Cascade Michael-Aldol reaction: efficient annulation of sulfonamide chalcones into novel cyclohexenones under solvent-free conditions

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Abstract
A simple, convenient and efficient synthesis of novel sulfonamide cyclohexenones from differently substituted sulfonamide chalcones has been developed. Syntheses of cyclohexenones have been achieved *via* cascade Michael-Aldol reaction under solvent free condition. This process features mild and solvent-free synthesis of the titled compounds with high yields (18 examples, up to 95% yield). The synthesized scaffold is a promising intermediate for the further transformation into various heterocyclic compounds.

Keywords: Cascade Michael-Aldol reaction, solvent-free synthesis, sulfonamide cyclohexenones, sulfonamide chalcones

Introduction

Development of clean synthetic methodologies with least environmental damage is the primary requirement of sustainable chemical process. Nowadays, large scale usage of organic solvents instigate serious environmental threat.[1, 2] To minimize damage to the environment due to waste stream of organic solvents, synthetic chemists are under constant pressure of developing synthetic strategies which includes use of more benign solvents like water, supercritical CO_2 and ionic liquids.[1] It has been said that 'the best solvent is no solvent'.[1] Solvent-free reactions obviously reduce pollution, and bring down handling costs due to simplification of experimental procedure, work up technique and thereby saving in labor. Reactions on solid support like clays,[3] zeolites,[4] silica,[5, 6] alumina.[7] using conventional heating[8] or irradiation with microwave[9, 10] or ultrasound[11] continue to witness exponential growth in the recent times. However, these are not supposed to be

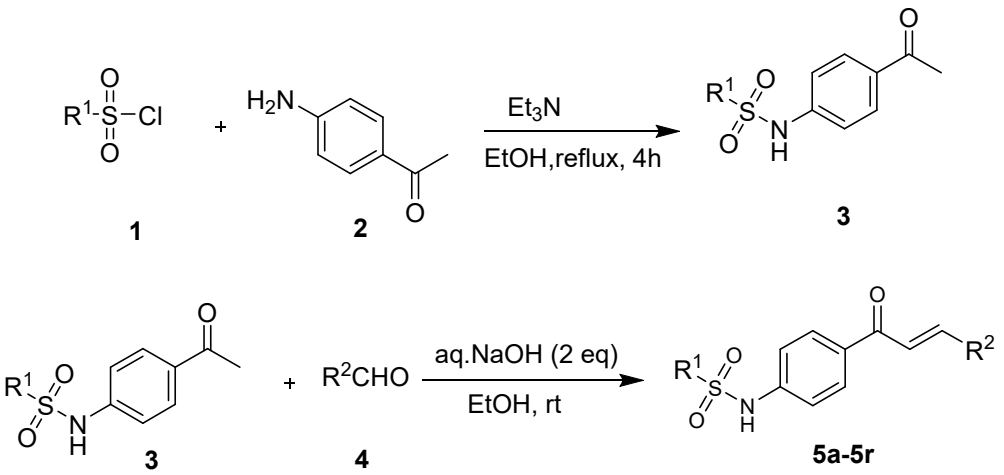
a 'true solvent-free' reaction as solvents are often used to pre-adsorb the substrate on the solid support.[12]

Sulfonamide chalcones identified as chemotherapeutic agents, possesses potent biological properties,[13, 14] provides a versatile platform for the synthesis of bioactive scaffolds such as cyanopyridines, isoxazoles, pyrazoles and pyrimidin-2-thiones.[15, 16] Cyclohexenones, being known to display important biological activities such as anticancer agents[17] and pheromones.[18-20] In addition, cyclohexenones have been widely found as a key structural skeleton in natural products and pharmaceuticals like saudin,[21] antroquinonol,[22] gabosines,[23] etc. A number of synthetic strategies have been reported for the construction of cyclohexenone skeleton which includes Hagemann condensation and Knoevenagel condensation,[24-26] reductive synthesis via cyclization of heavily functionalized dihydropyrines,[27] and Au-catalyzed cyclisation of alkene-functionalized propargyl acetate followed by base treatment.[28] Robinson annulation of chalcone motif promoted by various catalysts such as lanthanide complex,[29] Rhodium,[30] C-200,[31, 32] etc has also been documented. Specifically, addition of β-keto ester to chalcone moiety has also been accessed in the presence of base like sodium ethoxide,[33] potassium carbonate under MW irradiation.[34] Despite the progress, till date, there is only one report of transformation of sulfonamide chalcones to cyclohexenone skeleton. El-Sharief *et al.* reported transformation of sulfonamide chalcones to cyclohexenone skeleton using piperidine as a base and butanol as a solvent.[35]

In virtue of extending wide arena of this structurally interesting sulfonamide chalcones and cyclohexenone, herein we report annulations of sulfonamide chalcones with ethyl acetoacetate *via* cascade Michael-Aldol reaction in presence of anhydrous K_2CO_3 under solvent-free condition (**Scheme 2**).

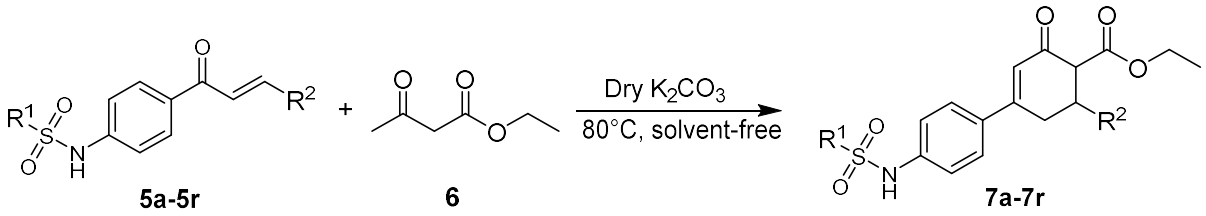
Results and Discussion

Aiming to construct cyclohexenone scaffolds (**7a-7r**), the precursor sulfonamide chalcones **5** were prepared by Claisen-Schmidt condensation of ketone **3** and differently substituted aldehydes **4** (Scheme 1). Ketone **3**, in turn was prepared easily by condensation of aryl/methane sulfonyl chloride **1** and 4-aminoacetophenone **2** in presence of triethyl amine as a base.[36]



Scheme 1. Synthesis of sulfonamide chalcones **(5a-5r).**

The concluding step was the annulation of **5a-5r** into cyclohexenones possessing sulfonamide unit **(7a-7r)** *via* cascade Michael-Aldol reaction. Anhydrous K_2CO_3 catalyzed annulation reaction was achieved from sulfonamide chalcones (**5a-5r)** with ethylacetoacetate at 80 °C under solvent-free condition. When tested the effect of temperature on the proposed reaction, low temperature i.e. 60 °C took longer time for completion with moderate yields while higher temperature i.e. 100 °C did not boost the reaction rate. After completion of reaction (TLC monitoring), simple extraction from ethanol at reaction temperature offers effortless isolation of pure product with better yields (**Scheme 2**).



Scheme 2. Synthesis of sulfonamide cyclohexenone derivatives **(7a-7r).**

Proving the generality of the aforesaid protocol, an array of varied substituted sulfonamide cyclohexenones **7a-7r** was synthesized by varying the substitution on the 3rd and 5th position of cyclohexenone ring and the outputs are summarized in **Table 1**. It can be contemplated that the substitution at phenyl ring of R^2 of sulfonamide chalcone profoundly affects the speed of reaction. Reactions with electron-withdrawing substituent at phenyl ring of R^2 were found to be more facile than that with electron-donating substituent (**Table 1**). It might be due to the increase in the electrophilicity of β-carbon of chalcone which thereon facilitates the nucleophilic attack of ethyl acetoacetate resulting into 1,4 addition which subsequently cyclizes to afford substituted sulfonamide cyclohexenones. Substitution at R^1 of phenylsulfonamido moiety shows little or no

effect on the speed and yield of reaction and reaction proceeds smoothly with better yields (**Table 1, entry 7l-7r**). Overall yields of the synthesized compounds **7a-7r** were found to be excellent.

Table 1. Physical data of sulfonamide cyclohexenones **(7a-7r)**

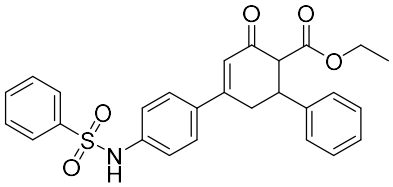
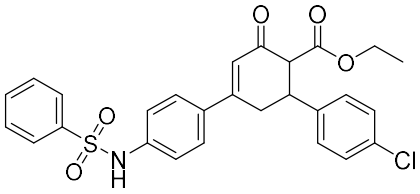
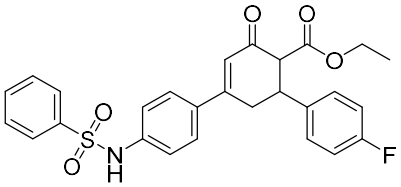
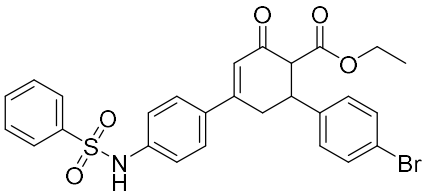
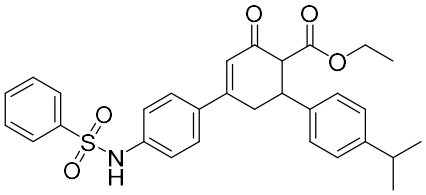
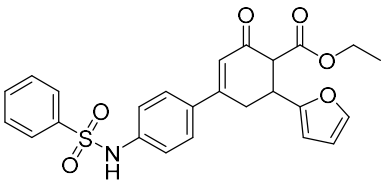
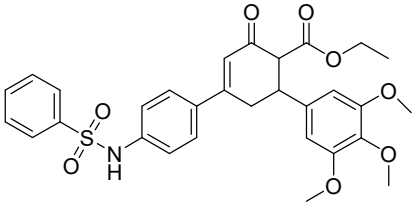
Entry	R^1	R^2	Product	Time (in min)	Yield (%)	Mp (°C)
7a	-Ph	-Ph		60	91	180-181
7b	-Ph	-4-Cl-C_6H_4		50	80	235-237
7c	-Ph	-4-F-C_6H_4		50	88	254-255
7d	-Ph	-4-Br-C_6H_4		50	80	270-272
7e	-Ph	-4-$CH(CH_3)_2$-C_6H_4		70	95	199-200
7f	-Ph	-2-furyl		60	72	196-198
7g	-Ph	-3,4,5-$(OCH_3)_3$-C_6H_2		70	80	241-243

Table 1 (continued)

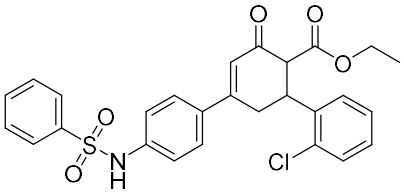
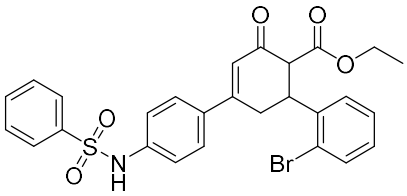
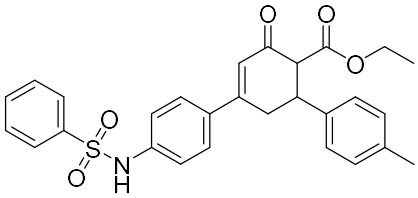
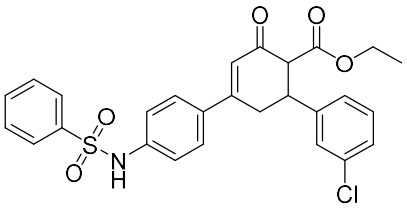
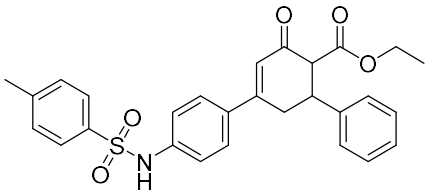
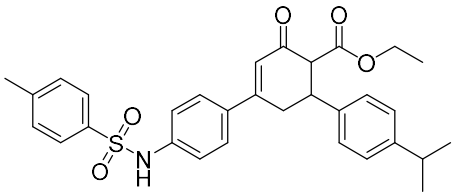
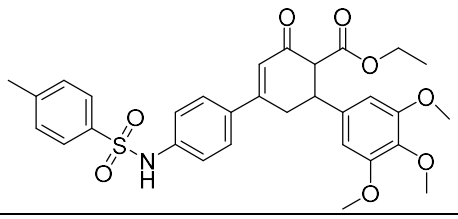
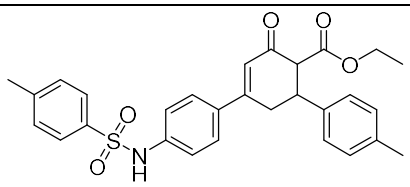
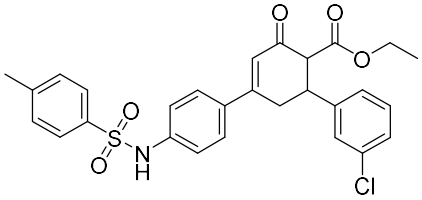
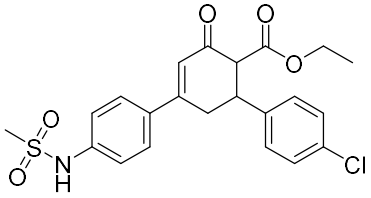
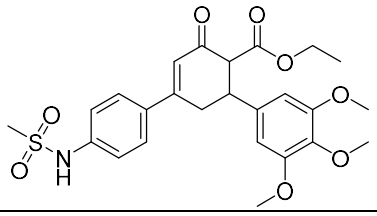
Entry	R^1	R^2	Product	Time (in min)	Yield (%)	Mp (°C)
7h	-Ph	-2-Cl-C_6H_4		50	81	210-211
7i	-Ph	-2-Br-C_6H_4		50	80	224-226
7j	-Ph	-4-CH_3-C_6H_4		70	89	193-194
7k	-Ph	-3-Cl-C_6H_4		50	90	236-237
7l	-4-CH_3-C_6H_4	-Ph		60	90	180-181
7m	-4-CH_3-C_6H_4	-4-$CH(CH_3)_2$-C_6H_4		70	95	211-212
7n	-4-CH_3-C_6H_4	-3,4,5-$(OCH_3)_3$-C_6H_2		70	93	256-257

Table 1 (continued)

Entry	R^1	R^2	Product	Time (in min)	Yield (%)	Mp (°C)
7o	-4-CH_3-C_6H_4	-4-CH_3-C_6H_4		70	80	201-202
7p	-4-CH_3-C_6H_4	-3-Cl-C_6H_4		50	91	240-241
7q	-CH_3	-4-Cl-C_6H_4		50	92	181-182
7r	-CH_3	-3,4,5-$(OCH_3)_3$-C_6H_2		70	84	194-195

Structures of newly synthesized sulfonamide cyclohexenones were characterized by IR, ^{1}H NMR, ^{13}C NMR, mass spectrometric and elemental analysis. IR spectrum clearly indicates two absorption peaks for ketone and ester carbonyl in the range of 1625–1658 cm^{-1} and 1716–1738 cm^{-1} respectively. N-H stretch at absorption band was observed around 3200 cm^{-1} while symmetric and asymmetric stretch of -SO_2NH group was observed around 1080 and 1350 cm^{-1} respectively. In ^{1}H spectrum, there was a singlet around δ 6.3 for the **H_5** proton of C_2-carbon of cyclohexenone ring. Methyl group of ethoxycarbonyl moiety resonated around δ 0.9, while quartet of corresponding methylene group of ethoxycarbonyl group merged with **H_4** and observed as complex multiplets around δ 3.8. The remainder protons **H_1** and **H_2** resonated around δ 2.9, while **H_3** observed as multiplet around δ 3.5 (**Figure 1**). ^{13}C NMR spectra showed requisite number of distinct resonances in agreement with the destined structure. ESI-MS of the compounds showed molecular ion peaks at their respective m/e value.

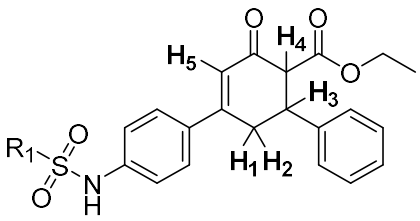


Figure 1. Cyclohexenone scaffold showing different types of proton.

Conclusions

We have illustrated an efficient synthesis of novel sulfonamide cyclohexenones *via* cascade Michael-Aldol reaction in the presence of anhydrous K_2CO_3 under solvent-free condition. The demonstrated protocol is wide in scope with the respect to the change in substituent at both the phenyl rings of the precursor chalcone. The fascinating merits of present protocol are the environmentally friendly conditions, simplicity of reaction, reasonable reaction times, very good yields and simple workup procedure. The synthesized scaffolds are the promising intermediate for further transformation into heterocycles, thus present research work likely to open gateway for the future scope for synthesis of the biologically potential heterocyclic skeletons.

Experimental Section

General. All solvents and chemicals were obtained commercially and were used as received. Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded using a Bruker instrument. NMR spectra were taken with a Bruker Avance II at 400 MHz / Bruker DMX spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) using DMSO-d_6 as the solvent. All chemical shifts are reported in ppm and are referenced to tetramethylsilane using residual ^{1}H signals of the deuterated solvents as internal standards. Electron spray ionization mass spectra were recorded on Bruker microTOFQ spectrometer. Elemental analyses (C, H, N) were obtained using Carlo Erba 1108 analyzer.

General procedure for the synthesis of sulfonamide ketone (3)
Aryl/methane sulphonyl chloride **1** (10 mmol), 4-aminoacetophenone **2** (10 mmol) and triethyl amine (10 mmol) in ethanol (15 ml) were refluxed until the TLC showed the complete consumption of starting material **2** i.e. for 4 hr. After completion of reaction**,** contents were cooled and poured into dilute HCl. The solid obtained was filtered, washed with 2% $NaHCO_3$ and again with water to get crude product which was then recystallized with ethanol- water (1:1) to get pure ketone **3.**

***N*-(4-acetylphenyl)benzenesulfonamide (3a).** Yellow crystal, yield 87 %, mp 126-127° C (lit. 127-130°C)[37].

***N*-(4-acetylphenyl)-4-methylbenzenesulfonamide (3b).** Yellow crystal, yield 90 %, mp 203-204° C (lit. 204-206°C)[38].

***N*-(4-acetylphenyl)methanesulfonamide (3c).** Yellow crystal, yield 85%, mp 157-158 °C (lit. 156-156.5°C)[39].

General procedure for the synthesis of sulfonamide chalcones (5a-5r)

To the solution of **3** (5 mmol) and aldehydes **4** (5 mmol) in ethanol (10 ml), aq. NaOH (10 mmol) was added drop-wise with constant stirring for 30 min during which a yellow cake was formed. It was then kept overnight at room temperature. The solid cake so obtained was acidified with dilute HCl . The solid obtained was filtered, washed with 2% $NaHCO_3$ and again with water to get crude product which was then recrystallized with ethanol to get yellow crystals of **(5a-5r)**.

***N*-(4-cinnamoylphenyl)benzenesulfonamide (5a).** White solid, yield 83%, mp 183-185°C (lit. 180°C),[40] Rf 0.5 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3219 (N-H str), 3057 (Ar C-H str), 1651 (C=O str), 1336 (asymm. S=O str), 1165 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.91 (s, 1H, SO_2NH), 8.04-8.02 (m, 2H, Ar-H), 7.86-7.82 (m, 5H, Ar-H), 7.70-7.56 (m, 4H, Ar-H+CH=CH), 7.44-7.43 (m, 3H, Ar-H), 7.27-7.25 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.87, 144.89, 140.75, 138.86, 134.78, 134.44, 133.44, 130.60, 130.16, 129.26, 128.95, 128.43, 127.19, 121.50, 119.33; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}NO_3S$ m/z 364.0929, observed 364.1125 $[M+H]^+$.

***N*-[4-(3-(4-chlorophenyl)-acryloyl)-phenyl]-benzenesulfonamide (5b).** Yellow solid, yield 74%, mp 200-202°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3280 (N-H str), 3064 (Ar C-H str), 1651 (C=O str), 1301 (asymm. S=O str), 1157 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.96 (s, 1H, SO_2NH), 8.07-8.05 (m, 2H, Ar-H), 7.90-7.85 (m, 5H, Ar-H), 7.69-7.56 (m, 4H, Ar-H+CH=CH), 7.52-7.50 (m, 2H, Ar-H), 7.29-7.25 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.78, 140.97, 140.65, 138.83, 135.47, 134.46, 133.19, 131.20, 130.85, 130.31, 129.27, 127.33, 127.18, 127.06, 124.36, 119.35; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{17}ClNO_3S$ m/z 398.0539, observed 398.0678 $[M+H]^+$.

***N*-[4-(3-(4-fluorophenyl)-acryloyl)-phenyl]-benzenesulfonamide (5c)**. Yellow solid, yield 64%, mp 165-167°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3273 (N-H str), 3066 (Ar C-H str), 1654 (C=O str), 1340 (asymm. S=O str), 1157 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.94 (s, 1H, SO_2NH), 8.06-8.04 (m, 2H, Ar-H), 7.95-7.91 (m, 2H, Ar-H), 7.87-7.80 (m, 4H, Ar-H+CH=CH), 7.70-7.56 (m, 4H, Ar-H), 7.31-7.24 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.84, 165.40, 163.07, 143.75, 143.72, 133.65, 130.57, 130.48, 130.35, 129.45, 127.32, 121.24, 119.43, 116.43, 116.18; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{17}FNO_3S$ m/z 382.0835, observed 382.0983 $[M+H]^+$.

***N*-[4-(3-(4-bromophenyl)-acryloyl)-phenyl]-benzenesulfonamide (5d).** Yellow solid, yield 71%, mp 205-207°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3278 (N-H str), 3055 (Ar C-H str), 1651 (C=C str), 1300 (asymm. S=O str), 1157 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.95 (s, 1H, SO_2NH), 8.06-8.04 (m, 2H, Ar-H), 7.91-7.80 (m, 5H, Ar-H), 7.66-7.58 (m, 6H, Ar-H+CH=CH), 7.26-7.24 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 188.49, 143.39, 140.84, 138.88, 134.25, 133.70, 133.45, 132.22, 130.17, 129.75, 129.27, 127.18, 124.88, 121.98, 119.32; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{17}BrNO_3S$ m/z 444.330, observed 444.0243 $[M+H]^+$.

***N*-(4-(3-(4-isopropylphenyl)acryloyl)phenyl)benzenesulfonamide (5e).** Yellow solid, yield 80%, mp 160-162°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3203 (N-H str), 3030 (Ar C-H str), 1649 (C=O str), 1328 (symm. S=O str), 1163 (asymm. S=O str); ^{1}H NMR (500MHz, DMSO-*d*$_6$): 7.80-7.70 (m, 4H, Ar-H+CH=CH), 7.63 (d, *J* 15.6 Hz, 1H, CH=CH), 7.42-7.37 (m, 3H, Ar-H), 7.33-7.26 (m, 3H, Ar-H), 7.13-7.07 (m, 4H, Ar-H), 2.78 (septet, *J* 6.9 Hz, 1H, C**H**$(CH_3)_2$), 1.11 (d, *J* 6.9 Hz, 6H, CH(C**H$_3$)$_2$**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.13, 152.07, 145.07, 140.82, 138.87, 134.44, 133.38, 132.40, 130.11, 129.23, 128.60, 127.17, 127.07, 120.57, 119.27, 34.11, 23.71; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{24}NO_3S$ m/z 405.1399, observed 405.6184 $[M+H]^+$.

***N*-(4-(3-(furan-2-yl)acryloyl)phenyl)benzenesulfonamide (5f).** Yellow solid, yield 73%, mp 142-144°C, Rf 0.5 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3251 (N-H str), 1604 (C=O str), 1331 (asymm. S=O str), 1156 (symm. S=O str); ^{1}H NMR (300MHz, DMSO-*d*$_6$): 10.93 (s, 1H, NH), 7.97-7.84 (m, 5H, Ar-H), 7.70-7.47 (m, 5H, Ar-H+CH=CH), 7.26-7.24 (m, 2H, Ar-H), 7.06-6.69 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.85, 151.30, 141.51, 133.53, 130.32, 129.30, 128.90, 127.19, 125.18, 124.22, 119.26, 116.51, 114.30, 110.18; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}NO_4S$ m/z 354.0722, observed 354.0846 $[M+H]^+$.

***N*-(4-(3-(3,4,5-trimethoxyphenyl)acryloyl)phenyl)benzenesulfonamide (5g).** Yellow solid, yield 90%, mp 190-192°C, Rf 0.3 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3219 (N-H str), 3080 (Ar C-H str), 1649 (C=O str), 1327 (asymm. S=O str), 1157 (symm. S=O str), 1124 (C-O str); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.94 – 7.84 (m, 4H, Ar-H), 7.70 (d, *J* 14.8 Hz, 1H, CH=CH), 7.58 – 7.45 (m, 3H, Ar-H), 7.33 (d, *J* 15.3 Hz, 1H, CH=CH), 7.22 (s, 2H, Ar-H), 6.89 – 6.79 (m, 2H, Ar-H), 3.91(s, 9H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 188.86, 153.49, 145.08, 140.71, 133.42, 130.14, 129.26, 127.17, 120.84, 119.34, 105.74, 61.00, 56.24; Anal. calcd for $C_{24}H_{23}NO_6S$ (453.50): C, 63.56; H, 5.11; N, 3.09 %. Found: C, 64.38; H, 5.29; N, 3.30 %.

***N*-(4-(3-(2-chlorophenyl)acryloyl)phenyl)benzenesulfonamide (5h).** Yellow solid, yield 72%, mp 169-170°C, Rf 0.6 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3211 (N-H str), 3062 (Ar C-H str), 1649 (C=O str), 1332 (asymm. S=O str), 1168 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.98 (s, 1H, SO_2NH), 8.18-8.15 (m, 1H, CH=CH), 8.08-8.05 (m, 2H, Ar-H), 8.00-7.93 (m, 2H, Ar-H)), 7.89-7.85 (m, 2H, ArH) 7.65-7.55 (m, 4H, Ar-H+CH=CH), 7.47- 7.44 (m,2H, ArH), 7.27-7.25 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.85, 140.90, 140.67, 138.83, 135.47, 134.13, 133.45, 133.16, 131.20, 130.31, 130.29, 129.27, 127.78, 127.18, 127.06, 124.35, 119.30; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{17}ClNO_3S$ m/z 398.0539, observed 398.2441 $[M+H]^+$.

***N*-(4-(3-(2-bromophenyl)acryloyl)phenyl)benzenesulfonamide (5i).** Yellow solid, yield 82%, mp 185-186°C, Rf 0.6 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3208 (N-H str), 3066 (Ar C-H str),

1650 (C=O str), 1338 (asymm. S=O str), 1158 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 – 8.06 (m, 1H, CH=CH), 7.94 – 7.91 (m, 2H, Ar-H), 7.89 – 7.85 (m, 2H, Ar-H), 7.70 (dd, *J* 7.8, 1.6 Hz, 1H, Ar-H), 7.63 (dd, *J* 8.0, 1.3 Hz, 1H, Ar-H), 7.59 – 7.55 (m, 1H, CH=CH), 7.48 (dd, *J* 8.5, 7.1 Hz, 2H, Ar-H), 7.38 – 7.33 (m, 2H, Ar-H), 7.27 – 7.20 (m, 3H, Ar-H); ^{13}C NMR (125 MHz, Chloroform-*d*) δ 188.86, 143.24, 140.91, 138.83, 134.98, 134.10, 133.56, 133.45, 131.35, 130.32, 129.27, 127.86, 127.69, 127.19, 125.85, 124.62, 119.31; Anal. calcd for $C_{21}H_{16}BrNO_3S$ (442.32): C, 57.02; H, 3.65; N, 3.17 %. Found: C, 57.28; H, 3.59; N, 3.30 %.

***N*-(4-(3-(p-tolyl)acryloyl)phenyl)benzenesulfonamide (5j).** Yellow solid, yield 88%, mp 171-172°C, Rf 0.52 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3206 (N-H str), 3048 (Ar C-H str), 1590 (C=O str), 1345 (asymm. S=O str), 1154 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.96 (m, 2H, Ar-H+CH=CH), 7.94 – 7.90 (m, 2H, Ar-H), 7.83 (d, *J* 15.6 Hz, 1H, CH=CH), 7.64 – 7.46 (m, 7H, Ar-H), 7.29 – 7.26 (m, 3H, Ar-H), 2.45 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.00, 145.01, 141.19, 140.67, 138.88, 134.60, 133.41, 132.05, 130.11, 129.70, 129.25, 128.47, 127.19, 120.50, 119.36, 21.52; Anal. calcd for $C_{22}H_{19}NO_3S$ (377.45): C, 70.01; H, 5.07; N, 3.71 %. Found: C, 69.88; H, 5.29; N, 3.60 %.

***N*-(4-(3-(3-chlorophenyl)acryloyl)phenyl)benzenesulfonamide (5k).** Yellow solid, yield 72%, mp 189-190°C, Rf 0.6 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3084 (N-H str), 1648 (C=O str), 1321 (asymm. S=O str), 1152 (symm. S=O str); ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.95 – 7.93 (m, 2H, Ar-H+CH=CH), 7.88 – 7.86 (m, 2H, Ar-H), 7.71 (d, *J* 15.6 Hz, 1H, CH=CH), 7.61 – 7.56 (m, 2H, Ar-H), 7.50 – 7.44 (m, 4H, Ar-H), 7.38 – 7.33 (m, 2H, Ar-H), 7.22 – 7.19 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.37, 143.07, 140.93, 136.63, 134.12, 133.47, 130.39, 130.21, 129.27, 127.84, 127.19, 126.79, 122.68, 119.29; Anal. calcd for $C_{21}H_{16}ClNO_3S$ (397.87): C, 63.39; H, 4.05; N, 3.52 %. Found: C, 63.22; H, 3.92; N, 3.60 %.

***N*-(4-cinnamoylphenyl)-4-methylbenzenesulfonamide (5l).** Yellow solid, yield 83%, mp 162-163°C (lit 160-161°C)[41], Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3219 (N-H str), 3032 (Ar C-H str), 1666 (C=C str), 1336 (asymm. S=O str), 1163 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94-7.92 (m, 2H, Ar-H+CH=CH), 7.80 – 7.75 (m, 3H, Ar-H), 7.62 – 7.61 (m, 2H, Ar-H), 7.47 (d, *J* 15.6 Hz, 1H, CH=CH), 7.42 – 7.40 (m, 3H, Ar-H), 7.27 – 7.21 (m, 4H, Ar-H), 2.38 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.90, 144.82, 144.44, 140.99, 135.85, 134.79, 134.21, 130.58, 130.15, 129.87, 128.94, 128.42, 127.26, 121.52, 119.11, 21.54; Anal. calcd for $C_{22}H_{19}NO_3S$ (377.45): C, 70.01; H, 5.07; N, 3.71 %. Found: C, 70.21; H, 4.92; N, 3.61 %.

***N*-(4-(3-(4-isopropylphenyl)acryloyl)phenyl)-4-methylbenzenesulfonamide (5m).** Yellow solid, yield 86%, mp 184-185°C, Rf 0.5 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3215 (N-H str), 3049 (Ar C-H str), 1670 (C=O str), 1328 (asymm. S=O str), 1157 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.92 (m, 2H, Ar-H+ CH=CH), 7.79 – 7.74 (m, 3H, Ar-H), 7.56 (d, *J* 8.1 Hz, 2H, Ar-H), 7.43 (d, *J* 15.6 Hz, 1H, CH=CH), 7.28 – 7.25 (m, 4H, Ar-H), 7.21 – 7.19 (m, 2H, Ar-H), 2.94 (hept, *J* 7.2 Hz, 1H, C**H**$(CH_3)_2$), 2.38 (s, 3H, CH_3), 1.27 (d, *J* 6.9 Hz, 6H, CH(C**H**$_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.99, 152.07, 144.95, 144.43, 140.80, 135.88, 134.49, 132.46, 130.11, 129.87, 128.60, 127.27, 127.10, 120.62, 119.20, 34.14, 23.74, 21.55; Anal. calcd for $C_{25}H_{25}NO_3S$ (419.53): C, 71.57; H, 6.01; N, 3.34 %. Found: C, 71.68; H, 5.89; N, 3.49 %.

4-methyl-*N*-(4-(3-(3,4,5-trimethoxyphenyl)acryloyl)phenyl)benzensulfonamide (5n). Yellow solid, yield 89%, mp 195-197°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3223 (N-H str), 1651 (C=O str), 1402 (asymm. S=O str), 1153 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.91 (m, 2H, Ar-H+CH=CH), 7.77 – 7.68 (m, 3H, Ar-H), 7.34 (d, *J* 15.5 Hz, 1H, CH=CH), 7.27 – 7.20 (m, 4H, Ar-H), 6.84 (s, 2H, Ar-H), 3.91 (s, 6H, OCH_3), 3.90 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.92, 153.47, 145.02, 144.42, 140.99, 135.91, 134.22, 130.25, 130.12, 129.86, 127.24, 120.85, 119.08, 105.73, 60.98, 56.23, 21.53; Anal. calcd for $C_{25}H_{25}NO_6S$ (467.53): C, 64.23; H, 5.39; N, 3.00 %. Found: C, 64.00; H, 5.65; N, 3.24 %.

4-methyl-*N*-(4-(3-(p-tolyl)acryloyl)phenyl)benzensulfonamide (5o). Yellow solid, yield 84%, mp 208-209°C, Rf 0.58 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3202 (N-H str), 1600 (C=C str), 1333 (asymm. S=O str), 1158 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.92 (m, 2H, Ar-H+CH=CH), 7.78 – 7.74 (m, 3H, Ar-H), 7.53 – 7.51 (m, 2H, Ar-H), 7.43 (d, *J* 15.6 Hz, 1H, CH=CH), 7.27 – 7.19 (m, 6H, Ar-H), 2.39 (s, 3H, CH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.99, 144.93, 144.42, 141.16, 140.85, 135.87, 134.42, 132.07, 130.10, 129.87, 129.70, 128.47, 127.26, 120.52, 119.17, 21.54, 21.52; Anal. calcd for $C_{23}H_{21}NO_3S$ (391.48): C, 70.57; H, 5.41; N, 3.58 %. Found: C, 70.36; H, 5.62; N, 3.71 %.

***N*-(4-(3-(3-chlorophenyl)acryloyl)phenyl)-4-methylbenzenesulfonamide (5p).** Yellow solid, yield 80%, mp 213-214°C, Rf 0.6 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3200 (N-H str), 1658 (C=O str), 1333 (asymm. S=O str), 1155 (symm. S=O str); ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.96 – 7.91 (m, 2H, Ar-H+CH=CH), 7.77 – 7.74 (m, 2H, Ar-H), 7.71 (d, *J* 15.7 Hz, 1H, CH=CH), 7.61 – 7.60 (m, 1H, Ar-H), 7.49 – 7.43 (m, 2H, Ar-H), 7.39-7.33 (m, 2H, Ar-H), 7.26 – 7.24 (m, 2H, Ar-H), 7.22- 7.19 (m,2H, ArH), 2.39 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.39, 144.50, 143.01, 141.14, 136.65, 135.84, 134.99, 133.93, 130.37, 130.21, 129.96, 129.89, 127.84, 127.27, 127.24, 126.78, 122.71, 119.09, 118.97, 21.55; Anal. calcd for $C_{22}H_{18}ClNO_3S$ (411.90): C, 64.15; H, 4.40; N, 3.40 %. Found: C, 64.99; H, 4.42; N, 3.64 %.

***N*-(4-(3-(4-chlorophenyl)acryloyl)phenyl)methanesulfonamide (5q).** Yellow solid, yield 75%, mp 159-161°C, Rf 0.6 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3183 (N-H str), 1651 (C=O str), 1340 (asymm. S=O str), 1140 (symm. S=O str); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* 8.2 Hz, 2H, Ar-H), 7.77 (d, *J* 15.6 Hz, 1H, CH=CH), 7.58 (d, *J* 8.1 Hz, 2H, Ar-H), 7.48 (d, *J* 15.6 Hz, 1H, CH=CH), 7.40 (d, *J* 8.1 Hz, 2H, Ar-H), 7.30 (d, *J* 8.4 Hz, 2H, Ar-H), 3.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.85, 140.18, 134.73, 130.51, 129.40, 128.74, 127.19, 125.17, 124.22, 119.24, 40.20; Anal. calcd for $C_{16}H_{14}ClNO_3S$ (335.80): C, 57.23; H, 4.20; N, 4.17 %. Found: C, 57.47; H, 4.34; N, 3.95 %.

N-(4-(3-(3,4,5-trimethoxyphenyl)acryloyl)phenyl)methanesulfonamide (5r). Yellow solid, yield 78%, mp 170-172°C, Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3208 (N-H str), 1643 (C=O str), 1318 (asymm. S=O str), 1115 (symm. S=O str); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.06 – 8.04 (m, 2H. Ar-H), 7.77 (d, *J* 15.7 Hz, 1H, CH=CH), 7.60 – 7.56 (m, 2H, Ar-H), 7.48 (d, *J* 15.6 Hz, 1H, CH=CH), 7.32 – 7.28 (m, 2H, Ar-H), 3.92 (s, 6H, OCH_3), 3.91 (s, 3H, OCH_3), 3.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.99, 151.36, 134.53, 130.36, 129.19, 128.92,

127.22, 125.12, 124.22, 119.26, 99.98, 61.36, 40.16, 30.75; Anal. calcd for $C_{19}H_{21}NO_6S$ (391.43): C, 58.30; H, 5.41; N, 3.58 %. Found: C, 58.52; H, 5.67; N, 3.32 %.

General procedure for the synthesis of cyclohexenones (7a-7r). A round-bottom flask was charged with sulfonamide chalcones (**5a-5r**) (1 mmol), ethylacetoacetate (1 mmol) and dry K_2CO_3 (2 mmol) and the mixture was heated at 80 °C for specified time (**Table 1**). The reaction progress was monitored by TLC. After completion of reaction, reaction mass is extracted from ethanol and the filtrate was evaporated to dryness. The residue was recrystallized from ethanol to obtain products **7a-7r** with high yield (up to 95%).

Ethyl 6-phenyl-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxylate (7a). Yellow solid, yield 91%, 0.43g, mp 180-181 °C (from EtOH), Rf 0.54 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3217 (N-H str), 1732 (ester C=O str), 1655 (ketone C=O str), 1372 (assym. S=O str), 1080 (symm. S=O str). ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.67-7.65 (m, 2H, Ar-H), 7.38-7.20 (m, 10H, Ar-H), 6.77-6.75 (m, 2H, Ar-H), 6.30 (s, 1H, H_5), 3.94-3.84 (m, 3H, H_4+O**CH_2**CH_3), 3.53-3.45 (m, 1H, H_3), 2.90-2.95 (m, 2H, H_1+H_2), 0.89 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.24, 169.63, 154.95, 147.13, 141.95, 129.13, 128.36, 128.26, 127.86, 126.85, 126.74, 125.96, 122.69, 120.08, 118.70, 117.07, 59.68, 58.73, 34.52, 18.50, 13.79; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{25}NNaO_5S$ is 498.14, found 498.22; Anal. calcd for $C_{27}H_{25}NO_5S$ (475.14): C, 68.19; H, 5.30; N, 2.95 %. Found: C, 68.28; H, 5.36; N, 2.89 %.

Ethyl 6-(4-chlorophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla - te (7b). Yellow solid, yield 80%, 0.40g, mp 235-236 °C (from EtOH), Rf 0.44 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3288 (N-H str), 1732 (ester C=O str), 1658 (ketone C=O str), 1369 (assym. S=O str), 1087 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.75-7.74 (m, 2H, Ar-H), 7.47-7.39 (m, 9H, Ar-H), 6.99-6.97 (m, 2H, Ar-H), 6.41 (s, 1H, H_5), 4.00 (m, 2H, O**CH_2**CH_3), 3.94 (m, 2H, H_3 H_4), 2.94 (m, 2H, H_1, H_2), 0.92 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.68, 169.38, 158.61, 142.73, 140.81, 131.60, 129.61, 128.79, 128.36, 127.49, 126.40, 119.63, 119.49, 60.01, 58.43, 43.00, 34.50, 13.89; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}ClNNaO_5S$ 532.10, observed 532.09; Anal. Calcd for $C_{27}H_{24}ClNO_5S$ (509.10): C, 63.59; H, 4.74; N, 2.75 %. Found: C, 63.43; H, 4.89; N, 2.84 %.

Ethyl 6-(4-fluorophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla - te (7c). Yellow solid, yield 88%, 0.39g, mp 254-255 °C (from EtOH), Rf 0.46 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3116 (N-H str), 1731 (ester C=O str), 1655 (ketone C=O str), 1372 (assym. S=O str), 1084 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.71-7.68 (m, 2H, Ar-H), 7.44-7.33 (m, 7H, Ar-H), 7.14-7.10 (m, 2H, Ar-H), 6.84-6.82 (m, 2H, Ar-H), 6.33 (s, 1H, H_5), 4.102 (m, 1H, H_4), 3.95-3.85 (m, 2H, O**CH_2**CH_3), 3.56-3.49 (m, 1H, H_3), 2.94-2.91 (m, 2H, H_1, H_2), 0.92 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.30, 169.53, 162.32, 159.09, 152.08, 145.60, 139.74, 138.60, 129.50, 128.92, 128.03, 127.14, 126.97, 126.04, 117.97, 115.09, 114.79, 59.80, 58.83, 43.09, 34.54, 13.81; MS (ESI): *m/z* $[M+Na]^+$ calc. for

$C_{27}H_{24}FNNaO_5S$ is 516.13, found 516.38; Anal. calcd for $C_{27}H_{24}FNO_5S$ (493.13): C, 65.71; H, 4.90; N, 2.84 %. Found: C, 65.67; H, 5.01; N, 2.90 %.

Ethyl 6-(4-bromophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla - te (7d). Yellow solid, yield 80%, 0.44g, mp 270-272 °C (from EtOH), Rf 0.46 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3115 (N-H str), 1732 (ester C=O str), 1656 (ketone C=O str), 1369 (assym. S=O str), 1084 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.68-6.74 (m, 13H, Ar-H), 6.30 (s, 1H, H_5), 3.95-3.86 (m, 3H, H_4+O**CH_2**CH_3), 3.54-3.48 (m, 1H, H_3), 2.88-2.84 (m, 2H, H_1+ H_2), 0.93 (t, 3H, *J* 6.8 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 192.99, 169.54, 159.21, 154.03, 146.98, 141.40, 131.17, 129.22, 127.90, 126.01, 122.74, 120.10, 119.95, 117.09, 59.84, 58.46, 43.23, 34.22, 13.83; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}BrNNaO_5S$ is 576.05, found 576.16; Anal. Calcd for $C_{27}H_{24}BrNO_5S$ (553.05): C, 58.49; H, 4.36; N, 2.53 %. Found: C, 58.32; H, 4.59; N, 2.33 %.

Ethyl 6-(4-isopropylphenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxy -late (7e). Yellow solid, yield 95%, 0.49g, mp 199-200 °C (from EtOH), Rf 0.46 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3015 (N-H str), 1725 (ester C=O str), 1634 (ketone C=O str), 1372 (assym. S=O str), 1082 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.68-7.65 (m, 2H, Ar-H), 7.34-7.26 (m, 7H, Ar-H), 7.18-7.15 (m, 2H, Ar-H), 6.76-6.74 (m, 2H, Ar-H), 6.29 (s, 1H, H_5), 3.92-3.83 (m, 3H, H_4+O**CH_2**CH_3), 3.71-3.49 (m, 1H, H_3), 2.97-2.81 (m, 3H, **C**H$(CH_3)_2$+H_1+H_2), 1.19-1.16 (m, 6H, CH(**CH_3**)$_2$), 0.87 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.83, 169.71, 159.39, 158.75, 154.38, 147.87, 141.50, 139.29, 129.16, 127.43, 126.74, 123.53, 120.09, 59.64, 58.84, 43.51, 40.12, 34.67, 33.00, 23.84, 23.84, 13.73; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{30}H_{31}NNaO_5S$ is 540.18, found 540.20; Anal. calcd for $C_{30}H_{31}NO_5S$ (527.18): C, 69.61; H, 6.04; N, 2.71 %. Found: C, 69.43; H, 6.23; N, 2.45 %.

Ethyl 6-(2-furyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxylate (7f). Yellow solid, yield 72%, 0.33g, mp 196-198 °C (from EtOH), Rf 0.40 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3011 (N-H str), 1716 (ester C=O str), 1625 (ketone C=O str), 1372 (assym. S=O str), 1080 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.69-7.68 (m, 3H, Ar-H), 7.35-7.33 (m, 6H, ArH+ furyl H), 6.80-6.77 (m, 2H, Ar-H), 6.39-6.30 (m, 2H, Furyl H+ H_5), 6.23-6.22 (m,1H, Furyl H), 4.05-4.03 (m, 2H, H_4+O**CH_2**CH_3), 3.68 (m, 1H, H_3), 3.12 (m, 1H, H_2), 2.89 (m, 1H , H_1), 1.086 (t, 3H, *J* 6.8 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 192.35, 169.67, 158.77, 155.67, 155.02, 147.64, 141.93, 129.65,129.27, 127.98, 126.65, 122.64, 120.13, 117.17, 110.37, 105.70 ,60.20, 57.11, 38.88, 13.98; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{25}H_{23}NNaO_6S$ is 488.11 found 488.11; Anal. calcd for $C_{25}H_{23}NO_6S$ (465.11): C, 64.50; H, 4.98; N, 3.01 %. Found: C, 64.80; H, 4.86; N, 3.14 %.

Ethyl 6-(3,4,5-trimethoxyphenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-ene - carboxylate (7g). Yellow solid, yield 80 %, 0.45g, mp 241-243 °C (from EtOH), Rf 0.32 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3107 (N-H str), 1720 (ester C=O str), 1630 (ketone C=O str), 1337 (assym. S=O str), 1129 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.64 (s, 1H, NH), 7.81-6.71 (m, 11H, Ar-H), 6.38 (s, 1H, H_5), 3.76 (s, 6H, OCH_3), 3.70 (s, 3H, OCH_3), 3.30-3.35 (m, 3H, H_4+ O**CH_2**CH_3), 2.92 (m, 1H, H_3), 2.82 (m, 1H, H_1), 2.50 (m, 1H, H_2), 0.93 (t, 3H, *J* 7.64 Hz,

$OCH_2\mathbf{CH_3}$); ^{13}C NMR (100 MHz, DMSO-d_6): 198.30, 157.59, 152.81, 139.63, 139.42, 136.09, 132.81, 129.37, 127.59, 126.61, 122.98, 119.03, 104.41, 60.91, 59.92, 57.59, 55.84, 43.50, 35.00, 25.84; MS (ESI): *m/z* $[M+Na]^+$ calc. for $C_{30}H_{31}NNaO_8S$ is 588.17, found 588.15; Anal. calcd for $C_{30}H_{31}NO_8S$ (565.17): C, 63.70; H, 5.52; N, 2.48 %. Found: C, 63.55; H, 5.78; N, 2.31 %.

Ethyl 6-(2-chlorophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla -te (7h). Yellow solid, yield 81%, 0.41g, mp 210-211 °C (from EtOH), Rf 0.44 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3402 (N-H str), 1720 (ester C=O str), 1636 (ketone C=O str), 1370 (assym. S=O str), 1080 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-d_6): 7.68-7.66 (m, 2H , Ar-H), 7.62-7.60 (m, 1H , Ar-H), 7.44-7.41 (m, 1H , Ar-H), 7.35-7.25(m, 7H , Ar-H), 6.77-6.75 (m, 2H , Ar-H), 6.33 (s, 1H, H_5), 4.18 (m, 1H, H_4), 3.89-3.86 (m, 3H, H_3+O$\mathbf{CH_2}CH_3$), 2.93-2.48 (m, 2H, H_1+H_2), 0.89 (t, 3H, *J* 8.0 Hz, $OCH_2\mathbf{CH_3}$); ^{13}C NMR (100 MHz, DMSO-d_6): 197.90, 169.30, 158.82, 155.07, 147.05, 138.89, 132.81, 129.45, 129.20, 128.52, 127.90, 127.45, 126,76, 125.98, 122.98, 122.14, 116.98, 59.87, 57.45, 42.40, 33.32, 13.71; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{27}H_{25}ClNO_5S$ is 510.11, found 510.31; Anal. calcd for $C_{27}H_{24}ClNO_5S$ (509.11): C, 63.59; H, 4.74; N, 2.75 %. Found: C, 63.43; H, 4.56; N, 2.87 %.

Ethyl 6-(2-bromophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-ene carboxyla -te (7i). Yellow solid, yield 80 %, 0.44g, mp 224-226 °C (from EtOH), Rf 0.48 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3056 (N-H str), 1720 (ester C=O str), 1636 (ketone C=O str), 1370 (assym. S=O str), 1080 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-d_6): 7.68-7.65 (m, 3H, Ar-H), 7.62-7.54 (m, 3H, Ar-H), 7.40-7.16 (m, 3H, Ar-H), 6.33 (d, 1H, H_5), 4.20-4.17 (m,1H, H_4), 4.02-3.86 (m, 3H, H_3+O$\mathbf{CH_2}CH_3$), 2.98-2.65 (m, 2H, H_1+H_2), 0.90 (t, 3H, *J* 6.8 Hz, $OCH_2\mathbf{CH_3}$) ^{13}C NMR (100 MHz, DMSO-d_6): 197.10, 169.29, 158.79, 155.08, 147.19, 147.06, 129.21, 128.20, 127.91, 126.99, 126.77, 126.01, 120.15, 116.99, 59.88, 57.54, 42.42, 33.47, 33.04, 13.74; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{27}H_{25}BrNO_5S$ is 554.06, found 554.10; Anal. calcd for $C_{27}H_{24}BrNO_5S$ (553.06): C, 58.49; H, 4.36; N, 2.53 %. Found: C, 58.55; H, 4.18; N, 2.34 %.

Ethyl 6-(4-methylphenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla -te (7j). Yellow solid, yield 89%, 0.44g, mp 193-194 °C (from EtOH), Rf 0.48 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3122 (N-H str), 1733 (ester C=O str), 1658 (ketone C=O str), 1371 (assym. S=O str), 1080 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-d_6): 7.71-7.69 (m, 2H, Ar-H), 7.34-7.24 (m, 7H, Ar-H), 7.12-7.11 (m, 2H, Ar-H), 6.79-6.77 (m, 2H, Ar-H), 6.32 (s, 1H, H_5), 3.92-3.87 (m, 3H, H_4+O$\mathbf{CH_2}CH_3$), 3.46-3.43 (m, 1H, H_3), 2.91-2.85 (m, 2H, H_1+H_2), 2.26 (s, 3H, CH_3), 0.93 (t, 3H, *J* 7.64 Hz, $OCH_2\mathbf{CH_3}$); ^{13}C NMR (100 MHz, DMSO-d_6): 193.42, 169.68, 159.36, 154.80, 147.00, 138.97, 135.90, 129.23, 128.85, 127.92, 127.39, 126.02, 117.18, 59.73, 58.83, 43.46, 39.28, 20.63, 13.87; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{28}H_{27}NNaO_5S$ is 512.15, observed 512.14; Anal. Calcd for $C_{28}H_{27}NO_5S$ (489.15): C, 68.69; H, 5.56; N, 2.86 %. Found: C, 68.74; H, 5.36; N, 2.90 %.

Ethyl 6-(3-chlorophenyl)-2-oxo-4-((4-phenylsulfonamido)phenyl)-cyclohex-3-enecarboxyla -te (7k). Yellow solid, yield 90%, 0.46g, mp 236-237 °C (from EtOH), Rf 0.46 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3131 (N-H str), 1736 (ester C=O str), 1650 (ketone C=O str), 1372 (assym. S=O str), 1085 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-d_6): 7.71-7.69 (m, 2H, Ar-

H), 7.51 (s, 1H, Ar-H), 7.36-7.29 (m, 9H, Ar-H), 6.80-6.78 (m, 1H, Ar-H), 6.33 (s, 1H, H_5), 4.02-3.98 (m, 1H, H_4), 3.92-3.90 (m,2H, O**CH_2**CH_3), 3.58-3.54 (m, 1H, H_3), 2.98-2.90 (m, 2H, H_1+H_2), 0.92 (t, 3H, *J* 6.48 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.00, 169.56, 159.26, 154.84, 146.95, 144.49, 130.19, 129.27, 127.62, 126.92, 126.44, 120.12, 117.06, 59.84, 58.39, 43.50, 34.00, 13.85; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}ClNNaO_5S$ are 532.10, found 532.10; Anal. calcd for $C_{27}H_{24}ClNO_5S$ (509.01): C, 63.59; H, 4.74; N, 2.75 %. Found: C, 63.48; H, 4.44; N, 2.50 %.

Ethyl 6-phenyl-2-oxo-4-((4-(4-methylphenylsulfonamido)phenyl))-cyclohex-3-enecarboxyl - ate (7l). Yellow solid, yield 90 %, 0.44g, mp 180-181 °C (From EtOH), Rf 0.60 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3235 (N-H str), 1724 (ester C=O str), 1637 (ketone C=O str), 1372 (assym. S=O str), 1079 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.55-7.53 (m, 2H, Ar-H), 7.38-7.36 (m, 2H, Ar-H),7.31-7.27 (m, 4H, Ar-H), 7.23-7.19 (m, 1H, Ar-H), 7.12-7.10 (m, 2H, Ar-H), 6.74-6.72 (m, 2H, Ar-H), 6.30 (s, 1H, H_5), 3.93-3.84 (m, 3H, H_4+O**CH_2**CH_3), 3.52-3.45 (m, 1H, H_3), 2.99-2.83 (m, 2H, H_1+H_2), 2.25 (s, 3H, CH_3), 0.89 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.23. 169.64, 159.35, 155.05, 144.26, 141.95, 138.68, 128.33, 128.27, 127.55, 126.97, 122.55, 120.04, 116.98, 59.67, 58.73, 43.85, 34.52, 20.72, 13.79; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{28}H_{27}NNaO_5S$ is 512.15, found 512.34; Anal. calcd for $C_{28}H_{27}NO_5S$ (489.15): C, 63.59; H, 4.74; N, 2.75 %. Found: C, 63.48; H, 4.44; N, 2.50 %.

Ethyl 6-(4-isopropylphenyl)-2-oxo-4-((4-(4-methylphenylsulfonamido)phenyl))-cyclohex-3-enecarboxylate (7m). Yellow solid, yield 95 %, 0.5g, mp 211-212 °C (from EtOH), Rf 0.35 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3171 (N-H str), 1727 (ester C=O str), 1635 (ketone C=O str), 1351 (assym. S=O str), 1083 (symm. S=O str) cm^{-1}; ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.66-7.64 (m, 2H, Ar-H), 7.52-7.50 (m, 2H, Ar-H), 7.29-7.27 (m, 4H, Ar-H), 7.18-7.16 (m, 2H, Ar-H), 7.04-7.02 (m, 2H, Ar-H), 6.42 (s, 1H, H_5), 3.99-3.96 (m, 1H, H_4), 3.91-3.89 (m, 2H, O**CH_2**CH_3), 3.52-3.49 (m, 1H, H_3), 2.93-2.91 (m, 2H, H_1+H_2), 2.84-2.82 (m, 1H, **C**H$(CH_3)_2$), 2.30 (s, 3H, CH_3), 1.16 (d, 6H, *J* 6.84 Hz, CH(**CH_3**)$_2$), 0.87 (t, 3H, *J* 7.24 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.94, 169.44, 158.49, 147.17, 142.17, 138.99, 138.63, 129.38, 127.45, 126.18, 120.32, 119.12, 59.78, 58.78, 43.50, 34.00, 33.05, 23.84, 20.86, 13.73; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{31}H_{33}NNaO_5S$ 554.20, observed 554.18; Anal. calcd for $C_{31}H_{33}NO_5S$ (531.20): C, 70.03; H, 6.26; N, 2.63 %. Found: C, 70.33; H, 6.06; N, 2.40 %.

Ethyl 6-(3,4,5-trimethoxyphenyl)-2-oxo-4-((4-(4-methylphenylsulfonamido)phenyl))-cyclo - hex-3-enecarboxylate (7n). Yellow solid, yield 93%, 0.54g, mp 256-257 °C (from EtOH), Rf 0.20 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3212 (N-H str), 1729 (ester C=O str), 1638 (ketone C=O str), 1327 (assym. S=O str), 1125 (symm. S=O str) cm^{-1}; ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.65 (s, 1H, NH), 7.69-7.62 (m, 4H, Ar-H), 7.35-7.33 (m, 2H, Ar-H), 7.16-7.14 (m, 2H, Ar-H), 6.72 (s, 2H, Ar-H), 6.47 (s, 1H, H_5), 4.12-4.09 (m, 1H, H_4), 3.96-3.94 (m, 2H, O**CH_2**CH_3), 3.74 (s, 6H, OCH_3), 3.62 (s, 3H, OCH_3), 3.56-3.52 (m, 1H, H_3), 2.96-2.91 (m, 2H, H_1+H_2), 2.32 (s, 3H, CH_3), 0.96 (t, 3H, *J* 6.88 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 194.23, 169.44, 158.81, 152.71, 143.55, 140.14, 137.35, 136.51, 136.30, 131.89, 131.89, 129.82, , 127.77, 126.70, 121.59, 118.80, 104.90, 104.40, 60.44, 59.94, 58.55, 55.86, 43.50, 35.00, 20.95, 13.93; MS (ESI): *m/z*

$[M+Na]^+$ calcd for $C_{31}H_{33}NNaO_8S$ 602.18, observed 602.17; Anal. calcd for $C_{31}H_{33}NO_8S$ (579.18): C, 64.23; H, 5.74; N, 2.42 %. Found: C, 64.43; H, 5.87; N, 2.54; %.

Ethyl 6-(4-methylphenyl)-2-oxo-4-((4-(4-methylphenylsulfonamido)phenyl))-cyclohex-3-ene carboxylate (7o). Yellow solid, yield 80%, 0.4g, mp 201-202 °C (from EtOH), Rf 0.37 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3234 (N-H str), 1738 (ester C=O str), 1657 (ketone C=O str), 1370 (assym. S=O str), 1085 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.59-7.57 (m, 2H, Ar-H), 7.30-7.24 (m, 4H, Ar-H), 7.15-7.12 (m, 4H, Ar-H), 6.79-6.77 (m, 2H, Ar-H), 6.32 (s, 1H, H_5), 3.92-3.87 (m, 3H, H_4+O**CH_2**CH_3), 3.46-3.43 (m, 1H, H_3), 2.91-2.85 (m, 2H, H_1+H_2), 2.26 (s, 6H, CH_3), 0.93 (t, 3H, *J* 7.64 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.45, 169.67. 159.89, 153.89, 143.63, 139.10, 138.95, 135.91, 128.86, 128.48, 127.40, 126.16, 123.31, 119.98, 117.39, 59.74, 58.83, 43.50, 34.50, 20.77, 20.64, 13.87; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{29}H_{29}NNaO_5S$ is 504.16, found 504.18; Anal. calcd for $C_{29}H_{29}NO_5S$ (489.16): C, 69.16; H, 5.80; N, 2.78 %. Found: C, 69.23; H, 5.90; N, 2.91 %.

Ethyl 6-(3-chlorophenyl)-2-oxo-4-((4-(4-methylphenylsulfonamido)phenyl))-cyclohex-3-ene carboxylate (7p). Yellow solid, yield 91%, 0.48, mp 240-241 °C (from EtOH), Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 1723 (ester C=O str), 1635 (ketone C=O str), 1369 (assym. S=O str), 1078 (symm. S=O str) cm^{-1}; ^{1}H NMR (400MHz, DMSO-*d*$_6$): 7.58-7.56 (m, 2H, Ar-H), 7.50 (s,1H, Ar-H), 7.36-7.32 (m, 5H, Ar-H), 7.15-7.13 (m, 2H, Ar-H), 6.79-6.76 (m, 2H, Ar-H), 6.33 (s, 1H, H_5), 4.01-3.98 (m, 1H, H_4), 3.92-3.90 (m, 2H, O**CH_2**CH_3), 3.56-3.53 (m, 1H, H_3), 3.01-2.90 (m, 2H, H_1+ H_2), 2.27 (s, 3H, CH_3), 0.92 (t, 3H, *J* 6.84 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 193.04, 169.57, 159.22, 154.13, 144.49, 143.69, 139.08, 132.94, 130.21, 128.49, 127.64, 126.46, 126.16, 123.08, 117.21, 59.86, 58.40, 38.88, 20.79, 13.86; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{28}H_{26}ClNNaO_5S$ 546.11, observed 546.10; Anal. calcd for $C_{28}H_{26}ClNO_5S$ (523.11): C, 64.18; H, 5.00; N, 2.67; %. Found: C, 64.08; H, 5.35; N, 2.76 %.

Ethyl 6-(4-chlorophenyl)-2-oxo-4-(4-methylsulfonamidophenyl)-cyclohex-3-ene carboxyl ate (7q). Yellow solid, yield 92%, 0.41g, mp 181-182 °C (from EtOH), Rf 0.4 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3268 (N-H str), 1726 (ester C=O str), 1652 (ketone C=O str),1334 (assym. S=O str), 1155 (symm. S=O str) cm^{-1}; ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.13 (s, 1H, NH), 7.76-7.71 (m, 2H, Ar-H), 7.34-7.33 (m, 2H, Ar-H), 7.25-7.23 (m, 2H, Ar-H), 6.76 (s, 2H, Ar-H), 6.53 (s, 1H, H_5), 4.16-4.12 (m, 1H, H_4), 3.97-3.96 (m, 2H, O**CH_2**CH_3), 3.63-3.57 (m, 3H, H_1+H_2+H_3), 3.08 (s, 3H, CH_3), 0.98 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): 194.24. 169.45, 158.44, 152.74, 140.74, 137.37, 136.33, 131.73, 127.93, 118.50, 104.96, 59.94, 58.61, 44.00, 35.00, 13.93; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{22}ClNNaO_5S$ is 470.08, found 470.08; Anal. calcd for $C_{22}H_{22}ClNO_5S$ (447.08): C, 58.99; H, 4.95; N, 3.13 %. Found: C, 58.78; H, 4.83; N, 3.07 %.

Ethyl 6-(3,4,5-trimethoxyphenyl)-2-oxo-4-(4-methylsulfonamidophenyl)-cyclohex-3-ene carboxylate (7r). Yellow solid, yield 84 %, 0.42g, mp 194-195 °C (from EtOH), Rf 0.32 (30% EtOAc:Hexane); IR (ν_{max},cm^{-1}): 3208 (N-H str), 1731 (ester C=O str), 1640 (ketone C=O str), 1331 (assym. S=O str), 1144 (symm. S=O str); ^{1}H NMR (400MHz, DMSO-*d*$_6$): 10.13 (s, 1H, NH), 7.75-7.73 (m, 2H, Ar-H), 7.26-7.24 (m, 2H, Ar-H), 6.76 (s, 2H, Ar-H), 6.53 (s, 1H, H_5), 4.16-4.12 (m,

1H, H_4), 3.97-3.96 (m, 3H, O**CH_2**CH_3+H_3), 3.76 (s, 6H, OCH_3), 3.63 (s, 3H, OCH_3), 3.59-3.57 (m, 2H, H_1+H_2), 3.05 (s, 3H, CH_3), 0.98 (t, 3H, *J* 7.2 Hz, OCH_2**CH_3**); ^{13}C NMR (100, MHz, DMSO-d_6): 193.2439,168.7763, 159.3245, 152.7751, 140.7433, 137.3793, 136.2544, 131.7323, 127.3735, 121.5796, 118.0432, 104.5045, 61.4086, 60.4450, 59.9409, 58.5544, 55.8612, 44.0001, 35.079, 20.9553, 13.9312; MS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{29}ClNNaO_8S$ is 526.15 found 526.16; Anal. calcd for $C_{22}H_{22}ClNO_5S$ (503.16): C, 59.63; H, 5.80; N, 2.78 %. Found: C, 59.40; H, 5.77; N, 2.65 %.

Supporting Information

Supporting information (Experimental details, ^{1}H and ^{13}C NMR spectra for the synthesized compounds), associated with this article can be found, in the online version.

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