

Supporting Information

Synthesis of oxaprozin analogs from 2*H*-azirines and cyclic anhydrides

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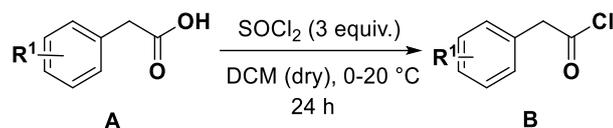
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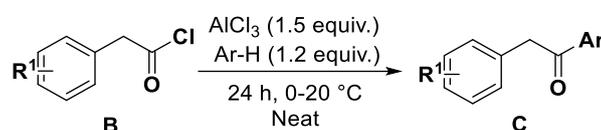
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1. Experimental procedures

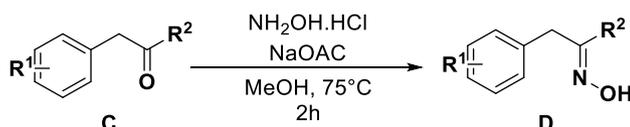
1.1. General procedure for the synthesis of 2*H*-azirines^{1,2}



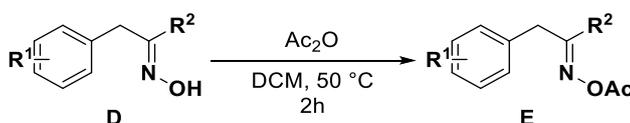
Step 1: Follow the reported procedure.^{1,2} To a solution of arylacetic acid **A** (30 mmol, 1 equiv.) in dry CH₂Cl₂ (75 mL) was added thionyl chloride (90 mmol, 3 equiv.) under an N₂ atmosphere at 0 °C. Then the mixture was stirred at room temperature overnight. After the completion of the reaction, the solvent and excess thionyl chloride were removed under reduced pressure, and the crude product **B** was used for the next step without further purification.



Step 2: Arylacetyl chloride **B** (20 mmol, 1 equiv.) and benzene (24 mmol, 1.2 equiv.) were added to the round-bottom flask. The reaction mixture was cooled to 0 °C, and then anhydrous AlCl₃ (30 mmol, 1.5 equiv.) was added in small portions. After the addition of AlCl₃, the resulting mixture was warmed to room temperature and stirred overnight. The reaction mixture was poured on ice and extracted with ethyl acetate. The combined organic phases were dried over Na₂SO₄, filtered, and concentrated under a vacuum, and the corresponding product **C** was used for the next step without further purification.

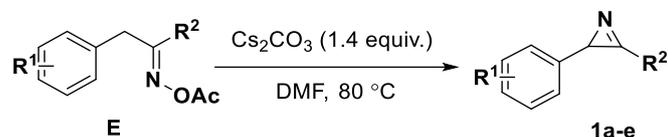


Step 3: The mixture of ketone **C** (15 mmol), NH₂OH·HCl (18 mmol, 1.2 equiv.), and NaOAc (22.5 mmol, 1.5 equiv.) was stirred in MeOH (60 mL) at 75 °C in an oil bath. After completion of the reaction (detected by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (75 mL × 2), and washed with brine (60 mL). The organic layers were dried over anhydrous Na₂SO₄ and evaporated in vacuo to afford crude ketoximes. The desired ketoximes were purified by recrystallization (*n*-hexane).

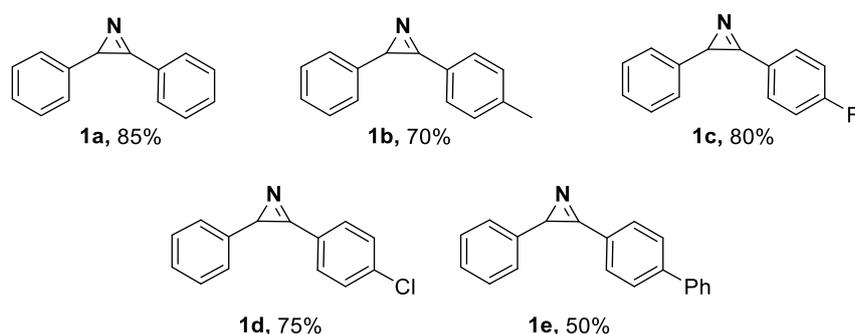


Step 4: The mixture of ketoxime **D** (10 mmol), and acetic anhydride (20 mmol, 2.0 equiv.) was stirred in dichloromethane at 50 °C and monitored by TLC until the reaction

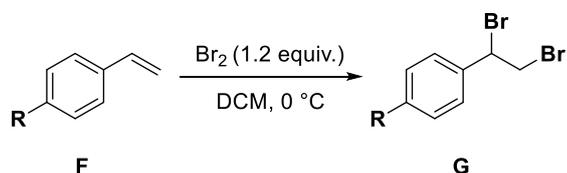
completion. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with H_2O (40 mL) and brine (20 mL). The organic layers were dried over anhydrous Na_2SO_4 and it evaporated in vacuo. The crude product was purified by recrystallization (*n*-hexane) to afford the corresponding ketoxime acetates.



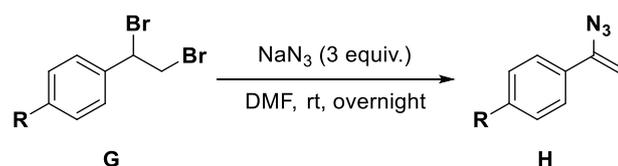
Step 5: In a 100 mL round-bottom flask, ketoxime acetate **E** (5 mmol), and Cs_2CO_3 (7 mmol, 1.4 equiv.) were stirred in DMF (15 mL) at 80 °C under Ar. After completion of the reaction (detected by TLC), the reaction mixture was cooled to room temperature, extracted with ethyl acetate, and washed with brine. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding *2H*-azirine **1a-e**.



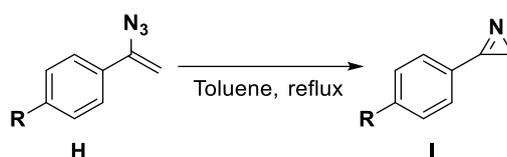
1.2. General procedure for the synthesis of monosubstituted *2H*-azirine³



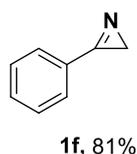
Step 1: To a solution of alkene **F** (5 mmol) in DCM (10 mL) cooled to 0 °C was added bromine (1.2 equiv.) dropwise. The resulting solution was stirred in an ice bath for 1 h. Upon completion, as indicated by TLC, the reaction was quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ and stirred vigorously until the orange color disappeared. The reaction was then filtered through a pad of Celite and washed with DCM. The filtrate was evaporated and purified by column chromatography using *n*-hexane: ether (99:1).



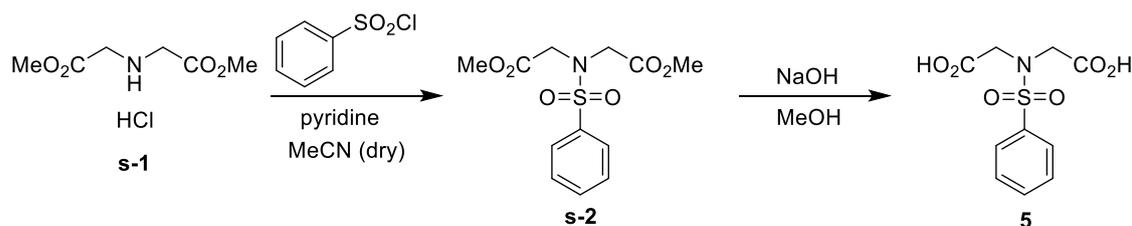
Step 2: To a solution of dibromide **G** (5 mmol, 1 equiv.) in DMF (20 mL) was added NaN_3 (3 equiv.). The mixture was stirred overnight at room temperature, then diluted with water and extracted with diethyl ether. The combined organic layers were washed three times with water, dried with MgSO_4 . After evaporation of solvents, the crude residue was purified by flash column chromatography (*n*-hexane: ethyl acetate = 99: 1) to give vinyl azide **H**.



Step 3: A solution of vinyl azide **H** (3 mmol) in toluene was heated in reflux until completion was shown by TLC. The reaction was allowed to cool to room temperature, and toluene was evaporated. The crude residue was purified by flash column chromatography (in pentane) to give 2*H*-azirine **1f**.



1.3. Procedure for the synthesis of 2,2'-((phenylsulfonyl)azanediyl)diacetic acid⁴



A mixture of dimethyl 2,2'-azanediyl diacetate hydrochloride **s-1** (20 mmol) and benzenesulfonyl chloride (20 mmol, 1 equiv.) in 80 mL of dry acetonitrile was prepared. To this mixture, a solution of pyridine (44 mmol, 2.2 equiv.) in acetonitrile was added dropwise at 0 °C. The reaction mixture was then stirred at room temperature for 48 hours. After which it was concentrated under reduced pressure, the resulting residue was diluted with 120 mL of ethyl acetate, and the organic layer was washed with 3M aqueous citric acid. The aqueous layer was subsequently extracted with 40 mL of ethyl acetate, and the combined organic extracts were washed with water and aqueous NaHCO_3 .

The organic phase was dried over MgSO₄ and concentrated in vacuo to yield dimethyl 2,2'-((phenylsulfonyl) azanediyl) diacetate as a yellow solid (3.9 g, 66%).

In the next step, to a suspension of dimethyl 2,2'-((phenylsulfonyl) azanediyl) diacetate **s-2** (12 mmol) in 40 mL methanol was added dropwise a solution of NaOH (4 equiv.) in 40 mL methanol at 0 °C. The resulting solution was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was dissolved in 6 mL of water, and 12N HCl was added dropwise at 0 °C to adjust the pH to 2–3. The resulting suspension was stirred for 2 hours, during which a precipitate formed. This precipitate was filtered and air-dried to yield 2,2'-((phenylsulfonyl) azanediyl) diacetic acid as a light colorless solid (2.6 g, 80%).

Compounds Characterization Data

3-(4,5-Diphenyloxazol-2-yl)propanoic acid^{11a} (3a) Colorless solid, (57 mg, Yield: 98%), (*n*-hexane/EtOAc = 10:1, R_f = 0.3); ¹H-NMR (250 MHz, DMSO-*d*₆) δ 12.09 (*br s*, 1H), 7.37-7.26 (*m*, 4H), 7.23-7.09 (*m*, 6H), 2.86 (*t*, *J* = 7.1 Hz, 2H), 2.59 (*t*, *J* = 7.1 Hz, 2H); ¹³C {¹H} NMR (63 MHz, DMSO-*d*₆) δ 173.5, 162.8, 149.9, 134.7, 132.4, 129.3, 129.2, 129.0, 128.8, 128.5, 127.7, 126.7, 30.6, 23.4; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₈H₁₆NO₃ 294.1125; Found: 294.1127.

3-(5-phenyl-4-(*p*-tolyl)oxazol-2-yl)propanoic acid^{11b} (3b) Colorless solid, (31 mg, Yield: 50%), (*n*-hexane/EtOAc = 10:1, R_f = 0.3); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.31 (*br s*, 1H), 7.55 (*d*, *J* = 5.7 Hz, 2H), 7.45-7.43 (*m*, 5H), 7.23 (*d*, *J* = 6.4 Hz, 2H), 3.08 (*t*, *J* = 7.0 Hz, 2H), 2.80 (*t*, *J* = 7.0 Hz, 2H), 2.43 (*s*, 3H); ¹³C {¹H} NMR (126 MHz, DMSO) δ 172.9, 162.0, 144.6, 138.3, 133.7, 132.0, 129.3, 128.4, 127.8, 127.1, 126.2, 125.5, 30.2, 22.8, 20.7; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₉H₁₈NO₃ 308.1281; Found: 308.1288.

3-(4-(4-fluorophenyl)-5-phenyloxazol-2-yl)propanoic acid (3c) Yellow solid, (49 mg, Yield: 79%), (*n*-hexane/EtOAc = 5:1, R_f = 0.2); ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.19 (*br s*, 1H), 7.64-7.45 (*m*, 4H), 7.44-7.32 (*m*, 3H), 7.30-7.19 (*m*, 2H), 3.04 (*t*, *J* = 7.1 Hz, 2H), 2.77 (*t*, *J* = 7.1 Hz, 2H); ¹³C {¹H} NMR (75 MHz, DMSO-*d*₆) δ 172.5, 163.4, 160.4 158.0 (¹*J*_{CF} = 243.2), 143.7, 134.2, 129.5, 128.9, 128.8, 128.6, 128.1, 127.3, 126.3, 116.1, 115.8, 115.7, 115.4 (²*J*_{CF} = 22.5), 30.3, 22.9; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₈H₁₅FNO₃ 312.1031; Found: 312.1036.

3-(4-(4-chlorophenyl)-5-phenyloxazol-2-yl)propanoic acid^{11b} (3d) Colorless solid, (106 mg, Yield: 81%), (*n*-hexane/EtOAc = 5:1, R_f = 0.2); ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.33 (*br s*, 1H), 7.95-7.87 (*m*, 2H), 7.53-7.44 (*m*, 5H), 7.42-7.29 (*m*, 2H), 3.04 (*t*, *J* = 5.6 Hz, 2H), 2.77 (*t*, *J* = 5.6 Hz, 2H); ¹³C {¹H} NMR (75 MHz, DMSO-*d*₆) δ 173.1, 162.6, 146.5, 135.1, 133.3, 131.1, 129.6, 129.1, 128.7, 127.9, 127.5, 28.6, 22.9; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₈H₁₄³⁵ClNO₃ 328.0735; Found: 328.0744.

4-(4,5-Diphenyloxazol-2-yl)butanoic acid^{11c} (3e) Colorless solid, (52 mg, Yield 85%), (*n*-hexane/EtOAc = 10:1, R_f = 0.25); ¹H NMR (250 MHz, DMSO-*d*₆) δ 12.10 (*br s*, 1H), 7.69-7.46 (*m*, 4H), 7.46-7.18 (*m*, 6H), 2.85 (*t*, *J* = 7.5 Hz, 2H), 2.38 (*t*, *J* = 7.5 Hz, 2H), 2.05-1.90 (*quintet*, 2H); ¹³C {¹H} NMR (63 MHz, DMSO-*d*₆) δ 174.4, 163.2, 145.0, 134.7, 132.4, 129.3, 129.2, 129.0, 128.9, 128.5, 127.7, 126.8, 33.1, 27.0, 22.2; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₉H₁₈NO₃ 308.1281; Found: 308.1281.

4-(5-phenyl-4-(p-tolyl)oxazol-2-yl)butanoic acid (3f) Colorless solid, (25 mg, Yield:40%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (301 MHz, DMSO- d_6) δ 12.18 (*br s*, 1H), 7.66 (d, $J = 7.5$ Hz, 2H), 7.53-7.33 (m, 5H), 7.27 (d, $J = 7.5$ Hz, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.42 (t, $J = 7.5$ Hz, 2H), 2.35 (s, 3H), 2.07-1.90 (quintet, 2H); ^{13}C { ^1H } NMR (76 MHz, DMSO- d_6) δ 174.4, 163.0, 145.2, 138.9, 134.2, 132.6, 129.9, 129.0, 128.4, 127.7, 126.9, 126.1, 33.2, 27.0, 22.3, 21.3; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_3$ 322.1438; Found: 322.1434.

2-(((4,5-Diphenyloxazol-2-yl)methyl)thio)acetic acid (3g) Brown solid, (40 mg, Yield:61.5%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.35$); ^1H NMR (400 MHz, DMSO- d_6) δ 12.82 (*br s*, 1H), 7.57-7.50 (m, 4H), 7.49-7.29 (m, 6H), 4.06 (s, 2H), 3.50 (s, 2H); ^{13}C { ^1H } NMR (101 MHz, DMSO- d_6) δ 171.3, 160.5, 145.7, 135.1, 132.2, 129.5, 129.4, 129.1, 128.7, 128.6, 127.9, 126.9, 34.0, 27.6; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{16}\text{NO}_3\text{S}$ 326.0846; Found: 326.0837.

2-(((5-phenyl-4-(p-tolyl)oxazol-2-yl)methyl)thio)acetic acid (3h) Colorless solid, (33 mg, Yield:47%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (300 MHz, DMSO- d_6) δ 12.50 (*br s*, 1H), 7.53 (d, $J = 7.8$ Hz, 2H), 7.46-7.30 (m, 5H), 7.16 (d, $J = 7.8$ Hz, 2H), 4.02 (s, 2H), 3.46 (s, 2H), 2.31 (s, 3H); ^{13}C { ^1H } NMR (75 MHz, DMSO- d_6) δ 170.7, 159.9, 144.9, 137.6, 134.8, 129.5, 129.1, 128.8, 128.5, 128.3, 127.3, 126.3, 33.60, 27.2, 20.8; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_3\text{S}$ 340.1002; Found: 340.1004.

2-(((4-(4-fluorophenyl)-5-phenyloxazol-2-yl)methyl)thio)acetic acid (3i) Colorless solid, (40 mg, Yield:58%), (*n*-hexane/EtOAc = 5:1, $R_f = 0.2$); ^1H NMR (300 MHz, acetone- d_6) δ 11.03 (*br s*, 1H), 7.73-7.63 (m, 2H), 7.62-7.56 (m, 2H), 7.50-7.34 (m, 3H), 7.27-7.09 (m, 2H), 4.08 (s, 2H), 3.55 (s, 2H); ^{13}C { ^1H } NMR (75 MHz, acetone- d_6) δ 169.5, 163.7, 160.4 ($^1J_{\text{CF}} = 244.5$), 159.6, 145.4, 134.0, 129.3, 129.2, 128.4, 128.3, 127.1, 126.2, 114.9, 114.7, ($^2J_{\text{CF}} = 21.7$), 32.6, 27.1; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{14}\text{FNO}_3\text{S}$ 344.0751; Found: 344.0749.

2-(((4-(4-chlorophenyl)-5-phenyloxazol-2-yl)methyl)thio)acetic acid (3j) Colorless solid, (56 mg, Yield:78%), (EtOAc /methanol = 5:1, $R_f = 0.2$); ^1H NMR (300 MHz, DMSO- d_6) δ 12.70 (*br s*, 1H), 7.61-7.49 (m, 4H), 7.48-7.34 (m, 5H), 4.03 (s, 2H), 3.47 (s, 2H); ^{13}C { ^1H } NMR (75 MHz, DMSO- d_6) δ 170.7, 160.2, 145.7, 133.6, 132.8, 130.6, 129.2, 129.1, 129.0, 128.7, 127.9, 126.6, 33.5, 27.2; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{14}^{35}\text{ClNO}_3\text{S}$ 360.0456; Found: 360.0459.

2-(((4-([1,1'-biphenyl]-4-yl)-5-phenyloxazol-2-yl)methyl)thio)acetic acid (3k) Colorless solid, (55 mg, Yield 69%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (500 MHz, DMSO- d_6) δ 12.86 (*br s*, 1H), 7.75-7.64 (m, 6H), 7.63-7.56 (m, 2H), 7.50-7.41 (m, 5H), 7.36 (t, $J = 7.4$ Hz, 1H), 4.06 (s, 2H), 3.49 (s, 2H); ^{13}C { ^1H } NMR (126 MHz, DMSO- d_6) δ 170.9, 160.1, 145.4, 139.7, 139.3, 134.3, 130.8, 129.0, 128.9, 128.7, 128.2, 127.8, 127.6, 126.8, 126.6, 126.5, 33.6, 27.1; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{20}\text{NO}_3\text{S}$ 402.1159; Found: 402.1165.

2-(((4,5-Diphenyloxazol-2-yl)methoxy)acetic acid (3l) Colorless solid, (51 mg, Yield:82%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (500 MHz, DMSO- d_6) δ 12.63 (*br s*, 1H), 7.63-7.48 (m, 4H), 7.47-7.32 (m, 6H), 4.72 (s, 2H), 3.75 (s, 2H); ^{13}C { ^1H } NMR (126 MHz, DMSO- d_6) δ 172.4, 160.2, 145.3, 134.4, 131.7, 129.0, 128.9, 128.6, 128.3, 128.2, 127.3, 126.5, 70.2, 63.2; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{16}\text{NO}_4$ 310.1074; Found: 310.1070.

2-(((4-(4-fluorophenyl)-5-phenyloxazol-2-yl)methoxy)acetic acid (3m) Colorless solid, (65 mg, Yield:80%), (*n*-hexane/EtOAc = 5:1, $R_f = 0.2$); ^1H NMR (300 MHz, acetone- d_6) δ 11.22 (*br s*, 1H), 7.73-7.65 (m, 2H), 7.64-7.56 (m, 2H), 7.50-7.30 (m, 3H), 7.29-7.04 (m, 2H), 4.82 (s, 2H), 4.32 (s,

2H); ^{13}C $\{^1\text{H}\}$ NMR (75 MHz, acetone- d_6) δ 169.6, 163.8, 160.5 ($^1J_{\text{CF}} = 244.5$), 158.9, 145.8, 133.9, 129.3, 129.2, 128.6, 128.4, 127.2, 126.4, 114.9, 114.7, ($^2J_{\text{CF}} = 21.7$), 66.9, 64.2; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{14}\text{FNO}_4$ 328.0979; Found: 328.0979.

2-((4-(4-chlorophenyl)-5-phenyloxazol-2-yl)methoxy)acetic acid (3n) Colorless solid, (69 mg, Yield:50%), (EtOAc /methanol = 5:1, $R_f = 0.2$); ^1H NMR (500 MHz, DMSO- d_6) δ 12.25 (*br s*, 1H), 7.59 (d, $J = 8.4$ Hz, 2H), 7.58-7.50 (m, 3H), 7.48-7.38 (m, 4H), 4.73 (s, 2H), 4.16 (s, 2H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 171.1, 159.3, 145.9, 133.3, 132.7, 130.4, 129.2, 128.9, 128.7, 128.1, 127.4, 126.7, 67.5, 63.8; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{14}^{35}\text{ClNO}_4$ 344.0683; Found: 344.0679.

2-((4-([1,1'-biphenyl]-4-yl)-5-phenyloxazol-2-yl)methoxy)acetic acid (3o) Colorless solid, (50 mg, Yield 65%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (500 MHz, DMSO- d_6) δ 12.92 (*br s*, 1H), 7.73-7.66 (m, 6H), 7.60 (d, $J = 6.7$ Hz, 2H), 7.50-7.42 (m, 5H), 7.38-7.34 (m, 1H), 4.74 (s, 2H), 4.19 (s, 2H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 171.1, 159.2, 145.7, 139.8, 139.3, 134.1, 130.7, 129.2, 129.0, 128.9, 128.1, 127.8, 127.7, 126.9, 126.8, 126.5, 67.3, 64.0.; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{20}\text{NO}_4$ 386.1387; Found: 386.1391.

2-((4-([1,1'-biphenyl]-4-yl)-5-phenyloxazol-2-yl)methyl)benzoic acid (3p) Colorless solid, (29 mg, Yield 33%), (*n*-hexane/EtOAc = 10:1, $R_f = 0.3$); ^1H NMR (400 MHz, DMSO- d_6) δ 12.68 (*br s*, 1H), 7.89 (dd, $J = 7.8, 1.4$ Hz, 2H), 7.71 (dd, $J = 7.7, 1.4$ Hz, 1H), 7.57 (d, $J = 7.7$ Hz, 1H), 7.50 (td, $J = 7.5, 1.5$ Hz, 2H), 7.44-7.35 (m, 5H), 7.33 (t, $J = 7.5$ Hz, 2H) 7.29-7.22 (m, 1H), 7.21-7.09 (m, 3H), 6.79 (d, $J = 7.7$ Hz, 1H), 3.93 (s, 2H); ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, DMSO- d_6) δ 172.9, 168.8, 143.0, 136.9, 136.7, 135.2, 132.7, 132.4, 132.2, 130.9, 130.8, 130.0, 129.3, 128.6, 128.2, 128.1, 127.9, 127.6, 127.4, 127.1, 126.8, 126.1, 45.7; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{29}\text{H}_{22}\text{NO}_3$ 432.1594; Found: 432.1587.

2-(((4-([1,1'-biphenyl]-4-yl)-5-phenyloxazol-2-yl)methyl)sulfonyl)acetic acid (4) Colorless solid, (41 mg, Yield 48%), (*n*-hexane/EtOAc = 1:1, $R_f = 0.2$); ^1H NMR (500 MHz, DMSO- d_6) δ 13.06 (*br s*, 1H), 7.78-7.68 (m, 6H), 7.65-7.60 (m, 2H), 7.54-7.45 (m, 5H), 7.41-7.36 (m, 1H), 5.11 (s, 2H), 4.55 (s, 2H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 164.1, 152.2, 146.7, 136.9, 139.2, 134.9, 130.2, 129.3, 129.0, 128.8, 127.8, 127.7, 127.6, 126.8, 126.7, 126.4, 57.6, 52.1; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{19}\text{NO}_5\text{S}$ 434.1057; Found: 434.1054.

2,2'-((Phenylsulfonyl)azanediyl)diacetic acid (5)^{11d} Colorless solid, (41 mg, Yield 48%), (*n*-hexane/EtOAc = 1:1, $R_f = 0.2$); ^1H NMR (500 MHz, DMSO- d_6) δ 7.77 (d, $J = 8.5$ Hz, 2H), 7.67 (tt, $J = 7.3, 1.3$ Hz, 1H), 7.60 (dd, $J = 8.4, 6.9$ Hz, 2H), 3.72 (s, 4H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 171.8, 138.8, 132.8, 129.3, 126.4, 53.8; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_6\text{S}$ 274.0379; Found: 274.0373

2-(4,5-diphenyloxazol-2-yl)benzoic acid (6) Colorless solid, (12 mg, Yield 17%), (*n*-hexane/EtOAc = 5:1, $R_f = 0.2$); ^1H NMR (500 MHz, DMSO- d_6) δ 13.32 (*br s*, 1H), 8.00 (dd, $J = 7.6, 1.4$ Hz, 1H), 7.75 (dd, $J = 7.4, 1.6$ Hz, 1H), 7.71 – 7.59 (m, 6H), 7.50 – 7.37 (m, 6H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, DMSO- d_6) δ 169.1, 158.8, 145.6, 135.7, 133.2, 131.7, 130.8, 130.6, 129.2, 129.1, 128.9, 128.8, 128.7, 128.4, 128.1, 127.5, 126.4, 125.0; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{15}\text{NO}_3$ 342.1123; Found: 342.1133.

Dihydrofuran-2,5-dione (2a) Colorless solid, (mixture of anhydride/acid = 94:6); ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 12.11 (*br s*, 2H, $-\text{CO}_2\text{H}$), 2.89 (*s*, 4H), 2.41 (*s*, 4H, $-\text{CH}_2-\text{CO}_2\text{H}$); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, $\text{DMSO-}d_6$) δ 173.5, 172.9, 28.6.

2. Computational Details

Gaussian 16ⁱ was used to fully optimize all the structures reported in this study at the B3LYP level of theory.ⁱⁱ For all the calculations, solvent effects were considered using the SMD solvation modelⁱⁱⁱ with *O*-xylene as the solvent. Grimme empirical dispersion was added with the GD3 term on all the calculations.^{iv} For geometry optimizations, the 6-31G(d) basis set was employed for all atoms.^v This basis set combination will be referred to as BS1. Frequency calculations were carried out at the same level of theory as those for structural optimization. Transition structures were located using the Berny algorithm. Intrinsic reaction coordinate (IRC) calculations were used to confirm the connectivity between transition structures and minima.^{vi} To enhance the precision of the energies derived from the SMD/B3LYP-D3/6-31G(d) calculations, we performed single-point energy calculations for all structures using the B3LYP functional method with the GD3 term and a larger basis set (BS2), with consideration of the SMD solvation model. This expanded basis set incorporates 6-311+G(2d,p) for all atoms. The overall solvation free energy values reported in this work were obtained by adding the free energy corrections from the frequency analysis to the single-point solvation free energies calculated using the SMD solvation model. Moreover, the overall free energy values were corrected by adding $\Delta G^{1\text{atm}\rightarrow 1\text{M}} = 1.89$ kcal/mol to account for the free-energy change associated with compressing 1 mol of an ideal gas from 1 atm to the 1 M solution phase standard state.

I) Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

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V) a) Bergner, A; Dolg, M.; Küchle, W.; Stoll, H.; Preuß, H.; Ab initio energy-adjusted pseudopotentials for elements of groups 13-17. *Mol. Phys.* **1993**, *80*, 1431-1441; b) Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. Energy-adjusted ab initio pseudopotentials for the first row transition elements. *J. Chem. Phys.* **1987**, *86*, 866-872; c) Hariharan, P.C.; Pople, J.A. The influence of polarization functions on molecular orbital hydrogenation energies. *Theor. Chim. Acta.* **1973**, *28*, 213-222.

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3. ^1H NMR, ^{13}C NMR, and HRMS/ Mass-ESI Spectra

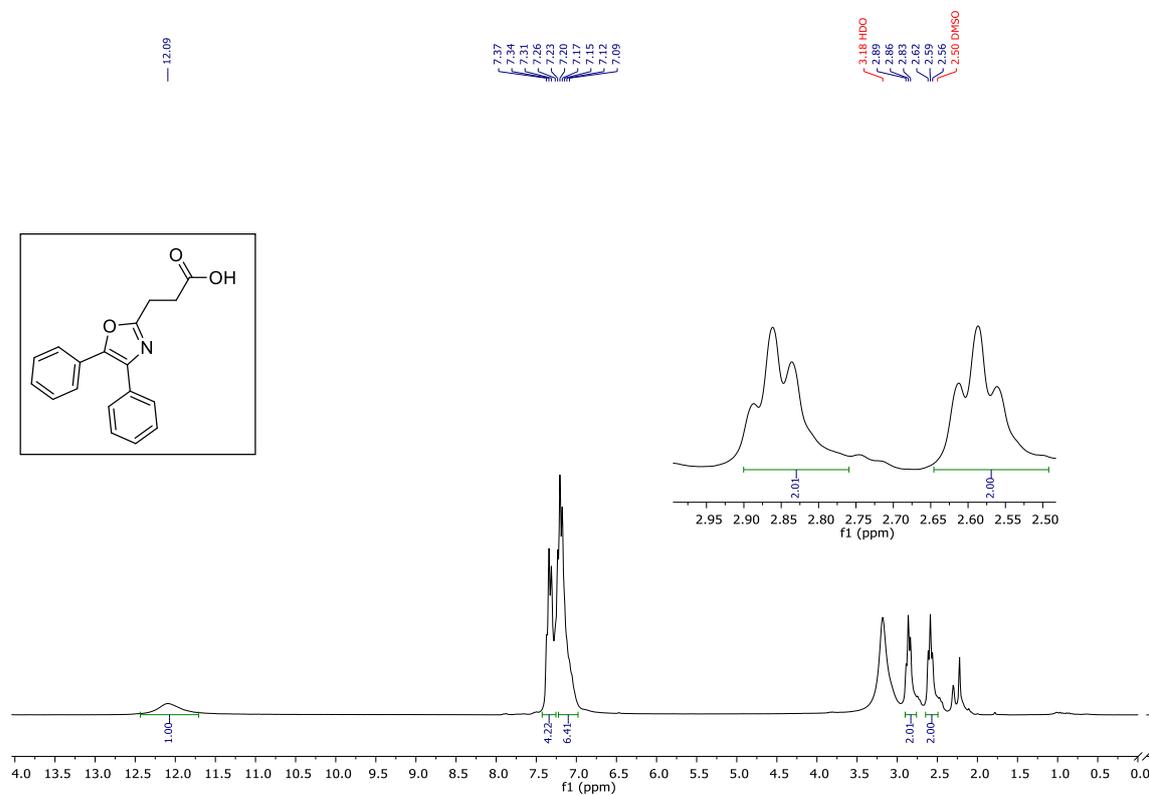


Figure S2: ^1H NMR Compound 3a (250 MHz, DMSO- d_6)

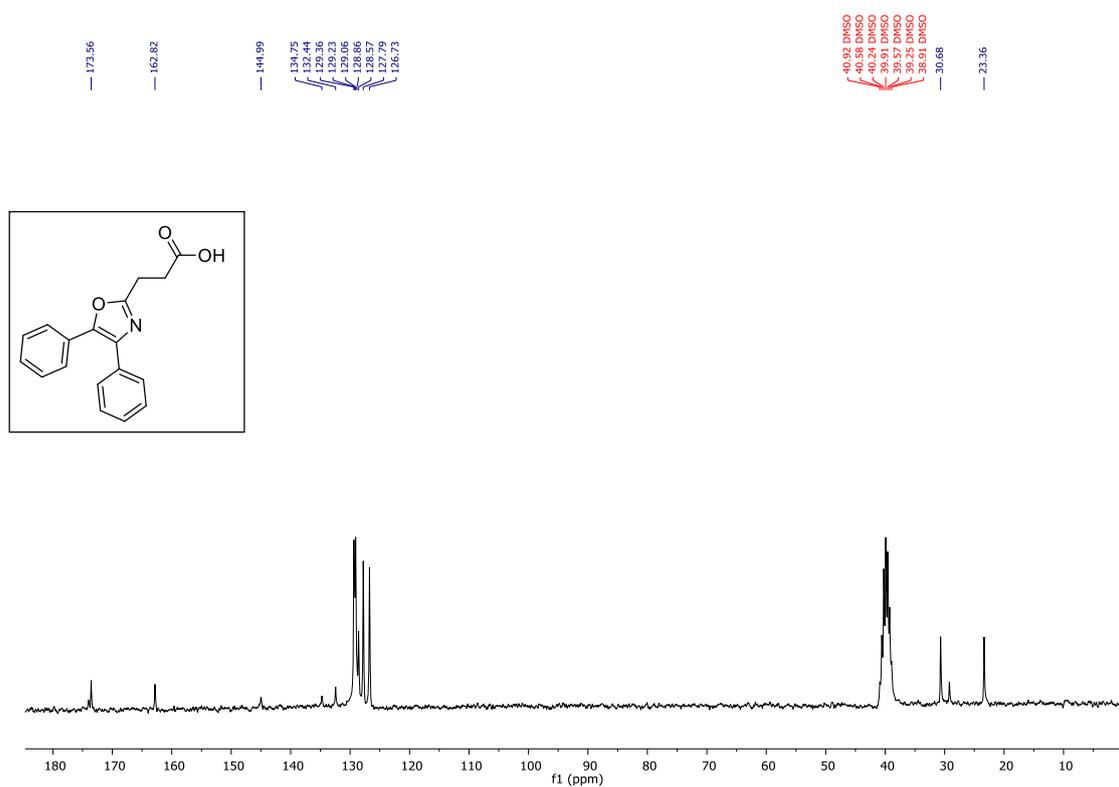
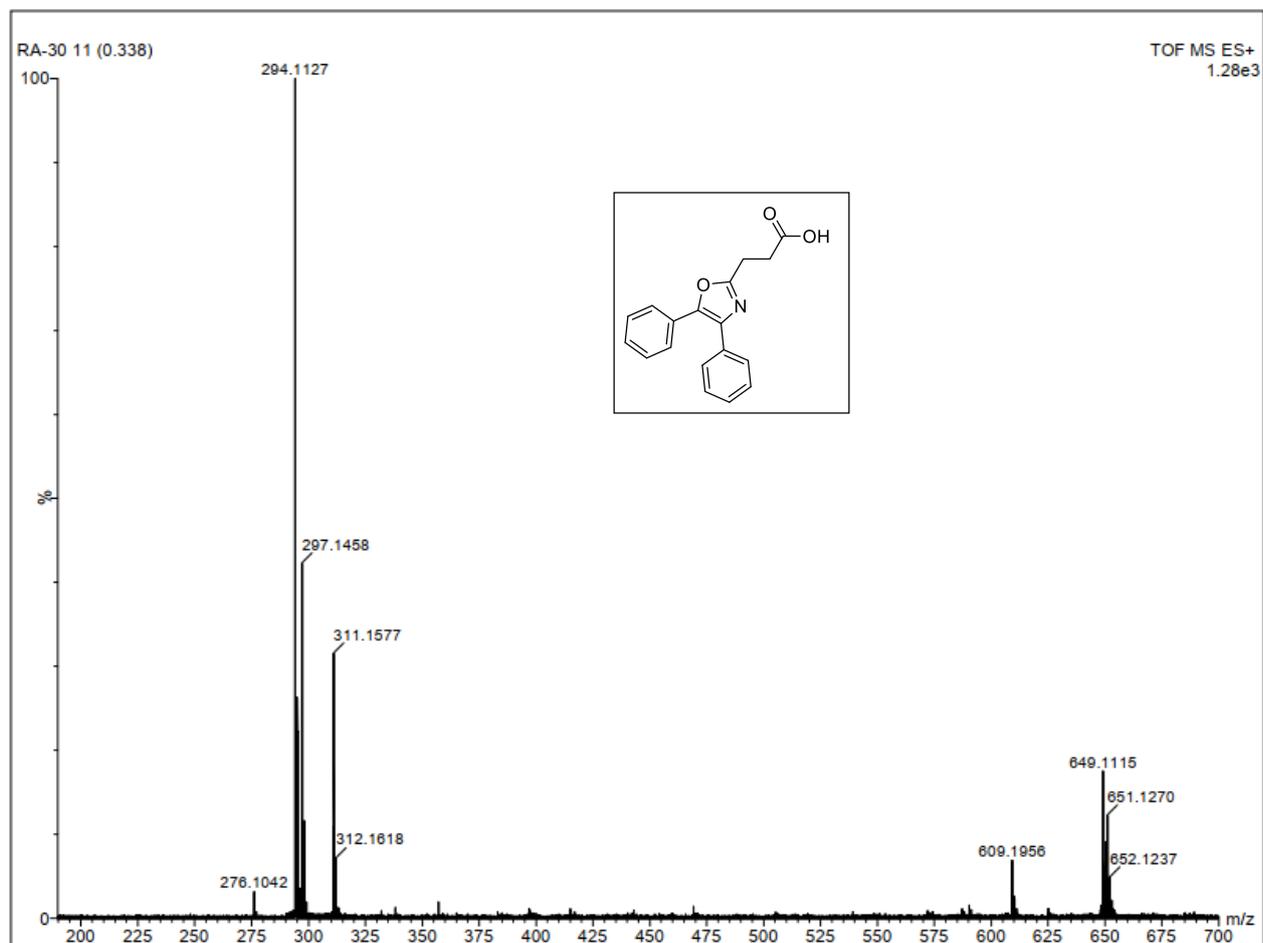
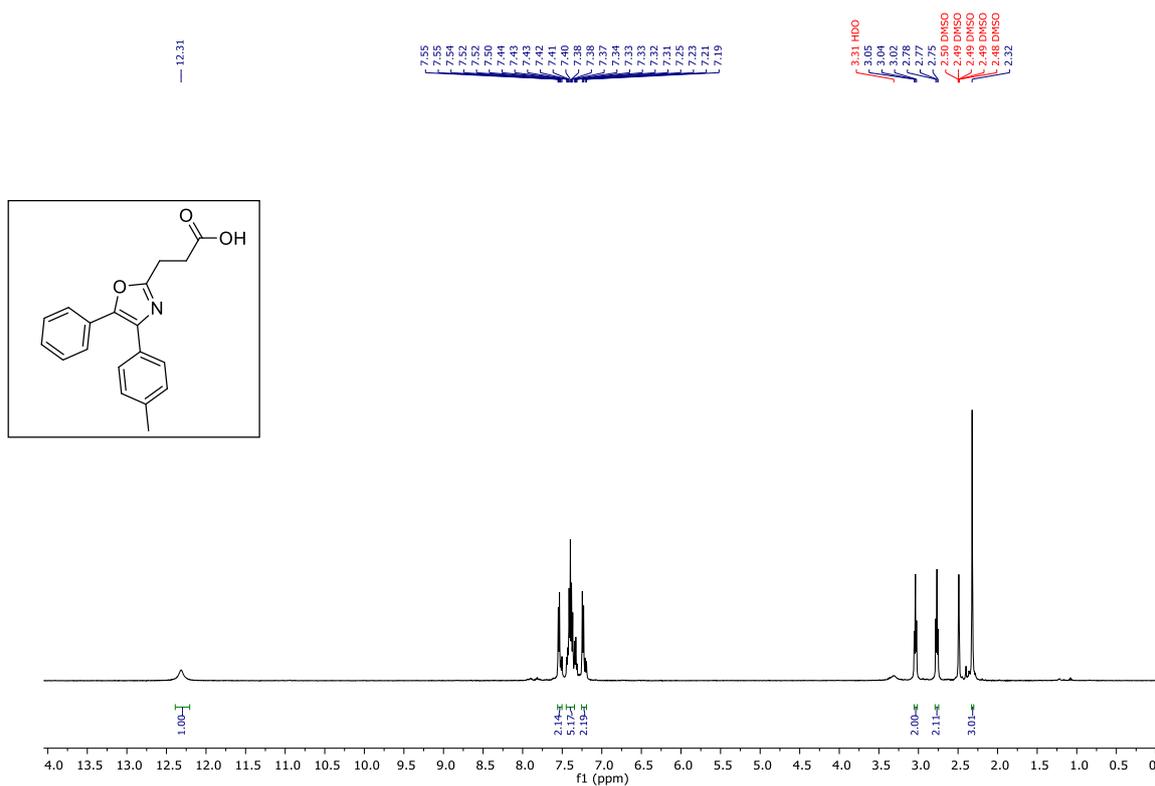
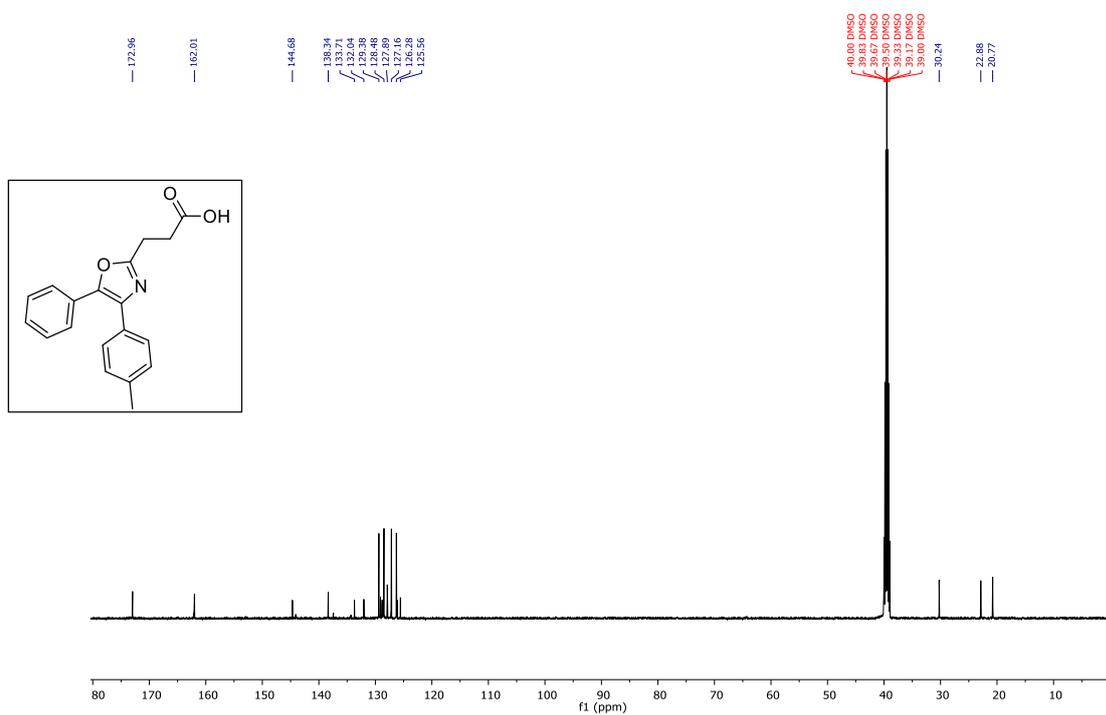
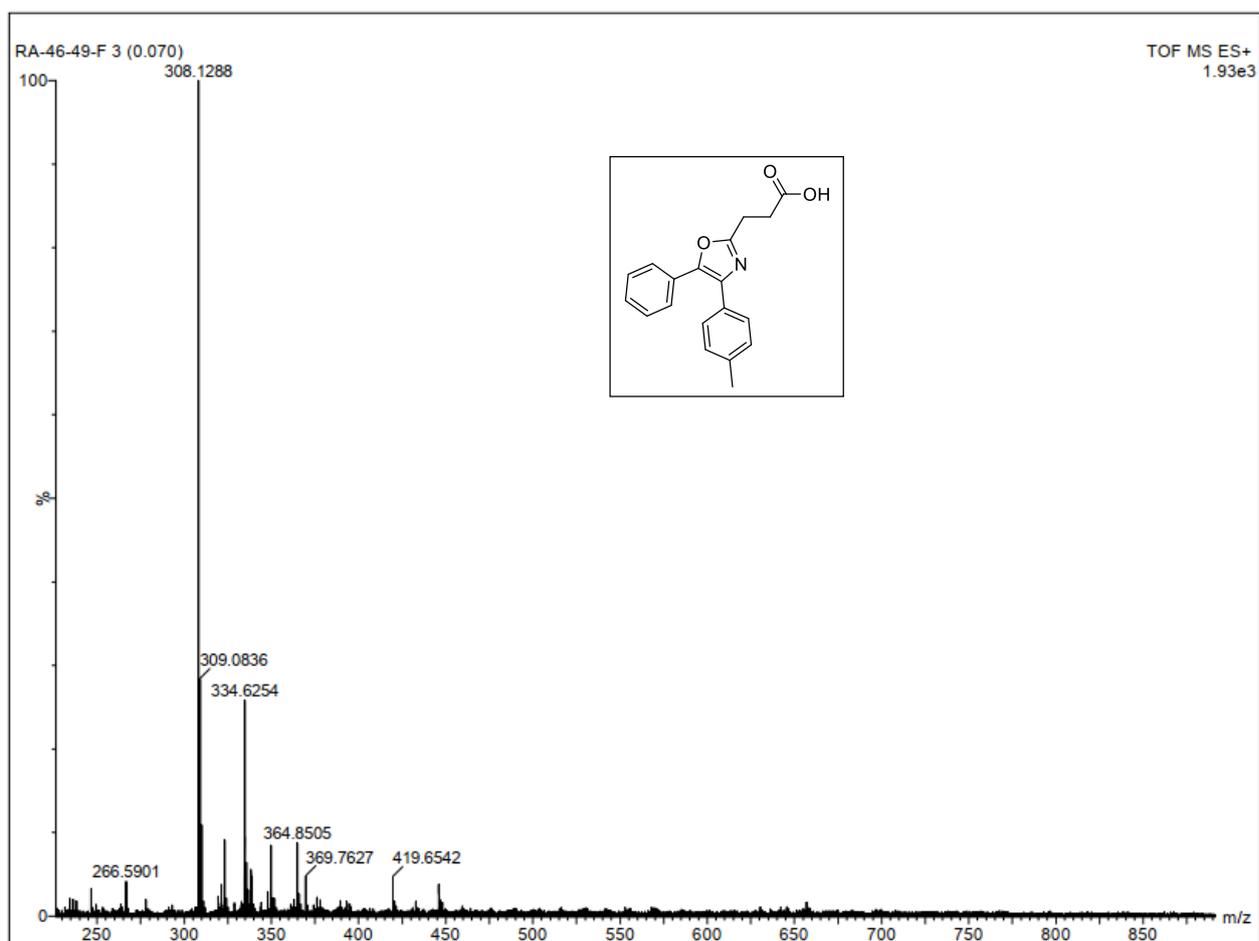
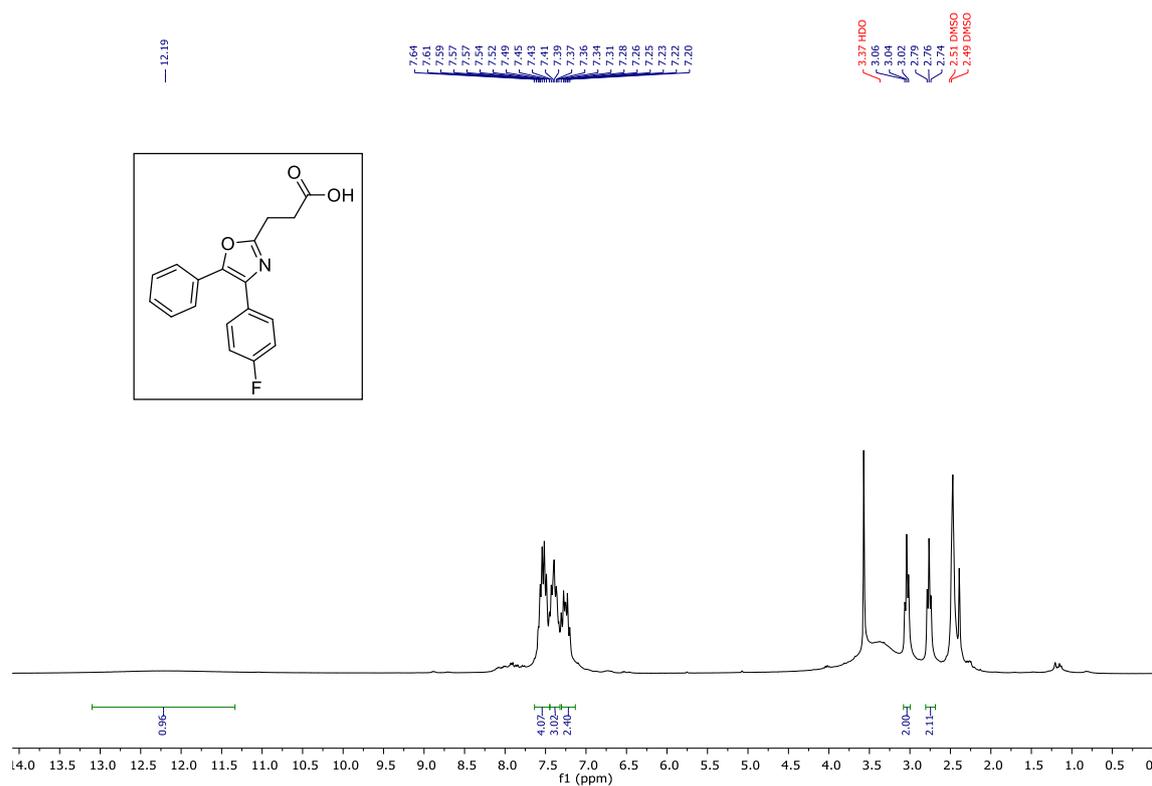
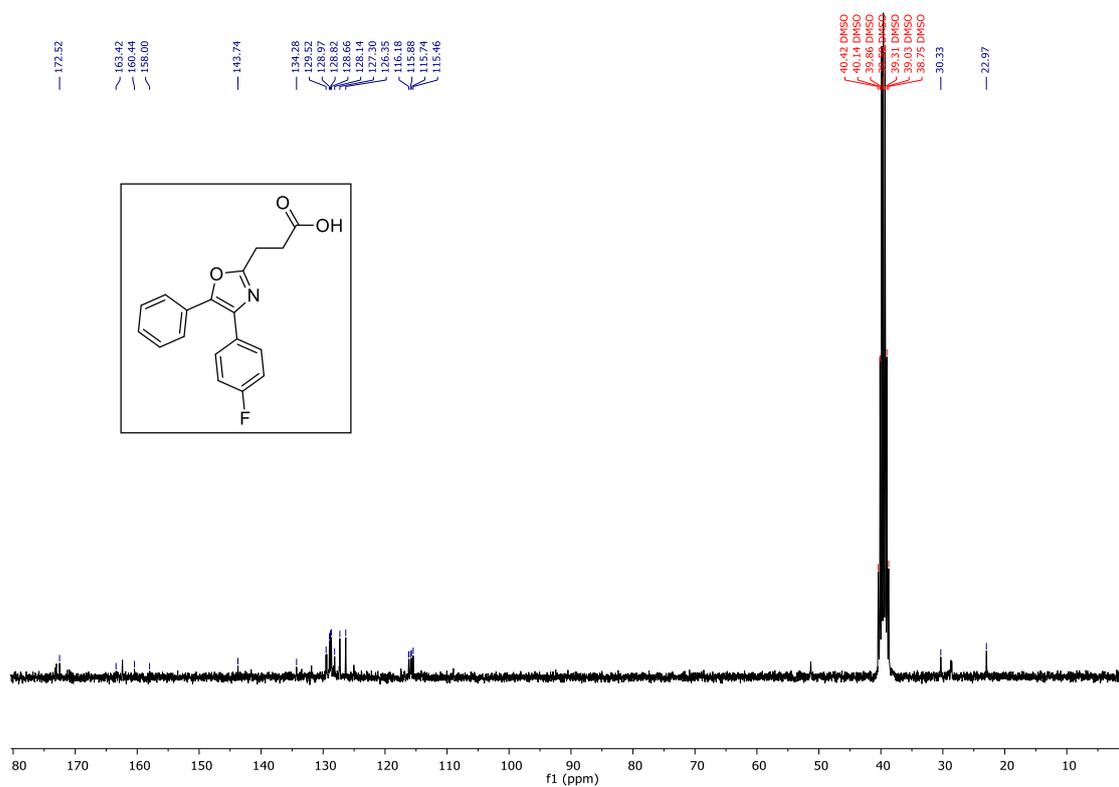
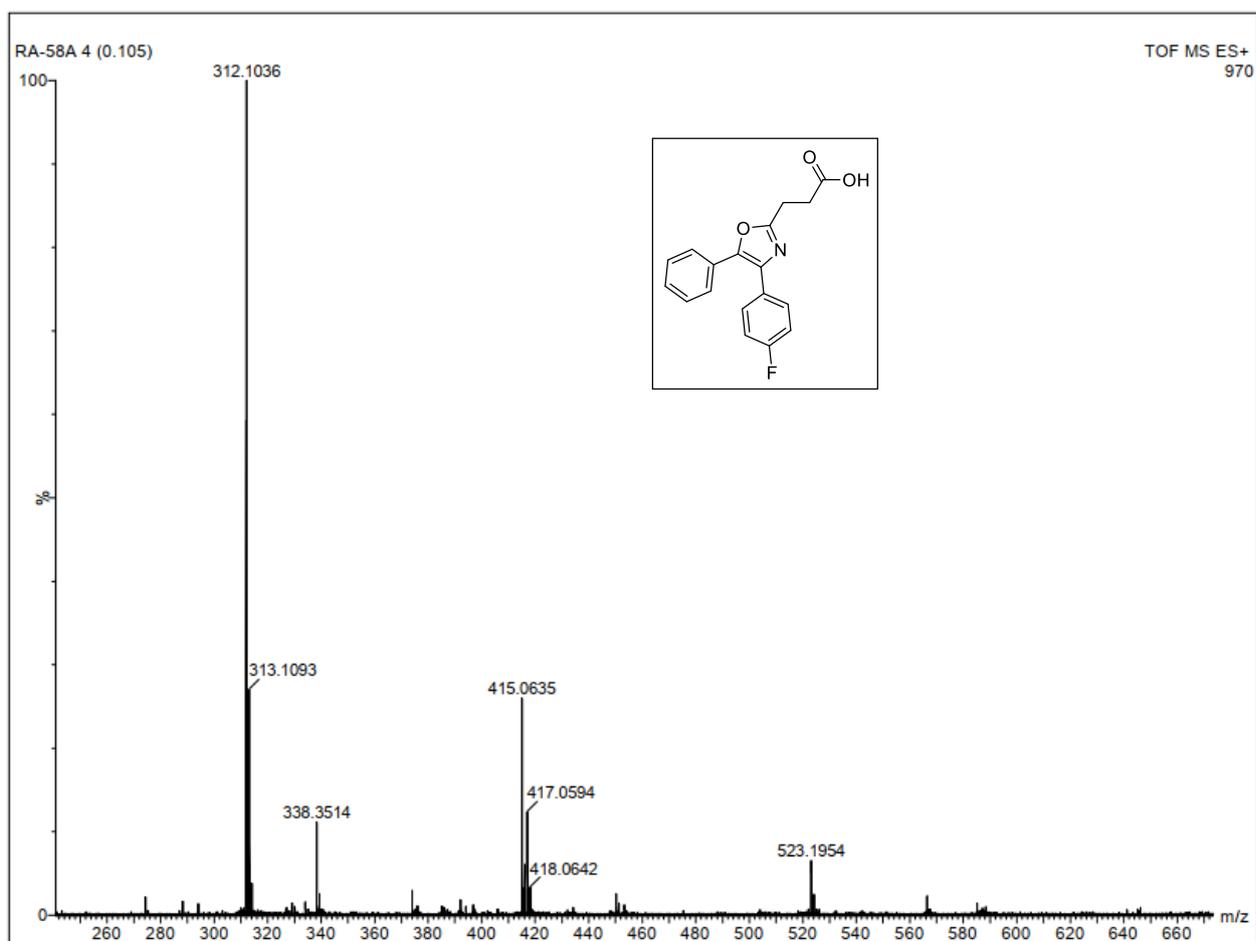


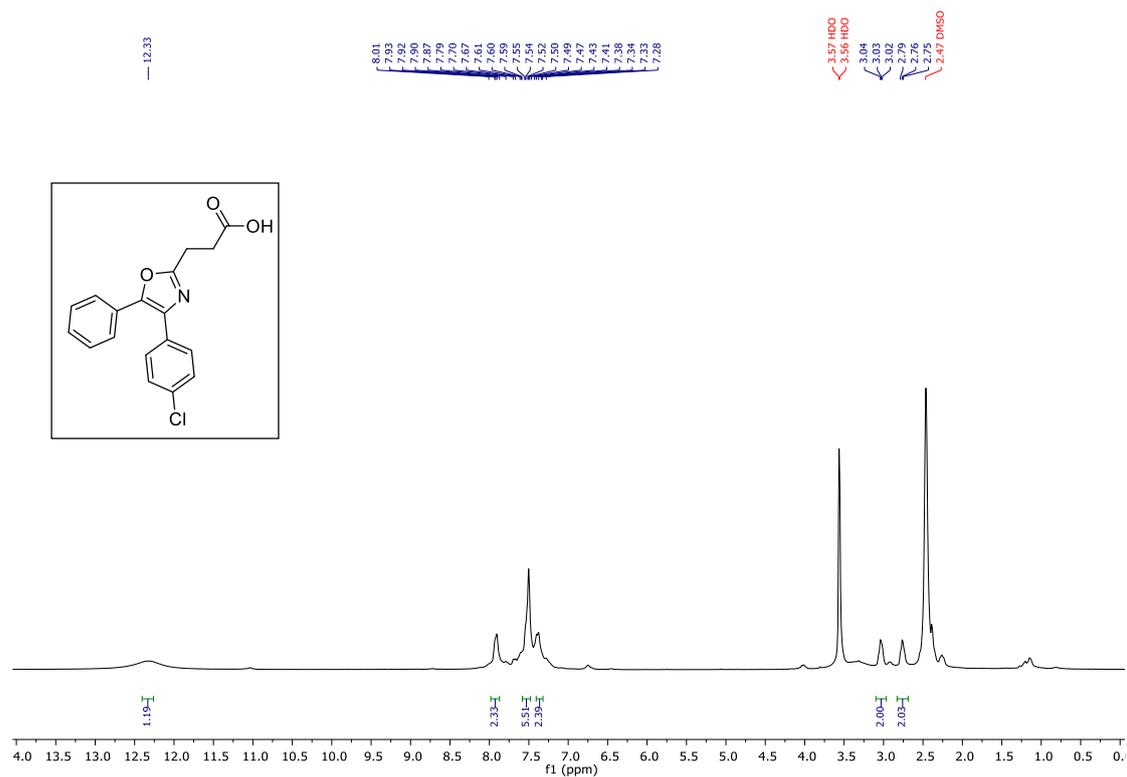
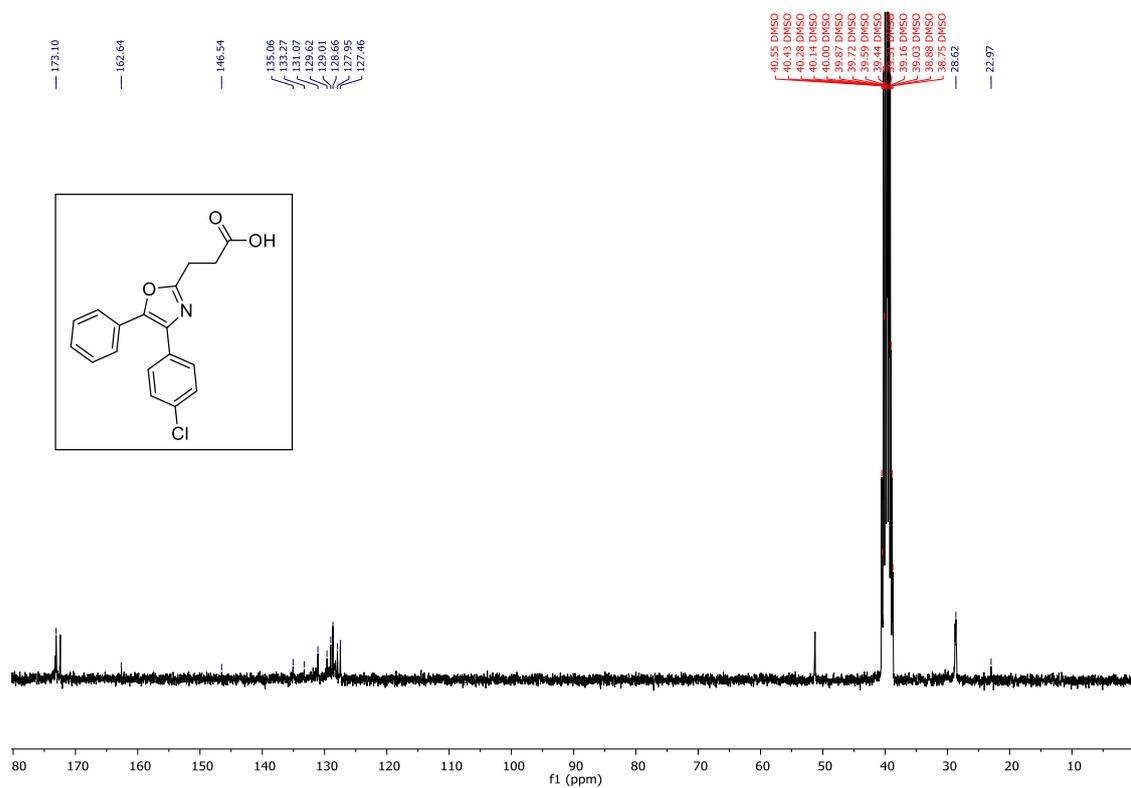
Figure S3: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **3a** (63 MHz, $\text{DMSO-}d_6$)Figure S4: HRMS (ESI) of **3a**

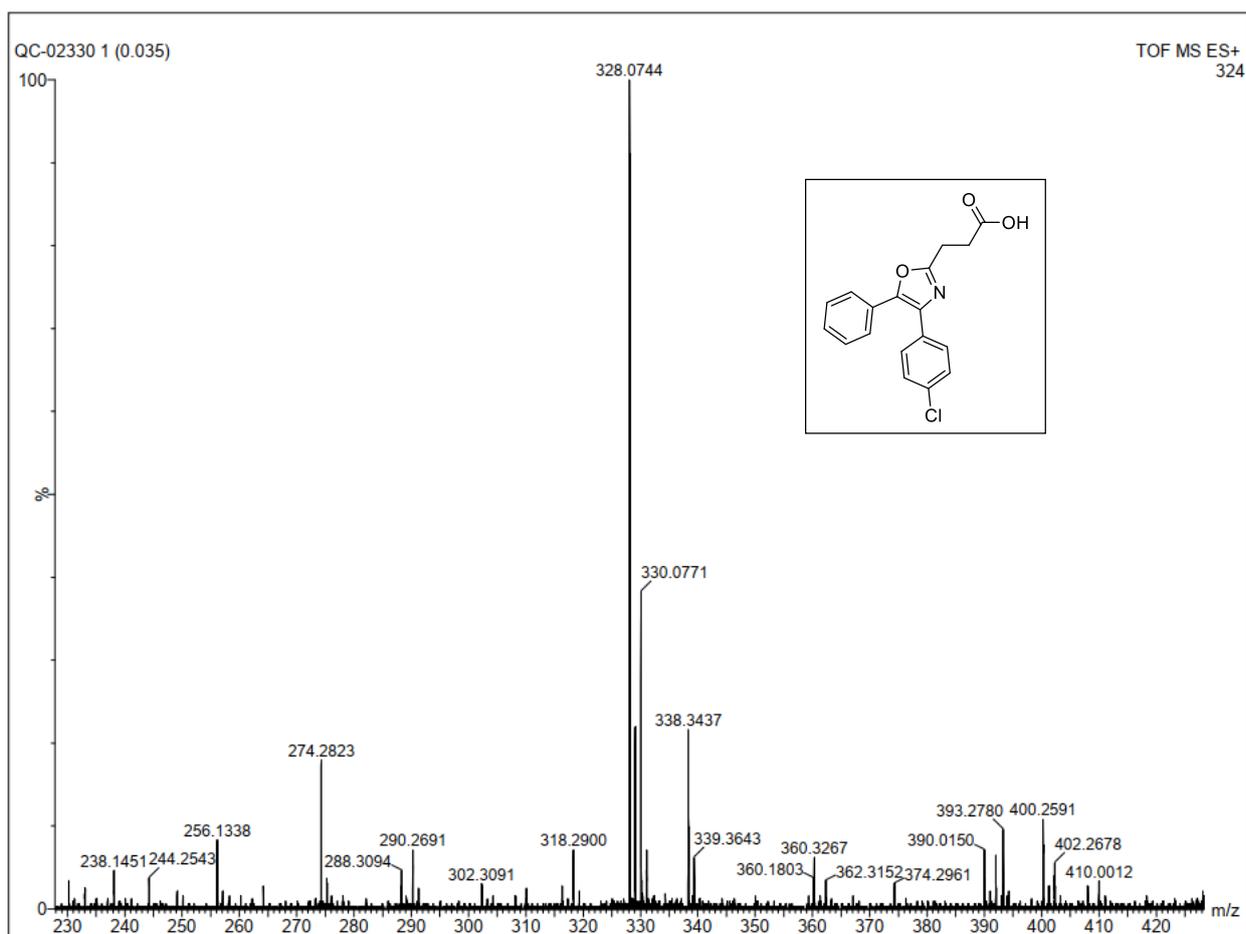
Figure S5: ^1H NMR Compound **3b** (500 MHz, $\text{DMSO-}d_6$)Figure S6: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **3b** (126 MHz, $\text{DMSO-}d_6$)

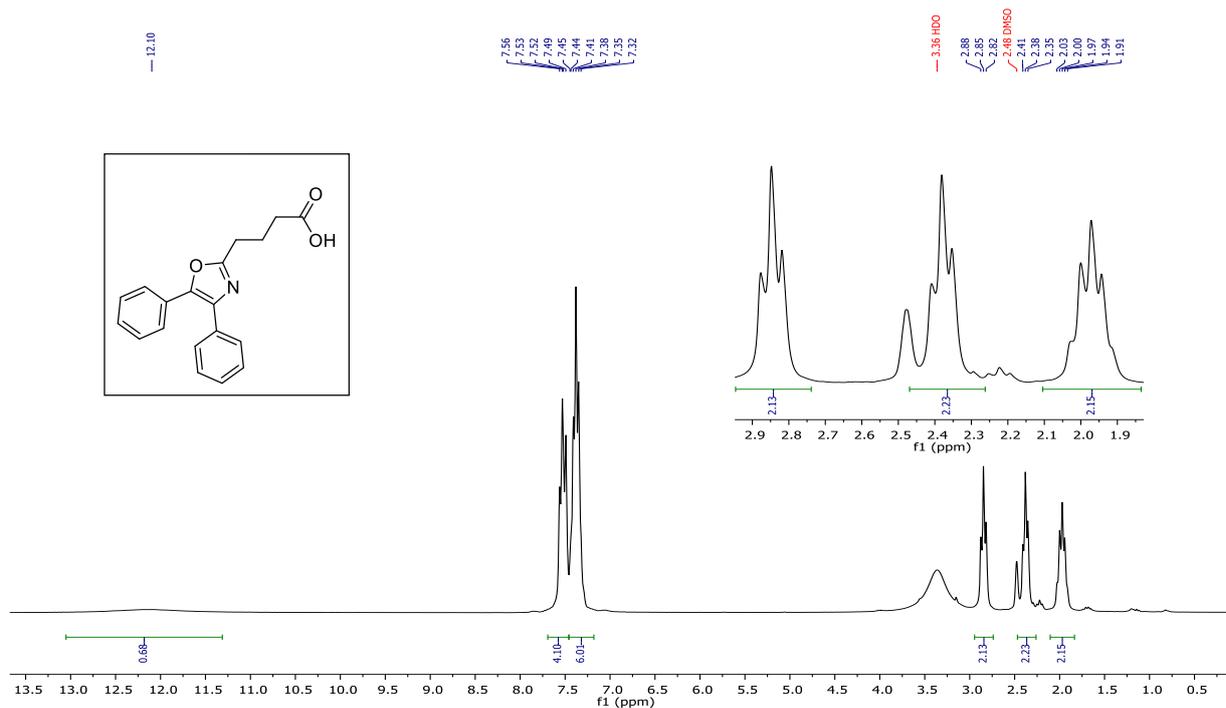
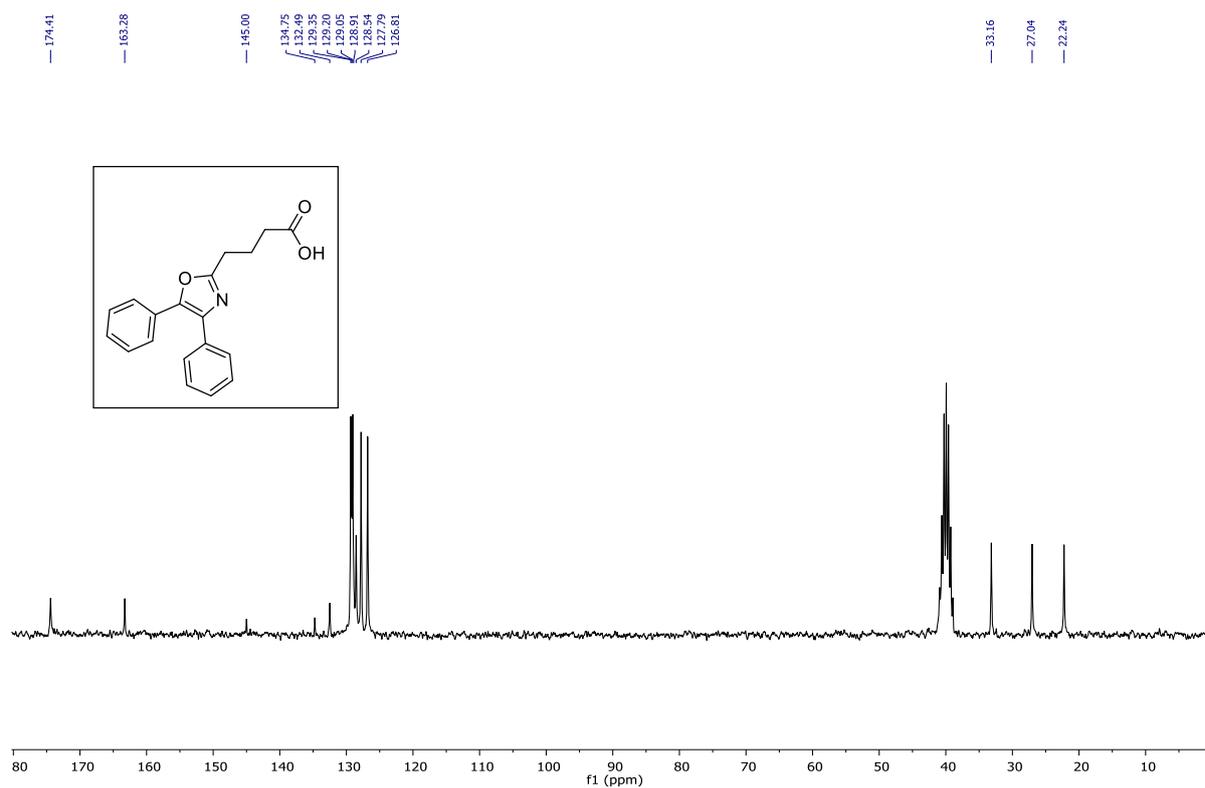
Figure S7: HRMS (ESI) of **3b**

Figure S8: ¹H NMR Compound 3c (300 MHz, DMSO-*d*₆)Figure S9: ¹³C {¹H} NMR Compound 3c (75 MHz, DMSO-*d*₆)

Figure S10: HRMS (ESI) of **3c**

Figure S11: ^1H NMR Compound 3d (300 MHz, $\text{DMSO-}d_6$)Figure S12: ^{13}C { ^1H } NMR Compound 3d (75 MHz, $\text{DMSO-}d_6$)

Figure S13: HRMS (ESI) of **3d**

Figure S14: ^1H NMR Compound 3e (250 MHz, $\text{DMSO-}d_6$)Figure S15: ^{13}C $\{^1\text{H}\}$ NMR Compound 3e (63 MHz, $\text{DMSO-}d_6$)

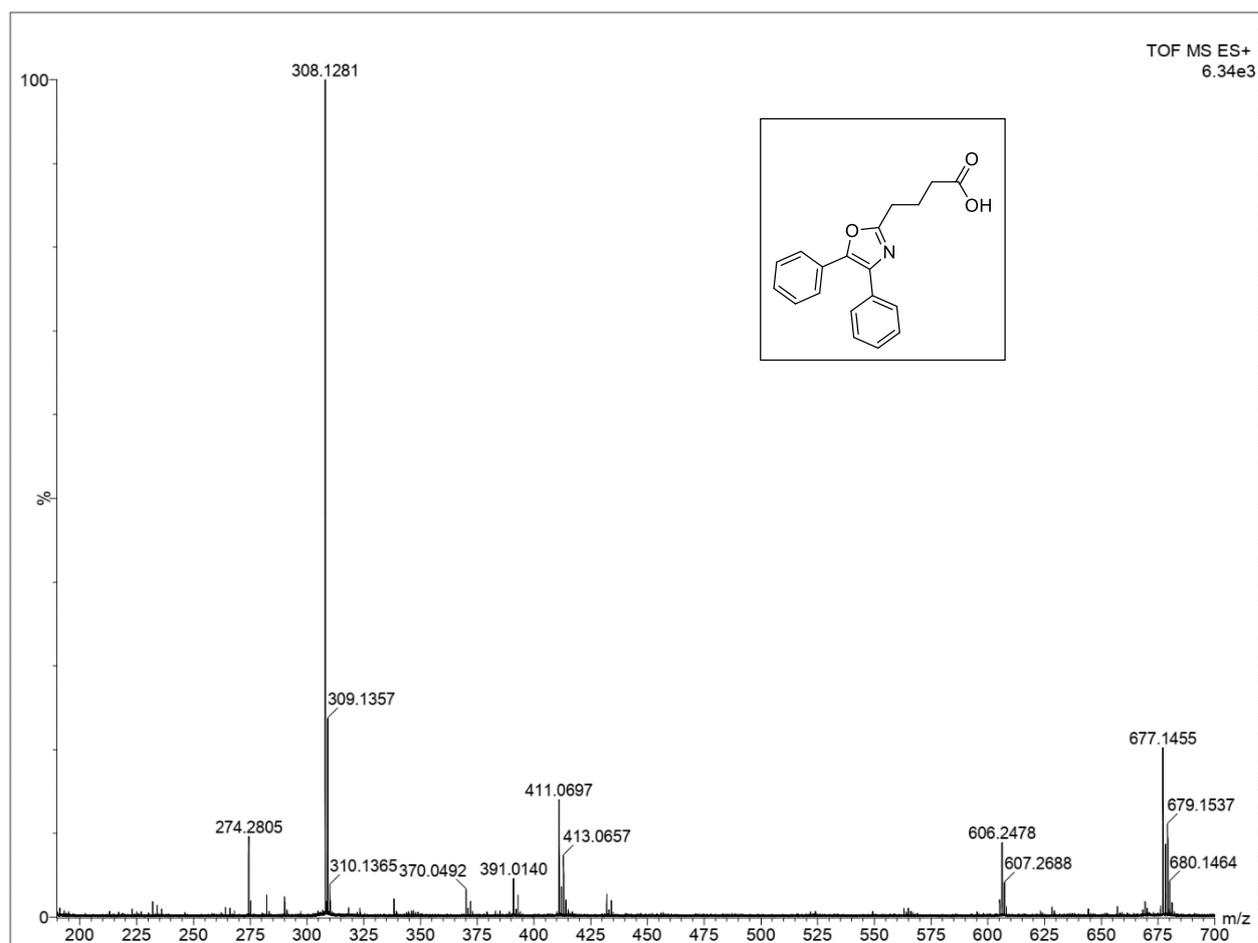
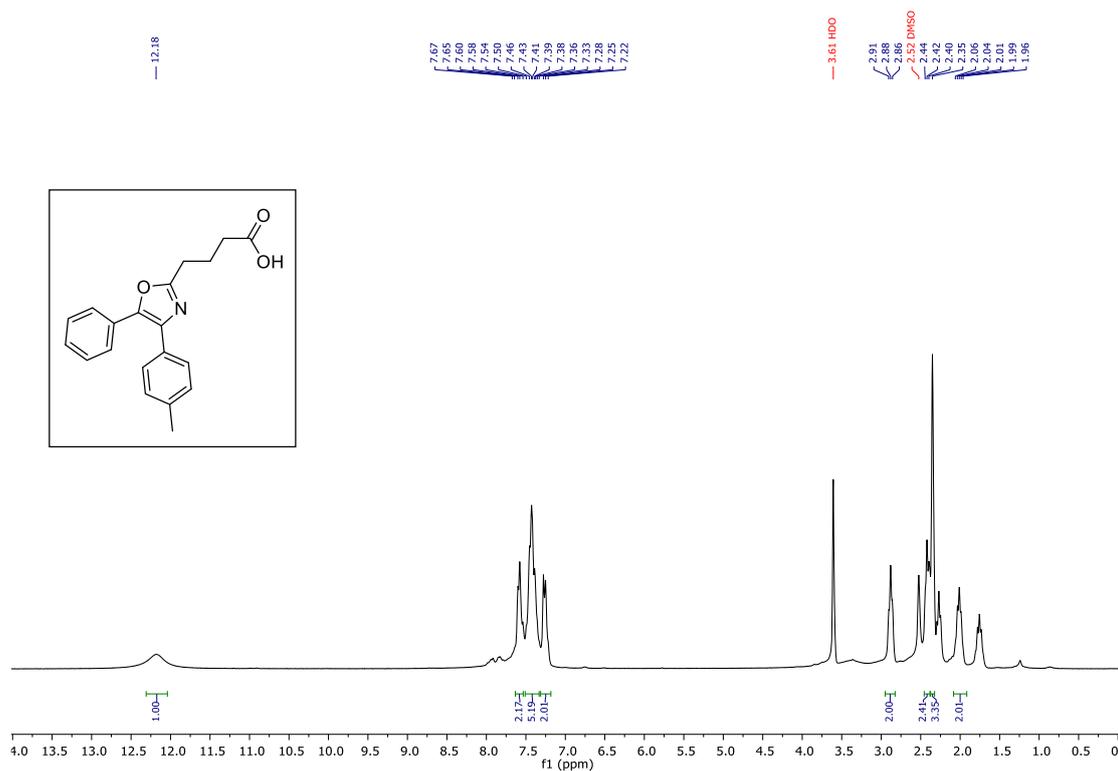
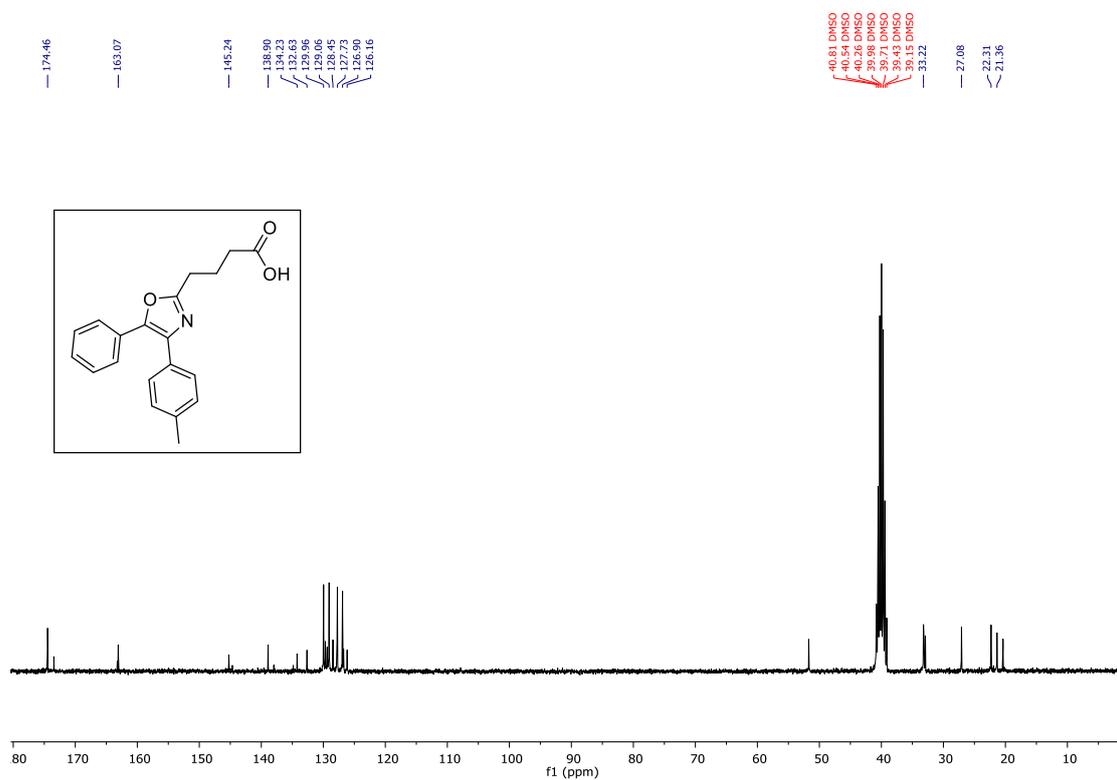
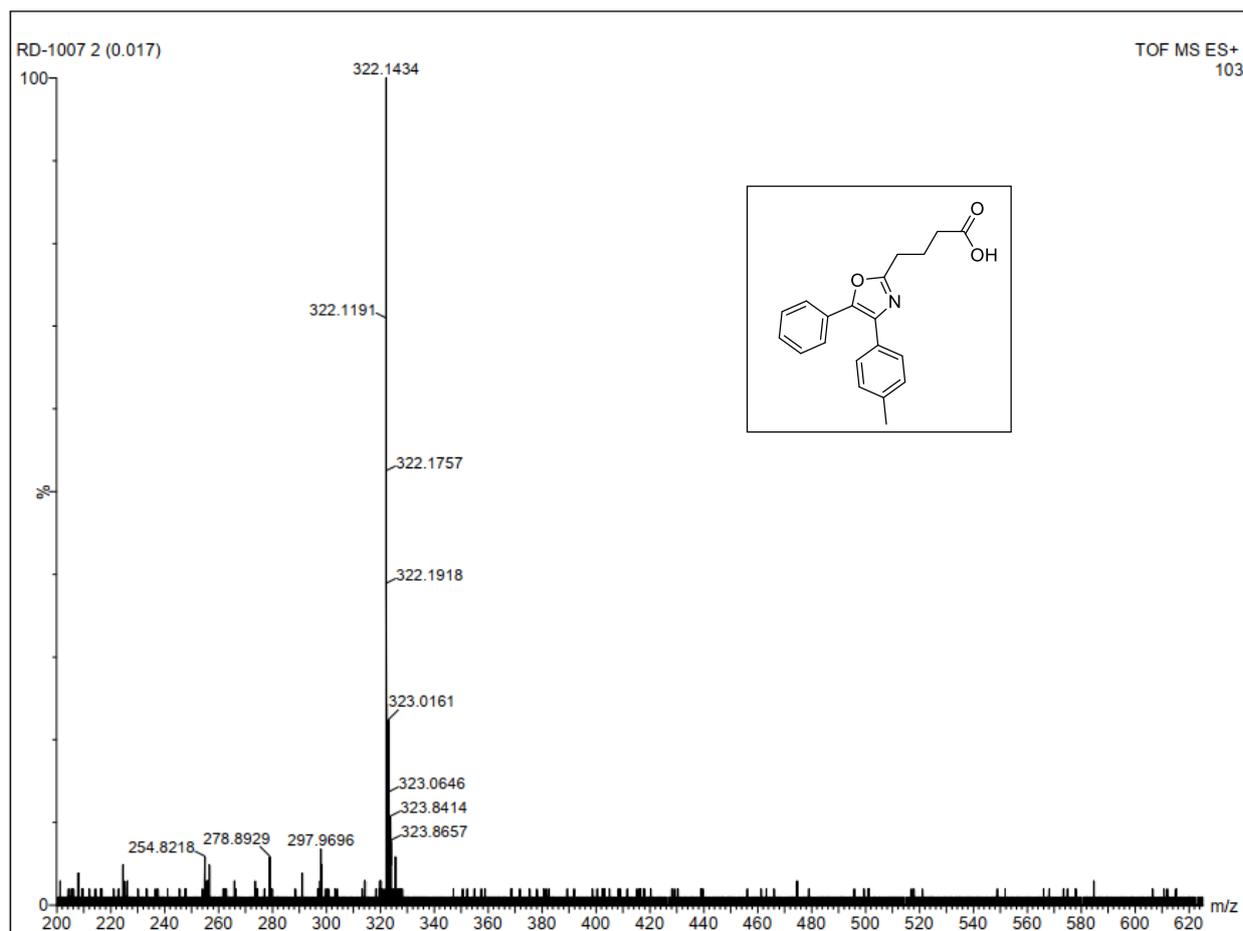
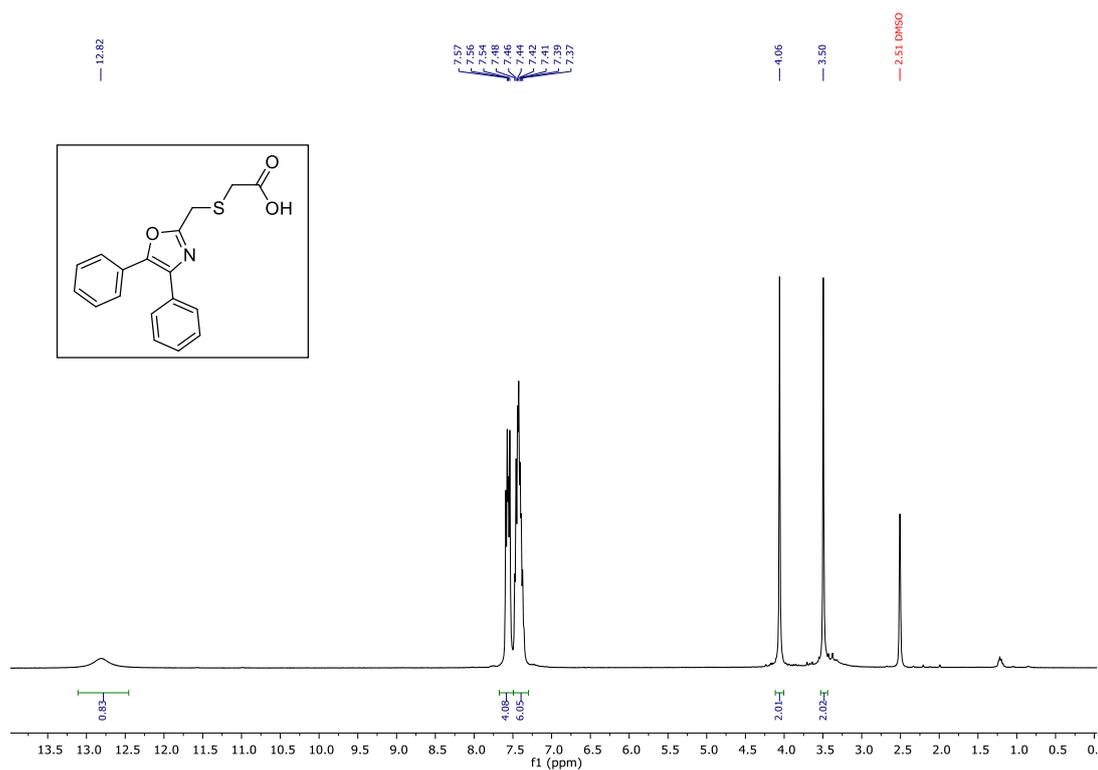
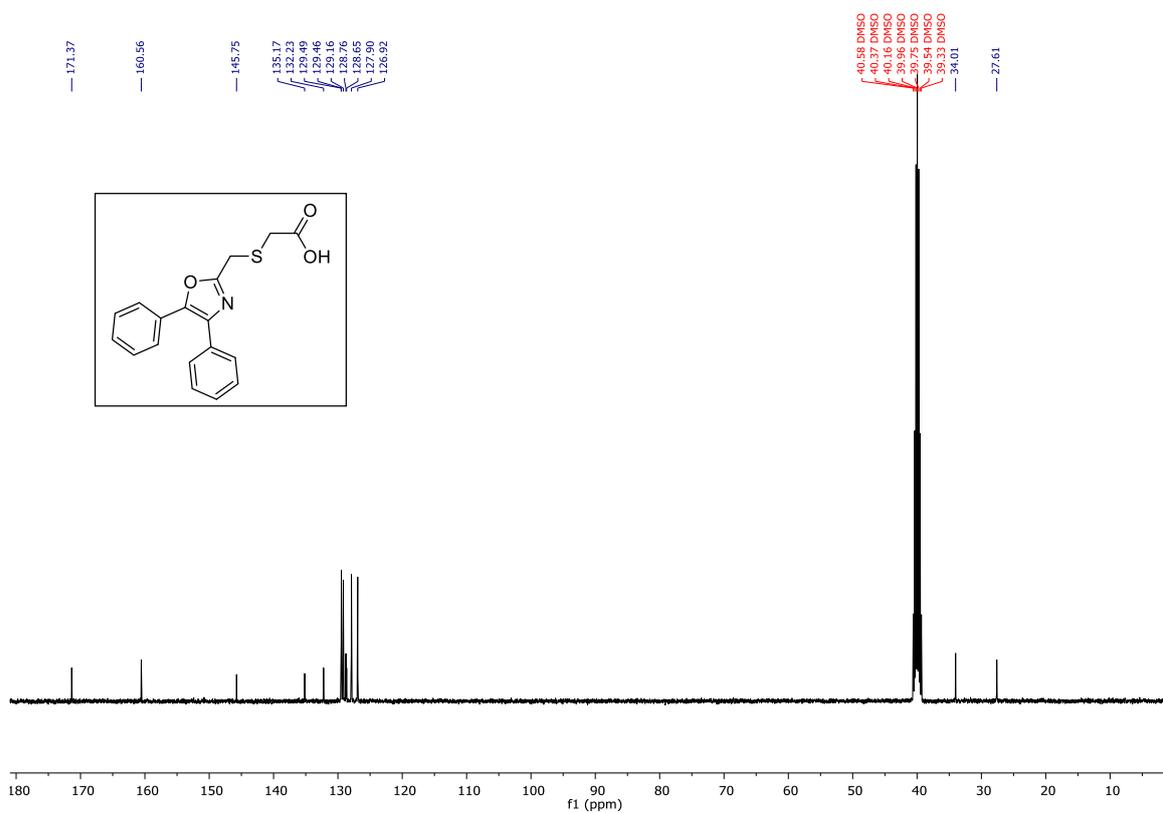
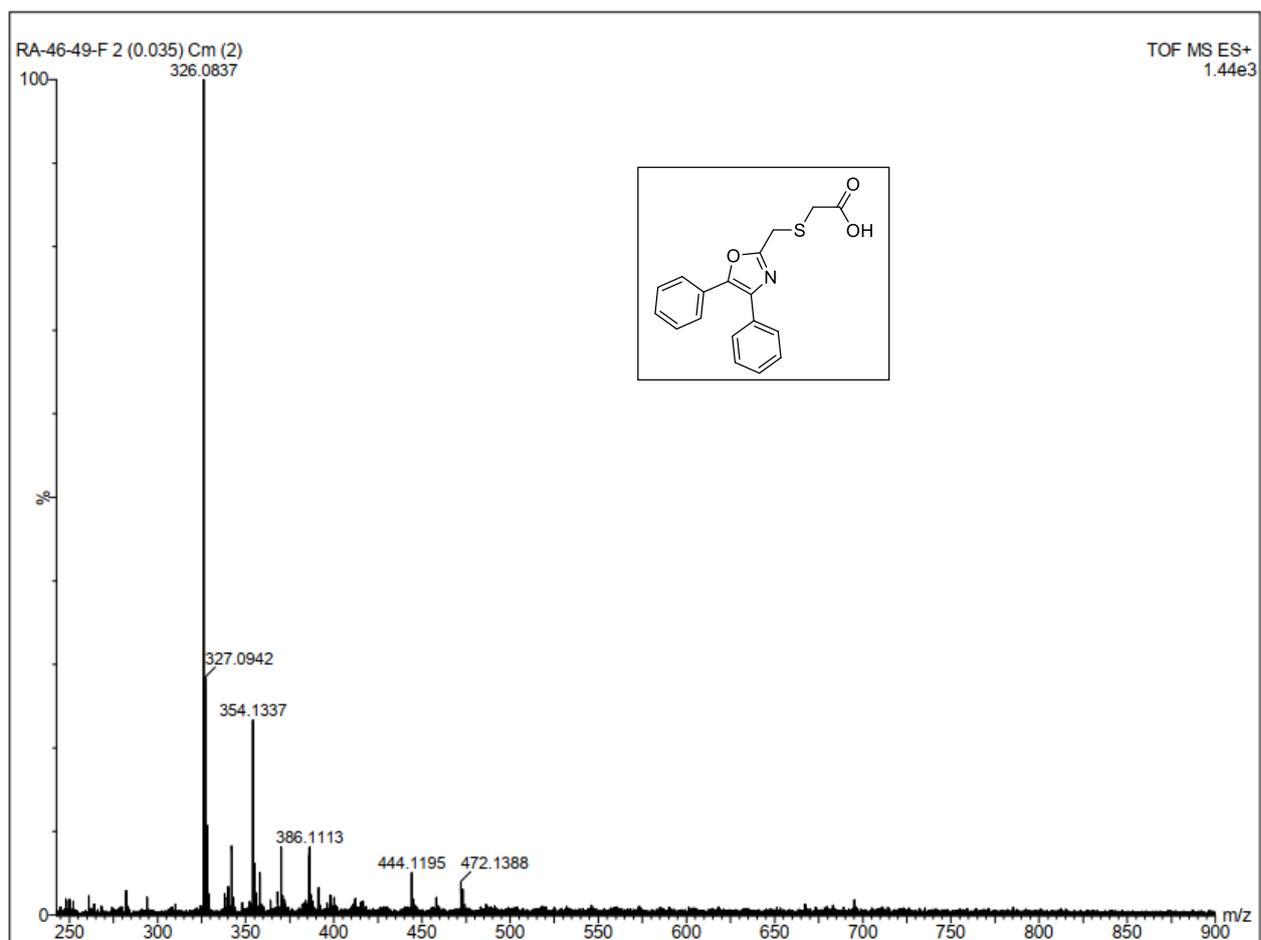


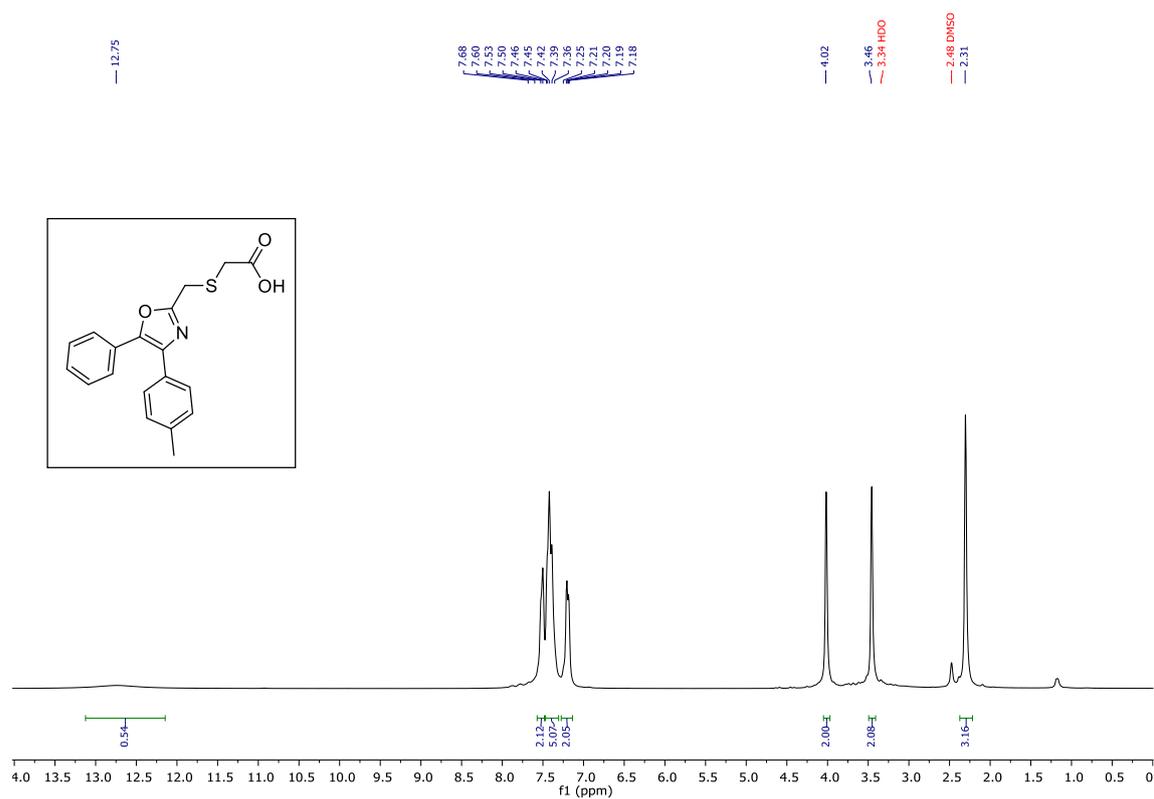
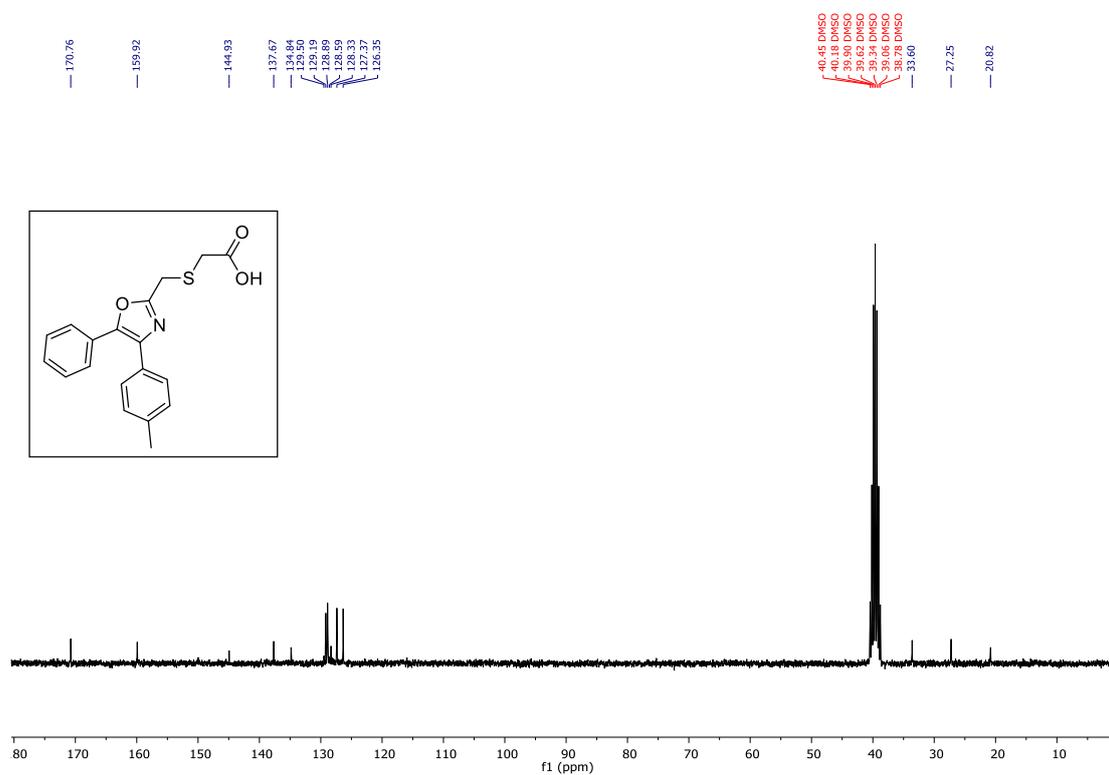
Figure S16: HRMS (ESI) of 3e

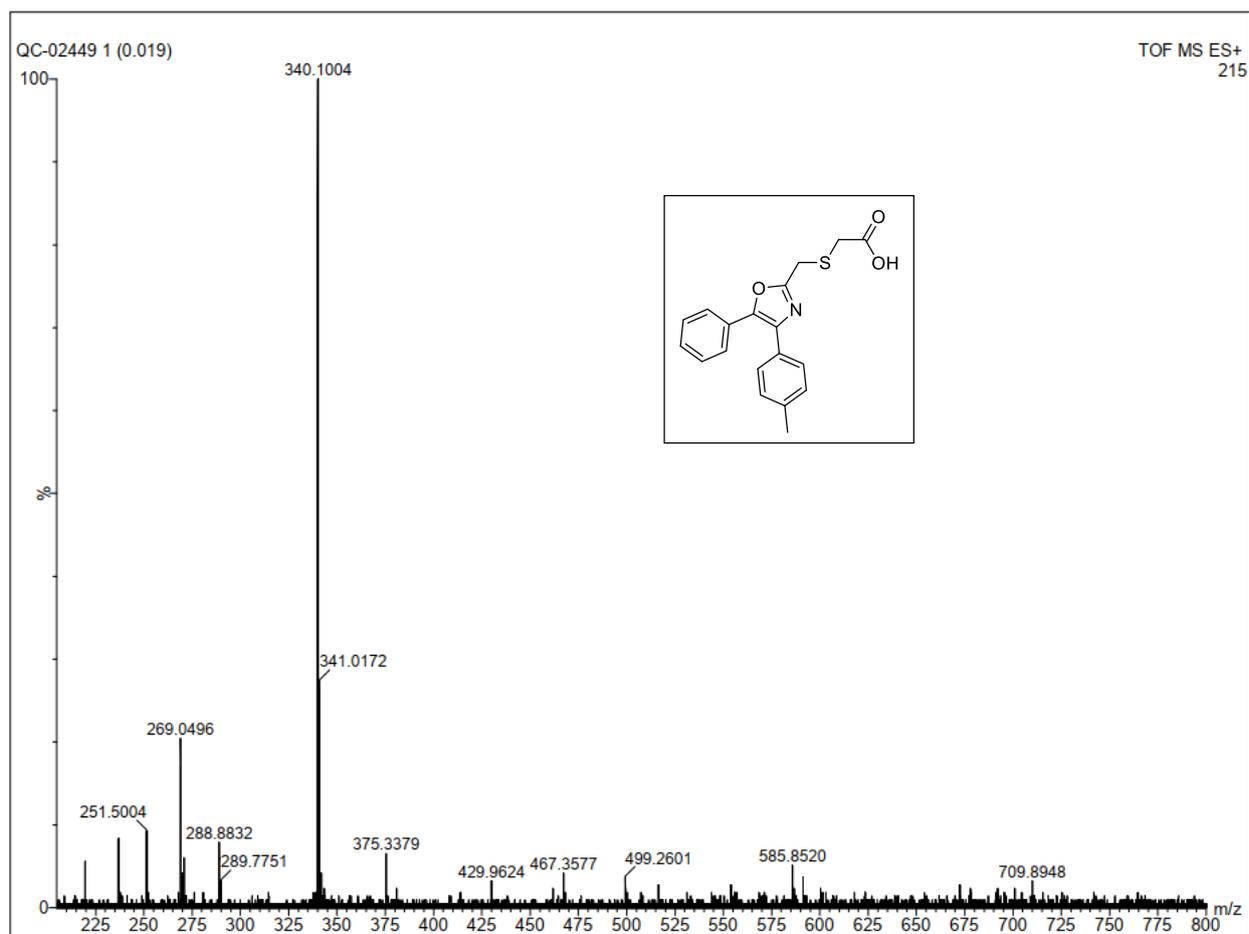
Figure S17: ¹H NMR Compound 3f (300 MHz, DMSO-*d*₆)Figure S18: ¹³C {¹H} NMR Compound 3f (75 MHz, DMSO-*d*₆)

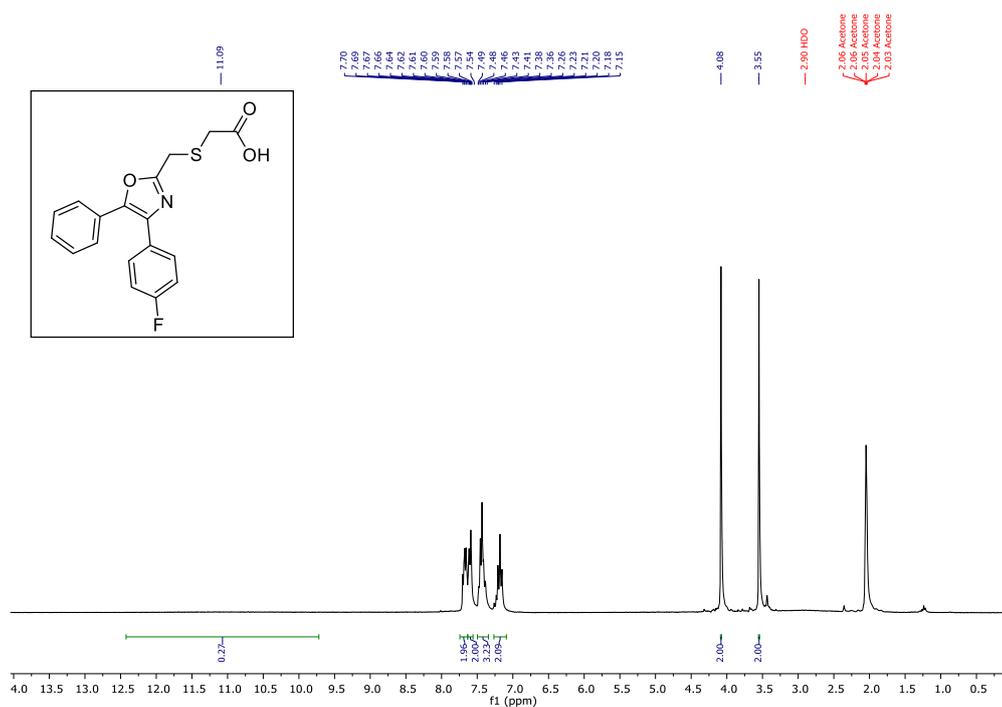
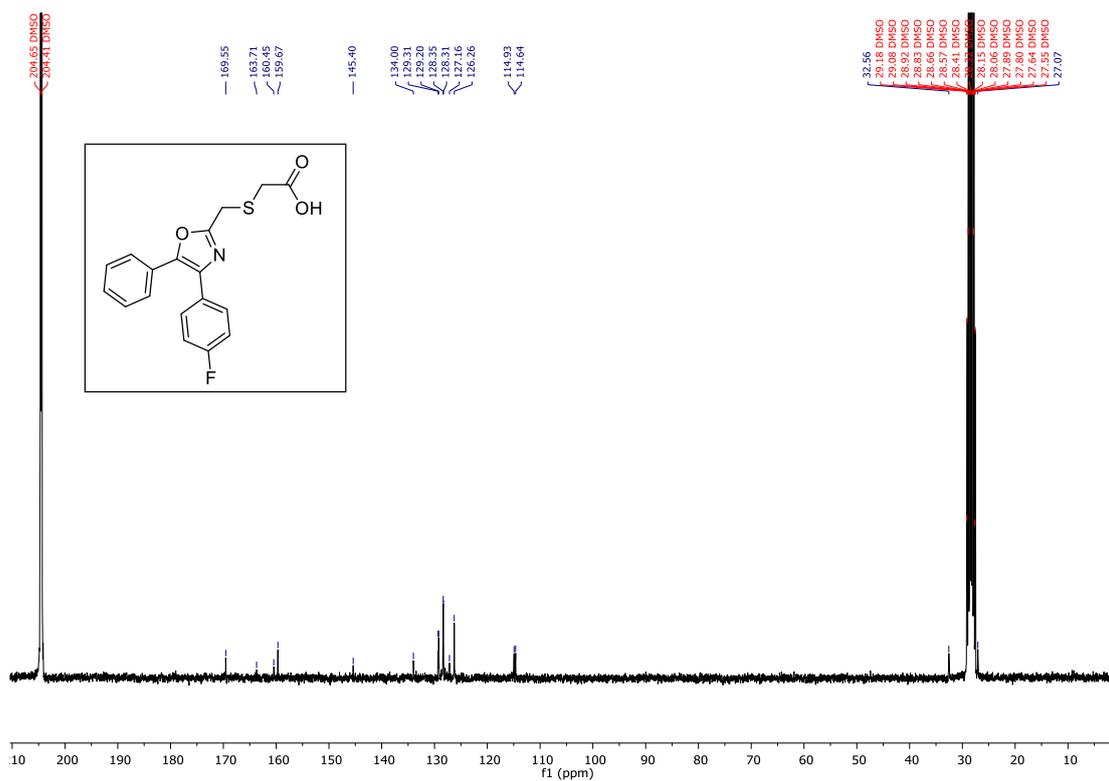
Figure S19: HRMS (ESI) of **3f**

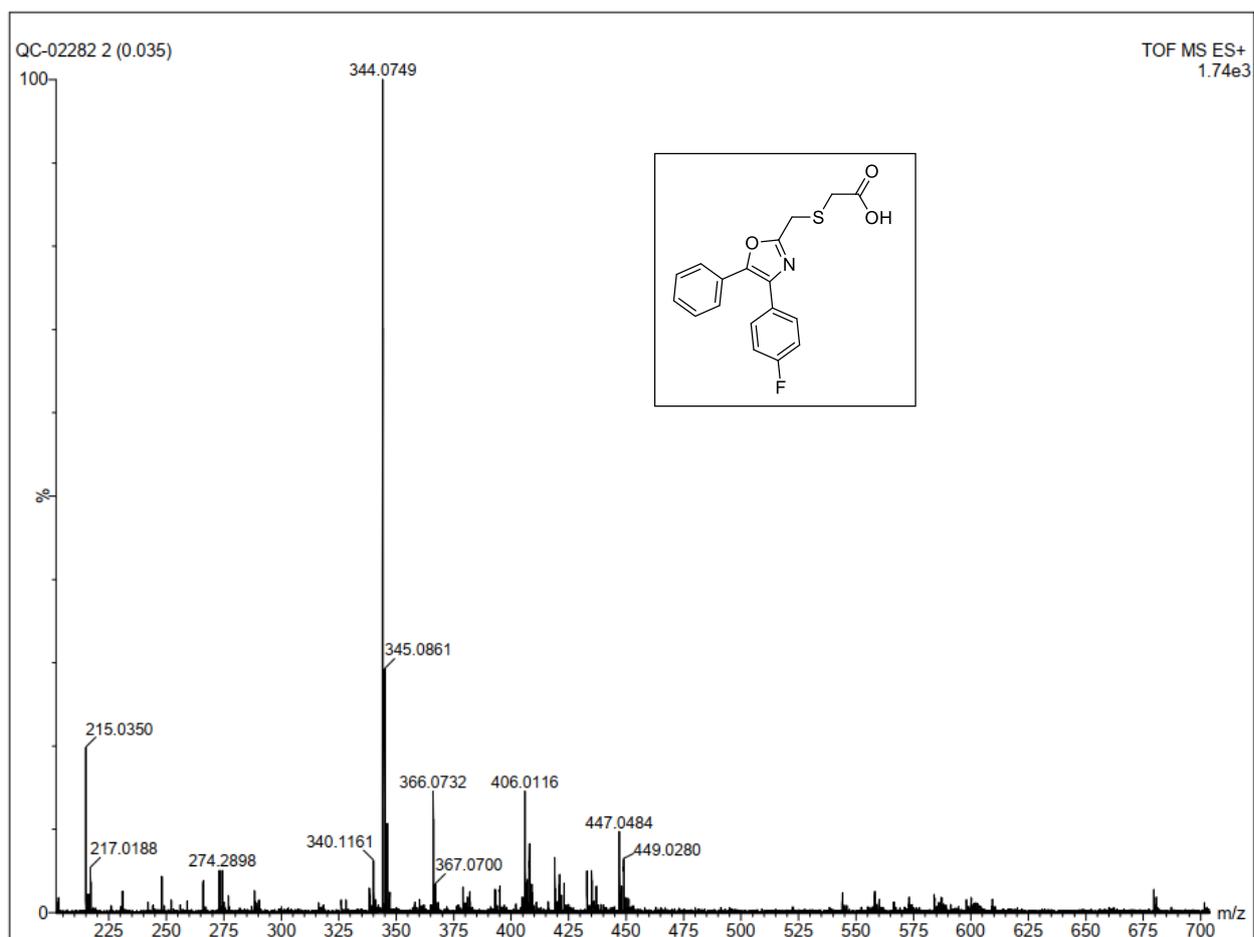
Figure S20: ^1H NMR Compound 3g (400 MHz, $\text{DMSO-}d_6$)Figure S21: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 3g (101 MHz, $\text{DMSO-}d_6$)

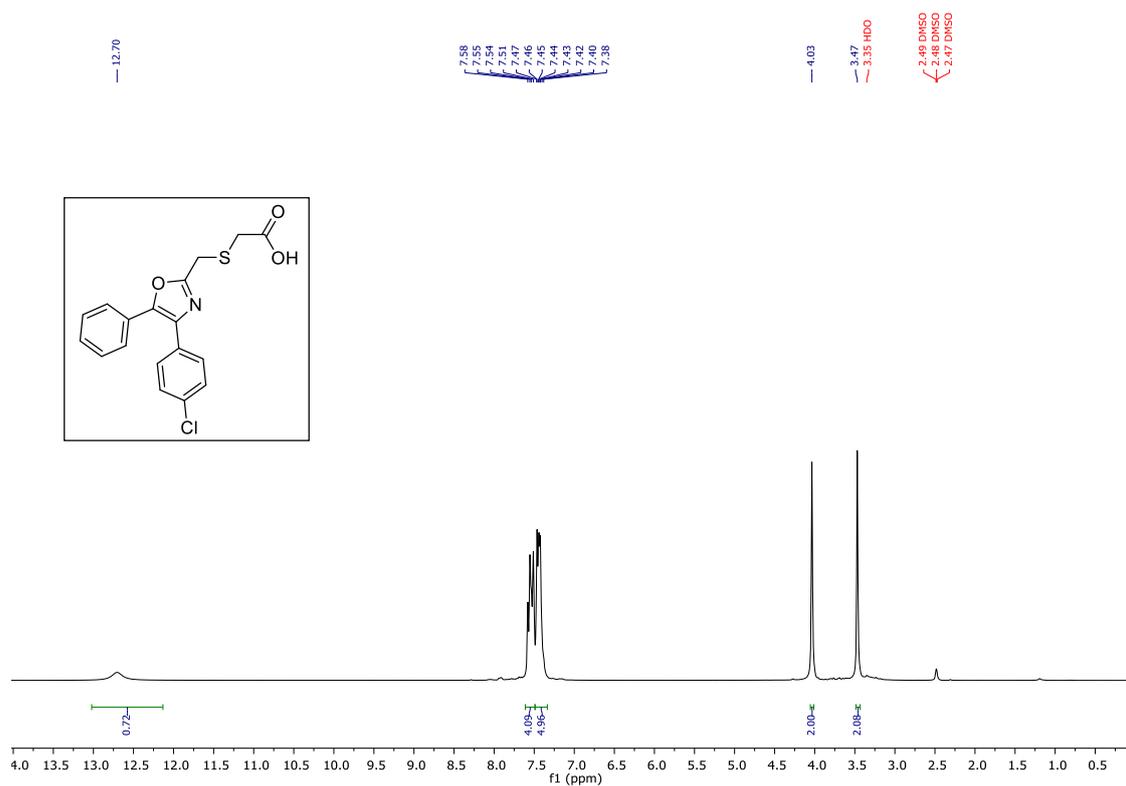
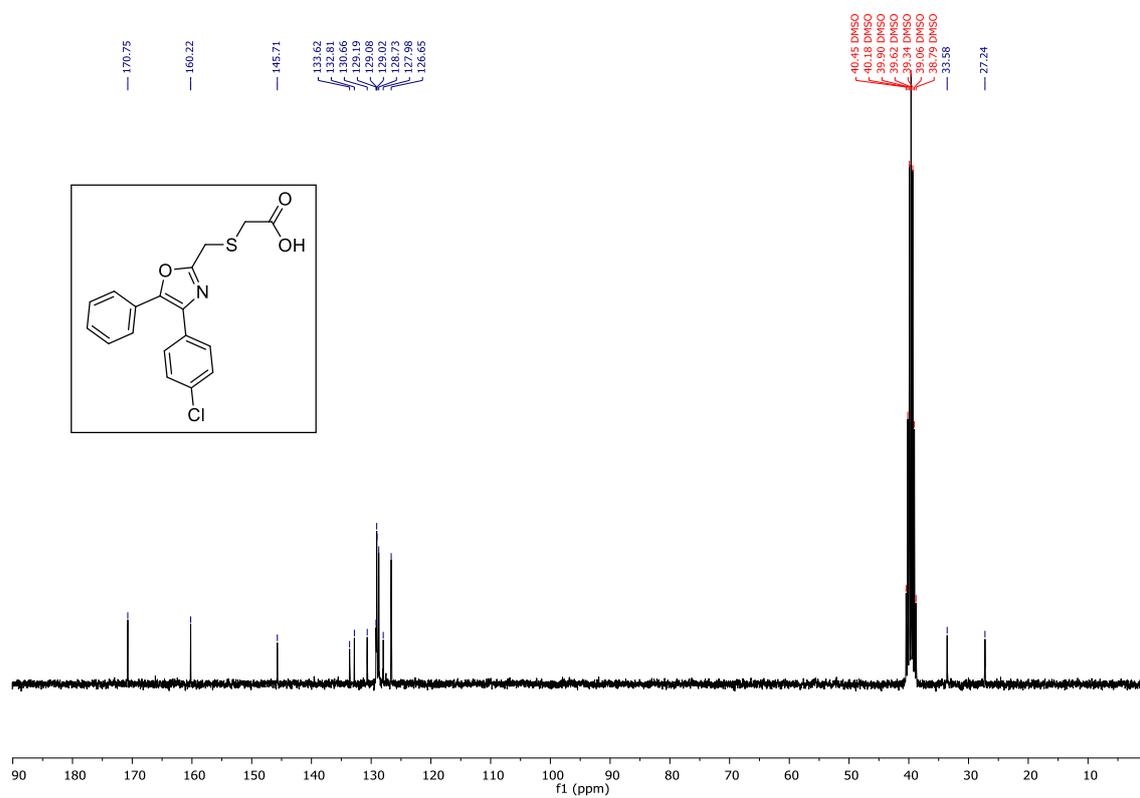
Figure S22: HRMS (ESI) of **3g**

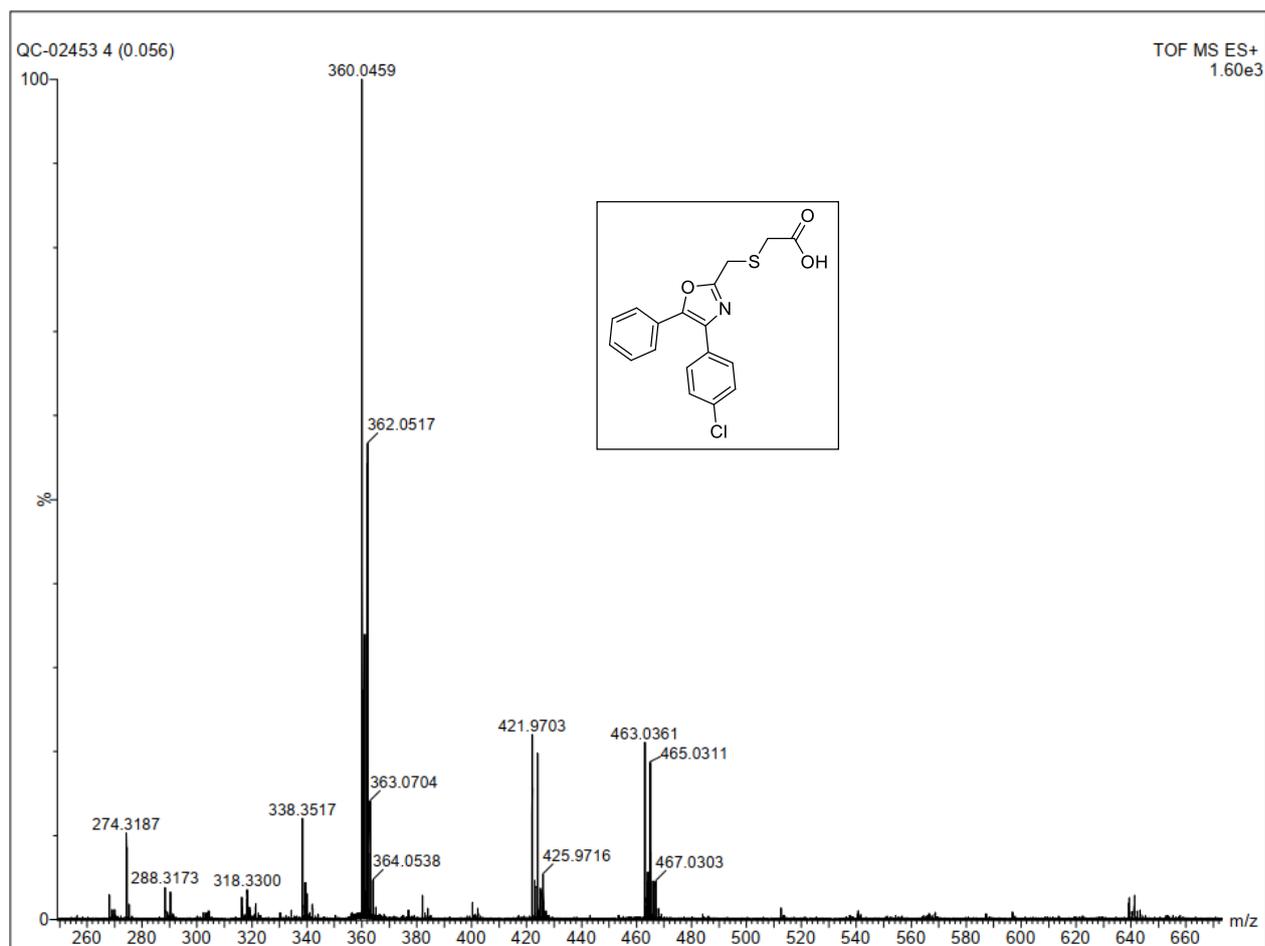
Figure S23: ^1H NMR Compound 3h (300 MHz, DMSO- d_6)Figure S24: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 3h (75 MHz, DMSO- d_6)

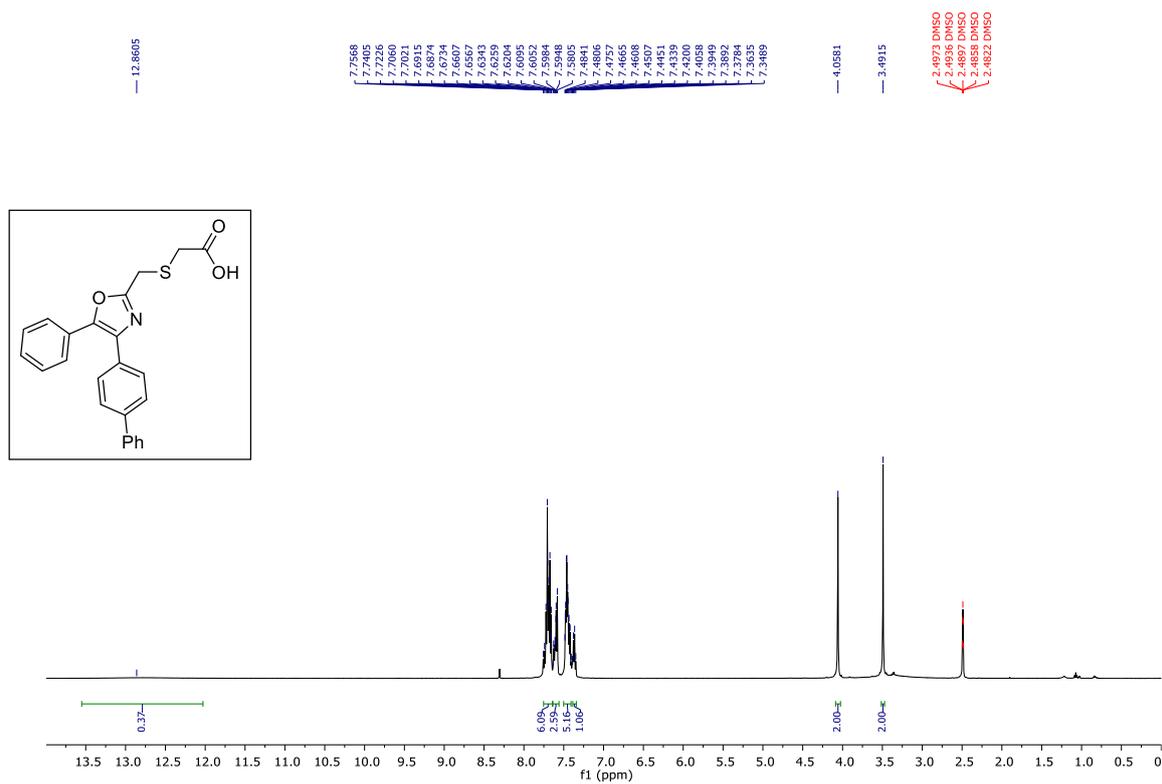
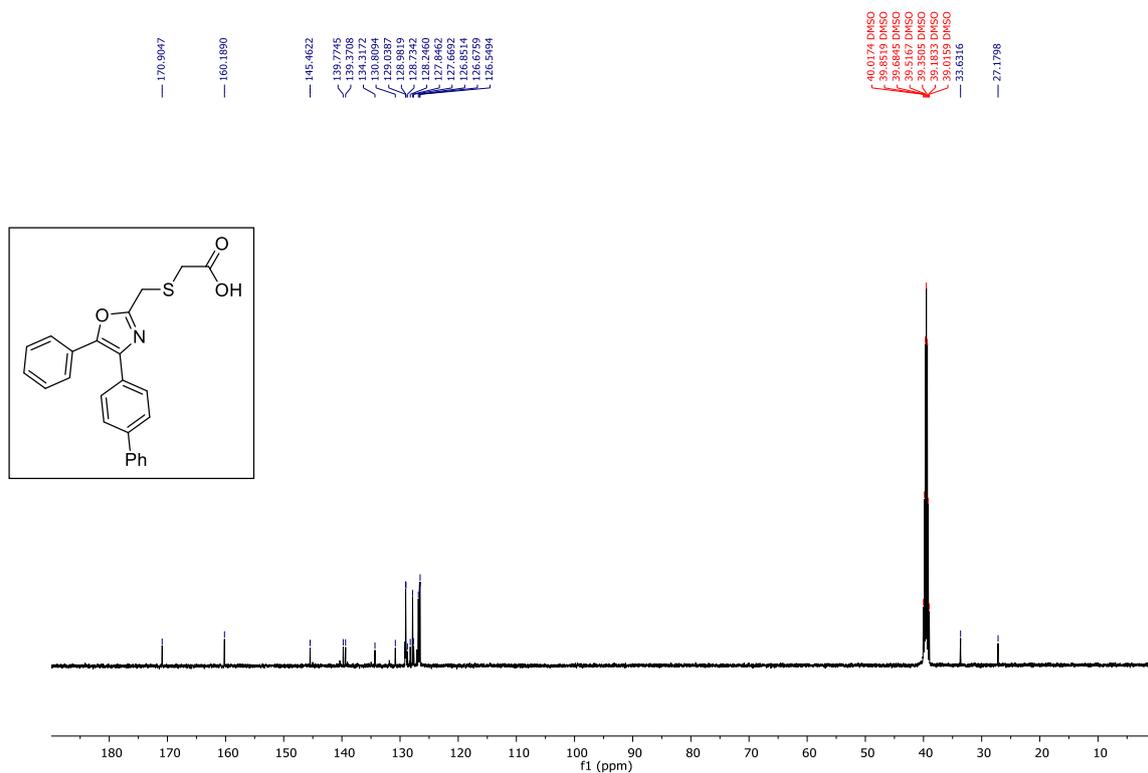
Figure S25: HRMS (ESI) of **3h**

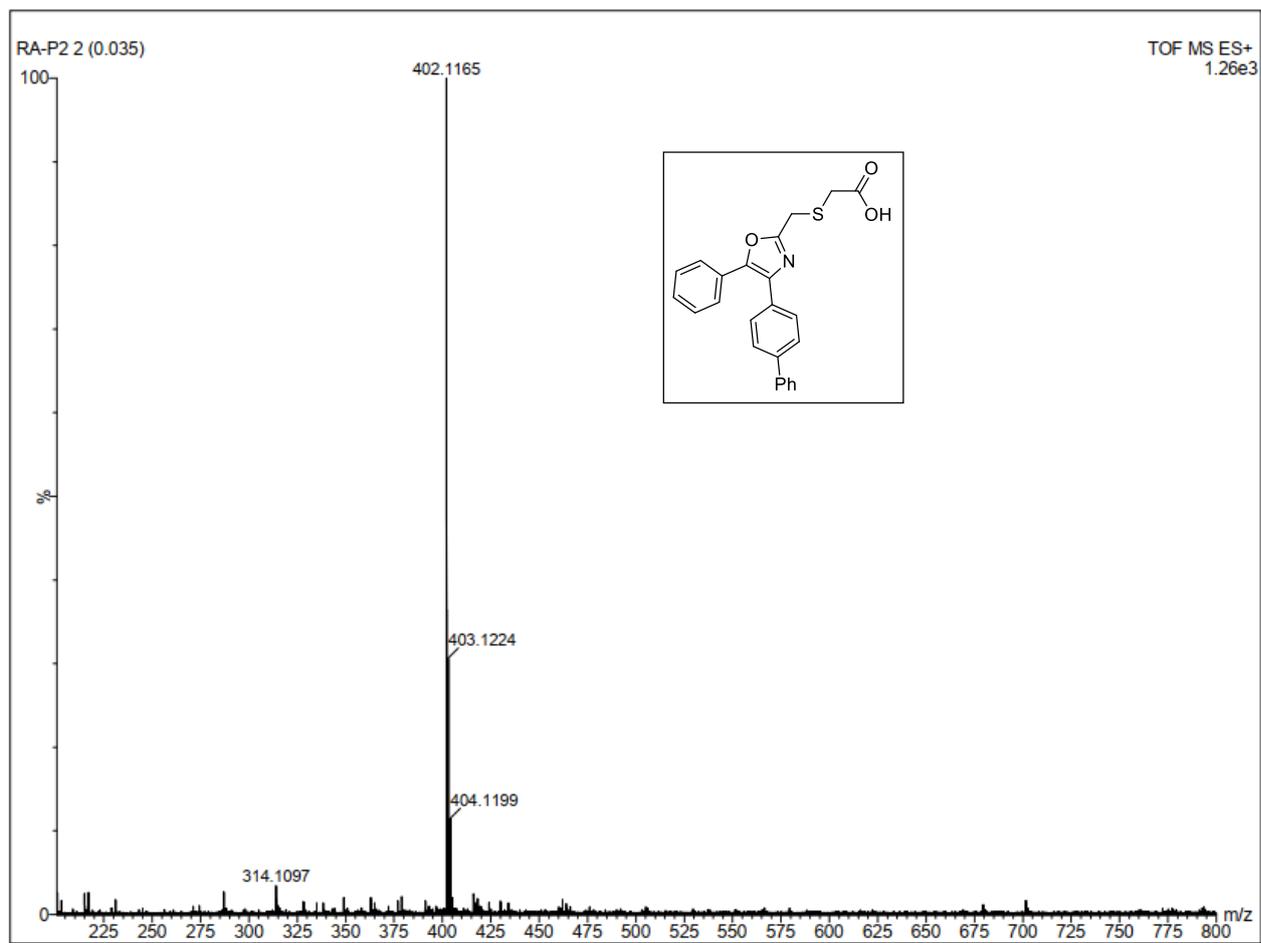
Figure S26: ¹H NMR Compound 3i (300 MHz, Acetone)Figure S27: ¹³C {¹H} NMR Compound 3i (75 MHz, Acetone)

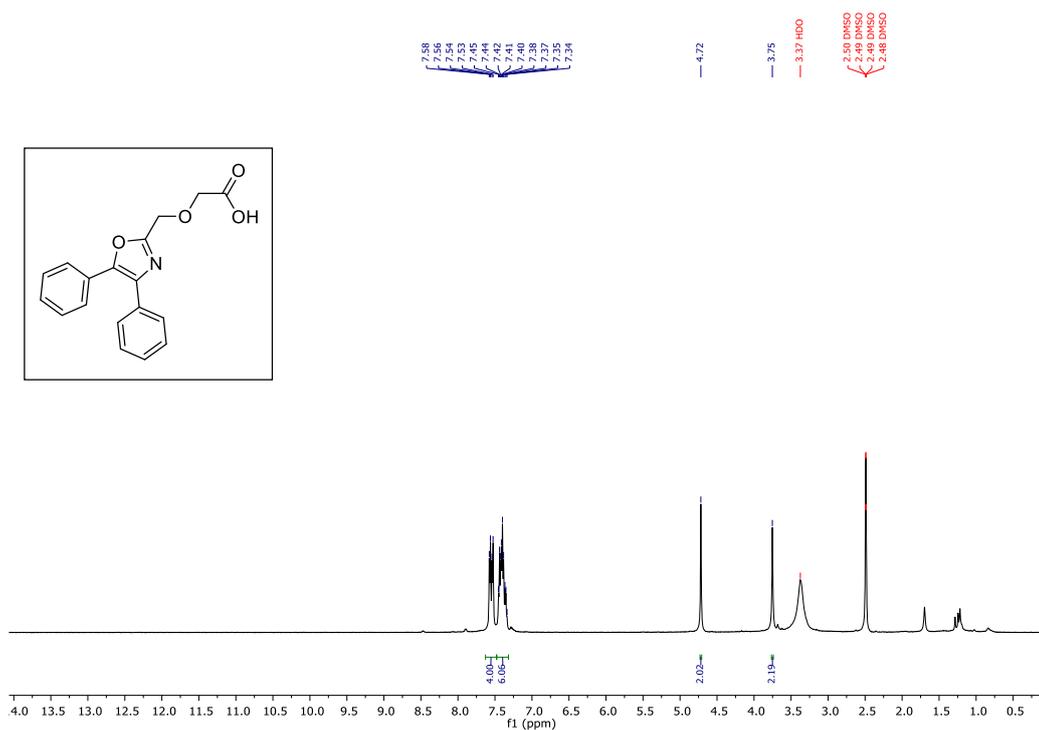
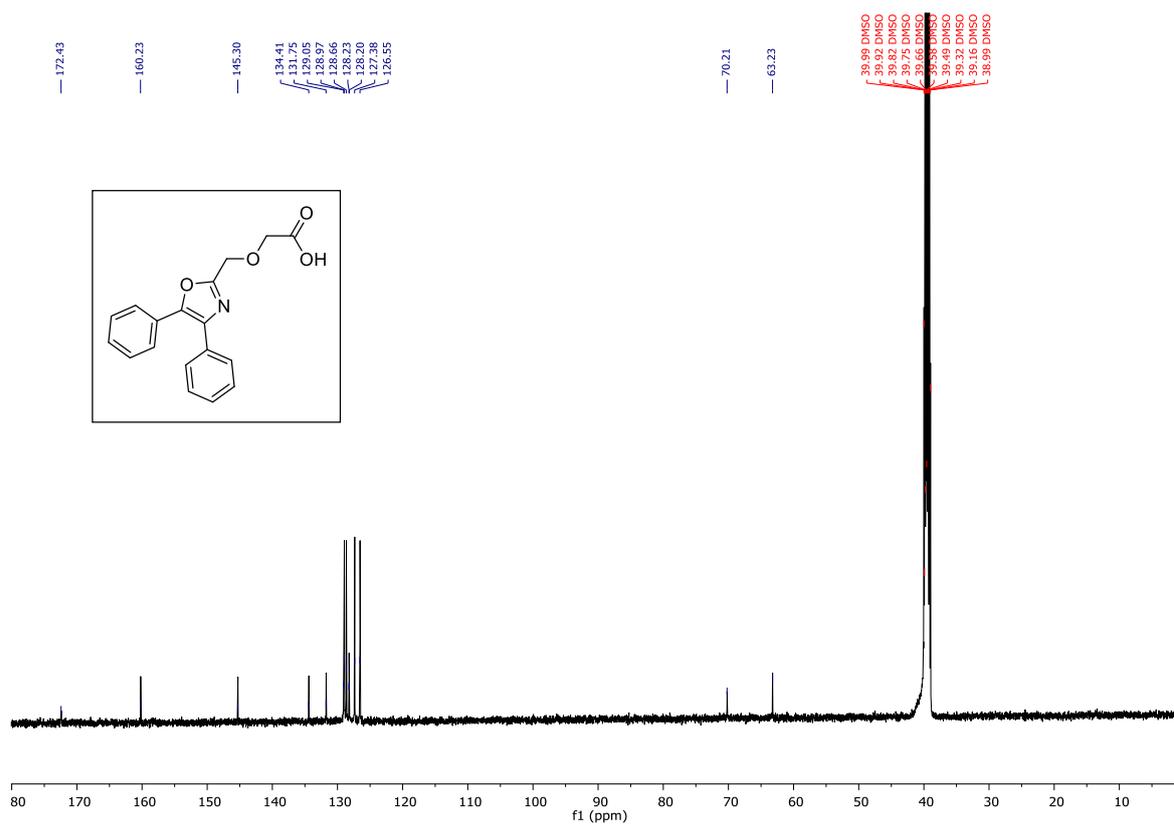
Figure S28: HRMS (ESI) of **3i**

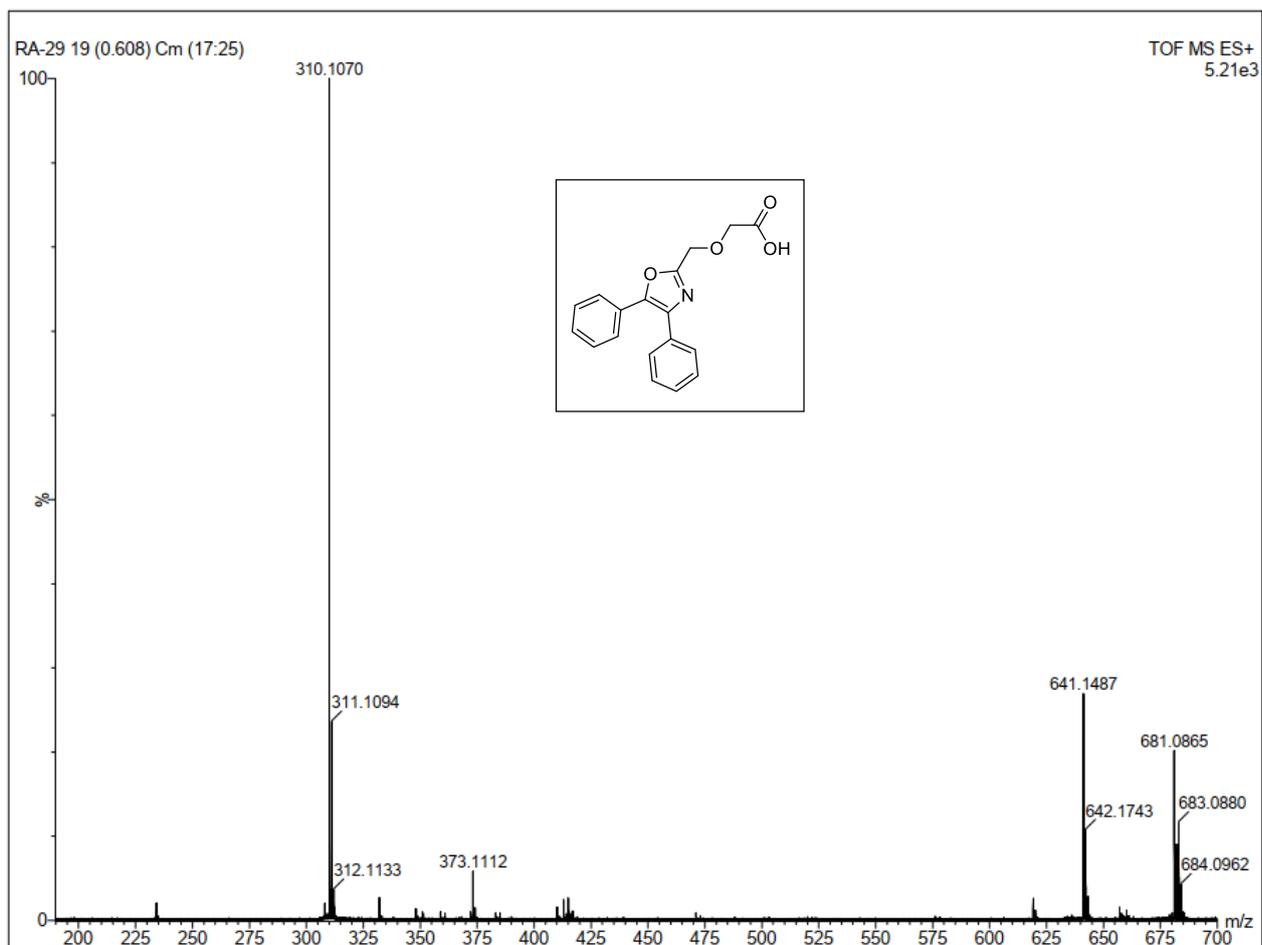
Figure S29: $^1\text{H NMR}$ Compound 3j (300 MHz, $\text{DMSO-}d_6$)Figure S30: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 3j (75 MHz, $\text{DMSO-}d_6$)

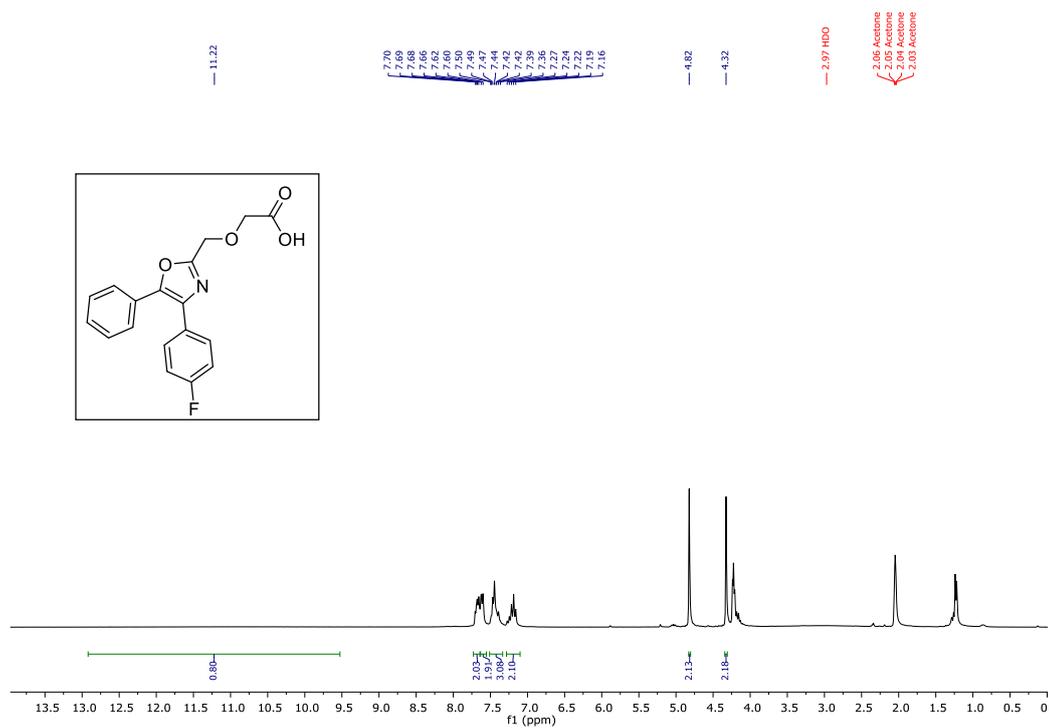
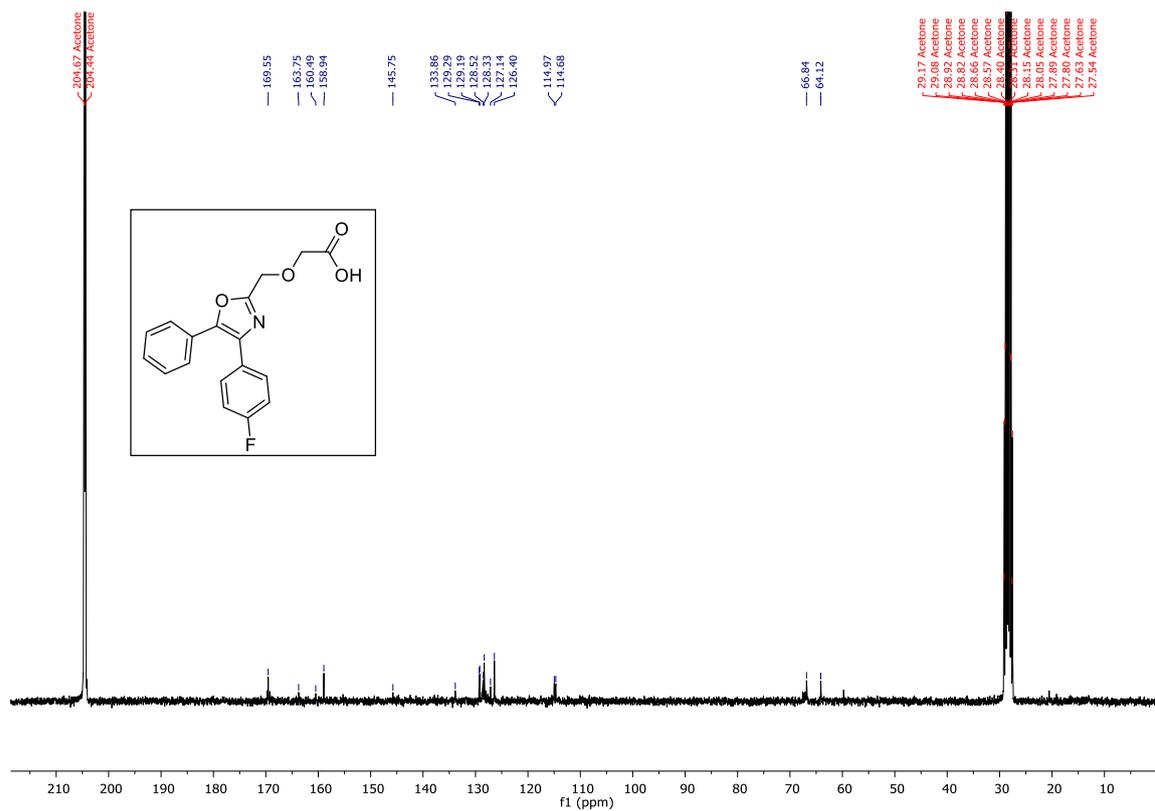
Figure S31: HRMS (ESI) of **3j**

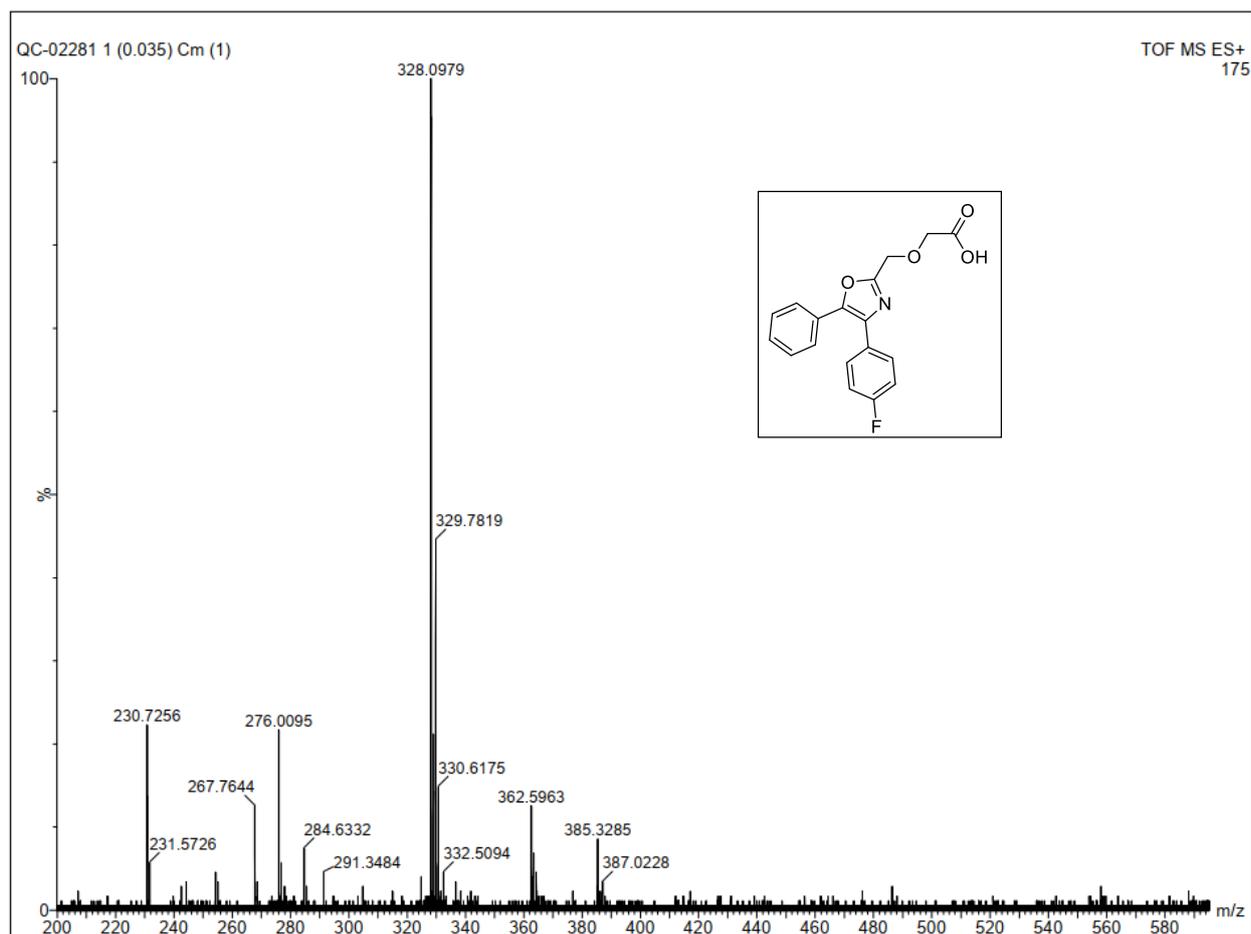
Figure S32: ^1H NMR Compound **3k** (500 MHz, $\text{DMSO-}d_6$)Figure S33: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **3k** (126 MHz, $\text{DMSO-}d_6$)

Figure S34: HRMS (ESI) of **3k**

Figure S35: ^1H NMR Compound 31 (500 MHz, $\text{DMSO-}d_6$)Figure S36: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 31 (126 MHz, $\text{DMSO-}d_6$)

Figure S37: HRMS (ESI) of **31**

Figure S38: ¹H NMR Compound 3m (300 MHz, Acetone)Figure S39: ¹³C {¹H} NMR Compound 3m (75 MHz, Acetone)

Figure S40: HRMS (ESI) of **3m**

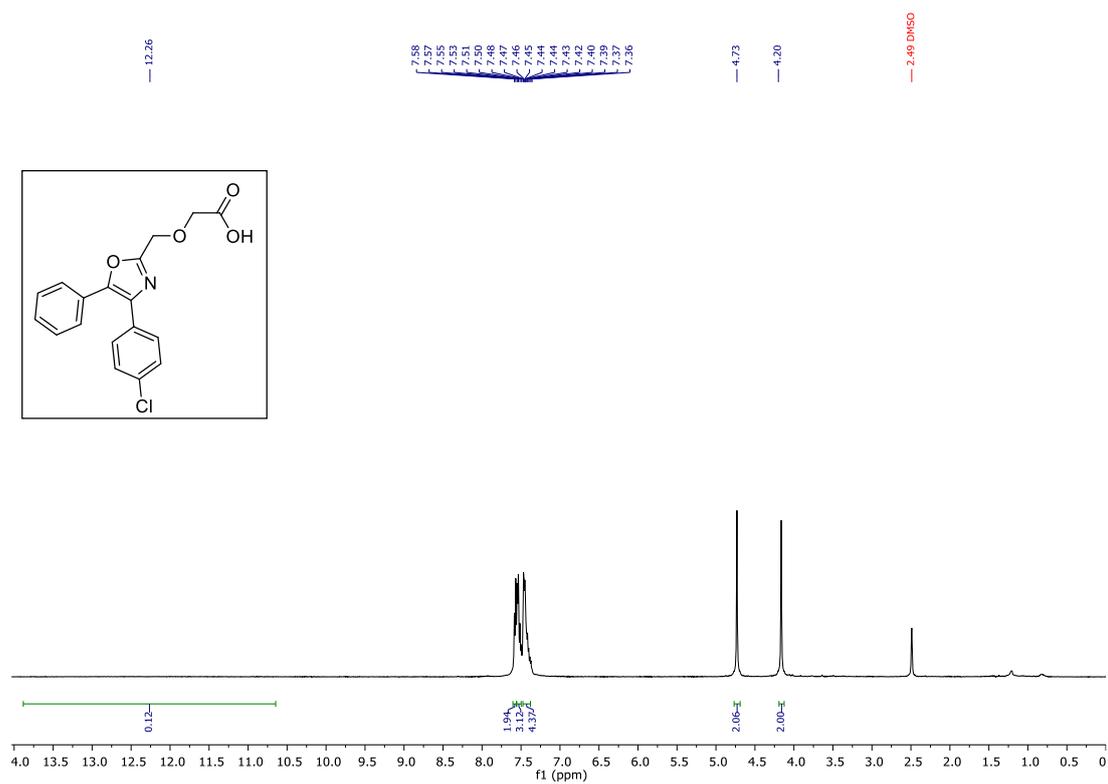


Figure 41: ^1H NMR Compound **3n** (500 MHz, $\text{DMSO-}d_6$)

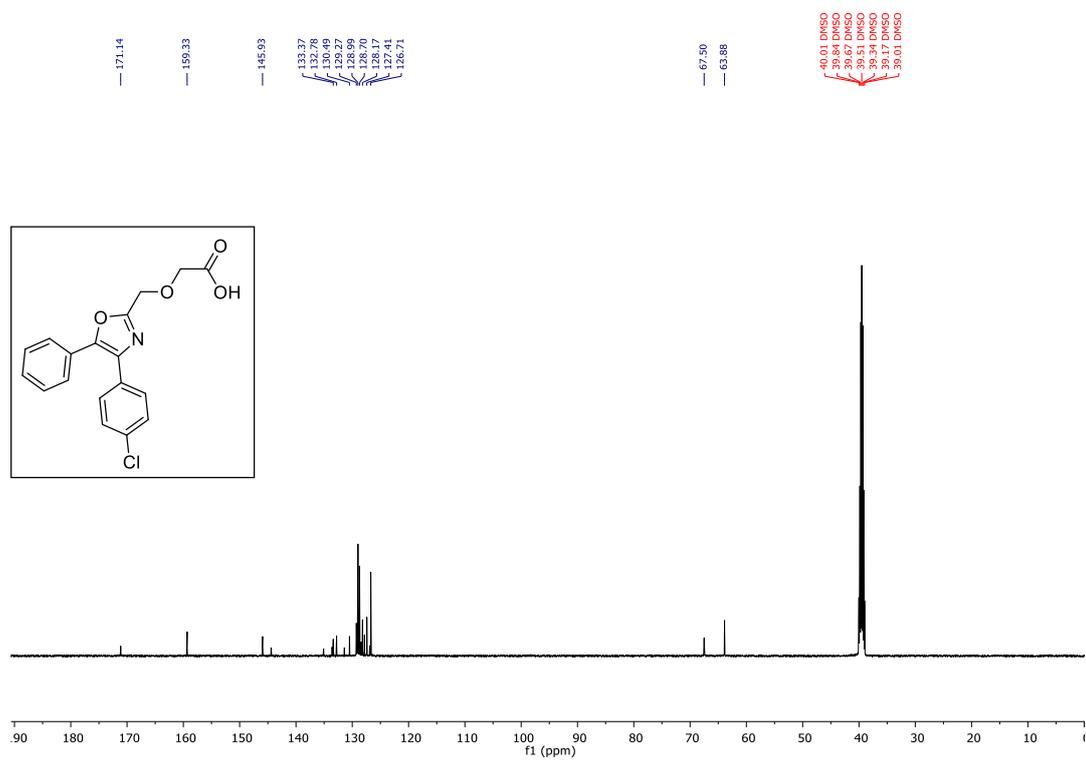


Figure S42: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **3n** (126 MHz, $\text{DMSO-}d_6$)

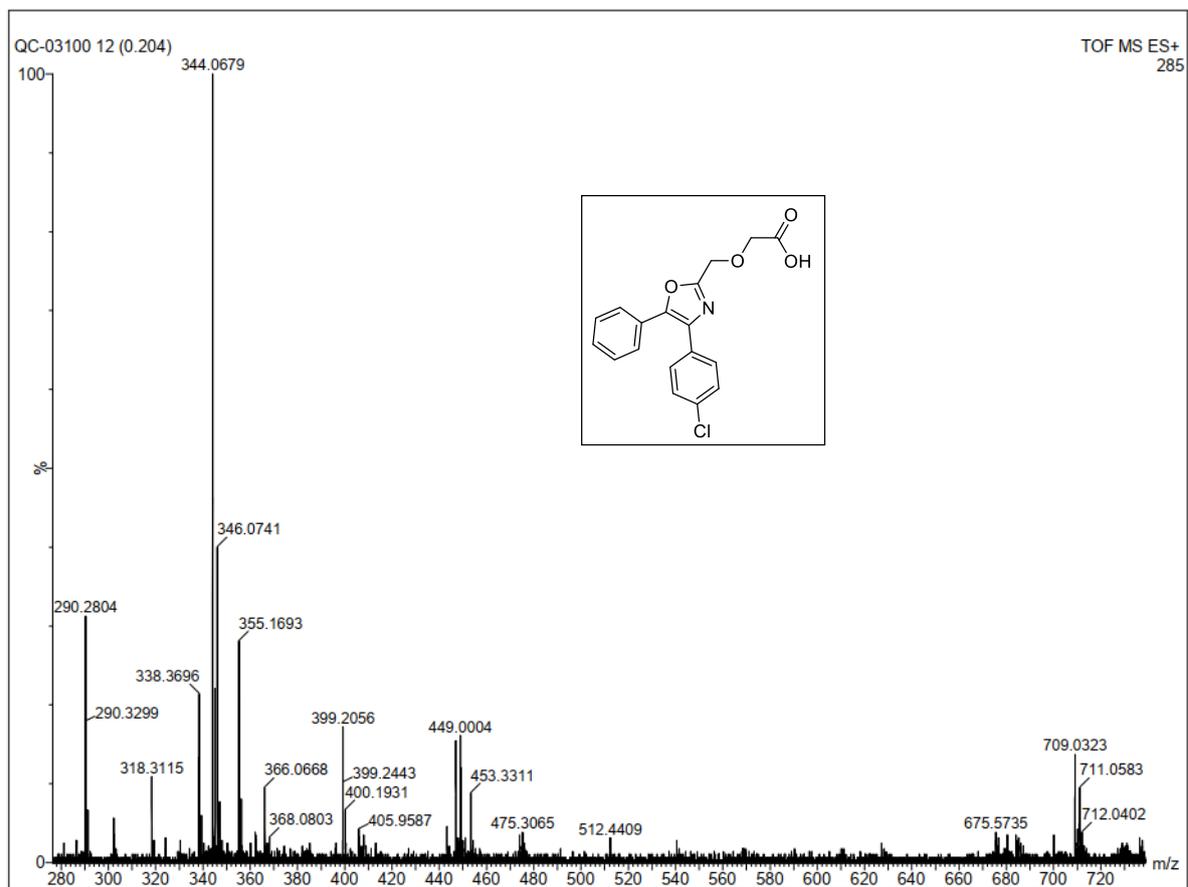
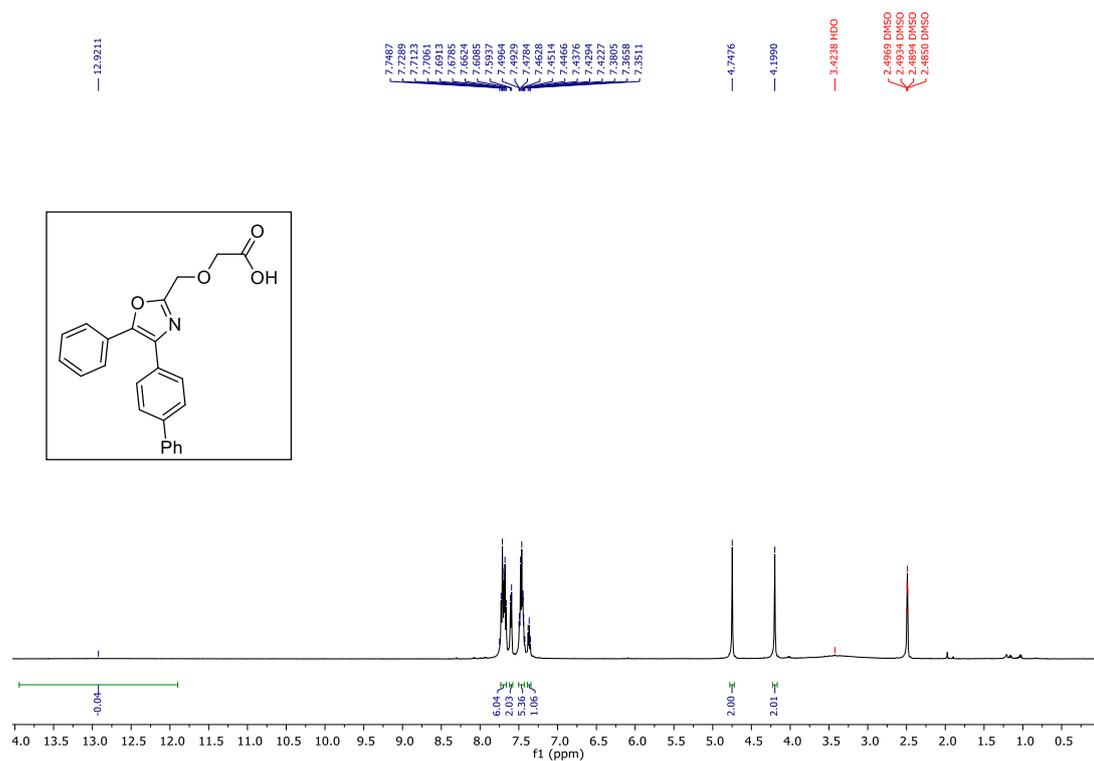
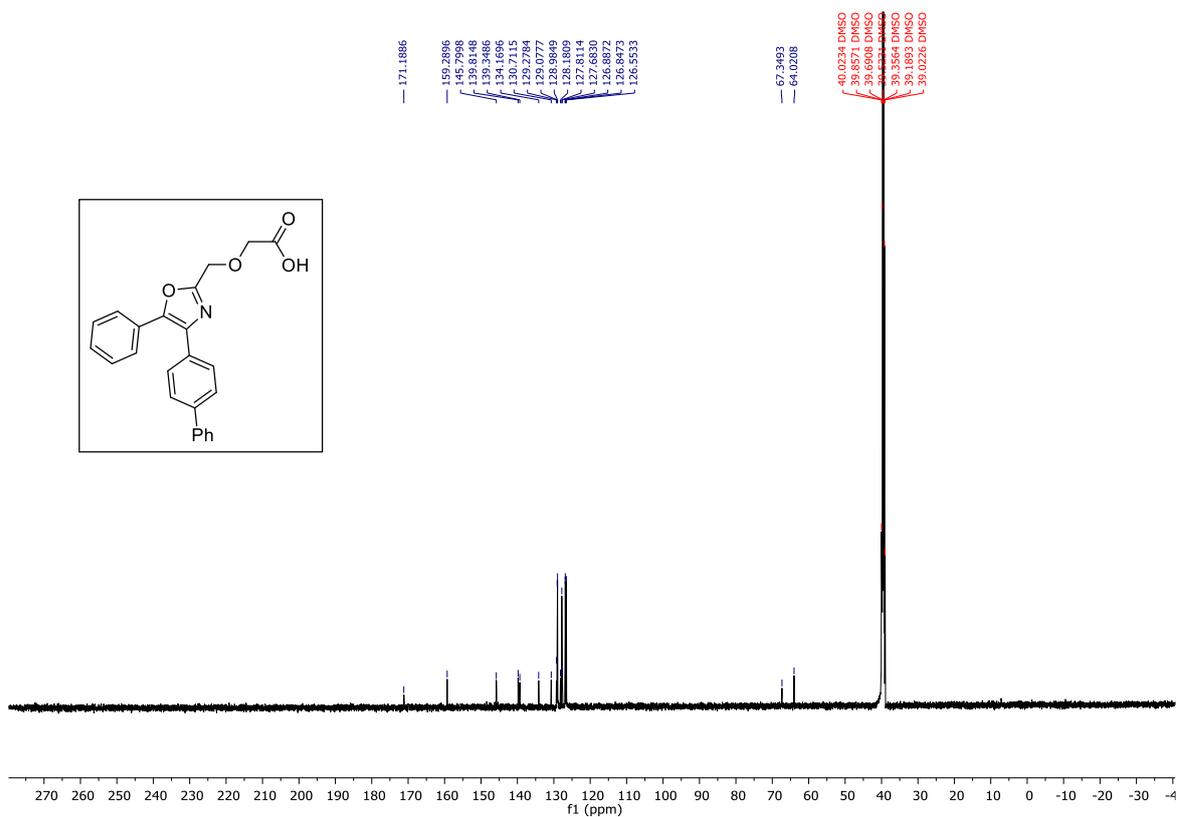
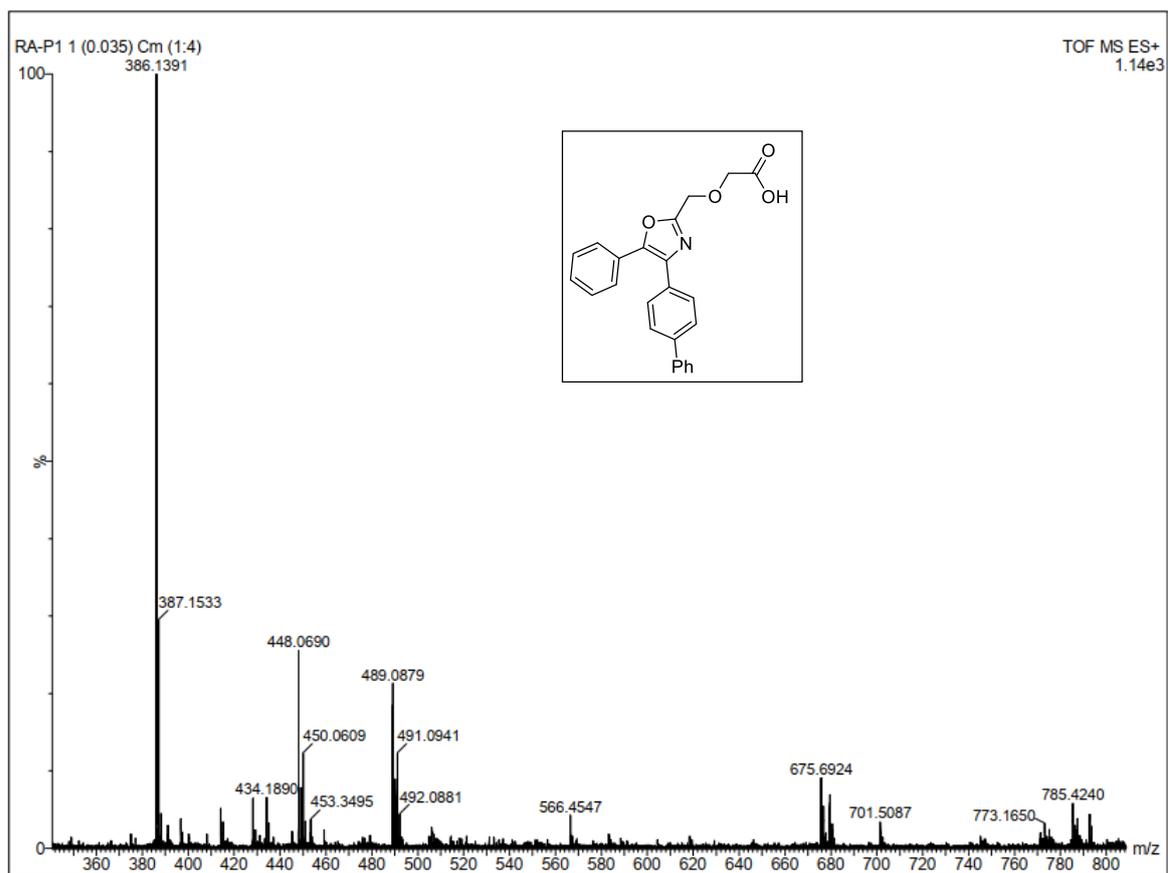
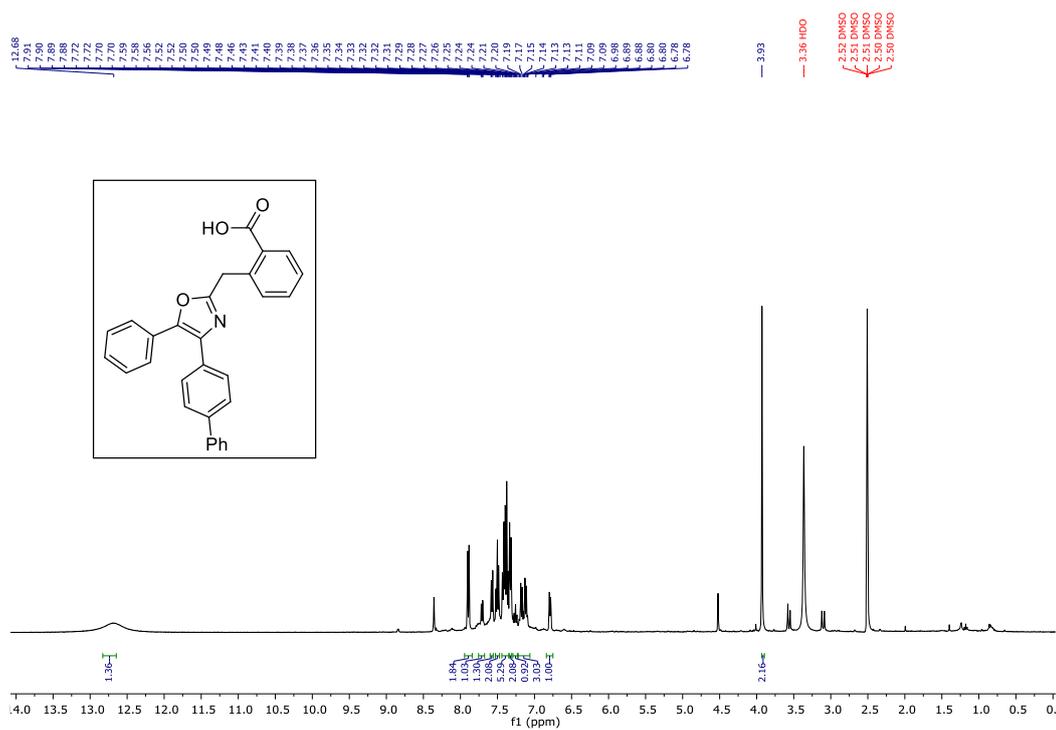
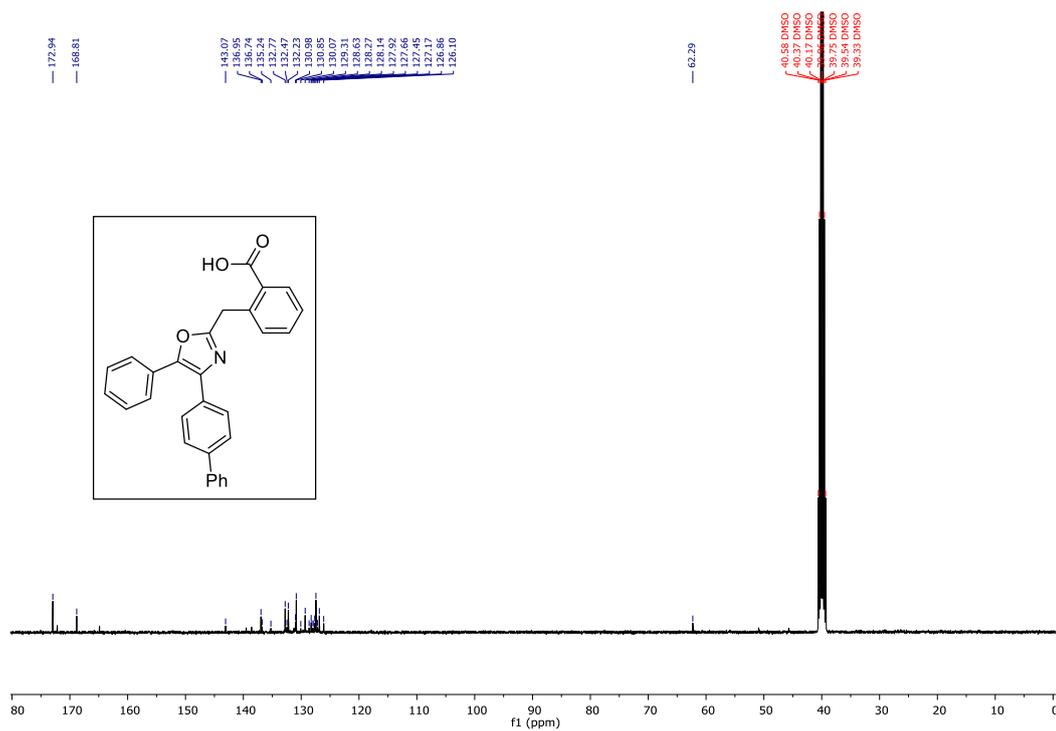
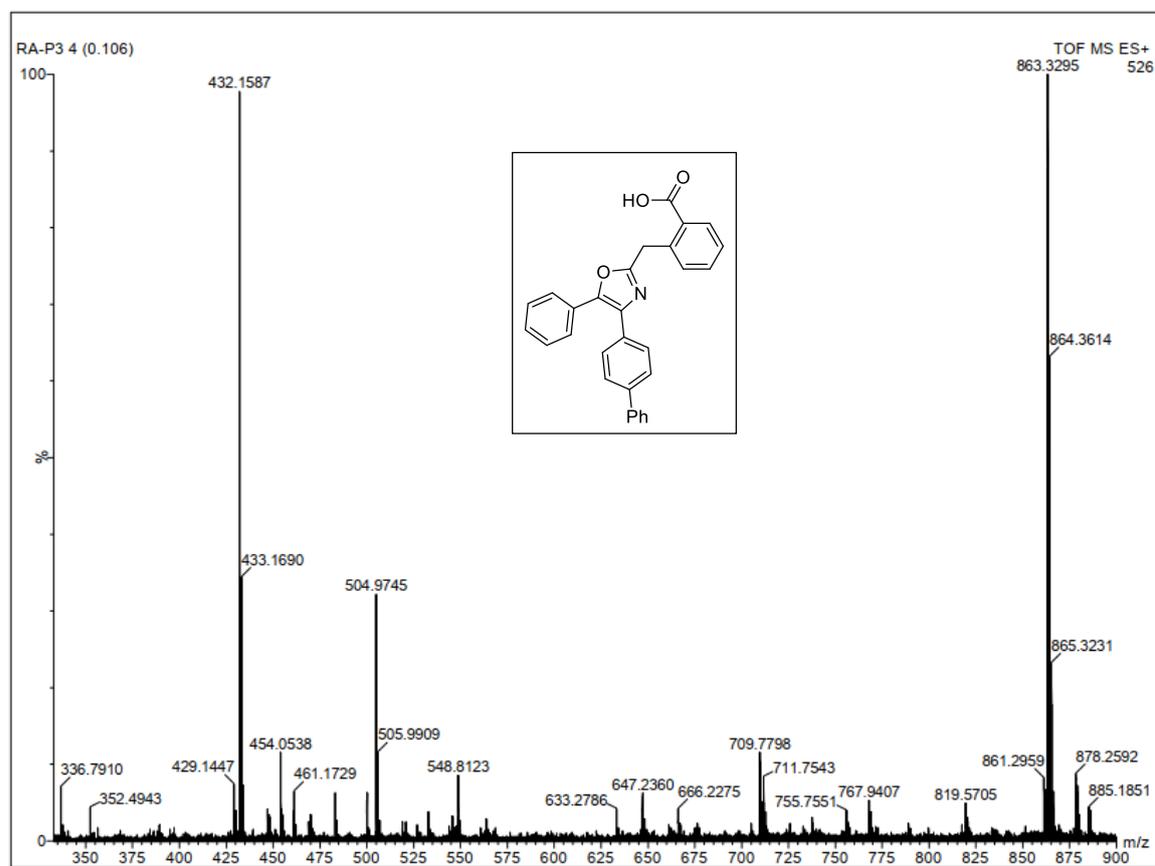


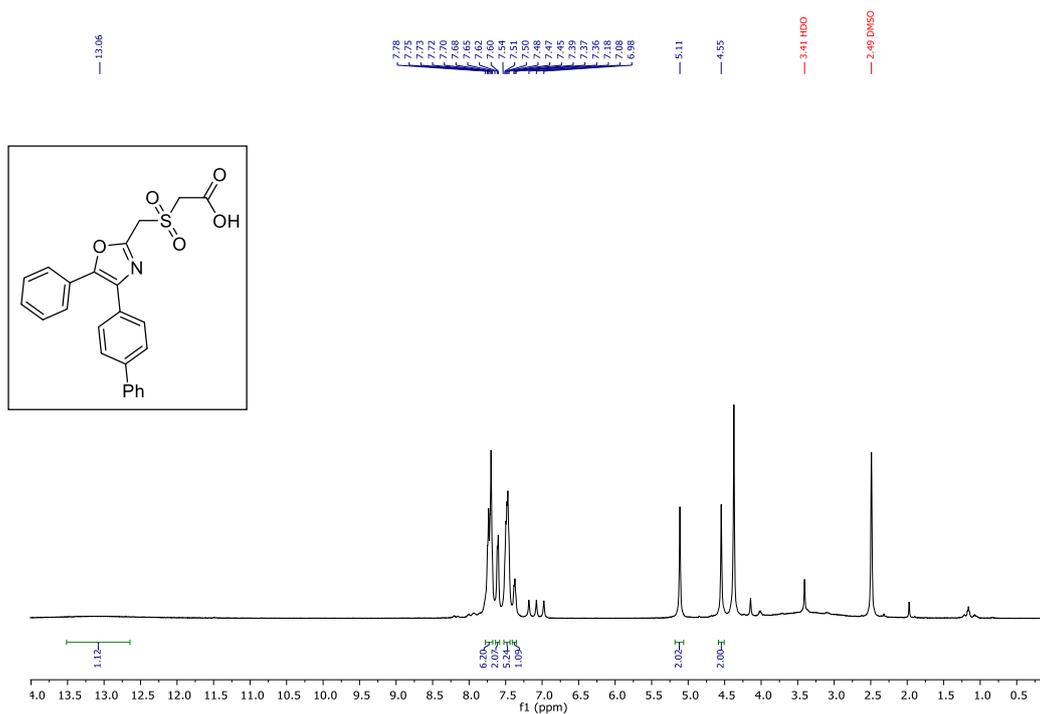
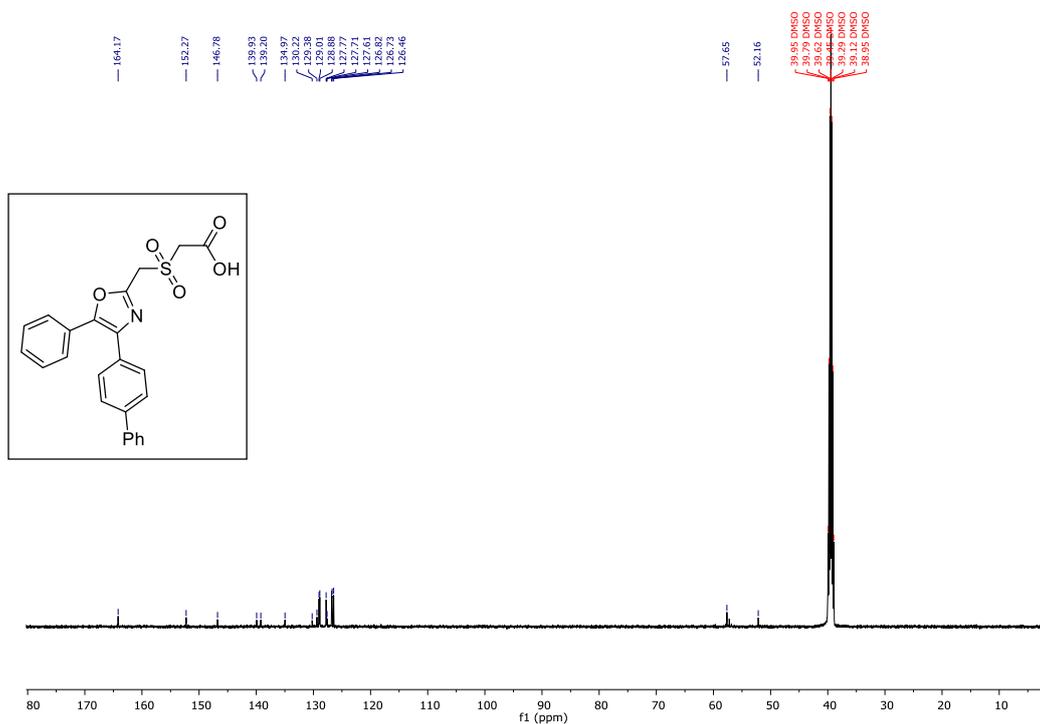
Figure S43: HRMS (ESI) of 3n

Figure S44: ¹H NMR Compound 3o (500 MHz, DMSO-*d*₆)Figure S45: ¹³C {¹H} NMR Compound 3o (126 MHz, DMSO-*d*₆)

Figure S46: HRMS (ESI) of **3o**

Figure S47: $^1\text{H NMR}$ Compound **3p** (400 MHz $\text{DMSO-}d_6$)Figure S48: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **3p** (101 MHz, $\text{DMSO-}d_6$)

Figure S49: HRMS (ESI) of **3p**

Figure S50: ¹H NMR Compound 4 (500 MHz, DMSO-*d*₆)Figure S51: ¹³C{¹H}NMR Compound 4 (126 MHz, DMSO-*d*₆)

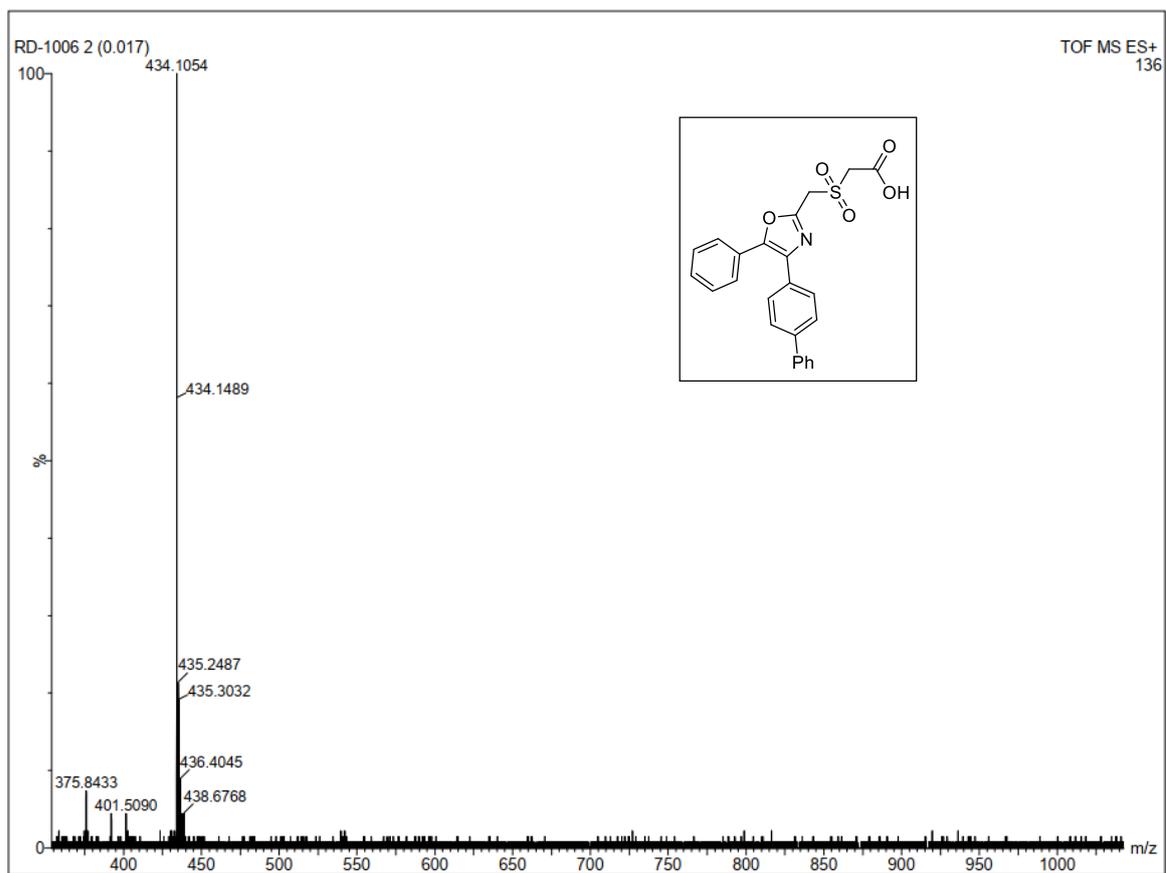
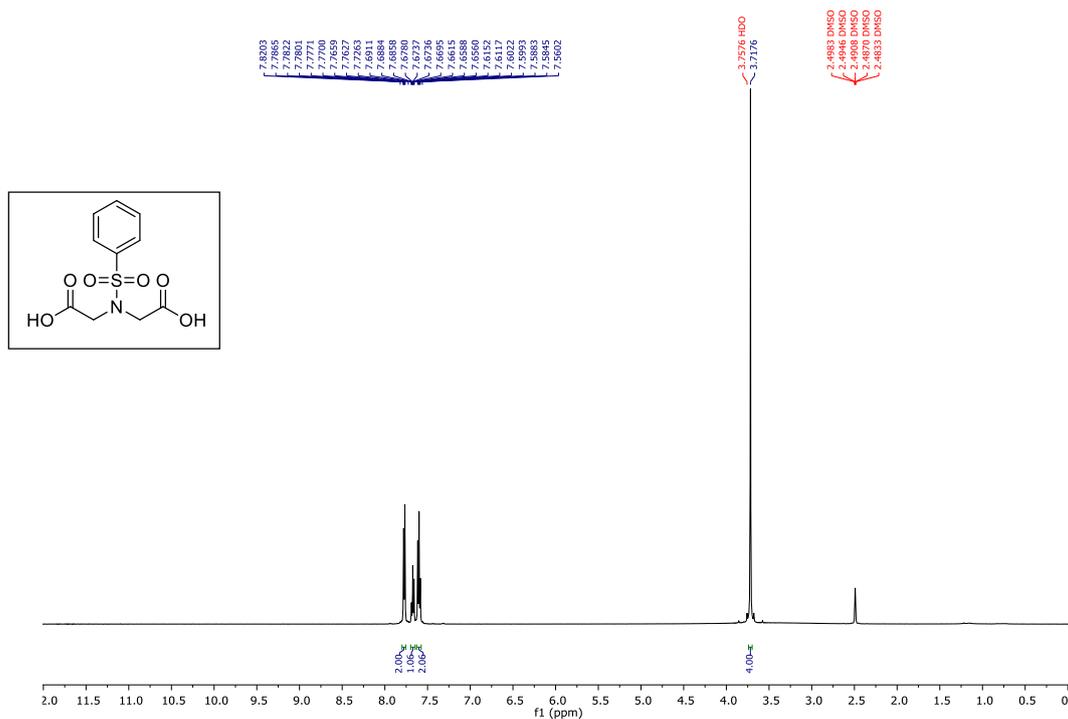
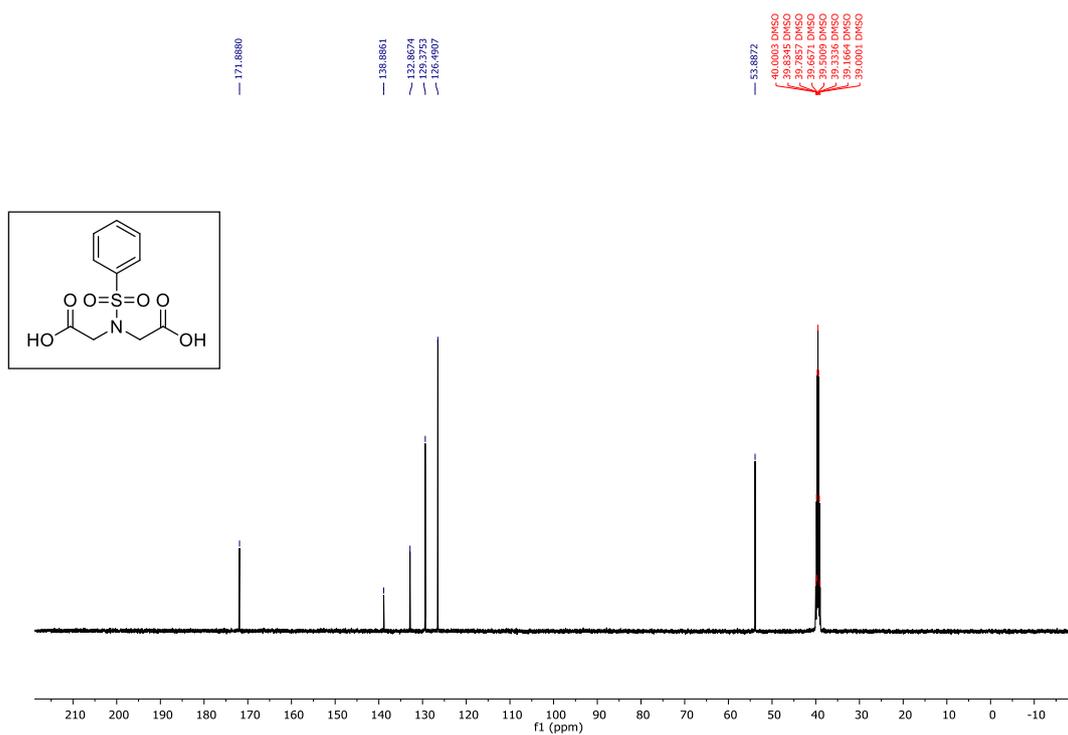


Figure S52: HRMS (ESI) of 4

Figure S53: ^1H NMR Compound 5 (500 MHz, DMSO- d_6)Figure S54: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 5 (126 MHz, DMSO- d_6)

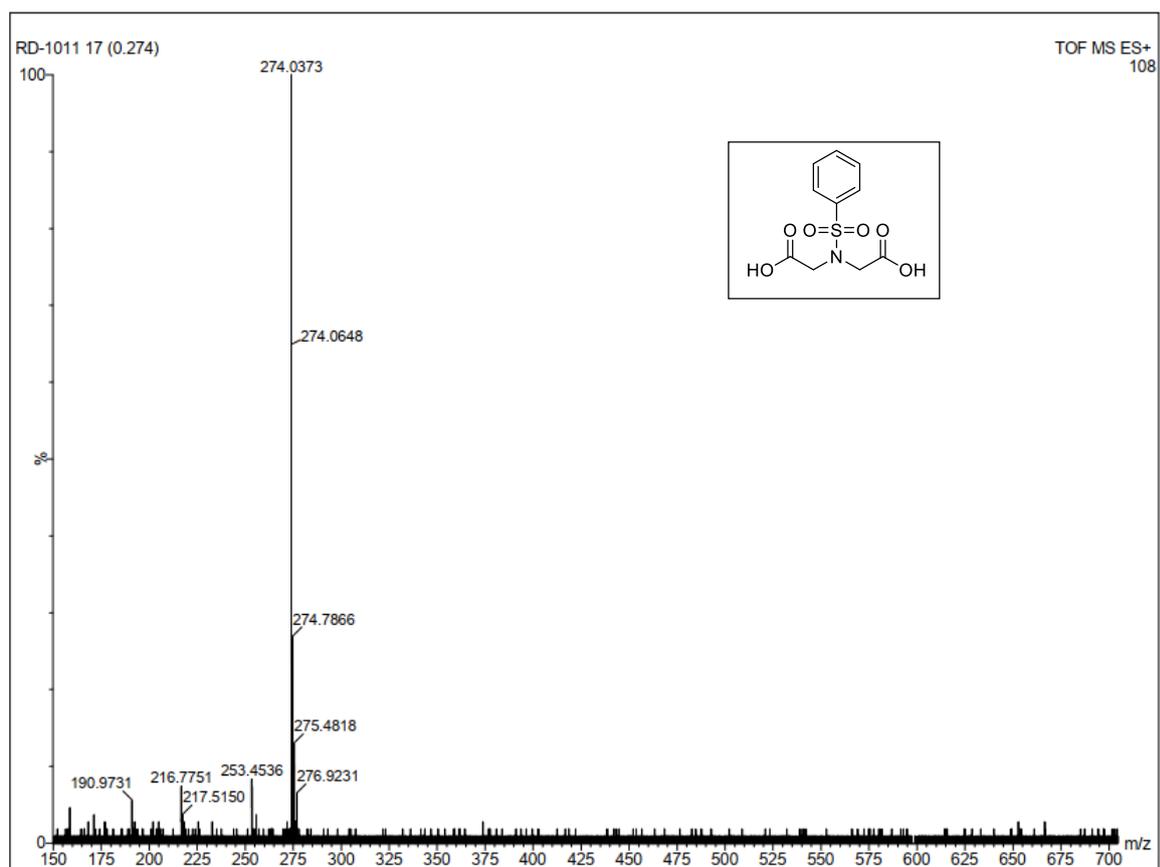
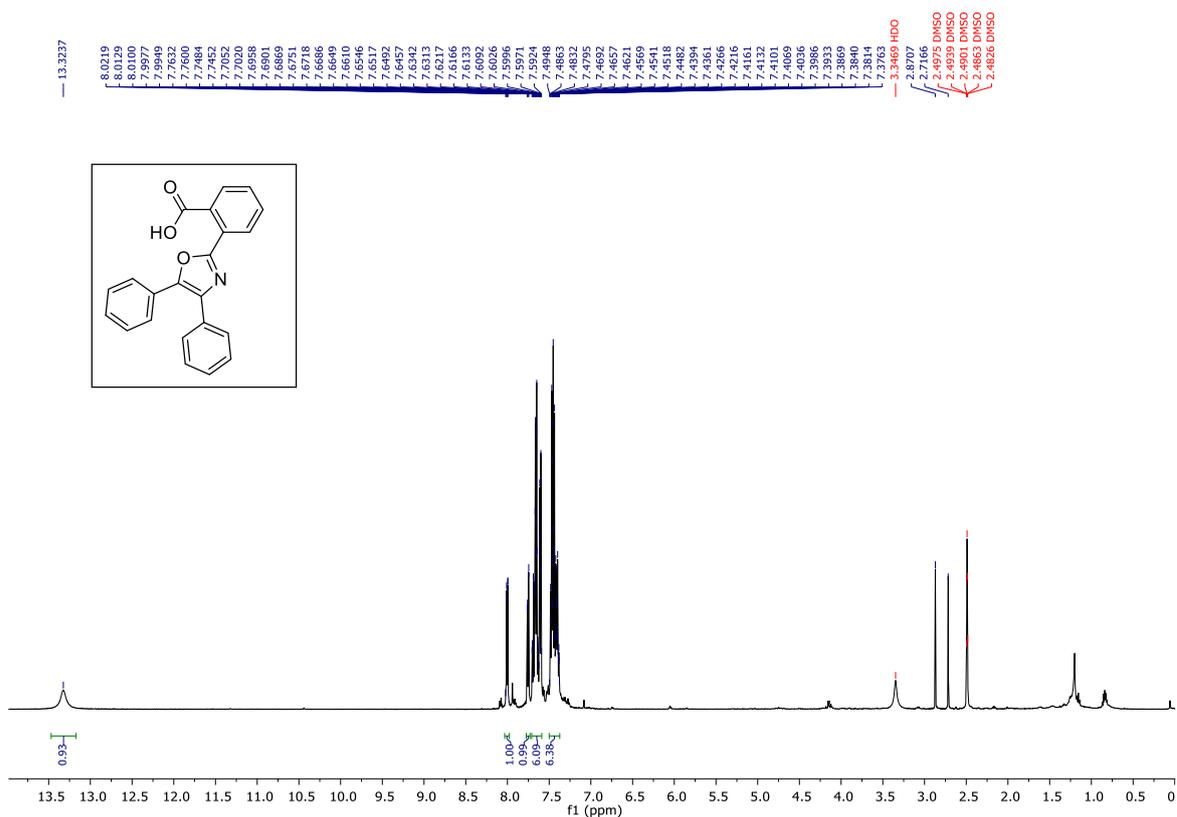
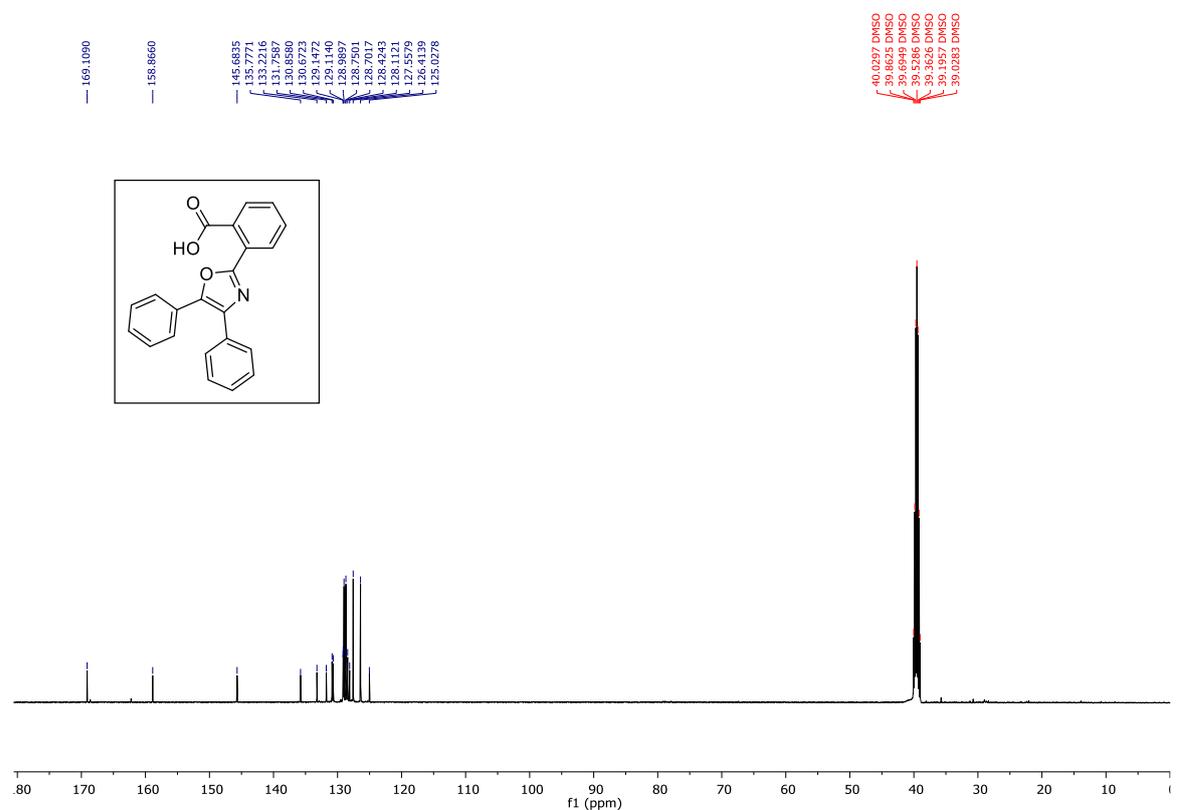


Figure S55: HRMS (ESI) of 5

Figure S56: $^1\text{H NMR}$ Compound 6 (500 MHz, $\text{DMSO-}d_6$)Figure S57: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound 6 (126 MHz, $\text{DMSO-}d_6$)

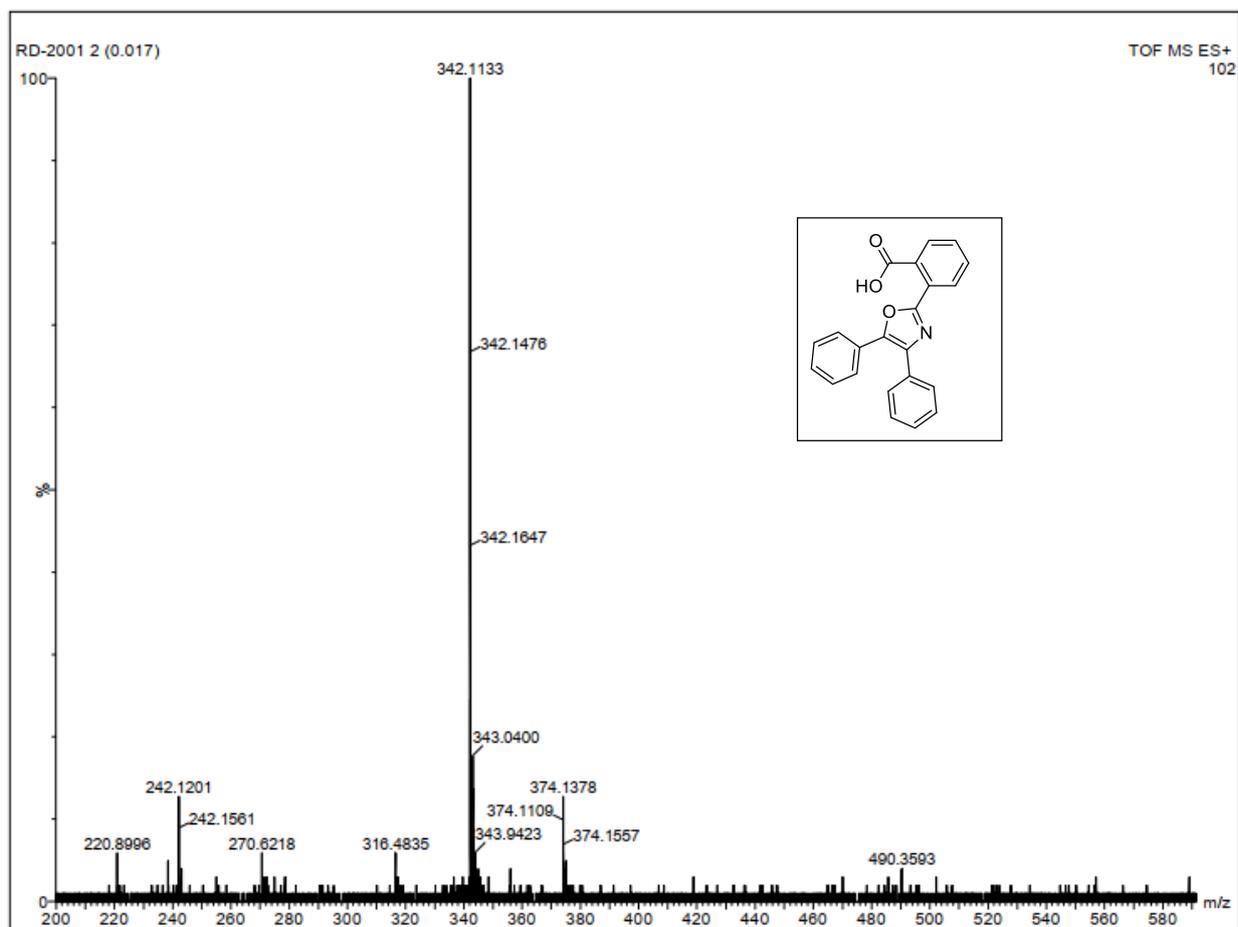
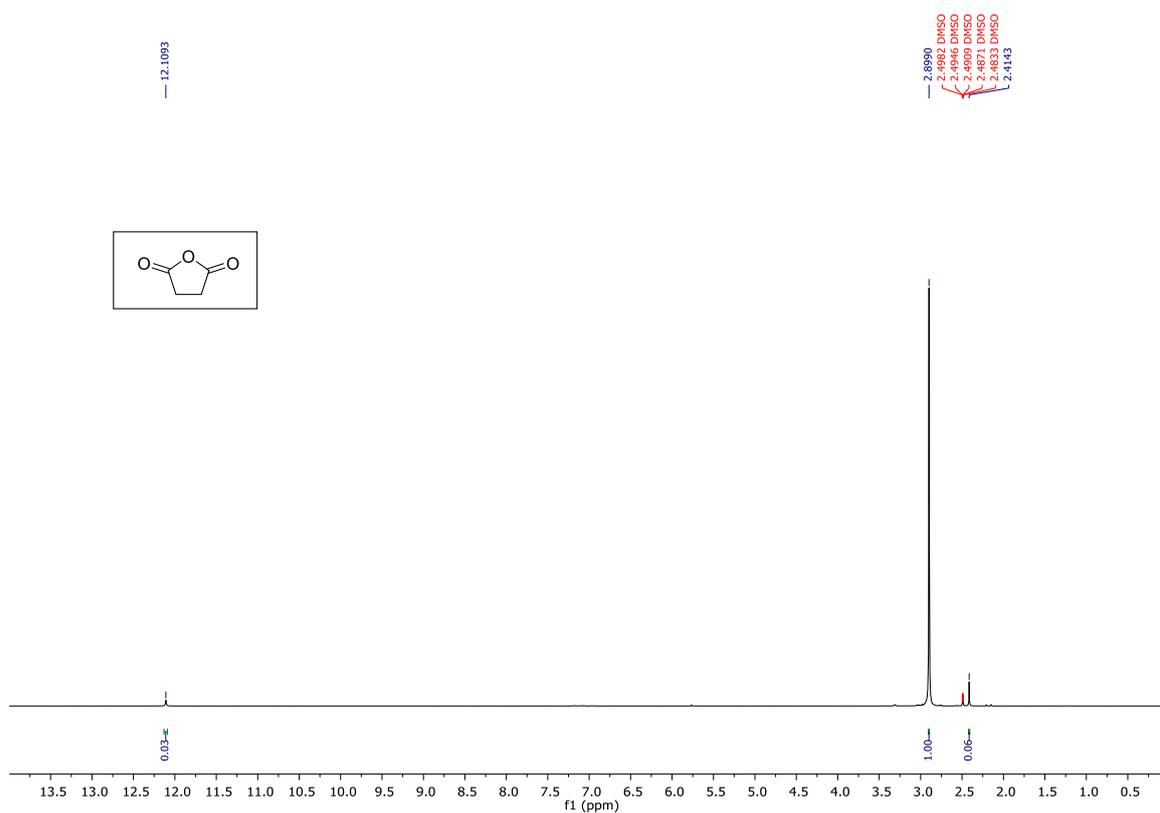
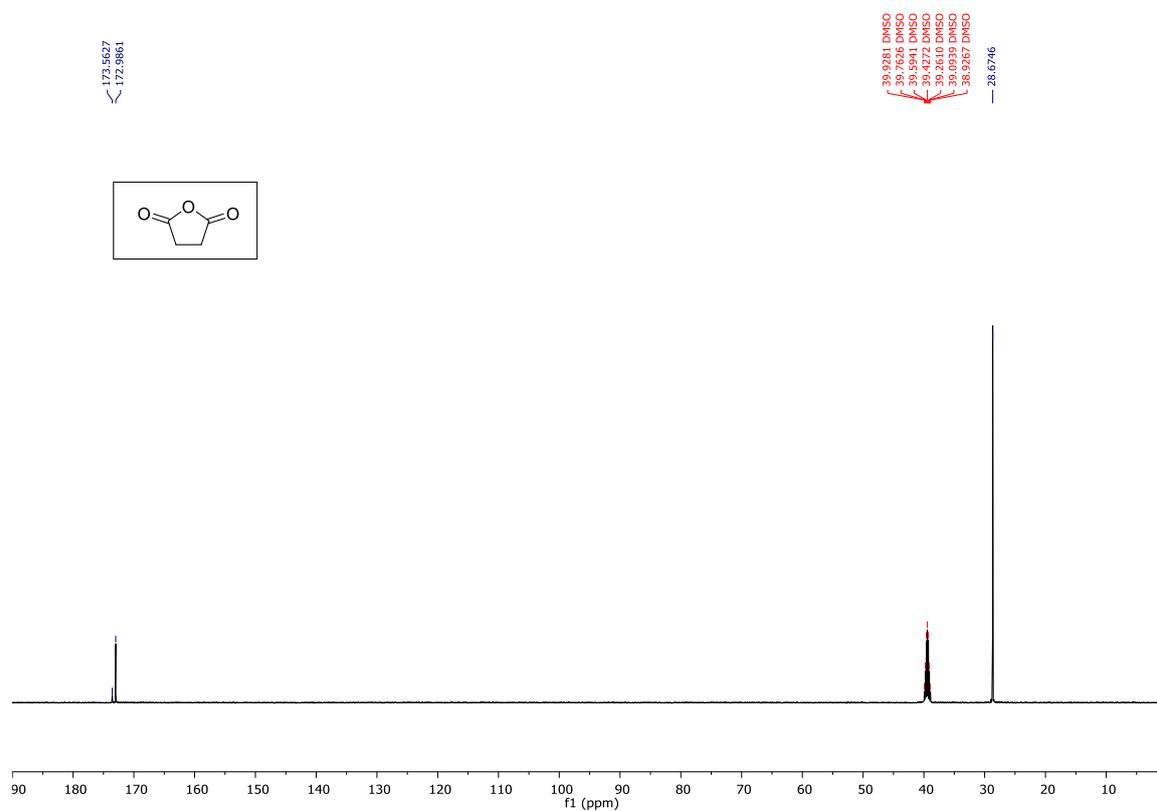


Figure S58: HRMS (ESI) of 6

Figure S59: ^1H NMR Compound **2a** (500 MHz, $\text{DMSO}-d_6$)Figure S60: $^{13}\text{C}\{^1\text{H}\}$ NMR Compound **2a** (126 MHz, $\text{DMSO}-d_6$)

4. X-ray Crystallographic Analysis

Chemistry : Saeed Balalaie
 Probe : RA.26
 File names : sba205.*
 Operator : F. Rominger
 Device : Bruker APEX-II Quazar area detector

Table 1: Crystal data and structure refinement for sba205.

Identification code	sba205
Empirical formula	C ₁₉ H ₁₇ NO ₃
Formula weight	307.33
Temperature	200(2) K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P $\bar{1}$
Z	2
Unit cell dimensions	a = 6.1263(5) Å α = 92.8750(18) deg. b = 10.1800(8) Å β = 98.3576(17) deg. c = 12.5965(10) Å γ = 90.9987(19) deg.
Volume	776.03(11) Å ³
Density (calculated)	1.32 g/cm ³
Absorption coefficient	0.09 mm ⁻¹
Crystal shape	plank
Crystal size	0.510 x 0.083 x 0.062 mm ³
Crystal colour	colourless
Theta range for data collection	1.6 to 27.8 deg.
Index ranges	-8 \leq h \leq 8, -12 \leq k \leq 12, -16 \leq l \leq 15
Reflections collected	10920
Independent reflections	3292 (R(int) = 0.0524)
Observed reflections	2317 (I > 2 σ (I))
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.96 and 0.74
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3292 / 0 / 212
Goodness-of-fit on F ²	1.04
Final R indices (I > 2 σ (I))	R1 = 0.047, wR2 = 0.096
Largest diff. peak and hole	0.18 and -0.18 eÅ ⁻³

Table 2: Atomic coordinates and equivalent isotropic displacement parameters (Å²) for sba205. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.)

Atom	x	y	z	U _{eq}
C1	0.5481(3)	0.7452(2)	0.7382(1)	0.0265(4)
C2	0.6682(3)	0.6636(2)	0.6834(1)	0.0271(4)
C4	0.4136(3)	0.7500(2)	0.5710(1)	0.0296(4)
O3	0.5829(2)	0.6664(1)	0.5751(1)	0.0293(4)

N5	0.3848(2)	0.7993(1)	0.6651(1)	0.0303(4)
N3B	0.5829(2)	0.6664(1)	0.5751(1)	0.0293(4)
O5B	0.3848(2)	0.7993(1)	0.6651(1)	0.0303(4)
C6	0.2803(3)	0.7742(2)	0.4664(1)	0.0324(4)
H6A	0.1481	0.8233	0.4800	0.039
H6B	0.2287	0.6884	0.4302	0.039
C7	0.4007(3)	0.8508(2)	0.3902(1)	0.0315(4)
H7A	0.4864	0.9253	0.4307	0.038
H7B	0.5051	0.7927	0.3588	0.038
C8	0.2360(3)	0.9028(2)	0.3007(1)	0.0334(4)
H8A	0.3174	0.9389	0.2459	0.040
H8B	0.1401	0.8290	0.2658	0.040
C9	0.0936(3)	1.0083(2)	0.3407(1)	0.0280(4)
O9	0.1456(2)	1.0777(1)	0.4204(1)	0.0381(3)
O10	-0.0950(2)	1.0187(1)	0.2756(1)	0.0445(4)
H10	-0.181(4)	1.082(2)	0.3009(17)	0.067
C11	0.5662(3)	0.7807(2)	0.8542(1)	0.0263(4)
C12	0.3861(3)	0.7617(2)	0.9073(1)	0.0348(4)
H12	0.2523	0.7244	0.8692	0.042
C13	0.4008(3)	0.7968(2)	1.0160(2)	0.0395(5)
H13	0.2771	0.7831	1.0520	0.047
C14	0.5932(3)	0.8514(2)	1.0719(1)	0.0358(4)
H14	0.6021	0.8763	1.1462	0.043
C15	0.7734(3)	0.8698(2)	1.0196(1)	0.0338(4)
H15	0.9069	0.9070	1.0581	0.041
C16	0.7606(3)	0.8345(2)	0.9114(1)	0.0307(4)
H16	0.8856	0.8470	0.8761	0.037
C21	0.8530(3)	0.5776(2)	0.7126(1)	0.0272(4)
C22	0.8807(3)	0.5190(2)	0.8111(2)	0.0366(5)
H22	0.7769	0.5335	0.8594	0.044
C23	1.0589(3)	0.4398(2)	0.8388(2)	0.0448(5)
H23	1.0779	0.4006	0.9063	0.054
C24	1.2094(3)	0.4175(2)	0.7686(2)	0.0445(5)
H24	1.3324	0.3637	0.7882	0.053
C25	1.1817(3)	0.4730(2)	0.6703(2)	0.0399(5)
H25	1.2839	0.4562	0.6216	0.048
C26	1.0049(3)	0.5533(2)	0.6425(1)	0.0325(4)
H26	0.9872	0.5922	0.5749	0.039

Table 3: Hydrogen coordinates and isotropic displacement parameters (\AA^2) for sba205.

Atom	x	y	z	U_{eq}
H6A	0.1481	0.8233	0.4800	0.039
H6B	0.2287	0.6884	0.4302	0.039
H7A	0.4864	0.9253	0.4307	0.038
H7B	0.5051	0.7927	0.3588	0.038
H8A	0.3174	0.9389	0.2459	0.040
H8B	0.1401	0.8290	0.2658	0.040
H10	-0.181(4)	1.082(2)	0.3009(17)	0.067

H12	0.2523	0.7244	0.8692	0.042
H13	0.2771	0.7831	1.0520	0.047
H14	0.6021	0.8763	1.1462	0.043
H15	0.9069	0.9070	1.0581	0.041
H16	0.8856	0.8470	0.8761	0.037
H22	0.7769	0.5335	0.8594	0.044
H23	1.0779	0.4006	0.9063	0.054
H24	1.3324	0.3637	0.7882	0.053
H25	1.2839	0.4562	0.6216	0.048
H26	0.9872	0.5922	0.5749	0.039

Table 4: Anisotropic displacement parameters (\AA^2) for sba205. The anisotropic displacement factor exponent takes the form: $-2 \pi^2 (h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12})$

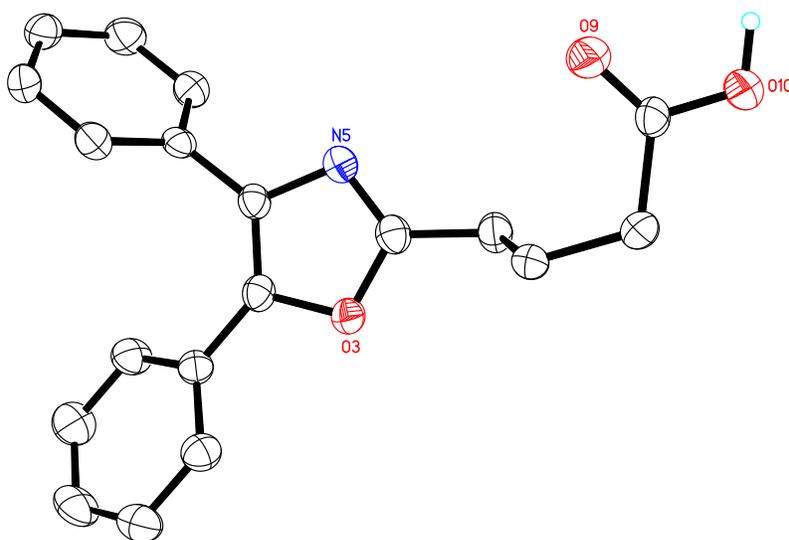
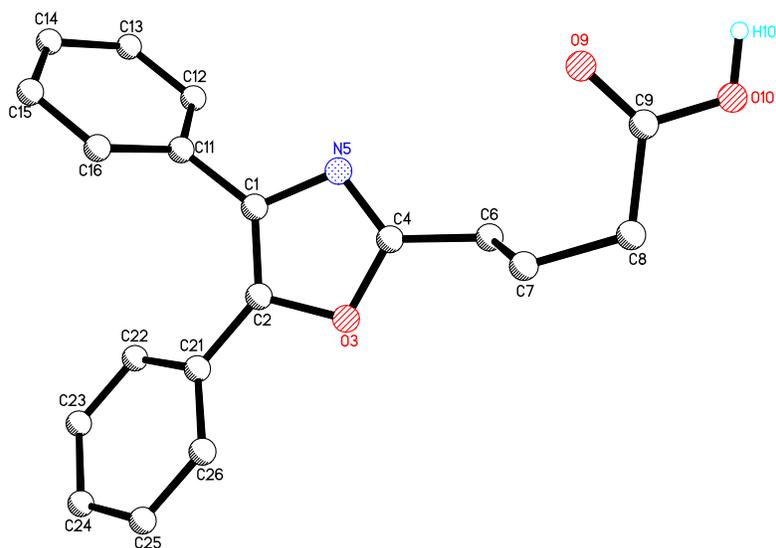
Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0281(9)	0.0251(9)	0.0257(9)	0.0046(7)	0.0009(7)	0.0024(7)
C2	0.0311(9)	0.0266(9)	0.0233(9)	0.0048(7)	0.0018(7)	0.0008(7)
C4	0.0300(10)	0.0280(9)	0.0303(10)	0.0050(8)	0.0018(8)	0.0006(8)
O3	0.0335(7)	0.0295(7)	0.0245(7)	0.0025(5)	0.0016(5)	0.0055(5)
N5	0.0307(8)	0.0310(8)	0.0287(8)	0.0033(6)	0.0015(6)	0.0047(6)
N3B	0.0335(7)	0.0295(7)	0.0245(7)	0.0025(5)	0.0016(5)	0.0055(5)
O5B	0.0307(8)	0.0310(8)	0.0287(8)	0.0033(6)	0.0015(6)	0.0047(6)
C6	0.0338(10)	0.0327(10)	0.0290(10)	0.0023(8)	-0.0017(8)	0.0029(8)
C7	0.0300(9)	0.0383(10)	0.0264(9)	0.0006(8)	0.0045(7)	0.0109(8)
C8	0.0380(10)	0.0397(10)	0.0235(9)	0.0015(8)	0.0071(8)	0.0100(8)
C9	0.0298(9)	0.0328(10)	0.0218(9)	0.0056(8)	0.0036(7)	0.0036(8)
O9	0.0358(7)	0.0379(7)	0.0383(7)	-0.0073(6)	0.0005(6)	0.0046(6)
O10	0.0391(8)	0.0541(9)	0.0366(8)	-0.0080(6)	-0.0061(6)	0.0195(7)
C11	0.0291(9)	0.0227(9)	0.0274(9)	0.0043(7)	0.0034(7)	0.0079(7)
C12	0.0290(10)	0.0390(11)	0.0359(10)	-0.0005(8)	0.0039(8)	0.0020(8)
C13	0.0370(11)	0.0488(12)	0.0356(11)	0.0032(9)	0.0148(9)	0.0060(9)
C14	0.0441(11)	0.0373(11)	0.0261(9)	0.0018(8)	0.0043(8)	0.0096(9)
C15	0.0328(10)	0.0352(10)	0.0310(10)	0.0001(8)	-0.0034(8)	0.0047(8)
C16	0.0274(9)	0.0348(10)	0.0306(10)	0.0061(8)	0.0050(8)	0.0043(8)
C21	0.0303(9)	0.0202(8)	0.0303(9)	-0.0001(7)	0.0020(7)	0.0015(7)
C22	0.0435(11)	0.0332(10)	0.0346(10)	0.0077(8)	0.0077(9)	0.0102(9)
C23	0.0568(13)	0.0351(11)	0.0429(12)	0.0135(9)	0.0030(10)	0.0135(10)
C24	0.0409(11)	0.0324(10)	0.0595(14)	0.0062(10)	0.0027(10)	0.0144(9)
C25	0.0356(11)	0.0364(11)	0.0489(12)	-0.0006(9)	0.0104(9)	0.0054(9)
C26	0.0360(10)	0.0279(9)	0.0338(10)	0.0008(8)	0.0060(8)	0.0015(8)

Table 5: Bond lengths (\AA) and angles (deg) for sba205.

C1-C2	1.348(2)	C1-C11	1.476(2)
C1-O5B	1.398(2)	C2-N3B	1.3896(19)
C1-N5	1.398(2)	C2-O3	1.3896(19)

C2-C21	1.460(2)	O5B-C4-C6	127.02(16)
C4-O5B	1.300(2)	N5-C4-C6	127.02(16)
C4-N5	1.300(2)	O3-C4-C6	119.83(15)
C4-O3	1.350(2)	N3B-C4-C6	119.83(15)
C4-N3B	1.350(2)	C4-O3-C2	105.24(12)
C4-C6	1.480(2)	C4-N5-C1	105.54(14)
C6-C7	1.528(2)	C4-N3B-C2	105.24(12)
C6-H6A	0.9900	C4-O5B-C1	105.54(14)
C6-H6B	0.9900	C4-C6-C7	114.90(15)
C7-C8	1.522(2)	C4-C6-H6A	108.5
C7-H7A	0.9900	C7-C6-H6A	108.5
C7-H7B	0.9900	C4-C6-H6B	108.5
C8-C9	1.508(2)	C7-C6-H6B	108.5
C8-H8A	0.9900	H6A-C6-H6B	107.5
C8-H8B	0.9900	C8-C7-C6	110.31(14)
C9-O9	1.1987(19)	C8-C7-H7A	109.6
C9-O10	1.325(2)	C6-C7-H7A	109.6
O10-H10	0.91(2)	C8-C7-H7B	109.6
C11-C12	1.387(2)	C6-C7-H7B	109.6
C11-C16	1.388(2)	H7A-C7-H7B	108.1
C12-C13	1.387(2)	C9-C8-C7	112.71(14)
C12-H12	0.9500	C9-C8-H8A	109.1
C13-C14	1.376(3)	C7-C8-H8A	109.1
C13-H13	0.9500	C9-C8-H8B	109.1
C14-C15	1.380(3)	C7-C8-H8B	109.1
C14-H14	0.9500	H8A-C8-H8B	107.8
C15-C16	1.383(2)	O9-C9-O10	123.35(16)
C15-H15	0.9500	O9-C9-C8	124.45(16)
C16-H16	0.9500	O10-C9-C8	112.18(15)
C21-C26	1.390(2)	C9-O10-H10	111.8(14)
C21-C22	1.393(2)	C12-C11-C16	119.05(16)
C22-C23	1.383(2)	C12-C11-C1	119.84(16)
C22-H22	0.9500	C16-C11-C1	121.10(15)
C23-C24	1.382(3)	C11-C12-C13	120.18(17)
C23-H23	0.9500	C11-C12-H12	119.9
C24-C25	1.375(3)	C13-C12-H12	119.9
C24-H24	0.9500	C14-C13-C12	120.42(17)
C25-C26	1.383(2)	C14-C13-H13	119.8
C25-H25	0.9500	C12-C13-H13	119.8
C26-H26	0.9500	C13-C14-C15	119.64(17)
C2-C1-O5B	108.60(14)	C13-C14-H14	120.2
C2-C1-N5	108.60(14)	C15-C14-H14	120.2
C2-C1-C11	130.87(15)	C14-C15-C16	120.30(17)
O5B-C1-C11	120.53(14)	C14-C15-H15	119.8
N5-C1-C11	120.53(14)	C16-C15-H15	119.8
C1-C2-N3B	107.49(14)	C15-C16-C11	120.39(16)
C1-C2-O3	107.49(14)	C15-C16-H16	119.8
C1-C2-C21	135.04(16)	C11-C16-H16	119.8
N3B-C2-C21	117.46(14)	C26-C21-C22	118.92(16)
O3-C2-C21	117.46(14)	C26-C21-C2	120.35(15)
N5-C4-O3	113.13(14)	C22-C21-C2	120.73(15)
O5B-C4-N3B	113.13(14)	C23-C22-C21	120.20(17)

C23-C22-H22	119.9
C21-C22-H22	119.9
C24-C23-C22	120.13(18)
C24-C23-H23	119.9
C22-C23-H23	119.9
C25-C24-C23	120.21(18)
C25-C24-H24	119.9
C23-C24-H24	119.9
C24-C25-C26	119.93(18)
C24-C25-H25	120.0
C26-C25-H25	120.0
C25-C26-C21	120.59(17)
C25-C26-H26	119.7
C21-C26-H26	119.7



Suggestion for a short experimental part:

sb205: colourless crystal (plank), dimensions 0.510 x 0.083 x 0.062 mm³, crystal system triclinic, space group $P\bar{1}$, $Z=2$, $a=6.1263(5)$ Å, $b=10.1800(8)$ Å, $c=12.5965(10)$ Å, $\alpha=92.8750(18)$ deg, $\beta=98.3576(17)$ deg, $\gamma=90.9987(19)$ deg, $V=776.03(11)$ Å³, $\rho=1.315$ g/cm³, $T=200(2)$ K, $\Theta_{\max}=27.827$ deg, radiation MoK α , $\lambda=0.71073$ Å, 0.5 deg omega-scans with CCD area detector, covering the asymmetric unit in reciprocal space with a mean redundancy of 2.97 and

a completeness of 89.4% to a resolution of 0.76 Å, 10920 reflections measured, 3292 unique ($R(\text{int})=0.0524$), 2317 observed ($I > 2\sigma(I)$), intensities were corrected for Lorentz and polarization effects, an empirical scaling and absorption correction was applied using SADABS^[1] based on the Laue symmetry of the reciprocal space, $\mu=0.09 \text{ mm}^{-1}$, $T_{\text{min}}=0.74$, $T_{\text{max}}=0.96$, structure solved with SHELXT-2018/2 (Sheldrick 2015)^[2] and refined against F^2 with a Full-matrix least-squares algorithm using the SHELXL-2018/3 (Sheldrick, 2018) software^[3], 212 parameters refined, hydrogen atoms were treated using appropriate riding models, except the acidic H10, which was refined restrained, goodness of fit 1.04 for observed reflections, final residual values $R1(F)=0.047$, $wR(F^2)=0.096$ for observed reflections, residual electron density -0.18 to $0.18 \text{ e}\text{\AA}^{-3}$. CCDC 2401252 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Lit. 1: (SADABS-2016/2 - Bruker AXS area detector scaling and absorption correction)
Krause, L., Herbst-Irmer, R., Sheldrick G.M. & Stalke D., *J. Appl. Cryst.* 48 (2015) 3-10.

Lit. 2: (SHELXT - Integrated space-group and crystal structure determination)
Sheldrick G. M., *Acta Cryst.* A71 (2015) 3-8.

Lit. 3: (program SHELXL-2018/3 (Sheldrick, 2018) for structure refinement)
Sheldrick G. M., *Acta Cryst.* (2015). C71, 3-8

Lit. APEX, APEX2, SMART, SAINT, SAINT-Plus:
Bruker (2007). "Program name(s)". Bruker AXS Inc., Madison, Wisconsin, USA.

5. Z-matrices

1a

E (SMD/B3LYP-D3/6-31G(d)) = -594.8315635 au

H (SMD/B3LYP-D3/6-31G(d)) = -594.609828 au

G (SMD/B3LYP-D3/6-31G(d)) = -594.662377 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -595.0089185 au

N	0.39004200	3.48425000	-2.32018900
C	0.51943200	2.83974900	-1.23913000
C	-0.88427800	2.95710300	-1.60889500
C	1.51634200	2.39983300	-0.28567000
C	1.11698100	1.72642900	0.87882300
C	2.87911800	2.64890100	-0.52588000
C	2.07572200	1.30468400	1.79844800
H	0.06033900	1.54492200	1.05353200
C	3.83099200	2.22253200	0.39534200
H	3.17271800	3.17265900	-1.43128000
C	3.43025200	1.55107000	1.55673000
H	1.76882300	0.78487700	2.70152500
H	4.88500300	2.41195600	0.21264700
H	4.17645600	1.22009200	2.27397100
C	-1.80735500	3.93351800	-0.96608800
C	-1.35086500	5.16417900	-0.46803900
C	-3.16989000	3.62275400	-0.84682000
C	-2.23608900	6.05646000	0.13606100
H	-0.30088900	5.42510800	-0.56611800
C	-4.05469300	4.51339300	-0.23716300
H	-3.53771800	2.67585200	-1.23648900

C	-3.59097100	5.73456300	0.25750000
H	-1.86694400	7.00713500	0.51256000
H	-5.10725200	4.25488100	-0.15320200
H	-4.27883600	6.43063600	0.73010900
H	-1.37131900	2.11257600	-2.09851100

7a

E (SMD/B3LYP-D3/6-31G(d)) = -456.9747304 au

H (SMD/B3LYP-D3/6-31G(d)) = -456.858706 au

G (SMD/B3LYP-D3/6-31G(d)) = -456.900305 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -457.152123 au

C	1.36002600	1.21708900	-2.34571400
O	1.46894100	2.40203500	-2.97024700
C	3.41001600	3.05800400	-0.51064000
C	2.69808800	1.76370000	-0.19656200
C	2.50806800	0.83364700	-1.40999200
H	3.27033200	1.25062900	0.58308100
H	1.73241900	2.02075700	0.26001200
H	3.44009800	0.78960100	-1.98745900
H	2.28954600	-0.17322100	-1.05050300
O	3.89500000	3.65120800	0.58633500
O	0.40151600	0.50077900	-2.53389300
O	3.54505800	3.54467200	-1.62488900
H	2.29241800	2.86211900	-2.68224100
H	4.31029000	4.49313200	0.30982200

A

E (SMD/B3LYP-D3/6-31G(d)) = -1051.831239 au

H (SMD/B3LYP-D3/6-31G(d)) = -1051.49136 au

G (SMD/B3LYP-D3/6-31G(d)) = -1051.570223 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1052.180941 au

N	-2.01394500	1.77580900	-0.13713600
C	-1.50153000	1.13152100	0.82460200
C	-2.89308800	1.49597700	1.08799400
C	-0.26153000	0.55285800	1.28029700
C	-0.20513300	-0.05281000	2.54634400
C	0.88065700	0.60357700	0.45947300
C	0.99217800	-0.60829900	2.99090200
H	-1.09534900	-0.07656000	3.16828300
C	2.07097700	0.04408000	0.91316000
H	0.81663000	1.08407000	-0.51223300
C	2.12690600	-0.56060600	2.17485300
H	1.04334100	-1.07607600	3.96969000
H	2.95800100	0.07980100	0.28727300
H	3.06005100	-0.99461300	2.52362700
C	-3.26566100	2.62936700	1.98137100
C	-2.44371400	3.75859500	2.11874200
C	-4.46347200	2.57040200	2.70718700
C	-2.81377100	4.80255100	2.96592300
H	-1.51782000	3.82253000	1.55391800
C	-4.83048200	3.61304800	3.55917700
H	-5.11145600	1.70300600	2.60179500
C	-4.00645900	4.73300600	3.69151400
H	-2.16922300	5.67261100	3.05959700
H	-5.76229200	3.55223800	4.11529600
H	-4.29219200	5.54695800	4.35226300

H	-3.66786900	0.74344000	0.93870400
C	2.42079400	4.10858800	-4.32772800
O	2.75660800	3.56048000	-3.14914600
C	-0.40926500	3.20842000	-2.82399900
C	-0.15221400	4.13040500	-3.99838300
C	1.04579500	3.73160500	-4.88192100
H	-1.06562600	4.15934600	-4.60066000
H	-0.02446700	5.14539500	-3.59777800
H	1.02290300	2.64870800	-5.05925200
H	0.95604200	4.22976300	-5.84887200
O	-1.63427600	3.30760600	-2.35175000
O	3.18326700	4.84820600	-4.91226300
O	0.44095500	2.44915500	-2.35304400
H	2.00445600	3.01125200	-2.81087200
H	-1.75173200	2.71282400	-1.54395300

2a

E (SMD/B3LYP-D3/6-31G(d)) = -380.5331942 au

H (SMD/B3LYP-D3/6-31G(d)) = -380.447097 au

G (SMD/B3LYP-D3/6-31G(d)) = -380.484803 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -380.6668914 au

C	-1.54073300	1.26992000	0.00000100
O	-0.15301400	1.28180200	0.00000100
C	0.34530800	2.57709600	0.00000500
C	-0.80629900	3.56764000	-0.00000100
C	-2.06393300	2.69574500	0.00000000
H	-0.71388000	4.20971500	0.88120700
H	-0.71387800	4.20971000	-0.88121200

H	-2.69750600	2.83418500	0.88131000
H	-2.69750500	2.83418300	-0.88131200
O	1.52487500	2.78798700	-0.00000200
O	-2.15251000	0.23961800	-0.00000300

TS_{A-B}

E (SMD/B3LYP-D3/6-31G(d)) = -1432.343205 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.917866 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.009184 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.822062 au

N	0.37323600	2.67935500	0.77261300
C	0.43258600	1.65701100	1.53913200
C	-0.67555700	1.80262400	2.49712100
C	1.18735400	0.39413400	1.46464800
C	1.26272400	-0.40431900	2.61845400
C	1.81011900	-0.03099400	0.27917200
C	1.94662000	-1.61818900	2.59250900
H	0.79771300	-0.06569900	3.54313900
C	2.48817100	-1.24695400	0.25937700
H	1.74841300	0.57725100	-0.61610200
C	2.55831200	-2.04055300	1.40927600
H	2.00551300	-2.22879600	3.48908600
H	2.95607600	-1.58134400	-0.66199400
H	3.09061200	-2.98767600	1.38319300
C	-0.91522200	2.87288000	3.37898200
C	0.05488400	3.88718100	3.62781000
C	-2.14840400	2.89879300	4.08998500
C	-0.20837200	4.87771700	4.55516400

H	0.98730900	3.87573700	3.07609600
C	-2.39880300	3.89612500	5.01820800
H	-2.89007700	2.13174900	3.88833300
C	-1.43076100	4.88286600	5.24882900
H	0.52675300	5.65224700	4.74862100
H	-3.33919100	3.91770600	5.55933400
H	-1.62830900	5.66627300	5.97522000
H	-1.44029300	1.03132800	2.42476900
C	-0.66929300	3.44511700	-5.49312300
O	-1.61385300	3.17989900	-4.58389200
C	0.79539500	2.67518800	-2.54463100
C	1.27993700	2.57090200	-3.99639000
C	0.74227900	3.66448600	-4.94908600
H	2.37213000	2.60567800	-3.98830500
H	0.99455600	1.57572400	-4.36457600
H	0.75766100	4.63592600	-4.43520200
H	1.39698800	3.74996200	-5.81954400
O	1.66001200	2.54641800	-1.63882900
O	-0.93356700	3.52739400	-6.67741800
O	-0.44772000	2.86102700	-2.33298100
H	-1.18922700	3.11044500	-3.65363400
H	0.86377700	2.60728400	-0.16908100
C	-1.12332500	0.10612000	-2.05580000
O	-1.34405900	0.39651500	-0.70333300
C	-2.50074100	1.12633200	-0.54023200
C	-3.12540400	1.40901600	-1.88764700
C	-2.34489400	0.51200600	-2.84950400
H	-4.20105100	1.22316100	-1.84699700

H	-2.96557000	2.46929000	-2.10438700
H	-2.89341800	-0.40421600	-3.10012000
H	-2.05032100	0.99894400	-3.77871300
O	-2.88725700	1.43792500	0.55819900
O	-0.11674200	-0.44018400	-2.40648000

B

E (SMD/B3LYP-D3/6-31G(d)) = -1432.352375 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.924939 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.018809 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.828131 au

N	0.42429100	2.61189300	0.29194500
C	0.30471800	1.69902200	1.16701000
C	-1.07706000	1.61550200	1.85069000
C	1.29041300	0.65010200	1.54803200
C	1.29808100	0.08689700	2.83591100
C	2.22260500	0.20252200	0.59568900
C	2.23029200	-0.89555300	3.16977900
H	0.59532000	0.43061100	3.58857500
C	3.14209600	-0.78892500	0.93333400
H	2.21019200	0.62327300	-0.40622900
C	3.15193600	-1.33816600	2.21837200
H	2.23717300	-1.31257000	4.17318800
H	3.85146500	-1.13653900	0.18716300
H	3.87342900	-2.10891200	2.47616300
C	-1.22048600	2.39031500	3.13192600
C	-0.78207600	3.72005600	3.20139200
C	-1.80001700	1.78708800	4.25453800

C	-0.92722600	4.43708000	4.38759200
H	-0.33112700	4.17923900	2.32676100
C	-1.93145400	2.50375400	5.44508700
H	-2.14357000	0.75689600	4.19777000
C	-1.49688000	3.82937600	5.51105500
H	-0.58863600	5.46797600	4.43869900
H	-2.37499200	2.02906100	6.31568600
H	-1.60012400	4.38895400	6.43666400
H	-1.36905900	0.57188700	1.98202300
C	-0.49971700	3.24492700	-5.73813500
O	-1.39935000	3.08217300	-4.76220600
C	1.01565700	2.10122000	-2.93149500
C	1.34021700	1.92829400	-4.42544900
C	0.96630400	3.13777300	-5.31667900
H	2.41352000	1.74415200	-4.51374100
H	0.82078400	1.03002100	-4.78677600
H	1.23247900	4.07051500	-4.79892000
H	1.54915800	3.11040400	-6.24050500
O	1.93525200	1.97326100	-2.10367100
O	-0.83518700	3.49070700	-6.88083100
O	-0.21359600	2.37255000	-2.64405700
H	-0.91957500	2.83328600	-3.88534100
H	1.28390400	2.56445800	-0.26884900
C	-1.92515700	0.46564900	-2.16037000
O	-1.60867900	0.68092300	-0.67370400
C	-2.12214400	1.80322700	-0.30782200
C	-2.85321400	2.54344200	-1.37638000
C	-2.96417600	1.49987200	-2.49218000

H	-3.80102300	2.94290300	-1.00992700
H	-2.19838000	3.37355800	-1.66414500
H	-3.93265900	0.98368100	-2.46876100
H	-2.79912100	1.88330900	-3.49924000
O	-2.07794600	2.21510200	0.89768500
O	-1.44845600	-0.46909700	-2.68810300

C

E (SMD/B3LYP-D3/6-31G(d)) = -1432.425025 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.994538 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.084016 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.899318 au

N	-0.12438600	1.73639200	-0.00400100
C	-0.00893700	1.21255700	1.16491900
C	-1.36186900	1.10930400	1.86554900
C	1.26580700	0.75695600	1.72787600
C	1.30467000	0.02285800	2.92590600
C	2.47205700	1.04321700	1.06019800
C	2.52142900	-0.42336800	3.43835300
H	0.38944000	-0.20056500	3.46255000
C	3.68396600	0.59960000	1.57778900
H	2.45131100	1.61844800	0.14073900
C	3.71180400	-0.13624100	2.76748600
H	2.53881800	-0.99272700	4.36303700
H	4.60867100	0.82764100	1.05561300
H	4.65979700	-0.48174800	3.17037300
C	-1.45443900	1.84050200	3.18852400
C	-1.07484400	3.18643600	3.27041100

C	-1.92631200	1.18810200	4.33094700
C	-1.16024500	3.86753300	4.48302200
H	-0.71095400	3.69753100	2.38253600
C	-2.01010900	1.86911600	5.54814800
H	-2.23390100	0.14671600	4.26821700
C	-1.62626500	3.20866100	5.62559300
H	-0.86147900	4.91067900	4.53930600
H	-2.37978800	1.35436700	6.43071000
H	-1.69130900	3.74008900	6.57108000
H	-1.62422600	0.05078800	1.99981300
C	-0.25348000	2.61626700	-6.46573300
O	-1.07602100	3.24518100	-5.61374300
C	0.60920700	1.66928200	-3.36441700
C	0.85735200	1.03211200	-4.71204400
C	1.03252200	2.03288800	-5.87331500
H	1.74151400	0.39373300	-4.63089100
H	0.00806300	0.36042000	-4.90030900
H	1.66753700	2.86677000	-5.54566500
H	1.54645600	1.53399000	-6.69679100
O	1.05408500	0.95421300	-2.35008900
O	-0.51170700	2.54715900	-7.64851400
O	0.02722100	2.74766200	-3.21916600
H	-0.71671700	3.18773500	-4.69192400
H	0.71785900	1.34644100	-1.48304100
C	-2.63944400	1.65440600	-2.29097200
O	-1.90495100	1.05507100	-1.30020200
C	-1.52848100	1.98997300	-0.27191400
C	-1.85872200	3.38791400	-0.82570900

C	-2.87473200	3.11024000	-1.93497000
H	-2.23567700	4.02049700	-0.02089600
H	-0.94715400	3.82071300	-1.23832100
H	-3.91072700	3.20383700	-1.58813100
H	-2.75959600	3.73168600	-2.82493100
O	-2.23997900	1.71138100	0.90714600
O	-3.01493300	1.03473400	-3.25093900

D

E (SMD/B3LYP-D3/6-31G(d)) = -975.4226531 au

H (SMD/B3LYP-D3/6-31G(d)) = -975.110478 au

G (SMD/B3LYP-D3/6-31G(d)) = -975.176674 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -975.7258291 au

N	-0.04128700	1.76245500	-0.02698600
C	0.03291000	1.23050500	1.13926100
C	-1.33671800	1.12362500	1.81362900
C	1.29778300	0.76986900	1.73049200
C	1.32837900	0.09309400	2.96096300
C	2.50504200	0.99525800	1.04302600
C	2.53991400	-0.34909500	3.49160900
H	0.41124600	-0.08640400	3.51075100
C	3.71168200	0.55761300	1.57847100
H	2.47644200	1.51372500	0.09032600
C	3.73275600	-0.11646000	2.80468500
H	2.55063000	-0.87278400	4.44330000
H	4.63802800	0.73904200	1.04051500
H	4.67625600	-0.45860500	3.22131600
C	-1.45909800	1.83378900	3.14600500

C	-1.06036100	3.17141200	3.26592400
C	-1.98091200	1.17168800	4.26113200
C	-1.17534600	3.83329500	4.48678900
H	-0.65556800	3.68978200	2.40040500
C	-2.09479600	1.83282600	5.48694100
H	-2.30271900	0.13668600	4.16961200
C	-1.69135100	3.16394100	5.60146600
H	-0.86006900	4.86977900	4.57154800
H	-2.50270700	1.30930400	6.34736000
H	-1.77929500	3.68016000	6.55361100
H	-1.61764500	0.06692000	1.92445900
C	-2.73967500	1.65115700	-2.19364600
O	-1.83063500	1.08158500	-1.34933500
C	-1.42814100	2.01604800	-0.31669500
C	-1.75455800	3.39905800	-0.89461300
C	-2.94502600	3.10894400	-1.80886300
H	-1.95875200	4.10920800	-0.09174500
H	-0.89093900	3.74387500	-1.47010200
H	-3.90132900	3.18536900	-1.27778100
H	-3.00475300	3.73180400	-2.70403700
O	-2.18336400	1.75713900	0.84741500
O	-3.26171200	1.02769200	-3.08235200

TS_{D-E}

E (SMD/B3LYP-D3/6-31G(d)) = -1432.401482 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.977147 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.064517 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.878678 au

N 0.00737100 2.26444400 0.09875800

C	-0.05816100	1.57396300	1.22511300
C	-1.42715700	1.70533400	1.85306600
C	1.00192600	0.72258900	1.69933600
C	0.78638300	-0.15198600	2.78613300
C	2.23748800	0.69408900	1.01243900
C	1.77872700	-1.04847100	3.16756500
H	-0.15757000	-0.16265700	3.31453200
C	3.23091100	-0.18656700	1.41550000
H	2.38815200	1.35649100	0.16682000
C	3.00055100	-1.06194700	2.48647400
H	1.58233100	-1.74584900	3.97532600
H	4.18069200	-0.20831100	0.88984600
H	3.77539400	-1.76274500	2.78467700
C	-1.50313400	2.24377100	3.25696100
C	-0.88303900	3.45996300	3.57354000
C	-2.18194900	1.52640900	4.24731800
C	-0.94592300	3.95585200	4.87394100
H	-0.35435400	4.01562300	2.80277500
C	-2.23354400	2.02089400	5.55201200
H	-2.65157700	0.57731100	4.00699700
C	-1.61948700	3.23466100	5.86515600
H	-0.46555900	4.89954800	5.11630800
H	-2.75490400	1.45656000	6.31954200
H	-1.66241700	3.61894000	6.88043900
H	-1.96420300	0.75043000	1.72636000
C	-1.10159900	-3.09350800	3.38303100
O	-1.72250100	-1.92492700	3.61186700
C	-1.68327300	-1.79052600	0.39844300

C	-0.95384800	-3.07078000	0.80427300
C	-1.46804600	-3.78434300	2.07127100
H	-1.00206800	-3.75770600	-0.04605200
H	0.10663500	-2.80789500	0.91983900
H	-2.55903600	-3.88483200	2.01535300
H	-1.03709200	-4.78699700	2.11379100
O	-1.49080800	-1.43196200	-0.81036500
O	-0.31127600	-3.55408200	4.18319600
O	-2.38179300	-1.15415600	1.23262500
H	-2.15687000	-1.62973400	2.75093400
H	-1.87407100	-0.27640500	-1.08506000
C	-2.97902100	1.38910300	-1.95510500
O	-1.98901600	0.88350200	-1.25270400
C	-1.23756000	2.75476400	-0.10302900
C	-1.69152100	3.50041900	-1.30599700
C	-3.01954600	2.92136900	-1.83312800
H	-1.81418900	4.55740500	-1.03324500
H	-0.89812200	3.43035400	-2.05303100
H	-3.84047800	3.17163100	-1.15076700
H	-3.26626900	3.35849400	-2.80403300
O	-2.06787200	2.61902300	0.90021700
O	-3.80165700	0.76917200	-2.60699500

E

E (SMD/B3LYP-D3/6-31G(d)) = -1432.402451 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.974601 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.06503 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.879669 au

N	0.12247600	2.33384500	0.03338400
C	0.06249500	1.61701600	1.15388400
C	-1.31749300	1.67743000	1.74531300
C	1.13790700	0.78789900	1.62189900
C	0.93743700	-0.09475800	2.70639100
C	2.37615200	0.78744400	0.93688600
C	1.94349500	-0.97631200	3.08339700
H	-0.00359200	-0.11963000	3.23855500
C	3.38379900	-0.07712500	1.33762400
H	2.51617500	1.45683500	0.09494000
C	3.16595500	-0.96369100	2.40286000
H	1.75813200	-1.68062200	3.88829200
H	4.33522700	-0.07940400	0.81459200
H	3.95280700	-1.65263900	2.69732700
C	-1.49603300	2.10251800	3.17465300
C	-0.76857800	3.18145800	3.69466500
C	-2.40133100	1.41069900	3.98680100
C	-0.94748700	3.56457100	5.02218800
H	-0.06172500	3.71497300	3.06373700
C	-2.57290700	1.79309400	5.31796800
H	-2.96003900	0.57392300	3.57944400
C	-1.84802900	2.86840600	5.83499600
H	-0.38178300	4.39989600	5.42495000
H	-3.26904700	1.24822700	5.94862800
H	-1.98027900	3.16312100	6.87232900
H	-1.81319400	0.70040400	1.54302900
C	-0.91952000	-3.08605400	3.55157200
O	-1.41527500	-1.86301100	3.78851400

C	-1.73472900	-1.85668100	0.57315300
C	-1.07542900	-3.18209300	0.97967900
C	-1.49642800	-3.79721700	2.33060800
H	-1.27509800	-3.89883000	0.17755700
H	0.00996900	-3.01105800	0.96697200
H	-2.59104000	-3.80060200	2.40452400
H	-1.14988400	-4.83231300	2.37512200
O	-1.66774900	-1.57519600	-0.65068000
O	-0.07253900	-3.57599100	4.27441500
O	-2.26439400	-1.12119000	1.47129900
H	-1.90545600	-1.55999200	2.95487600
H	-1.98539800	-0.20334400	-1.11607700
C	-3.05241900	1.37041800	-1.81898400
O	-1.93506600	0.81726100	-1.36091800
C	-1.11859400	2.80997400	-0.16061100
C	-1.60344900	3.47810400	-1.39651100
C	-2.96709400	2.90208200	-1.83491100
H	-1.69904200	4.55533400	-1.20408400
H	-0.83676000	3.34032400	-2.16160700
H	-3.76429700	3.26411400	-1.17708800
H	-3.20845700	3.25614800	-2.84161200
O	-1.96704000	2.61392000	0.81494000
O	-4.05278100	0.77668600	-2.16719900

TS_{E-F}

E (SMD/B3LYP-D3/6-31G(d)) = -1432.393332 au

H (SMD/B3LYP-D3/6-31G(d)) = -1431.969016 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.056323 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.87081 au

N	0.17648200	2.34634100	-0.14924200
C	0.19568200	1.66932300	1.02566500
C	-1.11214500	1.68807600	1.62607800
C	1.35320700	0.89446100	1.44167600
C	1.27196600	-0.01291400	2.51753700
C	2.55977400	1.00753800	0.72158400
C	2.37206200	-0.79254800	2.85931900
H	0.35514300	-0.12680000	3.08072200
C	3.66014800	0.23668100	1.08071600
H	2.61365800	1.69577300	-0.11496900
C	3.56822800	-0.66665100	2.14559400
H	2.28929100	-1.49909900	3.67988400
H	4.58870700	0.33098700	0.52531900
H	4.42723300	-1.27464000	2.41585600
C	-1.46378100	1.90314200	3.06407200
C	-0.54318600	2.44668800	3.96984600
C	-2.74926900	1.55682100	3.50588100
C	-0.90178300	2.62812900	5.30556700
H	0.45265700	2.71714300	3.63288100
C	-3.10776400	1.75345300	4.83845100
H	-3.45891900	1.12548100	2.80603100
C	-2.18296300	2.28371900	5.74157900
H	-0.18021100	3.04335200	6.00350800
H	-4.10436500	1.48091600	5.17371400
H	-2.45902300	2.42467600	6.78284500
H	-1.55107700	0.45168700	1.40204700
C	-1.13019700	-2.84397400	3.89091800

O	-1.26634800	-1.51852500	4.09280000
C	-1.59292000	-1.69302000	0.75839500
C	-1.30268300	-3.07968300	1.32634400
C	-1.90082400	-3.42270700	2.70658800
H	-1.65652200	-3.80066200	0.58376200
H	-0.20896600	-3.18245800	1.35102500
H	-2.94486800	-3.09028200	2.75062200
H	-1.88587600	-4.50737300	2.83306300
O	-1.44741600	-1.50908800	-0.45486800
O	-0.43819400	-3.51436600	4.62658200
O	-1.95481400	-0.77568600	1.61662400
H	-1.72286000	-1.12467300	3.30827300
H	-1.89571000	-0.16503900	-1.28962000
C	-3.12218600	1.32456500	-1.61630100
O	-1.91074200	0.76124200	-1.68378700
C	-1.06067600	2.79318100	-0.28443700
C	-1.65448800	3.43559200	-1.49261700
C	-3.04418300	2.83802800	-1.81202100
H	-1.74604300	4.51671500	-1.32803400
H	-0.95116000	3.28097600	-2.31283700
H	-3.81841200	3.27523700	-1.17648800
H	-3.31018300	3.07537700	-2.84844700
O	-1.86489200	2.52578300	0.73236500
O	-4.15751400	0.72869100	-1.40496700

F

E (SMD/B3LYP-D3/6-31G(d)) = -1432.442114 au

H (SMD/B3LYP-D3/6-31G(d)) = -1432.011108 au

G (SMD/B3LYP-D3/6-31G(d)) = -1432.098599 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1432.919208 au

N	-0.34562500	1.95022600	0.00167300
C	-0.17856200	1.71623600	1.36787700
C	-1.07379600	2.50417700	2.05777900
C	0.80190600	0.71679400	1.82036300
C	0.62271300	-0.02181200	3.00246000
C	1.92758400	0.44743600	1.02055100
C	1.56472400	-0.97165300	3.39731600
H	-0.26683200	0.12516900	3.60347500
C	2.86785700	-0.50314600	1.41688100
H	2.05309000	0.98907600	0.08859500
C	2.69552900	-1.21082500	2.61069900
H	1.39136100	-1.55046700	4.29888700
H	3.73537800	-0.69330100	0.79035500
H	3.42598700	-1.95436400	2.91779800
C	-1.38617500	2.79546300	3.45438900
C	-0.39289700	2.74000200	4.44850900
C	-2.69338400	3.16676300	3.81831400
C	-0.70771300	3.02545700	5.77505800
H	0.62452700	2.47928300	4.17688700
C	-3.00007900	3.45837900	5.14602800
H	-3.46456300	3.21772900	3.05608400
C	-2.01117000	3.38414400	6.13015900
H	0.07033300	2.97699900	6.53198100
H	-4.01550400	3.73848900	5.41308800
H	-2.25311000	3.60691900	7.16572200
H	-2.57158000	-0.83185100	0.27905600

C	-0.74690100	-3.33204600	3.14470800
O	-1.55456100	-2.27713500	3.35830900
C	-1.02540700	-1.97150700	-0.01993800
C	-0.07458900	-2.92809000	0.65676400
C	-0.68136800	-3.87748600	1.71734300
H	0.38800400	-3.51349300	-0.14135300
H	0.72592700	-2.31934200	1.09598300
H	-1.68762000	-4.18986100	1.41083200
H	-0.06124500	-4.77383200	1.77178900
O	-0.88738700	-1.61778200	-1.18535400
O	-0.13069100	-3.82748900	4.06296200
O	-2.01802300	-1.53629400	0.75682500
H	-1.90265700	-1.93990600	2.50544600
H	-1.76062100	-0.37902300	-1.94038300
C	-2.95473300	0.99760300	-1.37859600
O	-2.15836400	0.47294900	-2.28878600
C	-1.30618200	2.81788500	-0.09032500
C	-1.98699200	3.28282900	-1.33442800
C	-3.27483600	2.45236200	-1.61639300
H	-2.25081000	4.34220100	-1.26117500
H	-1.28265900	3.15293700	-2.15887700
H	-4.07745400	2.74081300	-0.93519900
H	-3.59388000	2.61708100	-2.64998000
O	-1.80619900	3.19882600	1.11170900
O	-3.34131400	0.40668400	-0.36743600

3a

E (SMD/B3LYP-D3/6-31G(d)) = -975.4302741 au

H (SMD/B3LYP-D3/6-31G(d)) = -975.11736 au

G (SMD/B3LYP-D3/6-31G(d)) = -975.186906 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -975.740744 au

N	-0.24343900	1.83359600	0.01797800
C	-0.09205400	1.64097000	1.39383600
C	-1.02294600	2.41474200	2.04941800
C	0.91548600	0.69531500	1.89817000
C	0.71233800	-0.04876500	3.07321700
C	2.09741900	0.49105400	1.16557500
C	1.67873500	-0.94981800	3.51732100
H	-0.21069000	0.07082400	3.63120400
C	3.06109300	-0.41250800	1.61146700
H	2.24857200	1.04563800	0.24475400
C	2.85890500	-1.13304600	2.79133600
H	1.50331600	-1.51878000	4.42661700
H	3.97191900	-0.55438700	1.03553900
H	3.61049900	-1.83711000	3.13841000
C	-1.36567900	2.73133100	3.43345700
C	-0.38784100	2.72606300	4.44464600
C	-2.68693900	3.08051900	3.76769500
C	-0.73050500	3.03969800	5.75795600
H	0.63971200	2.48324800	4.19565500
C	-3.02171700	3.40005500	5.08229300
H	-3.44683900	3.09242600	2.99268300
C	-2.04756600	3.37663200	6.08350900
H	0.03681300	3.03196800	6.52744600
H	-4.04771200	3.66304300	5.32546900
H	-2.31107300	3.62273800	7.10853500

H	-2.70487000	-0.36730100	-2.56405900
C	-3.31876600	1.09619200	-1.54757800
O	-2.71402000	0.60593300	-2.65359800
C	-1.23095500	2.66426000	-0.10950400
C	-1.87286100	3.16104500	-1.36007400
C	-3.30898600	2.60955400	-1.53542900
H	-1.91765600	4.25616500	-1.34759500
H	-1.24521300	2.85347900	-2.19945700
H	-3.94840900	2.93995400	-0.71427100
H	-3.71972400	2.98352400	-2.47938900
O	-1.76227600	3.05967800	1.07587000
O	-3.77853800	0.38839200	-0.67804400

H₂O

E (SMD/B3LYP-D3/6-31G(d)) = -76.41113166 au

H (SMD/B3LYP-D3/6-31G(d)) = -76.38632 au

G (SMD/B3LYP-D3/6-31G(d)) = -76.408424 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -76.46375141 au

O	-1.01932700	-0.25294800	0.00000000
H	-0.18370900	0.23923500	0.00000000
H	-1.69330000	0.44437700	0.00000000

1e

E (SMD/B3LYP-D3/6-31G(d)) = -532.9645699 au

H (SMD/B3LYP-D3/6-31G(d)) = -532.85253 au

G (SMD/B3LYP-D3/6-31G(d)) = -532.893912 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -533.1378639 au

C	-0.57650300	1.26999800	-0.55579500
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O	0.78990400	1.32150600	-0.26047800
C	1.30273000	2.58425100	-0.57869500
O	2.45896900	2.85863600	-0.40831500
O	-1.22880200	0.28044800	-0.36415700
C	-0.95888300	2.59236800	-1.09900100
C	0.18312100	3.39074700	-1.11335600
C	0.15316200	4.70199100	-1.57197900
C	-1.07959100	5.18945400	-2.02101200
C	-2.23026200	4.38514400	-2.00609100
C	-2.18787800	3.06539500	-1.54195400
H	1.04728000	5.31688700	-1.57960400
H	-1.14981300	6.20909200	-2.38809700
H	-3.16997900	4.79703000	-2.36187400
H	-3.07225600	2.43665300	-1.52651400

7e

E (SMD/B3LYP-D3/6-31G(d)) = -609.3997342 au

H (SMD/B3LYP-D3/6-31G(d)) = -609.258133 au

G (SMD/B3LYP-D3/6-31G(d)) = -609.304599 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -609.6155289 au

C	1.29620300	1.21368600	-2.51865600
O	2.04679500	2.00582600	-3.27910500
C	3.16164000	2.96832500	-0.51941100
O	3.39617200	3.74819900	0.54600400
O	0.29895600	0.69155200	-2.97894600
O	3.52435100	3.32668500	-1.63666000
H	2.77404100	2.43687900	-2.75955900
H	3.87987900	4.53423900	0.22256100

C	2.68443100	1.22304800	1.13988500
C	2.15854800	0.01014400	1.57081900
C	1.40075800	-0.75695000	0.68841000
C	1.17601800	-0.29960300	-0.60710500
C	1.71554000	0.90564500	-1.08073000
C	2.49240100	1.68345100	-0.17646100
H	3.26641000	1.82566200	1.82665200
H	2.33729900	-0.32596900	2.58775600
H	0.97592500	-1.70480700	1.00592600
H	0.55862500	-0.87466800	-1.28668000

TS_{A-B} for substrate 6

E (SMD/B3LYP-D3/6-31G(d)) = -1201.246112 au

H (SMD/B3LYP-D3/6-31G(d)) = -1200.907489 au

G (SMD/B3LYP-D3/6-31G(d)) = -1200.98596 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -1201.657616 au

N	0.60479400	2.67477200	0.83765400
C	0.61206600	1.61621200	1.58152500
C	-0.60985700	1.77195200	2.31784800
C	1.37473000	0.36056300	1.51738700
C	1.33530400	-0.49855000	2.62791200
C	2.12404500	0.00769600	0.38255200
C	2.03543100	-1.70263400	2.60836400
H	0.77026500	-0.21635800	3.51410100
C	2.81389600	-1.20193600	0.36786100
H	2.14806700	0.66334700	-0.48156500
C	2.77272700	-2.05560900	1.47479400
H	2.00783900	-2.36123500	3.47160600

H	3.38149000	-1.48226600	-0.51456800
H	3.31650300	-2.99613500	1.45460100
H	-1.26729100	0.93207900	2.51442000
C	-0.66107500	3.39974400	-5.34179300
O	-1.57499200	3.13728600	-4.39744300
C	0.91477800	2.64770600	-2.44450800
C	1.34595200	2.54958500	-3.91115100
C	0.76381500	3.63838100	-4.84377200
H	2.43718500	2.59536500	-3.94150400
H	1.05821200	1.55246800	-4.27264900
H	0.78433200	4.60945800	-4.32984000
H	1.38919700	3.73093800	-5.73452500
O	1.81176200	2.52543100	-1.56754500
O	-0.96583800	3.46252900	-6.51618000
O	-0.31985500	2.82508400	-2.18149900
H	-1.11957500	3.08071100	-3.48714800
H	1.07893400	2.59980700	-0.12718000
C	-1.09877300	0.10099800	-1.87648500
O	-1.16917200	0.53583000	-0.53125700
C	-2.19691700	1.40981600	-0.36344900
C	-3.00020100	1.55188100	-1.63403900
C	-2.34544000	0.55808600	-2.59714900
H	-4.05391700	1.35184100	-1.42125900
H	-2.91404000	2.58734100	-1.97225500
H	-2.96647200	-0.32614700	-2.78038400
H	-2.07895400	0.99153200	-3.56177000
O	-2.39043800	1.94634900	0.70895700
O	-0.17519500	-0.56065000	-2.24254300

H -0.89666200 2.75209200 2.67749300

A for substrate 6

E (SMD/B3LYP-D3/6-31G(d)) = -820.7611238 au

H (SMD/B3LYP-D3/6-31G(d)) = -820.507097 au

G (SMD/B3LYP-D3/6-31G(d)) = -820.573313 au

E (SMD/B3LYP-D3/6-311+G(2d,p)//SMD/B3LYP-D3/6-31G(d)) = -821.044323 au

N -1.96825400 1.92604100 -0.03716300

C -1.48005400 1.21077800 0.88565300

C -2.89571500 1.48937900 1.09172100

C -0.25275000 0.59020100 1.31947500

C -0.23613300 -0.15045100 2.51274300

C 0.91711900 0.73032100 0.54939000

C 0.94785600 -0.74972200 2.93617800

H -1.14863800 -0.24797700 3.09412300

C 2.09433000 0.12778200 0.98169000

H 0.88251400 1.30586500 -0.37081600

C 2.11037400 -0.61014200 2.17161700

H 0.96671000 -1.32351800 3.85811700

H 3.00182500 0.23183000 0.39394900

H 3.03322400 -1.07809500 2.50356700

H -3.64814600 0.74046100 0.84417900

C 2.40708700 4.10196800 -4.41154400

O 2.76660000 3.67972000 -3.18928500

C -0.38510400 3.25592200 -2.79581300

C -0.16203000 4.09311500 -4.03871100

C 1.03217900 3.65032800 -4.90716500

H -1.08334200 4.06236800 -4.62837700

H	-0.04610100	5.13672100	-3.71526300
H	1.03340200	2.55614600	-4.99441700
H	0.91584100	4.06377600	-5.91052500
O	-1.61488700	3.33649300	-2.33345900
O	3.14973000	4.79099000	-5.07787100
O	0.49655200	2.57500200	-2.26625300
H	2.03157600	3.14818900	-2.78980500
H	-1.71214500	2.79778200	-1.48338900
H	-3.21063900	2.26227800	1.79301100

6. References

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