

**First ^{97}Ru complex with pyridine-2,6-dicarboxamide conjugate
for potential use as radiopharmaceutical**

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Synthesis of the Peptidomimetic Pyridine-2,6-dicarboxamide (1)

Methionine Methyl Ester Hydrochloride

Thionyl chloride (10.88 ml, 150 mmol) was added dropwise to methanol (100 ml) cooled to -10 °C. The mixture was stirred at -10 °C for 30 min and then L-methionine (14.92 g, 100 mmol) was added in one portion. The reaction mixture was allowed to warm to room temperature and left under these conditions for 24–30 h with vigorous stirring. Then the mixture was evaporated to dryness in vacuo and the residue was treated with dry ethyl ether until a solid precipitated. The solid hydrochloride salt of the ester was filtered off, washed with ethyl ether, dried in vacuo to constant weight, and used without further purification.

Acylation of Methionine Methyl Ester. Preparation of Ester 2

Et₃N (4.21 ml, 30 mmol) was added to a solution of methionine methyl ester hydrochloride (6 g, 30 mmol) in dichloromethane (DCM, 100 ml). The mixture was stirred for 20 min and evaporated to dryness in vacuo. Methionine methyl ester was extracted from the solid residue with ethyl ether. The ether extract was evaporated in vacuo and the oily methionine methyl ester was dissolved in dry tetrahydrofuran (THF, 10 ml). Then pyridine-2,6-dicarbonyl dichloride (2.78 g, 13.64 mmol) was dissolved in dry THF (50 ml) and treated with a solution of methionine methyl ester and Et₃N (4.21 ml, 30 mmol). The mixture was stirred for 24 h, filtered and evaporated to dryness. Oily ester **2** was washed with ether–hexane (1 : 10) and dried in vacuo to give **2** as yellowish oil. Yield: 6.24 g (80%). ¹H NMR (500 MHz), δ : 8.28 (d, J 7.7 Hz, 2H), 8.15 (dd, J 8.2 Hz, J 7.3 Hz, 1H), 4.86 (dd, J 9.2 Hz, J 5.0 Hz, 2H), 3.74 (s, 6H), 2.71–2.52 (m, 4H), 2.29 (dtd, J 14.1 Hz, J 7.8 Hz, J 5.0 Hz, 2H), 2.16 (dddd, J 14.1 Hz, J 9.2 Hz, J 7.8 Hz, J 5.5 Hz, 2H), 2.07 (s, 6H). ¹³C NMR (126 MHz), δ : 173.60, 165.87, 149.90, 140.58, 126.44, 53.05, 31.72, 31.48, 15.36.

Preparation of Ligand 1

A solution of NaOH (180 mg, 4.5 mmol) in water (5 ml) was added to a solution of **2** (920 mg, 2 mmol) in ethanol (20 ml). The mixture was stirred for 2 days and then treated with 1 M HCl (4.5 ml) and evaporated to dryness. The product was extracted with THF, dried over Na₂SO₄, and reduced in volume by half. The resulting solution was diluted with ether and a white powder precipitated out. The powder was decanted from the mother liquor, washed with ether, and dried. Yield: 640 mg (74%). ¹H NMR (500 MHz), δ : 8.33–8.23 (m, 2H), 8.13 (dd, J 8.3 Hz, J 7.3 Hz, 1H), 4.85 (dd, J 9.3 Hz, J 4.8 Hz, 2H), 2.72–2.56 (m, 4H), 2.32 (dtd, J 14.1 Hz, J 7.8 Hz, J 4.8 Hz, 2H), 2.19 (dddd, J 14.4 Hz, J 9.3 Hz, J 7.9 Hz, J 5.3 Hz, 2H), 2.09 (s, 6H). ¹³C NMR (126 MHz), δ : 175.09, 165.87, 149.95, 140.48, 126.27, 53.04, 31.92, 31.58, 15.29.

NMR Spectra

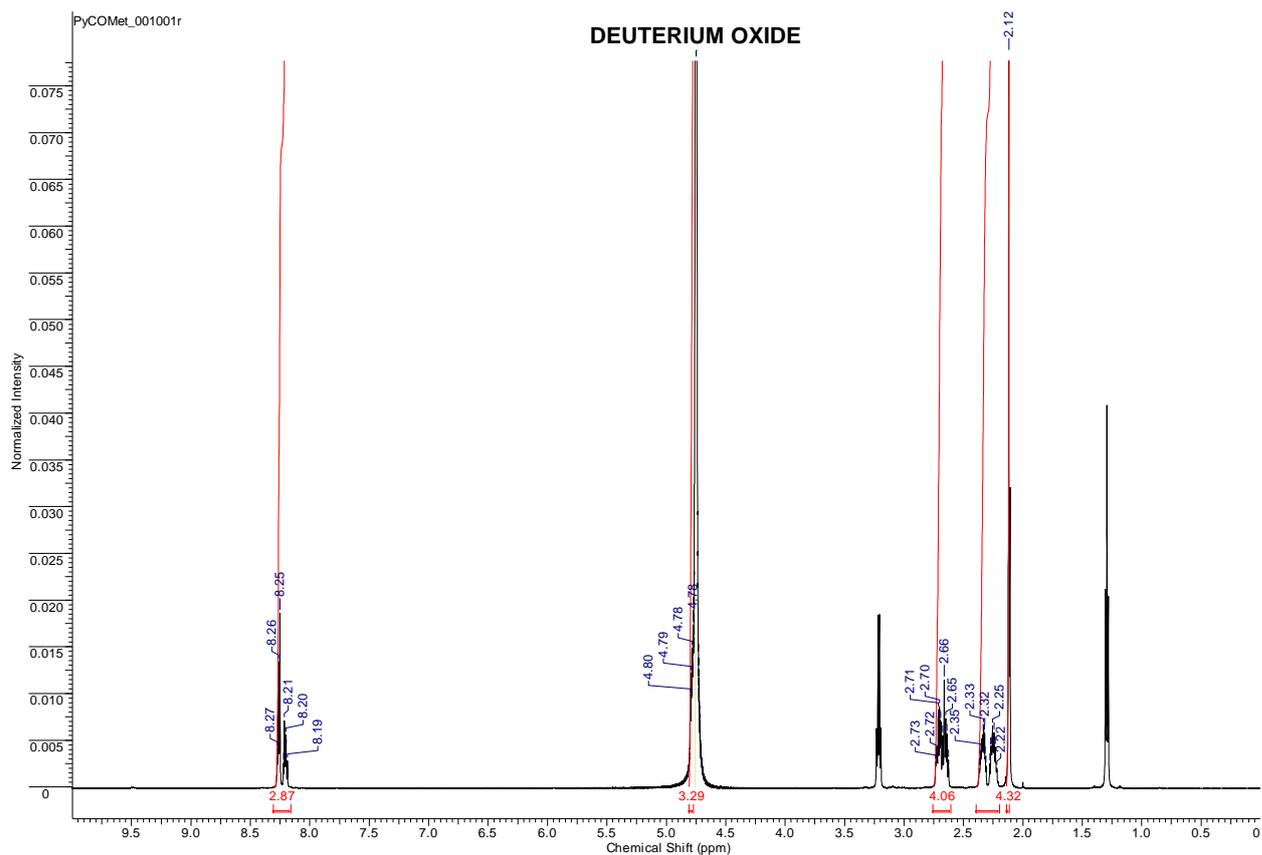


Figure S1 ^1H NMR spectrum of amide 1 in D_2O .

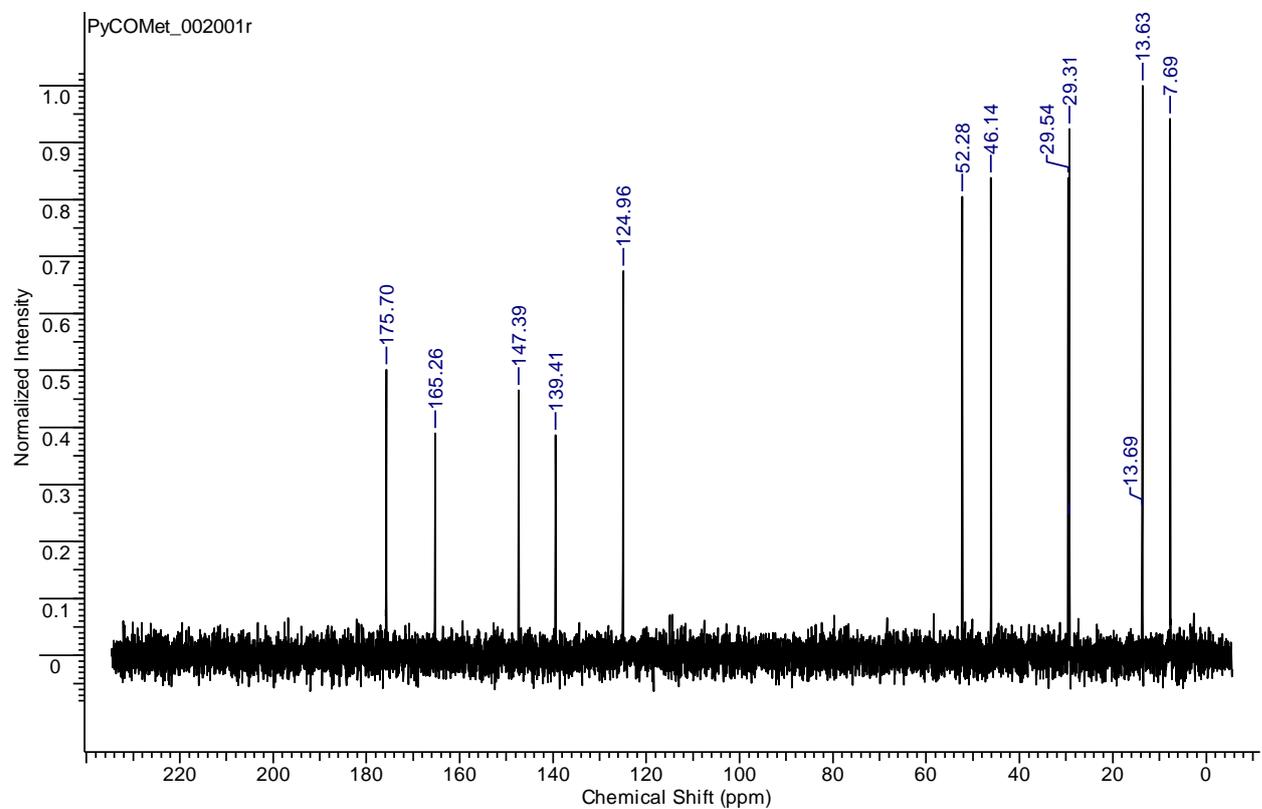


Figure S2 ^{13}C NMR spectrum of amide 1 in D_2O .

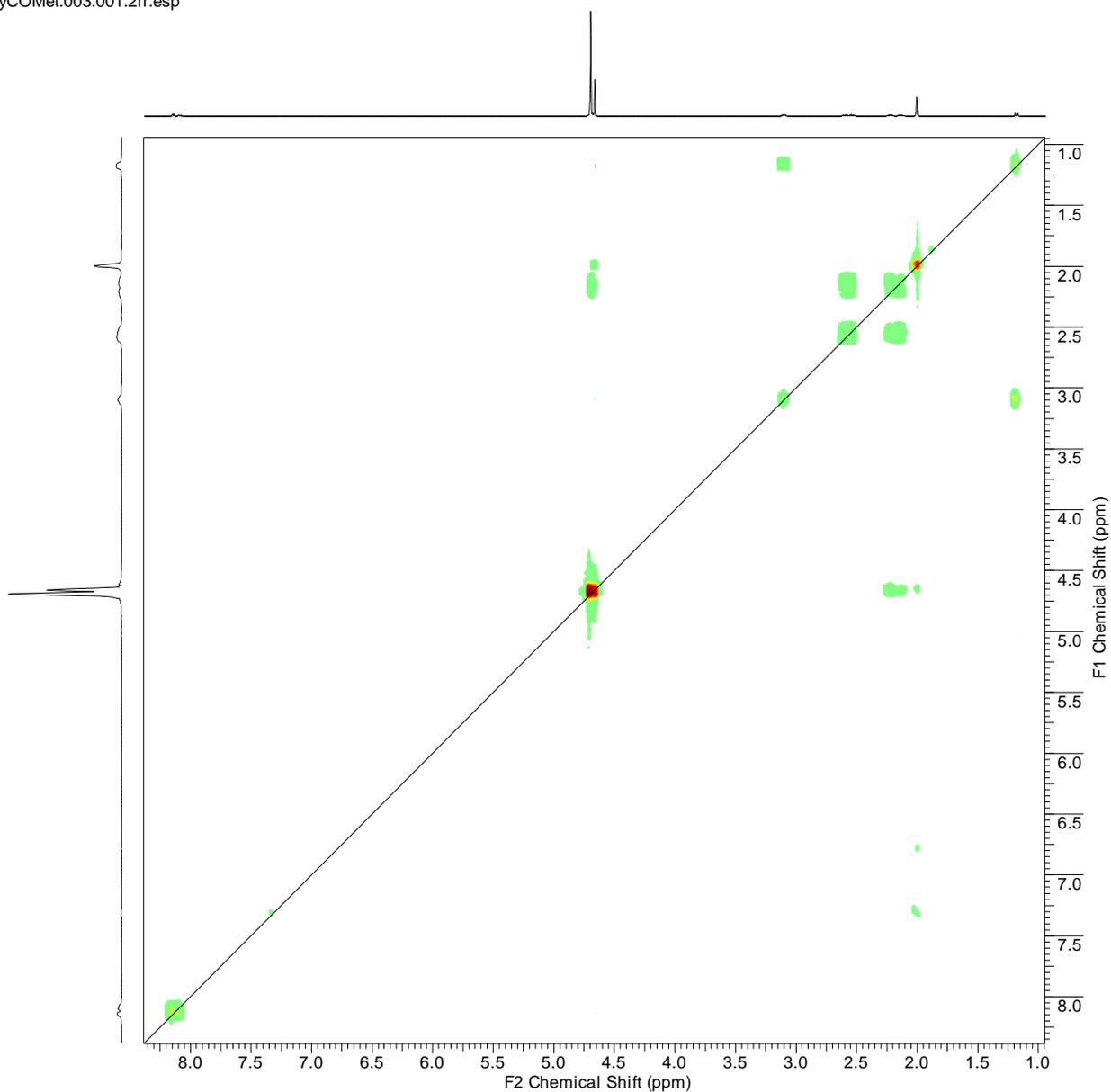


Figure S3 2D COSY spectrum of amide **1** in D₂O.

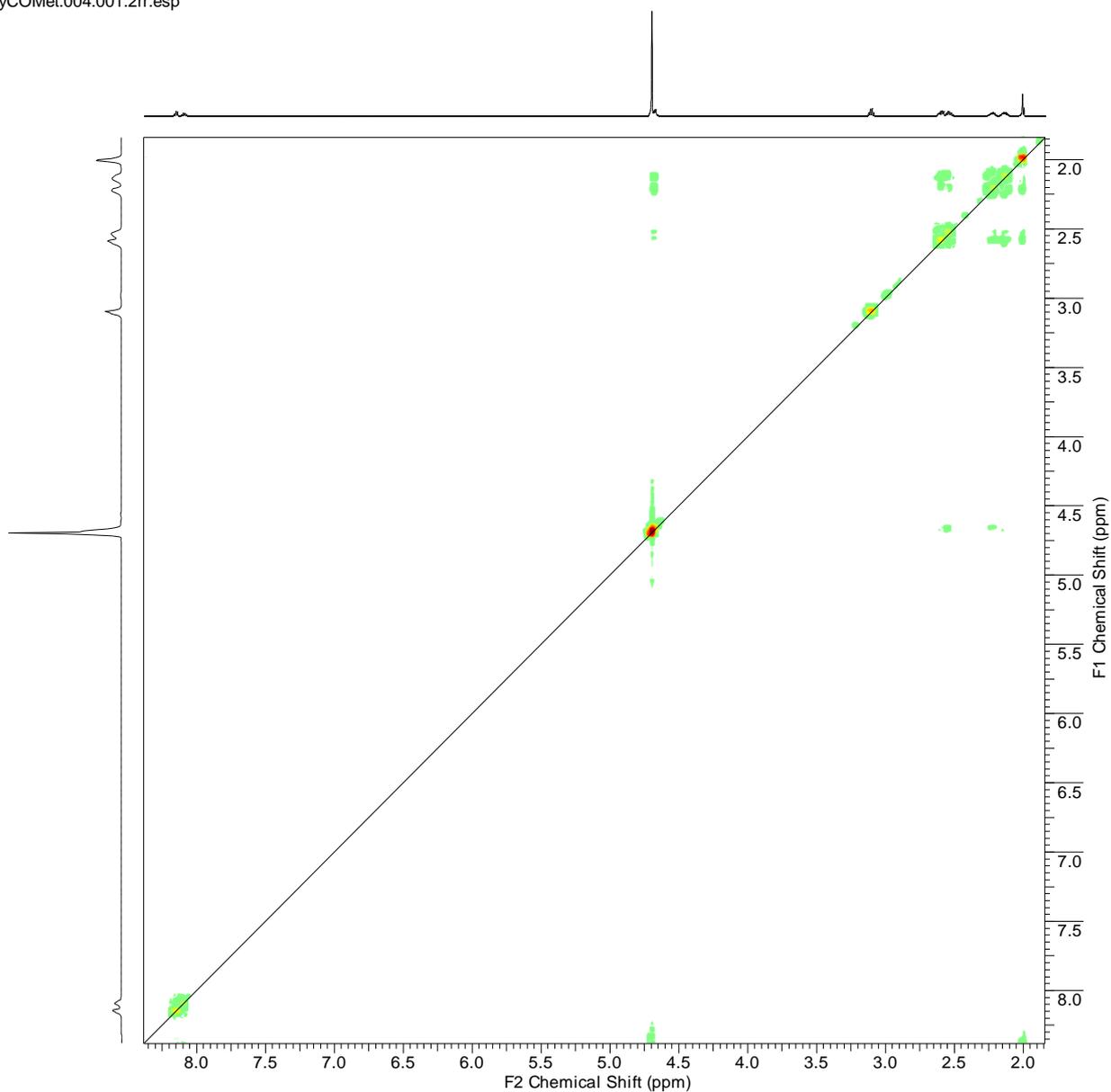


Figure S4 2D NOESY spectrum of amide **1** in D₂O.

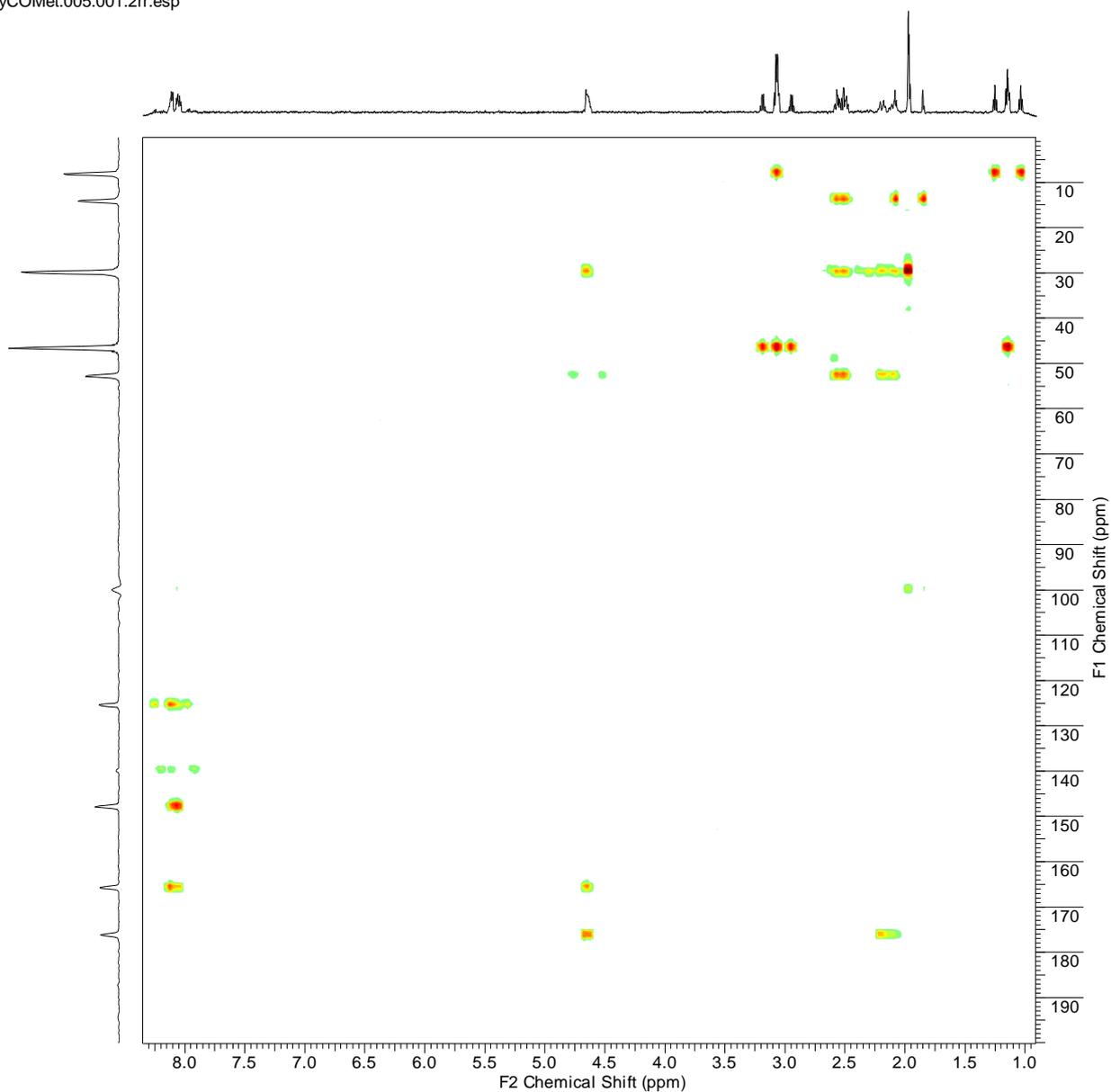


Figure S5 2D HMBC spectrum of amide **1** in D₂O.

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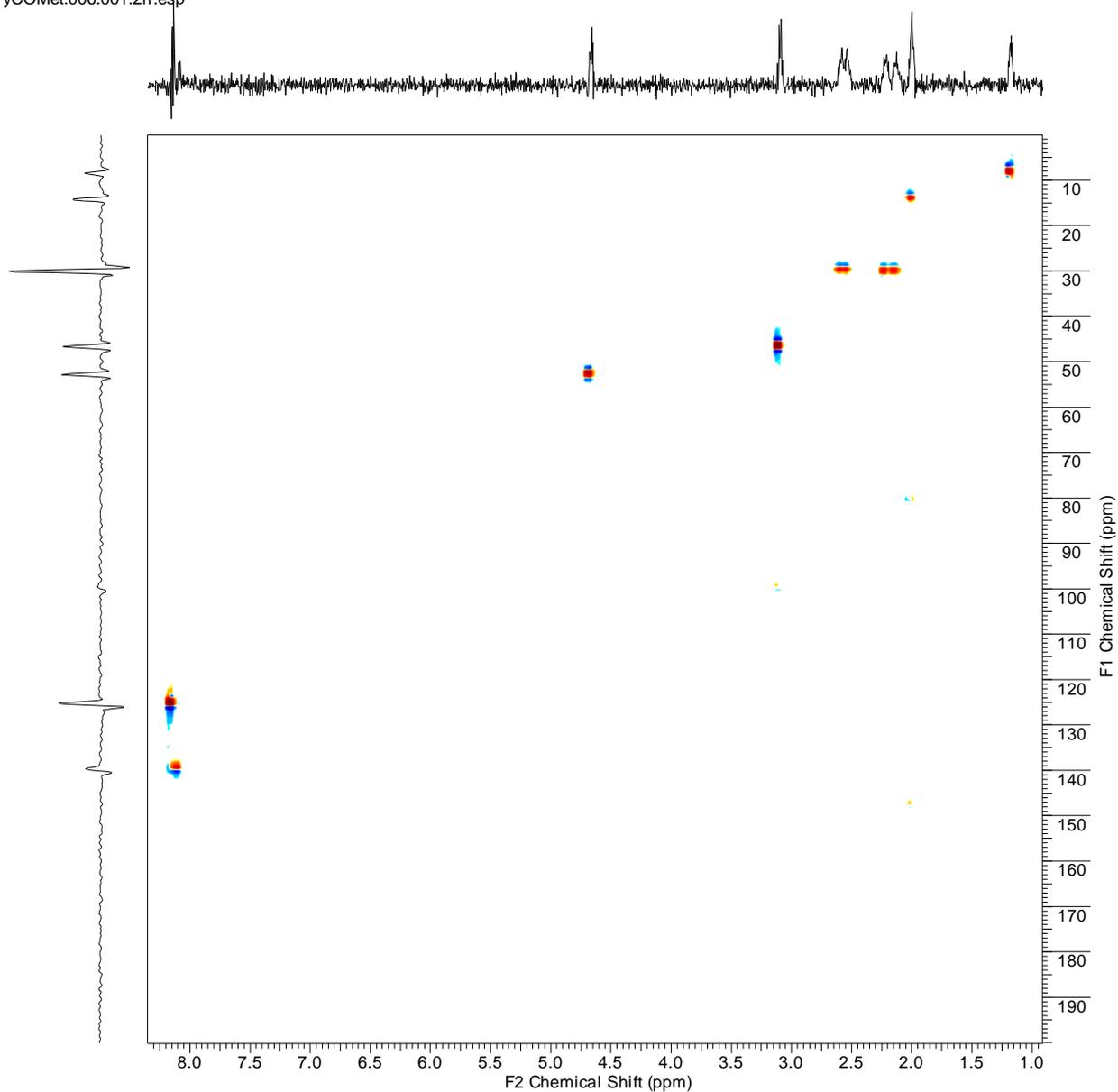


Figure S6 2D HSQC spectrum of amide **1** in D₂O.

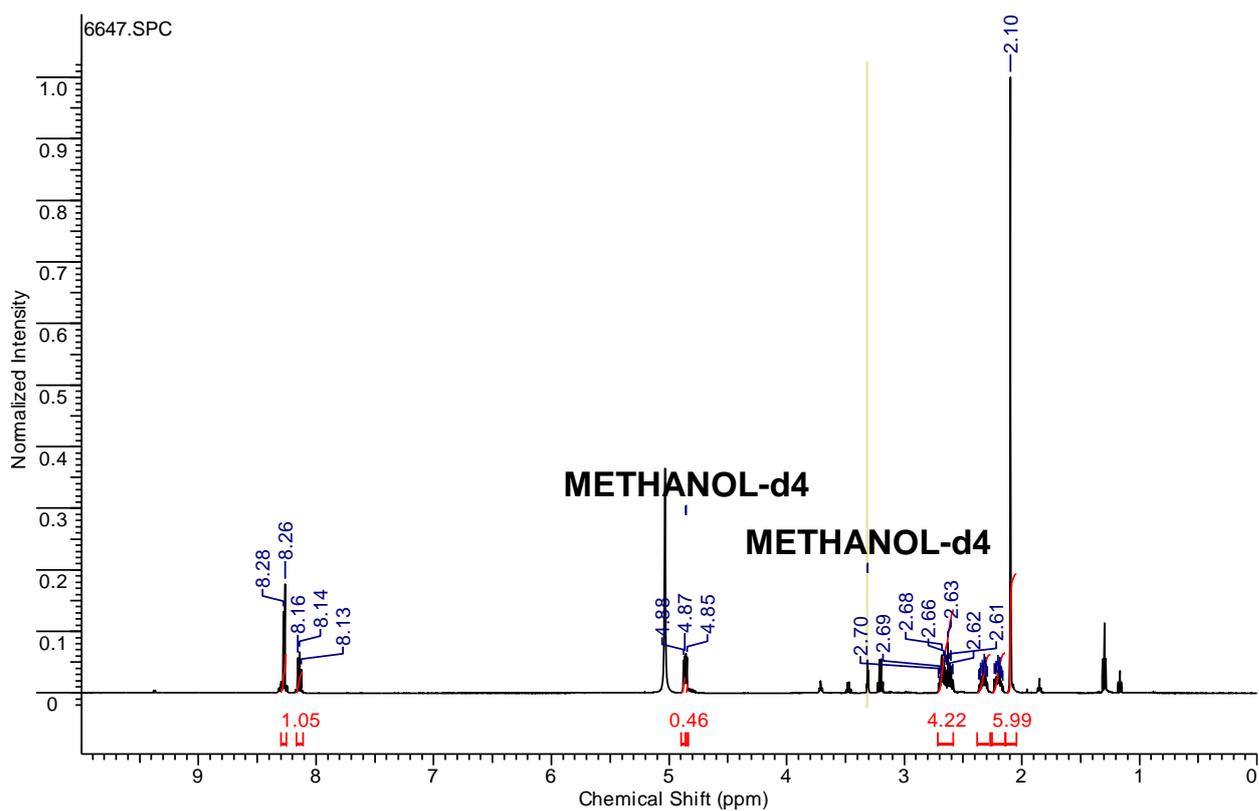


Figure S7 ^1H NMR spectrum of amide **1** in methanol- d_4 .

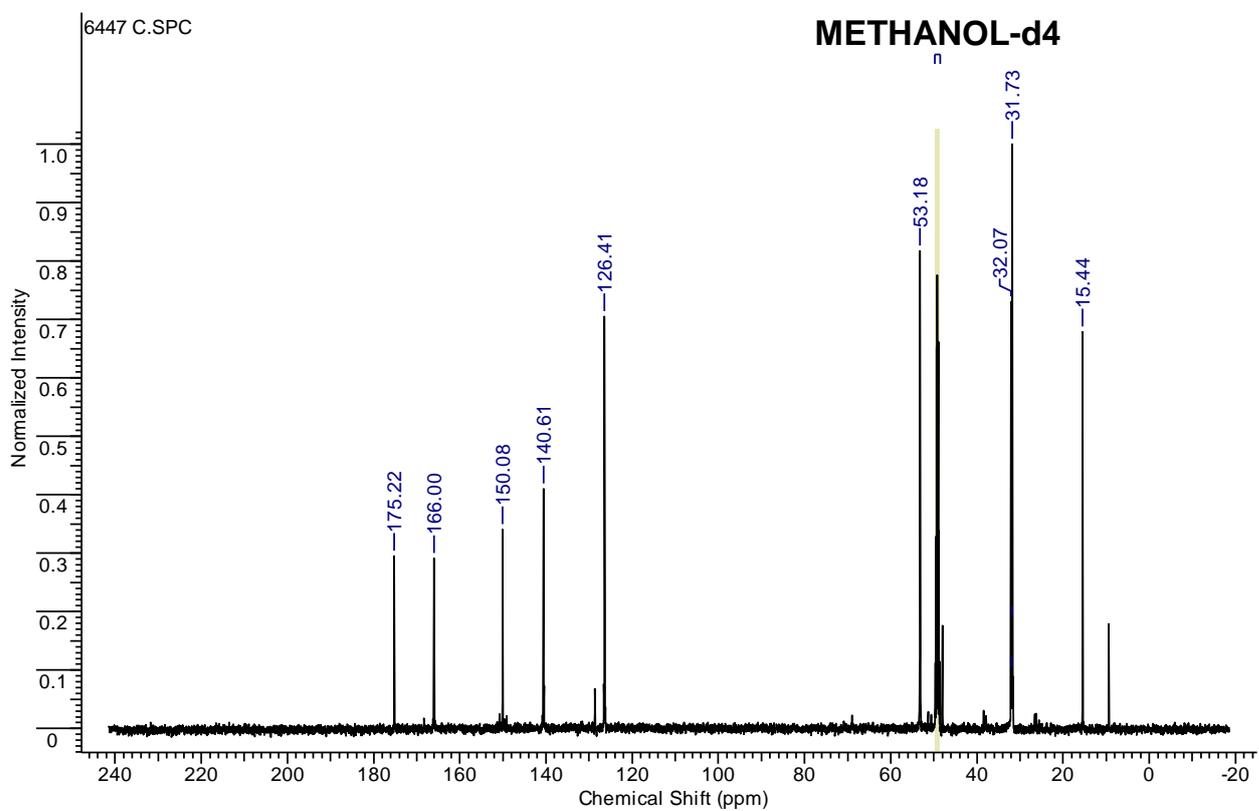


Figure S8 ^{13}C NMR spectrum of amide **1** in methanol- d_4 .

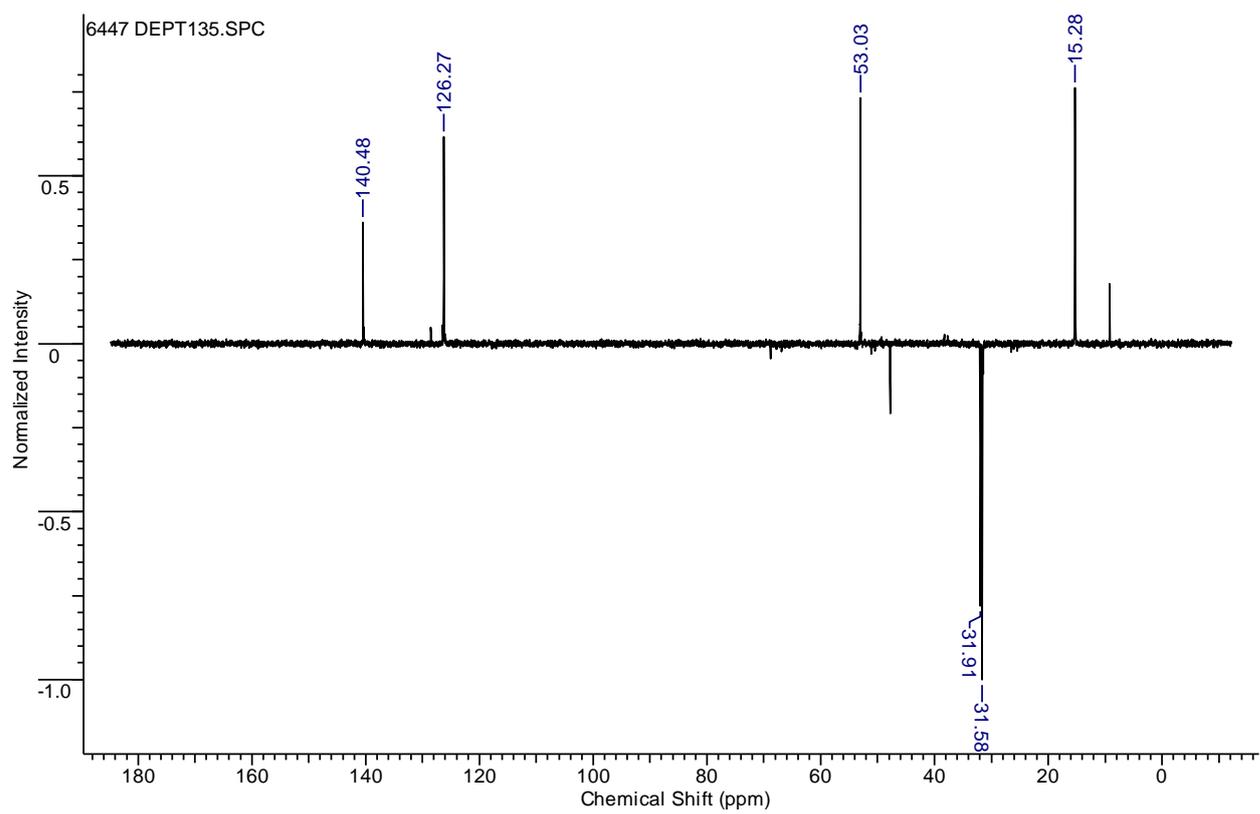


Figure S9 ^{13}C DEPT 135 spectrum of amide **1** in methanol- d_4 .

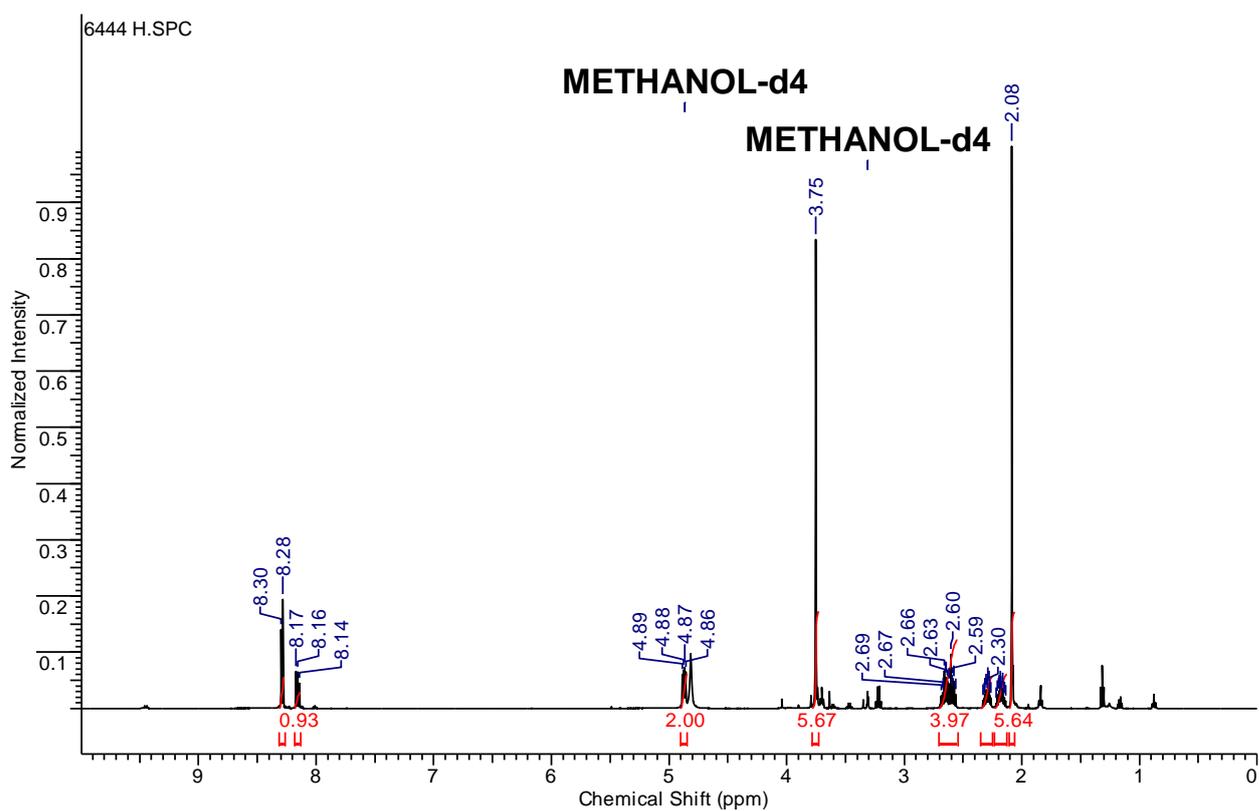


Figure S10 ¹H NMR spectrum of ester **2** in methanol-*d*₄.

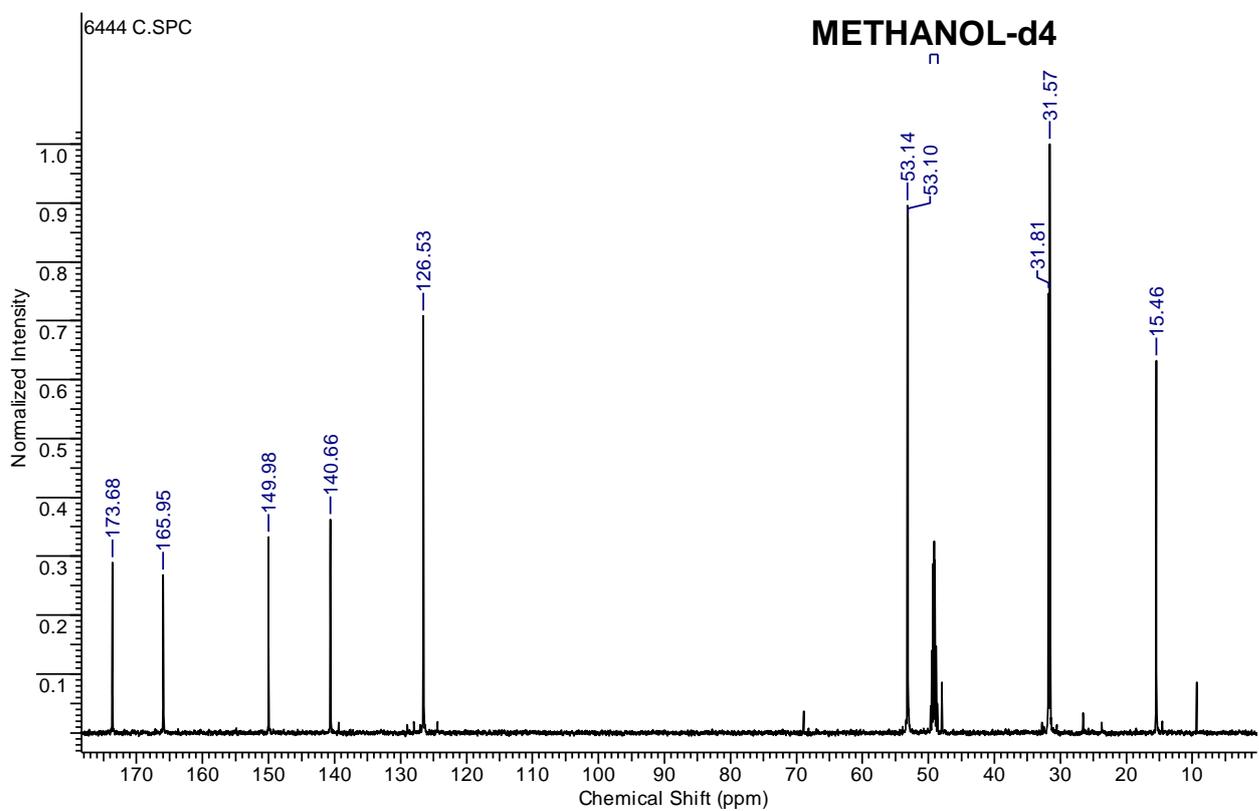


Figure S11 ¹³C NMR spectrum of ester **2** in methanol-*d*₄.