Electronic Supplementary Information (ESI)

Enantioselective Synthesis of Vicinal Diamines and β-Amino Amides by NiH-Catalyzed Hydroamidation of Alkenyl Amides

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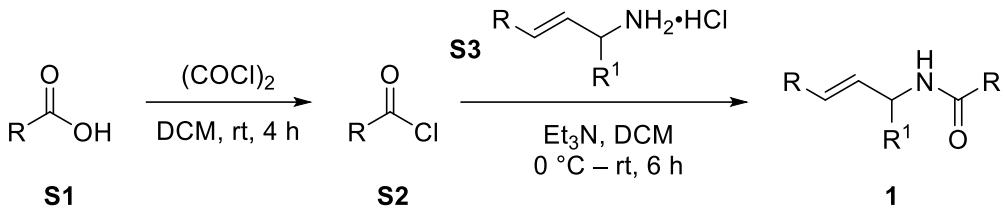
General information

All air- and moisture-sensitive solutions and chemicals were handled under a nitrogen atmosphere of a glovebox and solutions were transferred via "Titan" brand pipettor. Anhydrous solvents, including THF (Tetrahydrofuran), 1,4-Dioxane, 2-Me-THF, DMA (*N*,*N*-Dimethylacetamide), MeCN (Acetonitrile), DCE (1,2-Dichloroethane), MTBE (*tert*-Butyl methyl ether), CPME (Cyclopentyl methyl ether), and DME (1,2-Dimethoxyethane) were purchased from Sigma-Aldrich and used without further purification. Unless otherwise stated, all reagents were commercially available and used as received without further purification. Nickel Catalyst was purchased from Sigma-Aldrich and used as received. Chiral ligands were purchased from Bidepharm. Other chemicals were obtained from Sigma-Aldrich, Acros, TCI, Adamas and Alfa-Aesar. TLC was performed with Merck TLC Silica gel60 F_{254} plates with detection under UV light at 254 nm. Silica gel (200-300 mesh, Qingdao) was used for flash chromatography. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were obtained using a Brüker DRX 400/600 spectrometer at 400/600 MHz and 100/150 MHz, respectively. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. X-Ray crystal diffraction data were recorded on Brüker D8 VENTURE. High resolution mass spectra were taken on an AB QSTAR Pulsar mass spectrometer. Melting points were obtained on an XT-4 melting-point apparatus and were uncorrected. The enantiomeric excess was determined by chiral HPLC with *n*-hexane and *i*-propanol as eluents. Optical rotations were measured on a *JASCO* DIP-370 polarimeter.

Preparation and characterization of *N*-allyl-amides

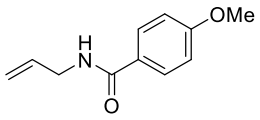


The reaction was performed following the literature procedures.[1]

Step 1: In a dried 100 ml round-bottom flask equipped with a magnetic stir bar, the corresponding acid **S1** (11 mmol, 1.1 equiv) was dissolved in 50ml anhydrous DCM. Then, 10 drops of anhydrous DMF were added. Under ice-bath conditions, oxalyl chloride (15 mmol, 1.5 equiv) was slowly added dropwise. After the completion of the addition, the reaction mixture was allowed to react at room temperature for 4 hours. After 4 hours, the crude product was separated from the solvent under vacuum. The obtained product **S2** was directly used for the next step reaction.

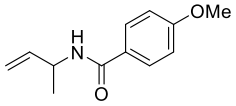
Step 2: In a dried 100 ml round-bottom flask equipped with a magnetic stir bar, the corresponding allylamine **S3** (10 mmol, 1.0 equiv) hydrochloride was dissolved in 50ml anhydrous DCM. Et_3N (35 mmol, 3.5 equiv) was added and stirred for 5 minutes. After 5 minutes, under ice-bath conditions, the crude product **S2** (if it was a solid, dissolved in a small amount of anhydrous DCM before adding) was slowly added dropwise to the mixture. After the completion of the addition, the reaction was allowed to proceed at room temperature for 6 hours, monitored by TLC. The reaction was quenched by slowly adding saturated $NaHCO_3$ solution and the organic phase was extracted. The aqueous phase was extracted with DCM (20 ml×3), and the organic phases were combined. The combined organic phase was collected and dried over Na_2SO_4. The extract was filtered, concentrated, and purified by silica gel column chromatography (eluent:petroleum ether:ethyl acetate = 4:1 to 3:1) to give *N*-allyl-amides (**1**).

N-Allyl-4-methoxybenzamide (1a)



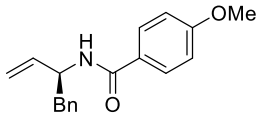
1a was prepared from allylamine hydrochloride and *p*-methoxybenzoic acid in 1.75 g, 92% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data.[1]

N-(But-3-en-2-yl)-4-methoxybenzamide (1b)



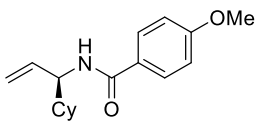
1b was prepared from but-3-en-2-amine hydrochloride and *p*-methoxybenzoic acid in 1.84 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). **Mp:** 144 – 146 °C**.** $\mathbf{R}_f$ = 0.25 (petroleum ether : ethyl acetate = 4 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.82 – 7.64 (m, 2H), 7.00 – 6.84 (m, 2H), 6.03 (d, *J* = 8.4 Hz, 1H), 5.99 – 5.82 (m, 1H), 5.29 – 4.98 (m, 2H), 4.76 (m, 1H), 3.83 (s, 3H), 1.33 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 166.3, 162.2, 139.8, 128.8, 127.1, 114.3, 113.8, 55.5, 47.2, 20.4 ppm. **HRMS** calc'd for $C_{12}H_{16}NO_2^+$ 206.1176, found 206.1179 $[M+H]^+$.

(*S*)-4-Methoxy-*N*-(1-phenylbut-3-en-2-yl)benzamide (1c)



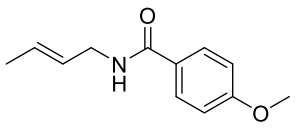
1c was prepared from (*S*)-1-phenylbut-3-en-2-amine hydrochloride and *p*-methoxybenzoic acid in 2.55 g, 91% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). **Mp:** 151 – 153 °C**.** $\mathbf{R}_f$ = 0.23 (petroleum ether : ethyl acetate = 4 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.72 – 7.56 (m, 2H), 7.36 – 7.27 (m, 2H), 7.26 – 7.18 (m, 3H), 6.94 – 6.84 (m, 2H), 5.99 – 5.87 (m, 2H), 5.21 – 5.09 (m, 2H), 5.03 – 4.89 (m, 1H), 3.84 (s, 3H), 2.99 (d, *J* = 6.4 Hz, 2H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 166.4, 162.3, 137.7, 137.3, 129.7, 128.8, 128.6, 127.0, 126.8, 115.5, 113.9, 55.6, 52.3, 41.1 ppm. **HRMS** calc'd for $C_{18}H_{20}NO_2^+$ 282.1489, found 282.1492 $[M+H]^+$; $\mathbf{[\alpha]_D^{20}}$ = -35.11 (*c* 1.0, MeOH).

(*S*)-*N*-(1-Cyclohexylallyl)-4-methoxybenzamide (1d)



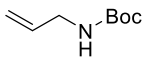
1d was prepared from (*S*)-1-cyclohexylprop-2-en-1-amine hydrochloride and *p*-methoxybenzoic acid in 2.45 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). **Mp:** 155 – 157 °C. $\mathbf{R}_f$ = 0.22 (petroleum ether : ethyl acetate = 4 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.86 – 7.62 (m, 2H), 6.96 – 6.82 (m, 2H), 6.03 (d, *J* = 8.8 Hz, 1H), 5.83 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.28 – 5.06 (m, 2H), 4.68 – 4.41 (m, 1H), 3.84 (s, 3H), 1.76 (m, *J* = 12.0, 9.2, 6.4 Hz, 4H), 1.70 – 1.59 (m, 1H), 1.54 (m, 1H), 1.27 – 0.99 (m, 5H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 166. 5, 162.2, 137.2, 128.8, 127.3, 115.8, 113.9, 56.5, 55.5, 42.4, 29.6, 29.0, 26.5, 26.3, 26.2 ppm. **HRMS** calc'd for $C_{17}H_{24}NO_2^+$ 274.1802, found 274.1807 $[M+H]^+$; $\mathbf{[\alpha]_D^{20}}$ = 24.59 (*c* 1.0, MeOH).

(*E*)-*N*-(But-2-en-1-yl)-4-methoxybenzamide (1e)



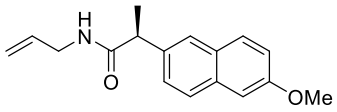
1e was prepared from (*E*)-but-2-en-1-amine hydrochloride and *p*-methoxybenzoic acid in 1.94 g, 95% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[2]

***tert*-Butyl allylcarbamate (1f)**



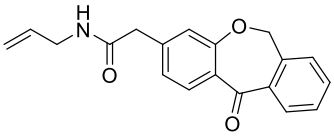
1f was prepared from allylamine hydrochloride and di-*tert*-butyl dicarbonate in 1.54 g, 98% yield as a Colorless oil. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). Synthetic method and the ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[3]

(*S*)-*N*-Allyl-2-(6-methoxynaphthalen-2-yl)propanamide (1g)



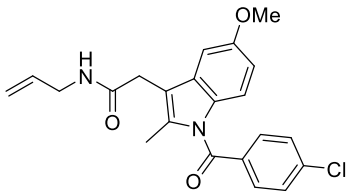
1g was prepared from allylamine hydrochloride and *(S)*-Naproxen in 2.50 g, 93% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[4]

***N*-Allyl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-3-yl)acetamide (1h)**



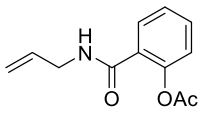
1h was prepared from allylamine hydrochloride and Isoxepac in 2.76 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). **Mp:** 182 – 184 °C. $\mathbf{R_f}$ = 0.20 (petroleum ether : ethyl acetate = 4 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.57 (td, *J* = 7.2, 1.2 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.42 – 7.34 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.97 – 5.69 (m, 1H), 5.53 (s, 1H), 5.20 (s, 2H), 5.11 (dq, *J* = 6.0, 1.6 Hz, 1H), 5.07 (t, *J* = 1.6 Hz, 1H), 3.86 (m, 2H), 3.59 (s, 2H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 191.0, 170.5, 160.8, 140.5, 136.6, 135.6, 134.1, 133.1, 132.6, 129.6, 129.5, 128.8, 128.0, 125.5, 121.8, 116.6, 73.8, 42.9, 42.2 ppm. **HRMS** calc'd for $C_{19}H_{18}NO_3^+$ 308.1281, found 308.1280 $[M+H]^+$.

***N*-Allyl-2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamide (1i)**



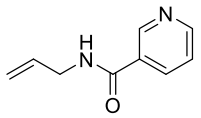
1i was prepared from allylamine hydrochloride and Indometacin in 3.48 g, 88% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 3 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[4]

2-(Allylcarbamoyl)phenyl acetate (1j)



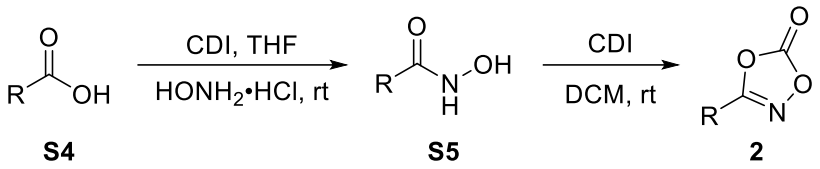
1j was prepared from allylamine hydrochloride and Aspirin in 1.97 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 3 : 1). **Mp**: 61 – 63 °C. $\mathbf{R_f}$ = 0.28 (petroleum ether : ethyl acetate = 3 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.57 (td, *J* = 7.2, 1.2 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.42 – 7.34 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.97 – 5.69 (m, 1H), 5.53 (s, 1H), 5.20 (s, 2H), 5.11 (dq, *J* = 6.0, 1.6 Hz, 1H), 5.07 (t, *J* = 1.6 Hz, 1H), 3.86 (m, 2H), 3.59 (s, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 191.0, 170.5, 160.8, 140.5, 136.6, 135.6, 134.1, 133.1, 132.6, 129.6, 129.5, 128.8, 128.0, 125.5, 121.8, 116.6, 73.8, 42.9, 42.2. **HRMS** calc'd for $C_{12}H_{14}NO_3^+$ 220.0968, found 220.0966 $[M+H]^+$.

***N*-Allylnicotinamide (1k)**



1k was prepared from allylamine hydrochloride and nicotinic acid in 1.39 g, 86% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[5]

Preparation of 1,4,2-dioxazol-5-ones

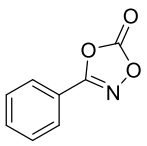


The reaction was performed following the literature procedures.[6]

Step 1: To a solution of corresponding carboxylic acid **S4** (10 mmol) in 40 ml anhydrous THF was added 1,1′-carbon-yldiimidazole (CDI, 15 mmol, 1.5 equiv). The reaction mixture was stirred for 1 h before hydroxylamine hydrochloride (20 mmol, 2.0 equiv) was added. The resulting mixture was stirred overnight. The mixture was diluted with 5% aq $KHSO_4$ (20 mL) and extracted with ethyl acetate. The combined organic phase was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. The extract was filtered and concentrated to give the residue **S5** that was used directly for the next step.

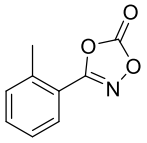
Step 2: To a solution of unpurified hydroxamic acid **S5** (10 mmol) in dry DCM (40 mL) was added CDI (11mmol, 1.1 equiv). The mixture was stirred for 5 min to 1 h until the reaction was completed. 2 N HCl solution (20 mL) was added and extracted with DCM. The combined organic phase was collected and dried over Na_2SO_4. The extract was filtered, concentrated, and purified by silica gel column chromatography (eluent: petroleum ether : ethyl acetate = 10 : 1 to 5 : 1) to give 3-substituted-1,4,2-dioxazol-5-ones (**2**).

3-Phenyl-1,4,2-dioxazol-5-one (2a)



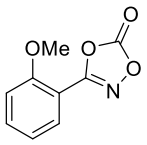
2a was prepared from benzoic acid in 1.31 g, 80% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data.[7]

3-(*o*-Tolyl)-1,4,2-dioxazol-5-one (2b)



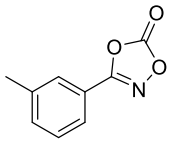
2b was prepared from 2-methylbenzoic acid in 1.47 g, 83% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data.[7]

3-(2-Methoxyphenyl)-1,4,2-dioxazol-5-one (2c)



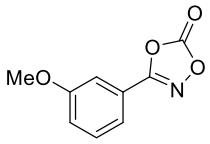
2c was prepared from 2-methoxybenzoic acid in 1.58 g, 82% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[8]

3-(*m*-Tolyl)-1,4,2-dioxazol-5-one (2d)



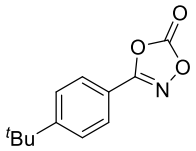
2d was prepared from 3-methylbenzoic acid in 1.51 g, 85% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[7]

3-(3-Methoxyphenyl)-1,4,2-dioxazol-5-one (2e)



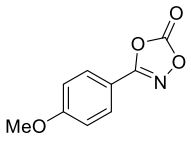
2e was prepared from 3-methoxybenzoic acid in 1.60 g, 84% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[9]

3-(4-(*tert*-Butyl)phenyl)-1,4,2-dioxazol-5-one (2f)



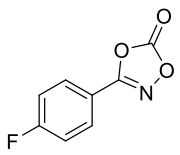
2f was prepared from 4-(*tert*-butyl)benzoic acid in 1.75 g, 80% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[9]

3-(4-Methoxyphenyl)-1,4,2-dioxazol-5-one (2g)



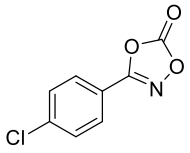
2g was prepared from 4-methoxybenzoic acid in 1.58 g, 82% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[7]

3-(4-Fluorophenyl)-1,4,2-dioxazol-5-one (2h)



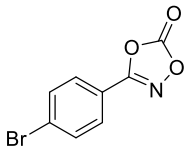
2h was prepared from 4-fluorobenzoic acid in 1.35 g, 75% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[8]

3-(4-Chlorophenyl)-1,4,2-dioxazol-5-one (2i)



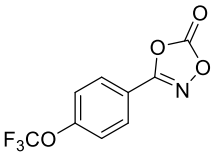
2i was prepared from 4-chlorobenzoic acid in 1.73 g, 78% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[8]

3-(4-Bromophenyl)-1,4,2-dioxazol-5-one (2j)



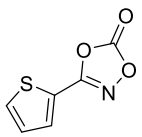
2j was prepared from 4-bromobenzoic acid in 1.92 g, 80% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[9]

3-(4-(Trifluoromethoxy)phenyl)-1,4,2-dioxazol-5-one (2k)



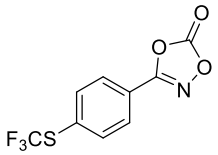
2k was prepared from 4-(trifluoromethoxy)benzoic acid in 1.92 g, 78% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[10]

3-(Thiophen-2-yl)-1,4,2-dioxazol-5-one (2l)



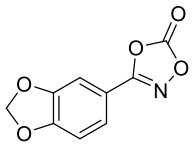
2l was prepared from thiophene-2-carboxylic acid in 1.34 g, 80% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[7]

3-(4-((Trifluoromethyl)thio)phenyl)-1,4,2-dioxazol-5-one (2m)



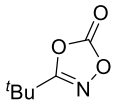
2m was prepared from 4-((trifluoromethyl)thio)benzoic acid in 1.78 g, 68% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[11]

3-(Benzo[*d*][*1,3*]dioxol-5-yl)-1,4,2-dioxazol-5-one (2n)



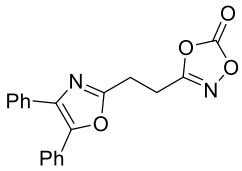
2n was prepared from benzo[*d*][*1,3*]dioxole-5-carboxylic acid in 1.71 g, 83% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 5 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[9]

3-(*tert*-Butyl)-1,4,2-dioxazol-5-one (2o)



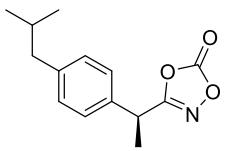
2o was prepared from pivalic acid in 1.17 g, 82% yield as a colourless liquid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[11]

3-(2-(4,5-Diphenyloxazol-2-yl)ethyl)-1,4,2-dioxazol-5-one (2p)



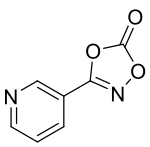
2p was prepared from Oxaprozin in 2.51 g, 78% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 5 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[12]

(*S*)-3-(1-(4-Isobutylphenyl)ethyl)-1,4,2-dioxazol-5-one (2q)



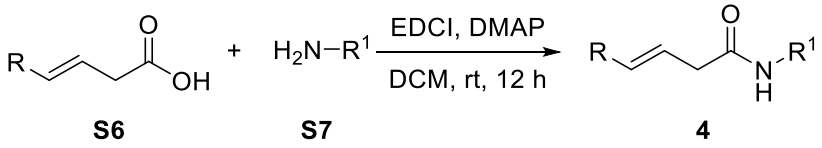
2q was prepared from (*S*)-Ibuprofen in 2.05 g, 83% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[6]

3-(Pyridin-3-yl)-1,4,2-dioxazol-5-one (2r)



2r was prepared from nicotinic acid in 0.98 g, 64% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 5 : 1). **Mp:** 51 – 53 °C. $\mathbf{R}_f$ = 0.46 (petroleum ether : ethyl acetate = 5 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.11 (d, *J* = 2.4 Hz, 1H), 8.89 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.16 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.52 (dd, *J* = 8.0, 4.8 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 162.1, 154.5, 153.4, 147.8, 134.0, 124.1, 117.1 ppm. **HRMS** calc'd for $C_7H_5N_2O_3^+$ 165.0295, found 165.0296 $[M+H]^+$

Preparation of but-3-enamides

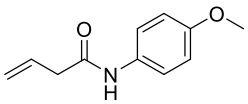


S6 **S7** **4**

The reaction was performed following the literature procedures.[13]

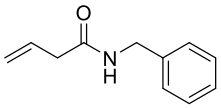
At room temperature, the corresponding amine (10 mmol, 1.0 equiv.) was added to a 100 ml dry round-bottom flask equipped with a magnetic stirrer. After adding 50ml of anhydrous DCM, EDCI (10 mmol, 1.0 equiv.) and DMAP (1 mmol, 0.1 equiv.) were sequentially added. Next, but-3-enoic acid (11 mmol, 1.1 equiv.) was slowly added to the mixture, which was stirred at room temperature for 12 hours. After completion of the reaction, the reaction was quenched using saturated $NaHCO_3$ solution. The organic phase was collected by extraction, while the aqueous phase was extracted with DCM (20 ml×3). The extract was filtered, concentrated, and purified by silica gel column chromatography (eluent: petroleum ether : ethyl acetate = 4 : 1) to give but-3-enamides (**4**).

***N*-(4-Methoxyphenyl)but-3-enamide (4a)**



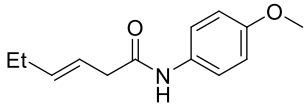
4a was prepared from but-3-enoic acid and 4-methoxyaniline in 1.72 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data[13].

***N*-Benzylbut-3-enamide (4b)**



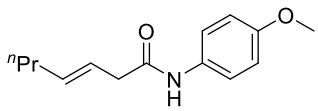
4b was prepared from but-3-enoic acid and phenylmethanamine in 1.61 g, 92% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data[14].

(*E*)-*N*-(4-Methoxyphenyl)hex-3-enamide (4c)



4c was prepared from (*E*)-hex-3-enoic acid and 4-methoxyaniline in 1.99 g, 91% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^1H and $^{13}C\{^1H\}$ data for this compound match the literature data.[15]

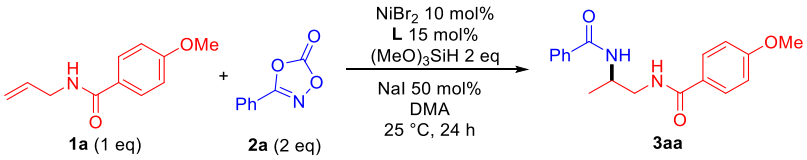
(*E*)-*N*-(4-Methoxyphenyl)hept-3-enamide (4d)



4d was prepared from (*E*)-hept-3-enoic acid and 4-methoxyaniline in 2.09 g, 90% yield as a white solid. Purification of the residue by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1). The ^{1}H and $^{13}C\{^{1}H\}$ data for this compound match the literature data.[16]

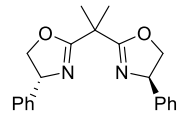
Optimisation of conditions for yield and ee value of product 3aa

Table S1. Screening of ligands for enantioselective synthesis of 3aa.[a,b,c,d]

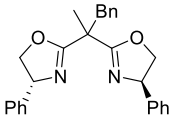


Entry	L	Yiled of **3aa**/%	ee% of **3aa**/%
1	**L1**	50	15
2	**L2**	60	40
3	**L3**	80	67
4	**L4**	<5	-
5	**L5**	83	93
6	**L6**	78	86
7	**L7**	<5	-
8	**L8**	50	<5
9	**L9**	<5	-
10	**L10**	<5	-
11	**L11-L14**	0	-
12	**L15**	25	<5
13	**L16**	<5	-
14	**L17**	<5	-
15	**L18**	<5	-
16	**L19**	<5	-
17	**L20**	23	<5
18	**L21**	<5	-
19	**L22**	<5	/
20	**L23**	62	32
21	**L24**	<5	-
22	**L25**	<5	-
23	**L26**	60	40
24	**L27**	55	15
25	**L28**	<5	-

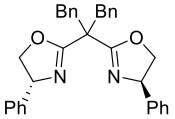
[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, $NiBr_2$ (10 mol%), Ligand (15 mol%), 2equiv. of $(MeO)_3SiH$ and 50 mol% of NaI in 1 mL of DMA at 25 °C for 48 h. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC. [d]Racemic **3aa** was obtained when using diethyl [2,2'-bipyridine]-6,6'-dicarboxylate **(L1)** as ligand.



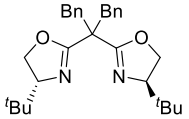
L1



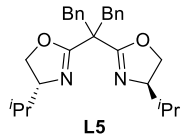
L2



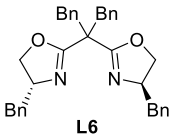
L3



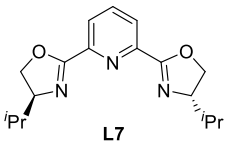
L4



L5



L6



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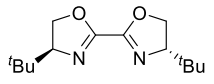
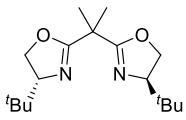
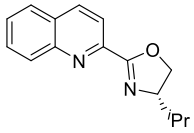


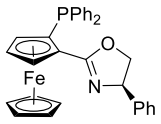
L8



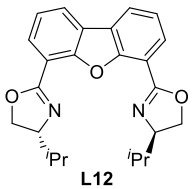
L9



L10



L11



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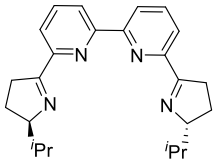

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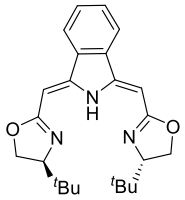

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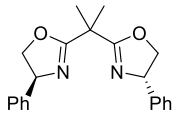

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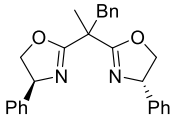

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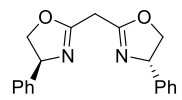

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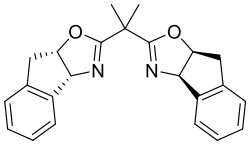

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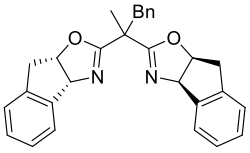
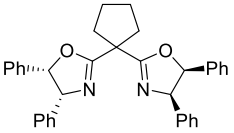


L19



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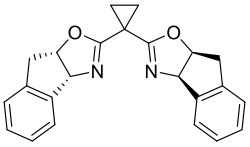

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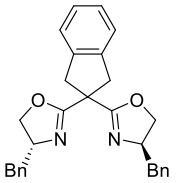

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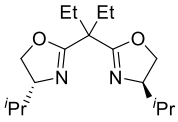

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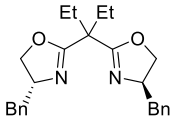

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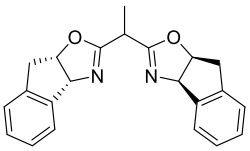

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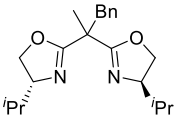

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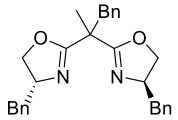
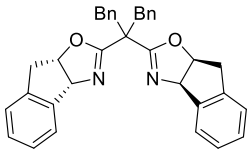
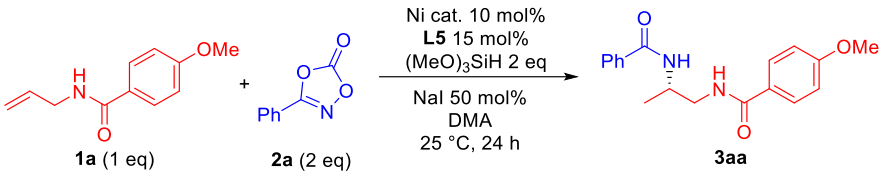


L27



L28

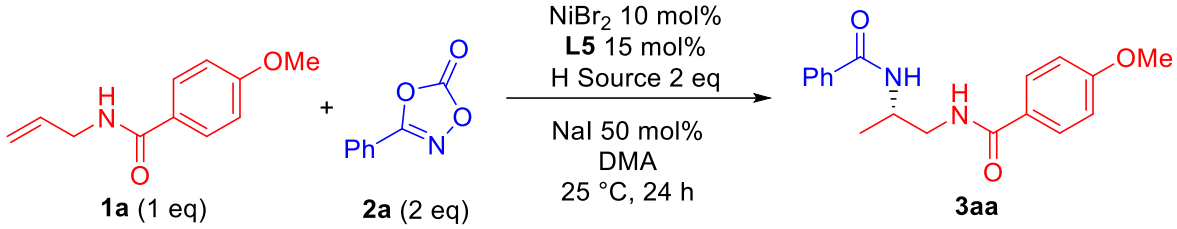
Table S2. Screening of Ni catalyst for enantioselective synthesis of 3aa.[a,b,c]



Entry	Ni Cat.	Yeild of **3**/%	ee% of **3**/%
1	$NiBr_2$	83	93
2	$NiBr_2$·DME	81	75
3	$NiCl_2$	45	75
4	$NiCl_2$·DME	60	86
5	$NiCl·6H_2O$	<5	-
6	NiI_2	66	89
7	$Ni(acac)_2$	<5	-
8	$Ni(COD)_2$	0	-

[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, Ni cat. (10 mol%), **L5** (15 mol%), 2equiv. of $(MeO)_3SiH$ and 50 mol% of NaI in 1 mL of DMA at 25 °C for 48 h. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC.

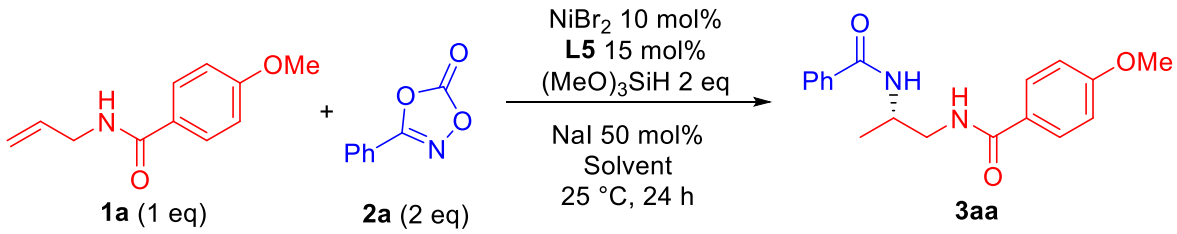
Table S3. Screening of hydrogen source for enantioselective synthesis of 3aa.[a,b,c]



Entry	H Source	Yeild of **3**/%	ee% of **3**/%
1	$(MeO)_3SiH$	83	93
2	$(MeO)_2MeSiH$	48	89
3	$(EtO)_3SiH$	77	89
4	PMHS	40	88
5	Ph_2SiH_2	/	/
6	HBPin	60	90

[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, $NiBr_2$ (10 mol%), **L5** (15 mol%), 2equiv. of hydrogen source and 50 mol% of NaI in 1 mL of DMA at 25 °C for 48 h. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC.

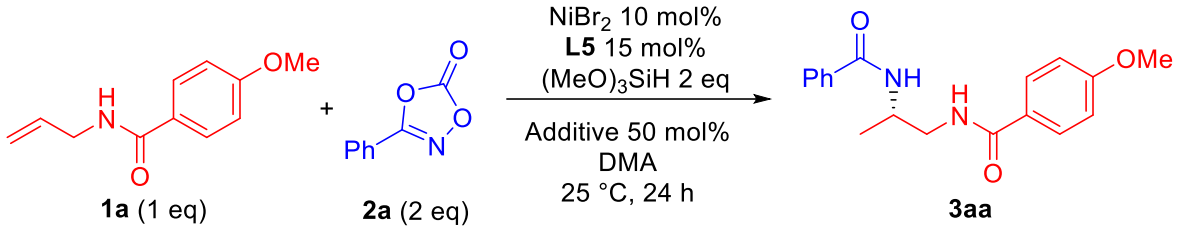
Table S4. Screening of solvent for enantioselective synthesis of 3aa.[a,b,c]



Entry	Solvent	Yeild of **3**/%	ee% of **3**/%
1	THF	70	90
2	Dioxane	Trace	/
3	2-Me-THF	56	90
4	DMA	83	93
5	MeCN	63	89
6	DCE	Trace	/
7	MTBE	60	87
8	CPME	Trace	/
9	DME	Trace	/

[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, $NiBr_2$ (10 mol%), **L5** (15 mol%), 2equiv. of $(MeO)_3SiH$ and 50 mol% of NaI in 1 mL of solvent at 25 °C for 48 h. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC.

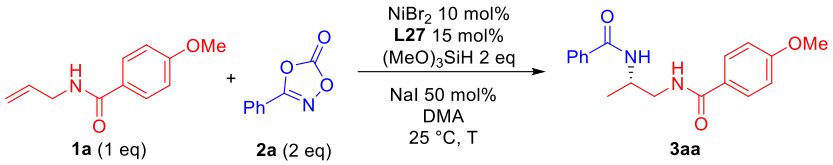
Table S5. Screening of additive for enantioselective synthesis of 3aa.[a,b,c]



Entry	Additive	Yeild of **3**/%	ee% of **3**/%
1	NaI	83	93
2	NaF	58	87
3	NaCl	60	88
4	NaBr	68	86
5	LiI	56	90
6	CsI	60	89
7	/	50	90

[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, $NiBr_2$ (10 mol%), L5 (15 mol%), 2equiv. of $(MeO)_3SiH$ and 50 mol% of additive in 1 mL of DMA at 25 °C for 48 h. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC.

Table S6. Screening of reaction time for enantioselective synthesis of 3aa.[a,b,c]



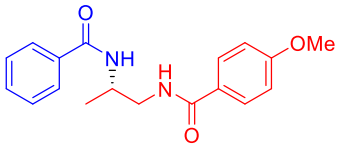
Entry	T/ h	Yeild of **3**/%	ee% of **3**/%
1	24	53	93
2	36	68	91
3	48	83	91
4	60	79	90

[a]Reactions conducted on a 0.1 mmol scale using 1.0 equiv. of **1a**, and 2.0 equiv. of **2a**, $NiBr_2$ (10 mol%), **L5** (15 mol%), 2equiv. of $(MeO)_3SiH$ and 50 mol% of NaI in 1 mL of DMA at 25 °C for different reaction time. [b]Isolated yield of **3aa** after flash chromatography on silica gel. [c]The *ee* (enantiomeric excess) of **3aa** was determined by chiral HPLC.

General procedure and characterization of NiH-catalyzed asymmetric hydroamidation of unactivated olefins

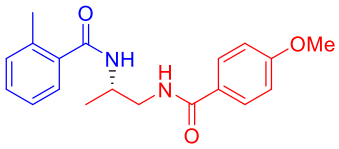
In a glove box under a nitrogen atmosphere, $NiBr_2$ (4.4 mg, 0.02 mmol, 10 mol%) and **L5** (12.6 mg, 0.03 mmol, 15 mol%) were added to a dry 8 ml reaction vial containing a magnetic stir bar. Then, 2 ml of anhydrous DMA was added to the mixture, which was stirred at room temperature for 10 minutes. Subsequently, $(MeO)_3SiH$ (50 mg, 0.4 mmol, 2.0 equiv.) and NaI (15 mg, 0.1 mmol, 50 mol%) were sequentially added to the mixture and stirred. *N*-allyl-amides **1** or but-3-enamides **3** were then added to the mixture and finally 1,4,2-dioxazol-5-ones **2** were added. The reaction vial was sealed and taken out of the glove box, and the mixture was stirred at room temperature for 48 hours or at 40 ℃ for 72 hours. After the completion of the reaction, 2 ml of EtOAc was added to the reaction vial for dilution. Extraction was performed using 50 ml of EA and 20 ml of saturated NaCl solution. The organic phase was further extracted using 2×30 ml of saturated NaCl solution. The organic phase was then dried using anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude material was loaded onto a silica gel column and purified by flash chromatography to obtain 1,2-diamines **3** or β-amino amides **5**.

(*S*)-*N*-(2-Benzamidopropyl)-4-methoxybenzamide (3aa)



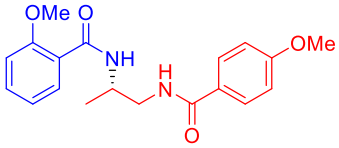
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3aa** (51.8 mg, 83% yield, 93% *ee*) as a white solid. **Mp**: 210 – 212 ℃. $\mathbf{R}_f$ = 0.28 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.45 (t, J = 6.4 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.90 – 7.73 (m, 4H), 7.54 – 7.48 (m, 1H), 7.45 (dd, J = 8.0, 6.4 Hz, 2H), 7.04 – 6.92 (m, 2H), 4.29 – 4.15 (m, 1H), 3.79 (s, 3H), 3.40 (t, J = 6.4 Hz, 2H), 1.16 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-*d*6) δ 166.3, 166.0, 161.5, 134.8, 131.0, 129.0, 128.2, 127.2, 126.8, 113.5, 55.3, 45.6, 44.2, 18.0 ppm. **HRMS** calc'd for $C_{18}H_{21}N_2O_3^+$ 313.1547, found 313.1545 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 20.99 min, t_{minor} = 23.22 min; $[\alpha]_D^{20}$ = 45.70 (*c* 1.0, MeOH).

(*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-2-methylbenzamide (3ab)



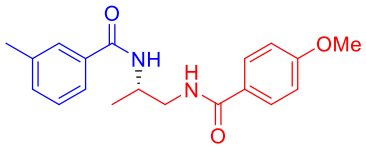
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(*o*-tolyl)-1,4,2-dioxazol-5-one **2b** (70.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ab** (53.5 mg, 82% yield, 97% *ee*) as a white solid. **Mp**: 173 – 175 °C. **R*f*** = 0.27 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.36 (t, *J* = 6.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.79 (m, 2H), 7.36 – 7.29 (m, 2H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.02 – 6.97 (m, 2H), 4.28 – 4.14 (m, 1H), 3.80 (s, 3H), 3.46 – 3.34 (m, 2H), 2.28 (s, 3H), 1.14 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 166.0, 161.5, 137.5, 135.0, 130.3, 129.1, 129.0, 127.0, 126.8, 125.4, 113.5, 55.3, 44.9, 44.3, 19.2, 18.0 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1702 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.21 min, t_{minor} = 8.45 min; $[\alpha]_D^{20}$ = 24.73 (*c* 1.0, MeOH).

(*S*)-2-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ac)



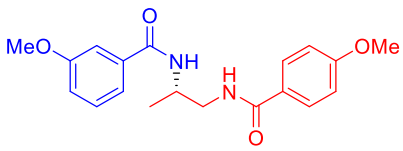
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(2-methoxyphenyl)-1,4,2-dioxazol-5-one **2c** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ac** (56.7 mg, 83% yield, 90% *ee*) as a white solid. **Mp**: 160 – 162 °C. **R*f*** = 0.20 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (t, *J* = 6.0 Hz, 1H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.89 – 7.79 (m, 2H), 7.72 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.49 – 7.35 (m, 1H), 7.09 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.05 – 6.94 (m, 3H), 4.25- 4.12 (m, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.48 – 3.37 (m, 2H), 1.16 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 164.7, 161.6, 157.0, 132.1, 130.3, 129.0, 126.6, 123.2, 120.4, 113.5, 111.9, 55.8, 55.4, 45.7, 43.9, 18.2 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_4^+$ 343.1652, found 343.1650 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 13.40 min, t_{minor} = 15.72 min; $[\alpha]_D^{20}$ = 40.37 (*c* 1.0, MeOH).

(*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-3-methylbenzamide (3ad)



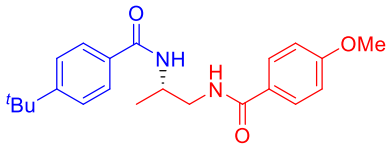
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(*m*-tolyl)-1,4,2-dioxazol-5-one **2d** (70.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ad** (56.7 mg, 83% yield, 92% *ee*) as a white solid. **Mp**: 197 – 199 °C. **R*f*** = 0.29 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, *J* = 6.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.77 (m, 2H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.61 (dt, *J* = 6.4, 2.0 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.02 – 6.95 (m, 2H), 4.28 – 4.15 (m, 1H), 3.79 (s, 3H), 3.44 – 3.38 (m, 2H), 2.35 (s, 3H), 1.16 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 166.1, 161.5, 137.4, 134.8, 131.6, 129.0, 128.1, 127.8, 126.8, 124.4, 113.5, 55.3, 45.5, 44.2, 21.0, 18.0 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1701 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.05 min, t_{minor} = 8.55 min; $[\alpha]_D^{20}$ = 41.40 (*c* 1.0, MeOH).

(*S*)-3-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ae)



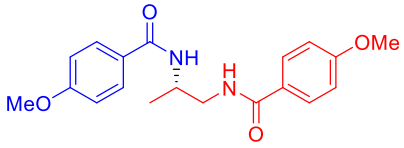
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(3-methoxyphenyl)-1,4,2-dioxazol-5-one **2e** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ae** (58.1 mg, 85% yield, 95% *ee*) as a white solid. **Mp**: 182 – 184 °C. **R*f*** = 0.24 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (t, *J* = 6.0 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.95 – 7.73 (m, 2H), 7.53 – 7.28 (m, 3H), 7.12 –7.04 (m, 1H), 7.02 – 6.87 (m, 2H), 4.32 – 4.15 (m, 1H), 3.80 (s, 6H), 3.49 – 3.37 (m, 2H), 1.17 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.4, 165.7, 161.5, 159.1, 136.3, 129.3, 129.0, 126.8, 119.5, 116.8, 113.5, 112.5, 55.3, 55.3, 45.7, 44.2, 18.0 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_4^+$ 343.1652, found 343.1649 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.97 min, t_{minor} = 11.34 min; $[\alpha]_D^{20}$ = 26.63 (*c* 1.0, MeOH).

(*S*)-4-(*tert*-Butyl)-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3af)



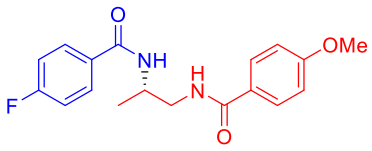
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-(tert-butyl)phenyl)-1,4,2-dioxazol-5-one **2f** (87.6 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3af** (58.1 mg, 79% yield, 94% *ee*) as a white solid. **Mp**: 210 – 212 °C. $\mathbf{R}_f$ = 0.28 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, J = 6.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.89 – 7.79 (m, 2H), 7.76 (dd, J = 8.4, 1.2 Hz, 2H), 7.45 (dd, J = 8.4, 1.2 Hz, 2H), 7.06 – 6.90 (m, 2H), 4.21 (h, J = 6.8 Hz, 1H), 3.79 (s, 3H), 3.40 (q, J = 6.0 Hz, 2H), 1.28 (s, 9H), 1.16 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 165.9, 161.5, 153.8, 132.1, 129.0, 127.1, 126.8, 125.0, 113.5, 55.3, 45.5, 44.3, 34.6, 31.0, 18.0 ppm. **HRMS** calc'd for $C_{22}H_{29}N_2O_3^+$ 369.2173, found 369.2172 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.52 min, t_{minor} = 9.31 min; $[\alpha]_D^{20}$ = 22.44 (*c* 1.0, MeOH).

(*S*)-*N*,*N*′-(Propane-1,2-diyl)bis(4-methoxybenzamide) (3ag)



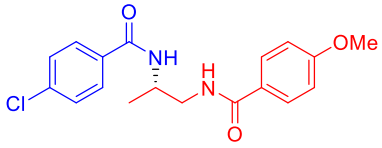
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-methoxyphenyl)-1,4,2-dioxazol-5-one **2g** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ag** (56.7 mg, 83% yield, 96% *ee*) as a white solid. **Mp**: 206 – 208 °C. $\mathbf{R}_f$ = 0.19 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, J = 6.0 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.88 – 7.75 (m, 4H), 7.05 – 6.91 (m, 4H), 4.25 – 4.16 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.39 (td, J = 6.4, 2.4 Hz, 2H), 1.15 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 165.4, 161.5, 161.5, 129.0, 127.0, 126.8, 113.5, 113.4, 55.3, 45.5, 44.3, 18.1 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_4^+$ 343.1652, found 343.1654 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.22 min, t_{minor} = 14.47 min; $[\alpha]_D^{20}$ = 9.84 (*c* 1.0, MeOH).

(*S*)-4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ah)



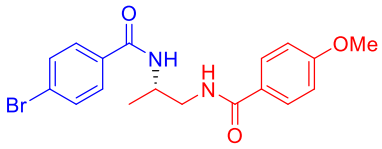
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-fluorophenyl)-1,4,2-dioxazol-5-one **2h** (72.4 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ah** (46.2 mg, 70% yield, 97% *ee*) as a white solid. **Mp**: 227 – 229 °C. **R*f*** = 0.26 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, J = 6.0 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.97 – 7.86 (m, 2H), 7.85 – 7.66 (m, 2H), 7.41 – 7.19 (m, 2H), 7.12 – 6.78 (m, 2H), 4.31 – 4.12 (m, 1H), 3.79 (s, 3H), 3.39 (dt, J = 6.4, 4.0 Hz, 2H), 1.16 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.8, 165.4, 165.2 (d, J_1 = 246.4 Hz), 162.0, 131.7 (d, J_4 = 2.3 Hz), 130.3 (d, J_3 = 9.1 Hz), 129.5, 127.3, 115.5 (d, J_2= 21.9 Hz), 113.9, 55.8, 46.1, 44.6, 18.4 ppm. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -109.78 ppm. **HRMS** calc'd for $C_{18}H_{20}FN_2O_3^+$ 331.1452, found 331.1450 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 9.30 min, t_{minor} = 11.74 min; **$[\alpha]_D^{20}$** = 69.56 (*c* 1.0, MeOH).

(*S*)-4-Chloro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ai)



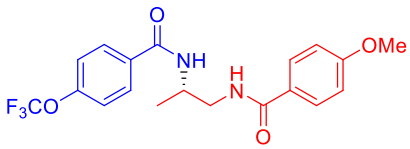
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-chlorophenyl)-1,4,2-dioxazol-5-one **2i** (78.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ai** (49.8 mg, 72% yield, 94% *ee*) as a white solid. **Mp**: 235 – 237 °C. **R*f*** = 0.27 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, J = 6.0 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.83 – 7.76 (m, 2H), 7.58 – 7.50 (m, 2H), 7.02 – 6.93 (m, 2H), 4.28 – 4.13 (m, 1H), 3.79 (s, 3H), 3.39 (dt, J = 6.4, 3.6 Hz, 2H), 1.15 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.8, 165.3, 162.0, 136.3, 134.0, 129.7, 129.5, 128.8, 127.2, 113.9, 55.8, 46.1, 44.6, 18.4 ppm. **HRMS** calc'd for $C_{18}H_{20}ClN_2O_3^+$ 347.1157, found 347.1161 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.70 min, t_{minor} = 11.11 min; **$[\alpha]_D^{20}$** = 56.85 (*c* 1.0, MeOH).

(*S*)-4-Bromo-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3aj)



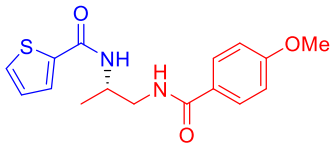
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-bromophenyl)-1,4,2-dioxazol-5-one **2j** (96.4 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3aj** (58.5 mg, 75% yield, 95% *ee*) as a white solid. **Mp**: 240 – 242 °C. **R$_f$** = 0.28 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.44 (t, J = 6.0 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.90 – 7.83 (m, 2H), 7.83 – 7.72 (m, 2H), 7.59 – 7.49 (m, 2H), 7.04 – 6.92 (m, 2H), 4.30 – 4.12 (m, 1H), 3.79 (s, 3H), 3.39 (td, J = 6.4, 1.6 Hz, 2H), 1.15 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 164.9, 161.5, 135.9, 133.6, 129.2, 129.0, 128.3, 126.8, 113.5, 55.3, 45.7, 44.1, 18.0 ppm. **HRMS** calc'd for $C_{18}H_{20}BrN_2O_3^+$ 391.0652, found 391.0650 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.50 min, t_{minor} = 10.36 min; **[α]$_D^{20}$** = 30.55 (*c* 1.0, MeOH).

(*S*)-4-Methoxy-*N*-(2-(4-(trifluoromethoxy)benzamido)propyl)benzamide (3ak)



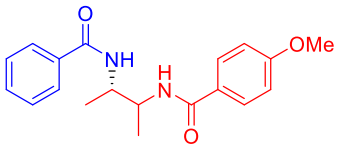
The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(4-(trifluoromethoxy)phenyl)-1,4,2-dioxazol-5-one **2k** (98.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ak** (61.8 mg, 78% yield, 99% *ee*) as a white solid. **Mp**: 203 – 205 °C. **R$_f$** = 0.23 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 – 8.37 (m, 2H), 7.98 – 7.93 (m, 2H), 7.83 – 7.78 (m, 2H), 7.49 – 7.42 (m, 2H), 7.00 – 6.94 (m, 2H), 4.29 – 4.16 (m, 1H), 3.79 (s, 3H), 3.45 – 3.36 (m, 2H), 1.16 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 164.7, 161.5, 150.2, 134.0, 129.6, 129.0, 126.8, 120.6, 119.9 (q, J_1 = 255.1 Hz), 113.5, 55.3, 45.7, 44.1, 17.9 ppm. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -56.70 ppm. **HRMS** calc'd for $C_{19}H_{20}F_3N_2O_4^+$ 397.1370, found 397.1372 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 15.93 min, t_{minor} = 13.69 min; **[α]$_D^{20}$** = 50.56 (*c* 1.0, MeOH).

(*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)thiophene-2-carboxamide (3al)



The reaction was performed with *N*-allyl-4-methoxybenzamide **1a** (38.2 mg, 0.2 mmol) and 3-(thiophen-2-yl)-1,4,2-dioxazol-5-one **2l** (67.6 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3al** (45.2 mg, 71% yield, 93% *ee*) as a white solid. **Mp**: 190 – 192 °C. **R*f*** = 0.25 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.45 (t, *J* = 6.0 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.74 – 7.68 (m, 2H), 7.14 (dd, *J* = 5.2, 3.6 Hz, 1H), 7.03 – 6.93 (m, 2H), 4.24 – 4.11 (m, 1H), 3.79 (s, 3H), 3.41 (td, *J* = 12.4, 11.6, 6.0 Hz, 2H), 1.15 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.3, 161.5, 160.7, 140.3, 130.6, 129.1, 128.0, 127.8, 126.7, 113.5, 55.3, 45.5, 44.1, 18.0 ppm. **HRMS** calc'd for $C_{16}H_{19}N_2O_3S^+$ 319.1111, found 319.1114 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 9.13 min, t_{minor} = 11.36 min; **$[\alpha]_D^{20}$** = 54.54 (c 1.0, MeOH).

***N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba)**



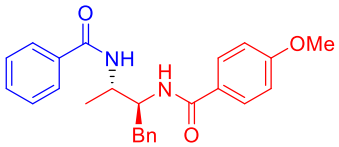
The reaction was performed with *N*-(but-3-en-2-yl)-4-methoxybenzamide **1b** (41.0 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ba** in two diastereoisomers (dr = 1.2:1) as a white solid.

Major diastereoisomer: (22.1 mg, 34% yield, 90% ee), **Mp**: 181 – 183 °C. **R*f*** = 0.28 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.23 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.84 – 7.73 (m, 4H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.44 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.03 – 6.93 (m, 2H), 4.18 (m, 2H), 3.79 (s, 3H), 1.17 (d, *J* = 5.8 Hz, 6H) ppm. **^{13}C NMR** (150 MHz, DMSO-d_6) δ 166.4, 165.8, 161.4, 135.0, 131.0, 129.1, 128.2, 127.2, 127.1, 55.3, 49.4, 49.2, 17.8, 17.8 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1706 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.53 min, t_{minor} = 14.05 min; **$[\alpha]_D^{20}$** = 36.53 (*c* 1.0, MeOH).

Minor diastereoisomer: (18.4 mg, 28% yield, 82% ee), **Mp**: 178 – 180 °C. **R*f*** = 0.26 (petroleum ether :

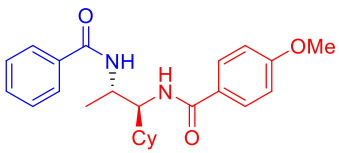
ethyl acetate = 1 : 1.5). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.39 (d, J = 7.2 Hz, 1H), 8.24 (d, J = 7.2 Hz, 1H), 7.85 (t, J = 7.2 Hz, 4H), 7.52 (t, J = 7.2Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 4.20 (m, 2H), 3.81 (s, 3H), 1.14 (d, J = 5.3 Hz, 6H) ppm. **^{13}C NMR** (150 MHz, DMSO-d_6) δ 166.0, 165.5, 161.5, 134.8, 131.1, 129.1, 128.2, 127.3, 126.9, 113.4, 55.4, 49.2, 49.1, 17.5, 17.4 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1704 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 19.03 min, t_{minor} = 20.07 min; **$[\alpha]_D^{20}$** = 16.87 (*c* 1.0, MeOH).

_N_-((2_S_,3_S_)-3-Benzamido-1-phenylbutan-2-yl)-4-methoxybenzamide (3ca)



The reaction was performed with (*S*)-4-methoxy-*N*-(1-phenylbut-3-en-2-yl)benzamide **1c** (56.2 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ca** (62.7 mg, 78% yield, 92% de) as a white solid. **Mp**: 201 – 203 °C. **R_f** = 0.26 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.27 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H), 7.89 – 7.80 (m, 2H), 7.76 – 7.68 (m, 2H), 7.54 – 7.45 (m, 3H), 7.28 – 7.19 (m, 4H), 7.16 – 7.10 (m, 1H), 6.99 – 6.93 (m, 2H), 4.39 – 4.23 (m, 2H), 3.78 (s, 3H), 2.96 (dd, J = 13.6, 4.4 Hz, 1H), 2.85 (dd, J = 13.6, 9.6 Hz, 1H), 1.20 (d, J = 6.4 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.4, 166.3, 161.5, 139.2, 135.1, 131.1, 129.1, 129.0, 128.3, 128.1, 127.3, 127.1, 126.0, 113.4, 55.3, 54.9, 48.5, 37.2, 18.1 ppm. **HRMS** calc'd for $C_{25}H_{27}N_2O_3^+$ 403.2016, found 403.2011 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 5.14 min, t_{minor} = 7.82 min; **$[\alpha]_D^{20}$** = 68.50 (*c* 1.0, MeOH).

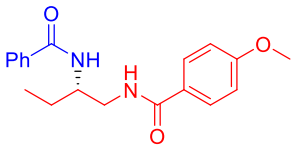
_N_-((1_S_,2_S_)-2-Benzamido-1-cyclohexylpropyl)-4-methoxybenzamide (3da)



The reaction was performed with (*S*)-*N*-(1-cyclohexylallyl)-4-methoxybenzamide **1d** (54.6 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3da** (53.6 mg, 68% yield, 90% de) as a white solid. **Mp**: 206 – 208 °C. **R_f** = 0.25 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.38 (t, J = 5.6 Hz,

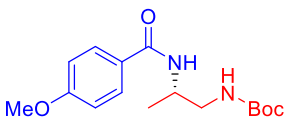
1H), 7.99 (d, J = 8.8 Hz, 1H), 7.91 – 7.84 (m, 2H), 7.84 – 7.77 (m, 2H), 7.54 – 7.47 (m, 1H), 7.47 – 7.39 (m, 2H), 7.02 – 6.93 (m, 2H), 3.87 (d, J = 3.1 Hz, 1H), 3.81 (s, 3H), 3.47 – 3.36 (m, 1H), 3.20 – 3.04 (m, 1H), 1.95– 1.85 (m, 1H), 1.83 – 1.64 (m, 5H), 1.63 – 1.55 (m, 1H), 1.55 – 1.44 (m, 1H), 1.22 – 1.09 (m, 3H), 1.03 – 0.89 (m, 2H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 166.5, 166.4, 161.9, 135.2, 131.5, 129.6, 128.7, 127.5, 113.8, 55.8, 52.2, 41.8, 37.4, 31.4, 29.9, 29.5, 26.5, 26.3, 26.2 ppm. **HRMS** calc'd for $C_{24}H_{31}N_2O_3^+$ 395.2329, found 395.2327 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.53 min, t_{minor} = 14.05 min; **$[\alpha]_D^{20}$** = 42.98 (*c* 1.0, MeOH).

(*S*)-*N*-(2-Benzamidobutyl)-4-methoxybenzamide (3ea)



The reaction was performed with (*E*)-*N*-(but-2-en-1-yl)-4-methoxybenzamide **1e** (41.0 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3ea** (26.7 mg, 41% yield, 93% *ee*) as a white solid. **Mp**: 219 – 221 °C. **R_f** = 0.35 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.37 (t, J = 6.6 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 6.6 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 7.54 – 7.49 (t, J = 8.4 Hz,, 1H), 7.45 (t, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 4.15 – 4.04 (m, 1H), 3.79 (s, 3H), 3.48 – 3.37 (m, 2H), 1.60 (m, 1H), 1.57 – 1.49 (m, 1H), 0.89 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (150 MHz, DMSO-d_6) δ 166.4, 166.2, 161.5, 134.9, 131.0, 129.0, 128.2, 127.3, 126.9, 113.4, 55.3, 51.2, 42.9, 24.6, 10.6 ppm. **HRMS** calc'd for $C_{19}H_{21}N_2O_3^-$ 325.1558, found 235.1556 $[M-H]^-$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.06 min, t_{minor} = 10.21 min; **$[\alpha]_D^{20}$** = 33.56 (*c* 1.0, MeOH).

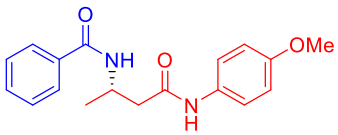
***tert*-Butyl-(*S*)-(2-(4-methoxybenzamido)propyl)carbamate (3fg)**



The reaction was performed with *tert*-butyl allylcarbamate **1f** (31.4 mg, 0.2 mmol) and 3-(4-methoxyphenyl)-1,4,2-dioxazol-5-one **2g** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **3fg** (22.2 mg, 36% yield, 94% *ee*) as a white solid. **Mp**: 158 – 160 °C. **R_f** = 0.50 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR**

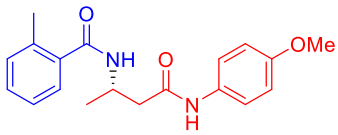
(400 MHz, DMSO-d_6) δ 7.96 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.93 (t, J = 6.0 Hz, 1H), 4.02 (m, 1H), 3.80 (s, 3H), 3.05 (m, 2H), 1.35 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 165.2, 161.4, 156.0, 129.1, 126.9, 113.3, 77.7, 55.3, 45.5, 44.8, 28.2, 17.9 ppm. **HRMS** calc'd for $C_{16}H_{25}N_2O_4^+$ 309.1809, found 309.1807 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK OJ-H *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 3.94 min, t_{minor} = 4.66 min; **$[\alpha]_D^{20}$** = 45.68 (*c* 1.0, MeOH).

(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aa)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5aa** (50.5 mg, 81% yield, 98% *ee*) as a white solid. **Mp**: 209 – 211 °C. **R_f** = 0.32 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.34 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 7.8 Hz, 2H), 7.48 – 7.35 (m, 5H), 6.86 (d, J = 8.4 Hz, 2H), 4.56 – 4.24 (m, 1H), 3.70 (s, 3H), 2.61 (dd, J = 14.4, 6.6 Hz, 1H), 2.49 – 2.45 (dd, J = 14.4, 6.6 Hz, 1H), 1.22 (d, J = 6.6 Hz, 3H) ppm. **^{13}C NMR** (150 MHz, DMSO-d_6) δ 168.7, 165.5, 155.1, 134.8, 132.3, 131.1, 128.2, 127.2, 120.8, 113.8, 55.1, 43.0, 42.9, 20.3 ppm. **HRMS** calc'd for $C_{18}H_{21}N_2O_3^+$ 313.1547, found 313.1552 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.57 min, t_{minor} = 17.81 min; **$[\alpha]_D^{20}$** = 62.58 (*c* 1.0, MeOH).

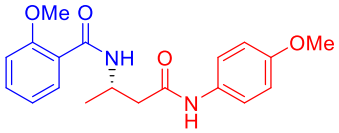
(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-2-methylbenzamide (5ab)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(*o*-tolyl)-1,4,2-dioxazol-5-one **2b** (70.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ab** (54.1 mg, 83% yield, 99% *ee*) as a white solid. **Mp**: 196 – 198 °C. **R_f** = 0.31 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (s, 1H), 7.46 – 7.39 (m, 2H), 7.35 (dd, J = 7.6, 1.6 Hz, 1H), 7.29 (td, J = 7.6, 1.6 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.90 –

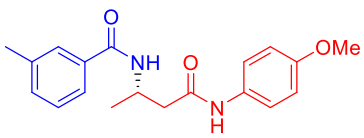
6.81 (m, 2H), 6.72 (d, J = 8.4 Hz, 1H), 4.57 (dt, J = 13.2, 6.4 Hz, 1H), 3.79 (s, 3H), 2.75 (dd, J = 15.2, 4.8 Hz, 1H), 2.63 (dd, J = 15.2, 4.8 Hz, 1H), 2.42 (s, 3H), 1.41 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 170.2, 169.2, 156.7, 136.3, 136.1, 131.2, 130.9, 130.1, 127.0, 126.0, 122.1, 114.3, 55.6, 43.4, 43.3, 20.6, 19.9 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1705 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.96 min, t_{minor} = 10.80 min; **$[\alpha]_D^{20}$** = 20.91 (*c* 1.0, MeOH).

(*S*)-2-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ac)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(2-methoxyphenyl)-1,4,2-dioxazol-5-one **2c** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ac** (59.5 mg, 87% yield, 97% *ee*) as a white solid. **Mp**: 198 – 200 °C. **R_f** = 0.21 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 7.79 (dd, J = 7.6, 2.0 Hz, 1H), 7.61 – 7.49 (m, 2H), 7.47 – 7.40 (m, 1H), 7.12 (dd, J = 8.4, 1.2 Hz, 1H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 6.93 – 6.78 (m, 2H), 4.47 – 4.29 (m, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 2.60 (dd, J = 14.4, 6.0 Hz, 1H), 2.54 – 2.51 (dd, J = 14.4, 6.0 Hz, 1H), 1.23 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.9, 163.9, 157.0, 155.2, 132.2, 130.5, 122.9, 120.8, 120.5, 113.8, 112.1, 55.8, 55.1, 42.7, 42.1, 20.1 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_4^+$ 343.1652, found 343.1647 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.78 min, t_{minor} = 15.98 min; **$[\alpha]_D^{20}$** = 19.24 (*c* 1.0, MeOH).

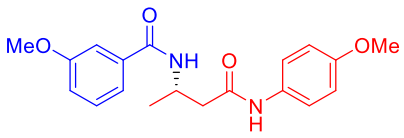
(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-3-methylbenzamide (5ad)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(m-tolyl)-1,4,2-dioxazol-5-one **2d** (70.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ad** (52.1 mg, 80% yield, 97% *ee*) as a white solid. **Mp**: 160 – 162 °C. **R_f** = 0.29 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.30 (d,

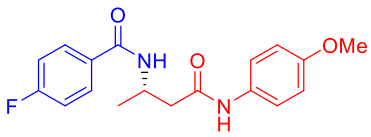
J = 8.0 Hz, 1H), 7.64 (d, J = 1.6 Hz, 1H), 7.61 (dt, J = 6.0, 2.4 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.38 – 7.29 (m, 2H), 6.89 – 6.83 (m, 2H), 4.50 – 4.34 (m, 1H), 3.71 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.50 – 2.44 (dd, J = 14.4, 6.4 Hz, 1H), 2.35 (s, 3H), 1.22 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 165.6, 155.1, 137.4, 134.8, 132.3, 131.6, 128.1, 127.7, 124.4, 120.8, 113.8, 55.1, 42.9, 20.9, 20.3 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_3^+$ 327.1703, found 327.1702 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 5.30 min, t_{minor} = 8.32 min; $[\alpha]_D^{20}$ = 12.35 (*c* 1.0, MeOH).

(*S*)-3-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ae)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(3-methoxyphenyl)-1,4,2-dioxazol-5-one **2e** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ae** (58.1 mg, 85% yield, 98% *ee*) as a white solid. **Mp**: 175 – 177 °C. **R$_f$** = 0.20 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.34 (d, J = 8.0 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.42 – 7.33 (m, 3H), 7.09 – 7.05 (m, 1H), 6.91 – 6.77 (m, 2H), 4.53 – 4.46 (m, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 2.62 (dd, J = 14.4, 6.4 Hz, 1H), 2.47 (dd, J = 14.4, 6.4 Hz, 1H), 1.22 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 165.3, 159.1, 155.2, 136.3, 132.3, 129.4, 120.8, 119.5, 116.8, 113.8, 112.6, 55.3, 55.1, 43.1, 42.9, 20.3 ppm. **HRMS** calc'd for $C_{19}H_{23}N_2O_4^+$ 343.1652, found 343.1656 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.28 min, t_{minor} = 16.84 min; $[\alpha]_D^{20}$ = 28.39 (*c* 1.0, MeOH).

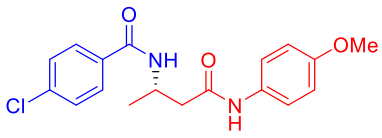
(*S*)-4-Fluoro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ah)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(4-fluorophenyl)-1,4,2-dioxazol-5-one **2h** (72.4 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ah** (49.5 mg, 75% yield, 96% *ee*) as a white solid. **Mp**: 227 – 229 °C. **R$_f$** = 0.28 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.38

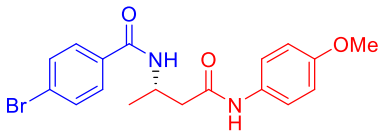
(d, J = 8.0 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.54 – 7.43 (m, 2H), 7.31 – 7.26 (m, 2H), 6.96 – 6.77 (m, 2H), 4.51 – 4.30 (m, 1H), 3.70 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.46 (dd, J = 14.4, 6.4 Hz, 1H), 1.21 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.6, 164.5, 163.8 (d, J_1 = 246.5 Hz), 155.2, 132.3, 131.2(d, J_4 = 3.2 Hz), 129.9 (d, J_3= 8.6 Hz), 120.8, 115.1 (d, J_2= 21.3 Hz), 113.8, 55.1, 43.1, 42.9, 20.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ -109.75 ppm. **HRMS** calc'd for $C_{18}H_{20}FN_2O_3^+$ 331.1452, found 331.1453 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.76 min, t_{minor} = 11.65 min; **$[\alpha]_D^{20}$** = 10.65 (*c* 1.0, MeOH).

(*S*)-4-Chloro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ai)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(4-chlorophenyl)-1,4,2-dioxazol-5-one **2i** (78.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ai** (50.5 mg, 73% yield, 91% *ee*) as a white solid. **Mp**: 236 – 238 °C. **R_f** = 0.26 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 7.97 – 7.82 (m, 2H), 7.57 – 7.52 (m, 2H), 7.51 – 7.45 (m, 2H), 6.90 – 6.83 (m, 2H), 4.56 – 4.23 (m, 1H), 3.71 (s, 3H), 2.62 (dd, J = 14.4, 6.4 Hz, 1H), 2.48 (dd, J = 14.4, 6.4 Hz, 1H), 1.22 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.6, 164.5, 155.2, 135.9, 133.5, 132.3, 129.2, 128.3, 120.8, 113.8, 55.1, 43.1, 42.9, 20.2 ppm. **HRMS** calc'd for $C_{18}H_{20}ClN_2O_3^+$ 347.1157, found 347.1155 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 9.12 min, t_{minor} = 13.10 min; **$[\alpha]_D^{20}$** = 27.38 (*c* 1.0, MeOH).

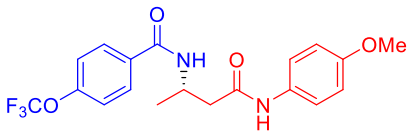
(*S*)-4-Bromo-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aj)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(4-bromophenyl)-1,4,2-dioxazol-5-one **2j** (96.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5aj** (59.4 mg, 76% yield, 99% *ee*) as a white solid. **Mp**: 253 – 255 °C. **R_f**

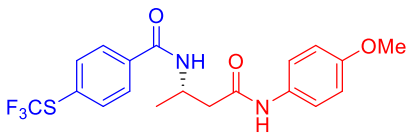
= 0.27 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 7.85 – 7.73 (m, 2H), 7.73 – 7.62 (m, 2H), 7.51 – 7.46 (m, 2H), 6.89 – 6.84 (m, 2H), 4.52 – 4.40 (m, 1H), 3.71 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.46 (dd, J = 14.4, 6.4 Hz, 1H), 1.22 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.5, 164.5, 155.1, 133.9, 132.3, 131.2, 129.4, 124.8, 120.8, 113.8, 55.1, 43.1, 42.8, 20.2 ppm. **HRMS** calc'd for $C_{18}H_{20}BrN_2O_3^+$ 391.0652, found 391.0647 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.09 min, t_{minor} = 17.14 min; $[\alpha]_D^{20}$ = 19.20 (*c* 1.0, MeOH).

(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-(trifluoromethoxy)benzamide (5ak)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(4-(trifluoromethoxy)phenyl)-1,4,2-dioxazol-5-one **2k** (98.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ak** (61.8 mg, 78% yield, 91% *ee*) as a white solid. **Mp**: 242 – 244 °C. **R_f** = 0.22 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.48 (d, J = 8.0 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.47 (dd, J = 9.2, 7.2 Hz, 4H), 6.89 – 6.83 (m, 2H), 4.52 – 4.30 (m, 1H), 3.70 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.47 (dd, J = 14.4, 6.4 Hz, 1H), 1.21 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.5, 164.3, 155.2, 150.2, 133.9, 132.3, 129.6, 120.8, 120.6, 119.9(q, J_1 = 255.3 Hz), 113.8, 55.1, 43.1, 42.8, 20.2 ppm. ^{19}F NMR (377 MHz, DMSO-d_6) δ -56.71 ppm. **HRMS** calc'd for $C_{19}H_{20}F_3N_2O_4^+$ 397.1370, found 397.1373 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.38 min, t_{minor} = 11.37 min; $[\alpha]_D^{20}$ = 36.35 (*c* 1.0, MeOH).

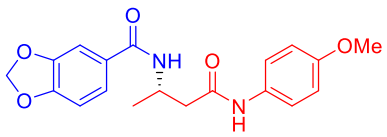
(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-((trifluoromethyl)thio)benzamide (5am)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(4-((trifluoromethyl)thio)phenyl)-1,4,2-dioxazol-5-one **2m** (104.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel

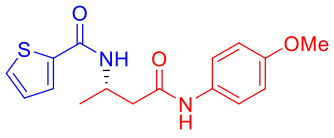
(petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5am** (54.4 mg, 66% yield, 99% *ee*) as a white solid. **Mp**: 246 – 248 °C. **R**$_f$ = 0.24 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.01 – 7.90 (m, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.53 – 7.41 (m, 2H), 6.91 – 6.81 (m, 2H), 4.52 – 4.36 (m, 1H), 3.70 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.47 (dd, J = 14.4, 6.4 Hz, 1H), 1.22 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.5, 164.6, 155.2, 137.5, 135.9, 132.3, 129.5(q, J_1 = 306.3 Hz), 128.7, 126.0, 120.8, 113.8, 55.1, 43.2, 42.8, 20.2 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ -41.70 ppm. **HRMS** calc'd for $C_{19}H_{20}F_3N_2O^+$ 413.1141, found 413.1139 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.16 min, t_{minor} = 15.35 min; **[α]$_D^{20}$** = 22.30 (*c* 1.0, MeOH).

(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzo[*d*][1,3]dioxole-5-carboxamide (5an)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(benzo[*d*][*1,3*]dioxol-5-yl)-1,4,2-dioxazol-5-one **2n** (82.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5an** (60.5 mg, 85% yield, 99% *ee*) as a white solid. **Mp**: 256 – 258 °C. **R**$_f$ = 0.18 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.42 (dd, J = 8.0, 1.6 Hz, 1H), 7.37 (d, J = 1.6 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.89 – 6.82 (m, 2H), 6.08 (s, 2H), 4.48 – 4.24 (m, 1H), 3.70 (s, 3H), 2.59 (dd, J = 14.4, 6.4 Hz, 1H), 2.46 (dd, J = 14.4, 6.4 Hz, 1H), 1.20 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 164.6, 155.2, 149.6, 147.3, 132.3, 128.8, 122.2, 120.8, 113.8, 107.8, 107.4, 101.6, 55.1, 43.0, 43.0, 20.3 ppm. **HRMS** calc'd for $C_{19}H_{21}N_2O_5^+$ 357.1445, found 357.1444 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.01 min, t_{minor} = 29.74 min; **[α]$_D^{20}$** = 12.18 (*c* 1.0, MeOH).

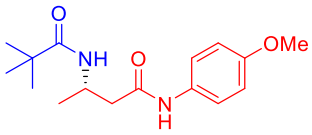
(*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)thiophene-2-carboxamide (5al)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(thiophen-2-yl)-1,4,2-dioxazol-5-one

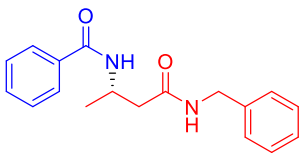
2l (67.6 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5al** (51.5 mg, 81% yield, 94% *ee*) as a white solid. **Mp**: 244 – 246 °C. **R_f** = 0.20 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 7.79 – 7.70 (dd, J = 8.0, 4.4 Hz, 2H), 7.53 – 7.44 (m, 2H), 7.13 (dd, J = 5.2, 3.6 Hz, 1H), 6.91 – 6.81 (m, 2H), 4.44 – 4.28 (m, 1H), 3.70 (s, 3H), 2.61 (dd, J = 14.4, 6.4 Hz, 1H), 2.46 (dd, J = 14.4, 6.4 Hz, 1H), 1.21 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.5, 160.3, 155.1, 140.3, 132.3, 130.6, 127.9, 127.8, 120.8, 113.8, 55.1, 43.0, 42.9, 20.3 ppm. **HRMS** calc'd for $C_{16}H_{19}N_2O_3S^+$ 319.1111, found 319.1115 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.91 min, t_{minor} = 14.26 min; **$[\alpha]_D^{20}$** = 21.04 (*c* 1.0, MeOH).

(*S*)-*N*-(4-Methoxyphenyl)-3-pivalamidobutanamide (5ao)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(tert-butyl)-1,4,2-dioxazol-5-one **2o** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ao** (38.5 mg, 66% yield, 91% *ee*) as a white solid. **Mp**: 153 – 155 °C. **R_f** = 0.30 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.51 – 7.42 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 6.91 – 6.79 (m, 2H), 4.17 (dt, J = 14.0, 6.8 Hz, 1H), 3.70 (s, 3H), 2.47 (dd, J = 14.0, 7.2 Hz, 1H), 2.37 (dd, J = 14.0, 7.2 Hz, 1H), 1.10 (d, J = 6.8 Hz, 3H), 1.06 (s, 9H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 176.5, 168.9, 155.1, 132.3, 120.8, 113.8, 55.1, 42.7, 42.4, 37.9, 27.4, 20.2 ppm. **HRMS** calc'd for $C_{16}H_{25}N_2O_3^+$ 293.1860, found 293.1855 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 4.72 min, t_{minor} = 10.44 min; **$[\alpha]_D^{20}$** = 20.20 (*c* 1.0, MeOH).

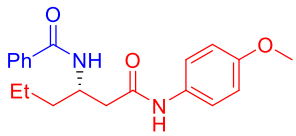
(*S*)-*N*-(4-(Benzylamino)-4-oxobutan-2-yl)benzamide (5ba)



The reaction was performed with *N*-benzylbut-3-enamide **4b** (35.0 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ba** (50.9 mg, 86% yield, 96% *ee*) as a

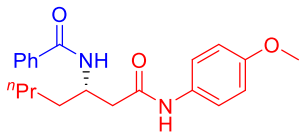
white solid. **Mp**: 192 – 194 °C. $\mathbf{R_f}$ = 0.33 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.41 (t, J = 6.0 Hz, 1H), 8.32 (d, J = 8.0 Hz, 1H), 7.91 – 7.74 (m, 2H), 7.59 – 7.52 (m, 1H), 7.50 – 7.39 (m, 2H), 7.33 – 7.11 (m, 5H), 4.44 – 4.34 (m, 1H), 4.36 – 4.19 (m, 2H), 2.53 (dd, J = 14.0, 7.6 Hz, 1H), 2.37 (dd, J = 14.0, 7.6 Hz, 1H), 1.18 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.2, 165.4, 139.5, 134.8, 131.0, 128.2, 127.2, 127.1, 126.7, 43.0, 42.0, 42.0, 20.3 ppm. **HRMS** calc'd for $C_{18}H_{21}N_2O_2^+$ 297.1598, found 297.1593 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.23 min, t_{minor} = 32.67 min; $\mathbf{[\alpha]_D^{20}}$ = 21.66 (*c* 1.0, MeOH).

(*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxohexan-3-yl)benzamide (5ca)



The reaction was performed with (*E*)-*N*-(4-methoxyphenyl)hex-3-enamide **4c** (43.8 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5ca** (25.8 mg, 38% yield, 98% *ee*) as a white solid. **Mp**: 200 – 202 °C. $\mathbf{R_f}$ = 0.35 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 7.88 – 7.77 (m, 2H), 7.54 – 7.49 (m, 1H), 7.49 – 7.43 (m, 4H), 6.86 (d, J = 8.8 Hz, 2H), 4.38 (m, 1H), 3.71 (s, 3H), 2.54 (m, 2H), 1.63 – 1.50 (m, 2H), 1.40 – 1.27 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 165.8, 155.1, 134.9, 132.3, 131.0, 128.2, 127.2, 120.8, 113.8, 55.2, 46.7, 42.0, 36.2, 19.0, 13.9 ppm. **HRMS** calc'd for $C_{20}H_{23}N_2O_3^-$ 339.1714, found 339.1733 $[M-H]^-$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.59 min, t_{minor} = 12.96 min; $\mathbf{[\alpha]_D^{20}}$ = 32.58 (*c* 1.0, MeOH).

(*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxoheptan-3-yl)benzamide (5da)



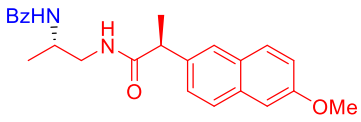
The reaction was performed with (*E*)-*N*-(4-methoxyphenyl)hept-3-enamide **4d** (46.6 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **5da** (21.2 mg, 30% yield, 95% *ee*) as a white solid. **Mp**: 208 – 210 °C. $\mathbf{R_f}$ = 0.33 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.25 (d, J =

8.4 Hz, 1H), 7.90 – 7.74 (m, 2H), 7.55 – 7.48 (m, 1H), 7.48 – 7.42 (m, 4H), 6.90 – 6.78 (m, 2H), 4.36 (h, *J* = 7.2 Hz, 1H), 3.70 (s, 3H), 2.53 (m, 2H), 1.57 (d, *J* = 6.8 Hz, 2H), 1.28 (m, 4H), 0.88 – 0.82 (t, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.7, 165.8, 155.1, 134.9, 132.3, 131.0, 128.2, 127.2, 120.8, 113.8, 55.1, 46.9, 42.0, 33.6, 27.9, 22.0, 14.0 ppm. **HRMS** calc'd for $C_{21}H_{25}N_2O_3^-$ 353.1871, found 353.1873 $[M-H]^-$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 10.47 min, t_{minor} = 13.40 min; $\mathbf{[\alpha]_D^{20}}$ = 35.39 (*c* 1.0, MeOH).

Hydroamidation of natural products and bioactive molecules derivatives

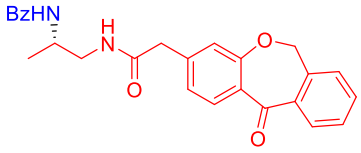
Same as standard condition, in a glove box under a nitrogen atmosphere, $NiBr_2$ (4.4 mg, 0.02 mmol, 10 mol%) and **L5** (12.6 mg, 0.03 mmol, 15 mol%) were added to a dry 8 ml reaction vial containing a magnetic stir bar. Then, 2 ml of anhydrous DMA was added to the mixture, which was stirred at room temperature for 10 minutes. Subsequently, $(MeO)_3SiH$ (50 mg, 0.4 mmol, 2.0 equiv.) and NaI (15 mg, 0.1 mmol, 50 mol%) were sequentially added to the mixture and stirred. *N*-allyl-amides **1** or but-3-enamides **3** were then added to the mixture and finally 1,4,2-dioxazol-5-ones **2** were added. The reaction vial was sealed and taken out of the glove box, and the mixture was stirred at room temperature for 48 hours. After the completion of the reaction, 2 ml of EA was added to the reaction vial for dilution. Extraction was performed using 50 ml of EA and 20 ml of saturated NaCl solution. The organic phase was further extracted using 2×30 ml of saturated NaCl solution. The organic phase was then dried using anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude material was loaded onto a silica gel column and purified by flash chromatography to to obtain **6-11**.

***N*-((*S*)-1-((*S*)-2-(6-Methoxynaphthalen-2-yl)propanamido)propan-2-yl)benzamide (6)**



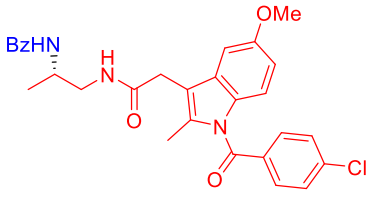
The reaction was performed with (*S*)-*N*-allyl-2-(6-methoxynaphthalen-2-yl)propanamide **1g** (53.8 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **6** (60.1 mg, 77% yield, 96% de) as a white solid. **Mp**: 202 – 204 °C. $\mathbf{R_f}$ = 0.23 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.22 – 8.05 (m, 2H), 7.78 – 7.72 (m, 2H), 7.72 – 7.67 (m, 2H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.39 (td, *J* = 8.4, 1.6 Hz, 3H), 7.22 (d, *J* = 2.4 Hz, 1H), 7.11 (dd, *J* = 9.2, 2.4 Hz, 1H), 4.16 – 4.00 (m, 1H), 3.85 (s, 3H), 3.74 (q, *J* = 7.2 Hz, 1H), 3.20 (td, *J* = 6.4, 3.6 Hz, 2H), 1.41 (d, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 174.0, 165.9, 157.0, 137.3, 134.7, 133.1, 131.0, 129.1, 128.4, 128.1, 127.2, 126.6, 126.5, 125.2, 118.5, 105.7, 55.1, 45.4, 45.1, 43.6, 18.5, 18.0 ppm. **HRMS** calc'd for $C_{24}H_{27}N_2O_3^+$ 391.2016, found 391.2013 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.62 min, t_{minor} = 13.28 min; $\mathbf{[\alpha]_D^{20}}$ = 5.55 (*c* 1.0, MeOH).

(*S*)-*N*-(1-(2-(11-oxo-6,11-Dihydrodibenzo[*b*,*e*]oxepin-3-yl)acetamido)propan-2-yl)benzamide (7)



The reaction was performed with *N*-allyl-2-(11-oxo-6,11-dihydrodibenzo[*b*,*e*]oxepin-3-yl)acetamide **1h** (61.4 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **7** (68.5 mg, 80% yield, 90% ee) as a white solid. **Mp**: 216 – 218 °C. **R**$_f$ = 0.20 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.24 (t, *J* = 6.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.77 (td, *J* = 7.6, 7.2, 1.2 Hz, 3H), 7.66 (td, *J* = 7.2, 1.2 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.50 – 7.38 (m, 4H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.25 (s, 2H), 4.19 – 3.96 (m, 1H), 3.46 (s, 2H), 3.22 (t, *J* = 6.8 Hz, 2H), 1.10 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 190.2, 170.6, 165.8, 159.6, 140.0, 136.5, 135.9, 134.7, 133.0, 131.4, 131.0, 130.2, 129.2, 128.8, 128.3, 128.1, 127.2, 124.5, 120.5, 72.7, 45.4, 43.6, 41.2, 18.0 ppm. **HRMS** calc'd for $C_{26}H_{25}N_2O_4^+$ 429.1809, found 429.1812 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 35.23 min, t_{minor} = 37.60 min; **[α]$_D^{20}$** = 19.64 (*c* 1.0, MeOH).

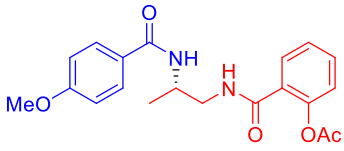
(*S*)-*N*-(1-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)propan-2-yl)benzamide (8)



The reaction was performed with *N*-allyl-2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamide **1i** (79.2 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one **2a** (57.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 2) to give the product **8** (83.9 mg, 81% yield, 91% ee) as a white solid. **Mp**: 196 – 198 °C. **R**$_f$ = 0.25 (petroleum ether : ethyl acetate = 1 : 2). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.16 (d, *J* = 8.0 Hz, 1H), 8.12 (t, *J* = 6.0 Hz, 1H), 7.78 – 7.69 (m, 2H), 7.69 – 7.57 (m, 4H), 7.52 – 7.43 (m, 1H), 7.38 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.11 (d, *J* = 2.4 Hz, 1H), 6.95 (d, *J* = 9.2 Hz, 1H), 6.69 (dd, *J* = 9.2, 2.4 Hz, 1H), 4.08 (dq, *J* = 15.2, 8.4 Hz, 1H), 3.73 (s, 3H), 3.53 (s, 2H), 3.32 – 3.13 (m, 2H), 2.17 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.0, 167.8, 165.9, 155.6, 137.5, 135.2, 134.7, 134.3, 131.1, 131.0, 130.9, 130.3, 129.0, 128.1, 127.2, 114.6, 114.2, 111.4, 101.7, 55.4, 45.5, 43.8, 31.1, 18.0,

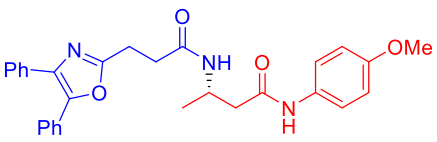
13.3 ppm. **HRMS** calc'd for $C_{29}H_{29}ClN_3O_4^+$ 518.1841, found 518.1844 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.58 min, t_{minor} = 11.02 min; $[\alpha]_D^{20}$ = -7.43 (c 1.0, MeOH).

(*S*)-2-((2-(4-Methoxybenzamido)propyl)carbamoyl)phenyl acetate (9)



The reaction was performed with 2-(allylcarbamoyl)phenyl acetate **1j** (43.8 mg, 0.2 mmol) and 3-(4-methoxyphenyl)-1,4,2-dioxazol-5-one **2g** (77.2 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 2) to give the product **9** (59.9 mg, 81% yield, 99% ee) as a white solid. **Mp**: 220 – 222 °C. $\mathbf{R}_f$ = 0.22 (petroleum ether : ethyl acetate = 1 : 2). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.39 (t, *J* = 6.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.80 (m, 2H), 7.55 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.49 (td, *J* = 7.6, 1.6 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.16 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.00 – 6.96 (m, 2H), 4.19 (dt, *J* = 13.6, 6.8 Hz, 1H), 3.80 (s, 3H), 3.32 (t, *J* = 11.6 Hz, 2H), 2.16 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 168.9, 165.7, 165.4, 161.5, 148.0, 131.2, 129.5, 129.1, 128.9, 127.0, 125.8, 123.3, 113.4, 55.4, 45.2, 44.1, 20.7, 18.0 ppm. **HRMS** calc'd for $C_{20}H_{23}N_2O_5^+$ 371.1601, found 371.1598 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 12.16 min, t_{minor} = 17.74 min; $[\alpha]_D^{20}$ = 18.22 (*c* 1.0, MeOH).

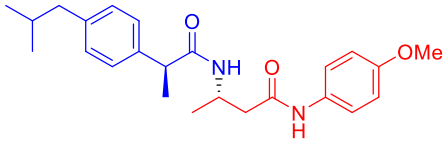
(*S*)-3-(3-(4,5-Diphenyloxazol-2-yl)propanamido)-*N*-(4-methoxyphenyl)butanamide (10)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and 3-(2-(4,5-diphenyloxazol-2-yl)ethyl)-1,4,2-dioxazol-5-one **2p** (133.6 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 2) to give the product **10** (69.6 mg, 72% yield, 93% ee) as a white solid. **Mp**: 232 – 234 °C. $\mathbf{R}_f$ = 0.18 (petroleum ether : ethyl acetate = 1 : 2). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.50 (m, 4H), 7.50 – 7.46 (m, 2H), 7.46 – 7.34 (m, 6H), 6.89 – 6.77 (m, 2H), 4.25 – 4.16 (m, 1H), 3.70 (s, 3H), 3.09 – 2.97 (m, 2H), 2.61 (td, *J* = 7.2, 1.6 Hz, 2H), 2.49 – 2.43 (m, 1H),

2.34 (dd, J = 14.0, 8.0 Hz, 1H), 1.09 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 169.6, 168.4, 162.7, 155.1, 144.5, 134.3, 132.3, 132.1, 129.0, 128.8, 128.7, 128.5, 128.1, 127.4, 126.4, 120.8, 113.8, 55.1, 43.1, 42.3, 31.9, 23.4, 20.2 ppm. **HRMS** calc'd for $C_{29}H_{30}N_3O_4^+$ 484.2231, found 484.2229 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.45 min, t_{minor} = 12.54 min; **$[\alpha]_D^{20}$** = 31.51 (*c* 1.0, MeOH).

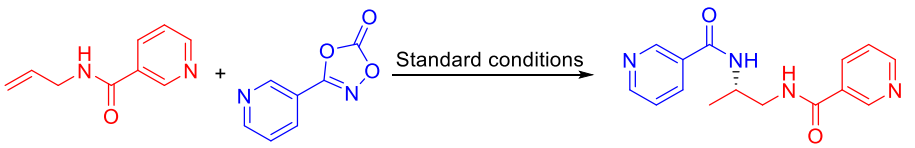
(*S*)-3-((*S*)-2-(4-Isobutylphenyl)propanamido)-*N*-(4-methoxyphenyl)butanamide (11)



The reaction was performed with *N*-(4-methoxyphenyl)but-3-enamide **4a** (38.2 mg, 0.2 mmol) and (*S*)-3-(1-(4-isobutylphenyl)ethyl)-1,4,2-dioxazol-5-one **2q** (98.8 mg, 0.4 mmol). The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 1.5) to give the product **11** (53.8 mg, 68% yield, 96% de) as a white solid. **Mp**: 194 – 196 °C. **R_f** = 0.22 (petroleum ether : ethyl acetate = 1 : 1.5). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.68 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.89 – 6.79 (m, 2H), 4.18 – 4.10 (m, 1H), 3.71 (s, 3H), 3.52 (q, J = 7.2 Hz, 1H), 2.40 (dd, J = 14.4, 6.0 Hz, 1H), 2.35 (d, J = 7.1 Hz, 2H), 2.26 (dd, J = 14.4, 6.0 Hz, 1H), 1.82 – 1.69 (m, 1H), 1.28 (d, J = 7.2 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 6H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 172.6, 168.4, 155.1, 139.5, 139.0, 132.3, 128.7, 126.9, 120.7, 113.7, 55.1, 44.6, 44.3, 42.8, 42.3, 29.6, 22.2, 20.2, 18.4 ppm. **HRMS** calc'd for $C_{24}H_{33}N_2O_3^+$ 397.2486, found 397.2490 $[M+H]^+$; **HPLC analysis:** Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 5.09 min, t_{minor} = 10.91 min; **$[\alpha]_D^{20}$** = 72.05 (*c* 1.0, MeOH).

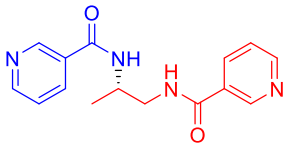
Synthesis of (*S*)-Nicaraven

Same as standard condition, in a glove box under a nitrogen atmosphere, $NiBr_2$ (4.4 mg, 0.02 mmol, 10 mol%) and **L5** (12.6 mg, 0.03 mmol, 15 mol%) were added to a dry 8 ml reaction vial containing a magnetic stir bar. Then, 2 ml of anhydrous DMA was added to the mixture, which was stirred at room temperature for 10 minutes. Subsequently, $(MeO)_3SiH$ (50 mg, 0.4 mmol, 2.0 equiv.) and NaI (15 mg, 0.1 mmol, 50 mol%) were sequentially added to the mixture and stirred. *N*-allylnicotinamide **1k** (32.4 mg, 0.2 mmol, 1.0 equiv.) was then added to the mixture and finally 3-(pyridin-3-yl)-1,4,2-dioxazol-5-one **2r** (65.6 mg, 0.4 mmol, 2.0 equiv.) were added. The reaction vial was sealed and taken out of the glove box, and the mixture was stirred at room temperature for 48 hours. After the completion of the reaction, 2 ml of EA was added to the reaction vial for dilution. Extraction was performed using 50 ml of EA and 20 ml of saturated NaCl solution. The organic phase was further extracted using 2×30 ml of saturated NaCl solution. The organic phase was then dried using anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude material was loaded onto a silica gel column and purified by flash chromatography to to obtain (*S*)-Nicaraven.



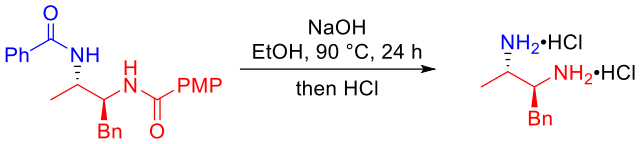
1i **2r** **(*S*)-Nicaraven**, 71% IY, 99% ee

(*S*)-*N*,*N*′-(Propane-1,2-diyl)dinicotinamide ((*S*)-Nicaraven)



The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 1 : 2) to give the product (40.3 mg, 71% yield, 99% *ee*) as a white solid. **Mp**: 154 – 156 °C. $\mathbf{R_f}$ = 0.16 (petroleum ether : ethyl acetate = 1 : 2). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.05 – 8.95 (m, 2H), 8.79 (t, J = 6.0 Hz, 1H), 8.68 (dt, J = 4.8, 1.2 Hz, 2H), 8.50 (d, J = 8.4 Hz, 1H), 8.15 (dd, J = 7.8, 5.6 Hz, 2H), 7.55 – 7.42 (m, 2H), 4.40 – 4.19 (m, 1H), 3.45 – 3.36 (m, 2H), 1.19 (d, J = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, DMSO-d_6) δ 165.4, 164.6, 151.8, 151.7, 148.5, 148.4, 135.1, 135.0, 130.3, 130.2, 123.5, 123.4, 45.4, 44.2, 17.9.ppm. **HRMS** calc'd for $C_{15}H_{17}N_4O_2^+$ 285.1346, found 285.1347 $[M+H]^+$; **HPLC analysis**: Daicel CHIRALPAK AD-3 *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 24.04 min; $[\alpha]_D^{20}$ = 28.02 (*c* 1.0, MeOH).

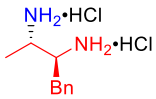
Hydrolysis of 3ca



3ca **12**, 95% yield

According to the literature.[17] In a dry 8 ml reaction vial containing a magnetic stirrer, **3ca** (38.7 mg, 0.1 mmol, 1.0 equiv), NaOH (80 mg, 2 nnol, 20.0 equiv), and finally 2 ml of anhydrous ethanol were added sequentially and after sealing the reaction vial, the reaction was carried out at 90°C for 24 h. After monitoring the completion of the reaction, the solvent was removed under vacuum. The crude product was dissolved using 10 ml of water and 20 ml of ethyl acetate, next 10 ml of 2N HCl solution was added to the mixture and the aqueous phase was collected. The aqueous phase was washed with ethyl acetate 20 ml×3 and the aqueous phase was evaporated directly under vacuum to give the product **12** in 22.5 mg, 95% yield.

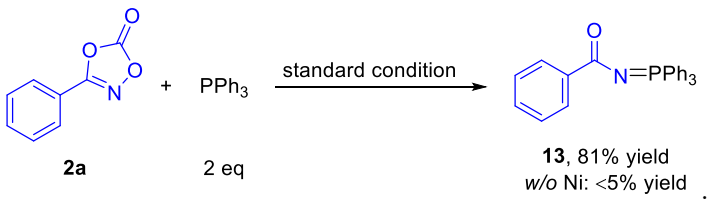
(2*S*,3*S*)-1-Phenylbutane-2,3-diaminium chloride (12)



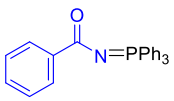
The product was obtained as white solid. **Mp**: 284 – 286 °C. **^{1}H NMR** (400 MHz, Deuterium Oxide) δ 7.74 (m, 5H), 4.38 – 4.23 (m, 2H), 3.58 (dd, *J* = 14.4, 3.2 Hz, 1H), 3.23 (dd, *J* = 14.4, 3.2 Hz, 1H), 1.83 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, Deuterium Oxide) δ 134.4, 130.0, 128.7, 54.7, 48.9, 32.8, 13.5 ppm, one resonance was not observed due to overlapping peaks. **HRMS** calc'd for $C_{10}H_{17}N_2^+$ ((2*S*,3*S*)-3-amino-1-phenylbutan-2-aminium) 165.1386, found 165.1380 $[M+H]^+$; $[\alpha]_D^{20}$ = -44.50 (*c* 1.0, MeOH).

Capture of metal-nitrenoid intermediate.

In a glove box under a nitrogen atmosphere, $NiBr_2$ (4.4 mg, 0.02 mmol, 10 mol%) and **L5** (12.6 mg, 0.03 mmol, 15 mol%) were added to a dry 8 ml reaction vial containing a magnetic stir bar. Then, 2 ml of anhydrous DMA was added to the mixture, which was stirred at room temperature for 10 minutes. Subsequently, $(MeO)_3SiH$ (50 mg, 0.4 mmol, 2.0 equiv.) and NaI (15 mg, 0.1 mmol, 50 mol%) were sequentially added to the mixture and stirred. Finally 3-phenyl-1,4,2-dioxazol-5-one **2a** (65.2 mg, 0.4 mmol) and **PPh_3** (209.8 mg, 0.8 mmol, 2.0 equiv.) were added. The reaction vial was sealed and taken out of the glove box, and the mixture was stirred at room temperature for 48 hours. After the completion of the reaction, 2 ml of EA was added to the reaction vial for dilution. Extraction was performed using 50 ml of EA and 20 ml of saturated NaCl solution. The organic phase was further extracted using 2×30 ml of saturated NaCl solution. The organic phase was then dried using anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude material was loaded onto a silica gel column and purified by flash chromatography to to obtain metal-nitrenoid intermediate **13.** In addition, no generation of **13** was detected in the absence of the Ni catalyst.



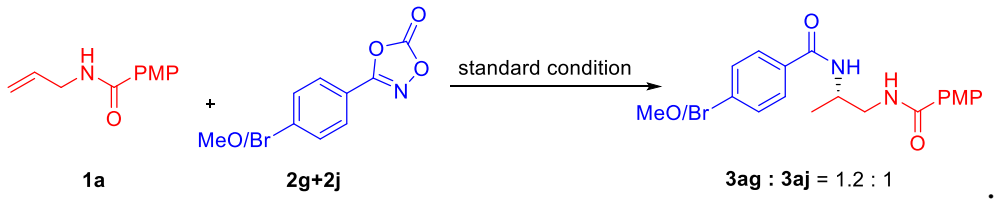
N-(Triphenyl-l5-phosphanylidene)benzamide (13)



The crude product was separated by flash chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1) to give the product (61.9 mg, 71% yield) as a white solid. $\mathbf{R}_f$ = 0.45 (petroleum ether : ethyl acetate = 4 : 1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.43 – 8.34 (m, 2H), 7.93 – 7.80 (m, 6H), 7.60 – 7.53 (m, 3H), 7.53 – 7.39 (m, 9H) ppm. **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 176.4 (d, $J_{C\text{-}P}$ = 7.7 Hz), 138.6 (d, $J_{C\text{-}P}$ = 20.5 Hz), 133.2 (d, $J_{C\text{-}P}$ = 9.9 Hz), 132.3 (d, $J_{C\text{-}P}$ = 3.0 Hz), 130.8, 129.6 (d, $J_{C\text{-}P}$ = 2.4 Hz), 128.8 (d, $J_{C\text{-}P}$ = 12.1 Hz), 128.4 (d, $J_{C\text{-}P}$ = 99.0 Hz), 127.7 ppm. **^{31}P NMR** (162 MHz, Chloroform-*d*) δ 20.73 ppm. The ^{1}H , ^{13}C{^{1}H} and ^{31}P data for this compound match the literature data.[18]

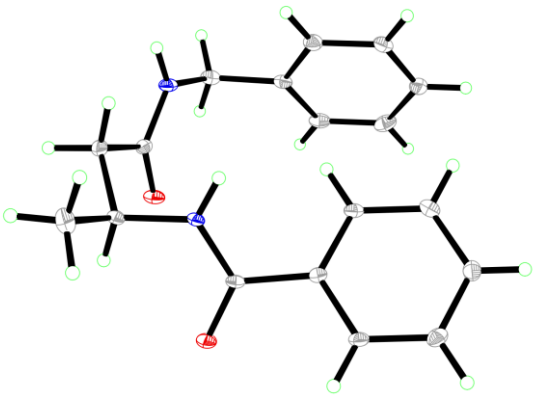
Competitive experiment

In a glove box under a nitrogen atmosphere, $NiBr_2$ (2.2 mg, 0.01 mmol, 10 mol%) and **L5** (6.3 mg, 0.015 mmol, 15 mol%) were added to a dry 8 ml reaction vial containing a magnetic stir bar. Then, 1 ml of anhydrous DMA was added to the mixture, which was stirred at room temperature for 10 minutes. Subsequently, $(MeO)_3SiH$ (25 mg, 0.2 mmol, 2.0 equiv.) and NaI (7.5 mg, 0.05 mmol, 50 mol%) were sequentially added to the mixture and stirred. Finally *N*-allyl-4-methoxybenzamide **1a** (19.1 mg, 0.1 mmol, 1.0 equiv.), 3-(4-Methoxyphenyl)-1,4,2-dioxazol-5-one **2g** (38.6 mg, 0.2 mmol, 2.0 equiv.)and 3-(4-Bromophenyl)-1,4,2-dioxazol-5-one **2j** (48.2 mg, 0.2 mmol, 2.0 equiv.) were added. The reaction vial was sealed and taken out of the glove box, and the mixture was stirred at room temperature for 48 hours. After the completion of the reaction, 2 ml of EA was added to the reaction vial for dilution. Extraction was performed using 50 ml of EA and 20 ml of saturated NaCl solution. The organic phase was further extracted using 2×30 ml of saturated NaCl solution. The organic phase was then dried using anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude material was loaded onto a silica gel column and purified by flash chromatography to to obtain **3ag** (24.6 mg, 36% yield) and **3aj** (23.4 mg, 30% yield),yield of **3ag** : **3aj** = 1.2 : 1



1a **2g+2j** **3ag : 3aj** = 1.2 : 1

X-ray crystal structure of compound 5ba



Crystal structure of 5ba (CCDC 2293468)

A specimen of $C_{18}H_{20}N_2O_2$, approximate dimensions 0.100 mm x 0.120 mm x 0.210 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å).

The integration of the data using a monoclinic unit cell yielded a total of 25726 reflections to a maximum θ angle of 77.36° (0.79 Å resolution), of which 3249 were independent (average redundancy 7.918, completeness = 99.7%, R_{int} = 5.30%, R_{sig} = 2.98%) and 3192 (98.25%) were greater than $2\sigma(F^2)$. The final cell constants of a = 36.827(3) Å, b = 5.0991(3) Å, c = 8.2493(6) Å, β = 92.460(2)°, volume = 1547.66(18) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.5856 and 0.7541.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group C 1 2 1, with Z = 4 for the formula unit, $C_{18}H_{20}N_2O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 176 variables converged at R1 = 6.06%, for the observed data and wR2 = 16.04% for all data. The goodness-of-fit was 1.091. The largest peak in the final difference electron density synthesis was 0.438 $e^-/Å^3$ and the largest hole was -0.265 $e^-/Å^3$ with an RMS deviation of 0.074 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.272 g/cm^3 and F(000), 632 e^-.

Table S7. Sample and crystal data for 5ba.

Identification code	5ba
Chemical formula	$C_{18}H_{20}N_2O_2$
Formula weight	296.36 g/mol
Wavelength	1.54178 Å

Crystal size	0.100 x 0.120 x 0.210 mm
Crystal system	monoclinic
Space group	C 1 2 1
Unit cell dimensions	a = 36.827(3) Å α = 90°
	b = 5.0991(3) Å β = 92.460(2)°
	c = 8.2493(6) Å γ = 90°
Volume	1547.66(18) $Å^3$
Z	4
Density (calculated)	1.272 g/cm^3
Absorption coefficient	0.668 mm^{-1}
F(000)	632

Table S8. Data collection and structure refinement for 5ba.

Theta range for data collection	2.40 to 77.36°
Index ranges	-46<=h<=46, -6<=k<=6, -10<=l<=10
Reflections collected	25726
Independent reflections	3249 [R(int) = 0.0530]
Max. and min. transmission	0.7541 and 0.5856
Structure solution technique	direct methods
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	3249 / 1 / 176
Goodness-of-fit on F^2	1.091
Final R indices	3192 data; I>2σ(I) R1 = 0.0606, wR2 = 0.1600
	all data R1 = 0.0613, wR2 = 0.1604
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0589P)^2+5.1821P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.04(16)
Largest diff. peak and hole	0.438 and -0.265 $eÅ^{-3}$
R.M.S. deviation from mean	0.074 $eÅ^{-3}$

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NMR spectra of the products

Figure S1. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of (*N*-(But-3-en-2-yl)-4-methoxybenz amide (1b).

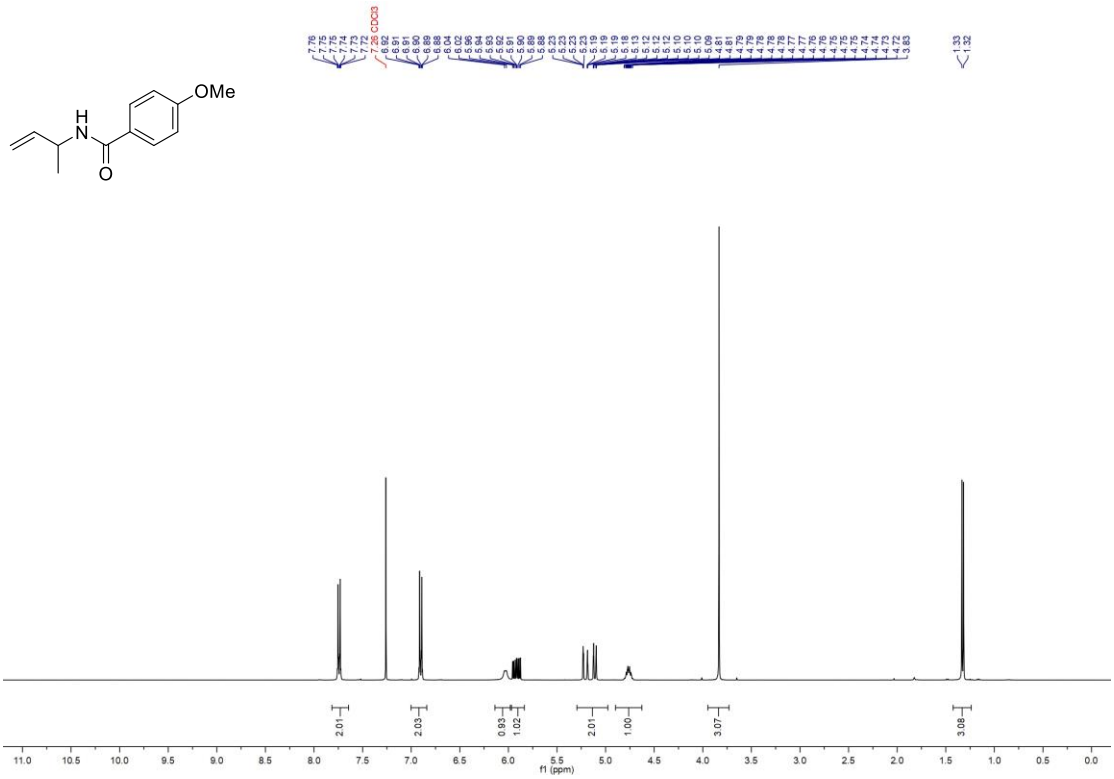


Figure S2. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of *N*-(But-3-en-2-yl)-4-methoxybenz amide (1b).

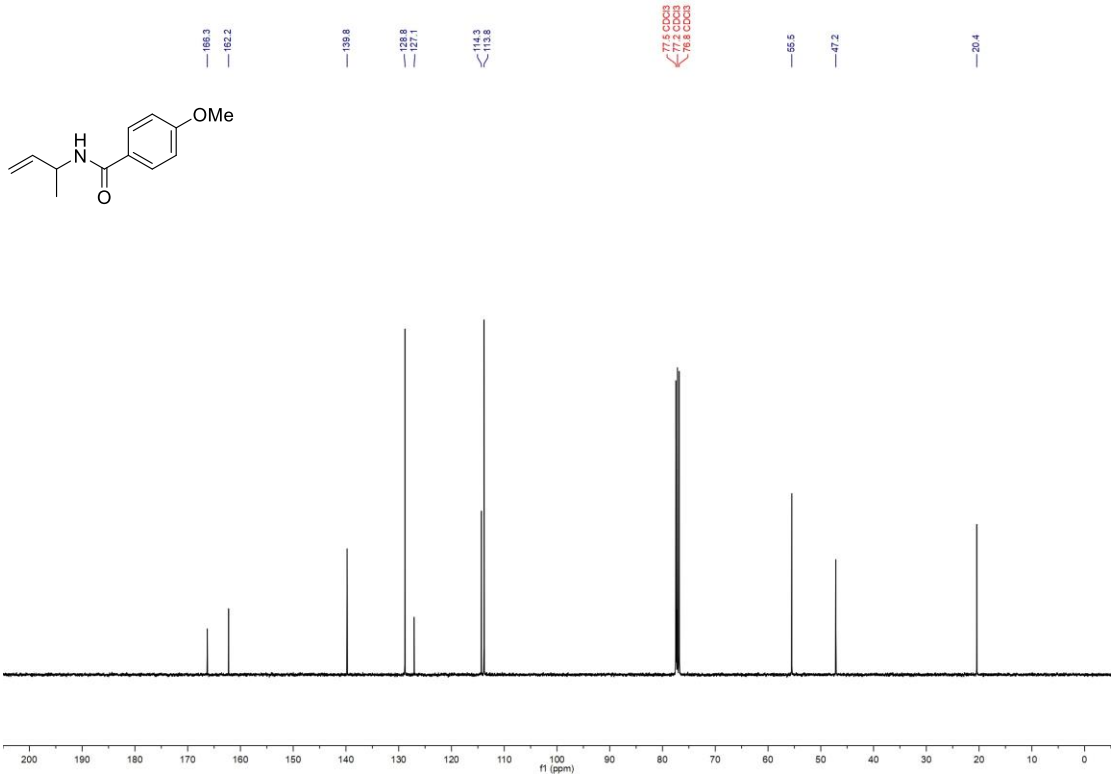


Figure S3. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of (*S*)-4-Methoxy-*N*-(1-phenylbut-3-en-2-yl)benzamide (1c).

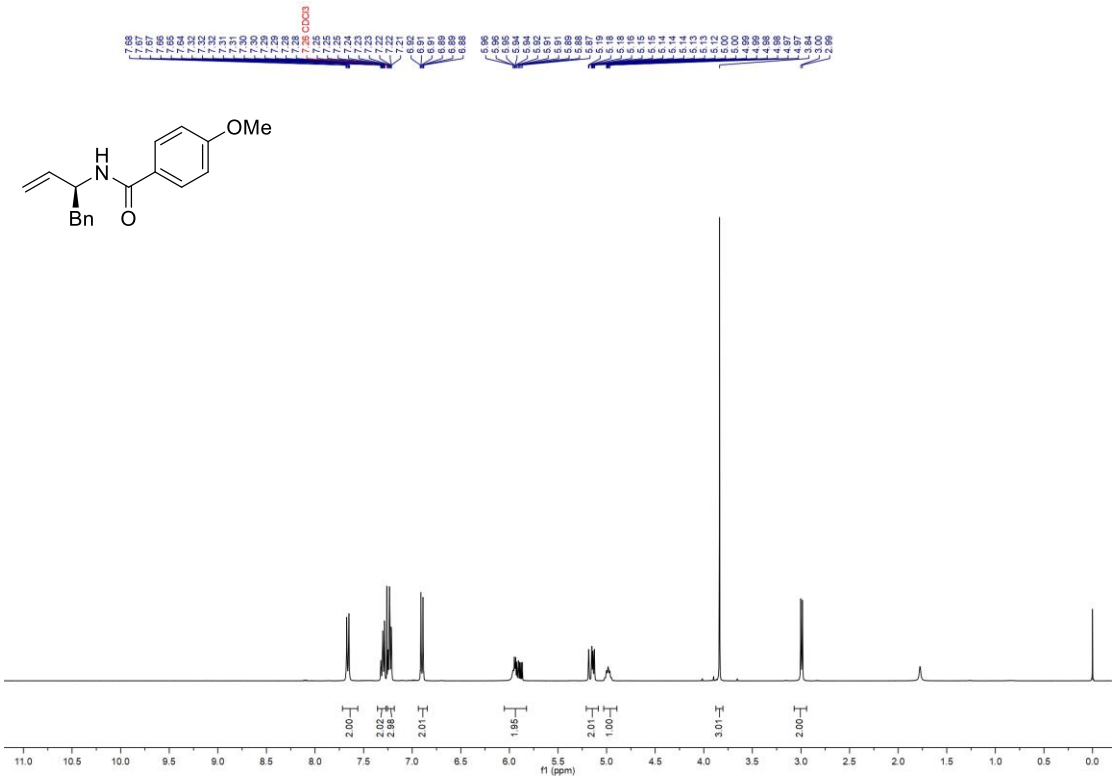


Figure S4. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of (*S*)-4-Methoxy-*N*-(1-phenylbut-3-en-2-yl)benzamide (1c).

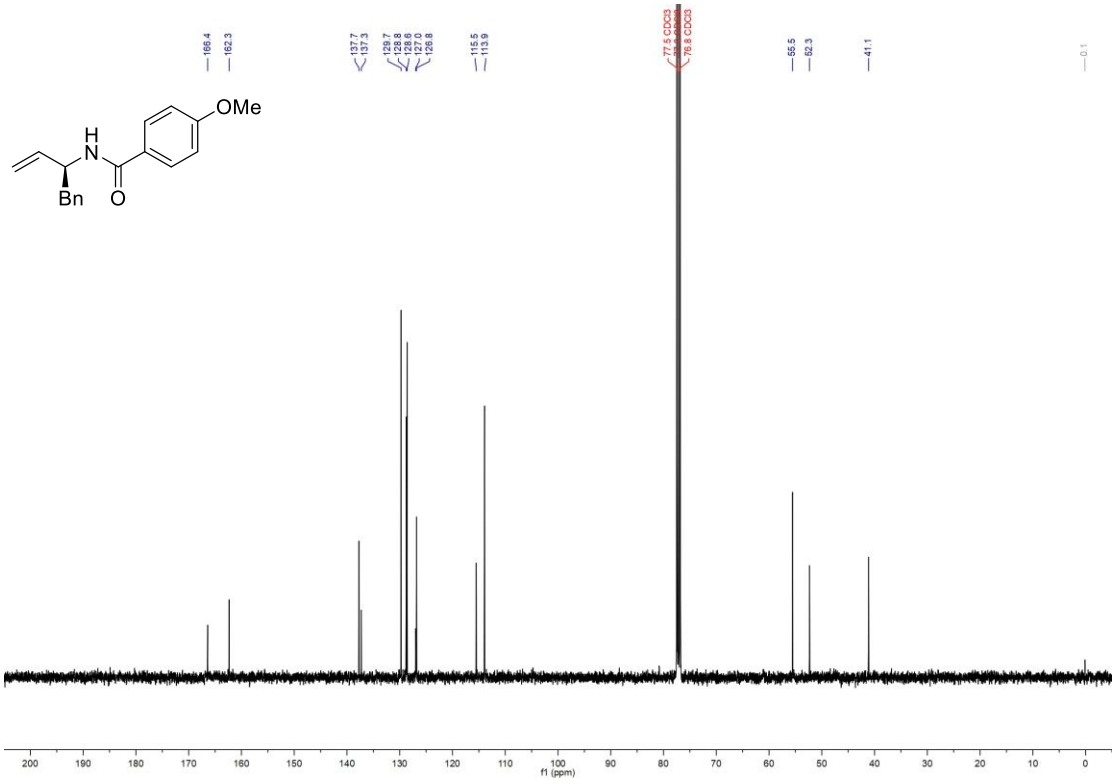


Figure S5. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of (*R*)-*N*-(1-Cyclohexylallyl)-4-metho xybenzamide (1d).

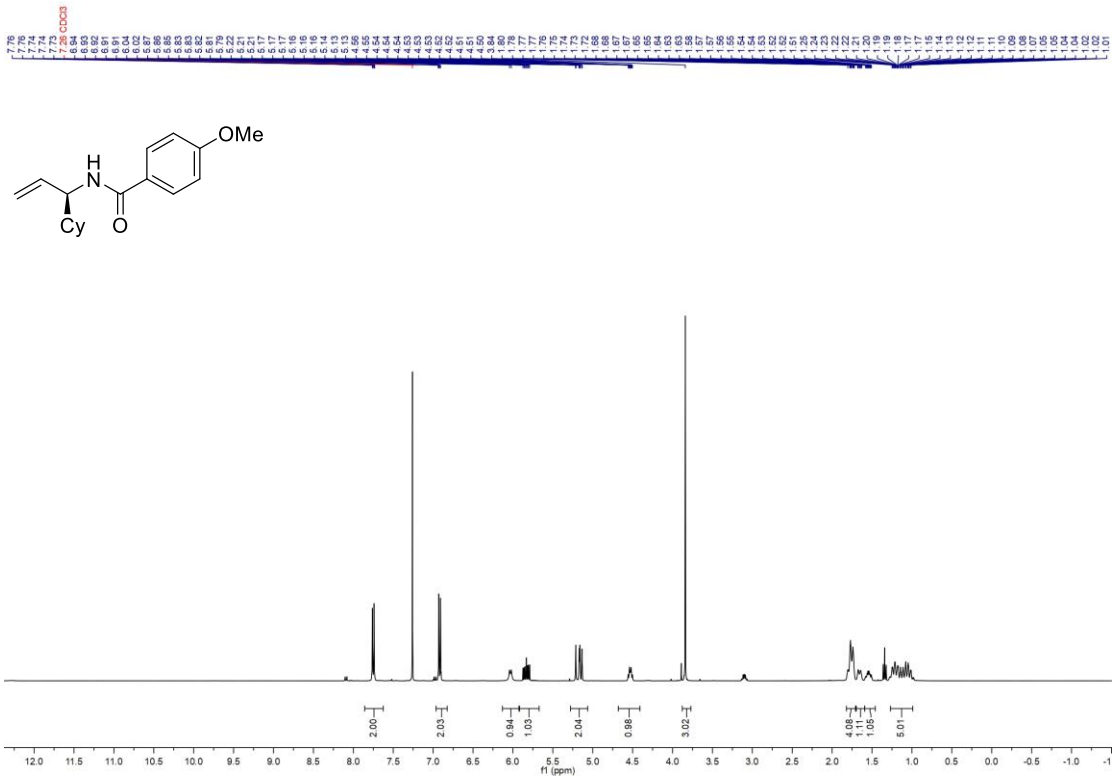


Figure S6. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of (*R*)-*N*-(1-Cyclohexylallyl)-4-metho xybenzamide (1d).

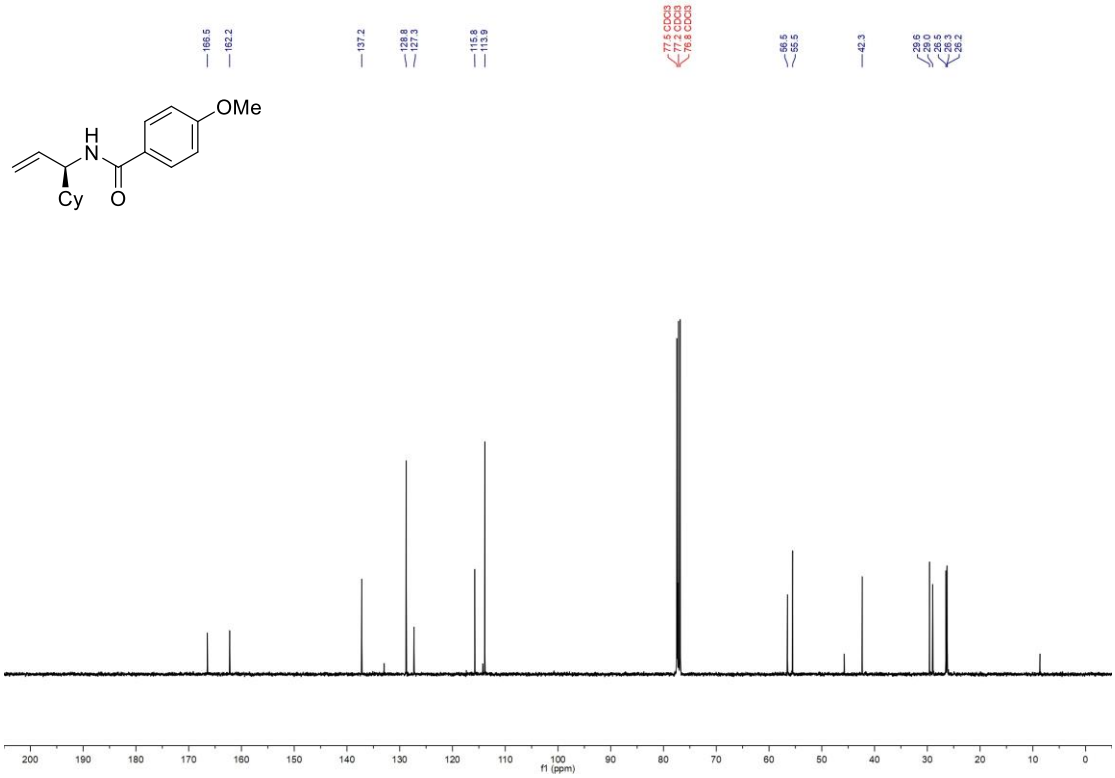


Figure S7. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of *N*-Allyl-2-(11-oxo-6,11-dihydrodib enzo[*b*,*e*]oxepin-3-yl)acetamide (1f).

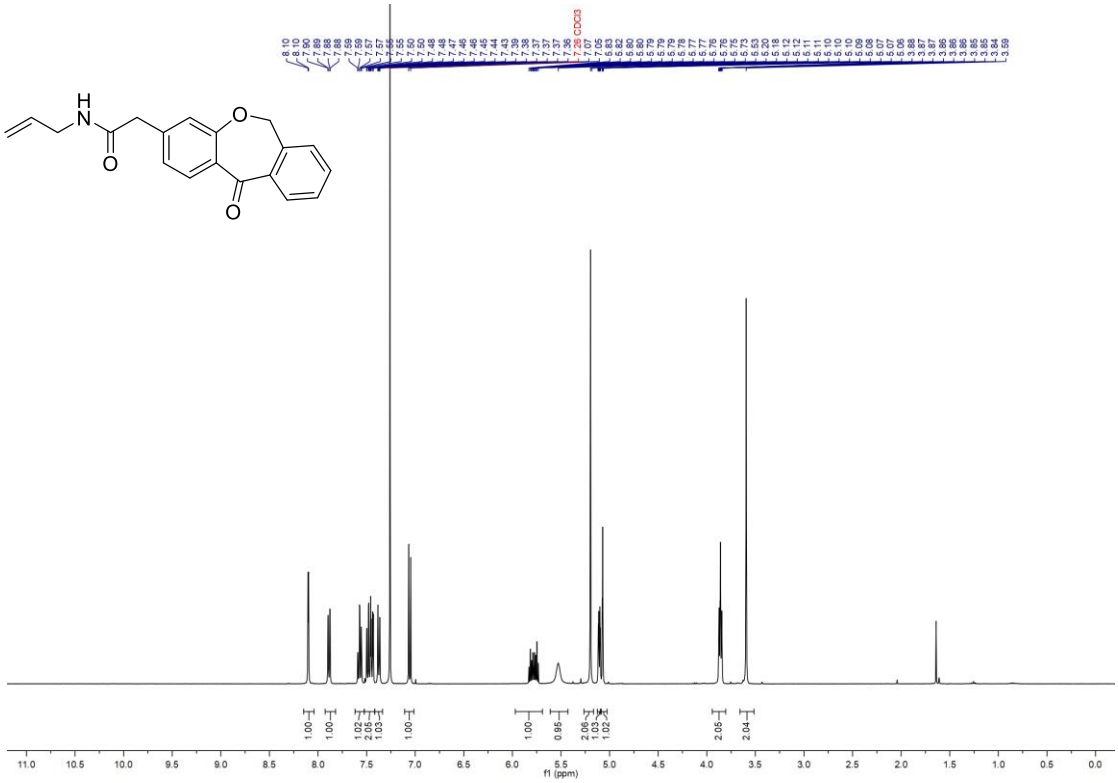


Figure S8. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of *N*-Allyl-2-(11-oxo-6,11-dihydrodib enzo[*b*,*e*]oxepin-3-yl)acetamide (1f).

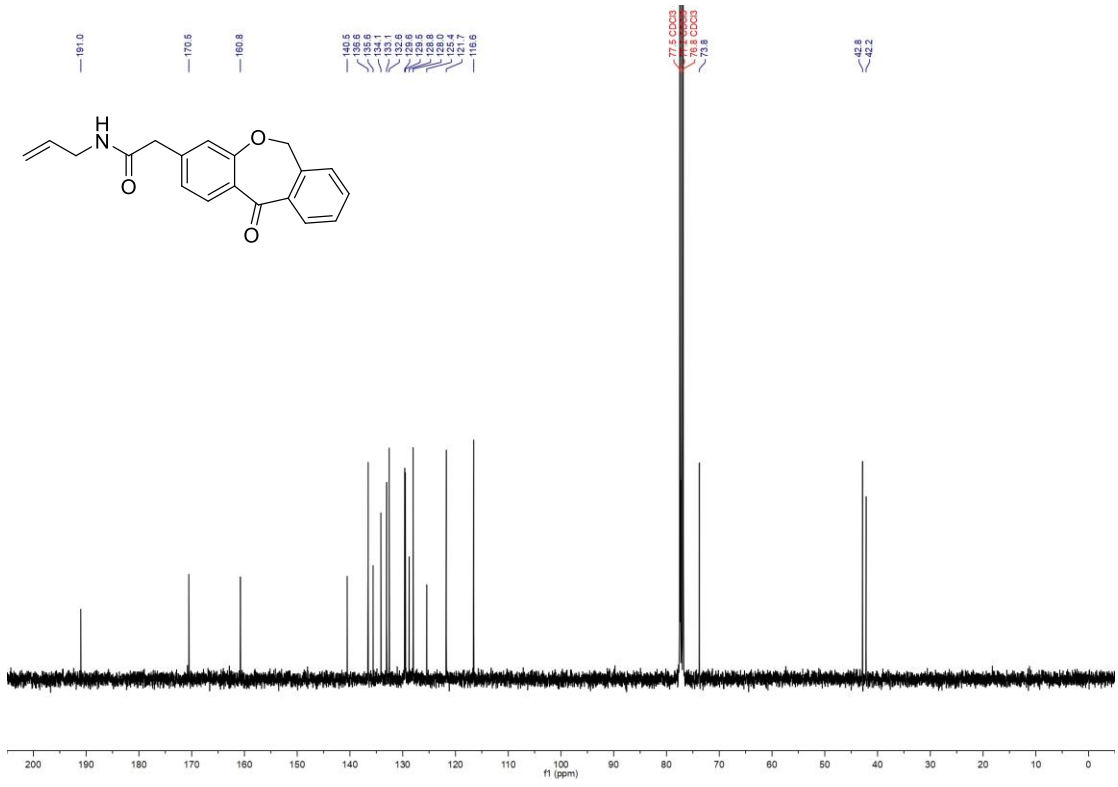


Figure S9. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of 2-(Allylcarbamoyl)phenyl acetate (1h).

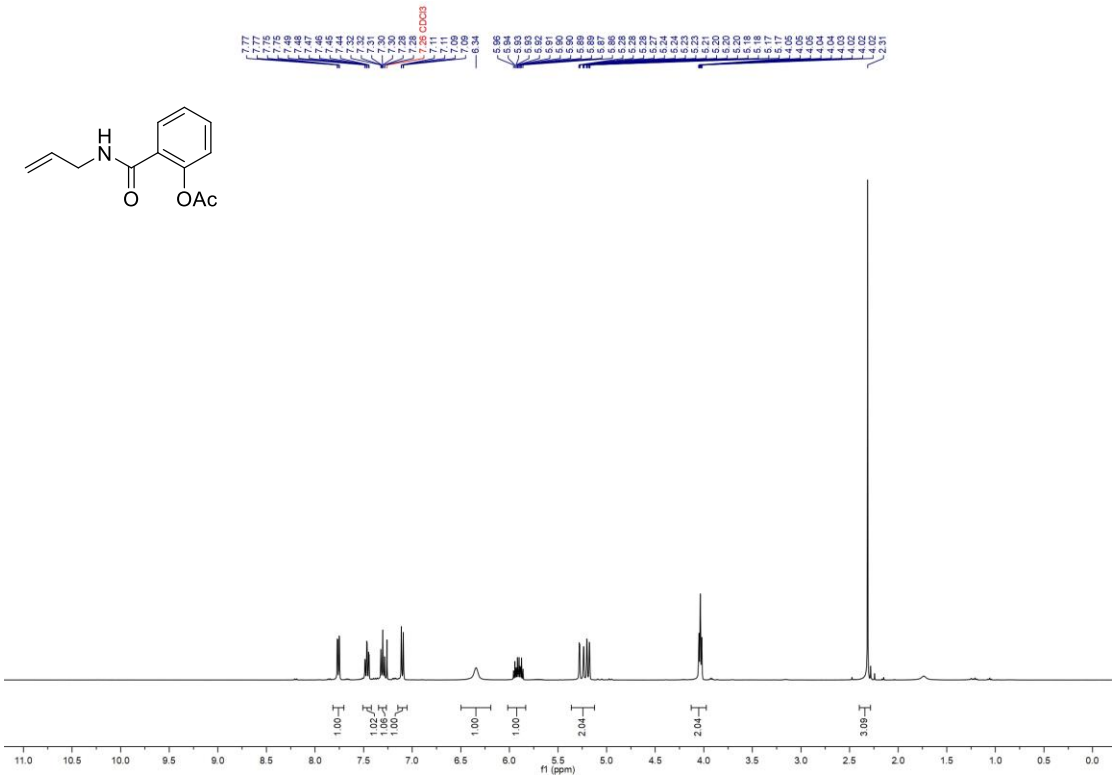


Figure S10. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of 2-(Allylcarbamoyl)phenyl acetate (1h).

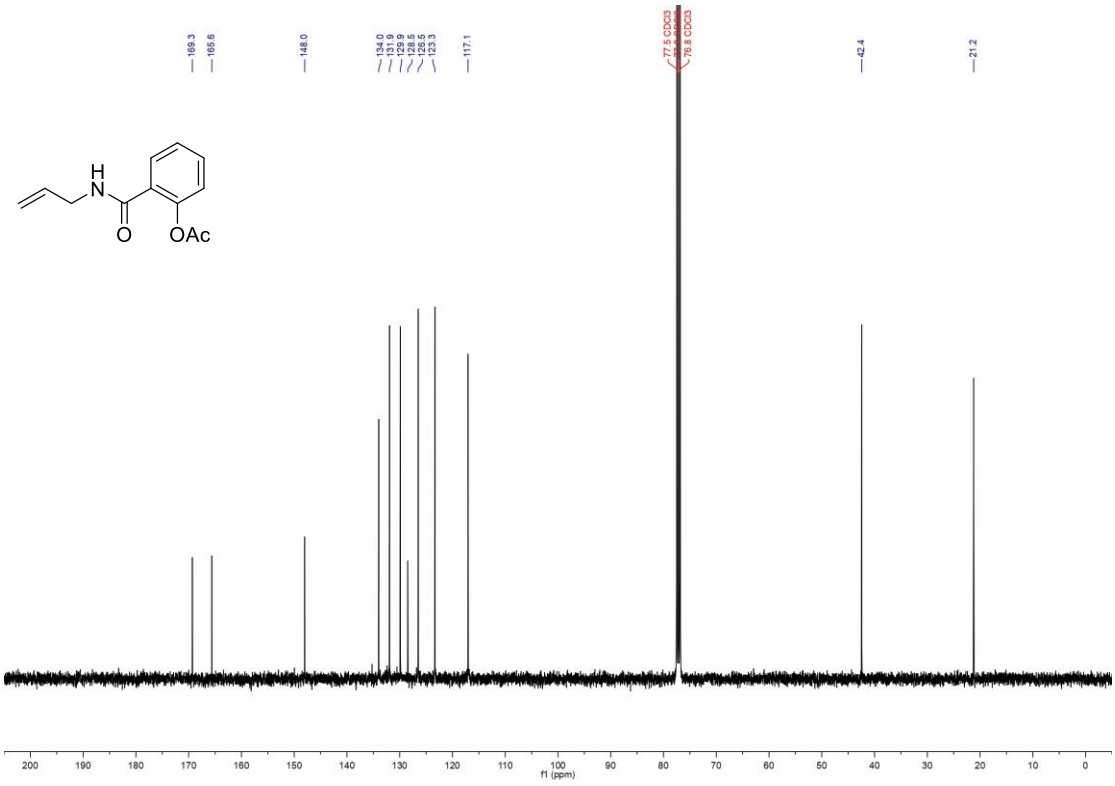


Figure S11. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of 3-(Pyridin-3-yl)-1,4,2-dioxazol-5-one (2r).

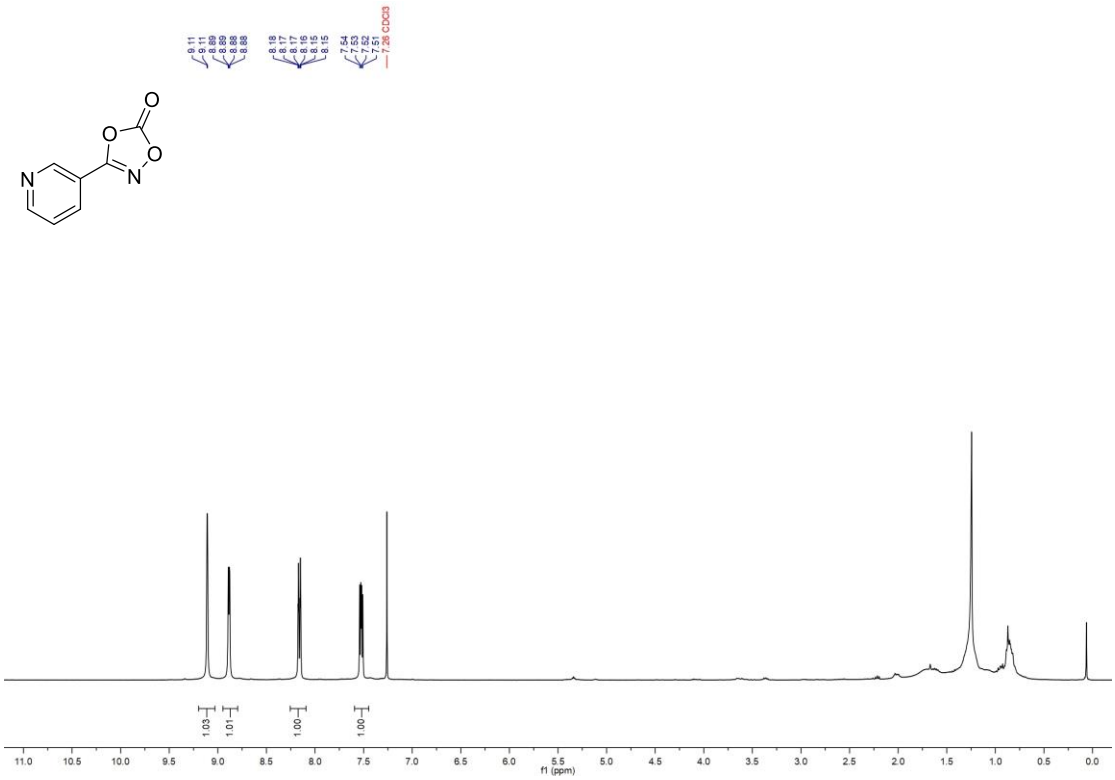


Figure S12. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of 3-(Pyridin-3-yl)-1,4,2-dioxazol-5-one (2r).

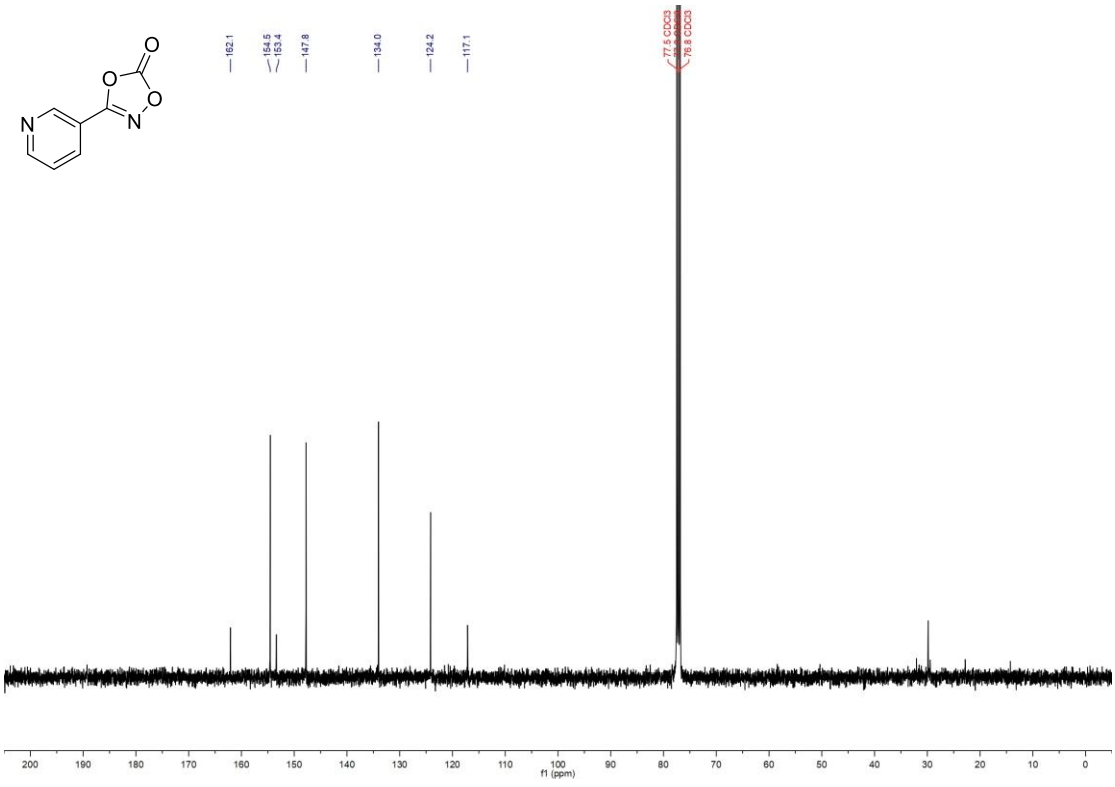


Figure S13. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(2-Benzamidopropyl)-4-methox ybenzamide (3aa).

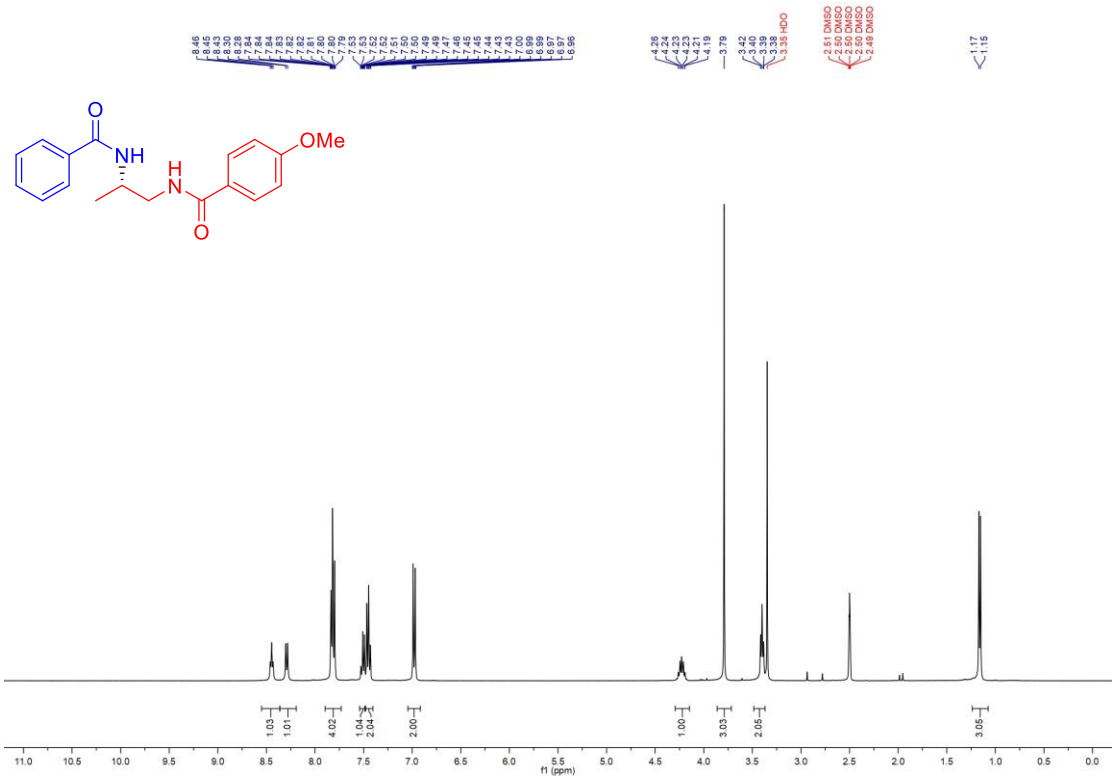


Figure S14. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(2-Benzamidopropyl)-4-metho xybenzamide (3aa).

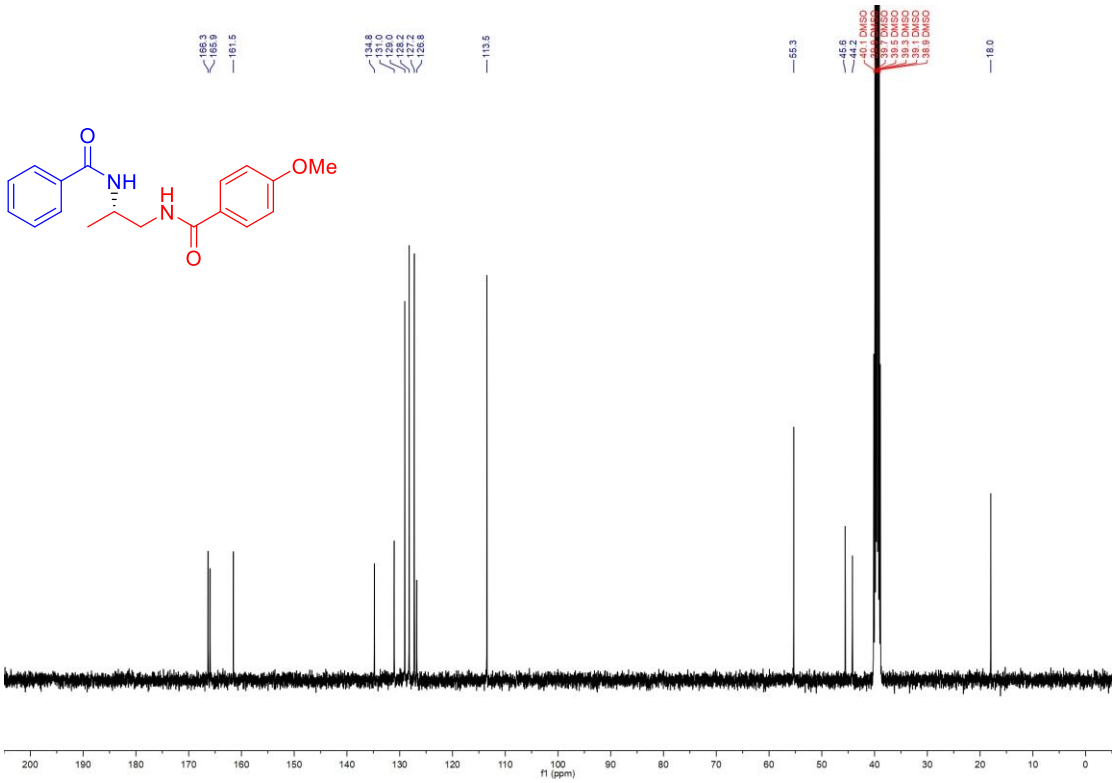


Figure S15. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-2-methylbenzamide (3ab).

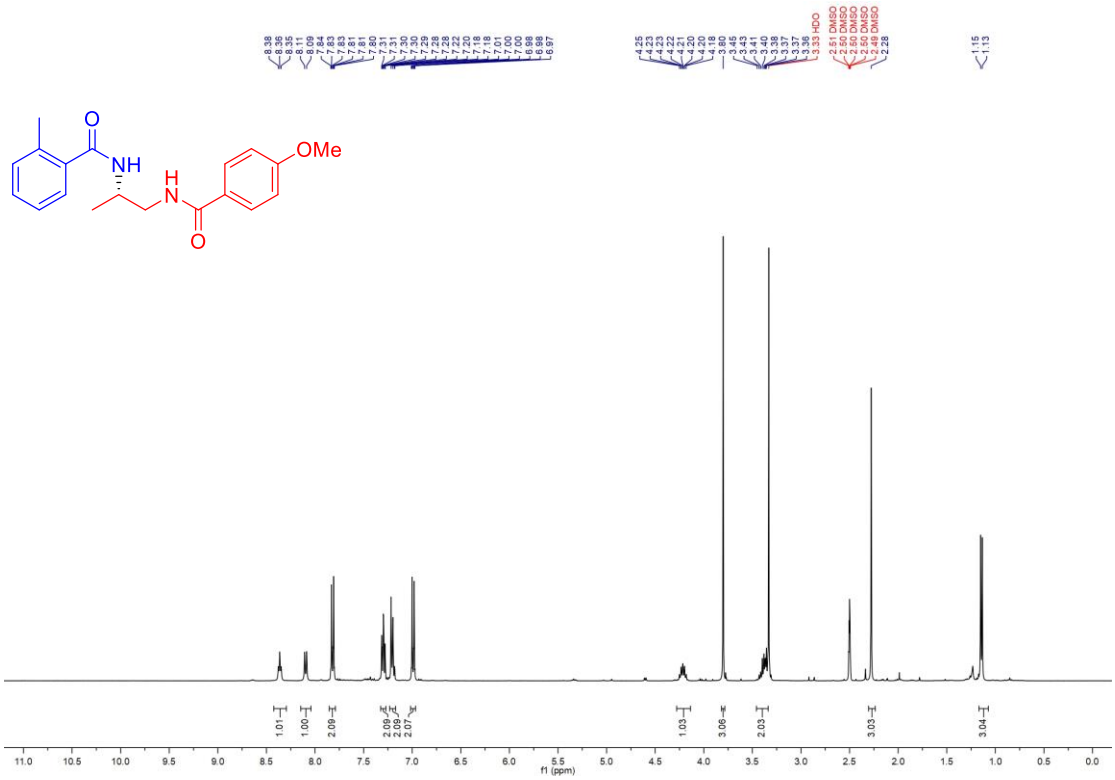


Figure S16. ^{13}C NMR spectra (100 MHz, DMSO-*d*6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-2-methylbenzamide (3ab).

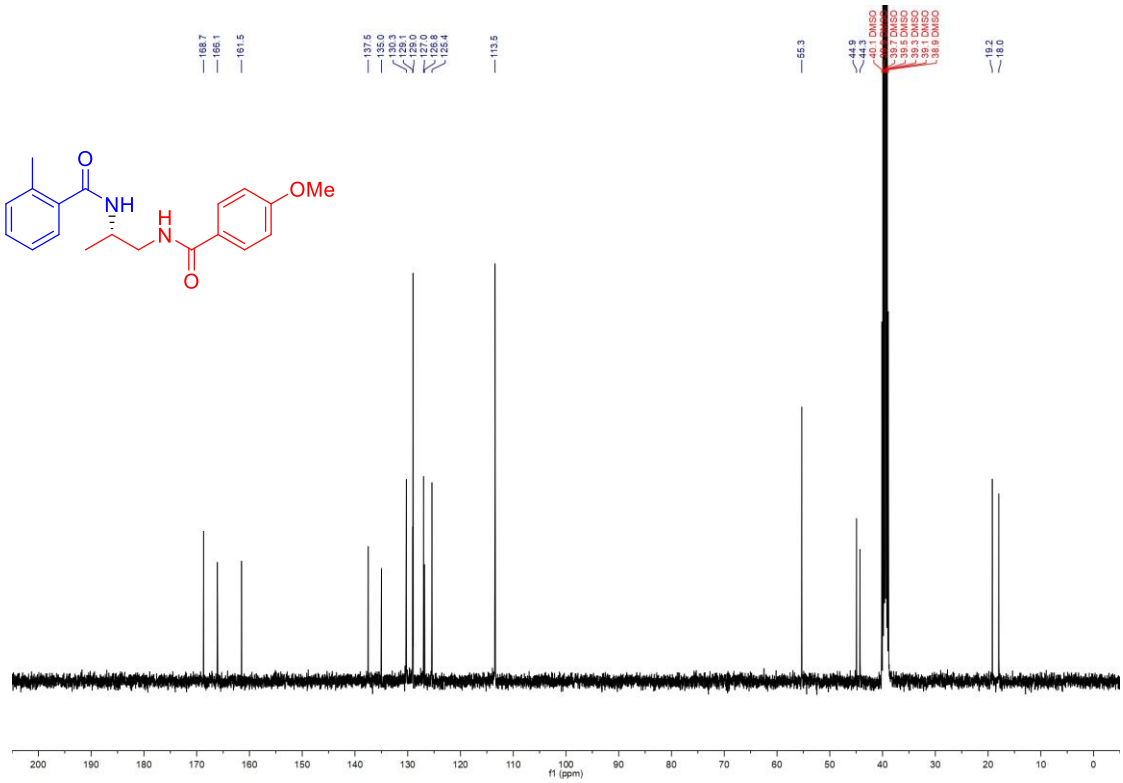


Figure S17. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-2-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ac).

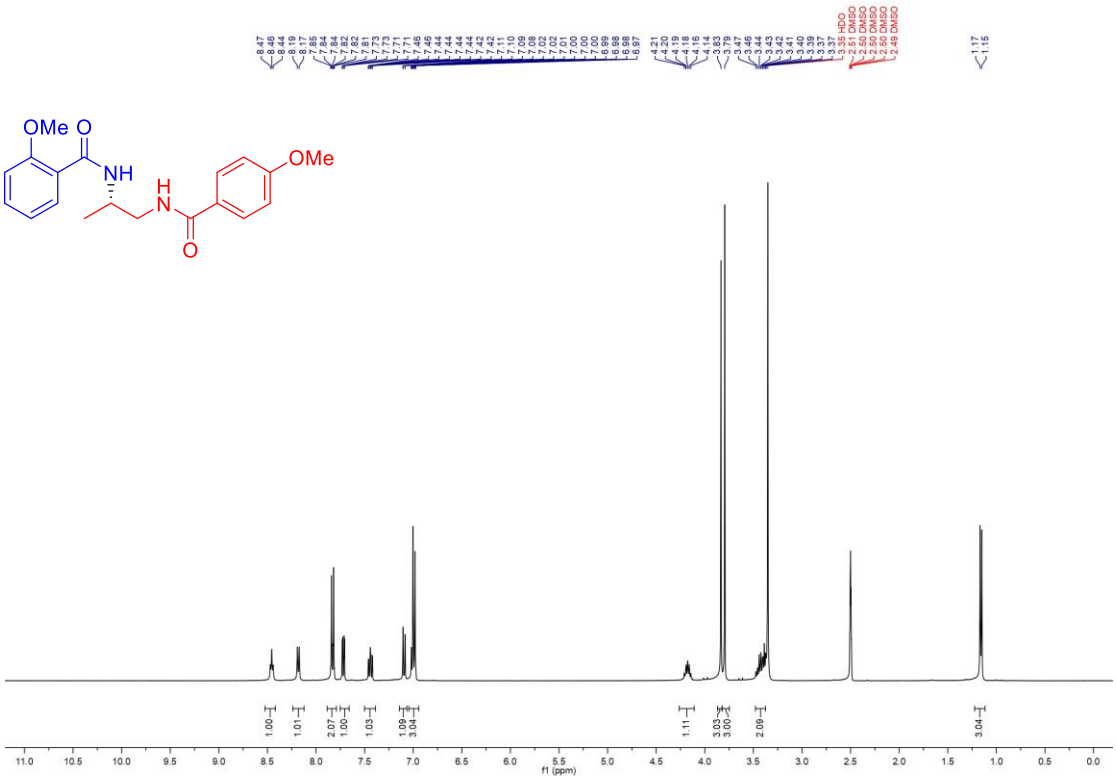


Figure S18. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-2-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ac).

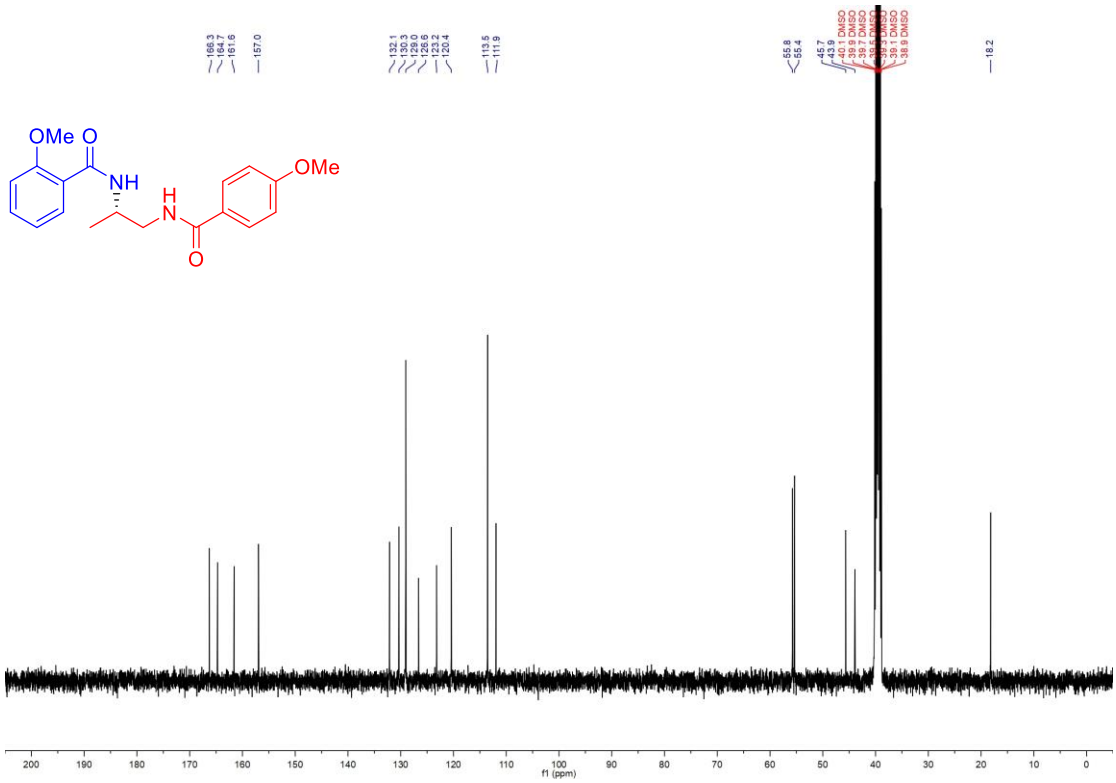


Figure S19. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-3-methylbenzamide (3ad).

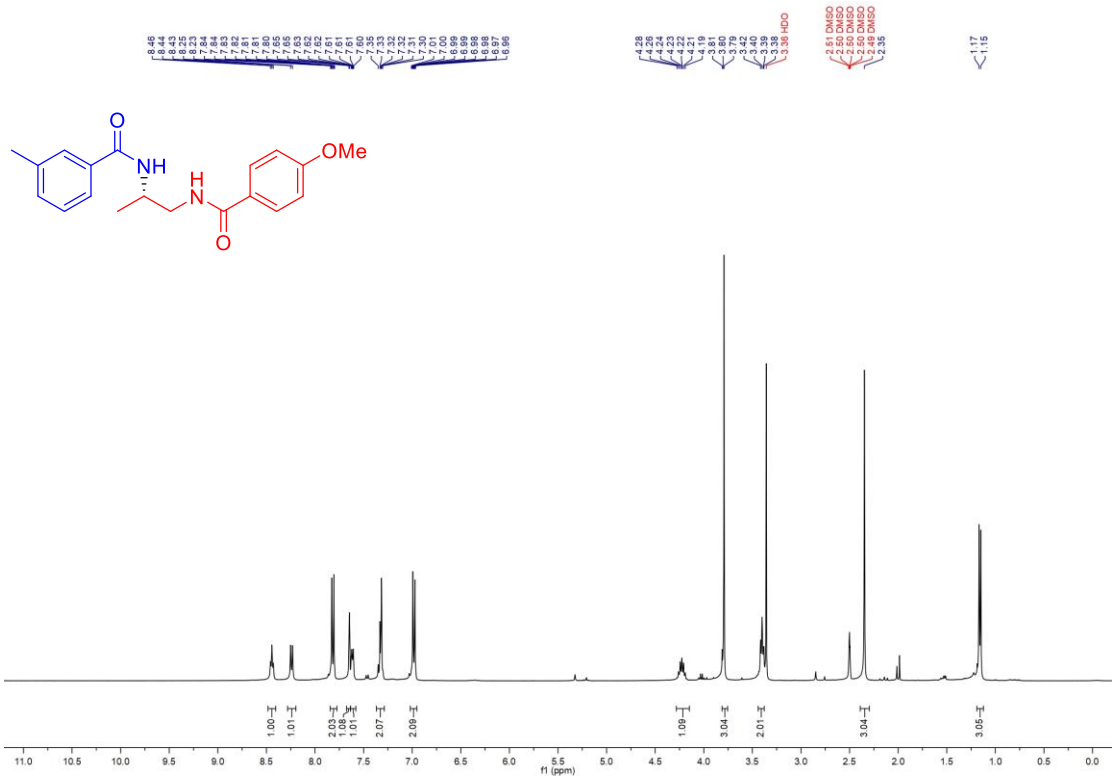


Figure S20. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-3-methylbenzamide (3ad).

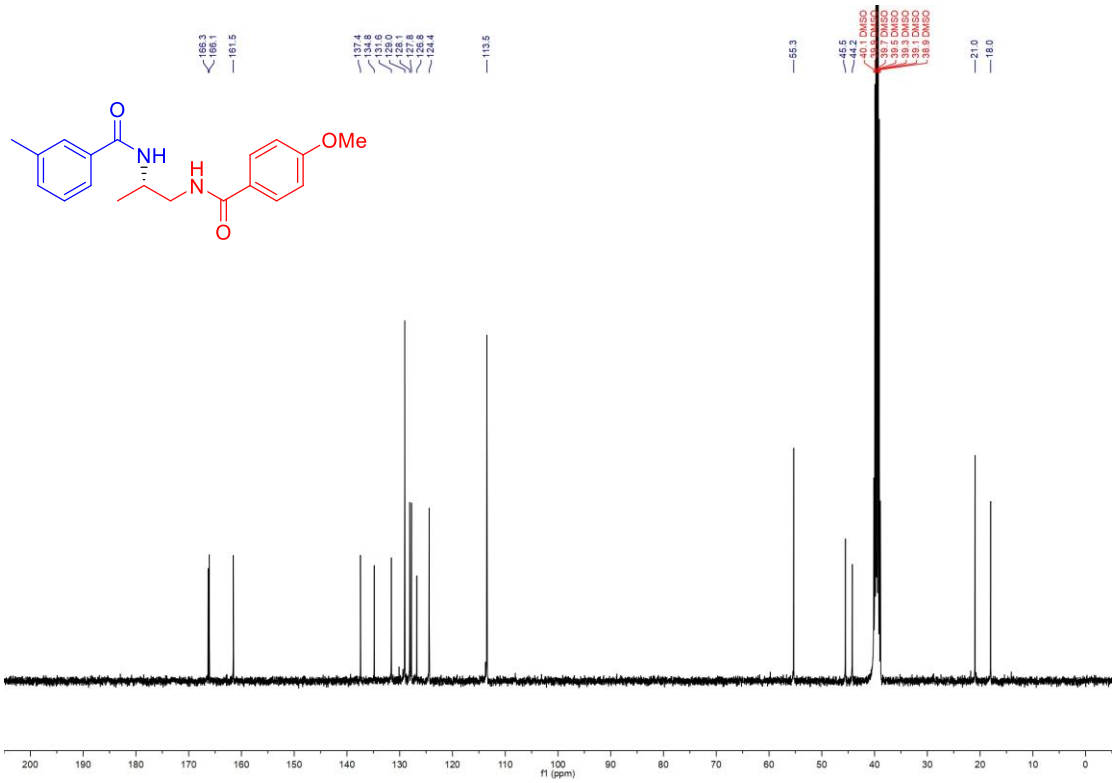


Figure S21. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-3-Methoxy-*N*-(1-(4-methoxybenza mido)propan-2-yl)benzamide (3ae).

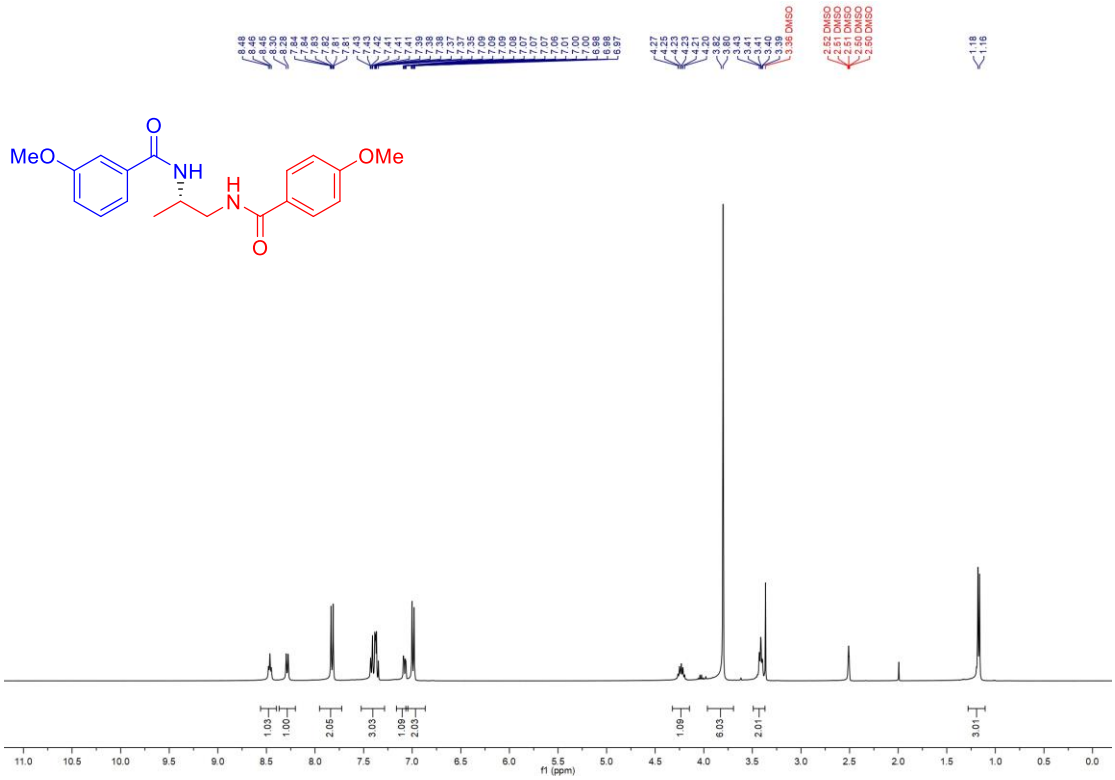


Figure S22. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-3-Methoxy-*N*-(1-(4-methoxybenz amido)propan-2-yl)benzamide (3ae).

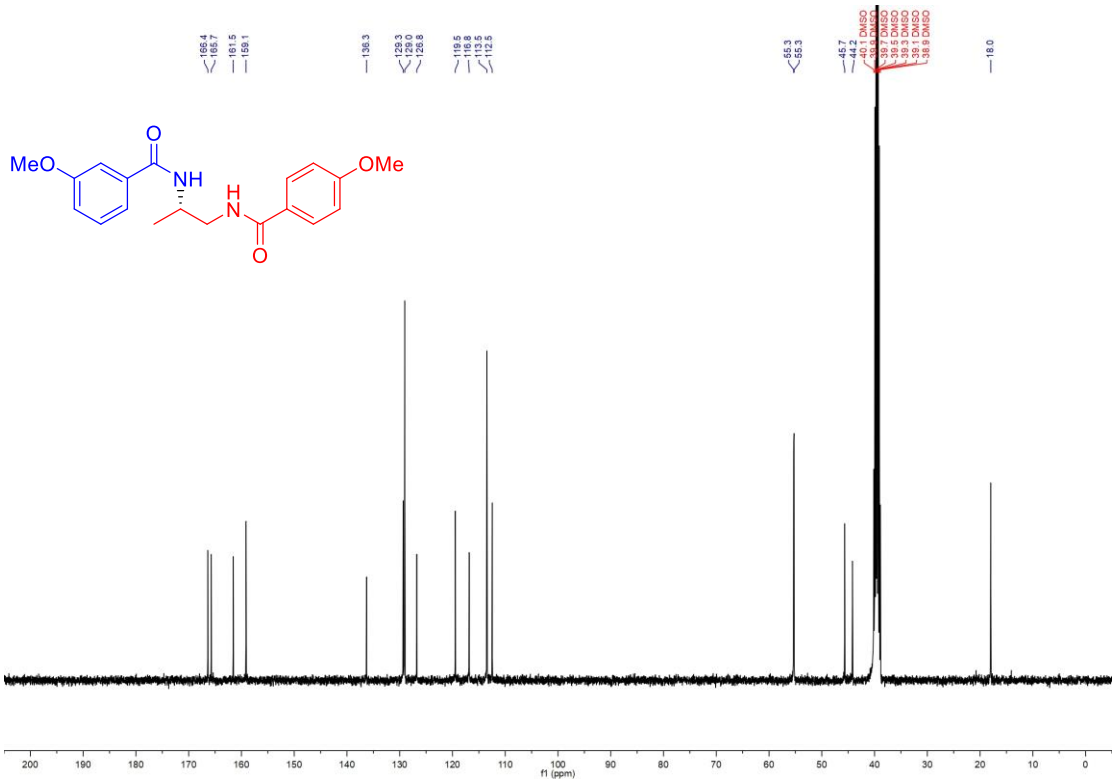


Figure S23. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-(*tert*-Butyl)-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3af).

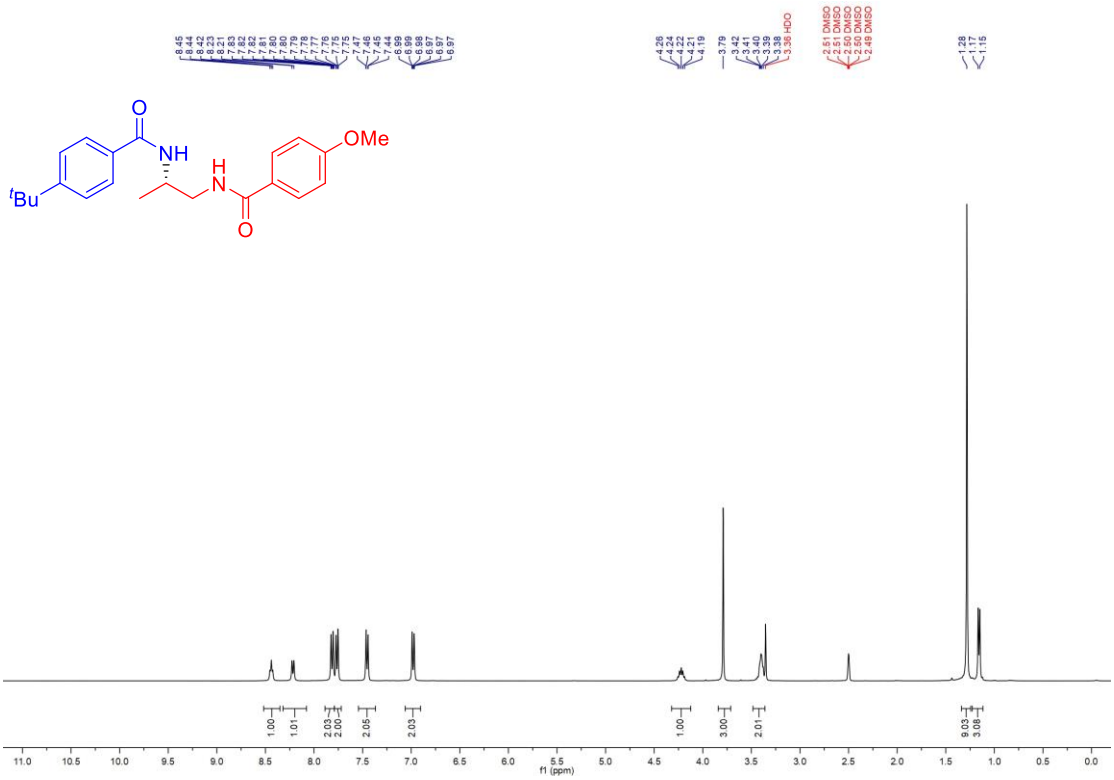


Figure S24. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-(*tert*-Butyl)-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3af).

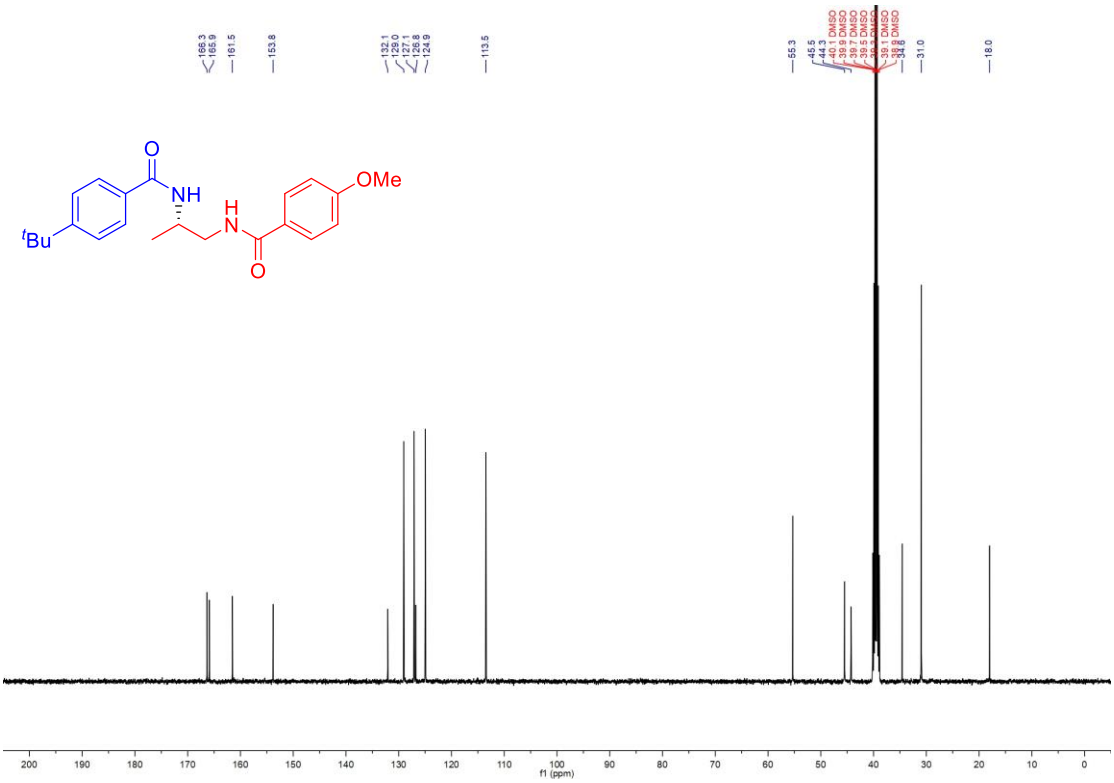


Figure S25. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*,*N*′-(Propane-1,2-diyl)bis(4-meth oxybenzamide) (3ag).

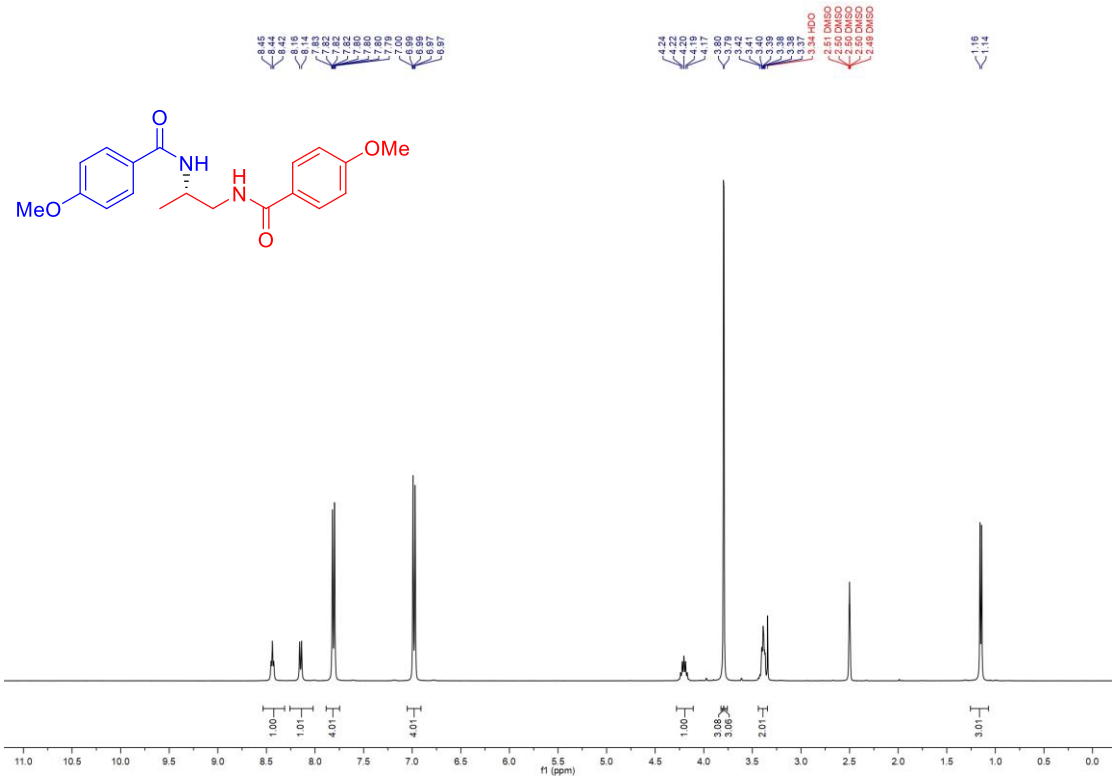


Figure S26. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*,*N*′-(Propane-1,2-diyl)bis(4-met hoxybenzamide) (3ag).

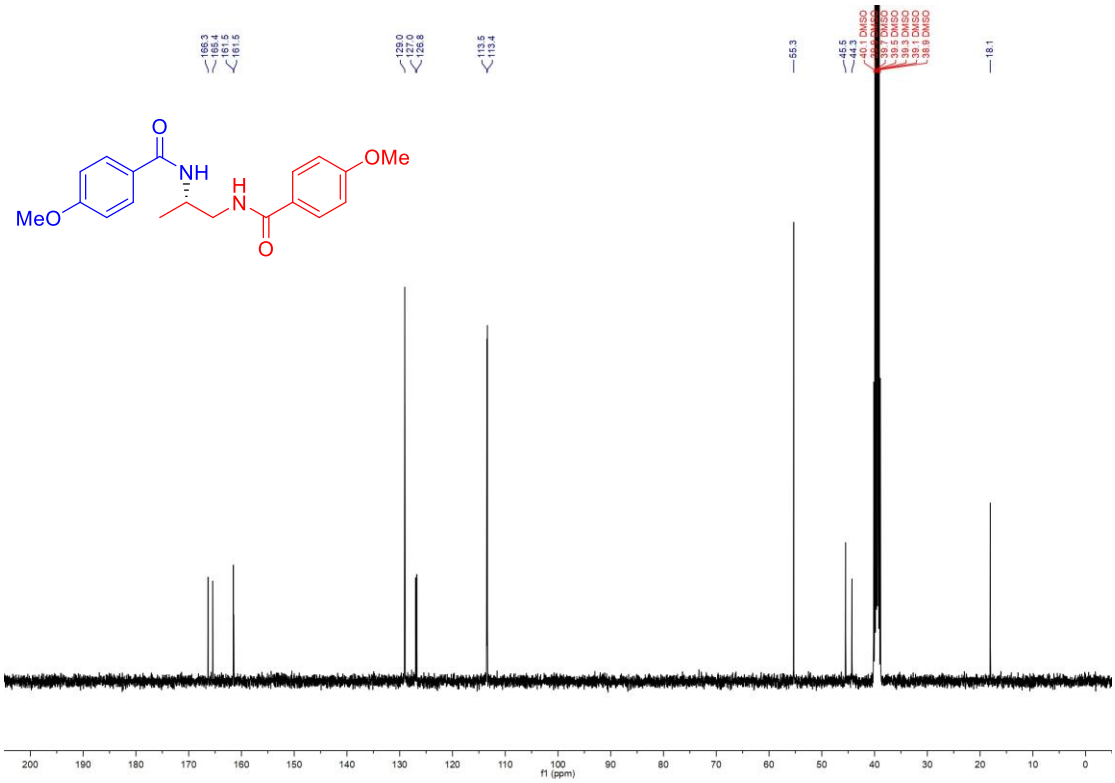


Figure S27. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ah).

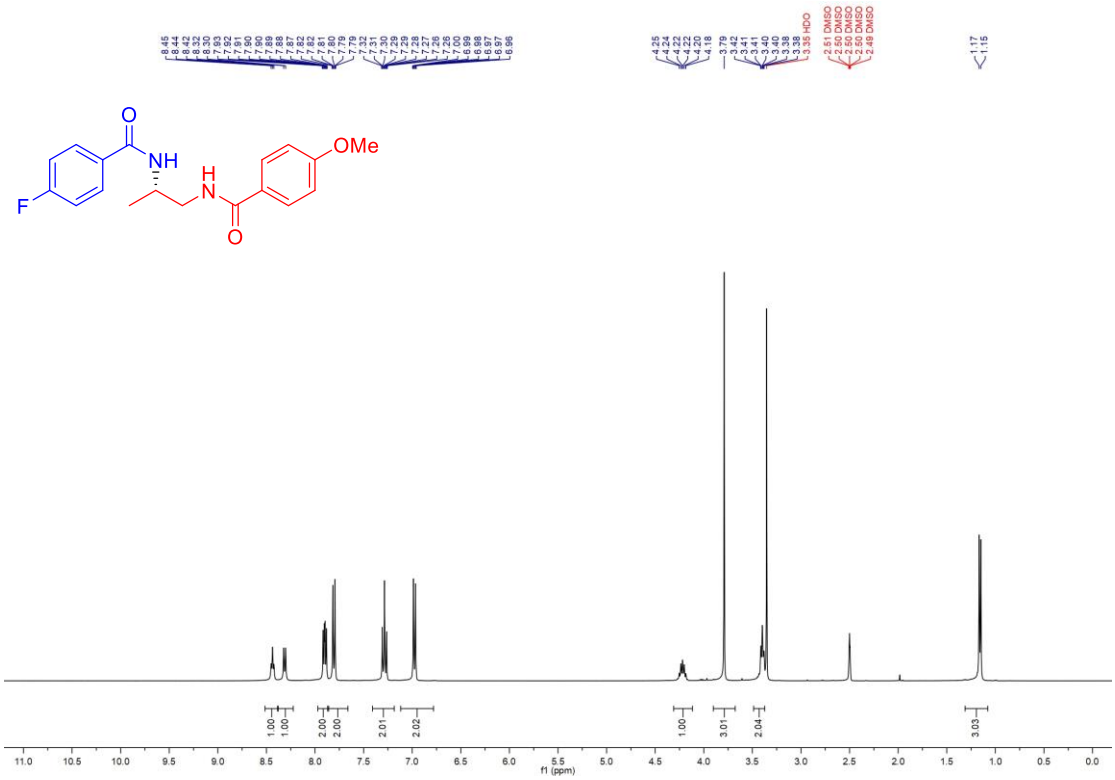


Figure S28. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ah).

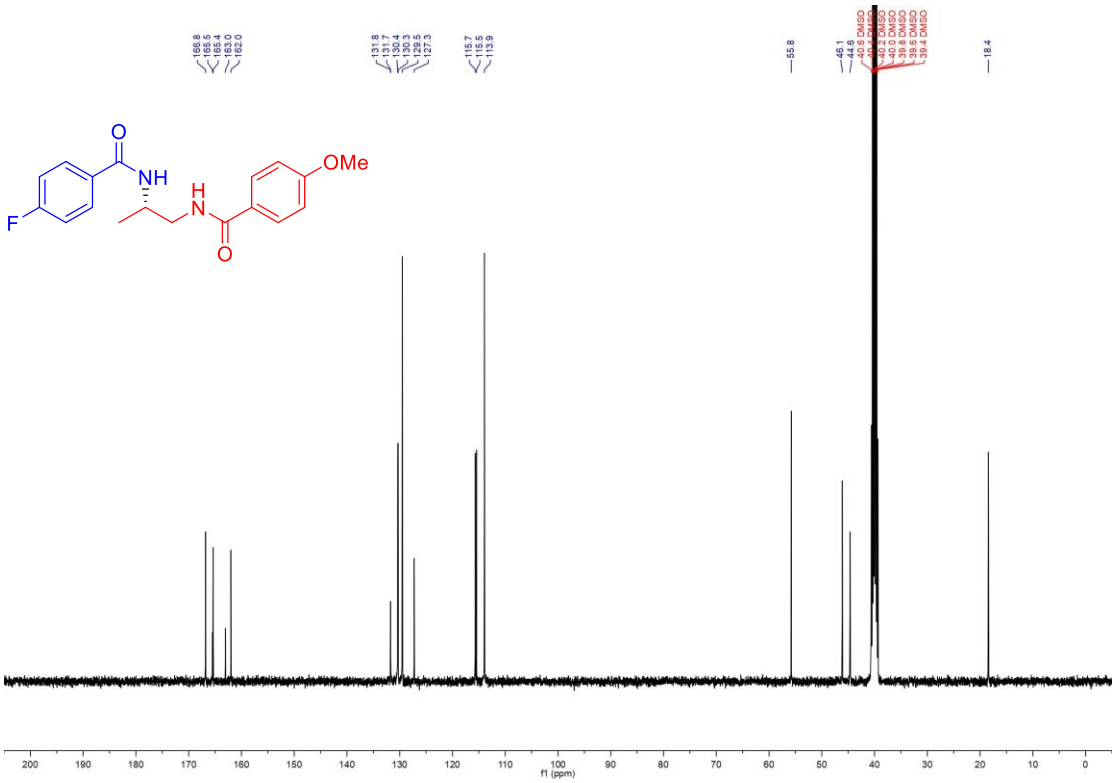


Figure S29. ^{19}F NMR spectra (376 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ah).

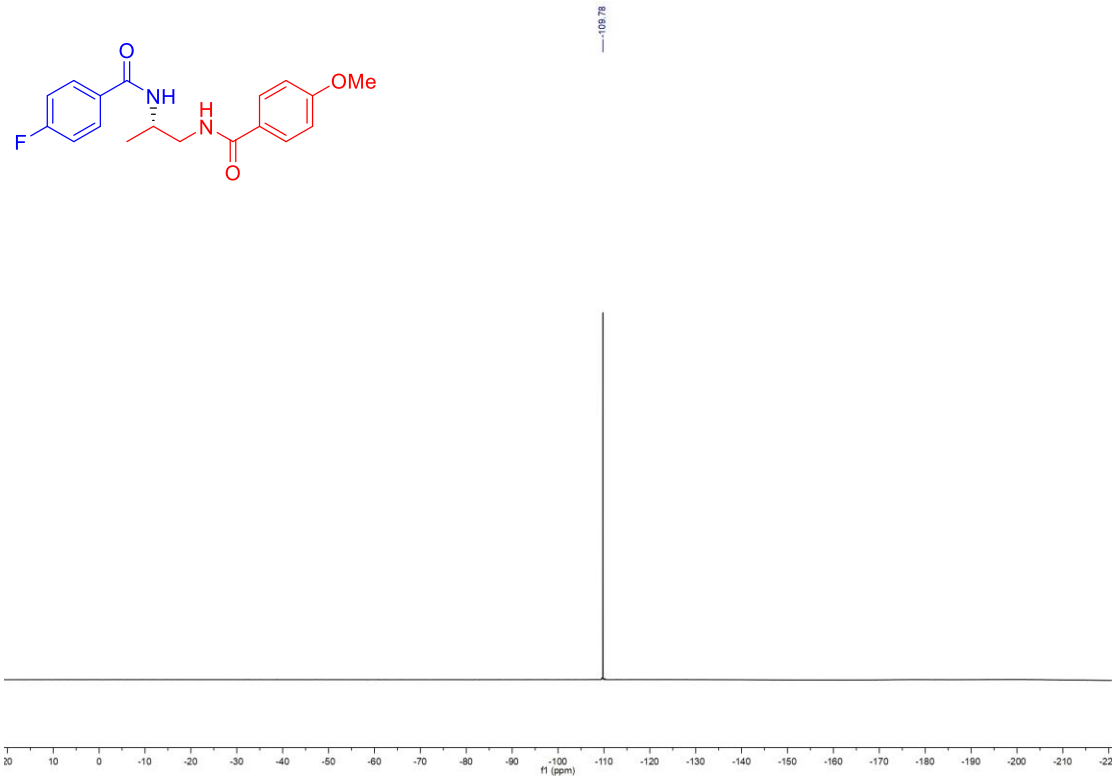


Figure S30. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Chloro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ai).

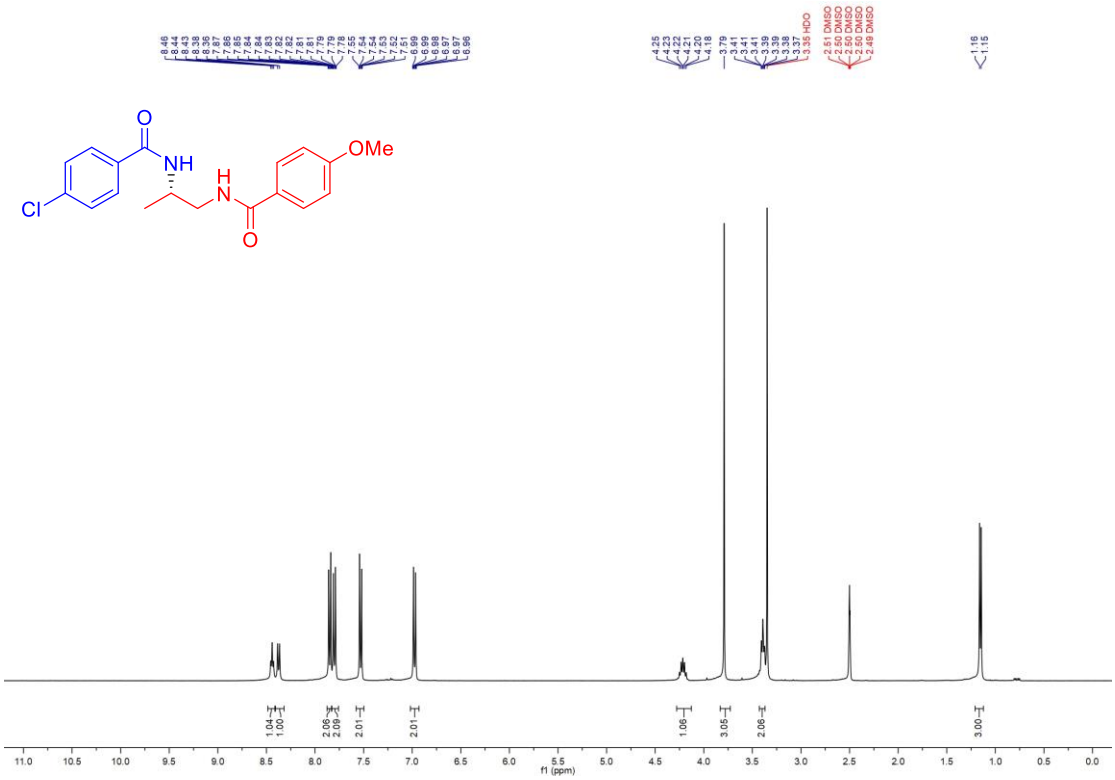


Figure S31. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Chloro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ai).

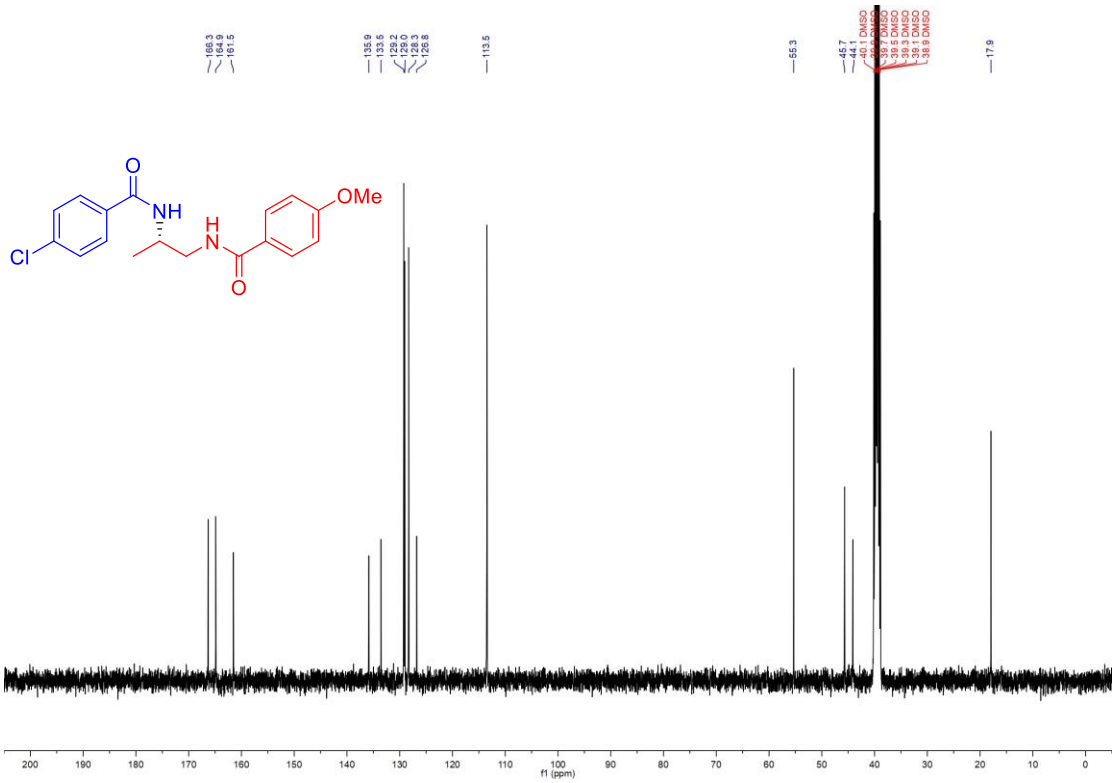


Figure S32. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Bromo-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3aj).

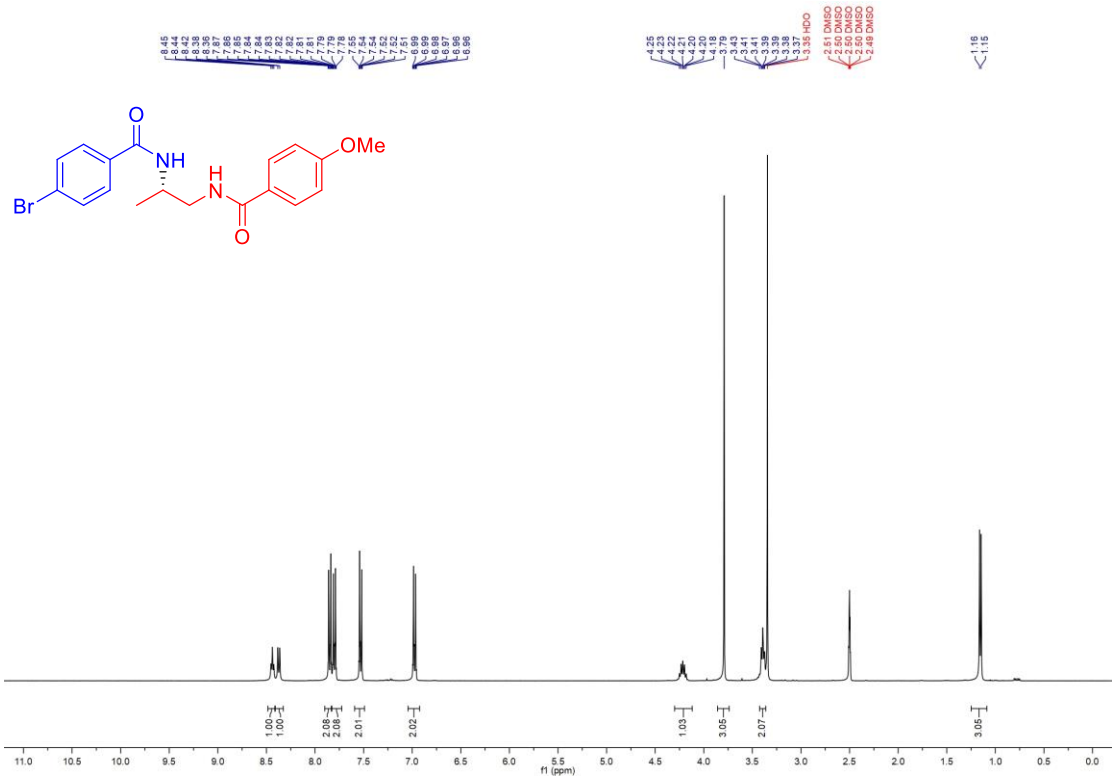


Figure S33. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Bromo-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3aj).

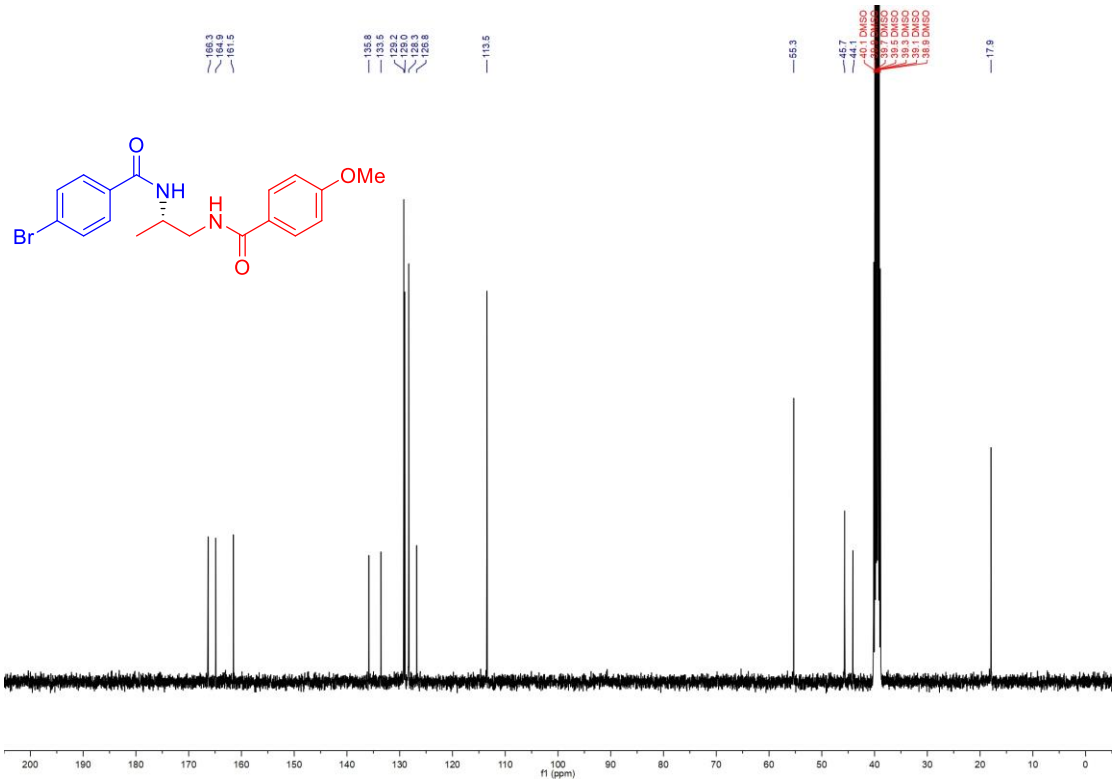


Figure S34. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Methoxy-*N*-(2-(4-(trifluoromethoxy)benzamido)propyl)benzamide (3ak).

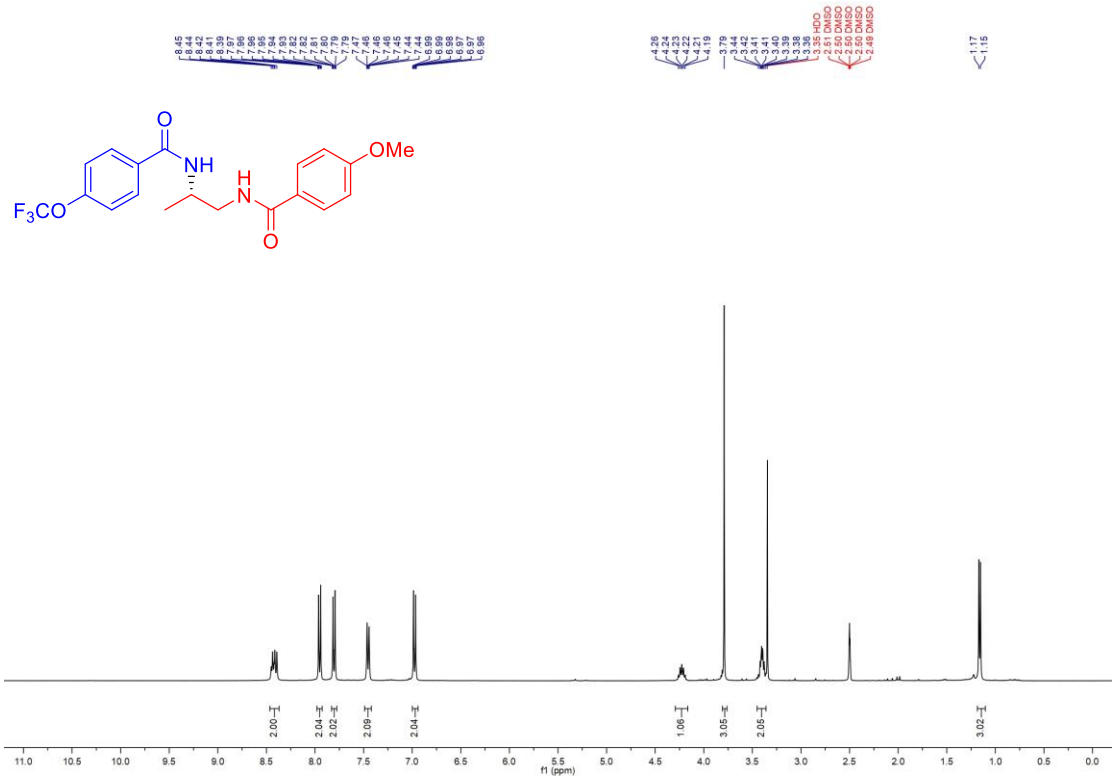


Figure S35. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Methoxy-*N*-(2-(4-(trifluoromethoxy)benzamido)propyl)benzamide (3ak).

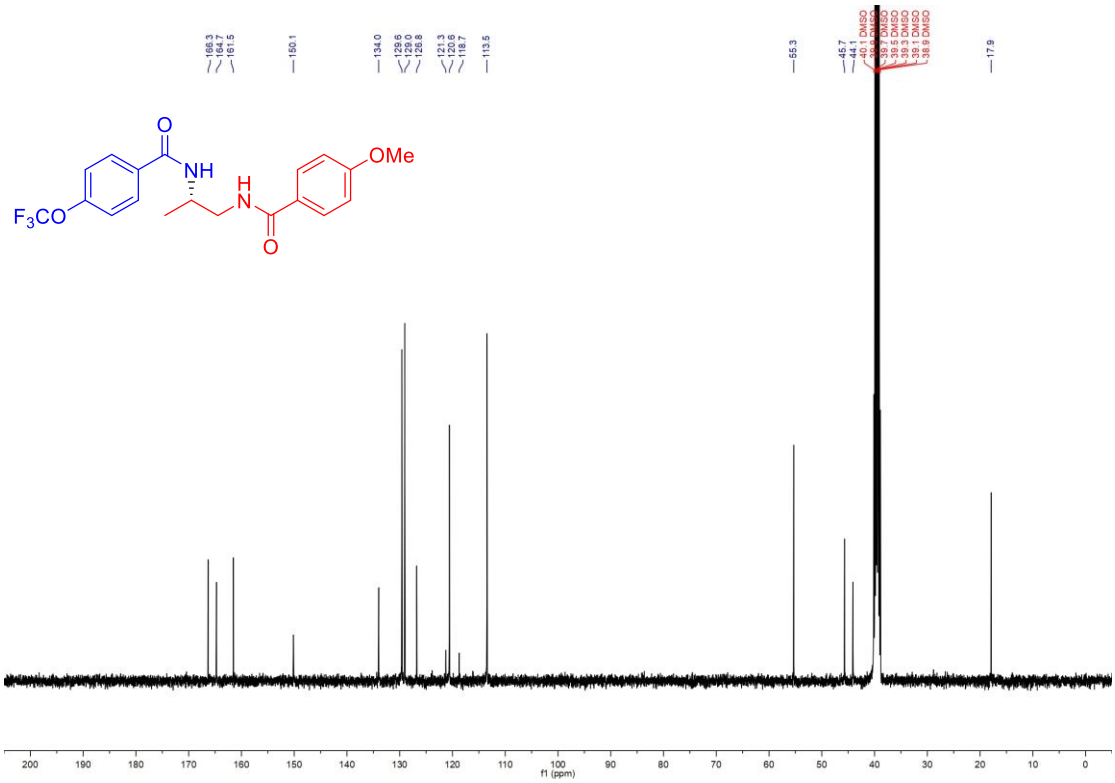


Figure S36. ^{19}F NMR spectra (376 MHz, DMSO-d_6) of (*S*)-4-Methoxy-*N*-(2-(4-(trifluoromethoxy)benzamido)propyl)benzamide (3ak).

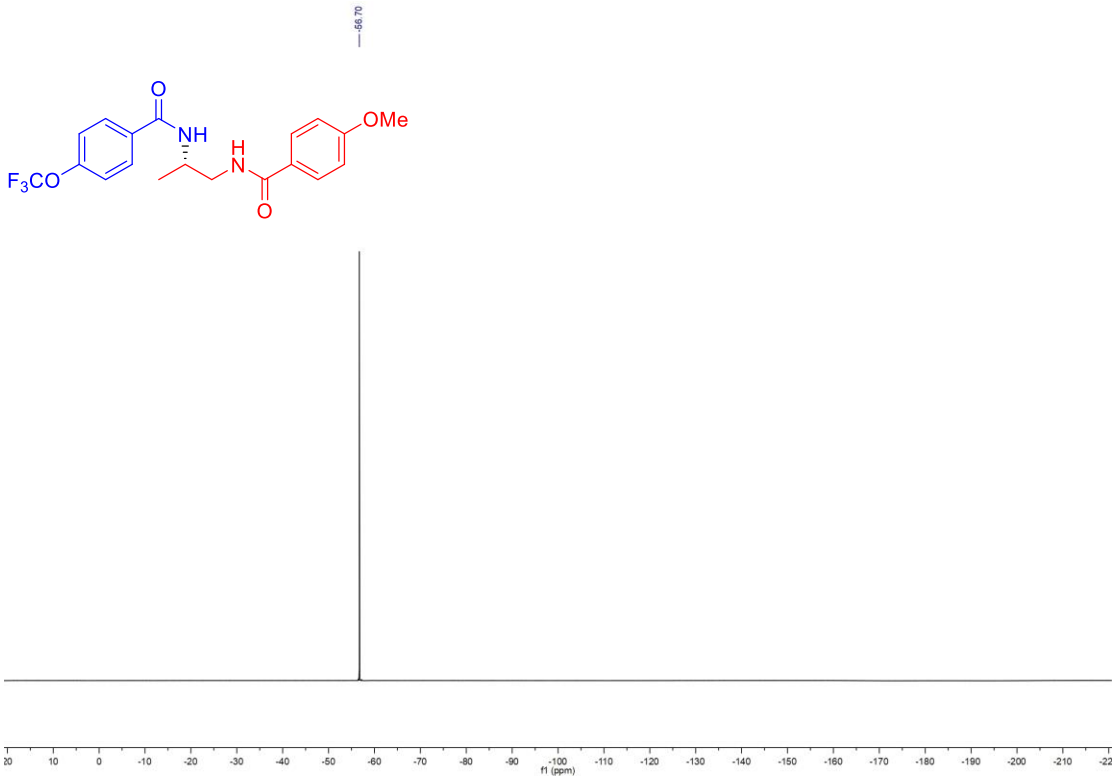


Figure S37. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)thiophene-2-carboxamide (3al).

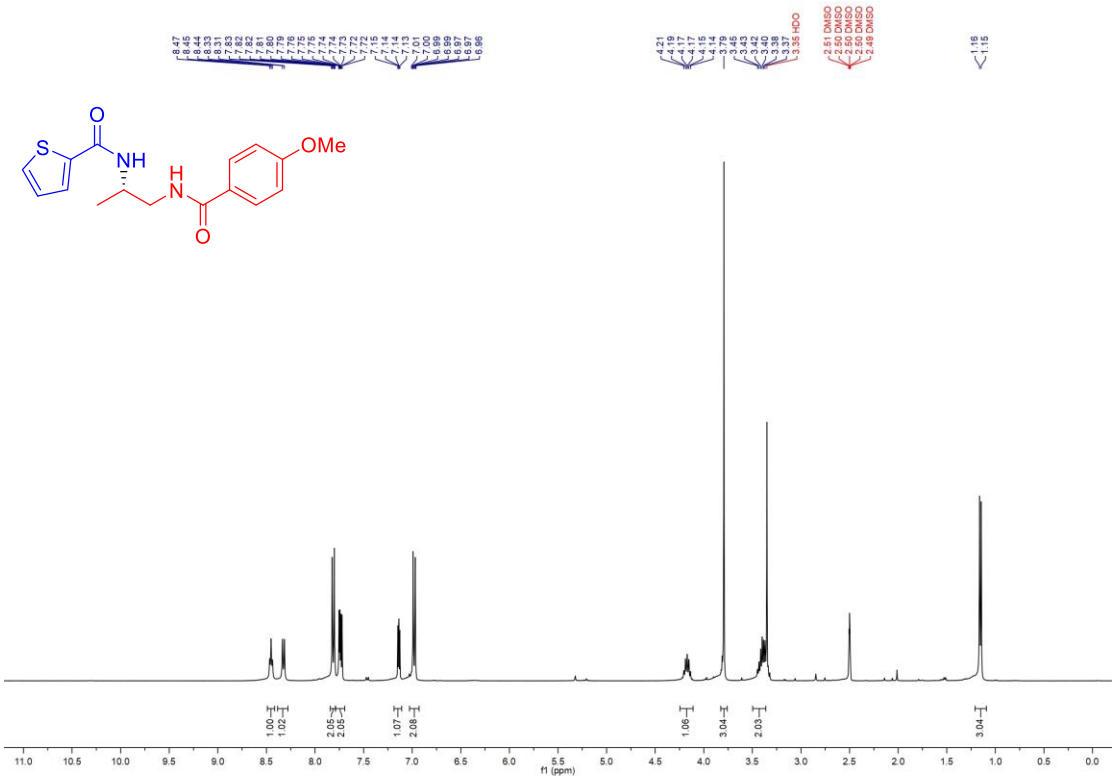


Figure S38. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)thiophene-2-carboxamide (3al).

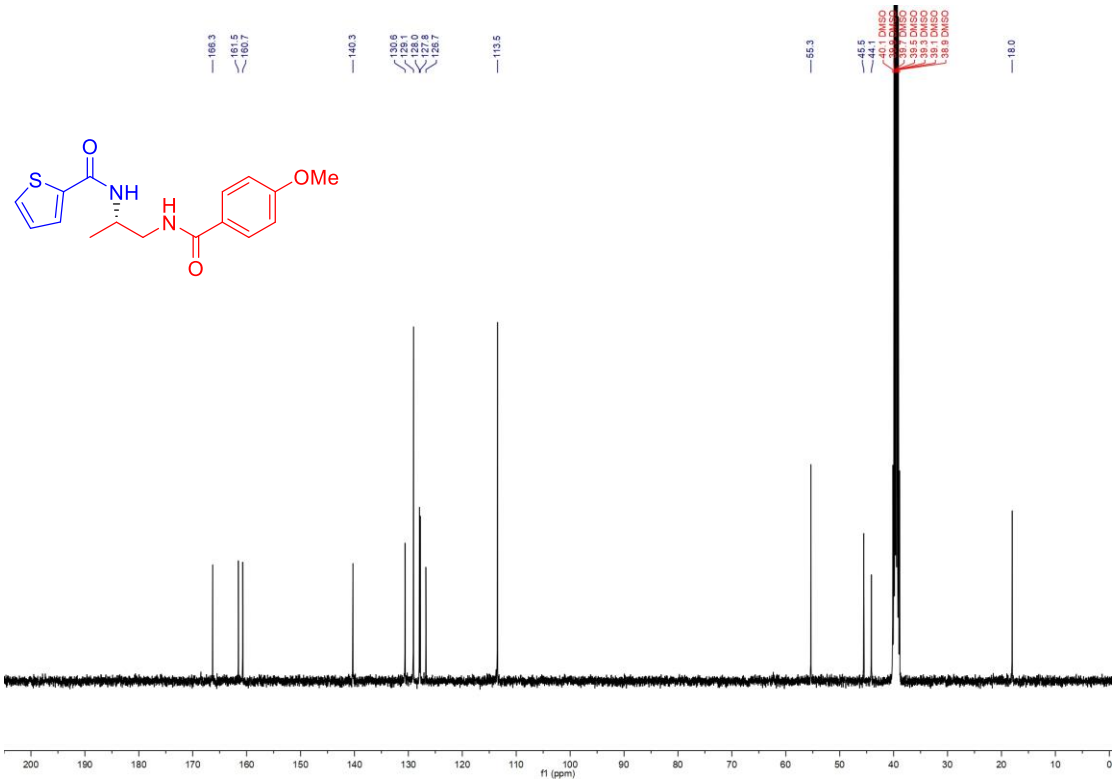


Figure S39. ^{1}H NMR spectra (600 MHz, DMSO-d_6) of *N*-(3*S*-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Major diastereoisomer).

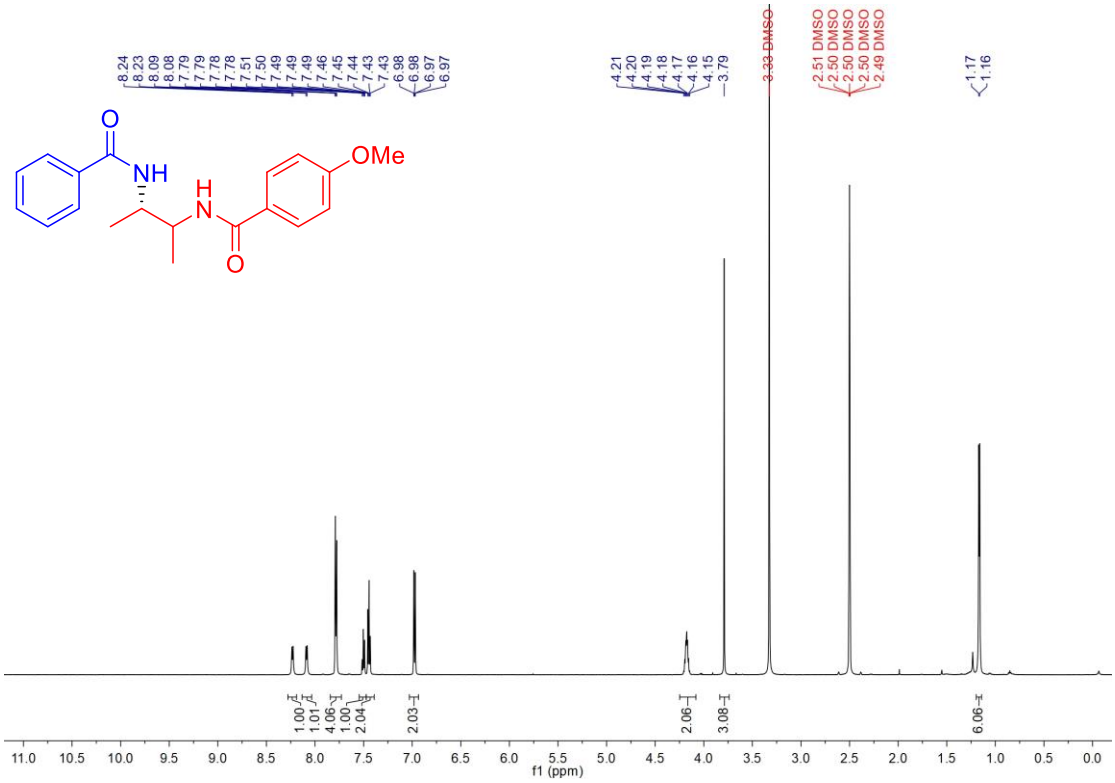


Figure S40. ^{13}C NMR spectra (150 MHz, DMSO-d_6) of *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Major diastereoisomer).

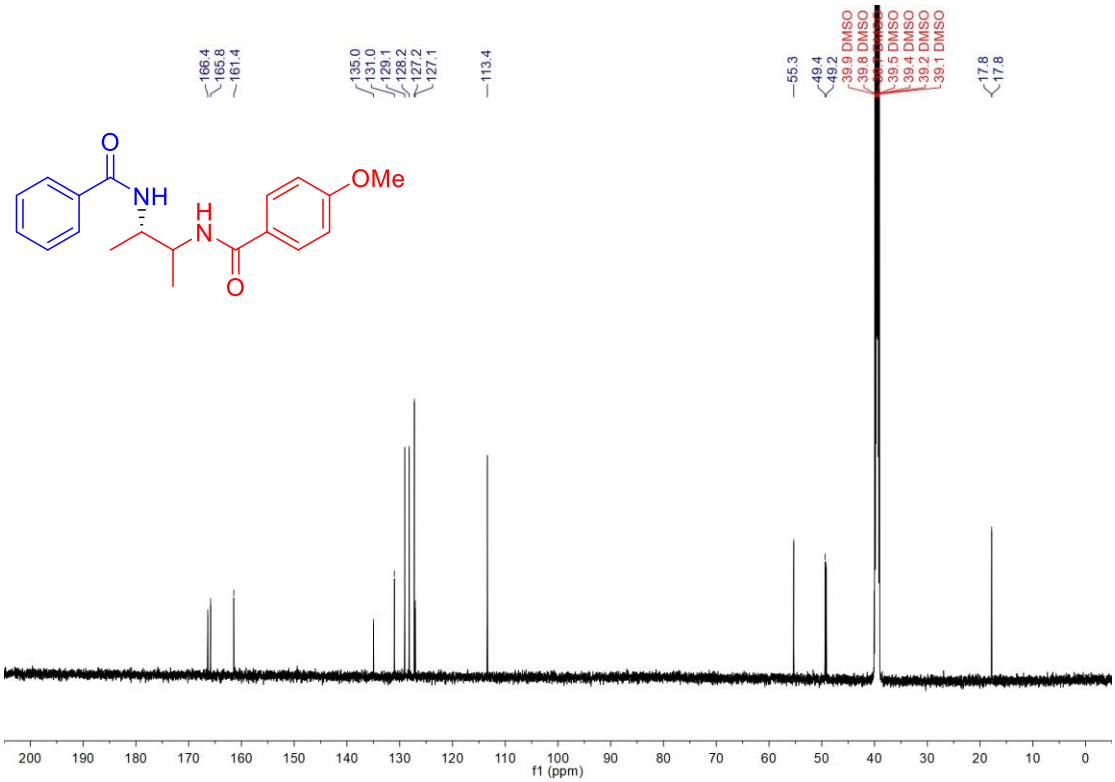


Figure S41. ^{1}H NMR spectra (600 MHz, DMSO-d_6) of *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-m ethoxybenzamide (3ba) (Minor diastereoisomer).

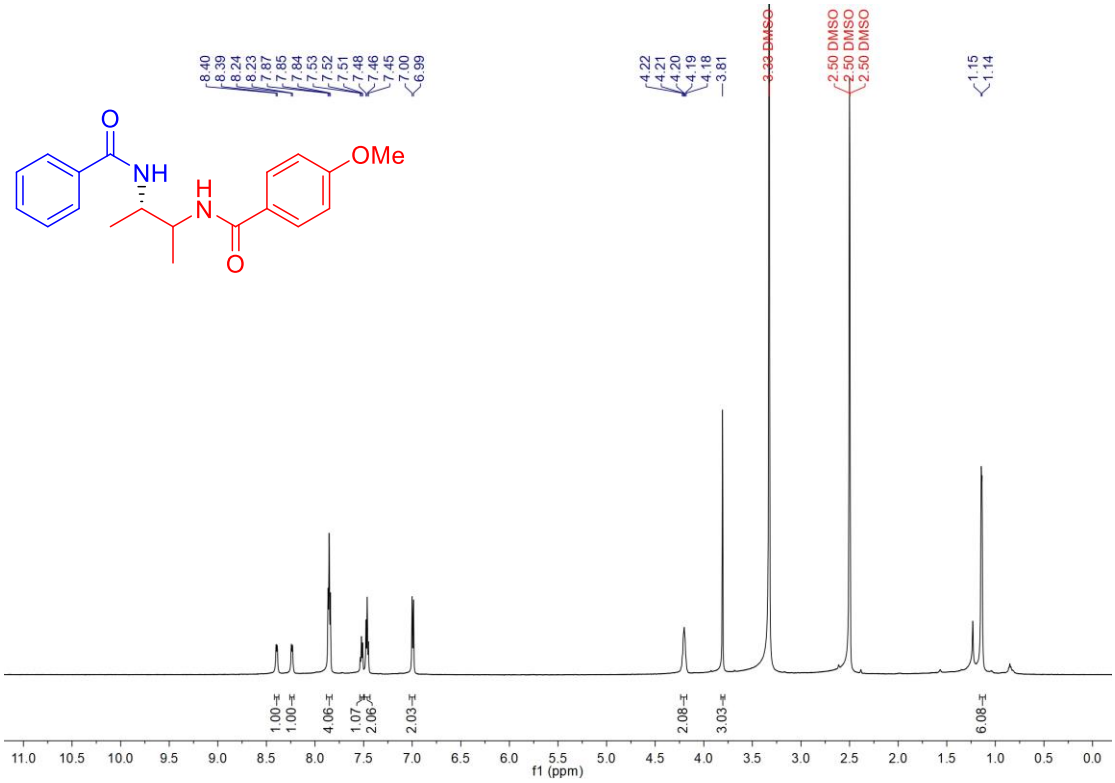


Figure S42. ^{13}C NMR spectra (150 MHz, DMSO-d_6) of *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-m ethoxybenzamide (3ba) (Minor diastereoisomer).

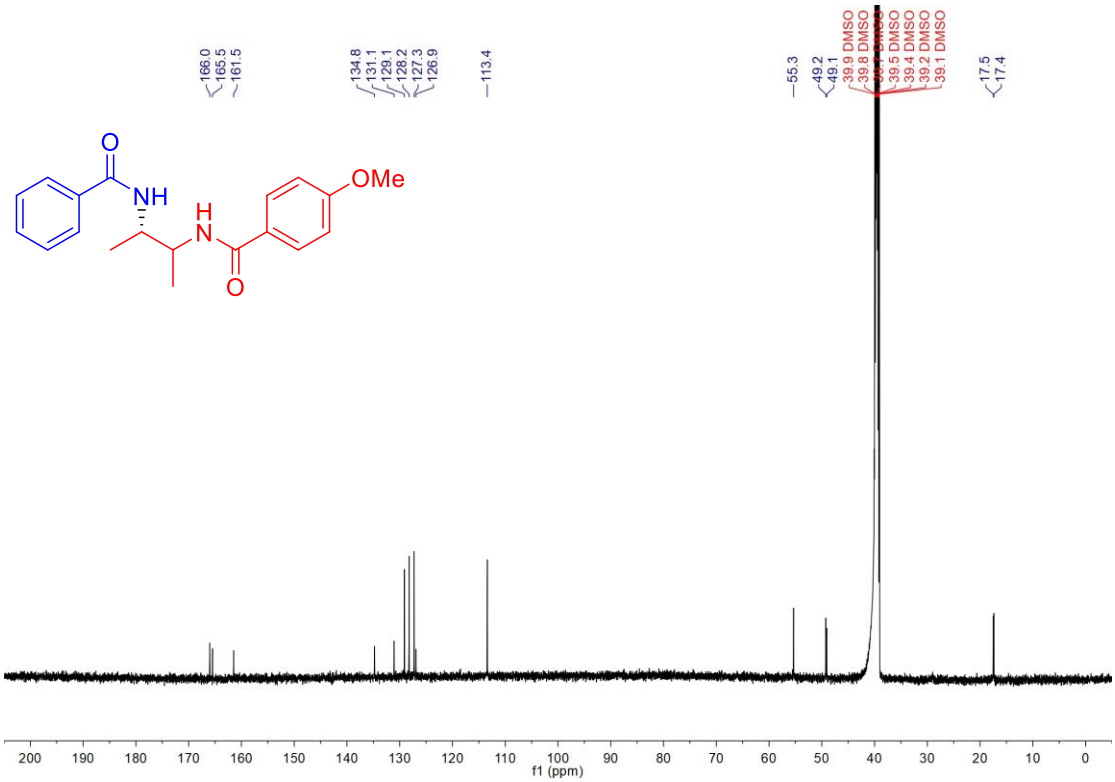


Figure S43. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of *N*-((2*S*,3*S*)-3-Benzamido-1-phenylbut an-2-yl)-4-methoxybenzamide (3ca).

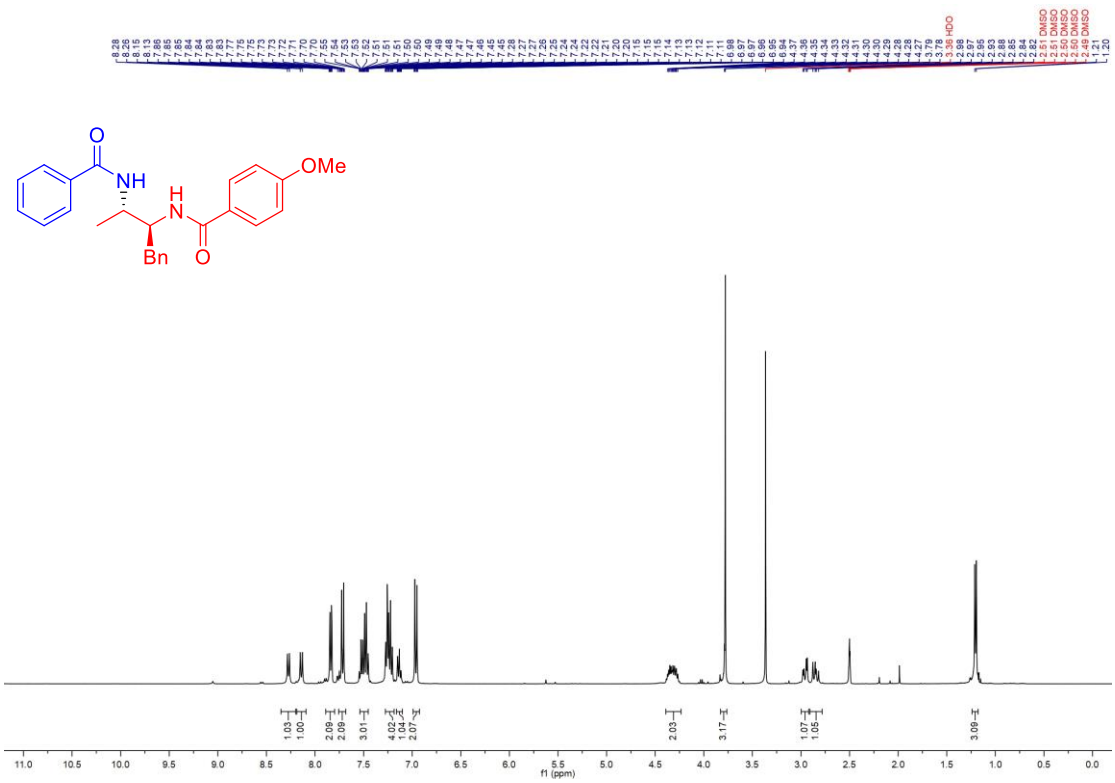


Figure S44. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of *N*-((2*S*,3*S*)-3-Benzamido-1-phenylbut an-2-yl)-4-methoxybenzamide (3ca).

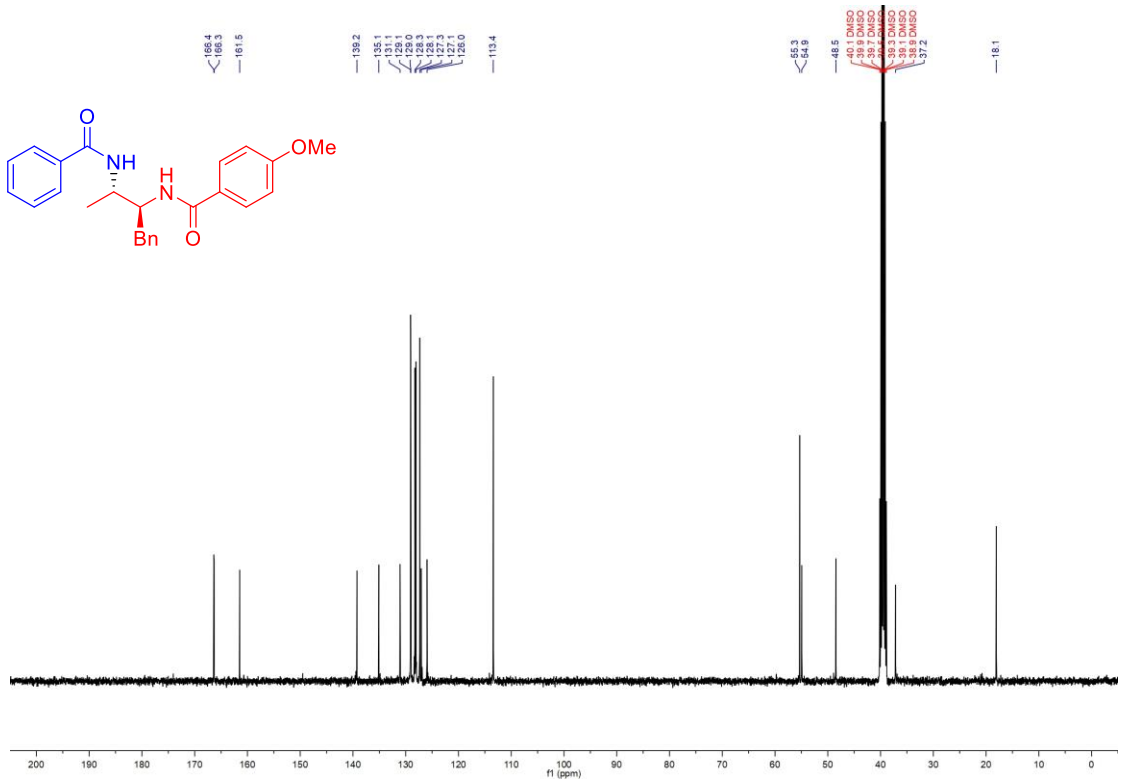


Figure S45. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of *N*-((1*S*,2*S*)-2-Benzamido-1-cyclohexyl propyl)-4-methoxybenzamide (3da).

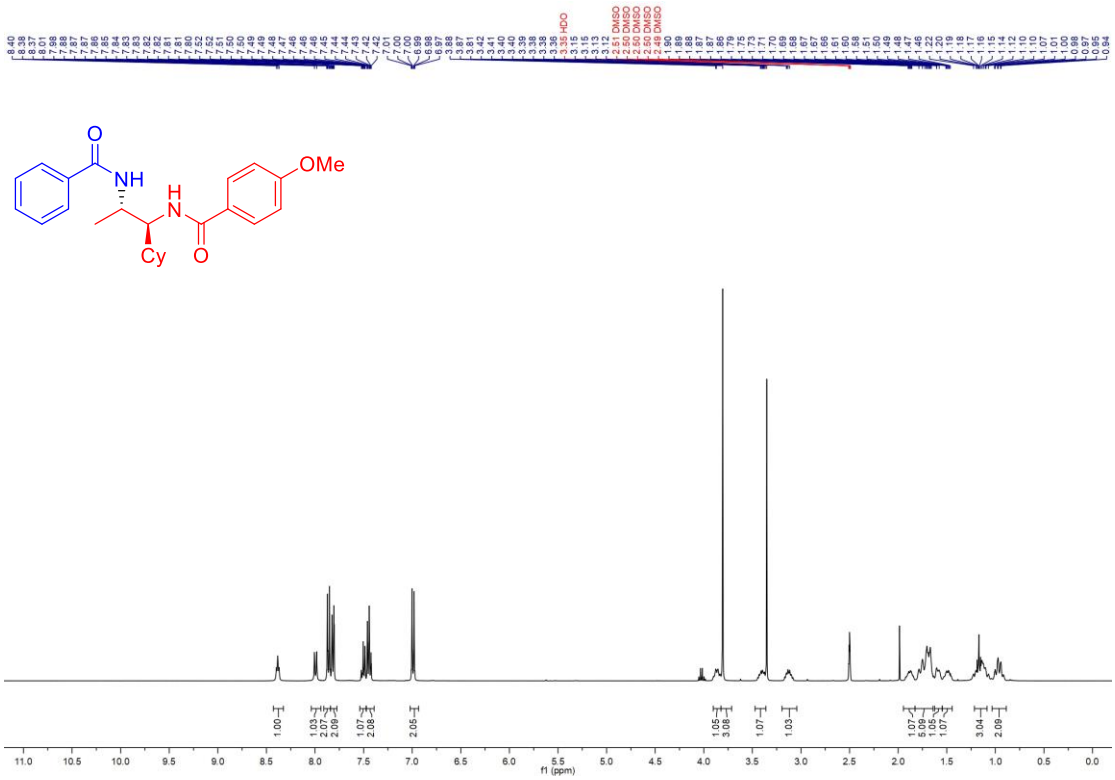


Figure S46. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of *N*-((1*S*,2*S*)-2-Benzamido-1-cyclohexy lpropyl)-4-methoxybenzamide (3da).

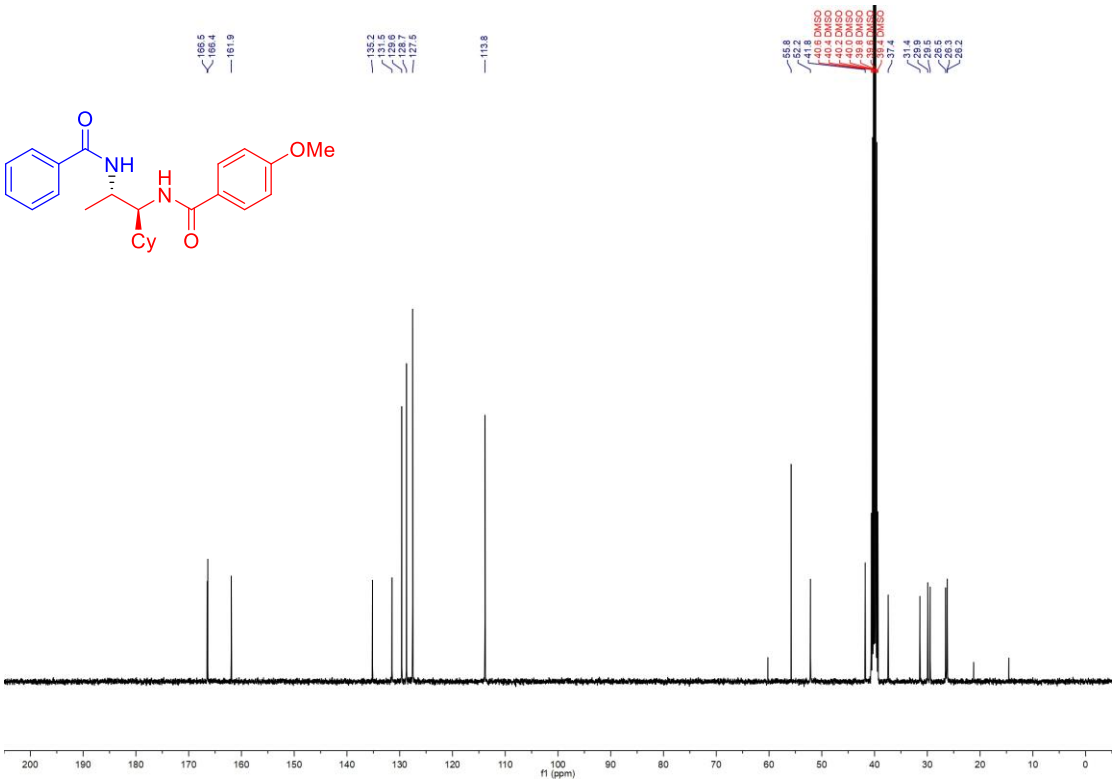


Figure S47. ^{1}H NMR spectra (600 MHz, DMSO-d_6) of (*S*)-*N*-(2-Benzamidobutyl)-4-methoxy benzamide (3ea)

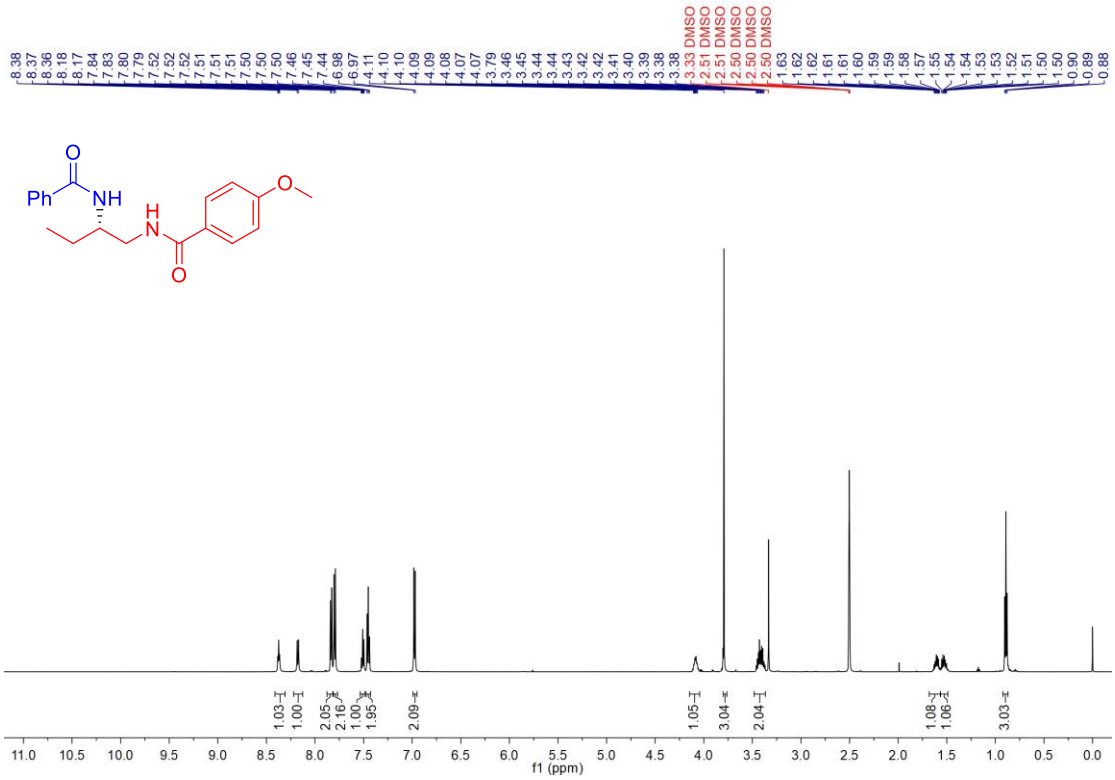


Figure S48. ^{13}C NMR spectra (150 MHz, DMSO-d_6) of (*S*)-*N*-(2-Benzamidobutyl)-4-methoxy benzamide (3ea)

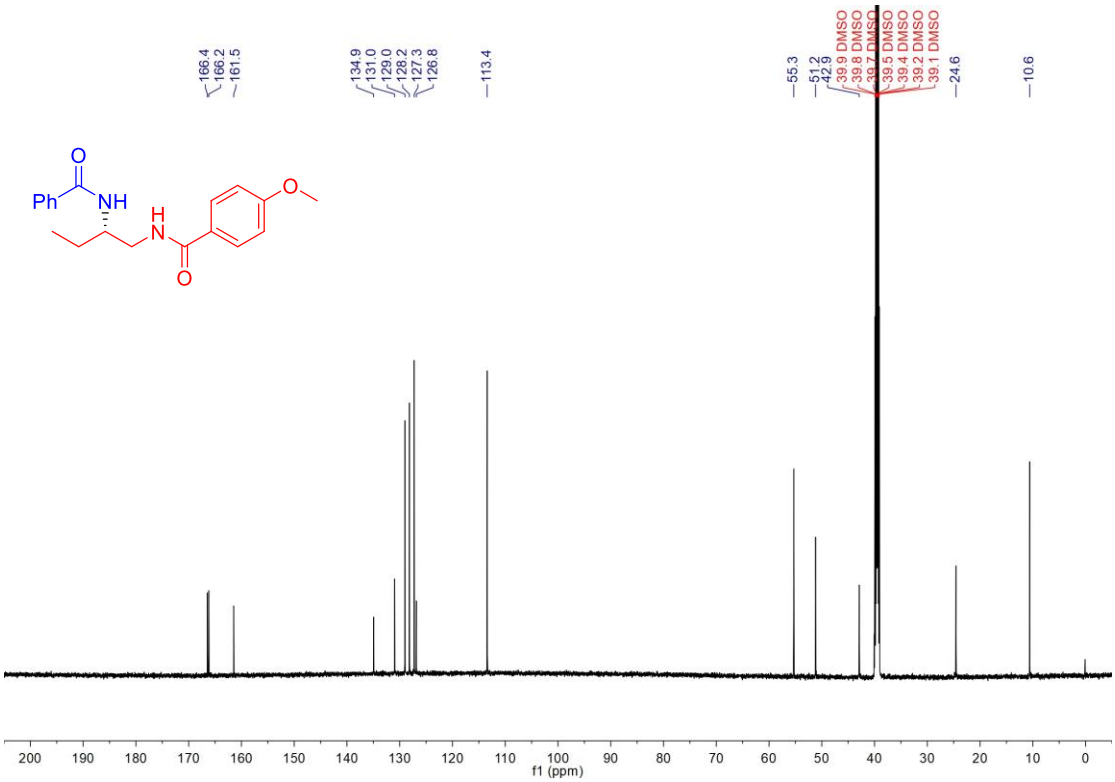


Figure S49. ^{1}H NMR spectra (600 MHz, DMSO-*d*$_6$) of *tert*-Butyl (*S*)-(2-(4-methoxybenzam ido)propyl)carbamate (3fg)

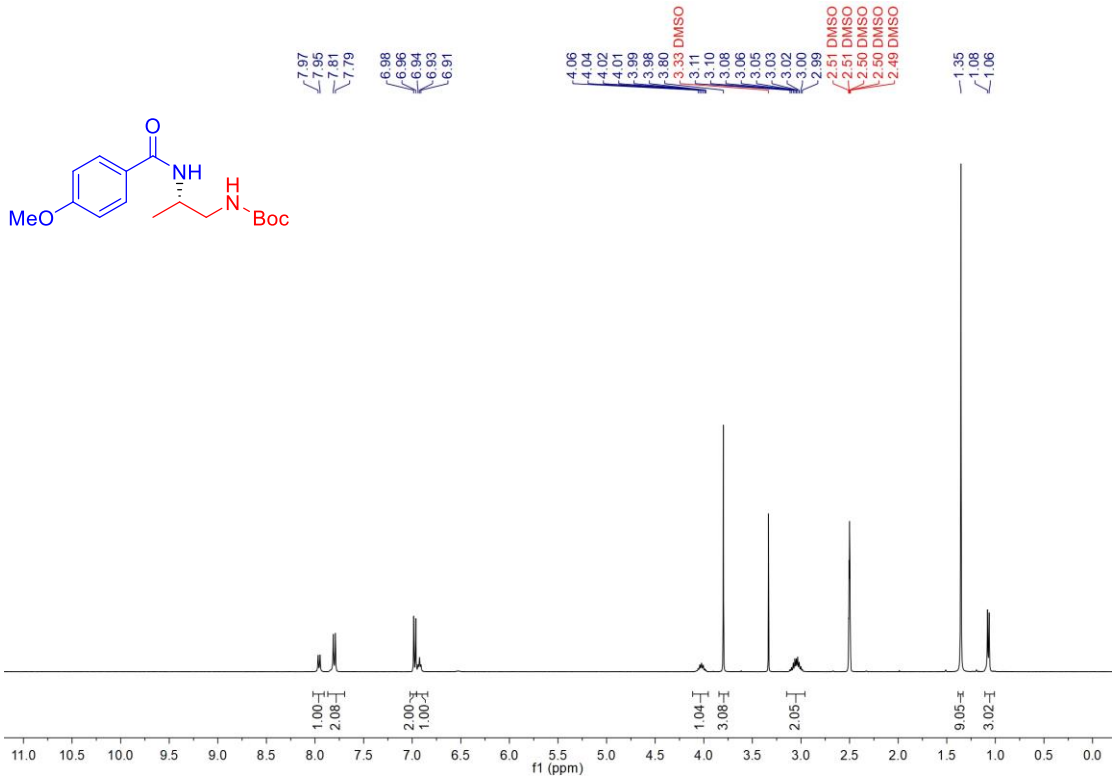


Figure S50. ^{13}C NMR spectra (150 MHz, DMSO-*d*$_6$) of *tert*-Butyl (*S*)-(2-(4-methoxybenza mido)propyl)carbamate (3fg)

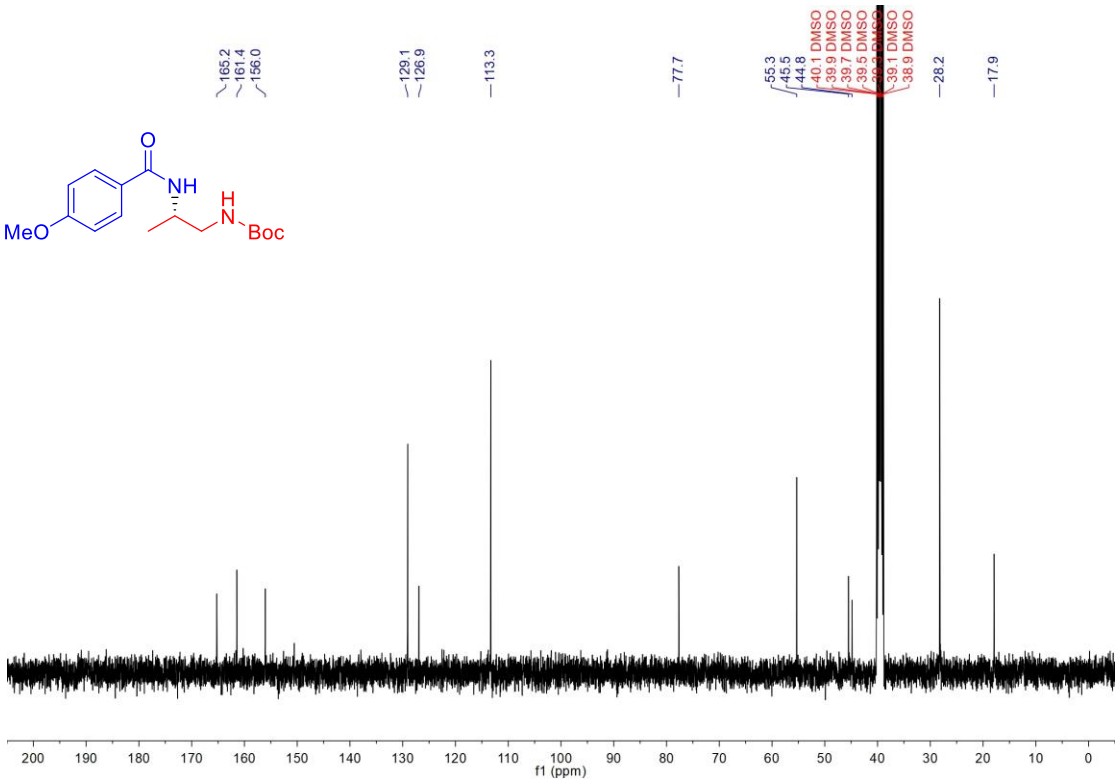


Figure S51. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aa).

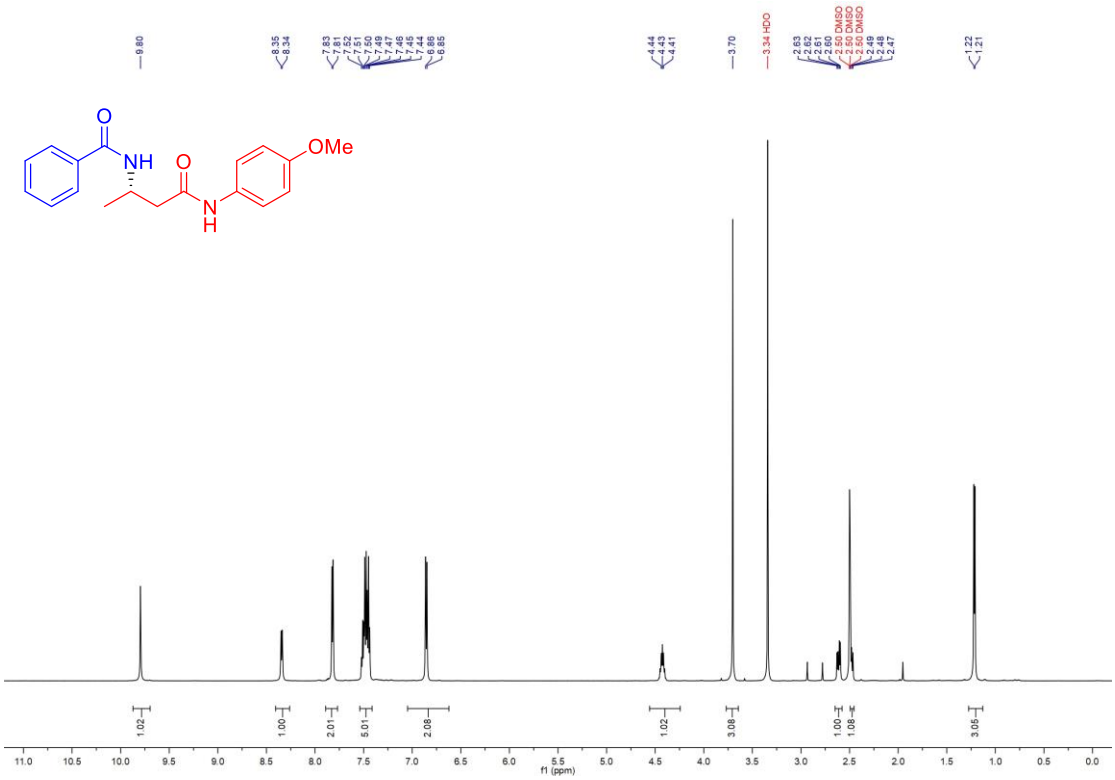


Figure S52. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aa).

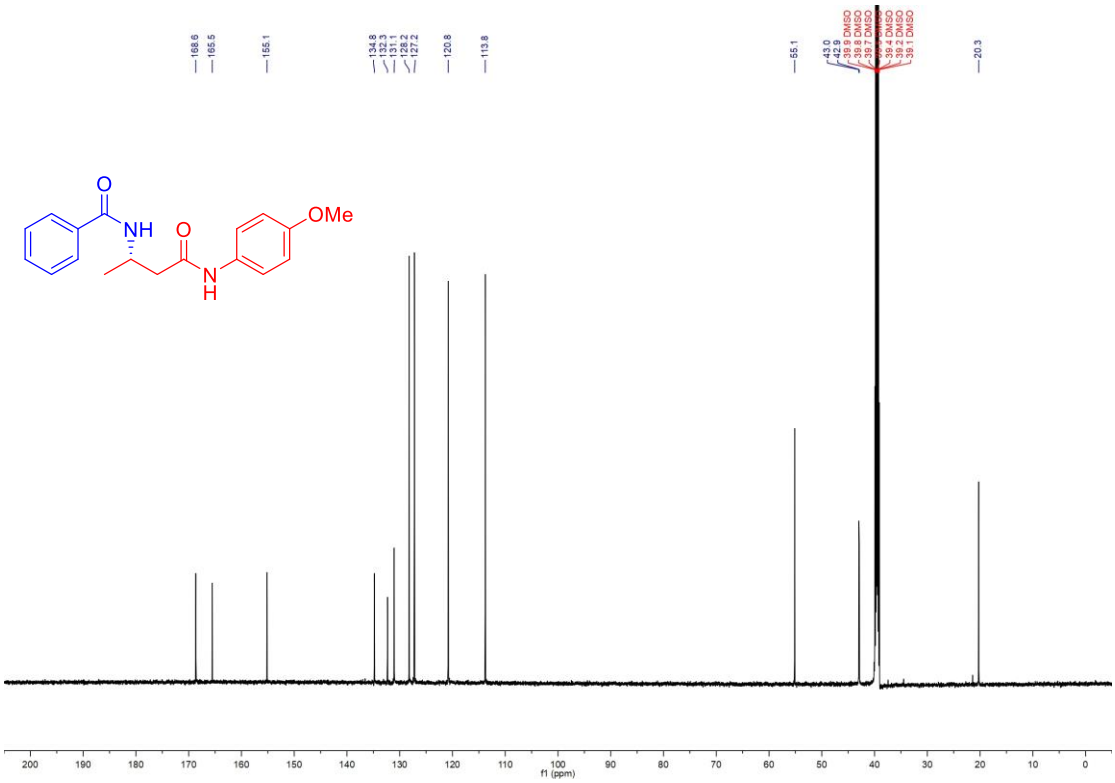


Figure S53. ^{1}H NMR spectra (400 MHz, Chloroform-*d*) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-2-methylbenzamide (5ab).

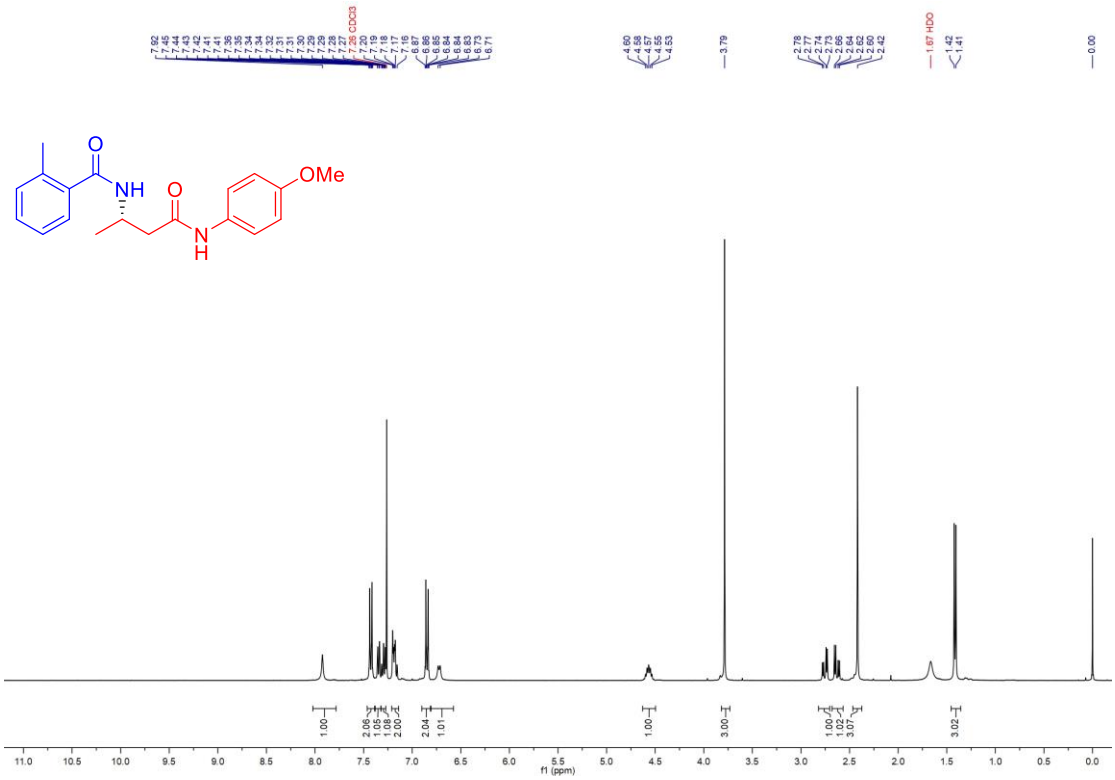


Figure S54. ^{13}C NMR spectra (100 MHz, Chloroform-*d*) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-2-methylbenzamide (5ab).

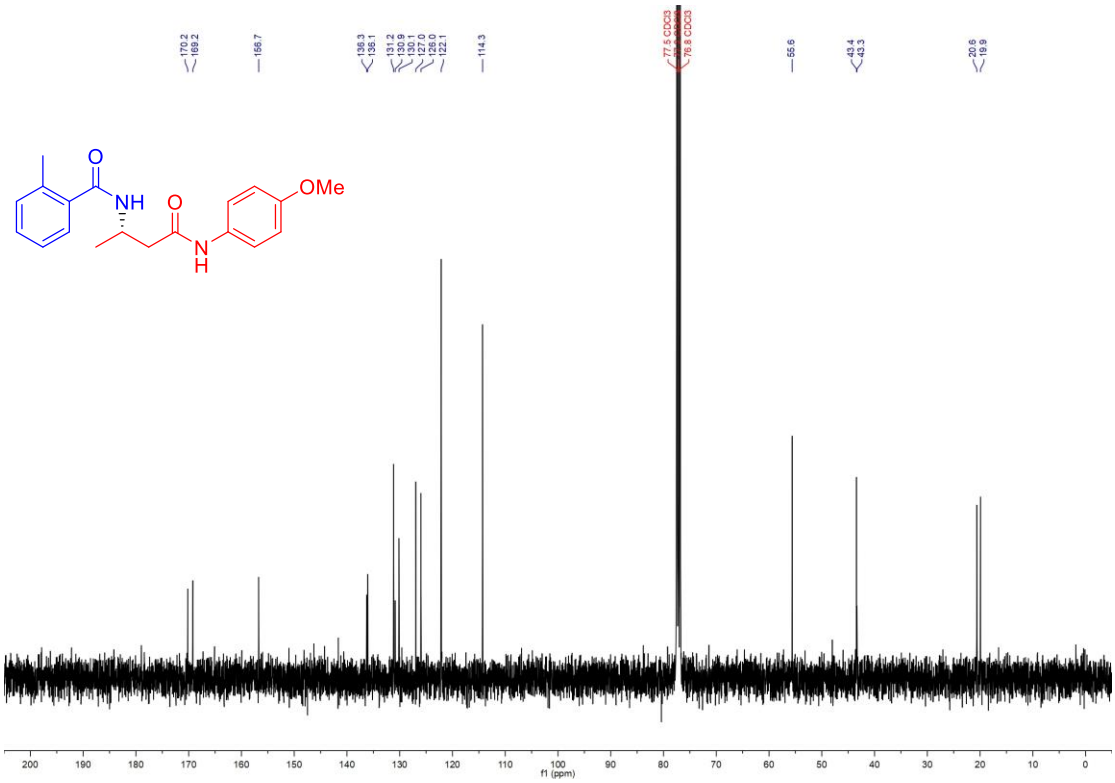


Figure S55. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-2-Methoxy-*N*-(4-((4-methoxyphen yl)amino)-4-oxobutan-2-yl)benzamide (5ac).

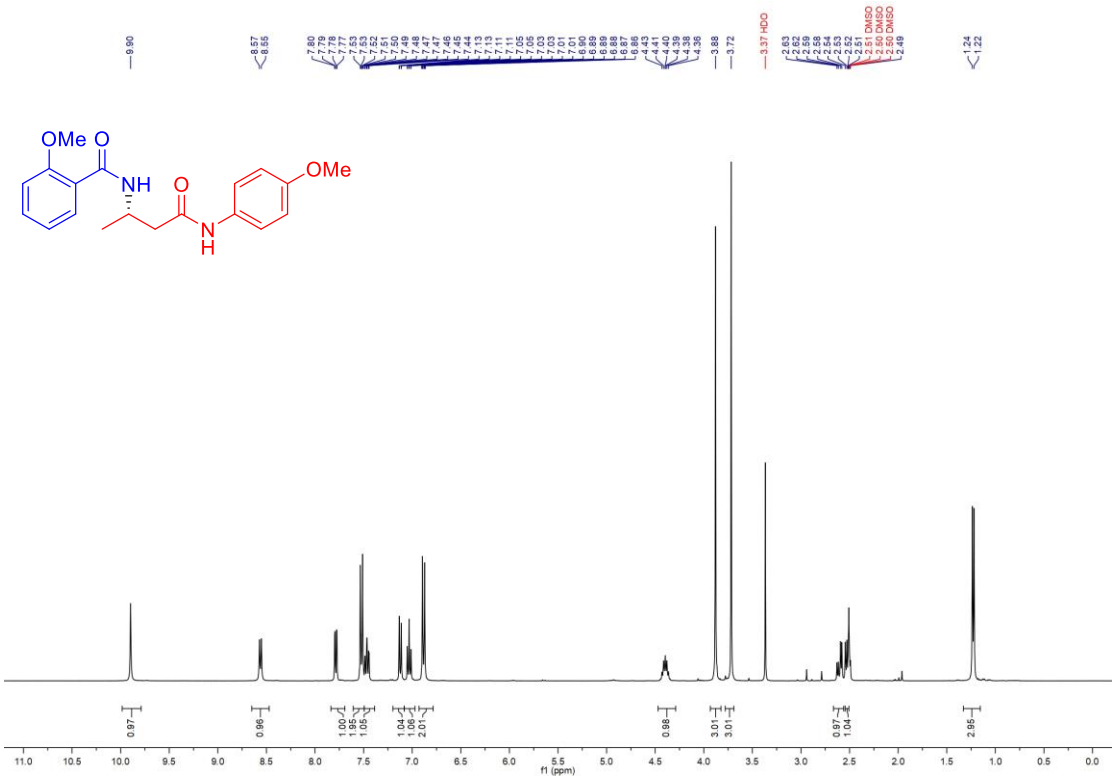


Figure S56. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-2-Methoxy-*N*-(4-((4-methoxyphe nyl)amino)-4-oxobutan-2-yl)benzamide (5ac).

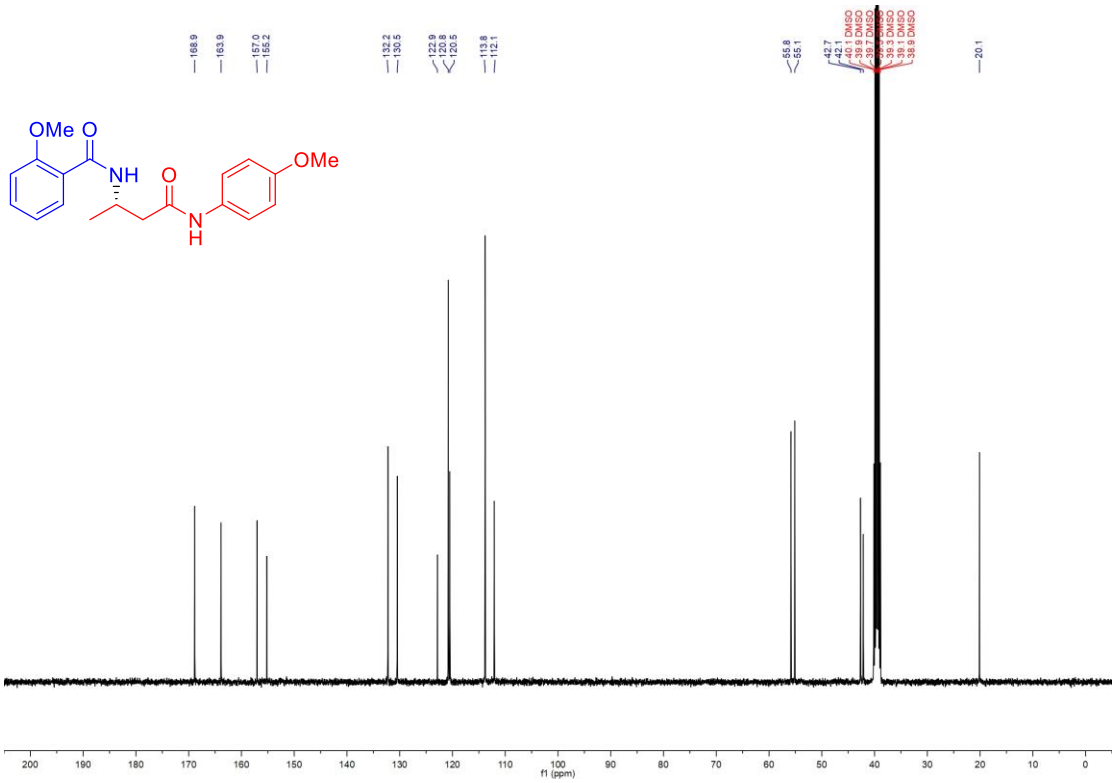


Figure S57. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-3-methylbenzamide (5ad).

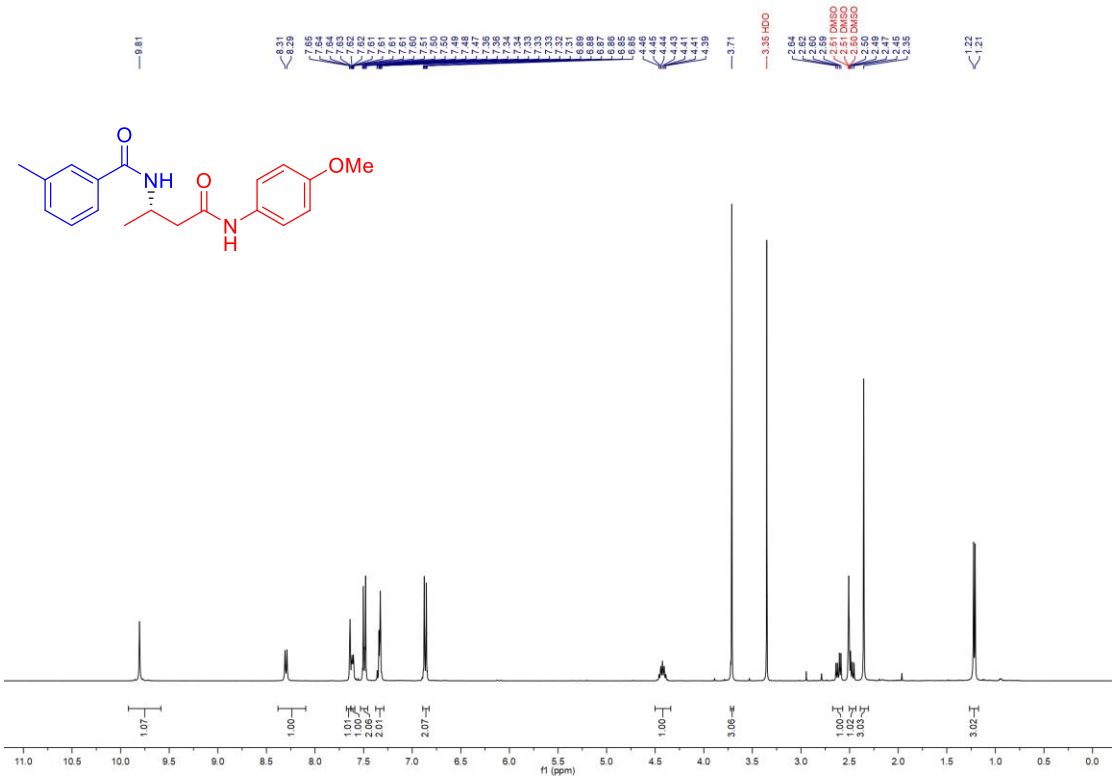


Figure S58. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-3-methylbenzamide (5ad).

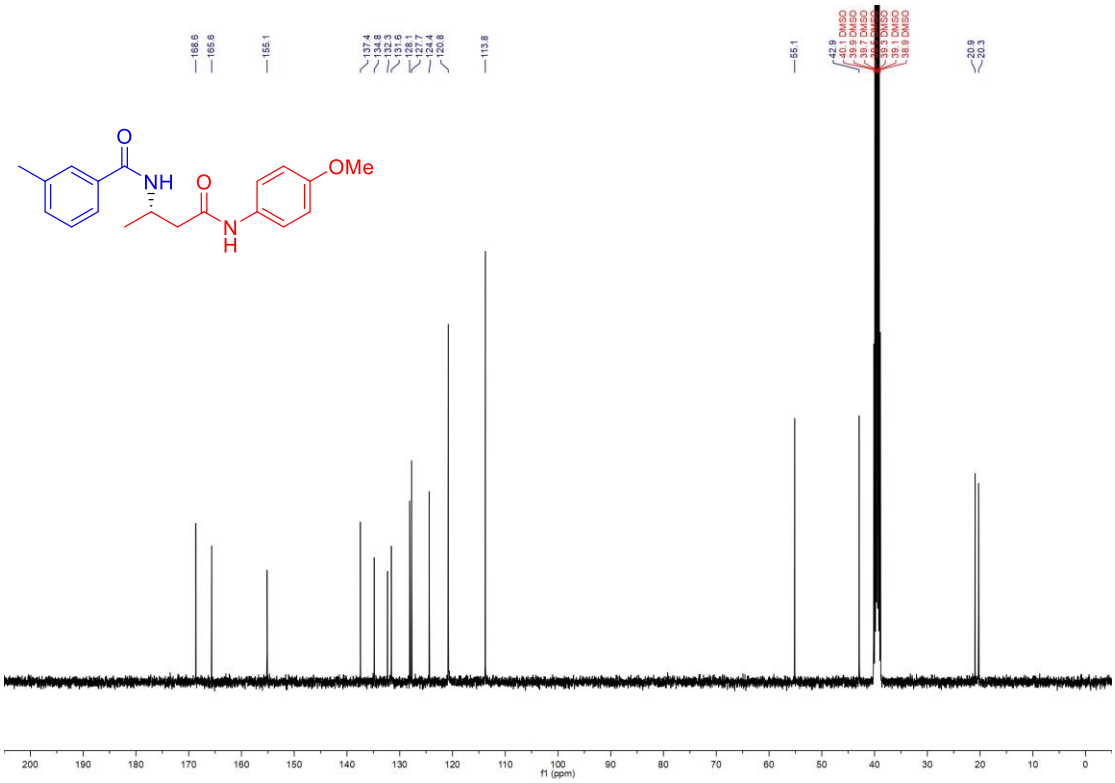


Figure S59. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-3-Methoxy-*N*-(4-((4-methoxyphen yl)amino)-4-oxobutan-2-yl)benzamide (5ae).

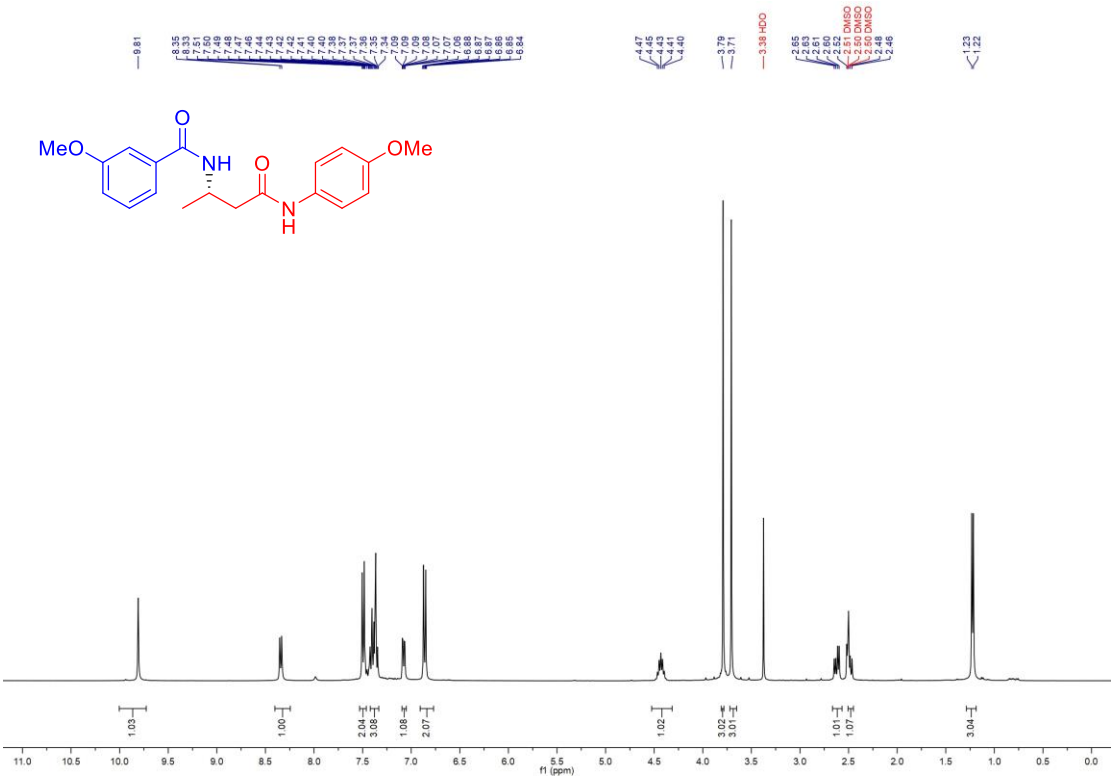


Figure S60. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-3-Methoxy-*N*-(4-((4-methoxyphe nyl)amino)-4-oxobutan-2-yl)benzamide (5ae).

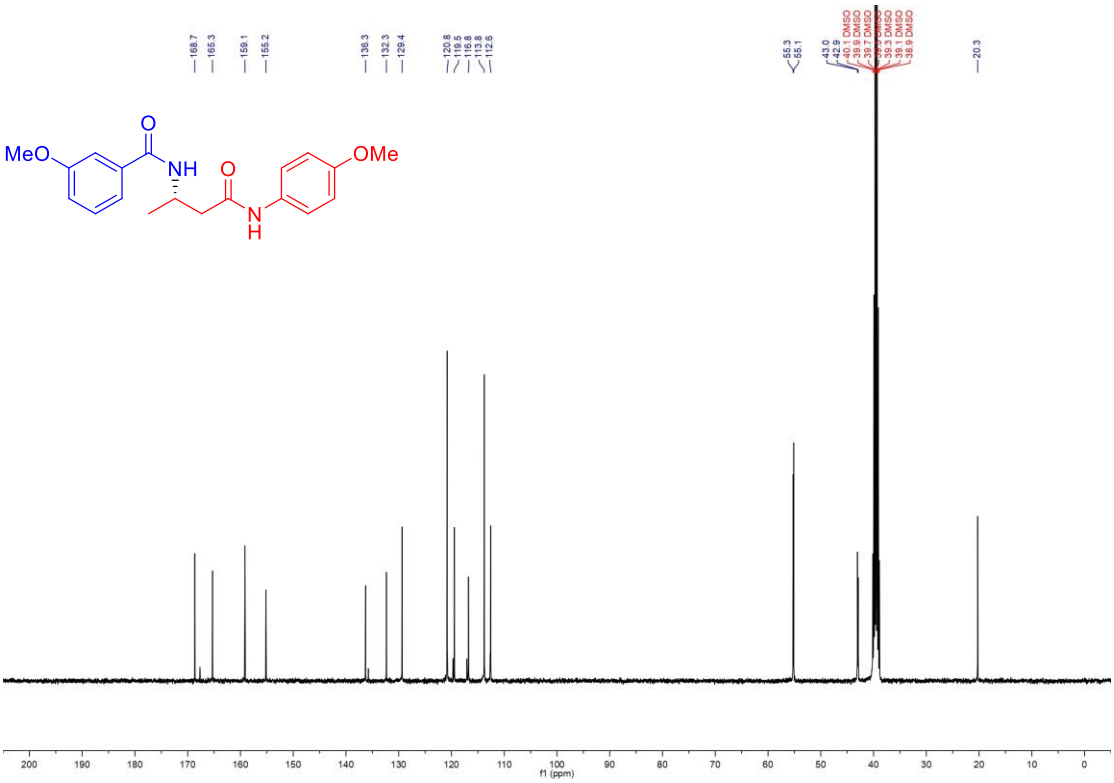


Figure S61. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5ah).

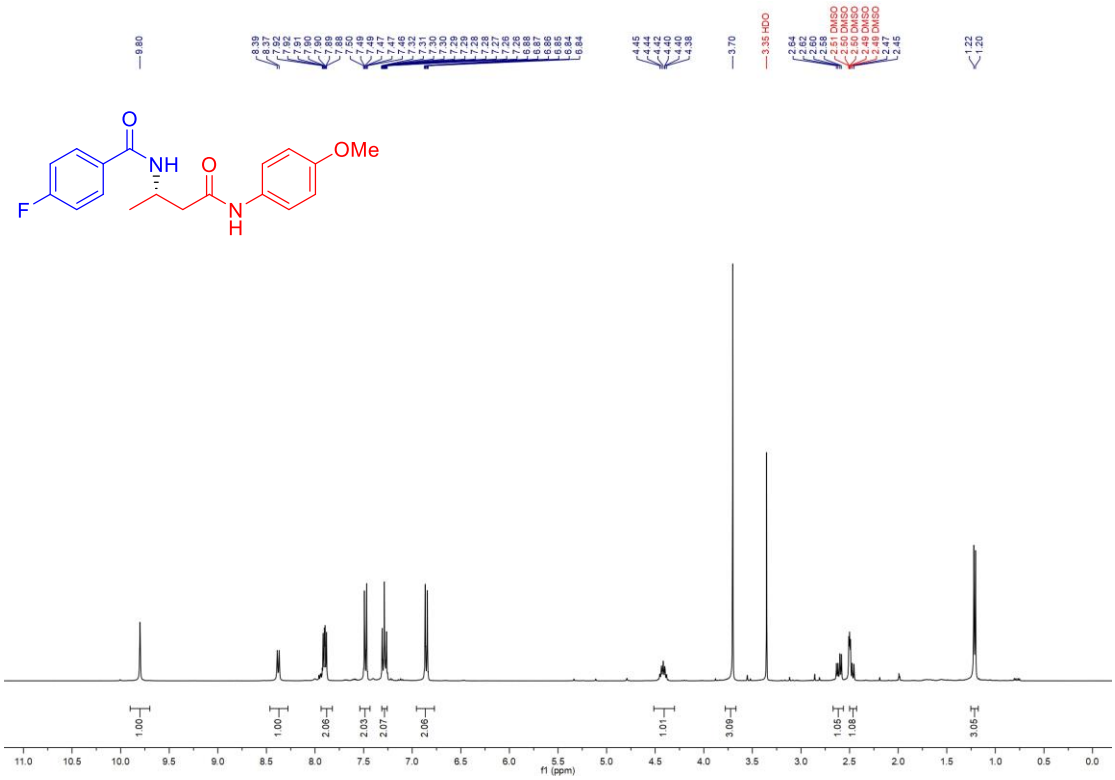


Figure S62. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5ah).

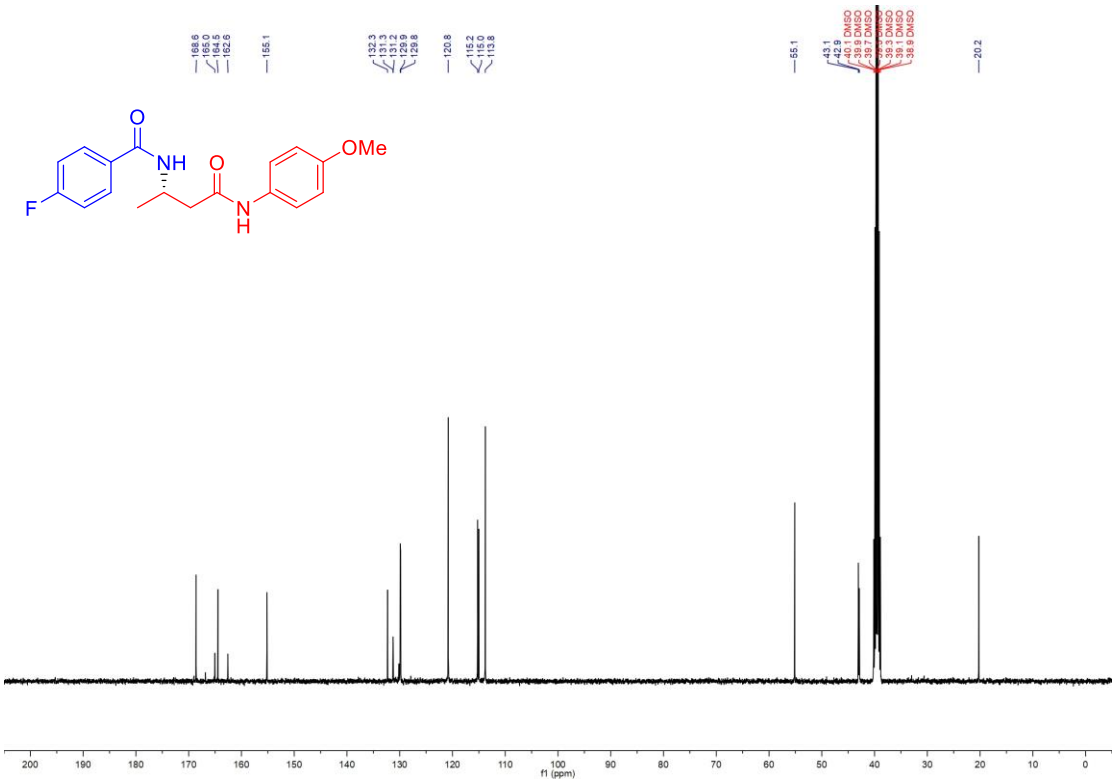


Figure S63. ^{19}F NMR spectra (376 MHz, DMSO-d_6) of (*S*)-4-Fluoro-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5ah).

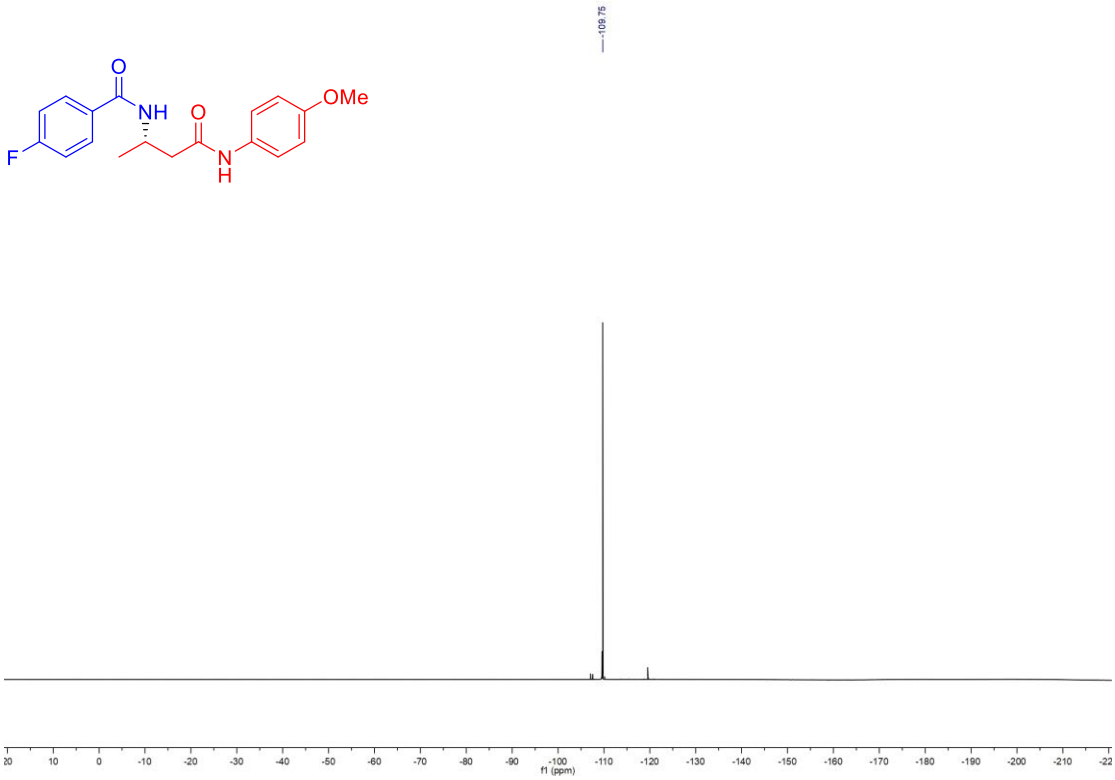


Figure S64. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Chloro-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5ai).

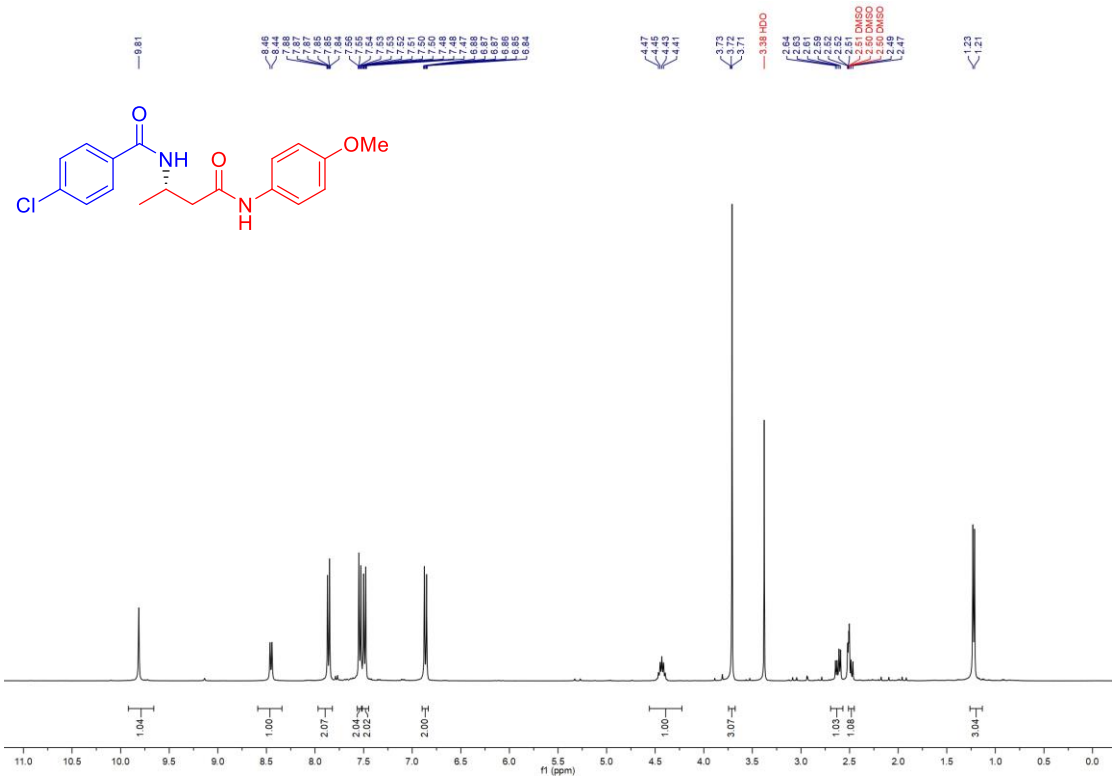


Figure S65. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Chloro-*N*-(4-((4-methoxypheny l)amino)-4-oxobutan-2-yl)benzamide (5ai).

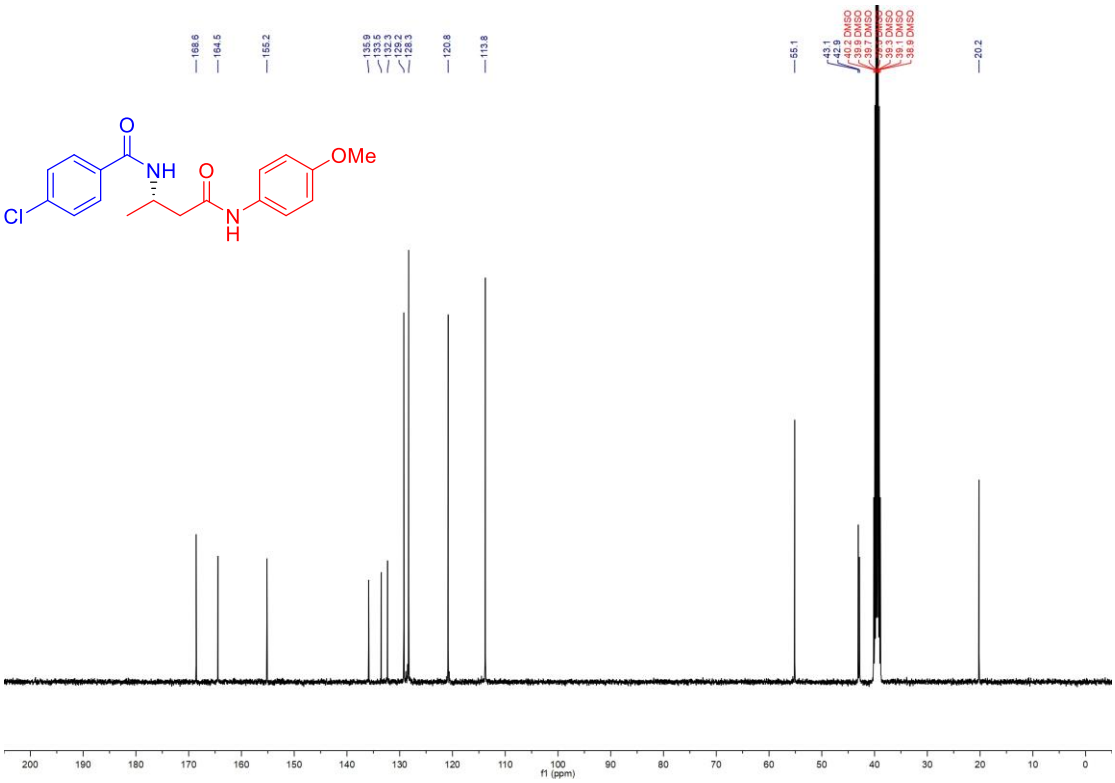


Figure S66. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-4-Bromo-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5aj).

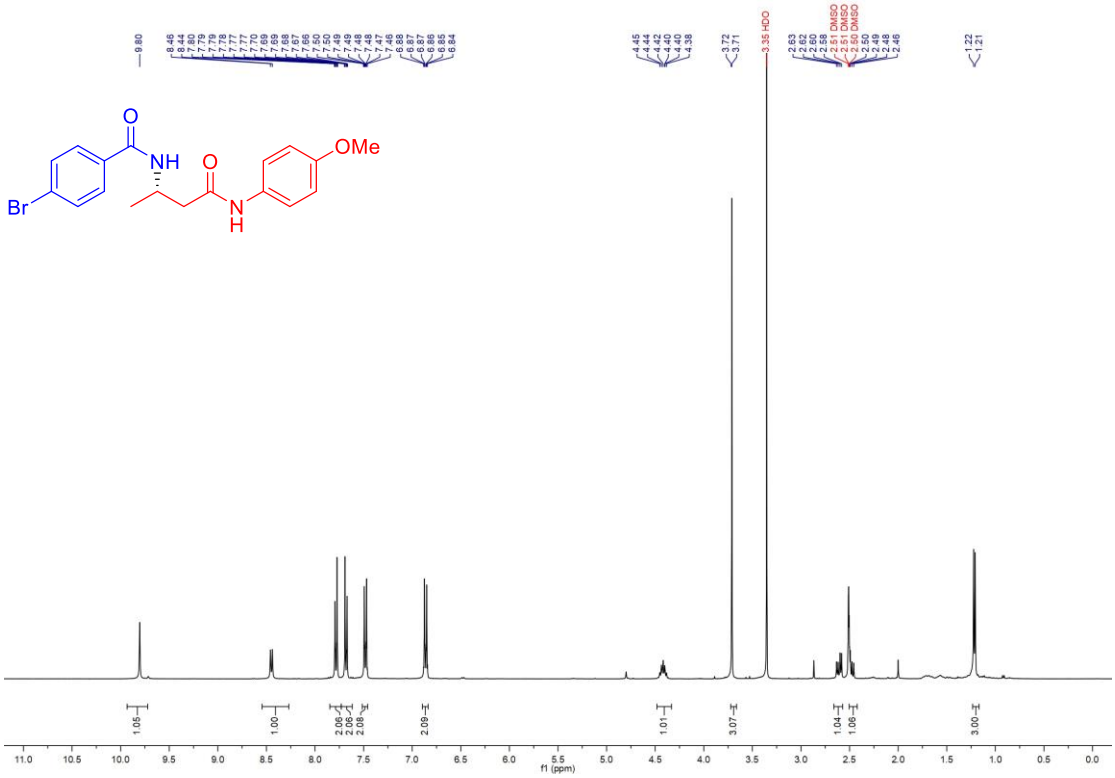


Figure S67. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-4-Bromo-*N*-(4-((4-methoxyphenyl) amino)-4-oxobutan-2-yl)benzamide (5aj).

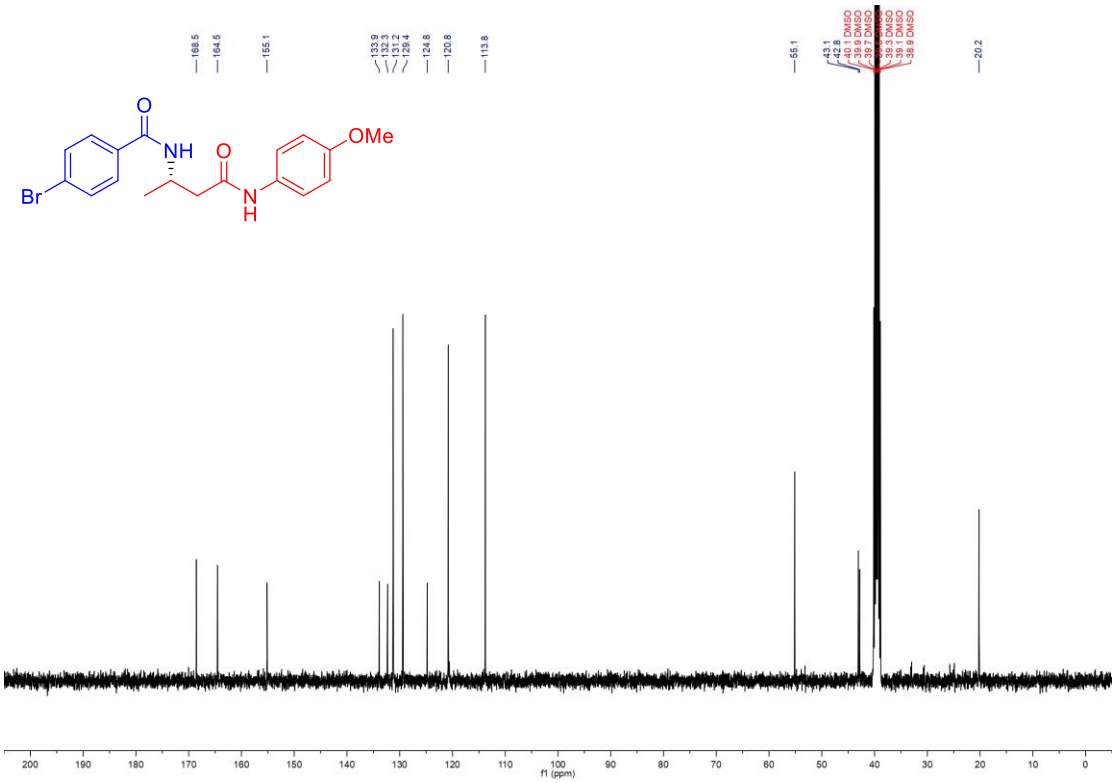


Figure S68. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-(trifluoromethoxy)benzamide (5ak).

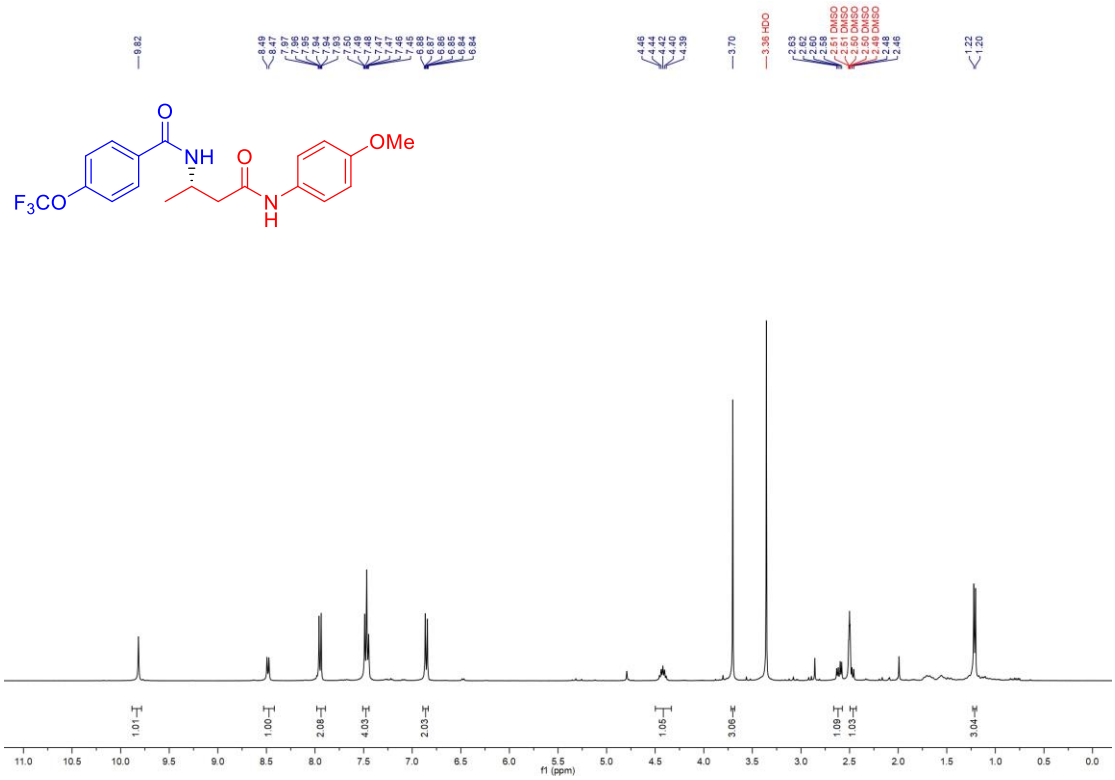


Figure S69. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-(trifluoromethoxy)benzamide (5ak).

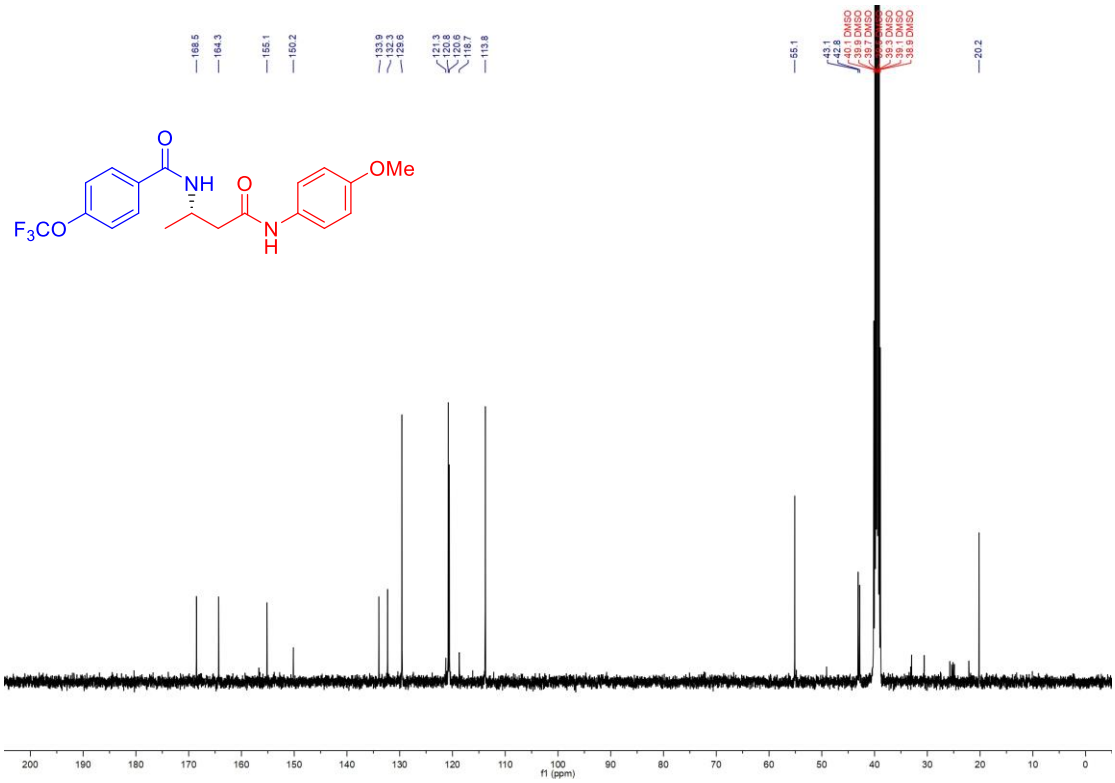


Figure S70. ^{19}F NMR spectra (376 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-(trifluoromethoxy)benzamide (5ak).

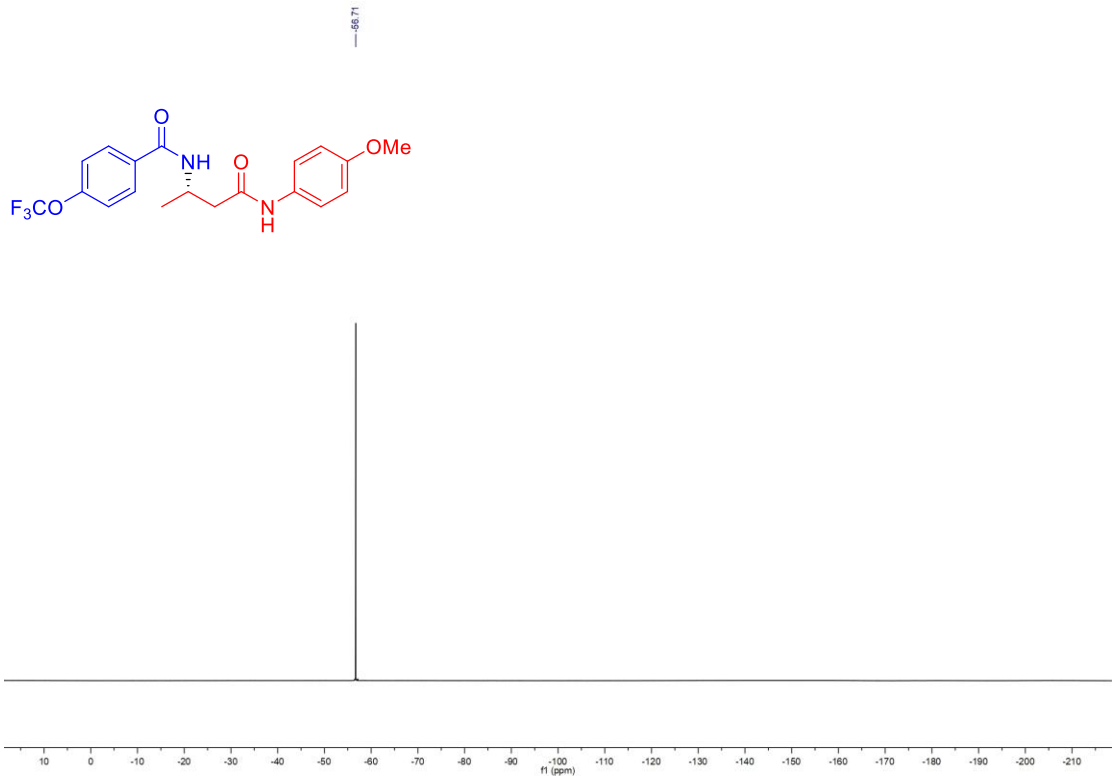


Figure S71. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-((trifluoromethyl)thio)benzamide (5am).

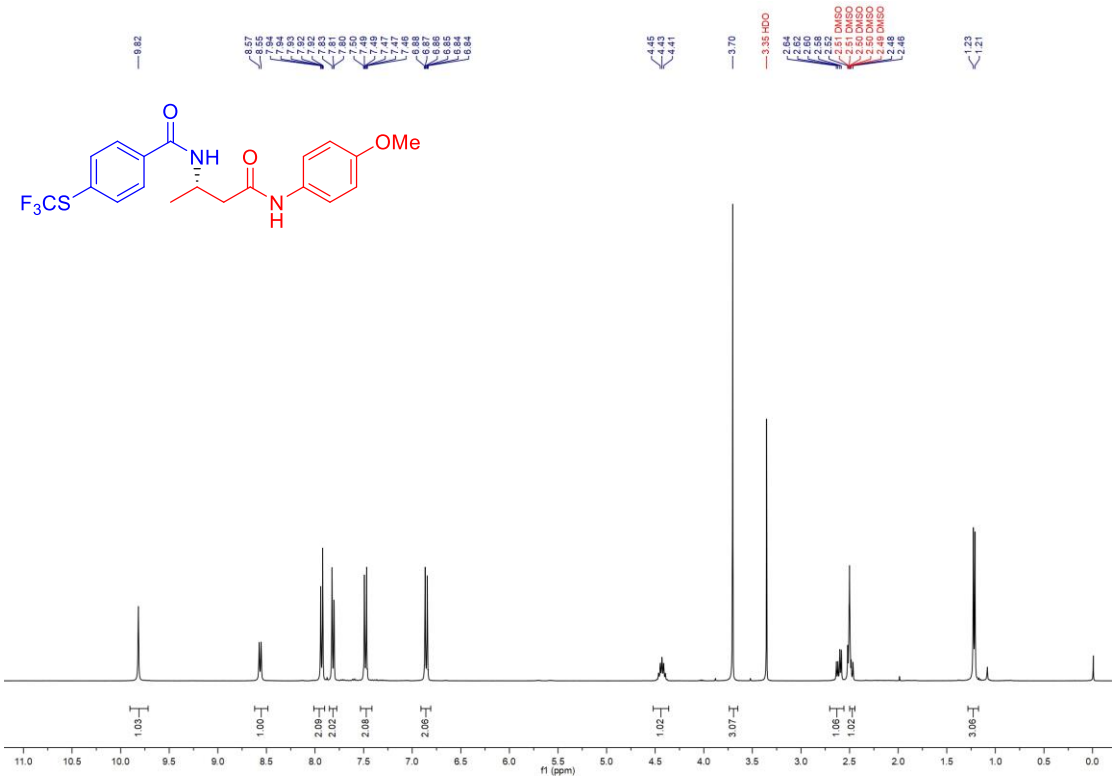


Figure S72. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-((trifluoromethyl)thio)benzamide (5am).

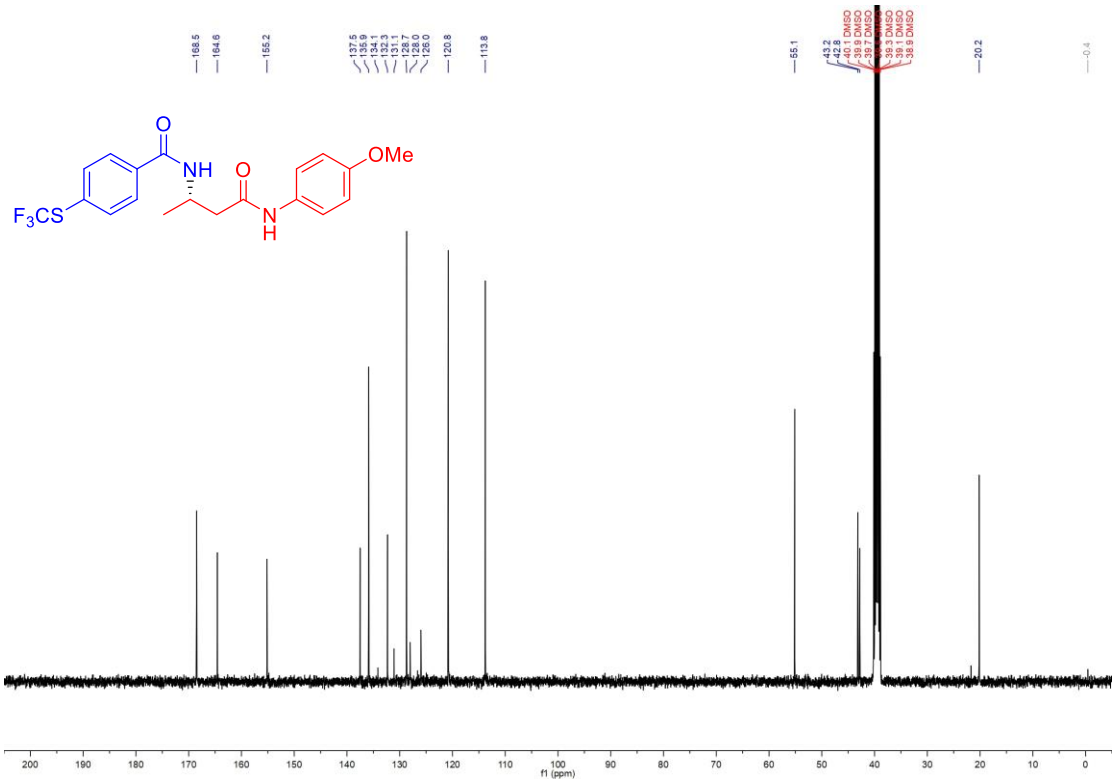


Figure S73. ^{19}F NMR spectra (376 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)-4-((trifluoromethyl)thio)benzamide (5am).

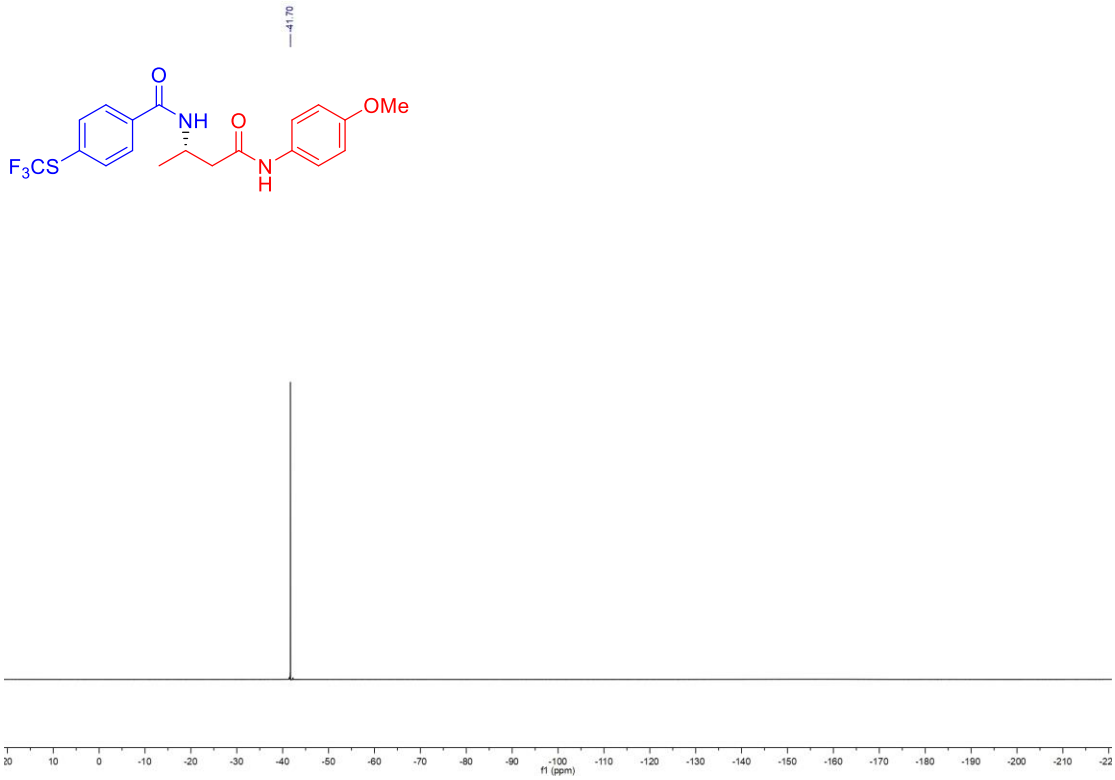


Figure S74. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzo[*d*][*1,3*]dioxole-5-carboxamide (5an).

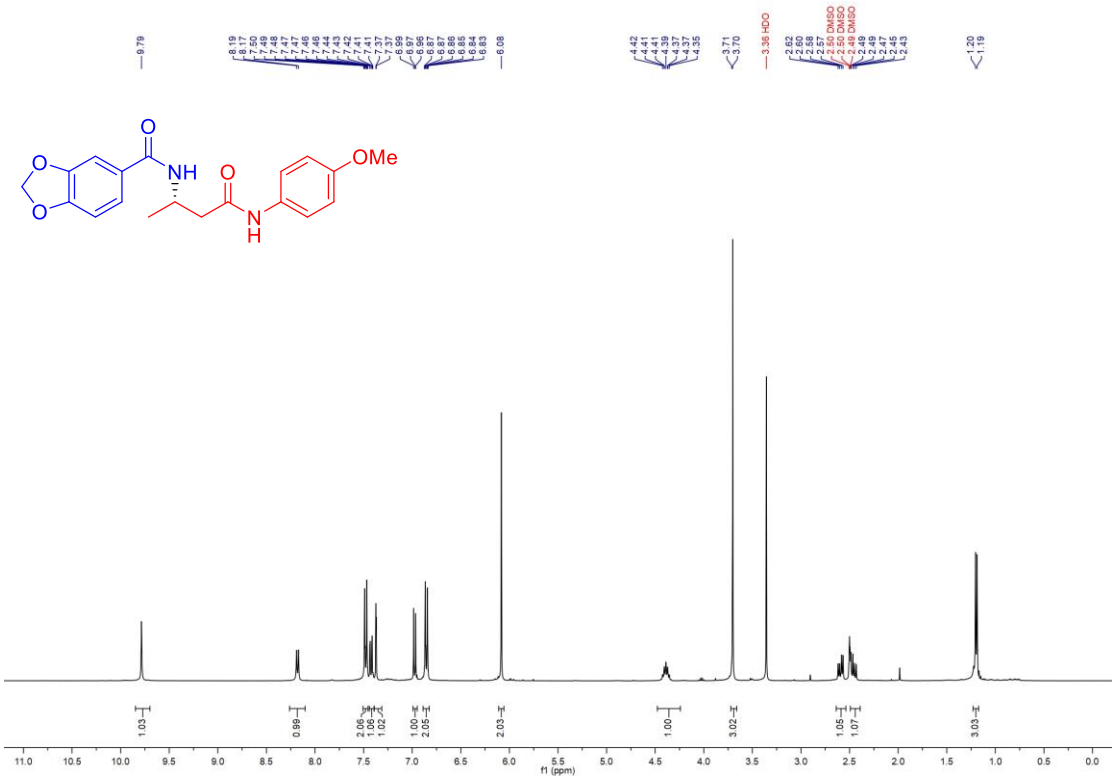


Figure S75. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)benzo[*d*][*1,3*]dioxole-5-carboxamide (5an).

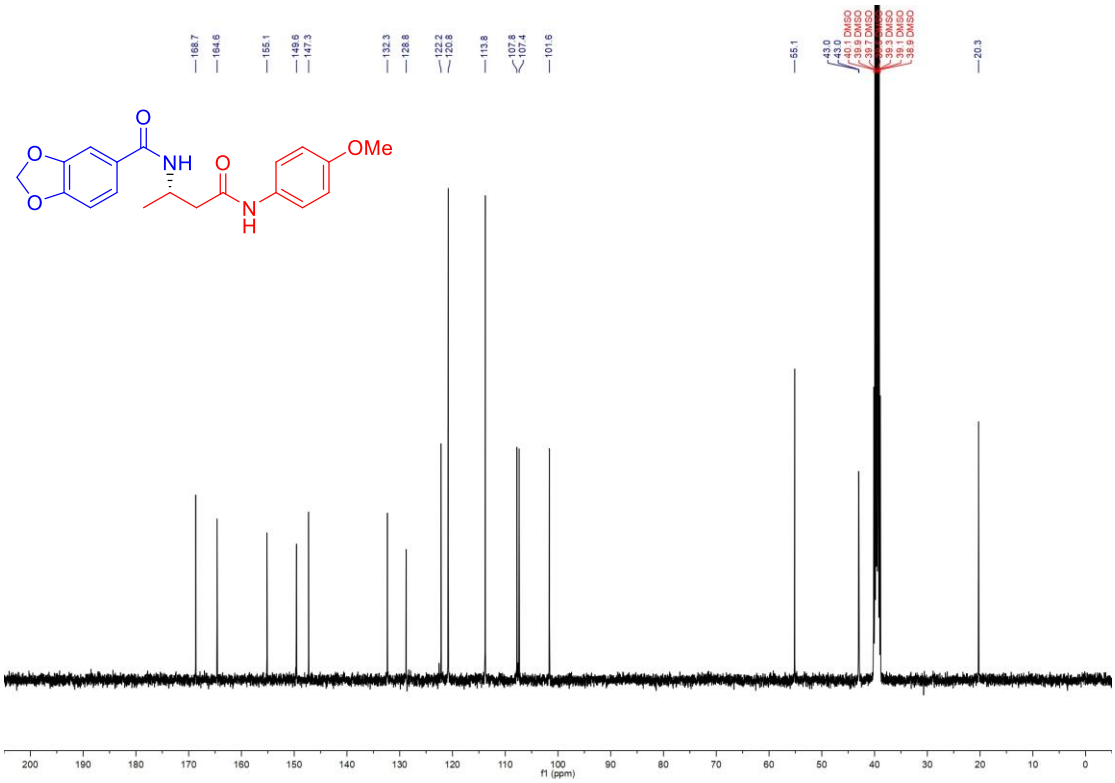


Figure S76. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)thiophene-2-carboxamide (5al).

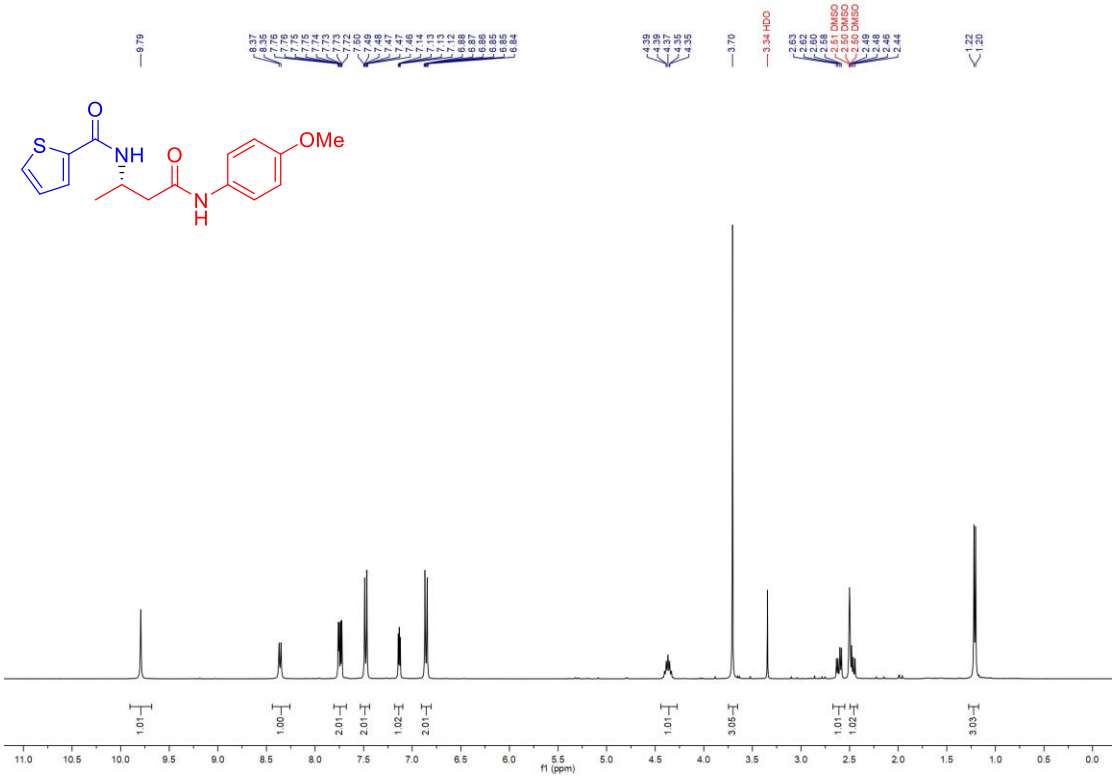


Figure S77. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl)thiophene-2-carboxamide (5al).

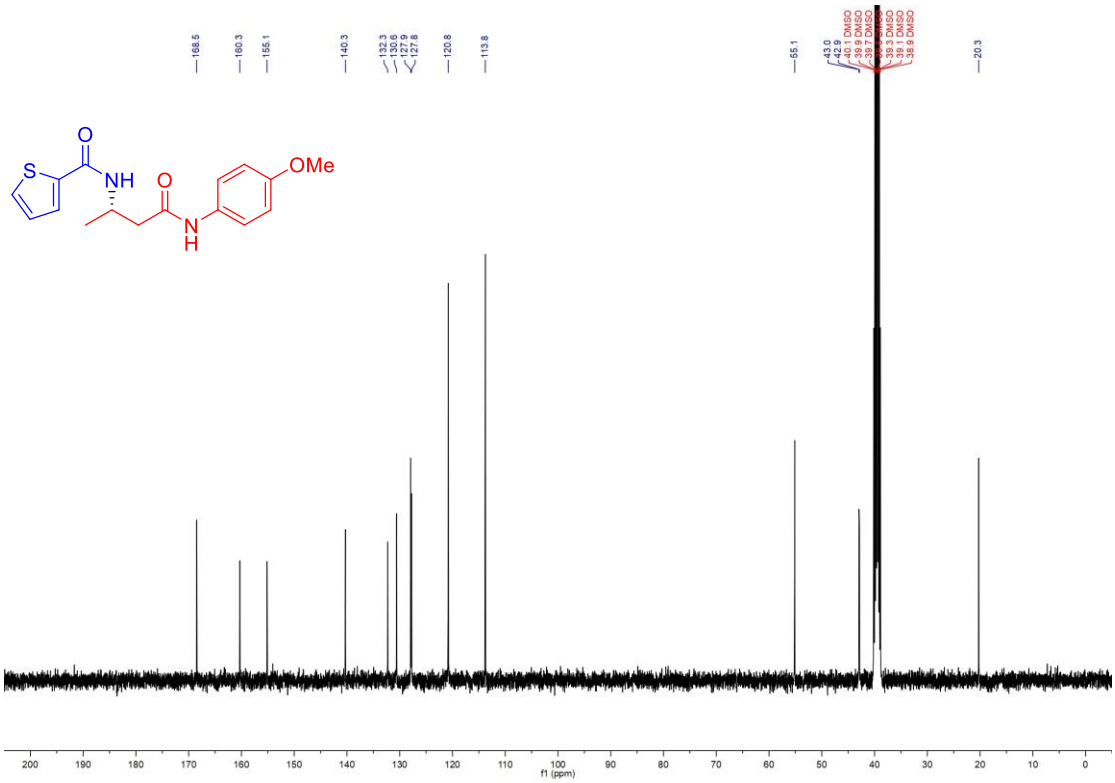


Figure S78. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(4-Methoxyphenyl)-3-pivalami dobutanamide (5ao).

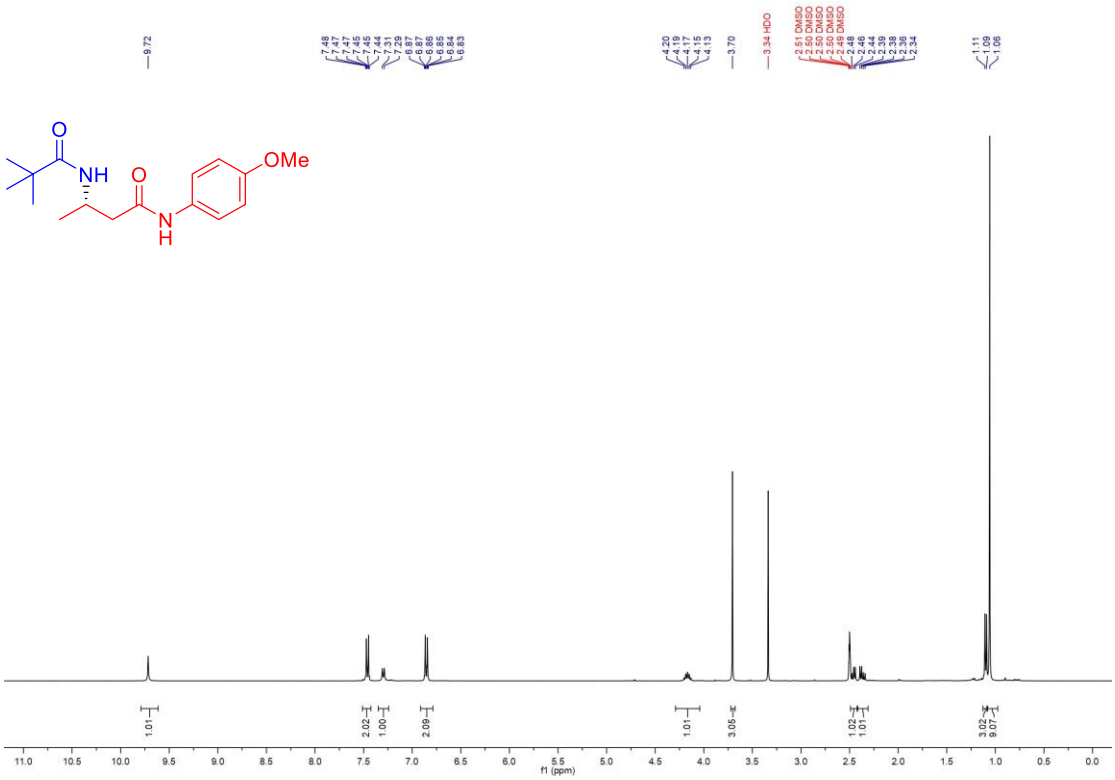


Figure S79. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(4-Methoxyphenyl)-3-pivalami dobutanamide (5ao).

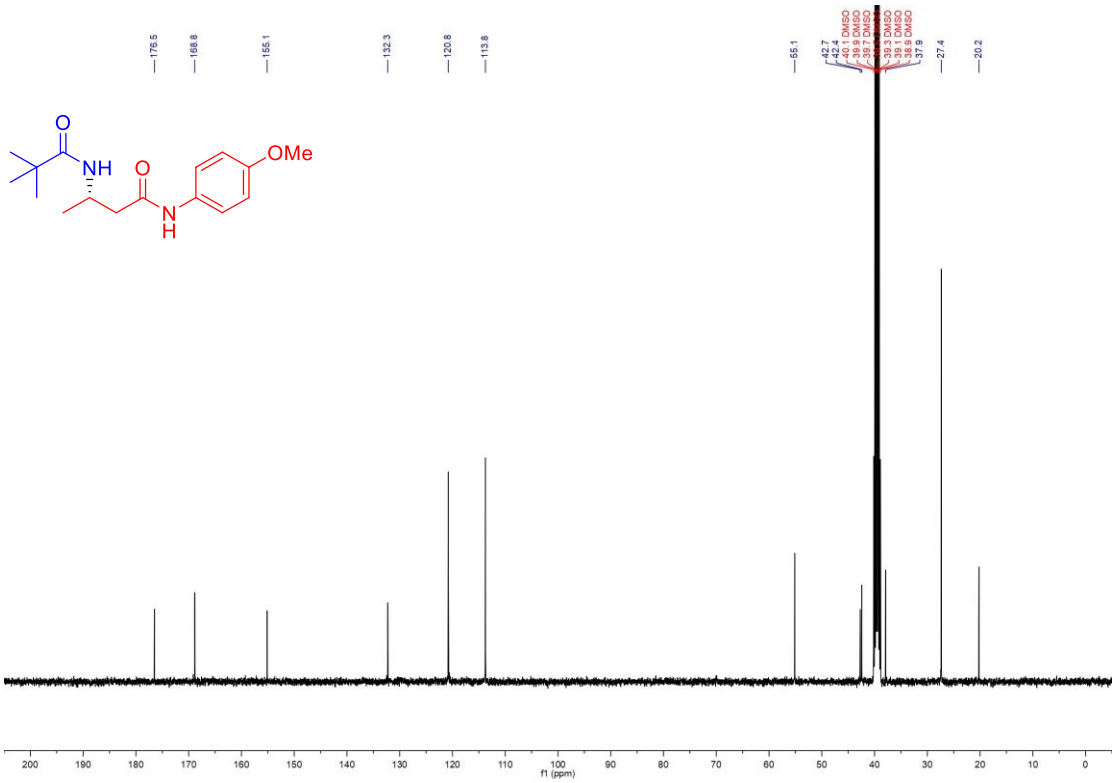


Figure S80. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(4-(Benzylamino)-4-oxobutan-2-yl)benzamide (5ba).

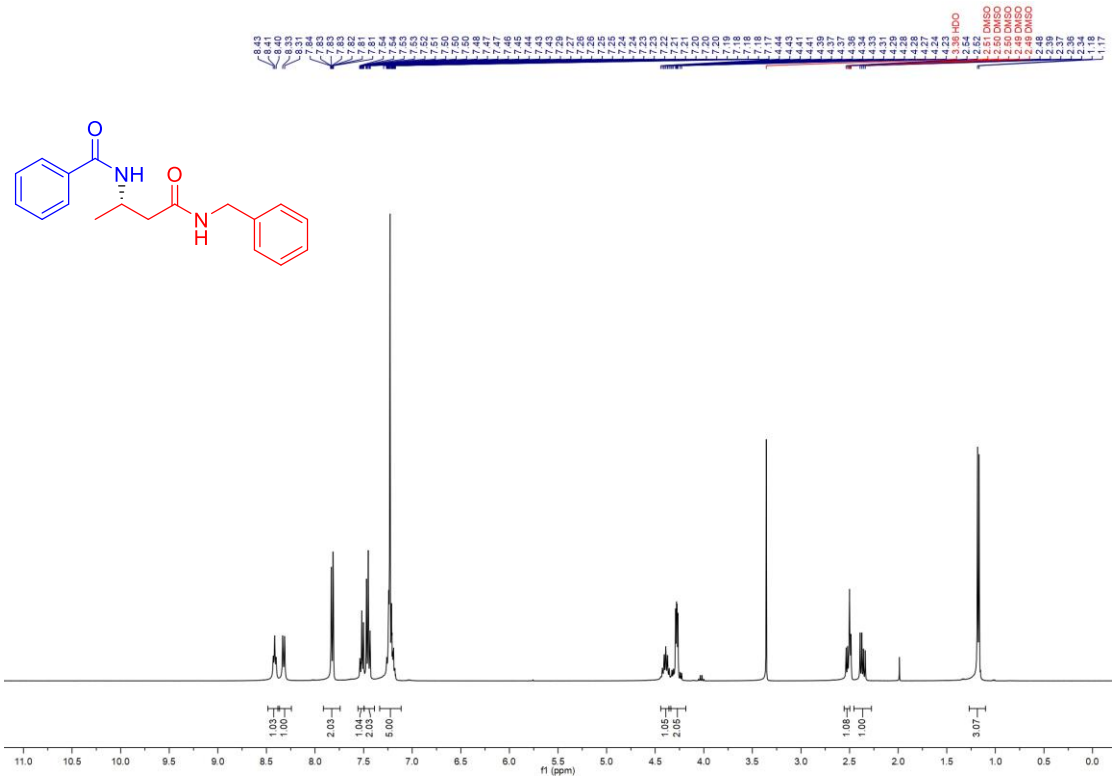


Figure S81. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(4-(Benzylamino)-4-oxobutan-2-yl)benzamide (5ba).

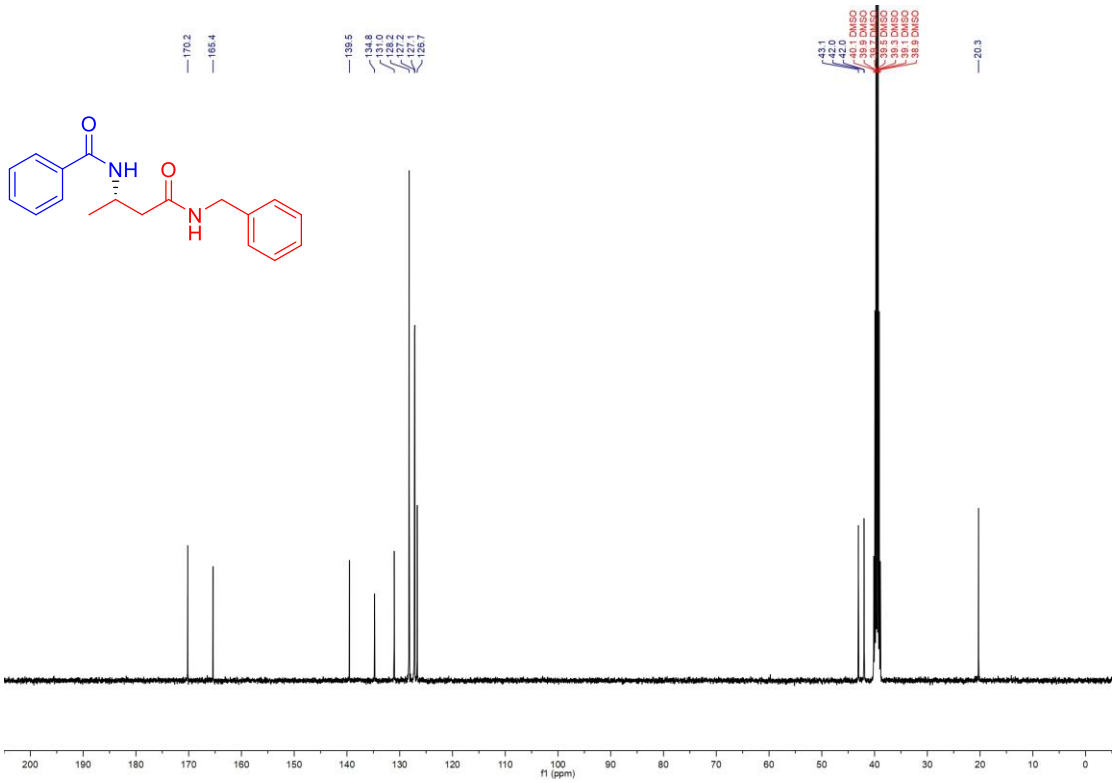


Figure S82. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxohexan-3-yl)benzamide (5ca)

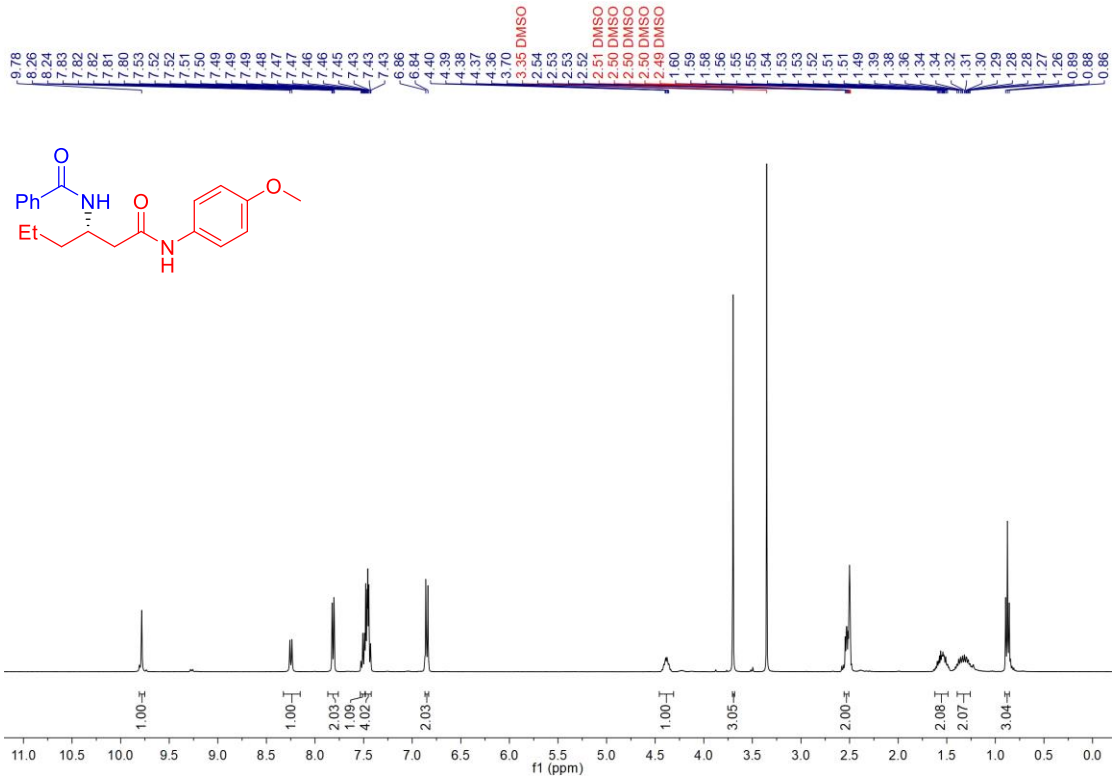


Figure S83. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxohexan-3-yl)benzamide (5ca)

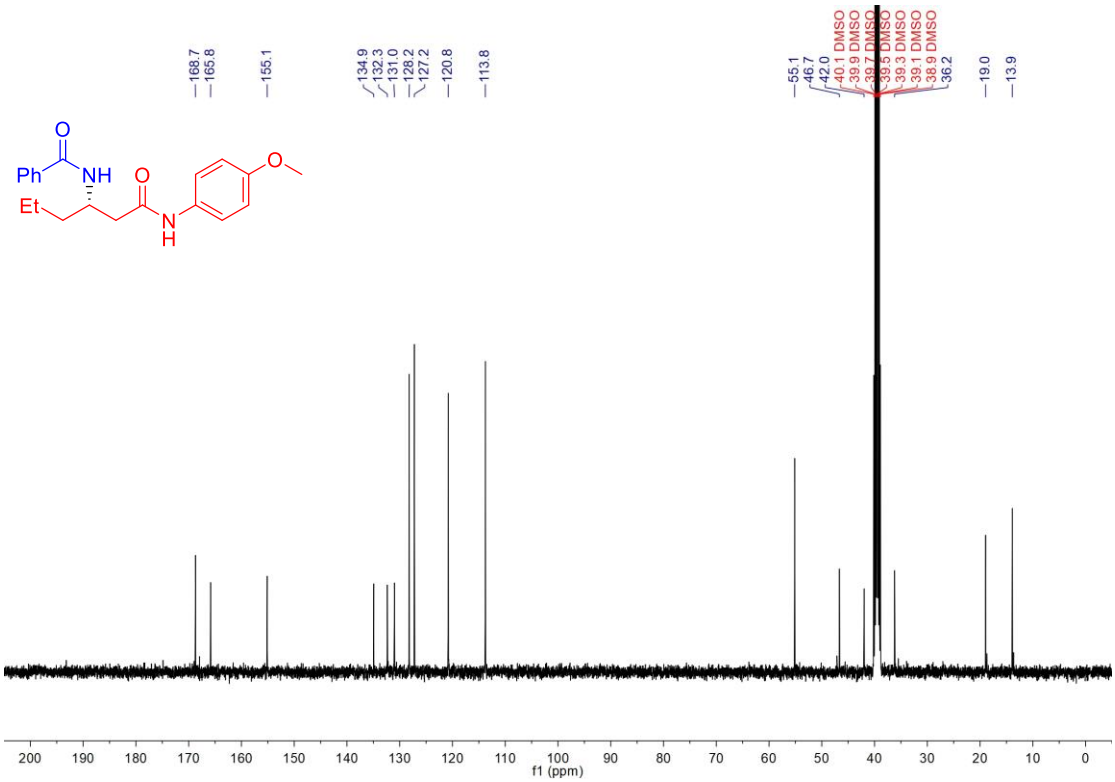


Figure S84 ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxoheptan-3-yl)benzamide (5da)

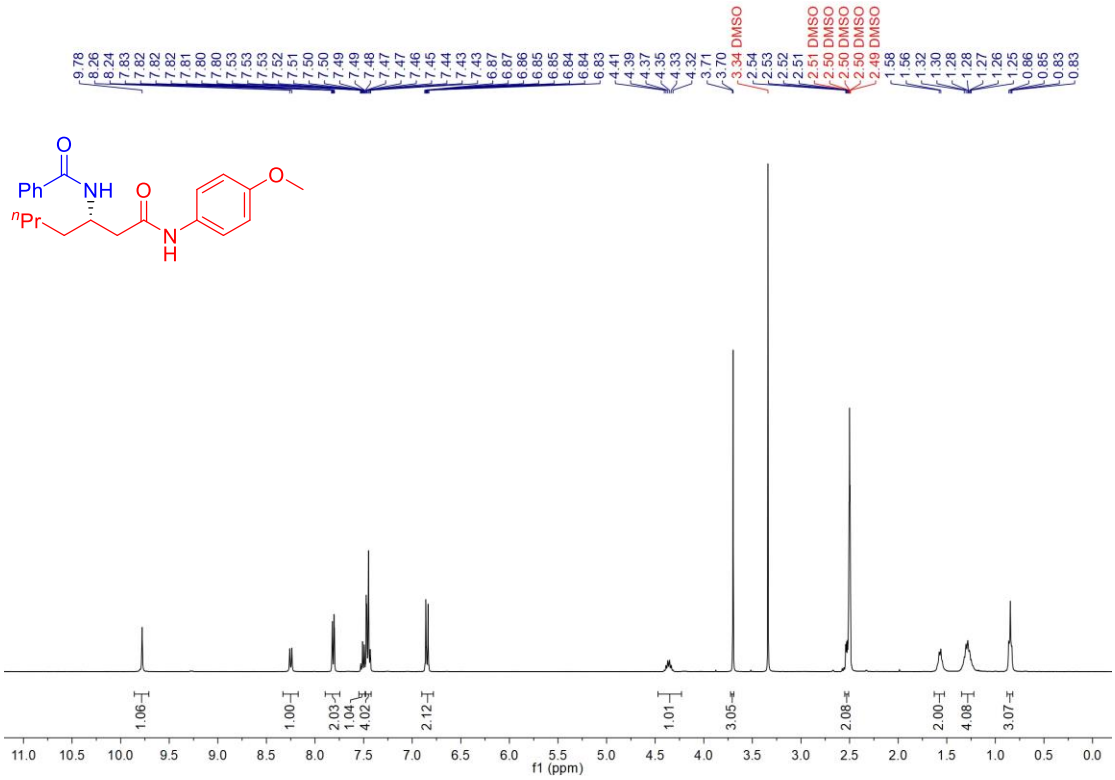


Figure S85. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxoheptan-3-yl)benzamide (5da)

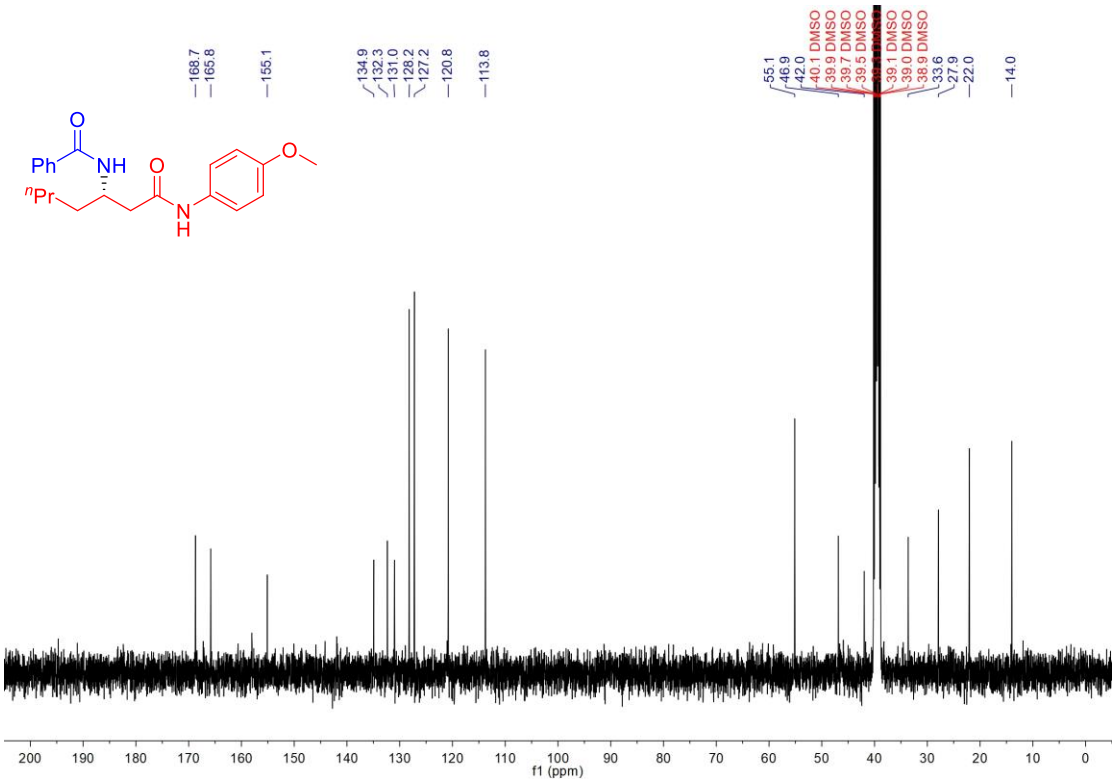


Figure S86. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of *N*-((*S*)-1-((*S*)-2-(6-Methoxynaphthalen-2-yl)propanamido)propan-2-yl)benzamide (6).

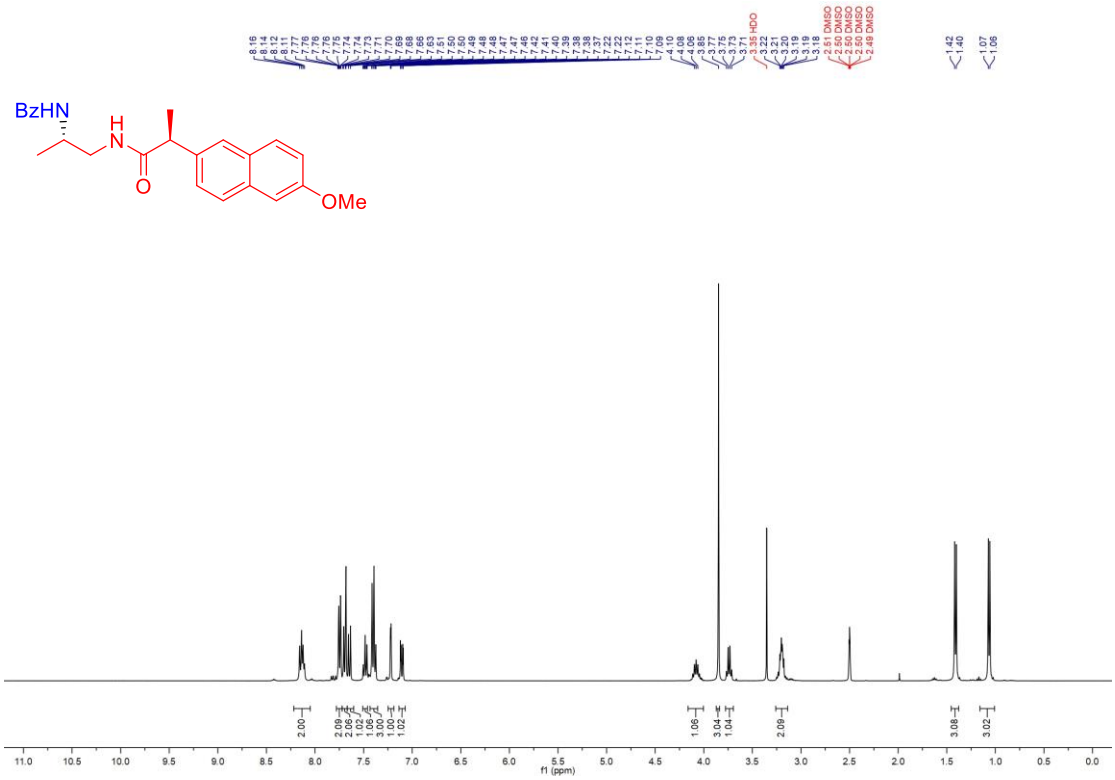


Figure S87. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of *N*-((*S*)-1-((*S*)-2-(6-Methoxynaphthalen-2-yl)propanamido)propan-2-yl)benzamide (6).

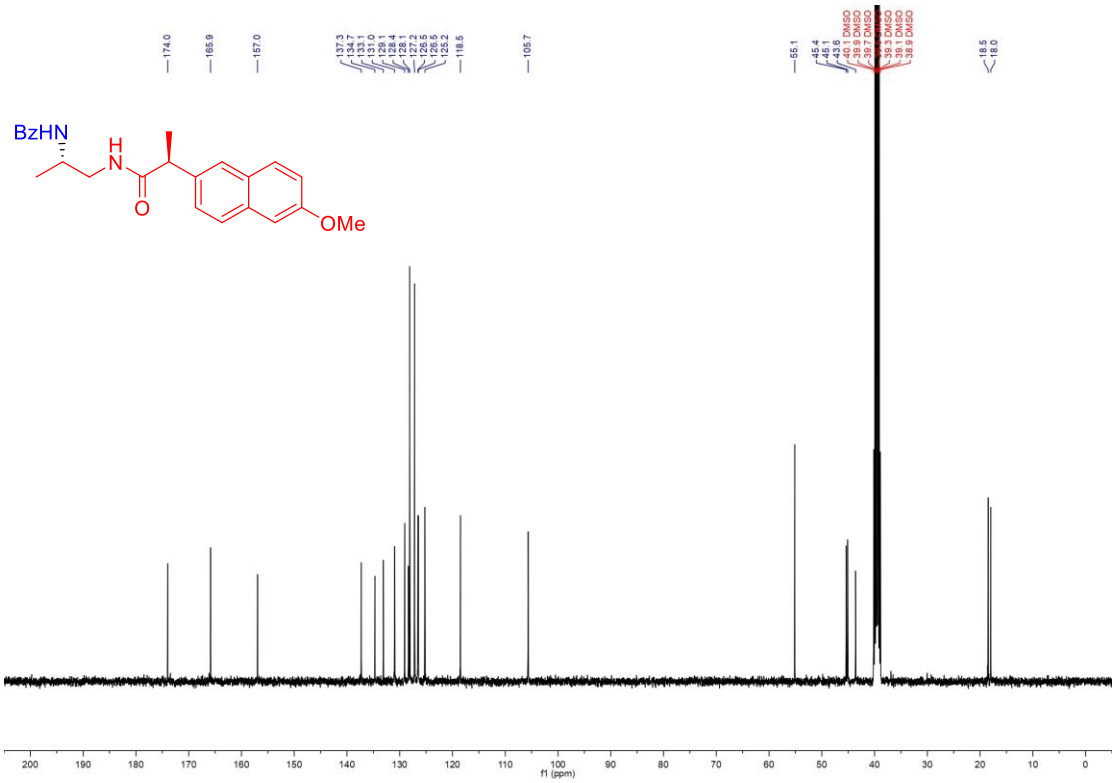


Figure S88. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-(2-(11-oxo-6,11-Dihydrodibenzo[*b*,*e*]oxepin-3-yl)acetamido)propan-2-yl)benzamide (7).

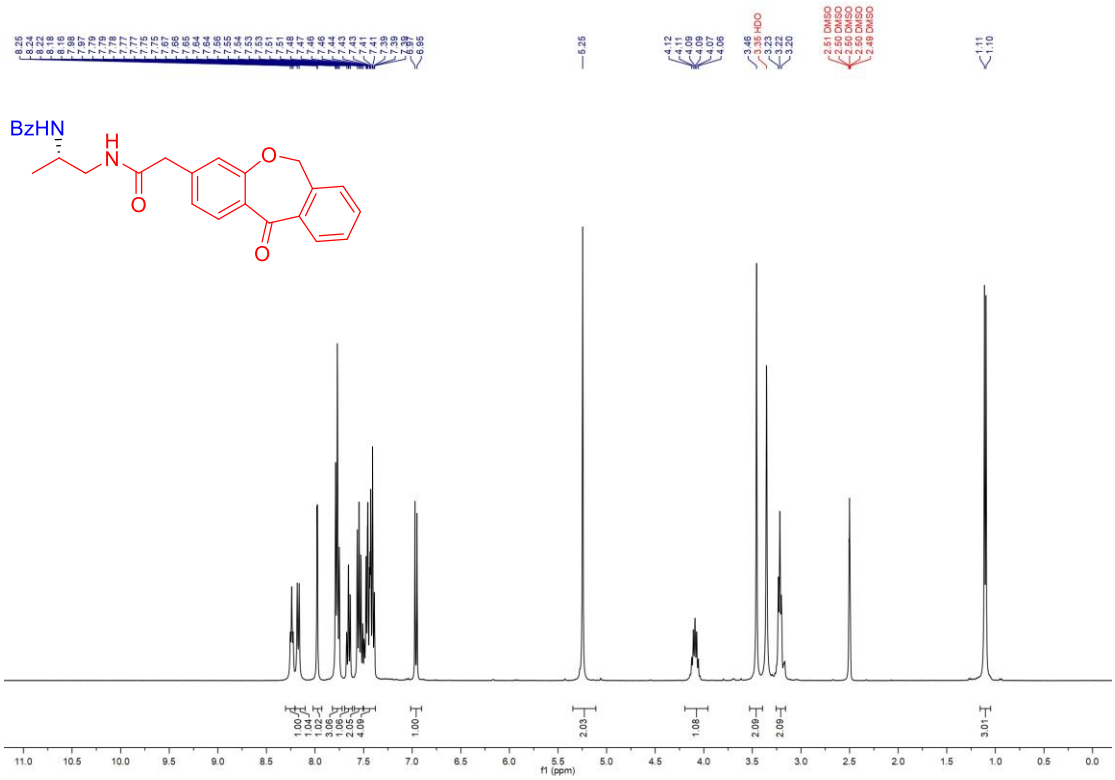


Figure S89. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(1-(2-(11-oxo-6,11-Dihydrodibenzo[*b*,*e*]oxepin-3-yl)acetamido)propan-2-yl)benzamide (7).

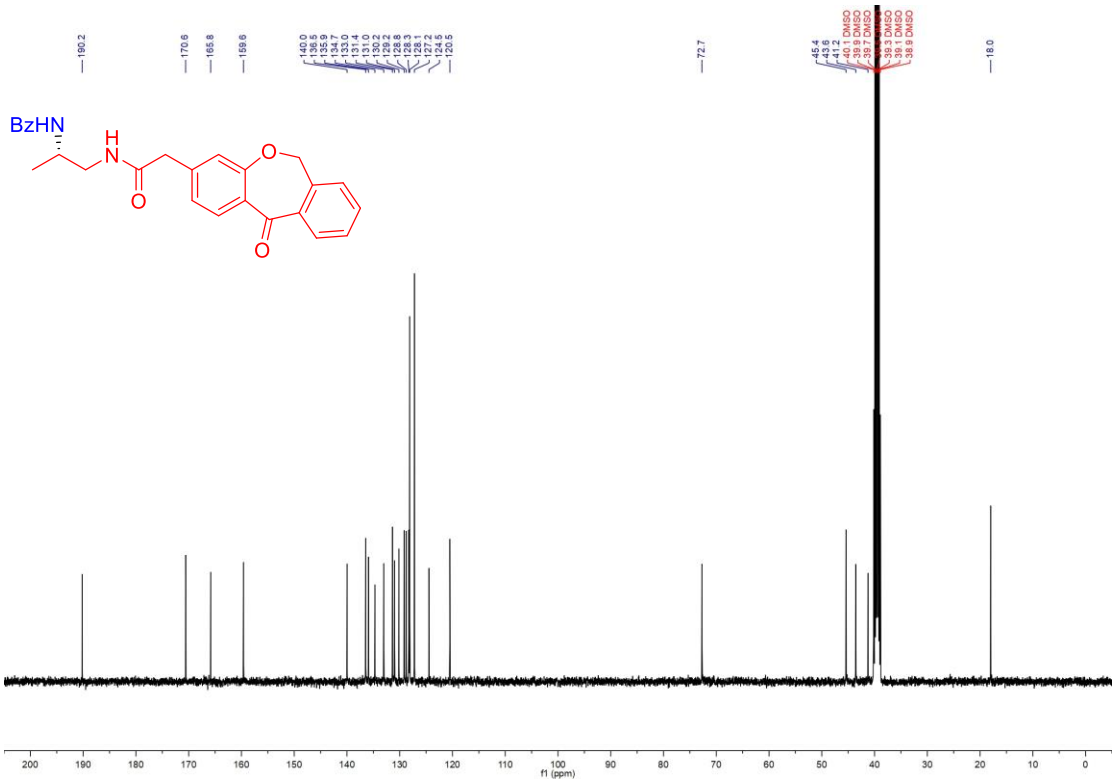


Figure S90. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*-(1-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)propan-2-yl)benzamide (8).

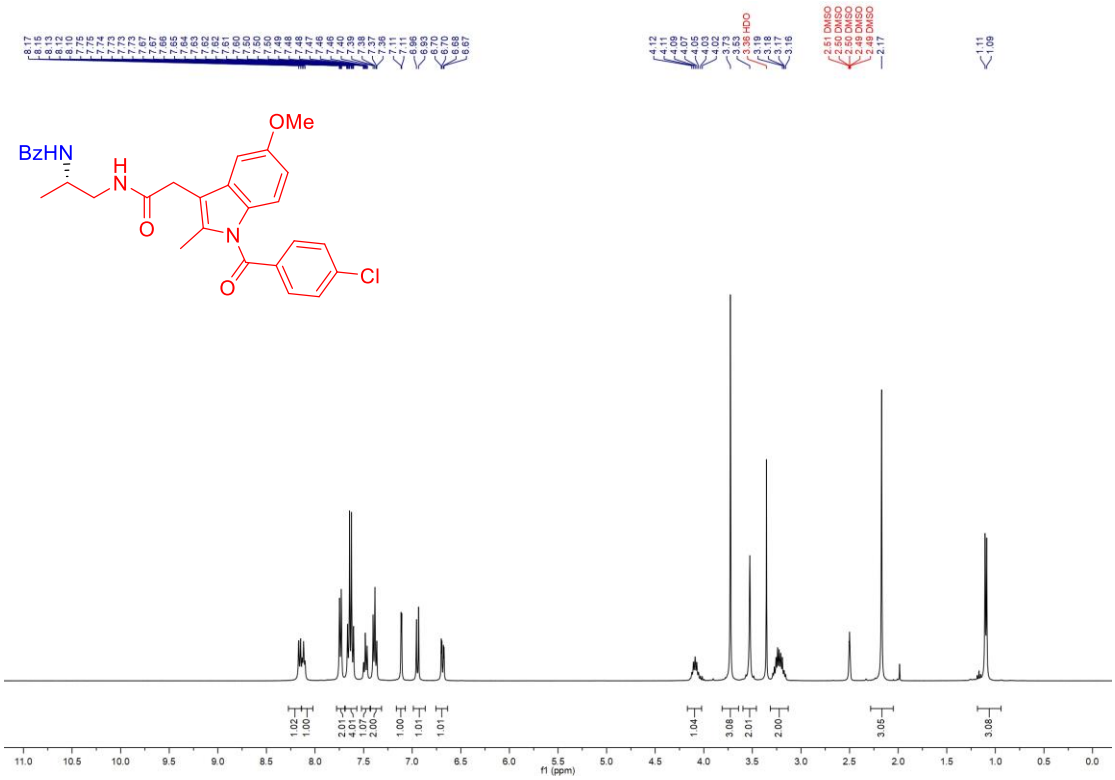


Figure S91. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*-(1-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)propan-2-yl)benzamide (8).

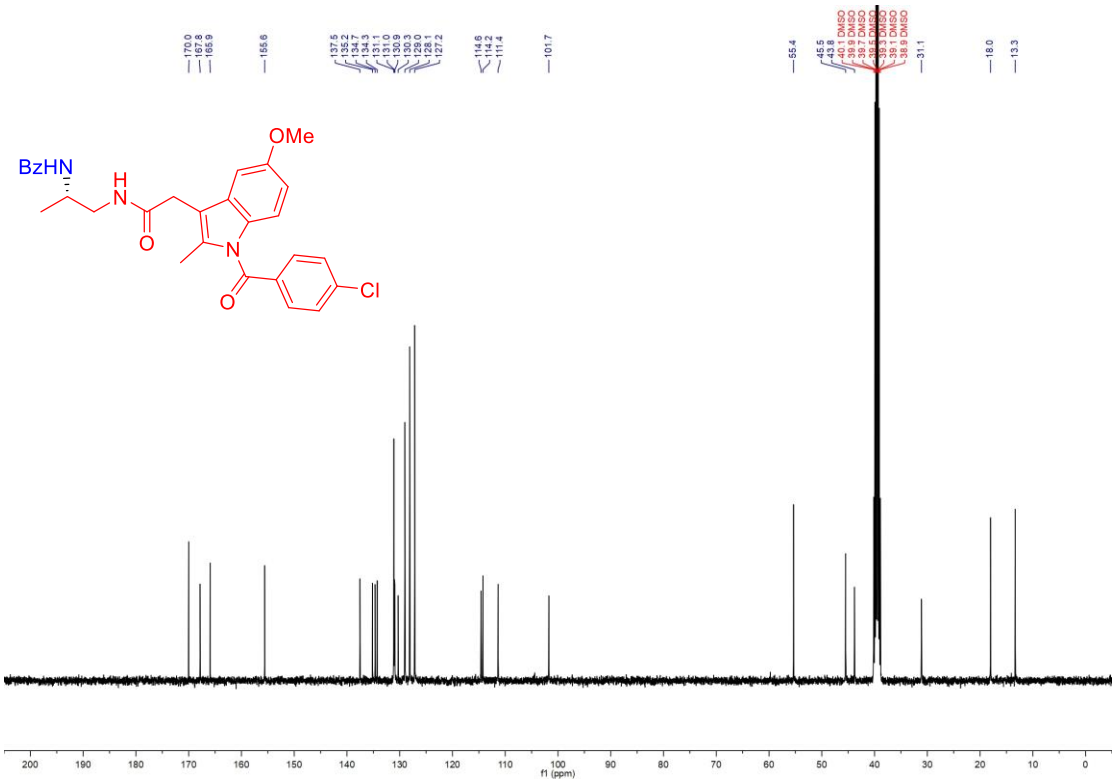


Figure S92. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-2-((2-(4-Methoxybenzamido)propyl)carbamoyl)phenyl acetate (9).

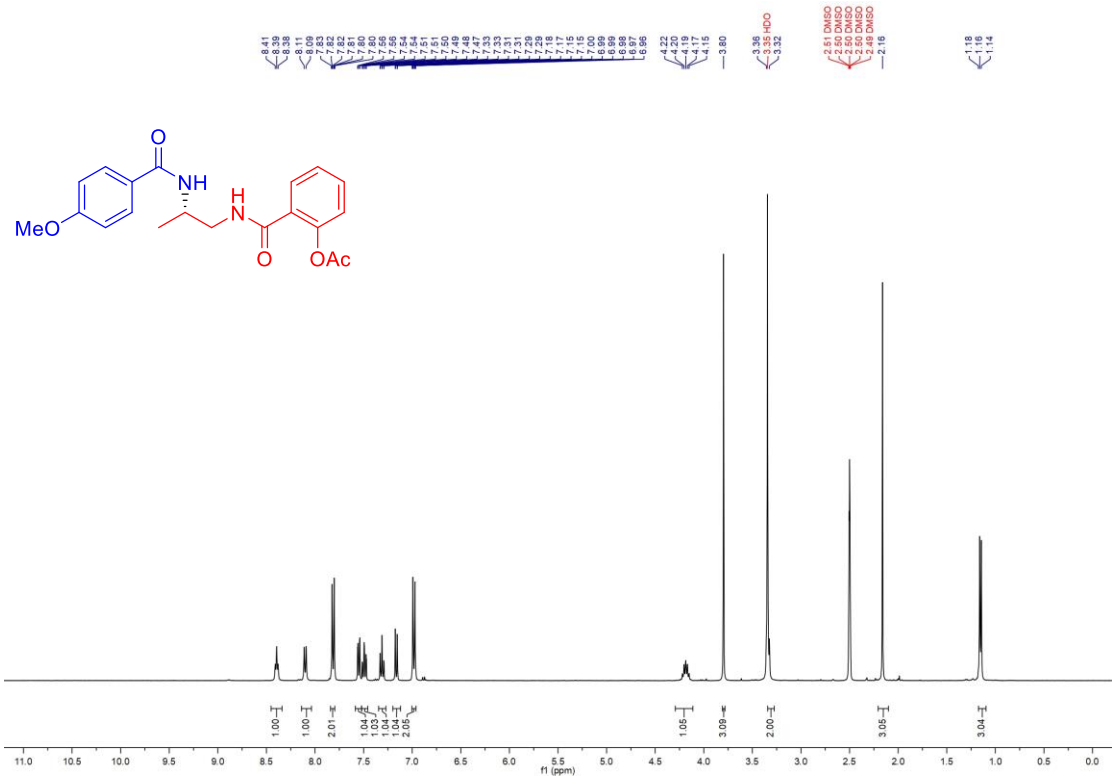


Figure S93. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-2-((2-(4-Methoxybenzamido)propyl)carbamoyl)phenyl acetate (9).

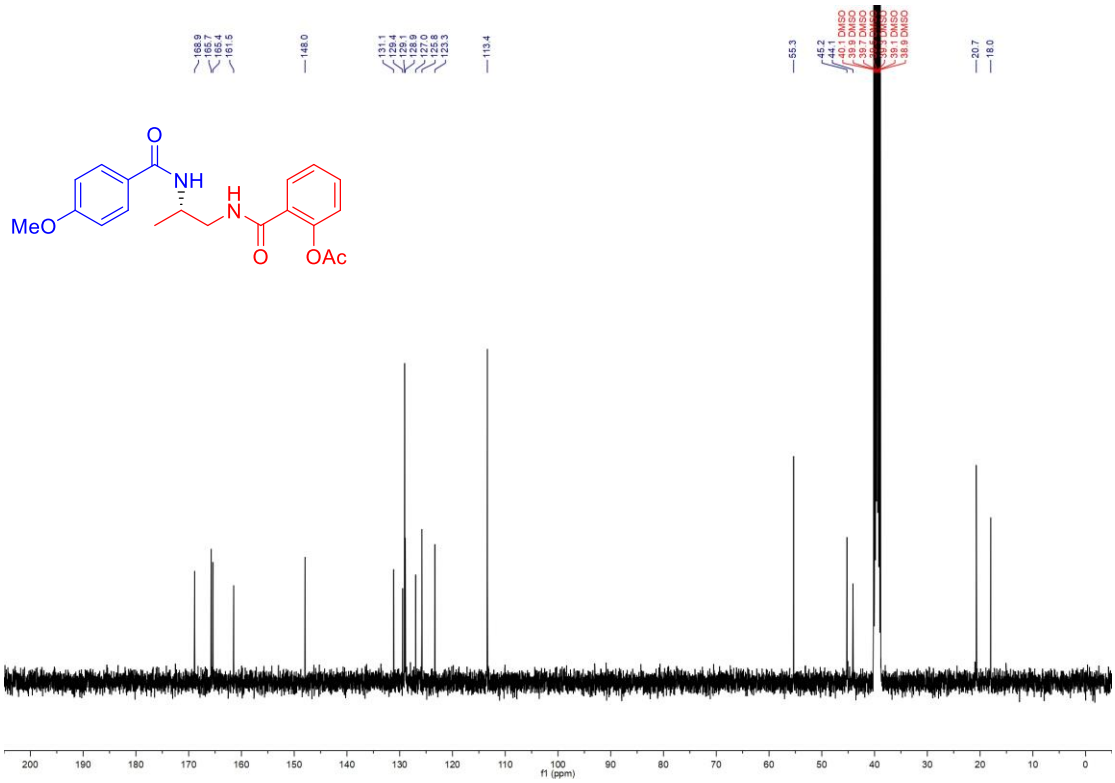


Figure S94. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-3-(3-(4,5-Diphenyloxazol-2-yl)propanamido)-*N*-(4-methoxyphenyl)butanamide (10).

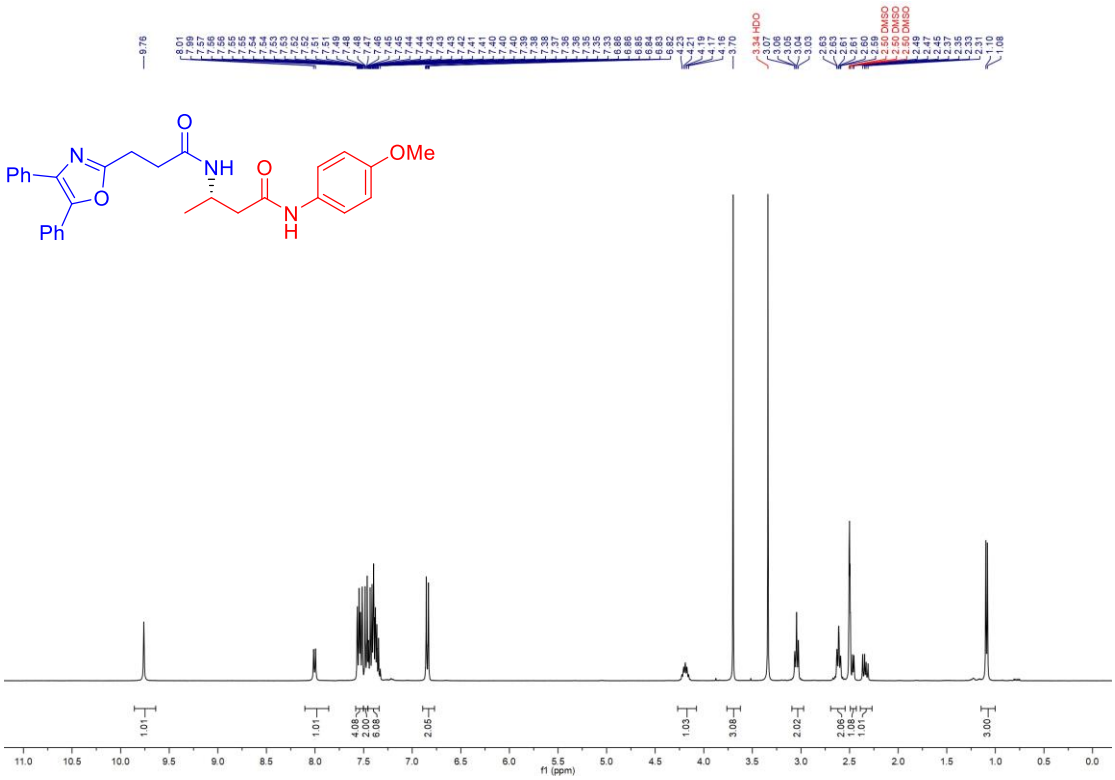


Figure S95. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-3-(3-(4,5-Diphenyloxazol-2-yl)propanamido)-*N*-(4-methoxyphenyl)butanamide (10).

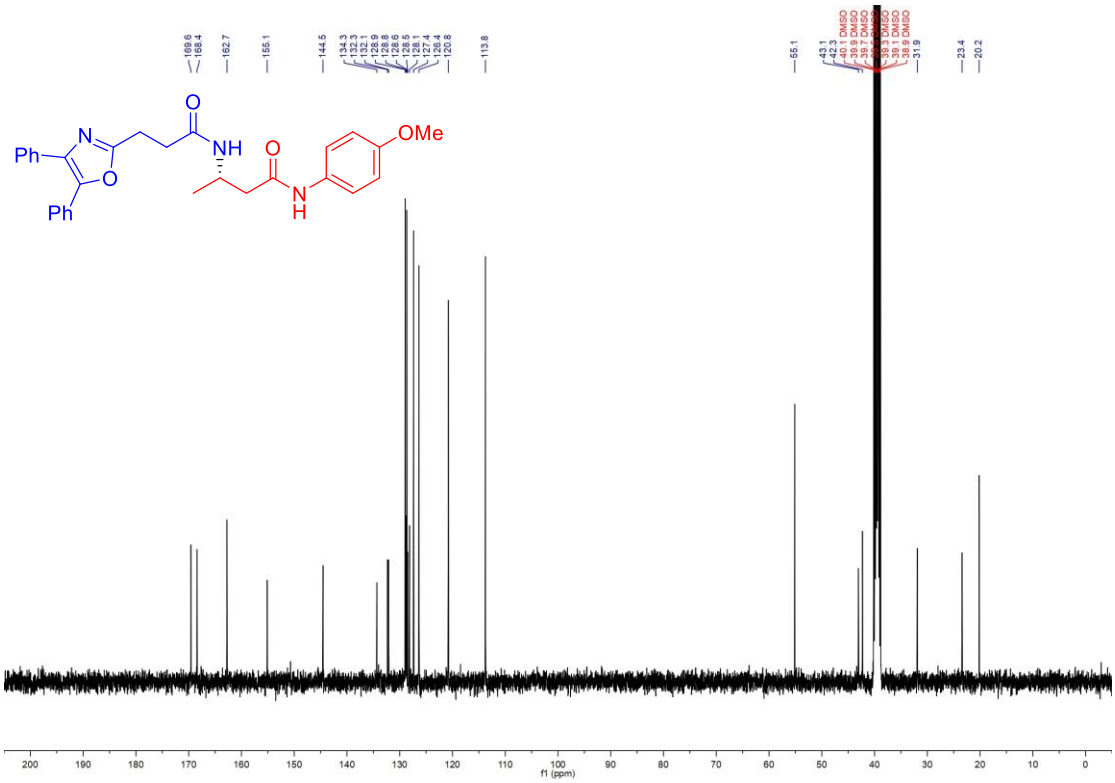


Figure S96. ^{1}H NMR spectra (400 MHz, DMSO-*d*$_6$) of (*S*)-3-((*S*)-2-(4-Isobutylphenyl)propan amido)-*N*-(4-methoxyphenyl)butanamide (11).

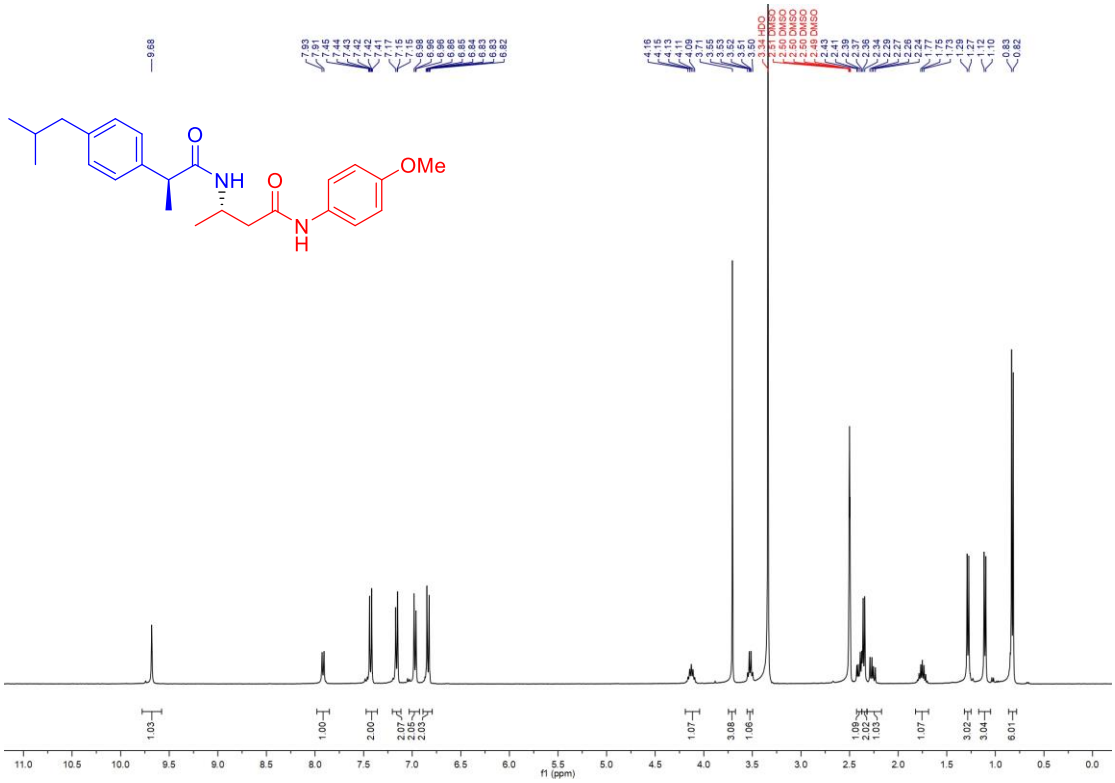


Figure S97. ^{13}C NMR spectra (100 MHz, DMSO-*d*$_6$) of (*S*)-3-((*S*)-2-(4-Isobutylphenyl)propa namido)-*N*-(4-methoxyphenyl)butanamide (11).

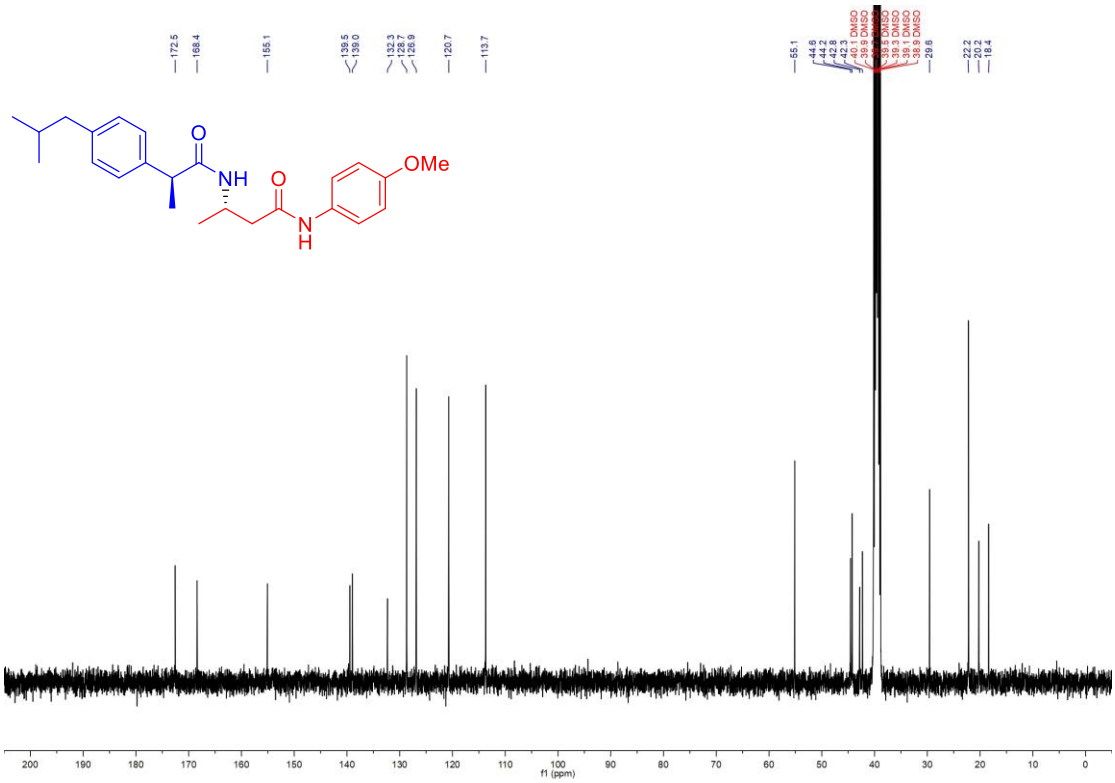


Figure S98. ^{1}H NMR spectra (400 MHz, DMSO-d_6) of (*S*)-*N*,*N*′-(Propane-1,2-diyl)dinicotinamide ((*S*)-Nicaraven).

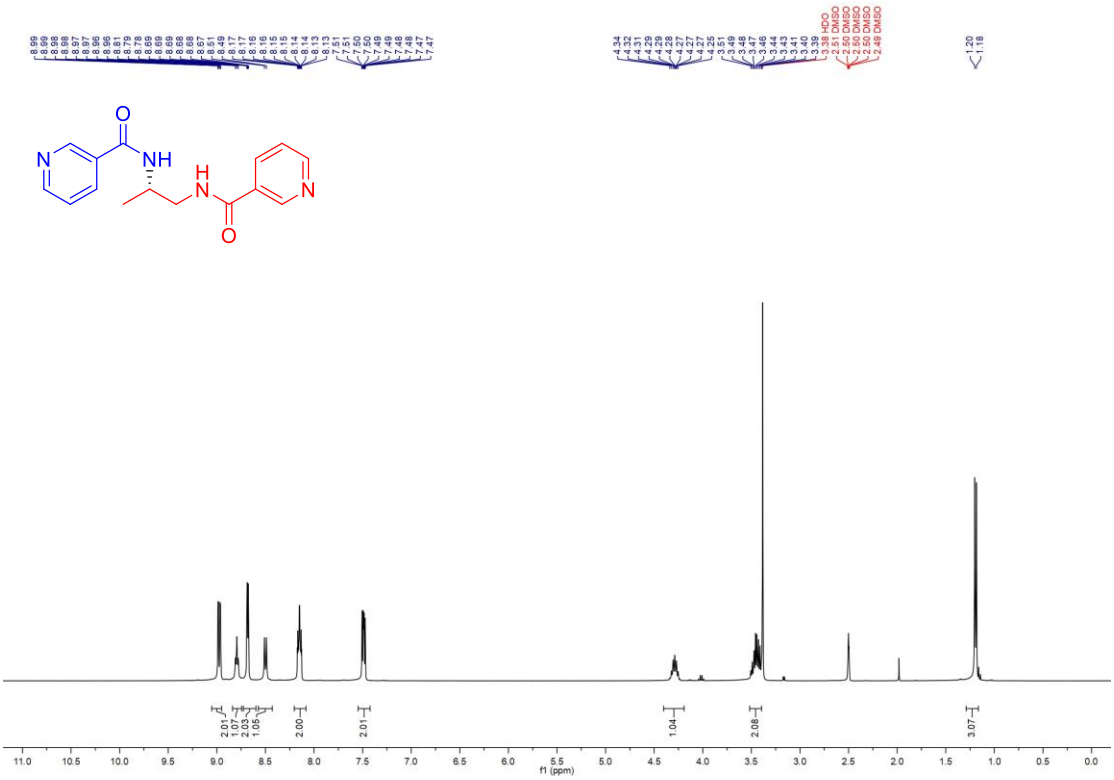


Figure S99. ^{13}C NMR spectra (100 MHz, DMSO-d_6) of (*S*)-*N*,*N*′-(Propane-1,2-diyl)dinicotinamide ((*S*)-Nicaraven).

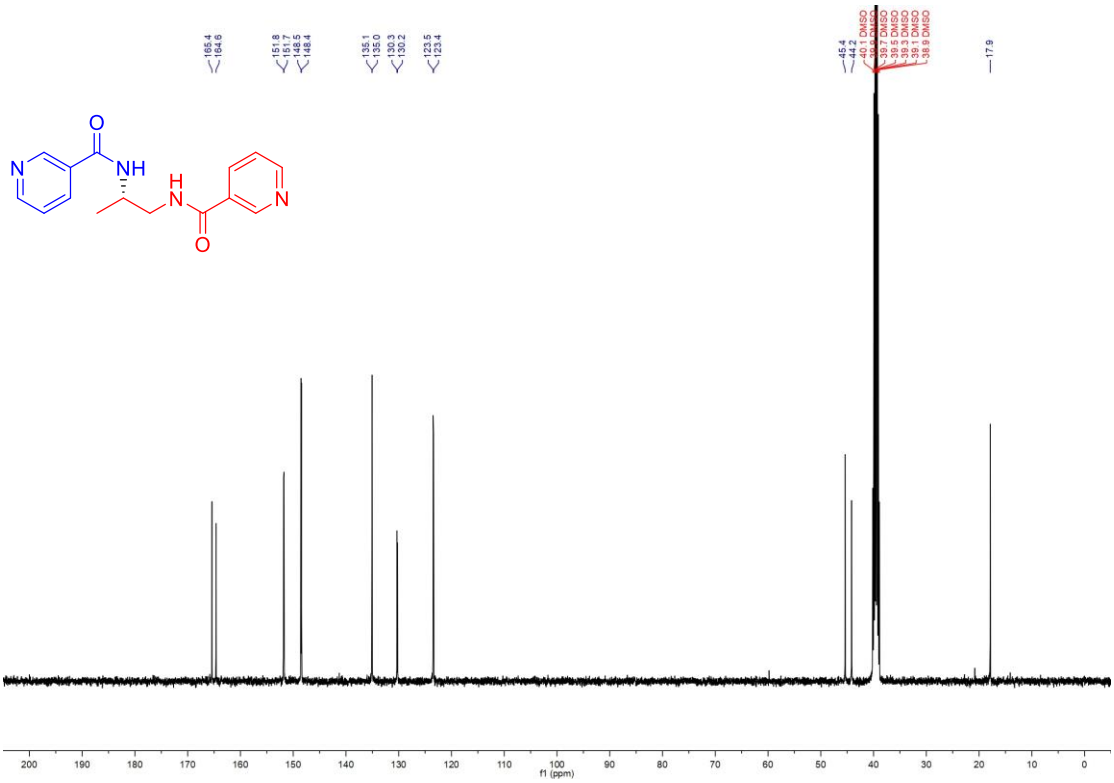


Figure S100. ^{1}H NMR spectra (400 MHz, Deuterium Oxide) of (2*S*,3*S*)-1-Phenylbutane-2,3-diaminium chloride (12).

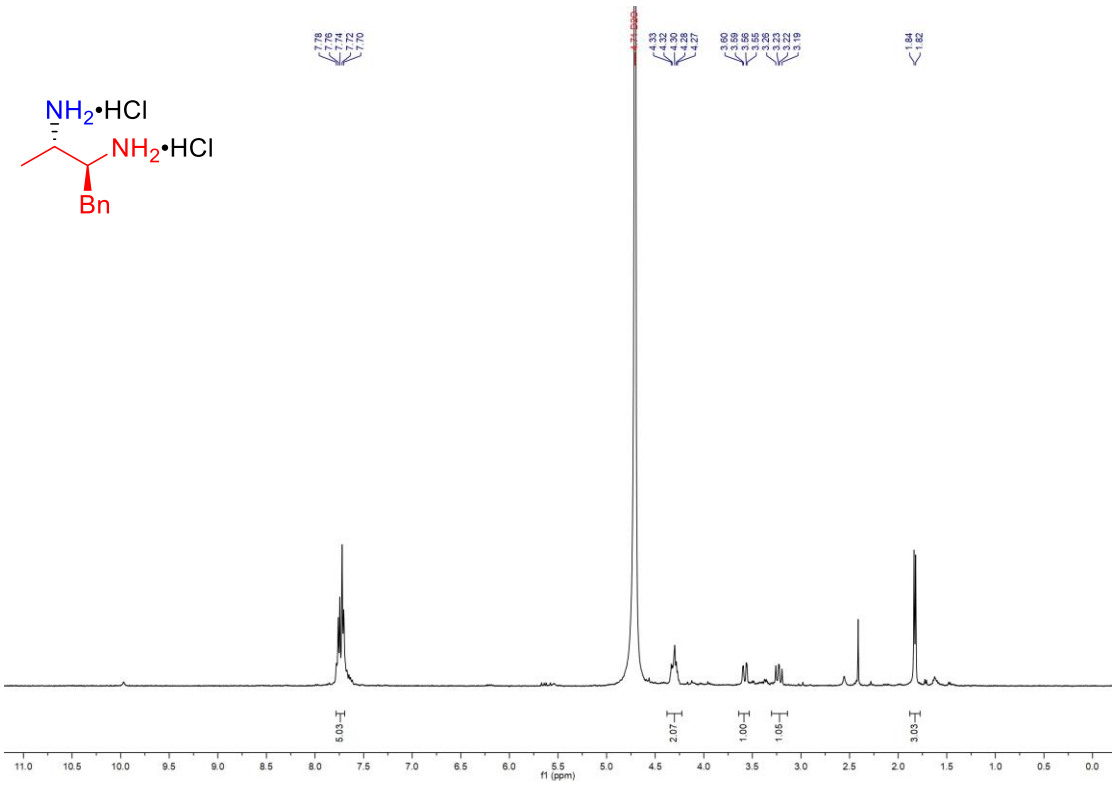
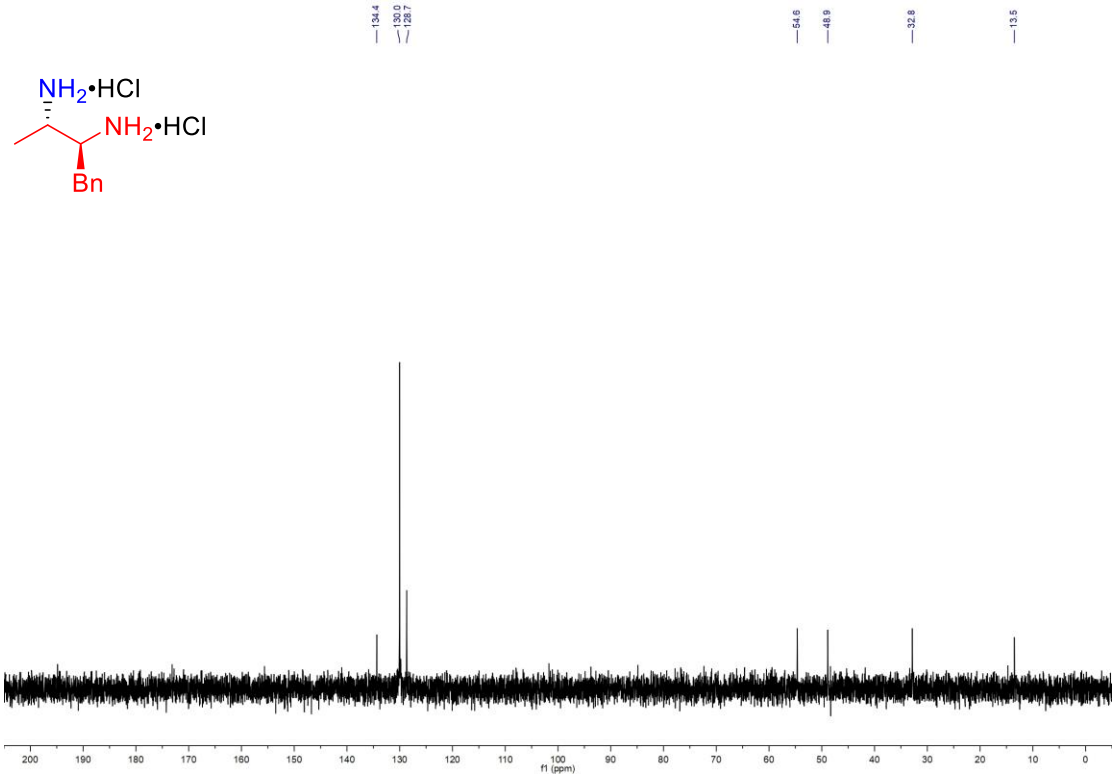
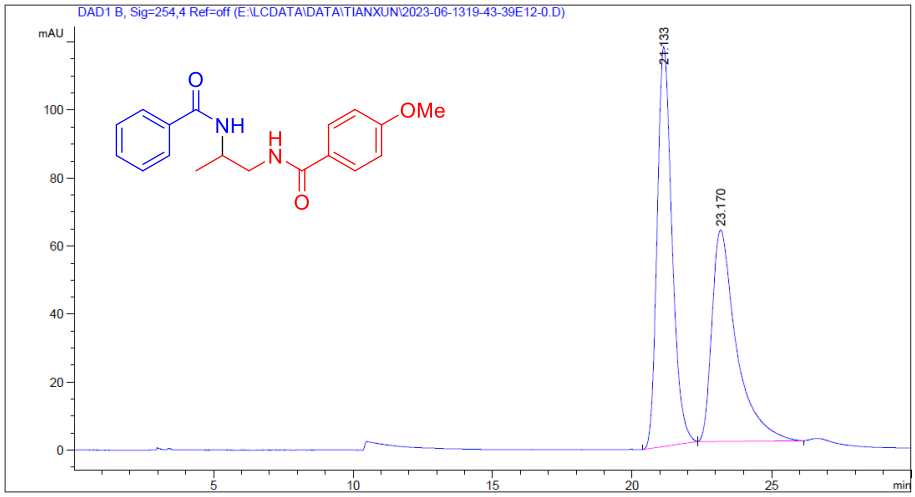


Figure S101. ^{13}C NMR spectra (400 MHz, Deuterium Oxide) of (2*S*,3*S*)-1-Phenylbutane-2,3-diaminium chloride (12).



HPLC spectra of the products

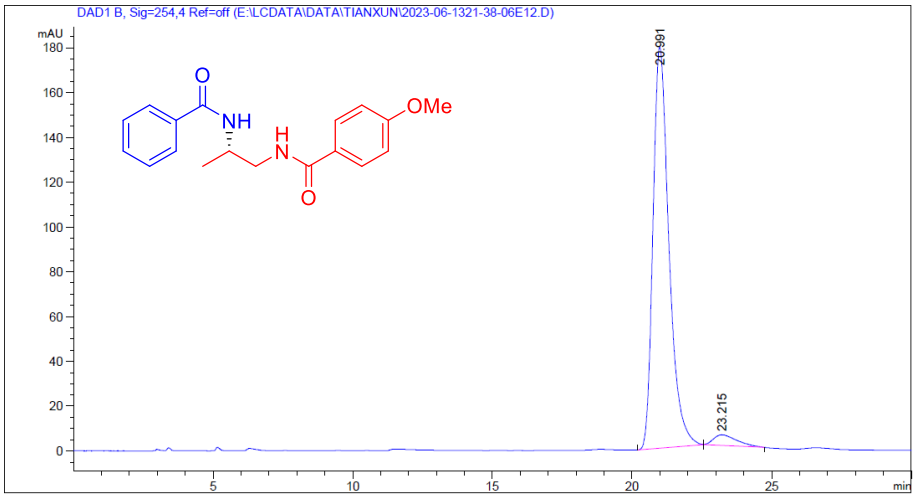
Figure S102. HPLC Chromatography of the Racemic *N*-(2-Benzamidopropyl)-4-methoxyben zamide (3aa).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.133	BB	0.5700	4329.34131	117.47626	53.4047
2	23.170	BB	0.8836	3777.32813	62.10092	46.5953
Totals :				8106.66943	179.57718	

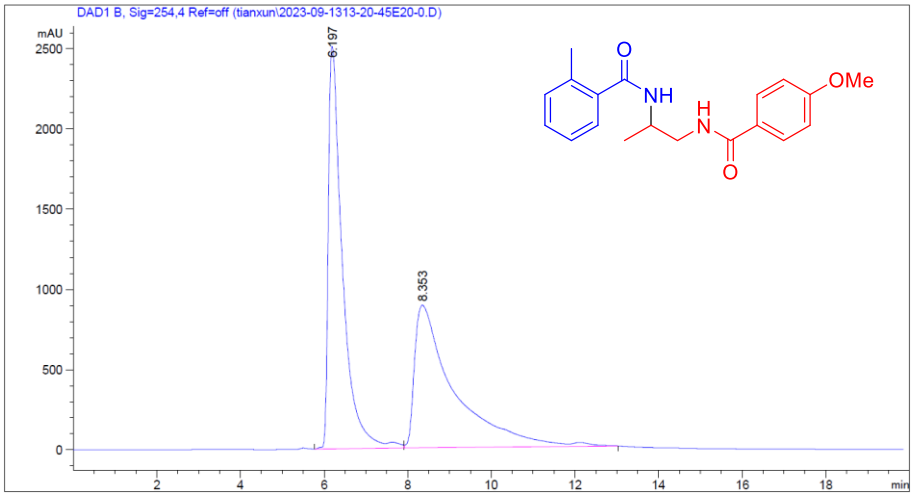
Figure S103. HPLC Chromatography of (*S*)-*N*-(2-Benzamidopropyl)-4-methoxybenzamide (3aa).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.991	BB	0.6023	7098.85742	179.14470	96.3106
2	23.215	BBA	0.6946	271.93640	4.67494	3.6894
Totals :				7370.79382	183.81964	

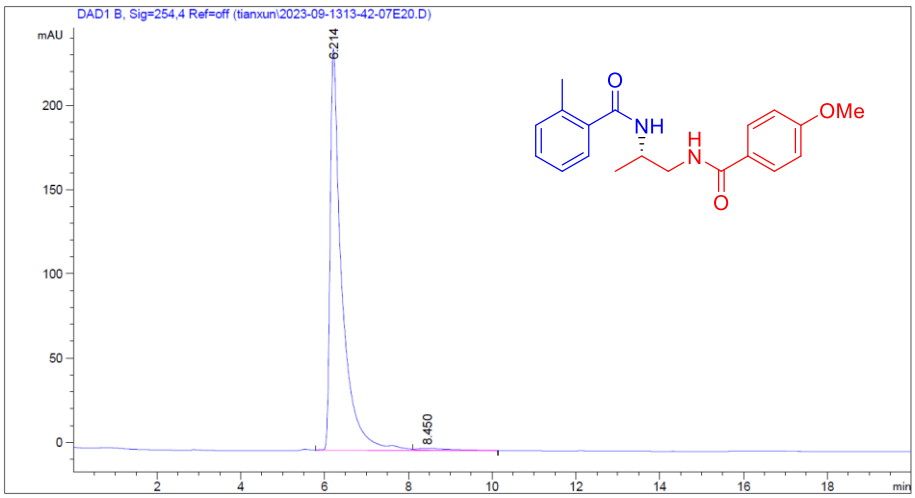
Figure S104. HPLC Chromatography of the Racemic *N*-(1-(4-Methoxybenzamido)propan-2-yl)-2-methylbenzamide (3ab).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.197	BV R	0.3290	5.91690e4	2509.68164	50.2855
2	8.353	VV R	0.9014	5.84972e4	890.25616	49.7145
Totals :				1.17666e5	3399.93781	

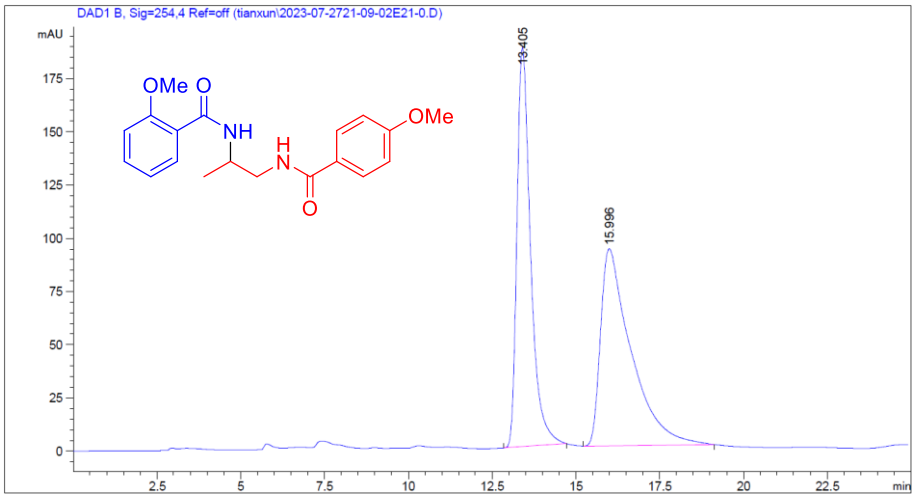
Figure S105. HPLC Chromatography of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-2-methylbenzamide (3ab).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.214	BV R	0.2696	4639.98486	238.41887	98.6727
2	8.450	VBAE	0.6939	62.41358	1.09343	1.3273
Totals :				4702.39845	239.51230	

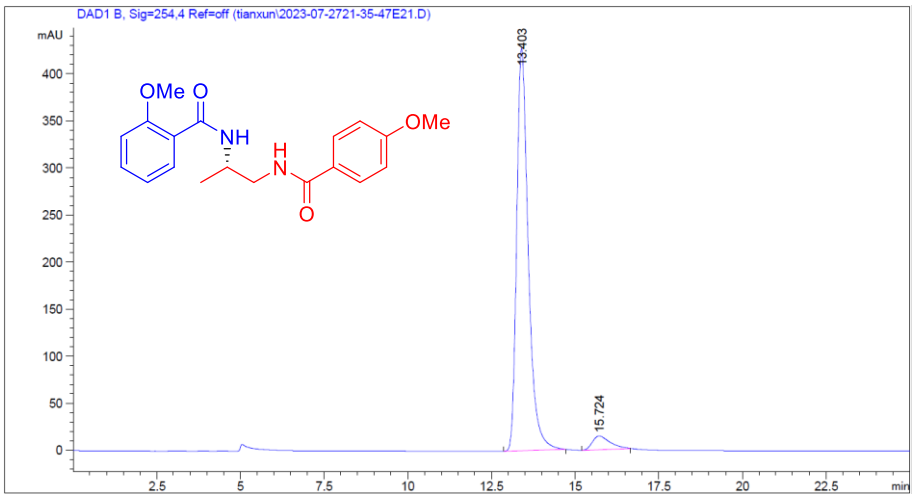
Figure S106. HPLC Chromatography of the Racemic 2-Methoxy-*N*-(1-(4-methoxybenzamido) propan-2-yl)benzamide (3ac).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.405	BBA	0.4275	5296.34326	187.55377	47.4452
2	15.996	BBA	0.8893	5866.73584	92.58383	52.5548
Totals :				1.11631e4	280.13760	

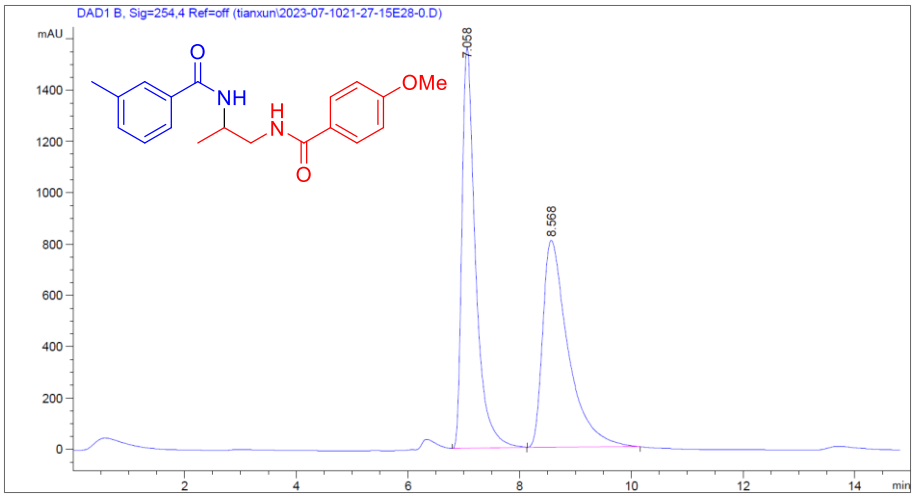
Figure S107. HPLC Chromatography of (*S*)-2-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ac).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.403	BBA	0.3647	1.02842e4	427.38065	95.0796
2	15.724	BBA	0.5428	532.21387	14.54898	4.9204
Totals :				1.08164e4	441.92963	

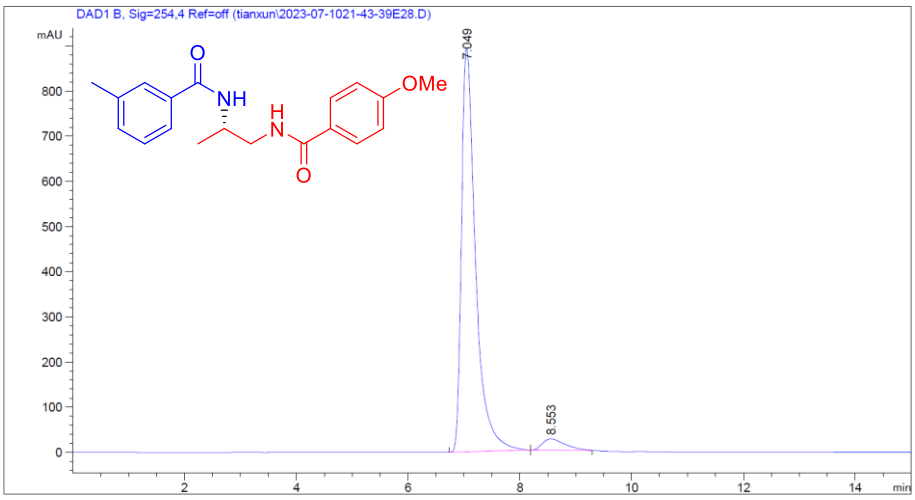
Figure S108. HPLC Chromatography of the Racemic *N*-(1-(4-Methoxybenzamido)propan-2-yl)-3-methylbenzamide (3ad).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.058	BB	0.2556	2.64628e4	1562.72876	50.8285
2	8.568	BBA	0.4687	2.56001e4	805.79364	49.1715
Totals :				5.20629e4	2368.52240	

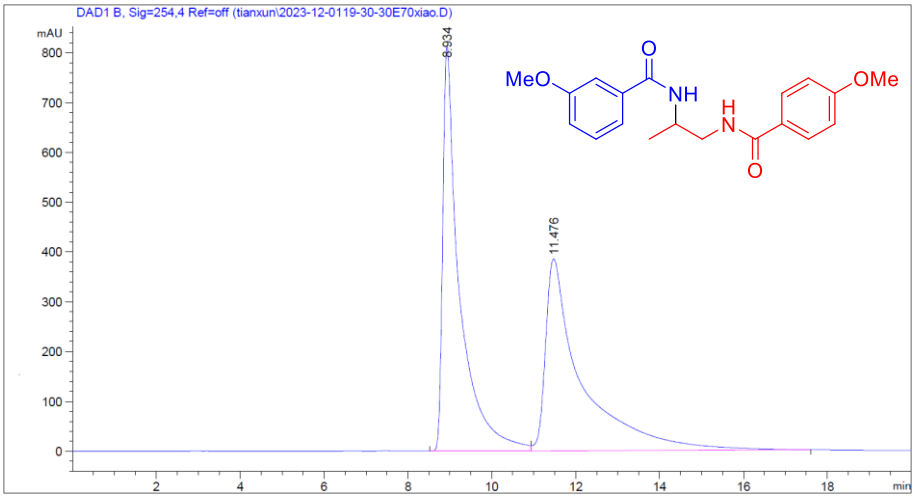
Figure S109. HPLC Chromatography of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)-3-methylbenzamide (3ad).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.049	BB	0.2615	1.55910e4	894.00549	95.7676
2	8.553	BBA	0.4224	689.02948	24.78358	4.2324
Totals :				1.62801e4	918.78908	

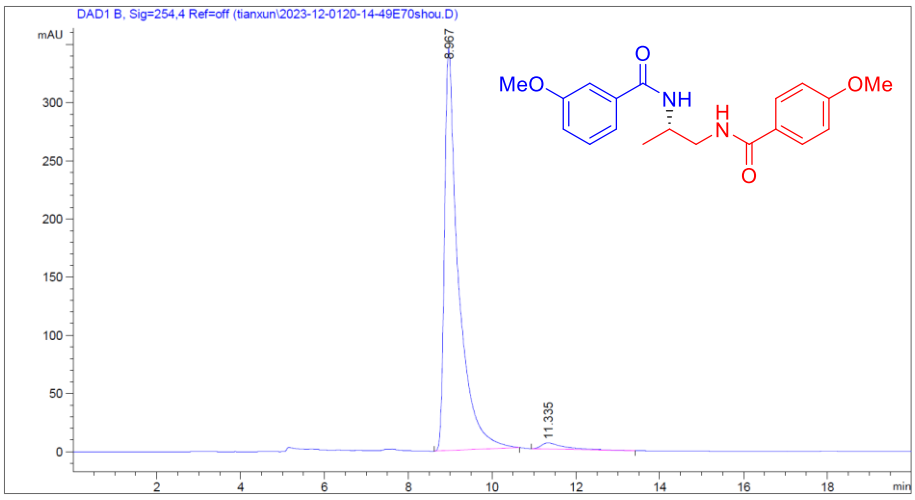
Figure S110. HPLC Chromatography of the Racemic 3-Methoxy-*N*-(1-(4-methoxybenzamido) propan-2-yl)benzamide (3ae).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.934	BV	0.3832	2.26260e4	811.68036	49.4229
2	11.476	VB	0.8068	2.31544e4	385.46683	50.5771
Totals :				4.57804e4	1197.14719	

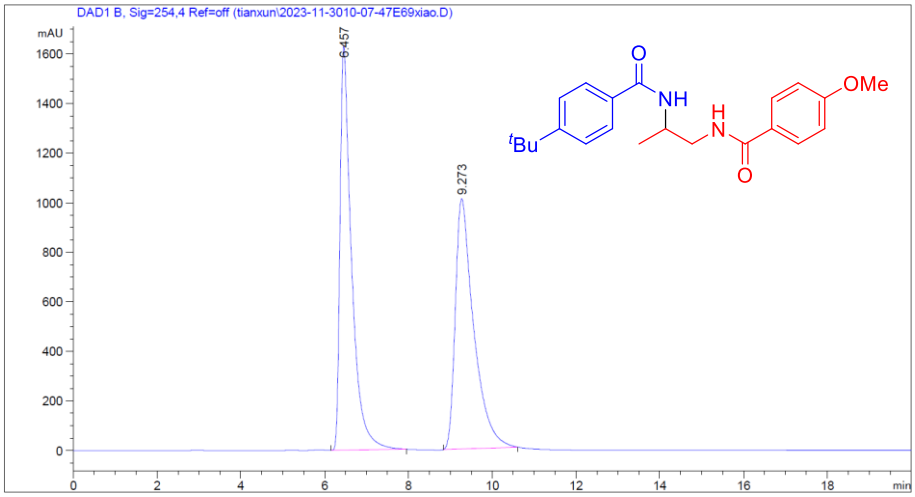
Figure S111. HPLC Chromatography of (*S*)-3-Methoxy-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ae).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.967	BBA	0.3237	7990.33740	345.63705	97.6094
2	11.335	BBA	0.5238	195.69550	5.23842	2.3906
Totals :				8186.03290	350.87548	

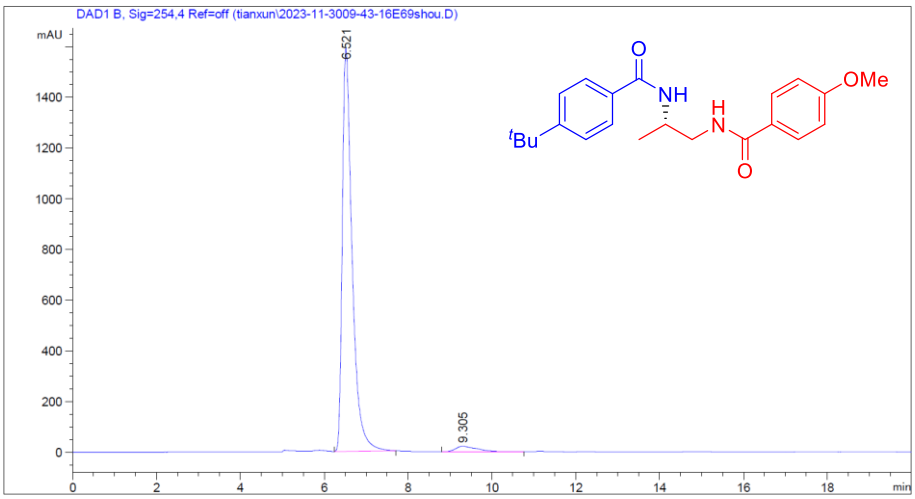
Figure S112. HPLC Chromatography of the Racemic 4-(*tert*-Butyl)-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3af).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.457	BBA	0.2732	3.11727e4	1629.38794	50.3644
2	9.273	BBA	0.4387	3.07216e4	1010.57623	49.6356
Totals :				6.18944e4	2639.96417	

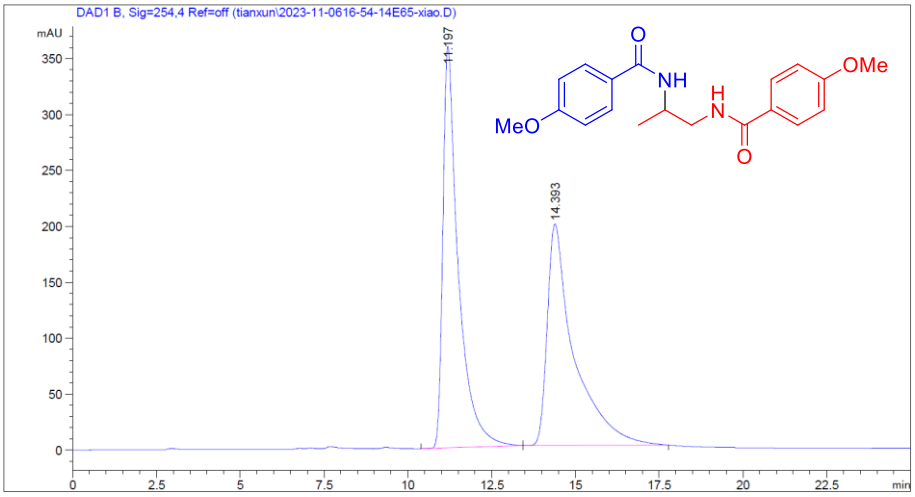
Figure S113. HPLC Chromatography of (*S*)-4-(*tert*-Butyl)-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3af).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.521	BBA	0.2460	2.58408e4	1586.63135	97.0962
2	9.305	BB	0.4811	772.79749	22.25761	2.9038
Totals :				2.66136e4	1608.88896	

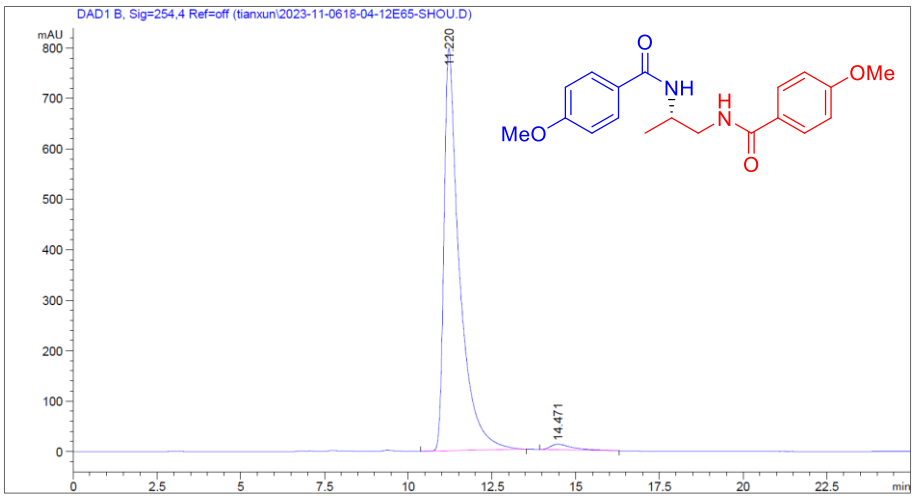
Figure S114. HPLC Chromatography of the Racemic *N*,*N*′-(Propane-1,2-diyl)bis(4-methoxyb enzamide) (3ag).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.197	BB	0.4552	1.14838e4	358.95984	51.1003
2	14.393	BBA	0.7697	1.09893e4	197.93706	48.8997
Totals :				2.24731e4	556.89690	

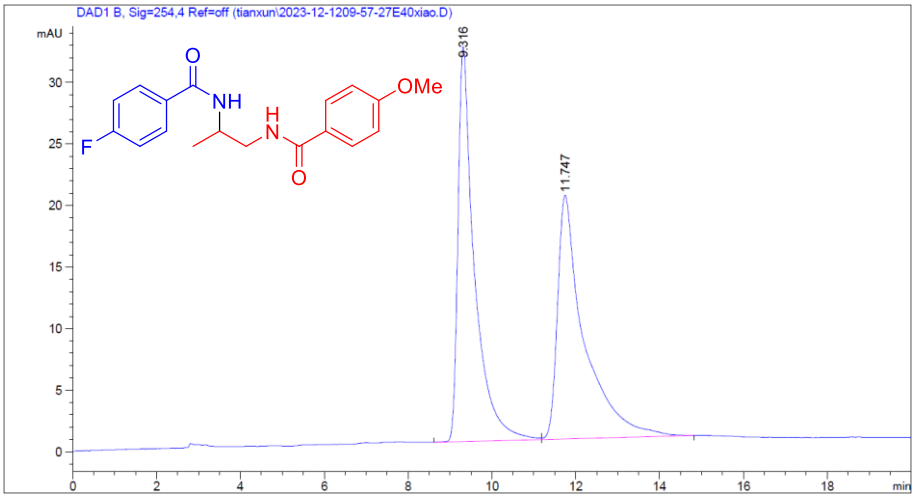
Figure S115. HPLC Chromatography of (*S*)-*N*,*N*′-(Propane-1,2-diyl)bis(4-methoxybenzamide) (3ag).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.220	BBA	0.4547	2.56343e4	798.23718	98.0145
2	14.471	BBA	0.6518	519.28333	11.18212	1.9855
Totals :				2.61536e4	809.41930	

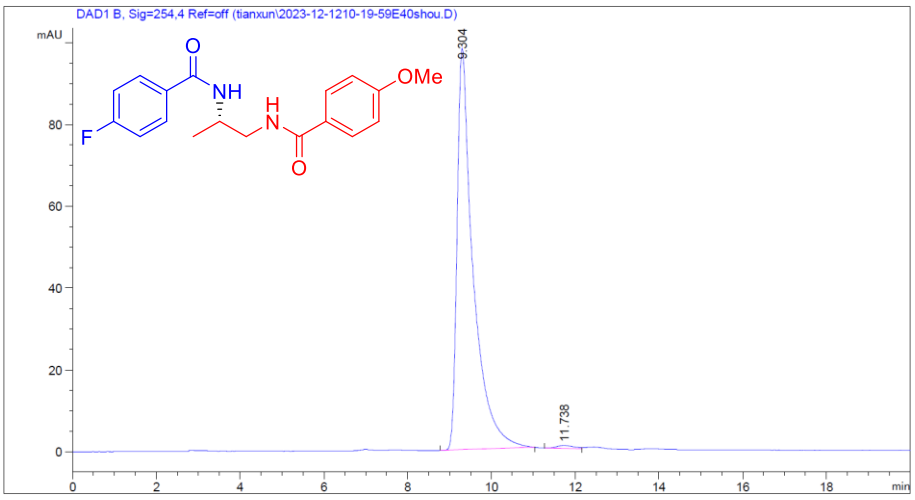
Figure S116. HPLC Chromatography of the Racemic 4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ah).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.316	BV	0.3835	872.69403	32.07031	50.0878
2	11.747	VB	0.6088	869.63373	19.78493	49.9122
Totals :				1742.32776	51.85524	

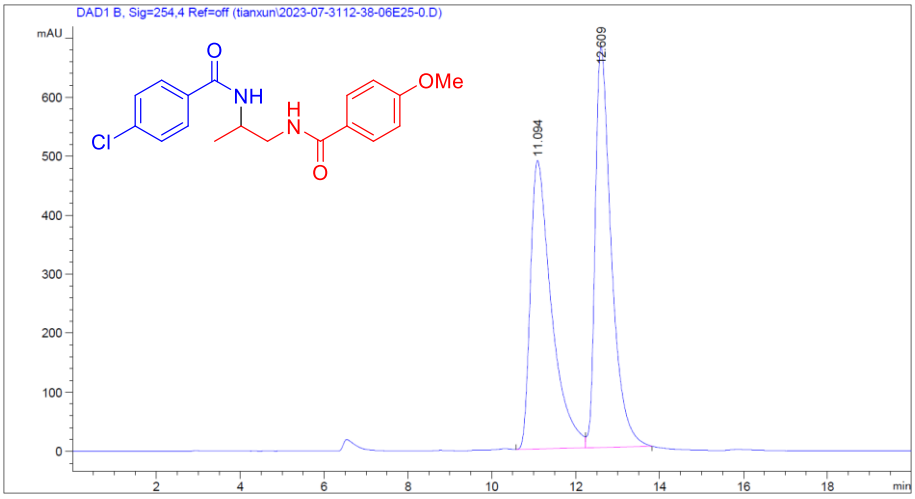
Figure S117. HPLC Chromatography of (*S*)-4-Fluoro-*N*-(1-(4-methoxybenzamido)propan-2-yl) benzamide (3ah).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.304	BBA	0.3762	2609.54102	98.14292	99.1677
2	11.738	BV	0.4094	21.90266	7.57336e-1	0.8323
Totals :				2631.44367	98.90026	

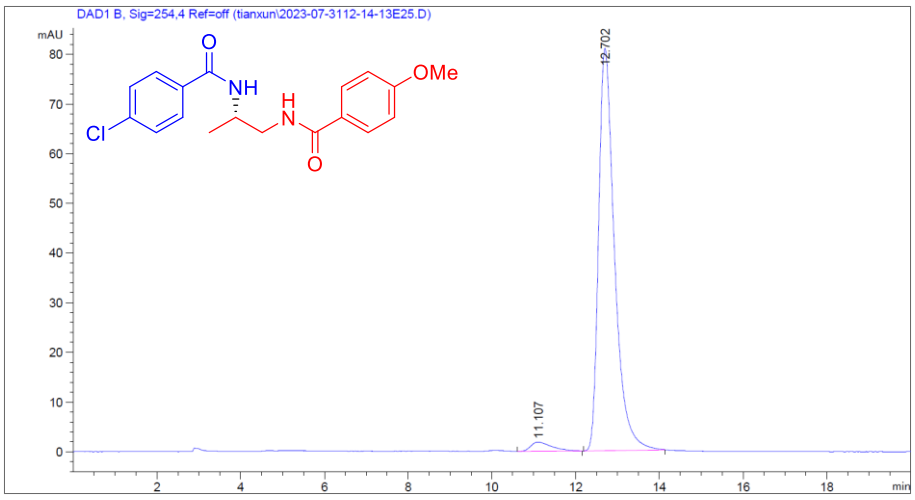
Figure S118. HPLC Chromatography of the Racemic 4-Chloro-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3ai).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.094	BV	0.5163	1.71043e4	488.70969	48.4639
2	12.609	VBA	0.4047	1.81885e4	678.65448	51.5361
Totals :				3.52927e4	1167.36417	

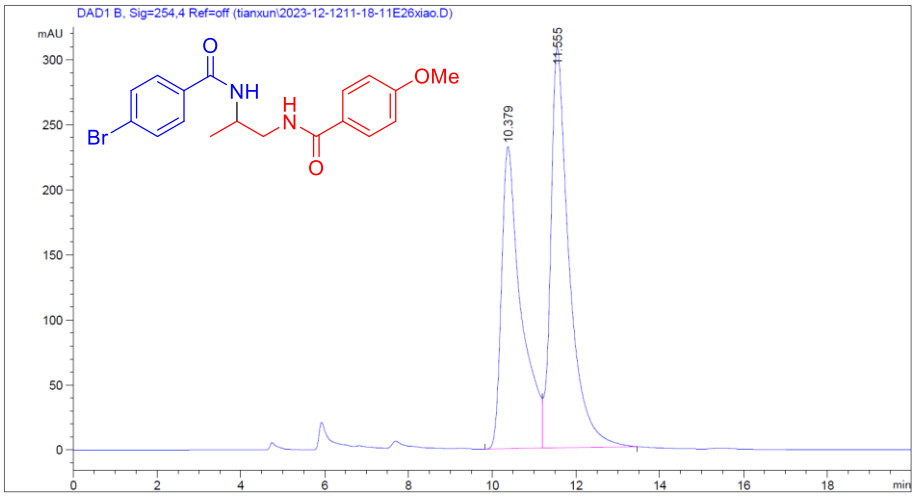
Figure S119. HPLC Chromatography of (*S*)-4-Chloro-*N*-(1-(4-methoxybenzamido)propan-2-yl) benzamide (3ai).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.107	BB	0.5013	63.28051	1.83962	2.8859
2	12.702	BBA	0.4028	2129.46045	80.96626	97.1141
Totals :				2192.74096	82.80588	

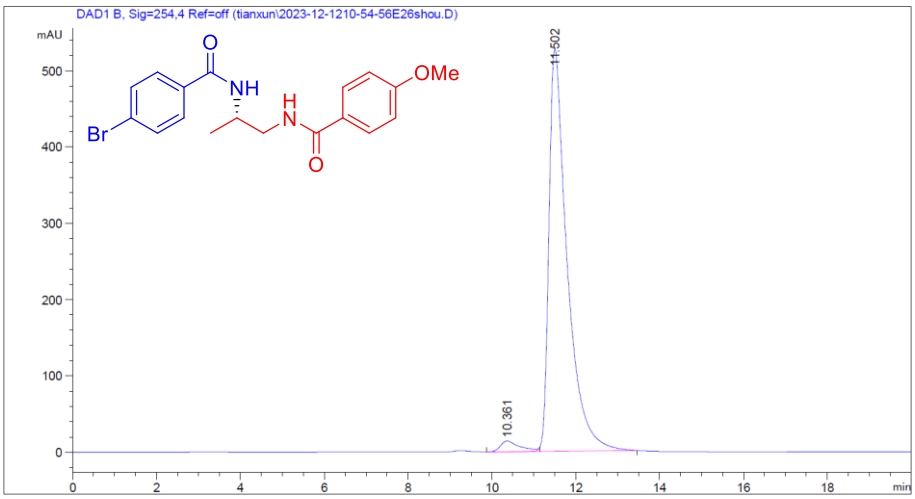
Figure S120. HPLC Chromatography of the Racemic 4-Bromo-*N*-(1-(4-methoxybenzamido)propan-2-yl)benzamide (3aj).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.379	BV	0.4611	7540.42773	232.05092	44.3948
2	11.555	VBA	0.4420	9444.52344	307.82132	55.6052
Totals :				1.69850e4	539.87224	

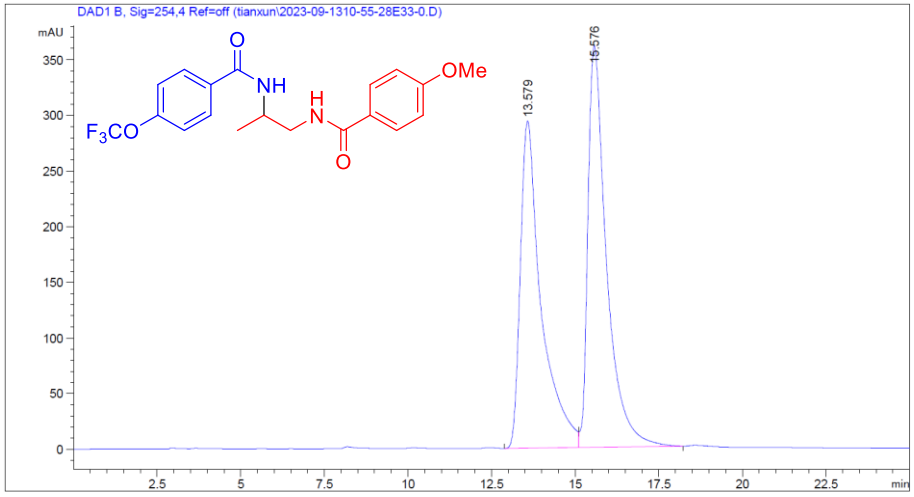
Figure S121. HPLC Chromatography of (*S*)-4-Bromo-*N*-(1-(4-methoxybenzamido)propan-2-yl) benzamide (3aj).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.361	BV E	0.4446	438.09735	14.01827	2.6853
2	11.502	VBAR	0.4349	1.58767e4	527.89636	97.3147
Totals :				1.63148e4	541.91463	

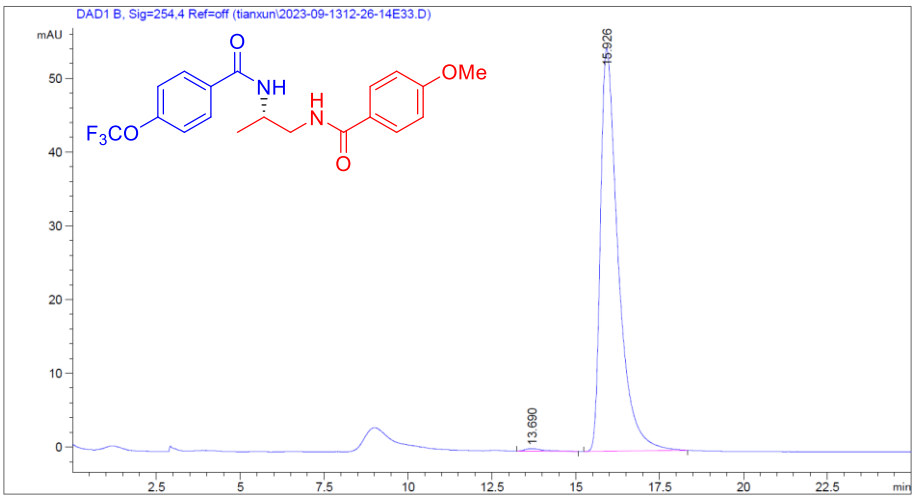
Figure S122. HPLC Chromatography of the Racemic 4-Methoxy-*N*-(2-(4-(trifluoromethoxy) benzamido)propyl)benzamide (3ak).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.579	BV	0.6211	1.27195e4	293.79965	47.6367
2	15.576	VB	0.5724	1.39816e4	360.60199	52.3633
Totals :				2.67011e4	654.40164	

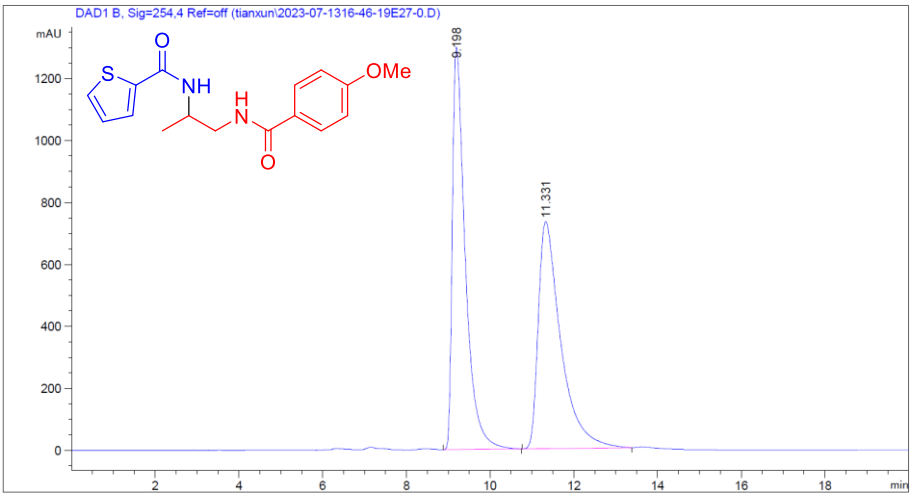
Figure S123. HPLC Chromatography of (*S*)-4-Methoxy-*N*-(2-(4-(trifluoromethoxy)benzamido) propyl)benzamide (3ak).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.690	BB	0.5053	13.61694	3.44384e-1	0.6733
2	15.926	BBA	0.5490	2008.79065	54.63310	99.3267
Totals :				2022.40759	54.97748	

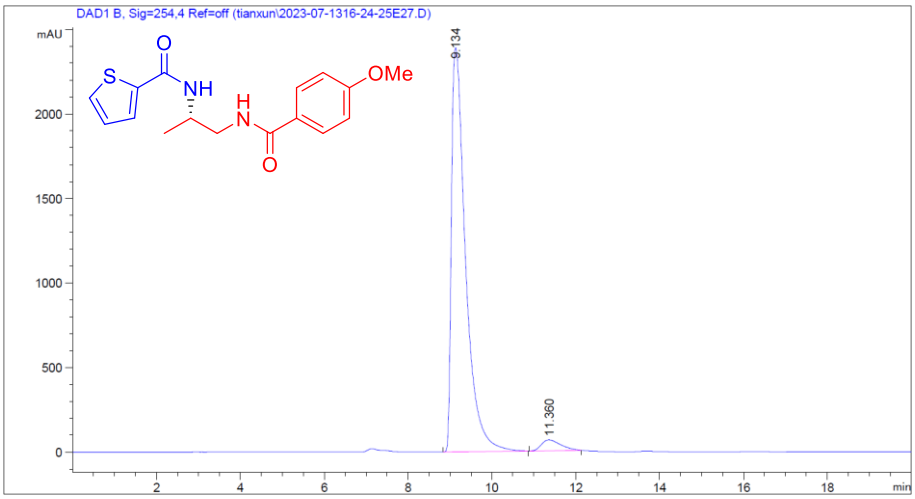
Figure S124. HPLC Chromatography of the Racemic *N*-(1-(4-Methoxybenzamido)propan-2-yl)thiophene-2-carboxamide (3al).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.198	BB	0.3156	2.77920e4	1298.90918	50.4623
2	11.331	BBA	0.5459	2.72828e4	733.59882	49.5377
Totals :				5.50748e4	2032.50800	

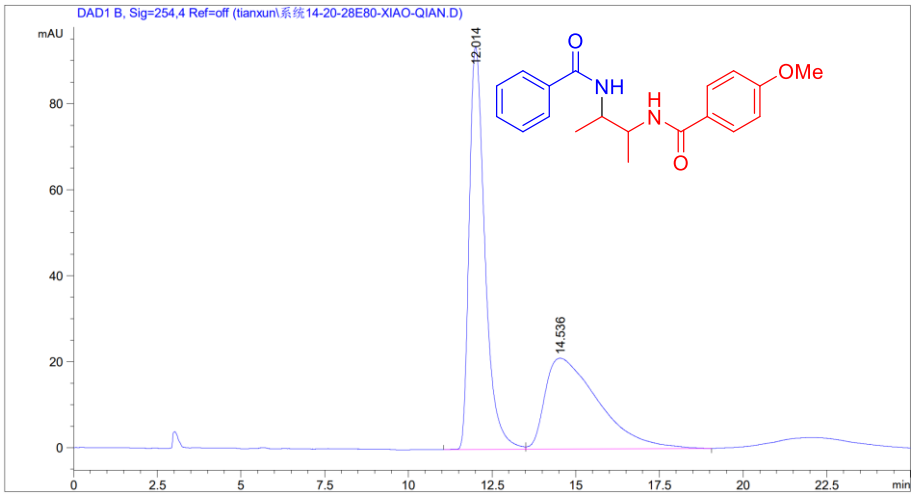
Figure S125. HPLC Chromatography of (*S*)-*N*-(1-(4-Methoxybenzamido)propan-2-yl)thiophene-2-carboxamide (3al).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.134	BB	0.3498	5.56589e4	2389.24463	96.4150
2	11.360	BBA	0.4827	2069.58618	64.79060	3.5850
Totals :				5.77284e4	2454.03523	

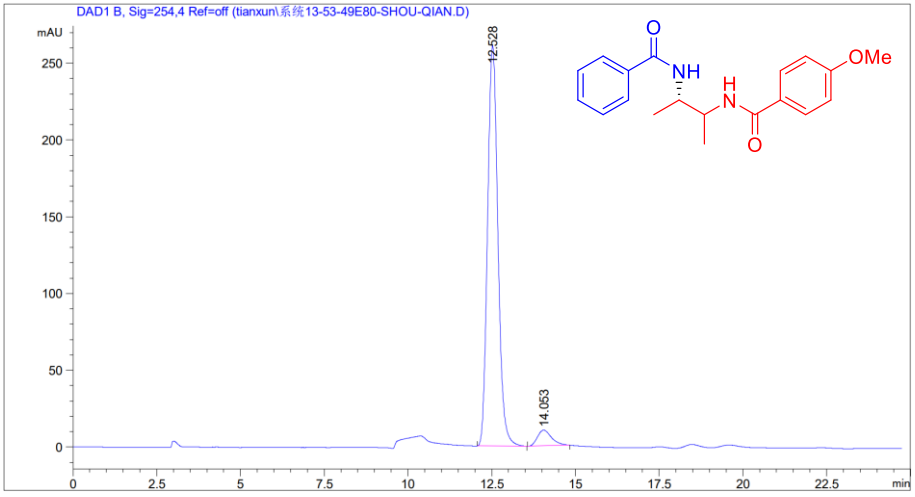
Figure S126. HPLC Chromatography of the Racemic *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Major diastereoisomer).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.014	BV	0.5019	3065.40088	93.63917	56.6626
2	14.536	VBA	1.5448	2344.52148	21.15731	43.3374
Totals :				5409.92236	114.79648	

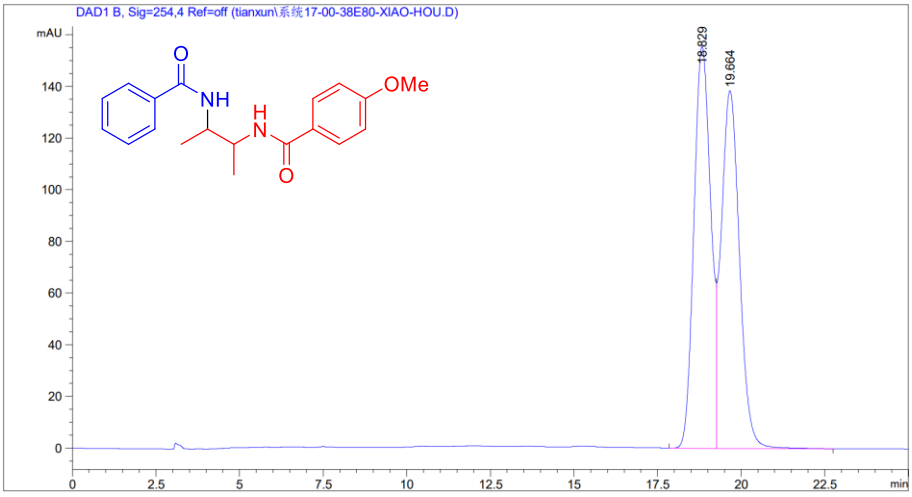
Figure S127. HPLC Chromatography of *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Major diastereoisomer).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.528	BB	0.3347	5599.23145	260.59082	94.9045
2	14.053	BBA	0.4542	300.62674	10.24944	5.0955
Totals :				5899.85818	270.84026	

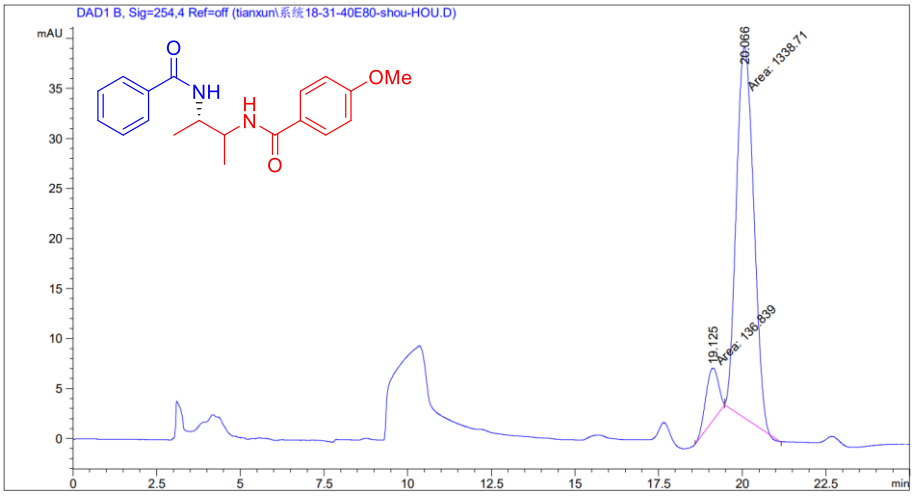
Figure S128. HPLC Chromatography of the Racemic *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Minor diastereoisomer).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.829	BV	0.5390	5428.87842	155.62836	50.8304
2	19.664	VB	0.5783	5251.50342	138.51923	49.1696
Totals :				1.06804e4	294.14758	

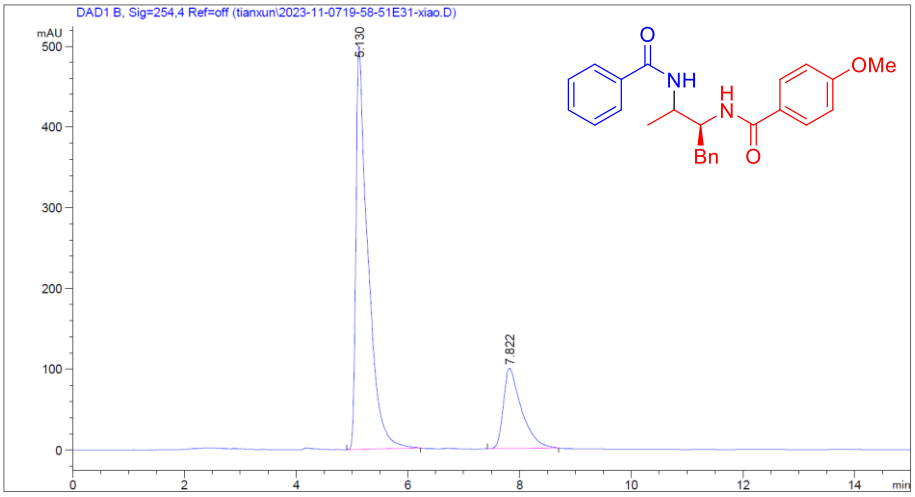
Figure S129. HPLC Chromatography of *N*-((3*S*)-3-Benzamidobutan-2-yl)-4-methoxybenzamide (3ba) (Minor diastereoisomer).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.125	MM	0.4328	136.83942	5.27004	9.2738
2	20.066	MM	0.6007	1338.70789	37.14119	90.7262
Totals :				1475.54730	42.41123	

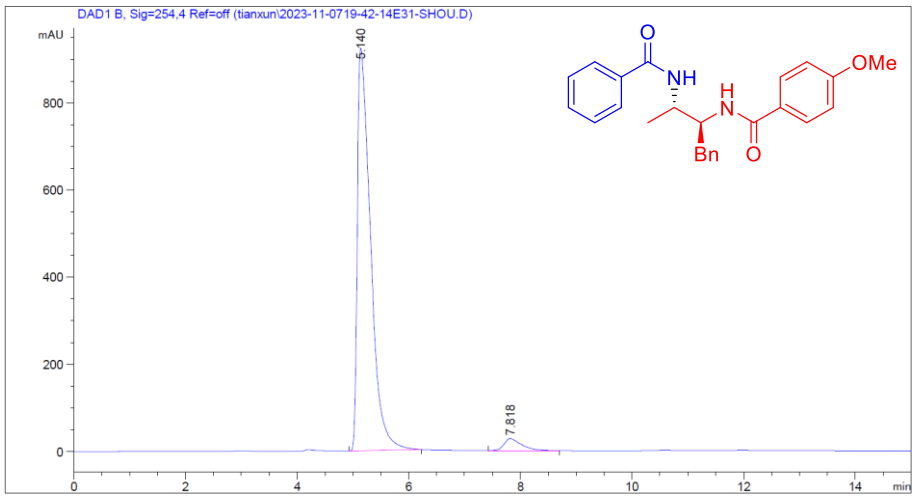
Figure S130. HPLC Chromatography of the Racemic *N*-((2*S*)-3-Benzamido-1-phenylbutan-2-yl)-4-methoxybenzamide (3ca).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.130	BBA	0.2059	7441.62158	499.23395	76.9339
2	7.822	BBA	0.3239	2231.12744	99.38867	23.0661
Totals :				9672.74902	598.62262	

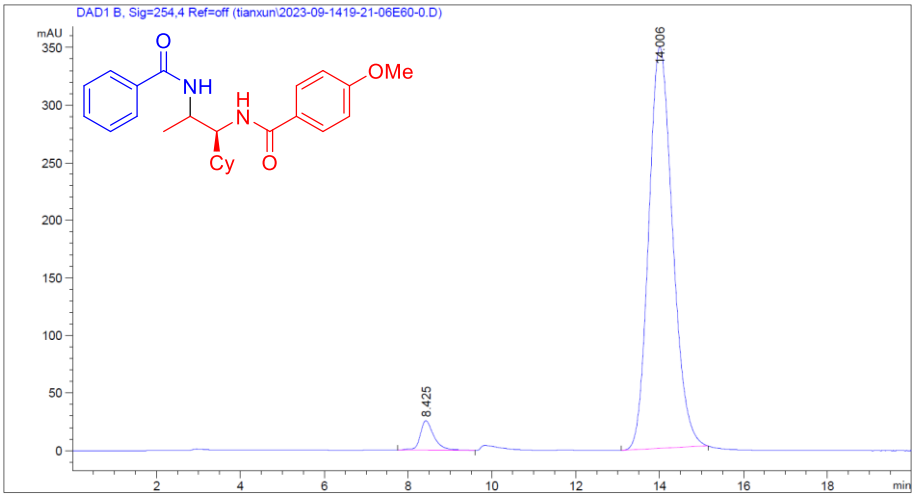
Figure S131. HPLC Chromatography of *N*-((2*S*,3*S*)-3-Benzamido-1-phenylbutan-2-yl)-4-methoxybenzamide (3ca).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.140	BBA	0.2435	1.51653e4	924.04755	96.1965
2	7.818	BBA	0.3174	599.62103	27.39000	3.8035
Totals :				1.57649e4	951.43755	

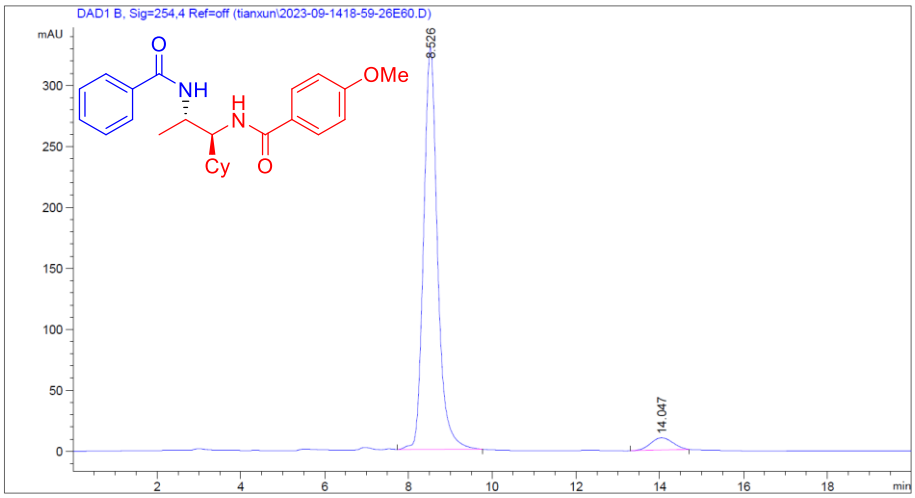
Figure S132. HPLC Chromatography of the Racemic *N*-((1*S*)-2-Benzamido-1-cyclohexylpropyl)-4-methoxybenzamide.



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.425	BB	0.3366	580.01459	25.56973	4.0378
2	14.006	BBA	0.6132	1.37847e4	348.68677	95.9622
Totals :				1.43648e4	374.25650	

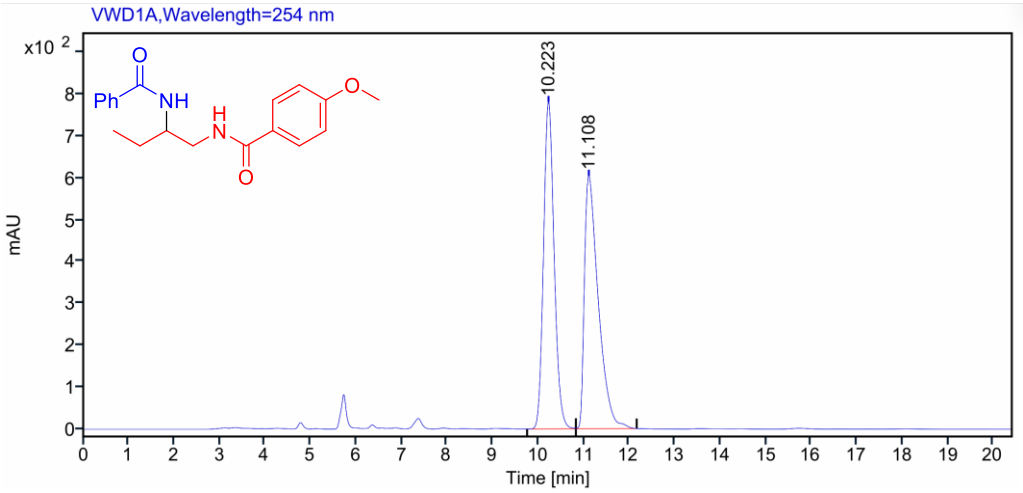
Figure S133. HPLC Chromatography of *N*-((1*S*,2*S*)-2-Benzamido-1-cyclohexylpropyl)-4-methoxybenzamide (3da).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.526	BBA	0.3528	7584.44971	329.24692	95.3609
2	14.047	BBA	0.5720	368.96878	10.05705	4.6391
Totals :				7953.41849	339.30397	

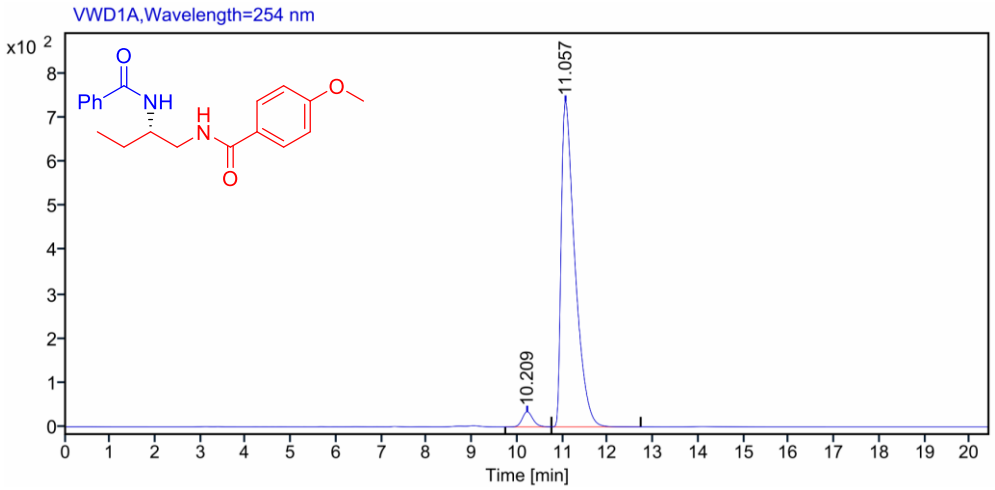
Figure S134. HPLC Chromatography of the Racemic *N*-(2-Benzamidobutyl)-4-methoxybenz amide (3ea)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
10.223	BM m	1.07	12645.94	780.48	49.70
11.108	MM m	1.34	12796.47	603.96	50.30
		Total	25442.41		

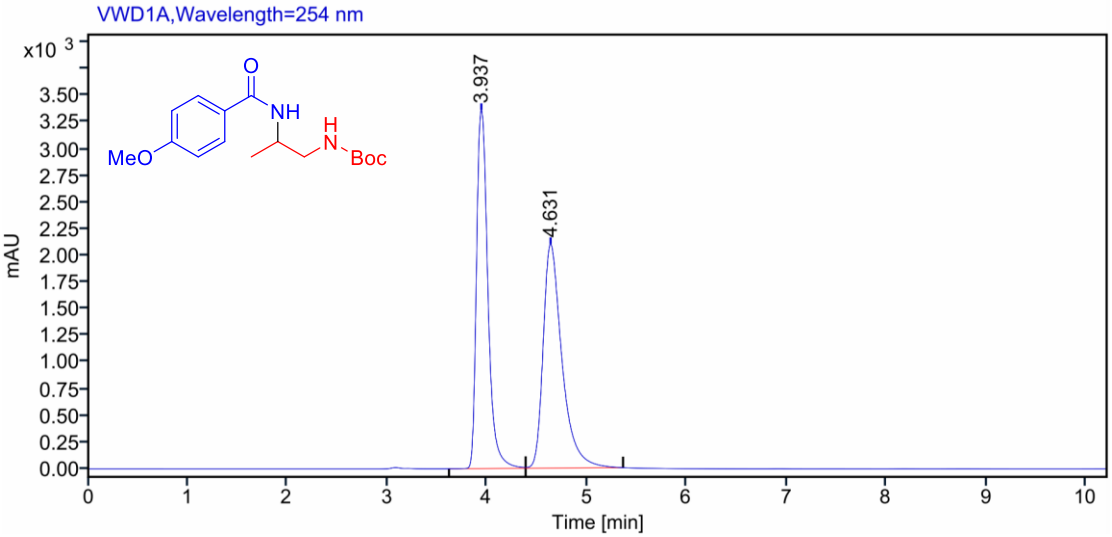
Figure S135. HPLC Chromatography of (*S*)-*N*-(2-Benzamidobutyl)-4-methoxybenzamide (3e a)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
10.209	BV	1.02	564.06	34.48	3.50
11.057	VB	1.97	15565.12	738.75	96.50
		Total	16129.18		

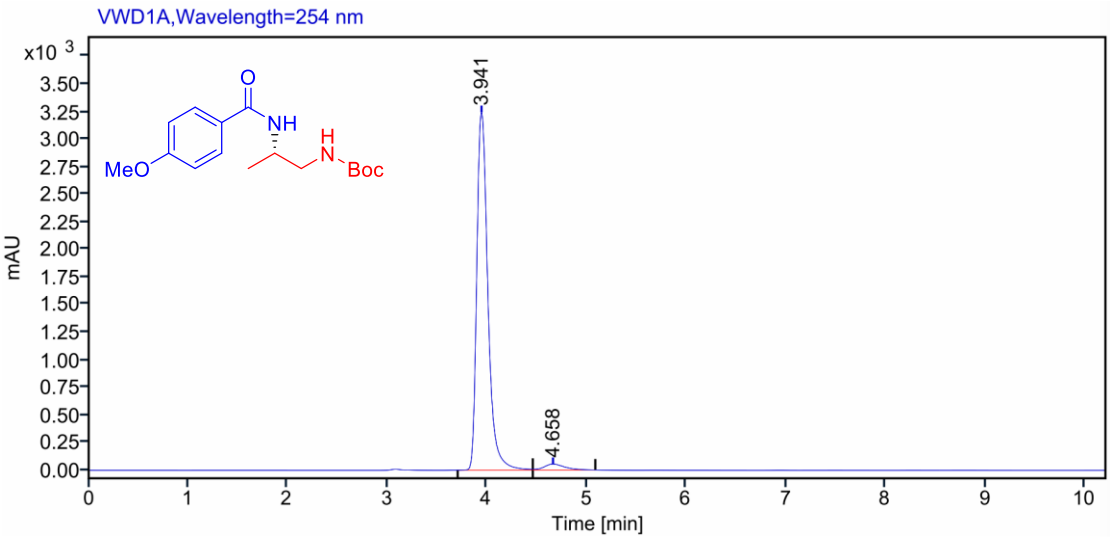
Figure S136. HPLC Chromatography of the Racemic *tert*-Butyl-(2-(4-methoxybenzamido)propyl)carbamate (3fg)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
3.937	MM m	0.77	26619.89	3364.79	49.12
4.631	MM m	0.98	27571.72	2103.19	50.88
		Total	54191.62		

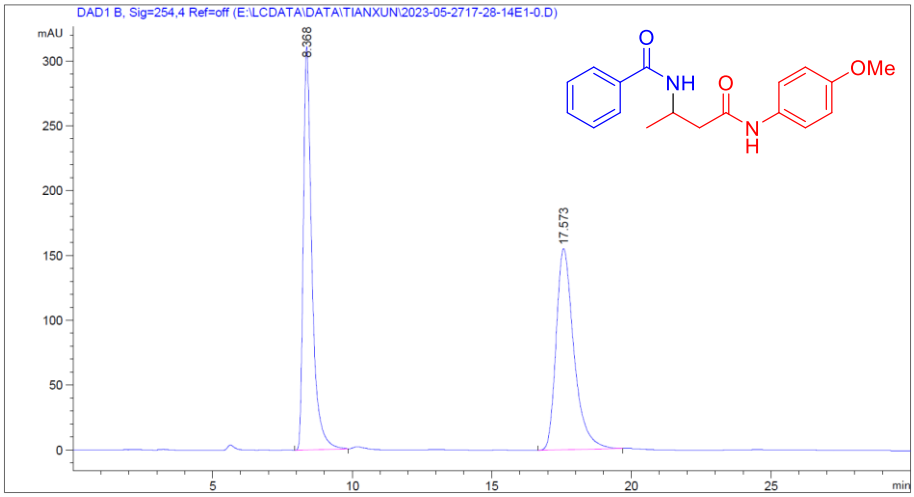
Figure S137. HPLC Chromatography of *tert*-Butyl (*S*)-(2-(4-methoxybenzamido)propyl)carbamate (3fg)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
3.941	BM m	0.75	25102.22	3245.01	97.00
4.658	MM m	0.63	777.68	53.86	3.00
		Total	25879.91		

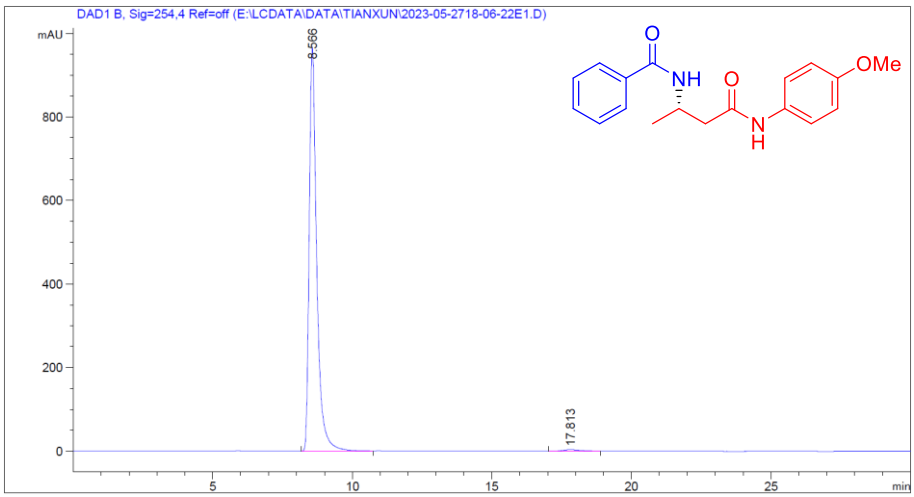
Figure S138. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)benzamide (5aa).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.368	BBA	0.3191	6635.75000	310.80490	49.1670
2	17.573	BB	0.6676	6860.60107	155.23618	50.8330
Totals :				1.34964e4	466.04108	

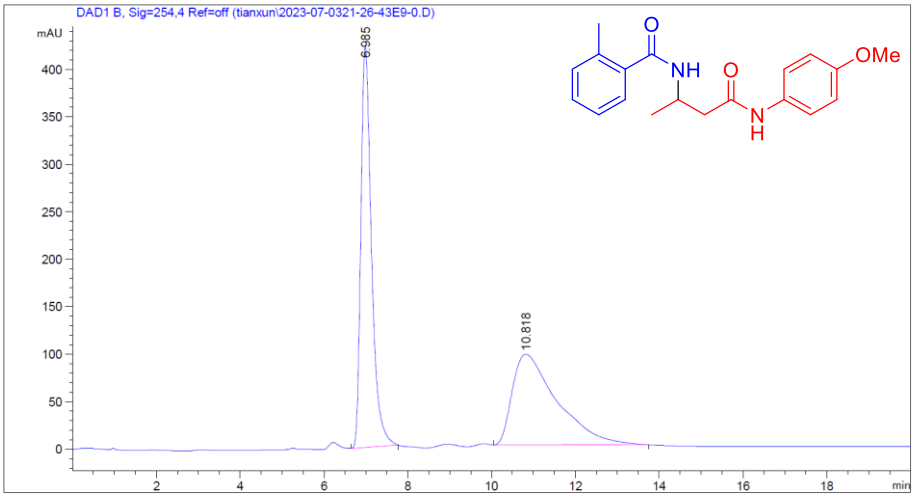
Figure S139. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) benzamide (5aa).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.566	BB	0.2818	1.81780e4	964.86133	99.0712
2	17.813	BBA	0.6050	170.41130	3.77243	0.9288
Totals :				1.83484e4	968.63375	

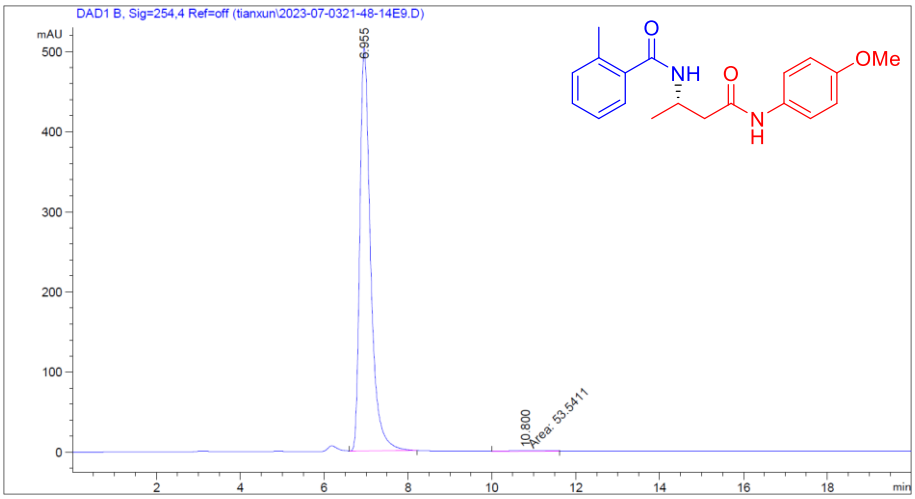
Figure S140. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)-2-methylbenzamide (5ab).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.985	BBA	0.2694	7430.88818	422.03644	51.2681
2	10.818	BBA	1.0790	7063.27930	95.49199	48.7319
Totals :				1.44942e4	517.52843	

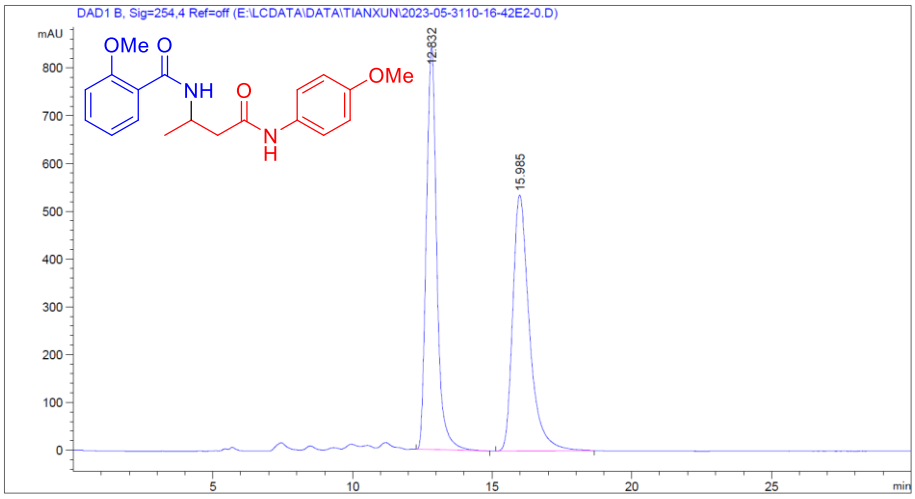
Figure S141. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) -2-methylbenzamide (5ab)



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.955	VBA	0.2707	8995.57617	502.92819	99.4083
2	10.800	MM	1.0580	53.54111	8.43457e-1	0.5917
Totals :				9049.11728	503.77165	

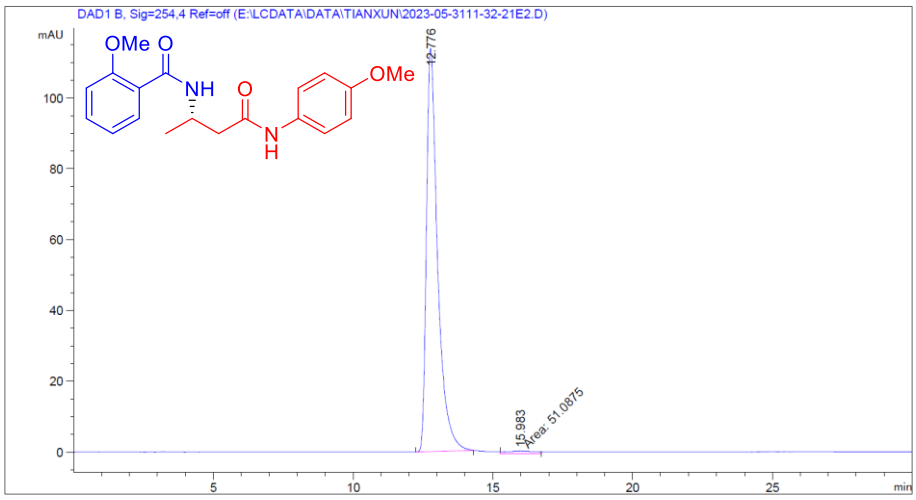
Figure S142. HPLC Chromatography of the Racemic 2-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ac).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.832	BB	0.4006	2.18179e4	841.14001	49.6159
2	15.985	BBA	0.6250	2.21557e4	535.20990	50.3841
Totals :				4.39735e4	1376.34991	

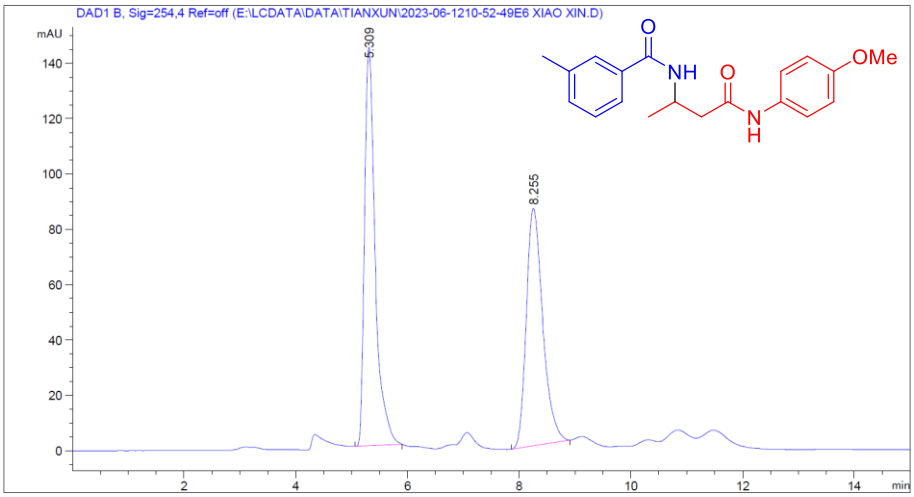
Figure S143. HPLC Chromatography of (*S*)-2-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ac).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.776	BBA	0.4136	3157.29907	113.83295	98.4077
2	15.983	MM	1.1800	51.08746	7.21572e-1	1.5923
Totals :				3208.38653	114.55453	

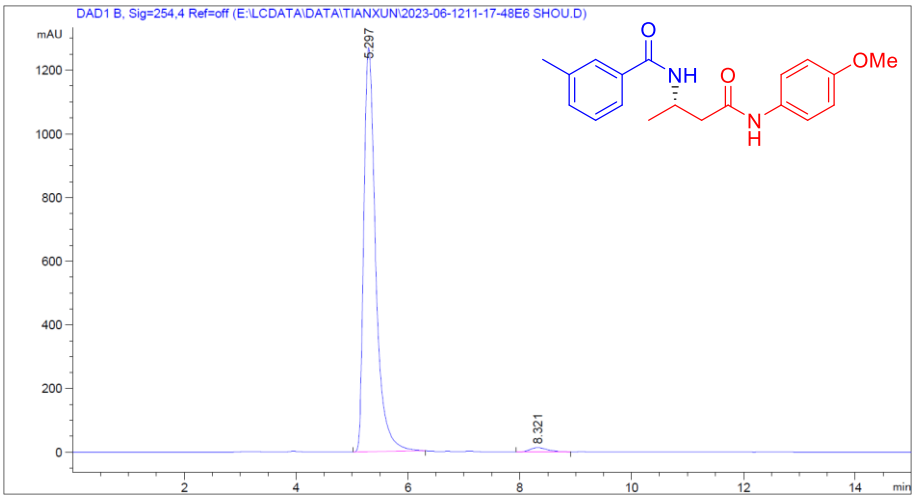
Figure S144. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)-3-methylbenzamide (5ad).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.309	BBA	0.2013	1892.05151	144.03728	51.9002
2	8.255	BB	0.3124	1753.50256	85.81213	48.0998
Totals :				3645.55408	229.84940	

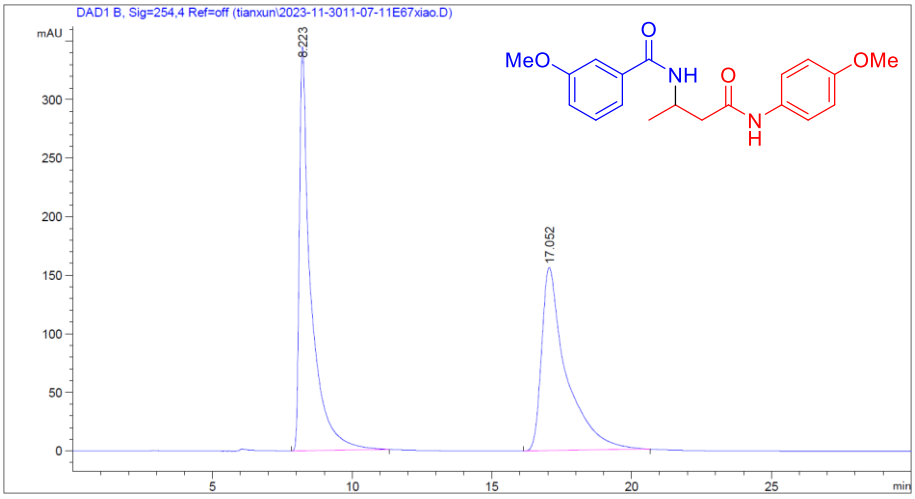
Figure S145. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) -3-methylbenzamide (5ad).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.297	BBA	0.2232	1.86152e4	1268.51575	98.4886
2	8.321	BB	0.3285	285.67627	13.41293	1.5114
Totals :				1.89008e4	1281.92868	

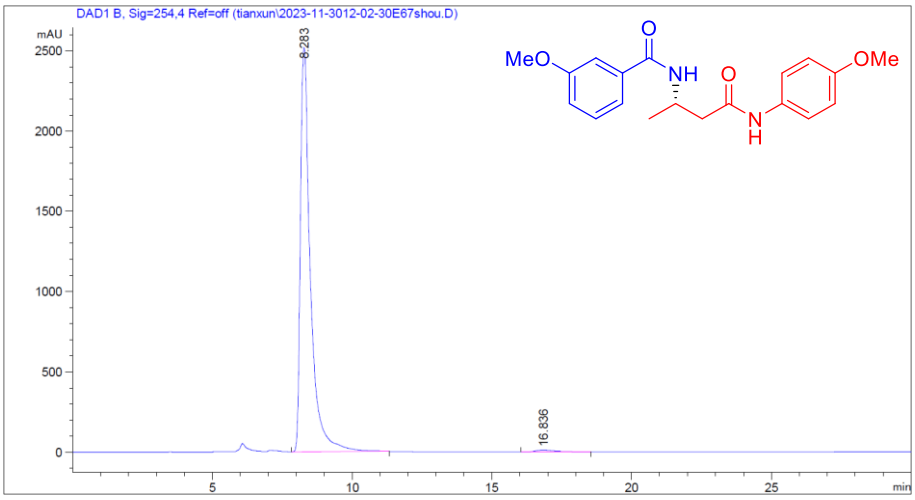
Figure S146. HPLC Chromatography of the Racemic 3-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ae).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.223	BBA	0.3931	9850.93262	345.04919	50.6478
2	17.052	BBA	0.8598	9598.95215	156.44342	49.3522
Totals :				1.94499e4	501.49261	

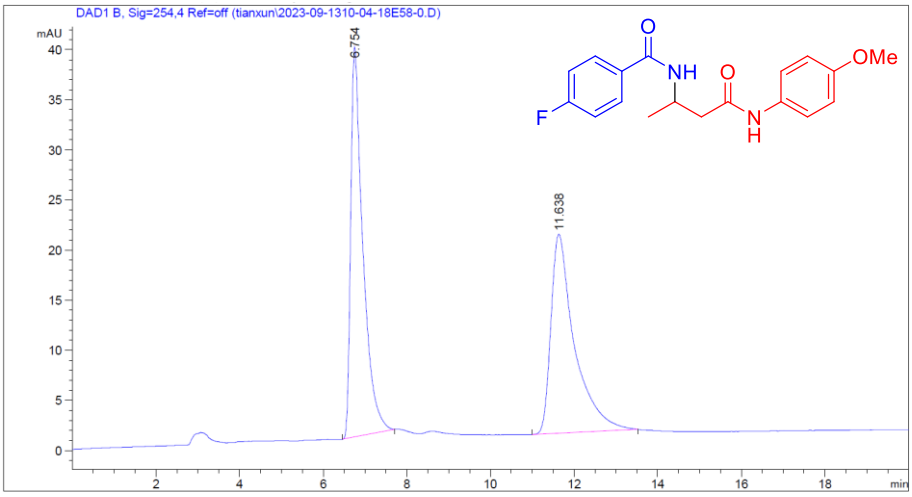
Figure S147. HPLC Chromatography of (*S*)-3-Methoxy-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ae).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.283	BBA	0.3591	6.23340e4	2515.13745	99.0371
2	16.836	BB	0.7093	606.03662	12.46344	0.9629
Totals :				6.29400e4	2527.60089	

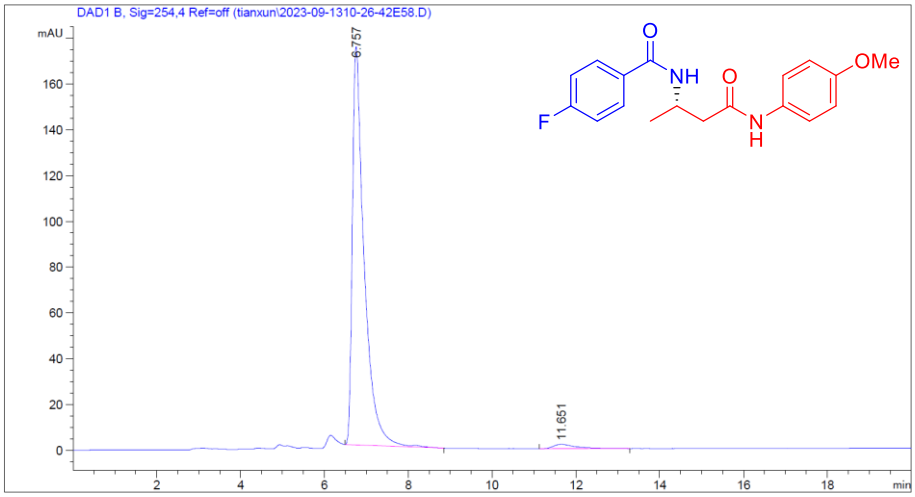
Figure S148. HPLC Chromatography of the Racemic 4-Fluoro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ah).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.754	BB	0.2874	785.34296	38.92079	50.3107
2	11.638	BBA	0.5597	775.64203	19.85961	49.6893
Totals :				1560.98499	58.78041	

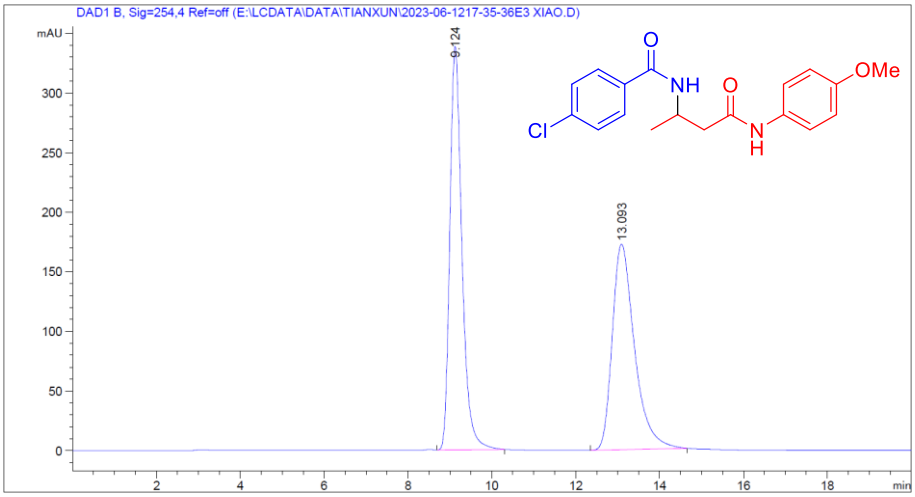
Figure S149. HPLC Chromatography of (*S*)-4-Fluoro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ah).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.757	BV R	0.2748	3392.02368	173.94601	97.8903
2	11.651	BB	0.5367	73.10411	1.93527	2.1097
Totals :				3465.12779	175.88129	

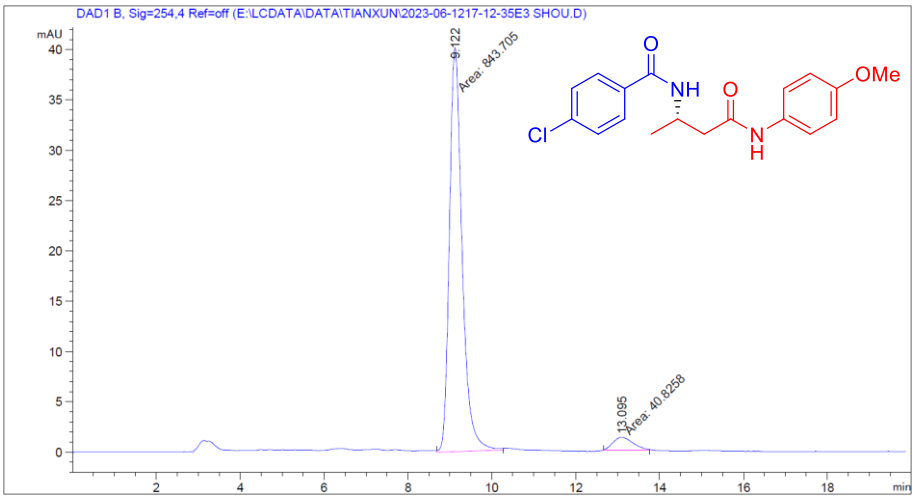
Figure S150. HPLC Chromatography of the Racemic 4-Chloro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ai).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.124	BBA	0.3032	6763.21289	338.41547	51.5429
2	13.093	BBA	0.5581	6358.30713	172.47862	48.4571
Totals :				1.31215e4	510.89409	

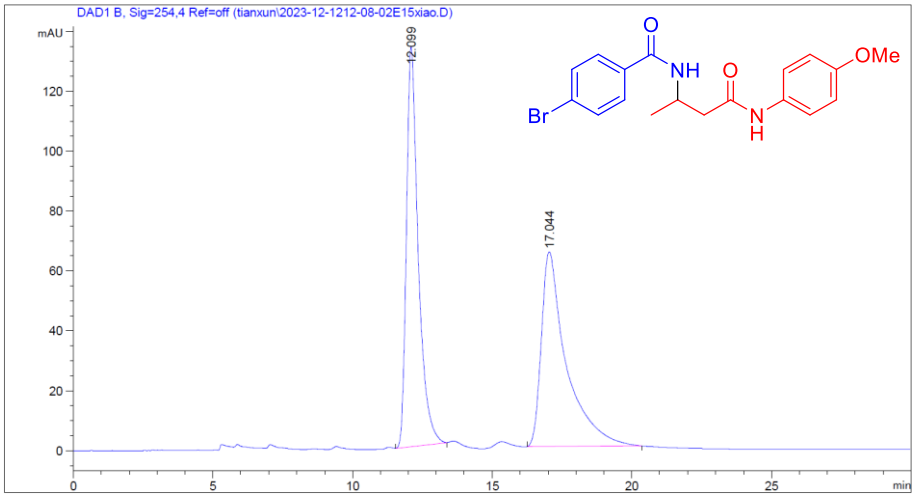
Figure S151. HPLC Chromatography of (*S*)-4-Chloro-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5ai).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.122	MM	0.3504	843.70477	40.13346	95.3845
2	13.095	MM	0.5428	40.82583	1.25351	4.6155
Totals :				884.53060	41.38697	

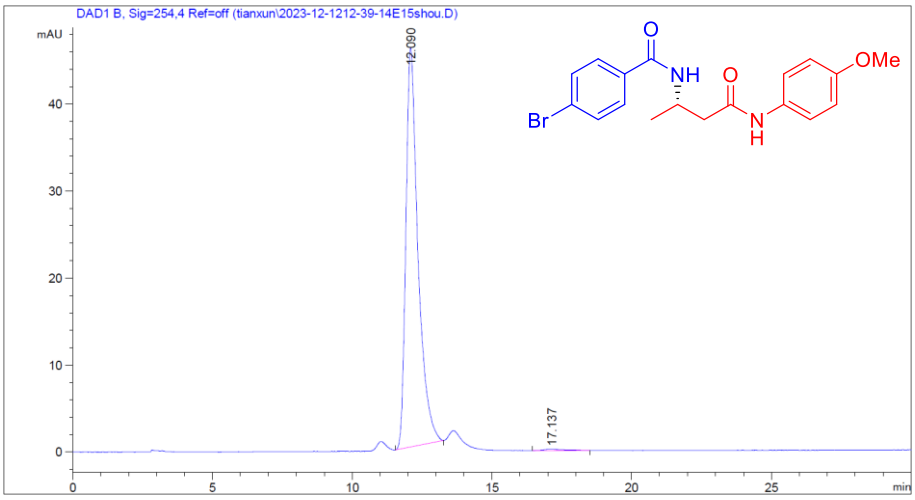
Figure S152. HPLC Chromatography of the Racemic 4-Bromo-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aj).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.099	BB	0.4341	3913.12769	133.46248	49.2719
2	17.044	BBA	0.8753	4028.77905	64.98422	50.7281
Totals :				7941.90674	198.44670	

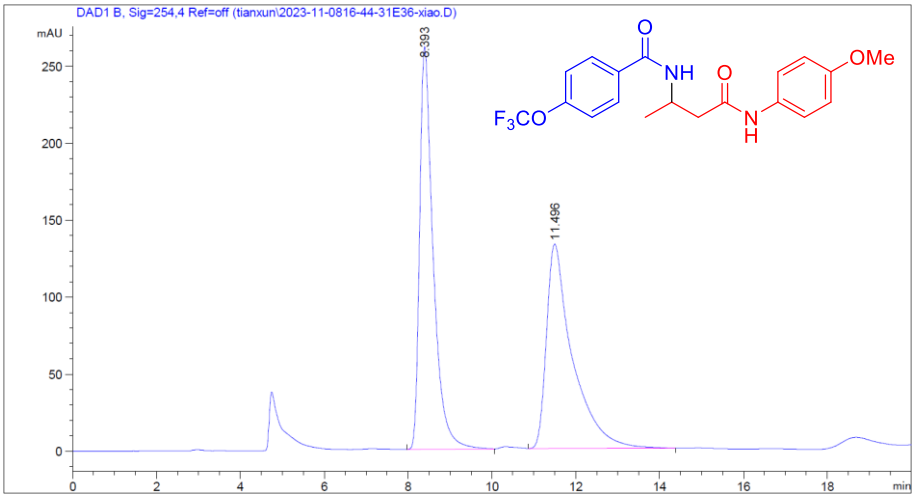
Figure S153. HPLC Chromatography of (*S*)-4-Bromo-*N*-(4-((4-methoxyphenyl)amino)-4-oxobutan-2-yl)benzamide (5aj).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.090	BB	0.4418	1383.19226	45.86885	99.3862
2	17.137	BB	0.6171	8.54301	1.64711e-1	0.6138
Totals :				1391.73528	46.03356	

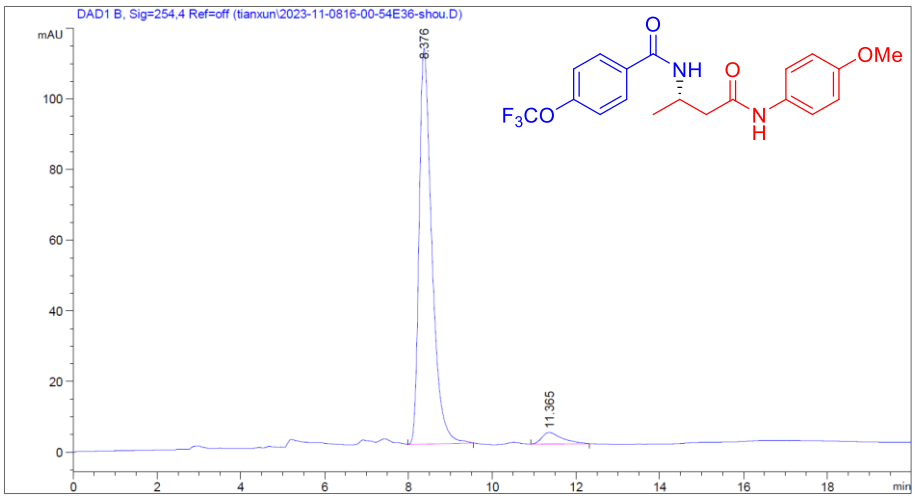
Figure S154. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)-4-(trifluoromethoxy)benzamide (5ak).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.393	BB	0.3296	5859.44629	261.27921	50.5895
2	11.496	BB	0.6069	5722.88232	132.76945	49.4105
Totals :				1.15823e4	394.04866	

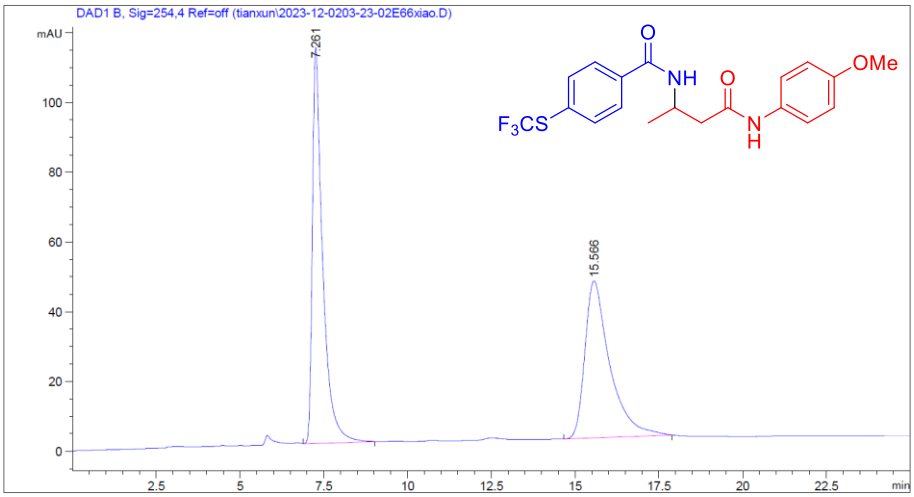
Figure S155. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) -4-(trifluoromethoxy)benzamide (5ak).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.376	BBA	0.3162	2363.60889	112.02225	95.6344
2	11.365	BBA	0.4759	107.89490	3.26232	4.3656
Totals :				2471.50378	115.28457	

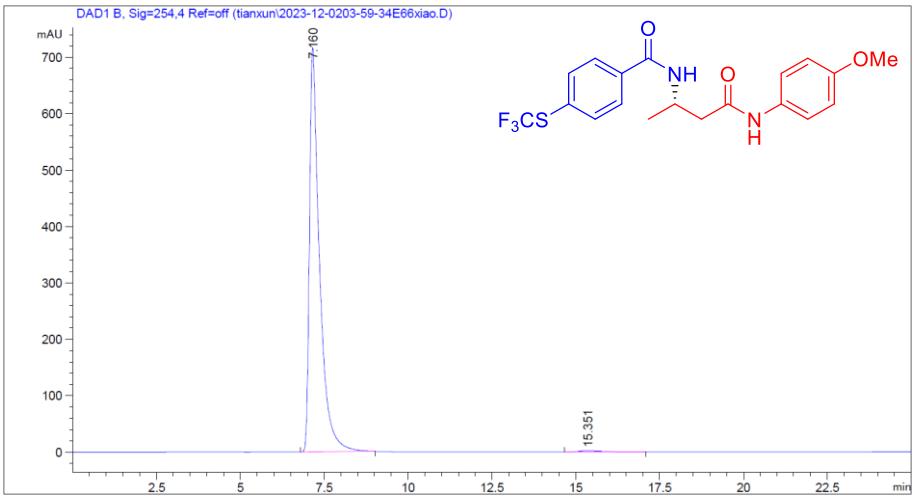
Figure S156. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)-4-((trifluoromethyl)thio)benzamide (5am).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.261	VBA	0.3025	2419.91187	113.61816	51.0206
2	15.566	BBA	0.7525	2323.09912	44.98688	48.9794
Totals :				4743.01099	158.60503	

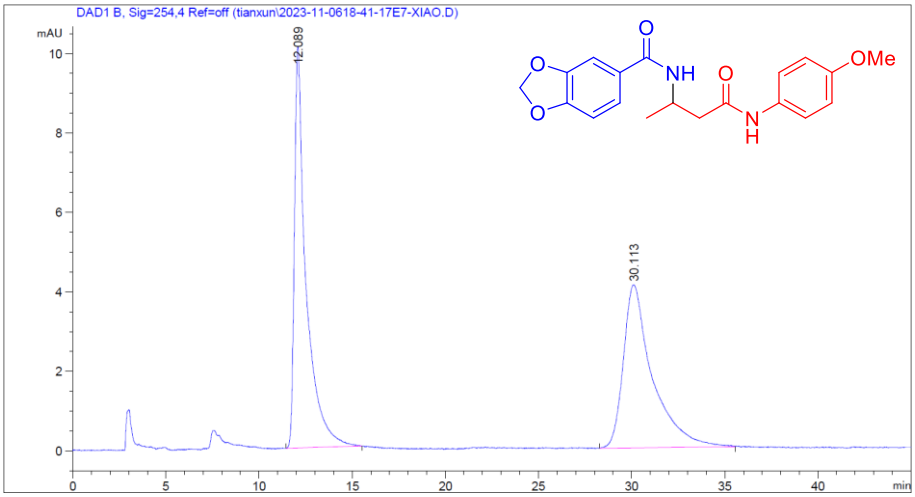
Figure S157. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) -4-((trifluoromethyl)thio)benzamide (5am).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.160	BBA	0.2934	1.49414e4	716.21411	99.2955
2	15.351	BBA	0.6538	106.00166	2.19359	0.7045
Totals :				1.50474e4	718.40770	

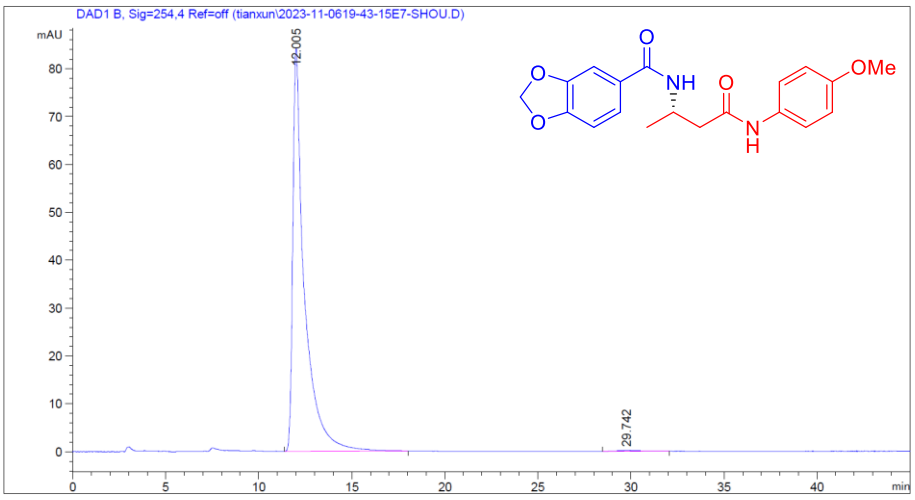
Figure S158. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)benzo[d][1,3]dioxole-5-carboxamide (5an).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.089	BB	0.6057	437.52765	10.09340	49.6600
2	30.113	BB	1.4818	443.51807	4.10093	50.3400
Totals :				881.04572	14.19433	

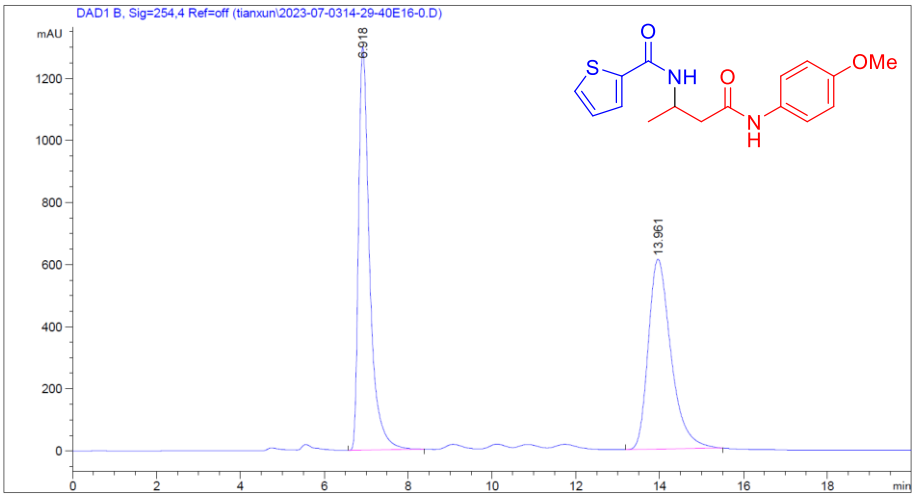
Figure S159. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) benzo[d][1,3]dioxole-5-carboxamide (5an).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.005	BB	0.5959	3635.67871	84.16940	99.5410
2	29.742	BB	1.0434	16.76502	1.91862e-1	0.4590
Totals :				3652.44373	84.36127	

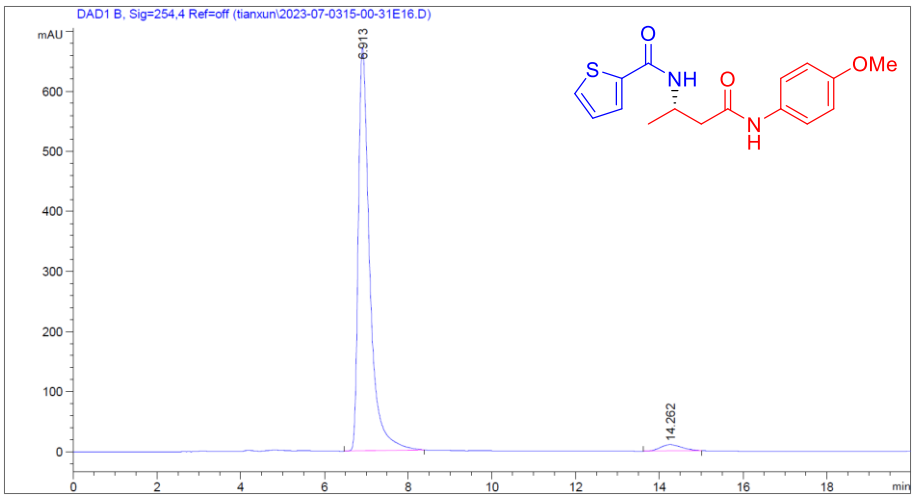
Figure S160. HPLC Chromatography of the Racemic *N*-(4-((4-Methoxyphenyl)amino)-4-oxo butan-2-yl)thiophene-2-carboxamide (5al).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.918	BBA	0.2765	2.38677e4	1297.96741	50.8576
2	13.961	BBA	0.5736	2.30628e4	612.12183	49.1424
Totals :				4.69305e4	1910.08923	

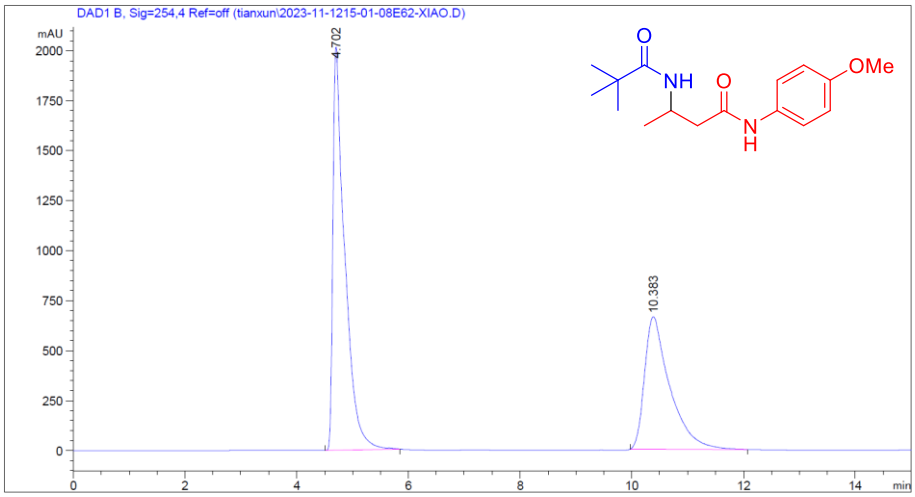
Figure S161. HPLC Chromatography of (*S*)-*N*-(4-((4-Methoxyphenyl)amino)-4-oxobutan-2-yl) thiophene-2-carboxamide (5al).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.913	BBA	0.2849	1.26949e4	670.32104	97.1797
2	14.262	BBA	0.5319	368.42691	10.43538	2.8203
Totals :				1.30633e4	680.75642	

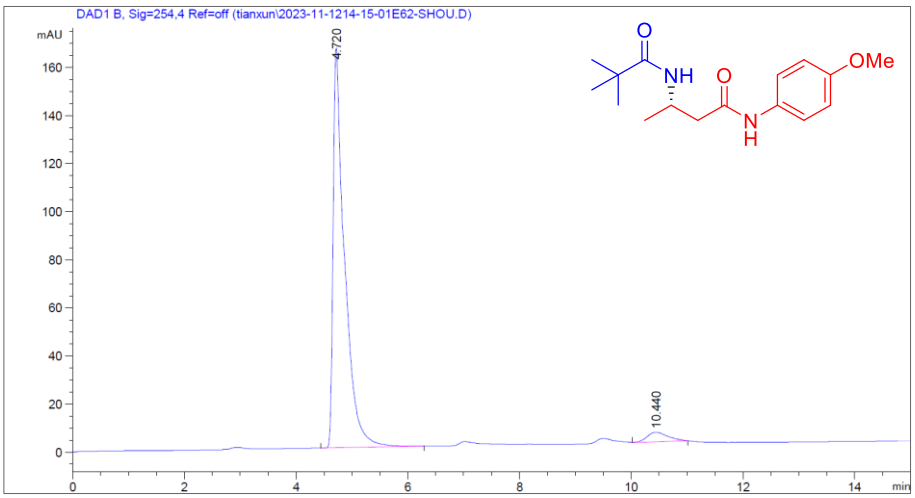
Figure S162. HPLC Chromatography of the Racemic *N*-(4-Methoxyphenyl)-3-pivalamidobut anamide (5ao).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.702	BV R	0.2003	2.94595e4	2017.91907	58.6690
2	10.383	BBA	0.4498	2.07536e4	661.90411	41.3310
Totals :				5.02131e4	2679.82318	

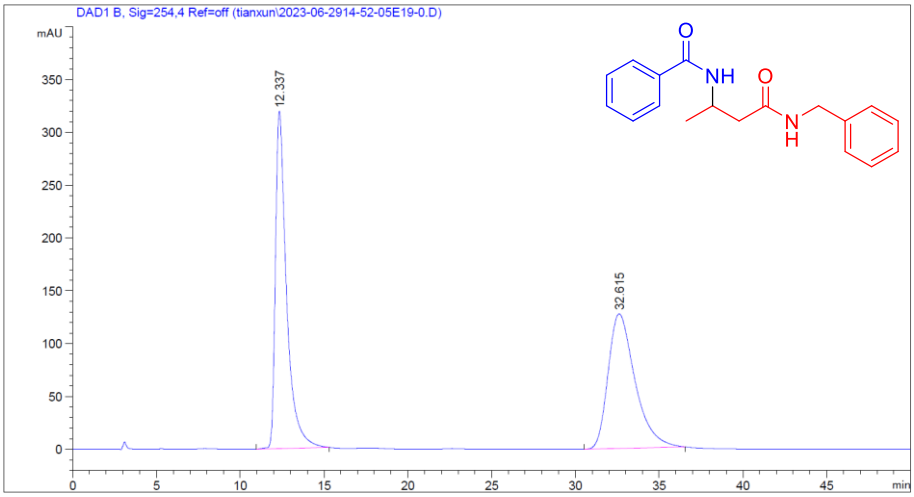
Figure S163. HPLC Chromatography of (*S*)-*N*-(4-Methoxyphenyl)-3-pivalamidobutanamide (5ao).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.720	BB	0.1960	2343.42725	166.67308	95.6796
2	10.440	VBA	0.3913	105.81750	4.07076	4.3204
Totals :				2449.24475	170.74384	

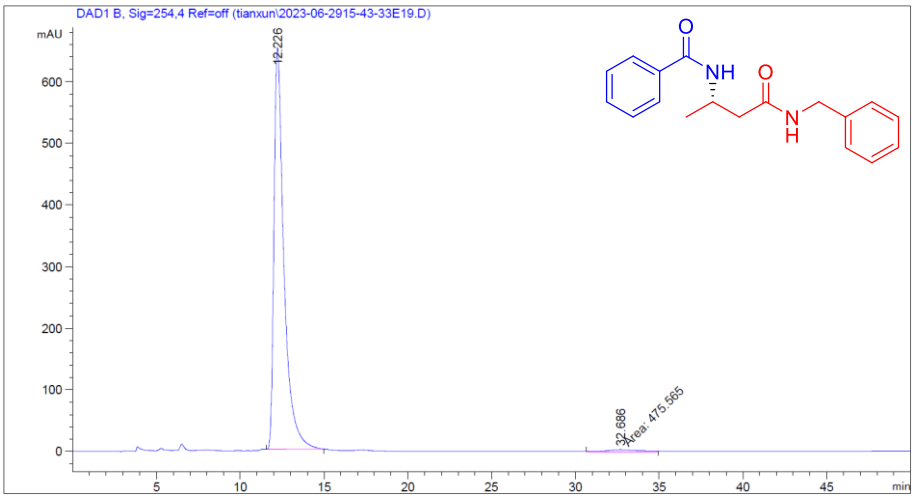
Figure S164. HPLC Chromatography of the Racemic *N*-(4-(Benzylamino)-4-oxobutan-2-yl)benzamide (5ba).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.337	BBA	0.6799	1.47216e4	319.30914	50.8710
2	32.615	BBA	1.6813	1.42175e4	127.46292	49.1290
Totals :				2.89391e4	446.77206	

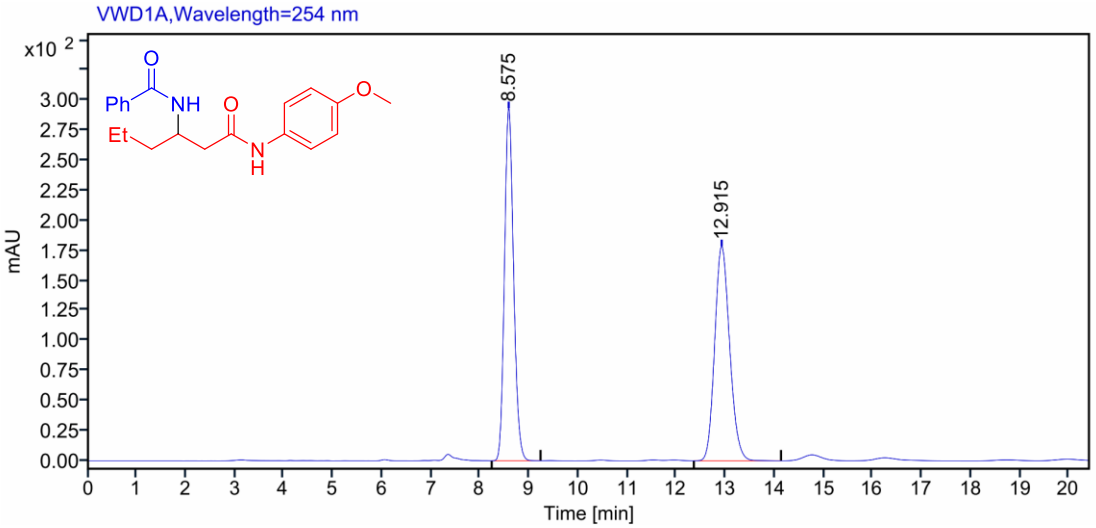
Figure S165. HPLC Chromatography of (*S*)-*N*-(4-(Benzylamino)-4-oxobutan-2-yl)benzamide (5ba).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.226	BBA	0.6094	2.69970e4	651.57886	98.2689
2	32.686	MM	2.3160	475.56491	3.42232	1.7311
Totals :				2.74726e4	655.00118	

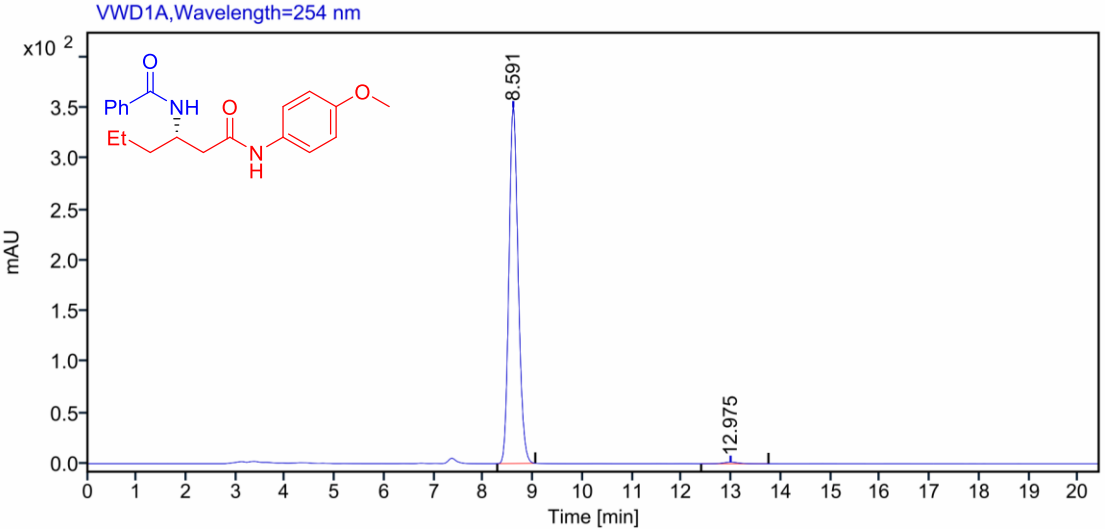
Figure S166. HPLC Chromatography of the Racemic *N*-(1-((4-Methoxyphenyl)amino)-1-oxo hexan-3-yl)benzamide (5ca)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
8.575	BB	0.99	3803.58	293.80	50.09
12.915	BB	1.78	3790.15	178.86	49.91
		Total	7593.73		

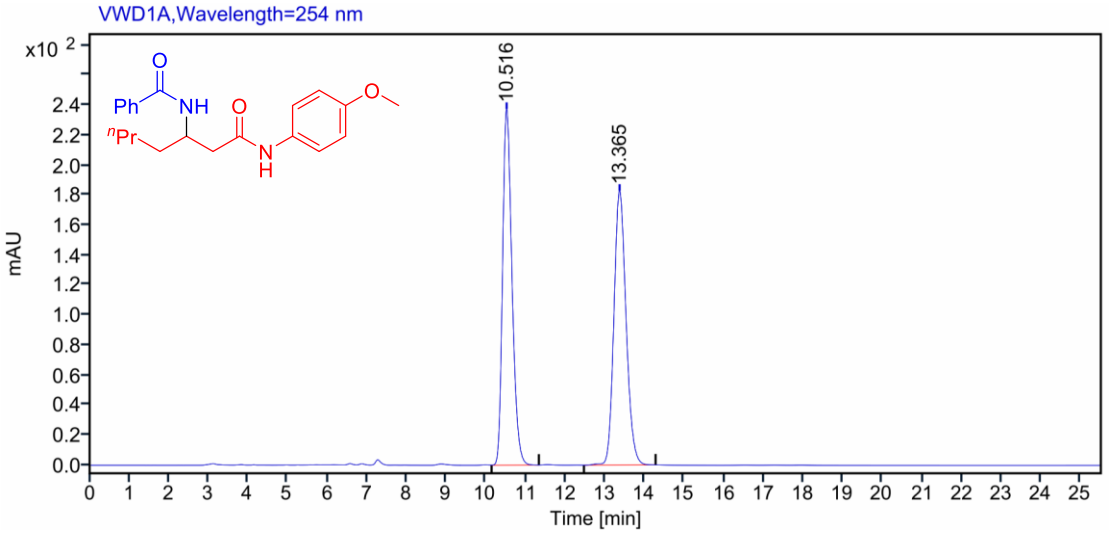
Figure S167. HPLC Chromatography of (*S*)-*N*-(1-((4-Methoxyphenyl)amino)-1-oxohexan-3-yl) benzamide (5ca)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
8.591	MM m	0.77	4556.83	350.29	99.28
12.975	MM m	1.36	33.12	1.55	0.72
		Total	4589.95		

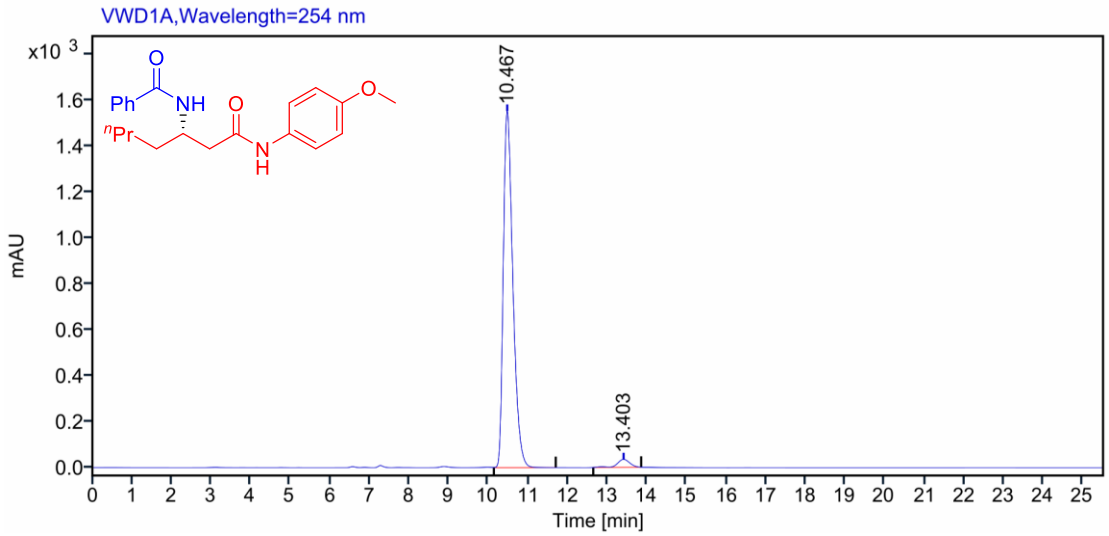
Figure S168. HPLC Chromatography of the Racemic *N*-(1-((4-Methoxyphenyl)amino)-1-oxo heptan-3-yl)benzamide (5da)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
10.516	VB	1.19	3921.53	237.50	50.17
13.365	BM m	1.81	3895.34	182.86	49.83
		Total	7816.87		

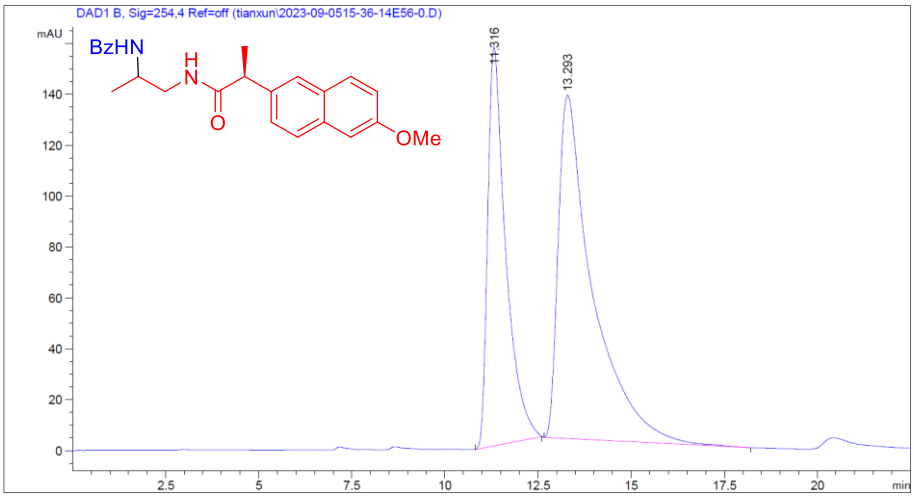
Figure S169. HPLC Chromatography of *(S)*-*N*-(1-((4-Methoxyphenyl)amino)-1-oxoheptan-3-yl) benzamide (5da)



Signal: VWD1A,Wavelength=254 nm

RT [min]	Type	Width [min]	Area	Height	Area%
10.467	VB	1.56	26102.47	1552.07	97.20
13.403	MM m	1.21	752.69	34.69	2.80
		Total	26855.16		

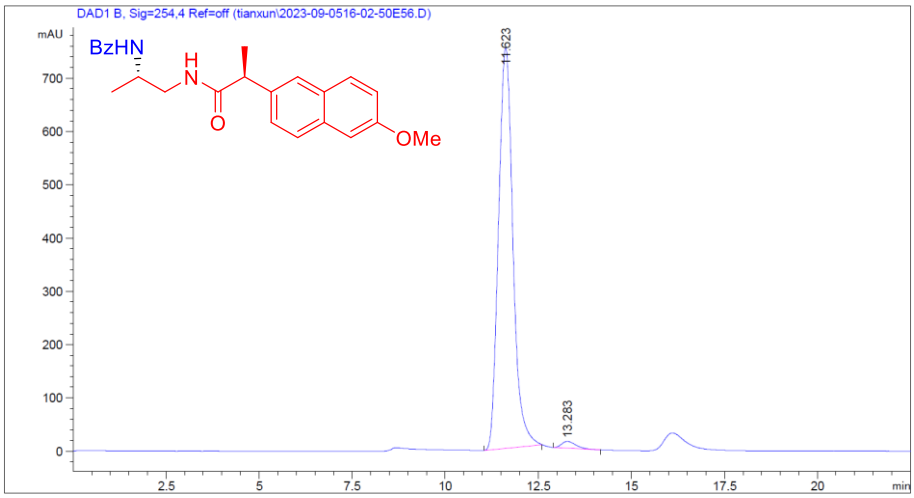
Figure S170. HPLC Chromatography of the Racemic *N*-(1-((*S*)-2-(6-Methoxynaphthalen-2-yl) propanamido)propan-2-yl)benzamide (6).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.316	BBA	0.4885	5267.99219	156.57556	37.9167
2	13.293	BB	0.9000	8625.61816	134.89653	62.0833
Totals :				1.38936e4	291.47209	

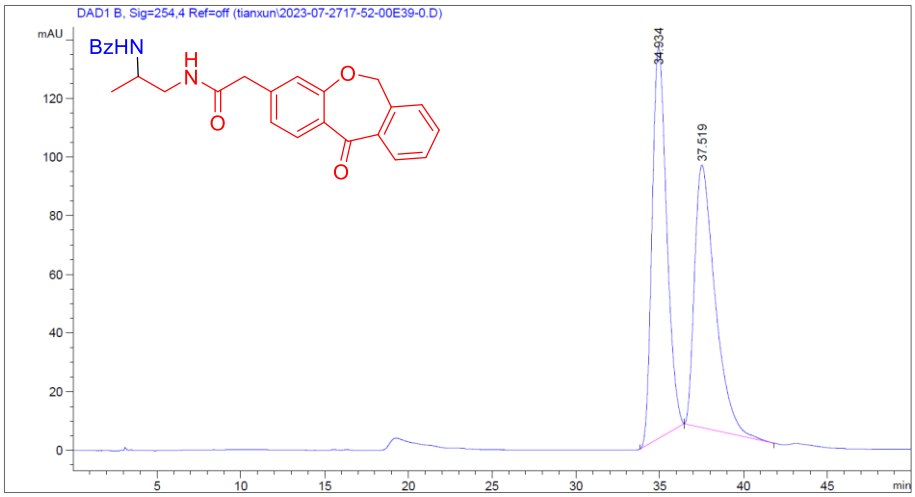
Figure S171. HPLC Chromatography of N-((*S*)-1-((*S*)-2-(6-Methoxynaphthalen-2-yl)propana mido)propan-2-yl)benzamide (6).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.623	BBA	0.4223	2.02561e4	751.91980	98.3591
2	13.283	BB	0.4094	337.92648	12.74286	1.6409
Totals :				2.05940e4	764.66266	

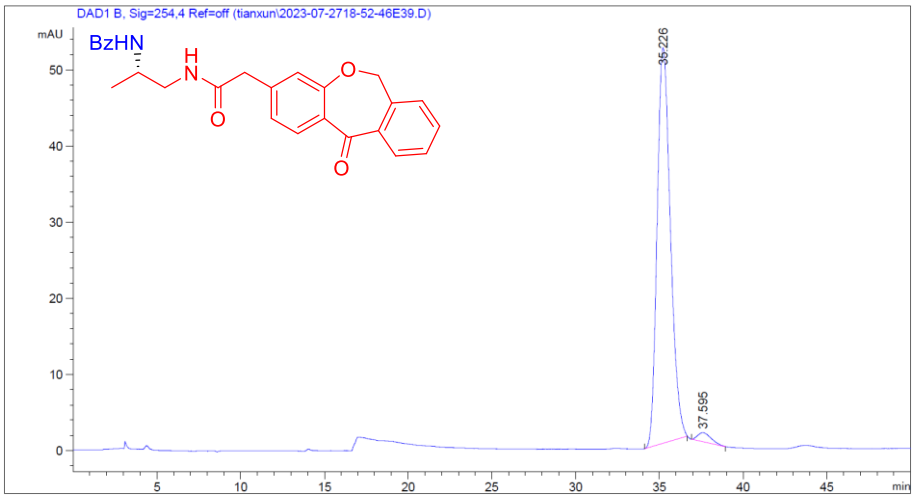
Figure S172. HPLC Chromatography of the Racemic *N*-(1-(2-(11-oxo-6,11-Dihydrodibenzo[*b*, *e*]oxepin-3-yl)acetamido)propan-2-yl)benzamide (7).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.934	BB	0.9332	8031.08838	133.23552	51.3313
2	37.519	BBA	1.2739	7614.50293	89.38248	48.6687
Totals :				1.56456e4	222.61800	

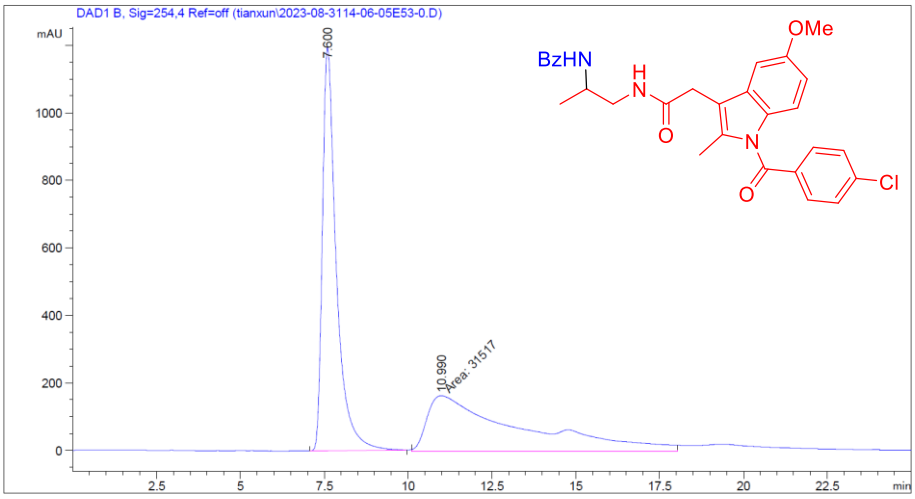
Figure S173. HPLC Chromatography of (*S*)-*N*-(1-(2-(11-oxo-6,11-Dihydrodibenzo[*b*,*e*]oxepin-3-yl)acetamido)propan-2-yl)benzamide (7).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.226	BBA	0.8493	2853.53882	51.90400	97.7819
2	37.595	BB	0.6812	64.73160	1.16331	2.2181
Totals :				2918.27042	53.06730	

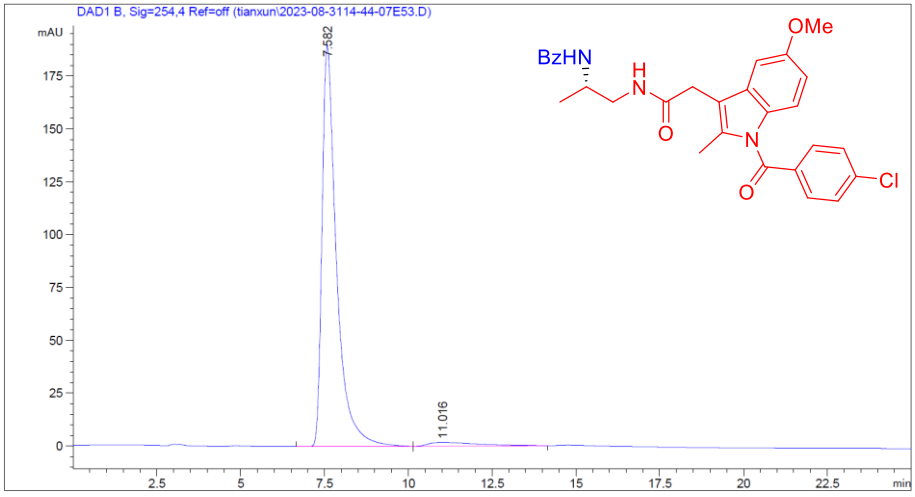
Figure S174. HPLC Chromatography of the Racemic *N*-(1-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)propan-2-yl)benzamide (8).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.600	BB	0.4219	3.44064e4	1195.00134	52.1915
2	10.990	MM	3.1929	3.15170e4	164.51656	47.8085
Totals :				6.59234e4	1359.51790	

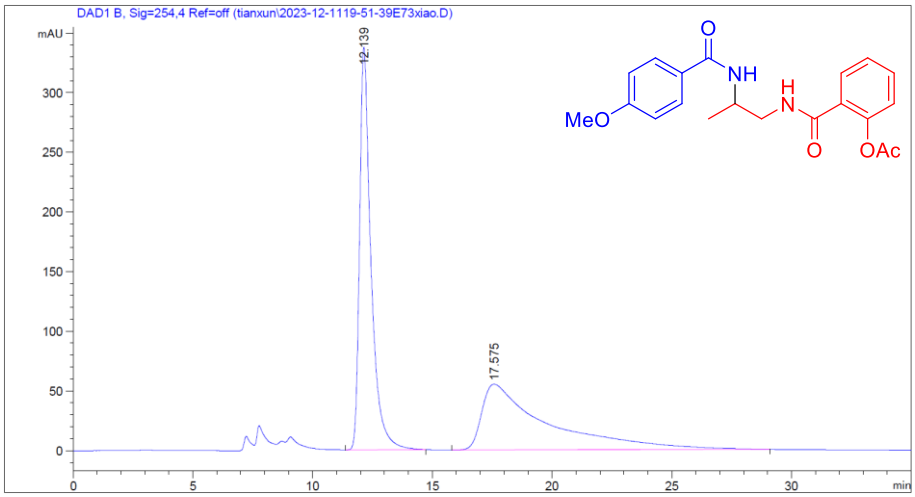
Figure S175. HPLC Chromatography of (*S*)-*N*-(1-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetamido)propan-2-yl)benzamide (8).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.582	BB	0.4432	5705.28906	189.52417	96.7637
2	11.016	BBA	1.2104	190.81352	1.86391	3.2363
Totals :				5896.10258	191.38808	

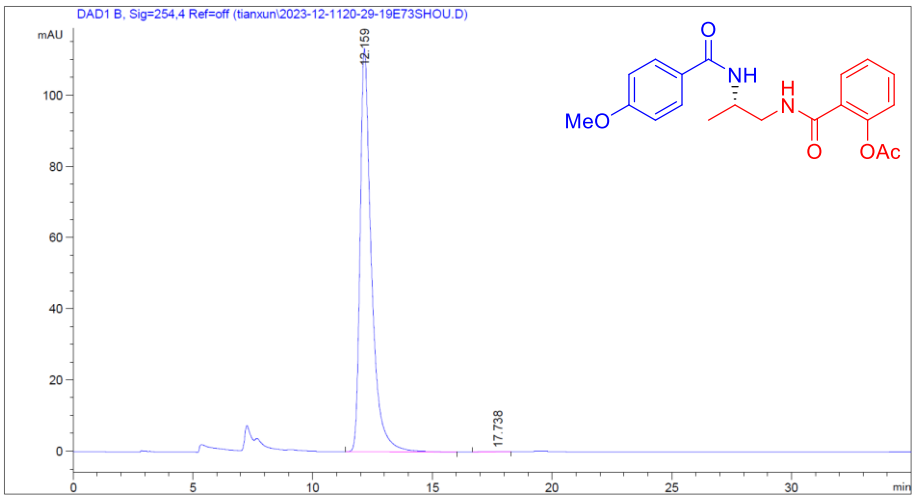
Figure S176. HPLC Chromatography of the Racemic 2-((2-(4-Methoxybenzamido)propyl)carbamoyl)phenyl acetate (9).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.139	BBA	0.4807	1.11769e4	337.24454	51.6134
2	17.575	BB	2.4429	1.04782e4	55.24165	48.3866
Totals :				2.16551e4	392.48618	

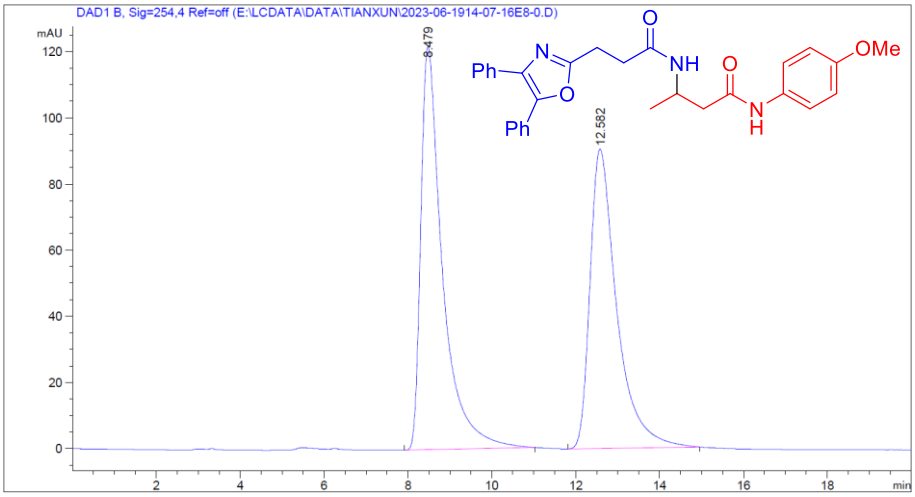
Figure S177. HPLC Chromatography of (*S*)-2-((2-(4-Methoxybenzamido)propyl)carbamoyl)phenyl acetate (9).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.159	BB	0.4802	3730.09302	113.26410	99.8613
2	17.738	BB	0.7580	5.18255	8.10523e-2	0.1387
Totals :				3735.27557	113.34515	

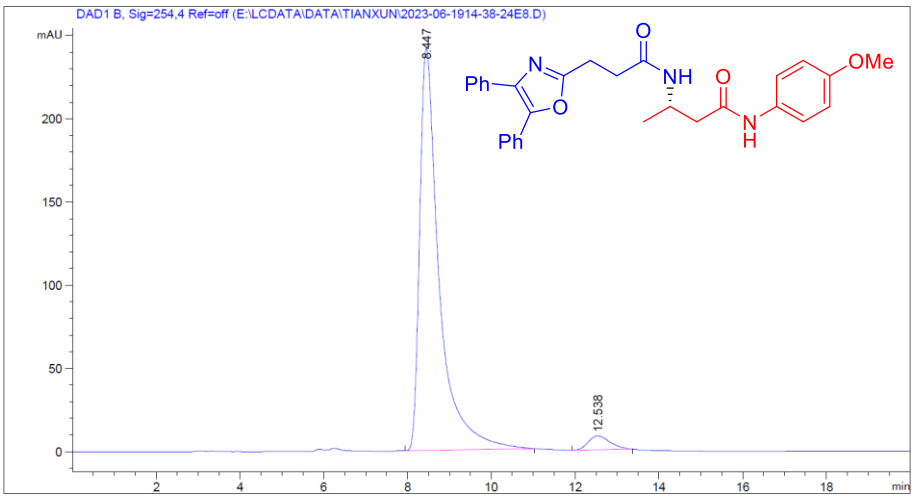
Figure S178. HPLC Chromatography of the Racemic 3-(3-(4,5-Diphenyloxazol-2-yl)propanamido)-*N*-(4-methoxyphenyl)butanamide (10).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.479	BBA	0.5227	4372.91992	121.85932	52.2196
2	12.582	BBA	0.6541	4001.17041	90.44542	47.7804
Totals :				8374.09033	212.30474	

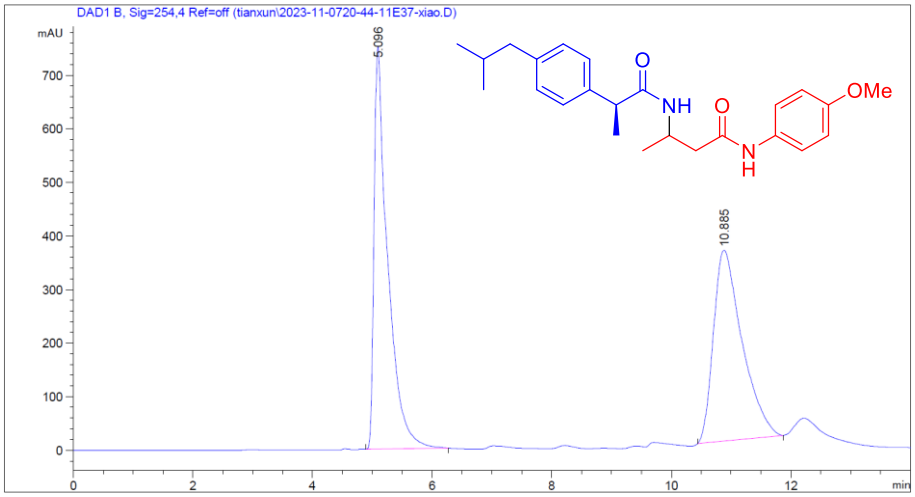
Figure S179. HPLC Chromatography of (*S*)-3-(3-(4,5-Diphenyloxazol-2-yl)propanamido)-*N*-(4-methoxyphenyl)butanamide (10).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.447	BBA	0.4709	7806.74121	241.65436	96.2610
2	12.538	BBA	0.5430	303.23257	8.40382	3.7390
Totals :				8109.97379	250.05818	

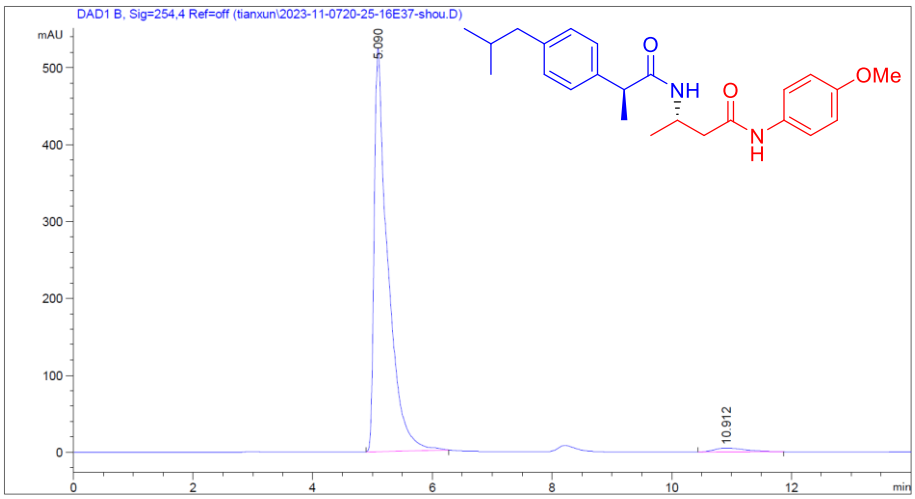
Figure S180. HPLC Chromatography of the Racemic 3-((*S*)-2-(4-Isobutylphenyl)propanamido)-*N*-(4-methoxyphenyl)butanamide (11).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.096	BBA	0.2179	1.18429e4	751.14294	49.9788
2	10.885	BBA	0.4903	1.18530e4	356.08624	50.0212
Totals :				2.36959e4	1107.22919	

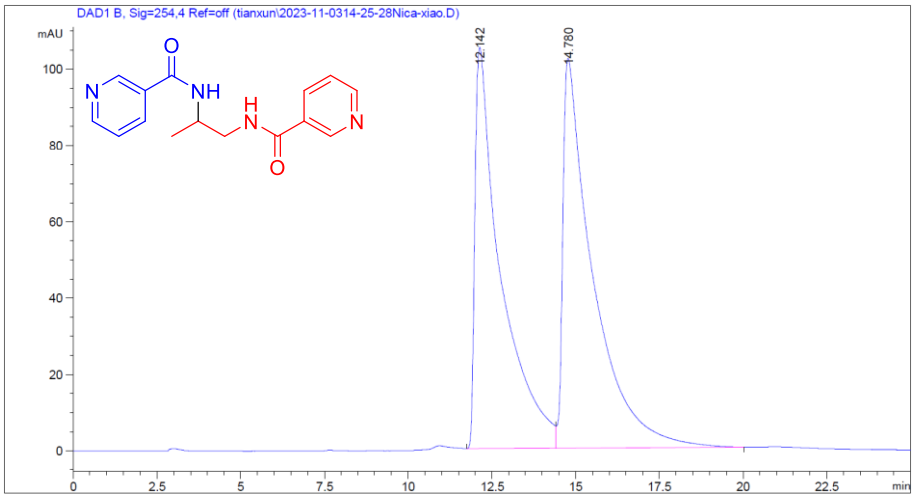
Figure S181. HPLC Chromatography of (*S*)-3-((*S*)-2-(4-Isobutylphenyl)propanamido)-*N*-(4-methoxyphenyl)butanamide (11).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.090	BBA	0.2174	8243.94238	524.38672	97.8475
2	10.912	BBA	0.5326	181.35062	5.05427	2.1525
Totals :				8425.29300	529.44098	

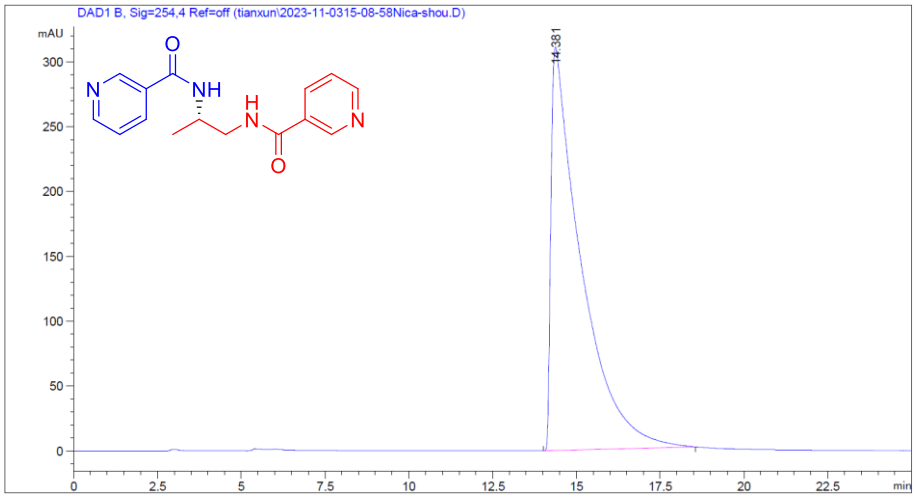
Figure S182. HPLC Chromatography of the Racemic *N*,*N*′-(Propane-1,2-diyl)dinicotinamide (Nicaraven).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.142	BV	0.7236	5617.49805	105.09461	46.9144
2	14.780	VB	0.8386	6356.44189	102.06170	53.0856
Totals :				1.19739e4	207.15631	

Figure S183. HPLC Chromatography of (*S*)-*N*,*N*′-(Propane-1,2-diyl)dinicotinamide ((*S*)-Nicaraven).



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.381	BBA	0.8206	1.93085e4	310.89749	100.0000
Totals :				1.93085e4	310.89749	