Supporting Information

Title: Identification of Inhibitors of Fungal Fatty Acid Biosynthesis

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Page S2: Figure S1. Schematic of the biochemical steps and enzymes involved in the fatty acid biosynthesis.

Page S3: Figure S2. Phylogenetic relationship of fungal and mammalian Δ9-fatty acid desaturase enzymes.

Page S4: Figure S3. Off-target inhibitors do not cause the expected population shifts in the expression pools.

Page S5: Figure S4. Structures of the primary hit compounds.

Page S6: Figure S5. Ole1p inhibitors have pH-dependent activity on Candida albicans.

Page S7: Table S1. Oligonucleotides used in this study.

Page S8: Table S2. Isoxazole derivatives have broad-spectrum antifungal activity, and are effective against azole resistant fungal isolates.

Page S9: Table S3. Thiadiazole derivatives have broad-spectrum antifungal activity, and are effective against azole resistant fungal isolates.

Page S10-12: Synthetic schemes and chemistry experiment procedures.
Page S13-24: Compound characterization

Page S25: References
Figure S1. Schematic of the biochemical steps and enzymes involved in the fatty acid biosynthesis. Note the FAS complex catalyzes multiple rounds of synthesis to sequentially elongate the hydrocarbon backbone 2-carbons at a time, with each round of elongation utilizing a molecule of malonyl-CoA. The Ole1p Δ9-desaturase predominantly acts upon the 16 and 18 carbon saturated palmitic and stearic acids. FAS = fatty acid synthase; Acc1p = acetyl-CoA carboxylase; Ole1p = Δ9-fatty acid desaturase.
Figure S2. Phylogenetic relationship of fungal and mammalian \( \Delta^9 \)-fatty acid desaturase enzymes. The amino acid sequences of fungal and mammalian \( \Delta^9 \)-desaturase enzymes were aligned (A), % identity calculated (B) and their phylogenetic relationships evaluated (C) using the phylogeny.fr server (http://www.phylogeny.fr/index.cgi). Six conserved histidine residues and a conserved asparagine responsible for coordinating the two bound iron atoms are indicated within the red boxes. The blue boxes indicate two residues positioned at the end of the substrate binding channel that are believed to be key determinants of substrate specificity. DmDESAT1 (Q7K4Y0) and DmDESAT2 (Q9VG68) = Drosophila melanogaster; HsSCD1 (O00767) and HsSCD5 (Q86SK9) = Homo sapiens; MmSCD1 (P13516), MmSCD2 (P13011) MmSCD3 (Q99PL7) and MmSCD4 (Q6T707) = Mus musculus (mouse); E.coli_desat (A0A6N7NMN0) = E. coli.
Figure S3. Off-target inhibitors do not cause the expected population shifts in the expression pools. (A) C. albicans Ole1p strains OLE1/OLE1+P_{TEF1}-OLE1 (OLE1_{HI}), OLE1/OLE1 (OLE1_{WT}), OLE1/ole1Δ (OLE1_{MED}), and P_{ACT1}-OLE1/ole1Δ (OLE1_{LO}) were tagged with CER, dTOM, GFPγ, and φYFP respectively, and were combined in equal proportions to create an expression pool. Approximately 1 × 10^3 cells of the combined pool was inoculated into YNB medium in the wells of a 96-well plate in the presence of a serial dilution of cerulenin. After 48 hours at 30°C, fluorescence was read at all four FP’s wavelengths, and expressed as a percentage of fluorescence of the untreated wells. Values presented are the averages and standard deviations of technical triplicates and are representative of two independent experiments. (B) C. albicans FAS strains FAS1/FAS1+P_{TEF1}-FAS1 (FAS1_{HI}), FAS1/FAS1 (FAS1_{WT}), FAS1/fas1Δ (FAS1_{MED}), and P_{TEF1}-FAS1/fas1Δ (FAS1_{PR}) were tagged with CER, dTOM, GFPγ, and φYFP respectively, and were combined in equal proportions to create an expression pool. Approximately 1 × 10^3 cells of the combined pool was inoculated into YNB medium in the wells of a 96-well plate in the presence of a serial dilution series of cerulenin. After 48 hours at 30°C, fluorescence was read at all four FP’s wavelengths, and expressed as a percentage of fluorescence of the untreated wells. Values presented are the averages and standard deviations of technical triplicates and are representative of two independent experiments.
| FAI # | Structure | FAI # | Structure |
|-------|-----------|-------|-----------|
| 53    | ![Structure 53](image1) | 58    | ![Structure 58](image2) |
| 54    | ![Structure 54](image3) | 59    | ![Structure 59](image4) |
| 55    | ![Structure 55](image5) | 4     | ![Structure 4](image6) |
| 1     | ![Structure 1](image7) | 60    | ![Structure 60](image8) |
| 56    | ![Structure 56](image9) | 61    | ![Structure 61](image10) |
| 57    | ![Structure 57](image11) | 62    | ![Structure 62](image12) |
| 3     | ![Structure 3](image13) | 63    | ![Structure 63](image14) |
| 2     | ![Structure 2](image15) | 64    | ![Structure 64](image16) |

Figure S4. Structures of the primary hit compounds. FAI = Fatty acid inhibitor.
Figure S5. Ole1p inhibitors have pH-dependent activity on *Candida albicans*. *C. albicans* Ole1p strains OLE1/OLE1+*pTEF1*-OLE1 (OLE1HI), OLE1/OLE1 (OLE1WT), OLE1/ole1Δ (OLE1MED), and *pACT1*-OLE1/ole1Δ (OLE1LO) were tagged with CER, dTOM, GFPγ, and φYFP respectively, and were combined in equal proportions to create an expression pool. Approximately 1 $\times$ 10$^3$ cells of the combined pool was inoculated into YNB medium buffered to pH 5, 6, or 7 in the wells of a 96-well plate in the presence of a serial dilution of ECC190, FAI54, FAI409, FAI429, FAI496. After 48 hours at 30°C, fluorescence was read at all four FP’s wavelengths, and expressed as a percentage of fluorescence of the untreated wells. Values presented are the averages and standard deviations of technical triplicates and are representative of two independent experiments.
Table S1. Oligonucleotides used in this study.

| Primer        | Sequence                                                                 |
|---------------|--------------------------------------------------------------------------|
| FAS10DSF      | TGAGGTATAAAACTTTCCCCCTTATTGTATAATTATATACAGTATTTCCTCAGTCACCGTATTTTTGATG |
| FAS10DSR      | AGAGAAATATATTTCTACAAACTTGGAGCTGACGGACATTTCTGCTAGATATAACAAAGATTGAG||
| FAS1AMPF      | TGTGGAATATGTTCAATACAGTCG                                                |
| FAS1AMPR      | AGACCAATGAGGCCAAGCTG                                                    |
| ARG4INTR2     | AATGACTGAATATATGCGTGC                                                   |
| ARG4INTR2     | AGACCTAGTGGGAAAGAAGAG                                                   |
| FAS1PRF       | CCAACATTTAAACACTTGGAGATCAACCTGATAGTGGAGGAGAGTCTGAGATAAAACAAGAGTTGAGC   |
| FAS1PRR       | TTGGGTTACCAAATGGGTATGCTCAATGGAACCACATGAGTTATGAGGAAAGGTCATAGTCATACGTCATG |
| FAS1ORFF-Sall | TCAAGCTCAATGCTGCAATGTGACCTGCTTCCG                                     |
| FAS1ORFR-MluI | TCAACCACTCAAGCTGCTTCAATACGAG                                              |
| FAS1qF2       | CAGGGTTTCTTTTGAG                                                       |
| FAS1qR2       | TACCTGATGATGAGG                                                         |
| OLE1DSF       | CAAAGAAGAGATGTTGCAAACTTGGAGCTGAAAGTGAATAGAGTCTGAGATTTTTTCCAGTCAAGTCTTT |
| OLE1DSR       | ATGGCTAAAGAGAGTTTGGAGAAGAGAGTTTGGAGTCAATACGTCATGAGCACTTTTGAGTTTGGAGCTA |
| OLE1AMPR-Sacl | TCAAGGGCTCTCAAGCTGAAATACCTGTTGAGCTGAAATTCCTACGAGGAGATTTATAGGAGAGGAGGG |
| OLE1AMPR-Sacl | TCAAGGGCTCTCAAGCTGAAATACCTGTTGAGCTGAAATTCCTACGAGGAGATTTATAGGAGAGGAGGG |
| OLE1PRF       | AAAGGAGCTTAAATACAGATCTGACTGAGATTTTCAATAATTACAGAGAGGAGGAGTTGAGAATCTCAT |
| OLE1PRR       | GTACCTGGATCAATGATATGCTGCAATTCCTACGTAAGTGATTCAGTTGGCTTGGAGCTGTTGCTTGGAG |
| OLE1ORFF-Sall | TCAAGGGCTCTCAAGCTGAAATACCTGTTGAGCTGAAATTCCTACGAGGAGATTTATAGGAGAGGAGGG |
| OLE1ORFR-MluI | TCAAGGGCTCTCAAGCTGAAATACCTGTTGAGCTGAAATTCCTACGAGGAGATTTATAGGAGAGGAGGG |
| OLE1qF2       | GGTATCTCTGACGATAACCTGTCATGAGGAGATTTATAGGAGAGGAGATTTATAGGAGAGGAGGG |
| OLE1qR2       | TTTGGGAATGCTTGGAGTTTGGAGTTTGGAGTTTGGAGTTTGGAGTTTGGAGTTTGGAGTTTGGAGTTTGGAGT
Table S2. Isoxazole derivatives have broad-spectrum antifungal activity, and are effective against azole resistant fungal isolates.

| Compound # | R   | SC5314 | TW17 | SM1 | SM3 | 381  | 384 | H99 | Afum |
|------------|-----|--------|------|-----|-----|------|-----|-----|------|
| 12         |     | ![Chemical Structure](image1) | 0.39 | 0.39 | 1.56 | 1.56 | 0.39 | 0.78 | 0.39 | 1.56 |
| 16         |     | ![Chemical Structure](image2) | 0.78 | 0.78 | 3.125 | 3.125 | 0.78 | 0.78 | 0.78 | 1.56 |

Note:
SC5314: *Candida albicans* azole susceptible strain. TW17: *Candida albicans* azole resistant strain. SM1: *Candida glabrata* azole susceptible strain. SM3: *Candida glabrata* azole resistant strain. 381: *Candida auris* azole susceptible strain. 384: *Candida auris* azole resistant strain. H99: *Cryptococcus neoformans*. Afum: *Aspergillus fumigatus*. All units are micromolar (µM).
Table S3. Thiadiazole derivatives have broad-spectrum antifungal activity and are effective against azole resistant fungal isolates.

| Compound # | R           | SC5314 | TW17 | SM1 | SM3 | 381 | 384 | H99 | Afum |
|------------|-------------|--------|------|-----|-----|-----|-----|-----|------|
| 1          |             | 1.56   | 1.56 | 6.25| 3.13| 1.56| 1.56| 1.56| 6.25 |
| 19         | F           | 0.78   | 0.78 | 3.125| 3.13| 0.78| 0.39| 0.39| 1.56 |
| 20         | F           | 0.78   | 0.78 | 3.13| 3.13| 0.78| 0.78| 0.78| 3.13 |
| 21         | F           | 0.39   | 0.39 | 0.78| 1.56| 0.78| 0.39| 0.39| 0.78 |
| 22         |             | 0.78   | 0.78 | 3.13| 1.56| 0.39| 0.39| 0.39| 0.78 |
| 24         |             | 0.78   | 0.78 | 6.25| 6.25| 0.39| 0.78| 0.78| 1.56 |
| 27         | O           | 0.78   | 0.78 | 3.13| 3.13| 0.39| 0.78| 0.78| 12.5 |
| 30         | C3F         | 1.56   | 1.56 | 6.25| 6.25| 1.56| 3.13| 3.13| >50  |
| 32         | Cl           | 0.39   | 0.39 | 1.56| 1.56| 0.39| 0.39| 0.39| 1.56 |
| 33         | Cl           | 0.39   | 0.39 | 0.78| 0.78| 0.39| 0.39| 0.39| 1.56 |

Note: SC5314: *Candida albicans* azole susceptible strain. TW17: *Candida albicans* azole resistant strain. SM1: *Candida glabrata* azole susceptible strain. SM3: *Candida glabrata* azole resistant strain. 381: *Candida auris* azole susceptible strain. 384: *Candida auris* azole resistant strain. H99: *Cryptococcus neoformans*. Afum: *Aspergillus fumigatus*. ND: Not determined. All units are micromolar (µM).
Chemistry experimental - General

Solvents and reagents were ACS reagent grade and used without further purification unless noted below. Acetonitrile (CH$_3$CN), dimethylformamide (DMF), toluene (PhMe), tetrahydrofuran (THF), dichloromethane (CH$_2$Cl$_2$) and diethyl ether (Et$_2$O) were passed through a column of molecular sieves and stored under argon. All reactions were carried out in oven-dried glassware under argon unless otherwise specified. All reagents, unless specified, were purchased from commercial sources and used without further purification. Hydrazines for $^{11}$ and $^{27}$ were synthesized due to purity issues and not being commercially available, respectively.

Compound purity for all final compounds was confirmed to be >95% by UPLC-MS-ELSD analysis.

Abbreviations

HATU – 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide hexafluorophosphate
NaH – Sodium hydride
MeI – Methyl iodide
Et$_3$N – Triethylamine
CuI – Copper (I) iodide
Cs$_2$CO$_3$ – Cesium carbonate
TFA – Trifluoroacetic acid
Brine – Aqueous saturated sodium chloride solution
Bicarb – Aqueous saturated sodium bicarbonate solution
EtOAc – Ethyl acetate
DIPEA – diisopropylethyl amine (Hünig’s base)
mL – Millilitre
DCM - Dichloromethane
**Synthesis procedures to construct acyl hydrazides**

General procedure for synthesis of acyl hydrazide (42).

To a 6 mL vial with a stir bar was added 1-methyl-1H-imidazole-5-carboxylic acid (31.3 mg, 0.248 mmol, 1 equiv.), 2-fluorophenylhydrazine hydrochloride (53.2 mg, 0.327 mmol, 1.3 equiv.), HATU (138.5 mg, 0.364 mmol, 1.4 equiv.), followed by 1 mL of DMF and stirred. To the stirred suspension was added DIPEA (175 µL, 1.002 mmol, 4 equiv.) and an immediate color change occurred. Reaction was monitored by TLC/UPLC until the carboxylic acid was no longer detectable. Upon completion the reaction was transferred to a 50 mL Erlenmeyer flask, quenched with water and bicarb (10 mL each), and extracted with EtOAc (3 x 20 mL). The organic extracts were washed with bicarb (2 x 10 mL) followed by brine (20 mL), dried over sodium sulfate and concentrated in vacuo. The resulting acyl hydrazide was purified via chromatography eluting a gradient from 20% EtOAc/hexanes to 50% EtOAc/hexanes. Compound #42 was obtained after fraction collection and concentration in 90% yield (52.3 mg, 0.223 mmol).

**Synthesis of 27:**

![Chemical structures](image)

Following literature precedent\(^1\), \#27 -int. 1 was synthesized from 3-iodoanisole (120 µL, 1.008 mmol, 1 equiv.) and tert-butylhydrazine carboxylate (162.5 mg, 1.230 mmol, 1.23 equiv.) to afford 116 mg of \#27 -int. 1. The compounds \(^1\)H NMR matched literature precedent\(^2\) and was used without further purification.

Compound 27 -int. 2 was synthesized following the same procedure to generate the acyl hydrazides from \#27 -int. 1 (116.0 mg, 0.487 mmol, 1 equiv.), 4-methyl-1,2,3-thiadiazole-5-carboxylic acid (86.9 mg, 0.603 mmol, 1.23 equiv.), HATU (296.3 mg, 0.779 mmol, 1.6 equiv.), and triethylamine (105 µL, 0.753 mmol, 1.5 equiv.) in 1.0 mL DMF (0.48 M). After work up and purification via chromatography, 104.0 mg of \#27 -int. 2 was isolated in 58.7% yield. The \(^1\)H NMR was consistent with the product and taken for deprotection without further characterization.

27 was obtained after utilizing tert-butyloxycarbony (Boc) deprotection conditions. 104 mg (0.285 mmol, 1 equiv.) of 27 -int. 2 was added to a 6 mL vial with a stir bar and dissolved in 1.5 mL of dry DCM. The solution was stirred and cooled in an ice bath for 20 minutes. Trifluoracetic acid (TFA, 0.5 mL, 6.49 mmol, 22 equiv.) was added slowly to the reaction mixture over 45 minutes. After addition the ice bath
was removed and the reaction warmed slowly to room temperature and monitored by UPLC. After ~ 4 hours, no more starting material was observed and the reaction was added to a 125 mL Erlenmeyer flask with an additional 20 mL of DCM and quenched with 10 mL of water, followed by 10 mL of saturated bicarbonate. The organic layer was removed and the aqueous layer extracted twice with 2 mL DCM. The combined organic extracts were washed twice with bicarbonate (2 x 20 mL) followed by water (1 x 20 mL). The reaction was dried over sodium sulfate, filtered and concentrated in vacuo, followed by purification by chromatography. The title compound was isolated in 15.6 mg, 20.6% yield.

Synthesis of 11:

Following literature precedent, 11-int. 1 was isolated in 40% yield from iodobenzene (112 µL, 1.001 mmol, 1 equiv.), tert-butylhydrazinecarboxylate (161.4 mg, 1.220 mmol, 1.22 equiv.), copper(I) iodide (201.3 mg, 1.057 mmol, 1.05 equiv.), and cesium carbonate (539.2 mg, 1.655 mmol, 1.65 equiv.) in DMSO (1 mL, 1 M reaction molarity). After work up, product was consistent with literature precedent and used without further purification.

11-int. 2 was synthesized by the same amide coupling procedure to synthesize the acyl hydrazides from 11-int. 1 (85.0 mg, 0.408 mmol, 1 equiv.), 4-methyl-1,2,3-thiadiazole-5-carboxylic acid (76.7 mg, 0.532 mmol, 1.30 equiv.), HATU (231.7 mg, 0.609 mmol, 1.49 equiv.), and triethylamine (85 µL, 0.610 mmol, 1.49 equiv.) in DMF (1 mL, 0.4 M reaction molarity). After work up and purification via chromatography, 101.5 mg of #11-int. 2 was isolated in 74.6% yield. The 1H NMR was consistent with the structure and was taken on without further classification.

11-int. 3 was synthesized by methylation of 11-int. 2. Sodium hydride (60% suspension in mineral oil, 16.0 mg, 0.4 mmol, 1.31 equiv.) was added to a dry 6 mL vial with a stir bar, sealed under argon and suspended in 1 mL of dry DMF. Reaction mixture was stirred and placed in an ice bath. A solution of 11-int. 2 (101.5 mg, 0.304 mmol, 1 equiv.) in 0.75 mL of dry DMF was added slowly over 20 minutes. The vial of #11-int. 2 was rinsed with an additional 0.25 mL of dry DMF and added to the reaction mixture, followed by methyl iodide (25 µL, 0.399 mmol, 1.31 equiv.). After 24 hours only 50% conversion was
observed by UPLC, so two additional aliquots of methyl iodide (25 µL each) were added and reaction was continued for another 24 hours. After ~48 hours, the reaction was completed and quenched with 5 mL of water. The reaction was transferred to a 125 mL Erlenmeyer, where an additional 5 mL of water was added, followed by 20 mL of EtOAc. The aqueous layer was extracted twice with 20 mL of EtOAc, then the combined extracts were washed twice with 20 mL of water and then three times with 50 mL of brine. The organic layer was dried over sodium sulfate, and then filtered. Some material was spilled upon filtration, an estimated 30% was lost. After concentration, 62.0 mg of #11-int. 3 was obtained in 58.6% yield. The $^1$H NMR was consistent with the product and was taken on for deprotection without further characterization.

11 was synthesized following the same Boc-deprotection procedure used for #27. #11-int. 3 (62.0 mg, 0.178 mmol, 1 equiv.), TFA (0.25 mL, 3.240 mmol, 18 equiv.) in dry DCM (1.000 mL, 0.14 M reaction molarity) afforded 15.3 mg of #11 in 34.6% yield.

**Compound characterization**

![Chemical structure of 1.](image1)

1. N’-(2-fluorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 10.63, 10.07 (1:2, s, 1H), 8.67, 7.97 (2:1, s, 1H), 7.08-6.93 (m, 4H), 2.95, 2.85 (1:1, s, 3H). $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 164.1, 164.1, 152.5, 150.6, 136.5, 136.5, 134.8, 134.8, 134.7, 125.5, 125.4, 122.2, 122.2, 116.1, 115.9, 115.4, 115.4, 15.2, 13.8. HRMS-ESI calculated for formula C$_{10}$H$_9$FN$_4$OS [M+H]$^+$ 253.0559, found: 253.0569.

![Chemical structure of 2.](image2)

2. N’-(2-fluorophenyl)-isoxazole-5-carbohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) δ 10.86 (s, 1H), 8.82 (d, J = 5 Hz, 2H), 8.06 (s, 1H), 7.21 (d, J = 5 Hz, 2H), 7.14-7.10 (m, 2H), 6.84-6.76 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 163.2, 152.2, 125.6, 125.6, 121.7, 121.6, 121.6, 116.1, 115.9, 115.6, 107.7. HRMS-ESI calculated for formula C$_{10}$H$_8$FN$_3$O$_2$ [M+H]$^+$ 222.0679, found: 222.0684.

![Chemical structure of 5.](image3)

5. N-(2-fluorobenzyl)isoxazole-5-carboxamide. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.3 (d, J = 5 Hz, 1H), 7.42 (t, J = 10 Hz, 1H), 7.33 (m, 1H), 7.09-7.17 (m, 2H), 7.03 (bs, 1H), 6.96 (d, J = 5 Hz, 1H) 4.71 (d, J = 10 Hz, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 162.6, 162.1, 160.1, 155.6, 151.1, 130.5, 130.4, 130.0, 129.9, 124.5, 124.5, 124.1, 124.0, 115.7, 115.5, 106.7, 37.7, 37.6. HRMS-ESI calculated for formula C$_{11}$H$_9$FN$_2$O$_2$ [M+H]$^+$ 221.0726, found: 221.0732.
6. N-(2-fluorobenzyl)-4-methyl-1,2,3-thiadiazole-5-carboxamide. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.34-7.42 (m, 2H), 7.11-7.19 (m, 2H), 6.35 (bs, 1H), 4.69 (d, $J$ = 5 Hz, 2H) 2.92 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 162.2, 160.2, 159.1, 159.0, 143.4, 130.6, 130.6, 130.1, 130.1, 124.6, 124.6, 124.0, 123.9, 115.8, 115.6, 38.9, 38.8, 13.8. HRMS-ESI calculated for formula C$_{11}$H$_{10}$FN$_3$OS [M+H]$^+$ 252.0607, found: 252.0613.

7. 2-((2-fluorophenyl)amino)-1-phenethan-1-one. Compound 4622 was synthesized according to literature precedent$^3$ and obtained in 55% yield. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.94 (d, $J$ = 10 Hz, 2H), 7.55 (t, $J$ = 10 Hz, 1H), 7.44 (t, $J$ = 10 Hz, 2H), 6.92-6.96 (m, 2H), 6.59-6.63 (m, 2H) 5.04 (bs, 1H), 4.56 (s, 2H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 194.6, 153.0, 135.9, 135.1, 133.8, 128.9, 127.7, 124.5, 124.5, 117.4, 117.3, 114.8, 114.7, 112.6, 112.5, 50.1.

8. N-(2-fluorophenyl)-4-methyl-1,2,3-thiadiazole-5-carboxamide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.65 (bs, 1H), 7.70 (t, $J$ = 10 Hz, 1H), 7.25-7.34 (m, 3H), 2.84 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 159.8, 158.4, 156.7, 154.8, 144.0, 128.1, 127.0, 125.1, 125.0, 125.0, 116.5, 116.4, 13.7. HRMS-ESI calculated for formula C$_{14}$H$_8$FN$_3$OS [M+H]$^+$ 238.0450, found: 238.0459.

10. N'-methyl-N'-phenylisoxazole-5-carboxyhydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 11.03 (s, 1H), 8.82 (d, $J$ = 5 Hz, 1H), 7.28 (t, $J$ = 10 Hz, 2H), 7.21 (d, $J$ = 5 Hz, 1), 6.85-6.90 (m, 3H), 3.24 (s, 3H). $^{13}$C NMR (125 MHz, MeOH-d$_4$) $\delta$ 163.1, 157.7, 152.3, 150.7, 130.1, 121.1, 114.5, 108.0, 41.0. HRMS-ESI calculated for formula C$_{11}$H$_9$FN$_2$O$_2$ [M+H]$^+$ 218.0929, found: 218.0935.
11. N, 4-dimethyl-N'-phenyl-1, 2, 3-thiadiazole-5-carboxhydrazide. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.25 (t, $J$ = 10 Hz, 2H), 6.99 (t, $J$ = 10 Hz, 1H), 6.73 (d, $J$ = 10 Hz, 2H), 6.27 (bs, 1H), 3.22 (s, 3H), 2.98 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.1, 142.8, 134.7, 130.0, 123.6, 114.7, 33.5, 15.4. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$OS [M+H]$^+$ 249.0810, found: 249.0820.

12. N'(4-fluorophenyl)-isoxazole-5-carboxhydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.84 (d, $J$ = 5 Hz, 1H), 8.81 (d, $J$ = 5 Hz, 1H), 8.08 (s, 1H), 7.20 (d, $J$ = 5 Hz, 1H), 7.02 (t, $J$ = 10 Hz, 2H), 6.80-6.77 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 161.9, 157.5, 156.3, 155.6, 152.1, 145.6, 115.9, 115.7, 114.1, 114.1, 106.8. HRMS-ESI calculated for formula C$_{10}$H$_8$FN$_3$O$_2$ [M+H]$^+$ 222.0679, found: 222.0683.

13. N'(2,4-difluorophenyl)-isoxazole-5-carboxhydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.88 (s, 1H), 8.81 (d, $J$ = 5 Hz, 1H), 8.01 (s, 1H), 7.21-7.17 (m, 2H), 6.91-6.81 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 161.8, 156.4, 154.6, 154.5, 152.1, 151.1, 149.1, 149.0, 133.5, 133.4, 133.4, 114.9, 114.8, 114.8, 111.5, 111.5, 111.4, 111.3, 107.0, 104.5, 104.4, 104.3, 104.1. HRMS-ESI calculated for formula C$_{10}$H$_7$F$_2$N$_3$O$_2$ [M+H]$^+$ 240.0584, found: 240.0590.

14. N'(phenyl)-isoxazole-5-carboxhydrazide. $^1$H NMR (500 MHz, MeOH-d$_4$) $\delta$ 8.55 (d, $J$ = 5 Hz, 1H), 7.24-7.20 (t, $J$ = 10 Hz, 2H), 7.04 (t, $J$ = 10 Hz, 2H), 6.90-6.82 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 161.6, 155.9, 151.5, 148.5, 128.8, 119.0, 112.4, 106.2. HRMS-ESI calculated for formula C$_{10}$H$_9$N$_3$O$_2$ [M+H]$^+$ 204.0773, found: 204.0778.

15. N'(o-tolyl)-isoxazole-5-carboxhydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 8.81 (d, $J$ = 5 Hz, 1H), 7.47 (s, 1H) 7.20 (d, $J$ = 5 Hz, 1H), 7.05-7.03 (m, 2H), 6.70-6.66 (m, 2H), 2.20 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 162.1, 156.3, 152.1, 146.4, 130.6, 127.0, 122.5, 119.5, 106.7, 17.8. HRMS-ESI calculated for formula C$_{11}$H$_{11}$N$_3$O$_2$ [M+H]$^+$ 218.0929, found: 218.0934.
16. N’-(m-tolyl)-isoxazole-5-carbohydrazide. $^1$H NMR (500 MHz, MeOH-d$_4$) $\delta$ 8.55 (d, $J = 5$ Hz, 1H), 7.11-7.07 (t, $J = 10$ Hz, 1H), 7.05 (d, $J = 5$ Hz, 1H), 6.71-6.67 (m, 3H), 2.28 (s, 3H). $^{13}$C NMR (125 MHz, MeOD-d$_4$) $\delta$ 163.0, 152.2, 149.5, 140.0, 129.9, 122.8, 122.4, 115.0, 111.6, 107.6, 21.6. HRMS-ESI calculated for formula C$_{11}$H$_{11}$N$_3$O$_2$ [M+H]$^+$ 218.0929, found: 218.0932.

17. N’-(p-tolyl)-isoxazole-5-carbohydrazide. $^1$H NMR (400 MHz, MeOH-d$_4$) $\delta$ 8.55 (d, $J = 4$ Hz, 1H), 7.03-7.01 (m, 3H) 6.79-6.77 (d, $J = 8$ Hz, 1H), 6.71-6.67 (m, 3H), 2.23 (s, 3H). $^{13}$C NMR (125 MHz, MeOD-d$_4$) $\delta$ 163.3, 152.2, 147.1, 131.1, 130.5, 114.7, 107.6, 20.5. HRMS-ESI calculated for formula C$_{11}$H$_{11}$N$_3$O$_2$ [M+H]$^+$ 218.0927, found: 218.0927.

18. N’-(o-anisolyl)-isoxazole-5-carbohydrazide. $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 8.76 (d, $J = 4$ Hz, 1H), 7.25 (bs, 1H), 7.16 (d, $J = 4$ Hz, 1H), 6.94-6.92 (dd, $J = 8$, 4 Hz, 1H), 6.78-6.77 (m, 2H), 6.73-6.71 (dd, $J = 8$, 4 Hz, 1H) 3.85 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 159.9, 152.1, 147.2, 124.4, 120.8, 119.5, 111.6, 110.8, 106.2, 55.6. HRMS-ESI calculated for formula C$_{11}$H$_{11}$N$_3$O$_3$ [M+H]$^+$ 234.0878, found: 234.0875.

19. N’-(3-fluorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.67, 10.19 (3:4, s, 1H), 8.90, 8.44 (4:3, s, 1H), 7.30-7.18 (m, 1H), 6.71-6.53 (m, 3H), 2.95, 2.84 (2:1, s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.1, 162.5, 149.5, 134., 131.6, 131.5, 131.1, 131.0, 110.0, 110.0, 108.8, 101.0, 100.8, 99.5, 99.3, 15.3, 13.8. HRMS-ESI calculated for formula C$_{10}$H$_5$FN$_4$OS [M+H]$^+$ 253.0559, found: 253.0599.

20. N’-(4-fluorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.57, 10.06 (1:3, s, 1H), 8.56, 8.02 (3:1, s, 1H), 7.11-7.07 (m, 2H), 6.89-6.86 (m, 2H), 2.95, 2.84 (3:1, s,
\textbf{21.} \textit{N’-(2,4-difluorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.} $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 10.69, 10.17 (1:2, s, 1H), 8.73, 8.04 (2:1, s, 1H), 7.31-7.24 (m, 1H), 6.98-6.92 (m, 2H), 2.95, 2.84 (2:1, s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 164.1, 164.0, 159.7, 157.9, 157.8, 156.0, 155.9, 152.2, 152.1, 150.2, 150.1, 149.1, 134.8, 131.5, 131.5, 131.5, 116.4, 116.3, 115.0, 112.0, 111.8, 111.6, 111.4, 105.8, 104.9, 104.6, 15.3, 13.8. HRMS-ESI calculated for formula C$_{10}$H$_8$F$_2$N$_4$OS $[\text{M+H}]^+$ 271.0465, found: 271.0475.

\begin{center}
\includegraphics[width=0.2\textwidth]{image1.png}
\end{center}

\textbf{22.} \textit{N’-(phenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.} $^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.31-7.27 (m, 2H), 6.99-6.90 (m, 3H), 3.02 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 165.5, 147.7, 130.5, 130.1, 123.2, 114.8, 114.4, 15.1. HRMS-ESI calculated for formula C$_{10}$H$_{10}$N$_4$OS $[\text{M+H}]^+$ 235.0653, found: 235.0661.

\begin{center}
\includegraphics[width=0.2\textwidth]{image2.png}
\end{center}

\textbf{23.} \textit{N’-(o-tolyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.} $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 7.19 (d, $J=10$ Hz, 1H), 7.12 (q, $J=10$ Hz, 1H), 6.88 (t, $J=10$ Hz, 1H), 6.83 (d, $J=5$ Hz, 1H), 3.02 (s, 3H), 2.39 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 164.8, 164.1, 143.9, 134.5, 130.4, 126.7, 123.5, 121.4, 111.4, 16.0, 13.8. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$OS $[\text{M+H}]^+$ 249.0810, found: 249.0812.

\begin{center}
\includegraphics[width=0.2\textwidth]{image3.png}
\end{center}

\textbf{24.} \textit{N’-(m-tolyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.} $^1$H NMR (500 MHz, MeOH-$d_4$) $\delta$ 7.16 (t, $J=10$ Hz, 1H), 6.80 (d, $J=10$ Hz, 1H), 6.72 (m, 2H), 3.02 (s, 3H), 2.30 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 165.5, 147.7, 140.6, 135.9, 130.3, 124.0, 122.4, 115.4, 112.0, 21.5, 15.1. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$OS $[\text{M+H}]^+$ 249.0810, found: 249.0814.
25.  N’-(p-tolyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.  
$^1$H NMR (500 MHz, MeOH-d$_4$) $\delta$ 7.10 (d, $J = 10$ Hz, 2H), 6.81 (d, $J = 10$ Hz, 2H), 3.01 (s, 3H), 2.27 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 165.4, 145.2, 135.9, 132.8, 130.9, 115.0, 114.7, 20.6, 15.1. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$OS [M+H]$^+$ 249.0810, found: 249.0813.

![Chemical structure](image)

26.  N’-(2-methoxyphenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.  
$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 9.98 (s, 1H), 8.25 (s, 1H), 7.02 (dd, $J = 1.5$, 8.5 Hz, 1H), 6.89 (dt, $J = 1.5$, 7.5 Hz, 1H), 6.83 (t, $J = 7.5$ Hz, 1H), 6.73 (dd, $J = 1.5$, 8.5 Hz, 1H), 3.89 (s, 3H), 2.94 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.3, 163.8, 148.0, 135.8, 134.9, 121.9, 121.4, 113.1, 111.6, 56.3, 15.3. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$O$_2$S [M+H]$^+$ 265.0759, found: 265.0767.

![Chemical structure](image)

27.  N’-(3-methoxyphenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.  
$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.14 (s, 1H), 8.66 (s, 1H), 7.02 (t, $J = 10$ Hz, 1H), 6.49 (m, 1H), 6.43 (m, 1H), 6.37 (m, 1H), 3.71 (s, 3H), 2.95 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.3, 164.0, 160.7, 148.6, 134.5, 130.8, 107.0, 106.4, 99.8, 55.5, 15.3. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$O$_2$S [M+H]$^+$ 265.0759, found: 265.0764.

![Chemical structure](image)

28.  N’-(4-methoxyphenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.  
$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.1 (s, 1H), 8.41 (s, 1H), 6.86 (d, $J = 10$ Hz, 2H), 6.80 (d, $J = 10$ Hz, 2H), 6.83 (t, $J = 7.5$ Hz, 1H), 6.73 (dd, $J = 1.5$, 8.5 Hz, 1H), 3.68 (s, 3H), 2.95 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.2, 163.9, 154.8, 140.3, 134.4, 115.4, 115.1, 55.7, 15.3. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$O$_2$S [M+H]$^+$ 265.0759, found: 265.0766.

![Chemical structure](image)

29.  N’-(2-(trifluoromethyl)phenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide.  
$^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.65 (s, 1H), 7.70 (t, $J = 10$ Hz, 1H), 7.24-7.34 (m, 3H), 2.84 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.2, 164.2, 160.2, 159.6, 149.6, 148.1, 134.5, 131.0, 130.6, 118.1, 118.0, 117.9, 109.9, 109.9, 15.3. HRMS-ESI calculated for formula C$_{11}$H$_9$F$_3$N$_4$OS [M+H]$^+$ 303.0527, found: 303.0531.
30. N’-(3-(trifluoromethyl)phenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. \(^1\)H NMR (500 MHz, DMSO-d\(_6\)) \(\delta\) 10.76, 10.25 (2:3, s, 1H), 9.04, 8.61 (3:2, s, 1H), 7.41-7.52 (m, 1H), 7.06-7.27 (m, 3H), 2.96, 2.84 (3:2, s, 3H). \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)) \(\delta\) 164.2, 160.2, 159.7, 149.6, 148.1, 134.5, 131.1, 130.6, 130.4, 118.1, 118.0, 117.9, 116.3, 109.9, 109.9, 15.3. HRMS-ESI calculated for formula C\(_{11}\)H\(_9\)F\(_3\)N\(_4\)OS [M+H]\(^+\) 303.0527, found: 303.0537.

31. N’-(4-(trifluoromethyl)phenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. \(^1\)H NMR (500 MHz, DMSO-d\(_6\)) \(\delta\) 10.78, 10.29 (3:4, s, 1H), 9.18, 8.78 (4:3, s, 1H), 7.61, 7.52 (4:3, d, \(J = 10\) Hz, 2H), 7.01, 6.92 (4:3, d, \(J = 10\) Hz, 2H), 6.83 (t, \(J = 7.5\) Hz, 1H), 6.73 (dd, \(J = 1.5, 8.5\) Hz, 1H), 3.68 (s, 3H), 2.95 (s, 3H). \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)) \(\delta\) 164.2, 164.1, 160.3, 150.8, 134.5, 127.2, 150.8, 134.5, 127.2, 126.8, 126.8, 113.8, 112.2, 15.2. HRMS-ESI calculated for formula C\(_{11}\)H\(_9\)F\(_3\)N\(_4\)OS [M+H]\(^+\) 303.0527, found: 303.0531.

32. N’-(2-chlorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. \(^1\)H NMR (500 MHz, DMSO-d\(_6\)) \(\delta\) 10.76, 10.19 (1:2, s, 1H), 8.66, 7.89 (2:1, s, 1H), 7.33-7.44 (m, 1H), 7.20-7.25 (m, 1H), 6.80-6.94 (m, 2H), 2.94, 2.86 (2:1, s, 3H). \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)) \(\delta\) 164.1, 144.4, 143.0, 134.9, 130.2, 128.7, 122.5, 119.2, 114.4, 15.2. HRMS-ESI calculated for formula C\(_{10}\)H\(_9\)ClN\(_4\)OS [M+H]\(^+\) 269.0264, found: 269.0270.

33. N’-(3-chlorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. \(^1\)H NMR (500 MHz, DMSO-d\(_6\)) \(\delta\) 10.69, 10.20 (1:2, s, 1H), 8.90, 8.45 (2:1, s, 1H), 7.19-7.30 (m, 1H), 6.76-6.96 (m, 3H), 2.95, 2.84 (2:1, s, 3H). \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)) \(\delta\) 164.2, 150.6, 148.9, 134.9, 134.5, 131.5, 121.4, 113.5, 112.7, 15.3. HRMS-ESI calculated for formula C\(_{10}\)H\(_9\)ClN\(_4\)OS [M+H]\(^+\) 269.0264, found: 269.0269.

34. N’-(4-chlorophenyl)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. \(^1\)H NMR (500 MHz, DMSO-d\(_6\)) \(\delta\) 10.67, 10.19 (1:2, s, 1H), 8.82, 8.34 (2:1, s, 1H), 7.22, 7.31 (1:2, d, \(J = 5\) Hz, 2H), 6.80, 6.88 (1:2, d, \(J = 5\) Hz,
(2H), 2.95, 2.84 (2:1, s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.2, 147.9, 146.2, 134.4, 129.6, 129.2, 115.7, 15.3. HRMS-ESI calculated for formula C$_{10}$H$_9$ClN$_4$O$_2$ [M+H]$^+$ 269.0264, found: 269.0269.

35. N’-(2-fluorophenyl)isonicotinohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.71 (bs, 1H), 8.79 (d, $J = 5$ Hz, 2H), 7.96 (bs, 1H), 7.83 (d, $J = 5$ Hz, 2H), 7.10-7.14 (m, 1H), 7.00 (t, $J = 5$ Hz, 1H), 6.86 (t, $J = 5$ Hz, 1H), 6.76 (m, 1H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 165.3, 150.9, 149.8, 140.3, 137.1, 137.0, 125.1, 125.1, 121.8, 119.6, 119.5, 115.5, 115.4, 114.2, 114.2. HRMS-ESI calculated for formula C$_{12}$H$_{10}$FN$_3$O [M+H]$^+$ 232.0886, found: 232.0896.

36. N’-(2-fluorophenyl)nicotinohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.62 (bs, 1H), 9.09 (d, $J = 2.5$ Hz, 1H), 8.78 (dd, $J = 2.5, 5$ Hz, 1H), 8.26 (dt, $J = 2.5, 5$ Hz, 1H), 7.92 (bs, 1H), 7.57 (dd, $J = 5, 10$ Hz, 1H), 7.12 (dd, $J = 5, 10$ Hz, 1H), 7.00 (t, $J = 5$ Hz, 1H), 6.89 (t, $J = 5$ Hz, 1H), 6.76 (m, 1H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 165.5, 152.9, 148.8, 137.3, 137.2, 135.6, 129.0, 125.1, 124.2, 119.5, 119.4, 115.5, 115.3, 114.3, 114.2. HRMS-ESI calculated for formula C$_{12}$H$_{10}$FN$_3$O [M+H]$^+$ 232.0886, found: 232.0901.

37. N’-(2-fluorophenyl)picolinohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.62 (bs, 1H), 8.71 (d, $J = 5$ Hz, 1H), 8.03 (m, 2H), 7.82 (bs, 1H), 7.67 (m, 1H), 7.11 (m, 1H), 6.97 (t, $J = 5$ Hz, 1H), 6.73-6.80 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.5, 151.7, 150.1, 149.8, 149.2, 138.3, 137.3, 137.2, 127.4, 125.0, 125.0, 122.8, 119.2, 119.1, 115.4, 115.2, 114.2, 114.1. HRMS-ESI calculated for formula C$_{12}$H$_{10}$FN$_3$O [M+H]$^+$ 232.0886, found: 232.0888.

38. N’-(2-fluorophenyl)benzohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 10.37 (bs, 1H), 7.94 (d, $J = 10$ Hz, 2H), 7.68 (bs, 1H), 7.58 (m, 1H), 7.51 (t, $J = 10$ Hz, 2H), 7.10 (dd, $J = 5, 10$ Hz, 1H), 7.02 (t, $J = 10$ Hz, 1H), 6.87 (t, $J = 10$ Hz, 1H), 6.73-6.79 (m, 1H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 166.8, 151.7, 149.8, 137.6, 137.5, 133.3, 132.2, 129.0, 127.8, 125.1, 125.0, 119.3, 119.3, 115.3, 115.4, 114.1. HRMS-ESI calculated for formula C$_{13}$H$_{11}$FN$_2$O [M+H]$^+$ 231.0933, found: 231.0937.
39. \(N'-(2\text{-fluorophenyl})\text{cyclohexanecarbohydrazide.}\) \(^1\text{H NMR (500 MHz, DMSO-d}\_6) \delta \) 9.62 (d, \(J = 5\) Hz, 1H), 7.54 (bs, 1H), 7.05 (dd, \(J = 10, 20\) Hz, 1H), 6.98 (t, \(J = 5\) Hz), 6.69-6.73 (m, 2H), 2.20-2.25 (m, 1H), 1.62-1.78 (m, 5H), 1.10-1.43 (m, 5H). \(^{13}\text{C NMR (125 MHz, DMSO-d}\_6) \delta \) 175.4, 151.5, 149.6, 137.6, 137.5, 125.0, 124.9, 119.0, 118.9, 115.3, 115.2, 113.7, 113.7, 42.5, 29.5, 25.8, 25.7. HRMS-ESI calculated for formula \(\text{C}_{13}\text{H}_{17}\text{FN}_{2}\text{O} [\text{M+H}]^+\) 237.1403, found: 237.1410.

40. \(N'-(2\text{-fluorophenyl})\text{pyridazine-3-carbohydrazide.}\) \(^1\text{H NMR (500 MHz, MeOH-d}_4) \delta \) 9.37 (dd, \(J = 10, 20\) Hz, 1H), 8.30 (dd, \(J = 10, 20\) Hz, 1H), 7.91 (dd, \(J = 10, 20\) Hz, 1H), 6.95-7.08 (m, 3H), 6.82-6.86 (m, 1H). \(^{13}\text{C NMR (125 MHz, DMSO-d}_6) \delta \) 165.1, 154.6, 154.3, 154.1, 151.7, 137.6, 137.5, 129.9, 127.5, 125.6, 125.6, 121.6, 121.6, 116.1, 115.9, 115.7, 115.7. HRMS-ESI calculated for formula \(\text{C}_{11}\text{H}_9\text{FN}_4\text{O} [\text{M+H}]^+\) 233.0838, found: 233.0839.

41. \(N'-(2\text{-fluorophenyl})\text{pyrazine-2-carbohydrazide.}\) \(^1\text{H NMR (500 MHz, DMSO-d}_6) \delta \) 10.81 (bs, 1H), 9.18 (d, \(J = 10\) Hz, 1H), 8.92 (d, \(J = 10\) Hz, 1H), 8.80 (dd, \(J = 5, 10\) Hz, 1H), 7.92 (bs, 1H), 7.11 (dd, 10, 20 Hz, 1H), 6.98 (t, \(J = 10\) Hz, 1H), 6.82 (t, \(J = 10\) Hz, 1H), 6.74 (m, 1H). \(^{13}\text{C NMR (125 MHz, DMSO-d}_6) \delta \) 163.6, 151.7, 149.8, 148.4, 145.1, 144.1, 137.1, 137.0, 125.0, 125.0, 119.4, 119.3, 115.4, 115.3, 114.2, 114.2. HRMS-ESI calculated for formula \(\text{C}_{11}\text{H}_{9}\text{FN}_4\text{O} [\text{M+H}]^+\) 233.0838, found: 233.0840.

42. \(N'-(2\text{-fluorophenyl})\text{-1-methyl-1H-imidazole-5-carbohydrazide.}\) \(^1\text{H NMR (500 MHz, DMSO-d}_6) \delta \) 10.20 (bs, 1H), 7.83 (s, 1H), 7.80 (bs, 1H), 7.76 (s, 1H), 7.10 (dd, 10, 20 Hz, 1H), 7.00 (t, 10 Hz, 1H), 6.82 (t, \(J = 10\) Hz, 1H), 6.74 (m, 1H), 3.80 (s, 3H). \(^{13}\text{C NMR (125 MHz, DMSO-d}_6) \delta \) 160.7, 151.6, 150.0, 142.9, 137.6, 137.5, 133.0, 125.1, 125.0, 124.5, 119.3, 119.2, 115.4, 115.3, 114.1, 114.1, 34.0. HRMS-ESI calculated for formula \(\text{C}_{11}\text{H}_{11}\text{FN}_4\text{O} [\text{M+H}]^+\) 235.0995, found: 235.1003.
43. N’-(2-fluorophenyl)-1-methyl-1H-pyrrole-2-carbohydrazide. 1H NMR (500 MHz, MeOD-d₄) δ 6.89-7.05 (m, 5H), 6.79-6.81 (m, 1H), 6.12 (dd, J = 5, 10 Hz, 1H), 3.89 (s, 3H). 13C NMR (125 MHz, MeOD-d₄) δ 153.9, 151.5, 138.5, 138.4, 130.0, 125.5, 125.5, 124.9, 121.0, 115.9, 115.7, 115.4, 115.3, 114.6, 108.5, 36.7. HRMS-ESI calculated for formula C₁₂H₁₂FN₃O [M+H]⁺ 234.1042, found: 234.1047.

44. N’-(2-fluorophenyl)-1-methyl-1H-pyrrole-2-carbohydrazide. 1H NMR (500 MHz, MeOD-d₄) δ 7.51 (d, J = 5 Hz, 1H), 7.01-7.06 (m, 2H), 6.91-6.96 (m, 2H), 6.82-6.85 (m, 1H), 4.12 (s, 3H). 13C NMR (125 MHz, MeOD-d₄) δ 162.3, 154.0, 138.9, 137.8, 137.7, 135.2, 125.6, 125.6, 121.5, 121.4, 116.1, 115.9, 115.5, 108.6, 39.3. HRMS-ESI calculated for formula C₁₁H₁₁FN₂O [M+H]⁺ 235.0995, found: 235.1001.

45. N’-(4-fluorophenyl)benzohydrazide. 1H NMR (400 MHz, DMSO-d₆) δ 10.32 (d, J = 4 Hz, 1H), 7.91 (d, J = 4 Hz, 2H), 7.77 (d, J = 4 Hz, 1H), 7.49-7.58 (m, 3H), 6.99 (t, J = 8 Hz, 2H), 6.81 (dd, J = 4, 8 Hz, 2H), 4.12 (s, 3H). 13C NMR (100 MHz, DMSO-d₆) δ 166.4, 157.1, 146.0, 133.0, 131.6, 128.4, 127.2, 115.2, 115.0, 113.7, 113.6. HRMS-ESI calculated for formula C₁₃H₁₁FN₂O [M+H]⁺ 231.0933, found: 231.0942.

46. N’-(4-fluorophenyl)furan-2-carbohydrazide. 1H NMR (500 MHz, DMSO-d₆) δ 10.30 (d, J = 2.9 Hz, 1H), 7.86-7.88 (m, 2H), 7.23 (d, J = 3.4 Hz, 1H), 6.99 (t, J = 10 Hz, 2H), 6.74 (dd, J = 4.5, 9 Hz, 2H), 6.65 (dd, J = 1.8, 3.5 Hz, 1H). 13C NMR (125 MHz, DMSO-d₆) δ 158.5, 157.3, 146.9, 146.3, 146.1, 115.8, 115.6, 114.6, 113.9, 113.9, 112.3. HRMS-ESI calculated for formula C₁₁H₉FN₂O₂ [M+H]⁺ 221.0726, found: 221.0732.

47. N’-(4-fluorophenyl)thiophene-2-carbohydrazide. 1H NMR (500 MHz, DMSO-d₆) δ 10.41 (d, J = 5 Hz, 1H), 7.92 (bs, 1H), 7.89 (d, J = 5 Hz, 1H), 7.84 (d, J = 5 Hz, 1H), 7.20 (t, J = 5 Hz, 1H), 7.00 (t, J = 10 Hz, 2H),
6.78 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 161.8, 157.3, 155.5, 146.4, 146.8, 138.1, 131.8, 129.0, 128.6, 115.8, 115.6, 114.0, 113.9. HRMS-ESI calculated for formula C$_{11}$H$_9$FN$_2$OS [M+H]$^+$ 237.0498, found: 237.0492.

52. N’-methyl-N’-phenyl-4-methyl-1,2,3-thiadiazole-5-carbohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) δ 10.24 (bs, 1H), 7.31-7.35 (m, 2H), 7.01-7.06 (m, 3H), 6.85-6.90 (m, 3H), 3.18 (s, 3H), 2.97 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 163.5, 162.6, 148.9, 129.2, 128.9, 122.0, 115.2, 42.8, 14.7. HRMS-ESI calculated for formula C$_{11}$H$_{12}$N$_4$OS [M+H]$^+$ 249.0810, found: 249.0817.

65. N’-(3-chlorophenyl)pyrazine-2-carbohydrazide. $^1$H NMR (500 MHz, DMSO-d$_6$) δ 10.84 (d, J = 5 Hz, 1H), 9.18 (d, J = 5 Hz, 1H), 8.92 (d, J = 5 Hz, 1H), 8.79 (m, 1H), 8.30 (d, J = 5 Hz, 1H), 7.17 (t, J = 10 Hz, 1H), 6.75 (m, 3H). $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 163.6, 151.1, 148.4, 145.1, 144.2, 144.1, 133.9, 130.9, 118.6, 112.0, 111.5. HRMS-ESI calculated for formula C$_{11}$H$_8$ClN$_2$O [M+H]$^+$ 249.0543, found: 249.0545.
Supporting References.

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