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Sulfonamide Synthesis via Oxyma-*O*-sulfonates – Compatibility to Acid Sensitive Groups and Solid-Phase Peptide Synthesis

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A milder and more efficient procedure for the synthesis of sulfonamides by activating sulfonic acid groups as the corresponding sulfonate esters of ethyl 2-cyano-2-(hydroxyimino)-acetate (Oxyma) is reported. This method is greener than all other existing protocols for the purpose. Other important advantages lie in (a) its applicability to less nucleophilic anilines under ambient and milder conditions and (b) its compatibility with solid phase peptide synthesis and acid-labile groups such as trityl (Trt) and *t*Bu, which empowers the solid phase synthesis of sulfonamides of various peptides. To illustrate this, the syntheses of three sulfonamide derivatives of the peptide GAILG-NH_2, which is relevant in the context of drug design against type 2 diabetes, are demonstrated by using Fmoc-based solid-phase peptide synthesis (SPPS).

Introduction

The importance of the sulfonamide unit in medicinal chemistry is unabated, as it exhibits a wide range of biological activities.[1] Also, sulfonylation is used as a protection technique for OH and NH functionalities as it enables crystallization and the protecting group can be easily removed under mild conditions.[2]. Moreover, the 2,4-dinitrobenzenesulfonamides (dNBS) of various peptides and amino acids have drawn considerable attention as they are very important synthetically[3] and biologically.[4] To date, most of these transformations have been achieved from sulfonyl chlorides and the corresponding amines in the presence of inorganic/organic bases, which generates stoichiometric amounts of HCl.[5] Owing to the synthetic importance of sulfonamides of peptides and amino acids, it is important to develop a method that acid-labile protecting groups can tolerate, as they can be used as the precursors for native chemoselective ligation (NCL).[3] Furthermore, dNBS are of great interest as they are useful synthons for ureas, thioureas, and thioamides.[6] In addition to their synthetic importance, they have recently drawn attention as antituberculosis drugs as they act as prodrugs for the in vivo generation of SO_2.[7]

A thorough literature survey for the HCl-free synthesis of sulfonamides revealed that only five such synthetic strategies have been disclosed, which includes the methods in which the sulfonic acids have been activated as the corresponding 3-methylimidazolium triflates,[8] pentafluorophenolates,[9] sulfonyl benzotriazoles,[10] *p*-nitrophenolate esters,[1b] and trichlorophenolates.[11] However, all the reported methods need either prolonged heating conditions, harsh reagents such as trifluoromethanesulfonic anhydride (Tf_2O), or the use of harsh bases. Additionally, for less nucleophilic aniline derivatives, strong bases such as lithium hexamethyldisilylamide (LHMDSA) or *n*BuLi are used. Thus, it is important to develop a method in which the sulfonic acid moiety is activated and undergoes amidation under ambient conditions such that there will be no HCl production; such a method would be compatible with all acid-labile groups and resins for Fmoc-based SPPS (Solid Phase Peptide Synthesis). We recently reported a method in which the sulfonic acid is activated as the corresponding *N*-hydroxybenzotriazole ester.[12] However, this methodology has the limitation that triazoles are explosive on heating,[13] although it serves the purpose well.

In addition to the above, we needed an HCl-free method for the synthesis of peptide-based sulfonamides under ambient conditions as part of our drug discovery endeavor for type 2 diabetes. Thus, we began an investigation into auxiliaries that are better leaving groups for the nucleophilic attack of amines to form sulfonamides, while retaining all the benefits of an activated species. In this context, Oxyma [ethyl 2-cyano-2-(hydroxyimino)acetate] was found to be a good candidate as it can be heated [unlike hydroxybenzotriazole (HOBt)] and has been used in peptide synthesis since its introduction as a coupling reagent and a racemization suppressant.[14] The ability of Oxyma to withstand various temperatures also opens a way to prepare the corresponding sulfonate esters.

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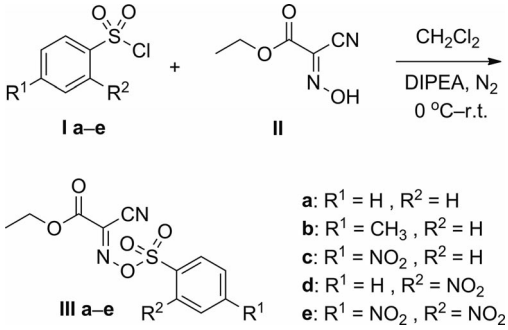
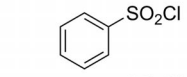
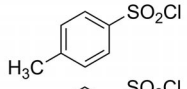
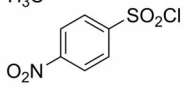
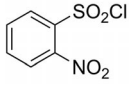
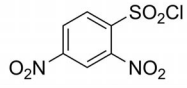
Results and Discussion

Initially, we prepared a few Oxyma esters from sulfonyl chlorides (Scheme 1, Table 1) by using a reported protocol.[15] All the sulfonate esters were characterized by ^1H and ^{13}C NMR spectroscopy and ESI-MS. *p*-NO_2–$C_6H_4SO_3XY$ was also characterized by single-crystal XRD (Figure 1).



Scheme 1. Synthesis of the sulfonate esters of Oxyma.

Table 1. Synthesis of sulfonate esters.

Entry	Sulfonyl chloride	Yield III[a]	Time (h)[b]
1		79	2
2		81	2
3		64	1.5
4		63	1.5
5		71	1.5

[a] Yields refer to the isolated yield after recrystallization. [b] Reaction monitored by TLC every 30 min.

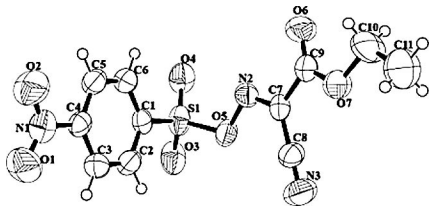
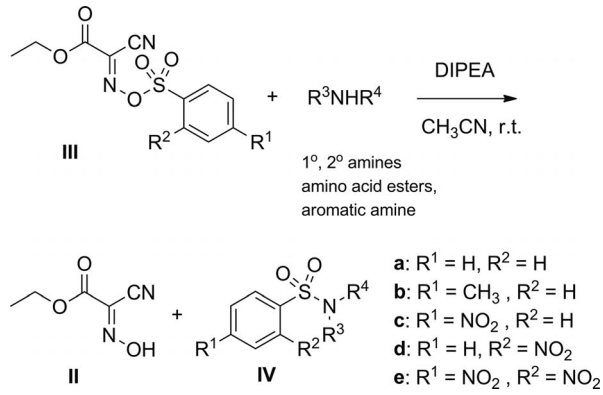


Figure 1. ORTEP diagram for 4-NO_2–Ph–SO_3XY with 50% probability ellipsoids.

With the activated esters in hand, we investigated their ability to undergo amidation with various amines (Scheme 2) in green solvents. Initially, we took (ethyl 2-cyano-2-(tosyloxyimino)acetate (TsOXY) and benzylamine (1 equiv. each) in the presence of 1 equiv. of *N*,*N*-diisopropylethylamine (DIPEA) in acetonitrile. The reaction progressed smoothly and generated the desired product in very good yield within 2 h. This encouraged us to pursue further verification of the applicability of this method to various amines. Although, the reactions work equally well in CH_2Cl_2, we proceeded with acetonitrile with green chemistry aspects in mind.

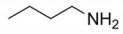
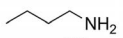
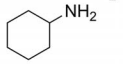
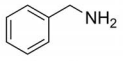
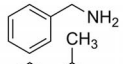
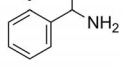
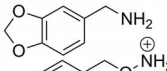
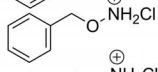
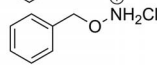
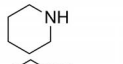
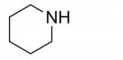
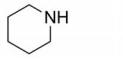
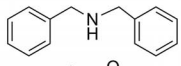
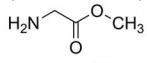
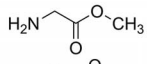
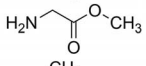
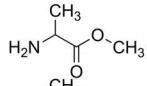
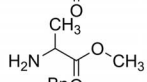
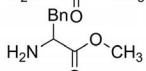
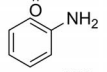
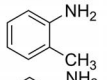
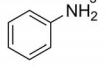
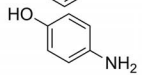
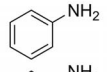
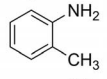
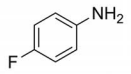


Scheme 2. Synthesis of various sulfonamides.

This methodology is applicable to a wide variety of amines that include primary amines (Table 2, Entries 1–7), protected hydroxylamines (Table 2, Entries 8 & 9), secondary amines (Table 2, Entries 10–13), and amino acid esters including those with sterically hindered side chains (Table 2, Entries 14–19). This methodology is also sensitive electronic and steric factors as its previous counterpart (HOBt).[12] For example, in the case of Table 2, Entries 4 and 6, in which a sterically hindered amine is subjected to the reaction conditions, the yield was found to be lower than that of its sterically less hindered analogue. A similar argument holds for the decrease in the yields of the reactions indicated in Table 2, Entries 15 and 19 respectively.

This method has disadvantages in the case of less nucleophilic amines such as anilines. The change of base from DIPEA to diazabicycloundecene (DBU) and the temperature from ambient to 100 °C did not alter the course of the reaction towards aniline for esters **IIIa**–**b**. However, the presence of electron-withdrawing groups on the benzene ring of the sulfonic acid moiety (e.g., 2,4-dinitrobenzene sulfonate ester of Oxyma (**IIIc and IIIe**)] did make a difference as shown in Table 2, Entries 20–26. However, it is worth mentioning that these reactions with aniline derivatives took slightly longer than those of the other substrates (3 h). Unlike the previous reports, the sulfonamides of anilines were synthesized in good-to-excellent yields without the use of harsh reagents such as *n*BuLi and LHMDSA or elevated temperature.[11]

Table 2. Synthesis of various sulfonamides.

Entry	Sulfonate ester **III**	Amine	Yield **IV**[a]
1	$R^1 = CH_3$, $R^2 = H$		84
2	$R^1 = NO_2$, $R^2 = NO_2$		86
3	$R^1 = CH_3$, $R^2 = H$		89
4	$R^1 = CH_3$, $R^2 = H$		79
5	$R^1 = NO_2$, $R^2 = NO_2$		83
6	$R^1 = CH_3$, $R^2 = H$		61
7	$R^1 = CH_3$, $R^2 = H$		69
8	$R^1 = CH_3$, $R^2 = H$		73
9	$R^1 = H$ $R^2 = NO_2$		76
10	$R^1 = CH_3$, $R^2 = H$		90
11	$R^1 = H$, $R^2 = H$		92
12	$R^1 = NO_2$, $R^2 = H$		96
13	$R^1 = CH_3$, $R^2 = H$		54
14	$R^1 = CH_3$, $R^2 = H$		84
15	$R^1 = NO_2$, $R^2 = H$		88
16	R1 = H, $R^2 = NO_2$		84
17	$R^1 = CH_3$, $R^2 = H$		79
18	$R^1 = NO_2$ $R^2 = NO_2$		74
19	$R^1 = NO_2$, $R^2 = H$		53
20[b]	$R^1 = CH_3$, $R^2 = H$		n.d.
21[b]	$R^1 = CH_3$, $R^2 = H$		n.d.
22[c]	$R^1 = NO_2$, $R^2 = H$		24
23[c]	$R^1 = NO_2$, $R^2 = H$		30
24[c]	$R^1 = NO_2$ $R^2 = NO_2$		56
25[c]	$R^1 = NO_2$ $R^2 = NO_2$		68
26[c]	$R^1 = NO_2$ $R^2 = NO_2$		79

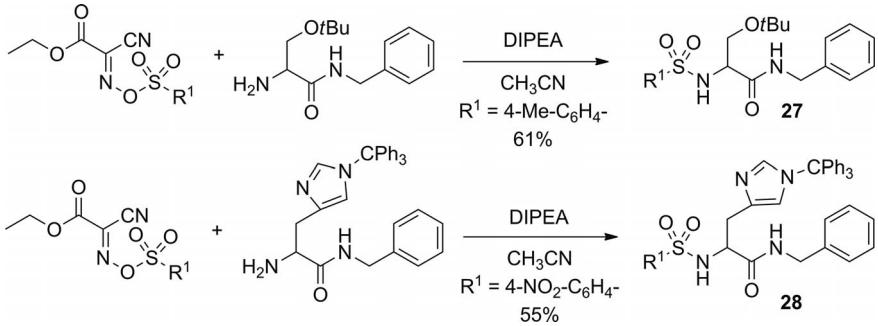
[a] Yields refer to the isolated product after column chromatography. All the reported products were characterized by ^1H NMR spectroscopy and compared with the reported data. The rest are characterized fully and the data is provided in Supporting Information. [b] The reaction was aborted as there was no progress even after 5 h. [c] It took 3 h for the completion of the reaction.

To examine whether the present protocol can tolerate acid-labile groups, we took H-Ser(*t*Bu)–NHBn and H-His(Trt)–NHBn (Scheme 3) and subjected them to the reaction conditions. Interestingly, no significant cleavage of any of these groups was noticed (see Supporting Information). Therefore, the current strategy of synthesizing the sulfonamides of substrates that have acid-labile functionalities makes the sulfonate esters of Oxyma a better auxiliary in the synthesis of natural products and peptide chemistry.

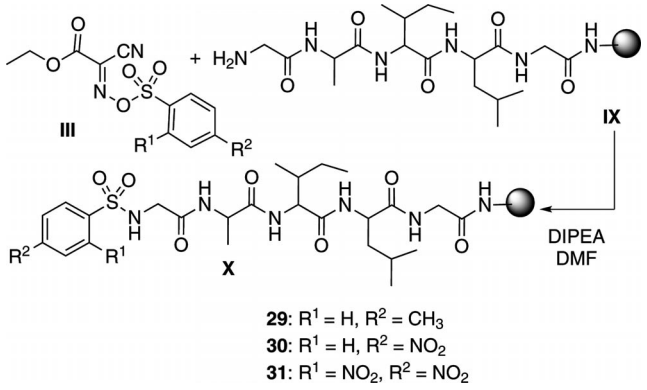
To extend the applicability of the current methodology, we further envisaged the course of the reaction for solid phase peptide synthesis. GAIL is part of the core sequence of the amylin peptide and is believed to be responsible for the initiation of aggregation of amylin, which causes type 2 diabetes. We have coupled the desired amino acid residues on Rink amide MBHA resin following Fmoc/*t*Bu protection. C-terminus glycine was added as a spacer. Sulfonamide attachment at the N-terminus was performed by using 2 or 3 equiv. of the corresponding sulfonate ester of Oxyma (**III**) in the presence of DIPEA (see Supporting Information for Scheme and characterization data). The attempts resulted in good yields of the corresponding sulfonamides of peptide GAILG–NH_2 (Scheme 4), which demonstrates the robustness of the current methodology over the existing reports and compatibility with Fmoc-based SPPS.

Conclusions

We have shown a new activation of sulfonic acid as corresponding Oxyma esters, which has the following advantages: (i) room temperature reactions, (ii) very good to excellent yields, (iii) shorter reaction times compared to those of other activation methods, (iv) easy handling and purification, (v) avoidance of the use of bases such as DBU, *N*-methylmorpholine (NMM), *N*-methylpyrrolidinone (NMP), or NaH, (vi) wide substrate scope (vii) applicability to those substrates that have acid-labile groups such as trityl (Trt) and *t*Bu, and (viii) compatible with Fmoc-based solid phase peptide synthesis strategy. Moreover, the current methodology gives a way for easy synthesis of dNBS derivatives, which are important as antituberculosis drugs. Apart from these, Oxyma is a better auxiliary than its counterparts HOBt, pentafluorophenyl (PFP), *p*-NO_2PhOH, and trichlorophenyl (TCP) in terms of green chemistry practice. Furthermore, if desired, the byproduct Oxyma can be recovered easily and reused for reagent preparation, and can be used in the same pool. Although the present methodology could necessitate the use of sulfonyl chlorides for reagent preparation, it gives access to the HCl-free sulfonamide synthesis under milder conditions. By taking advantage of this acid free sulfonamide synthesis method, we will report the synthesis of some biologically important peptide conjugates in due course.



Scheme 3. Application of the present method to acid-labile substrates.



Scheme 4. Application of the current protocol for the on-resin synthesis of various sulfonamide derivatives of the peptide GAILG–NH_2.

Experimental Section

General Procedure for the Synthesis of Sulfonate Esters from Sulfonyl Chloride and Oxyma: An oven-dried 25 mL round-bottomed flask equipped with a magnetic stir bar was loaded with Oxyma[14] (1 mmol, 1 equiv.) dissolved in dry CH_2Cl_2 (1 mL). To this solution, DIPEA (1 mmol, 1 equiv.) was added under nitrogen. The mixture was cooled to 0 °C, and sulfonyl chloride (1 mmol, 1 equiv.) predissolved in dry dichloromethane (DCM) was added slowly with a syringe over 30 min. The reaction mixture was then stirred at room temperature, and the reaction progress was monitored by TLC. After completion of the reaction, the reaction mixture was washed with saturated NaCl solution (2× 10 mL) and dried with anhydrous $CaCl_2$. It was then dried in vacuo and purified by recrystallization from hexane and CH_2Cl_2.

General Procedure for the Synthesis of Sulfonamides from the Sulfonate Esters of Oxyma: An oven-dried 25 mL round-bottomed flask equipped with a magnetic stir bar was loaded with Oxyma sulfonate (1 mmol, 1 equiv.) dissolved in CH_3CN (1 mL). To this solution, a solution of amine (1 mmol, 1 equiv.) and DIPEA (1 mmol, 1 equiv.) in CH_3CN (1 mL) was added slowly over 2 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was concentrated by rotary evaporation, diluted with ethyl acetate (10 mL), washed with 5% HCl (3× 10 mL), 5% $NaHCO_3$ (3× 10 mL), and saturated NaCl solution (2× 10 mL), and dried with anhydrous Na_2SO_4. The product was dried in vacuo and purified by column chromatography.

General Procedure for the Solid Phase Synthesis of Sulfonamide Derivatives of Peptide from the Sulfonate Esters of Oxyma: To the resin-connected peptide, which was synthesized by using a solid phase peptide synthesis strategy following Fmoc/*t*Bu protection on Rink amide MBHA resin (Scheme is provided in Supporting Information), 2 or 3 equiv. of the corresponding sulfonate esters and DIPEA (2.5 equiv.) in *N*,*N*-dimethylformamide (DMF, 1 mL) were added into a sintered syringe and subjected to gentle rotation by using a blood tube rotator. The reaction was monitored by using the Kaiser test. After completion, the reaction mixture was thoroughly washed with DMF (five times). The peptide was then cleaved from the resin by using a trifluoroacetic acid/dichloromethane (TFA/DCM) cleavage cocktail followed by precipitation with cold ether. The peptide was purified by semipreparative HPLC followed by lyophilization. The yields reported are for peptides purified as mentioned above.

(*E*)-Ethyl 2-Cyano-2-(phenylsulfonyloxyimino)acetate: This compound (Table 2, Entry 1) was prepared by using the general procedure for the synthesis of sulfonate esters. R_f = 0.48 (EtOAc/hexane 1:4). Yield 223 mg, 79%, colorless crystalline solid, m.p. 96 °C. IR (KBr): $\tilde{\nu}$ = 3093, 2977, 1754, 1591, 942, 764 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.04–5.02 (m, 2 H, 2× Ar*H*), 7.75–7.73 (m, 1 H, 1× Ar*H*), 7.62–7.59 (m, 2 H, 2× Ar*H*), 4.41–4.36 (q, 2 H, CH_2), 1.37–1.33 (t, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 135.8, 133.1, 131.5, 129.7, 129.4, 106.1, 64.7, 13.8 ppm. HRMS (ESI): calcd. for $C_{11}H_{11}N_2O_5S$ $[M + H]^+$ 283.0389; found 283.0384.

(*E*)-Ethyl 2-Cyano-2-(tosyloxyimino)acetate: This compound (Table 1, Entry 2) was prepared by using the general procedure for the synthesis of sulfonate esters. R_f = 0.46 (EtOAc/hexane 1:4). Yield 240 mg, 81%, colorless crystalline solid, m.p. 70–71 °C. IR (KBr): $\tilde{\nu}$ = 3011, 2923, 1759, 1593, 949, 769 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.35–7.33 (d, J = 8 Hz, 2 H, 2× Ar*H*), 4.37–4.31 (q, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 1.30 (t, J = 7.6 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 147.5, 131.5, 130.4, 130.1, 129.5, 106.2, 64.6, 21.9, 13.9 ppm. MS (ESI): m/z = 297.05 $[M + H]^+$.

(*E*)-Ethyl 2-Cyano-2-(4-nitrophenylsulfonyloxyimino)acetate: This compound (Table 1, Entry 3) was prepared by using the general procedure for the synthesis of sulfonate esters. R_f = 0.42 (EtOAc/hexane 1:4). Yield 209 mg, 64%, pale yellow solid, m.p. 111 °C. IR (KBr): $\tilde{\nu}$ = 3113, 2991, 1768, 1604, 932, 745 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.40–8.39 (d, J = 6.8 Hz, 2 H, 2× Ar*H*), 8.21–8.8.18 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 4.39–4.34 (q, 2 H, CH_2), 1.39–1.30 (t, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 151.9, 138.7, 132.7, 131.1, 124.9, 105.9, 65.1, 14.0 ppm. MS (ESI): m/z = 328.02 $[M + H]^+$.

(*E*)-Ethyl 2-Cyano-2-(2-nitrophenylsulfonyloxyimino)acetate: This compound (Table 1, Entry 4) was prepared by using the general

procedure for the synthesis of sulfonate esters. R_f = 0.58 (EtOAc/hexane 1:4). Yield 246 mg, 75%, colorless crystalline solid, m.p. 113 °C. IR (KBr): ṽ = 3103, 2988, 1748, 1544, 928, 742 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27–8.25 (d, J = 8.0 Hz, 1 H, 1× Ar*H*), 7.95–7.85 (m, 3 H, 3× Ar*H*), 4.47–4.42 (q, 2 H, CH_2), 1.40–1.37 (t, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 148.0, 137.1, 133.4, 132.8, 126.3, 125.5, 105.9, 65.1, 13.9 ppm. HRMS (ESI): calcd. for $C_{11}H_{10}N_3O_7S$ [M + H]$^+$ 328.0239; found 328.0237.

(*E*)-Ethyl 2-Cyano-2-(2,4-dinitrophenylsulfonyloxyimino)acetate: This compound (Table 1, Entry 5) was prepared by using the general procedure for the synthesis of sulfonate esters. R_f = 0.39 (EtOAc/hexane 1:4). Yield 201 mg, 54%, yellow crystalline solid, m.p. 109 °C. IR (KBr): ṽ = 3121, 2989, 1752, 1602, 985, 767 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.91–8.90 (d, J = 2.4 Hz, 1 H, 1× Ar*H*), 8.54–8.50 (m, 1 H, 1× Ar*H*), 7.95–7.92 (d, J = 9.2 Hz, 1 H, 1× Ar*H*), 4.51–4.46 (q, 2 H, 2× CH_2), 1.40–1.37 (t, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 154.2, 144.0, 137.5, 131.7, 129.6, 118.8, 106.6, 64.9, 14.0 ppm. HRMS (ESI): calcd. for $C_{11}H_9N_4O_9S$ [M + H]$^+$ 373.0090; found 373.0098.

***N*-Butyl-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 1) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.52 (EtOAc/hexane 1:4). Yield 275 mg, 84%, white solid, m.p. 44 °C. IR (KBr): ṽ = 3470, 3090, 1652, 1358, 1163 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77–7.75 (d, J = 8 Hz, 2 H, 2× Ar*H*), 7.31–7.29 (d, J = 8 Hz, 2 H, 2× Ar*H*), 5.12 (br. s, 1 H, N*H*), 2.91 (t, J = 6.8 Hz, 2 H, NHCH_2), 2.42 (s, 3 H, CH_3), 1.45–1.41 (m, 2 H, NHCH$_2$CH_2), 1.30–1.25 (m, 2 H, CH_2CH$_3$), 0.85–0.83 (t, J = 5.6 Hz, 3 H, CH$_2$CH_3) ppm. MS (ESI): m/z = 228.10 [M + H]$^+$

***N*-Butyl-2,4-dinitrobenzenesulfonamide:** This compound (Table 2, Entry 2) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 1:6). Yield 261 mg, 86%, pale yellow solid, m.p. 151 °C. IR (KBr): ṽ = 3262, 2943, 1729, 1532, 1350, 1336, 1236, 1159, 830, 736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.14–9.13 (d, J = 2.4 Hz, 1 H, 1× Ar*H*), 8.56 (s, 1 H), 8.28–8.28 (d, ^1J = 2.4, 2.8 Hz, 1 H, 1× Ar*H*), 6.94–6.91 (d, 1 H, 1× Ar*H*), 3.44–3.40 (m, 2 H, CH_2CH$_2$), 1.81–1.74 (m, 2 H, CH$_2$CH_2CH$_2$), 1.54–1.48 (m, 2 H, CH$_2$CH$_2$CH_2), 1.03–0.98 (m, 3 H, CH$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 135.5, 130.1, 129.9, 123.9, 114.1, 43.2, 30.6, 20.0, 13.5 ppm. MS (ESI): m/z = 304.06 [M + H]$^+$.

***N*-Cyclohexyl-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 3) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.61 (EtOAc/hexane 1:4). Yield 226 mg, 89%, white solid, m.p. 87–89 °C. IR (KBr): ṽ = 3328, 2937, 1755, 1684 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.77 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.32–7.28 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 4.97 (br. s, 1 H, N*H*), 3.11–3.09 (m, 1 H, NHC*H*), 2.42 (s, 3 H, CH_3), 1.74–1.72 (m, 4 H, 2× NHCHCH_2), 1.63–1.60 (m, 4 H, 2× NHCHCH$_2$CH_2), 1.27–1.07 (m, 2 H, NHCHCH$_2$CH$_2$CH_2) ppm. MS (ESI): m/z = 254.12 [M + H]$^+$.

***N*-Benzyl-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 4) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.58 (EtOAc/hexane 1:4). Yield 206 mg, 79%, white solid, m.p. 87–89 °C. IR (KBr): ṽ = 3262, 3027, 1594, 1492, 1450, 1320, 1156 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77–7.75 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.31–7.26 (m, 5 H, 5× Ar*H*), 7.20–7.18 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 4.74 (br. s, 1 H, N*H*), 4.11 (s, 2 H, CH_2), 2.43 (s, 3 H, CH_3) ppm. MS (ESI): m/z = 261.02 [M]$^+$.

***N*-Benzyl-2,4-dinitrobenzenesulfonamide:** This compound (Table 2, Entry 5) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane, 1:6). Yield 298 mg, 83%, white solid, m.p. 151 °C. IR (KBr): ṽ = 3379, 3096, 2346, 1532, 1336, 1159 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.16–9.15 (s, J = 2.4 Hz, 1 H, 1× Ar*H*), 8.91 (s, 1 H, 1× Ar*H*), 8.24–8.21 (dd, ^1J = 2.4, ^2J = 2.8 Hz, 1 H, 1× ArH), 7.43–7.26 (m, 5 H, 5× Ar*H*), 6.92–6.90 (d, J = 5.2 Hz, 1 H, 1× Ar*H*), 4.66–4.64 (d, ^1J = 5.6 Hz, 2 H, CH$_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 136.2, 135.7, 130.6, 130.2, 129.2, 128.2, 127.1, 124.0, 114.6, 47.4 ppm. MS (ESI): m/z = 338.04 [M]$^+$.

4-Methyl-*N*-(1-phenylethyl)benzenesulfonamide: This compound (Table 2, Entry 6) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.46 (EtOAc/hexane 1:4). Yield 168 mg, 61%, white solid, m.p. 78 °C. IR (KBr): ṽ = 3307, 2931, 2854, 1926, 1597, 1494, 1427, 1159, 1092, 925 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.53 (d, J = 8 Hz, 2 H, 2× Ar*H*), 7.09–7.07 (d, J = 8 Hz, 5 H, 5× Ar*H*), 7.02–7.01 (m, 2 H, 2× Ar*H*), 5.22–5.21 (d, J = 3.6 Hz, 1 H, N*H*), 4.38–4.35 (t, J = 12 Hz, 1 *H*, C*H*Ar), 2.29 (s, 3 H, ArCH_3), 1.33–1.32 (d, J = 6.8 Hz, 3 H, CHCH_3) ppm. MS (ESI): m/z = 276.10 [M + H]$^+$.

***N*-(Benzo-1,3-dioxol-5-ylmethyl)-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 7) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.59 (EtOAc/hexane 2:3). Yield 211 mg, 69%, white solid, m.p. 139 °C (lit. 134–137 °C). IR (KBr): ṽ = 3268, 1586, 1337, 1263, 1089, 926 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.33–7.31 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 6.58–6.65 (m, 3 H, 2× Ar*H*), 5.9 (s, 2 H, CH_2), 4.92 (t, J = 6.4 Hz, N*H*), 4.20 (d, J = 6.4 Hz, 2 H, CH_2), 2.43 (s, 3 H, CH_3) ppm. MS (ESI): m/z = 306.08 [M + H]$^+$.

***N*-Benzyloxy-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 8) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.46 (EtOAc/hexane 1:6). Yield 202 mg, 73%, white solid, m.p. 74 °C (lit. 72 °C). IR (KBr): ṽ = 3268, 1586, 1337, 1263, 1089, 926 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.80 (d, J = 8.0 Hz, 2 H, 2× Ar*H*), 7.37–7.26 (m, 7 H, 2× Ar*H*), 4.97 (s, 2 H, CH_2), 2.43 (s, 3 H, CH_3) ppm. MS (ESI): m/z = 278.08 [M + H]$^+$.

***N*-Benzyloxy-4-nitrobenzenesulfonamide:** This compound (Table 2, Entry 9) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.42 (EtOAc/hexane 1:4). Yield 234 mg, 76%, white solid, m.p. 91–93 °C. IR (KBr): ṽ = 2946, 1739, 1446, 1337, 1263 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.02 (d, 1 H, 1× Ar*H*), 8.71–8.69 (dd, J = 2.8 Hz, 1 H, 1× Ar*H*), 8.41–8.38 (dd, J = 2.6 Hz, 1 H, 1× Ar*H*), 8.18–8.04 (m, 2 H, 2× Ar*H*), 8.76–7.26 (m, 4 H, 4× Ar*H*), 5.06 (s, 2 H, CH_2) ppm. MS (ESI): m/z = 309.05 [M + H]$^+$.

1-Tosylpiperidine: This compound (Table 2, Entry 10) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.42 (EtOAc/hexane 1:4). Yield 216 mg, 90%, white solid, m.p. 82 °C. IR (KBr): ṽ = 2946, 1739, 1446, 1337, 1263 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.33–7.31 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 2.97 (t, J = 5.6 Hz, 4 H, 2× CH_2), 2.43 (s, 3 H, CH_3), 1.66–1.61 (m, 4 H, 2× CH_2), 1.42–1.39 (m, 2 H, CH_2) ppm. MS (ESI): m/z = 240.10 [M + H]$^+$.

1-(Phenylsulfonyl)piperidine: This compound (Table 2, Entry 11) was prepared by using the general procedure for the synthesis of

sulfonamides from sulfonate esters of Oxyma. R_f = 0.42 (EtOAc/hexane 1:4). Yield 207 mg, 92%, white solid, m.p. 91–93 °C. IR: $\tilde{\nu}$ = 1630, 1485, 1470, 1450, 1340, 1180 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.33–7.31 (d, J = 8.4 Hz, 3 H, 3× Ar*H*), 2.97 (t, J = 5.6 Hz, 4 H, 2× CH_2), 1.66–1.61 (m, 4 H, 2× CH_2), 1.42–1.39 (m, 2 H, CH_2) ppm. MS (ESI): m/z = 226.09 $[M + H]^+$.

1-(4-Nitrophenylsulfonyl)piperidine: This compound (Table 2, Entry 12) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.51 (EtOAc/hexane 1:4). Yield 281 mg, 96%, yellow solid, m.p. 174 °C. IR (KBr): $\tilde{\nu}$ = 3113, 2928, 1608, 1525, 1160, 1073 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.30 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 7.88–7.86 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 2.99–2.94 (m, 4 H, 2× NCH_2), 1.62–1.55 (m, 4 H, 2× NCH_2CH_2), 1.40–1.37 (m, 2 H, NHCH_2CH_2CH_2) ppm. MS (ESI): m/z = 293.10 $[M + Na]^+$.

***N*,*N*-Dibenzyl-4-methylbenzenesulfonamide:** This compound (Table 2, Entry 13) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.38 (EtOAc/hexane 1:4). Yield 189 mg, 54%, colorless crystalline solid. IR (KBr): $\tilde{\nu}$ = 3012, 2976, 1739, 1455, 1337, 1263 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.70 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.29–7.27 (d, J = 8.0 Hz, 2 H, 2× Ar*H*), 7.20–7.18 (m, 6 H, 6× Ar*H*), 7.04–7.01 (m, 4 H, 4× Ar*H*), 4.29 (s, 4 H, 2× CH_2), 2.42 (s, 3 H, CH_3) ppm. MS (ESI): m/z = 351.13 $[M]^+$.

Methyl 2-(4-Methylphenylsulfonamido)acetate: This compound (Table 2, Entry 14) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 1:6). Yield 204 mg, 84%, white solid, m.p. 151 °C. IR (KBr): $\tilde{\nu}$ = 3262, 2943, 1729, 1532, 1350, 1336, 1236, 1159, 830, 736 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.77–7.74 (d, J = 8 Hz, 2 H, 2× ArH), 7.32–7.30 (d, J = 8 Hz, 2 H, 2× Ar*H*), 5.06 (br. s, 1 H, N*H*), 3.80 (d, J = 4 Hz, 2 H, CH_2), 3.64 (s, 3 H, OCH_3), 2.43 (s, 3 H, CH_3) ppm. MS (ESI): m/z = 244.06 $[M + H]^+$.

Methyl (4-Nitrophenylsulfonylamino)acetate: This compound (Table 2, Entry 15) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.26 (EtOAc/hexane 1:4). Yield 241 mg, 88%, pale yellow solid. IR (KBr): $\tilde{\nu}$ = 3344, 1743, 1541, 1403, 1369, 1347, 1225, 1163, 1127, 837, 785 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.36–8.34 (d, J = 9.2 Hz, 2 H, 2× Ar*H*), 8.06–8.04 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 5.35 (br. s, 1 H, N*H*), 3.86 (d, J = 4 Hz, 2 H, CH_2), 3.65 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 152.3, 148.4, 126.4, 124.2, 50.4, 41.8 ppm. MS (ESI): m/z = 274.03 $[M]^+$.

Methyl (2-Nitrophenylsulfonylamino)acetate: This compound (Table 2, Entry 16) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.58 (EtOAc/hexane 1:9). Yield 230 mg, 84%, pale yellow solid, m.p. 109 °C. IR (KBr): $\tilde{\nu}$ = 3305, 1752, 1539, 1439, 1358, 1208, 1169, 976 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 1 H, Ar*H*), 7.95–7.92 (m, 1 H, Ar*H*), 7.76–7.73 (m, 2 H, 2× Ar*H*), 6.08 (br. s, 1 H, N*H*), 4.02 (s, 2 H, CH_2), 3.61 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 147.6, 135.8, 133.5, 132.8, 129.4, 122.5, 52.6, 48.7 ppm. MS (ESI): m/z = 275.03 $[M + H]^+$.

Methyl 2-(4-Methylphenylsulfonamido)proponoate: This compound (Table 2, Entry 17) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.58 (EtOAc/hexane 1:9). Yield 203 mg, 79%, white solid, m.p. 137–139 °C. IR (KBr): $\tilde{\nu}$ = 3342, 3026, 1734, 1589, 1340, 1160 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.72 (d, J = 8 Hz, 2 H, 2× ArH), 7.30–7.28 (d, J = 8 Hz, 2 H, 2× Ar*H*), 5.37 (d, J = 8.4 Hz, 1 H, N*H*), 4.00–3.96 (q, J = 7.2 Hz, 1 H, C*H*), 3.54 (s, 3 H, OCH_3), 2.42 (s, 3 H, CH_3), 1.38–1.37 (d, J = 7.2 Hz, 3 H, CH_3) ppm. MS (ESI): m/z = 242.08 $[M + H]^+$.

Methyl 2-(2,4-Dinitrophenylsulfonamido)propanoate: This compound (Table 2, Entry 18) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 1:6). Yield 247 mg, 74%, colorless foam. IR (KBr): $\tilde{\nu}$ = 2934, 1727, 1548, 1346, 1332, 830, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.75 (d, J = 2.4 Hz, 1 H, 1× Ar*H*), 8.29 (dd, ^1J = 2.4, ^1J = 2.8 Hz, 1 H, 1× Ar*H*), 6.14 (dd, 1 H, 1× Ar*H*), 4.32 (m, 1 H, α-C*H*), 3.59 (s, 1 H, N*H*), 3.56 (s, 3 H, OCH_3), 1.53 (d, J = 7.2 Hz, 3 H, CH_3) ppm. MS (ESI): m/z = 334.03 $[M + H]^+$.

Methyl 2-(4-Nitrophenylsulfonamido)-3-phenylproponoate: This compound (Table 2, Entry 19) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.23 (EtOAc/hexane 1:4). Yield 193 mg, 53%, pale yellow solid, m.p. 153 °C. IR (KBr): $\tilde{\nu}$ = 3272, 1722, 1523, 1347, 1313, 1168, 1092, 1008, 855, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = (400 MHz, $CDCl_3$) 8.16–8.14 (d, J = 8 Hz, 2 H, 2× Ar*H*), 7.78–7.76 (d, J = 8 Hz, 2 H, 2× Ar*H*), 7.16–7.14 (m, 3 H, 3× Ar*H*), 6.99–6.96 (m, 2 H, 2× Ar*H*), 5.30 (s, 1 H, N*H*), 4.21–4.16 (m, 1 H, C*H*), 3.54 (s, 3 H, OC*H*$_3$), 3.07–3.02 (dd, ^1J = 5.6, ^2J = 4.8 Hz, 1 H, C*H*HAr), 3.00–2.94 (dd, ^1J = 7.2, ^2J = 7.2 Hz, 1 H, CH*H*Ar) ppm. MS (ESI): m/z = 365.08 $[M + H]^+$.

4-Nitro-*N*-phenylbenzenesulfonamide: This compound (Table 2, Entry 22) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.38 (EtOAc/hexane 2:3). Yield 67 mg, 24%, pale yellow crystalline solid, m.p. 172 °C. IR (KBr): $\tilde{\nu}$ = 3279, 1337, 1159, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.30 (d, J = 8.8 Hz, 2× Ar*H*), 7.90–7.88 (d, J = 8.4 Hz, 2× Ar*H*), 7.29 (t, J = 6.8 Hz, 2× Ar*H*), 7.21 (t, J = 7.2 Hz, 1× Ar*H*), 7.22–7.18 (m, 1× Ar*H*), 7.08 (d, J = 8.4 Hz, 2× Ar*H*), 6.57 (br. s, 1N*H*) ppm. MS (ESI): m/z = 279.04 $[M + H]^+$.

***N*-(4-Hydroxyphenyl)-4-nitrobenzenesulfonamide:** This compound (Table 2, Entry 23) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 3:2). Yield 88 mg, 30%, white solid. m.p. 172 °C. IR (KBr): $\tilde{\nu}$ = 3320, 1324, 1159, 920 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.34–8.32 (d, J = 8.8 Hz, 2× Ar*H*), 7.99–7.97 (d, J = 8.4 Hz, 2× Ar*H*), 6.72–6.69 (d, J = 8.8 Hz, 2× Ar*H*), 6.52–6.50 (d, J = 8.8 Hz, 2× Ar*H*), 3.73 (br. s, O*H*) ppm. MS (ESI): m/z = 295.03 $[M + H]^+$.

2,4-Dinitro-*N*-phenylbenzenesulfonamide: This compound (Table 2, Entry 24) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.26 (EtOAc/hexane 1:4). Yield 181 mg, 56%, pale yellow solid, m.p. 112–115 °C. IR (KBr): $\tilde{\nu}$ = 3344, 1743, 1541, 1403, 1369, 1347, 1225, 1163, 1127, 837, 785 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.72 (s, 1 H, 1× Ar*H*), 9.18 (s, 1 H, 1× Ar*H*), 8.17–8.15 (d, J = 9.6 Hz, 1 H, 1× Ar*H*), 7.50–7.47 (m, 2 H, 2× Ar*H*), 7.42–7.38 (m, 1 H, 1× Ar*H*), 7.31–7.25 (m, 2 H, 2× Ar*H*) ppm. MS (ESI): m/z = 324.02 $[M + H]^+$.

2,4-Dinitro-*N*-*o*-tolylbenzenesulfonamide: This compound (Table 2, Entry 25) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 1:6). Yield 229 mg, 68%, white solid, m.p. 151 °C. IR (KBr): $\tilde{\nu}$ = 3262, 2943, 1729, 1532, 1350, 1336, 1236, 1159, 830, 736 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.82 (s, 1 H, 1× Ar*H*),

9.17 (d, J = 2.8 Hz, 1 H, 1× Ar*H*), 8.75–8.74 (d, J = 2.4 Hz, 1 H, 1Ar× *H*), 8.41–8.38 (dd, J = 2.8 Hz, 1 H, 1× Ar*H*), 8.15–8.12 (dd, J = 2.8 Hz, 1 H, 1× Ar*H*), 7.82–7.78 (m, 1 H, 1× Ar*H*), 7.40–7.24 (m, 2 H, 2× Ar*H*), 2.26 (s, 3 H, C*H*$_3$) ppm. HRMS (ESI): calcd. for $C_{13}H_{12}N_3O_6S$ $[M + H]^+$ 338.0447; found 338.0448.

***N*-(4-Fluorophenyl)-2,4-dinitrobenzenesulfonamide:** This compound (Table 2, Entry 26) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.21 (EtOAc/hexane 1:6). Yield 270 mg, 79%, white solid, m.p. 129 °C. IR (KBr): ṽ = 3286, 1552, 1350, 1165 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.04 (s, 1 H), 8.87 (s, 1 H, 1× Ar*H*), 8.60–8.58 (d, J = 8.6 Hz, 1 H, 1× Ar*H*), 8.19–8.16 (dd, ^1J = 1.9, ^2J = 2.4 Hz, 1 H), 7.14–7.15 (m, 4 H, 4× Ar*H*) ppm. MS (ESI): m/z = 342.01 $[M + H]^+$.

***N*-Benzyl-3-*tert*-butoxy-2-(tolyl-4-sulfonylamino)propionamide:** This compound (**27**) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.09 (EtOAc). Yield 259 mg, 61%, red semisolid. IR (KBr): ṽ = 3276, 1552, 1364, 1165 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.89 (d, J = 8.4 Hz, 2 H, 2× Ar*H*), 7.72–7.66 (m, 2 H, 2× Ar*H*), 7.40–7.35 (m, 3 H, 3× Ar*H*), 7.30–7.27 (m, 2 H, 2× Ar*H*), 5.71 (s, 2 H, CH_2), 4.41–4.36 (m, 2 H, CH_2), 2.46 (s, 3 H, CH_3), 1.36 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 144.6, 142.1, 136.7, 109.9, 109.2, 100.6, 76.1, 68.1, 61.6, 54.2, 46.7, 34.6, 19.9 ppm. HRMS (ESI): calcd. for $C_{21}H_{29}N_2O_4S$ $[M + H]^+$ 406.1926; found 406.1926.

***N*-Benzyl-3-(4-nitrophenylsulfonyl)-2-(1-trityl-1*H*-imidazol-4-ylmethyl)propionamide:** This compound (**28**) was prepared by using the general procedure for the synthesis of sulfonamides from sulfonate esters of Oxyma. R_f = 0.12 (EtOAc). Yield 369 mg, 55%, yellow semisolid. IR (KBr): ṽ = 3344, 1749, 1552, 1210, 1165 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21–8.19 (d, J = 9.2 Hz, 2 H, 2× Ar*H*), 8.08–8.06 (d, J = 8.8 Hz, 2 H, 2× Ar*H*), 7.84–7.81 (t, 1 H, C*H*=N), 7.63–7.61 (d, 1 H, NH), 7.32–7.06 (m, 20 H, Ar*H*), 6.64 (s, 1 H, C*H*=C), 4.32 (s, 2 H, CH_2), 3.86 (m, 1 H, α-CH), 3.06–2.95 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 161.1, 154.5, 146.6, 142.1, 139.2, 138.1, 136.7, 130.4, 129.2, 128.8, 128.0, 127.6, 127.2, 126.5, 120.6, 73.9, 54.2, 49.9, 30.6 ppm. HRMS (ESI): calcd. for $C_{39}H_{35}N_4O_5S$ $[M + H]^+$ 672.2281; found 672.2281.

CCDC-877997 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra, solid phase synthesis scheme, MS spectra, HPLC chromatographs, and crystallographic data.

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