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Desulfonylation of Amides using Tributyltin Hydride, Samarium Diiodide or Zinc/Titanium Tetrachloride. A Comparison of Methods

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Abstract—Deprotection of *N*-sulfonylated amides can be achieved by reaction with Bu_3SnH, SmI_2 or $TiCl_4/Zn$. All three methods gave good yields (typically >60%) when using *N*-benzoyl or related amides while the corresponding *N*-acetyl derivatives proved to be inert to deprotection under the same reaction conditions. The mechanistic implications of this are discussed.

Introduction

The preparation of *N*-sulfonamides constitutes a common method of amine protection in synthesis.[1] The product sulfonamides are often crystalline and stable to a variety of reaction conditions (e.g. alkaline hydrolysis and catalytic reduction). Whereas carbamate protecting groups can undergo nucleophilic attack, sulfonamides are much more resistant. Sulfonamides derived from primary amines are readily deprotonated and the anion can react with a variety of electrophiles including alkyl and acyl halides.[2] Deprotection of the resulting *N*-alkyl or *N*-acyl sulfonamides produces secondary amines or amides, respectively. As sulfonamides are amongst the most stable of the nitrogen protecting groups, harsh deprotection conditions are required which often limit the scope of the procedures. Thus, arylsulfonamides are cleaved by sodium in liquid ammonia,[3] sodium naphthalenide or anthracenide[4] and by heating to reflux in strong acid (e.g. 48% HBr in the presence of phenol).[5] These harsh conditions have led to the development of new methods of deprotection of *N-alkyl* sulfonamides. This has included the deprotection of arene- and pyridine-2-sulfonamides using SmI_2[6,7]or electrolysis.[7] We now wish to report[8] that the deprotection of *N-acyl* sulfonamides can be achieved under mild reaction conditions using Bu_3SnH, SmI_2 or $TiCl_4/Zn$.

Results and Discussion

Preliminary results

The deprotection of *N*-acyl sulfonamides using tributyltin hydride was first observed serendipitously, from the attempted radical cyclisation of halides bearing an unsaturated amide side-chain. It was envisaged that precursors of this type could undergo 5-*exo* radical cyclisation so as to form substituted pyrrolidinones (Scheme 1). Initially, however, reaction of the secondary amide **1a** with Bu_3SnH yielded only the protected alanine **2** (derived from simple reduction) and oxazoline **3** (formed by an ionic cyclisation reaction[9]). The lack of radical cyclisation was thought to be due to the conformation of the amide bond and in an attempt to perturb the amide conformer population and facilitate radical cyclisation, a bulky protecting group was then introduced on nitrogen.[10] Thus, the introduction of an *N*-benzyl group in chloride **1b**† did promote cyclisation to give the desired pyrrolidinone **4**, but only in 26% yield. A number of other products were formed including diester **5**, which presumably was derived from hydrolysis of the intermediate iminium ion **6**.

The formation of both **3** and **5** results from an initial nucleophilic displacement of the halogen by the amide group (to form, e.g. **6**) and in an attempt to inhibit this side-reaction, a (bulky) electron-withdrawing sulfonyl group was introduced on nitrogen (Scheme 2). Unexpectedly, however, reaction of the primary chlorides **7a**,**b** with (1.1 equiv. of) Bu_3SnH led to chemoselective desulfonylation and the formation of secondary amide **8** in 64–83% yield. No

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† The corresponding primary bromide was unstable and could not be purified by column chromatography.

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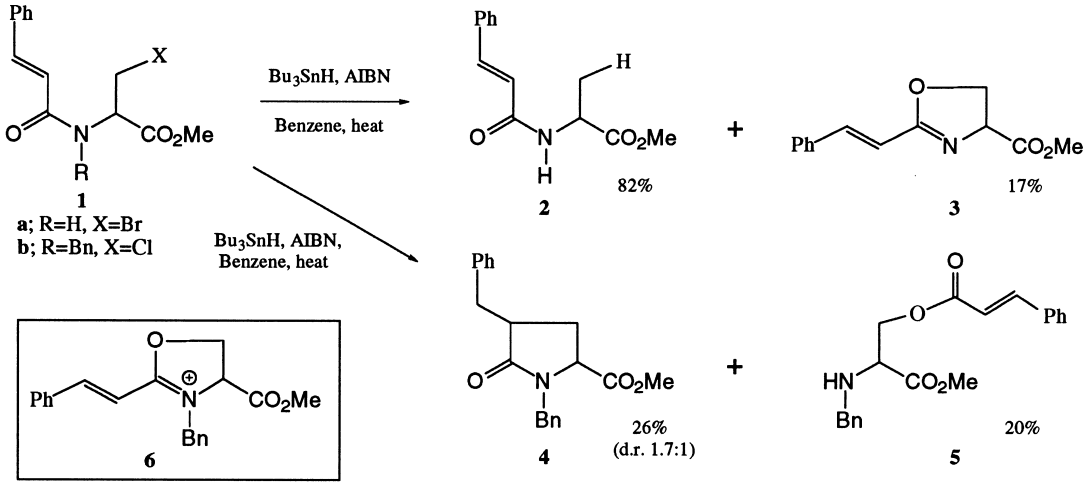
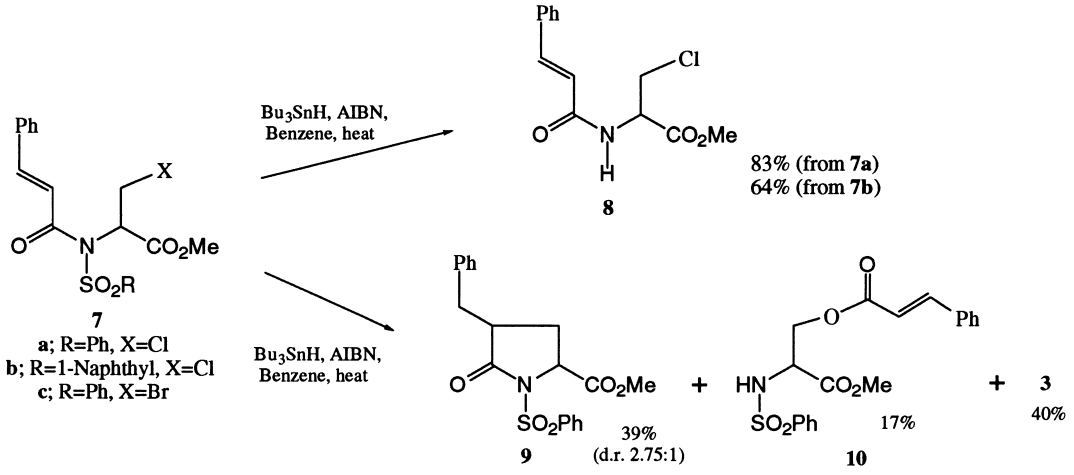


Scheme 1.



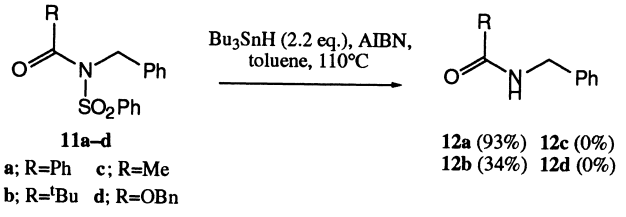
Scheme 2.

products derived from homolysis of the carbon–chlorine bond were recovered from these reactions. Even the bromide precursor **7c** (with a weaker carbon–halogen bond) underwent deprotection, in addition to cyclisation (which gave **9**), to give secondary amide **1a**, which then underwent cyclisation to form the oxazolidine **3** in 40% yield. The diester **10** was also isolated in 17% yield from this reaction.

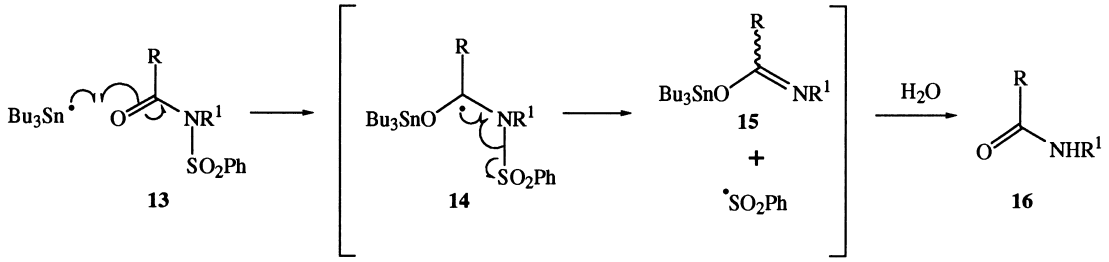
Although the radical cyclisation of these halo-amide precursors proved problematic, the unforeseen *N*-sulfonyl deprotection of **7a**–**c** using Bu_3SnH was of considerable interest and this prompted us to investigate the mechanism and generality of this mild method of deprotection.

Tin hydride deprotections

The deprotection of *N*-benzenesulfonamides **11a**–**d**, prepared on sulfonylation followed by acylation of benzylamine, was first investigated (Scheme 3). Initially, the reaction of **11a** with 1.1 equiv. of Bu_3SnH and 0.1 equiv. of AIBN in boiling benzene was examined and deprotection to give **12a** was observed, but only in 40% yield. This could be improved to an excellent 93% yield when using 2.2 equiv. of Bu_3SnH in boiling toluene and adding the AIBN portionwise (0.1 equiv. added every 0.5 h). A total of 0.4 equiv. of AIBN was required for the complete conversion of **11a** and this presumably reflects a short radical chain length. The presence of an amide carbonyl is crucial for the deprotection of **11a** because when *N*,*N*-dibenzylbenzenesulfonamide (Bn_2NSO_2Ph) was reacted with Bu_3SnH and AIBN for 48 h, only starting material was recovered. In order to investigate the influence of the amide side chain, the deprotection of **11b**–**d** was then explored using the optimised reaction conditions (for **11a** to **12a**). Thus, reaction of the *tert*-butyl analogue **11b** was moderately successful and a 34% yield of secondary amide **12b** together with 45% of recovered starting material was



Scheme 3.



Scheme 4.

isolated after 12 h. The importance of the nature of the amide carbonyl was also evident from reaction of the *N*-acetyl derivative **11c** or carbamate **11d**. Neither of these reactions led to deprotection.

These results indicate that the nature of the amide substituent plays an important role in the deprotection reaction and it was initially proposed that the tributyltin radical attacks the amide bond of the sulfonamide **13** to give the intermediate tertiary radical **14** (Scheme 4).[11] Clearly this addition reaction is expected to be favoured if the amide substituent (*R*) is able to stabilise the resultant tertiary radical **14**. Fragmentation of **14** to eliminate the phenylsulfonyl radical ($PhSO_2^{\cdot}$) could then occur to afford a tin(IV) enolate **15** which would undergo hydrolysis during aqueous work-up to give the deprotected amide **16**.

In order to substantiate the proposed mechanism a series of experiments were undertaken in order to provide evidence for the phenylsulfonyl radical and/or the tin enolate. Initial experiments using EPR spectroscopy[12] to establish the formation of the phenylsulfonyl radical in the deprotection of **11a** were unsuccessful. Hence irradiation of **11a** with Me_6Sn_2 showed no evidence for the formation of $PhSO_2^{\cdot}$ although one intense singlet (g=2.0057) together with two weak singlet signals (g=2.0050 and 2.0064) due to unidentified transient species was obtained (and these disappeared immediately on cessation of photolysis). It should be noted that irradiation of a solution of **11a** with Bu_3SnH/AIBN afforded **12a** and so the EPR spectra are a result of the desulfonylation rather than an alternative photochemical process.

Experiments designed to trap the phenylsulfonyl radical by reaction with a vinyl ether were then investigated. Electrophilic sulfonyl radicals are known[13] to add to the electron-rich double bond of vinyl ethers and so the desulfonylation of **11a** was performed using *tert*-butyl vinyl ether ($^tBuO–CH=CH_2$), rather than toluene, as the solvent. However, although tin-hydride mediated deprotection of **11a** to **12a** was observed, no products derived from addition of the sulfonyl radical to the alkene were isolated.

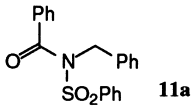
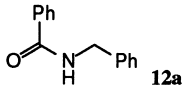
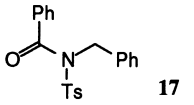
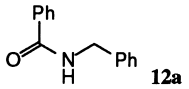
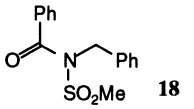
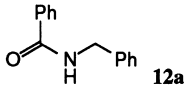
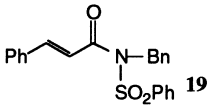
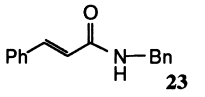
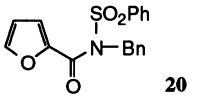
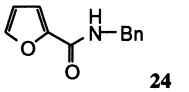
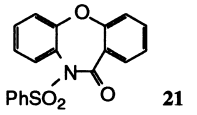
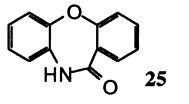
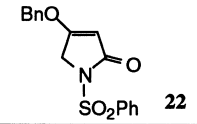
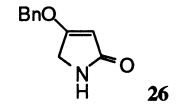
Our attention was then turned towards trapping the tin(IV) enolate by alkylation with alkyl halides.[14] Thus, sulfonamide **11a** was reacted with Bu_3SnH/AIBN in boiling toluene (according to the standard procedure) and when TLC indicated consumption of starting material, the reaction mixture was cooled to rt and benzyl bromide (3.3 equiv.) and DMPU were added. However, after heating overnight, column chromatography of the crude reaction mixture gave the deprotected amide **12a** in 64% yield and, unexpectedly, benzylphenylsulfone ($BnSO_2Ph$) in 85% yield. A similar reaction using allyl bromide as the alkylating agent also produced **12a** and allylphenylsulfone ($CH_2=CHCH_2SO_2Ph$) in 70% yield. It therefore appears that the alkyl bromide reacts with the sulfinate anion ($PhSO_2^-$) rather than with the tin(IV) enolate. Sulfinate anions are known to undergo this type of alkylation[15] and although the sulfones could be formed by a radical coupling reaction, the formation of sulfonyl and alkyl radicals (from $RBr/Bu_3Sn^{\cdot}$) would also be expected to give products derived from radical dimerisation (e.g. $PhSSO_2Ph$, $PhSO_2OSO_2Ph$,[16] $PhCH_2CH_2Ph$). The unexpected formation of the sulfinate anion could arise from reduction of the sulfonyl radical or, alternatively, from reduction of tertiary radical **14** followed by β-elimination of the sulfinate anion. An electron transfer pathway is also possible in which a radical anion is produced on reduction of **13** and this could fragment to give the sulfinate anion together with an amidyl radical. Although tributyltin hydride does not usually react by donating an electron to organic precursors, the tributyltin radical ($Bu_3Sn^{\cdot}$) could donate an electron to the radicals highlighted above (and so form the tributyltin cation). Indeed, this may explain why the optimum yield for deprotection of **11a** required 2.2 equiv. of Bu_3SnH and more than catalytic quantities of the initiator (AIBN); one equivalent of the tin radical adds to the amide carbonyl while the second reduces, for example, the sulfonyl radical.

Deprotections using tributyltin hydride, samarium diiodide or titanium tetrachloride/zinc

The mechanistic investigations of the Bu_3SnH reaction led us to investigate the deprotection of different *N*-sulfonyl amides, which contain a radical stabilising group in the amide side chain. This work also suggested that alternative metal reducing agents such as samarium diiodide or low-valent titanium, which are known[17] to readily donate an electron to carbonyl groups, could be employed to deprotect these types of compound. The successful use of these three reagents in the deprotection of amides **11a** and **17**–**22** is shown in Table 1.

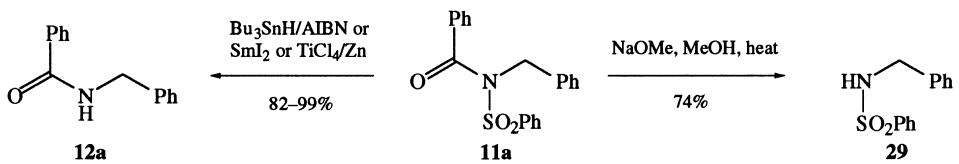
Compared to the Bu_3SnH reaction, the deprotection of **11a** using SmI_2 was slightly higher yielding (i.e. quantitative) and the conversion was much quicker (typically 10 min rather than 2 h). The reaction was also carried out at 0°C followed by warming to rt (rather than at 110°C) using 3 equiv. of SmI_2 to ensure complete consumption of the starting material. It should be noted that whereas the SmI_2 deprotection of *N*-alkyl-arenesulfonamides[6b] required the

Table 1.

Sulfonamide	Product	Yield(%)		
		Bu_3SnH	SmI_2 [a]	$TiCl_4/Zn$ [b]
 **11a**	 **12a**	93	99	82
 **17**	 **12a**	83	87	NA
 **18**	 **12a**	71	71	68
 **19**	 **23**	94	NA	94
 **20**	 **24**	82	88	67
 **21**	 **25**	77	62	88
 **22**	 **26**	35 (79[c])	74	NA

[a] SmI_2 (3.0 equiv.), THF, 0°C to rt.
[b] $TiCl_4$ (3 equiv.), Zn (18 equiv.), THF, 65°C.
[c] Based on recovered starting material; N/A=not attempted.

use of DMPU as a co-solvent (to increase the reduction potential of SmI_2), this was not necessary for the deprotection of **11a** (or subsequent *N*-acylsulfonamide deprotections). In contrast, the $TiCl_4/Zn$ reaction required the in situ generation of the low-valent titanium reductant by treatment of $TiCl_4$ with excess zinc. It was found that addition of 18 equiv. of zinc to 3 equiv. of $TiCl_4$ in dry, refluxing tetrahydrofuran gave the best deprotection results and this resulted in the isolation of **12a** in 82% yield after 17 h. When the equivalents of zinc was reduced, the rate of the reaction was much slower. For example, when a 1:4 ratio of $TiCl_4/Zn$ was used the reaction took 40 h to give a 78% yield of **12a**. It is believed that low-valent titanium is the reductant as attempted deprotection of **11a** using only Zn (or Me_3SiCl/Zn[17]) was found to be ineffective. In addition, when **11a** was heated overnight with 3 equiv. of $TiCl_4$ only starting material was recovered and so the deprotection is not due to the acidic reaction conditions. The reaction of related amide precursors **17**–**22** using each of these methods were generally found to give comparable yields of deprotected products. It is envisaged that the mechanism of the deprotection reactions using SmI_2 or $TiCl_4/Zn$ follows a similar path to that outlined for the Bu_3SnH reaction (Scheme 4). Electron transfer is expected to generate a radical intermediate of type **14** (or a radical anion) together with, for example, Sm(III). The resultant tertiary radical could then fragment to expel the sulfonyl radical, which in the presence of a further equivalent of the reducing agent is expected to form the sulfinate anion by-product.



Scheme 5.

Conclusions

Three novel metal-mediated deprotections of *N*-sulfonyl amides have been developed. These methods complement the known[18] cleavage of the amide N–CO bond which occurs on treatment of these compounds with base. Thus, for example, we found that on treatment of **11a** with sodium methoxide, the sulfonamide **29** was isolated in 74% yield (Scheme 5). The yields from each of the deprotection methods are generally comparable although the reaction conditions vary considerably. Whereas, for example, the Bu_3SnH/AIBN reactions take place in refluxing toluene, the $TiCl_4$/Zn deprotections are conducted at 65°C while the SmI_2 reactions can be carried out at 0°C to rt. All three methods gave rise to products of high purity and the metal by-products (e.g. tin oxides) were easily removed on work-up and chromatography. It is anticipated that the mild and chemoselective nature of these deprotection reactions should lead to their application in synthesis.[19] In addition, these results could promote interest in the reaction of radicals with amides, which to our knowledge has been unexplored.

Experimental

IR spectra were recorded on an ATI Mattson Genesis FT IR spectrometer. ^{1}H NMR and ^{13}C spectra were recorded on a Jeol EX 270 or Bruker AMX500 spectrometer. The spectra were assigned using DEPT experiments. Coupling constants (*J*) were recorded in Hertz to the nearest 0.5 Hz. Mass spectra were recorded on a Fisons Instruments VG Analytical Autospec Spectrometer system. Thin layer chromatography (TLC) was performed on Merck aluminium-backed silica gel plates. Compounds were visualised under a UV lamp, using basic potassium permanganate solution, acidic cerium(IV) sulfate-molybdic acid solution and/or iodine. Column chromatography was perfomed using silica gel (Matrex Silica 60, 70–200 μm Fisons or ICN flash silica 60, 32–63 μm). Solvents were purified/dried using standard literature methods. Petroleum ether refers to the fraction with bp 40–60°C. Bu_3SnH was purchased from Lancaster Synthesis Ltd and was distilled immediately before use. Samarium diiodide was purchased from Aldrich Chemical Company as a 0.1 M solution in tetrahydrofuran.

Methyl (*E*)-2-cinnamamido-3-bromopropanoate 1a. To a stirred solution of D,L-serine methyl ester hydrochloride (0.5 g, 3.24 mmol) in dichloromethane (20 cm^3) was added triethylamine (0.81 g, 8.1 mmol) at 0°C. After 0.5 h, a solution of *trans*-cinnamoyl chloride (0.6 g, 3.56 mmol) in dichloromethane (10 cm^3) was added. The mixture was allowed to warm to rt and stirred for 2 h. Water (20 cm^3) and dichloromethane (20 cm^3) were then added and the mixture stirred vigorously for 1 h. The organic layer was separated, washed with water, brine, dried ($MgSO_4$), evaporated under reduced pressure and purified by column chromatography to give methyl (*E*)-2-cinnamamido-3-hydroxypropanoate (0.65 g, 81%) as a colourless oil. To a stirred solution of the alcohol (0.1 g, 0.4 mmol) in tetrahydrofuran (5 cm^3) was added triphenylphosphine (140 mg, 0.52 mmol) followed by *N*-bromosuccinimide (93 mg, 0.52 mmol). After 2 h, the solvent was removed in vacuo to afford a pale yellow oil. Chromatography of the residue (silica; dichloromethane) afforded the bromide **1a** (102 mg, 81%) as a yellow oil; R_f 0.2 (dichloromethane); ν_{max} (thin film) 1738 (s), 1652 (s), 1622 (s), 1569 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.70 (1H, d, *J*=15.5 Hz, PhC*H*=CH), 7.63–7.21 (5H, m, aromatics), 6.65 (1H, d, *J*=15.5 Hz, PhCH=C*H*), 4.62–4.58 (1H, m, NC*H*O), 4.51 (1H, br s, N*H*), 3.96–3.85 (2H, m, CH_2Br), 3.69 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 169.9 (CO_2CH_3), 165.3 (N*C*O), 142.3 (Ph*C*H=CH), 134.5, 130.2, 128.9, 127.5 (aromatics), 118.6 (PhCH=*C*H), 55.8 (N*C*HCO), 53.2 (CO_2CH_3), 34.0 (*C*H_2Br); *m*/*z* (CI, NH_3) 314 (^{81}M+H$^+$, 4%), 232 (100), 172 (15), 148 (25), 131 (11).

Methyl (*E*)-2-(*N*-benzylcinnamamido)-3-chloropropanoate 1b. To a stirred solution of (2*RS*)-methyl 2-(*N*-benzylamino)-3-*tert*-butyldimethylsiloxypropanoate[20] (2.77 g, 8.58 mmol) in dichloromethane (50 cm^3) was added triethylamine (0.95 g, 9.43 mmol) while the solution was stirred at 0°C. After 0.5 h a solution containing *trans*-cinnamoyl chloride (1.57 g, 9.43 mmol) in dichloromethane (20 cm^3) was added gradually. The solution was allowed to warm to rt and stirred for 2 h. Water (50 cm^3) and dichloromethane (50 cm^3) were then added and the solution was stirred vigorously for 0.1 h. The organic layer was separated, washed with water (×2), brine, dried ($MgSO_4$), and evaporated to form the amide (3.34 g, 83%) as a colourless oil. To a solution of the amide (0.66 g, 1.46 mmol) in methanol (10 cm^3) was added 4-toluenesulfonic acid (catalytic) and the solution was stirred for 24 h. The methanol was then removed, the residue dissolved in ethyl acetate, washed with water, brine, dried ($MgSO_4$), evaporated and purified by column chromatography to give the primary alcohol (0.46 g, 94%) as a white solid (mp 173–176°C). To a solution of the alcohol (0.2 g, 0.59 mmol) in chloroform (20 cm^3) was added phosphorus pentachloride (135 mg, 0.65 mmol) and the resulting solution was allowed to stir for 12 h. The chloroform was removed in vacuo and the crude product was washed with water, brine, dried ($MgSO_4$) and then purified by column chromatography (silica; petroleum ether–diethyl ether, 1:1) to afford chloride **1b** (137 mg, 87%) as a white solid; mp 110–113°C; R_f 0.3 (petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 1742 (s), 1650 (s), 1612 (s), 1433 (m), 1205 (s) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.70 (1H, d, *J*=15.5 Hz, PhC*H*=CH), 7.55–7.18 (10H, m, aromatics), 6.73 (1H, d, *J*=15.5 Hz, PhCH=C*H*), 4.94 (1H, d, *J*=17 Hz, PhC*H*N), 4.70 (1H, d, *J*=17 Hz, PhC*H*N), 4.40–4.33 (1H, m, C*H*Cl), 4.08–4.06 (1H, m, C*H*Cl), 3.88–3.85 (1H, m, NC*H*O), 3.62 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 168.6 (CO_2CH_3), 165.8 (N*C*O), 144.7 (Ph*C*H=CH), 136.6, 134.7, 130.6, 130.0, 129.6, 128.7, 128.6, 128.5, 128.0 (aromatics), 116.5 (PhCH=*C*H), 62.1 (N*C*HCO), 53.4 (*C*H_2Cl), 52.5 (CO_2CH_3), 42.4 (Ph*C*H_2); *m*/*z* (CI, NH_3) 360 (^{37}M+H$^+$, 25%), 340 (30), 322 (100), 131 (15); Found: ^{35}M+H$^+$, 358.1222. $C_{20}H_{20}ClNO_3$ requires for ^{35}M+H$^+$, 358.1210.

Typical procedure for the preparation of 7a–c

To a solution of D,L-serine methyl ester hydrochloride (0.78–6.43 mmol) in pyridine (5–20 cm^3) at −5°C was added a solution of benzene- or naphthalene-sulfonyl chloride (0.85–7.39 mmol) in pyridine (1–3 cm^3). The

mixture was allowed to warm to rt and stirred for 24 h. The pyridine was then removed in vacuo and the crude product dissolved in ethyl acetate, washed with a saturated solution of copper sulfate (50 cm^3), water (50 cm^3), brine (50 cm^3), dried ($MgSO_4$), evaporated and purified by column chromatography to give the sulfonamides (48–68%). To a stirred solution of the alcohol (0.31–7.97 mmol) in dry tetrahydrofuran (10–60 cm^3) was added triphenylphosphine (0.37–12.0 mmol) followed by *N*-chlorosuccinimide or *N*-bromosuccinimide (0.37–12.0 mmol). After stirring overnight, the solvent was removed in vacuo and the product purified by column chromatography to afford primary chlorides or bromide (73–91%). To a stirred solution of the halide (0.17–1.20 mmol) in dry tetrahydrofuran (10–30 cm^3) at −15°C under nitrogen, was added sodium hydride (0.17–1.20 mmol) and the solution was stirred for 0.5 h. A solution of *trans*-cinnamoyl chloride (0.17–1.20 mmol) in dry tetrahydrofuran (0.5–1 cm^3) was then added, the reaction was allowed to warm to rt and then stirred for a further 0.5–24 h. Ethyl acetate (15–30 cm^3) and water (15–30 cm^3) were then added and the mixture stirred vigorously for 0.5 h. The organic layer was separated, washed with water (15–30 cm^3), brine (15–30 cm^3), dried ($MgSO_4$), evaporated in vacuo and purified by column chromatography to afford amides **7a–c** (34–61%) as oils.

Methyl (*E*)-2-(*N*-benzenesulfonylcinnamamido)-3-chloropropanoate 7a. R_f 0.3 (silica; petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 1744 (s), 1677 (m), 1616 (s), 1448 (m), 1349 (m), 1163 (s) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 8.27–7.34 (12H, m, PhC*H*=C*H* and 2× aromatics), 5.51–5.46 (1H, m, NC*H*O), 4.40 (1H, dd, *J*=12 and 5 Hz, C*H*Cl), 4.18 (1H, dd, *J*=12 and 9 Hz, C*H*Cl), 3.85 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 167.8 (CO_2CH_3), 165.3 (N*C*O), 146.8 (Ph*C*H=CH), 139.6, 134.0, 130.9, 129.7, 128.9, 128.8, 128.6, 128.3, 128.1 (aromatics), 117.3 (PhCH=*C*H), 61.0 (N*C*HCO), 52.9 (CO_2CH_3), 41.5 (CH_2Cl); *m*/*z* (CI, NH_3) 427 ($^{37}M+NH_4^+$, 2%), 410 ($^{37}M+H^+$, 3), 232 (90), 131 (100); Found: $^{35}M+H^+$, 408.0670. $C_{19}H_{18}ClNO_5S$ requires for $^{35}M+H^+$, 408.0672.

Methyl (*E*)-2-(*N*-benzenesulfonylcinnamamido)-3-bromopropanoate 7b. R_f 0.3 (silica; petroleum ether–diethyl ether, 2:1); ν_{max} (thin film) 1746 (s), 1676 (m), 1617 (m), 1488 (m), 1349 (m), 1330 (m), 1201 (s) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 8.10–7.17 (12H, m, PhC*H*=C*H* and 2×aromatics), 5.34 (1H, dd, *J*=9.5 and 5 Hz, NC*H*O), 4.13 (1H, dd, *J*=11 and 5 Hz, C*H*Br), 3.85 (1H, dd, *J*=11 and 9.5 Hz, C*H*Br), 3.69 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 167.7 (CO_2CH_3), 165.3 (N*C*O), 146.8 (Ph*C*H=CH), 139.6, 134.2, 134.0, 130.9, 129.4, 128.9, 128.4, 128.2 (aromatics), 117.4 (PhCH=*C*H), 61.0 (N*C*HCO), 52.9 (CO_2CH_3), 29.1 (CH_2Br); *m*/*z* (CI, NH_3) 454 ($^{81}M+H^+$, 1%), 232 (100); Found: $^{79}M+H^+$, 452.0167. $C_{19}H_{18}BrNO_5S$ requires for $^{79}M+H^+$, 452.0167.

Methyl (*E*)-2-(*N*-naphthalene-1-sulfonylcinnamamido)-3-chloropropanoate 7c. R_f 0.4 (silica; petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 1744 (s), 1676 (s), 1616 (s), 1347 (s), 1262 (w), 1235 (w), 1200 (s), 1160 (s), 1136 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.98–7.30 (9H, m, PhC*H*=C*H* and aromatics), 5.27 (1H, dd, *J*=7.5 and 5.5 Hz, NC*H*O), 4.37 (1H, dd, *J*=12 and 5.5 Hz, C*H*Cl), 3.92 (1H, dd, *J*=12 and 7.5 Hz, C*H*Cl), 3.60 (3H, s, CO_2CH_3); *m*/*z* (FAB) 482 ($^{37}M+Na^+$, 6%), 460 ($^{37}M+H^+$, 11), 422 (15), 422 (15), 250 (30), 131 (100).

Typical procedure for reaction of 1a–b or 7a–c with tributyltin hydride

A 0.02 mol dm^{-3} solution containing tributyltin hydride (0.30 mmol) and azobisisobutyronitrile (5 mg, 0.03 mmol) in benzene was added dropwise over 1 h to a 0.03 mol dm^{-3} solution of **1a**,**b** or **7a–c** (0.27 mmol) in boiling benzene while stirring under nitrogen. The solution was then heated to reflux for a further 2–12 h and then the solvent was removed in vacuo. Diethyl ether (15–20 cm^3) and aqueous potassium fluoride (8%, 20–25 cm^3) were added to the residue, and the mixture stirred overnight. The organic layer was separated, washed with water, brine, dried ($MgSO_4$), evaporated in vacuo and purified by column chromatography (silica) to afford products generally as oils.

Methyl (*E*)-2-*N*-cinnamamidopropanoate 2. R_f 0.4 (silica; dichloromethane–ethyl acetate, 10:1); ν_{max} (thin film) 3341 (br, s), 1742 (s), 1658 (s), 1652 (s), 1542 (m), 1211 (w) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.57 (1H, d, *J*=17 Hz, PhC*H*=CH), 7.42–7.19 (5H, m, aromatics), 6.38 (1H, d, *J*=15.5 Hz, PhCH=C*H*), 6.25 (1H, br s, N*H*), 4.71–4.66 (1H, m, NC*H*O), 3.71 (3H, s, CO_2CH_3), 1.40 (3H, d, *J*=8 Hz, $CHCH_3$); δ_C (67.5 MHz; $CDCl_3$) 173.6 (CO_2CH_3), 165.2 (N*C*O), 141.6 (Ph*C*H=CH), 134.6, 129.8, 128.8, 127.8 (aromatics), 120.0 (PhCH=*C*H), 52.5 (CO_2CH_3), 48.2 (N*C*HCO), 18.6 ($CHCH_3$); *m*/*z* (CI, NH_3) 234 ($M+H^+$, 100%).

Oxazoline 3. R_f 0.2 (silica; petroleum ether–diethyl ether, 2:5); ν_{max} (thin film) 1737 (s), 1649 (s), 1608 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.41–6.99 (6H, m, aromatics and PhC*H*=CH), 6.59 (1H, d, *J*=16 Hz, PhCH=C*H*), 4.83 (1H, dd, *J*=10.5 and 8 Hz, NC*H*CO), 4.57–4.44 (2H, m, NCH_2O), 3.75 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 171.5 (CO_2CH_3), 141.3 (CH*C*=N), 134.8 (*C*=CH), 129.8, 128.7, 127.5 (aromatics), 127.8 (Ph*C*H=CH), 114.3 (PhCH=*C*H), 69.1 (CH_2O), 68.4 (N*C*HCO), 52.7 (CO_2CH_3); *m*/*z* (CI, NH_3) 232 ($M+H^+$, 100%), 172 (10); Found: $M+H^+$, 232.0968. $C_{13}H_{14}NO_3$ requires for $M+H^+$, 232.0974.

Methyl *N*-benzyl-4-benzylpyroglutamate 4. R_f 0.3 (silica; petroleum ether–diethyl ether, 2:5); ν_{max} (thin film) 1743 (s), 1648 (s), 1452 (m), 1207 (s), 700 (w) cm^{-1}; δ_H (500 MHz; $CDCl_3$) (major diastereoisomer) 7.71–7.16 (10H, m, aromatics), 5.62 (1H, d, *J*=16 Hz, PhC*H*N), 4.24–4.21 (1H, m, NC*H*CO), 3.89 (1H, d, *J*=16 Hz, PhC*H*N), 3.78 (3H, s, CO_2CH_3), 3.23–3.19 (1H, m, $PhCH_2CH$), 2.98 (1H, dd, *J*=10 and 3 Hz, PhC*H*CH), 2.62 (1H, dd, *J*=10 and 6 Hz, PhC*H*CH), 2.41 (1H, app. dd, *J*=9 and 2 Hz, CHC*H*CH), 2.29–2.24 (1H, m, CHC*H*CH); δ_C (67.5 MHz; $CDCl_3$) (major diastereoisomer) 172.1, 169.5 (CO_2CH_3, N*C*O), 142.6, 140.1 (*C*=CH), 128.8, 128.7, 128.5, 128.4, 127.7, 127.1, 126.6, 126.4 (*C*H=C), 58.0 (N*C*HCO), 52.7 (CO_2CH_3), 49.1 ($PhCH_2N$), 39.6 ($CHCH_2CH$ or $PhCH_2CH$), 35.6 ($PhCH_2CH$), 33.0 ($CHCH_2CH$ or $PhCH_2CH$); *m*/*z* (EI) 323 (M^+, 100%), 264 (100), 237 (12), 167 (10), 149 (20), 131 (94), 91 (95);

Found: M^+, 323.1524. $C_{20}H_{21}NO_3$ requires for M^+, 323.1521. The presence of the minor diastereoisomer was indicated by: δ_H (500 MHz; $CDCl_3$) 4.66 (1H, d, J=16 Hz, PhC*H*N), 4.18–4.16 (1H, m, NC*H*CO), 3.81 (1H, d, J=16 Hz, PhC*H*N), 3.70 (3H, s, CO_2CH_3), 3.15–3.13 (1H, m, $PhCH_2CH$), 2.89–2.81 (1H, m, PhC*H*), 2.74 (1H, dd, J=11 and 3 Hz, PhC*H*); δ_C (67.5 MHz; $CDCl_3$) 170.1, 169.0 (CO_2CH_3, NCO), 143.2, 142.9 (*C*=CH), 58.5 (NCHCO), 52.5 (CO_2CH_3), 48.7 ($PhCH_2N$), 39.5 ($CHCH_2CH$ or $PhCH_2CH$), 34.1 ($PhCH_2CH$), 29.7 ($CHCH_2CH$ or $PhCH_2CH$).

2-(*N*-Benzylamino)-2-methoxycarbonylethyl (*E*)-3-phenylpropenoate 5. R_f 0.8 (silica; ethyl acetate); ν_{max} (thin film) 1738 (s), 1716 (s), 1637 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.72–7.68 (1H, d, J=15 Hz, PhC*H*=CH), 7.45–7.10 (10H, m, aromatics), 6.32 (1H, d, J=15 Hz, PhCH=C*H*), 4.49–4.25 (2H, m, CH_2O), 3.83 (3H, s, CO_2CH_3), 3.79–3.61 (2H, m, $PhCH_2$), 3.55 (1H, t, J=6 Hz, NC*H*CO); δ_C (67.5 MHz; $CDCl_3$) 168.7, 167.6 (CO_2CH_3, NCO), 145.3 (PhCH=CH), 136.4, 134.9 (*C*=CH), 130.3, 130.0, 129.1, 128.9, 128.7, 128.4, 127.7 (*C*H=C), 117.0 (PhCH=*C*H), 62.3 (CH_2O), 53.1 ($PhCH_2$), 52.1 (CO_2CH_3); *m/z* (CI, NH_3) 340 ($M+H^+$, 100%), 192 (10), 131 (10), 91 (10); Found: $M+H^+$, 323.1554. $C_{20}H_{22}NO_4$ requires for $M+H^+$, 340.1549.

Methyl (*E*)-3-chloro-2-cinnamamidopropanoate 8. White solid; mp 145–146°C; R_f 0.5 (silica; diethyl ether); ν_{max} (thin film) 3233 (s), 1742 (s), 1652 (s), 1618 (s), 1525 (s), 1441 (w), 1358 (m), 1211 (s) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.77 (1H, d, J=16 Hz, PhC*H*=CH), 7.63–7.36 (5H, m, aromatics), 6.76 (1H, d, J=7 Hz, N*H*), 6.63 (1H, d, J=16 Hz, PhCH=C*H*), 5.25–5.23 (1H, m, NC*H*CO), 4.15 (1H, dd, J=11.5 and 3 Hz, C*H*Cl), 4.07 (1H, dd, J=11.5 and 3.5 Hz, C*H*Cl), 3.93 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 171.4, 169.4 (CO_2CH_3 and NCO), 142.5 (PhCH=CH), 130.0, 128.9, 128.0 (aromatics), 119.5 (PhCH=*C*H), 52.3 (CO_2CH_3), 53.1 (NCHCO), 45.2 (CH_2Cl); *m/z* (CI, NH_3) 270 ($^{37}M+H^+$, 15%), 234 (55), 232 (100); Found: $^{35}M+H^+$, 268.0738. $C_{13}H_{14}ClNO_3S$ requires for $^{35}M+H^+$, 268.0740.

***N*-Benzenesulfonyl-4-benzylpyroglutamate 9.** R_f 0.5 (silica; petroleum ether–diethyl ether, 2:5); ν_{max} (thin film) 1743 (s), 1447 (s), 1361 (m), 1210 (w), 1167 (s), 1140 (m), 1083 (w) cm^{-1}; δ_H (270 MHz; $CDCl_3$) (major diastereoisomer) 8.33–7.21 (10H, m, aromatics), 4.96 (1H, dd, J=6 and 4 Hz, NC*H*CO), 3.91 (3H, s, CO_2CH_3), 3.34 (1H, dd, J=14 and 4.5 Hz, PhC*H*), 3.05 (1H, dd, J=10 and 4.5 Hz, $PhCH_2CH$), 2.79 (1H, dd, J=14 and 9 Hz, PhC*H*), 2.35–2.30 (2H, m, $CHCH_2CH$); δ_C (67.5 MHz; $CDCl_3$) (major diastereoisomer) 173.7, 170.9 (CO_2CH_3 and NCO), 137.7 (*C*=CH), 134.3, 129.1, 128.8, 128.7, 128.6, 126.8 (*C*H=C), 57.4 (NCHCO), 52.8 (CO_2CH_3), 43.0 ($PhCH_2CH$), 35.8, 29.7 ($PhCH_2CH$ and $CHCH_2CH$); *m/z* (CI, NH_3) 391 ($M+NH_4^+$, 100%), 374 ($M+H^+$, 71), 314 (8), 310 (10), 234 (41), 232 (35), 172 (10); Found: $M+H^+$, 374.1050. $C_{19}H_{19}NO_5S$ requires for $M+H^+$, 374.1062. The presence of the minor diastereoisomer was indicated by: δ_H (270 MHz; $CDCl_3$) 4.92–4.89 (1H, m, NC*H*CO), 3.99 (3H, s, CO_2CH_3), 2.62 (1H, dd, J=12 and 9 Hz, PhC*H*); δ_C (67.5 MHz; $CDCl_3$) 174.1, 171.5 (CO_2CH_3 and NCO), 137.6 (*C*=CH), 58.0 (NCHCO), 52.9 (CO_2CH_3), 43.9 ($PhCH_2CH$), 36.4, 27.8 ($PhCH_2CH$ and $CHCH_2CH$).

2-(*N*-Benzenesulfonylamino)-2-methoxycarbonylethyl (*E*)-3-phenylpropenoate 10. R_f 0.2 (silica; petroleum ether–ethyl acetate, 5:2); ν_{max} (thin film) 3320 (s), 1738 (s), 1716 (s), 1639 (m), 1642 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.90–7.49 (10H, m, aromatics), 7.74 (1H, d, J=16 Hz, PhC*H*=CH), 6.42 (1H, d, J=16 Hz, PhCH=C*H*), 5.64 (1H, d, J=8.5 Hz, N*H*), 4.44–4.39 (1H, m, NC*H*CO), 3.74 (1H, dd, J=10.5 and 3.5 Hz, C*H*OCO), 3.59 (1H, dd, J=10.5 and 4 Hz, C*H*OCO), 3.64 (3H, s, CO_2CH_3); δ_C (67.5 MHz; $CDCl_3$) 169.7, 166.6 (CO_2CH_3 and OCOCH), 146.5 (PhCH=CH), 140.2, 134.4 (CH=*C*), 131.1, 129.6, 129.3, 128.7, 127.5 (*C*H=C), 117.1 (PhCH=*C*H), 64.9 (CH_2O), 55.4 (NCHCO), 53.5 (CO_2CH_3); *m/z* (CI, NH_3) 407 ($M+NH_4^+$, 6%), 390 ($M+H^+$, 3), 259 (85), 242 (60), 177 (10), 166 (12), 148 (35), 102 (100); Found: $M+NH_4^+$, 407.1279. $C_{19}H_{19}NO_6S$ requires for $M+NH_4^+$, 407.1277.

General procedure for acylation of *N*-sulfonylamines to give 11a–d and 17–20

To a stirred solution of the amine (0.68–2.34 mmol) in dry tetrahydrofuran (10–20 cm^3) at 0°C under a nitrogen atmosphere was added sodium hydride (0.82–2.84 mmol) and the reaction was allowed to stir for 1 h. A solution of the acid chloride (0.82–2.84 mmol) in tetrahydrofuran (1–2 cm^3) was then added and the reaction was allowed to warm to rt and stirred overnight. The solvent was removed in vacuo and the residue dissolved in ethyl acetate, washed with water, dried ($MgSO_4$) and evaporated in vacuo to afford crude product, purified by column chromatography (silica) to afford the amide (63–99%).

***N*-Benzoyl-*N*-benzylbenzenesulfonamide 11a.** White solid; mp 78–79°C; R_f 0.3 (petroleum ether–ethyl acetate, 3:1); ν_{max} (thin film) 1688 (s), 1448 (s), 1358 (s), 1324 (m), 1170 (s), 1087 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.73–7.18 (15H, m, aromatics), 4.91 (2H, s, $PhCH_2$); δ_C (67.5 MHz; $CDCl_3$) 171.5 (NCO), 138.8, 136.0, 134.8 (*C*=CH), 133.6, 131.8, 128.7, 128.5, 128.4, 128.2, 127.9, 127.8 (*C*H=C), 51.3 ($PhCH_2$); *m/z* (CI, NH_3) 369 ($M+NH_4^+$, 15%), 352 ($M+H^+$, 45), 212 (100); Found: $M+H^+$, 352.1013. $C_{20}H_{17}NO_3S$ requires for $M+H^+$, 352.1007.

***N*-Benzyl-*N*-(2,2-dimethylpropionyl)benzenesulfonamide 11b.** White solid; mp 100–102°C; R_f 0.4 (petroleum ether–ethyl acetate, 2:1); ν_{max} (thin film) 2925 (m), 2936 (m), 1686 (s), 1447 (m), 1148 (m), 1350 (s), 1310 (w), 1169 (s), 1088 (m), 971 (w), 739 (w) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.81–7.21 (10H, m, aromatics), 5.02 (2H, s, NCH_2), 1.25 (9H, s, C*Me*$_3$); δ_C (67.5 MHz; $CDCl_3$) 181.8 (NCO), 139.0, 136.0 (*C*=CH), 133.2, 128.4, 127.7, 127.4 (*C*H=C), 51.0 ($PhCH_2$), 42.6 (*C*Me$_3$), 27.9 (C*Me*$_3$); *m/z* (CI, NH_3) 349 ($M+NH_4^+$, 17%), 332 ($M+H^+$, 78), 265 (30), 248 (17), 192 (100); Found: $M+H^+$, 332.1315. $C_{18}H_{21}NO_3S$ requires for $M+H^+$, 332.1313.

***N*-Benzyl-*N*-ethanoylbenzenesulfonamide 11c.** White solid; mp 72–75°C; R_f 0.3 (petroleum ether–diethyl ether, 2:3); ν_{max} (thin film) 1705 (s), 1448 (m), 1354 (s), 1236 (s), 1168 (m), 1090 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.89–7.16

(10H, m, aromatics), 5.10 (2H, s, NCH_2), 2.29 (3H, s, COCH_3); δ_C (67.5 MHz; $CDCl_3$) 171.5 (N*C*O), 138.9, 136.2 (*C*=CH), 131.8, 128.7, 128.0, 127.7, 127.5 (*C*H=C), 53.2 (Ph*C*H_2), 32.1 (CO*C*H_3); *m/z* (CI, NH_3) 307 ($M+NH_4^+$, 100%), 290 ($M+H^+$, 18), 265 (15), 167 (20).

***N*-Benzyl-*N*-(benzyloxycarbonyl)benzenesulfonamide 11d.** White solid; mp 106–108°C; R_f 0.4 (petroleum ether–ethyl acetate, 5:2); ν_{max} (thin film) 1802 (s), 1677 (s), 1587 (w), 1541 (w), 1342 (m), 1300 (m), 1283 (m), 1162 (s), 1059 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.55–7.02 (15H, m, aromatics), 5.01 (4H, s, PhCH_2O and NCH_2); δ_C (67.5 MHz; $CDCl_3$) 152.3 (N*C*O_2), 139.2, 136.7, 134.3 (*C*=CH), 133.3, 128.6, 128.5, 128.4, 128.3, 127.9 (*C*H=C), 69.2 (Ph*C*H_2O), 50.0 (Ph*C*H_2); *m/z* (CI, NH_3) 399 ($M+NH_4^+$, 100%), 382 ($M+H^+$, 22), 265 (10), 242 (19), 196 (50), 181 (42), 91 (10); Found: $M+NH_4^+$, 399.1380. $C_{21}H_{19}NO_3S$ requires for $M+NH_4^+$, 399.1379.

***N*-Benzoyl-*N*-benzyl-4-methylbenzenesulfonamide 17.** White solid; mp 82–83°C; R_f 0.4 (petroleum ether–ethyl acetate, 2:1); ν_{max} (thin film) 2955 (m), 2924 (m), 2854 (m), 1677 (s), 1597 (w), 1540 (w), 1352 (m), 1302 (m), 1285 (m), 1162 (s), 1059 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.54–7.11 (14H, m, aromatics), 4.91 (2H, s, PhCH_2), 2.34 (3H, s, CH_3–C=C); δ_C (67.5 MHz; $CDCl_3$) 170.1 (N*C*O), 142.2, 134.6, 136.1 (*C*=CH), 129.8, 128.4, 127.5, 127.2, 127.1 (*C*H=C), 51.2 (Ph*C*H_2), 21.6 (*C*H_3–C=C); *m/z* (CI, NH_3) 366 ($M+H^+$, 42%), 212 (100), 105 (10); Found: $M+H^+$, 366.1146. $C_{21}H_{19}NO_3S$ requires for $M+H^+$, 366.1146.

***N*-Benzoyl-*N*-benzyl-methanesulfonamide 18.** White solid; mp 81–84°C; R_f 0.3 (petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 1682 (s), 1351 (s), 1320 (w), 1302 (m), 1163 (s), 952 (w) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.58–7.07 (10H, m, aromatics), 4.92 (2H, s, PhCH_2), 2.97 (3H, s, $SO_2C$$H_3$); δ_C (67.5 MHz; $CDCl_3$) 172.6 (N*C*O), 135.6, 133.8 (*C*=CH), 132.2, 128.5, 127.1 (*C*H=C), 52.2 (Ph*C*H_2), 42.9 (SO_2*C*H_3); *m/z* (CI, NH_3) 307 ($M+NH_4^+$, 15%), 290 ($M+H^+$, 55), 212 (100), 122 (12), 105 (35), 91 (20); Found: $M+H^+$, 290.0854. $C_{15}H_{15}NO_3S$ requires for $M+H^+$, 290.0851.

***N*-Benzyl-*N*-cinnamoylbenzenesulfonamide 19.** White solid; mp 90–94°C; R_f 0.3 (petroleum ether–ethyl acetate, 3:1); ν_{max} (thin film) 1678 (s), 1618 (s), 1149 (s), 1356 (s), 1160 (s) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.72–7.13 (15H, m, aromatics), 7.57 (1H, d, *J*=15.5 Hz, PhC*H*=CH), 7.16 (1H, d, *J*=15.5 Hz, PhCH=C*H*), 5.08 (2H, s, PhCH_2); δ_C (67.5 MHz; $CDCl_3$) 166.1 (N*C*O), 146.3 (Ph*C*H=CH), 139.7, 136.6 (*C*=CH), 130.6, 129.5, 128.9, 128.6, 128.3, 127.9, 127.7, 127.5 (*C*H=C), 117.9 (PhCH=*C*H), 49.4 (Ph*C*H_2); *m/z* (CI, NH_3) 378 ($M+H^+$, 42%), 238 (100), 48 (11), 131 (23), 106 (30); Found: $M+H^+$, 378.1159. $C_{22}H_{19}NO_3S$ requires for $M+H^+$, 378.1164.

***N*-Benzyl-*N*-(2-furoyl)-benzenesulfonamide 20.** White solid; mp 93–97°C; R_f 0.4 (petroleum ether–ethyl acetate, 2:1); ν_{max} (thin film) 2956 (m), 2924 (m), 2855 (m), 1727 (s), 1675 (s), 1471 (m), 1148 (m), 1387 (w), 1339 (s), 1268 (m), 1164 (s), 1086 (m), 1073 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.83–7.01 (12H, m, benzene and 2× furan C=C*H*), 6.39–6.35 (1H, m, furan C=C*H*), 5.20 (2H, s, PhCH_2); δ_C (67.5 MHz; $CDCl_3$) 159.4 (N*C*O), 146.4 (NCO*C*), 138.8, 136.3 (*C*=CH), 146.1, 133.6, 129.1, 128.7, 127.8, 127.6, 127.1, 120.5, 12.2 (*C*H=C), 50.6 (Ph*C*H_2); *m/z* (CI, NH_3) 359 ($M+NH_4^+$, 15%), 342 ($M+H^+$, 100), 265 (9), 202 (35), 200 (31), 106 (10); Found: $M+H^+$, 342.0793. $C_{18}H_{15}NO_4S$ requires for $M+H^+$, 342.0799.

General procedure for preparation of amides 21–22

To a stirred solution of the amide **25**–**26** (1.42–1.59 mmol) in dry tetrahydrofuran (10–20 cm^3) was added sodium hydride (2.13–2.39 mmol) and the solution was allowed to stir for 1 h at −5°C under nitrogen. A solution of the sulfonyl chloride (2.13–2.39 mmol) in tetrahydrofuran (2 cm^3) was then added and the reaction was warmed to rt and stirred overnight. The solvent was removed in vacuo and the residue dissolved in ethyl acetate, washed with water, brine, dried ($MgSO_4$) and evaporated to give crude product. Purification by column chromatography (silica) afforded the desired sulfonamide (61–64%).

10-Benzenesulfonyl-dihydroben[*b,f*][1,4]oxazepin-11-one 21. White solid; mp 174–175°C; R_f 0.3 (petroleum ether–diethyl ether, 1:1); ν_{max} (thin film) 1687 (s), 1604 (m), 1492 (m), 1476 (m), 1450 (s), 1364 (s), 1308 (s), 1277 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 8.13–7.01 (8H, m, aromatics); δ_C (67.5 MHz; $CDCl_3$) 167.5 (N*C*O), 146.4 (NCO*C*), 159.7, 150.9, 131.9, 130.6, 125.0 (*C*=CH), 134.5, 125.9, 125.8, 125.2, 121.7, 121.3, 120.8 (*C*H=C); *m/z* (EI) 351 (M^+, 1%), 287 (60), 210 (10), 182 (100), 154 (10), 127 (10); Found: M^+, 351.0566. $C_{19}H_{13}NO_4S$ requires for M^+, 351.0565.

***N*-Benzenesulfonyl-4-benzyloxy-3-pyrrolidin-2-one 22.** White solid; mp 126–128°C; R_f 0.3 (hexane–ethyl acetate, 2:1); ν_{max} (thin film) 1724 (s), 1615 (s), 1148 (m), 1356 (m), 1307 (m), 1238 (w), 1160 (s), 1090 (w), 1034 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 8.16–7.42 (10H, m, aromatics), 5.18 (1H, s, COC*H*=C), 5.06 (2H, s, PhCH_2O), 4.45 (2H, s, NCH_2); δ_C (67.5 MHz; $CDCl_3$) 174.1 (N*C*O), 168.4 (NCH_2*C*=C), 138.5, 133.8 (*C*=CH), 133.6, 129.1, 128.8, 127.9, 127.8 (*C*H=C), 95.2 (NCO*C*H=C), 73.9 (N*C*H_2), 46.8 (Ph*C*H_2); *m/z* (CI, NH_3) 330 ($M+H^+$, 100%), 190 (26), 108 (10), 91 (11); Found: $M+H^+$, 330.0787. $C_{17}H_{15}NO_4S$ requires for $M+H^+$, 330.0802.

General procedures for desulfonylation

Using tributyltin hydride. A solution of the sulfonamide (0.12–0.57 mmol) in degassed toluene (10–20 cm^3) was heated to reflux and tributyltin hydride (0.27–1.25 mmol) and azobisisobutyronitrile (0.07–0.13 mmol) were added in one portion as a solution in toluene (5 cm^3) under a nitrogen atmosphere. 0.1 equiv. of azobisisobutyronitrile was added portionwise until the reaction had gone to completion (2–48 h) as indicated by TLC analysis. The toluene was then removed in vacuo and diethyl ether (20 cm^3) and aqueous potassium fluoride (8%, 20 cm^3) were added to the residue and the mixture stirred for 2 h. The organic layer was separated, washed with water, brine, dried ($MgSO_4$), evaporated and purified by column chromatography (silica) to give the deprotected amide (34–99%).

Using samarium diiodide. To a solution of the sulfonamide

(0.11–0.44 mmol) in dry tetrahydrofuran (3–5 cm^3) was added samarium diiodide (3.3–13.1 cm^3 of a 0.1 M solution in tetrahydrofuran, 0.33–1.31 mmol) at 0°C under a nitrogen atmosphere. The reaction mixture was stirred at this temperature for 0.2 h, allowed to warm to rt and then quenched by the addition of aqueous saturated sodium bicarbonate solution (15 cm^3). The aqueous phase was extracted with ethyl acetate (×2) and the combined organic phase was then washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give crude product, which on column chromatography gave the secondary amide (57–99%).

Using titanium tetrachloride and zinc. To a stirred suspension of zinc (4.86–6.30 mmol) in dry tetrahydrofuran (25 cm^3) under nitrogen was added titanium tetrachloride (0.81–1.05 mmol) dropwise and the solution was heated for 2 h. The reaction mixture was then allowed to cool to rt and the sulfonamide (0.27–0.35 mmol) in dry tetrahydrofuran (5 cm^3) was added over 0.75 h. The reaction was then heated to reflux for 17 h, the solvent removed and 3% aqueous HCl solution (125 cm^3) added to the residue. The aqueous phase was extracted with chloroform (×3) and the combined organic phase was then washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give crude product which on column chromatography gave the secondary amide (67–94%).

***N*-Benzylbenzamide 12a.** White solid; mp 102–105°C (lit.[21] 106–107°C); R_f 0.2 (petroleum ether–ethyl acetate, 1:1); ν_{max} (thin film) 3322 (br, s), 1640 (s), 1541 (m), 1363 (w), 1323 (w), 1162 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.91–7.36 (10H, m, aromatics), 6.74 (1H, br t, *J*=6 Hz, N*H*), 4.72 (2H, d, *J*=6 Hz, PhCH_2); δ_C (67.5 MHz; $CDCl_3$) 167.4 (N*C*O), 138.1, 134.3 (*C*=CH), 131.4, 128.7, 128.5, 127.8, 127.5, 126.9 (*C*H=C), 44.0 (Ph*C*H_2); *m/z* (EI) 211 (M^+, 65%), 105 (100), 77 (65).

***N*-Benzyl-*N*-cinnamamide 23.** White solid; mp 107–110°C (lit.[22] 109–110°C); R_f 0.3 (petroleum ether–diethyl ether, 1:2); ν_{max} (thin film) 3441 (w), 3010 (m), 1667 (s), 1629 (s), 1511 (s), 1452 (w), 1331 (w), 1190 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.69 (1H, d, *J*=15.5 Hz, PhC*H*=CH), 7.50–7.47 and 7.38–7.33 (10H, m, aromatics), 6.41 (1H, d, *J*=15.5 Hz, PhCH=C*H*), 5.83 (1H, br t, *J*=6.0 Hz, NH), 4.59 (2H, d, *J*=6.0 Hz, PhCH_2); *m/z* (CI, NH_3) 238 ($M+H^+$, 100%), 131 (8), 106 (5).

***N*-Benzylfuran-2-carboxylic acid amide 24.** White solid; mp 108–109°C (lit.[23] 111–111.5°C); R_f 0.4 (petroleum ether–ethyl acetate, 1:1); ν_{max} (thin film) 3285 (s), 1639 (s), 1573 (s), 1542 (s), 1475 (m), 1403 (m), 1389 (w), 1251 (m), 1230 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 7.35–7.07 (7H, m, benzene and 2× furan C*H*=C), 6.58 (1H, br t, *J*=6.0 Hz, N*H*), 6.44 (1H, d, *J*=1.5 Hz, furan C*H*=C), 4.55 (2H, d, *J*=6.0 Hz, PhCH_2); δ_C (67.5 MHz; $CDCl_3$) 158.2 (N*C*O), 143.8 (NCO*C*), 134.1 (*C*=CH), 128.7, 127.8, 127.6, 114.1, 112.2 (*C*H=C), 43.1 (Ph*C*H_2); *m/z* (CI, NH_3) 202 ($M+H^+$, 100%), 106 (35), 95 (37), 39 (15): Found: $M+H^+$, 202.0867. $C_{12}H_{11}NO_2S$ requires for $M+H^+$, 202.0868.

10,11-Dihydrodibenz[*b,f*][1,4]oxazepin-11-one 25. White solid; mp 210–212°C (lit.[24] 215–217°C); R_f 0.2 (petroleum ether–diethyl ether, 10:1); ν_{max} (thin film) 1633 (s), 1599 (m), 1497 (m), 1451 (s), 1338 (m), 1261 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$) 8.96 (1H, br s, NH), 8.08–7.18 (8H, m, aromatics); δ_C (67.5 MHz; $CDCl_3$) 167.5 (N*C*O), 159.6, 150.9, 134.5, 130.6 (*C*=CH), 132.0, 125.9, 125.8, 125.2, 121.6, 121.2, 120.2 (*C*H=C); *m/z* (EI) 211 ($M+H^+$, 100%).

4-Benzyloxy-3-pyrrolidin-2-one 26. White solid; R_f 0.15 (ethyl acetate); ν_{max} (thin film) 1720 (s), 1619 (s), 1447 (m), 1350 (m), 1219 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$)[25] 7.51–7.45 (5H, m, aromatics), 5.55 (1H, br s, N*H*), 5.25 (1H, s, COC*H*=C), 5.08 (2H, s, PhCH_2O), 4.06 (2H, s, NCH_2); δ_C (67.5 MHz; $CDCl_3$)[25] 175.5, 174.5 (N*C*O and NCH_2*C*), 134.6 (*C*=CH), 130.1, 128.7, 127.9 (*C*H=C), 95.2 (NCH_2*C*H), 73.2 (N*C*H_2), 46.8 (Ph*C*H_2); *m/z* (CI, NH_3) 207 ($M+NH_4^+$, 55%), 190 ($M+H^+$, 100): Found: $M+H^+$, 190.0866. $C_{11}H_{11}NO_2$ requires for $M+H^+$, 190.0868.

General procedure for tributyltin hydride deprotection followed by alkylation

A solution of the sulfonamide (0.28 mmol) in degassed toluene (10 cm^3) and tributyltin hydride (0.62 mmol) was heated to reflux under a nitrogen atmosphere. Azobisisobutyronitrile (5 mg every 0.3 h) was added until TLC showed disappearance of starting material. The reaction was then cooled to 0°C and dimethylpropylene urea (DMPU) (1.4 mmol) was added followed by benzyl or allyl bromide (0.93 mmol) and the mixture heated overnight. The solvent was then removed and ethyl acetate (20 cm^3) and 10% aqueous potassium fluoride (10 cm^3) added to the residue. After stirring for 5 h, the organic layer was separated, washed with brine, dried ($MgSO_4$) and purified by column chromatography (silica).

Benzylphenylsulfone. 85%; white solid; mp 142–144°C (lit.[26] 145–147°C); R_f 0.3 (petroleum ether–diethyl ether, 3:2); ν_{max} (thin film) 2921 (w), 1447 (m), 1290 (s), 1151 (s), 1124 (m), 1080 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$)[15,27] 7.65–7.07 (10H, m, aromatics), 4.31 (2H, s, NCH_2); δ_C (67.5 MHz; $CDCl_3$) 133.7, 130.8 (*C*=CH), 128.9, 128.8, 128.6, 128.5 (*C*H=C), 62.9 (Ph*C*H_2); *m/z* (CI, NH_3) 250 ($M+NH_4^+$, 55%), 108 (10).

Allylphenylsulfone. 70%; oil; R_f 0.3 (petroleum ether–diethyl ether, 3:2); ν_{max} (thin film) 2959 (m), 2926 (m), 2855 (w), 1675 (w), 1447 (m), 1319 (s), 1294 (m), 1237 (w), 1211 (w), 1147 (s), 1085 (m) cm^{-1}; δ_H (270 MHz; $CDCl_3$)[28] 7.89–7.86 and 7.66–7.53 (5H, m, aromatics), 5.80 (1H, ddt, *J*=7, 10 and 10 Hz, CH=C*H*CH_2), 5.33 (1H, d, *J*=10 Hz, CH=C*H*), 5.15 (1H, dd, *J*=17 and 1.0 Hz, CH=C*H*), 3.82 (2H, m, NCH_2); δ_C (67.5 MHz; $CDCl_3$)[28] 137.0, 133.8, 129.1, 128.5, 124.8, 121.0 (CH=*C*H_2, CH=*C* and *C*H=C), 60.9 (Ph*C*H_2); *m/z* (CI, NH_3) 200 ($M+NH_4^+$, 100%): Found: $M+NH_4^+$, 200.0741. $C_9H_{10}O_2S$ requires for $M+NH_4^+$, 200.0745.

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