Stereoelectronic Effects Dictate Molecular Conformation and Biological Function of Heterocyclic Amides

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Supporting Information

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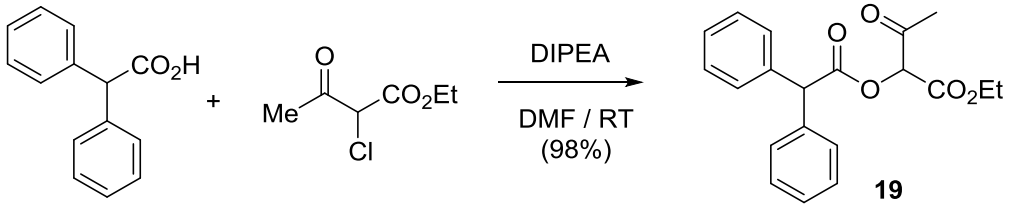
General Purification and Compound Characterization Procedures

Thin-layer chromatography (TLC) was carried out on 0.25 mm Merck silica gel plates (60F-254) and visualized using UV light and iodine vapor. Flash column chromatography was conducted on Merck silica gel 60 (particle size 0.063–0.200 mm).[1] The progress of reactions and purity of products was assessed by UPLC-MS on a Shimadzu Nexera system using a Zorbax eclipse plus C18 100x2.1 mm 1.8 μm column and MeCN/water (both containing 0.1% formic acid) gradients at flow rate 0.5 $mLmin^{-1}$. All final compounds were purified by preparative reverse-phase HPLC on a Phenomenex Luna C18 10 μm, 250 × 21 mm column. Standard conditions were used for elution of all compounds: 100% A to 100% B linear gradient over 20 min at a flow rate of 20 $mLmin^{-1}$ where solvent A was H_2O + 0.1% TFA and solvent B was 90% MeCN, 10% H_2O + 0.1% TFA. Detection was by UV and pure fractions as assessed ≥ 99% by UPLC were combined and lyophilized. Low resolution electrospray ionization mass spectra measurements were obtained on a Micromass LCT. High-resolution mass spectra (HRMS) measurements were obtained on a Bruker microTOF mass spectrometer equipped with a Dionex LC system (Chromeleon) in positive ion mode by direct infusion in MeCN at 100 μL/h using sodium formate clusters as an internal calibrant. Data were processed using Bruker Daltonics DataAnalysis 3.4 software. Mass accuracy was consistently better than 1 ppm error. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 600 equipped with a TCI cryoprobe or Varian 400 spectrometers at 298 K in the deuterated solvents indicated and were referenced to the residual solvent peaks; DMSO-d_6 δ_H 2.49, δ_C 39.51 ppm, $CDCl_3$ δ_H referenced to internal TMS 0 ppm and δ_C 77.01. H_2O/D_2O δ_H referenced to DSS, δ_C CH_3OH 49.50 ppm. Microwave reactions were conducted in a Biotage Initiator 8. Stock solutions of compounds for assay were prepared 10 mM in DMSO-d_6 and the exact concentration was additionally confirmed by the quantitative ^{1}H NMR integration experiment PULCON.[2] NMR spectra reproduced below (pages S12-S19) are from the actual stock solutions used for the biological assays. *Ab initio* calculations were performed with Gaussian 09.[3]

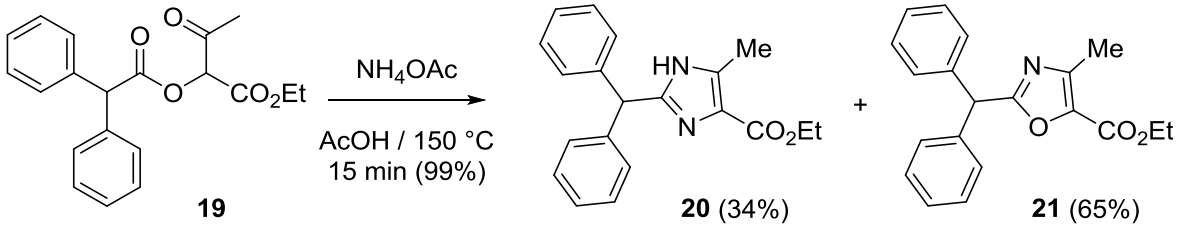
Ethyl 2-(2,2-diphenylacetoxy)-3-oxobutanoate (19)



A solution of diphenylacetic acid (2.12 g, 10 mmol) and ethyl 2-chloroacetoacetate (1.88 g, 11 mmol) in dry DMF (5 mL) was treated with DIPEA (2 mL, 11 mmol) and stirred at RT 17h. Ether (150 mL) was added and the solution was washed with 2M HCl, 1M $NaHCO_3$, brine and dried over $MgSO_4$. Removal of solvent gave **19**, a pale yellow oil 3.33 g, 98%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.25 (m, 10H), 5.50 (s, 1H), 5.23 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 2.20 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 171.1, 164.3, 137.8, 137.7,

128.7, 128.6, 127.54, 127.48, 78.2, 62.5, 56.4, 27.0, 13.9. Two carbons of the diastereotopic phenyls overlap and are not resolved. m/z: 363.1 $[MNa]^+$.

Ethyl 2-benzhydryl-5-methyl-1*H*-imidazole-4-carboxylate (20)

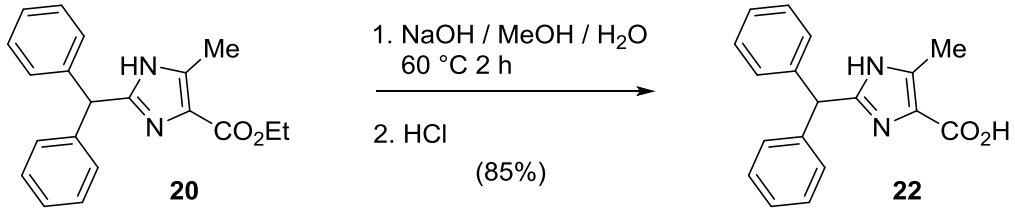


A solution of ethyl 2-(2,2-diphenylacetoxy)-3-oxobutanoate **19** (2.55 g, 7.5 mmol) and NH_4OAc (2.88 g 5 equiv.) in glacial acetic acid (12.5 mL) was stirred and heated until homogeneous then heated in a microwave reactor at 150 °C for 15 min. The mixture was diluted with EtOAc 200 mL and water 50 mL containing conc. NH_3 (15 mL, d 0.88, slight excess) and shaken well. The organic layer was washed with brine and dried over $MgSO_4$ and evaporated to an oil (2.45 g). Flash chromatography 25-40% EtOAc / petrol afforded the imidazole **20** as a white powder (820 mg, 34%) and the oxazole **21** as a pale yellow oil (1.56 g, 65%). Alternatively, the EtOAc solution was concentrated to about 15 mL and left at RT overnight, then in a refrigerator for a further 4h. The crystalline imidazole **20** was filtered off and washed with cooled 50% EtOAc/petrol and dried in air, the oxazole **21** was recovered from the mother liquor and purified by flash chromatography giving an oil.

Imidazole **20** ^{1}H NMR (400 MHz, $CDCl_3$): tautomers ratio 2.9:1 δ9.03 and 8.76 (broad s, 1H), 7.36-7.22 (m, 6H), 7.18-7.08 (m, 4H), 5.74 and 5.62 (s, 1H), 4.35 and 4.29 (q, J = 7.1 Hz, 2H), 2.47 (s, 3H), 1.36 and 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.9, 150.8, 146.4, 140.3, 128.9, 128.7, 127.4, 60.6, 51.2, 50.9, 14.7, 14.4. m/z: 321.2 MH^+.

Oxazole **21** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.23 (m, 10H), 5.61 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 2.47 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 158.7, 146.0, 139.1, 137.7, 128.7, 128.6, 127.4, 61.0, 51.0, 14.3, 13.5. m/z 322.1 MH^+.

2-Benzhydryl-5-methyl-1*H*-imidazole-4-carboxylic acid (22)

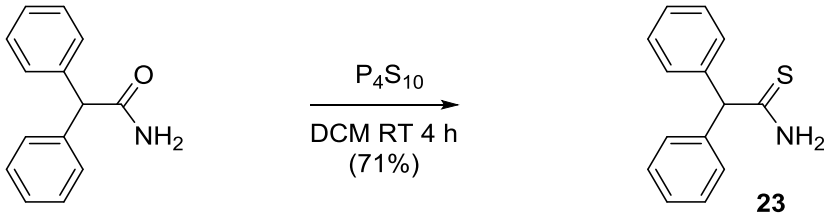


Ethyl 2-benzhydryl-4-methyl-1*H*-imidazole-5-carboxylate **20** (444 mg, 1.38 mmol) and NaOH (200 mg, 4 equiv) in MeOH / water (1:1, 5 mL) were stirred and heated at 60 °C for 2 h. The clear solution was acidified to pH 3 with HCl and the precipitate was collected and air dried

giving the carboxylic acid **22** as a white powder (340 mg, 85%). Note: hydrolysis does not proceed without heating but that extended heating (microwave) leads to decarboxylation of the product.

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 7.34-7.17 (m, 10H), 5.61 (s, 1H), 2.48 (s, 3H). m/z: 293.1 MH^+. ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 140.6, 128.5, 128.1, 126.5, 50.4. some signals not observed due to broadening caused by equilibrating tautomers.

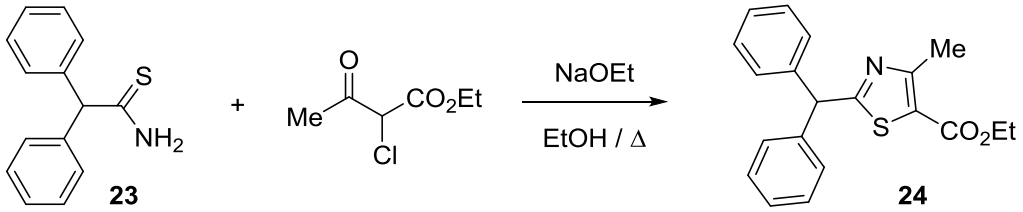
2,2-Diphenylthioacetamide (23)



23

A suspension of 2,2-diphenylacetamide (7.00 g 33.1 mmol) and phosphorus pentasulfide (3.00 g, 6.75 mmol) in DCM (35 mL) was stirred at RT for 4h when TLC revealed complete conversion (R_f thioamide 0.60 50% EtOAc/petrol, amide R_f 0.29). The mixture was filtered and the yellow solution was washed with 10% Na_2CO_3, dried over $MgSO_4$ and evaporated to dryness. The solid residue was recrystallised twice from MeOH (5 mL/g). The mother liquor was evaporated and purified by flash chromatography (15-50% EtOAc/petrol) to remove a yellow oil impurity (R_f 0.89 50% EtOAc/petrol) then the product was recrystallised from MeOH and combined with the above giving the thioamide **23** as white prisms (5.31 g, 71%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.38-7.23 (m, 10H), 6.81 (s, 1H), 5.63 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 209.0, 139.6, 129.0, 128.8, 127.7, 66.4. m/z 228.1 MH^+.

Ethyl 2-diphenylmethyl-4-methyl thiazole-5-carboxylate (24)

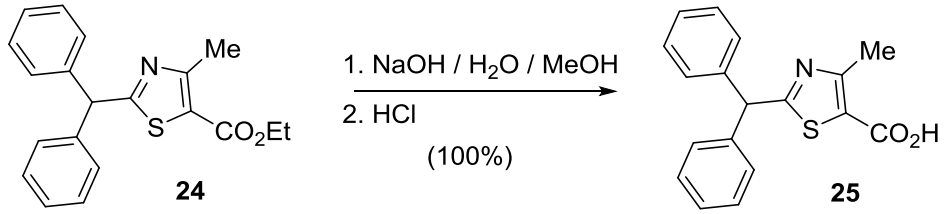


23 **24**

Diphenylthioacetamide **23** (700 mg, 3.08 mmol), ethyl 2-chloroacetoacetate (640 µL, 4.62 mmol) and NaOEt (315 mg, 4.62 mmol) were dissolved in EtOH (5 mL) and stirred at RT overnight. The solution was evaporated and the residue was dissolved in ether and washed with brine, dried over $MgSO_4$ and evaporated. Purification by flash chromatography gave the thiazole **24** a pale yellow oil 810 mg, 78% (r.f 0.85, 50% EtOAc/petrol).

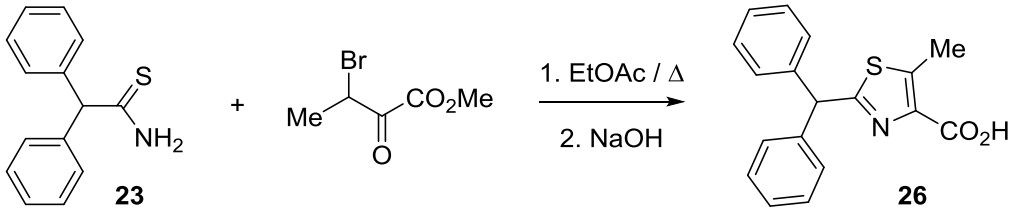
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.21 (m, 10H), 5.77 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.72 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 162.1, 160.3, 141.1, 128.8, 128.6, 127.3, 122.4, 61.0, 55.2, 17.3, 14.2. m/z: 338.1 MH^+.

2-Diphenylmethyl-4-methyl thiazole-5-carboxylic acid (25)



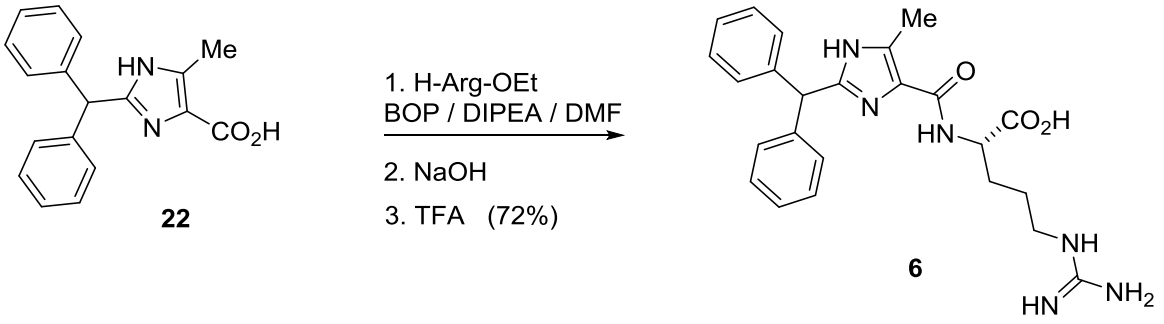
The ethyl ester **24** (750 mg, 2.23 mmol) was dissolved in MeOH (8 mL) then a solution of NaOH (200 mg, 5 mmol) in water (2 mL) was added. The mixture was stirred at RT for 1h then acidified with HCl. The precipitate was extracted into DCM, washed with water and the solution was dried over $MgSO_4$. Removal of solvent gave the acid **25** as a white solid (690 mg, 100%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35-7.20 (m, 10H), 5.81 (s, 1H), 2.71 (s, 3H). m/z: 310.1 MH^+. ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4, 166.8, 161.8, 141.0, 128.9, 128.8, 127.5, 122.2, 55.2, 17.5.

2-Benzhydryl-4-methylthiazole-5-carboxylic acid (26)



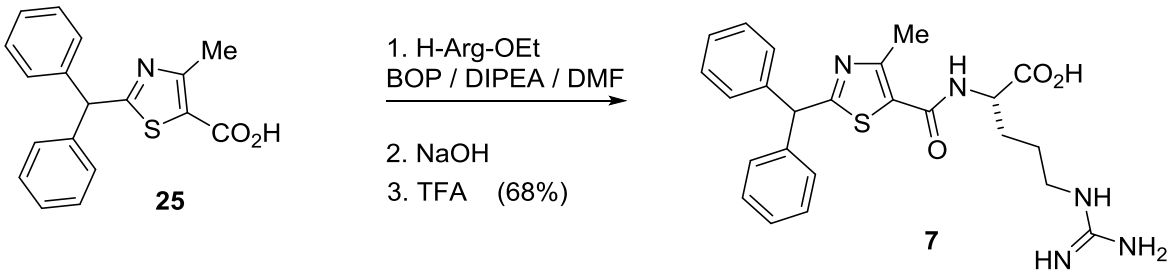
Bromine (0.47 mL, 9.16 mmol, neat) was added dropwise with stirring and cooling on ice to methyl 2-oxobutanoate (1.0 mL, 9.20 mmol, neat, Aldrich). After 15 min the mixture was diluted with EtOAc and washed with 10% $NaHCO_3$, brine, dried over $MgSO_4$ and concentrated to a volume of about 10 mL. Diphenylthioacetamide **23** (910 mg, 4.0 mmol) was added and the solution was refluxed for 2h washed with 10% $NaHCO_3$, brine dried over $MgSO_4$ and evaporated to dryness. The residue was purified by flash chromatogtaphy (20-50% EtOAc/petrol) giving the ester (860 mg, 67%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.18 (m, 10H), 5.90 (s, 1H), 3.91 (s, 3H), 2.72 (s, 3H). The ester was dissolved in MeOH (10 mL) and NaOH (200 mg in water 2 mL) was added. The solution was stirred at rt for 2 h, acidified with HCl and the precipitate was extracted into ether. The solution was washed with brine, dried over $MgSO_4$ and evaporated to dryness giving the acid **26** as a white powder (820 mg, 66% over 2 steps). m/z: 310.1 (MH^+).
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.19 (m, 10H), 5.75 (s, 1H), 2.75 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 162.0, 145.8, 141.1, 140.0, 128.8, 127.5, 54.8, 12.8.

(2-Benzhydryl-5-methyl-1*H*-imidazole-4-carbonyl)-L-arginine (6)



The carboxylic acid **22** (66 mg, 0.23 mmol) and L-arginine ethyl ester dihydrochloride (124 mg, 0.46 mmol) were dissolved in DMF (1 mL) and DIPEA (120 μL) with stirring. When homogeneous, BOP (120 mg, 0.27 mmol) was added and the solution was stirred a RT for 17h. The solvent was evaporated at 0.05 mbar and the residue was dissolved in MeOH (2 mL) and water (2 mL) then NaOH (100 mg) was added. After stirring at RT for 4h the solution was acidified with TFA (250 μL) and the product was isolated by preparative reverse phase HPLC to afford the product **6** (TFA salt) as a white powder after lyophilisation (93 mg, 72%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.91 (d, *J* = 7.5 Hz, 1H), 7.65 (t, *J* = 5.6 Hz, 1H), 7.37-7.32 (m, 4H), 7.30-7.24 (m, 6H), 5.69 (s, 1H), 4.38 (m, 1H), 3.16-3.05 (m, 2H), 2.41 (s, 3H), 1.83 (m, 1H), 1.72 (m, 1H), 1.55-1.46 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 173.4, 161.7, 156.8, 146.7, 140.3, 132.4, 128.7, 128.6, 127.1, 51.1, 49.4, 40.3, 28.5, 25.3, 10.6. One aromatic carbon is overlapped and not resolved. HRMS calculated for $C_{24}H_{29}N_6O_3^+$ 449.2296, found 449.2295.

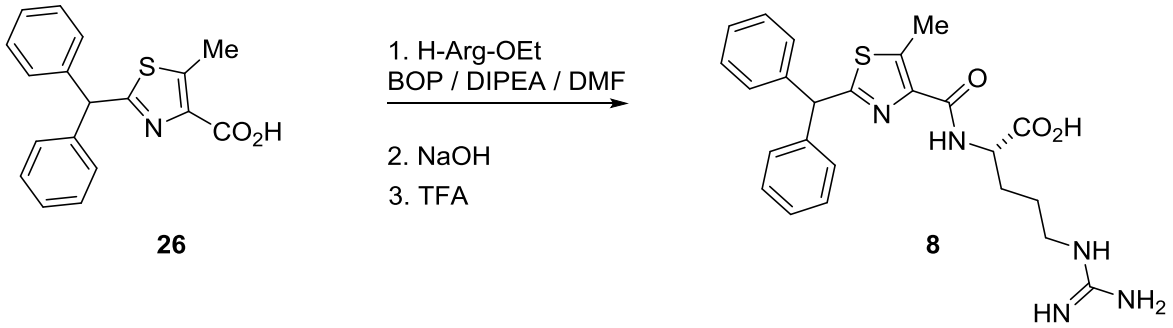
(2-Benzhydryl-4-methylthiazole-5-carbonyl)-L-arginine (7)



The acid **25** (108 mg, 0.35 mmol) and L-arginine ethyl ester dihydrochloride (193 mg, 0.70 mmol 2 equiv) were dissolved in DMF (2 mL) and DIPEA (187 μL 3 equiv). After the solution was homogeneous BOP (185 mg, 0.42 mmol, 1.2 equiv) was added and the solution was stirred at RT for 17 h. The solvent was removed at 0.05 mbar and the residue was dissolved in MeOH (5 mL) and water (1 mL) and NaOH (200 mg) was added. After stirring at RT for 4h the solution was acidified with TFA (500 μL) and the product was isolated by preparative reverse phase HPLC giving **7** (TFA salt) as a white powder (138 mg, 68% for 2 steps) after lyophilisation. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.41 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 5.6 Hz, 1H), 7.39-7.26 (m, 10H), 5.94 (s, 1H), 4.29 (m, 1H), 3.13-3.04 (m, 2H), 2.52 (s, 3H), 1.81 (m, 1H), 1.67 (m, 1H),

1.57-1.44 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 173.1, 172.6, 161.4, 156.6, 154.9, 141.7, 128.67, 128.66 127.2, 125.5, 53.7, 52.2, 40.3, 27.5, 25.4, 17.0. HRMS calculated for $C_{24}H_{28}N_5O_3S^+$ 466.1907, found 466.1907.

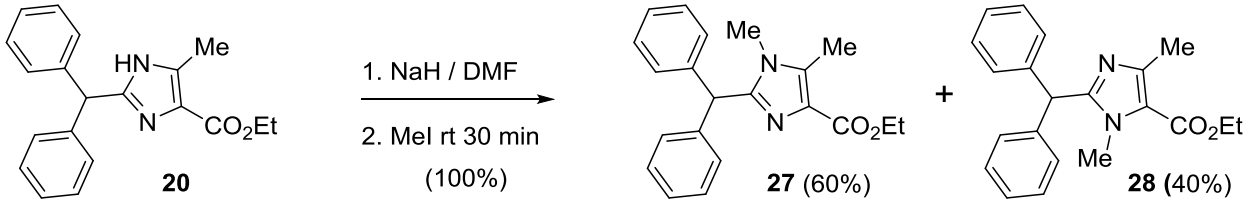
(2-Benzhydryl-5-methylthiazole-4-carbonyl)-L-arginine (8)



26 **8**

Compound **8** was prepared from **26** using the same procedure above for compound **7**.
^{1}H NMR (600 MHz, DMSO-d_6): δ 8.13 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 5.7 Hz, 1H), 7.38-7.25 (m, 10H), 5.93 (s, 1H), 4.38 (m, 1H), 3.14-3.04 (m, 2H), 2.67 (s, 3H), 1.85 (m, 1H), 1.75 (m, 1H), 1.51-1.43 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 173.1, 168.4, 161.8, 156.6, 142.3, 141.8, 140.8, 128.7, 128.6, 127.21, 127.19, 53.5, 51.3, 40.3, 28.2, 25.3, 12.2. HRMS calculated for $C_{24}H_{28}N_5O_3S^+$ 466.1907, found 466.1907.

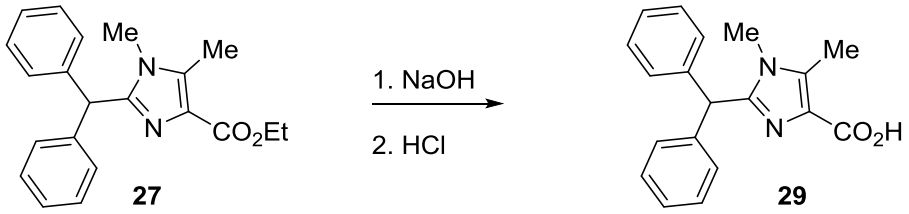
Ethyl 2-benzhydryl-1,5-dimethyl-1H-imidazole-4-carboxylate 27



20 **27** (60%) **28** (40%)

The imidazole **20** (256 mg, 0.80 mmol) was dissolved in dry DMF (2 mL) then NaH (60% dispersion in oil, 50 mg, 1.25 mmol, 1.6 equiv.) was added with stirring. After 1 min MeI (0.5 mL, 8 mmol 10 equiv.) was added and stirring at RT was continued for 30 min. EtOAc was added and the solution was washed with brine 2x, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by flash chromatography (30-50% EtOAc/petrol) to give **27** (160 mg, 60%. R_f 0.34 50% EtOAc/petrol) and **28** (108 mg, 40%. R_f 0.61 50% EtOAc/petrol) as white solids. Data for the major isomer **27** ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33-7.18 (m, 10H), 5.69 (s, 1H), 4.34 (q, J=7.1 Hz, 2H), 3.24 (s, 3H), 2.51 (s, 3H), 1.36 (t, J=7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.0, 147.9, 139.8, 136.7, 128.8, 128.5, 127.8, 126.9, 60.1, 50.0, 30.8, 14.4, 10.3. Data for the minor isomer **28** ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33-7.14 (m, 10H), 5.53 (s, 1H), 4.30 (q, J=7.1 Hz, 2H), 3.70 (s, 3H), 2.45 (s, 3H), 1.36 (t, J=7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.6, 151.8, 147.0, 140.1, 129.0, 128.6, 127.0, 119.3, 60.1, 49.4, 32.7, 16.2, 14.4.

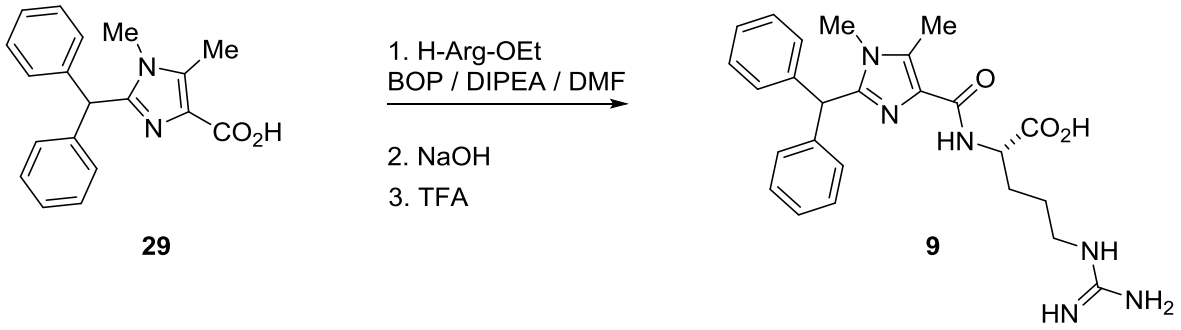
2-Benzhydryl-1,5-dimethyl-1H-imidazole-4-carboxylic acid 29



27 **29**

The ethyl ester **27** was hydrolysed with NaOH in MeOH / water solution at rt. After acidification to pH 3 with HCl the acid was extracted into EtOAc, dried and evaporated to give **29** as a white solid, m/z: 307.1 (MH^+). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40-7.30 (m, 6H), 7.16-7.11 (m, 4H), 6.00 (s, 1H), 3.40 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.3, 148.3, 137.1, 135.8, 129.5, 128.9, 128.5, 122.6, 48.3, 32.0, 9.5.

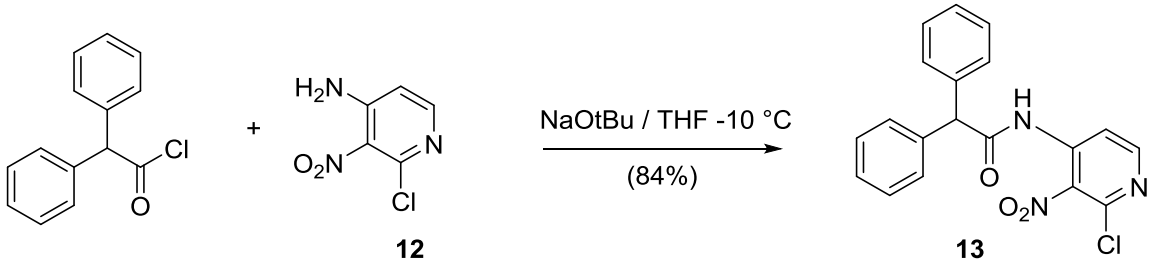
(2-benzhydryl-5-methyl-1H-imidazole-4-carbonyl)-L-arginine (9)



29 **9**

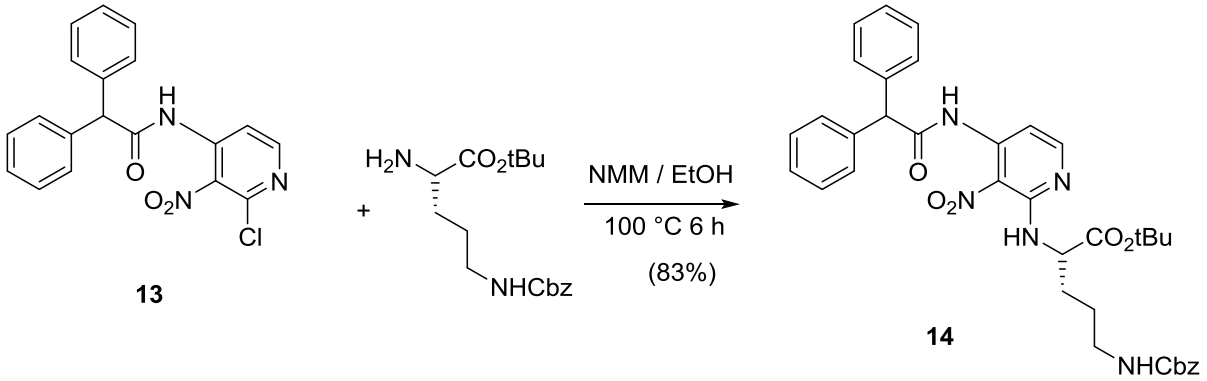
Compound **9** was prepared from **29** using the same procedure above for compounds **7** and **8**. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.59 (d, J = 7.9 Hz, 1H), 7.55 (t, J = 5.7 Hz, 1H), 7.34-7.20 (m, 14H), 5.78 (s, 1H), 4.38 (m, 1H), 3.38 (s, 3H), 3.16-3.04 (m, 2H), 2.44 (s, 3H), 1.82 (m, 1H), 1.70 (m, 1H), 1.51-1.42 (m, 2H). A strong NOE was observed between the two methyl groups. ^{13}C NMR (150 MHz, DMSO-d_6): δ 173.4, 162.9, 156.6, 146.8, 141.11, 141.06, 132.9, 128.8, 128.7, 128.4, 126.7, 50.8, 47.4, 40.3, 30.2, 28.8, 25.2, 9.47. HRMS calculated for $C_{25}H_{31}N_6O_3^+$ 463.2452, found 463.2452.

N-(2-Chloro-3-nitropyridin-4-yl)-2,2-diphenylacetamide (13)



4-Amino-2-chloro-3-nitropyridine **12** (1.00 g, 5.78 mmol) was dissolved in dry THF (15 mL) then cooled to -15 °C under N_2. NaO^{t}Bu (625 mg, 6.51 mmol, 1.1 equiv) was added in several portions then stirring at -10 °C was continued for a further 15 min. A solution of diphenylacetyl chloride (1.40 g, 6.08 mmol) in THF (5 mL) was added dropwise at -10 °C over 5 min then the mixture was stirred at -5 °C for 30 min. Water (5 mL) was added and the mixture was warmed to RT and extracted with EtOAc. The extracts were washed with brine, dried over $MgSO_4$ and evaporated to a yellow solid. Digestion with DCM dissolved the product allowing separation of the unreacted starting material, which was insoluble. Flash chromatography 12-30% EtOAc/petrol gave pure product **13** as a white crystalline solid (1.78 g, 84%) (R_f 0.37 25% EtOAc/petrol). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.71 (s, 1H), 8.55 (d, J = 5.8 Hz, 1H), 8.38 (d, J = 5.8 Hz, 1H), 7.43-7.38 (m, 4H), 7.38-7.33 (m, 2H), 7.30-7.25 (m, 4H), 5.13 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.1, 151.5, 144.2, 140.1, 137.2, 134.6, 129.3, 128.8, 128.2, 114.4, 60.6. HRMS calculated for $C_{19}H_{15}N_3O_3Cl^+$ 368.0796, found 368.0795.

tert-Butyl (*S*)-5-(((benzyloxy)carbonyl)amino)-2-((4-(2,2-diphenylacetamido)-3-nitropyridin-2-yl)amino)pentanoate (14)

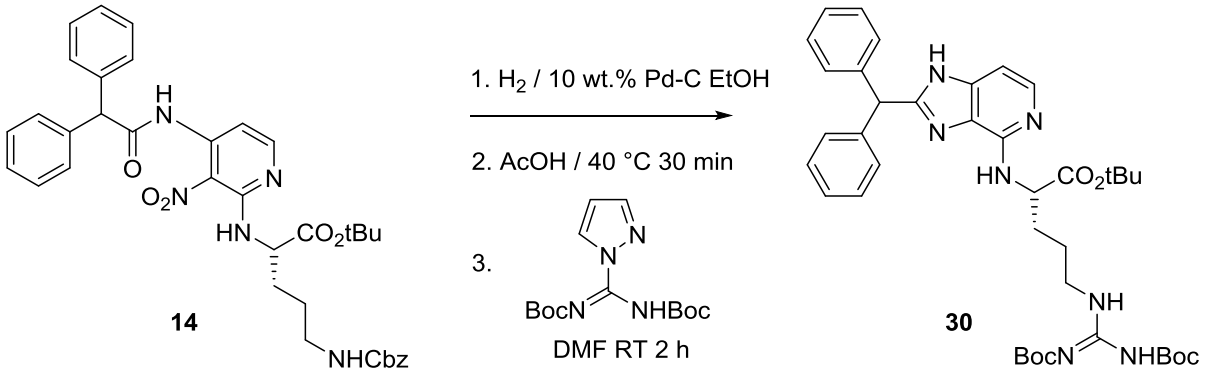


A solution of the 2-chloropyridine derivative **13** (700 mg, 1.91 mmol), H-Orn(Cbz)-OtBu (920 mg, 2.86 mmol) and N-methyl morpholine (0.5 mL) in absolute EtOH (10 mL) was heated in a microwave reactor at 100 °C for 6 h. The solution was diluted with EtOAc and washed with 5% citric acid, brine, dried over $MgSO_4$ and evaporated to an orange oil. Flash chromatography 15-40% EtOAc/petrol gave **14** as an orange oil (2.19 g, 83%) r.f 0.16 25% EtOAc/petrol, R_f 0.47 40% EtOAc/petrol, R_f 0.66 50% EtOAc/petrol.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.90 (d, J = 6.6 Hz, 1H), 8.12 (d, J = 5.6 Hz, 1H), 8.09 (d, J = 5.6 Hz, 1H),7.40-7.29 (m, 15H), 5.14 (s, 1H), 5.08 (s, 2H), 4.77 (m, 1H), 3.31-3.17 (m, 2H), 1.94 (m,

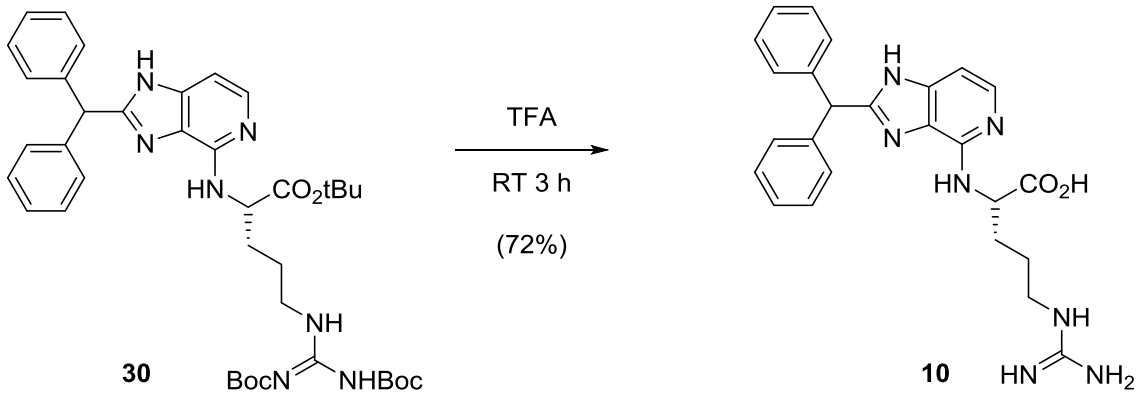
1H), 1.85 (m, 1H), 1.46 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.9, 171.1, 156.4, 155.2, 153.1, 144.4, 137.7, 136.5, 129.07, 129.06, 128.9, 128.5, 128.1, 127.9, 118.5, 103.9, 82.4, 66.7, 61.4, 54.4, 40.3, 29.5, 28.0, 25.7. HRMS calculated for $C_{36}H_{40}N_5O_7^+$ 654.2922, found 654.2922.

tert-Butyl (2-benzhydryl-1*H*-imidazo[4,5-c]pyridin-4-yl)-N$^{\omega}$,N$^{\omega'}$-bis(tert-butoxycarbonyl)-L-argininate (30)



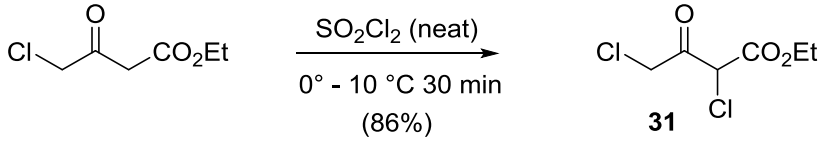
The nitro compound **14** (308 mg, 0.49 mmol) was dissolved in EtOH (10 mL) and hydrogenated over 10 wt. % Pd on activated carbon (30 mg) at RT and 1 atm (balloon) for 40 min. The characteristic orange colour had disappeared and mass spec confirmed total hydrogenolysis of the Cbz group had accompanied reduction of the nitro group. The catalyst was filtered off using a 0.45 micron nylon syringe filter and washed with EtOH and the dark filtrate was evaporated to dryness giving a black gum. This material was immediately dissolved in glacial acetic acid (10 mL) and warmed to 40 °C for 60 min. The AcOH was evaporated under reduced pressure and the residue was dissolved in EtOAc, washed with $NaHCO_3$, brine, dried over $MgSO_4$ and evaporated giving the imidazopyridine intermediate as a red gum. This material was dissolved in DMF (4 mL) then N,N'-di-Boc-1*H*-pyrazole-1-carboxamidine (180 mg, 0.58 mmol) and *N*-methylmorpholine (100 μL) were added and the solution was stirred at RT for 2 h. The solution was evaporated to dryness at 0.05 mbar and the residue was purified by flash chromatography, first column 0-6% MeOH / DCM, second column 25-80% EtOAc/petrol to give the di-Boc protected guanidine **30** (129 mg, 37% over 3 steps) R_f 0.35 5% MeOH/DCM. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.22 (s, 1H), 8.34 (t, J = 5.0 Hz, 1H), 7.75 (d, *J* = 5.8 Hz, 1H), 7.35-7.30 (m, 4H), 7.30-7.23 (m, 3H), 7.23-7.16 (m, 5H), 6.56 (d, *J* = 5.8 Hz, 1H), 5.83 (d, *J* = 7.8 Hz, 1H), 5.79 (s, 1H), 4.82 (m, 1H), 3.46-3.36 (m, 2H), 1.97 (m, 1H), 1.82 (m, 1H), 1.78-1.64 (m ,2H), 1.48 (s, 18H), 1.43 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.8, 163.6, 156.2, 153.2, 152.6, 150.3, 140.6, 140.55, 140.50, 137.8, 133.8, 128.9, 127.4, 105.1, 97.9, 83.0, 81.3, 79.2, 53.8, 51.7, 40.6, 30.1, 28.3, 28.1, 28.0, 25.3. HRMS calculated for $C_{39}H_{52}N_7O_6^+$ 714.3974, found 714.3976.

(2-Benzhydryl-1*H*-imidazo[4,5-c]pyridin-4-yl)-L-arginine (10)



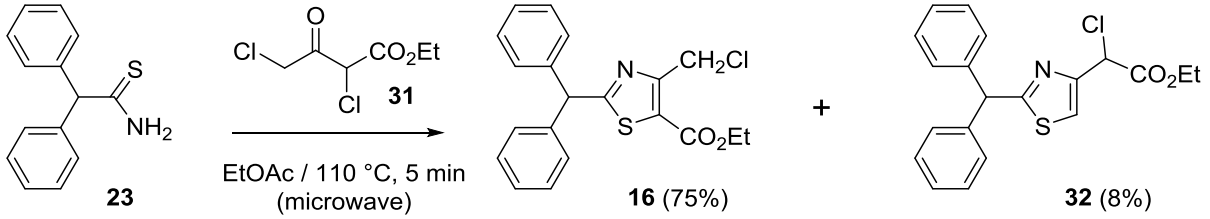
The Boc protected tert-butyl ester **30** (50 mg, 0.07 mmol) was dissolved in neat TFA (2 mL) and stirred at RT for 3 h. TFA was removed in a stream of N_2 and the residue was purified by preparative reverse phase HPLC to give **10** (TFA salt) as a white powder (29 mg, 72%) after lyophilisation. ^{1}H NMR (600 MHz, 90% H_2O + 10% D_2O + DSS): δ 8.28 (broad s, 1H), 7.66 (d, J = 7.2 Hz, 1H), 7.51-7.34 (m, 10H), 7.23 (broad t, J = 5.0 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 5.96 (s, 1H), 4.8 (m, 1H, under H_2O peak), 3.31-3.18 (m, 2H), 2.16 (m, 1H), 2.04 (m, 1H), 1.86-1.71 (m, 2H). ^{13}C NMR (150 MHz, 90% H_2O + 10% D_2O, Ref MeOH 49.5 ppm): δ 175.4, 163.4 (q, $^2J_{C\text{-}F}$ = 35.4 Hz, TFA), 158.8, 157.7, 146.6, 141.7, 140.26, 140.22, 129.54, 129.52, 129.45, 129.34, 129.28, 128.2, 125.8, 116.8 (q, $^1J_{C\text{-}F}$ = 291.7 Hz, TFA), 101.4, 56.1, 51.2, 41.1, 28.9, 24.7. HRMS calculated for $C_{25}H_{28}N_7O_2^+$ 458.2299, found 458.2299.

Ethyl 2,4-dichloro-3-oxobutanoate (31)



Ethyl 4-chloroacetoacetate (5 mL, 37 mmol) was stirred under N_2 in an ice bath while sulfuryl chloride (neat 3 mL, 37 mmol) was added in 6 portions of 0.5 mL over 5 min keeping the temperature below 10 °C. The mixture was then stirred at RT for 30 min then distilled on a kugelrohr apparatus with oven temperature 160 °C at 13 mbar giving a clear colourless liquid (6.35 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.10 (s, 1H), 4.50 and 4.45 (AB quartet J_{AB} = 16.1 Hz, 2H), 4.32 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H) a minor enol tautomer is also present. ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 164.2, 63.6, 62.8, 58.6, 45.7, 40.2, 14.0, 13.9 (a minor enol tautomer is also present).

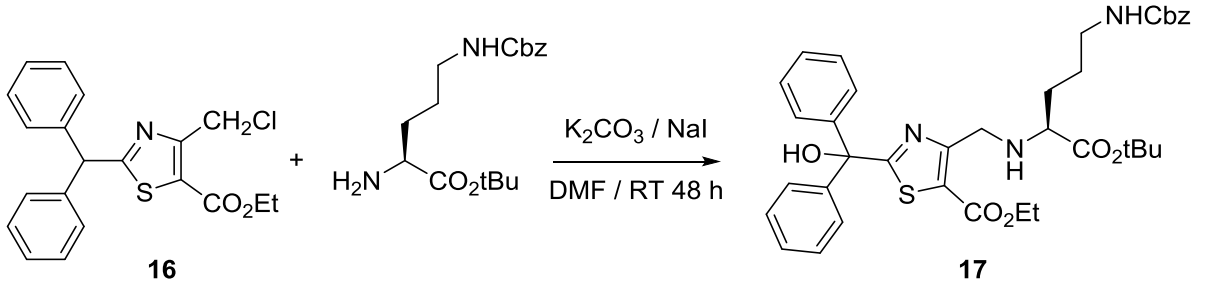
Ethyl 2-benzhydryl-4-(chloromethyl)thiazole-5-carboxylate (16)



A solution of 2,2-diphenylthioacetamide **23** (1.00 g, 4.41 mmol) and ethyl 2,4-dichloro-3-oxobutanoate **31** (1.00 g, 5.0 mol 1.1 equiv) in EtOAc (10 mL) was heated in a microwave reactor at 110 °C for 5 min. After cooling the solution was diluted with EtOAc and washed with 5% $NaHCO_3$, brine, dried over $MgSO_4$ and evaporated to an oil (1.64 g). Purification by flash chromatography 10-20% EtOAc/petrol gave ethyl 2-benzhydryl-4-(chloromethyl)thiazole-5-carboxylate **16** as a pale yellow oil (1.23 g, 75%) R_f 0.51 25% EtOAc/petrol. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36-7.27 (m, 10H), 5.82 (s, 1H), 5.03 (s, 2H), 4.32 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.9, 161.0, 157.5, 141.0, 128.9, 128.8, 127.6, 125.8, 61.8, 55.3, 38.6, 14.2. m/z: 372.1 MH^+.

Data for the minor (8%) isomer ethyl 2-(2-benzhydrylthiazol-4-yl)-2-chloroacetate **32**:
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.44 (s, 1H), 7.34-7.20 (m, 10H), 5.82 (s, 1H), 5.57 (d, J = 0.5 Hz, 1H), 4.29-4.21 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.4, 167.4, 150.5, 141.6, 128.92, 128.90, 128.6, 127.31, 127.29, 118.8, 62.7, 54.9, 54.3, 13.9.

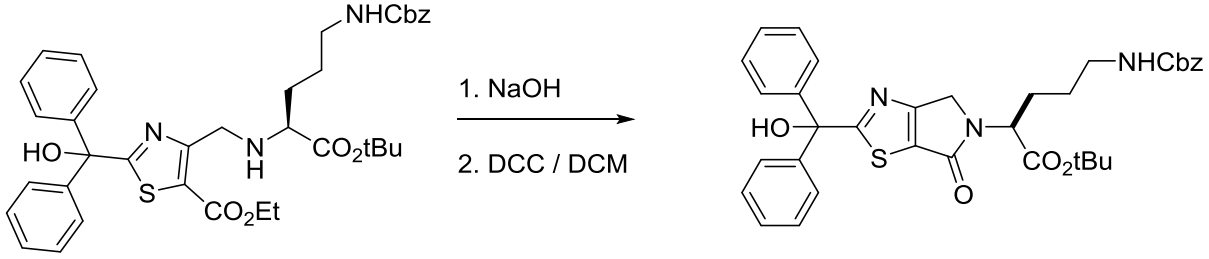
Ethyl (*S*)-4-(((5-(((benzyloxy)carbonyl)amino)-1-(tert-butoxy)-1-oxopentan-2-yl)amino)methyl)-2-(hydroxydiphenylmethyl)thiazole-5-carboxylate (17)



The chloromethyl thiazole **16** (371 mg, 1 mmol) and H-Orn(Cbz)-O^{t}Bu (480 mg, 1.5 mmol) were dissolved in DMF (1 mL) then NaI (100 mg) and anhydrous K_2CO_3 (400 mg, finely ground) were added and the mixture was stirred at RT under Ar for 48 h. The mixture was diluted with DCM and ether 1:2 and washed with 5% sodium thiosulfate, brine and dried over $MgSO_4$ and evaporated to give a brown gum (668 mg, 99% crude). The product **17** had the hydroxylated benzhydryl group as indicated by mass spectrum m/z 674.3 MH^+ and NMR shows absence of the benzhydryl CH proton expected to be near δ_H 5.9 ppm but a quaternary carbon δ_C 79.7 ppm with $^2J_{C\text{-}H}$ coupling to an OH proton δ_H 7.54 ppm in the HMBC spectrum. Possible explanations for this observation could be halogenation followed by hydrolysis or direct reaction with oxygen (air), however, this has no consequences for continuing the synthesis because the hydroxyl group is removed during subsequent steps when the tert-butyl ester is deprotected. An

analytical sample of **17** was purified by reverse phase HPLC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.54 (s, 1H, OH), 7.47-7.20 (m, 16H), 4.98 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 3.06 (m, 1H), 2.96-2.88 (m, 2H), 1.51-1.34 (m, 4H), 1.31 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 181.8, 173.6, 161.8, 161.3, 156.0, 144.9, 144.8, 137.3, 128.3, 127.8, 127.73, 127.70, 127.66, 127.4, 127.2, 122.4, 80.0, 79.7, 65.0, 61.1, 60.2, 45.7, 40.2, 30.2, 27.6, 25.8, 14.1.

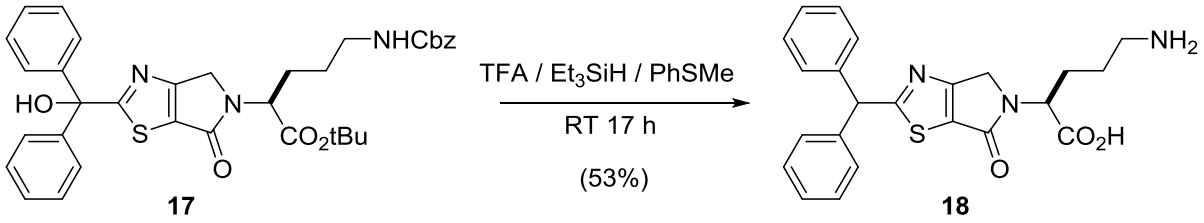
tert-Butyl (*S*)-5-(((benzyloxy)carbonyl)amino)-2-(2-(hydroxydiphenylmethyl)-6-oxo-4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-5-yl)pentanoate (33)



17 **33**

The ethyl ester **17** (650 mg, 0.96 mmol) was dissolved in MeOH, THF, water (1:1:1, 4 mL) then KOH (100 mg, 1.5 equiv) was added. The solution was stirred and heated at 50 °C 2 h and the hydrolysis was monitored by LCMS. Transesterification to the methyl ester (m/z 660.3 MH^+) occurred first followed by hydrolysis to the acid (m/z 646.3 MH^+) which had longer retention time than the methyl ester. The solvents were partially evaporated and the aqueous residue was acidified to pH 5.8 with citric acid and extracted with DCM. After drying over $MgSO_4$ and filtration the solvent was evaporated to give the acid (zwitterion) as an orange foam (604 mg). The zwitterion was dissolved in DCM (5 mL) then dicyclohexylcarbodiimide (230 mg, 1.12 mmol) was added followed by DIPEA (175 μL 1.0 mmol). The solution was stirred at RT for 2h, diluted with DCM and washed with 1M HCl, dried over $MgSO_4$ and evaporated. Purification by flash chromatography 25-75% EtOAc/petrol gave the lactam **33** as a yellow foam (170 mg, 28% over 2 steps) (R_f 0.36 50% EtOAc/petrol). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48-7.26 (m, 15H), 5.07 (s, 2H), 4.88 (m, 1H, NH), 4.86 (dd, J = 10.6, 5.1 Hz, 1H), 4.66 (d, J = 17.6 Hz, 1H), 4.28 (d, J = 17.6 Hz, 1H), 4.06 (s, 1H, OH), 3.27-3.17 (m, 2H), 2.08-1.99 (m, 1H), 1.82-1.73 (m, 1H), 1.58-1.49 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 188.3, 170.3, 167.9, 164.2, 156.4, 144.19, 144.17, 136.5, 128.5, 128.35, 128.32, 128.27, 128.10, 128.08, 128.00, 127.45, 127.43, 82.5, 81.3, 66.7, 54.4, 46.2, 40.4, 28.0, 27.4, 26.9. HRMS calculated for $C_{35}H_{38}N_3O_6S^+$ 628.2476, found 628.2476.

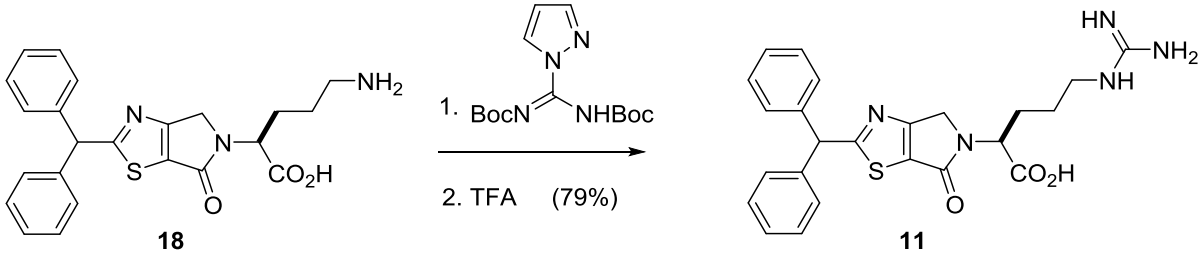
(*S*)-5-Amino-2-(2-benzhydryl-6-oxo-4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-5-yl)pentanoic acid (18)



17 **18**

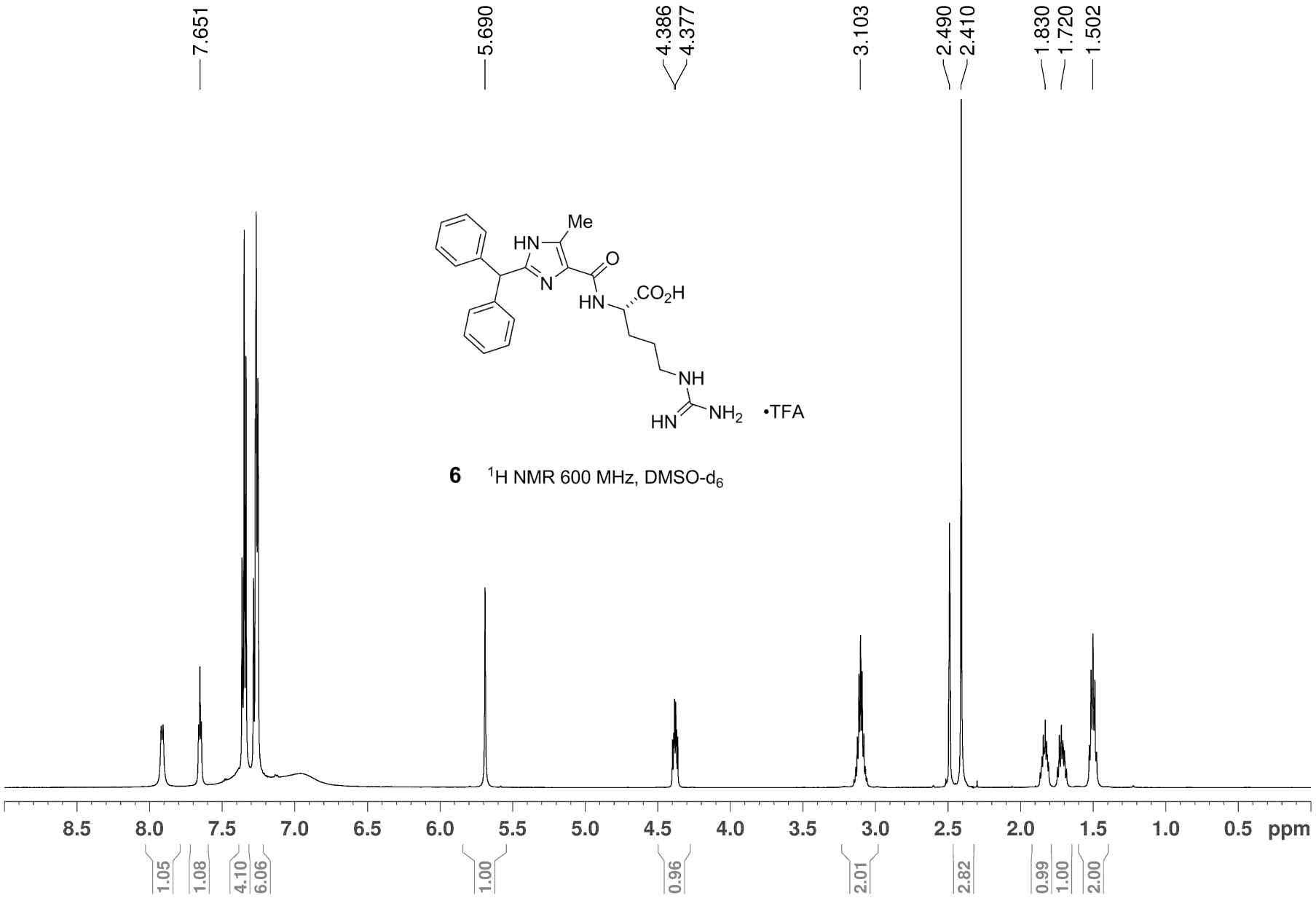
The protected lactam **33** (165 mg, 0.26 mmol) was dissolved in TFA (5 mL) then triethylsilane (250 μL) and thioanisole (40 mg) were added. The solution was stirred at RT for 17 h then evaporated under a stream of N_2. The residue was dissolved in 80% MeCN / water and washed with 20% diethyl ether in pentane then the aqueous MeCN layer was lyophilised. The residue was purified by preparative reverse phase HPLC to give **18** (TFA salt) as a white powder (73 mg, 53%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.64 (broad s, 3H), 7.38-7.32 (m, 8H), 7.31-7.25 (m, 2H), 6.16 (s, 1H), 4.68 (dd, *J* = 11.4, 4.2 Hz, 1H), 4.56 (d, *J* = 18.4 Hz, 1H), 4.53 (d, *J* = 18.4 Hz, 1H), 2.85-2.74 (m, 2H), 2.03 (m, 1H), 1.85 (m, 1H), 1.57-1.44 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 183.1, 172.1, 168.1, 163.0, 141.23, 141.19, 128.75, 128.70, 128.68, 127.3, 126.6, 54.2, 53.6, 46.2, 40.0, 38.3, 26.0, 24.1.
HRMS calculated for $C_{23}H_{23}N_3O_3S^+$ 422.1533, found 422.1533.

(*S*)-2-(2-Benzhydryl-6-oxo-4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-5-yl)-5-guanidinopentanoic acid (11)

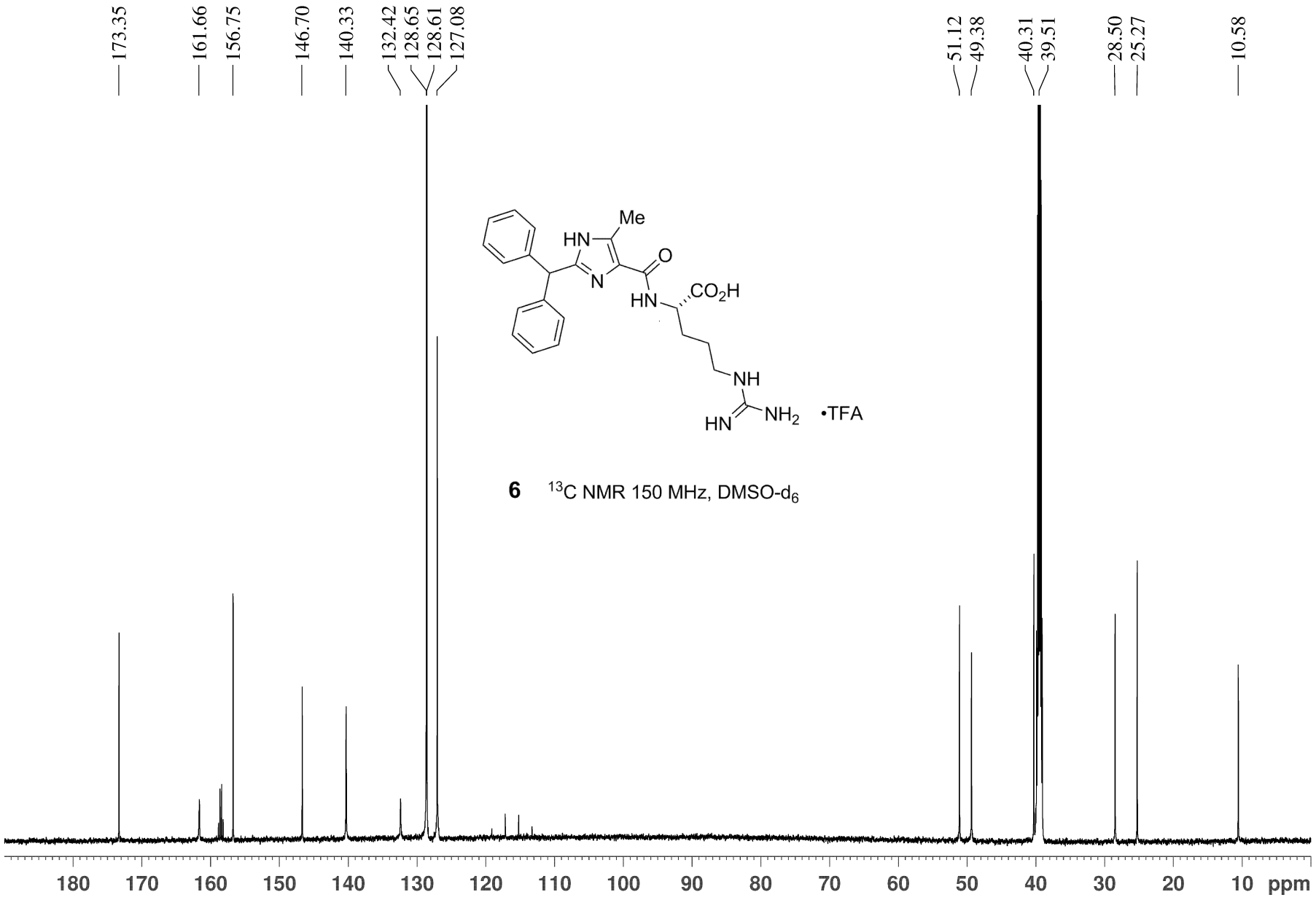


18 **11**

The amine **18** (13 mg, 0.024 mmol) and N,N'-di-Boc-1*H*-pyrazole-1-carboxamidine (15 mg, 0.48 mmol 2 equiv) were dissolved in DMF (200 μL) then *N*-methylmorpholine (10 μL) was added. The solution was stirred at RT for 2 h then evaporated to dryness at 0.05 mbar. The residue was dissolved in TFA (3 mL) and stirred at RT for 3 h. The TFA was removed under a stream of N_2 and the residue was purified by preparative reverse phase HPLC to give the guanidine **11** (TFA salt) as a white powder (11 mg, 79%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.53 (t, *J* = 5.3 Hz, 1H), 7.38-7.33 (m, 8H), 7.31-7.26 (m, 2H), 6.15 (s, 1H), 4.68 (dd, *J* = 11.3, 4.3 Hz, 1H), 4.57 (d, *J* = 18.3 Hz, 1H), 4.52 (d, *J* = 18.3 Hz, 1H), 3.13-3.07 (m, 2H), 2.00 (m, 1H), 1.81 (m, 1H), 1.49-1.41 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 183.1, 172.3, 168.2, 163.1, 156.7, 141.25, 141.22, 128.76, 128.70, 128.68, 127.3, 126.6, 54.3, 53.8, 46.3, 40.2, 40.0, 26.1, 25.6. HRMS calculated for $C_{24}H_{26}N_5O_3S^+$ 464.1751, found 464.1751.



6 ^{1}H NMR 600 MHz, DMSO-d_6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28.50
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Me
HN
O
N
HN
CO2H
NH
HN
NH2
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150
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70
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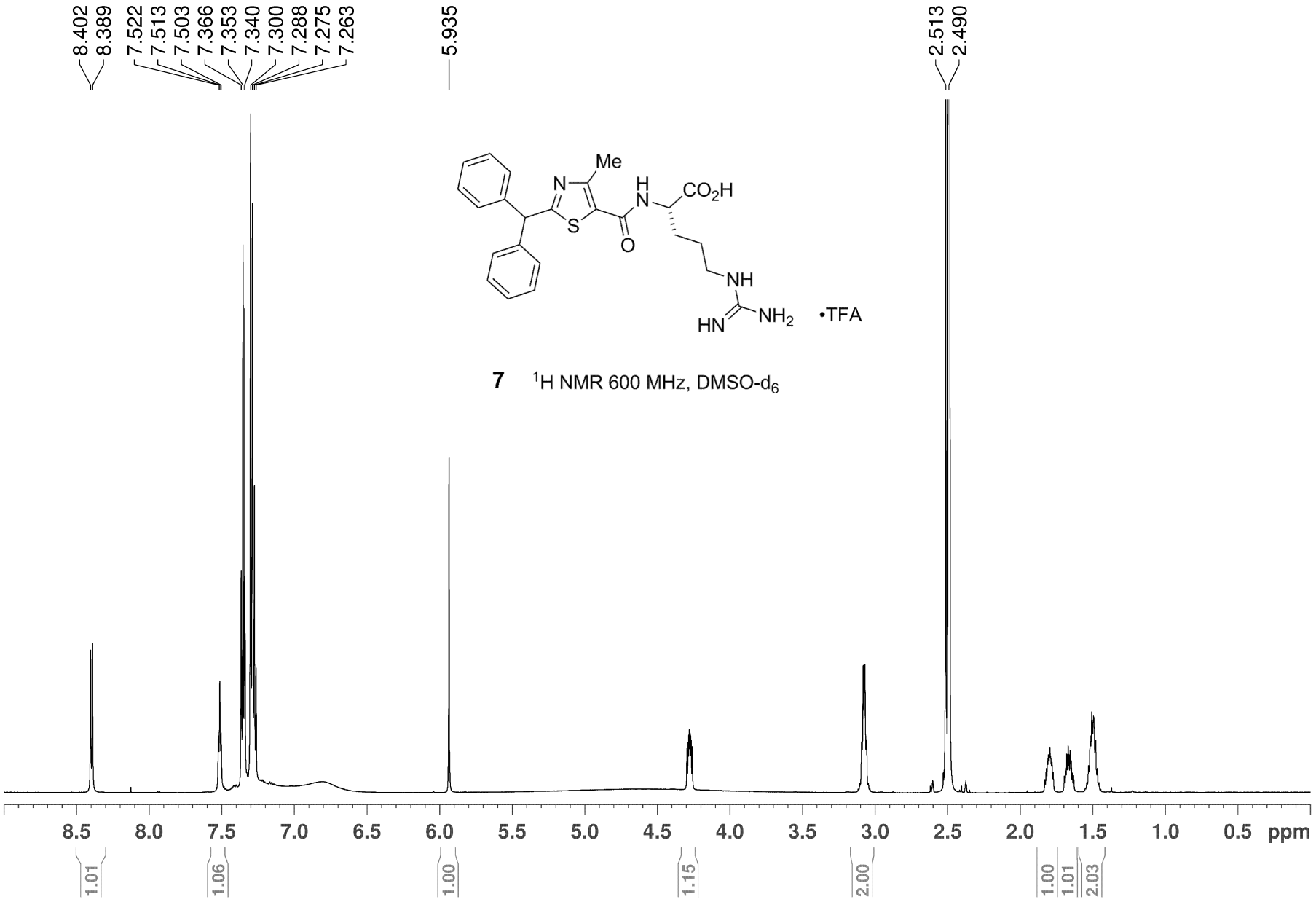
10
ppm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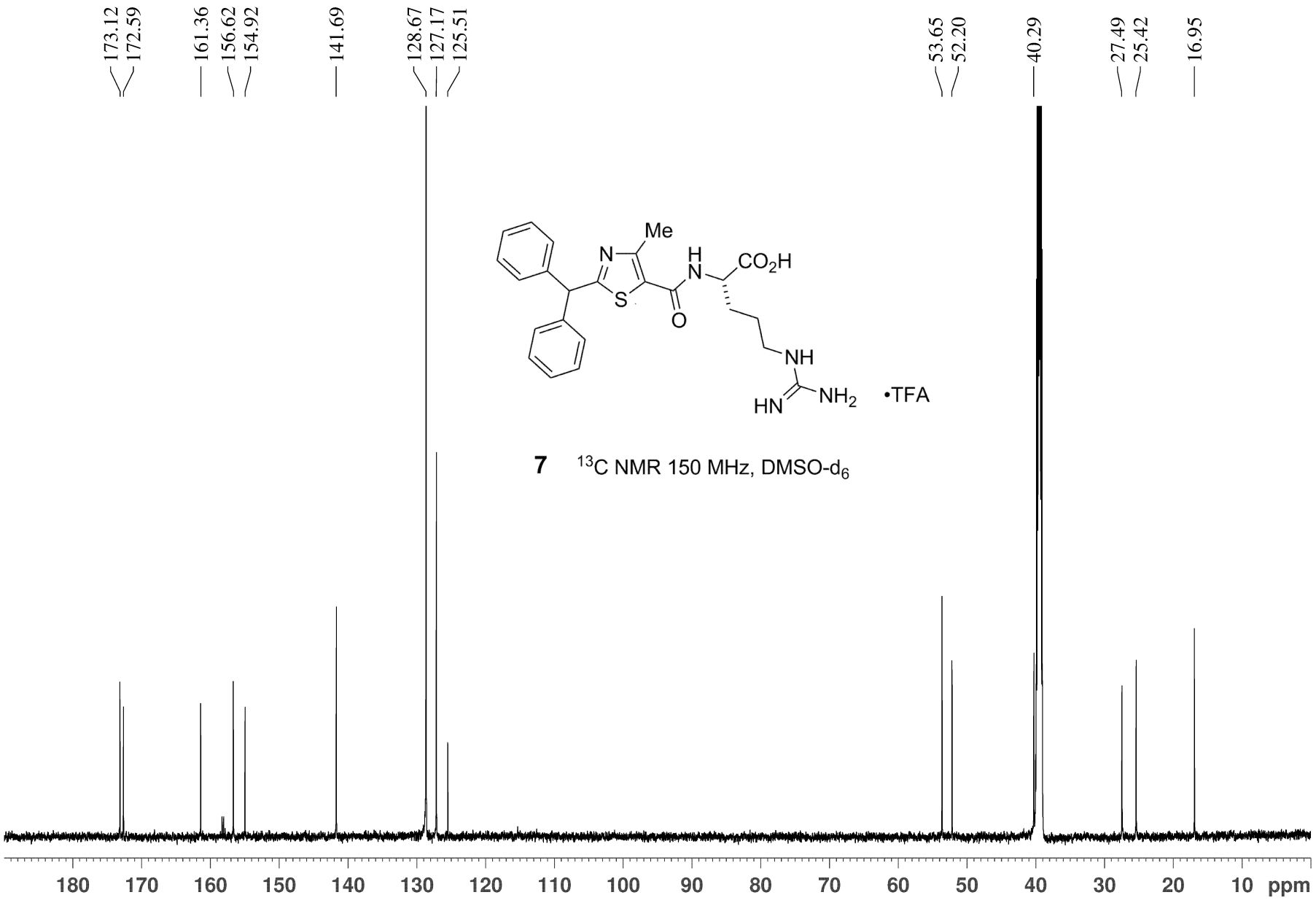
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NH
HN
NH2
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150
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80
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60
50
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30
20
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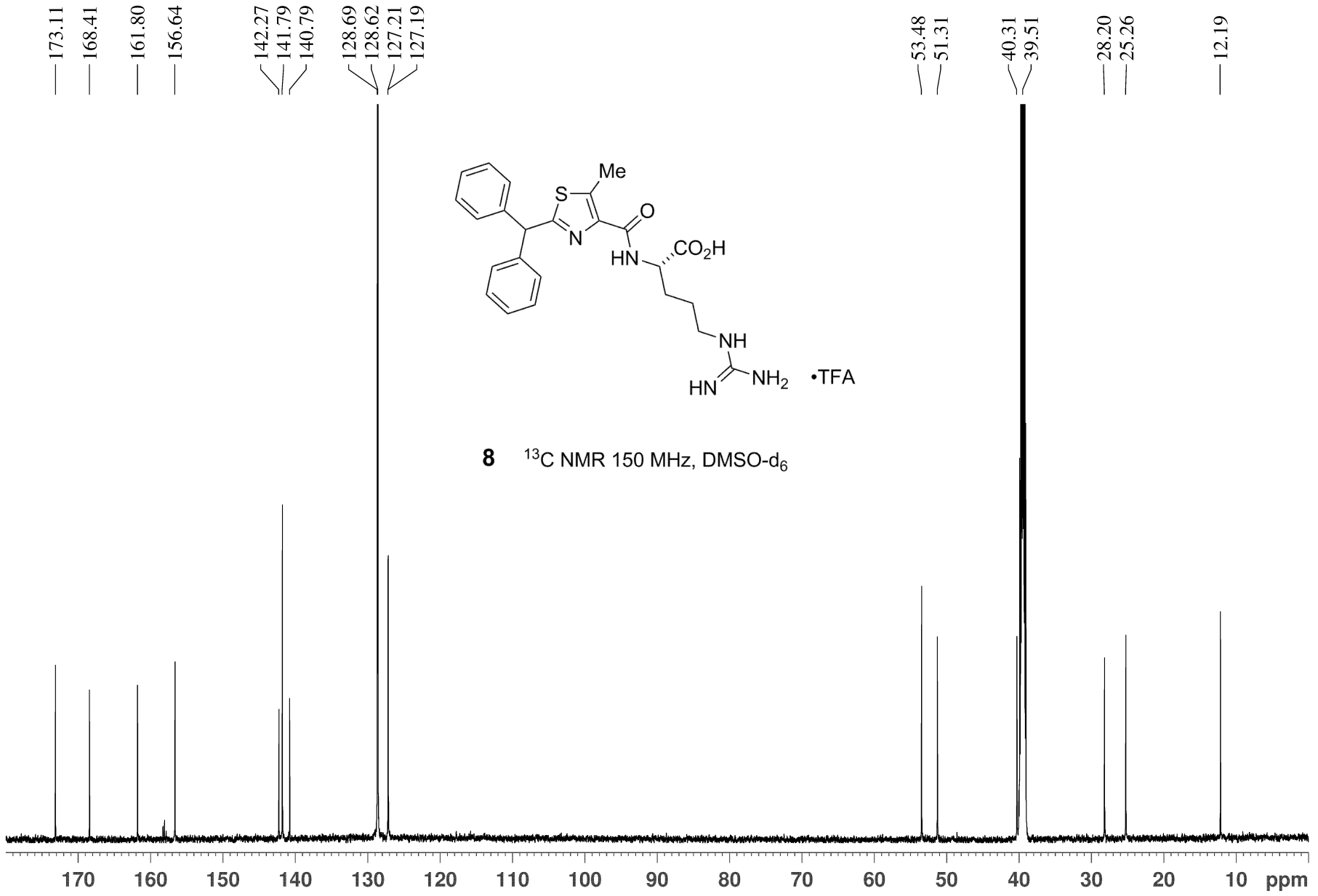
ppm

8 ^{1}H NMR 600 MHz, DMSO-d_6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39.51
28.20
25.26
12.19
Me
S
N
O
HN
CO2H
NH
HN
NH2
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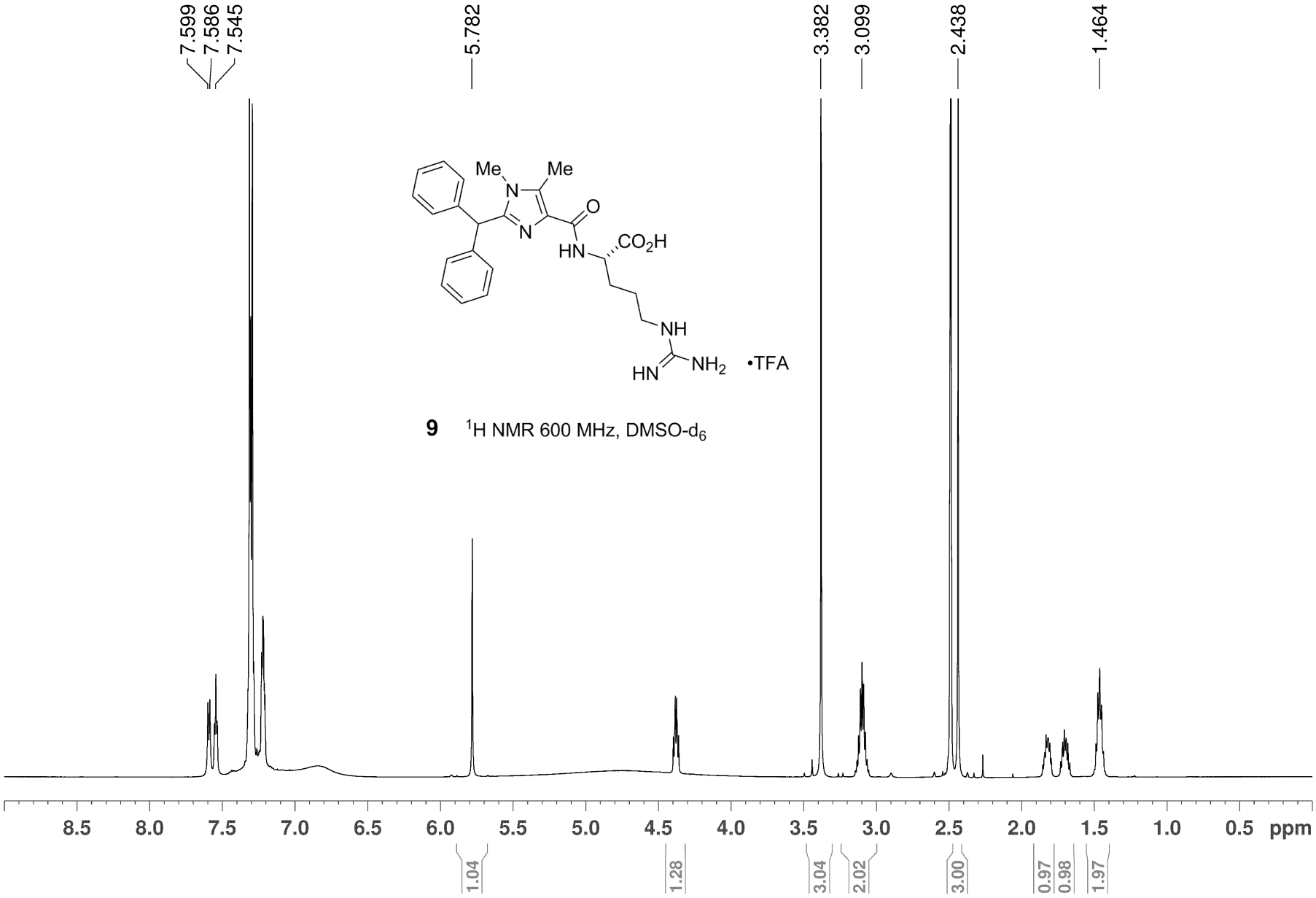
110
100
90
80
70
60
50
40
30
20
10
ppm


7.599
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7.545
5.782
3.382
3.099
2.438
1.464
Me
Me
N
N
O
HN
CO2H
NH
HN
NH2
•TFA
9 1H NMR 600 MHz, DMSO-d6
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.02
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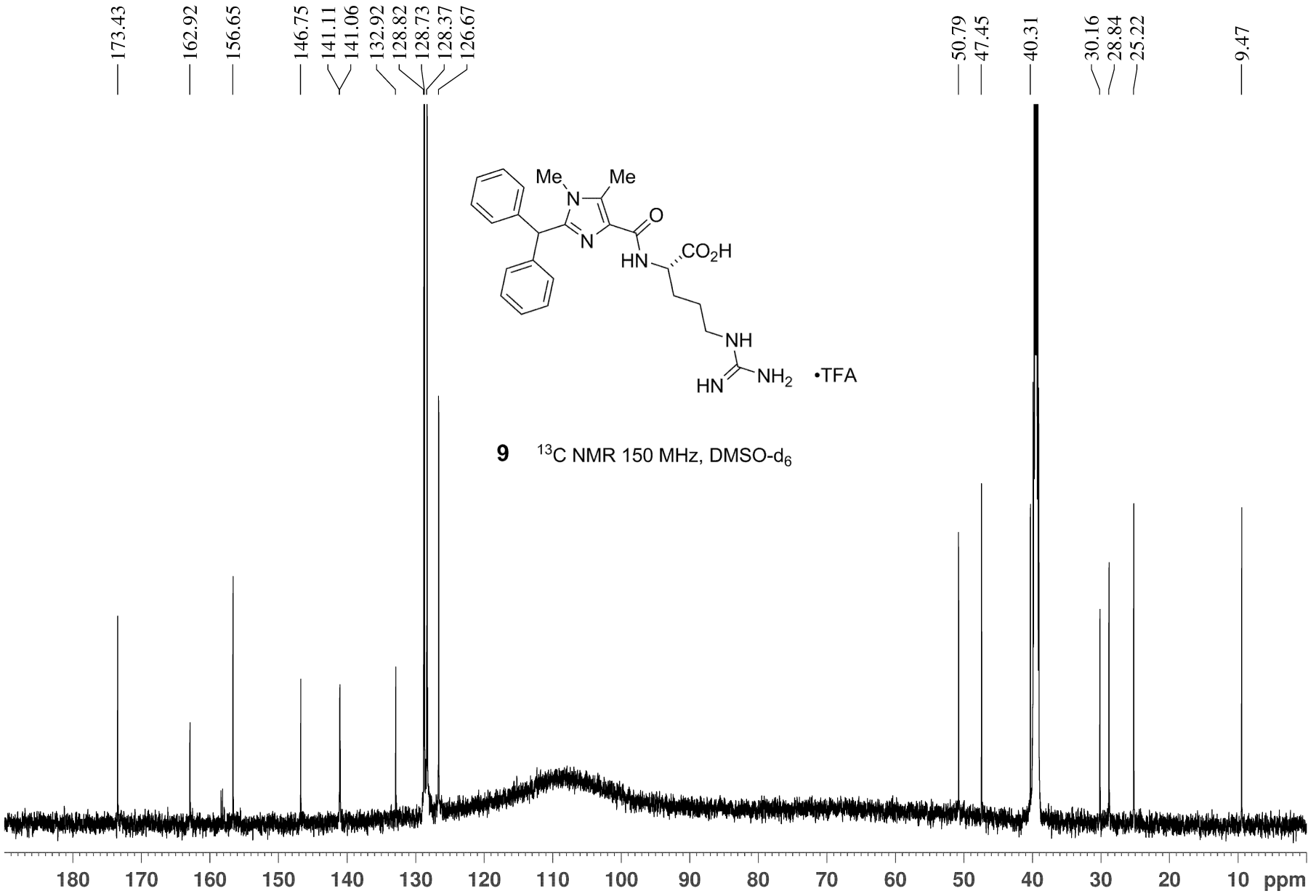
0.97
0.98
1.97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162.92
156.65
146.75
141.11
141.06
132.92
128.82
128.73
128.37
126.67
50.79
47.45
40.31
30.16
28.84
25.22
9.47
Me
Me
N
N
O
HN
CO2H
NH
HN
NH2
•TFA
9 13C NMR 150 MHz, DMSO-d6
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160
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140
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110
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70
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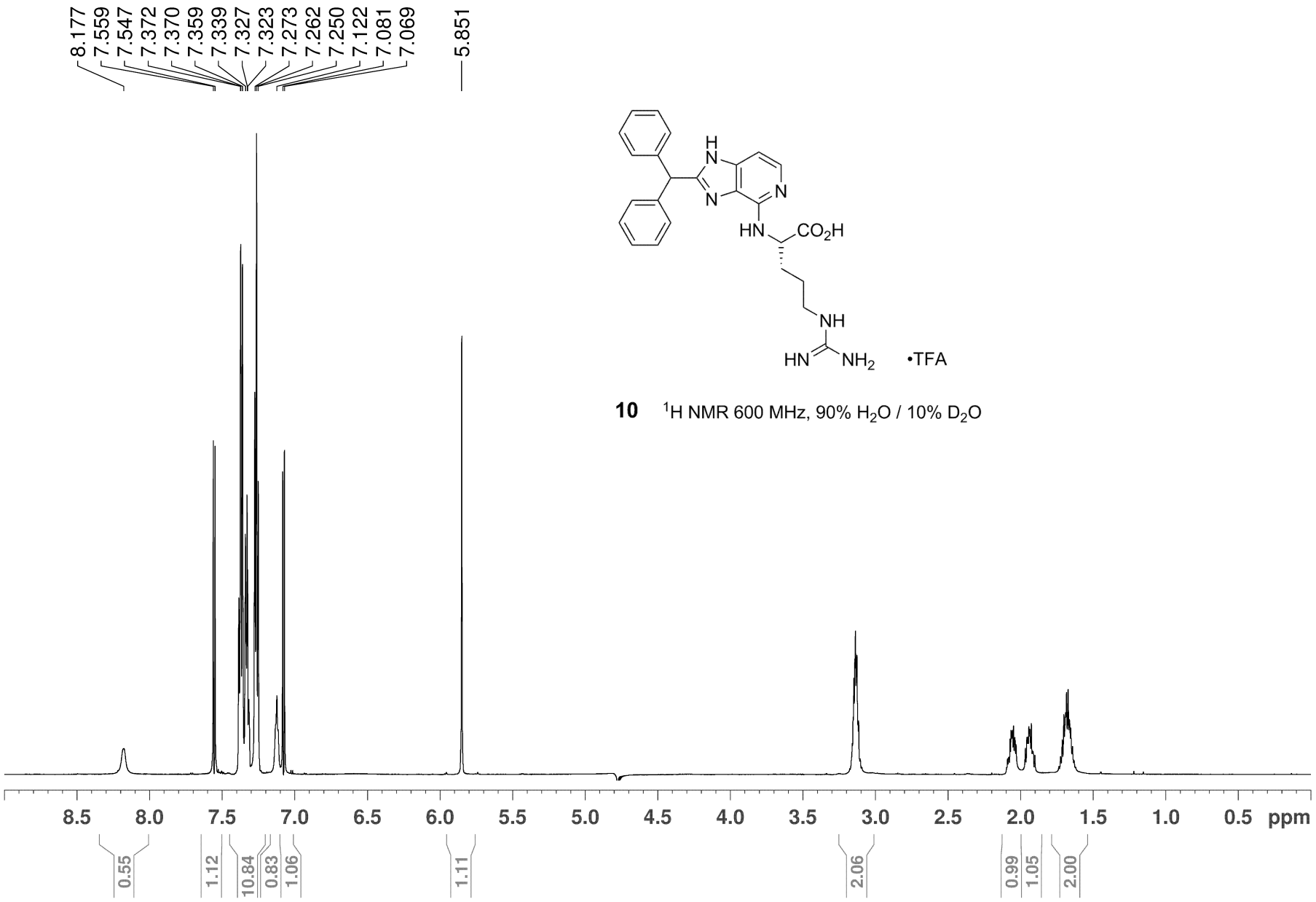
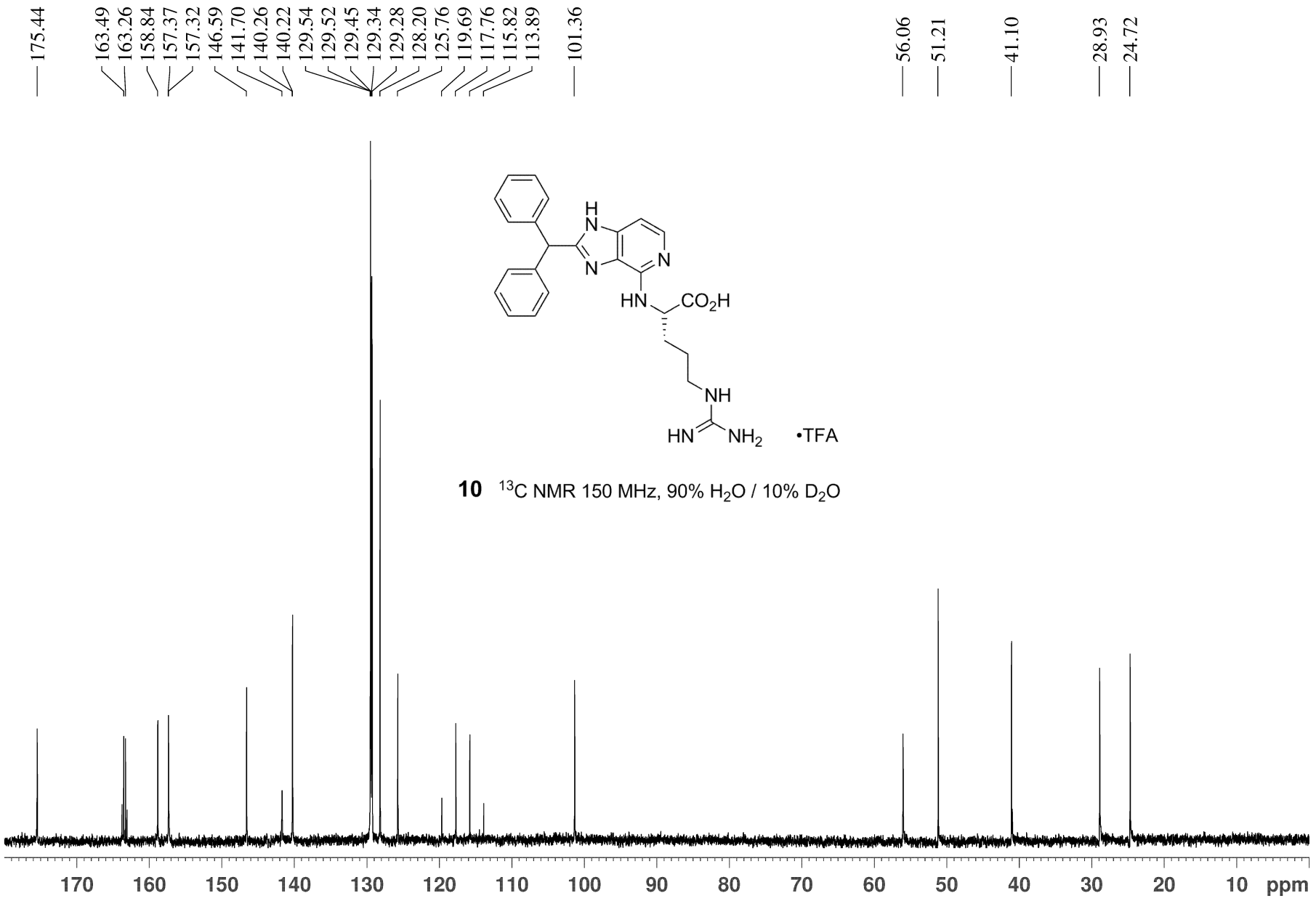
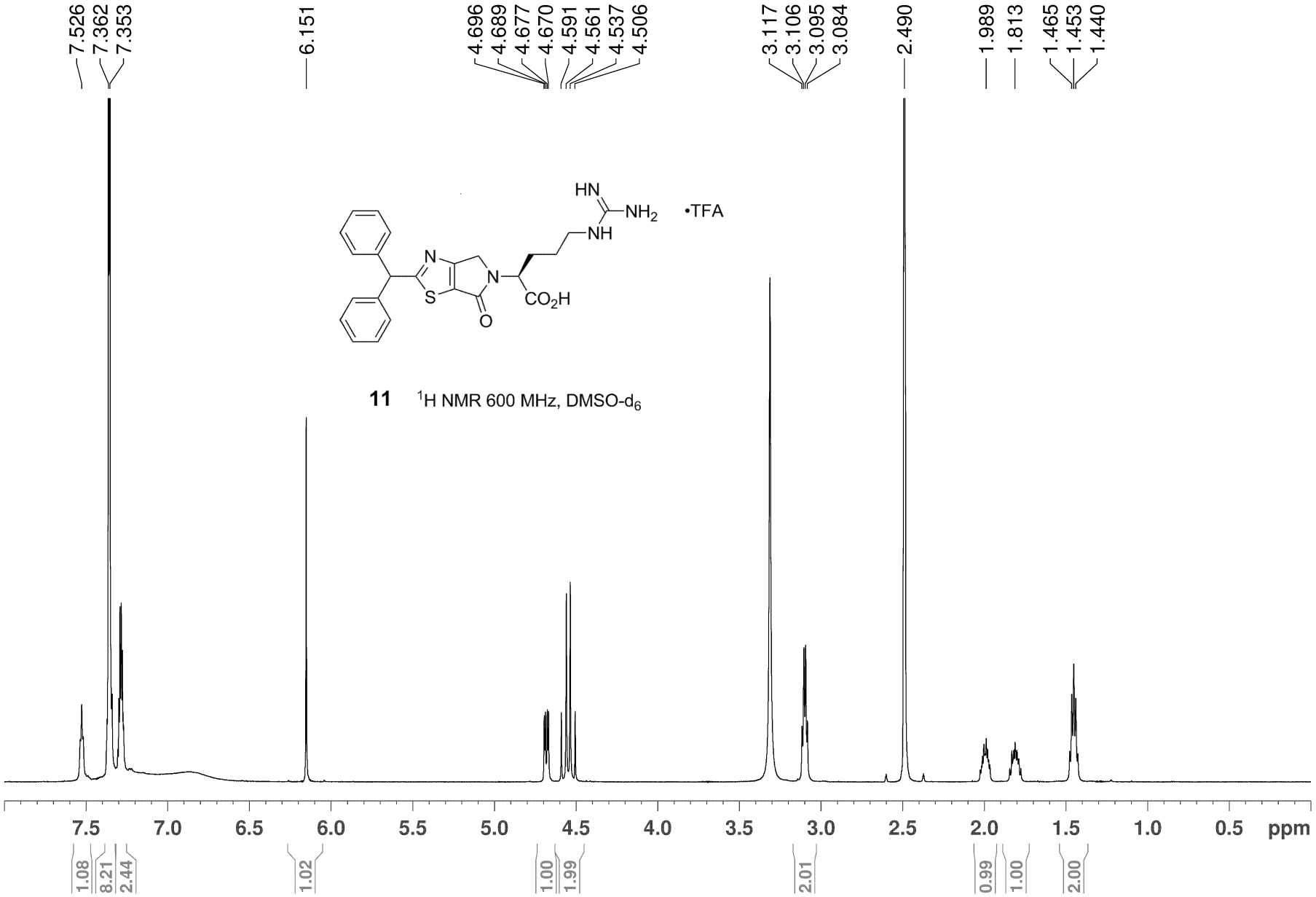
10
ppm



10 ^{1}H NMR 600 MHz, 90% H_2O / 10% D_2O



10 ^{13}C NMR 150 MHz, 90% H_2O / 10% D_2O


7.526
7.362
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6.151
4.696
4.689
4.677
4.670
4.591
4.561
4.537
4.506
3.117
3.106
3.095
3.084
2.490
1.989
1.813
1.465
1.453
1.440
HN
NH2
NH
•TFA
N
S
N
O
CO2H
11 1H NMR 600 MHz, DMSO-d6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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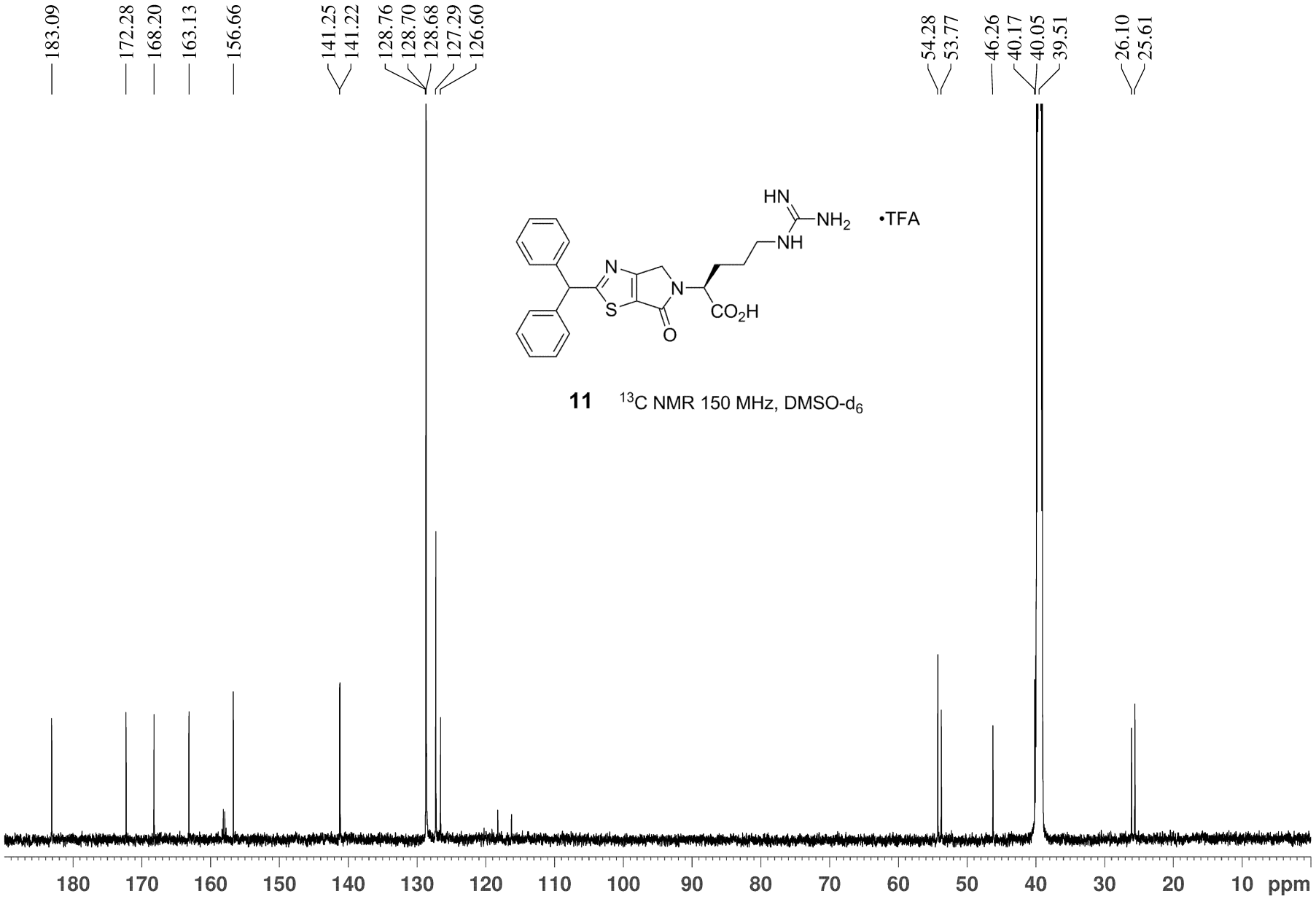
1.02
1.00
1.99
2.01
0.99
1.00
2.00



11 ^{13}C NMR 150 MHz, DMSO-d_6

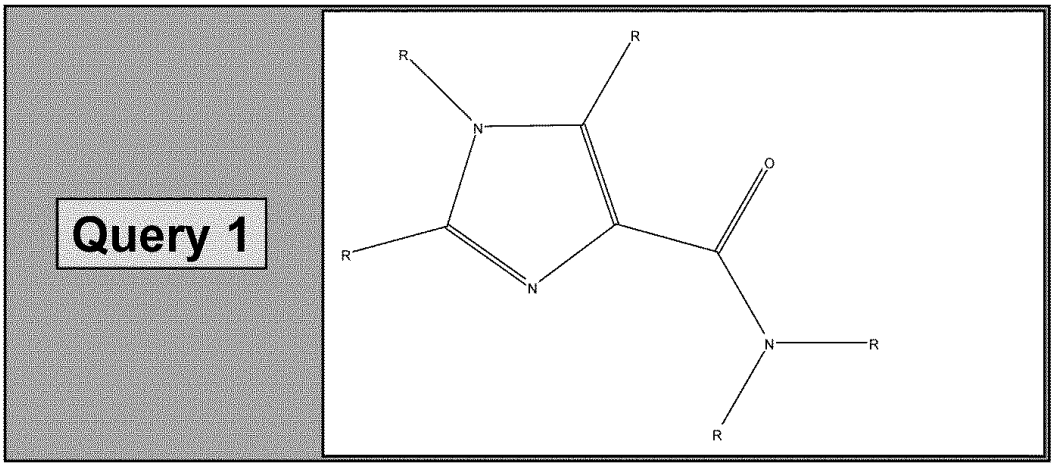
Search Overview

Search:	search1
Date/Time done:	Tue Feb 18 09:20:35 2014
Database(s):	CSD version 5.34 updates (Nov 2012) CSD version 5.34 (November 2012)
Restriction Info:	No refcode restrictions applied
Filters:	3D coordinates determined Not disordered No errors
Percentage Completed:	100%
Number of Hits:	39

Single query used. Search found structures that:

match

Query 1



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 1-4

BEZYAG

Reference: N.B.Brovtsyna, V.S.Fundamenskii, V.L.Gol'dfarb, K.A.Moshkov, Yu.S.Borodkin (1982) *Zh.Strukt.Khim.(Russ.)(J.Struct.Chem.)* ,**23**,92-2

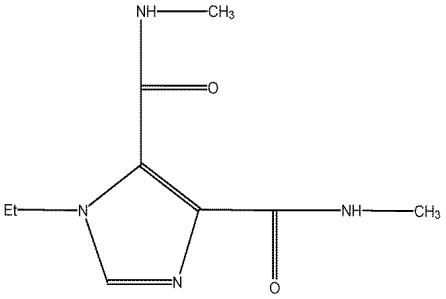
Formula: $C_9 H_{14} N_4 O_2$

Compound Name: 1-Ethyl-4,5-bis(N-methylcarbamoyl)-imidazole

Synonym: Ethimizole

Space Group:	Fdd2	***Cell:***	***a*** 18.496(6)	***b*** 28.666(8)	***c*** 8.301(2)
Space Group No.:	43	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.90 ***Temperature(K):*** 295 ***Density(g/cm³):*** 1.269



EKOMOG

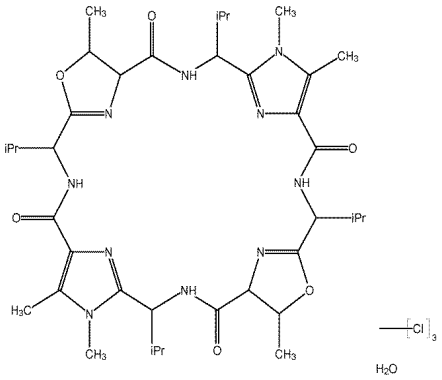
Reference: G.Haberhauer, F.Rominger (2003) *Eur.J.Org.Chem.* ,3209

Formula: $C_{38} H_{58} N_{10} O_6.0.5(C_1 H_1 Cl_3).H_2 O_1$

Compound Name: 7,13,14,21,27,28-Hexamethyl-4,11,18,25-tetraisopropyl-2,9,16,23-tetraoxo-3,10,13,17,24,27,29,30,31,32-decaaza-6,20-dioxapentacyclo(24.2.1.1^{5,8}.1^{12,15}.1^{19,22})doconta-1(28),5(32),12(31),14,19(30),26(29)-hexaene chloroform solvate monohydrate

Space Group:	P212121	***Cell:***	***a*** 15.503(0)	***b*** 20.517(0)	***c*** 27.532(0)
Space Group No.:	19	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 5.53 ***Temperature(K):*** 200 ***Density(g/cm³):*** 1.257



FAFMOQ

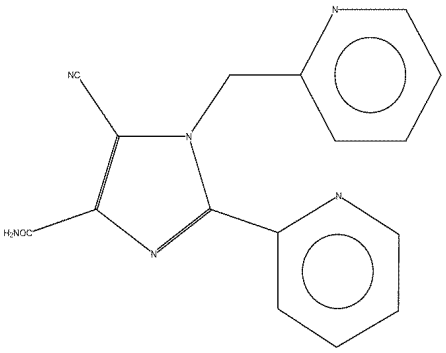
Reference: M.Altaf, H.Stoeckli-Evans (2010) *Acta Crystallogr.,Sect.C:Cryst.Struct.Commun.* ,**66**,o441

Formula: $C_{16} H_{12} N_6 O_1$

Compound Name: 5-Cyano-2-(pyridin-2-yl)-1-(pyridin-2-ylmethyl)-1H-imidazole-4-carboxamide

Space Group:	P21/c	***Cell:***	***a*** 10.573(1)	***b*** 7.046(0)	***c*** 21.261(2)
Space Group No.:	14	***(Å,°)***	α 90.00	β 114.50(0)	γ 90.00

R-Factor (%): 3.65 ***Temperature(K):*** 173 ***Density(g/cm³):*** 1.403



GASSEZ

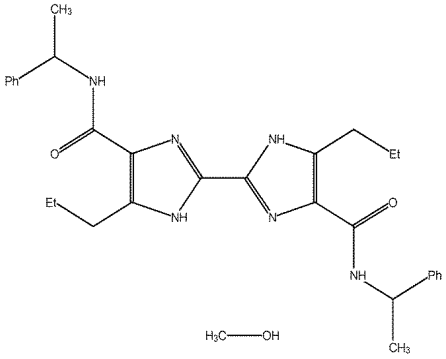
Reference: D.K.Barnhill, A.L.Sargent, W.E.Allen (2005) *Tetrahedron* , **61**,8366

Formula: $C_{30} H_{36} N_6 O_2.2(C_1 H_4 O_1)$

Compound Name: meso-5,5'-Dipropyl-1H,1'H-(2,2')biimidazolyl-4,4'-dicarboxylic acid bis((1-phenylethyl)amide) methanol solvate

Space Group:	P212121	***Cell:***	***a*** 9.829(0)	***b*** 12.789(0)	***c*** 24.777(0)
Space Group No.:	19	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 4.90 ***Temperature(K):*** 173 ***Density(g/cm³):*** 1.230



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 5-8

HEPHIU

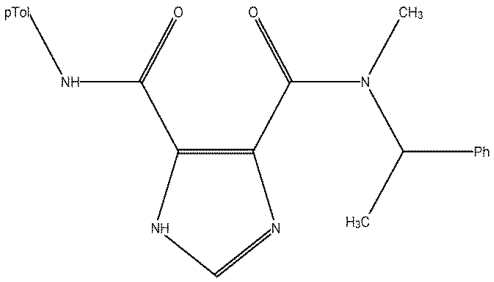
Reference: P.W.Baures, A.W.Caldwell, C.R.Cashman, M.T.Masse, E.B.Van Arnam, R.R.Conry (2006) *Cryst.Growth Des.* ,**6**,2047

Formula: $C_{21}H_{22}N_4O_2$

Compound Name: N-Methyl-N-(1-phenylethyl)-N'-p-tolyl-imidazole-4,5-dicarboxamide

Space Group:	P21	***Cell:***	***a*** 6.341(0)	***b*** 25.017(3)	***c*** 12.435(1)
Space Group No.:	4	***(Å,°)***	α 90.00	β 102.64(0)	γ 90.00

R-Factor (%): 5.82 ***Temperature(K):*** 296 ***Density(g/cm³):*** 1.251



HUKGOJ

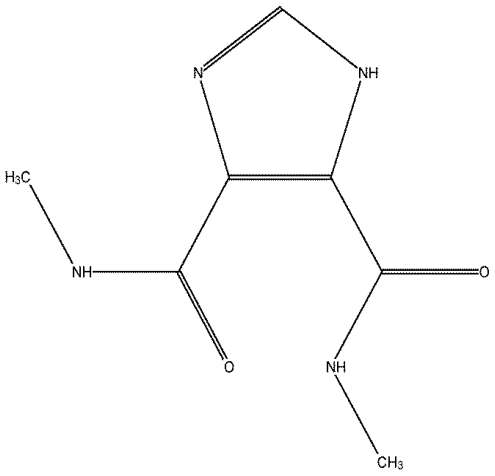
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_7H_{10}N_4O_2$

Compound Name: 4,5-bis((Methylamino)carbonyl)-1H-imidazole

Space Group:	P-1	***Cell:***	***a*** 4.890(0)	***b*** 9.109(1)	***c*** 9.506(1)
Space Group No.:	2	***(Å,°)***	α 94.85(0)	β 94.49(0)	γ 96.86(0)

R-Factor (%): 3.69 ***Temperature(K):*** 203 ***Density(g/cm³):*** 1.450



HUKGUP

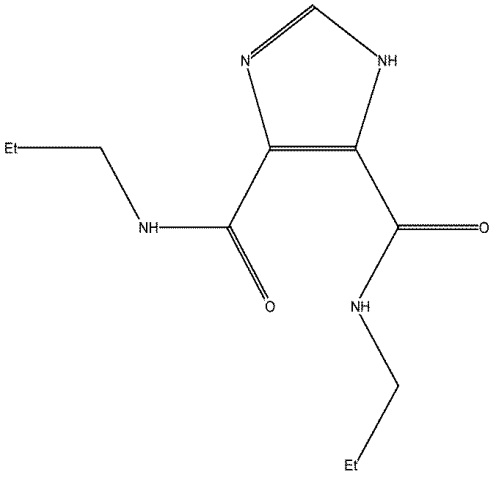
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{11}H_{18}N_4O_2$

Compound Name: 4,5-bis((Propylamino)carbonyl)-1H-imidazole

Space Group:	P-1	***Cell:***	***a*** 13.407(2)	***b*** 14.641(3)	***c*** 14.813(2)
Space Group No.:	2	***(Å,°)***	α 94.42(0)	β 101.66(0)	γ 116.36(0)

R-Factor (%): 5.22 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.264



HUKHAW

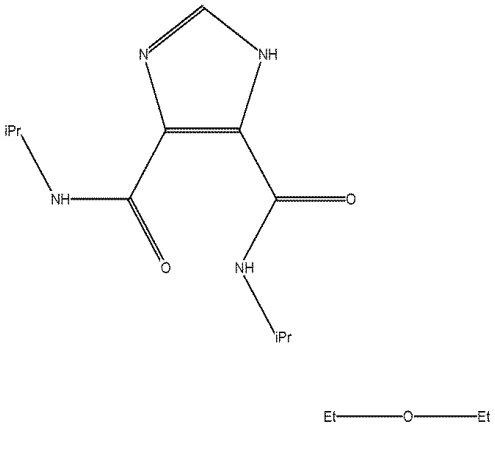
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{11}H_{18}N_4O_2.0.5(C_4H_{10}O_1)$

Compound Name: 4,5-bis((Isopropylamino)carbonyl)-1H-imidazole

Space Group:	P21/c	***Cell:***	***a*** 23.220(3)	***b*** 8.770(1)	***c*** 15.362(1)
Space Group No.:	14	***(Å,°)***	α 90.00	β 96.14(0)	γ 90.00

R-Factor (%): 4.36 ***Temperature(K):*** 203 ***Density(g/cm³):*** 1.176



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 9-12

HUKHIE

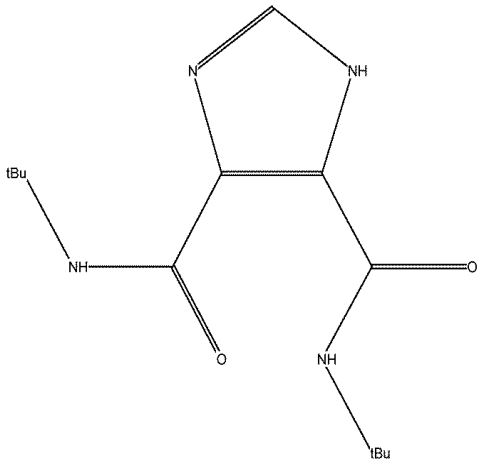
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{13}H_{22}N_4O_2$

Compound Name: 4,5-bis((t-Butylamino)carbonyl)-1H-imidazole

Space Group:	C2/c	***Cell:***	***a*** 24.853(6)	***b*** 9.431(3)	***c*** 17.448(4)
Space Group No.:	15	***(A,°)***	α 90.00	β 133.10(0)	γ 90.00

R-Factor (%): 3.81 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.185



HUKHUQ

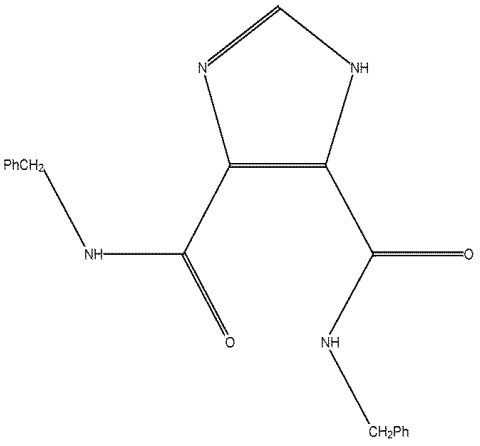
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{19}H_{18}N_4O_2$

Compound Name: 4,5-bis((Benzylamino)carbonyl)-1H-imidazole

Space Group:	P21/n	***Cell:***	***a*** 28.386(6)	***b*** 9.579(2)	***c*** 38.379(8)
Space Group No.:	14	***(A,°)***	α 90.00	β 109.41(0)	γ 90.00

R-Factor (%): 9.56 ***Temperature(K):*** 233 ***Density(g/cm³):*** 1.354



HUKJAY

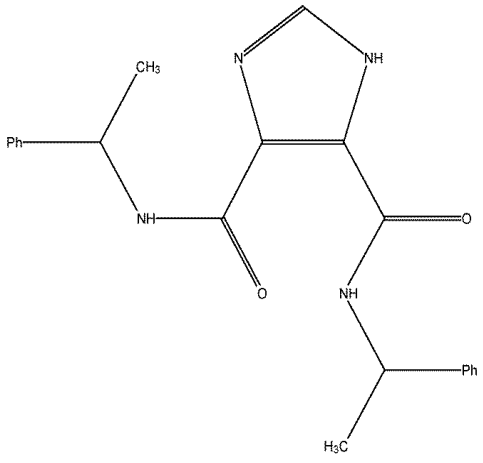
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{21}H_{22}N_4O_2$

Compound Name: 4,5-bis((R-α-Methylbenzylamino)carbonyl)-1H-imidazole

Space Group:	P21	***Cell:***	***a*** 10.139(1)	***b*** 5.813(1)	***c*** 16.709(3)
Space Group No.:	4	***(A,°)***	α 90.00	β 94.24(0)	γ 90.00

R-Factor (%): 4.29 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.226



HUKJEC

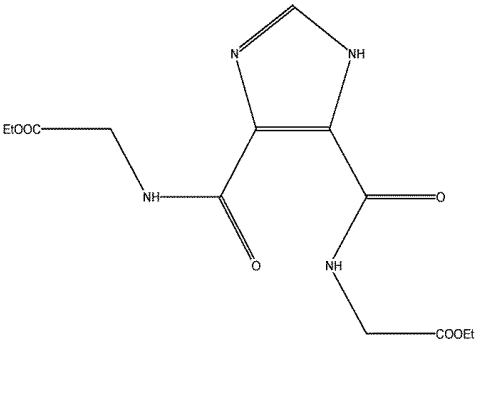
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{13}H_{18}N_4O_6$

Compound Name: 4,5-bis((Ethoxyglycyl)carbonyl)-1H-imidazole

Space Group:	P-1	***Cell:***	***a*** 11.029(1)	***b*** 12.203(1)	***c*** 13.128(1)
Space Group No.:	2	***(A,°)***	α 90.28(0)	β 107.85(0)	γ 111.66(0)

R-Factor (%): 5.00 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.399



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 13-16

HUKJOM

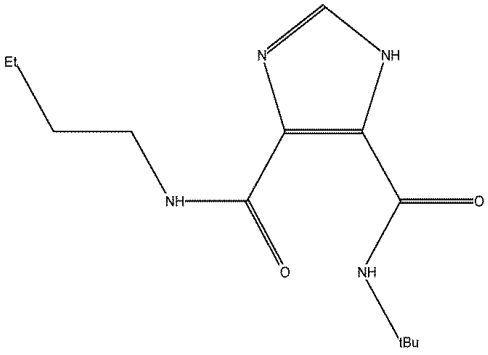
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{13}H_{22}N_4O_2$

Compound Name: 4-Butylaminocarbonyl-5-t-butylaminocarbonyl-1H-imidazole

Space Group:	C2/c	***Cell:***	***a*** 25.942(5)	***b*** 12.372(3)	***c*** 19.168(4)
Space Group No.:	15	***(A,°)***	α 90.00	β 102.23(0)	γ 90.00

R-Factor (%): 4.74 ***Temperature(K):*** 233 ***Density(g/cm³):*** 1.177



HUKJUS

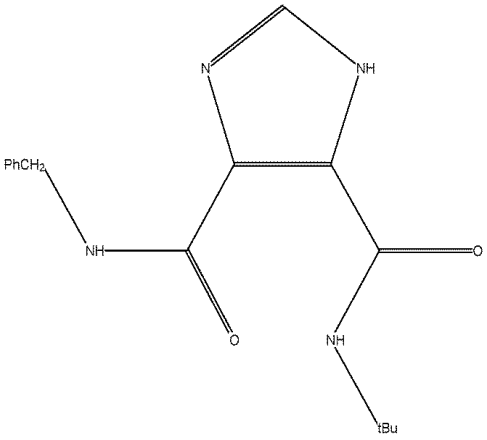
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{16}H_{20}N_4O_2$

Compound Name: 4-Benzylaminocarbonyl-5-t-butylaminocarbonyl-1H-imidazole

Space Group:	C2/c	***Cell:***	***a*** 22.342(4)	***b*** 16.167(3)	***c*** 8.944(1)
Space Group No.:	15	***(A,°)***	α 90.00	β 94.44(0)	γ 90.00

R-Factor (%): 3.91 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.239



HUKLEE

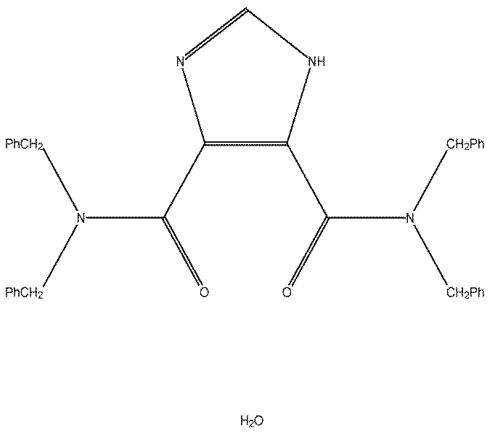
Reference: P.W.Baures, J.R.Rush, A.V.Wiznycia, J.Desper, B.A.Helfrich, A.M.Beatty (2002) *Cryst.Growth Des.* ,**2**,653

Formula: $C_{33}H_{30}N_4O_2.0.25(H_2O_1)$

Compound Name: 4,5-bis((N,N-Dibenzylamino)carbonyl)-1H-imidazole hydrate

Space Group:	C2/c	***Cell:***	***a*** 30.244(7)	***b*** 10.456(2)	***c*** 19.804(5)
Space Group No.:	15	***(A,°)***	α 90.00	β 116.30(0)	γ 90.00

R-Factor (%): 4.22 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.228



IWOMIR

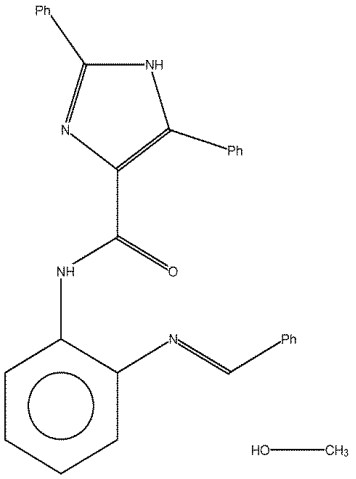
Reference: V.A.Mamedov, N.A.Zhukova, T.N.Beschastnova, A.T.Gubaidullin, D.V.Rakov, I.Kh.Rizvanov (2011) *Tetrahedron Lett.* , **52**,4280

Formula: $C_{29}H_{22}N_4O_1,C_1H_4O_1$

Compound Name: N-(2-(Benzylideneamino)phenyl)-2,5-diphenyl-1H-imidazole-4-carboxamide methanol solvate

Space Group:	Pbca	***Cell:***	***a*** 7.532(0)	***b*** 23.637(2)	***c*** 27.950(2)
Space Group No.:	61	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 5.94 ***Temperature(K):*** 296 ***Density(g/cm³):*** 1.267



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 17-20

KATSAZ

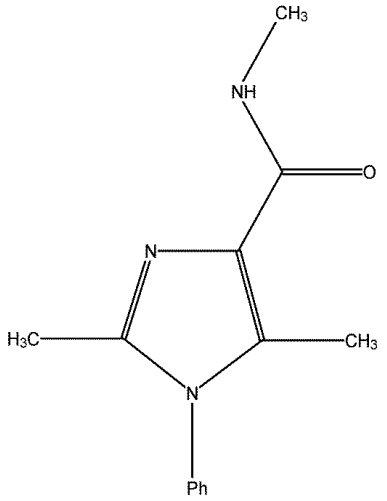
Reference: T.Ueda, I.Matsuura, N.Murakami, S.Nagai, J.Sakakibara, M.Goto (1988) *Tetrahedron Lett.* ,**29**,4607

Formula: $C_{13}H_{15}N_3O_1$

Compound Name: 2,5-Dimethyl-4-methylcarbamoyl-1-phenyl-1H-imidazole

Space Group:	P21/c	***Cell:***	***a*** 8.784(6)	***b*** 16.217(7)	***c*** 9.466(3)
Space Group No.:	14	***(A,°)***	α 90.00	β 108.17(5)	γ 90.00

R-Factor (%): 6.50 ***Temperature(K):*** 295 ***Density(g/cm³):*** 1.189



MOQHOQ

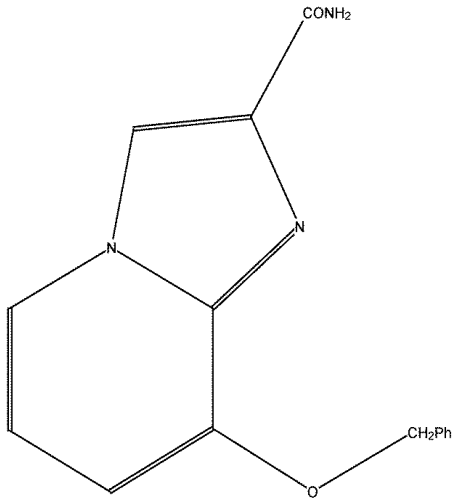
Reference: U.Groselj, J.Bezensek, A.Meden, J.Svete, B.Stanovnik, M.Oblak, P.S.Anderluh, U.Urleb (2008) *Heterocycles* ,**75**,1355

Formula: $C_{15}H_{13}N_3O_2$

Compound Name: 8-(Benzyloxy)imidazo[1,2-a]pyridine-2-carboxamide

Space Group:	P21/a	***Cell:***	***a*** 8.361(0)	***b*** 13.638(0)	***c*** 11.970(0)
Space Group No.:	14	***(A,°)***	α 90.00	β 93.20(0)	γ 90.00

R-Factor (%): 4.90 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.303



NCBXRF

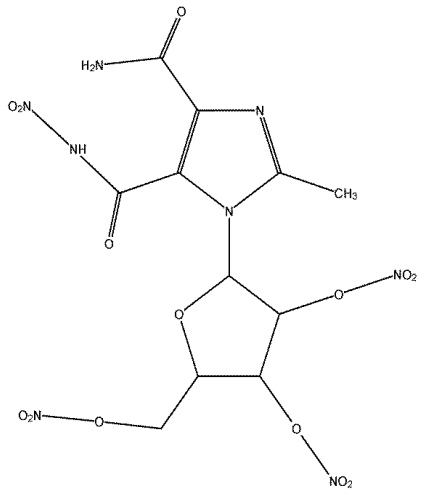
Reference: P.C.Wyss, P.Schonholzer, W.Arnold (1980) *Dissertation Abstr.B* ,**63**,1353

Formula: $C_{11}H_{12}N_6O_{14}$

Compound Name: 2-Methyl-5-(N-nitrocarboxamido)-1-(2',3',5'-tri-O-nitro-β-D-ribofuranosyl)-imidazole-4-carboxamide

Space Group:	P21	***Cell:***	***a*** 10.647(4)	***b*** 8.946(3)	***c*** 10.589(4)
Space Group No.:	4	***(A,°)***	α 90.00	β 111.55(3)	γ 90.00

R-Factor (%): 7.03 ***Temperature(K):*** 295 ***Density(g/cm³):*** 1.700



SARYUG

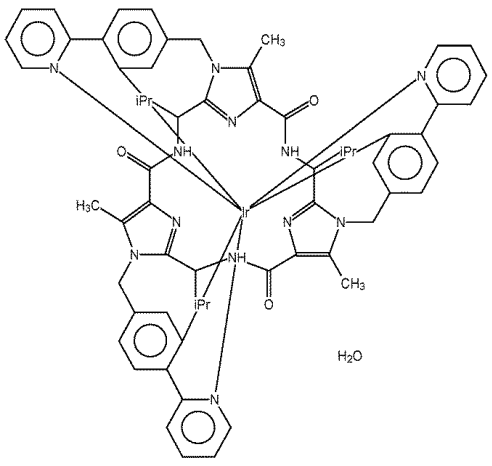
Reference: G.Haberhauer, T.Oeser, F.Rominger (2005) *Chem.Commun.* ,2799

Formula: $C_{63}H_{63}Ir_1N_{12}O_3.7.8(H_2O_1)$

Compound Name: Λ-(1⁵,5⁵,9⁵-Trimethyl-1¹,5¹,9¹-tris((4-(2-pyridyl)-1,3-phenylene)methyl)-4,8,12-tri-isopropyl-2,6,10-trioxo-3,7,11-triaza-1(4,2),5,9(2,4)-tri-imidazolacyclododecaphane)-iridium hydrate

Space Group:	R3	***Cell:***	***a*** 16.214(1)	***b*** 16.214(1)	***c*** 22.071(1)
Space Group No.:	146	***(A,°)***	α 90.00	β 90.00	γ 120.00

R-Factor (%): 4.73 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.357



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 21-24

SARZAN

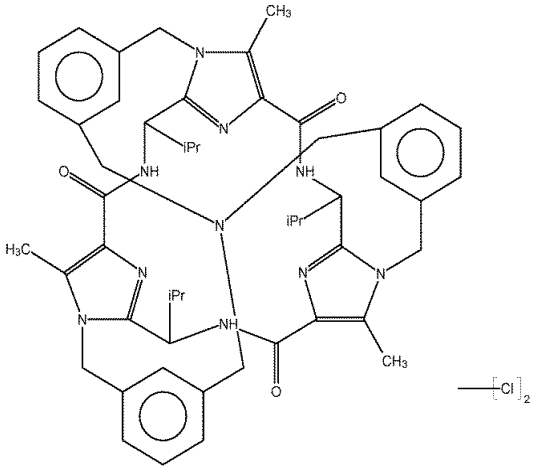
Reference: G.Haberhauer, T.Oeser, F.Rominger (2005) *Chem.Commun.* ,2799

Formula: $C_{51}\ H_{60}\ N_{10}\ O_3,2(C_1\ H_2\ Cl_2)$

Compound Name: $1^5,5^5,9^5$-Trimethyl-11,5^1,9^1-(3,3',3''-(nitrilo-trimethyl)-tribenzyl)-4,8,12-tri-isopropyl-2,6,10-trioxo-3,7,11-triaza-1(4,2),5,9(2,4)-tri-imidazolacyclododecaphane dichloromethane solvate

Space Group:	P21	***Cell:***	***a***	13.062(0)	***b***	15.430(0)	***c*** 13.675(0)
Space Group No.:	4	***(A,°)***	α	90.00	β	92.06(0)	γ 90.00

R-Factor (%): 5.95 ***Temperature(K):*** 200 ***Density(g/cm^3):*** 1.243



VAWSUJ

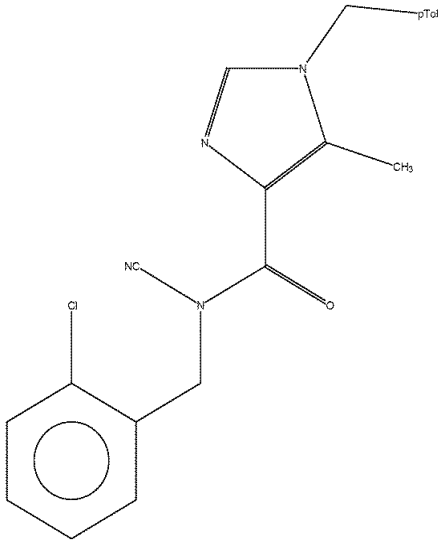
Reference: Wen-Chao Yang, Jing Li, Hun Li, Qiong Chen, Guang-Fu Yang (2012) *Bioorg.Med.Chem.Lett.* ,**22**,1455

Formula: $C_{21}\ H_{19}\ Cl_1\ N_4\ O_1$

Compound Name: N-(2-Chlorobenzyl)-N-cyano-5-methyl-1-(4-methylbenzyl)-1H-imidazole-4-carboxamide

Space Group:	P-1	***Cell:***	***a***	8.303(0)	***b***	10.757(1)	***c*** 11.820(1)
Space Group No.:	2	***(A,°)***	α	73.26(0)	β	80.44(0)	γ 71.65(0)

R-Factor (%): 6.32 ***Temperature(K):*** 294 ***Density(g/cm^3):*** 1.316



WETKAH

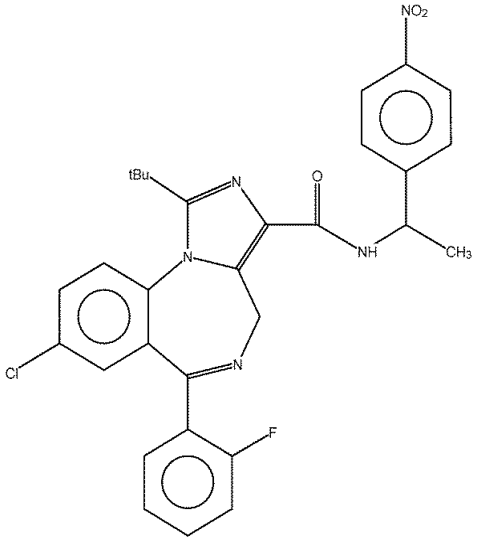
Reference: N.W.Gilman, P.Rosen, J.V.Earley, C.M.Cook, J.F.Blount, L.J.Todaro (1993) *J.Org.Chem.* ,**58**,3285

Formula: $C_{30}\ H_{27}\ Cl_1\ F_1\ N_5\ O_3$

Compound Name: (R)-(-)-(R)-8-Chloro-1-(1,1-dimethylethyl)-6-(2-fluorophenyl)-N-(4-nitro-1-phenylethyl)-4H-imidazo(1,5-a)(1,4)benzodiazepine-3-carboxamide

Space Group:	P21	***Cell:***	***a***	18.547(3)	***b***	8.417(2)	***c*** 18.138(3)
Space Group No.:	4	***(A,°)***	α	90.00	β	94.17(1)	γ 90.00

R-Factor (%): 4.30 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.317



WETLAI

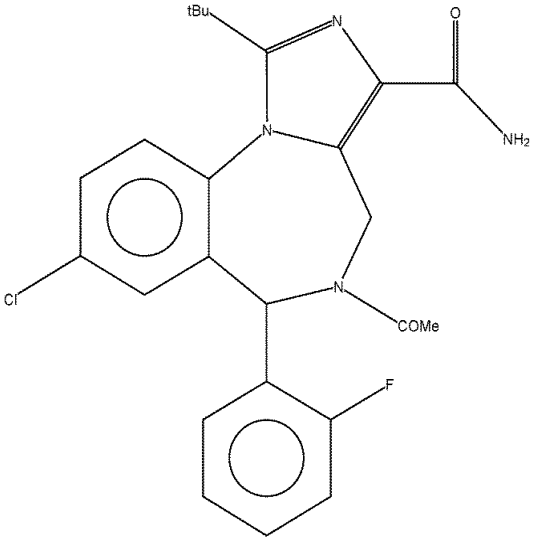
Reference: N.W.Gilman, P.Rosen, J.V.Earley, C.M.Cook, J.F.Blount, L.J.Todaro (1993) *J.Org.Chem.* ,**58**,3285

Formula: $C_{24}\ H_{24}\ Cl_1\ F_1\ N_4\ O_2$

Compound Name: 5-Acetyl-8-chloro-1-(1,1-dimethylethyl)-5,6,dihydro-6-(2-fluorophenyl)-4H-imidazo(1,5-a)(1,4)benzodiazepine-3-carboxamide

Space Group:	P21/a	***Cell:***	***a***	11.901(3)	***b***	21.634(4)	***c*** 9.028(2)
Space Group No.:	14	***(A,°)***	α	90.00	β	101.86(1)	γ 90.00

R-Factor (%): 3.80 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.328



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WETLEM

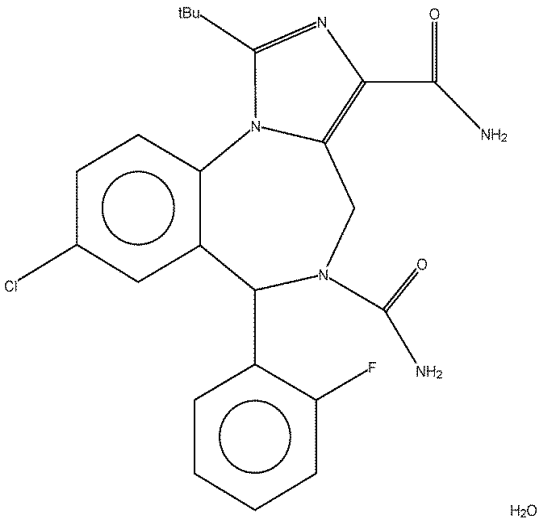
Reference: N.W.Gilman, P.Rosen, J.V.Earley, C.M.Cook, J.F.Blount, L.J.Todaro (1993) *J.Org.Chem.* ,**58**,3285

Formula: $C_{23}\,H_{23}\,Cl_1\,F_1\,N_5\,O_2,H_2\,O_1$

Compound Name: (R)-(6S)-(+)-8-Chloro-1-t-butyl-6-(2-fluorophenyl)-4,6-dihydro-5H-imidazo(1,5-a)(1,4)benzodiazepine-3,5-dicarboxamide monohydrate

Space Group:	A2	***Cell:***	***a*** 28.036(5)	***b*** 10.058(2)	***c*** 16.701(2)
Space Group No.:	5	***(A,°)***	α 90.00	β 106.23(1)	γ 90.00

R-Factor (%): 3.80 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.392



WETLOW

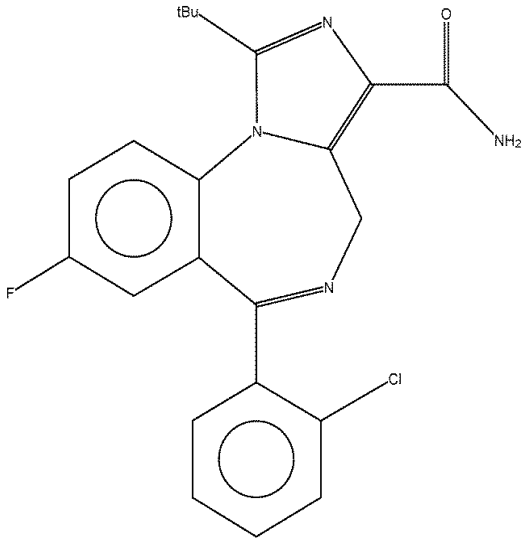
Reference: N.W.Gilman, P.Rosen, J.V.Earley, C.M.Cook, J.F.Blount, L.J.Todaro (1993) *J.Org.Chem.* ,**58**,3285

Formula: $C_{22}\,H_{20}\,Cl_1\,F_1\,N_4\,O_1$

Compound Name: (S)-(+)-6-(2-Chlorophenyl)-1-t-butyl-8-fluoro-4H-imidazo(1,5-a)(1,4) benzodiazepine-3-carboxamide

Space Group:	P212121	***Cell:***	***a*** 9.205(2)	***b*** 9.589(2)	***c*** 22.711(5)
Space Group No.:	19	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.30 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.361



WONJEO

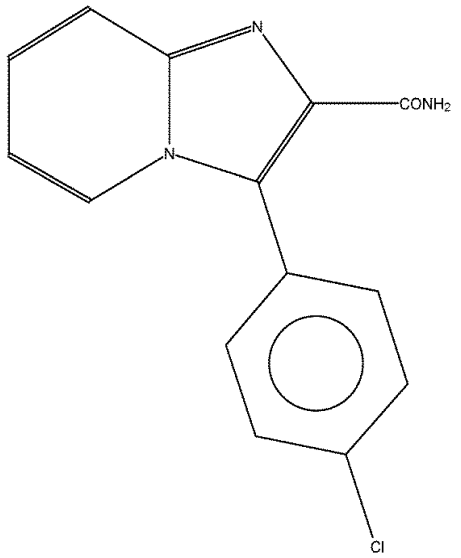
Reference: N.Lah, I.Leban, A.Majcen Le Marechal, V.Ferk, P.Le Grel, J.Sieler (2000) *J.Chem.Cryst.* ,**30**,109

Formula: $C_{14}\,H_{10}\,Cl_1\,N_3\,O_1$

Compound Name: 3-(4-chlorophenyl)imidazo(1,2-a)pyridine-2-carboxamide

Space Group:	Pca21	***Cell:***	***a*** 28.813(2)	***b*** 9.369(1)	***c*** 9.361(1)
Space Group No.:	29	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 4.77 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.428



WUPZUC

Reference: T.W.Hambley, A.Katsifis, R.B.Knott, F.Mattner, B.Dikic (2002) *Aust.J.Chem.* ,**55**,737

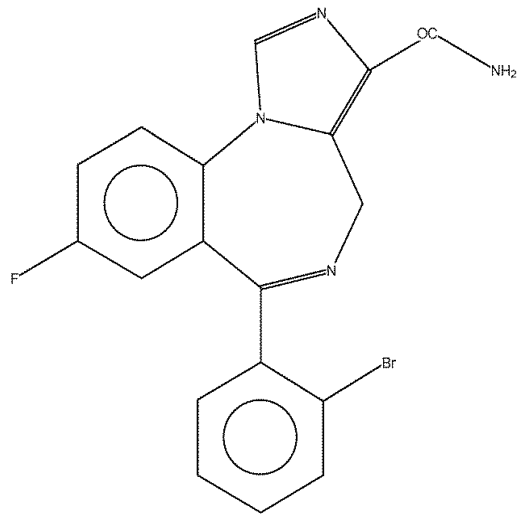
Formula: $C_{18}\,H_{12}\,Br_1\,F_1\,N_4\,O_1$

Compound Name: 6-(2'-Bromophenyl)-8-fluoro-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxamide

Synonym: Imidazenil

Space Group:	P-1	***Cell:***	***a*** 12.537(4)	***b*** 18.211(5)	***c*** 7.852(2)
Space Group No.:	2	***(A,°)***	α 91.07(2)	β 106.26(2)	γ 77.86(3)

R-Factor (%): 5.60 ***Temperature(K):*** 294 ***Density(g/cm^3):*** 1.577



Search: search1 (Tue Feb 18 09:20:35 2014): Hits 29-32

WUQBAL

Reference: T.W.Hambley, A.Katsifis, R.B.Knott, F.Mattner, B.Dikic (2002) *Aust.J.Chem.* ,**55**,737

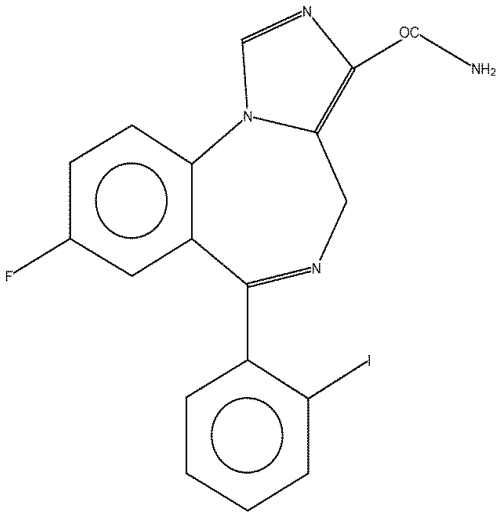
Formula: $C_{18}H_{12}F_1I_1N_4O_1$

Compound Name: 6-(2'-Iodophenyl)-8-fluoro-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxamide

Synonym: Iodoimidazenil

Space Group:	P21/a	***Cell:***	***a*** 12.185(2)	***b*** 7.558(2)	***c*** 18.287(2)
Space Group No.:	14	***(A,°)***	α 90.00	β 95.23(1)	γ 90.00

R-Factor (%): 4.80 ***Temperature(K):*** 294 ***Density(g/cm³):*** 1.767



XUQHUM

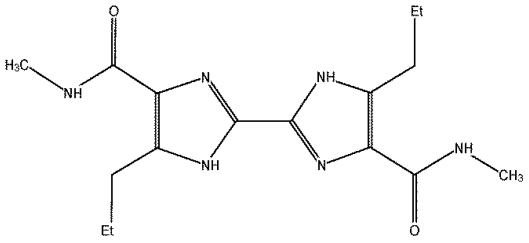
Reference: C.P.Causey, W.E.Allen (2002) *J.Org.Chem.* ,**67**,5963

Formula: $C_{16}H_{24}N_6O_2$

Compound Name: 5,5'-Dipropyl-1H,1'H-(2,2')bi-imidazolyl-4,4'-dicarboxylic acid bis(methylamide)

Space Group:	R-3	***Cell:***	***a*** 28.158(0)	***b*** 28.158(0)	***c*** 6.479(0)
Space Group No.:	148	***(A,°)***	α 90.00	β 90.00	γ 120.00

R-Factor (%): 6.74 ***Temperature(K):*** 153 ***Density(g/cm³):*** 1.117



YAJXEO

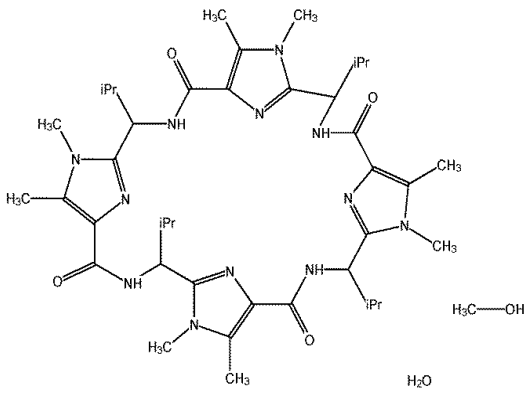
Reference: P.Comba, N.Dovalil, G.R.Hanson, G.Linti (2011) *Inorg.Chem.* ,**50**,5165

Formula: $C_{40}H_{60}N_{12}O_4.0.25(H_2O_1),C_1H_4O_1$

Compound Name: $1^1,1^5,5^1,5^5,9^1,9^5,13^1,13^5$-octamethyl-4,8,12-16-tetra-isopropyl-2,6,10-14-tetraoxa-3,11,7,15-tetra-aza-1,5,9,13(2,4)-tetra-imidazolacyclohexadecaphane methanol solvate hydrate

Space Group:	I-4	***Cell:***	***a*** 19.861(3)	***b*** 19.861(3)	***c*** 6.922(1)
Space Group No.:	82	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 9.42 ***Temperature(K):*** 200 ***Density(g/cm³):*** 0.985



YAJXIS

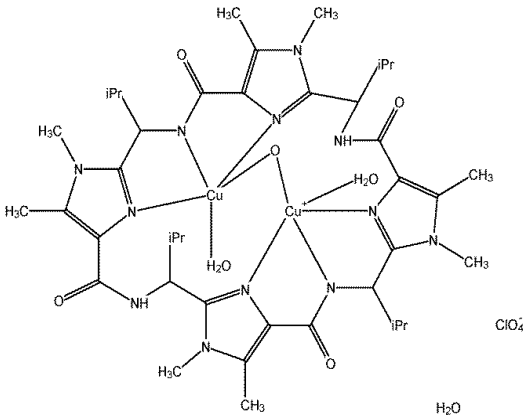
Reference: P.Comba, N.Dovalil, G.R.Hanson, G.Linti (2011) *Inorg.Chem.* ,**50**,5165

Formula: $C_{40}H_{62}Cu_2N_{12}O_7{}^{1+},Cl_1O_4{}^{1-},2(H_2O_1)$

Compound Name: (μ_2-$1^1,1^5,5^1,5^5,9^1,9^5,13^1,13^5$-octamethyl-4,8,12-16-tetra-isopropyl-2,6,10-14-tetraoxa-3,11-diazanide-7,15-diaza-1,5,9,13(2,4)-tetra-imidazolacyclohexadecaphane)-(μ_2-oxo)-diaqua-di-copper(ii) perchlorate dihydrate

Space Group:	P2/c	***Cell:***	***a*** 11.876(2)	***b*** 11.599(2)	***c*** 18.240(4)
Space Group No.:	13	***(A,°)***	α 90.00	β 102.09(3)	γ 90.00

R-Factor (%): 5.03 ***Temperature(K):*** 200 ***Density(g/cm³):*** 1.467



Search Overview

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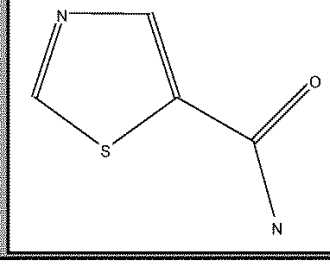
Date/Time done:	Tue Feb 18 09:20:52 2014
Database(s):	CSD version 5.34 updates (Nov 2012) CSD version 5.34 (November 2012)
Restriction Info:	No refcode restrictions applied
Filters:	3D coordinates determined Not disordered No errors
Percentage Completed:	100%
Number of Hits:	5

Single query used. Search found structures that:

match

Query 2

Query 2



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EYOZIB

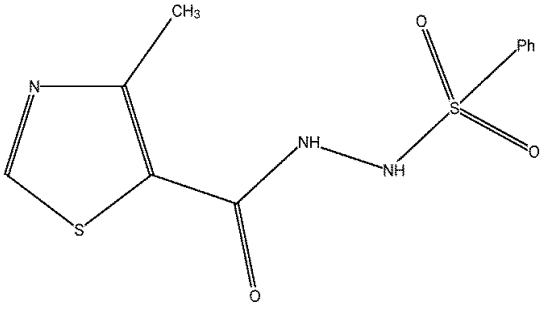
Reference: Qing Bao Song, Zhi Min Jin, Hai Bin Wang, Biao Jiang (2004) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**60**,o1292

Formula: $C_{11}H_{11}N_3O_3S_2$

Compound Name: N'-(Benzenesulfonyl)-4-methylthiazole-5-carbohydrazide

Space Group:	P21/c	***Cell:***	***a*** 10.559(0)	***b*** 12.898(1)	***c*** 10.188(0)
Space Group No.:	14	***(Å,°)***	α 90.00	β 111.70(0)	γ 90.00

R-Factor (%): 3.37 ***Temperature(K):*** 293 ***Density(g/cm^3):*** 1.532



HAYPON

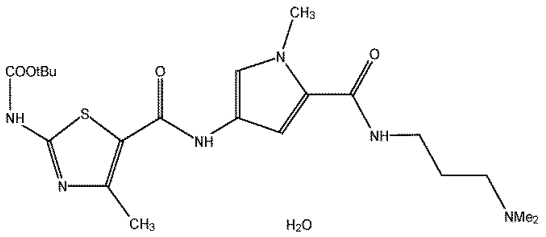
Reference: K.Benschawel, U.Pindur, D.Schollmeyer (2005) *Private Communication* ,

Formula: $C_{21}H_{32}N_6O_4S_1,H_2O_1$

Compound Name: (5-(5-(3-Dimethylaminopropylcarbamoyl)-1-methyl-1H-pyrrol-3-ylcarbamoyl)-4-methylthiazol-2-yl)carbamic acid t-butyl ester monohydrate

Space Group:	P-1	***Cell:***	***a*** 10.356(1)	***b*** 10.816(1)	***c*** 12.755(2)
Space Group No.:	2	***(Å,°)***	α 111.70(1)	β 106.24(1)	γ 92.92(1)

R-Factor (%): 4.46 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.277



PUMNUH

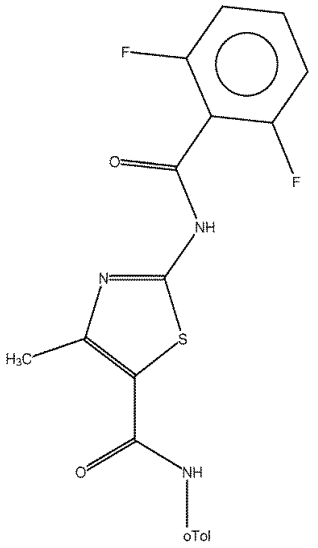
Reference: Hua Cai, Ying Guo, Jian-Gang Li, Yun-Ling Zou (2010) *J.Chem.Cryst.* ,**40**,100

Formula: $C_{19}H_{15}F_2N_3O_2S_1$

Compound Name: 2-((2,6-Difluorobenzoyl)amino)-4-methyl-N-(2-methylphenyl)-1,3-thiazole-5-carboxamide

Space Group:	Pca21	***Cell:***	***a*** 21.840(2)	***b*** 7.532(0)	***c*** 22.365(2)
Space Group No.:	29	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.28 ***Temperature(K):*** 296 ***Density(g/cm^3):*** 1.399



XISZOP

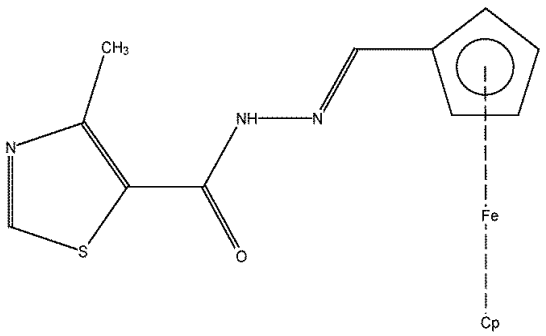
Reference: Jie Zhang (2008) *Appl.Organomet.Chem.* ,**22**,6

Formula: $C_{16}H_{15}Fe_1N_3O_1S_1$

Compound Name: (E)-N'-Ferrocenylidene-4-methylthiazole-5-carbohydrazide

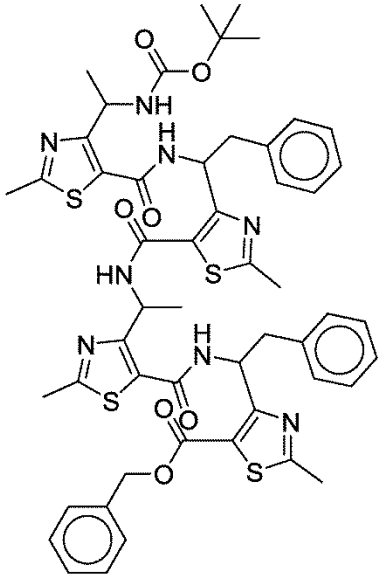
Space Group:	P42/n	***Cell:***	***a*** 21.041(3)	***b*** 21.041(3)	***c*** 7.121(1)
Space Group No.:	86	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.24 ***Temperature(K):*** 293 ***Density(g/cm^3):*** 1.488



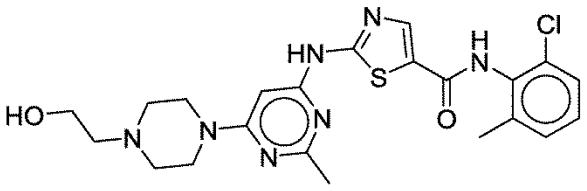
Search of WebCSD updates to 18th February 2014 (two structures)

Refcode: AGEZAP
Source Database as531be
Reliability Score Fully curated CSD
Author(s) L.Mathieu, B.Legrand, C.Deng, L.Vezenkov, M.Amblard, M.C.Averland-Petit, E.Wenger, C.Didierjean, N.Masurier, V.Lisowski, J.Martinez, T.L.Maillard
Reference Angew.Chem.,Int.Ed. (**2013**), 52, 6006, doi:10.1002/anie.201302106
Formula C_{52} H_{56} N_8 O_7 S_4,C_6 H_{14} O
Compound Name
Benzyl 4-(1-(((4-(1-(((4-(1-(((4-(1-((t-butoxycarbonyl)amino)ethyl)-2-methyl-1, 3-thiazol-5-yl)carbonyl)amino)-2- phenylethyl)-2-methyl-1,3-thiazol-5-yl)carbonyl)amino)ethyl)-2-methyl-1,3-thiazol-5-yl)carbonyl)amino)-2- phenylethyl)-2-methyl-1,3-thiazole-5- carboxylate di-isopropyl ether solvate
Space Group P 21 21 21
Cell Lengths a 15.640(1) b 15.821(2) c 24.894(3)
Cell Angles α 90 β 90 γ 90
Cell Volume 6159.78
Z, Z' Z: 4 Z': 1
R-Factor (%) 7.22



AGEZAP

Refcode: RAVPUB
Source Database as531be
Reliability Score Fully curated CSD
Author(s)
S.Roy, R.Quinones, A.J.Matzger
Reference Cryst.Growth Des. (**2012**), 12, 2122, doi:10.1021/cg300152p
Formula C_{22} H_{26} Cl N_7 O_2 S
Compound Name
N-(2-Chloro-6-methylphenyl)-2-((6-(4-(2-hydroxyethyl)piperazin-1-yl)-2-methylpyrimidin-4-yl)amino)-1,3- thiazole-5-carboxamide
Space Group P 21/n
Cell Lengths a 14.1400(7) b 8.1804(4) c 22.1356(12)
Cell Angles α 90 β 105.415(3) γ 90
Cell Volume 2468.33
Z, Z' Z: 4 Z': 1
R-Factor (%) 8.46



RAVPUB

Search Overview

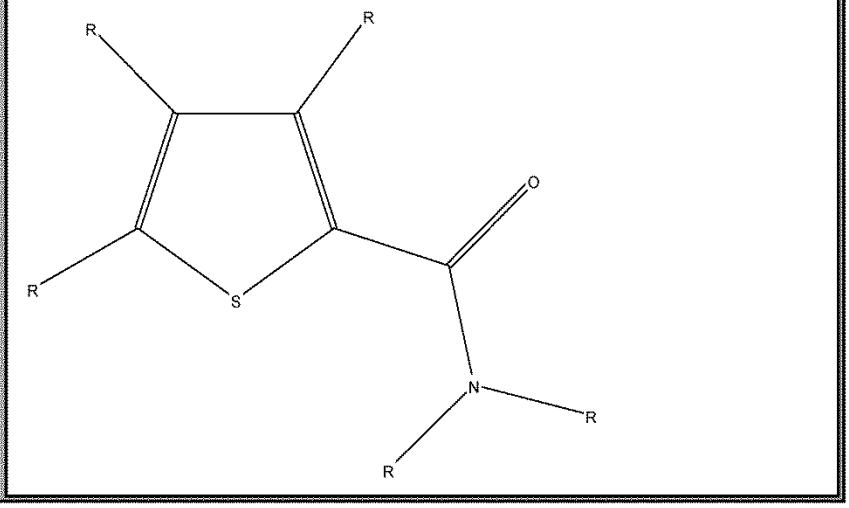
Search:	search3
Date/Time done:	Tue Feb 18 09:21:02 2014
Database(s):	CSD version 5.34 updates (Nov 2012) CSD version 5.34 (November 2012)
Restriction Info:	No refcode restrictions applied
Filters:	3D coordinates determined Not disordered No errors
Percentage Completed:	100%
Number of Hits:	60

Single query used. Search found structures that:

match

Query 3

Query 3



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 1-4

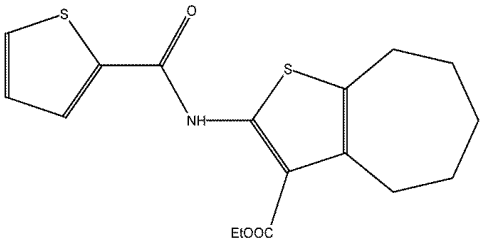
AVAJIR

Reference: A.M.Mahran (2008) *Egypt.J.Phys.* ,**51**,539

Formula: $C_{17}H_{19}N_1O_3S_2$

Compound Name: Ethyl 2-((2-thienylcarbonyl)amino)-5,6,7,8-tetrahydro-4H-cyclohepta[b]thiophene-3-carboxylate

Space Group:	C2/c	***Cell:***	***a*** 20.797(0)	***b*** 8.640(0)	***c*** 19.844(0)
Space Group No.:	15	***(Å,°)***	α 90.00	β 105.75(0)	γ 90.00
R-Factor (%):	6.60	***Temperature(K):***	298	***Density(g/cm³):***	1.353



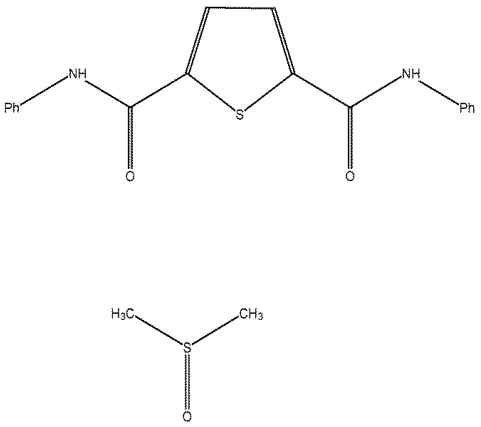
BILXEA

Reference: P.A.Gale, M.B.Hursthouse, M.E.Light, C.N.Warriner (2004) *Collect.Czech.Chem.Commun.* ,**69**,1301

Formula: $C_{18}H_{14}N_2O_2S_1,2(C_2H_6O_1S_1)$

Compound Name: N,N'-Diphenylthiophene-2,5-dicarboxamide dimethylsulfoxide solvate

Space Group:	P21/n	***Cell:***	***a*** 8.598(0)	***b*** 28.229(0)	***c*** 9.551(0)
Space Group No.:	14	***(Å,°)***	α 90.00	β 99.43(0)	γ 90.00
R-Factor (%):	3.69	***Temperature(K):***	120	***Density(g/cm³):***	1.390



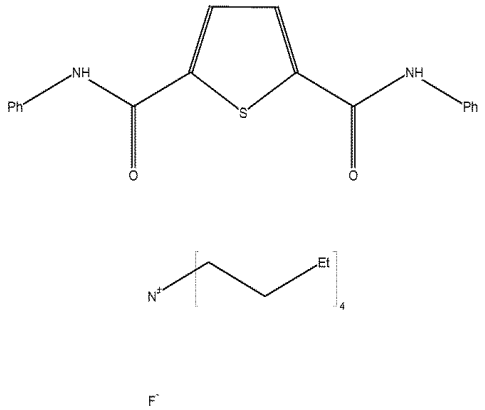
BILXIE

Reference: P.A.Gale, M.B.Hursthouse, M.E.Light, C.N.Warriner (2004) *Collect.Czech.Chem.Commun.* ,**69**,1301

Formula: $C_{18}H_{14}N_2O_2S_1,C_{16}H_{36}N_1{}^{1+},F_1{}^{1-}$

Compound Name: N,N'-Diphenylthiophene-2,5-dicarboxamide tetra-n-butylammonium fluoride

Space Group:	P21/c	***Cell:***	***a*** 9.555(0)	***b*** 17.704(0)	***c*** 19.341(0)
Space Group No.:	14	***(Å,°)***	α 90.00	β 93.89(0)	γ 90.00
R-Factor (%):	3.98	***Temperature(K):***	120	***Density(g/cm³):***	1.188



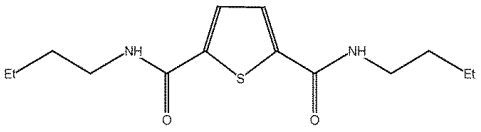
BILXOK

Reference: P.A.Gale, M.B.Hursthouse, M.E.Light, C.N.Warriner (2004) *Collect.Czech.Chem.Commun.* ,**69**,1301

Formula: $C_{14}H_{22}N_2O_2S_1$

Compound Name: N,N'-Dibutylthiophene-2,5-dicarboxamide

Space Group:	P1	***Cell:***	***a*** 9.750(5)	***b*** 9.970(5)	***c*** 15.582(5)
Space Group No.:	1	***(Å,°)***	α 87.57(0)	β 87.55(0)	γ 84.23(0)
R-Factor (%):	8.64	***Temperature(K):***	120	***Density(g/cm³):***	1.247



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 5-8

BUFCOV

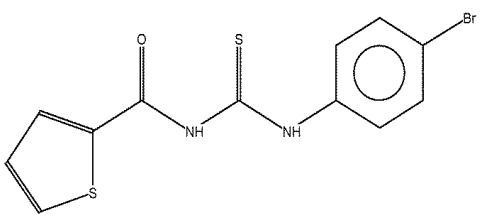
Reference: S.Saeed, N.Rashid, R.Hussain, P.G.Jones (2009)
Acta Crystallogr.,Sect.E:Struct.Rep.Online ,**65**,o2568

Formula: $C_{12}\,H_9\,Br_1\,N_2\,O_1\,S_2$

Compound Name: 1-(4-Bromophenyl)-3-(2-thienylcarbonyl)thiourea

Space Group:	P21/n	***Cell:***	***a*** 13.148(0)	***b*** 4.426(0)	***c*** 22.671(1)
Space Group No.:	14	***(A,°)***	α 90.00	β 90.41(0)	γ 90.00

R-Factor (%): 2.51 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.718



BUVLAG

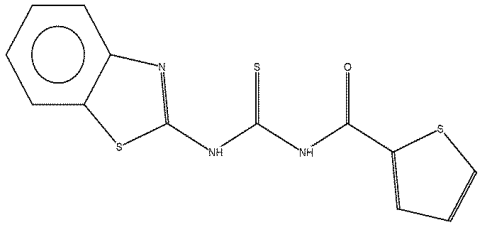
Reference: S.Saeed, N.Rashid, P.G.Jones, M.Ali, R.Hussain (2010)
Eur.J.Med.Chem. ,**45**,1323

Formula: $C_{13}\,H_9\,N_3\,O_1\,S_3$

Compound Name: N-(1,3-Benzothiazol-2-ylcarbamothioyl)thiophene-2-carboxamide

Space Group:	C2/c	***Cell:***	***a*** 24.631(0)	***b*** 5.889(0)	***c*** 18.790(0)
Space Group No.:	15	***(A,°)***	α 90.00	β 102.51(0)	γ 90.00

R-Factor (%): 2.58 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.595



CEMTAQ

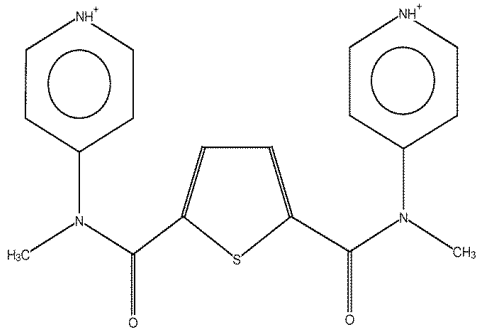
Reference: N.L.S.Yue, M.C.Jennings, R.J.Puddephatt (2006)
Dalton Trans. ,3886

Formula: $C_{18}\,H_{18}\,N_4\,O_2\,S_1\,^{2+}$,2($Cl_1\,^{1-}$),4($H_2\,O_1$)

Compound Name: cis,cis,syn-N,N'-dimethyl-N,N'-bis(4-pyridyl)thiophene-2,5-dicarboxamide bis(hydrochloride) tetrahydrate

Space Group:	Pnma	***Cell:***	***a*** 8.327(0)	***b*** 14.732(0)	***c*** 19.190(0)
Space Group No.:	62	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 8.71 ***Temperature(K):*** 150 ***Density(g/cm³):*** 1.403



Cl^- H_2O

CEMTUK

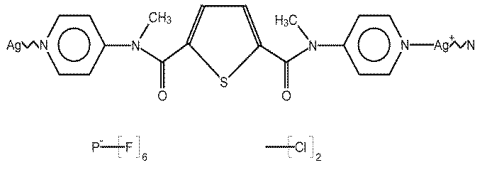
Reference: N.L.S.Yue, M.C.Jennings, R.J.Puddephatt (2006)
Dalton Trans. ,3886

Formula: ($C_{18}\,H_{16}\,Ag_1\,N_4\,O_2\,S_1\,^{1+}$)n,n($F_6\,P_1\,^{1-}$),2n($C_1\,H_2\,Cl_2$)

Compound Name: catena-((μ2-N,N'-dimethyl-N,N'-bis(4-pyridyl)thiophene-2,5-dicarboxamide)-silver(i) hexafluorophosphate dichloromethane solvate)

Space Group:	P21/n	***Cell:***	***a*** 11.560(0)	***b*** 19.778(0)	***c*** 12.834(0)
Space Group No.:	14	***(A,°)***	α 90.00	β 109.26(0)	γ 90.00

R-Factor (%): 4.90 ***Temperature(K):*** 150 ***Density(g/cm³):*** 1.859



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 9-12

CEMVAS

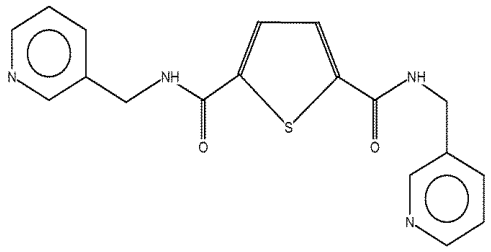
Reference: N.L.S.Yue, M.C.Jennings, R.J.Puddephatt (2006) *Dalton Trans.* ,3886

Formula: $C_{18}H_{16}N_4O_2S_1$

Compound Name: N,N'-bis(3-pyridylmethyl)thiophene-2,5-dicarboxamide

Space Group:	P1	***Cell:***	***a*** 6.077(0)	***b*** 7.347(1)	***c*** 9.783(1)
Space Group No.:	1	***(Å,°)***	α 102.25(0)	β 91.96(0)	γ 109.73(0)

R-Factor (%): 4.35 ***Temperature(K):*** 150 ***Density(g/cm^3):*** 1.466



CEMVEW

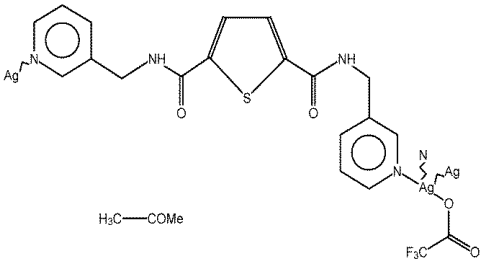
Reference: N.L.S.Yue, M.C.Jennings, R.J.Puddephatt (2006) *Dalton Trans.* ,3886

Formula: $(C_{20}H_{16}Ag_1F_3N_4O_4S_1)n,0.5n(C_3H_6O_1)$

Compound Name: catena-{(μ_2-N,N'-bis(3-pyridylmethyl)thiophene-2,5-dicarboxamide)-(trifluoroacetato)-silver(i) acetone solvate}

Space Group:	P-1	***Cell:***	***a*** 7.706(1)	***b*** 12.748(1)	***c*** 14.185(2)
Space Group No.:	2	***(Å,°)***	α 112.98(0)	β 104.11(0)	γ 94.87(0)

R-Factor (%): 8.75 ***Temperature(K):*** 150 ***Density(g/cm^3):*** 1.642



DUBFUB

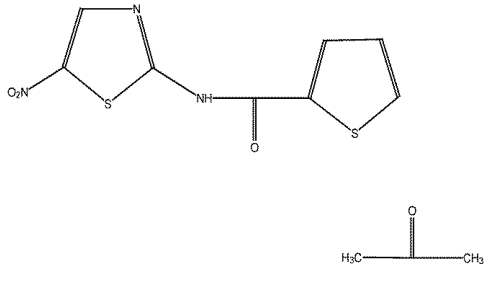
Reference: N.H.Dung, B.Viossat, J.-C.Lancelot, M.Robba (1986) *Chem.Pharm.Bull.* ,**34**,951

Formula: $C_8H_5N_3O_3S_2.C_3H_6O_1$

Compound Name: 5-Nitro-2-(2-thenoylamino)-thiazole acetone solvate

Space Group:	C2/c	***Cell:***	***a*** 25.660(40)	***b*** 7.360(5)	***c*** 11.050(80)
Space Group No.:	15	***(Å,°)***	α 90.00	β 105.00(30)	γ 90.00

R-Factor (%): 4.00 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 2.065



ENUFUP

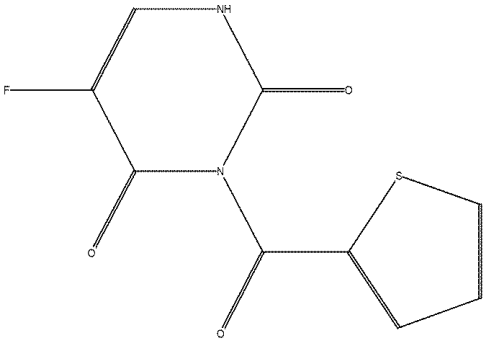
Reference: Yi-Feng Zhu, Mei-Rong Li, Xiao-Qing Cai, Mao-Lin Hu (2011) *Z.Kristallogr.-New Cryst.Struct.* ,**226**,107

Formula: $C_9H_5F_1N_2O_3S_1$

Compound Name: 5-Fluoro-3-(2-thienylcarbonyl)pyrimidine-2,4(1H,3H)-dione

Space Group:	P21/c	***Cell:***	***a*** 5.574(4)	***b*** 19.770(15)	***c*** 8.866(7)
Space Group No.:	14	***(Å,°)***	α 90.00	β 100.49(1)	γ 90.00

R-Factor (%): 5.19 ***Temperature(K):*** 298 ***Density(g/cm^3):*** 1.661



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 13-16

EPAGAE

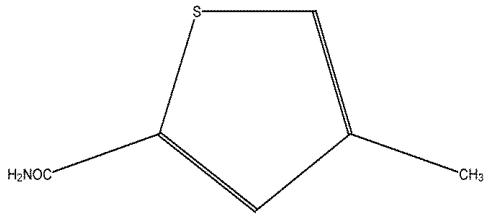
Reference: S.L.Huth, M.B.Hursthouse (2007)
University of Southampton, Crystal Structure Report Archive ,374

Formula: $C_6 H_7 N_1 O_1 S_1$

Compound Name: 4-Methylthiophene-2-carboxamide

Space Group:	P-1	***Cell:***	***a***	10.085(0)	***b***	10.472(0)	***c***	10.915(0)
Space Group No.:	2	***(A,°)***	α	106.72(0)	β	111.47(0)	γ	95.60(0)

R-Factor (%): 6.99 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.406



FIWLUS

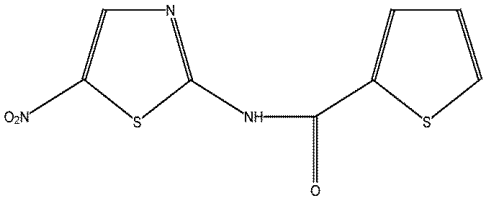
Reference: B.Viossat, Nguyen-Huy Dung, J.-C.Lancelot, F.Robert, M.Robba (1987) *Chem.Pharm.Bull.* ,**35**,2419

Formula: $C_8 H_5 N_3 O_3 S_2.C_3 H_7 N_1 O_1$

Compound Name: 5-Nitro-2-({2'-thenoyl}amino)-1,3-thiazole dimethylformamide solvate

Space Group:	P21/n	***Cell:***	***a***	10.370(3)	***b***	8.180(8)	***c***	17.900(10)
Space Group No.:	14	***(A,°)***	α	90.00	β	104.30(4)	γ	90.00

R-Factor (%): 4.90 ***Temperature(K):*** 295 ***Density(g/cm³):*** 1.482



GOKREE

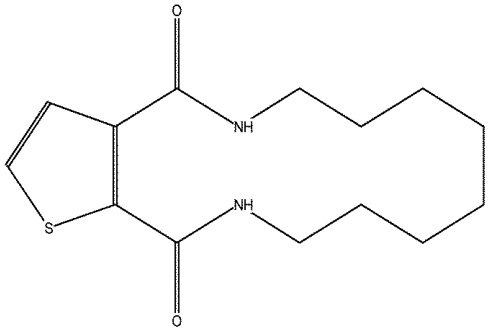
Reference: K.Mereiter, E.Horkel, C.Hametner, J.Frohlich (2008)
Private Communication ,

Formula: $C_{14} H_{20} N_2 O_2 S_1$

Compound Name: 5,6,7,8,9,10,11,12,13,14-Decahydrothieno(2,3-c)(1,6) diazacyclotetradecine-4,15-dione

Space Group:	P212121	***Cell:***	***a***	9.684(0)	***b***	10.082(0)	***c***	14.564(0)
Space Group No.:	19	***(A,°)***	α	90.00	β	90.00	γ	90.00

R-Factor (%): 3.67 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.310



GUPHOP

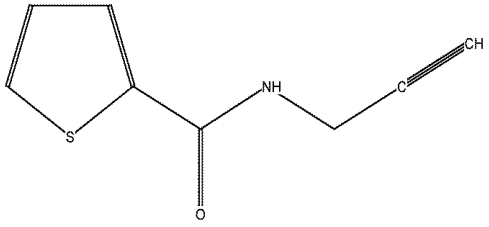
Reference: J.W.Weyrauch, A.S.K.Hashmi, A.Schuster, T.Hengst, S.Schetter, A.Littmann, M.Rudolph, M.Hamzic, J.Visus, F.Rominger, W.Frey, J.W.Bats (2010) *Chem.-Eur.J.* ,**16**,956

Formula: $C_8 H_7 N_1 O_1 S_1$

Compound Name: N-(Prop-2-yn-1-yl)thiophene-2-carboxamide

Space Group:	P21	***Cell:***	***a***	9.818(2)	***b***	4.231(1)	***c***	19.688(5)
Space Group No.:	4	***(A,°)***	α	90.00	β	93.09(0)	γ	90.00

R-Factor (%): 6.06 ***Temperature(K):*** 200 ***Density(g/cm³):*** 1.344



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 17-20

HAMNUG

Reference: J.Spencer, H.Patel, S.K.Callear, S.J.Coles, J.J.Deadman (2011) *Tetrahedron Lett.* ,**52**,5905

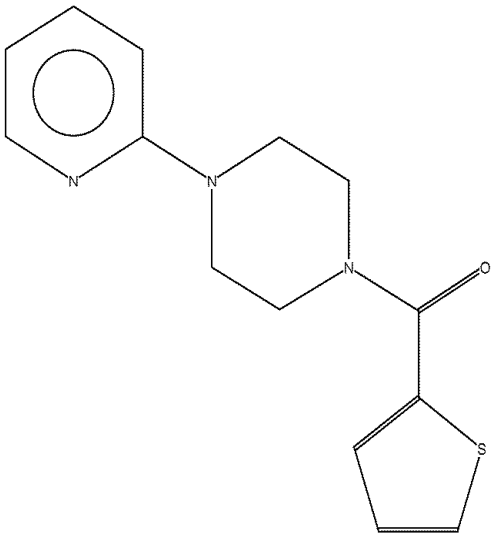
Formula: $C_{14}H_{15}N_3O_1S_1$

Compound Name: (4-(Pyridin-2-yl)piperazin-1-yl)(2-thienyl)methanone

Synonym: 1-(Pyridin-2-yl)-4-(thiophen-2-ylcarbonyl)piperazine

Space Group:	P21	***Cell:***	***a*** 6.278(0)	***b*** 7.574(0)	***c*** 13.906(0)
Space Group No.:	4	***(Å,°)***	α 90.00	β 101.88(0)	γ 90.00

R-Factor (%): 4.74 ***Temperature(K):*** 120 ***Density(g/cm^3):*** 1.403



HAMQET

Reference: J.Spencer, H.Patel, S.K.Callear, S.J.Coles, J.J.Deadman (2011) *Tetrahedron Lett.* ,**52**,5905

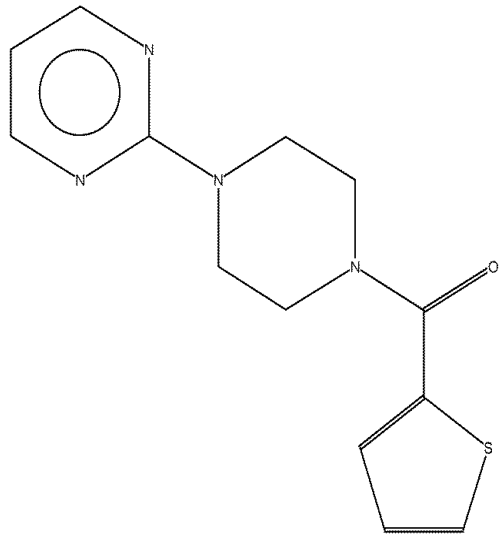
Formula: $C_{13}H_{14}N_4O_1S_1$

Compound Name: (4-(Pyrimidin-2-yl)piperazin-1-yl)(2-thienyl)methanone

Synonym: 2-(4-(Thiophen-2-ylcarbonyl)piperazin-1-yl)pyrimidine

Space Group:	P21	***Cell:***	***a*** 6.219(0)	***b*** 7.672(0)	***c*** 13.711(0)
Space Group No.:	4	***(Å,°)***	α 90.00	β 101.55(0)	γ 90.00

R-Factor (%): 3.75 ***Temperature(K):*** 120 ***Density(g/cm^3):*** 1.421



HIXXAO

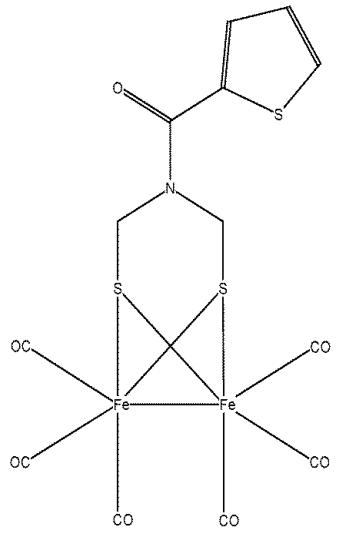
Reference: Li-Cheng Song, Liang-Xing Wang, Bang-Shao Yin, Yu-Long Li, Xiao-Guang Zhang, Yuan-Wei Zhang, Xiang Luo, Qing-Mei Hu (2008) *Eur.J.Inorg.Chem.* ,291

Formula: $C_{13}H_7Fe_2N_1O_7S_3$

Compound Name: (μ_2-2-(2-Thiophenecarbonyl)-2-azapropane-1,3-dithiolato-S,S,S',S')-hexacarbonyl-di-iron

Space Group:	P21/n	***Cell:***	***a*** 16.057(3)	***b*** 6.767(1)	***c*** 16.874(3)
Space Group No.:	14	***(Å,°)***	α 90.00	β 100.23(0)	γ 90.00

R-Factor (%): 3.50 ***Temperature(K):*** 294 ***Density(g/cm^3):*** 1.830



HUFMUR

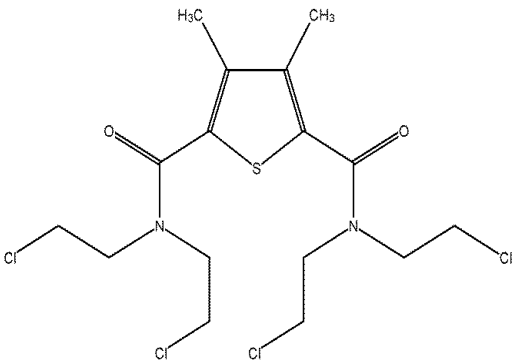
Reference: Yi-Dan Tang, Rong-Xia Geng, Cheng-He Zhou (2010) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**66**,o100

Formula: $C_{16}H_{22}Cl_4N_2O_2S_1$

Compound Name: N^2,N^2,N^5,N^5-tetrakis(2-Chloroethyl)-3,4-dimethylthiophene-2,5-dicarboxamide

Space Group:	P21/c	***Cell:***	***a*** 7.924(0)	***b*** 21.171(1)	***c*** 12.619(0)
Space Group No.:	14	***(Å,°)***	α 90.00	β 99.24(0)	γ 90.00

R-Factor (%): 4.23 ***Temperature(K):*** 298 ***Density(g/cm^3):*** 1.425



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 21-24

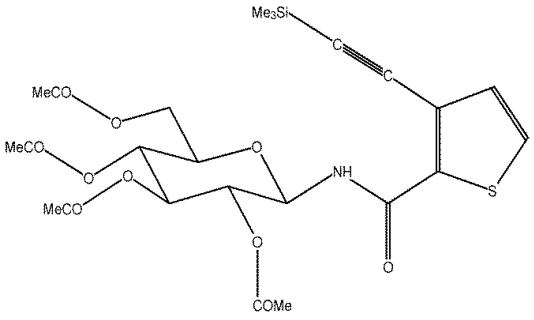
IDEQEO

Reference: S.L.Rawe, D.Doyle, V.Zaric, I.Rozas, K.McMahon, M.Tosin, H.M.Bunz, E.P.Murphy, K.M.O'Boyle, P.V.Murphy (2006) *Carbohydr.Res.* ,**341**,1370

Formula: $C_{24}H_{31}N_1O_{10}S_1Si_1$

Compound Name: N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(2-(trimethylsilyl) ethynyl)thiophene-2-(Z-anti)-carboxamide

Space Group:	P212121	***Cell:***	***a*** 8.606(7)	***b*** 11.163(9)	***c*** 30.420(20)
Space Group No.:	19	***(Å,°)***	α 90.00	β 90.00	γ 90.00
R-Factor (%):	4.47	***Temperature(K):***	100	***Density(g/cm³):***	1.258



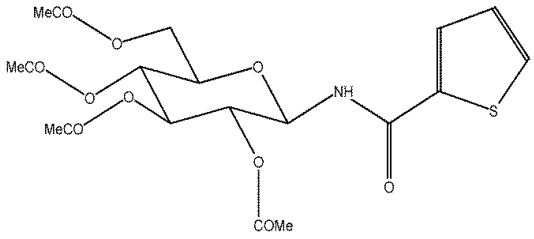
IDEQIS

Reference: S.L.Rawe, D.Doyle, V.Zaric, I.Rozas, K.McMahon, M.Tosin, H.M.Bunz, E.P.Murphy, K.M.O'Boyle, P.V.Murphy (2006) *Carbohydr.Res.* ,**341**,1370

Formula: $C_{19}H_{23}N_1O_{10}S_1$

Compound Name: N-(2,3,4,6-Tetra-O-acetyl-D-glucopyranosyl)thiophene-2-(Z-anti)-carboxamide

Space Group:	C2	***Cell:***	***a*** 16.221(1)	***b*** 14.087(1)	***c*** 11.170(1)
Space Group No.:	5	***(Å,°)***	α 90.00	β 124.95(0)	γ 90.00
R-Factor (%):	3.37	***Temperature(K):***	100	***Density(g/cm³):***	1.452



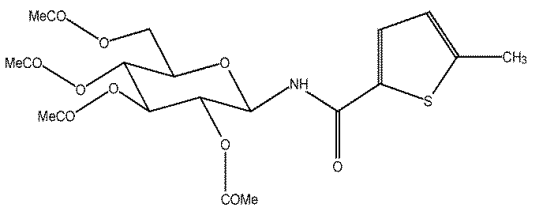
IDEQUE

Reference: S.L.Rawe, D.Doyle, V.Zaric, I.Rozas, K.McMahon, M.Tosin, H.M.Bunz, E.P.Murphy, K.M.O'Boyle, P.V.Murphy (2006) *Carbohydr.Res.* ,**341**,1370

Formula: $C_{20}H_{25}N_1O_{10}S_1$

Compound Name: N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-5-methylthiophene-2-(Z-anti)-carboxamide

Space Group:	C2	***Cell:***	***a*** 16.235(1)	***b*** 14.556(0)	***c*** 11.272(0)
Space Group No.:	5	***(Å,°)***	α 90.00	β 124.12(0)	γ 90.00
R-Factor (%):	2.88	***Temperature(K):***	100	***Density(g/cm³):***	1.420



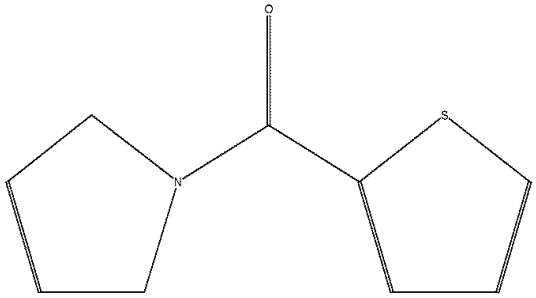
IWEMON

Reference: A.S.K.Hashmi, A.M.Schuster, S.Litters, F.Rominger, M.Pernpointner (2011) *Chem.-Eur.J.* ,**17**,5661

Formula: $C_9H_9N_1O_1S_1$

Compound Name: 2,5-Dihydro-1H-pyrrol-1-yl(2-thienyl)methanone

Space Group:	P21	***Cell:***	***a*** 5.827(0)	***b*** 5.242(0)	***c*** 13.818(1)
Space Group No.:	4	***(Å,°)***	α 90.00	β 91.75(0)	γ 90.00
R-Factor (%):	3.93	***Temperature(K):***	200	***Density(g/cm³):***	1.411



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 25-28

JALCIJ

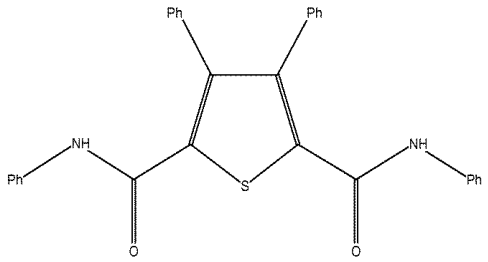
Reference: S.J.Coles, P.A.Gale, M.B.Hursthouse, M.E.Light, C.N.Warriner (2004) *Supramol.Chem.* ,**16**,469

Formula: $C_{30}H_{22}N_2O_2S_1$

Compound Name: 3,4-Diphenylthiophene-2,5-dicarboxylic acid diphenylamide

Space Group:	P-1	***Cell:***	***a***	9.476(0)	***b***	9.749(0)	***c***	26.135(0)
Space Group No.:	2	***(A,°)***	α	97.49(0)	β	90.72(0)	γ	92.98(0)

R-Factor (%): 4.14 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.319



JALDOQ

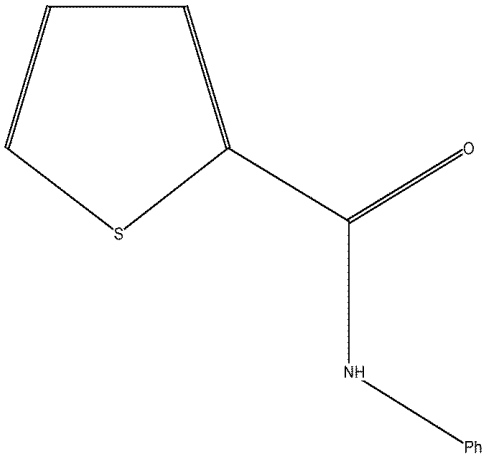
Reference: S.J.Coles, P.A.Gale, M.B.Hursthouse, M.E.Light, C.N.Warriner (2004) *Supramol.Chem.* ,**16**,469

Formula: $C_{11}H_9N_1O_1S_1$

Compound Name: Thiophene-2-carboxylic acid phenylamide

Space Group:	Pna21	***Cell:***	***a***	9.980(1)	***b***	16.761(1)	***c***	5.622(0)
Space Group No.:	33	***(A,°)***	α	90.00	β	90.00	γ	90.00

R-Factor (%): 4.30 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.435



KUSXAY

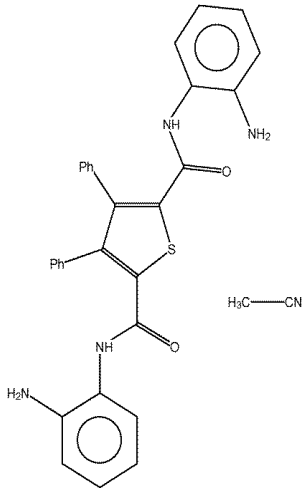
Reference: R.K.Askerov, V.V.Roznyatovsky, E.A.Katayev, A.M.Maharramov, V.N.Khrustalev (2010) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**66**,o793

Formula: $C_{30}H_{24}N_4O_2S_1,C_2H_3N_1$

Compound Name: N,N'-Bis(2-aminophenyl)-3,4-diphenylthiophene-2,5-dicarboxamide acetonitrile solvate

Space Group:	P-1	***Cell:***	***a***	9.031(0)	***b***	11.547(1)	***c***	13.014(1)
Space Group No.:	2	***(A,°)***	α	93.21(0)	β	92.50(0)	γ	90.02(0)

R-Factor (%): 4.79 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.339



KUYYUZ

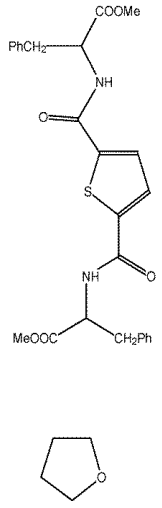
Reference: GuangMing Xia, Jing Liu, Zhen Li, MuWei Ji, GuoXin Sun (2010) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**66**,o2489

Formula: $C_{26}H_{26}N_2O_6S_1,C_4H_8O_1$

Compound Name: Dimethyl 3,3'-diphenyl-2,2'-[(S)-thiophene-2,5-diylbis(carbonylazanediyl)]dipropanoate tetrahydrofuran solvate

Space Group:	P212121	***Cell:***	***a***	8.304(0)	***b***	12.181(0)	***c***	29.679(1)
Space Group No.:	19	***(A,°)***	α	90.00	β	90.00	γ	90.00

R-Factor (%): 4.66 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.254



Search: search3 (Tue Feb 18 09:21:02 2014): Hits 29-32

LIKGUH

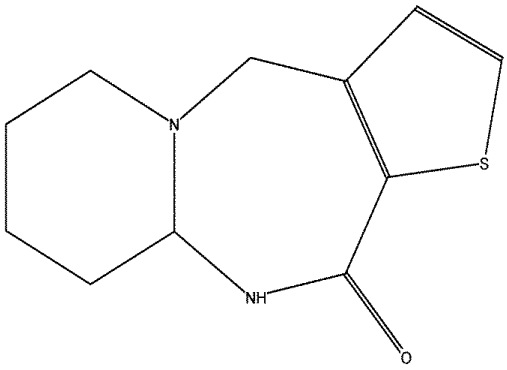
Reference: J.Kozisek, L.Ulicky, S.Marchalin, Z.Zak, B.Decroix (1995) *Acta Crystallogr.,Sect.C:Cryst.Struct.Commun.* ,**51**,151

Formula: $C_{11}H_{14}N_2O_1S_1$

Compound Name: 4,6,7,8,9,9a-Hexahydro-11H-pyrido(1,2-a)thieno(2,3-e)(1,3)diazepin-11(10H)-one

Space Group:	P21/n	***Cell:***	***a***	9.028(7)	***b***	5.256(2)	***c***	23.022(16)
Space Group No.:	14	***(A,°)***	α	90.00	β	92.78(6)	γ	90.00

R-Factor (%): 4.77 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.353



LOQSAL

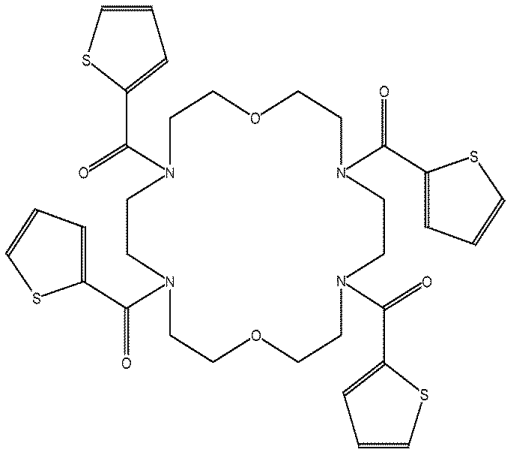
Reference: Xinhao Yang, D.C.Craig, N.Kumar, D.B.Hibbert (1999) *J.Inclusion Phenom.Macrocyclic Chem.* ,**33**,135

Formula: $C_{32}H_{36}N_4O_6S_4$

Compound Name: 4,7,13,16-Tetrakis(thienoyl)-1,10-dioxa-4,7,13,16-tetraazacyclooctadecane

Space Group:	P21/c	***Cell:***	***a***	10.315(4)	***b***	13.635(2)	***c***	14.357(6)
Space Group No.:	14	***(A,°)***	α	90.00	β	124.63(2)	γ	90.00

R-Factor (%): 5.40 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.401



MACQUE

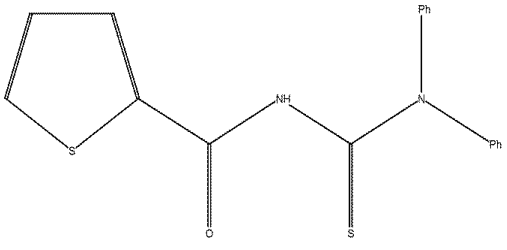
Reference: S.Saeed, N.Rashid, M.Ali, R.Hussain, P.Jones (2010) *Eur.J.Chem.* ,**1**,221

Formula: $C_{18}H_{14}N_2O_1S_2$

Compound Name: N-(Diphenylcarbamothioyl)thiophene-2-carboxamide

Space Group:	P21	***Cell:***	***a***	11.747(0)	***b***	6.085(0)	***c***	12.579(0)
Space Group No.:	4	***(A,°)***	α	90.00	β	117.74(0)	γ	90.00

R-Factor (%): 2.91 ***Temperature(K):*** 103 ***Density(g/cm^3):*** 1.412



NUQPEV

Reference: S.Saeed, N.Rashid, W.-T.Wong (2010) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**66**,o1162

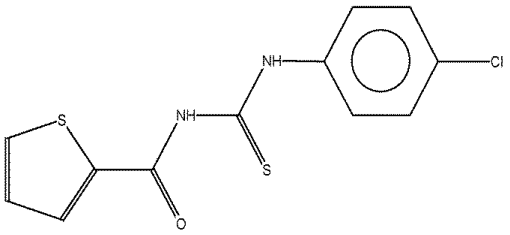
Formula: $C_{12}H_9Cl_1N_2O_1S_2$

Compound Name: N-((4-Chlorophenyl)carbamothioyl)thiophene-2-carboxamide

Synonym: 1-(4-Chlorophenyl)-3-(2-thienylcarbonyl)thiourea

Space Group:	P21/n	***Cell:***	***a***	4.655(0)	***b***	11.660(2)	***c***	23.630(4)
Space Group No.:	14	***(A,°)***	α	90.00	β	95.63(0)	γ	90.00

R-Factor (%): 3.84 ***Temperature(K):*** 300 ***Density(g/cm^3):*** 1.544



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OPAVAD

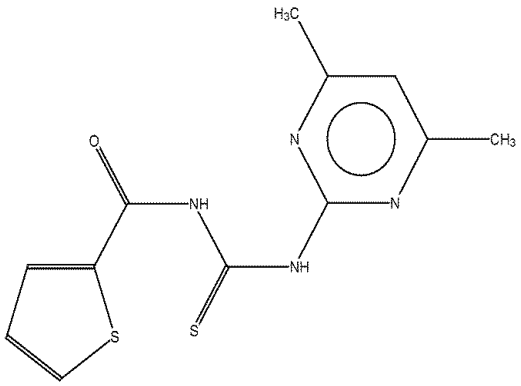
Reference: S.Saeed, N.Rashid, P.G.Jones, A.Tahir (2011) *J.Heterocycl.Chem.* ,**48**,74

Formula: $C_{12}H_{12}N_4O_1S_2$

Compound Name: N-((4,6-Dimethylpyrimidin-2-yl)carbamothioyl)thiophene-2-carboxamide

Space Group:	P21/c	***Cell:***	***a*** 9.694(0)	***b*** 6.918(0)	***c*** 19.837(0)
Space Group No.:	14	***(Å,°)***	α 90.00	β 95.21(0)	γ 90.00

R-Factor (%): 2.68 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.466



PAWJAA

Reference: D.P.Singh, S.Pratap, R.J.Butcher, S.K.Gupta (2012) *Acta Crystallogr.,Sect.E:Struct.Rep.Online* ,**68**,o1765

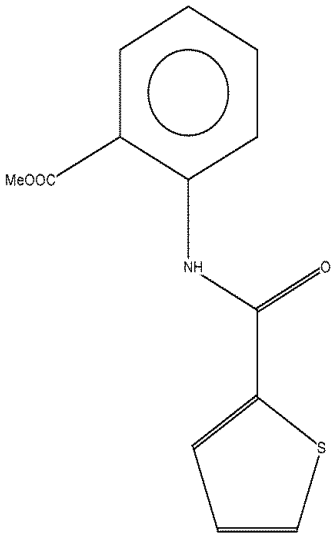
Formula: $C_{13}H_{11}N_1O_3S_1$

Compound Name: Methyl 2-((2-thienylcarbonyl)amino)benzoate

Synonym: Methyl 2-(thiophene-2-carboxamido)benzoate

Space Group:	Pca21	***Cell:***	***a*** 19.285(0)	***b*** 3.868(0)	***c*** 15.643(0)
Space Group No.:	29	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.32 ***Temperature(K):*** 123 ***Density(g/cm³):*** 1.488



QOBKAU

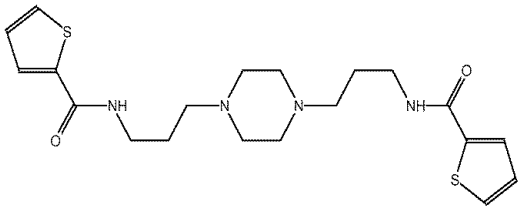
Reference: A.Balaban, N.Colak, H.Unver, B.Erk, T.N.Durlu, D.M.Zengin (2008) *J.Chem.Cryst.* ,**38**,369

Formula: $C_{20}H_{28}N_4O_2S_2$

Compound Name: N,N'-bis(3-(thiophene-2-carboxamido)propyl)piperazine

Space Group:	P21/c	***Cell:***	***a*** 9.768(0)	***b*** 12.895(1)	***c*** 10.083(1)
Space Group No.:	14	***(Å,°)***	α 90.00	β 115.12(1)	γ 90.00

R-Factor (%): 3.88 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.215



QOTVOL

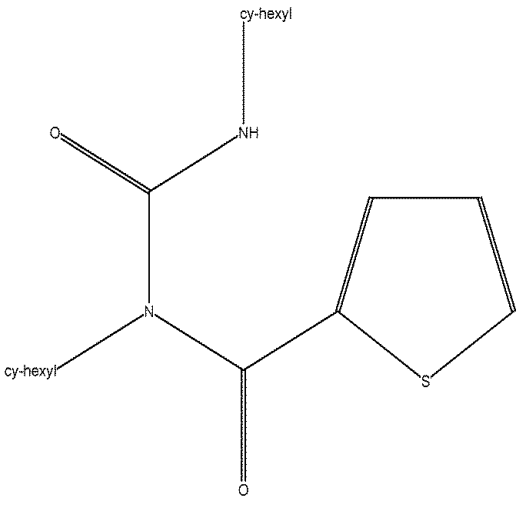
Reference: Xiao-Qing Cai, Xiao-Wei Yan, Xiao-Nuan Xie (2009) *Z.Kristallogr.-New Cryst.Struct.* ,**224**,211

Formula: $C_{18}H_{26}N_2O_2S_1$

Compound Name: 1,3-Dicyclohexyl-1-(thiophene-2-carbonyl)-urea

Space Group:	Pna21	***Cell:***	***a*** 11.779(2)	***b*** 16.454(3)	***c*** 9.601(1)
Space Group No.:	33	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 7.16 ***Temperature(K):*** 298 ***Density(g/cm³):*** 1.194



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REJJOF

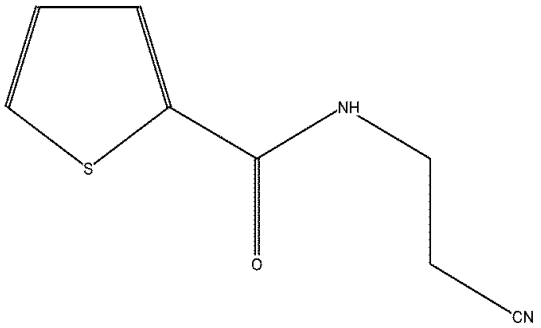
Reference: R.S.Kusurkar, M.S.Wadia, D.K.Bhosale, S.S.Tavale, V.G.Puranik (1996) *J.Chem.Res.* ,**478**,2701

Formula: $C_8 H_8 N_2 O_1 S_1$

Compound Name: 2-(N-(2-Cyanoethyl)carbamoyl)thiophene

Space Group:	P21nb	***Cell:***	***a*** 5.149(1)	***b*** 9.825(4)	***c*** 17.822(4)
Space Group No.:	33	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 4.47 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.328



SUWQOR

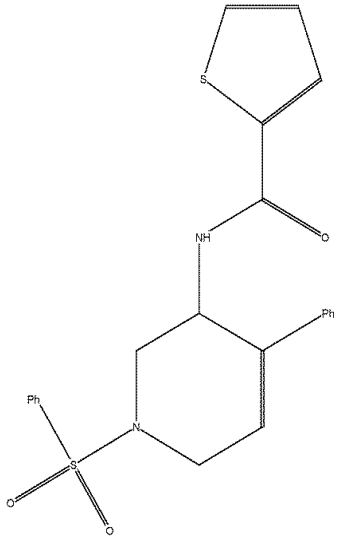
Reference: Meng-Yang Chang, Chung-Han Lin, Yeh-Long Chen, Ru-Ting Hsu, Ching-Yao Chang (2010) *Tetrahedron Lett.* ,**51**,4886

Formula: $C_{22} H_{20} N_2 O_3 S_2$

Compound Name: N-(4-Phenyl-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridin-3-yl)thiophene-2-carboxamide

Space Group:	Pna21	***Cell:***	***a*** 23.956(1)	***b*** 14.617(0)	***c*** 5.789(0)
Space Group No.:	33	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.72 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 1.391



TUKPOF

Reference: J.N.Low, A.Quesada, L.M.N.B.F.Santos, B.Schroder, L.R.Gomes (2009) *J.Chem.Cryst.* ,**39**,747

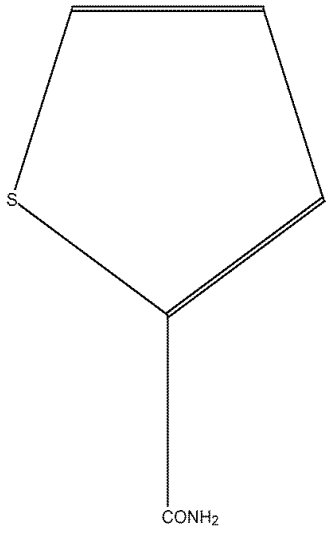
Formula: $C_5 H_5 N_1 O_1 S_1$

Compound Name: Thiophene-2-carboxamide

Synonym: 2-thiophenecarboxamide

Space Group:	Pna21	***Cell:***	***a*** 10.044(3)	***b*** 14.203(4)	***c*** 15.941(3)
Space Group No.:	33	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 4.48 ***Temperature(K):*** 120 ***Density(g/cm^3):*** 1.486



UFUSOE

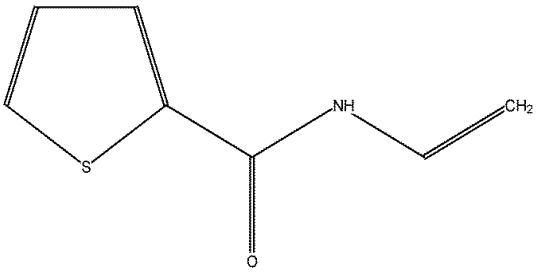
Reference: P.Arsenyan, A.Petrenko, S.Belyakov (2008) *Tetrahedron Lett.* ,**49**,5255

Formula: $C_7 H_7 N_1 O_1 S_1$

Compound Name: N-Vinyl-2-thiophenecarboxamide

Space Group:	Pbca	***Cell:***	***a*** 9.924(0)	***b*** 12.123(0)	***c*** 12.706(0)
Space Group No.:	61	***(Å,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 5.80 ***Temperature(K):*** 293 ***Density(g/cm^3):*** 1.331



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UFUSUK

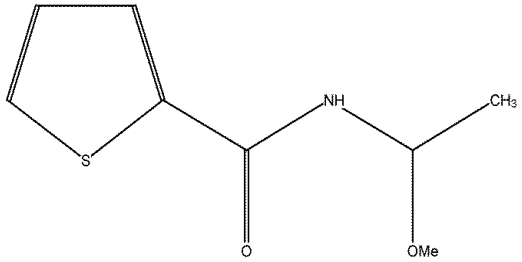
Reference: P.Arsenyan, A.Petrenko, S.Belyakov (2008) *Tetrahedron Lett.* ,**49**,5255

Formula: $C_8 H_{11} N_1 O_2 S_1$

Compound Name: N-(1-Methoxyethyl)-2-thiophenecarboxamide

Space Group:	Pc21b	***Cell:***	***a*** 8.367(0)	***b*** 9.552(0)	***c*** 11.817(0)
Space Group No.:	29	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 6.77 ***Temperature(K):*** 293 ***Density(g/cm^3):*** 1.303



UMEZUI

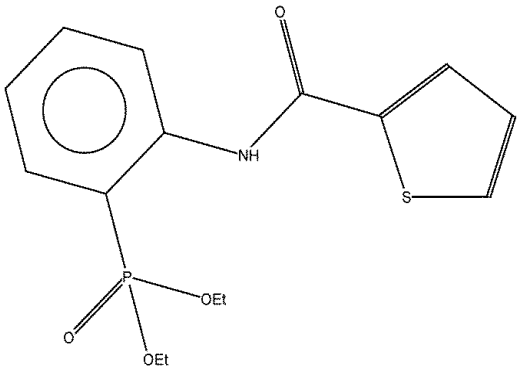
Reference: B.R.Aluri, B.Niaz, M.K.Kindermann, P.G.Jones, J.Heinicke (2011) *Dalton Trans.* ,**40**,211

Formula: $C_{15} H_{18} N_1 O_4 P_1 S_1$

Compound Name: Diethyl (2-((2-thienylcarbonyl)amino)phenyl)phosphonate

Space Group:	P21/n	***Cell:***	***a*** 10.432(2)	***b*** 13.442(2)	***c*** 12.006(2)
Space Group No.:	14	***(A,°)***	α 90.00	β 107.82(0)	γ 90.00

R-Factor (%): 3.91 ***Temperature(K):*** 133 ***Density(g/cm^3):*** 1.406



VAWPEQ

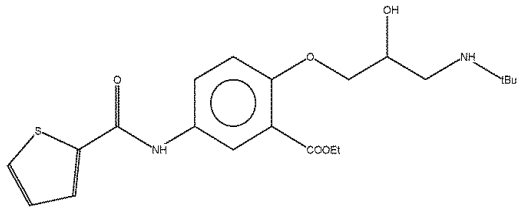
Reference: N.Mahe, B.Do, B.Nicolai, I.B.Rietveld, M.Barrio, J.-L.Tamarit, R.Ceolin, C.Guechot, J.-M.Teulon (2012) *Int.J.Pharm.* , **422**,47

Formula: $C_{21} H_{28} N_2 O_5 S_1$

Compound Name: Ethyl 2-(3-(t-butylamino)-2-hydroxypropoxy)-5-((2-thienylcarbonyl)amino) benzoate

Space Group:	Iba2	***Cell:***	***a*** 10.069(5)	***b*** 45.831(10)	***c*** 9.822(5)
Space Group No.:	45	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 7.50 ***Temperature(K):*** 298 ***Density(g/cm^3):*** 1.232



VORWII

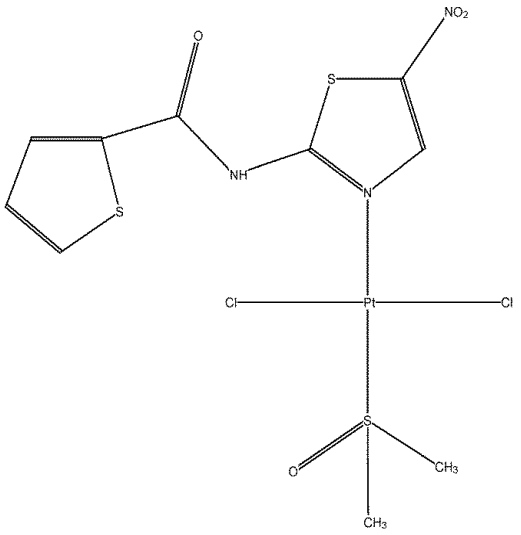
Reference: B.Viossat, N.H.Dung, J.-C.Lancelot, M.Robba (1991) *Chem.Pharm.Bull.* ,**39**,3023

Formula: $C_{10} H_{11} Cl_2 N_3 O_4 Pt_1 S_3$

Compound Name: Dichloro-(dimethylsulfoxide-S)-(tenonitrozolato-N)-platinum(ii)

Space Group:	Pna21	***Cell:***	***a*** 10.120(1)	***b*** 22.660(1)	***c*** 7.631(0)
Space Group No.:	33	***(A,°)***	α 90.00	β 90.00	γ 90.00

R-Factor (%): 3.40 ***Temperature(K):*** 295 ***Density(g/cm^3):*** 2.275



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WIZVOQ

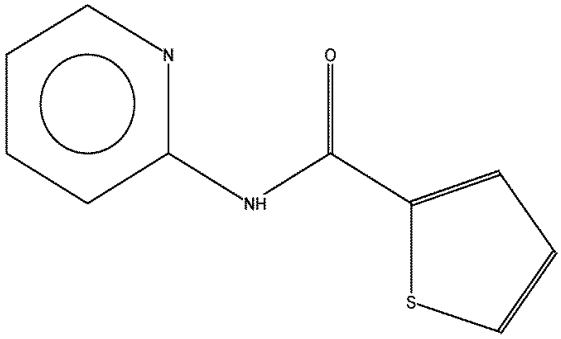
Reference: G.D.Fallon, M.Percy, T.D.Smith (2000) *Private Communication* ,

Formula: $C_{10}H_8N_2O_1S_1$

Compound Name: 2-(2-Pyridylaminocarbonyl)thiophene

Space Group:	P21/n	***Cell:***	***a*** 5.391(0)	***b*** 12.512(0)	***c*** 13.555(0)
Space Group No.:	14	***(A,°)***	α 90.00	β 100.34(0)	γ 90.00

R-Factor (%): 4.10 ***Temperature(K):*** 123 ***Density(g/cm^3):*** 1.508



WUCYAU

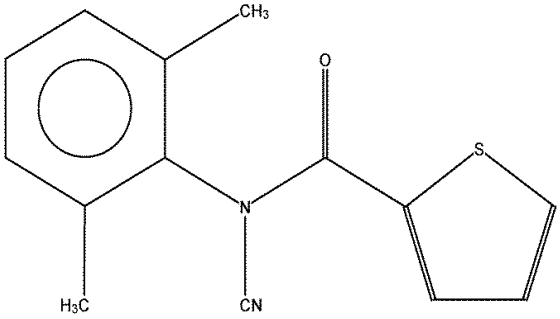
Reference: Yong-Joo Kim, Young-Seon Joo, Jin-Taek Han, Won Seok Han, Soon W.Lee (2002) *J.Chem.Soc.,Dalton Trans.* ,3611

Formula: $C_{14}H_{12}N_2O_1S_1$

Compound Name: N-(2,6-Dimethylphenyl)-N-(2-thienoyl)cyanamide

Space Group:	Pc	***Cell:***	***a*** 8.085(1)	***b*** 11.637(2)	***c*** 14.389(3)
Space Group No.:	7	***(A,°)***	α 90.00	β 105.83(1)	γ 90.00

R-Factor (%): 8.24 ***Temperature(K):*** 293 ***Density(g/cm^3):*** 1.307



WUFXUR

Reference: L.R.Gomes, J.N.Low, A.Quesada, L.M.N.B.F.Santos, M.A.A.Rocha, B.Schroder (2009) *J.Mol.Struct.* ,**936**,37

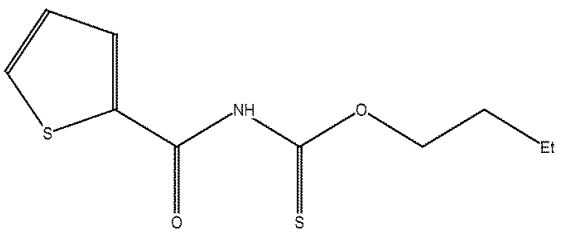
Formula: $C_{10}H_{13}N_1O_2S_2$

Compound Name: O-Butyl (2-thienylcarbonyl)carbamothioate

Synonym: N-Thenoylthiocarbamic O-n-butyl ester

Space Group:	P21/n	***Cell:***	***a*** 8.352(2)	***b*** 16.856(5)	***c*** 9.211(1)
Space Group No.:	14	***(A,°)***	α 90.00	β 115.45(1)	γ 90.00

R-Factor (%): 5.42 ***Temperature(K):*** 120 ***Density(g/cm^3):*** 1.380



WUFYAY

Reference: L.R.Gomes, J.N.Low, A.Quesada, L.M.N.B.F.Santos, M.A.A.Rocha, B.Schroder (2009) *J.Mol.Struct.* ,**936**,37

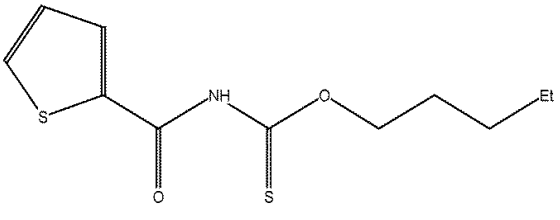
Formula: $C_{11}H_{15}N_1O_2S_2$

Compound Name: O-Pentyl (2-thienylcarbonyl)carbamothioate

Synonym: N-Theonylthiocarbamic O-n-pentyl ester

Space Group:	P21/n	***Cell:***	***a*** 8.596(1)	***b*** 17.009(2)	***c*** 9.146(1)
Space Group No.:	14	***(A,°)***	α 90.00	β 112.98(0)	γ 90.00

R-Factor (%): 5.48 ***Temperature(K):*** 120 ***Density(g/cm^3):*** 1.389



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WUFYEC

Reference: L.R.Gomes, J.N.Low, A.Quesada, L.M.N.B.F.Santos, M.A.A.Rocha, B.Schroder (2009) *J.Mol.Struct.* ,**936**,37

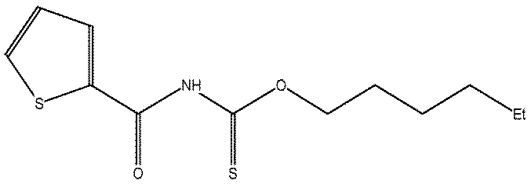
Formula: $C_{12}H_{17}N_1O_2S_2$

Compound Name: N-Theonylthiocarbamic O-n-hexyl ester

Synonym: O-Hexyl (2-thienylcarbonyl)carbamothioate

Space Group:	P21/c	***Cell:***	***a***	8.863(0)	***b***	16.853(0)	***c***	9.555(0)
Space Group No.:	14	***(A,°)***	α	90.00	β	102.52(0)	γ	90.00

R-Factor (%): 4.16 ***Temperature(K):*** 120 ***Density(g/cm³):*** 1.294



WUQFAQ

Reference: T.Kobayashi, S.Sasaki, N.Tomita, S.Fukui, N.Kuroda, M.Nakayama, A.Kiba, Y.Takatsu, T.Ohtaki, F.Itoh, A.Baba (2010) *Bioorg.Med.Chem.* ,**18**,3841

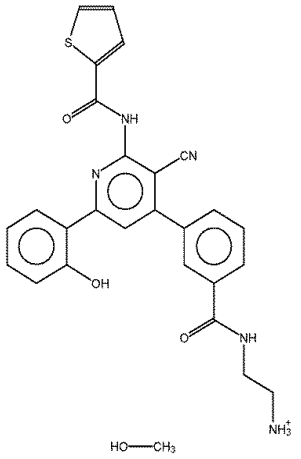
Formula: $C_{26}H_{22}N_5O_3S_1^{1+}.2(C_1H_4O_1).Cl_1^{1-}$

Compound Name: 2-((3-(3-Cyano-6-(2-hydroxyphenyl)-2-((2-thienylcarbonyl)amino)pyridin-4-yl)benzoyl)amino)ethanaminium chloride methanol solvate

Synonym: N-[4-(3-[(2-Aminoethyl)carbamoyl]phenyl)-3-cyano-6-(2-hydroxyphenyl) pyridin-2-yl]thiophene-2-carboxamide hydrochloride methanol solvate

Space Group:	P21/n	***Cell:***	***a***	7.170(3)	***b***	25.267(9)	***c***	15.745(5)
Space Group No.:	14	***(A,°)***	α	90.00	β	93.54(3)	γ	90.00

R-Factor (%): 10.79 ***Temperature(K):*** 100 ***Density(g/cm³):*** 1.363



XOBZUJ

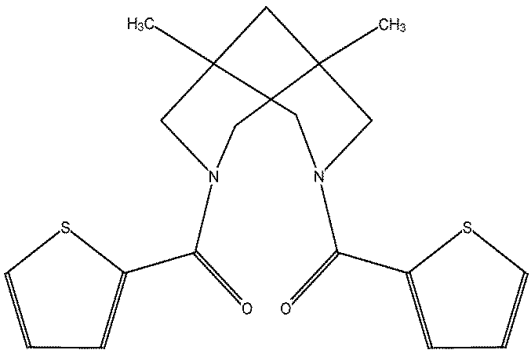
Reference: V.A.Palyulin, S.V.Emets, K.A.Potekhin, A.E.Lysov, Yu.G.Sumskaya, N.S.Zefirov (2001) *Dokl.Akad.Nauk SSSR(Russ.)(Proc.Nat.Acad.Sci.USSR)* ,**380**,639

Formula: $C_{19}H_{22}N_2O_2S_2$

Compound Name: 3,7-bis(2-Thienylcarbonyl)-1,5-dimethyl-3,7-diazabicyclo(3.3.1)nonane

Space Group:	P-1	***Cell:***	***a***	9.921(6)	***b***	14.086(5)	***c***	14.672(6)
Space Group No.:	2	***(A,°)***	α	74.57(3)	β	76.13(3)	γ	69.42(3)

R-Factor (%): 8.60 ***Temperature(K):*** 293 ***Density(g/cm³):*** 1.362



Isolation of Human Monocyte-derived Macrophages (HMDM)

To obtain human monocyte-derived macrophages (HMDM), peripheral blood mononuclear cells (PBMCs) were first isolated by Ficoll-paque density centrifugation (GE healthcare Bio-Science, Uppsala, Sweden) from buffy coat of anonymous human donors provided by Australian Red Cross Blood Service, Brisbane. $CD14^+$ monocytes were positively selected using $CD14^+$ MACS magnetic beads (Miltenyi Biotech, Auburn, CA, USA) after successive magnetic sorting and washings. The $CD14^+$ monocytes were then cultured at 37 °C, with 5% CO_2 and differentiated to HMDM in complete media containing 10^4 U/mL (100ng/mL) recombinant human macrophage colony stimulating factor (M-CSF) (PeptroTech Inc, Rocky Hill, New Jersey, USA) at 1.5 $x10^6$ monocytes/mL. HMDM were kept in a complete media, consisting of IMDM with 10% FBS, 10 U/mL penicillin, 10 U/mL streptomycin and 2 mM L-glutamine (Invitrogen). HMDM were supplemented after 5 days with fresh medium containing 10^2 U/mL M-CSF. Cells were harvested by gentle scraping in saline solution on day 7.

Intracellular Calcium Release Assay

Harvested HMDM were washed with 0.9% NaCl solution by centrifugation at 2500 rpm for 5 min, followed by resuspension of the cell pellet with complete media. Cells were plated at 5 x 10^4 cells/well in a 96-well cleared-bottomed black-walled assay plate (Corning) with equal amounts of medium added and incubated overnight at 37 ^oC. Before assay, the medium was removed and cells were incubated with dye-loading buffer (12 mL assay buffer, 4 μM Fluo-3 AM, 25 μL Pluronic acid F-127 and 1% fetal bovine serum) for an hour at 37 ^oC. After an hour, cells were washed once with assay buffer (HBSS supplemented with 2.5 mM probenecid and 20 mM HEPES, pH 7.4). Compounds were dissolved in DMSO to make a 10 mM stock solution, then further diluted with HBSS buffer to the desired concentrations for intracellular calicum release assay. The final concentration of DMSO was less than 2% in the assay. For antagonist assay, the cells were pre-incubated with desired concentrations of the synthesised compounds for 15 min before the addition of agonist (human C3a protein, 100 nM).[4] FLIPR was used to monitor the intracellular release of Ca^{2+} via fluorescence measurement for 5 min (excitation 495 nm, emission 520 nm). The agonist assay was conducted in a similar manner, except that the intracellular Ca^{2+} release was monitored immediately for 5 min after the injection of the desired concentration of the synthesised compounds. Duplicate measurements were made for each data point, mean ± SEM are reported from experiments as indicated. Net changes in fluorescence were calculated as a percentage relative to the maximum response given by the test compound. Changes in fluorescence (% response) were plotted against logarithmic compound concentrations. The half maximal effective concentration (EC_{50}) and inhibitory concentration (IC_{50}) values were derived from the concentration response curve using nonlinear regression curve fitting in GraphPad Prism v6.

References

[1] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923-2925.

[2] L. Dreier, G. Wider, *Magn. Reson. Chem.* **2006**, *44*, S206-S212.

[3] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox Gaussian Inc., Wallingford CT, **2009**.