, 18-CH₃), 3.14 (dt, $^2J_{\text{H,H}} = 10.2$ Hz, $^3J_{\text{H,H}} = 7.1$ Hz, 1H, 15-CH_b), 1.90-1.65 (m, 2H, 13-CH_a, 14-CH_a), 1.65-1.43 (m, 2H, 13-CH_b, 14-CH_b) ppm. ^{13}C NMR (75 MHz, DMSO-*d*₆): $\delta = 181.7$ (3-CO), 159.2 (2-CO), 146.7 (d, $^1J_{\text{C,F}} = 250.3$ Hz, 7-CF), 141.2 (d, $^2J_{\text{C,F}} = 13.6$ Hz, 8-CN), 131.5 (d, $^3J_{\text{C,F}} = 4.0$ Hz, 5-CSO₂), 123.0 (d, $^2J_{\text{C,F}} = 20.2$ Hz, 6-CH), 120.6 (d, $^3J_{\text{C,F}} = 4.5$ Hz, 9-CCO), 119.0 (d, $^4J_{\text{C,F}} = 3.1$ Hz, 4-CH), 74.4 (16-CH₂), 58.7 (12-CH), 58.4 (18-CH₃), 48.9 (15-CH₂), 28.1 (13-CH₂), 23.5 (14-CH₂) ppm. ^{19}F NMR (282 MHz, DMSO-*d*₆): $\delta = -130.5$ (s, 1F, 7-CF) ppm.

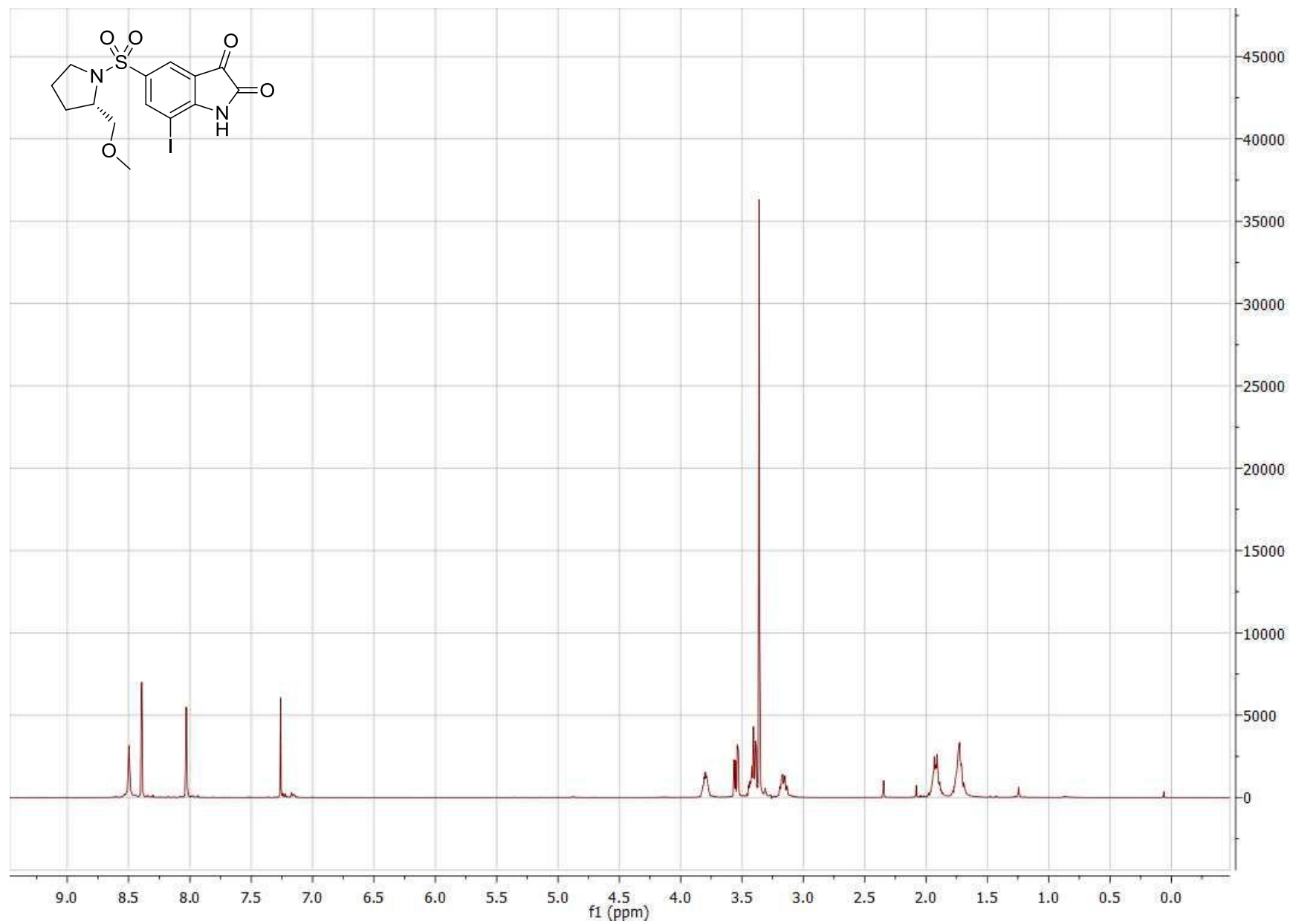
4.6.4 (S)-N-Butyl-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**38**)

^1H NMR (300 MHz, CDCl₃): $\delta = 7.85$ (dd, $^3J_{\text{H,F}} = 11.2$ Hz, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 6-CH), 7.85 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 4-CH), 3.91 (td, $^3J_{\text{H,H}} = 7.4$ Hz, $^5J_{\text{H,F}} = 1.6$ Hz, 2H, 19-CH₂), 3.82-3.73 (m, 1H, 12-CH), 3.56 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 3.9$ Hz, 1H, 16-CH_a), 3.48-3.37 (m, 1H, 15-CH_a), 3.43-3.35 (m, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.22-3.10 (m, 1H, 15-CH_b), 2.03-1.64 (m, 4H, 13-CH₂, 14-CH₂), 1.81-1.64 (m, 2H, 20-CH₂), 1.42 (sextet, $^3J_{\text{H,H}} = 7.3$ Hz, 2H, 21-CH₂), 0.98 (t, $^3J_{\text{H,H}} = 7.3$ Hz, 3H, 22-CH₃) ppm. ^{13}C NMR (75 MHz, CDCl₃): $\delta = 181.4$ (d, $^4J_{\text{C,F}} = 3.0$ Hz, 3-CO), 157.5 (2-CO), 147.2 (d, $^1J_{\text{C,F}} = 253.1$ Hz, 7-CF), 140.5 (d, $^2J_{\text{C,F}} = 8.8$ Hz, 8-CN), 134.7 (d, $^3J_{\text{C,F}} = 4.1$ Hz, 5-CSO₂), 125.5 (d, $^2J_{\text{C,F}} = 22.8$ Hz, 6-CH), 120.3 (d, $^4J_{\text{C,F}} = 3.4$ Hz, 4-CH), 120.0 (d, $^3J_{\text{C,F}} = 2.8$ Hz, 9-CCO), 74.7 (16-CH₂), 59.3 (12-CH), 59.1 (18-CH₃), 49.4 (15-CH₂), 42.7 (d, $^4J_{\text{C,F}} = 4.8$ Hz, 19-CH₂), 30.8 (d, $^5J_{\text{C,F}} = 2.6$ Hz, 20-CH₂), 28.8 (13-CH₂), 24.2 (14-CH₂), 19.9 (21-CH₂), 13.6 (22-CH₃) ppm. ^{19}F NMR (282 MHz, CDCl₃): $\delta = -130.7$ (s, 1F, 7-CF) ppm.

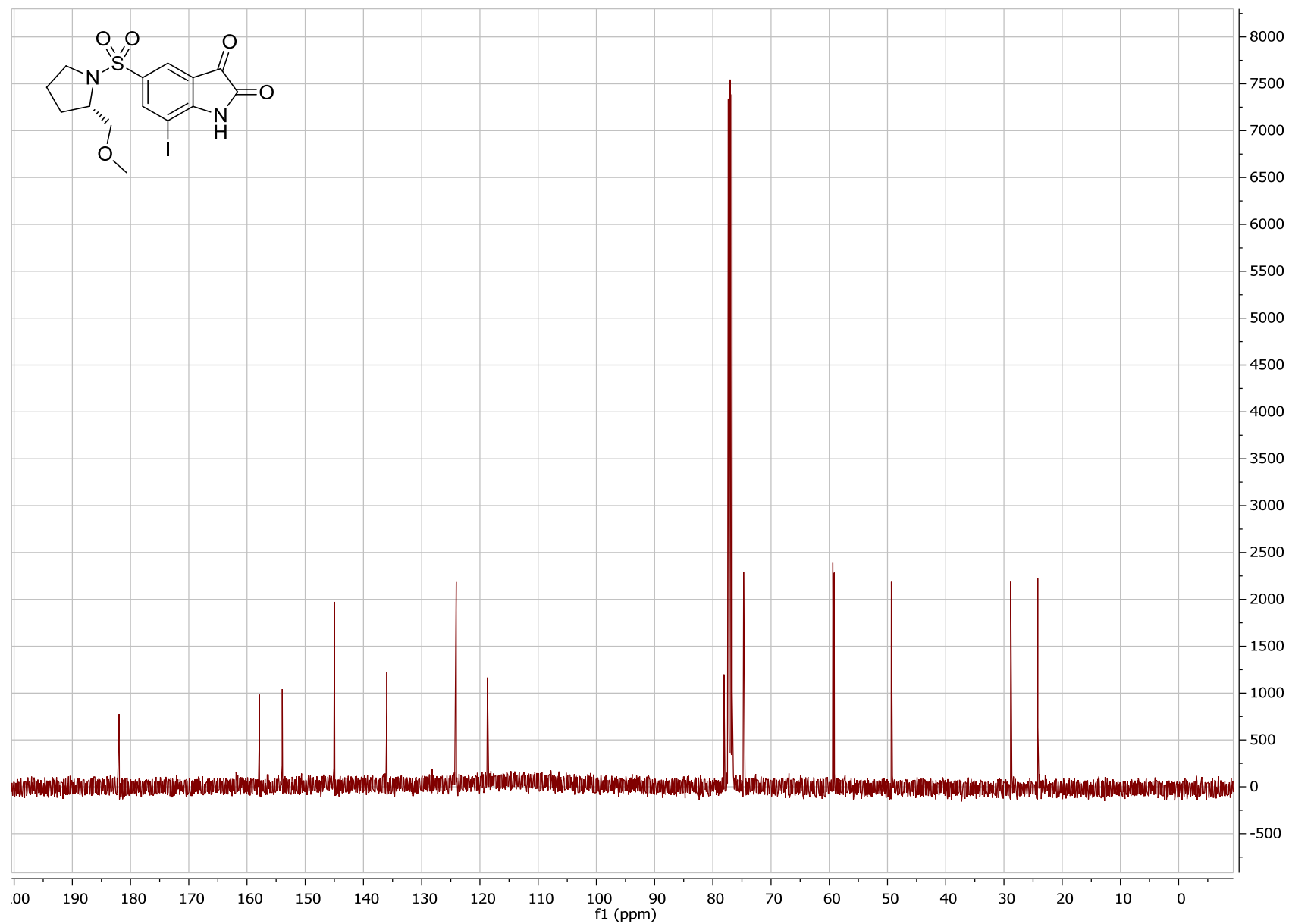
4.6.5 (S)-N-(4-Fluorobutyl)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**39**)

^1H NMR (400 MHz, CDCl₃): $\delta = 7.86$ (dd, $^3J_{\text{H,F}} = 11.1$ Hz, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 6-CH), 7.85 (d, $^4J_{\text{H,H}} = 1.5$ Hz, 1H, 4-CH), 4.50 (dt, $^2J_{\text{H,F}} = 47.6$ Hz, $^3J_{\text{H,H}} = 5.6$ Hz, 2H, 22-CH₂), 3.97 (t, $^3J_{\text{H,H}} = 6.7$ Hz, 2H, 19-CH₂), 3.81-3.73 (m, 1H, 12-CH), 3.55 (dd, $^2J_{\text{H,H}} = 9.5$ Hz, $^3J_{\text{H,H}} = 3.9$ Hz, 1H, 16-CH_a), 3.47-3.38 (m, 1H, 15-CH_a), 3.40 (dd, $^2J_{\text{H,H}} = 9.8$ Hz, $^3J_{\text{H,H}} = 2.5$ Hz, 1H, 16-CH_b), 3.36 (s, 3H, 18-CH₃), 3.21-3.12 (m, 1H, 15-CH_b), 2.02-1.64 (m, 8H, 13-CH₂, 14-CH₂, 20-CH₂, 21-CH₂) ppm. ^{13}C NMR (100 MHz, CDCl₃): $\delta = 181.2$ (d, $^4J_{\text{C,F}} = 3.1$ Hz, 3-CO), 157.5 (2-CO), 147.2 (d, $^1J_{\text{C,F}} = 252.9$ Hz, 7-CF), 140.3 (d, $^2J_{\text{C,F}} = 8.8$ Hz, 8-CN), 135.0 (d, $^3J_{\text{C,F}} = 4.1$ Hz, 5-CSO₂), 125.5 (d, $^2J_{\text{C,F}} = 22.7$ Hz, 6-CH), 120.3 (d, $^4J_{\text{C,F}} = 3.4$ Hz, 4-CH), 120.0 (d, $^3J_{\text{C,F}} = 2.8$ Hz, 9-CCO), 83.2 (d, $^1J_{\text{C,F}} = 165.5$ Hz, 22-CH₂), 74.7 (16-CH₂), 59.4 (12-CH), 59.1 (18-CH₃), 42.4 (d, $^4J_{\text{C,F}} = 4.8$ Hz, 19-CH₂), 49.3 (15-CH₂), 28.8 (13-CH₂), 27.5 (d, $^2J_{\text{C,F}} = 20.2$ Hz, 21-CH₂), 25.0 (dd, $^3J_{\text{C,F}} = 4.3$ Hz, $^5J_{\text{C,F}} = 2.7$ Hz, 20-CH₂), 24.2 (14-CH₂) ppm. ^{19}F NMR (282 MHz, CDCl₃): $\delta = -131.0$ (s, 1F, 7-CF), -219.5 (s, 1F, 22-CH₂F) ppm.

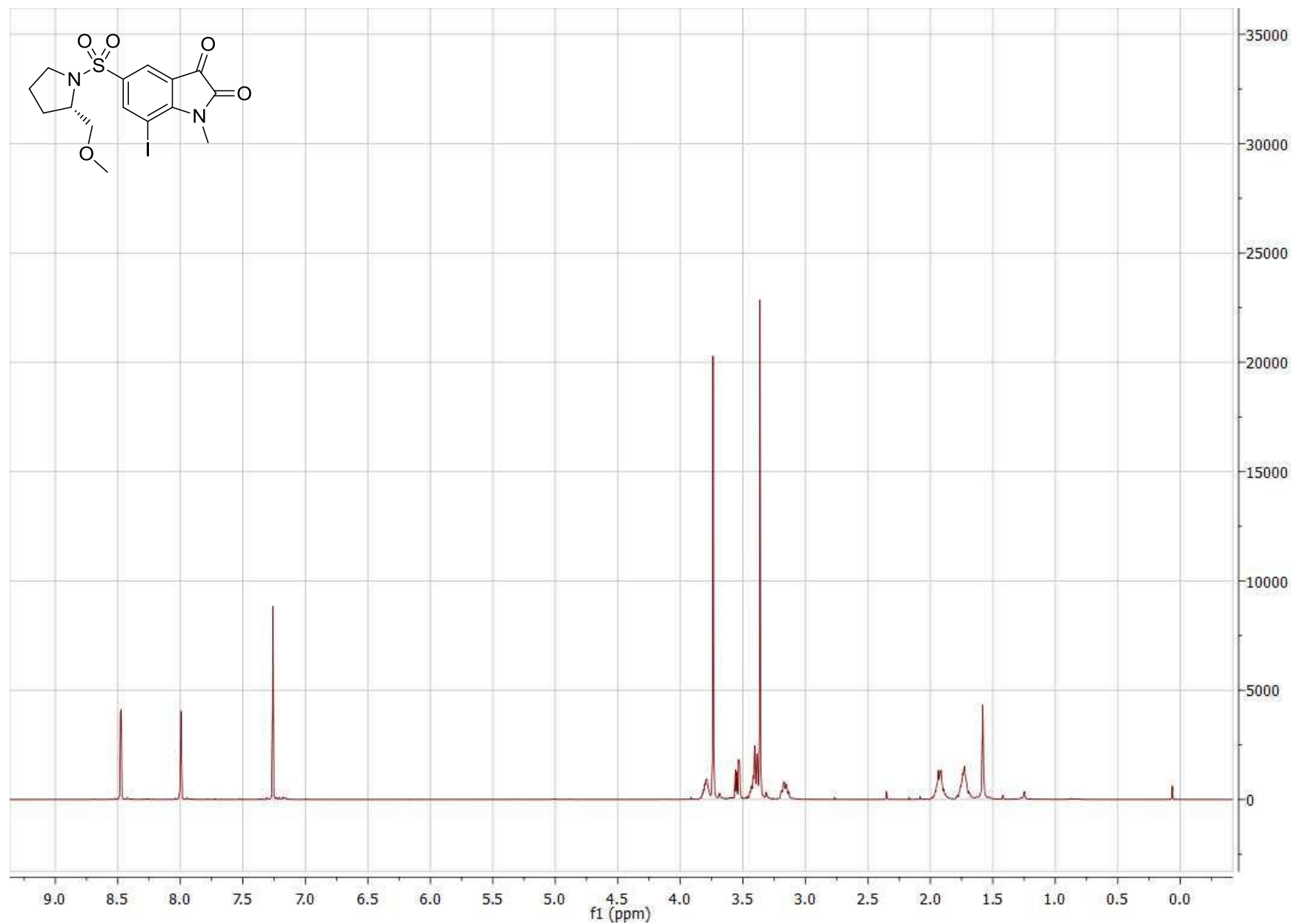
^1H NMR spectrum of (*S*)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**10**)



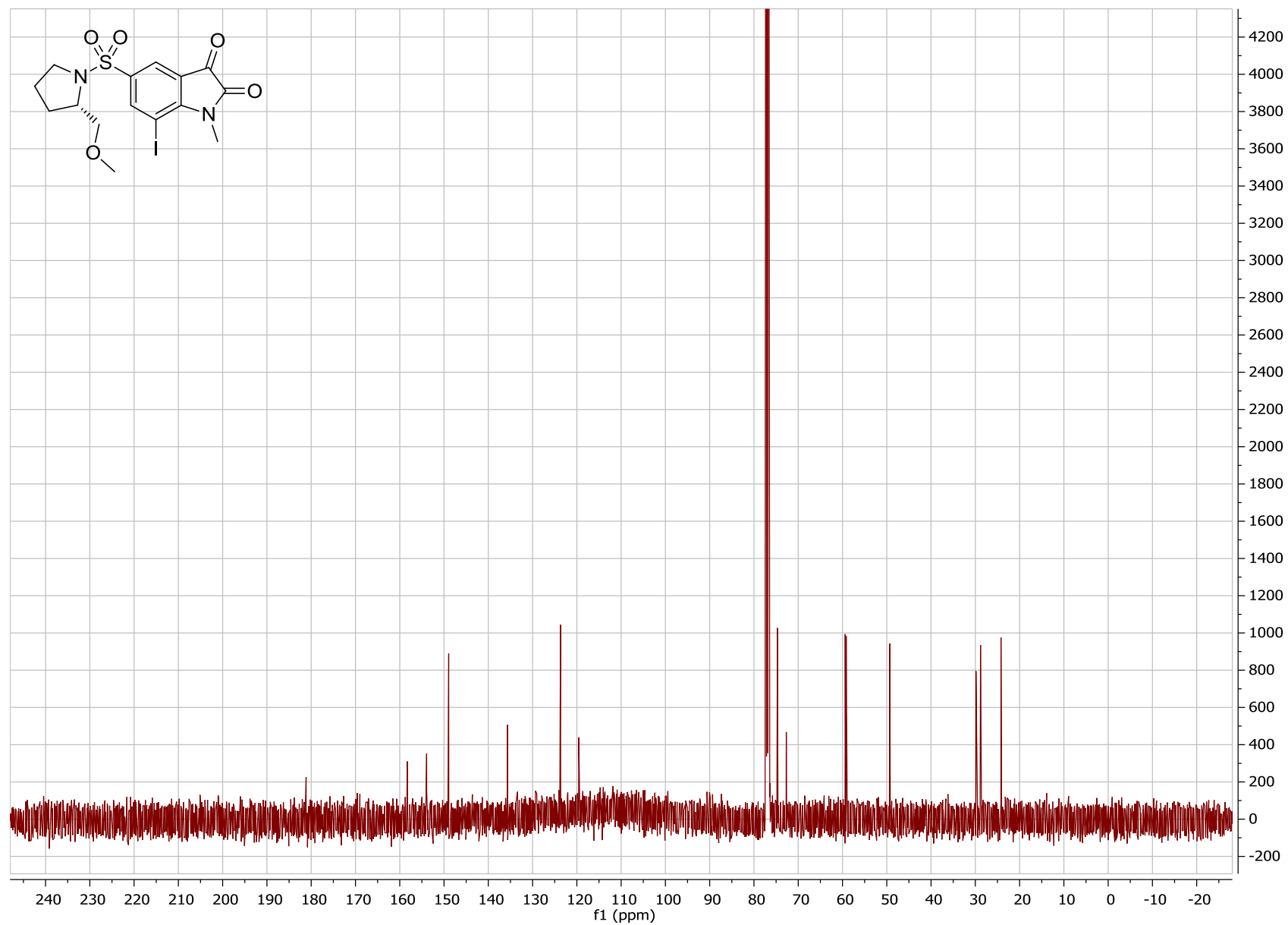
¹³C NMR spectrum of (S)-7-iodo-5-[1-(2-methoxymethylpyrrolidiny]sulfonyl]isatin (**10**)



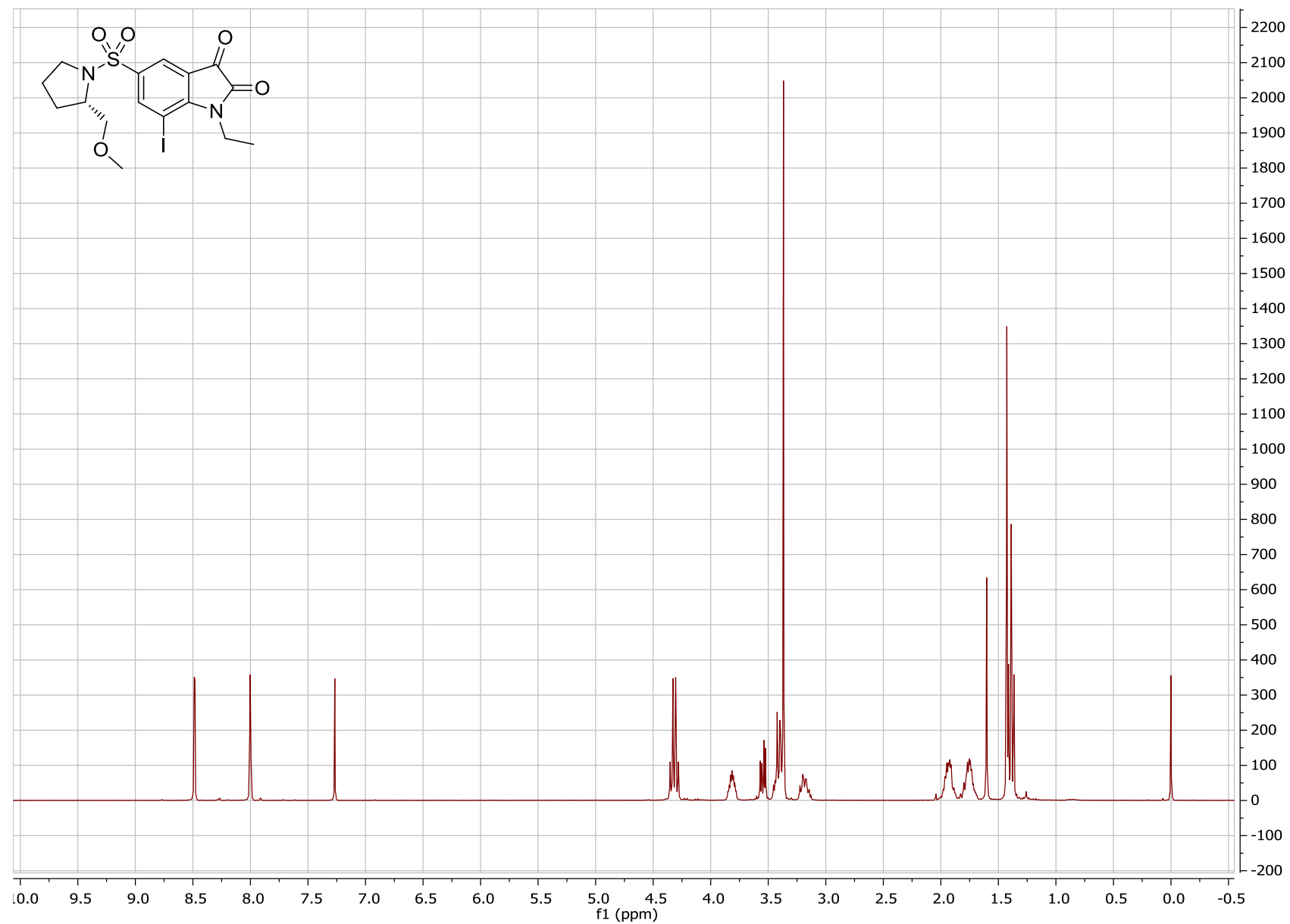
^1H NMR spectrum of (*S*)-*N*-methyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**11**)



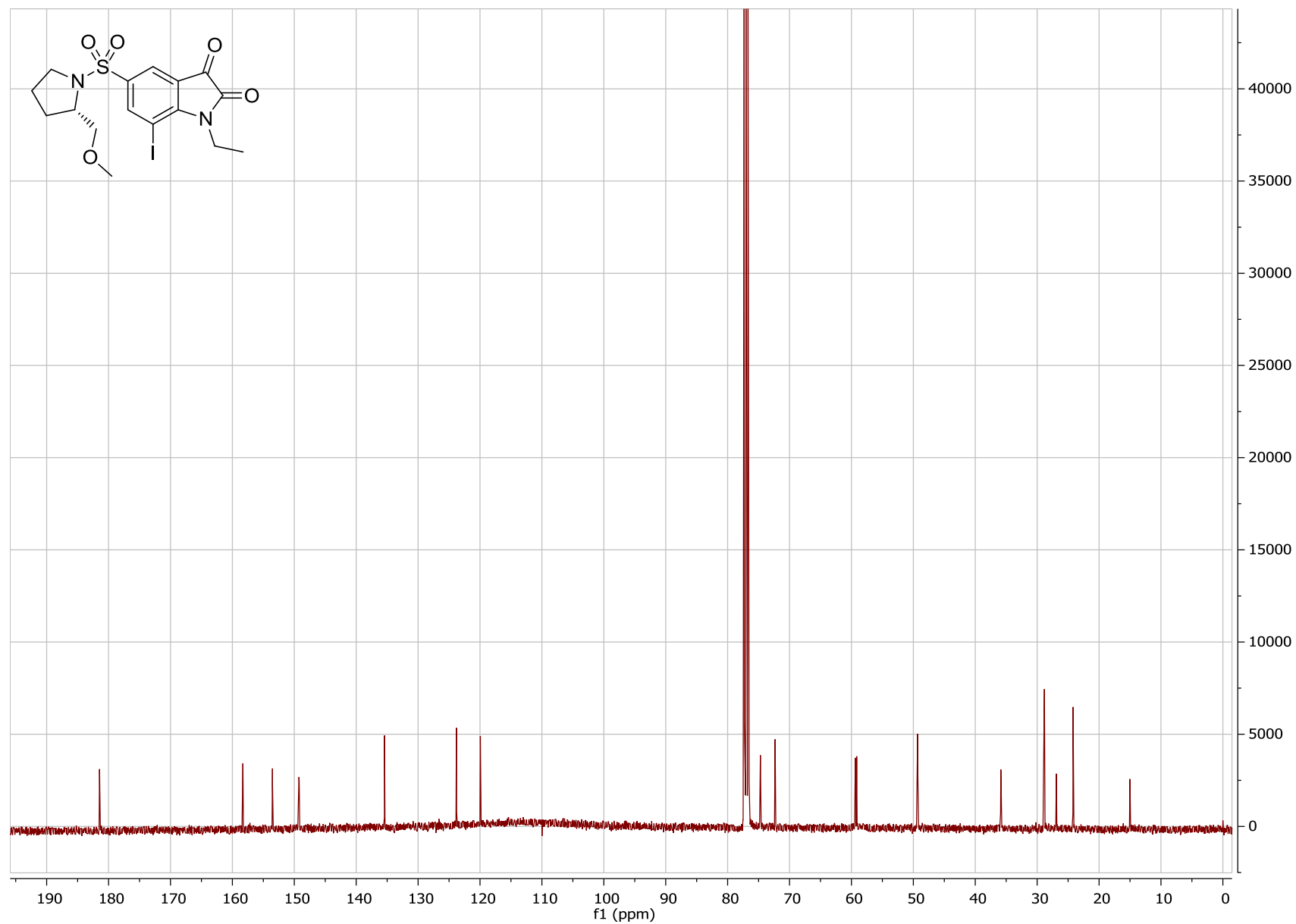
¹³C NMR spectrum of (S)-N-methyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**11**)



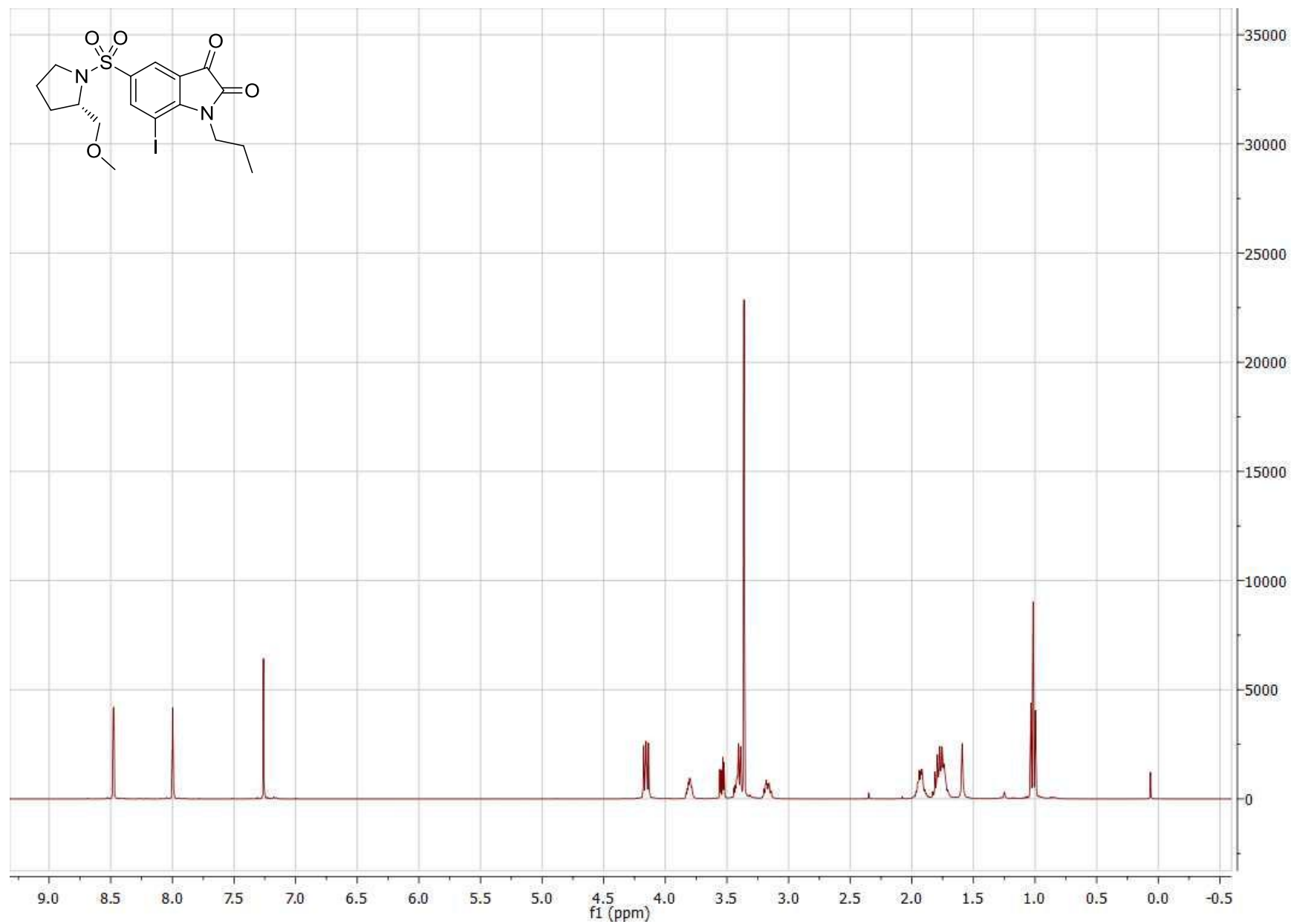
^1H NMR spectrum of (*S*)-*N*-ethyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**12**)



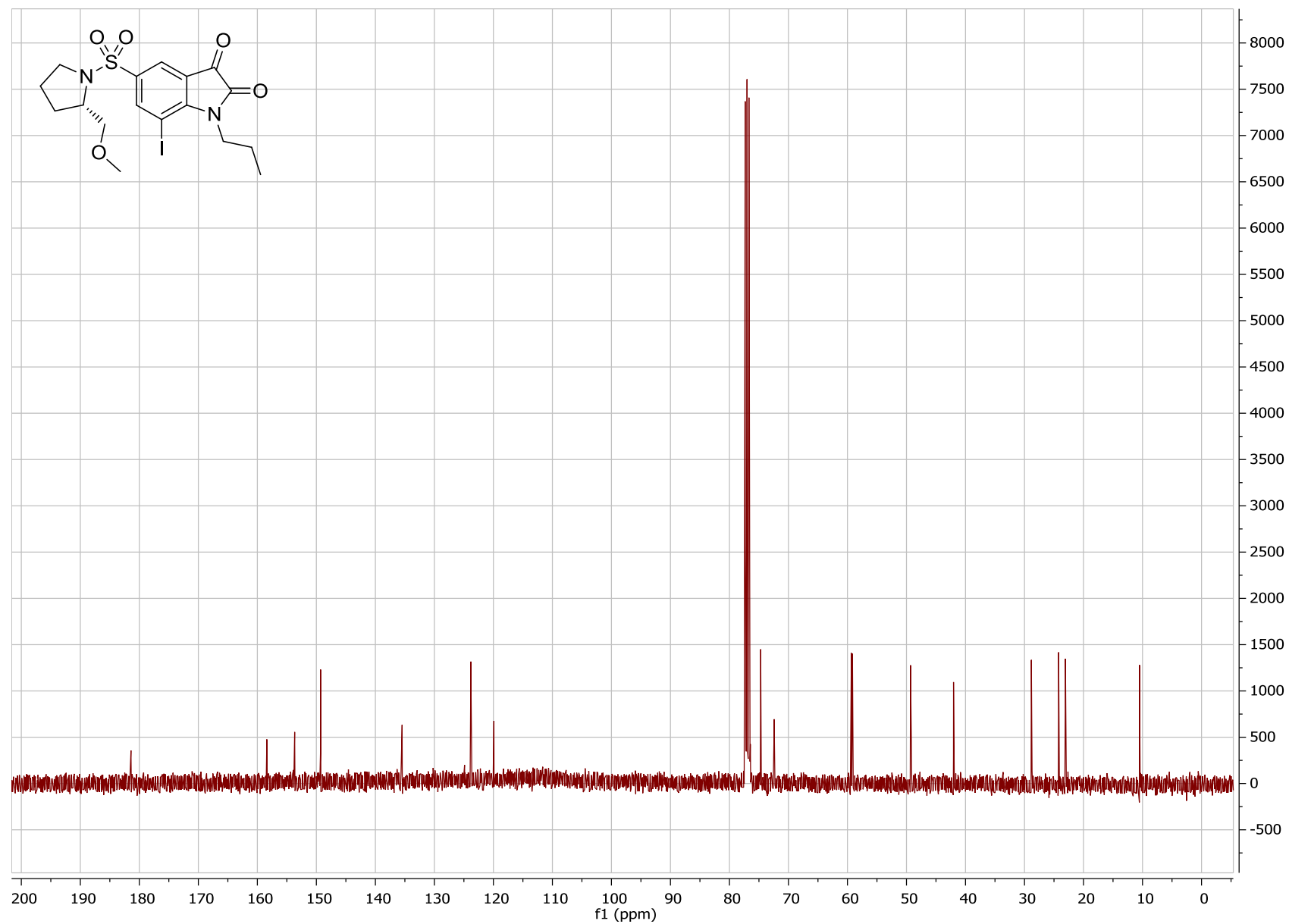
^{13}C NMR spectrum of (S)-N-ethyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**12**)



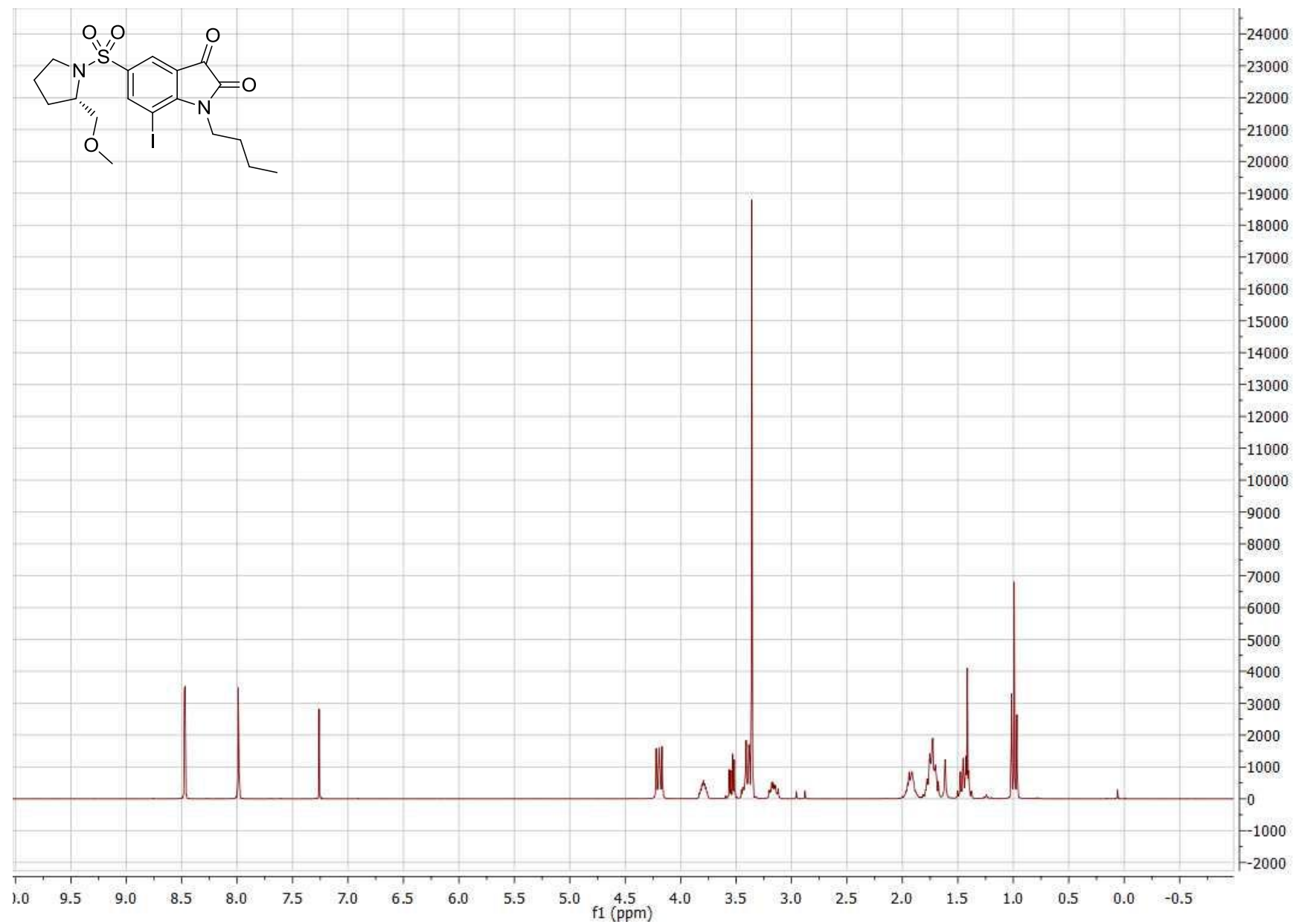
^1H NMR spectrum of (*S*)-*N*-propyl-7-iodo-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatin (**13**)



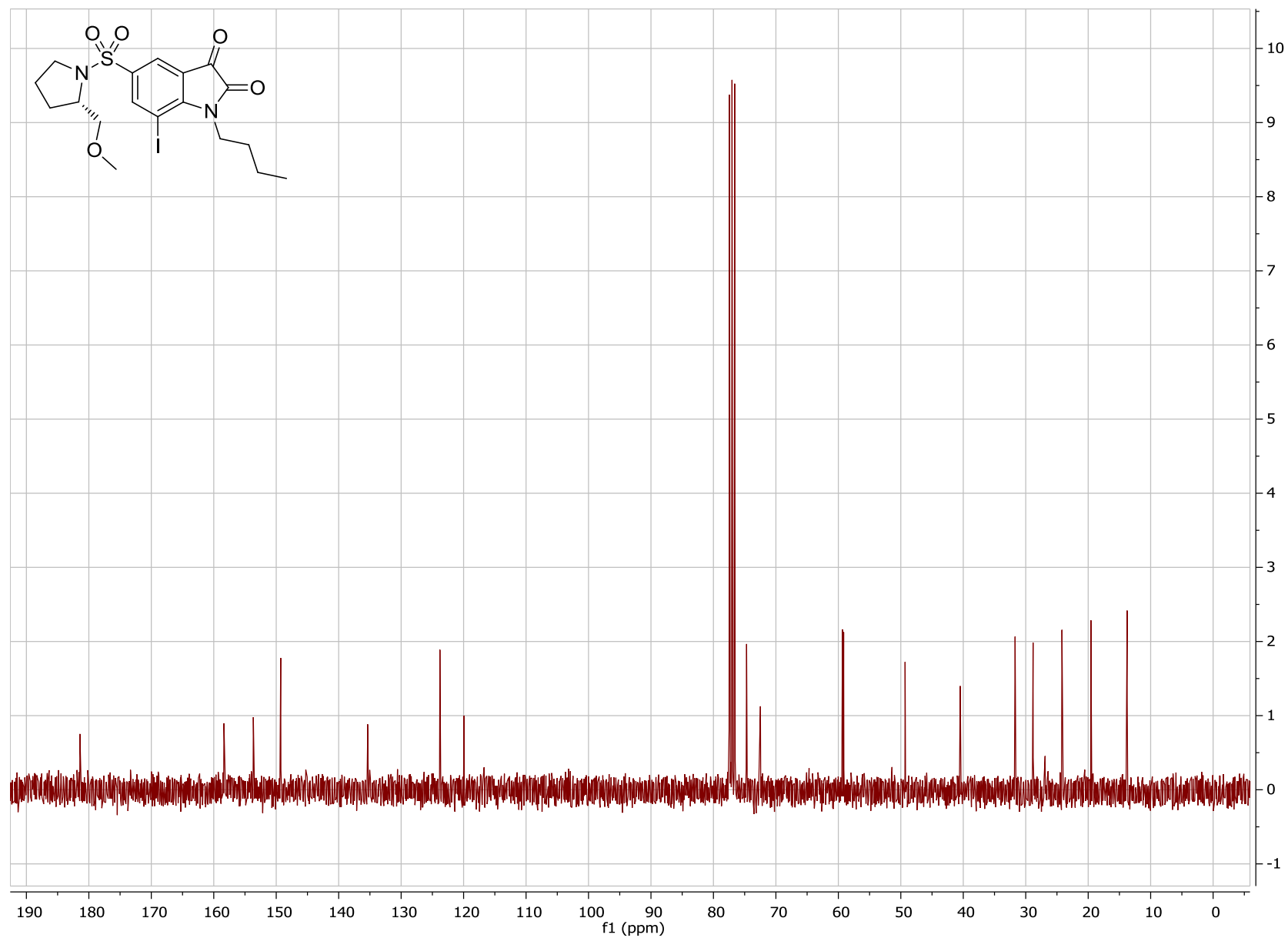
^{13}C NMR spectrum of (S)-N-propyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**13**)



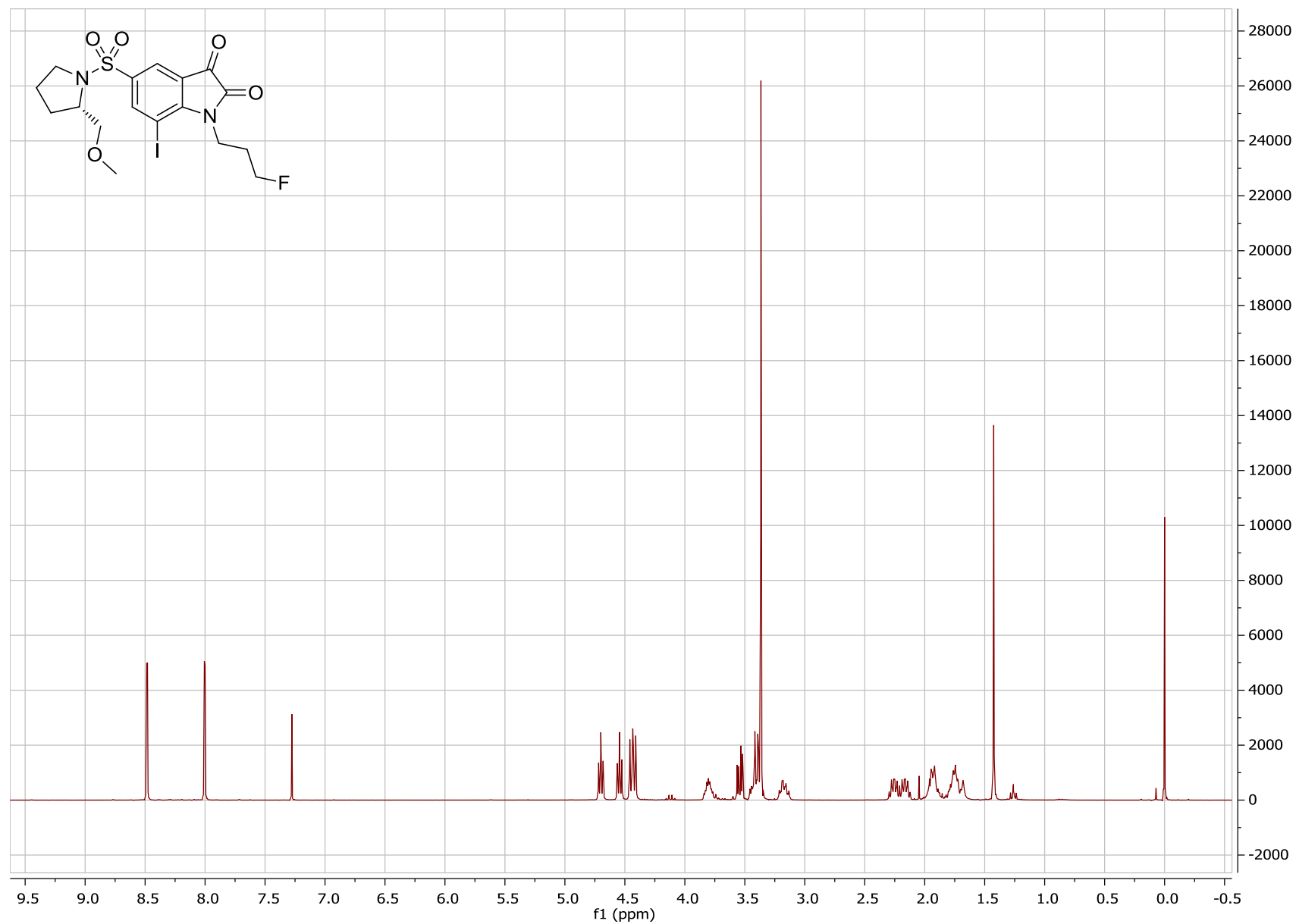
^1H NMR spectrum of (*S*)-*N*-butyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**14**)



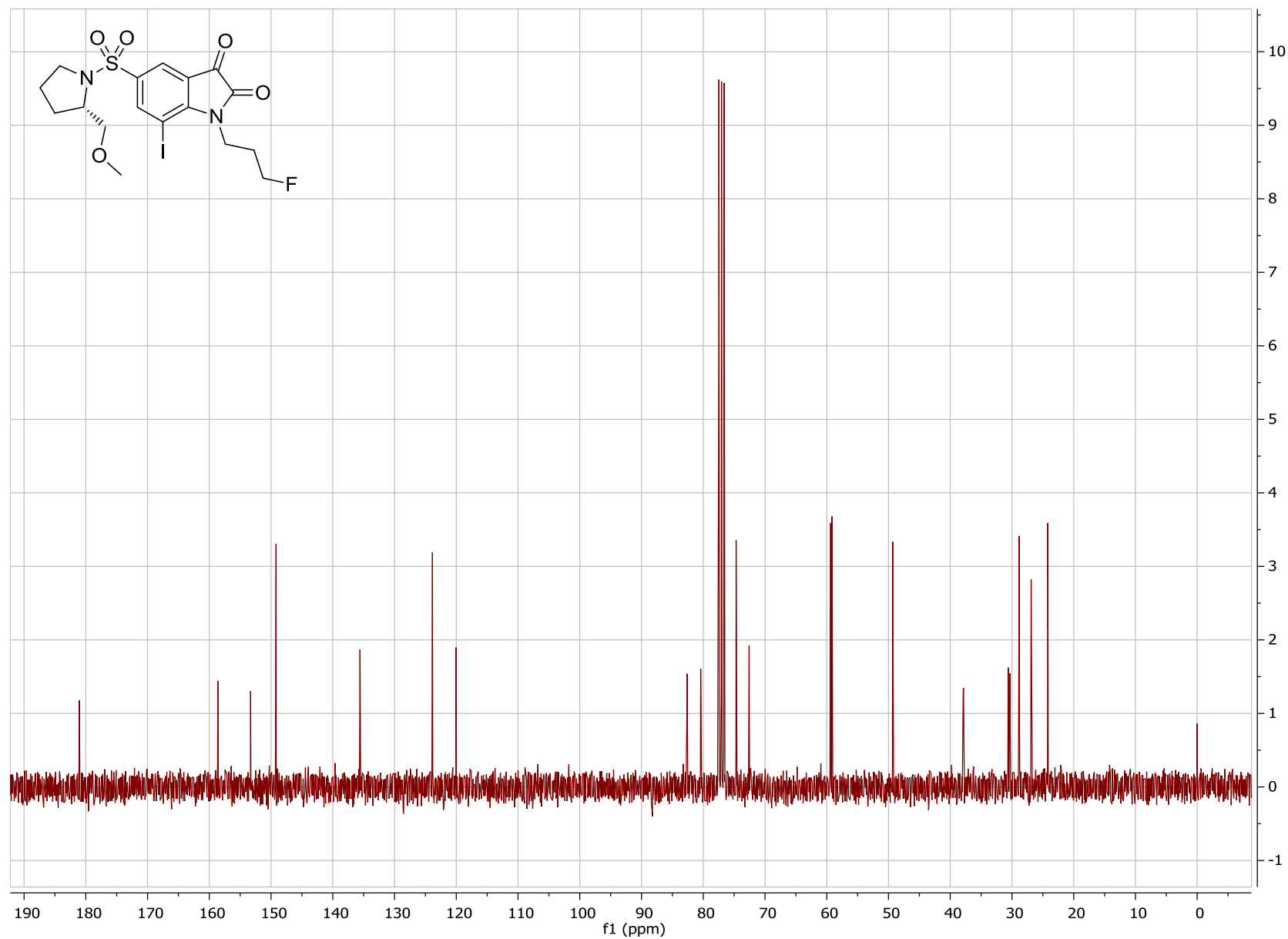
^{13}C NMR spectrum of (S)-N-butyl-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**14**)



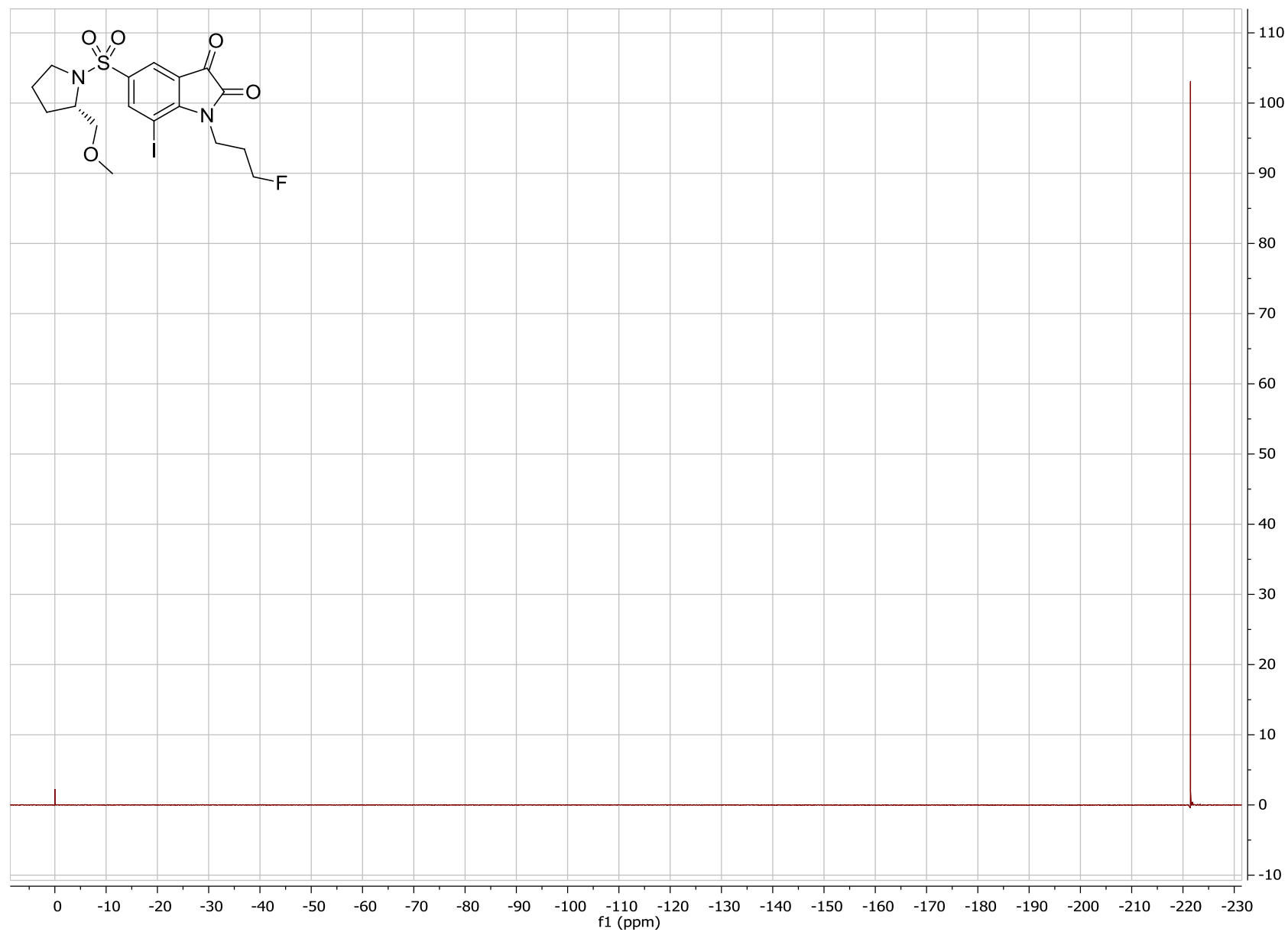
^1H NMR spectrum of (S)-N-(3-fluoropropyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**15**)



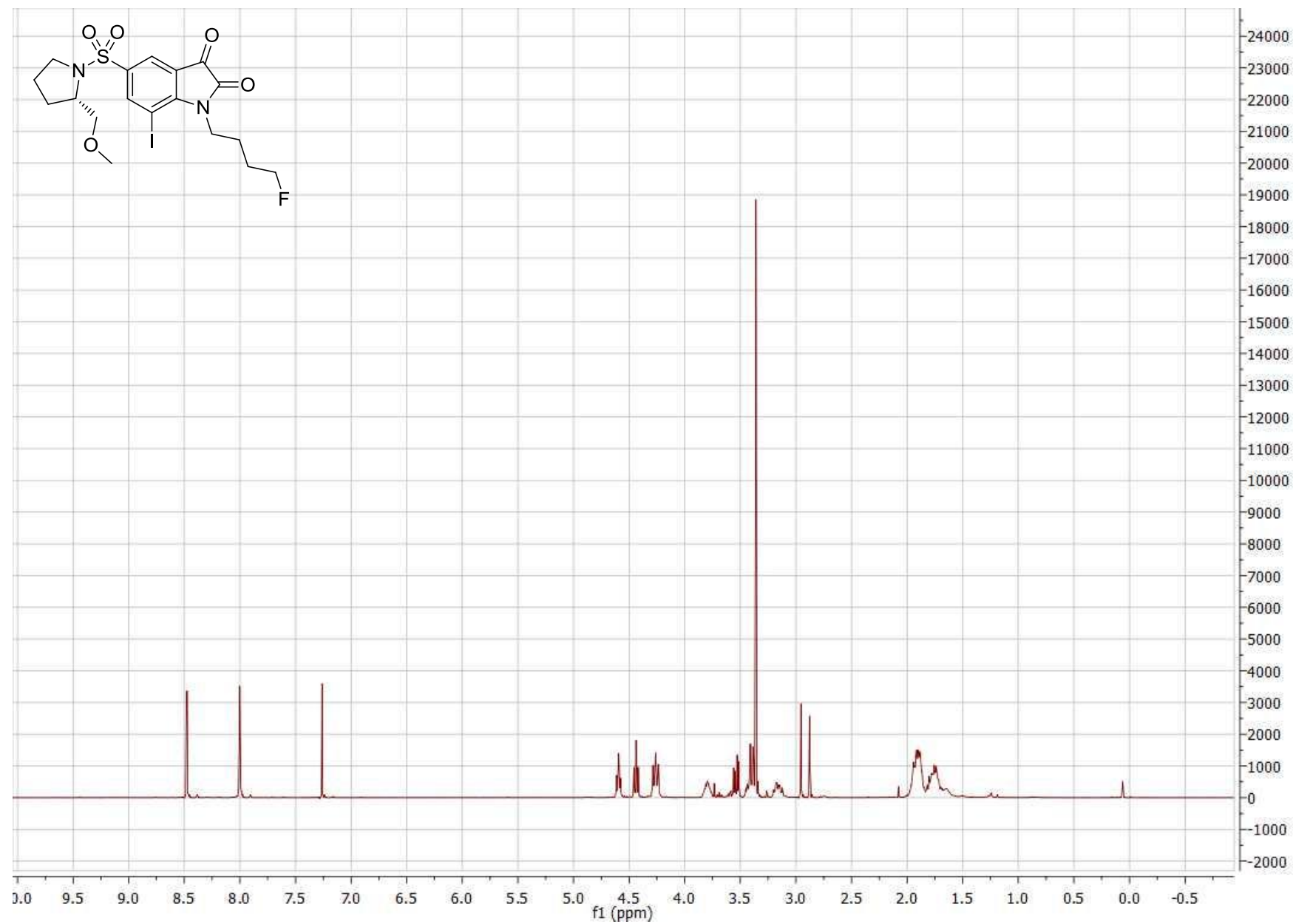
¹³C NMR spectrum of (S)-N-(3-fluoropropyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**15**)



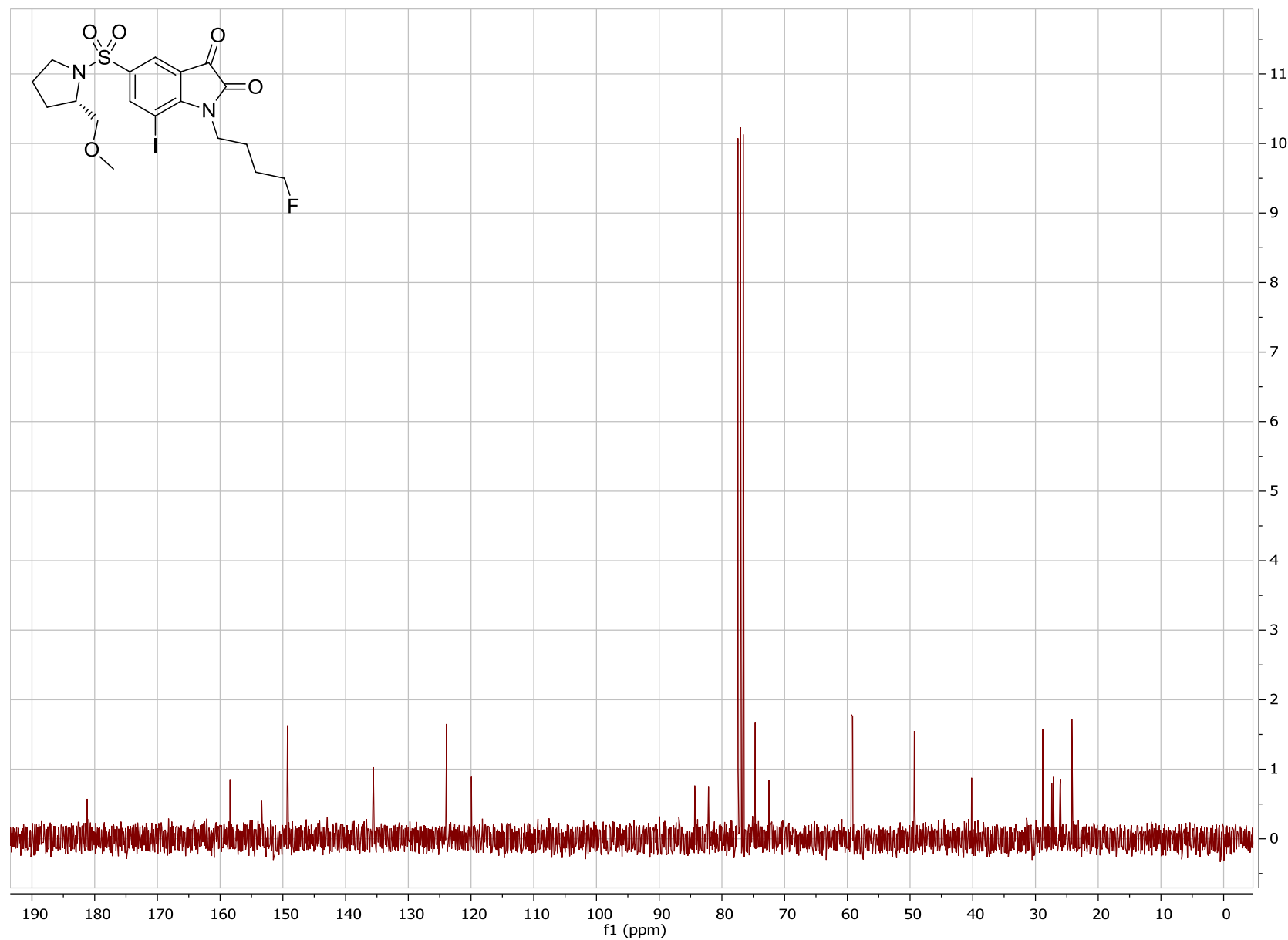
^{19}F NMR spectrum of (S)-N-(3-fluoropropyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**15**)



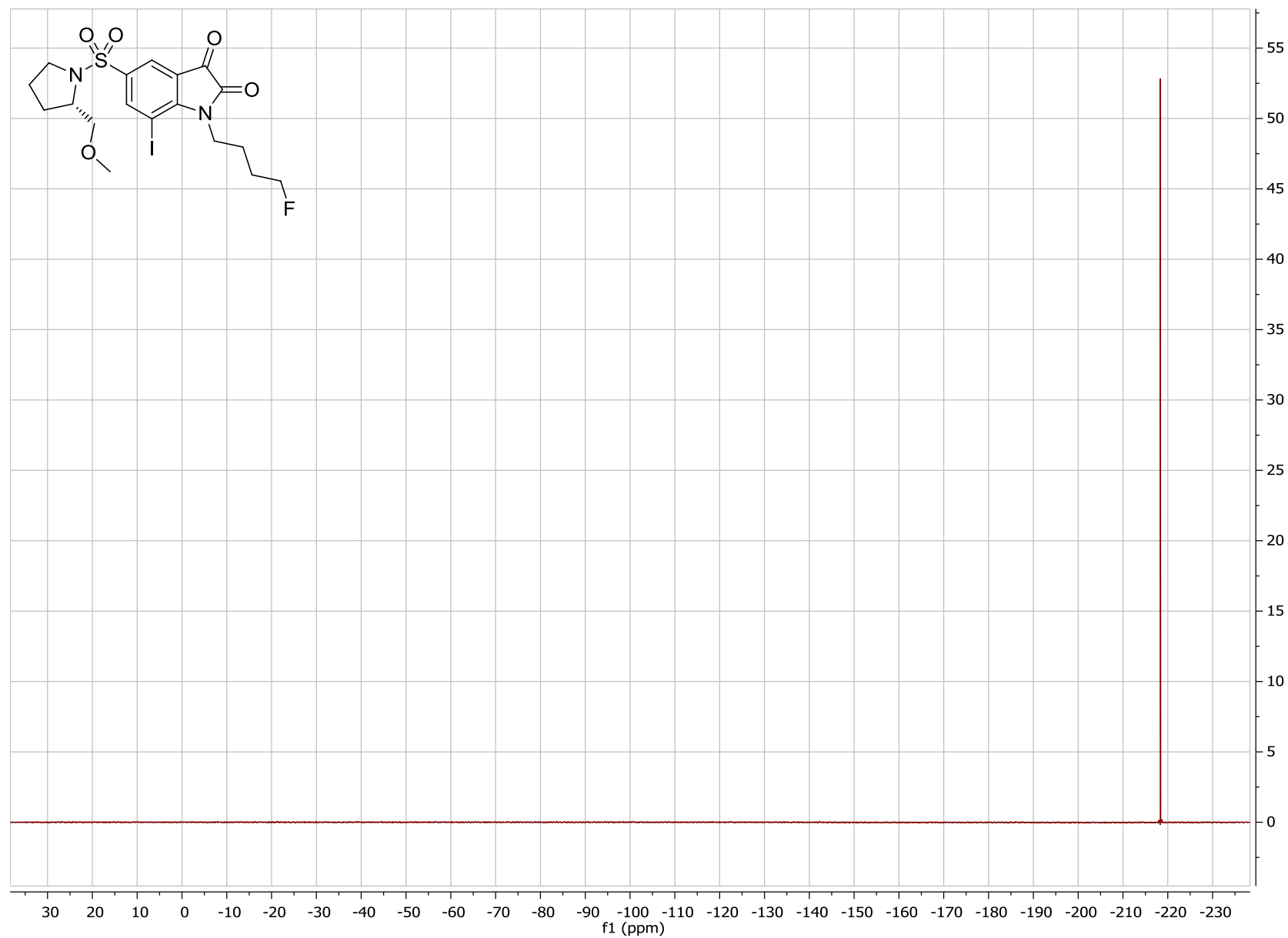
^1H NMR spectrum of (S)-N-(4-fluorobutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**16**)



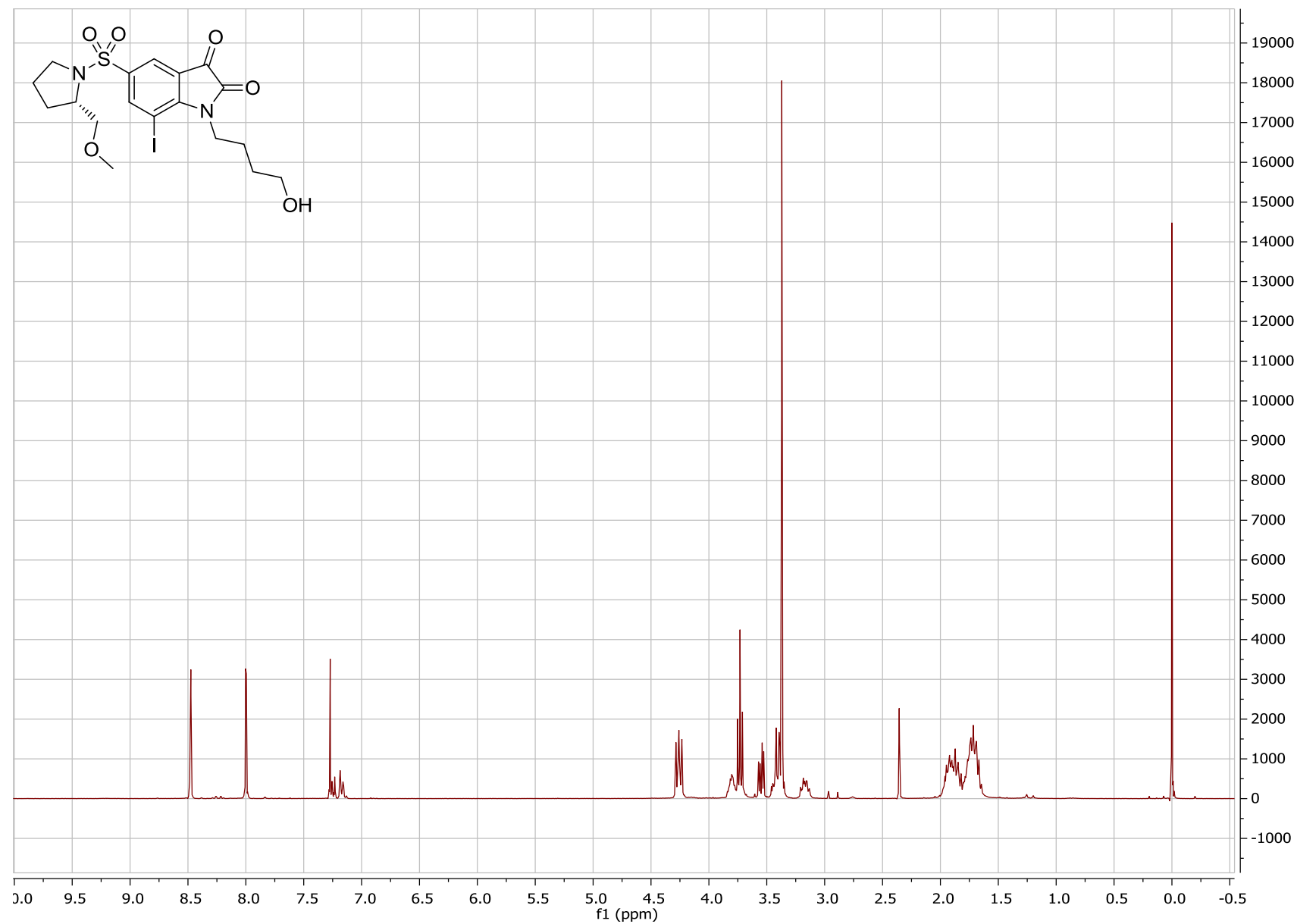
¹³C NMR spectrum of (S)-N-(4-fluorobutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**16**)



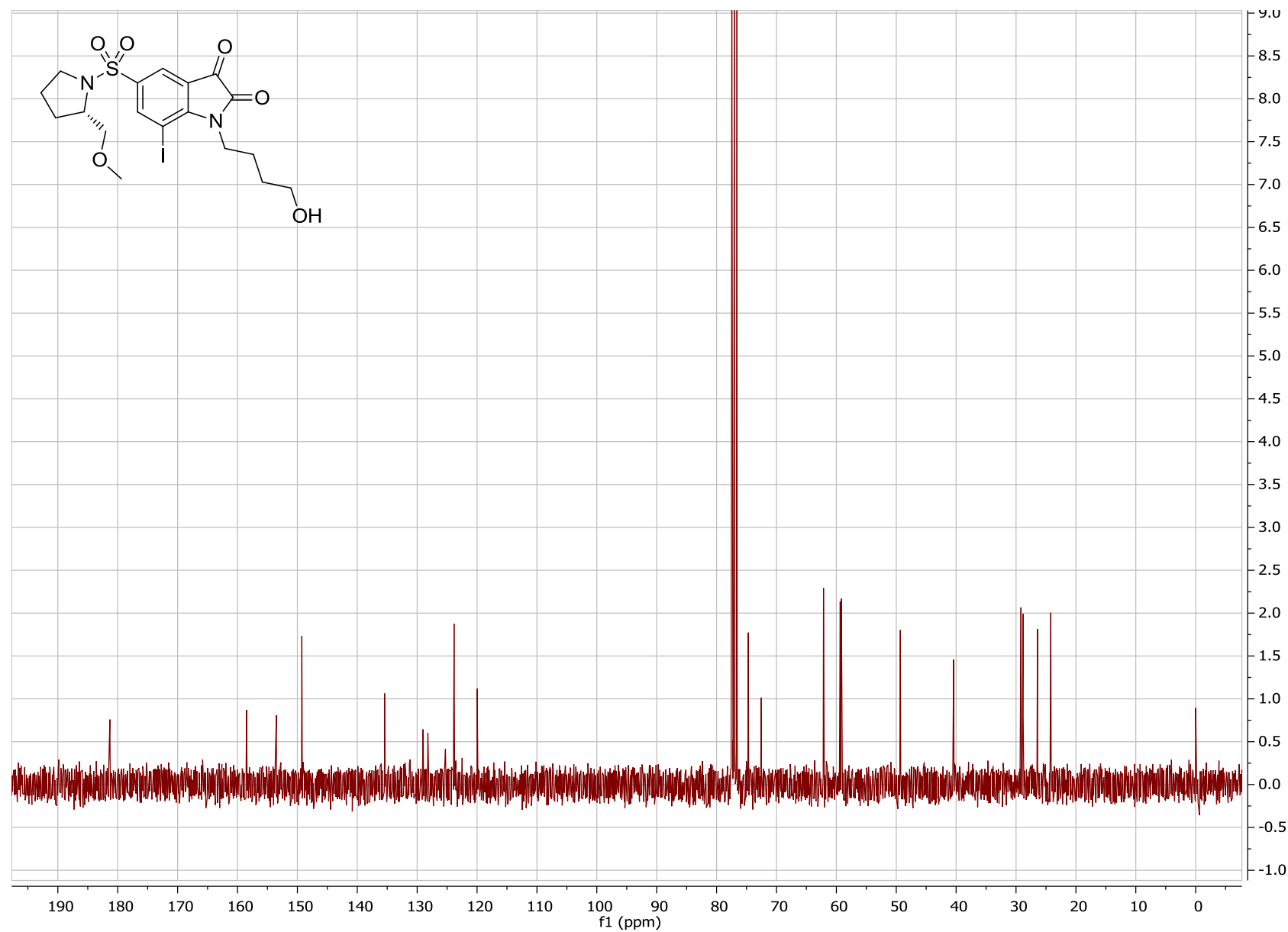
^{19}F NMR spectrum of (S)-N-(4-fluorobutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**16**)



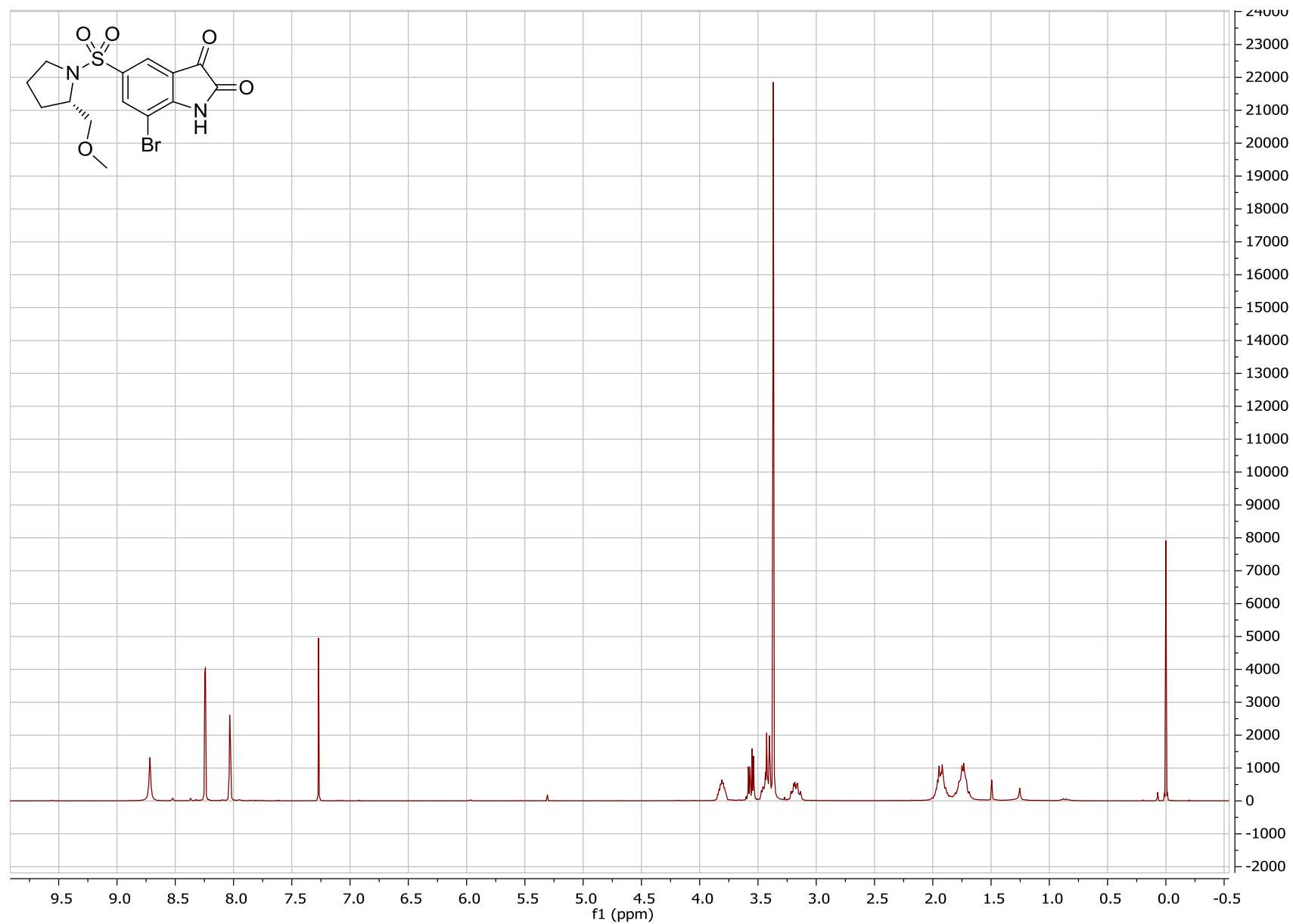
^1H NMR spectrum of (*S*)-*N*-(4-hydroxybutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**17**)



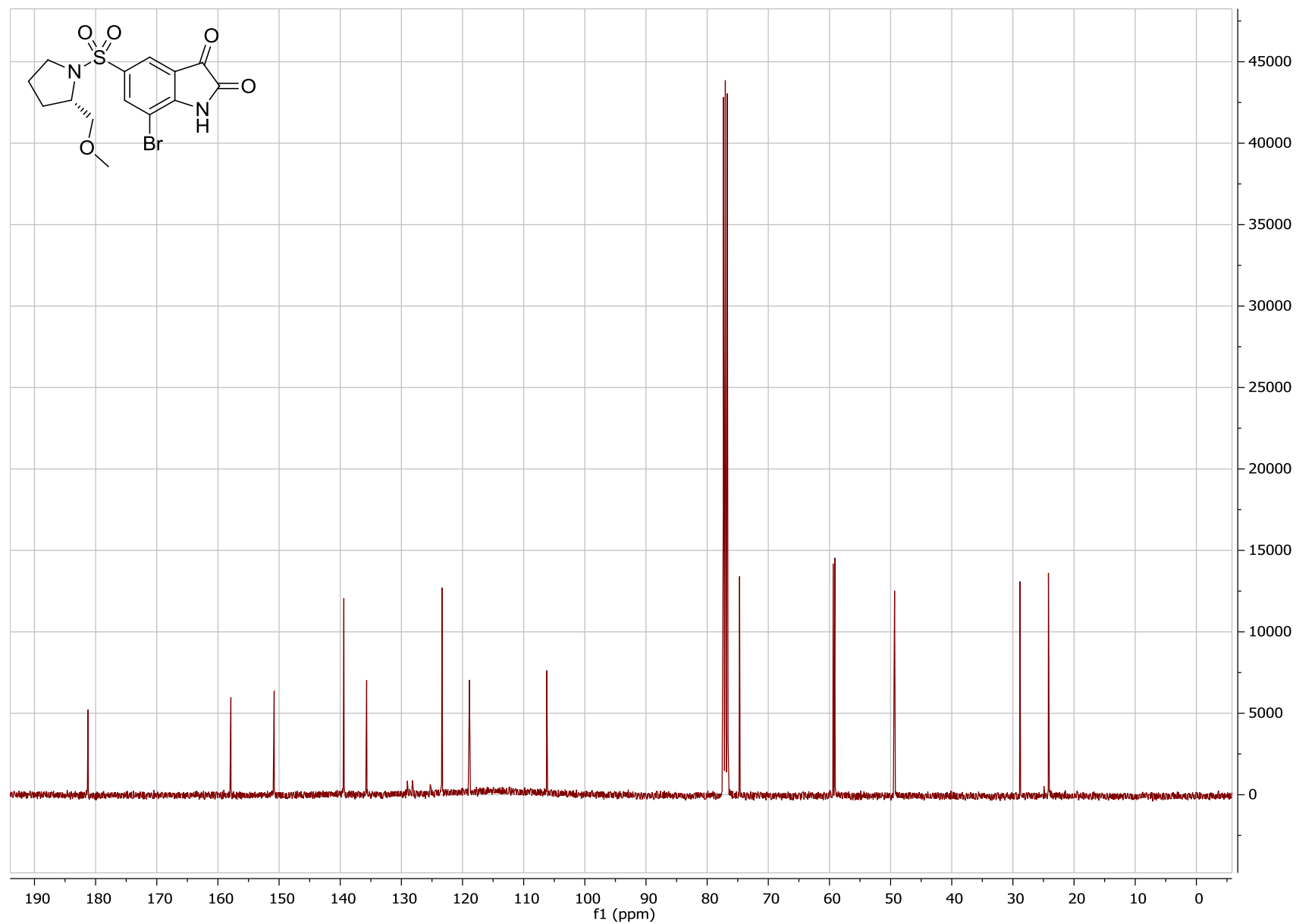
¹³C NMR spectrum of (S)-N-(4-hydroxybutyl)-7-iodo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**17**)



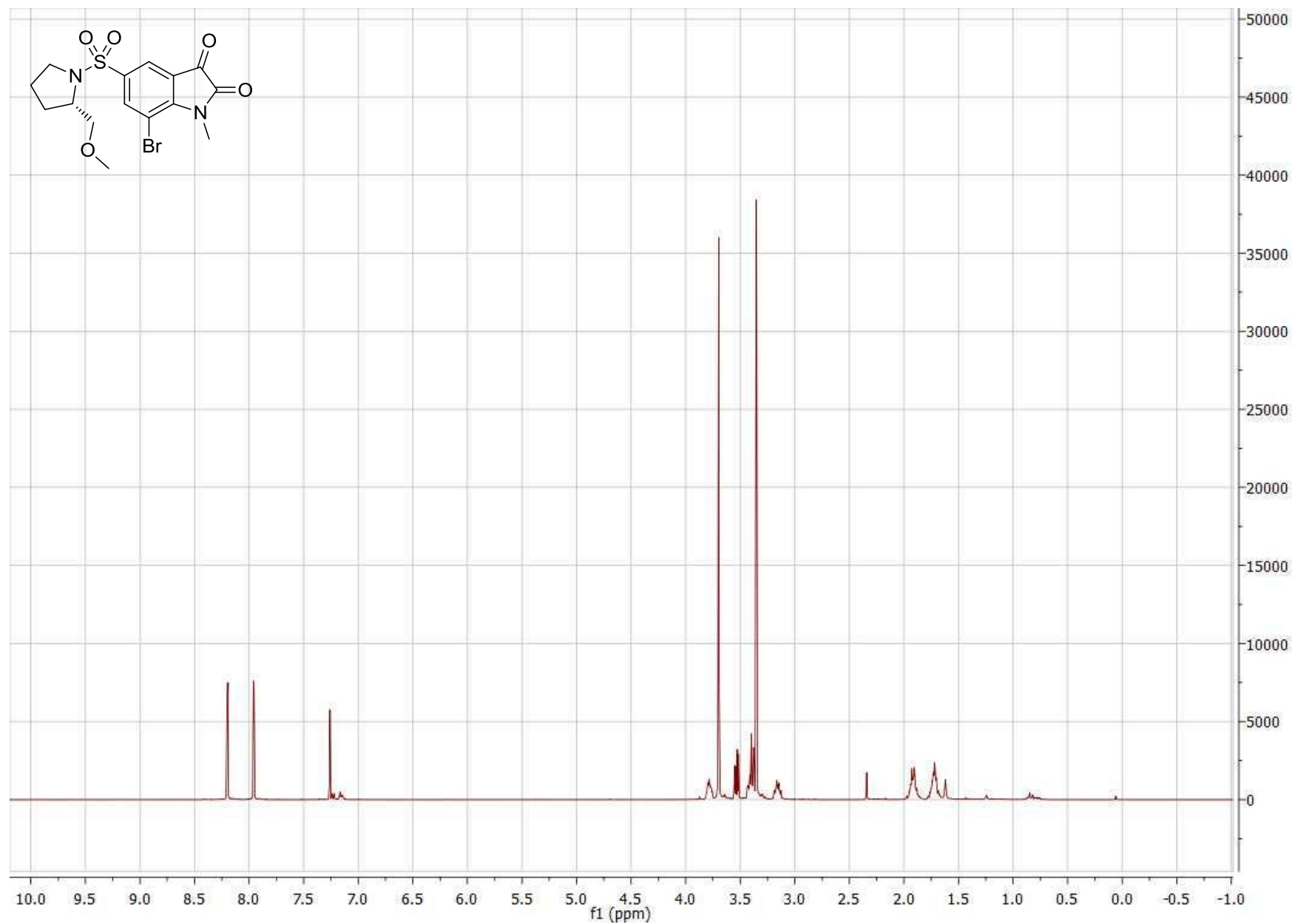
¹H NMR spectrum of (S)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**18**)



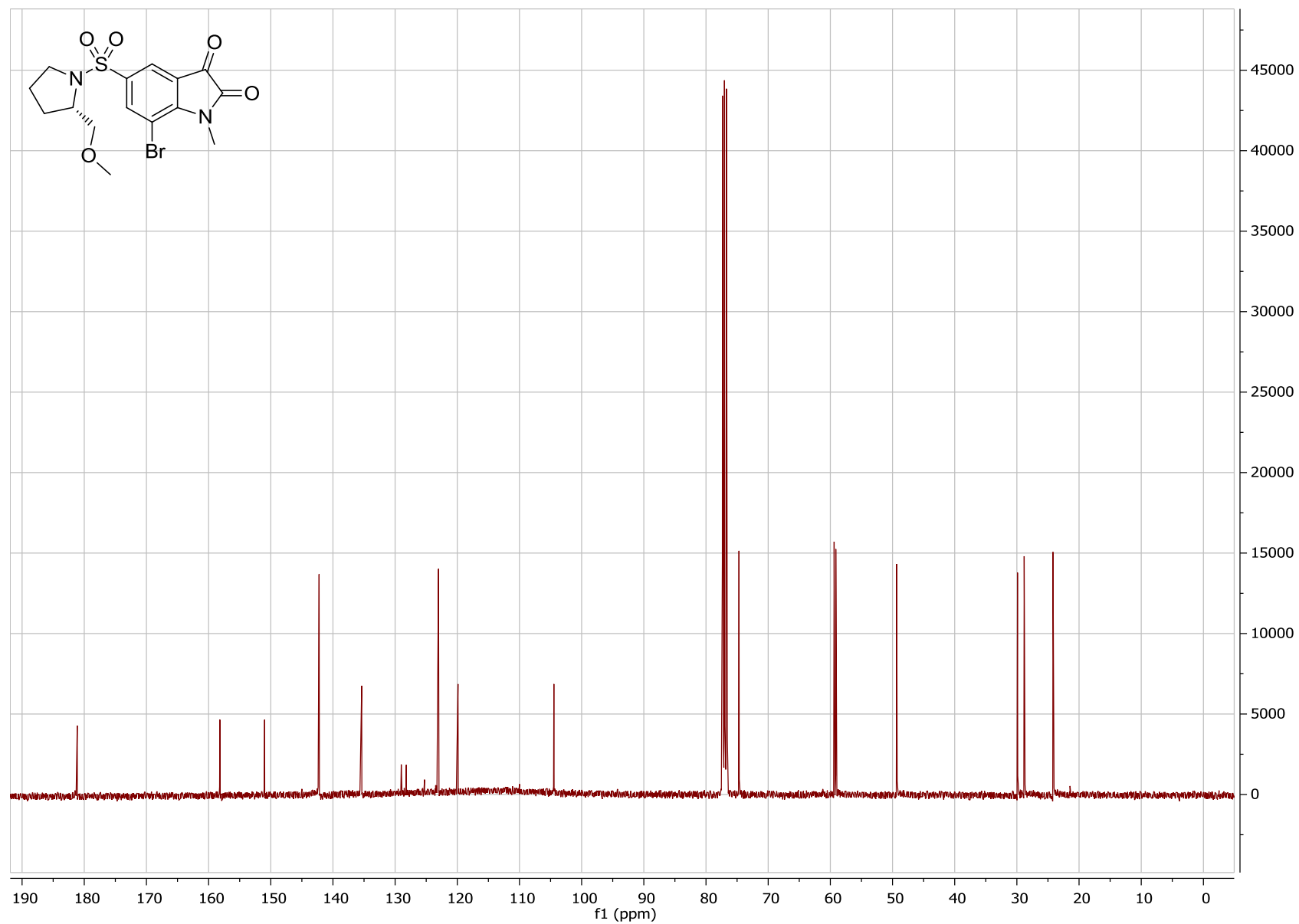
^{13}C NMR spectrum of (S)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**18**)



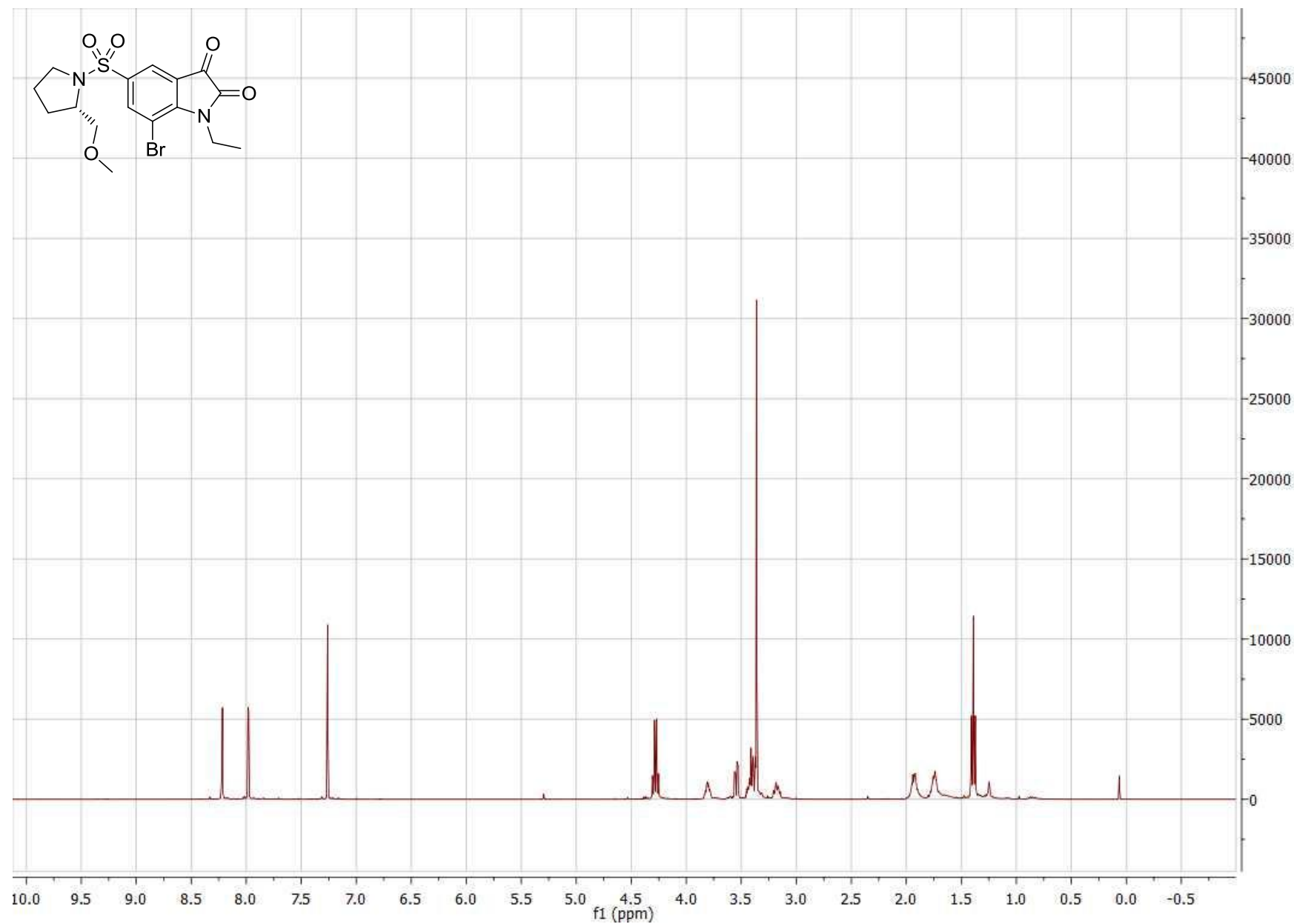
^1H NMR spectrum of (*S*)-*N*-methyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**19**)



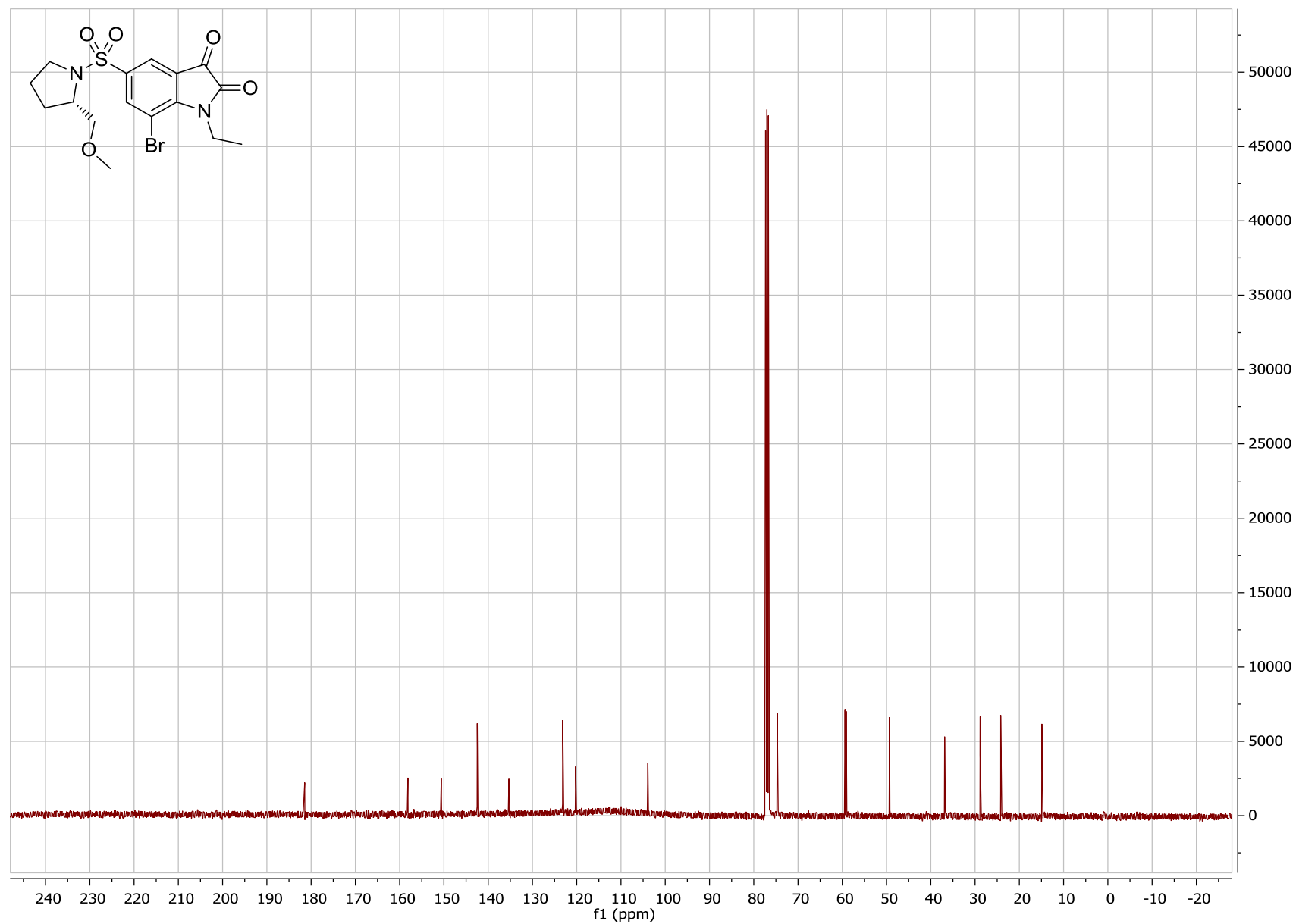
¹³C NMR spectrum of (S)-N-methyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**19**)



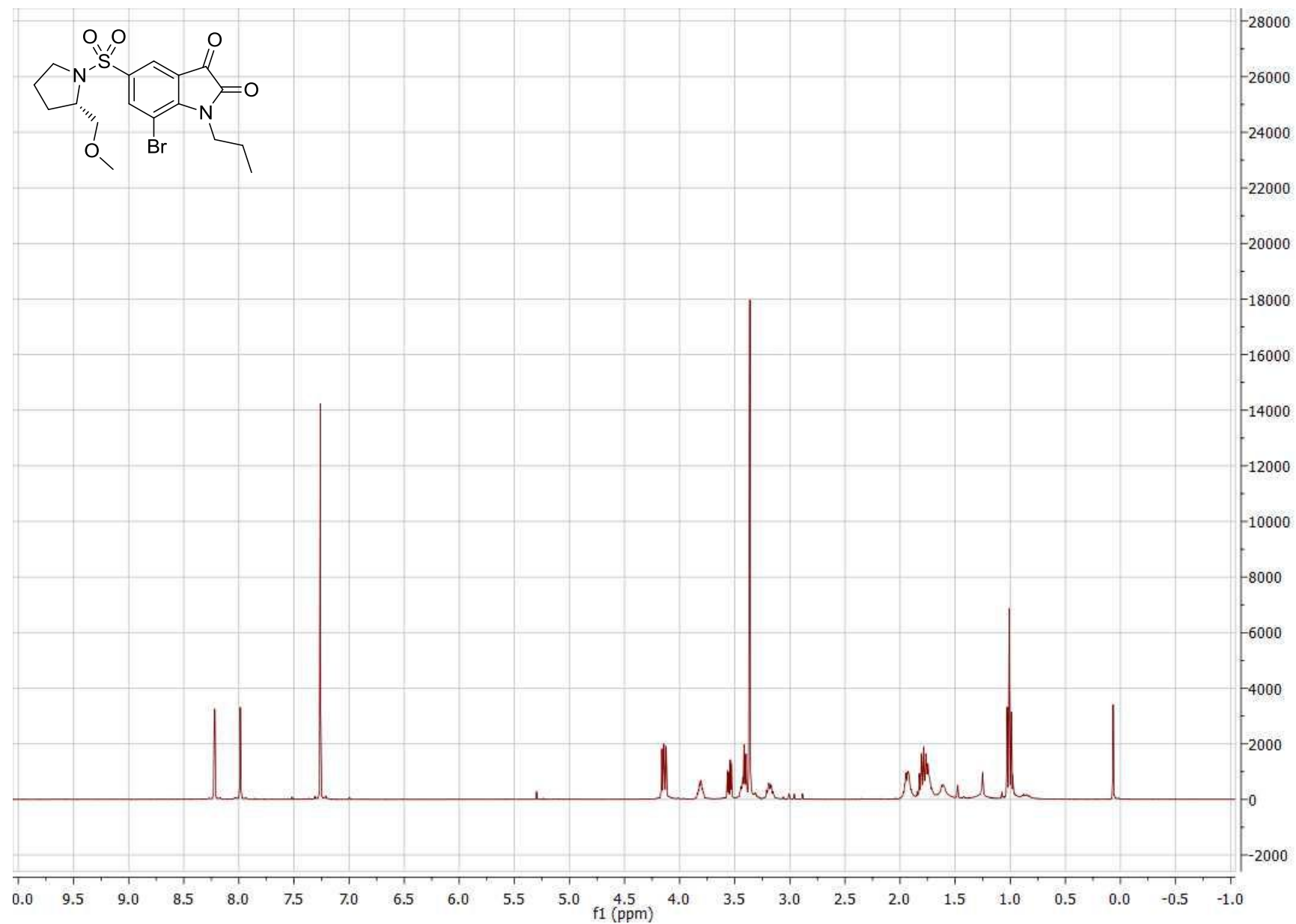
^1H NMR spectrum of (*S*)-*N*-ethyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**20**)



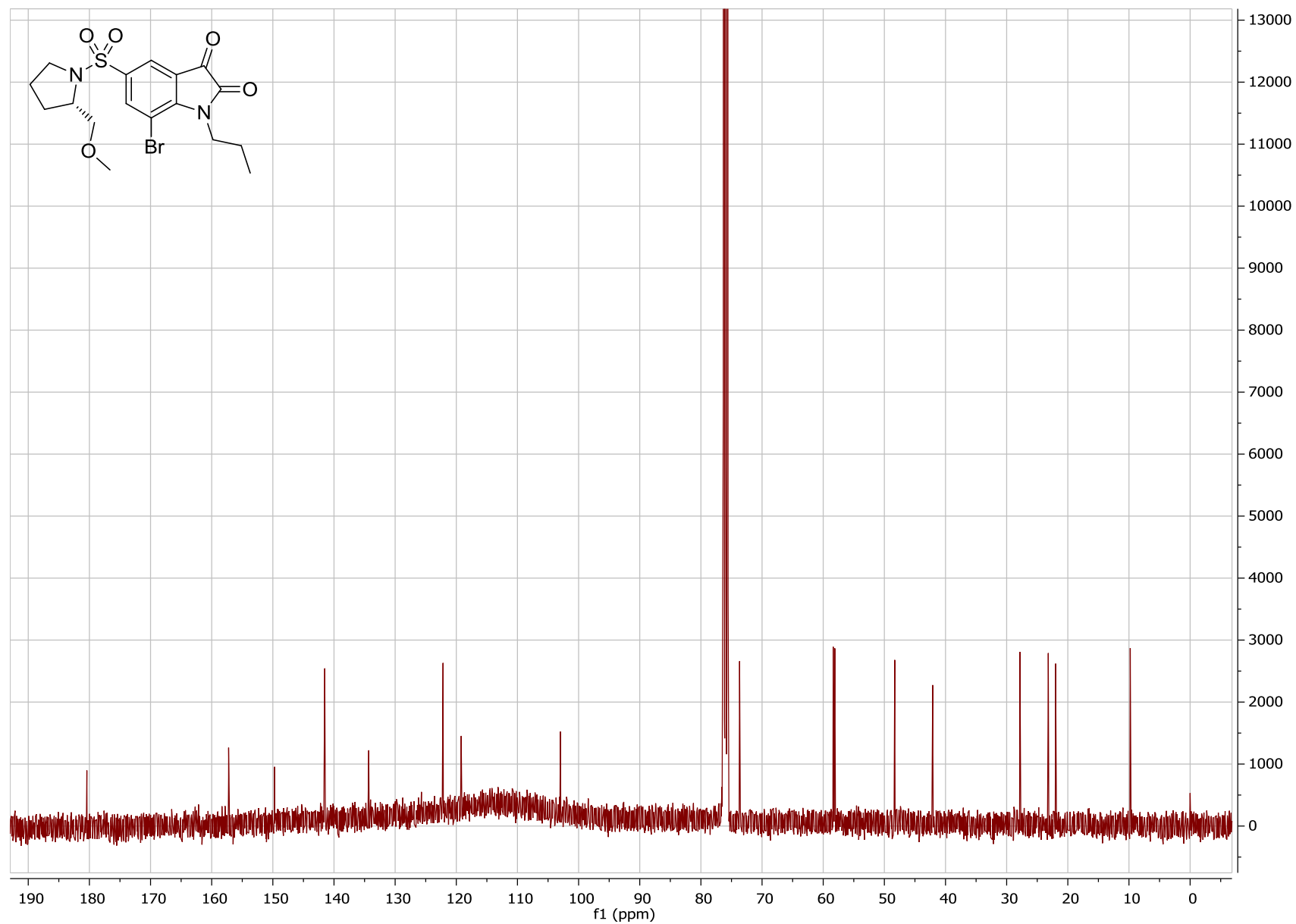
¹³C NMR spectrum of (S)-N-ethyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**20**)



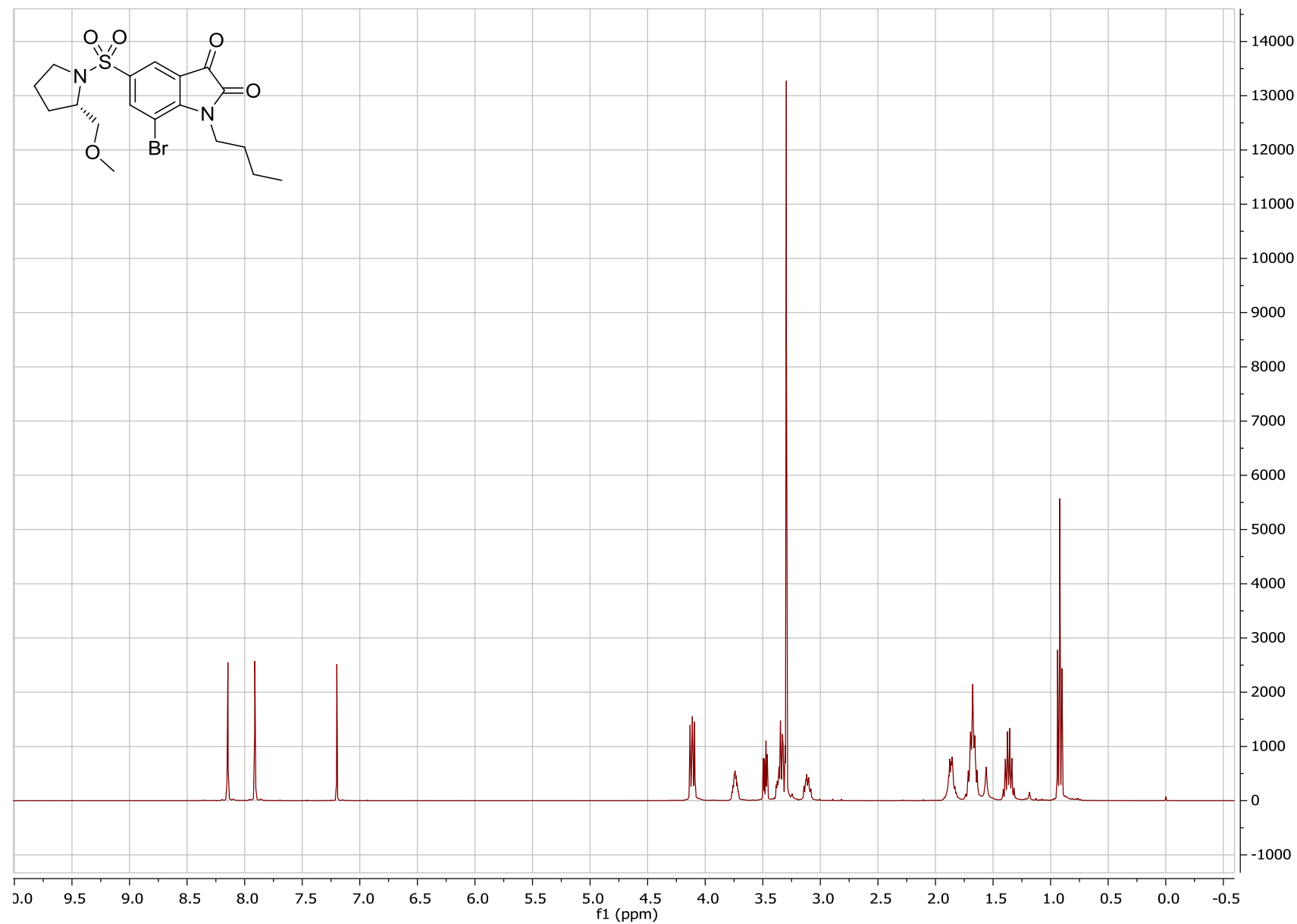
^1H NMR spectrum of (*S*)-*N*-propyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**21**)



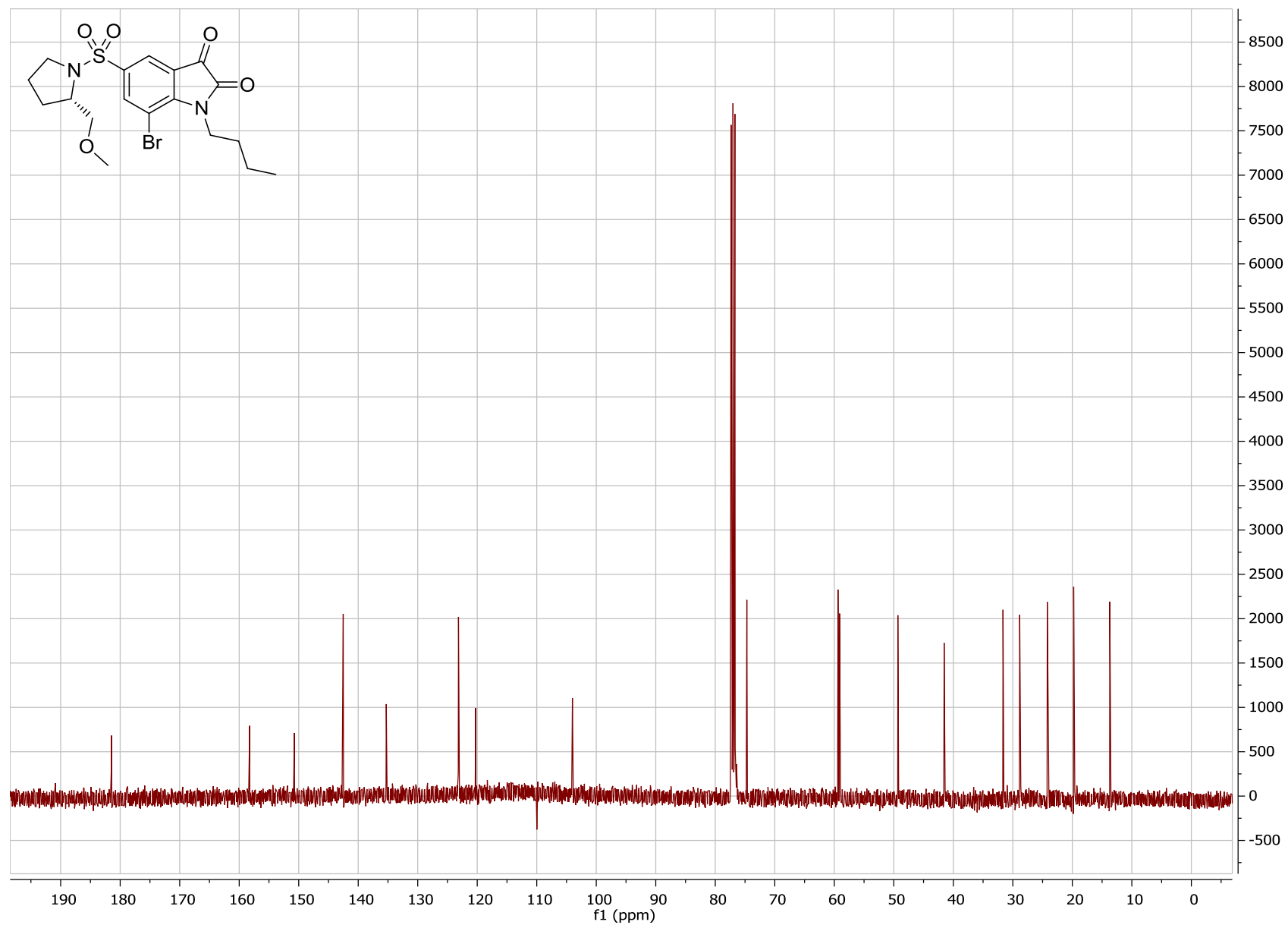
^{13}C NMR spectrum of (S)-N-propyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**21**)



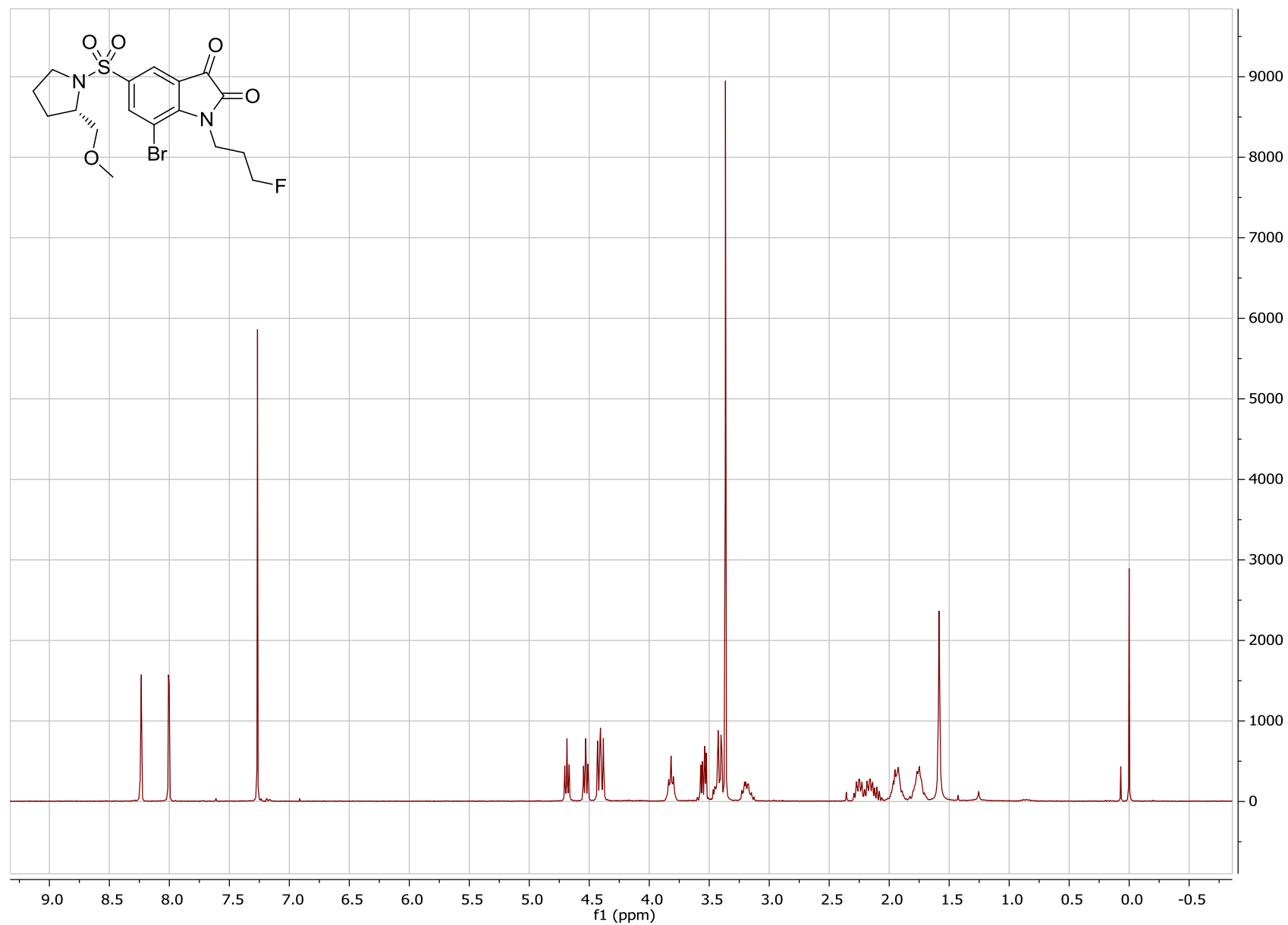
¹H NMR spectrum of (S)-N-butyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**22**)



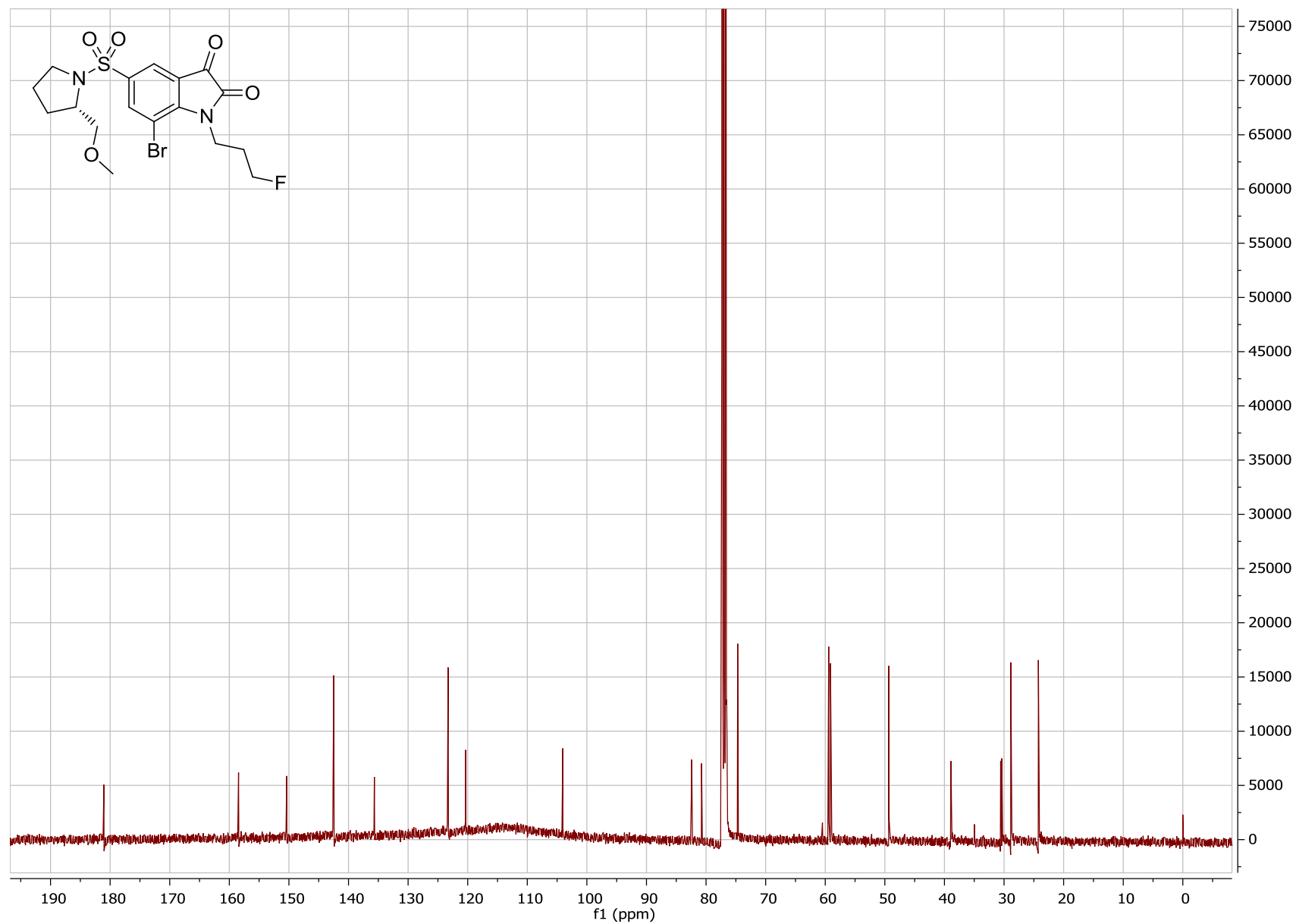
¹³C NMR spectrum of (S)-N-butyl-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**22**)



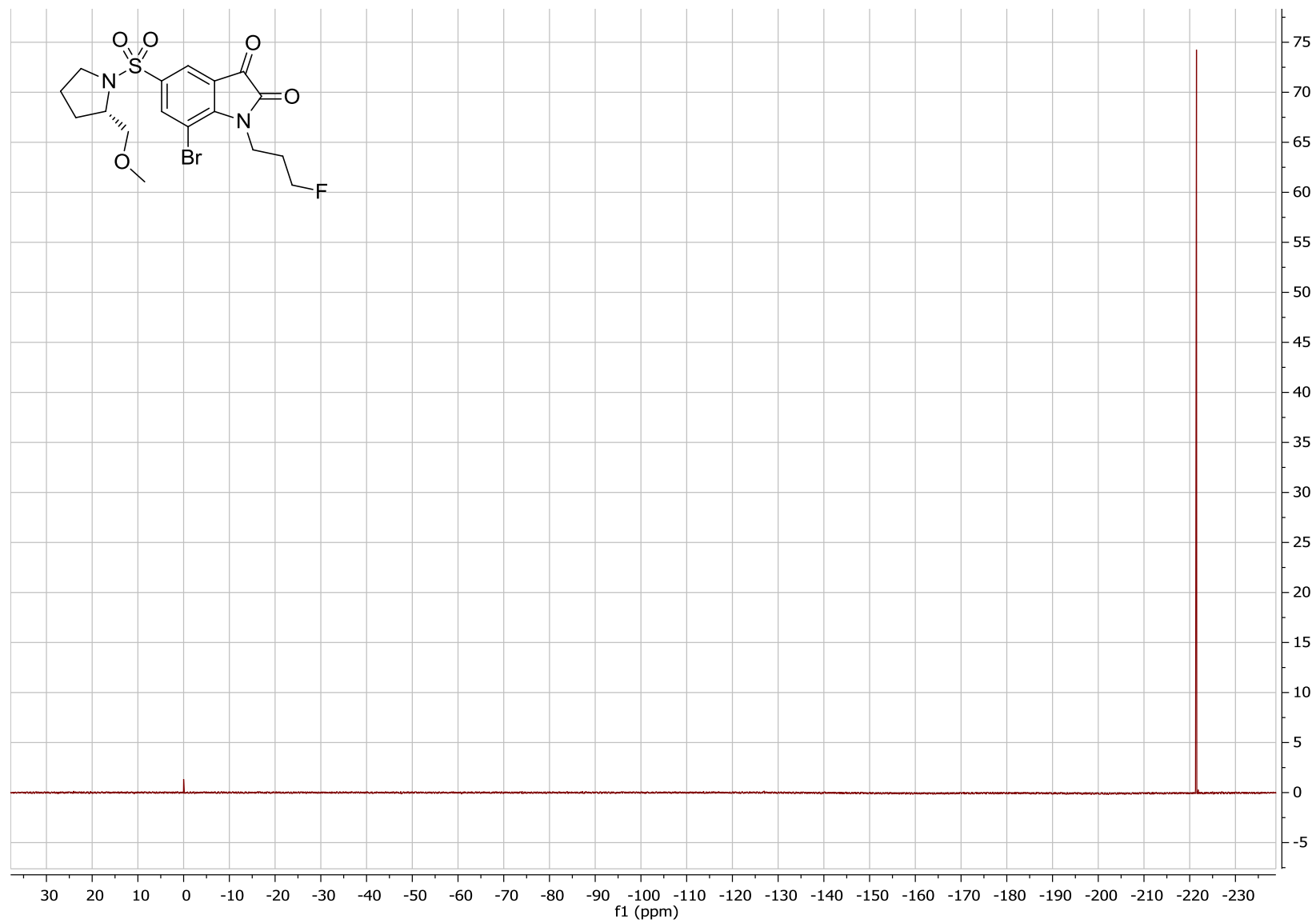
^1H NMR spectrum of (*S*)-*N*-(3-fluoropropyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**23**)



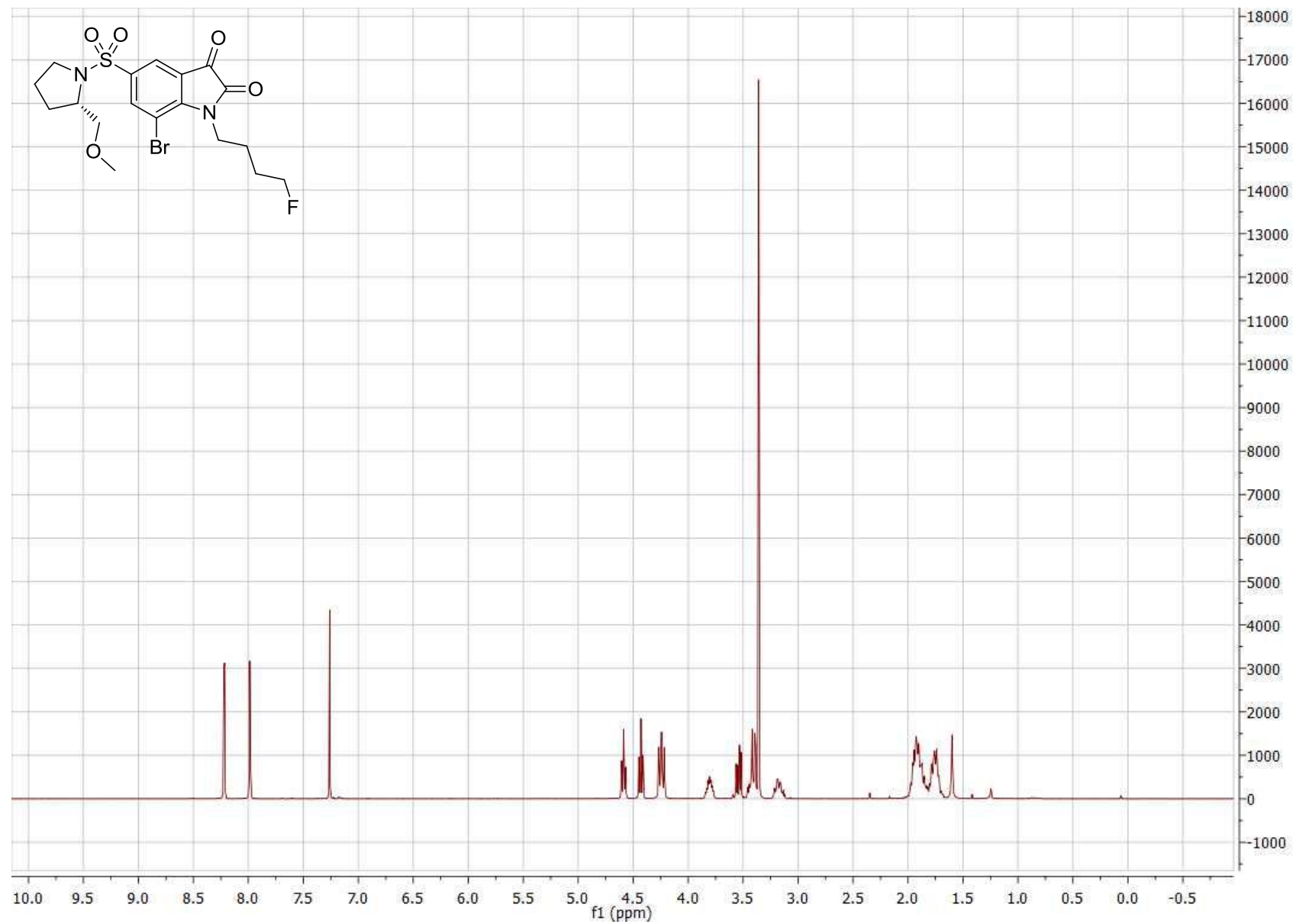
¹³C NMR spectrum of (S)-N-(3-fluoropropyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**23**)



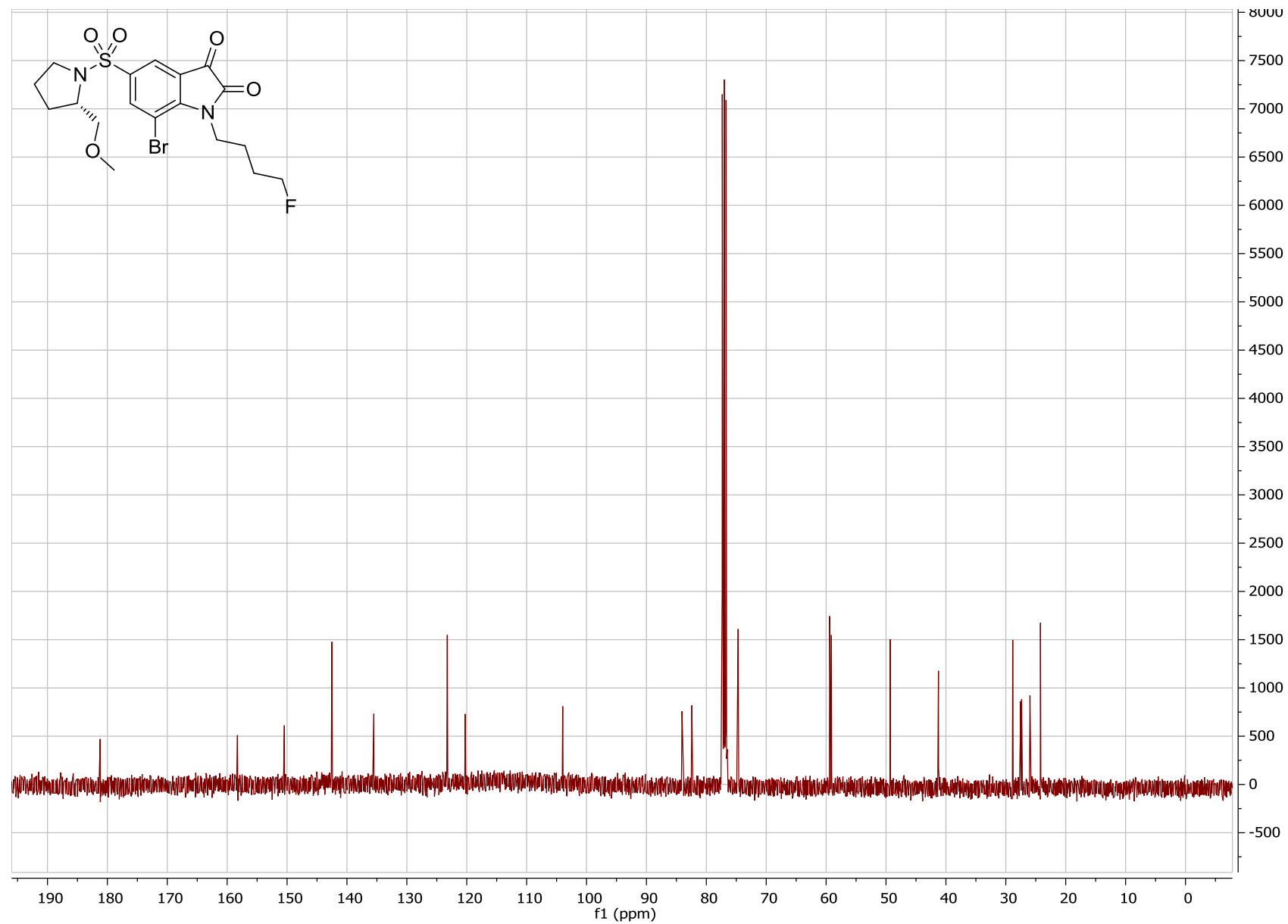
^{19}F NMR spectrum of (S)-N-(3-fluoropropyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**23**)



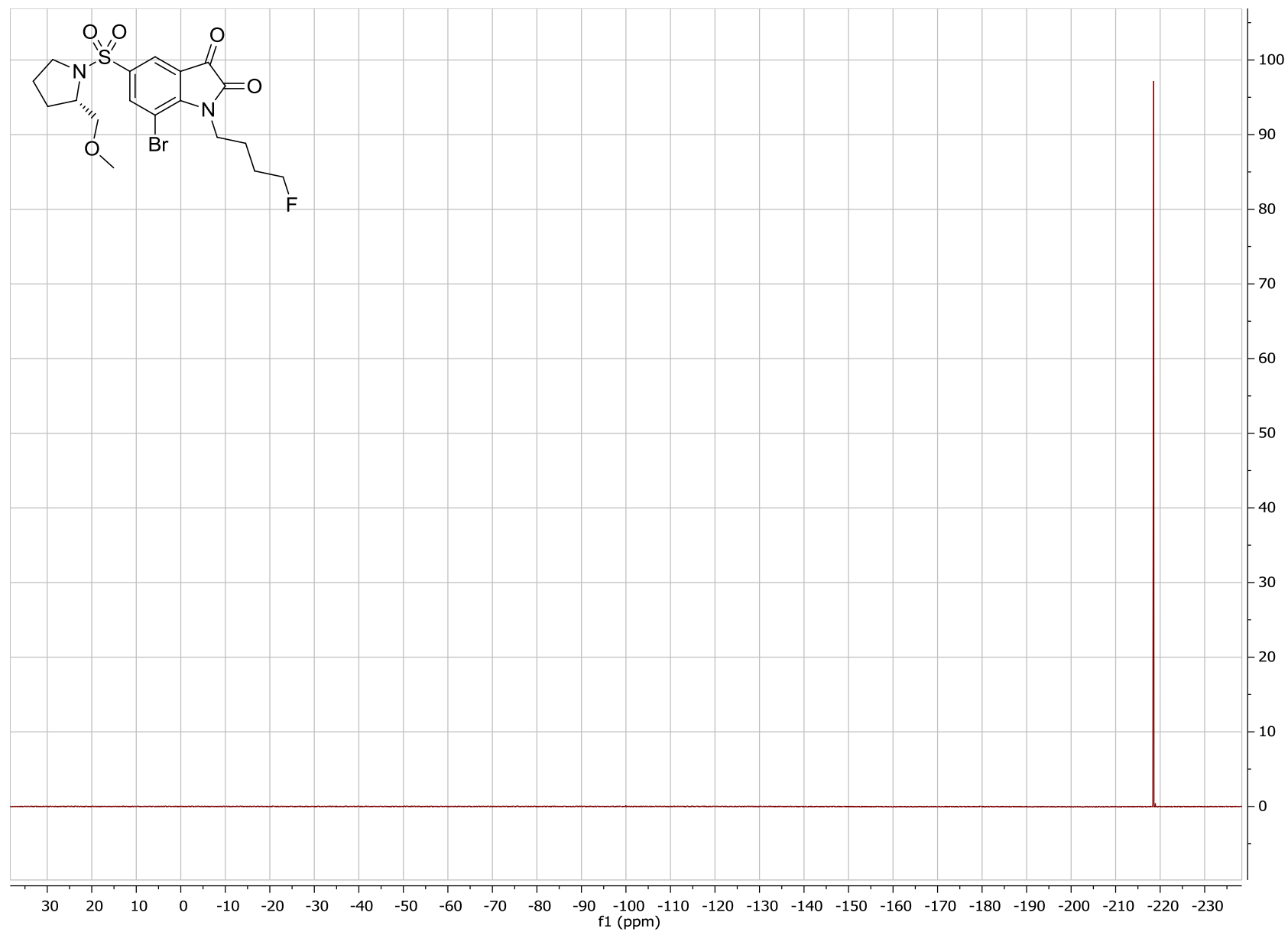
^1H NMR spectrum of (*S*)-*N*-(4-fluorobutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**24**)



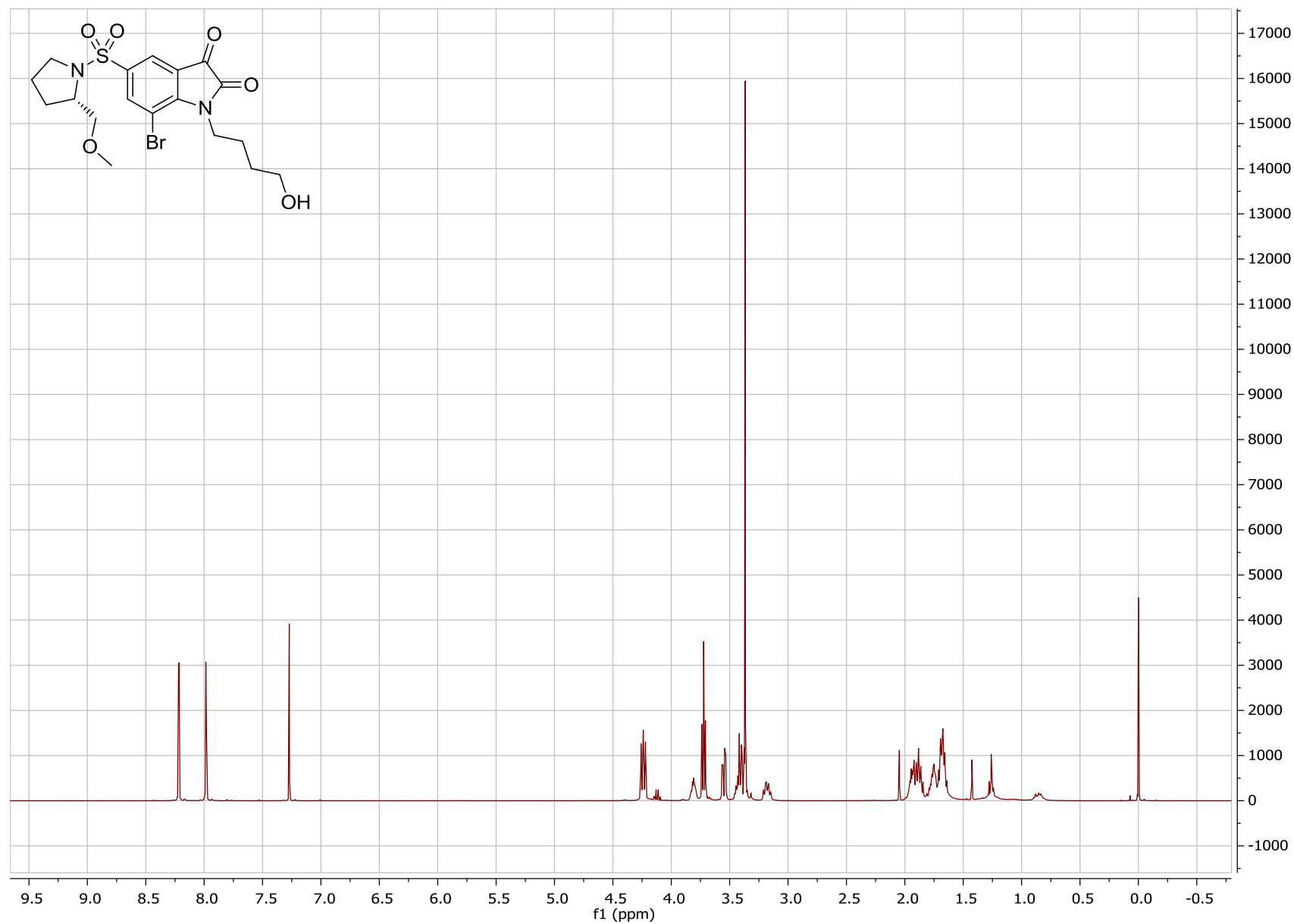
¹³C NMR spectrum of (S)-N-(4-fluorobutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**24**)



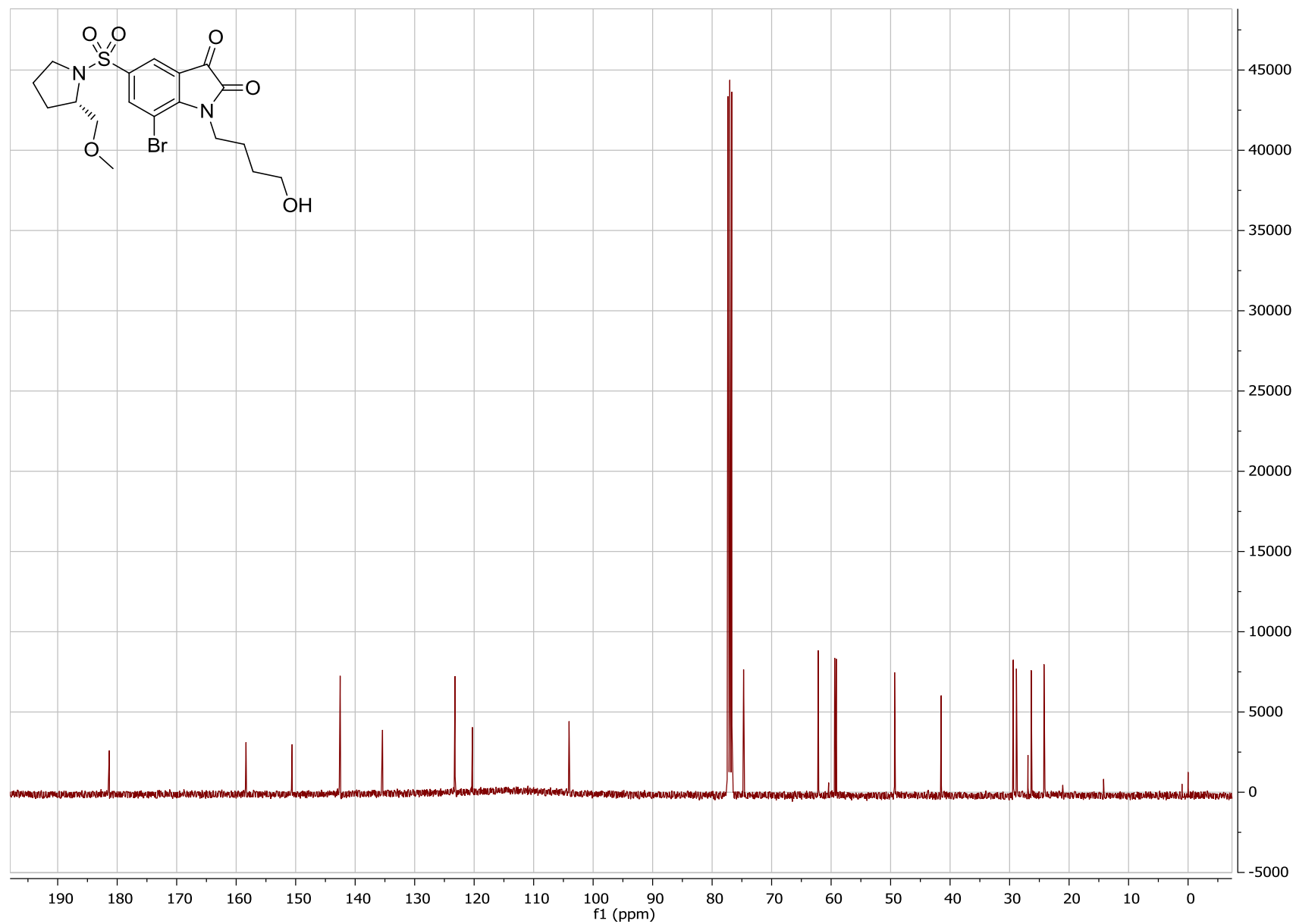
¹⁹F NMR spectrum of (S)-N-(4-fluorobutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**24**)



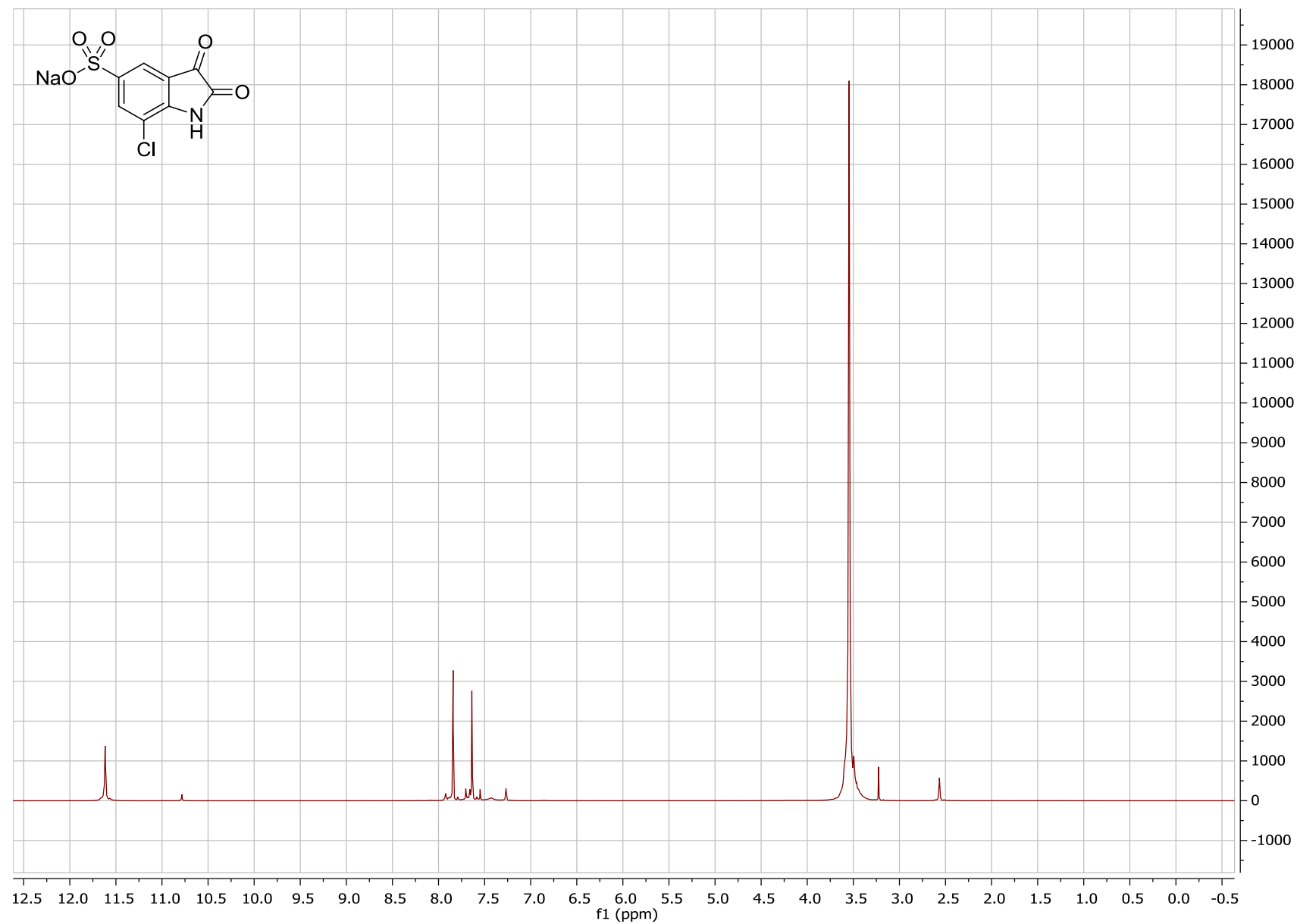
¹H NMR spectrum of (S)-N-(4-hydroxybutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**25**)



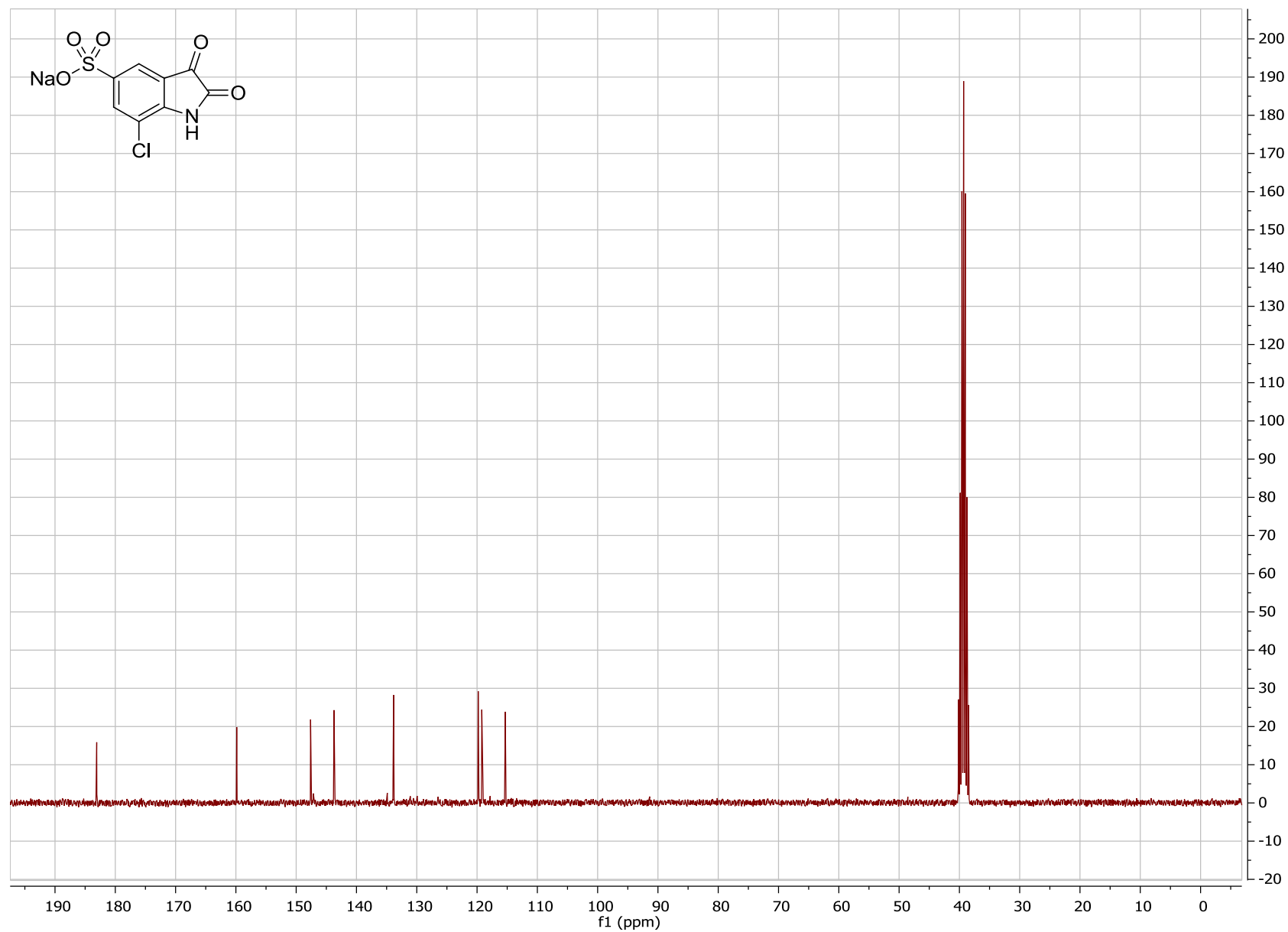
¹³C NMR spectrum of (S)-N-(4-hydroxybutyl)-7-bromo-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**25**)



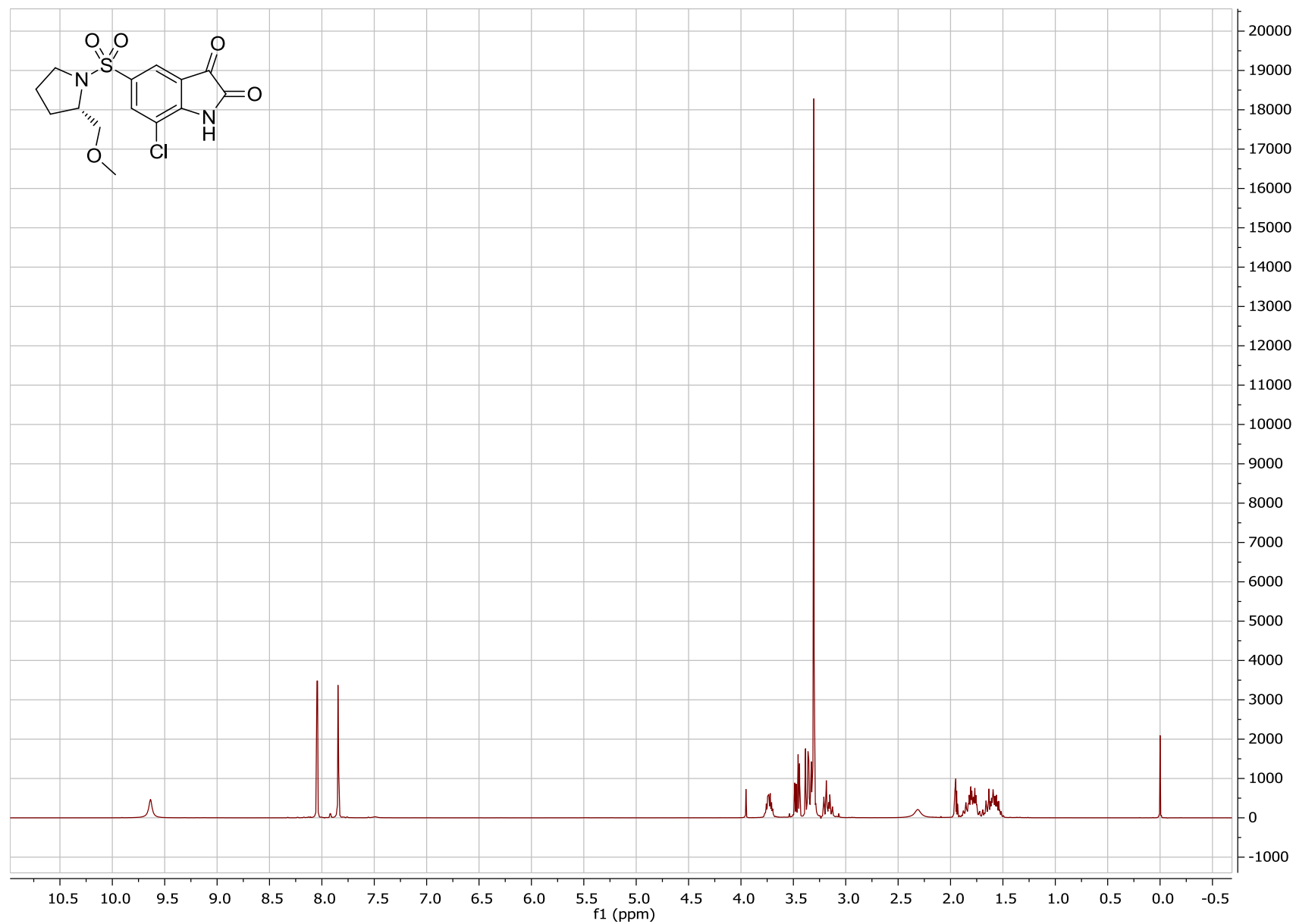
^1H NMR spectrum of sodium 7-chloro-2,3-dioxindoline-5-sulfonate (**29**)



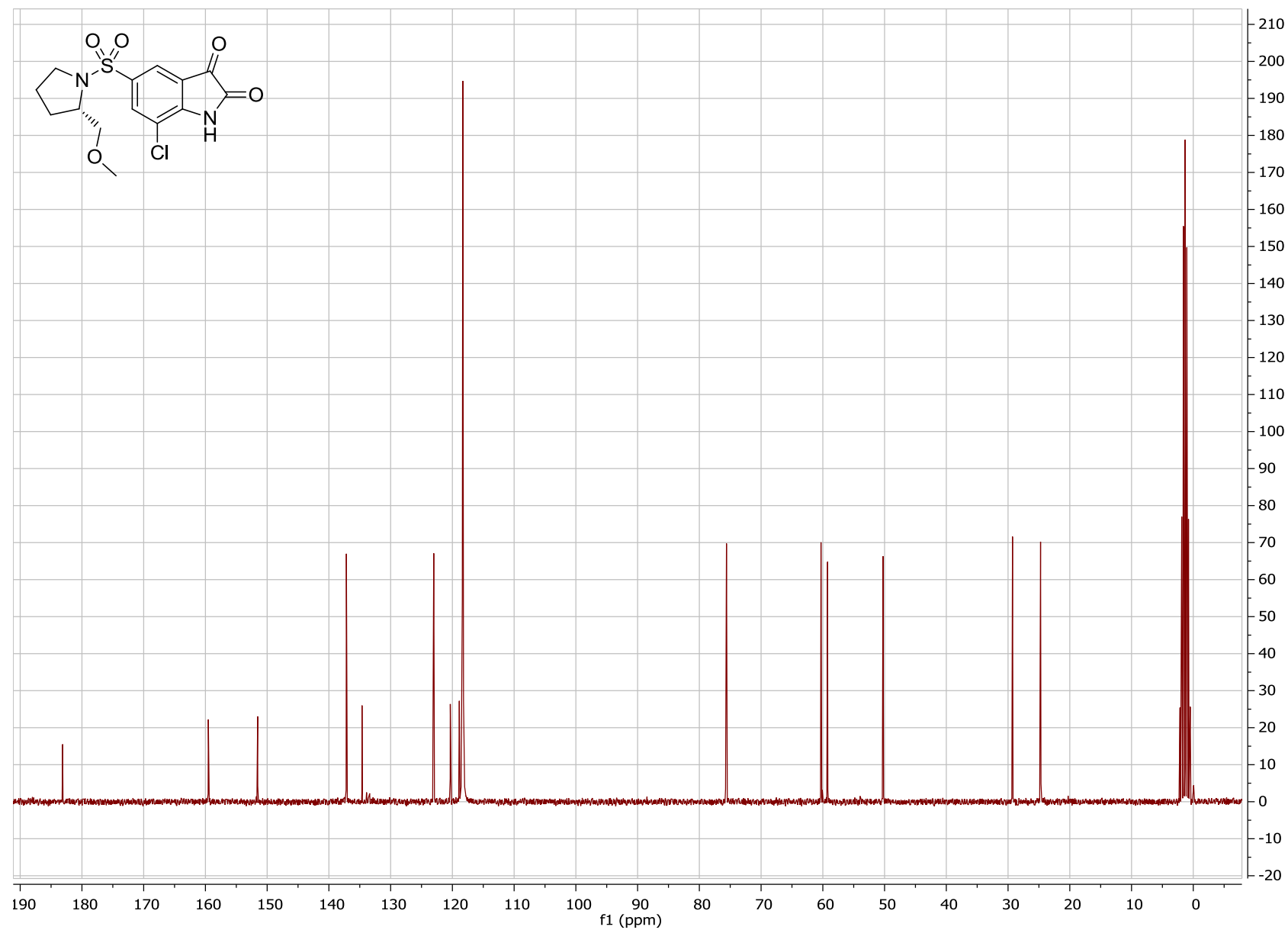
^{13}C NMR spectrum of sodium 7-chloro-2,3-dioxoindoline-5-sulfonate (**29**)



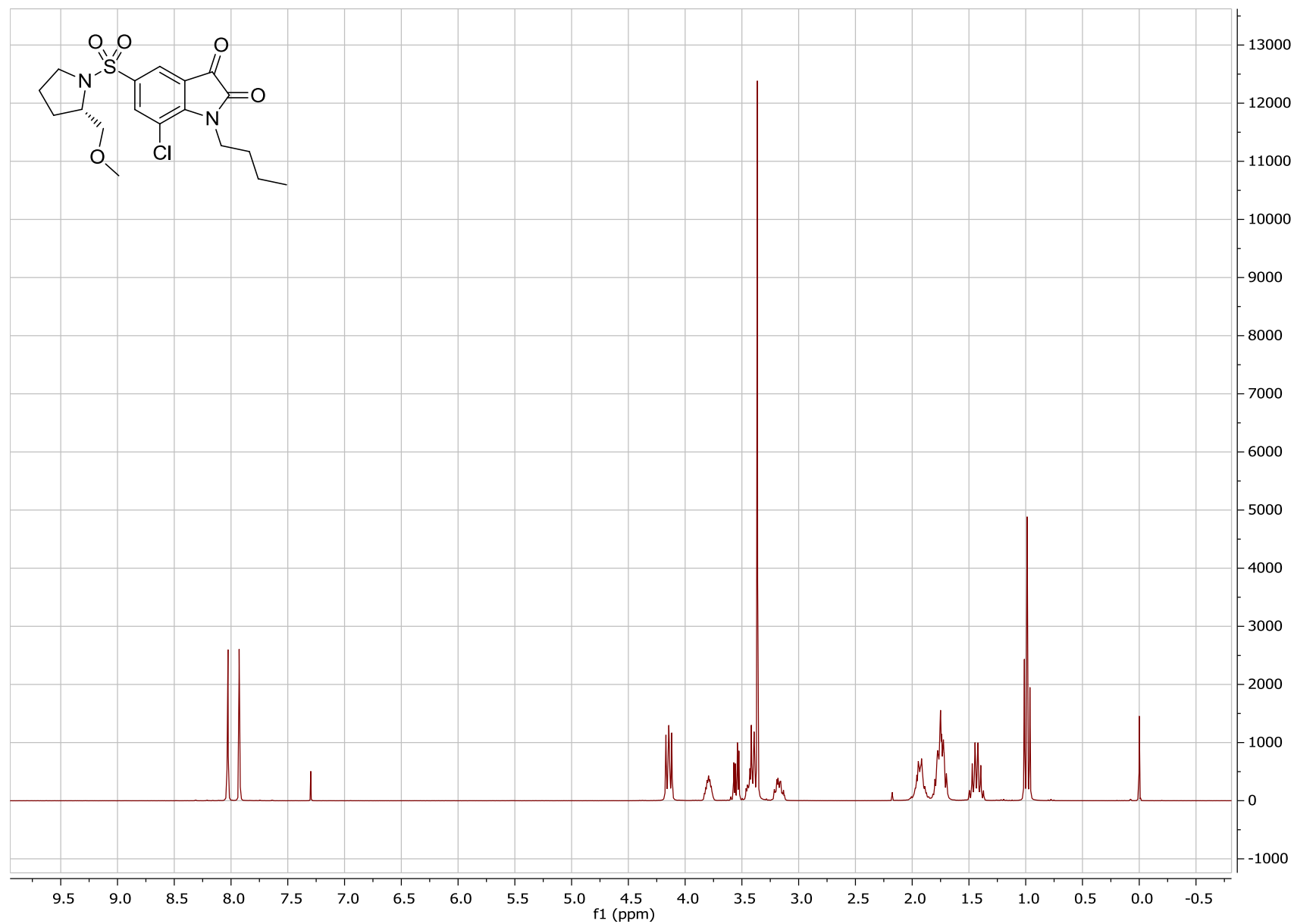
¹H NMR spectrum of (S)-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**31**)



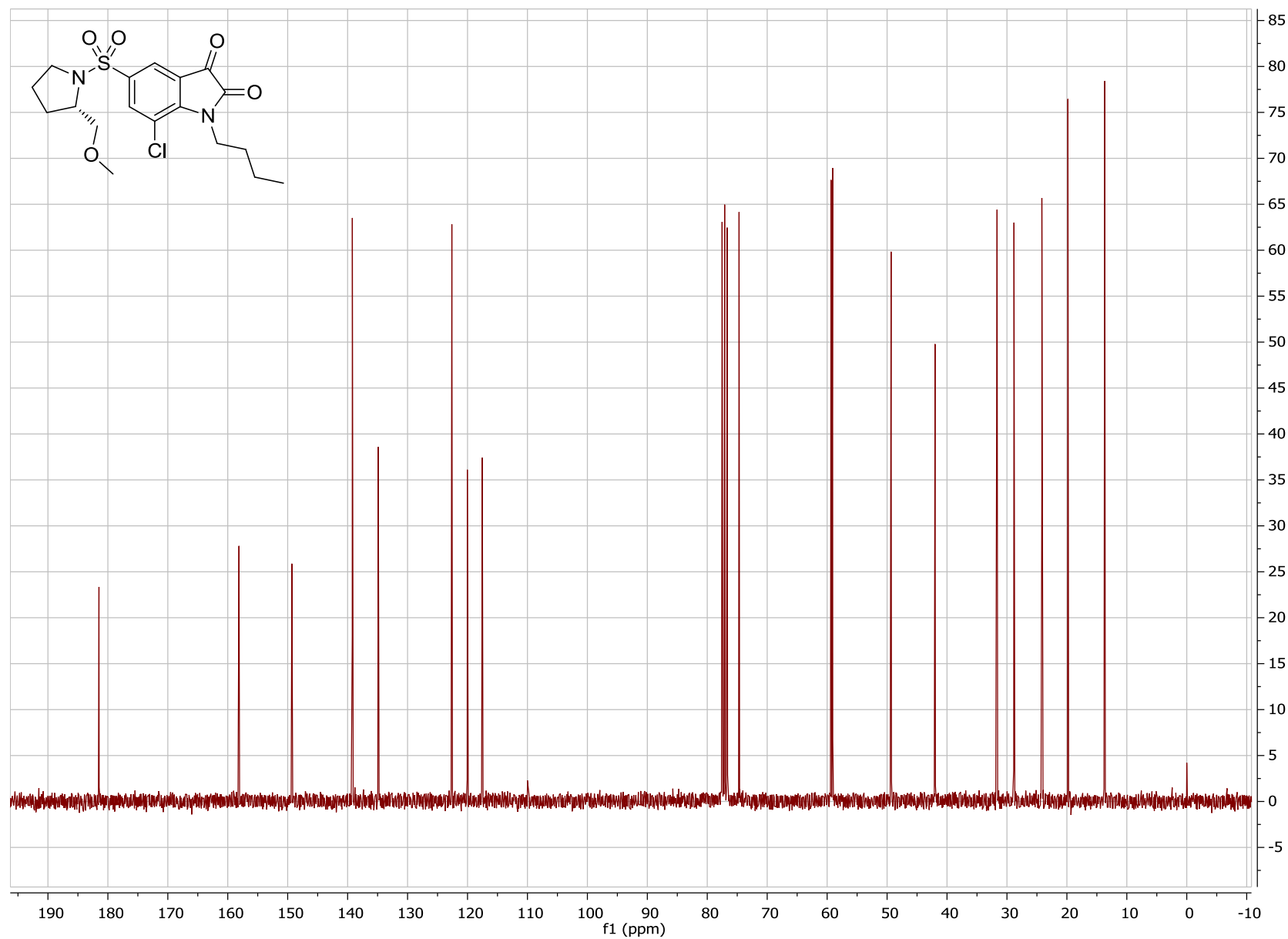
^{13}C NMR spectrum of (S)-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**31**)



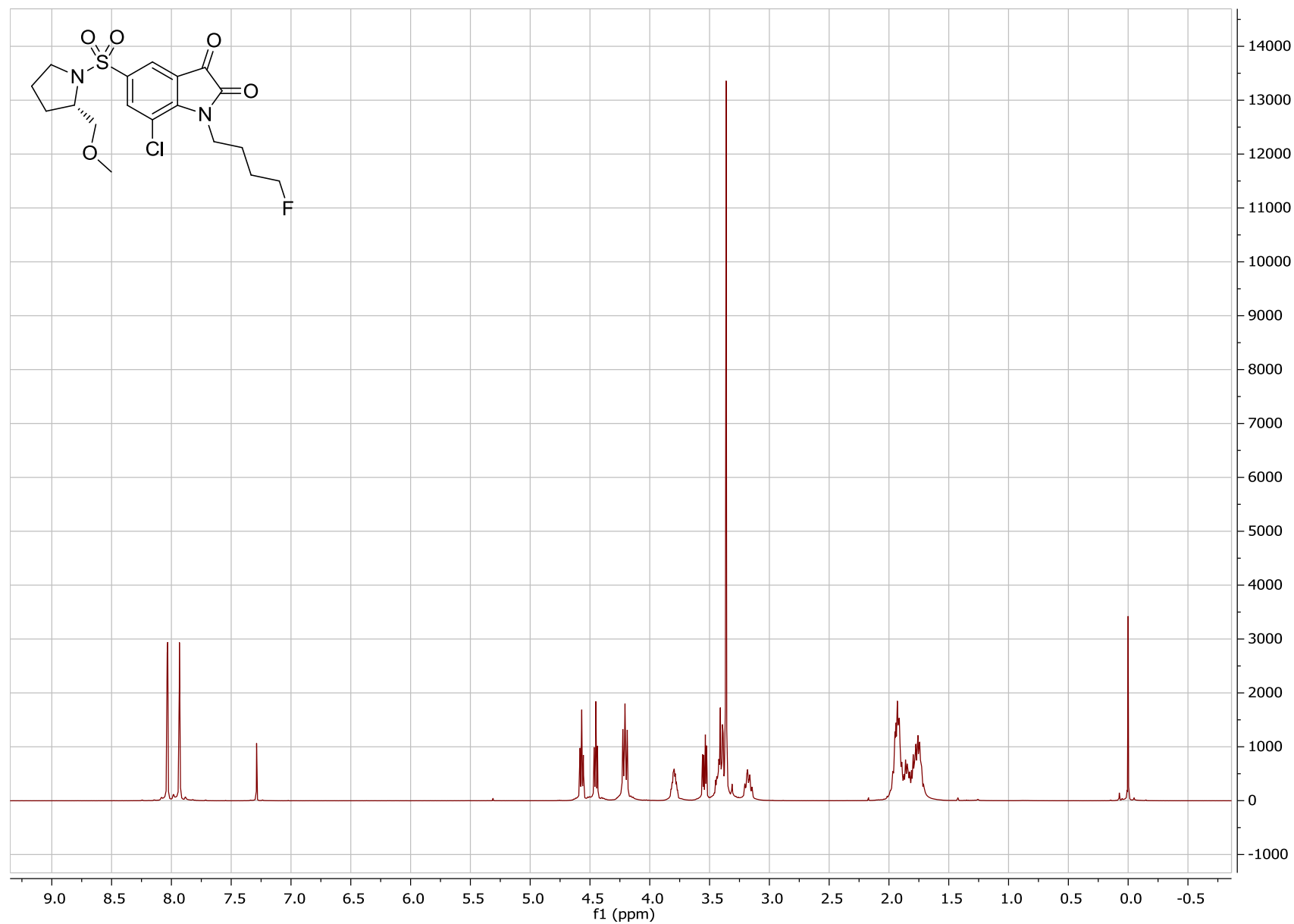
^1H NMR spectrum of (*S*)-*N*-butyl-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**32**)



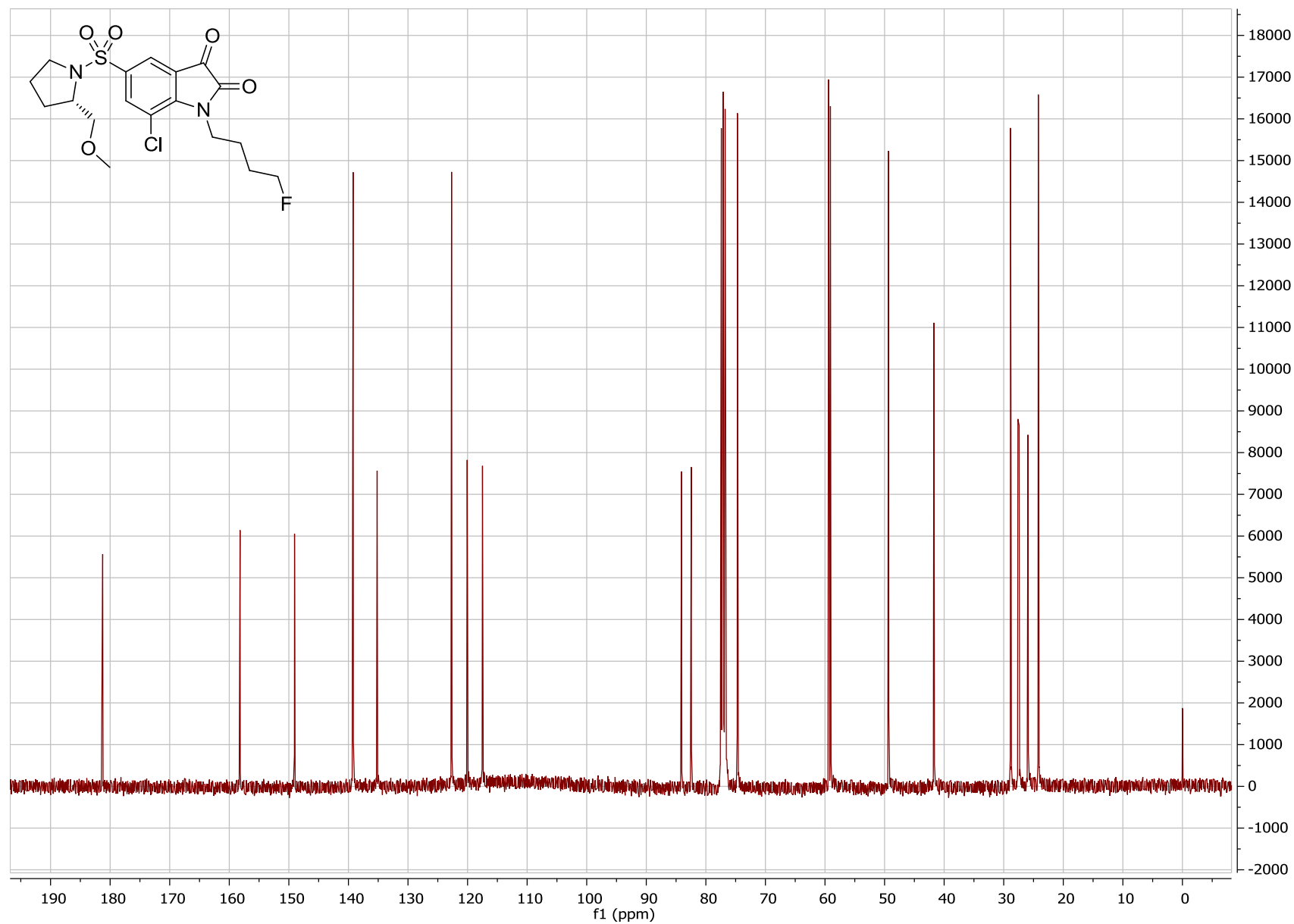
^{13}C NMR spectrum of (S)-N-butyl-7-chloro-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatin (**32**)



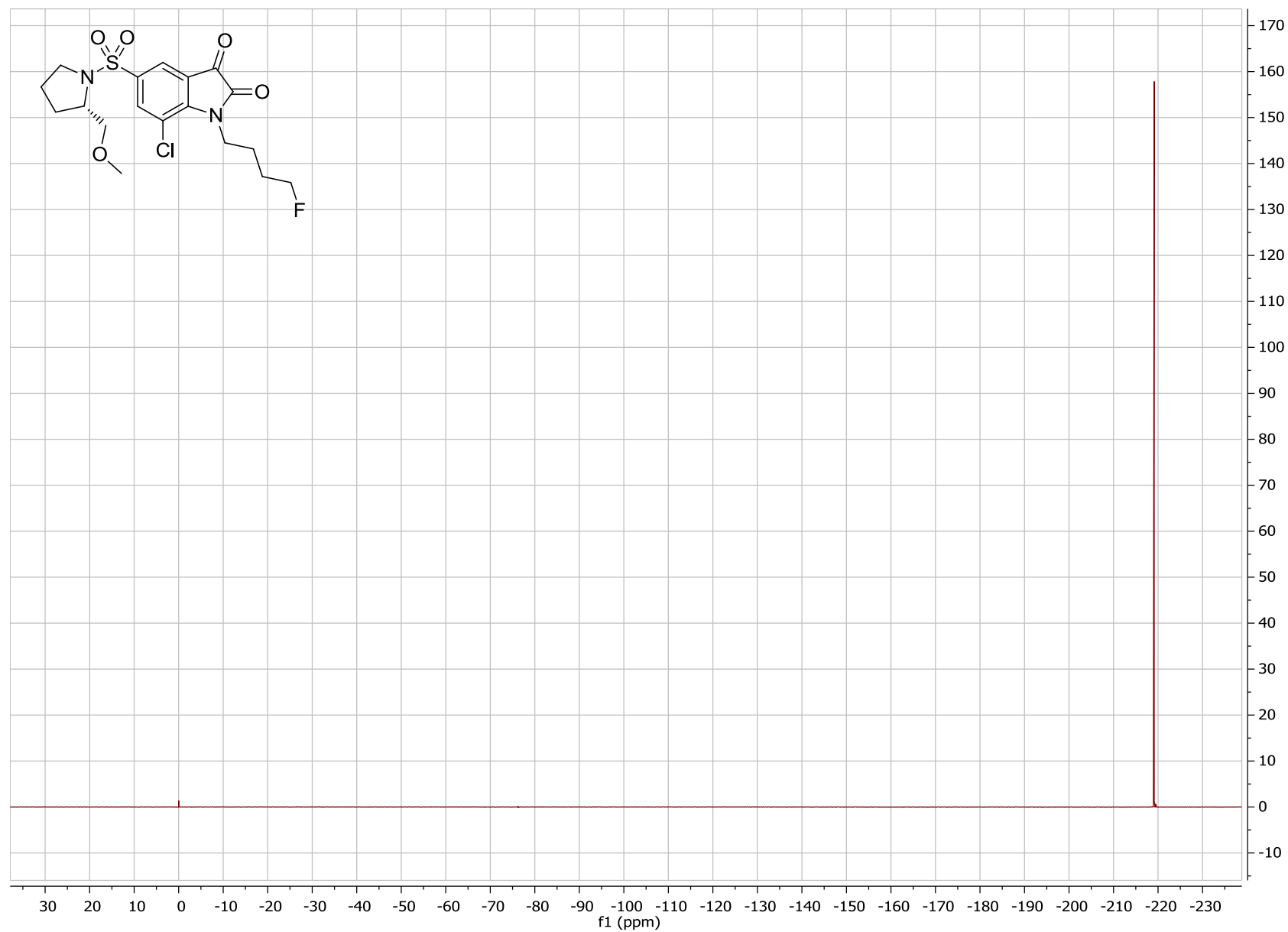
^1H NMR spectrum of (*S*)-*N*-(4-fluorobutyl)-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**33**)



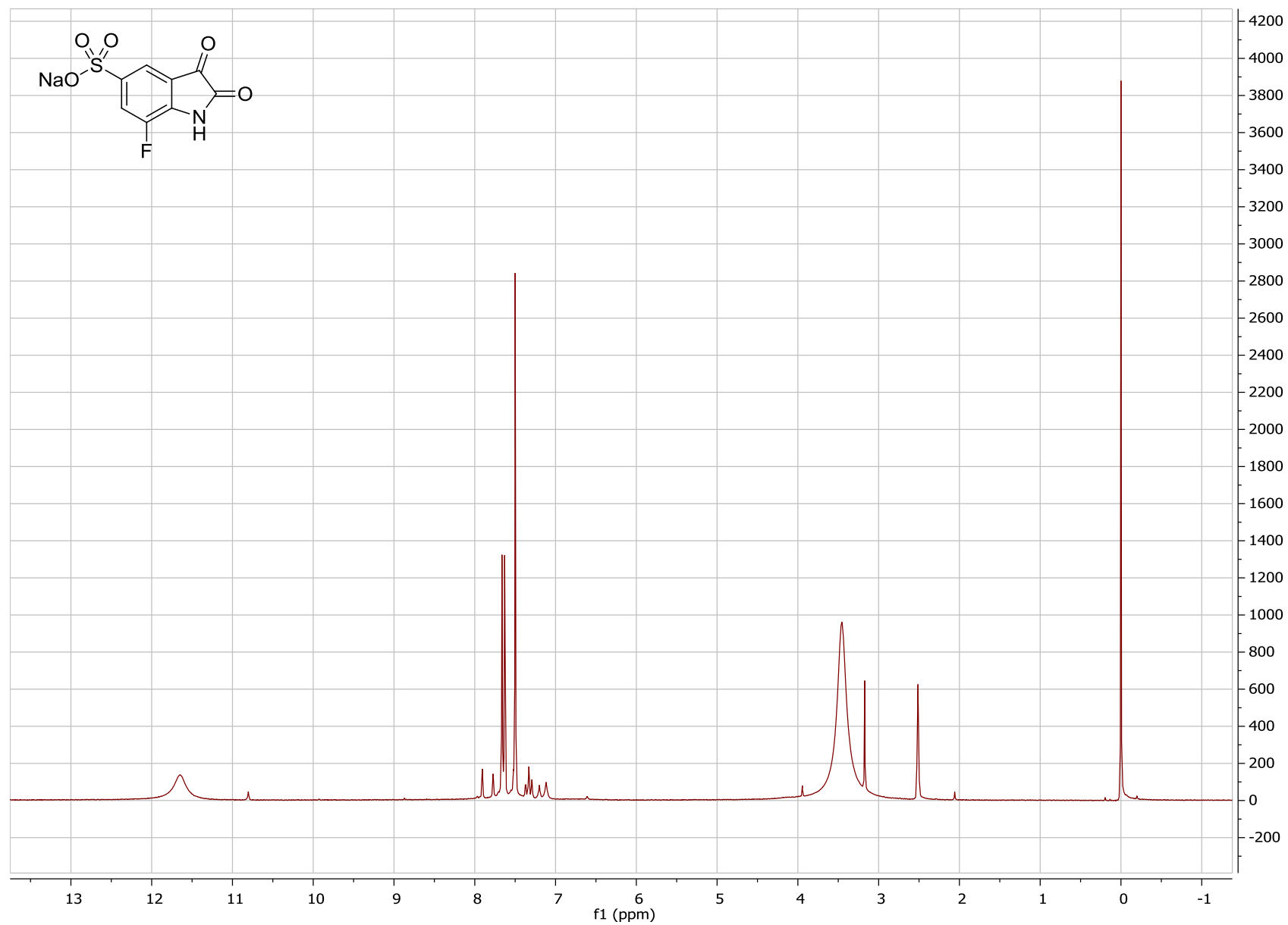
^{13}C NMR spectrum of (S)-N-(4-fluorobutyl)-7-chloro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**33**)



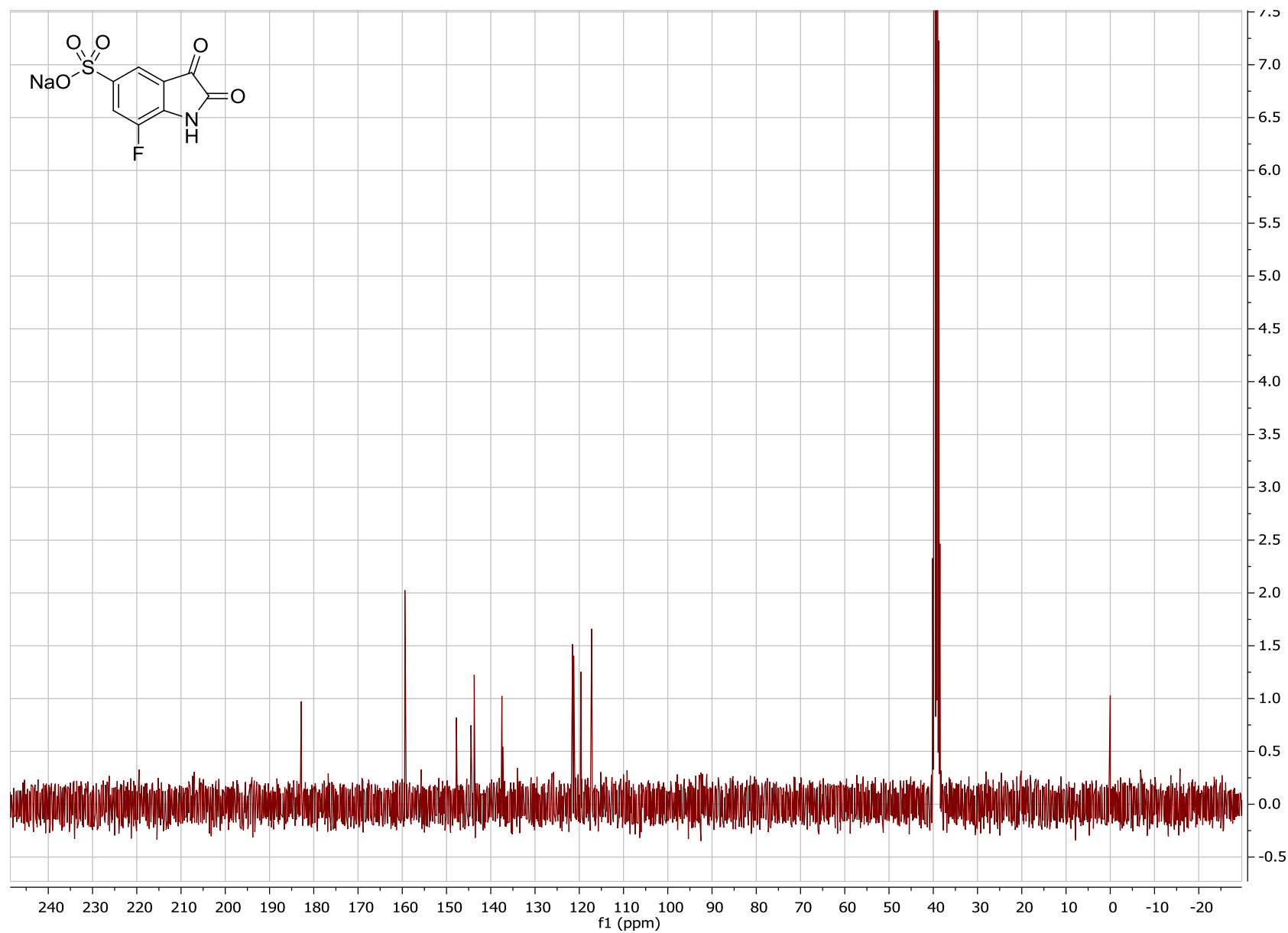
¹⁹F NMR spectrum of (S)-N-(4-fluorobutyl)-7-chloro-5-[1-(2-methoxymethylpyrrolidiny]sulfonyl]isatin (**33**)



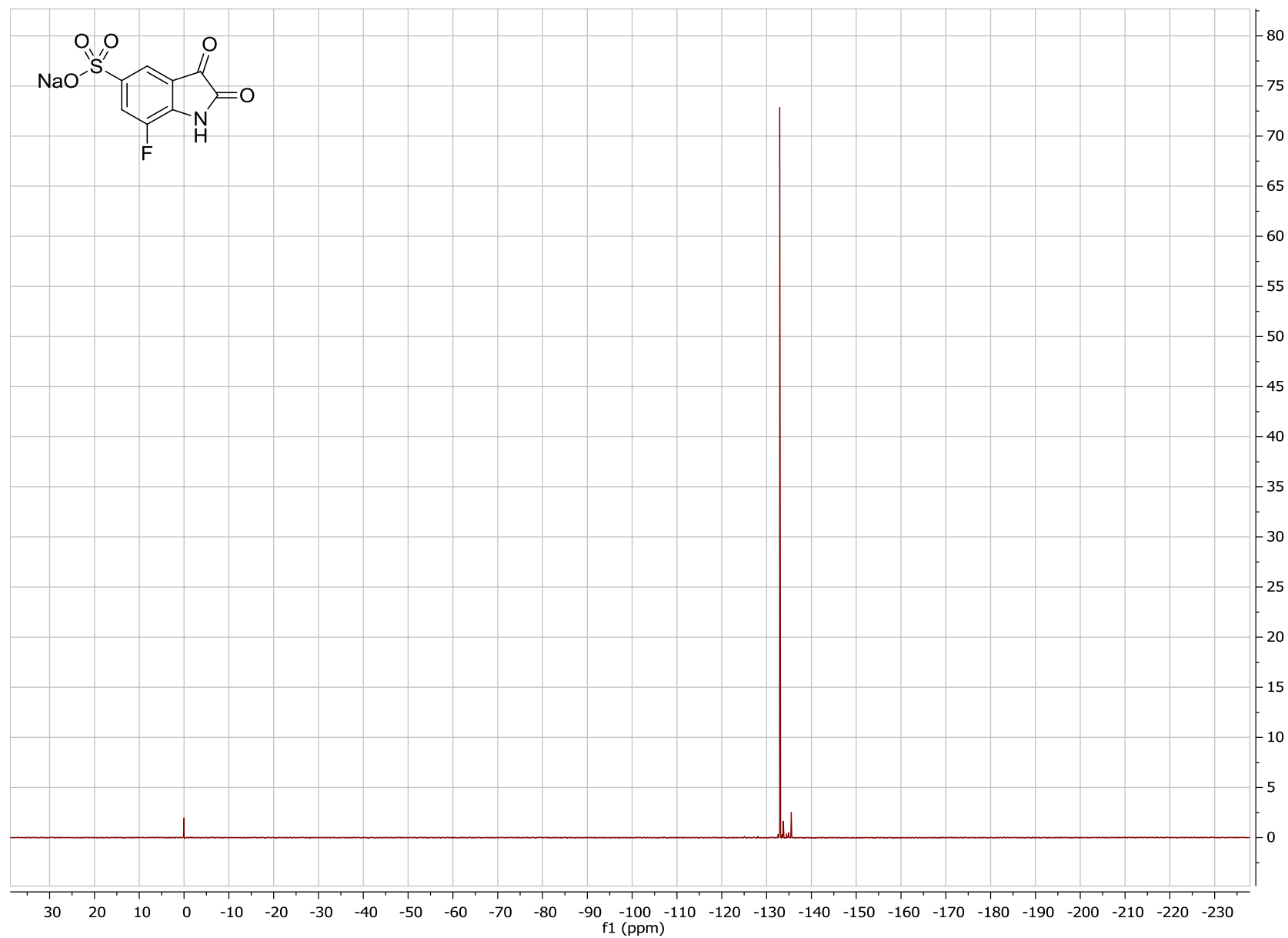
^1H NMR spectrum of sodium 7-fluoroisatin-5-sulfonate (**35**)



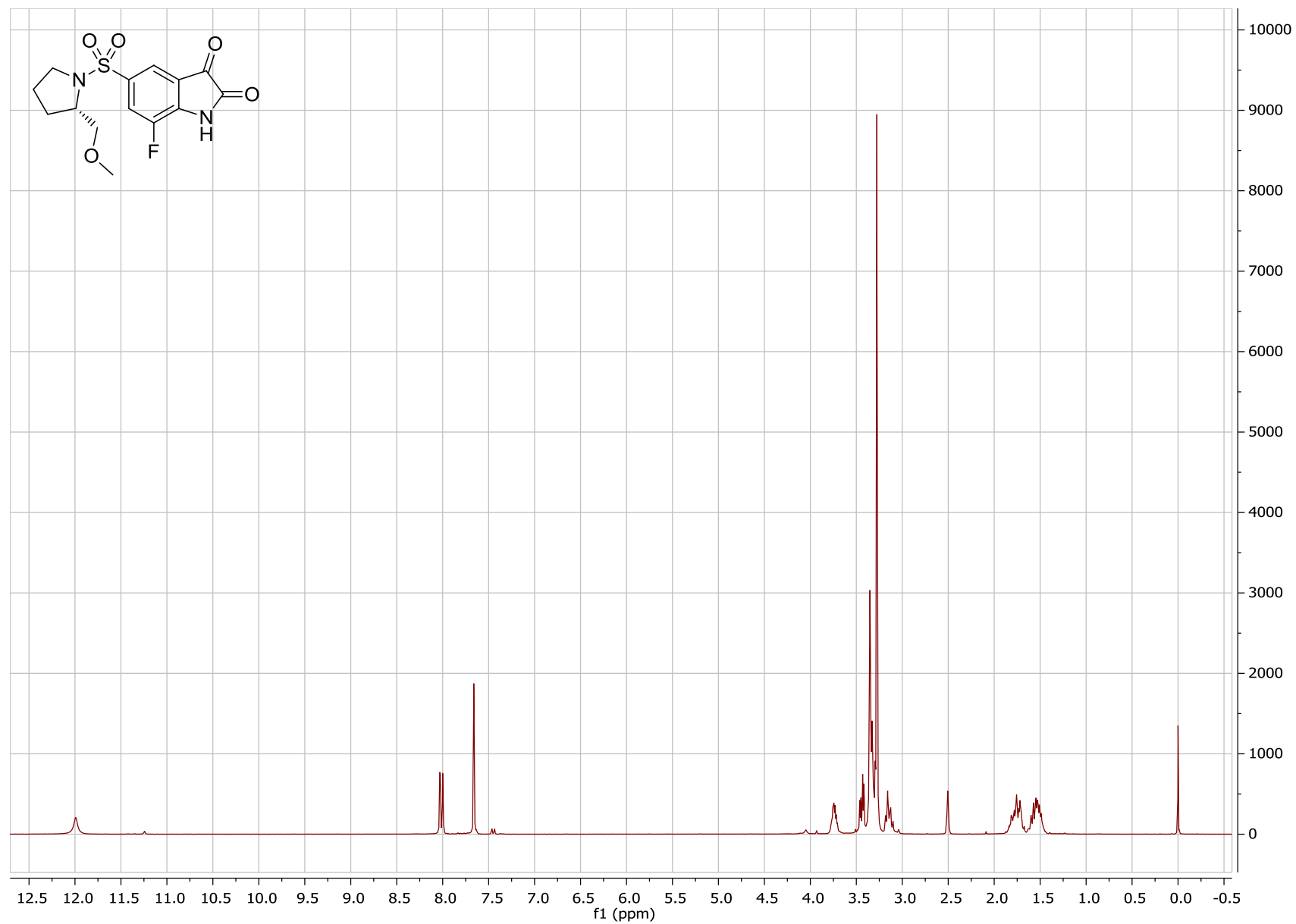
^{13}C NMR spectrum of sodium 7-fluoroisatin-5-sulfonate (**35**)



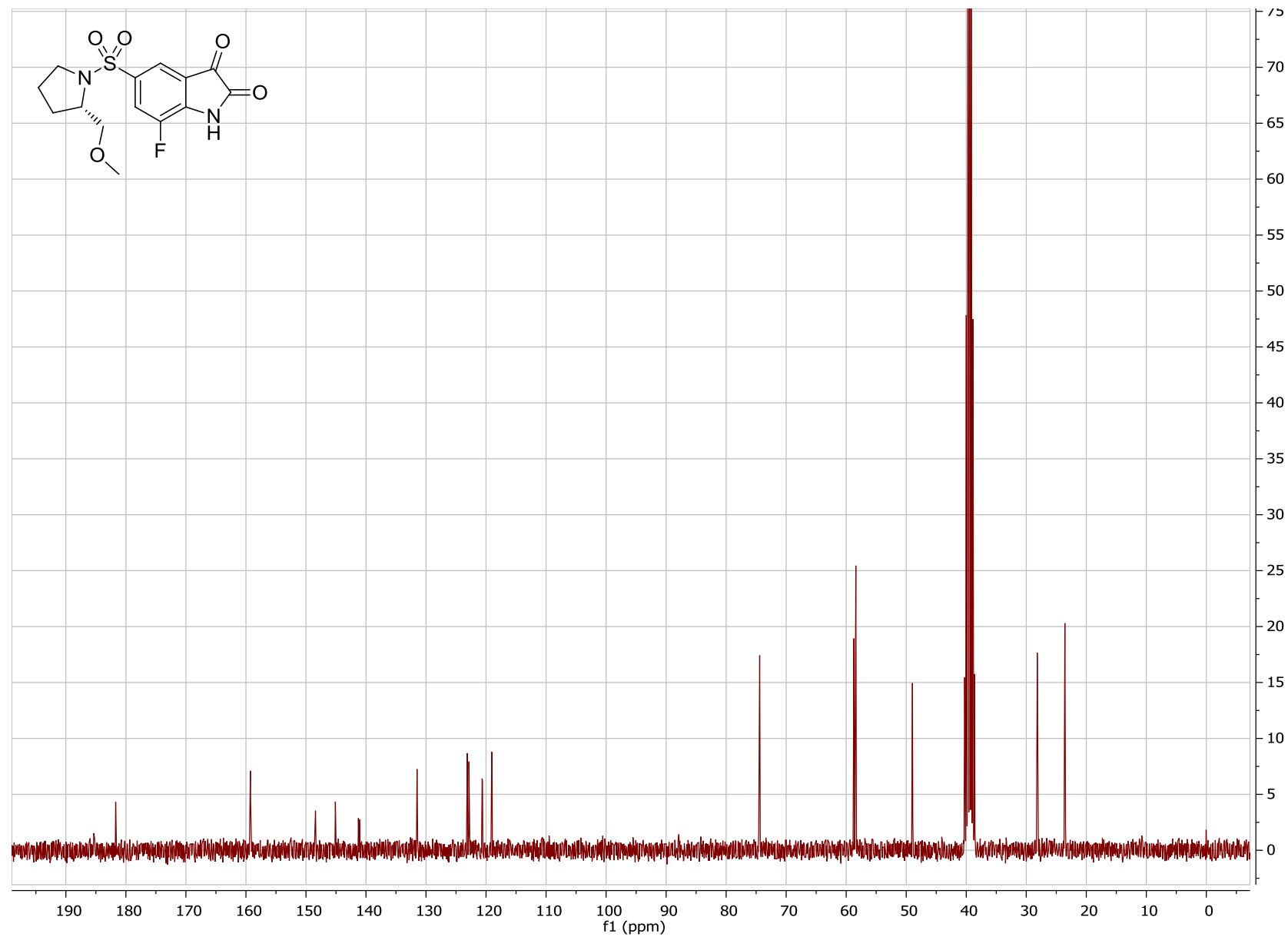
^{19}F NMR spectrum of sodium 7-fluoroisatin-5-sulfonate (**35**)



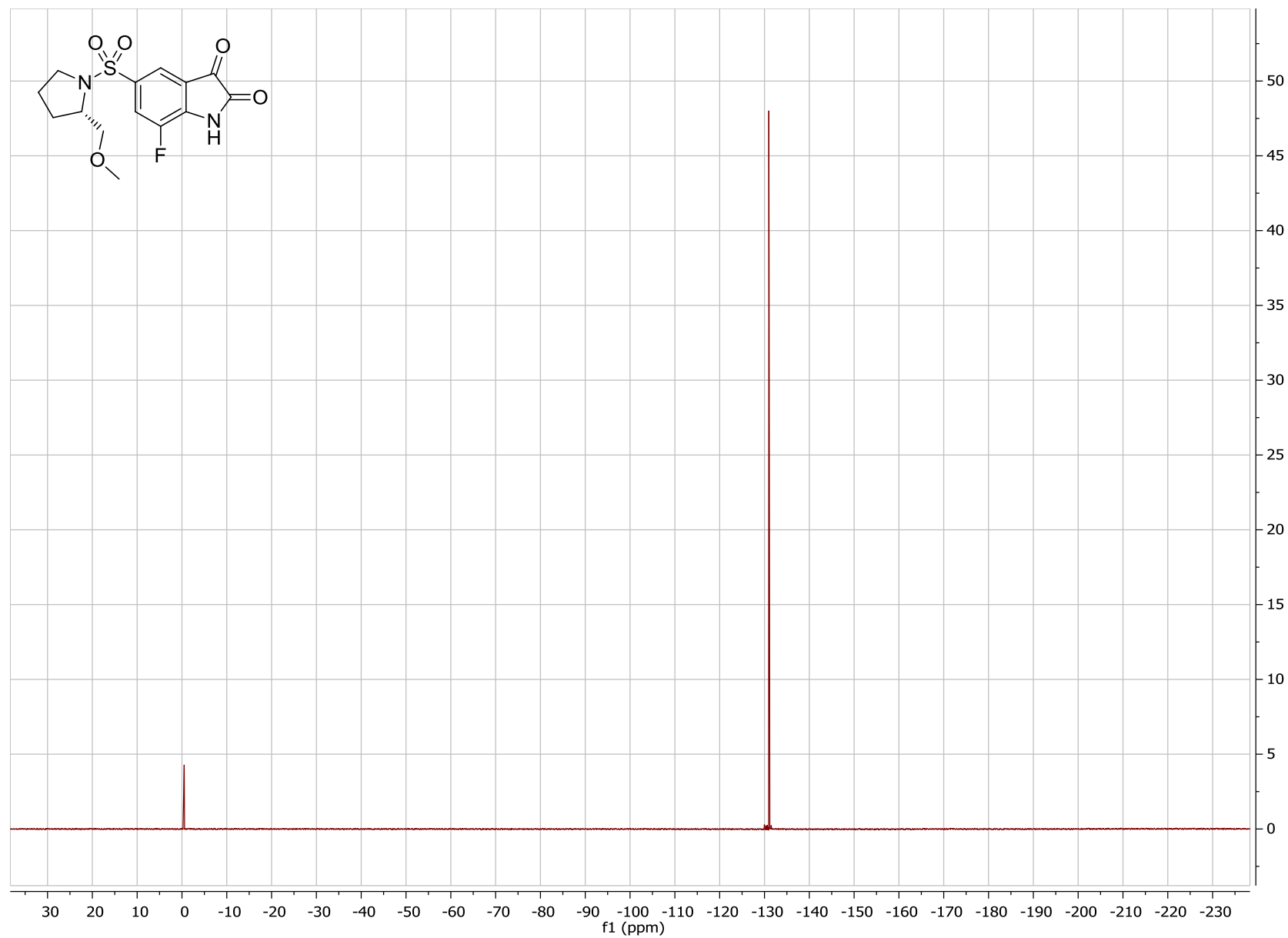
¹H NMR spectrum of (S)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**37**)



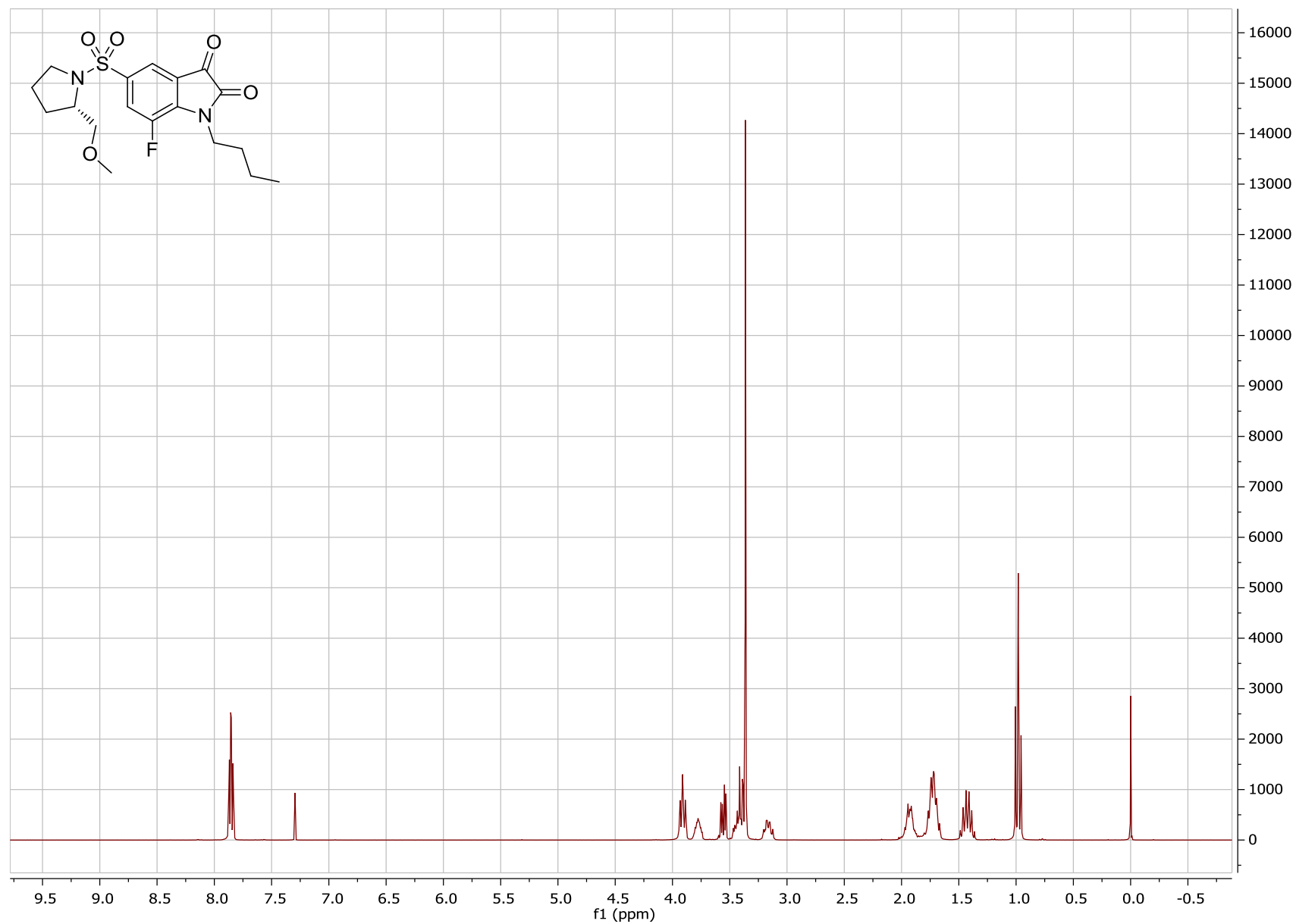
¹³C NMR spectrum of (S)-7-fluoro-5-[1-(2-methoxymethylpyrrolidiny)sulfonyl]isatin (**37**)



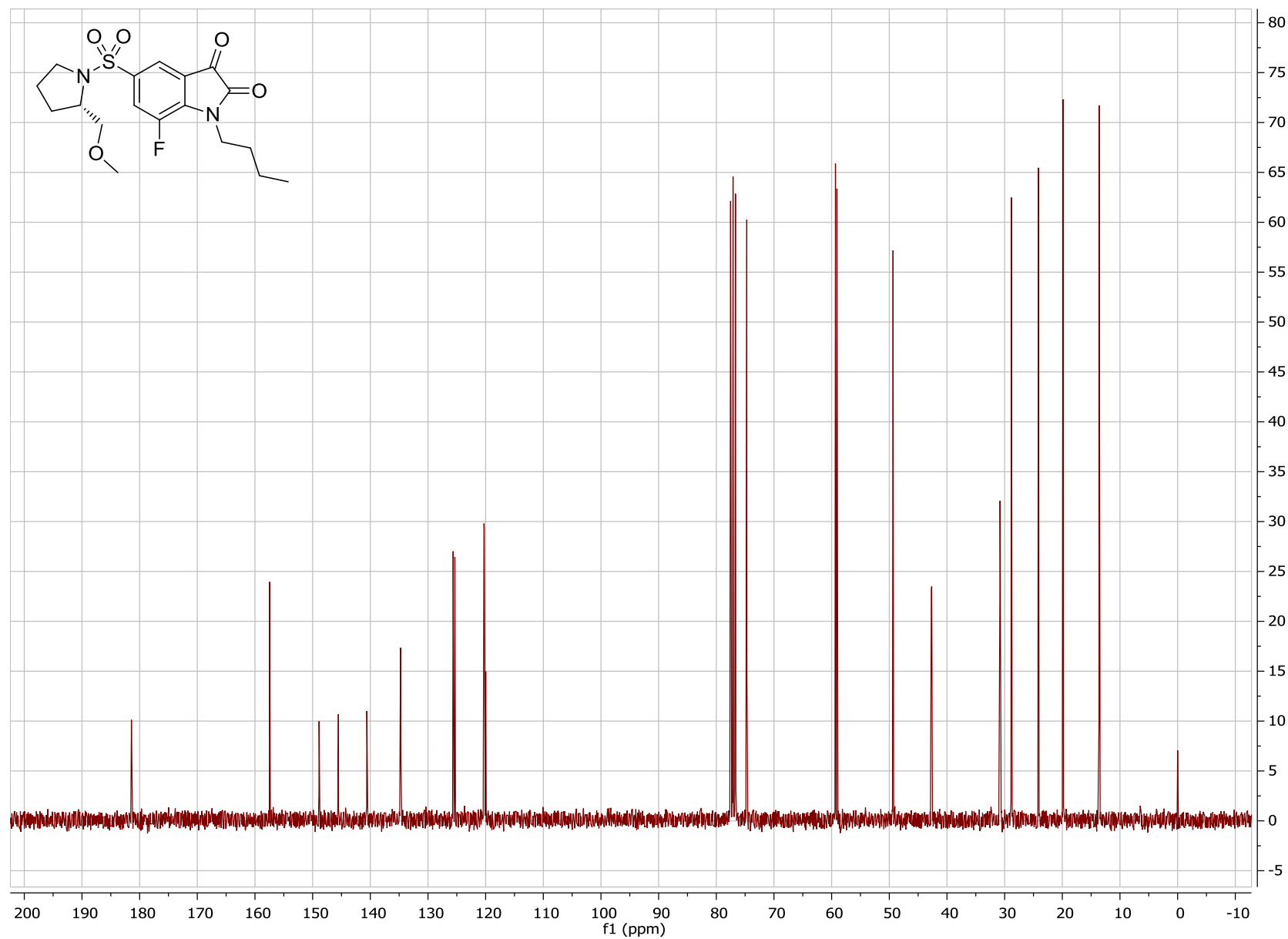
¹⁹F NMR spectrum of (S)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**37**)



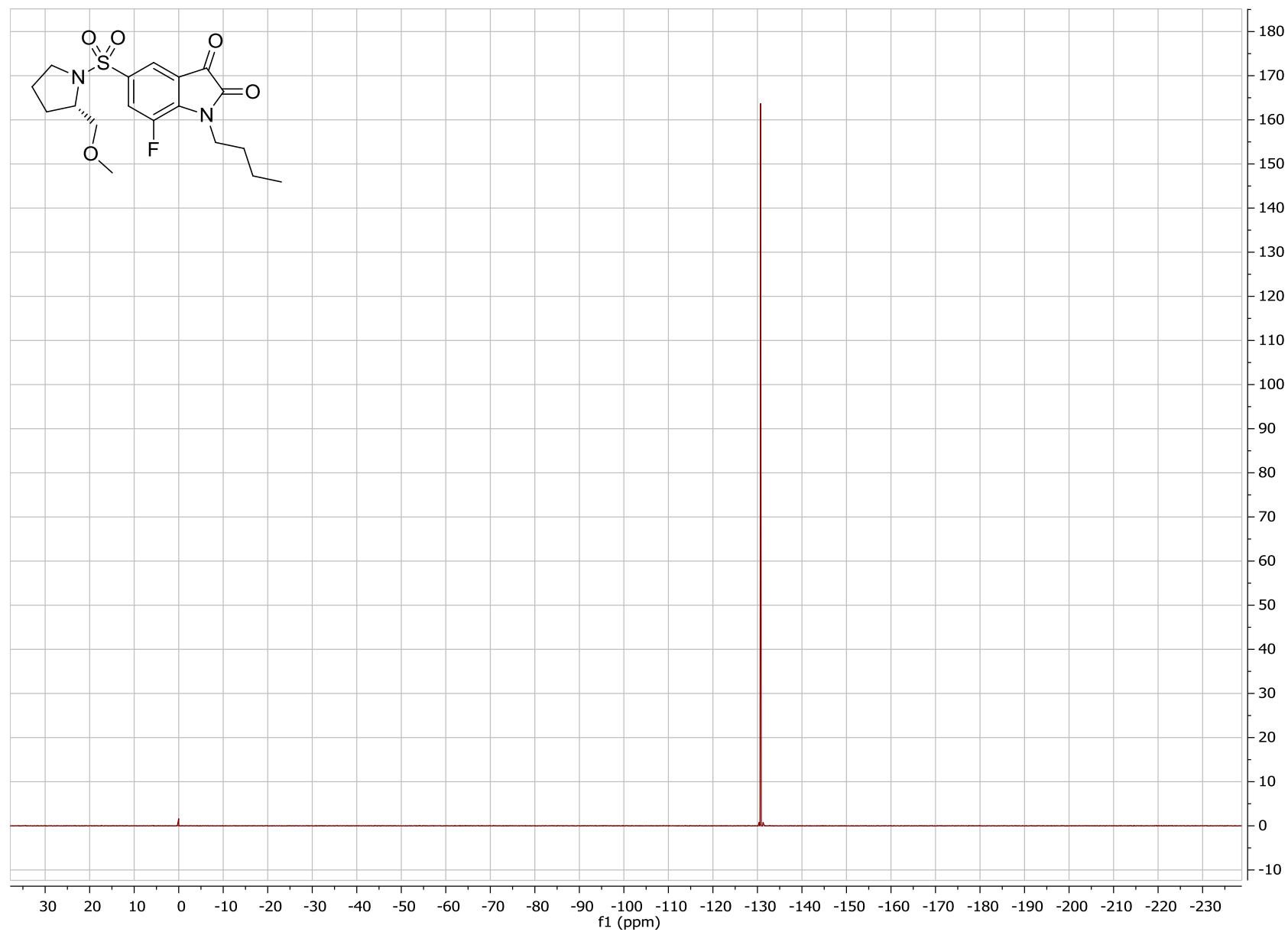
^1H NMR spectrum of (*S*)-*N*-butyl-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**38**)



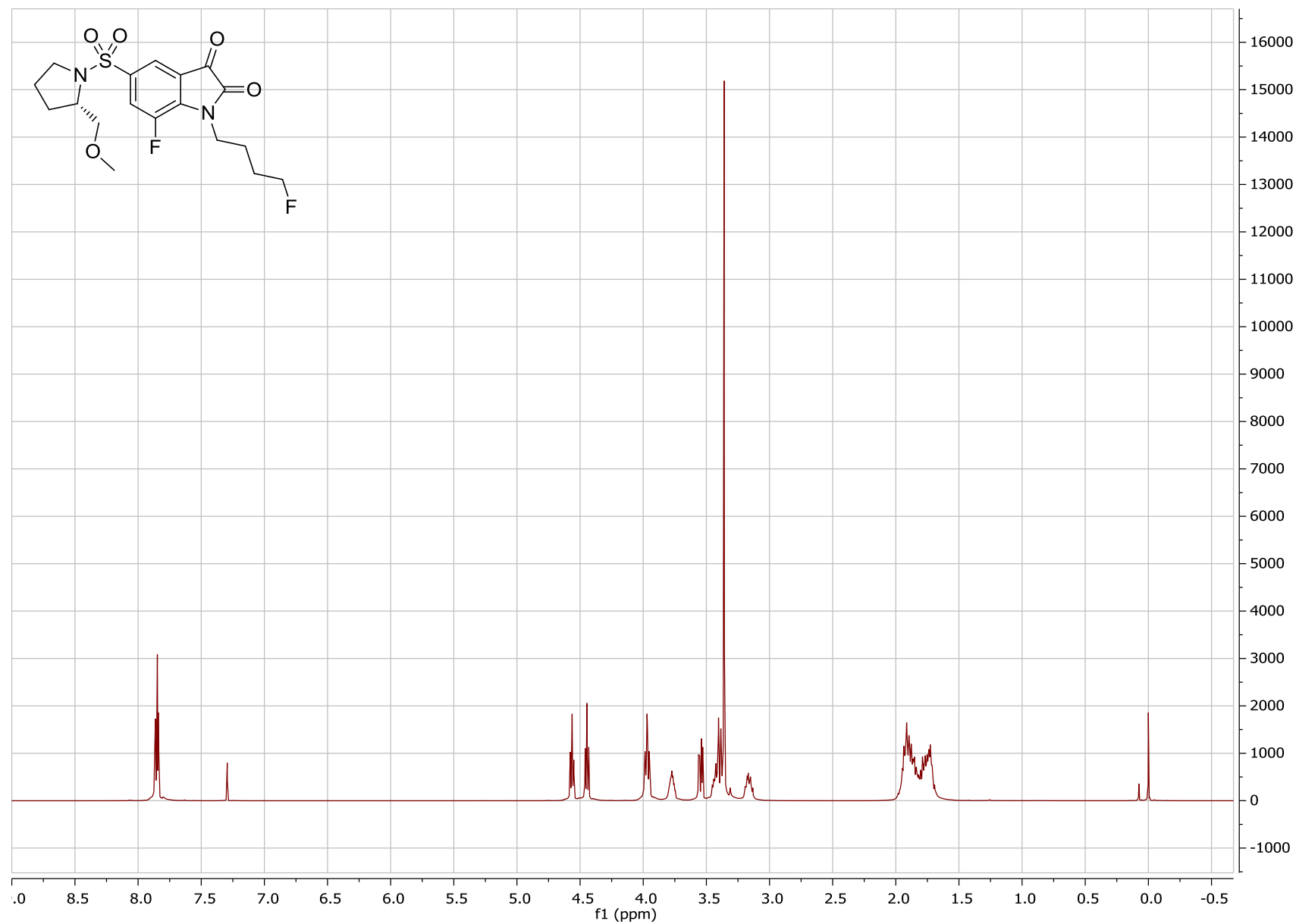
^{13}C NMR spectrum of (S)-N-butyl-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**38**)



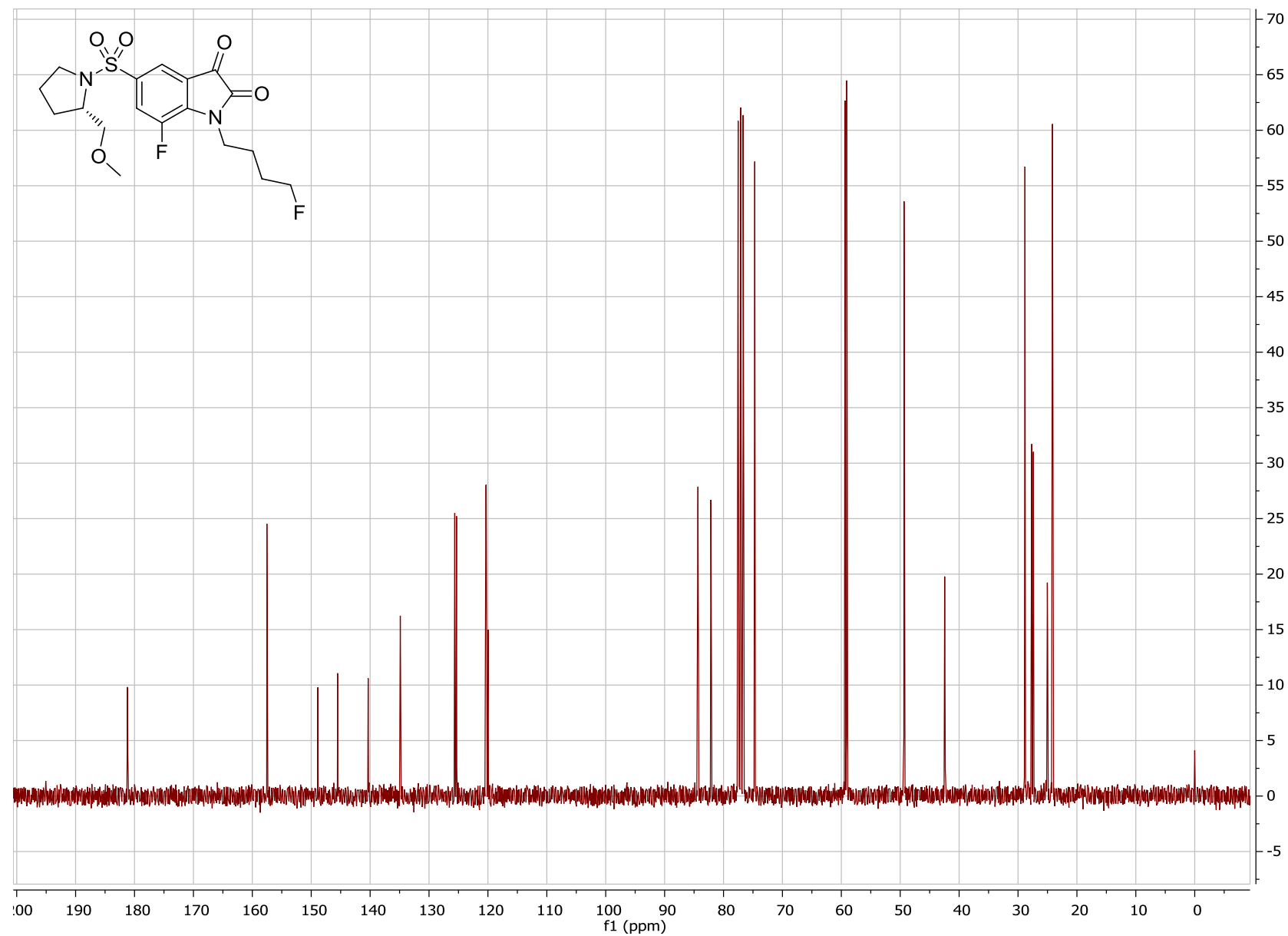
^{19}F NMR spectrum of (S)-N-butyl-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**38**)



^1H NMR spectrum of (S)-N-(4-fluorobutyl)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**39**)



¹³C NMR spectrum of (S)-N-(4-fluorobutyl)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**39**)



^{19}F NMR spectrum of (S)-N-(4-fluorobutyl)-7-fluoro-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatin (**39**)

