Supplementary Material

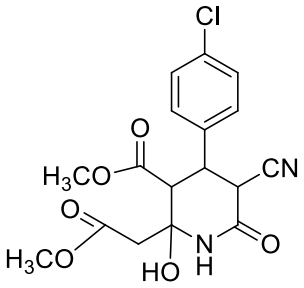
Trisodium citrate dihydrate catalyzed synthesis of fully and diversely functionalized novel piperidinone derivatives

Bubun Banerjee[1,2]*, Manmeet Kaur[1], Arvind Singh[1], Anu Priya,[1] and Aditi Sharma[1]

[1]Department of Chemistry, Akal University, Talwandi Sabo, Bathinda, Punjab-151302, India
[2]Visiting Researcher, Eternal University, Baru Sahib, Himachal Pradesh - 173101, India
Email: banerjeebubun@gmail.com

Table of Contents

Characterization data along with scanned spectra of all the synthesized compounds are given below:



4a

Methyl-4-(4-chlorophenyl)-5-cyano-2-hydroxy-2-(2-methoxy-2-oxoethyl)-6-oxopiperidine-3-carboxylate (**4a**). Light yellow solid, yield 97%; mp 142°C; FTIR (cm^{-1}): 3421, 1726, 1682, 1359, 1219, 1087, 615, 507, 434; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.67 (s, 1H, -N*H*), 7.39 (d, *J* = 8.5 Hz, 2H, aromatic H), 7.33 (d, *J* = 8.5 Hz, 2H, aromatic H), 6.57 (s, 1H, -O*H*), 4.33, (d, *J* = 12 Hz, 1H, -CH), 3.91 (t, *J* = 12.5 Hz, 1H, -CH), 3.69 (d, *J* = 12.5 Hz, 1H, aromatic H), 3.62 (s, 3H, -OCH_3) 3.33 (s, 3H, -OCH_3), 2.87 (d, *J* = 17 Hz, 1H), 2.77 (d, *J* = 17 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 170.22, 169.88, 168.84, 162.94, 159.07, 138.59, 132.82, 130.49 (2C), 129.09 (2C), 80.75, 52.57, 52.14, 52.07, 43.11, 41.97); HRMS (ESI-TOF) m/z: For $C_{17}H_{17}ClN_2O_6$ Calcd. $[M]^+$ 380.0775; Found $[M-H]^-$ 379.0355.

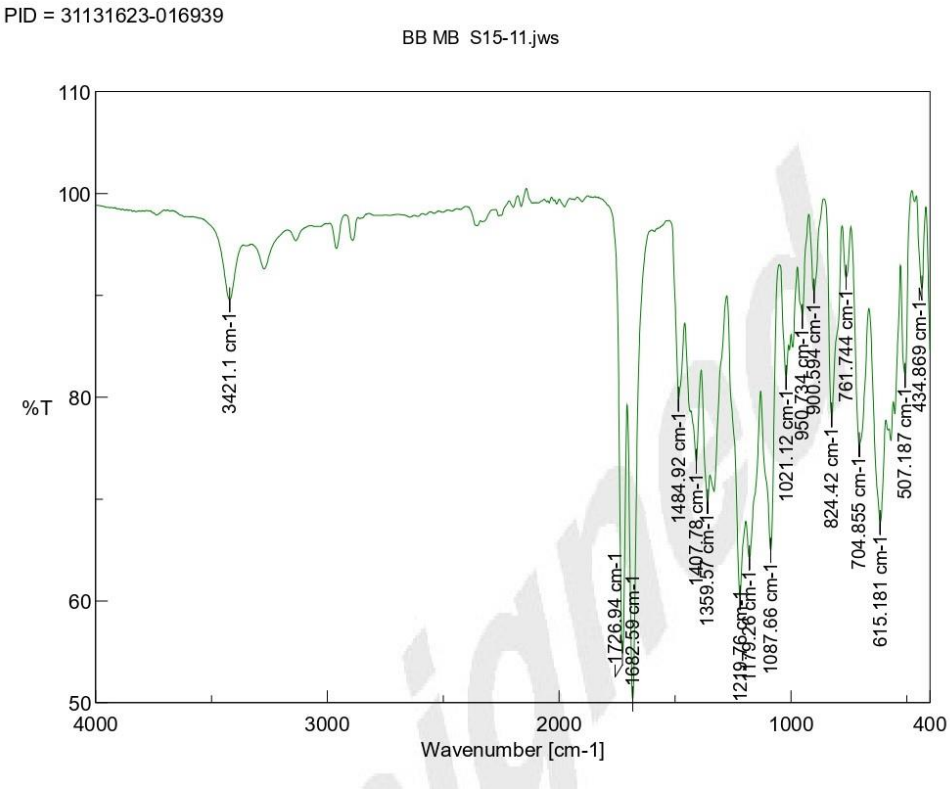


Figure S1. FTIR spectrum of **4a**

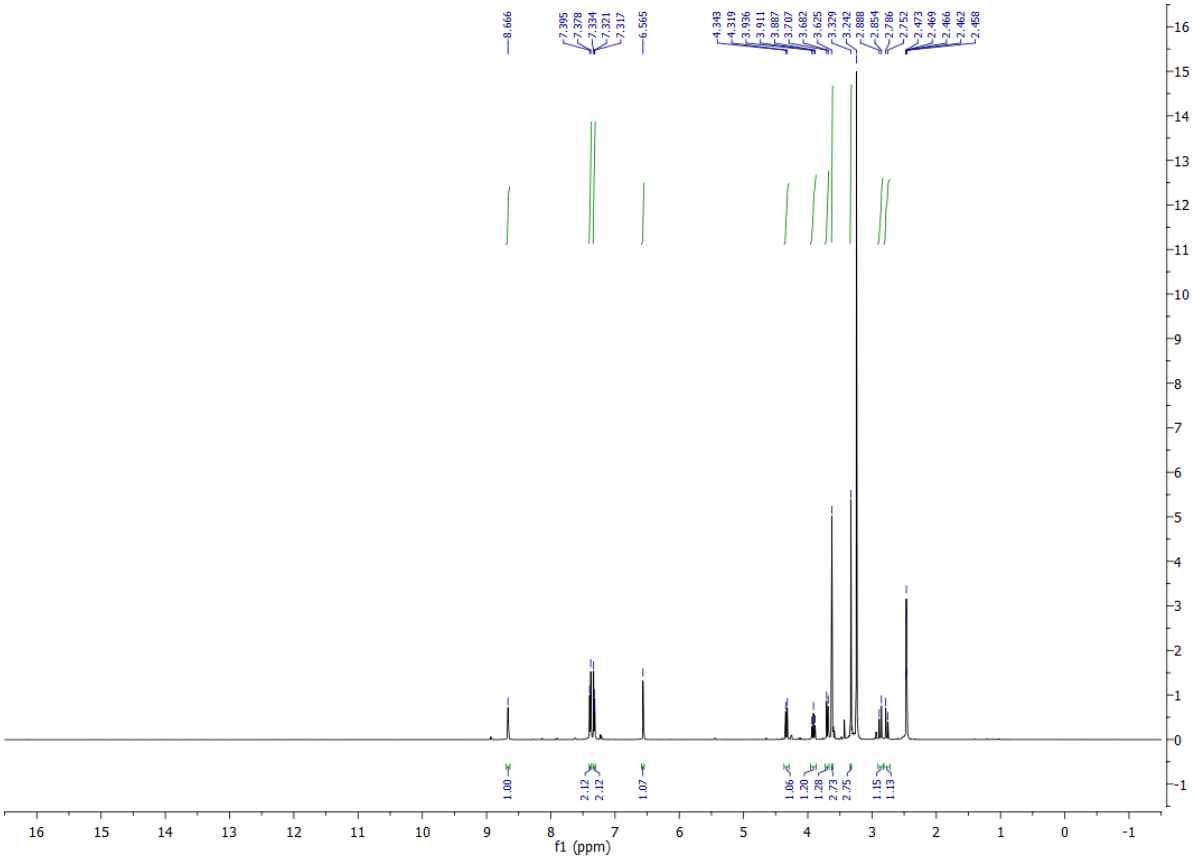


Figure S2. ^{1}H NMR spectrum of **4a**

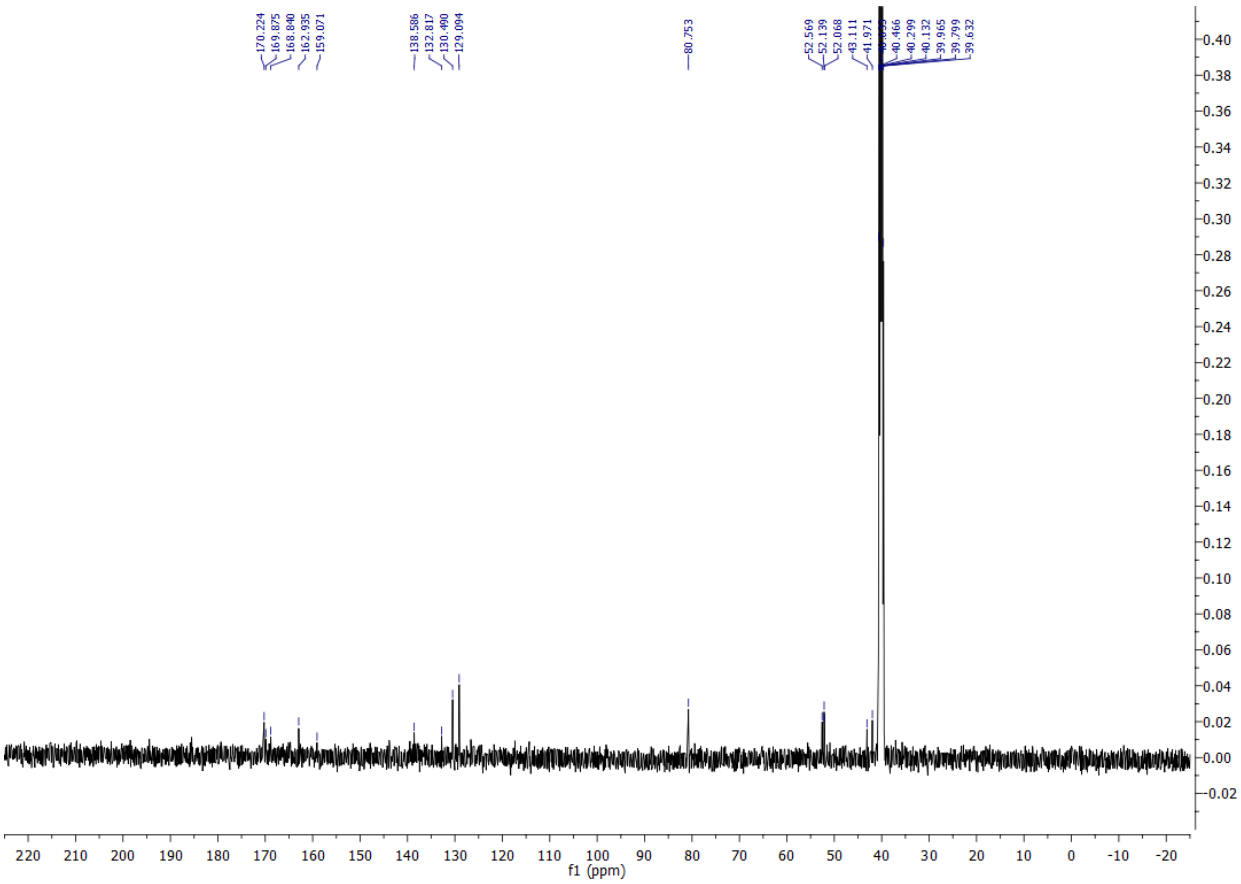


Figure S3. ^{13}C NMR spectrum of **4a**

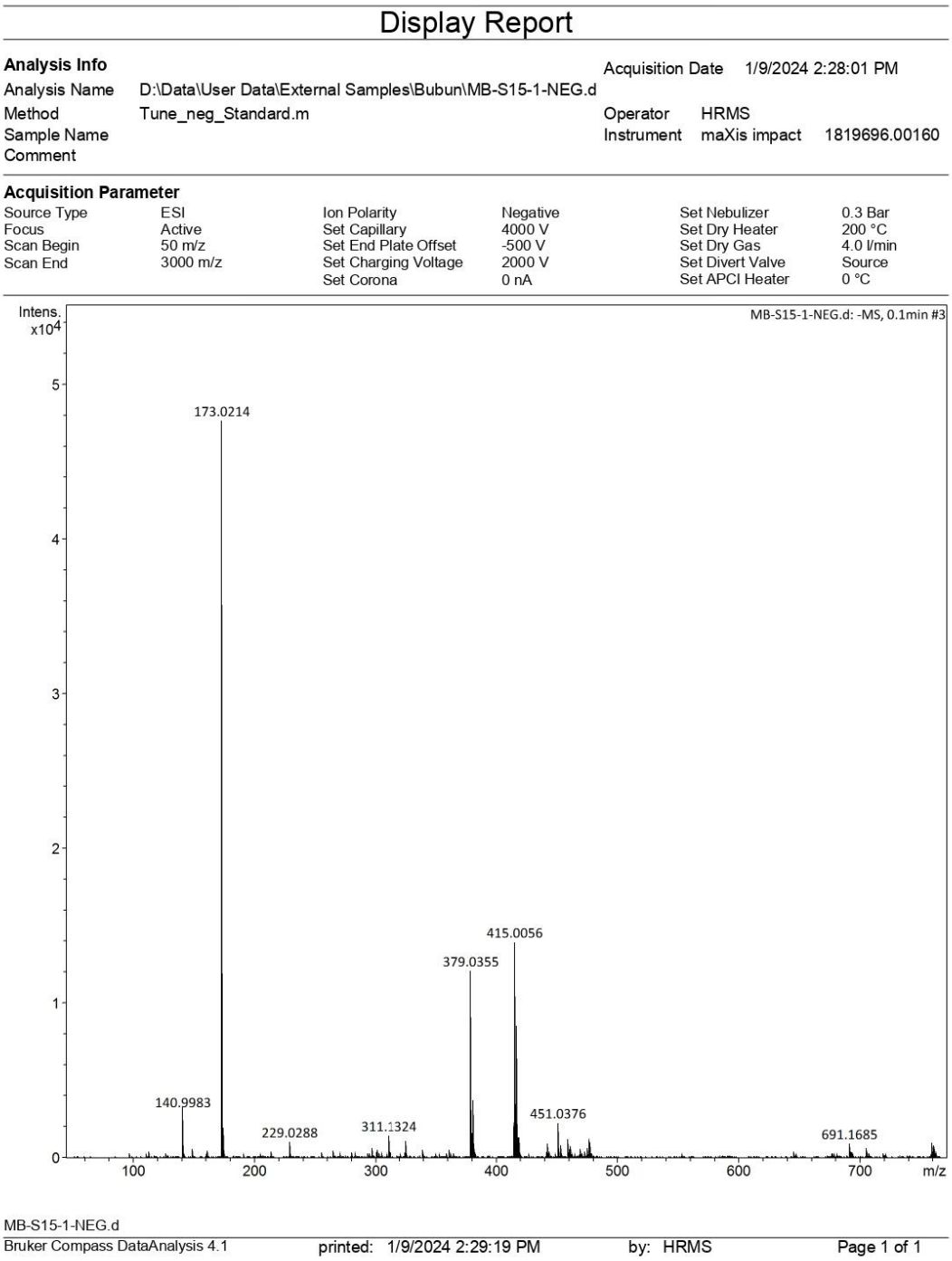
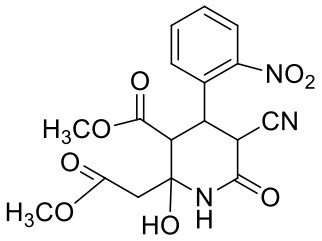


Figure S4. HRMS spectrum of **4a**



4b

Methyl-5-cyano-2-hydroxy-2-(2-methoxy-2-oxoethyl)-4-(2-nitrophenyl)-6-oxopiperidine-3-carboxylate (**4b**). Light yellow solid, yield 90%; mp 153-155°C; FTIR (cm^{-1}): 3423, 2355, 1681, 1344, 1218 848, 699, 617; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.80 (s, 1H, -N*H*), 7.88-7.86 (m, 1H, aromatic H), 7.77-7.69 (m, 2H, aromatic H), 7.52-7.49 (m, 1H, aromatic H), 6.79 (s, 1H, O*H*), 4.65-4.63 (m, 2H, -C*H*), 3.71-3.69 (m, 1H, -C*H*), 3.68 (s, 3H, -OCH_3), 3.26 (s, 3H, -OCH_3), 2.88 (dd, *J* = 17 Hz, 2H, -CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 170.25, 168.73, 167.74, 162.86, 151.05, 134.05, 133.74, 129.48, 128.96, 124.96, 116.66, 80.74, 53.61, 52.41, 52.11, 42.94, 40.94); HRMS (ESI-TOF) m/z: For $C_{17}H_{17}N_3O_8$ Calcd. $[M+Na]^+$ 414.1016; Found $[M+Na]^+$ 414.1050.

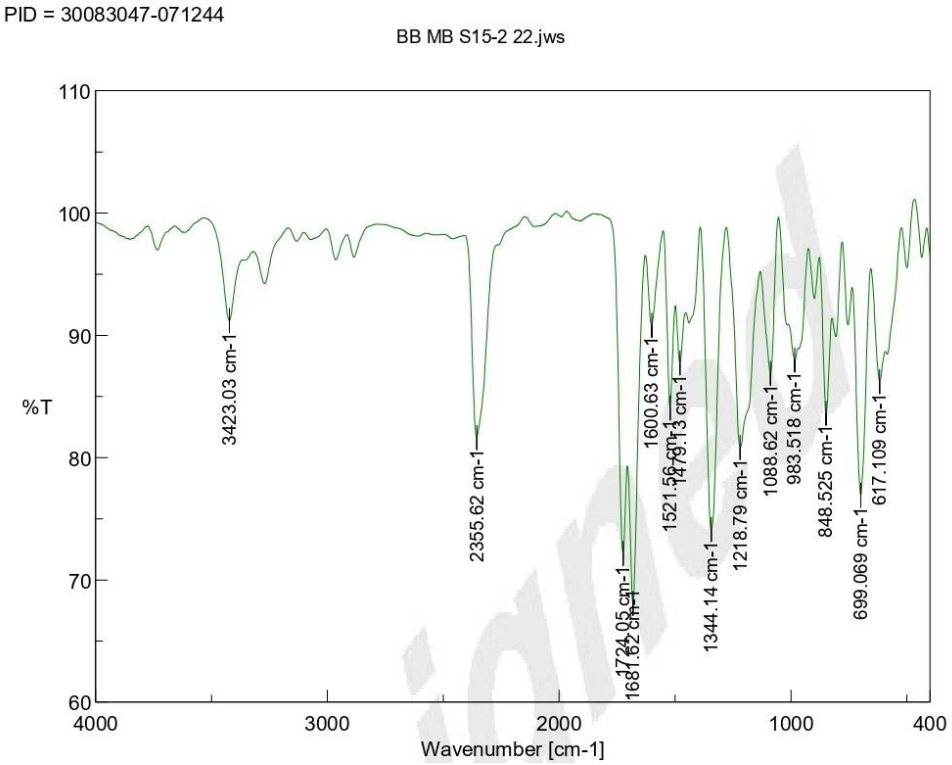


Figure S5. FTIR spectrum of **4b**

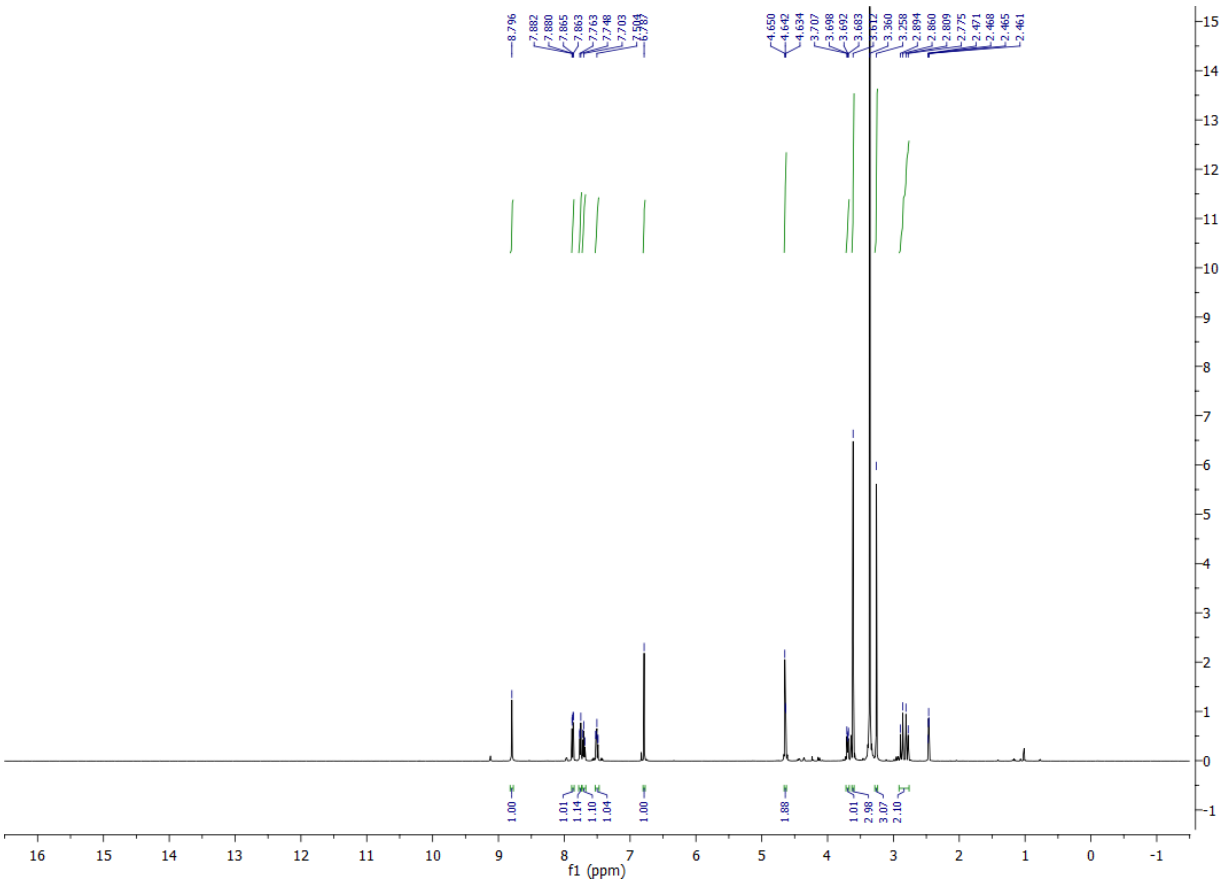


Figure S6. ^{1}H NMR spectrum of **4b**

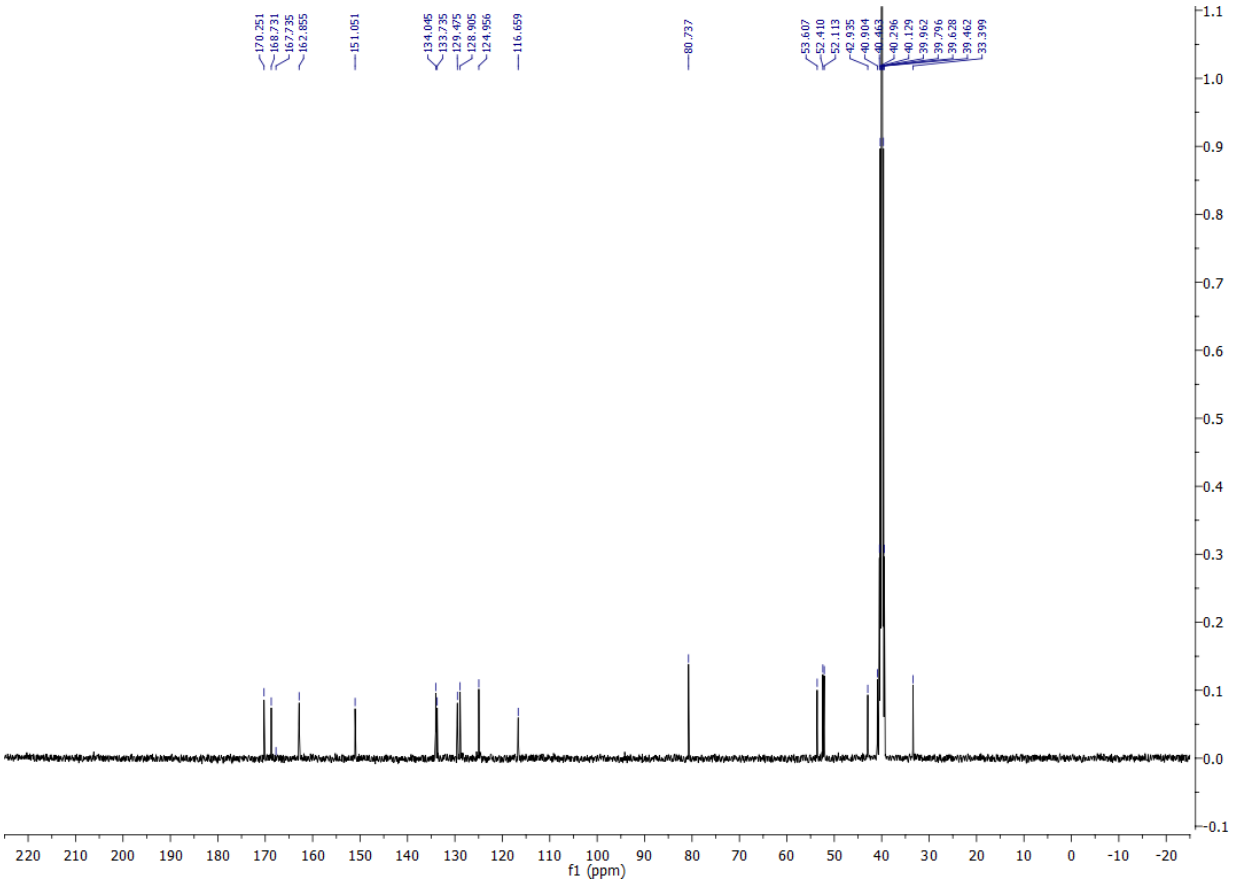


Figure S7. ^{13}C NMR spectrum of **4b**

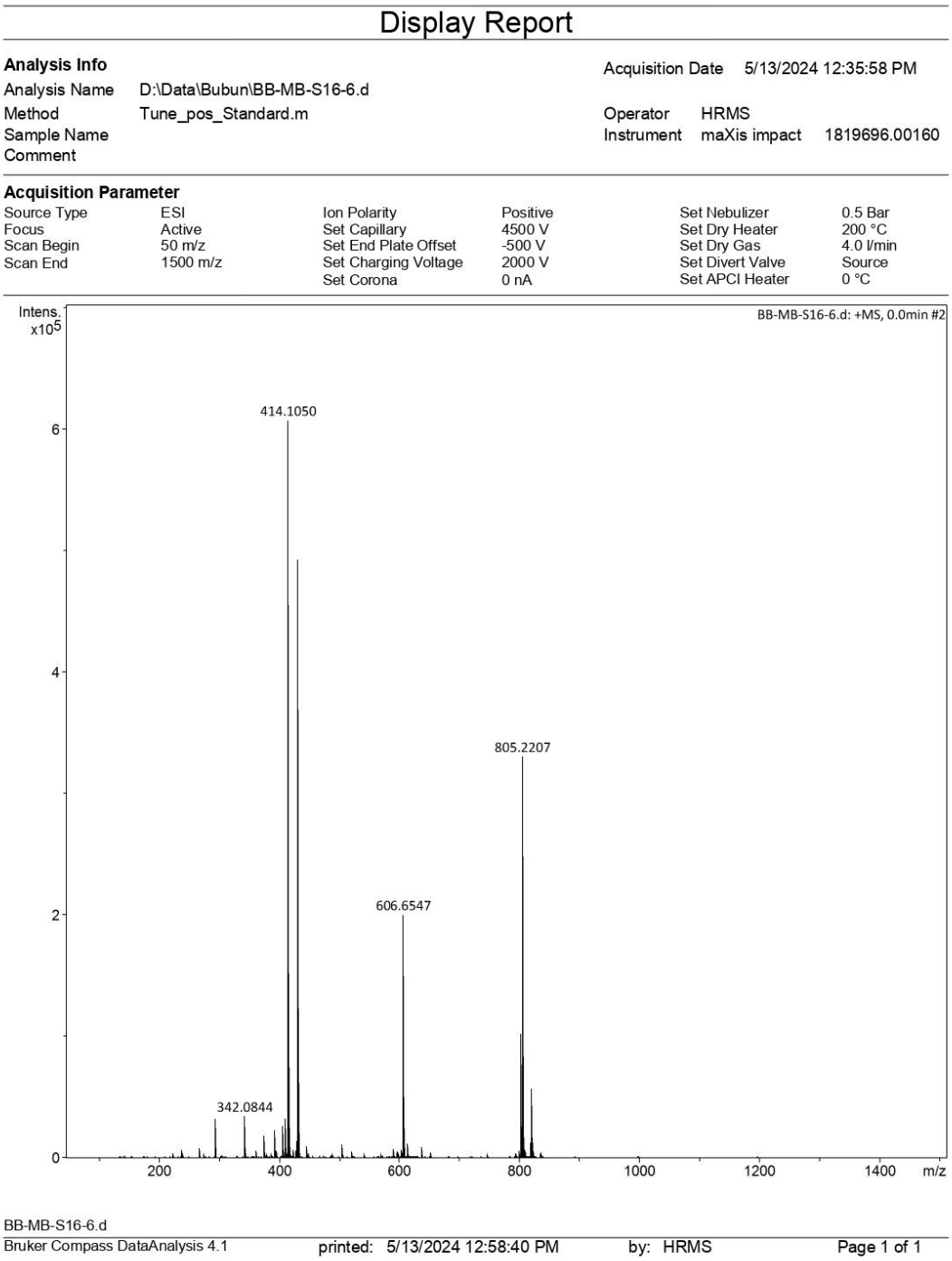
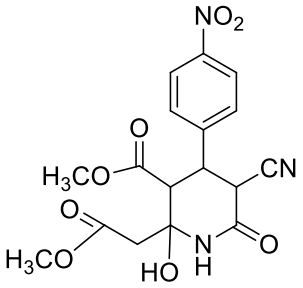


Figure S8. HRMS spectrum of **4b**



4c

Methyl-5-cyano-2-hydroxy-2-(2-methoxy-2-oxoethyl)-4-(4-nitrophenyl)-6-oxopiperidine-3-carboxylate (**4c**). Light yellow solid, yield 94%; mp 140°C; FTIR (cm^{-1}): 3423, 2355, 1681, 1344, 1218, 848, 699, 617; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.75 (s, 1H, -N*H*), 8.19 (d, *J* = 9Hz, 2H, aromatic H), 7.61 (d, *J* = 8.5 Hz, 2H, aromatic H), 6.64 (s, 1H, -O*H*), 4.46 (d, *J* = 12.5 Hz, 1H, -CH), 4.09 (t, *J* = 12.5 Hz, 1H, -CH), 3.81 (d, *J* = 12.5 Hz, 1H, aromatic H), 3.63 (s, 3H, -OCH_3), 3.32 (s, 3H, -OCH_3), 2.85 (dd, *J* = 17 Hz, 2H, -C*H*$_2$); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 170.20, 168.68, 162.63, 147.59 (2C), 147.18, 130.02, 124.32 (2C), 124.12 (2C), 117.13, 117.10, 80.83, 52.11, 40.62, 40.46); HRMS (ESI-TOF) m/z: For $C_{17}H_{17}N_3O_8$ Calcd. $[M+Na]^+$ 414.1016; Found $[M+Na]^+$414.1050

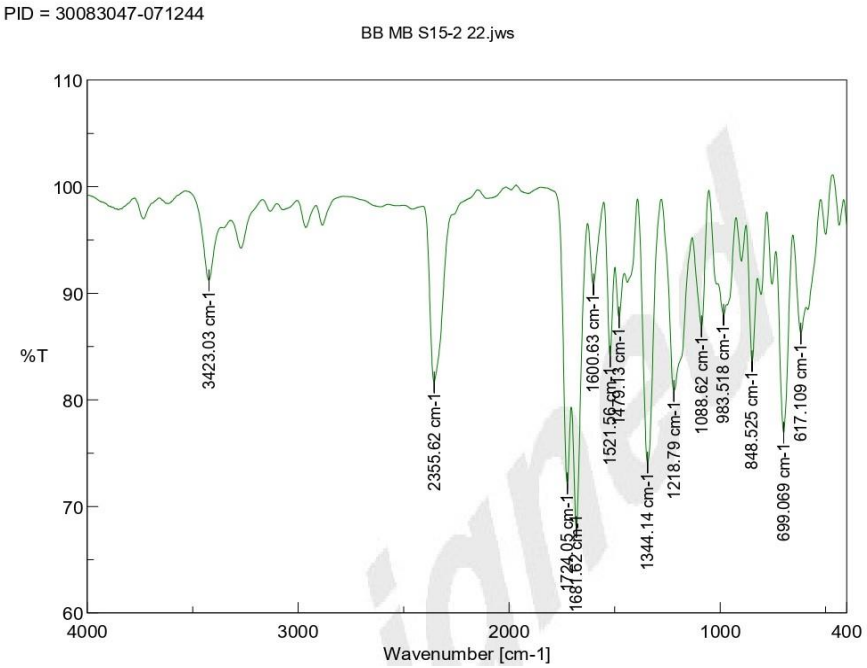


Figure S9. FTIR spectrum of **4c**

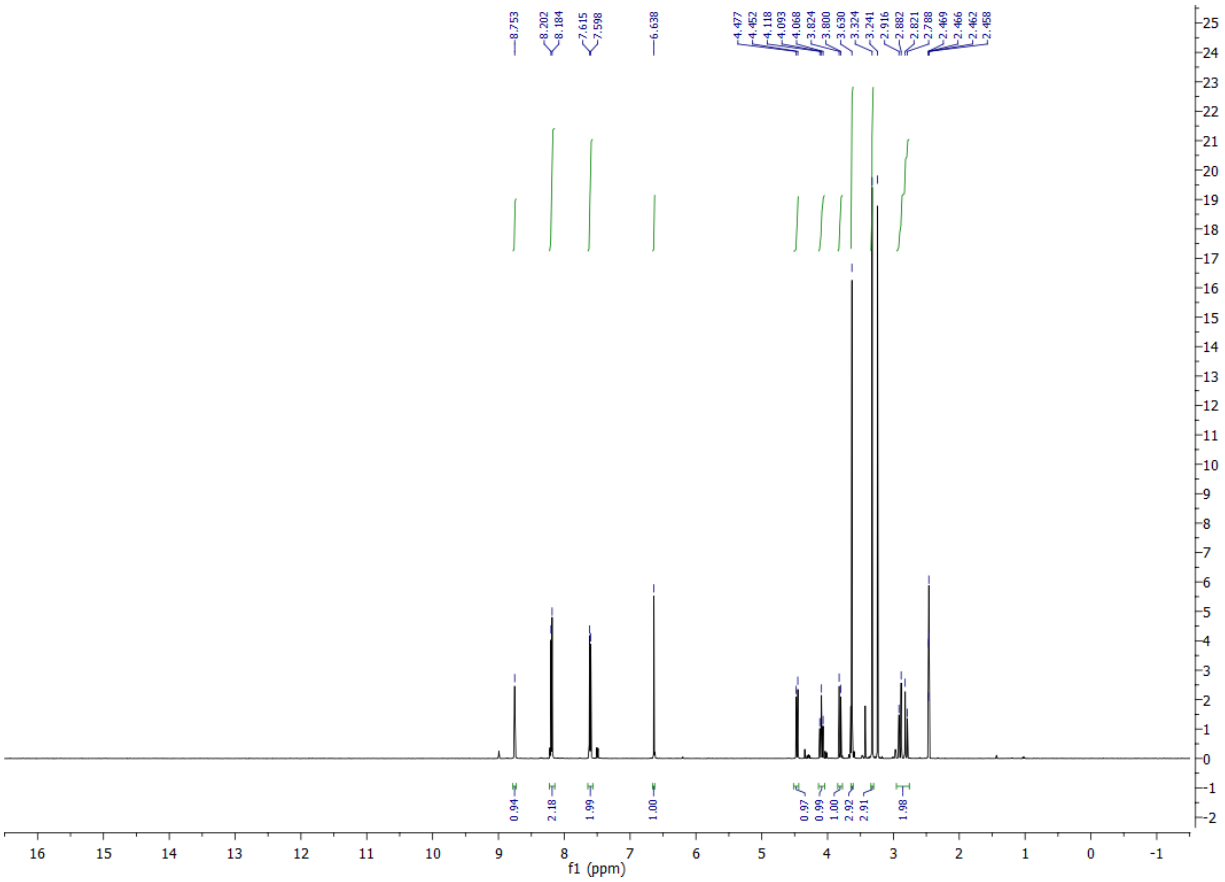


Figure S10. ^{1}H NMR spectrum of **4c**

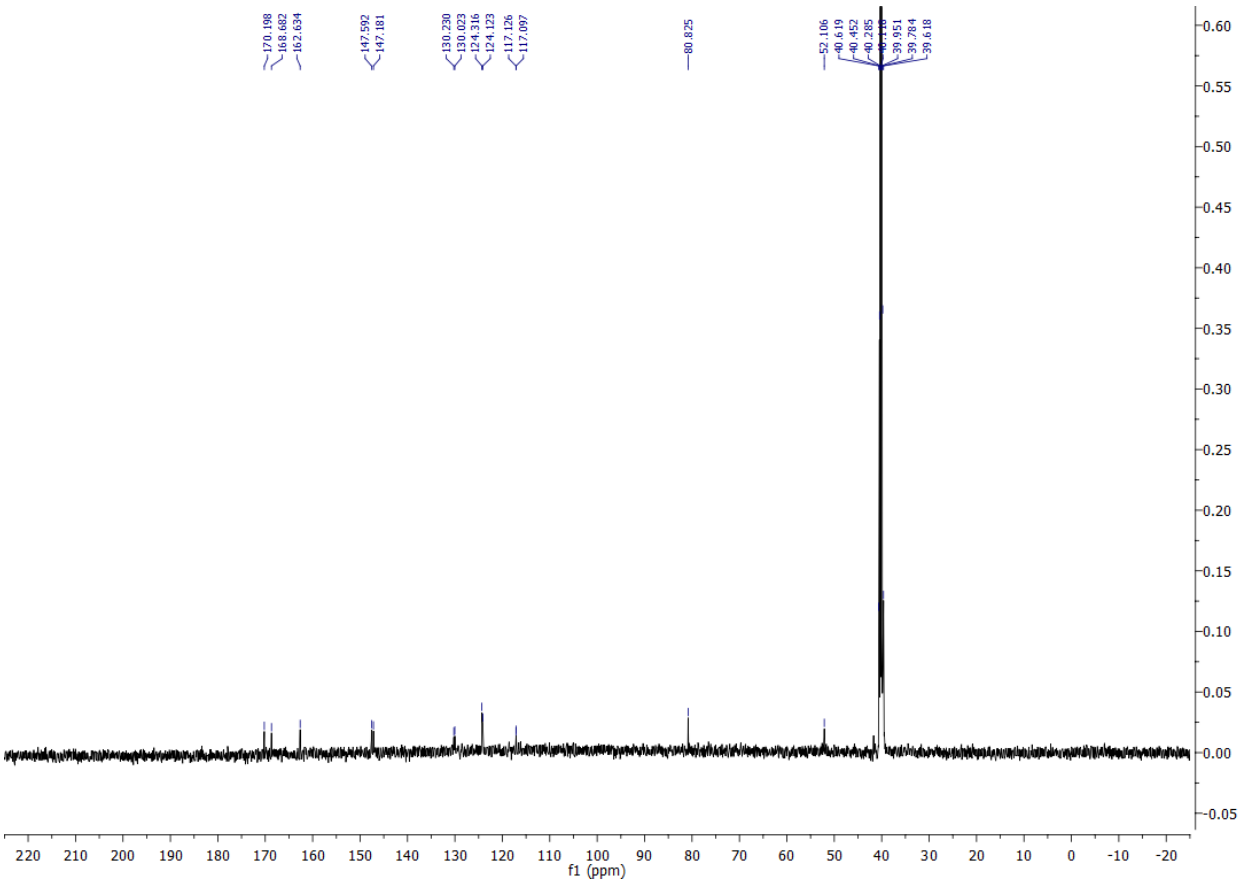


Figure S11. ^{13}C NMR spectrum of **4c**

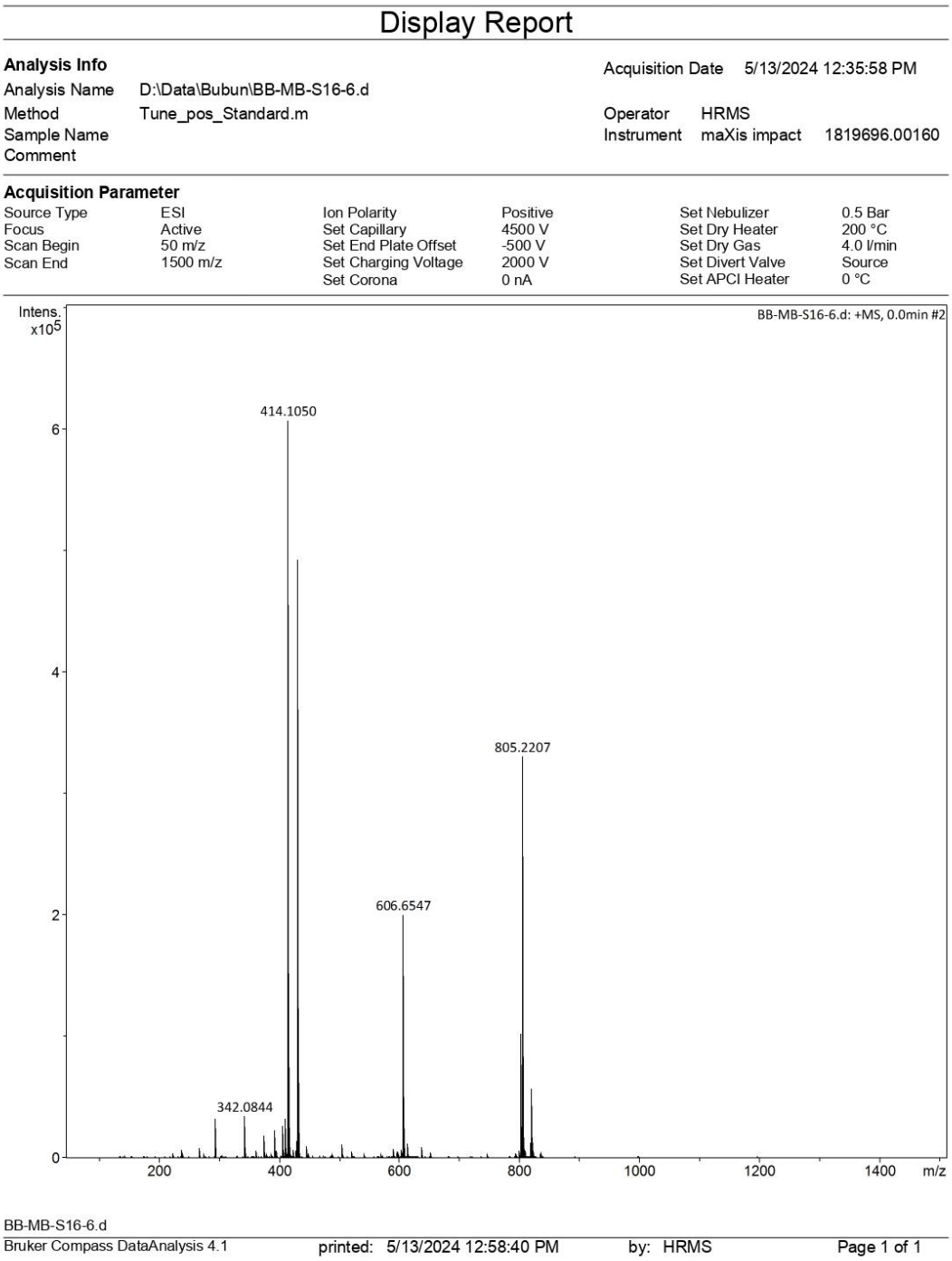
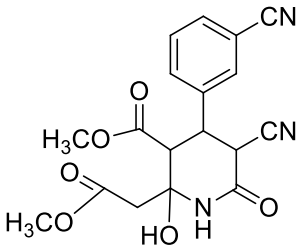


Figure S12. HRMS spectrum of **4c**



4d

Methyl-5-cyano-4-(3-cyanophenyl)-2-hydroxy-2-(2-methoxy-2-oxoethyl)-6-oxopiperidine-3-carboxylate **(4d)** White solid, yield 91%; mp 163°C; 3422, 2355, 1722, 1679, 1348, 1216, 619, 548, 458; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ_H/ppm: 8.77 (s, 1H, -N*H*), 7.81 (s, 1H, aromatic H), 7.75 (d, *J* = 8 Hz, 1H, aromatic H), 7.75 (d, *J* = 8 Hz, 1H, -CH), 7.55 (d, *J* = 8 Hz, 1H, -CH), 6.65 (s, 1H, -O*H*), 4.47 (d, *J* = 12Hz, 1H, -CH), 3.99 (t, *J* = 12.5 Hz, 1H, -CH), 3.75 (d, *J* = 12.5 Hz, 1H, -CH), 3.63 (s, 3H, -OC*H*$_3$), 3.32 (s, 3H, -OC*H*$_3$), 2.83 (dd, *J* = 17 Hz, 2H, -C*H*$_2$); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ_C/ppm: 170.17, 168.75, 162.81, 141.18, 134.14, 132.20, 132.00 (2C), 119.10, 117.24, 112.10, 80.76, 52.27 (2C), 52.09 (2C), 42.97, 41.60); HRMS (ESI-TOF) m/z: For $C_{18}H_{17}N_3O_6$ Calcd. $[M]^+$ 371.1117; Found $[M\text{-}H]^-$ 370.0476.

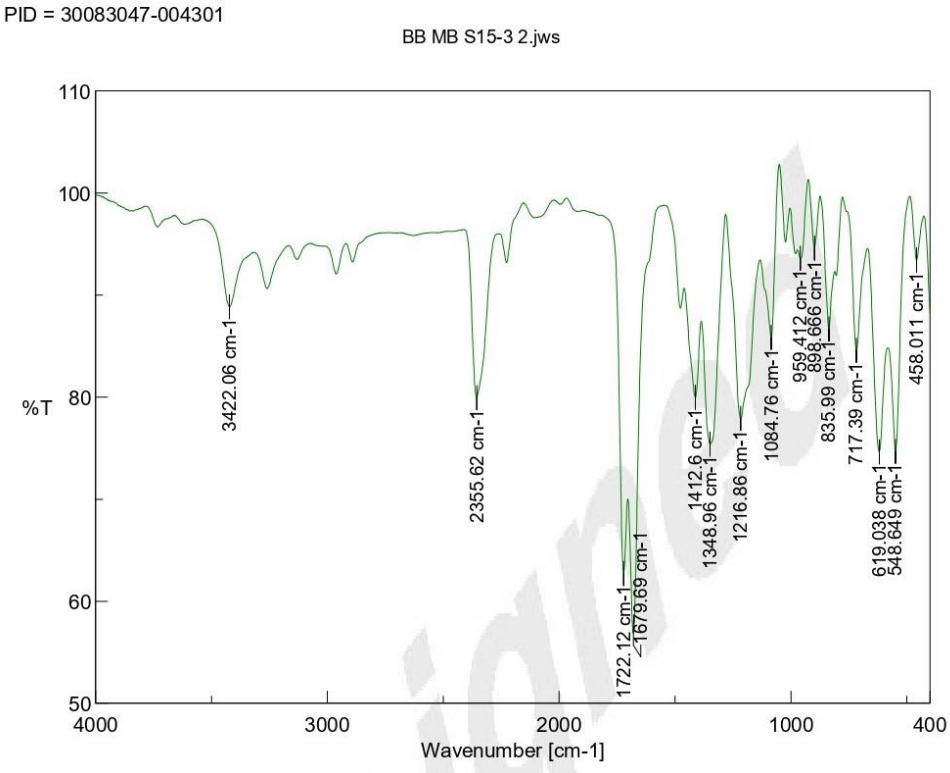


Figure S13. FTIR spectrum of **4d**

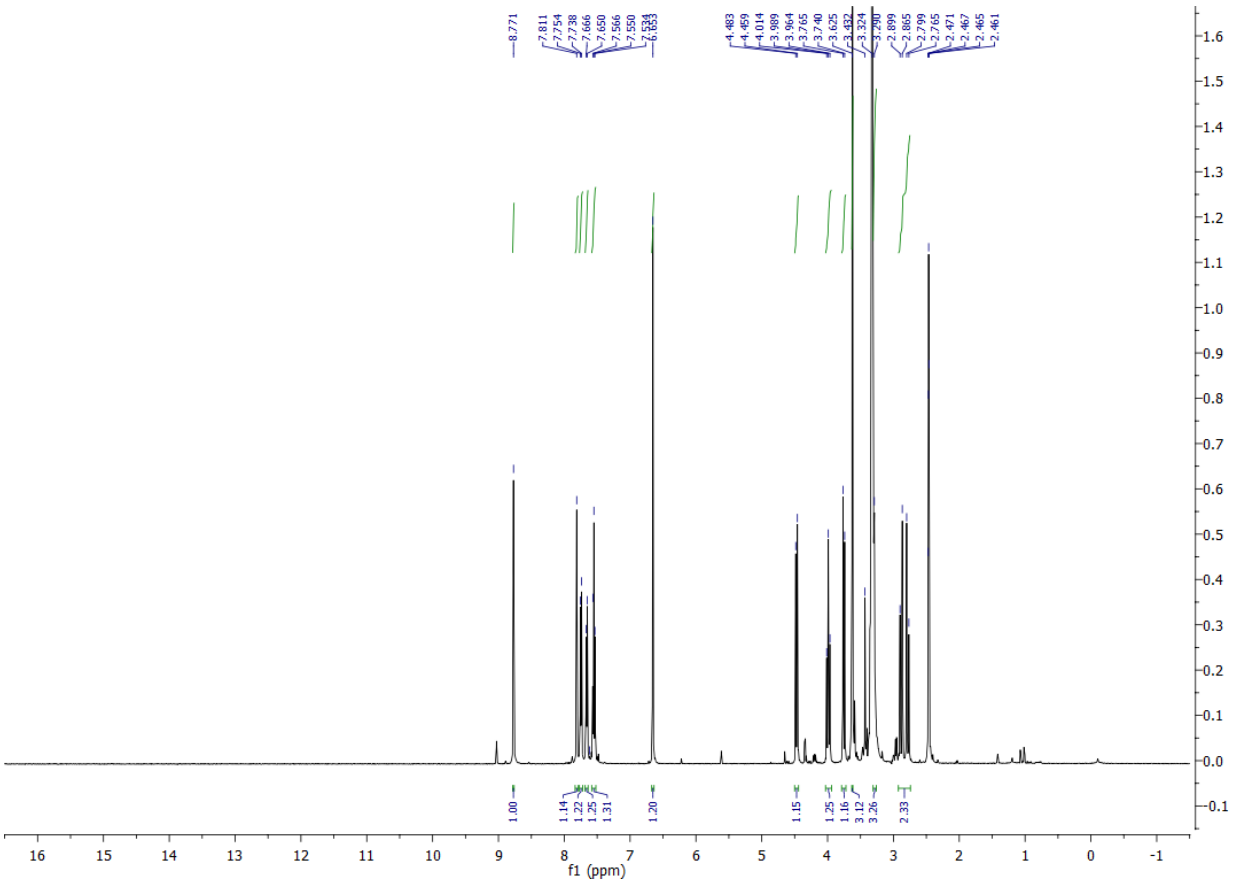


Figure S14. ^{1}H NMR spectrum of **4d**

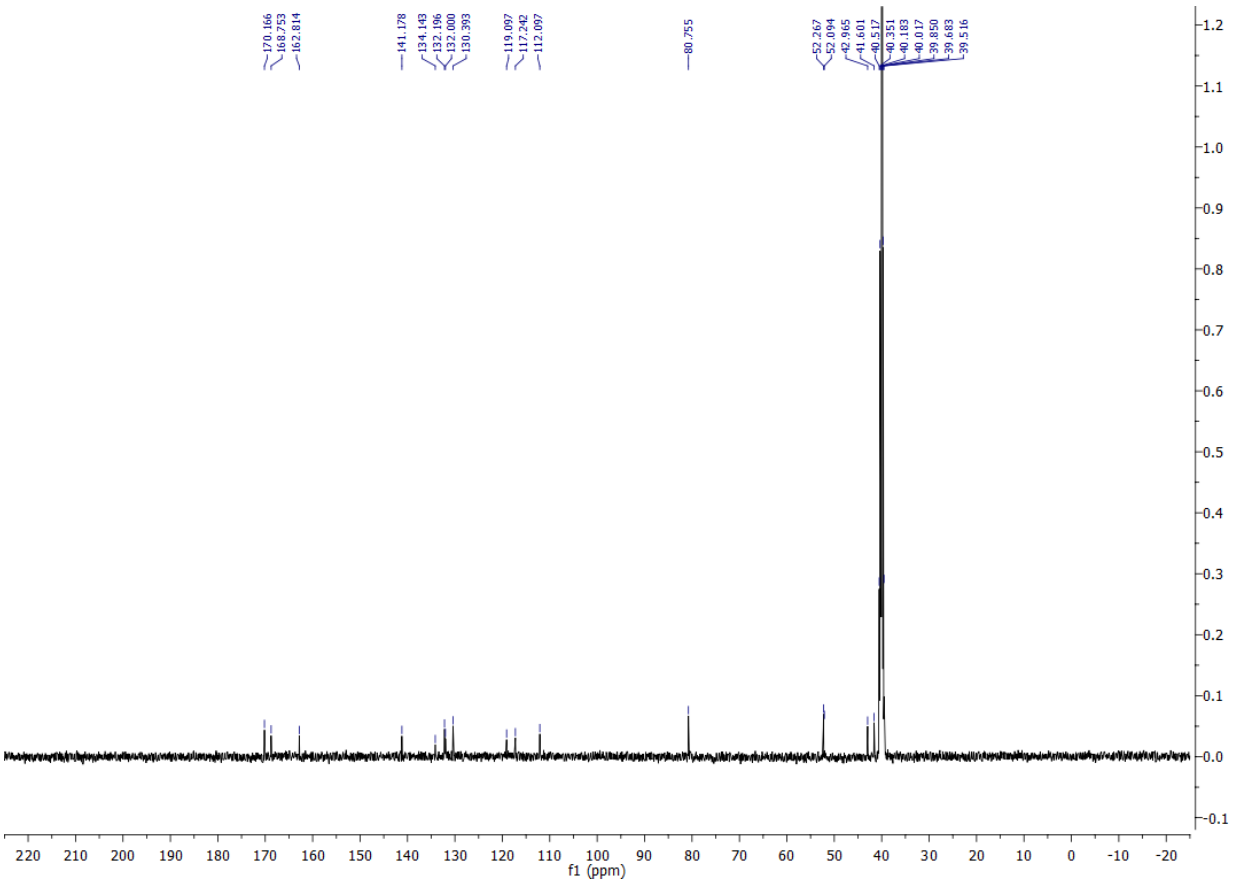


Figure S15. ^{13}C NMR spectrum of **4d**

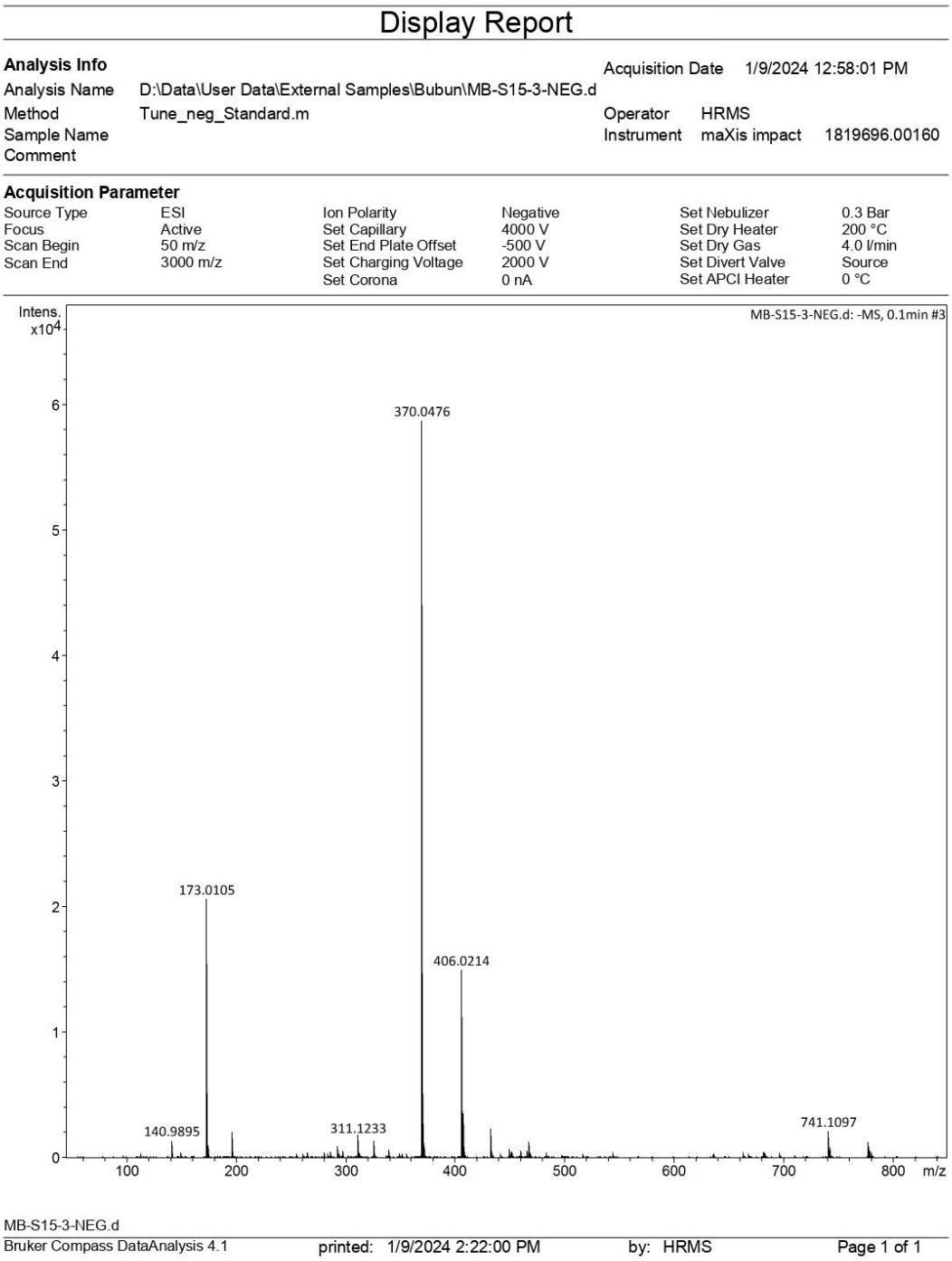
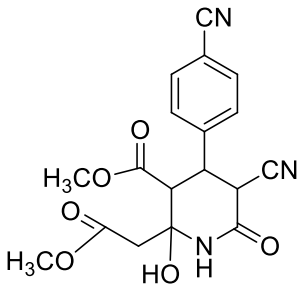


Figure S16. HRMS spectrum of **4d**



4e

Methyl-5-cyano-4-(4-cyanophenyl)-2-hydroxy-2-(2-methoxy-2-oxoethyl)-6-oxopiperidine-3-carboxylate (**4e**). White solid, yield 95%; mp 151°C; FTIR (cm^{-1}): 3422, 2355, 1722, 1679, 1348, 1216, 619, 548, 458;^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.73 (s, 1H, -N*H*), 7.81(d, *J* = 8.5 Hz, 2H, aromatic H), 7.52 (d, *J* = 8 Hz, 2H, aromatic H), 6.61 (s, 1H, -O*H*), 4.43 (d, *J* = 12 Hz, 1H, -CH), 4.02 (t, *J* = 12.5 Hz, 1H, -CH), 3.77 (d, *J* = 12 Hz, 1H, aromatic H), 3.63 (s, 3H, -OCH_3), 3.32 (s, 3H, -OCH_3), 2.84 (dd, *J* = 17 Hz, 2H, -CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 170.18, 168.71, 162.72, 145.15, 133.05 (2C), 129.80 (2C), 119.03, 117.15, 111.20, 80.81, 52.23 (2C), 52.07 (2C), 43.06, 41.54); HRMS (ESI-TOF) m/z: For $C_{18}H_{17}N_3O_6$ Calcd. $[M]^+$ 371.1117; Found $[M\text{-}H]^-$ 370.0476

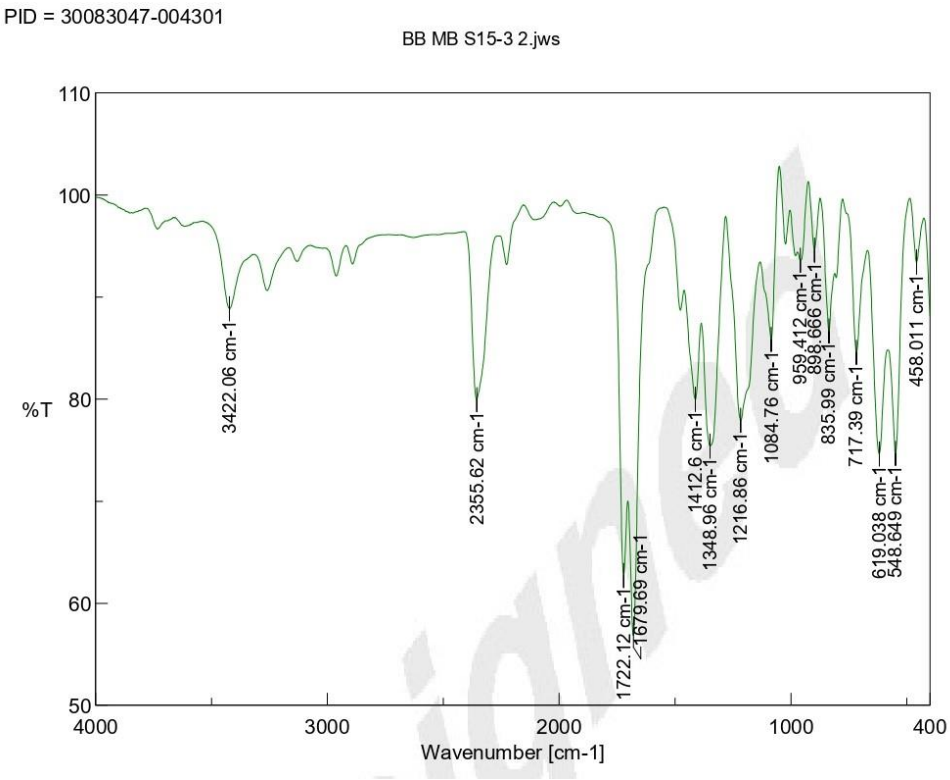


Figure S17. FTIR spectrum of **4e**

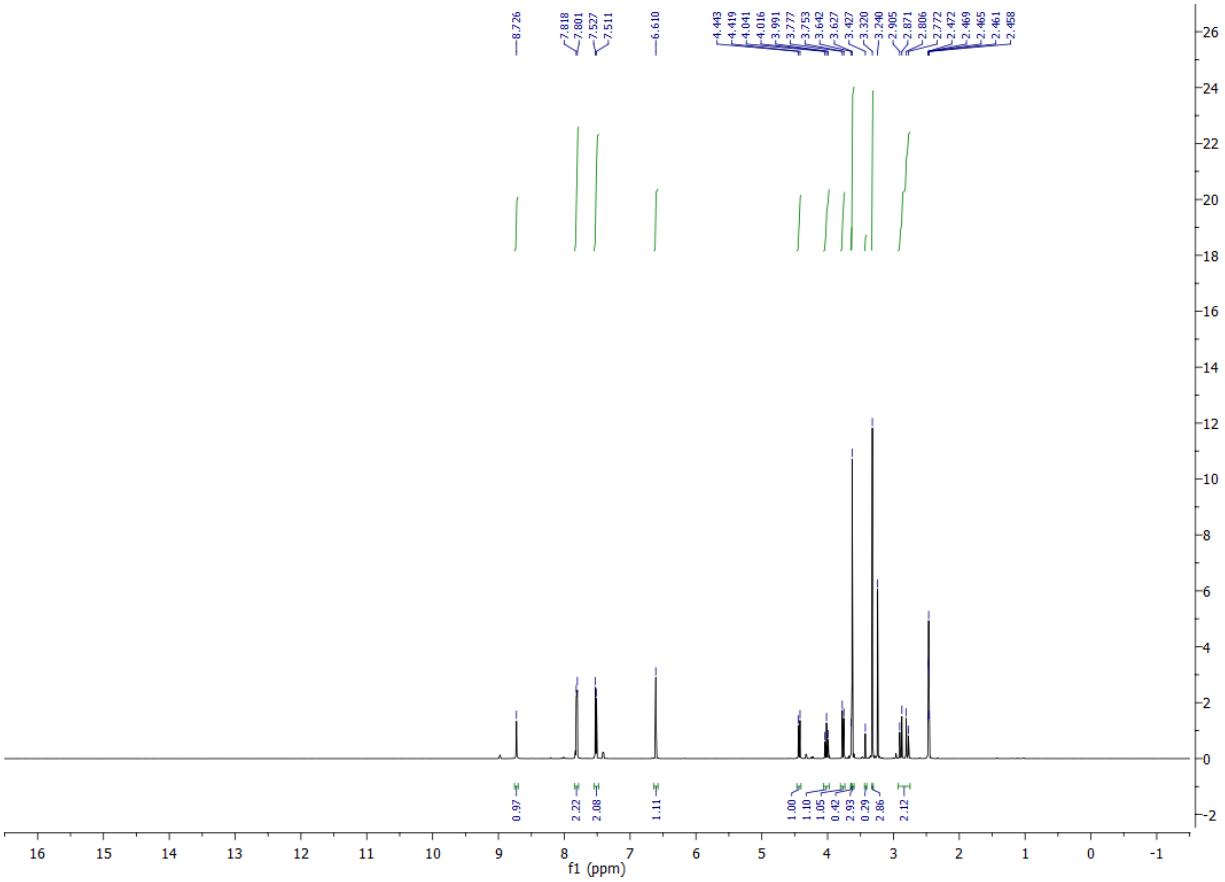


Figure S18. ^{1}H NMR spectrum of **4e**

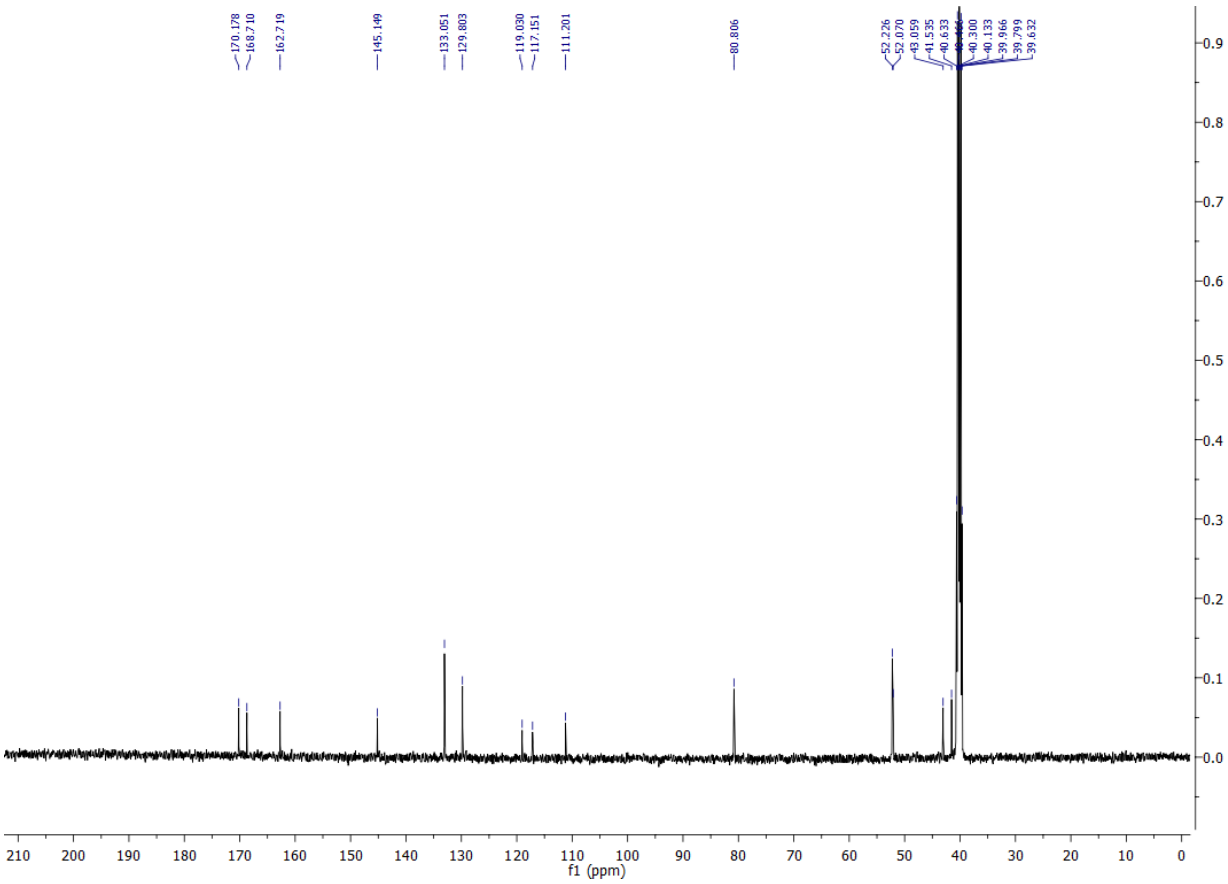


Figure S19. ^{13}C NMR spectrum of **4e**

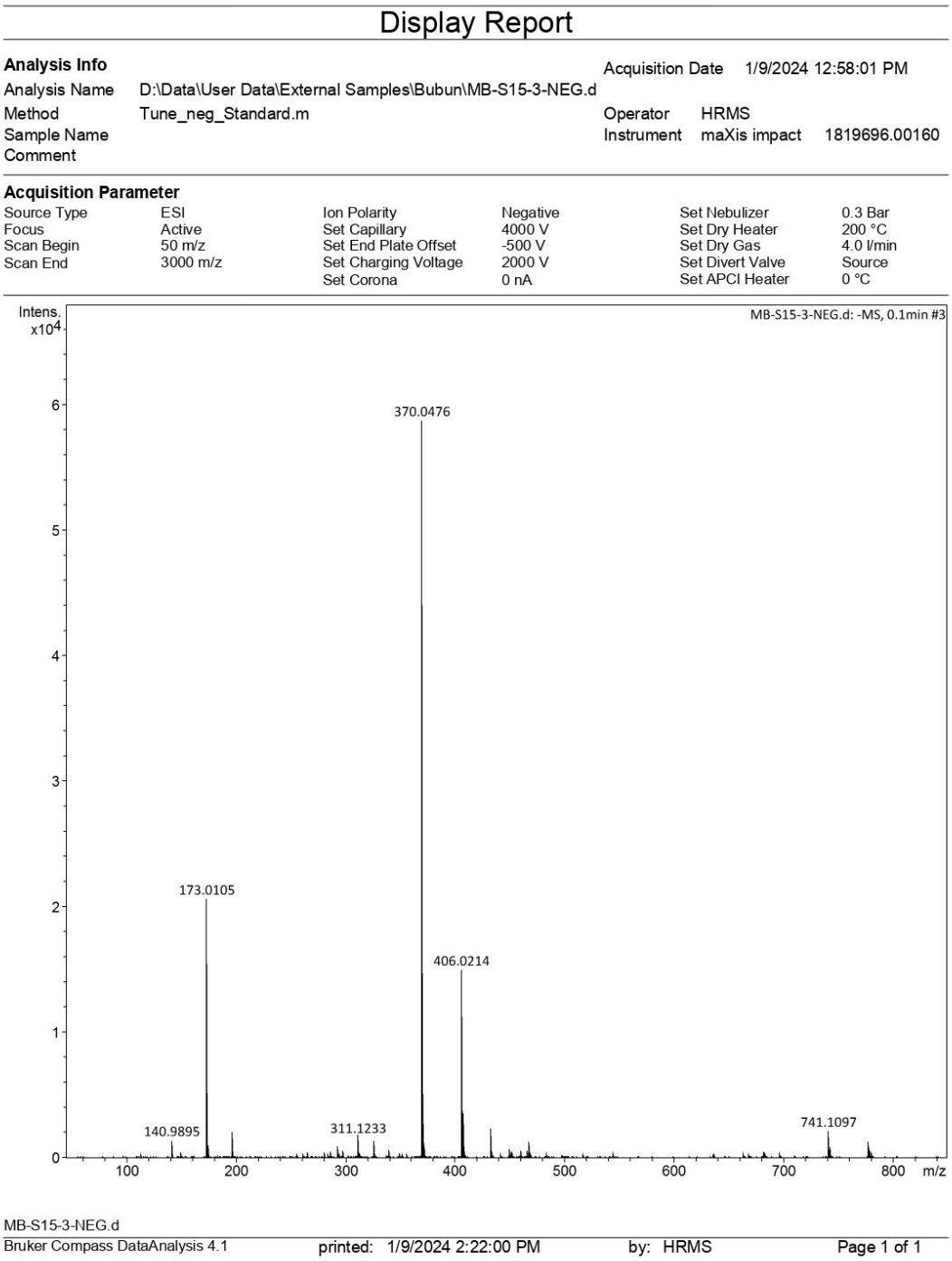
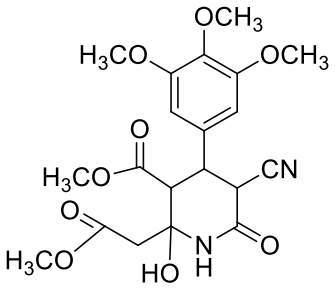


Figure S20. HRMS spectrum of **4e**



4f

Methyl-cyano-2-hydroxy-2-(2-methoxy-2-oxoethyl)-6-oxo-4-(3,4,5-trimethoxyphenyl)piperidine-3-carboxylate **(4f)** White solid, yield 98%; mp 181-182°C; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ_H/ppm: 8.65 (s, 1H, -N*H*), 6.59 (s, 2H, aromatic H), 6.61 (s, 1H, -O*H*), 4.41 (d, *J* = 12 Hz, 1H, -CH), 3.80 (t, *J* = 12.5 Hz, 1H, -CH), 3.73 (s, 6H, 2X -OC*H*$_3$), 3.64 (d, *J* = 8.5 Hz, 1H, -CH), 3.62 (s, 3H, -OC*H*$_3$), 3.61 (s, 3H, -OC*H*$_3$), 3.36 (s, 3H, -OC*H*$_3$), 2.79 (dd, *J* = 16.5 Hz, 2H, -C*H*$_2$); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ_C/ppm: 170.25, 169.07, 163.31, 153.21 (2C), 137.23, 135.07, 117.65, 105.99, 80.67, 60.48 (2C), 56.49 (2C), 52.84 (2C), 52.14, 52.09, 43.06, 41.99); HRMS (ESI-TOF) m/z: For $C_{20}H_{24}N_2O_9$ Calcd. $[M+Na]^+$ 459.1482; Found $[M+Na]^+$ 459.1274

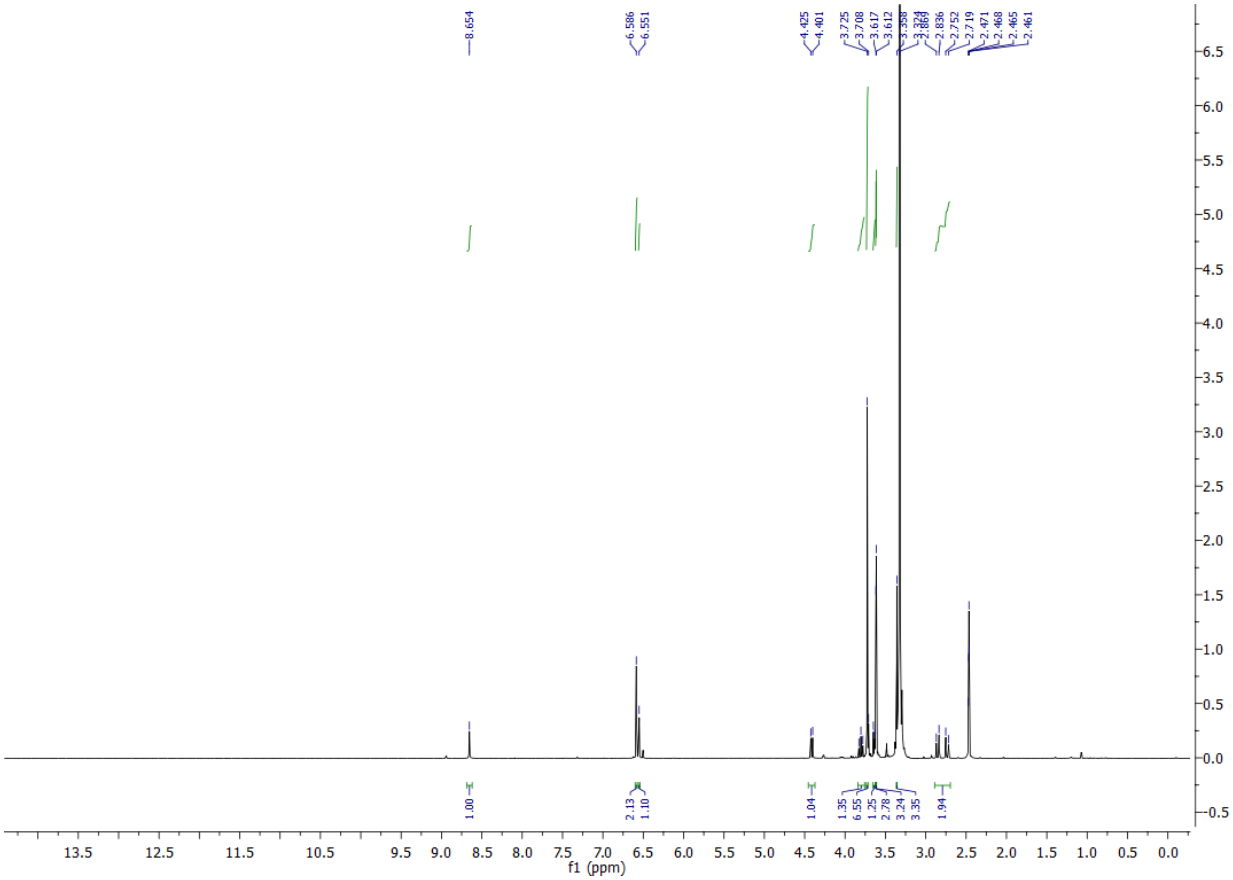


Figure S21. ^{1}H NMR spectrum of **4f**

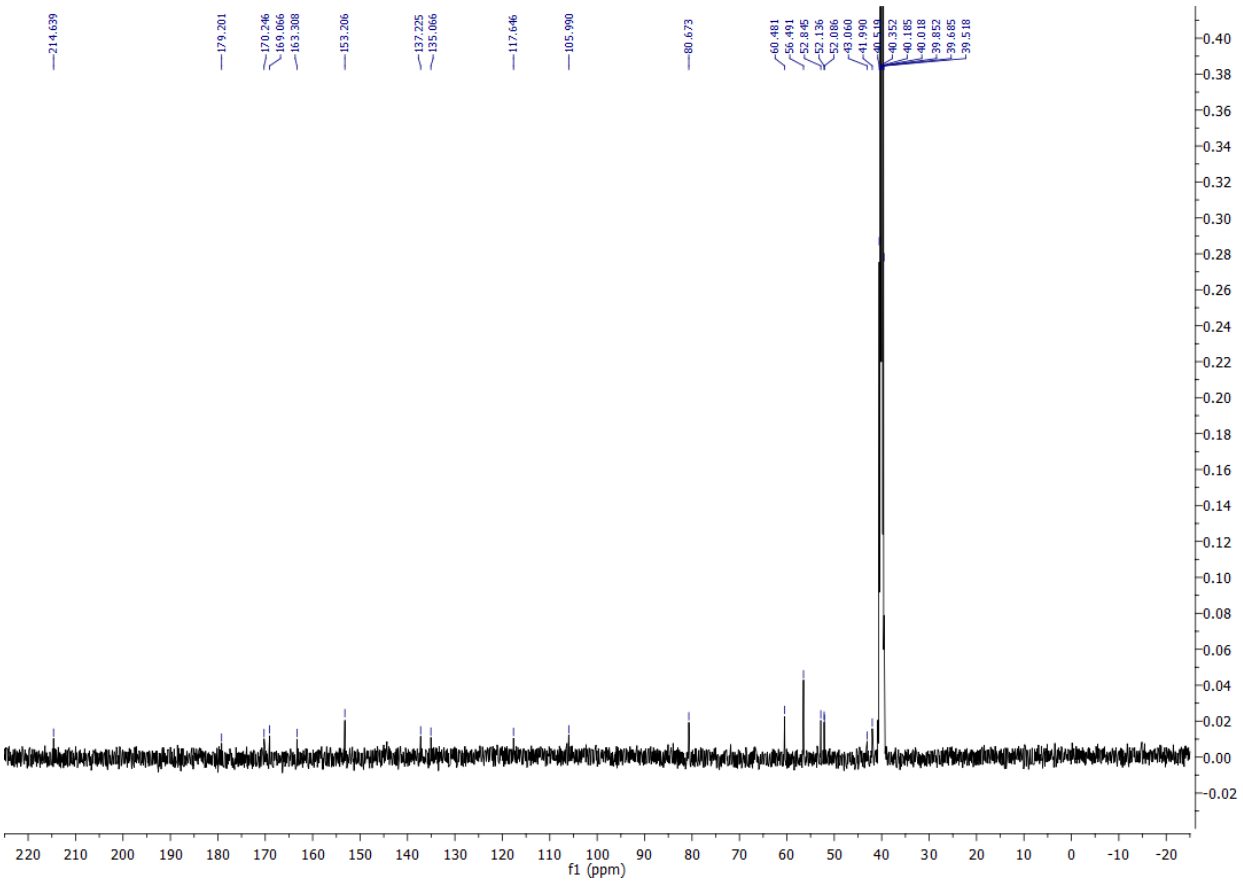


Figure S22. ^{13}C NMR spectrum of **4f**

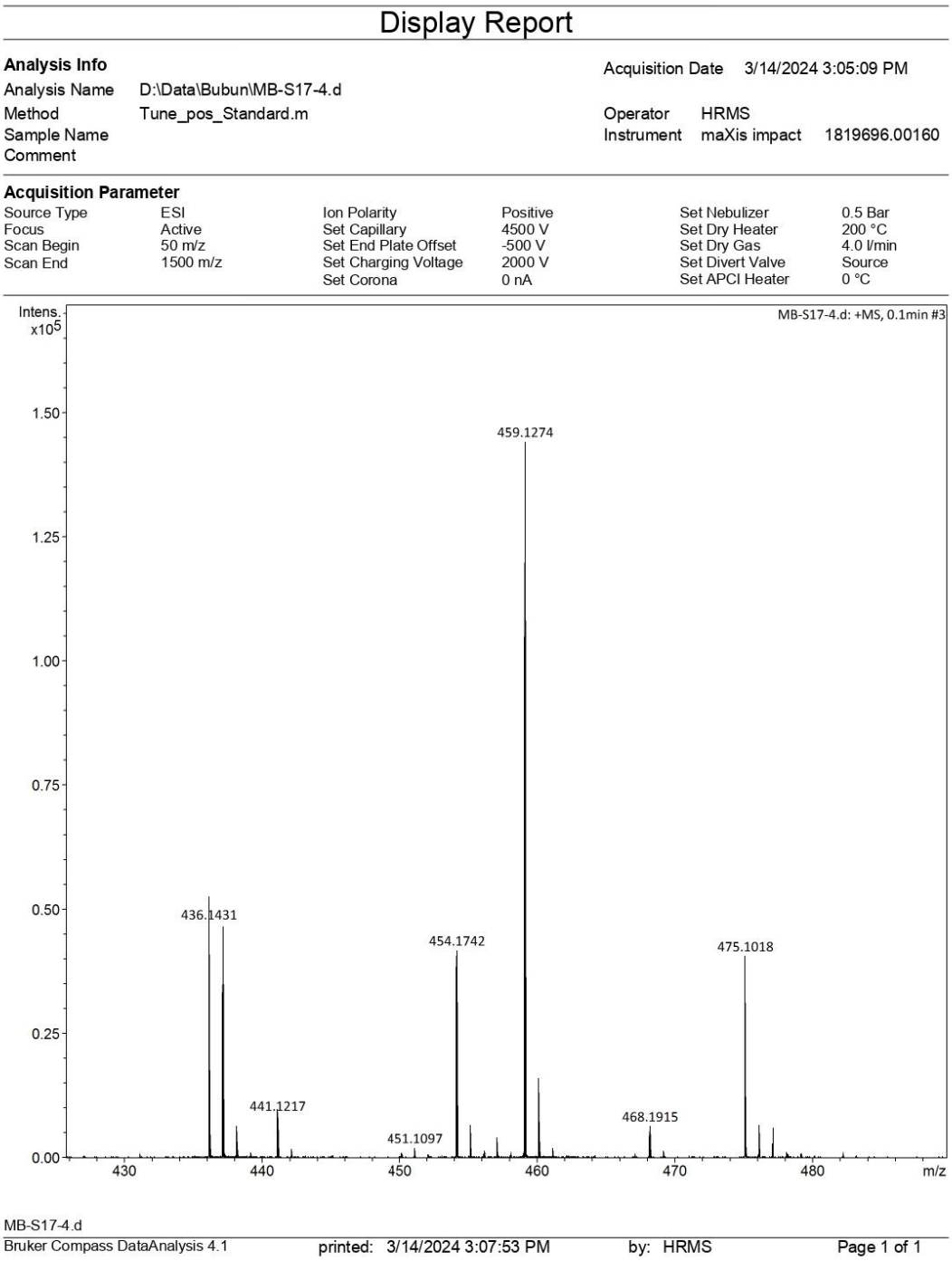
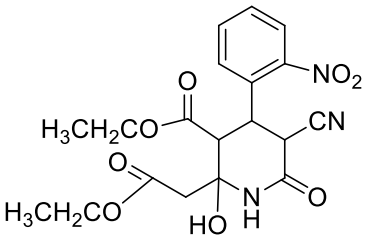


Figure S23. HRMS spectrum of **4f**



4g

Ethyl-5-cyano-2-(2-ethoxy-2-oxoethyl)-2-hydroxy-4-(2-nitrophenyl)-6-oxopiperidine-3-carboxylate (**4g**). Light yellow solid, yield 89%; mp 161-163°C; FTIR (cm^{-1}): 3742, 3307, 3153, 2361, 1738, 1356, 1053, 649, 537, 436; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.76 (s, 1H, -N*H*), 7.89 (d, *J* = 8.5 Hz, 1H, aromatic H), 7.76-7.71 (m, 1H, aromatic H), 7.70 (d, *J* = 8 Hz, 1H, aromatic H), 7.51 (td, *J* = 17 Hz, *J* = 8 Hz, *J* = 7.5 Hz, 1H, aromatic H), 6.71, (s, 1H, O*H*), 4.69-4.59 (m, 2H, -C*H*), 4.11-4.060 (m, 2H, -OCH_2), 3.80-3.77 (m, 1H, -C*H*), 3.71-3.67 (m, 2H, -OCH_2), 2.88 (d, *J* = 17 Hz, 1H, -CH_2), 2.76 (d, *J* = 17 Hz, 1H, -CH_2), 1.17 (t, *J* = 7 Hz, 3H, -CH_3), 0.78 (t, *J* = 7 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 169.74, 168.21 (2C), 162.86, 134.07, 133.99, 129.39, 128.96, 125.02, 116.64, 80.74, 61.17, 60.70, 53.41, 41.15, 40.56, 33.43, 14.58, 13.91; HRMS (ESI-TOF) m/z: For $C_{19}H_{21}N_3O_8$ Calcd. $[M+Na]^+$ 442.1329; Found $[M+Na]^+$ 442.1194

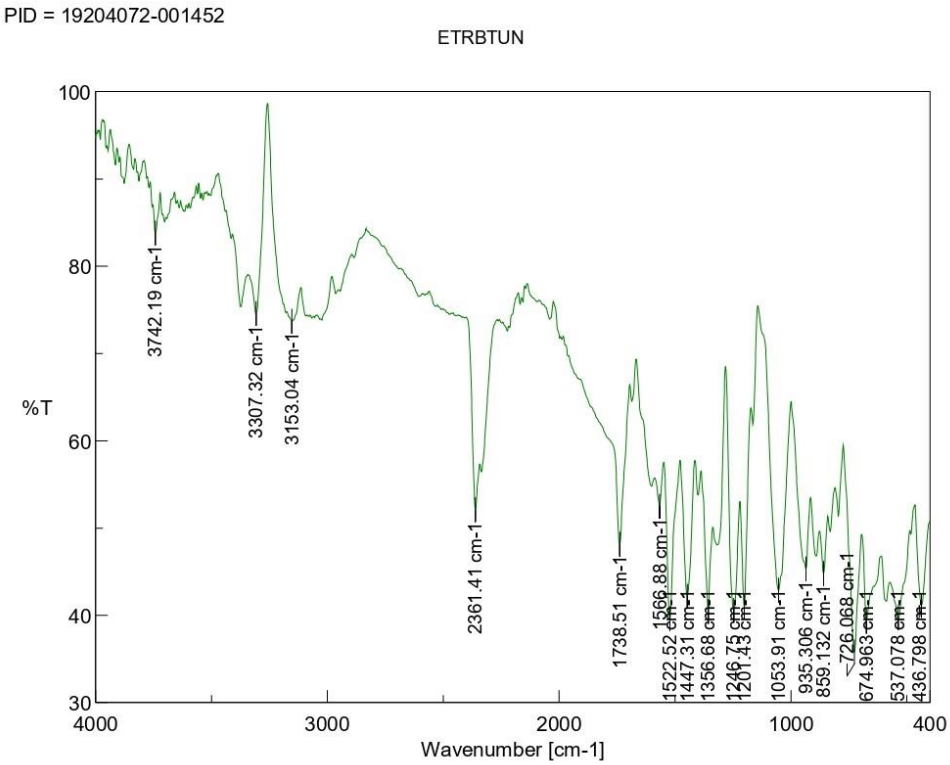


Figure S24. FTIR spectrum of **4g**

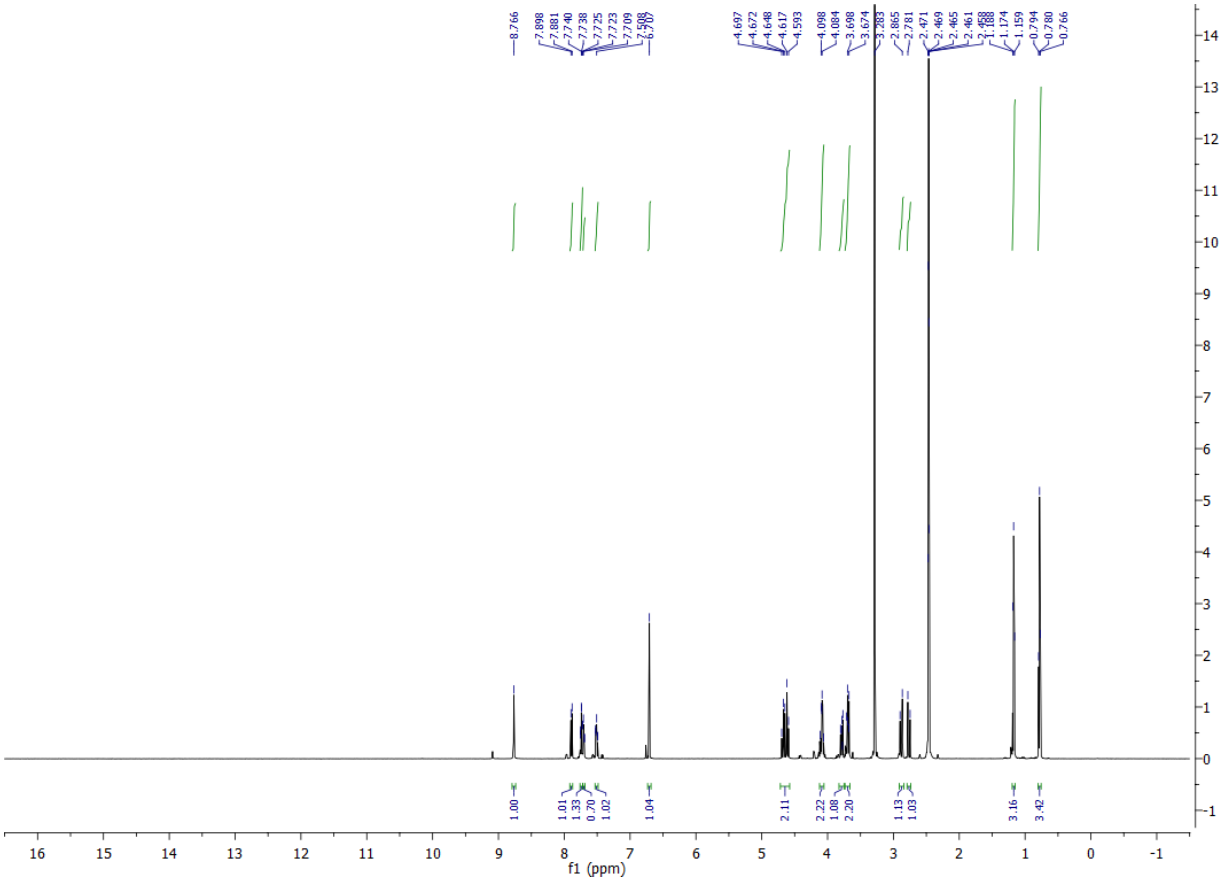


Figure S25. ^{1}H NMR spectrum of **4g**

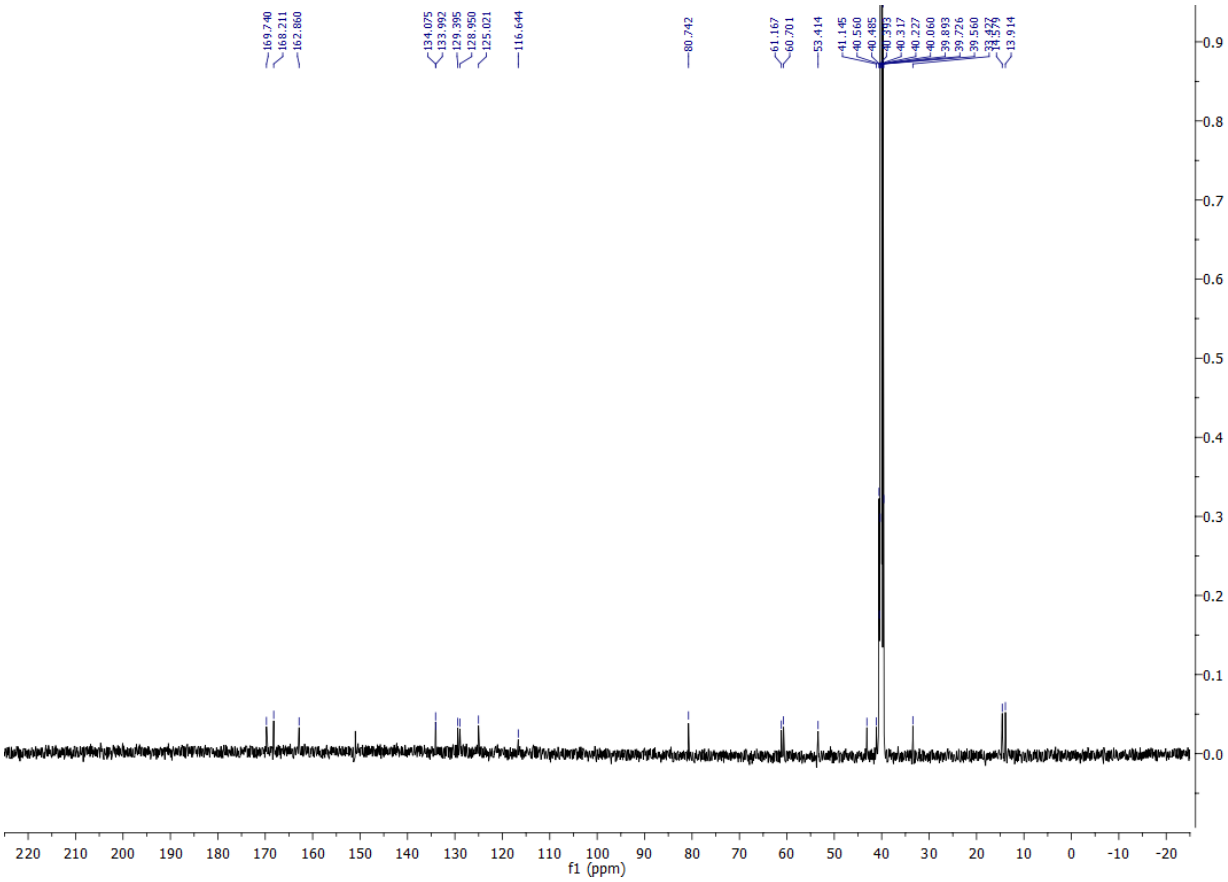


Figure S26. ^{13}C NMR spectrum of **4g**

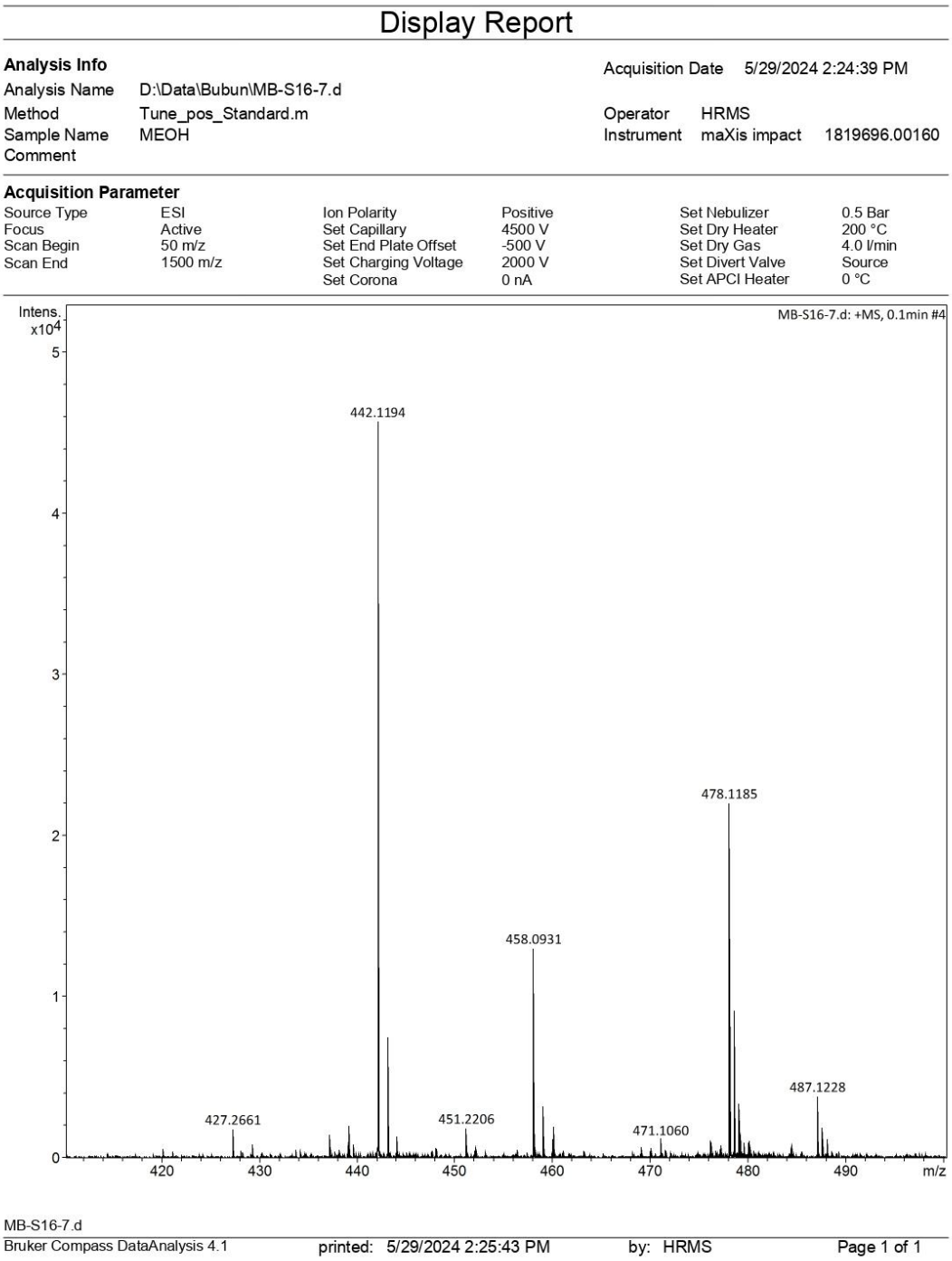
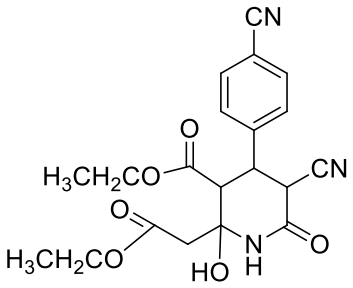


Figure S27.HRMS spectrum of **4g**



4h

Ethyl-5-cyano-4-(4-cyanophenyl)-2-(2-ethoxy-2-oxoethyl)-2-hydroxy-6-oxopiperidine-3-carboxylate (**4h**). Light yellow solid, yield 93%; mp 155°C; FTIR (cm^{-1}): 3741, 3304, 3192, 2361, 1733, 1318, 1060, 721, 526, 437; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.78 (s, 1H, -N*H*), 7.82 (d, *J* = 8 Hz, 2H, aromatic H), 7.51 (d, *J* = 8.5 Hz, 2H, aromatic H), 6.60 (s, 1H, O*H*), 4.57-4.33 (d, *J* = 12 Hz, 1H, -C*H*), 4.10-4.078 (m, 2H, -OCH_2), 4.00 (t, *J* = 12.5 Hz, 1H, -C*H*), 3.85-3.81 (m, 1H, -C*H*), 3.75-3.70 (m, 2H, -OCH_2), 2.88 (d, *J* = 17 Hz, 1H, -CH_2), 2.76 (d, *J* = 17 Hz, 1H, -CH_2), 1.77 (t, *J* = 7 Hz, 3H, -CH_3), 0.82 (t, *J* = 7 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 169.67, 168.19 (2C), 162.76, 145.20, 133.07 (2C), 129.89, 119.22, 119.072, 111.10, 107.99, 80.78, 60.94, 60.70, 51.95, 43.03, 41.58, 14.59, 14.03; HRMS (ESI-TOF) m/z: For $C_{20}H_{21}N_3O_8$ Calcd. $[M+K]^+$ 438.1430; Found $[M+K]^+$ 438.1109

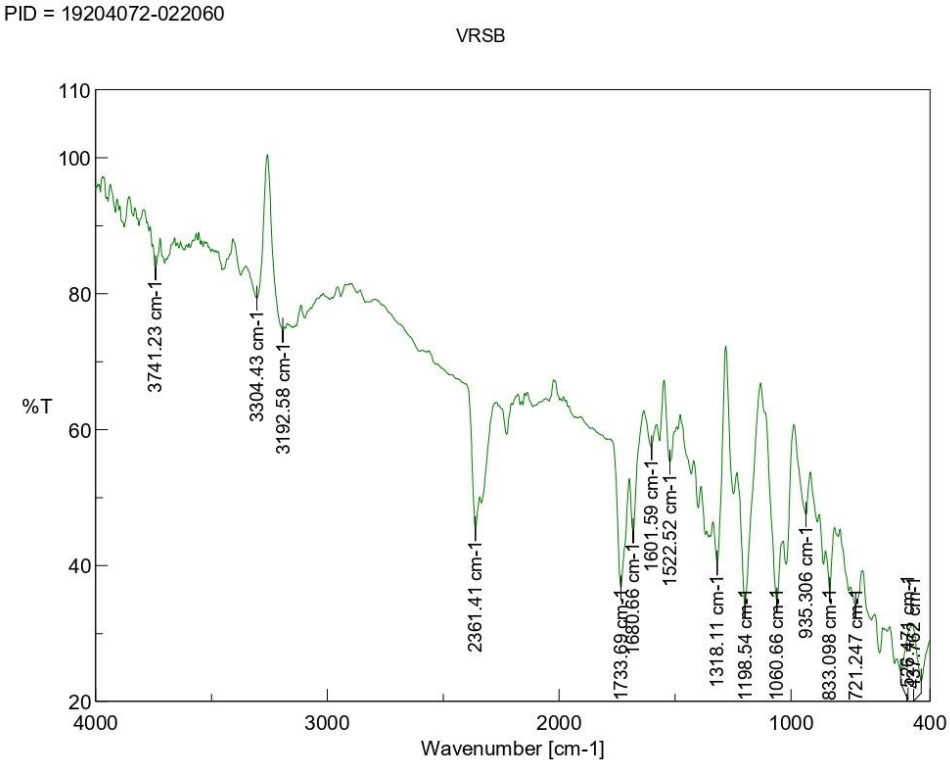


Figure S28. FTIR spectrum of **4h**

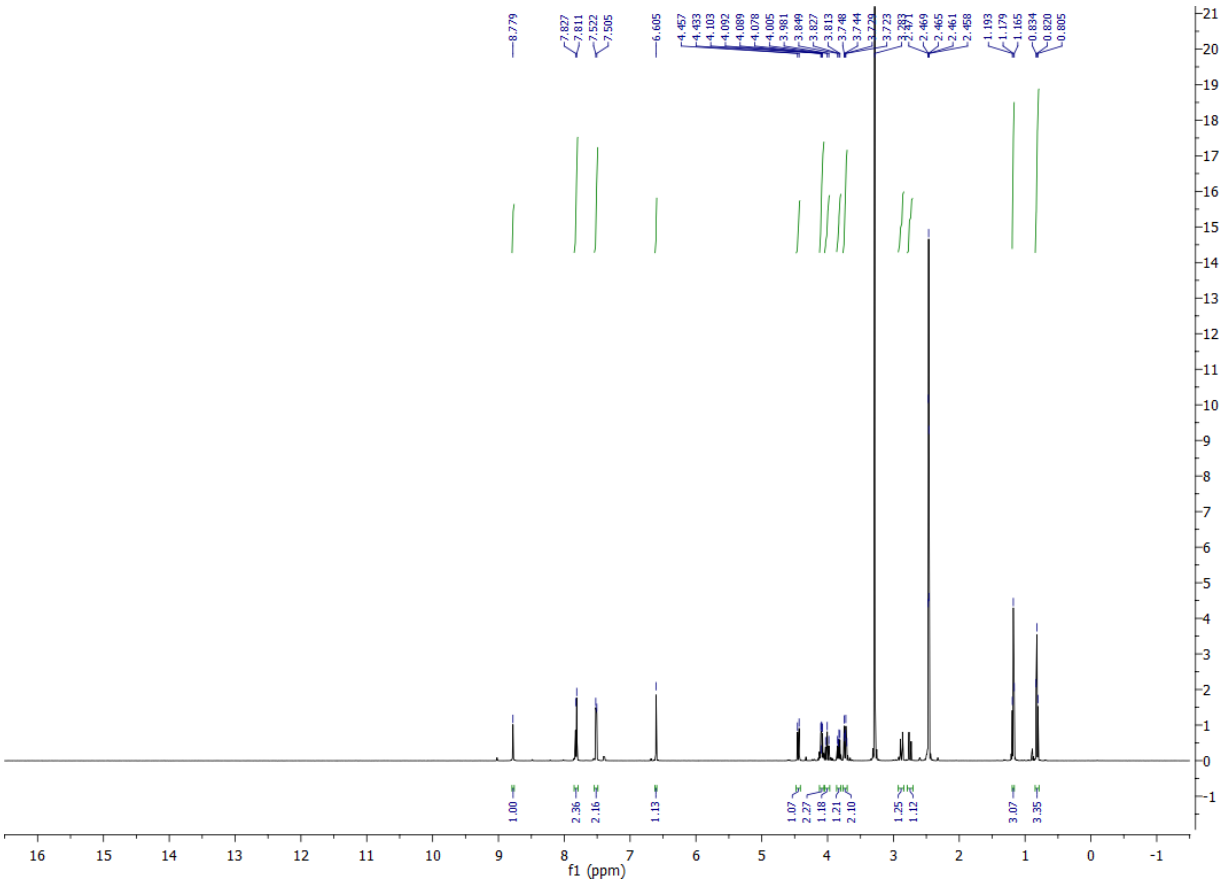


Figure S29. ^{1}H NMR spectrum of **4h**

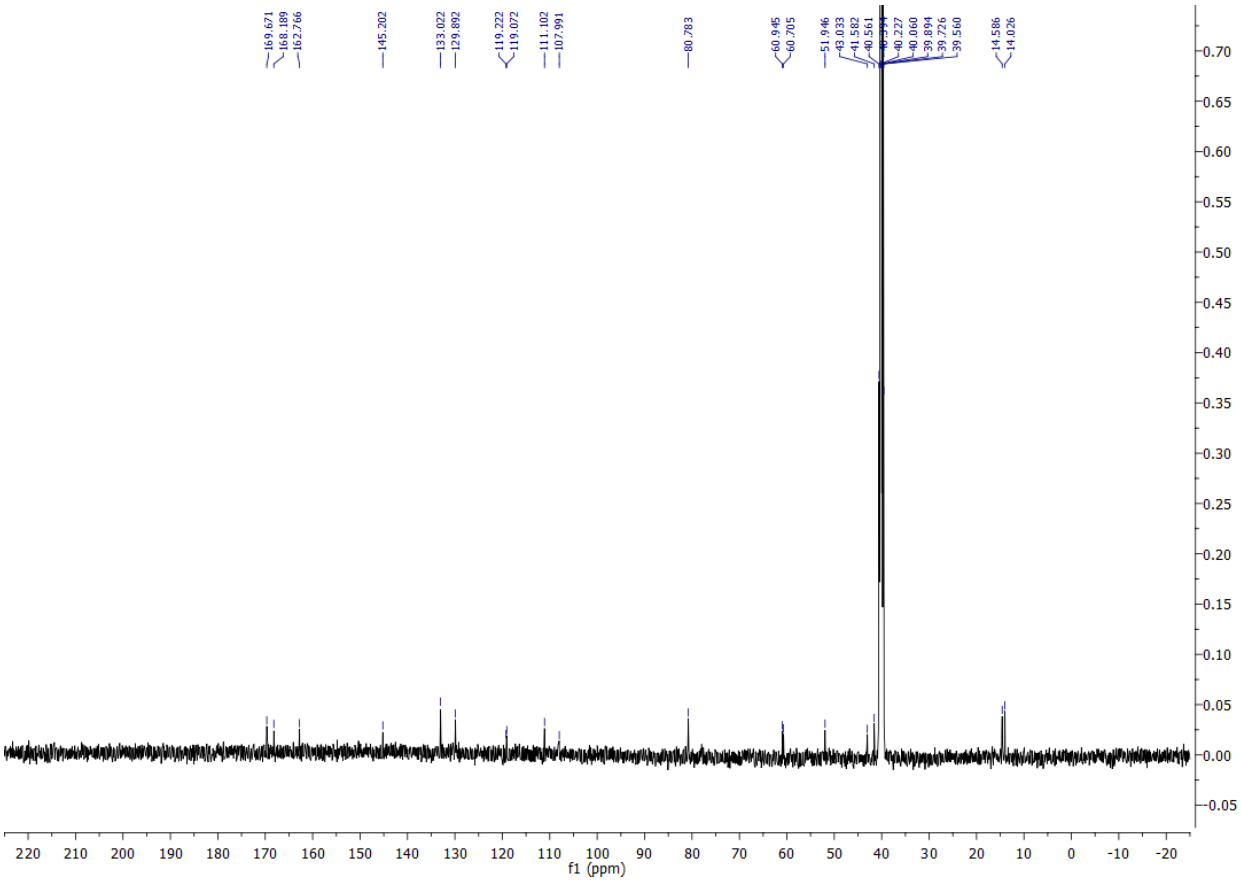


Figure S30. ^{13}C NMR spectrum of **4h**

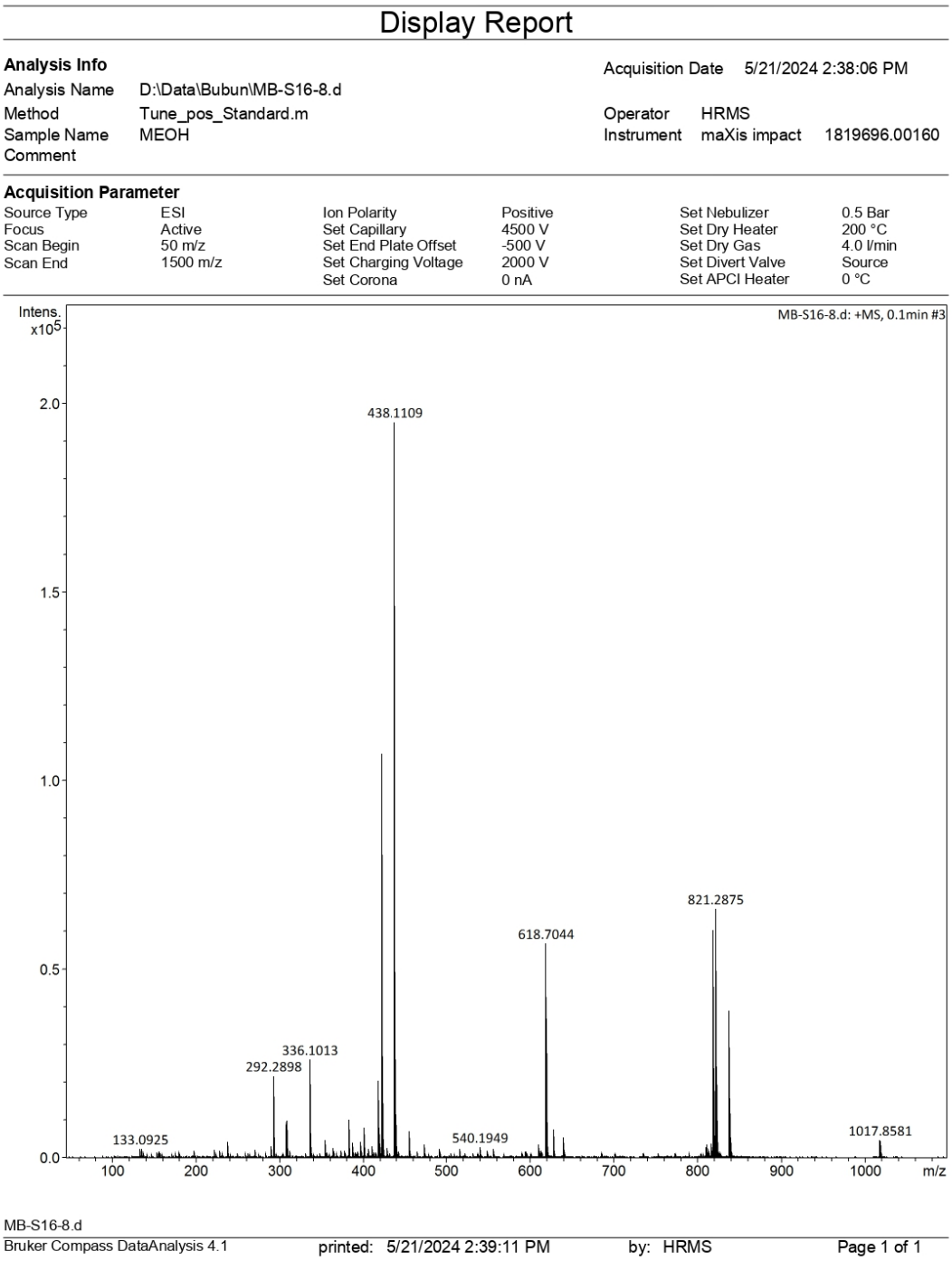
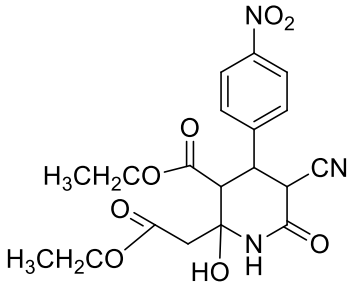


Figure S31.HRMS spectrum of **4h**



4i

Ethyl-5-cyano-2-(2-ethoxy-2-oxoethyl)-2-hydroxy-4-(4-nitrophenyl)-6-oxopiperidine-3-carboxylate (**4i**). Light yellow solid, yield 91%; mp 162°C; FTIR (cm^{-1}): 3742, 3307, 3153, 2361, 1738, 1356, 1053, 649, 537, 436; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.76 (s, 1H, -N*H*), 8.20 (d, *J* = 9 Hz, 2H, aromatic H), 7.61 (d, *J* = 8.5 Hz, 2H, aromatic H), 6.61 (s, 1H, O*H*), 4.45 (d, *J* = 12.5 Hz, 1H, -C*H*), 4.11-4.06 (m, 2H, -OCH_2, 1H, -CH), 3.85-3.71 (m, 2H, -OCH_2, 1H, -CH), 2.89 (d, *J* = 17 Hz, 1H, -CH_2), 2.78 (d, *J* = 17 Hz, 1H, -CH_2), 1.87 (t, *J* = 7 Hz, 3H, -CH_3), 0.84 (t, *J* = 7 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 169.70, 168.15, 162.65, 147.58, 147.23, 130.22 (2C), 124.17 (2C), 117.14, 80.84, 61.01, 60.72, 52.04, 43.10, 41.61 (2C), 14.58, 14.04; HRMS (ESI-TOF) m/z: For $C_{19}H_{21}N_3O_8$ Calcd. $[M+Na]^+$ 442.1329; Found $[M+Na]^+$ 442.1194

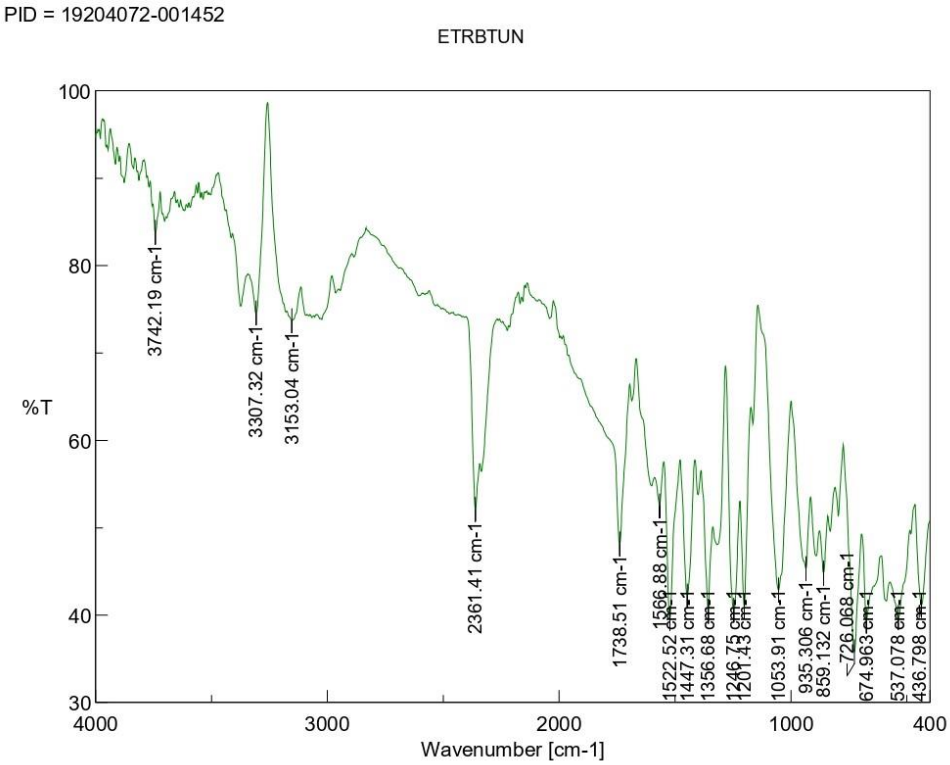


Figure S32.FTIR spectrum of **4i**

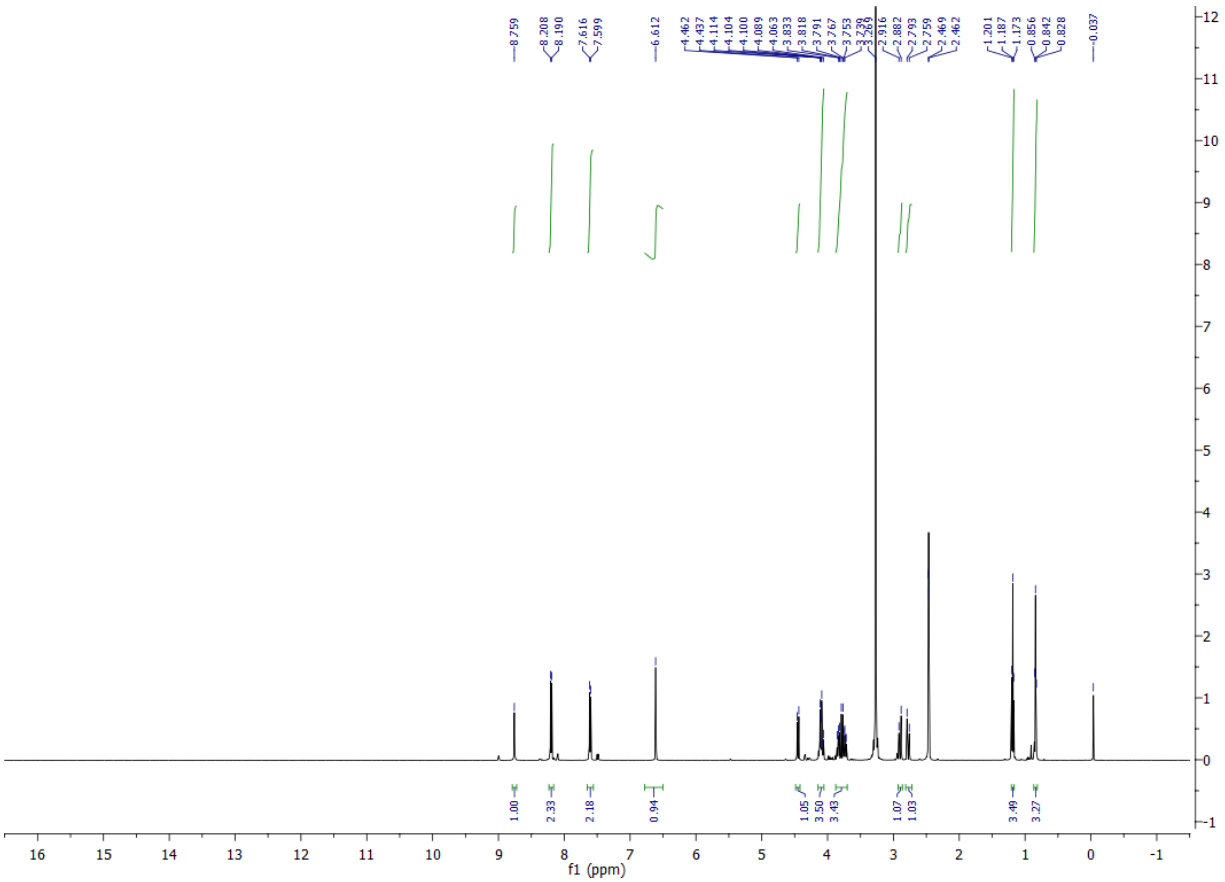


Figure S33. ^{1}H NMR spectrum of **4i**

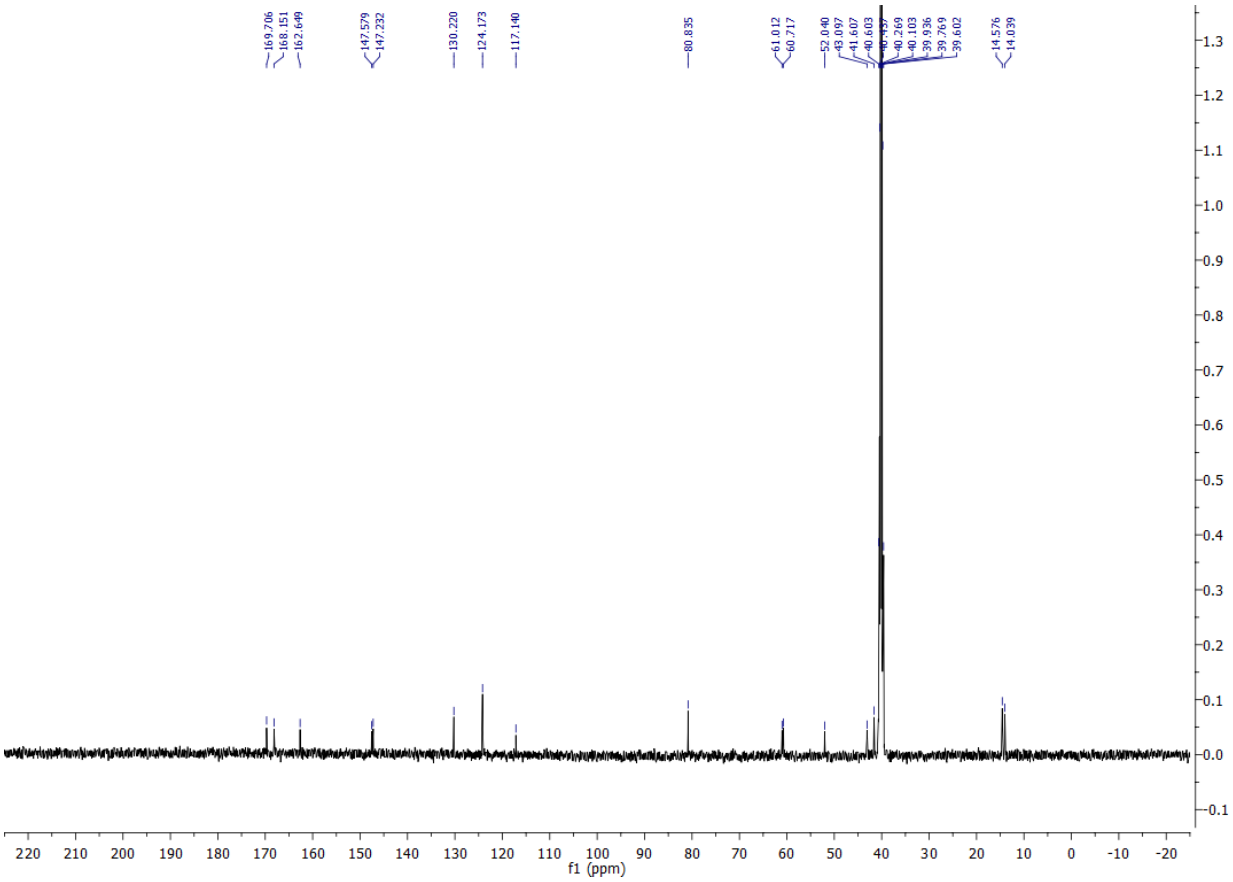


Figure S34. ^{13}C NMR spectrum of **4i**

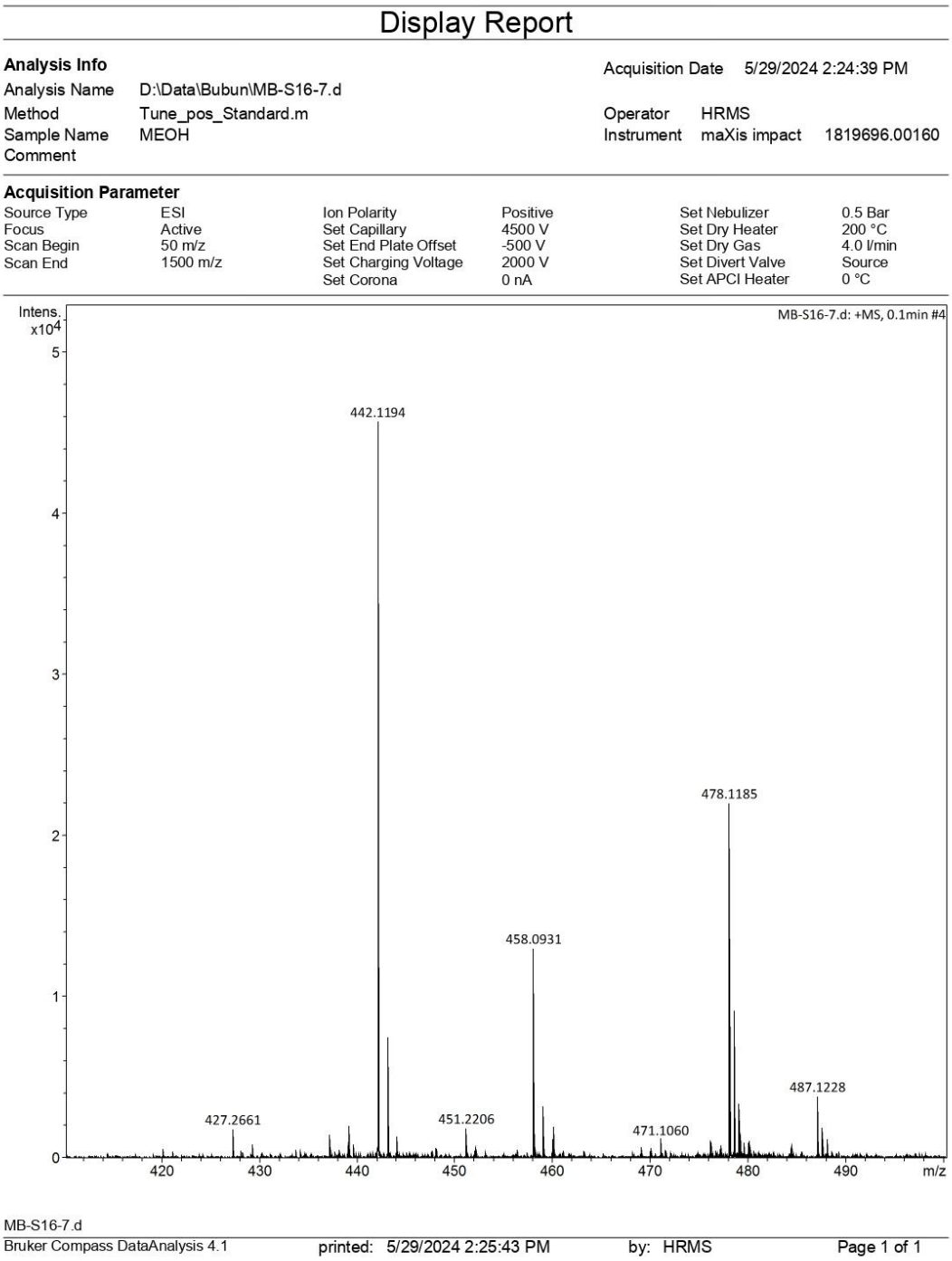
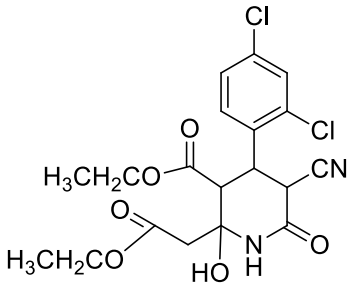


Figure S35.HRMS spectrum of **4i**



4j

Ethyl-5-cyano-4-(2,4-dichlorophenyl)-2-(2-ethoxy-2-oxoethyl)-2-hydroxy-6-oxopiperidine-3-carboxylate (**4j**). White solid, yield 94%; mp 174°C; FTIR (cm^{-1}): 3741, 3377, 3297, 2360, 1717, 1519, 1355, 1054, 625, 518, 436; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.70 (s, 1H, -N*H*), 7.60 (d, *J* = 2 Hz, 1H, aromatic H), 7.48 (d, *J* = 8.5 Hz, 1H, aromatic H), 7.43 (dd, *J* = 2 Hz, 1H, aromatic H) 6.66 (s, 1H, O*H*), 4.60 (d, *J* = 12 Hz, 1H, -C*H*), 4.31 (d, *J* = 12 Hz, 1H, -C*H*), 4.12-4.08 (m, 2H, -OCH_2), 3.87-3.83 (m, 1H, -C*H*), 3.76-3.71 (m, 2H, -OCH_2), 2.90 (d, *J* = 16.5 Hz, 1H, -CH_2), 2.78 (d, *J* = 17 Hz, 1H, -CH_2), 1.18 (t, *J* = 7 Hz, 3H, -CH_3), 0.84 (t, *J* = 7 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 169.77, 168.16, 162.74, 136.91, 136.03, 133.22, 129.72, 128.42, 117.47, 116.75, 80.83, 60.96, 60.71, 52.54, 43.26, 41.59 (2C), 14.57, 13.96; HRMS (ESI-TOF) m/z: For $C_{19}H_{20}Cl_2N_2O_6$ Calcd. $[M+Na]^+$ 465.0596; Found $[M+Na]^+$ 465.0704

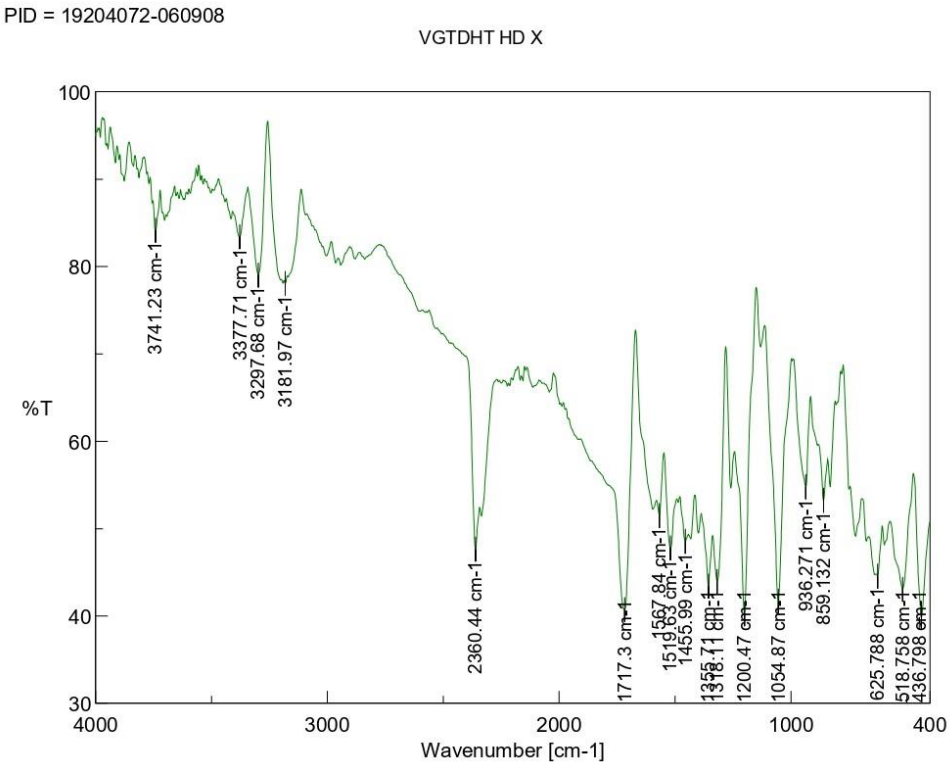


Figure S36.FTIR spectrum of **4j**

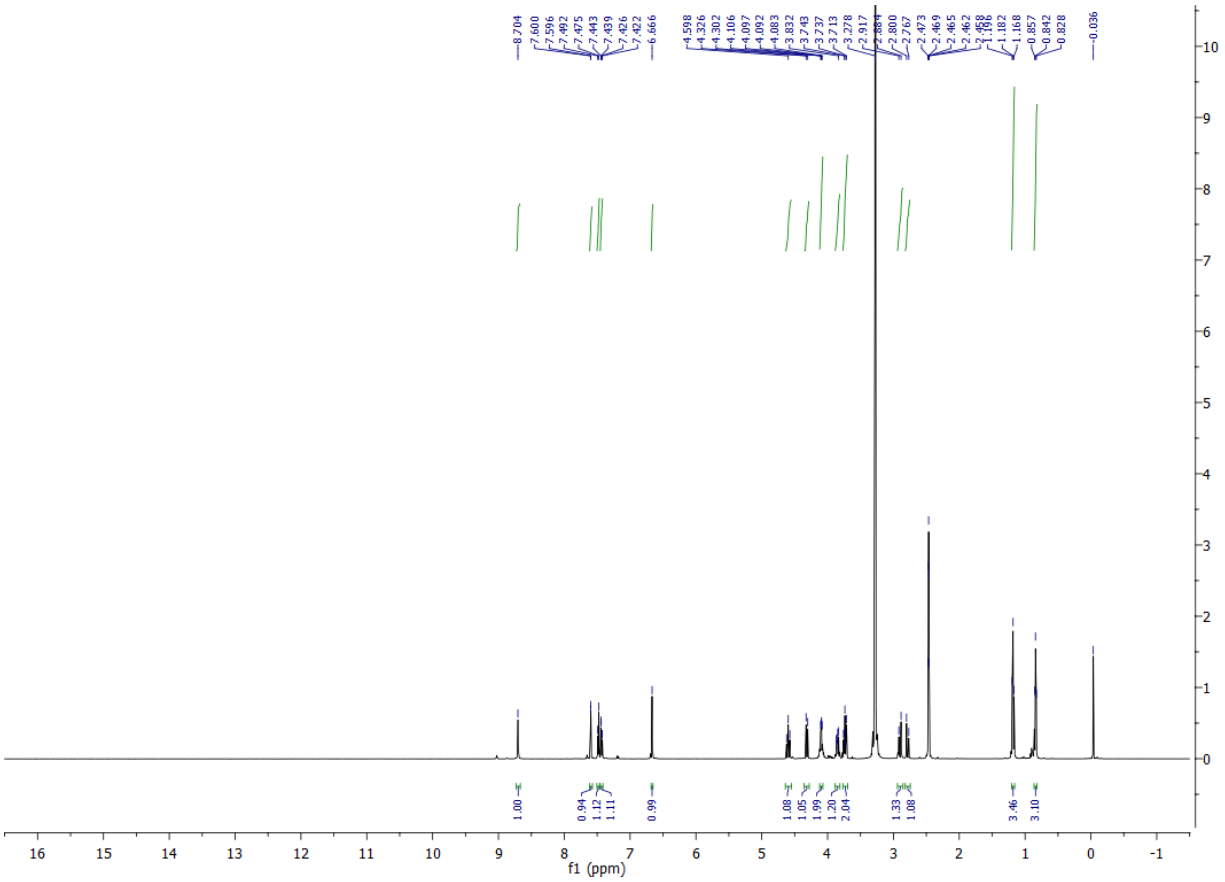


Figure S37. ^{1}H NMR spectrum of **4j**

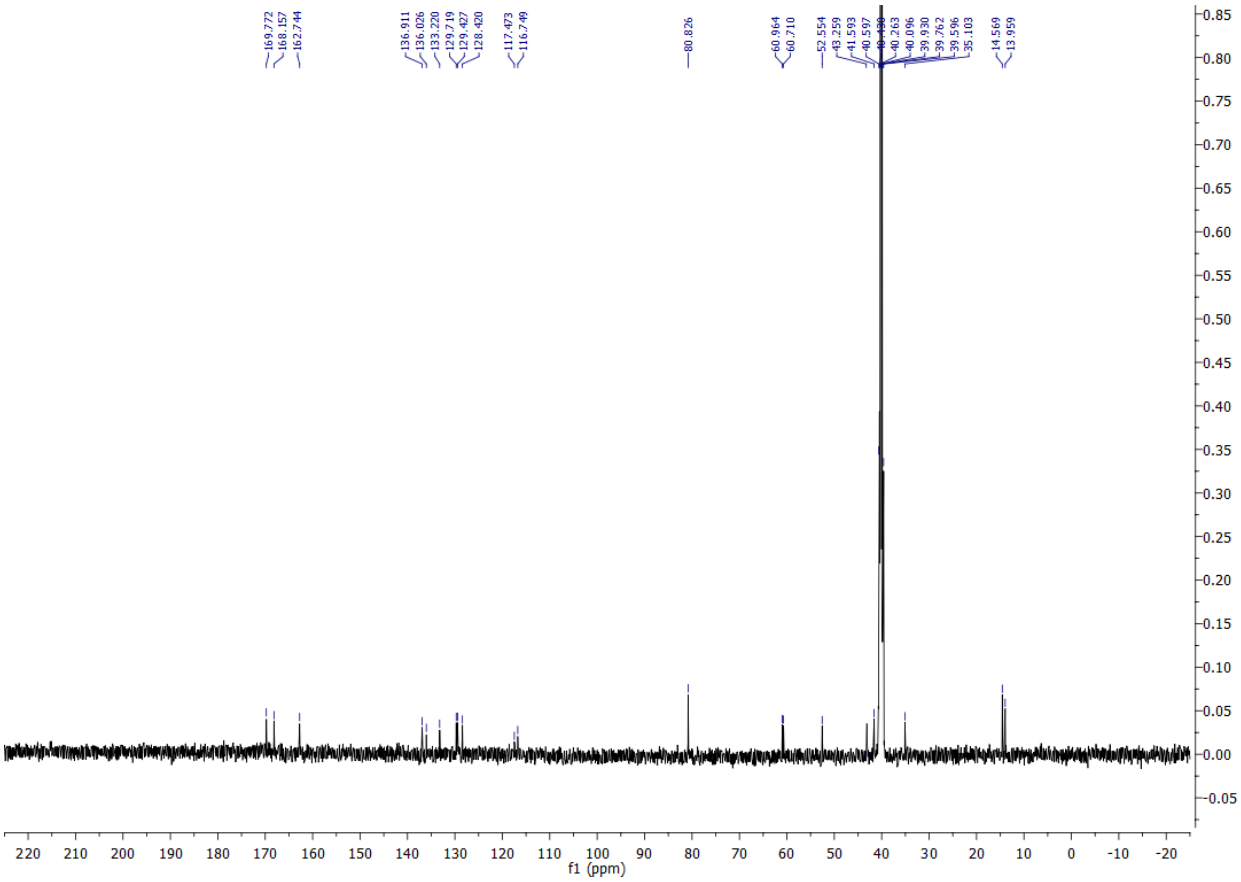


Figure S38. ^{13}C NMR spectrum of **4j**

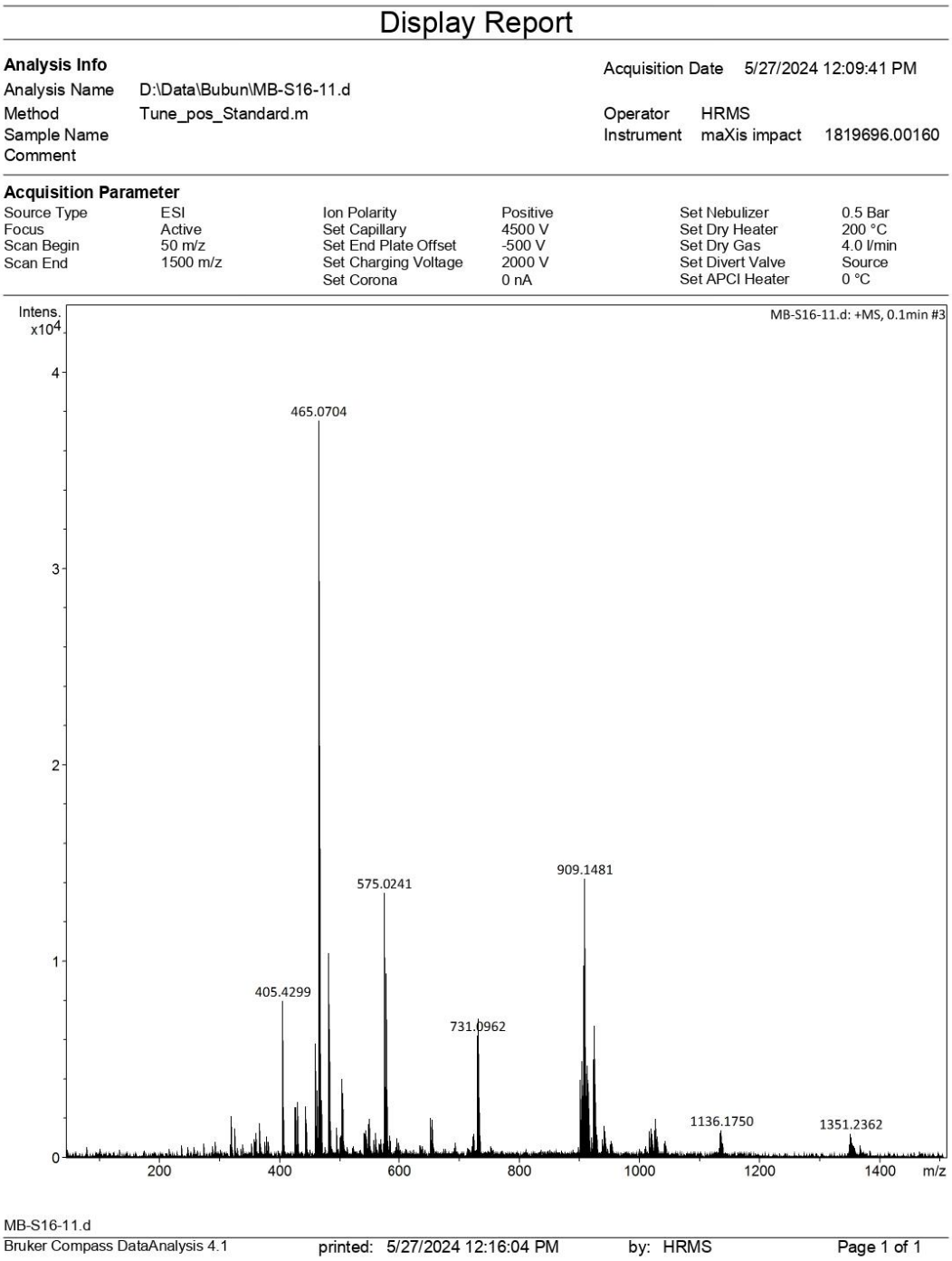
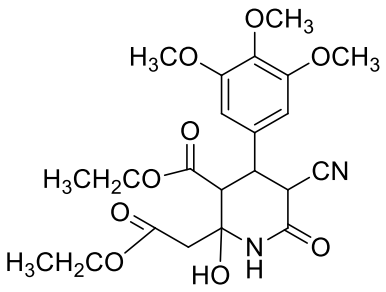


Figure S39.HRMS spectrum of **4j**



4k

Ethyl-5-cyano-2-(2-ethoxy-2-oxoethyl)-2-hydroxy-6-oxo-4-(3,4,5-trimethoxyphenyl)piperidine-3-carboxylate (**4k**). White solid, yield 98%; mp 197°C; FTIR (cm^{-1}): 3741, 3305, 3155, 2361, 1725, 1517, 1317, 1054, 627, 519, 435; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H/ppm: 8.67 (s, 1H, -N*H*), 6.59 (s, 2H, aromatic H), 6.49 (s, 1H, O*H*), 4.39 (d, *J* = 12.5 Hz, 1H, -C*H*), 4.11 (m, 2H, -OCH_2), 3.88-3.79 (m, 2H, -OCH_2, 1H, -CH), 3.72 (s, 6H, 2 x -OCH_3), 3.6 (t, 3H, -OCH_3, 1H, -CH), 2.85 (d, *J* = 16.5 Hz, 1H, -CH_2), 2.70 (d, *J* = 17 Hz, 1H, -CH_2), 1.19-1.165 (m, 3H, -CH_3), 0.83 (t, *J* = 7 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ_C/ppm: 169.71, 168.55, 164.54, 163.30, 153.18, 137.30, 135.05, 117.66, 106.05, 80.68, 78.71, 60.74, 60.64, 60.49, 56.47, 52.64 (2C), 43.24, 42.12 (2C), 14.54, 14.12; HRMS (ESI-TOF) m/z: For $C_{22}H_{28}N_2O_9$ Calcd. $[M+Na]^+$ 487.1693; Found $[M+Na]^+$ 487.1756

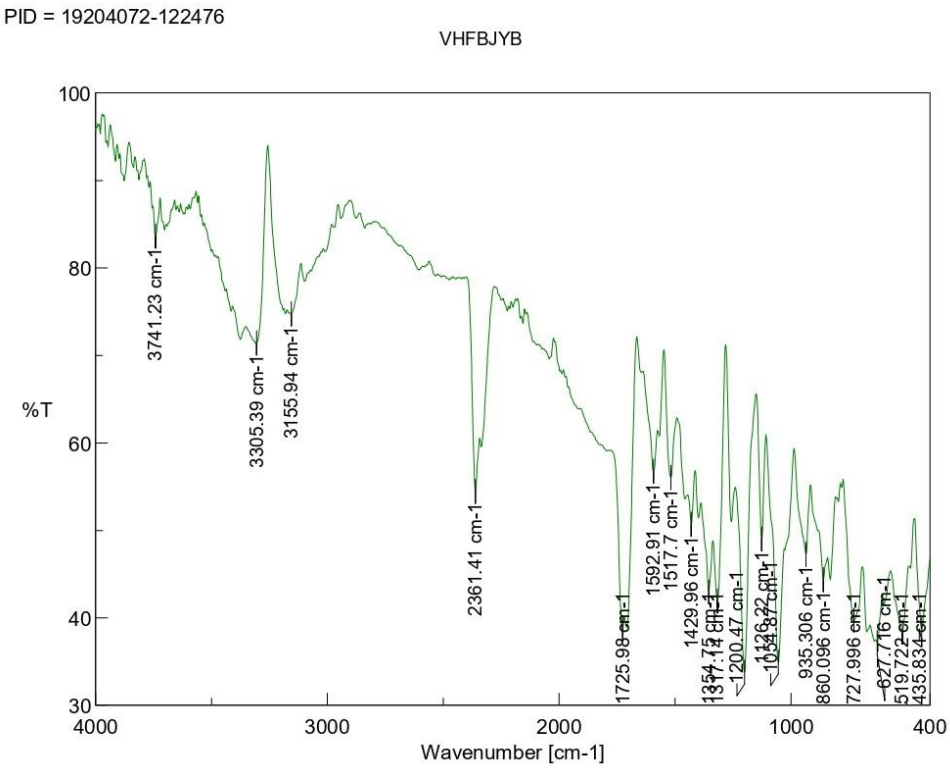


Figure S40. FTIR spectrum of **4k**

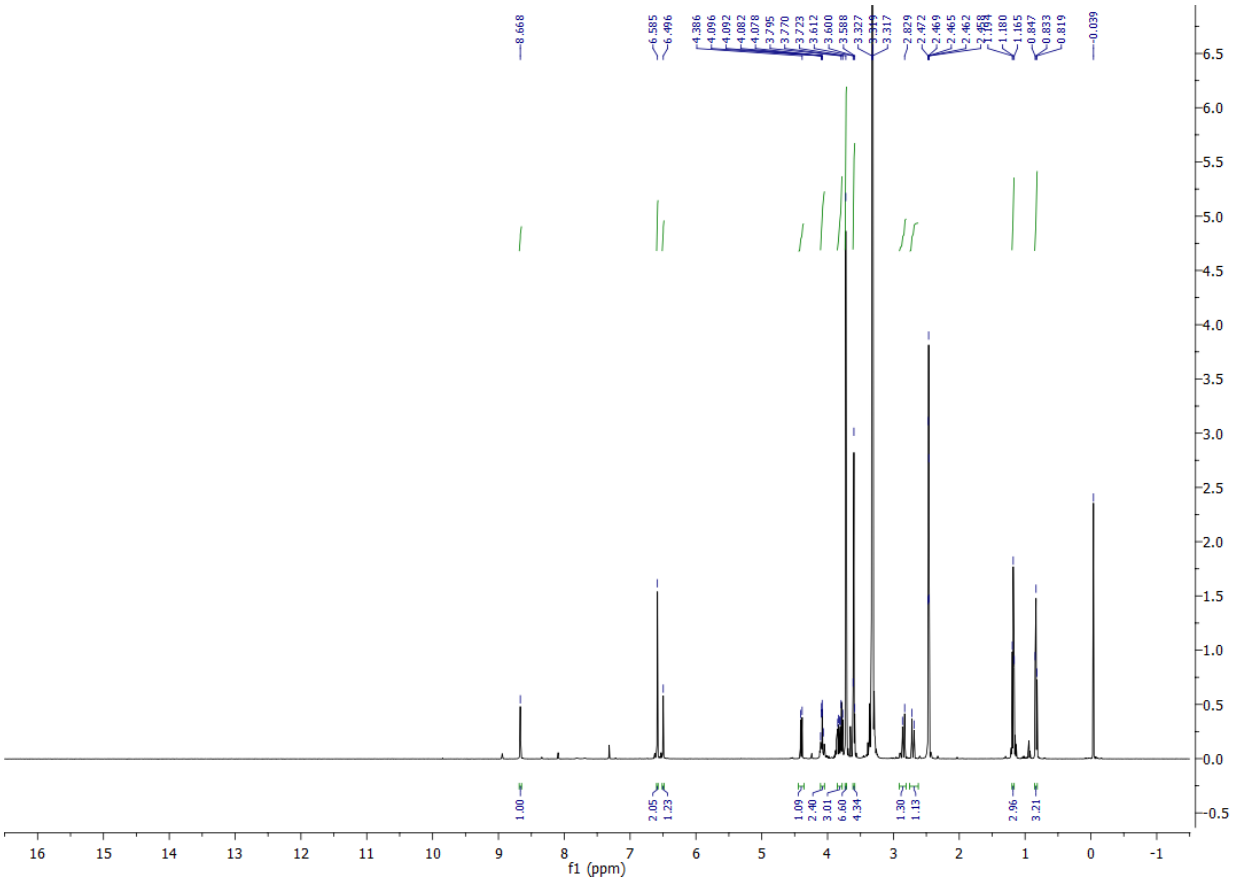


Figure S41. ^{1}H NMR spectrum of **4k**

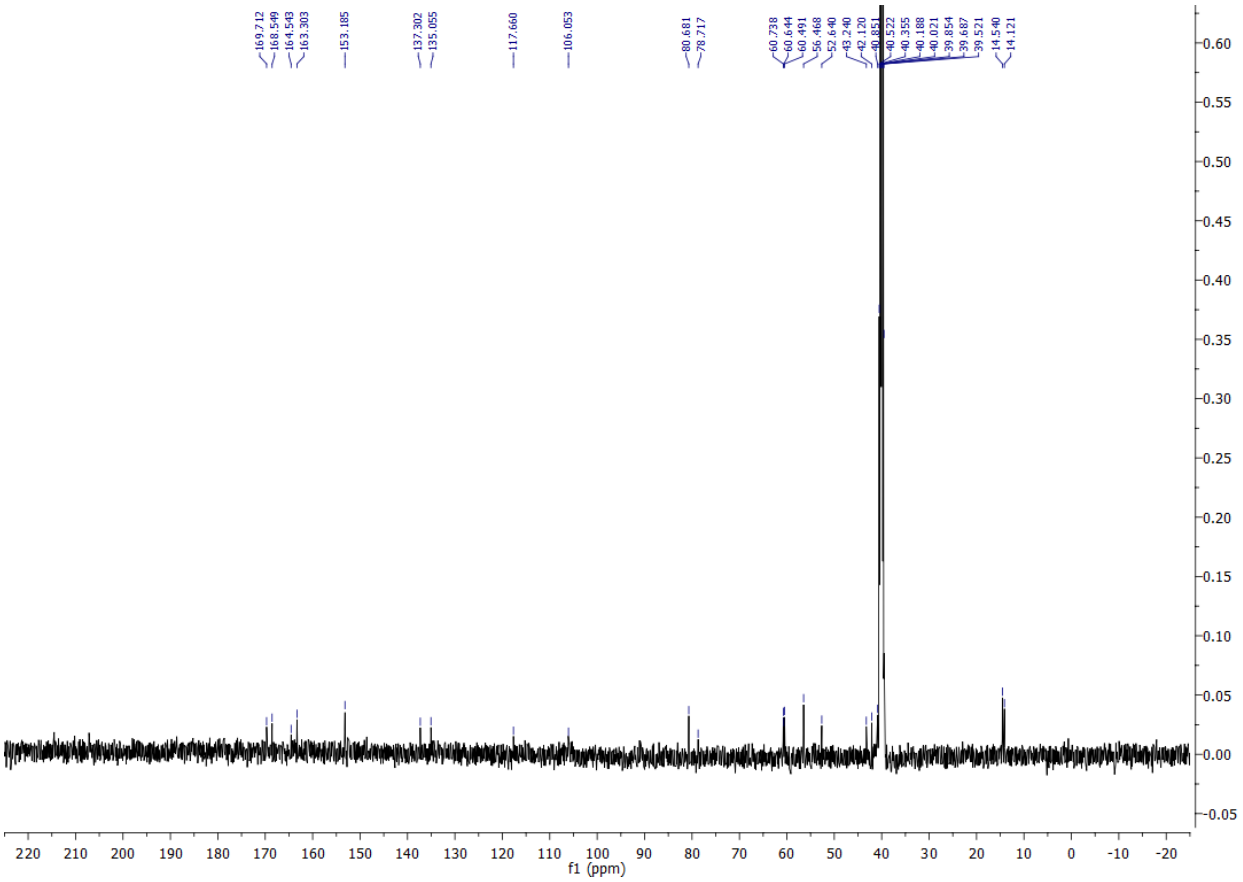


Figure S42. ^{13}C NMR spectrum of **4k**

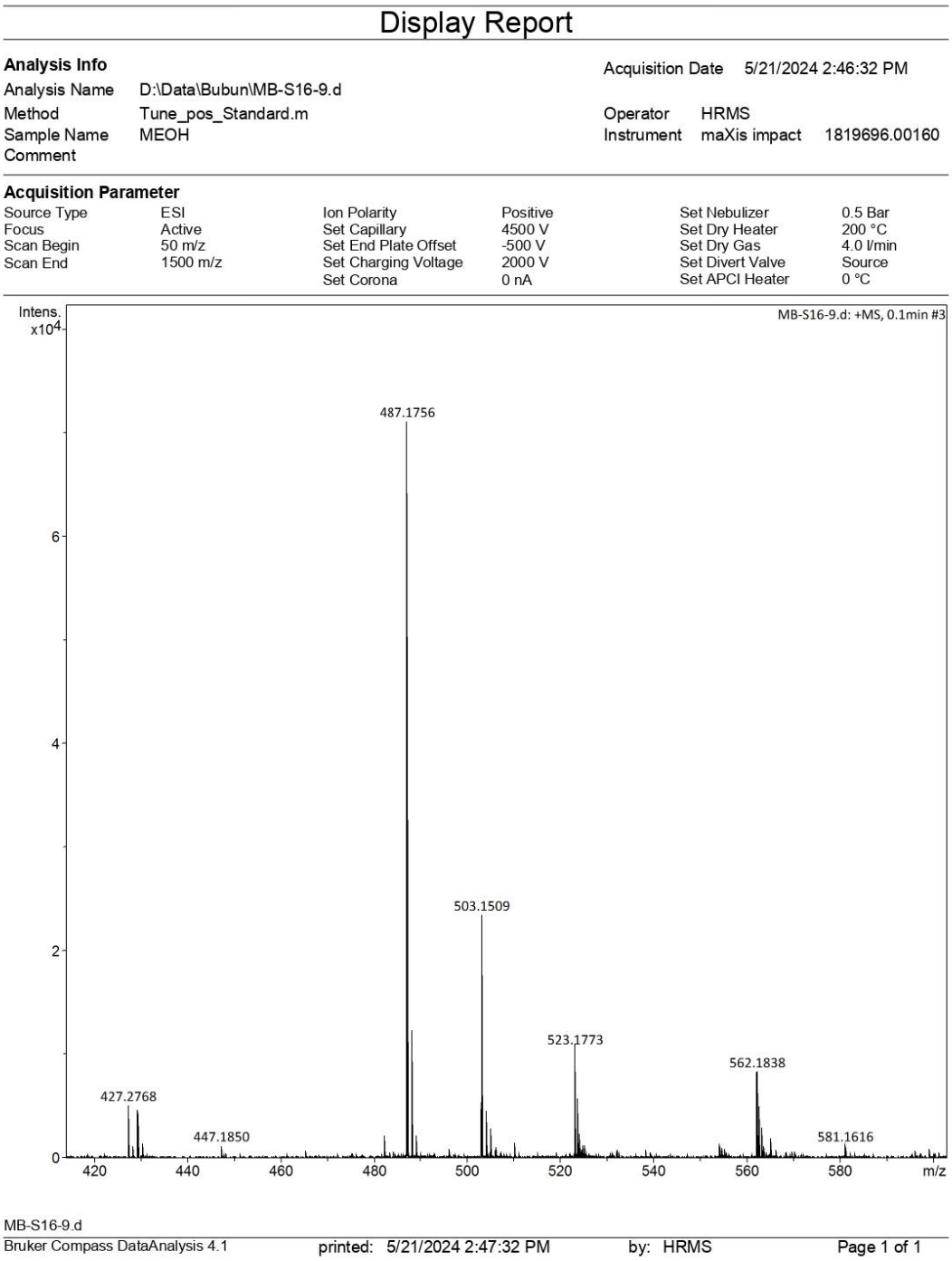


Figure S43. HRMS spectrum of **4k**

