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SUPPORTING INFORMATION

Synthesis of a 6-Hydroxyindole Metabolite of AM2201

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The synthesis of 1*H*-indol-6-yl acetate (2).

In a round bottom flask, 1H-indol-6-ol (1.0 g, 7.52 mmol) was disssolved in dichloromethane (DCM, 20 mL), and acetic anhydride (782 μL, 8.27 mmol) and triethylamine (2.09 mL, 15.04 mmol) were added. The mixture was stirred at room temperature for 3 hours. Upon completion of the reaction, water (100 mL) and DCM (50 mL) were added for extraction. The organic phase was separated, and the aqueous layer was extracted with DCM (3 × 30 mL). The combined organic extracts were dried over anhydrous sodium sulfate (Na_2SO_4), and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was purified by column chromatography using a gradient of hexane and ethyl acetate (from 3:1 to 1:1) to afford compound **2** as an off-white solid (1.25 g, 7.14 mmol, 95% yield). The solid were dried in high vacuum for at least 8h for the next reaction.

The synthesis of 3-(1-naphthoyl)-1H-indol-6-yl acetate (3).

A solution of compound **2** (600 mg, 3.42 mmol) in anhydrous toluene (10 mL) was cooled to 0 °C under a nitrogen atmosphere and treated with 1-naphthoyl chloride (535 μL, 2.85 mmol). The mixture was stirred at 0 °C for 30 minutes, followed by the dropwise addition of ethylaluminum dichloride (0.9 M in heptane, 4.8 mL, 19.1 mmol, 5.58 equiv.) while maintaining the same temperature. The reaction was then allowed to warm to room temperature and stirred overnight. Upon completion, water (100 mL) and ethyl acetate (50 mL) were added. The organic phase was separated, and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate (Na_2SO_4), and concentrated under reduced pressure using a rotary evaporator. The resulting crude product was dissolved in 20 mL of ethyl acetate, and the precipitated solid was collected by filtration and washed with ethyl acetate (3 × 5 mL) to yield compound **3** as an off-white solid (595 mg, 1.81 mmol, 53% yield). The solid was dried with high vacuum for 8h.

The synthesis of 3-(1-naphthoyl)-1-(5-fluoropentyl)-1*H*-indol-6-yl acetate (4).

Compound **3** (500 mg, 1.52 mmol) was dissolved in anhydrous dimethylformamide (DMF, 10 mL) and cooled to 0 °C under a nitrogen atmosphere. Sodium hydride (73 mg, 1.82 mmol) was added, and the reaction mixture was stirred at 0 °C for 20 minutes. Subsequently, 1-bromo-5-fluoropentane (282 μL, 2.28 mmol) was added dropwise while maintaining the temperature. The reaction was then allowed to reach room temperature and stirred for an additional 2 hours. Upon completion, water (100 mL) and ethyl acetate (50 mL) were added for extraction. The organic phase was separated, and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate (Na_2SO_4), and concentrated under reduced pressure using a rotary evaporator. The crude product was purified by column chromatography using a gradient elution of hexane and ethyl acetate (from 5:1 to 3:1), yielding compound **4** as a white solid (285.2 mg, 0.68 mmol, 45% yield). The solid was dried with vacuum pump for 8h.

The synthesis of (1-(5-fluoropentyl)-6-hydroxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (5).

Compound **4** (285.2 mg, 0.68 mmol) was dissolved in methanol (3 mL) and treated with 1 N sodium hydroxide solution (3 mL). The reaction mixture was stirred at room temperature for 1 hour. Upon completion, the solvent was removed under reduced pressure, and the resulting resi-

due was acidified to pH 4 using 1 N hydrochloric acid. Water (50 mL) and ethyl acetate (50 mL) were then added for extraction. The organic phase was separated, and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous sodium sulfate (Na_2SO_4) and concentrated using a rotary evaporator. The crude product was purified by column chromatography using a hexane:ethyl acetate gradient (from 3:1 to 1:1), affording compound **5** as a yellow solid (234.6 mg, 0.63 mmol, 92% yield). The product was dried under high vacuum overnight.

The synthesis of (1-(5-fluoropentyl)-6-methoxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (7).

Compound **6** (30 mg, 0.3 mmol) was dissolved in DMF (3 mL), and 60% sodium hydride (4.8 mg) was added under stirring. Subsequently, 1-bromo-5-fluoropentane (18.5 μL) was introduced to the reaction mixture. Upon completion, the mixture was subjected to extraction with ethyl acetate and water. The organic phase was separated, dried over anhydrous sodium sulfate (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography to yield compound **7** (15.6 mg, 40% yield).

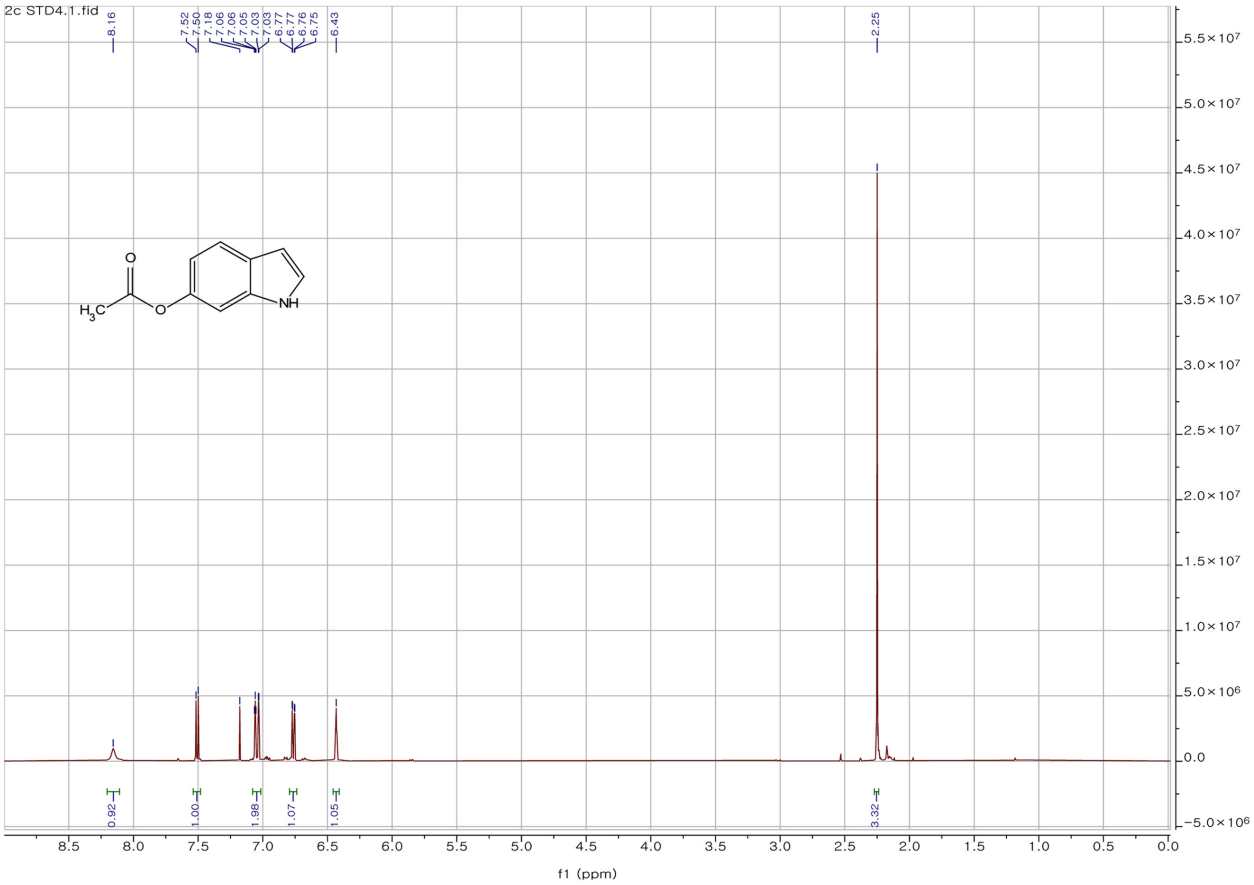


***Figure* S1.** ^{1}H-NMR of 1*H*-indol-6-yl acetate (**2**).

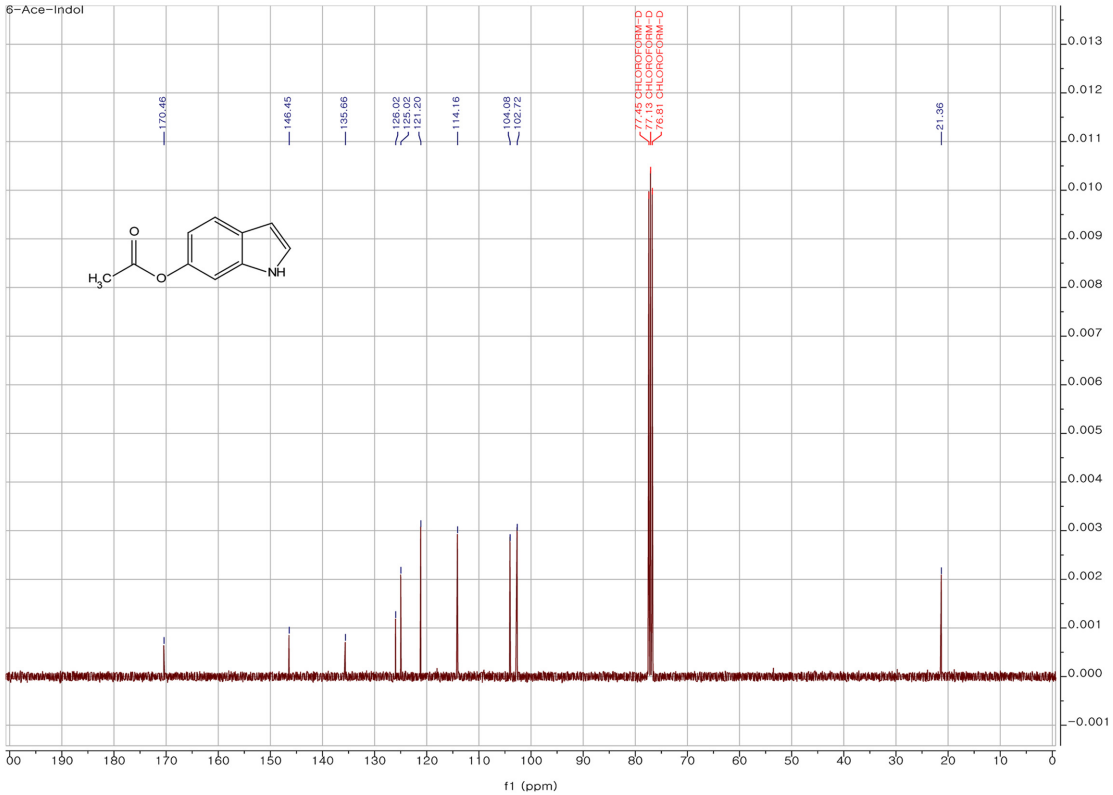


***Figure* S2.** ^{13}C-NMR of 1*H*-indol-6-yl acetate (**2**).

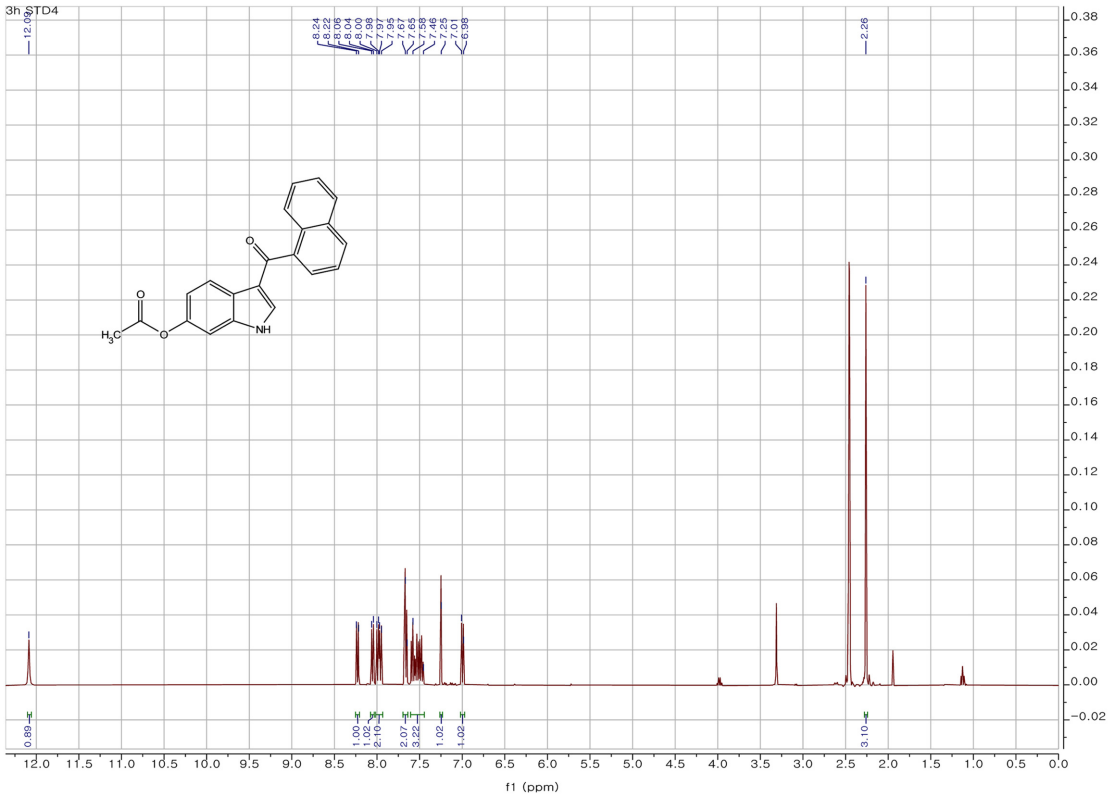


***Figure* S3.** ^{1}H-NMR of 3-(1-naphthoyl)-1*H*-indol-6-yl acetate (**3**).

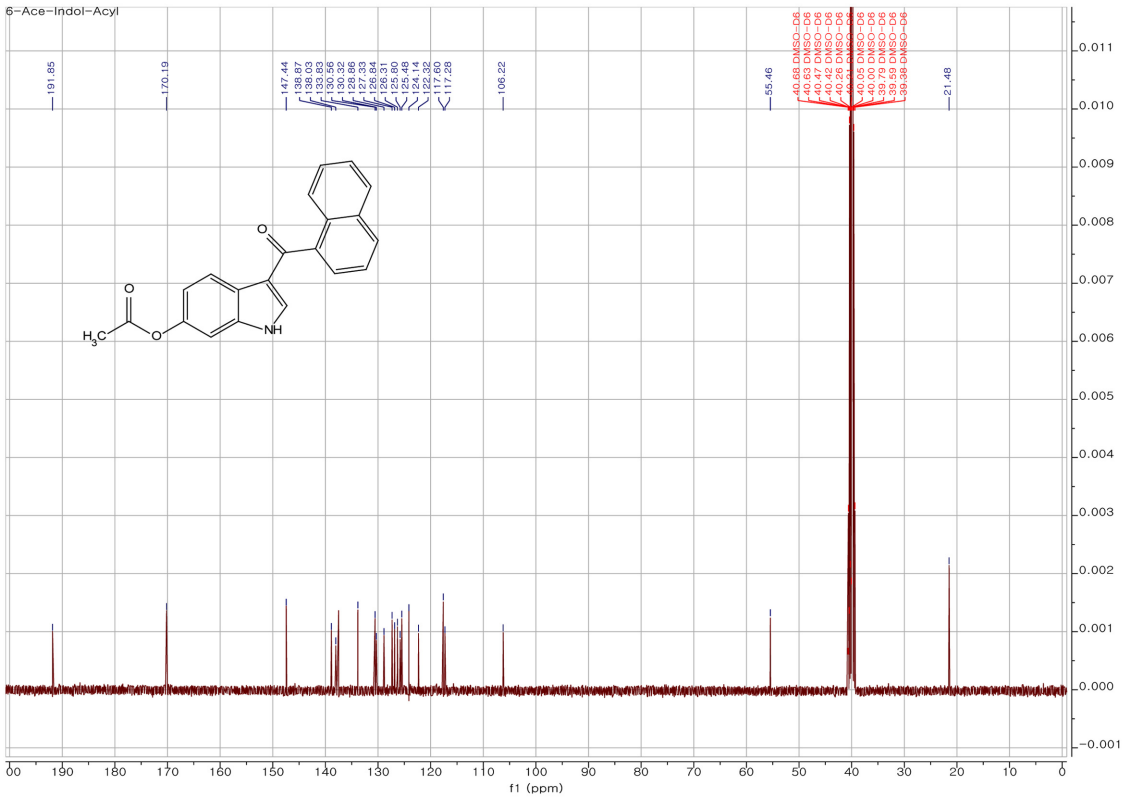


***Figure* S4.** ^{13}C-NMR of 3-(1-naphthoyl)-1*H*-indol-6-yl acetate (**3**).

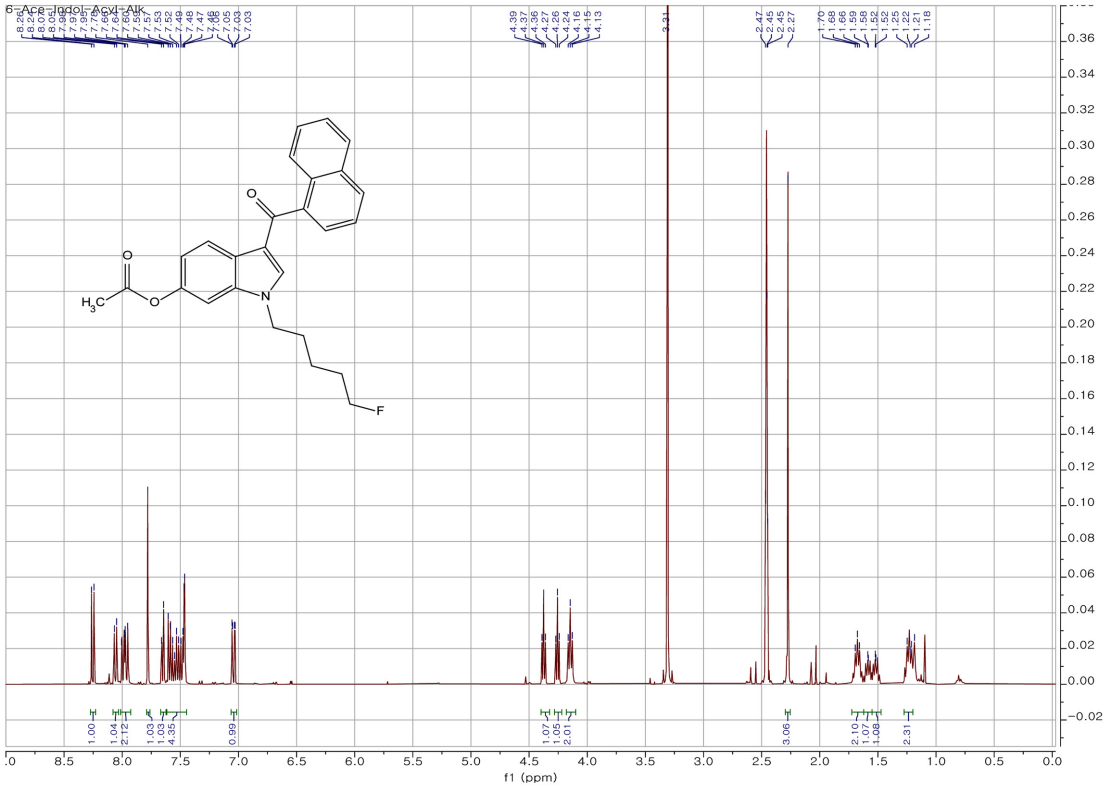


***Figure* S5.** ^{1}H-NMR of 3-(1-naphthoyl)-1-(5-fluoropentyl)-1*H*-indol-6-yl acetate (**4**).

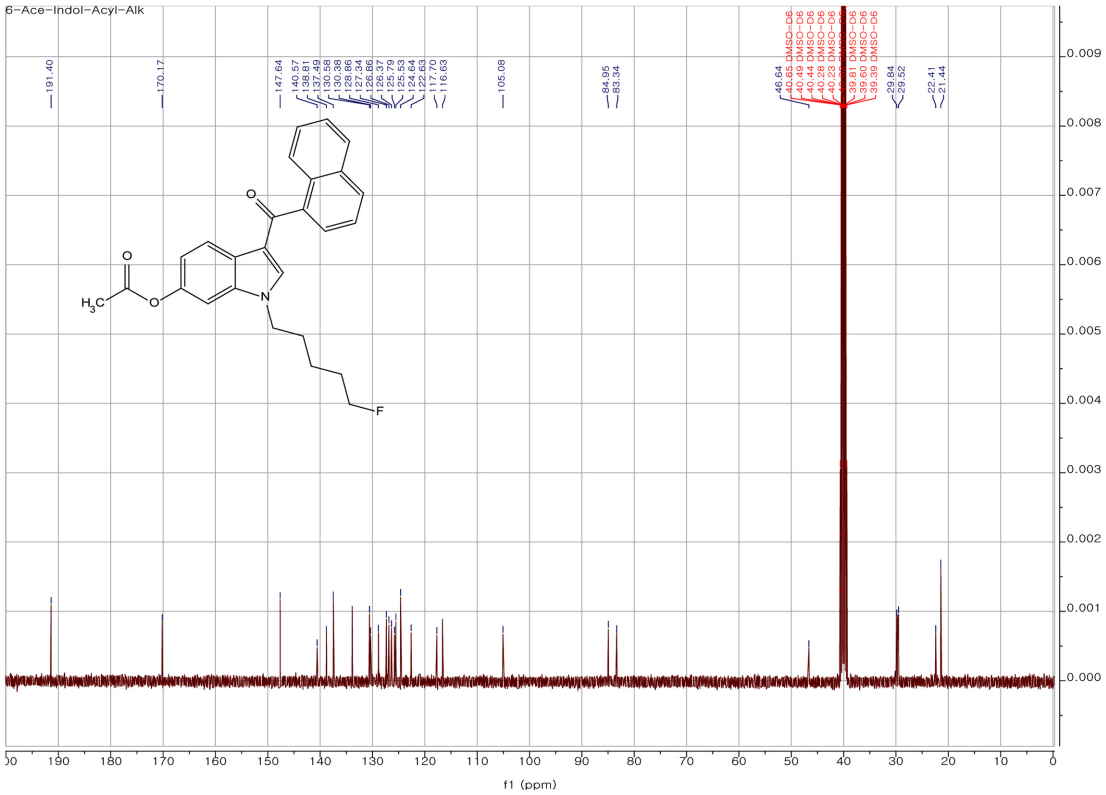


***Figure* S6.** ^{13}C-NMR of 3-(1-naphthoyl)-1-(5-fluoropentyl)-1*H*-indol-6-yl acetate (**4**).

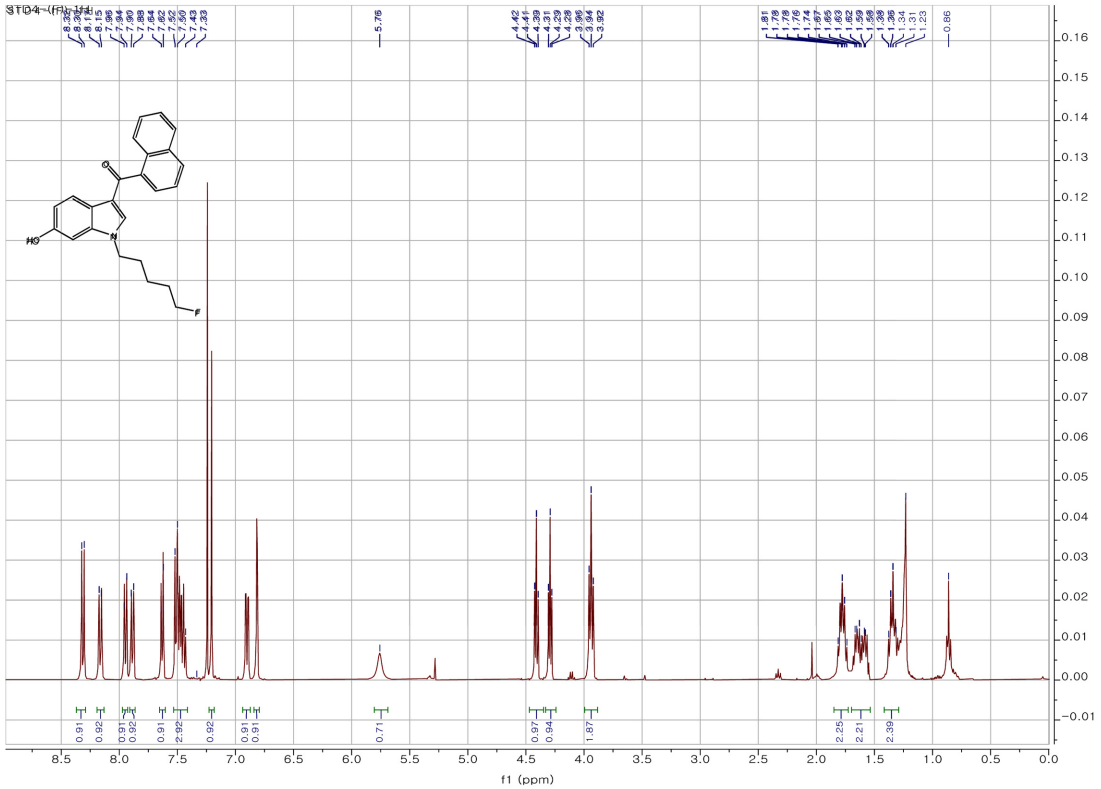
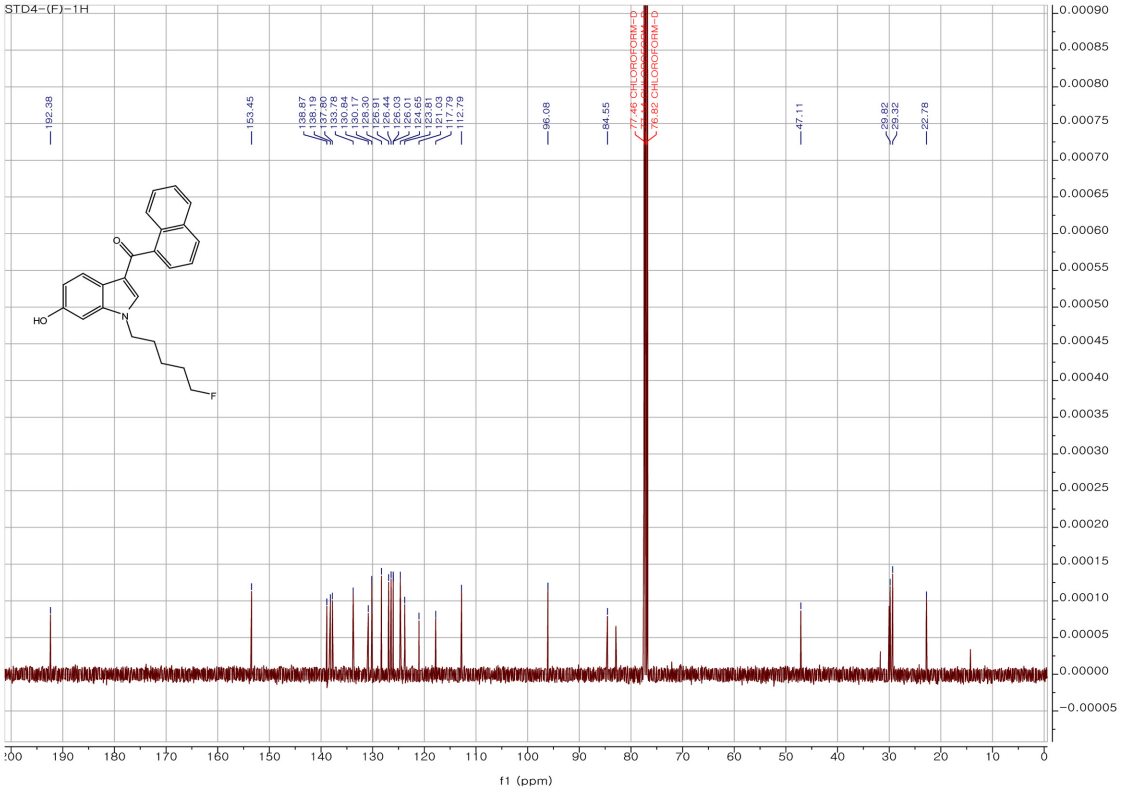


***Figure* S7.** ^{1}H-NMR of (1-(5-fluoropentyl)-6-hydroxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (**5**).



***Fiure* S8.** ^{13}C-NMR of (1-(5-fluoropentyl)-6-hydroxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (**5**).

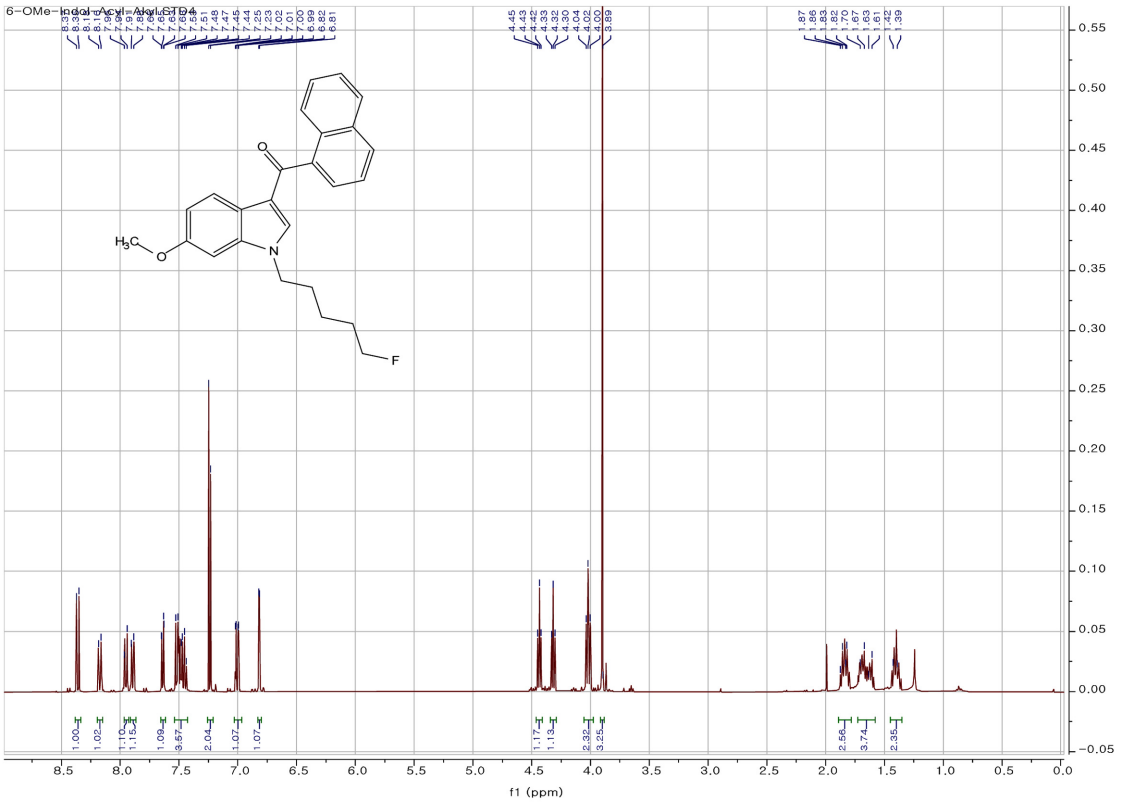


***Figure* S9.** ^{1}H NMR of (1-(5-fluoropentyl)-6-methoxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (**8**).

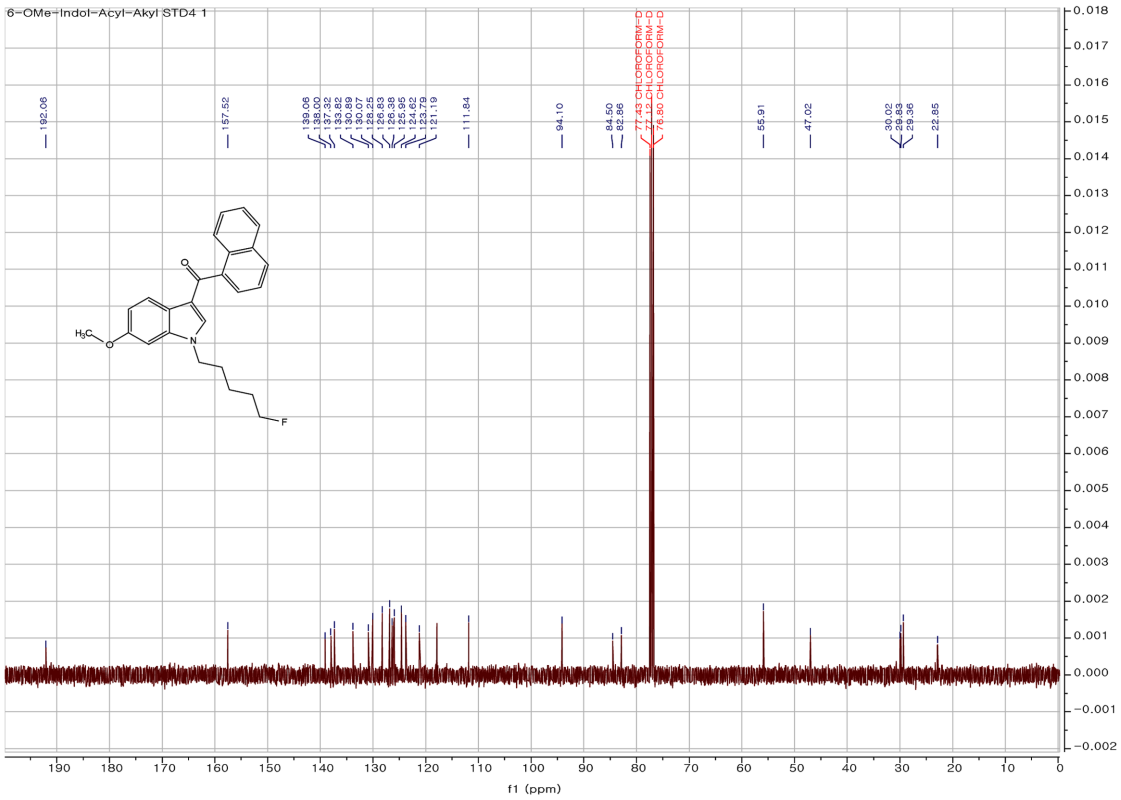


***Figure* S10.** ^{13}C NMR of (1-(5-fluoropentyl)-6-methoxy-1*H*-indol-3-yl)(naphthalen-1-yl)methanone (**8**).