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Synthesis of α-sulfanyl-β-amino acid derivatives by using nanocrystalline magnesium oxide

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ABSTRACT

The Mannich-type reaction between alkyl, aryl and heterocyclic aldimines and sulfonium salts for the synthesis of α-sulfanyl-β-amino acid derivatives by using nanocrystalline magnesium oxide (NAP-MgO) is described. These products are obtained in moderate to high yields with moderate diastereoselectivities. The configuration of ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (major isomer) has been confirmed by X-ray diffraction technique to be *anti*, and consistent with the assignment based on ^{1}H NMR spectroscopy. These α-sulfanyl-β-amino acid derivatives are important building blocks for pharmaceuticals with potent biological activity.

1. Introduction

β-Amino acids and their derivatives, although far less abundant in nature than their α-analogues, are pharmacologically important compounds.[1a] They can be used as precursors for medicinally important β-lactam antibiotics,[1b] antifungal cyclic β-amino acids[1c,d] and as constituents of biologically active unnatural peptides.[1e,f] The Mannich reaction is one of the direct approaches for the preparation of these useful class of compounds, and has been actively investigated for many years.[2] The Mannich reaction produces two adjacent stereogenic centres, constructed simultaneously with concomitant C–C bond formation. This provides a unique opportunity for directly and selectively introducing substituents at both the α and β-positions through the choice of electrophile and nucleophile employed.[3]

Based on these considerations, numerous reports for the synthesis of β-amino acids (esters) have been investigated to date. For example, Lewis acid and Lewis base promoted addition of silyl enol ethers to aldimines[4] and addition of Li and Ti ester enolates to aldimines[5] are widely used for the synthesis of β-amino esters. The most prevalent methods for asymmetric Mannich reactions rely on Shibasaki's (*S*,*S*)-linked-binol complexes,[6a,b] Jacobsen's urea derivatives,[6c] Trost's dinuclear zinc complexes[6d] and List's proline organo catalysis[6e] for the synthesis of chiral β-amino acids. Another promising route for the synthesis of β-amino esters is the one-pot Ni, Rh or Zn catalyzed Reformatsky-type reaction of an aldehyde, amine and ester.[7]

In addition, the synthesis of sulfur containing amino acid derivatives has received considerable attention due to the unique biological properties imparted by the sulfur atom.[8] For example, pseudotripeptides containing α-mercapto-β-amino acid residues have been shown to be potent inhibitors of aminopeptidase A,[9a] tetanus neurotoxin[9b] and botolinum neurotoxin type B,[9c–f] while azetidinones derived from α-mercapto-β-amino acids display potent inhibition of cholesterol absorption.[9g] Some amino acid drugs containing the thiol moiety, such as captopril, are well-known angiotensin-converting enzyme inhibitors.[10] As a result of the biological activity associated with these α-mercapto-β-amino acid derivatives, the synthesis of these derivatives has evoked a lot of interest.[11–14]

The procedures used for the synthesis of β-amino acid derivatives often involve the use of undesirable toxic and hazardous metal salts. The development of suitable ecofriendly reagents is of great significance and the use of relatively benign heterogeneous catalysts has been reported recently.[15]

Nanocrystalline metal oxides have found excellent applications as active adsorbents for gases, for the destruction of hazardous chemicals,[16] and as catalysts for various organic transformations.[17] These high reactivities are due to high surface areas combined with unusually reactive morphologies. In continuation of our work on the application of nanomaterials in organic methodologies, we report an effective Mannich-type reaction between *N*-sulfonyl aldimines[18] and

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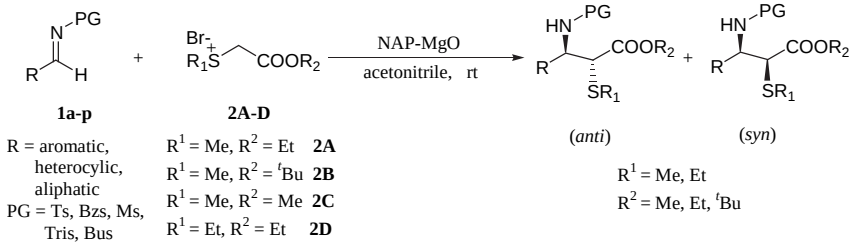
various sulfonium salts to afford α-sulfanyl-β-amino acid derivatives in moderate to high yields with moderate diastereoselectivities using nanocrystalline magnesium oxide (NAP-MgO).

2. Results and discussion

N-Sulfonyl aldimines **1** react with sulfonium salts **2** in a Mannich-type reaction in the presence of a nanocrystalline MgO catalyst to afford α-sulfanyl-β-amino acid derivatives (Scheme 1). These results are in contrast to many reports in which aziridine, aziridinyl carboxamide or β-amino alkenes are the final products.[19] In order to understand the relationship between structure and reactivity, various forms of magnesium oxide crystals [CM-MgO (commercial MgO, SSA: 30 m^2/g), NA-MgO (NanoActive MgO, conventionally prepared MgO, SSA: 250 m^2/g), NAP-MgO (NanoActive Plus MgO, aerogel prepared MgO, SSA: 590 m^2/g) and silylated MgO, Sil-NAP-MgO] were initially evaluated in the reaction between *N*-tosyl benzaldimine **1a** (PG=Ts, R=Ph) and (ethoxycarbonylmethyl)dimethylsulfonium bromide **2A** (Scheme 1). It was found that all forms of MgO catalyze the reaction in high yields, however, the high surface area NAP-MgO was found to be superior to that of NA-MgO and CM-MgO (Table 1).



1a-p

R = aromatic, heterocylic, aliphatic
PG = Ts, Bzs, Ms, Tris, Bus

2A-D

R^1 = Me, R^2 = Et **2A**
R^1 = Me, R^2 = ^{t}Bu **2B**
R^1 = Me, R^2 = Me **2C**
R^1 = Et, R^2 = Et **2D**

(*anti*) (*syn*)

R^1 = Me, Et
R^2 = Me, Et, ^{t}Bu

Scheme 1. NAP-MgO catalyzed Mannich-type reaction between *N*-sulfonyl aldimines **1** and ester sulfonium salts **2A**–**D**.

Table 1
Mannich-type reaction between *N*-tosyl benzaldimine **1a** and (ethoxycarbonylmethyl)dimethylsulfonium bromide **2A** with various catalysts[a]

Entry	Catalyst	Time (h)	Yield[b] (%)	*anti*/*syn*[c]
1	NAP-MgO	12, 15[d]	91, 89[d]	76:24
2	NA-MgO	21	90	72:28
3	CM-MgO	32	87	62:38
4	Sil-NAP-MgO	22	85	71:29
5	None	48	N.R[e]	—

[a] Reaction conditions: *N*-tosyl benzaldimine **1a** (1 mmol), (ethoxycarbonylmethyl)dimethylsulfonium bromide **2A** (2 mmol), catalyst (0.1 g), acetonitrile (5 mL) at room temperature.
[b] Isolated yield of both diastereomers.
[c] The ratio of *anti*/*syn* isomers was determined by ^{1}H NMR spectroscopy of the crude reaction mixture.
[d] Fourth cycle.
[e] No Reaction.

Based on these initial results, the effect of various solvents on the reaction between **1a** and **2A** was investigated using NAP-MgO as catalyst. The nature of the solvent had a striking effect on the yields as well as diastereoselectvity of the reaction product. The use of a non-coordinating solvent like toluene led to lower yields with lower diastereoselectivity when compared to polar solvents. Using the highly polar, protic solvent methanol, the starting imine was converted to *p*-tosyl amine and only traces of the product were isolated (Table 2, entry 5). In polar, aprotic solvents (THF, DCM, DMF and $CHCl_3$), the products were obtained in moderate yields with moderate diastereoselectivities. However, in acetonitrile, a reasonable yield was obtained with good selectivity (Table 2, entry 7), which was therefore selected for future reactions. At low temperature, a decrease in the diastereoselectivity and yield was observed (Table 2, entry 8). Conversely, using an excess sulfonium salt (Table 2, entries 9 and 10) gave higher yields; there was also a slight improvement in diastereoselectivity, which led us to adopt these conditions as optimal for this reaction (Table 2, entry 10). Using dried solvent and performing the reaction under an inert atmosphere did not significantly alter the yield or diastereoselectivity (Table 2, entry 11). Subsequently, when we used 0.5, 1.0, 2.0 equiv of water in combination with acetonitrile did not significantly effect the yield or diastereoselectivity (Table 2, entries 12–14). When 50.0 equiv of water in acetonitrile and water without any organic solvent were used, it showed no reaction because more water content decomposes the catalyst and sulfonium salt (Table 2, entries 15 and 16).

Table 2
Optimization of the Mannich-type reaction of *N*-tosyl benzaldimine **1a** with (ethoxycarbonylmethyl)dimethylsulfonium bromide **2A** catalyzed by NAP-MgO[a]

Entry	Solvent	Time (h)	Yield[b] (%)	*anti*/*syn*[c]
1	THF	24	64	62:38
2	DCM	24	65	66:34
3	DMF	12	56	60:40
4	$CHCl_3$	24	61	56:44
5	Methanol	6	Trace[h]	—
6	Toluene	24	36	50:50
7	Acetonitrile	24	72	72:28
8	Acetonitrile[d]	24	61	68:32
9	Acetonitrile[e]	16	84	72:28
10	Acetonitrile[f]	12	91	76:24
11	Dry acetonitrile[f,g]	12	89	75:25
12	Acetonitrile[i]	12	90	72:28
13	Acetonitrile[j]	16	89	70:30
14	Acetonitrile[k]	24	84	72:28
15	Acetonitrile[l]	24	NR[m]	—
16	Water	24	NR[m]	—

[a] Reaction conditions: *N*-tosyl benzaldimine **1a** (1 mmol), (ethoxycarbonylmethyl)dimethylsulfonium bromide **2A** (1 mmol), NAP-MgO catalyst (0.1 g), solvent (5 mL) at room temperature.
[b] Isolated yield of both diastereomers.
[c] The ratio of *anti*/*syn* isomers was determined by ^{1}H NMR spectroscopy of the crude reaction mixture.
[d] Reaction conducted at 0 °C.
[e] Reaction using 1.5 mmol sulfonium salt.
[f] Reaction using 2 mmol sulfonium salt.
[g] Under N_2 atmosphere.
[h] Tosyl amine was isolated almost quantitatively.
[i] Water (0.5 equiv)was added.
[j] Water (1.0 equiv) was added.
[k] Water (2.0 equiv) was added.
[l] Water (50.0 equiv) was added (excess).
[m] Due to more water content, catalyst and sulfonium salt were decomposed.

Using the optimized conditions above, the reaction between various aldimines **1** and sulfonium salts **2** was investigated and the results are summarized in Table 3. In all cases, the reaction proceeded smoothly to provide the desired α-sulfanyl-β-amino esters in high yields with moderate diastereoselectivity. As expected, the rate of the reaction was faster for electron-poor imines (**1c**, **1d**, **1i** and **1m**) than for electron-rich imines (**1b**, **1j** and **1n**). Heterocyclic aldimines (**1p** and **1f**) reacted with the sulfonium salts **2A** and **2B**, respectively, to afford the products with poor

Table 3
NAP-MgO catalyzed Mannich-type reaction between *N*-sulfonyl aldimines **1** and ester sulfonium salts **2A**–**D**[a]

Sl. no.	Aldimine **1**			Sulfonium salt **2**	Time (h)	Products	
	R	PG				Yield[b] (%)	*anti*/*syn*[c]
1	Ph	Ts	**1a**	**2A**	12	91	76:24
2	4-OMePh	Ts	**1b**	**2A**	24	86	78:22
3	4-NO_2Ph	Ts	**1c**	**2A**	15	82	79:71
4	4-Cl,3-NO_2Ph	Ts	**1d**	**2A**	12	92	81:19
5	Cinnamyl	Ts	**1e**	**2A**	20	73	76:24
6	2-Furyl	Ts	**1f**	**2A**	18	94	69:31
7	Cyclohexyl	Ts	**1g**	**2A**	12	88	67:33
8	Ph	Bzs	**1h**	**2A**	6	82	75:25
9	4-ClPh	Bzs	**1i**	**2A**	6	94	78:22
10	4-MePh	Bzs	**1j**	**2A**	10	89	71:29
11	2-Napthyl	Bzs	**1k**	**2A**	7	85	78:22
12	Ph	Ms	**1l**	**2A**	8	84	75:25
13	4-ClPh	Ms	**1m**	**2A**	6	86	68:32
14	4-OMePh	Ms	**1n**	**2A**	18	83	70:30
15	4-NO_2Ph	TIP Bzs	**1o**	**2A**	14	77	90:10
16	2-Pyridyl	Bus	**1p**	**2A**	8	89	52:48
17	4-OMePh	Ts	**1b**	**2B**	24	90	92:8
18	2-Furyl	Ts	**1f**	**2B**	12	91	55:45
19	4-ClPh	Bzs	**1i**	**2B**	8	92	90:10
20	Ph	Ms	**1l**	**2B**	12	88	86:14
21	Ph	Ts	**1a**	**2C**	8	87	58:42
22	4-MePh	Bzs	**1j**	**2C**	10	94	55:45
23	Ph	Ms	**1l**	**2C**	7	91	52:48
24	Ph	Ts	**1a**	**2D**	16	82	89:11
25	4-ClPh	Bzs	**1i**	**2D**	10	89	85:15
26	Ph	Ms	**1l**	**2D**	12	79	83:17

[a] Reaction conditions: aldimine **1** (1 mmol), sulfonium salt **2A**–**D** (2 mmol), NAP-MgO catalyst (0.1 g), acetonitrile (5 mL) at room temperature.
[b] Isolated yield of both diastereomers.
[c] The ratio of *anti*/*syn* isomers was determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

diastereoselectivity (*syn*/*anti* ratio 52:48 and 55:45, respectively) (Table 3, entries 16 and 18). The furfural-derived imine **1f** reacted with **2A** (Table 3, entry 6) to afford the corresponding product in high yield with moderate diastereoselectivity. This reaction is of particular interest as the furan moiety can be readily derivatized into several useful functional groups. The reaction of the cyclohexyl aldimine **1g** with **2A** gave the β-amino ester in high yield with moderate selectivity (Table 3, entry 7), indicating that the reaction is not only restricted to aromatic aldimines and the scope of the transformation may be further extended to include alkyl aldimines.

The protecting group on the aldimine was varied to determine if this has any influence on the reaction outcome. A variety of structurally different aldimines containing *N*-*p*-toluene sulfonyl (Ts), *N*-benzene sulfonyl (Bzs), *N*-methane sulfonyl (Ms), *N*-2,4,6-triisopropylbenzene sulfonyl (Tris) and *N*-*tert*-butyl sulfonyl (Bus) groups were reacted with the sulfonium salts **2A**–**D**, afforded the expected products in high yields and moderate diastereoselectivities. Replacement of the Ts group by the much bulkier Tris group (Table 3, entries 3 and 15) gave a higher proportion of the *anti* configuration, suggesting the diastereoselectivity is influenced by the steric bulk of the imine protecting group.

Greater diastereoselectivity was also observed when sulfonium salts containing bulkier substituents were used. Changing the ester functionality from ethyl to *tert*-butyl resulted in a significant increase in the proportion of the *anti* configuration (Table 3, entries 2 and 17). A similar effect was observed by increasing the alkyl chain length at the sulfonium centre from methyl to ethyl (Table 3, entries 1 and 24).

The *syn* and *anti* diastereomers were generally distinguishable by ^{1}H NMR spectroscopy. The $^3J_{H-H}$ coupling in the (PG-NH) *CH*R–*CH*(SR^1)(COOR^2) unit were typically larger for the *anti* diastereomer compared to its *syn* analogue. Similar observations have been observed in the literature.[12a] Additional confirmation for the assignments was obtained by a single crystal X-ray analysis of compound ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (major isomer) (Table 3, rntry 3). Crystal was grown from $CHCl_3$ and was shown to be the *anti* configuration (Fig. 1),[20] and consistent with the NMR spectroscopic assignments.

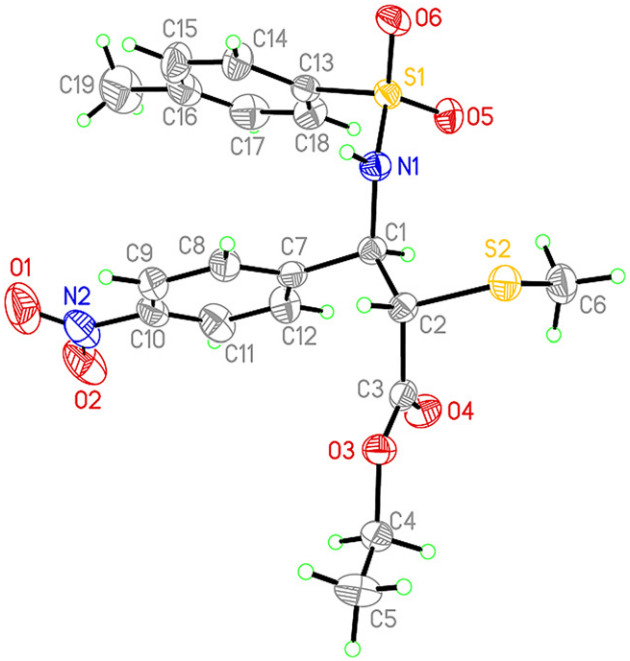
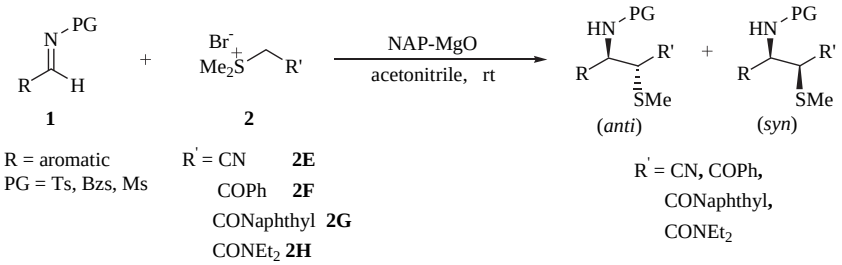


Figure 1. Thermal ellipsoidal plot of compound ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (major isomer) (Table 3, entry 3). Displacement ellipsoids are drawn at the 25% probability level except for the hydrogen atoms, which are shown as circles of arbitrary radius.

The results of the structural studies gave us great confidence in assigning the *anti* configuration to the major isomers and *syn* configuration to the minor isomers on the basis of chemical shift, coupling constant trends and response factors (R_f) of isomers.[21] Most of the *syn* and *anti* diastereomers were easily separated by means of column chromatography; but those compounds obtained from heterocyclic and aliphatic imines, and those with *tert*-butyl ester sulfonium salts could not be separated.

The results from these reactions prompted us to expand our investigation using other sulfonium salts as nucleophiles. Using the optimized reaction conditions, other sulfonium salts (**2E**, **2F**, **2G**, **2H**) reacted with *N*-sulfonyl aldimines to give the corresponding α-sulfanyl-β-amino nitriles, ketones and amides, respectively (Scheme 2) and the results are summarized in Table 4. It is worth noting that relatively few systems have been developed for the preparation of these β-amino nitriles, ketones and amides.[22]

Moderate yields of the coupled products were obtained using cyanomethyl dimethylsulfonium bromide **2E**, however the diastereoselectivity was poor, which might be due to the lower steric requirements of the linear cyanogroup. Good diastereoselectivity was obtained from the reactions of the ketonic sulfonium salts [$Me_2SCH_2C(O)R'$]Br (R′=Ph (**2F**), Naphthyl (**2G**)) and from the amido sulfonium salt (R′=NEt_2 (**2H**)). Uniquely, the *syn* isomer was the major diastereomer formed from the later reaction, however the reasons for this are not clear. The diastereomers containing the nitrile functional group could be readily separated by column chromatography, while those containing the ketone and amide groups were obtained as inseparable mixtures.



Scheme 2. NAP-MgO catalyzed Mannich-type reaction between *N*-sulfonyl aldimines **1** and nitrile/ketone/amide sulfonium salts **2E**–**H**.

Table 4
NAP-MgO catalyzed Mannich-type reaction between *N*-sulfonyl aldimines **1** and nitrilo/ketonic/amido sulfonium salts **2E**–**H**[a]

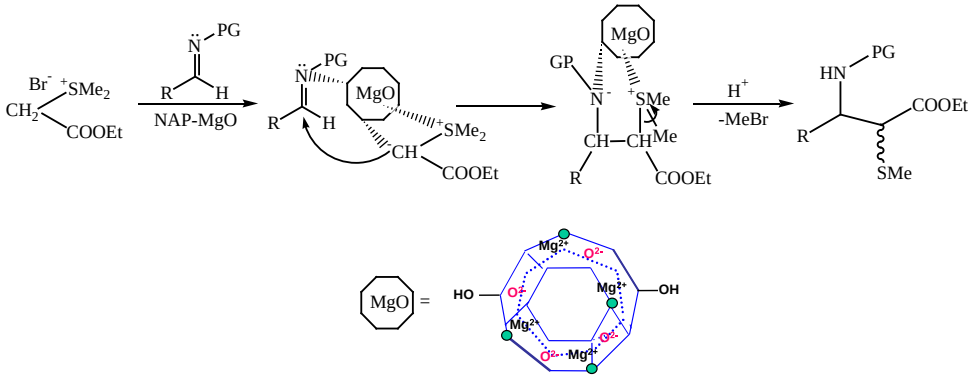
Sl. No.	Aldimine **1**			Sulfonium salt **2**	Time (h)	Products	
	R	PG				Yield[b] (%)	*anti*/*syn*[c]
1	Ph	Ts	**1a**	**2E**	36	64	53:47
2	4-NO_2Ph	Ts	**1c**	**2E**	36	69	55:45
3	4-MePh	Bzs	**1j**	**2E**	40	53	50:50
4	Ph	Ts	**1a**	**2F**	36	55	76:24
5	4-ClPh	Bzs	**1i**	**2F**	36	52	65:35
6	4-ClPh	Bzs	**1i**	**2G**	40	73	77:23
7	4-MePh	Bzs	**1j**	**2G**	48	62	61:39
8	Ph	Ms	**1l**	**2G**	36	64	66:34
9	4-NO_2Ph	Ts	**1c**	**2H**	36	74	37:63

[a] Reaction conditions: aldimine **1** (1 mmol), sulfonium salt **2E**–**H** (2 mmol), NAP-MgO catalyst (0.1 g), acetonitrile (5 mL) at room temperature.
[b] Isolated yield of both diastereomers.
[c] The ratio of *anti*/*syn* isomers was determined by ^{1}H NMR spectroscopy of the crude reaction mixtures.

On treatment with NAP-MgO, sulfonium salts **2** were converted into sulfur ylides, similar to phosphorous ylides.[17d] Meanwhile, imine **1** was activated by Mg^{2+}/Mg^{+} (Lewis acid) of NAP-MgO, then the carbanionoid carbon of sulfur ylide attacks the electrophilic carbon of the imine and forms the intermediate betaine.[19a,23] We assume that the betaine forms a complex with NAP-MgO as imine and the carbonyl oxygen of the ylide is coordinated to the unsaturated Mg^{2+}/Mg^{+} (Lewis acid).[17d,24] Sulfur of the ylide was coordinated to O^{2-}/O^{-} (Lewis base) of NAP-MgO, resulting in the polarization of one of the alkyl subtituents on sulfur, and the O^{2-}/O^{-} (Lewis base) of NAP-MgO directs dealkylation to form α-sulfanyl-β-amino acid derivative as Mannich product. This type of C–S bond cleavage with demethylation was earlier observed in the synthesis of methylthio-substituted heterocycles from hetero aryl(dimethyl)sulfonium salts in the presence of triethylamine as a base (Scheme 3).[25]

To understand the relationship between structure and reactivity of the NAP-MgO catalyst in the Mannich-type reaction, it is important to know the structure and nature of the reactive sites. NAP-MgO has a single-crystallite, three-dimensional polyhedral structure, with high surface concentrations of edge/corner and various exposed crystal planes (such as 002, 001, 111). This leads to an inherently high surface reactivity per unit area. In addition, the NAP-MgO contains Lewis acid sites (Mg^{2+}), Lewis base sites (O^{2-} and O^{-}), lattice-bound and isolated Bronsted hydroxyls and anionic and cationic vacancies.[26] Generally, Mannich-type reactions are known to be driven by basic catalysts,[4a,d,5a,b,e] and accordingly, the surface –OH, and O^{2-} sites of these oxide crystals are expected to trigger these reactions. To examine the role of hydroxyl groups in the coupling reaction, the silylated catalyst, Sil-NAP-MgO,[26e] devoid of free –OH groups, was tested using the optimized reaction conditions. In this case, the rate of the reaction was slow and a longer reaction time was required (Table 1, entry 4). Although both NAP-MgO and NA-MgO possess defined shapes and the same average concentrations of surface –OH groups, a possible rationale for the display of higher reactivity in the Mannich-type reaction of NAP-MgO is the presence of more surface Mg^{2+} Lewis acid sites (20%) and –OH groups present on the edge and corner sites on the NAP-MgO. These are stretched in three-dimensional space, and are thus more isolated and accessible to the reactants. Indeed, NAP-MgO displayed the highest activity compared to NA-MgO and CM-MgO. In the Mannich-type reaction, O^{2-}/O^{-} (Lewis base) of NAP-MgO activates the sulfonium salts **2**, to form sulfur ylides, which may coordinate to the unsaturated Mg^{2+}/Mg^{+} (Lewis acid) of the NAP-MgO. The Mannich-type reaction proceeds via dual activation of both substrates (electrophiles and nucleophiles) by NAP-MgO. Thus, the Lewis base moieties (O^{2-}/O^{-}) of the catalyst activate the sulfonium salt and the Lewis acid moieties (Mg^{2+}/Mg^{+}) activate the aldimine.[27]

The NAP-MgO was reused for four cycles with consistent activity (Table 1, entry 1). After completion of the reaction, the catalyst was centrifuged and washed with ethyl acetate several times. The recovered catalyst was activated at 250 °C for 1 h under a nitrogen atmosphere before reuse.



Scheme 3. The plausible mechanism for the Mannich-type reaction between *N*-sulfonyl aldimines **1** and sulfonium salts **2** catalyzed by NAP-MgO.

3. Conclusion

Nanocrystalline MgO has been shown to be an effective catalyst for the Mannich-type reaction of various alkyl, aryl and heterocyclic *N*-sulfonyl aldimines with a variety of sulfonium salts to afford the corresponding α-sulfanyl-β-amino acid derivatives in moderate to high yields with moderate diastereoselectivities. NMR spectroscopic data suggest the *anti* diastereomer is the major isomer product, and is consistent with that found by a single crystal X-ray diffraction study on one example.

4. Experimental section

4.1. General remarks

Nanocrystalline MgO samples were obtained from NanoScale Materials Inc. (formally Nantek, Inc.) Manhattan, Kansas, USA. All catalysts were calcined at 400 °C for 4 h before use. Other chemicals were purchased from Aldrich Chemicals and S.D Fine Chemicals, Pvt. Ltd. India and used as received. All solvents used were LR grade and used as received from S.D Fine Chemicals Pvt. Ltd. India. ACME silica gel (100–200 mesh) was used for column chromatography and thin layer chromatography was performed on Merck precoated silica gel 60-F_{254} plates. Melting points were measured in open glass capillary tubes and are uncorrected. The IR spectra of all compounds were recorded on a NEXUS 670 FTIR spectrometer (Necolet Corporation Ltd, USA) as KBr discs and values are reported in reciprocal centimetres (cm^{-1}). The ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 MHz or Bruker Avance 300 MHz spectrometer. Chemical shifts (δ) are reported in parts per million, using TMS (δ=0) as an internal standard in $CDCl_3$. Mass spectra were recorded on a QSTAR XL high resolution mass spectrometer (Applied Biosystems, Foster City, USA).

4.2. Preparation of nanocrystalline MgO catalysts[26c–e]

4.2.1. Preparation of NA-MgO[26c,d]. Several grams of commercially available MgO was refluxed in 500 mL of distilled water overnight. After cooling, the slurry was filtered and the filter cake was dried in an oven at 120 °C. The dried powder was broken into pieces and dried at 500 °C under vacuum in a Pyrex reaction tube placed in a cylindrical furnace. Heating took about 12 h, and the sample was maintained at 500 °C for several hours, usually overnight. The vacuum reached about 1×10^{-3} Torr.

4.2.2. Preparation of NAP-MgO[26c,d]. In a three-necked 2 L round bottom flask equipped with a mechanical stirrer, water cooled condenser and argon inlet with a three-way stopcock was placed 300 mL of toluene. In another flask, 2.4 g (0.1 mol) of Mg turnings was allowed to react with 100 mL of CH_3OH under argon. The resulting 1 M solution of $Mg(OCH_3)_2$ was added dropwise to the toluene with vigorous stirring under argon. Distilled water (4 mL, 0.22 mol) was added dropwise from a syringe over a 30 min period. This solution was stirred at room temperature under argon overnight. The resulting slightly turbid mixture was placed in an autoclave and slowly heated to 265 °C to give a $Mg(OH)_2$ aerogel.[26c] After cooling, the slurry was filtered, and the filter cake was dried in an oven at 120 °C. The dried powder was broken into pieces and heat treated to 500 °C under vacuum in a Pyrex reaction tube placed in a cylindrical furnace. Heating took about 12 h, and the sample was maintained at 500 °C for several hours, usually overnight. The vacuum reached about 1×10^{-3} Torr.

4.2.3. Preparation of Sil-NAP-MgO[26e]. A mixture of 0.5 g of NAP-MgO and 0.3 g of methoxytrimethylsilane in 20 mL of toluene was refluxed for 7 h and the reaction mixture was allowed to cool and centrifuged to obtain silylated NAP-MgO, which was washed several times with *n*-pentane.

4.3. Preparation of aldimines[18]

The imines **1a**–**f**,[18a,b] **1g**,[18c] **1h**–**o**[18a,b] and **1p**[18d,e] were prepared according to literature methods.

Typical procedure. Under a nitrogen atmosphere, the sulfonamide (25 mmol) and $Si(OEt)_4$ (25 mmol) were added to a flask equipped with a reflux condenser and downward distillation condenser attached to a receiving flask. The aldehyde (25 mmol) was slowly added and the reaction mixture was stirred at 160 °C under nitrogen for 6 h, during which time ethanol was collected in the receiving flask. After cooling to room temperature, the reaction mixture was suspended in diethyl ether and filtered. The precipitate was washed with diethyl ether and the crude product was recrystallized from ethyl acetate/hexane (6:4).

4.4. Typical procedure for the preparation of sulfonium salts 2A–H[19f]

To a dry flask, the bromo derivative (α-bromo acetate/nitrile/ketone/amide) (25 mmol) and dimethyl sulfide (25 mmol) were added at 0 °C under a nitrogen atmosphere and stirred for 30 min. The reaction mixture was warmed to room temperature and further stirred for 6–12 h until the mixture solidified. In the case of the diethyl sulfide analogues, the mixture was stirred for 18 h to give a viscous liquid (sometimes it is difficult to reproduce **2D**). The resulting sulfonium salts **2A**–**H** were dried under high vacuum at 0 °C for 2 h and stored at sub-zero temperatures.

4.5. Typical procedure for the Mannich-type reaction between *N*-sulfonyl aldimines and sulfonium salts

To a stirred solution of sulfonium salt **2A**–**H** (2 mmol) in acetonitrile (5 mL) was added NAP-MgO (0.1 g). After 5–10 min, the aldimine **1** (1 mmol) was added and the reaction mixture stirred at room temperature. After completion of the reaction (as monitored by TLC), the catalyst was centrifuged, and washed with ethyl acetate (3×5 mL). The combined organic solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (100–200 mesh) using ethyl acetate/hexane in varying proportions as an eluent to afford the pure products. All products were characterized by ^1H NMR, ^{13}C NMR, IR and high resolution mass spectroscopies.

4.5.1. Ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-phenylpropanoate[12a] *(Table 3, entry 1). anti*: R_f 0.4 (hexane/EtOAc 7:3); white solid; mp 127–128 °C; IR: 3259, 2924, 1729, 1332, 1156 cm^{-1}; ^1H NMR (200 MHz): δ 1.01 (t, 3H, *J*=7.2 Hz), 2.05 (s, 3H), 2.35 (s, 3H), 3.3 (d, 1H, *J*=10.6 Hz), 3.93 (q, 2H, *J*=7.2 Hz), 4.55 (dd, 1H, *J*=10.6, 3.0 Hz), 5.68 (d, 1H, *J*=3.0 Hz), 7.04 (d, 2H, *J*=8.3 Hz), 7.1 (m, 5H), 7.43 (d, 2H, *J*=8.3 Hz); ^{13}C NMR (50 MHz): δ 12.1, 13.7, 21.3, 52.5, 55.9, 61.2, 127.2, 127.9, 128.1, 129.1, 136.9, 137.1, 143.0, 168.6; ESI-MS: *m*/*z* 416 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{23}NO_4NaS_2$: 416.0966, found: 416.0970.

syn: R_f 0.36 (hexane/EtOAc 7:3); white solid; mp 136–137 °C; IR: 3194, 2924, 1713, 1335, 1162 cm^{-1}; ^1H NMR (300 MHz): δ 1.17 (t, 3H, *J*=7.2 Hz), 2.06 (s, 3H), 2.34 (s, 3H), 3.44 (d, 1H, *J*=6.0 Hz), 4.03–4.13 (m, 2H), 4.79 (dd, 1H, *J*=6.0, 9.1 Hz), 6.13 (d, 1H, *J*=9.1 Hz), 7.05–7.15 (m, 7H), 7.53 (d, 2H, *J*=8.3 Hz); ^{13}C NMR (75 MHz): δ 13.9, 15.3, 21.3, 53.9, 59.0, 61.6, 126.7, 127.0, 127.8, 128.3, 129.0, 137.6, 137.8, 142.8, 170.6; ESI-MS: *m*/*z* 416 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{23}NO_4NaS_2$: 416.0966, found: 416.0965.

4.5.2. Ethyl-3-(4-methoxyphenyl)-3-{[(4-methylphenyl)sulfonyl] amino}-2-(methylsulfanyl)propanoate (Table 3, entry 2). anti: R_f 0.38 (hexane/EtOAc 6:4); colourless solid; mp 123–125 °C; IR: 3307, 2956, 1705, 1332, 1157 cm^{-1}; ^1H NMR (200 MHz): δ 1.04 (t, J=7.2 Hz, 3H), 2.05 (s, 3H), 2.36 (s, 3H), 3.25 (d, J=10.6 Hz, 1H), 3.73 (s, 3H), 3.94 (q, J=7.2 Hz, 2H), 4.48 (dd, J=10.6, 3.0 Hz, 1H), 5.53 (d, J=3.0 Hz, 1H), 6.59 (d, J=8.3 Hz, 2H), 6.99 (d, J=9.1 Hz, 2H), 7.06 (d, J=8.3 Hz, 2H), 7.4 (d, J=9.1 Hz, 2H); ^{13}C NMR (50 MHz): δ 12.1, 13.8, 21.3, 52.5, 55.1, 55.3, 61.2, 113.5, 127.3, 128.9, 129.1, 129.2, 136.9, 143.0, 159.3, 168.7; ESI-MS: m/z 446 $[M+Na]^+$, HRMS (ESI) calcd for $C_{20}H_{25}NO_5NaS_2$: 446.1071, found: 446.1057.

syn: R_f 0.33 (hexane/EtOAc 6:4); colourless solid; mp 131–133 °C; IR: 3289, 2963, 1721, 1342, 1156 cm^{-1}; ^1H NMR (300 MHz): δ 1.17 (t, J=7.2 Hz, 3H), 2.08 (s, 3H), 2.34 (s, 3H), 3.46 (d, J=6.0 Hz, 1H), 3.74 (s, 3H), 4.08 (m, 2H), 4.78 (dd, J=6.0, 9.1 Hz, 1H), 6.04 (d, J=9.1 Hz, 1H), 6.68 (d, J=8.7 Hz, 2H), 7.01 (d, J=8.7 Hz, 2H), 7.11 (d, J=8.0 Hz, 2H), 7.54 (d, J=8.0 Hz, 2H); ESI-MS: m/z 446 $[M+Na]^+$, HRMS (ESI) calcd for $C_{20}H_{25}NO_5NaS_2$: 446.1071, found: 446.1066.

4.5.3. Ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (Table 3, entry 3). anti: R_f 0.4 (hexane/EtOAc 6:4); yellow solid; mp 133–135 °C; IR: 3253, 2923, 1721, 1521, 1340, 1155 cm^{-1}; ^1H NMR (300 MHz): δ 1.07 (t, J=7.2 Hz, 3H), 2.01 (s, 3H), 2.37 (s, 3H), 3.28 (d, J=10.6 Hz, 1H), 3.89–4.02 (m, 2H), 4.6 (dd, J=10.6, 3.0 Hz, 1H), 5.79 (d, J=3.0 Hz, 1H), 7.1 (d, J=8.3 Hz, 2H), 7.33 (d, J=9.1 Hz, 2H), 7.46 (d, J=8.3 Hz, 2H), 7.97 (d, J=9.1 Hz, 2H); ^{13}C NMR (75 MHz): δ 11.9, 13.7, 21.3, 51.8, 55.0, 61.6, 123.2, 127.2, 129.0, 129.4, 136.1, 143.9, 144.8, 147.4, 168.1; ESI-MS: m/z 461 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{22}N_2O_6NaS_2$: 461.0817, found: 461.0809.

syn: R_f 0.35 (hexane/EtOAc 6:4); yellow solid; mp 136–138 °C; IR: 3233, 2924, 1711, 1520, 1345, 1162 cm^{-1}; ^1H NMR (300 MHz): δ 1.25 (t, J=7.2 Hz, 3H), 2.03 (s, 3H), 2.34 (s, 3H), 3.48 (d, J=7.6 Hz, 1H), 4.07–4.22 (m, 2H), 4.86 (dd, J=7.6, 9.1 Hz, 1H), 6.61 (d, J=9.1 Hz, 1H), 7.07 (d, J=8.3 Hz, 2H), 7.32 (d, J=9.1 Hz, 2H), 7.51 (d, J=8.3 Hz, 2H), 7.99 (d, J=9.1 Hz, 2H); ESI-MS: m/z 461 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{22}N_2O_6NaS_2$: 461.0817, found: 461.0815.

4.5.4. Ethyl-3-(3-chloro-4-nitrophenyl)-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)propanoate (Table 3, entry 4). anti: R_f 0.37 (hexane/EtOAc 7:3); white solid; mp 121–122 °C; IR: 3318, 2921, 1703, 1536, 1340, 1159 cm^{-1}; ^1H NMR (300 MHz): δ 1.11 (t, J=7.2 Hz, 3H), 2.09 (s, 3H), 2.39 (s, 3H), 3.26 (d, J=10.6 Hz, 1H), 3.92–4.1 (m, 2H), 4.61 (dd, J=10.6, 2.7 Hz, 1H), 5.78 (d, J=2.7 Hz, 1H), 7.09 (d, J=8.3 Hz, 2H), 7.31 (d, J=8.3 Hz, 1H), 7.36 (d, J=2.1 Hz, 1H), 7.42 (d, J=8.3 Hz, 2H), 7.46 (d, J=2.1 Hz, 1H); ^{13}C NMR (75 MHz): δ 12.1, 13.8, 21.4, 51.7, 54.7, 61.8, 125.2, 127.2, 129.5, 131.6, 133.1, 136.2, 138.0, 144.2, 147.3, 168.2; ESI-MS: m/z 495 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{21}N_2O_6NaS_2Cl$: 495.0427, found: 495.0425.

syn: R_f 0.33 (hexane/EtOAc 7:3); white solid; mp 137–139 °C; IR: 3174, 2920, 1703, 1537, 1341, 1160 cm^{-1}; ^1H NMR (300 MHz): δ 1.26 (t, J=7.2 Hz, 3H), 2.11 (s, 3H), 2.38 (s, 3H), 3.45 (d, J=6.8 Hz, 1H), 4.08–4.27 (m, 2H), 4.8 (dd, J=6.8, 9.1 Hz, 1H), 6.36 (d, J=9.1 Hz, 1H), 7.1 (d, J=8.3 Hz, 2H), 7.33–7.49 (m, 5H); ESI-MS: m/z 495 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{21}N_2O_6NaS_2Cl$: 495.0427, found: 495.0427.

4.5.5. Ethyl-(E)-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-5-phenyl-4-pentenoate (Table 3, entry 5). anti: R_f 0.43 (hexane/EtOAc 7:3); colourless solid; mp 129–131 °C; IR: 3244, 2923, 1725, 1329, 1153 cm^{-1}; ^1H NMR (200 MHz): δ 1.22 (t, J=7.2 Hz, 3H), 2.11 (s, 3H), 2.3 (s, 3H), 3.31 (d, J=7.6 Hz, 1H), 4.13 (q, J=7.2 Hz, 2H), 5.35 (d, J=5.1 Hz, 1H), 5.78 (dd, J=16.1, 8.5 Hz, 1H), 6.25 (d, J=16.1 Hz, 1H), 7.04–7.22 (m, 7H), 7.69 (d, J=8.5 Hz, 2H); ^{13}C NMR (50 MHz): δ 13.7, 14.1, 21.3, 51.6, 55.6, 61.5, 124.4, 126.5, 127.5, 128.0, 128.4, 129.5, 134.5, 135.8, 137.3, 143.5, 169.6; ESI-MS: m/z 442 $[M+Na]^+$, HRMS (ESI) calcd for $C_{21}H_{25}NO_4NaS_2$: 442.1122, found: 442.1127.

syn: R_f 0.36 (hexane/EtOAc 7:3); colourless solid; mp 121–123 °C; IR: 3289, 2925, 1720, 1331, 1160 cm^{-1}; ^1H NMR (200 MHz): δ 1.28 (t, J=7.2 Hz, 3H), 2.18 (s, 3H), 2.27 (s, 3H), 3.33 (d, J=5.5 Hz, 1H), 4.19 (m, 2H), 4.4 (m, 1H), 5.63 (d, J=9.6 Hz, 1H), 5.8 (dd, J=15.8, 7.2 Hz, 1H), 6.26 (d, J=15.8 Hz, 1H), 7.05–7.22 (m, 7H), 7.71 (d, J=8.2 Hz, 1H); ESI-MS: m/z 442 $[M+Na]^+$, HRMS (ESI) calcd for $C_{21}H_{25}NO_4NaS_2$: 442.1122, found: 442.1118.

*4.5.6. Ethyl-3-(2-furyl)-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)propanoate (Table 3, entry 6). syn*and *anti* (inseparable isomers): R_f 0.33 (hexane/EtOAc 7:3); colourless solid; mp 118–120 °C; IR: 3254, 3183, 2925, 1722, 1372, 1334, 1159 cm^{-1}; ^1H NMR (300 MHz): δ 1.16 (t, J=7.2 Hz, 3H)^{anti}, 1.25 (t, J=7.2 Hz, 3H)^{syn}, 2.05 (s, 3H)^{anti}, 2.07 (s, 3H)^{syn}, 2.38 (s, 3H)^{anti}, 2.39 (s, 3H)^{syn}, 3.55 (d, J=9.5 Hz, 1H)^{anti}, 3.57 (d, J=6.8 Hz, 1H)^{syn}, 4.05 (q, J=7.2 Hz, 2H)^{anti}, 4.14 (q, J=7.2 Hz, 2H)^{syn}, 4.77 (dd, J=9.44, 6.6 Hz, 1H)^{anti}, 4.87 (dd, J=6.8, 9.8 Hz, 1H)^{syn}, 5.42 (s, br, 1H)^{anti}, 5.73 (d, J=9.8 Hz, 1H)^{syn}, 6.02–6.14 (m, 4H), 7.1–7.18 (m, 6H), 7.57 (d, J=8.3 Hz, 2H), 7.62 (d, J=8.3 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.8, 13.9, 14.0, 15.1, 21.4, 50.4, 50.8, 51.4, 53.0, 61.4, 61.6, 108.4, 109.2, 110.1, 110.2, 126.9, 127.0, 129.2, 137.0, 137.5, 142.0, 142.3, 143.0, 143.1, 149.6, 150.3, 168.8, 170.1; ESI-MS: m/z 406 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{21}NO_5NaS_2$: 406.0758, found: 406.0754.

4.5.7. Ethyl-3-cyclohexyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)propanoate (Table 3, entry 7). syn and *anti* (inseparable isomers): R_f 0.3 (hexane/EtOAc 8:2); colourless solid; mp 113–114 °C; IR: 3276, 2924, 2851, 1727, 1372, 1313, 1151 cm^{-1}; ^1H NMR (300 MHz): δ 0.82–1.2 (m, 12H), 1.25 (t, J=7.2 Hz, 3H)^{syn}, 1.28 (t, J=7.2 Hz, 3H)^{anti}, 1.43–1.8 (m, 10H), 1.96 (s, 3H)^{anti}, 2.03 (s, 3H)^{syn}, 2.42 (s, 3H)^{syn}, 2.43 (s, 3H)^{anti}, 3.23 (d, J=6.8 Hz, 1H)^{anti}, 3.25 (d, J=4.5 Hz, 1H)^{syn}, 3.57–3.63 (m, 2H)^{syn,anti}, 4.04–4.09 (m, 2H)^{syn}, 4.13 (q, J=7.2 Hz, 2H)^{anti}, 4.86 (d, J=8.3 Hz, 1H)^{anti}, 5.36 (d, J=9.8 Hz, 1H)^{syn}, 7.22–7.27 (m, 4H), 7.72–7.76 (m, 4H); ^{13}C NMR (75 MHz): δ 14.0, 14.4, 15.7, 21.4, 26.0, 26.1, 26.2, 27.7, 29.2, 29.6, 29.9, 30.4, 40.9, 41.7, 50.5, 51.5, 58.4, 60.3, 61.4, 61.5, 127.0, 127.2, 129.1, 129.3, 138.4, 138.5, 142.8, 143.1, 170.1, 171.4; ESI-MS: m/z 422 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{29}NO_4NaS_2$: 422.1435, found: 422.1428.

4.5.8. Ethyl-2-(methylsulfanyl)-3-phenyl-3-[(phenylsulfonyl)amino] propanoate (Table 3, entry 8). anti: R_f 0.4 (hexane/EtOAc 7:3); white solid; mp 107–108 °C; IR: 3271, 2926, 1724, 1322, 1161 cm^{-1}; ^1H NMR (300 MHz): δ 1.0 (t, J=7.2 Hz, 3H), 2.06 (s, 3H), 3.29 (d, J=10.4 Hz, 1H), 3.92 (q, J=7.2 Hz, 2H), 4.58 (dd, J=10.4, 3.0 Hz, 1H), 5.67 (d, J=3.0 Hz, 1H), 7.07–7.09 (m, 5H), 7.25 (t, J=7.7 Hz, 2H), 7.37 (t, J=7.6 Hz, 1H), 7.53 (d, J=8.5 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.1, 13.7, 52.5, 56.0, 61.2, 127.1, 127.8, 128.0, 128.1, 128.5, 132.2, 136.9, 139.9, 168.6; ESI-MS: m/z 397 $[M+NH_4]^+$, HRMS (ESI) calcd for $C_{18}H_{25}N_2O_4S_2$: 397.1255, found: 397.1269.

syn: R_f 0.35 (hexane/EtOAc 7:3); white solid; mp104–105 °C; IR: 3274, 2925, 1727, 1332, 1162 cm^{-1}; ^1H NMR (300 MHz): δ 1.23 (t, J=7.2 Hz, 3H), 1.98 (s, 3H), 3.48 (d, J=7.7 Hz, 1H), 4.05–4.23 (m, 2H), 4.79 (dd, J=7.7, 9.8 Hz, 1H), 6.62 (d, J=9.8 Hz, 1H), 7.08–7.1 (m, 5H), 7.22 (t, J=7.7 Hz, 2H), 7.32 (t, J=7.6 Hz, 1H), 7.61 (d, J=8.5 Hz, 2H); ESI-MS: m/z 397 $[M+NH_4]^+$, HRMS (ESI) calcd for $C_{18}H_{25}N_2O_4S_2$: 397.1255, found: 397.1251.

4.5.9. Ethyl-3-(4-chlorophenyl)-2-(methylsulfanyl)-3-[(phenylsulfonyl)amino]propanoate (Table 3, entry 9). anti: R_f 0.44 (hexane/EtOAc 7:3); white solid; mp 120–122 °C; IR: 3322, 2924, 1705, 1337, 1161 cm^{-1}; ^1H NMR (300 MHz): δ 1.05 (t, J=7.2 Hz, 3H), 2.04 (s, 3H), 3.27 (d, J=10.6 Hz, 1H), 3.87–4.02 (m, 2H), 4.55 (dd, J=10.6, 3.8 Hz, 1H), 5.85 (d, J=3.8 Hz, 1H), 7.01–7.04 (m, 4H), 7.25–7.32 (m, 2H), 7.44 (t, J=7.6 Hz, 1H), 7.56 (d, J=7.6 Hz, 2H); ^{13}C NMR (75 MHz):

δ 12.0, 13.7, 52.1, 55.2, 61.4, 127.1, 128.3, 128.6, 129.3, 132.5, 134.0, 135.6, 139.6, 168.4; ESI-MS: *m/z* 436 $[M+Na]^+$, HRMS (ESI) calcd for $C_{18}H_{20}NO_4NaS_2Cl$: 436.0419, found: 436.0420.

syn: R_f 0.41 (hexane/EtOAc 7:3); white solid; mp133–134 °C; IR: 3295, 2926, 1716, 1341, 1163 cm^{-1}; ^1H NMR (200 MHz): δ1.24 (t, *J*=7.2 Hz, 3H), 2.01 (s, 3H), 3.44 (d, *J*=7.8 Hz, 1H), 4.03–4.22 (m, 2H), 4.76 (dd, *J*=7.8, 9.6 Hz, 1H), 6.58 (d, *J*=9.6 Hz, 1H), 7.06–7.09 (m, 4H), 7.24–7.32 (m, 2H), 7.41 (t, *J*=7.8 Hz, 1H), 7.63 (d, *J*=7.8 Hz, 2H); ESI-MS: *m/z* 436 $[M+Na]^+$, HRMS (ESI): calcd for $C_{18}H_{20}NO_4NaS_2Cl$: 436.0419, found: 436.0413.

4.5.10. Ethyl-3-(4-methylphenyl)-2-(methylsulfanyl)-3-[(phenylsulfonyl)amino]propanoate (Table 3, entry 10). anti: R_f 0.4 (hexane/EtOAc 7:3); white solid; mp 106–107 °C; IR: 3323, 2924, 1709, 1333, 1159 cm^{-1}; ^1H NMR (300 MHz): δ 1.05 (t, *J*=7.2 Hz, 3H), 2.06 (s, 3H), 2.26 (s, 3H), 3.33 (d, *J*=10.4 Hz, 1H), 3.95 (q, *J*=7.2 Hz, 2H), 4.56 (dd, *J*=10.4, 4.2 Hz, 1H), 5.84 (d, *J*=4.2 Hz, 1H), 6.88 (d, *J*=8.1 Hz, 2H), 6.99 (d, *J*=8.1 Hz, 2H), 7.25–7.3 (m, 2H), 7.4 (t, *J*=7.6 Hz, 1H), 7.58 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.2, 13.7, 20.9, 52.5, 55.7, 61.2, 127.2, 127.7, 128.4, 128.8, 132.1, 133.9, 137.8, 139.9, 168.6; ESI-MS: *m/z* 416 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{23}NO_4NaS_2$: 416.0966, found: 416.0966.

syn: R_f 0.36 (hexane/EtOAc 7:3); white solid; mp 117–118 °C; IR: 3278, 2920, 1732, 1325, 1162 cm^{-1}; ^1H NMR (300 MHz): δ 1.22 (t, *J*=7.2 Hz, 3H), 2.0 (s, 3H), 2.24 (s, 3H), 3.45 (d, *J*=7.6 Hz, 1H), 4.03–4.21 (m, 2H), 4.74 (dd, *J*=7.6, 9.8 Hz, 1H), 6.45 (d, *J*=9.8 Hz, 1H), 6.89 (d, *J*=8.3 Hz, 2H), 6.96 (d, *J*=8.3 Hz, 2H), 7.21–7.27 (m, 2H), 7.36 (t, *J*=7.6 Hz, 1H), 7.62 (d, *J*=9.1 Hz, 2H); ESI-MS: *m/z* 416 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{23}NO_4NaS_2$: 416.0966, found: 416.0969.

4.5.11. Ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(2-naphthyl)propanoate (Table 3, entry 11). anti: R_f 0.37 (hexane/EtOAc 7:3); white solid; mp 124–126 °C; IR: 3305, 2922, 1759, 1315, 1173 cm^{-1}; ^1H NMR (300 MHz): δ 0.91 (t, *J*=7.2 Hz, 3H), 2.11 (s, 3H), 3.47 (d, *J*=10.6 Hz, 1H), 3.78–3.93 (m, 2H), 4.77 (dd, *J*=10.6, 4.3 Hz, 1H), 6.04 (d, *J*=4.3 Hz, 1H), 7.03 (t, *J*=7.6 Hz, 2H), 7.16 (t, *J*=7.6 Hz, 2H), 7.37–7.65 (m, 8H); ^{13}C NMR (75 MHz): δ 12.2, 13.7, 52.3, 56.1, 61.3, 124.8, 126.0, 126.2, 127.1, 127.4, 127.9, 128.1, 128.3, 132.1, 132.7, 132.9, 134.1, 139.8, 168.6; ESI-MS: *m/z* 452 $[M+Na]^+$, HRMS (ESI): calcd for $C_{22}H_{23}NO_4NaS_2$: 452.0966, found: 452.0979.

syn: R_f 0.32 (hexane/EtOAc 7:3); white solid; mp 138–139 °C; IR: 3313, 2909, 1742, 1327, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.11 (t, *J*=7.2 Hz, 3H), 2.12 (s, 3H), 3.6 (d, *J*=5.8 Hz, 1H), 3.97–4.15 (m, 2H), 5.02 (dd, *J*=5.8, 9.1 Hz, 1H), 6.31 (d, *J*=9.1 Hz, 1H), 7.14–7.24 (m, 4H), 7.42–7.45 (m, 2H), 7.51 (s, 1H), 7.62–7.75 (m, 5H); ESI-MS: *m/z* 452 $[M+Na]^+$, HRMS (ESI) calcd for $C_{22}H_{23}NO_4NaS_2$: 452.0966, found: 452.0966.

4.5.12. Ethyl-2-(methylsulfanyl)-3-[(methylsulfonyl)amino]-3-phenylpropanoate (Table 3, entry 12). anti: R_f 0.37 (hexane/EtOAc 6:4); white solid; mp 143–145 °C; IR: 3306, 2926, 1728, 1384, 1157 cm^{-1}; ^1H NMR (300 MHz): δ 1.06 (t, *J*=7.2 Hz, 3H), 2.21 (s, 3H), 2.45 (s, 3H), 3.39 (d, *J*=10.6 Hz, 1H), 3.99 (q, *J*=7.2 Hz, 2H), 4.73 (dd, *J*=10.6, 3.0 Hz, 1H), 5.44 (d, *J*=3.0 Hz, 1H), 7.3–7.5 (m, 5H); ^{13}C NMR (75 MHz): 12.4, 13.9, 42.1, 52.3, 56.0, 61.4, 128.0, 128.8, 128.9, 137.9, 168.8; ESI-MS: *m/z* 340 $[M+Na]^+$, HRMS (ESI) calcd for $C_{13}H_{19}NO_4NaS_2$: 340.0653, found: 340.0648.

syn: R_f 0.33 (hexane/EtOAc 6:4); colourless solid; mp 131–132 °C; IR: 3255, 2923, 1729, 1319, 1147 cm^{-1}; ^1H NMR (300 MHz): δ 1.22 (t, *J*=7.2 Hz, 3H), 2.16 (s, 3H), 2.72 (s, 3H), 3.51 (d, *J*=6.8 Hz, 1H), 4.08–4.21 (m, 2H), 4.86 (t, *J*=8.7 Hz, 1H), 6.1 (d, *J*=9.1 Hz, 1H), 7.29–7.39 (m, 5H); ESI-MS: *m/z* 340 $[M+Na]^+$, HRMS (ESI) calcd for $C_{13}H_{19}NO_4NaS_2$: 340.0653, found: 340.0656.

4.5.13. Ethyl-3-(4-chlorophenyl)-2-(methylsulfanyl)-3-[(methylsulfonyl)amino]propanoate (Table 3, entry 13). anti: R_f 0.33 (hexane/EtOAc 7:3); white solid; mp 120–122 °C; IR: 3313, 2928, 1723, 1329, 1160 cm^{-1}; ^1H NMR (300 MHz): δ 1.14 (t, *J*=7.2 Hz, 3H), 2.23 (s, 3H), 2.55 (s, 3H), 3.38 (d, *J*=10.6 Hz, 1H), 3.99–4.1 (m, 2H), 4.75 (dd, *J*=10.6, 3.8 Hz, 1H), 5.62 (d, *J*=3.8 Hz, 1H), 7.34–7.38 (m, 4H); ^{13}C NMR (75 MHz): δ 12.4, 13.8, 42.1, 52.0, 55.3, 61.5, 129.0, 129.3, 134.6, 136.5, 168.6; ESI-MS: *m/z* 374 $[M+Na]^+$, HRMS (ESI) calcd for $C_{13}H_{18}NO_4NaS_2Cl$: 374.0263, found: 374.0258.

syn: R_f 0.29 (hexane/EtOAc 7:3); white solid; mp 106–108 °C; IR: 3274, 2928, 1725, 1329, 1153 cm^{-1}; ^1H NMR (300 MHz): δ 1.27 (t, *J*=7.2 Hz, 3H), 2.1 (s, 3H), 2.72 (s, 3H), 3.47 (d, *J*=7.9 Hz, 1H), 4.11–4.26 (m, 2H), 4.81 (dd, *J*=7.9, 9.6 Hz, 1H), 6.34 (d, *J*=9.6 Hz, 1H), 7.31–7.35 (m, 4H); ESI-MS: *m/z* 374 $[M+Na]^+$, HRMS (ESI) calcd for $C_{13}H_{18}NO_4NaS_2Cl$: 374.0263, found: 374.0268.

4.5.14. Ethyl-3-(4-methoxyphenyl)-2-(methylsulfanyl)-3-[(methylsulfonyl)amino]propanoate (Table 3, entry 14). anti: R_f 0.42 (hexane/EtOAc 1:1); white solid; mp 123–124 °C; IR: 3303, 2928, 1719, 1384, 1252, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.09 (t, *J*=7.2 Hz, 3H), 2.2 (s, 3H), 2.44 (s, 3H), 3.36 (d, *J*=10.6 Hz, 1H), 3.79 (s, 3H), 3.99 (q, *J*=7.2 Hz, 2H), 4.67 (dd, *J*=10.6, 2.2 Hz, 1H), 5.48 (d, *J*=2.2 Hz, 1H), 6.85 (d, *J*=8.3 Hz, 2H), 7.29 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.1, 13.8, 42.0, 52.0, 55.2, 61.3, 114.2, 129.3, 159.7, 168.8; ESI-MS: *m/z* 370 $[M+Na]^+$, HRMS (ESI) calcd for $C_{14}H_{21}NO_5NaS_2$: 370.0758, found: 370.0741.

syn: R_f 0.36 (hexane/EtOAc 1:1); colourless solid; mp 118–120 °C; IR:.3214, 2926, 1705, 1333, 1259, 1154 cm^{-1}; ^1H NMR (300 MHz): δ 1.28 (t, *J*=7.2 Hz, 3H), 2.08 (s, 3H), 2.63 (s, 3H), 3.46 (d, *J*=8.3 Hz, 1H), 3.78 (s, 3H), 4.13–4.26 (m, 2H), 4.76 (t, *J*=8.7 Hz, 1H), 6.24 (d, *J*=9.8 Hz, 1H), 6.85 (d, *J*=8.7 Hz, 2H), 7.27 (d, *J*=8.7 Hz, 2H); ESI-MS: *m/z* 370 $[M+Na]^+$, HRMS (ESI) calcd for $C_{14}H_{21}NO_5NaS_2$: 370.0758, found: 370.0752.

4.5.15. Ethyl-2-(methylsulfanyl)-3-(4-nitrophenyl)-3-{[(2,4,6-triisopropylphenyl)sulfonyl]amino}propanoate (Table 3, entry 15). anti: R_f 0.4 (hexane/EtOAc 8:2); pale yellow solid; mp 140–143 °C; IR: 3224, 2967, 1727, 1520, 1385, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.06 (t, *J*=7.2 Hz, 3H), 1.12 (d, *J*=6.8 Hz, 6H), 1.2 (d, *J*=7.6 Hz, 6H), 1.26 (d, *J*=6.8 Hz, 6H), 2.07 (s, 3H), 2.78–2.87 (m, 1H), 3.29 (d, *J*=10.6 Hz, 1H), 3.9–4.02 (m, 4H), 4.83 (dd, *J*=10.6, 2.3 Hz, 1H), 5.83 (d, *J*=2.3 Hz, 1H), 6.99 (s, 2H), 7.33 (d, *J*=9.1 Hz, 2H), 7.92 (d, *J*=9.1 Hz, 2H); ^{13}C NMR (75 MHz): δ 11.7, 13.8, 23.5, 23.6, 24.5, 25.0, 29.8, 34.1, 52.0, 54.7, 61.6, 123.0, 123.4, 129.0, 132.9, 145.0, 147.5, 150.0, 153.4, 168.1; ESI-MS: *m/z* 551 $[M+H]^+$, HRMS (ESI) calcd for $C_{27}H_{39}N_2O_6S_2$: 551.2249, found: 551.2251.

syn: R_f 0.32 (hexane/EtOAc 8:2); pale yellow solid; mp 109–111 °C; IR: 3283, 2962, 1721, 1525, 1345, 1160 cm^{-1}; ^1H NMR (300 MHz): δ 1.18 (t, *J*=9.1 Hz, 3H), 1.19 (d, *J*=9.1 Hz, 6H), 1.24 (d, *J*=6.8 Hz, 6H), 1.29 (d, *J*=6.8 Hz, 6H), 2.11 (s, 3H), 2.79–2.94 (m, 1H), 3.56 (d, *J*=6.0 Hz, 1H), 3.92–4.0 (m, 2H), 4.05–4.1 (m, 2H), 5.03 (dd, *J*=6.0, 8.3 Hz, 1H), 6.34 (d, *J*=8.3 Hz, 1H), 7.13 (s, 2H), 7.34 (d, *J*=9.1 Hz, 2H), 8.02 (d, *J*=9.1 Hz, 2H); ESI-MS: *m/z* 551 $[M+H]^+$, HRMS (ESI) calcd for $C_{27}H_{39}N_2O_6S_2$: 551.2249, found: 551.2241.

4.5.16. Ethyl-3-[(tert-butylsulfonyl)amino]-2-(methylsulfanyl)-3-(3-pyridyl)propanoate (Table 3, entry 16). syn and *anti* (inseparable isomers): R_f 0.45 (hexane/EtOAc 6:4); white solid; mp 102–104 °C; IR: 3346, 3248, 2985, 2928, 1726, 1308, 1129, 1124 cm^{-1}; ^1H NMR (300 MHz): δ 1.12 (t, *J*=7.2 Hz, 3H)^{anti}, 1.25 (t, *J*=7.2 Hz, 3H)^{syn}, 1.28 (s, 9H)^{syn}, 1.37 (s, 9H)^{anti}, 2.12 (s, 3H)^{syn}, 2.16 (s, 3H)^{anti}, 3.76 (d, *J*=9.1 Hz, 1H)^{anti}, 3.79 (d, *J*=7.4 Hz, 1H)^{syn}, 3.95–4.05 (m, 2H)^{anti}, 4.15 (q, *J*=7.2 Hz, 2H)^{syn}, 4.84 (dd, *J*=9.1, 8.7 Hz, 1H)^{anti}, 4.89 (dd, *J*=7.4, 10.2 Hz, 1H)^{syn}, 5.25 (d, *J*=8.7 Hz, 1H)^{anti}, 5.56 (d, *J*=10.2 Hz, 1H)^{syn}, 7.18–7.22 (m, 2H), 7.35 (d, *J*=7.7 Hz, 1H), 7.48 (d, *J*=7.9 Hz, 1H), 7.61–7.72 (m, 2H), 8.54–8.58 (m, 2H); ^{13}C NMR (75 MHz): δ 13.9, 14.0, 14.2, 15.2, 24.0, 24.1, 29.6, 52.0, 53.5, 57.6, 59.3, 60.2, 60.6, 61.4, 61.7, 123.8, 124.2, 124.7, 138.7, 139.4, 146.7, 147.6, 157.3, 157.4, 169.4,

170.6; ESI-MS: *m/z* 361 $[M+H]^+$, HRMS (ESI) calcd for $C_{15}H_{25}N_2O_4S_2$: 361.1255, found: 361.1266.

4.5.17. tert-Butyl-3-(4-methoxyphenyl)-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)propanoate (Table 3, entry 17). ***syn*** and ***anti*** (inseparable isomers): R_f 0.31 (hexane/EtOAc 7:3); white solid; mp 165–167 °C; IR: 3324, 2922, 1697, 1384, 1362, 1297, 1254, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.21 (s, 9H)^{anti}, 1.22 (s, 9H)^{syn}, 2.03 (s, 3H)^{anti}, 2.06 (s, 3H)^{syn}, 2.35(s, 3H)^{syn}, 2.36 (s, 3H)^{anti}, 3.15 (d, *J*=10.6 Hz, 1H)^{anti}, 3.29 (d, *J*=6.0 Hz, 1H)^{syn}, 3.73 (s, 3H)^{anti}, 3.74 (s, 3H)^{syn}, 4.41 (dd, *J*=10.6, 3.0 Hz, 1H)^{anti}, 4.68 (dd, *J*=6.0, 9.1 Hz, 1H)^{syn}, 5.52 (d, *J*=3.0 Hz, 1H)^{anti}, 6.08 (d, *J*=9.1 Hz, 1H)^{syn}, 6.59 (d, *J*=8.3 Hz, 2H), 6.63 (d, *J*=8.3 Hz, 2H), 7.0 (d, *J*=8.3 Hz, 4H), 7.06 (d, *J*=8.3 Hz, 4H), 7.41 (d, *J*=8.3 Hz, 2H), 7.51 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (75 MHz): 11.9, 15.3, 21.4, 27.6, 27.8, 29.6, 53.2, 54.7, 55.2, 55.4, 58.6, 82.0, 113.4, 113.6, 127.1, 127.3, 128.0, 129.0, 129.1, 129.4, 136.9, 143.0, 159.1, 159.3, 167.8; ESI-MS: *m/z* 474 $[M+Na]^+$, HRMS (ESI) calcd for $C_{22}H_{29}NO_5NaS_2$: 474.1384, found: 474.1403.

4.5.18. tert-Butyl-3-(2-furyl)-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)propanoate (Table 3, entry 18). ***syn*** and ***anti*** (inseparable isomers): R_f 0.41 (hexane/EtOAc 7:3); colourless solid; mp 132–135 °C; IR: 3245, 3173, 2928, 1725, 1696, 1598, 1384, 1158 cm^{-1}; ^1H NMR (200 MHz): δ 1.33 (s, 9H)^{anti}, 1.44 (s, 9H)^{syn}, 2.05 (s, 3H)^{anti}, 2.06 (s, 3H)^{syn}, 2.38(s, 6H)^{syn,anti}, 3.45 (d, *J*=9.6 Hz, 1H)^{anti}, 3.46 (d, *J*=6.9 Hz, 1H)^{syn}, 4.7 (dd, *J*=9.6, 6.1 Hz, 1H)^{anti}, 4.8 (dd, *J*=6.9, 9.6 Hz, 1H)^{syn}, 5.39 (d, *J*=6.1 Hz, 1H)^{anti}, 5.79 (d, *J*=9.6 Hz, 1H)^{syn}, 6.01–6.11 (m, 4H), 7.1–7.17 (m, 6H), 7.54–7.62 (m, 4H); ^{13}C NMR (50 MHz): δ 12.6, 15.1, 21.4, 27.7, 27.8, 50.4, 51.6, 52.3, 53.2, 82.3, 82.7, 108.3, 109.3, 110.1, 110.2, 127.0, 127.1, 129.2, 129.3, 141.9, 142.2, 143.0, 143.1, 149.8, 150.7, 167.9, 169.4; ESI-MS: *m/z* 434 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{25}NO_5NaS_2$: 434.1071, found: 434.1070.

4.5.19. tert-Butyl-3-(4-chlorophenyl)-2-(methylsulfanyl)-3-[(phenylsulfonyl)amino]propanoate (Table 3, entry 19). ***syn*** and ***anti*** (inseparable isomers): R_f 0.3 (hexane/EtOAc 8:2); white solid; mp 152–155 °C; IR: 3311, 2925, 1699, 1365, 1159 cm^{-1}; ^1H NMR (300 MHz): δ 1.22 (s, 9H)^{anti}, 1.39 (s, 9H)^{syn}, 2.02 (s, 3H)^{anti}, 2.06 (s, 3H)^{syn}, 3.14 (d, *J*=10.6 Hz, 1H)^{anti}, 3.29 (d, *J*=6.0 Hz, 1H)^{syn}, 4.48 (dd, *J*=10.6, 2.3 Hz, 1H)^{anti}, 4.72 (dd, *J*=6.0, 9.1 Hz, 1H)^{syn}, 5.67 (d, *J*=2.3 Hz, 1H)^{anti}, 6.31 (d, *J*=9.1 Hz, 1H)^{syn}, 7.04–7.12 (m, 8H), 7.25–7.65 (m, 10H); ^{13}C NMR (75 MHz): 11.9, 15.4, 27.6, 27.7, 27.9, 53.0, 54.3, 55.4, 58.7, 82.4, 83.2, 127.0, 127.2, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8, 129.6, 132.3, 132.5, 134.0, 135.8, 136.4, 139.7, 167.7; ESI-MS: *m/z* 464 $[M+Na]^+$, HRMS (ESI) calcd for $C_{20}H_{24}NO_4NaS_2Cl$: 464.0732, found: 464.0732.

4.5.20. tert-Butyl-2-(methylsulfanyl)-3-[(methylsulfonyl)amino]-3-phenylpropanoate (Table 3, entry 20). ***syn*** and ***anti*** (inseparable isomers): R_f 0.31 (hexane/EtOAc 7:3); colourless solid; mp 104–106 °C; IR: 3300, 3211, 2929, 1721, 1693, 1327, 1156 cm^{-1}; ^1H NMR (300 MHz): δ 1.21 (s, 9H)^{anti}, 1.47 (s, 9H)^{syn}, 2.01 (s, 3H)^{syn}, 2.23(s, 3H)^{anti}, 2.5(s, 3H)^{anti}, 2.57(s, 3H)^{syn}, 3.36 (d, *J*=10.6 Hz, 1H)^{anti}, 3.39 (d, *J*=6.4 Hz, 1H)^{syn}, 4.67 (dd, *J*=10.6, 5.3 Hz, 1H)^{anti}, 4.73 (dd, *J*=6.4, 9.8 Hz, 1H)^{syn}, 5.94 (d, *J*=5.3 Hz, 1H)^{anti}, 6.46 (d, *J*=9.8 Hz, 1H)^{syn}, 7.27–7.4 (m, 10H); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 75 MHz): 12.0, 13.8, 27.0, 27.3, 41.1, 41.3, 52.4, 53.7, 55.9, 58.6, 81.0, 81.5, 126.8, 127.4, 127.7, 127.8, 128.0, 128.1, 138.3, 138.6, 167.8, 168.9; ESI-MS: *m/z* 368 $[M+Na]^+$, HRMS (ESI) calcd for $C_{15}H_{23}NO_4NaS_2$: 368.0966, found: 368.0972.

4.5.21. Methyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-phenylpropanoate (Table 3, entry 21). ***anti***: R_f 0.41 (hexane/EtOAc 7:3); white solid; mp 139–141 °C; IR: 3277, 2925, 1730, 1326, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 2.05 (s, 3H), 2.34 (s, 3H), 3.32 (d, *J*=10.6 Hz, 1H), 3.48 (s, 3H), 4.56 (dd, *J*=10.6, 3.0 Hz, 1H), 5.55 (d, *J*=3.0 Hz, 1H), 7.04 (d, *J*=8.3 Hz, 2H), 6.98–7.22 (m, 5H), 7.4 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.2, 21.4, 52.1, 52.5, 55.9, 127.3, 127.9, 128.0, 128.2, 129.1, 137.2, 142.9, 169.1; ESI-MS: *m/z* 402 $[M+Na]^+$, HRMS (ESI) calcd for $C_{18}H_{21}NO_4NaS_2$: 402.0809, found: 402.0794.

syn: R_f 0.34 (hexane/EtOAc 7:3); colourless solid; mp 136–139 °C; IR: 3251, 2924, 1740, 1326, 1163 cm^{-1}; ^1H NMR (300 MHz): δ 2.03 (s, 3H), 2.33 (s, 3H), 3.48 (d, *J*=6.8 Hz, 1H), 3.64 (s, 3H), 4.77 (dd, *J*=6.8, 9.1 Hz, 1H), 6.3 (d, *J*=9.1 Hz, 1H), 7.03–7.13 (m, 7H), 7.52 (d, *J*=8.3 Hz, 2H); ESI-MS: *m/z* 402 $[M+Na]^+$, HRMS (ESI) calcd for $C_{18}H_{21}NO_4NaS_2$: 402.0809, found: 402.07816.

4.5.22. Methyl-3-(4-methylphenyl)-2-(methylsulfanyl)-3-[(phenylsulfonyl)amino]propanoate (Table 3, entry 22). ***anti***: R_f 0.4 (hexane/EtOAc 7:3); colourless solid; mp 152–154 °C; IR: 3270, 2924, 1730, 1316, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 2.03 (s, 3H), 2.24 (s, 3H), 3.31 (d, *J*=9.8 Hz, 1H), 3.49 (s, 3H), 4.54 (dd, *J*=9.8, 3.0 Hz, 1H), 5.59 (d, *J*=3.0 Hz, 1H), 6.87 (d, *J*=8.3 Hz, 2H), 6.96 (d, *J*=8.3 Hz, 2H), 7.25 (t, *J*=7.6 Hz, 2H), 7.39 (t, *J*=7.6 Hz, 1H), 7.53 (d, *J*=7.6 Hz, 2H); ^{13}C NMR (75 MHz): δ 12.3, 21.0, 52.2, 52.5, 55.7, 127.1, 127.6, 128.5, 128.9, 132.1, 133.9, 137.8, 139.9, 169.1; ESI-MS: *m/z* 402 $[M+Na]^+$, HRMS (ESI) calcd for $C_{18}H_{21}NO_4NaS_2$: 402.0809, found: 402.0800.

syn: R_f 0.32 (hexane/EtOAc 7:3); white solid; mp 126–129 °C; IR: 3252, 2922, 1730, 1326, 1160 cm^{-1}; ^1H NMR (200 MHz): δ 2.08 (s, 3H), 2.27 (s, 3H), 3.45 (d, *J*=6.3 Hz, 1H), 3.61 (s, 3H), 4.77 (dd, *J*=6.3, 9.4 Hz, 1H), 6.08 (d, *J*=9.4 Hz, 1H), 6.93–6.96 (m, 4H), 7.29–7.32 (m, 3H), 7.66 (d, *J*=7.8 Hz, 2H); ESI-MS: *m/z* 402 $[M+Na]^+$, HRMS (ESI) calcd for $C_{18}H_{21}NO_4NaS_2$: 402.0809, found: 402.0816.

4.5.23. Methyl-2-(methylsulfanyl)-3-[(methylsulfonyl)amino]-3-phenylpropanoate (Table 3, entry 23). ***anti***: R_f 0.39 (hexane/EtOAc 1:1); white solid; mp 150–151 °C; IR: 3309, 2927, 1729, 1322, 1155 cm^{-1}; ^1H NMR (300 MHz): δ 2.21 (s, 3H), 2.44 (s, 3H), 3.42 (d, *J*=10.6 Hz, 1H), 3.55 (s, 3H), 4.74 (dd, *J*=10.6, 3.0 Hz, 1H), 5.46 (d, *J*=3.0 Hz, 1H), 7.29–7.4 (m, 5H); ^{13}C NMR (75 MHz): δ 12.3, 42.0, 52.1, 52.3, 55.8, 127.9, 128.8, 128.9, 137.7, 169.2; ESI-MS: *m/z* 326 $[M+Na]^+$, HRMS (ESI) calcd for $C_{12}H_{17}NO_4NaS_2$: 326.0496, found: 326.0497.

syn: R_f 0.34 (hexane/EtOAc 1:1); colourless solid; mp 120–122 °C; IR: 3228, 2921, 1729, 1313, 1145 cm^{-1}; ^1H NMR (300 MHz): δ 2.11 (s, 3H), 2.69 (s, 3H), 3.53 (d, *J*=6.8 Hz, 1H), 3.71 (s, 3H), 4.84 (dd, *J*=6.8, 9.1 Hz, 1H), 6.24 (d, *J*=9.1 Hz, 1H), 7.29–7.36 (m, 5H); ESI-MS: *m/z* 326 $[M+Na]^+$, HRMS (ESI) calcd for $C_{12}H_{17}NO_4NaS_2$: 326.0496, found: 326.0488.

4.5.24. Ethyl-2-(ethylsulfanyl)-3-{[(4-methylphenyl)sulfonyl]amino}-3-phenylpropanoate (Table 3, entry 24). ***anti***: R_f 0.39 (hexane/EtOAc 7:3); white solid; mp 116–118 °C; IR: 3252, 2927, 1731, 1328, 1157 cm^{-1}; ^1H NMR (300 MHz): δ 1.03 (t, *J*=7.3 Hz, 3H), 1.24 (t, *J*=7.3 Hz, 3H), 2.37 (s, 3H), 2.47–2.63 (m, 2H), 3.35 (d, *J*=9.7 Hz, 1H), 3.94 (q, *J*=7.3 Hz, 2H), 4.55 (dd, *J*=9.7, 2.8 Hz, 1H), 5.59 (d, *J*=2.8 Hz, 1H), 7.07 (d, *J*=8.3 Hz, 2H), 7.11–7.15 (m, 5H), 7.43 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (75 MHz): δ 13.7, 13.9, 21.3, 24.4, 52.9, 56.9, 61.2, 127.2, 127.9, 128.1, 129.1, 136.9, 137.2, 143.1, 169.2; ESI-MS: *m/z* 430 $[M+Na]^+$, HRMS (ESI) calcd for $C_{20}H_{25}NO_4NaS_2$: 430.1122, found: 430.1114.

syn: R_f 0.35 (hexane/EtOAc 7:3); white solid; mp 109–110 °C; IR: 3211, 2922, 1719, 1337, 1161 cm^{-1}; ^1H NMR (300 MHz): δ 1.12 (t, *J*=7.2 Hz, 3H), 1.2 (t, *J*=7.2 Hz, 3H), 2.32 (s, 3H), 2.39–2.47 (m, 2H), 3.52 (d, *J*=6.8 Hz, 1H), 4.04–4.16 (m, 2H), 4.73 (dd, *J*=6.8, 9.8 Hz, 1H), 6.39 (d, *J*=9.8 Hz, 1H), 7.03 (d, *J*=8.3 Hz, 2H), 7.07–7.12 (m, 5H), 7.51 (d, *J*=8.3 Hz, 2H); ESI-MS: *m/z* 430 $[M+Na]^+$, HRMS (ESI) calcd for $C_{20}H_{25}NO_4NaS_2$: 430.1122, found: 430.1129.

4.5.25. Ethyl-3-(4-chlorophenyl)-2-(ethylsulfanyl)-3-[(phenylsulfonyl)amino]propanoate (Table 3, entry 25). ***anti***: R_f 0.4 (hexane/

EtOAc 7:3); pale yellow solid; mp 94–95 °C; IR: 3251, 2931, 1721, 1329, 1157 cm^{-1}; ^1H NMR (300 MHz): δ 1.07 (t, J=7.3 Hz, 3H), 1.23 (t, J=7.3 Hz, 3H), 2.45–2.64 (m, 2H), 3.3 (d, J=7.3 Hz, 1H), 3.96 (q, J=10.3 Hz, 2H), 4.54 (dd, J=10.3, 3.0 Hz, 1H), 5.75 (d, J=3.0 Hz, 1H), 7.02–7.07 (m, 4H), 7.3 (t, J=8.5 Hz, 2H), 7.41–7.46 (m, 1H), 7.53 (d, J=8.5 Hz, 2H); ^{13}C NMR (75 MHz): δ 13.7, 13.9, 24.5, 52.5, 56.3, 61.5, 127.2, 128.3, 128.6, 129.4, 132.4, 134.0, 135.7, 139.8, 169.0; ESI-MS: m/z 450 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{22}NO_4NaS_2Cl$: 450.0576, found: 450.0571.

syn: R_f 0.36 (hexane/EtOAc 7:3); pale yellow solid; mp 92–94 °C; IR: 3184, 2926, 1704, 1340, 1164 cm^{-1}; ^1H NMR (300 MHz): δ 1.16 (t, J=7.3 Hz, 3H), 1.21 (t, J=7.3 Hz, 3H), 2.53 (q, J=7.3 Hz, 2H), 3.47 (d, J=5.1 Hz, 1H), 4.0–4.15 (m, 2H), 4.76 (dd, J=5.1, 8.8 Hz, 1H), 6.21 (d, J=8.8 Hz, 1H), 7.04 (d, J=8.8 Hz, 2H), 7.13 (d, J=8.8 Hz, 2H), 7.33 (t, J=8.1 Hz, 2H), 7.41–7.48 (m, 1H), 7.67 (d, J=8.1 Hz, 2H); ESI-MS: m/z 450 $[M+Na]^+$, HRMS (ESI) calcd for $C_{19}H_{22}NO_4NaS_2Cl$: 450.0576, found: 450.0582.

4.5.26. Ethyl-2-(ethylsulfanyl)-3-[(methylsulfonyl)amino]-3-phenylpropanoate (Table 3, entry 26). anti: R_f 0.45 (hexane/EtOAc 6:4); white solid; mp 115–117 °C; IR: 3305, 2930, 1727, 1323, 1156 cm^{-1}; ^1H NMR (300 MHz): δ 1.07 (t, J=7.3 Hz, 3H), 1.3 (t, J=7.3 Hz, 3H), 2.48 (s, 3H), 2.64–2.78 (m, 2H), 3.45 (d, J=10.2 Hz, 1H), 3.99 (q, J=7.3 Hz, 2H), 4.74 (dd, J=10.2, 3.9 Hz, 1H), 5.55 (d, J=3.9 Hz, 1H), 7.3–7.39 (m, 5H); ^{13}C NMR (75 MHz): δ 13.8, 14.1, 24.6, 42.0, 52.6, 56.9, 61.4, 128.0, 128.7, 137.8, 169.3; ESI-MS: m/z 354 $[M+Na]^+$, HRMS (ESI) calcd for $C_{14}H_{21}NO_4NaS_2$: 354.0809, found: 354.0802.

syn: R_f 0.39 (hexane/EtOAc 6:4); colourless solid; mp 83–85 °C; IR: 3254, 2925, 1723, 1324, 1149 cm^{-1}; ^1H NMR (300 MHz): δ 1.21 (t, J=7.3 Hz, 3H), 1.25 (t, J=7.3 Hz, 3H), 2.58 (q, J=7.3 Hz, 2H), 2.72 (s, 3H), 3.57 (d, J=6.6 Hz, 1H), 4.07–4.19 (m, 2H), 4.82 (dd, J=6.6, 9.6 Hz, 1H), 6.18 (d, J=9.6 Hz, 1H), 7.31–7.36 (m, 5H); ESI-MS: m/z 354 $[M+Na]^+$, HRMS (ESI) calcd for $C_{14}H_{21}NO_4NaS_2$: 354.0809, found: 354.0798.

4.5.27. N-[2-Cyano-2-(methylsulfanyl)-1-phenylethyl]-4-methyl-1-benzenesulfonamide (Table 4, entry 1). anti: R_f 0.47 (hexane/EtOAc 6:4); white solid; mp 136–138 °C; IR: 3236, 2920, 2231, 1319, 1151 cm^{-1}; ^1H NMR (300 MHz): δ 2.01 (s, 3H), 2.39 (s, 3H), 3.93 (d, J=7.6 Hz, 1H), 4.44 (t, J=6.8 Hz, 1H), 5.59 (d, J=6.0 Hz, 1H), 7.16 (d, J=8.3 Hz, 2H), 7.2–7.25 (m, 5H), 7.57 (d, J=8.3 Hz, 2H); ^{13}C NMR (75 MHz): δ 13.9, 21.5, 41.1, 58.3, 115.9, 127.1, 127.4, 128.8, 129.2, 129.6, 135.1, 136.4, 143.9; ESI-MS: m/z 369 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{18}N_2O_2NaS_2$: 369.0707, found: 369.0698.

syn: R_f 0.41 (hexane/EtOAc 6:4); colourless solid; mp 160–162 °C; IR: 3213, 2915, 2234, 1321, 1150 cm^{-1}; ^1H NMR (300 MHz): δ 2.02 (s, 3H), 2.45 (s, 3H), 3.84 (d, J=4.5 Hz, 1H), 4.77 (dd, J=4.5, 9.1 Hz, 1H), 5.53 (d, J=9.1 Hz, 1H), 7.12–7.31 (m, 7H), 7.8 (d, J=8.3 Hz, 2H); ESI-MS: m/z 369 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{18}N_2O_2NaS_2$: 369.0707, found: 369.0703.

4.5.28. N-[2-Cyano-2-(methylsulfanyl)-1-(4-nitrophenyl)ethyl]-4-methyl-1-benzenesulfonamide (Table 4, entry 2). anti: R_f 0.42 (hexane/EtOAc 6:4); colourless solid; mp 130–131 °C; IR: 3237, 2923, 2244, 1350, 1153 cm^{-1}; ^1H NMR (300 MHz): δ 2.21(s, 3H), 2.39 (s, 3H), 3.91 (d, J=7.6 Hz, 1H), 4.57 (t, J=6.8 Hz, 1H), 6.16 (d, J=6.0 Hz, 1H), 7.16 (d, J=7.6 Hz, 2H), 7.39 (d,, J=9.1 Hz, 2H), 7.55 (d, J=7.6 Hz, 2H), 8.08 (d,, J=9.1 Hz, 2H); ^{13}C NMR (75 MHz): δ 13.9, 21.5, 40.7, 57.3, 115.3, 123.8, 127.2, 128.7, 129.7, 136.1, 142.2, 144.6, 148.3; ESI-MS: m/z 414 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{17}N_3O_4NaS_2$: 414.0558, found: 414.0547.

syn: R_f 0.36 (hexane/EtOAc 6:4); colourless solid; mp 159–162 °C; IR: 3257, 2922, 2241, 1355, 1160 cm^{-1}; ^1H NMR (300 MHz): δ 2.21 (s, 3H), 2.37 (s, 3H), 3.85 (d, J=5.3 Hz, 1H), 4.86 (t, J=6.8 Hz, 1H), 5.84 (d, J=8.3 Hz, 1H), 7.16 (d, J=8.3 Hz, 2H), 7.38 (d, J=9.1 Hz, 2H), 7.57 (d, J=8.3 Hz, 2H), 8.09 (d, J=9.1 Hz, 2H); ESI-MS: m/z 414 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{17}N_3O_4NaS_2$: 414.0558, found: 414.0563.

4.5.29. N-[2-Cyano-1-(4-methylphenyl)-2-(methylsulfanyl)ethyl]-1-benzenesulfonamide (Table 4, entry 3). anti: R_f 0.33 (hexane/EtOAc 7:3); colourless solid; mp 105–107 °C; IR: 3237, 2922, 2244, 1515, 1445, 1350, 1152 cm^{-1}; ^1H NMR (300 MHz): δ 2.02 (s, 3H), 2.29 (s, 3H), 3.95 (d, J=7.6 Hz, 1H), 4.42 (t, J=6.8 Hz, 1H), 6.06 (d, J=6.0 Hz, 1H), 6.99 (d, J=8.3 Hz, 2H), 7.06 (d, J=8.3 Hz, 2H), 7.36 (t, J=7.6 Hz, 2H), 7.46 (t,, J=7.6 Hz, 1H), 7.71 (d, J=7.6 Hz, 2H); ESI-MS: m/z 369 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{18}N_2O_2NaS_2$: 369.0707, found: 369.0695.

syn: R_f 0.3 (hexane/EtOAc 7:3); colourless solid; mp 131–133 °C; IR: 3257, 2922, 2241, 1520, 1456, 1346, 1159 cm^{-1}; ^1H NMR (300 MHz): δ 2.15 (s, 3H), 2.29 (s, 3H), 3.82 (d, J=5.3 Hz, 1H), 4.74 (dd, J=5.3, 9.1 Hz, 1H), 5.64 (d, J=9.1 Hz, 1H), 6.99–7.05 (m, 4H), 7.31–7.54 (m, 3H), 7.7 (d, J=7.6 Hz, 2H); ESI-MS: m/z 369 $[M+Na]^+$, HRMS (ESI) calcd for $C_{17}H_{18}N_2O_2NaS_2$: 369.0707, found: 369.0701.

4.5.30. N-[2-(Methylsulfanyl)-3-oxo-1,3diphenylpropyl]-4-methyl-1-benzenesulfonamide (Table 4, entry 4). syn and *anti* (inseparable isomers): R_f 0.31 (hexane/EtOAc 7:3); colourless solid; mp 170–171 °C; IR: 3316, 2922, 1662, 1596, 1450, 1330, 1157 cm^{-1}; ^1H NMR (300 MHz): δ 1.85 (s, 3H)^{anti}, 2.02 (s, 3H)^{syn}, 2.33 (s, 3H)^{syn}, 2.35 (s, 3H)^{anti}, 4.31 (d, J=10.6 Hz, 1H)^{anti}, 4.46 (d, J=6.0 Hz, 1H)^{syn}, 4.78 (dd, J=10.6, 3.0 Hz, 1H)^{anti}, 5.0 (dd, J=6.0, 9.1 Hz, 1H)^{syn}, 5.74 (d, J=3.0 Hz, 1H)^{anti}, 6.37 (d, J=9.1 Hz, 1H)^{syn}, 7.01–7.15 (m, 14H), 7.28–7.77 (m, 14H); ^{13}C NMR (75 MHz): δ 10.3, 14.0, 21.4, 29.6, 51.6, 51.8, 54.2, 59.9, 127.0, 127.3, 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 129.0, 129.2, 133.2, 133.5, 135.6, 136.8, 137.9, 143.1, 190.9, 195.1; ESI-MS: m/z 448 $[M+Na]^+$, HRMS (ESI) calcd for $C_{23}H_{23}NO_3NaS_2$: 448.1017, found: 448.1016.

4.5.31. N-[1-(4-Chlorophenyl)-2-(methylsulfanyl)-3-oxo-3-phenylpropyl]-1-benzenesulfonamide (Table 4, entry 5). syn and *anti* (inseparable isomers): R_f 0.31 (hexane/EtOAc 7:3); colourless solid; mp 184–186 °C; IR: 3311, 2922, 1664, 1589, 1446, 1330, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.83 (s, 3H)^{anti}, 1.97 (s, 3H)^{syn}, 4.29 (d, J=10.6 Hz, 1H)^{anti}, 4.44 (d, J=6.0 Hz, 1H)^{syn}, 4.79 (dd, J=10.6, 3.0 Hz, 1H)^{anti}, 4.99 (dd, J=6.0, 9.1 Hz, 1H)^{syn}, 5.91 (d, J=3.0 Hz, 1H)^{anti}, 6.53 (d, J=9.1 Hz, 1H)^{syn}, 6.95–7.79 (m, 28H); ^{13}C NMR (75 MHz): δ 10.2, 14.1, 29.6, 31.9, 51.3, 53.6, 59.5, 127.0, 127.3, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.6, 132.2, 132.5, 133.5, 133.8, 135.3, 136.4, 138.6, 139.6, 190.5; ESI-MS: m/z 468 $[M+Na]^+$, HRMS (ESI) calcd for $C_{22}H_{20}NO_3NaS_2Cl$: 468.0470, found: 468.0448.

4.5.32. N-[1-(4-Chlorophenyl)-2-(methylsulfanyl)-3-(2-naphthyl)-3-oxo-propyl]-1-benzenesulfonamide (Table 4, entry 6). syn and *anti* (inseparable isomers): R_f 0.33 (hexane/EtOAc 7:3); white solid; mp 170–172 °C; IR: 3311, 2923, 2363, 1658, 1335, 1161 cm^{-1}; ^1H NMR (200 MHz): δ 1.88 (s, 3H)^{anti}, 2.05 (s, 3H)^{syn}, 4.44 (d, J=10.6 Hz, 1H)^{anti}, 4.6 (d, J=5.5 Hz, 1H)^{syn}, 4.86 (dd, J=10.6, 2.3 Hz, 1H)^{anti}, 5.06 (dd, J=5.5, 9.4 Hz, 1H)^{syn}, 5.82 (d, J=2.3 Hz, 1H)^{anti}, 6.52 (d, J=9.3 Hz, 1H)^{syn}, 6.94–7.86 (m, 30H), 8.18 (s, 1H)^{anti}, 8.28 (s, 1H)^{syn}; ^{13}C NMR (50 MHz): δ 10.3, 14.1, 26.9, 51.4, 53.7, 59.5, 123.6, 123.8, 126.9, 127.3, 127.6, 128.4, 128.6, 128.7, 129.0, 129.5, 129.6, 129.8, 130.2, 132.3, 132.5, 133.7, 135.6, 135.7, 136.4, 139.6, 190.5, 194.3; ESI-MS: m/z 518 $[M+Na]^+$, HRMS (ESI) calcd for $C_{26}H_{22}NO_3NaS_2Cl$: 518.0627, found: 518.0636.

4.5.33. N-[1-(4-Methylphenyl)-2-(methyl sulfanyl)-3-(2-naphthyl)-3-oxo-propyl]-1-benzenesulfonamide (Table 4, entry 7). syn and *anti* (inseparable isomers): R_f 0.33 (hexane/EtOAc 7:3); colourless solid; mp 155–157 °C; IR: 3308, 2922, 2362, 1659, 1329, 1159 cm^{-1}; ^1H NMR (200 MHz): δ 1.88 (s, 3H)^{anti}, 2.04 (s, 3H)^{syn}, 2.15 (s, 3H)^{anti}, 2.21 (s, 3H)^{syn}, 4.51 (d, J=10.2 Hz, 1H)^{anti}, 4.63 (d, J=5.5 Hz, 1H)^{syn}, 4.84 (dd, J=10.2, 2.3 Hz, 1H)^{anti}, 5.06 (dd, J=5.5, 8.6 Hz, 1H)^{syn}, 5.84 (d, J=2.3 Hz, 1H)^{anti}, 6.52 (d, J=8.6 Hz, 1H)^{syn}, 6.79–7.89 (m, 30H),

8.18 (s, 1H)^{anti}, 8.27 (s, 1H)^{syn}; ^{13}C NMR (50 MHz): δ 10.4, 13.9, 20.9, 51.5, 51.7, 54.1, 59.8, 123.8, 123.9, 126.8, 126.9, 127.0, 127.3, 128.0, 128.4, 128.5, 128.6, 128.7, 128.9, 129.1, 129.5, 129.7, 130.1, 131.9, 132.2, 132.3, 132.8, 133.3, 134.7, 135.2, 135.5, 135.7, 137.5, 139.9, 140.7, 190.8, 195.1; ESI-MS: *m*/*z* 498 $[M+Na]^+$, HRMS (ESI) calcd for $C_{27}H_{25}NO_3NaS_2$: 498.1173, found: 498.1172.

4.5.34. N-[2-(Methylsulfanyl)-3-(2-naphthyl)-3-oxo-1-phenylpropyl] methanesulfonamide (Table 4, entry 8). ***syn*** and ***anti*** (inseparable isomers): R_f 0.47 (hexane/EtOAc 1:1); white solid; mp 149–150 °C; IR: 3291, 2924, 2362, 1658, 1318, 1158 cm^{-1}; ^{1}H NMR (200 MHz): δ 2.0 (s, 3H)^{syn}, 2.07 (s, 3H)^{anti}, 2.45 (s, 3H)^{anti}, 2.64 (s, 3H)^{syn}, 4.66 (d, *J*=10.6 Hz, 1H)^{anti}, 4.72 (d, *J*=5.5 Hz, 1H)^{syn}, 5.06 (dd, *J*=10.6, 4.3 Hz, 1H)^{anti}, 5.11 (dd, *J*=5.5, 9.2 Hz, 1H)^{syn}, 5.94 (d, *J*=4.3 Hz, 1H)^{anti}, 6.4 (d, *J*=9.2 Hz, 1H)^{syn}, 7.15–7.95 (m, 22H), 8.26 (s, 1H)^{anti}, 8.42 (s, 1H)^{syn}; ^{13}C NMR (50 MHz): δ 10.7, 13.7, 41.8, 42.1, 51.2, 51.3, 54.4, 59.3, 123.8, 123.9, 126.8, 126.9, 127.2, 127.6, 128.2, 128.3, 128.5, 128.6, 128.9, 129.5, 129.7, 130.1, 132.3, 132.7, 133.3, 135.5, 135.7, 138.5, 139.1, 190.8, 194.9; ESI-MS: *m*/*z* 422 $[M+Na]^+$, HRMS (ESI) calcd for $C_{21}H_{21}NO_3NaS_2$: 422.0860, found: 422.0852.

4.5.35. N,N-Diethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanamide (Table 4, entry 9). ***syn*** and ***anti*** (inseparable isomers): R_f 0.38 (hexane/EtOAc 1:1); yellow solid; mp 143–145 °C; IR: 3246, 2924, 1616, 1552, 1347, 1158 cm^{-1}; ^{1}H NMR (300 MHz): δ 0.83 (t, *J*=6.8 Hz, 3H)^{syn}, 0.89 (t, *J*=6.8 Hz, 3H)^{anti}, 1.0 (t, *J*=6.8 Hz, 3H)^{syn}, 1.8 (s, 3H)^{anti}, 2.16 (s, 3H)^{syn}, 2.35 (s, 3H)^{syn}, 2.39 (s, 3H)^{anti}, 2.85–3.35 (m, 8H)^{anti,syn}, 3.39 (d, *J*=10.6 Hz, 1H)^{anti}, 3.6 (d, *J*=4.5 Hz, 1H)^{syn}, 4.68 (dd, *J*=10.6, 2.3 Hz, 1H)^{anti}, 4.89 (dd, *J*=3.7, 8.3 Hz, 1H)^{syn}, 5.88 (d, *J*=2.3 Hz, 1H, N*H*)^{anti}, 7.08(d, *J*=8.3 Hz, 2H), 7.16 (d, *J*=8.3 Hz, 2H), 7.31 (d, *J*=8.3 Hz, 2H), 7.43 (d, *J*=8.3 Hz, 2H), 7.53 (d, *J*=8.3 Hz, 4H), 7.53 (d, *J*=8.3 Hz, 1H, N*H*)^{syn}, 7.98 (d, *J*=8.3 Hz, 4H); ^{13}C NMR (75 MHz): δ 10.2, 12.6, 12.7, 14.2, 14.4, 21.3, 21.4, 40.8, 40.9, 42.1, 42.4, 47.6, 47.8, 54.9, 59.9, 123.0, 123.3, 126.8, 127.3, 128.0, 129.1, 129.3, 129.5, 135.9, 138.0, 143.1, 143.9, 146.4, 146.5, 147.1, 147.2, 165.3, 167.9; ESI-MS: *m*/*z* 488 $[M+Na]^+$, HRMS (ESI) calcd for $C_{21}H_{27}N_3O_5NaS_2$: 488.1289, found: 488.1281.

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Supplementary data

X-ray crystallographic data of compound ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (major isomer) (Table 3, entry 3). Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.002. This data include MOL files and InChiKey of the most important compound described in this article.

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20. Crystal structure and refinement data for compound ethyl-3-{[(4-methylphenyl)sulfonyl]amino}-2-(methylsulfanyl)-3-(4-nitrophenyl)propanoate (major isomer) (Table 3, entry 3) is available in Supplementary data. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 701498.
21. In addition to having larger C*H*(NHPG)–C*H*(SR^1) coupling constants, the C*H*(SR^1) resonates at up field for the *anti* isomers compared to their *syn* analogues. The reverse trend in chemical shift was evident for the nitrile compounds. In all cases where separation was possible, the *anti* isomers eluted prior to their *syn* analogues during column chromatography, i.e, R_f values are larger for the *anti* isomer.
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