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Accepted Article

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Design, synthesis, and cytotoxic activity of 3-aryl-N-hydroxy-2(sulfonamido)propanamides in HepG2, HT-1080, KB, and MCF-7 cells

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Abstract: A new series of compounds containing (sulfonamido) propanamide (**6a1-13, 6b1-15, 7c1-5, 6d1-5, 6e1-6**) was designed and synthesized. All the synthesized compounds were characterized by NMR and mass spectrometry. The target compounds were evaluated for their in vitro cytotoxic activity against hepatocellular carcinoma (HepG2), fibrosarcoma (HT-1080), mouth epidermal carcinoma (KB), and breast adenocarcinoma (MCF-7) cells with the *sulforhodamine B* (SRB) assay, with *gemcitabine* and *mitomycin C* as positive controls. Most of these compounds exhibit a more potent cytotoxic effect than the positive control group on various cancer cell lines and the most potent compound, **6a7**, shows the IC50 values of 29.78 ± 0.516 μM, 30.70 ± 0.61 μM, and 64.89 ± 3.09 μM in HepG2, HT-1080, KB, and MCF-7 cells, respectively. Thus, these compounds with potent cytotoxic activity have potential for development as new chemotherapy agents.

Keywords: Sulfonamido; Cytotoxic; Synthesis; SRB Assay.

Introduction

Cancer is a major illness that seriously endangers human life and health.[1 - 3] In recent years, cancers have been responsible for 8.2 million human deaths worldwide.[4 - 5] According to the World Health Organization (WHO), tumours have been the main cause of morbidity and mortality.[6] Cancer is one of the most serious threats against humans, and the clinical prognosis remains relatively poor.[7 - 10] Surpassing cardiovascular diseases, cancer has taken the position as the number one killer due to various worldwide factors.[11 - 13] Cancer is a pathological condition that occurs due to genetic factors during development, resulting in cell death via excessive proliferation and apoptosis.[14]

Currently, there is no absolute effective treatment for cancer patients in clinical practice, but chemotherapy is still the most widely used form of cancer treatment.[15 - 20] The FDA approved anticancer drugs can be devided into two main gropus: cytotoxic antineoplastics and targeted antineoplastics. The cytotoxic antibiotics are a varied group of drugs having various mechanisms of action which contains alkylating agents, antimicrotubule agents, topoisomerase inhibitors and antimetabolites; while most of the targeted antineoplastics belong to signal transduction inhibitors, gene expression modulators, apoptosis induces, hormone therapies, and monoclonal antibodies.[21] There are many successful anticancer drugs such as: vincristine, paclitaxel and its derivates docetaxel and cabazitaxel, irinotecan, topotecan, carboplatin, cisplatin and imatinib in the history of anticancer drugs development. However, the majority of cancers are either resistant to chemotherapy, or they acquire resistance during treatment.[22 - 25] Thus, studies involving the synthesis of new compounds and the investigation of their bioactive potential represent an important goal for the development of new cancer drugs.[26 - 30]

Herein, we communicate the synthesis, biological data and structure - activity relationship (SAR) of a series of novel 3-aryl-N-hydroxy-2-(sulfonamido)propanamide based cytotoxic reagents. In the present study, 2-(sulfonamido) propanamide was used as the parent compound for the design of new anticancer compounds. In total, **44** novel 3-aryl-N-hydroxy-2-(sulfonamido)propenamide compounds were designed

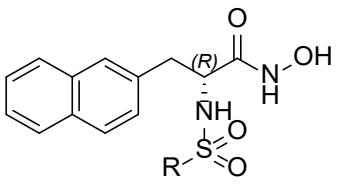
and synthesized by the sulfonyl esterification of naphthylpropionamide (D/L), phenylpropionamide (D/L), and hydroxypropionamide (D) with different sulfonyl chlorides in an alkaline medium, followed by amination via aqueous hydroxylamine solution.

Results and Discussion

Chemistry

Compounds **6a - b, d - e,** and **7c** (**Tables 1 - 4**) with diferent aromantic group substitutions and chiral centers were designed to expore their cytotoxic effect. The target compounds were obtained through the route depicted in Scheme 1. The synthesis of novel derivatives was completed using 3-(2-Naphthyl)-D-alanine (a), 3 - (2 - naphthyl) - L - alanine (b), 4 - bromo - L - phenylalanine (c), 4 - bromo - D - phenylalanine (d) and D - tyrosine ethyl ester hydrochloride (e) as key starting materials. The conversion of the starting materials (**1a - e**) to the corresponding esters (**2a - b, d - e,** and **3c**) was conducted in the presence of $SOCl_2$ and methanol. Then, the intermediates **4(a - b, d - e**) and **5c** were synthesized by the sulfonylation of **2a - b, d - e,** and **3c** with different sulfonyl chlorides in the presence of DIPEA. Subsequently, aminolysis of the ester moiety with aqueous hydroxylamine (50 percent w/w) led to the target hydroxamic acid (**6a - b, d - e, 7c**).

Table 1. The structures of the compounds 6a1 - 6a13



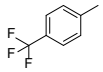
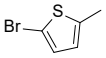
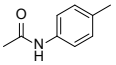
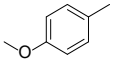
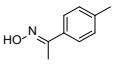
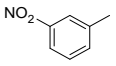
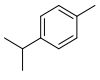
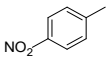
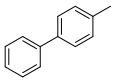
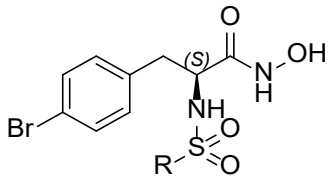
Compound (D)	R	Compound (D)	R
6a$_1$		**6a$_8$**	
6a$_2$		**6a$_9$**	
6a$_3$		**6a$_{10}$**	
6a$_4$		**6a$_{11}$**	
6a$_5$		**6a$_{12}$**	
6a$_6$		**6a$_{13}$**	
6a$_7$			

Table 2. The structures of the compounds 6b1 - 6b15



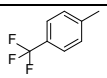
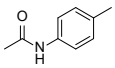
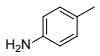
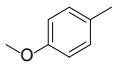
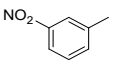
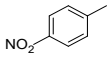
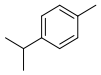
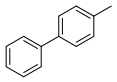
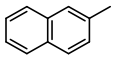
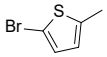
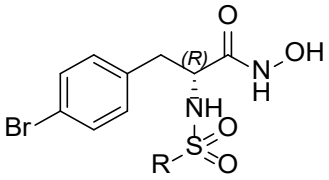
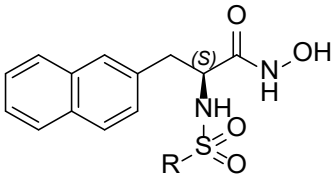
Compound (L)	R	Compound (L)	R
6b1		6b9	
6b2		6b10	
6b3		6b11	
6b4		6b12	
6b5		6b13	
6b6		6b14	
6b7		6b15	
6b8			

Table 3. The structures of the compounds 6d1 - 6d5, 6e1 - 6e6





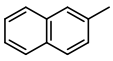
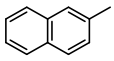
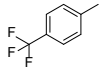
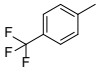
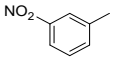
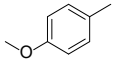
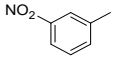
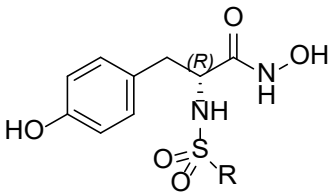
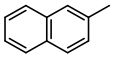
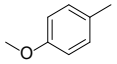
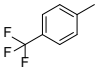
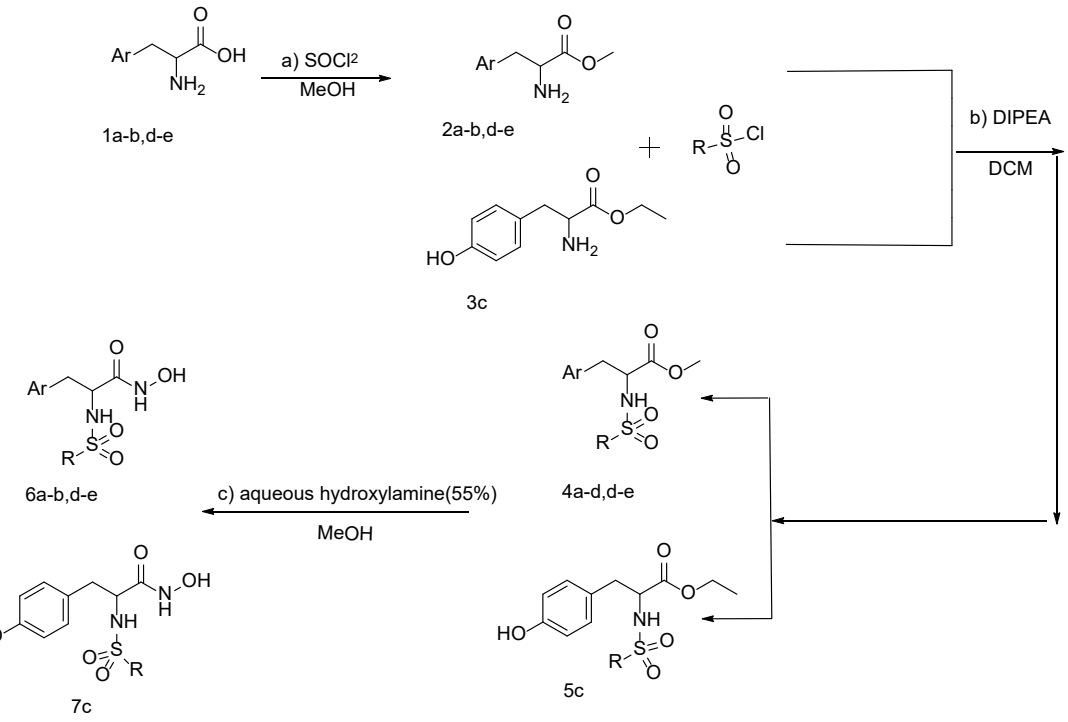
Compound (D)	R	Compound (L)	R
6d1		6e1	
6d2		6e2	
6d3		6e3	
6d4		6e4	
6d5		6e5	
		6e6	

Table 4. The structures of the compounds 7c1 - 7c5



Compound(D)	R	Compound (D)	R
7c1		7c4	
7c2		7c5	
7c3			



Scheme 1. Synthesis of compounds 6a1 - a13, 6b1 - b15, 6d1 - d5, 6e1 - e5, 7c1 - c5. ***Reagents and conditions:*** a) MeOH, $SOCl_2$, 0 °C, 4 h;. b) CH_2Cl_2, DIPEA, rt, 6 h; c) MeOH, aqueous hydroxylamine(55%), rt, 12 h.

Biological evaluation

1. SRB assay

The cytotoxicities of the tested compounds against the human cancer cell lines HepG2 (hepatocellular carcinoma), MCF-7 (breast adenocarcinoma), KB (mouth epidermal carcinoma) and HT-1080 (fibrosarcoma) were evaluated by the sulforhodamine B (SRB) assay using

a standard protocol developed by the NCI (National Cancer Institute). HepG2, HT-1080 and MCF-7 cells were maintained in Dulbecco's modified Eagle's medium (DMEM, HyClone), and KB cells were maintained in RPMI 1640 medium (HyClone.) All media contained 100 units/mL of penicillin, 100 mg/mL of streptomycin and 10% foetal bovine serum. For the cytotoxicity assays, the cells were inoculated in 96 - well plates at a concentration of 4000 cells per well. After incubation at 37 °C under a humidified atmosphere containing 5% CO_2 for 24 h, the cells were treated with various concentrations of the test compounds in triplicate and were further incubated for 48 h. Cell proliferation was determined by the SRB assay. The IC50 value was defined as the compound concentration that produces 50% inhibition of cell growth during 2 days of treatment. IC50 values were calculated using SigmaPlot 10.0 software with nonlinear regression fit analysis.

2. In vitro cytotoxic activity against the cancer cell lines HepG2, HT1080, KB, MCF-7

The cytotoxic activities of the target compounds were evaluated in parallel against four humancancer cell lines (HepG2, HT1080, KB, and MCF-7) by sulforhodamine B (SRB) assay. Gemcitabine and mitomycin C were used as the reference compounds. The results are summarized in **Tables 5 - 7**, and values represent the average of at least three independent measurements. Most of the compounds showed higher inhibitory activity than the compounds in the positive control group, except for the compounds **7c1 - 7c5**, each of which bears a 3′ - hydroxyphenyl group. These compounds almost had no inhibitory activity against any test cell lines. The results suggest that the hydroxyl group on position 3 of the phenyl ring reduces the cytotoxic properties. Most compounds had a good effect on the proliferation of the cell lines HepG2, HT1080, and KB but had no sensitivity to the cell line MCF-7.

As shown in **Tables 5 - 6**, most of the compounds showed higher inhibitory activity than those in the positive control group on the four cell lines. Among these compounds, **6a1**, **6a6**, **6a7**, **6b1**, **6b5**, **6b6**, **6b8**, **6d2**, **6e1**, and **6e2** showed good inhibition for cancer cell proliferation. Compound **6a7** represented the best cytotoxic activity against HepG2, HT1080 and KB cell lines, with IC50 values of 30.18 ± 0.069 μM, 29.78 ± 0.52 μM, and 30.70 ± 0.61 μM, respectively. Moreover, the different substituent groups had a significant impact on cytotoxic activity. Compounds **6a11 - 13**, each of which bears a nitryl group on the benzosulfonyl moiety, were not active in the HT1080, KB, and MCF-7 cell lines, and compounds **6a9 - 10** also showed limited inhibition in the SRB assay. The result clearly indicates that a phenyl, alkyl, trifluoromethyl group or bromine atom substitution on the benzenesulfonyl ring is favourable, while an electron withdrawing nitryl group on different positions of benzenesulfonyl ring is unfavourable for its cytotoxic activity in the 4 tested cell lines. The activities of compounds **6b3** and **6b9 - 13** also revealed that hydrogen-bonding substituents reduce the inhibition of cell proliferation. Each of compounds **6a1** and **6b1** bears an electron withdrawing trifluoromethyl group instead of an electron donating naphthyl group and showed better activity than compounds **6a2** and **6b2**.In addition, the preliminary structure activity relationship also revealed that the stereo-configuration had little effect on the cytotoxic activity. There was no significant difference between the effect of the D - and L - configurations (**6a1 - 3** vs **6e3 - 5**, **6b1 - 2** vs **6d3 - 4** and **6b12** vs **6d5**).

Table 5. The IC50 values of the target compounds 6a1 - 6a13

Compound	IC50[μM]			
	HepG2	HT1080	KB	MCF-7

6a1	36.29±2.17	42.19±11.53	35.41±0.18	69.72±15.49
6a2	54.69±3.5	55.37±1.24	63.60±14.72	>100
6a3	64.91±0.09	62.21±6.11	98.15±2.31	>100
6a4	72.74±0.26	81.34±2.72	82.81±1.13	>100
6a5	>100	>100	>100	63.87±17.33
6a6	31.74±1.78	35.59±2.84	32.80±0.10	64.88±3.08
6a7	30.17±0.06	29.78±0.516	30.69±0.60	>100
6a8	44.79±13.04	40.17±6.88	35.70±0.48	>100
6a9	>100	>100	>100	>100
6a10	58.51±5.62	69.73±22.36	>100	>100
6a11	74.34±72.12	>100	>100	>100
6a12	65.55±30.4	>100	>100	>100
6a13	39.94±1.06	>100	>100	>100
GEM	87.49±4.5	69.22±0.23	34.66±0.19	>100
MMC	66.22±1.73	4.75±0.28	59.33±6.47	25.71±1.16

Table 6. The IC50 values of the target compounds 6b1 - 4b15

Compound	IC50 [μM]			
	HepG2	HT1080	KB	MCF-7
6b1	33.70±0.44	31.86±1.11	>100	80.49±3.83
6b2	57.95±13.18	>100	>100	>100
6b3	>100	> 100	>100	>100
6b4	56.01±7.95	45.33±0.18	39.70±7.3	51.23±19.22
6b5	32.51±0.20	35.31±3.06	33.59±0.23	83.97±5.26
6b6	31.02±0.35	33.77±1.74	34.49±2.57	65.74±4.45
6b7	>100	>100	>100	>100
6b8	40.20±4.19	46.69±9.06	33.40±0.46	>100
6b9	>100	>100	>100	>100
6b10	>100	>100	>100	>100
6b11	>100	>100	>100	>100
6b12	>100	>100	>100	>100
6b13	>100	>100	>100	>100
6b14	52.98±12.19	51.3±2.32	39.23±4.97	86.76±2.58
6b15	43.75±12.62	54.05±5.25	41.23±9.55	88.45±3.23
GEM	87.49±4.5	69.22±0.23	34.66±0.19	>100
MMC	66.22±1.73	4.75±0.28	59.33±6.47	25.71±1.16

Table 7. The IC50 values of the target compounds 7c1 - 4c5, 6d1 - 4d5, 6e1 - 4e6

Compound	IC50 [μM]			
	HepG2	HT1080	KB	MCF-7

7c1	>100	>100	>100	>100
7c2	>100	>100	>100	>100
7c3	>100	>100	>100	>100
7c4	>100	>100	>100	>100
7c5	>100	>100	>100	>100
6d1	52.01±11.48	>100	40.87±5.23	46.35±12.09
6d2	37.06±1.96	31.96±0.25	35.69±0.28	84.30±0.71
6d3	>100	>100	>100	>100
6d4	>100	>100	>100	>100
6d5	>100	>100	>100	>100
6e1	34.52±0.26	46.84±14	38.56±0.37	55.45±20.29
6e2	37.25±5.45	33.85±2.64	35.75±0.31	74.51±17.45
6e3	60.99±9.22	59.84±3.89	65.48±15.72	86.74±5.63
6e4	44.65±2.74	46.14±8.85	57.14±13.10	>100
6e5	71.17±11.42	>100	>100	>100
6e6	>100	>100	>100	>100
GEM	87.49±4.5	69.22±0.23	34.66±0.19	>100
MMC	66.22±1.73	4.75±0.28	59.33±6.47	25.71±1.16

Conclusions

In this paper, we designed and synthesized a series of sulfonyl - propionamide derivatives containing a total of **44** compounds. The structures of these compounds were confirmed by 1HNMR, 13CNMR and ESI - MS, and their cytotoxic effect were evaluated with the SRB assay. Most compounds showed moderate to excellent inhibitory effects on cell proliferation, and compounds **6a1**, **6a6**, **6a7**, **6a13**, **6b1**, **6b5**, **6b6**, **6b8**, **6d2**, **6e1**, and **6e2** were identified as the most promising cytotoxic compounds.

The cytotoxic effect of these compounds was inferior to that of the leading compound mitomycin C. Analysis of the test results revealed that the introduction of an electron donating group at the C-4 position of the sulfonyl group showed a significant decrease in the cytotoxic effect compared to the introduction of an electron withdrawing group. A hydrogen-bonding substituent on the benzosulfonyl ring was also unfavourable for the cytotoxic effect. The introduction of a hydroxyl group at the 3 - position of the benzene ring of propionamide increased the cytotoxic activity of the compound. These compounds were selective for cancer cells. Most of the compounds showed higher inhibitory activity than the positive control on three of four cell lines; compounds had a good effect on the proliferation of the cell lines HepG2, HT1080, and KB but had no sensitivity to the cell line MCF-7 Experimental Section

Experimental Section

General information

Reagents were from Shanghai Chemical Reagent Company and used without further purification. Melting points were taken on a MP70 melting point apparatus, uncorrected and reported in degrees Centigrade. ^{1}HNMR and ^{13}CNMR spectra were recorded in DMSO on a BRUKER AVANCE Ⅲ HD (600 MHz) using TMS as internal standard. Column chromatography at Teledyne Isco - Combiflash Rf 200. The spectrum

Abbreviations used. DIPEA, N,N-diisopropylethylamine; HNMR, Nuclear magnetic resonance; min, Minute; TLC, Thin layer chromatography; ESI - MS, Electron spray ionization mass spectrum; h, Hour ; DCM, Dichloromethane; δ(ppm), chemical shift.

Synthesis of Methyl (R)-2-amino-3-(naphthalen-2-yl) propanoate (**2a**)

To a solution of the 3-(2-Naphthyl)-D-alanine (1g, 6.05 mmol) in the 10ml of anhydrous methanol, $SOCl_2$ (7.14g, 60.05 mmol) was added at 0 °C. Then the solution was stirred at room temperature for 4 h until the completion of the reaction monitored by TLC.

General synthesis of compounds **4a-b,d-e** and **5c**

A suspension of D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol), i-Pr2NEt (1.1 mL, 6.54 mmol) and 4-(trifluoromethyl) benzenesulfonyl chloride (0.64 g, 2.62 mmol) in CH_2Cl_2 (50 mL) was stirred at rt overnight. The solution was washed with 10 percent $NaHCO_3$(20 mL), dried ($NaSO_4$), concentrated, then chromatographed (CH_2Cl_2 to 1 percent MeOH/CH_2Cl_2) and concentrated to provide 0.6 g of the sulfonamide ester.

Synthesis of Methyl(R)-3-(naphthalene-2-yl)-2-((4-(trifluoromethyl) phenyl) sulfonamide) propanoate (**4a1**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4-(trifluoromethyl) benzenesulfonyl chloride (0.64 g, 2.62 mmol), the target product was obtained as a white solid (0.6g)^{1}H NMR (600 MHz, Chloroform - d) δ 7.79 – 7.75 (m, 1H), 7.71 – 7.67 (m, 1H), 7.67 – 7.62 (m, 3H), 7.50 (d, J = 1.6 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.14 – 7.10 (m, 1H), 5.47 (d, J = 9.2 Hz, 1H), 4.38 – 4.12 (m, 1H), 3.60 (s, 3H), 3.29 – 3.24 (m, 1H), 3.10 – 3.05 (m, 1H). 13C NMR (151 MHz, $CDCl_3$) δ 171.3, 143.1, 134.0, 133.3, 132.4, 132.4, 128.4, 128.3, 127.6, 127.5, 127.4(2C), 126.9, 126.4, 126.0, 125.8, 125.7, 123.0, 57.1, 52.7, 39.3; ESI - Mass for $C_{21}H_{18}F_3NO_4S$: m/z [M + Na]+ : 460.3.

Synthesis of Methyl(R)-2-((4-methylphenyl) sulfonamide)-3-(naphthalene-2-yl) propanoate (**4a2**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4 - methylbenzenesulfonyl chloride (0.498 g, 2.62 mmol), the target product was obtained as a white solid (0.56 g).1H NMR (600 MHz, Chloroform - d) δ 7.81 – 7.76 (m, 1H), 7.74 – 7.68 (m, 2H), 7.58 – 7.52 (m, 2H), 7.50 – 7.49 (m, 1H), 7.48 – 7.44 (m, 2H), 7.20 – 7.14 (m, 1H), 7.11 – 7.02 (m, 2H), 5.15 (d, J = 9.1 Hz, 1H), 4.47 – 4.07 (m, 1H), 3.53 (s, 3H), 3.26 – 3.20 (m, 1H), 3.16 – 3.10 (m, 1H), 2.31 (s, 3H). 13C NMR (151 MHz, $CDCl_3$) δ 171.4, 143.5, 136.6, 133.3, 132.6, 132.5, 129.4(2C), 128.3, 128.2, 127.6, 127.6, 127.2, 127.1(2C), 126.1, 125.8, 56.8, 52.5, 39.6, 21.5. ESI - Mass for $C_{21}H_{21}F_3NO_4S$: m/z [M+Na]$^+$: 406.4.

Synthesis of Methyl (R)-2-((4-methoxyphenyl) sulfonamide)-3-(naphthalene-2-yl) propanoate (**4a3**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4 - methoxybenzenesulfonyl chloride (0.54 g, 2.616 mmol), the target product was obtained as a white solid (0.57 g). 1H NMR (600 MHz, Chloroform - d) δ 7.82 – 7.77 (m, 1H), 7.74 – 7.68 (m, 2H), 7.61 – 7.56 (m, 2H), 7.52 – 7.50 (m, 1H), 7.49 – 7.43 (m, 2H), 7.20 – 7.15 (m, 1H), 6.78 – 6.71 (m, 2H), 5.09 (d, J = 9.1 Hz, 1H), 4.32 – 4.23 (m, 1H), 3.77 (s, 3H), 3.55 (s, 3H), 3.26 – 3.18 (m, 1H), 3.16 – 3.08 (m, 1H). 13C NMR (151 MHz, $CDCl_3$) δ 171.48, 162.8, 133.3, 132.6, 132.6, 131.0, 129.2(2C), 128.3, 128.2, 127.6, 127.6, 127.2, 126.2, 125.8, 113.9(2C), 56.8, 55.6, 52.5, 39.5.ESI - Mass for $C_{21}H_{21}F_3NO_5S$: m/z [M+Na]$^+$: 422.3.

Synthesis of methyl (R)-3-(naphthalene-2-yl)-2-(quinolone-8-sulfonamido) propanoate (**4a4**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and quinolone - 8 - sulfonyl chloride (0.6 g, 2.62 mmol), the target product was obtained as a white solid (0.57 g). 1H NMR (600 MHz, Chloroform - d) δ 8.58 – 8.53 (m, 1H), 8.30 – 8.24 (m, 1H), 8.09 – 7.95 (m, 1H), 7.90 – 7.85 (m, 1H), 7.71 – 7.66 (m, 1H), 7.62 – 7.57 (m, 1H), 7.52 – 7.45 (m, 2H), 7.45 – 7.40 (m, 3H), 7.24 – 7.20 (m, 1H), 7.12 – 7.00 (m, 1H), 6.84 (d, J = 7.0 Hz, 1H), 4.54 – 4.41 (m, 1H), 3.38 (s, 3H), 3.30 – 3.22 (m, 1H), 3.18 – 3.11 (m, 1H). 13C NMR (151 MHz, $CDCl_3$) δ

171.2, 150.6, 142.7, 136.4, 136.3, 133.1, 133.0, 132.7, 132.3, 1291.0, 128.4, 128.1, 127.9, 127.7, 127.6, 126.8, 126.0, 125.7, 125.2, 121.8, 57.7, 52.1, 39.2.ESI-Mass for $C_{23}H_{20}N_2O_4S$: m/z $[M+Na]^+$: 443.4.

Synthesis of methyl(R)-2-((4-isopropylphenyl)sulfonamide)-3-(naphthalene-2-yl) propanoate (**4a5**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4 - isopropylbenzenesulfonylchloride (0.83 g, 3.27 mmol), the target product was obtained as a white solid (0.58 g). 1H NMR (600 MHz, Chloroform - d) δ 7.81 – 7.77 (m, 1H), 7.75 – 7.69 (m, 2H), 7.62 – 7.59 (m, 2H), 7.53 (s, 1H), 7.48 – 7.44 (m, 2H), 7.20 – 7.15 (m, 3H), 5.43 – 5.05 (m, 1H), 4.45 – 4.10 (m, 1H), 3.48 (s, 3H), 3.24 – 3.20 (m, 1H), 3.18 – 3.13 (m, 1H), 2.95 – 2.84 (m, 1H), 1.59 – 0.76 (m, 6H). 13C NMR (151 MHz, $CDCl_3$) δ 171.4, 154.3, 136.8, 133.4, 132.6, 132.5, 128.3, 128.3, 127.7, 127.6, 127.3(2C), 127.3, 1261.0(2C), 126.2, 125.9, 56.8, 52.4, 39.5, 34.1, 23.6, 23.6.ESI - Mass for $C_{23}H_{25}F_3NO_4S$: m/z $[M+Na]^+$: 434.4.

Synthesis of methyl(R)-2-([1, 1′-biphenyl]-4-sulfonamido)-3-(naphthalene-2-yl) propanoate (**4a6**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and [1, 1′-biphenyl]-4-sulfonyl chloride (0.83 g, 3.27 mmol), the target product was obtained as a white solid (0.72 g).1H NMR (600 MHz, Chloroform - d) δ 7.77 – 7.66 (m, 6H), 7.55 – 7.50 (m, 3H), 7.50 – 7.45 (m, 4H), 7.44 – 7.40 (m, 3H), 5.29 – 5.20 (m, 1H), 4.40 – 4.29 (m, 1H), 3.54 (s, 3H), 3.28 – 3.24 (m, 1H), 3.18 – 3.14 (m, 1H). 13C NMR (151 MHz, $CDCl_3$) δ 171.4, 145.5, 139.1, 1371.0, 133.3, 132.5, 132.5, 1281.0(2C), 128.5, 128.3, 128.3, 127.6, 127.4, 127.6, 127.3(2C), 127.2(2C), 127.2(2C), 126.2, 125.9, 56.9, 52.5, 39.5. ESI - Mass for $C_{26}H_{23}NO_4S$: m/z $[M+Na]+$:468.4.

Synthesis of methyl(R)-3-(naphthalene-2-yl)-2-(naphthalene-1-sulfonamido) propanoate (**4a7**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and naphthalene - 1 - chloride (0.6 g, 2.62 mmol), the target product was obtained as a white solid (0.59 g).^{1}H NMR (600 MHz, Chloroform - d) δ 8.44 (d, J = 8.4 Hz, 1H), 8.18 – 8.12 (m, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 6.0, 3.0 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.50 – 7.35 (m, 7H), 7.30 (s, 1H), 6.99 – 6.92 (m, 1H), 5.59 – 5.14 (m, 1H), 4.42 – 4.13 (m, 1H), 3.43 (s, 2H), 3.13 – 3.08 (m, 1H), 3.05 – 3.00 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ13C NMR (151 MHz, $CDCl_3$) δ 171.2, 134.4, 134.1, 1331.0, 133.1, 132.3, 129.5, 128.8, 128.1, 128.1(2C), 128.0, 127.9, 127.6, 127.6, 126.8, 126.7, 126.0, 125.7, 124.2, 123.8, 57.1, 52.4, 39.3.ESI - Mass for $C_{24}H_{21}NO_4S$: m/z $[M+Na]^+$: 442.4.

Synthesis of methyl(R)-2-((5-bromothiophene)-2-sulfonamido-3-(naphthalene-2-yl) propanote (**4a8**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 3 - bromocyclopenta - 1, 3 - diene - 1 - sulfonyl chloride (0.685 g, 0.62 mmol), the target product was obtained as a white solid (0.62 g).1H NMR (600 MHz, DMSO-d6) δ 8.96 (d, J = 8.9 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.81 – 7.74 (m, 2H), 7.65 (s, 1H), 7.51 – 7.45 (m, 2H), 7.32 – 7.29 (m, 1H), 7.10 (d, J = 4.0 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 4.18 – 4.13 (m, 1H), 3.53 (s, 3H), 3.18 – 3.13 (m, 1H), 2.97 – 2.92 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.6, 143.0, 134.3, 133.3, 132.4, 132.4, 131.1, 128.3, 128.2, 1271.0, 127.9, 127.8, 126.6, 126.1, 118.7, 57.9, 52.6, 38.0.ESI - Mass for $C_{18}H_{16}BrNO_4S$: m/z $[M+Na]^+$: 476.2/478.2.

Synthesis of methyl (R)-2-((4-acetamidophenyl) sulfonamido)-3-(naphthalene-2-yl)propanoate (**4a9**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4 - acetamidobenzenesulfonyl chloride (0.61 g, 2.62 mmol), the target product was obtained as a white solid (0.51 g).1H NMR (600 MHz, DMSO-d6) δ 10.17 (s, 1H), 8.42 (d, J = 8.8 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.79 – 7.73 (m, 2H), 7.59 (s, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.51 – 7.44 (m, 4H), 7.29 – 7.24 (m, 1H), 4.12 – 4.04 (m, 1H), 3.37 (s, 3H),

3.10 – 3.06 (m, 1H), 2.95 – 2.89 (m, 1H), 2.07 (s, 3H). 13C NMR (151 MHz, DMSO) δ 171.7, 169.3, 143.1, 134.7, 134.4, 133.3, 132.4, 128.2, 128.0, 127.9, 127.8, 127.8(2C), 126.4(2C), 126.1, 118.7(2C), 57.7, 52.3, 38.3, 24.6. ESI - Mass for $C_{22}H_{22}N_2O_5S$: m/z $[M+Na]^+$: 449.3.

Synthesis of methyl(R)-2-((4-acetylphenyl) sulfonamido)-3-(naphthalene-2-yl) propanoate (**4a10**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 4 - acetylbenzenesulfonyl chloride (0.57 g, 2.62mmol), the target product was obtained as a white solid (0.54 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.79 (d, J = 9.0 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.72 – 7.65 (m, 4H), 7.57 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.46 – 7.40 (m, 2H), 7.29 – 7.25 (m, 1H), 4.27 – 3.91 (m, 1H), 3.48 (s, 3H), 3.19 – 3.10 (m, 1H), 2.96 – 2.86 (m, 1H), 2.47 (s, 3H). 13C NMR (151 MHz, DMSO) δ 197.3, 171.7, 144.8, 139.1, 134.4, 133.2, 132.3, 128.7(2C), 128.2, 128.2, 127.9(2C), 127.8, 126.6(2C), 126.4, 126.1, 571.0, 52.5, 38.1, 27.3.ESI - Mass for $C_{22}H_{21}NO_5S$: m/z [M + Na]+ : 434.3.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-((3-nitrophenyl) sulfonamide) propanamide (**4a11**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 3 - nitrobenzenesulfonyl chloride (0.58 g, 2.62 mmol), the target product was obtained as a white solid (0.52 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.96 (d, J = 8.9 Hz, 1H), 8.13 – 8.02 (m, 1H), 7.93 (d, 1H), 7.85 – 7.78 (m, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.67 – 7.59 (m, 2H), 7.53 (s, 1H), 7.49 – 7.35 (m, 3H), 7.31 – 7.22 (m, 1H), 4.34 – 4.11 (m, 1H), 3.54 (s, 3H), 3.22 – 3.12 (m, 1H), 2.95 – 2.81 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.7, 147.4, 142.8, 134.3, 133.1, 132.2, 132.2, 130.9, 128.2, 128.0, 127.8, 127.8, 127.7, 126.4, 126.4, 126.1, 120.9, 58.0, 52.6, 371.0. ESI - Mass for $C_{20}H_{18}N_2O_6S$: m/z $[M+Na]^+$:437.3.

Synthesis of methyl(R)-3-(naphthalene-2-yl)-2-((4-nitrophenyl) sulfonamido propanate (**4a12**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 3 - nitrobenzenesulfonyl chloride (0.58 g, 2.62 mmol), the target product was obtained as a white solid (0.6 g).^{1}H NMR (600 MHz, DMSO-d6) δ 9.06 – 8.90 (m, 1H), 7.81 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H), 7.57 – 7.48 (m, 3H), 7.45 – 7.33 (m, 2H), 7.30 – 7.24 (m, 1H), 4.27 – 4.16 (m, 1H), 3.59 (s, 3H), 3.23 – 3.11 (m, 1H), 2.92 – 2.75 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.3, 148.2, 146.2, 133.8, 132.4, 131.7, 127.7, 127.6, 127.4, 127.2, 127.1, 1261.0(2C), 125.8, 125.6, 123.6(2C), 57.6, 52.1, 37.4. ESI - Mass for $C_{20}H_{18}N_2O_6S$: m/z $[M+Na]^+$: 437.3.

Synthesis of methyl(R)-3-(naphthalene-2-yl)-2-((2-nitrophenyl) sulfonamido propanate (**4a13**)

Starting material: D-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 2 - nitrobenzenesulfonyl chloride (0.58 g, 2.62 mmol), the target product was obtained as a white solid (0.61 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.85 (d, J = 9.0 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.73 – 7.69 (m, 1H), 7.68 – 7.65 (m, 2H), 7.63 – 7.58 (m, 1H), 7.55 – 7.51 (m, 1H), 7.49 – 7.43 (m, 3H), 7.36 – 7.27 (m, 2H), 4.39 – 4.20 (m, 1H), 3.53 (s, 3H), 3.27 – 3.18 (m, 1H), 3.08 – 2.98 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 146.6, 1331.0, 133.2, 132.8, 132.7, 131.9, 131.8, 129.0, 127.9, 127.6, 127.4, 127.4, 127.4, 125.9, 125.5, 123.7, 57.7, 52.1, 37.3.ESI - Mass for $C_{20}H_{18}N_2O_6S$: m/z $[M+Na]^+$: 437.3.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-((trifluoromethyl) phenyl)sulfonamide) propanoate (**4b1**)

Starting material: L - bromophenylalanine methyl ester. (0.3 g, 1.17 mmol) and 2 - nitrobenzenesulfonyl chloride (0.343 g, 1.41 mmol), the target product was obtained as a white solid (0.38 g). ^{1}H NMR (600 MHz, DMSO-d6) δ 8.79 (d, J = 9.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 7.30 (d, 2H), 7.06 (d, J = 8.4 Hz, 2H), 4.09 – 4.00 (m, 1H), 3.44 (s, 3H), 2.99 – 2.91 (m, 1H), 2.78 – 2.66 (m, 1H). 13C NMR (151 MHz, DMSO) δ 1701.0, 144.6, 135.6, 131.8, 131.4, 130.9, 127.0, 126.0, 1251.0, 1251.0, 124.4, 122.6, 119.9, 57.0, 51.9, 36.6. ESI - Mass for $C_{17}H_{15}BrF_3NO_4S$: m/z [M + Na]+ : 488.2/490.3.

Synthesis of methyl (R)-3-(4-bromophenyl)-2-((4-methylphenyl)sulfonamido) propanoate(**4b2**)

Starting material: L - bromophenylalanine methyl ester. (0.3 g, 1.17 mmol) and 4 - methylbenzenesulfonyl chloride (0.27 g, 1.404 mmol), the target product was obtained as a white solid (0.202 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.40 (d, J = 9.0 Hz, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.3 Hz, 2H), 3.99 – 3.87 (m, 1H), 3.41 (s, 3H), 2.94 – 2.85 (m, 1H), 2.78 – 2.65 (m, 1H), 2.37 (s, 3H). 13C NMR (151 MHz, DMSO) δ 1701.0, 142.3, 137.6, 135.6, 131.2, 130.8, 129.1, 1251.0, 119.8, 56.9, 51.7, 36.6, 20.9. ESI - Mass for $C_{17}H_{18}BrNO_4S$: m/z $[M+Na]^+$: 434.2/436.2.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-((4-methoxyphenyl) sulfonamide) propanoate(**4b3**)

Starting material: L - bromophenylalanine methyl ester. (0.3 g, 1.17 mmol) and 4 - methoxylbenzenesulfonyl chloride (0.29 g, 1.404 mmol), the target product was obtained as a white solid (0.38 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.33 (d, J = 9.1 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.98 – 3.87 (m, 1H), 3.82 (s, 3H), 3.41 (s, 3H), 2.95 – 2.85 (m, 1H), 2.76 – 2.65 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.7, 162.5, 136.3, 132.8, 131.9, 131.48, 128.8, 120.4, 114.4, 57.6, 56.1, 52.4, 37.3. ESI - Mass for $C_{17}H_{18}BrNO_5S$: m/z $[M+Na]^+$: 450.2/452.3.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-(naphthalene-1-sulfonamido) propanoate (**4b4**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and naphthalene - 1 - sulfonyl chloride (0.212 g, 0.936 mmol) in CH_2Cl_2 (50ml), the target product was obtained as a white solid (0.25 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.81 (d, J = 9.3 Hz, 1H), 8.45 (d, 1H), 8.12 (d, J = 8.2 Hz, 1H), 8.02 (d, J = 6.7, 2.7 Hz, 1H), 7.88 (d, J = 7.3, 1.1 Hz, 1H), 7.70 – 7.56 (m, 2H), 7.52 – 7.45 (m, 1H), 7.00 – 6.93 (m, 2H), 6.85 (d, J = 8.3 Hz, 2H), 3.98 – 3.80 (m, 1H), 3.32 (s, 3H), 2.90 – 2.82 (m, 1H), 2.72 – 2.61 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.3, 135.4, 135.2, 130.8, 130.4, 128.7, 128.1, 127.4, 127.2, 126.6, 124.7, 124.0, 119.6, 57.2, 51.7, 36.5. ESI - Mass for $C_{20}H_{18}BrNO_4S$: m/z $[M+Na]^+$: 470.2/472.3.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-((4-isopropylphenyl) sulfonamido) propanoate(**4b5**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and 4 - isopropylbenzenesulfonyl chloride (0.204 g, 0.936 mmol)in CH_2Cl_2 (50ml), the target product was obtained as a white solid (0.27 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.41 (d, J = 9.2 Hz, 1H), 7.45 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 5.4 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 3.98 – 3.86 (m, 1H), 3.37 (s, 3H), 2.98 – 2.92 (m, 1H), 2.92 – 2.87 (m, 1H), 2.75 – 2.69 (m, 1H), 1.21 (d, J = 6.9 Hz, 6H). 13C NMR (151 MHz, DMSO) δ 171.6, 153.5, 138.5, 136.3, 131.9, 131.5, 127.2, 126.9, 120.4, 57.5, 52.3, 37.3, 33.8, 231.0, 23.9. ESI - Mass for $C_{19}H_{22}BrNO_4S$: m/z $[M + Na]^+$: 462.2/464.2.

Synthesis of methyl (R)-2-([1,1′-biphenyl]-4-sulfonamido)-3-(4-bromophenyl)propanoate(**4b6**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and [1, 1′ - biphenyl] - 4 - sulfonyl chloride (0.237 g, 0.936 mmol), the target product was obtained as a white solid (0.26 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.55 (d, J = 9.1 Hz, 1H), 7.74 (t, J = 8.9 Hz, 4H), 7.61 (d, J = 8.3 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.47 – 7.41 (m, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.3 Hz, 2H), 4.05 – 3.89 (m, 1H), 3.40 (s, 3H), 2.96 – 2.87 (m, 1H), 2.79 – 2.60 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 143.7, 139.4, 138.5, 135.7, 131.4, 1301.0, 129.1, 128.4, 127.0, 1261.0, 126.8, 119.9, 57.1, 51.8, 36.8.ESI - Mass for $C_{22}H_{20}BrNO_4S$: m/z $[M+Na]^+$: 474.3/476.3.

Synthesis of methyl (R)-3-(4-bromophenyl)-2-(quinolone-8-sulfonamido) propanoate (**4b7**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and uinolone - 8 - sulfonyl chloride (0.16 g, 0.696 mmol), the target product was obtained as a white solid (0.22 g).^{1}H NMR (500 MHz, DMSO-d6) δ 8.91 (dd, J = 4.2, 1.9 Hz, 1H), 8.47 (d, J = 8.3, 1.9 Hz, 1H), 8.24 – 8.12 (m, 2H), 7.92 (d, J = 8.4 Hz, 1H), 7.71 – 7.60 (m, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 4.61 – 4.21 (m, 1H), 2.97 – 2.89 (m, 1H), 2.85 – 2.73 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 171.2, 135.3, 133.6, 132.6, 131.7, 128.5, 128.2, 127.4, 127.4, 127.2, 127.0, 126.4, 125.8, 125.4, 124.54, 123.9, 57.4, 51.6, 37.5. ESI - Mass for $C_{19}H_{17}BrN_2O_4S$: m/z $[M+Na]^+$: 449.3/451.3.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-((5-bromothiophene)-2-sulfonamido) propanoate (**4b8**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and 5 - bromothiophene - 2 - sulfonyl chloride (0.25 g, 0.936 mmol), the target product was obtained as a white solid (0.31 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.88 (d, J = 8.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 2H), 7.17 – 7.13 (m, 2H), 7.10 (d, J = 8.1 Hz, 2H), 4.18 – 3.87 (m, 1H), 3.54 (s, 3H), 3.07 – 2.85 (m, 1H), 2.78 – 2.64 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 171.00, 142.6, 135.7, 132.0, 131.4(2C), 131.0 (2C), 130.1, 120.0, 118.4, 57.2, 52.1, 36.6. ESI - Mass for $C_{19}H_{17}BrN_2O_4S$: m/z $[M+Na]^+$: 504.1/506.1.

Synthesis of methyl(R)-2-((4-acetamidophenyl) sulfonamide)-3-(4-bromophenyl) propanoate (**4b9**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and 4 - acetamidobenzenesulfonyl chloride (0.22 g, 0.936 mmol), the target product was obtained as a white solid (0.23 g).^{1}H NMR (600 MHz, DMSO-d6) δ 10.26 (s, 1H), 7.63 (d, 2H), 7.48 (d, 2H), 7.36 (d, 2H), 7.06 (d, 2H), 3.38 (s, 3H), 2.95 – 2.82 (m, 1H), 2.74 – 2.61 (m, 1H), 2.07 (s, 3H). 13C NMR (151 MHz, DMSO) δ 170.6, 168.4, 142.2, 135.2, 133.8, 130.9, 130.5, 126.9, 119.4, 117.8, 56.5, 51.4, 36.4, 23.7. ESI - Mass for $C_{18}H_{19}BrN_2O_5S$: (m/z) $[M+Na]^+$: 477.2/479.2.

Synthesis of methyl(R)-2-((4-acetylphenyl) sulfonamido)-3-(4-bromophenyl) propanoate(**4b10**)

Starting material: L-bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and 4 - acetamidobenzenesulfonyl chloride (0.204 g, 0.936 mmol), the target product was obtained as a white solid (0.25 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.71 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 4.13 – 3.96 (m, 1H), 3.46 (s, 3H), 2.94 (dd, J = 13.8, 5.1 Hz, 1H), 2.70 (dd, J = 13.7, 10.1 Hz, 1H), 2.64 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 197.2, 171.1, 144.5, 139.0, 135.7, 131.4(2C), 130.9 (2C), 128.6 (2C), 126.3 (2C), 120.0, 57.2, 52.0, 36.7, 27.0. ESI - Mass for $C_{18}H_{18}BrNO_5S$: (m/z) $[M+Na]^+$: 462.3/464.2.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-((3-nitrophenyl) sulfonamido) propanoate(**4b11**)

Starting material: L - bromophenylalanine methyl ester. (0.2 g, 0.78 mmol) and 3 - nitrobenzenesulfonyl chloride (0.154 g, 0.696 mmol), the target product was obtained as a white solid (0.24 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.97 – 8.85 (m, 1H), 8.43 – 8.36 (m, 1H), 8.23 – 8.17 (m, 1H), 7.98 – 7.90 (m, 1H), 7.78 – 7.60 (m, 1H), 7.25 – 7.20 (m, 2H), 7.11 – 7.00 (m, 2H), 4.21 – 4.03 (m, 1H), 3.50 (s, 3H), 3.00 – 2.91 (m, 1H), 2.76 – 2.63 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.0, 147.4, 135.6, 132.1, 131.4, 130.9, 130.8, 126.5, 120.8, 119.9, 57.1, 52.1, 36.6. ESI - Mass for $C_{16}H_{15}BrN_2O_6S$: m/z $[M+Na]^+$: 466.3/468.2.

Synthesis of methyl (R)-3-(4-bromophenyl)-2-((4-nitrophenyl) sulfonamide)propanoate(**4b12**).

Starting material: L - bromophenylalanine methyl ester. (0.15 g, 0.58 mmol) and 4 - nitrobenzenesulfonyl chloride (0.154 g, 0.696 mmol), the target product was obtained as a white solid (0.16 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.53 – 8.35 (m, 1H), 8.04 – 7.88 (m, 1H), 7.51 – 7.34 (m, 1H), 7.25 – 7.09 (m, 1H), 5.16 (s, 1H), 4.72 – 4.47 (m, 1H), 3.71 (s, 2H), 3.39 – 3.24 (m, 1H), 3.14 – 2.93 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.6, 148.9, 146.7, 136.2, 131.3, 130.7, 127.4, 124.1, 119.8, 55.7, 40.0, 37.6. ESI - Mass for C16H15BrN2O6S: m/z [M + Na]$^+$: 466.3/468.2.

Synthesis of methyl (R)-3-(4-bromophenyl)-2-((2-nitropheny) sulfonamido) propanoate (**4b13**)

Starting material: L - bromophenylalanine methyl ester. (0.15 g, 0.58 mmol) and 2 - nitrobenzenesulfonyl chloride (0.154 g, 0.696 mmol), the target product was obtained as a white solid (0.19 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.79 (d, J = 9.0 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.80 – 7.77 (m, 1H), 7.67 – 7.63 (m, 2H), 7.31 – 7.23 (m, 2H), 7.16 – 7.04 (m, 2H), 4.24 – 4.09 (m, 1H), 3.52 (s, 3H), 3.07 – 2.99 (m, 1H), 2.86 – 2.75 (m, 1H). 13C NMR (151 MHz, DMSO) δ 170.9, 146.8, 135.8, 133.6, 1321.0, 132.3, 131.5, 130.9, 129.3, 124.1, 1191.0, 57.4, 52.1, 36.4. ESI - Mass for C16H15BrN2O6S: m/z [M+Na]$^+$: 466.3/468.2.

Synthesis of methyl(R)-3-(4-bromophenyl)-2-(naphthalene-2-sulfonamido) propanoate (**4b14**)

Starting material: L - bromophenylalanine methyl ester. (0.5 g, 1.95 mmol) and naphthalene - 2 - sulfonyl chloride (0.53 g, 2.34 `mmol), the target product was obtained as a white solid (0.62 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.59 (d, J = 9.0 Hz, 1H), 8.28 – 8.17 (m, 1H), 8.11 – 7.91 (m, 3H), 7.76 – 7.61 (m, 2H), 7.57 – 7.50 (m, 1H), 7.32 – 7.19 (m, 2H), 7.04 (d, J = 8.1 Hz, 2H), 4.23 – 3.85 (m, 1H), 3.29 (s, 3H), 2.96 – 2.86 (m, 1H), 2.78 – 2.67 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.6, 138.1, 136.1, 134.4, 1311.0, 131.8, 131.4, 129.5, 129.48, 129.1, 128.2, 127.9, 127.4, 122.4, 120.4, 57.5, 52.3, 37.3.ESI - Mass for C19H17BrN2O4S : m/z [M+Na]$^+$: 471.2/473.2.

Synthesis of (R)-3-(4-bromophenyl)-2-((4-bromophenyl) sulfonamido)-N-hydroxypropanamide (**4b15**)

Starting material: L - bromophenylalanine methyl ester. (0.5 g, 1.95 mmol) and 4 - bromobenzenesulfonyl chloride (0.6 g, 2.34 mmol), the target product was obtained as a white solid (0.49 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.63 (d, J = 9.1 Hz, 1H), 7.65 (d, J = 8.9, 2.5 Hz, 2H), 7.44 (d, J = 9.0, 2.6 Hz, 2H), 7.35 (d, J = 8.9, 2.5 Hz, 2H), 7.08 (d, J = 8.7, 2.6 Hz, 2H), 4.05 – 3.92 (m, 1H), 3.46 (s, 3H), 2.99 – 2.88 (m, 1H), 2.79 – 2.65 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.5, 140.5, 136.1, 132.3, 131.9, 131.4, 128.6, 126.4, 120.5, 57.5, 52.4, 37.2. ESI - Mass for C16H15Br2NO4S : m/z [M+Na]$^+$: 497.9/500.1.

Synthesis of methyl (S)-3-(4-bromophenyl)-2-(naphthalene-2-sulfonamido) propanoate (**4d1**)

Starting material: D - bromophenylalanine methyl ester (0.3 g, 1.17 mmol) and naphthalene - 2 - sulfonyl chloride (0.32 g, 1.404 mmol), the target product was obtained as a white solid (0.37 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.59 (d, J = 9.1 Hz, 1H), 8.21 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.7 Hz, 1H), 7.73 – 7.62 (m, 1H), 7.53 (d, J = 8.6, 1.9 Hz, 1H), 7.23 (d, J = 8.8, 2.5 Hz, 2H), 7.04 (d, J = 8.7, 2.6 Hz, 2H), 4.13 – 3.93 (m, 1H), 3.29 (s, 3H), 2.95 – 2.85 (m, 1H), 2.78 – 2.68 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 137.6, 135.6, 133.9, 131.4, 131.3(2C), 130.8(2C), 129.0, 128.9, 128.5, 127.7, 127.4, 126.9, 121.9, 119.9, 57.0, 51.7, 36.8. ESI - Mass for C20H18BrNO4S: m/z [M+Na]$^+$: 470.4.

Synthesis of methyl (S)-3-(4-bromophenyl)-2-((4-bromophenyl) sulfonamido)propanoate(**4d2**)

Starting material: D - bromophenylalanine methyl ester (0.3 g, 1.17 mmol) and 4 - bromobenzenesulfonyl chloride (0.36 g, 1.404 mmol), the target product was obtained as a white solid (0.34 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.61 (d, J = 9.0 Hz, 1H), 7.64 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.3 Hz, 2H), 4.04 – 3.93 (m, 1H), 3.45 (s, 3H), 2.96 – 2.87 (m, 1H), 2.75 – 2.66 (m, 1H). 13C NMR (151 MHz, DMSO) δ 1701.0, 1391.0, 135.6, 131.8(2C), 131.3(2C), 130.9(2C), 128.1(2C), 125.9, 1191.0, 561.0, 51.9, 36.7. ESI - Mass for $C_{20}H_{18}BrNO_4S$: m/z $[M+Na]^+$: 498.3.

Synthesis of methyl(S)-3-(4-bromophenyl)-2-((4-trifluoromethyl) phenyl) sulfonamido) propanoate. (**4d3**)

Starting material: D - bromophenylalanine methyl ester (0.4 g, 1.55 mmol) and 4-(trifluoromethyl) benzenesulfonyl chloride (0.454 g, 1.86 mmol), the target product was obtained as a white solid (0.47 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.79 (s, 1H), 7.76 (dd, J = 54.7, 8.1 Hz, 4H), 7.31 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.1 Hz, 2H), 4.09 – 4.00 (m, 1H), 3.45 (s, 3H), 3.01 – 2.90 (m, 1H), 2.77 – 2.66 (m, 1H). 13C NMR (151 MHz, DMSO) δ 1701.0, 144.6, 135.6, 131.8, 131.4(2C), 130.9(2C), 1261.0(2C), 1251.0, 125.9, 123.4, 119.9, 57.0, 51.9, 36.6.ESI - Mass for $C_{17}H_{15}BrF_3NO_4S$: m/z $[M+Na]^+$: 488.1.

Synthesis of methyl (S)-3-(4-bromophenyl)-2-((4-methylphenyl) sulfonamido)propanoate(**4d4**)

Starting material: D - bromophenylalanine methyl ester (0.4 g, 1.55 mmol) and 4 - methylbenzenesulfonyl chloride (0.354 g, 1.86 mmol), the target product was obtained as a white solid (0.44 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.39 (d, J = 9.0 Hz, 1H), 7.41 (d, J = 7.8 Hz, 2H), 7.36 – 7.32 (m, 2H), 7.23 (d, J = 7.8 Hz, 2H), 7.07 – 7.03 (m, 2H), 3.92 (td, J = 9.4, 5.7 Hz, 1H), 3.42 (s, 3H), 2.95 – 2.84 (m, 1H), 2.76 – 2.65 (m, 1H), 2.37 (s, 3H). 13C NMR (151 MHz, DMSO) δ 171.1, 142.4, 137.8, 135.7, 131.3（2C）, 130.9(2C), 129.2(2C), 126.1(2C), 119.9, 57.0, 51.8, 36.8, 201.0.ESI - Mass for $C_{17}H_{18}BrNO_4S$: m/z $[M+Na]^+$: 434.1.

Synthesis of methyl (S)-3-(4-bromophenyl)-2-((3-nitrophenyl) sulfonamido) propanoate (**4d5**)

Starting material: D - bromophenylalanine methyl ester (0.5 g, 1.95 mmol) and 3 - nitrobenzenesulfonyl chloride (0.52 g, 2.34 mmol), the target product was obtained as a white solid (0.53 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.90 (d, J = 9.0 Hz, 1H), 8.39 (d, J = 8.1, 2.5 Hz, 1H), 8.23 – 8.16 (m, 1H), 7.96 – 7.91 (m, 1H), 7.80 – 7.69 (m, 1H), 7.26 – 7.19 (m, 2H), 7.04 (d, J = 6.6, 4.5 Hz, 2H), 4.19 – 4.09 (m, 1H), 3.50 (s, 3H), 3.03 – 2.93 (m, 1H), 2.76 – 2.64 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 142.4, 137.8, 135.7, 131.3(2C), 130.9(2C), 129.2(2C), 126.1(2C), 119.9, 57.0, 51.8, 36.8, 201.0. ESI - Mass for $C_{16}H_{15}BrN_2O_6S$: m/z $[M+Na]^+$: 465.2.

Synthesis of methyl (S)-3-(naphthalene-2-yl)-2-(naphthalene-2-sulfonamido) propanoate(**4e1**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.3 g, 1.31 mmol) and naphthalene - 2 - sulfonyl chloride (0.36 g, 1.572 mmol), the target product was obtained as a white solid (0.35 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.66 (d, J = 9.0 Hz, 1H), 8.19 (d, J = 1.8 Hz, 1H), 7.96 – 7.91 (m, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.70 – 7.57 (m, 6H), 7.53 – 7.49 (m, 1H), 7.45 – 7.40 (m, 2H), 7.25 – 7.21 (m, 1H), 4.22 – 4.09 (m, 1H), 3.27 (s, 3H), 3.15 – 3.07 (m, 1H), 2.98 – 2.89 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.2, 137.6, 133.8, 133.8, 132.7, 131.8, 131.4, 128.9, 128.8, 128.4, 127.6, 127.6(2C), 127.3, 127.3, 127.2(2C), 126.8, 125.9, 125.5, 121.9, 57.3, 51.7, 37.7. ESI - Mass for $C_{24}H_{21}NO_4S$: m/z $[M+Na]^+$: 442.2.

Synthesis of methyl (S)-2-((4-bromophenyl) sulfonamido)-3-(naphthalene-2-yl) propanoate(**4e2**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.4 g, 1.57 mmol) and 4 - bromobenzenesulfonyl chloride (0.3 g, 1.31 mmol), the target product was obtained as a white solid (0.48 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.69 (d, J = 8.8 Hz, 1H), 7.88 – 7.83 (m, 1H), 7.78 – 7.75 (m, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.61 (s, 1H), 7.53 – 7.45 (m, 2H), 7.42 – 7.35 (m, 4H), 7.26 (d, J = 8.4 Hz, 1H), 4.16 – 4.06 (m, 1H), 3.46 (s, 3H), 3.17 – 3.09 (m, 1H), 2.98 – 2.88 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 139.9, 133.8, 132.7, 131.9, 131.6(2C), 127.9(2C), 127.7, 127.6, 127.4, 127.3, 127.3, 126.0, 125.8, 125.6, 57.3, 51.9, 37.6. ESI - Mass for C20H18BrNO4S: m/z [M+Na]$^+$: 470.2/472.3.

Synthesis of methyl (S)-3-(naphthalene-2-yl)-2-((4-(trifluoromethyl) phenyl) sulfonamido)Propanoate (**4e3**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.3 g, 1.31 mmol) and 4-(trifluoromethyl) benzenesulfony chloride (0.384 g, 1.572 mmol), the target product was obtained as a white solid (0.36 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.86 (d, J = 9.0 Hz, 1H), 7.84 – 7.78 (m, 1H), 7.77 – 7.72 (m, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 7.8 Hz, 3H), 7.54 (d, J = 8.1 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.32 – 7.16 (m, 1H), 4.22 – 4.10 (m, 1H), 3.45 (s, 3H), 3.22 – 3.10 (m, 1H), 2.96 – 2.88 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.1, 144.6, 133.8, 132.7, 131.8, 131.6, 127.7, 127.6, 127.3, 127.3, 126.9, 1251.0, 125.7, 125.6, 125.6, 123.3, 57.3, 51.9, 37.5. ESI - Mass for C21H18F3NO4S: m/z [M+Na]+: 450.3.

Synthesis of methyl (S)-2-((4-methylphenyl) sulfonamido)-3-(naphthalene-2-yl) propanoate(**4e4**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.3 g, 1.31 mmol) and 4 - methylbenzenesulfonyl chloride (0.3 g, 1.572 mmol), the target product was obtained as a white solid (0.38 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.46 (d, J = 8.9 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.78 – 7.70 (m, 2H), 7.61 – 7.57 (m, 1H), 7.51 – 7.44 (m, 2H), 7.40 – 7.34 (m, 2H), 7.27 – 7.21 (m, 1H), 7.06 – 7.01 (m, 2H), 4.08 – 3.99 (m, 1H), 3.40 (s, 3H), 3.13 – 3.05 (m, 1H), 2.96 – 2.86 (m, 1H), 2.22 (s, 3H). 13C NMR (151 MHz, DMSO) δ 171.2, 142.2, 137.7, 133.9, 132.8, 131.9, 1281.0(2C), 127.6, 127.6, 127.4(2C), 127.3, 126.1(2C), 125.9, 125.5, 57.3, 51.7, 37.7, 20.8. ESI - Mass for C21H21NO4S : m/z [M+Na]$^+$: 406.2.

Synthesis of methyl (S)-2-((4-methoxyphenyl) sulfonamido)-3-(naphthalene-2-yl) propanoate(**4e5**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.3 g, 1.31 mmol) and 4 - methoxylbenzenesulfonyl chloride (0.324 g, 1.572 mmol), the target product was obtained as a white solid (0.31 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.39 (d, J = 9.0 Hz, 1H), 7.89 – 7.82 (m, 1H), 7.80 – 7.71 (m, 2H), 7.60 (s, 1H), 7.52 – 7.38 (m, 4H), 7.30 – 7.24 (m, 1H), 6.80 – 6.74 (m, 2H), 4.08 – 3.98 (m, 1H), 3.71 (s, 3H), 3.41 (s, 3H), 3.16 – 3.04 (m, 1H), 2.98 – 2.87 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.3, 161.8, 133.9, 132.8, 132.3, 131.9, 128.3(2C), 127.7, 127.6, 127.4(2C), 125.9(2C), 125.5, 113.7(2C), 57.3, 55.4, 51.8, 37.7.ESI - Mass for C21H21NO5S: m/z [M+Na]$^+$: 422.4.

Synthesis of methyl(S)-3-(naphthalene-2-yl)-2-((3-nitrophenyl) sulfonamido) propanoate (**4e6**)

Starting material: L-Napthylalanine hydrochloride methyl ester (0.5 g, 2.18 mmol) and 3 - nitrobenzenesulfonyl chloride (0.58 g, 2.62 mmol), the target product was obtained as a white solid (0.62 g).^{1}H NMR (600 MHz, DMSO-d6) δ 8.95 (d, J = 9.0 Hz, 1H), 8.11 – 8.07 (m, 1H), 7.97 – 7.88 (m, 1H), 7.83 – 7.79 (m, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.66 – 7.58 (m, 2H), 7.54 (s, 1H), 7.47 – 7.38 (m, 3H), 7.29 – 7.23 (m, 1H), 4.32 – 4.13 (m, 1H), 3.54 (s, 3H), 3.21 – 3.09 (m, 1H), 2.93 – 2.78 (m, 1H). 13C NMR (151 MHz, DMSO) δ 171.2, 146.9, 142.3, 133.7, 132.6, 131.7, 130.4, 127.7, 127.5, 127.3（2C）, 127.2, 125.9, 125.9, 125.6, 120.4(2C), 57.6, 52.1, 37.5. ESI - Mass for C20H18N2O6S : m/z [M+Na]$^+$: 437.2.

Synthesis of ethyl(naphthalene-2-ylsulfonyl)-D-tyrosinate (**5c1**)

Starting material: D - tyrosine ethyl ester hydrochloride (0.3 g, 1.32 mmol) and naphthalene-2-sulfonyl chloride (0.39 g, 1.584 mmol), the target product was obtained as a white solid (0.48 g). ESI - Mass for $C_{21}H_{21}NO_5S$: m/z $[M+Na]^+$: 422.4.

Synthesis of ethyl ((4-bromophenyl) sulfonyl)-D-tyrosinate (**5c2**)

Starting material: D - tyrosine ethyl ester hydrochloride (0.25 g, 1.01 mmol) and 4 - bromobenzenesulfonyl chloride (0.34 g, 1.404 mmol), the target product was obtained as a white solid (0.35 g). ESI - Mass for $C_{17}H_{18}BrNO_5S$: m/z $[M+Na]^+$: 426.2/428.2.

Synthesis of ethy ((4-trifluoromethyl) phenyl) sulfonyl)-D-tyrosinate (**5c3**)

Starting material: D - tyrosine ethyl ester hydrochloride (0.5 g, 2.04 mmol) and 4 - (trifuoromethyl) benzenesulfonyl chloride (0.6 g, 2.448 mmol), the target product was obtained as a white solid (0.48 g).ESI - Mass for $C_{18}H_{18}F_3NO_5S$: m/z $[M+Na]^+$: 440.3.

Synthesis of ethyl tosyl-D-tyrosinate (**5c4**)

Starting material: D - tyrosine ethyl ester hydrochloride (0.5 g, 2.04 mmol) and 4 - methylbenzenesulfonyl chloride (0.772 g, 3.14 mmol), the target product was obtained as a white solid (0.52 g). ESI - Mass for $C_{17}H_{18}BrNO_5S$: m/z $[M+Na]^+$: 386.3.

Synthesis of ethyl ((4-methoxyphenyl) sulfonyl)-D-tyrosinate. (**5c5**)

Starting material: D - tyrosine ethyl ester hydrochloride (0.5 g, 2.04 mmol) and 4 - methoxybenzenesulfonyl chloride (0.78 g, 3.14 mmol), the target product was obtained as a white solid (0.49 g).ESI - Mass for $C_{18}H_{21}NO_6S$: m/z $[M+Na]^+$: 402.4.

General synthesis of compounds 6a-b,d-e and 7c

The material (4a1) was dissolved in Methanol (5 mL) and Tetrahydrofuran (5 mL), 10 mL of aqueous hydroxylamine (50 percent w/w) was added. The mixture was stirred for 24 h at rt, then concentrated onto silica, chromatographed (2 percent to 10 percent MeOH /CH_2Cl_2), and dried to provide white solid(Yield 63.1%).

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-((4-(trifluoromethyl) phenyl)sulfonamide) propanamide(**6a1**)

Starting material: 4a1 (0.2 g, 0.458 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), the target product was obtained as a white solid (0.15 g, Yield 63.1%).1H NMR (600 MHz, DMSO) δ 10.73 (s, 1H), 8.95 (s, 1H), 8.67 (s, 1H), 7.78 (d, J = 6.2 Hz, 1H), 7.71 (d, J = 6.3 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.57 (d, J = 5.3 Hz, 3H), 7.49 – 7.40 (m, 5H), 7.22 (d, J = 7.9 Hz, 1H), 3.98 – 3.89 (m, 1H), 3.01 – 2.92 (m, 1H), 2.88 – 2.79 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.4, 145.4, 131.0, 133.2, 132.2, 131.8, 128.2, 127.9, 127.9, 127.8, 127.7, 127.2, 126.4, 126.0, 1251.0, 125.9, 124.7, 122.9, 56.2, 39.0.HRMS (ESI): calcd for $C_{20}H_{17}F_3N_2O_4S$ $[M-H]^-$: 437.0782; found, 437.0976.

Synthesis of (R)-N-hydroxy-2-((4-methylphenyl) sulfonamido)-3-(naphthalene-2-yl) propanamide (**6a2**)

Starting material: 4a2 (0.26 g, 0.679 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.2 g, Yield 35.4 %).1H NMR (600 MHz, DMSO-d6) δ 10.66 (s, 1H), 8.90 (s, 1H), 8.20 (d, J = 8.1 Hz, 1H), 7.86 – 7.81 (m, 1H), 7.73 – 7.70 (m, 1H), 7.67 (d, J =

8.4 Hz, 1H), 7.52 (s, 1H), 7.50 – 7.43 (m, 2H), 7.33 (d, J = 7.9 Hz, 2H), 7.22 – 7.19 (m, 1H), 6.92 (d, J = 7.9 Hz, 2H), 3.93 – 3.79 (m, 1H), 2.99 – 2.89(m, 1H), 2.80 – 2.70 (m, 1H), 2.17 (s, 3H). 13C NMR (151 MHz, DMSO) δ 167.5, 142.3, 138.7, 135.0, 133.3, 132.4, 129.4(2C), 129.2, 128.0, 128.0, 127.9, 127.9, 127.8, 126.4(2C), 126.3, 125.9, 56.0, 39.1, 21.3.HRMS (ESI): calcd for $C_{20}H_{20}N_2O_4S$ $[M-H]^-$: 383.1065; found, 383.1060.

Synthesis of (R)-N-hydroxy-2-((4-methoxyphenyl) sulfonamide)-3-(naphthalene-2-yl) propanamide. (**6a3**)

Starting material: **4a3** (0.25 g, 0.627 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.22 g, Yield 58.1 %). ^{1}H NMR (600 MHz, DMSO) δ 7.79 (d, J = 1.5 Hz, 1H), 7.75 (dt, J = 7.5, 1.5 Hz, 2H), 7.70 (dd, J = 7.4, 1.4 Hz, 1H), 7.45 (td, J = 7.4, 1.6 Hz, 1H), 7.42 – 7.34 (m, 4H), 7.32 – 7.27 (m, 2H), 5.65 (s, 1H), 4.56 (s, 1H), 4.47 – 4.39 (m, 1H), 3.80 (s, 3H), 3.72 – 3.60 (m, 1H), 3.15 – 2.98 (m, 1H). 13C NMR (151 MHz, DMSO) δ 137.7, 134.8, 134.3, 133.1, 129.5(2C), 128.6, 127.9, 127.6, 127.4, 126.2, 126.1, 125.1, 115.6(2C), 59.7, 55.4, 37.8 HRMS (ESI): calcd for $C_{20}H_{20}N_2O_5S$ $[M-H]^-$: 399.1014; found, 399.1011.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-(quinolone-8-sulfonamido) propanamide (**6a4**)

Starting material: 4a4 (0.34 g, 0.81 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.3 g, Yield 55 %).1H NMR (600 MHz, DMSO-d6) δ 10.62 (s, 1H), 8.82 (dd, J = 4.3, 1.7 Hz, 1H), 8.24 (dd, J = 8.3, 1.7 Hz, 1H), 8.08 (dd, J = 7.3, 1.4 Hz, 1H), 8.04 – 7.99 (m, 1H), 7.73 – 7.67 (m, 1H), 7.61 – 7.56 (m, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.44 – 7.39 (m, 4H), 7.11 – 7.06 (m, 1H), 6.45 (s, 1H), 4.42 – 4.08 (m, 1H), 2.99 – 2.93 (m, 1H), 2.90 – 2.83 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.5, 151.2, 142.7, 137.2, 136.9, 134.6, 133.7, 1321.0, 132.1, 129.7, 128.7, 128.0, 127.9, 127.8, 127.6, 127.5, 126.2, 125.9, 125.6, 122.5, 56.7, 39.4.HRMS (ESI): calcd for $C_{22}H_{19}N_3O_4S$ $[M - H]^-$:420.1017; found, 420.1021.

Synthesis of (R)-N-hydroxy-2-((4-isopropylphenyl) sulfonamide)-3-(naphthalene-2-yl) propanamide (**6a5**)

Starting material: **4a5** (0.15 g, 0.36 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.1 g, Yield 44.2 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.64 (s, 1H), 8.91 (s, 1H), 7.87 – 7.83 (m, 1H), 7.78 – 7.73 (m, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.56 (s, 1H), 7.49 – 7.45 (m, 2H), 7.37 (d, J = 7.9 Hz, 2H), 7.21 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 7.9 Hz, 2H), 3.93 – 3.81 (m, 1H), 2.99 – 2.91 (m, 1H), 2.84 – 2.70 (m, 2H), 1.18 – 1.04 (m, 7H). ^{13}C NMR (151 MHz, DMSO) δ 167.1, 152.4, 138.6, 134.7, 132.7, 131.8, 127.6, 127.6, 127.5, 127.4, 127.3, 126.4 (2C), 126.2 (2C), 125.9, 125.4, 55.5, 38.6, 33.1, 23.4, 23.3. HRMS (ESI): calcd for $C_{22}H_{24}N_2O_4S$[M-H]-: 411.1378; found, 411.1396.

Synthesis of (R)-2-([1, 1'-biphenyl]-4-sulfonamido)-N-hydroxy-3-(naphthalene-2-yl) propanamide (**6a6**)

Starting material: **4a6** (0.26 g, 0.58 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.22 g, Yield 61.3 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.68 (s, 1H), 8.90 (s, 1H), 8.35 (s, 1H), 7.75 – 7.70 (m, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.58 – 7.53 (m, 3H), 7.53 – 7.46 (m, 4H), 7.44 – 7.34 (m, 5H), 7.24 (dd, J = 8.4, 1.7 Hz, 1H), 3.99 – 3.85 (m, 1H), 3.02 – 2.91 (m, 1H), 2.88 – 2.74 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 167.0, 143.2, 139.9, 138.4, 134.6, 132.8, 131.8, 128.9 (2C), 128.3 (2C), 127.6, 127.6, 127.5, 127.3, 127.3, 126.9 (2C) 126.6, 126.6 (2C), 125.9, 125.3, 55.6, 38.6. HRMS (ESI) : calcd for $C_{25}H_{22}N_2O_4S$ $[M - H]^-$:445.1221; found, 445.1224.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-(naphthalene-1-sulfonamido) propanamide (**6a7**)

Starting material: **4a7** (0.27 g, 0.6 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.2 g, Yield 52.4 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.65 (s, 1H), 8.91 (d, J = 1.5 Hz, 1H), 8.62 (d, J = 9.0 Hz, 1H), 8.44 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.2

Hz, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.77 (d, J = 8.1, 1.5 Hz, 1H), 7.70 – 7.67 (m, 1H), 7.56 – 7.51 (m, 1H), 7.45 – 7.34 (m, 7H), 7.31 – 7.27 (m, 1H), 7.01 – 6.97 (m, 1H), 3.96 – 3.86 (m, 1H), 2.93 – 2.86 (m, 1H), 2.76 – 2.67 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 167.71, 136.39, 134.77, 133.95, 133.79, 133.00, 132.05, 128.84, 128.16, 127.84, 127.81 (2C), 127.68, 127.64, 127.52, 127.51, 126.81, 126.11, 125.71, 125.23, 124.26, 56.11, 39.09. HRMS (ESI): calcd for $C_{23}H_{20}N_2O_4S$ [M - H]$^-$:419.1065; found, 419.1062.

Synthesis of (R)-2-((5-bromothiophene)-2-sulfonamido)-N-hydroxy-3-(naphthalene-2-yl) propanamide (**6a8**)

Starting material: 4a8 (0.2 g, 0.44 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.18 g, Yield 62.8 %).1H NMR (600 MHz, DMSO-d6) δ 10.73 (s, 1H), 8.97 (s, 1H), 8.74 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.75 (d, J = 14.3, 8.2 Hz, 2H), 7.62 (s, 1H), 7.53 – 7.43 (m, 2H), 7.28 (d, J = 8.3 Hz, 1H), 7.03 (d, J = 3.9 Hz, 1H), 6.88 (d, J = 3.9 Hz, 1H), 3.98 – 3.91 (m, 1H), 3.02 – 2.96 (m, 1H), 2.88 – 2.81 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.2, 143.5, 1341.0, 133.3, 132.3, 1311.0, 1301.0, 128.2, 128.0, 1271.0, 1271.0, 127.8, 126.48, 1251.0, 118.3, 56.3, 381.0.HRMS (ESI): calcd for $C_{17}H_{15}BrN_2O_4S_2$[M-H]-: 452.9578; found, 452.9574/454.9532.

Synthesis of (R)-2-((4-acetamidophenyl) sulfonamide)-N-hydroxy-3-(naphthalene-2-yl) propanamide (**6a9**)

Starting material: 4a9 (0.31 g, 0.73 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.18 g, Yield 47.9 %).1H NMR (600 MHz, DMSO-d6) δ 10.61 (s, 1H), 10.10 (s, 1H), 8.87 (s, 0H), 7.83 – 7.79 (m, 1H), 7.74 – 7.68 (m, 3H), 7.52 (s, 1H), 7.45 (d, J = 7.3 Hz, 6H), 7.21 (d, J = 8.4 Hz, 1H), 4.01 – 3.75 (m, 1H), 2.98 – 2.91 (m, 1H), 2.78 – 2.71 (m, 1H), 2.06 (s, 3H). 13C NMR (151 MHz, DMSO) δ 169.2, 167.3, 142.8, 135.3, 1341.0, 133.3, 132.3, 128.0, 1271.0, 1271.0, 127.8, 127.8, 127.6(2C), 126.3, 125.9, 118.6, 55.9, 39.1, 24.6.HRMS (ESI): calcd for $C_{21}H_{21}N_3O_5S$[M-H]-: 426.1123; found, 426.1137.

Synthesis of (R,E)-N-hydroxy-2-((4-(1-(hydroxyimino) ethyl)phenyl) sulfonamido)-3-(naphthalene-2-yl) propanamide (**6a10**).

Starting material: **4a10** (0.35 g, 0.85 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.27 g, Yield 44.6 %).^{1}H NMR (600 MHz, DMSO-d6) δ 11.49 (s, 1H), 10.69 (s, 1H), 8.93 (s, 1H), 8.25 (s, 1H), 7.81 – 7.78 (m, 1H), 7.74 – 7.71 (m, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 1.6 Hz, 1H), 7.48 – 7.40 (m, 6H), 7.25 – 7.21 (m, 1H), 3.97 – 3.88 (m, 1H), 3.01 – 2.93 (m, 1H), 2.84 – 2.77 (m, 1H), 2.06 (s, 3H). 13C NMR (151 MHz, DMSO) δ 167.4, 152.3, 141.3, 140.3, 135.0, 133.3, 132.3, 128.1, 128.0, 1271.0, 127.8, 127.8, 126.5(2C), 126.3(2C), 125.9(2C), 56.1, 39.1, 11.8.HRMS (ESI): calcd for $C_{21}H_{21}N_3O_5S$[M-H]-: 426.1123; found, 426.1142.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-(3-nitrophenyl) sulfonamide propanmide (**6a11**)

Starting material: **4a11** (0.25 g, 0.61 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.23 g, Yield 53.3 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.79 (s, 1H), 8.96 (s, 1H), 8.73 (s, 1H), 8.13 – 8.07 (m, 1H), 7.90 – 7.82 (m, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.48 (s, 1H), 7.45 – 7.38 (m, 2H), 7.38 – 7.34 (m, 1H), 7.26 – 7.21 (m, 1H), 4.06 – 3.91 (m, 1H), 3.00 – 2.88 (m, 1H), 2.87 – 2.76 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.3, 147.2, 143.1, 134.9, 133.0, 132.1, 132.1, 130.6, 128.1, 127.9, 127.9, 127.8, 127.6, 126.4, 126.2, 126.0, 120.9, 56.5, 38.9. HRMS (ESI) : calcd for $C_{21}H_{21}N_3O_5S$ [M - H]$^-$: 414.0759; found, 414.0779.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-(4-nitrophenyl)sulfonamide propanamide(**6a12**)

Starting material: **4a12** (0.3 g, 0.72 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.19 g, Yield 42.7 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.78 (s, 1H), 8.97 (s, 1H), 7.77 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.54 – 7.45 (m, 3H), 7.43 – 7.31 (m, 2H), 7.25 (d, J = 8.5 Hz, 1H), 4.02 – 3.91 (m, 1H), 2.99 – 2.90 (m, 1H), 2.88 – 2.77 (m, 1H). 13C NMR (151 MHz, DMSO) δ 1661.0, 148.1, 146.5, 134.4, 132.4, 131.7, 127.7, 127.6(2C), 127.1(2C), 126.9(2C), 125.8, 125.5, 123.5(2C), 56.2, 38.4.HRMS (ESI): calcd for $C_{21}H_{21}N_3O_5S$[M-H]-: 414.0759; found, 414.0768.

Synthesis of (R)-N-hydroxy-3-(naphthalene-2-yl)-2-(4-nitrophenyl)sulfonamide propanamide (**6a13**)

Starting material: **4a13** (0.32 g, 0.77 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.22 g, Yield 47 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.71 (s, 1H), 8.97 (s, 1H), 8.19 (s, 0H), 7.82 – 7.76 (m, 1H), 7.71 – 7.68 (m, 1H), 7.66 (d, 2H), 7.57 (d, J = 8.0, 1.2 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.48 – 7.41 (m, 3H), 7.32 (d, J = 8.3, 1.8 Hz, 1H), 7.27 – 7.22 (m, 1H), 4.08 – 4.00 (m, 1H), 3.06 – 3.01 (m, 1H), 2.99 – 2.94 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 146.6, 134.4, 133.1, 133.0, 132.6, 131.8(2C), 128.8, 127.8, 127.6, 127.5, 127.4, 127.3, 125.9, 125.4, 123.7, 56.3, 38.5.HRMS (ESI) : calcd for $C_{21}H_{21}N_3O_5S$[M-H]-: 414.0759; found, 414.0765.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((trifluoromethyl) phenyl) sulfonamio) propanamide **(6b1**)

Starting material: **4b1** (0.23 g, 0.49 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.2 g, Yield 49.7 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.70 (s, 1H), 8.95 (s, 1H), 8.60 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 7.00 (d, J = 8.3 Hz, 2H), 3.83 – 3.74 (m, 1H), 2.79 – 2.71 (m, 1H), 2.67 – 2.60 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 1441.0, 136.2, 131.3(2C), 130.8(2C), 126.8(2C), 125.9, 125.9, 124.4, 122.6, 119.7, 55.5, 37.7. HRMS (ESI) : calcd for $C_{16}H_{14}BrF_3N_2O_4S$ [M - H]$^-$:464.9731; found, 464.9716/466.9686.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((4-methylphenyl) sulfonamide) propanamide (**6b2**)

Starting material: **4b2** (0.15 g, 0.36 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.14 g, Yield 68.1 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.61 (s, 1H), 8.91 (s, 1H), 8.09 (s, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.97 (d, J = 8.3 Hz, 2H), 3.76 – 3.66 (m, 1H), 2.76 – 2.67 (m, 1H), 2.62 – 2.52 (m, 1H), 2.37 (s, 3H). 13C NMR (151 MHz, DMSO) δ 166.9, 142.0, 138.3, 136.3, 131.3, 130.7, 129.1, 1251.0, 119.7, 55.3, 37.7, 21.0. HRMS (ESI) : calcd for $C_{16}H_{17}BrN_2O_4S$[M-H]-: 411.0013; found, 411.0001/466.0024.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((4-methoxyphenyl) sulfonamide) propanamide (**6b3**)

Starting material: **4b3** (0.22 g, 0.52 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.2 g, Yield 66.2 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 8.88 (s, 1H), 7.46 – 7.41 (m, 2H), 7.34 – 7.30 (m, 2H), 6.99 (d, J = 8.3 Hz, 2H), 6.92 – 6.88 (m, 2H), 3.82 (d, J = 6.3 Hz, 3H), 3.75 – 3.64 (m, 1H), 2.77 – 2.68 (m, 1H), 2.58 – 2.52 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.9, 161.8, 136.4, 132.9, 131.4, 130.8, 128.2, 119.6, 113.8, 55.5, 55.3, 37.7.HEMS (ESI) : calcd for $C_{16}H_{17}BrN_2O_4S$ [M - H]$^-$:411.0013; found, 411.0001/466.0000.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-(naphthalene-1-sulfonamido) propanamide(**6b4**)

Starting material: **4b4** (0.15 g, 0.33 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.12 g, Yield 65.3 %).^{1}H NMR (600 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.45 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.85 (d, J = 6.6

Hz, 1H), 7.63 – 7.53 (m, 2H), 7.48 – 7.42 (m, 1H), 6.80 (d, J = 8.3 Hz, 2H), 6.72 (d, J = 8.3 Hz, 2H), 3.76 – 3.68 (m, 1H), 2.67 – 2.60 (m, 1H), 2.56 – 2.51 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.9, 136.3, 136.3, 134.1, 133.8, 131.1, 130.5, 129.2, 128.2, 127.7, 127.7, 126.9, 125.5, 124.4, 119.8, 56.2, 38.1.HRMS (ESI): (m/z): $[M - H]^-$:calcd for $C_{20}H_{18}BrNO_4S$, 447.0013; found, 447.0038/448.9980.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((4-isopropylphenyl) sulfonamido) propanamide (**6b5**)

Starting material: **4b5** (0.15 g, 0.33 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.12 g, Yield 40.2 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 10.62 (s, 1H), 8.92 (s, 1H), 8.16 (s, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 6.98 (d, J = 8.2 Hz, 2H), 3.69 (dd, J = 9.1, 5.5 Hz, 1H), 2.99 – 2.90 (m, 1H), 2.72 (dd, J = 13.6, 5.4 Hz, 1H), 2.56 (dd, J = 13.5, 9.4 Hz, 1H), 1.22 (d, J = 6.9 Hz, 6H). 13C NMR (151 MHz, DMSO) δ 167.0, 152.6, 138.6, 136.4, 131.4, 130.8, 126.5, 126.2, 119.6, 55.3, 37.7, 33.3, 23.5, 23.4.HRMS (ESI) : calcd for $C_{18}H_{21}BrN_2O_4S$, $[M - H]^-$:439.0326; found, 439.0333/441.0288.

Synthesis of (R)-2-([1, 1'-biphenyl]-4-sulfonamido)-3-(4-bromophenyl)-N-hydroxypropanamide (**6b6**)

Starting material: **4b6** (0.18 g, 0.38 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.16 g, Yield 62.7 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.66 (s, 1H), 8.92 (s, 1H), 8.31 (s, 1H), 7.73 (d, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.51 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.31 (d, J = 8.3 Hz, 2H), 7.03 (t, J = 7.7 Hz, 2H), 3.84 – 3.73 (m, 1H), 2.82 – 2.72 (m, 1H), 2.64 – 2.55 (m, 1H). 13C NMR (151 MHz, DMSO) δ 167.3, 143.9, 140.4, 139.1, 136.8, 131.9, 131.3, 129.5, 128.8, 127.5, 127.4, 127.2, 120.2, 55.9, 38.3.
HRMS (ESI) : calcd for $C_{21}H_{19}BrN_2O_4S$, $[M - H]^-$:473.017; found, 473.0164/475.0136.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-(quinolone-8-sulfonamido) propanamide (**6b7**)

Starting material: **4b7** (0.15 g, 0.33 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.1 g, Yield 57.5 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 10.60 (s, 1H), 8.99 – 8.76 (m, 2H), 8.46 (d, J = 8.3, 1.7 Hz, 1H), 8.19 (d, J = 8.2, 1.4 Hz, 1H), 8.10 (d, J = 7.2, 1.4 Hz, 1H), 7.73 – 7.57 (m, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 4.25 – 4.06 (m, 1H), 2.85 – 2.58 (m, 2H). 13C NMR (151 MHz, DMSO) δ 167.0, 150.9, 142.3, 1361.0, 136.7, 135.8, 133.3, 130.9, 130.1, 129.3, 128.3, 125.2, 122.3, 119.5, 56.1, 37.9.HRMS (ESI) : calcd for $C_{18}H_{16}BrN_3O_4S$[M-H]-: 447.9966; found, 447.9954/449.9977.

Synthesis of (R)-3-(4-bromophenyl)-2-((5-bromothiophene)-2-sulfonamido-N-hydroxypropanamide (**6b8**)

Starting material: **4b8** (0.15 g, 0.32 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.07 g, Yield 37.5 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.70 (s, 1H), 8.97 (s, 1H), 8.64 (s, 1H), 7.45 – 7.34 (m, 2H), 7.16 – 7.03 (m, 4H), 3.90 – 3.73 (m, 1H), 2.81 – 2.74 (m, 1H), 2.69 – 2.62 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 166.6, 143.1, 136.3, 131.6, 131.4 (2C), 130.9 (2C), 130.7, 119.8, 118.0, 55.6, 37.6. HRMS (ESI) : calcd for $C_{13}H_{12}Br_2N_2O_4S_2$ $[M - H]^-$:4480.8526; found, 480.8544/482.8506/484.8457.

Synthesis of (R)-2-((4-acetamidophenyl) sulfonamido)-3-(4-bromophenyl)-N-hydroxypropanamide (**6b9**)

Starting material: **4b9** (0.15 g, 0.33 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.14 g, Yield 47.3 %).^{1}H NMR (600 MHz, DMSO-d6) δ 7.59 – 7.55 (m, 1H), 7.49 – 7.44 (m, 1H), 7.30 (dt, J = 7.6, 1.1 Hz, 1H), 6.72 – 6.54 (m, 1H), 5.90 (s, 1H), 4.75 (s, 1H), 4.68 – 4.60 (m, 1H), 4.51 (s, 1H), 3.57 – 3.46 (m, 0H), 3.26 – 3.11 (m, 1H). ^{13}C NMR (151 MHz, DMSO) δ 166.7, 152.3, 136.4, 131.3

(2C), 130.8 (2C), 128.2 (2C), 126.2, 119.6, 112.4 (2C), 54.9, 37.7. HRMS (ESI) : [M - H] - calcd for $C_{17}H_{18}BrN_3O_5S$ [M - H]$^-$ 454.0072; found, 454.0096/456.0027.

Synthesis of (R)-2-((4-acetyphenyl) sulfonamide)-3-(4-bromophenyl)-N-hydroxypropanamide(**6b10**)

Starting material: **4b10** (0.15 g, 0.34 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.075 g, Yield 36.7 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 8.14 – 8.08 (m, 1H), 7.99 – 7.89 (m, 1H), 7.43 – 7.32 (m, 1H), 7.21 – 7.09 (m, 1H), 5.46 (s, 1H), 4.77 (s, 1H), 4.52 – 4.30 (m, 1H), 3.64 – 3.41 (m, 1H), 2.99 – 2.80 (m, 1H), 2.51 (s, 2H). ^{13}C NMR (151 MHz, DMSO) δ 197.4, 172.7, 144.3, 138.3, 132.9, 131.7 (2C), 131.2 (2C), 128.5 (2C), 127.4 (2C), 120.1, 59.7, 38.1, 26.8. HRMS (ESI) : calcd for $C_{15}H_{16}BrN_3O_4S$ [M - H]$^-$ 411.9966; found, 412.0013/414.0038.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((3-nitrophenyl) sulfonamide propanamide(**6b11**)

Starting material: **4b11** (0.15 g, 0.34 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.075 g, Yield 46.7 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.70 (d, J = 1.8 Hz, 1H), 8.91 (d, J = 1.7 Hz, 1H), 8.74 (d, J = 9.0 Hz, 1H), 8.46 – 8.31 (m, 1H), 8.22 – 8.14 (m, 1H), 7.98 – 7.87 (m, 1H), 7.77 – 7.62 (m, 1H), 7.27 – 7.13 (m, 2H), 7.01 – 6.92 (m, 2H), 4.00 – 3.71 (m, 1H), 2.77 – 2.70 (m, 1H), 2.67 – 2.59 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.4, 147.3, 142.7, 136.2, 1311.0, 131.3, 130.7, 130.7, 126.3, 120.8, 119.7, 55.6, 37.6. HRMS (ESI) : calcd for $C_{13}H_{12}Br_2N_2O_4S_2$ [M - H]$^-$: 441.9708; found, 440.9971/482.8506/438.9957.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((4-nitrophenyl) sulfonamido)propanamide(**6b12**)

Starting material: 4b12 (0.15 g, 0.34 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.1 g, Yield 41.7 %).1H NMR (600 MHz, DMSO-d6) δ 10.72 (s, 1H), 8.92 (s, 1H), 8.75 (s, 1H), 8.25 – 8.16 (m, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 7.00 (d, J = 8.2 Hz, 2H), 2.78 – 2.70 (m, 1H), 2.67 – 2.59 (m, 1H). 13C NMR (151 MHz, DMSO) δ 172.7, 150.0, 143.3, 132.9, 131.7(2C), 131.2(2C), 128.3(2C), 126.3(2C), 120.1, 581.0, 52.5, 39.5. HRMS (ESI) : calcd for $C_{15}H_{14}BrN_3O_6S$[M-H]-: 441.9708; found, 441.9710/443.9728.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-((2-nitropheny) sulfonamido) propanamide(**6b13**)

Starting material: **4b13** (0.15 g, 0.34 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.083 g, Yield 41.1 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.68 (s, 1H), 8.95 (s, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.79 – 7.73 (m, 1H), 7.63 – 7.58 (m, 2H), 7.28 – 7.22 (m, 2H), 7.17 – 7.01 (m, 2H), 3.97 – 3.83 (m, 1H), 2.90 – 2.68 (m, 2H). 13C NMR (151 MHz, DMSO) δ 166.6, 146.8, 136.1, 133.4, 133.2, 132.2, 131.4, 130.7, 129.1, 124.1, 119.8, 56.1, 37.6.HRMS (ESI) : calcd for $C_{15}H_{14}BrN_3O_6S$[M-H]-: 441.9708; found, 441.9708/443.9738.

Synthesis of (R)-3-(4-bromophenyl)-N-hydroxy-2-(naphthalene-2-sulfonamido) propanamide(**6b14**)

Starting material: **4b14** (0.15 g, 0.33 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.23 g, Yield 64.1 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.64 (s, 1H), 8.89 (s, 1H), 8.35 (s, 1H), 8.17 (s, 1H), 8.03 – 7.97 (m, 2H), 7.89 (d, J = 8.7 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.52 – 7.47 (m, 1H), 7.17 – 7.12 (m, 2H), 6.98 – 6.92 (m, 2H), 3.86 – 3.76 (m, 1H), 2.77 – 2.70 (m, 1H), 2.64 – 2.56 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.9, 138.2, 136.2, 133.9, 131.4, 131.3, 130.7, 1281.0, 128.9, 128.4, 127.8, 127.3, 126.6, 121.9, 119.7, 55.4, 37.8. HRMS (ESI) : calcd for $C_{19}H_{17}BrN_2O_4S$[M-H]-: 447.0013; found, 447.0018/449.0024.

Synthesis of (R)-3-(4-bromophenyl)-2-((4-bromophenyl) sulfonamido)-N-hydroxypropanamide (**6b15**)

Starting material: **4b15** (0.15 g, 0.315 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.16 g, Yield 43.2 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.65 (s, 1H), 8.92 (s, 1H), 8.41 (s, 1H), 7.63 – 7.55 (m, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.8, 2.6 Hz, 2H), 7.01 (d, J = 6.6, 4.3 Hz, 2H), 3.75 (s, 1H), 2.77 – 2.70 (m, 1H), 2.64 – 2.56 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 140.4, 136.2, 131.7, 131.3, 130.8, 127.9, 125.7, 119.8, 55.4, 37.7.HRMS (ESI): calcd for $C_{15}H_{14}Br_2N_2O_4S$ [M - H]$^-$:474.8962; found, 474.8969/476.8975.

Synthesis of (S)-3-(4-bromophenyl)-N-hydroxy-2-(naphthalene-2-sulfonamido) propanamide(**6d1**)

Starting material: **4d1** (0.3 g, 0.67 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.25 g, Yield 48.5 %).^{1}H NMR (600 MHz, DMSO-d6) δ 8.87 (s, 1H), 8.18 – 8.14 (m, 1H), 7.99 (d, J = 13.8, 8.0 Hz, 2H), 7.88 (d, J = 8.7 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.51 – 7.45 (m, 1H), 7.14 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 7.9 Hz, 2H), 3.85 – 3.76 (m, 1H), 2.76 – 2.68 (m, 1H), 2.64 – 2.55 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.8, 138.2, 136.2, 133.9, 131.4, 131.2(2C), 130.6(2C), 1281.0, 128.9, 128.4, 127.7, 127.3, 126.6, 121.9, 119.7, 55.4, 37.8.HRMS (ESI) : calcd for $C_{19}H_{17}BrN_2O_4S$[M-H]-: 447.0013; found, 447.0036/448.9977.

Synthesis of (S)-3-(4-bromophenyl-2-((4-bromophenyl)sulfonamido)-N-hydroxypropanamide(**6d2**)

Starting material: **4d2** (0.25 g, 0.56 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.19 g, Yield 41.2 %). ^{1}H NMR (600 MHz, /llkjm,n) δ 10.65 (s, 1H), 8.91 (s, 1H), 8.39 (s, 1H), 7.63 – 7.56 (m, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.01 (d, J = 8.1 Hz, 2H), 3.78 – 3.71 (m, 1H), 2.77 – 2.69 (m, 1H), 2.65 – 2.57 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 140.4, 136.2, 131.7(2C), 131.3(2C), 130.8(2C), 127.9(2C), 125.7, 119.8, 55.4, 37.7.HRMS (ESI) : calcd for $C_{15}H_{14}Br_2N_2O_4S$[M-H]-: 474.9322; found, 474.8968/476.8973/478.8939.

Synthesis of (S)-3-(4-bromophenyl)-N-hydroxy-2-((4-(trifluoromethyl) phenyl) sulfonamido)propanamide (**6d3**)

Starting material: **4d3** (0.15 g, 0.32 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.1 g, Yield 60.1 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.69 (s, 1H), 8.94 (s, 1H), 8.44 (s, 1H), 7.75 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 7.01 (d, J = 8.1 Hz, 2H), 3.82 – 3.75 (m, 1H), 2.78 – 2.70 (m, 1H), 2.66 – 2.59 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 1441.0, 136.2, 131.6, 131.3, 130.7, 126.8, 125.8, 125.8, 123.5, 119.6, 55.5, 37.7.HRMS (ESI) : calcd for $C_{17}H_{17}BrF_2N_2O_4S$[M-H]-: 464.9731; found, 464.9733/466.9724.

Synthesis of (S)-3-(4-bromophenyl)-N-hydroxy-2-((4-methylphenyl) sulfonamido)propanamide (**6d4**)

Starting material: **4d4** (0.15 g, 0.36 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.24 g, Yield 48.3 %).^{1}H NMR (600 MHz, DMSO-d6) δ 8.88 (s, 1H), 7.37 (d, J = 7.7 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 7.7 Hz, 2H), 6.97 (d, J = 7.8 Hz, 2H), 6.50 (s, 1H), 3.78 – 3.68 (m, 1H), 2.71 (dd, J = 13.4, 5.5 Hz, 1H), 2.56 (dd, J = 13.6, 9.3 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 166.9, 142.0, 138.3, 136.3, 131.3(2C), 130.7(2C), 129.1(2C), 1251.0(2C), 119.7, 55.4, 37.7, 21.0. HRMS (ESI) : calcd for $C_{16}H_{17}BrF_2N_2O_4S$ [M-H]$^-$: 411.0013; found, 411.0007/413.0022.

Synthesis of (S)-3-(4-bromophenyl)-N-hydroxy-2-((3-nitrophenyl) sulfonamido)propanamide(**6d5**)

Starting material: **4d5** (0.4 g, 0.36 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.36 g, Yield 53.4 %).[1]H NMR (600 MHz, DMSO-d6) δ 10.69 (s, 1H), 8.91 (s, 1H), 8.40 – 8.33 (m, 1H), 8.24 – 8.13 (m, 1H), 7.96 – 7.86 (m, 1H), 7.77 – 7.67 (m, 1H), 7.20 (d, J = 7.6 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 6.45 (s, 1H), 3.92 – 3.71 (m, 1H), 2.77 – 2.68 (m, 1H), 2.67 – 2.61 (m, 1H). [13]C NMR (151 MHz, DMSO) δ 167.0, 147.8, 143.3, 136.7, 132.5, 131.8（2C）, 131.3, 131.2 (2C), 126.9, 121.3, 120.2, 56.16, 38.1. HRMS (ESI) : calcd for C15H14BrN3O6S[M-H]-: 441.9708; found, 441.9693/443.9632.

Synthesis of (S)-N-hydroxy-3-(naphthalene-2-yl)-2-(naphthalene-2-sulfonamido) propanamide (**6e1**)

Starting material: **4e1** (0.2 g, 0.48 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.18 g, Yield 38.6 %).[1]H NMR (600 MHz, DMSO-d6) δ 10.66 (s, 1H), 8.87 (s, 1H), 8.42 – 8.32 (m, 1H), 8.14 (s, 1H), 7.84 (dd, J = 18.6, 8.1 Hz, 2H), 7.72 – 7.68 (m, 1H), 7.64 – 7.54 (m, 4H), 7.54 – 7.48 (m, 2H), 7.47 – 7.36 (m, 3H), 7.16 (dd, J = 8.4, 1.7 Hz, 1H), 4.14 – 3.87 (m, 1H), 3.00 – 2.91 (m, 1H), 2.82 – 2.71 (m, 1H). [13]C NMR (151 MHz, DMSO) δ 166.9, 138.2, 134.5, 133.8, 132.8, 131.7, 131.4, 128.9, 128.6, 128.3, 127.6, 127.5, 127.4, 127.3, 127.30, 127.2, 127.2, 126.6, 125.8, 125.4, 121.9, 55.6, 38.6. HRMS (ESI) : calcd for C23H20N2O4S [M-H]$^-$: 419.1065; found, 419.1059.

Synthesis of (S)-2-((4-bromophenyl) sulfonamido)-N-hydroxy-3-(naphthalene-2-yl) propanamide (**6e2**)

Starting material: **4e2** (0.2 g, 0.45 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.17 g, Yield 42 %). [1]H NMR (600 MHz, DMSO-d6) δ 10.65 (s, 1H), 8.91 (s, 1H), 7.87 – 7.81 (m, 1H), 7.75 – 7.71 (m, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.56 (s, 1H), 7.52 – 7.44 (m, 2H), 7.35 – 7.27 (m, 4H), 7.24 – 7.16 (m, 1H), 3.92 – 3.81 (m, 1H), 2.99 – 2.91 (m, 1H), 2.85 – 2.72 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.8, 140.3, 134.5, 132.7, 131.8, 131.4(2C), 127.8(2C), 127.6, 127.4, 127.4, 127.4, 127.2, 125.9, 125.5, 125.5, 55.6, 38.6. HRMS (ESI) : calcd for C19H17BrN2O4S[M-H]-: 447.0013; found, 447.0030/448.0085.

Synthesis of (S)-N-hydroxy-3-(naphthalene-2-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)propanamide (**6e3**)

Starting material: **4e3** (0.15 g, 0.34 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.1 g, Yield 43 %). 1H NMR (600 MHz, DMSO-d6) δ 8.00 – 7.94 (m, 1H), 7.84 – 7.77 (m, 1H), 7.78 – 7.72 (m, 1H), 7.70 (dd, J = 7.5, 1.4 Hz, 0H), 7.48 – 7.43 (m, 1H), 7.42 – 7.37 (m, 0H), 7.31 (d, J = 7.5, 1.4 Hz, 0H), 5.59 (s, 0H), 4.81 (s, 0H), 4.51 – 4.38 (m, 1H), 3.78 – 3.63 (m, 1H), 3.14 – 2.98 (m, 1H). 13C NMR (151 MHz, DMSO) δ 172.7, 144.8, 136.5, 134.8, 134.3, 133.1, 128.6, 128.1, 128.1, 127.9, 127.6, 127.4, 126.7, 126.6, 126.5, 126.4, 126.2, 126.1, 125.1, 123.2, 59.7, 37.8. HRMS (ESI) : calcd for C19H17BrN2O4S [M - H]$^-$: 438.0861; found, 437.0782/437.0774.

Synthesis of (S)-N-hydroxy-2-((4-methyphenyl) sulfonamido)-3-(naphthalene-2-yl) propanamide (**6e4**)

Starting material: **4e4** (0.2 g, 0.52 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.18 g, Yield 44 %).[1]H NMR (600 MHz, DMSO-d6) δ 10.64 (s, 1H), 8.89 (s, 1H), 8.17 (s, 1H), 7.88 – 7.80 (m, 1H), 7.75 – 7.63 (m, 2H), 7.54 – 7.43 (m, 3H), 7.33 (d, J = 7.8 Hz, 2H), 7.23 – 7.17 (m, 1H), 6.92 (d, J = 7.9 Hz, 2H), 3.87 (dd, J = 8.9, 5.7 Hz, 1H), 2.98 – 2.88 (m, 1H), 2.82 – 2.67 (m, 1H), 2.17 (s, 3H). 13C NMR (151 MHz, DMSO) δ 1661.0, 141.8, 138.2, 134.5, 132.8, 131.8, 128.9(2C), 127.5, 127.6, 127.4, 127.3, 127.3, 125.9(2C), 125.8, 125.3, 55.5, 38.6, 20.8.HRMS (ESI) : calcd for C20H20N2O4S [M - H] - : 383.1065; found, 383.1057.

Synthesis of (S)-N-hydroxy-2-((4-methoxyphenyl) sulfonamido)-3-(naphthalene-2-yl) propanamide. (**6e5**)

Starting material: **4e5**(0.15 g, 0.375 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.13 g, Yield 46 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.63 (s, 1H), 8.87 (s, 1H), 7.88 – 7.81 (m, 1H), 7.77 – 7.67 (m, 2H), 7.53 (s, 1H), 7.49 – 7.43 (m, 3H), 7.41 – 7.37 (m, 2H), 7.23 – 7.19 (m, 1H), 6.66 (d, J = 8.9 Hz, 2H), 3.90 – 3.81 (m, 1H), 3.68 (s, 3H), 2.99 – 2.91 (m, 1H), 2.78 – 2.70 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.9, 161.5, 134.6, 132.9, 132.8, 131.8, 128.1(2C), 127.6, 127.5, 127.4, 127.3, 127.3, 125.8, 125.4, 113.5(2C), 55.5, 55.3, 38.6.HRMS (ESI) : calcd for C20H20N2O5S[M-H]-: 399.1014; found, 399.1030.

Synthesis of (S)-N-hydroxy-3-(naphthalene-2-yl)-2-((3-nitrophenyl) sulfonamido) propanamide (**6e6**)

Starting material: **4e6**(0.15 g, 0.36 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.12 g, Yield 44.6 %).^{1}H NMR (600 MHz, DMSO-d6) δ 10.77 (s, 1H), 8.94 (s, 1H), 8.75 (s, 1H), 8.13 – 8.06 (m, 1H), 7.88 – 7.84 (m, 1H), 7.80 – 7.77 (m, 1H), 7.73 – 7.70 (m, 1H), 7.61 – 7.56 (m, 2H), 7.48 – 7.47 (m, 1H), 7.44 – 7.38 (m, 2H), 7.38 – 7.34 (m, 1H), 7.26 – 7.21 (m, 1H), 4.07 – 3.90 (m, 1H), 2.97 – 2.89 (m, 1H), 2.85 – 2.76 (m, 1H). 13C NMR (151 MHz, DMSO) δ 166.7, 146.7, 142.6, 134.4, 132.5, 131.6, 131.6, 130.2, 127.6, 127.4, 127.4, 127.3, 127.1, 125.9, 125.7, 125.5, 120.4, 551.0, 38.4. HRMS (ESI) : calcd for C19H17N3O5S [M - H]$^-$:414.0759; found, 414.0758.

Synthesis of (R)-N-hydroxy-3-(4-hydroxyphenyl)-2-(naphthalene-2-sulfonamido) propanamide (**7c1**)

Starting material: **5c1** (0.3 g, 0.78 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.21 g, Yield 49.5 %).^{1}H NMR (600 MHz, DMSO-d6) δ 8.57 (s, 1H), 8.21 (d, 2H), 8.11 (d, J = 8.2 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.81 – 7.76 (m, 1H), 7.74 – 7.68 (m, 1H), 7.19 – 7.09 (m, 2H), 6.96 – 6.86 (m, 2H), 3.27 – 3.08 (m, 1H), 2.86 – 2.71 (m, 1H), 2.65 – 2.52 (m, 1H). 13C NMR (151 MHz, DMSO) δ 170.9, 147.4, 138.2, 1341.0, 131.6, 131.4(2C), 130.7, 130.1, 129.9, 129.9, 129.6, 128.0, 1271.0, 122.5, 121.48(2C), 54.1, 40.4.HRMS (ESI) : calcd for C19H18N2O5S[M-H]-: 385.0857; found, 385.0844.

Synthesis of (R)-2-((4-bromophenyl) sulfonamido)-N-hydroxy-3-(4-hydroxyphenyl) propanamide (**7c2**)

Starting material: **5c2** (0.25 g, 0.59 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.17 g, Yield 43.2 %).^{1}H NMR (600 MHz, DMSO-d6) δ 7.90 – 7.85 (m, 2H), 7.78 – 7.72 (m, 2H), 7.20 (d, 2H), 6.94 (d, 2H), 3.25 – 3.15 (m, 1H), 2.85 – 2.73 (m, 1H), 2.65 – 2.55 (m, 1H). 13C NMR (151 MHz, DMSO) δ 170.8, 147.2, 138.4, 133.6, 132.9(2C), 130.8(2C), 130.0(2C), 129.1, 121.5(2C), 54.1, 40.5. HRMS (ESI) : [M - H] - calcd for C15H15BrN2O5S[M-H]-: 412.9806; found, 412.9836/414.9799.

Synthesis of (R)-N-hydroxy-3-(4-hydroxyphenyl)-2-((4-(trifluoromethyl) phenyl) sulfonamido)propanamide (**7c3**)

Starting material: **5c3** (0.4 g, 0.96 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.32 g, Yield 57.8 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 8.19 – 7.96 (m, 4H), 7.29 – 7.13 (m, 2H), 7.01 – 6.88 (m, 2H), 3.24 – 3.16 (m, 1H), 2.85 – 2.74 (m, 1H), 2.67 – 2.57 (m, 1H). 13C NMR (151 MHz, DMSO) δ 170.8, 147.1, 138.6, 138.3, 134.5, 130.8(2C), 129.2(2C), 1261.0, 126.9, 121.5(2C), 54.1, 40.5.HRMS (ESI) : calcd for C16H15F3N2O5S [M - H]$^-$:403.0575; found, 403.0577.

Synthesis of (R)-N-hydroxy-3-(4-hydroxyphenyl)-2-((4-methylphenyl) sulfonamido) propanamide (**7c4**)

Starting material: **5c4** (0.4 g, 1.1 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.36 g, Yield 44.4 %). ^{1}H NMR (600 MHz, DMSO-d6) δ 7.81 – 7.69 (m, 2H), 7.46 (d, J = 7.9 Hz, 2H), 7.24 – 7.14 (m, 2H), 6.96 – 6.85 (m, 2H), 3.24 – 3.15 (m, 1H), 2.86

– 2.74 (m, 1H), 2.64 – 2.55 (m, 1H), 2.42 (s, 3H). 13C NMR (151 MHz, DMSO) δ 170.9, 147.4, 145.6, 138.1, 131.6, 130.6(2C), 130.1(2C), 128.1(2C), 121.5(2C), 54.1, 40.6, 21.1.HRMS (ESI) : calcd for C16H18N2O5S[M-H]-: 349.0857; found, 349.0860.

Synthesis of (R)-N-hydroxy-3-(4-hydroxyphenyl)-2-((4-methoxyphenyl) sulfonamide) propanamide (**7c5**)

Starting material: **5c5** (0.3 g, 0.75 mmol) and 10 mL of aqueous hydroxylamine (50 percent w/w), obtained as white solid (0.25 g, Yield 55.1 %).^{1}H NMR (600 MHz, DMSO-d6) δ 7.77 – 7.72 (m, 2H), 7.21 – 7.13 (m, 4H), 6.92 – 6.87 (m, 2H), 3.87 (s, 3H), 3.24 – 3.16 (m, 1H), 2.83 – 2.73 (m, 1H), 2.66 – 2.54 (m, 1H). 13C NMR (151 MHz, DMSO) δ 170.8, 163.9, 147.4, 138.0, 130.6(2C), 130.5(2C), 125.6, 121.5(2C), 114.9(2C), 55.9, 54.1, 40.5.HRMS (ESI) : calcd for C16H18N2O6S[M-H]-: 365.0807; found, 365.0812.

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Author Contribution Statement

Duan-Yang Shao, Dong-Hui Li,Ju-Xian Wang and Yu-Cheng Wang designed and planned the experiments. Duan-Yang Shao, Guo-Ning Zhang, Mei Zhu and Zi-Qiang Li synthesized the compounds.Wei-Xiao Niu tested their cytotoxic effect. Duan-Yang Shao wrote the the manuscript with support from Guo-Ning Zhang and Dong-Hui Li. Yucheng Wang supervised the project.

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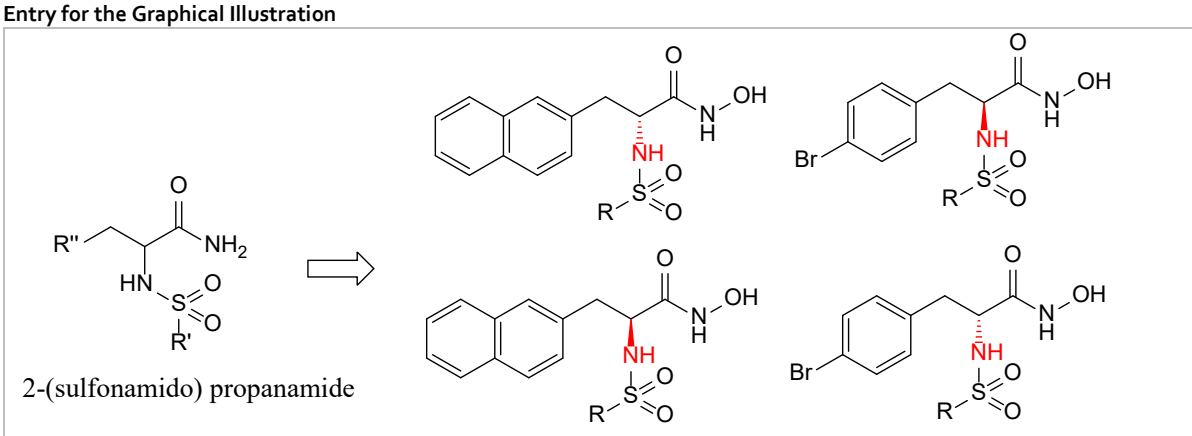

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