Substituted anilides from chitin-based 3-acetamido-furfural

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Material and methods

S1. Reagents

(R)-*N*-(5-(1,2-dihydroxyethyl)furan-3-yl)acetamide (**Di-HAF**) and *N*-(5-acetylfuran-3-yl)acetamide (**3A5AF**) were prepared according to reference [1] and pyrrolidin-1-amine according to [2]. All other reagents were acquired from commercial sources and used without further purification. Specifically, 1,1-dimethylhydrazine was purchased from SigmaAldrich. Sodium periodate (99.8+%, ACS reagent), 3-chloroperoxybenzoic acid (70-75%), ethyl acrylate (99.5%, stabilized), *tert*-butyl acrylate (99%, stabilized), acrylonitrile (99+%), dimethyl maleate (96%), dimethyl fumarate (99%), diethyl vinylphosphonate (97%) and methyl vinyl ketone (95%, stabilized) from ThermoFisher Scientific Chemicals. Fumaronitrile and (methylsulfonyl)ethene from Combi-Blocks, Inc., 1-methyl-1H-pyrrole-2,5-dione and 1-benzyl-1H-pyrrole-2,5-dione from Ambeed, Inc. and 1-phenyl-1H-pyrrole-2,5-dione from TCI Europe. Thin-layer chromatography (TLC) was carried out on Merck silica gel 60 F254 aluminum plates. Visualization of compounds by TLC was done by potassium permanganate stain. Automated flash column chromatography cartridges were acquired from Screening Devices (UltraPure Irregular Silica Gel, 40 – 63 um, 60A, 5/1P). As internal standard for quantitative analysis was used ethylene carbonate, standard for quantitative NMR, TraceCERT® (SigmaAldrich).

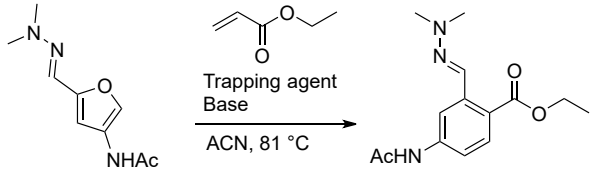
[1] *Org. Biomol. Chem.*, 2021, **19**, 10105–10111.
[2] *Syn. Com.,* 2015, **45**, 1367-1373.

S2. Equipment

^{1}H-NMR and ^{13}C-NMR analyses were performed on a Bruker Avance NEO (400 MHz) at 25 °C. High-resolution mass spectrometry (HRMS) was performed on a Thermo Scientific LTQ Orbitrap XL (FTMS). DSC was recorded on a TA instruments DSC Q20 and Infrared spectra (IR) spectra were recorded on a PerkinElmer Spectrum Two FT-IR Spectrometer. Automated flash column chromatography was carried out on a Buchi Sepacore® Flash System X10 (Pumps: 601, control unit: 620, detector: 640, fraction collector: 660). Ozonolysis was performed using an ozone generator from Ozone Tech Systems (Model: OT-20, Typ. no: 32000-03).

Supplemental Research data

S3. **Reaction optimization of 1 with ethyl acrylate to 7**



1 **7**

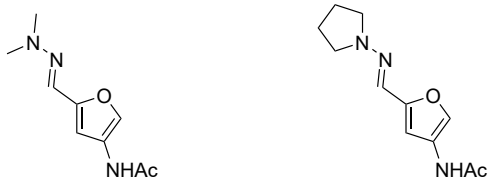
Scheme 1*. Reaction optimization of* ***1*** *with ethyl acrylate to* ***7****.*

Table 1. *Reaction optimization of* ***1*** *and ethyl acrylate. Parameters studied: trapping agent (type/eq.), type of base, concentration, and equivalents of dienophile.*

#	DIENOPHILE	TRAPPING AGENT	BASE	CONCENTRATION	YIELD*
1	Ethyl acrylate (2 eq)	Ac_2O (1 eq)	triethylamine (2.5 eq)	0.5M	55%
2	Ethyl acrylate (2 eq)	Ac_2O (2 eq)	triethylamine (2.5 eq)	0.5M	49%
3	Ethyl acrylate (2 eq)	Ac_2O (4 eq)	triethylamine (2.5 eq)	0.5M	48%
4	Ethyl acrylate (2 eq)	MsCl (2 eq)	triethylamine (2.5 eq)	0.5M	-
5	Ethyl acrylate (2 eq)	Tf_2O (4 eq)	triethylamine (2.5 eq)	0.5M	-
6	Ethyl acrylate (2 eq)	Ac_2O (2 eq)	DBU (2.5 eq)	0.5M	-
7	Ethyl acrylate (2 eq)	Ac_2O (2 eq)	DABCO (2.5 eq)	0.5M	43%
8	**Ethyl acrylate (2 eq)**	**Ac_2O (1 eq)**	**triethylamine (2.5 eq)**	**1.0M**	**73%**
9	Ethyl acrylate (4 eq)	Ac_2O (1 eq)	triethylamine (2.5 eq)	1.0M	72%
10	Ethyl acrylate (6 eq)	Ac_2O (1 eq)	triethylamine (2.5 eq)	1.0M	75%

**yield determined by qNMR, IS: ethylene carbonate (4.48 ppm) vs. aromatic protons (7.98 ppm, 7.79 ppm and 7.69 ppm).*

S4. **Stability monitoring 1 and 12 under procedure A and B**



1 **12**

Scheme 2*. Hydrazone* ***1*** *and* ***12.***

Table 2. *The stability of hydrazone* ***1*** *and* ***12*** *under the reaction conditions was monitored by quantitative ^{1}H-NMR in the absence of a dienophile. At room temperature a minimal decrease in substrate concentration was observed. At 81 °C both* ***1*** *and* ***12*** *show a similar degree of decomposition*.

#	SUBSTRATE	CONDITIONS	TEMP.	T = 0	T = 2	T = 18
1	1	Protocol **A**	RT	97%	-	95%
2	1	protocol **B**	81 °C	97%	82%	41%
3	12	protocol **B**	81°C	100%	87%	47%

S5. ^{1}H-NMR comparison of 1 and 12

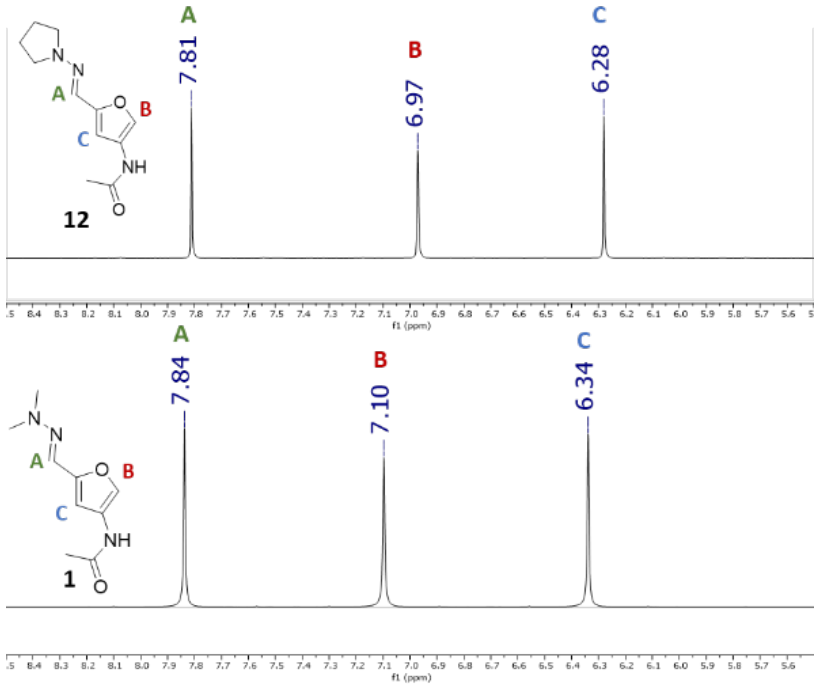
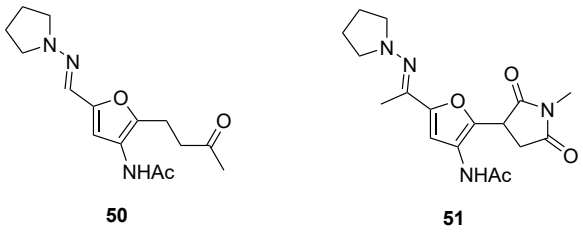


Figure 1. *^{1}H-NMR comparison **1** and **12**. An upfield shift is observed of protons **B** and **C**, indicating a relative elevated HOMO for **12**.*

S6. **1,4-addition side products**



Scheme 3*. Side products formed via 1,4-addition pathway.* ***50****: Major product of the reaction between **12** and methyl vinyl ketone.* ***51****: Major product of the reaction between **28** and N-methylmaleimide.* ***Note****: In both cases complex product mixtures were obtained consisting of cycloaddition product, 1,4-addition product, a combination of both and other unidentified products. Depicted products were identified by LCMS and ^{1}H-NMR analysis of the reaction mixtures and were not isolated.*

Experimental procedures

S7. Synthesis of 3A5F

***N*-(5-formylfuran-3-yl)acetamide (3A5F).** Sodium periodate (14.4 g, 1.25 eq., 67.5 mmol) was added to a solution of (R)-*N*-(5-(1,2-dihydroxyethyl)furan-3-yl)acetamide (**Di-HAF**) (10.0 g, 1 eq., 54.0 mmol) in water (250 mL) at room temperature. A suspension formed within 5 min and was stirred for 1 h. The mixture was diluted with brine (250 mL) and extracted with ethyl acetate (3 x 300 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to afford a brown solid (~8 g). The product was triturated in TBME (50 mL) for 1 h, filtered and dried *in vacuo* (45 °C) to afford *N*-(5-formylfuran-3-yl)acetamide (6.9 g, 45 mmol, 83%) as beige solid (purity by qNMR: 97%, IS: ethylene carbonate). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.29 (s, 1H), 9.57 (d, 1H), 8.29 (t, 1H), 7.36 (d, 1H), 2.03 (s, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 178.76, 167.75, 150.09, 136.78, 127.35, 115.31, 22.78. HRMS (ESI) calculated for $C_7H_7NO_3$ ($M+H^+$): 154.0499; found ($M+H^+$): 154.0498. MP (DSC): 160 °C.

S8. Synthesis of 1

***N*-(5-((2,2-dimethylhydrazineylidene)methyl)furan-3-yl)acetamide (1).** 1,1-Dimethylhydrazine (3.3 g, 4.2 mL, 1.5 eq., 55 mmol) was added to a suspension of *N*-(5-formylfuran-3-yl)acetamide (**3A5F**) (5.6 g, 1 eq., 37 mmol) in ethanol (150 mL). The suspension became a solution and was stirred at room temperature for 16 h. The mixture was concentrated *in vacuo* to afford a brown solid, which was triturated in DCM (100 mL) for 1 h. The solids were filtered, washed with ice-cold DCM and dried *in vacuo* to afford *N*-(5-((2,2-dimethylhydrazineylidene)methyl)furan-3-yl)acetamide (**1**) (3.5 g, 18 mmol, 49%) (purity by qNMR: 97%, IS: ethylene carbonate). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.99 (s, 1H), 7.84 (s, 1H), 7.10 (s, 1H), 6.34 (s, 1H), 2.86 (s, 6H), 1.99 (s, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.14, 150.26, 129.89, 126.44, 122.65, 100.81, 42.36, 22.79. HRMS (ESI) calculated for $C_9H_{13}N_3O_2$ ($M+H^+$): 196.1081; found ($M+H^+$):196.1079 MP (DSC): 130 °C.

S9. Synthesis of 2

***N*-(7-((2,2-dimethylhydrazineylidene)methyl)-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (2)**. 1-Methyl-1H-pyrrole-2,5-dione (213 mg, 1.5 eq., 1.92 mmol) was added to a solution of *N*-(5-((2,2-dimethylhydrazineylidene)methyl)furan-3-yl)acetamide (**1**) (250 mg, 1 eq., 1.28 mmol) and acetic anhydride (261 mg, 0.24 mL, 2 eq., 2.56 mmol) in acetonitrile (2.5 mL). The mixture was stirred for 1 h at room temperature. The suspension was diluted with TBME (10 mL), the solids were filtered and dried *in vacuo* (45 °C) to afford *N*-(7-((2,2-dimethylhydrazineylidene)methyl)-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (**2**) (284 mg, 0.98 mmol, 77%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.46 (s, 1H), 8.08 (d, 1H), 8.05 (d, 1H), 7.91 (s, 1H), 3.06 (s, 6H), 2.98 (s, 3H), 2.09 (s, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.16, 168.22, 167.66, 143.97, 136.16, 133.71, 123.17, 118.86, 115.68, 110.97, 42.20, 24.15, 23.49. HRMS (ESI) calculated for $C_{14}H_{16}N_4O_3$ ($M+H^+$): 289.1295; found ($M+H^+$): 289.1292. MP (DSC): 276 °C.

S10. Synthesis of 7

Ethyl 4-acetamido-2-((2,2-dimethylhydrazineylidene)methyl)benzoate (7). Ethyl acrylate (256 mg, 0.27 mL, 2 eq., 2.56 mmol) was added to a solution of *N*-(5-((2,2-dimethylhydrazineylidene)methyl)furan-3-yl)acetamide (**1**) (250 mg, 1 eq., 1.28 mmol), triethylamine (324 mg, 0.45 mL, 2.5 eq., 3.20 mmol) and acetic anhydride (144 mg, 0.13 mL, 1.1 eq., 1.41 mmol) in acetonitrile (1 mL). The mixture was stirred at 81 °C for 18 h, concentrated *in vacuo* and the crude was purified by automated column chromatography (heptane/ethyl acetate) to afford ethyl 4-acetamido-2-((2,2-dimethylhydrazineylidene)methyl)benzoate (**7**) (228 mg, 0.82 mmol, 64%) as an off-white solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.21 (s, 1H), 8.02 (d, 1H), 7.98 (s, 1H), 7.79 (d, 1H), 7.69 (dd, 1H), 4.28 (q, 2H), 2.96 (s, 6H), 2.07 (s, 3H), 1.32 (t, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.31, 166.87, 142.93, 138.77, 132.07, 130.19, 121.81,

117.28, 114.86, 60.93, 42.89, 24.58, 14.62. HRMS (ESI) calculated for $C_{14}H_{19}N_3O_3$ ($M+H^+$): 278.1499; found ($M+H^+$): 278.1495. MP (DSC): 144 °C.

S11. **Synthesis of 12**

***N*-(5-((pyrrolidin-1-ylimino)methyl)furan-3-yl)acetamide (12).** Pyrrolidin-1-amine (6.0 g, 1.25 eq., 70 mmol) was added to a suspension of *N*-(5-formylfuran-3-yl)acetamide (**3A5F**) (8.6 g, 1 eq., 56 mmol) in ethanol (200 mL) at 10 °C. The mixture was stirred at room temperature for 4 h, during which a solution was obtained. The mixture was concentrated *in vacuo*, and the crude was purified by automated column chromatography (330 g column, solid load (~ 18 g celite), product dissolved in DCM with small amount of MeOH). Concentration of the fractions with product afforded *N*-(5-((pyrrolidin-1-ylimino)methyl)furan-3-yl)acetamide (**12**) (10.16 g, 45.92 mmol, 82%) as a yellow solid (purity by qNMR: 100%, IS: ethylene carbonate). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.97 (s, 1H), 7.81 (s, 1H), 6.97 (s, 1H), 6.28 (s, 1H), 3.28 – 3.12 (m, 4H), 1.99 (s, 3H), 1.93 – 1.79 (m, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.10, 150.51, 129.55, 126.45, 121.60, 99.91, 50.36, 23.04, 22.79. HRMS (ESI) calculated for $C_{11}H_{15}N_3O_2$ ($M+H^+$): 222.1237; found ($M+H^+$): 222.1236. MP (DSC): 151 °C.

S12. **Protocol A**

***Protocol A (maleimides and fumaronitrile*):** To a mixture of *N*-(5-((pyrrolidin-1-ylimino)methyl)furan-3-yl)acetamide (**12**) (250 mg, 1 eq., 1.13 mmol) in acetonitrile (2 mL) was added triethylamine (286 mg, 0.39 mL, 2.5 eq., 2.82 mmol), acetic anhydride (127 mg, 0.12 mL, 1.1 eq., 1.24 mmol.) and the appropriate dienophile (2.26 mmol, 2 eq.). The suspension was stirred for 18 h at room temperature. The product was filtered off, washed with ethyl acetate (5 mL) and dried *in vacuo* to afford the target compound.

S13. **Protocol B**

Protocol B (maleates and mono-activated alkenes): To a mixture of *N*-(5-((pyrrolidin-1-ylimino)methyl)furan-3-yl)acetamide (**12**) (250 mg, 1 eq., 1.13 mmol) in acetonitrile (1 mL) was added triethylamine (286 mg, 0.39 mL, 2.5 eq., 2.82 mmol) , acetic anhydride (127 mg, 0.12 mL, 1.1 eq., 1.24 mmol.) and the appropriate dienophile (2.26 mmol, 2 eq.). The suspension was stirred for 18 h at 81 °C. The volatiles were removed *in vacuo* and the crude was purified by automated column chromatography (heptane/ethyl acetate) to afford the target compound.

S14. **Synthesis of 13**

Ethyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (13). Prepared according to protocol **B** with ethyl acrylate (226 mg, 0.24 mL, 2 eq., 2.26 mmol) as dienophile. Ethyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (**13**) (244 mg, 0.80 mmol, 71%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.19 (s, 1H), 7.99 (d, 1H), 7.87 (s, 1H), 7.76 (d, 1H), 7.66 (dd, 1H), 4.26 (q, 2H), 3.38 – 3.26 (m, 4H), 2.05 (s, 2H), 1.95 – 1.86 (m, 3H), 1.30 (t, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.79, 142.41, 138.72, 131.61, 128.72, 120.82, 116.33, 113.76, 60.36, 50.40, 24.08, 23.15, 14.15. HRMS (ESI) calculated for $C_{16}H_{21}N_3O_3$ ($M+H^+$): 304.1656; found ($M+H^+$): 304.1655. MP (DSC): 153 °C.

S15. **Synthesis of 14**

***N*-(2-methyl-1,3-dioxo-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (14).** Prepared according to protocol **A** with 1-methyl-1H-pyrrole-2,5-dione (126 mg, 1 eq., 1.13 mmol) as dienophile. *N*-(2-methyl-1,3-dioxo-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (**14**) (315 mg, 1.00 mmol, 89%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.41 (s, 1H), 8.01 (d, 1H), 7.98 (d, 1H), 7.72 (s, 1H), 3.41 – 3.34 (m, 4H), 2.95 (s, 3H), 2.08 (s, 3H), 1.99 – 1.92 (m, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.13, 168.20, 167.69, 143.92, 136.58, 133.72, 122.65, 118.32, 115.25, 110.57, 50.20, 24.14, 23.38 (d). HRMS (ESI) calculated for $C_{16}H_{18}N_4O_3$ ($M+H^+$): 315.1452; found ($M+H^+$): 315.1450. MP (DSC): 299 °C.

S16. **Synthesis of 15**

***N*-(2-benzyl-1,3-dioxo-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (15).** Prepared according to protocol **A** with 1-benzyl-1H-pyrrole-2,5-dione (423 mg, 2 eq., 2.26 mmol) as dienophile. The product was triturated in DCM for 1 h to afford *N*-(2-benzyl-1,3-dioxo-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (**15**) (399 mg, 1.02 mmol, 90%) as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.49 (s, 1H), 8.11 (d, 1H), 8.06 (d, 1H), 7.80 (s, 1H), 7.37 – 7.21 (m, 5H), 4.71 (s, 2H), 3.43 – 3.36 (m, 4H), 2.09 (s, 3H), 1.99 – 1.90 (m, 4H).^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.23, 144.21, 137.06, 136.89, 133.57, 128.57, 127.39 (d), 122.42, 117.94, 115.64, 110.90, 50.27, 40.70, 24.16, 23.32. HRMS (ESI) calculated for $C_{22}H_{22}N_4O_3$ (M+H$^+$): 391.1765; found (M+H$^+$): 391.1760. MP (DSC): 300 °C.

S17. **Synthesis of 16**

***N*-(1,3-dioxo-2-phenyl-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (16).** Prepared according to protocol **A** with 1-phenyl-1H-pyrrole-2,5-dione (391 mg, 2 eq., 2.26 mmol) as dienophile. *N*-(1,3-dioxo-2-phenyl-7-((pyrrolidin-1-ylimino)methyl)isoindolin-5-yl)acetamide (**16**) (380 mg, 1.01 mmol, 89%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.52 (s, 1H), 8.16 (d, 1H), 8.13 (d, 1H), 7.85 (s, 1H), 7.55 – 7.46 (m, 2H), 7.42 (dt, 3H), 3.46 – 3.35 (m, 4H), 2.11 (s, 3H), 2.01 – 1.94 (m, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.28, 167.20, 166.69, 144.32, 137.26, 133.57, 131.99, 128.73, 127.85, 127.34, 122.50, 117.90, 115.82, 110.94, 50.28, 24.19, 23.32. HRMS (ESI) calculated for $C_{21}H_{20}N_4O_3$ (M+H$^+$): 377.1608; found (M+H$^+$): 377.1610. MP (DSC): 314 °C.

S18. **Synthesis of 17**

Dimethyl 5-acetamido-3-((pyrrolidin-1-ylimino)methyl)phthalate (17). Prepared according to protocol **B** with dimethyl maleate (326 mg, 0.28 mL, 2 eq., 2.26 mmol) or dimethyl fumarate (326 mg, 2 eq., 2.26 mmol) as dienophile. Dimethyl 5-acetamido-3-((pyrrolidin-1-ylimino)methyl)phthalate (**17**) (244 mg, 0.70 mmol, 62%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.27 (s, 1H), 8.08 (s, 2H), 6.92 (s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.32 – 3.26 (m, 4H), 2.06 (s, 3H), 1.94 – 1.86 (m, 4H).^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.87, 168.19, 165.95, 140.12, 135.70, 129.31, 124.75, 117.40, 117.07, 52.61, 52.26, 50.21, 24.03, 23.16. HRMS (ESI) calculated for $C_{17}H_{21}N_3O_5$ (M+H$^+$): 348.1554; found (M+H$^+$): 348.1549. MP (DSC): 186 °C.

S19. **Synthesis of 18**

***N*-(3,4-dicyano-5-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (18).** Prepared according to protocol **A** with fumaronitrile (176 mg, 2 eq., 2.26 mmol) as dienophile. *N*-(3,4-dicyano-5-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (**18**) (260 mg, 0.92 mmol, 82%) was obtained as off-white solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.57 (s, 1H), 8.06 (d, 1H), 8.03 (d, 1H), 6.97 (s, 1H), 3.51 – 3.37 (m, 4H), 2.08 (s, 3H), 2.01 – 1.88 (m, 4H).^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.63, 143.04, 142.81, 121.26, 120.27, 116.29, 115.90, 115.67, 115.34, 102.56, 50.33, 24.23, 23.40. HRMS (ESI) calculated for $C_{15}H_{15}N_5O$ (M+H$^+$): 282.1349; found (M+H$^+$): 282.1348. MP (DSC): 284 °C.

S20. **Synthesis of 19**

***N*-(4-cyano-3-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (19).** Prepared according to protocol **B** with acrylonitrile (120 mg, 0.15 mL, 2 eq., 2.26 mmol) as dienophile. *N*-(4-cyano-3-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (**19**) (242 mg, 0.94 mmol, 84%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.28 (s, 1H), 7.99 (d, 1H), 7.63 (dd, 1H), 7.59 (dd, 1H), 7.10 (s, 1H), 3.42 – 3.34 (m, 4H), 2.06 (s, 3H), 1.98 – 1.85 (m, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.04, 143.17, 140.87, 133.87, 123.65, 118.11, 116.66, 112.51, 101.23, 50.22, 24.15, 23.28. HRMS (ESI) calculated for $C_{14}H_{16}N_4O$ (M+H$^+$): 257.1397; found (M+H$^+$): 257.1394. MP (DSC): 198 °C.

S21. **Synthesis of 20**

***tert*-Butyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (20).** Prepared according to protocol **B** with *N*-(5-((pyrrolidin-1-ylimino)methyl)furan-3-yl)acetamide (**12**) (1.0 g, 1 eq., 4.5 mmol) and *tert*-butyl acrylate (1.2 g, 1.3 mL, 2 eq., 9.0 mmol) as dienophile. *tert*-Butyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (**20**) (1.1 g, 3.3 mmol, 73%) was obtained as yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.16 (s, 1H), 7.97 (d, 1H), 7.81 (s, 1H), 7.69 (d, 1H), 7.63 (dd, 1H), 3.32 – 3.29 (m, 4H), 2.04 (s, 3H), 1.95 – 1.88 (m, 4H), 1.53 (s, 8H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.73, 166.03, 142.03, 138.10, 131.57, 128.73, 122.72, 116.36, 113.70, 80.64, 50.45, 27.92, 24.07, 23.15. HRMS (ESI) calculated for $C_{18}H_{25}N_3O_3$ (M+H$^+$): 332.1969; found (M+H$^+$): 332.1967. MP (DSC): 151 °C.

S22. **Synthesis of 21**

***N*-(4-(methylsulfonyl)-3-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (21).** Prepared according to protocol **B** with (methylsulfonyl)ethene (240 mg, 0.2 mL, 2 eq., 2.26 mmol) as dienophile. After column chromatography the product was triturated in TBME (5 mL) to afford *N*-(4-(methylsulfonyl)-3-((pyrrolidin-1-ylimino)methyl)phenyl)acetamide (**21**) (261 mg, 0.84 mmol, 75%) as light yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.32 (s, 1H), 8.08 (d, 1H), 7.77 (d, 1H), 7.73 (dd, 1H), 7.66 (s, 1H), 3.46 – 3.37 (m, 4H), 3.16 (s, 3H), 2.07 (s, 3H), 2.00 – 1.91 (m, 4H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.01, 143.46, 136.82, 129.98, 129.50, 124.40, 116.04, 113.79, 50.32, 44.18, 24.11, 23.24. HRMS (ESI) calculated for $C_{14}H_{19}N_3O_3S$ (M+H$^+$): 310.1220; found (M+H$^+$): 310.1214. MP (DSC): 196 °C.

S23. **Synthesis of 22**

Diethyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)phenyl)phosphonate (22). Prepared according to protocol **B** with diethyl vinylphosphonate (927 mg, 0.87 mL, 5 eq., 5.65 mmol) as dienophile. Diethyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)phenyl)phosphonate (**22**) (278 mg, 0.76 mmol, 67%) was obtained as light orange solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.18 (s, 1H), 8.03 – 7.98 (m, 1H), 7.68 – 7.66 (m, 1H), 7.67 – 7.61 (m, 1H), 7.57 (s, 1H), 4.10 – 3.88 (m, 4H), 3.32 – 3.28 (m, 4H), 2.05 (s, 3H), 1.96 – 1.87 (m, 4H), 1.21 (t, 6H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.82, 142.78, 140.60 (d), 134.46 (d), 128.35 (d), 117.73 (d), 116.09 (d), 113.12 (d), 61.41 (d), 50.33, 24.07, 23.15, 16.16 (d). HRMS (ESI) calculated for $C_{17}H_{26}N_3O_4P$ (M+H$^+$): 368.1734; found (M+H$^+$): 368.1728. MP (DSC): 197 °C.

S24. **Synthesis of 25**

***tert*-Butyl 4-acetamido-2-formylbenzoate (25).** A solution of *tert*-butyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (**20**) (350 mg, 1 eq., 1.06 mmol) in DCM (5.0 mL) was cooled to -78 °C. The mixture was subjected to ozonolysis for 3 min, during which a color change was observed: yellow → dark orange → brown → dark yellow → greenish-blue. The mixture was purged with N_2 for 5 min to afford a yellow solution, concentrated *in vacuo* and was purified by automated column chromatography (heptane/ethyl acetate) to furnish *tert*-butyl 4-acetamido-2-formylbenzoate (**25**) (186 mg, 0.71 mmol, 67%) as a white solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.43 (s, 2H), 8.01 (d, 1H), 7.89 (dd, 1H), 7.85 (d, 1H), 2.09 (s, 3H), 1.55 (s, 9H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 192.54, 169.13, 164.69, 142.76, 138.06, 131.35, 127.13, 121.94, 117.21, 82.06, 27.74, 24.13. HRMS (ESI) calculated for $C_{14}H_{17}NO_4$ (M+Na$^+$): 286.1050; found (M+Na$^+$): 286.1046. MP (DSC): 129 °C.

S25. **Synthesis of 26**

***tert*-Butyl 4-acetamido-2-cyanobenzoate (26).** A solution of *tert*-butyl 4-acetamido-2-((pyrrolidin-1-ylimino)methyl)benzoate (**20**) (350 mg, 1 eq., 1.06 mmol) in DCM (5.0 mL) was cooled to 0 °C. *m*CPBA (325 mg, 70% Wt, 1.25 eq., 1.32 mmol) was added portionwise while maintaining a temperature < 10 °C. The cooling was removed, and the mixture was stirred for 1 h at room temperature. The mixture was diluted with ethyl acetate (50 mL) and washed with $NaHCO_3$ (aq., sat.) + $Na_2S_2O_3$ (aq., 10%) (1:1) (5 x 50 mL) (thoroughly) and brine (1 x 25 mL). The organic phase was dried over Na_2SO_4, concentrated *in vacuo* and the crude product was purified by automated column

chromatography (heptane/ethyl acetate). *tert*-Butyl 4-acetamido-2-cyanobenzoate (**26**) (218 mg, 0.84 mmol, 79%) was isolated as a light yellow solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.55 (s, 1H), 8.18 (d, 1H), 8.00 (d, 1H), 7.84 (dd, 1H), 2.10 (s, 3H), 1.56 (s, 9H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.45, 162.43, 143.13, 132.17, 126.76, 123.61, 122.09, 117.55, 112.29, 82.49, 27.65, 24.16. HRMS (ESI) calculated for $C_{14}H_{16}N_2O_3$ (M+Na$^+$): 283.1053; found (M+H$^+$): 283.1053. MP (DSC): 188 °C.

S26. **Synthesis of 27**

***N*-(5-(1-(2,2-dimethylhydrazineylidene)ethyl)furan-3-yl)acetamide (27).** A mixture of *N*-(5-acetylfuran-3-yl)acetamide (**3A5AF**) (1.30 g, 1 eq., 7.78 mmol), 1,1-dimethylhydrazine (701 mg, 0.88 mL, 1.5 eq., 11.7 mmol) and acetic acid (467 mg, 0.45 mL, 1 eq., 7.78 mmol) in ethanol (25 mL) was stirred at reflux temperature for 6 h. The mixture was diluted with ethyl acetate (200 mL) and washed with $NaHCO_3$ (aq., sat., 2 x 200 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to afford a black oil (1.46 g). The crude was purified by automated column chromatography (DCM/MeOH) to afford *N*-(5-(1-(2,2-dimethylhydrazineylidene)ethyl)furan-3-yl)acetamide (**27**) (1.18 g, 5.64 mmol, 73%) as a light brown oil that solidified upon standing. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.04 (s, 1H), 7.95 (s, 1H), 6.66 (s, 1H), 2.49 (s, 6H), 2.15 (s, 3H), 2.00 (s, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.30, 151.89, 150.16, 131.80, 126.48, 104.01, 47.01, 22.82, 14.18. HRMS (ESI) calculated for $C_{10}H_{15}N_3O_2$ (M+H$^+$): 210.1237; found (M+H$^+$): 210.1235. MP (DSC): 85 °C.

S27. **Synthesis of 32**

***N*-(7-(1-(2,2-Dimethylhydrazineylidene)ethyl)-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (32).** A solution of *N*-(5-(1-(2,2-dimethylhydrazineylidene)ethyl)furan-3-yl)acetamide (**27**) (1.25 g, 1 eq., 5.97 mmol), acetic anhydride (671 mg, 0.62 mL, 1.1 eq., 6.57 mmol) and 1-methyl-1H-pyrrole-2,5-dione (1.33 g, 2.0 eq., 11.9 mmol) in acetonitrile (6 mL) was stirred at reflux temperature for 20 h. The mixture was concentrated *in vacuo* and the crude was purified by automated column chromatography (DCM/MeOH, *see chromatogram below*). **Fraction 1**: *N*-(7-acetyl-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (**33**) (657 mg, 2.52 mmol, 42%), **Faction 2**: *N*-(7-(1-(2,2-dimethylhydrazineylidene)ethyl)-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (**32**) as cis/trans mixture (2:8) (830 mg, 2.75 mmol, 46%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.56 (s, 1H), 8.20 (s, 1H), 8.14 (s, 1H), 7.62 (s, 1H), 7.53 (s, 1H), 2.99 (s, 3H), 2.81 (s, 3H), 2.55 (s, 6H), 2.30 (s, 2H), 2.22 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 169.36, 167.40, 167.02, 160.42, 144.22, 139.01, 137.46, 134.06, 122.20, 121.79, 120.68, 112.30, 46.66, 24.21, 23.72, 18.93. HRMS (ESI) calculated for $C_{15}H_{18}N_4O_3$ (M+H$^+$): 303.1452; found (M+H$^+$): 303.1451. MP (DSC): 172 °C.

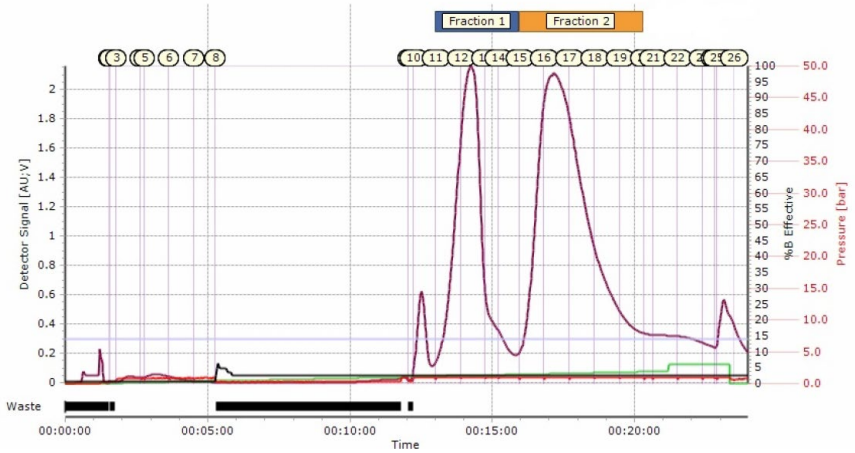


Figure 2. *Chromatogram of purification of* ***32****. F1 (blue): ketone* ***33****, F2 (orange):* ***32***

S28. **Synthesis of 33**

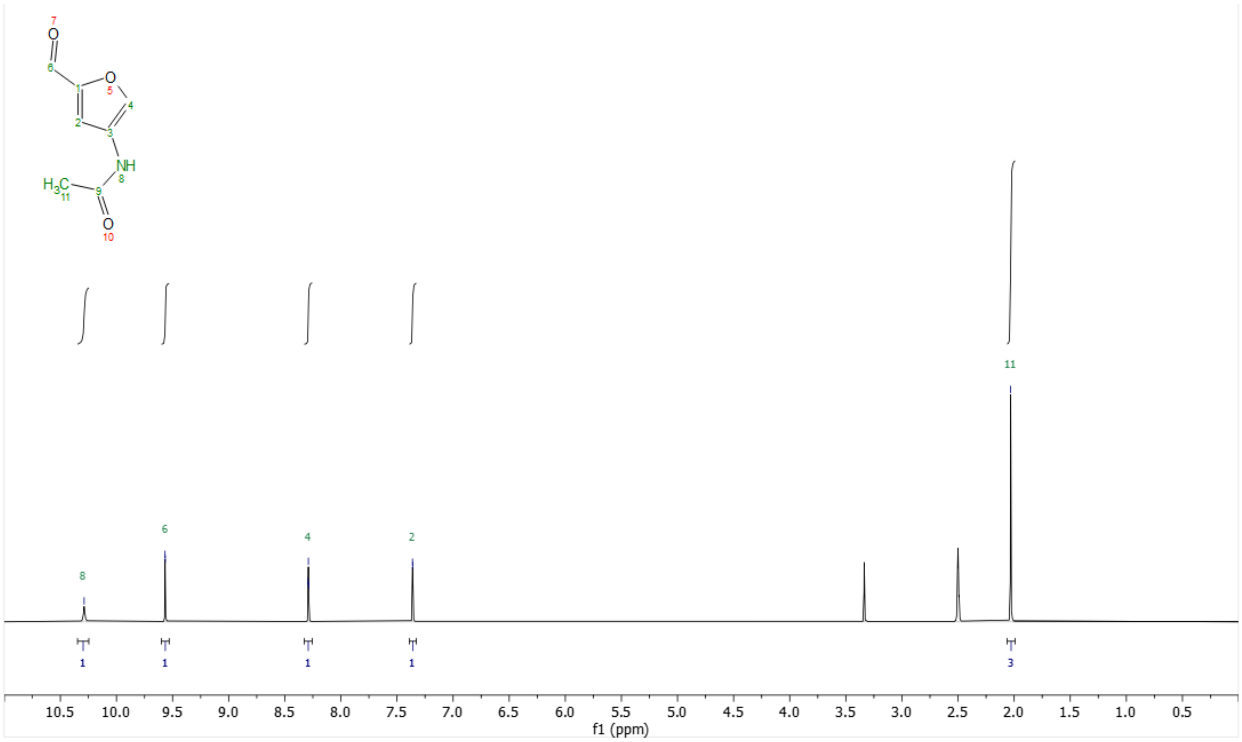
***N*-(7-acetyl-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (33).** A solution of *N*-(7-(1-(2,2-dimethylhydrazineylidene)ethyl)-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (**32**) (250 mg, 1 eq., 0.83 mmol) in DCM (5.0 mL) was cooled to -78 °C. The mixture was subjected to ozonolysis for 5 min, during which a color change was observed: dark green/brown → dark greenish-blue. The mixture was purged with N_2 for 5 min to afford a yellow solution. The mixture was concentrated *in vacuo* and was purified by automated column chromatography (heptane/ethyl acetate) to furnish *N*-(7-acetyl-2-methyl-1,3-dioxoisoindolin-5-yl)acetamide (**33**) (131 mg, 0.50 mmol, 61%) as a white solid. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.65 (s, 1H), 8.21 (d, 1H), 7.79 (d, 1H), 3.01 (s, 3H), 2.67 (s, 3H), 2.12 (s, 3H). ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 200.74, 169.50, 167.02, 166.80, 144.58, 138.68, 134.07, 121.35, 120.49, 113.88, 30.71, 24.21, 23.88. HRMS (ESI) calculated for $C_{13}H_{12}N_2O_4$ ($M+H^+$): 261.0870; found ($M+H^+$): 261.0868. MP (DSC): 196 °C.

Characterization

S29. **Spectra of 3A5F**

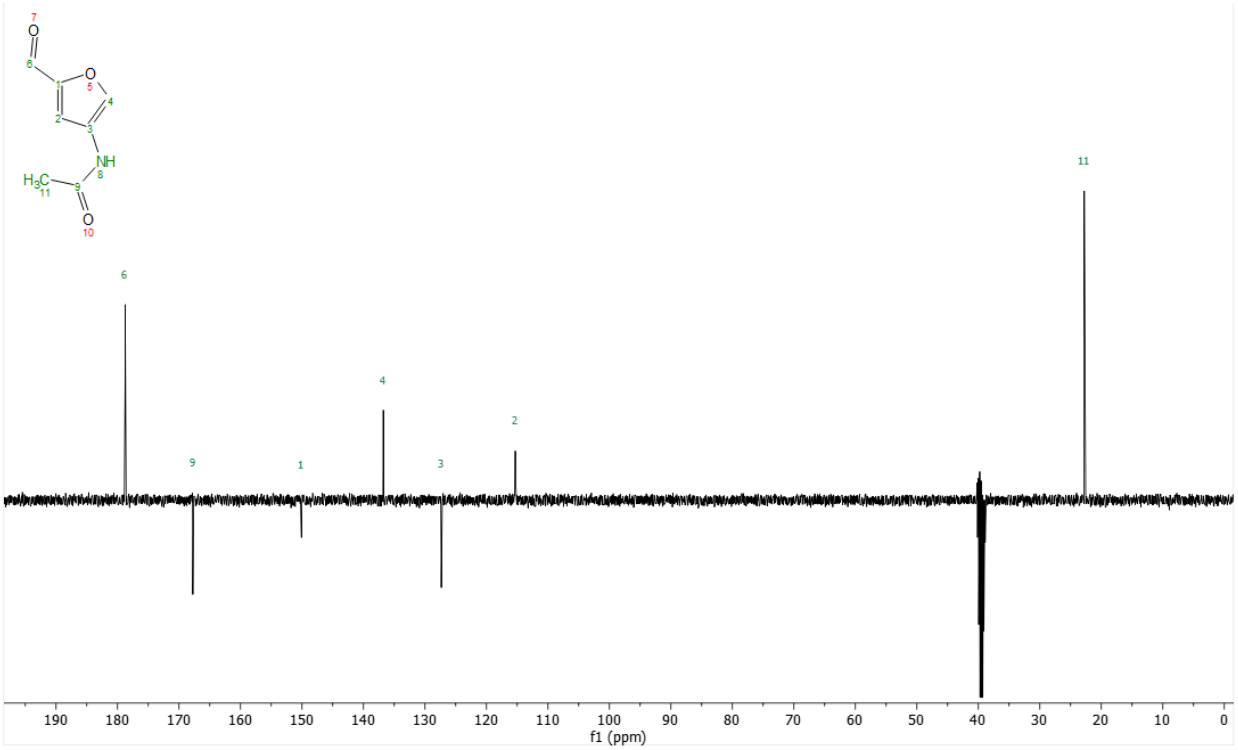
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.29 (s, 1H), 9.57 (d, 1H), 8.29 (t, 1H), 7.36 (d, 1H), 2.03 (s, 3H)

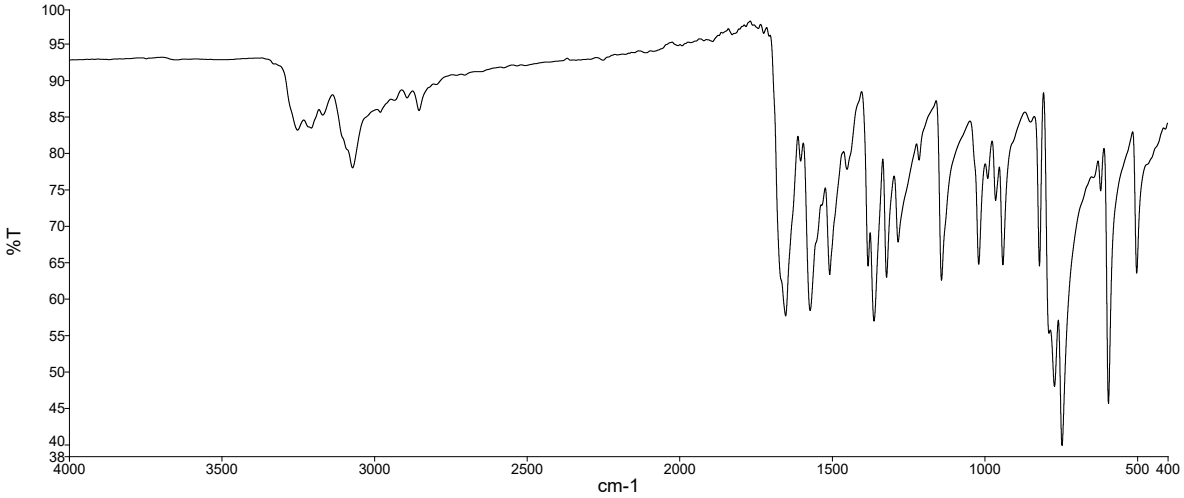


^{13}C-NMR (DMSO-d_6)

^{13}C-NMR (101 MHz, DMSO-d_6) δ = 178.76, 167.75, 150.09, 136.78, 127.35, 115.31, 22.78



IR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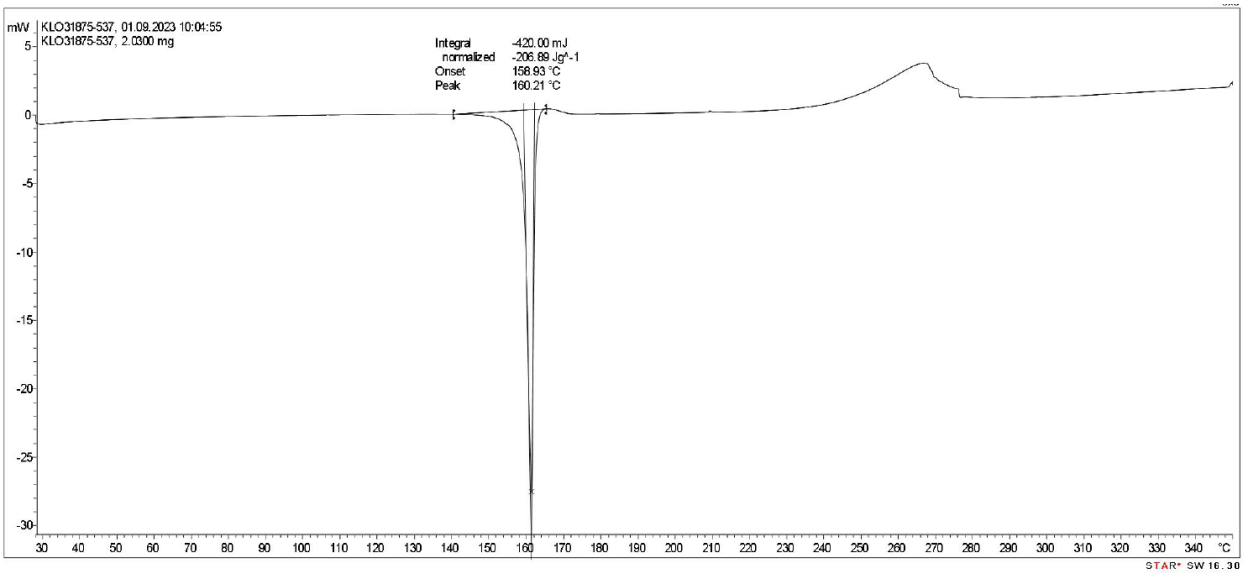
cm-1

DSC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normalized -206.89 Jg^-1
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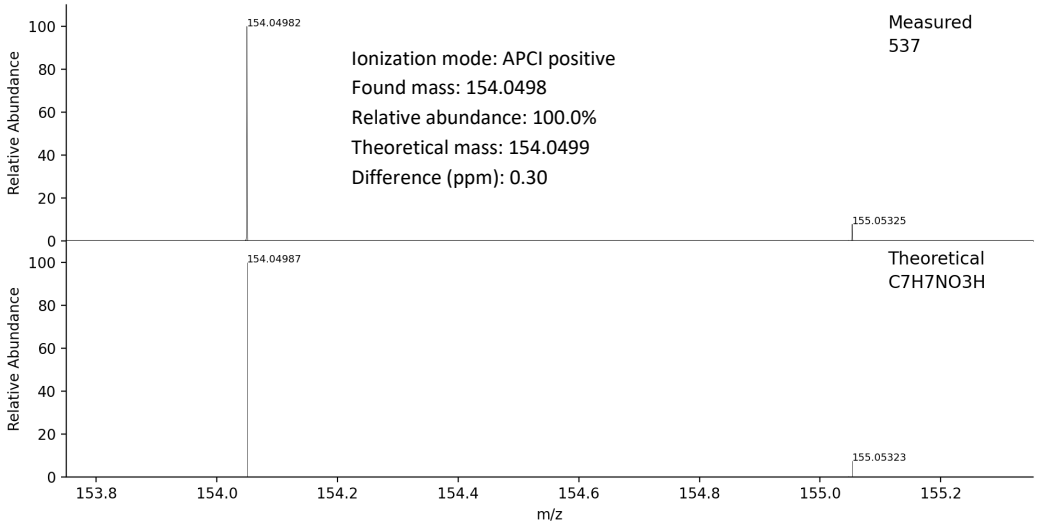
Peak 160.21 °C
°C
STARe SW 16.30

HRMS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Measured
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Theoretical mass: 154.0499
Difference (ppm): 0.30
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154.04987
Theoretical
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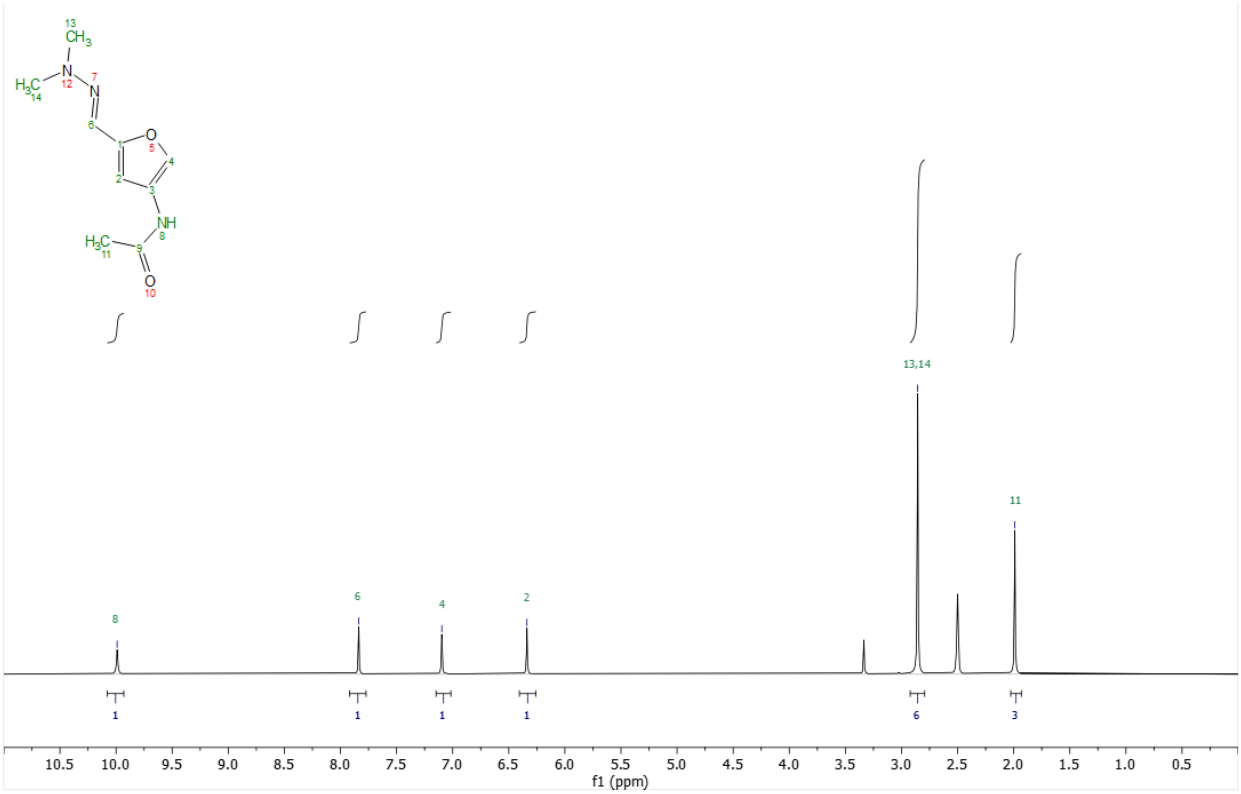
155.05323
m/z

S30. **Spectra of 1**

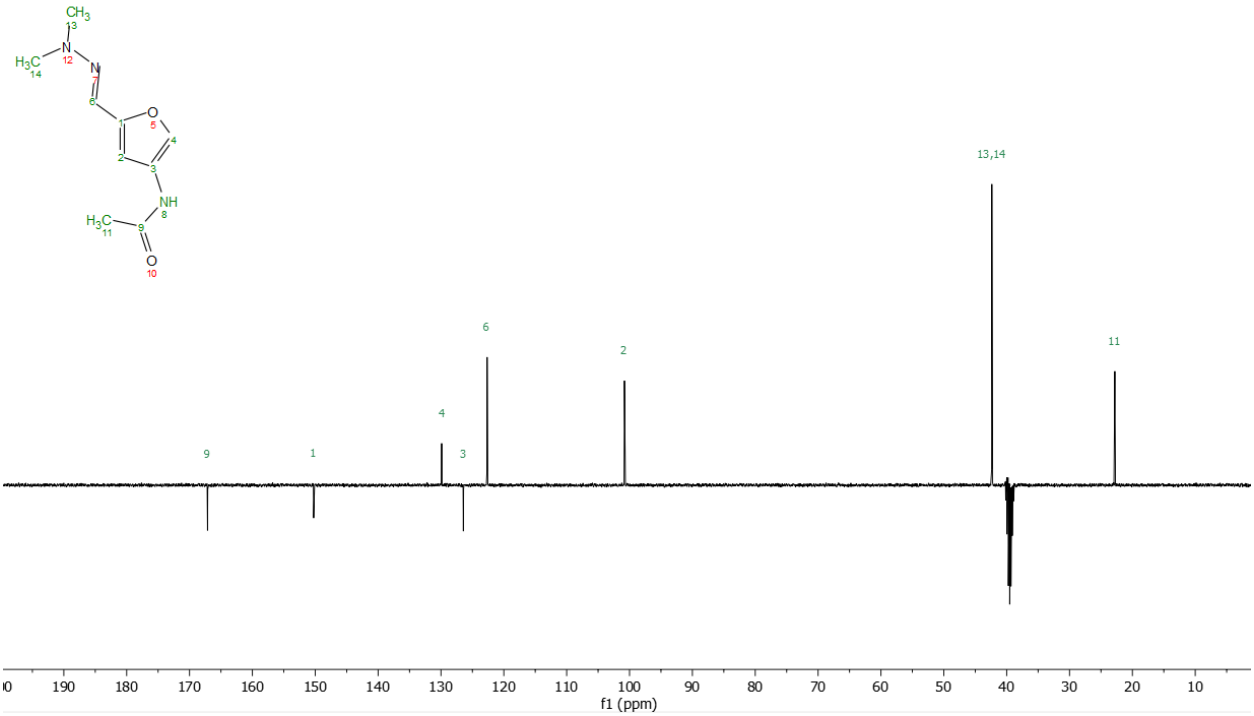
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.99 (s, 1H), 7.84 (s, 1H), 7.10 (s, 1H), 6.34 (s, 1H), 2.86 (s, 6H), 1.99 (s, 3H)

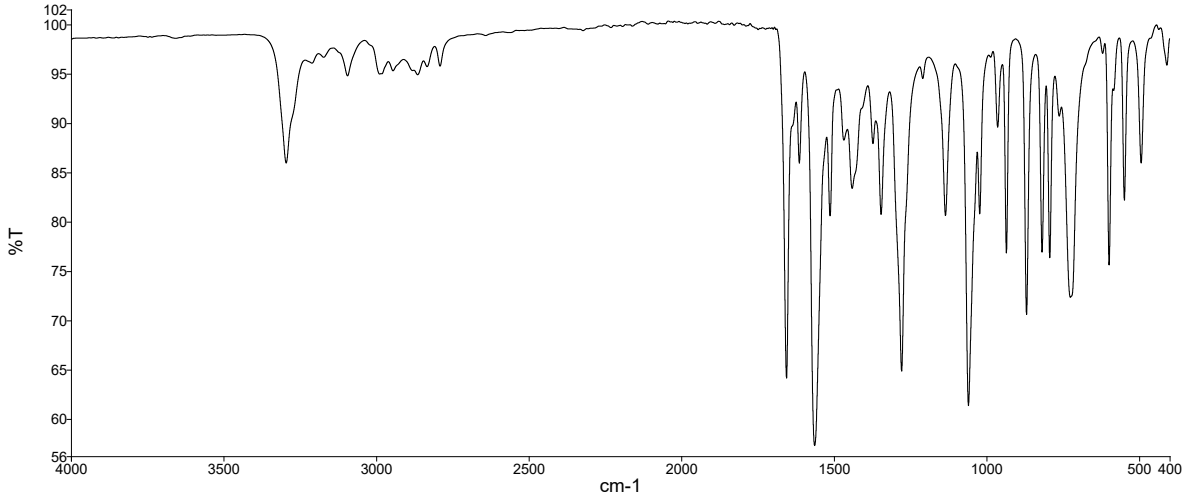


^{13}C-NMR (DMSO-d_6)

^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.14, 150.26, 129.89, 126.44, 122.65, 100.81, 42.36, 22.79



IR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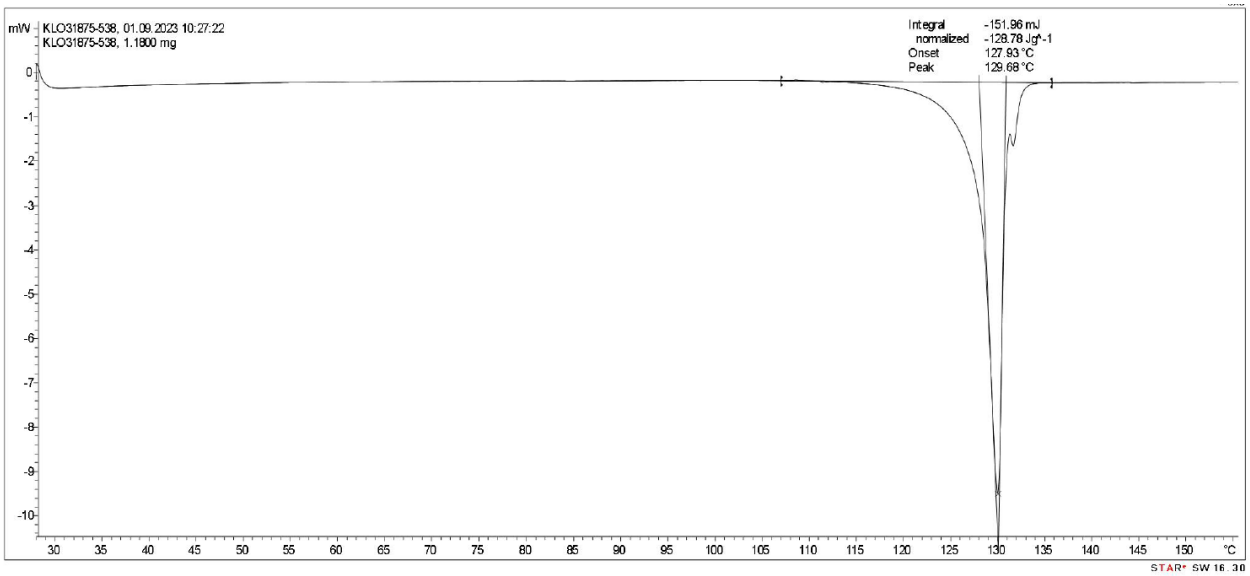
cm-1

DSC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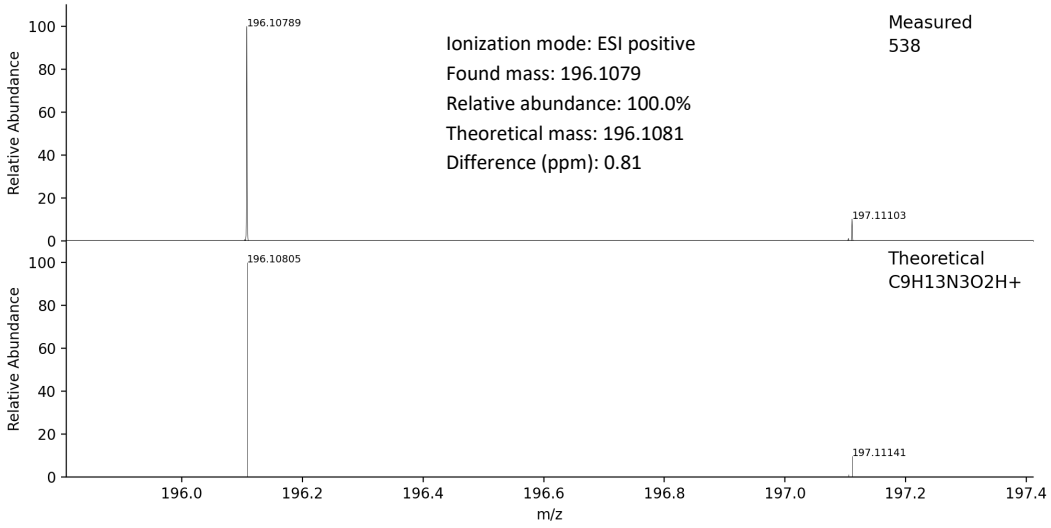
normalized -128.78 Jg^-1
Onset 127.93 °C
Peak 129.68 °C
°C

HRMS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Theoretical
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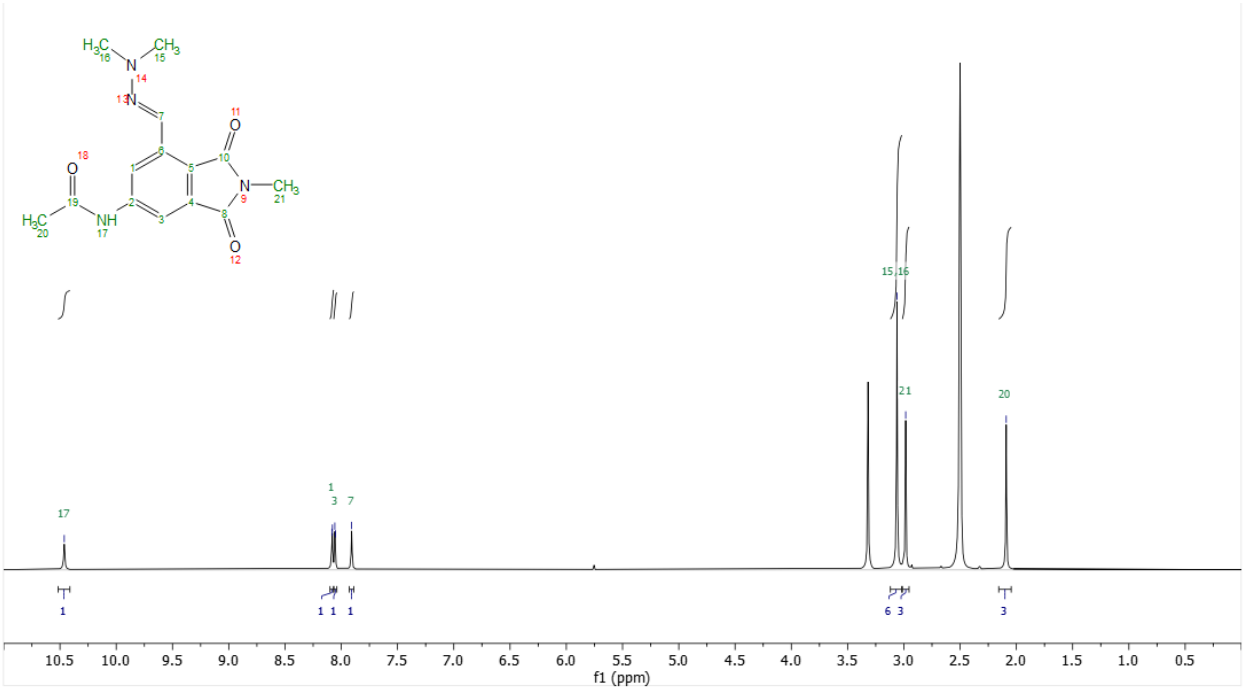
m/z

S31. **Spectra of 2**

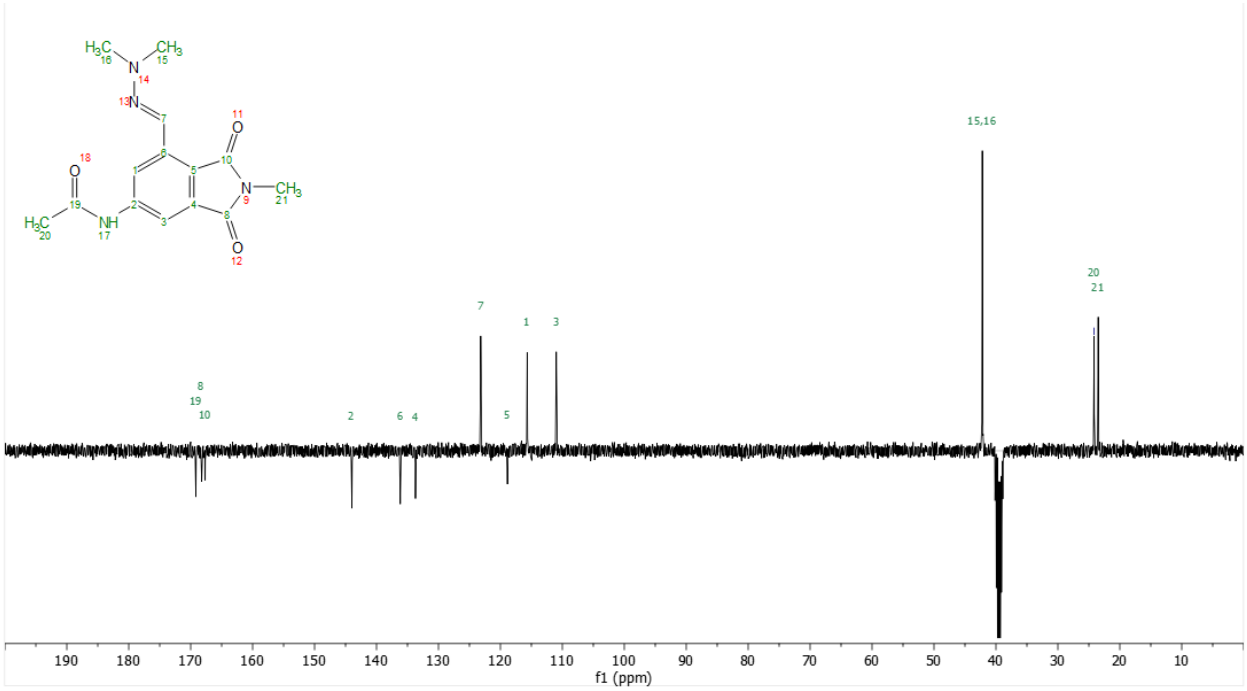
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.46 (s, 1H), 8.08 (d, 1H), 8.05 (d, 1H), 7.91 (s, 1H), 3.06 (s, 6H), 2.98 (s, 3H), 2.09 (s, 3H)



^{13}C-NMR (DMSO-d_6)

^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.16, 168.22, 167.66, 143.97, 136.16, 133.71, 123.17, 118.86, 115.68, 110.97, 42.20, 24.15, 23.49



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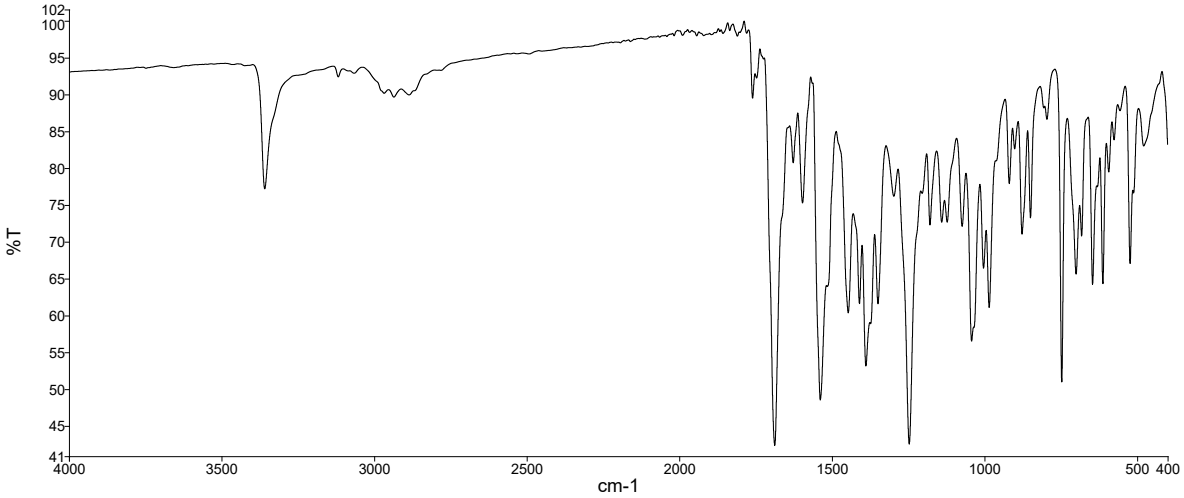
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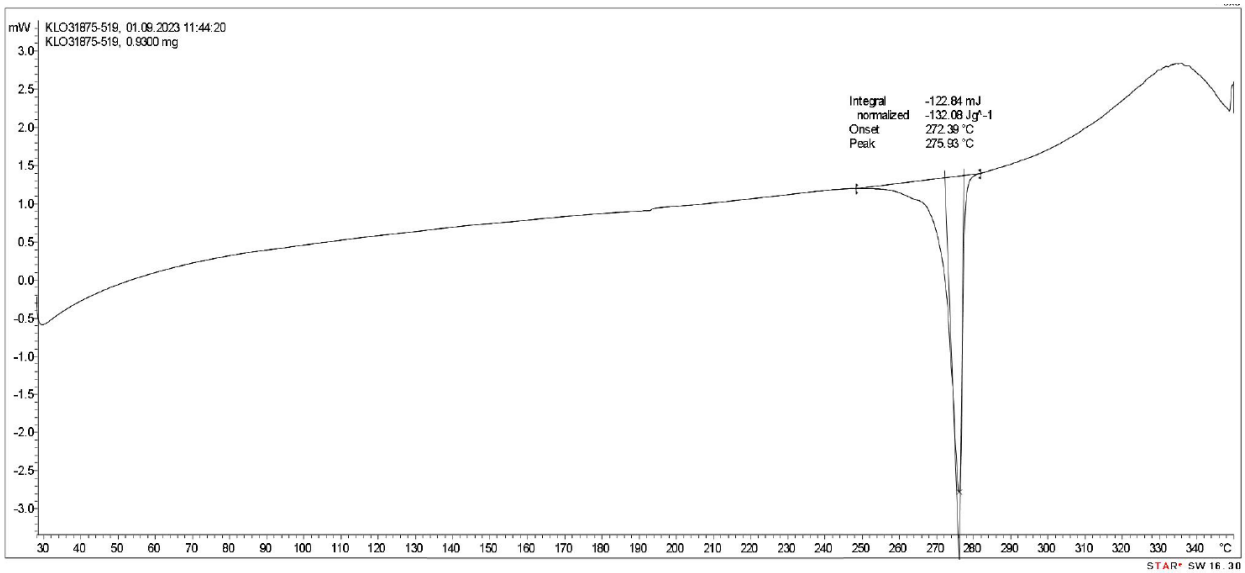
3000
2500
2000
1500
1000
500
400

DSC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normalized -132.08 Jg^-1
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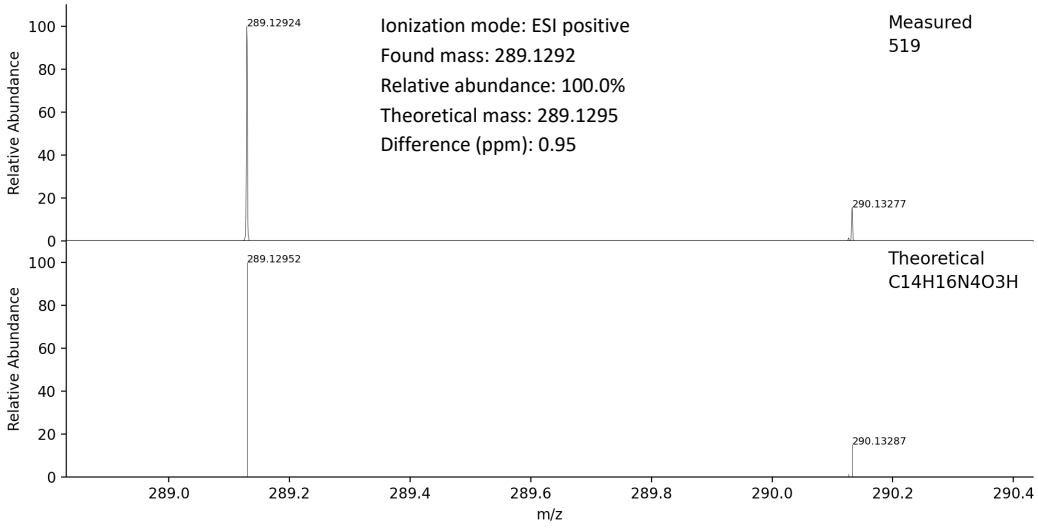
Peak 275.93 °C
°C
STAR° SW 16.30

HRMS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Difference (ppm): 0.95
Measured
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289.12952
Theoretical
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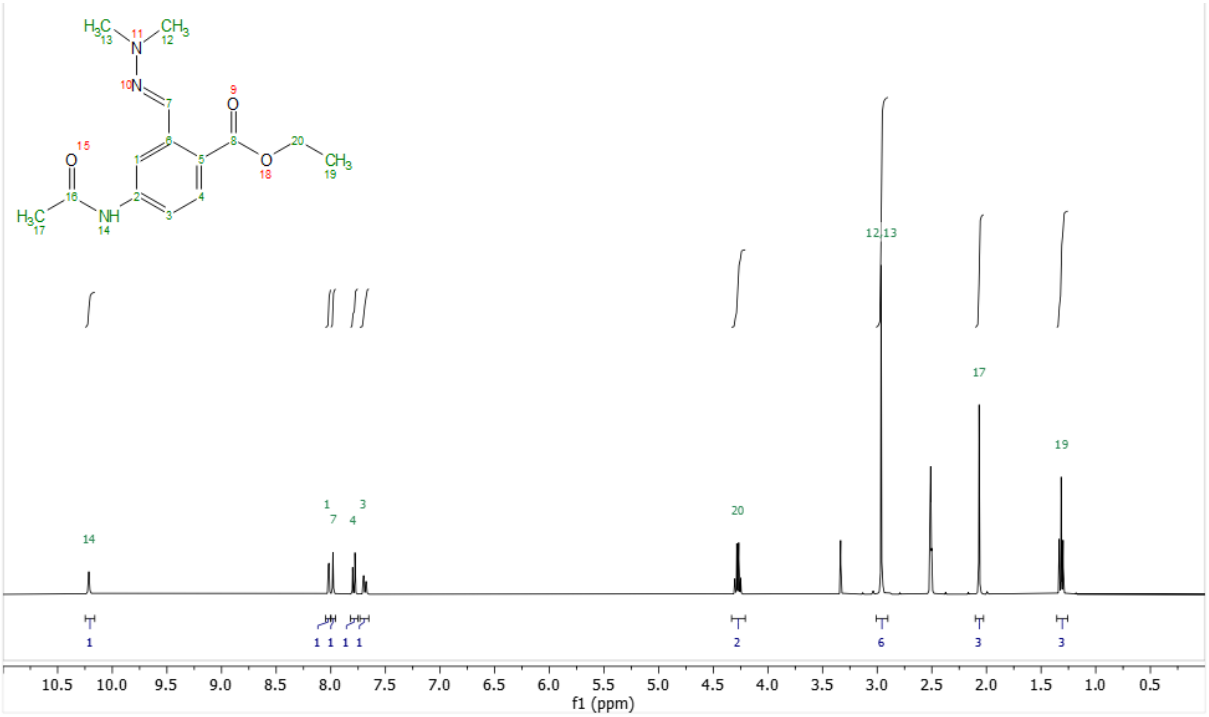
290.13287
m/z

S32. **Spectra of 7**

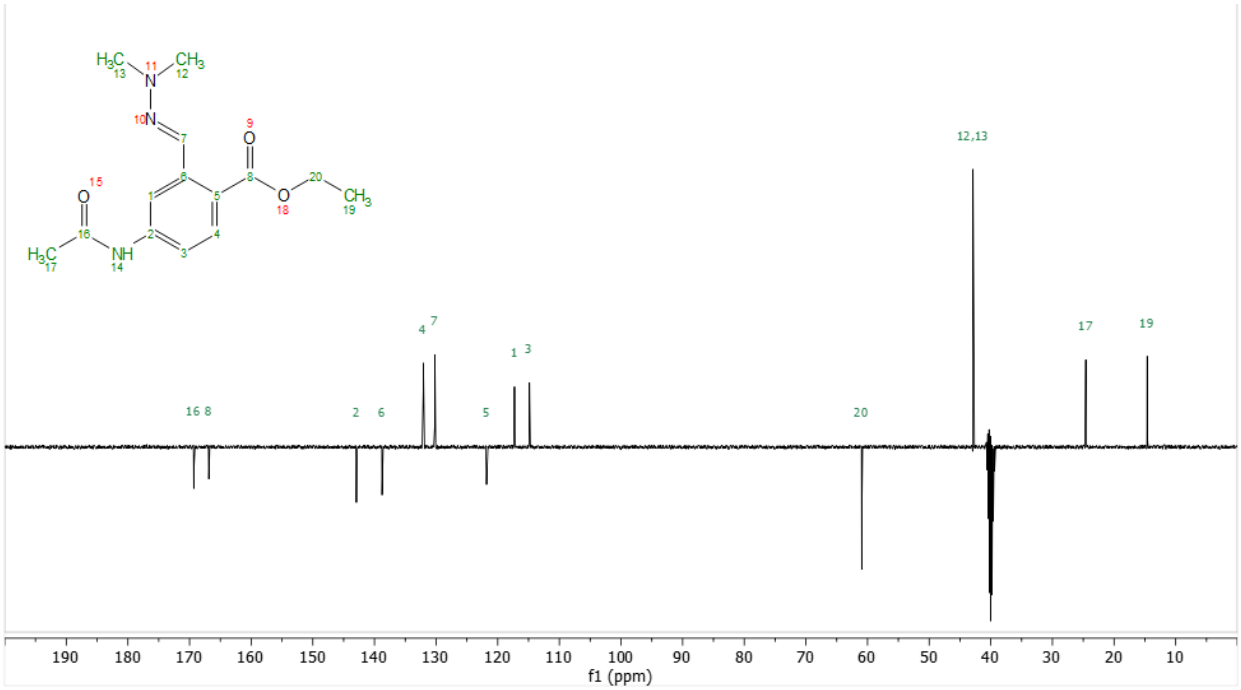
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.21 (s, 1H), 8.02 (d, 1H), 7.98 (s, 1H), 7.79 (d, 1H), 7.69 (dd, 1H), 4.28 (q, 2H), 2.96 (s, 6H), 2.07 (s, 3H), 1.32 (t, 3H)



^{13}C-NMR (DMSO-d_6)

^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.31, 166.87, 142.93, 138.77, 132.07, 130.19, 121.81, 117.28, 114.86, 60.93, 42.89, 24.58, 14.62



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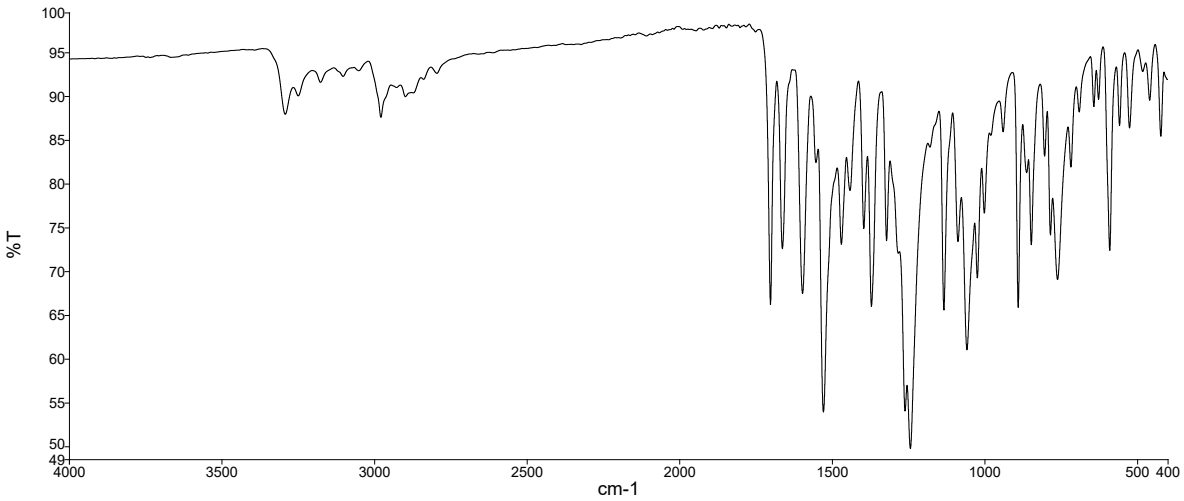
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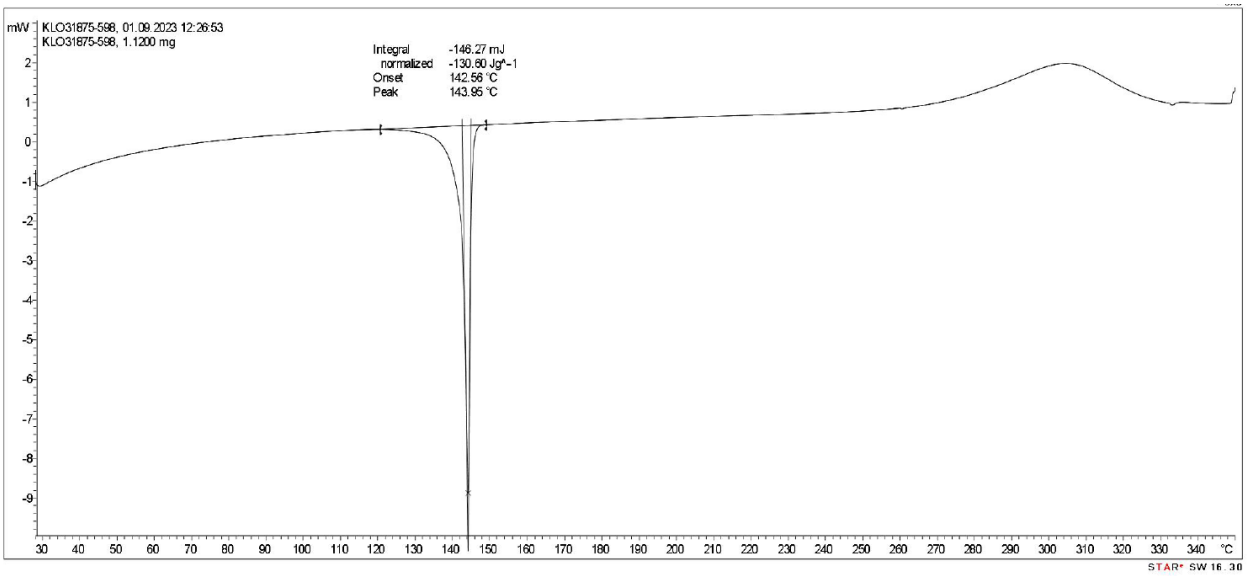
cm-1

DSC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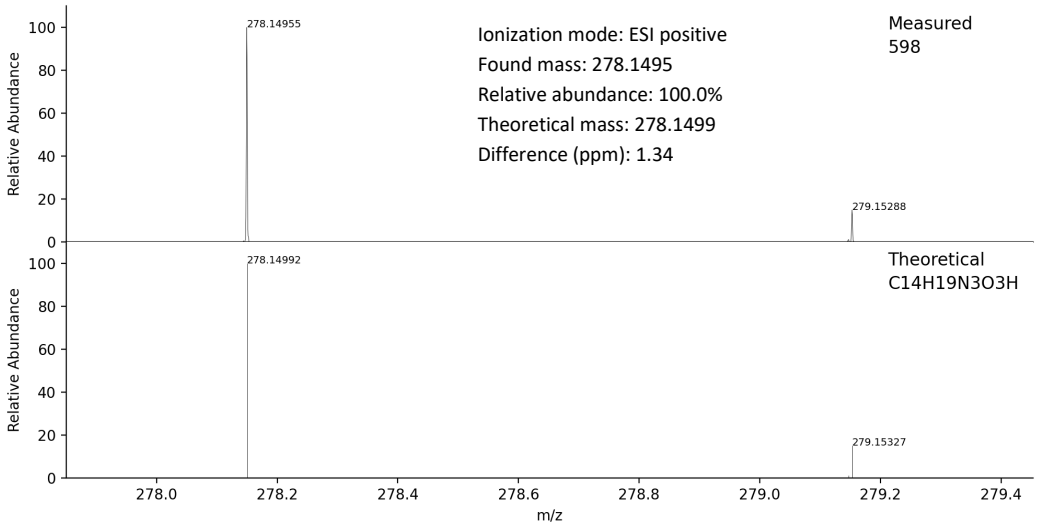
KLO31875-598, 1.1200 mg
Integral -146.27 mJ
normalized -130.60 Jg^-1
Onset 142.56 °C
Peak 143.95 °C
°C

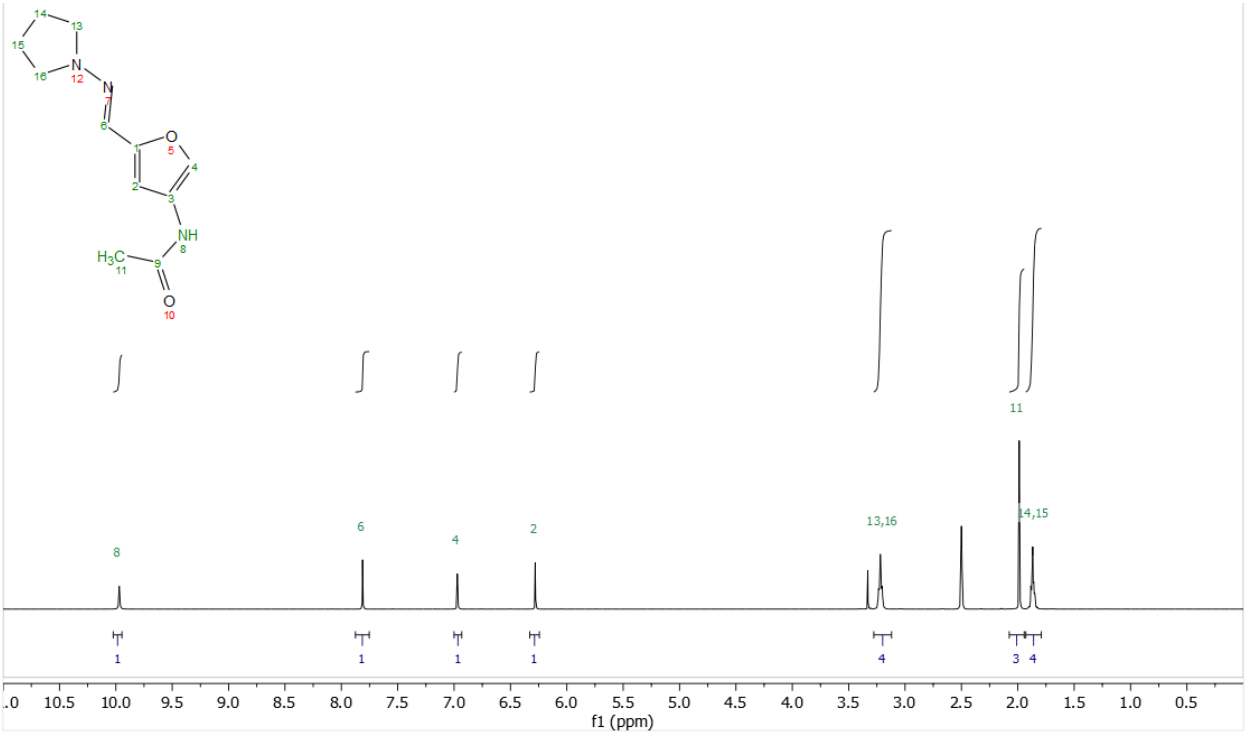
HRMS


Relative Abundance
278.14955
279.15288
Ionization mode: ESI positive
Found mass: 278.1495
Relative abundance: 100.0%
Theoretical mass: 278.1499
Difference (ppm): 1.34
Measured
598
278.14992
279.15327
Theoretical
C14H19N3O3H
m/z

S33. **Spectra of 12**

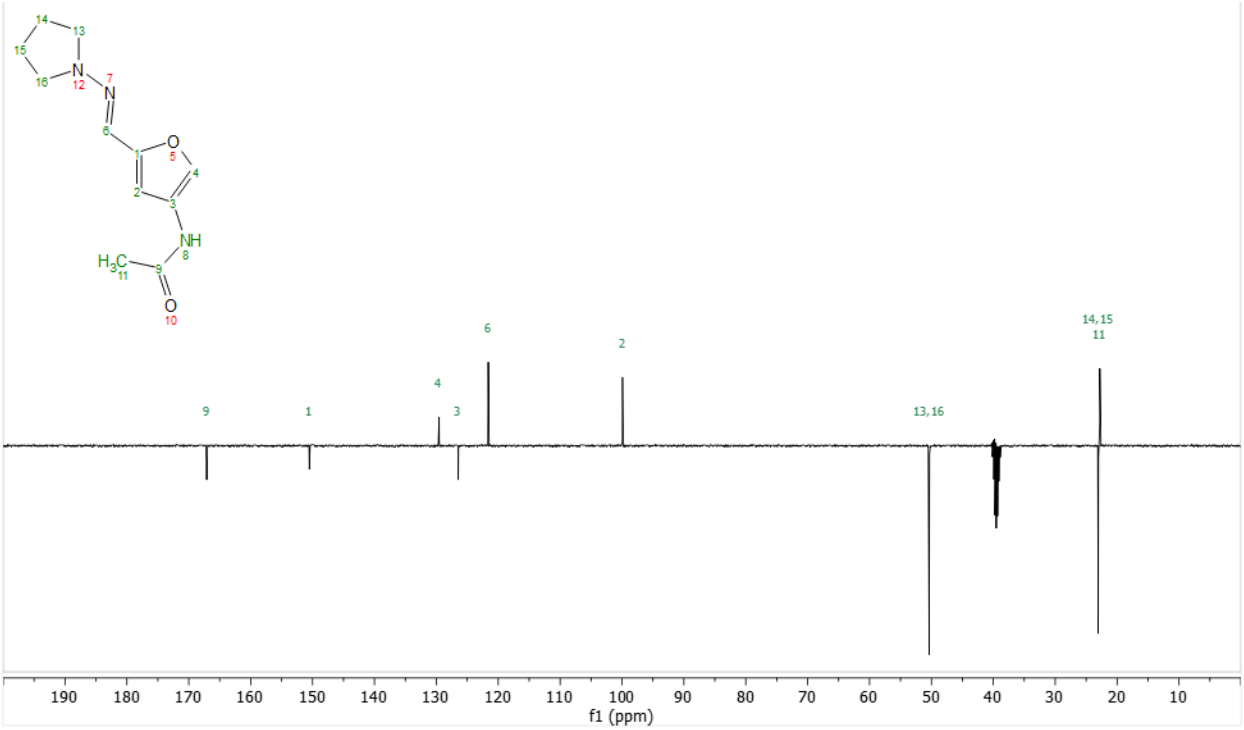
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.97 (s, 1H), 7.81 (s, 1H), 6.97 (s, 1H), 6.28 (s, 1H), 3.28 – 3.12 (m, 4H), 1.99 (s, 3H), 1.93 – 1.79 (m, 4H)

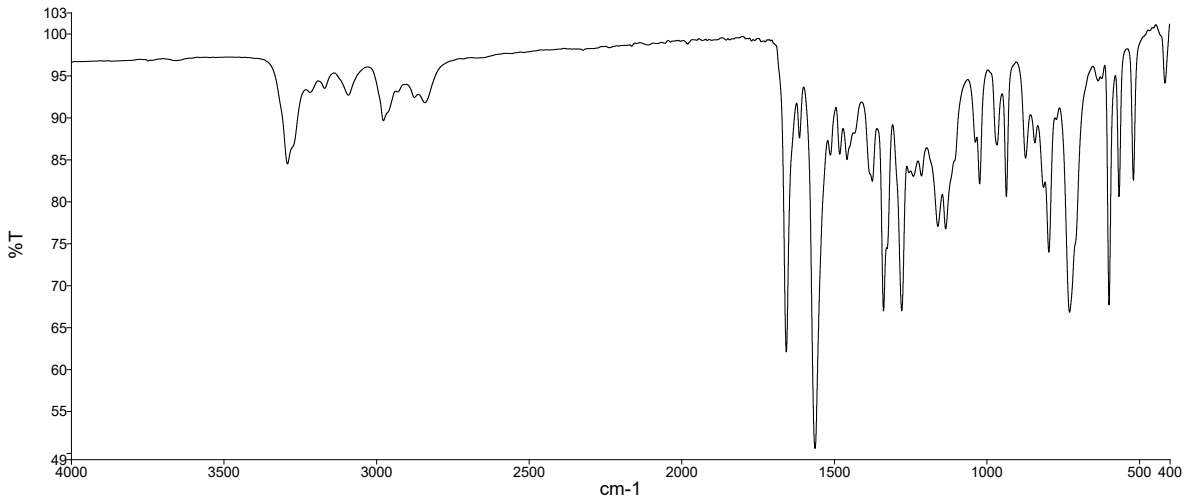


^{13}C-NMR (DMSO-d_6)

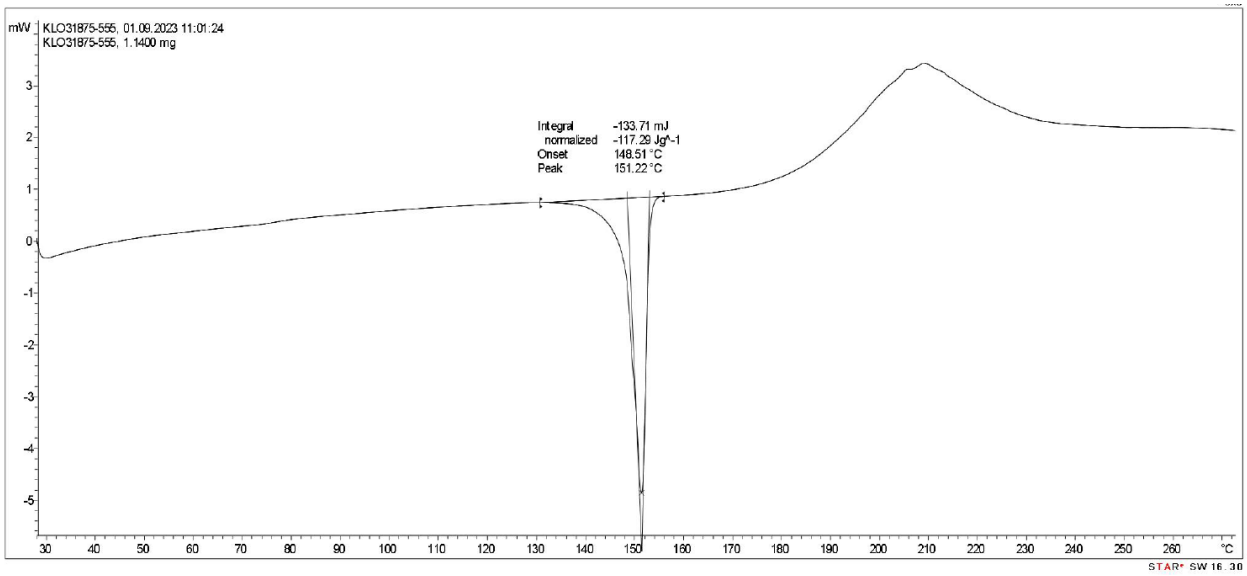
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.10, 150.51, 129.55, 126.45, 121.60, 99.91, 50.36, 23.04, 22.79



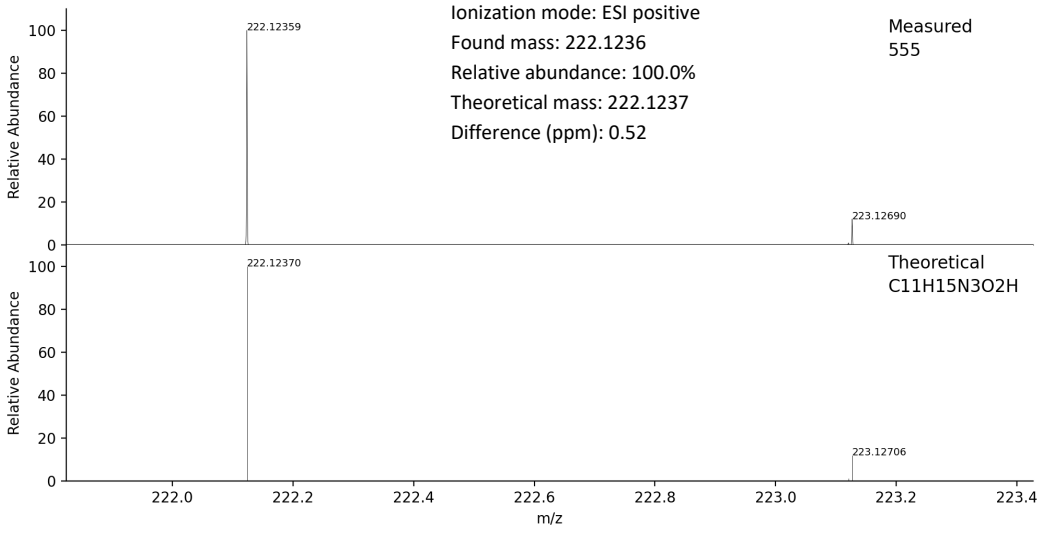
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500 400

DSC


mW
KLO31875-555, 01.09.2023 11:01:24
KLO31875-555, 1.1400 mg
Integral -133.71 mJ
normalized -117.29 Jg^-1
Onset 148.51 °C
Peak 151.22 °C
°C

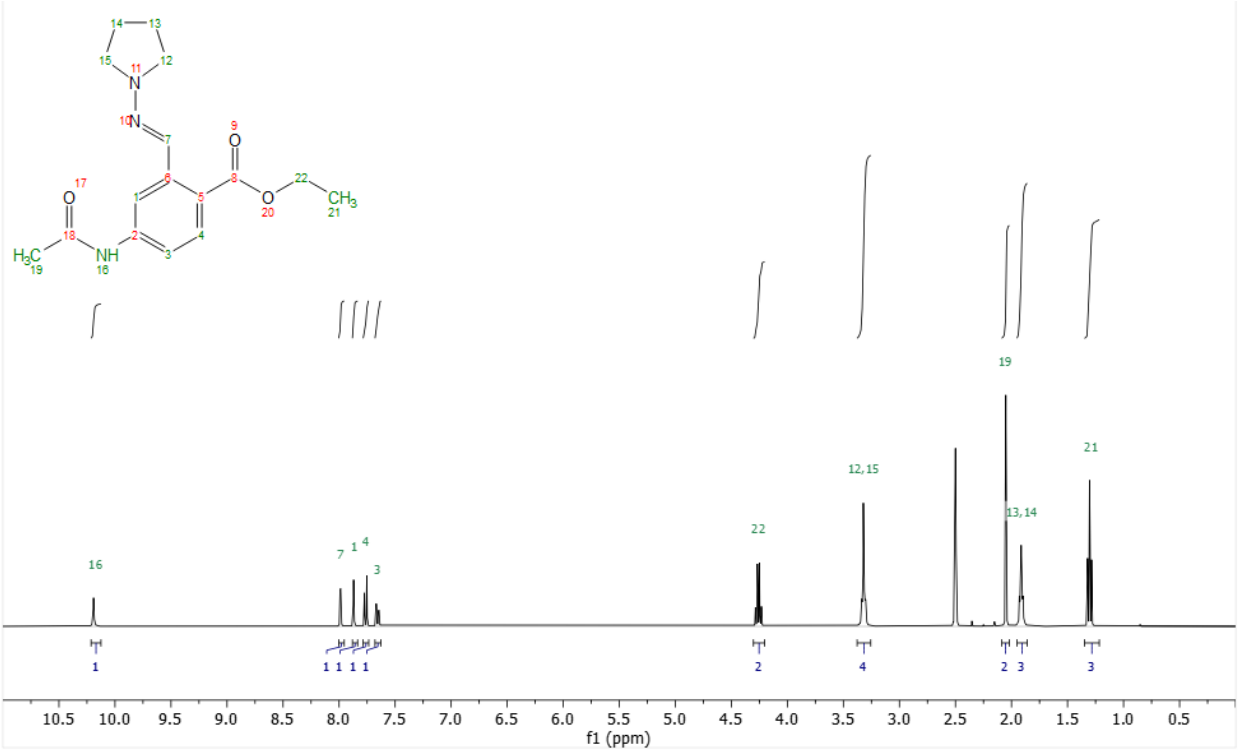
HRMS


Ionization mode: ESI positive
Found mass: 222.1236
Relative abundance: 100.0%
Theoretical mass: 222.1237
Difference (ppm): 0.52
Measured
555
222.12359
223.12690
Theoretical
C11H15N3O2H
222.12370
223.12706
Relative Abundance
m/z

S34. **Spectra of 13**

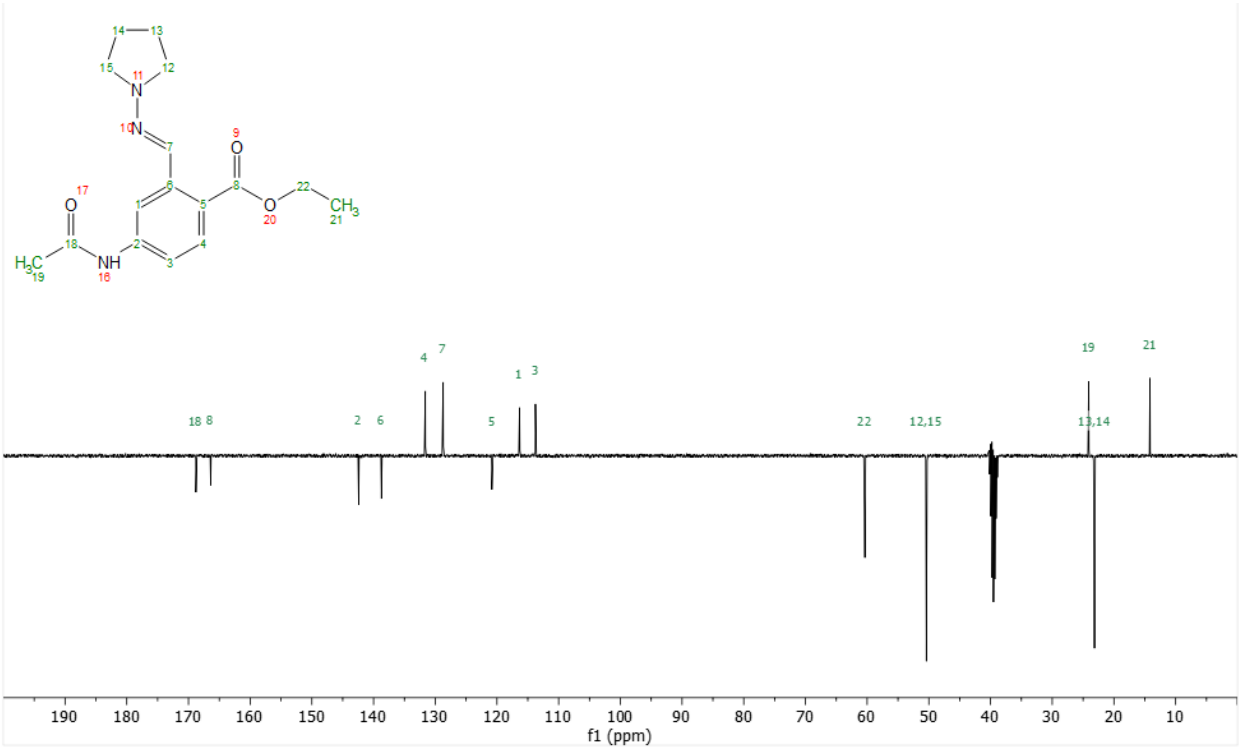
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.19 (s, 1H), 7.99 (d, 1H), 7.87 (s, 1H), 7.76 (d, 1H), 7.66 (dd, 1H), 4.26 (q, 2H), 3.38 – 3.26 (m, 4H), 2.05 (s, 2H), 1.95 – 1.86 (m, 3H), 1.30 (t, 3H)

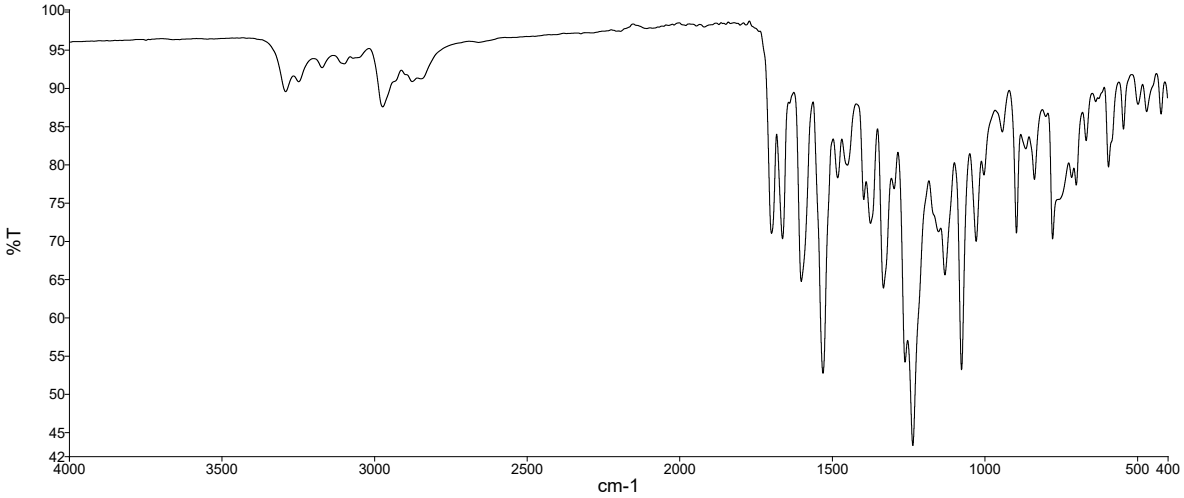


^{13}C-NMR (DMSO-d_6)

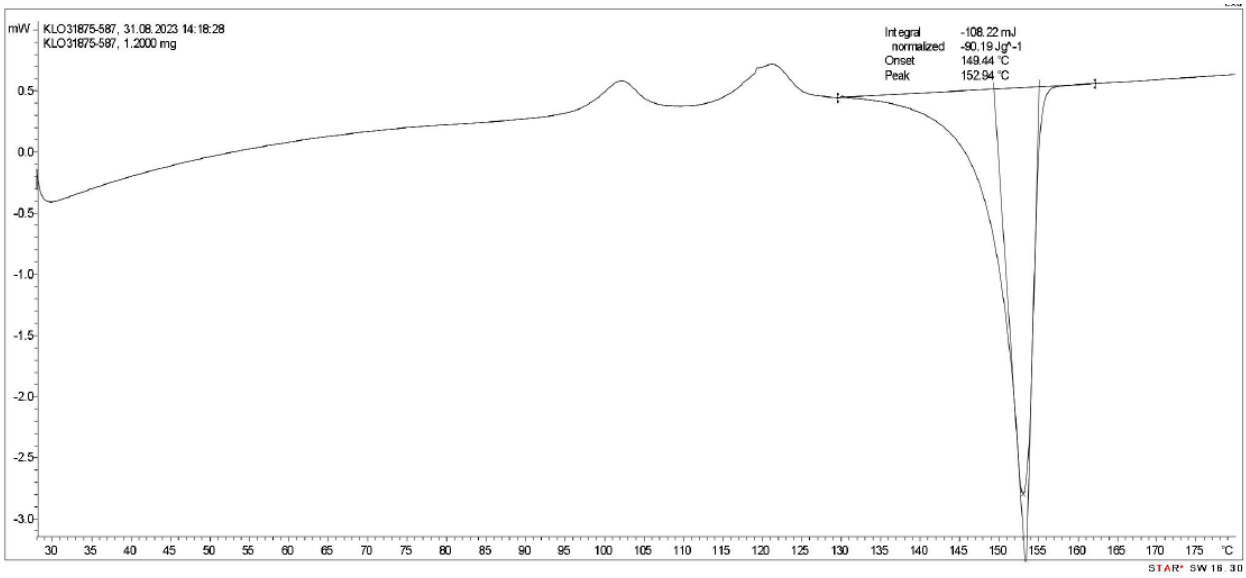
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.79, 142.41, 138.72, 131.61, 128.72, 120.82, 116.33, 113.76, 60.36, 50.40, 24.08, 23.15, 14.15



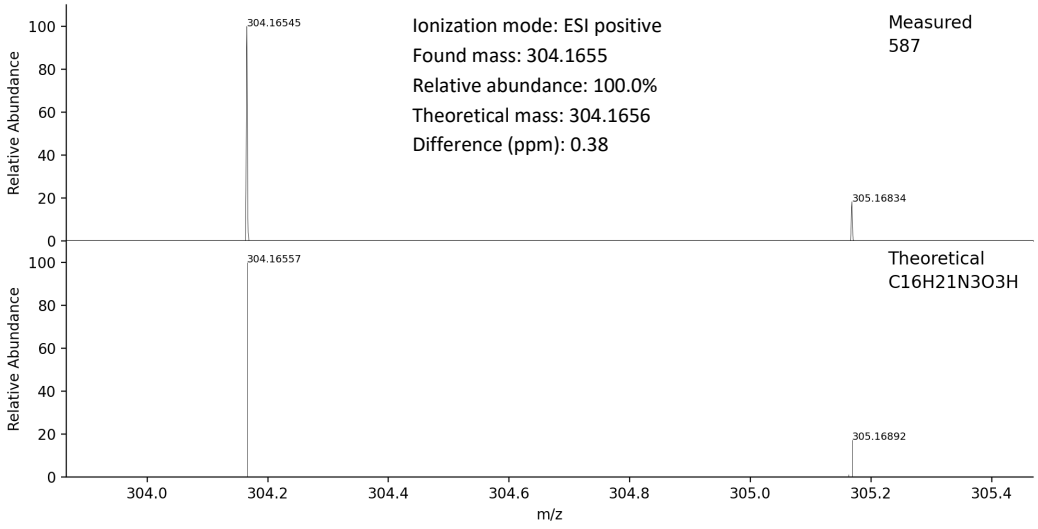
IR


%T
cm-1

DSC


mW
KLO31875-587, 31.08.2023 14:18:28
KLO31875-587, 1.2000 mg
Integral -108.22 mJ
normalized -90.19 Jg^-1
Onset 149.44 °C
Peak 152.94 °C
°C

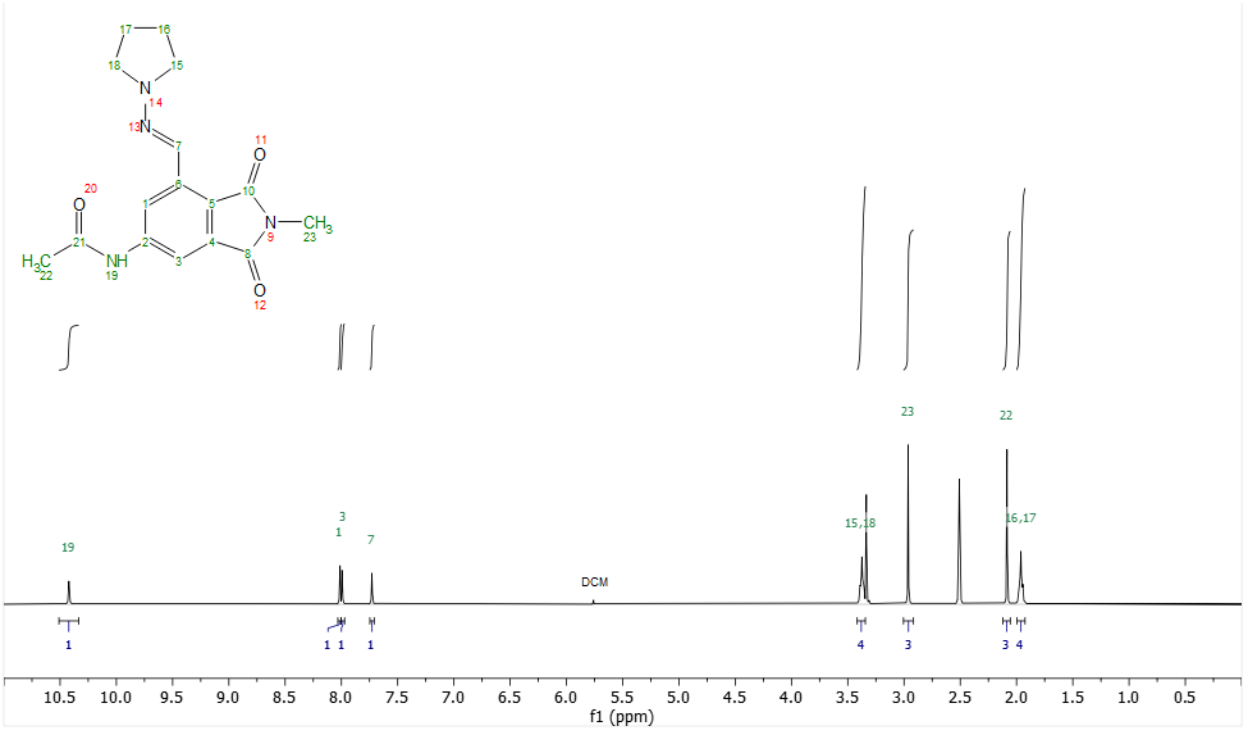
HRMS


304.16545
Ionization mode: ESI positive
Found mass: 304.1655
Relative abundance: 100.0%
Theoretical mass: 304.1656
Difference (ppm): 0.38
Measured
587
305.16834
Relative Abundance
304.16557
Theoretical
C16H21N3O3H
305.16892
m/z

S35. **Spectra of 14**

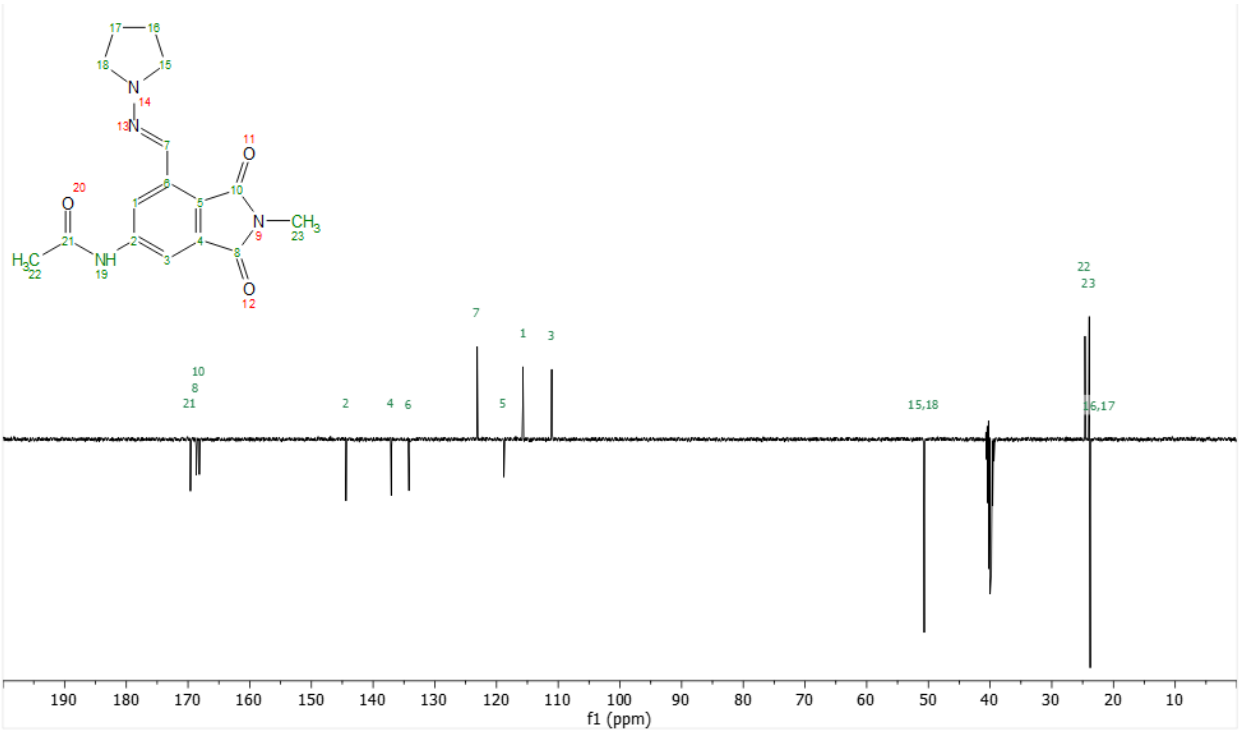
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.41 (s, 1H), 8.01 (d, 1H), 7.98 (d, 1H), 7.72 (s, 1H), 3.41 – 3.34 (m, 4H), 2.95 (s, 3H), 2.08 (s, 3H), 1.99 – 1.92 (m, 4H)

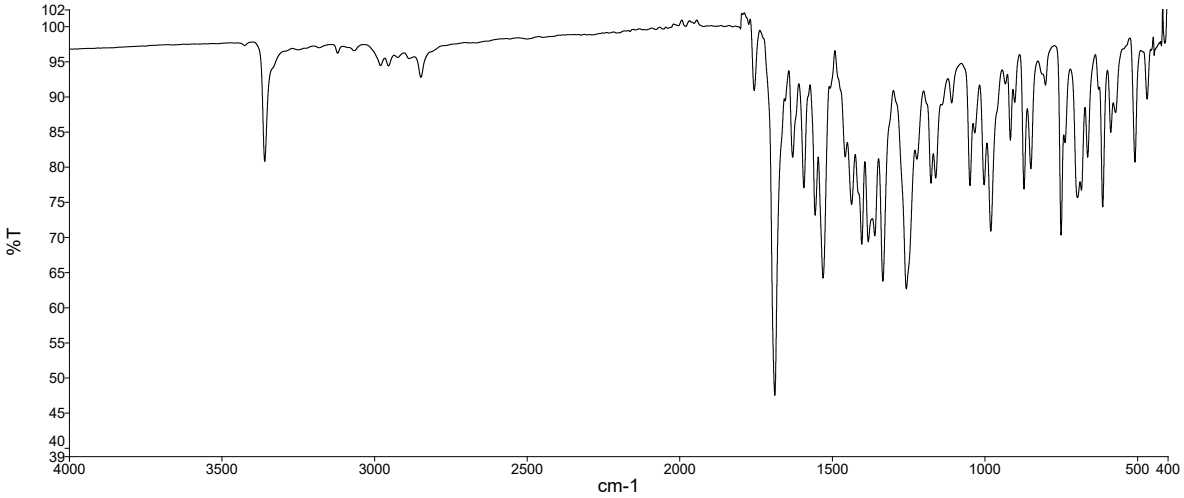


^{13}C-NMR (DMSO-d_6)

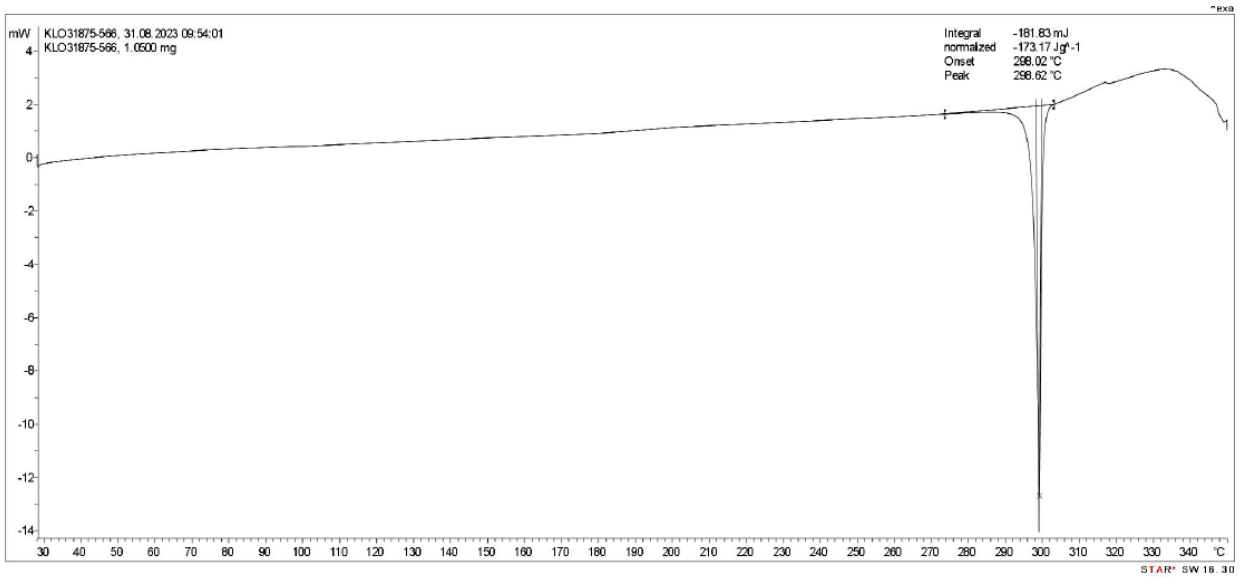
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.13, 168.20, 167.69, 143.92, 136.58, 133.72, 122.65, 118.32, 115.25, 110.57, 50.20, 24.14, 23.38



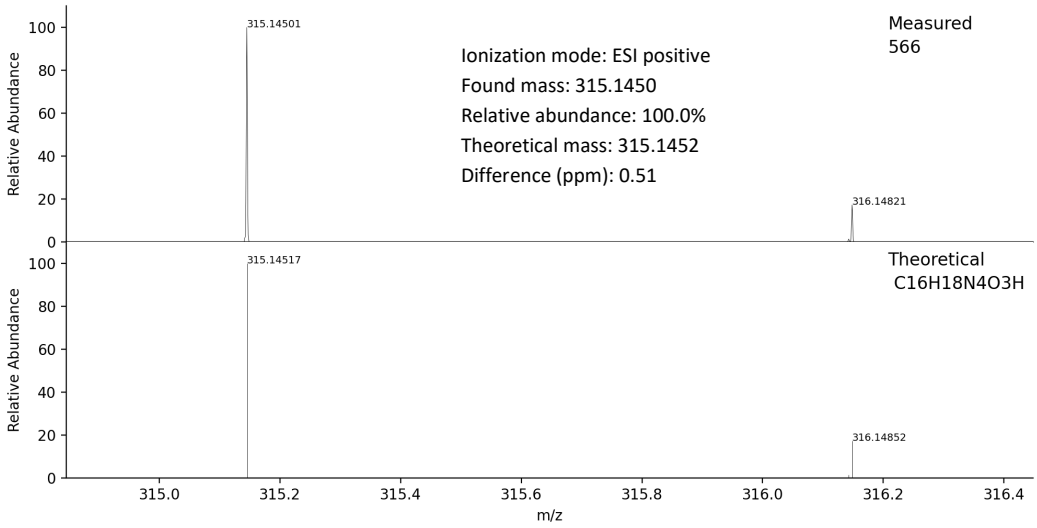
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500
400

DSC


mW
KLO31875-566, 31.08.2023 09:54:01
KLO31875-566, 1.0500 mg
Integral -181.83 mJ
normalized -173.17 Jg^-1
Onset 298.02 °C
Peak 298.62 °C
°C

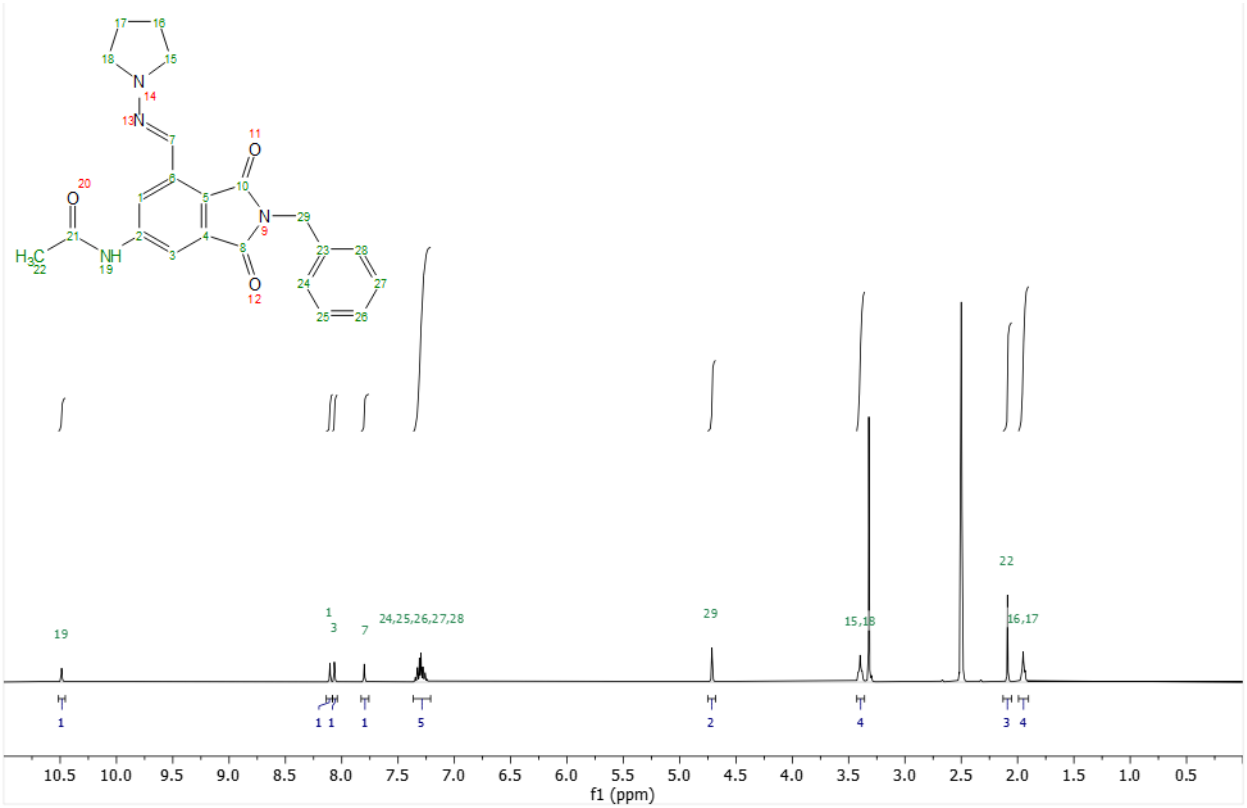
HRMS


Relative Abundance
315.14501
316.14821
Measured
566
Ionization mode: ESI positive
Found mass: 315.1450
Relative abundance: 100.0%
Theoretical mass: 315.1452
Difference (ppm): 0.51
315.14517
316.14852
Theoretical
C16H18N4O3H
m/z

S36. **Spectra of 15**

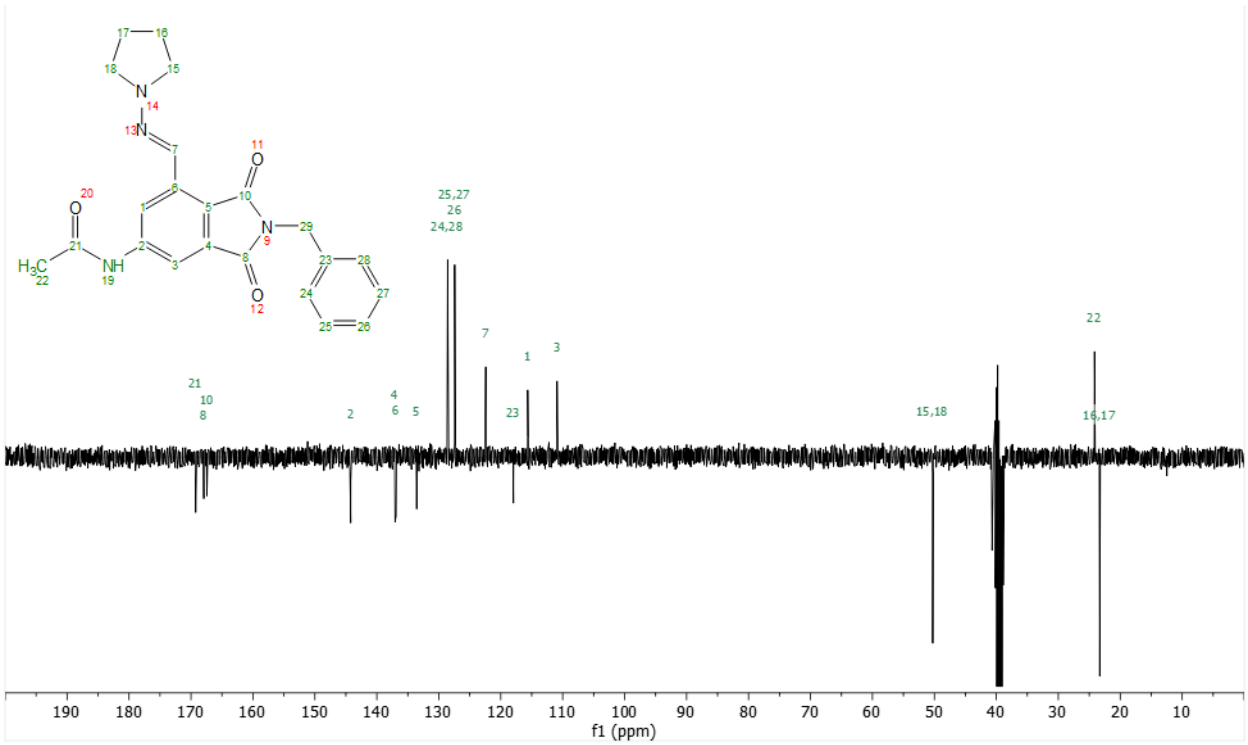
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.49 (s, 1H), 8.11 (d, 1H), 8.06 (d, 1H), 7.80 (s, 1H), 7.37 – 7.21 (m, 5H), 4.71 (s, 2H), 3.43 – 3.36 (m, 4H), 2.09 (s, 3H), 1.99 – 1.90 (m, 4H)

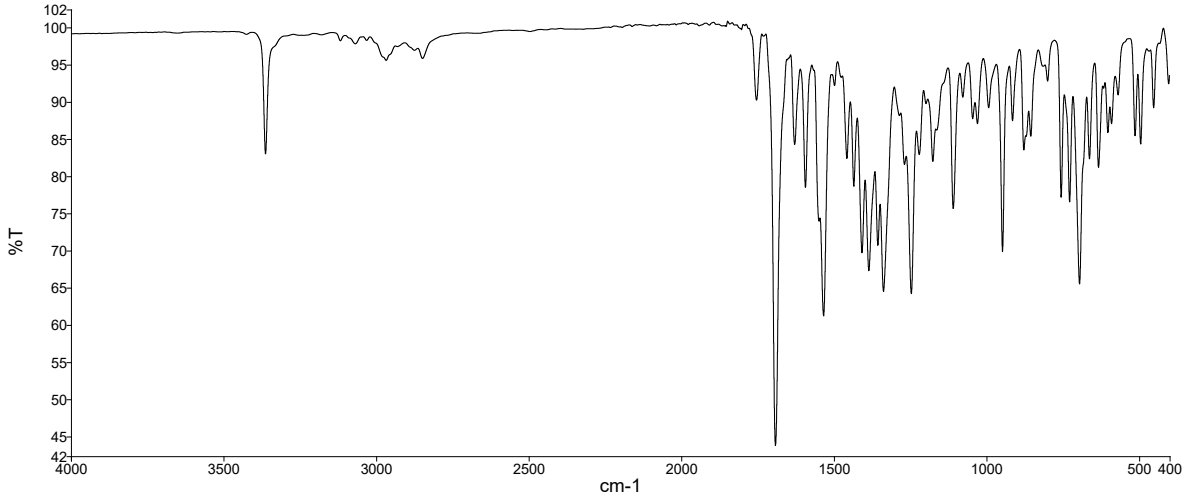


^{13}C-NMR (DMSO-d_6)

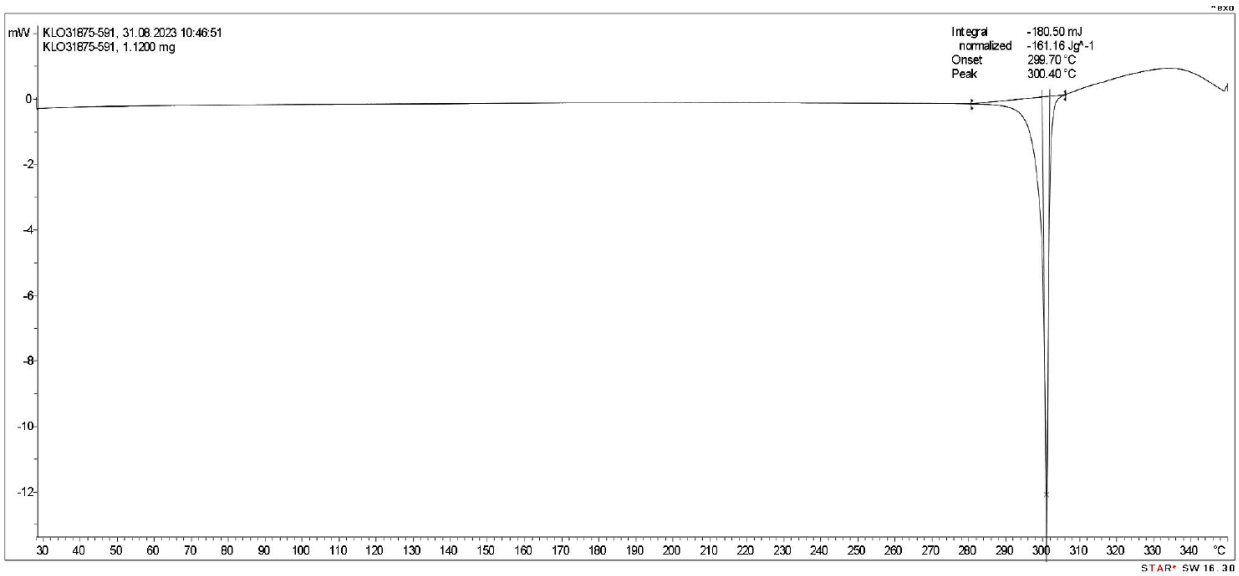
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.23, 144.21, 137.06, 136.89, 133.57, 128.57, 127.39 (d), 122.42, 117.94, 115.64, 110.90, 50.27, 40.70, 24.16, 23.32



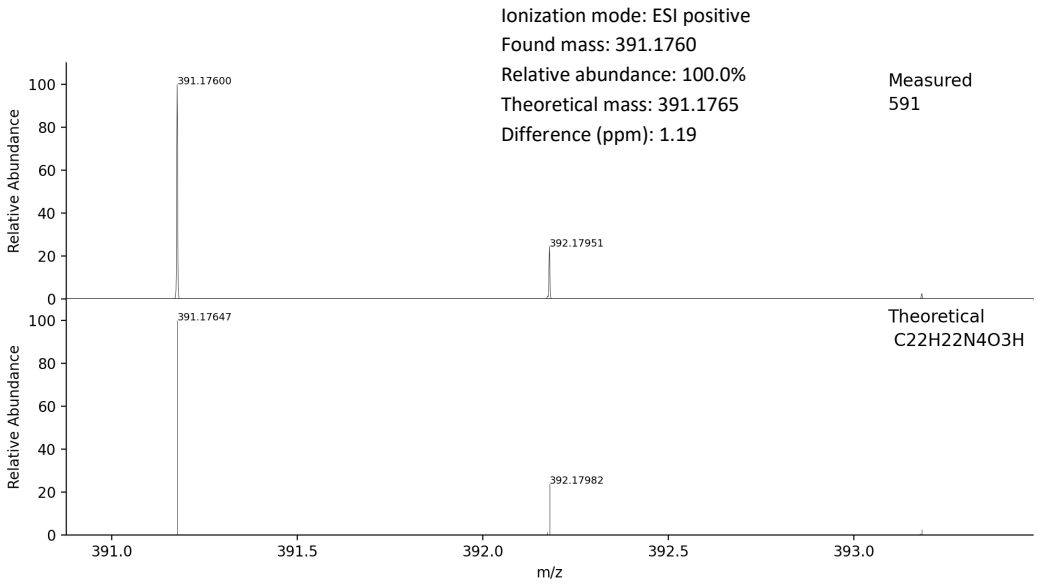
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500

DSC


mW
KLO31875-591, 31.08.2023 10:46:51
KLO31875-591, 1.1200 mg
Integral -180.50 mJ
normalized -161.16 Jg^-1
Onset 299.70 °C
Peak 300.40 °C
°C

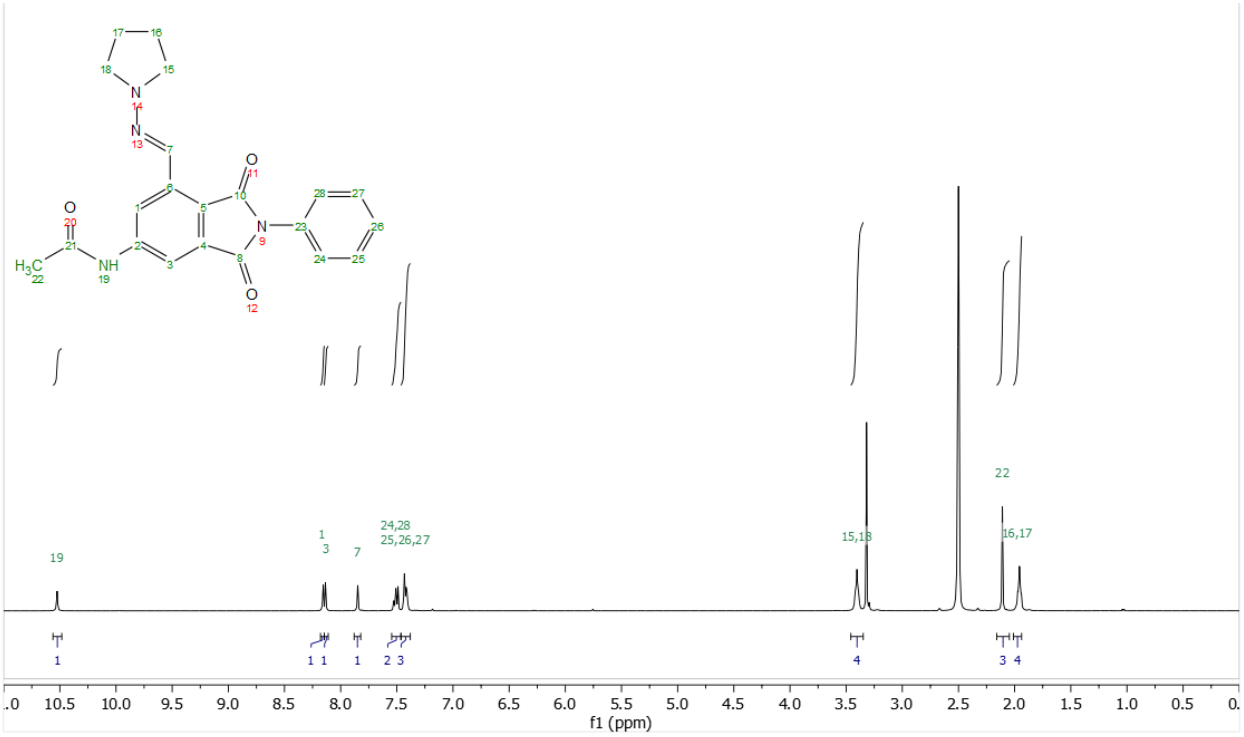
HRMS


Ionization mode: ESI positive
Found mass: 391.1760
Relative abundance: 100.0%
Theoretical mass: 391.1765
Difference (ppm): 1.19
Measured
591
391.17600
392.17951
Relative Abundance
Theoretical
C22H22N4O3H
391.17647
392.17982
m/z

S37. **Spectra of 16**

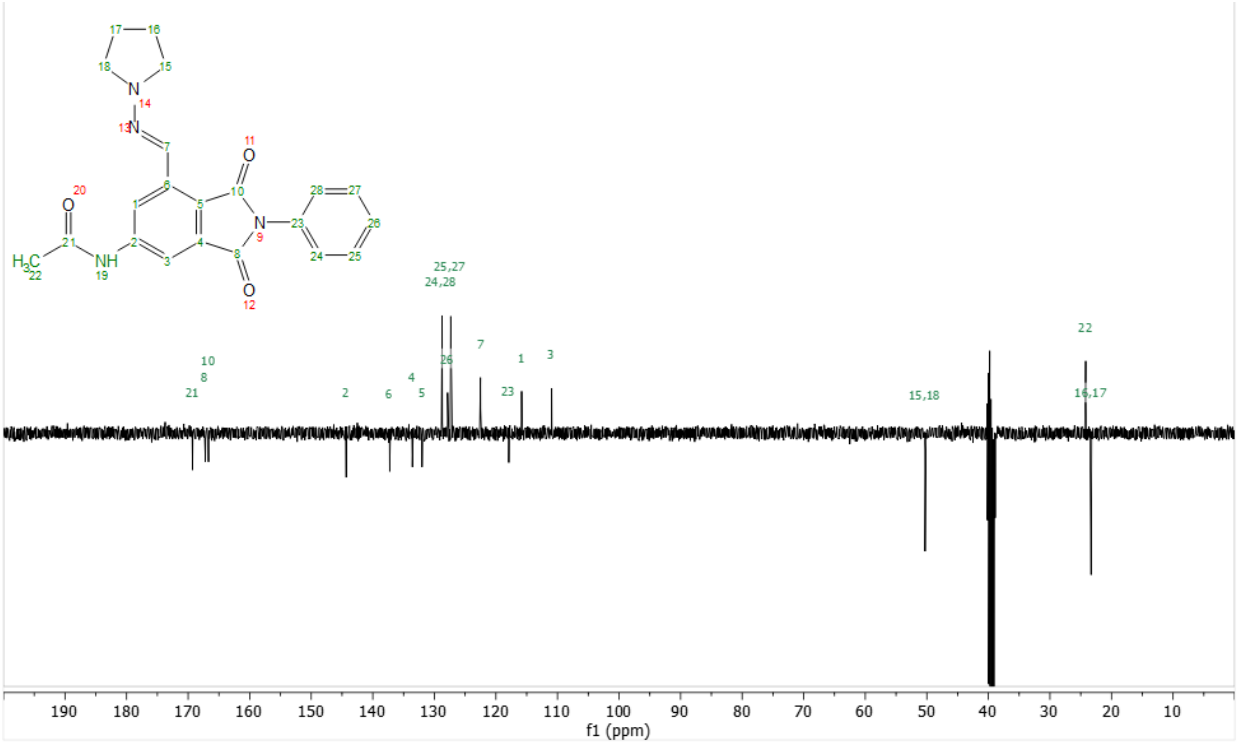
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.52 (s, 1H), 8.16 (d, 1H), 8.13 (d, 1H), 7.85 (s, 1H), 7.55 – 7.46 (m, 2H), 7.42 (dt, 3H), 3.46 – 3.35 (m, 4H), 2.11 (s, 3H), 2.01 – 1.94 (m, 4H)

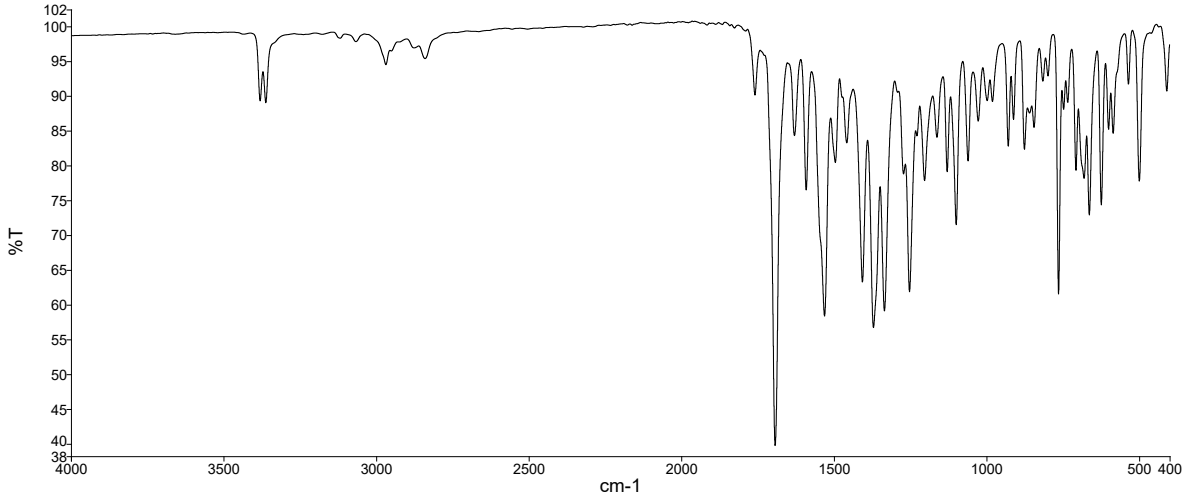


^{13}C-NMR (DMSO-d_6)

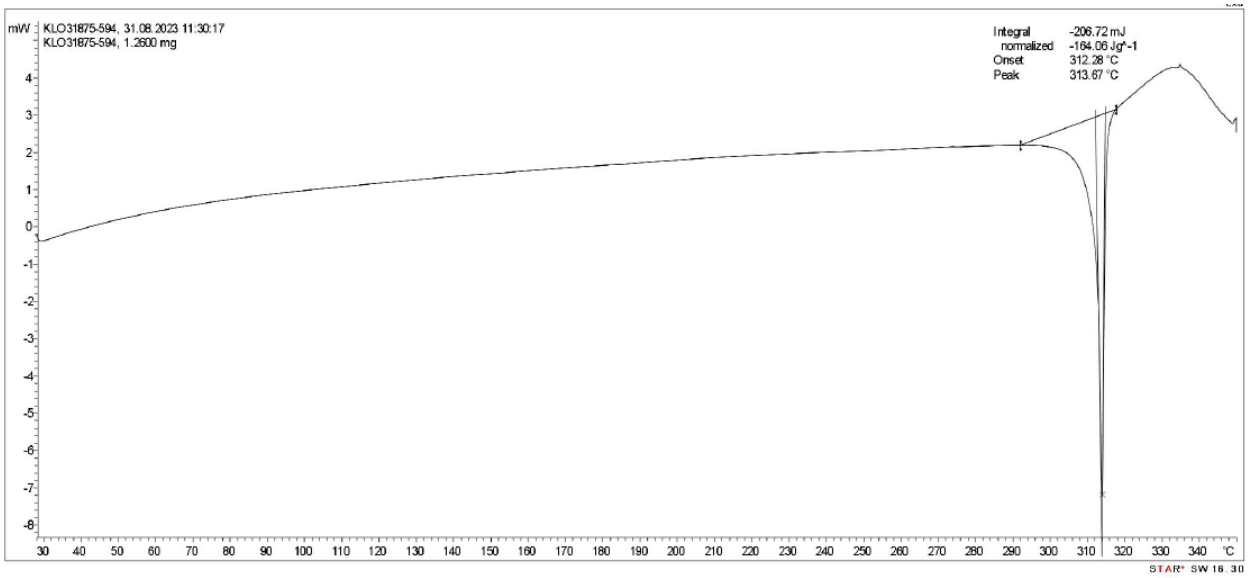
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.28, 167.20, 166.69, 144.32, 137.26, 133.57, 131.99, 128.73, 127.85, 127.34, 122.50, 117.90, 115.82, 110.94, 50.28, 24.19, 23.32



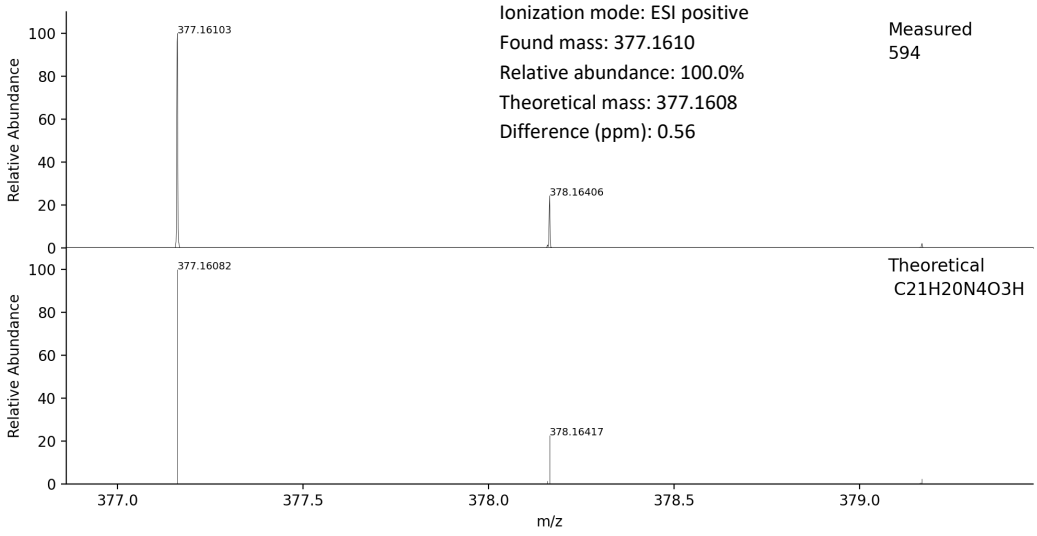
IR


%T
cm-1

DSC


mW
KLO31875-594, 31.08.2023 11:30:17
KLO31875-594, 1.2600 mg
Integral -206.72 mJ
normalized -164.06 Jg^-1
Onset 312.28 °C
Peak 313.67 °C
°C
STAR° SW 16.30

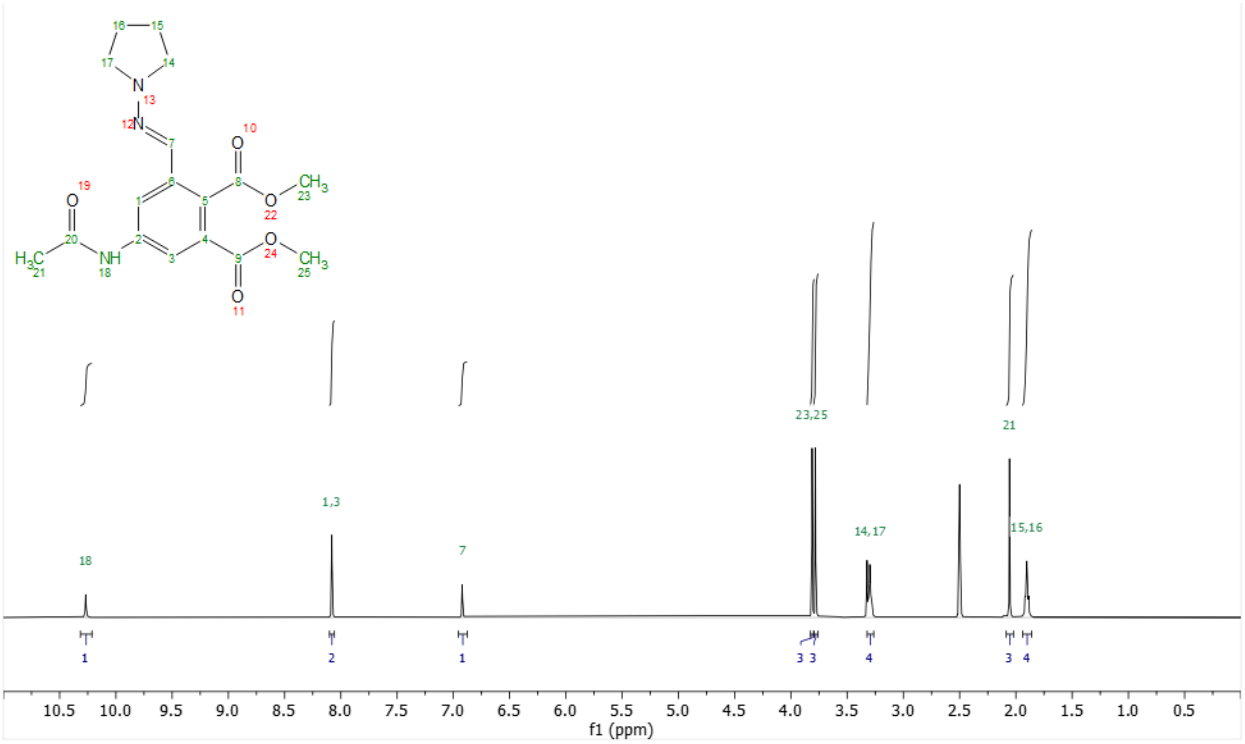
HRMS


Ionization mode: ESI positive
Found mass: 377.1610
Relative abundance: 100.0%
Theoretical mass: 377.1608
Difference (ppm): 0.56
Measured
594
377.16103
378.16406
Theoretical
C21H20N4O3H
377.16082
378.16417
Relative Abundance
m/z

S38. **Spectra of 17**

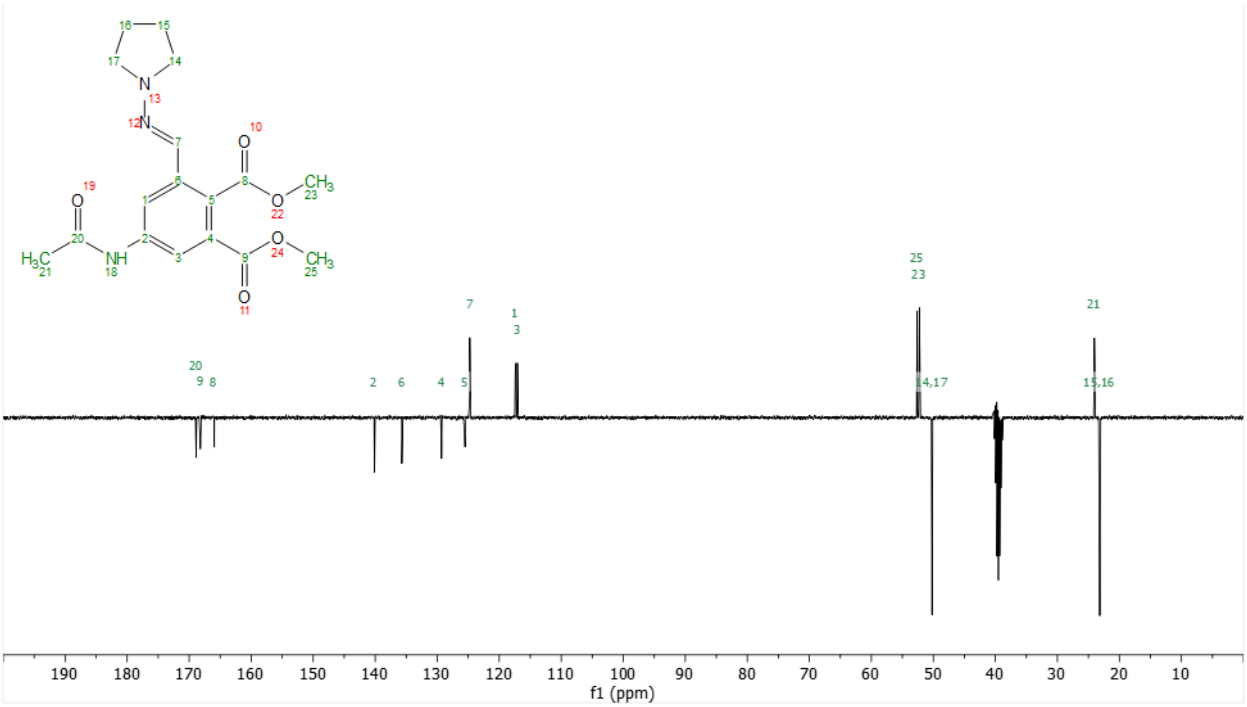
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.27 (s, 1H), 8.08 (s, 2H), 6.92 (s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.32 – 3.26 (m, 4H), 2.06 (s, 3H), 1.94 – 1.86 (m, 4H)

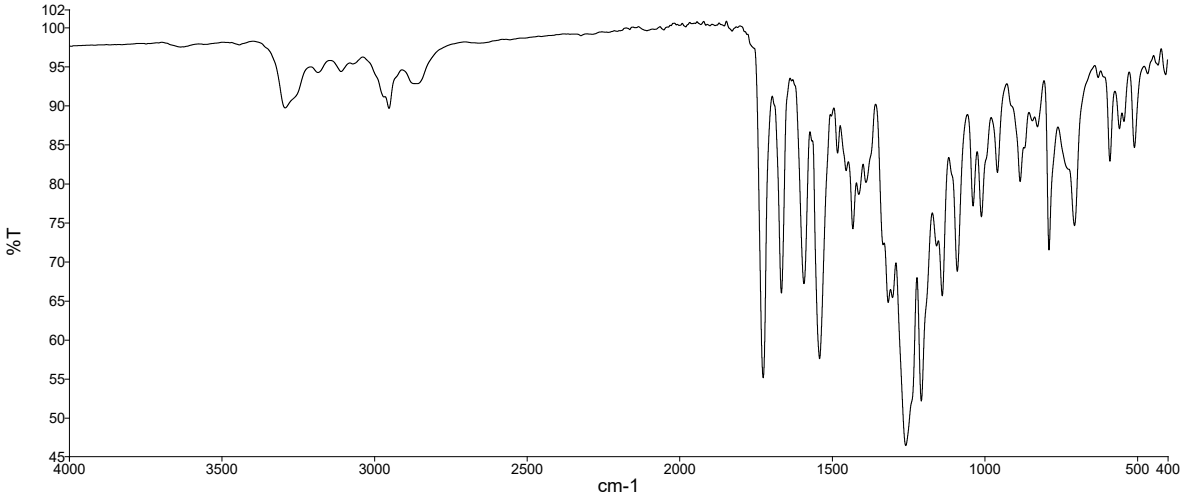


^{13}C-NMR (DMSO-d_6)

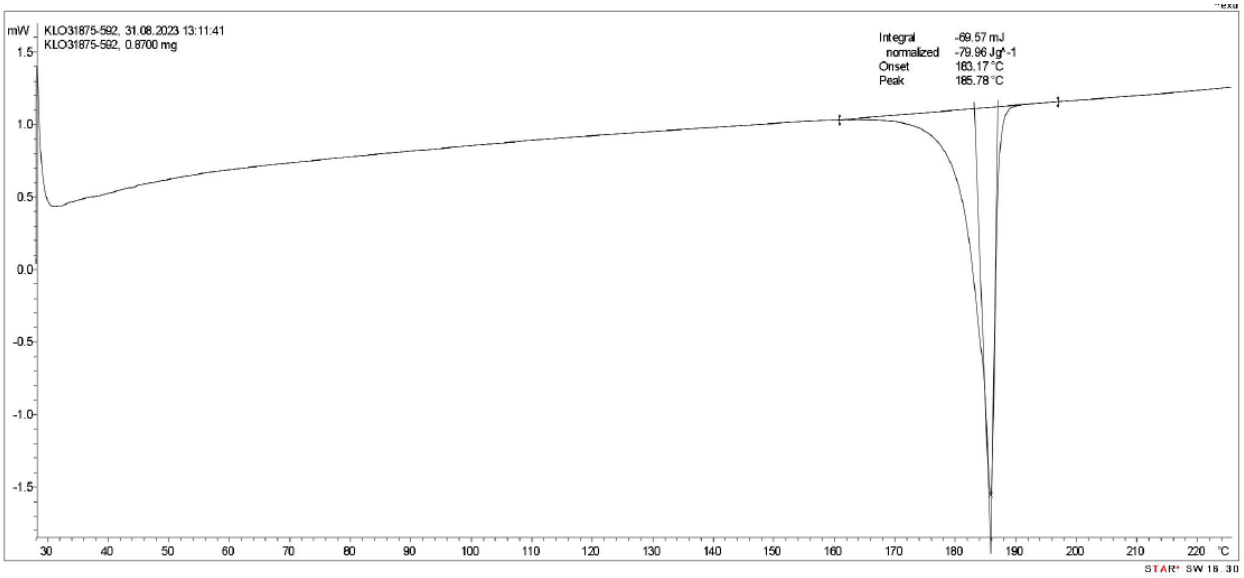
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.87, 168.19, 165.95, 140.12, 135.70, 129.31, 124.75, 117.40, 117.07, 52.61, 52.26, 50.21, 24.03, 23.16



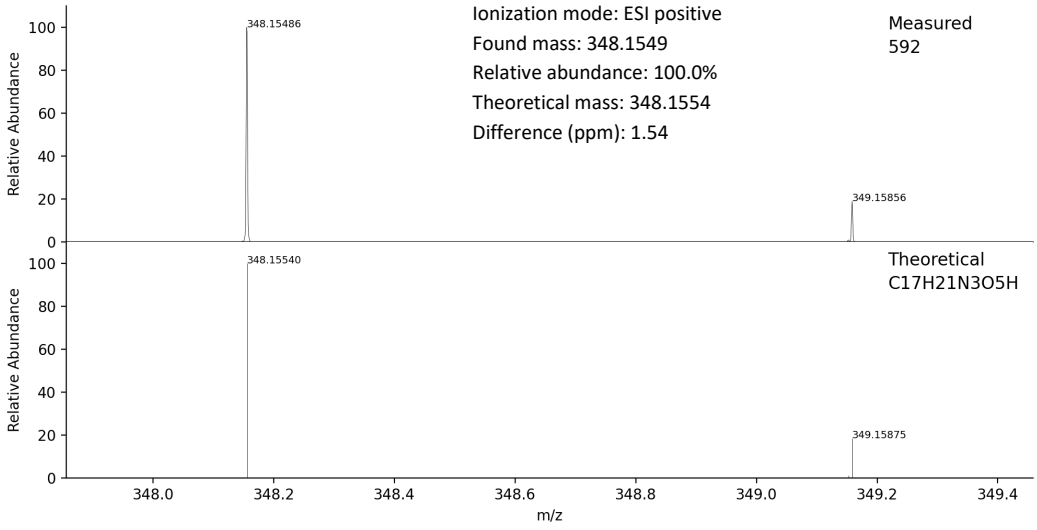
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500
400

DSC


mW
KLO31875-592, 31.08.2023 13:11:41
KLO31875-592, 0.8700 mg
Integral -69.57 mJ
normalized -79.96 Jg^-1
Onset 183.17 °C
Peak 185.78 °C
°C

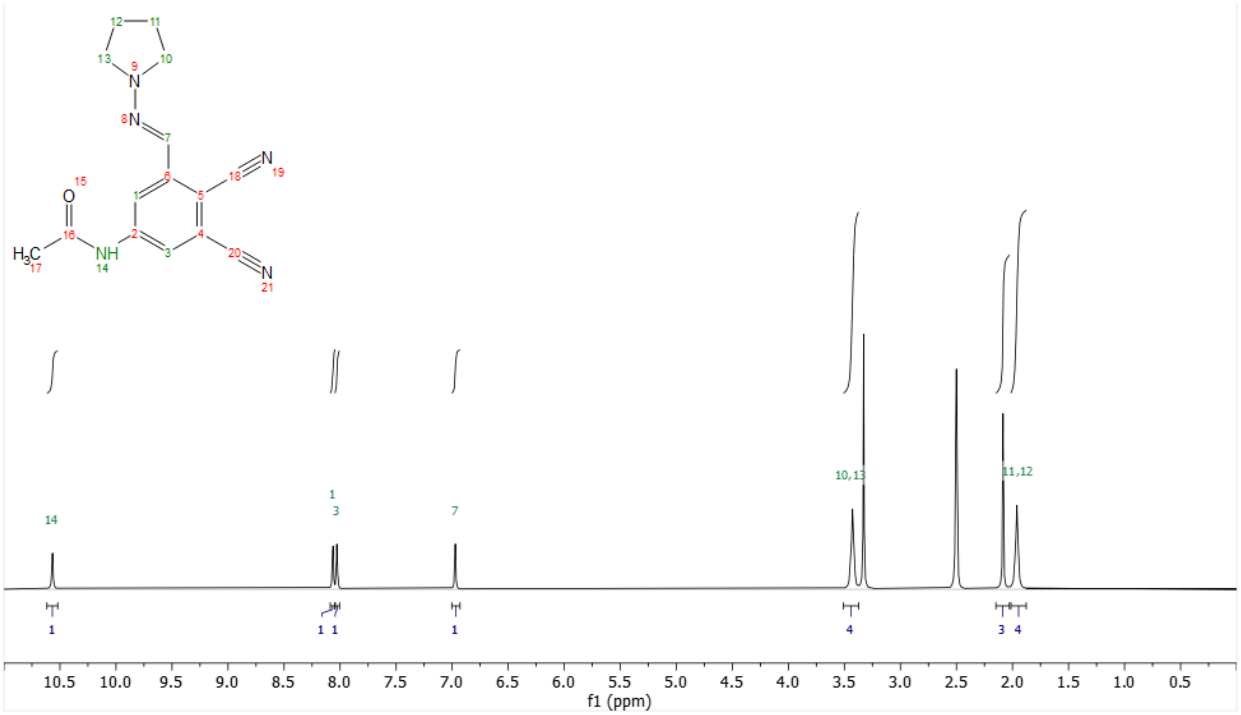
HRMS


Ionization mode: ESI positive
Found mass: 348.1549
Relative abundance: 100.0%
Theoretical mass: 348.1554
Difference (ppm): 1.54
Measured
592
348.15486
349.15856
Theoretical
C17H21N3O5H
348.15540
349.15875
Relative Abundance
m/z

S39. **Spectra of 18**

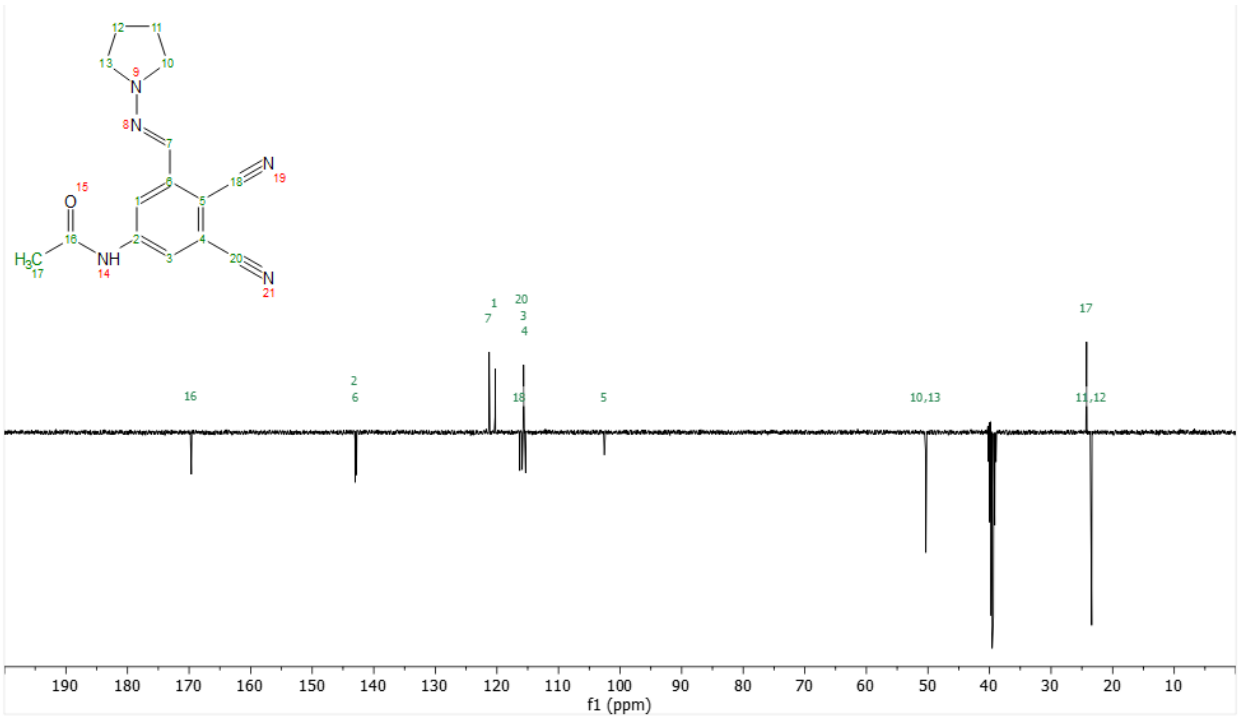
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.57 (s, 1H), 8.06 (d, 1H), 8.03 (d, 1H), 6.97 (s, 1H), 3.51 – 3.37 (m, 4H), 2.08 (s, 3H), 2.01 – 1.88 (m, 4H)

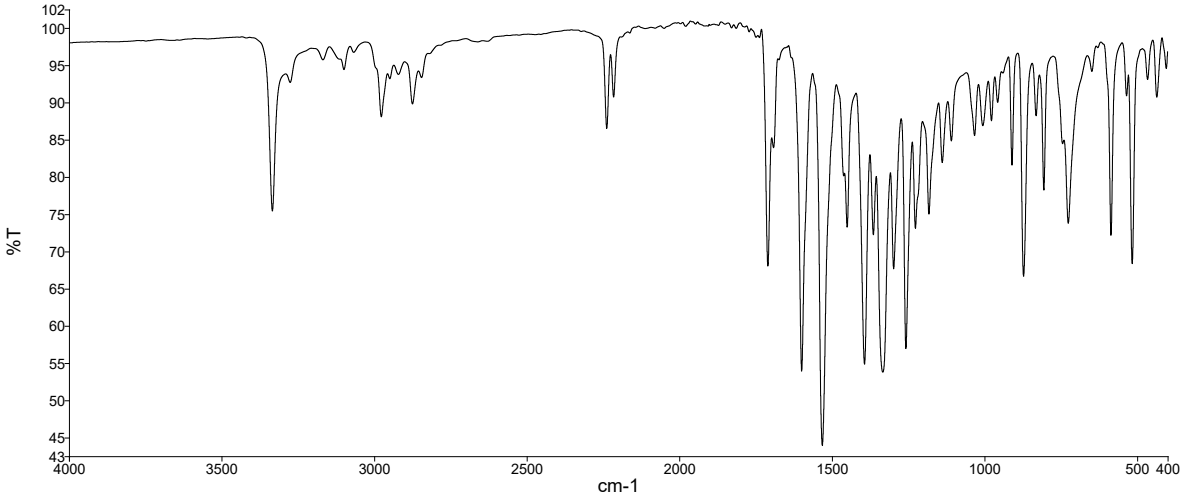


^{13}C-NMR (DMSO-d_6)

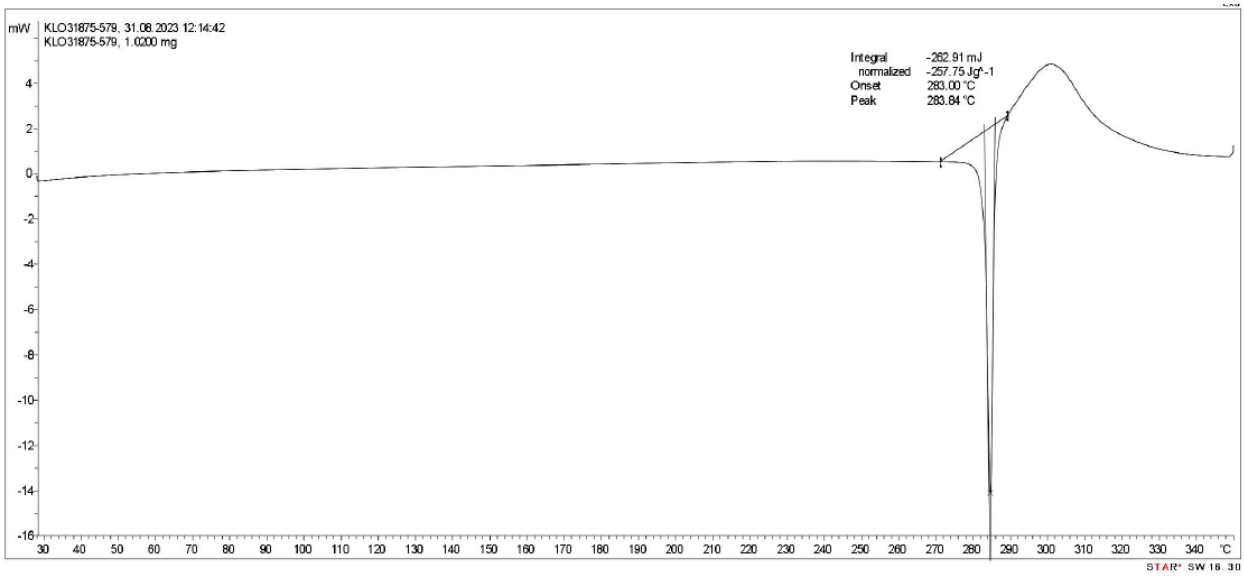
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.63, 143.04, 142.81, 121.26, 120.27, 116.29, 115.90, 115.67, 115.34, 102.56, 50.33, 24.23, 23.40



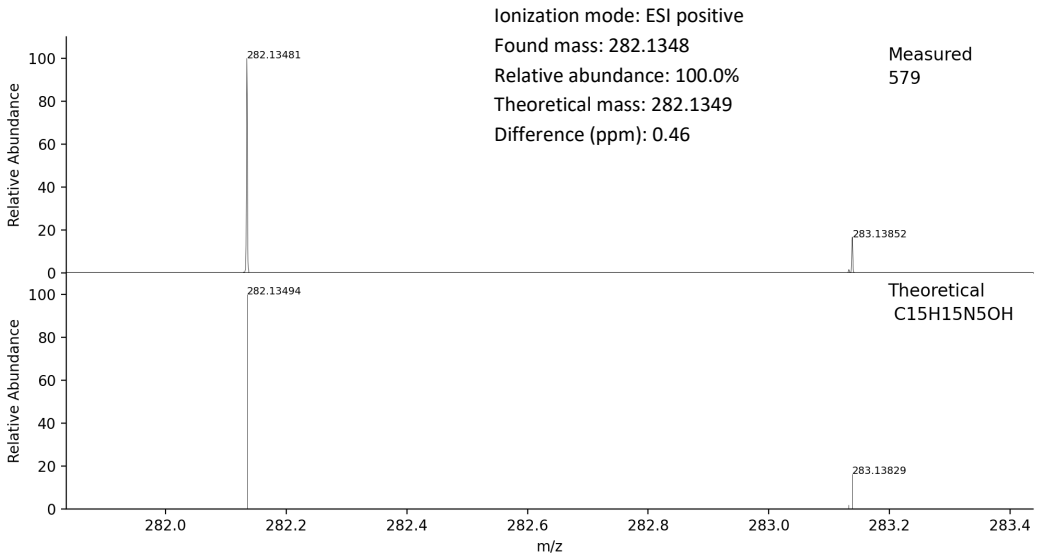
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500 400

DSC


mW
KLO31875-579, 31.08.2023 12:14:42
KLO31875-579, 1.0200 mg
Integral -262.91 mJ
normalized -257.75 Jg^-1
Onset 283.00 °C
Peak 283.84 °C
°C

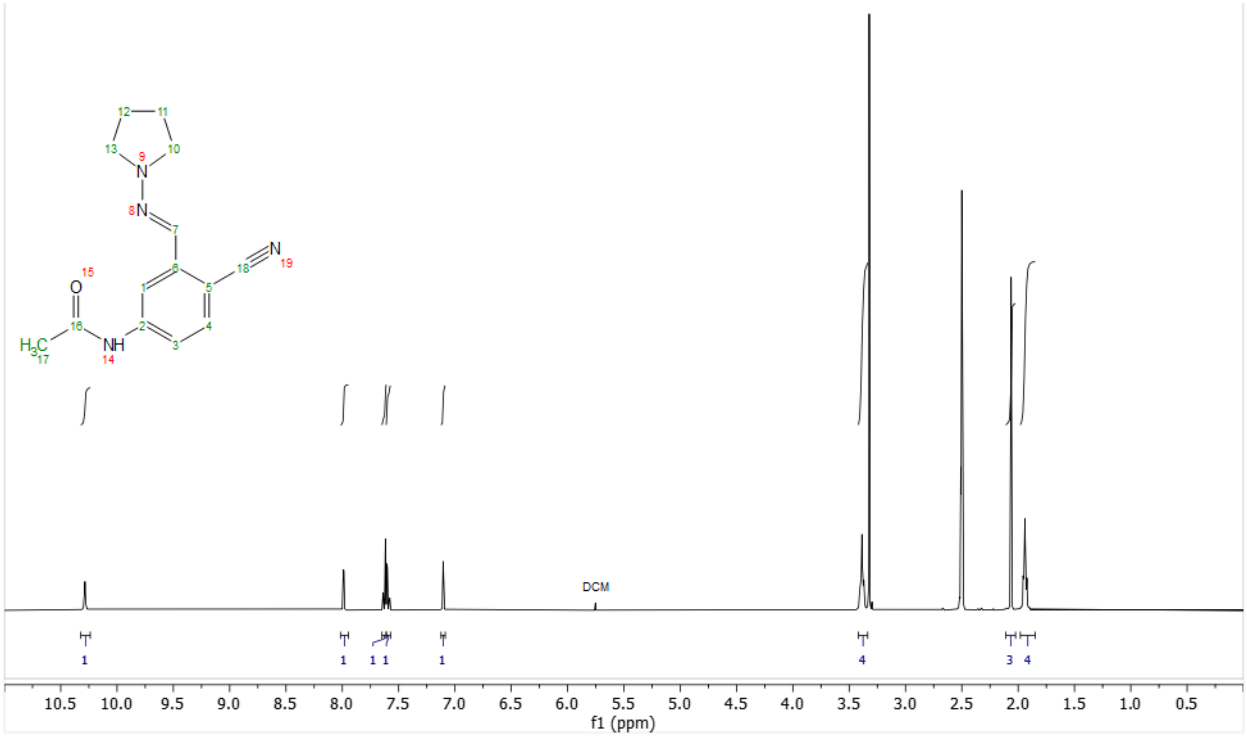
HRMS


Ionization mode: ESI positive
Found mass: 282.1348
Relative abundance: 100.0%
Theoretical mass: 282.1349
Difference (ppm): 0.46
Measured
579
282.13481
283.13852
Theoretical
C15H15N5OH
282.13494
283.13829
Relative Abundance
m/z

S40. **Spectra of 19**

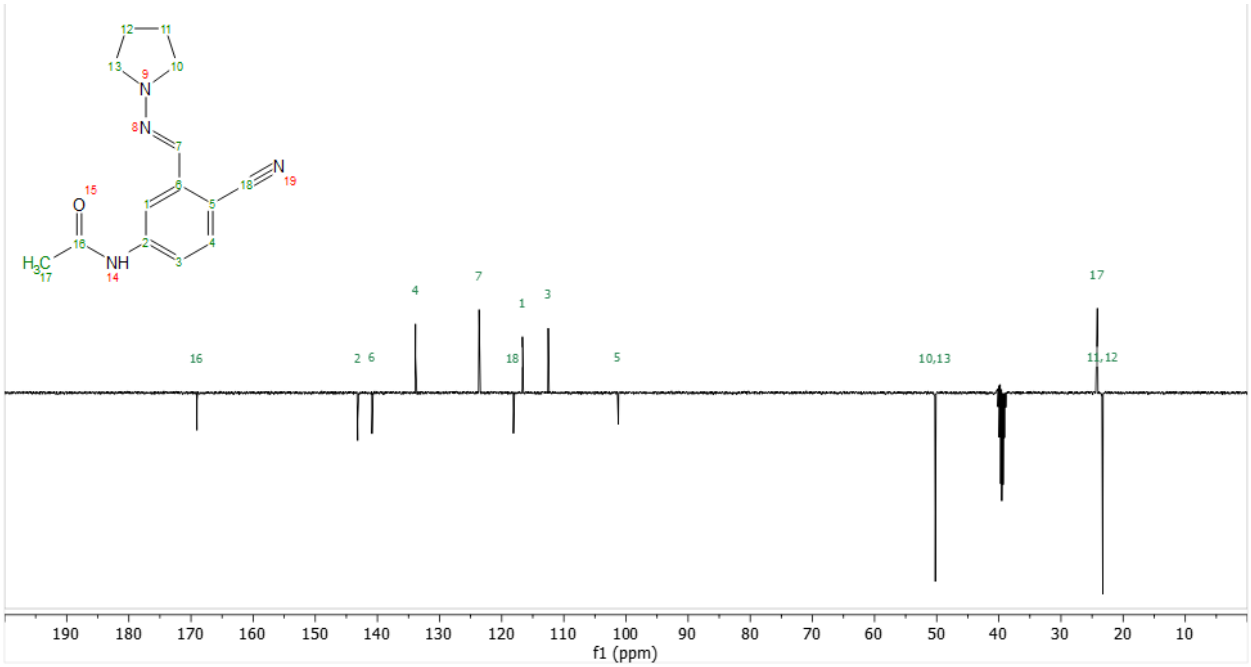
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.28 (s, 1H), 7.99 (d, 1H), 7.63 (dd, 1H), 7.59 (dd, 1H), 7.10 (s, 1H), 3.42 – 3.34 (m, 4H), 2.06 (s, 3H), 1.98 – 1.85 (m, 4H)

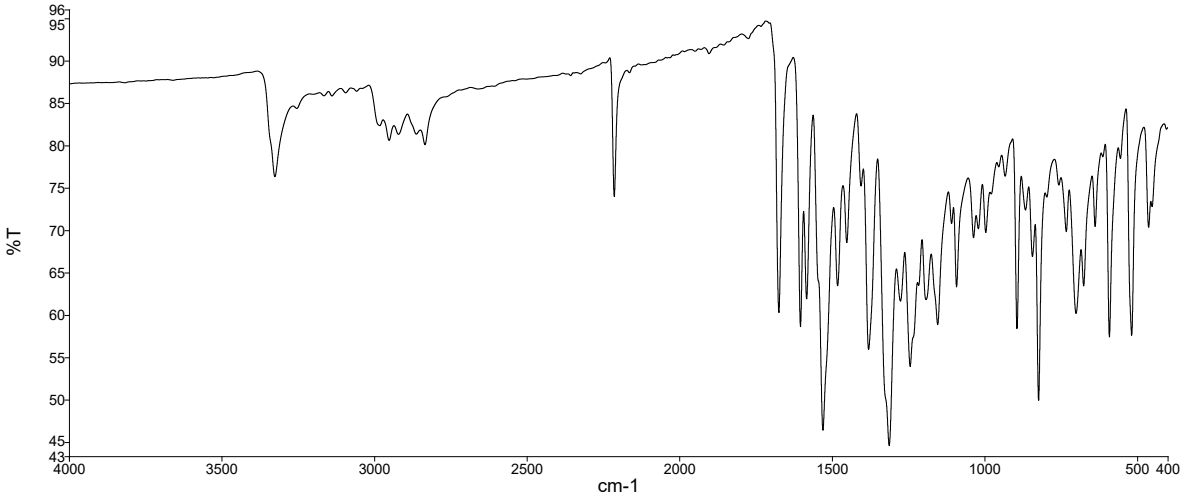


^{13}C-NMR (DMSO-d_6)

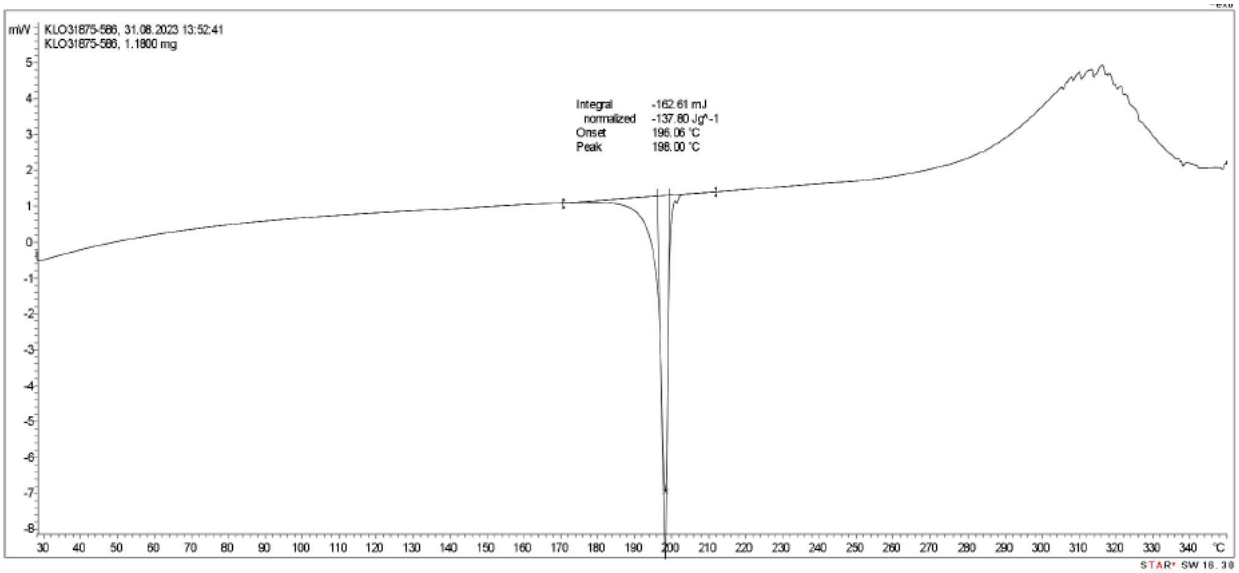
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.04, 143.17, 140.87, 133.87, 123.65, 118.11, 116.66, 112.51, 101.23, 50.22, 24.15, 23.28



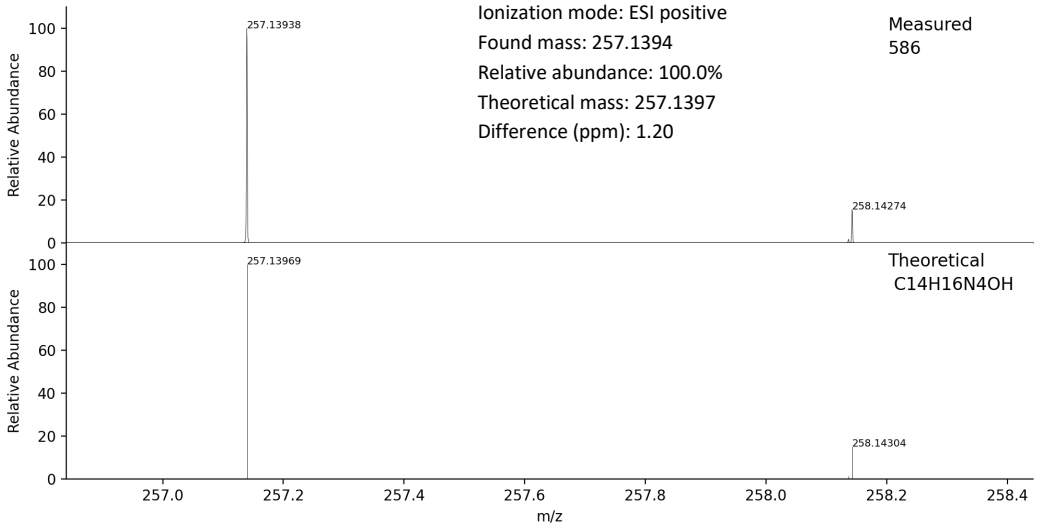
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500
400

DSC


mW
KLO31875-586, 31.08.2023 13:52:41
KLO31875-586, 1.1800 mg
Integral -162.61 mJ
normalized -137.80 Jg^-1
Onset 196.06 °C
Peak 198.00 °C
°C
STARe SW 16.30

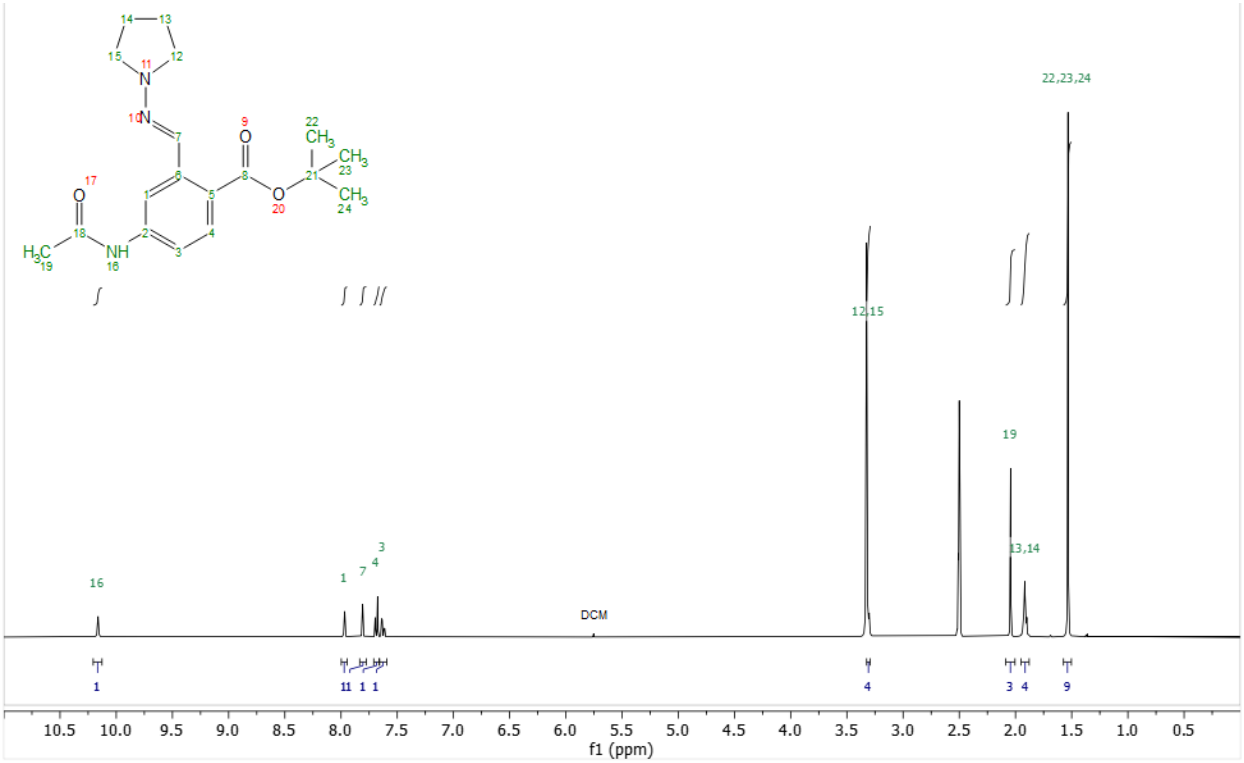
HRMS


Ionization mode: ESI positive
Found mass: 257.1394
Relative abundance: 100.0%
Theoretical mass: 257.1397
Difference (ppm): 1.20
Measured
586
257.13938
258.14274
Theoretical
C14H16N4OH
257.13969
258.14304
Relative Abundance
m/z

S41. **Spectra of 20**

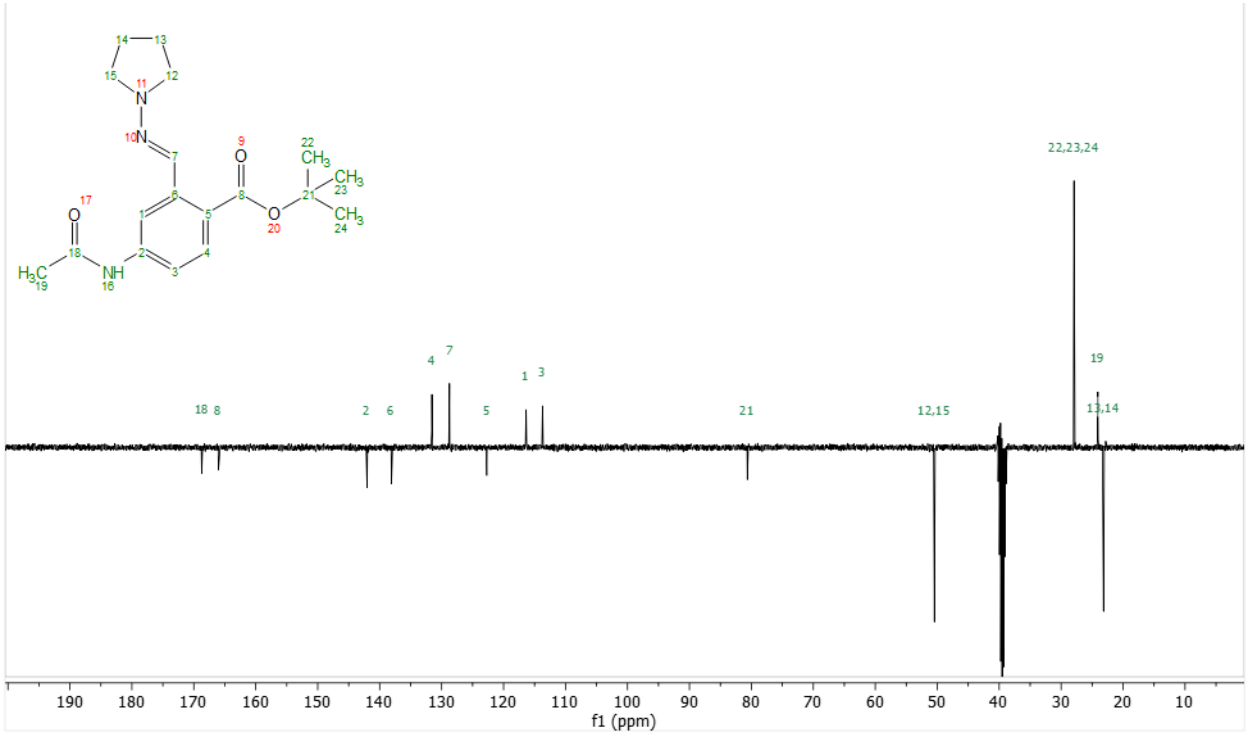
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.16 (s, 1H), 7.97 (d, 1H), 7.81 (s, 1H), 7.69 (d, 1H), 7.63 (dd, 1H), 3.32 – 3.29 (m, 4H), 2.04 (s, 3H), 1.95 – 1.88 (m, 4H), 1.53 (s, 8H)

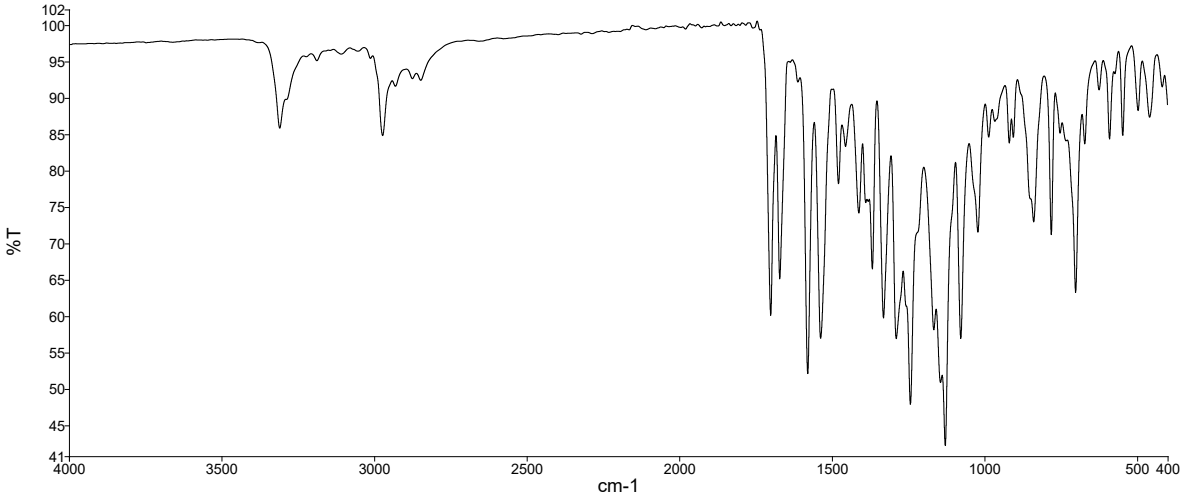


^{13}C-NMR (DMSO-d_6)

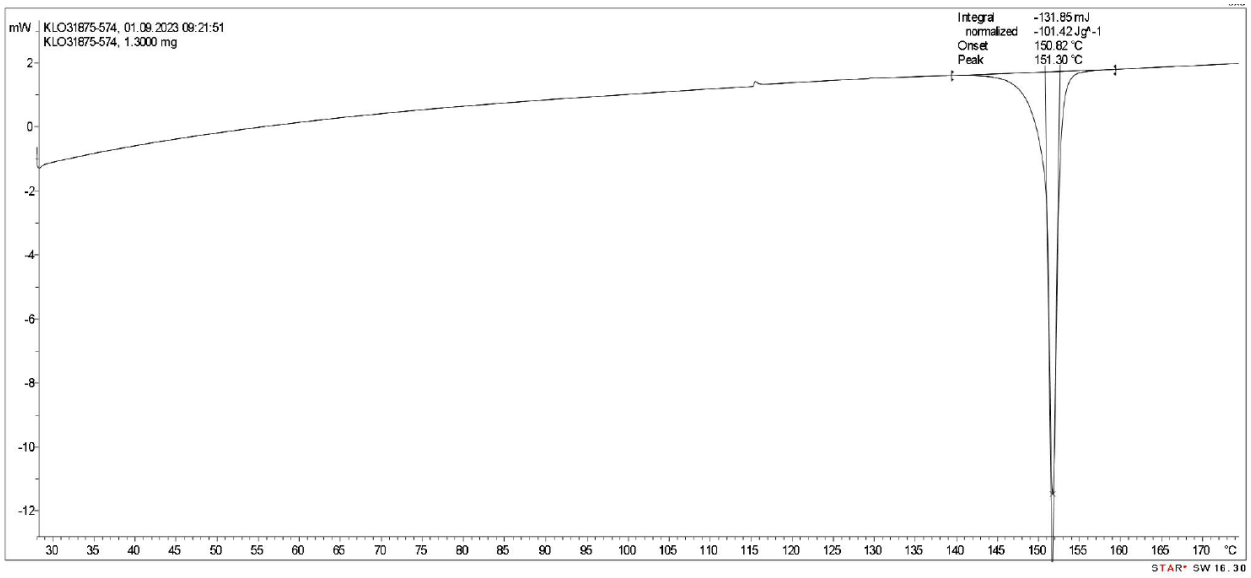
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.73, 166.03, 142.03, 138.10, 131.57, 128.73, 122.72, 116.36, 113.70, 80.64, 50.45, 27.92, 24.07, 23.15



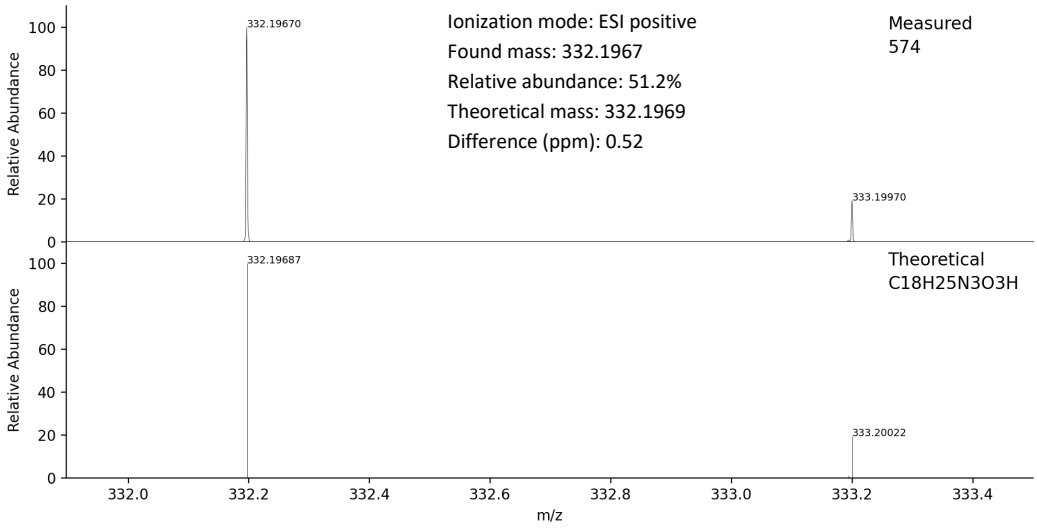
IR


%T
cm-1

DSC


mW
KLO31875-574, 01.09.2023 09:21:51
KLO31875-574, 1.3000 mg
Integral -131.85 mJ
normalized -101.42 Jg^-1
Onset 150.62 °C
Peak 151.30 °C
°C
STAR° SW 16.30

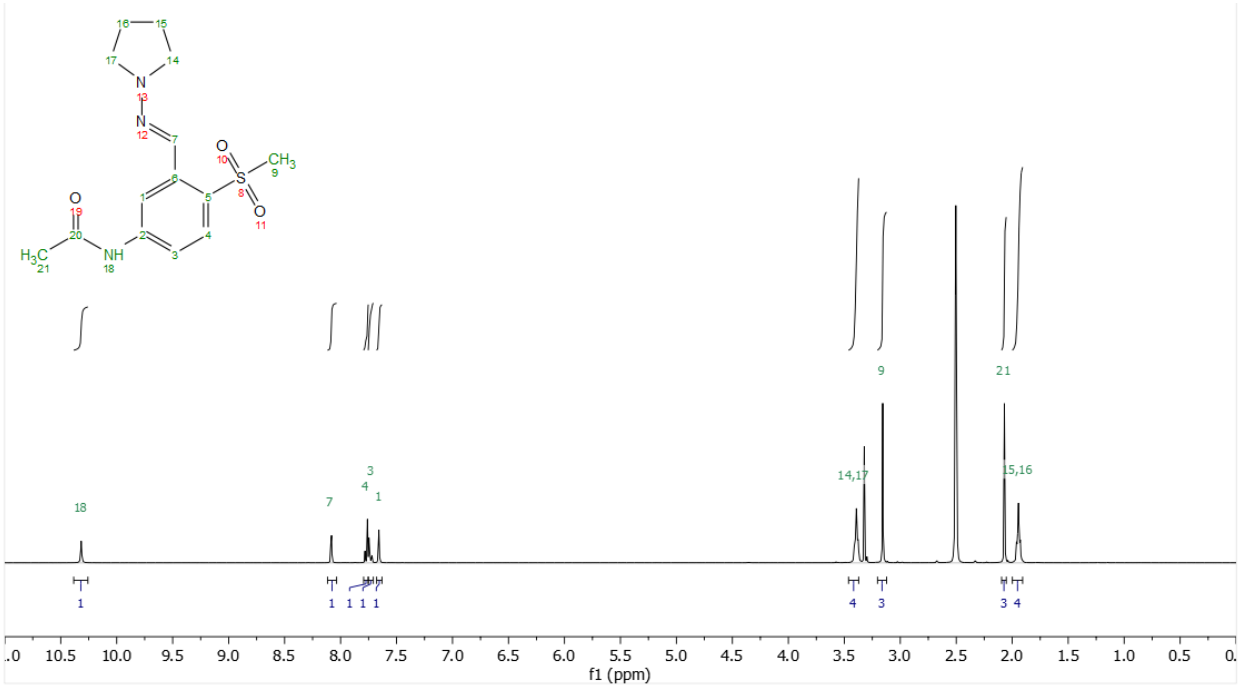
HRMS


Ionization mode: ESI positive
Found mass: 332.1967
Relative abundance: 51.2%
Theoretical mass: 332.1969
Difference (ppm): 0.52
Measured
574
332.19670
333.19970
Theoretical
C18H25N3O3H
332.19687
333.20022
Relative Abundance
m/z

S42. **Spectra of 21**

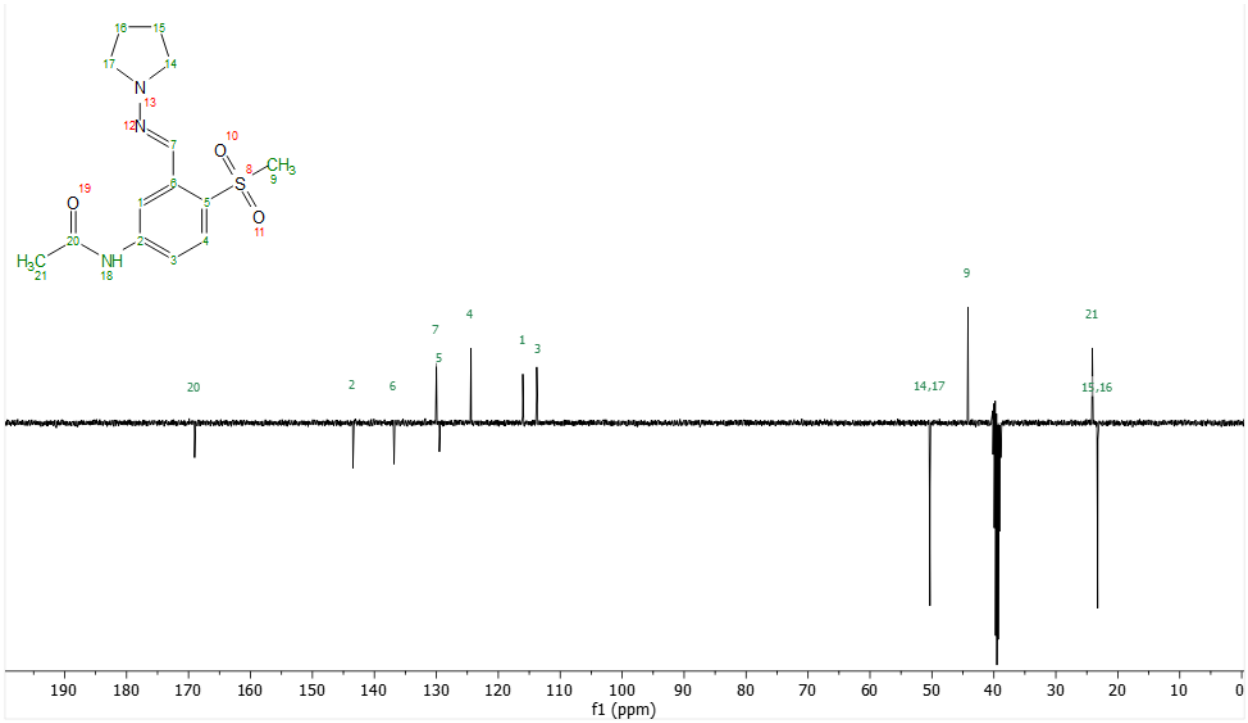
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.32 (s, 1H), 8.08 (d, 1H), 7.77 (d, 1H), 7.73 (dd, 1H), 7.66 (s, 1H), 3.46 – 3.37 (m, 4H), 3.16 (s, 3H), 2.07 (s, 3H), 2.00 – 1.91 (m, 4H)

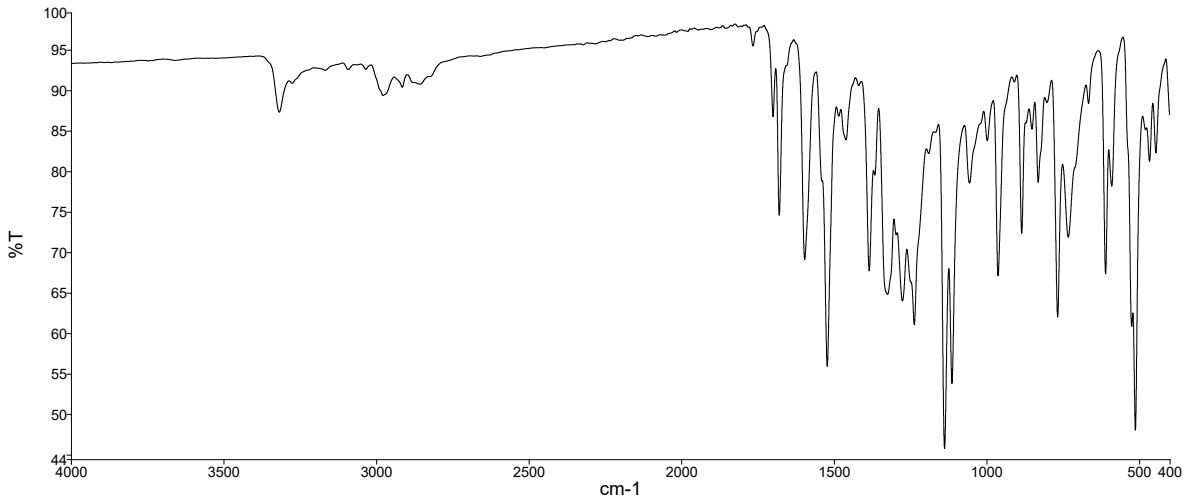


^{13}C-NMR (DMSO-d_6)

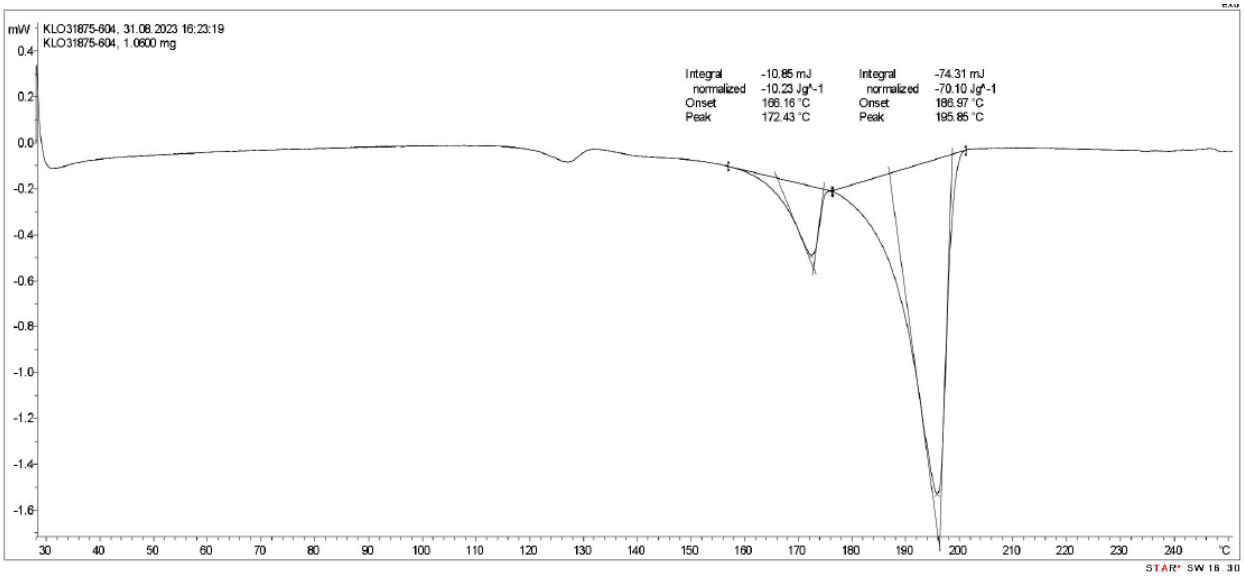
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.01, 143.46, 136.82, 129.98, 129.50, 124.40, 116.04, 113.79, 50.32, 44.18, 24.11, 23.24



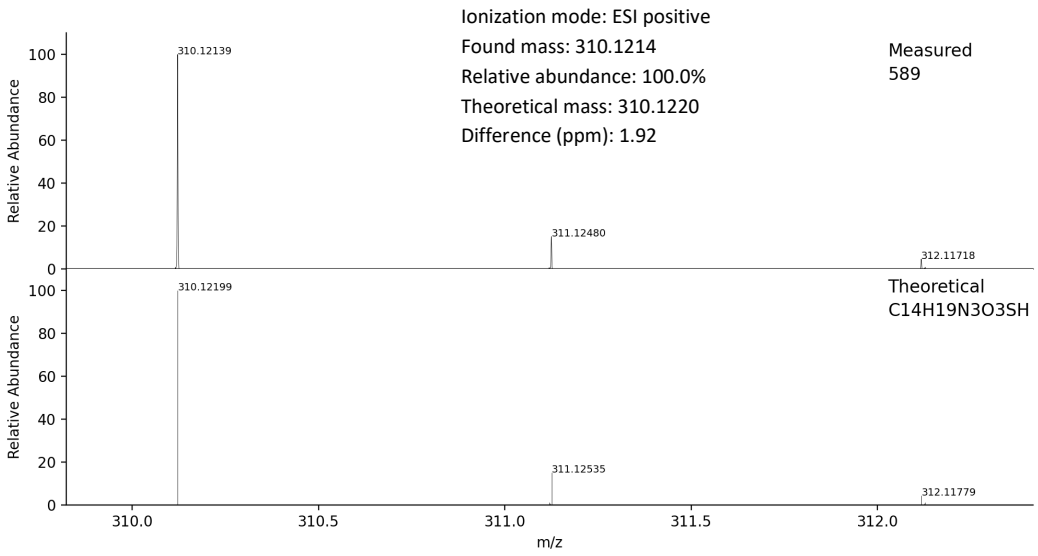
IR


%T
cm-1
100
95
90
85
80
75
70
65
60
55
50
44
4000
3500
3000
2500
2000
1500
1000
500 400

DSC


mW
KLO31875-604, 31.08.2023 16:23:19
KLO31875-604, 1.0600 mg
Integral -10.85 mJ
normalized -10.23 Jg^-1
Onset 166.16 °C
Peak 172.43 °C
Integral -74.31 mJ
normalized -70.10 Jg^-1
Onset 186.97 °C
Peak 195.85 °C
°C
STAR° SW 16.30

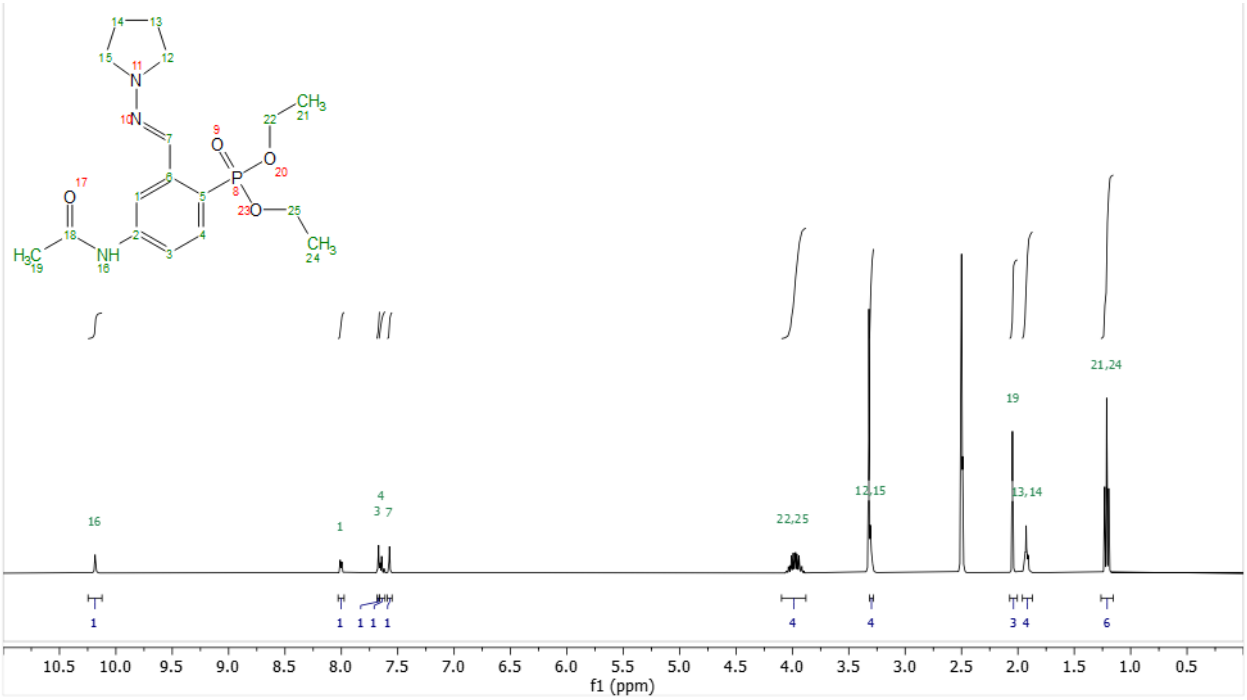
HRMS


Ionization mode: ESI positive
Found mass: 310.1214
Relative abundance: 100.0%
Theoretical mass: 310.1220
Difference (ppm): 1.92
Measured
589
Theoretical
C14H19N3O3SH
Relative Abundance
m/z
310.12139
311.12480
312.11718
310.12199
311.12535
312.11779

S43. **Spectra of 22**

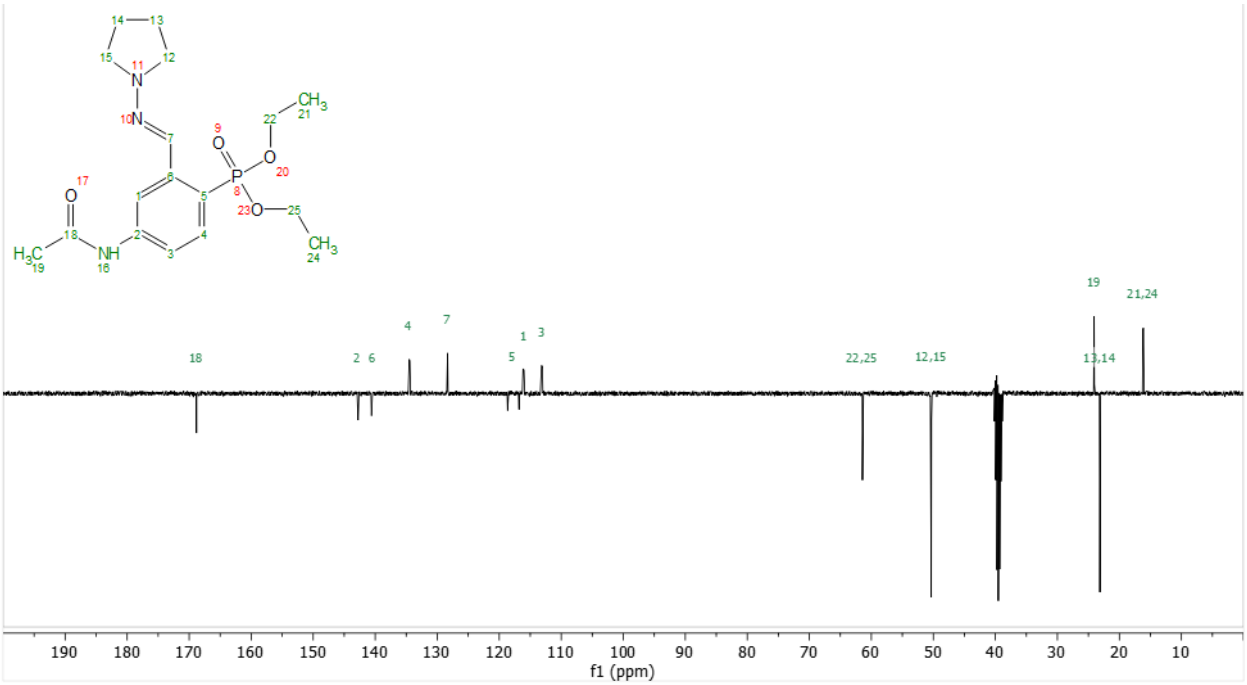
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.18 (s, 1H), 8.03 – 7.98 (m, 1H), 7.68 – 7.66 (m, 1H), 7.67 – 7.61 (m, 1H), 7.57 (s, 1H), 4.10 – 3.88 (m, 4H), 3.32 – 3.28 (m, 4H), 2.05 (s, 3H), 1.96 – 1.87 (m, 4H), 1.21 (t, 6H)

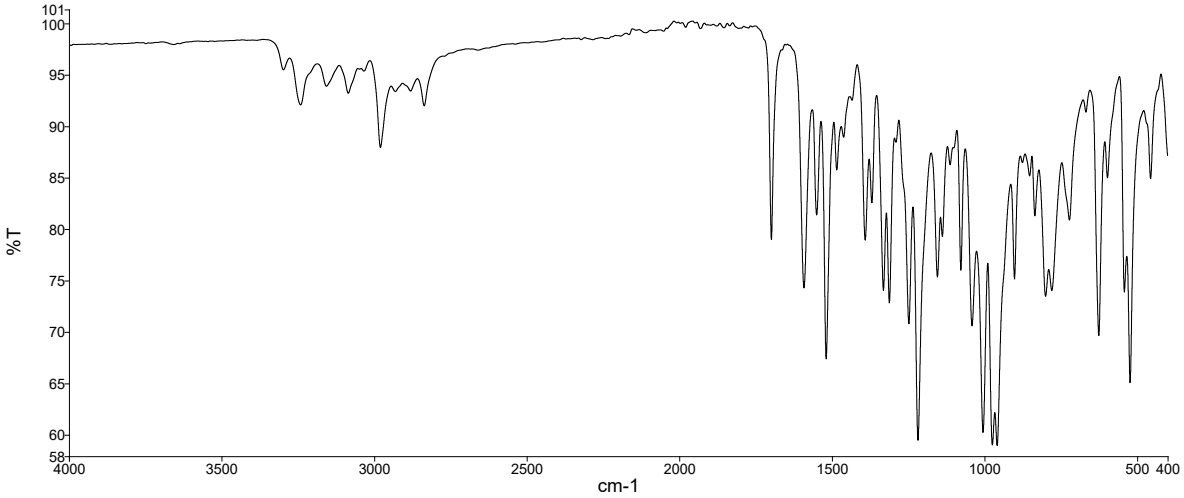


^{13}C-NMR (DMSO-d_6)

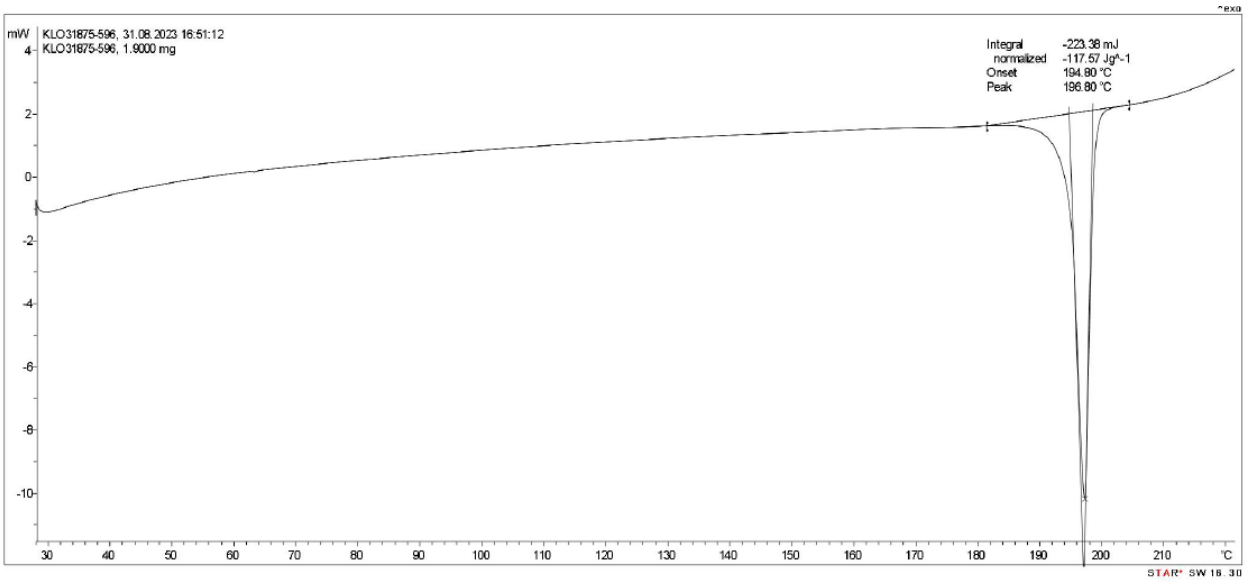
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 168.82, 142.78, 140.60 (d), 134.46 (d), 128.35 (d), 117.73 (d), 116.09 (d), 113.12 (d), 61.41 (d), 50.33, 24.07, 23.15, 16.16 (d).



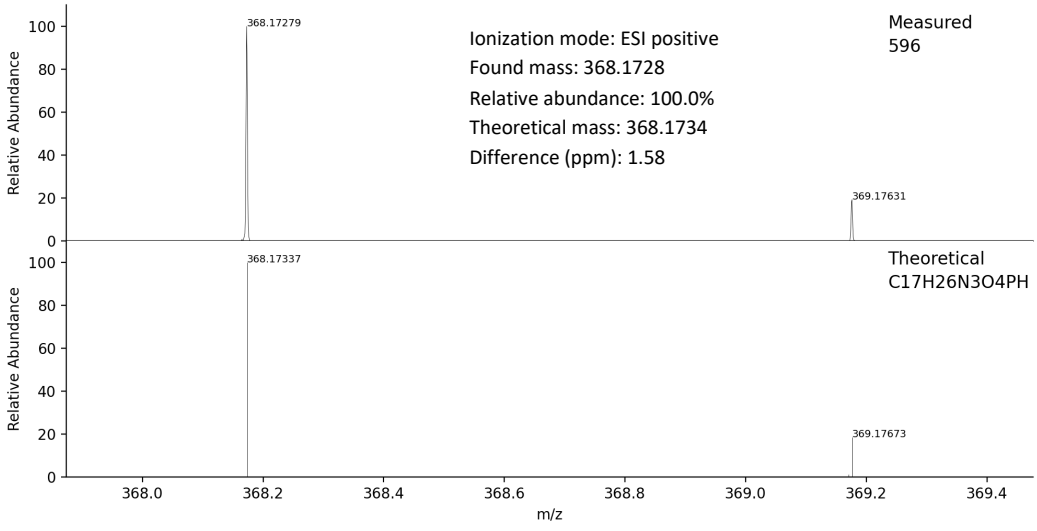
IR


%T
cm-1

DSC


mW
KLO31875-596, 31.08.2023 16:51:12
KLO31875-596, 1.9000 mg
Integral -223.38 mJ
normalized -117.57 Jg^-1
Onset 194.80 °C
Peak 196.80 °C
°C
STAR° SW 16.30

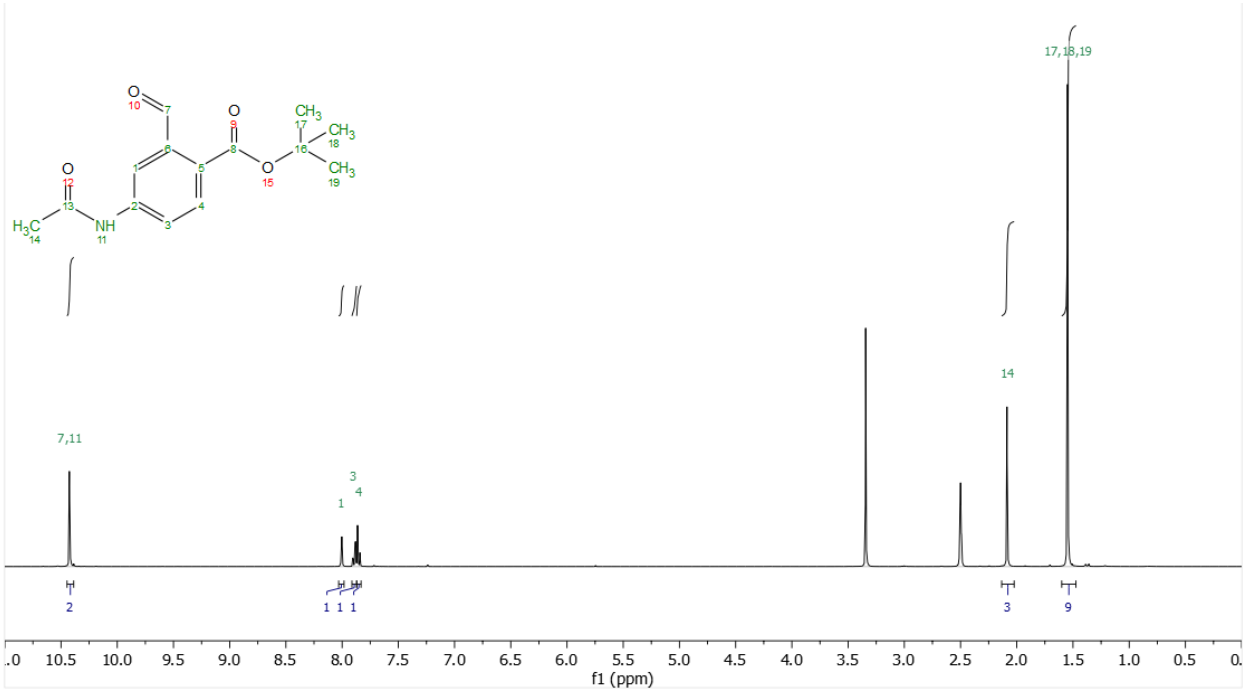
HRMS


Relative Abundance
368.17279
369.17631
Ionization mode: ESI positive
Found mass: 368.1728
Relative abundance: 100.0%
Theoretical mass: 368.1734
Difference (ppm): 1.58
Measured
596
368.17337
369.17673
Theoretical
C17H26N3O4PH
m/z

S44. **Spectra of 25**

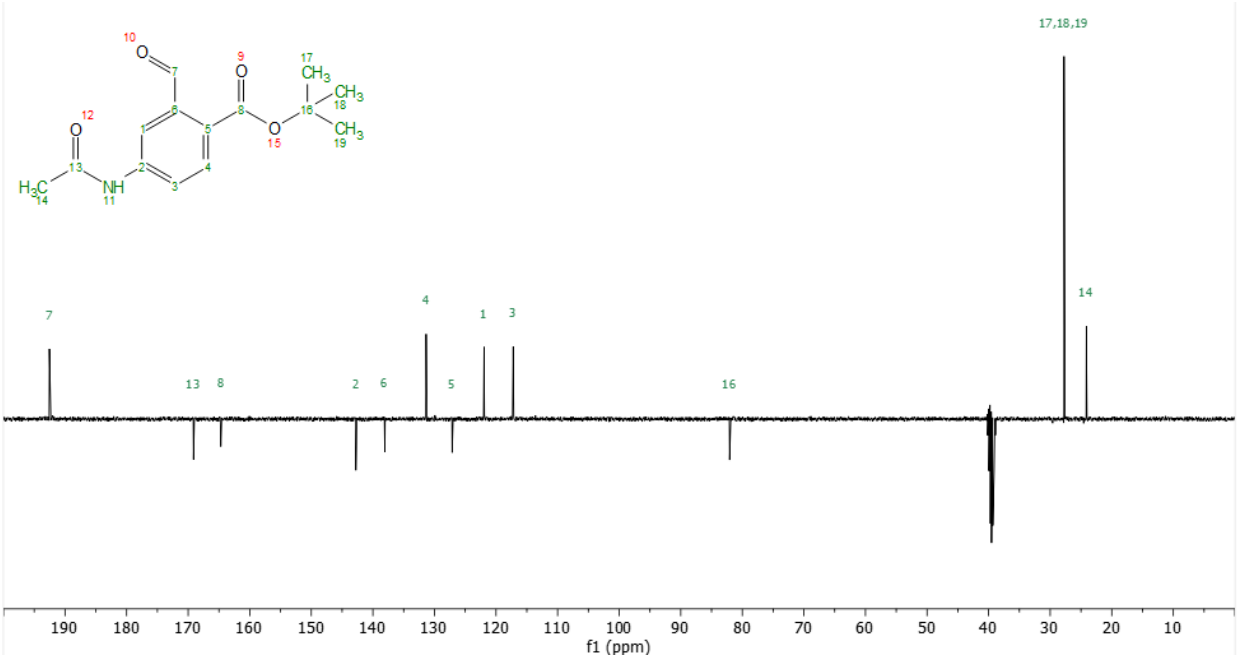
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.43 (s, 2H), 8.01 (d, 1H), 7.89 (dd, 1H), 7.85 (d, 1H), 2.09 (s, 3H), 1.55 (s, 9H).

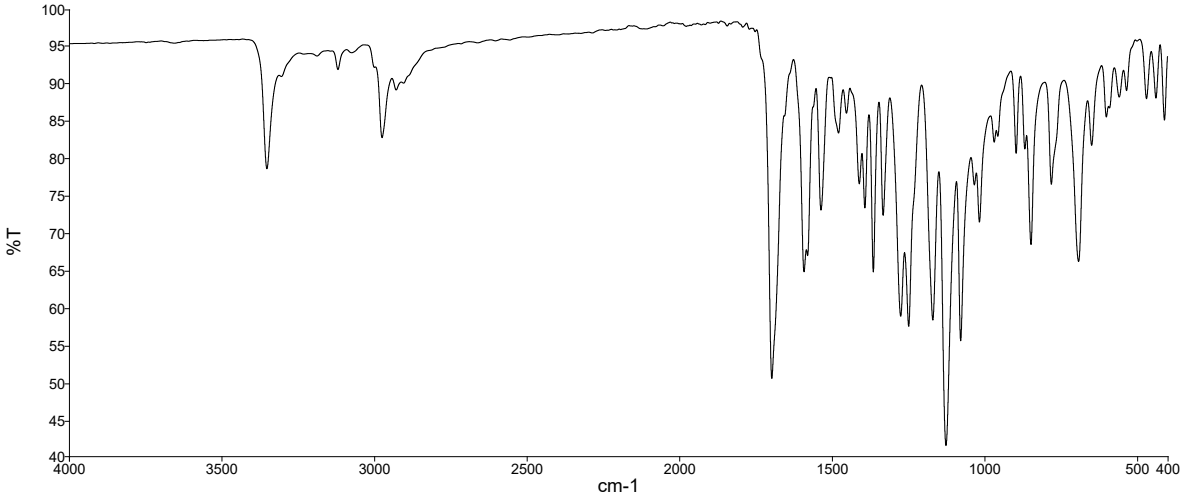


^{13}C-NMR (DMSO-d_6)

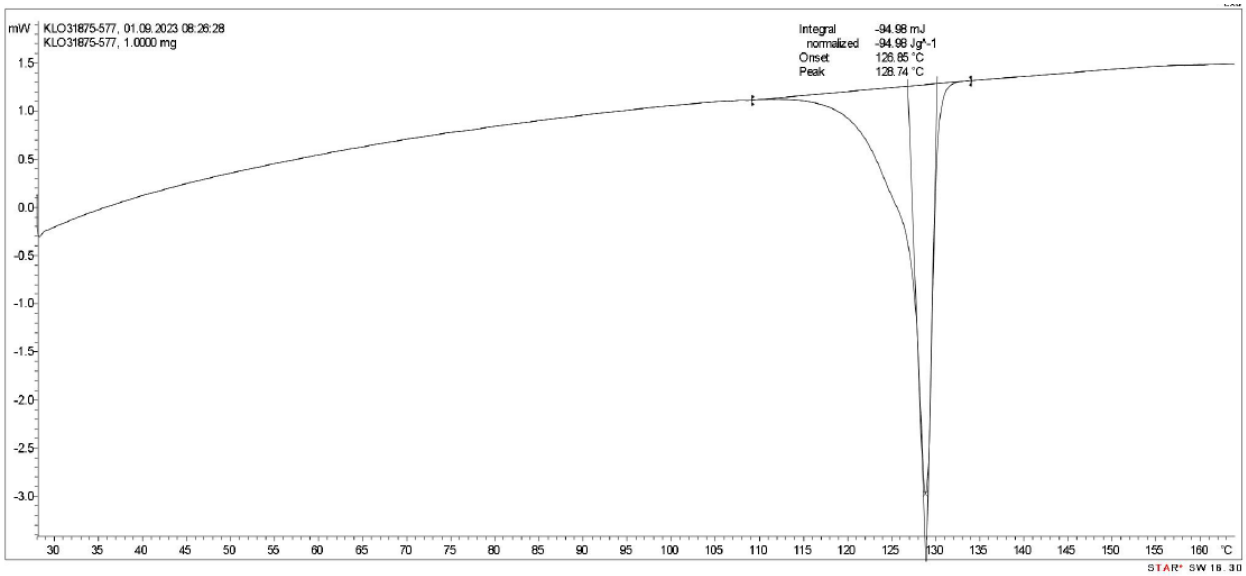
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 192.54, 169.13, 164.69, 142.76, 138.06, 131.35, 127.13, 121.94, 117.21, 82.06, 27.74, 24.13



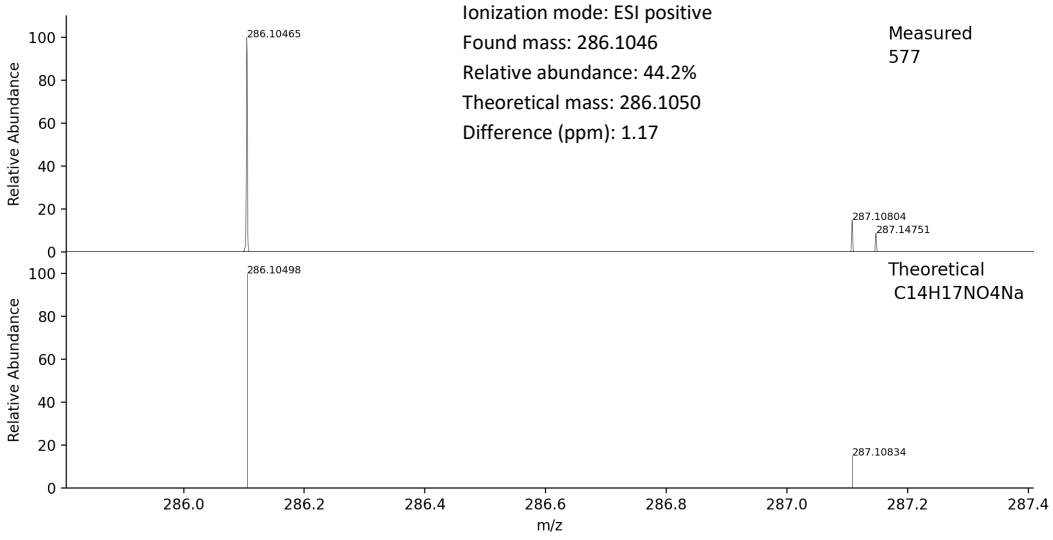
IR


%T
cm-1
100
95
90
85
80
75
70
65
60
55
50
45
40
4000
3500
3000
2500
2000
1500
1000
500 400

DSC


mW
KLO31875-577, 01.09.2023 08:26:28
KLO31875-577, 1.0000 mg
Integral -94.98 mJ
normalized -94.98 Jg^-1
Onset 126.85 °C
Peak 128.74 °C
°C

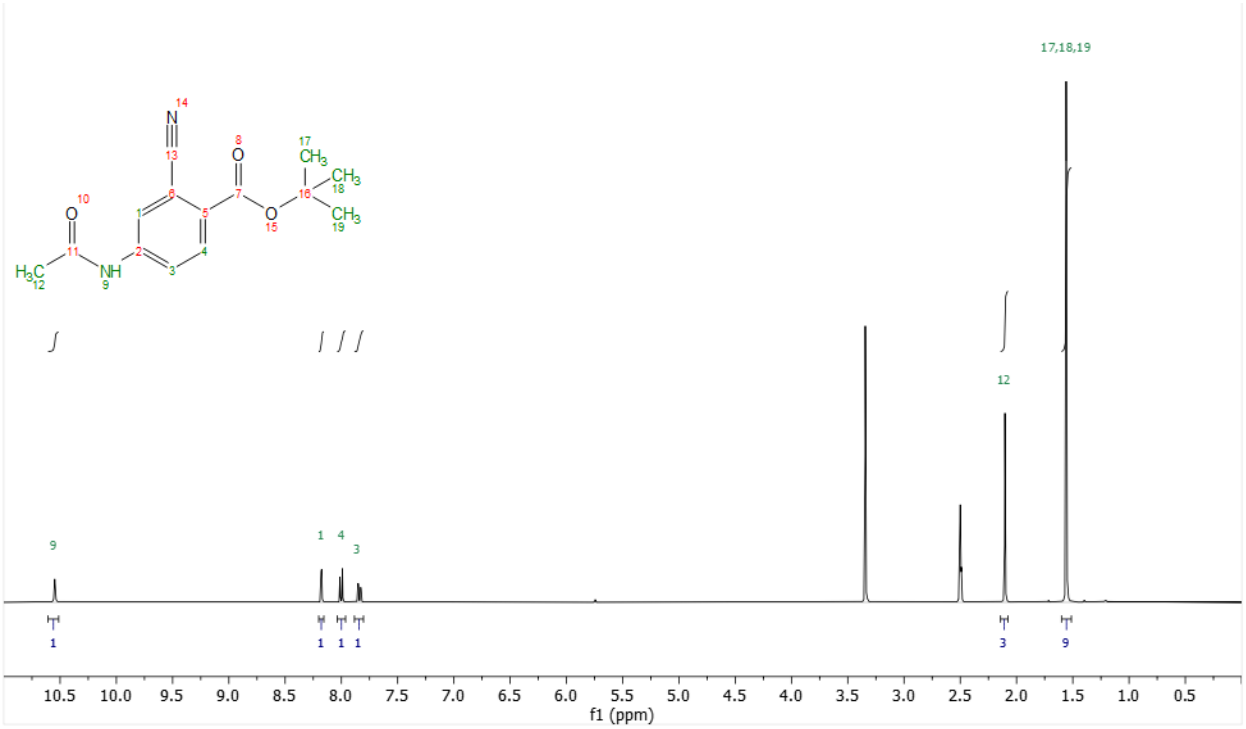
HRMS


Ionization mode: ESI positive
Found mass: 286.1046
Relative abundance: 44.2%
Theoretical mass: 286.1050
Difference (ppm): 1.17
Measured
577
286.10465
287.10804
287.14751
Theoretical
C14H17NO4Na
286.10498
287.10834
Relative Abundance
m/z

S45. **Spectra of 26**

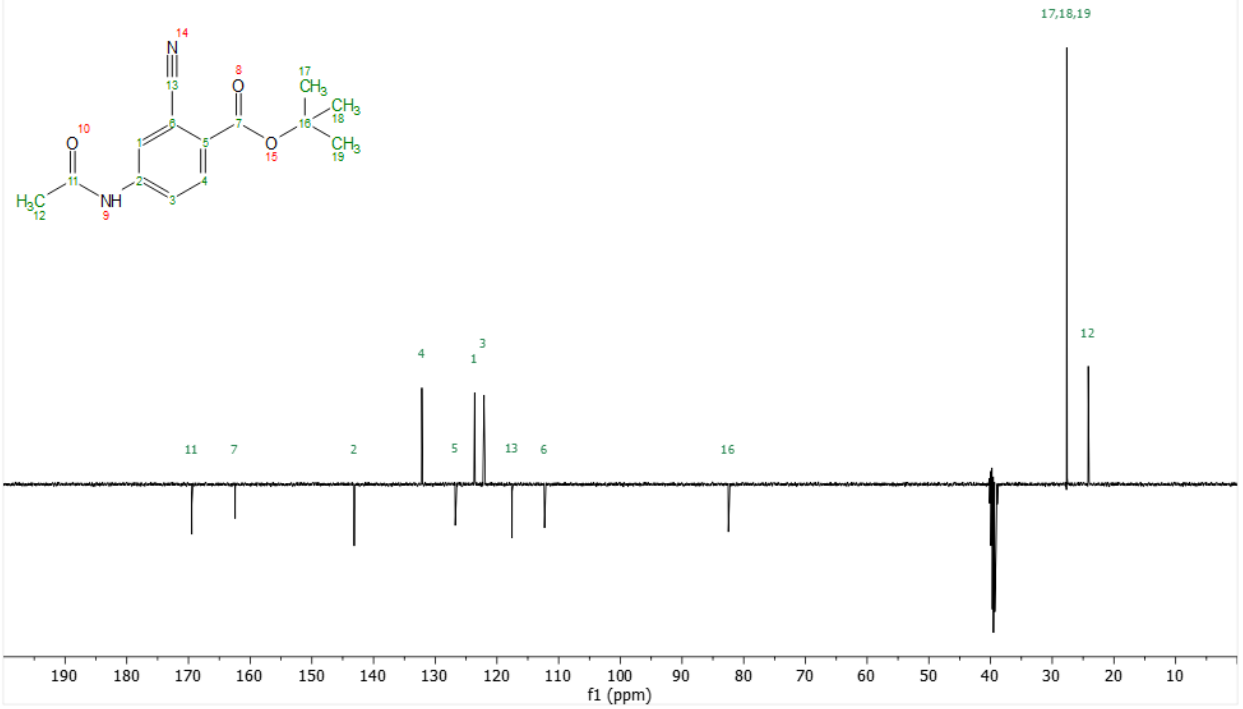
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.55 (s, 1H), 8.18 (d, 1H), 8.00 (d, 1H), 7.84 (dd, 1H), 2.10 (s, 3H), 1.56 (s, 9H)

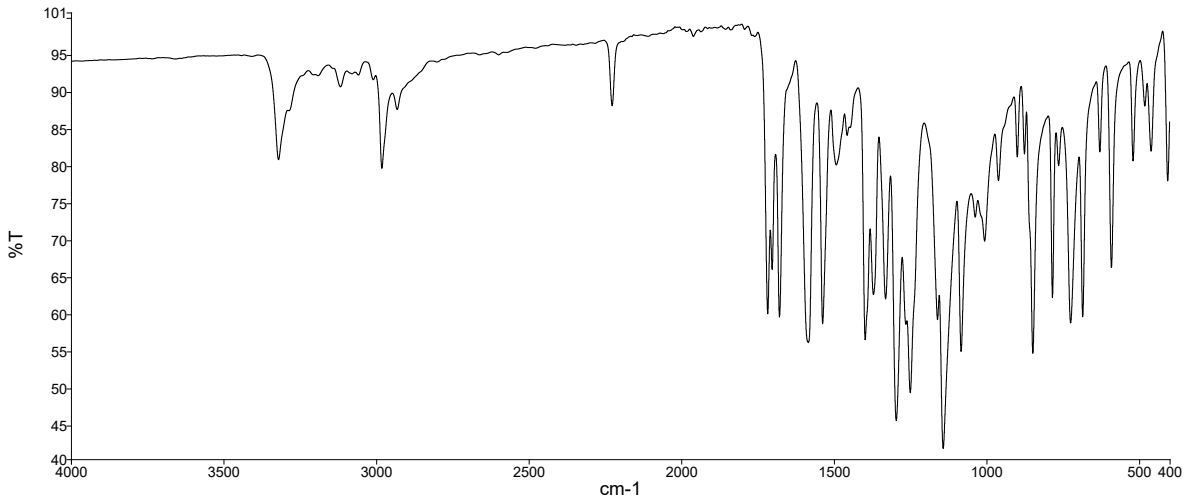


^{13}C-NMR (DMSO-d_6)

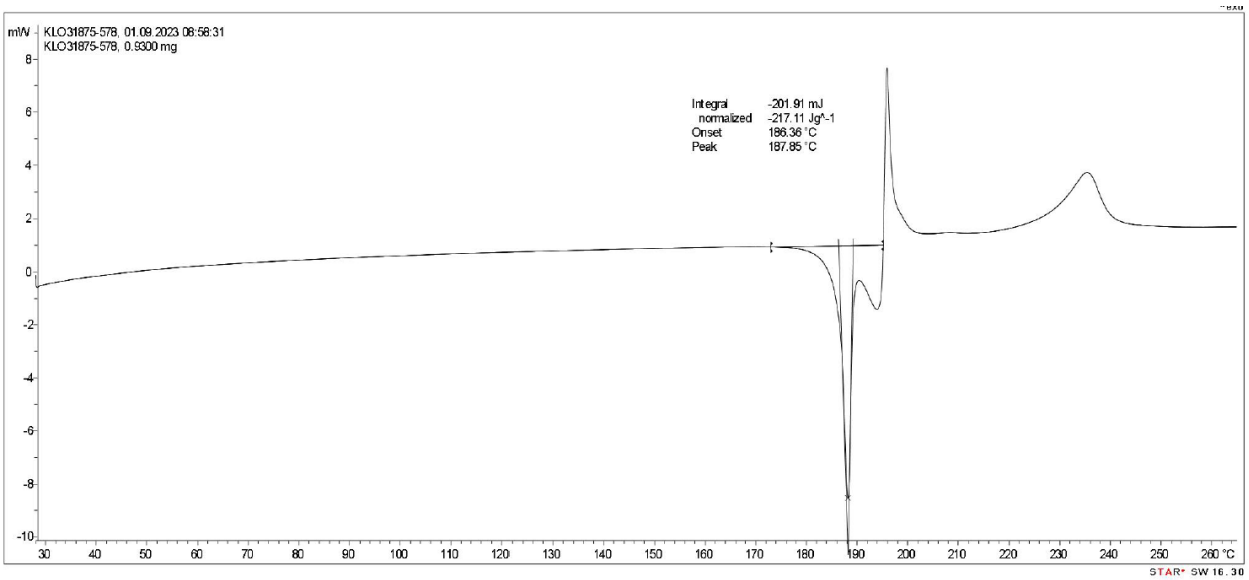
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 169.45, 162.43, 143.13, 132.17, 126.76, 123.61, 122.09, 117.55, 112.29, 82.49, 27.65, 24.16



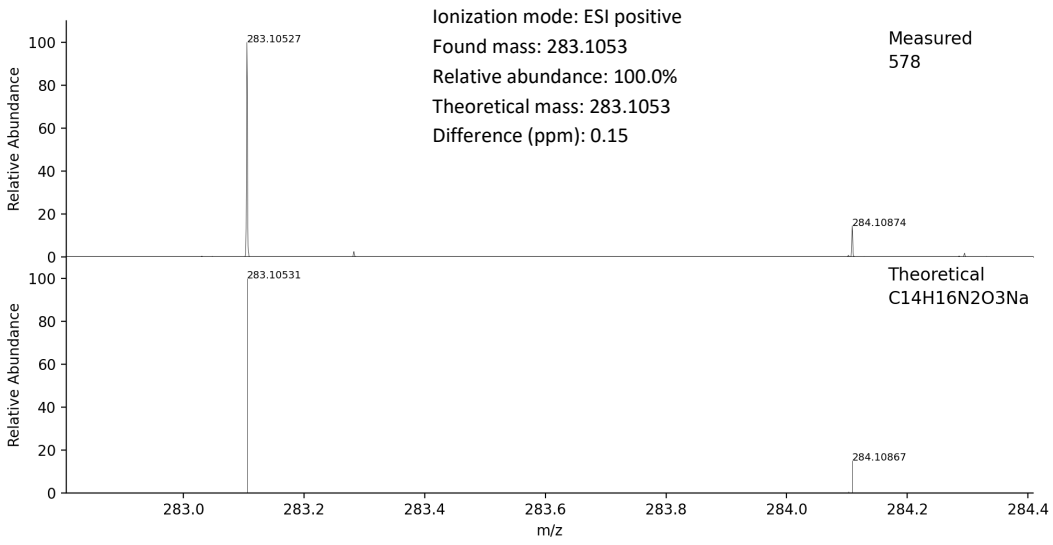
IR


%T
cm-1
4000
3500
3000
2500
2000
1500
1000
500 400

DSC


mW
KLO31875-578, 01.09.2023 08:58:31
KLO31875-578, 0.9300 mg
Integral -201.91 mJ
normalized -217.11 Jg^-1
Onset 186.36 °C
Peak 187.85 °C
°C
STAR° SW 16.30

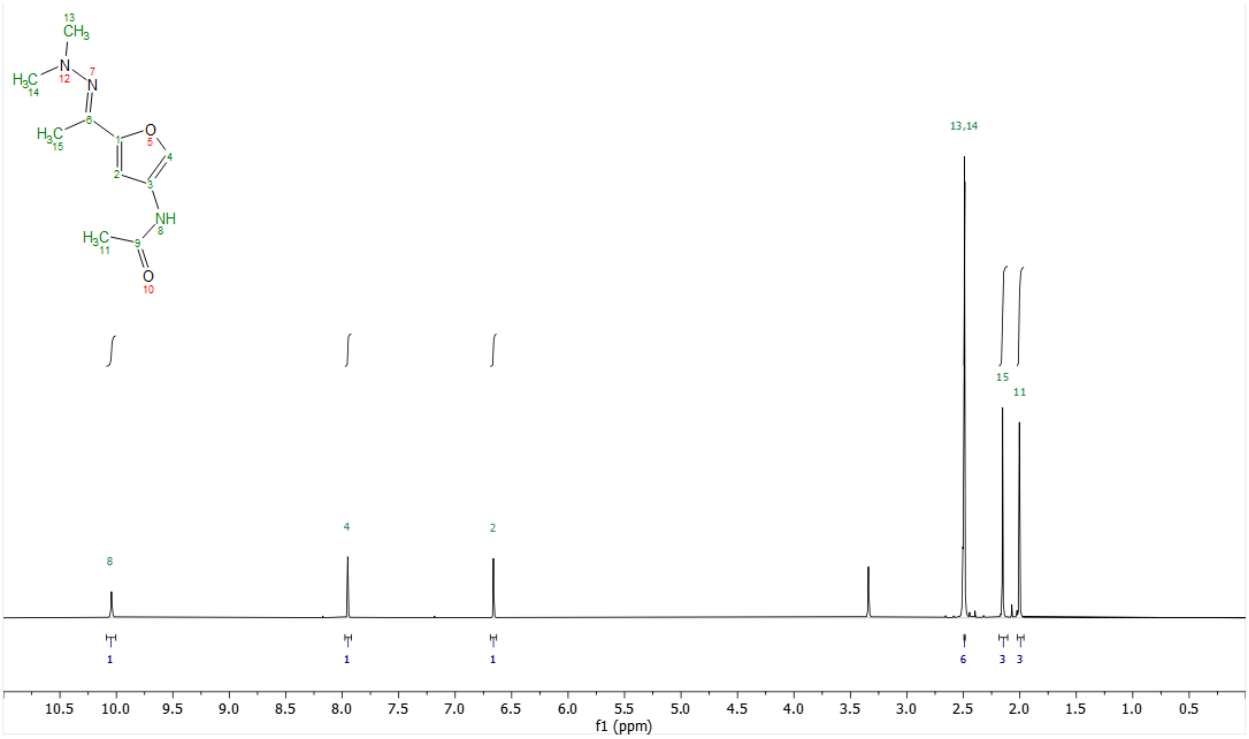
HRMS


Ionization mode: ESI positive
Found mass: 283.1053
Relative abundance: 100.0%
Theoretical mass: 283.1053
Difference (ppm): 0.15
Measured
578
283.10527
284.10874
Theoretical
C14H16N2O3Na
283.10531
284.10867
Relative Abundance
m/z

S46. **Spectra of 27**

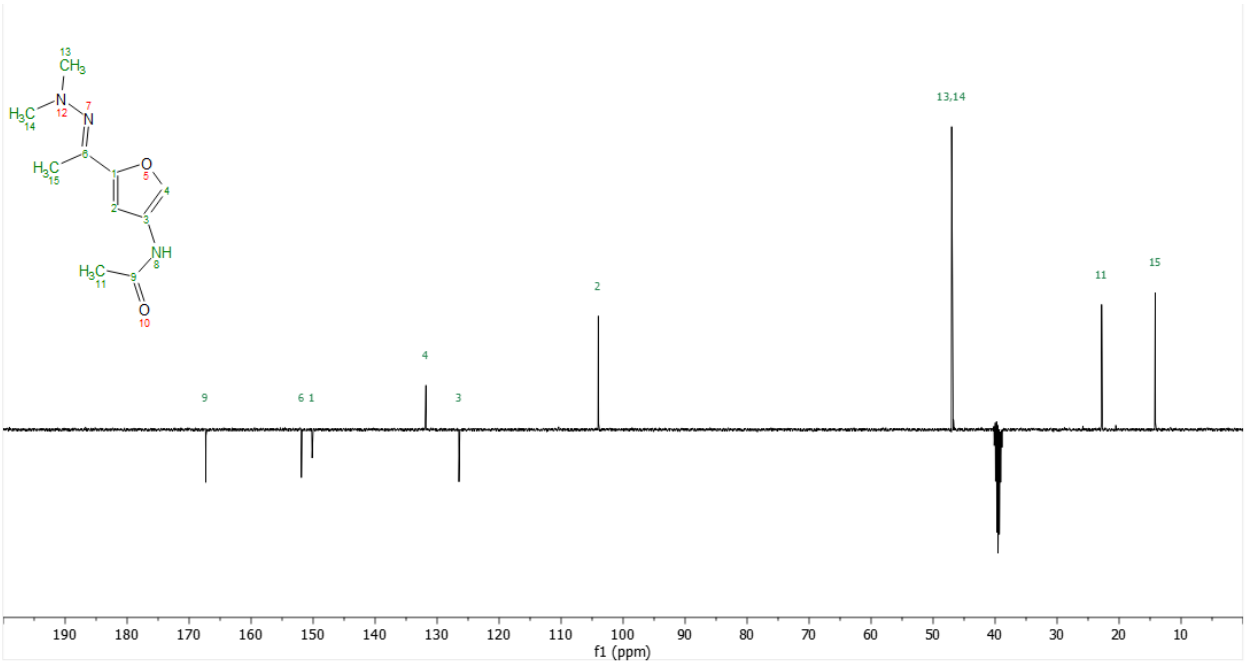
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.04 (s, 1H), 7.95 (s, 1H), 6.66 (s, 1H), 2.49 (s, 6H), 2.15 (s, 3H), 2.00 (s, 3H)

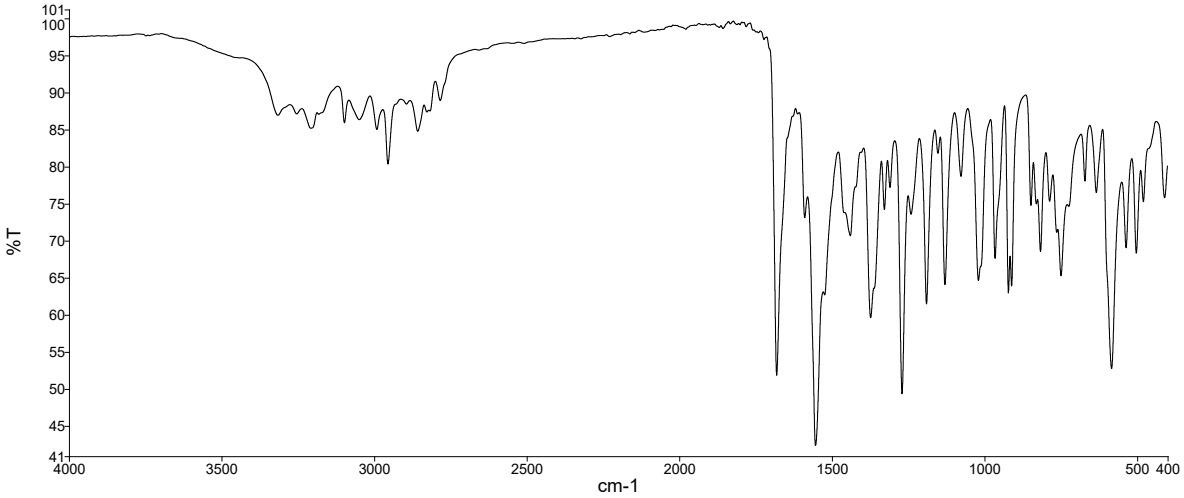


^{13}C-NMR (DMSO-d_6)

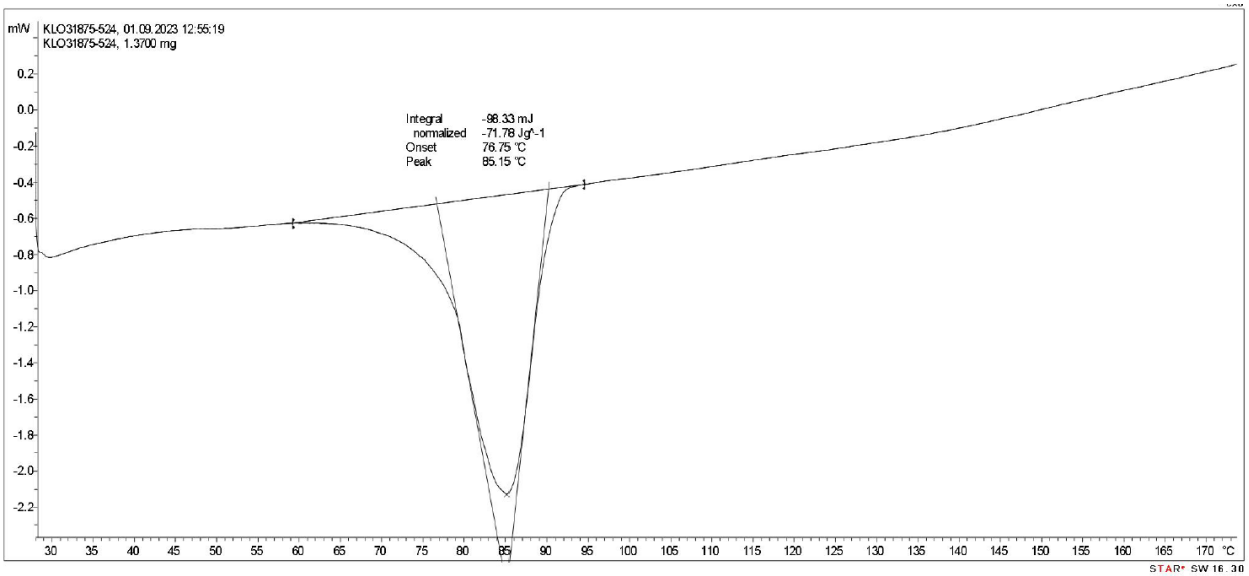
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 167.30, 151.89, 150.16, 131.80, 126.48, 104.01, 47.01, 22.82, 14.18



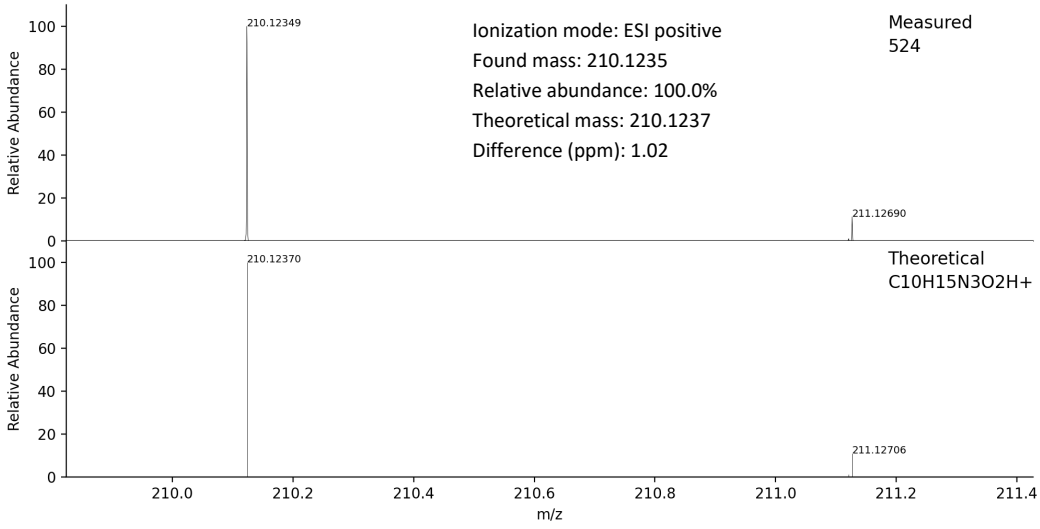
IR


%T
cm-1

DSC


mW
KLO31875-524, 01.09.2023 12:55:19
KLO31875-524, 1.3700 mg
Integral -98.33 mJ
normalized -71.78 Jg^-1
Onset 76.75 °C
Peak 85.15 °C
°C

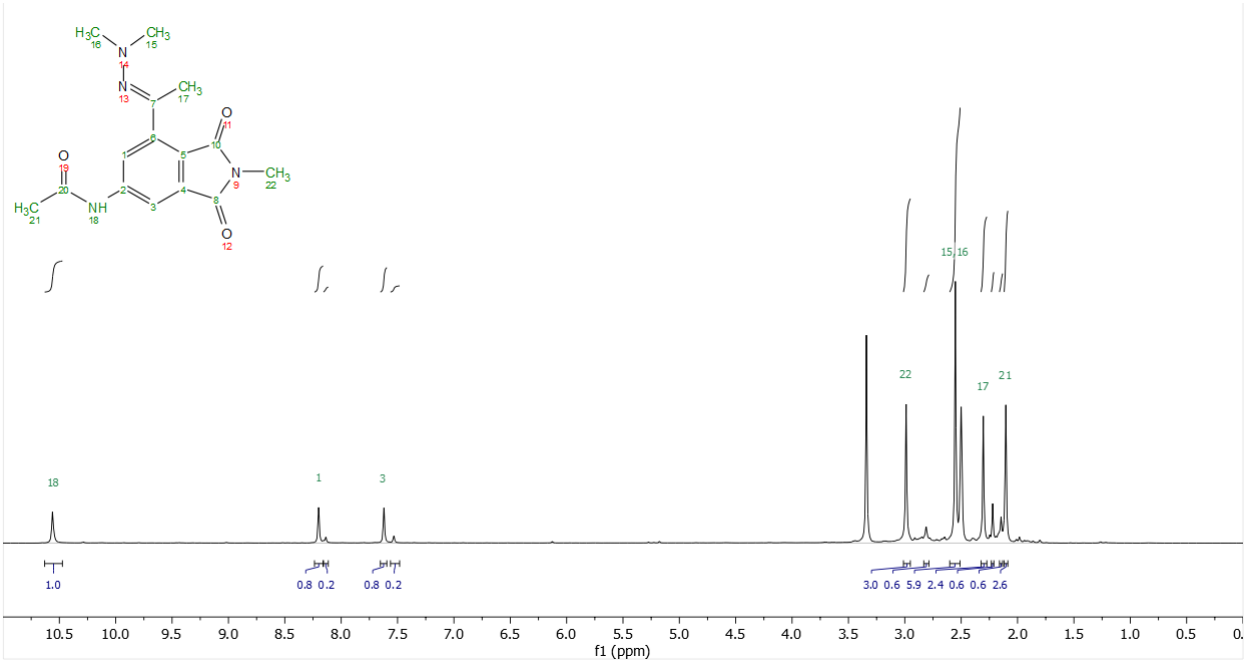
HRMS


Relative Abundance
210.12349
211.12690
Ionization mode: ESI positive
Found mass: 210.1235
Relative abundance: 100.0%
Theoretical mass: 210.1237
Difference (ppm): 1.02
Measured
524
210.12370
211.12706
Theoretical
C10H15N3O2H+
m/z

S47. **Spectra of 32**

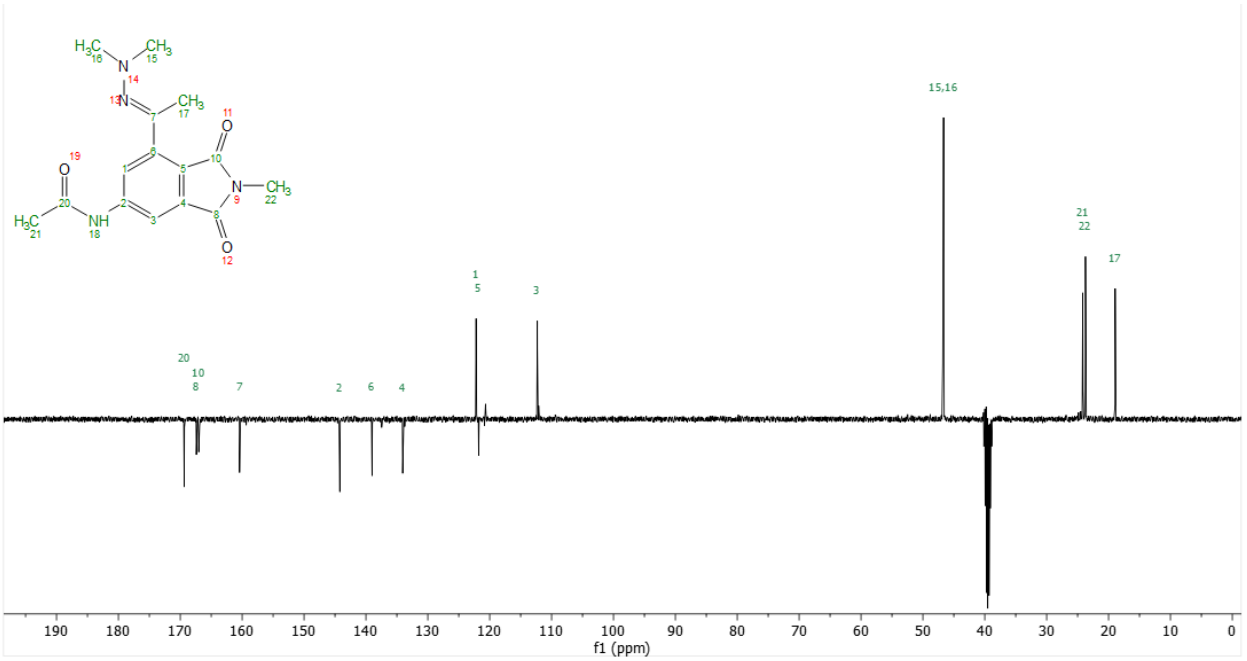
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.56 (s, 1H), 8.20 (s, 1H), 8.14 (s, 1H), 7.62 (s, 1H), 7.53 (s, 1H), 2.99 (s, 3H), 2.81 (s, 3H), 2.55 (s, 6H), 2.30 (s, 2H), 2.22 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H)

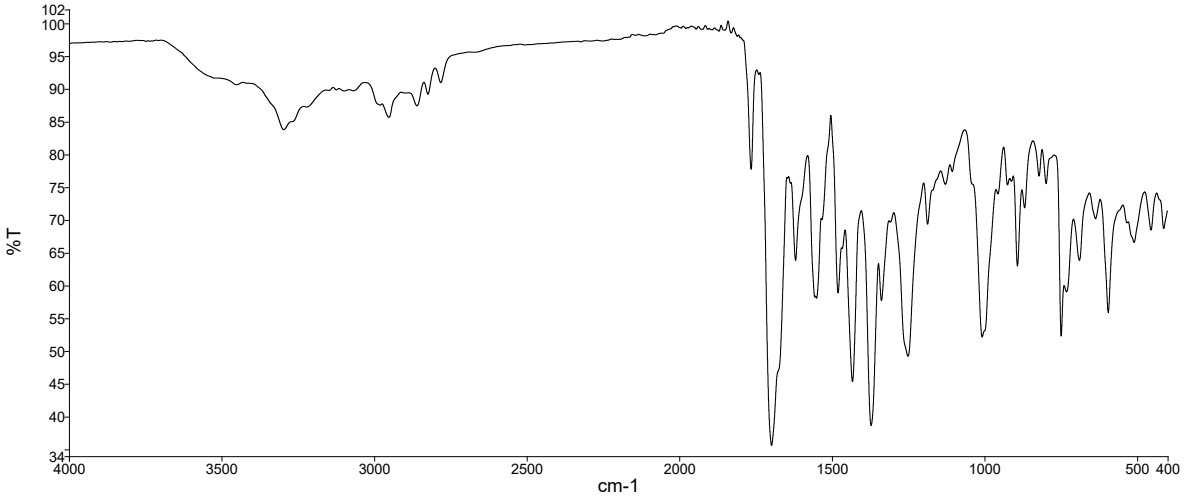


^{13}C-NMR (DMSO-d_6)

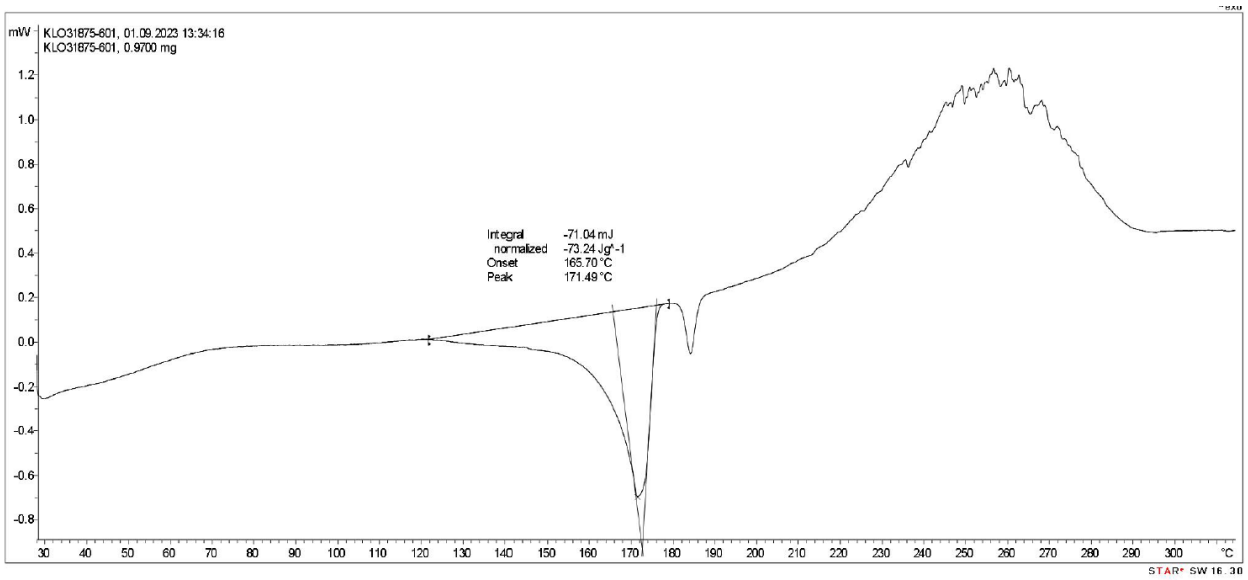
^{13}C NMR (101 MHz, DMSO-d_6) δ = 169.36, 167.40, 167.02, 160.42, 144.22, 139.01, 137.46, 134.06, 122.20, 121.79, 120.68, 112.30, 46.66, 24.21, 23.72, 18.93



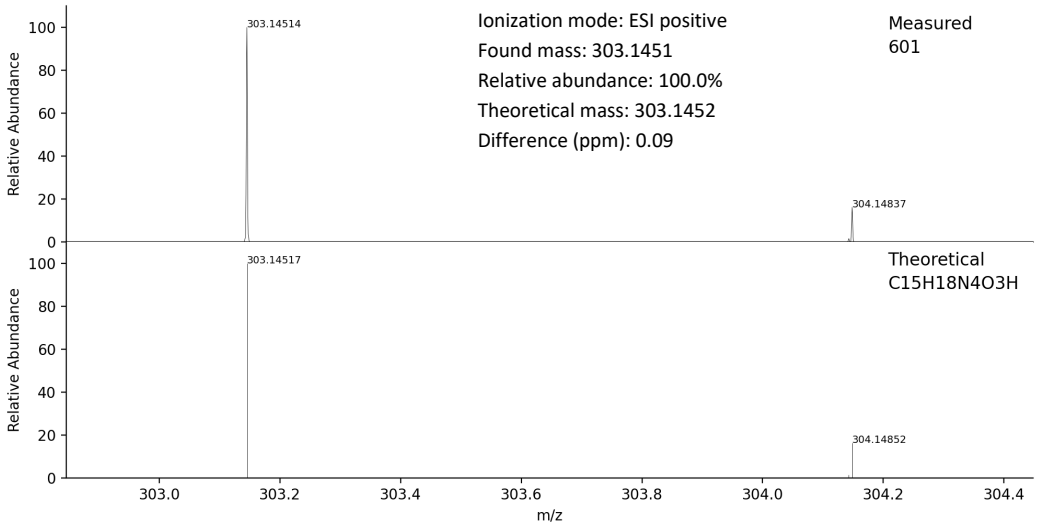
IR


%T
cm-1

DSC


mW
KLO31875-601, 01.09.2023 13:34:16
KLO31875-601, 0.9700 mg
Integral -71.04 mJ
normalized -73.24 Jg^-1
Onset 165.70 °C
Peak 171.49 °C
°C
STARe SW 16.30

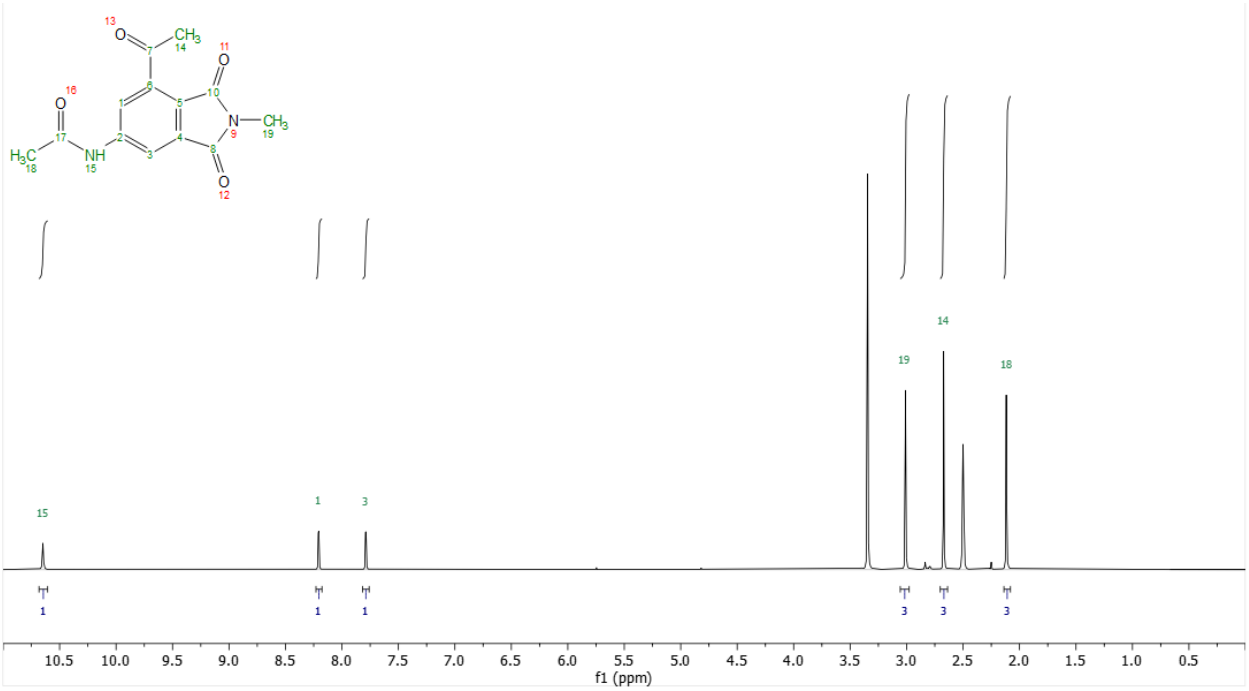
HRMS


Ionization mode: ESI positive
Found mass: 303.1451
Relative abundance: 100.0%
Theoretical mass: 303.1452
Difference (ppm): 0.09
Measured
601
303.14514
304.14837
Theoretical
C15H18N4O3H
303.14517
304.14852
Relative Abundance
m/z

S48. **Spectra of 33**

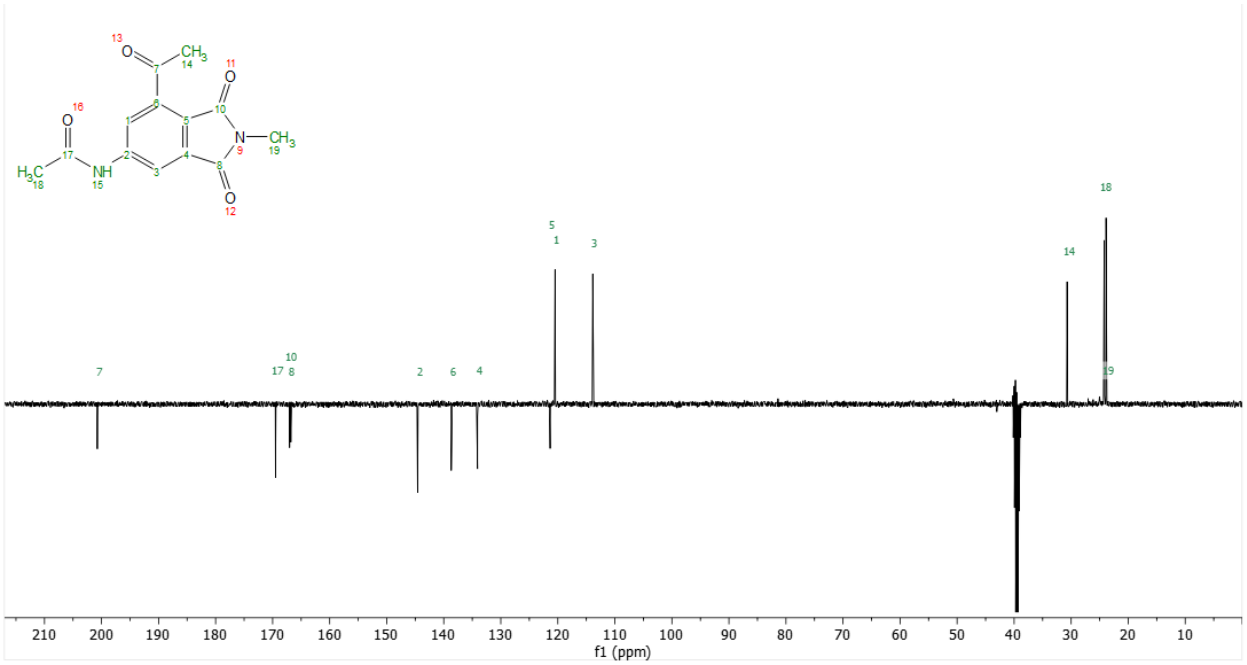
^{1}H-NMR (DMSO-d_6)

^{1}H-NMR (400 MHz, DMSO-d_6) δ = 10.65 (s, 1H), 8.21 (d, 1H), 7.79 (d, 1H), 3.01 (s, 3H), 2.67 (s, 3H), 2.12 (s, 3H)

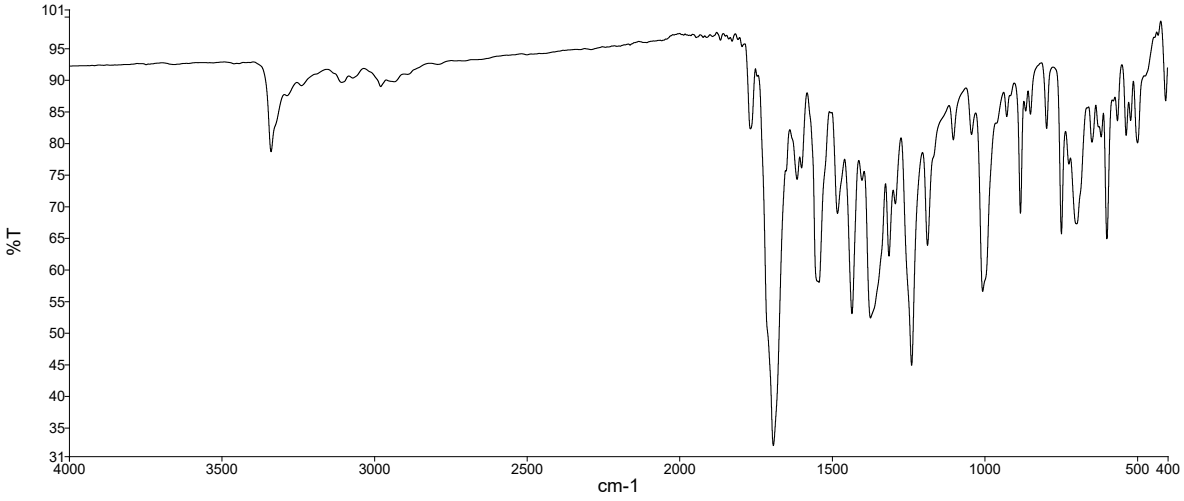


^{13}C-NMR (DMSO-d_6)

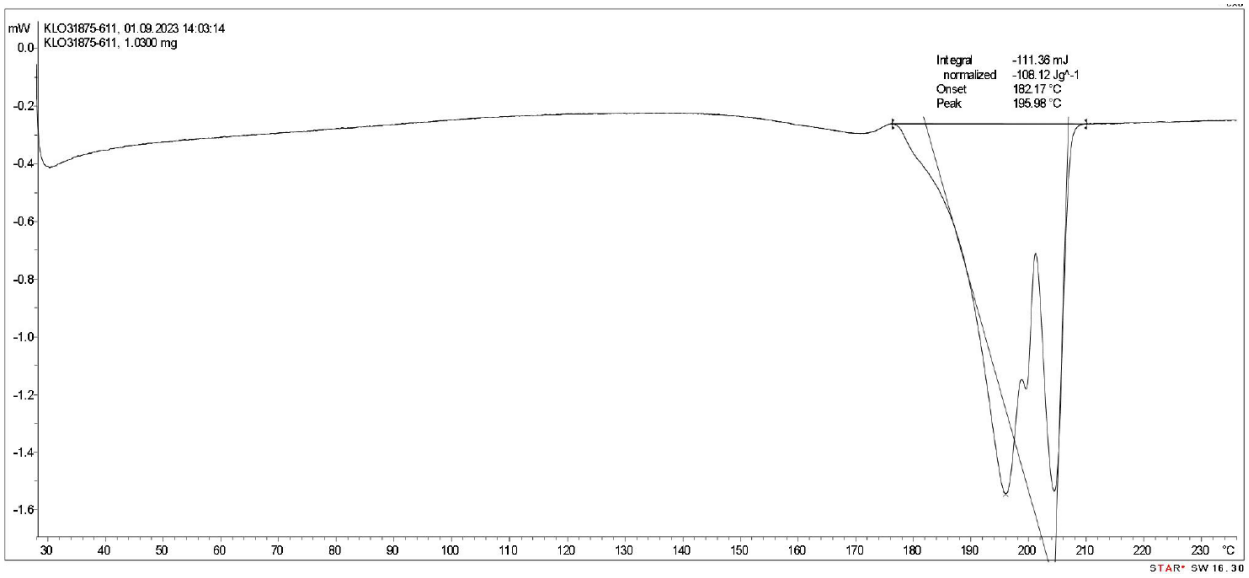
^{13}C-NMR (101 MHz, DMSO-d_6) δ = 200.74, 169.50, 167.02, 166.80, 144.58, 138.68, 134.07, 121.35, 120.49, 113.88, 30.71, 24.21, 23.88



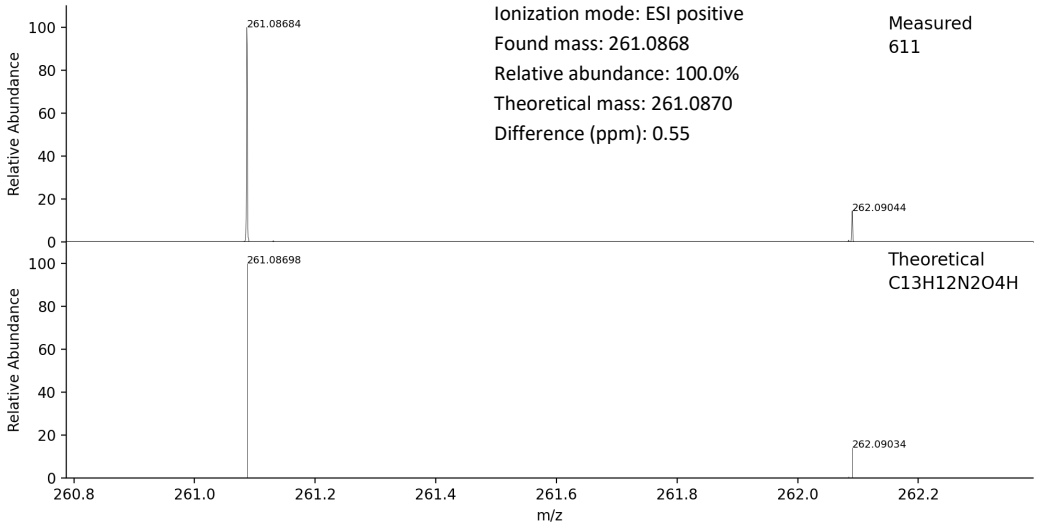
IR


%T
cm-1

DSC


mW
KLO31875-611, 01.09.2023 14:03:14
KLO31875-611, 1.0300 mg
Integral -111.36 mJ
normalized -108.12 Jg^-1
Onset 182.17 °C
Peak 195.98 °C
°C
STAR° SW 16.30

HRMS


Ionization mode: ESI positive
Found mass: 261.0868
Relative abundance: 100.0%
Theoretical mass: 261.0870
Difference (ppm): 0.55
Measured
611
261.08684
262.09044
Theoretical
C13H12N2O4H
261.08698
262.09034
Relative Abundance
m/z