Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Mechanistic Studies and Radiofluorination of Structurally Diverse Pharmaceuticals with Spirocyclic Iodonium(III) Ylides

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Reagents, solvents and chromatography: All commercial reagents were purchased from Sigma-Aldrich, Alfa Aesar, Fisher Scientific, Acros, Strem Chemicals, Oakwood Chemical, or Matrix Scientific and, unless otherwise stated, used as received. All solvents were of reagent or anhydrous grade quality and purchased from Sigma-Aldrich, Alfa Aesar, or Fisher Scientific. All deuterated solvents were purchased from Cambridge Isotopes. Analytical thin-layer chromatography (TLC) was performed on pre-coated glass-backed plates (EMD TLC Silica gel 60 F_{254}) and visualized using a UV lamp (254 nm), potassium permanganate, and/or iodine stain. Flash column chromatography was performed using a Biotage Isolera One system and preloaded Biotage Zip or refillable Snap silica gel columns. Silica gel for flash chromatography was high purity grade 40–63 μm pore size and purchased from Sigma-Aldrich. Yields refer to purified and spectroscopically pure compounds.

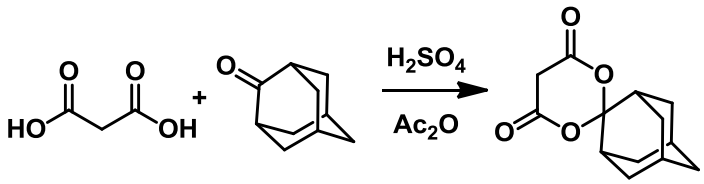
Spectroscopy: ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker 300 MHz or a Varian Unity/Inova 500 spectrometer, and resonances given in parts per million (ppm) relative residual solvent (^{19}F chemical shifts are uncorrected). Peak multiplicities are designated by the following abbreviations: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets; ddd, doublet of doublet of doublets; br, broad; and *J*, coupling constant in Hz. UV spectra were recorded on either a Hitachi U-1100 Spectrophotometer of a Spectronic Genesys 2 instrument.

Mass spectrometry: HRMS spectra were recorded on a Bruker microTOFII ESI LCMS using positive electrospray ionization (ESI^{+}).

Synthetic Procedures and Characterization Data

Auxiliary acids, aryl iodides, diacetoxyiodoarenes, and aryl fluorides were obtained from commercial sources, prepared as described previously[1] or herein.

Synthesis of adamantyl substituted auxiliary acid (SPIAd)

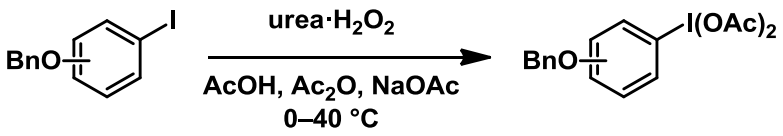


This procedure is based on a literature report.[2] A mixture of malonic acid (5.0 g, 48 mmol), acetic anhydride (4.8 mL), and conc. H_2SO_4 (24 µL) was heated with stirring to 60 ℃ for 15 min. The mixture was then cooled to room temperature, and 2-adamantanone (48 mmol), was added dropwise over 0.5–1 h. The mixture for stirred for an additional 1 h, prior to removal of volatiles by rotary evaporation. The residue was resolubilized in Et_2O, and washed three times with water. The organics were dried with $MgSO_4$, filtered and concentrated. The product was precipitated using Et_2O and hexanes, and cooling to -25 ℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.60 (s, 2H), 2.25–2.08 (m, 6H), 1.91 (s, 2H), 1.83–1.71 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.94, 109.56, 37.72, 36.77, 36.50, 33.51, 26.12 ppm. HRMS (ESI/[M-H]$^-$) calcd. for $C_{13}H_{15}O_4$: 235.0976, found 235.0979.

General procedure for synthesis of aryliodonium(III) ylides

To a solution of the auxiliary acid (0.25 mmol) in 10% $Na_2CO_{3(aq)}$ (w/v, 0.75 mL, 0.33 M solution) was added ethanol (1 mL) followed quickly by diacetoxyiodoarene (0.25 mmol). The reaction mixture was vigorously stirred at room temperature for 0.5–4 h, until full conversion of starting materials was determined by TLC. The reaction mixture was then diluted with water (~ 8 mL), and extracted with DCM (3 x 10 mL). The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated. To the residue was added ethyl acetate and hexanes to induce precipitation (at room temperature or -25 ℃). Solids were collected by filtration and purified by flash chromatography if necessary.

Synthesis of benzyloxyphenyliodonium ylides

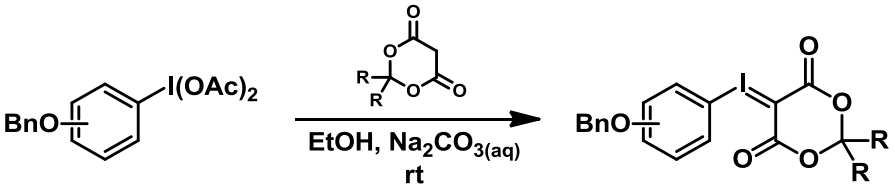


A solution of acetic acid (2.3 mL) and acetic anhydride (0.9 mL) was treated with urea ħydrogen peroxide adduct (1.36 g, 14.5 mmol) at room temperature. *Ortho-* or *para-*

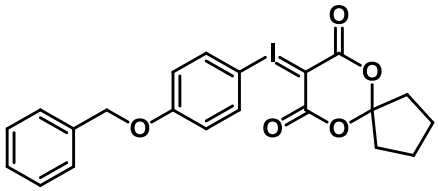
benzyloxyphenyliodide (1 g, 3.22 mmol) was added, and the resultant mixture cooled to 0 ℃. Anhydrous sodium acetate (0.53 g, 6.45 mmol) was then slowly added to the mixture. After completion of the addition, the mixture was heated to 40 ℃ for 2 h. The reaction mixture was cooled to room temperature, diluted with water and extracted three times with dichloromethane. The combined organic fractions were dried over sodium sulfate, filtered and concentrated. The residue was washed with a mixture of hexanes and ethyl ether and filtered to yield a colourless solid.

Para-benzyloxyphenyliododiacetate (2.42 g, 5.64 mmol, 88% yield) matched previously published spectroscopic data.[3]

Ortho-benzyloxyphenyliododiacetate (356 mg, 0.83 mmol, 26% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (dd, *J* = 1.4, 7.9 Hz, 1H), 7.56 (td, *J* = 1.4, 8.4 Hz, 1H), 7.44–7.33 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 5.29 (s, 2H), 1.97 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.8, 155.5, 137.9, 135.7, 134.5, 128.9, 128.4, 127.0, 123.2, 113.9, 113.5, 71.4, 20.5 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{17}H_{17}INaO_5$ 451.0018, found 451.0013.

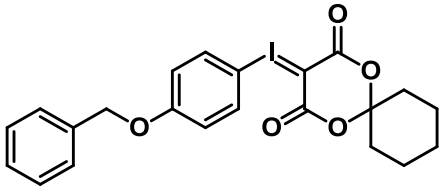


Benzyloxyphenyliodonium(III) ylides were prepared according to the general procedure described above.



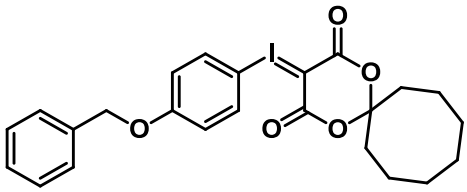
6,10-dioxaspiro[4.5]decane-7,9-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 9.0 Hz, 2H), 7.40–7.36 (m, 5H), 6.98 (d, *J* = 9.0 Hz, 2H), 5.09 (s, 2H), 2.14 (m, 4H), 1.78 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.4, 162.1, 138.4, 136.4, 129.0, 127.6, 118.6, 117.4, 114.2, 102.8, 70.6, 58.0, 37.5, 23.5 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{21}H_{19}INaO_5$ 501.0175, found 501.0172.



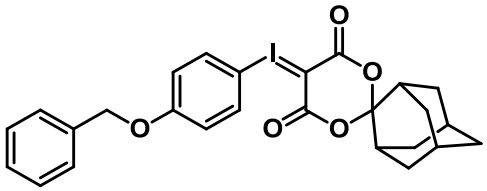
1,5-dioxaspiro[5.5]undecane-2,4-dione-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 76% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 9.1 Hz, 2H), 7.41–7.39 (m, 5H), 6.98 (d, *J* = 9.1 Hz, 2H), 5.09 (s, 2H), 1.97 (m, 4H), 1.67 (m, 4H), 1.46 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.5, 162.1, 136.4, 135.6, 129.0, 128.6, 127.6, 118.6, 105.3, 103.1, 70.6, 56.9, 34.8, 24.8, 22.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{21}INaO_5$ 515.0331, found 515.0330.



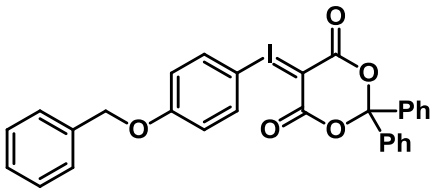
1,5-dioxaspiro[5.7]tridecane-2,4-dion-[4-benzyloxyphenyliodonium] ylide

Yellow solid, 18% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 9.0 Hz, 2H), 7.40–7.34 (m, 5H), 6.97 (d, *J* = 9.0 Hz, 2H), 5.09 (s, 2H), 2.17 (m, 4H), 1.66 (br s, 4H), 1.57 (br s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.4, 162.1, 136.4, 135.6, 129.0, 128.6, 127.6, 118.6, 109.0, 103.1, 70.6, 56.9, 33.8, 27.8, 24.6, 21.5 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{25}INaO_4$ 543.0644, found 543.0640.



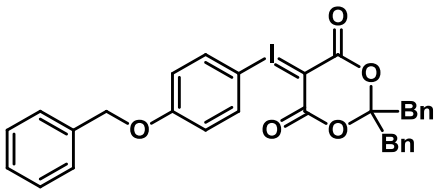
(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 86% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, *J* = 9.0 Hz, 2H), 7.40–7.34 (m, 5H), 6.97 (d, *J* = 9.0, 2H), 5.09 (s, 2H), 2.40 (br s, 2H), 2.17 (br s, 2H), 2.13 (br s, 2H), 1.84 (br s, 2H), 1.66 (br s, 4H), 1.62 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.5, 162.1, 136.3, 135.7, 128.9, 128.6, 127.6, 118.5, 107.6, 103.1, 70.6, 57.0, 37.3, 35.7, 33.9, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{26}H_{25}INaO_5$ 567.0644, found 567.0641.



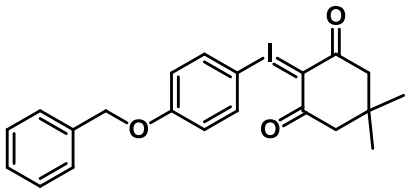
2,2-diphenyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 56% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63–7.59 (m, 4H), 7.40–7.34 (m, 8H), 7.30–7.27 (m, 5H), 6.82 (d, *J* = 9.0 Hz), 5.07 (s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 161.7, 140.6, 135.7, 134.5, 129.0, 128.9, 128.6, 128.6, 127.5, 126.0, 118.8, 104.9, 102.2, 70.6, 58.8 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{29}H_{21}INaO_5$ 599.0331, found 599.0334.



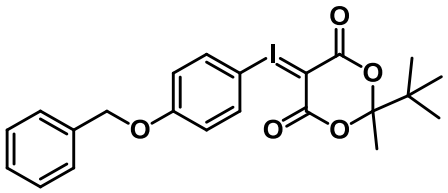
2,2-dibenzyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Pale yellow solid, 57% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63–7.59 (m, 4H), 7.40–7.34 (m, 8H), 7.30–7.27 (m, 5H), 6.82 (d, *J* = 9.0 Hz), 5.07 (s, 2H), 3.19 (s, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.9, 162.1, 136.3, 135.6, 134.4, 131.2, 128.9, 128.6, 128.3, 127.6, 127.1, 118.6, 106.1, 103.2, 70.6, 56.7, 44.0 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{31}H_{25}INaO_5$ 627.0644, found 627.0642.



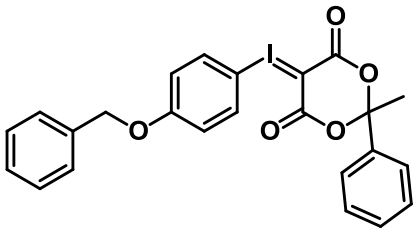
5,5-dimethylcyclohexane-1,3-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, *J* = 9.0 Hz, 2H), 7.38 (m, 5H), 6.92 (d, *J* = 9.0 Hz, 2H), 5.06 (s, 2H), 2.48 (s, 4H), 1.04 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.5, 161.6, 136.7, 135.8, 128.9, 128.6, 127.6, 118.3, 100.8, 95.4, 70.5, 50.9, 32.2, 28.3 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{21}H_{21}INaO_3$ 471.0433, found 471.0428.



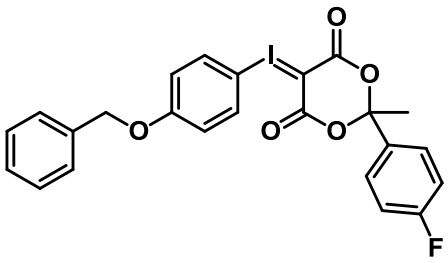
2-(*tert*-butyl)-2-methyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 86% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (d, *J* = 9.1 Hz, 2H), 7.39 (m, 5H), 6.98 (d, *J* = 9.1 Hz, 2H), 5.09 (s, 2H), 1.61 (s, 3H), 1.08 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.8, 162.1, 136.4, 135.6, 129.0, 128.6, 127.6, 118.6, 109.7, 103.2, 70.6, 56.9, 39.0, 24.7, 18.5 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{23}INaO_5$ 517.0488, found 517.0490.



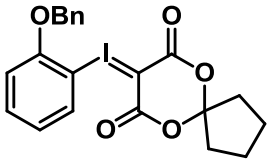
2-methyl-2-phenyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 93% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54–7.52 (m, 3H), 7.40–7.34 (m, 9H), 6.82 (d, *J* = 9.1 Hz, 2H), 5.07 (s, 2H), 11.87 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.7, 161.7, 142.0, 138.4, 135.7, 134.5, 129.0, 128.7, 128.6, 127.5, 125.1, 118.7, 104.9, 102.2, 70.6, 58.6, 29.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{19}INaO_5$ 537.0175, found 537.0180.



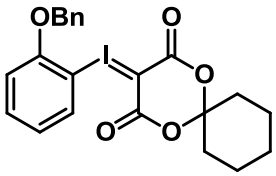
2-(4-fluorophenyl)-2-methyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 67% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52–7.39 (m, 9H), 6.95 (t, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 7.2 Hz), 5.08 (s, 2H), 1.85 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.5, 161.9, 138.0, 135.6, 135.1, 129.0, 128.8, 128.6, 127.6, 127.0 (d), 124.4, 118.6, 115.5 (d), 103.4 (d), 70.6, 58.9, 29.6 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): 109.2 (m) ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{18}FINaO_5$ 555.0081, found 555.0083.



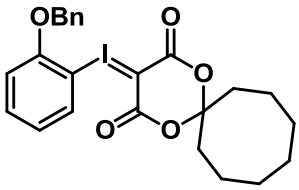
6,10-dioxaspiro[4.5]decane-7,9-dion-[2-benzyloxyphenyliodonium] ylide

Colourless solid, 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48–7.41 (m, 6H), 7.35 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.11 (t, *J* = 8.1 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 5.21 (s, 2H), 2.25 (m, 4H), 1.84 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 154.5, 134.8, 129.2, 129.1, 128.5, 127.9, 124.9, 114.4, 113.8, 102.2, 72.3, 48.2, 37.6, 23.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{21}H_{19}INaO_5$ 501.0175, found 501.0173.



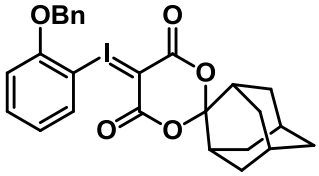
1,5-dioxaspiro[5.5]undecane-2,4-dione-[2-benzyloxyphenyliodonium] ylide

Colourless solid, 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48–7.41 (m, 6H), 7.34 (dd, *J* = 1.1, 8.1 Hz, 1H), 7.10 (t, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 5.21 (s, 2H), 2.08 (m, 4H), 1.73 (m, 4H), 1.49 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.7, 154.5, 134.8, 132.7, 129.2, 129.1, 128.7, 127.8, 124.9, 113.8, 105.5, 102.4 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{21}INaO_5$ 515.0331, found 515.0336.



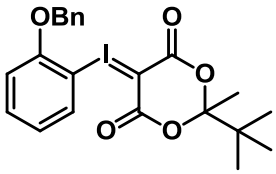
1,5-dioxaspiro[5.7]tridecane-2,4-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45–7.41 (m, 6H), 7.33 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 5.20 (s, 2H), 2.28 (m, 4H), 1.72 (br s, 4H), 1.60 (br s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 154.5, 134.8, 132.7, 129.2, 129.1, 128.6, 127.8, 124.9, 113.8, 109.2, 102.5, 72.3, 47.1, 33.9, 27.8, 24.6, 21.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{25}INaO_5$ 543.0644, found 543.0642.



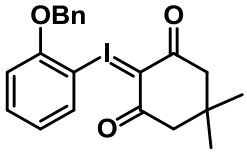
(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[2-benzyloxyphenyliodonium] ylide

Colourless solid, 76% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45–7.42 (m, 6H), 7.33 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.10 (t, *J* = 8.1 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 5.21 (s, 2H), 2.53 (br s, 2H), 2.23 (br s, 2H), 2.19 (br s, 2H), 1.88 (br s, 2H), 1.75 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 154.5, 134.9, 132.7, 129.2, 129.1, 128.7, 127.8, 124.9, 113.8, 107.8, 102.5, 72.3, 60.5, 37.3, 35.8, 33.9, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{26}H_{25}INaO_5$ 567.0644, found 567.0647.



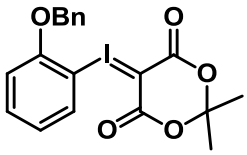
2-(*tert*-butyl)-2-methyl-1,3-dioxane-4,6-dion-[4-benzyloxyphenyliodonium] ylide

Colourless solid, 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (m, 6H), 7.32 (dd, *J* = 1.4, 8.1 Hz, 1H), 7.10 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 5.21 (s, 2H), 1.75 (s, 3H), 1.15 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.0, 154.6, 134.8, 132.7, 129.2, 129.1, 128.6, 127.9, 124.9, 113.8, 109.8, 102.6, 72.3, 47.2, 39.2, 24.8, 18.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{23}INaO_5$ 517.0488, found 517.0491.



5,5-dimethylcyclohexane-1,3-dion-[2-benzyloxyphenyliodonium] ylide

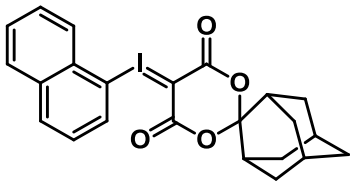
Colourless solid, 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44–7.36 (m, 6H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.02–6.97 (m, 2H), 5.21 (s, 2H), 2.58 (s, 4H), 1.16 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.5, 155.0, 135.1, 132.2, 129.8, 129.1, 128.9, 127.7, 124.5, 113.6, 101.0, 87.3, 72.0, 51.0, 32.2, 28.5 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{21}H_{21}INaO_3$ 471.0433, found 471.0430.



2,2-dimethyl-1,3-dioxane-4,6-dion-[2-benzyloxyphenyliodonium] ylide

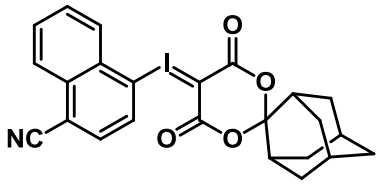
Colourless solid, 31% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45–7.33 (m, 7H), 7.10–7.00 (m, 2H), 5.18 (s, 2H), 1.77 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.8, 154.6, 134.9, 132.8, 129.1, 129.1, 128.8, 127.9, 124.9, 113.8, 104.8, 102.4, 72.2, 47.7, 26.1 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{19}H_{17}INaO_5$ 475.0018, found 475.0021.

Synthesis of (hetero)arene iodonium ylides



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[1-naphthyliodonium] ylide

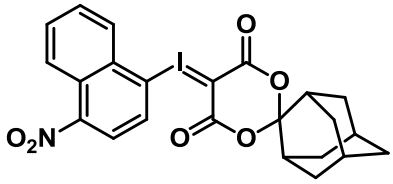
This compound was prepared according the general procedure described above from naphthyl-1-iododiacetate.[4]
Colourless solid, 55% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 7.5 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.1 Hz), 7.74 (t, *J* = 7.5 Hz, 1H) 7.63 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 2.34 (br s, 2H), 2.14–2.09 (overlapping br s, 4H), 1.82 (br s, 2H), 1.67 (br s, 4H), 1.62 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.4, 135.8, 135.2, 133.6, 131.5, 129.9, 129.2, 128.8, 128.2, 127.2, 116.3, 107.7, 54.6, 37.3, 35.7, 33.8, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{23}H_{21}INaO_4$ 511.0382, found 511.0387.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[4-cyanonaphthyl-1-iodonium] ylide

A solution of 4-iodo-1-naphthonitrile (56 mg, 0.2 mmol) in acetic acid (1.3 mL) was treated with mCPBA (49 mg, 0.22 mmol) at room temperature. The reaction was heated to 55 ℃ for 24 h following the procedure of Togo *et al.*[5] When TLC indicated no remaining starting material, water was added to the reaction mixture and the product extracted with dichloromethane and precipitated with diethyl ether and hexanes at -78 ℃. After filtration, the crude residue was immediately dissolved in ethanol and the general procedure for iodonium(III) ylide preparation was completed.

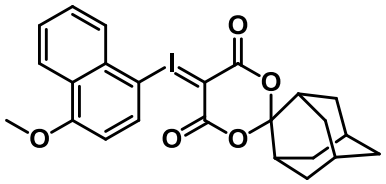
Colourless solid, 16% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (m, 3H), 7.87 (m, 3H), 2.35 (br s, 2H), 2.13–2.08 (overlapping br s, 4H), 1.83 (br s, 2H), 1.70–1.64 (overlapping br s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 133.7, 133.6, 133.0, 131.4, 131.1, 130.8, 129.6, 126.7, 121.2, 116.1, 115.6, 108.2, 54.6, 37.2, 35.8, 33.8, 26.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{20}INNaO_4$ 536.0335, found 536.0337.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[4-nitronaphthyl-1-iodonium] ylide

This compound was prepared from 1-iodo-4-methoxynaphthalene following a similar procedure to that used to prepare the cyano-substituted analogue described above, carrying out the oxidation at 55 ℃ for 72 h.

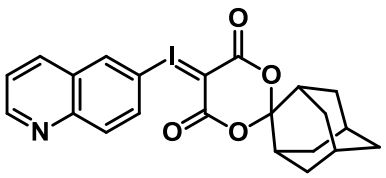
Colourless solid, 29% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46–8.42 (m, 1H), 8.36–8.31 (m, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.91–7.88 (m, 2H), 2.38 (br s, 2H), 2.16 (br s, 2H), 2.12 (br s, 2H), 1.85 (br s, 2H), 1.71 (br s, 4H), 1.67 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 150.4, 133.4, 132.2, 131.3, 131.2, 129.4, 126.3, 124.4, 123.7, 120.9, 108.2, 54.8, 37.2, 35.8, 33.8, 26.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{23}H_{20}INNaO_6$ 556.0233, found 556.0235.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[4-methoxynaphthyl-1-iodonium] ylide

A solution of 1-iodo-4-methoxynaphthalene (85 mg, 0.3 mmol) in acetone and acetic acid (4:1, 2.2 mL) was cooled to 0 ℃ and treated with a solution of DMDO in acetone. The reaction mixture was stirred at 0 ℃ for 1 h, then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then concentrated, diluted with ethanol (1.2 mL), treated with (1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dione (71 mg) in 10% aqueous sodium carbonate (0.9 mL) and the pH was adjusted to ~10 using 10% aqueous sodium carbonate. The reaction was then stirred for 2–4 h, and worked up and purified as described above.

Colourless solid, 25% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30–8.21 (m, 3H), 7.74 (dt, *J* = 1.3, 8.4 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 4.05 (s, 3H), 2.31 (br s, 2H), 2.13 (br s, 2H), 2.08 (br s, 2H), 1.80 (br s, 2H), 1.64 (overlapping br s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 156.5, 137.0, 134.8, 133.2, 131.9, 128.3, 126.8, 126.1, 122.6, 111.5, 105.7, 88.2, 55.8, 38.1, 36.7, 33.6, 26.1 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{24}H_{23}INaO_5$ 541.0488, found 541.0487.

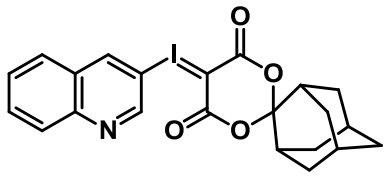


(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[quinolin-6-iodonium] ylide

Under a nitrogen atmosphere, 6-iodoquinoline (102 mg, 0.4 mmol) was dissolved in anhydrous acetonitrile (2.4 mL). A solution of trimethylsilylacetate (0.15 mL, 1 mmol) in acetonitrile (2.4 mL) was added, followed by SelectFluor (184 mg, 0.52 mmol). This mixture was stirred at room temperature for 3–8 h or until complete consumption of the aryl iodide was observed by TLC.

Volatiles were removed under reduced pressure, and the residue was taken up in dichloromethane and filtered to remove solids. The filtrate was washed with acetate buffer (0.5 M, 1:1 NaOAc:AcOH), dried over anhydrous sodium sulfate, filtered and concentrated. The crude aryliodonium(III) diacetate was then immediately subjected to the general procedure for iodonium(III) ylide formation, as described above.

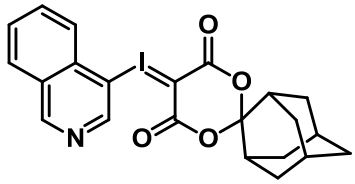
Colourless solid, 33% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.06 (dd, *J* = 1.7, 4.3 Hz, 1H), 8.43 (d, *J* = 1.9 Hz), 8.21 (dd, *J* = 1.7, 6.9 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 1H) 8.10 (dd, *J* = 1.9, 9.1 Hz, 1H), 7.56 (dd, *J* = 4.2, 8.3 Hz, 1H), 2.44 (br s, 2H), 2.19 (br s, 2H), 2.15 (br s, 2H), 1.86 (br s, 2H), 1.72 (br s, 4H), 1.68 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.7, 153.1, 148.7, 136.3, 134.0, 133.7, 131.9, 129.8, 122.8, 111.7, 107.9, 56.3, 37.2, 35.7, 33.9, 26.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{20}INNaO_4$ 512.0335, found 512.0332.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[quinolin-3-iodonium] ylide

This compound was prepared from 3-iodoquinoline following a similar procedure to that used to prepare 6-substituted isomer described above.

Colourless solid, 48% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.23 (d, *J* = 2.1 Hz, 1H), 8.82 (d, *J* = 1.6 Hz, 1H), 8.17 (d, *J* = 8.9 Hz, 1H), 7.92–7.86 (m, 2H), 7.70 (t, *J* = 7.1 Hz, 1H), 2.41 (br s, 2H), 2.17 (br s, 2H), 2.13 (br s, 2H), 1.85 (br s, 2H), 1.71 (br s, 4H), 1.59 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.7, 150.5, 148.3, 142.5, 132.6, 129.8, 129.7, 128.7, 128.5, 109.7, 107.9, 56.4, 37.2, 35.7, 33.8, 26.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{20}INNaO_4$ 512.0335, found 512.0332.

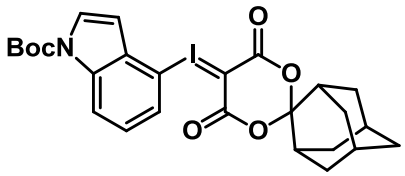


(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[isoquinolin-4-iodonium] ylide

This compound was prepared from 4-iodoisoquinoline following a similar procedure to that used to prepare the quinoline iodonium ylides described above.

Yellow solid, 12% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.41 (s, 1H), 9.24 (s, 1H), 8.37 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.83 (t, *J* = 7.2 Hz), 2.32 (br s, 2H), 2.14 (br s, 2H), 2.09 (br s, 2H), 1.82 (br s, 2H), 1.67 (br s, 4H), 1.63 (br s, 2H) ppm. ^{13}C

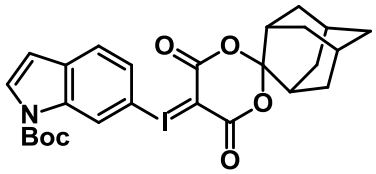
NMR (75 MHz, $CDCl_3$): δ 163.3, 157.14, 152.7, 150.7, 134.3, 132.2, 130.9, 130.0, 128.9, 128.5, 107.8, 39.4, 37.3, 35.7, 33.8, 26.6 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{20}INNaO_4$ 512.0335, found 512.0337.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[*N*-Boc-indol-4-iodonium] ylide

A solution of 1-Boc-4-iodoindole[6] (103 mg, 0.3 mmol) in acetone and acetic acid (4:1, 2.2 mL) was cooled to 0 ℃ and treated with a solution of DMDO in acetone. The reaction mixture was stirred at 0 ℃ for 1 h, then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then concentrated, diluted with ethanol (1.2 mL), treated with (1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dione (71 mg) in 10% aqueous sodium carbonate (0.9 mL) and the pH was adjusted to ~10 using 10% aqueous sodium carbonate. The reaction was then stirred for 2–4 h, and worked up and purified as described above.

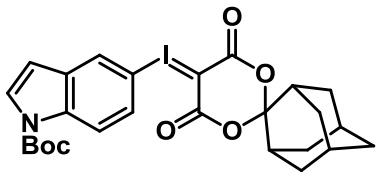
Colourless solid, 55% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 3.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 3.8 Hz, 1H), 2.34 (br s, 2H), 2.15 (br s, 2H), 2.11 (br s, 2H), 1.68 (s, 9H), 1.63 (br s, 2H), 1.58 (br s, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 149.0, 136.0, 132.6, 130.4, 128.8, 125.9, 119.9, 108.4, 107.5, 104.9, 85.4, 55.9, 37.3, 35.7, 33.8, 28.2, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{26}H_{28}INNaO_6$ 600.0859, found 600.0860.



(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[*N*-Boc-indol-5-iodonium] ylide

This compound was prepared from *N*-Boc-6-iodoindole[7] following a similar procedure to that used to prepare the indole iodonium ylide described above.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.71 (s, 1H), 7.68–7.72 (m, 2H), 7.58–7.62 (m, 1H), 6.63 (d, *J* = 3.2 Hz, 1H), 2.44 (br s, 2H), 2.20 (br s, 2H), 2.16 (br s, 2H), 1.84 (br s, 2H), 1.69 (overlapping br s, 6H), 1.21 (s, 9H) ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{26}H_{28}INNaO_6$ 600.0859, found 600.0963.



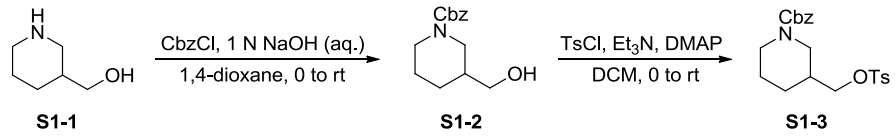
(1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dion-[*N*-Boc-indol-5-iodonium] ylide

This compound was prepared from *N*-Boc-5-iodoindole[8] following a similar procedure to that used to prepare the indole iodonium ylide described above.

Colourless solid, 14% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.9 Hz, 1H), 8.12 (d, *J* = 1.8 Hz, 1H), 7.76 (dd, *J* = 1.9, 8.9 Hz, 1H), 7.65 (d, *J* = 3.7 Hz, 1H), 2.37 (br s, 2H), 2.14 (br s, 2H), 2.10 (br s, 2H), 1.84 (br s, 2H), 1.80 (br s, 2H), 1.66 (br s, 4H), 1.64 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.0, 163.7, 133.2, 132.8, 129.9, 128.9, 128.4, 127.6, 118.6, 107.7, 107.0, 85.3, 56.8, 47.1, 35.6, 33.9, 28.2, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{26}H_{28}INNaO_6$ 600.0859, found 600.0863.

Syntheses and characterization of drug fragment precursors and ^{19}F-standards

1. filorexant

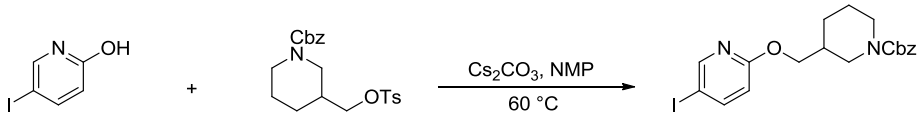


S1-1 **S1-2** **S1-3**

To a solution of piperidin-3-ylmethanol **S1-1** (1.2 g, 10.4 mmol) and 1 N NaOH (14.5 mL, 14.5 mmol) in 1,4-dioxane (14 mL) was added CbzCl (2.1 mL, 14.5 mmol) dropwise (using dropping funnel) at 0 °C. After stirring for 30 min at room temperature, the mixture was diluted with H_2O, acidified with 10% HCl to pH 1 and extracted with ethyl acetate (15 mL × 3). The organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified with flash column chromatography (Hexanes/EtOAc = 1/1) to afford benzyl 3-(hydroxymethyl) piperidine-1-carboxylate **S1-2** (2.37 g, yield 91 %) as a colorless oil.

To a solution of **S1-2** (2.37 g, 9.5 mmol), dimethylaminopyridine (58 mg, 0.48 mmol) and triethylamine (2.6 ml, 19.0 mmol) in dichloromethane (50 ml) at 0 °C was added *p*-toluenesulfonyl chloride (2.0 g, 10.5 mmol) and the reaction stirred for 18 hours at room temperature. The mixture was diluted with 100 ml of dichloromethane and washed saturated sodium bicarbonate (15 mL × 3), water (20 mL) and brine (50 mL). The organics were dried over sodium sulfate, filtered and concentrated under reduced pressure to afford **S1-3** (3.7 g, 97 %) as a white solid.

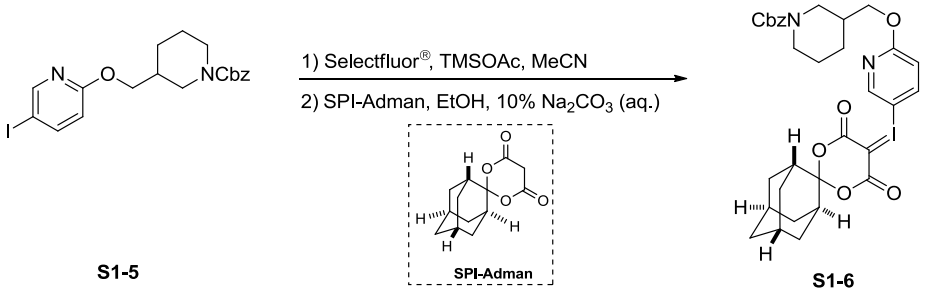
Characterized according to a literature procedure.[9]



S1-4 **S1-3** **S1-5**

In a 100 mL reaction vessel was charged the solution of piperidine **S1-3** (1.0 g, 2.48 mmol) in NMP (24 mL), 5-iodopyridin-2-ol **S1-4** (657 mg, 2.97 mmol), and Cs_2CO_3 (2.2 g, 6.65 mmol). The mixture was heated to 60 ℃ and stirred for 26 h. It was cooled to 15 °C before addition of water (100 mL) over 5 min, keeping the temperature below 25 °C. The solution was extracted with ethyl ether (25 mL × 3). The organic layer was washed with 10 wt % LiCl (20 mL × 2) and brine (20 mL × 2). The organics were dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford benzyl 3-(((5-iodopyridin-2-yl)oxy)methyl)piperidine-1-carboxylate **S1-5** (1.04 g, 2.3 mmol) as colorless oil.[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30-8.29 (m, 1H), 7.76 (dd, *J* = 8.8, 2.4

Hz, 1H), 7.34-7.26 (m, 5H), 6.55 (d, *J* = 8.2 Hz), 5.12 (s, 2H), 4.19-4.11 (m, 2H), 4.08-3.98 (m, 2H), 2.91 (br s, 1H), 2.71 (br s, 1H), 2.04-2.01 (m, 1H), 1.91-1.85 (m, 1H), 1.73-1.67 (m, 1H), 1.57-1.49 (m, 1H), 1.33-1.21 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 155.3, 152.5, 146.3, 136.9, 128.4, 127.8, 127.7, 113.5, 82.1, 68.0, 66.9, 47.2, 44.6, 35.6, 27.2; HRMS (m/z): $[M+Na]^+$ calculated for $C_{19}H_{21}IN_2NaO_3$ 475.0495, found 475.0496.

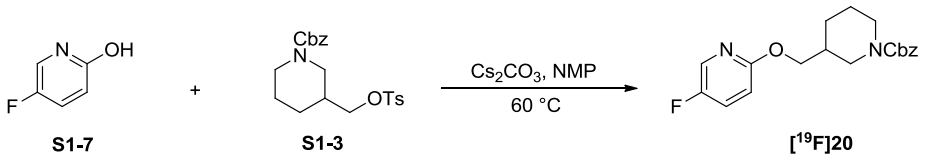


In a N_2 charged round-bottom flask, iodide **S1-5** (200 mg, 0.44 mmol) was dissolved in dry MeCN (2 mL). Trimethylsilyl acetate (175 mg, 1.33 mmol) and a solution of Selectfluor® (313 mg, 0.89 mmol) in dry MeCN (2 mL) were dropwisely added sequentially. The reaction mixture was allowed to stir at room temperature for 15 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (10 mL). The mixture was extracted with dichloromethane (5 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 5 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (10 mL) and dichloromethane (1.0 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The solvent was decanted away and the remaining solid was dried under vacuum for 4 h. The obtained diacetoxyiodoarene (220 mg, ~0.39 mmol) was used in the next step.

A solution of diacetoxyiodoarene (220 mg, ~0.39 mmol) in EtOH (6 mL) was added a solution of SPI-Adaman (91 mg, 0.39 mmol) in 10% Na_2CO_3 (3.0 mL), followed by addition of 10% Na_2CO_3 (3.0 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 4 h, then diluted with H_2O (15 mL), extracted with DCM (10 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To the residue was added ethyl acetate and pentane to induce precipitation and stored at -25 °C in freezer overnight. After decantation, the ylide **S1-6** was obtained as white solid (239 mg, yield over two steps 78%).

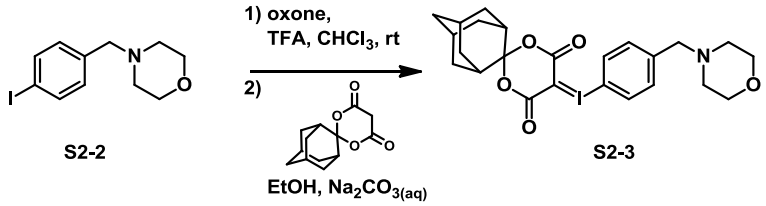
^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.61 (d, *J* = 2.2 Hz, 1H), 8.10 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.35 (s, 5H), 6.82 (br s, 1H), 5.35 (s, 2H), 4.35-4.05 (m, 3H), 3.95 (br s, 1H), 2.95 (t, *J* = 11.3 Hz, 1H), 2.76 (br s, 1H), 2.37 (s, 2H), 2.07 (d, *J* = 12.4 Hz, 6H), 1.82 (br s, 3H), 1.71 (d, *J* = 11.4 Hz, 6H), 1.58-1.44 (m, 1H), 1.42-1.25 (m, 1H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 165.4, 163.0, 155.1, 151.8,

143.7, 137.2, 128.4, 127.8, 127.5, 115.1, 107.0, 103.3, 68.9, 66.7, 56.3, 46.9, 44.4, 37.0, 35.5, 35.4, 33.7, 27.0, 26.6; HRMS (m/z): $[M+Na]^+$ calculated for $C_{32}H_{35}IN_2NaO_7$ 709.1387, found 709.1389.



In a 100 mL reaction vessel was charged the solution of piperidine **S1-3** (428 mg, 1.09 mmol) in NMP (10 mL), 5-fluoropyridin-2-ol **S1-7** (149 mg, 1.33 mmol), and Cs_2CO_3 (926 mg, 2.84 mmol). The mixture was heated to 60 ℃ and stirred for 26 h. It was cooled to 15 ℃ before addition of water (60 mL) over 5 min, keeping the temperature below 25 ℃. The solution was extracted with ethyl ether (15 mL × 3). The organic layer was washed with 10 wt % LiCl (10 mL × 2) and brine (10 mL × 2). The organics were dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford benzyl 3-(((5-iodopyridin-2-yl)oxy)methyl)piperidine-1-carboxylate **[^{19}F]20** (1.04 g, 2.3 mmol) as colorless oil.[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 3.2 Hz, 1H), 7.34-7.28 (m, 6H), 6.68 (d, *J* = 7.4 Hz, 1H), 5.12 (s, 2H), 4.26-4.13 (m, 2H), 4.10-3.99 (m, 2H), 2.90 (br s, 1H), 2.71 (br s, 1H), 2.10-1.95 (m, 1H), 1.94-1.82 (m, 1H), 1.77-1.64 (m, 1H), 1.60-1.43 (m, 1H), 1.41-1.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 156.9, 155.3, 153.7, 136.9, 132.9 (d, *J* = 27 Hz), 128.4, 127.8 (d, *J* = 11 Hz), 126.5 (d, *J* = 22 Hz), 111.6, 68.2, 66.9, 47.2, 44.6, 35.7, 27.3; HRMS (m/z): $[M+Na]^+$ calculated for $C_{19}H_{21}FN_2NaO_3$ 345.1614, found 345.1615.

2. mosapride

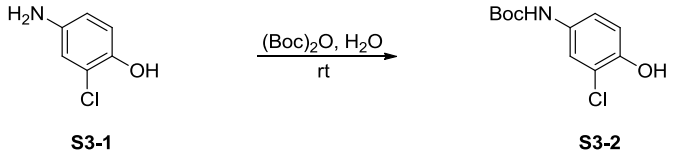


A solution of *N*-(*para*-iodobenzyl)morpholine **S2-2** (106 mg, 0.35 mmol; prepared by reductive amination of 4-iodobenzaldehyde[10]) in chloroform (350 μL) was treated with trifluoroacetic acid (1.1 mL, 14 mmol) followed by oxone monopersulfate (172 mg, 0.56 mmol). The heterogeneous mixture was stirred at room temperature for 4 h and then concentrated under reduced pressure. The residue was suspended in ethanol (1.4 mL) and treated with the adamantyl substituted auxiliary acid (83 mg, 0.35 mmol) and a solution of 10% sodium carbonate in water, which was used to adjust the pH to ~10 (~5 mL). The reaction was stirred at room temperature for 3 h and

then diluted with water and extracted with dichloromethane three times. The combined organic layers were dried with anhydrous sodium sulfate, filtered and concentrated. The product was purified by flash chromatography on silica (mobile phase gradient: 50 → 100% ethyl acetate/hexanes, then 0 → 20% methanol/ethyl acetate) to yield the product **S2-3** as a white solid (0.15 mmol, 44%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 3.69 (m, 4H), 3.50 (s, 2H), 2.41 (m, 6H), 2.16 (br s, 2H), 2.12 (br s, 2H), 1.84 (br s, 2H), 1.70 (br s, 4H), 1.66 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 137.6, 133.6, 132.5, 107.7, 67.0, 62.5, 56.0, 53.7, 39.4, 37.3, 35.7, 33.9, 33.6, 26.7 ppm. $[M+Na]^+$ calculated for $C_{24}H_{28}INNaO_5$ 560.0910, found 560.0908.

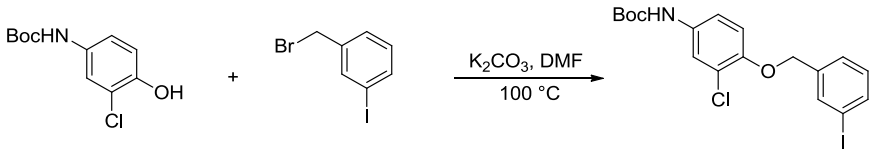
The ^{19}F-standard is a known compound that was also prepared by reductive amination.[11]

3. lapatinib



S3-1 **S3-2**

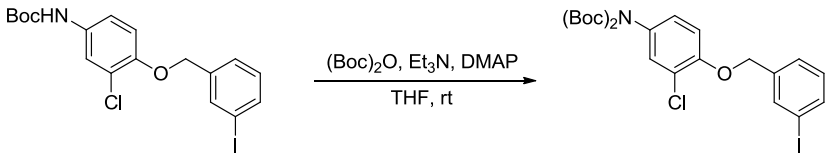
A well-stirred solution of 4-amino-2-chlorophenol **S3-1** (2.0 g, 14.0 mmol) in H_2O (16 mL) was treated with *t*-Boc_2O (3.36 g, 15.4 mmol). The mixture was stirred at room temperature for 22 h and then extracted with ethyl acetate (30 mL × 3), washed with brine, dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 5/1) to afford *tert*-butyl (3-chloro-4-hydroxyphenyl) carbamate **S3-2** (3.3 g, yield 97%) as white solid. Characterized according to a literature procedure.[12]



S3-2 **S3-3** **S3-4**

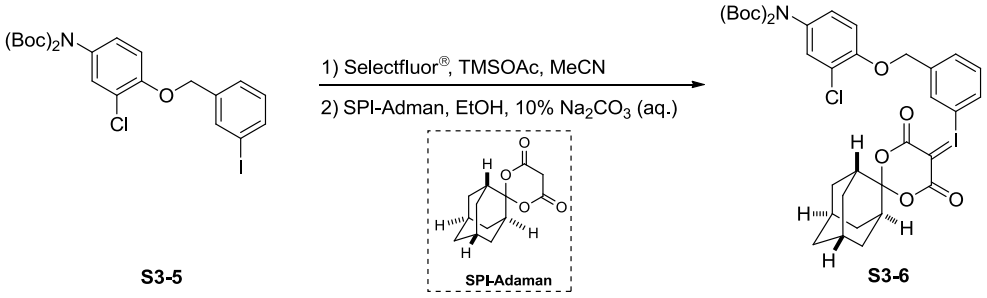
A solution of the *tert*-butyl (3-chloro-4-hydroxyphenyl) carbamate **S3-2** (347.2 mg, 1.43 mmol) in anhydrous DMF (5 mL) was added K_2CO_3 (984 mg, 7.12 mmol) and 1-(bromomethyl)-3-iodobenzene **S3-3** (444 mg, 1.5 mmol). The resulting solution was then stirred at 100 ℃ for 3 h under Ar. The reaction mixture was cooled down to ambient temperature and quenched with water (50 mL), and then extracted with ethyl ether (15 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 5/1) to

afford *tert*-butyl (3-chloro-4-((3-iodobenzyl)oxy)phenyl) carbamate **S3-4** (644 mg, yield 98%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 2.6 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.14-7.07 (m, 2H), 6.83 (d, *J* = 8.9 Hz, 1H), 6.41 (br s, 1H), 5.02 (s, 2H), 1.51 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 149.8, 138.9, 137.0, 136.0, 132.8, 130.3, 126.3. 123.8, 121.2, 118.1, 114.9, 94.4, 80.8, 70.5, 28.3; HRMS (m/z): $[M+Na]^+$ calculated for $C_{18}H_{19}ClINNaO_3$ 481.9996, found 481.9998.



S3-4 **S3-5**

A solution of the *tert*-butyl (3-chloro-4-((3-iodobenzyl)oxy) phenyl) carbamate **S3-4** (667 mg, 1.45 mmol) in anhydrous THF (5 mL) was added Et_3N (0.6 mL, 4.35 mmol), DMAP (88 mg, 0.73 mmol) and *t*-Boc_2O (633 mg, 2.9 mmol). The resulting solution was stirred at ambient temperature for 15 h under Ar. The reaction was quenched with water (50 mL), and then extracted with ethyl acetate (15 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 5/1) to afford iodide **S3-5** (666 mg, yield 82%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.21 (d, *J* = 2.6 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 6.99 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 5.09 (s, 2H), 1.43 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 151.7, 138.6, 137.1, 135.9, 133.0, 130.3, 130.1, 127.3, 126.2, 122.9, 133.5, 94.4, 83.0, 70.0, 27.9; HRMS (m/z): $[M+Na]^+$ calculated for $C_{23}H_{27}ClINNaO_5$ 582.0520, found 582.0521.



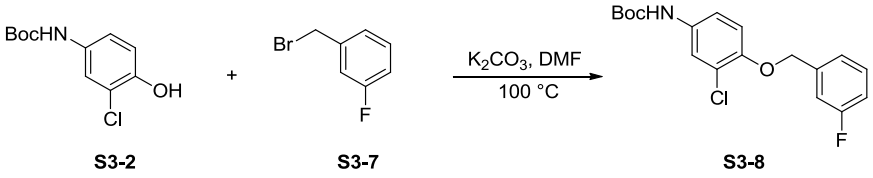
S3-5 **S3-6**

In a N_2 charged round-bottom flask, iodide **S3-5** (200 mg, 0.36 mmol) was dissolved in dry MeCN (2 mL). Trimethylsilyl acetate (141 mg, 1.1 mmol) and a solution of Selectfluor® (316 mg, 0.89 mmol) in dry MeCN (2 mL) were dropwisely added sequentially. The reaction mixture

was allowed to stir at room temperature for 15 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (10 mL). The mixture was extracted with dichloromethane (5 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 5 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (15 mL) and dichloromethane (1.5 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The solvent was decanted away and the remaining solid was dried under vacuum for 4 h. The obtained diacetoxyiodoarene (214 mg, ~0.32 mmol) was used in the next step.

A solution of diacetoxyiodoarene (214 mg, ~0.32 mmol) in EtOH (5 mL) was added a solution of SPI-Adaman (75 mg, 0.32 mmol) in 10% Na_2CO_3 (2.5 mL), followed by addition of 10% Na_2CO_3 (2.5 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 4 h, then diluted with H_2O (15 mL), extracted with DCM (10 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To the residue was added ethyl acetate and pentane to induce precipitation and stored at -25 °C in freezer overnight. After decantation, the ylide **S3-6** (209 mg, yield over two steps 74%) was obtained as white solid.

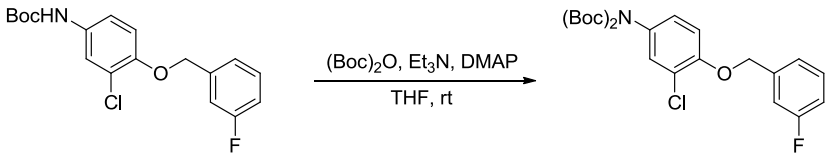
^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.94 (s, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.02 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 1H), 5.13 (s, 2H), 2.40 (s, 2H), 2.07 (d, *J* = 12.4 Hz, 4H), 1.82 (s, 2H), 1.69 (d, *J* = 11.4 Hz, 6H), 1.41 (s, 18H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 163.0, 152.8, 151.7, 140.0, 133.0, 132.3, 131.4, 131.1, 130.0, 128.3, 121.5, 116.7, 114.3, 105.5, 82.8, 69.7, 57.9, 36.9, 35.2, 33.6, 27.9, 26.4; HRMS (m/z): $[M+Na]^+$ calculated for $C_{36}H_{41}ClINNaO_9$ 816.1412, found 816.1417.



S3-2 **S3-7** **S3-8**

A solution of the *tert*-butyl (3-chloro-4-hydroxyphenyl) carbamate **S3-2** (449 mg, 1.84 mmol) in anhydrous DMF (7 mL) was added K_2CO_3 (1.27 g, 9.2 mmol) and 1-(bromomethyl)-3-fluorobenzene **S3-7** (365 mg, 1.9 mmol). The resulting solution was then stirred at 100 °C for 3 h under Ar. The reaction mixture was cooled down to ambient temperature and quenched with water (50 mL), and then extracted with ethyl ether (15 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 5/1) to afford *tert*-butyl (3-chloro-4-((3-fluorobenzyl)oxy) phenyl)carbamate **S3-8** (552 mg, yield 85%)

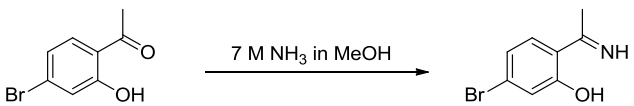
as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.5 Hz, 1H), 7.37-7.29 (m, 1H), 7.21-7.10 (m, 3H), 6.99 (td, *J* = 8.8, 2.0 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 1H), 6.45 (s, 1H), 5.08 (s, 2H), 1.51 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 152.8, 149.8, 139.1 (d, *J* = 7.2 Hz), 132.7, 130.1 (d, *J* = 8.2 Hz), 123.7, 122.4 (d, *J* = 2.8 Hz), 121.2, 118.1, 114.8 (t, *J* = 10.6 Hz), 113.9 (d, *J* = 22.2 Hz), 80.7, 70.5 (d, *J* = 2.2 Hz), 28.3 ; HRMS (m/z): $[M+Na]^+$ calculated for $C_{23}H_{27}ClFNNaO_5$ 474.1459, found 474.1460.



S3-8 **[^{19}F]24**

A solution of the *tert*-butyl (3-chloro-4-((3-fluorobenzyl)oxy) phenyl)carbamate **S3-8** (524 mg, 1.49 mmol) in anhydrous THF (5 mL) was added Et_3N (0.6 mL, 4.35 mmol), DMAP (176 mg, 1.49 mmol) and *t*-Boc_2O (654 mg, 3.0 mmol). The resulting solution was stirred at ambient temperature for 15 h under Ar. The reaction was quenched with water (50 mL), and then extracted with ethyl acetate (15 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 5/1) to afford compound **[^{19}F]24** (572 mg, yield 85%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.31 (m, 1H), 7.23-7.17 (m, 3H), 7.01 (td, *J* = 8.7, 2.5 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 1H), 5.15 (s, 2H), 1.43 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 153.1, 151.7, 138.8 (d, *J* = 7.2 Hz), 132.9, 130.1 (d, *J* = 7.7 Hz), 127.3, 122.9, 122.3 (d, *J* = 2.8 Hz), 114.9 (d, *J* = 21.2 Hz), 113.9 (d, *J* = 22.2 Hz), 113.5, 82.9, 70.1 (d, *J* = 1.7 Hz), 27.9; HRMS (m/z): $[M+Na]^+$ calculated for $C_{18}H_{19}ClFNNaO_3$ 374.0935, found 374.0936.

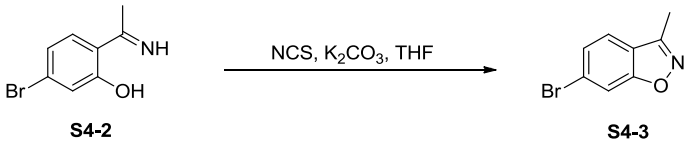
4. risperidone



S4-1 **S4-2**

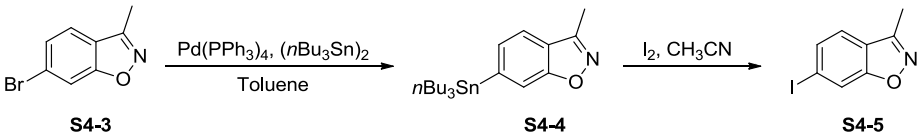
1-(4-bromo-2-hydroxyphenyl) ethan-1-one **S4-1** (1.02 g, 4.7 mmol) in 7 M ammonia in MeOH (3.5 ml, 23.6 mmol) was stirred at ambient temperature for 2 h to give a yellow slurry. The slurry

was filtered and the cake was dried to afford 5-bromo-2-(1-iminoethyl) phenol **S4-2** (1.0 g, yield 99%) as bright yellow solid, which was used in the next step without further purification.



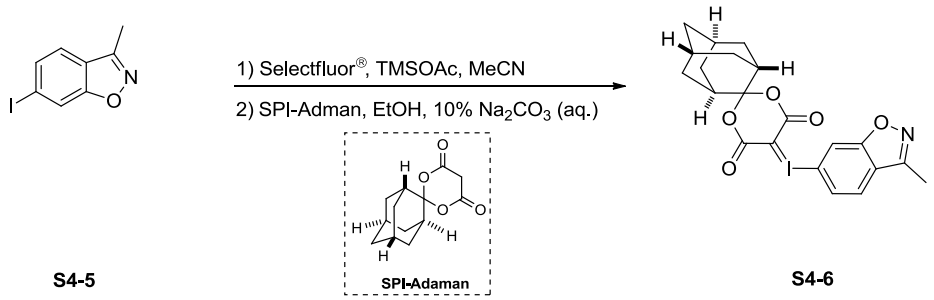
S4-2 **S4-3**

A mixture of hydroxy imine **S4-2** (1.0 g, 4.67 mmol), NCS (935 mg, 7 mmol) and K_2CO_3 (1.29 g, 9.34 mmol) in THF (15 mL) was stirred at ambient temperature for 12 h. Ethyl acetate (20 mL) and water (15 mL) was added to the reaction mixture and the organic layer was separated, dried over $MgSO_4$, and concentrated in vacuum. The crude product was purified by flash chromatography (Hexanes/EtOAc = 5/1) to afford 6-bromo-3-methylbenzo[*d*]isoxazole **S4-3** (570 mg, yield 58%) as yellow oil. Characterized according to a literature procedure.[13]



S4-3 **S4-4** **S4-5**

A solution of **S4-3** (300 mg, 1.42 mmol), hexabutylditin (1.64 g, 2.83 mmol) and $Pd(PPh_3)_4$ (164 mg, 0.15 mmol) in toluene (7 ml) was refluxed for 2 days. The solvent was evaporated and the residue purified by column chromatography (Hexanes/EtOAc = 10/1) to give **S4-4** as a yellow oil (270 mg), which was dissolved in CH_3CN (6 mL). The round-bottomed flask was shielded with tin foil papers. To this mixture was added iodine (324 mg, 1.26 mmol). The mixture was stirred at ambient temperature for 3 hours, then quenched with saturated $Na_2S_2O_3$ (5 mL), water (5 mL), and extracted with ethyl acetate (10 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 6/1) to afford compound **S4-5** (160 mg, yield over two steps 43%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95-7.94 (m, 1H), 7.60 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.35 (dd, *J* = 8.3, 0.6 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 155.0, 132.4, 126.9, 122.2, 119.3, 95.7, 9.9; HRMS (m/z): $[M+Na]^+$ calculated for C_8H_6INNaO 281.9392, found 281.9395.

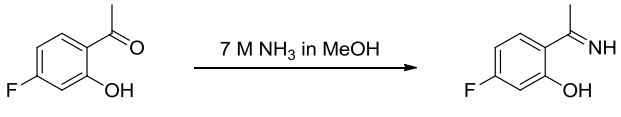


S4-5 **S4-6**

In a N_2 charged round-bottom flask, iodide **S4-5** (200 mg, 0.77 mmol) was dissolved in dry MeCN (5 mL). Trimethylsilyl acetate (307 mg, 2.32 mmol) and Selectfluor® (545 mg, 1.54 mmol) were added sequentially. The reaction mixture was allowed to stir at room temperature for 15 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (10 mL). The mixture was extracted with dichloromethane (5 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 5 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (10 mL) and dichloromethane (1.0 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The solvent was decanted away and the remaining solid was dried under vacuum for 4 h. The obtained diacetoxyiodoarene (97 mg, ~0.26 mmol) was used in the next step.

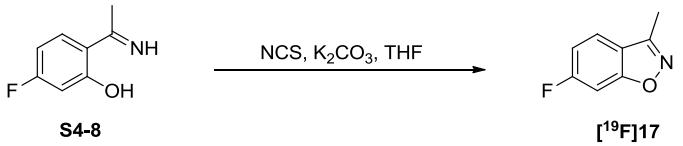
A solution of diacetoxyiodoarene (97 mg, ~0.26 mmol) in EtOH (2 mL) was added a solution of SPI-Adaman (42 mg, 0.18 mmol) in 10% Na_2CO_3 (1.0 mL), followed by addition of 10% Na_2CO_3 (1.5 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 4 h, then diluted with H_2O (15 mL), extracted with DCM (10 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To the residue was added ethyl acetate and pentane to induce precipitation and stored at -25 °C in freezer overnight. After decantation, the ylide **S4-6** (74 mg, yield over two steps 19%) was obtained as white solid.

^{1}H NMR (300 MHz, DMSO) δ 8.14 (s, 1H), 7.93 (d, J = 8.6 Hz, 1H), 7.68 (d, J = 8.2 Hz, 1H), 2.53 (s, 3H), 2.31 (s, 2H), 1.90 (d, J = 13.1 Hz, 4H), 1.76 (s, 2H), 1.61 (d, J = 10.8 Hz, 6H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 163.0, 162.1, 156.1, 126.9, 124.9, 124.1, 118.3, 114.4, 105.7, 58.7, 36.9, 35.3, 33.6, 26.4, 10.0. HRMS (m/z): $[M+Na]^+$ calculated for $C_{21}H_{20}INNaO_5$ 516.0248, found 516.0289.



S4-7 **S4-8**

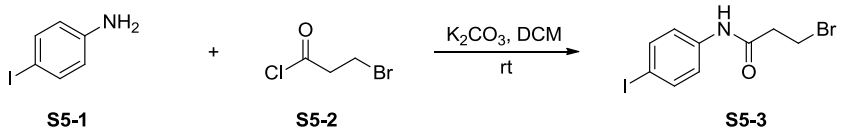
1-(4-fluoro-2-hydroxyphenyl) ethan-1-one **S4-7** (1.0 g, 6.49 mmol) in 7 M ammonia in MeOH (4.6 ml, 32.4 mmol) was stirred at ambient temperature for 2 h to give a yellow slurry. The slurry was filtered and the cake was dried to afford 5-fluoro-2-(1-iminoethyl) phenol **S4-8** (466 mg, yield 47%) as bright yellow solid, which was used in the next step without further purification.



S4-8 **[^{19}F]17**

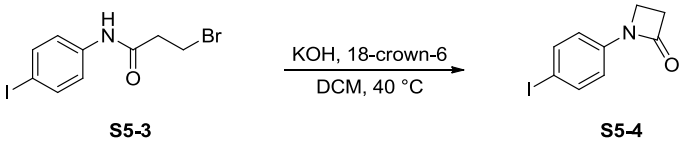
A mixture of hydroxy imine **S4-8** (466 mg, 3.04 mmol), NCS (607 mg, 4.55 mmol) and K_2CO_3 (837 mg, 6.06 mmol) in THF (9 mL) was stirred at ambient temperature for 12 h. Ethyl acetate (20 mL) and water (15 mL) was added to the reaction mixture and the organic layer was separated, dried over $MgSO_4$, and concentrated in vacuum. The crude product was purified by flash chromatography (Hexanes/EtOAc = 6/1) to afford 6-fluoro-3-methylbenzo[*d*]isoxazole **[^{19}F]17** (300 mg, yield 66%) as yellow solid. Characterized according to a literature procedure.[14] HRMS (m/z): $[M+Na]^+$ calculated for C_8H_6FNNaO 152.0512, found 152.0514.

5. ezetimibe



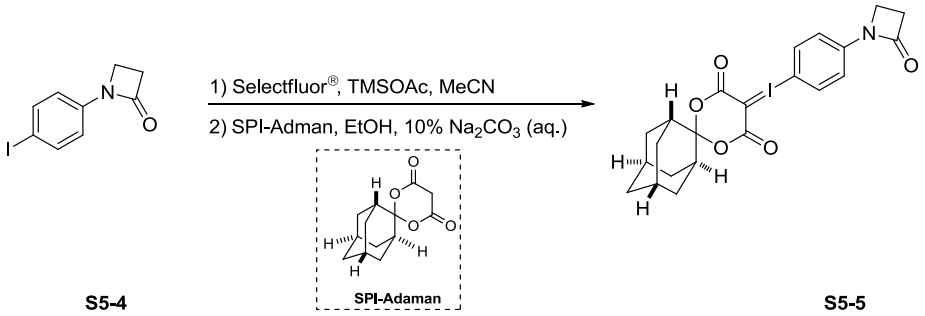
S5-1 **S5-2** **S5-3**

A mixture of 3-bromopropionyl chloride **S5-2** (0.46 mL, 4.57 mmol) in dichloromethane (5 mL) was added dropwise to a mixture of 4-iodoaniline **S5-1** (1.0 g, 4.57 mmol) and K_2CO_3 (1.6 g, 11.4 mmol) in dichloromethane (15 mL) and the reaction was stirred for 18 hours. The mixture was quenched with water (50 mL) slowly. The organic layer was separated and washed twice with water, dried with $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 3/1) to afford 3-bromo-N-(4-iodophenyl) propanamide **S5-3** (1.54 g, yield 95%) as white solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 10.14 (s, 1H), 7.63 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 3.71 (t, J = 6.3 Hz, 2H), 2.93 (t, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 168.8, 139.2, 137.8, 121.7, 87.2, 39.5, 29.5; HRMS (m/z): $[M+Na]^+$ calculated for $C_9H_9BrINNaO$ 375.8810, found 375.8814.



S5-3 **S5-4**

To a solution of 3-bromo-N-(4-iodophenyl) propanamide **S5-3** (1.0 g, 2.82 mmol) in DCM (7.0 mL) were added KOH (174 mg, 3.1 mmol) and 18-crown-6 (820 mg, 3.1 mmol). The reaction mixture was stirred at 40 °C overnight, then quenched with NH_4Cl (aq., 20 mL) and extracted with ethyl acetate (30 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (Hexanes/EtOAc = 1/1, then EtOAc/MeOH = 50:1) to afford lactam **S5-4** (352 mg, yield 46%) as white solid. ^{1}H NMR (300 MHz, d_6-DMSO) δ 7.66 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 3.58 (t, J = 4.4 Hz, 2H), 3.05 (t, J = 4.5 Hz, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 165.2, 138.6, 138.2, 118.5, 87.1, 38.4, 36.5; HRMS (m/z): $[M+Na]^+$ calculated for C_9H_8INNaO 295.9548, found 295.9549.

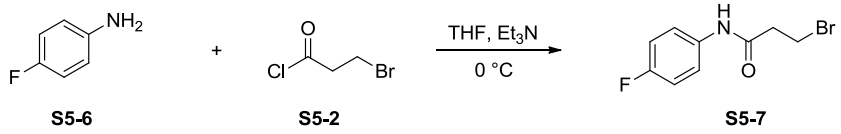


S5-4 **S5-5**

In a N_2 charged round-bottom flask, iodide **S5-4** (201 mg, 0.74 mmol) was dissolved in dry MeCN (4 mL). Trimethylsilyl acetate (292 mg, 2.21 mmol) and a solution of Selectfluor® (652 mg, 1.84 mmol) in dry MeCN (6 mL) were dropwisely added sequentially. The reaction mixture was allowed to stir at room temperature for 18 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (10 mL). The mixture was extracted with dichloromethane (5 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 5 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (15 mL) and dichloromethane (1.5 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The solvent was decanted away and the remaining solid was dried under vacuum for 4 h. The obtained diacetoxyiodoarene (260 mg, ~0.66 mmol) was used in the next step.

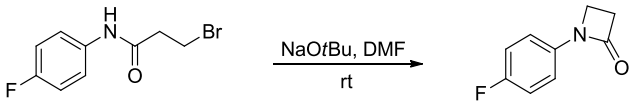
A solution of diacetoxyiodoarene (260 mg, ~0.66 mmol) in EtOH (5 mL) was added a solution of SPI-Adaman (157 mg, 0.66 mmol) in 10% Na_2CO_3 (5 mL), followed by addition of 10% Na_2CO_3 (3 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 5 h, then diluted with H_2O (30 mL), extracted with DCM (10 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To the residue was added ethyl acetate and pentane (v/ v = 1/ 1, 7 mL) to induce precipitation and stored at -25 °C for 1 h. After decantation, the crude compound was dispersed in a vial (25 mL) with ethyl acetate and pentane (v/ v = 1/ 1, 7 mL). The mixture was stirred for 5 min and allowed the solid to settle. The supernatant was decanted and this process was repeated for ten more times. After decantation and dryness using a vacuum pump, the ylide **S5-5** (153 mg, yield over two steps 41%) was obtained as white solid.

^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.82 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 3.65 (t, *J* = 4.7 Hz, 2H), 3.15 (t, *J* = 4.7 Hz, 2H), 2.37 (s, 2H), 2.07 (d, *J* = 12.3 Hz, 4H), 1.83 (s, 2H), 1.70 (d, *J* = 12.5 Hz, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 164.8, 163.0, 141.5, 134.7, 118.7, 106.9, 106.1, 56.3, 38.4, 37.0, 36.7, 35.6, 33.7, 26.6; HRMS (m/z): $[M+Na]^+$ calculated for $C_{22}H_{22}INNaO_5$ 530.0440, found 530.0443.



S5-6 **S5-2** **S5-7**

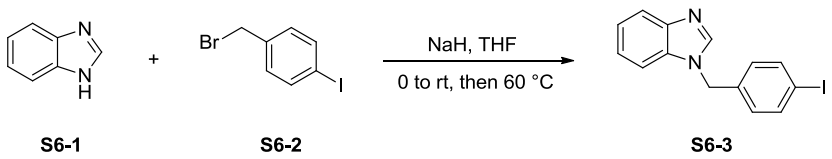
3-bromo-N-(4-fluorophenyl) propanamide **S5-7** was synthesized according to a literature procedure.[15]



S5-7 **[^{19}F]22**

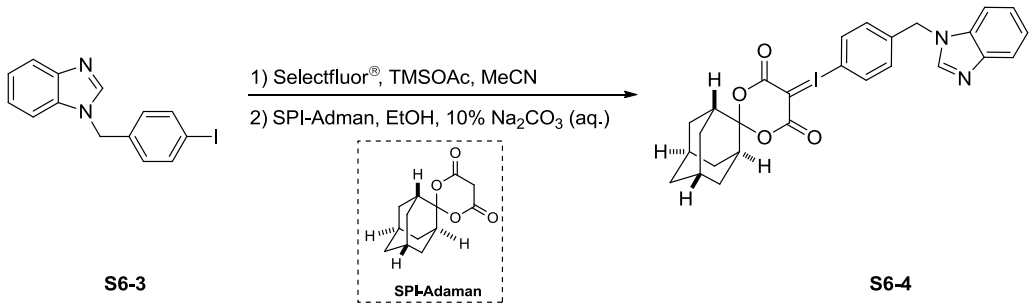
1-(4-fluorophenyl)azetidin-2-one **[^{19}F]22** was synthesized according to a literature procedure.[16] HRMS (m/z): $[M+Na]^+$ calculated for C_9H_8FNNaO 188.0488, found 188.0490.

6. astemizole



S6-1 S6-2 S6-3

NaH (washed with hexanes for five times to remove mineral oil and dried in vacuo for 3 h, 55 mg, 2.3 mmol)) was added in portions to a solution of benzimidazole **S6-1** (180 mg, 1.53 mmol) in dry THF under argon atmosphere at 0 ℃. The solution was stirred at rt for 3 h. At 0 ℃ 1-(bromomethyl)-4-iodobenzene **S6-2** (500 mg, 1.68 mmol) was added carefully and the reaction mixture was heated at 60 ℃ for 15 h. The reaction was quenched with H_2O (15 mL) and extracted with EtOAc (15 mL × 3). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by flash chromatography (Hexanes/EtOAc = 1/1 to 0/1, then EtOAc/MeOH = 50:1) to afford 1-(4-iodobenzyl)-1*H*-benzo[*d*]imidazole **S6-3** (301 mg, yield 59%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.84 (d, *J* = 7.4 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.31-7.24 (m, 3H), 6.92 (d, *J* = 8.3 Hz, 2H), 5.32 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 143.0, 138.2, 135.0, 133.6, 128.9, 123.4, 122.6, 120.4, 110.0, 93.8, 48.4; HRMS (m/z): $[M+Na]^+$ calculated for $C_{14}H_{11}IN_2Na$ 356.9865, found 356.9867.



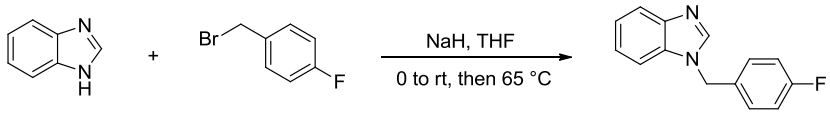
S6-3 SPI-Adaman S6-4

In a N_2 charged round-bottom flask, iodide **S6-3** (200 mg, 0.6 mmol) was dissolved in dry MeCN (2 mL). Trimethylsilyl acetate (238 mg, 1.8 mmol) and a solution of Selectfluor® (531 mg, 1.5 mmol) in dry MeCN (5 mL) were dropwisely added sequentially. The reaction mixture was allowed to stir at room temperature for 18 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (10 mL). The mixture was extracted with dichloromethane (10 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 5 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (10 mL) and dichloromethane (1.0 mL) were added

to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The mixture was stored at -20 °C in freezer for 1 h, and the solvent was decanted away. This process was repeated once more. The remaining solid was dried under vacuum for 2 h. The obtained diacetoxyiodoarene (200 mg, ~0.44 mmol) was used in the next step.

A solution of diacetoxyiodoarene (200 mg, ~0.44 mmol) in EtOH (4 mL) was added a solution of SPI-Adaman (105 mg, 0.44 mmol) in 10% Na_2CO_3 (3.5 mL), followed by addition of 10% Na_2CO_3 (3.5 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 3 h, then diluted with H_2O (25 mL), extracted with DCM (20 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To resulting solid was added ethyl acetate (6 mL), sonicated, allowed to settle and decanted. This process was repeated for three more times. After dryness using a vacuum pump, the ylide **S6-4** (189 mg, yield over two steps 55%) was obtained as white solid.

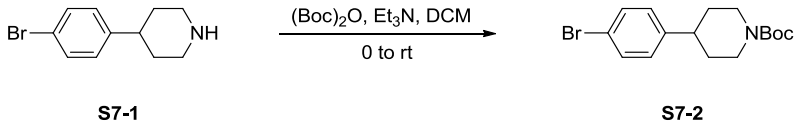
^{1}H NMR (300 MHz, d_6-DMSO) δ 8.38 (s, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.66-7.63 (m, 1H), 7.47-7.43 (m, 1H), 7.32 (d, J = 8.3 Hz, 2H), 7.20-7.16 (m, 2H), 5.54 (s, 2H), 2.28 (s, 2H), 1.90 (d, J = 11.8 Hz, 4H), 1.76 (s, 2H), 1.60 (d, J = 13.5 Hz, 6H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 163.0, 144.7, 144.0, 140.3, 133.9, 133.2, 130.2, 123.0, 122.1, 120.0, 115.5, 111.0, 105.5, 58.0, 47.4, 36.9, 35.2, 33.6, 26.4; HRMS (m/z): $[M+Na]^+$ calculated for $C_{27}H_{25}IN_2NaO_4$ 591.0757, found 591.0759.



S6-1 **S6-5** **[^{19}F]19**

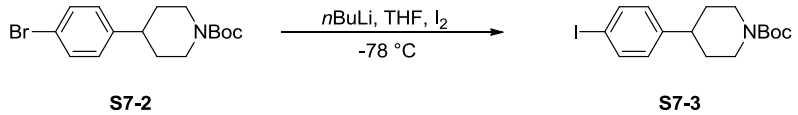
NaH (washed with hexanes for five times to remove mineral oil and dried in vacuo for 3 h, 55 mg, 2.3 mmol)) was added in portions to a solution of benzimidazole **S6-1** (180 mg, 1.53 mmol) in dry THF under argon atmosphere at 0 ℃. The solution was stirred at rt for 3 h. At 0 ℃ 1-(bromomethyl)-4-fluorobenzene **S6-5** (317 mg, 1.67 mmol) was added carefully and the reaction mixture was heated at 65 °C for 15 h. The reaction was quenched with H_2O (15 mL) and extracted with EtOAc (15 mL × 3). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by flash chromatography (Hexanes/EtOAc = 2/1 to 0/1, then EtOAc/MeOH = 50:1) to afford 1-(4-fluorobenzyl)-1*H*-benzo[*d*]imidazole **[^{19}F]19** (251 mg, yield 73%) as colorless oil. Characterized according to a literature procedure.[17] HRMS (m/z): $[M+Na]^+$ calculated for $C_{14}H_{11}FN_2Na$ 249.0804, found 249.0805.

7. paroxetine



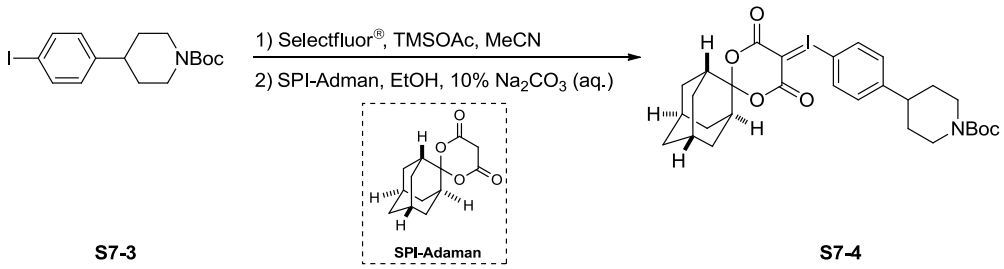
S7-1 **S7-2**

A well-stirred solution of 4-(4-bromophenyl) piperidine **S7-1** (460 mg, 1.92 mmol) in DCM (5 mL) was treated with triethylamine (583 mg, 5.76 mmol), followed by addition of *t*-Boc_2O (503 mg, 2.3 mmol) at 0 °C. The mixture was stirred at room temperature for 20 h and then quenched with H_2O (10 mL), extracted with dichloromethane (10 mL × 3), washed with brine, dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 12/1) to afford *tert*-butyl 4-(4-bromophenyl) piperidine-1-carboxylate **S7-2** (582 mg, yield 89%) as colorless oil. Identity confirmed by comparison with published characterization data.[18]



S7-2 **S7-3**

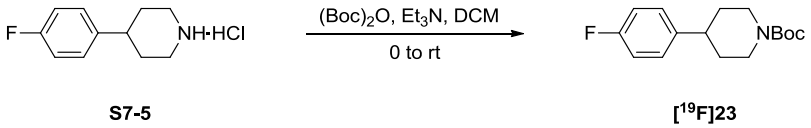
n-Butyllithium (2.5 M solution, 0.6 mL, 1.49 mmol) was added at -78 °C under stirring to the solution of bromide **S7-2** (460 mg, 1.35 mmol) in THF (4 mL) under argon. The mixture was stirred at -78 °C for 30 minutes and then the solution of iodine (412 mg, 1.62 mmol) in THF (2.5 mL) was added. After stirring at -78 °C for 2 hours the mixture was warmed to room temperature, diluted with water (10 mL), and extracted with ethyl acetate (10 mL × 3). The organic layers were combined, washed with water (20 mL × 1), saturated $Na_2S_2O_3$ solution (10 mL × 3), brine (10 mL × 2), and dried with Na_2SO_4. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 12/1) to afford tert-butyl 4-(4-iodophenyl) piperidine-1-carboxylate **S7-3** (410 mg, yield 78%) as colorless oil. Identity confirmed by comparison with published characterization data.[18]



In a N_2 charged round-bottom flask, iodide **S7-3** (410 mg, 1.06 mmol) was dissolved in dry MeCN (10 mL). Trimethylsilyl acetate (420 mg, 3.18 mmol) and Selectfluor® (938 mg, 2.65 mmol) were added sequentially. The reaction mixture was allowed to stir at room temperature for 15 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (20 mL). The mixture was extracted with dichloromethane (15 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 10 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (15 mL) and dichloromethane (1.5 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The mixture was stored at -20 °C in freezer for 1 h, and the solvent was decanted away. This process was repeated once more. The remaining solid was dried under vacuum for 2 h. The obtained diacetoxyiodoarene (405 mg, ~0.80 mmol) was used in the next step.

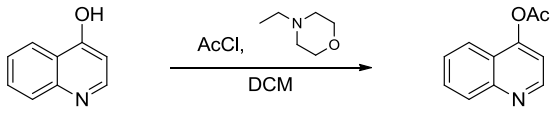
A solution of diacetoxyiodoarene (405 mg, ~0.80 mmol) in EtOH (6 mL) was added a solution of SPI-Adaman (190 mg, 0.80 mmol) in 10% Na_2CO_3 (6.5 mL), followed by addition of 10% Na_2CO_3 (2.0 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 3 h, then diluted with H_2O (25 mL), extracted with DCM (20 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To resulting solid was added ethyl acetate/pentane (v/ v = 1/ 1, 10 mL), sonicated, allowed to settle and decanted. This process was repeated for three more times. After dryness using a vacuum pump, the ylide **S7-4** (392 mg, yield over two steps 60%) was obtained as white solid.

^{1}H NMR (300 MHz, d_6-DMSO) δ 7.67 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.07-4.00 (m, 2H), 2.75-2.66 (m, 3H), 2.32 (br s, 2H), 1.91 (d, J = 12.1 Hz, 4H), 1.75 (d, J = 13.5 Hz, 3H), 1.66 (t, J = 10.5 Hz, 7H), 1.47 (td, J = 13.0, 4.5 Hz, 2H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 162.8, 154.1, 149.0, 132.8, 129.8, 113.6, 105.3, 78.9, 57.8, 41.6, 36.8, 35.1, 33.5, 32.7, 28.4, 26.3; HRMS (m/z): $[M+Na]^+$ calculated for $C_{29}H_{36}INNaO_6$ 644.1485, found 644.1487.



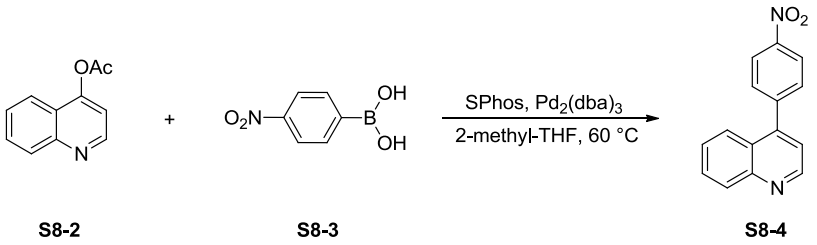
A well-stirred solution of 4-(4-fluorophenyl)piperidine hydrochloride salt **S7-5** (430 mg, 2.00 mmol) in DCM (10 mL) was treated with triethylamine (1.0 g, 10.0 mmol), followed by addition of *t*-Boc_2O (523 mg, 2.4 mmol) at 0 °C. The mixture was stirred at room temperature for 20 h and then quenched with H_2O (20 mL), extracted with dichloromethane (15 mL × 3), washed with brine, dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 8/1) to afford *tert*-butyl 4-(4-fluorophenyl) piperidine-1-carboxylate **[^{19}F]23** (508 mg, yield 91%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17-7.11 (m, 2H), 7.02-6.95 (m, 2H), 4.24 (dt, *J* = 13.4, 2.1 Hz, 2H), 2.78 (td, *J* = 10.5, 2.7 Hz, 2H), 2.62 (tt, *J* = 12.2, 3.7 Hz, 1H), 1.82-1.76 (m, 2H), 1.59 (td, *J* = 12.5, 4.3 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 159.7, 154.7, 141.3 (d, *J* = 3.3 Hz), 128.0 (d, *J* = 7.7 Hz), 115.1 (d, *J* = 20.9 Hz), 79.4, 44.3, 41.9; HRMS (m/z): $[M+Na]^+$ calculated for $C_{16}H_{22}FNNaO_2$ 302.1532, found 302.1535.

8. pitavastatin



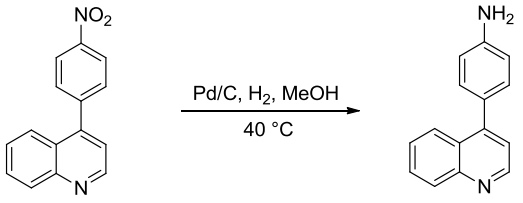
S8-1 **S8-2**

To an oven-dried flask (25 mL) were charged of 4-quinolinol **S8-1**(500 mg, 3.44 mmol) and DCM (7 mL), the mixture was cooled down to 0 °C. To the mixture was added N-ethylmorpholine (475 mg, 4.13 mmol). The mixture was stirred at 0 °C for 10 min, then AcCl (324 mg, 4.13 mmol) was added dropwise. The mixture was stirred at room temperature for 12 h, and quenched with water (10 mL), extracted with dichloromethane (8 mL × 3), washed with brine, dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford quinolin-4-yl acetate **S8-2** (514 mg, yield 80%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (d, *J* = 5.0 Hz, 1H), 8.75 (d, *J* = 8.7 Hz, 1H), 7.99-7.95 (m, 1H), 7.79-7.73 (m, 1H), 7.61-7.56 (m, 1H), 7.33 (d, *J* = 4.9 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 154.1, 150.6, 149.7, 130.2, 129.3, 127.0, 122.2, 121.2, 112.8, 21.1; HRMS (m/z): $[M+Na]^+$ calculated for $C_{11}H_9INNaO_2$ 210.0531, found 210.0534.



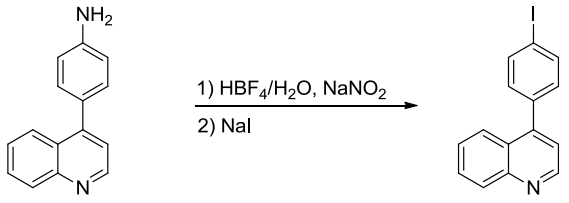
S8-2 **S8-3** **S8-4**

To an oven-dried flask (50 mL) under an argon atmosphere were charged of 2-methyl-THF (10 mL), quinolin-4-yl acetate **S8-2** (374 mg, 2 mmol), (4-nitrophenyl) boronic acid **S8-3** (401 mg, 2.4 mol), $Pd_2(dba)_3$ (23 mg, 0.04 mmol) and SPhos (33 mg, 0.08 mmol). The mixture was degassed with argon for 15 min, and then agitated at 65 °C for 20 h. To the agitated solution was charged ethyl acetate (20 mL), followed by 5% NaOH (10 mL).The mixture was stirred for 10 min. The aqueous phase was cut. The organic phase was washed with 10% brine (10 mL), dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford crude product, which was recrystallized from EtOAc/Pentane = 1/5 at -20 °C overnight. After filtration, the pure compound 4-(4-nitrophenyl) quinoline **S8-4** (210 mg, yield 42%) was obtained as white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (d, *J* = 4.4 Hz, 1H), 8.39 (d, *J* = 8.5 Hz, 2H), 8.23 (d, *J* = 9.0 Hz, 1H), 7.80-7.75 (m, 2H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.55 (t, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 148.4, 147.9, 146.1, 144.5, 130.5, 130.0, 129.9, 127.4, 125.9, 125.0, 123.8, 121.1; HRMS calc'd for $C_{15}H_{11}N_2O_2$ $[M + H]^+$, 251.0821; found 251.0819.



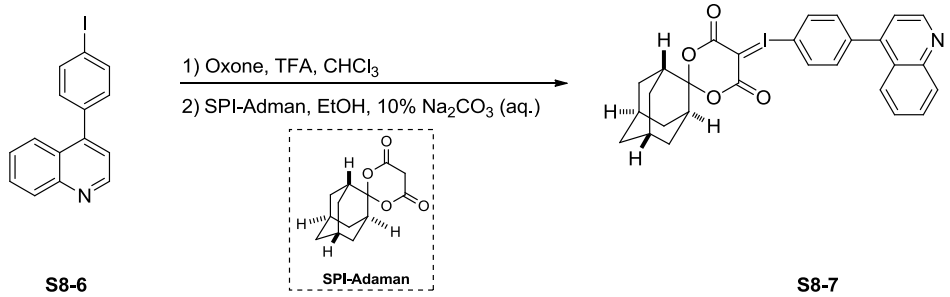
S8-4 **S8-5**

A mixture of 4-(4-nitrophenyl) quinoline **S8-4** (210 mg, 0.84 mmol) and Pd-C (10%, 70 mg) in MeOH (8 mL) was hydrogenated under balloon H_2 for 24 h. The mixture was then filtered through celite. The filtrate was concentrated in vacuo to give 4-(quinolin-4-yl) aniline **S8-5** (~210 mg) as a yellow solid, which was used in the next step without further purification.



S8-5 **S8-6**

4-(quinolin-4-yl) aniline **S8-5** (50 mg, 0.23 mmol) was dissolved in 48% aqueous HBF_4 (1.0 mL) and cooled to -10 °C. To the resulting slurry was added powdered $NaNO_2$ (17.2 mg, 0.25 mmol). After 30 min, NaI (54 mg, 0.36 mmol) was added to the mixture. The reaction was stirred for 30 min, then decolorized by adding saturated $Na_2S_2O_3$ (2 mL), neutralized with saturated aqueous Na_2CO_3 (2 mL), and extracted with chloroform (3 x 5 mL). The organic layer was dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford 4-(4-iodophenyl) quinoline **S8-6** (20 mg, yield 27%) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (d, *J* = 4.3 Hz, 1H), 8.20 (d, *J* = 8.6 Hz, 1H), 7.87 (dt, *J* = 8.3, 1.8 Hz, 3H), 7.74 (tt, J = 8.5, 1.4 Hz, 1H), 7.52 (tt, *J* = 8.4, 1.2 Hz, 1H), 7.30 (d, *J* = 4.5 Hz, 1H), 7.25 (dt, *J* = 8.4, 1.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 148.4, 147.5, 137.8, 137.3, 131.3, 129.7, 129.6, 126.9, 126.3, 125.5, 121.1, 94.6; HRMS (m/z): $[M+Na]^+$ calculated for $C_{15}H_{10}INNa$ 353.9756, found 353.9757.

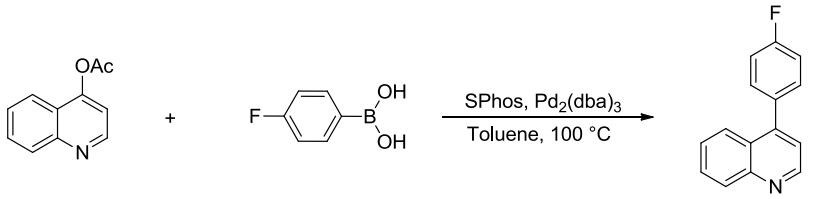


S8-6 **S8-7**

A solution of 4-(4-iodophenyl) quinoline **S8-6** (20 mg, 0.06 mmol) in a mixture of trifluoroacetic acid (1.2 mL) and chloroform (0.5 mL) was added Oxone (73 mg, 0.12 mmol) under stirring at room temperature. The reaction mixture was stirred at room temperature for 1.5 hours. The solvent was evaporated under vacuum, and the residue was treated with chloroform (2 mL). The insoluble residue of inorganic salts was collected by filtration, washed with chloroform (2 mL), and discarded. Evaporation of combined chloroform extracts under reduced pressure afforded crude products, which was dried under vacuum for 30 min and dissolved in EtOH (0.5 mL). The mixture was added a solution of SPI-Adaman (5.3 mg, 0.023 mmol) in 10% Na_2CO_3 (0.1 mL),

followed by addition of 10% Na_2CO_3 (0.2 mL) to adjust pH value of the mixture to be around 9. The reaction was stirred at ambient temperature for 10 h, then diluted with H_2O (5 mL), extracted with DCM (5 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To resulting mixture was recrystallized from Pentane/EtOAc = 10/1 to afford the ylide **S8-7** (17 mg, yield over two steps 51%) as white solid.

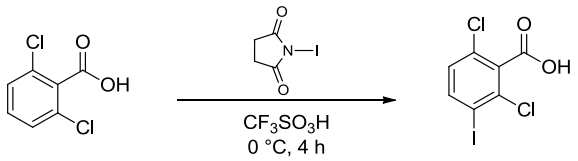
^{1}H NMR (300 MHz, d_6-DMSO) δ 8.96 (d, *J* = 4.2 Hz, 1H), 8.11 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.83-7.76 (m, 2H), 7. 46 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 4.3 Hz, 1H), 2.37 (s, 3H), 1.95 (d, *J* = 12.6 Hz, 4H), 1.80 (s, 2H), 1.66 (d, *J* = 10.9 Hz, 6H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 163.0, 150.6, 148.5, 146.2, 140.0, 132.8, 132.3, 130.1, 127.8, 125.9, 125.5, 122.0, 116.4, 105.6, 57.9, 36.9, 35.2, 33.7, 26.4; HRMS (m/z): $[M+Na]^+$ calculated for $C_{28}H_{24}INNaO_4$ 588.0648, found 588.0649.



S8-2 **S8-8** **[^{19}F]18**

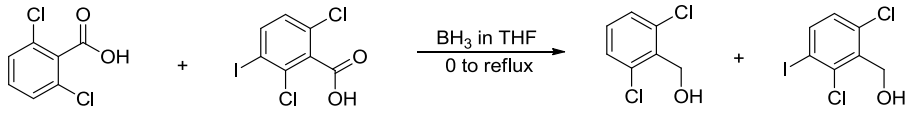
To an oven-dried flask (10 mL) under an argon atmosphere were charged of toluene (1.0 mL), quinolin-4-yl acetate **S8-2** (30 mg, 0.16 mmol), (4-fluorophenyl) boronic acid **S8-8** (27 mg, 0.19 mol), $Pd_2(dba)_3$ (1.84 mg, 0.0032 mmol) and SPhos (2.6 mg, 0.0064 mmol). The mixture was degassed with argon for 15 min, and then agitated at 100 °C for 20 h. To the agitated solution was charged ethyl acetate (3 mL), followed by 5% NaOH (0.5 mL).The mixture was stirred for 10 min. The aqueous phase was cut. The organic phase was washed with 10% brine (10 mL), dried over sodium sulfate, filtered and evaporated in *vacuo*. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 3/1) to afford 4-(4-fuorophenyl) quinoline **[^{19}F]18** (27 mg, yield 75%) as light purple oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (d, *J* = 4.3 Hz, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.75 (dt, J =6.8, 1.3 Hz, 1H), 7.56-7.46 (m, 3H), 7.33 (d, *J* = 4.5 Hz, 1H), 7.26-7.20 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 149.6, 148.3, 147.8, 133.8 (d, J = 3.4 Hz), 131.2 (d, J = 8.2 Hz), 129.6, 126.9, 125.6, 121.3, 115.8, 115.5; HRMS (m/z): $[M+Na]^+$ calculated for $C_{15}H_{10}FNNa$ 246.0695, found 246.0698.

9. crizotinib



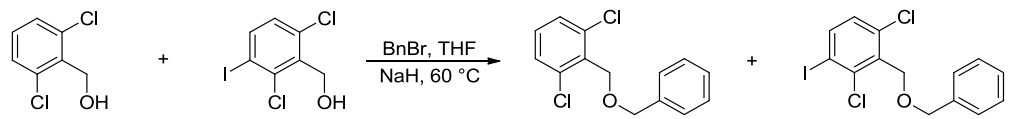
S9-1 **S9-2**

To a stirred solution of 2,6-dichlorobenzoic acid (2.5 g, 13.1 mmol) in trifluoromethanesulfonic acid (10 mL) cooled to 0 ℃ was added *N*-iodosuccinimide (2.67 g, 11.9 mmol) in small portions over 30 min, with vigorous stirring. After 4 h, the reaction mixture was quenched with water. The product was extracted with dichloromethane, washed with 10% sodium thiosulfate (3×) and brine (1×). The organics were dried with anhydrous sodium sulfate, filtered and concentrated. The product could be purified by flash chromatography or used in the next step without purification. The product **S9-2** is light sensitive and produces **S9-1** on standing. The product can be isolated in >90% purity as a pale brown solid (3.26 g, 10.3 mmol, 79% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 5.61 (br s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5, 141.6, 136.0, 133.5, 131.8, 129.2, 97.0 ppm.



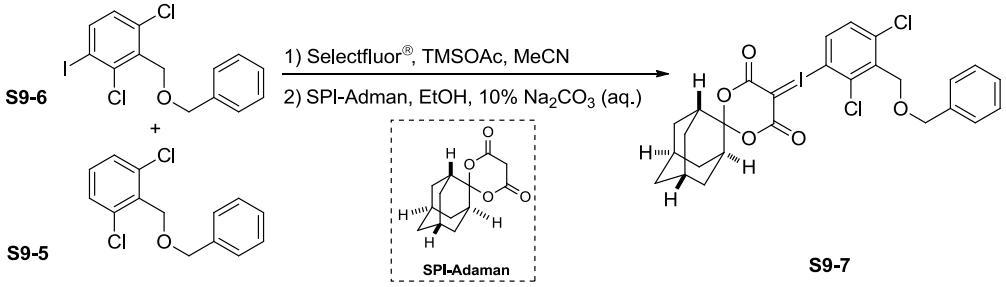
S9-1 **S9-2** **S9-3** **S9-4**

To a mixture of 2,6-dichlorobenzoic acid **S9-1** and 2,6-dichloro-3-iodobenzoic acid **S9-2** (molar ratio is about 1:1, 235 mg) was added dropwise BH_3·THF (1 M, 2.3 mL, 2.3 mmol) at ambient temperature. After addition, the resulting mixture was refluxed for 20 h. Methanol (10 mL) was added to quench the excess borane. Solvents and trimethyl borate by-product were evaporated under reduced pressure to dryness. The same process was repeated one more time. The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 4/1) to afford a mixture of **S9-3** and **S9-4** (molar ratio from ^{1}H NMR was 1:1, total 160 mg) as light yellow oil, which was used in the next step without further purification.



S9-3 **S9-4** **S9-5** **S9-6**

NaH (washed with hexanes for five times to remove mineral oil and dried in vacuo for 3 h, 12 mg, 0.5 mmol) was added to a well-stirred suspension of the benzyl alcohols **S9-3** and **S9-4** (total 78 mg, 0.158 mmol of each one) in dry THF (1.0 mL) at room temperature under argon. After 30 min, the benzyl bromide (68 mg, 0.4 mmol) in THF (1 mL) were added dropwise, and the reaction mixture was stirred at 60 °C for 12 h. The mixture was then cooled to 0 °C, and the excess sodium hydride was quenched with water (1 mL). The reaction mixture was then extracted with ethyl acetate (3 mL × 3). The organic layers were combined and were washed with brine (5 mL). The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 10/1) to afford a mixture of **S9-5** and **S9-6** (molar ratio from ^{1}H NMR was 1:1, total 108 mg) as light yellow solid, which was used in the next step without further purification.

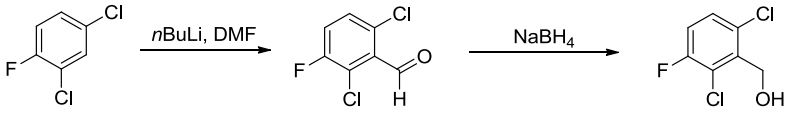


In a N_2 charged round-bottom flask, the mixture of **S9-5** and **S9-6** (total 108 mg, 0.164 mmol of each one) was dissolved in dry MeCN (2 mL). Trimethylsilyl acetate (54 mg, 0.41 mmol) and Selectfluor® (116 mg, 0.33 mmol) were added sequentially. The reaction mixture was allowed to stir at room temperature for 12 h. Acetonitrile was removed by evaporation and the remaining yellow oil was treated with H_2O (3 mL). The mixture was extracted with dichloromethane (3 mL × 3). The organic layers were combined, washed with aqueous acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5, 3 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. Pentane (5 mL) and dichloromethane (0.5 mL) were added to the oil and mixture was placed in an ultrasonic bath and sonicated until the compound solidified. The solvent was decanted away, and the same procedure was repeated one more time. The remaining solid was dried under vacuum for 2 h. The obtained diacetoxyiodoarene (33 mg, 0.065 mmol) was used in the next step.

A solution of diacetoxyiodoarene (33 mg, 0.065 mmol) in EtOH (0.5 mL) was added a solution of SPI-Adaman (15.3 mg, 0.065 mmol) in 10% Na_2CO_3 (0.25 mL), followed by addition of 10% Na_2CO_3 (0.2 mL) to adjust pH value of the mixture to be around 10. The reaction was stirred at ambient temperature for 3 h, then diluted with H_2O (2 mL), extracted with DCM (3 mL × 3). The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. To

resulting solid was added ethyl acetate/pentane (v/ v = 1/ 1, 2 mL), sonicated, allowed to settle and decanted. This process was repeated for three more times. After dryness using a vacuum pump, the ylide **S9-7** (41 mg, yield over two steps 39%) was obtained as white solid.

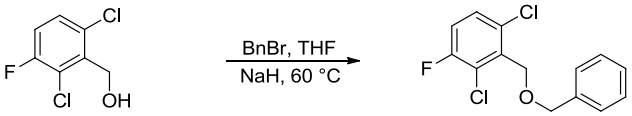
^{1}H NMR (300 MHz, d_6-DMSO) δ 7.82 (d, J = 8.6 Hz, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.34-7.27 (m, 5H), 4.77 (s, 2H), 4.57 (s, 2H), 2.25 (br s, 2H), 1.88 (d, J = 12.4 Hz, 4H), 1.75 (s, 2H), 1.60 (d, J = 11.7 Hz, 6H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 162.6, 139.0, 138.8, 138.2, 137.8, 137.0, 135.2, 131.0, 128.7, 128.1, 118.8, 105.6, 72.7, 67.9, 59.4, 36.9, 35.3, 33.6, 26.3. HRMS (m/z): $[M+Na]^+$ calculated for $C_{27}H_{25}Cl_2INaO_5$ 649.0021, found 649.0025.



S9-8 **S9-9** **S9-10**

To 2,4-dichloro-1-fluorobenzene **S9-8** (2.0 g, 12.1 mmol) in THF (28 mL) was added dropwise *n*BuLi (2.5 M, 5.3 mL, 13.3 mmol) at -78 °C over a period of 30 min. After 1.0 h stirring at -78 °C, methyl formate (1.45 g, 24.2 mmol) was added slowly and the reaction mixture was stirred overnight, warming up to rt. The reaction was diluted with EtOAc (20 mL) and quenched with sat. aqueous NH_4Cl (20 mL). The organic layer was separated and dried over Na_2SO_4. The organic solvents were removed and the crude material was crystallized from hexanes to give the light yellow solid **S9-9** (crude compound, 1.1 g), which was used without further purification.

To 2,6-dichloro-3-fluorobenzaldehyde **S9-9** (390 mg, 2.02 mmol) in MeOH (7 mL) was added $NaBH_4$ (115 mg, 3.03 mmol) at 0 °C. After stirring for 2 h at 0 °C, the reaction was diluted with EtOAc (10 mL) and quenched with sat. brine (10 mL). The organic layer was separated and dried over Na_2SO_4. The organic solvents were removed and the crude material was purified by column chromatography on silica gel (Hexanes/EtOAc = 10/1) to afford benzyl alcohol **S9-10** (389 mg, yield 99%) as colorless oil. Identity confirmed by comparison with published characterization data.[19]



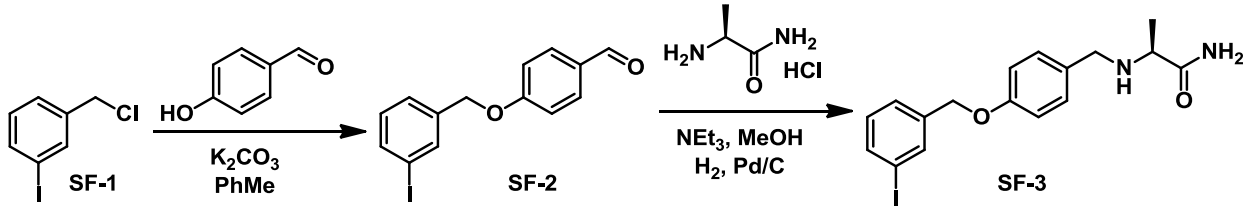
S9-10 **[^{19}F]16**

NaH (washed with hexanes for five times to remove mineral oil and dried in vacuo for 3 h, 72 mg, 3.0 mmol) was added to a well-stirred suspension of the benzyl alcohols **S9-10** (389 mg, 2.0 mmol) in dry THF (6.0 mL) at room temperature under argon. After 30 min, the benzyl bromide (376 mg, 2.2 mmol) in THF (2 mL) were added dropwise, and the reaction mixture was stirred at 60 °C for 2.5 h. The mixture was then cooled to 0 °C, and the excess sodium hydride was

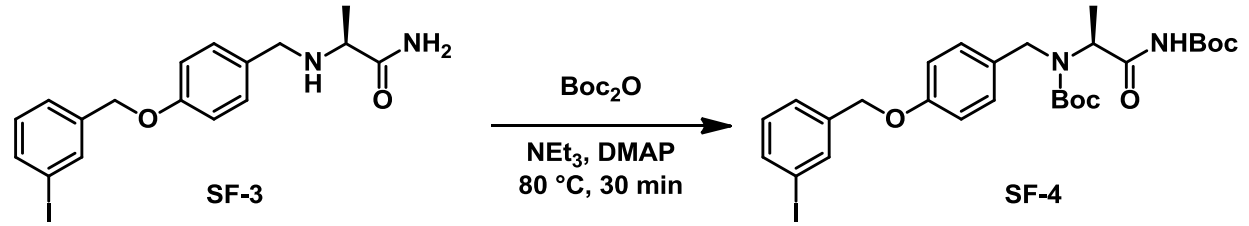
quenched with water (4 mL). The reaction mixture was then extracted with ethyl acetate (4 mL × 3). The organic layers were combined and were washed with brine (5 mL). The residue was purified by column chromatography on silica gel (Hexanes/EtOAc = 15/1) to afford 2-((benzyloxy)methyl)-1,3-dichloro-4-fluorobenzene **[^{19}F]16** (479 mg, yield 84%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.28 (m, 6H), 7.09 (t, *J* = 8.3 Hz, 1H), 4.83 (s, 2H), 4.66 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 155.4, 137.8, 135.3, 131.3 (d, *J* = 3.9 Hz), 128.5 (d, *J* = 7.2 Hz), 128.3, 127.8 (d, *J* = 5.5 Hz), 124.0 (d, *J* = 18.2 Hz), 116.8 (d, *J* = 23.1 Hz), 73.0, 66.6 (*J* = 2.1 Hz). HRMS (m/z): $[M+Na]^+$ calculated for $C_{14}H_{11}Cl_2FNaO$ 307.0069, found 307.0073.

Preparation of precursor to [^{18}F]safinamide

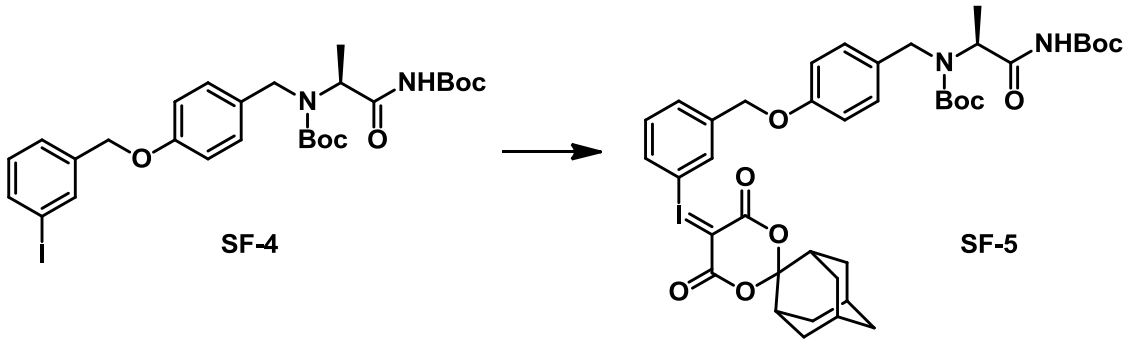
The aryliodide analog of safinamide was prepared using similar procedures to those for the preparation of safinamide.[20]



Iododefluorosafinamide (**SF-3**) was isolated as colourless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 5.64 (br s, 1H), 4.99 (s, 2H), 3.71 (apparent q, *J* = 7.7, 13.0 Hz, 2H), 3.24 (q, *J* = 7.0 Hz, 1H), 1.77 (br s, 1H), 1.34 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.9, 157.7, 139.3, 137.0, 132.1, 130.3, 129.3, 126.5, 114.9, 94.4, 69.0, 57.6, 51.9, 19.6 ppm.



Iododefluorosafinamide (**SF-3**, 500 mg, 1.2 mmol) was added to neat di-*tert*-butyl dicarbonate (5.24 g, 24 mmol), heated to 40 ℃. Triethylamine (1 mL, 7.2 mmol) and *N*,*N*-dimethylaminopyridine (74 mg, 0.6 mmol) were added and the reaction mixture heated to 80 ℃ for 30 min. The reaction mixture was diluted with ethyl acetate, and washed sequentially with water, 1 M HCl, and brine. The organic fraction was collected, dried with Na_2SO_4, filtered and concentrated. The product was then purified by flash chromatography (5–50% EA/Hex) to yield a colourless residue (**SF-4**, 400 mg, 0.66 mmol, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 2H, obscured by solvent residual signal), 7.11 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.98 (s, 2H), 4.56 (d, *J* = 15.3 Hz, 1H), 4.33 (d, *J* = 15.3 Hz, 1H), 1.60 (s, 9H), 1.48 (s, 3H), 1.29 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 164.9, 158.5, 152.2, 146.0, 139.3, 137.2, 136.3, 130.4, 130.3, 128.7, 126.6, 115.1, 94.6, 86.0, 84.6, 69.1, 68.3, 44.2, 28.0, 27.6 ppm.

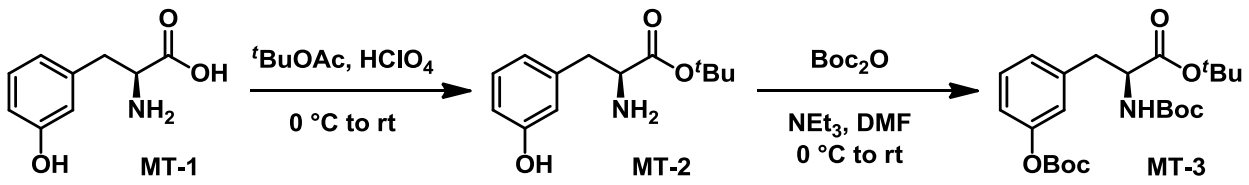


A solution of di-Boc-protected iododefluorosafinamide (**SF-4**, 183 mg, 0.3 mmol) in acetone and acetic acid (4:1, 2.2 mL) was cooled to 0 ℃ and treated with a solution of DMDO in acetone.[21] The reaction mixture was stirred at 0 ℃ for 1 h, then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then concentrated, diluted with ethanol (1.2 mL), treated with (1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dione (71 mg) in 10% aqueous sodium carbonate (0.9 mL) and the pH was adjusted to ~10 using 10% aqueous sodium carbonate. The reaction was then stirred for 2–4 h, and then diluted with water and extracted three times with dichoromethane. The pooled organics were dried using sodium sulfate, filtered concentrated and purified by flash chromatography (SiO_2, 50–100% EA/Hex) to yield a colourless solid (**SF-5**, 78 mg, 31% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.27 (d, 2H, obscured by solvent residual signal), 6.88 (d, *J* = 8.6 Hz, 2H), 5.04 (s, 2H), 4.60 (d, *J* = 15.3 Hz, 1H), 4.28 (d, *J* = 15.4 Hz, 1H), 2.43 (br s, 2H), 2.18 (br s, 2H), 2.14 (br s, 2H), 1.85 (br s, 2H), 1.71 (br s, 4H), 1.67 (br s, 2H), 1.59 (s, 9H), 1.48 (m, 3H), 1.32 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 163.5, 158.1, 152.2, 146.0, 141.6, 132.8, 132.1, 131.7, 130.8, 130.4, 129.2, 115.1, 114.4, 107.8, 86.0, 84.6, 68.7, 68.4, 55.9, 44.3, 37.3, 35.7, 33.9, 28.0, 27.7, 26.6, 18.4 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{45}H_{57}IN_2NaO_{13}$ 983.2803, found 983.2805.

The ^{19}F-standard safinamide was prepared according to literature conditions.[20]

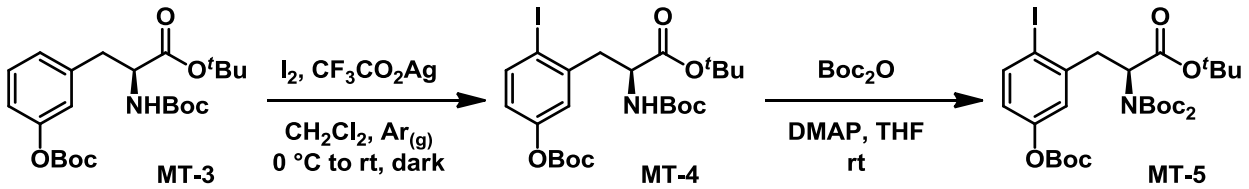
Preparation of precursor to 6-[^{18}F]fluoro-*meta*-tyrosine

Protected 6-iodo-*meta*-tyrosine was prepared based on the procedures of VanBrocklin *et al.*[22]



To a mixture of L-*meta*-tyrosine (**MT-1**, 1.0 g, 5.5 mmol) and *tert*-butyl acetate (11 mL) at 0 ℃ was slowly added perchloric acid (0.5 mL, 8.3 mmol).[23,24] The reaction mixture was then warmed to room temperature and stirred for 4 h, before sequential extraction with water and 1 M HCl. The aqueous fractions were then adjusted to pH 9 by addition of 10% K_2CO_3 and extracted three times with dichloromethane. The pooled organic fractions were dried with anhydrous sodium sulfate, filtered, and concentrated. The crude product (**MT-2**) was used in the following step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.72–6.68 (m, 2H), 3.63 (t, *J* = 5.4 Hz, 1H), 3.01 (dd, *J* = 5.4, 13.6 Hz, 1H), 2.83 (dd, *J* = 7.7, 13.6 Hz, 1H), 1.45 (s, 9H) ppm.

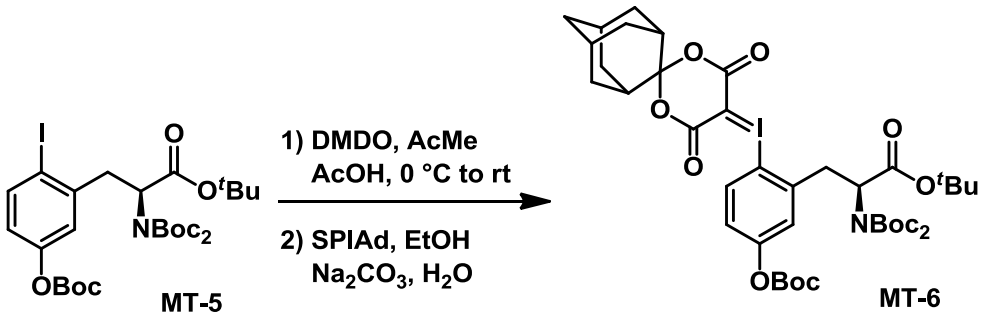
To a solution of L-*meta*-tyrosine *tert*-butyl ester (**MT-2**, ~5.5 mmol) in DMF (4 mL) was slowly added triethylamine (2.3 mL, 16.5 mmol). The reaction mixture was then cooled to 0 ℃, and a solution of di-*tert*-butyl dicarbonate (3.00 g, 13.75 mmol) in DMF (4 mL) was added over 10 minutes. The reaction mixture was then warmed to room temperature and stirred for 48 h. The reaction mixture was then diluted with ethyl acetate and washed with brine (3 × 100 mL). The pooled organic phases were then extracted with ethyl acetate and then the combined organic phases were dried with sodium sulfate, filtered, and concentrated. The crude mixture was purified by flash chromatography (SiO_2, 5–25% EA/Hex) to yield a pale yellow oil (**MT-3**, 2 g, 4.6 mmol, 83% yield over two steps. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (t, *J* = 7.7 Hz, 1H), 7.05–6.98 (m, 3H), 5.00 (d, *J* = 7.7 Hz, 1H), 4.44 (dd, *J* = 6.0, 13.6 Hz, 1H) 3.06 (d, *J* = 6.0 Hz, 1H), 1.55 (s, 9H), 1.42 (s, 9H), 1.39 (s, 9H) ppm.



To a solution of **MT-3** (2 g, 4.6 mmol) in dichloromethane (38 mL) at room temperature and under argon was added silver(I) trifluoroacetate (1.25 g, 5.7 mmol), followed by iodine (1.28 g, 5.1 mmol). The flask was sealed from light and vigorously stirred at room temperature for 48 h. The mixture was then filtered through a small pad of Celite over a glass frit to remove solids. The filtrate was concentrated and purified by flash chromatography (SiO_2, 10–25% EA/Hex) to yield a yellow oil (**MT-4**, 1.86 g, 3.3 mmol, 72% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d,

J = 8.4 Hz, 1H), 7.07 (d, *J* = 2.8 Hz, 1H), 6.81 (d, *J* = 8.4, 1H), 5.04 (d, *J* = 8.7 Hz, 1H), 4.53 (dd, *J* = 9.3, 15.3 Hz, 1H), 3.22 (dd, *J* = 5.9, 14.2 Hz, 1H), 3.03 (dd, *J* = 8.2, 13.6, 1H), 1.54 (s, 9H), 1.41 (s, 9H), 1.38 (s, 9H) ppm.

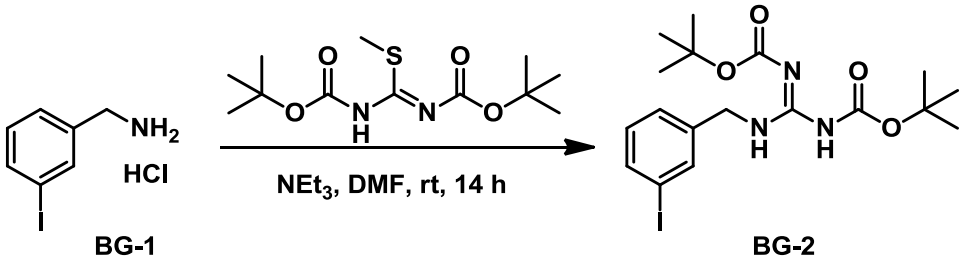
To a solution of **MT-4** (1.86 g, 3.3 mmol) in anhydrous THF (22 mL) under argon was added *N*,*N*-dimethylaminopyridine (2.02 g, 16.5 mmol). The solution was cooled to 0 ℃, and di-*tert*-buty dicarbonate (2.7 g, 12.4 mmol) was added and the reaction was stirred at room temperature overnight. The reaction mixture was then diluted with ethyl acetate, washed twice with water, and once with brine. The organic fractions were then dried over sodium sulfate, filtered, concentrated and purified by flash chromatography (SiO_2, 2–25% EA/Hex) to yield a yellow oil (**MT-5**, 87% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.6 Hz, 1H), 6.99 (d, *J* = 2.7 Hz, 1H), 6.77 (dd, *J* = 2.7, 8.6 Hz, 1H), 5.16 (dd, *J* = 4.4, 10.7 Hz, 1H), 3.52 (dd, *J* = 4.4, 14.3 Hz, 1H), 3.36 (dd, *J* = 10.7, 14.3 Hz, 1H), 1.53 (s, 9H), 1.47 (s, 9H), 1.40 (s, 18H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 152.3, 152.2, 151.4, 151.3, 142.6, 140.2, 139.9, 124.0, 121.5, 96.6, 83.7, 82.9, 81.9, 81.1, 58.2, 28.1, 28.0, 27.8 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{28}H_{42}INNaO_8$ 686.1802, found 686.1805.



A solution of **MT-5** (199 mg, 0.3 mmol) in acetone and acetic acid (4:1, 2.2 mL) was cooled to 0 ℃ and treated with a solution of DMDO in acetone.[21] The reaction mixture was stirred at 0 ℃ for 1 h, then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then concentrated, diluted with ethanol (1.2 mL), treated with (1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dione (71 mg) in 10% aqueous sodium carbonate (0.9 mL) and the pH was adjusted to ~10 using 10% aqueous sodium carbonate. The reaction was then stirred for 2–4 h, and then diluted with water and extracted three times with dichoromethane. The pooled organics were dried using sodium sulfate, filtered concentrated and purified by flash chromatography (SiO_2, 10–50% EA/Hex) to yield a colourless solid (**MT-6**, 85 mg, 32% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 2.8 Hz, 1H), 7.05 (dd, *J* = 2.8, 8.8 Hz, 1H), 4.94 (dd, *J* = 5.3, 9.1, 1H), 3.88 (dd, *J* = 9.2, 14.2 Hz, 1H), 3.25 (dd, *J* = 5.3, 14.2 Hz, 1H), 2.40 (br s, 2H), 2.18 (br s, 2H), 2.14 (br s, 2H), 1.83 (br s, 2H), 1.70 (br s, 4H), 1.65 (br s, 2H), 1.55 (s, 9H), 1.49 (s, 18H), 1.42 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5, 164.2, 153.7, 152.4, 150.9, 141.6, 136.3, 124.4, 123.3, 119.2, 107.3,

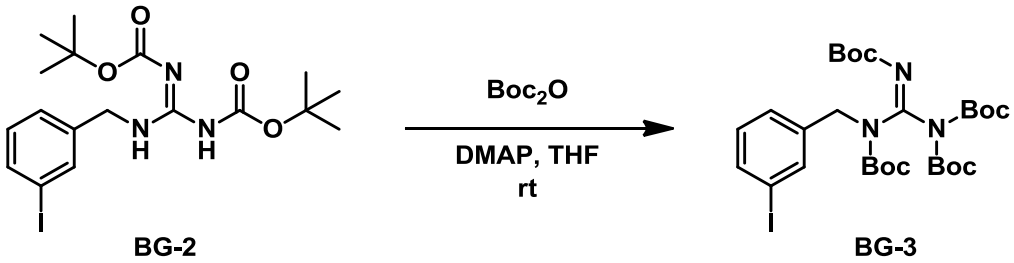
84.5, 84.0, 83.3, 59.6, 56.5, 39.9, 37.4, 35.7, 33.9, 28.2, 28.0, 27.8, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{41}H_{56}INNaO_{13}$ 920.2694, found 920.2699.

Preparation of precursor to [^{18}F]*meta*-fluorobenzylguanidine



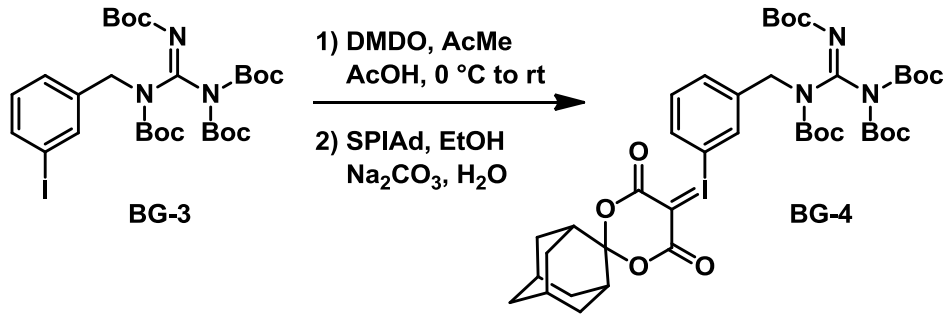
BG-1 BG-2

To a mixture of *meta*-iodobenzylamine hydrochloride (BG-2, 270 mg, 1.0 mmol), triethylamine (0.42 mL, 3.0 mmol), and dimethylformamide (0.5 mL) was added 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thiopseudourea (348 mg, 1.2 mmol) and an additional aliquot of dimethylformamide (0.5 mL). The heterogeneous reaction mixture was stirred at room temperature for 14 h, then diluted with ethyl acetate, and washed sequentially with water and brine. The pooled organic fractions were dried with sodium sulfate, filtered, and concentrated to yield a solid with a slight residual scent of methyl sulfide. The product was purified by flash chromatography to yield a colourless solid (**BG-2**, 440 mg, 0.93 mmol, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.53 (br s, 1H), 8.58 (br s, 1H), 7.66 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 4.57 (d, *J* = 5.4 Hz, 2H), 1.51 (s, 9H), 1.48 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.5, 156.1, 153.2, 139.8, 136.9, 136.7, 130.4, 127.1, 94.5, 83.3, 79.5, 44.1, 28.3, 28.0, ppm. The product was characterized in accordance with the literature.[25]



BG-2 BG-3

To a solution of **BG-2** (238 mg, 0.5 mmol) in tetrahydrofuran (3.33 mL) under argon was added *N*,*N*-dimethylaminopyridine (305 mg, 2.5 mmol). The mixture was cooled to 0 ℃ and di-*tert*-butyl dicarbonate (409 mg, 1.88 mmol) was added over 10 minutes. The reaction was stirred at room temperature for 2 hours, diluted with ethyl acetate, and washed with water. The organic fraction was dried with anhydrous sodium sulfate, filtered, concentrated, and purified by flash chromatography (SiO_2, 2–20% EA/Hex) to yield colourless oil (**BG-3**, 316 mg, 0.47 mmol, 94% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 4.95 (s, 2H), 1.49 (s, 9H), 1.45 (s, 18H), 1.41 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4, 151.2, 147.4, 144.5, 140.0, 136.9, 136.4, 130.1, 127.4, 94.1, 84.2, 83.9, 82.2, 49.5, 28.1, 28.0, 27.9 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{28}H_{42}IN_3NaO_8$ 698.1914, found 689.1917. The product was characterized in accordance with the literature.[25]

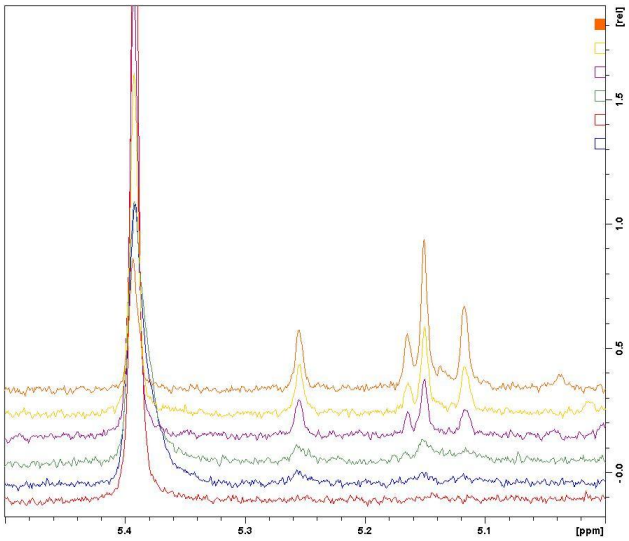


A solution of **BG-3** (173 mg, 0.26 mmol) in acetone and acetic acid (4:1, 2.2 mL) was cooled to 0 ℃ and treated with a solution of DMDO in acetone.[21] The reaction mixture was stirred at 0 ℃ for 1 h, then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was then concentrated, diluted with ethanol (1.2 mL), treated with (1*r*,3*r*,5*r*,7*r*)-spiro[adamantane-2,2'-[1,3]dioxane]-4',6'-dione (71 mg) in 10% aqueous sodium carbonate (0.9 mL) and the pH was adjusted to ~10 using 10% aqueous sodium carbonate. The reaction was then stirred for 2–4 h, and then diluted with water and extracted three times with dichoromethane. The pooled organics were dried using sodium sulfate, filtered concentrated and purified by flash chromatography (SiO_2, 50–100% EA/Hex) to yield a colourless solid (**BG-4**, 106 mg, 45% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 5.02 (s, 2H), 2.43 (br s, 2H), 2.19 (br s, 2H), 2.15 (br s, 2H), 1.85 (br s, 2H), 1.72 (br s, 4H), 1.68 (br s, 2H), 1.49 (s, 9H), 1.46 (s, 18H), 1.42 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.4, 157.3, 151.1, 147.4, 144.6, 142.2, 132.6, 131.9, 131.5, 114.0, 107.7, 84.9, 84.2, 84.0, 82.5, 55.6, 49.7, 37.3, 35.8, 33.9, 33.6, 28.1, 28.0, 26.7 ppm. HRMS (m/z): $[M+Na]^+$ calculated for $C_{41}H_{56}IN_3NaO_{12}$ 932.2806, found 932.2807.

Stability of Iodonium(III) Ylides Under Radiolabeling Conditions in Absence of ^{18}F

The stability of iodonium(III) ylides were evaluated by reaction monitoring with ^{1}H NMR under conditions designed to closely mimic those of radiofluorination, in the absence of ^{18}F. Specifically, 3.5 μmol of iodonium(III) ylide (1.4–1.9 mg) was added to 700 μL of a stock solution of *N*,*N*,*N*′,*N*′-tetraethylammonium bicarbonate (4.8 mg·mL^{-1}, 25 mM) in DMF-d_7 to produce a 5 mM solution in an NMR tube. No fluoride source was added to the reaction mixture. A baseline ^{1}H NMR spectrum (300 MHz, 8 scans) was acquired. The NMR tubes were heated to 120 °C for 1 min, rapidly cooled to room temperature, and a ^{1}H NMR spectrum acquired (t = 1 min). This process was repeated to acquire ^{1}H NMR spectra for 2, 3, 5, and 10 minute time points. Each spectrum underwent Fourier transform, phase correction, and was referenced to the solvent residual formyl proton signal at 8.01 ppm. Integral regions were applied as follows: 5.36–5.42 (parent compound), 5.24–5.27 and 5.09–5.17 (products) ppm. The parent fraction of the total of all regions was corrected for baseline and used to evaluate precursor stability. Experiments were conducted with each of the substrates in parallel, and repeated with freshly prepared stock solution. In the absence of heating, no measurable decomposition was observed in solution over 1 h. In the absence of base, dioxodione-based ylides (*e.g.*, SPIAd, Meldrum's) did not show appreciable levels of decomposition, as evaluated by ^{1}H NMR, over 1 h at 120 °C. Analytical HPLC (stationary phase: Eclipse Plus C18, 3.5 μm, 4.6 × 100 mm; mobile phase: 50% CH_3CN / 0.1% $NH_4OH_{(aq)}$, 1 min, linear gradient to 90% CH_3CN, 8 min, 90% CH_3CN, 3 min, 1 mL·min^{-1}) was conducted on the terminal samples (*i.e.*, after the 10 min time point was acquired). Independently prepared samples of various benzyloxyphenyl species were then evaluated by ^{1}H NMR and analytical HPLC to determine their presence in the decomposition of iodonium ylides.

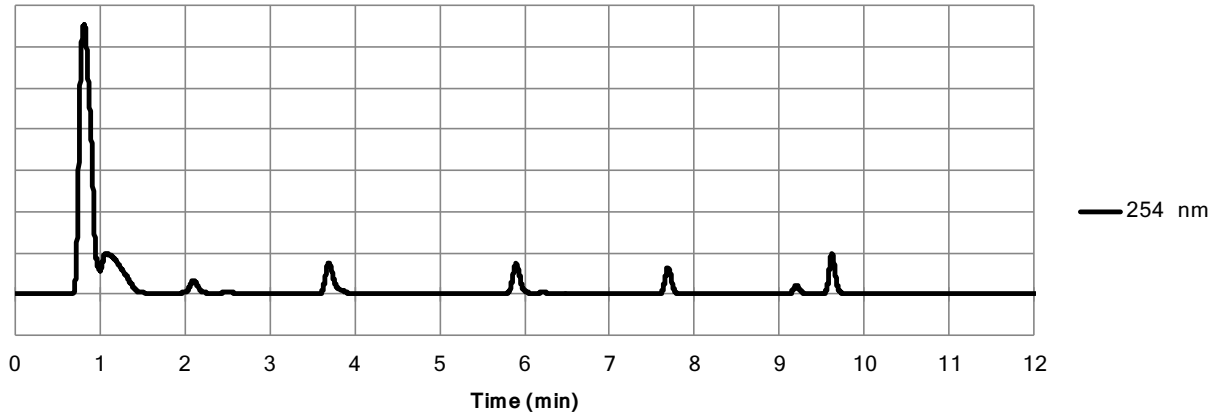
Representative stacked ^{1}H NMR spectra from a given stability experiment:

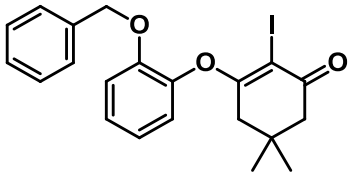


Representative analytical HPLC chromatogram of product solution

Stationary phase: Eclipse Plus C18, 100 × 4.6 mm, 3.5 μm

Mobile phase: 50% CH_3CN / 0.1% $NH_4OH_{(aq)}$, 1 min, linear gradient to 90% CH_3CN, 8 min, 90% CH_3CN, 3 min, 1 mL min^{-1}





3-(2-(benzyloxy)phenoxy)-2-iodo-5,5-dimethylcyclohex-2-enone

A suspension of 5,5-dimethylcyclohexane-1,3-dion-[2-benzyloxyphenyliodonium] ylide (50 mg, 110 μmol) in toluene (1.1 mL) was heated to 100 °C for 2 h. The resulting solution was concentrated under reduced pressure and purified by flash chromatography (SiO_2, 5–25% EA/Hex) to give the product as a colourless solid (83% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28–7.40 (m, 5H), 7.22 (dt, *J* = 7.5, 1.7 Hz, 1H), 7.15 (dd, *J* = 8.0, 1.7, 1H), 7.06 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.01 (dt, *J* = 7.5, 1.4 Hz, 1H), 5.09 (s, 2H), 2.34 (s, 2H), 2.22 (s, 2H), 0.93 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.2, 175.1, 150.3, 142.8, 136.2, 128.7, 128.4, 127.3, 127.2, 122.8, 122.1, 115.2, 82.8, 71.3, 50.1, 42.0, 32.9, 28.0 ppm.

Radiochemical Procedures and Characterization Data

General methods for radioisotope production and preparation

A GE PETtrace 16.5 MeV cyclotron was used for [^{18}F]fluoride production by the ^{18}O(p,n)^{18}F nuclear reaction to irradiate ^{18}O-enriched water. [^{18}F]fluoride was delivered to a lead-shielded hot cell in ^{18}O-enriched water by nitrogen gas pressure. [^{18}F]Fluoride was prepared for radiofluorination of aromatics by one of two methods: (A) A solution of base (*e.g.*, tetraethylammonium bicarbonate, 7 mg) in acetonitrile and water (1 mL, 7:3) was added to an aliquot of target water (≤ 1 mL) containing the appropriate amount of [^{18}F]fluoride in a V-shaped vial sealed with a teflon-lined septum. The vial was heated to 110 ℃ while nitrogen gas was passed through a P_2O_5-Drierite™ column followed by the vented vial. When no liquid was visible in the vial, it was removed from heat, anhydrous acetonitrile (1 mL) was added, and the heating was resumed until dryness. This step was repeated an additional three times. The vial was then cooled at room temperature under nitrogen pressure. The contents were resolubilized in the desired solvent (*e.g.* DMF). (B) An aliquot of target water containing the appropriate amount of [^{18}F]fluoride was slowly passed through an anion exchange cartridge (MP1, ORTG, Tennessee, USA), preactivated by flushing with $NaHCO_{3(aq)}$ (8%, 1 mL) and water (2–3 mL, until neutral by pH indicator). [^{18}F]Fluoride was eluted using a solution of base (*e.g.*, tetraethylammonium bicarbonate, 7 mg) in acetonitrile and water (1 mL, 7:3) into a V-shaped vial sealed with a teflon-lined septum. Drying and resolublization were then performed as described above. For preparations involving crypt-222, drying was conducted at 95 ℃.

General methods for analysis of radiofluorination reactions

Radioactivity was quantified using a Capintec Radioisotope Calibrator (CRC-712M) ion chamber. Radiochemical incorporation yields were determined by radioTLC. EMD TLC Silica gel 60 plates (10 x 2 cm) were spotted with an aliquot (1–5 μL) of crude reaction mixture approximately 1.5 cm from the bottom of the plate (baseline). Unless otherwise noted, TLC plates were developed in a chamber containing ethyl acetate until within 2 cm of the top of the plate (front). Analysis was performed using a Bioscan AR-2000 radio-TLC imaging scanner and WinScan software. Radiochemical identity and purity were determined by radioHPLC with a Waters 1515 Isocratic HPLC Pump equipped with a Waters 2487 Dual λ Absorbance Detector, a Bioscan Flow-Count equipped with a NaI crystal, and Breeze software or a Shimadzu LC-10AD binary variable pump equipped with an SPD-10AD single wavelength UV detector, a Carroll-Ramsey 105S-1 single-channel high sensitivity radiation detector, and Clarity software.

In order to account for immobilized radioactivity (which would not be accounted for by radioTLC), reaction vessels were decanted after quenching and residual and solution radioactivity were separately quantified. In all cases, ≥95% of radioactivity remained in solution.

Auxiliary Optimization for Electron-rich Arenes

An array of structurally diverse auxiliaries were surveyed for conversion to *para*-[^{18}F]fluorobiphenyl, and spirocyclic diester-based auxiliaries and particularly the cyclopentyl-substituted congener SPI5 performed best, achieving up to 85% RCC. SPI5-based precursors were proven to be useful for radiofluorination of electron-neutral, sterically hindered, and electron-rich arenes, albeit the latter proceeded with generally <20% RCC. Targeting improvement for this class of compounds, we prepared two isomeric electron-rich substrates, *para*- and *ortho*-benzyloxyphenyl (**3–4**), and evaluated an expanded collection of ylide auxiliaries (**a–k**) for radiofluorination of these arenes (Table S1). In the event, while SPI5 remained among the most capable auxiliaries for radiofluorination, higher conversions were achieved using either larger spirocyclic rings such as SPI6 and SPI8, or by auxiliaries with bulkier substituents, such as *tert*-butyl groups (**4e**). Conversely, manipulation of electronic properties of the auxiliaries had little influence on RCC (**3f–g**). With these findings in hand, we proceeded to design a sterically hindered spirocyclic auxiliary for iodonium ylides featuring an adamantyl substituent. Iodonium ylides activated by this auxiliary, SPIAd (**3d**, **4d**), had greater RCCs for electron-rich substrates under our screening conditions. By increasing the concentration of TEAB, radiochemical conversion to electron-rich [^{18}F]**6** could be increased to 77 ± 3%. Direct comparison of the SPIAd-based precursor under identical conditions to the Meldrum's acid analog **4k** clearly demonstrates the significant role auxiliary substitution plays in radiofluorination.

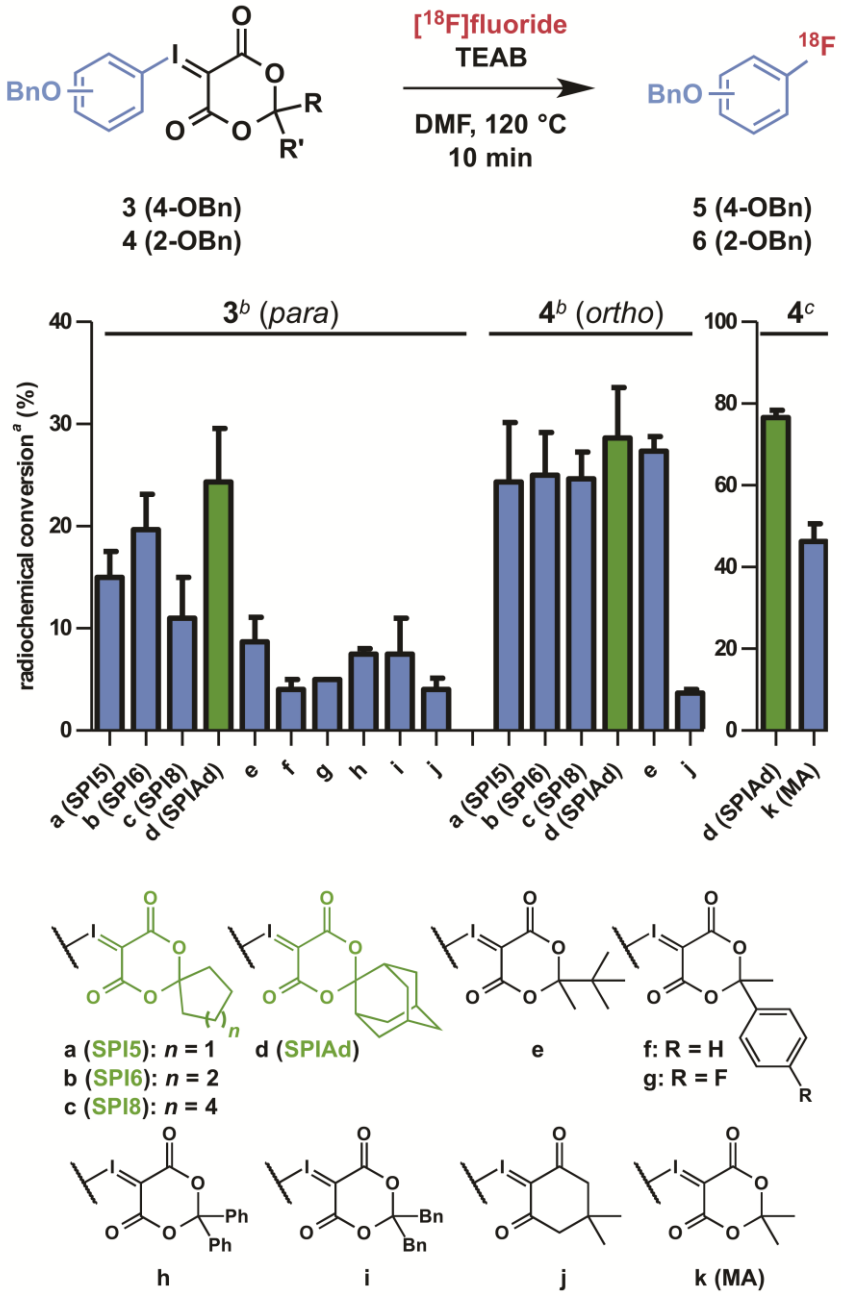
General procedure for radiofluorination of arenes

Azeotropically dried [^{18}F]Et_4NF (typically 50–500 μCi, 2–20 MBq), resolubilized in DMF (400 μL), was added to a V-vial containing iodonium(III) ylide precursor (2 mg). The reaction was heated at 120 ℃ for 10 min, and quenched with HPLC buffer (*e.g.*, 60:40 CH_3CN:H_2O + 0.1 N ammonium formate, 1 mL). Fluorine incorporation and product identities were determined by radioTLC and radioHPLC ($n \geq 3$).

Procedures for measurement of time-course of radiofluorination

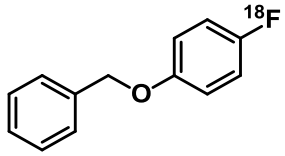
To evaluate the extent of radiofluorination over time, reactions were constructed under the specified conditions and based on the procedure described above. Immediately upon addition of resolubilized [^{18}F]fluoride salts to the vial containing precursor, an aliquot (1–10 μL) was removed and quenched in a test tube containing water or aqueous buffer (50–100 μL). This sample represented t_0. The vials were then heated to the prescribed temperature in heating blocks and additional samples withdrawn at predetermined times and immediately quenched in the same way. For reactions conducted at ambient temperature, samples were withdrawn at predetermined times after addition of [^{18}F]fluoride. Quenched samples were analyzed by rTLC and rHPLC, if suitable. In cases where time-courses were used for direct comparison of precursors or radiofluorination conditions, a common batch of dried and resolubilized [^{18}F]fluoride was used simultaneously for each condition. All time-course experiments were conducted in triplicate.

Table S1. Auxiliary Optimization for Electron-rich Arenes



[a]Radiochemical conversion determined by radioTLC (mean of n = 3, error bars represent SEM); product identity confirmed by radioHPLC co-injection with non-radiolabeled standard; [b]Conditions: precursor (3.5 μmol), anhydrous DMF (0.4 mL), TEAB (0.6 mg), [^{18}F]fluoride (ca. 50 μCi), 120 ℃, 10 min; see SI for detailed procedure; [c]TEAB (4 mg)

Characterization of ^{18}F-arenes and -heteroarenes
[^{18}F]*para*-benzyloxyphenylfluoride

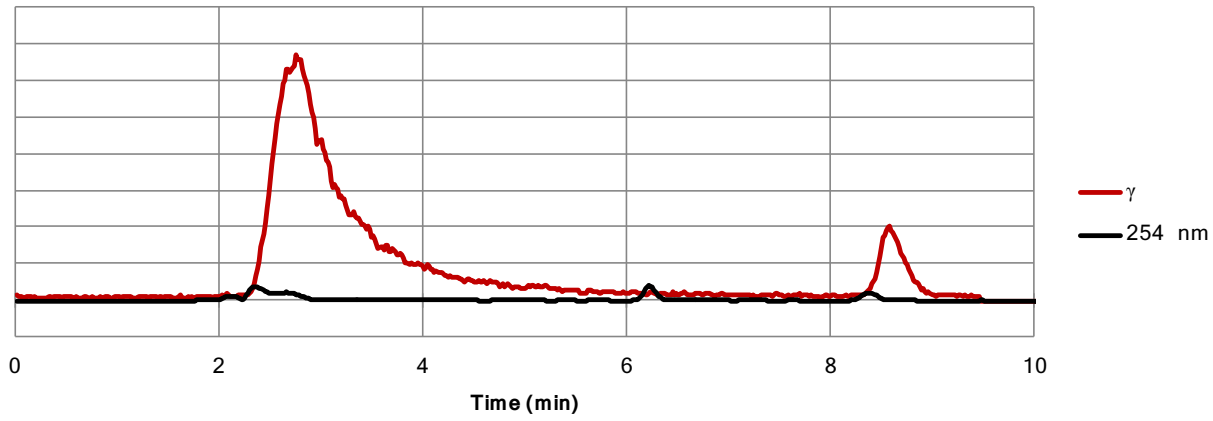


RadioHPLC chromatography

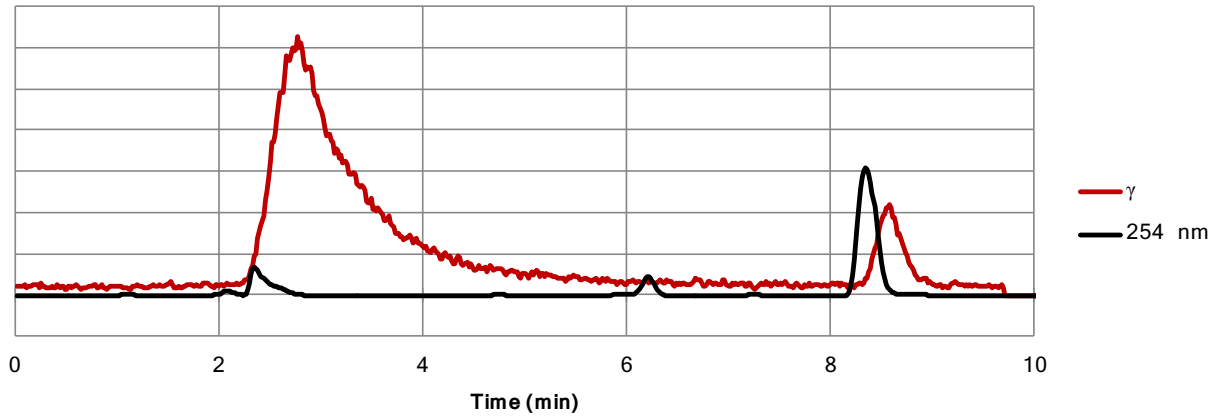
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 70% acetonitrile, 30% 0.1 M ammonium formate, 1 mL/min

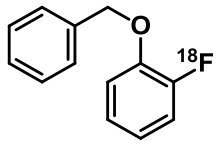
Crude:



Coinjection with standard:



[^{18}F]*ortho*-benzyloxyphenylfluoride

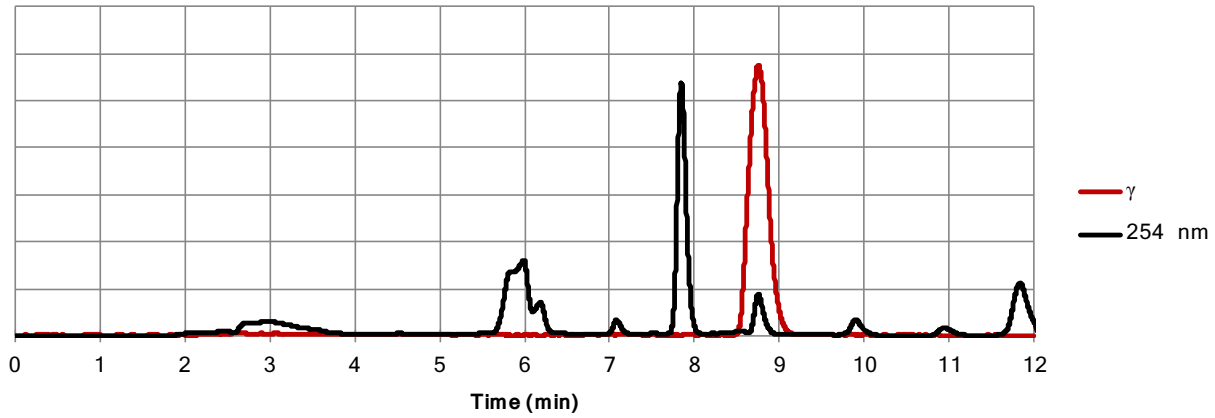


RadioHPLC chromatography

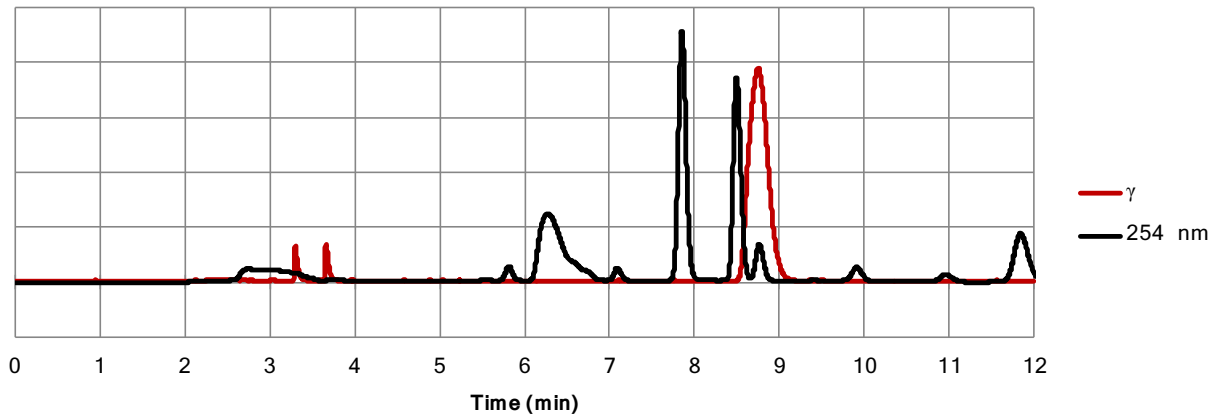
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 1:1 acetonitrile:0.1 M ammonium formate, 1 mL/min, 1 min; linear gradient to 9:1, 4 min; 9:1, 5 min; 1:1, 2 min

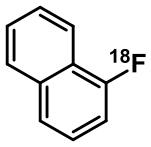
Crude:



Coinjection with standard:



[^{18}F]1-fluoronaphthalene

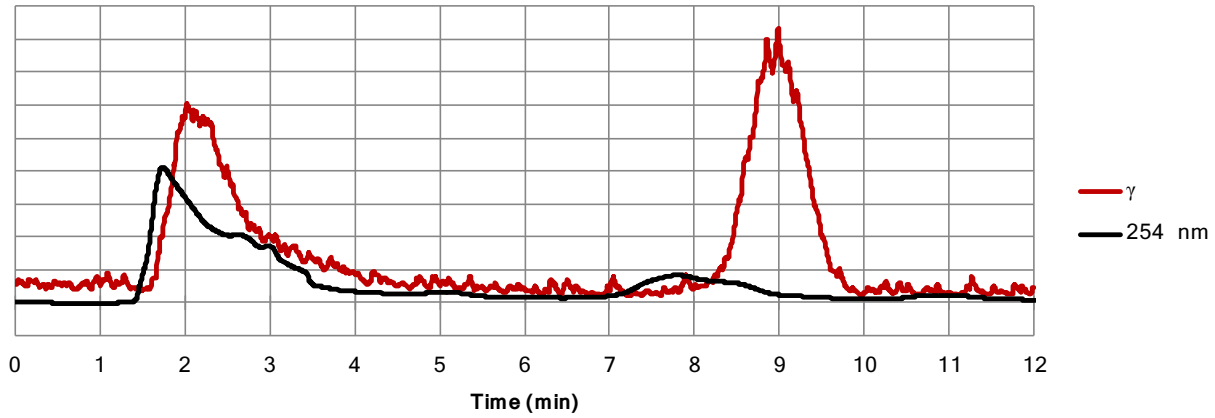


RadioHPLC chromatography

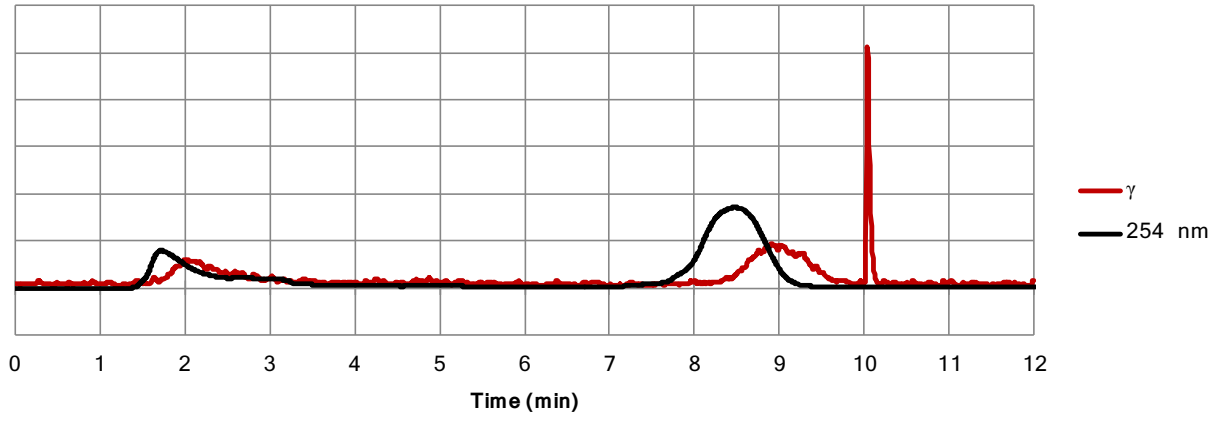
Stationary phase: Luna C18, 5 μm, 100 Å, 250 × 4.6 mm

Mobile phase: 1:1 acetonitrile:0.1 M ammonium formate, 1 mL/min, 1 min; linear gradient to 9:1, 4 min; 9:1, 5 min; 1:1, 2 min

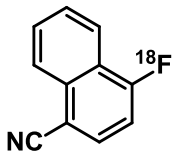
Crude:



Coinjection with standard:



[^{18}F]4-fluoro-1-naphthonitrile

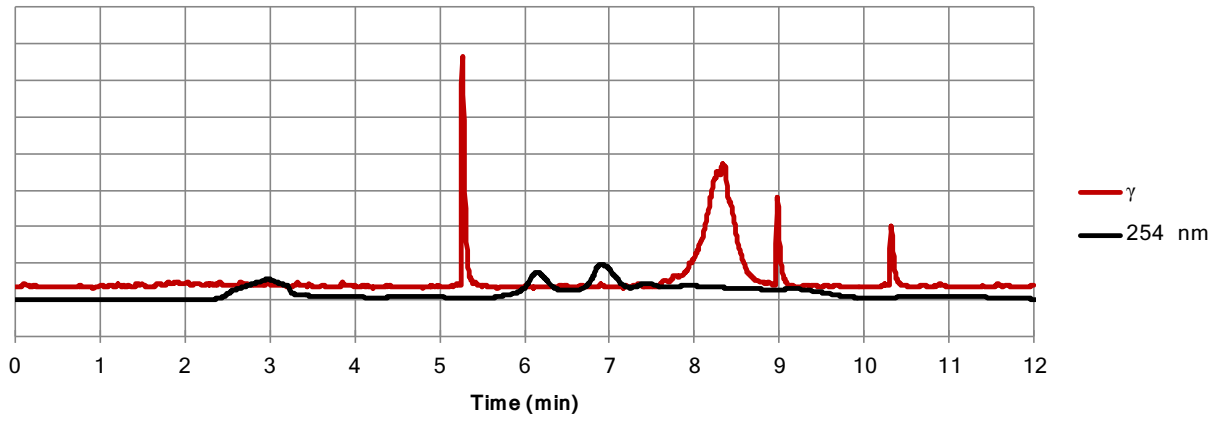


RadioHPLC chromatography

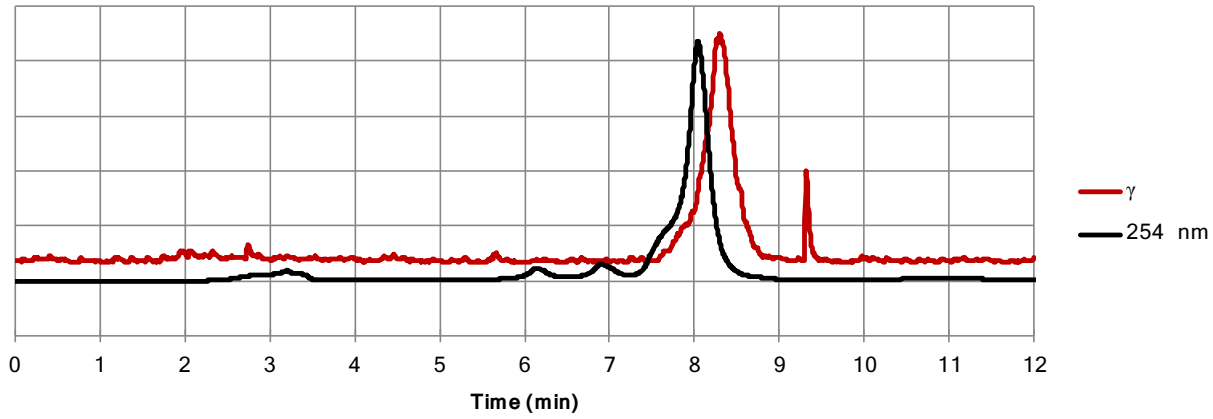
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 1:1 acetonitrile:0.1 M ammonium formate, 1 mL/min, 1 min; linear gradient to 9:1, 4 min; 9:1, 5 min; 1:1, 2 min

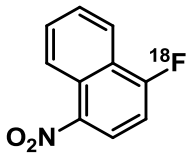
Crude:



Coinjection with standard:



[^{18}F]1-fluoro-4-nitronaphthalene

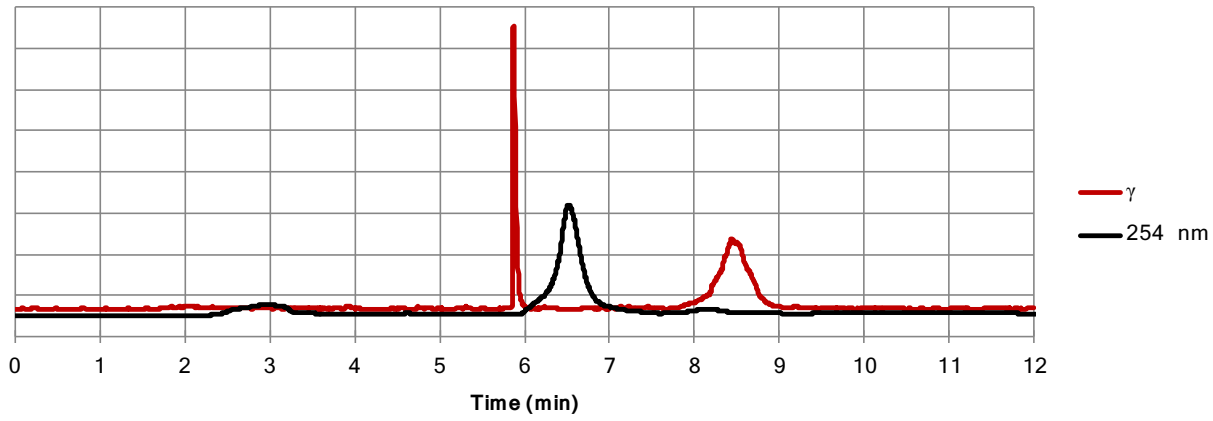


RadioHPLC chromatography

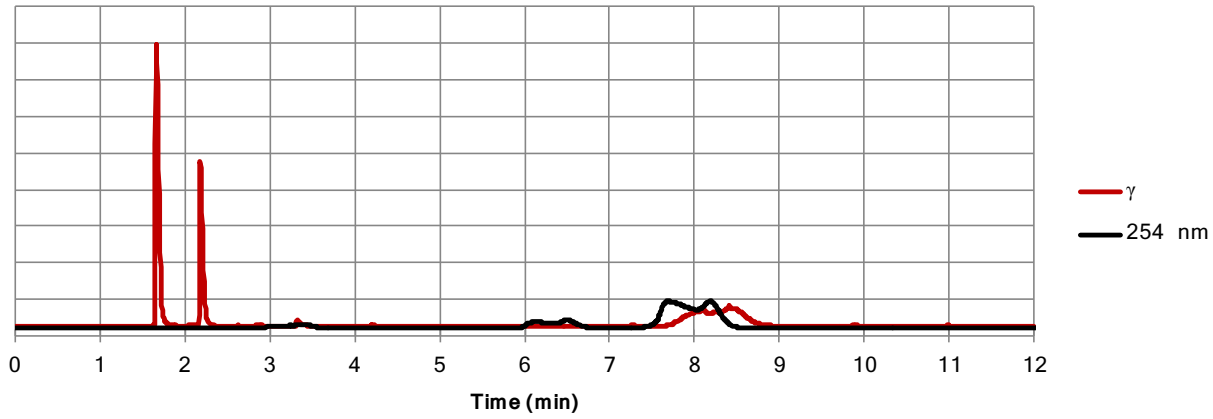
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 1:1 acetonitrile:0.1 M ammonium formate, 1 mL/min, 1 min; linear gradient to 9:1, 4 min; 9:1, 5 min; 1:1, 2 min

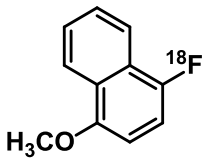
Crude:



Coinjection with standard:



[^{18}F]1-fluoro-4-methoxynaphthalene

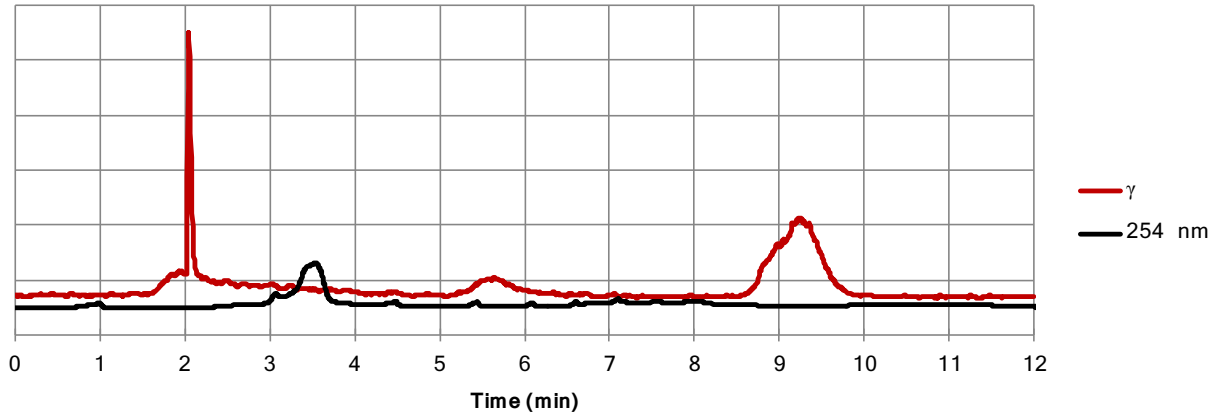


RadioHPLC chromatography

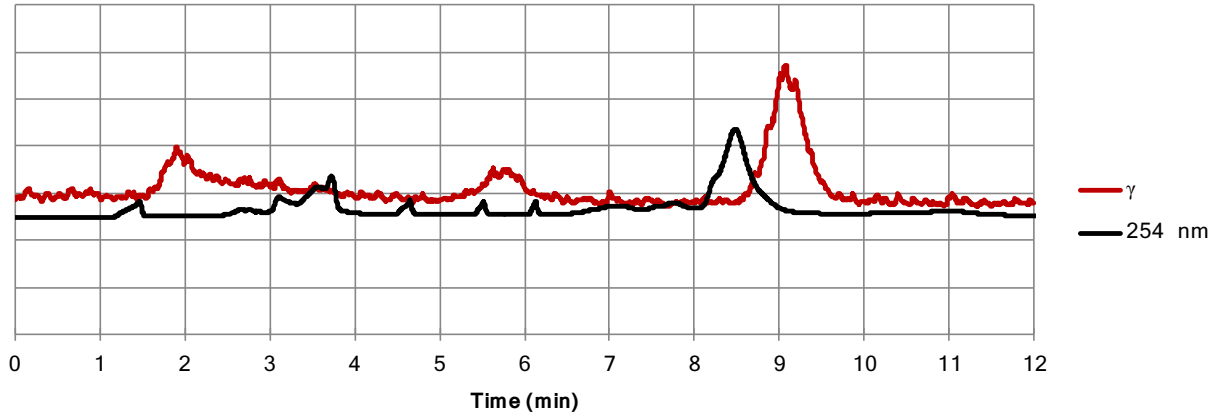
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 1:1 acetonitrile:0.1 M ammonium formate, 1 mL/min, 1 min; linear gradient to 9:1, 4 min; 9:1, 5 min; 1:1, 2 min

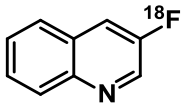
Crude:



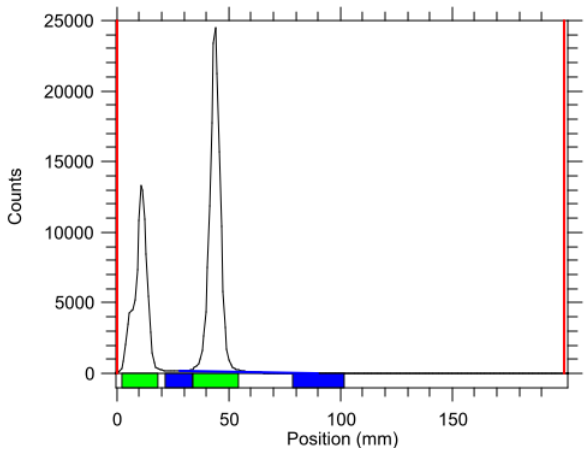
Coinjection with standard:



[^{18}F]3-fluoroquinoline



RadioTLC chromatography



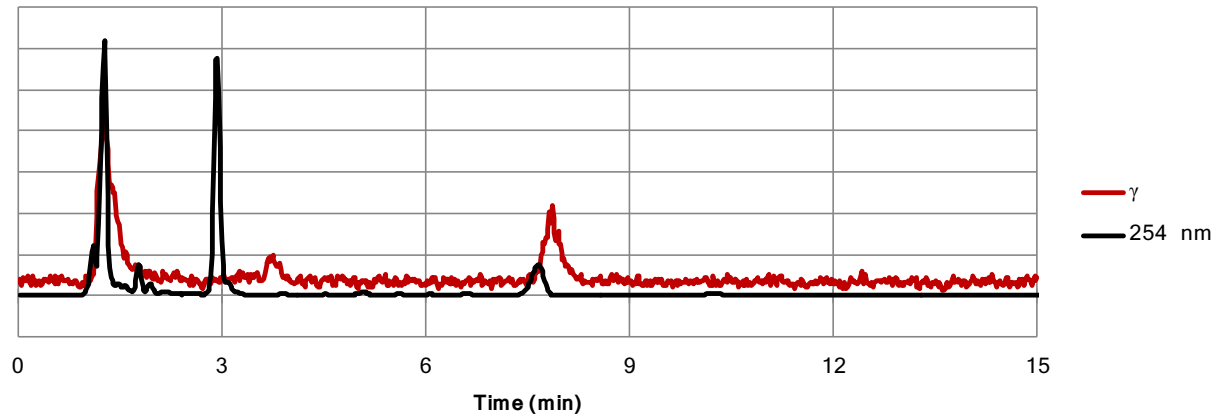
	1	2	3	mean	standard deviation
RCC (%)	56	68	62	62	6

RadioHPLC chromatography

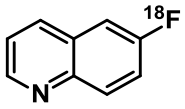
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

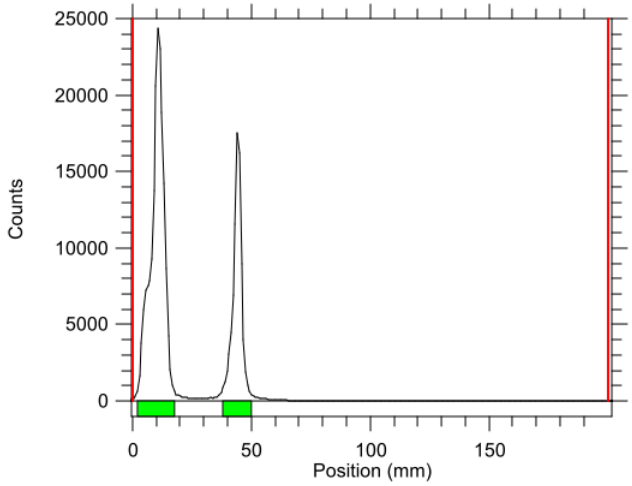
Coinjection with standard:



[^{18}F]6-fluoroquinoline



RadioTLC chromatography



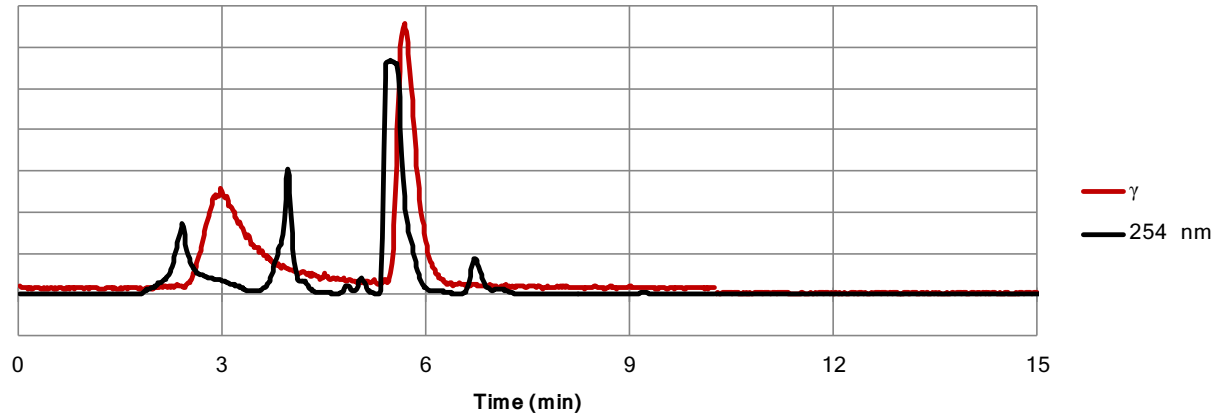
	1	2	3	mean	standard deviation
RCC (%)	54	84	82	73	17

RadioHPLC chromatography

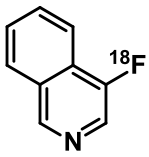
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

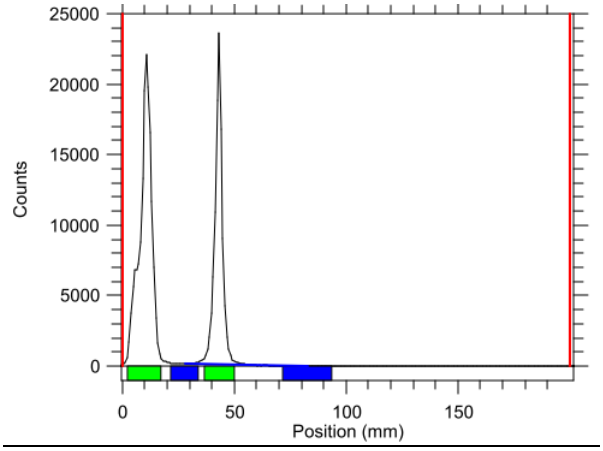
Coinjection with standard:



[^{18}F]4-fluoroisoquinoline



RadioTLC chromatography



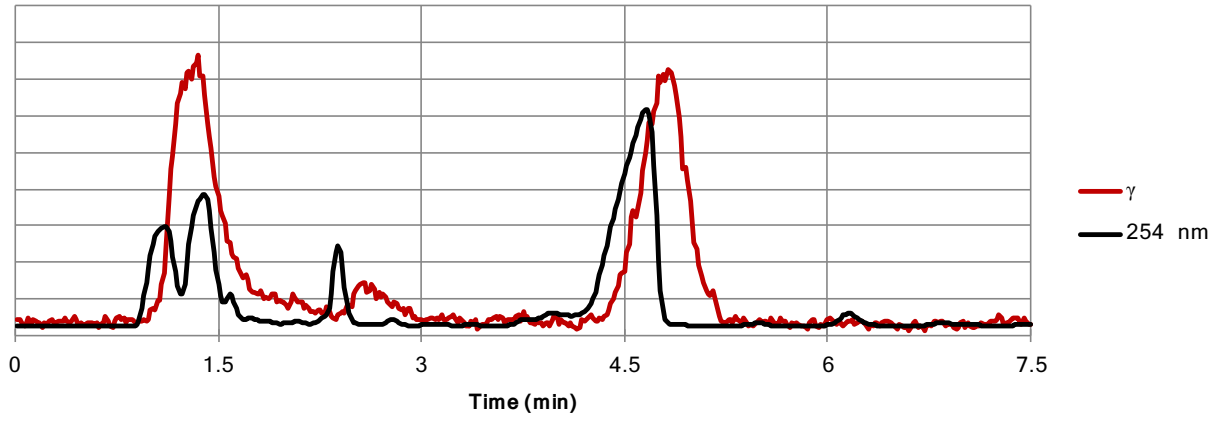
	1	2	3	mean	standard deviation
RCC (%)	73	80	86	80	7

RadioHPLC chromatography

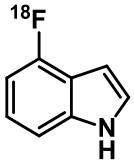
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

Coinjection with standard:

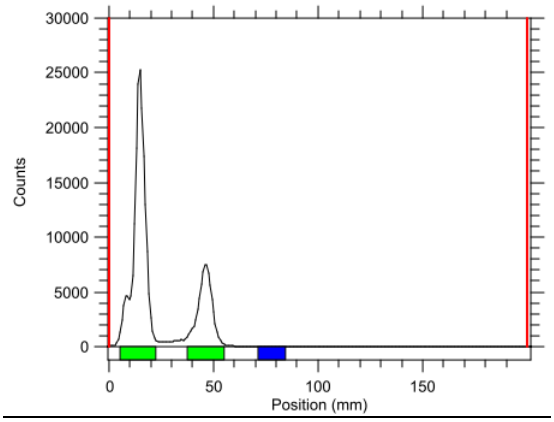


[^{18}F]4-fluoroindole



Note: N-Boc indole is spontaneously deprotected during radiofluorination.

RadioTLC chromatography



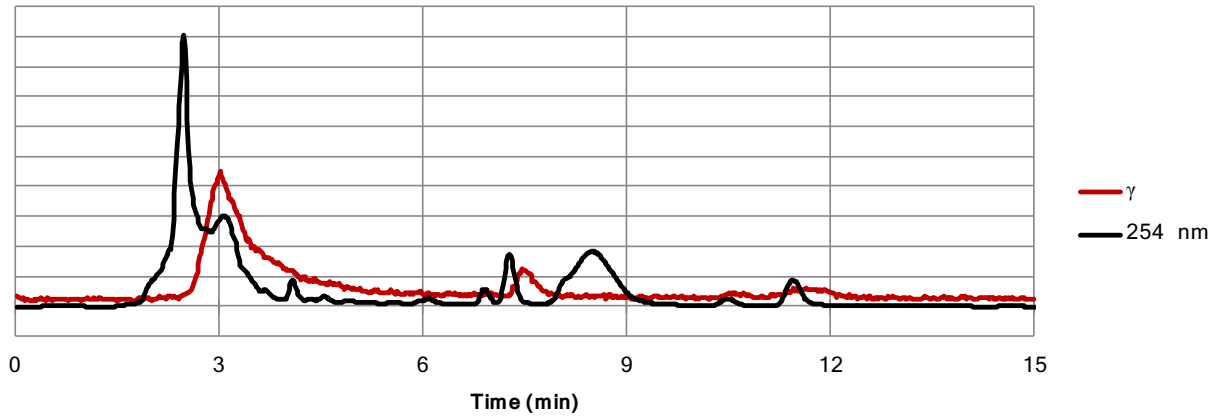
	1	2	3	mean	standard deviation
RCC (%)	45	29	35	36	8

RadioHPLC chromatography

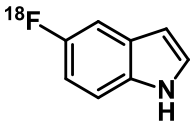
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

Coinjection with standard:

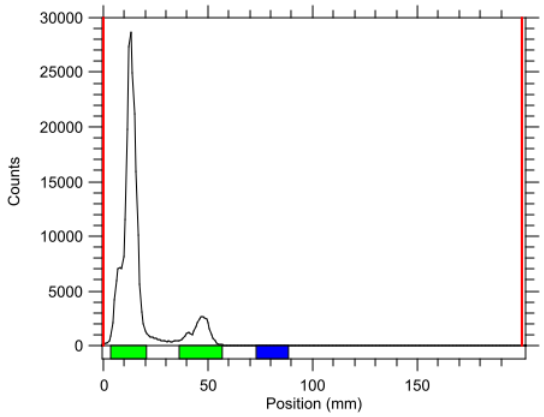


[^{18}F]5-fluoroindole



Note: N-Boc indole is spontaneously deprotected during radiofluorination.

RadioTLC chromatography



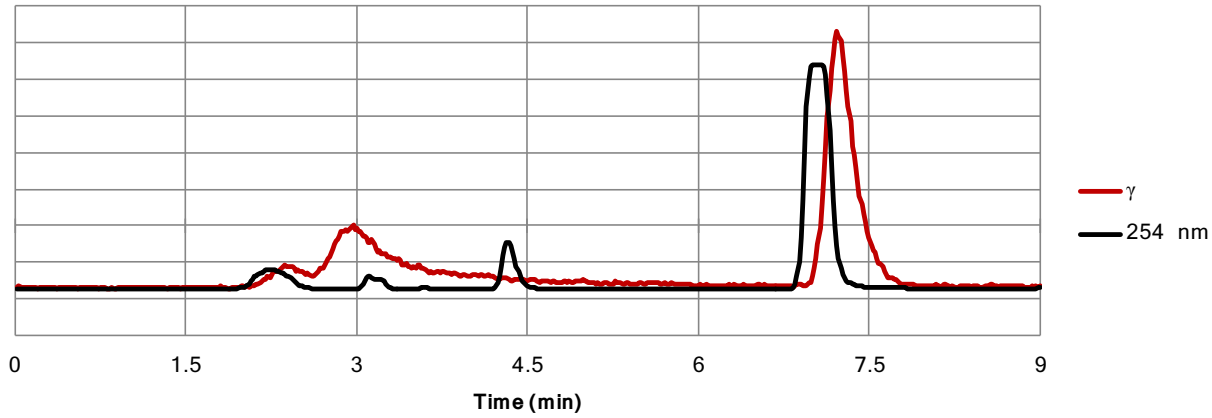
	1	2	3	mean	standard deviation
RCC (%)	5	13	6	8	4

RadioHPLC chromatography

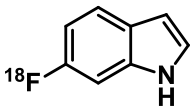
Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

Coinjection with standard:

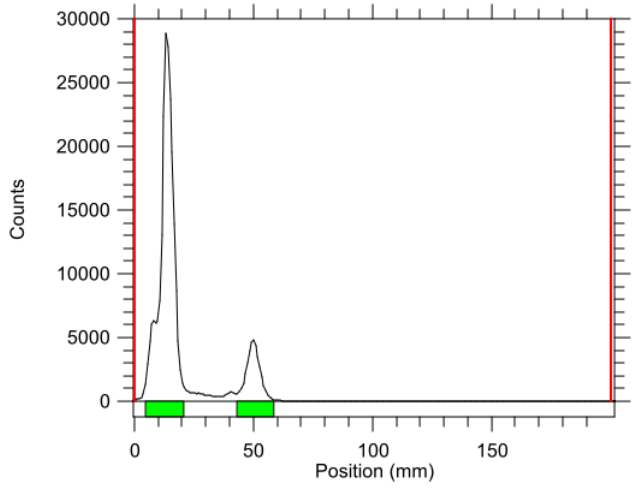


[^{18}F]6-fluoroindole



Note: N-Boc indole is spontaneously deprotected during radiofluorination.

RadioTLC chromatography



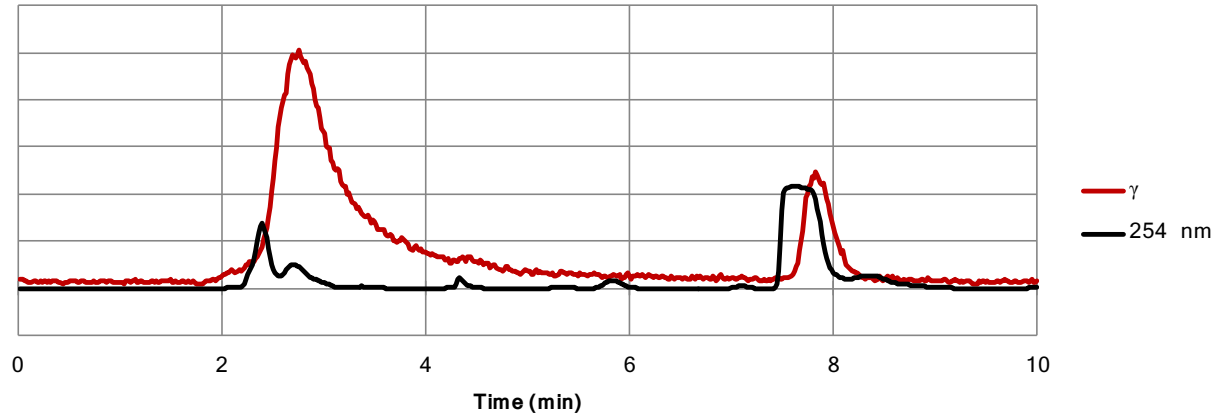
	1	2	3	mean	standard deviation
RCC (%)	27	23	18	23	5

RadioHPLC chromatography

Stationary phase: Luna C18, 5 µm, 100 Å, 250 × 4.6 mm

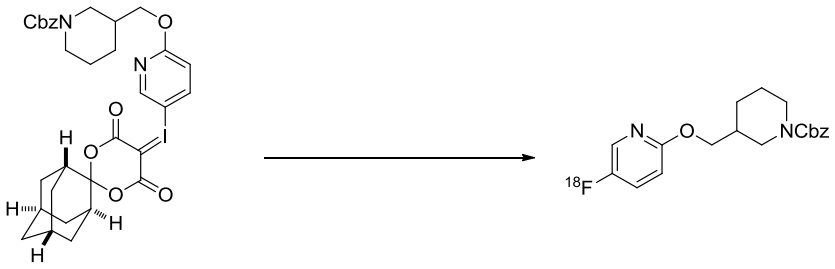
Mobile phase: 60% acetonitrile 40% 0.1 M ammonium formate, 1 mL/min

Coinjection with standard:



Radiofluorination and characterization of labeled drug fragments

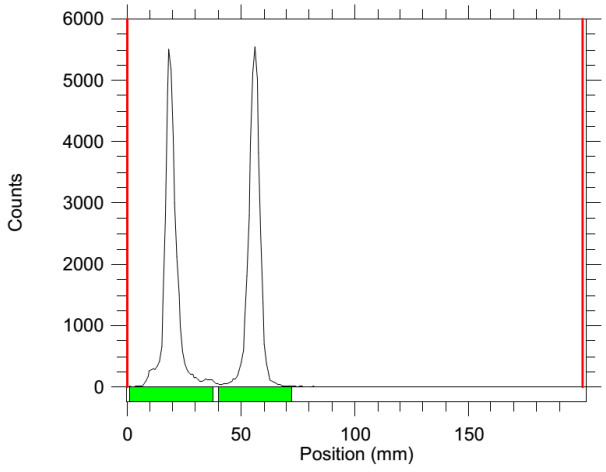
1. filorexant



S1-6 **20**

(1) Method: TEAB (3 mg) was used to dry [^{18}F]fluoride. A solution of precursor (6 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 150 °C for 10 min, and then quenched with HPLC mobile phase (75% CH_3CN, 25% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (24 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]20**.

(2) RadioTLC chromatogram of unpurified mixture:



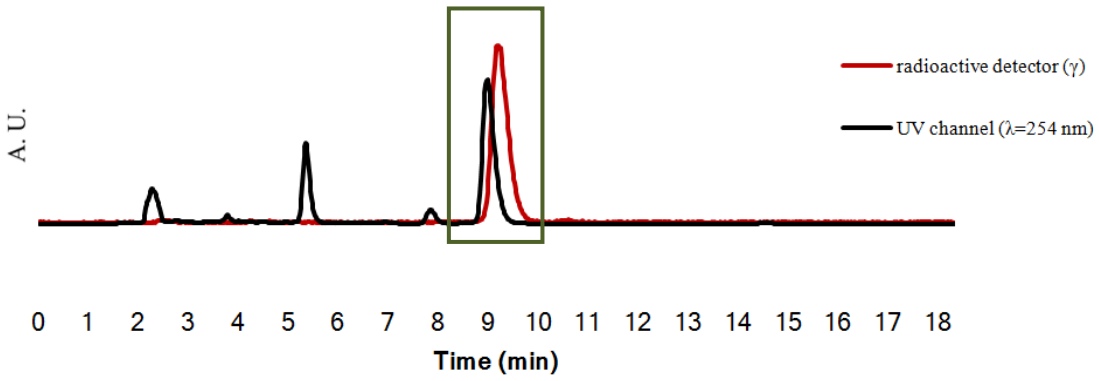
	1	2	3	4	5	mean	standard deviation
RCC (%)	50	42	47	42	43	45	4

(3) RadioHPLC chromatogram:

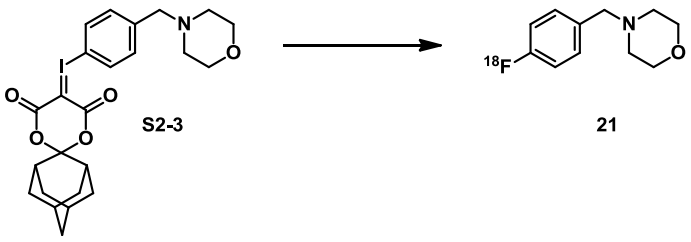
Column: luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 75% CH_3CN, 25% 0.1 M NH_4HCO_2(aq)

Flow rate: 1mL/min



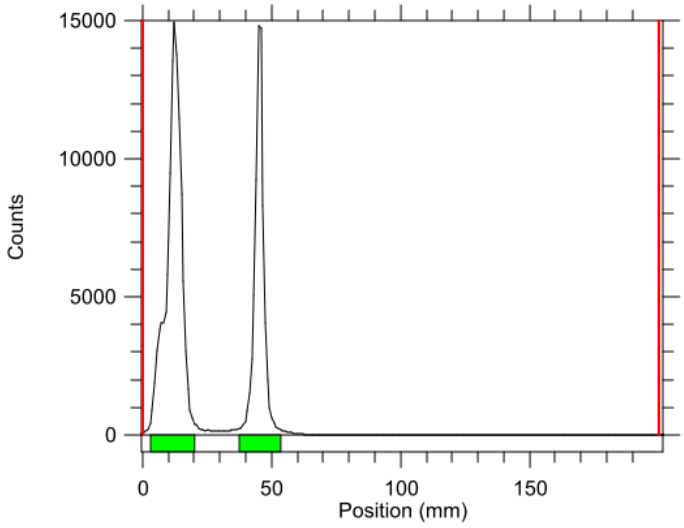
2. mosapride



(1) Method: TEAB (2 mg) was used to dry [^{18}F]fluoride. A solution of precursor (2 mg) in DMF (0.4 mL) was added to the vial and the mixture heated to 120 ℃ for 10 min, then quenched with water. A silica gel TLC plate was spotted with the crude mixture and developed with 100% EtOAc to determine radiochemical conversion (RCC). The identity of the product was confirmed

by coinjection with the nonradioactive standard **[^{19}F]21** by HPLC and in-line UV and radiation detectors.

(2) RadioTLC chromatogram of unpurified mixture:

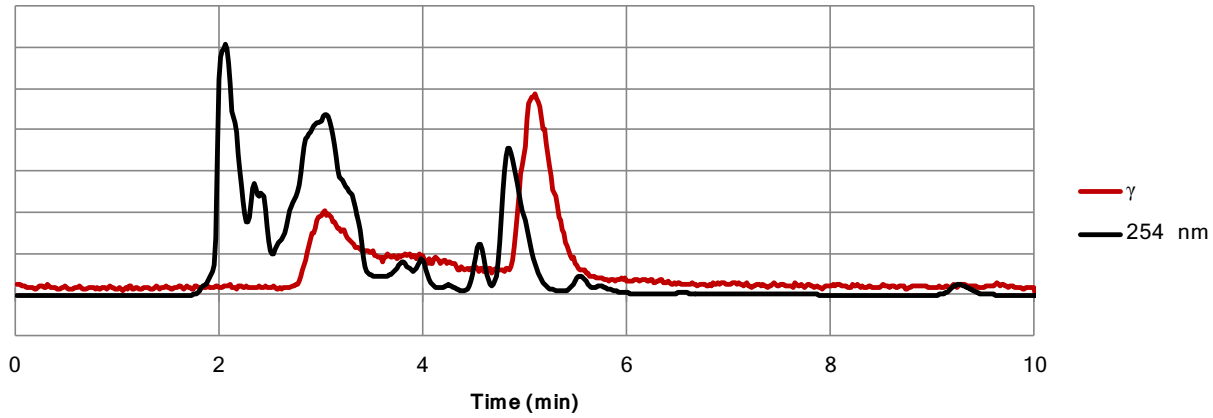


	1	2	3	mean	standard deviation
RCC (%)	38	39	29	35	6

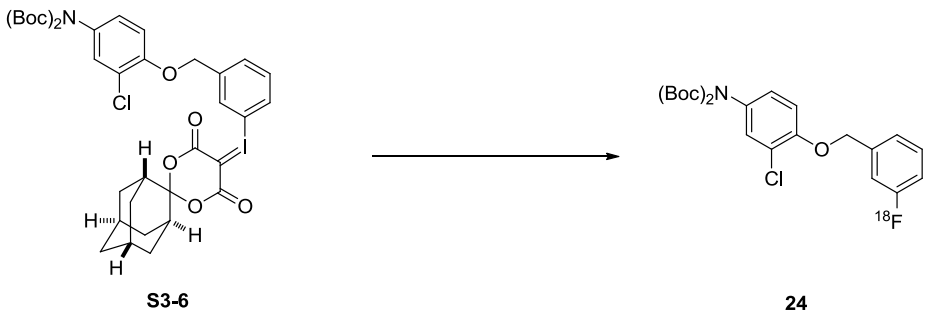
(3) RadioHPLC chromatogram:

Stationary phase: Luna C18, 5 μm, 100 Å, 250 × 4.6 mm

Mobile phase: 60% acetonitrile, 40% 0.1 M ammonium formate, 1 mL/min

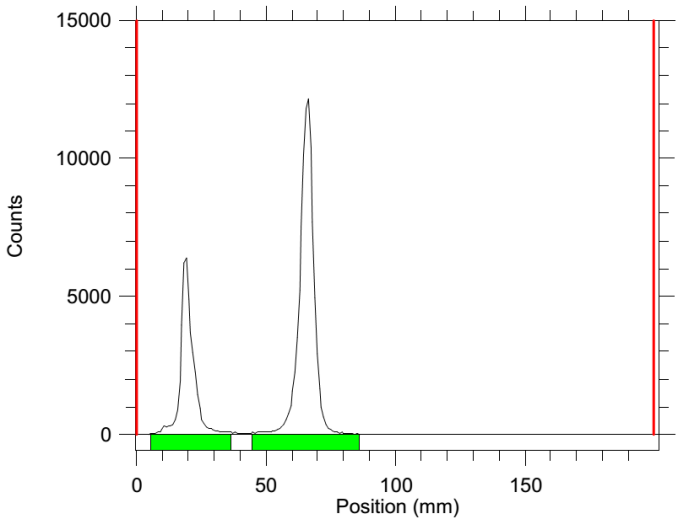


3. lapatinib



(1) Method: TEAB (3 mg) was used to dry [^{18}F]fluoride. A solution of precursor (4 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 95 °C for 11 min, and then quenched with HPLC mobile phase (75% CH_3CN, 25% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]24**.

(2) RadioTLC chromatogram of unpurified mixture:



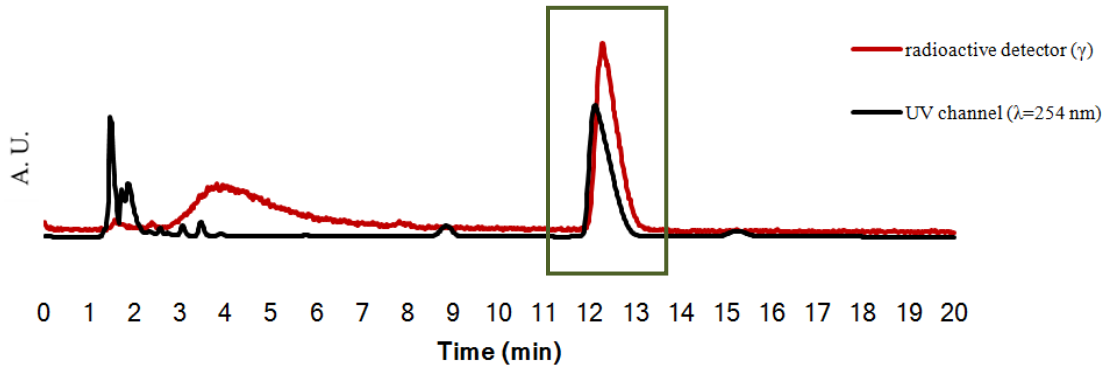
	1	2	3	4	mean	standard deviation
RCC (%)	69	58	61	76	66	8

(3) RadioHPLC chromatogram:

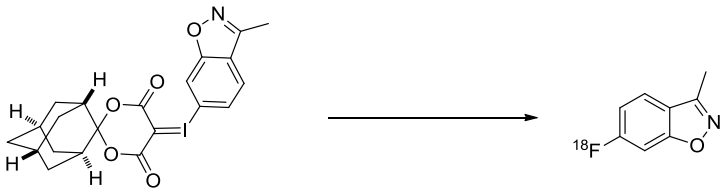
Column: luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 75% CH_3CN, 25% 0.1 M NH_4HCO_2(aq)

Flow rate: 1.5 mL/min

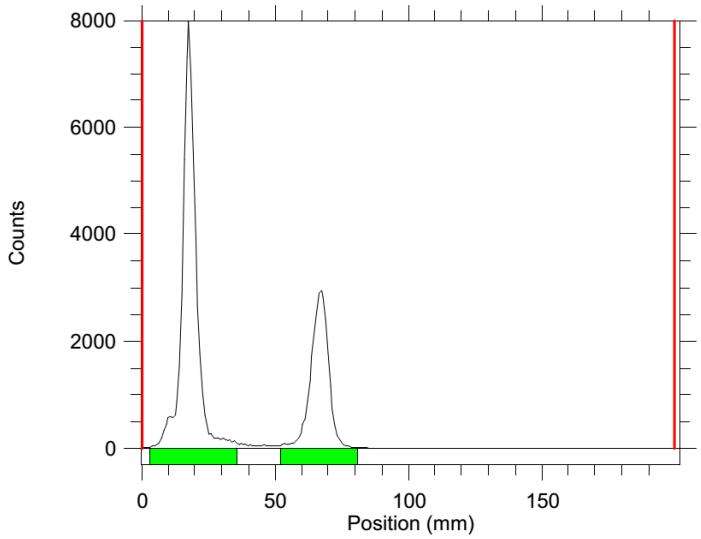


4. risperidone



(1) Method: TEAB (2 mg) was used to dry [^{18}F]fluoride. A solution of precursor (2.5 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 120 °C for 15 min, and then quenched with HPLC mobile phase (60% CH_3CN, 40% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]17**.

(2) RadioTLC chromatogram of unpurified mixture:



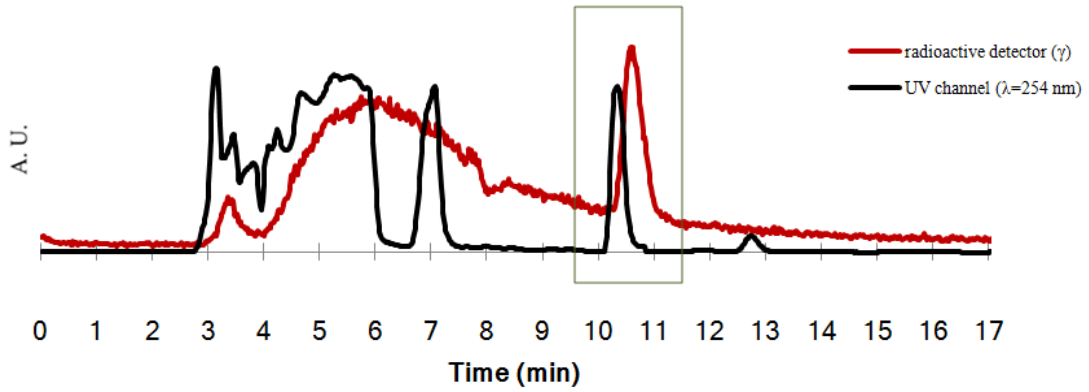
	1	2	3	mean	standard deviation
RCC (%)	24	30	22	25	4

(3) RadioHPLC chromatogram:

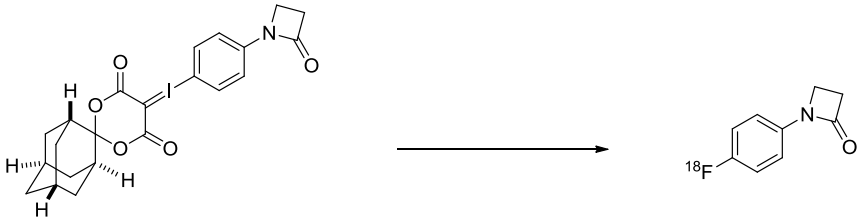
Column: luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M NH_4HCO_2(aq)

Flow rate: 1.5 mL/min

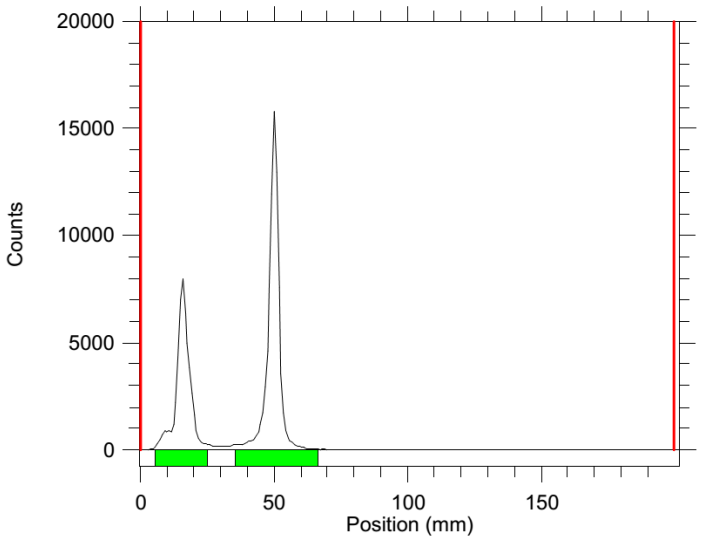


5. ezetimibe



(1) Method: TEAB (3 mg) was used to dry [^{18}F]fluoride. A solution of precursor (5 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 130 °C for 12 min, and then quenched with HPLC mobile phase (40% CH_3CN, 60% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (24 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]22**.

(2) RadioTLC chromatogram of unpurified mixture:



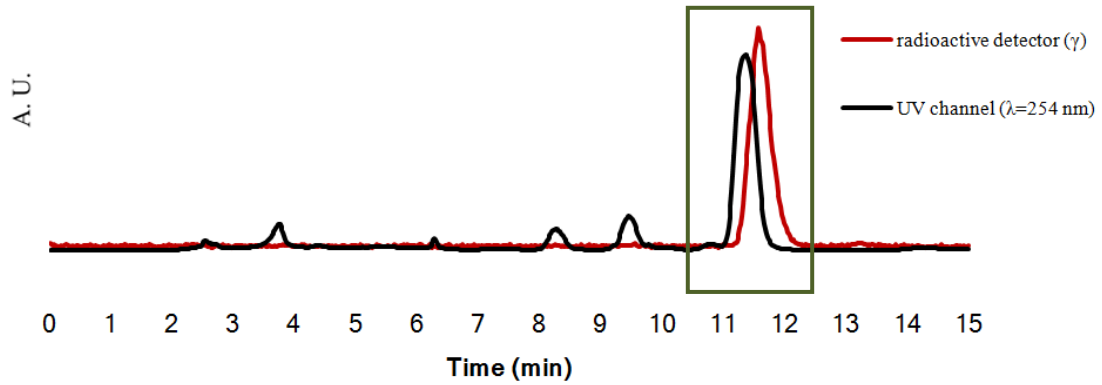
	1	2	3	mean	standard deviation
RCC (%)	61	86	65	71	13

(3) RadioHPLC chromatogram:

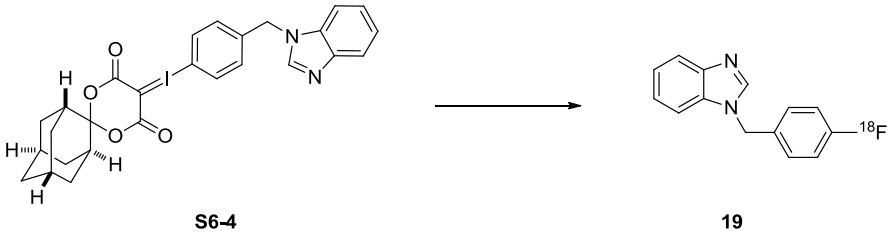
Column: luna 5u C18 100 Å 250 ×4.6 mm

Mobile phase: 40% CH_3CN, 60% 0.1 M NH_4HCO_2(aq)

Flow rate: 1mL/min

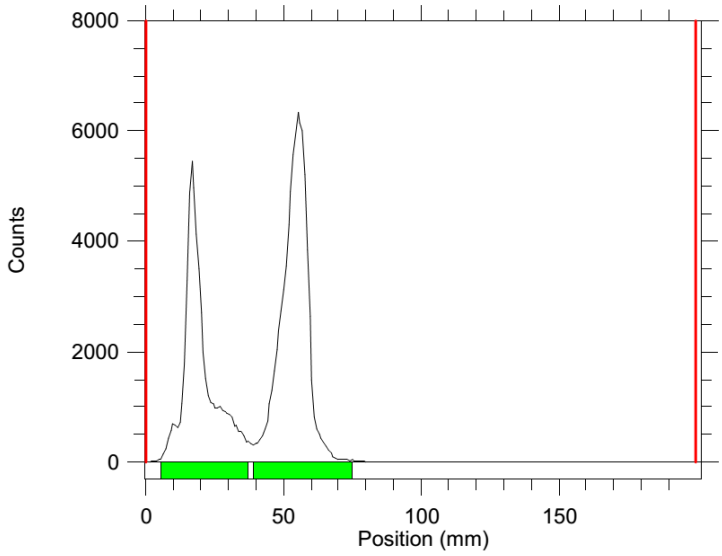


6. astemizole



(1) Method: TEAB (3 mg) was used to dry [^{18}F]fluoride. A solution of precursor (6 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 140 ˚C for 11 min, and then quenched with HPLC mobile phase (50% CH_3CN, 50% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (30 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]19**.

(2) RadioTLC chromatogram of unpurified mixture:



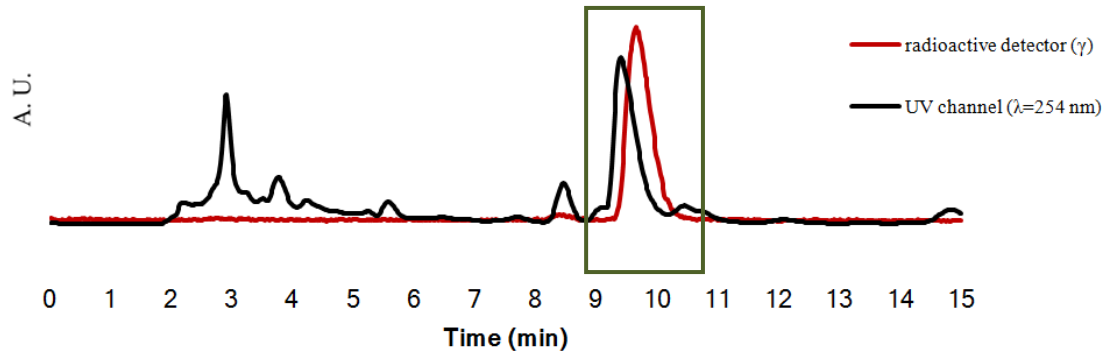
	1	2	3	mean	standard deviation
RCC (%)	59	44	51	51	7

(3) RadioHPLC chromatogram:

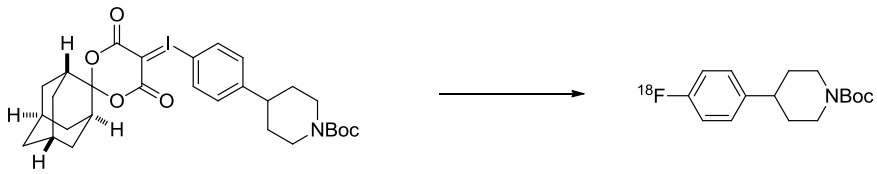
Column: luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 50% CH_3CN, 50% 0.1 M NH_4HCO_2(aq)

Flow rate: 1mL/min



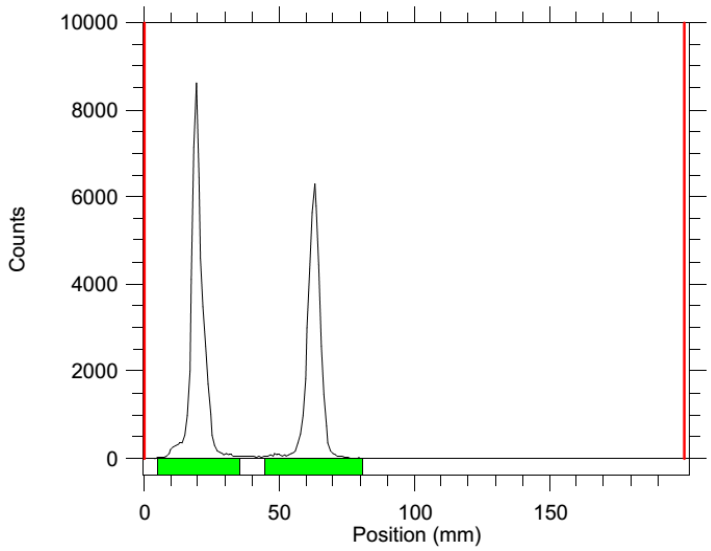
7. paroxetine



S7-4 **23**

(1) Method: TEAB (3 mg) was used to dry [^{18}F]fluoride. A solution of precursor (5.4 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 110 °C for 12 min, and then quenched with HPLC mobile phase (70% CH_3CN, 30% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (30 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]23**.

(2) RadioTLC chromatogram of unpurified mixture:



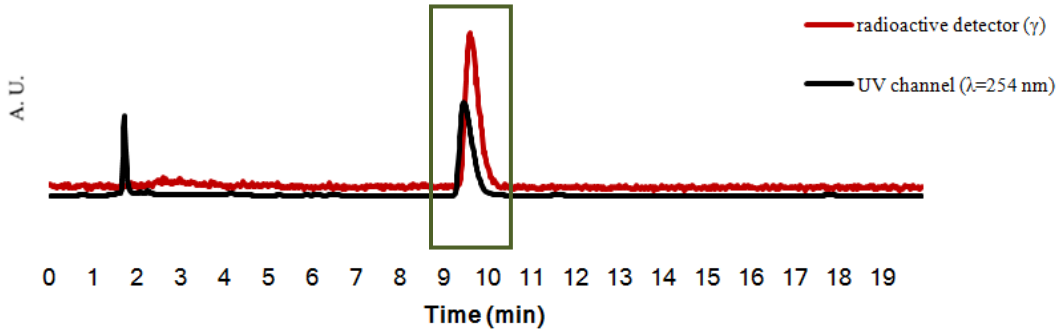
	1	2	3	mean	standard deviation
RCC (%)	46	39	38	41	4

(3) RadioHPLC chromatogram:

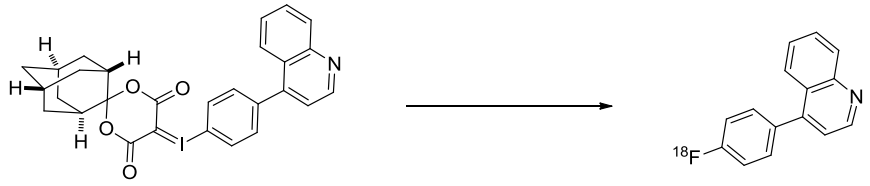
Column: luna 5u C18 100 Å 250 ×4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M NH_4HCO_2(aq)

Flow rate: 1.5 mL/min



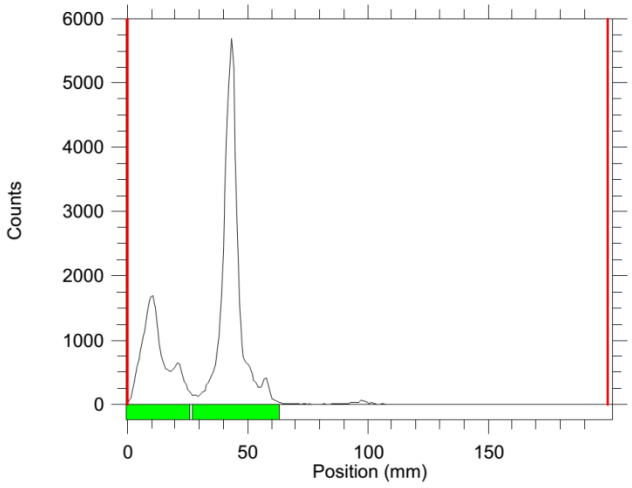
8. pitavastatin



S8-7 **18**

(1) Method: TEAB (2.5 mg) was used to dry [^{18}F]fluoride. A solution of precursor (5.2 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 110 °C for 12 min, and then quenched with HPLC mobile phase (70% CH_3CN, 30% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (10 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]18**.

(2) RadioTLC chromatogram of unpurified mixture:



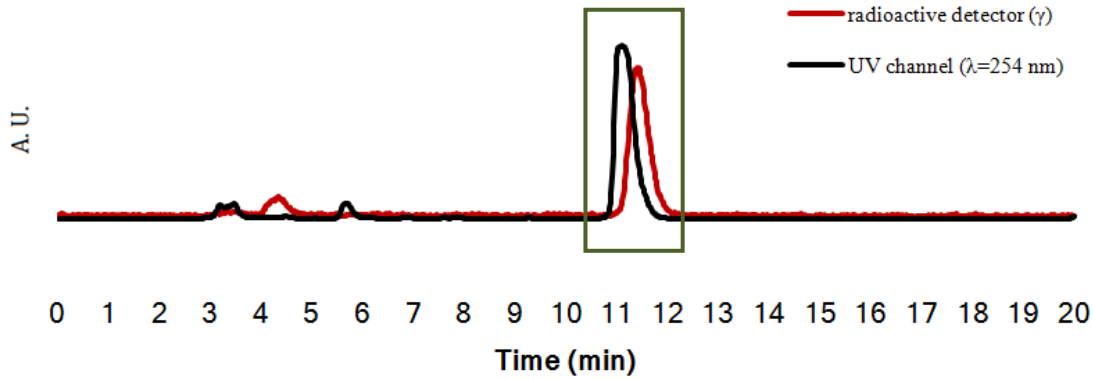
	1	2	3	mean	standard deviation
RCC (%)	68	50	54	57	9

(3) RadioHPLC chromatogram:

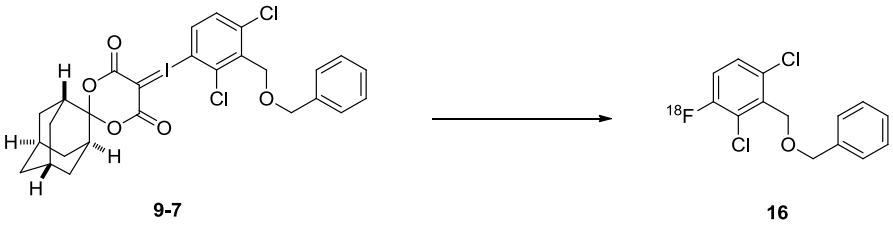
Column: luna 5u C18 100 Å 250 × 4.6 mm

Mobile phase: 70% CH_3CN, 30% 0.1 M NH_4HCO_2(aq)

Flow rate: 1.5 mL/min



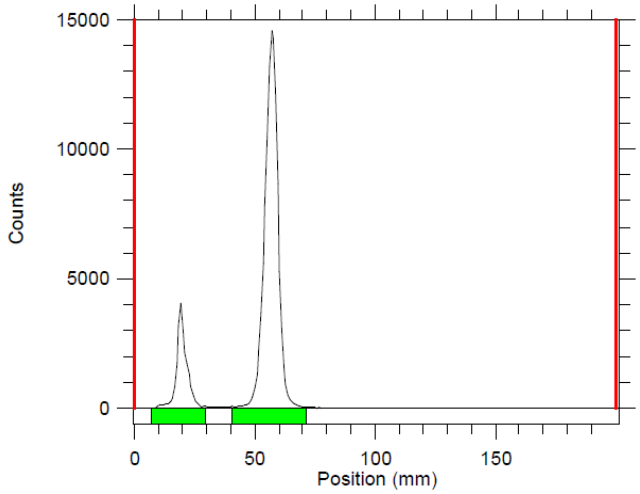
9. crizotinib



9-7 16

(1) Method: TEAB (2.0 mg) was used to dry [^{18}F]fluoride. A solution of precursor (1.4 mg) in DMF (0.4 mL) was added in the vial. The mixture was heated at 100 °C for 12 min, and then quenched with HPLC mobile phase (80% CH_3CN, 20% 0.1 M NH_4HCO_2(aq), 0.2 mL). TLC plate was spotted with crude mixture (2 μL) and developed with 100% EtOAc to determine the radiochemical conversion (RCC). Then the solution was diluted with water (15 mL), passed through C18 cartridge, washed with water (20 mL), and eluted with acetonitrile (1.5 mL) into a new vial. The mixture (20 μL) was injected into the radio-HPLC to determine the identity via coinjection with standard **[^{19}F]16**.

(2) RadioTLC chromatogram of unpurified mixture:



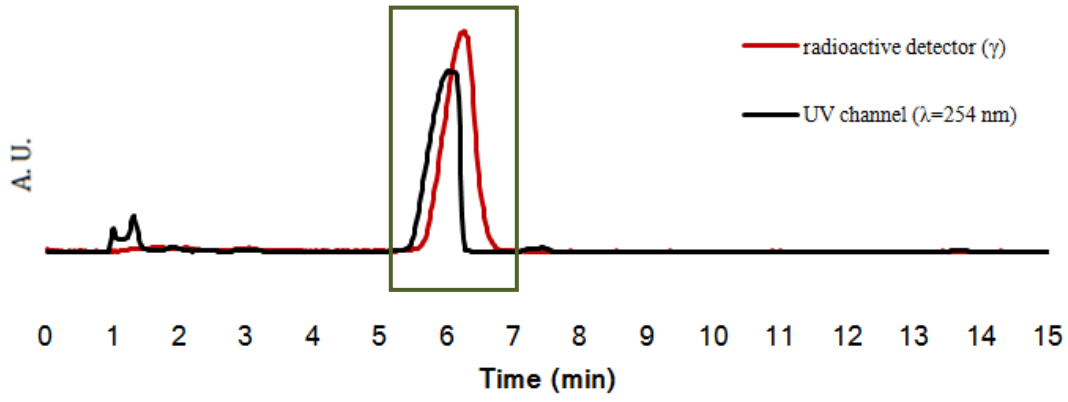
	1	2	3	4	mean	standard deviation
RCC (%)	83	75	80	89	82	6

(3) RadioHPLC chromatogram:

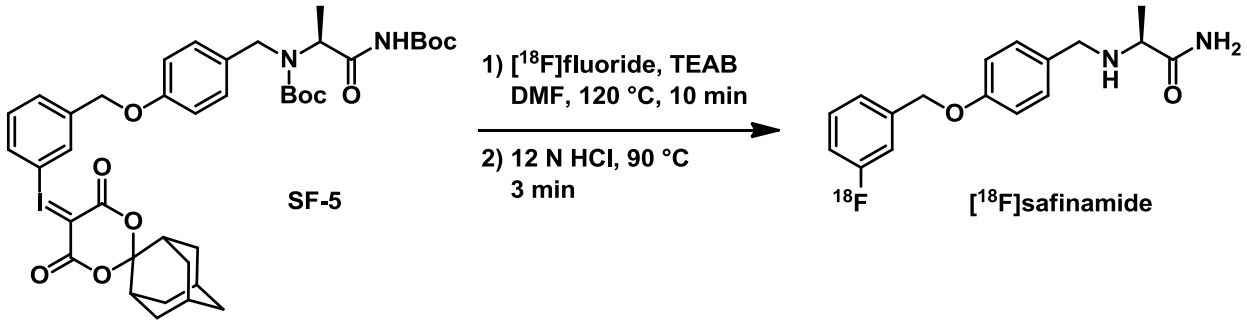
Column: XBridge^{TM} C18 3.5 μm 100 × 4.6 mm

Mobile phase: 60% CH_3CN, 40% 0.1 M NH_4HCO_2(aq)

Flow rate: 1.0 mL/min

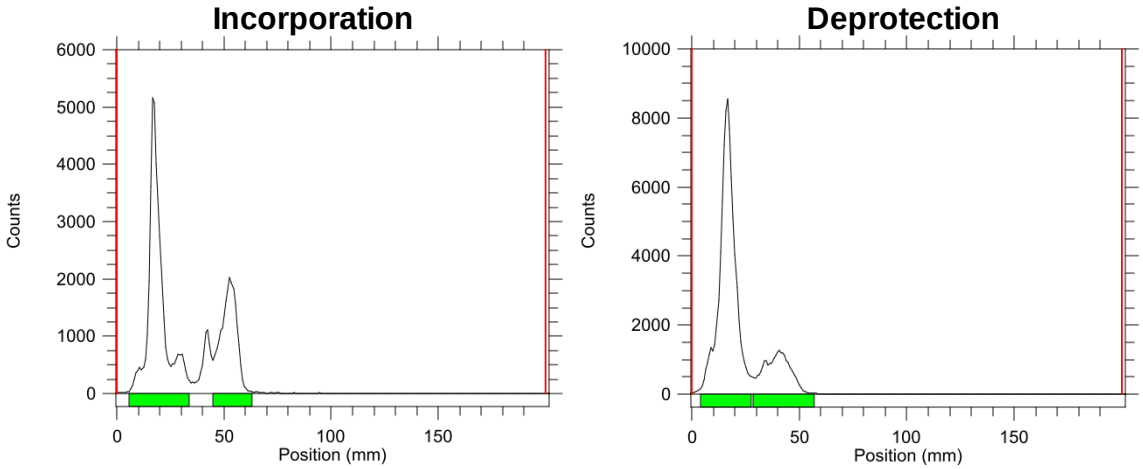


Preparation of [^{18}F]safinamide



(1) Method: [^{18}F]Fluoride was dried by iterative azeotropic evaporation of anhydrous acetonitrile in the presence of *N*,*N*,*N*,*N*-tetraethylammonium bicarbonate (TEAB). The residue was diluted with anhydrous *N*,*N*-dimethylformamide to produce a 10 mg mL^{-1} solution of TEAB. A 400 µL aliquot of this solution was added to V-vial containing 2 mg of precursor **SF-5**. The mixture was heated to 120 °C for 10 min, and then cooled to room temperature. An aliquot of 12 N HCl (0.2 mL) was added to the vial, which was then heated to 90 °C for 3 minutes. A sample of the crude reaction mixture was withdrawn and neutralized with aqueous sodium bicarbonate. The sample was analyzed by radioTLC (SiO_2, developed with EtOAc) to determine the radiochemical conversion (RCC), and radioHPLC coinjection with nonradioactive standard to confirm identity.

(2) RadioTLC chromatograms:



^{18}F-Incorporation

	1	2	3	mean	standard deviation
RCC (%)	19	13	12	15	4

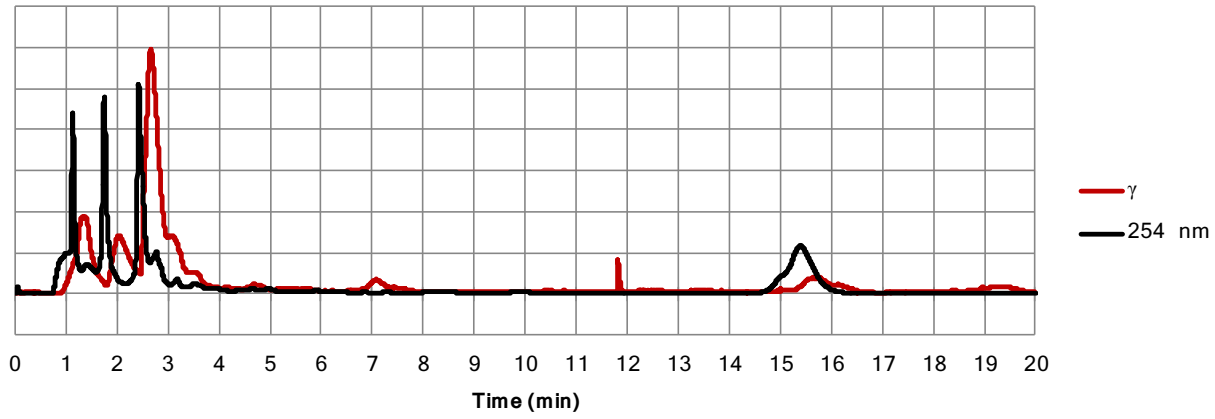
(3) RadioHPLC chromatograms:

Analytical:

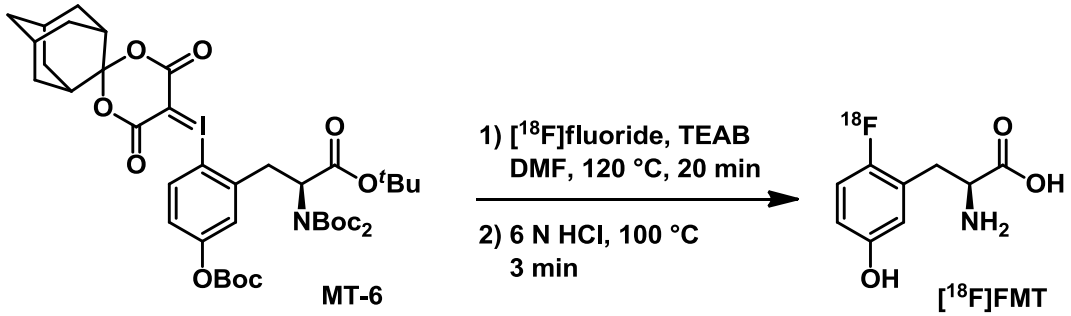
Stationary phase: Eclipse Plus C18, 100 × 4.6 mm, 3.5 µm

Mobile phase: 30% CH_3CN, 0.1% $NH_4OH_{(aq)}$, 1 mL min^{-1}

Note: Sharp peaks in the radiation chromatogram are artifacts from the radiation detector.

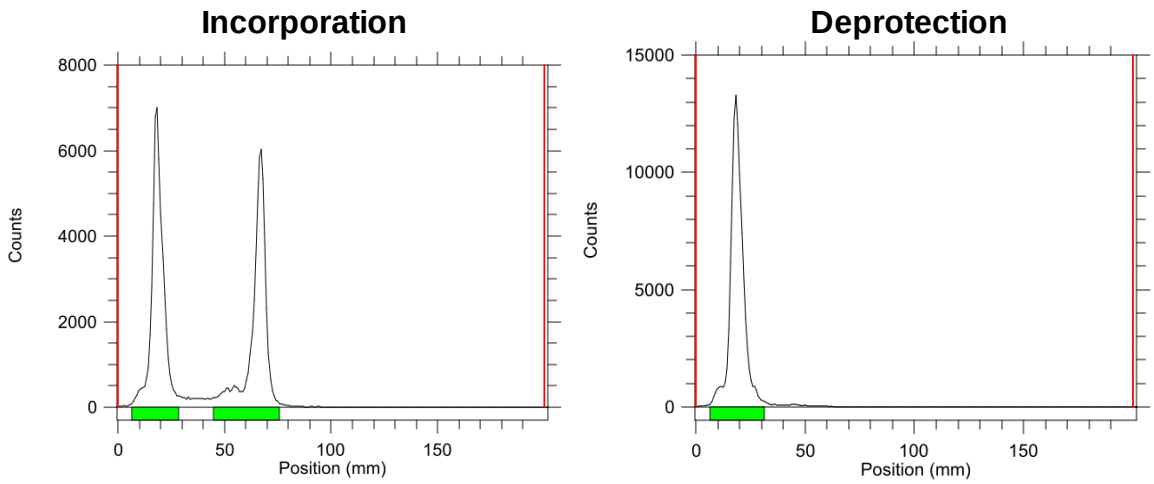


Preparation of 6-[^{18}F]fluoro-*meta*-tyrosine



(1) Method: An aliquot (0.1–0.5 mL) of cyclotron target water containing [^{18}F]fluoride (0.5–1.5 mCi, measured in a dose calibrator, t_0) was added to a V-vial containing *N*,*N*,*N*,*N*-tetraethylammonium bicarbonate (TEAB, 2.0 mg). Acetonitrile (1 mL) was added and the mixture heated to 110 ℃ with nitrogen gas flowing through the vial until no bulk liquid was visible. This drying step was then repeated three more times using anhydrous acetonitrile. The vial was cooled for 2 minutes in a room temperature water bath, before addition of a solution of precursor **MT-6** (4.0 mg) in anhydrous DMF (0.2 mL). The vial was then sealed and heated to 120 ℃ for 20 minutes, after which it was again cooled in a room temperature water bath. A sample of the reaction mixture (1–2 μL) was withdrawn and spotted on a silica-coated TLC plate that was then developed using ethyl acetate to quantify radioactive incorporation. A solution of 6 N HCl (0.2 mL) was added to the reaction vial, which was then heated to 100 ℃ for 3 minutes, followed by cooling to room temperature. Again, a sample of the reaction mixture was withdrawn and radioTLC conducted as described above to determine the extent of deprotection. The reaction mixture was partially neutralized with 5 N NaOH (0.2 mL), and diluted with HPLC mobile phase (5% MeOH, 0.1% HCO_2H, 1.0 mL). The contents of the reactor were then loaded into an injector loop and purified by semi-preparative HPLC (stationary phase: Luna C18, 250 × 10 mm, 100 Å, 5 μm; mobile phase as described above, 5 mL·min^{-1}; t_R = ~8 min). Fractions containing product were collected and radioactivity measured in a dose calibrator to determine isolated yield (EOS). The total time from t_0 to EOS was 60 ± 1 min.

(2) RadioTLC chromatograms:



^{18}F-Incorporation

	1	2	3	4	5	mean	standard deviation
RCC (%)	62	56	53	51	56	56	4

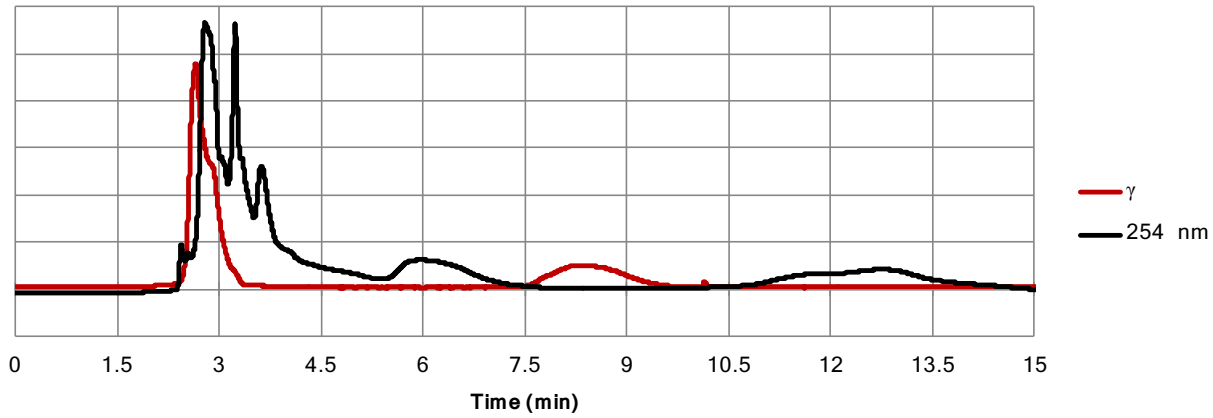
Deprotection: Extent of deprotection was evaluated at different time points. Under the conditions employed, no non-polar radioactive compound was observed by rTLC after 2 min reaction time. Therefore, isolation experiments were performed using 3 min heating for deprotection. Extent of deprotection was uniformly ≥99%.

(3) RadioHPLC chromatograms:

Semipreparative purification:

Stationary phase: Luna C18, 250 × 10 mm, 100 Å, 5 µm

Mobile phase: 5% MeOH, 0.1% HCO_2H, H_2O, 5 mL min^{-1}



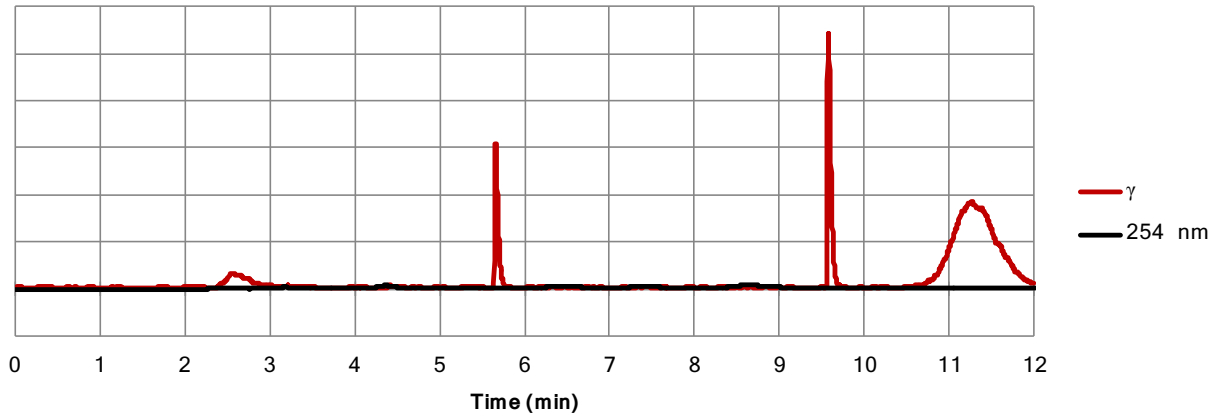
Analytical:

Stationary phase: Luna C18, 250 × 4.6 mm, 100 Å, 5 µm

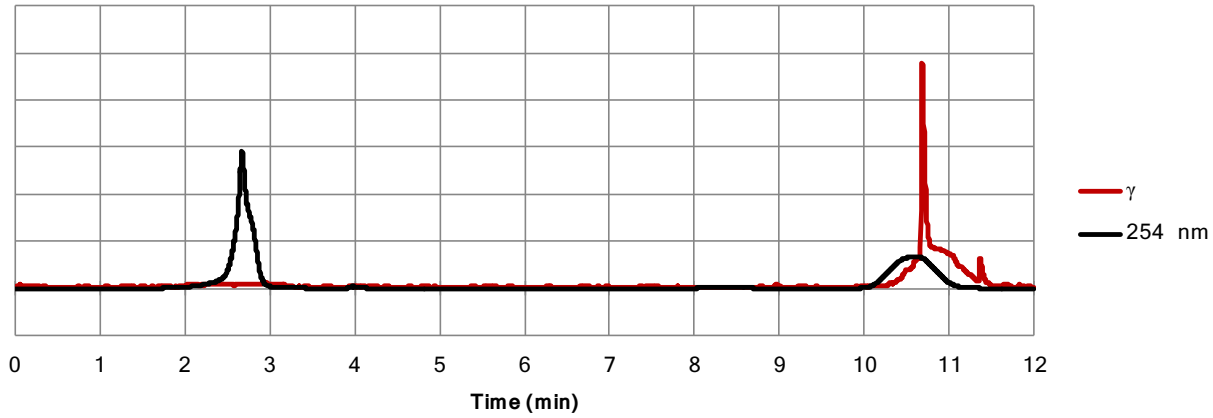
Mobile phase: 5% MeOH, 0.1% HCO_2H, H_2O, 1 mL min^{-1}

Note: Sharp peaks in the radiation chromatogram are artifacts from the radiation detector.

Purified product:



Coinjection with standard:



Radiochemical purity ranged from 95–99% for this product.

(4) Yield calculation:

Isolated yields were calculated as the quotient of measured activity isolated at end-of-synthesis and the measured activity in cyclotron target water at beginning-of-synthesis, and expressed as a

percentage. No corrections for decay or material losses (*e.g.*, activity withdrawn for analysis, potentially volatile radioactive species, or residual activity in vials, syringes, or purification equipment) are factored into the calculation. Product must be identified as ≥95% radiochemically pure to qualify.

(5) Optimization using SPI5-Precursor

Prior to the discovery of SPIAd-activated iodonium(III) ylides, significant efforts were undertaken to develop a radiofluorination precursor based on a SPI5-precursor for 6-[^{18}F]fluoro-*meta*-tyrosine. This included optimization of the base and base-loading, temperature, precursor loading, and reaction time. Conditions were evaluated by time-course measurements as described above, using rTLC to measure radiochemical conversion. The results are presented in the following plots:

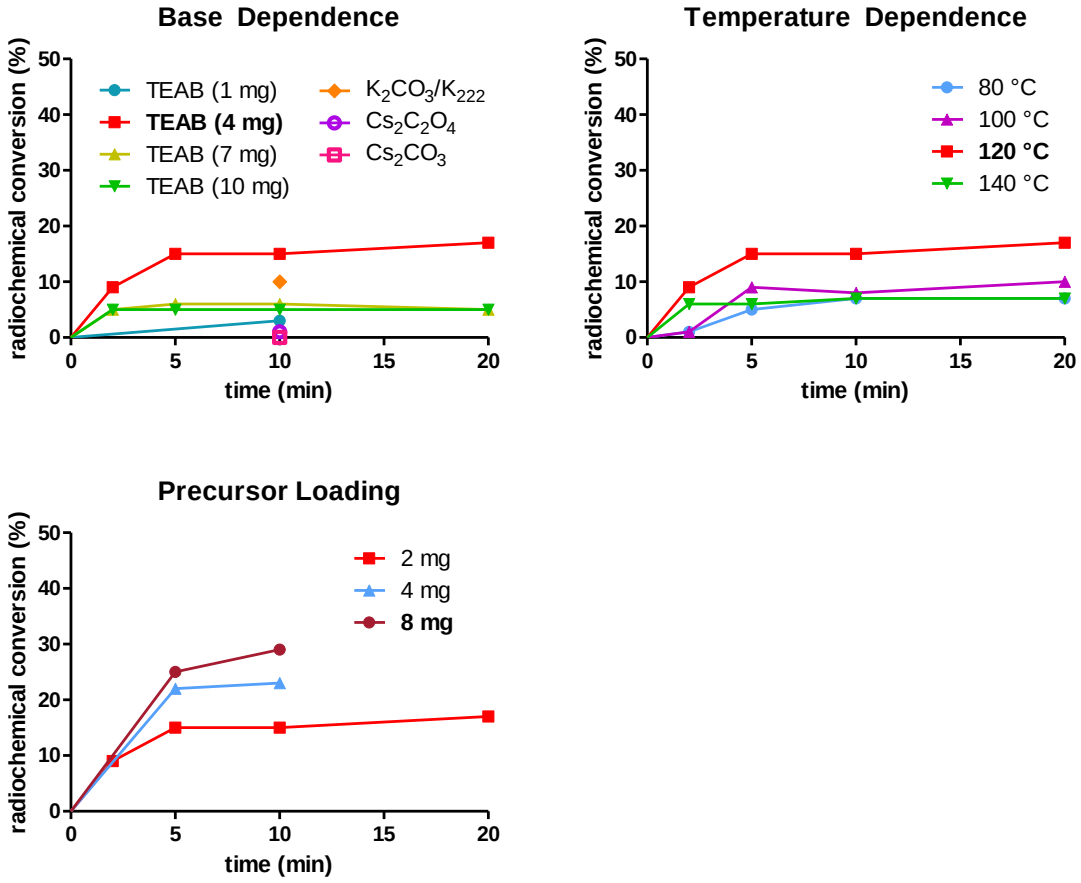
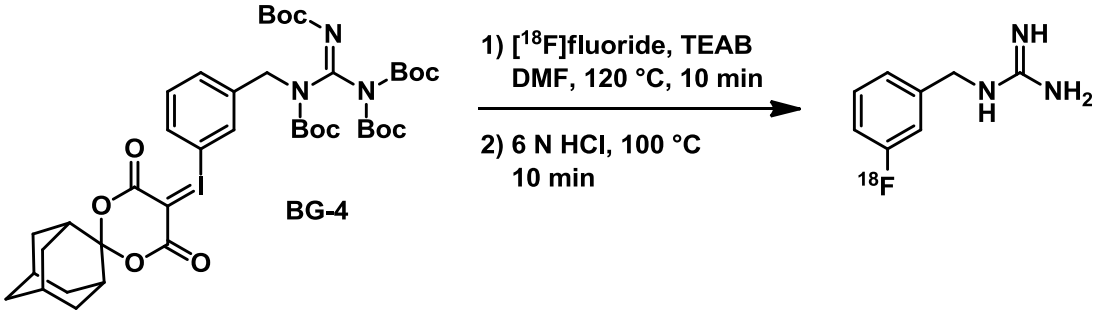


Figure S1 Optimization of [^{18}F]FMT with SPI5-precursor

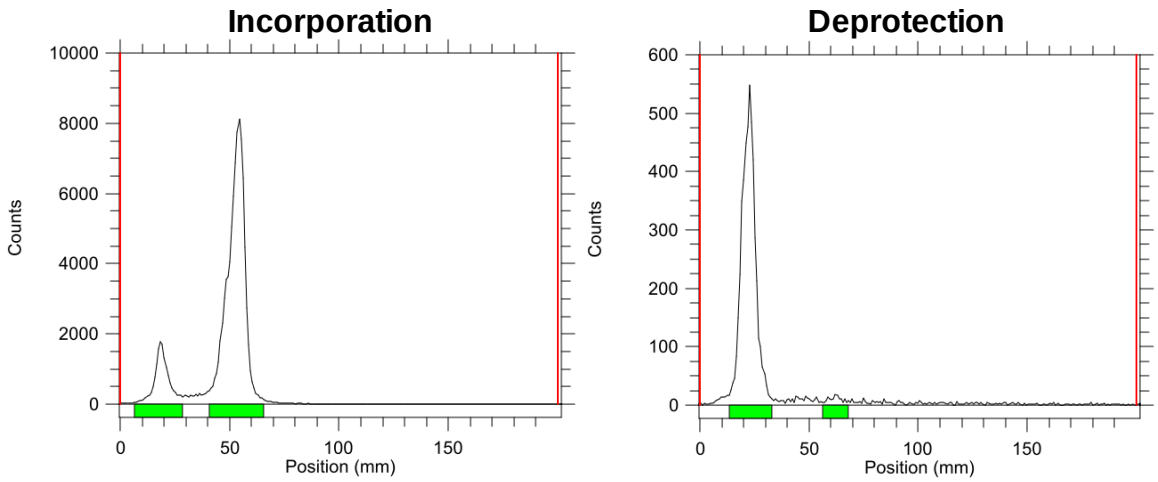
Both the maximum conversion from the first two and the third plot was confirmed by quantitative deprotection and solid-phase extraction purification. All attempts to further improve RCC using this precursor were unsuccessful. Isolation of [^{18}F]fluoro-*meta*-tyrosine from these reactions yielded at most 5% isolated radiochemical yield.

Preparation of [^{18}F]*meta*-fluorobenzylguanidine ([^{18}F]mFBG)



(1) Method: An aliquot (0.1–0.5 mL) of cyclotron target water containing [^{18}F]fluoride (0.5–1.5 mCi, measured in a dose calibrator, t_0) was added to a V-vial containing *N*,*N*,*N*,*N*-tetraethylammonium bicarbonate (TEAB, 4.0 mg). Acetonitrile (1 mL) was added and the mixture heated to 110 °C with nitrogen gas flowing through the vial until no bulk liquid was visible. This drying step was then repeated three more times using anhydrous acetonitrile. The vial was cooled for 2 minutes in a room temperature water bath, before addition of a solution of precursor **BG-4** (4.0 mg) in anhydrous DMF (0.2 mL). The vial was then sealed and heated to 120 °C for 20 minutes, after which it was again cooled in a room temperature water bath. A sample of the reaction mixture (1–2 µL) was withdrawn and spotted on a silica-coated TLC plate that was then developed using ethyl acetate to quantify radioactive incorporation. A solution of 6 N HCl (0.2 mL) was added to the reaction vial, which was then heated to 100 °C for 10 minutes, followed by cooling to room temperature. Again, a sample of the reaction mixture was withdrawn and radioTLC conducted as described above to determine the extent of deprotection. The reaction mixture was partially neutralized with 5 N NaOH (0.2 mL), and diluted with HPLC mobile phase (10% EtOH, 28 mM HCl, 20 mM NH_4OAc, pH 2, 0.5 mL). The contents of the reactor were then loaded into an injector loop and purified by semi-preparative HPLC (stationary phase: Hamilton PRP-1, 250 × 10 mm, 10 µm; mobile phase as described above, 3.5 mL·min^{-1}; t_R = ~17 min). Fractions containing product were collected and radioactivity measured in a dose calibrator to determine isolated yield (EOS). The total time from t_0 to EOS was 75 ± 2 min.

(2) RadioTLC chromatograms:



^{18}F-Incorporation

	1	2	3	4	mean	standard deviation
RCC (%)	70	80	84	85	80	7

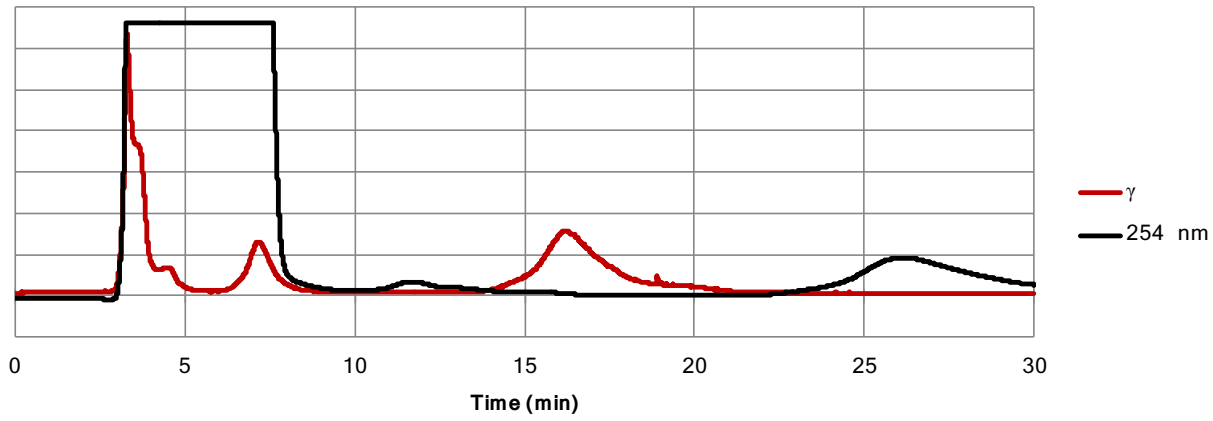
Deprotection: Extent of deprotection was typically ≥98%, with one exception for which a nonpolar radioactive peak accounted for 14% of total activity on the TLC plate.

(3) RadioHPLC chromatograms:

Semipreparative purification:[25]

Stationary phase: Hamilton PRP-1, 250 × 10 mm, 10 μm

Mobile phase: 10% EtOH, 28 mM HCl, 20 mM NH_4OAc, pH 2, 3.5 mL min^{-1}



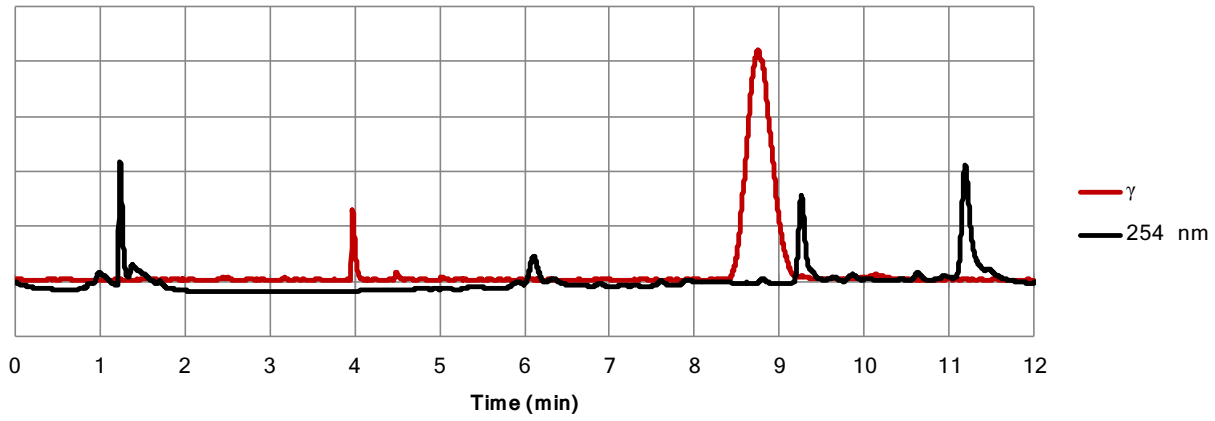
Analytical:

Stationary phase: Eclipse Plus C18, 100 × 4.6 mm, 3.5 µm

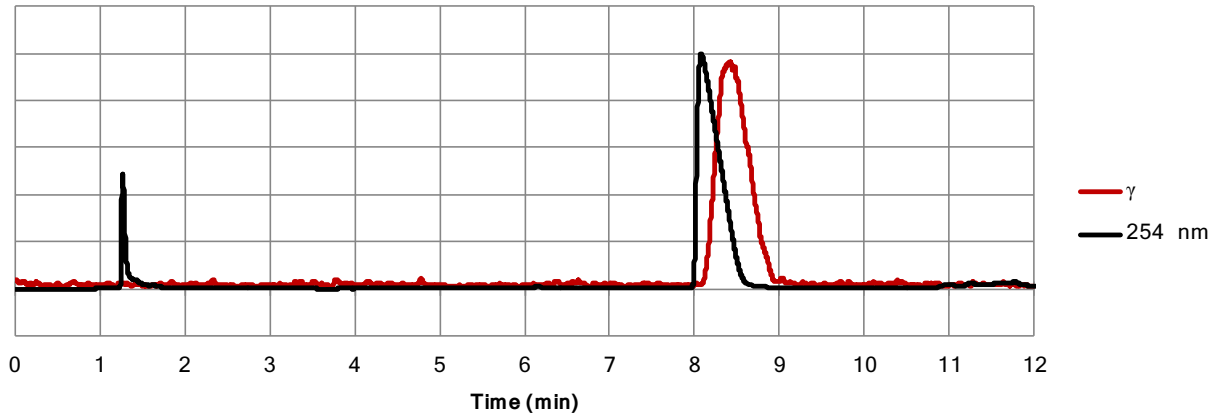
Mobile phase: 1% ACN, 10 mM phosphate buffer, pH 7–8, 1 mL min^{-1}, 1 min; linear gradient to 20% ACN, 8 min; 20% ACN, 3 min

Note: Sharp peaks in the radiation chromatogram are artifacts from the radiation detector.

Purified product:



Coinjection with standard:



Radiochemical purity ranged from 95–99% for this product.

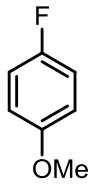
(4) Yield calculation:

Isolated yields were calculated as the quotient of measured activity isolated at end-of-synthesis and the measured activity in cyclotron target water at beginning-of-synthesis, and expressed as a percentage. No corrections for decay or material losses (*e.g.*, activity withdrawn for analysis,

potentially volatile radioactive species, or residual activity in vials, syringes, or purification equipment) are factored into the calculation. Product must be identified as ≥95% radiochemically pure to qualify.

Computational Experiments

Calculated Structures



Compound Label: AnisF
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ): -445.67035669 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.01311703 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.09304200 hartree
Energy (electronic + dispersion + thermal correction): -445.59043172 hartree

Geometry:

C	-1.832734	-0.118766	0.000037
C	-1.339407	1.183238	0.000036
C	0.037544	1.380214	-0.000066
C	0.914263	0.282899	-0.000189
C	0.396705	-1.018801	-0.000124
C	-0.988393	-1.218045	-0.000040
H	-2.027080	2.022702	0.000047
H	0.454285	2.382488	-0.000076
H	1.051283	-1.881997	-0.000163
H	-1.405294	-2.219944	-0.000013
O	2.245799	0.589435	0.000042
C	3.182919	-0.483786	0.000124
H	4.169615	-0.018283	-0.000029
H	3.075978	-1.109179	0.894967
H	3.075909	-1.109474	-0.894495
F	-3.176275	-0.313723	0.000085

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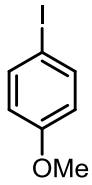

Compound Label: AnisI
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -357.30715559 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.01593501 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.08787700 hartree
Energy (electronic + dispersion + thermal correction): -357.23521360 hartree

Geometry:

C	0.184918	0.079667	0.000380

C	-0.416284	1.341411	0.000515
C	-1.804527	1.434807	0.000123
C	-2.598432	0.276163	-0.000413
C	-1.983877	-0.982505	0.000104
C	-0.587777	-1.076862	0.000394
H	0.182008	2.246139	0.000877
H	-2.292644	2.404512	0.000339
H	-2.569143	-1.894373	0.000646
H	-0.124813	-2.057402	0.000644
I	2.330280	-0.078916	-0.000105
O	-3.944286	0.479682	-0.000536
C	-4.800193	-0.661454	0.000042
H	-5.818210	-0.269778	-0.000116
H	-4.645365	-1.276092	-0.894777
H	-4.645372	-1.275291	0.895356

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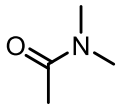

Compound Label: DMF
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ): -248.31622299 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.00692656 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.07347800 hartree
Energy (electronic + dispersion + thermal correction): -248.24967155 hartree

Geometry:

O	-1.942311	-0.097500	0.000327
C	-0.861789	-0.649271	-0.000181
H	-0.755042	-1.750605	-0.000325
N	0.345237	-0.021660	-0.000901
C	1.590995	-0.750489	0.000320
H	2.186606	-0.506351	-0.887468
H	2.184024	-0.508255	0.890400
H	1.388283	-1.824304	-0.001177
C	0.411512	1.424029	0.000068
H	0.940791	1.784122	-0.889927
H	-0.608187	1.808517	0.000522
H	0.941052	1.782882	0.890426

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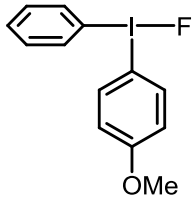

Compound Label: FAnisPh-GS
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -688.46309280
hartree

Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03242528 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.17047700 hartree
Energy (electronic + dispersion + thermal correction): -688.32504108 hartree

Geometry:

C	-0.914376	0.272027	0.000054
C	-2.093531	0.996568	0.000109
C	-0.885061	-1.117869	0.000020
C	-3.308293	0.303150	0.000110
H	-2.029103	2.080081	0.000153
C	-2.098496	-1.800577	0.000020
H	0.043628	-1.675064	0.000019
C	-3.315265	-1.098506	0.000054
H	-4.232900	0.868582	0.000134
H	-2.118568	-2.885878	-0.000026
O	-4.437676	-1.866899	0.000001
C	-5.706101	-1.214152	0.000031
H	-5.835381	-0.594427	-0.895143
H	-6.450419	-2.011429	0.000194
H	-5.835262	-0.594208	0.895072
C	2.170881	-0.378334	-0.000043
C	2.602632	-0.925162	1.211969
C	2.602321	-0.925542	-1.211993
C	3.467376	-2.023529	1.210283
H	2.273177	-0.500561	2.156050
C	3.467056	-2.023911	-1.210181
H	2.272619	-0.501212	-2.156109
C	3.898786	-2.572601	0.000083
H	3.802626	-2.447607	2.152806
H	3.802053	-2.448306	-2.152651
H	4.571668	-3.425510	0.000117
I	0.943421	1.427401	-0.000066
F	-0.454624	3.163232	-0.000025

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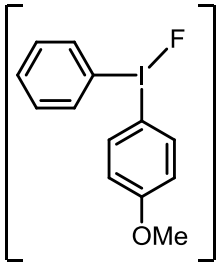

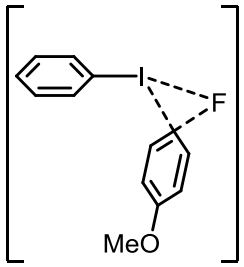

Compound Label: FAnisPh-pseudo
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)

Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -688.43408490 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03144110 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.16847000 hartree
Energy (electronic + dispersion + thermal correction): -688.29705600 hartree

Geometry:

C	-0.924233	-0.526998	0.098344
C	-1.649727	-0.291192	-1.064753
C	-1.507562	-0.350166	1.355550
C	-2.971854	0.156516	-0.982808
H	-1.203297	-0.444232	-2.042417
C	-2.821716	0.094792	1.441957
H	-0.948632	-0.550486	2.264301
C	-3.561874	0.352070	0.274428
H	-3.522793	0.344971	-1.896585
H	-3.296085	0.247796	2.406366
O	-4.835525	0.780510	0.468658
C	-5.647177	1.047074	-0.675195
H	-5.781646	0.146311	-1.285177
H	-6.612808	1.369589	-0.284248
H	-5.216707	1.845555	-1.290597
C	1.916146	0.776272	-0.024586
C	2.134307	1.427117	-1.236611
C	2.228371	1.369984	1.196237
C	2.661353	2.722612	-1.220014
H	1.899103	0.945611	-2.180545
C	2.754158	2.666046	1.199695
H	2.066014	0.844578	2.132166
C	2.969029	3.340018	-0.005130
H	2.830830	3.244127	-2.157834
H	2.995897	3.143645	2.145032
H	3.380599	4.345111	0.002559
I	1.127955	-1.285736	-0.043145
F	2.092977	-3.365281	-0.157586

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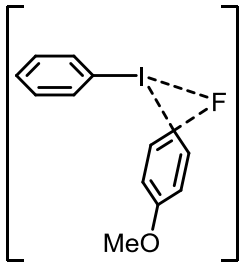

Compound Label: FAnisPh-ts
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -688.42482169 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03145492 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.16840400 hartree
Energy (electronic + dispersion + thermal correction): -688.28787261 hartree

Geometry:

C	-1.062346	-0.800244	0.049195
C	-1.650501	-0.288896	-1.095277

```
C    -1.569590  -0.563616   1.323401
C    -2.829202   0.461208  -0.966052
H    -1.230025  -0.465194  -2.078193
C    -2.737961   0.185344   1.436607
H    -1.085002  -0.959726   2.207652
C    -3.377494   0.702133   0.298198
H    -3.290608   0.853768  -1.864846
H    -3.165929   0.382392   2.415044
O    -4.513848   1.426664   0.531258
C    -5.202876   1.968483  -0.590386
H    -5.540812   1.179016  -1.273363
H    -6.070393   2.491814  -0.185313
H    -4.575036   2.679393  -1.142156
C     2.186249   0.486033  -0.020822
C     2.412856   1.199774  -1.199765
C     2.602840   0.985790   1.215106
C     3.081171   2.425727  -1.138204
H     2.082280   0.809225  -2.156865
C     3.271292   2.212145   1.265691
H     2.418351   0.429747   2.128661
C     3.509496   2.931130   0.091754
H     3.264357   2.983000  -2.052491
H     3.602281   2.603261   2.223573
H     4.028038   3.884522   0.135473
I     1.151258  -1.403141  -0.106378
F    -0.794111  -2.816457  -0.109542
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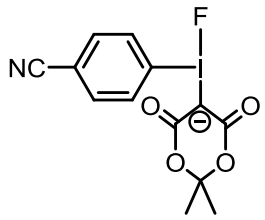


```
Compound Label: F_CNPhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -967.63110161
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03707043 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.15740500 hartree
Energy (electronic + dispersion + thermal correction): -967.51076704 hartree

Geometry:
C    -1.757569  -0.265856   0.000024
C    -3.041092  -0.796808  -0.000261
C    -1.496690   1.095319   0.000467
C    -4.115811   0.089128  -0.000092
H    -3.115445  -1.886372  -0.000626
C    -2.575090   1.977975   0.000628
H    -0.472816   1.457444   0.000673
C    -3.889782   1.478480   0.000351
H    -5.135495  -0.285616  -0.000313
H    -2.405788   3.050493   0.000970
F    -1.800653  -3.138634  -0.000644
I    -0.083152  -1.670733  -0.000213
C     1.391881  -0.165060   0.000099
O     1.375931   0.149089  -2.370440
```

```
O     1.378447   0.145697   2.371087
C     1.834278   0.355133   1.258091
C     1.832784   0.357119  -1.257600
C     3.701593   1.251391  -0.000134
C     4.643811   0.038660  -0.001535
H     5.277710   0.057361  -0.894288
H     5.278690   0.056054   0.890547
H     4.065152  -0.888535  -0.001894
C     4.464102   2.572187   0.000412
H     5.093565   2.644738   0.892868
H     5.092593   2.646036  -0.892621
H     3.749763   3.400070   0.001404
O     2.908906   1.256740   1.181898
O     2.907607   1.258484  -1.181286
C    -5.000414   2.384762   0.000513
N    -5.904875   3.118606   0.000643
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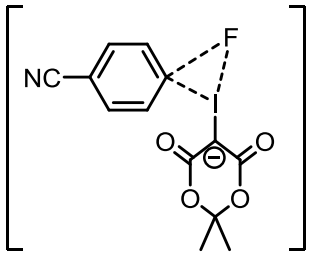

Compound Label: F_CNPhR-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -967.60958255 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03644956 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.15653900 hartree
Energy (electronic + dispersion + thermal correction): -967.48949311 hartree

Geometry:

```
C     1.857683  -0.539475  -0.041316
C     2.462024  -0.251135   1.190956
C     2.190538   0.180066  -1.194961
C     3.483116   0.683341   1.241252
H     2.150376  -0.775626   2.086226
C     3.219893   1.112616  -1.135343
H     1.642500   0.024492  -2.116502
C     3.885729   1.372291   0.076662
H     3.975509   0.896928   2.185712
H     3.497654   1.665943  -2.027983
F     2.203602  -2.557952  -0.217345
I     0.006498  -1.690657  -0.082082
C    -1.485888  -0.231481   0.011693
O    -1.600378  -0.207138   2.402439
O    -1.209965   0.414266  -2.275426
C    -1.763264   0.496514  -1.188817
C    -1.962938   0.169309   1.300297
C    -3.668904   1.347298   0.041456
C    -4.687463   0.220564  -0.183119
H    -5.384845   0.174630   0.659785
H    -5.249727   0.402313  -1.105002
H    -4.174917  -0.740978  -0.268017
```

```
C    -4.335914   2.713033   0.162720
H    -4.883935   2.948266  -0.754956
H    -5.028935   2.720390   1.009768
H    -3.568449   3.474739   0.324222
O    -2.787329   1.442117  -1.074411
O    -2.971043   1.143423   1.265252
C     4.937855   2.336223   0.134350
N     5.800407   3.119851   0.182198
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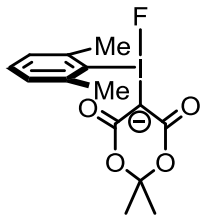


```
Compound Label: F_diMePhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -954.01173774
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.04328106 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.21588000 hartree
Energy (electronic + dispersion + thermal correction): -953.83913880 hartree

Geometry:
C     1.918829   0.396534   0.041018
C     2.565132   0.557022  -1.192260
C     2.052105   1.294543   1.105870
C     3.327300   1.719932  -1.368384
C     2.831993   2.440955   0.876955
C     3.451208   2.661844  -0.349496
H     3.829419   1.874959  -2.320942
H     2.952852   3.157949   1.686243
F     2.686520  -2.199401   0.243651
I     0.644794  -1.348729   0.267131
C    -1.174453  -0.244672   0.066551
O    -1.616184   0.007738   2.404941
O    -0.899312   0.070316  -2.289661
C    -1.538976   0.166035  -1.248799
C    -1.916786   0.127698   1.219723
C    -3.733867   0.578390  -0.318301
C    -4.355248  -0.821128  -0.448502
H    -5.104745  -0.974147   0.335341
H    -4.831868  -0.930895  -1.428462
H    -3.580474  -1.585352  -0.347503
C    -4.776230   1.684309  -0.453257
H    -5.260921   1.630099  -1.433261
H    -5.533954   1.587747   0.330942
H    -4.283331   2.655267  -0.353544
O    -2.792723   0.796606  -1.359379
O    -3.158703   0.738811   0.972289
H     4.043529   3.560929  -0.506623
C     1.472092   1.055071   2.479558
H     0.405046   0.810849   2.464784
H     1.983301   0.210211   2.960602
H     1.619722   1.937254   3.112410
C     2.496952  -0.496557  -2.265540
```

```
H     2.775124  -1.451158  -1.803047
H     1.473513  -0.574089  -2.651249
H     3.175080  -0.260008  -3.092843

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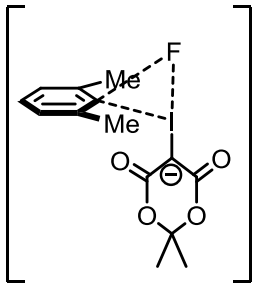


```
Compound Label: F_diMePhR-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -953.99073556
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.04245938 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.21511200 hartree
Energy (electronic + dispersion + thermal correction): -953.81808294 hartree

Geometry:
C    -2.177013   0.119436   0.189624
C    -2.520183  -0.644354   1.308546
C    -2.506184   1.467420   0.027166
C    -3.210036   0.018064   2.332895
C    -3.196949   2.075939   1.084514
C    -3.537491   1.370433   2.237993
H    -3.492979  -0.552730   3.215823
H    -3.467893   3.125758   0.985442
F    -2.904025  -0.910403  -1.480233
I    -0.521506  -0.705863  -1.155184
C     1.289682  -0.153575  -0.250067
O     1.311707   2.056852  -1.176525
O     1.331658  -2.022050   1.249897
C     1.812178  -1.003042   0.773696
C     1.801400   1.155049  -0.510310
C     3.811777   0.349460   0.574314
C     4.508482  -0.346890  -0.604413
H     5.132199   0.370894  -1.147573
H     5.138108  -1.164408  -0.237441
H     3.764984  -0.757305  -1.292197
C     4.809782   0.942788   1.563422
H     5.445542   0.153828   1.977401
H     5.437048   1.688675   1.065154
H     4.263705   1.424378   2.379059
O     3.039193  -0.588313   1.313796
O     3.028250   1.441123   0.107360
H    -4.065461   1.866056   3.049401
C    -2.194162   2.212353  -1.244150
H    -1.113180   2.349820  -1.374866
H    -2.568693   1.623616  -2.088793
H    -2.676332   3.196489  -1.248153
C    -2.229105  -2.120419   1.377179
H    -2.594096  -2.580882   0.452789
H    -1.152451  -2.317631   1.457148
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H   -2.733966 -2.579058   2.234980

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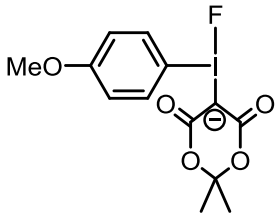

Compound Label: F_MeOPhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -989.89467802 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03821613 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.19053200 hartree
Energy (electronic + dispersion + thermal correction): -989.74236216 hartree

Electronic Energy with Solvation (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)/PCM(solvent=DMF)): -989.9795102 hartree
Energy with Solvation (electronic + dispersion + thermal correction): -989.8271943 hartree

Geometry:
C   -1.672503 -0.447888 -0.000050
C   -2.926837 -1.047456   0.000128
C   -1.500751   0.921772 -0.000217
C   -4.048973 -0.224041   0.000130
H   -2.946339 -2.137910   0.000266
C   -2.633166   1.746987 -0.000210
H   -0.503538   1.351443 -0.000356
C   -3.907849   1.171310 -0.000044
H   -5.052036 -0.642401   0.000263
H   -2.499456   2.823290 -0.000327
F   -1.540095 -3.332940 -0.000275
I   0.078099 -1.754278 -0.000092
C   1.473577 -0.162658   0.000036
O   1.453010   0.144036 -2.373067
O   1.452535   0.144064   2.373136
C   1.885931   0.381280   1.256237
C   1.886208   0.381240 -1.256090
C   3.696866   1.391191   0.000253
C   4.710540   0.236410   0.000364
H   5.342937   0.291149 -0.892214
H   5.342755   0.291162   0.893070
H   4.186320 -0.722594   0.000317
C   4.381393   2.754818   0.000314
H   5.004870   2.865605   0.893252
H   5.005053   2.865593 -0.892498
H   3.619122   3.538941   0.000230
O   2.906126   1.350480   1.180775
O   2.906368   1.350462 -1.180429
O   -5.082811   1.888978 -0.000020
C   -4.992787   3.297860 -0.000301
H   -4.474342   3.675728   0.892640
H   -4.474188   3.675354 -0.893308
H   -6.021259   3.668726 -0.000462

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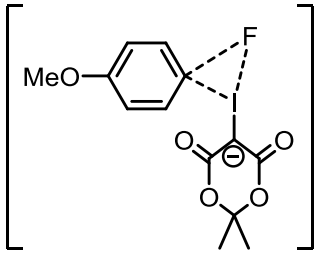

Compound Label: F_MeOPhR-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -989.86219636 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03737582 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.18914000 hartree
Energy (electronic + dispersion + thermal correction): -989.71043218 hartree

Electronic Energy with Solvation (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)/PCM(solvent=DMF)): -989.9469704 hartree
Energy with Solvation (electronic + dispersion + thermal correction): -989.7952062 hartree

Geometry:

C	1.832667	-0.733453	-0.019076
C	2.443401	-0.620402	1.234645
C	2.171728	0.125125	-1.056871
C	3.455838	0.312081	1.414573
H	2.144422	-1.272623	2.046415
C	3.206016	1.057144	-0.869680
H	1.633265	0.099760	-1.996811
C	3.851839	1.151708	0.362012
H	3.956886	0.407370	2.374215
H	3.463599	1.714567	-1.693696
F	2.035268	-2.712820	-0.361181
I	-0.166738	-1.741698	-0.194821
C	-1.591872	-0.216085	-0.012566
O	-1.827168	-0.425742	2.361892
O	-1.215752	0.619289	-2.225246
C	-1.792924	0.629352	-1.147870
C	-2.110548	0.077579	1.287300
C	-3.703163	1.461757	0.089776
C	-4.764328	0.414954	-0.282248
H	-5.499623	0.324044	0.524276
H	-5.276654	0.711118	-1.203828
H	-4.293418	-0.558632	-0.439649
C	-4.312355	2.841438	0.318504
H	-4.810627	3.190305	-0.591592
H	-5.038860	2.802727	1.136373
H	-3.518059	3.545338	0.581384
O	-2.773591	1.618124	-0.976426
O	-3.068920	1.106968	1.311551
O	4.871011	2.040949	0.654444
C	5.266334	2.926804	-0.366388
H	5.650054	2.393445	-1.249441
H	4.441337	3.580464	-0.687218
H	6.066931	3.542761	0.053345

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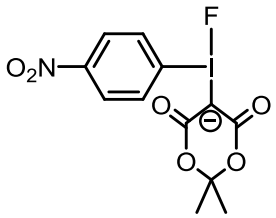

Compound Label: F_NO2PhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -1079.84084739 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03781368 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.15981300 hartree
Energy (electronic + dispersion + thermal correction): -1079.71884807 hartree

Geometry:

C	-1.458618	0.526439	-0.000017
C	-2.688161	1.175444	-0.000257
C	-1.325405	-0.854649	0.000272
C	-3.842162	0.395442	-0.000206
H	-2.660332	2.266999	-0.000487
C	-2.479946	-1.634648	0.000319
H	-0.339646	-1.309966	0.000456
C	-3.722741	-0.996973	0.000079
H	-4.827878	0.845088	-0.000392
H	-2.431297	-2.716571	0.000537
F	-1.235132	3.389656	-0.000194
I	0.337050	1.768280	-0.000083
C	1.665985	0.134017	0.000075
O	1.622067	-0.175010	2.370592
O	1.620576	-0.176617	-2.370212
C	2.057807	-0.425690	-1.257943
C	2.058705	-0.424730	1.258236
C	3.837565	-1.485673	-0.000074
C	4.886443	-0.364032	-0.000807
H	5.516803	-0.439415	0.891469
H	5.516227	-0.440044	-0.893436
H	4.395178	0.612299	-0.000992
C	4.475796	-2.870700	0.000203
H	5.095039	-3.001669	-0.892719
H	5.095634	-3.001039	0.892804
H	3.688517	-3.629535	0.000733
O	3.046739	-1.419784	-1.181709
O	3.047515	-1.418946	1.182034
O	-4.812529	-3.042653	0.000374
O	-6.027824	-1.236437	-0.000075
N	-4.937098	-1.814545	0.000124

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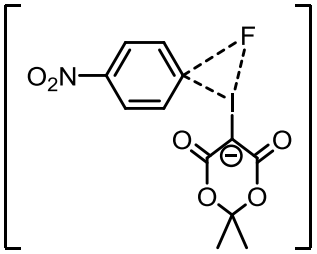

Compound Label: F_NO2PhR-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -1079.82197478 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03725813 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.15974500 hartree
Energy (electronic + dispersion + thermal correction): -1079.69948791 hartree

Geometry:

C	1.516343	-0.775021	-0.058199
C	2.161419	-0.568861	1.172146
C	1.913204	-0.084129	-1.211348
C	3.276589	0.248644	1.222465
H	1.803812	-1.068256	2.064385
C	3.036711	0.730603	-1.156749
H	1.340969	-0.171607	-2.127063
C	3.719255	0.887439	0.053969
H	3.812034	0.410527	2.150100
H	3.379970	1.267789	-2.032675
F	1.681528	-2.842869	-0.247384
I	-0.406420	-1.772070	-0.099168
C	-1.761049	-0.186573	0.013049
O	-1.862530	-0.172265	2.404022
O	-1.439300	0.450218	-2.269942
C	-1.980293	0.571835	-1.180706
C	-2.196705	0.243434	1.307060
C	-3.799569	1.575036	0.065647
C	-4.914861	0.544745	-0.161155
H	-5.610338	0.554985	0.684541
H	-5.462738	0.781569	-1.079188
H	-4.490297	-0.457955	-0.254431
C	-4.341489	2.993775	0.200170
H	-4.873244	3.282730	-0.711688
H	-5.024282	3.057640	1.053023
H	-3.507791	3.682839	0.359399
O	-2.918702	1.600116	-1.054860
O	-3.116424	1.300782	1.284306
O	5.259502	2.297346	-0.933967
O	5.460939	1.883294	1.197253
N	4.884745	1.743398	0.109053

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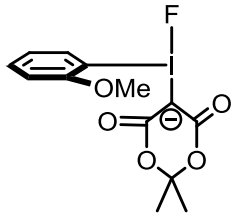

Compound Label: F_o-MeOPhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -989.88370058 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03877986 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.19083300 hartree
Energy (electronic + dispersion + thermal correction): -989.73164744 hartree

Electronic Energy with Solvation (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)/PCM(solvent=DMF)): -989.9725681 hartree
Energy with Solvation (electronic + dispersion + thermal correction): -989.8205149 hartree

Geometry:

C	1.689624	0.597074	-0.281963
C	1.387112	1.798324	-0.904093
C	2.753987	0.491372	0.628796
C	2.169372	2.932286	-0.644758
C	3.529936	1.631216	0.880691
C	3.239082	2.839737	0.239227
H	1.935835	3.872817	-1.136845
H	4.357231	1.583708	1.580741
F	2.535595	-1.678458	-1.354959
I	0.523543	-1.135807	-0.748937
C	-1.299833	-0.233709	-0.085604
O	-1.129088	-1.014422	2.171366
O	-1.596943	1.111689	-2.042332
C	-1.974485	0.658417	-0.963453
C	-1.716415	-0.449752	1.260627
C	-3.868330	0.385749	0.519829
C	-4.486534	-0.907901	-0.034980
H	-5.002734	-1.450531	0.764293
H	-5.202037	-0.672498	-0.830272
H	-3.702153	-1.548446	-0.445610
C	-4.925967	1.324456	1.093934
H	-5.642465	1.608847	0.316476
H	-5.459204	0.836080	1.915994
H	-4.436800	2.225792	1.473545
O	-3.232462	1.109714	-0.527645
O	-2.982222	0.092007	1.587350
H	3.856341	3.710961	0.448543
O	2.938386	-0.701543	1.244658
C	4.041058	-0.855806	2.107609
H	3.979029	-0.187991	2.979801
H	4.008568	-1.892577	2.449070
H	4.992224	-0.676910	1.586412
H	0.535011	1.846326	-1.576222

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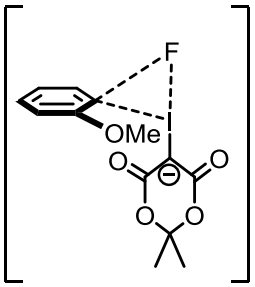

Compound Label: F_o-MeOPhR-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -989.85953456 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03916889 hartree

Electronic Energy with Solvation (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)/PCM(solvent=DMF)): -989.9430927 hartree
Energy with Solvation (electronic + dispersion + thermal correction): -989.7919336 hartree

Geometry:

C	2.092226	0.529877	-0.066036
C	2.035622	1.907358	0.142062
C	2.802286	-0.303896	0.813530
C	2.764590	2.474073	1.193489
C	3.516924	0.284088	1.857784
C	3.509160	1.669337	2.053899
H	2.722674	3.550775	1.343877
H	4.097873	-0.366646	2.507712
F	2.828497	-0.050958	-1.855990
I	0.509655	-0.341685	-1.358288
C	-1.284684	-0.074070	-0.298563
O	-1.168386	-2.132972	0.922812
O	-1.460379	2.238964	-0.894464
C	-1.879913	1.226676	-0.355416
C	-1.720764	-1.087057	0.606222
C	-3.802000	0.154472	0.657936
C	-4.503921	-0.411529	-0.585544
H	-5.075816	-1.306473	-0.318465
H	-5.184026	0.337308	-1.005066
H	-3.765651	-0.680008	-1.345323
C	-4.791367	0.540221	1.752780
H	-5.479240	1.308981	1.386857
H	-5.364718	-0.336500	2.070210
H	-4.240796	0.935074	2.610919
O	-3.099888	1.346070	0.327942
O	-2.949514	-0.829802	1.231706
H	4.074159	2.106252	2.873778
O	2.847837	-1.663386	0.614296
C	2.119632	-2.441039	1.567466
H	1.040458	-2.270726	1.480085
H	2.338712	-3.487190	1.332272
H	2.449936	-2.231076	2.595518
H	1.414159	2.526094	-0.495200

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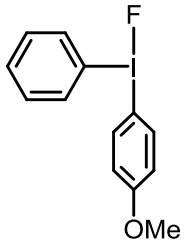

Compound Label: FPhAnis-GS
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -688.46354973 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03241842 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.17063100 hartree
Energy (electronic + dispersion + thermal correction): -688.32533715 hartree

Geometry:

C	1.000071	-0.550866	0.094171
C	1.736006	-0.316831	-1.068396
C	1.614392	-0.375983	1.342112
C	3.072324	0.088148	-1.002164
H	1.279484	-0.449591	-2.045242
C	2.942171	0.026567	1.421839
H	1.060451	-0.556142	2.259057
C	3.680890	0.261513	0.249127
H	3.620504	0.262314	-1.920581
H	3.429587	0.164134	2.382220
O	4.970121	0.649084	0.432622
C	5.777530	0.896285	-0.718069
H	5.366132	1.710937	-1.325381
H	6.757008	1.186477	-0.336083
H	5.877903	-0.004684	-1.334489
C	-1.908700	0.682704	-0.011369
C	-3.291324	0.744396	-0.088152
C	-1.091096	1.799262	0.071671
C	-3.884525	2.011368	-0.081630
H	-3.843735	-0.188215	-0.148396
C	-1.708657	3.056224	0.077169
H	-0.012588	1.718514	0.130933
C	-3.098681	3.163329	0.000499
H	-4.966571	2.091094	-0.141113
H	-1.091341	3.947711	0.141840
H	-3.567514	4.143100	0.005103
I	-1.023428	-1.328979	-0.028724
F	-3.163446	-1.966572	-0.147480

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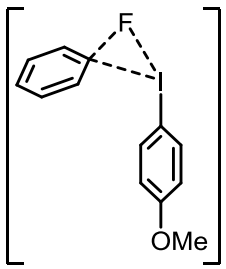

Compound Label: FPhAnis-ts
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -688.42960351 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03145385 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.16863500 hartree
Energy (electronic + dispersion + thermal correction): -688.29242236 hartree

Geometry:

C	1.089266	-0.627456	0.091681
C	1.809810	-0.337232	-1.066456
C	1.654967	-0.386330	1.350173
C	3.106452	0.176097	-0.980816
H	1.377924	-0.513214	-2.046527
C	2.943100	0.125483	1.442221
H	1.101226	-0.602880	2.258113
C	3.678749	0.409339	0.278108
H	3.651778	0.388121	-1.892731
H	3.400913	0.312856	2.408491
O	4.927353	0.902993	0.477044
C	5.732063	1.203151	-0.663559
H	5.266510	1.975884	-1.286163
H	6.678071	1.575146	-0.268677
H	5.914576	0.306579	-1.267193
C	-2.228337	0.430624	-0.039163
C	-2.339671	1.133876	-1.233634
C	-2.502288	0.995256	1.201982
C	-2.801868	2.453174	-1.173057
H	-2.095014	0.676091	-2.184752
C	-2.961249	2.316265	1.230626
H	-2.383204	0.429685	2.118486
C	-3.113630	3.049857	0.051038
H	-2.905932	3.012683	-2.099107
H	-3.191328	2.768328	2.191943
H	-3.463463	4.077080	0.086245
I	-0.896871	-1.425609	-0.057911
F	-3.293436	-1.302851	-0.188892

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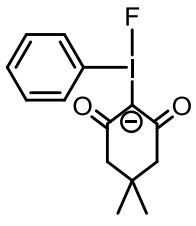

Compound Label: FPh_diketone_gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -803.62845287 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.04024310 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.20820100 hartree
Energy (electronic + dispersion + thermal correction): -803.46049497 hartree

Geometry:
C 2.139518 0.519484 0.000013
C 3.514213 0.331578 0.000110
C 1.540374 1.768306 0.000066
C 4.323994 1.471365 0.000275
H 3.860246 -0.705771 0.000048
C 2.368233 2.895995 0.000226
H 0.457599 1.854530 0.000016
C 3.757436 2.749378 0.000329
H 5.406709 1.358708 0.000357
H 1.922253 3.888447 0.000263
H 4.396508 3.630230 0.000448
F 2.962389 -2.273603 0.000138
I 0.890131 -1.272537 -0.000237
C -0.949571 -0.194342 0.000004
O -1.033982 -0.112368 2.381752
O -1.033747 -0.111008 -2.381698
C -1.541044 0.105084 -1.270109
C -1.541170 0.104339 1.270235
C -3.785453 0.510229 0.000070
C -4.257466 -0.958265 -0.000347
H -4.867598 -1.171853 0.887323
H -4.867526 -1.171370 -0.888182
H -3.406595 -1.646103 -0.000499
C -5.023417 1.425552 0.000270
H -5.645965 1.248407 -0.887296
H -5.646051 1.247916 0.887678
H -4.734821 2.484655 0.000582
C -2.923048 0.794210 1.243043
H -3.441003 0.504653 2.165926
H -2.743744 1.879045 1.315791
C -2.922953 0.794891 -1.242679
H -2.743655 1.879763 -1.314823
H -3.440827 0.505817 -2.165761

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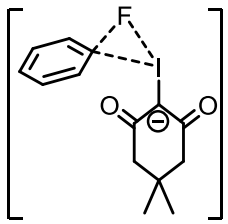

Compound Label: FPh_diketone_ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -803.60309651 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03957286 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.20762000 hartree
Energy (electronic + dispersion + thermal correction): -803.43504937 hartree

Geometry:
C 2.350959 0.228238 0.027811
C 2.885428 0.412678 1.307213
C 2.441853 1.223928 -0.945426
C 3.600401 1.576933 1.576261

H	2.770343	-0.357760	2.060704
C	3.170830	2.381618	-0.653472
H	1.934302	1.111273	-1.895958
C	3.757367	2.567781	0.598777
H	4.037152	1.711546	2.564534
H	3.253709	3.154600	-1.415658
H	4.311715	3.476896	0.820080
F	3.186685	-1.571448	-0.494620
I	0.798892	-1.317221	-0.283016
C	-1.023749	-0.267719	0.001516
O	-1.356928	-1.196363	2.172839
O	-0.798769	0.834705	-2.100321
C	-1.428982	0.603075	-1.054828
C	-1.716400	-0.467424	1.235977
C	-3.769762	0.677155	0.102577
C	-4.344935	-0.600125	-0.543100
H	-5.055389	-1.093645	0.133294
H	-4.876483	-0.361342	-1.473904
H	-3.550889	-1.314338	-0.780868
C	-4.929754	1.643758	0.403327
H	-5.465088	1.918356	-0.515810
H	-5.656429	1.189622	1.090756
H	-4.564726	2.569322	0.866629
C	-3.027226	0.330463	1.406764
H	-3.663827	-0.245564	2.089670
H	-2.768110	1.263521	1.931701
C	-2.762596	1.350788	-0.847641
H	-2.507401	2.347793	-0.455453
H	-3.195320	1.511828	-1.842985

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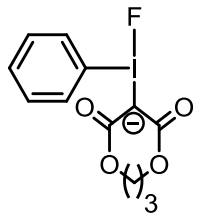

Compound Label: FPh_exp-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.40957418 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03524808 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.16409200 hartree
Energy (electronic + dispersion + thermal correction): -875.28073026 hartree

Geometry:

C	-1.897725	0.652949	-0.067577
C	-3.279450	0.677096	-0.192581
C	-1.110446	1.792588	-0.100092
C	-3.893965	1.918553	-0.382394
H	-3.792187	-0.283753	-0.117601
C	-1.745236	3.025405	-0.285603
H	-0.037791	1.721360	0.036073
C	-3.132824	3.089697	-0.432257
H	-4.975866	1.969128	-0.490291
H	-1.149791	3.935673	-0.308427

```
H    -3.619757   4.051918  -0.577842
F    -3.138721  -1.936858   0.302285
I    -0.955597  -1.303365   0.195456
C     1.043509  -0.571518   0.035912
O     1.430519  -1.869725  -1.920803
O     1.064587   0.579942   2.130666
C     1.620269   0.015748   1.190408
C     1.744807  -0.959748  -1.166707
O     3.029375  -0.140163   1.221587
O     2.878375  -0.234605  -1.566309
C     3.079298   1.138470  -1.253265
H     3.359018   1.619821  -2.200892
H     2.143643   1.597343  -0.911644
C     3.760871   1.074390   1.205703
H     3.139018   1.887201   1.604949
H     4.628065   0.963193   1.870326
C     4.205743   1.359126  -0.232176
H     4.574747   2.393196  -0.312529
H     5.034039   0.694873  -0.509242
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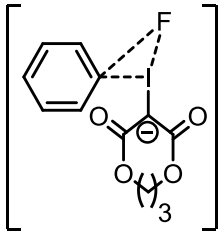


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Compound Label: FPh_exp-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.38358221
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03453773 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.16271000 hartree
Energy (electronic + dispersion + thermal correction): -875.25540994 hartree

Geometry:
C     2.105793   0.385510  -0.003467
C     2.027409   1.333466  -1.024555
C     2.579871   0.728397   1.267422
C     2.527297   2.618571  -0.787467
H     1.563967   1.085299  -1.971942
C     3.063825   2.016330   1.482175
H     2.600637  -0.013157   2.057784
C     3.050138   2.970799   0.457173
H     2.478297   3.355464  -1.587376
H     3.453938   2.276412   2.464819
H     3.424227   3.976171   0.635523
F     3.225426  -1.261443  -0.415720
I     0.831737  -1.422373  -0.236571
C    -1.132420  -0.687069  -0.034992
O    -1.492891  -1.757025   2.058216
O    -1.116487   0.358353  -2.190667
C    -1.682856  -0.070620  -1.188763
C    -1.767298  -0.882895   1.248998
O    -3.095359  -0.030114  -1.126861
O    -2.773284   0.005030   1.645109
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C	-2.782947	1.376808	1.254710
H	-2.913525	1.947436	2.184393
H	-1.816430	1.659632	0.820998
C	-3.647489	1.278268	-1.142978
H	-2.949540	1.967446	-1.636348
H	-4.568660	1.251780	-1.739805
C	-3.938426	1.706377	0.298464
H	-4.144593	2.786928	0.332386
H	-4.832410	1.191716	0.672645

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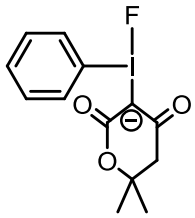

Compound Label: FPh_ketoester-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -839.53836092 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03732550 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.18530500 hartree
Energy (electronic + dispersion + thermal correction): -839.39038142 hartree

Geometry:

C	2.113825	0.508317	0.023411
C	3.488166	0.321816	-0.003603
C	1.514015	1.754096	0.098698
C	4.298152	1.460120	0.053749
H	3.836921	-0.711229	-0.069264
C	2.341813	2.880427	0.155091
H	0.431774	1.841503	0.113955
C	3.730957	2.735258	0.133213
H	5.380760	1.348245	0.036118
H	1.895307	3.870791	0.213580
H	4.369611	3.615295	0.176691
F	2.913038	-2.278309	-0.169198
I	0.860251	-1.282770	-0.065136
C	-0.972460	-0.216496	0.048876
O	-1.133035	-0.412734	2.426244
O	-0.972339	0.351397	-2.268269
C	-1.524772	0.291619	-1.178270
C	-1.579312	-0.049262	1.327642
C	-3.689894	0.510809	-0.015623
C	-4.224703	-0.925790	-0.147849
H	-4.943805	-1.149589	0.650055
H	-4.725118	-1.049236	-1.114781
H	-3.405632	-1.647749	-0.086881
C	-4.838610	1.516304	-0.143543
H	-5.354092	1.387762	-1.102293
H	-5.566446	1.381142	0.665937
H	-4.452858	2.540519	-0.098797
O	-2.831839	0.798384	-1.138665
C	-2.918011	0.711424	1.291424
H	-3.512034	0.393653	2.155615
H	-2.702314	1.782239	1.421288

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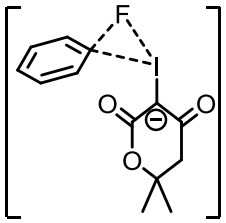

Compound Label: FPh_ketoester-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -839.51161893 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03660183 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.1837300 hartree
Energy (electronic + dispersion + thermal correction): -839.36448776 hartree

Geometry:

C	2.328360	0.223406	-0.002643
C	2.862515	0.467226	1.266415
C	2.410746	1.175557	-1.018947
C	3.569361	1.647544	1.482687
H	2.749453	-0.267948	2.054570
C	3.131229	2.350477	-0.779598
H	1.906667	1.016791	-1.964866
C	3.717834	2.595424	0.462450
H	4.004775	1.829394	2.463906
H	3.206800	3.089951	-1.574922
H	4.265143	3.517633	0.642996
F	3.148897	-1.591322	-0.457910
I	0.767293	-1.337751	-0.236636
C	-1.051106	-0.306407	0.029090
O	-1.250753	-0.895096	2.337840
O	-0.922618	0.691028	-2.137380
C	-1.511098	0.476831	-1.085401
C	-1.648652	-0.309142	1.320650
C	-3.673042	0.672041	0.086015
C	-4.335804	-0.660045	-0.305292
H	-5.090748	-0.951818	0.435478
H	-4.824046	-0.560396	-1.281141
H	-3.589841	-1.456920	-0.370497
C	-4.719852	1.789535	0.135523
H	-5.223429	1.884531	-0.833377
H	-5.475132	1.581087	0.903143
H	-4.241611	2.747348	0.366727
O	-2.769394	1.073295	-0.966009
C	-2.913469	0.563725	1.411327
H	-3.552899	0.153678	2.200843
H	-2.601734	1.568521	1.730801

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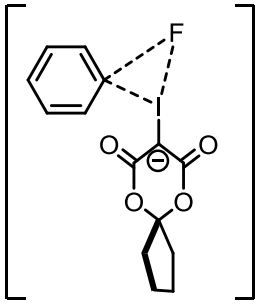

Compound Label: FPh_pent_ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -952.77344875 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03901231 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.1946360 hartree
Energy (electronic + dispersion + thermal correction): -952.61782506 hartree

Geometry:

C	-2.793333	0.218706	-0.065081
C	-3.125509	0.847262	1.135214
C	-3.025615	0.822504	-1.301137
C	-3.780713	2.081125	1.082503
H	-2.892919	0.386774	2.088642
C	-3.681892	2.056831	-1.326608
H	-2.716264	0.343302	-2.223095
C	-4.066056	2.691947	-0.142098
H	-4.056364	2.568377	2.014759
H	-3.879768	2.525386	-2.287779
H	-4.567409	3.654838	-0.172446
F	-3.634088	-1.612325	-0.079659
I	-1.181707	-1.375881	0.019702
C	0.628139	-0.333051	0.092613
O	0.753304	-0.005339	-2.274571
O	0.529287	0.045834	2.453575
C	1.085480	0.129840	1.363650
C	1.204232	0.103170	-1.138836
C	3.149806	0.591611	0.208856
C	3.865915	-0.773186	0.210745
H	4.163395	-0.998023	1.242504
H	3.225858	-1.584256	-0.145333
C	4.281628	1.640208	0.216923
H	4.360556	2.067619	1.220182
H	4.022911	2.450201	-0.470330
C	5.575533	0.887781	-0.197017
H	6.134411	1.416883	-0.974837
H	6.241581	0.788958	0.667731
C	5.105725	-0.511951	-0.655109
H	5.877135	-1.279497	-0.537190
H	4.817754	-0.490125	-1.712830
O	2.307504	0.796353	1.338009
O	2.418198	0.771324	-1.010131

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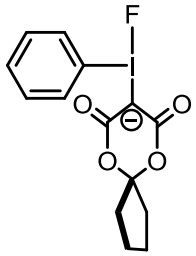

Compound Label: FPh_pent_gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -952.80389278 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03987913 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.19773445 hartree
Energy (electronic + dispersion + thermal correction): -952.64603746 hartree

Geometry:

C	-2.519014	0.510368	-0.070481
C	-3.891587	0.325300	-0.130790
C	-1.910040	1.754133	-0.063655
C	-4.697049	1.468095	-0.187521
H	-4.259629	-0.698653	-0.131355
C	-2.734374	2.884563	-0.121281
H	-0.829995	1.849741	-0.015345
C	-4.122912	2.742599	-0.182763
H	-5.777503	1.358093	-0.235445
H	-2.283940	3.873457	-0.117633
H	-4.755867	3.624607	-0.226816
F	-3.323902	-2.329558	-0.075638
I	-1.261784	-1.292794	0.022853
C	0.560528	-0.239777	0.112329
O	0.782724	0.007344	-2.255070
O	0.465193	0.141023	2.469859
C	1.039837	0.188047	1.386062
C	1.205870	0.120242	-1.107990
C	3.148082	0.512970	0.269929
C	3.798775	-0.882103	0.296637
H	4.121410	-1.079994	1.325737
H	3.106300	-1.674326	0.000360
C	4.339101	1.475899	0.286665
H	4.622266	1.634767	1.332145
H	4.058258	2.444220	-0.136983
C	5.465765	0.754501	-0.495655
H	5.619331	1.210343	-1.478561
H	6.416036	0.830737	0.042037
C	5.012253	-0.730338	-0.639290
H	5.810579	-1.436020	-0.390115
H	4.711009	-0.932745	-1.672241
O	2.304282	0.776818	1.382542
O	2.455301	0.721425	-0.964757

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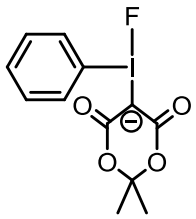

Compound Label: FPhR-gs
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.45337006 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03448570 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.16176800 hartree
Energy (electronic + dispersion + thermal correction): -875.32608776 hartree

Geometry:

C	-2.081813	0.518366	0.000157
C	-3.457742	0.348734	-0.000335
C	-1.459624	1.755545	0.000752
C	-4.252145	1.500623	-0.000209
H	-3.837273	-0.670922	-0.000783
C	-2.272955	2.895352	0.000874
H	-0.377409	1.838889	0.001127
C	-3.664335	2.768896	0.000395
H	-5.334805	1.402579	-0.000584
H	-1.811751	3.879272	0.001353
H	-4.288854	3.657981	0.000488
F	-2.917508	-2.312975	-0.000314
I	-0.841323	-1.298425	-0.000099
C	0.993744	-0.264232	0.000018
O	1.065663	0.029543	-2.369989
O	1.066724	0.027317	2.370291
C	1.563124	0.117679	1.250729
C	1.562621	0.118798	-1.250582
C	3.604448	0.507767	-0.000154
C	4.208682	-0.899069	-0.000859
H	4.830572	-1.036395	-0.890585
H	4.830985	-1.037109	0.888467
H	3.422928	-1.659159	-0.000981
C	4.663343	1.600649	0.000120
H	5.293849	1.513540	0.889594
H	5.293545	1.514299	-0.889643
H	4.180291	2.581915	0.000623
O	2.821623	0.710682	1.181481
O	2.821180	0.711681	-1.181339

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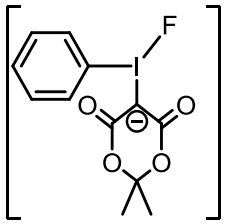

Compound Label: FPhR-pseudo

Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.42806283 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03359038 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.15999800 hartree
Energy (electronic + dispersion + thermal correction): -875.30165521 hartree

Geometry:

C	-2.166605	-0.487523	0.011317
C	-3.083976	-0.565898	1.055827
C	-2.086573	-1.473134	-0.971595
C	-3.943295	-1.669043	1.120671
H	-3.134619	0.209968	1.813839
C	-2.944881	-2.574073	-0.891369
H	-1.361500	-1.391382	-1.774975
C	-3.872545	-2.670709	0.150234
H	-4.661067	-1.743313	1.933132
H	-2.889251	-3.353405	-1.646766
H	-4.539960	-3.526171	0.204358
F	-1.467450	3.564821	-0.350067
I	-0.847222	1.279280	-0.124050
C	0.958247	0.185828	0.014625
O	1.031504	0.234393	2.403231
O	0.964141	-0.440667	-2.292249
C	1.476237	-0.400535	-1.175275
C	1.506399	-0.049471	1.308873
C	3.501438	-0.743253	0.114667
C	4.193965	0.608050	-0.077728
H	4.832372	0.823139	0.784372
H	4.815211	0.581871	-0.977945
H	3.459777	1.411289	-0.180422
C	4.487357	-1.893075	0.259191
H	5.111580	-1.966601	-0.635729
H	5.131547	-1.727822	1.127335
H	3.942600	-2.831903	0.392716
O	2.717680	-0.736038	1.313586
O	2.692740	-1.054427	-1.028478

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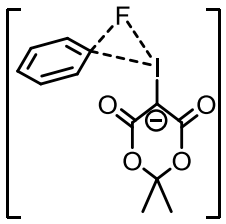

Compound Label: FPhR-TS
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.42285458 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03366179 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.15888200 hartree
Energy (electronic + dispersion + thermal correction): -875.29763437 hartree

Geometry:
C -2.346786 0.201971 0.000003
C -2.629899 0.818375 1.219222
C -2.629745 0.818420 -1.219233
C -3.286706 2.052529 1.205572
H -2.358685 0.348769 2.157968
C -3.286546 2.052580 -1.205610
H -2.358488 0.348813 -2.157965
C -3.621778 2.675670 -0.000028
H -3.523966 2.530408 2.153135
H -3.523685 2.530504 -2.153181
H -4.123822 3.638686 -0.000040
F -3.184218 -1.630281 0.000000
I -0.730012 -1.388809 -0.000018
C 1.073996 -0.333148 0.000014
O 1.088020 0.002201 -2.368201
O 1.087877 0.002179 2.368220
C 1.586661 0.118774 1.253426
C 1.586651 0.118871 -1.253347
C 3.588706 0.678470 -0.000030
C 4.315663 -0.668526 -0.000272
H 4.947932 -0.748826 -0.889567
H 4.947550 -0.749342 0.889245
H 3.601759 -1.496254 -0.000666
C 4.544901 1.862156 0.000149
H 5.180527 1.831377 0.889594
H 5.180105 1.831961 -0.889615
H 3.975554 2.795870 0.000597
O 2.789019 0.813070 -1.181020
O 2.789224 0.812627 1.181280

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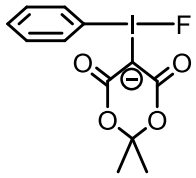

Compound Label: FRPh-GS
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.44563387 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03462698 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.16238300 hartree
Energy (electronic + dispersion + thermal correction): -875.31787785 hartree

Geometry:
C -2.376328 0.130908 0.009848
C -3.422670 -0.260134 0.846581
C -2.420448 1.366496 -0.640025
C -4.520444 0.587547 1.035553
H -3.391565 -1.219226 1.358165
C -3.515009 2.214238 -0.444898
H -1.603214 1.662120 -1.292138
C -4.565894 1.825841 0.391650
H -5.332520 0.281891 1.690395
H -3.549090 3.176538 -0.949816
H -5.416389 2.485766 0.540370

```
F     1.161628  -2.490076  -0.590335
I    -0.703420  -1.255818  -0.328523
C     0.758883   0.162254   0.116943
O     0.686601   1.207422  -2.031079
O     1.049455  -0.612922   2.359732
C     1.425404  -0.006248   1.363353
C     1.238036   0.953050  -0.960780
C     3.330997   0.895105   0.216168
C     3.839023  -0.434245  -0.354450
H     4.356219  -0.249098  -1.301768
H     4.554429  -0.876842   0.346793
H     3.020172  -1.144682  -0.519931
C     4.447101   1.880226   0.523497
H     5.130935   1.453087   1.262296
H     5.008301   2.106696  -0.387412
H     4.025407   2.807391   0.922161
O     2.467732   1.553138  -0.725256
O     2.635217   0.676757   1.450978
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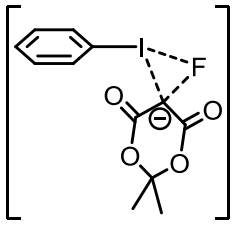


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Compound Label: FRPh-ts
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -875.38195818
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03363977 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.15895000 hartree
Energy (electronic + dispersion + thermal correction): -875.25664795 hartree

Geometry:
C    -2.509175   0.184130   0.012747
C    -3.525765   0.038579   0.958609
C    -2.403174   1.344831  -0.757062
C    -4.464010   1.063233   1.116376
H    -3.594220  -0.859235   1.565061
C    -3.341711   2.366523  -0.585234
H    -1.599366   1.449150  -1.479934
C    -4.372580   2.226286   0.347442
H    -5.260993   0.951536   1.846508
H    -3.265178   3.270979  -1.182682
H    -5.100715   3.021948   0.477397
F     1.331136  -2.154474  -0.496557
I    -1.032357  -1.352491  -0.256141
C     1.066464  -0.149590   0.038801
O     0.966604   0.640952  -2.218301
O     1.380665  -0.856942   2.302751
C     1.679403  -0.214054   1.302464
C     1.463875   0.576378  -1.094664
C     3.447871   0.991239   0.204381
C     4.205680  -0.257445  -0.263801
H     4.757425  -0.031819  -1.181936
```

H 4.920998 -0.564130 0.506041
H 3.508779 -1.079578 -0.454169
C 4.362665 2.167816 0.506126
H 5.067588 1.900695 1.298448
H 4.926657 2.444576 -0.389141
H 3.768739 3.026374 0.832295
O 2.540373 1.438091 -0.813767
O 2.730822 0.717177 1.415507

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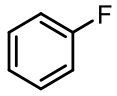

Compound Label: PhF
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ): -331.23069429 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.00952244 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.06382000 hartree
Energy (electronic + dispersion + thermal correction): -331.17639673 hartree

Geometry:
C 0.929548 0.000015 -0.000004
C 0.260864 -1.218933 -0.000018
C -1.136115 -1.209703 0.000017
C -1.836360 -0.000004 0.000000
C -1.136137 1.209688 -0.000016
C 0.260862 1.218939 0.000013
H 0.827279 -2.144494 -0.000017
H -1.675253 -2.152736 0.000022
H -2.922218 -0.000022 0.000007
H -1.675256 2.152732 -0.000016
H 0.827227 2.144532 0.000025
F 2.284694 -0.000003 0.000003

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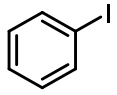

Compound Label: PhI
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -242.86552400
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.01231850 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.05846300 hartree
Energy (electronic + dispersion + thermal correction): -242.81937950 hartree

Geometry:
C -0.585527 0.000019 0.000003
C -1.265325 -1.217528 0.000000
C -2.663871 -1.208193 0.000003
C -3.364166 -0.000009 -0.000003
C -2.663906 1.208177 -0.000002

C	-1.265339	1.217532	0.000005
H	-0.726121	-2.158394	0.000005
H	-3.200413	-2.152905	-0.000002
H	-4.450158	-0.000035	-0.000002
H	-3.200434	2.152896	-0.000008
H	-0.726183	2.158427	0.000008
I	1.568908	0.000000	0.000000

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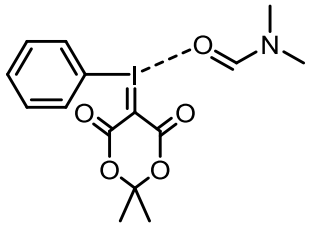


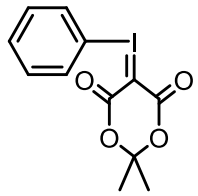
Compound Label: PhR-DMF
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -1023.89832033 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.04440783 hartree
Imaginary Frequencies: 1
Thermal Correction to Gibbs Free Energy (298 K): 0.25478600 hartree
Energy (electronic + dispersion + thermal correction): -1023.68794216 hartree

Geometry:

C	0.070047	0.638677	0.036732
O	0.709036	0.531304	2.337806
O	-0.100544	0.899925	-2.332828
C	0.152941	1.325594	-1.212542
C	0.573646	1.129926	1.280642
C	0.519431	3.288283	0.166630
C	-0.925300	3.707902	0.439041
H	-0.981695	4.236276	1.395092
H	-1.271234	4.376615	-0.354345
H	-1.587482	2.838896	0.478901
C	1.477293	4.466522	0.095640
H	1.176186	5.144287	-0.707708
H	1.467745	5.013321	1.042382
H	2.491486	4.107842	-0.100145
C	-2.682807	-1.009569	-0.022925
C	-3.442061	-1.500253	1.035999
C	-3.246312	-0.315612	-1.092299
C	-4.824604	-1.287634	1.015858
H	-2.981596	-2.032133	1.861651
C	-4.627975	-0.104776	-1.089434
H	-2.629438	0.057743	-1.902694
C	-5.413973	-0.591211	-0.041210
H	-5.433395	-1.662139	1.833479
H	-5.086294	0.436018	-1.912237
H	-6.487335	-0.426594	-0.048528
I	-0.549917	-1.349997	-0.024121
O	2.271563	-1.982259	-0.030764
C	3.172422	-1.138850	-0.124759
H	2.949486	-0.063201	-0.203779
N	4.491574	-1.409774	-0.143371
C	4.977438	-2.780372	-0.048207
H	5.610629	-2.896902	0.838900

```
H     4.120064  -3.448873   0.024152
H     5.568513  -3.034519  -0.935493
C     5.486890  -0.352940  -0.257374
H     4.990096   0.618038  -0.316904
H     6.150844  -0.357470   0.614746
H     6.094254  -0.495292  -1.158727
O     1.001680   2.445238   1.224595
O     0.610928   2.624821  -1.105996
```

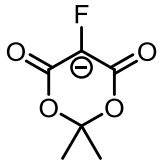
==========



```
Compound Label: PhR-GS
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -775.57148365
hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.03262343 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.16182100 hartree
Energy (electronic + dispersion + thermal correction): -775.44228608 hartree

Geometry:
C    -0.973553  -0.318277  -0.073209
O    -1.047109  -0.956438   2.231559
O    -0.817006   0.941599  -2.099717
C    -1.392107   0.624854  -1.066229
C    -1.506628  -0.385316   1.255127
C    -3.429774   0.711412   0.251285
C    -4.189731  -0.493027  -0.303450
H    -4.860695  -0.889435   0.464035
H    -4.785679  -0.185866  -1.167624
H    -3.503163  -1.285067  -0.613122
C    -4.345310   1.842291   0.690636
H    -4.939581   2.191739  -0.157858
H    -5.020763   1.491997   1.475706
H    -3.748248   2.673054   1.076285
C     2.335232   0.098976   0.006056
C     3.202859  -0.167256   1.059624
C     2.399114   1.249536  -0.774248
C     4.200184   0.775326   1.332979
H     3.117318  -1.069635   1.654298
C     3.398524   2.179987  -0.473715
H     1.692066   1.423869  -1.577454
C     4.295427   1.941963   0.571207
H     4.893499   0.593354   2.148628
H     3.472578   3.088669  -1.063662
H     5.070120   2.669509   0.793648
I     0.783378  -1.354457  -0.456212
O    -2.570472   1.269015  -0.760378
O    -2.674405   0.335979   1.414783
```

==========

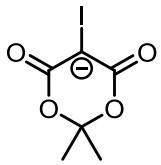


Compound Label: RF-GS
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ): -632.62450839 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.01465203 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.08400000 hartree
Energy (electronic + dispersion + thermal correction): -632.55516042 hartree

Geometry:

C	-1.296424	0.000008	0.065765
O	-1.207604	-2.360726	-0.206202
O	-1.207550	2.360741	-0.206228
C	-0.681894	1.246819	-0.156804
C	-0.681923	-1.246813	-0.156825
C	1.390072	-0.000011	0.042194
C	1.570745	0.000030	1.563687
H	2.128367	-0.889509	1.872060
H	2.128403	0.889564	1.872005
H	0.600878	0.000067	2.066573
C	2.718840	-0.000032	-0.699756
H	3.298180	0.889451	-0.435739
H	3.298172	-0.889507	-0.435694
H	2.538549	-0.000058	-1.778452
O	0.699584	1.182565	-0.379129
O	0.699573	-1.182602	-0.379078
F	-2.664563	0.000018	0.250531

==========



Compound Label: RI-GS
Charge: -1
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ/PCM(solvent=DMF)
Electronic Energy (PBE0/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I)): -544.27778749 hartree
Dispersion Correction (Grimme D3 for PBE0, BJ-damped): -0.01772147 hartree
Imaginary Frequencies: 0
Thermal Correction to Gibbs Free Energy (298 K): 0.07893900 hartree
Energy (electronic + dispersion + thermal correction): -544.21656996 hartree

Geometry:

C	-0.066315	0.000000	-0.104685
O	0.087904	-2.376836	-0.340361
O	0.087906	2.376839	-0.340360
C	0.578170	1.253117	-0.259219
C	0.578174	-1.253115	-0.259221
C	2.626293	0.000002	0.100647

C	2.681411	0.000003	1.631952
H	3.212462	-0.889401	1.984681
H	3.212467	0.889404	1.984680
H	1.674642	0.000006	2.057381
C	4.011948	-0.000003	-0.530185
H	4.567171	0.889518	-0.218924
H	4.567168	-0.889524	-0.218920
H	3.920991	-0.000005	-1.620093
I	-2.199143	0.000000	0.075782
O	1.970944	1.178226	-0.375954
O	1.970944	-1.178229	-0.375945

G2 Benchmark Calculation

For details, please see *J. Chem. Phys.* **1995**, *103*, 1878. A sample G09 input file with required basis sets is reproduced below.

```
%chk=Ph2IF-ts.chk
%mem=18000MB
%nprocshared=12
# genecp qcisd=(t,e4t)

diphenyliodonium fluoride reductive elimination TS G2(ECP)

0 1
 C           -1.77256800  -0.05312100  -0.00013500
 C           -2.31562700   0.37031000  -1.20946600
 C           -2.31671400   0.36844600   1.20935600
 C           -3.41694500   1.21926100  -1.20399300
 H           -1.88928500   0.04257500  -2.14714100
 C           -3.41805200   1.21737700   1.20420300
 H           -1.89121500   0.03925600   2.14690600
 C           -3.96751500   1.64285400   0.00018400
 H           -3.84253400   1.54870500  -2.14238400
 H           -3.84451100   1.54533600   2.14271900
 C            1.74988400   0.09674300   0.00012400
 C            2.09465400   0.65267900  -1.21761200
 C            2.09430000   0.65249500   1.21804100
 C            2.83546700   1.83145200  -1.19990600
 H            1.82250600   0.17999400  -2.14799200
 C            2.83510800   1.83127900   1.20071300
 H            1.82188100   0.17968600   2.14827900
 C            3.20574000   2.42618000   0.00050200
 H            3.12161300   2.27909100  -2.14274300
 H            3.12096800   2.27879100   2.14369700
 H            3.78035400   3.34164900   0.00065300
 I           -0.06507600  -1.34237300  -0.00029700
 F            2.26962900  -1.79206600   0.00015400
 H           -4.82379900   2.30356200   0.00030600

-H -C -O -F -Cl -N 0
6-311G(d,p)
****
-I     0
S   1   1.00
      2.1227650              1.0
S   1   1.00
      1.7704810              1.0
S   1   1.00
      0.3130840              1.0
S   1   1.00
      0.1240710              1.0000000
P   1   1.00
      2.4328870              1.0
P   1   1.00
      2.1372490              1.0
P   1   1.00
      0.3145460              1.0
P   1   1.00
```

```
      0.1049450                1.0000000
D    1    1.00
      0.276                    1.0000000
****

I    0
I-ECP    4    46
g-ul potential
  1
2     1.000000000          0.000000000
s-ul potential
  2
2     3.51120000          83.11386300
2     1.75560000           5.20187600
p-ul potential
  2
2     2.96880000          82.81110900
2     1.48440000           3.37968200
d-ul potential
  2
2     1.90660000          10.30427700
2     0.95330000           7.58803200
f-ul potential
  1
2     2.30750000         -21.47793600

--Link1--
%chk=Ph2IF-ts.chk
%mem=18000MB
%nprocshared=12
# Geom=AllCheck Guess=Check MP4/GenECP

-H -C -O -F -Cl -N 0
6-311+G(d,p)
****
-I     0
S   1   1.00
      2.1227650                1.0
S   1   1.00
      1.7704810                1.0
S   1   1.00
      0.3130840                1.0
S   1   1.00
      0.1240710                1.0000000
P   1   1.00
      2.4328870                1.0
P   1   1.00
      2.1372490                1.0
P   1   1.00
      0.3145460                1.0
P   1   1.00
      0.1049450                1.0000000
S   1   1.00
      0.0405                   1.0000000
P   1   1.00
      0.0328                   1.0000000
D   1   1.00
      0.276                    1.0000000
****
```

```
I    0
I-ECP    4    46
g-ul potential
  1
2      1.000000000           0.000000000
s-ul potential
  2
2      3.51120000           83.11386300
2      1.75560000            5.20187600
p-ul potential
  2
2      2.96880000           82.81110900
2      1.48440000            3.37968200
d-ul potential
  2
2      1.90660000           10.30427700
2      0.95330000            7.58803200
f-ul potential
  1
2      2.30750000          -21.47793600

--Link1--
%chk=Ph2IF-ts.chk
%mem=18000MB
%nprocshared=12
# Geom=AllCheck Guess=Check MP4/GenECP

-H -C -O -F -Cl -N 0
6-311G(2df,p)
****
-I      0
S   1   1.00
      2.1227650              1.0
S   1   1.00
      1.7704810              1.0
S   1   1.00
      0.3130840              1.0
S   1   1.00
      0.1240710              1.0000000
P   1   1.00
      2.4328870              1.0
P   1   1.00
      2.1372490              1.0
P   1   1.00
      0.3145460              1.0
P   1   1.00
      0.1049450              1.0000000
D   1   1.00
      0.414                  1.0000000
D   1   1.00
      0.184                  1.0000000
F   1   1.00
      0.434                  1.0000000
****

I   0
I-ECP    4    46
```

```
g-ul potential
  1
2     1.000000000           0.000000000
s-ul potential
  2
2     3.51120000           83.11386300
2     1.75560000            5.20187600
p-ul potential
  2
2     2.96880000           82.81110900
2     1.48440000            3.37968200
d-ul potential
  2
2     1.90660000           10.30427700
2     0.95330000            7.58803200
f-ul potential
  1
2     2.30750000          -21.47793600

--Link1--
%chk=Ph2IF-ts.chk
%mem=18000MB
%nprocshared=12
# Geom=AllCheck Guess=Check MP2/GenECP

-H -C -O -F -Cl -N 0
6-311+G(3df,2p)
****
-I     0
S   1   1.00
      2.1227650              1.0
S   1   1.00
      1.7704810              1.0
S   1   1.00
      0.3130840              1.0
S   1   1.00
      0.1240710              1.0000000
P   1   1.00
      2.4328870              1.0
P   1   1.00
      2.1372490              1.0
P   1   1.00
      0.3145460              1.0
P   1   1.00
      0.1049450              1.0000000
S   1   1.00
      0.0405                 1.0000000
P   1   1.00
      0.0328                 1.0000000
D   1   1.00
      0.552                  1.0000000
D   1   1.00
      0.276                  1.0000000
D   1   1.00
      0.138                  1.0000000
F   1   1.00
      0.434                  1.0000000
****
I   0
```

```
I-ECP     4     46
g-ul potential
  1
2       1.000000000           0.000000000
s-ul potential
  2
2       3.51120000           83.11386300
2       1.75560000            5.20187600
p-ul potential
  2
2       2.96880000           82.81110900
2       1.48440000            3.37968200
d-ul potential
  2
2       1.90660000           10.30427700
2       0.95330000            7.58803200
f-ul potential
  1
2       2.30750000          -21.47793600
```

Extrapolation procedure:
QCISD(T) = QCISD(T)/6-311G(d)/1st custom basis set
Δ+ = MP4SDTQ/6-311+G(d)/2nd custom basis set – MP4SDTQ/6-311G(d)/1st custom basis set
Δ2df = MP4SDTQ/6-311G(2df)/3rd custom basis set – MP4SDTQ/6-311G(d)/1st custom basis set
Δ3df = MP2/6-311+G(3df)/4th custom basis set – MP2/6-311G(2df)/3rd custom basis set – MP2/6-311+G(d)/2nd custom basis set + MP2/6-311G(d)/1st custom basis set
Higher-level corrections = 1.14 * number of electron pairs – 0.19 * number of alpha electrons – 5.95 * number of beta electrons

energy in hartree	Ph2IF ground state	reductive elimination TS	pseudorotation TS
QCISD(T)	–572.993781	–572.957132	–572.957852
Δ+	–0.034062	–0.036674	–0.041618
Δ2df	–0.364704	–0.362116	–0.364268
Δ3df	–0.034948	–0.033933	–0.034182
higher–level corrections	–0.245000	–0.245000	–0.245000
total	–573.672494	–573.634855	–573.642919

Geometries used for G2[ECP] calculations

```
Ground state
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ
Imaginary Frequencies: 0

C         -1.43848800        0.45847700        0.00003600
C         -2.80536200        0.23816600        0.00004700
C         -0.88625900        1.72808700        0.00012400
C         -3.64604800        1.34808600        0.00014300
H         -3.18278800       -0.77348500       -0.00000500
C         -1.74732200        2.82245800        0.00022000
H          0.18088300        1.88242600        0.00011700
C         -3.12354300        2.63539600        0.00022900
```

H	-4.71679800	1.19414000	0.00015600
H	-1.33033000	3.82059400	0.00028900
C	1.66988600	-0.08154000	-0.00001500
C	2.28614600	0.24463400	-1.20569300
C	2.28605400	0.24456300	1.20572800
C	3.50955200	0.90774500	-1.20406600
H	1.81809700	-0.01492800	-2.14645900
C	3.50946000	0.90767200	1.20423400
H	1.81793200	-0.01505600	2.14644300
C	4.12038100	1.23967400	0.00011800
H	3.98528700	1.16102500	-2.14232300
H	3.98512400	1.16089500	2.14254300
H	5.07265400	1.75286200	0.00017000
I	-0.15527700	-1.28661500	-0.00011500
F	-2.00233600	-2.40319200	-0.00020000
H	-3.78610300	3.49033000	0.00030700

Reductive elimination transition state
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ
Imaginary Frequencies: 1

C	-1.77256800	-0.05312100	-0.00013500
C	-2.31562700	0.37031000	-1.20946600
C	-2.31671400	0.36844600	1.20935600
C	-3.41694500	1.21926100	-1.20399300
H	-1.88928500	0.04257500	-2.14714100
C	-3.41805200	1.21737700	1.20420300
H	-1.89121500	0.03925600	2.14690600
C	-3.96751500	1.64285400	0.00018400
H	-3.84253400	1.54870500	-2.14238400
H	-3.84451100	1.54533600	2.14271900
C	1.74988400	0.09674300	0.00012400
C	2.09465400	0.65267900	-1.21761200
C	2.09430000	0.65249500	1.21804100
C	2.83546700	1.83145200	-1.19990600
H	1.82250600	0.17999400	-2.14799200
C	2.83510800	1.83127900	1.20071300
H	1.82188100	0.17968600	2.14827900
C	3.20574000	2.42618000	0.00050200
H	3.12161300	2.27909100	-2.14274300
H	3.12096800	2.27879100	2.14369700
H	3.78035400	3.34164900	0.00065300
I	-0.06507600	-1.34237300	-0.00029700
F	2.26962900	-1.79206600	0.00015400
H	-4.82379900	2.30356200	0.00030600

Pseudorotation transition state
Charge: 0
Multiplicity: 1
Geometry: B3LYP/6-31g(d)/LANL2DZ
Imaginary Frequencies: 1

C	-1.54670500	-0.25304200	-0.00002700
C	-2.05139700	-0.70658800	-1.21053200
C	-2.05150900	-0.70628100	1.21054600
C	-3.06668700	-1.65842100	-1.20474200
H	-1.66496100	-0.32940000	-2.14735700
C	-3.06679900	-1.65811400	1.20490400
H	-1.66516000	-0.32885300	2.14731000
C	-3.57141600	-2.13421800	0.00011800
H	-3.46400000	-2.02225700	-2.14292600
H	-3.46420000	-2.02171000	2.14314400

C	1.54670700	-0.25304100	0.00007700
C	2.05138700	-0.70632500	1.21068400
C	2.05152200	-0.70654000	-1.21039300
C	3.06667800	-1.65815800	1.20511000
H	1.66494100	-0.32893400	2.14742300
C	3.06681300	-1.65837200	-1.20453600
H	1.66518200	-0.32931700	-2.14724300
C	3.57141900	-2.13421500	0.00035800
H	3.46398200	-2.02178900	2.14337700
H	3.46422200	-2.02217100	-2.14269300
H	4.36336500	-2.87078400	0.00046800
I	-0.00000100	1.30243300	-0.00014600
F	-0.00000200	3.50188400	-0.00037200
H	-4.36336200	-2.87078800	0.00017500

Effect of solvation on single point energy calculations

The general effect of solvation on the single point energies of reductive elimination and pseudorotation barriers of diphenyliodonium(III) fluoride was examined as a model reaction. While solvation modeling greatly affected barriers at the double-zeta level, solvation has only minimal effects with larger basis sets.

Table S2. Effect of solvation on calculated barriers to reductive elimination and pseudorotation of diphenyliodonium(III) fluoride

	barrier (kcal/mol)			
	without solvation	*with solvation*	*without solvation*	*with solvation*
	PBE0/cc-pVDZ/ LANL2DZ	PBE0/cc-pVDZ/ LANL2DZ/PCM(DMF)	PBE0/cc-pVTZ/ LANL2DZ	PBE0/cc-pVTZ/ LANL2DZ/PCM(DMF)
reductive elimination	17.1	16.4	19.7	18.8
pseudorotation	25.2	20.2	22.8	20.8

Predicted influence of auxiliary structure on reductive elimination barrier

Activation energies for reductive elimination of fluorobenzene from iodonium(III) fluoride species were calculated to determine the effect of ring atom substitution and spirocyclic auxiliaries. As shown in the figure below, substitution at the 4-position is not expected to have a strong influence on barriers to reductive elimination.

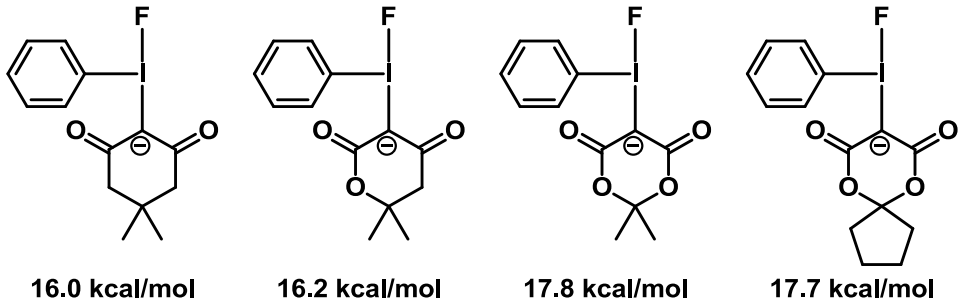
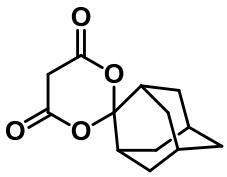
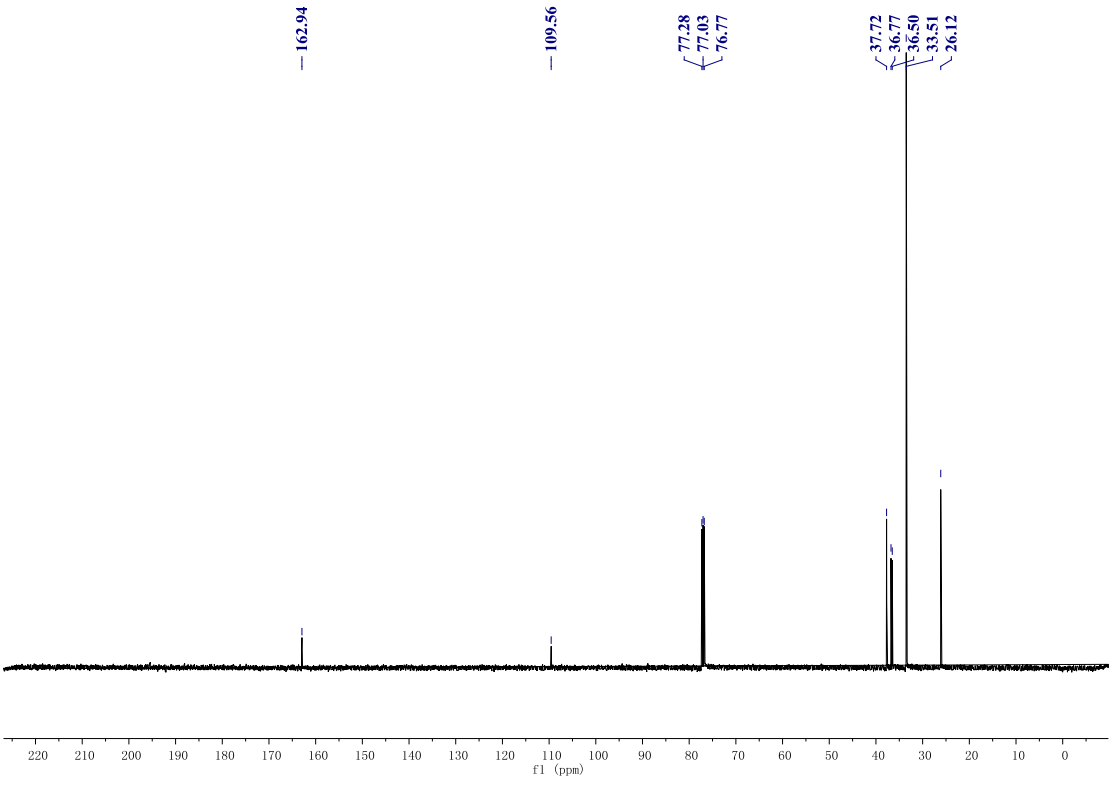
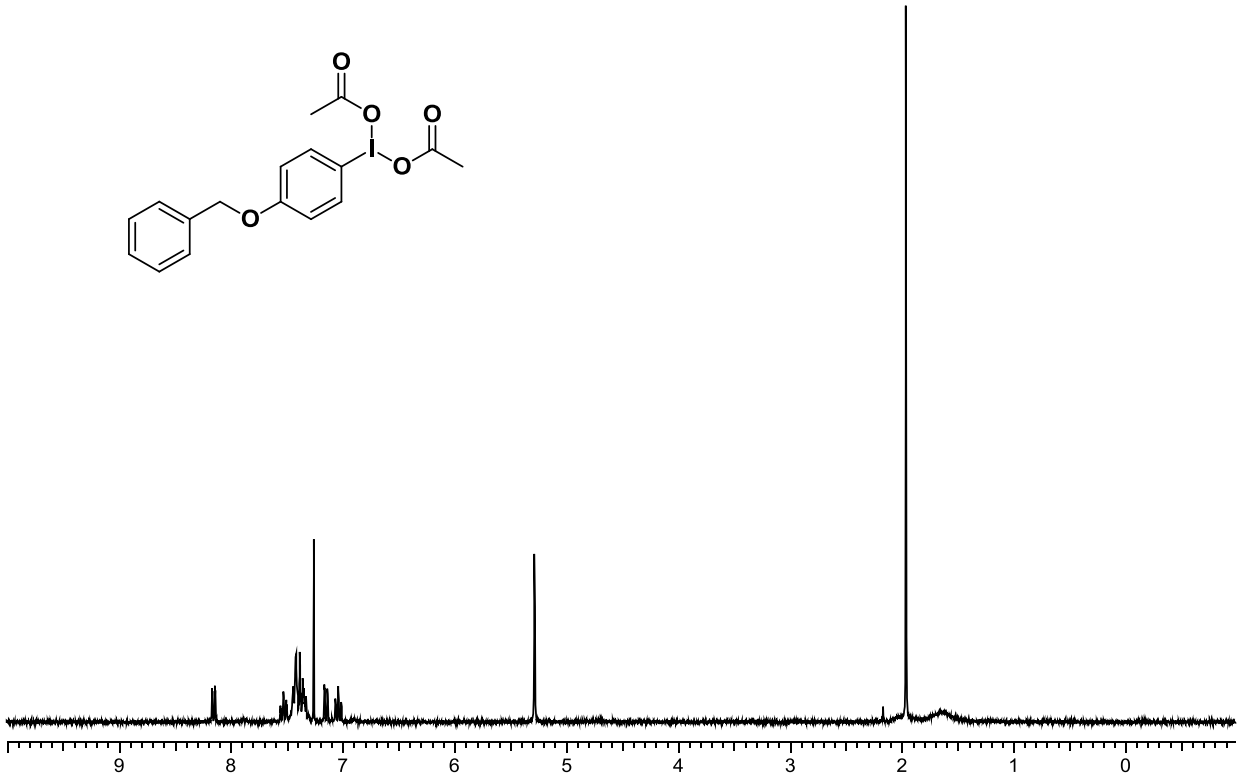


Figure S2 Calculated barriers of reductive elimination with different auxiliaries. PBE0-D3/aug-cc-pVTZ/SDB-aug-cc-pVTZ(I) single point, B3LYP/6-31G(d)/LANL2DZ(I)/PCM(DMF) geometry and vibrational correction.

Spectroscopic Data



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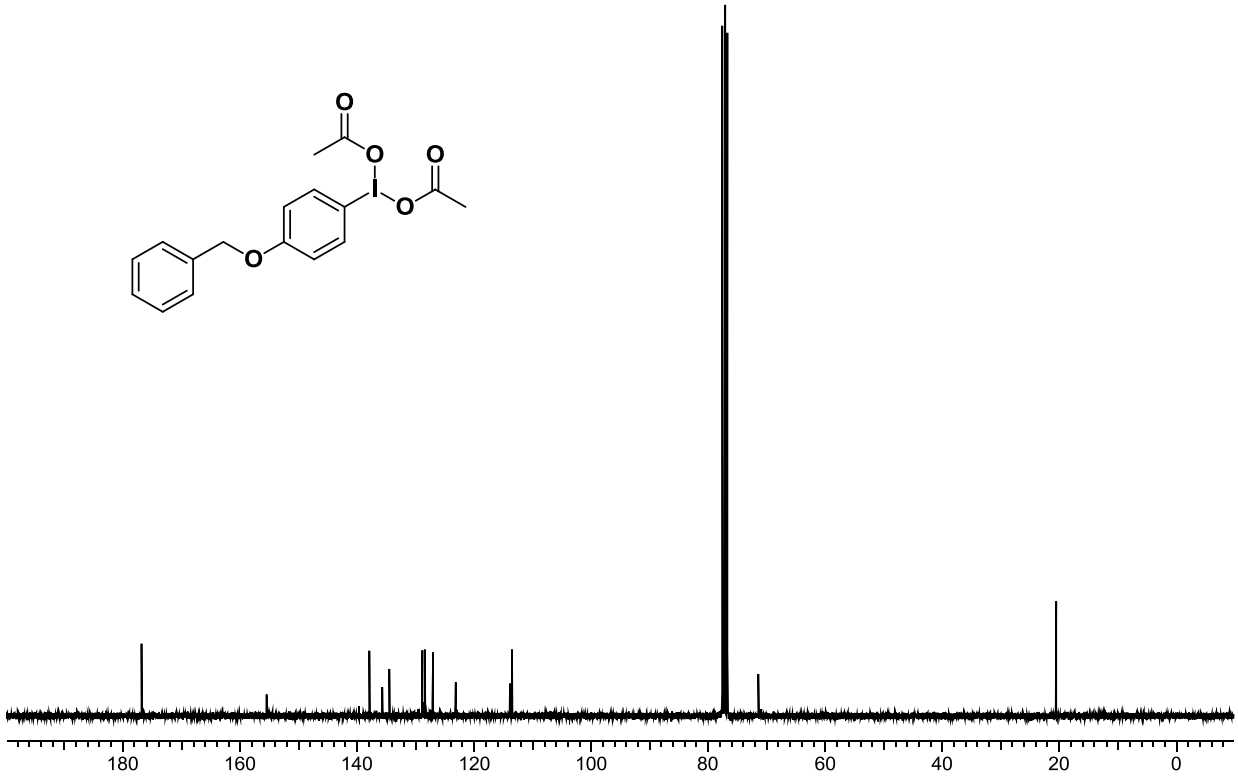
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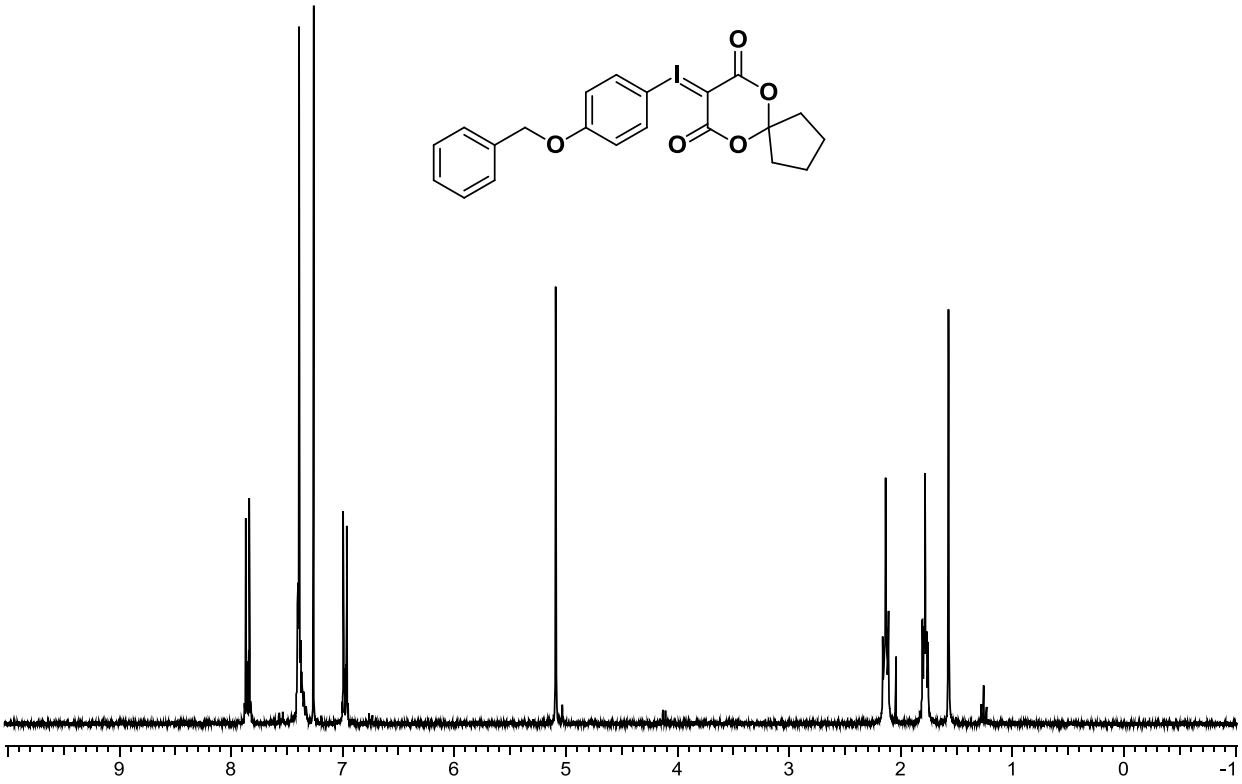
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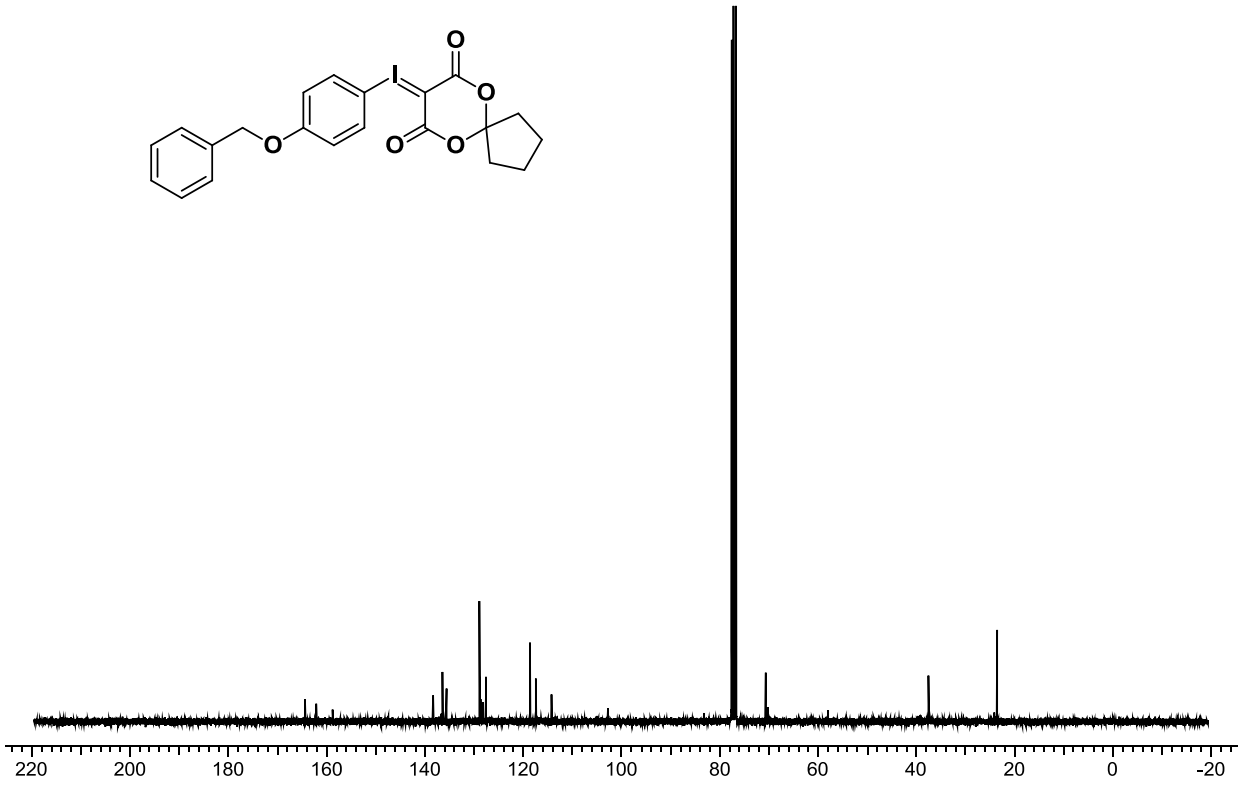
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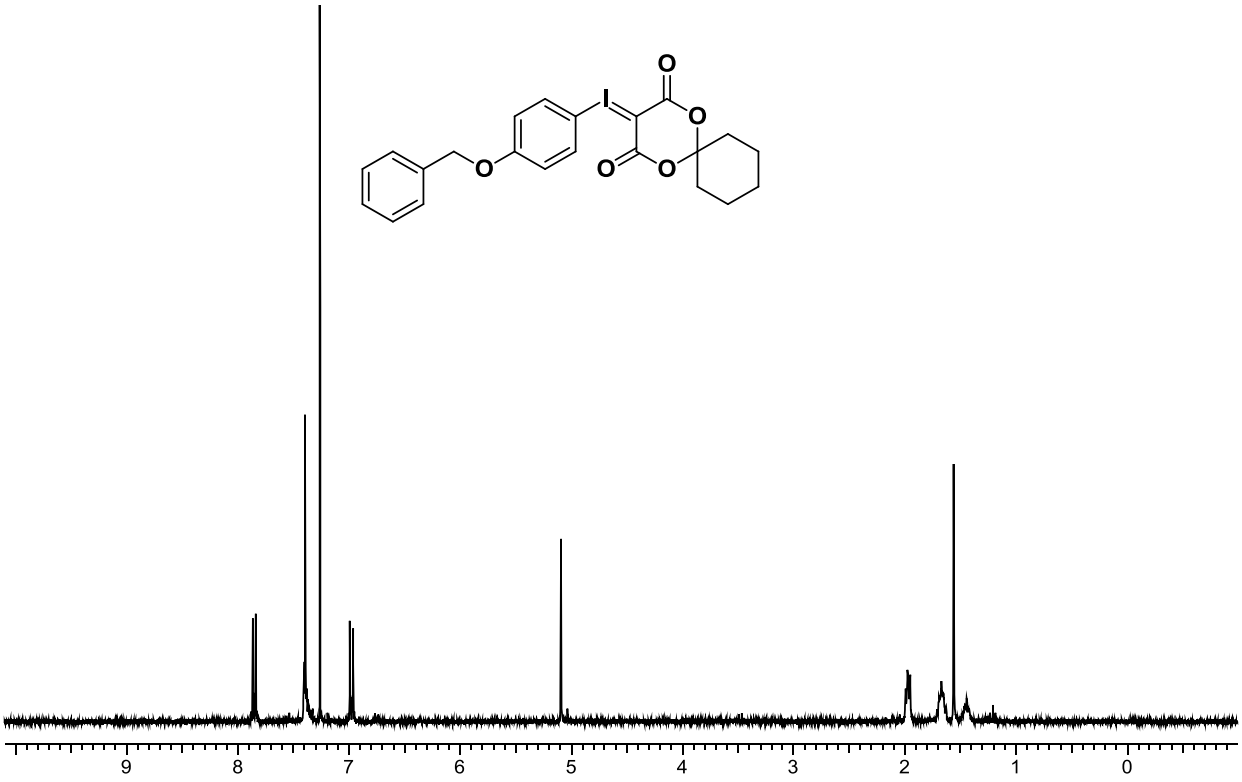
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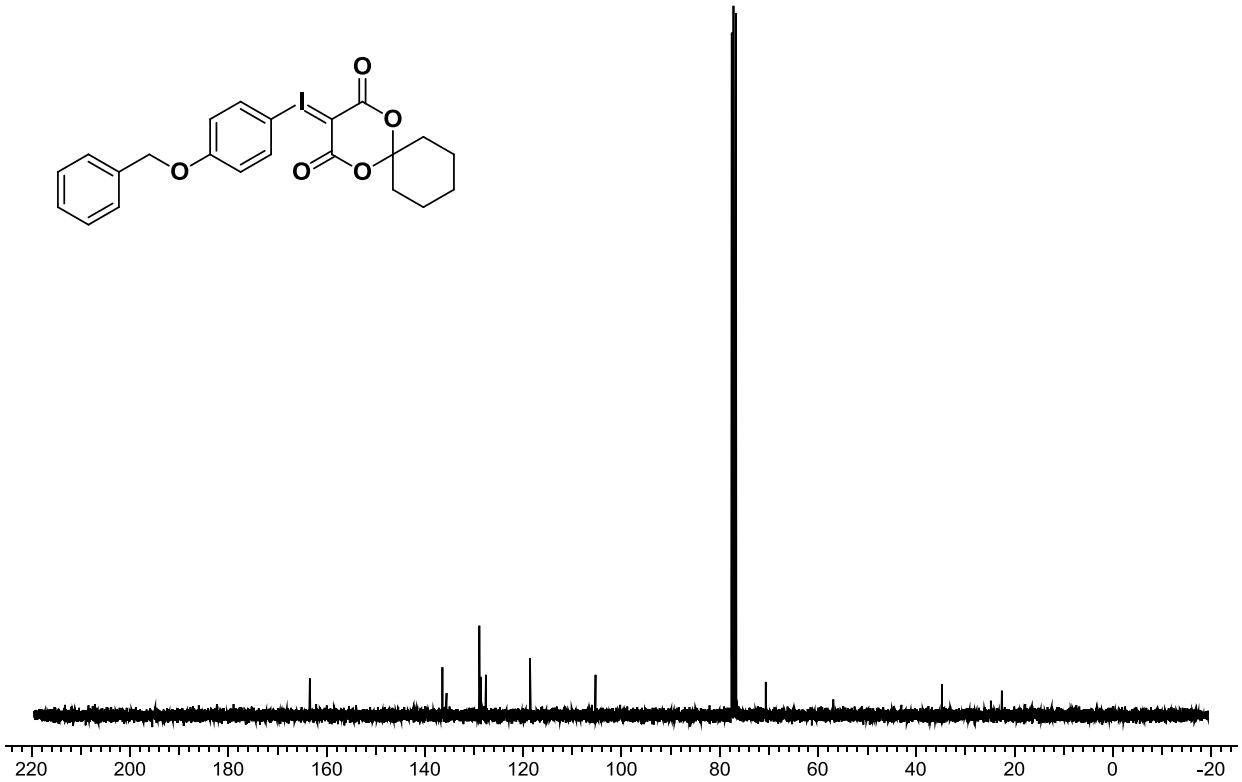
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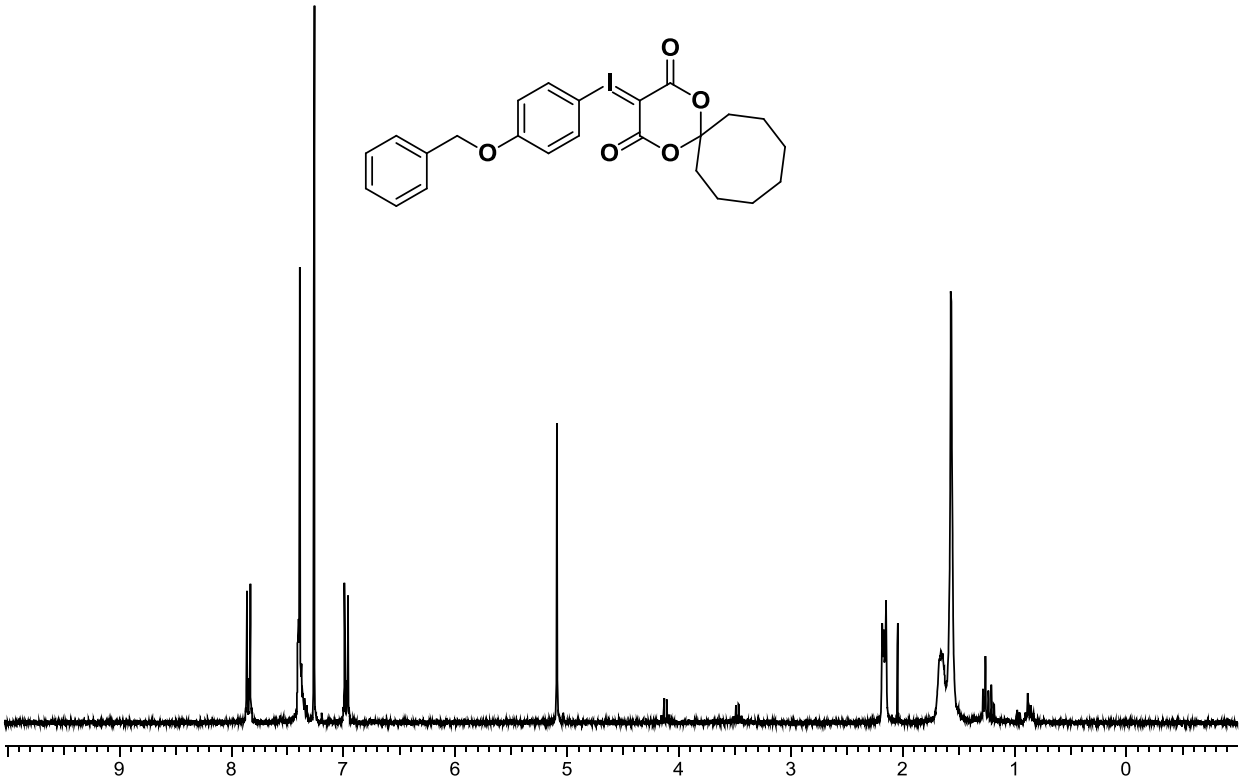
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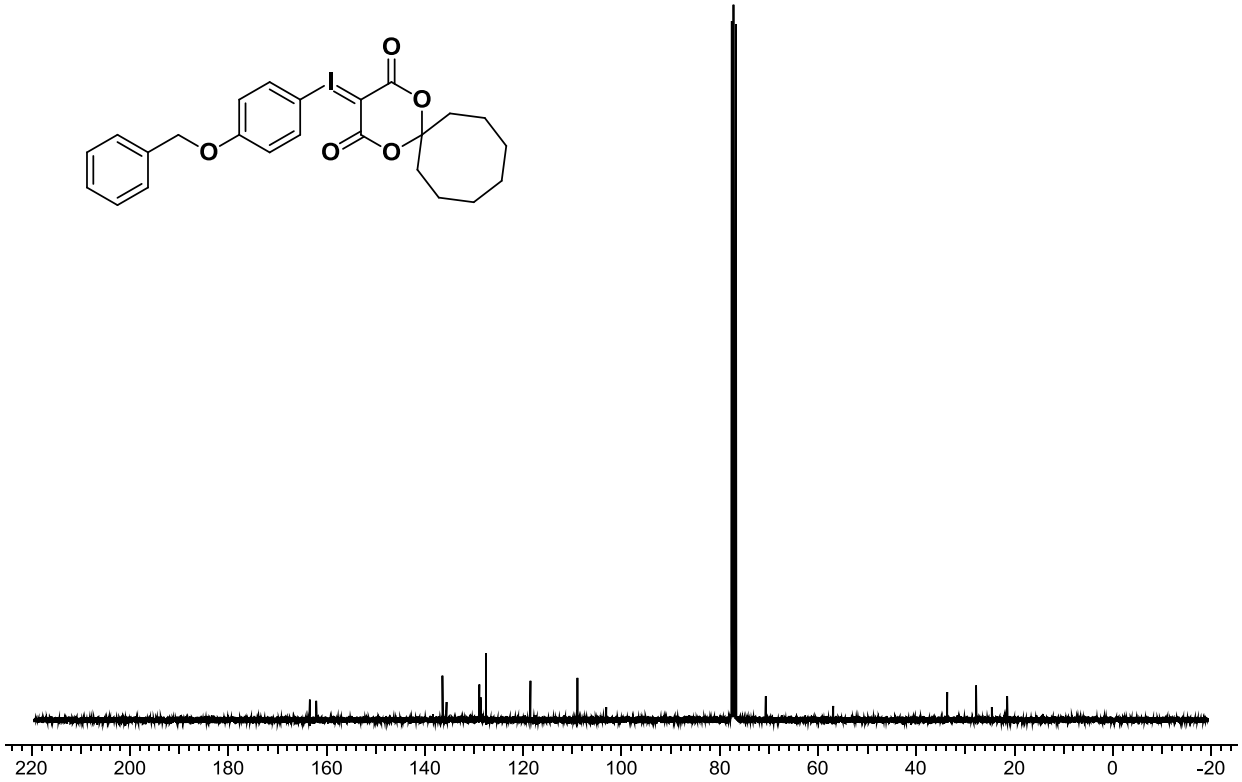
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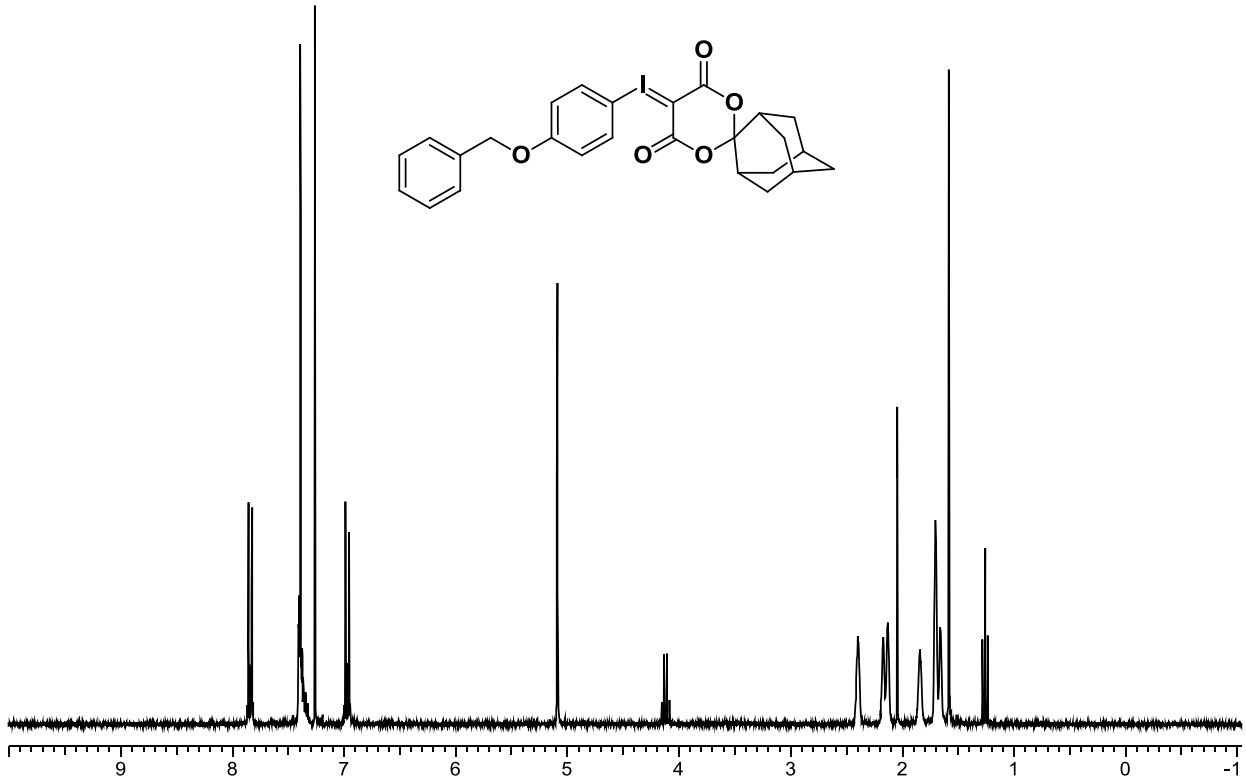
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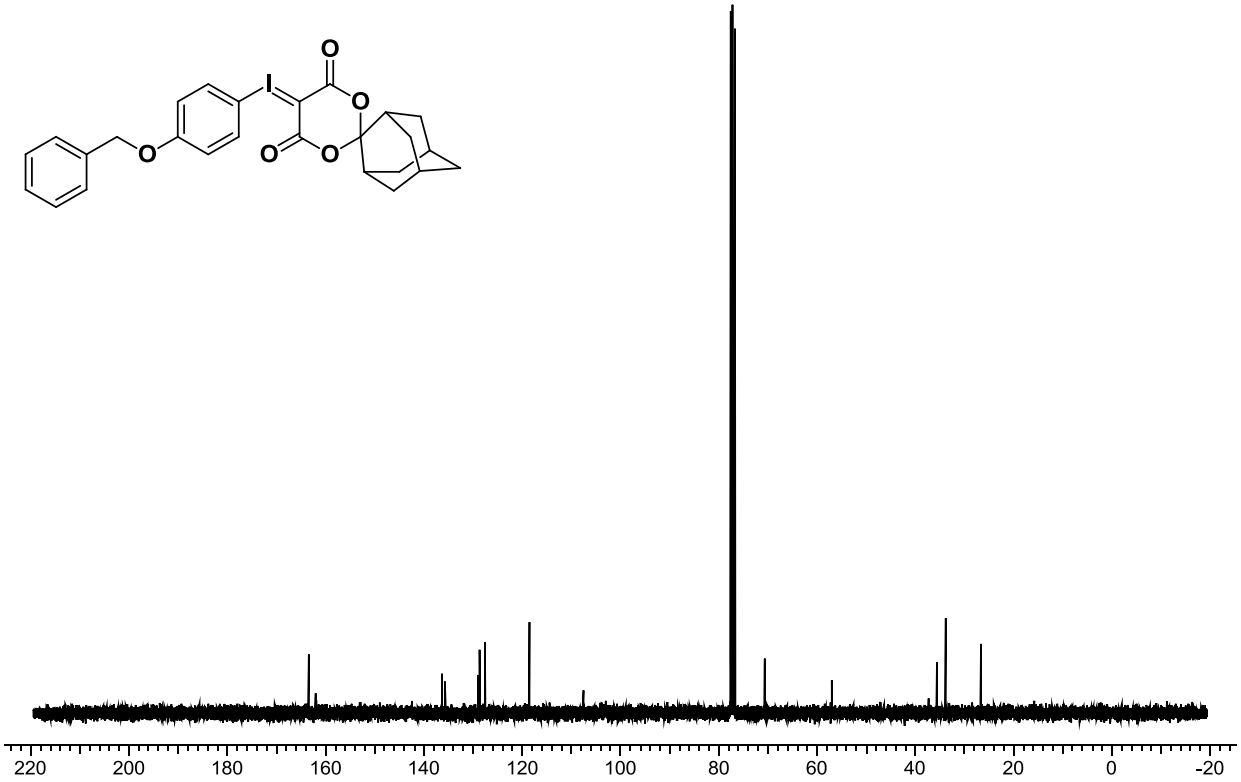
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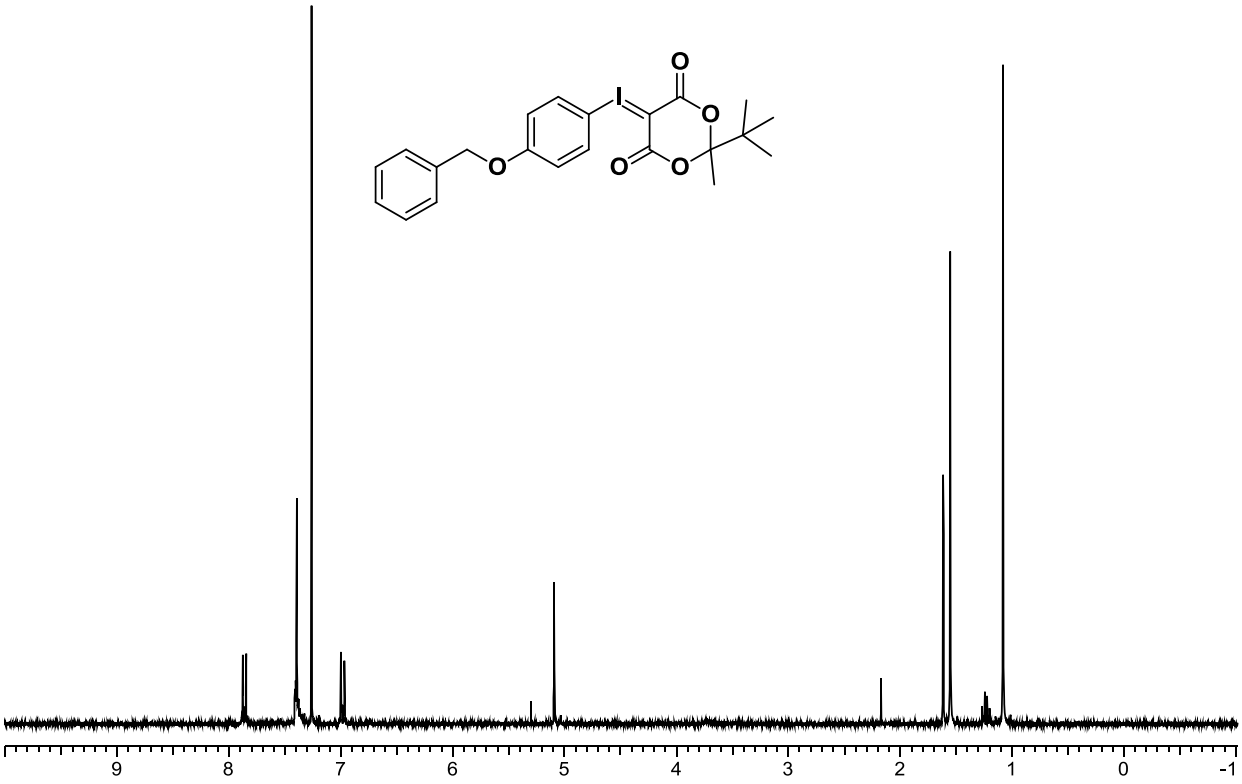
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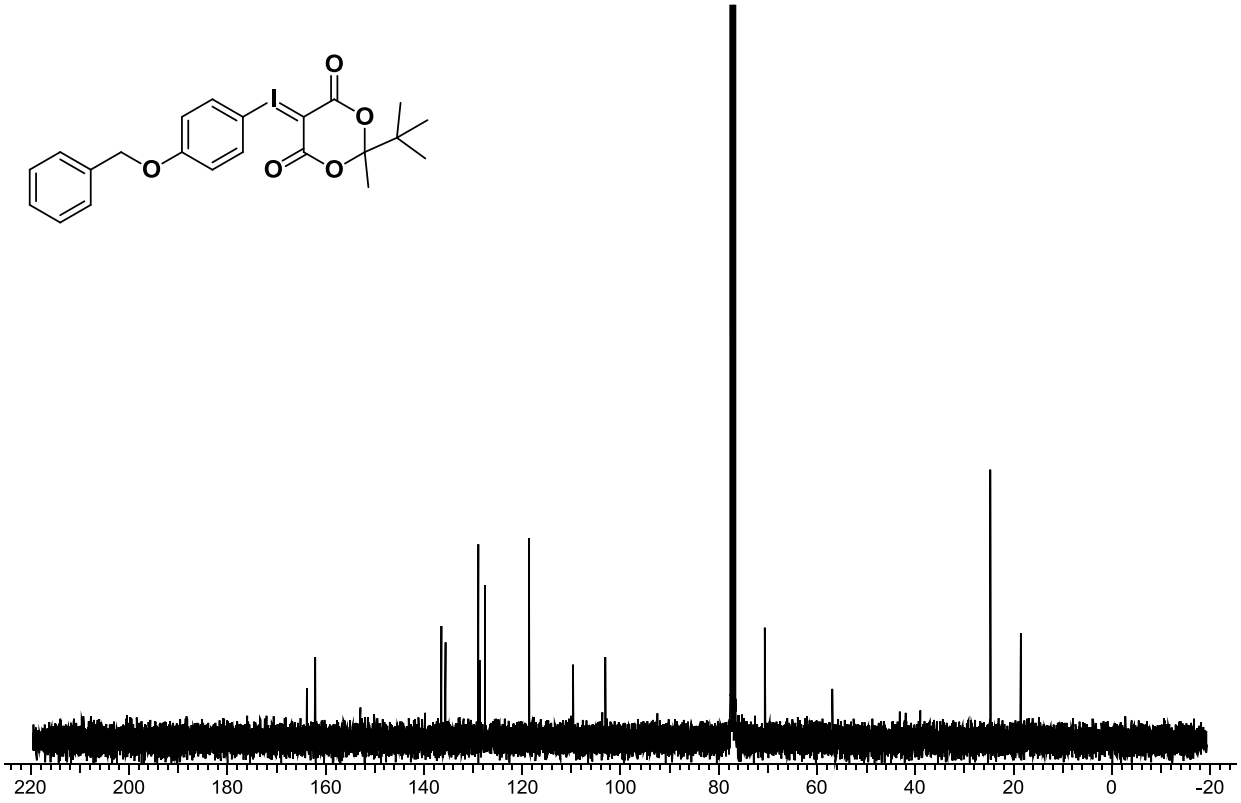
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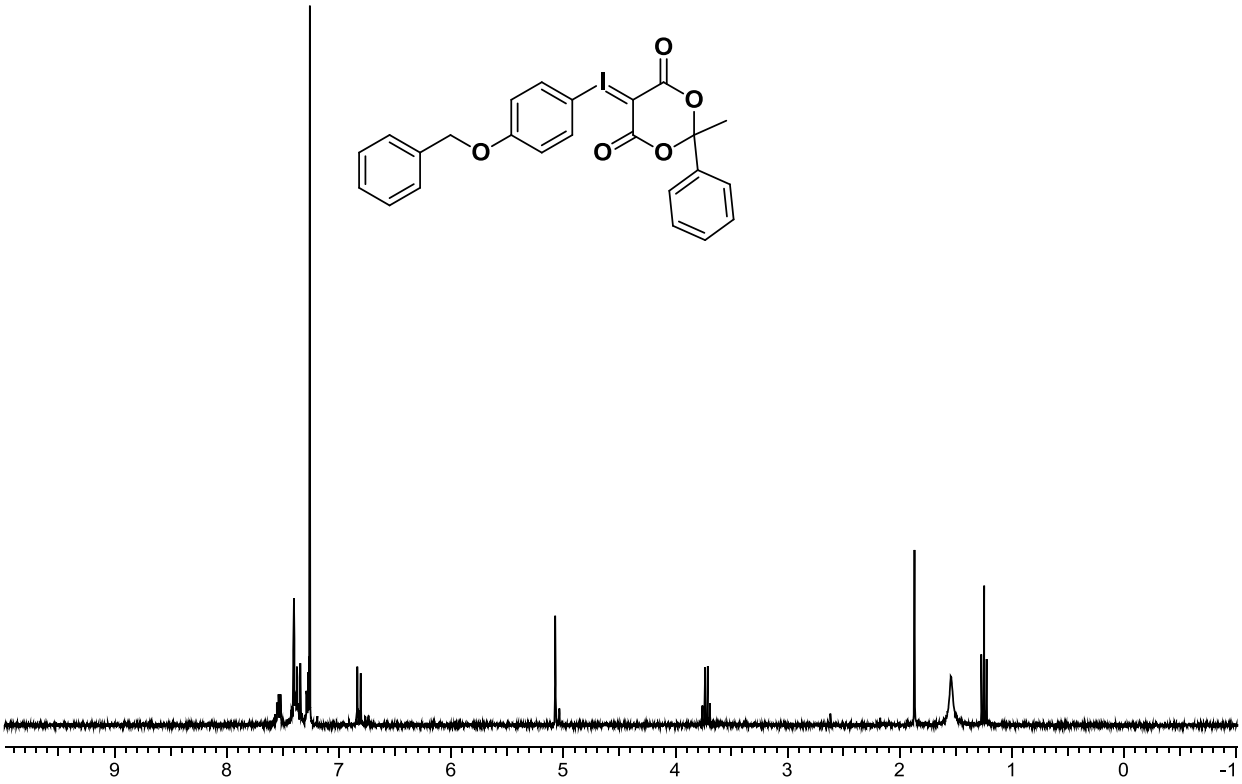
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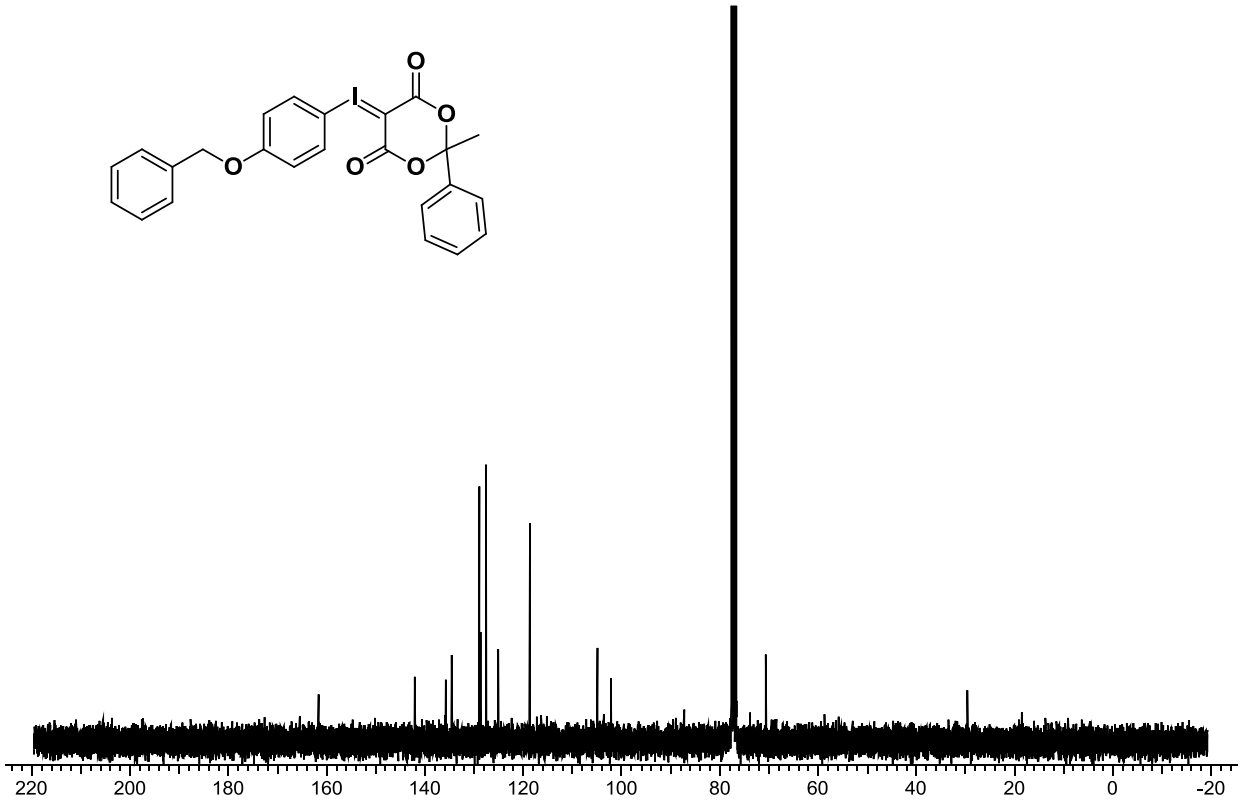
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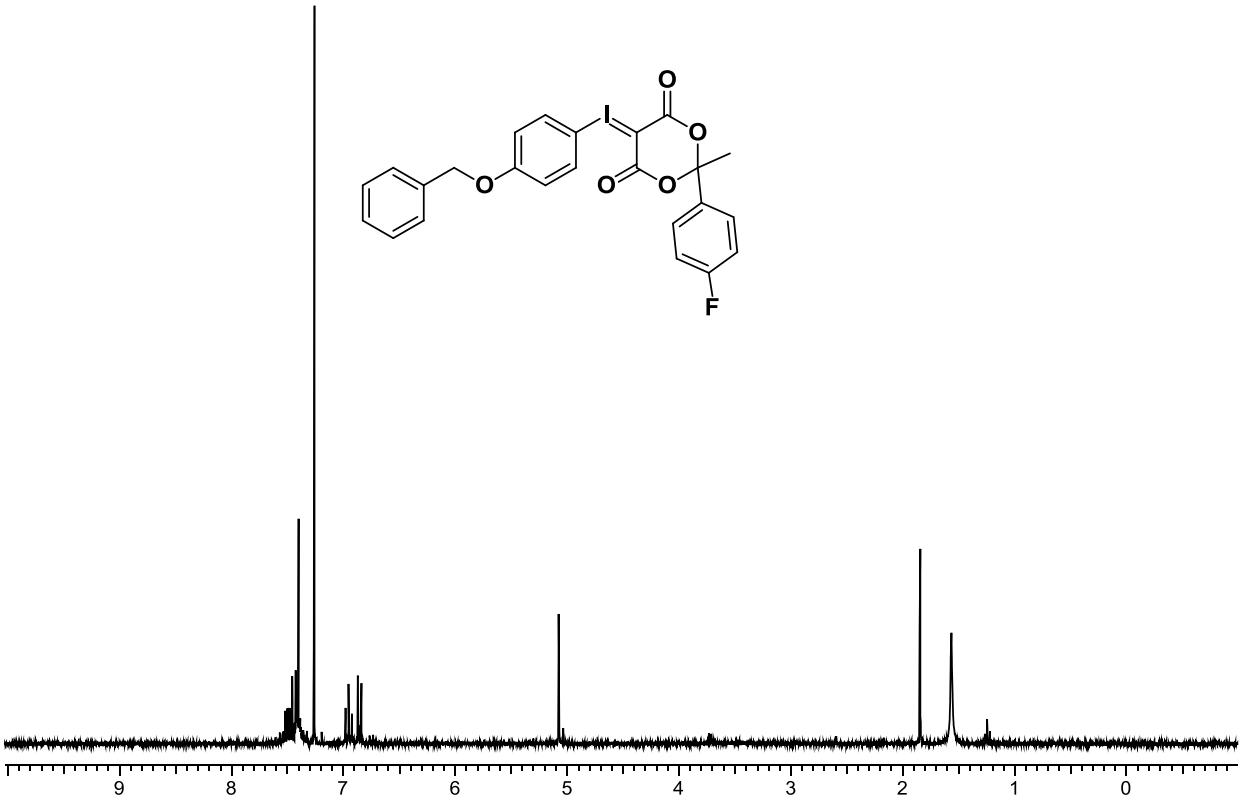
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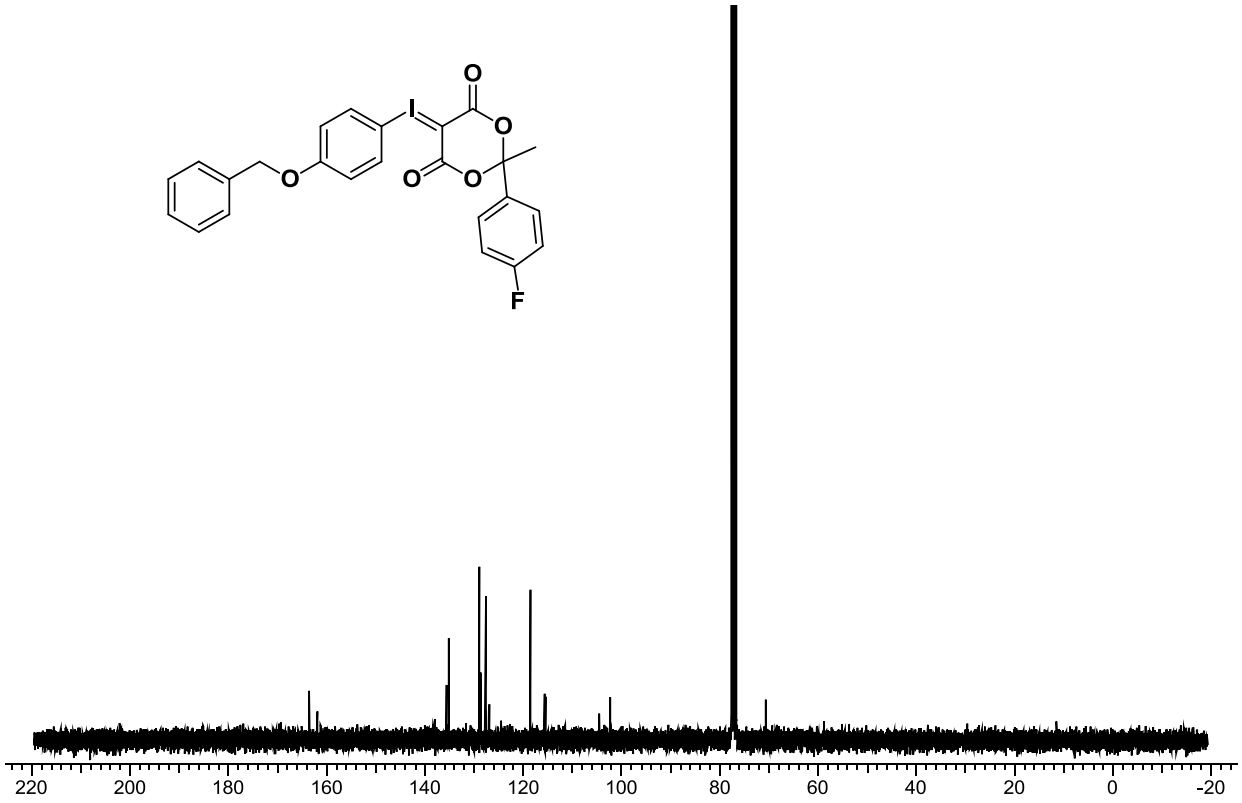
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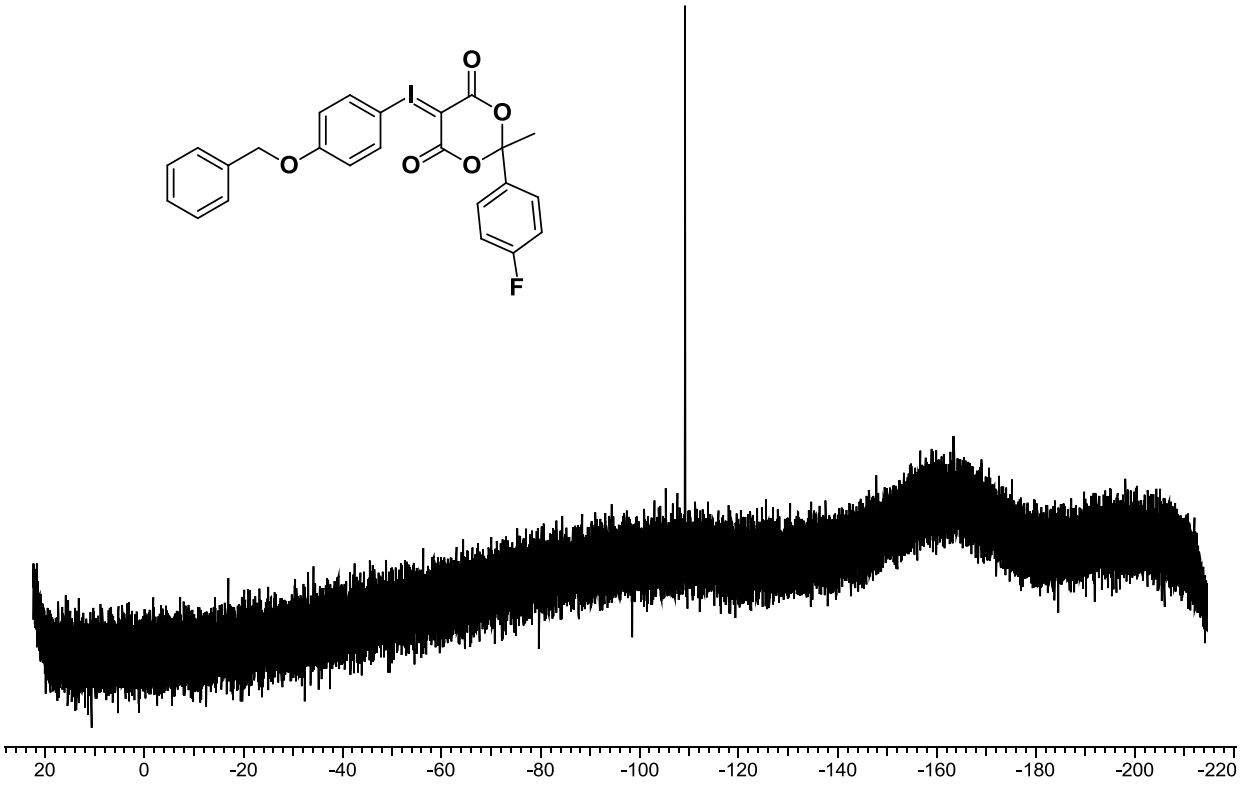
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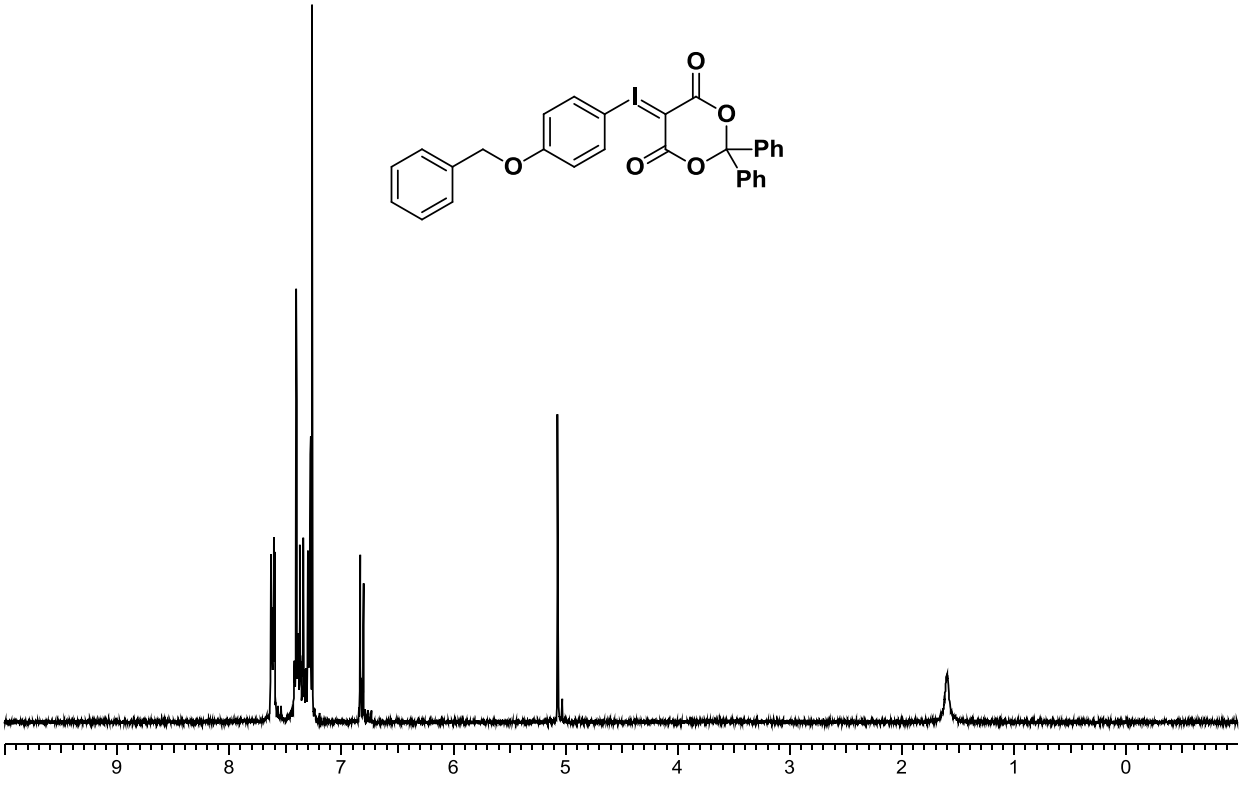
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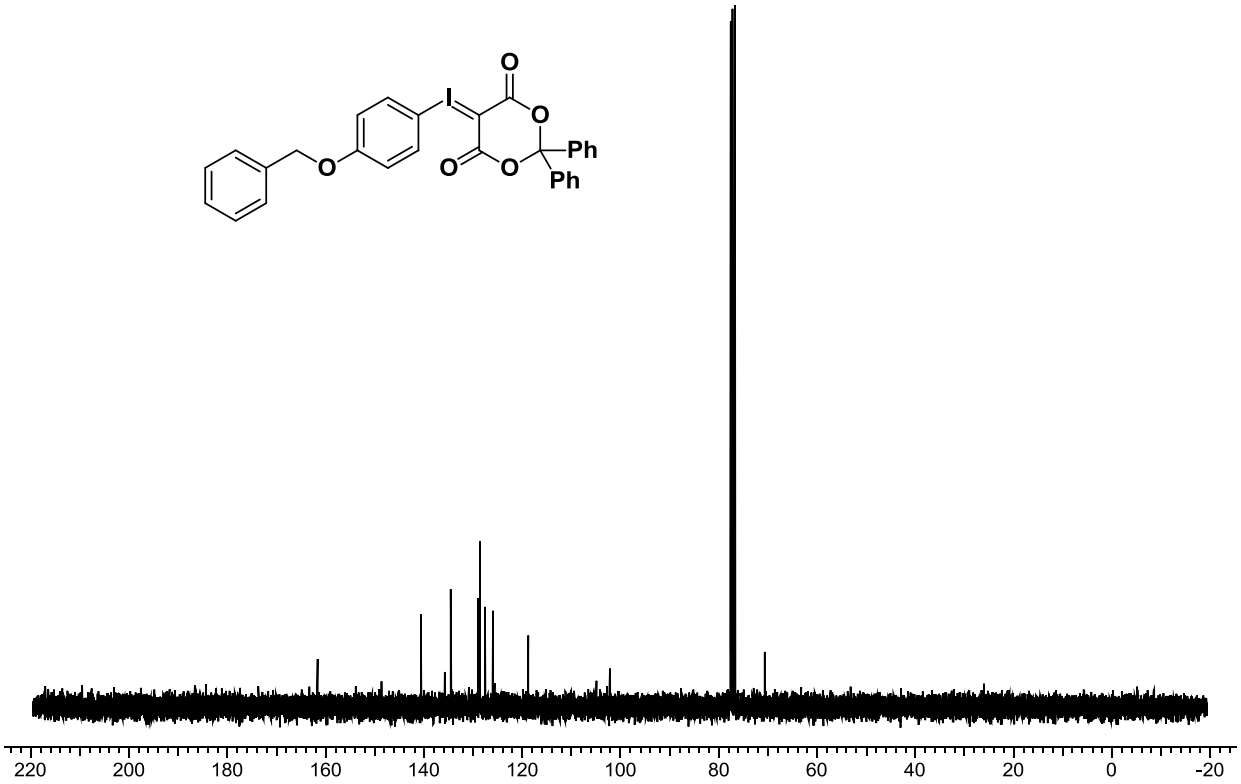
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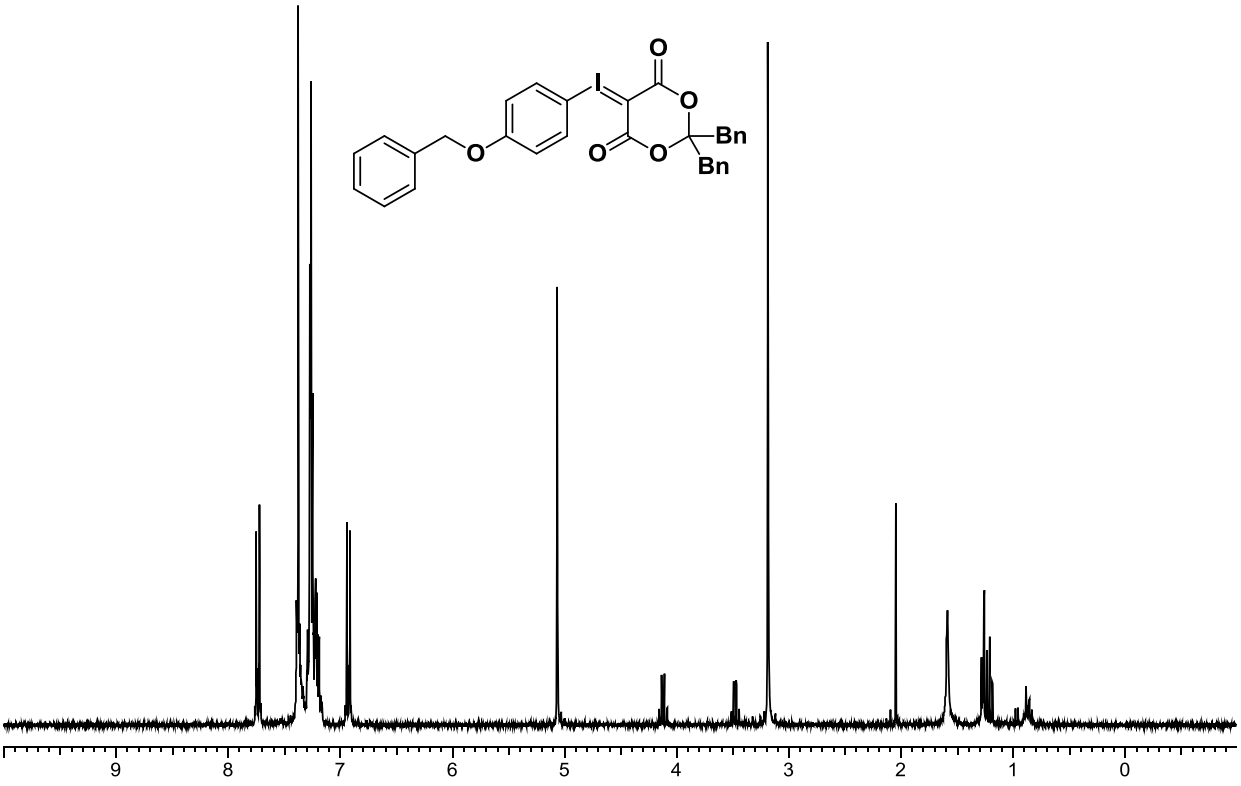
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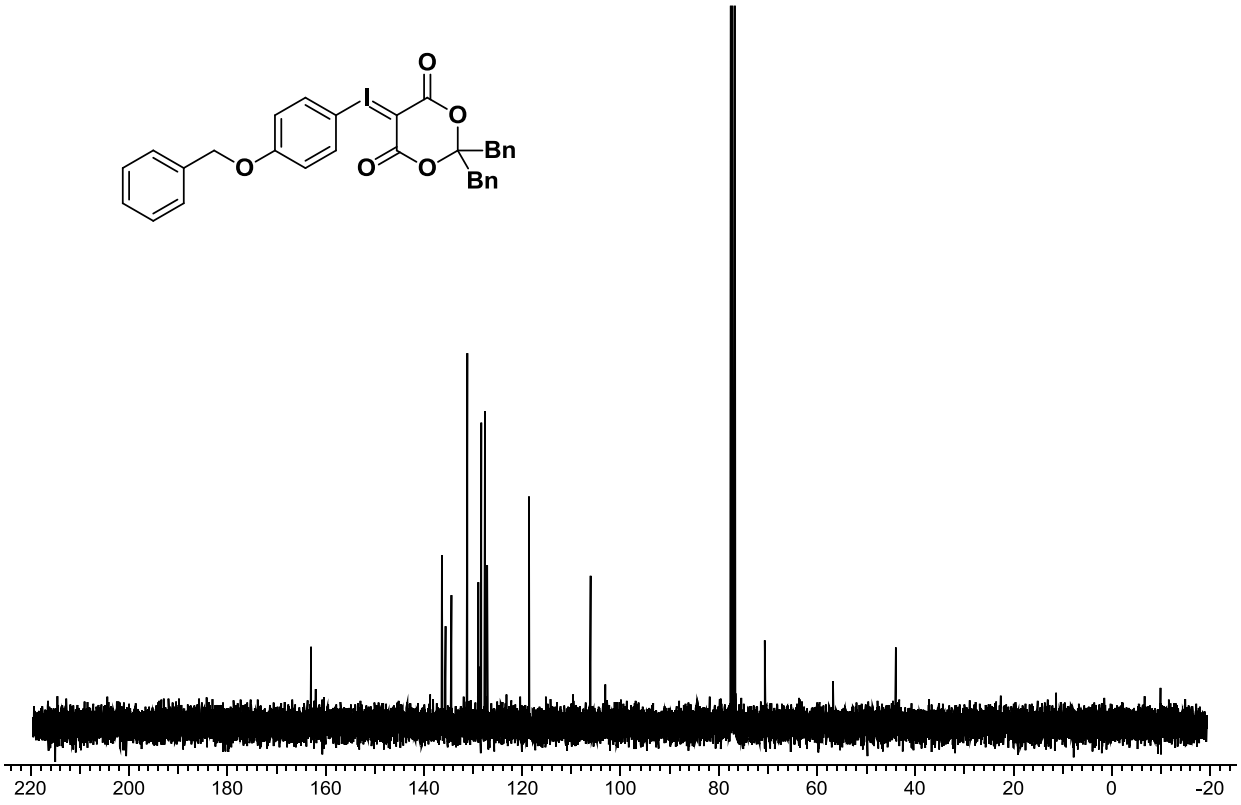
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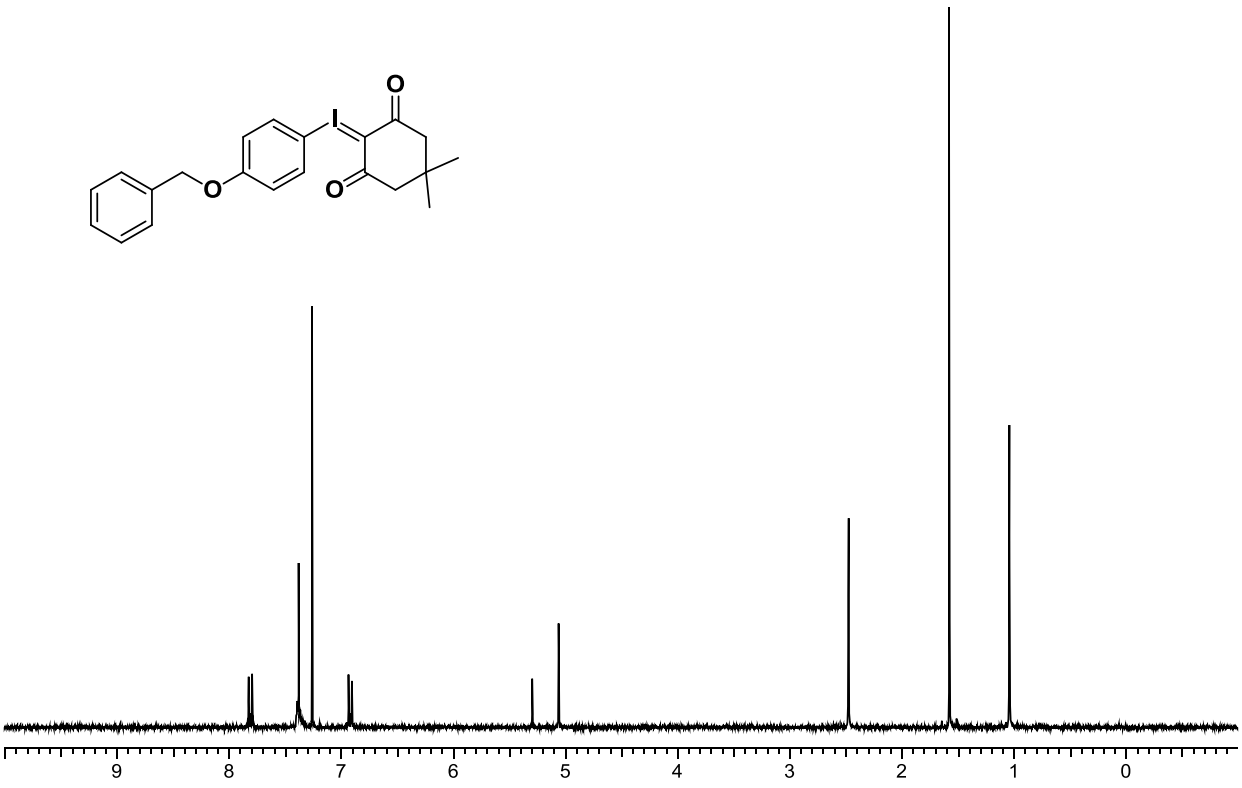
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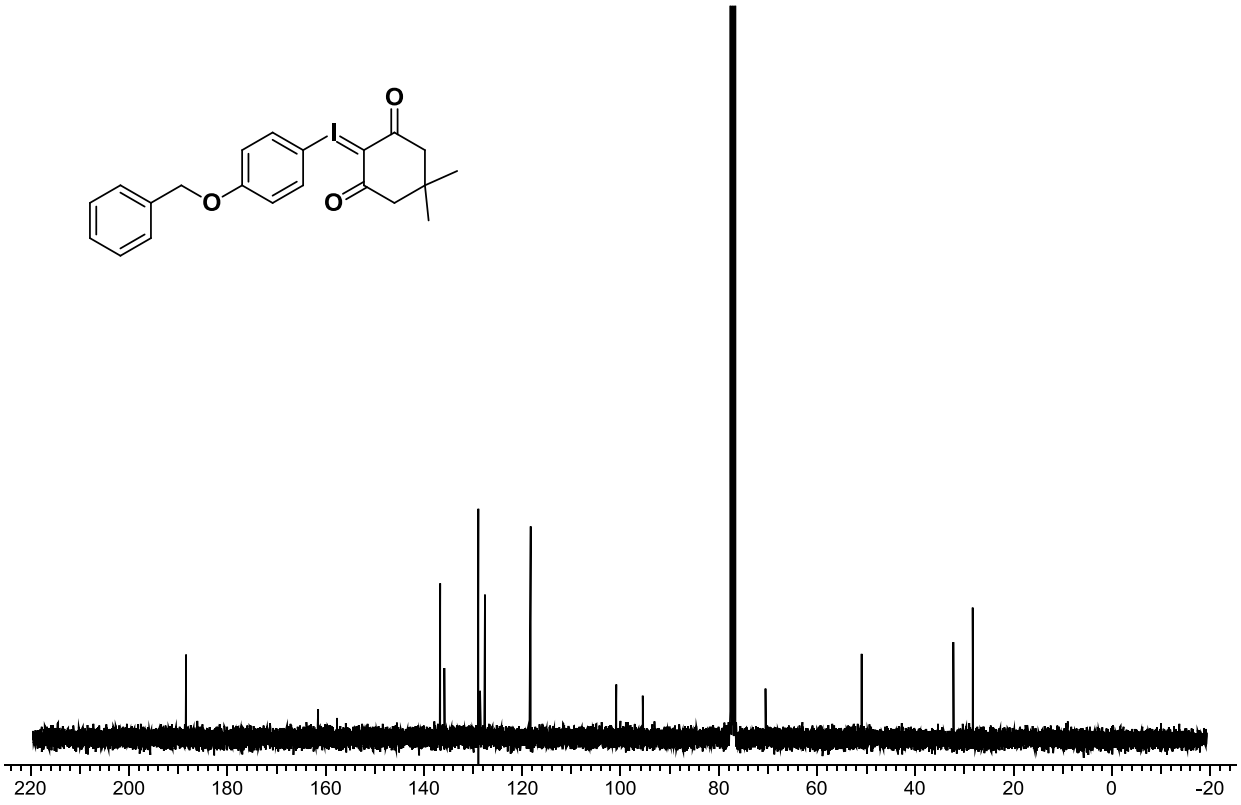
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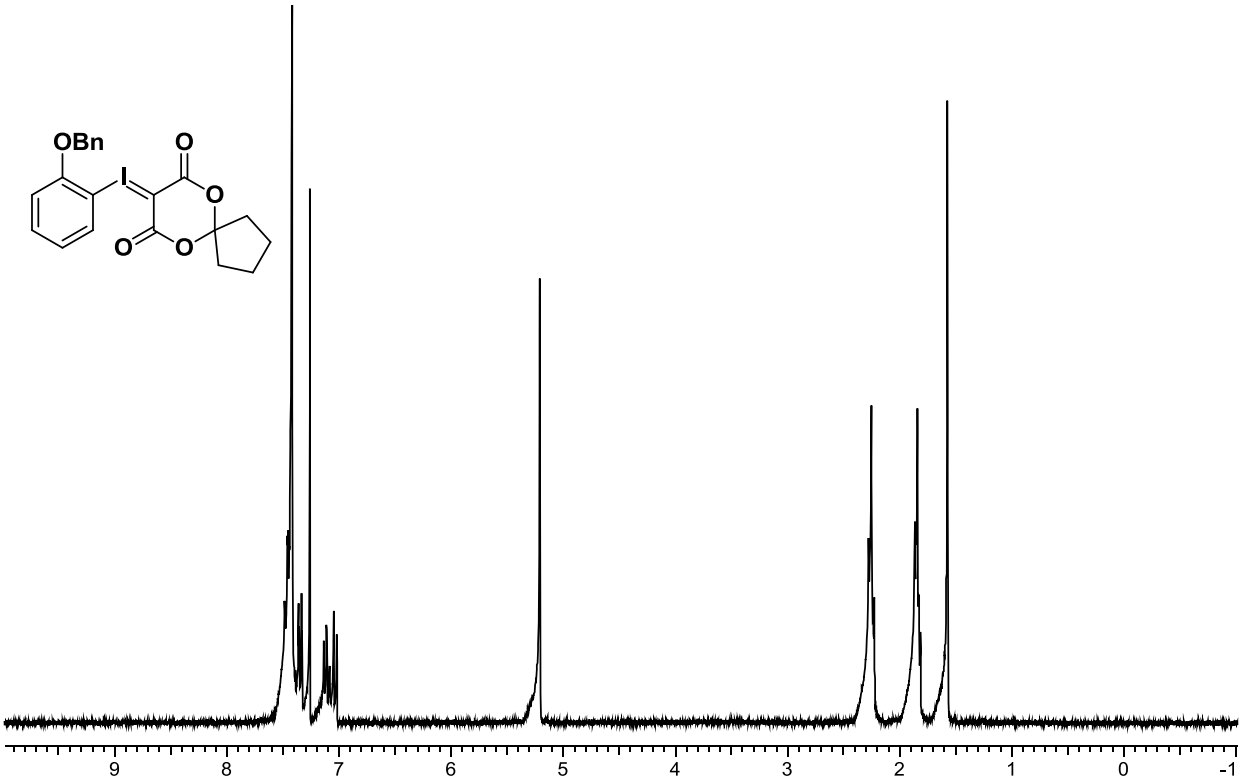
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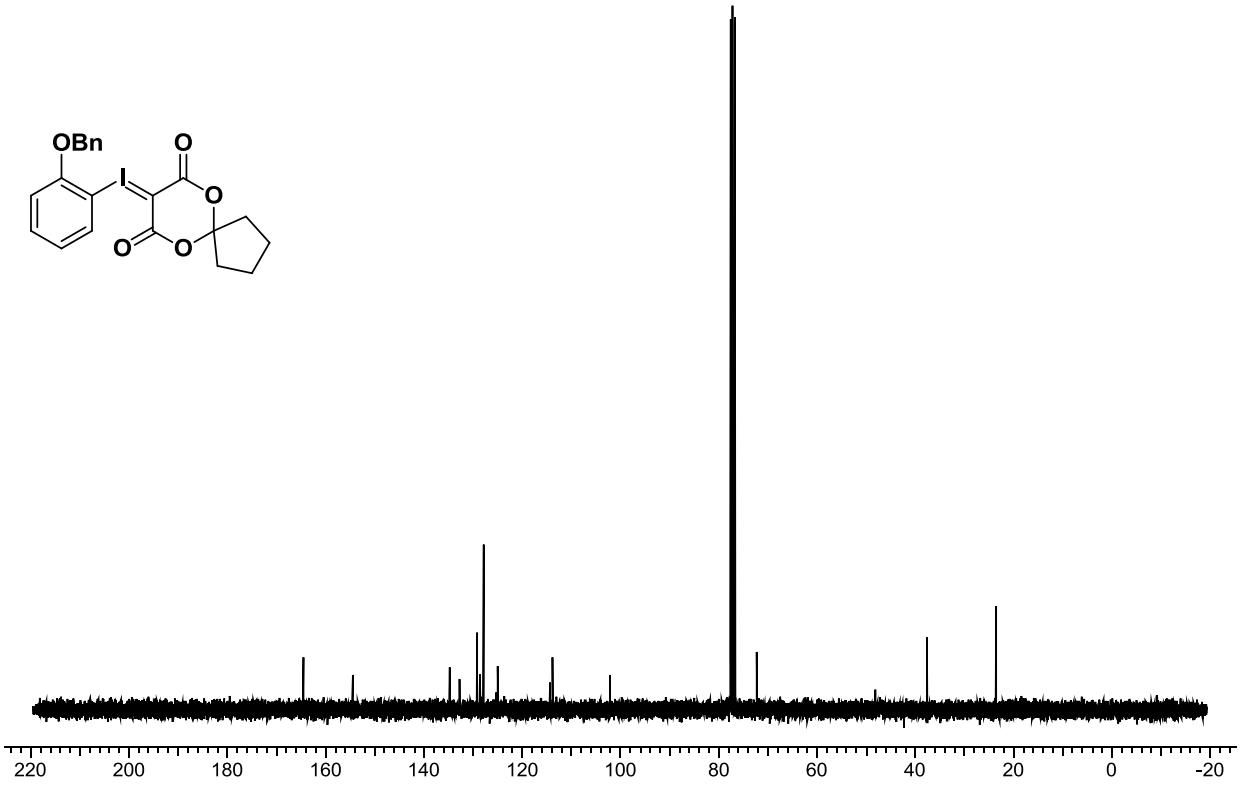
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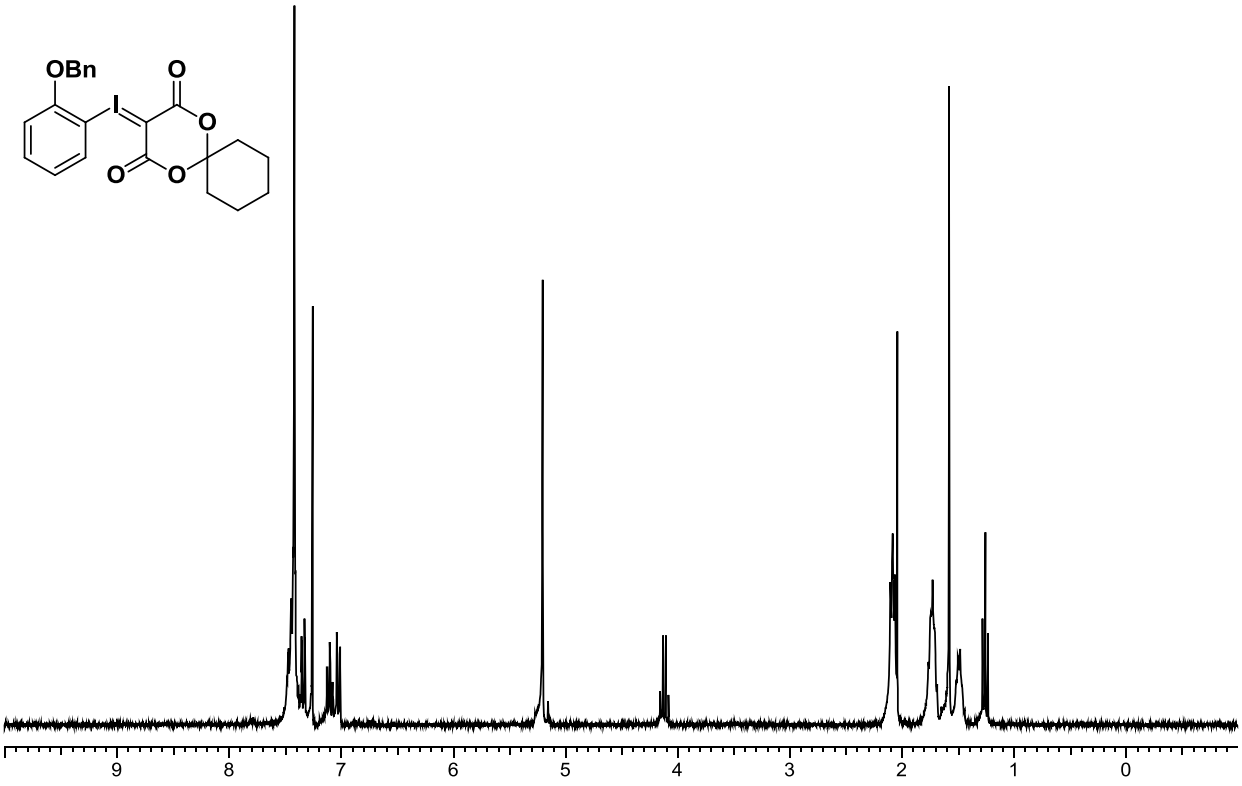
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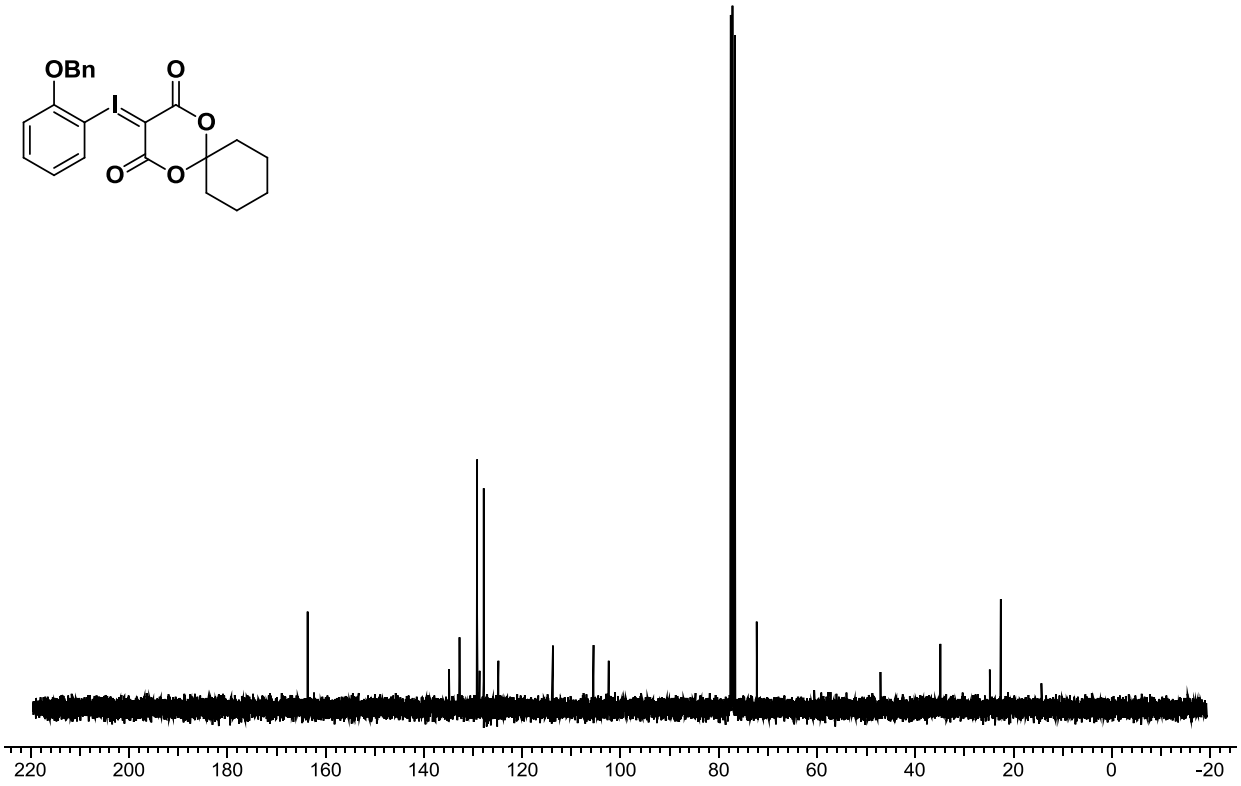
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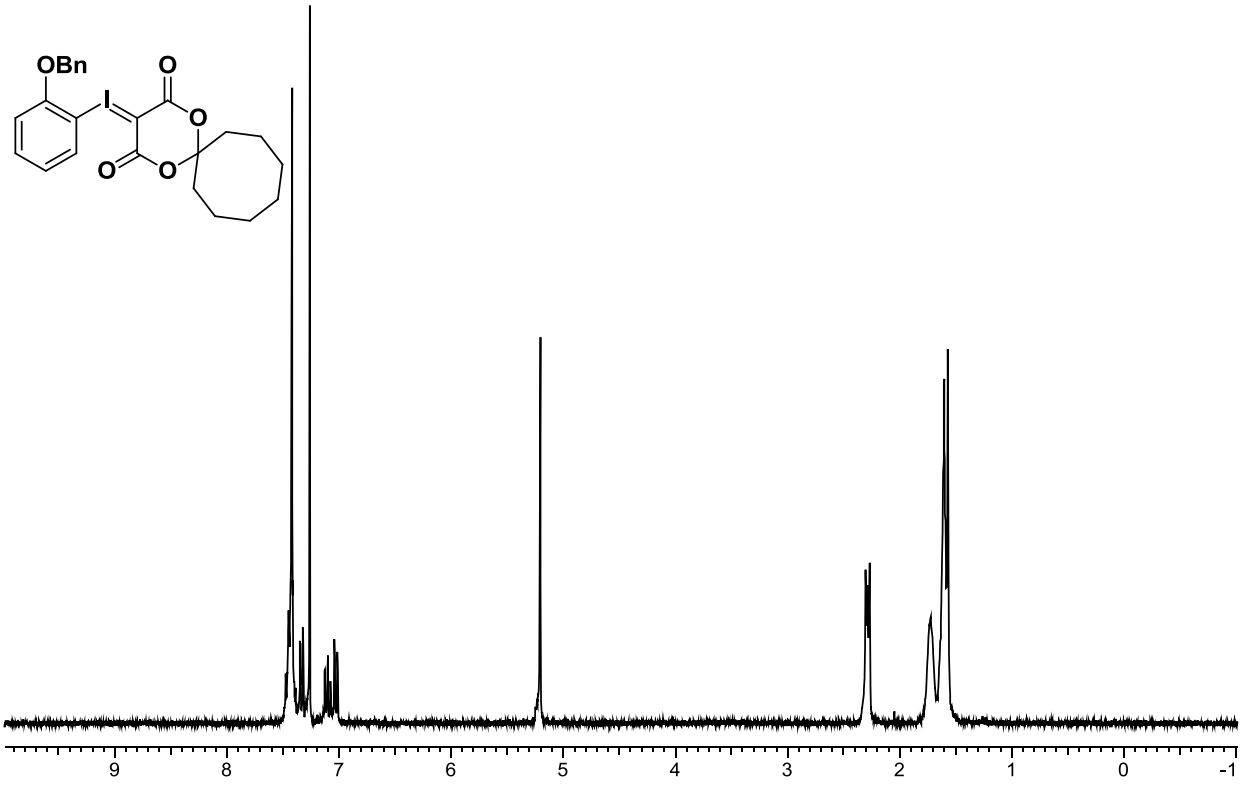
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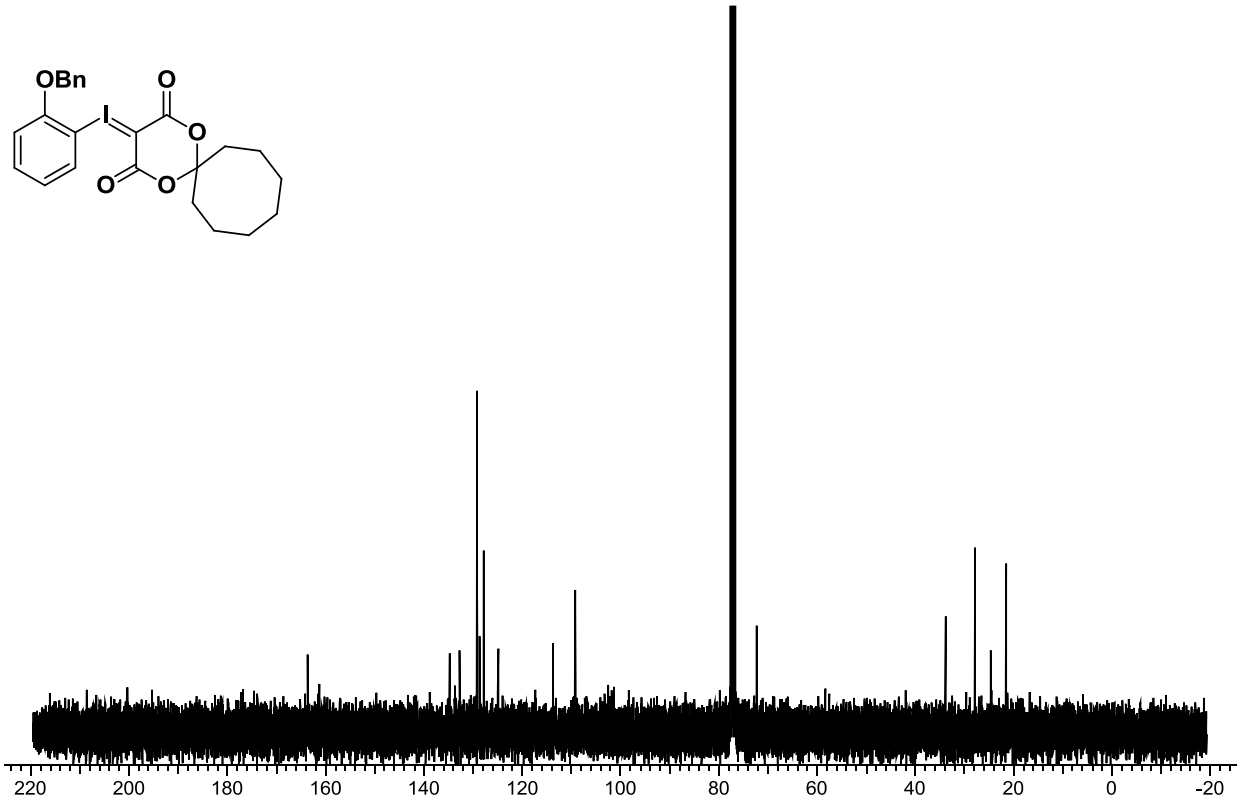
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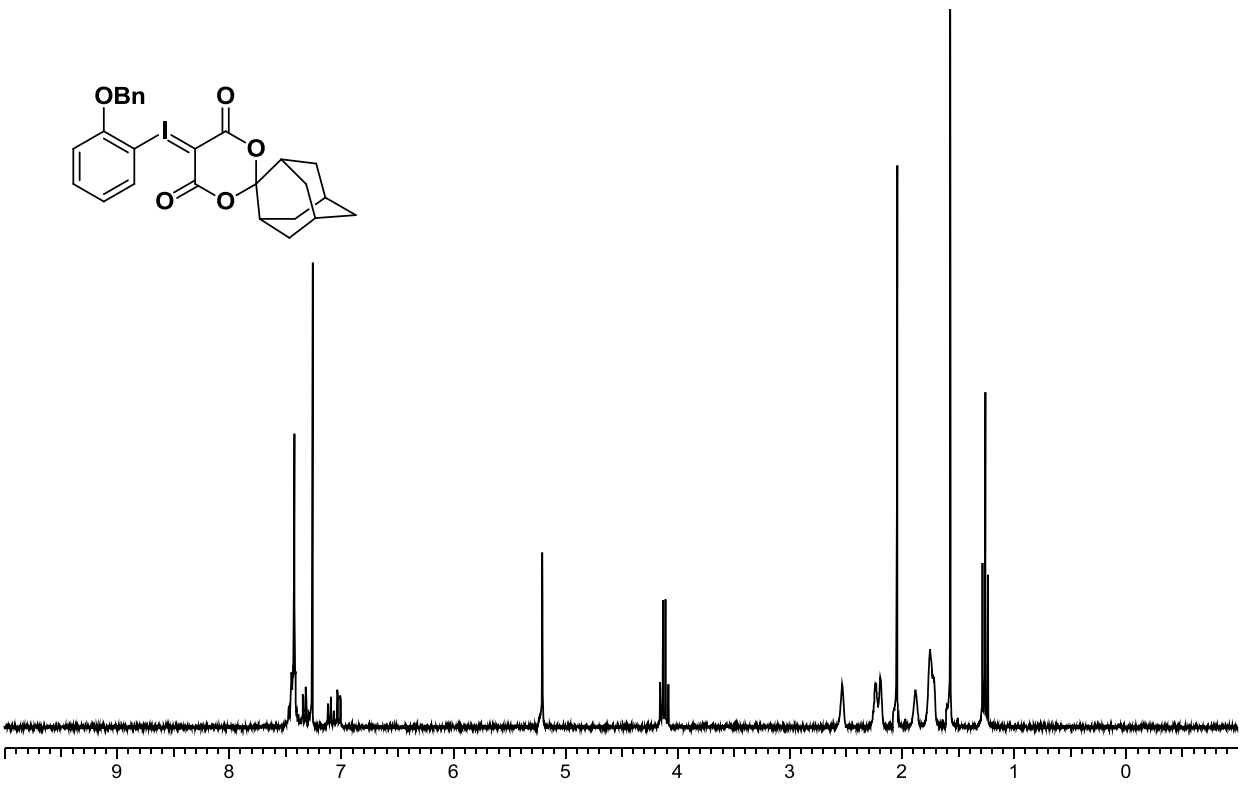
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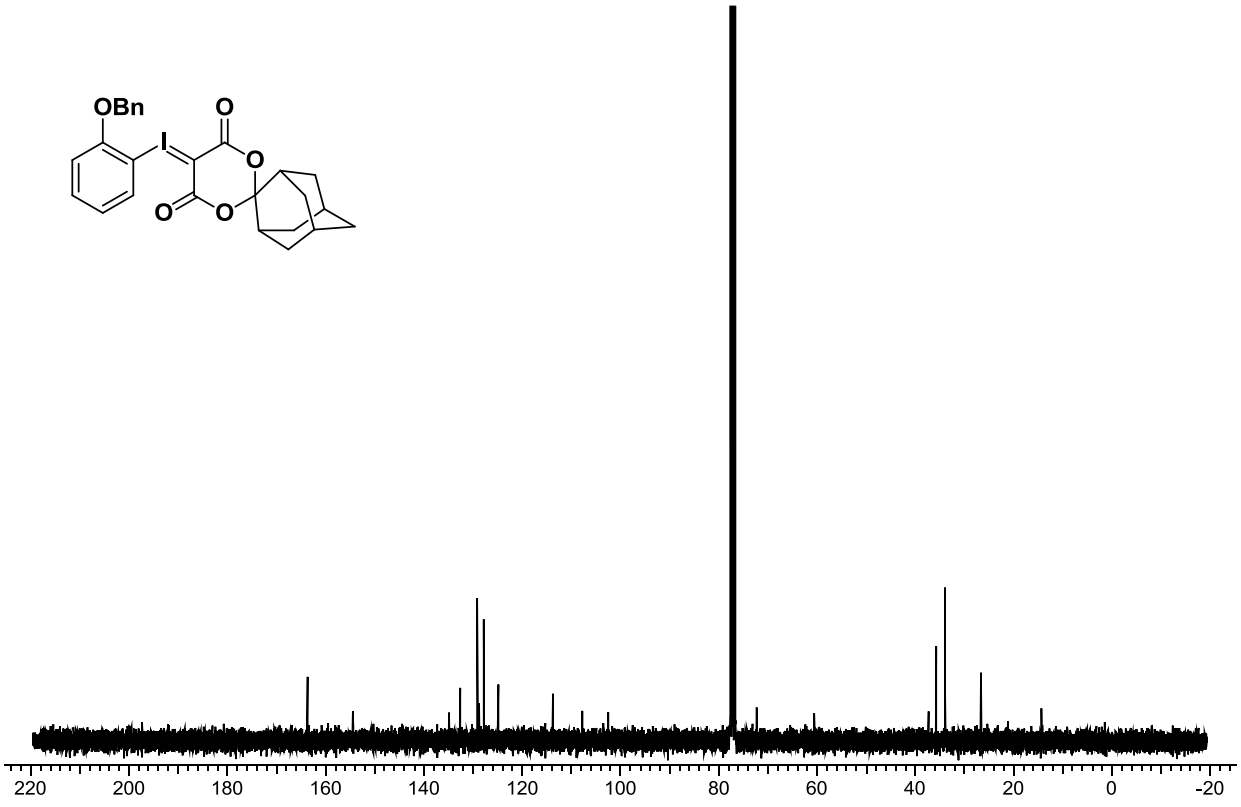
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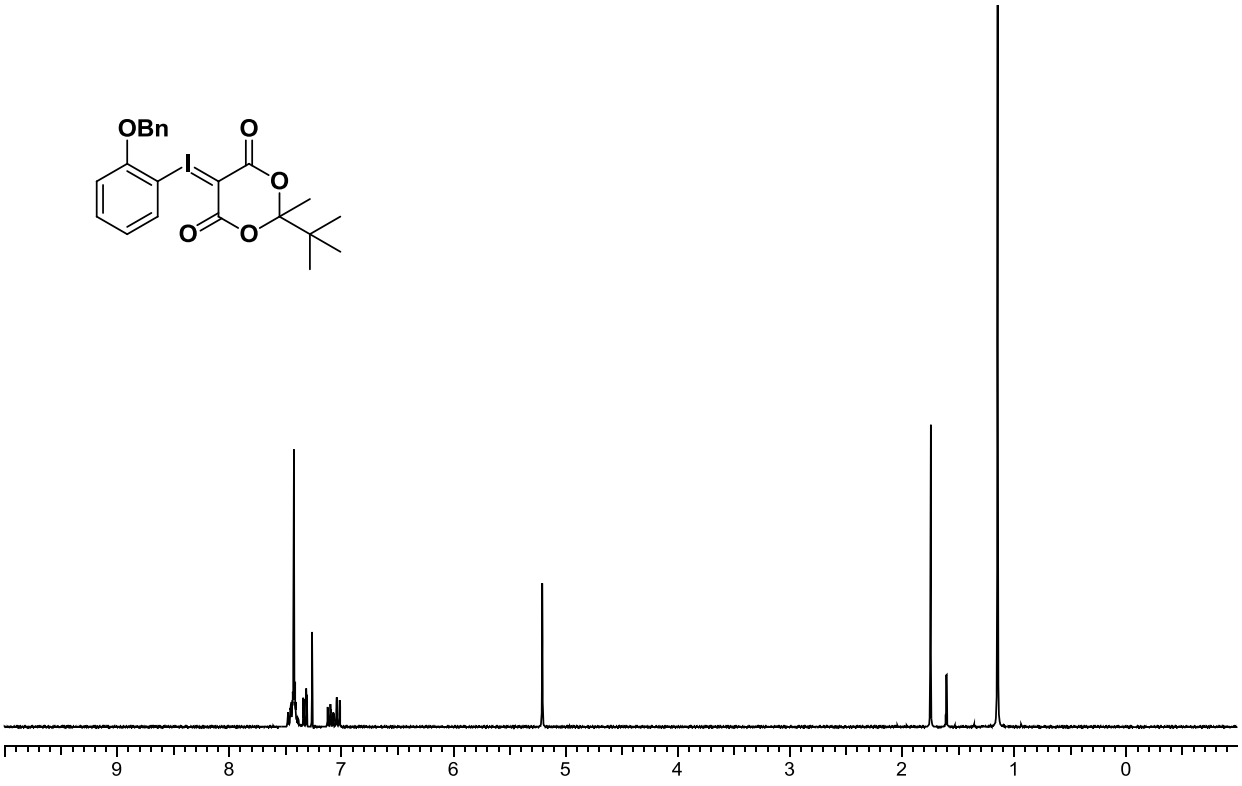
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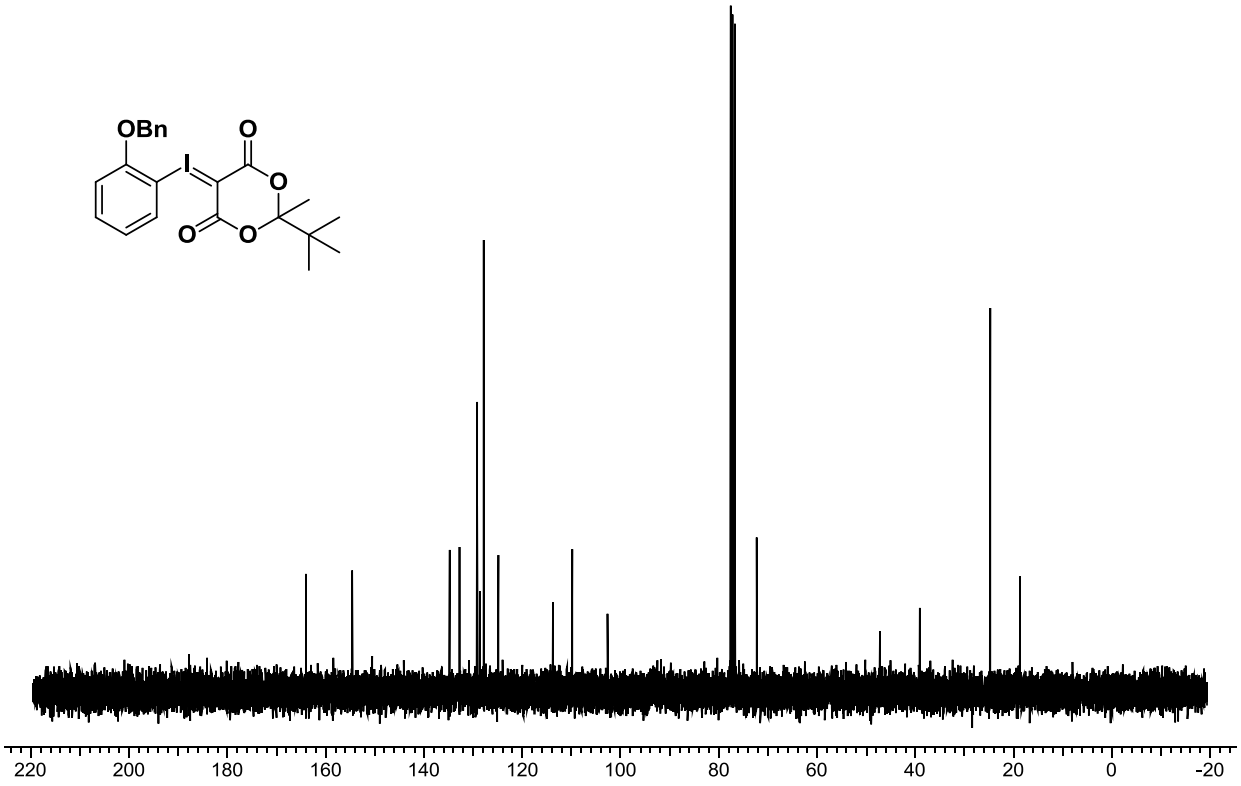
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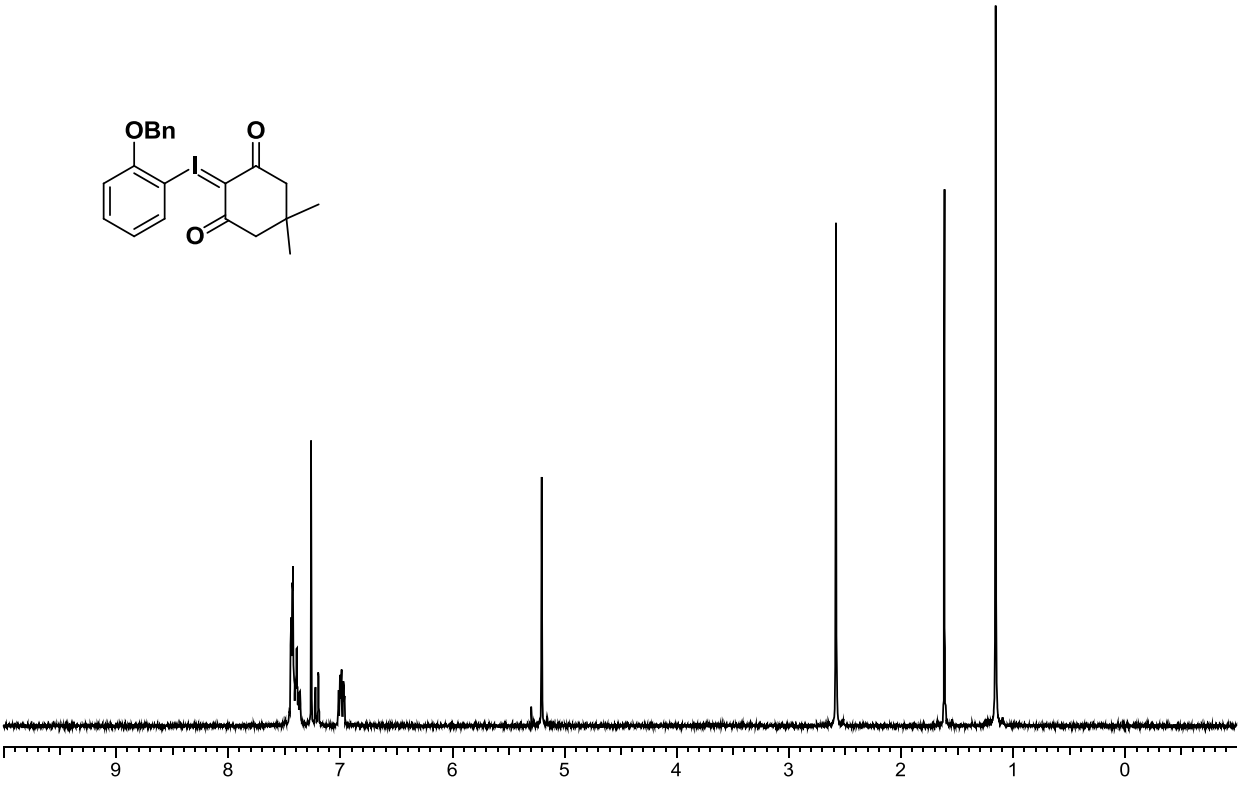
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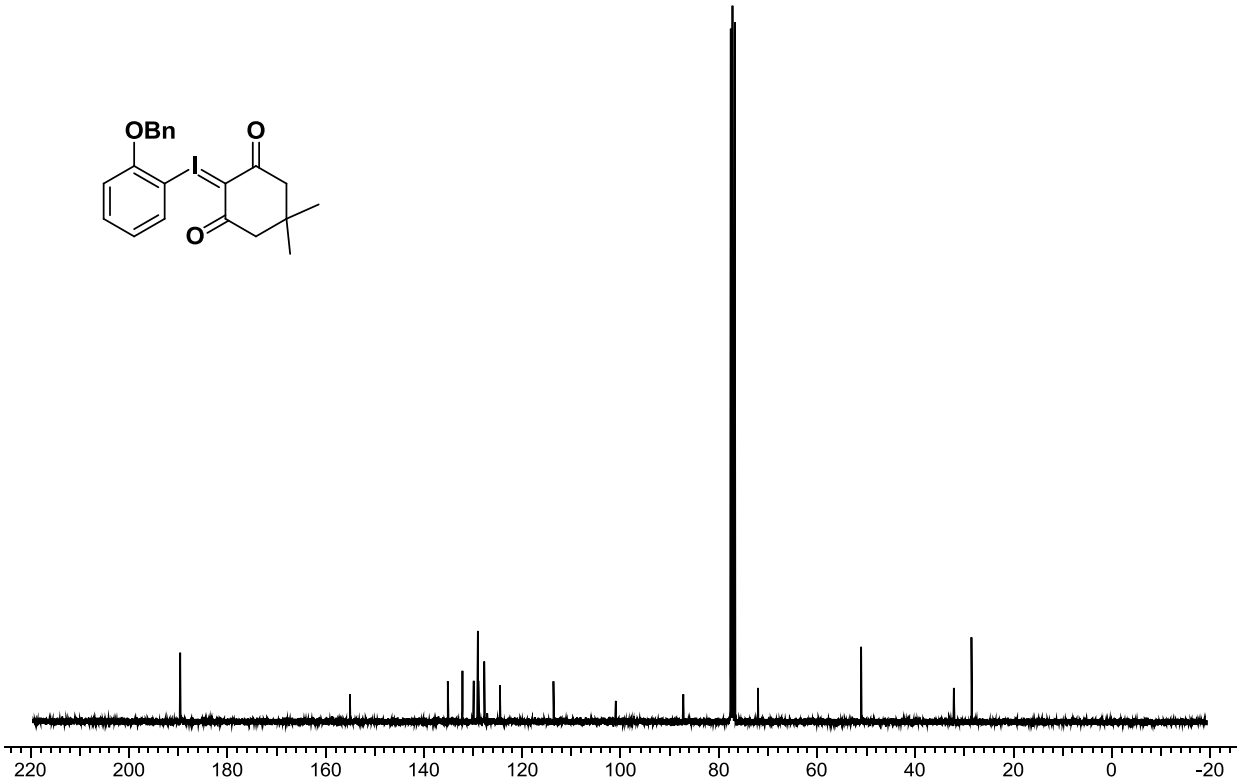
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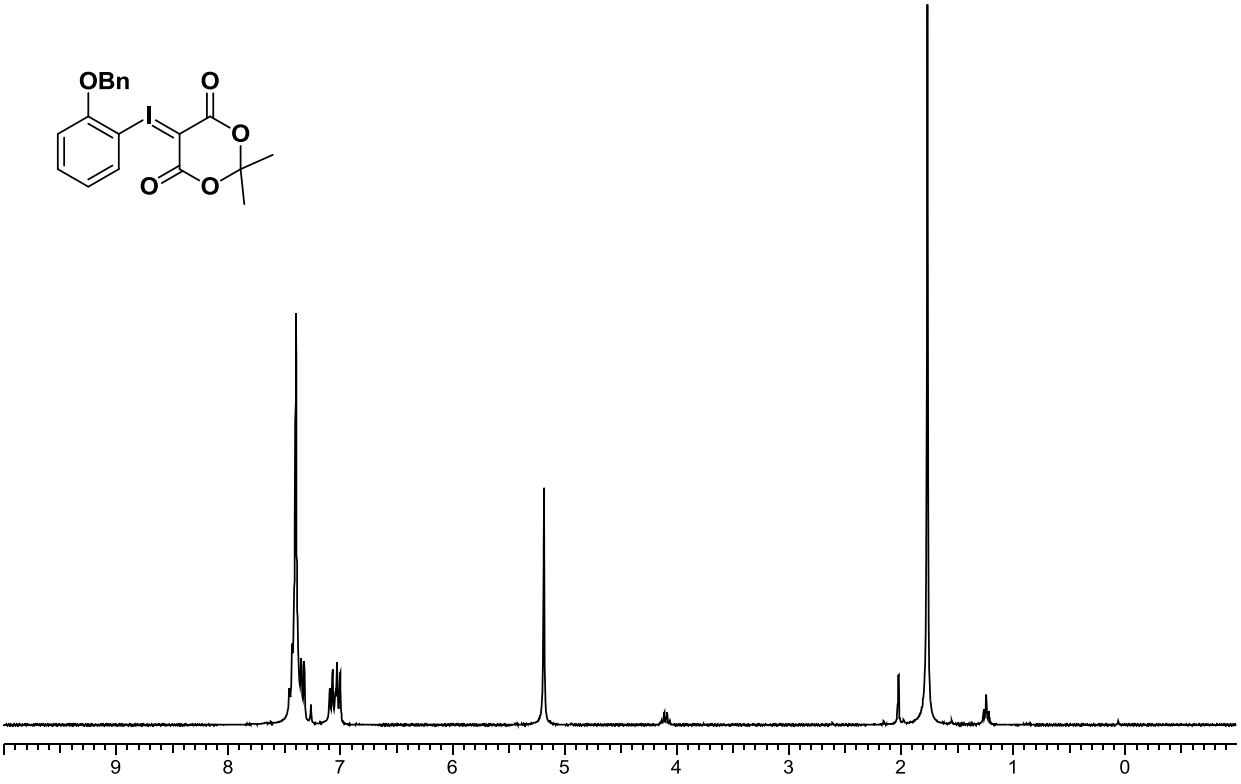
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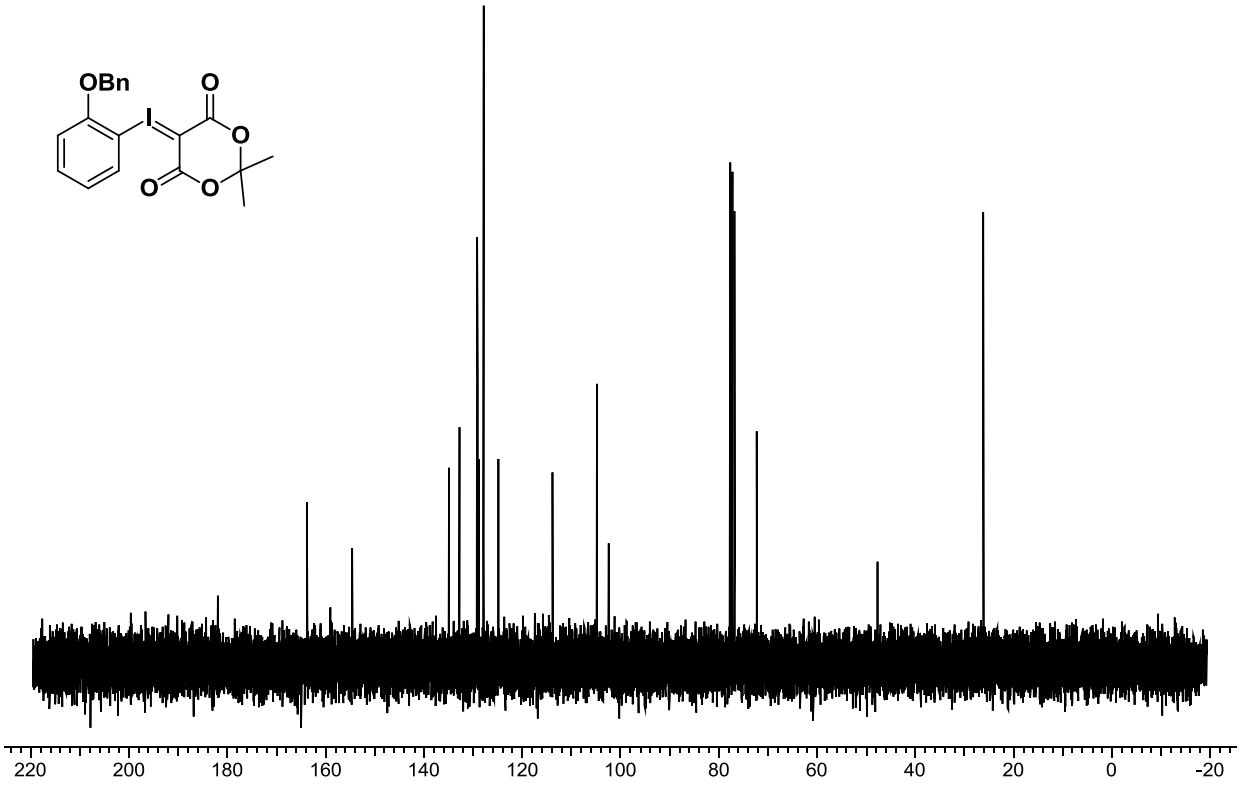
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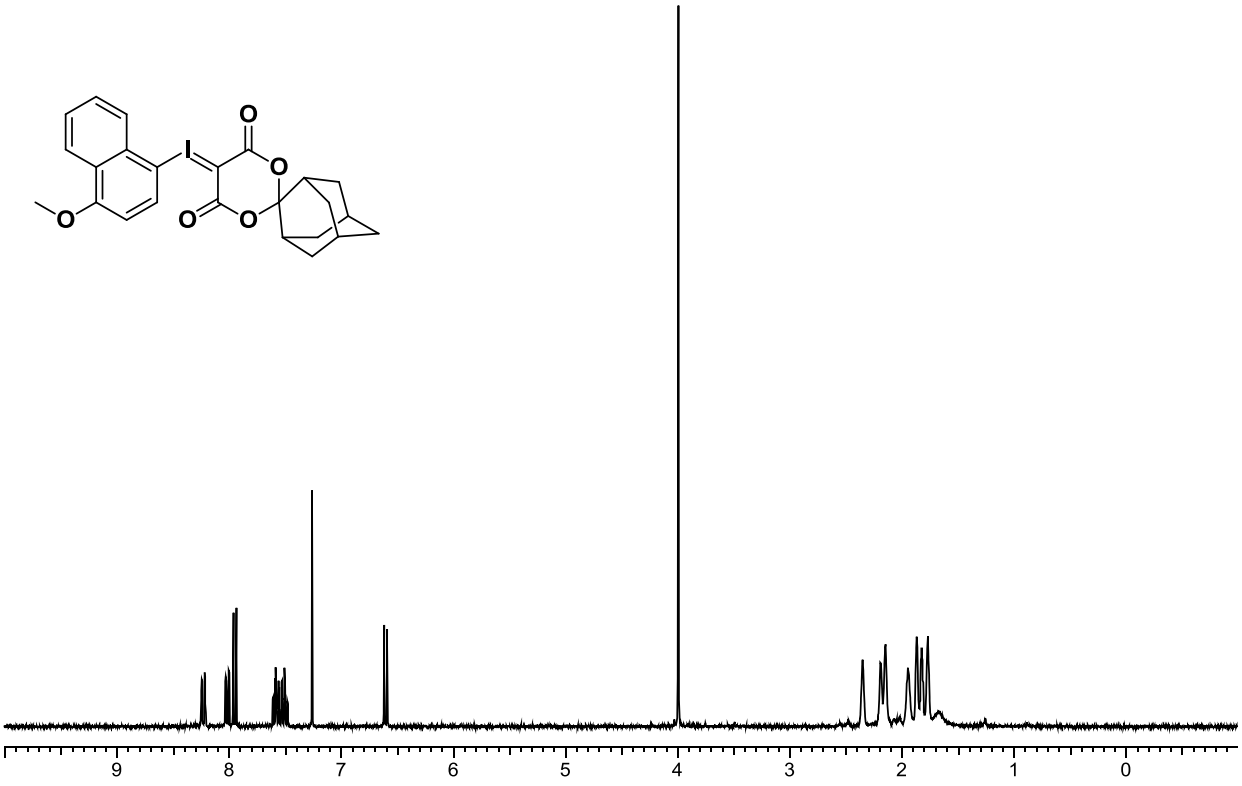
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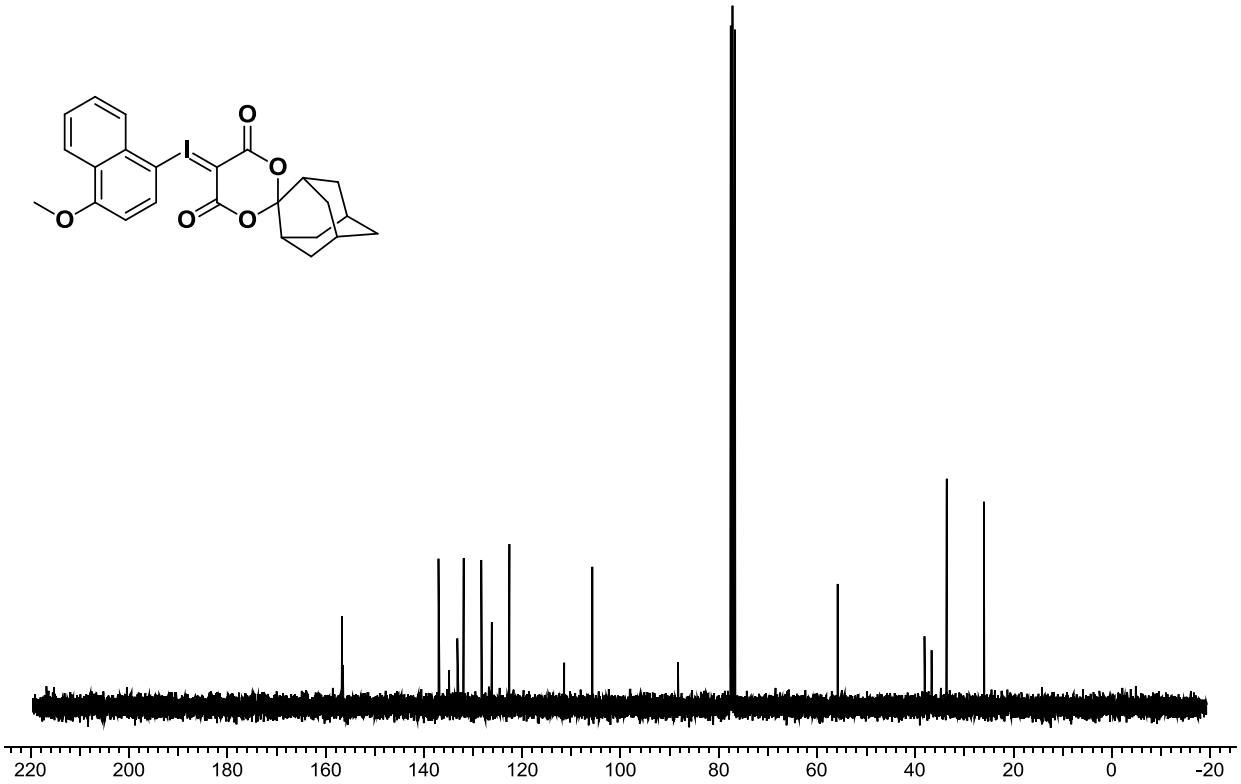
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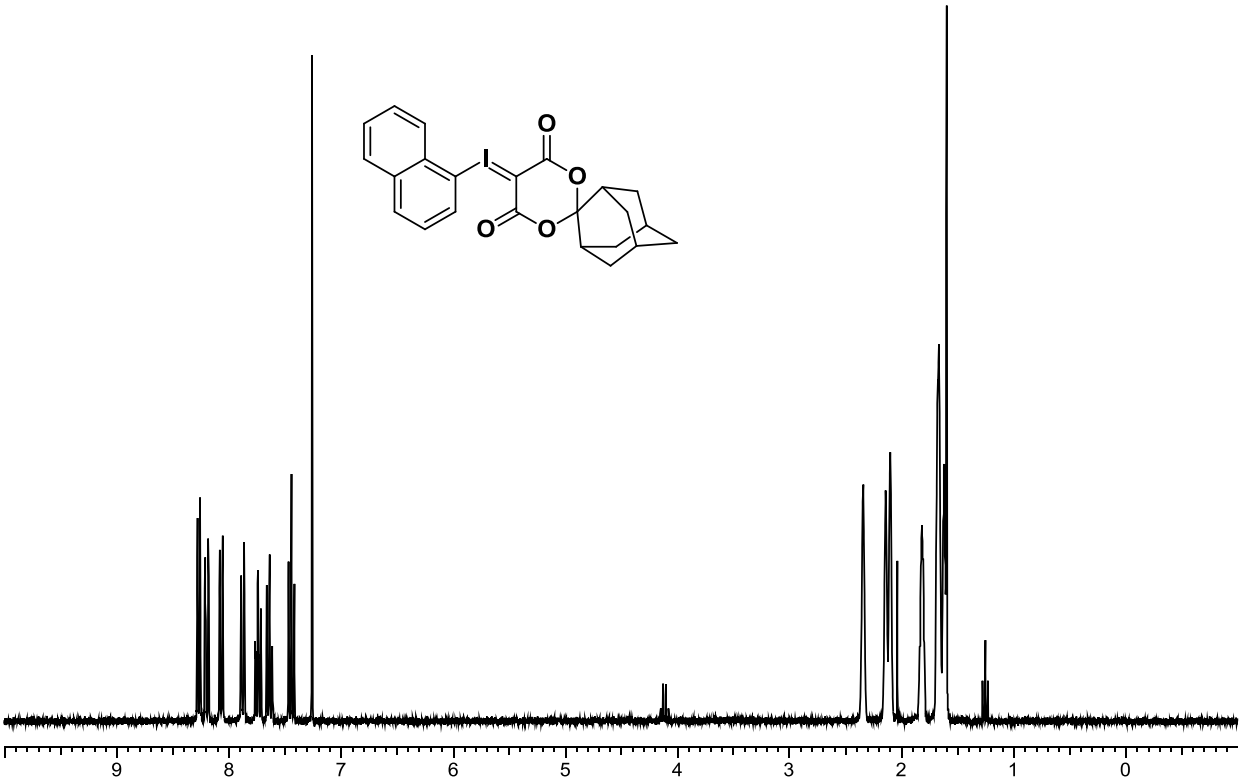
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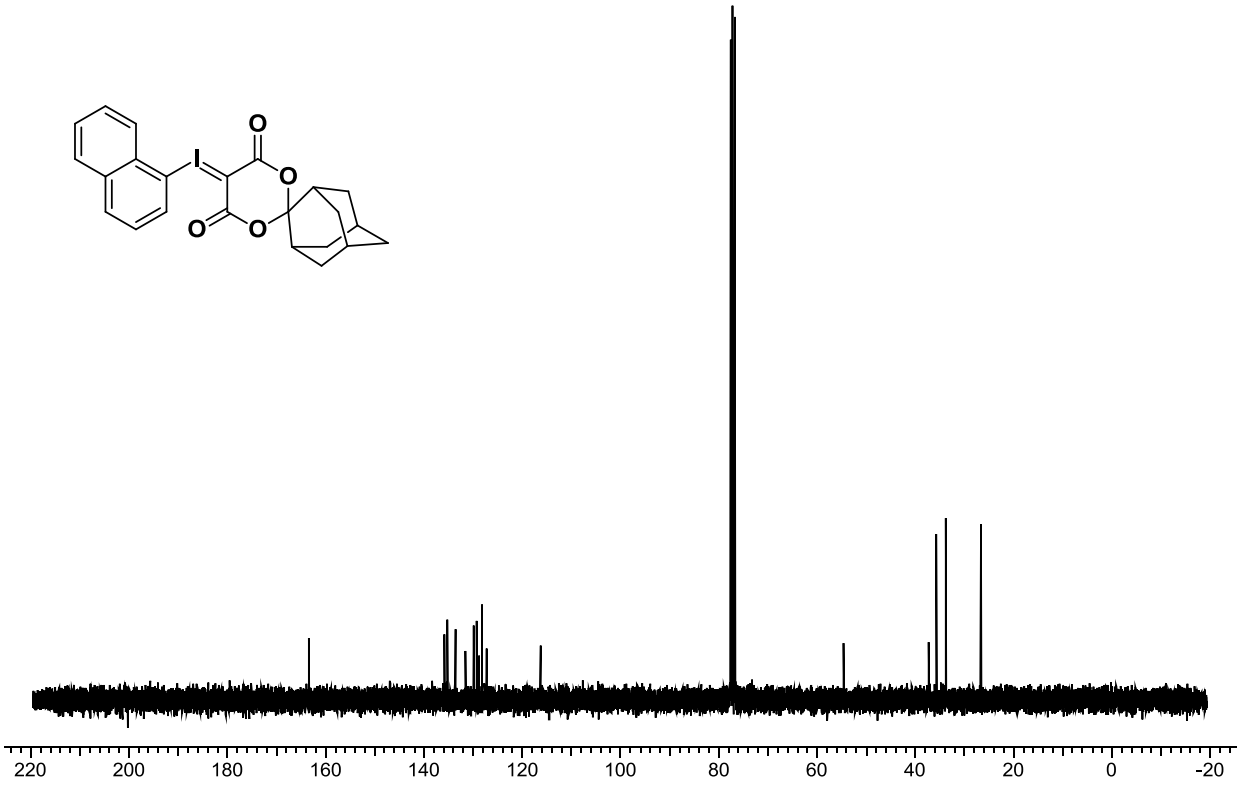
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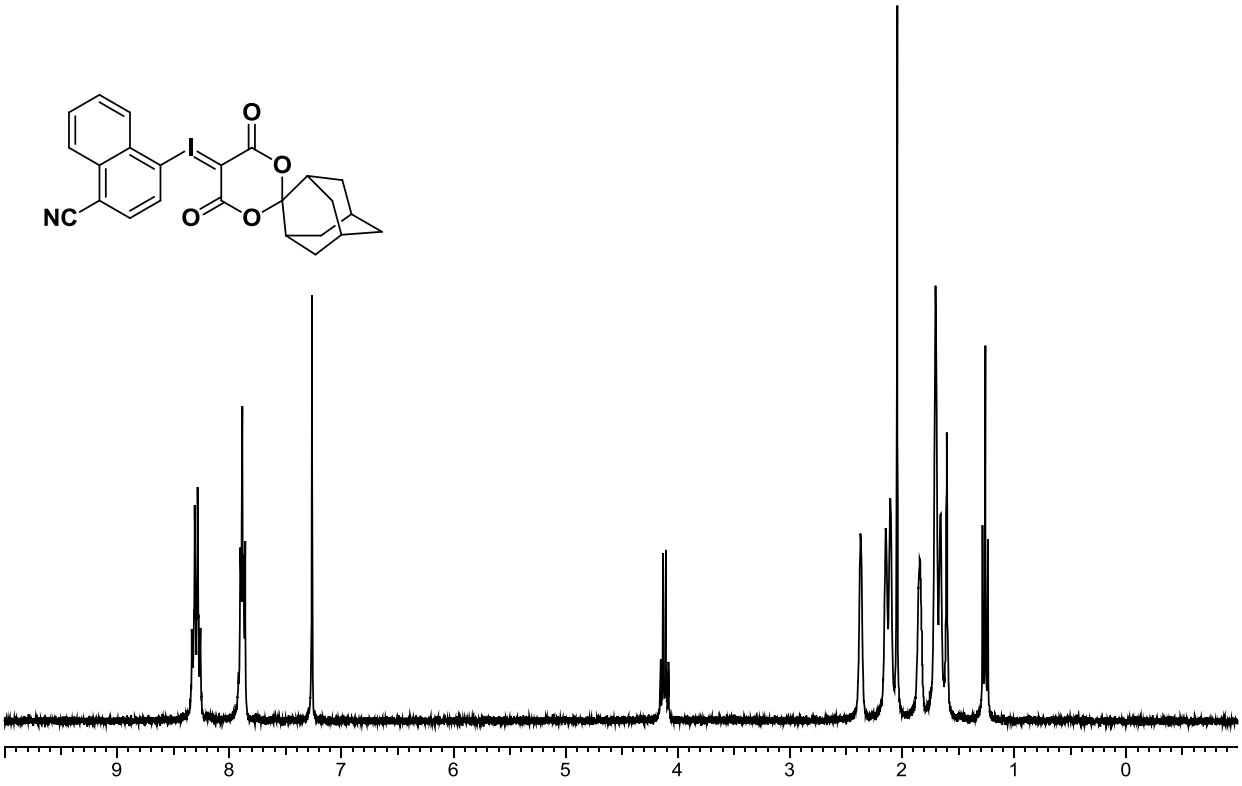
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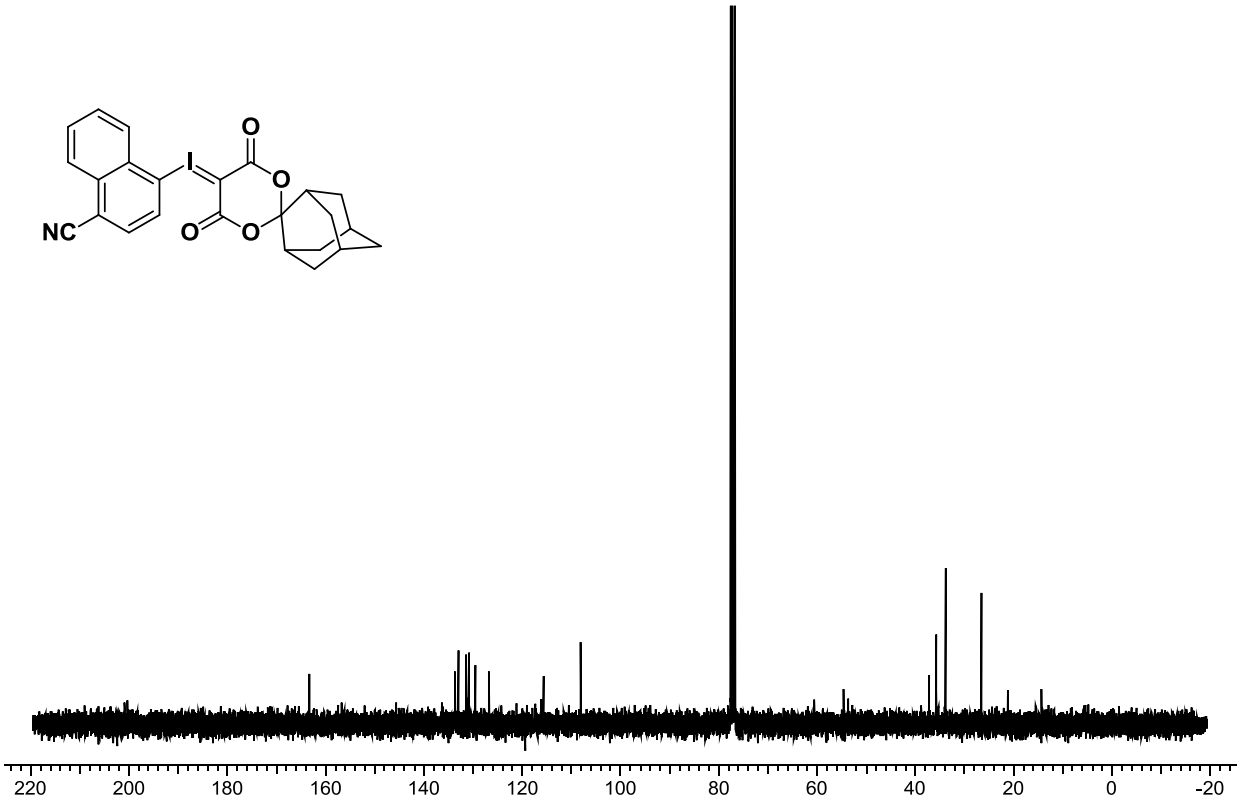
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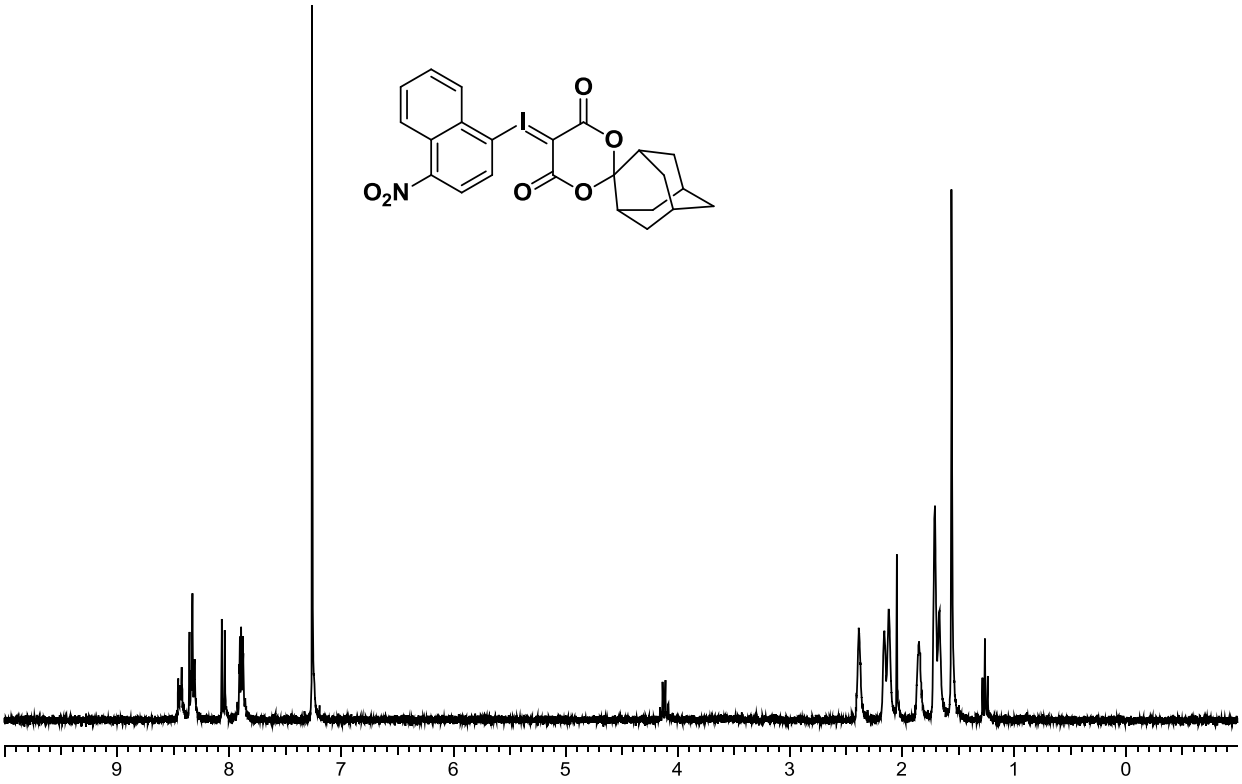
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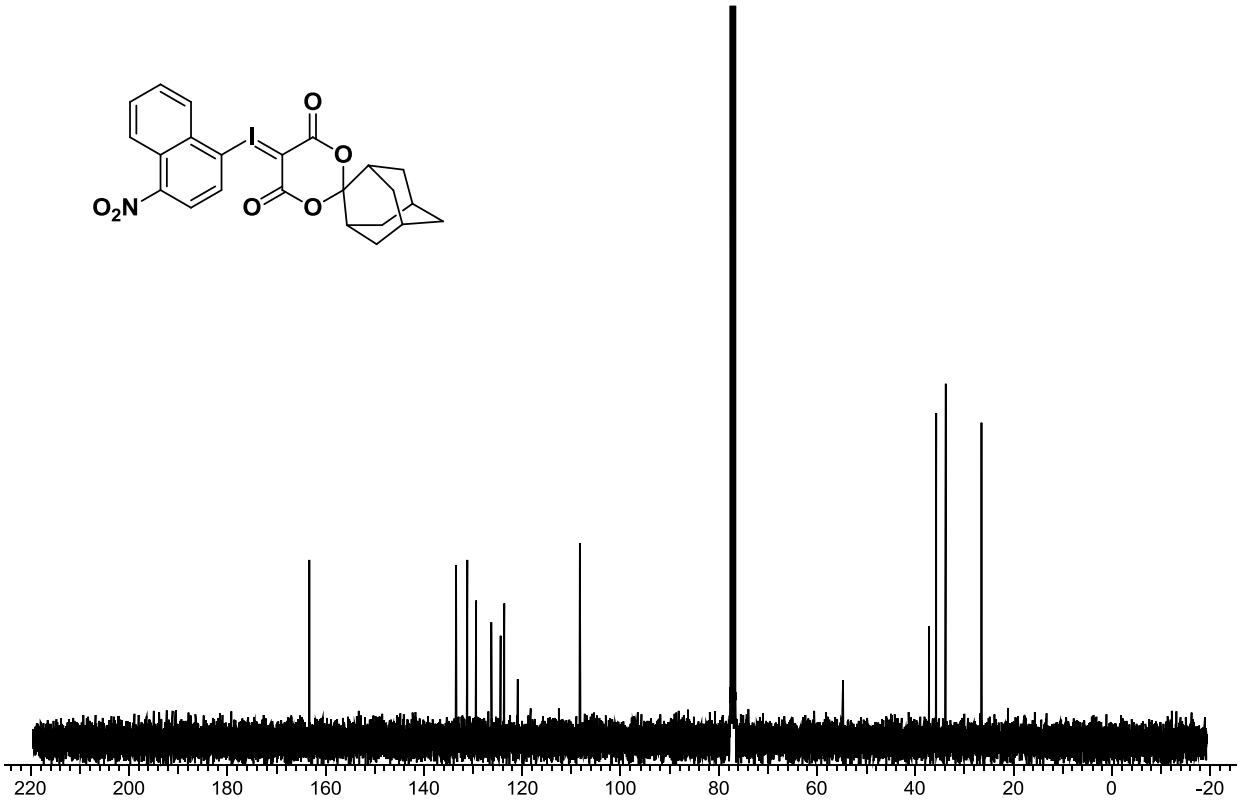
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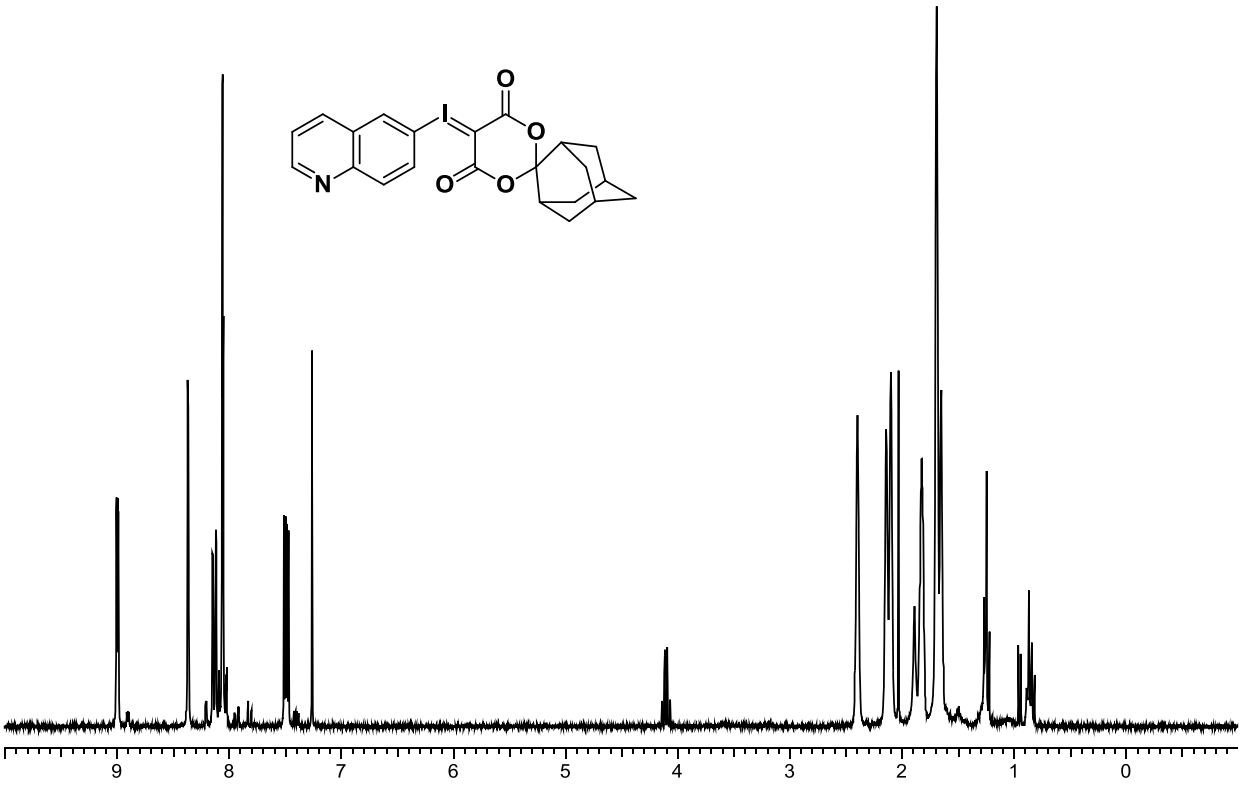
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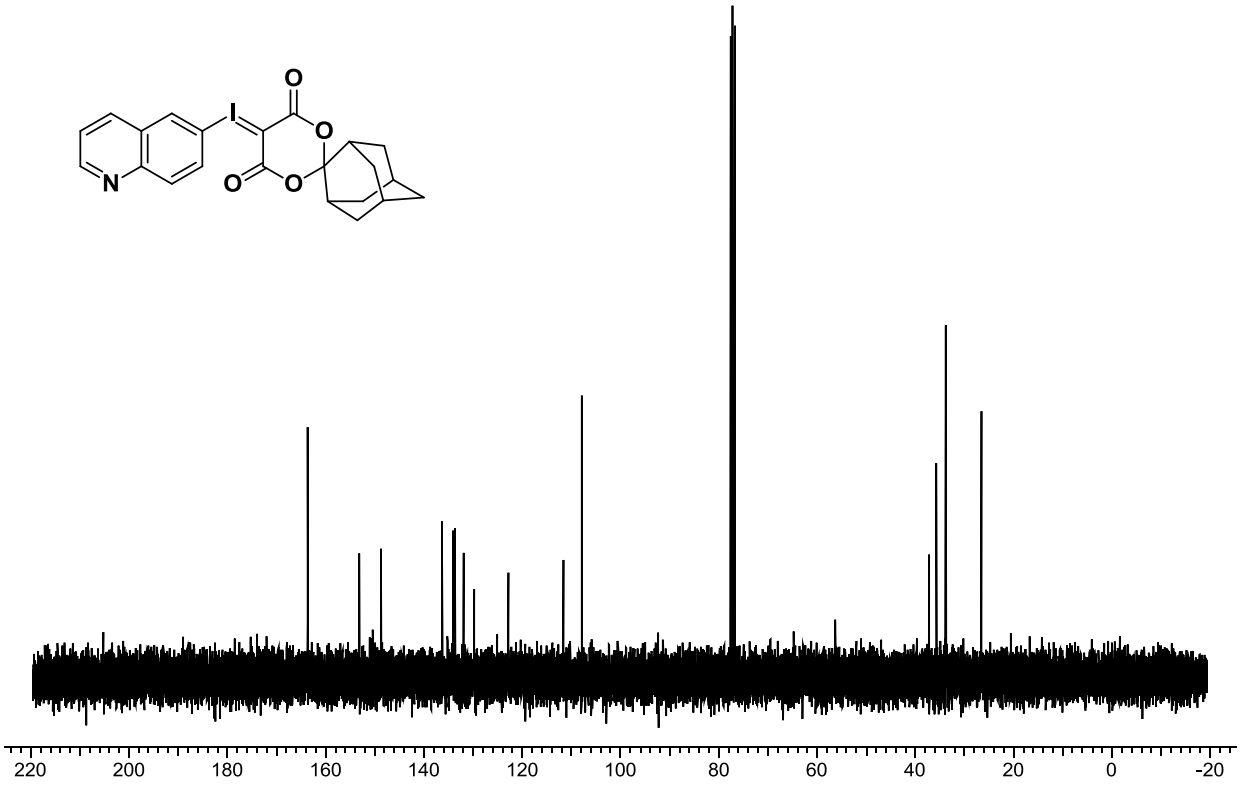
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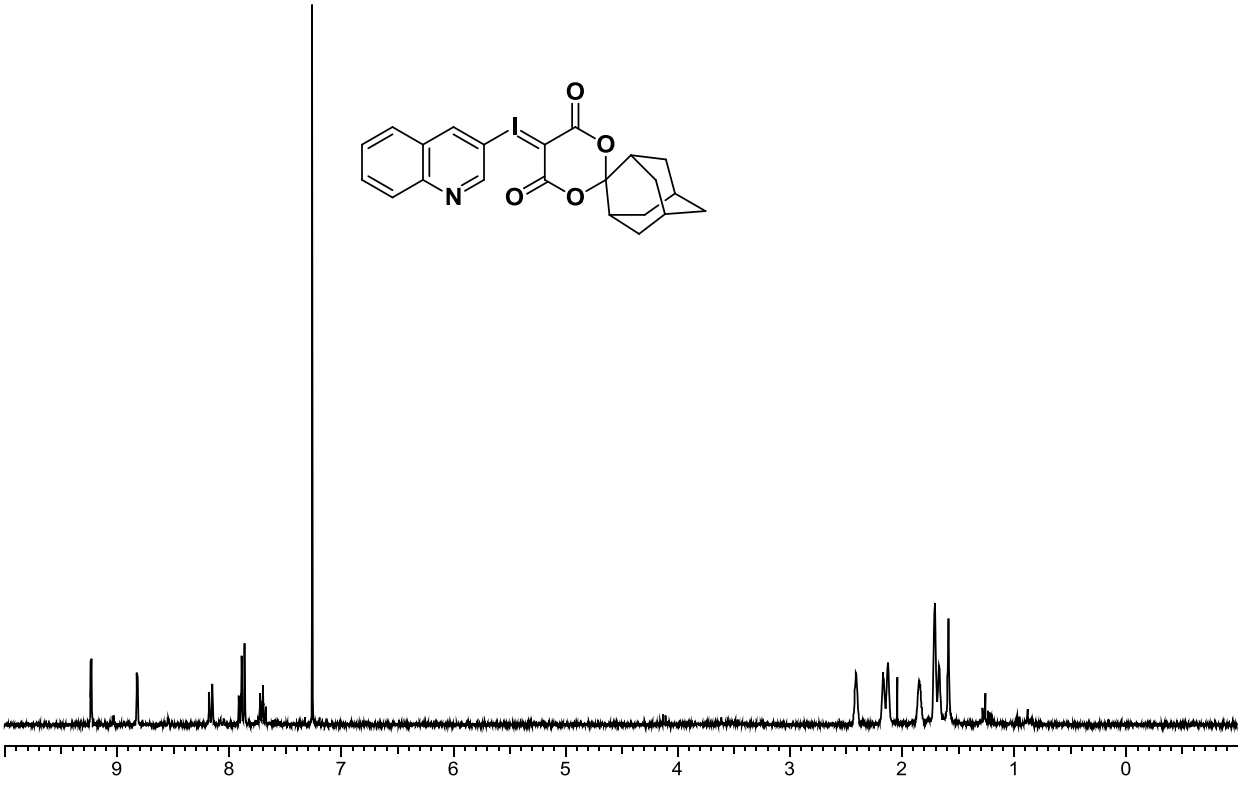
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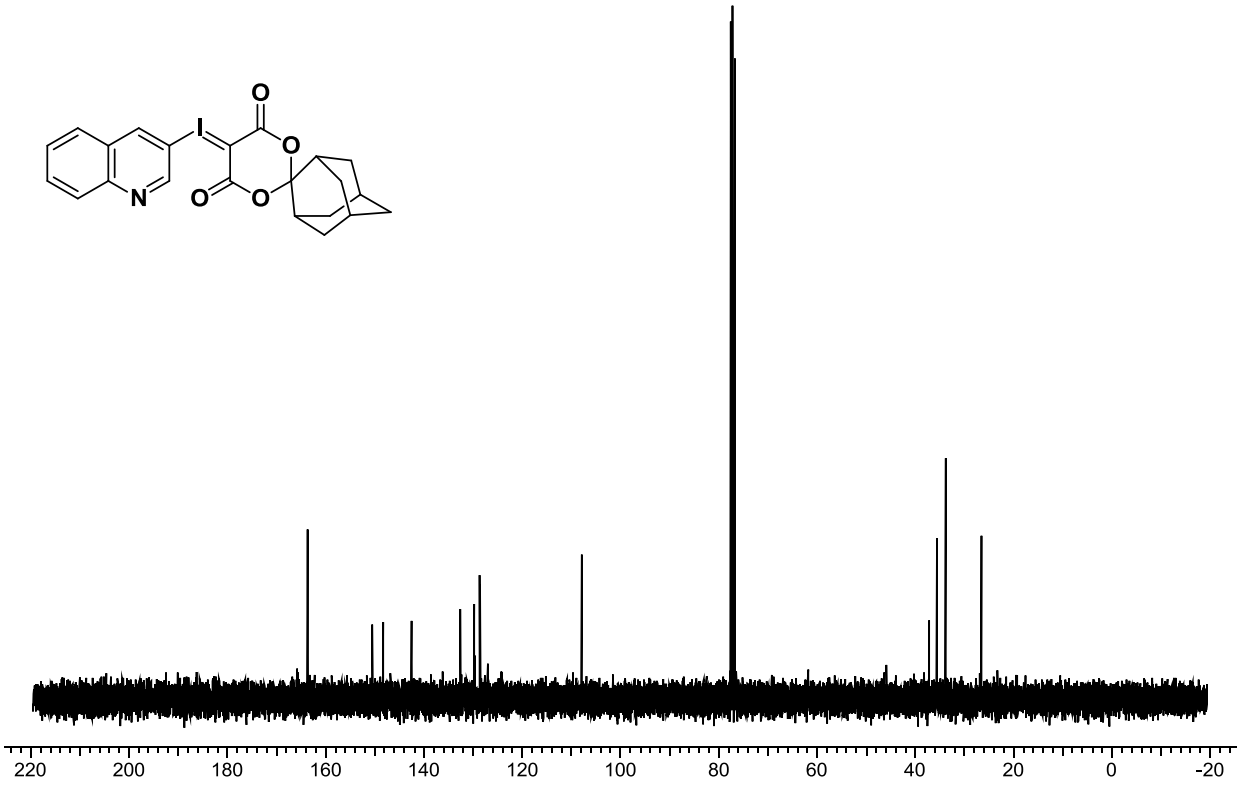
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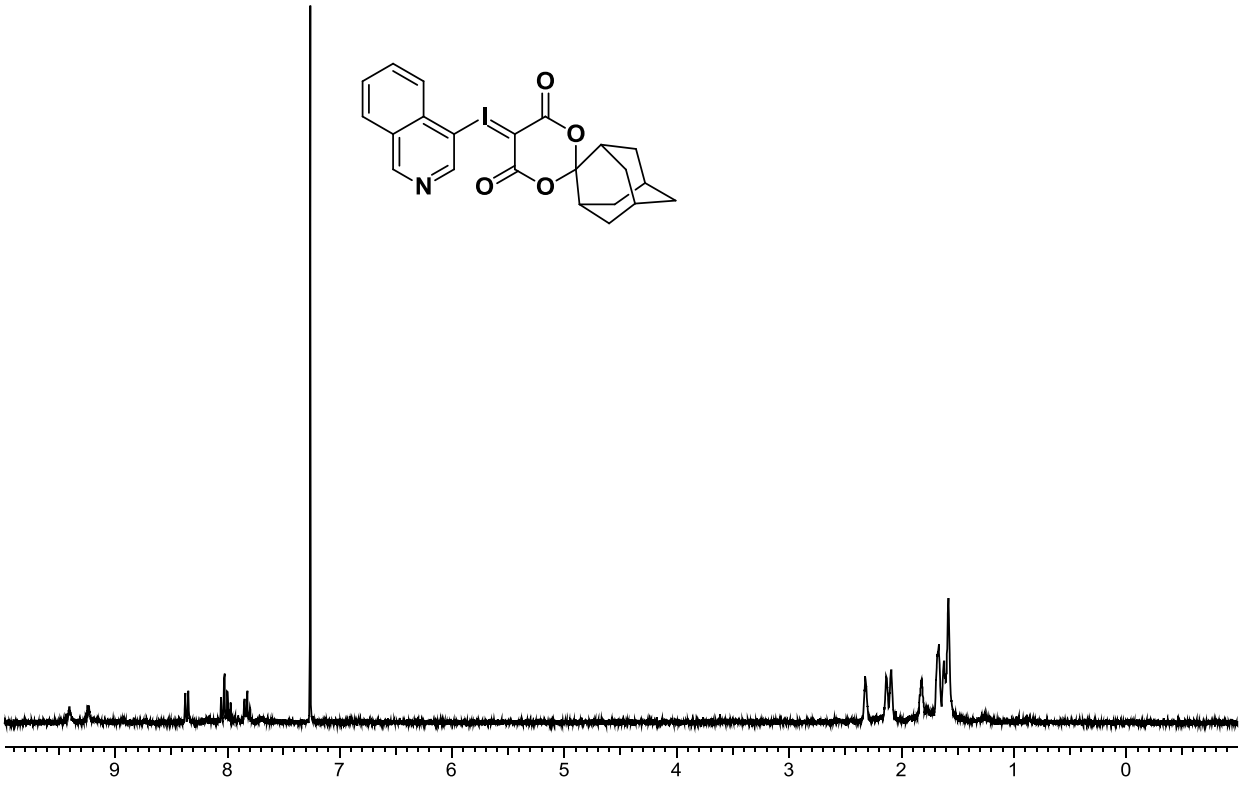
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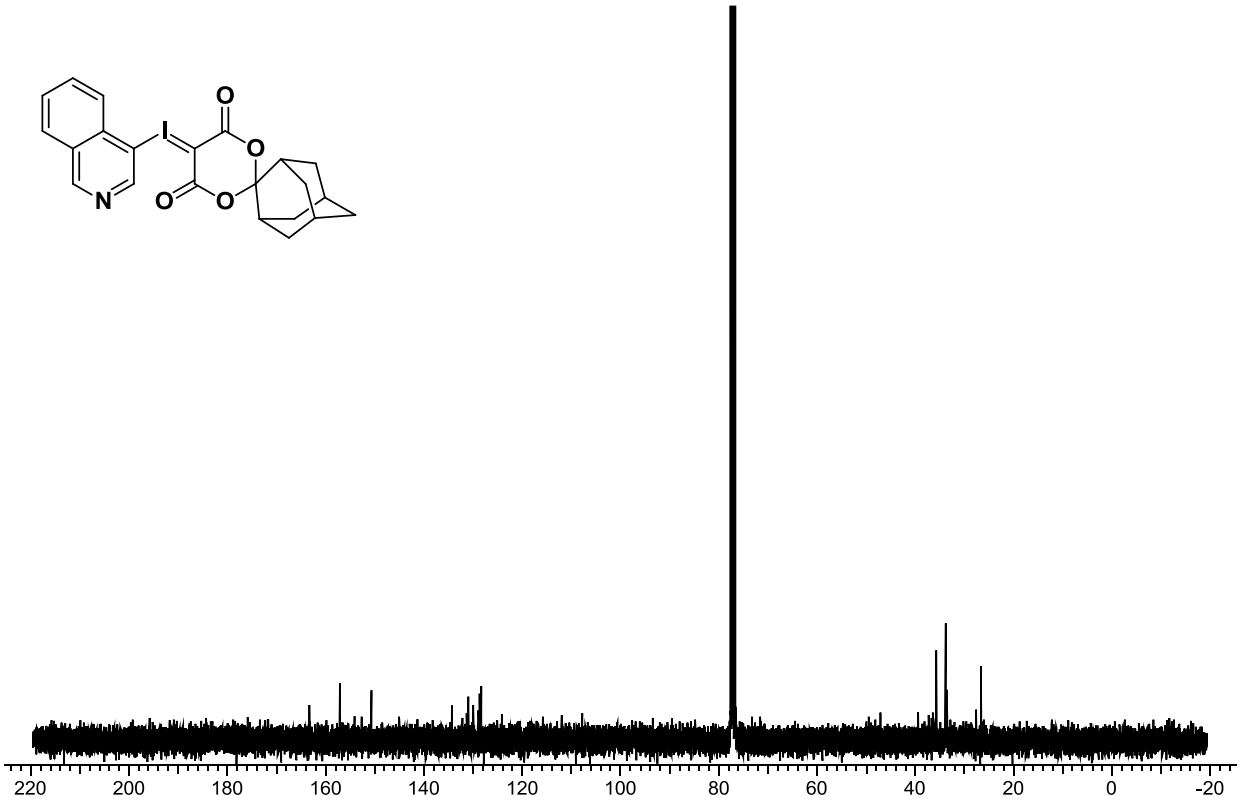
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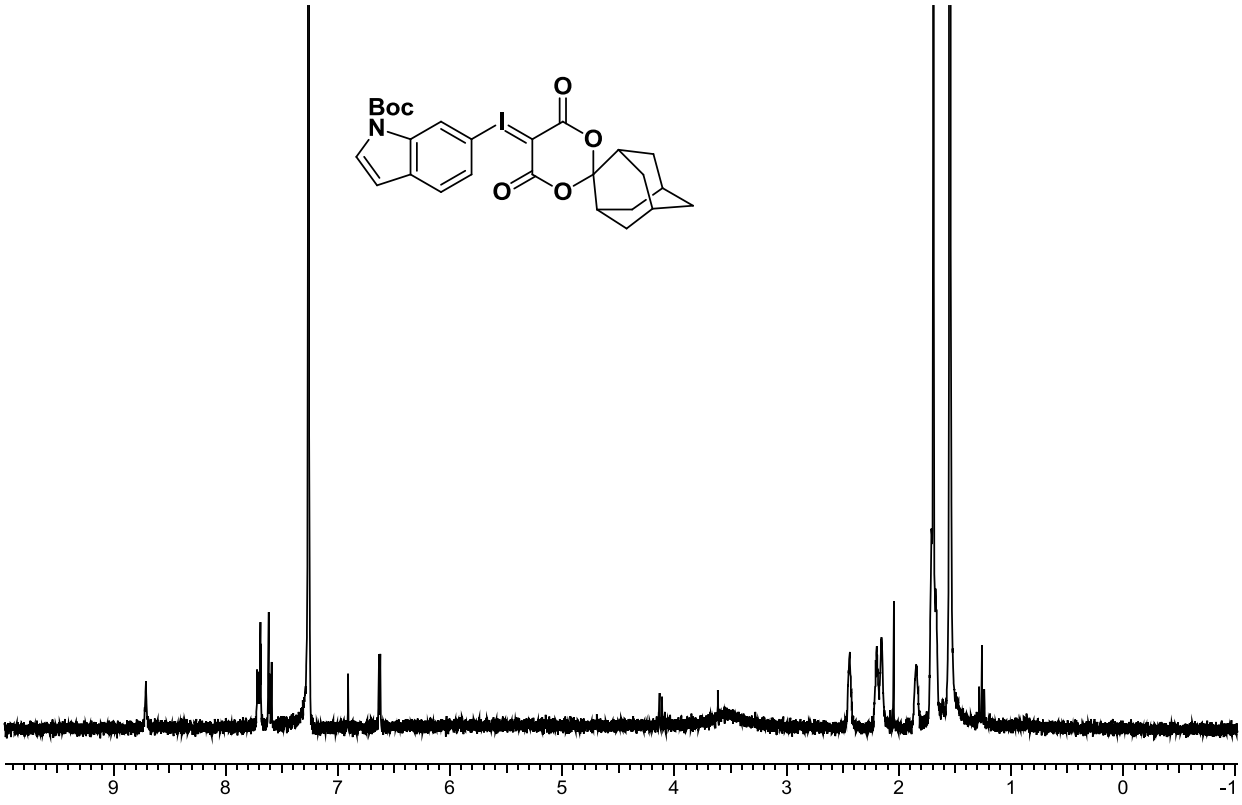
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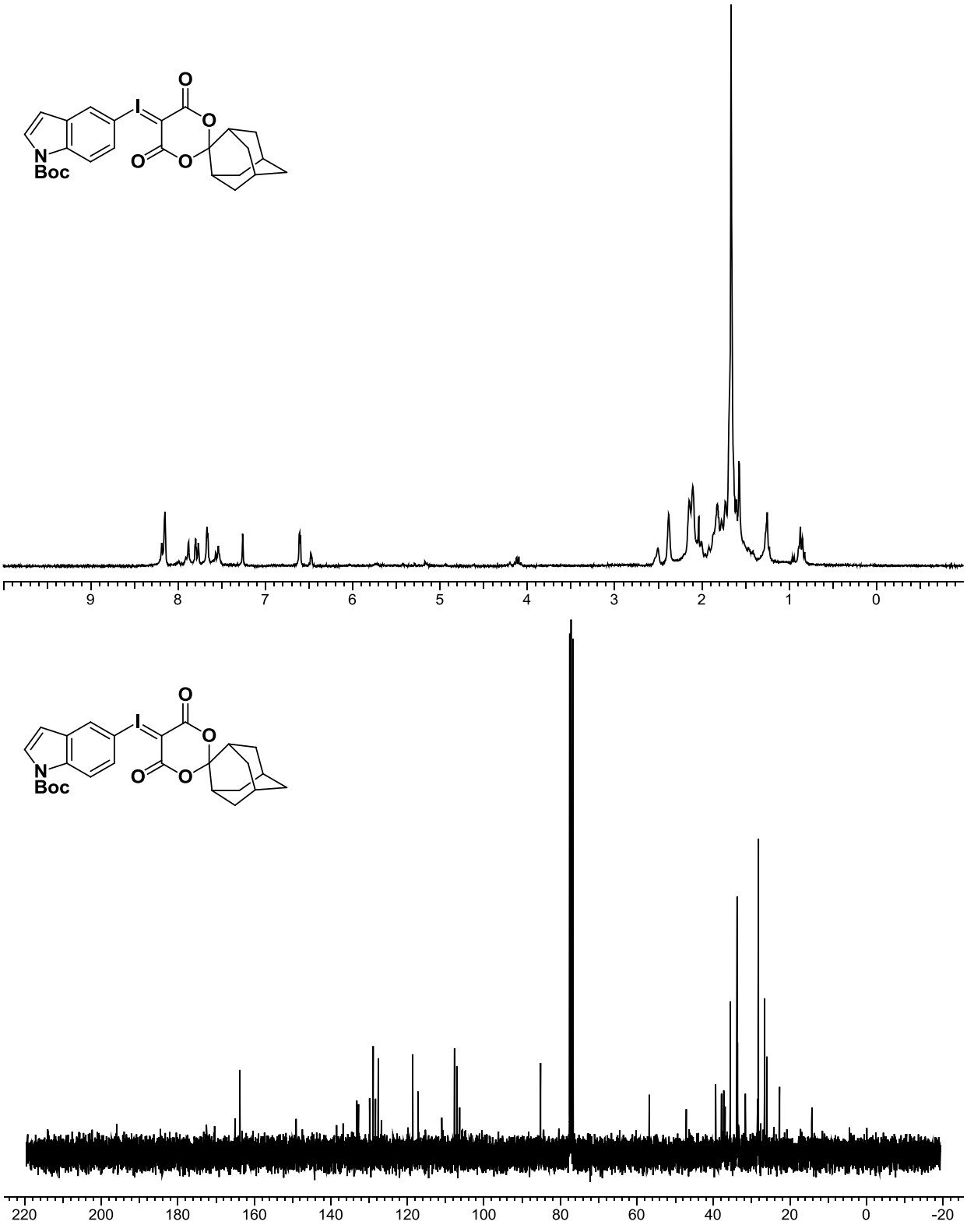
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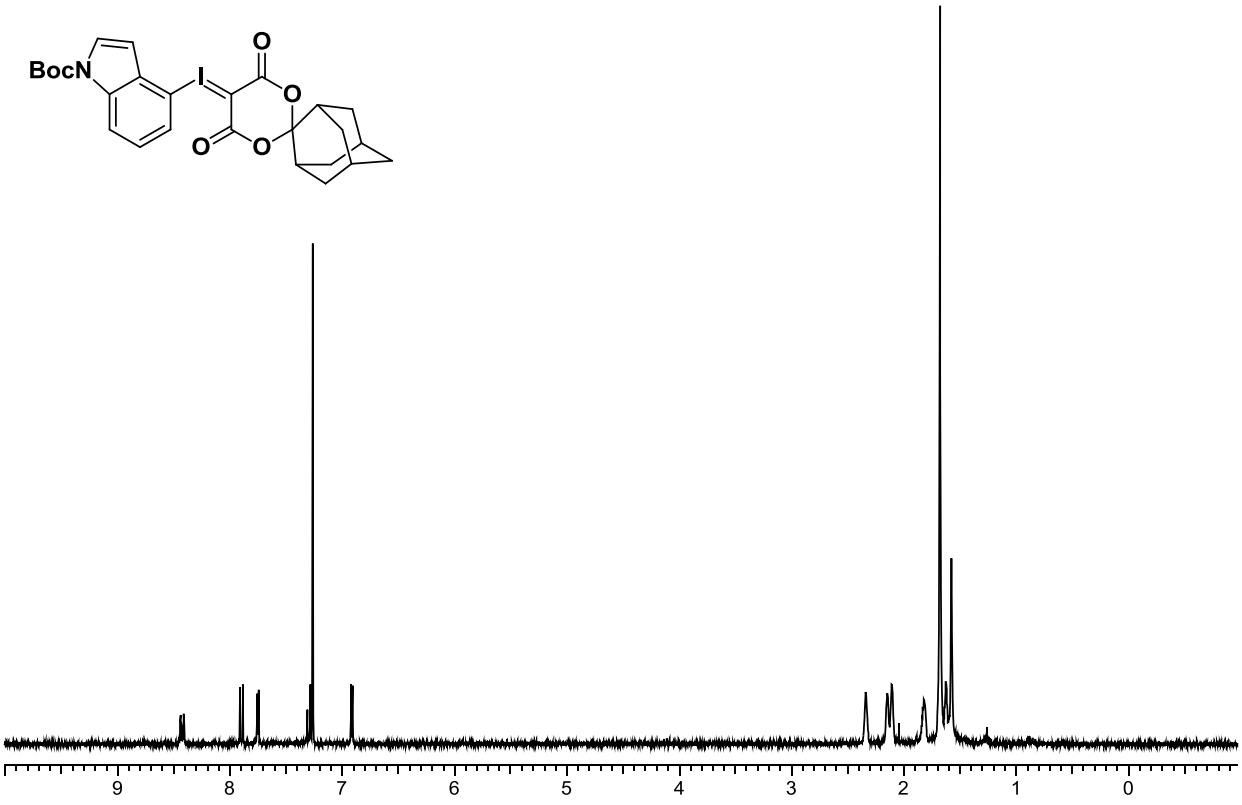
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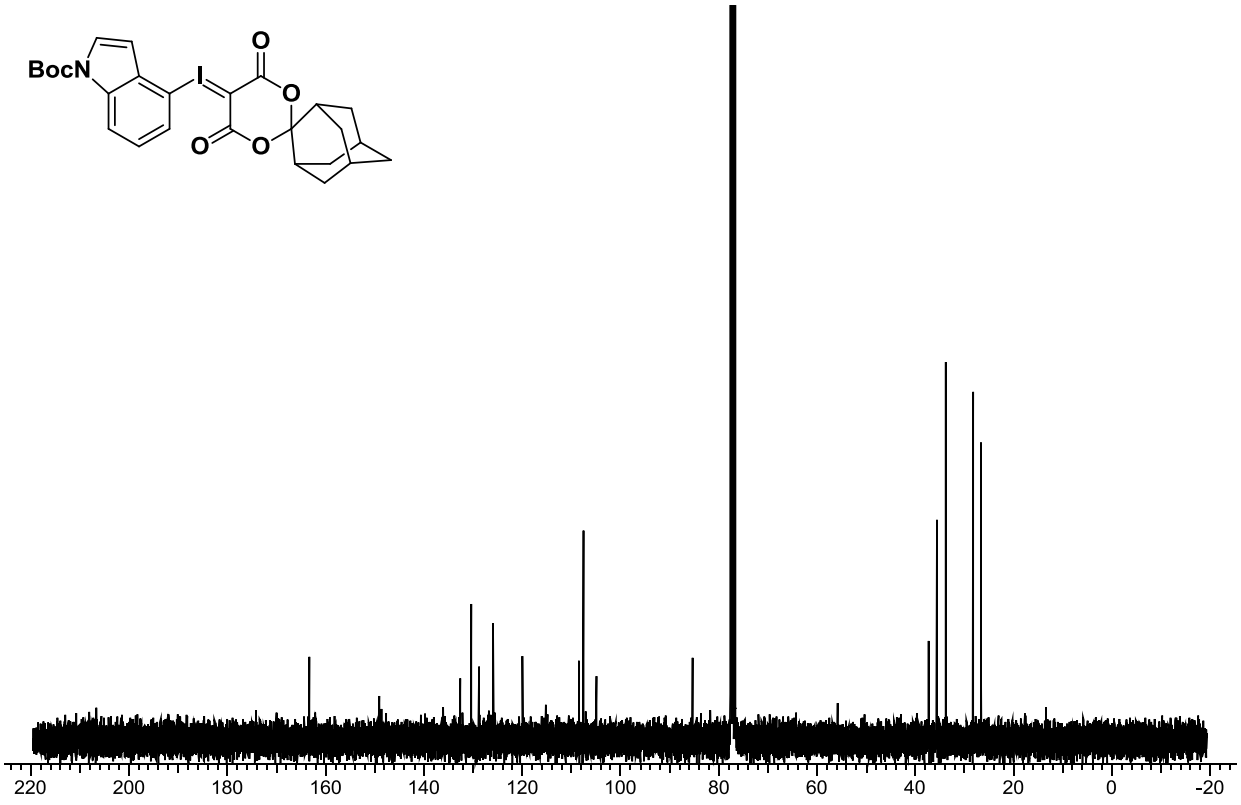
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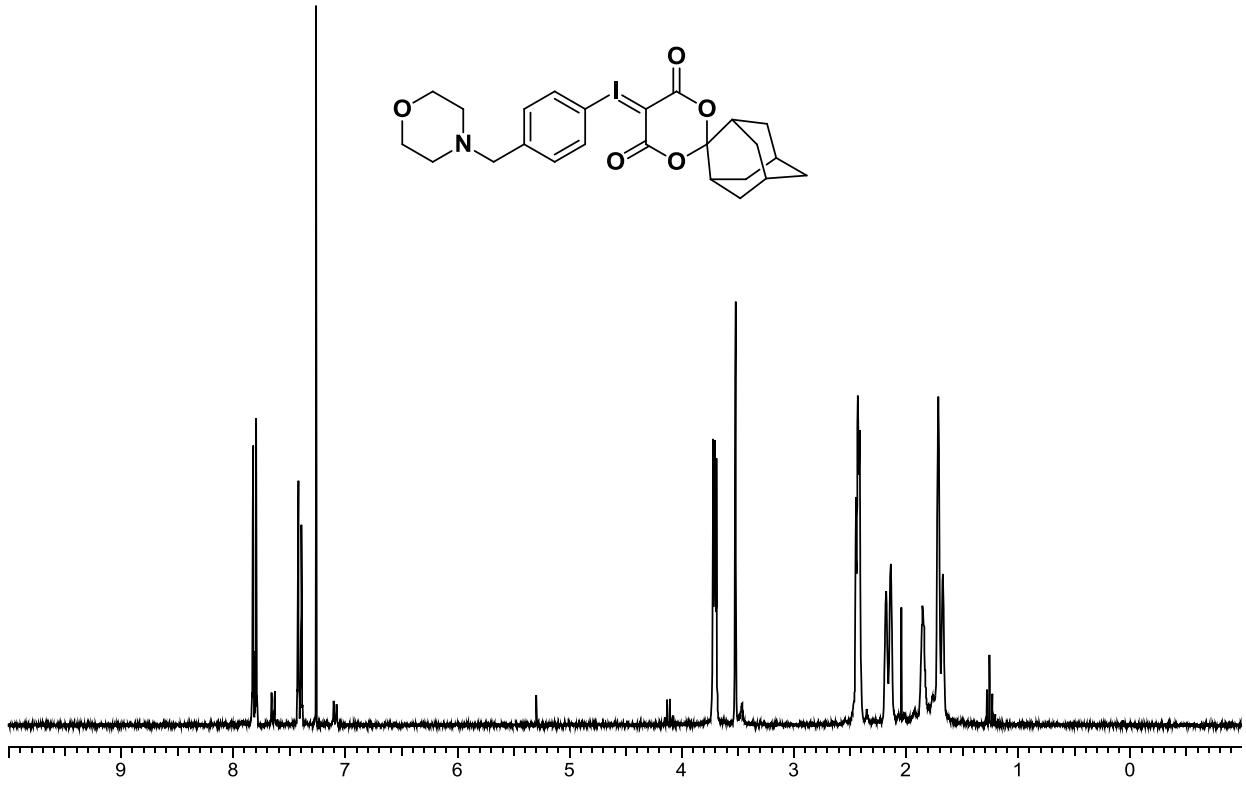
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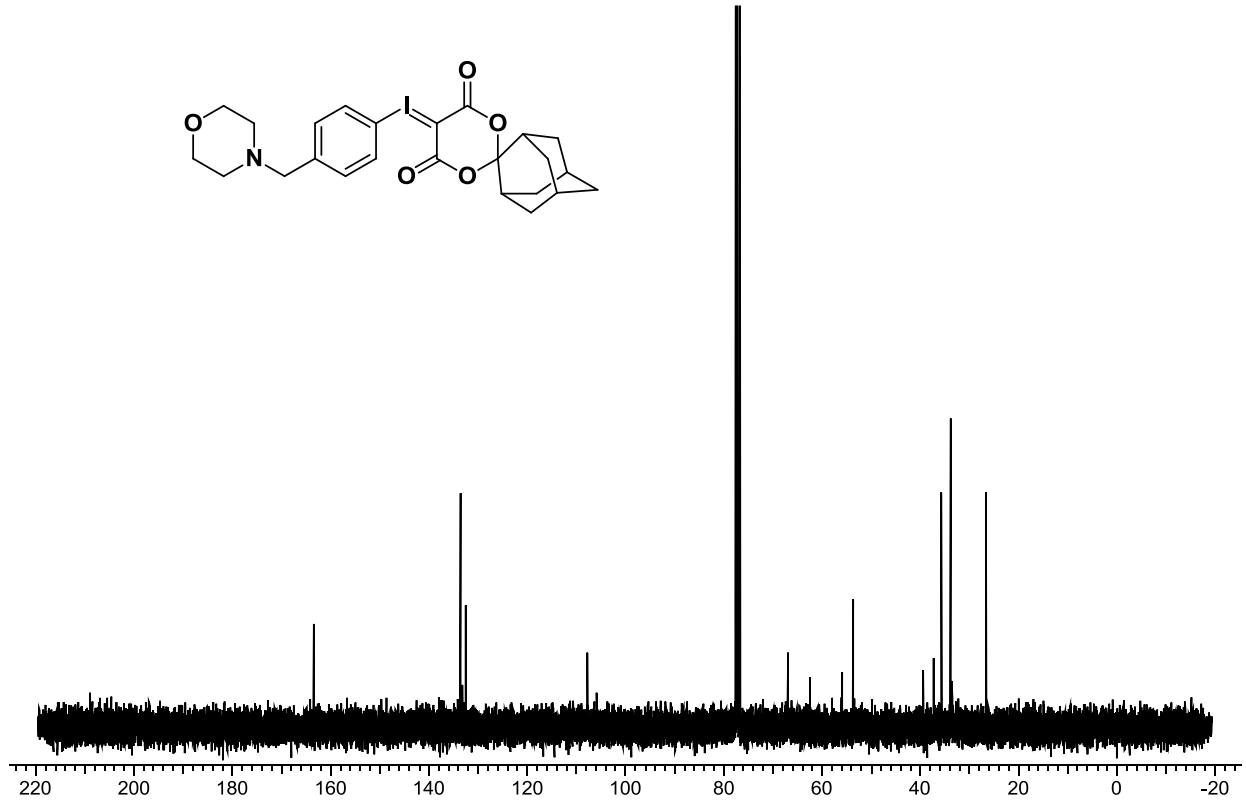
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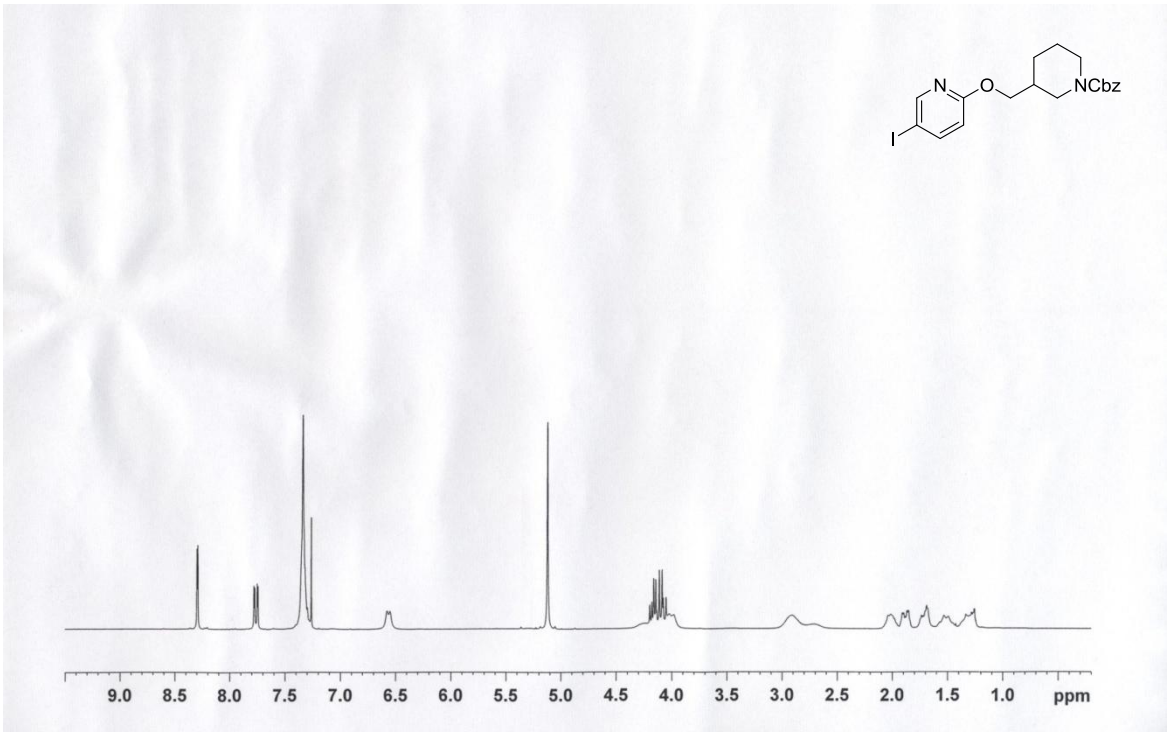
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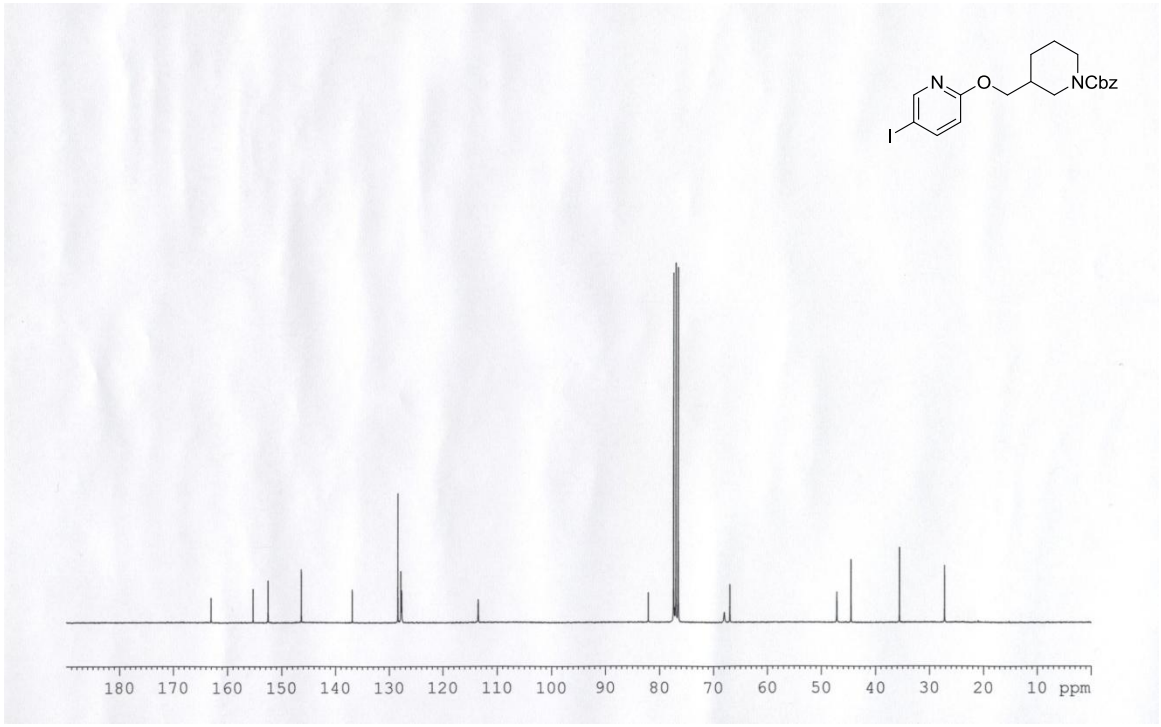
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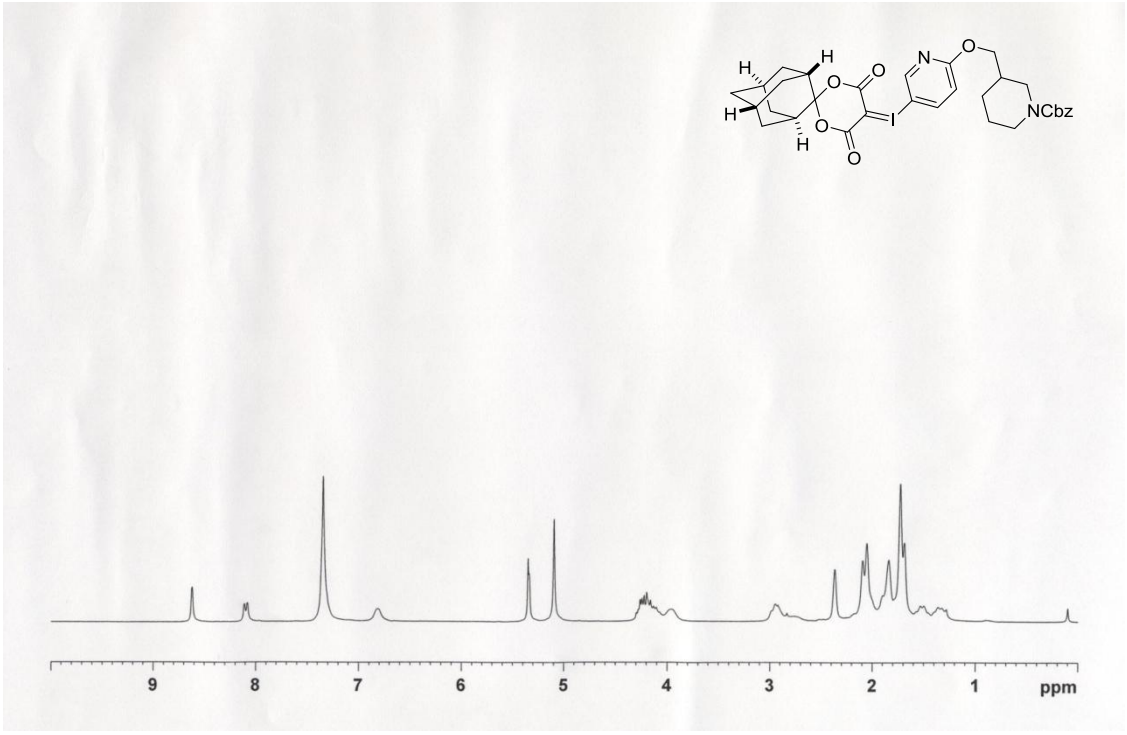
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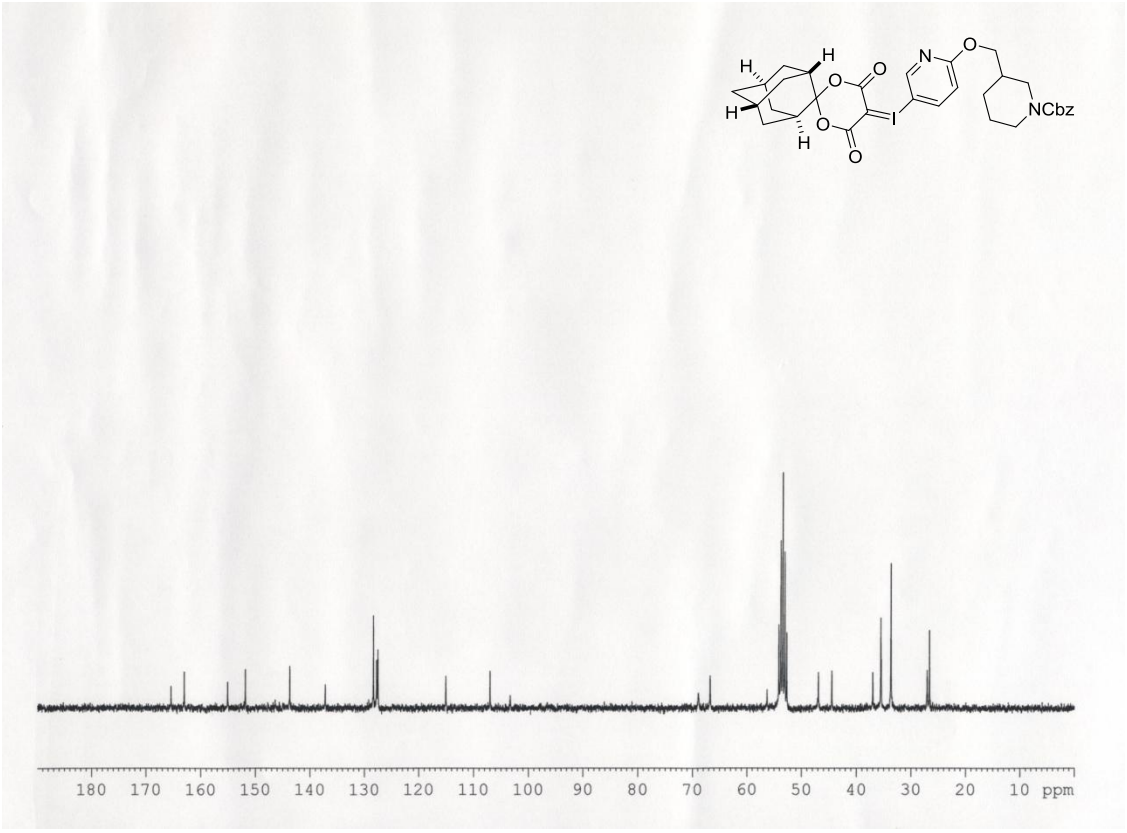
ppm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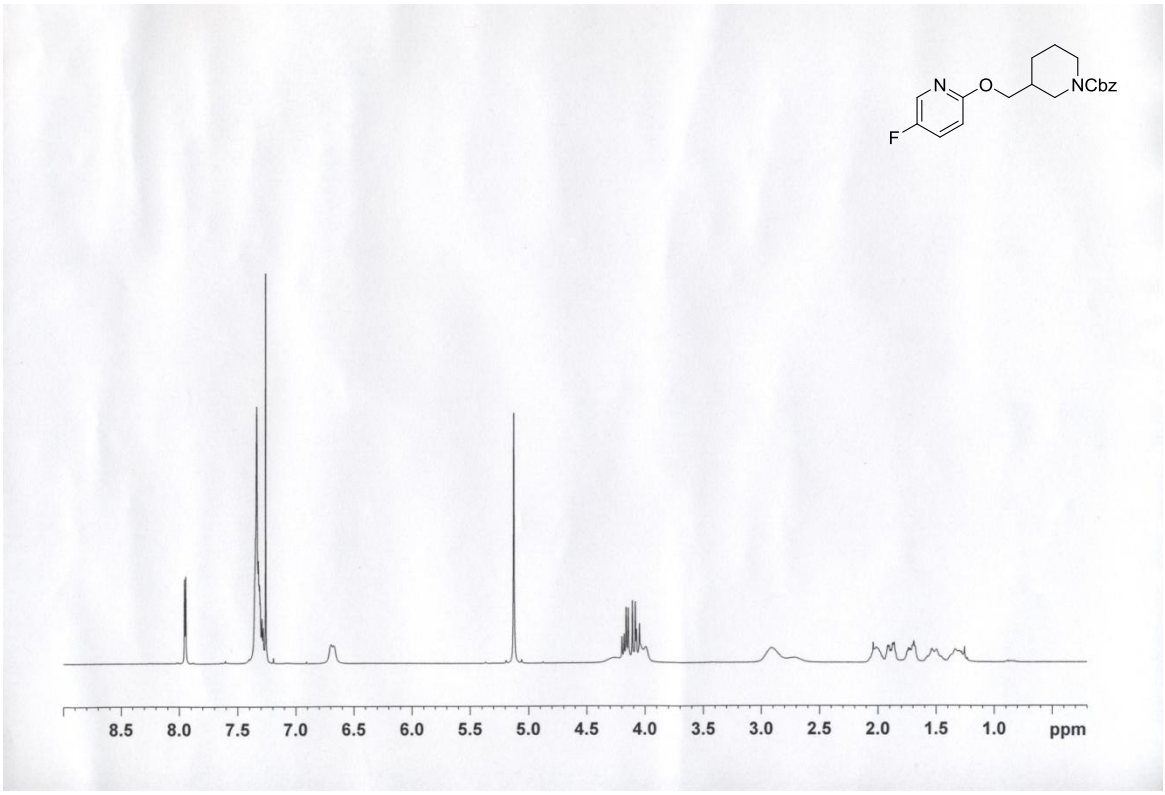
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NCbz
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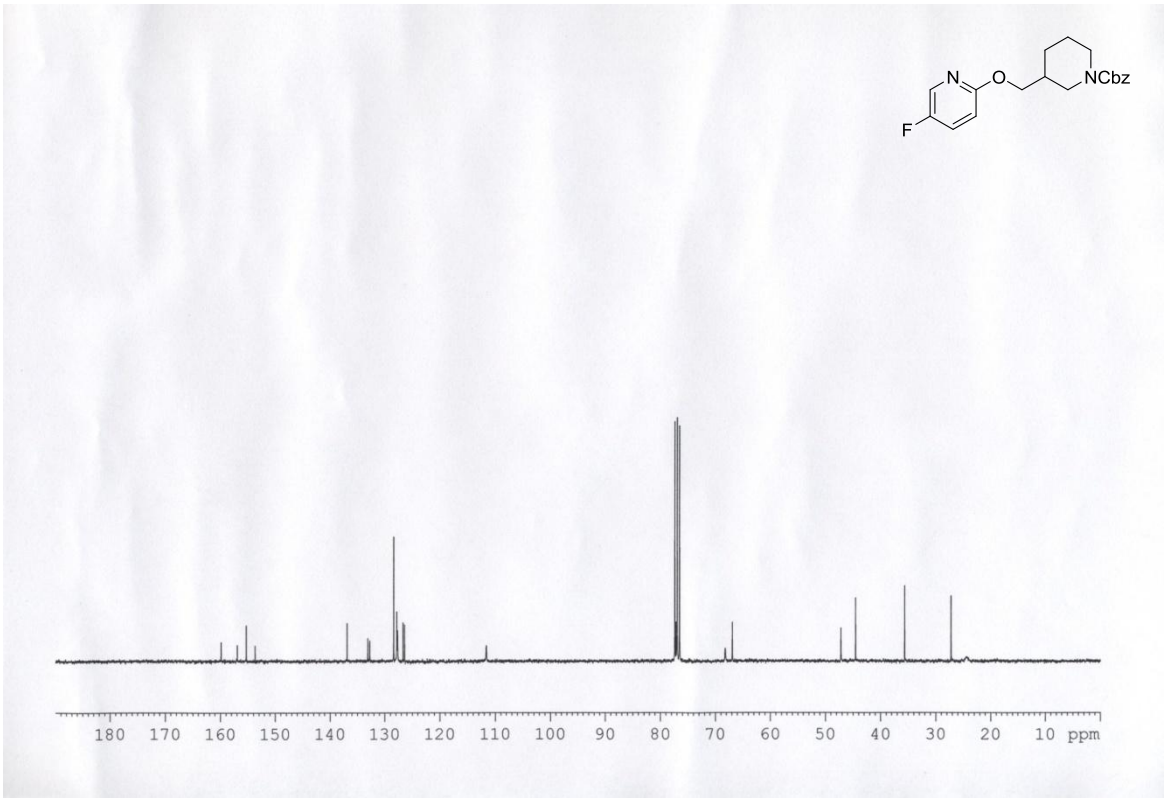
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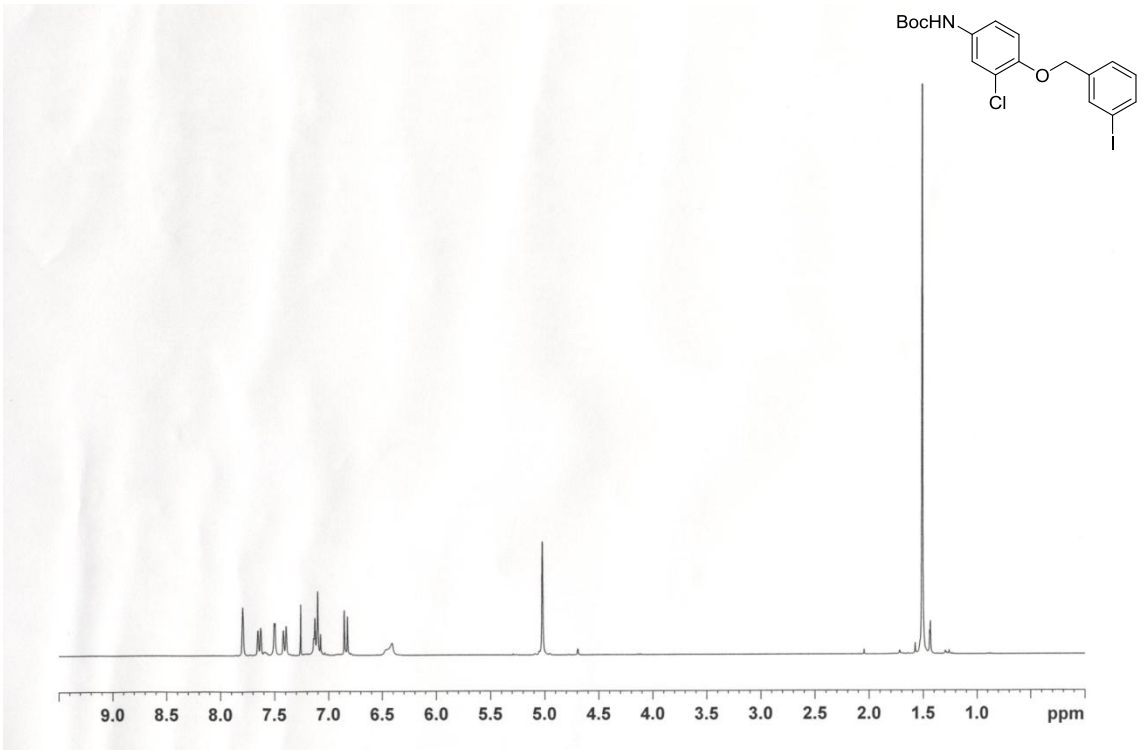
BocHN
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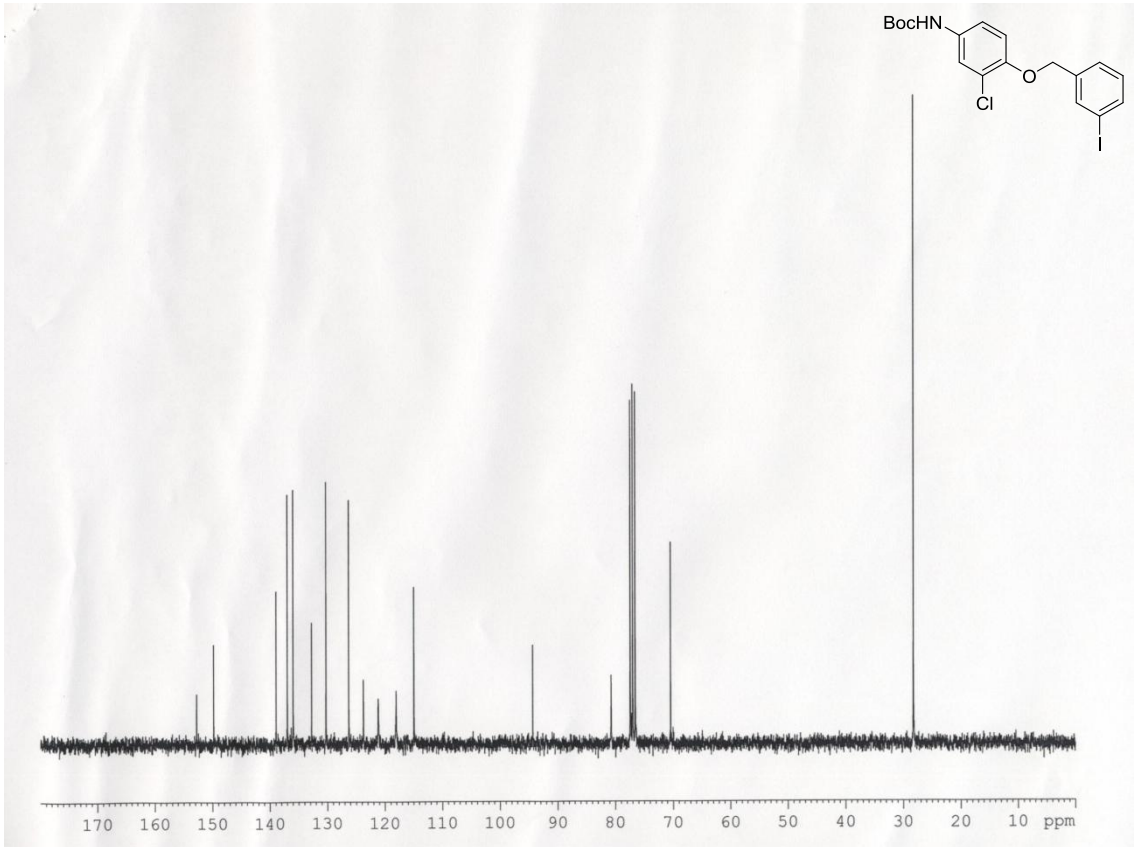
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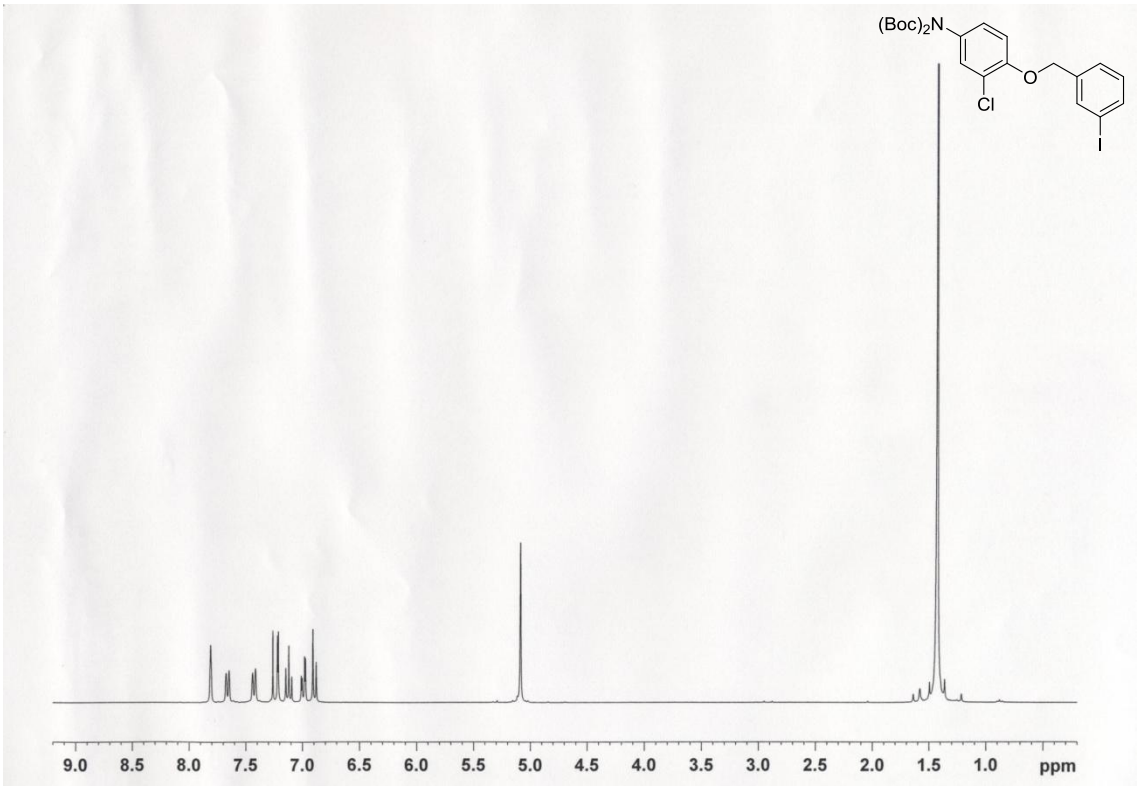
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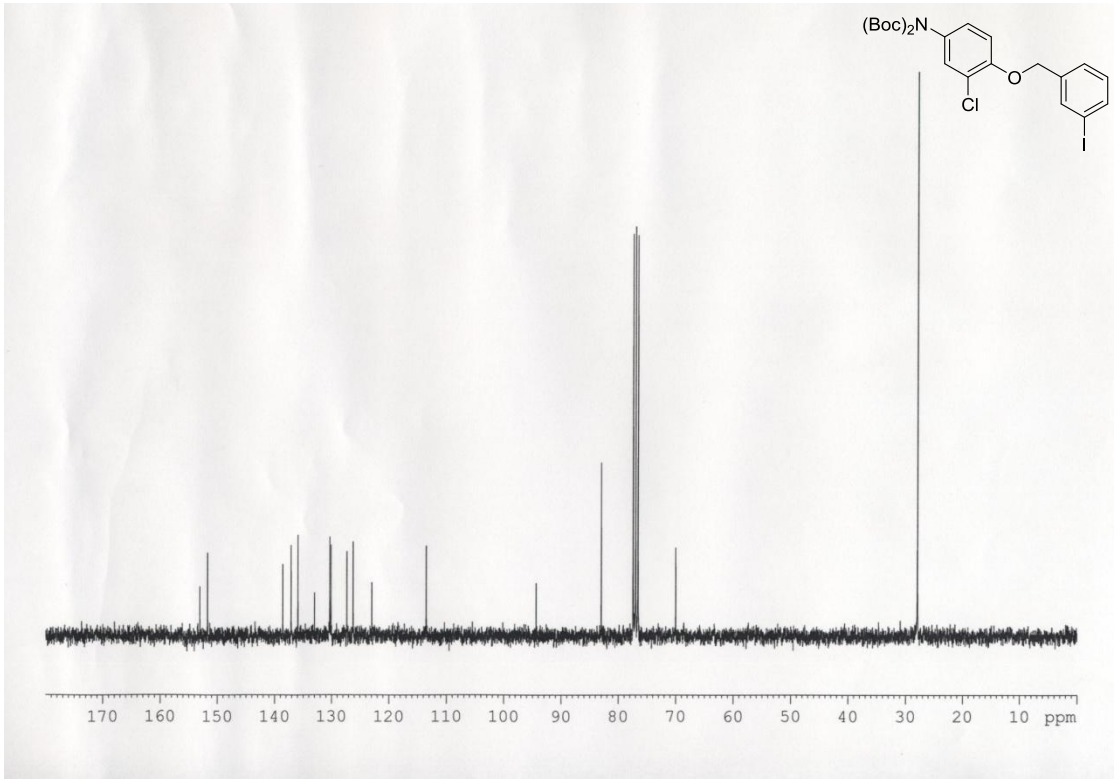
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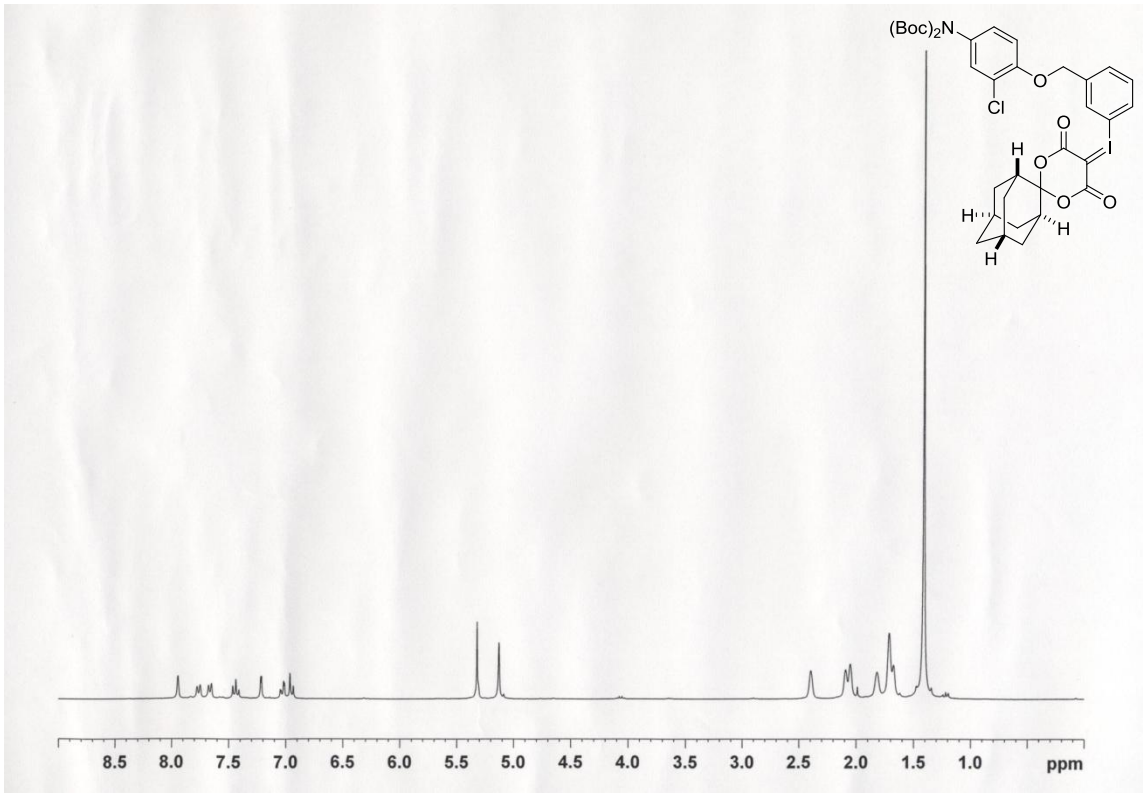
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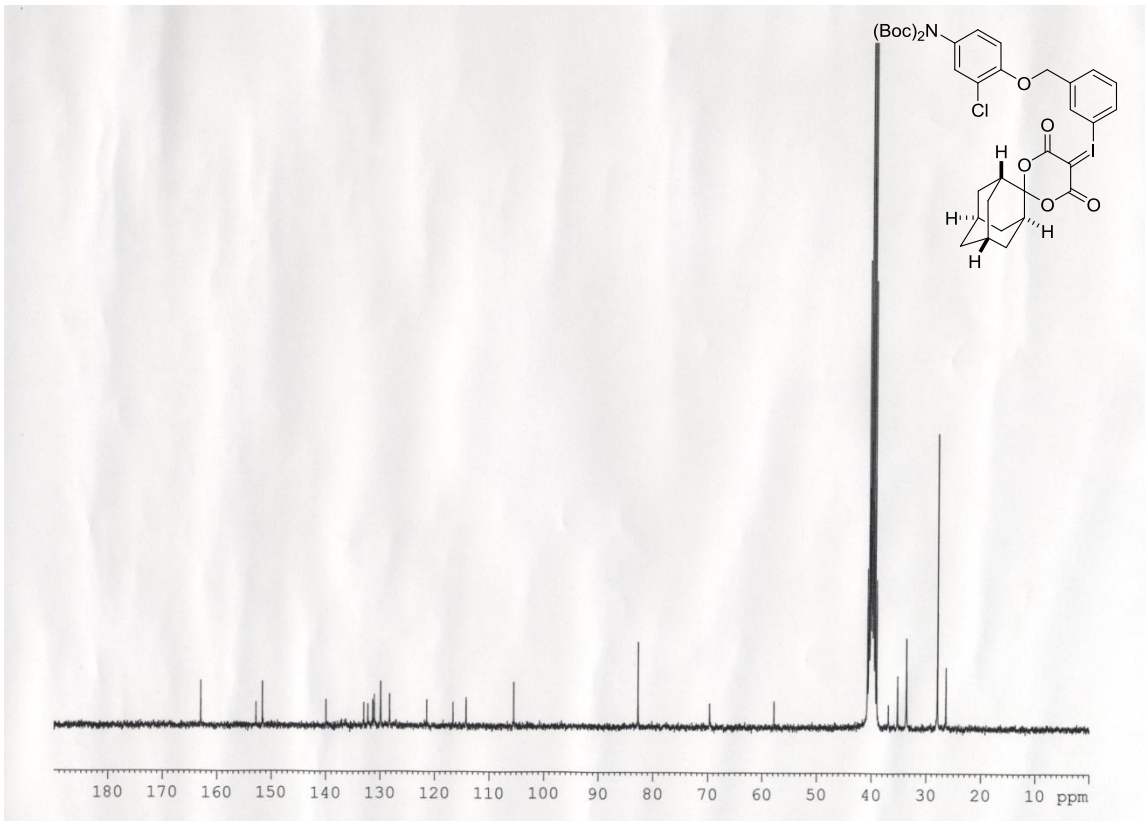
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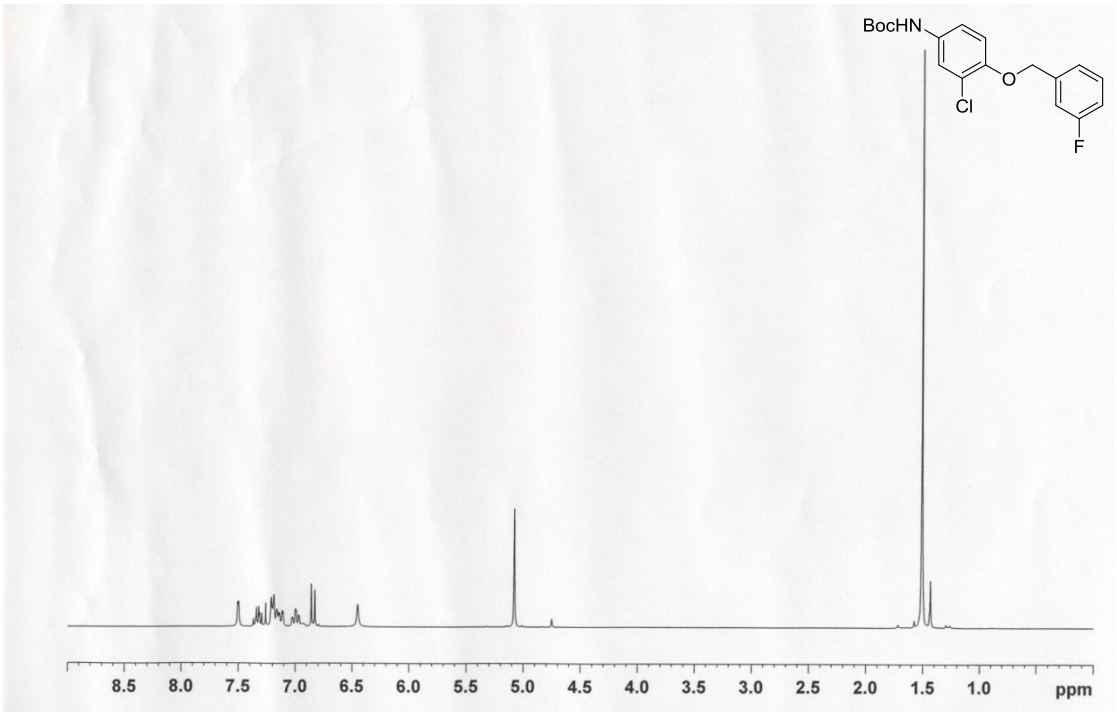
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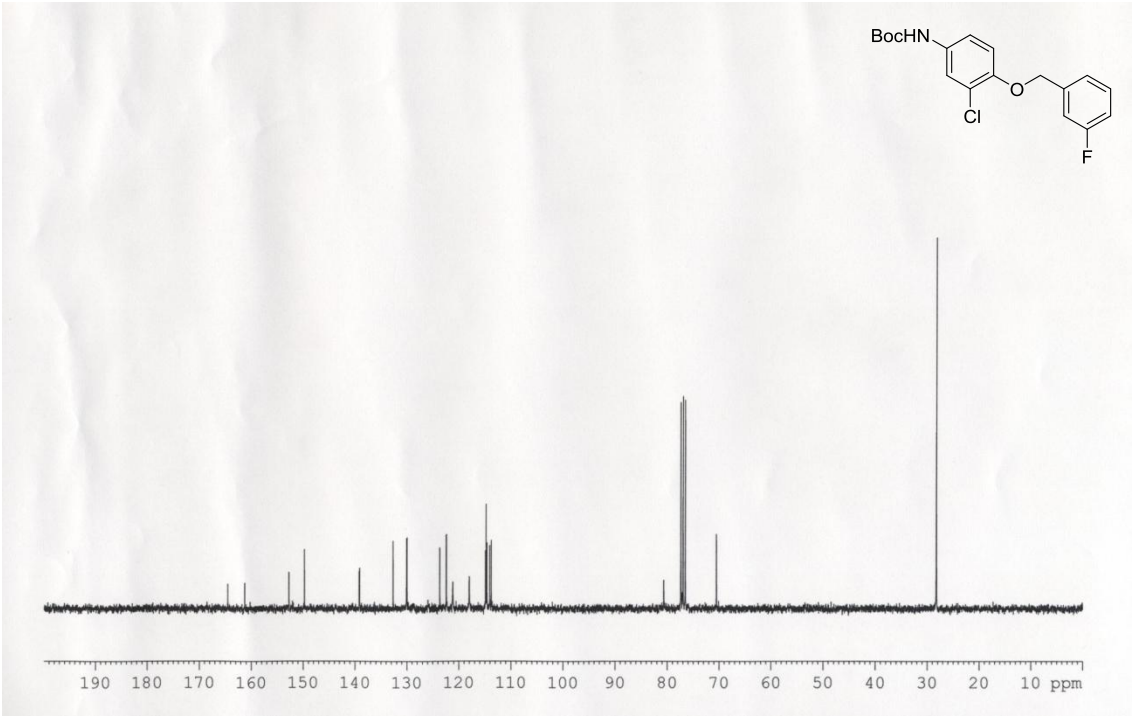
ppm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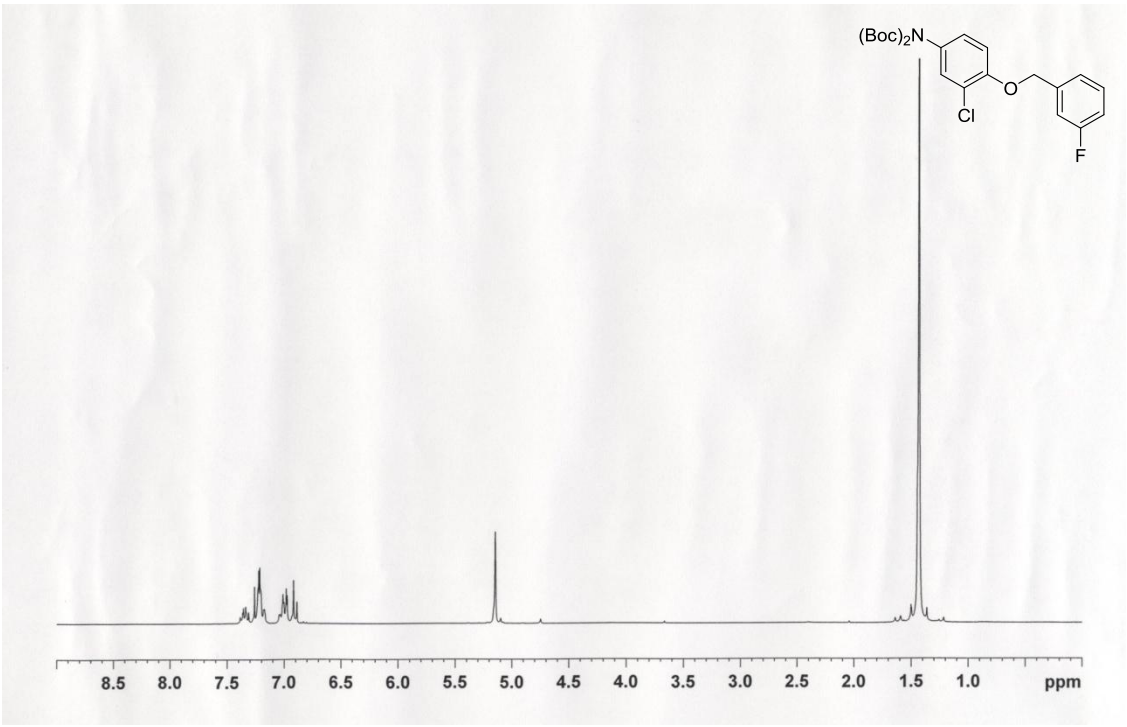
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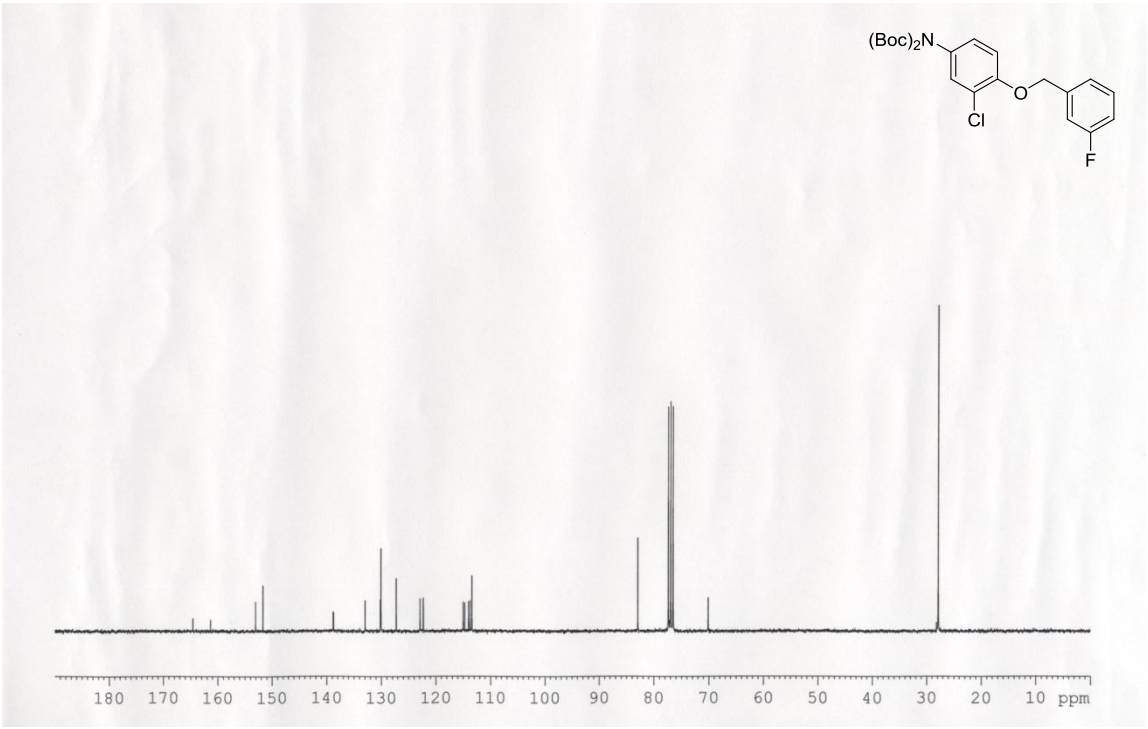
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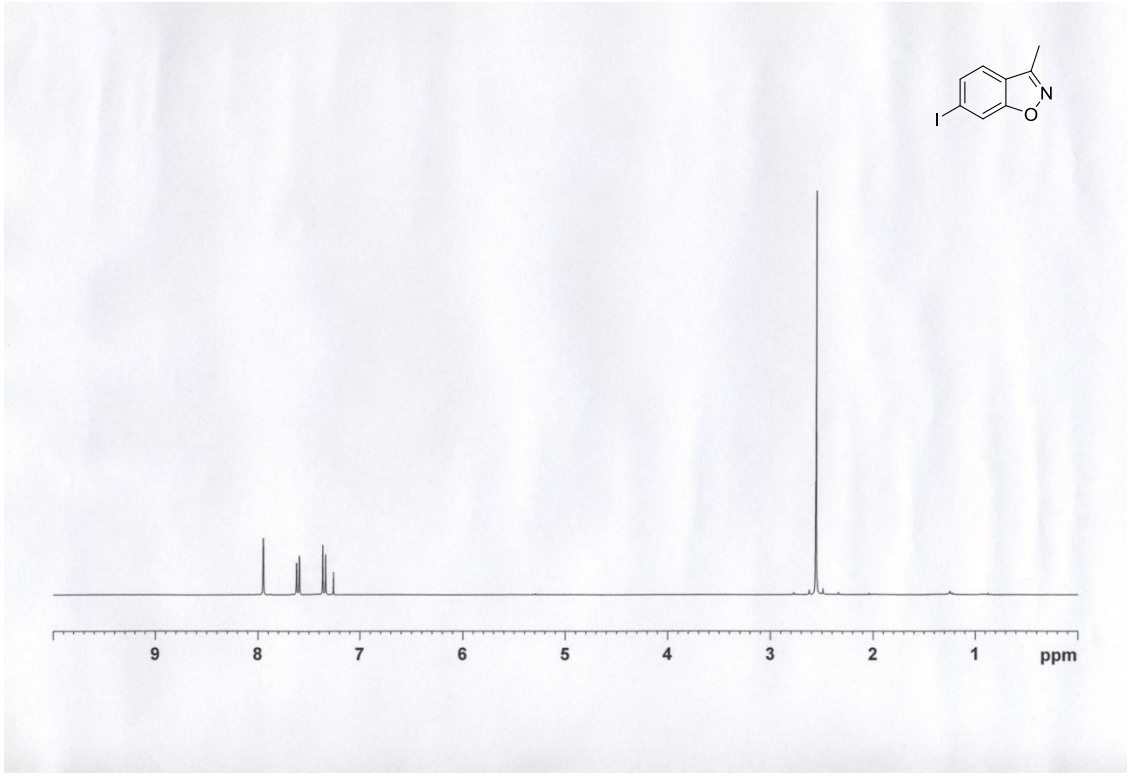
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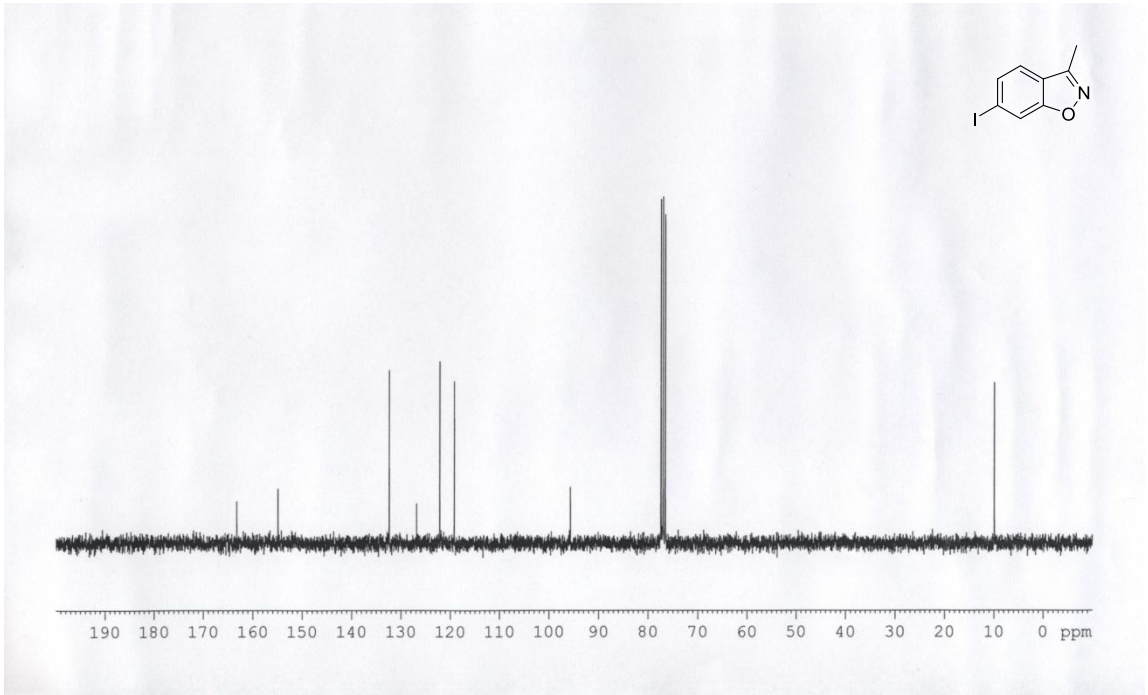
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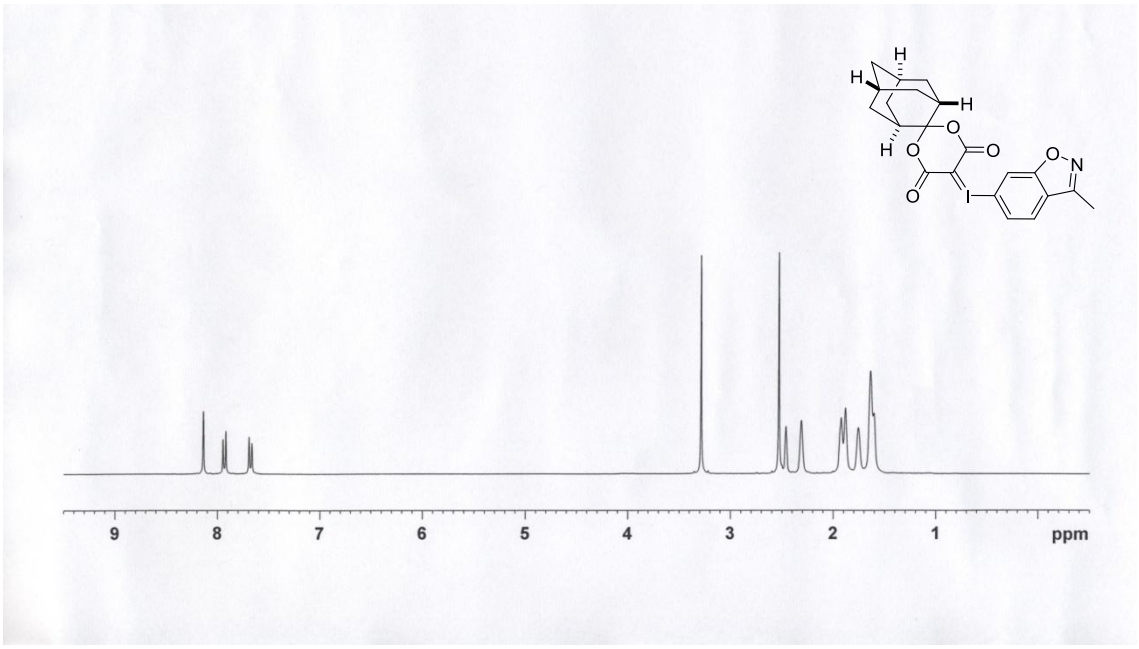
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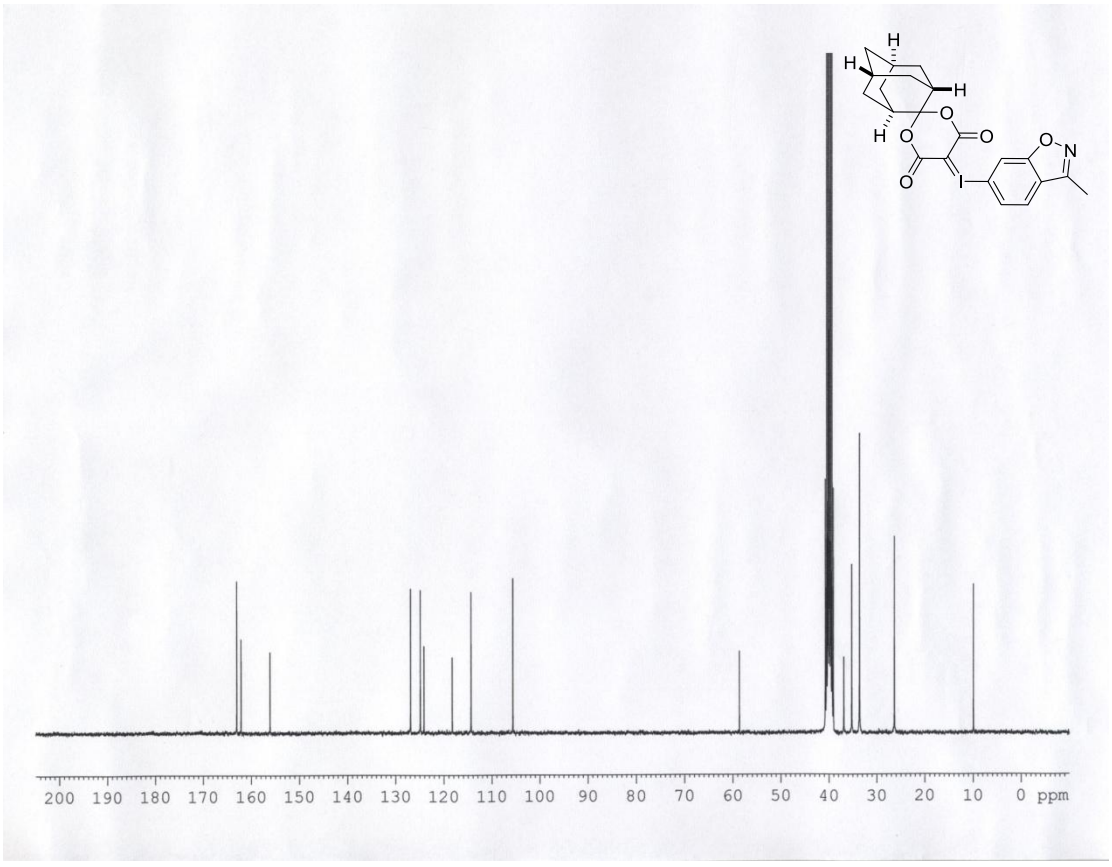
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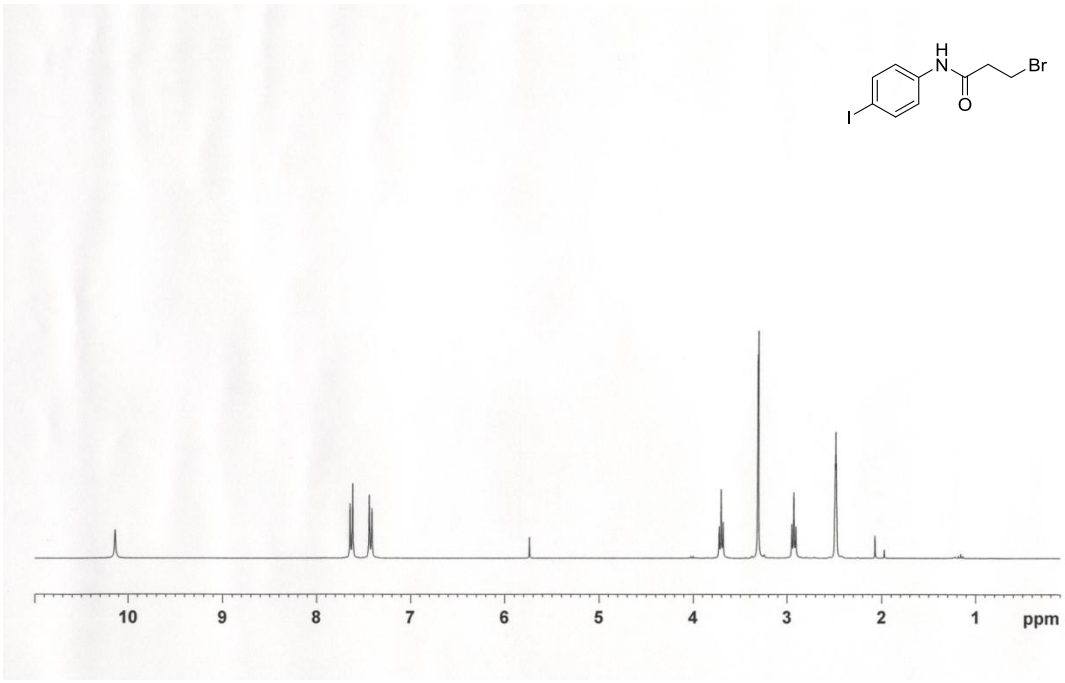
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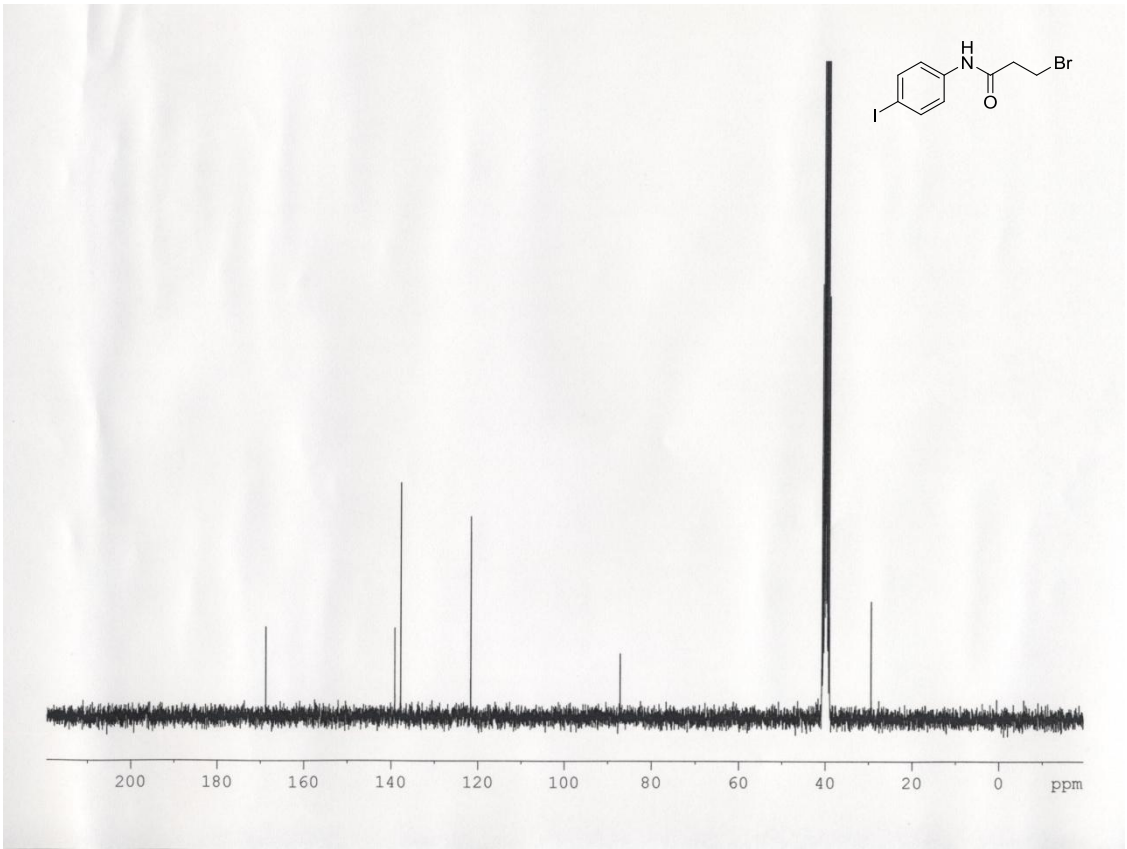
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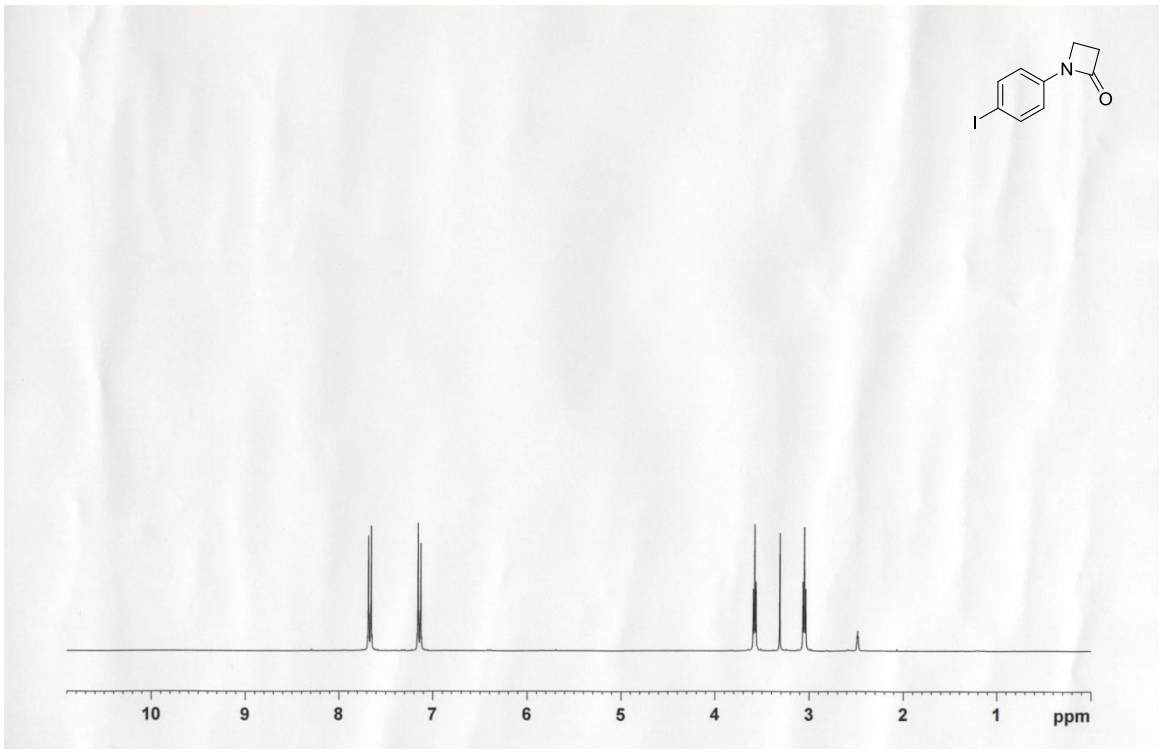
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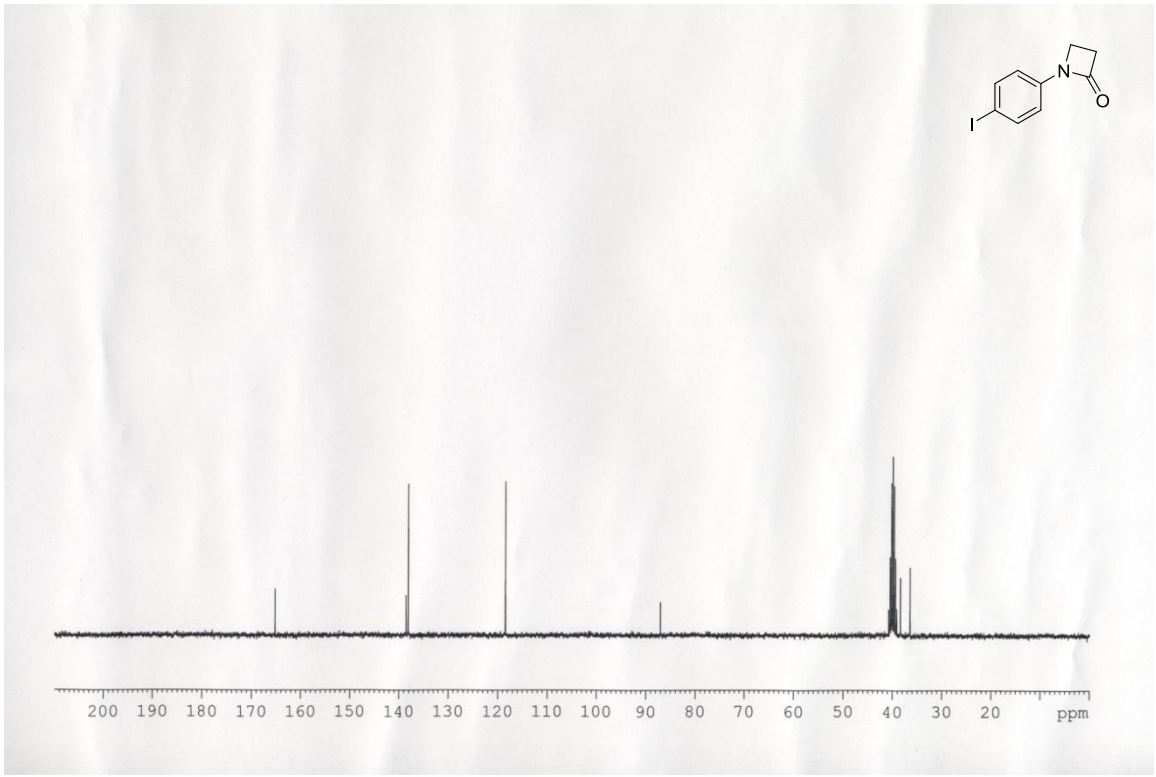
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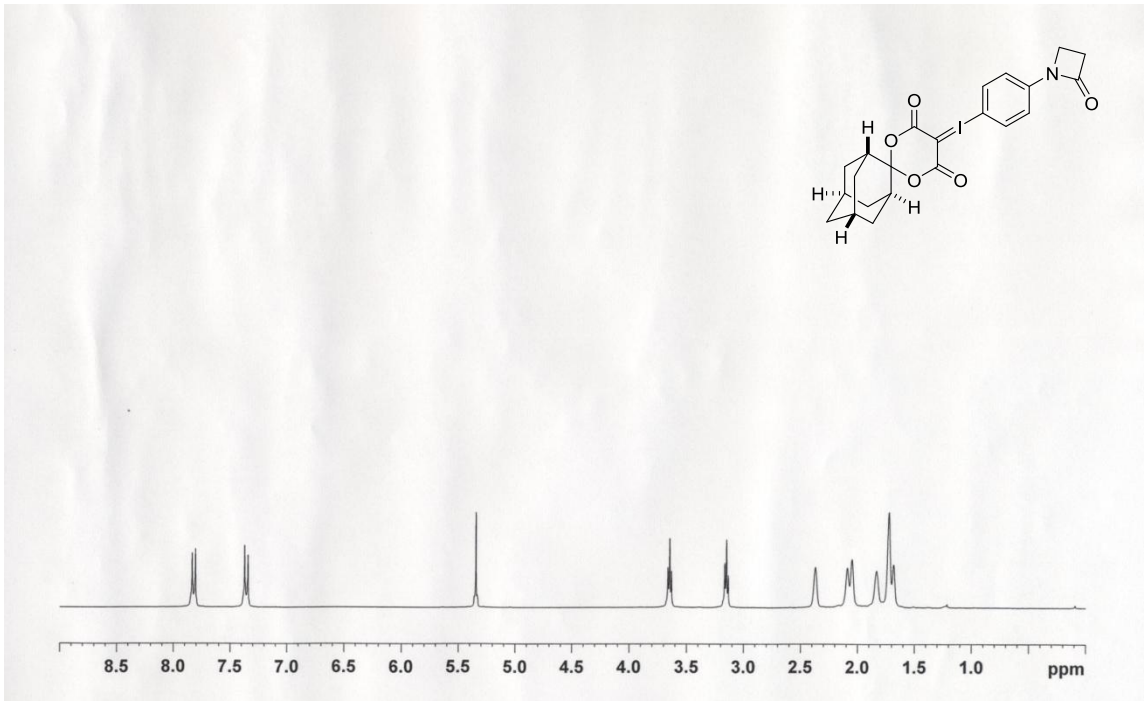
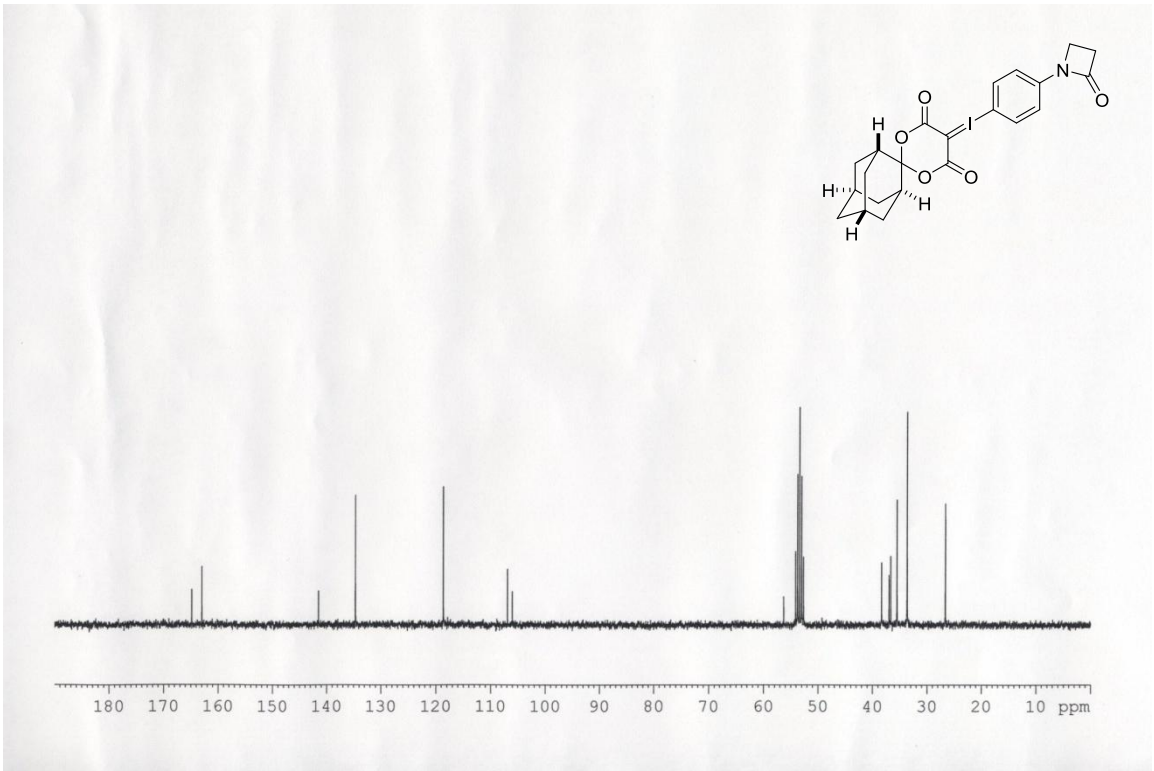
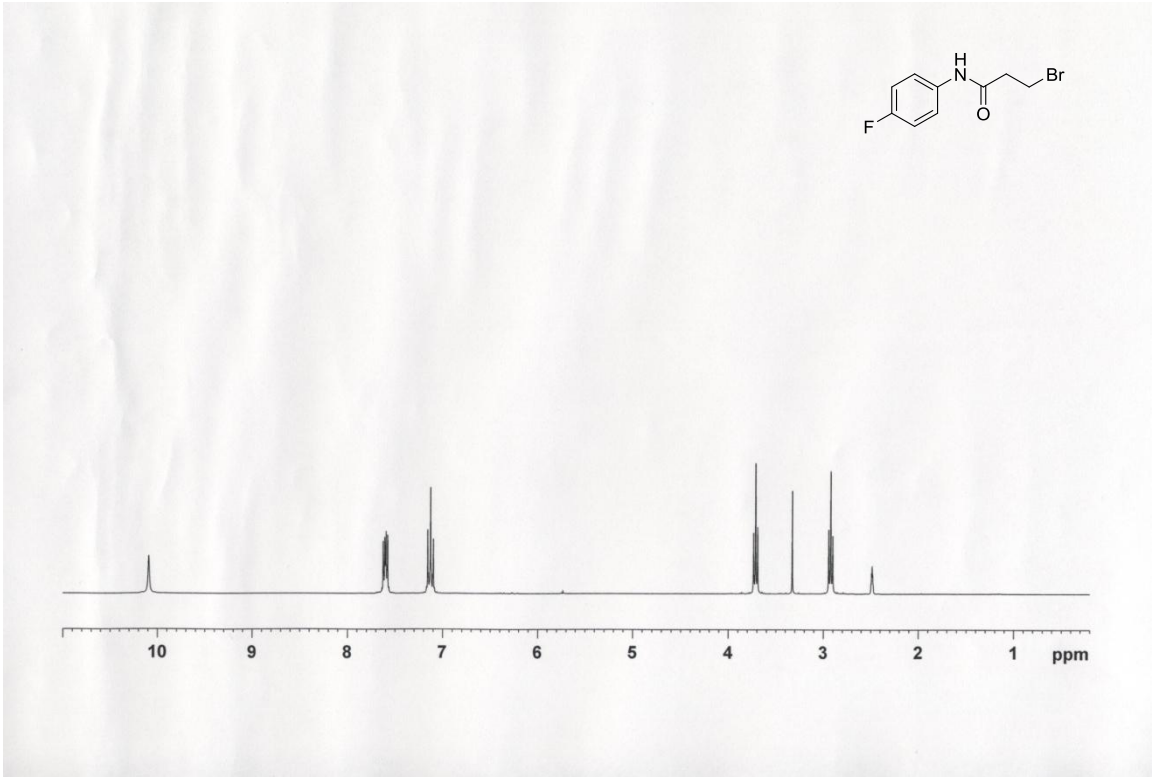
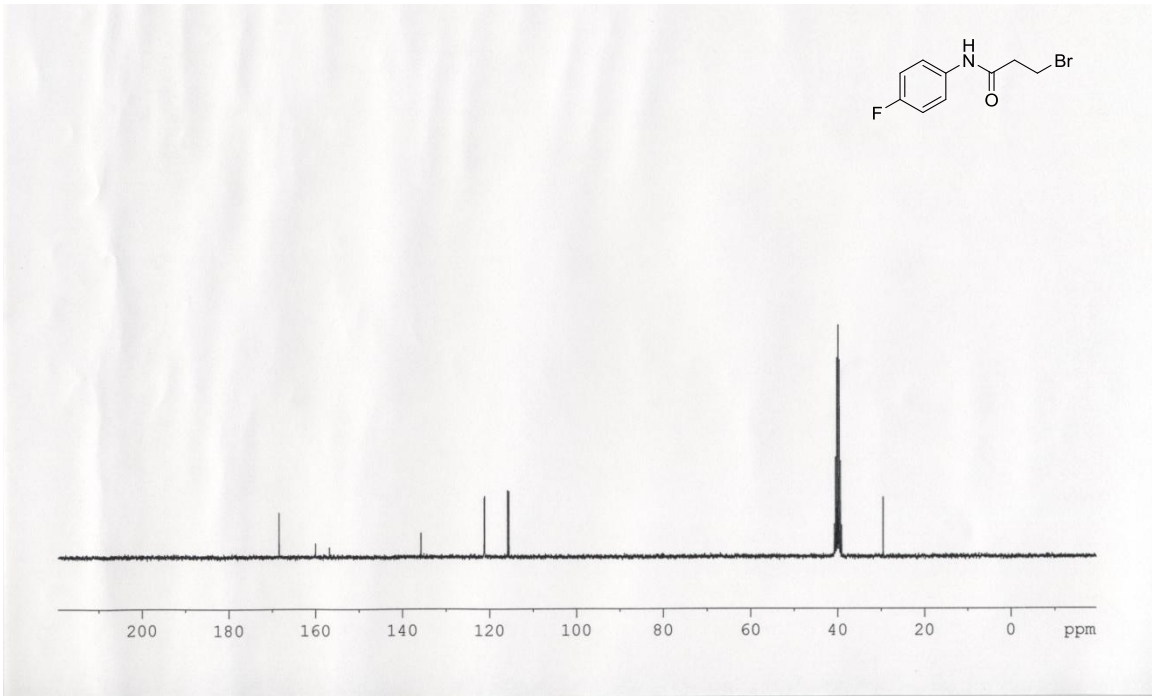
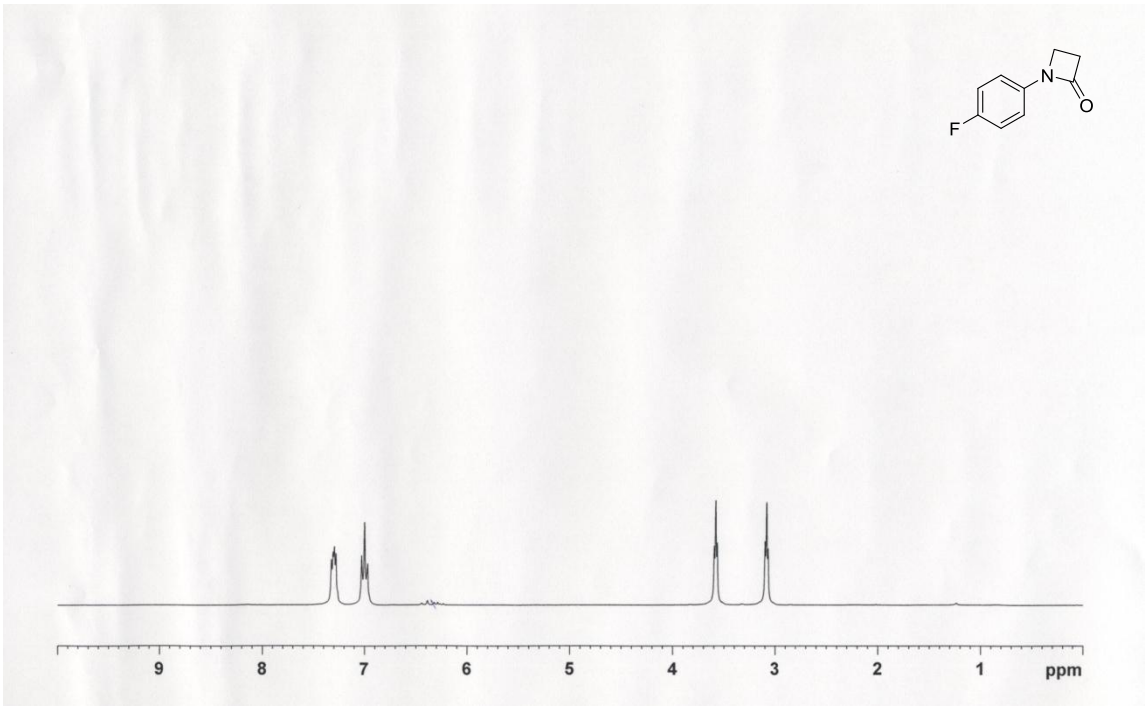
20
ppm

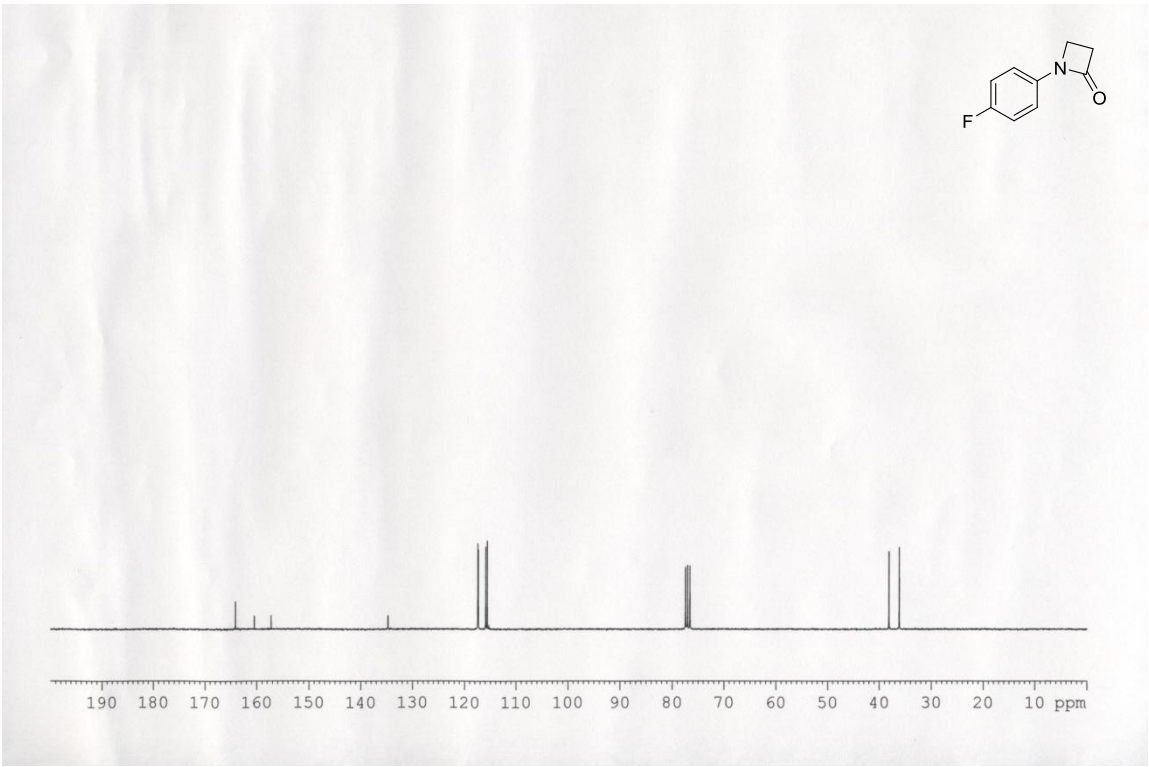

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

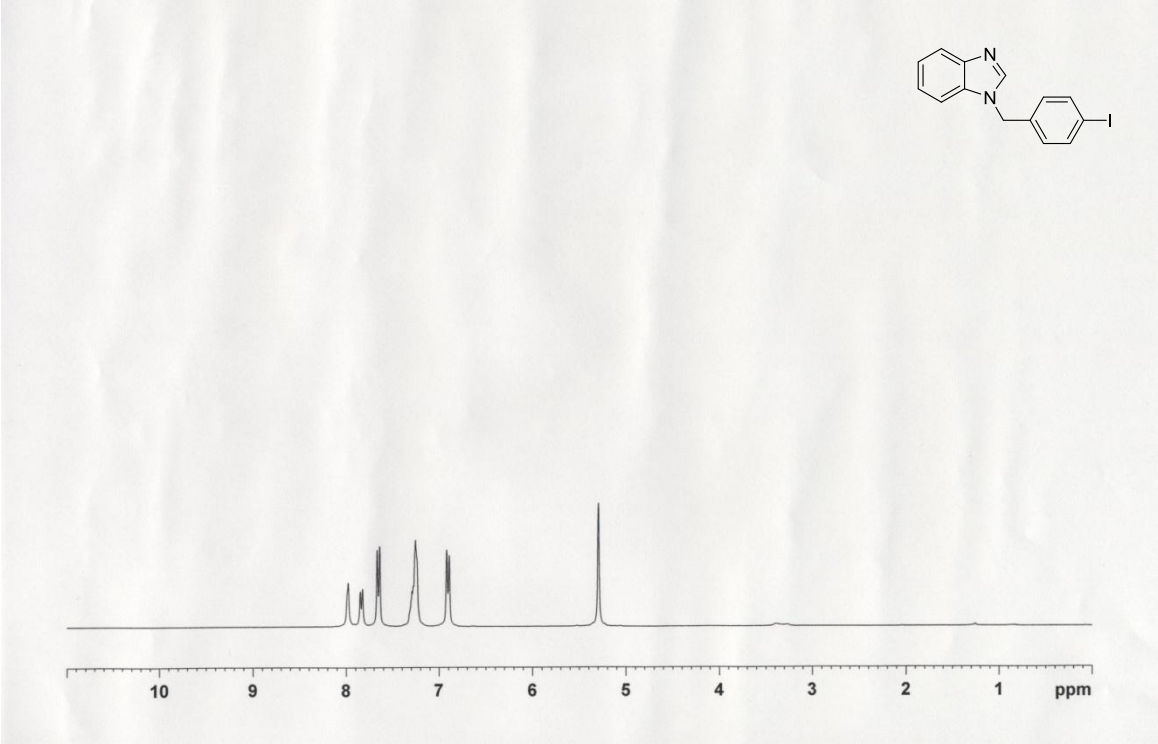

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

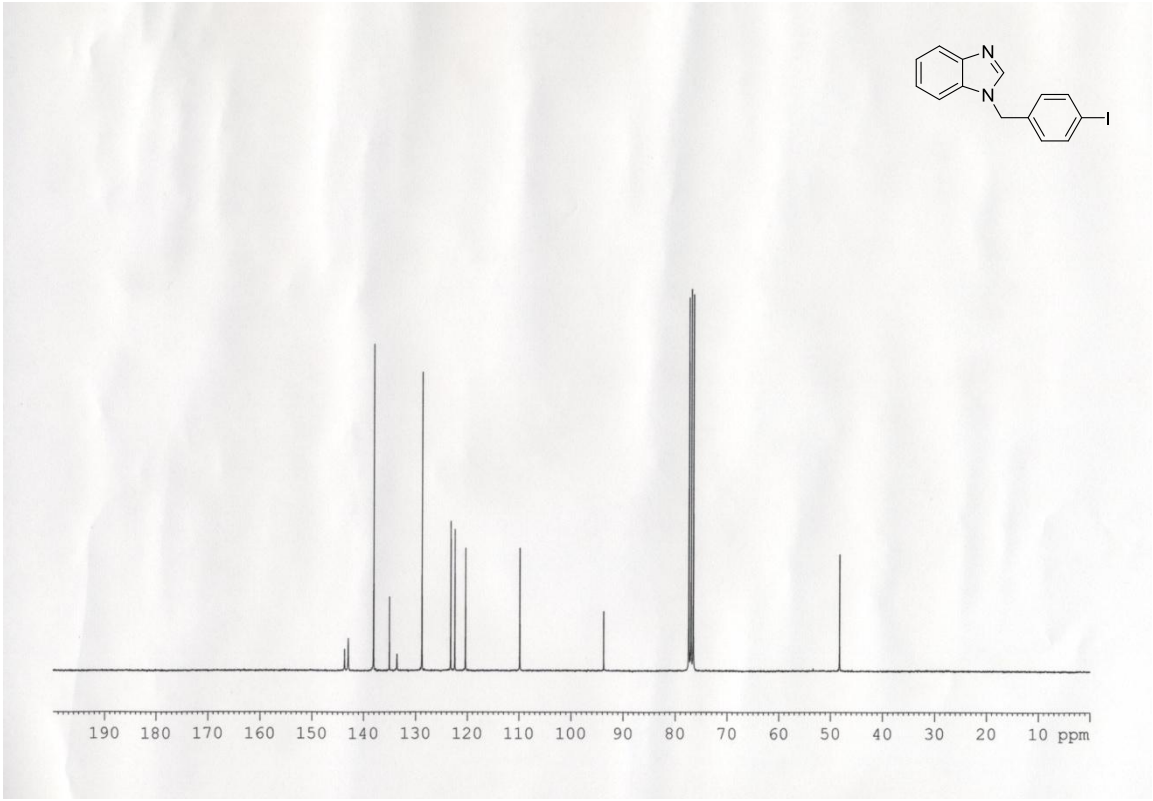

H
N
Br
O
F
10
9
8
7
6
5
4
3
2
1
ppm

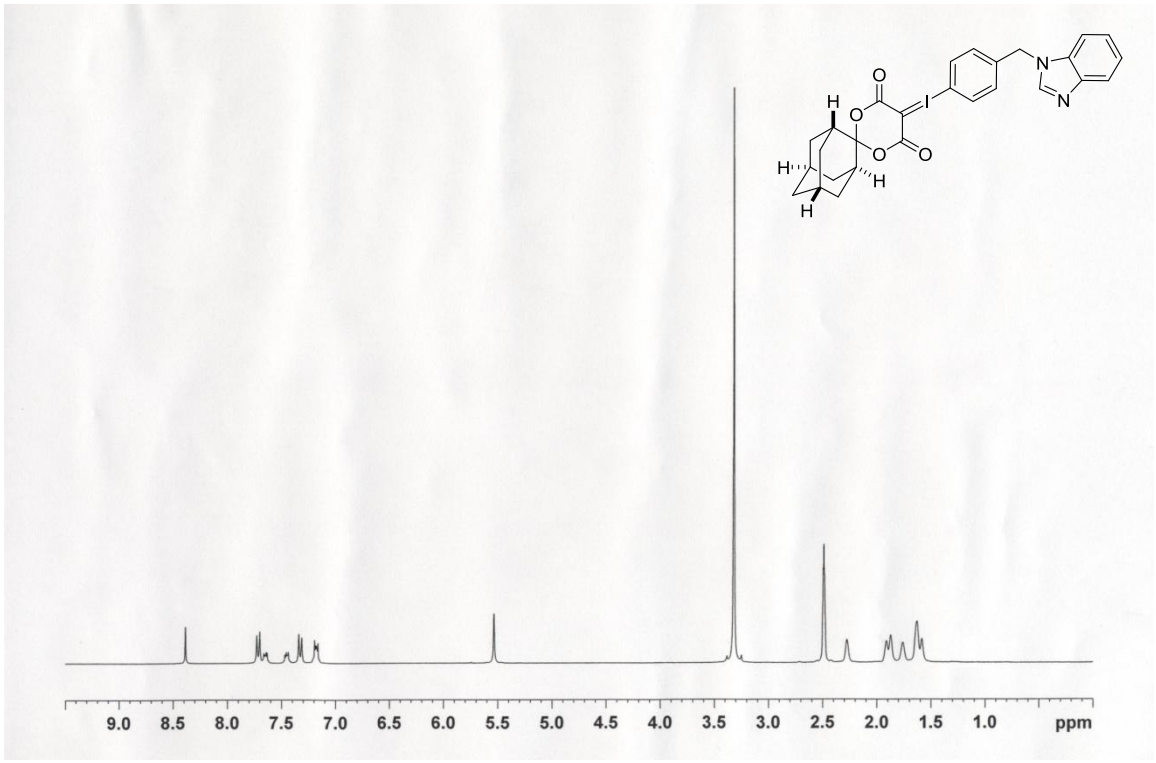

H
N
Br
O
F
200
180
160
140
120
100
80
60
40
20
0
ppm

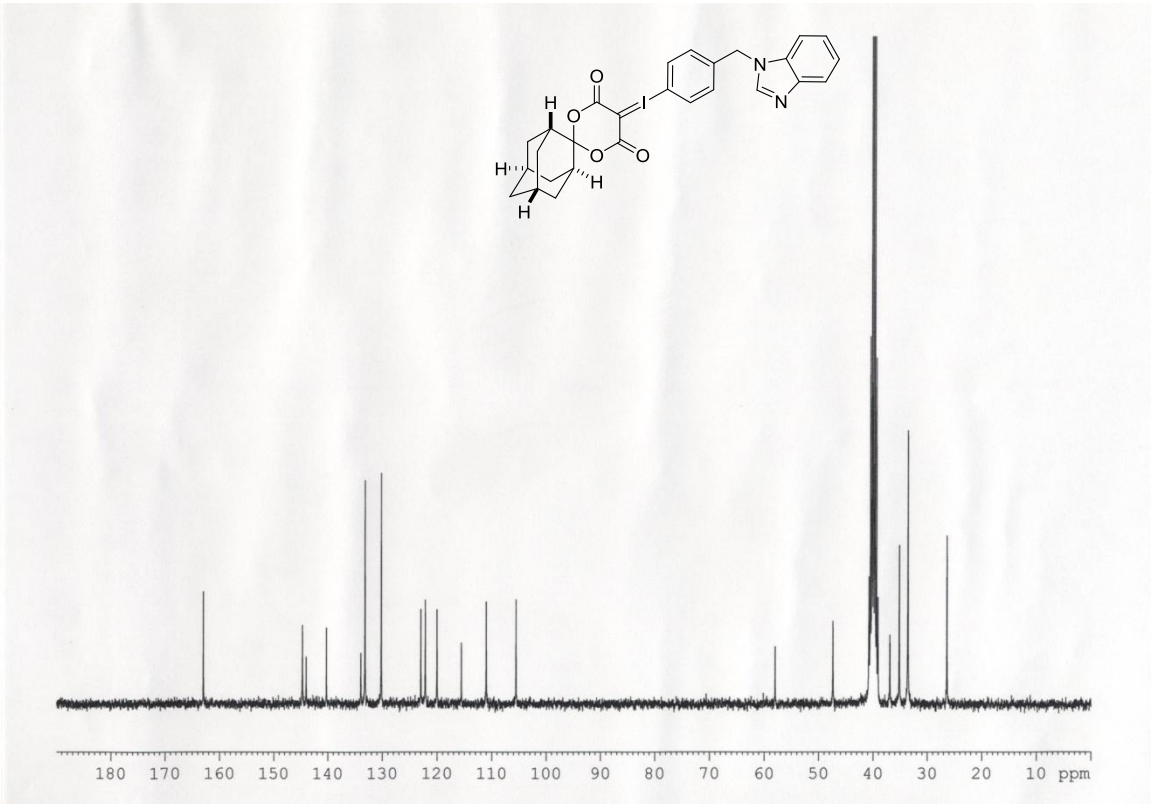

F
N
O
9
8
7
6
5
4
3
2
1
ppm

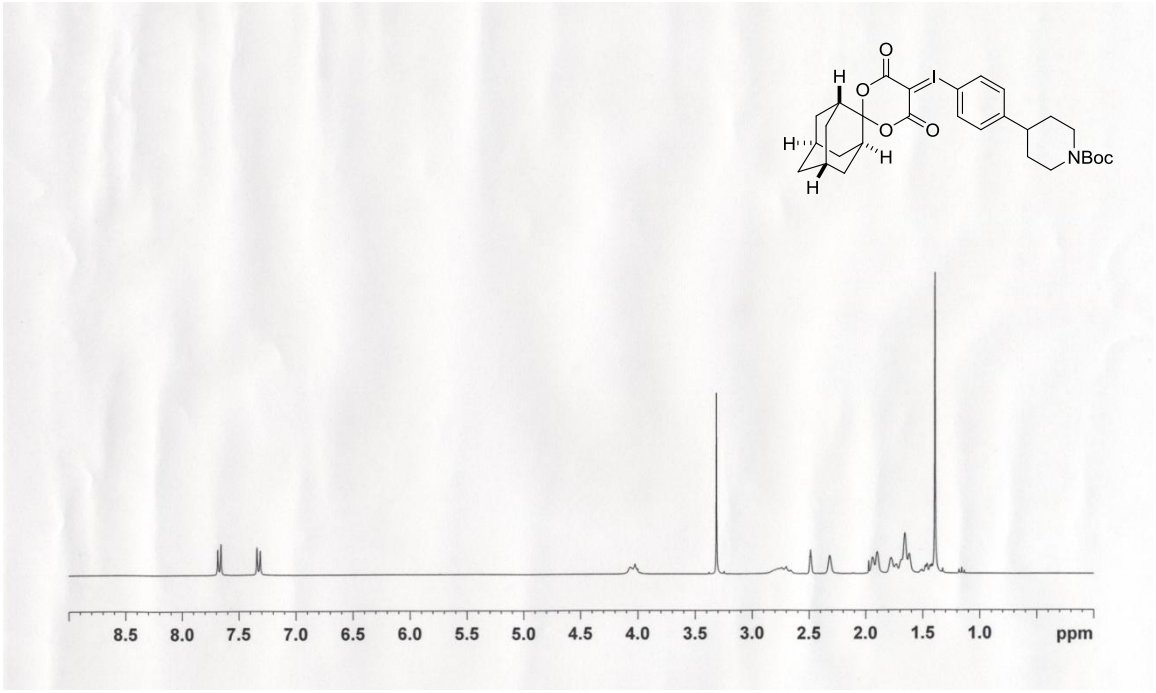

F
N
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

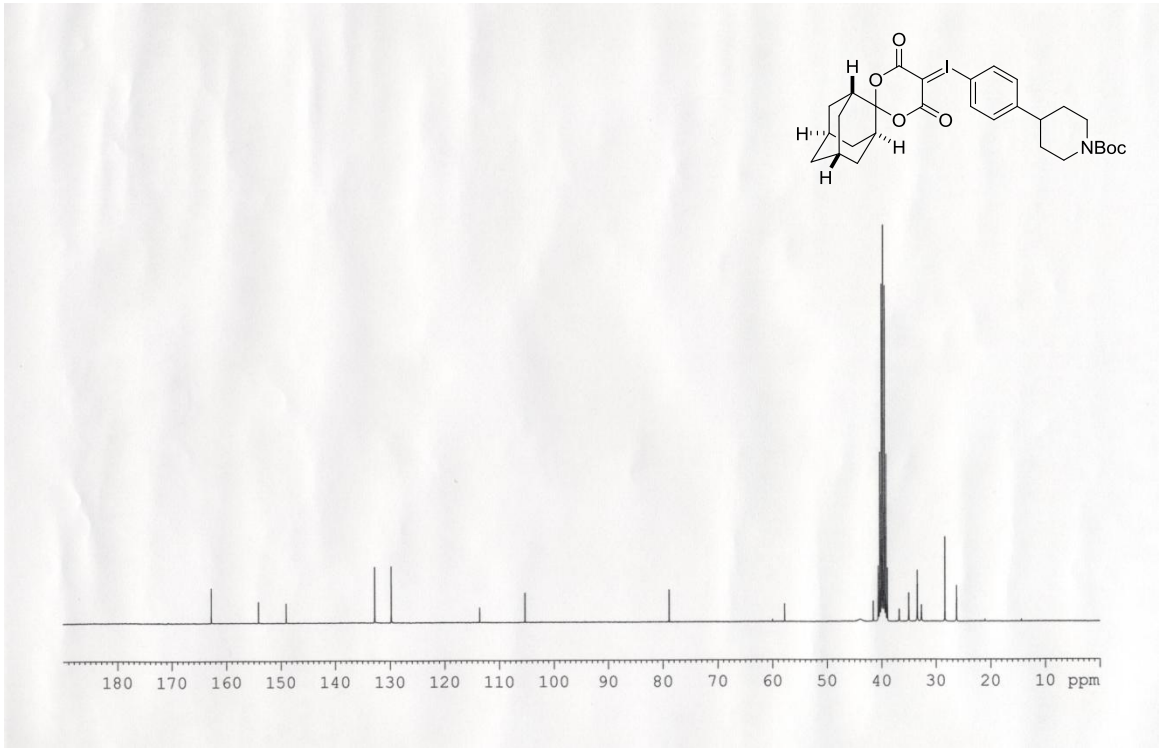

N
N
I
10
9
8
7
6
5
4
3
2
1
ppm

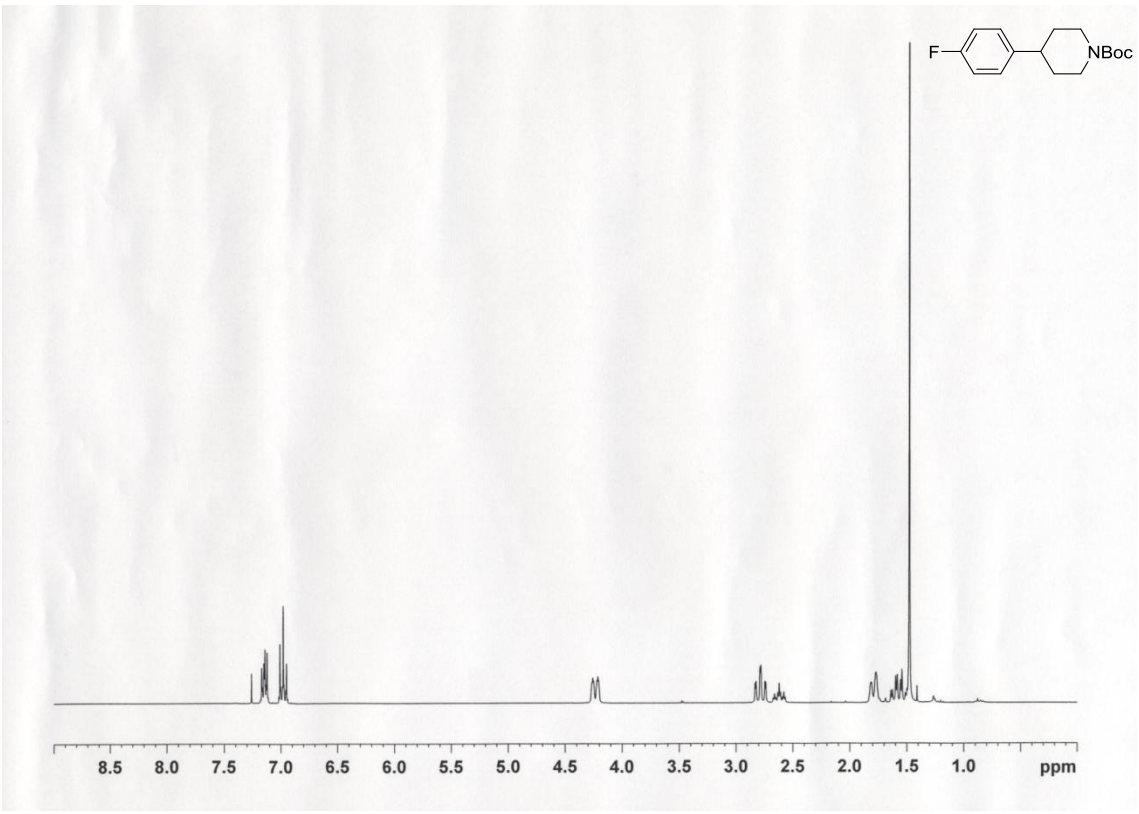

N
N
I
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

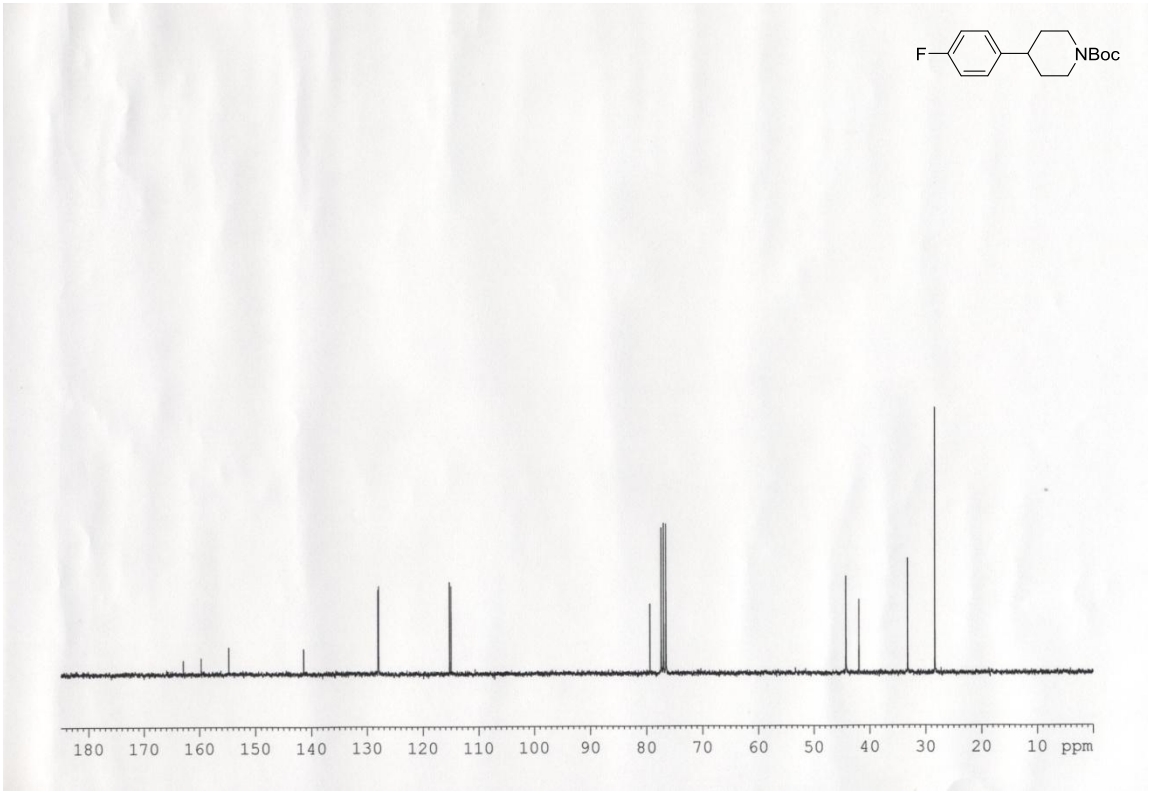

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

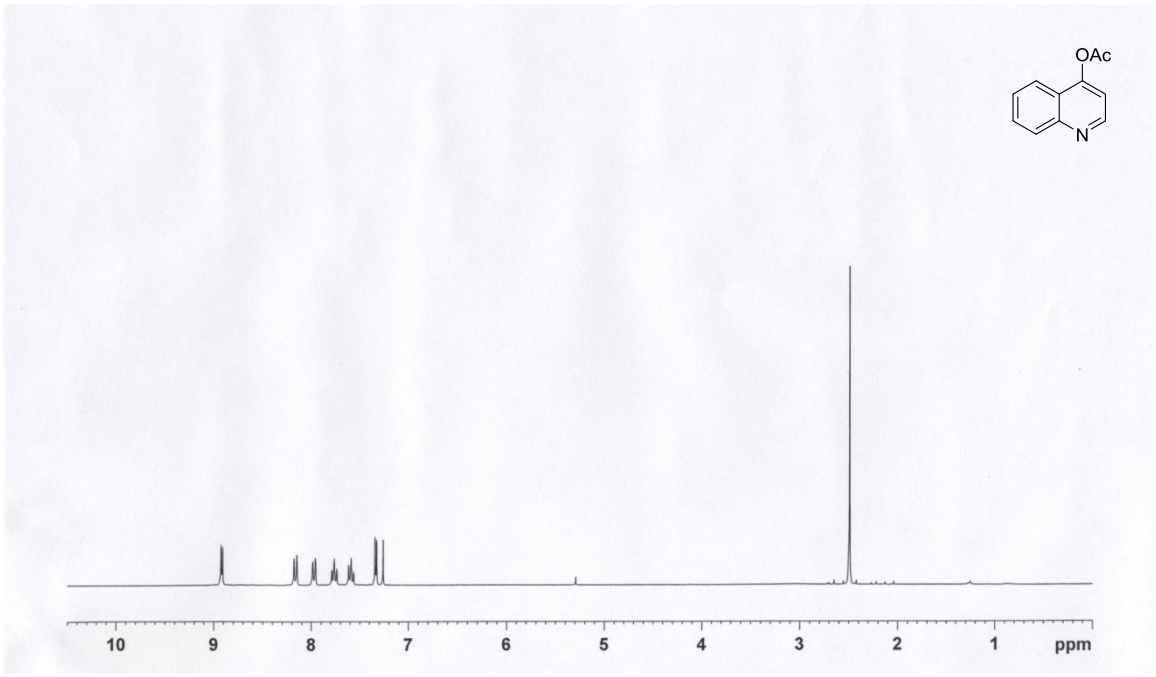

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

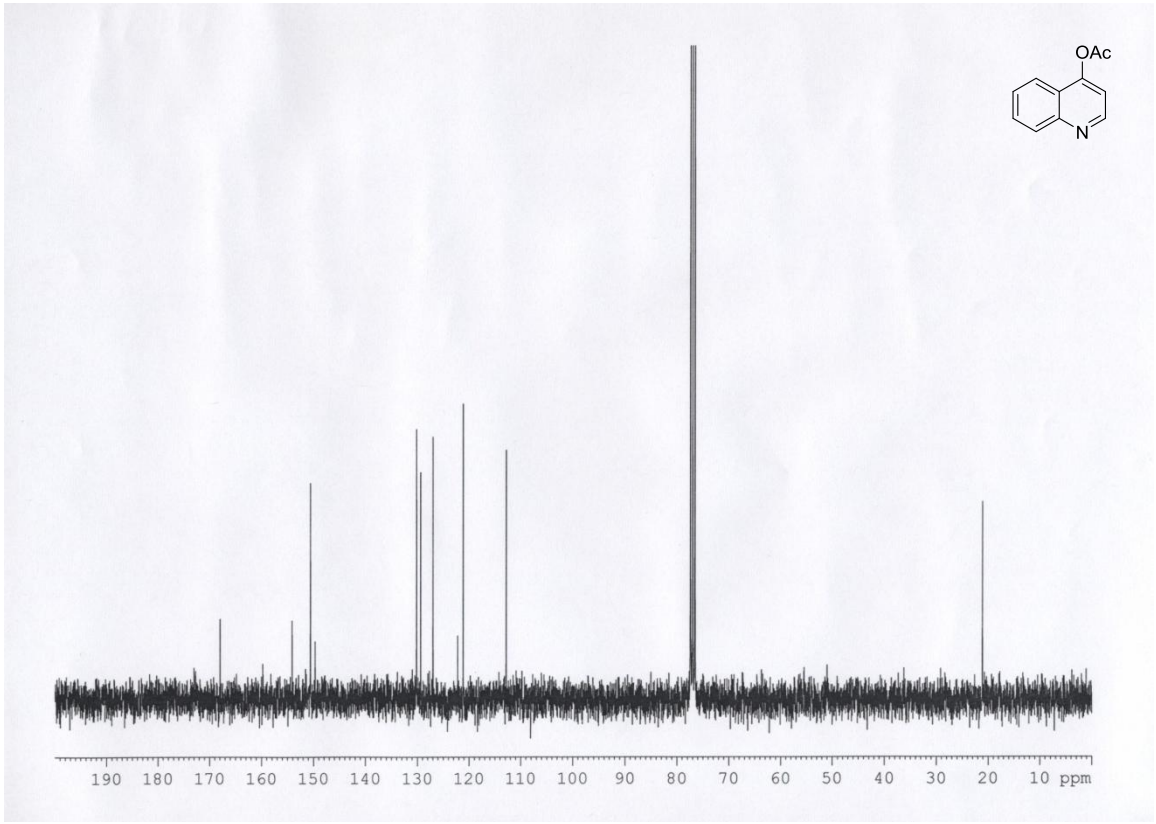

O
H
O
I
O
O
H
H
H
NBoc
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

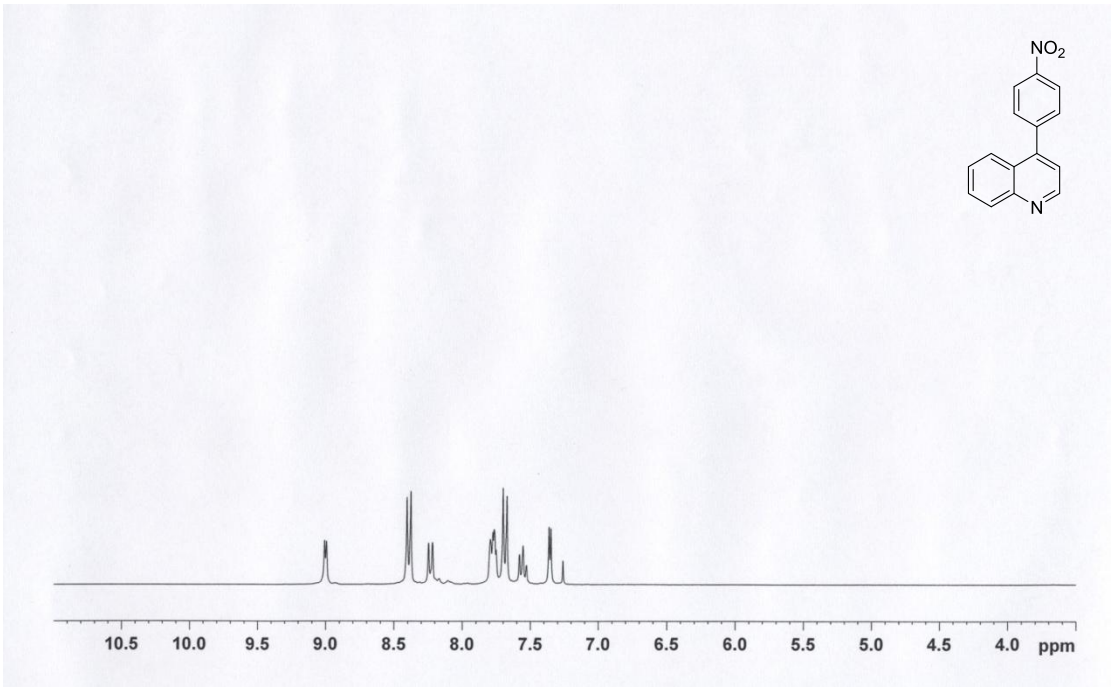

O
H
O
I
O
O
H
H
H
NBoc
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

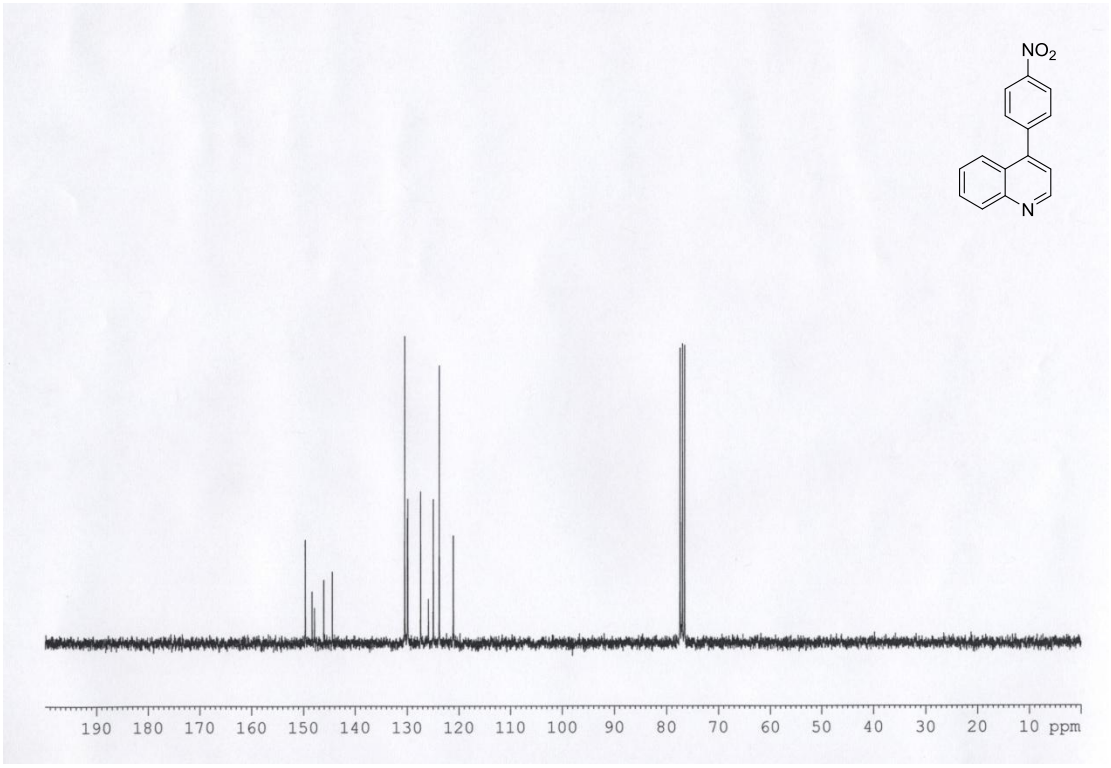

F
NBoc
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

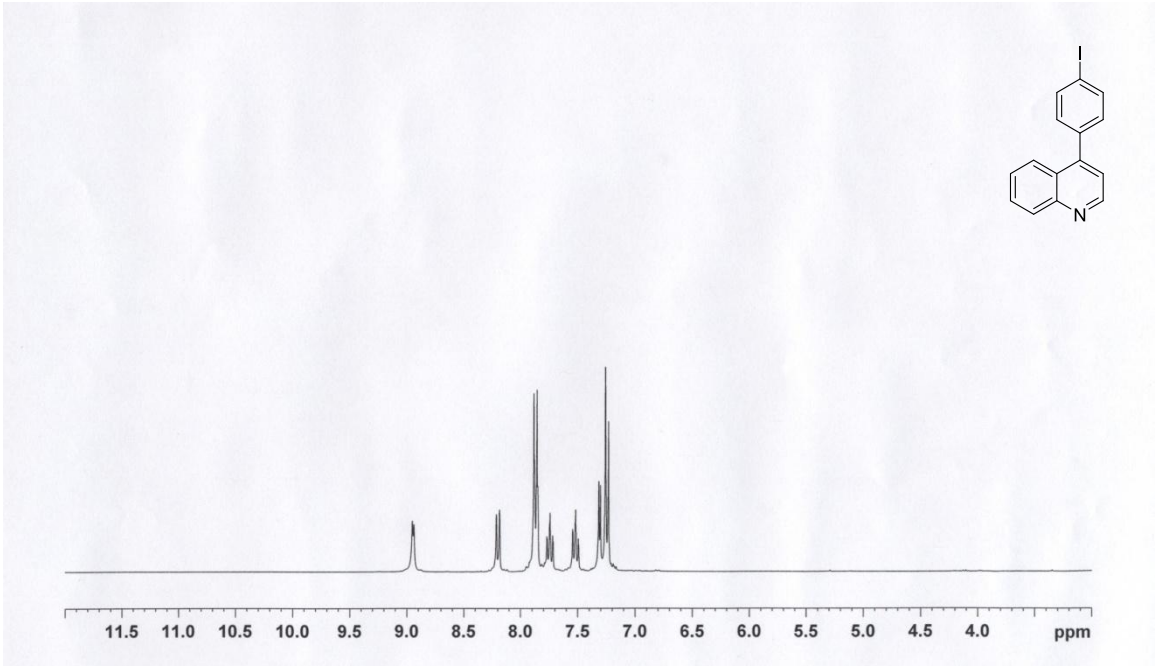

F
NBoc
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

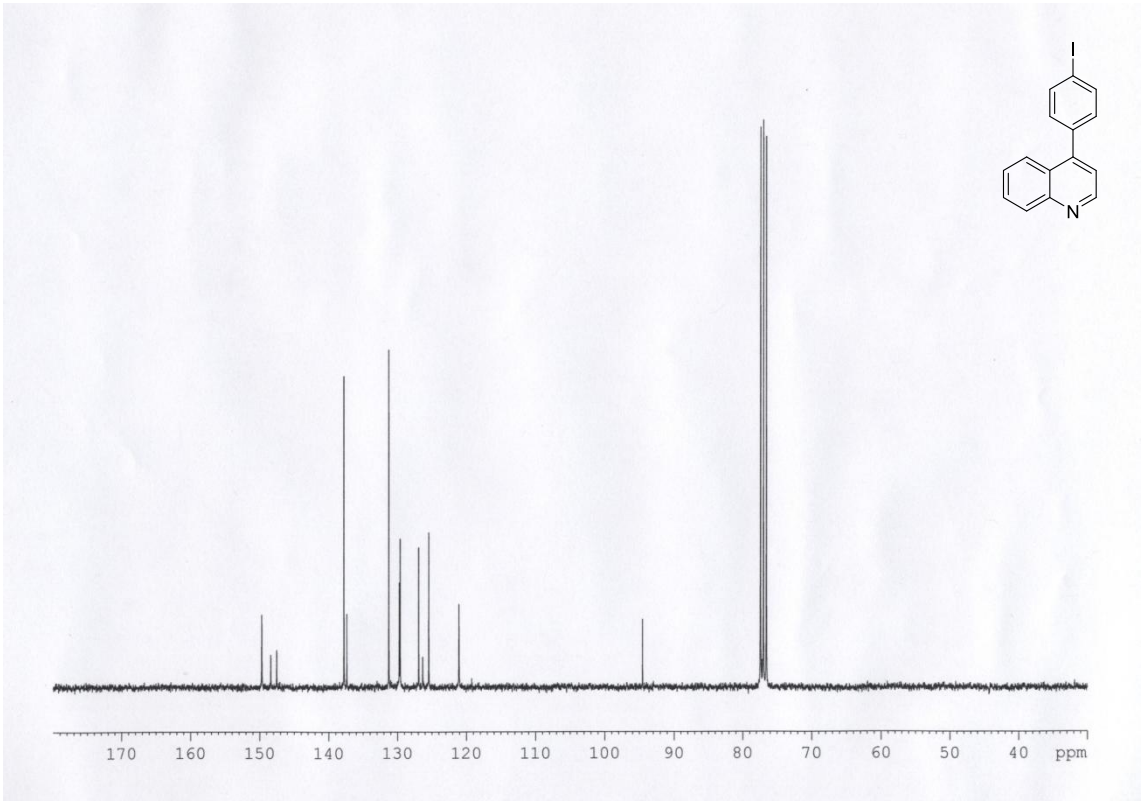

OAc
N
10
9
8
7
6
5
4
3
2
1
ppm

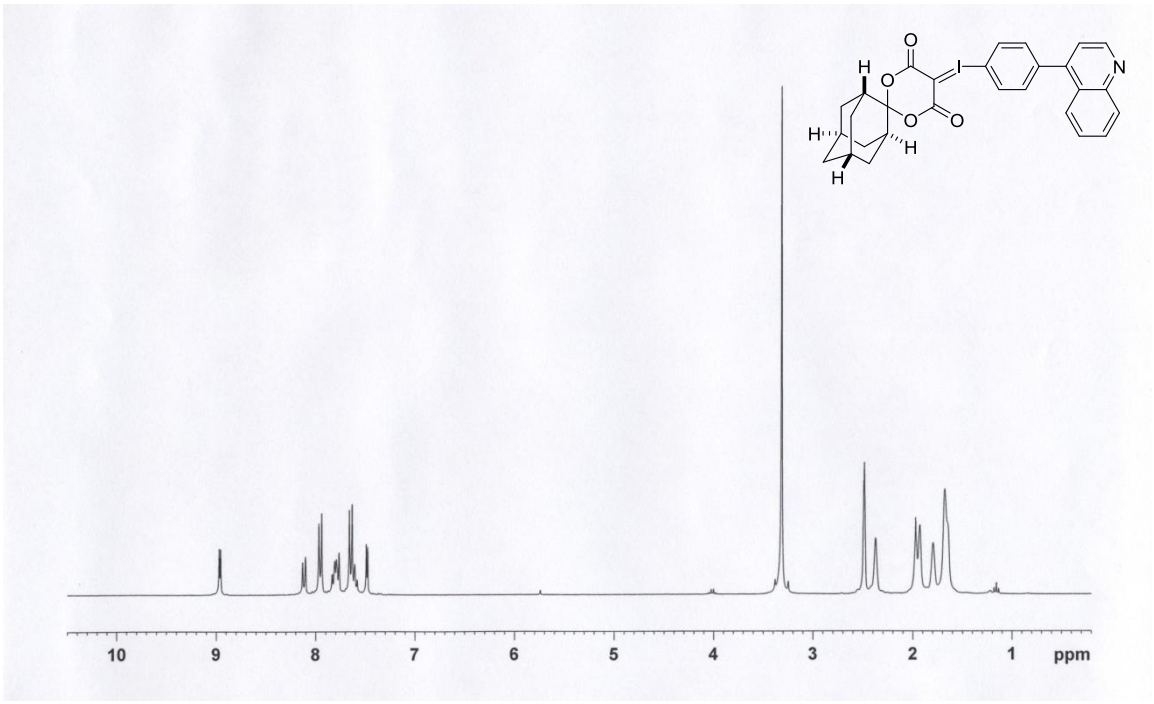

OAc
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

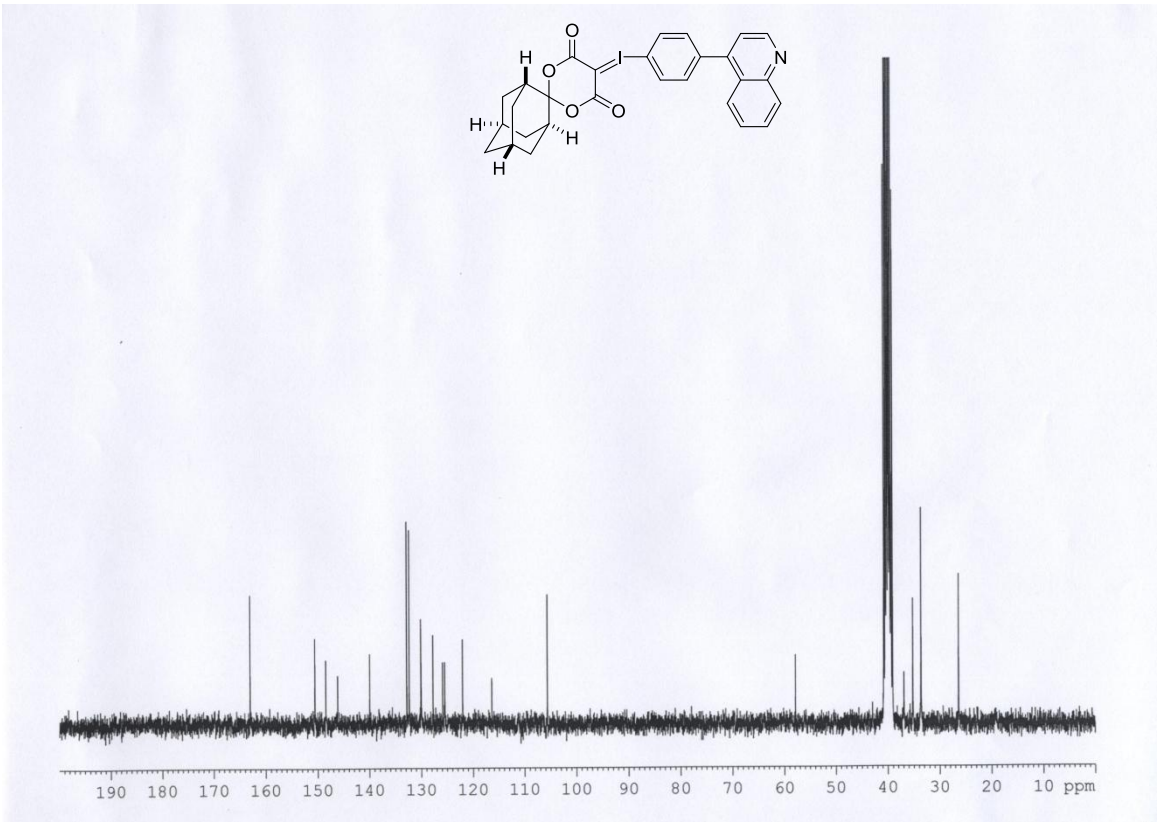

NO2
N
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm

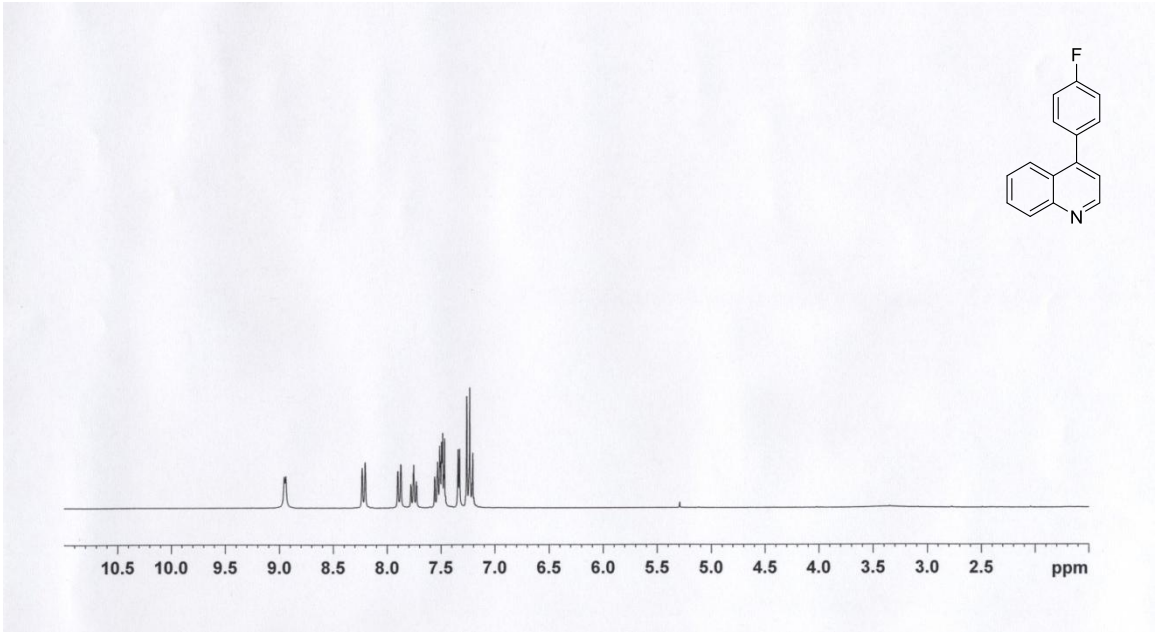

NO2
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

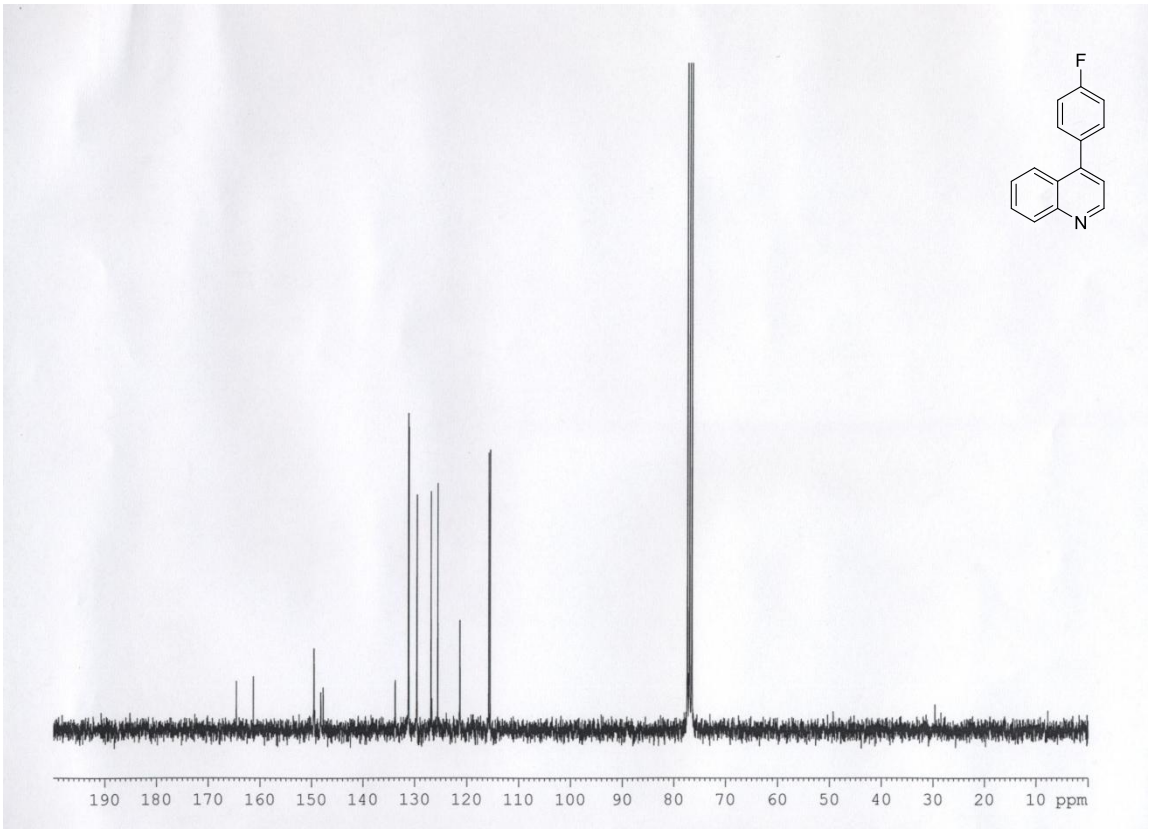

I
N
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0
ppm

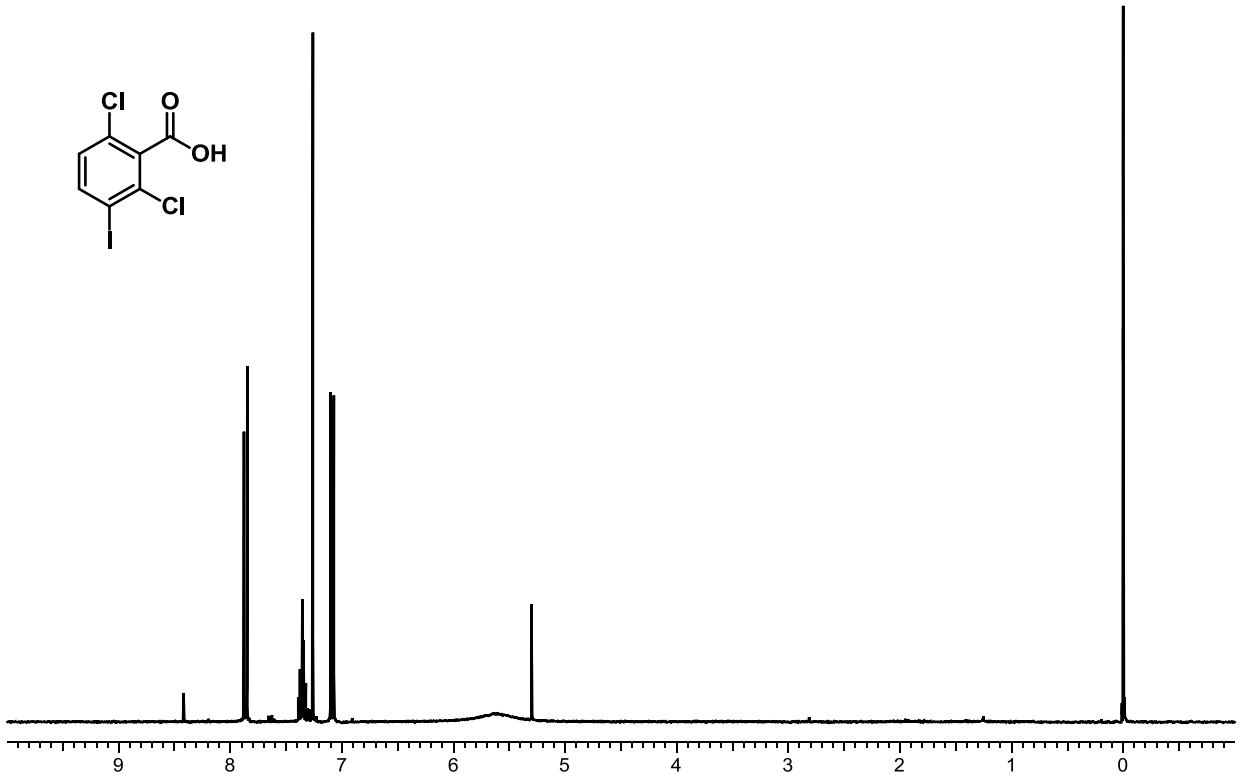

I
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 ppm

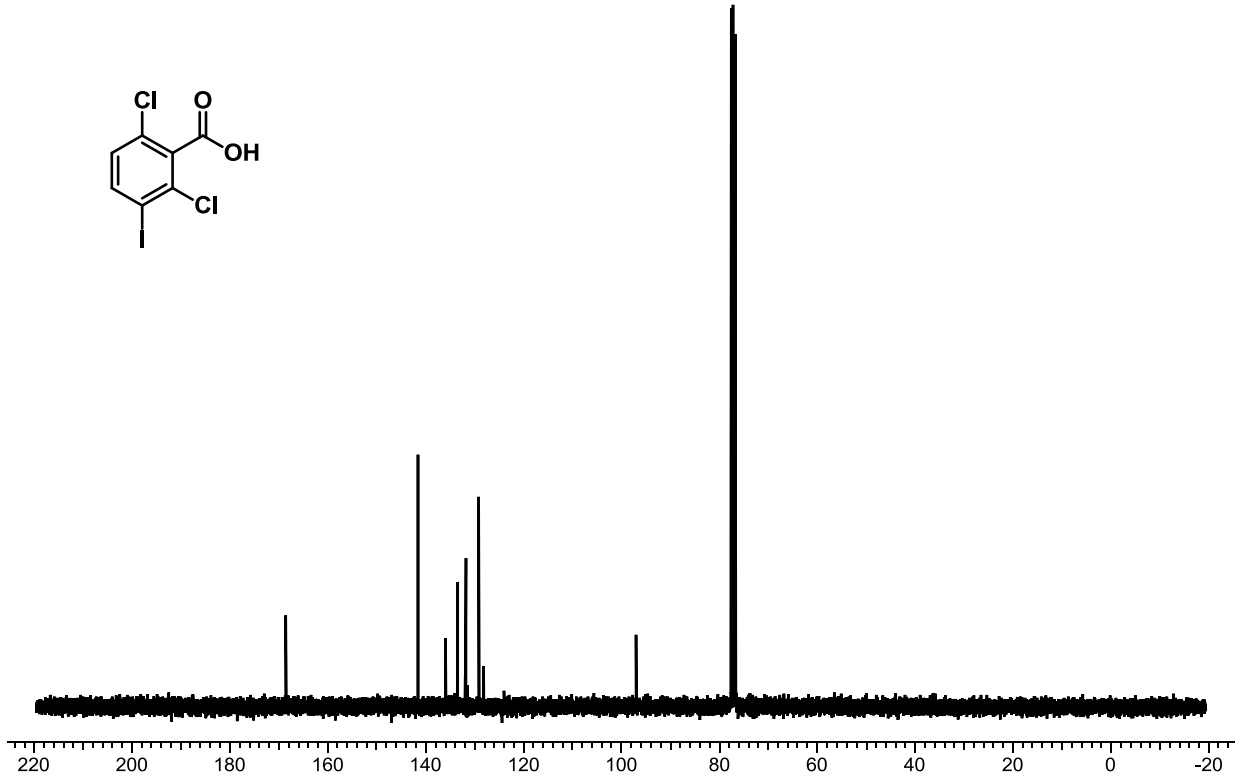

10
9
8
7
6
5
4
3
2
1
ppm

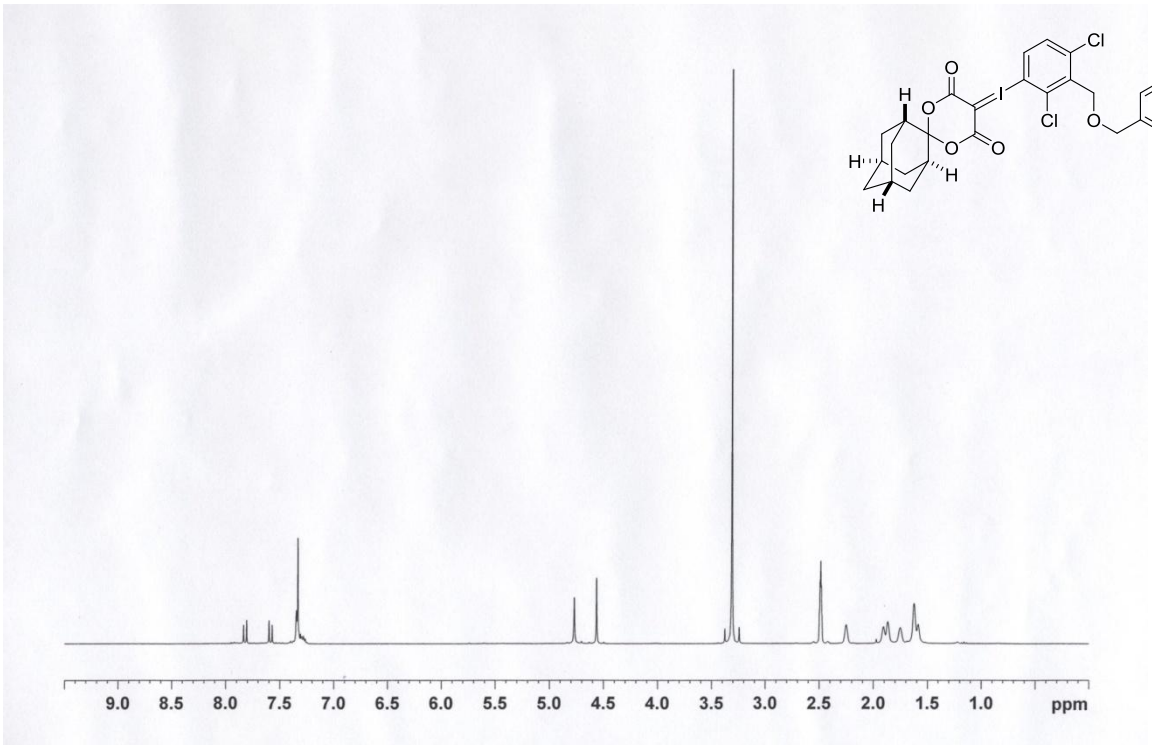

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

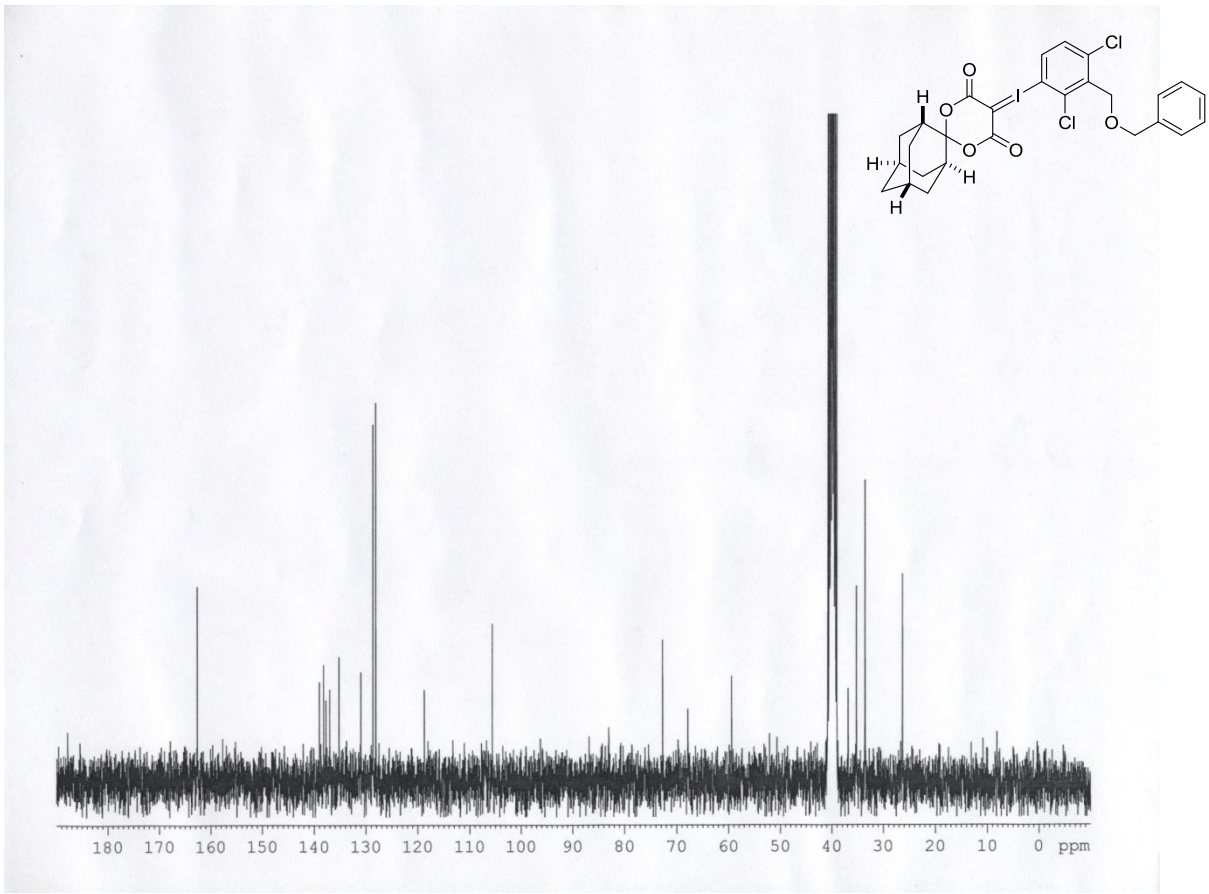

F
N
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 ppm

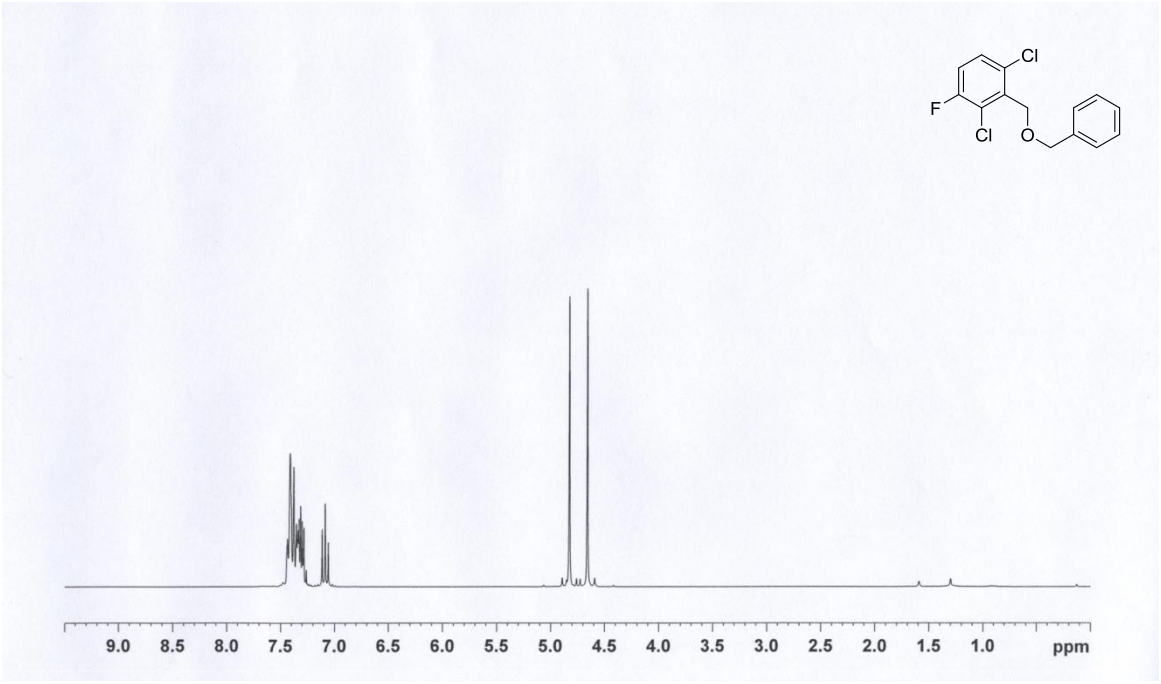

F
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

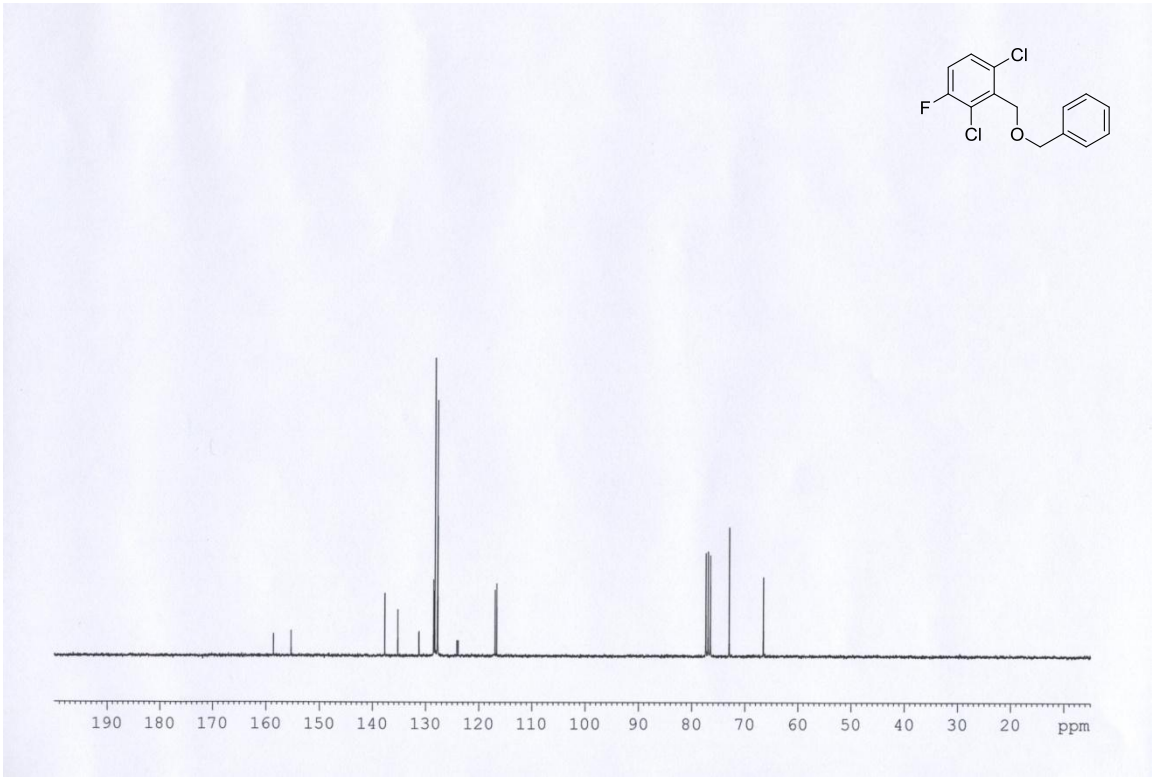

Cl
O
OH
Cl
9
8
7
6
5
4
3
2
1
0

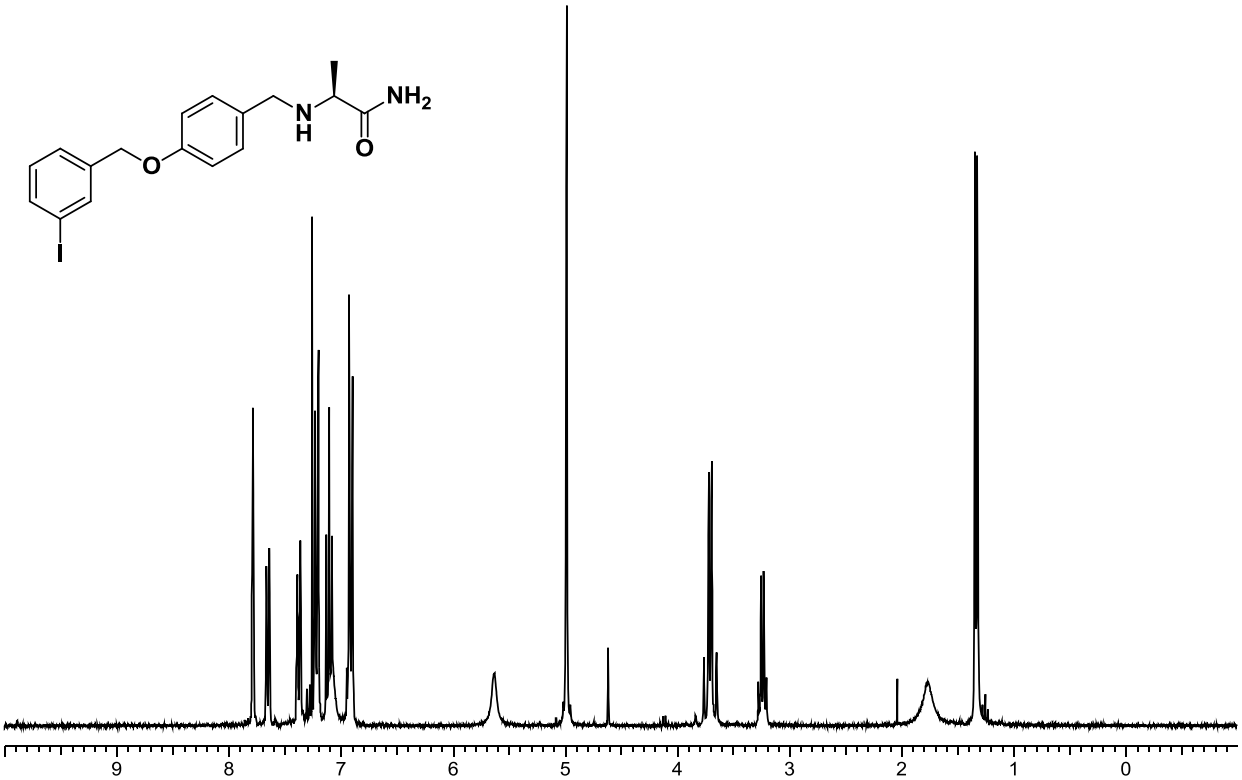

Cl
O
OH
Cl
220
200
180
160
140
120
100
80
60
40
20
0
-20

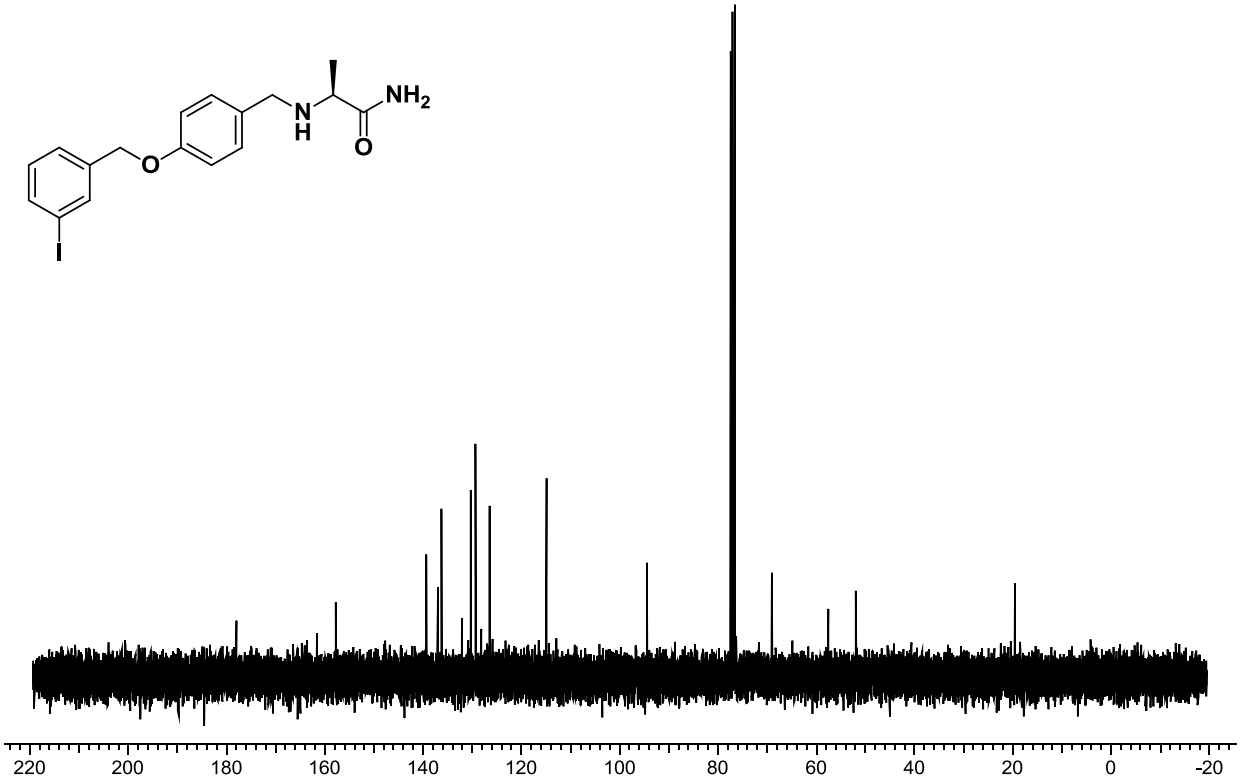

Cl
O
H
O
I
Cl
O
O
H
O
H
H
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

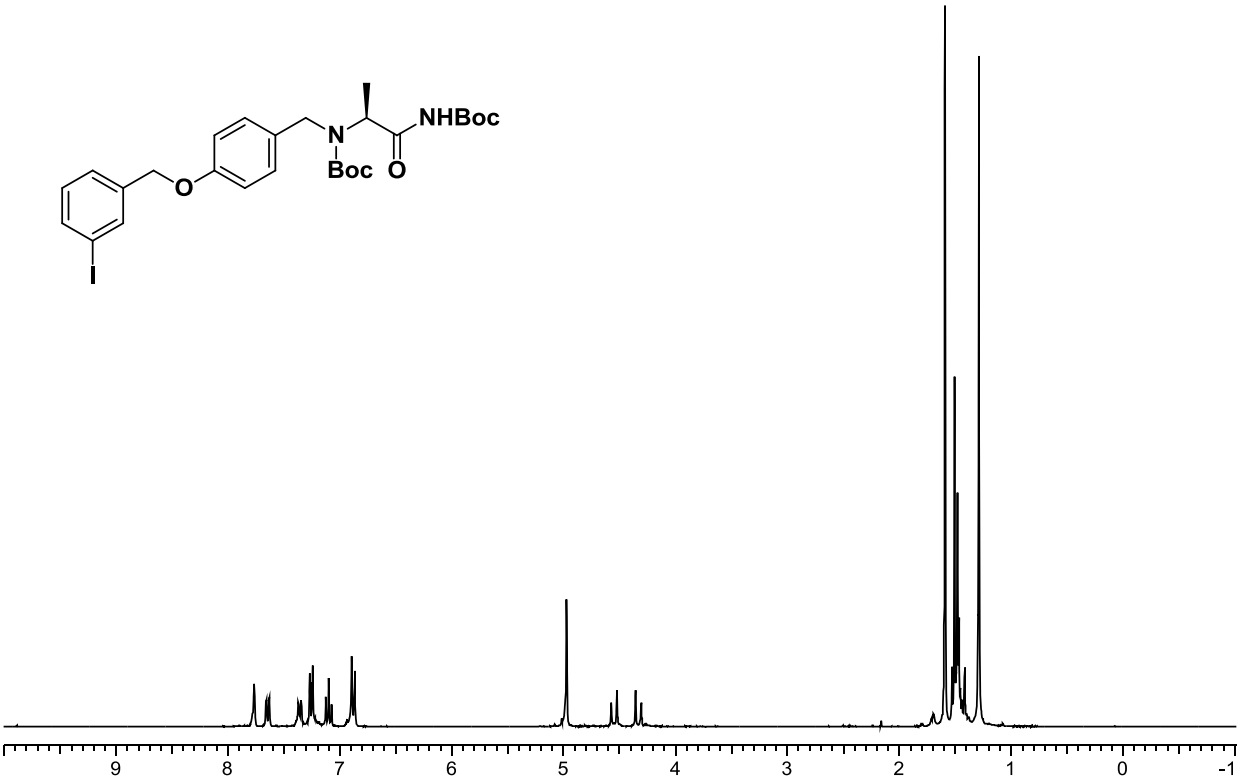

Cl
O
H
O
I
Cl
O
O
H
O
H
H
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

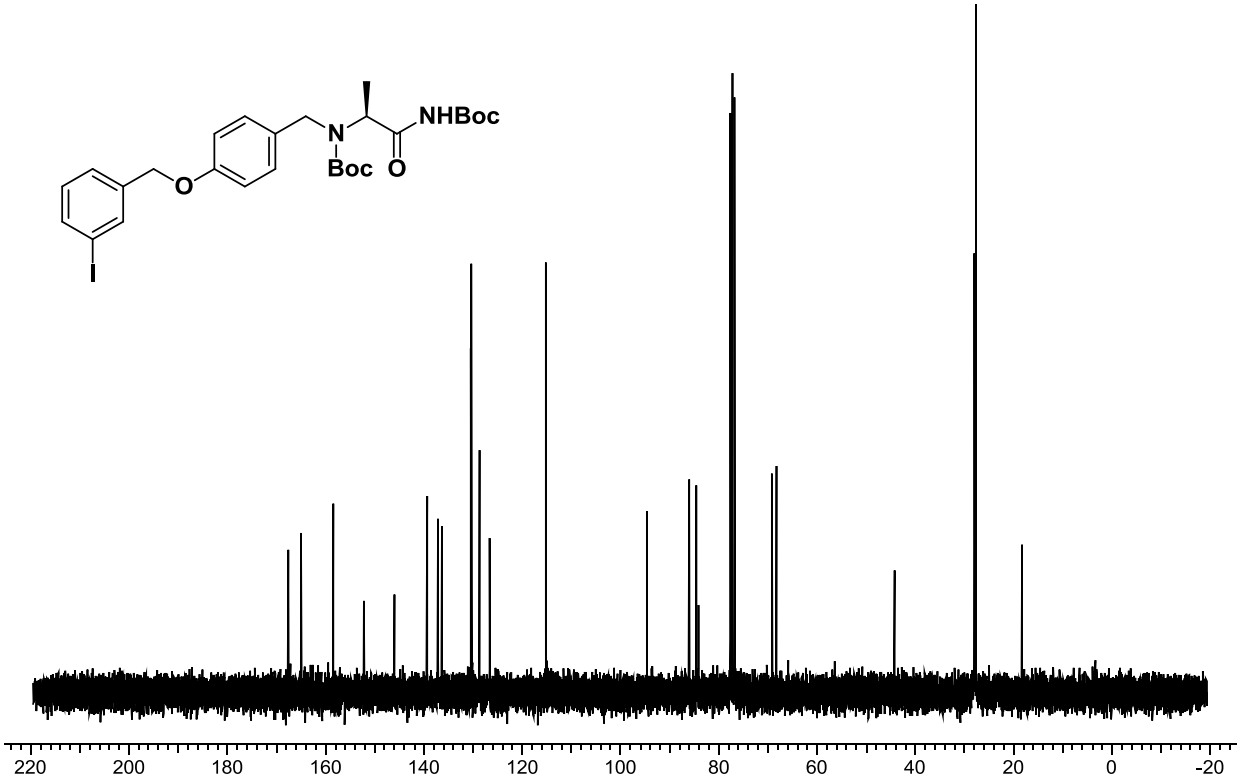

Cl
F
Cl
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

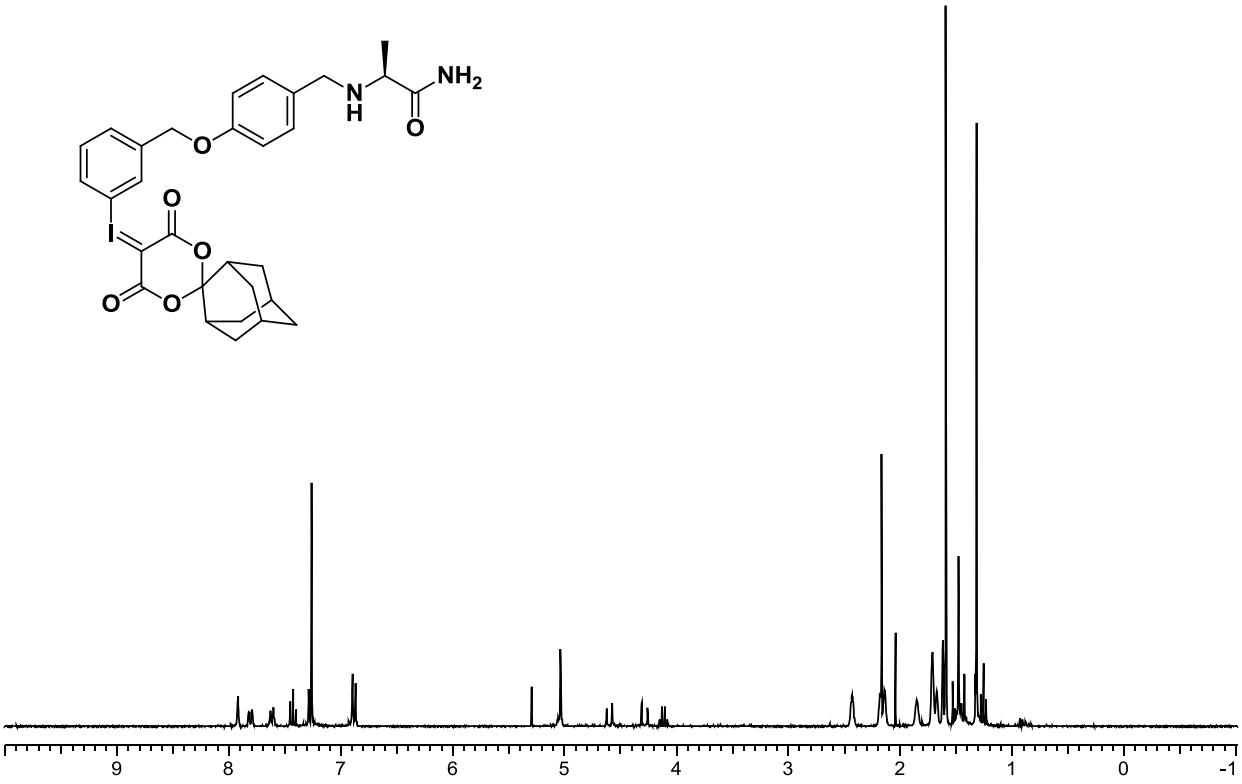

Cl
F
Cl
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

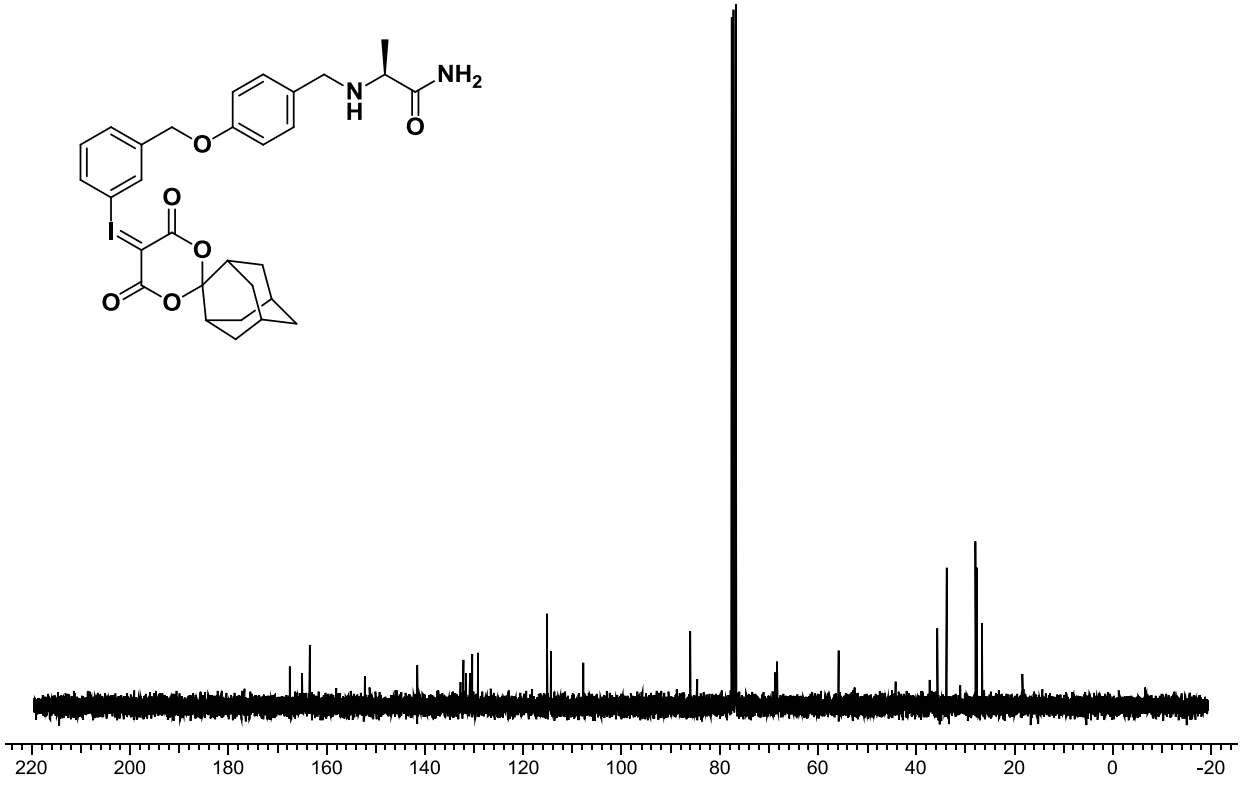

NH2
N
H
O
O
I
9
8
7
6
5
4
3
2
1
0

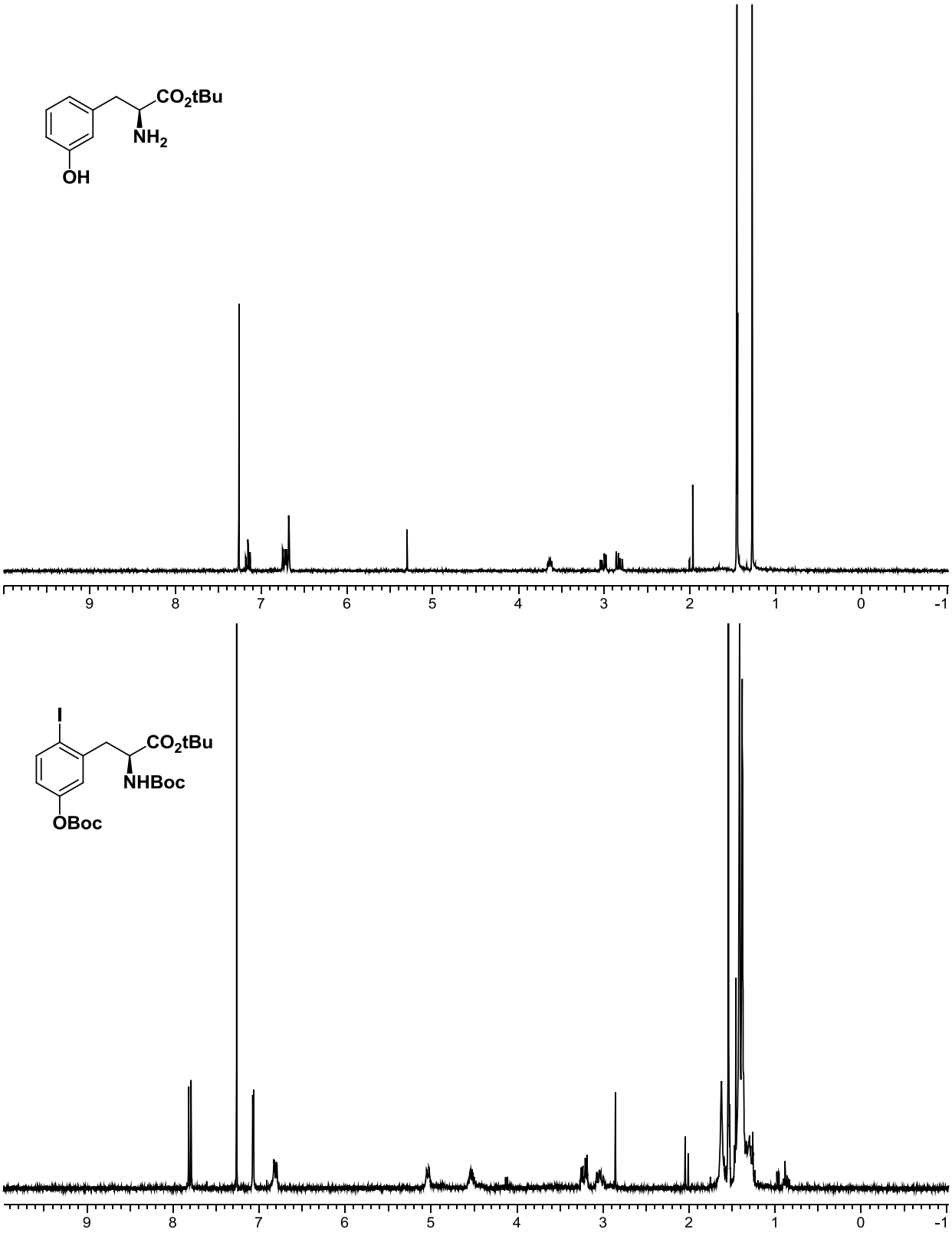

NH2
N
H
O
O
I
220
200
180
160
140
120
100
80
60
40
20
0
-20

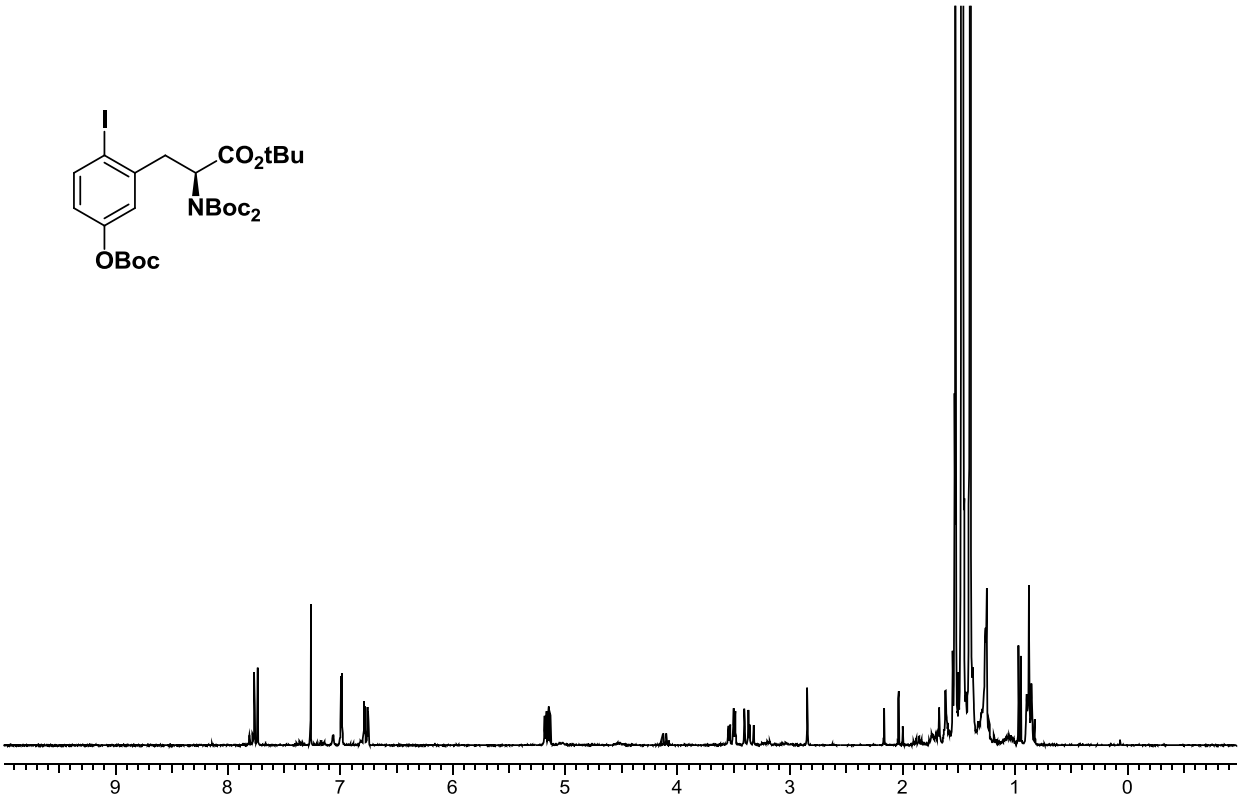

NHBoc
N
Boc
O
O
I
9
8
7
6
5
4
3
2
1
0
-1

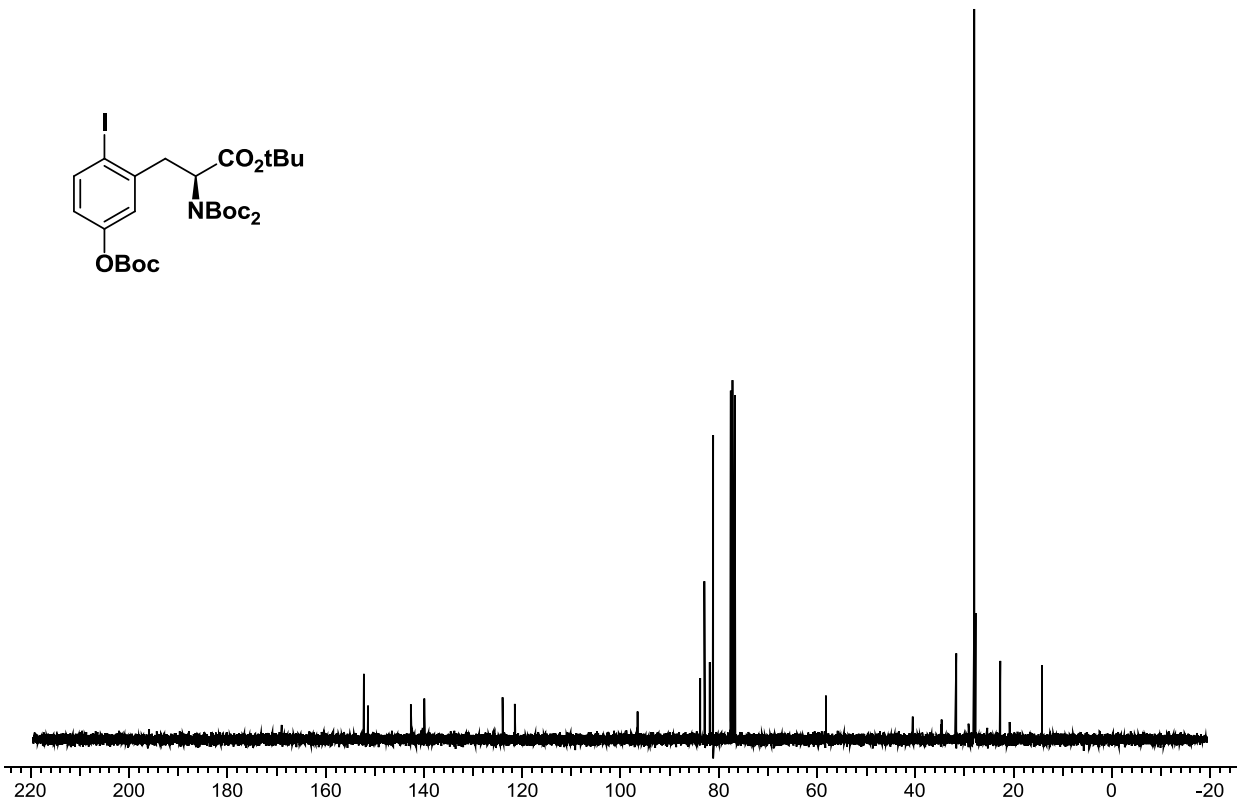

NHBoc
N
Boc
O
O
I
220
200
180
160
140
120
100
80
60
40
20
0
-20

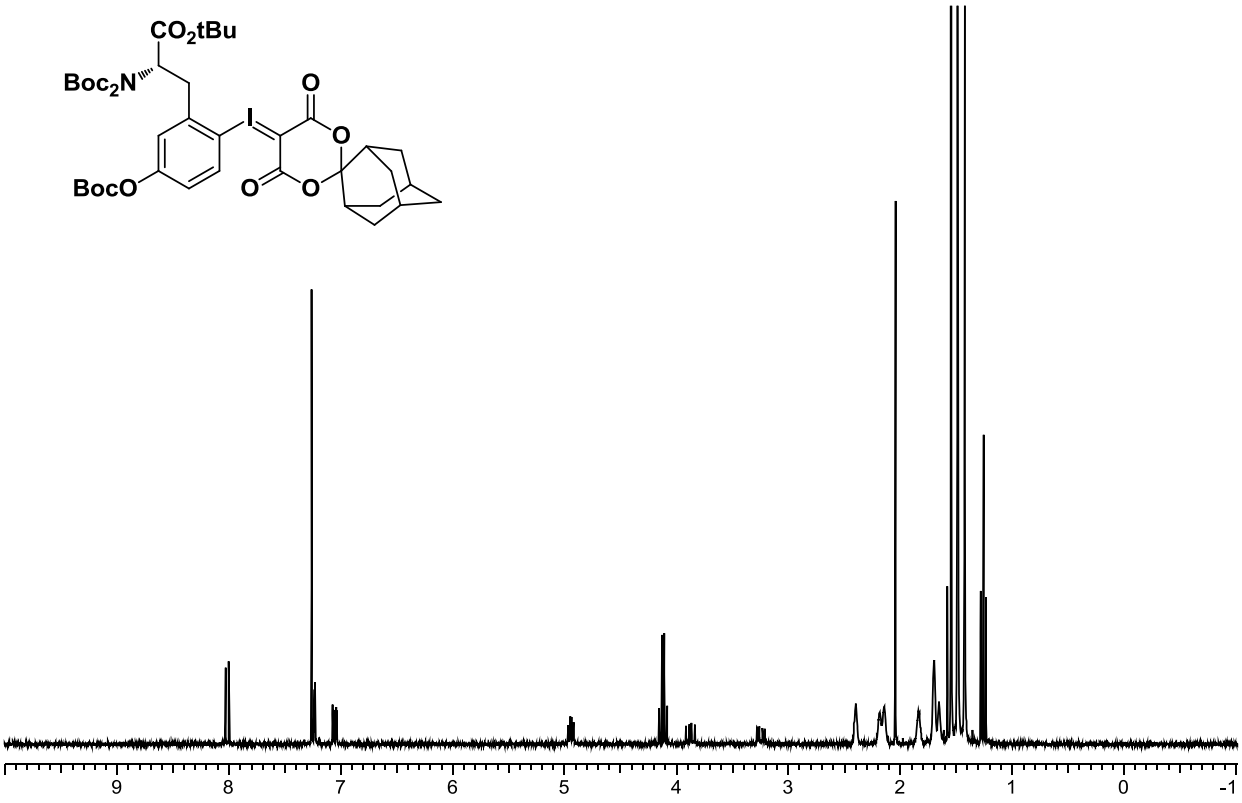

NH2
N
H
O
O
I
O
O
O
O
9
8
7
6
5
4
3
2
1
0
-1

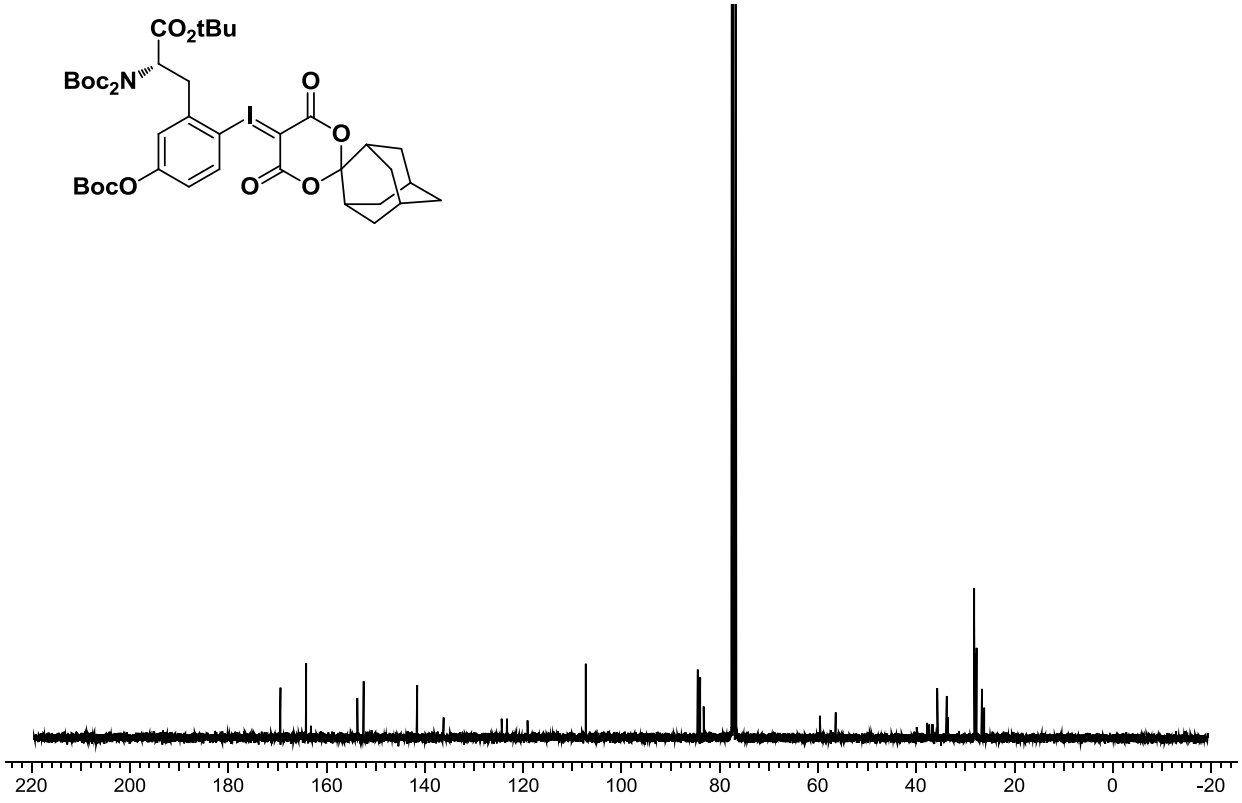

NH2
N
H
O
O
I
O
O
O
O
220
200
180
160
140
120
100
80
60
40
20
0
-20

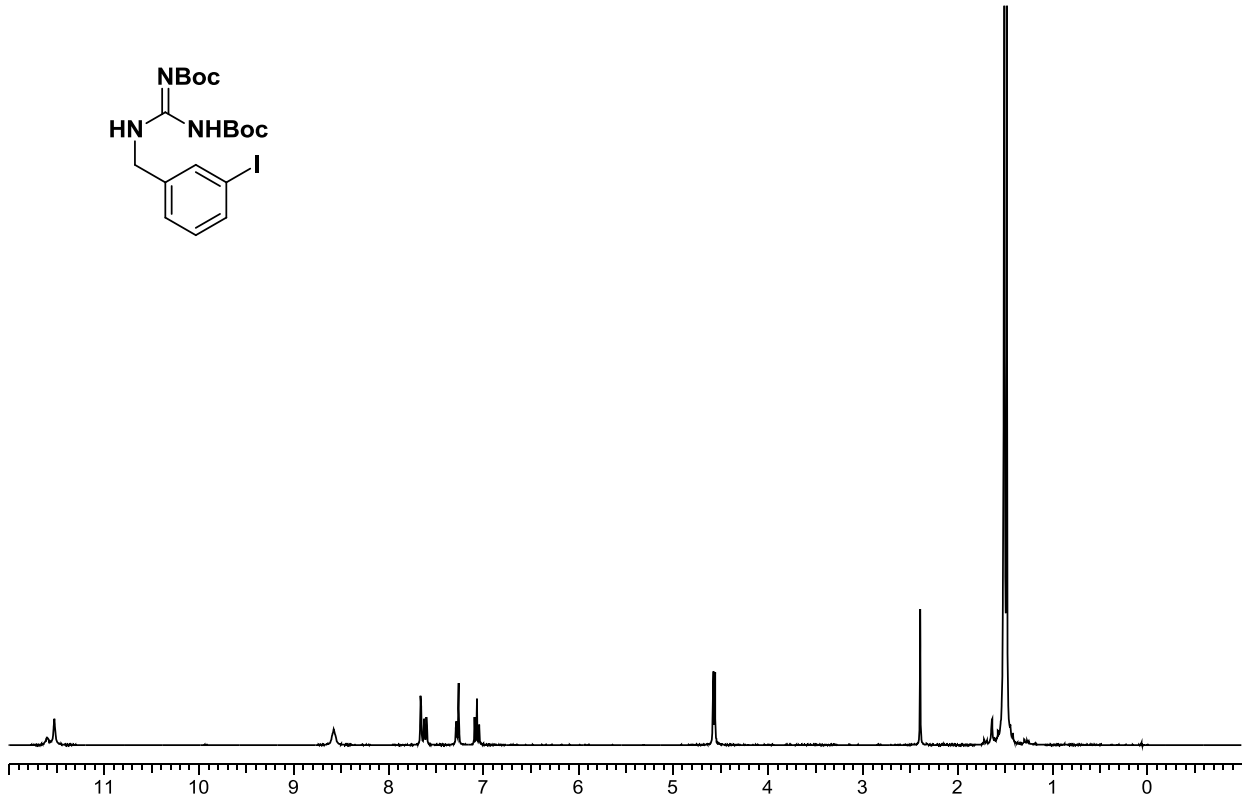

CO2tBu
NH2
OH
9
8
7
6
5
4
3
2
1
0
-1
I
CO2tBu
NHBoc
OBoc
9
8
7
6
5
4
3
2
1
0
-1

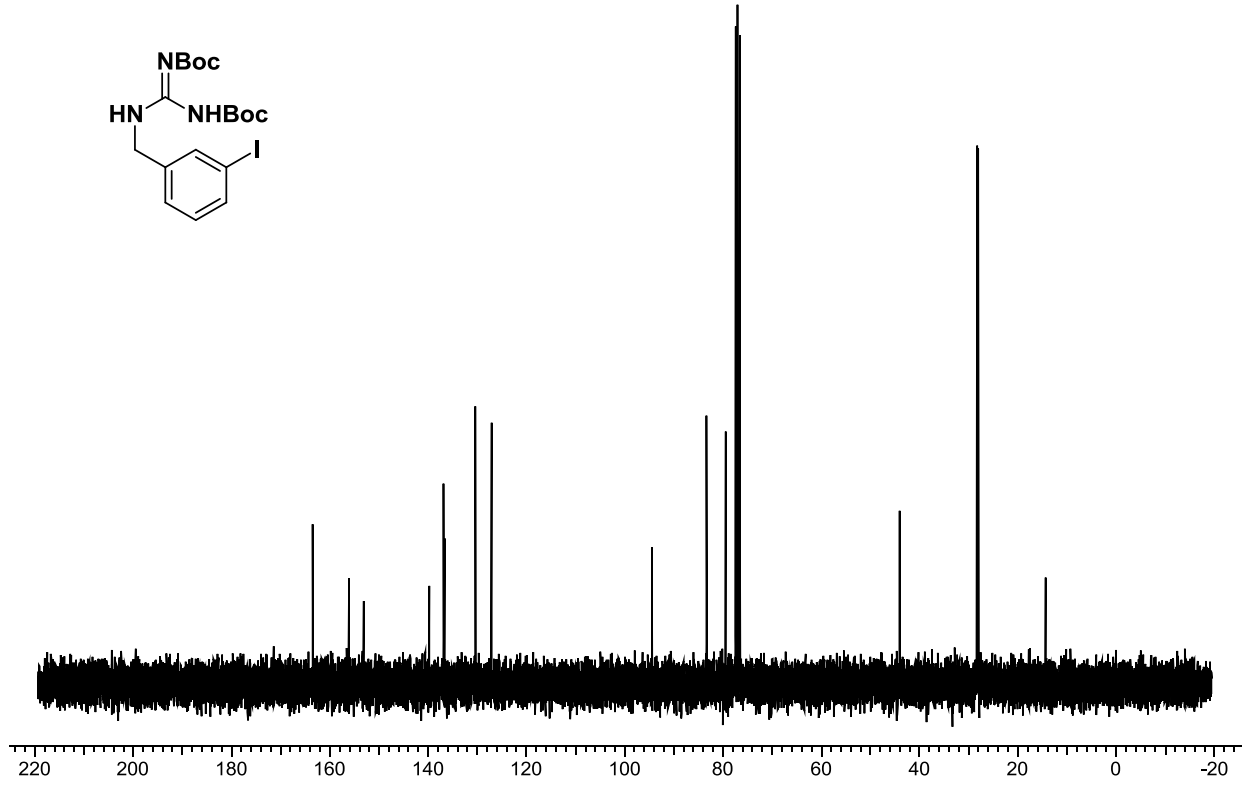

I
CO2tBu
NBoc2
OBoc
9
8
7
6
5
4
3
2
1
0

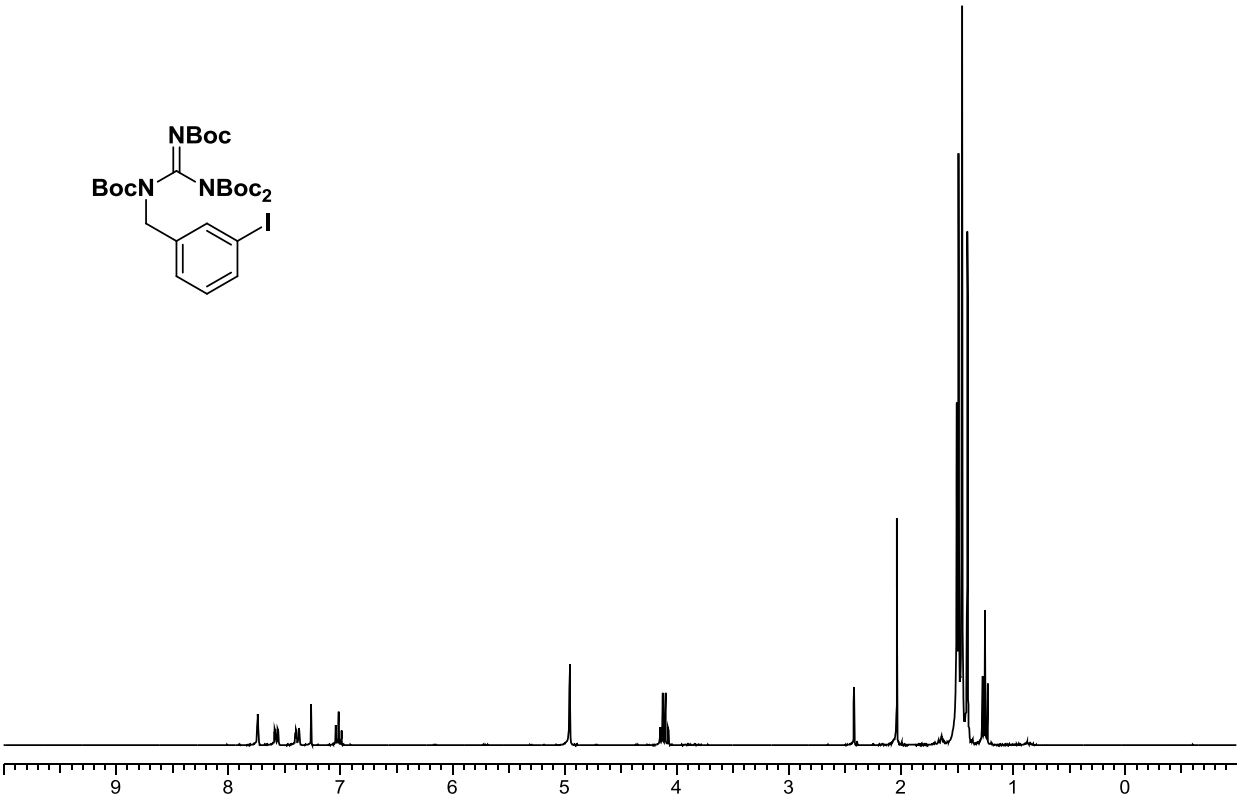

I
CO2tBu
NBoc2
OBoc
220
200
180
160
140
120
100
80
60
40
20
0
-20


CO2tBu
Boc2N
I
O
O
O
O
BocO
9
8
7
6
5
4
3
2
1
0
-1


CO2tBu
Boc2N
I
O
O
O
O
BocO
220
200
180
160
140
120
100
80
60
40
20
0
-20


NBoc
HN
NHBoc
I
11
10
9
8
7
6
5
4
3
2
1
0


NBoc
HN
NHBoc
I
220
200
180
160
140
120
100
80
60
40
20
0
-20


NBoc
BocN
NBoc2
I
9
8
7
6
5
4
3
2
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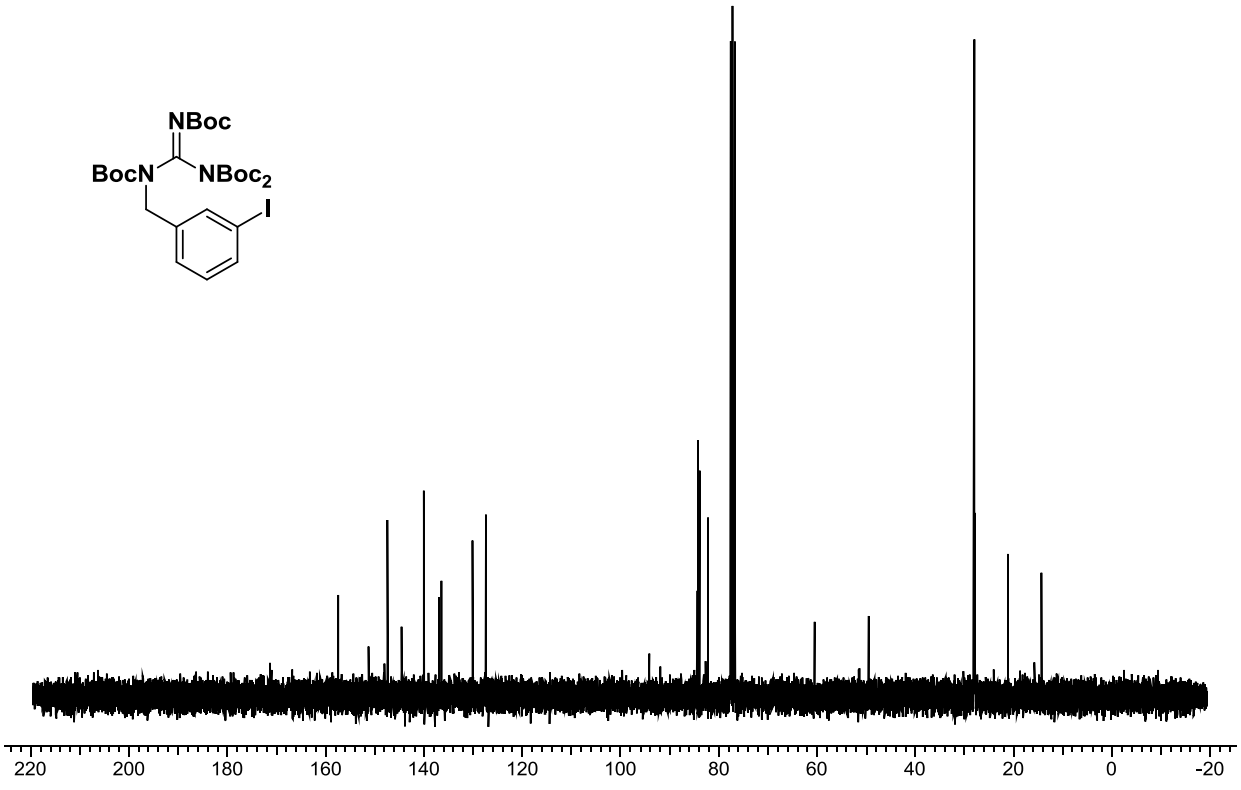
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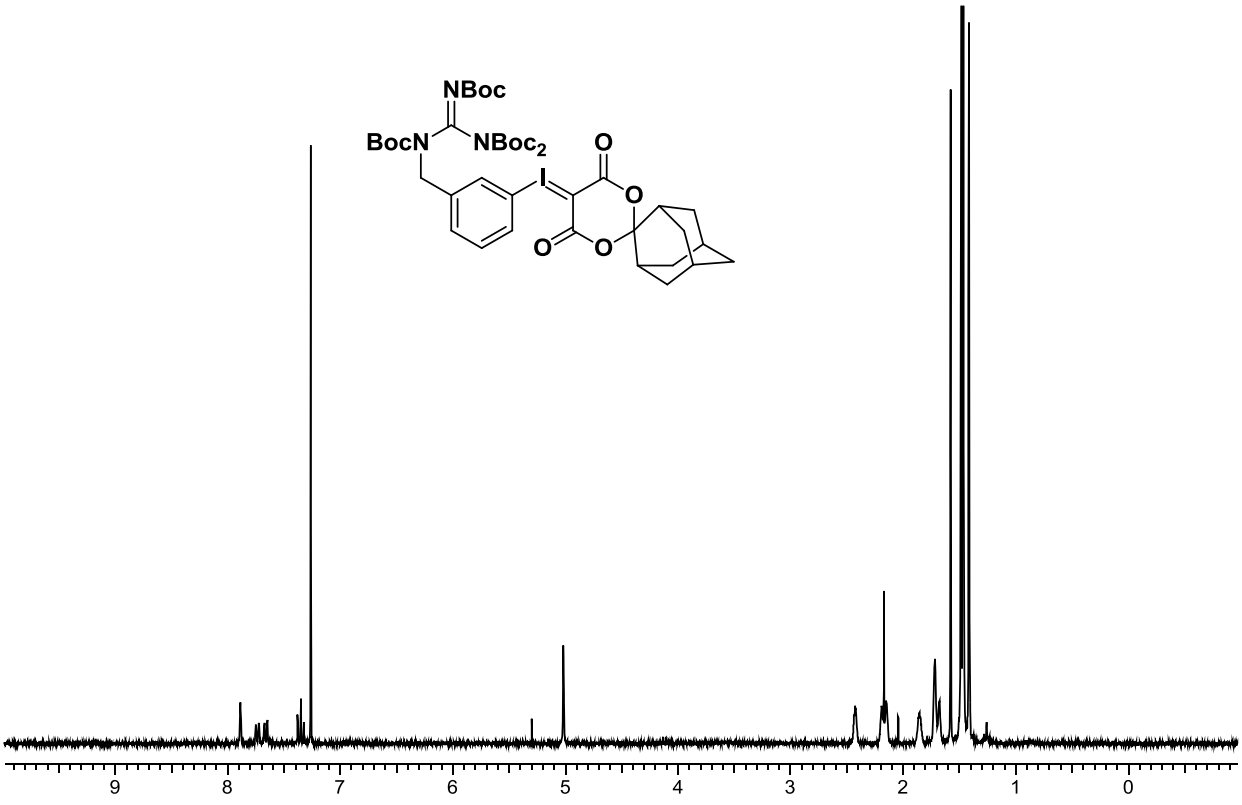
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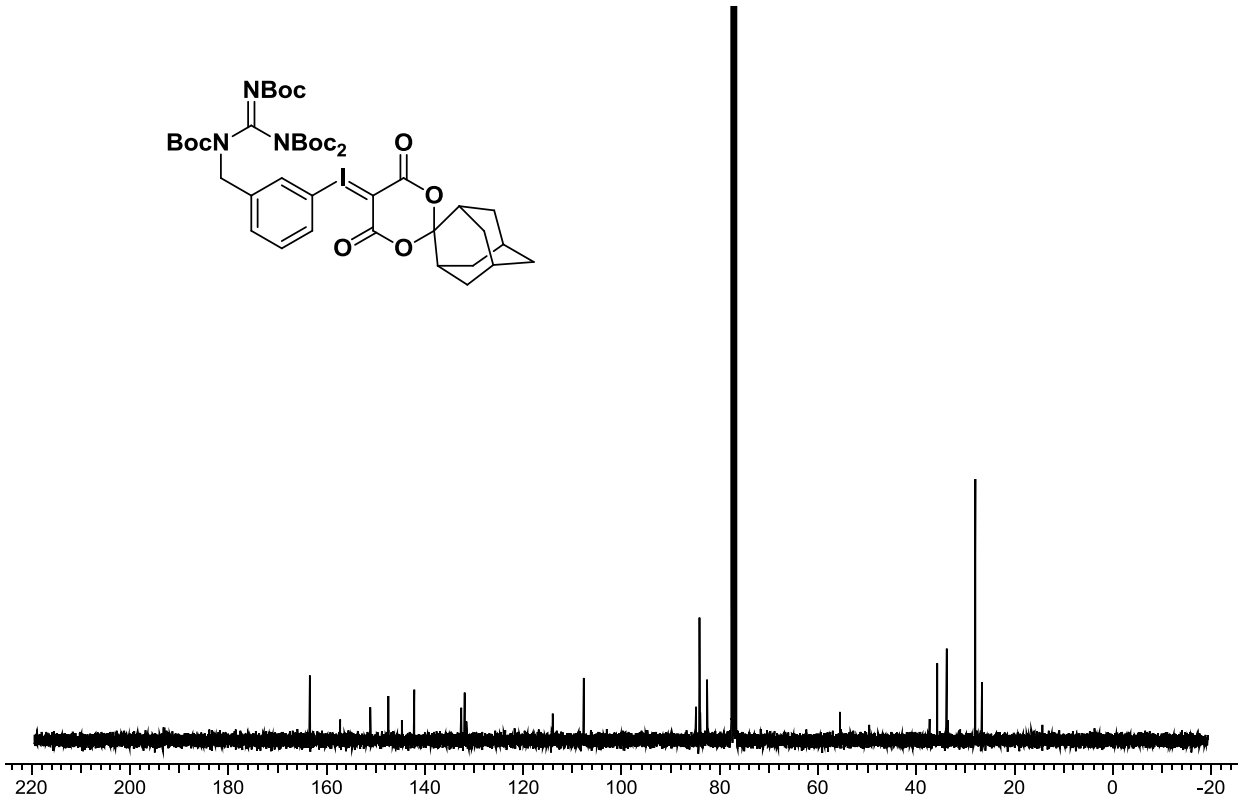
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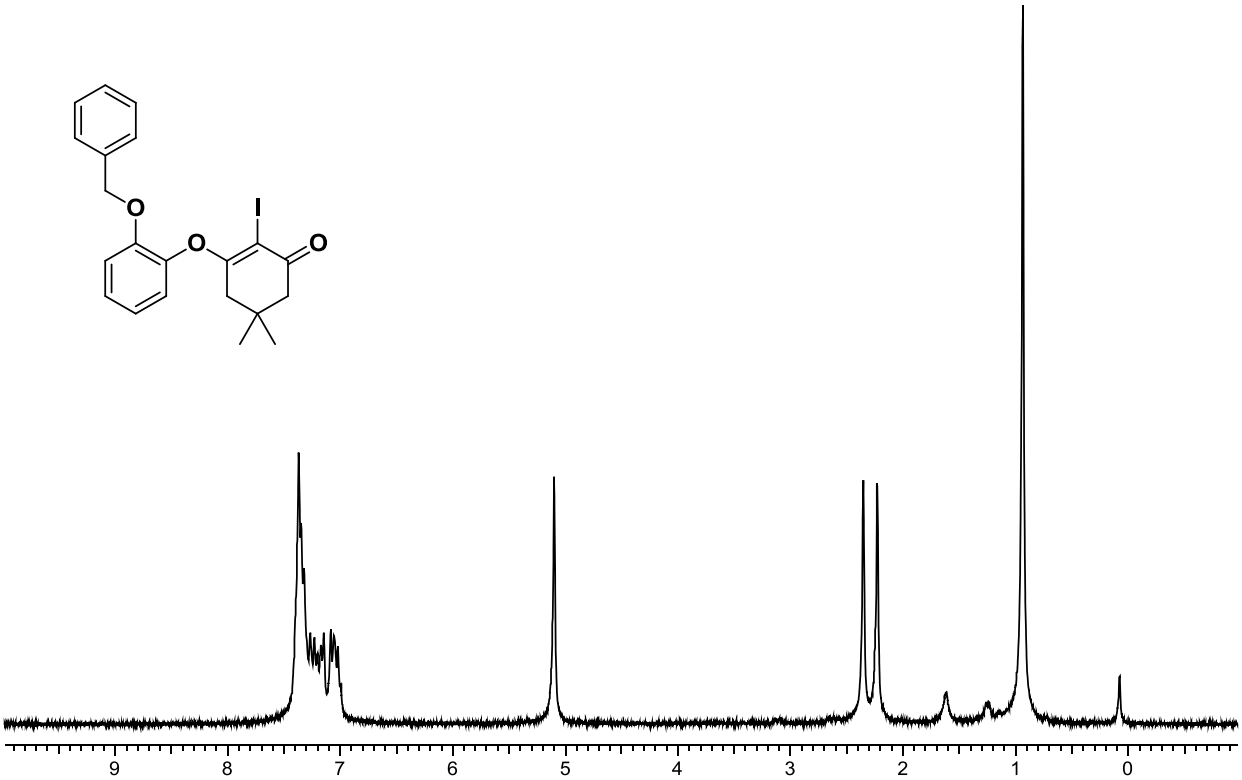
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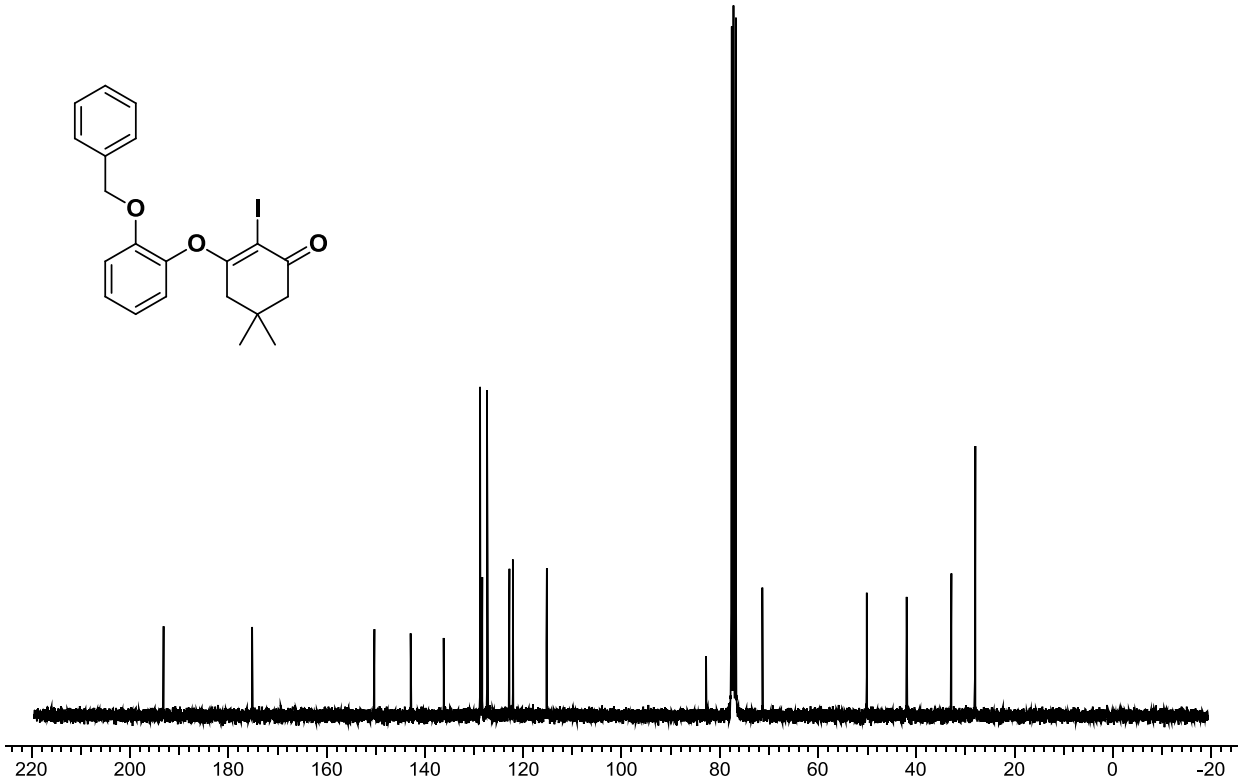
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