SUPPORTING INFORMATION

Discovery of G Protein-biased D2 Dopamine Receptor Partial Agonists

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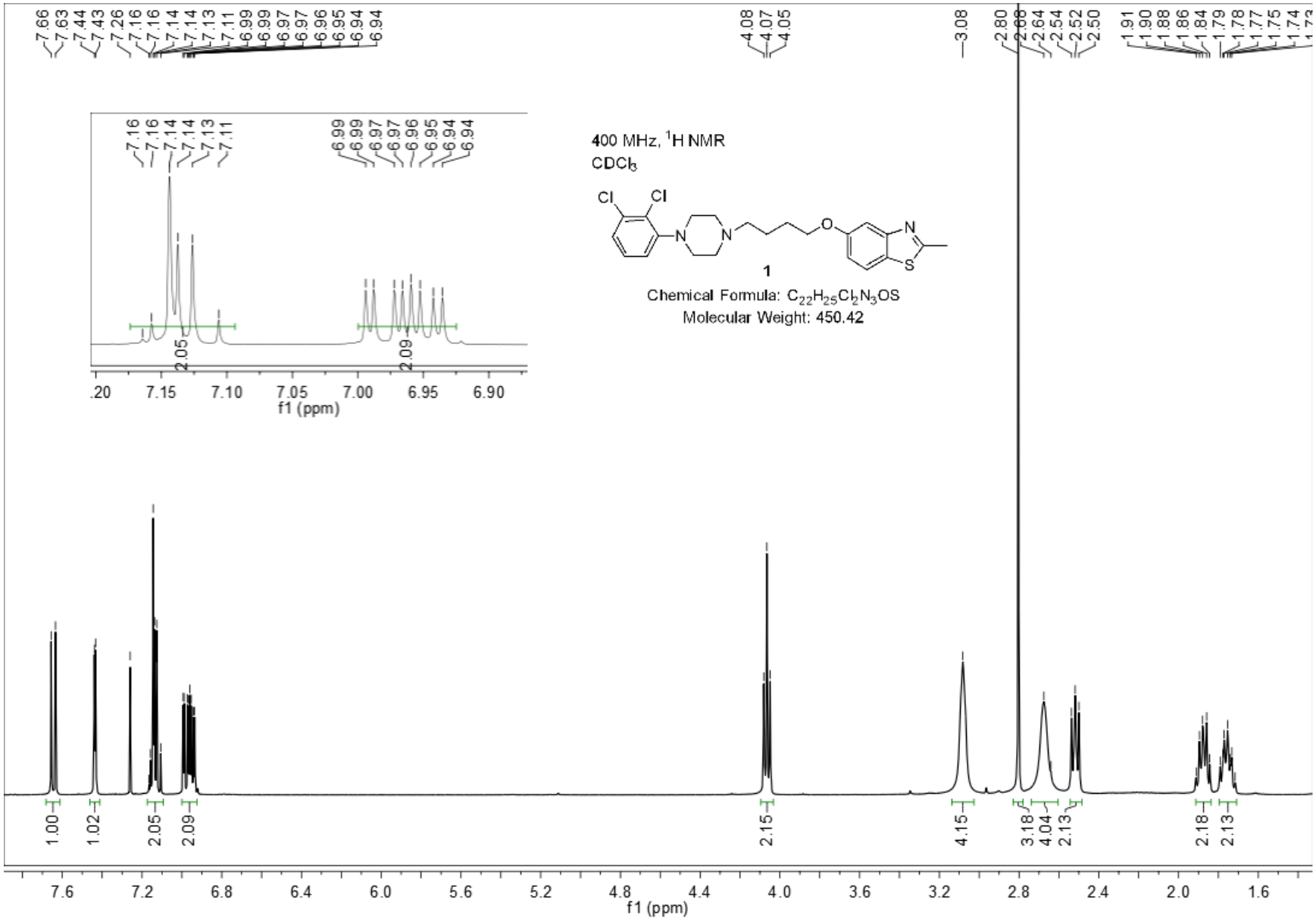
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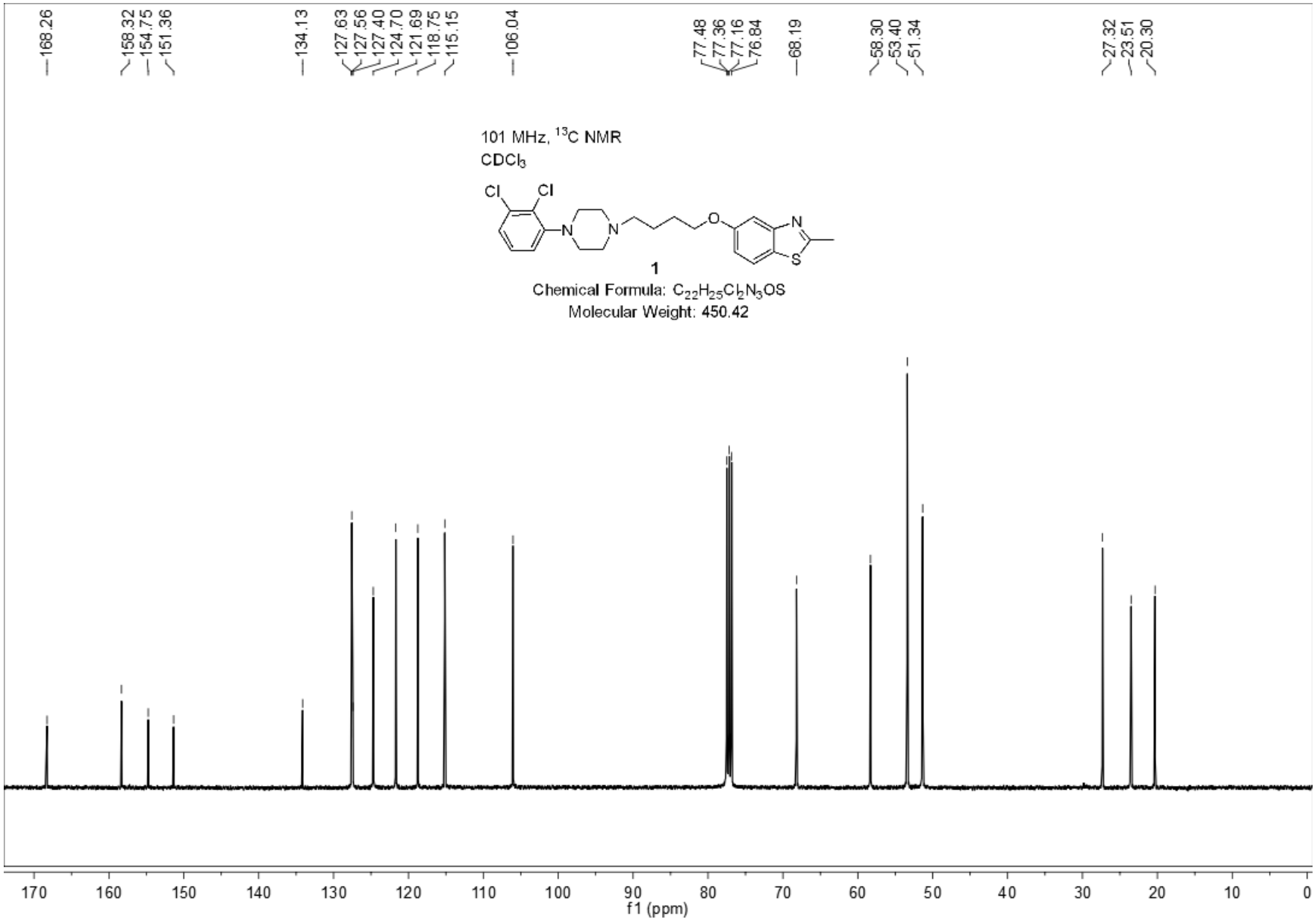
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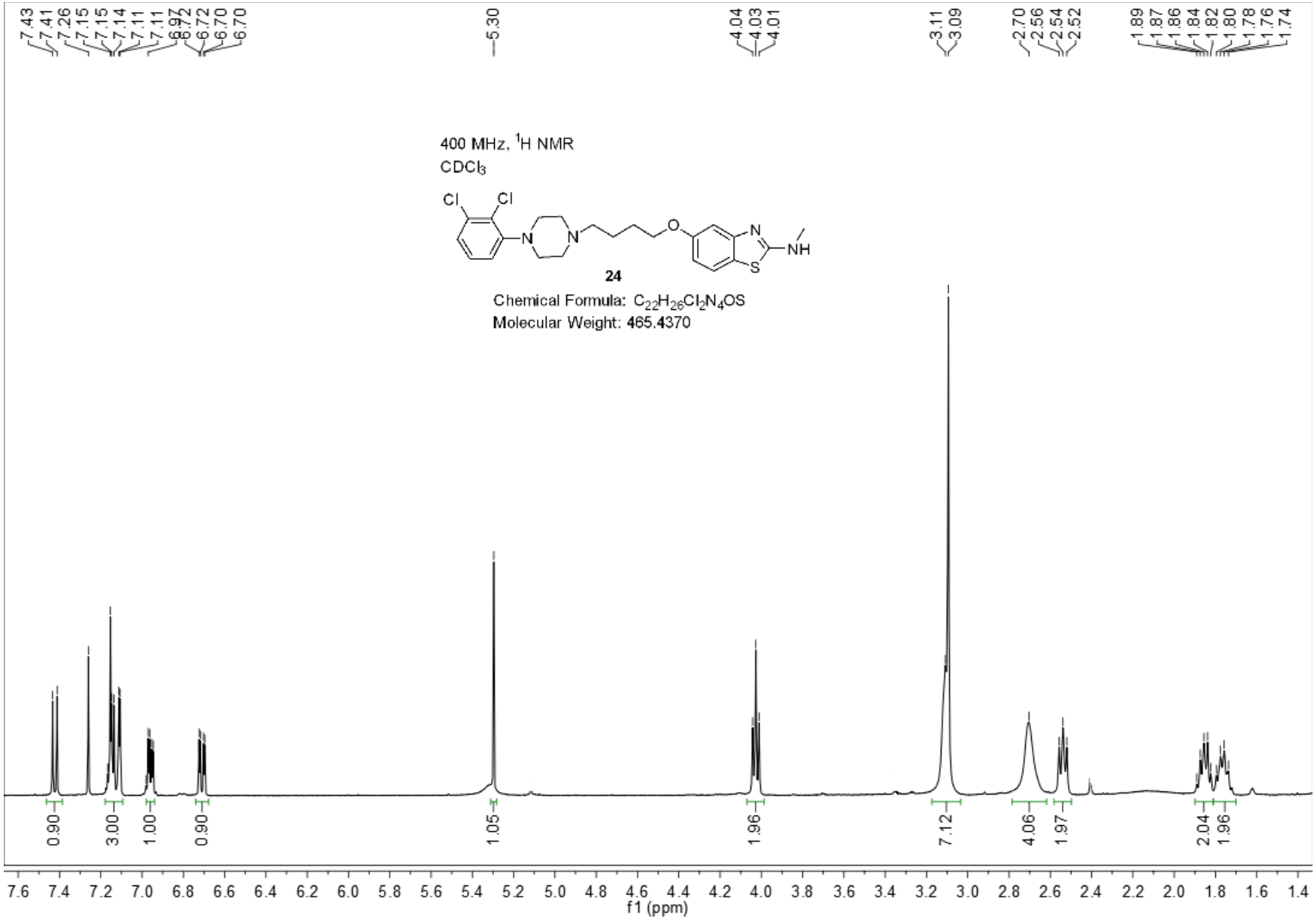
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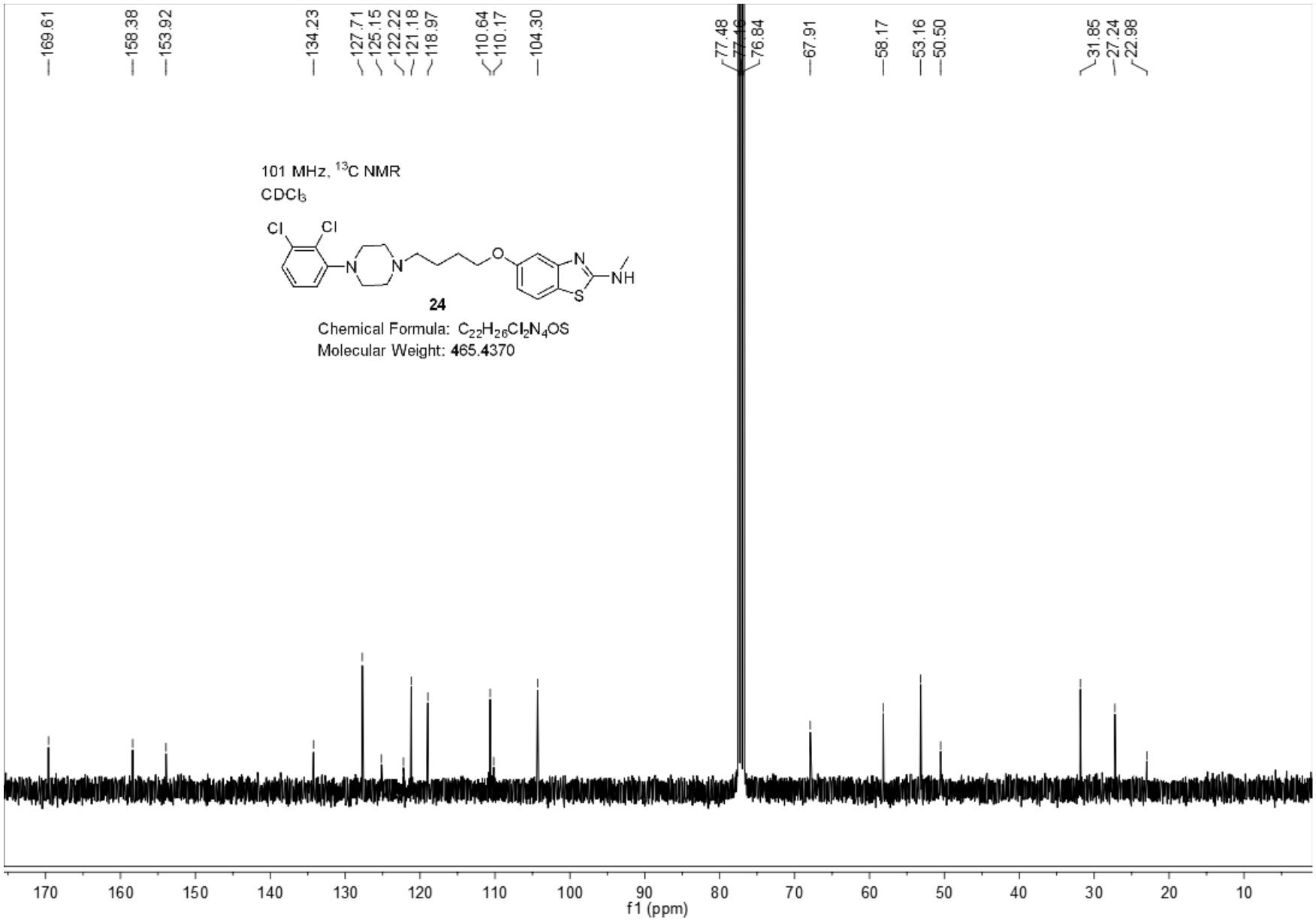
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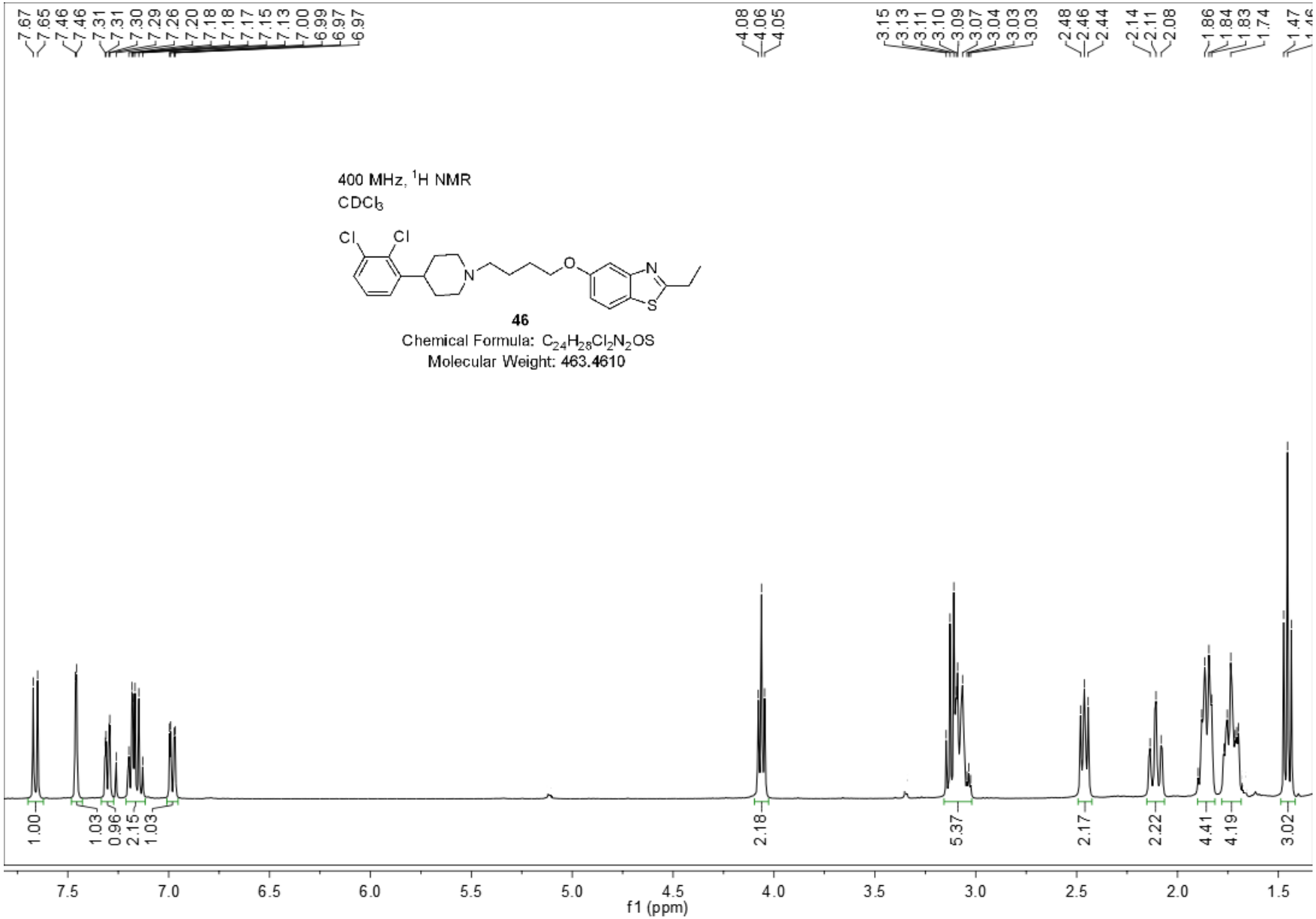
f1 (ppm)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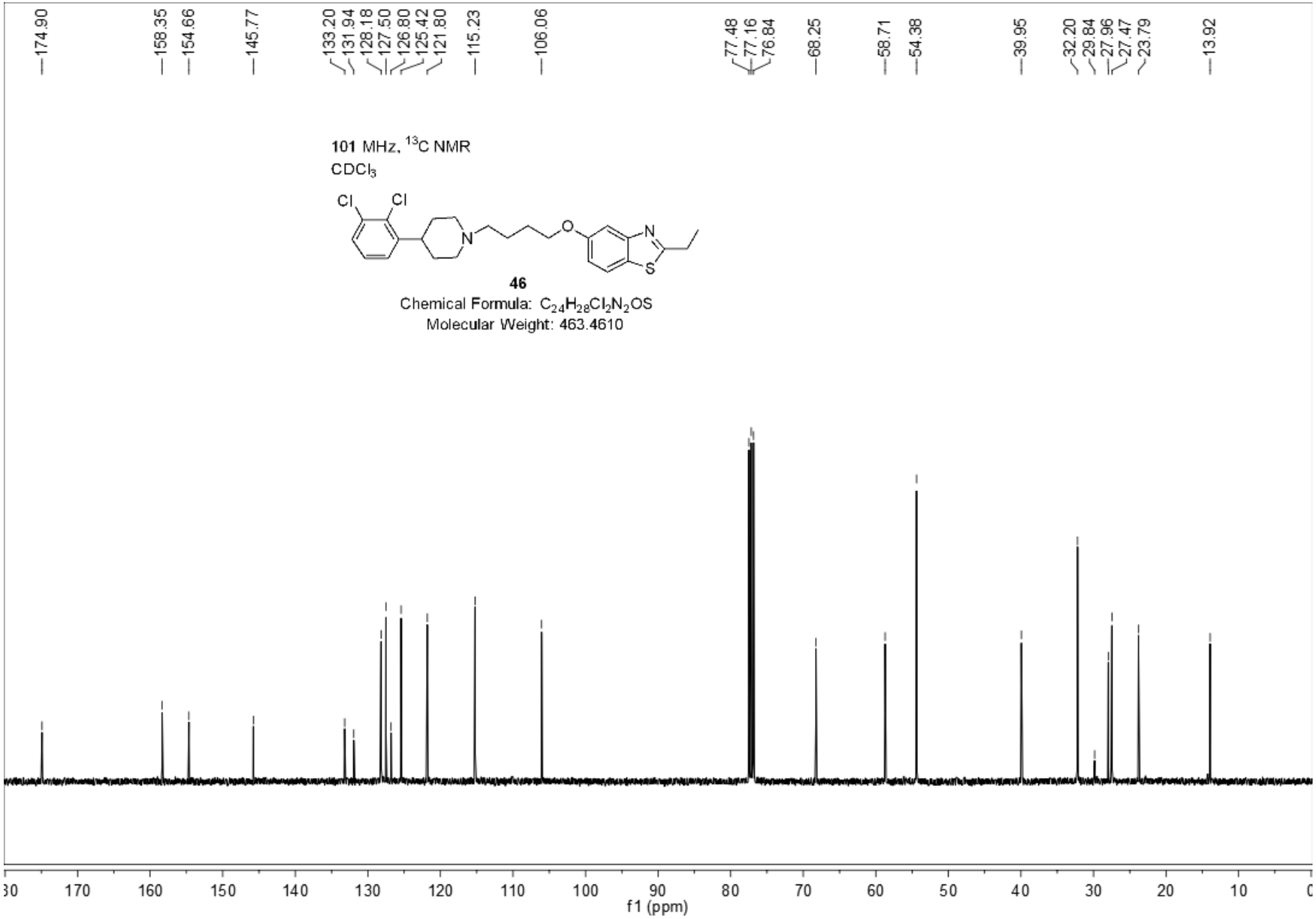
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68.25
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27.47
23.79
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101 MHz, 13C NMR
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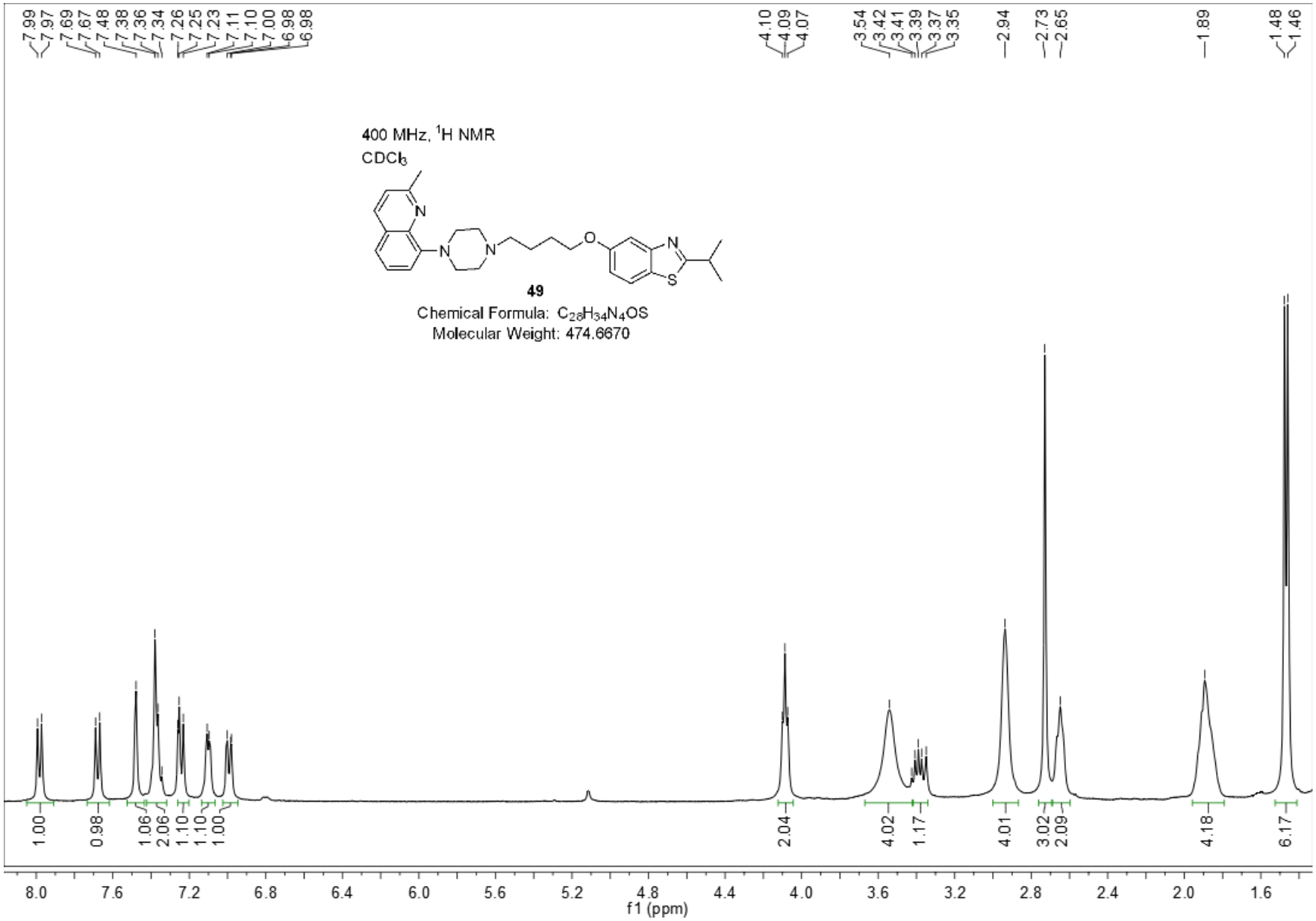
f1 (ppm)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400 MHz, 1H NMR
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S
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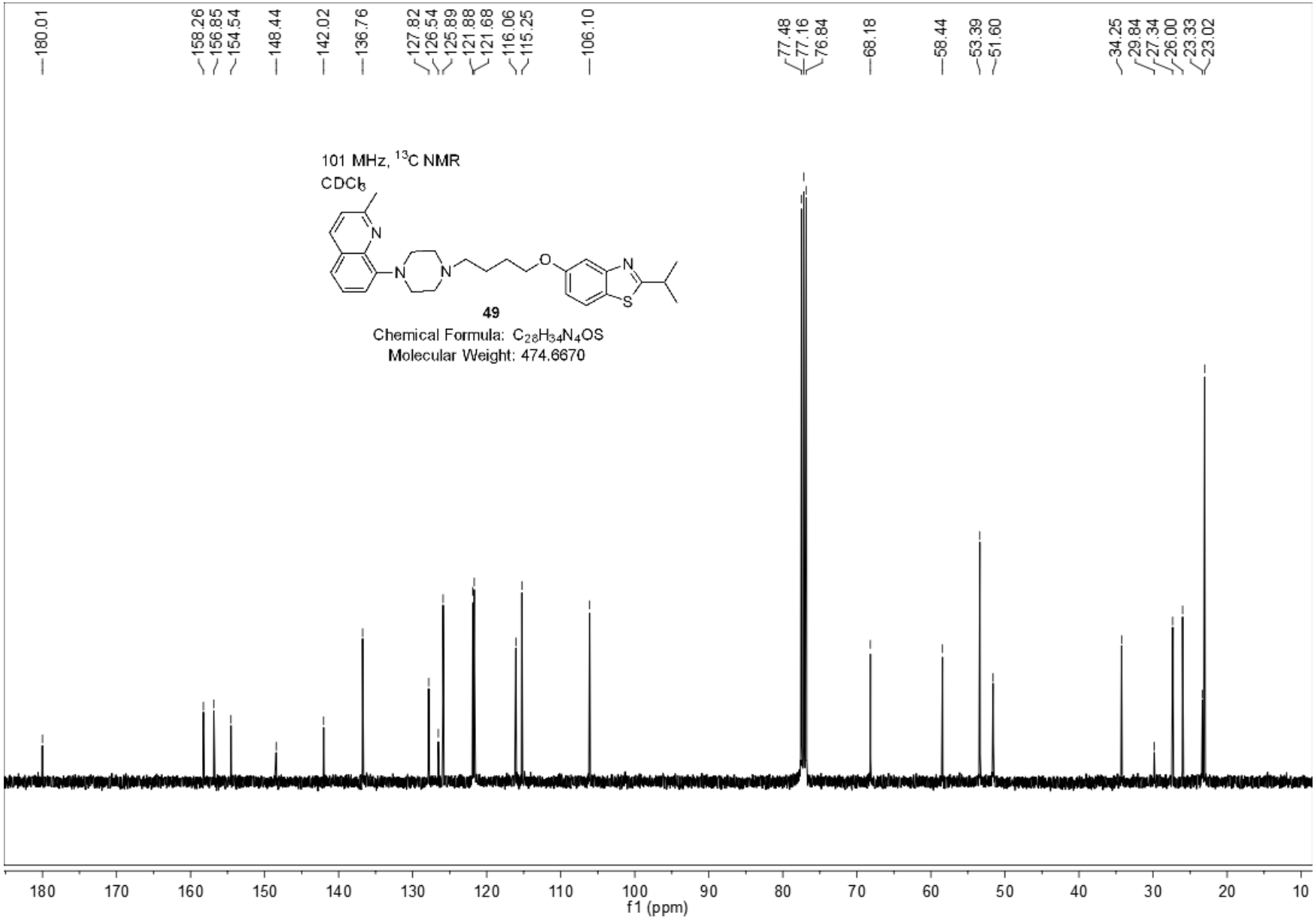
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101 MHz, 13C NMR
CDCl3
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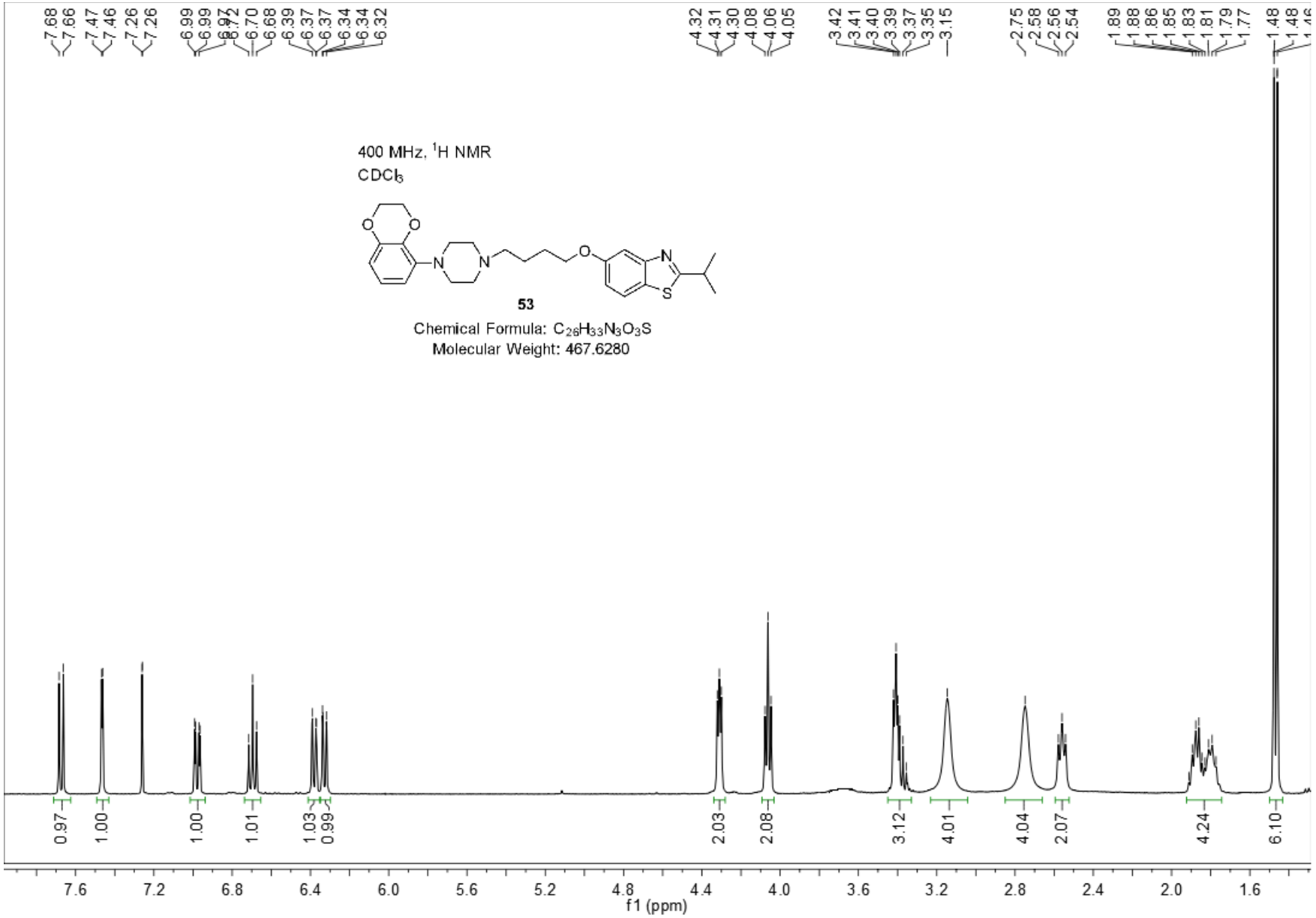
Molecular Weight: 474.6670
f1 (ppm)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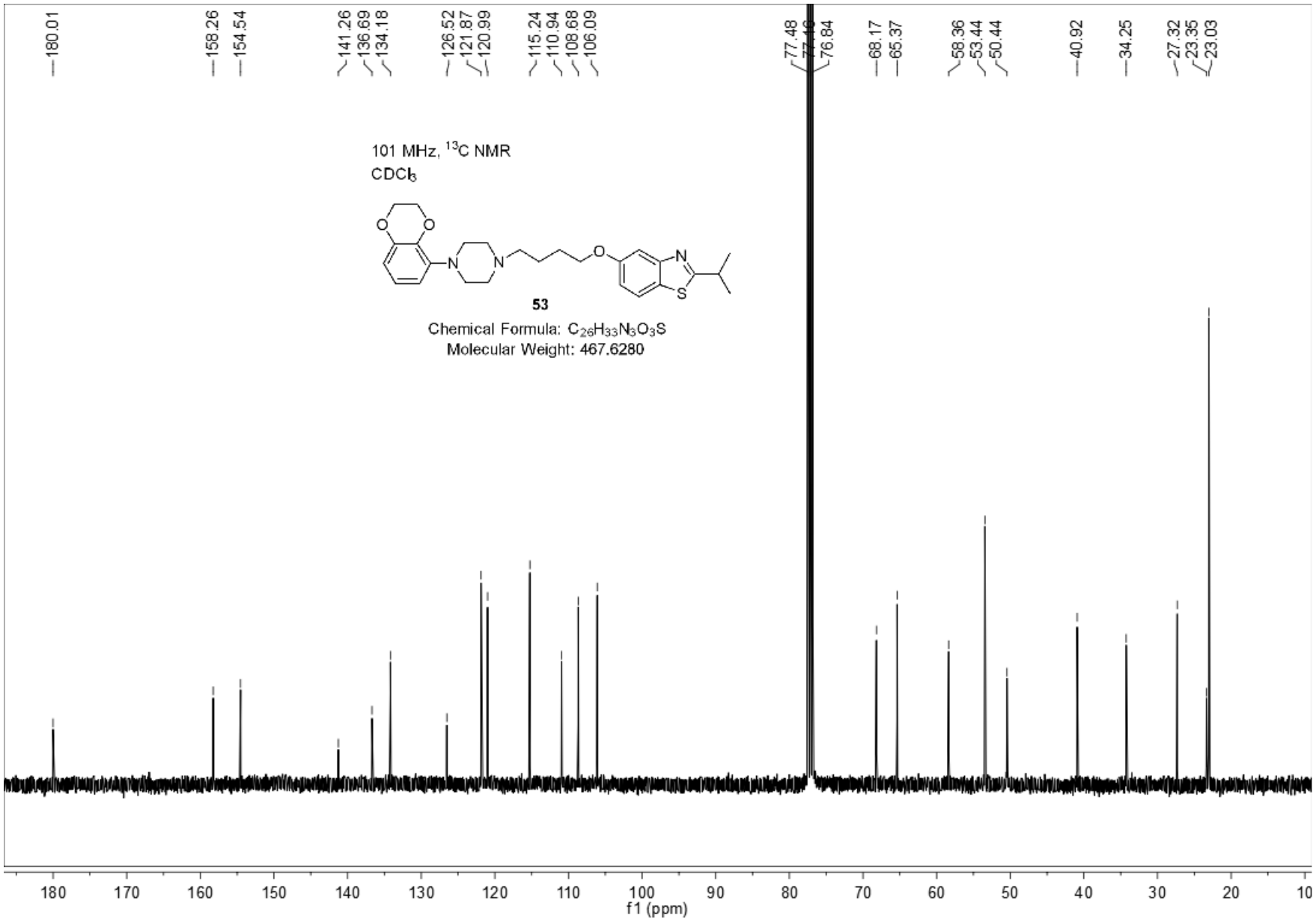
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53.44
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101 MHz, 13C NMR
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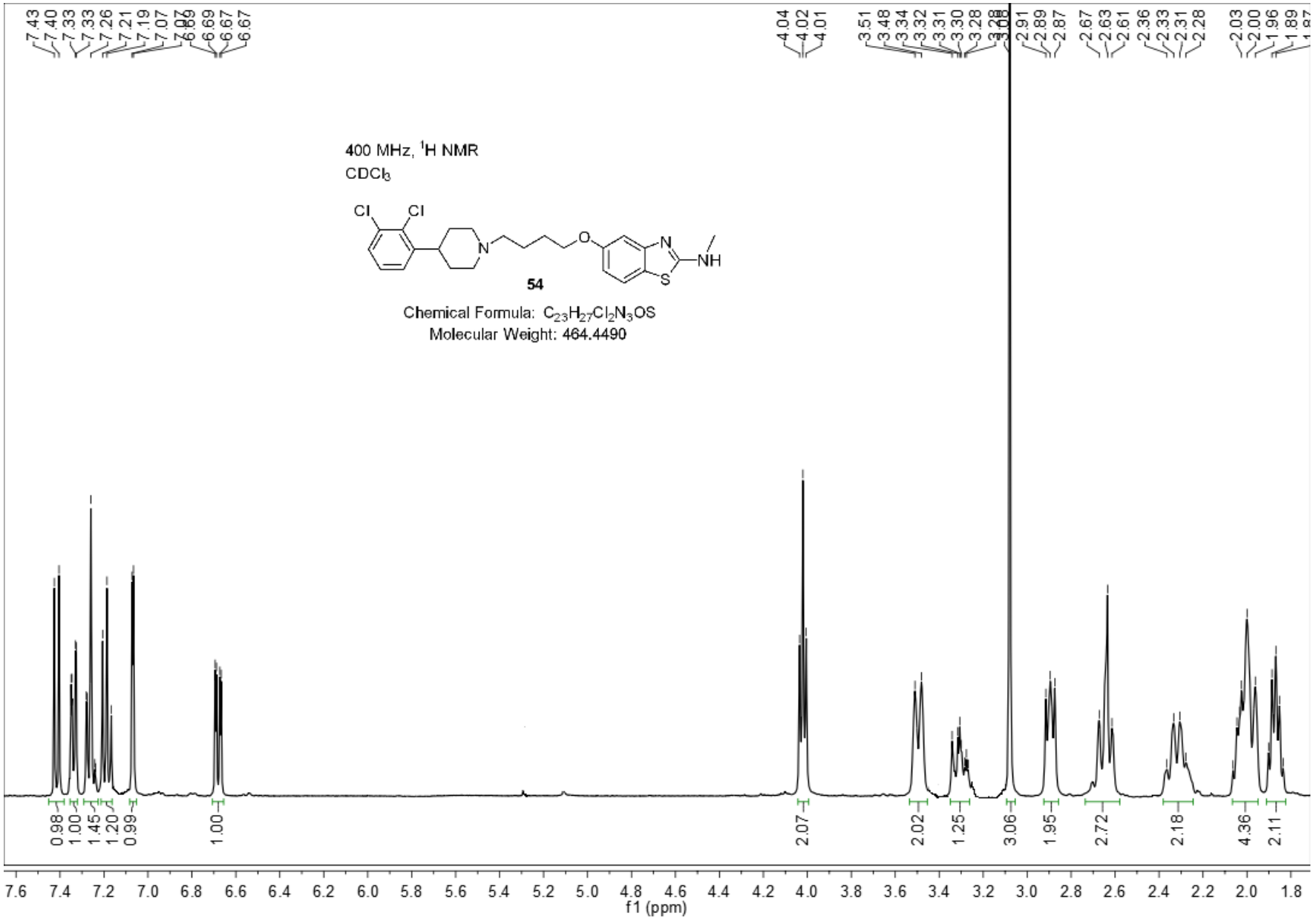
f1 (ppm)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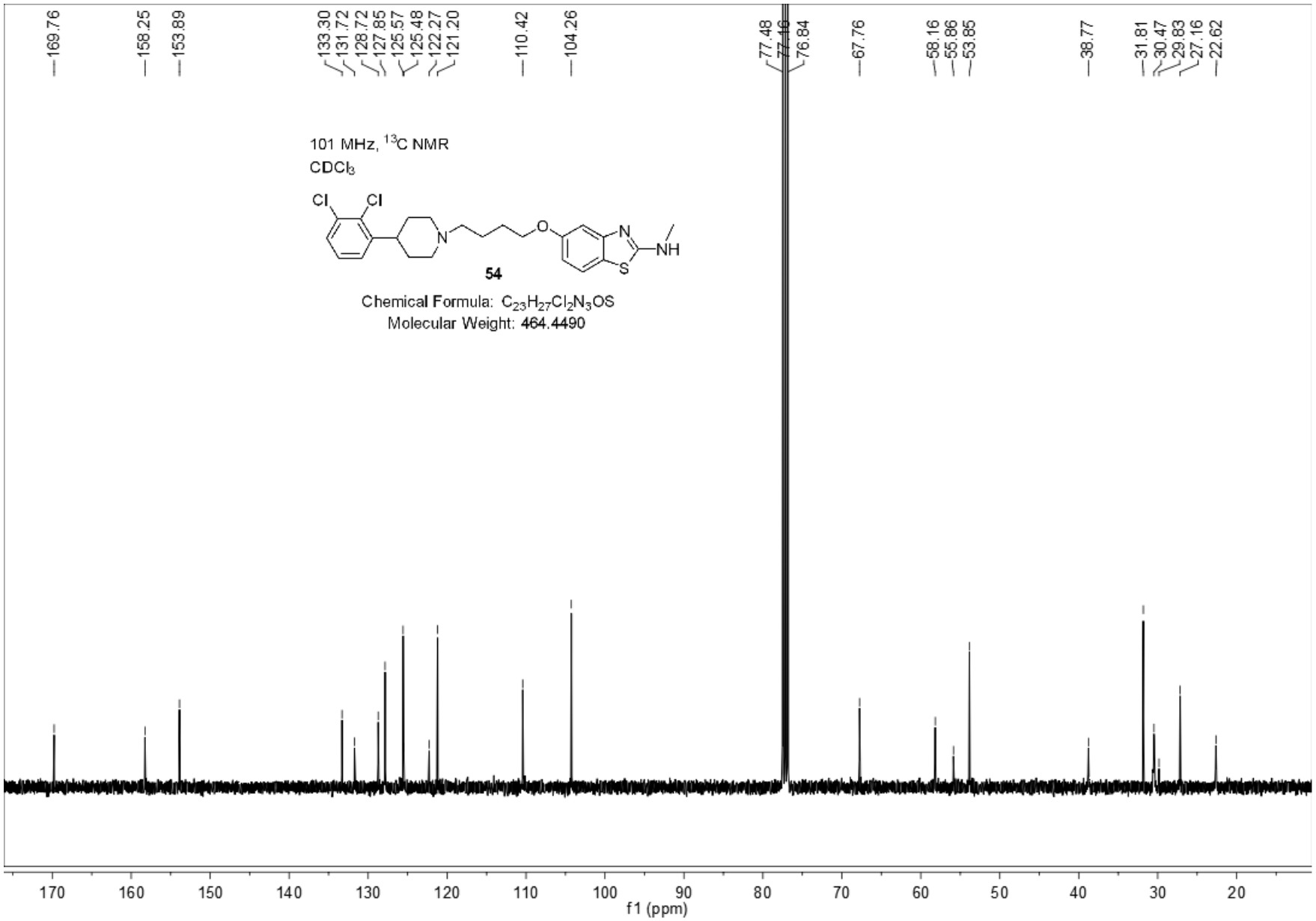
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101 MHz, 13C NMR
CDCl3
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Cl
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54
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Molecular Weight: 464.4490
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90
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50
40
30
20
f1 (ppm)

Table S1. K_d and B_{MAX} estimates comparing D2R GloSensor and D2R Tango cell types[a]

Cell Type	K_d, nM (pK_d ± SEM)	B_{MAX} (fmol/mg protein)
D2R GloSensor (HEKT)	0.11 (9.97 ± 0.08)	1290 ± 105
D2R Tango (HTLA)	0.12 (9.95 ± 0.12)	1284 ± 107

[a]Estimates of K_d and B_{MAX} were obtained by radioligand saturation assays using [^{3}H] N-methyl spiperone and 5 μM (+)-butaclamol to define non-specific binding. Human $D2R_{Long}$ receptors were expressed in either HEKT cells expressing GloSensor or in HTLA cells expressing β-arrestin-2-TEV protease. Data represent average and standard error of the mean (SEM; n=4).

Figure S1. GloSensor cAMP inhibition with no D2R expressed.

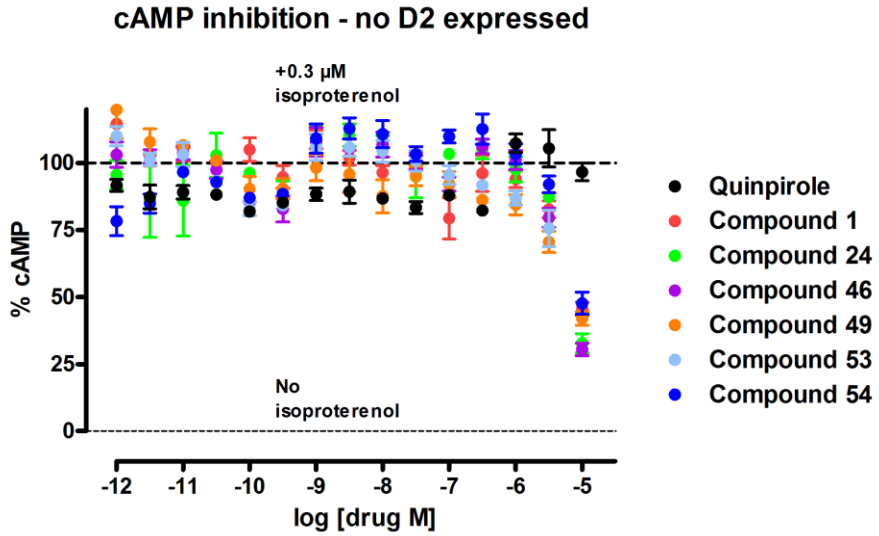

Figure S2. D2R G protein antagonism by compound **1**.