Electronic Supplementary Material (ESI) for RSC Advances.

Transition metal free, late-stage, regiospecific, aromatic fluorination on preparative scale using KF/Crypt-222 complex

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Experimental part

Reactants, reagents and solvents used herein were procured from Sigma-Aldrich (Sigma-Aldrich AS, Norway) or Fluorochem (UK) in analytical quality unless specified otherwise. Reactions were performed under an atmosphere of nitrogen. Solid phase extraction (SPE) cartridges were purchased from VWR (VWR International, Darmstadt, Germany). Nuclear magnetic resonance spectra were recorded on a Bruker AVII 400 NMR instrument (Bruker ASX Nordic AB). Chemical shifts (δ) for ^{1}H (400 MHz), ^{13}C (100 MHz) and ^{19}F (377 MHz). Resonances are reported in parts per million (ppm), relative to the solvent signal ($CDCl_3$ δ = 7.226 ppm), downfield from the expected tetramethylsilane signal (TMS, δ = 0 ppm). Mass spectrometry was conducted on a Q-Tof-2 mass analyser (Micromass, Q-Tof-2™) using electron spray ionization in positive mode (+ESI). For quality control and analysis of the radiochemical yield, a Phenomenex Luna PFP(2) column (5 µm, 100 Å, 250 mm × 4.6 mm) was used as a stationary phase with an isocratic mixture of MeCN-water as a mobile phase at a flow rate of 1.5 ml/min. RadioTLC was conducted on Silica gel 60 F_{254} coated aluminum TLC plates (Supelco, USA). RadioTLC plates were analysed using a raytest miniGita radioTLC scanner (Raytest GmBH, Straubenhardt, Germany). All other radioactivity measurements during labelling experiments and radiotracer productions were performed using a Wallac Wizard well counter (PerkinElmer, Oslo, Norway). Additional Reference compounds were synthesised by Jakobsson *et. al*.[1] (**11**) or purchased from Sigma Aldrich and Fluorochem (**2-10**).

Synthesis

KF/Crypt-222/K_2CO_3 (3:4:1). To (4,7,13,16,21,24-Hexaoxa-1,10-diazabicyclo[8.8.8] hexacosane) (200 µmol, 75.3 mg) in MeCN (5 ml) was added KF (17.4 mg, 150 µmol) and potassium carbonate * 1.5 hydrate (6.9 mg, 50 µmol) from water (1 ml). The solvents were removed under reduced pressure at 50 ^{0}C with portion wise additions of MeCN until reaction mixture solidified. The mixture was dried on high vac overnight, powdered and dried an additional day.

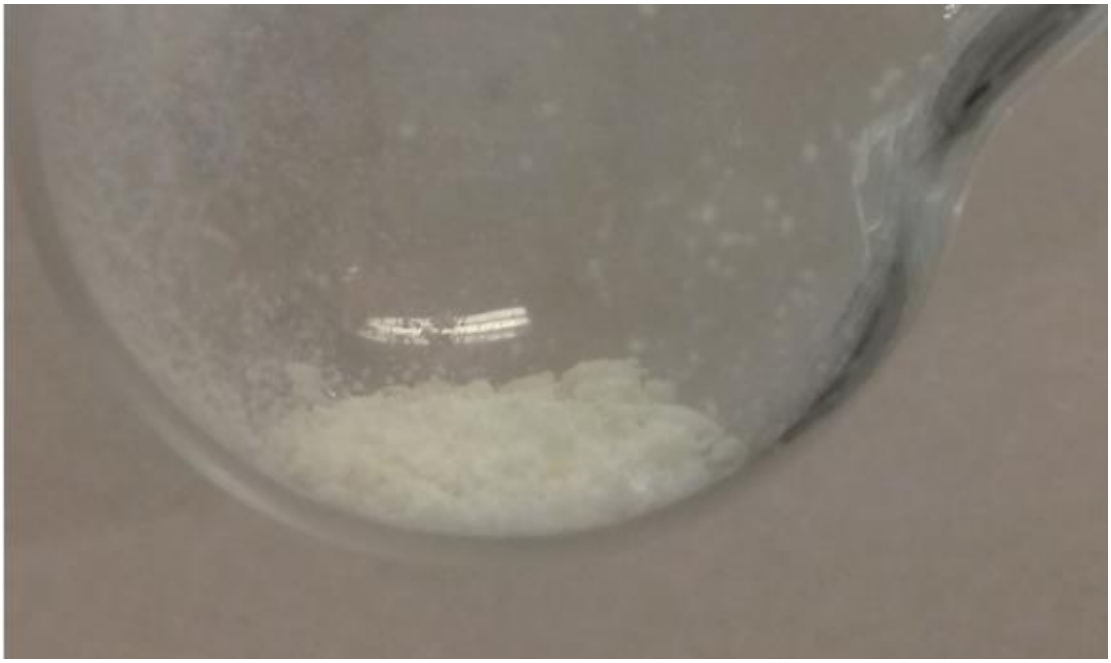


Figure 1: Shows KF/Crypt-222 complex after drying

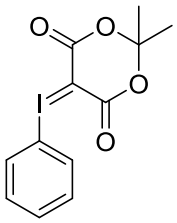
Tetrabutylammonium tetra(*tert*butyl alcohol) was synthesised in accordance with Kim *et. al.*[2] Analytical data matched.

Typical procedure A (ylide synthesis) (procedure is based on Cardinale *et. al.*[3]

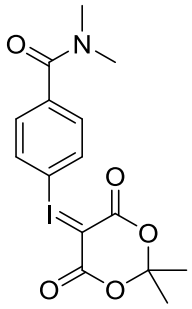
Reaction mixtures were kept in the dark at all times. In a glass vial was 3-chloroperbenzoic acid (77%, 1.4 mmol, 310 mg) dissolved in DCM (5 ml) and left for 5 minutes (excess water adhered to glass walls of vial). To iodoarene (1 mmol) in a capped argon flushed vial was added the 3-chloroperbenzoic acid solution, care was taken to avoid transferring water droplets. The reaction mixture was heated to 39 degrees for 80 minutes. Major to full consumption of starting material was indicated via TLC analysis (8% MeOH in DCM), (under UV light was all intermediate compounds visible in red that upon iodine staining yielded cream white coloured crescents. The reaction mixture was cooled to 10-15 ^{o}C. In one portion was added KOH (10 mmol, 560 mg) and 2,2-dimethyl-1,3-dioxane-4,6-dione (1.3 mmol, 187 mg). The reaction mixture was kept for 10– 60 minutes until complete conversion of intermediate was observed via TLC analysis (8% MeOH in DCM) (new in UV light visible bands that upon iodine staining stain in cream white, typically R_f is similar to intermediate). The reaction mixture was diluted with DCM (10 ml), filtered through a filter paper, washed with DCM (10 ml) and dried over sodium sulfate. The drying agent was filtered off and solvent removed under reduced pressure at 20-22 ^{o}C. The crude solids were dissolved in a minimal amount of DCM and filtered through a filter paper. The compounds were purified via precipitation from addition of hexanes (20 ml). The flasks were left at -20 for 1 hour. The pure ylides were obtained via decanting the solvents and solids washed with hexanes.

Typical procedure B (ylide synthesis)

To λ^3-iodane diacetate (1 mmol) in DCM (5 ml) at 10-15 ^oC was added in one portion KOH (10 mmol, 560 mg) and 2,2-dimethyl-1,3-dioxane-4,6-dione (1.3 mmol, 187 mg) and the reaction mixture kept for 10 min – 60 minutes until complete conversion of intermediate was observed via TLC analysis (8% MeOH in DCM) (new in UV light visible bands that upon iodine staining stain in cream white, typically Rf is very similar to intermediate). The reaction mixture was diluted with DCM (10 ml), filtered through cotton and glass wool, washed with DCM (10 ml) and dried over sodium sulfate. The drying agent was filtered off and the solvent removed in an aluminium foil wrapped round bottom flask under reduced pressure at 22 ^oC. The crude solids were purified via precipitation from dissolving in DCM (10 ml) and adding hexanes (20 ml). The flasks were left at -20 for 1 hour. The pure ylides were obtained via decanting the solvents and washed with hexanes.

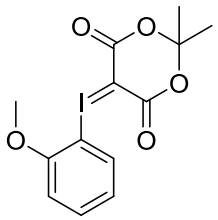


Synthesised according to typical procedure B. 2,2-dimethyl-5-(phenyl-l3-iodaneylidene)-1,3-dioxane-4,6-dione. Reaction performed on 1 mmol scale yielding target compound in 60% yield (206 mg, 0.6 mmol) as white solids. ^1H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.75 (m, 2H), 7.60 – 7.51 (m, 1H), 7.46 (dd, *J* = 8.4, 7.0 Hz, 2H), 1.56 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.8, 132.5, 131.0, 130.6, 116.3, 102.7, 57.8, 25.6. Analytical data was in accordance to that previously reported.[4] HR-ESIMS: *m/z* 368.9595 $[M+Na]^+$ ($C_{12}H_{11}INaO_4^+$, calculated 368.9594)

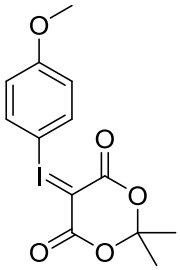


Synthesised according to typical procedure A. **4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-N,N-dimethylbenzamide.** Reaction performed on 0.5 mmol scale yielding target compound in 14% yield (60 mg, 0.14 mmol) as white solids.^1H NMR (400 MHz, DMSO-d_6) δ 7.86 – 7.80 (m, 1H), 7.51 – 7.44 (m, 1H), 2.98 (s, 2H), 2.86 (s, 2H), 1.58 (s,

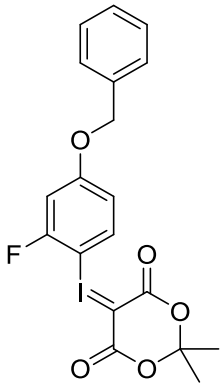
3H). ^{13}C NMR (101 MHz, DMSO) δ 168.7, 162.9, 138.7, 132.3, 129.3, 116.7, 102.8, 57.8, 38.9, 34.7, 25.6. HR-ESIMS: *m/z* 439.9966 $[M+Na]^+$ ($C_{15}H_{16}INNaO_5^+$, calculated 439.9965)



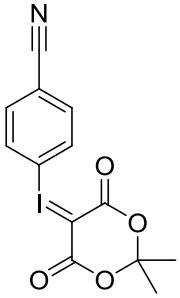
Synthesised according to typical procedure A. 5-((2-methoxyphenyl)-l3- iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione. Reaction performed on 2 mmol scale yielding target compound in 50% yield (379 mg, 1.01 mmol) as white solids. 1H NMR (400 MHz, Chloroform-d) δ 7.47 (ddd, J = 8.4, 7.4, 1.5 Hz, 1H), 7.35 (dd, J = 8.1, 1.5 Hz, 1H), 7.09 (ddd, J = 8.4, 7.4, 1.3 Hz, 1H), 6.97 (dd, J = 8.2, 1.2 Hz, 1H), 3.97 (s, 3H), 1.79 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 163.75, 155.29, 132.85, 128.82, 124.62, 112.48, 104.82, 101.81, 57.12, 47.56, 26.16. HR-ESIMS: m/z 398.9700 [M+Na]+ (C13H13INaO5+, calculated 398.9700)



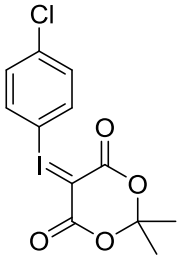
Synthesised according to typical procedure A. **5-((4-methoxyphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.** Reaction performed on 1 mmol scale yielding target compound in 54% yield (203 mg, 0.54 mmol) as white solids. Analytical data was in accordance to that previously reported.[ii] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 – 7.68 (m, 2H), 7.04 – 6.98 (m, 2H), 3.78 (s, 3H), 1.54 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.8, 161.1, 134.7, 116.6, 105.8, 102.6, 58.5, 55.5, 25.6. **HR-ESIMS:** *m/z* 398.9700 $[M+Na]^+$ ($C_{13}H_{13}INaO_5^+$, calculated 398.9700)



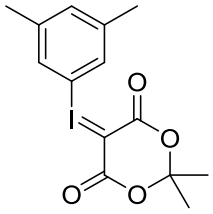
Synthesised according to typical procedure A. **5-((4-(benzyloxy)-2-fluorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.** Reaction performed on 1 mmol scale yielding target compound in 41% yield (192 mg, 0.41 mmol) as beige solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (dd, J = 8.8, 7.0 Hz, 1H), 7.59 – 7.30 (m, 5H), 7.15 (dd, J = 10.4, 2.7 Hz, 1H), 6.94 (dd, J = 8.9, 2.7 Hz, 1H), 5.17 (s, 2H), 1.50 (s, 6H). ^{19}F NMR (377 MHz, DMSO) δ -96.5. ^{13}C NMR (101 MHz, DMSO) δ 162.6, 162.4 (d, $^{3}J_{CF}$ = 11 Hz), 160.5 (d, $^{1}J_{CF}$ = 248 Hz), 136.9 (d, $^{4}J_{CF}$ = 4 Hz), 135.9, 128.5, 128.2, 127.9, 113.8 (d, $^{3}J_{CF}$ = 3 Hz), 103.0 (d, $2J_{CF}$ = 26 Hz),102.5, 93.8 (d, $2J_{CF}$ = 26 Hz), 70.1, 59.3, 25.5. HR-ESIMS: *m/z* 492.9919 $[M+Na]^+$ ($C_{19}H_{16}FINaO_5^+$, calculated 492.9919)



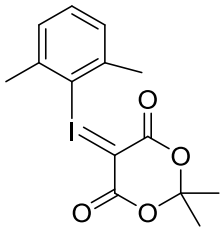
Synthesised according to typical procedure A. **4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzonitrile.** Reaction performed on 1 mmol scale yielding target compound in 21% yield (77 mg, 0.21 mmol) as white solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.91 – 7.82 (m, 4H), 1.51 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.9, 134.3, 132.9, 121.3, 117.7, 113.4, 103.0, 58.2, 25.6. **HR-ESIMS:** *m/z* 393.9546 $[M+Na]^+$ ($C_{13}H_{10}INNaO_4^+$, calculated 393.9547)



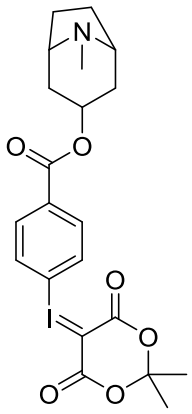
Synthesised according to typical procedure A. **5-((4-chlorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.** Reaction performed on 2 mmol scale yielding target compound in 25% yield (194 mg, 0.50 mmol) as white solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 – 7.76 (m, 2H), 7.58 – 7.52 (m, 2H), 1.57 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.8, 135.8, 134.2, 130.9, 114.2, 102.8, 58.3, 25.6. HR-ESIMS: *m/z* 402.9205$[M+Na]^+$ ($C_{12}H_{10}ClINaO_4^+$, calculated 402.9204)



Synthesised according to typical procedure A. **5-((3,5-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.** Reaction performed on 2 mmol scale yielding target compound in 41% yield (310 mg, 0.83 mmol) as white solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44 – 7.39 (m, 2H), 7.19 (dt, J = 1.7, 0.9 Hz, 1H), 2.29 (s, 6H), 1.56 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.8, 140.4, 132.2, 129.9, 116.3, 102.6, 57.7, 25.6, 20.7. HR-ESIMS: *m/z* 396.9907[M+Na]$^+$ ($C_{14}H_{15}INaO_4^+$, calculated 396.9907)

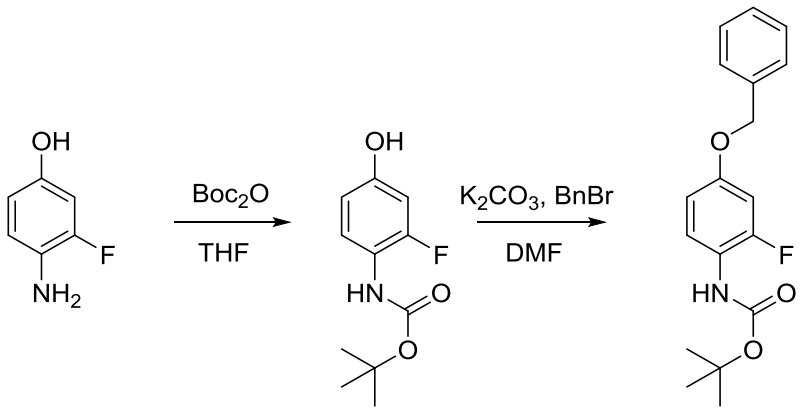


Synthesised according to typical procedure A. **5-((2,6-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.** Reaction performed on 1.4 mmol scale yielding target compound in 34% yield (180 mg, 0.48 mmol) as white solids. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.35 (dd, J = 8.0, 6.8 Hz, 1H), 7.24 (d, J = 7.4 Hz, 2H), 2.68 (s, 6H), 1.46 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.6, 141.5, 131.4, 127.9, 126.6, 102.4, 56.7, 26.5, 25.5. HR-ESIMS: *m/z* 396.9908[M+Na]$^+$ ($C_{14}H_{15}INaO_4^+$, calculated 396.9907)



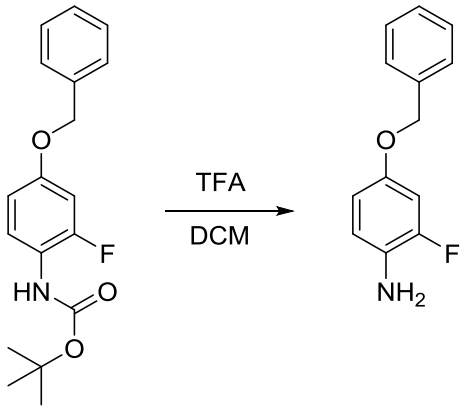
8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzoate. To 8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-iodobenzoate (165 mg, 0.44 mmol) in $CHCl_3$ (1.5 ml) was added TFA (4 ml) and oxone monopersulphate (220 mg, 0.70 mmol) and left at room temperature for 3 hours. The solvent was removed over a stream of nitrogen and the residues dissolved in EtOH (5 ml) and pH adjusted to ~10 via addition of 10% w/v Na_2CO_3. 2,2-dimethyl-1,3-dioxane-4,6-

dione (95mg, 0.66 mmol) was added from 10% w/v Na_2CO_3 (2 ml) and the reaction was left at room temperature for 50 minutes. The reaction mixture was poured into DCM (25 ml) and extracted with 2x25 ml DCM. The combined organic phases were washed with 0.5M $Na_2S_2O_3$ and dried over sodium sulphate. The solvents were removed under reduced pressure and the crude dissolved in DCM and hexanes was added to induce precipitation. The cloudy suspension was subjected to freezer and the target compound (95 mg, 0.19 mmol) was afforded as white solids in 42% via filtration and washed with hexanes. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.99 – 7.94 (m, 4H), 5.12 (t, *J* = 5.2 Hz, 1H), 3.08 (broad s, 2H), 2.20 (s, 3H), 2.15 – 2.05 (m, 2H), 2.05 – 1.88 (m, 4H), 1.71 (d, *J* = 14.8 Hz, 2H), 1.58 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 164.1, 162.8, 132.8, 132.2, 131.1, 121.3, 102.8, 68.6, 59.0, 58.0, 39.7, 35.7, 25.6, 25.6. HR-ESIMS: *m/z* 514.0721 $[M+H]^+$ ($C_{21}H_{25}INO_6^+$, calculated 514.0721).

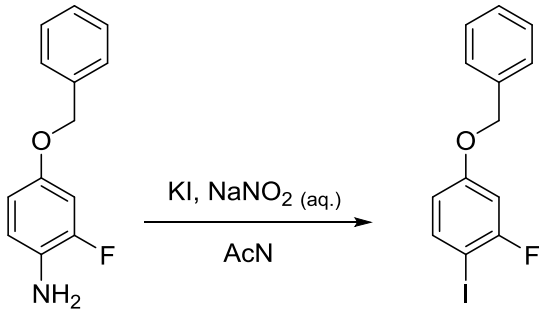


tert-butyl (4-(benzyloxy)-2-fluorophenyl)carbamate. To 4-amino-3-fluorophenol (5.59g, 44 mmol) in THF (40 ml) on ice was added di-*tert*-butyl dicarbonate (48.4 mmol, 10.6g) from THF (20 ml). The reaction mixture was stirred overnight. The solvents were removed under reduced pressure. The crude was dissolved in DCM and washed with water and aqueous sat. $NaHCO_3$. The organic phase was dried over sodium sulfate and evaporated to dryness under reduced pressure. The black crude was used in the next step without further purification.

To the crude in DMF (30 ml) was added K_2CO_3 (9.12 g, 66 mmol) and benzyl bromide (5.23 ml, 50.8 mmol) and left over night. The crude was dissolved in DCM and washed with water. The organic phase was dried over sodium sulfate and evaporated to dryness under reduced pressure. The black crude was recrystallized from EtOH yielding the target compound (6.99 g, 22.0 mmol) as brown solids in 50% over 2 steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (s, 1H), 7.45 – 7.30 (m, 5H), 6.77 – 6.69 (m, 2H), 6.46 (s, 1H), 5.02 (s, 2H), 1.52 (s, 9H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -129.2. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0 (d, $^3J_{CF}$ = 11 Hz), 153.2 (d, $^1J_{CF}$ = 244 Hz), 152.9, 128.8, 128.2, 127.6, 121.8 (broad), 120.2 (d, $^2J_{CF}$ = 11 Hz), 110.6 (d, $^4J_{CF}$ = 3 Hz), 102.9 (d, $^2J_{CF}$ = 23 Hz), 80.9, 70.7, 28.5. HR-ESIMS: *m/z* 340.1319 $[M+Na]^+$ ($C_{18}H_{20}FNNaO_3^+$, calculated 340.1319).

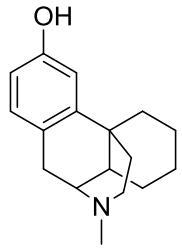


4-(benzyloxy)-2-fluoroaniline. To tert-butyl (4-(benzyloxy)-2-fluorophenyl)carbamate (6.41 g, 20.2 mmol) in DCM (45 ml) on ice was added dropwise trifluoroacetic acid (10 ml, 0.13 mol) and left for 4 hours. The crude was diluted with DCM and washed with aqueous sat. K_2CO_3. The organic phase was dried over sodium sulfate and evaporated to dryness under reduced pressure yielding the target compound (4.3 g, 19.8 mmol) in 98% as dark brown solids. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.29 (m, 5H), 6.78 – 6.66 (m, 2H), 6.61 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.98 (d, *J* = 3.4 Hz, 2H), 3.41 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.07 (d, $^1J_{CF}$ = 239 Hz), 152.05 (d, $^3J_{CF}$ = 9 Hz), 137.1, 128.7, 128.2 (d, $^2J_{CF}$ = 13 Hz), 128.1, 127.6, 117.7 (d, $^3J_{CF}$ = 5 Hz), 111.1 (d, $^4J_{CF}$ = 3 Hz), 104.0 (d, $^2J_{CF}$ = 22 Hz), 71.0 ^{19}F NMR (376 MHz, Chloroform-*d*) δ -131.81 (dd, *J* = 12.4, 10.1 Hz). HR-ESIMS: *m/z* 218.0976 $[M+H]^+$ ($C_{13}H_{13}FNO^+$, calculated 218.0976).

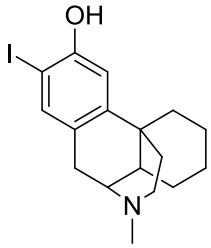


4-(benzyloxy)-2-fluoro-1-iodobenzene To 4-(benzyloxy)-2-fluoroaniline (2.41 g, 11.1 mmol) in MeCN (45 ml) on ice was added dropwise a solution of KI (4.6 g, 27.7 mmol) and $NaNO_2$ (1.53 g, 22.2 mmol) in water (8 ml). After effervescence had ceased the reaction mixture was allowed to reach room temperature and stirred for 1 hour. The reaction mixture was diluted with DCM and washed with water, 1M sodium thiosulfate and saturated $NaHCO_3$. The organic phase was dried over sodium sulfate and evaporated to dryness under reduced pressure. The crude was purified via flash column chromatography (0-20% DCM in hexanes) yielding the target compound (1.45 g, 4.43 mmol) in 40% as pale yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 8.7, 7.4 Hz, 1H), 7.45 – 7.33 (m, 4H), 6.74 (dd, *J* = 9.8, 2.8 Hz, 1H), 6.60 (ddd, *J* = 8.8, 2.8, 0.8 Hz, 1H), 5.04 (s, 2H). ^{19}F NMR (377 MHz,

Chloroform-*d*) δ -92.05 (dd, *J* = 9.8, 7.3 Hz) ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{CF}$ = 245 Hz), 160.6 (d, $^3J_{CF}$ = 10 Hz), 139.2 (d, $^3J_{CF}$ = 3 Hz), 136.1, 128.9, 128.4, 127.6, 113.2 (d, $^4J_{CF}$ = 3 Hz), 103.4 (d, $^2J_{CF}$ = 27 Hz), 70.61, 69.9 (d, $^2J_{CF}$ = 26 Hz) ^{19}F NMR (376 MHz, Chloroform-*d*) δ -131.81 (dd, *J* = 12.4, 10.1 Hz). HR-ESIMS: *m/z* 350.9653 $[M+Na]^+$ ($C_{13}H_{10}FINaO^+$, calculated 350.9653).

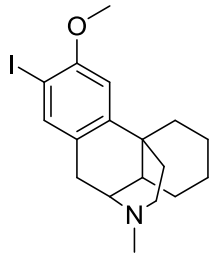


Dextrorphan. To dextmethorphan hydrobromide monohydrate (4.6 g, 12.4 mmol) was added 48 % HBr (25 ml) and heated to reflux overnight. The reaction mixture was basified via addition of potassium carbonate and extracted with diethyl ether. The combined organic phases were dried over sodium sulfate affording dextrorphan in 100% (3.2g, 12.4 mmol) as pale green solids. The crude was used in the next step without further purification. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (d, *J* = 8.2 Hz, 1H), 6.71 (d, *J* = 2.6 Hz, 1H), 6.61 (dd, *J* = 8.2, 2.6 Hz, 1H), 2.98 (d, *J* = 18.3 Hz, 1H), 2.91 (dd, *J* = 5.8, 3.1 Hz, 1H), 2.68 (dd, *J* = 18.3, 5.8 Hz, 1H), 2.59 – 2.50 (m, 1H), 2.44 (s, 3H), 2.32 – 2.25 (m, 1H), 2.21 (td, *J* = 12.5, 3.3 Hz, 1H), 1.93 (dt, *J* = 12.8, 3.2 Hz, 1H), 1.81 (td, *J* = 12.8, 4.7 Hz, 1H), 1.63 (d, *J* = 11.4 Hz, 1H), 1.53 – 1.23 (m, 6H), 1.14 (qd, *J* = 12.2, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 141.4, 128.9, 128.3, 113.6, 112.3, 58.5, 47.5, 44.5, 42.6, 41.4, 37.1, 36.5, 26.8, 26.5, 23.8, 22.3.

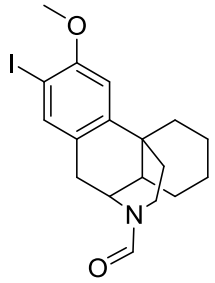


2-iodo-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol. To dextrorphan (1.00g, 3.90 mmol) in MeCN (20 ml) in the dark on ice was added (NIS) (964 mg, 4.29 mmol) and paratoluenesulfonic acid monohydrate (1.48 g, 7.8 mmol) and allowed to reach room temperature and kept overnight. The reaction mixture was diluted with water, 1M $Na_2S_2O_3$ and basified with Na_2CO_3. The aqueous phase was extracted with DCM and the combined organic phases were dried over sodium sulfate and evaporated to dryness under reduced pressure yielding the target compound as brown solids in 92% (3.6 mmol, 1.38 g). The crude was used in the next step without further purification. ^{1}H NMR

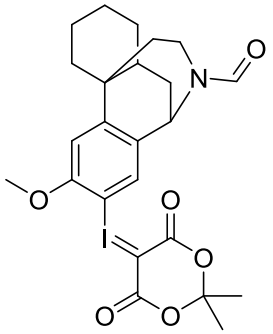
(400 MHz, Chloroform-*d*) δ 7.42 (s, 1H), 6.82 (s, 1H), 5.23 (broad s, 1H), 2.94 (d, *J* = 18.3 Hz, 1H), 2.85 (dd, *J* = 5.8, 3.2 Hz, 1H), 2.61 (dd, *J* = 18.4, 5.9 Hz, 1H), 2.50 (dt, *J* = 12.0, 3.2 Hz, 1H), 2.41 (s, 3H), 2.30 – 2.21 (m, 1H), 2.13 (td, *J* = 12.4, 3.3 Hz, 1H), 1.86 (dt, *J* = 12.9, 3.2 Hz, 1H), 1.76 (td, *J* = 12.8, 4.8 Hz, 1H), 1.63 (d, *J* = 11.9 Hz, 1H), 1.49 (d, *J* = 11.6 Hz, 1H), 1.44 – 1.37 (m, 1H), 1.37 – 1.19 (m, 4tH), 1.09 (qd, *J* = 12.5, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 142.9, 137.3, 131.5, 112.4, 83.4, 58.1, 47.3, 44.6, 42.7, 41.6, 37.2, 36.5, 26.8, 26.5, 23.3, 22.3. HR-ESIMS: *m/z* 384.0820 $[M+H]^+$ ($C_{17}H_{23}INO^+$, calculated 384.0819).



2-iodo-3-methoxy-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene. To 2-iodo-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol. (1.10 g, 2.87 mmol) in MeCN/MeOH (1:1; 35ml) was added DIPEA (1.5 ml, 8.6 mmol) and 2M TMS-diazomethane in ether (2.87 ml, 5.74 mmol) and left overnight. The reaction mixture was diluted with water and extracted with DCM. The combined organic phases were washed with brine and dried over sodium sulphate. The crude was purified via flash column chromatography using 8-22% MeOH in DCM affording the target compound as beige solids in 42% (480mg, 1.21 mmol). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.59 (s, 1H), 6.83 (s, 1H), 3.82 (s, 3H), 3.20 (dd, *J* = 6.0, 3.1 Hz, 1H), 3.07 (d, *J* = 19.1 Hz, 1H), 2.87 (dd, *J* = 19.1, 6.0 Hz, 1H), 2.78 (dd, *J* = 12.0, 3.0 Hz, 1H), 2.64 (s, 3H), 2.53 – 2.46 (m, 1H), 2.39 (td, *J* = 12.9, 3.5 Hz, 1H), 1.95 (dt, *J* = 12.7, 3.4 Hz, 1H), 1.84 (td, *J* = 13.3, 4.7 Hz, 1H), 1.73 – 1.65 (m, 1H), 1.63 – 1.55 (m, 1H), 1.50 (ddd, *J* = 13.5, 3.5, 1.7 Hz, 2H), 1.41 (ddt, *J* = 16.6, 13.7, 3.6 Hz, 2H), 1.29 (tt, *J* = 13.3, 3.1 Hz, 1H), 1.18 – 1.06 (m, 1H). ^{13}C NMR (101 MHz, MeOD) δ 159.0, 141.7, 139.8, 131.2, 109.2, 84.5, 60.3, 56.9, 48.4, 44.6, 42.0, 41.0, 37.9, 36.8, 27.4, 27.2, 24.4, 23.1. HR-ESIMS: *m/z* 398.0975 $[M+H]^+$ ($C_{18}H_{25}INO^+$, calculated 398.0975).

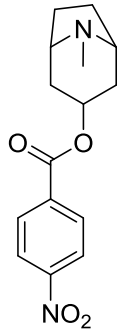


2-iodo-3-methoxy-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene-11-carbaldehyde. To **2-iodo-3-methoxy-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene** (80 mg, 0.20 mmol) in MeCN (1 ml) was added DIAD (59 µl, 0.30 mmol) and heated at 80 degrees for 1 hour. The solvent was removed under reduced pressure. The crude was dissolved in 2M HCl in dioxane/water (1:1; 4ml) and refluxed for 2 hours. The reaction mixture was basified with 2M NaOH and extracted with DCM. The combined organic phases were dried over sodium sulfate and evaporated to dryness under reduced pressure. To the crude on ice in THF (1 ml) was added freshly prepared acetic formic anhydride (formic acid (95 µl, 2.5 mmol) and acetic anhydride (190 µl, 2.0 mmol) heated at 65 ^{o}C for 30 minutes) and stirred for 10 minutes. The solvents were removed under reduced pressure and the crude purified via flash column chromatography 50% EtOAc in hexanes affording the product as off white solids in 57% (47 mg, 0.11 mmol) over 3 steps. NMR show a mixture of rotary isomers in roughly 1:1 ratio. ^{1}H NMR (400 MHz, Chloroform-*d*) δ (8.13, 7.98) (s, 1H), (7.52, 7.50 (s, 1H), (4.65 – 4.56, 3.69 – 3.65) (m, 1H), 3.85 (s, 1H), (3.28, 3.14), (td, *J* = 18.1, 5.9 Hz, 1H), 3.14 (td, *J* = 18.1, 5.9 Hz, 1H), (2.95, 2.45) (td, *J* = 13.2, 3.9 Hz, 1H), 2.63 (t, *J* = 18.9 Hz, 1H). 2.40 – 2.30 (m, 1H), 1.71 – 1.46 (m, 5H), 1.39 – 1.21 (m, 4H), 1.13 – 1.03 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 160.7, 157.5, 157.4, 140.8, 140.7, 139.0, 138.9, 130.7, 130.1, 108.2, 108.2, 83.9, 83.9, 56.6, 56.6, 53.6, 46.2, 45.0, 43.7, 42.0, 41.1, 40.8, 39.2, 39.0, 36.7, 36.6, 34.9, 32.0, 30.7, 26.4, 26.2, 26.2, 22.0, 22.0, 21.8. HR-ESIMS: *m/z* 434.0587 $[M+Na]^+$ ($C_{18}H_{22}INNaO_2^+$, calculated 434.0587).

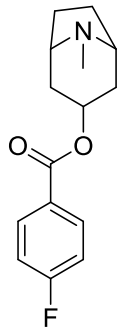


7-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-6-methoxy-1,3,4,9,10,10a-hexahydro-2H-9,4a-(epiminoethano)phenanthrene-11-carbaldehyde. To **2-iodo-3-methoxy-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene-11-carbaldehyde (**36 mg, 0.09 mmol) was added 77% mCPBA (31 mg, 0.14 mmol) in DCM (1 ml) and heated to 38 degrees for 80 minutes. The reaction mixture ws cooled to 10 degrees and KOH (56 mg, 10 mmol) together with 2,2-dimethyl-1,3-dioxane-4,6-dione (19 mg, 0.13 mmol) was added in one portion. The reaction mixture was kept between 10 and 15 degrees for 40 minutes. The reaction mixture was diluted with DCM (5 ml), filtered through a filter paper, washed with DCM (5 ml) and dried over sodium sulfate. The drying agent was filtered off and solvent removed under reduced pressure at 20-22 ^{o}C. The crude was dissolved in DCM (~5ml) and filtered

through a filter paper. The crude was purified via precipitation from slow addition of hexanes (10 ml). The flask was left at -20 for 1 hour. The product was obtained as white solids in 22% (11 mg, 0.020 mmol) via filtration and washed with hexanes. NMR was recorded as a mixture of rotary isomers in ~1:1 ratio. 8.09 (s, 0.5 H), 7.93 (s, 0.5H), 7.28 (s, 1H), 7.09 (s, 0.5H), 4.44 (dd, *J* = 4.9, 3.1 Hz, 0.5H), 3.98 (*J* = dd, 13.8, 5.1 Hz, 0.5H), 3.91 (s, 3H), 3.85 (dd, *J* = 5.5, 3.5 Hz, 0.5H), 3.41 (dd, *J* = 13.6, 5.1 Hz, 0.5H), 3.11 (td, *J* = 18.3, 6.0 Hz, 1H), 2.67 – 2.61 (m, 1H), 2.55 – 2.53 (m, 0.5H), 2.16 (td, *J* = 13.2, 4.2 Hz, 0.5H), 1.68 – 1.65 (m, 0.5H), 1.61 – 1.39 (m, 12.5H), 1.36 – 1.28 (m, 2H), 1.14 – 1.07 (m, 1H), 0.90 (tdd, *J* = 12.9, 8.9, 4.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 162.6, 160.7, 160.5, 155.1, 144.2, 131.42, (131.35, 131.3), (109.82, 109.78), 102.8, (102.6, 102.5), 57.1, (54.40, 54.35), (51.7, 45.0), (43.9, 42.8), (41.0, 40.1), (38.93, 38.89), (35.6, 35.5), (33.9, 31.9), (30.5, 21.7), (25.9, 25.8), 25.57, (25.52, 25.48). HR-ESIMS: *m/z* 576.0853 $[M+Na]^+$ ($C_{24}H_{28}INNaO_6^+$, calculated 576.0854).



8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-nitrobenzoate. To Tropine (282 mg, 2.0 mmol) in PhMe (3 ml) was added triethylamine (307 µl, 2.2 mmol) and heated to reflux. 4-nitrobenzoyl chloride (408 mg, 2.2 mmol) was added in one portion and the reaction mixture heated at reflux for 3 hours. The crude was diluted with $CHCl_3$ and washed with sat. $NaHCO_3$. The organic phase was dried over sodium sulphate and evaporated to dryness under reduced pressure. The crude was purified via flash column chromatography (8-25% MeOH in DCM) affording the target compound (122 mg, 0.42 mmol) as pale yellow solids in 21%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 – 8.29 (m, 2H), 8.21 – 8.17 (m, 2H), 5.31 (t, *J* = 5.3 Hz, 1H), 3.21 (s, 2H), 2.34 (s, 3H), 2.29 (d, *J* = 15.6 Hz, 2H), 2.18 – 2.10 (m, 2H), 2.06 – 1.97 (m, 2H), 1.87 (d, *J* = 15.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 150.7, 136.3, 130.7, 123.8, 69.6, 59.9, 40.6, 36.8, 26.0. HR-ESIMS: *m/z* 291.1339 $[M+H]^+$ ($C_{15}H_{19}N_2O_4^+$, calculated 291.1339).



8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-fluorobenzoate. To Tropine (282 mg, 2.0 mmol) in PhMe (2 ml) at reflux was added 4-iodobenzoyl chloride (260 µl, 2.2 mmol) and kept for 5.5 hours. The crude was diluted with DCM, washed with sat. $NaHCO_3$ and brine. The solvents were removed under reduced pressure and the crude purified via flash column chromatography (0-25% MeOH in DCM) affording the target compound (212 mg, 0.81 mmol) as white solids in 40%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.96 (m, 2H), 7.18 – 7.09 (m, 2H), 5.33 (t, *J* = 5.2 Hz, 1H), 3.51 (s, 2H), 2.71 (s, 2H), 2.57 (s, 3H), 2.25 (s, 4H), 2.00 (d, *J* = 15.5 Hz, 2H). ^{19}F NMR (377 MHz, Chloroform-*d*) δ -105.1 (s).

NMR reactions screening

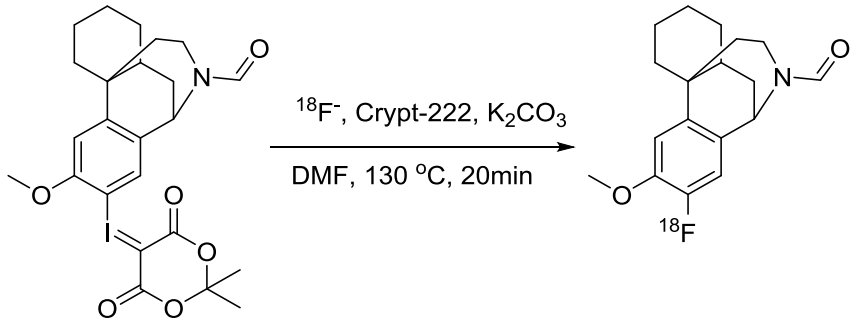
Typical procedure

To iodonium ylide (5 µmol) was added reference compound 4-fluorobiphenyl (0.50 mg, 2.3 µmol), KF/ crypt-222/K_2CO_3 (10 µmol KF) and DMF (0.5 ml). The reaction mixture was purged with argon for 1 minute and heated at 130 ^{o}C for 20 minutes. The reaction mixture was analysed via 19F-NMR, spiked with reference compound and reanalysed again to confirm signal assignment.

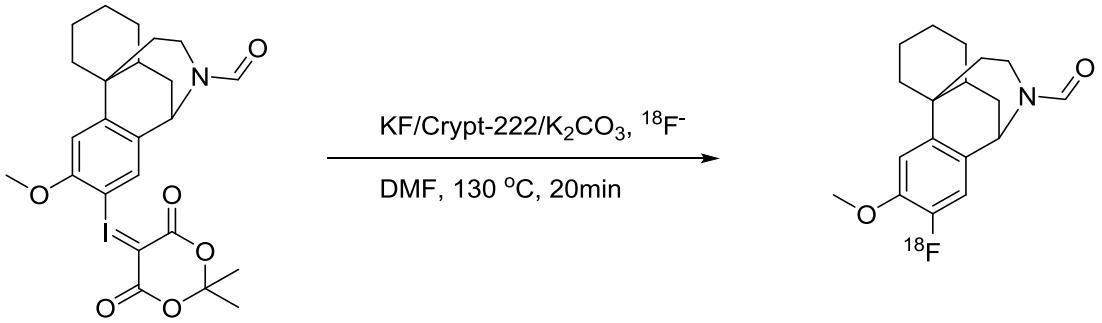
NMR analysis

The acquired FID file was opened in MestReNova V11.0.04, the spectra was phase adjusted to fit the reference compound and baseline corrected via Whittaker Smoother. The reference signal was integrated and noted down. The product signal was now phase adjusted and the signal integrated. The integrals were compared with added quantities to the reaction mixtures and a yield was calculated.

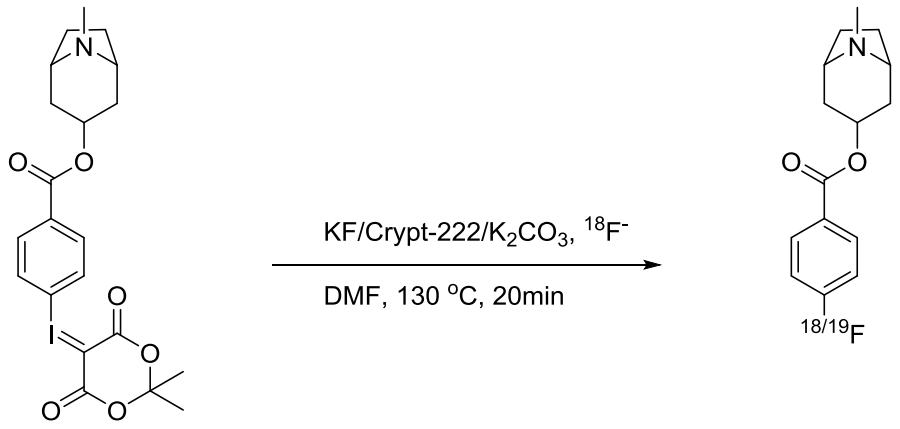
Radiochemistry



Aqueous target mixtures containing $^{18}F^-$ (~ 500 MBq) was loaded onto a QMA cartridge and subsequently eluted with crypt-222 (5 mg, 13 µmol) and K_2CO_3 (0.92 mg, 5.6 µmol) in 30/70 water/acetonitrile (0.5 ml) into a V-vial. The vial was heated at 85°C under a stream of nitrogen. After evaporation of bulk solvents, MeCN (1 ml) was added. The process was repeated 2 consecutive times. The vials content (400 MBq) was dissolved in DMF (200 µl). Iodonium ylide (2.04 mg, 3.7 µmol) was added from DMF (0.3 ml). The capped V-vial was bubbled with nitrogen for 1 minute and heated in a heating block at 130 °C for 20 minutes. The reaction mixture was allowed to cool to room temperature and a sample was taken for radioTLC analysis. The reaction mixture was diluted with water (7 ml), passed through a C18 cartridge (HR-P Chromafix) washed with water (10 ml) and eluted with DCM/THF (4:1; 5 ml) through a Si cartridge. RadioTLC was used to determine radiochemical purity, yielding the radiotracer in 38% RCY (150 MBq, > 95% RCP).



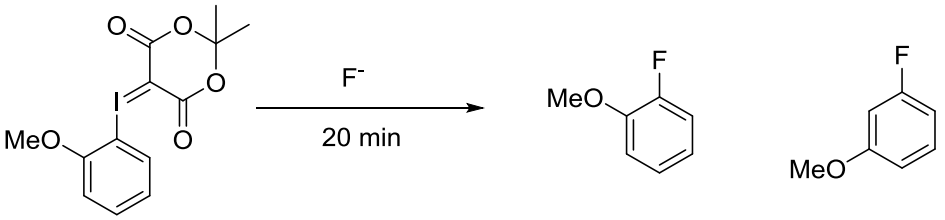
Aqueous target mixtures containing $^{18}F^-$ (~ 500 MBq) was loaded onto a QMA cartridge and subsequently eluted with crypt-222 (1 mg, 2.6 µmol) and K_2CO_3 (0.09 mg, 0.56 µmol) in 30/70 water/acetonitrile (0.5 ml) into a V-vial. The vial was heated at 85°C under a stream of nitrogen. After evaporation of bulk solvents, MeCN (1 ml) was added. The process was repeated 2 consecutive times. The vials content was dissolved in DMF (500 µl) and a portion (100 µl) was added to crypt-222/KF/K2CO3 (4:3:1, 5.65 mg, 8.6 µmol). Iodonium ylide (2.07 mg, 3.7 µmol) was added from DMF (0.3 ml). The capped V-vial was bubbled with nitrogen for 1 minute and heated in a heating block at 130 °C for 20 minutes. The reaction mixture was allowed to cool to room temperature and a sample was taken for radioTLC analysis. The reaction mixture was diluted with water (7 ml), passed through a C18 cartridge (HR-P Chromafix) washed with water (10 ml) and eluted with DCM/THF (4:1; 5 ml) through a Si cartridge. RadioTLC was used to determine radiochemical purity (> 95% RCP). Isolated yield was calculated after decay correction.



Aqueous target mixtures containing $^{18}F^-$ (~ 500 MBq) was loaded onto a QMA cartridge and subsequently eluted with crypt-222 (1 mg, 2.6 µmol) and K_2CO_3 (0.09 mg, 0.56 µmol) in 30/70 water/acetonitrile (0.5 ml) into a V-vial. The vial was heated at 85°C under a stream of nitrogen. After evaporation of bulk solvents, MeCN (1 ml) was added. The process was repeated 2 consecutive times. The vials content was dissolved in DMF (500 µl) and a portion (100 µl) was added to crypt-222/KF/K2CO3 (4:3:1, 5.90 mg, 8.9 µmol). Iodonium ylide (2.74 mg, 5.3 µmol) was added from DMF (0.3 ml). The capped V-vial was bubbled with nitrogen for 1 minute and heated in a heating block at 130 °C for 20 minutes. The reaction mixture was allowed to cool to room temperature and a sample was taken for radioTLC analysis. The reaction mixture was diluted with water (7 ml), passed through a C_{18} cartridge (HR-P Chromafix) washed with water (10 ml) and eluted with DCM/THF (4:1; 5 ml) through a Si cartridge. RadioTLC was used to determine radiochemical purity (> 95% RCP). Isolated yield was calculated after decay correction.

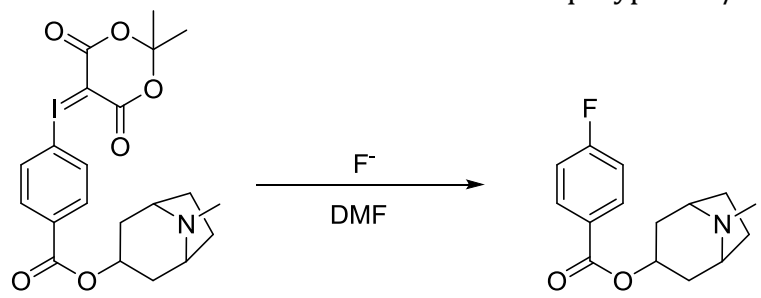
Additional experiments

Fluorination experiments were performed in accordance to typical procedure with the indicated variations, yield are ^{19}F NMR yields using 4-fluorobiphenyl as internal reference.

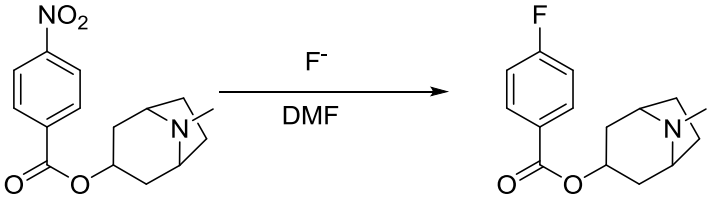


4F anisole	3F anisole	Conditions	Temperature
26%	0.8%	2 eq TBAF 4*tBuOH	110 °C
21%	0.8%	2 eq TBAF 4*tBuOH	120 °C
37%	0.9%	2 eq TBAF 4*tBuOH	140 °C
33%	1.4%	2 eq TBAF 4*tBuOH	130 °C m.w. heating
32±1%	1±0.2%	1.5 eq TBAF 4*tBuOH	130 °C
2%	0	1 eq Crypt-222, 4 eq KF	130 °C

4F anisole	3F anisole	Conditions	Additive
56%	0%	2 eq Crypt-222/K_2CO_3/KF, 130°C	+20% PPh3
34%	0%	2 eq Crypt-222/K_2CO_3/KF, 130°C	+10% PPh3
36%	0%	2 eq Crypt-222/K_2CO_3/KF, 130°C	+100% PPh3
46%	0%	2 eq Crypt-222/K_2CO_3/KF, 130°C	+5% PPh3
58%	0%	2 eq Crypt-222/K_2CO_3/KF, 130°C	+1% PPh3



19F NMR yield	Conditions	Temperature	Time
33 %	2 eq Crypt-222/K2CO3/KF	r.t.	60 min



19F NMR yield	**Conditions**	**Temperature**	**Time**
traces	2 eq Crypt-222/K_2CO_3/KF	r.t.	60 min
traces	2 eq TBAF*4tBuOH	r.t.	60 min
25 %	2 eq TBAF*4tBuOH	130 degrees	20 min
34 %	2 eq Crypt-222/K_2CO_3/KF	130 degrees	20 min

Solubility experiments

To solid reagents and a magnetic stirrer bar was added DMF (0.5 ml). The mixture was stirred for 30 seconds. Solubility was visually evaluated. The samples were heated for 10 + 10 + 100 minutes at 130 degrees, evaluated visually and after 2 hours by ^{13}C-NMR after diluting with $CDCl_3$ (1/5 volume).

Solubility of fluorinating reagent
(Dissolved (yes/no)

Reagents added	r.t.	10 min 130°C	20 min 130°C	2 h 130°C
4:3:1 : K222:KF:K2CO3 pre-complex (10 µmol with respect to KF	yes	yes	yes	yes
KF (10 µmol), Crypt-222 (12.5 µmol) K2CO3 (2.5 µmol)	no	no	no	no
KF (10 µmol). Crypt-222 (12.5 µmol)	no	no	no	no
KF (10 µmol)	no	no	no	no

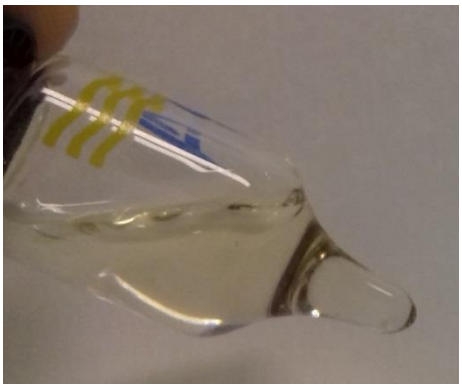


Figure 2: *4:3:1 :* K222:KF:K2CO3 pre-complex (10 µmol with respect to KF (no visible solids after 2 hours)

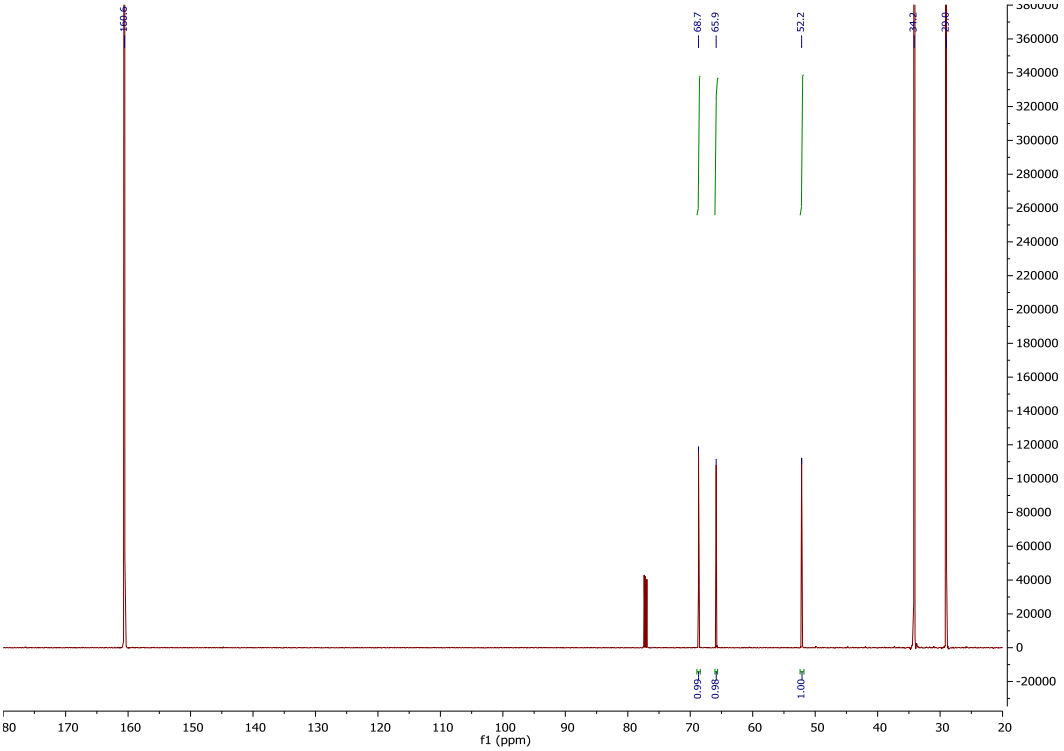
Figure 3: KF (10 µmol), Crypt-222 (12.5 µmol) K2CO3 (2.5 µmol) (visible solids in bottom after 2 hours)

Figure 4: KF (10 µmol). Crypt-222 (12.5 µmol) (visible solids in bottom after 2 hours)

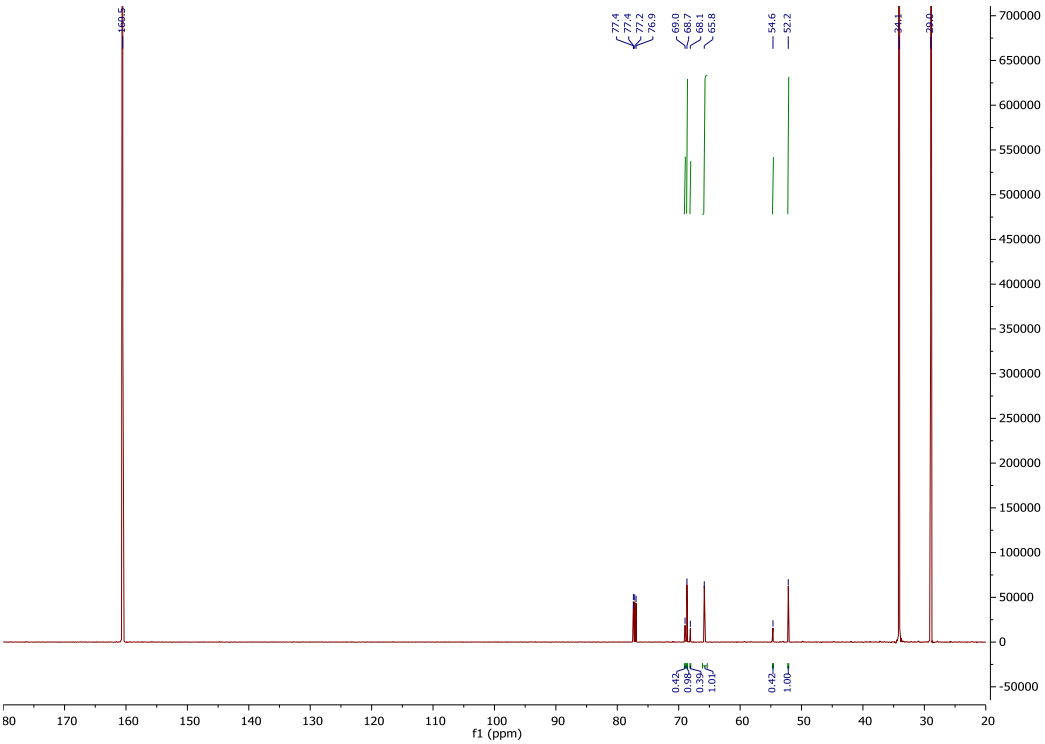
Figure 5: KF (10 µmol) (visible solids in bottom after 2 hours)

NMR

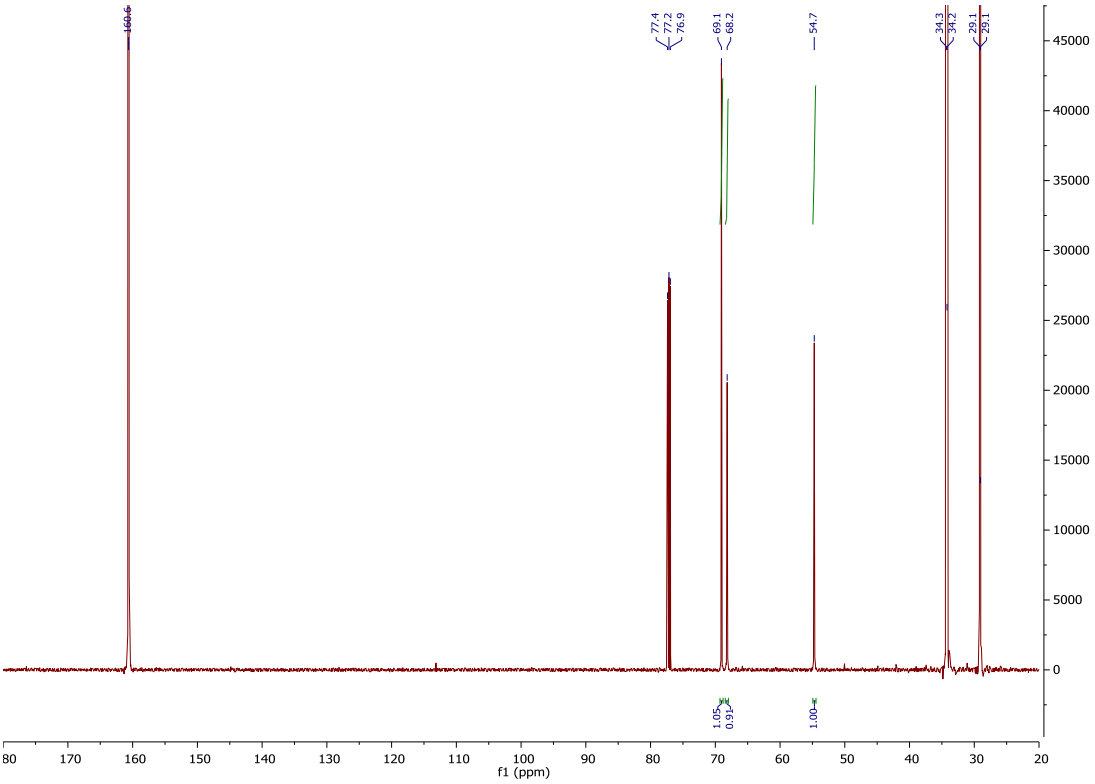
Premade Crypt-222/KF/K2CO$_3$ (4:3:1) complex in DMF/CDCl3 (5:1) after 2 hour heating at 130^{o}C



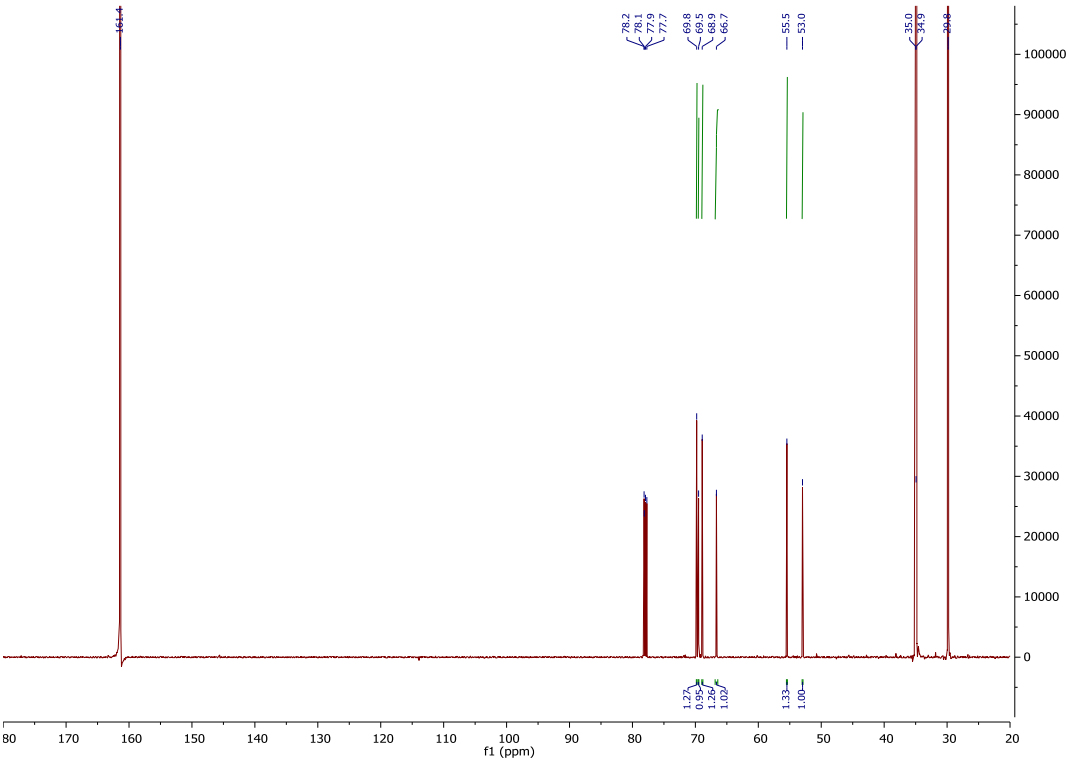
Crypt-222 (12.5 µmol), KF (10 µmol) and K_2CO_3 (2.5 µmol) in DMF/CDCl3 (5:1) after 2 hour heating at 130^{o}C



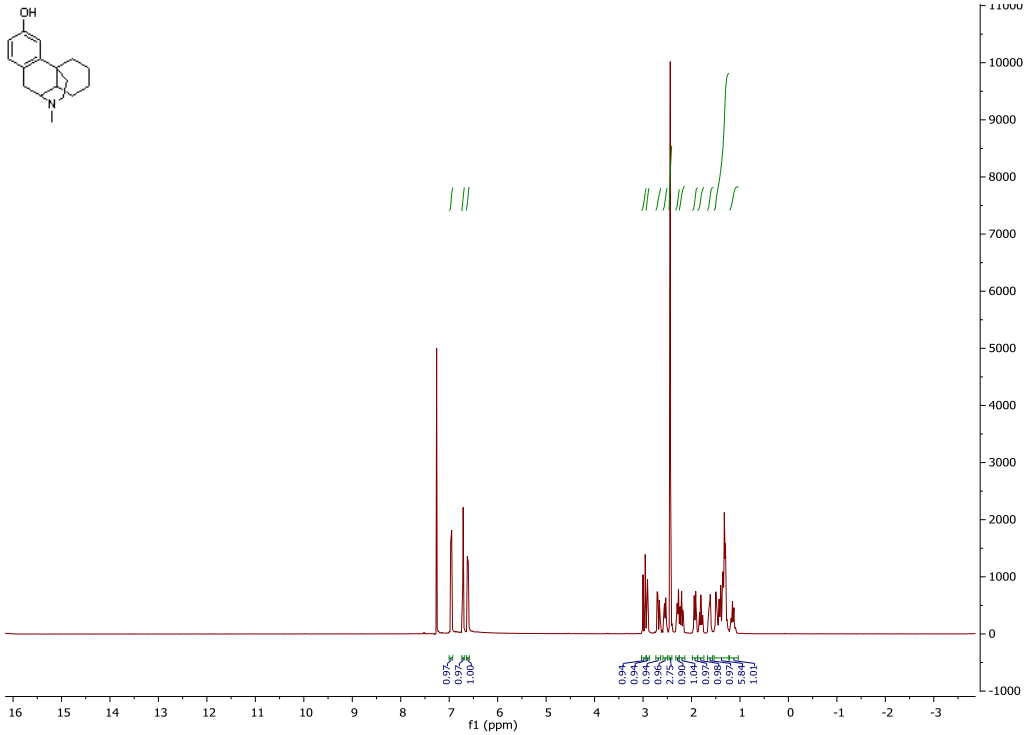
Crypt-222 in DMF/CDCl3 (5:1)



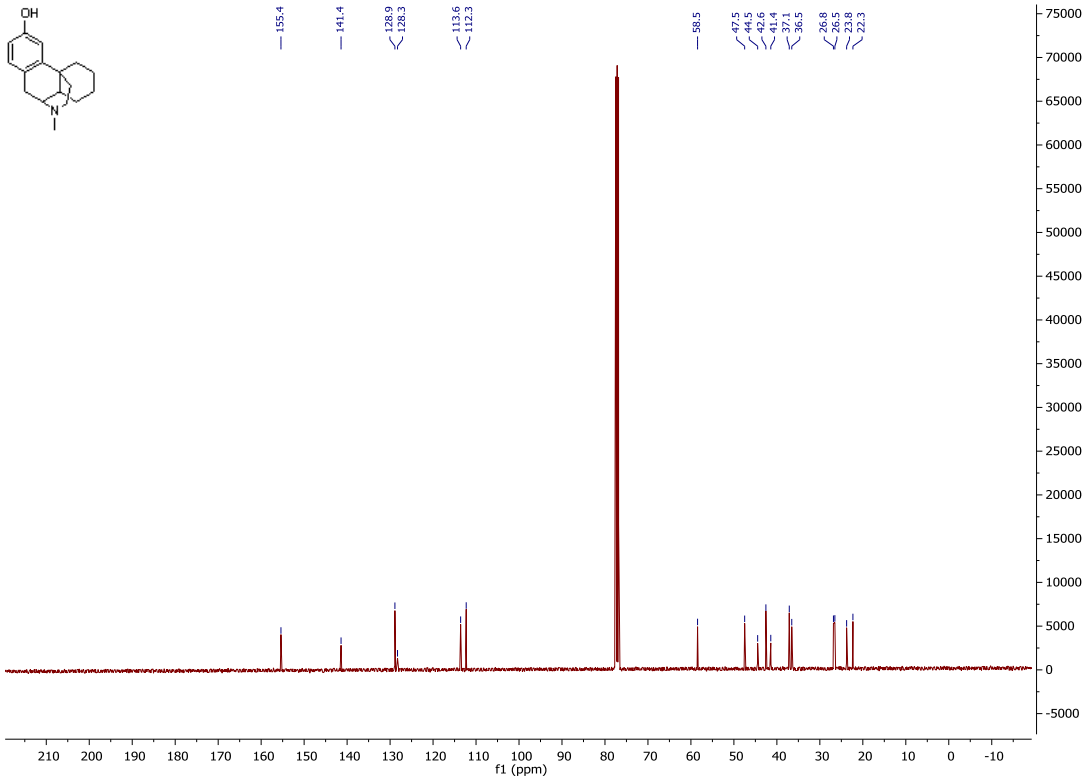
Crypt-222 (12.5 µmol) and KF (10 µmol) in DMF/CDCl3 (5:1) after 2 hour heating at 130^{o}C



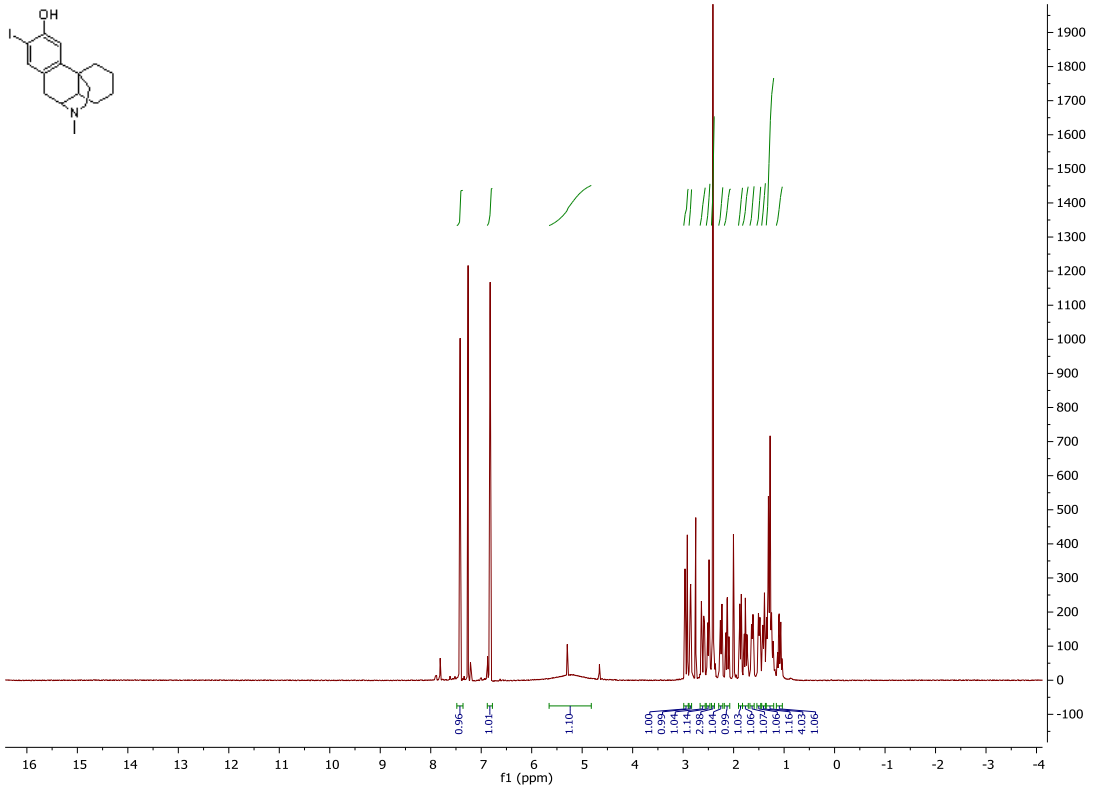
11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol



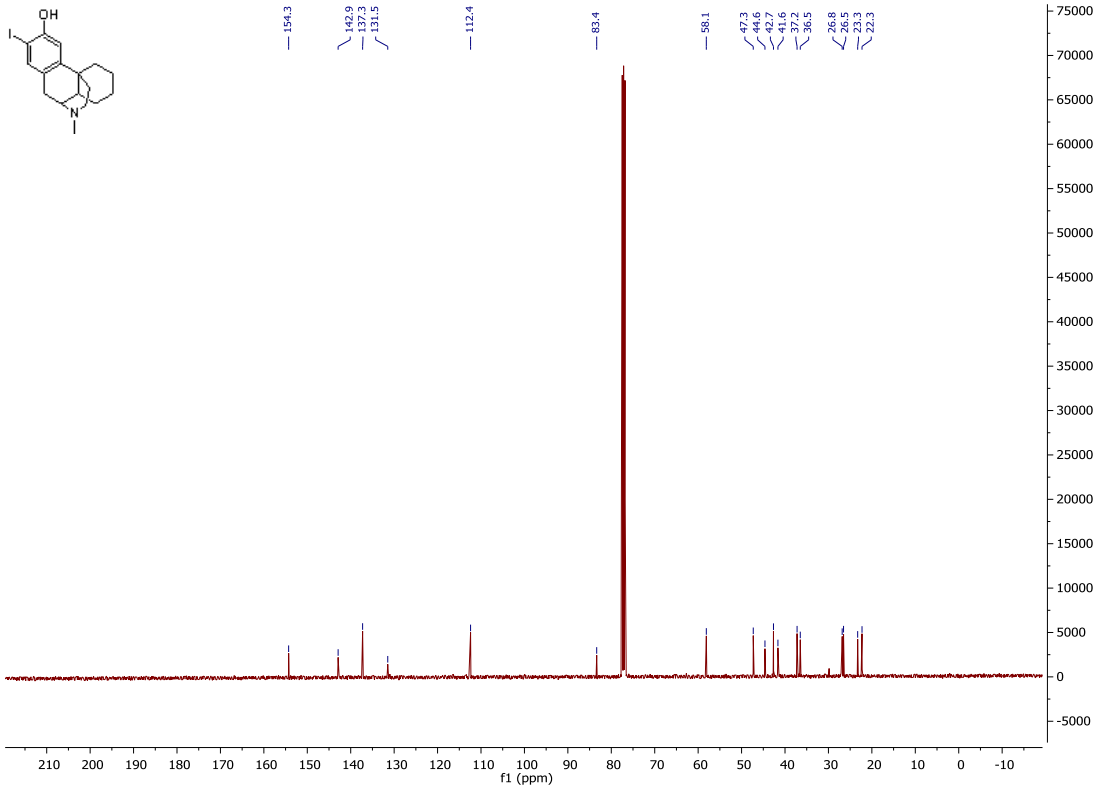
11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol



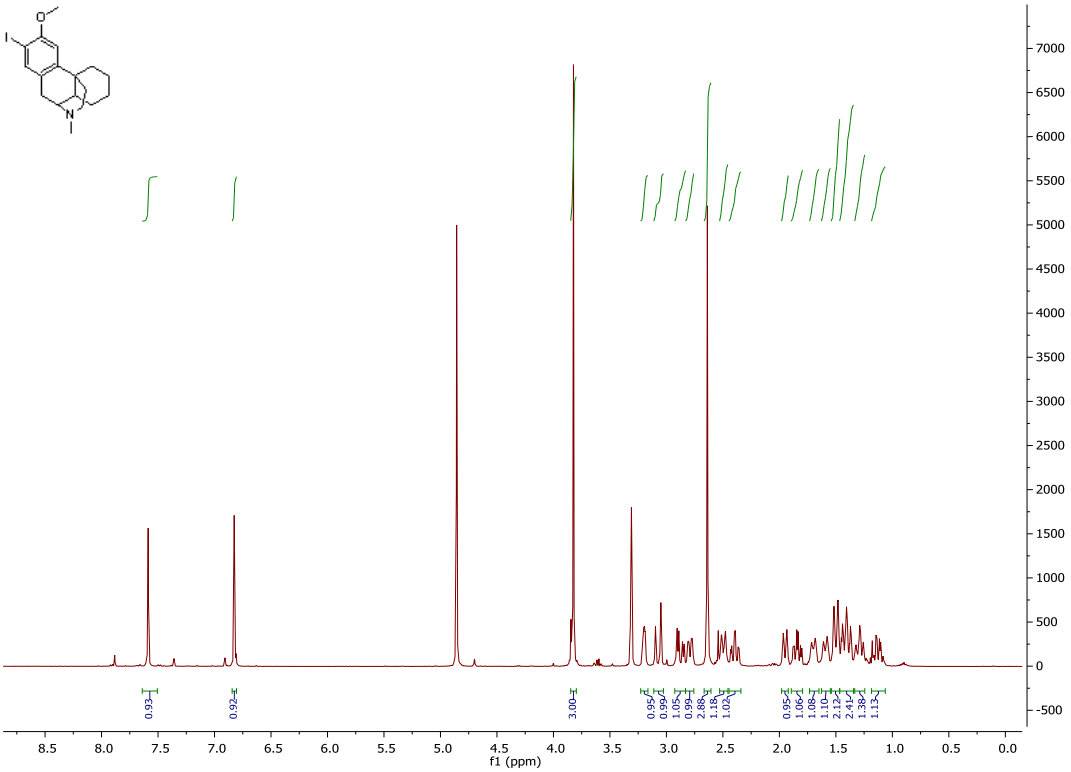
2-iodo-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol



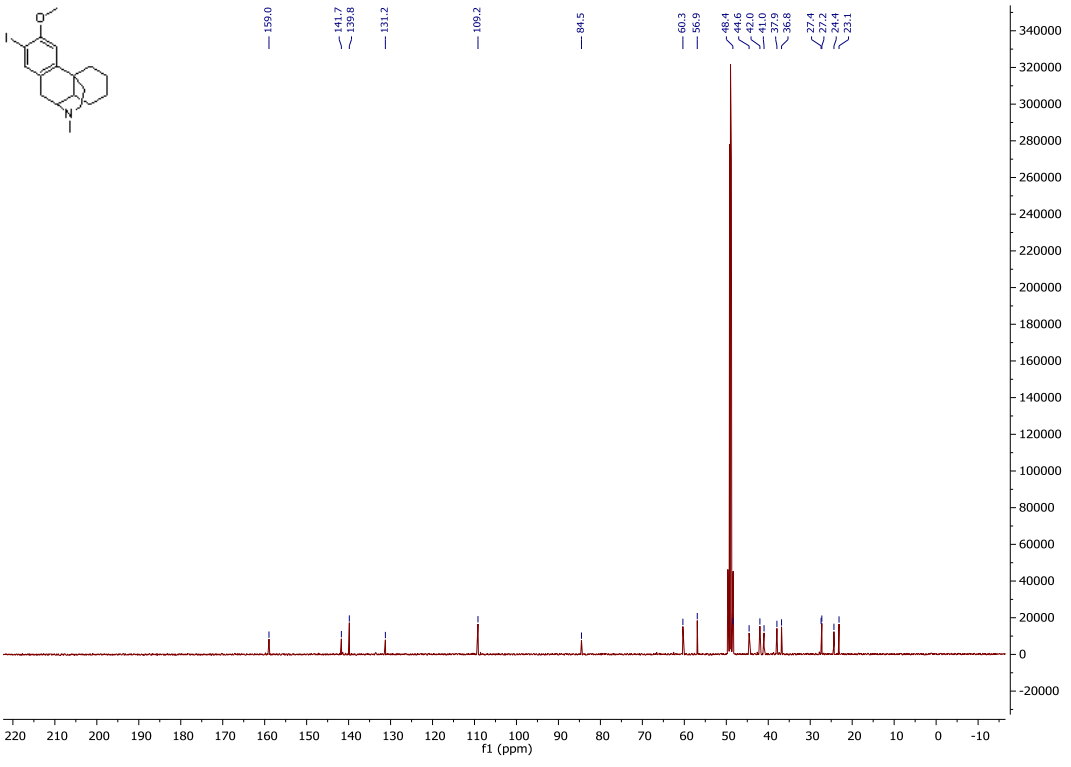
2-iodo-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol



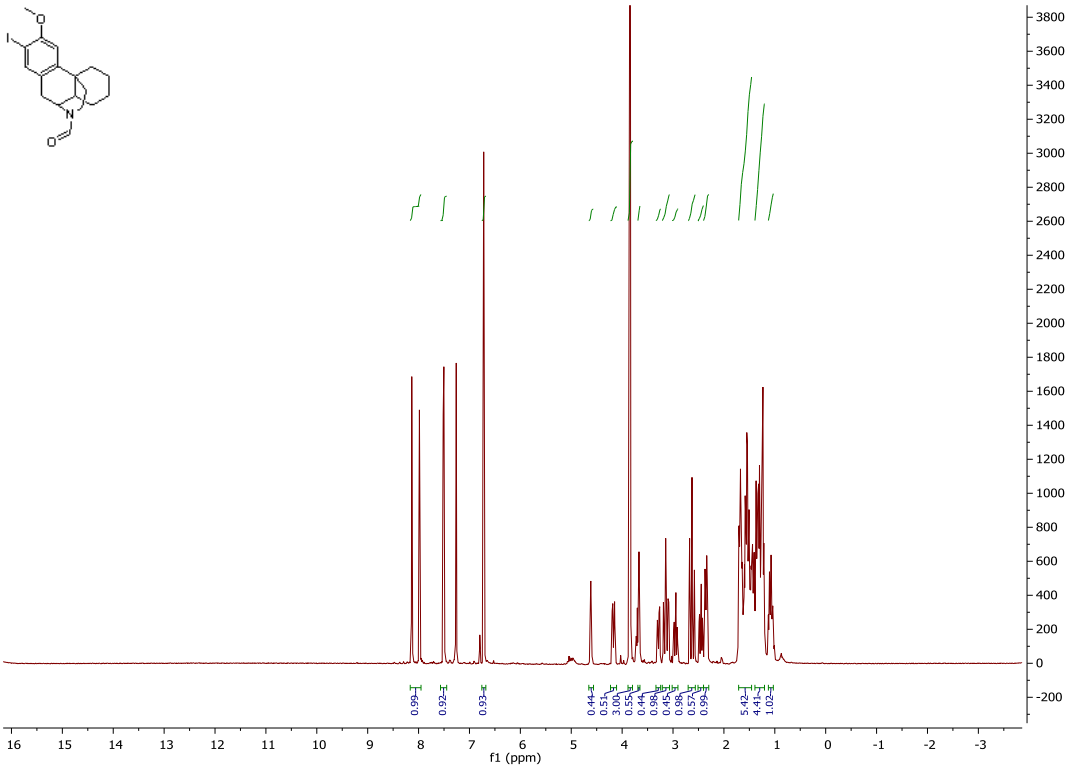
2-iodo-3-methoxy-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene



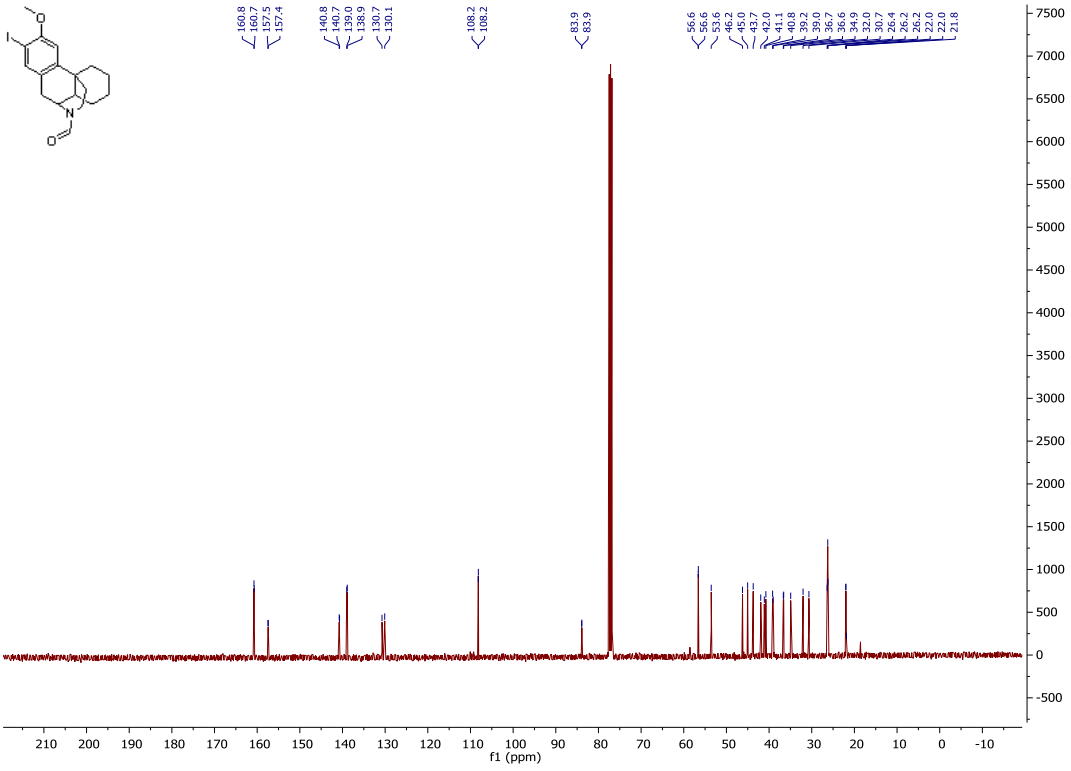
2-iodo-3-methoxy-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene



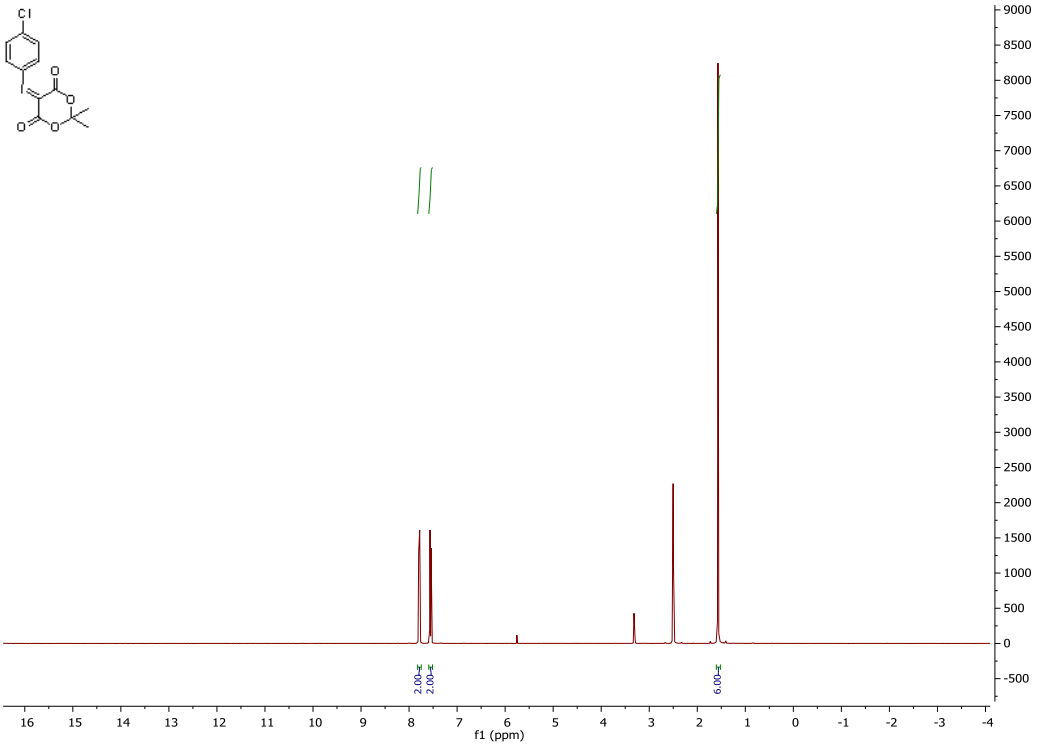
2-iodo-3-methoxy-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene-11-carbaldehyde



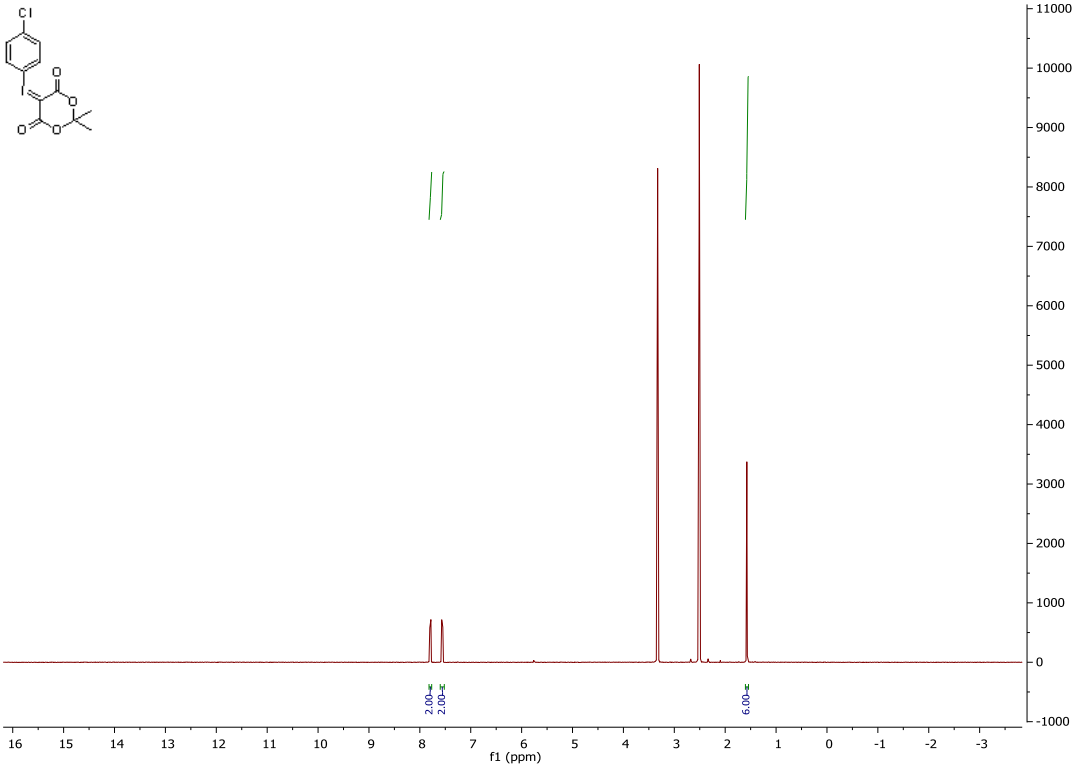
2-iodo-3-methoxy-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthrene-11-carbaldehyde



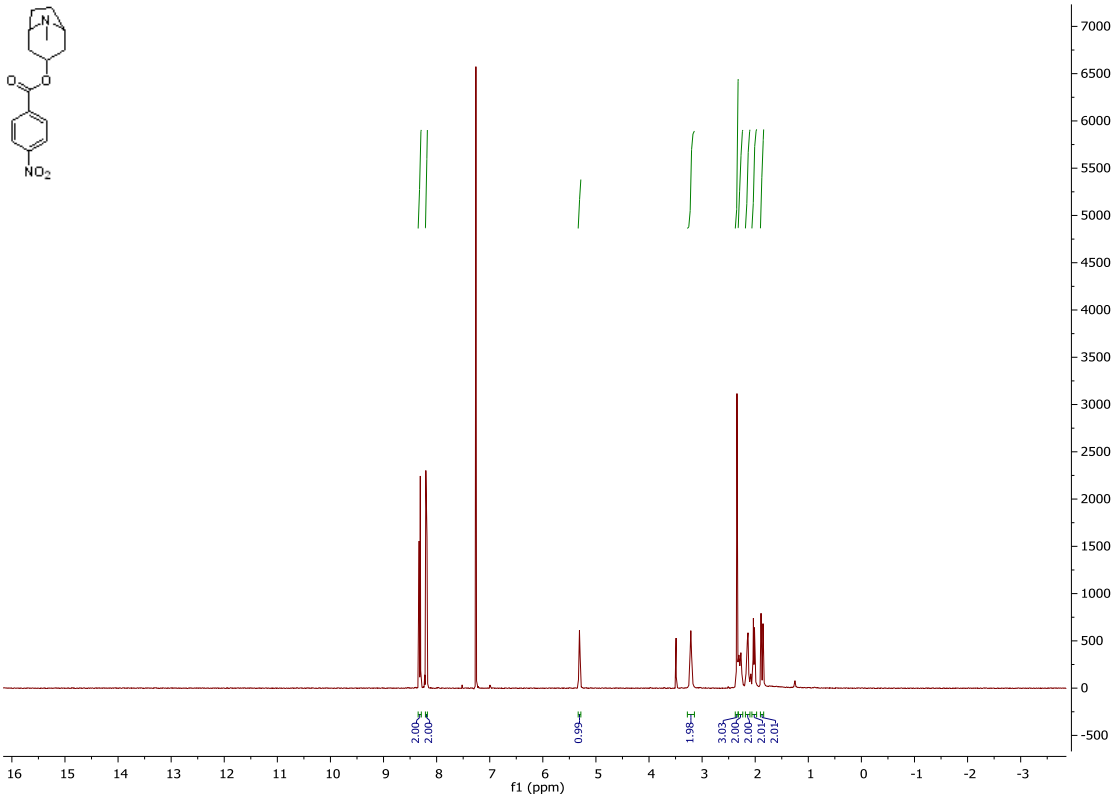
Original sample of 5-((4-chlorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione.



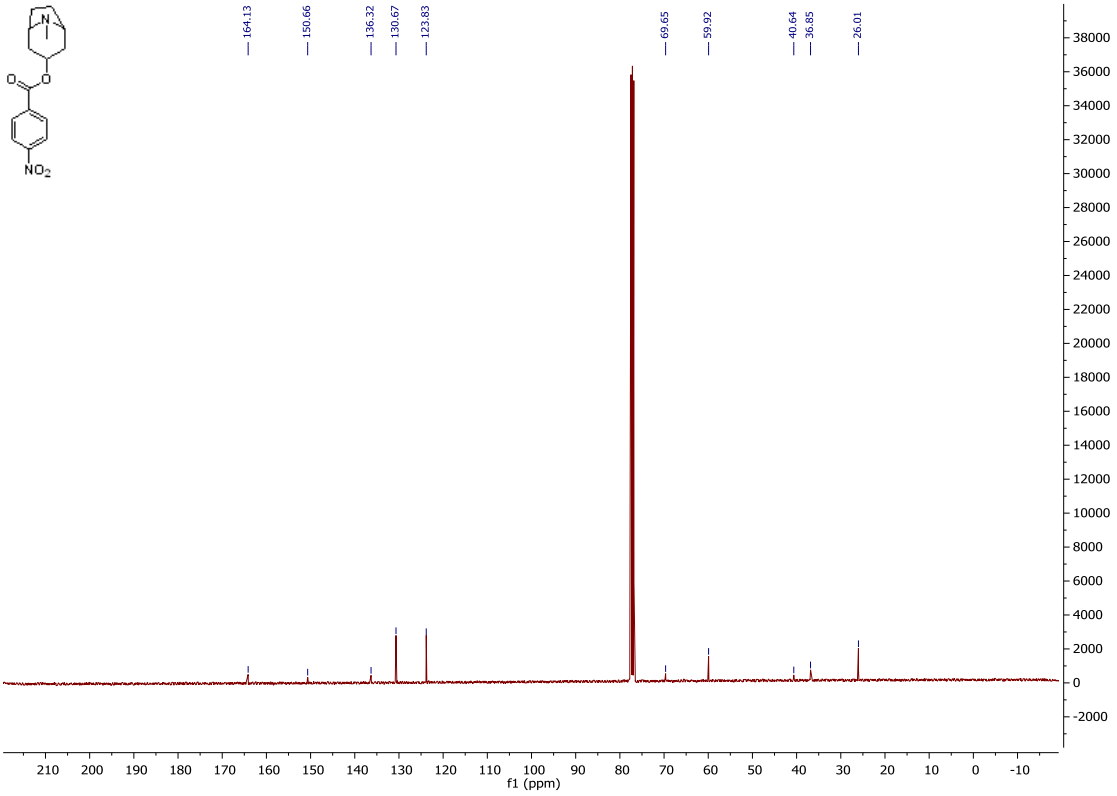
Sample of 5-((4-chlorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione after 6 months in freezer.



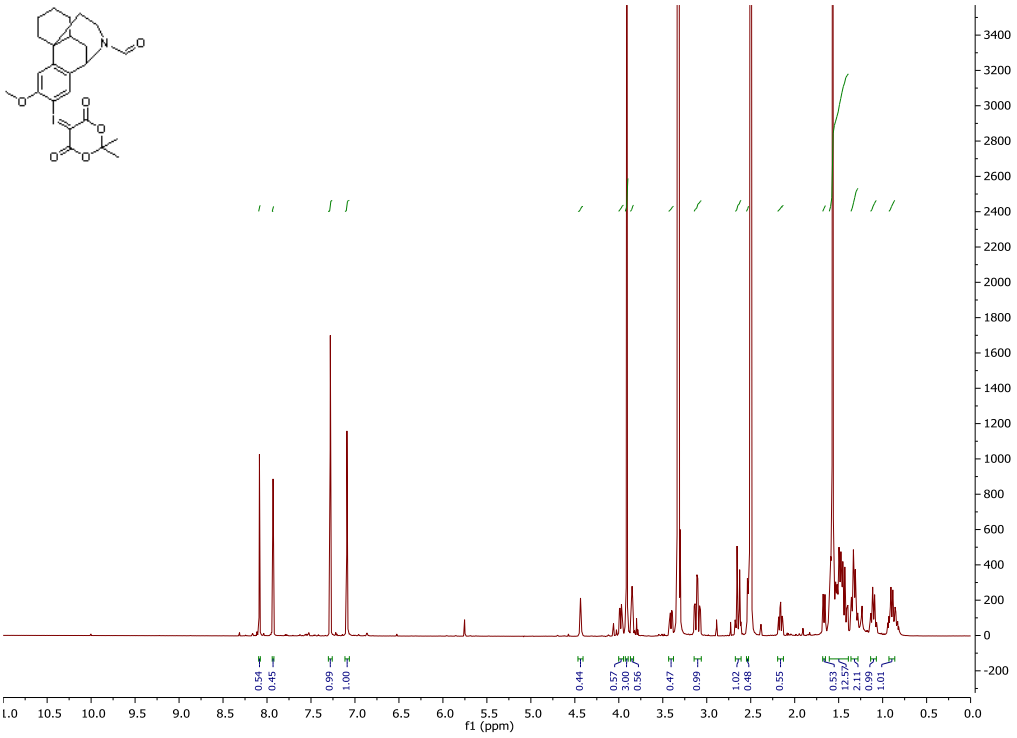
8-methyl-8-azabicyclo[3.2.1]octan-3-yl **4-nitrobenzoate**



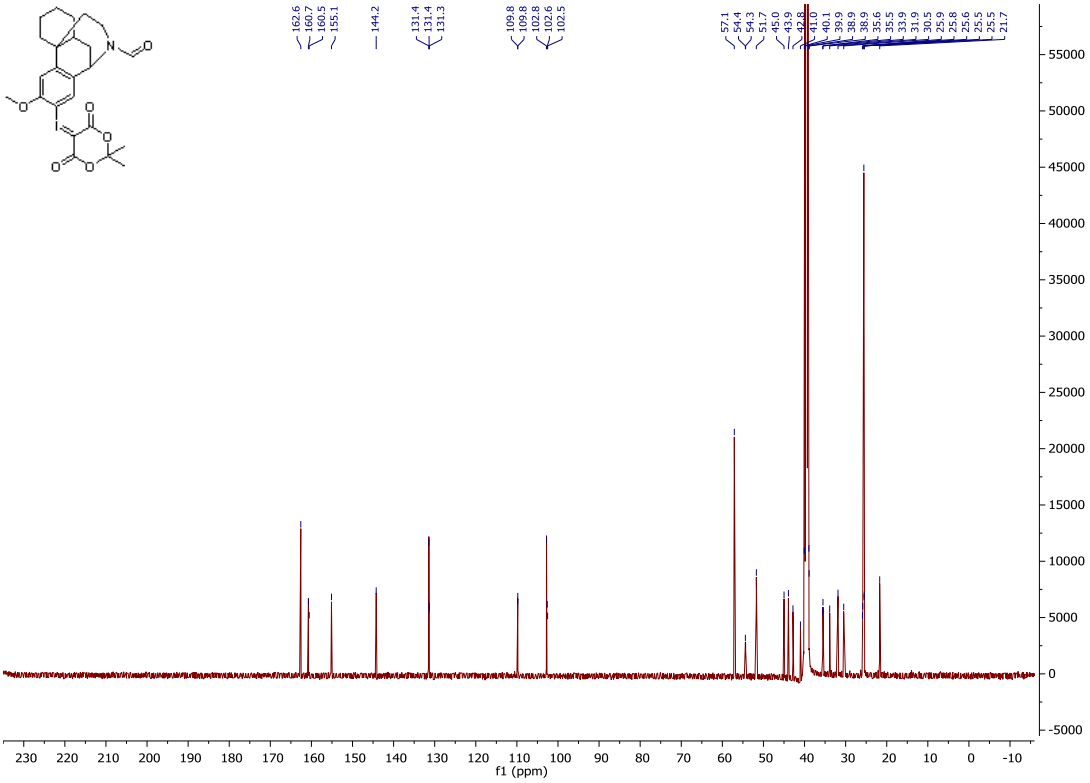
8-methyl-8-azabicyclo[3.2.1]octan-3-yl **4-nitrobenzoate**



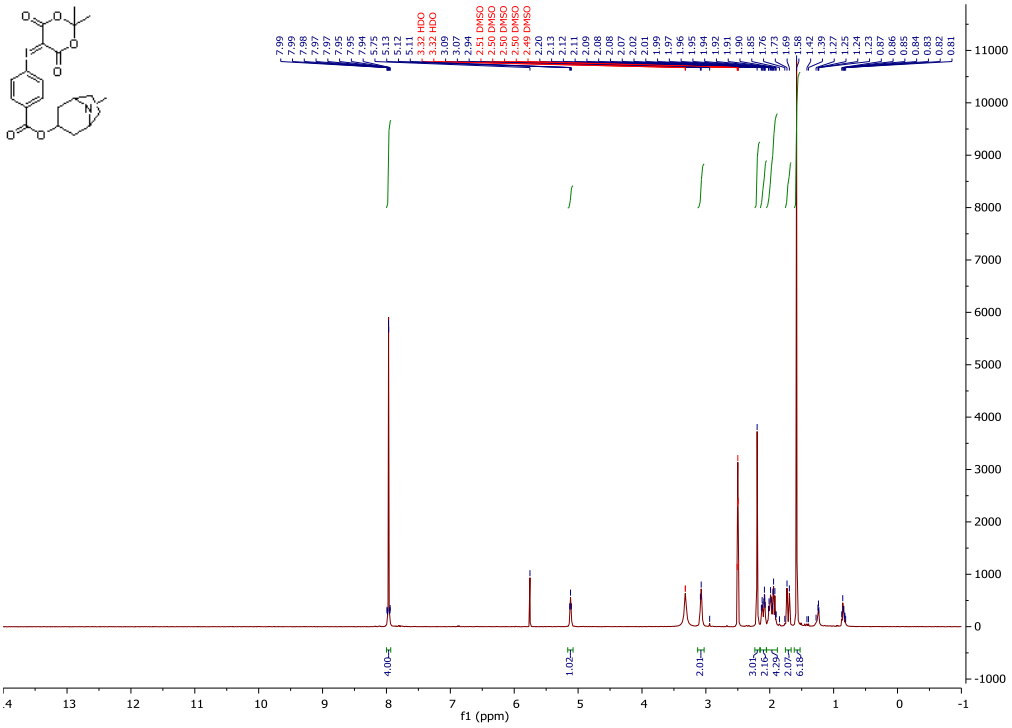
7-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-6-methoxy-1,3,4,9,10,10a-hexahydro-2H-9,4a-(epiminoethano)phenanthrene-11-carbaldehyde



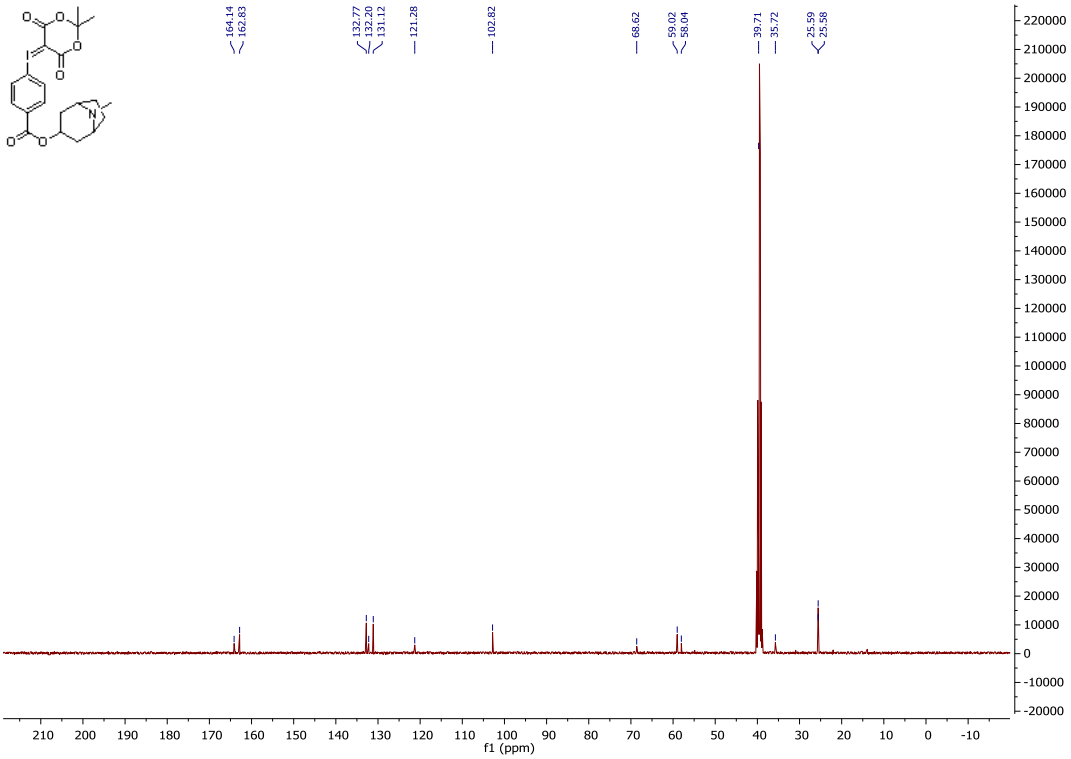
7-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-6-methoxy-1,3,4,9,10,10a-hexahydro-2H-9,4a-(epiminoethano)phenanthrene-11-carbaldehyde



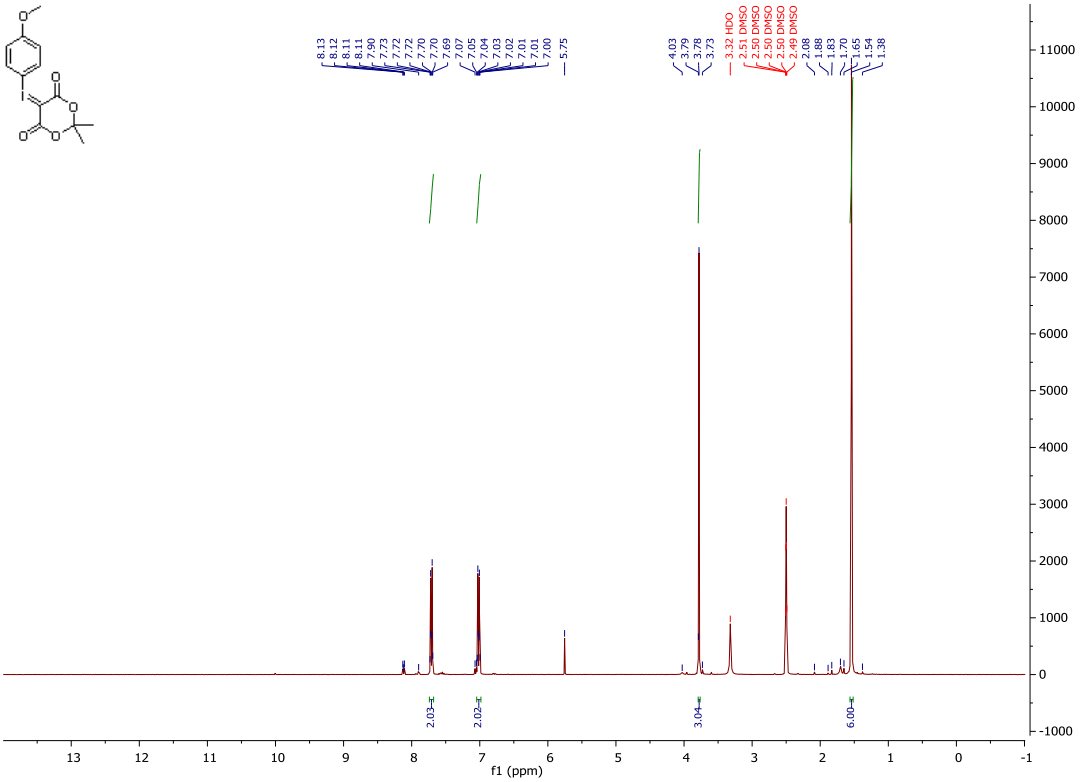
8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzoate



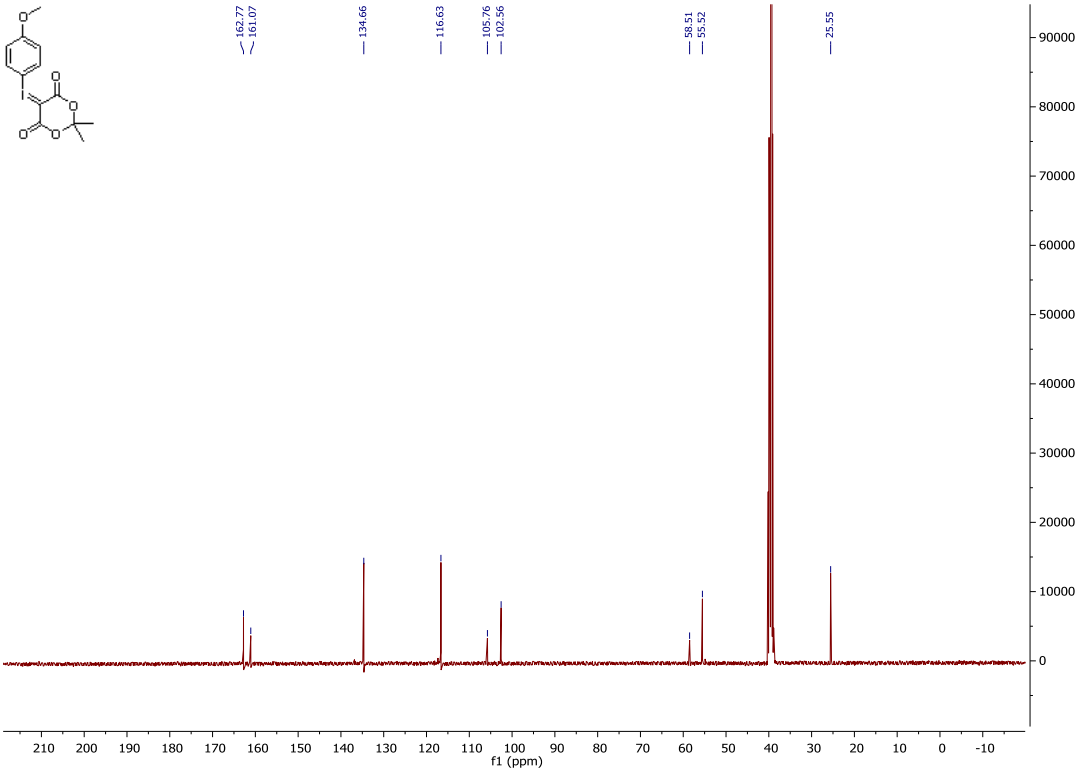
8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzoate



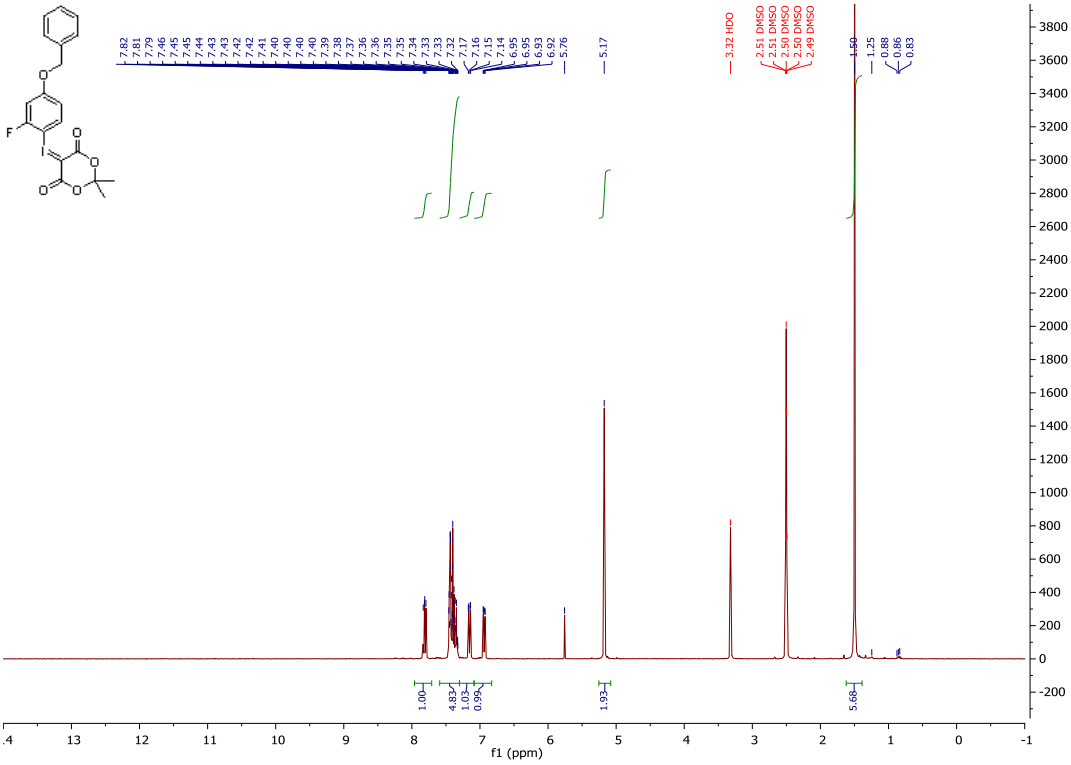
5-((4-methoxyphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



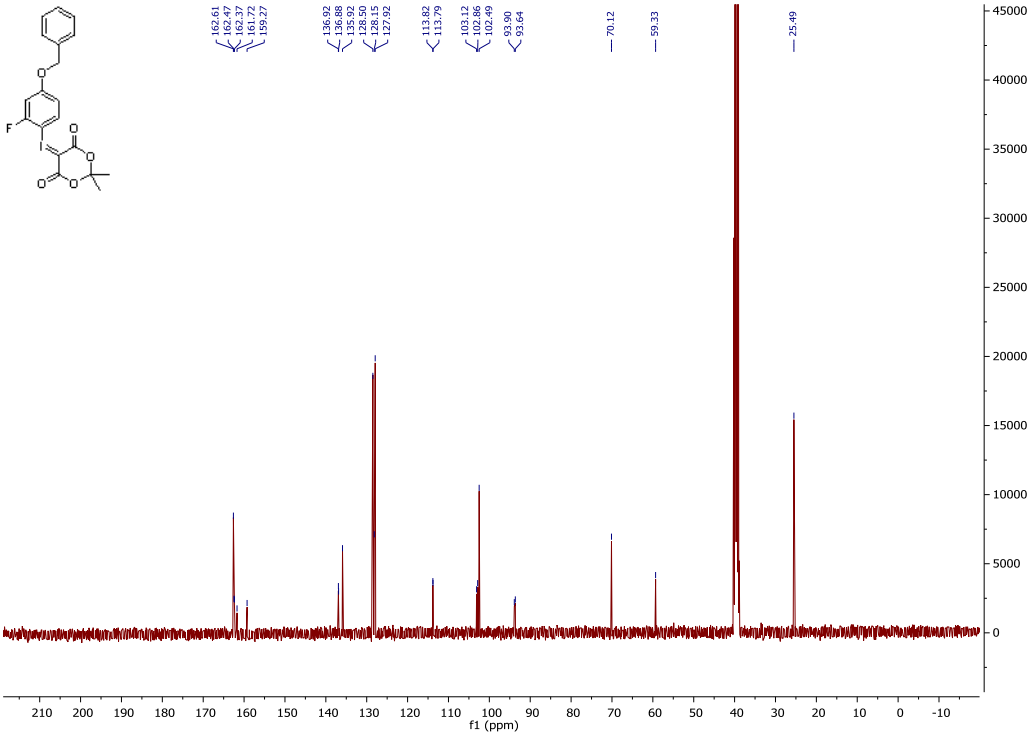
5-((4-methoxyphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



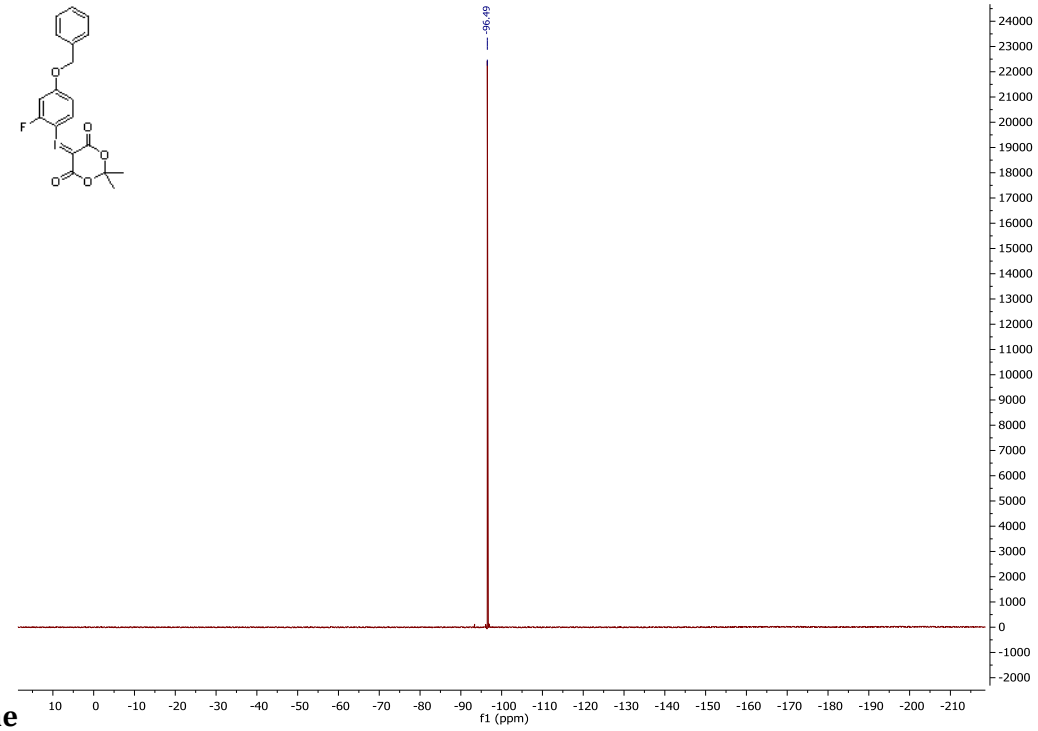
5-((4-(benzyloxy)-2-fluorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



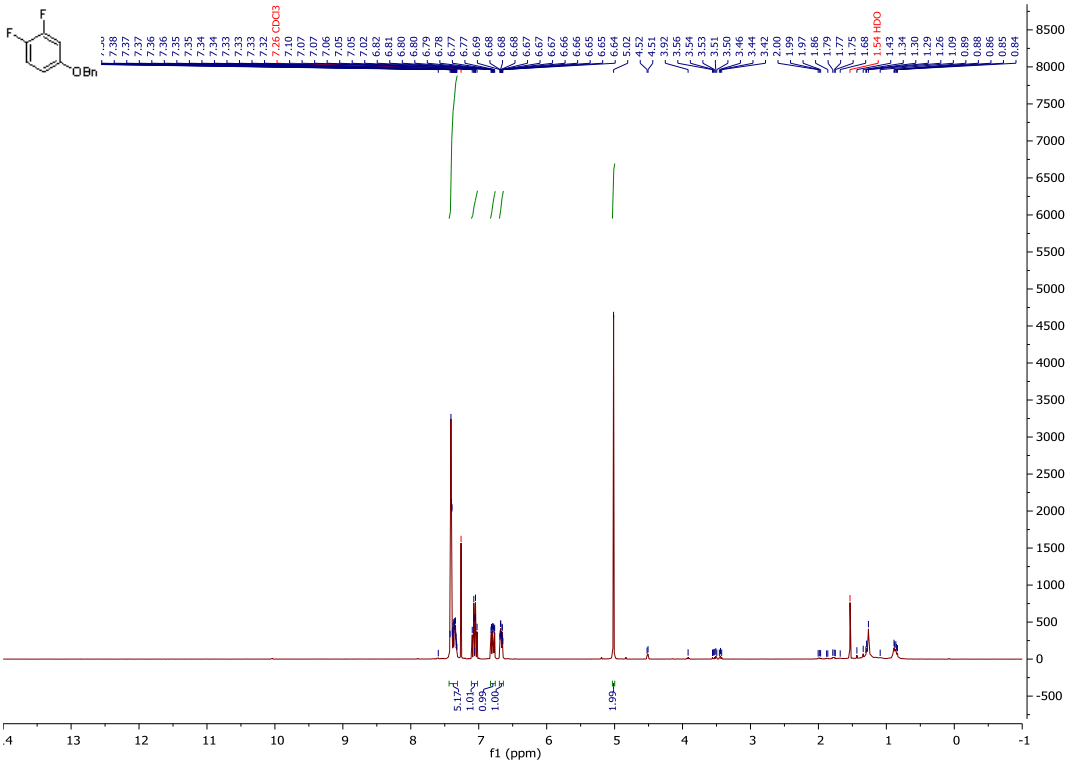
5-((4-(benzyloxy)-2-fluorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



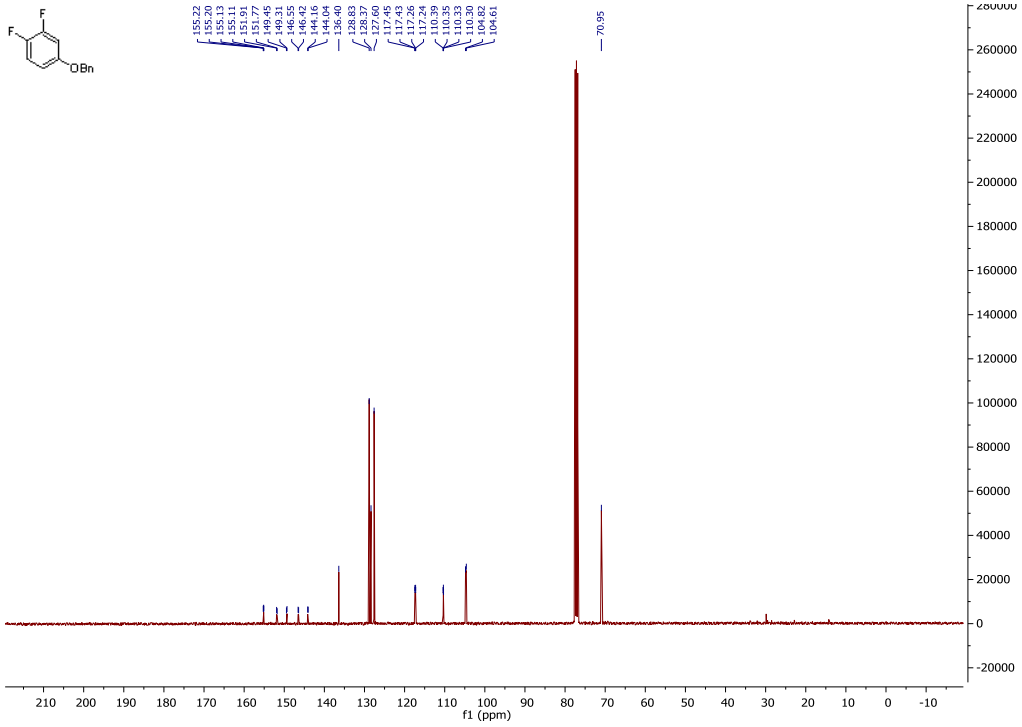
5-((4-(benzyloxy)-2-fluorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



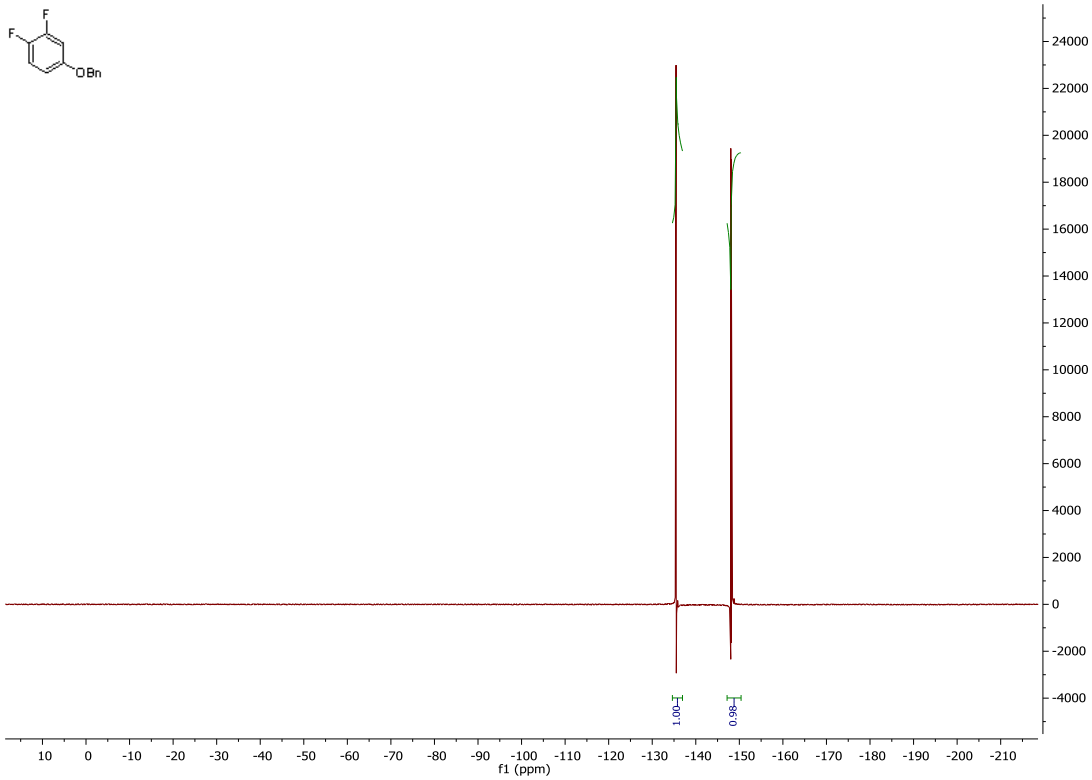
4-(benzyloxy)-1,2-difluorobenzene



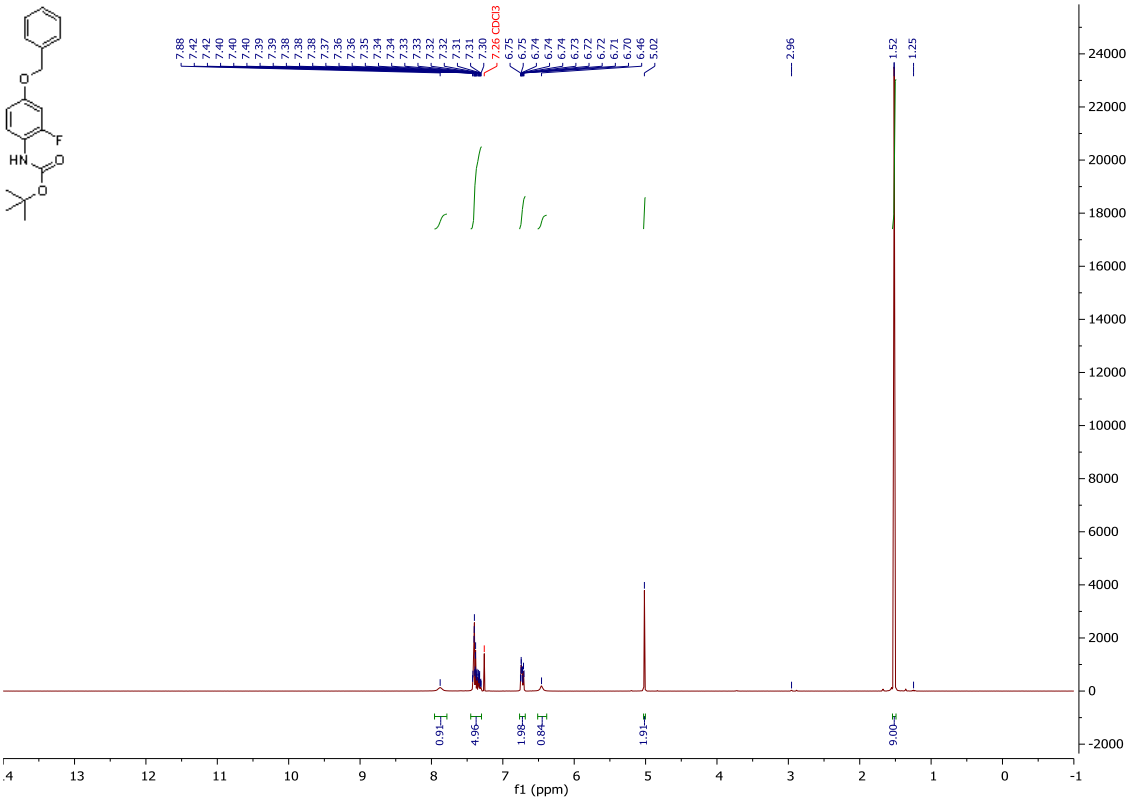
4-(benzyloxy)-1,2-difluorobenzene



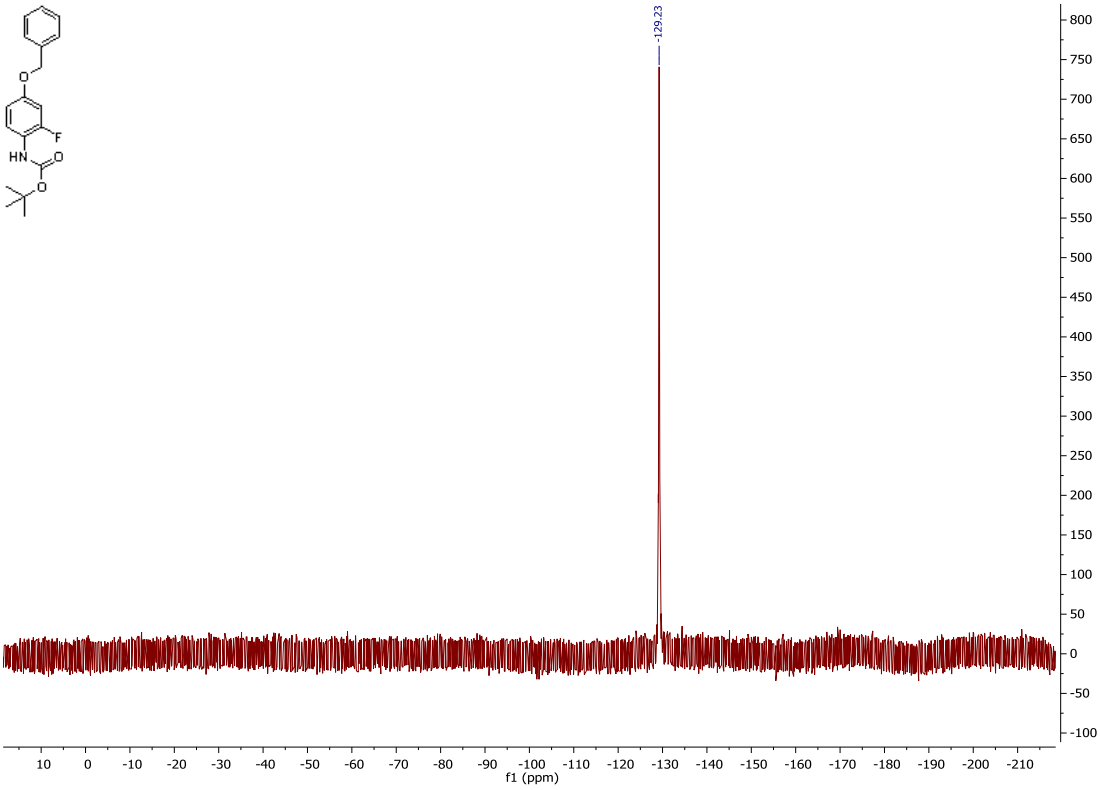
4-(benzyloxy)-1,2-difluorobenzene



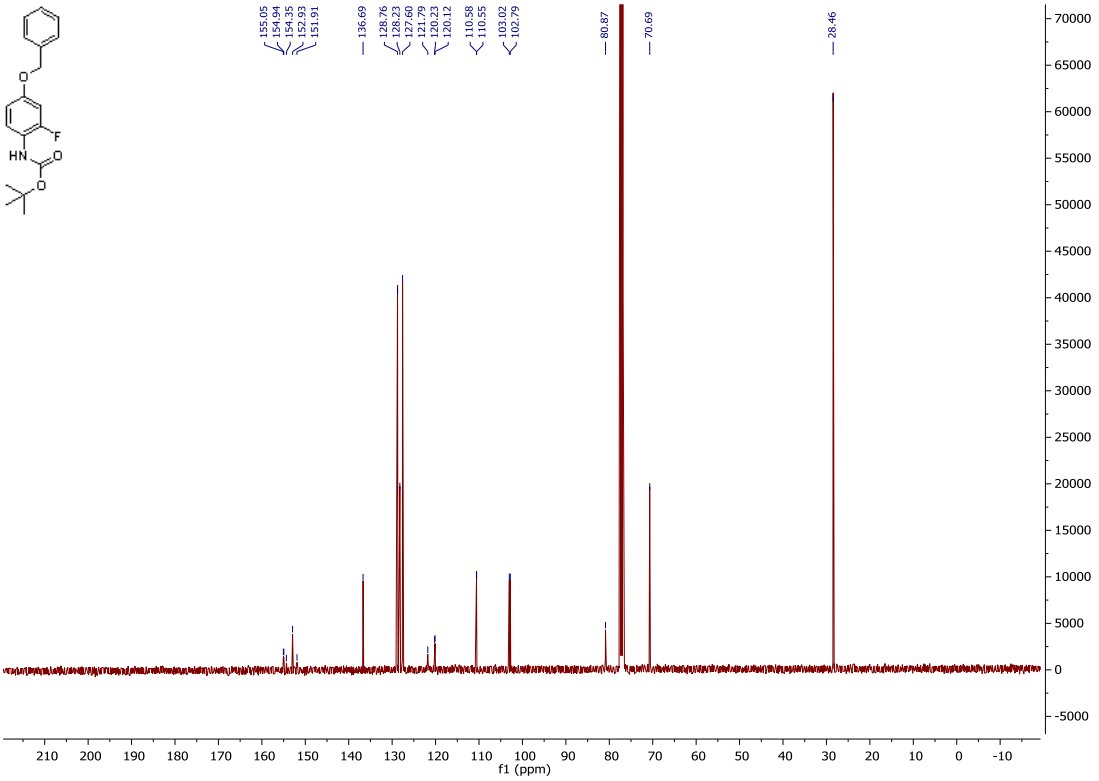
tert-butyl (4-(benzyloxy)-2-fluorophenyl)carbamate



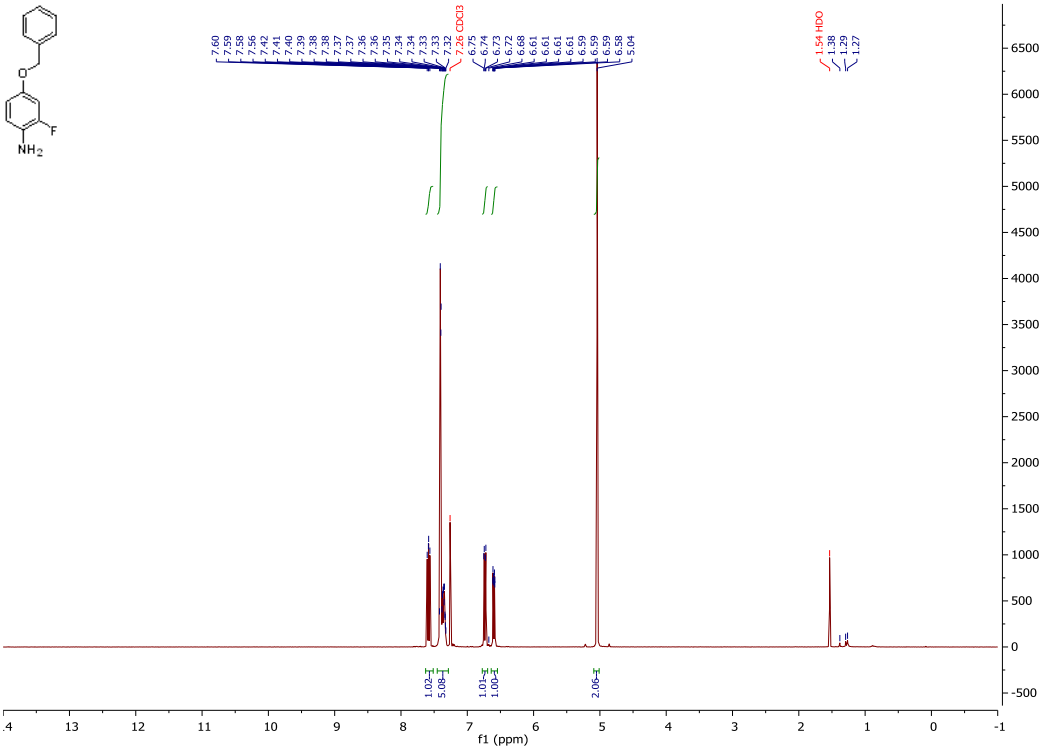
tert-butyl (4-(benzyloxy)-2-fluorophenyl)carbamate



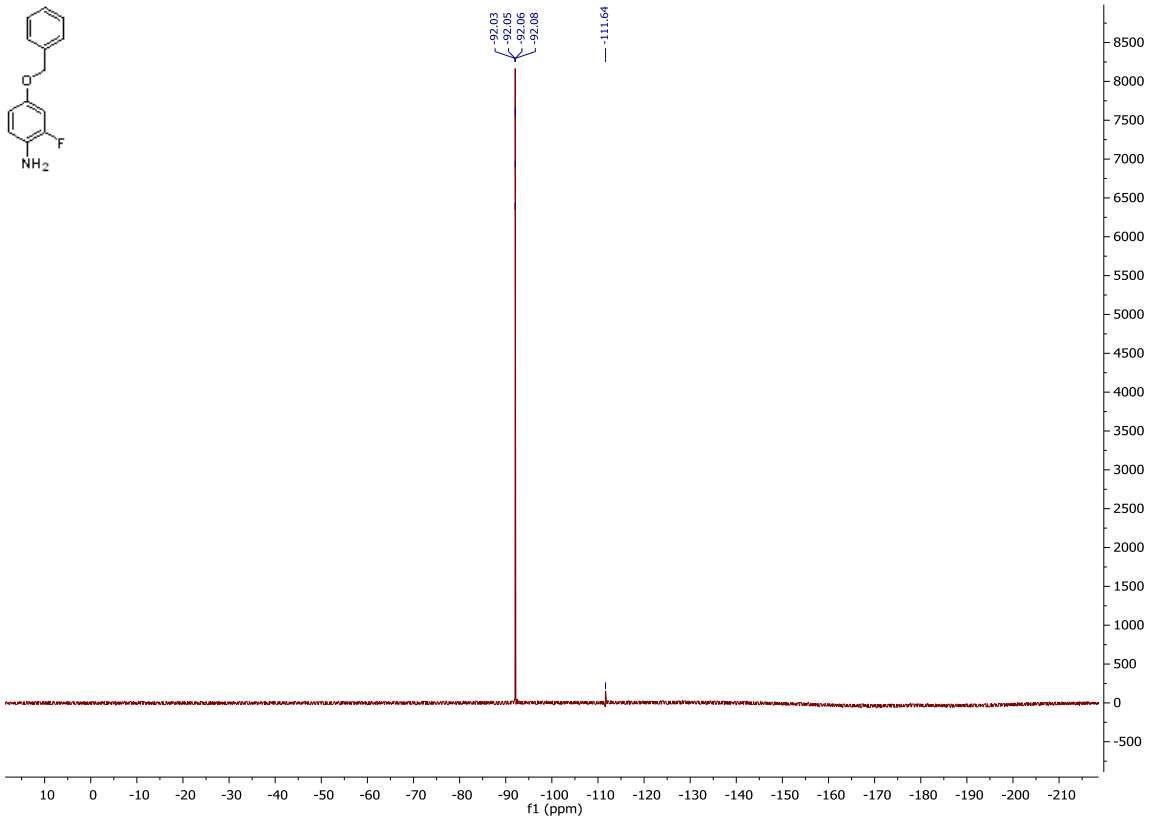
tert-butyl (4-(benzyloxy)-2-fluorophenyl)carbamate



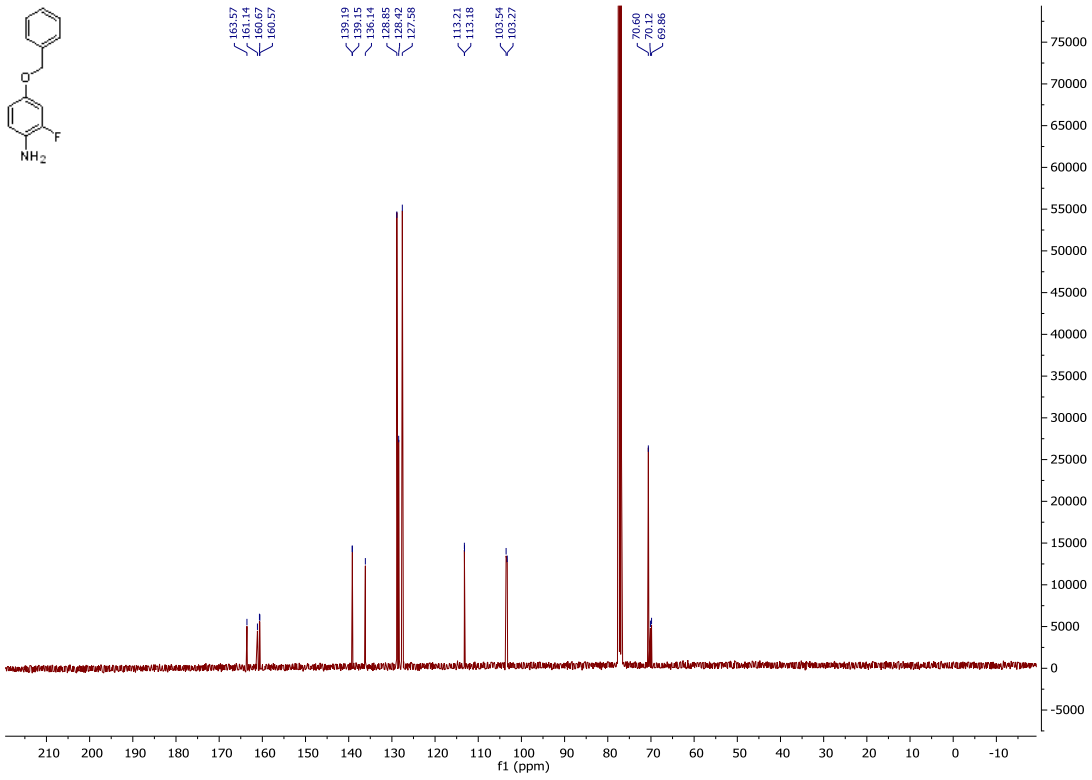
4-(benzyloxy)-2-fluoroaniline



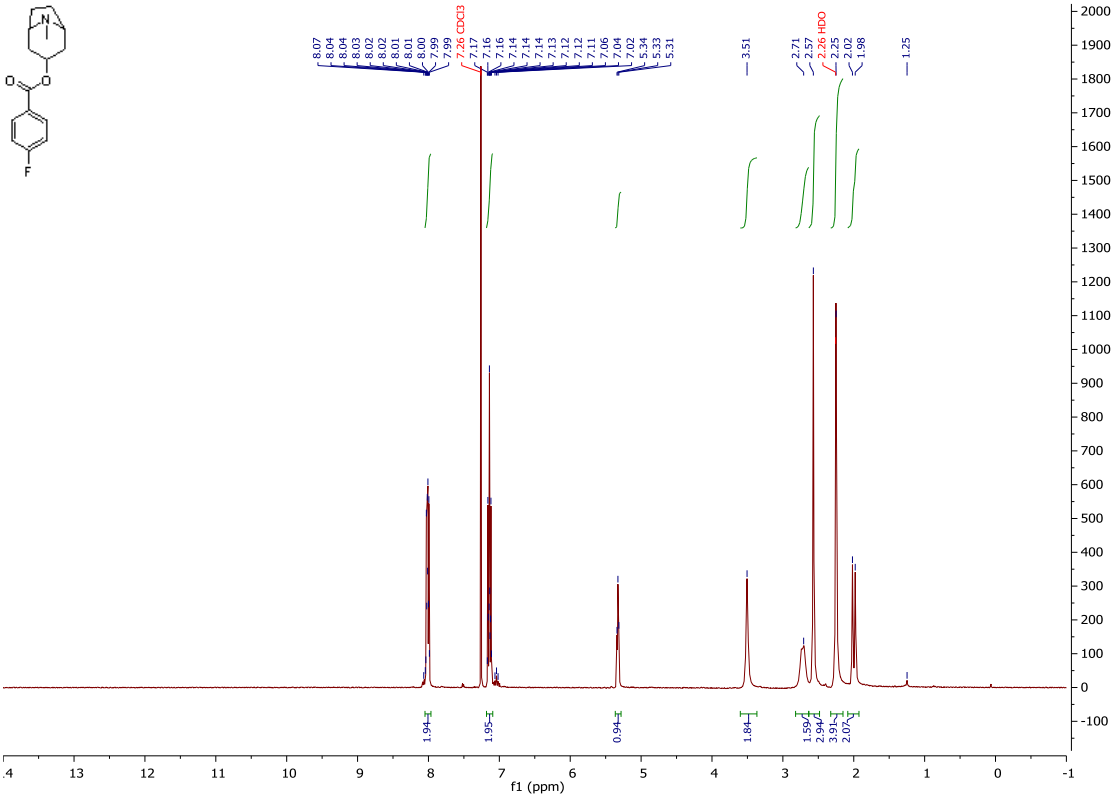
4-(benzyloxy)-2-fluoroaniline



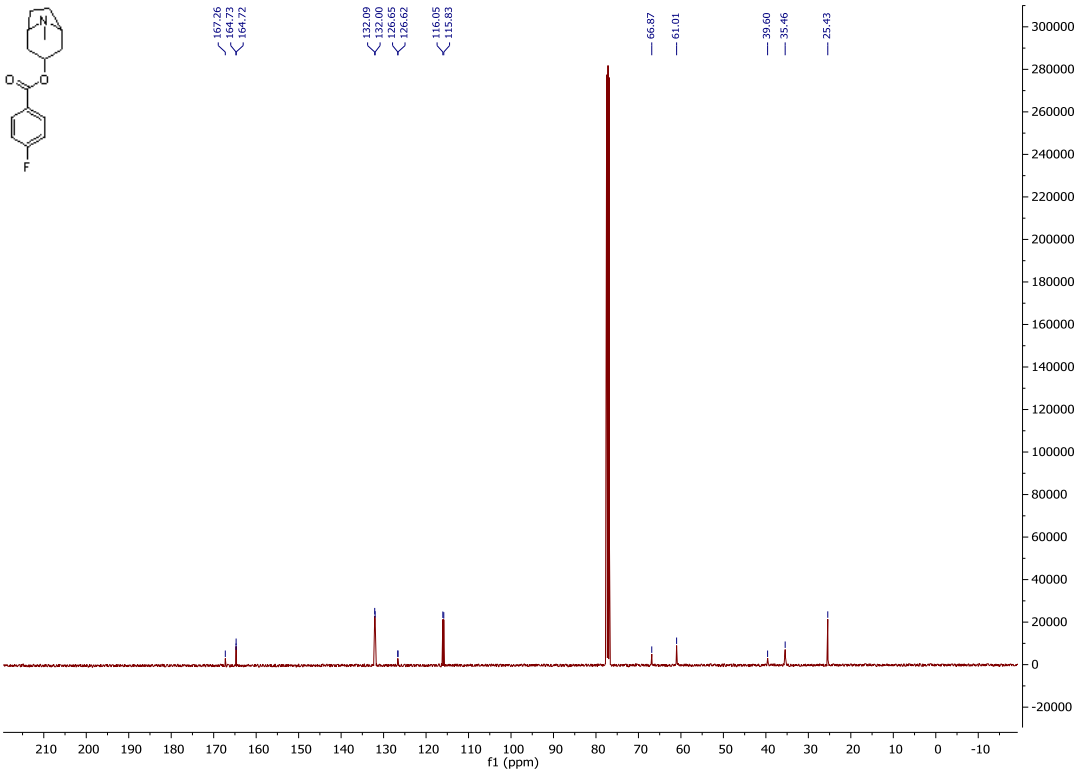
4-(benzyloxy)-2-fluoroaniline



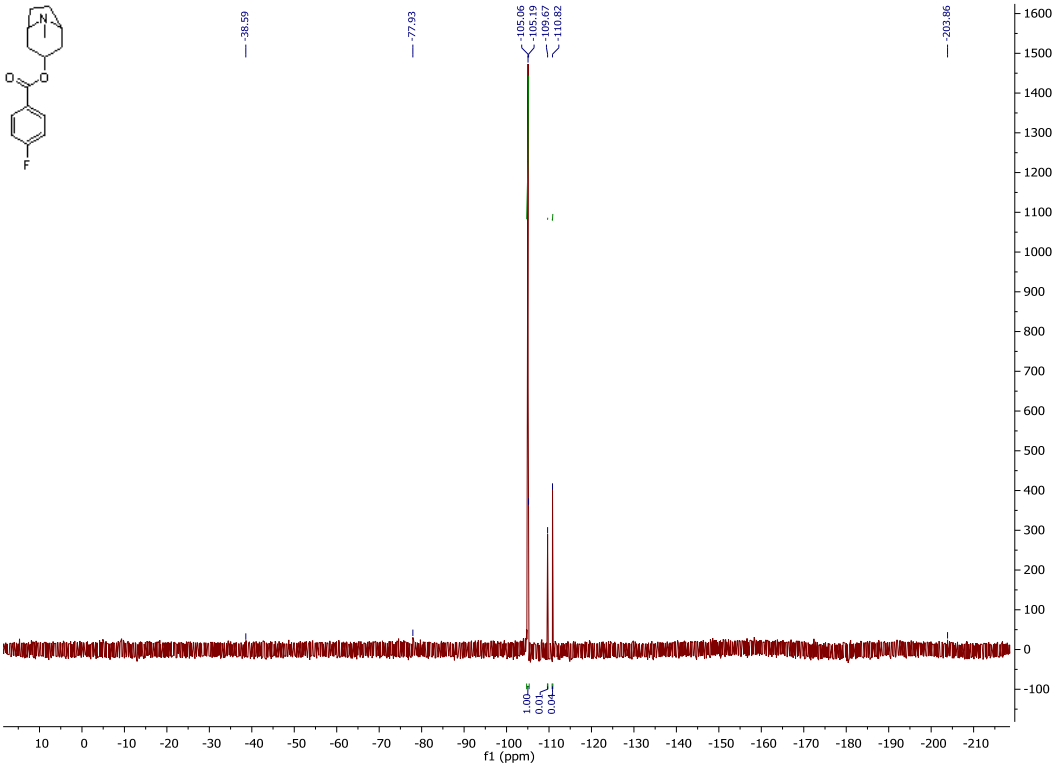
8-methyl-8-azabicyclo[3.2.1]octan-3-yl **4-fluorobenzoate**



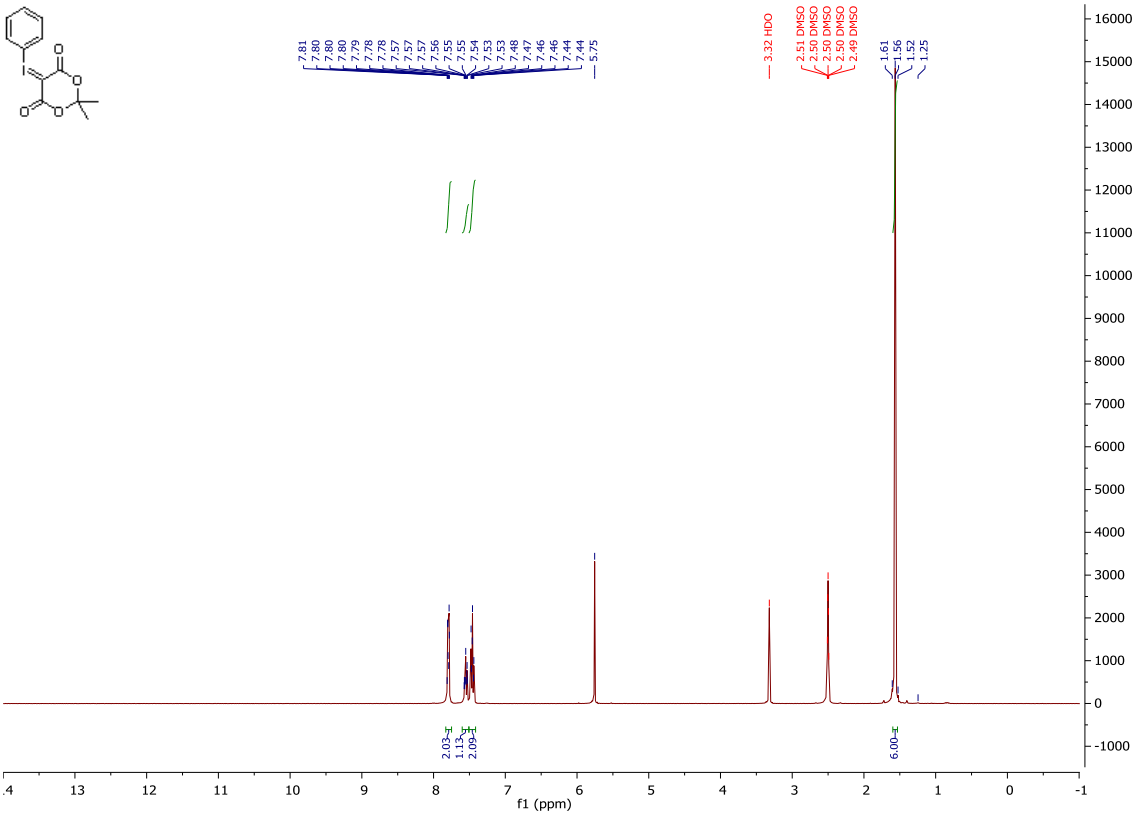
8-methyl-8-azabicyclo[3.2.1]octan-3-yl **4-fluorobenzoate**



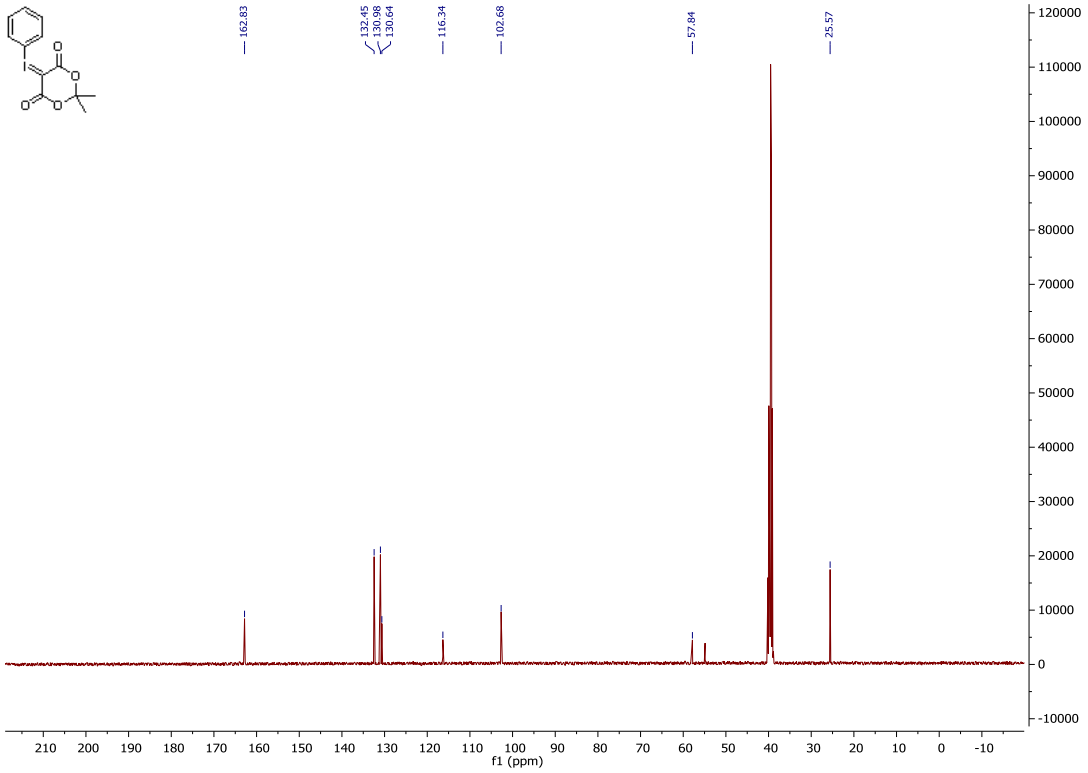
8-methyl-8-azabicyclo[3.2.1]octan-3-yl 4-fluorobenzoate



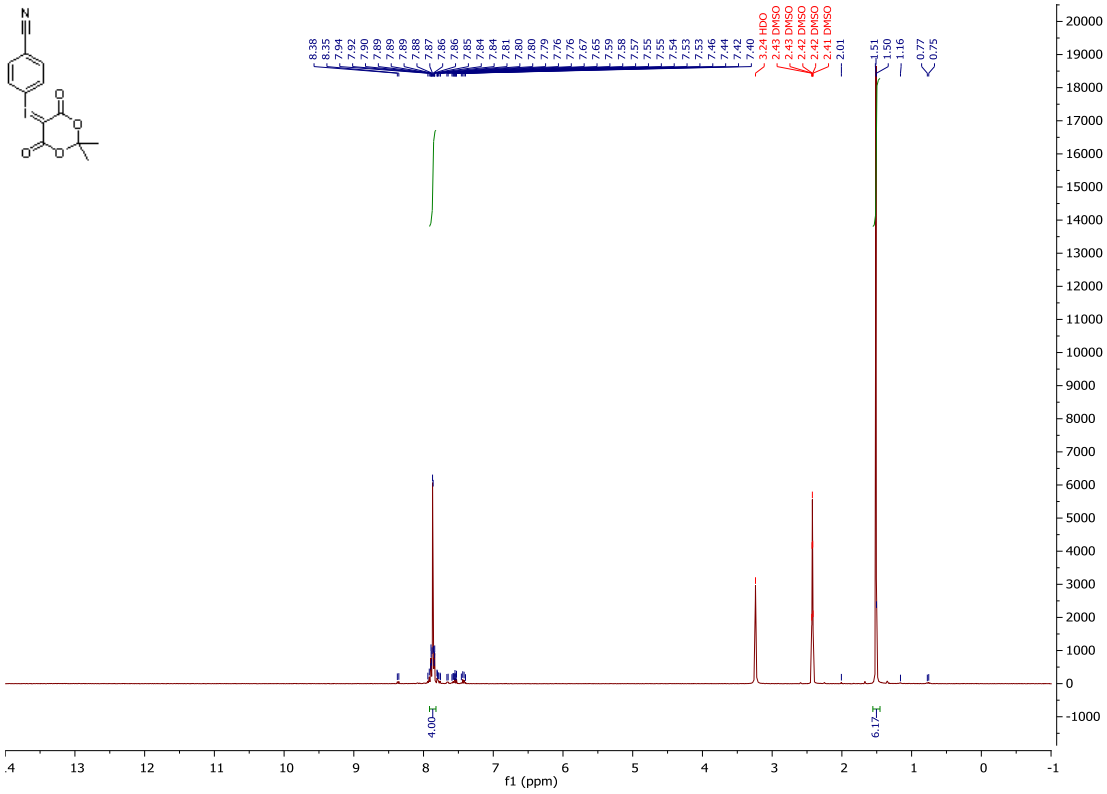
2,2-dimethyl-5-(phenyl-l3-iodaneylidene)-1,3-dioxane-4,6-dione



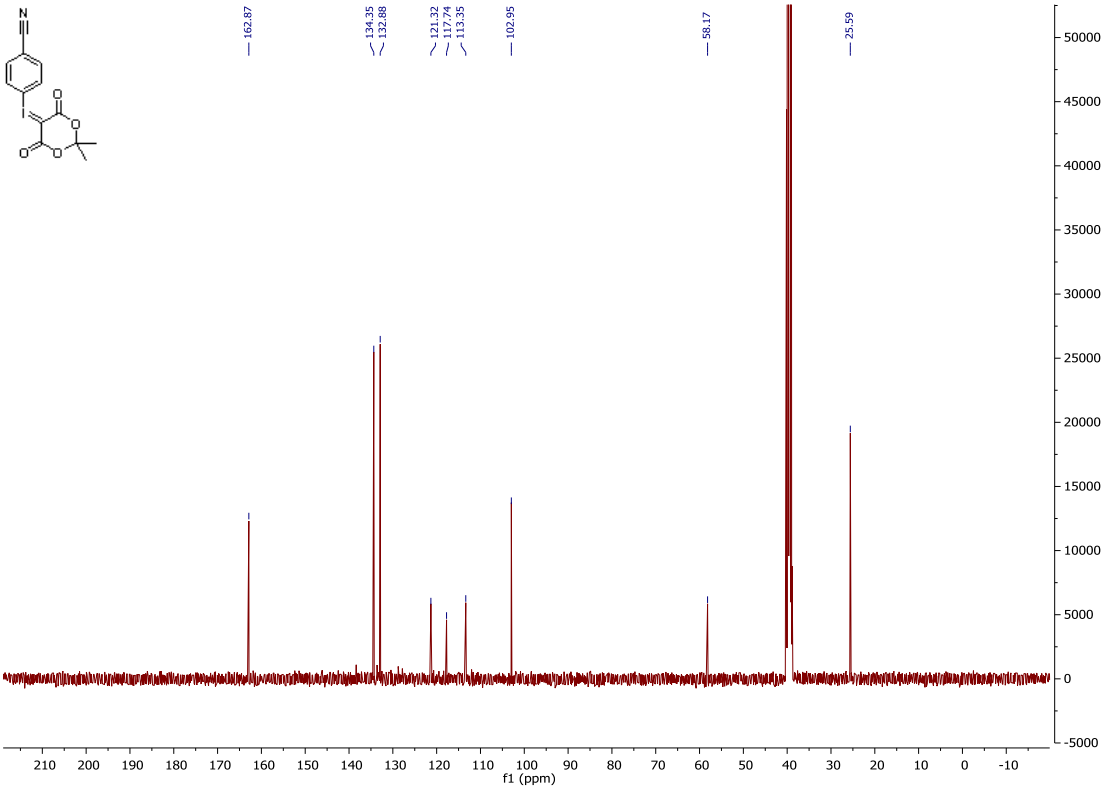
2,2-dimethyl-5-(phenyl-l3-iodaneylidene)-1,3-dioxane-4,6-dione



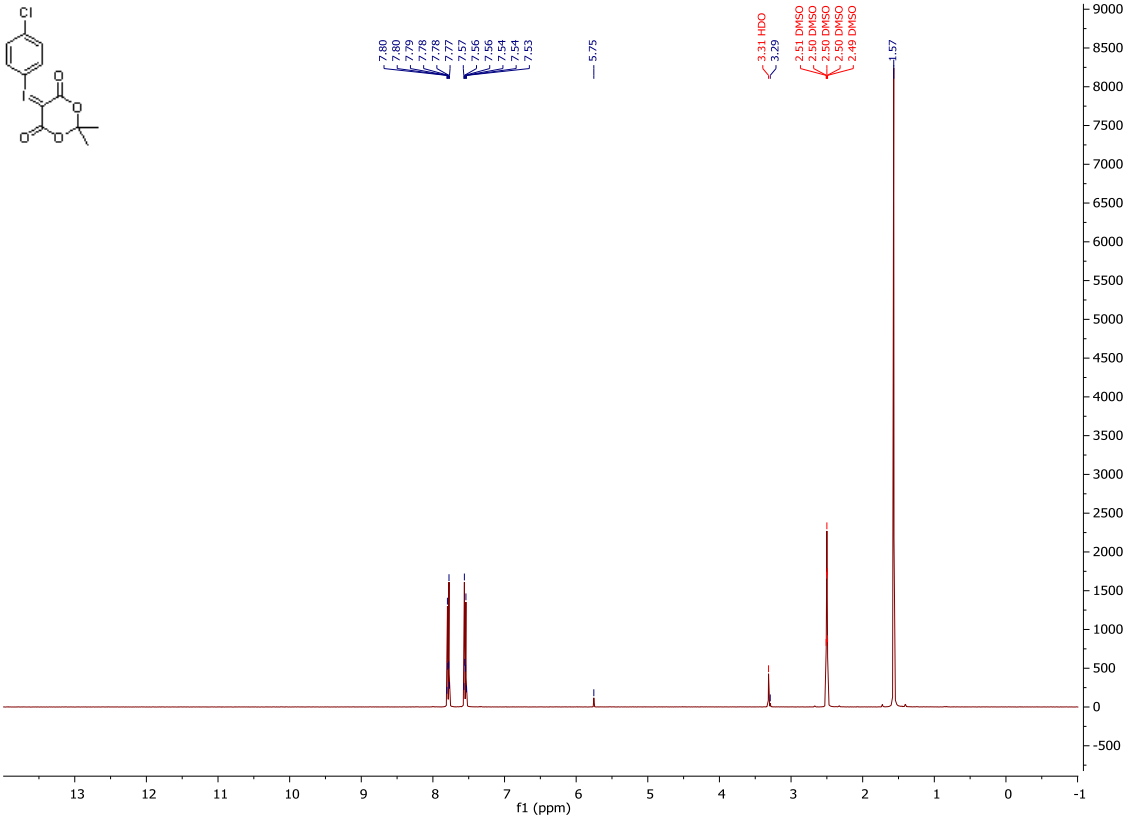
4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzonitrile



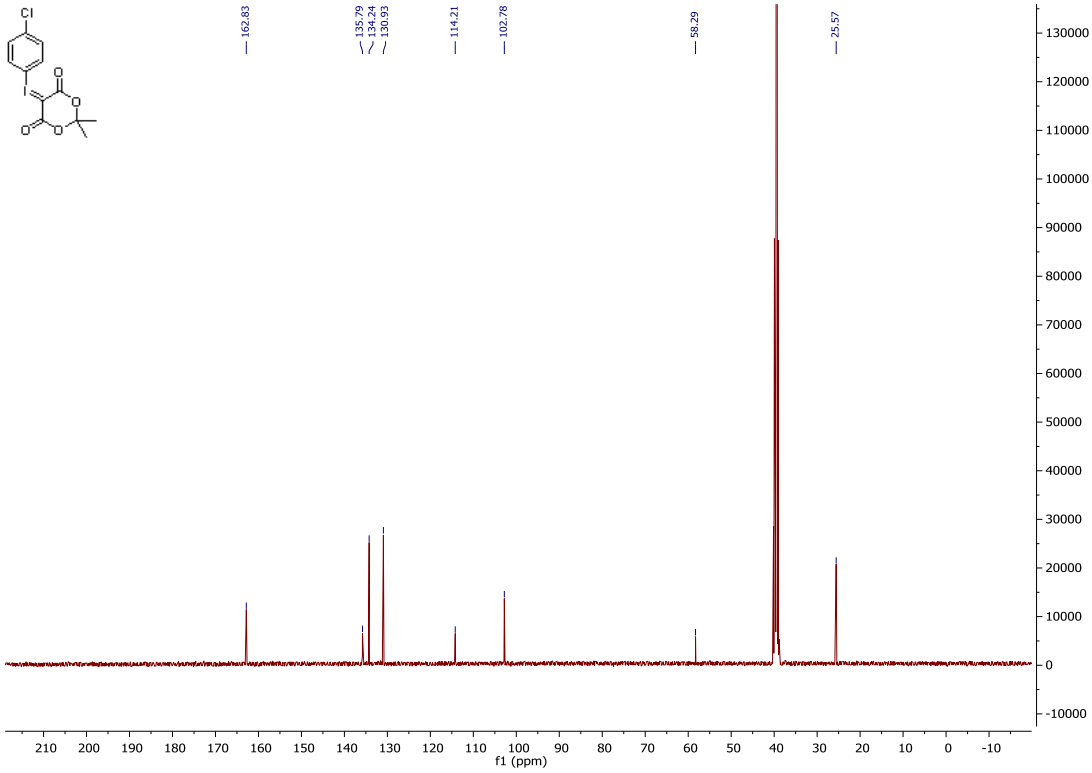
4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)benzonitrile



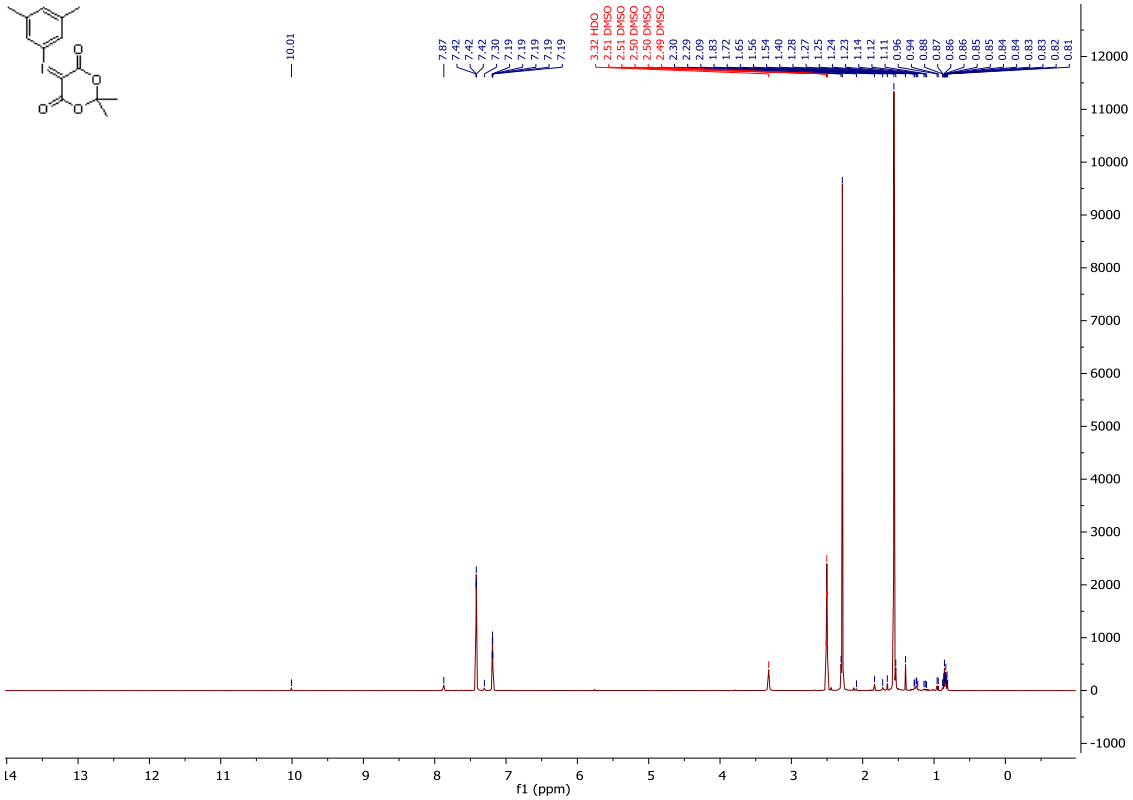
5-((4-chlorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



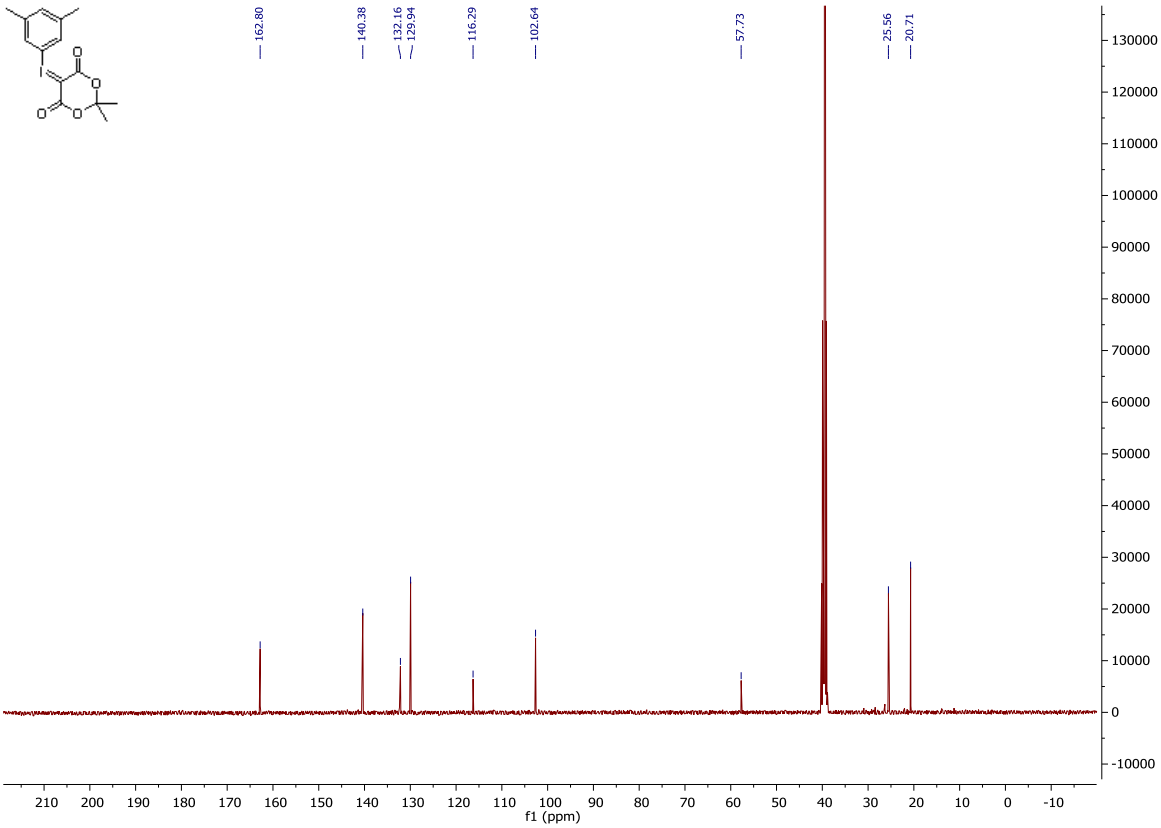
5-((4-chlorophenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



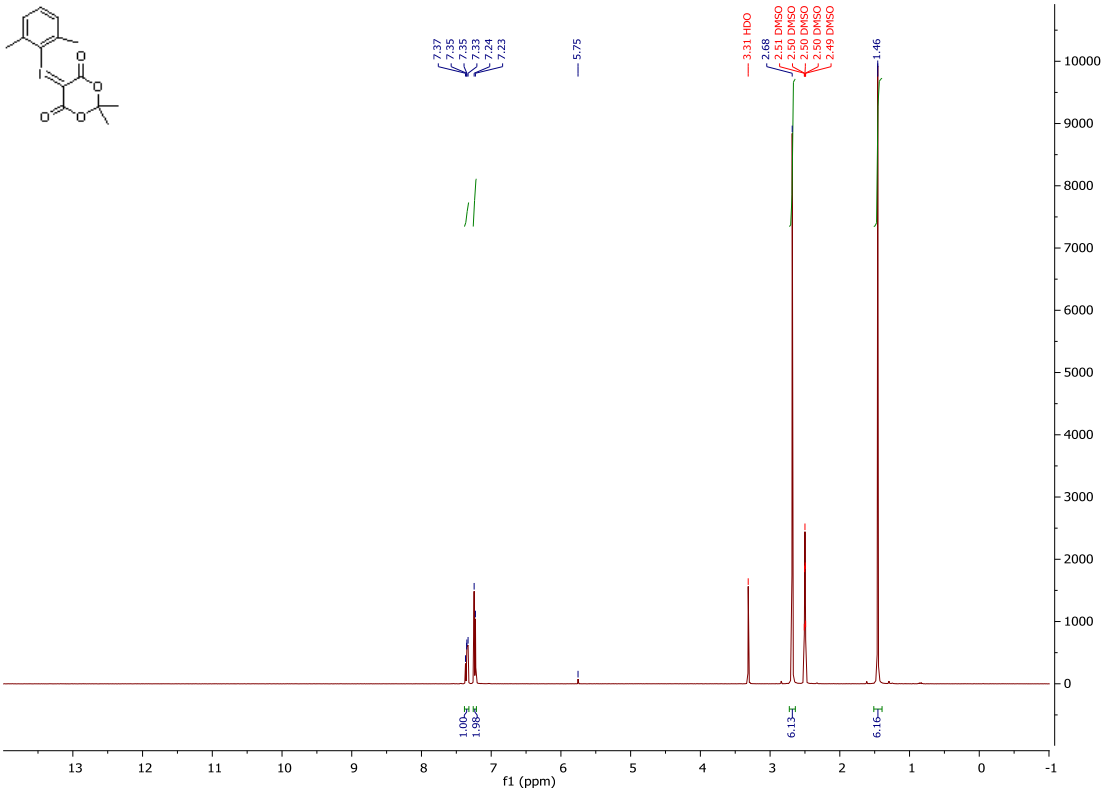
5-((3,5-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



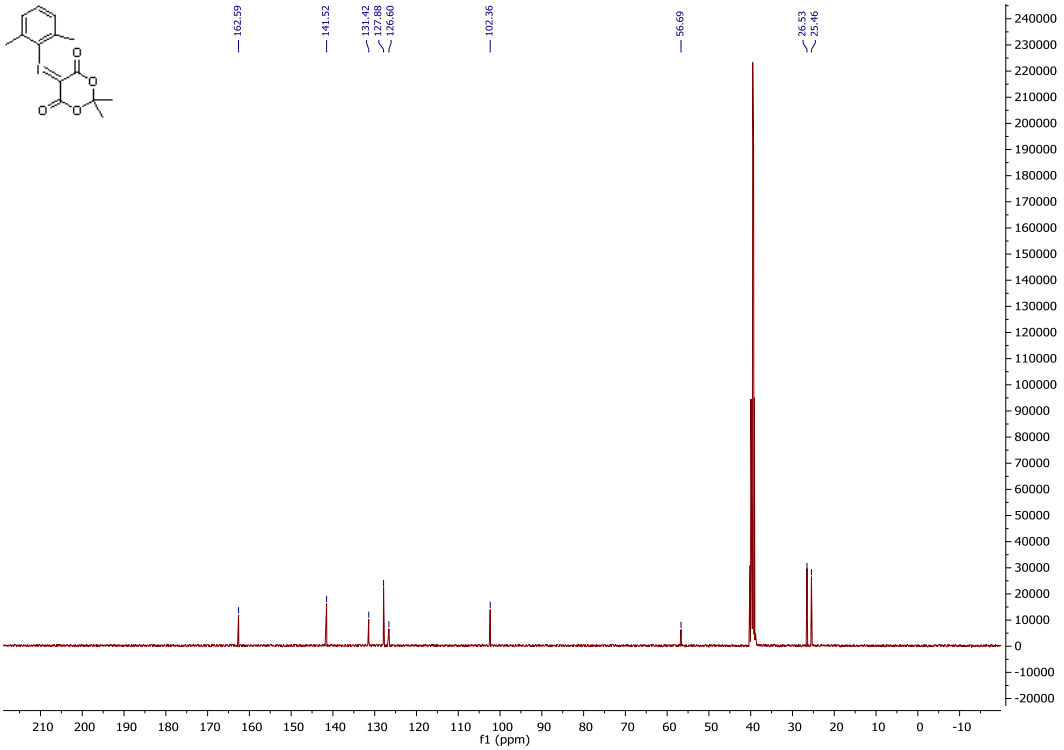
5-((3,5-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



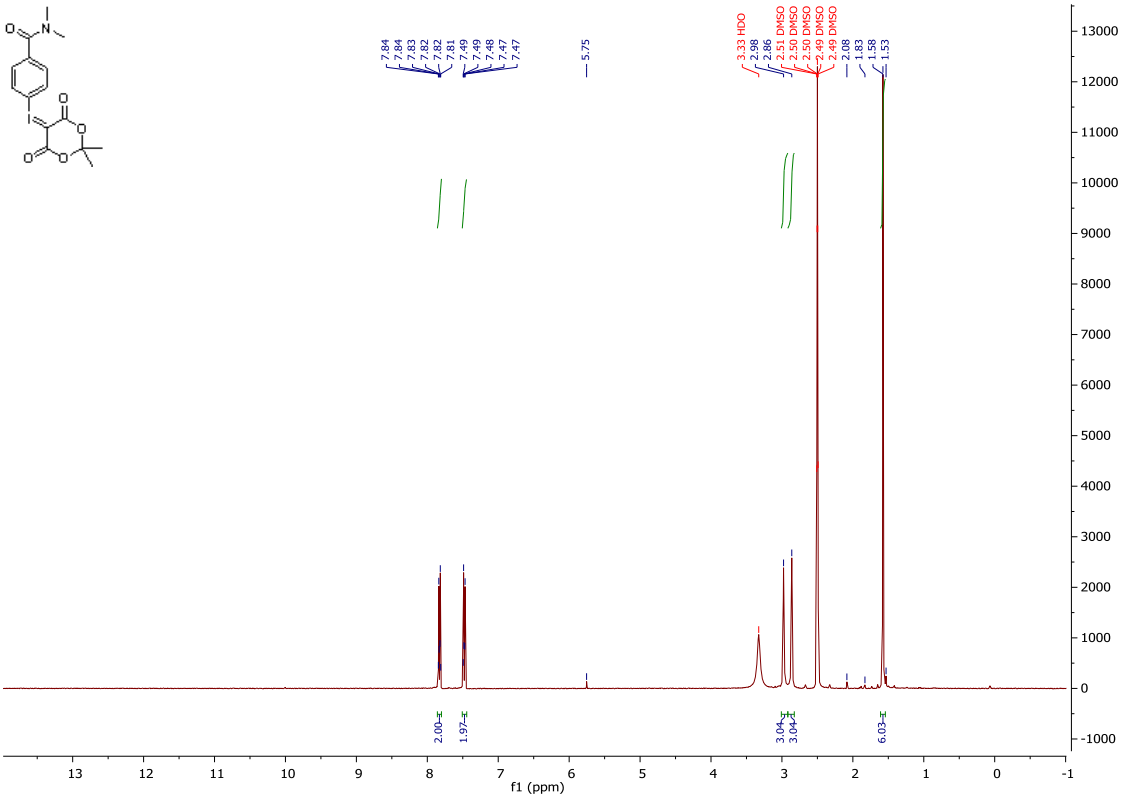
5-((2,6-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



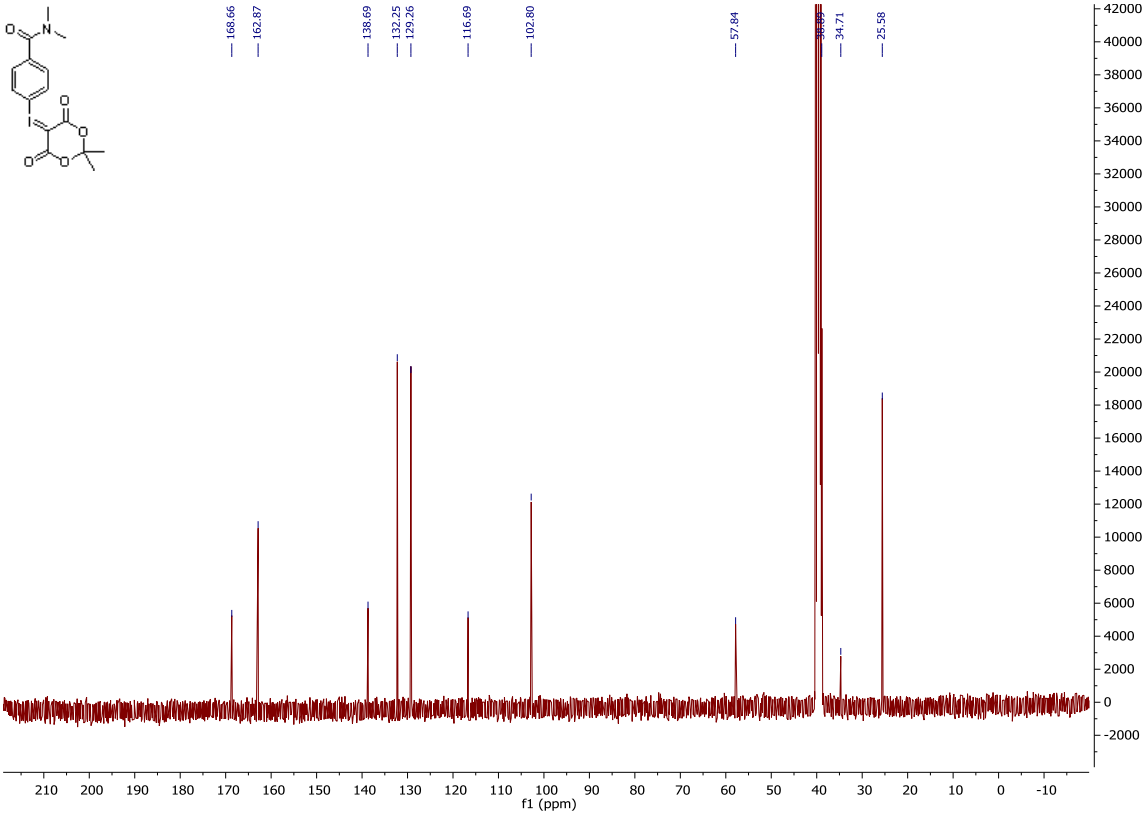
5-((2,6-dimethylphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



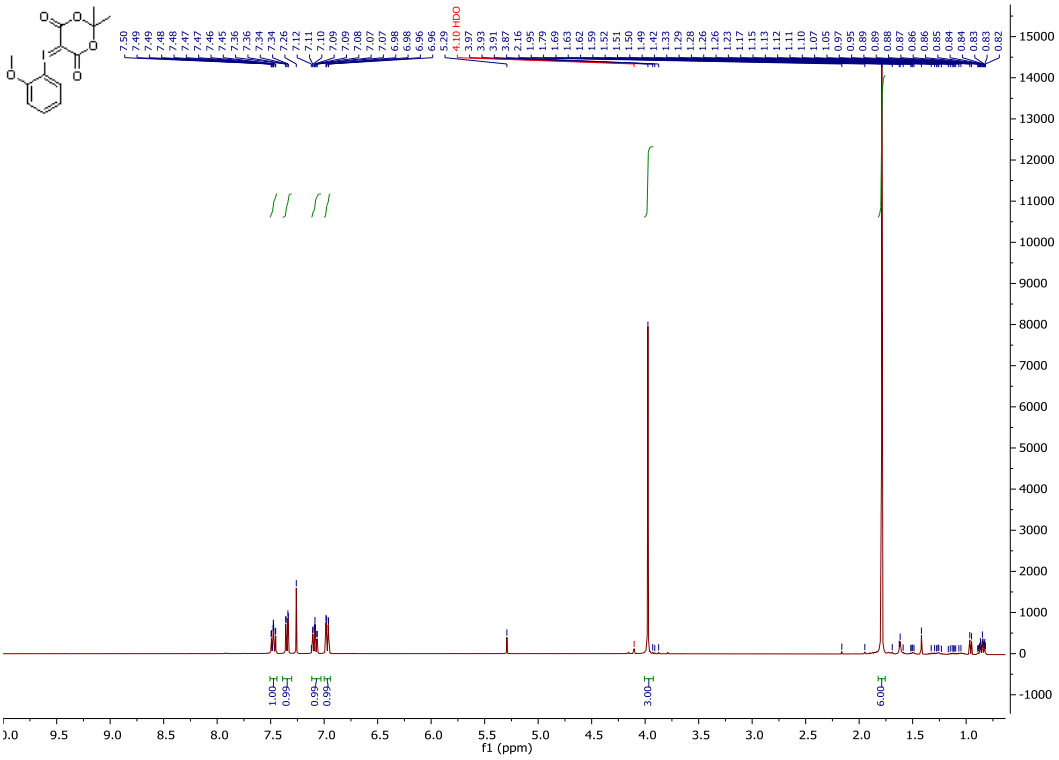
4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-N,N-dimethylbenzamide



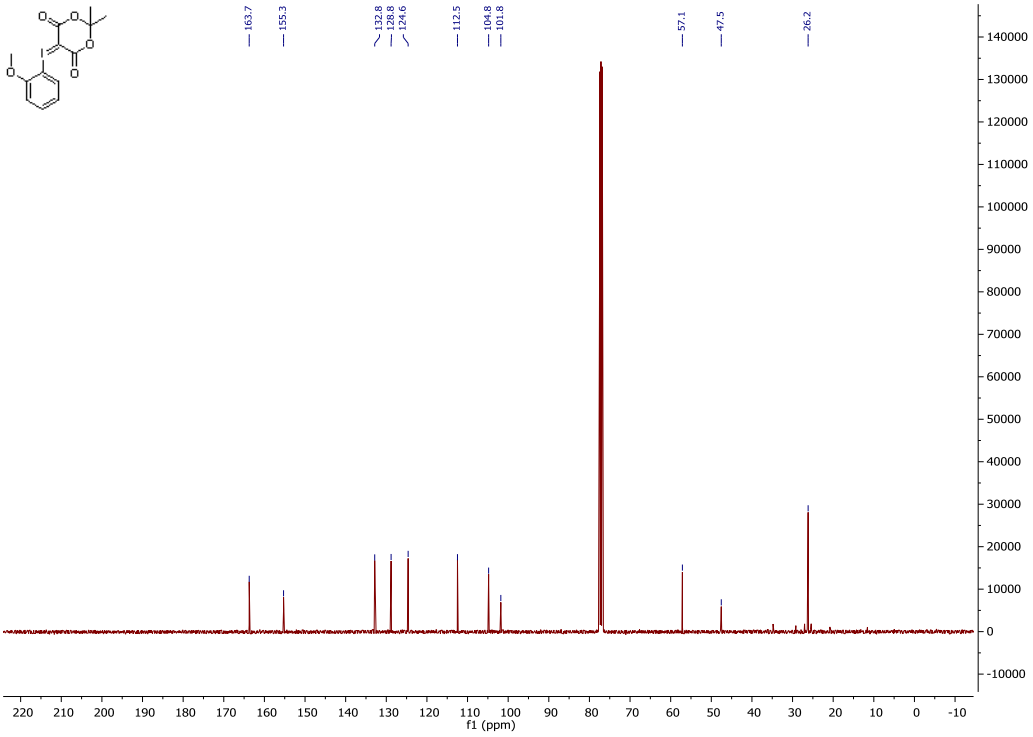
4-((2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-l3-iodaneyl)-N,N-dimethylbenzamide



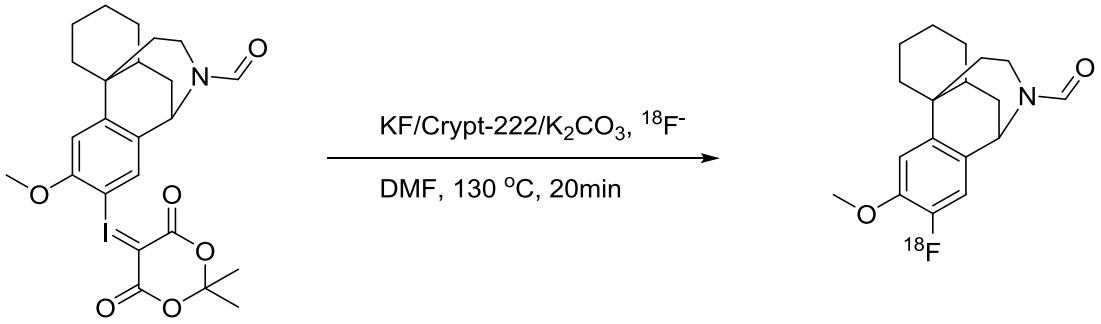
5-((2-methoxyphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



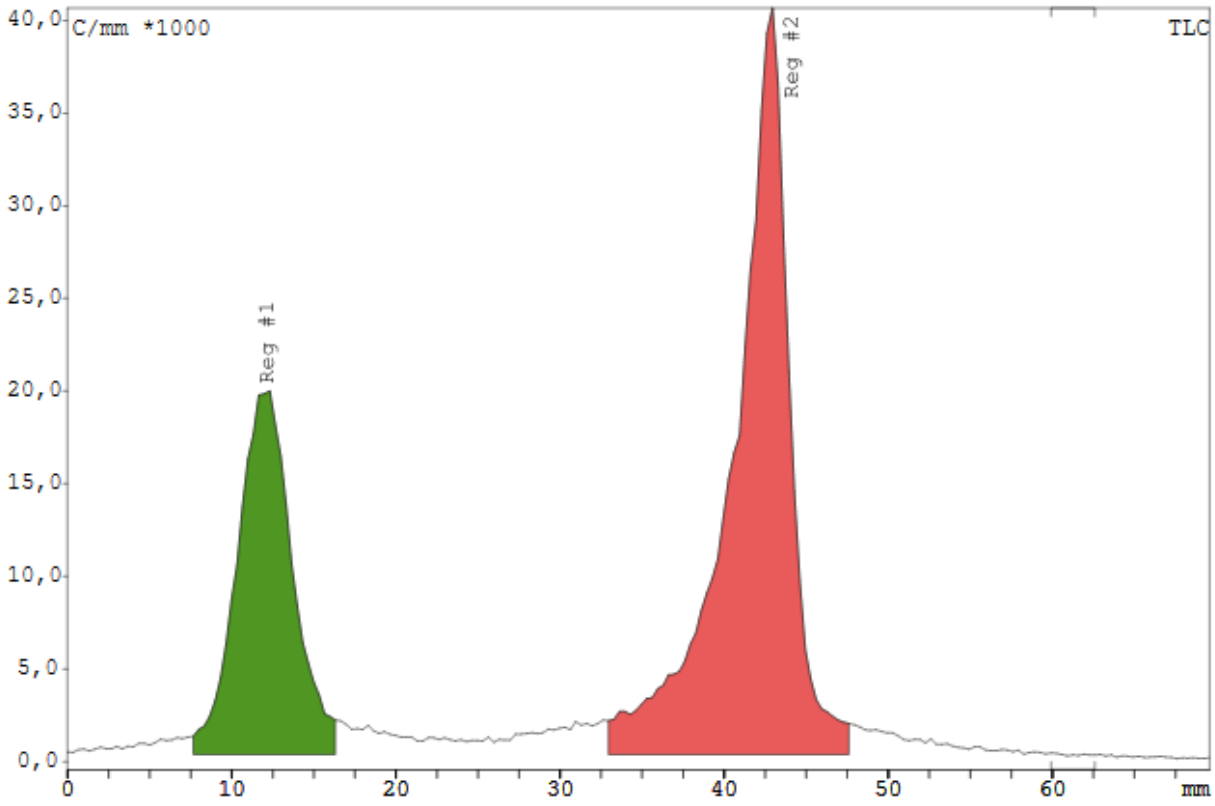
5-((2-methoxyphenyl)-l3-iodaneylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione



RadioTLC



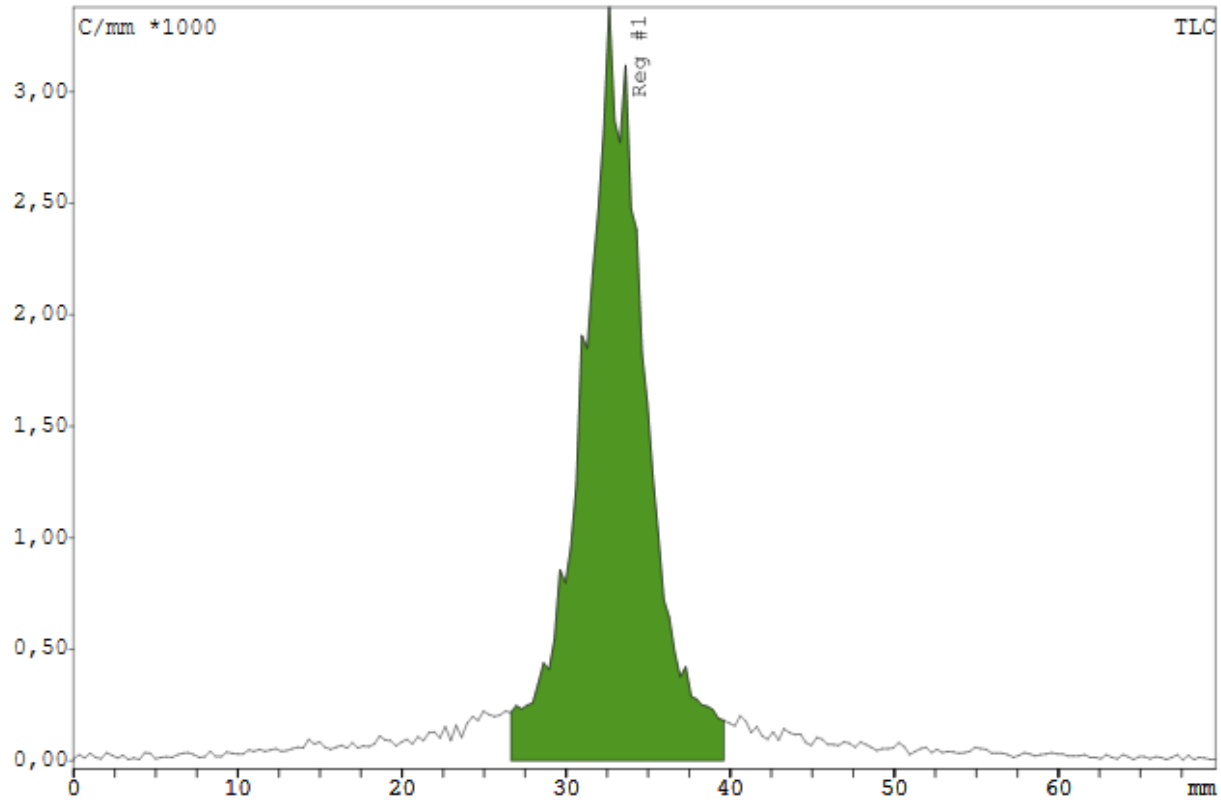
Crude reaction mixture radioTLC for radiofluorination experiment.



Integration TLC

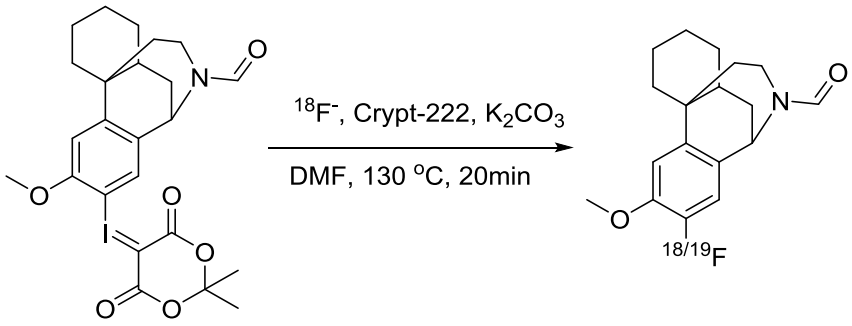
Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,171	28,82	DD	76808,8	32,48
Reg #2	0,610	59,92	DD	159701,5	67,52
Sum in ROI				236510,3	
Total area				266504,4	
Area RF				266437,8	
BKG1				386,35	
Remainder RF				29927,50	11,23
Remainder (Tot)				29994,13	11,25

radioTLC after C18 and Si cartridge purification

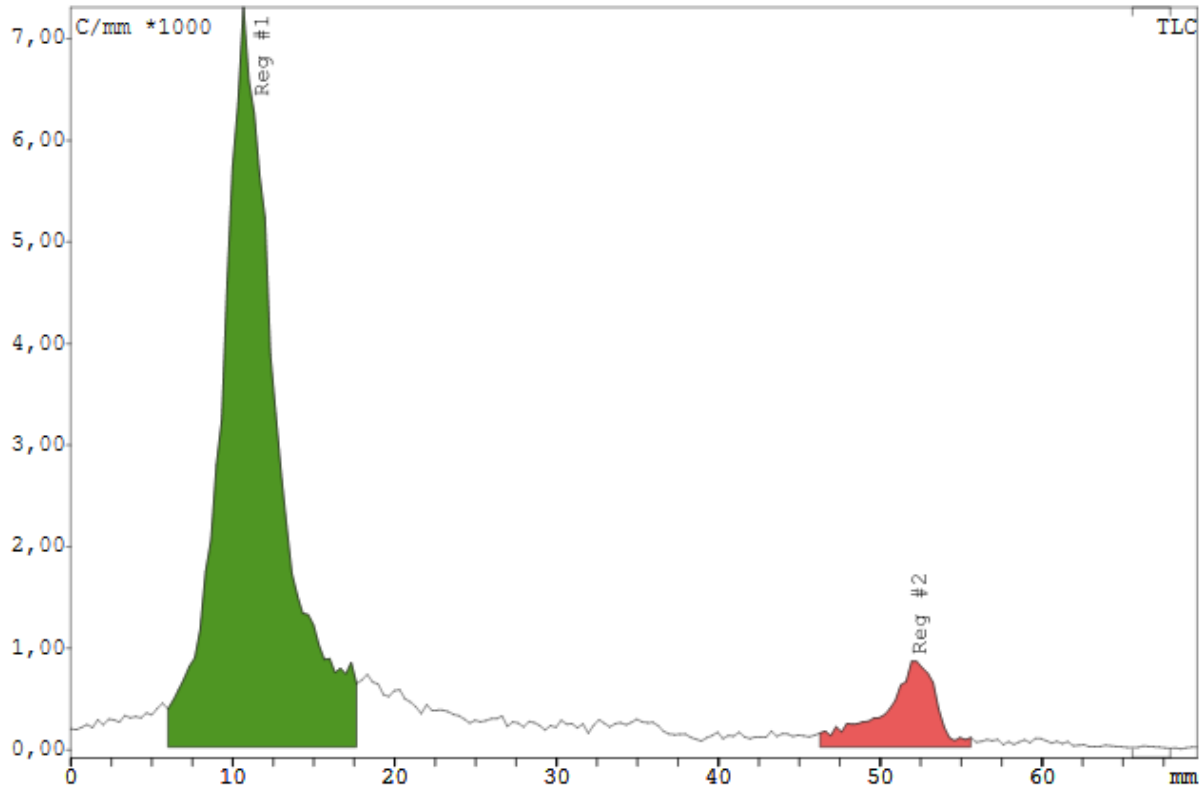


Integration TLC

Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,471	81,20	DD	14932,00	100,00
Sum in ROI				14932,00	
Total area				18390,00	
Area RF				18392,00	



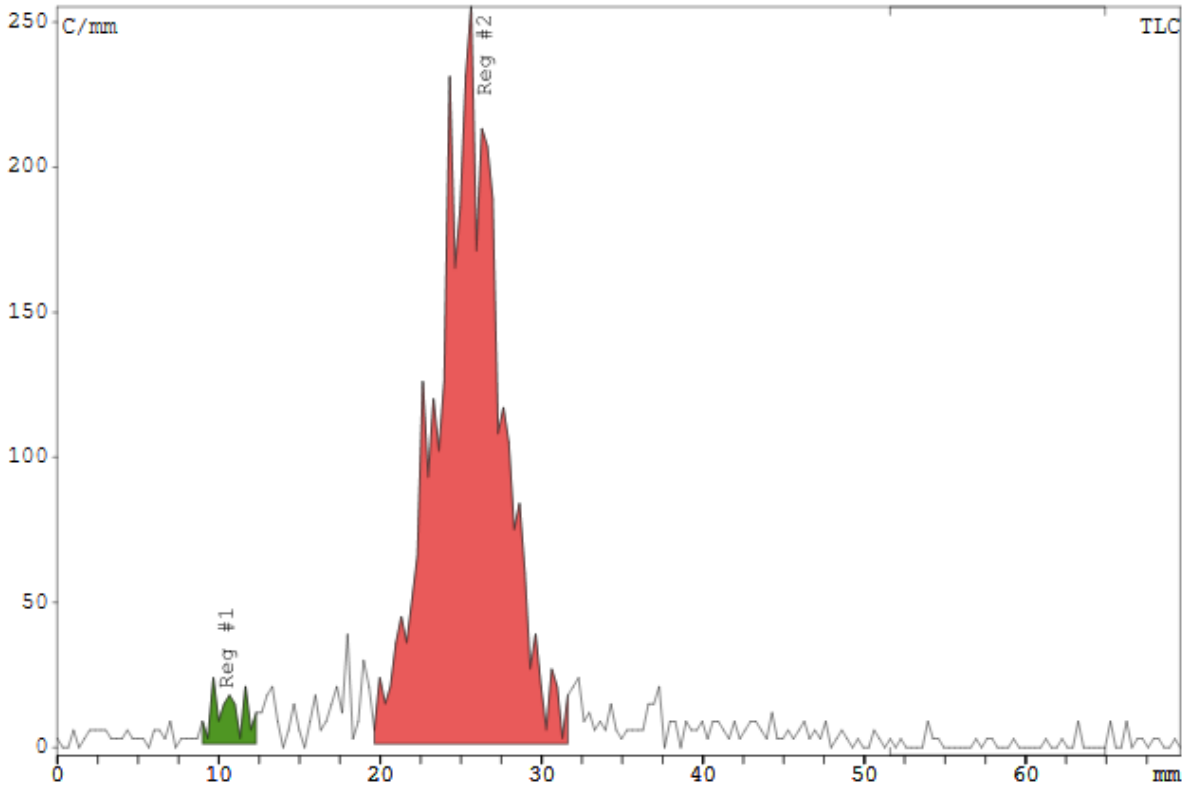
Crude reaction mixture radioTLC for carrier added radiofluorination experiment.



Integration TLC

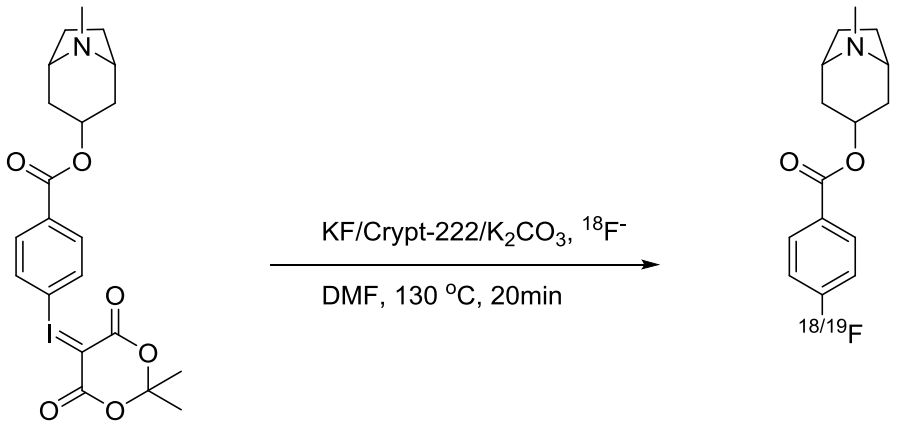
Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,152	70,15	DD	28978,00	90,04
Reg #2	0,748	7,76	DD	3204,00	9,96
Sum in ROI				32182,00	
Total area				41308,29	
Area RF				41308,00	
BKG1				27,892	
Remainder RF				9126,00	22,09
Remainder (Tot)				9126,29	22,09

radioTLC after C18 and Si cartridge purification

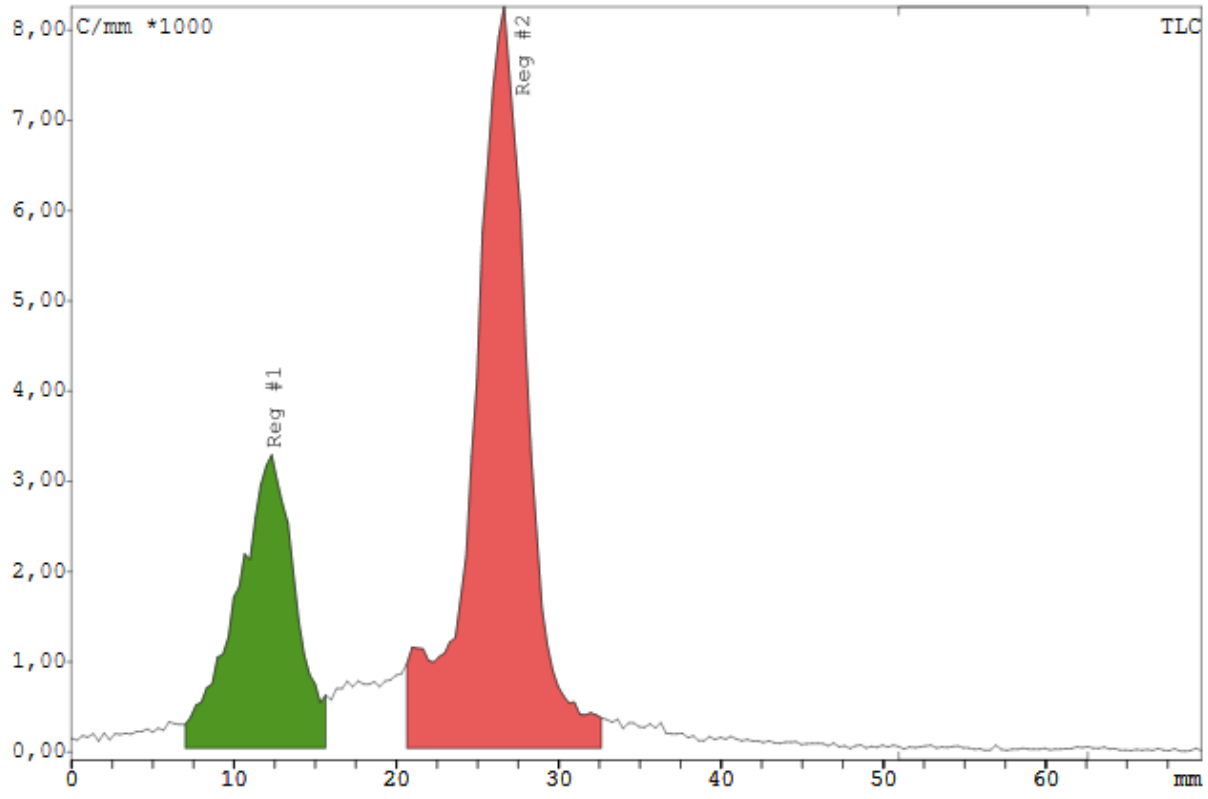


Integration TLC

Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,148	2,67	DD	37,000	3,19
Reg #2	0,371	80,84	DD	1121,600	96,81
Sum in ROI				1158,600	
Total area				1387,400	
Area RF				1388,000	
BKG1				1,2015	
Remainder RF				229,40	16,53
Remainder (Tot)				228,80	16,49



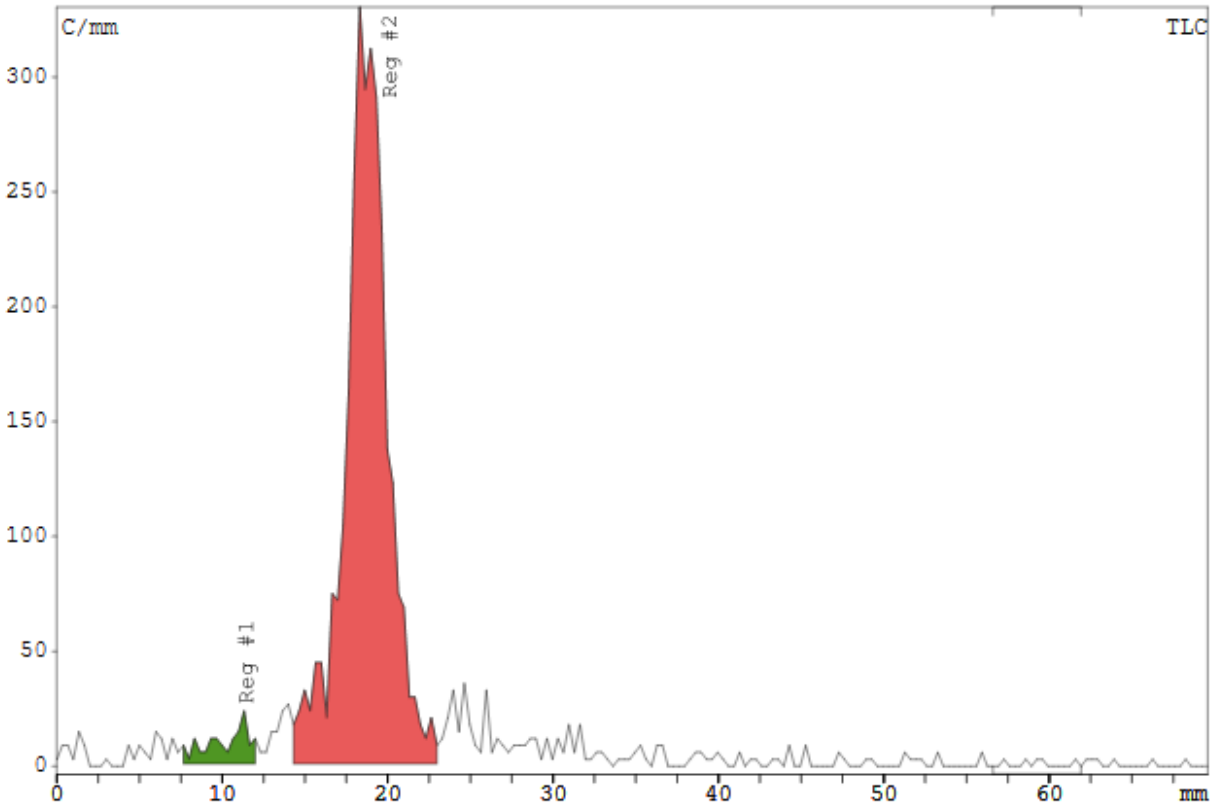
Crude reaction mixture radioTLC for radiofluorination experiment.



Integration TLC

Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,176	25,98	DD	13447,83	29,86
Reg #2	0,381	61,03	DD	31586,69	70,14
Sum in ROI				45034,51	
Total area				51756,31	
Area RF				51756,00	
BKG1				42,996	
Remainder RF				6721,49	12,99
Remainder (Tot)				6721,80	12,99

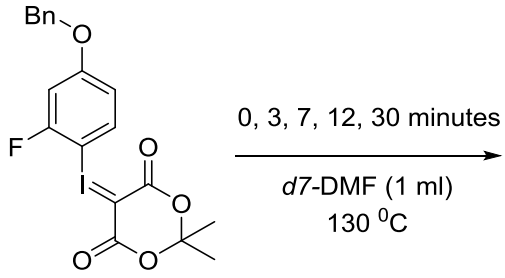
radioTLC after C18 and Si cartridge purification



Integration TLC

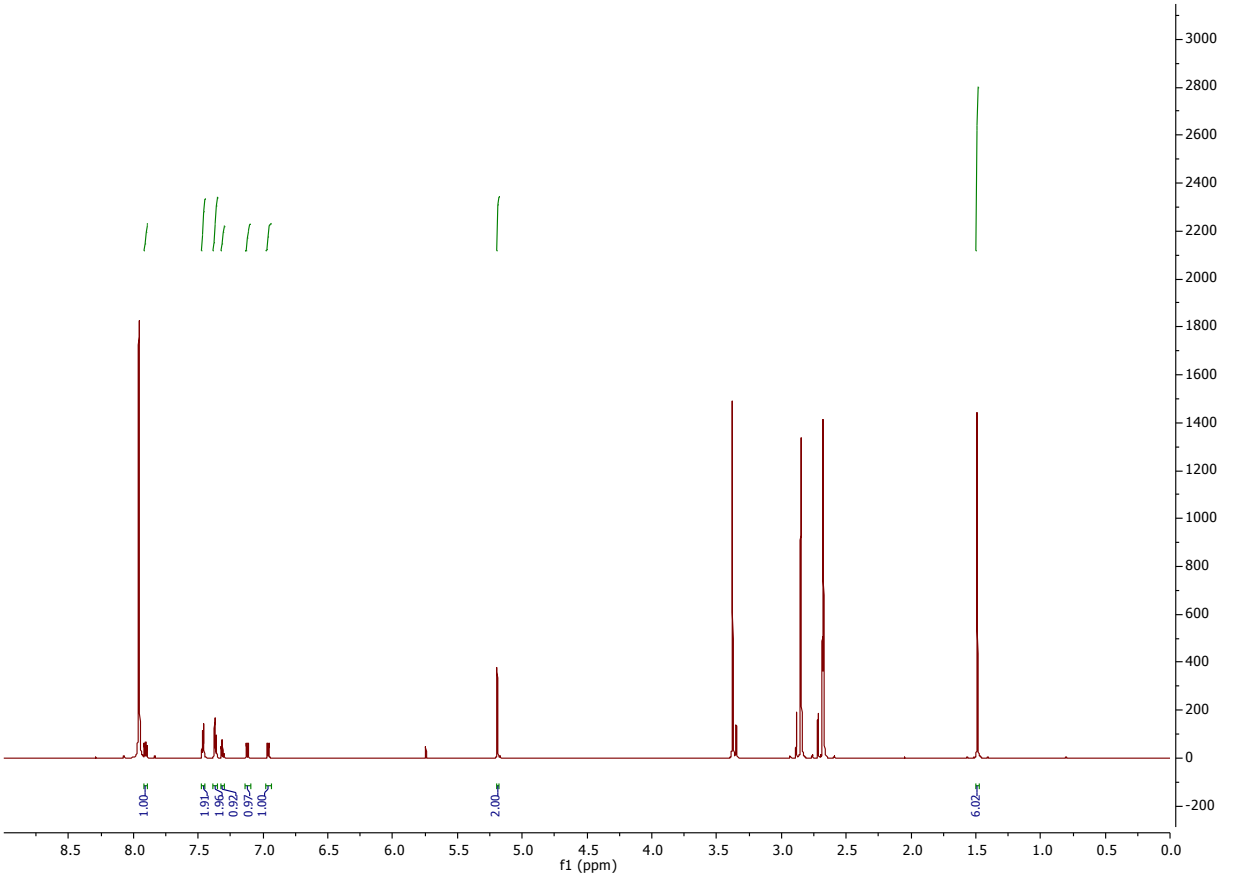
Substance	R/F	%Total	Type	Area	%Area
		%		Counts	%
Reg #1	0,162	3,42	DD	40,9375	4,16
Reg #2	0,267	78,87	DD	943,8750	95,84
Sum in ROI				984,8125	
Total area				1196,6875	
Area RF				1196,3750	
BKG1				0,93866	
Remainder RF				211,56	17,68
Remainder (Tot)				211,88	17,71

NMR degradation experiment

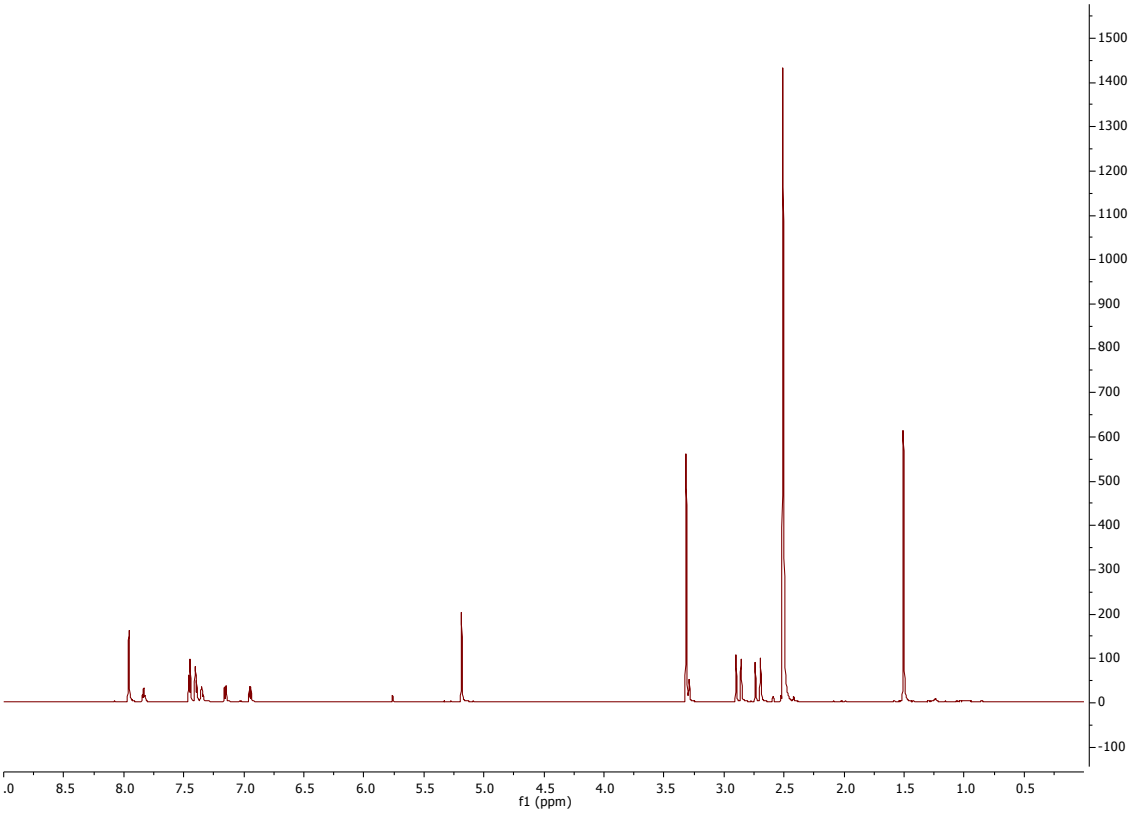


To iodonium ylide (4.7 mg, 10 µmol) in DMF-*d7* (1 ml) was heated at 130 ^{0}C. At the intervals 0, 3, 7, 12 and 30 minutes was 100 µl withdrawn, diluted with DMSO-*d6* and analysed via 1H NMR at a field strength of 800 MHz.

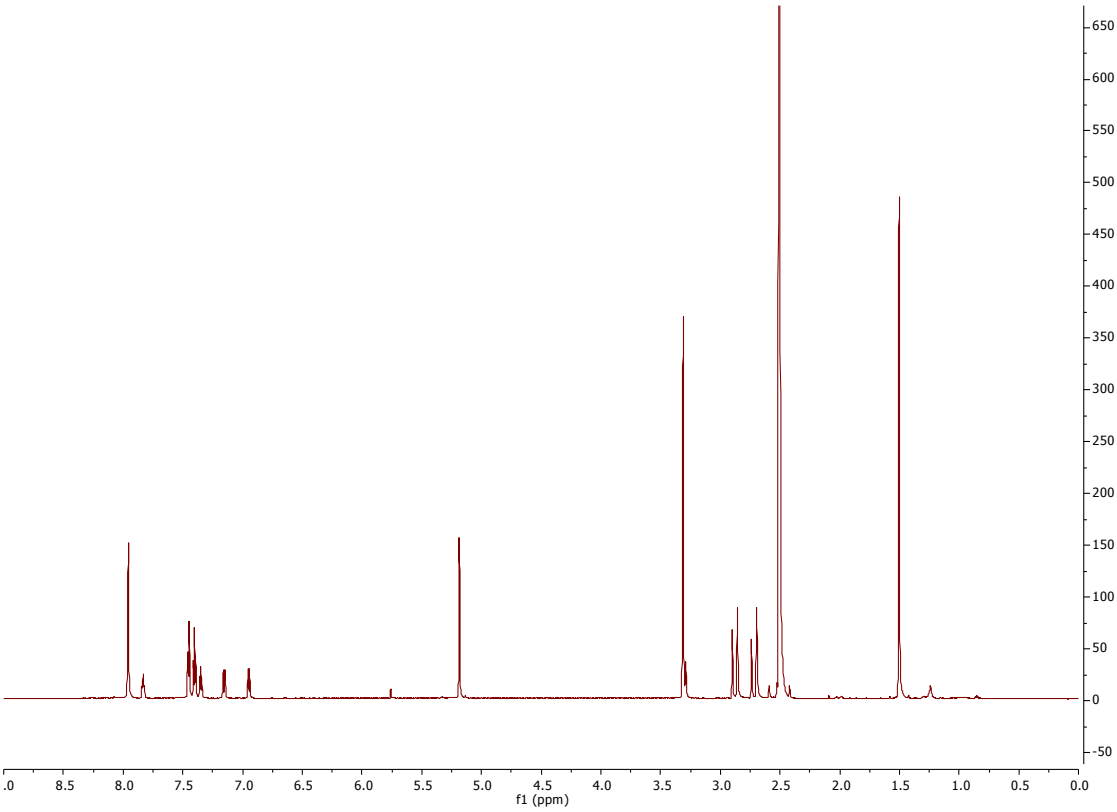
In DMF-*d7*



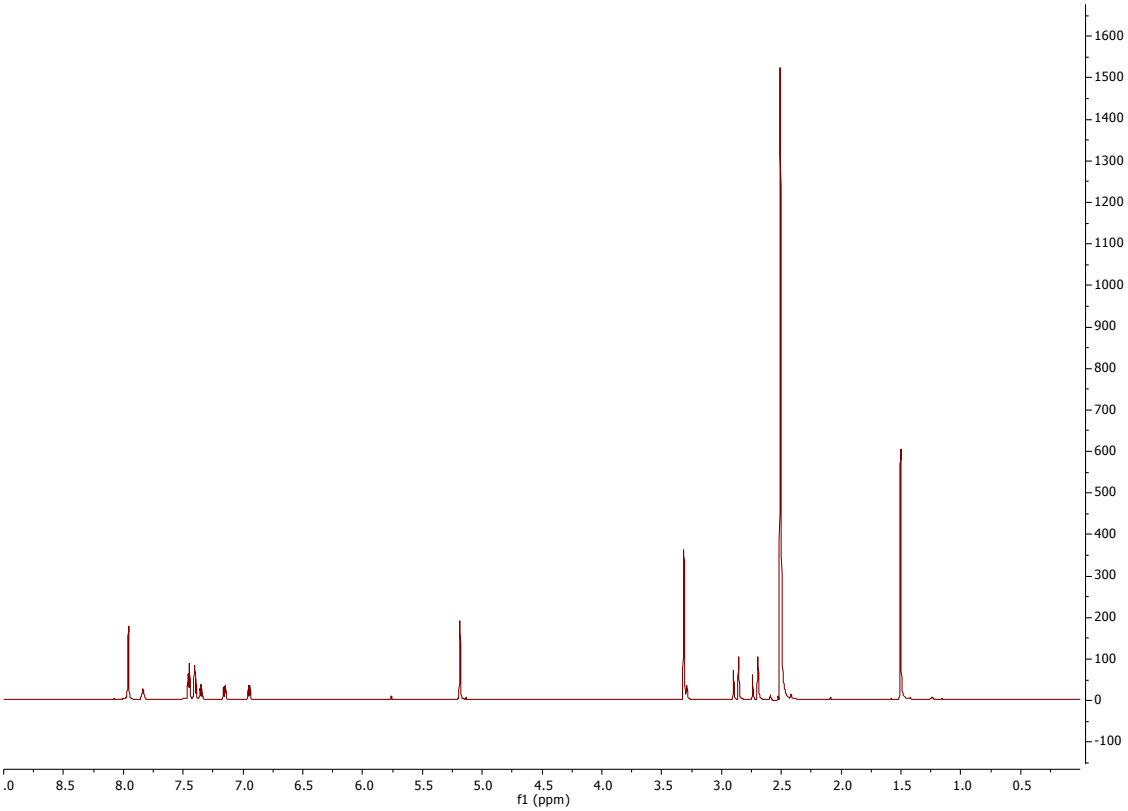
0 minutes



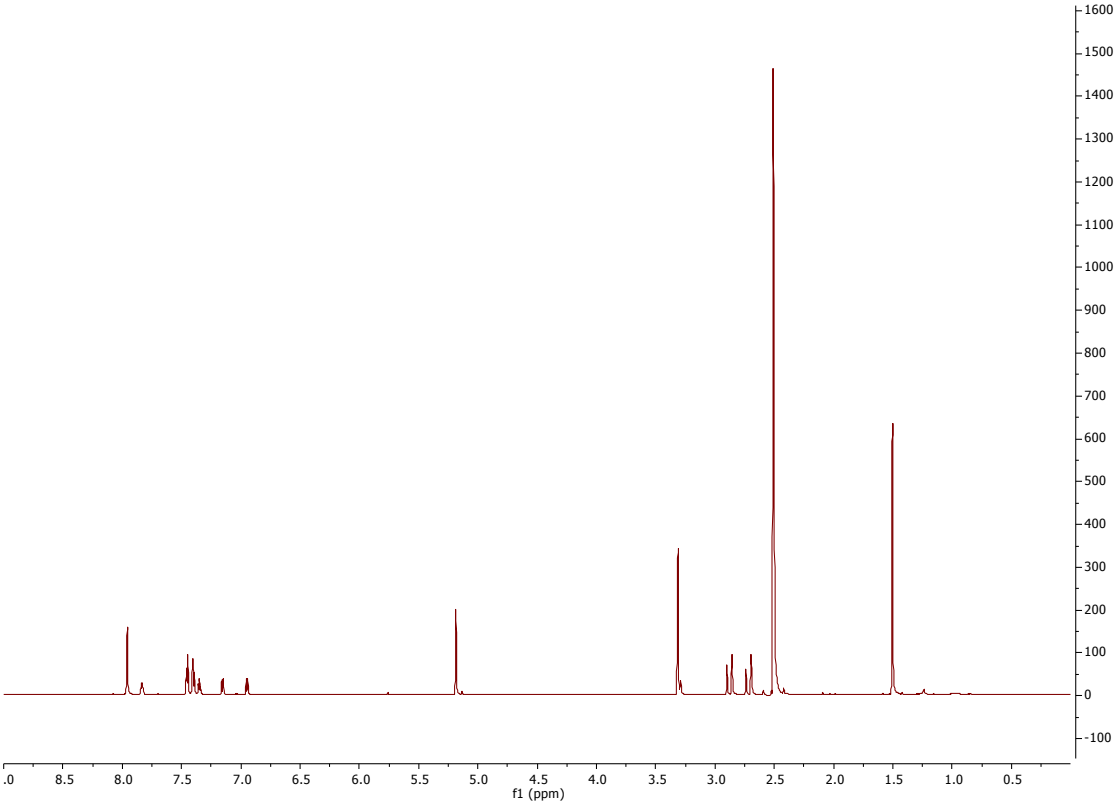
3 minutes



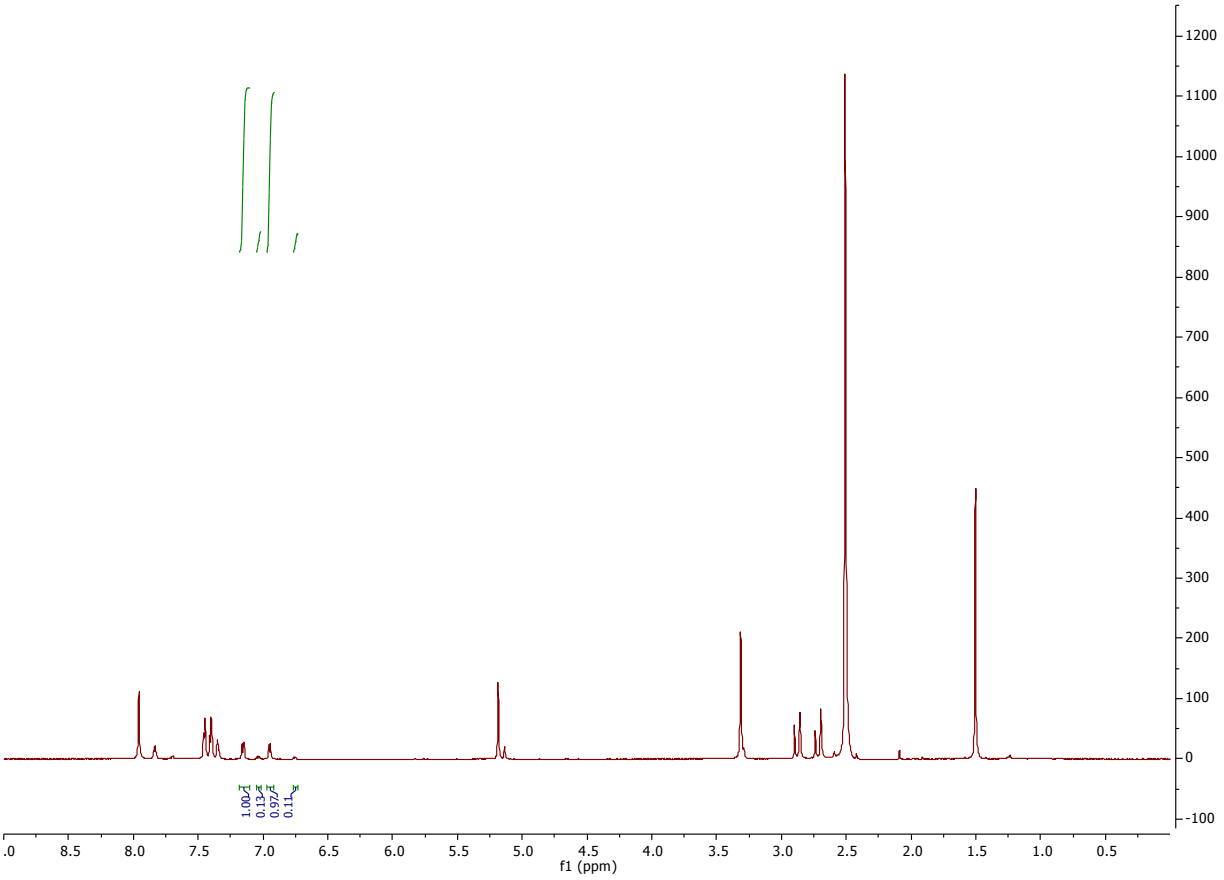
7 minutes



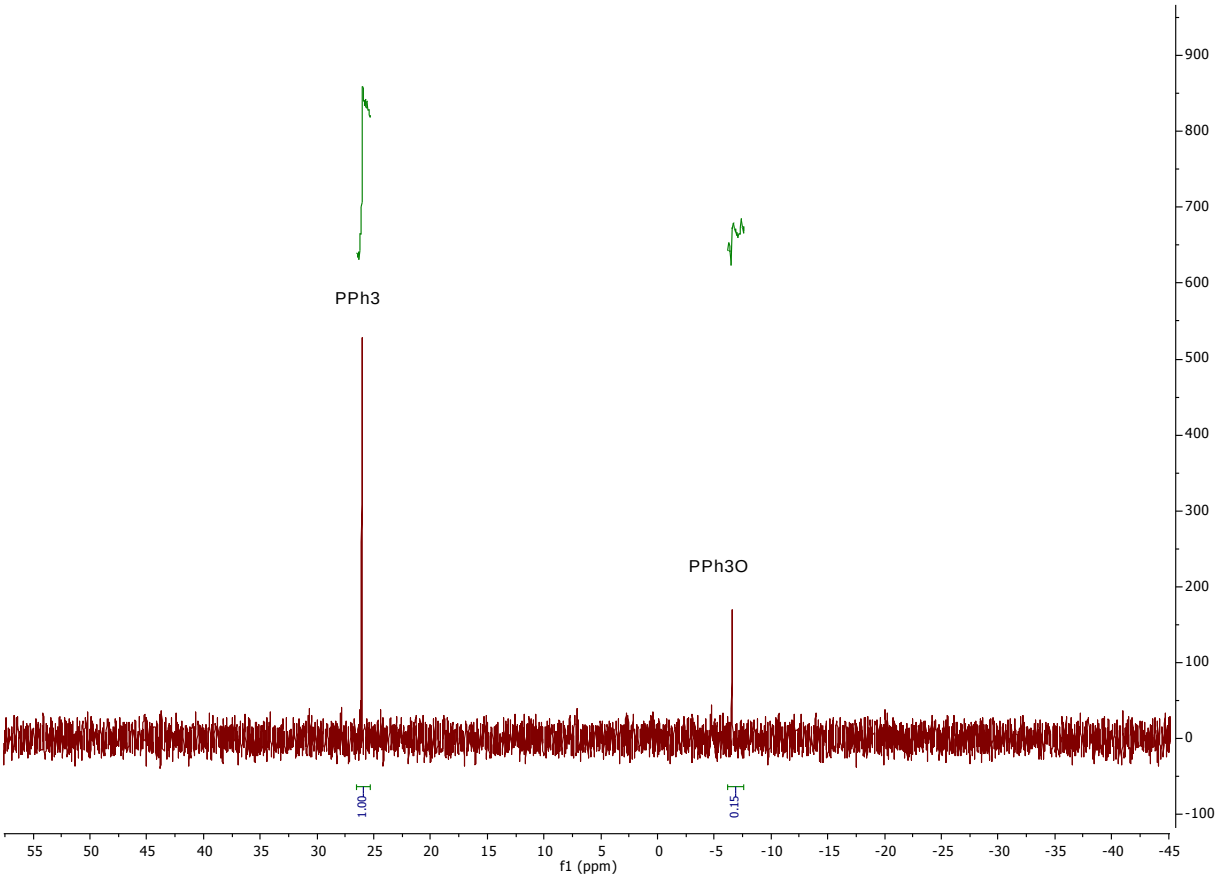
12 minutes



30 minutes


1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
1.00
0.13
0.97
0.11
.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
0.5
f1 (ppm)

Additional NMR spectra



31P NMR following typical NMR reaction procedure with 20% added triphenylphosphane.

1. J. E. Jakobsson, G. Gronnevik and P. J. Riss, *Chem Commun (Camb)*, 2017, **53**, 12906-12909.
2. D. W. Kim, H. J. Jeong, S. T. Lim and M. H. Sohn, *Angew Chem Int Edit*, 2008, **47**, 8404-8406.
3. J. Cardinale, J. Ermert, S. Humpert and H. H. Coenen, *Rsc Adv*, 2014, **4**, 17293-17299.
4. S. R. Goudreau, D. Marcoux and A. B. Charette, *J Org Chem*, 2009, **74**, 470-473.