PERKIN 1

N–H Insertion reactions of rhodium carbenoids. Part 3.[1] The development of a modified Bischler indole synthesis and a new protecting-group strategy for indoles

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Received (in Cambridge, UK) 15th March 2002, Accepted 13th May 2002
First published as an Advance Article on the web 18th June 2002

A modified version of the Bischler indole synthesis has been developed in which the key step is the N–H insertion reaction of rhodium carbene intermediates derived from α-diazo-β-ketoesters with anilines. Thus *N*-methylanilines **1** react with diazoketoesters **2** in the presence of dirhodium(II) acetate to give (*N*-arylamino)ketones **3**, cyclisation of which using boron trifluoride–ethyl acetate or acidic ion exchange resin gives the indoles **4**. In order to extend this method to the synthesis of *N*-unsubstituted indoles, a new protecting group strategy for indoles was developed. In this, anilines are reacted with α,β-unsaturated-esters or -sulfones to give the conjugate addition products **6** and **9**, cyclisation of which gives indoles **8** and **11**. The *N*-(2-ethoxycarbonylethyl)- and -(2-sulfonylethyl)- protecting groups are readily removed from indoles **8** and **11** by treatment with base.

Introduction

The wide-ranging biological activity associated with many indole derivatives, both naturally occurring and synthetic, ensures that the synthesis of this important ring system continues to attract the attention of synthetic organic chemists [2–4] Among the many routes to indoles, those which start from a simple aniline derivative are probably the most useful, since they do not require the presence of an additional *ortho*-substituent such as an alkyl group (Madelung reaction), a halide (various transition-metal catalysed reactions such as the Larock method), or an acyl group.[2–4] Although the Fischer indole synthesis could be considered as starting from an aniline, the need for prior conversion into the arylhydrazine (there are relatively few arylhydrazines that are commercially available), or into the hydrazone (*via* the Japp–Klingemann method) renders it less attractive than routes which start directly from anilines, such as the Bischler indole synthesis (Scheme 1a). The Bischler reaction, discovered

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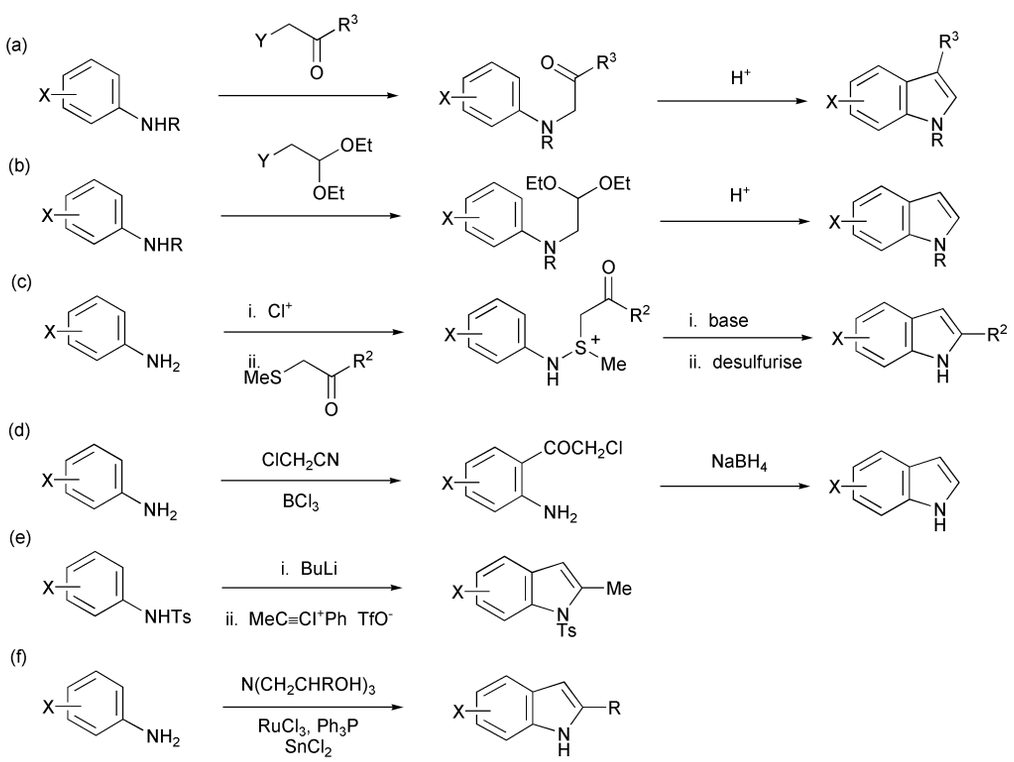

Scheme 1

 DOI: 10.1039/b202666j

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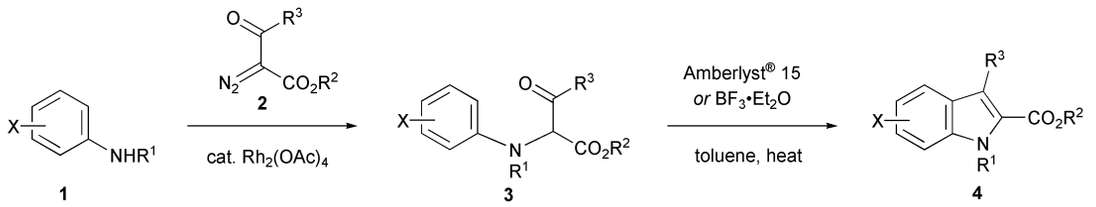


Scheme 2 [Diazo compound **2**; **a**, $R^2 = R^3 = Me$; **b**, $R^2 = Me$, $R^3 = Et$; **c**, $R^2 = Et$, $R^3 = Ph$.]

Table 1 Reaction of anilines **1** with diazoketoesters **2** in the presence of $Rh_2(OAc)_4$ and cyclisation of the resulting (*N*-arylamino)ketones **3** to indoles **4**

2, **3**	X	R^1	R^2	R^3	Yield (%)	Indole **4** X	**4**	Indole **4** Yield (%) Amberlyst® 15	Indole **4** Yield (%) BF_3–Et_2
a	H	Me	Me	Me	82	H	**a**	81	69
b	2-Br	Me	Me	Me	78	7-Br	**b**	52	—
c	2-MeO	Me	Me	Me	60	7-MeO	**c**	56	13
d	3-MeO	Me	Me	Me	84	4-MeO	**d**[1]	22	—
						6-MeO	**d**[2]	55	—
e	4-Cl	Me	Me	Me	77	5-Cl	**e**	87	62
f	4-NO_2	Me	Me	Me	75	5-NO_2	**f**	80	0[a]
g	4-MeO	Me	Me	Me	76	5-MeO	**g**	82	88
h	4-MeO	Me	Me	Et	70	5-MeO	**h**	50	49
i	4-MeO	Me	Et	Ph	89	5-MeO	**i**	54	42
j	2,4-$(MeO)_2$	Me	Me	Me	75	5,7-$(MeO)_2$	**j**	31	—
k	H	Bn	Me	Me	73	H	**k**	23	—

[a] Starting material recovered unchanged.

100 years ago,[5,6] involves the reaction of anilines with α-haloketones followed by acid catalysed cyclisation of the resulting α-(*N*-arylamino)ketones. Subsequent modification by Nordlander and by Sundberg and their co-workers allowed the formation of 2,3-unsubstituted indoles by using the corresponding acetals (Scheme 1b).[7,8] Examples of more recent routes which also start from anilines are the Gassman method (Scheme 1c),[9] the Sugasawa method (Scheme 1d),[10] the Feldman method (Scheme 1e),[11] and ruthenium catalysed routes from ethanolamines (Scheme 1f).[12]

We now report the details of a modification of the Bischler indole synthesis in which the key step is the N–H insertion reaction of anilines with rhodium carbenes derived from α-diazocarbonyl compounds,[13,14] during which we have also developed a new protecting group strategy for indoles.[15]

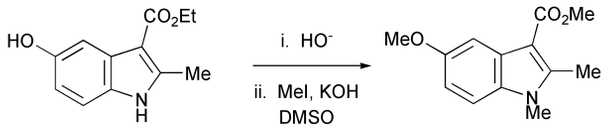
Results and discussion

The reaction of anilines with diazocarbonyl compounds to give products derived from an N–H insertion reaction is a known reaction of carbene and metal carbene intermediates.[16] Although the reaction of aniline with ethyl diazoacetate was first carried out by Curtius under thermal conditions over 100 years ago,[17] nowadays the reaction is usually carried out in the presence of a metal catalyst, following Yates' first report of the copper–bronze catalysed decomposition of diazoacetophenone in the presence of aniline to give α-anilinoacetophenone in 33% yield.[18] Further reactions of anilines with diazocarbonyl compounds catalysed by a range of transition-metal complexes, including copper,[19–22] rhodium,[1,23–29] rhenium,[30] and ruthenium,[31] have been reported. The diazocarbonyl compounds used in the present study were α-diazo-β-ketoesters **2**, readily prepared by a diazo-transfer reaction to the corresponding β-ketoester. The initial substrates investigated were simple *N*-methylanilines **1** (R^1 = Me) which were reacted with the α-diazo-β-ketoesters **2** in the presence of dirhodium(II) tetraacetate (2 mol%) in boiling chloroform or toluene. This resulted in N–H insertion of the intermediate metal carbenes, and gave the α-(*N*-arylamino)-β-ketoesters **3a**–**j** in good yield (Scheme 2, Table 1). For the most part, the ketones **3** were characterisable solids that existed as keto–enol mixtures in solution; on occasion, however, they were unstable oils (*e.g.* **3j**) that could not be completely characterised, and were therefore used without further purification.

A number of acids and Lewis acids have been used to effect the cyclisation of α-(*N*-arylamino)ketones or -acetals in the classical Bischler reaction or in its Nordlander modification. Initially we used boron trifluoride–diethyl ether in toluene, but in some cases the yields of product were unsatisfactory, with the nitro-derivative **3f** failing to cyclise at all under these conditions. Therefore an alternative method using acidic ion-exchange resin (Amberlyst® 15) was adopted.[32] Thus the (*N*-arylamino)-ketones **3** were heated with the ion-exchange resin in toluene to give the corresponding *N*-methyl indoles **4a**–**j** in a range of yields (Scheme 2, Table 1). In the case of the *m*-substituted aniline derivative **3d**, a mixture of indoles was formed on cyclisation with the 6-methoxyindole predominating (2.5 : 1). The overall method also works for *N*-benzylanilines, with **1k** undergoing N–H insertion (73%) followed by cyclisation to the *N*-benzylindole **4k** which is obtained in low yield (Table 1). However the sequence fails when *N*-acetyl- or *N*-tosyl-anilines are used as starting materials; 4-methoxyacetylanilide failed to undergo the N–H insertion reaction, and *N*-tosyl-4-anisidine gave the insertion product in only 27% yield.

One feature of the Bischler indole synthesis is the propensity for rearrangements to occur.[2,3] Thus α-anilinoacetophenones, $ArNRCH_2COPh$, often give 2-phenylindoles upon cyclisation in addition to, or instead of the expected 3-phenylindoles. In order to confirm that no similar rearrangements were occurring in the present work, one indole-3-ester **5** was prepared independently for comparison with its regioisomer **4g**. Thus the known ethyl 5-hydroxy-2-methylindole-3-carboxylate, prepared by the Nenitzescu reaction of ethyl 3-aminobut-2-enoate with 1,4-benzoquinone, was hydrolysed to the corresponding acid, and trimethylated to give **5** (Scheme 3) which is clearly spectroscopically distinguishable from regioisomer **4g**.

Although many synthetic routes to indoles lead directly to *N*-unsubstituted derivatives, many also lead to *N*-substituted or

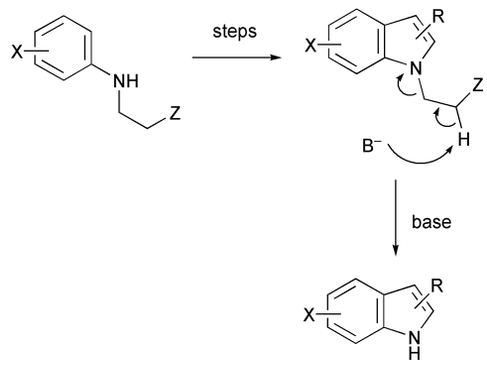


Scheme 3

-protected indoles, and whereas protecting group strategies for basic nitrogen atoms are well worked out,[33,34] the choice of suitable protecting groups for non-basic heterocyclic NH groups is more problematic. Electron-withdrawing carbonyl or sulfonyl based protecting groups, although easy to remove, often markedly affect the reactions leading to, and the reactivity of, the heterocyclic ring. Therefore one often has to resort to alkyl based protecting groups which are usually more difficult to remove.[35]

The modified Bischler indole synthesis described above suffers from this exact problem, in that whereas *N*-methylanilines were readily converted into *N*-methylindoles, indoles with readily removable protecting groups (*e.g.* acetyl or tosyl) could not be obtained. Although the reaction could be extended to the synthesis of *N*-benzylindoles, the benzyl protecting group can be difficult to remove, and overall we considered the N–H insertion–cyclisation sequence unsatisfactory for the synthesis of *N*-unsubstituted indoles. Therefore, in order to extend the methodology, we required an alkyl protecting group that functioned as a simple *N*-alkylaniline but was also readily removable following the conversion of the aniline into the corresponding indole. Since indole is a much better leaving group than aniline in a 1,2-elimination reaction, as reflected in the difference of *ca.* 15 in their pK_a values, it seemed that a protecting group that could be removed in a base-mediated elimination would be suitable. Therefore a retro-Michael strategy involving a CH_2CH_2Z group (Z = CN, CO_2R or SO_2R) was considered (Scheme 4).

Although there are reports of the base mediated removal of the 2-cyanoethyl group from heteroaromatic rings such as imidazoles[36] and purines,[37] we concentrated on the 2-ethoxycarbonyl- and 2-arylsulfonylethyl groups both of which have found some use as protecting groups although not, as far as we are aware, for indoles. Thus the 2-ethoxycarbonylethyl group can be removed from 2-aminoprop-2-enoate esters by treatment with sodium in xylene,[38] from pyrroles by reaction with sodium methoxide,[39] and from tetrazoles by reaction with DBN.[40]

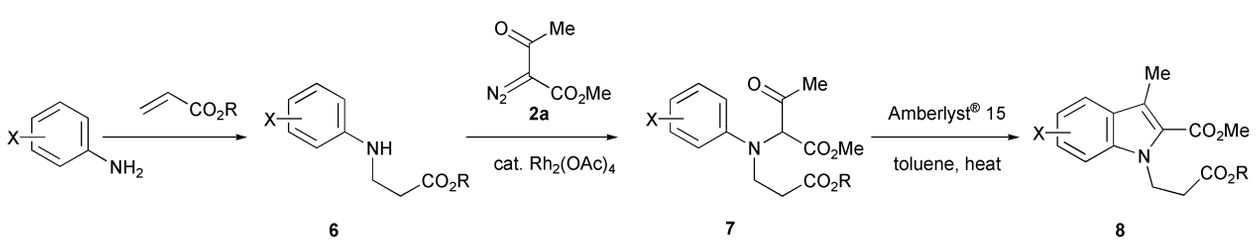


Scheme 4

Similarly the 2-sulfonylethyl group has been used as a protecting group for the NH group of amides, carbamates and β-lactams,[41] tetrazoles,[40] imidazoles,[36] and pyrroles.[42,43] Therefore we investigated the use of such 2-substituted ethyl protecting groups in our modified Bischler indole synthesis.

The 2-ethoxycarbonylethyl group was investigated first. The starting *N*-substituted anilines **6a**–**d** were readily prepared by conjugate addition of the aniline to ethyl acrylate in ethanol.[44] The amines **6e** and **6f** were similarly prepared by addition to benzyl acrylate (Scheme 5, Table 2), the reactions taking some three days to go to completion. Reaction of the anilines **6a**–**d** with methyl 2-diazo-3-oxobutanoate **2a** in chloroform in the presence of dirhodium(II) tetraacetate resulted in the formation of the N–H insertion products **7**; although these were separated from catalyst and other polar impurities by chromatography, no attempt was made to purify the amines **7** completely for characterisation. Rather, they were cyclised directly to the desired indoles **8** by heating in toluene with acidic ion-exchange resin (Scheme 5, Table 2). With one exception, the indoles **8** were formed in good yield, although when the 2-benzyloxycarbonylethyl anilines **6e** and **6f** were subjected to the same reaction sequence, the corresponding indoles were not isolated.

The reaction was extended to the conversion of *N*-(2-phenylsulfonylethyl)anilines **9a**–**f** into indoles **11**. Thus conjugate addition of anilines to phenyl vinyl sulfone gave the anilines **9a**–**g** in a range of yields (Scheme 6, Table 3), the reaction again taking three days. Treatment with methyl 2-diazo-3-oxobutanoate **2a** or -pentanoate **2b** in boiling chloroform in the presence of dirhodium(II) tetraacetate resulted in the formation

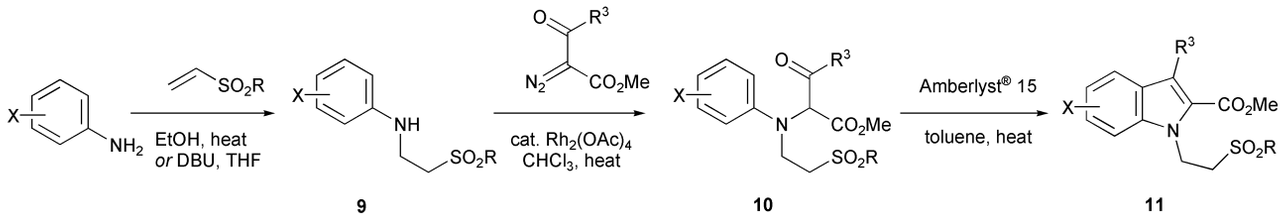


Scheme 5

Table 2 Conjugate addition of anilines to acrylates, reaction of the *N*-(2-ethoxycarbonylethyl)anilines **6** with diazoketoesters **2** in the presence of $Rh_2(OAc)_4$ and cyclisation of the resulting (*N*-arylamino)ketones **3** to indoles **8**

			6	**7**	Indole **8**	Indole **8**
	X	R	Yield (%)	Yield (%)[a]	X	Yield (%)
a	4-Me	Et	41	76	5-Me	76
b	4-MeO	Et	49	74	5-MeO	60
c	4-MeO_2C	Et	22	63	5-MeO_2C	22
d	4-^{t}Bu	Et	22	55	5-^{t}Bu	64
e	4-Me	Bn	88			
f	4-MeO	Bn	84			

[a] Compounds not characterised; yields refer to partially purified material.

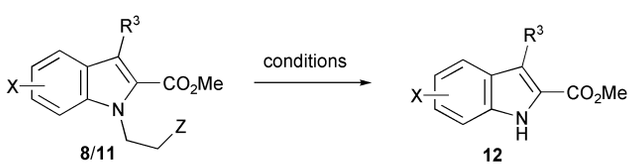


Scheme 6

Table 3 Conjugate addition of anilines to vinyl sulfones, reaction of the *N*-(2-sulfonylethyl)anilines **9** with diazoketoesters **2** in the presence of $Rh_2(OAc)_4$ and cyclisation of the resulting (*N*-arylamino)ketones **10** to indoles **11**

			9			**10**		Indole **11**	Indole **11**
9	X	R	Yield (%)	R^3	**10**	Yield (%)[a]	**11**	X	Yield (%)
a	4-Me	Ph	99	Me	**a**	62	**a**	5-Me	71
b	4-Me	Ph	—	Et	**b**	63	**b**	5-Me	66
c	4-MeO	Ph	68	Me	**c**	78	**c**	5-MeO	49
d	2-Me	Ph	68	Me	**d**	73	**d**	7-Me	51
e	2-MeO	Ph	74	Me	**e**	90	**e**	7-MeO	48
f	4-Br	Ph	17	Me	**f**	36	**f**	5-Br	79
g	3-MeO	Ph	75	Me	**g**	63	**g**[1]	4-MeO (6%)	30
							g[2]	6-MeO (24%)	—
h	4-Me	Bn	87,74[b]	Me	**h**	65	**h**	5-Me	62
i	4-MeO	Bn	89	Me	**i**	98	**i**	5-MeO	37
j	2-Me	Bn	73,67[b]	Me	**j**	60	**j**	7-Me	78
k	2-NO_2	Bn	50[b]						

[a] Compounds not characterised; yields refer to partially purified material. [b] Reaction carried out in the presence of DBU – see Experimental Section.



Scheme 7

Table 4 Base mediated deprotection of 1-(2-ethoxycarbonylethyl)- and 1-(2-sulfonylethyl)-indoles **8** and **11**

8,**11**	Z	X	R^3	**12**	Conditions	Yield (%)
8a	CO_2Et	5-Me	Me	**12a**	*t*-BuOK, DMF	60
11a	SO_2Ph	5-Me	Me	**12a**	*t*-BuOK, DMF	87
					DBN, Et_3N, DMF	59
					DBU, Et_3N, DMF	42
11h	SO_2Bn	5-Me	Me	**12a**	*t*-BuOK, DMF	70[a]
8b	CO_2Et	5-MeO	Me	**12b**	*t*-BuOK, DMF	77
11i	SO_2Bn	5-MeO	Me	**12b**	*t*-BuOK, DMF	91
11b	SO_2Ph	5-Me	Et	**12c**	DBN, toluene	27
11e	SO_2Ph	7-MeO	Me	**12d**	*t*-BuOK, DMF	55
11g[2]	SO_2Ph	6-MeO	Me	**12e**	*t*-BuOK, DMF	34
11j	SO_2Bn	7-Me	Me	**12f**	*t*-BuOK, DMF	58[b]

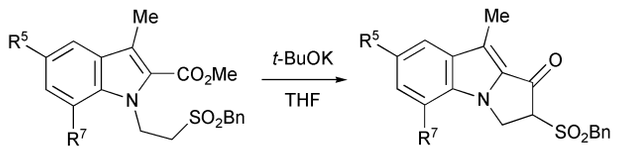
[a] Cyclopent[*a*]indole **13a** also formed (9%). [b] Cyclopent[*a*]indole **13b** also formed (11%).

of the N–H insertion products **10a**–**g** in modest to good yields (Table 3). Again the intermediate *N*-arylamino ketones **10** were not completely purified, but were cyclised by treatment with acidic ion-exchange resin to the indoles **11a**–**g** (Scheme 6, Table 3). As in the case of the *meta*-substituted *N*-methylaniline derivative **3d**, cyclisation of **10g** produced a mixture of 4- and 6-substituted indoles with the 6-methoxy isomer predominating.

With a view to the development of a solid phase variant of our modified Bischler indole synthesis (*q.v.*), the reaction was extended to 1-(2-benzylsulfonylethyl)indoles. Thus benzyl vinyl sulfone, prepared by a slight modification of the literature procedure,[45] underwent conjugate addition of 4-toluidine in boiling ethanol to give the *N*-substituted aniline **9h** in good yield (Scheme 6, Table 3). However, the reaction time was still inconveniently long, and therefore the conjugate addition was repeated in the presence of various additives [KOH, DBU, $Yb(OTF)_3$]. Of these, the use of DBU in THF proved successful, and reduced the reaction time to 13 hours. The addition of other anilines to benzyl vinyl sulfone gave the expected products **9i**–**k** (Table 3). Conversion into the corresponding *N*-(2-benzylsulfonylethyl) indoles **11h**–**j** proved uneventful (Table 3), although the 2-nitro compound **9k** failed to give the required indole.

With a range of appropriately *N*-substituted indoles **8** and **11** available, their base-mediated deprotection was investigated (*cf.* Scheme 4). The use of potassium *tert*-butoxide in DMF proved the most satisfactory, although amine bases could also be used (Scheme 7, Table 4). Hence methyl 3,5-dimethylindole-2-carboxylate **12a** was obtained by deprotection of the *N*-(2-ethoxycarbonylethyl)-, (2-phenylsulfonylethyl)-, and (2-benzylsulfonylethyl)indoles **8a**, **11a** and **11h**. Likewise, indoles **12b**–**12f** were obtained by base-mediated deprotection of the corresponding indoles **8** and **11** (Scheme 7, Table 4). During the deprotection of indoles **11h** and **11j** using potassium *tert*-

butoxide in DMF, byproducts (*ca.* 10%) were also formed. These were identified as the pyrrolo[1,2-*a*]indoles **13**, formed by intramolecular acylation of the sulfone stabilised anion (Scheme 8). Interestingly, when the reaction was repeated in

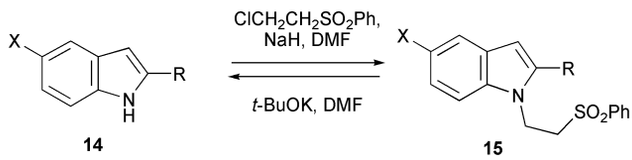


11h/11j **13a/13b**

Scheme 8 [**11h**, **13a**, R^5 = Me, R^7 = H; **11j**, **13b**, R^5 = H, R^7 = Me].

THF as solvent, the pyrrolo[1,2-*a*]indole **13** was the sole product.

We also briefly investigated the use of the 2-phenylsulfonylethyl protecting group on preformed indoles. The group was readily introduced by reaction of the indole with 2-chloroethyl phenyl sulfone in DMF using sodium hydride as base, and removed using potassium *tert*-butoxide also in DMF. Two examples are shown in Scheme 9 and Table 5.



14 **15**

Scheme 9

Table 5 Protection and deprotection of indoles using the 2-phenylsulfonylethyl protecting group

	X	R^2	Protection Yield (%)	Deprotection Yield (%)
a	MeO	H	73	91
b	H	CO_2Et	67	100

Finally, given the current interest in solid-phase organic synthesis, we attempted to adapt our modified Bischler indole synthesis for use on resin. A number of other indole syntheses have recently been adapted for resin, including the Fischer,[46] Nenitzescu,[47] various palladium-mediated syntheses,[48–52] including one very recent example involving a rhodium carbene N–H insertion reaction.[29] Our original intention had been to use the REM-resin, but in view of the failure to isolate any indoles from the benzyl acrylate derived anilines **6e** and **6f**, we turned our attention to vinylsulfonylmethyl polystyrene resin. Vinyl sulfone resins were developed as traceless linkers for amine synthesis,[53,54] the first step being conjugate addition of an amine, and therefore seemed ideal for our purpose. Therefore commercially available vinylsulfonylmethyl polystyrene resin was treated with 4-toluidine in THF in the presence of DBU as described above for benzyl vinyl sulfone. The appearance of a signal at 3390 cm^{-1} in the IR spectrum of the resin suggested the formation of the desired functionalised resin **16** (Scheme 10). Subsequent treatment with diazo compound **2a** in the presence of dirhodium(II) tetraacetate resulted in a resin that showed the absence of an NH absorption in its IR spectrum, but which did contain a carbonyl absorption at 1740 cm^{-1}, consistent with the desired structure **17**. Unfortunately, cyclisation with boron trifluoride–diethyl ether, followed by base-mediated cleavage from the resin gave a solution which clearly did not contain the expected indole **12a** (Scheme 10). Further studies are in progress.

Experimental

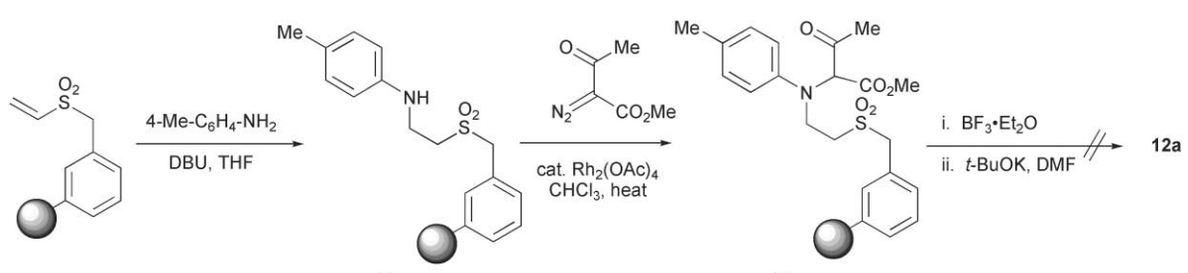
General experimental details

Commercially available reagents were used throughout without further purification unless otherwise stated; solvents were dried by standard procedures. Light petroleum refers to the fraction with bp 40–60 °C and ether refers to diethyl ether. Reactions were routinely carried out under a nitrogen atmosphere. Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF_{254}. Plates were visualised under UV light (at 254 and/or 360 nm). Flash chromatography was carried out using Merck Kieselgel 60 H silica or Matrex silica 60. Fully characterised compounds were chromatographically homogeneous. IR spectra were recorded in the range 4000–600 cm^{-1} using a Nicolet Magna FT-550 spectrometer. ^1H and ^{13}C NMR spectra were recorded using Bruker 250, 300 and 400 MHz instruments (^1H frequencies, corresponding ^{13}C frequencies are 63, 75 and 100 MHz); *J* values were recorded in Hz. In the ^{13}C NMR spectra, signals corresponding to CH, CH_2 or CH_3 groups are noted; all others are C. High and low-resolution mass spectra were recorded on a Kratos HV3 instrument, or at the EPSRC Mass Spectrometry Service (Swansea).

Preparation of α-(*N*-arylamino)-β-ketoesters 3 by N–H insertion reactions

General method. A mixture of the substituted aniline **1** (2 mmol), diazo compound **2** (2.6 mmol) and dirhodium(II) acetate (0.04 mmol) in toluene or chloroform (25 ml) was heated under reflux for 1 h. The solvent was removed *in vacuo* and the residue purified by column chromatography to give the α-(*N*-arylamino)-β-ketoesters **3**.

Methyl 2-(*N*-methyl-*N*-phenylamino)-3-oxobutanoate 3a. Reaction solvent toluene, purified by column chromatography (light petroleum : ether, 9 : 1 elution), recrystallised (light petroleum) to give the *title compound* (82%) as a colourless crystalline solid, mp 52–53 °C (Found: C, 65.1; H, 6.7; N, 6.2. $C_{12}H_{15}NO_3$ requires C, 65.1; H, 6.8; N, 6.3%); ν_{max} (KBr)/cm^{-1} 2953, 2884, 1655, 1600, 1501; δ_H (250 MHz; $CDCl_3$) 12.26 (1H, s, enol), 7.21 (2H, m, ArH), 6.73 (1H, t, *J* 7.7, ArH), 6.61 (2H, d, *J* 8.2, ArH), 3.67 (3H, s, OMe), 3.03 (3H, s, NMe), 1.95 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 175.9, 172.5, 148.8, 129.6 (CH), 116.7 (CH), 111.5 (CH), 110.6, 51.6 (Me), 38.7 (Me), 17.4 (Me); *m*/*z* (EI) 221 (M^+, 10%), 193 (15), 134 (100), 118 (51), 106 (52), 77 (65).



Scheme 10

Methyl 2-[*N*-(2-bromophenyl)-*N*-methylamino]-3-oxobutanoate 3b. Reaction solvent toluene, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution) to yield the *title compound* (78%) as a colourless oil (Found: MH^+, 300.0235. $C_{12}H_{14}{}^{79}BrNO_3$ + H requires 300.0236); ν_{max} (KBr)/cm^{-1} 3059, 3013, 2960, 2809, 1756, 1729, 1657, 1618, 1591; δ_H (300 MHz; $CDCl_3$) (keto/enol) 9.85 (1H, s, enol), 7.58–6.69 (4H, m, ArH), 4.84 (1H, s, NCH), 3.75/3.74 (3H, 2 × s, 2 × OMe), 3.07/2.98 (3H, 2 × s, 2 × NMe), 2.41/1.92 (3H, 2 × s, 2 × Me); δ_C (100 MHz; $CDCl_3$) (keto/enol) 202.9, 174.2, 172.4, 169.0, 148.9, 148.4, 134.8 (CH), 133.9 (CH), 128.3 (CH), 127.8 (CH), 125.4 (CH), 124.2 (CH), 121.5 (CH), 119.8 (CH), 119.6, 113.0, 112.8, 110.7 (CH), 51.9 (Me), 51.6 (Me), 41.6 (Me), 37.4 (Me), 28.4 (Me), 18.2 (Me); *m*/*z* (CI) 302/300 (M^+, 19%) 291/289 (42), 166 (91), 150 (100).

Methyl 2-[*N*-(2-methoxyphenyl)-*N*-methylamino]-3-oxobutanoate 3c. Reaction solvent toluene, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution) to yield the *title compound* (60%) as an off white crystalline solid, mp 60–62 °C (Found: C, 61.5; H, 6.9; N, 5.5. $C_{13}H_{17}NO_4{\cdot}0.2H_2O$ requires C, 61.2; H, 6.9; N, 5.5%) (Found: M^+, 251.1158. $C_{13}H_{17}NO_4$ requires 251.1157); ν_{max} (KBr)/cm^{-1} 3063, 3002, 2961, 2874, 1755, 1728, 1647, 1593; δ_H (300 MHz; $CDCl_3$) (keto/enol) 9.91 (1H, s, enol), 7.07–6.77 (4H, m, ArH), 5.08 (1H, s, NCH), 3.85/3.77/3.74/3.70 (6H, 4 × s, 4 × OMe), 3.03/2.96 (3H, 2 × s, 2 × NMe), 2.33/1.94 (3H, 2 × s, 2 × Me); δ_C (75.5 MHz; $CDCl_3$) (keto/enol) 173.3, 173.0, 169.4, 151.7, 150.7, 140.0, 139.6, 129.8, 122.9 (CH), 121.2 (CH), 121.1 (CH), 120.1 (CH), 120.0 (CH), 117.2 (CH), 113.7, 112.7 (CH), 111.6 (CH), 73.2 (CH), 56.1 (Me), 55.5 (Me), 51.8 (Me), 51.5 (Me), 40.9 (Me), 36.3 (Me), 28.2 (Me), 17.7 (Me); *m*/*z* (EI) 251 (M^+, 8%), 180 (12), 138 (100), 134 (38), 124 (40).

Methyl 2-[*N*-(3-methoxyphenyl)-*N*-methylamino]-3-oxobutanoate 3d. Reaction solvent toluene, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution), recrystallised (dichloromethane–light petroleum) to yield the *title compound* (84%) as a colourless crystalline solid, mp 39–40 °C (Found: C, 61.9; H, 6.8; N, 5.5. $C_{13}H_{17}NO_4$ requires C, 62.1; H, 6.8; N, 5.6%); ν_{max} (CH_2Cl_2)/cm^{-1} 3006, 2954, 2908, 2833, 1669, 1617, 1496; δ_H (300 MHz; $CDCl_3$) 9.75 (1H, s, enol), 7.12 (1H, t, *J* 8.2, ArH), 6.31 (1H, dd, *J* 8.2, 2.3, ArH), 6.24 (1H, dd, *J* 8.2, 2.3, ArH), 6.18 (1H, t, *J* 2.3, ArH), 3.78 (3H, s, OMe), 3.69 (3H, s, OMe), 3.03 (3H, s, NMe), 1.96 (3H, s, Me); δ_C (75.5 MHz; $CDCl_3$) 175.9, 172.4, 160.8, 150.4, 129.8 (CH), 110.6, 105.1 (CH), 101.7 (CH), 98.6 (CH), 55.1 (Me), 51.8 (Me), 38.8 (Me), 17.4 (Me); *m*/*z* (EI) 251 (M^+, 9%), 223 (38), 176 (19), 164 (100), 149 (96).

Methyl 2-[*N*-(4-chlorophenyl)-*N*-methylamino]-3-oxobutanoate 3e. Reaction solvent toluene, purified by column chromatography (light petroleum : ether, 1 : 1 elution), recrystallised (light petroleum–ether) to yield the *title compound* (77%) as a colourless crystalline solid, mp 109–111 °C (Found: C, 56.4; H, 5.4; N, 5.5. $C_{12}H_{14}ClNO_3$ requires C, 56.3; H, 5.5; N, 5.5%); ν_{max} (KBr)/cm^{-1} 2951, 2906, 2819, 1654, 1618, 1596; δ_H (250 MHz; $CDCl_3$) 12.23 (1H, s, enol), 7.14 and 6.50 (4H, AA′XX′, *J* 9.1, ArH), 3.68 (3H, s, OMe), 3.0 (3H, s, NMe), 1.95 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 176.0, 172.2, 147.6, 128.9 (CH), 122.0, 113.0 (CH), 110.5, 51.8 (Me), 39.0 (Me), 17.4 (Me); *m*/*z* (EI) 257/255 (M^+, 4/9%), 154/152 (9/22), 113/111 (9/22), 75 (39).

Methyl 2-[*N*-methyl-*N*-(4-nitrophenyl)amino]-3-oxobutanoate 3f. Reaction solvent toluene, purified by column chromatography (light petroleum : ether, 1 : 1 elution), recrystallised (light petroleum–ether) to yield the *title compound* (75%) as a yellow crystalline solid, mp 138–140 °C (Found: C, 53.9; H, 5.1; N, 10.5. $C_{12}H_{14}N_2O_5$ requires C, 54.1; H, 5.3; N, 10.5%); ν_{max} (KBr)/cm^{-1} 2825, 1648, 1597, 1508; δ_H (250 MHz; $CDCl_3$) 12.28 (1H, s, enol), 6.56 (4H, AA′XX′, *J* 9.3, ArH), 3.72 (3H, s, OMe), 3.15 (3H, s, NMe), 1.95 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 175.9, 171.2, 154.0, 138.5, 126.1 (CH), 111.1 (CH), 109.9, 52.2 (Me), 39.6 (Me), 17.5 (Me); *m*/*z* (EI) 266 (M^+, 34%), 206 (15), 163 (100).

Methyl 2-[*N*-(4-methoxyphenyl)-*N*-methylamino]-3-oxobutanoate 3g. Reaction solvent toluene, purified by column chromatography (dichloromethane elution), recrystallised (light petroleum) to yield the *title compound* (76%) as an off white crystalline solid, mp 85–86 °C (Found: C, 62.2; H, 7.1; N, 5.5. $C_{13}H_{17}NO_4$ requires C, 62.1; H, 6.8; N, 5.6%); ν_{max} (KBr)/cm^{-1} 3006, 2904, 2835, 1655, 1600, 1511; δ_H (250 MHz; $CDCl_3$) 12.23 (1H, s, enol), 6.80 and 6.55 (4H, AA′XX′, *J* 9.1, ArH), 3.75 (3H, s, OMe), 3.66 (3H, s, OMe), 3.00 (3H, s, NMe), 1.97 (3H, Me); δ_C (100 MHz; $CDCl_3$) 176.3, 173.1, 152.0, 143.8, 115.2 (CH), 113.0 (CH), 111.5, 56.1 (Me), 52.0 (Me), 39.4 (Me), 17.8 (Me); *m*/*z* (EI) 251 (M^+, 38%), 219 (19), 208 (14), 148 (100).

Methyl 2-[*N*-(4-methoxyphenyl)-*N*-methylamino]-3-oxopentanoate 3h. Reaction solvent chloroform, purified by column chromatography (dichloromethane elution), recrystallised (light petroleum–ether) to yield the *title compound* (70%) as a pale yellow solid, mp 74–75 °C (Found: C, 63.5; H, 7.0; N, 5.1. $C_{14}H_{19}NO_4$ requires C, 63.4; H, 7.2; N, 5.3%); ν_{max} (KBr)/cm^{-1} 2994, 1648, 1600, 1512; δ_H (250 MHz; $CDCl_3$) 12.33 (1H, s, enol), 6.79 and 6.55 (4H, AA′XX′, *J* 9.0, ArH), 3.75 (3H, s, OMe), 3.66 (3H, s, OMe), 3.00 (3H, s, NMe), 2.32 (2H, q, *J* 7.6, CH_2CH_3), 1.10 (3H, t, *J* 7.6, CH_2CH_3); δ_C (100 MHz; $CDCl_3$) 180.3, 173.3, 152.0, 144.1, 115.1 (CH), 113.1 (CH), 110.61, 56.1 (Me), 52.7 (Me), 39.9 (Me), 24.6 (CH_2), 10.9 (Me); *m*/*z* (EI) 265 (M^+, 29%), 208 (23), 162 (14), 148 (71), 57 (100).

Ethyl 2-[*N*-(4-methoxyphenyl)-*N*-methylamino]-3-oxo-3-phenylpropanoate 3i. Reaction solvent chloroform, purified by column chromatography (dichloromethane elution) to yield the *title compound* (89%) as a yellow oil (Found: M^+, 327.1471. $C_{19}H_{21}NO_4$ requires 327.1470); ν_{max} (film)/cm^{-1} 3400, 2984, 2936, 2905, 2833, 1748, 1640, 1572; δ_H (250 MHz; $CDCl_3$) (keto/enol) 12.85 (1H, s, enol), 7.79–7.27 (5H, m, ArH), 6.87–6.62 (4H, m, ArH), 5.72 (1H, s, NCH), 4.28–4.11 (2H, 2q, *J* 7.1, CH_2CH_3), 3.79/3.76 (3H, 2 × s, 2 × OMe), 2.91 (3H, s, NMe), 1.30/1.11 (3H, 2 × t, *J* 7.1, 2 × CH_2CH_3); δ_C (100 MHz; $CDCl_3$) (keto/enol) 173.3, 170.2, 169.7, 152.9, 151.8, 143.9, 142.9, 135.2 (CH), 133.9, 133.4, 130.6 (CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 115.0 (CH), 114.8 (CH), 114.6 (CH), 113.3 (CH), 111.6, 61.4 (CH_2), 60.9 (CH_2), 55.7 (Me), 55.5 (Me), 39.2 (Me), 35.7 (Me), 14.2 (Me), 14.1 (Me); *m*/*z* (EI) 327 (M^+, 9%), 281 (11), 222 (13), 148 (24), 105 (100), 77 (40).

Methyl 2-[*N*-(2,4-dimethoxyphenyl)-*N*-methylamino]-3-oxobutanoate 3j. Reaction solvent chloroform, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution) to yield the *title compound* (75%) as an unstable yellow oil, δ_H (300 MHz; $CDCl_3$) (keto/enol) 9.97 (1H, s, enol), 7.08–6.37 (3H, m, ArH), 4.87 (1H, s, NCH), 3.85–3.36 (9H, m, 3 × OMe), 3.20/2.97 (3H, 2 × s, 2 × NMe), 2.32/1.97 (3H, 2 × s, 2 × Me); ν_{max} (film)/cm^{-1} 3421, 3000, 2967, 1749, 1683, 1657. The compound was used without further purification.

Methyl 2-(*N*-benzyl-*N*-phenylamino)-3-oxobutanoate 3k. Reaction solvent toluene, purified by column chromatography (dichloromethane : light petroleum, 3 : 7 elution), recrystallised (light petroleum) to yield the *title compound* (73%) as a colourless crystalline solid, mp 41–42 °C (Found: C, 72.3; H, 6.4; N, 4.7. $C_{18}H_{19}NO_3$ requires C, 72.7; H, 6.4; N, 4.7%) (Found: M^+, 297.1365. $C_{18}H_{19}NO_3$ requires 297.1365); ν_{max} (KBr)/cm^{-1} 3068, 3027, 2951, 1667, 1597; δ_H (300 MHz; $CDCl_3$) 9.85 (1H, s, enol),

7.33–7.18 (7H, m, ArH), 6.79–6.70 (3H, m, ArH), 4.72 (2H, AB, *J* 15.4, C*H*$_2$Ph), 3.70 (3H, s, OMe), 1.84 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 176.9, 172.6, 148.8, 138.3, 129.2 (CH), 128.3 (CH), 128.1 (CH), 127.1 (CH), 117.7 (CH), 113.0 (CH), 109.8, 56.2 (CH_2), 51.7 (Me), 18.2 (Me); *m*/*z* (EI) 297 (M^+, 6%), 254 (5), 206 (32), 104 (100), 91 (90).

Preparation of indoles 4

General method 1. To a stirring solution of α-(*N*-arylamino)-β-ketoester **3** (1.5 mmol) in toluene (25 ml) was added boron trifluoride–diethyl ether (0.2 ml). The solution was heated under reflux overnight. The toluene was removed *in vacuo* and the residue purified by column chromatography to give the indole **4**.

General method 2. To a stirring solution of α-(*N*-arylamino)-β-ketoester **3** (1.5 mmol) in toluene (25 ml) was added Amberlyst® 15 (0.3 g). The solution was heated under reflux overnight. The resin was filtered off and the filtrate removed *in vacuo* and the residue purified by column chromatography to give the indole **4**.

Methyl 1,3-dimethylindole-2-carboxylate 4a. Method 1 (69%), method 2 (81%), purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution), recrystallised (light petroleum) to give the *title compound* as a colourless crystalline solid, mp 76–78 °C (lit.,[55] mp 76–77 °C) (Found: C, 70.7; H, 6.4; N, 7.0. $C_{12}H_{13}NO_2$ requires C, 70.9; H, 6.4; N, 6.9%); ν_{max} (KBr)/cm^{-1} 3061, 2949, 1720, 1603, 1570, 1530; δ_H (250 MHz; $CDCl_3$) 7.65 (1H, m, ArH), 7.33 (2H, m, ArH), 7.13 (1H, m, ArH), 3.98 (3H, s, OMe), 3.93 (3H, s, NMe), 2.57 (3H, s, Me).

Methyl 7-bromo-1,3-dimethylindole-2-carboxylate 4b. Method 2; purified by column chromatography (dichloromethane : light petroleum, 3 : 7 elution), recrystallised (light petroleum) to yield the *title compound* (52%) as a colourless crystalline solid, mp 47–48 °C (Found: C, 51.2; H, 4.3; N, 5.0. $C_{12}H_{12}BrNO_2$ requires C, 51.2; H, 4.3; N, 5.0%); ν_{max} (KBr)/cm^{-1} 3061, 2999, 2951, 1708, 1563; δ_H (300 MHz; $CDCl_3$) 7.58 (1H, dd, *J* 8.0, 1.0, ArH), 7.50 (1H, dd, *J* 7.5, 1.0, ArH), 6.95 (1H, t, *J* 7.8, ArH), 4.33 (3H, s, OMe), 3.95 (3H, s, NMe), 2.52 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.0, 135.6, 130.7 (CH), 130.3, 127.5, 120.7, 120.6 (CH), 120.1 (CH), 104.3, 51.6 (Me), 34.6 (Me), 10.6 (Me); *m*/*z* (EI) 283/281 (M^+, 96), 268/266 (50), 224/222 (35), 143 (51), 115 (100).

Methyl 7-methoxy-1,3-dimethylindole-2-carboxylate 4c. Method 1 (13%), method 2 (56%), purified by column chromatography (dichloromethane : light petroleum, 3 : 7 elution), recrystallised (light petroleum) to give the *title compound* as a colourless crystalline solid, mp 61–63 °C (Found: C, 66.7; H, 6.4; N, 5.9. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%); ν_{max} (KBr)/cm^{-1} 2954, 2848, 1729, 1584; δ_H (300 MHz; $CDCl_3$) 7.23 (1H, dd, *J* 8.1, 0.9, ArH), 7.01 (1H, t, *J* 7.8, ArH), 6.71 (1H, d, *J* 7.8, ArH), 4.28 (3H, s, OMe), 3.93 (6H, s, NMe, OMe), 2.53 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.4, 148.0, 129.3, 129.2, 125.8, 120.8, 119.8 (CH), 113.2 (CH), 105.5 (CH), 55.5 (Me), 51.3 (Me), 35.0 (Me), 10.9 (Me); *m*/*z* (EI) 233 (M^+, 100), 219 (9), 218 (65), 159 (19), 130 (29).

Methyl 1,3-dimethyl-4-methoxyindole-2-carboxylate 4d^1 and methyl 1,3-dimethyl-6-methoxyindole-2-carboxylate 4d^2. Method 2 yielded a 77% mixture of 2 products in a 1 : 2.5 ratio, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution).

Methyl 1,3-dimethyl-4-methoxyindole-2-carboxylate ***4d^1***. Recrystallised (light petroleum), mp 90–92 °C (Found: C, 66.7; H, 6.7; N, 5.9. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%); ν_{max} (KBr)/cm^{-1} 2999, 2980, 2841, 1703, 1611, 1578; δ_H (300 MHz; $CDCl_3$) 7.22 (1H, t, *J* 8.1, ArH), 6.91 (1H, d, *J* 8.4, ArH), 6.44 (1H, d, *J* 7.7, ArH), 3.94 (3H, s, OMe), 3.93 (3H, s, OMe), 3.92 (3H, s, NMe), 2.77 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.6, 156.7, 140.5, 126,0 (CH), 123.9, 122.0, 117.3, 103.0 (CH), 99.3 (CH), 55.1 (Me), 51.2 (Me), 32.3 (Me), 12.8 (Me); *m*/*z* (EI) 233 (M^+, 100%), 219 (8), 218 (69), 174 (19), 130 (23), 89 (34).

Methyl 1,3-dimethyl-6-methoxyindole-2-carboxylate ***4d^2***. Recrystallised (light petroleum) to give a colourless crystalline solid, mp 93–94 °C; (Found : C, 66.9; H, 6.7; N, 5.9); ν_{max} (KBr)/cm^{-1} 3019, 2954, 2848, 1710, 1637, 1571; δ_H (300 MHz; $CDCl_3$) 7.53 (1H, d, *J* 8.8, ArH), 6.81 (1H, dd, *J* 8.8, *J* 2.2, ArH), 6.72 (1H, d, *J* 6.7, ArH), 3.96 (3H, s, OMe), 3.92 (3H, s, OMe), 3.90 (3H, s, NMe), 2.28 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.4, 159.1, 139.9, 123.8, 121.6 (CH), 121.5, 111.0 (CH), 92.0 (CH), 55.5 (Me), 51.1 (Me), 32.0 (Me), 10.9 (Me); one ArC unobserved; *m*/*z* (EI) 233 (M^+, 100%), 219 (12), 218 (89), 190 (19), 131 (23), 89 (35).

Methyl 5-chloro-1,3-dimethylindole-2-carboxylate 4e. Method 1 (62%), method 2 (87%), purified by column chromatography (light petroleum : ether, 1 : 1 elution), recrystallised (light petroleum–ether) to give the *title compound* as an off white solid, mp 64–66 °C (Found: C, 60.6; H, 4.8; N, 5.7. $C_{12}H_{12}ClNO_2$ requires C, 60.6; H, 5.1; N, 5.9%); ν_{max} (KBr)/cm^{-1} 2951, 1701, 1527; δ_H (250 MHz; $CDCl_3$) 7.59 (1H, d, *J* 2.0, ArH), 7.24 (2H, m, ArH), 3.95 (3H, s, OMe), 3.94 (3H, s, NMe), 2.51 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.2, 137.1, 128.0, 126.0, 125.6, 125.5 (CH), 125.4, 120.0 (CH), 111.1 (CH), 51.5 (Me), 32.6 (Me), 10.7 (Me); *m*/*z* (EI) 239/237 (M^+, 38/95%), 224/222 (27/83), 222 (83), 180/178 (19/54).

Methyl 1,3-dimethyl-5-nitroindole-2-carboxylate 4f. Method 1 gave only starting material. Method 2 (80%), purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution), recrystallised (dichloromethane–light petroleum) to give the *title compound* as a pale yellow crystalline solid, mp 178–180 °C (Found: C, 57.6; H, 4.6; N, 11.1. $C_{12}H_{12}NO_4$ requires C, 58.0; H, 4.9; N, 11.3%) (Found: M^+, 248.0797. $C_{12}H_{12}N_2O_4$ requires 248.0797); ν_{max} (KBr)/cm^{-1} 3105, 2960, 1710, 1618, 1578; δ_H (300 MHz; $CDCl_3$) 8.66 (1H, d, *J* 2.2, ArH), 8.22 (1H, dd, *J* 9.2, 2.2, ArH), 7.38 (1H, d, *J* 9.2, ArH), 4.05 (3H, s, OMe), 3.98 (3H, s, NMe), 2.62 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 162.6, 141.6, 140.8, 127.8, 126.2, 122.9, 120.1 (CH), 118.2 (CH), 110.1 (CH), 51.8 (Me), 32.6 (Me), 10.7 (Me); *m*/*z* (EI) 248 (M^+, 100), 234 (11), 233 (83), 187 (47), 143 (38), 115 (37).

Methyl 5-methoxy-1,3-dimethylindole-2-carboxylate 4g. Method 1 (88%), method 2 (82%), purified by column chromatography (dichloromethane elution), recrystallised (light petroleum) to give the *title compound* as a colourless crystalline solid, mp 81–82 °C (Found: C, 67.0; H, 6.3; N, 5.9. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%); ν_{max} (KBr)/cm^{-1} 2948, 1702, 1520, 1495; δ_H (400 MHz; $CDCl_3$) 7.23 (1H, m, ArH), 7.02 (2H, m, ArH), 3.96 (3H, s, OMe), 3.93 (3H, s, OMe), 3.86 (3H, NMe), 2.54 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.5, 154.2, 134.5, 127.2, 125.3, 120.0, 116.8 (CH), 111.0 (CH), 101.0 (CH), 55.8 (Me), 51.2 (Me), 32.2 (Me), 10.8 (Me); *m*/*z* (EI) 233 (M^+, 100%), 218 (60), 190 (25).

Methyl 3-ethyl-5-methoxy-1-methylindole-2-carboxylate 4h. Method 1 (49%), method 2 (50%), purified by column chromatography (dichloromethane elution), recrystallised (light petroleum) to give the *title compound* as a pale crystalline solid, mp 55–56 °C (Found: C, 66.8; H, 6.9; N, 5.7. $C_{14}H_{17}NO_3 \cdot 0.25H_2O$ requires C, 66.8; H, 7.0; N, 5.6%) (Found: M^+, 247.1208. $C_{14}H_{17}NO_3$ requires 247.1208); ν_{max} (KBr)/cm^{-1} 2952, 1702, 1523; δ_H (250 MHz; $CDCl_3$) 7.25 (2H, m, ArH), 7.05 (1H, m, ArH), 3.97 (3H, s, OMe), 3.94 (3H, s, OMe), 3.88 (3H, s, NMe), 3.05 (2H, q, *J* 7.5, C*H*$_2$CH$_3$), 1.24 (3H, t, *J* 7.5,

CH_2CH_3); δ_C (100 MHz; $CDCl_3$) 171.1, 163.3, 154.2, 134.6, 126.6, 126.3, 116.7 (CH), 111.1 (CH), 101.0 (CH), 60.4 (CH_2), 55.9 (Me), 51.3 (Me), 32.2 (Me), 15.6 (Me); *m/z* (EI) 247 (M^+, 24%), 232 (49), 202 (14), 200 (16), 172 (15).

Ethyl 5-methoxy-1-methyl-3-phenylindole-2-carboxylate 4i. Method 1 (42%), method 2 (54%), purified by column chromatography (dichloromethane elution) to give the *title compound* as a colourless oil (Found: M^+, 309.1365. $C_{19}H_{19}NO_3$ requires 309.1365); ν_{max} (CH_2Cl_2)/cm^{-1} 3059, 3032, 2986, 2960, 2900, 2848, 1703, 1617; δ_H (300 MHz; $CDCl_3$) 7.44–7.30 (6H, m, ArH), 7.06 (1H, dd, *J* 9.0, 2.4, ArH), 6.92 (1H, d, *J* 2.4, ArH), 4.16 (2H, q, *J* 7.1, CH_2CH_3), 4.05 (3H, s, OMe), 3.78 (3H, s, NMe), 1.04 (3H, t, *J* 7.1, CH_2CH_3); δ_C (100 MHz; $CDCl_3$) 162.6, 155.0, 135.2, 134.0, 130.5 (CH), 127.8 (CH), 126.8 (CH), 126.7, 125.3, 123.9, 116.9 (CH), 111.1 (CH), 101.4 (CH), 60.4 (CH_2), 55.7 (Me), 32.0 (Me), 13.7 (Me); *m/z* (EI) 309 (M^+, 100), 281 (30), 181 (35), 165 (32), 152 (31).

Methyl 5,7-dimethoxy-1,3-dimethylindole-2-carboxylate 4j. Method 1, purified by column chromatography (dichloromethane : light petroleum, 1 : 1 elution) to yield the *title compound* (31%) as a colourless crystalline solid, mp 102–104 °C (Found: C, 63.8; H, 6.7; N, 5.2. $C_{14}H_{17}NO_4$ requires C, 63.8; H, 6.5; N, 5.3%); ν_{max} (KBr)/cm^{-1} 3000, 2967, 2848, 1710, 1630, 1591; δ_H (300 MHz; $CDCl_3$) 6.56 (1H, d, *J* 2.1, ArH), 6.41 (1H, d, *J* 2.1, ArH), 4.23 (3H, s, OMe), 3.92 (3H, s, OMe), 3.90 (3H, s, OMe), 3.86 (3H, s, NMe), 2.49 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.3, 154.4, 148.6, 128.5, 125.9, 125.0, 120.1. 98.2 (CH), 92.1 (CH), 55.6 (Me), 55.5 (Me), 51.2 (Me), 34.9 (Me), 11.0 (Me); *m/z* (EI) 263 (M^+, 100), 248 (65), 220 (25), 205 (20).

Methyl 1-benzyl-3-methylindole-2-carboxylate 4k. Method 1, purified by column chromatography (dichloromethane : light petroleum, 3 : 7 elution), recrystallised (light petroleum) to yield the *title compound* (23%) as a colourless crystalline solid, mp 43–45 °C (Found: C, 77.4; H, 6.2; N, 5.1. $C_{18}H_{17}NO_2$ requires C, 77.4; H, 6.1; N, 5.0%); ν_{max} (KBr)/cm^{-1} 3079, 3039, 2947, 1696, 1552; δ_H (300 MHz; $CDCl_3$) 7.72 (1H, dt, *J* 8.0, 1.0, ArH), 7.33 (2H, m, ArH), 7.22 (4H, m, ArH), 7.04 (2H, m, ArH), 5.97 (2H, s, CH_2Ph), 3.89 (3H, s, OMe), 2.64 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.3, 138.8, 138.7, 128.5 (CH), 127.4, 127.0 (CH), 126.2 (CH), 125.6 (CH), 124.5, 121.7, 120.9 (CH), 120.1 (CH), 110.6 (CH), 51.4 (Me), 48.2 (CH_2), 11.0 (Me); *m/z* (EI) 279 (M^+, 14), 188 (8), 128 (10), 91 (100).

Methyl 5-methoxy-1,2-dimethylindole-3-carboxylate 5. A solution of ethyl 5-hydroxy-2-methylindole-3-carboxylate (0.56 g, 2.5 mmol) in THF (15 ml) and sodium hydroxide solution (5%; 10 ml) was heated under reflux overnight. The mixture was acidified with hydrochloric acid (3 M) and extracted with ethyl acetate. The organic layer was dried ($MgSO_4$) and concentrated to yield 5-hydroxy-2-methylindole-3-carboxylic acid as a pale brown solid (0.41 g, 85%) which was used directly in the next step without purification; δ_H (300 MHz; CD_3OD) 7.44 (1H, d, *J* 2.4, ArH), 7.12 (1H, d, *J* 8.6, ArH), 6.66 (1H, dd, *J* 8.6, 2.4, ArH), 2.64 (3H, s, Me).

A solution of the above acid (0.10 g, 0.52 mmol), potassium hydroxide (0.12 g, 2.1 mmol) and iodomethane (0.30 g, 2.1 mmol) in DMSO (5 ml) was stirred overnight. Hydrochloric acid (3 M; 20 ml) was added and the mixture extracted with ethyl acetate. The organic layer was washed twice with hydrochloric acid (1 M) and then water. The organic layer was separated, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (dichloromethane elution) and recrystallised (light petroleum–ethyl acetate) to yield the *title compound* (0.075 g, 62%) as a colourless solid, mp 127–128 °C (Found: C, 66.9; H, 6.1; N, 5.9. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%) (Found: M^+, 233.1052. $C_{13}H_{15}NO_3$ requires 233.1052); ν_{max} (KBr)/cm^{-1} 3006, 2947, 2841, 1710, 1624, 1585; δ_H (300 MHz; $CDCl_3$) 7.63 (1H, d, *J* 2.5, ArH), 7.18 (1H, d, *J* 8.8, ArH), 6.87 (1H, dd, *J* 8.8, 2.5, ArH), 3.92 (3H, s, OMe), 3.89 (3H, s, OMe), 3.67 (3H, s, NMe), 2.74 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 166.5, 155.7, 145.3, 131.6, 127.4, 111.6 (CH), 109.7 (CH), 103.7 (CH), 103.5, 55.8 (Me), 50.6 (Me), 29.7 (Me), 12.0 (Me); *m/z* (EI) 233 (M^+, 100%), 218 (54), 202 (93), 190 (37), 130 (42).

Conjugate addition reactions to acrylates; preparation of 3-arylaminopropanoates 6

Ethyl 3-(4-methylphenylamino)propanoate 6a. A stirred solution of 4-toluidine (3.00 g, 28 mmol) and ethyl acrylate (3.34 ml, 30.8 mmol, 1.1 equiv.) in EtOH (30 ml) was heated at reflux for 3 days. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (2.39 g, 41%) as a brown oil (lit.,[56] bp 142–144 °C, 2–3 mmHg) (Found: MH^+, 208.1337. $C_{12}H_{17}NO_2$ + H requires 208.1337); ν_{max} (film)/cm^{-1} 3398, 2981, 2920, 1734, 1618, 1522, 1028, 810; δ_H (300 MHz; $CDCl_3$) 6.97 (2H, m, ArH), 6.53 (2H, m, ArH), 4.13 (2H, q, *J* 7.1, OCH_2Me), 3.40 (2H, t, *J* 6.4, NCH_2), 2.57 (2H, t, *J* 6.4, NCH_2CH_2), 2.22 (3H, s, Me), 1.24 (3H, t, *J* 7.1, OCH_2Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 172.5, 145.4, 129.8 (CH), 126.9, 113.3 (CH), 60.6 (CH_2), 39.9 (Me), 33.9 (CH_2), 20.4 (CH_2), 14.3 (Me); *m/z* (EI) 207 (M^+, 90%), 131 (42), 117 (100), 106 (33), 91 (95), 76 (52), 64 (52).

Ethyl 3-(4-methoxyphenylamino)propanoate 6b. A stirred solution of 4-anisidine (4.44 g, 36.1 mmol) and ethyl acrylate (3.97 g, 39.7 mmol, 1.1 equiv.) was heated at reflux in ethanol (30 ml) for 3 days. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (3.91 g, 49%) as an orange oil (lit.,[44] bp 155–159 °C, 0.5 mmHg); ν_{max} (film)/cm^{-1} 3383, 2983, 2937, 1730, 1514, 1236, 1180, 1035, 822; δ_H (300 MHz; $CDCl_3$) 6.78 (2H, m, ArH), 6.60 (2H, m, ArH), 4.15 (2H, q, *J* 7.1, OCH_2Me), 3.74 (3H, s, OMe), 3.39 (2H, t, *J* 6.38, NCH_2), 2.59 (2H, t, *J* 6.4, $NHCH_2CH_2$), 1.26 (3H, t, *J* 7.1, OCH_2Me); NH not observed.

Ethyl 3-(4-methoxycarbonylphenylamino)propanoate 6c. A stirred solution of methyl 4-aminobenzoate (2.0 g, 13.2 mmol) and ethyl acrylate (2.15 ml, 14.6 mmol, 1.5 equiv.) in EtOH (10 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (727 mg, 22%) as a pale yellow crystalline solid, mp 80 °C (Found: MH^+, 252.1234. $C_{13}H_{17}NO_4$ + H requires 252.1236); ν_{max} (KBr)/cm^{-1} 3391, 2950, 1706, 1610, 1280, 1180, 1110, 773; δ_H (300 MHz; $CDCl_3$) 7.87 (2H, m, ArH), 6.58 (2H, m, ArH), 4.60 (1H, br s, NH), 4.17 (2H, q, *J* 7.1, OCH_2Me), 3.86 (3H, s, OMe), 3.51 (2H, t, *J* 6.4, NCH_2), 2.63 (2H, t, *J* 6.4, NCH_2CH_2), 1.27 (3H, t, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 172.1, 167.3, 151.4, 131.6 (CH), 118.6, 111.6 (CH), 60.8 (CH_2), 51.6 (Me), 38.8 (CH_2), 33.7 (CH_2), 14.2 (CH_2); *m/z* (EI) 251 (M^+, 56%), 220 (25), 165 (46), 164 (100), 162 (33), 132 (49), 91 (26), 77 (27).

Ethyl 3-(4-*tert*-butylphenylamino)propanoate 6d. A solution of 4-*tert*-butylaniline (2.13 ml, 13.4 mmol) and ethyl acrylate (2.18 ml, 20.10 mmol, 1.5 equiv.) in EtOH (10 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (741 mg, 22%) as a pale yellow solid, mp 52–54 °C (Found: MH^+, 250.1806. $C_{15}H_{23}NO_2$ + H requires 250.1807); ν_{max} (KBr)/cm^{-1} 3398, 2962, 1720, 1525, 1319, 1192; δ_H (300 MHz; $CDCl_3$) 7.22 (2H, m, ArH), 6.59 (2H, m, ArH), 4.14 (2H, q, *J* 7.2, OCH_2Me), 3.44 (2H, t, *J* 6.4, NCH_2), 2.62 (2H, t, *J* 6.4, NCH_2CH_2), 1.30 (9H, s, CMe_3), 1.26 (3H, t, *J* 7.2, OCH_2Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 172.5, 145.3, 140.5, 126.1 (CH), 112.8 (CH), 60.6

(CH_2), 39.7 (CH_2), 34.1 (CH_2), 33.9, 31.5 (CMe_3), 14.2 (Me); *m*/*z* (EI) 249 (M^+, 40%), 234 (100), 162 (86), 146 (98), 118 (34), 91 (34).

Benzyl 3-(4-methylphenylamino)propanoate 6e. A stirred solution of 4-toluidine (3.00 g, 28 mmol) and benzyl acrylate (14.03 g, 84 mmol) in EtOH (40 ml) was heated at reflux for 3 days. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 10) to give the *title compound* (6.63 g, 88%) as an orange crystalline solid, mp 49–50 °C (Found: MH^+, 270.1492. $C_{17}H_{19}NO_2$ + H requires 270.1494); ν_{max} (KBr)/cm^{-1} 3447, 3392, 1720, 1618, 1522, 1321, 1186, 796, 723 (ArH); δ_H (300 MHz; $CDCl_3$) 7.36 (5H, m, PhH), 7.01 (2H, d, *J* 8.5, ArH), 6.56 (2H, d, *J* 8.5, ArH), 5.15 (2H, s, CH_2), 3.47 (2H, t, *J* 6.3, NCH_2), 2.68 (2H, t, *J* 6.3, NCH_2CH_2), 2.25 (3H, s, Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 172.1, 135.6, 129.8 (CH), 128.6 (CH), 128.4, 128.3 (CH), 128.2 (CH), 128.1, 114.0 (CH), 66.5 (CH_2),40.4 (CH_2), 33.6 (CH_2), 20.4 (Me); *m*/*z* (CI) 270 (MH^+, 32%), 135 (20), 120 (46), 108 (100), 91 (70), 78 (19).

Benzyl 3-(4-methoxyphenylamino)propanoate 6f. A stirred solution of 4-anisidine (333 mg, 2.7 mmol) and benzyl acrylate (500 mg, 3.0 mmol) in EtOH (15 ml) was heated at reflux for 3 days. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (663 mg, 84%) as a pale brown crystalline solid, mp 38–39 °C (ethyl acetate–light petroleum) (Found: MH^+, 286.1445. $C_{17}H_{19}NO_3$ + H requires 286.1443); ν_{max} (KBr)/cm^{-1} 3377, 2953, 2910, 1722, 1515, 1268, 1236, 1211, 808, 732; δ_H (300 MHz; $CDCl_3$) 7.39 (5H, m, PhH), 6.82 (2H, d, *J* 8.8, ArH), 6.62 (2H, d, *J* 8.8, ArH), 5.18 (2H, s, CH_2), 3.77 (3H, s, OMe), 3.45 (2H, t, *J* 6.3, NCH_2), 2.68 (2H, t, *J* 6.3, NCH_2CH_2); NH not observed; δ_C (75 MHz; $CDCl_3$) 172.2, 152.5, 141.5 (CH), 135.7, 128.6 (CH), 128.3 (CH), 128.2 (CH), 114.9 (CH), 114.7 (CH), 66.4 (CH_2), 55.7 (Me), 40.6 (CH_2), 33.9 (CH_2); *m*/*z* (EI) 285 (M^+, 90%), 226 (33), 195 (27), 194 (39), 149 (29), 148 (45), 134 (99), 120 (99), 107 (66), 91 (100), 77 (67), 64 (64).

Preparation of indoles 8

Methyl 1-(2-ethoxycarbonylethyl)-3,5-dimethylindole-2-carboxylate 8a. A solution of **6a** (100 mg, 0.48 mmol), diazo compound **2a** (137 mg, 0.96 mmol, 2 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (6 ml) was heated at reflux for 1.5 h. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the intermediate **7a** (118 mg, 76%) as a pale yellow oil.

This was then dissolved in toluene (5 ml), Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 10) to give the *title compound* (84 mg, 76%) as a colourless solid, mp 45–46 °C (Found: MH^+, 304.1551. $C_{17}H_{21}NO_4$ + H requires 304.1549); ν_{max} (KBr)/cm^{-1} 3446, 2956, 1734, 1700, 1257, 1188, 1124, 773; δ_H (300 MHz; $CDCl_3$) 7.43 (1H, s, ArH), 7.33 (1H, m, ArH), 7.19 (1H, m, ArH), 4.78 (2H, t, *J* 7.4, NCH_2), 4.10 (2H, q, *J* 7.1, OCH_2Me), 3.94 (3H, s, OMe), 2.80 (2H, t, *J* 7.4, NCH_2CH_2), 2.56 (3H, s, Me), 2.47 (3H, s, Me), 1.20 (3H, t, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 171.7, 163.4, 136.6, 129.3, 127.5 (CH), 127.4, 123.9, 121.1, 120.2 (CH), 109.9 (CH), 60.7 (CH_2), 51.4 (Me), 40.8 (CH_2), 35.5 (CH_2), 21.4 (Me), 14.1 (Me), 10.9 (Me); *m*/*z* (EI) 303 (M^+, 54%), 244 (42), 216 (100).

Methyl 1-(2-ethoxycarbonylethyl)-5-methoxy-3-methylindole-2-carboxylate 8b. A solution of **6b** (277 mg, 1.24 mmol), diazo compound **2a** (353 mg, 2.48 mmol, 2 equiv.) and dirhodium(II) acetate (10 mg) in distilled chloroform (10 ml) was heated at reflux for 1.5 h. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the intermediate **7b** (298 mg, 71%).

The intermediate **7b** was then heated at reflux overnight in toluene (3 ml) in the presence of Amberlyst® (110 mg). The reaction mixture was filtered, concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the *title compound* (178 mg, 63%) as a yellow solid, mp 44–45 °C (from ethyl acetate–light petroleum) (Found: C, 63.8; H, 6.6; N, 4.3. $C_{17}H_{21}NO_5$ requires C, 63.9; H, 6.6; N, 4.4%); ν_{max} (KBr)/cm^{-1} 2981, 2953, 2833, 1733, 1700, 1441, 1213; δ_H (300 MHz; $CDCl_3$) 7.32 (1H, m, ArH), 7.02 (2H, m, ArH), 4.77 (2H, t, *J* 7.3, NCH_2), 4.08 (2H, t, *J* 7.1, OCH_2Me), 3.95 (3H, s, OMe), 3.89 (3H, s, OMe), 2.79 (2H, t, *J* 7.3, NCH_2CH_2), 2.55 (3H, s, Me), 1.19 (3H, t, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 171.6, 163.3, 154.3, 133.6, 130.1, 124.2, 120.8, 117.0 (CH), 111.2 (CH), 100.9 (CH), 60.7 (CH_2), 55.8 (Me), 51.4 (Me), 40.9 (CH_2), 35.6 (CH_2), 14.1 (Me), 11.0 (Me); *m*/*z* (EI) 319 (M^+, 86%), 260 (70), 233 (41), 232 (100), 187 (25), 172 (30).

Dimethyl 1-(2-ethoxycarbonylethyl)-3-methylindole-2,5-dicarboxylate 8c. A solution of **6c** (100 mg, 0.40 mmol), diazo compound **2a** (113 mg, 0.80 mmol, 2 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (6 ml) was heated at reflux for 1.5 h. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the intermediate **7c** (91 mg, 63%) as a pale yellow oil.

This was then dissolved in toluene (5 ml) and Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (30 mg, 22%) as a pale yellow solid, mp 85–86 °C (Found: MH^+, 348.1448. $C_{18}H_{21}NO_6$ + H requires 348.1447); ν_{max} (KBr)/cm^{-1} 3437, 2945, 1731, 1701, 1319, 1259, 1244, 1180, 1134, 768; δ_H (300 MHz; $CDCl_3$) 8.44 (1H, d, *J* 1.5, H-4), 8.02 (1H, dd, *J* 8.8, 1.5, H-6), 7.44 (1H, d, *J* 8.8, H-7), 4.81 (2H, t, *J* 7.4, NCH_2), 4.07 (2H, q, *J* 7.1, OCH_2Me), 3.96 (3H, s, OMe), 3.95 (3H, s, OMe), 2.82, (2H, t, *J* 7.4, NCH_2CH_2), 2.61 (3H, s, Me), 1.17 (3H, t, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 171.4, 167.7, 163.0, 140.2, 126.9, 126.3 (CH), 125.3, 124.2 (CH), 123.2, 122.1, 109.9 (CH), 60.8 (CH_2), 52.0 (Me), 51.7 (Me), 41.1 (CH_2), 35.4 (CH_2), 14.1 (Me), 10.9 (Me); *m*/*z* (EI) 347 (M^+, 36%), 288 (40), 260 (100), 242 (12), 156 (16), 128 (14), 83 (20), 59 (12).

Methyl 5-*tert*-butyl-1-(2-ethoxycarbonylethyl)-3-methylindole-2-carboxylate 8d. A solution of **6d** (100 mg, 0.40 mmol), diazo compound **2a** (113 mg, 0.80 mmol, 2 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (6 ml) was heated at reflux for 1.5 h. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the intermediate **7d** (80 mg, 55%) as a pale yellow oil.

This was then dissolved in toluene (5 ml), Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (49 mg, 64%) as a pale yellow oil (Found: MH^+, 346.2023. $C_{20}H_{27}NO_4$ + H requires 346.2018); ν_{max} (film)/cm^{-1} 3446, 2962, 1733, 1701, 1541, 1178, 1132, 802; δ_H (300 MHz; $CDCl_3$) 7.61 (1H, d, *J* 1.9, H-4), 7.47 (1H, dd, *J* 8.8, 1.9, H-6), 7.38 (1H, d, *J* 8.8, H-7), 4.78 (2H, t, *J* 7.4, NCH_2), 4.10 (2H, q, *J* 7.1, OCH_2Me), 3.95 (3H, s, OMe), 2.80 (2H, t, *J* 7.4, NCH_2CH_2), 2.59 (3H, s, Me), 1.40 (9H, s, CMe_3), 1.19 (3H, t, *J* 7.1, OCH_2Me); δ_C (75 MHz; $CDCl_3$) 171.7, 163.4, 142.9, 136.5, 126.9, 124.3 (CH), 123.9, 121.7, 116.1 (CH), 109.8 (CH), 60.6 (CH_2), 51.4 (Me), 40.8 (CH_2), 35.5 (CH_2), 34.7, 31.7 (Me), 14.1 (Me), 10.9 (Me); *m*/*z* (EI) 345 (M^+, 82%), 330 (100), 258 (53), 256 (58), 242 (44).

2-Benzylsulfanylethanol. Benzyl bromide (3.8 ml, 31.9 mmol) and 2-mercaptoethanol (2.24 ml, 32.0 mmol) were added to a stirred suspension of potassium carbonate (11.05 g, 80 mmol), 18-crown-6 (100 mg) and potassium iodide (100 mg) in dry acetone (80 ml). The mixture was stirred at reflux for 15 h, cooled to room temperature, filtered and concentrated under reduced pressure. Water (75 ml) was then added to the residue and this was then extracted with ether (3 × 75 ml). The combined organic layers were washed with water (75 ml), brine (75 ml) and dried ($MgSO_4$). This was then concentrated under reduced pressure and purified on a silica gel column eluting with ethyl acetate–light petroleum (1 : 3) to give the title compound (4.75 g, 88%) as a yellow oil; δ_H (300 MHz; $CDCl_3$) 7.33–7.28 (5H, m, ArH), 3.73 (2H, s, CH_2), 3.68 (2H, t, *J* 6.0, C*H*$_2$OH), 2.64 (2H, t, *J* 6.0, SCH_2), 2.02 (1H, br s, OH).

2-Benzylsulfonylethanol. To a stirred solution of 2-benzylsulfanylethanol (3.5 g, 20 mmol) in dichloromethane (70 ml), *m*-chloroperbenzoic acid (17.3 g, 100 mmol) in dichloromethane (200 ml) was added dropwise at room temperature. The reaction mixture was stirred further for 3 h. The reaction was quenched using saturated sodium sulfite solution and washed with water, sodium hydrogen carbonate and water to obtain the crude product as a colourless solid (3.9 g, 94%), mp 65–66 °C (ethyl acetate–light petroleum); [lit.,[45] mp 70 °C (ethyl acetate)]; ν_{max} (neat)/cm^{-1} 3533 (br), 2925, 1790, 1763, 1574; δ_H (300 MHz; $CDCl_3$) 7.95–7.30 (5H, m, ArH), 4.26 (2H, s, CH_2), 3.97 (2H, t, *J* 5.2, C*H*$_2$OH), 2.99 (2H, t, *J* 5.2, SO_2CH_2), 2.28 (1H, br s, OH).

Benzyl vinyl sulfone. Methanesulfonyl chloride (3.5 ml, 45 mmol) was added to a stirred solution of 2-benzylsulfonylethanol (4.6 g, 23 mmol) in dry dichloromethane (150 ml) at 0 °C under nitrogen, and the reaction mixture stirred at room temperature for 15 h. Water (100 ml) was added and the aqueous layer extracted with dichloromethane (3 × 100 ml). The combined organic layers were washed with water (120 ml), brine (100 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale yellow solid. This was then purified by silica gel chromatography (1 : 4, ethyl acetate : light petroleum) to obtain the *title compound* (3.0 g, 72%) as a colourless solid, mp 93–95 °C (ethyl acetate–light petroleum) [lit.,[45] 94–95 °C (ethyl acetate–light petroleum)]; ν_{max} (KBr)/cm^{-1} 3058, 2966, 2925, 1603, 1491, 1455, 1388, 1312, 1260, 1153, 1107, 968, 784, 692; δ_H (300 MHz; $CDCl_3$) 7.36 (5H, s, ArH), 6.51 (1H, dd, *J* 16.5, 9.9, =CH), 6.29 (1H, d, *J* 16.5, =C*H*H), 6.09 (1H, d, *J* 9.9, =CH*H*), 4.24 (2H, s, CH_2).

Conjugate addition reactions to vinyl sulfones; preparation of *N*-(2-phenylsulfonylethyl)- and *N*-(2-benzylsulfonylethyl)anilines 9

4-Methyl-*N*-(2-phenylsulfonylethyl)aniline 9a. A stirred solution of 4-toluidine (1.86 g, 17.3 mmol) and phenyl vinyl sulfone (3.5 g, 20.8 mmol) in EtOH (20 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the *title compound* (4.76 g, 99%) as a colourless solid, mp 78–79 °C (from light petroleum – ethyl acetate) (Found: MH$^+$, 276.1061. $C_{15}H_{17}NO_2S$ + H requires 276.1058); ν_{max} (KBr)/cm^{-1} 3410, 2967, 2927, 1616, 1519, 1288, 1142, 1082, 808, 752; δ_H (300 MHz; $CDCl_3$) 7.93 (2H, m, PhH), 7.69 (1H, m, PhH), 7.59 (2H, m, PhH), 6.99 (2H, d, *J* 8.5, ArH), 6.47 (2H, d, *J* 8.5, ArH), 3.59 (2H, t, *J* 6.3, NC*H*$_2$), 3.37 (2H, t, *J* 6.3, NCH_2CH_2), 2.24 (3H, s, Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 144.2, 139.0, 134.0 (CH), 129.9 (CH), 129.5 (CH), 128.0 (CH), 127.7, 113.4 (CH), 54.8 (CH_2), 38.0 (CH_2), 20.4 (Me); *m*/*z* (CI) 275 (M$^+$, 100%), 134 (2), 132 (10).

4-Methoxy-*N*-(2-phenylsulfonylethyl)aniline 9c. A stirred solution of 4-anisidine (133 mg, 1.1 mmol), and phenyl vinyl sulfone (200 mg, 1.2 mmol, 1.1 equiv.) in ethanol (5 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (218 mg, 68%) as an off-white solid, mp 86–88 °C (Found: MH$^+$, 292.1004. $C_{15}H_{17}NO_3S$ + H requires 292.1007); ν_{max} (KBr)/cm^{-1} 3361, 2937, 1516, 1308, 1240, 1145, 742; δ_H (300 MHz; $CDCl_3$) 7.93 (2H, m, PhH), 7.69 (1H, m, PhH), 7.59 (2H, m, PhH), 6.77 (2H, m, ArH), 6.53 (2H, m, ArH), 3.75 (3H, s, OMe), 3.56 (2H, t, *J* 6.3, NC*H*$_2$), 3.35 (2H, t, *J* 6.3, NCH_2CH_2); NH not observed; δ_C (75 MHz; $CDCl_3$) 152.8, 140.5, 139.1, 134.0 (CH), 129.5 (CH), 128.0 (CH), 115.0 (CH), 114.8 (CH), 55.7 (Me), 54.8 (CH_2), 38.8 (CH_2); *m*/*z* (EI) 291 (M$^+$, 60%), 276 (25), 150 (46), 148 (100), 135 (99), 133 (83), 122 (50), 107 (48), 76 (75), 51 (46).

2-Methyl-*N*-(2-phenylsulfonylethyl)aniline 9d. A solution of 2-toluidine (0.57 ml, 5.35 mmol) and phenyl vinyl sulfone (900 mg, 5.35 mmol) in ethanol (20 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (996 mg, 68%) as a grey crystalline solid, mp 57–59 °C (Found: MH$^+$, 276.1059. $C_{15}H_{17}NO_2S$ + H requires 276.1058); ν_{max} (KBr)/cm^{-1} 3417, 2913, 1508, 1299, 1282, 1139, 755; δ_H (300 MHz; $CDCl_3$) 7.94 (2H, m, PhH), 7.69 (1H, m, PhH), 7.59 (2H, m, PhH), 7.09 (2H, m, ArH), 6.70 (1H, m, ArH), 6.48 (1H, m, ArH), 4.21 (1H, br s, NH), 3.64 (2H, t, *J* 6.2, NC*H*$_2$), 3.43 (2H, t, *J* 6.2, NCH_2CH_2), 2.11 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 144.7, 138.9, 134.1 (CH), 130.5 (CH), 129.5 (CH), 128.0 (CH), 127.1 (CH), 122.9, 117.9 (CH), 109.4 (CH), 54.9 (CH_2), 37.6 (CH_2), 17.4 (Me); *m*/*z* (EI) 275 (M$^+$, 55%), 133 (60), 120 (71), 117 (100), 91 (62), 77 (61), 65 (30).

2-Methoxy-*N*-(2-phenylsulfonylethyl)aniline 9e. A stirred solution of 2-anisidine (0.60 ml, 5.32 mmol) and phenyl vinyl sulfone (900 mg, 5.32 mmol) in EtOH was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4), and recrystallised from light petroleum–ethyl acetate to give the *title compound* as a grey crystalline solid (1.14g, 74%), mp 76–77 °C (Found: MH$^+$, 292.1007. $C_{15}H_{17}NO_3S$ + H requires 292.1007); ν_{max} (KBr)/cm^{-1} 3429, 2943, 1603, 1140, 744; δ_H (300 MHz; $CDCl_3$) 7.94 (2H, m, PhH), 7.68 (1H, m, PhH), 7.57 (2H, m, PhH), 6.84 (1H, m, ArH), 6.73 (2H, m, ArH), 6.47 (1H, m, ArH), 4.59 (1H, br s, NH), 3.81 (3H, s, OMe), 3.63 (2H, t, *J* 6.6, NC*H*$_2$), 3.41 (2H, t, *J* 6.6, NCH_2CH_2); δ_C (75 MHz; $CDCl_3$) 147.2, 139.1, 136.3, 133.9 (CH), 129.4 (CH), 128.0 (CH), 121.2 (CH), 117.5 (CH), 109.7 (CH), 109.6 (CH), 55.4 (CH_2), 54.9 (CH_2), 37.3 (Me); *m*/*z* (EI) 291 (M$^+$, 28%) 149 (56), 134 (57), 120 (55), 85 (46), 83 (68).

4-Bromo-*N*-(2-phenylsulfonylethyl)aniline 9f. A stirred solution of 4-bromoaniline (500 mg, 2.9 mmol) and phenyl vinyl sulfone (978 mg, 5.8 mmol) in ethanol (20 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (172 mg, 17%) as a pale orange solid, mp 91–93 °C (Found: M$^+$, 338.9934. $C_{14}H_{14}{}^{79}BrNO_2S$ requires 338.9929); ν_{max} (KBr)/cm^{-1} 3367, 2991, 2946, 1594, 1292, 1147, 808; δ_H (400 MHz; $CDCl_3$) 7.91 (2H, m, PhH), 7.67 (1H, m, PhH), 7.57 (2H, m, PhH), 7.23 (2H, m, ArH), 6.40 (2H, m, ArH), 3.55 (2H, t, *J* 6.2, NC*H*$_2$), 3.34 (2H, t, *J* 6.2, NCH_2CH_2); NH not observed; δ_C (100 MHz; $CDCl_3$) 145.5, 138.9, 134.1 (CH), 132.1 (CH), 129.5 (CH), 127.9 (CH), 114.6 (CH), 110.0, 54.5 (CH_2), 37.7 (CH_2); *m*/*z* (EI) 340/338 (M$^+$, 34%), 196 (100), 195 (17), 183 (54), 117 (20).

3-Methoxy-*N*-(2-phenylsulfonylethyl)aniline 9g. A stirred solution of 3-anisidine (0.46 ml, 4.04 mmol) and phenyl vinyl sulfone (1.36 g, 8.12 mmol) in ethanol (20 ml) was heated at reflux for 3 days. The reaction mixture was concentrated

in vacuo and purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the *title compound* (887 mg, 75%) as a grey crystalline solid, mp 48–49 °C (Found: M^+, 291.0923. $C_{15}H_{17}NO_3S$ requires 291.0929); ν_{max} (KBr)/cm^{-1} 3439, 2952, 1618, 1515, 1294, 1169, 1143, 756; δ_H (400 MHz; $CDCl_3$) 7.91 (2H, m, PhH), 7.67 (1H, m, PhH), 7.57 (2H, m, PhH), 7.06 (1H, t, *J* 8.1, ArH), 6.30 (1H, dd, *J* 8.1, 2.3, ArH), 6.14 (1H, dd, *J* 8.1, 2.2, ArH), 6.08 (1H, m, ArH), 3.74 (3H, s, OMe), 3.56 (2H, t, *J* 6.2, NCH_2), 3.36 (2H, t, *J* 6.2, NCH_2CH_2); NH not observed; δ_C (100 MHz; $CDCl_3$) 160.8, 147.9, 138.9, 134.0 (CH), 130.1 (CH), 129.4 (CH), 127.9 (CH), 106.0 (CH), 103.4 (CH), 99.1 (CH), 55.1 (Me), 54.7 (CH_2), 37.6 (CH_2); *m*/*z* (EI) 291 (M^+, 72%), 150 (14), 149 (100), 148 (56), 136 (83), 135 (10), 134 (12), 77 (40).

4-Methyl-*N*-(2-benzylsulfonylethyl)aniline 9h. *Method A.* A stirred solution of 4-toluidine (120 mg, 1.1 mmol) and benzyl vinyl sulfone (182 mg, 1.0 mmol) in absolute ethanol (15 ml) was heated at reflux for 3 days. The reaction was then concentrated under reduced pressure and the residue purified on silica gel eluting with ethyl acetate–light petroleum (1 : 2) to give the *title compound* (250 mg, 87%) as a pale yellow solid, mp 96–98 °C (Found: M^+, 289.1124. $C_{16}H_{19}NO_2S$ requires 289.1137); ν_{max} (KBr)/cm^{-1} 3355, 2940, 2909, 1609, 1522, 1291, 1112, 810, 692, 513; δ_H (300 MHz; $CDCl_3$) 7.42–7.34 (5H, m, PhH), 7.03 (2H, d, *J* 8.1, ArH), 6.55 (2H, d, *J* 8.1, ArH), 4.26 (2H, s, CH_2Ph), 3.64 (2H, t, *J* 6.0, NCH_2), 3.10 (2H, t, *J* 6.0, NCH_2CH_2), 2.27 (3H, s, Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 144.2, 130.7 (CH), 130.1 (CH), 129.13 (CH), 129.07 (CH), 127.9, 127.8, 113.5 (CH), 60.8 (CH_2), 49.9 (CH_2), 37.9 (CH_2), 20.4 (Me); *m*/*z* (EI) 289 (M^+, 53%), 133 (95), 120 (41), 106 (13), 91 (100), 77 (15).

Method B. A stirred solution of 4-toluidine (40 mg, 0.37 mmol) and benzyl vinyl sulfone (60 mg, 0.33 mmol) in dry THF (8 ml) was heated at reflux in the presence of DBU (10 mg, 0.07 mmol) for 13 h. The reaction mixture was concentrated and the residue purified by silica gel column chromatography to afford the *title compound* (70 mg, 74%), mp 96–98 °C.

4-Methoxy-*N*-(2-benzylsulfonylethyl)aniline 9i. A stirred solution of 4-anisidine (245 mg, 2.0 mmol) and benzyl vinyl sulfone[45] (545 mg, 3.0 mmol) in ethanol (20 ml) was heated at reflux for 3 days. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 2) to give the *title compound* (541 mg, 89%) as a pale orange solid, mp 84–86 °C (Found: M^+, 305.1091. $C_{16}H_{19}NO_3S$ requires 305.1086); ν_{max} (KBr)/cm^{-1} 2286, 2913, 1515, 1241, 1114, 815, 703; δ_H (300 MHz; $CDCl_3$) 7.33–7.35 (5H, m, PhH), 6.81 (2H, m, ArH), 6.60 (2H, m, ArH), 4.28 (2H, s, CH_2Ph), 3.77 (3H, s, OMe), 3.63 (2H, t, *J* 6.0, NCH_2), 3.09 (2H, t, *J* 6.0, NCH_2CH_2); NH not observed; δ_C (75 MHz; $CDCl_3$) 152.9, 140.6, 130.7 (CH), 129.1 (CH), 129.0 (CH), 127.8, 115.0 (CH), 114.8 (CH), 60.8 (CH_2), 55.8 (Me), 49.9 (CH_2), 38.5 (CH_2); *m*/*z* (EI) 305 (M^+, 100), 150 (25), 149 (82), 136 (45), 134 (23), 122 (28), 119 (20), 91 (66), 85 (21), 71 (26), 69 (22).

2-Methyl-*N*-(2-benzylsulfonylethyl)aniline 9j. *Method A.* A stirred solution of 2-toluidine (360 mg, 3.4 mmol) and benzyl vinyl sulfone (546 mg, 3.0 mmol) in absolute ethanol (20 ml) was heated at reflux for 8 days. The reaction was followed by NMR spectroscopy for the disappearance of distinct vinyl protons. The reaction mixture was then concentrated under reduced pressure and the residue purified on silica gel eluting with ethyl acetate–light petroleum (1 : 2) to give the *title compound* (630 mg, 73%) as a pale orange solid, mp 113–115 °C (Found: M^+, 289.1130. $C_{16}H_{19}NO_2S$ requires 289.1137); ν_{max} (KBr)/cm^{-1} 3360, 3027, 2971, 2909, 1603, 1516, 1450, 1327, 1286, 1112, 748, 687, 477; δ_H (300 MHz; $CDCl_3$) 7.32–7.20 (5H, m, PhH), 7.16–7.08 (2H, m, ArH), 6.73 (1H, t, *J* 7.4, ArH), 6.55 (1H, d, *J* 7.9, ArH), 4.25 (2H, s, CH_2Ph), 3.73 (2H, t, *J* 6.0, NCH_2), 3.15 (2H, t, *J* 6.0, NCH_2CH_2), 2.15 (3H, s, Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 144.6, 130.7 (CH), 130.6 (CH), 129.2 (CH), 129.1 (CH), 127.6, 127.2 (CH), 123.0, 118.1 (CH), 109.6 (CH), 60.8 (CH_2), 49.8 (CH_2), 37.3 (CH_2), 17.5 (Me); *m*/*z* (EI) 289 (M^+, 42%), 134 (18), 133 (28), 120 (41), 118 (100), 106 (14), 77 (9).

Method B. A stirred solution of 2-toluidine (260 mg, 2.4 mmol) and benzyl vinyl sulfone (365 mg, 2.0 mmol) in dry THF (15 ml) was heated at reflux in the presence of DBU (30 mg, 0.2 mmol) for 50 h. The reaction mixture was concentrated and the residue purified by silica gel column chromatography to afford the *title compound* (390 mg, 67%).

2-Nitro-*N*-(2-benzylsulfonylethyl)aniline 9k. A stirred solution of 2-nitroaniline (345 mg, 2.5 mmol) and benzyl vinyl sulfone (365 mg, 2.0 mmol) in dry THF (15 ml) was heated at reflux in the presence of DBU (45 mg, 0.3 mmol) for 6 days. The reaction mixture was concentrated and the residue purified by silica gel column chromatography to afford the *title compound* (320 mg, 50%) as a yellow crystalline solid, mp 172–173 °C (dichloromethane–light petroleum) (Found: M^+, 320.0822. $C_{15}H_{16}N_2O_4S$ requires 320.0831); ν_{max} (KBr)/cm^{-1} 3385, 1624, 1568, 1358, 1312, 1265, 1224, 1127, 738, 697, 513; δ_H (400 MHz; $CDCl_3$) 8.20 (1H, dd, *J* 8.5, 2.0, ArH), 8.17 (1H, br s, NH), 7.47 (1H, t, *J* 8.5, ArH), 7.42–7.36 (5H, m, PhH), 6.81 (1H, d, *J* 8.5, ArH), 6.74 (1H, dt, *J* 7.5, 2.0, ArH), 4.30 (2H, s, CH_2Ph), 3.82 (2H, t, *J* 6.8, NCH_2), 3.18 (2H, t, *J* 6.8, NCH_2CH_2); δ_C (100 MHz; $CDCl_3$) 144.0, 136.5 (CH), 130.6 (CH), 129.4 (CH), 129.3 (CH), 127.4, 127.2 (CH), 116.5 (CH), 113.0 (CH), 61.1 (CH_2), 49.6 (CH_2), 36.0 (CH_2); 1 C not observed; *m*/*z* (EI) 320 (M^+, 23%), 286 (4), 221 (6), 164 (17), 134 (51), 91 (100).

Preparation of indoles 11

Methyl 3,5-dimethyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11a. A solution of 4-methyl-*N*-(2-phenylsulfonylethyl)aniline **9a** (500 mg, 1.82 mmol), diazo compound **2a** (522 mg, 3.67 mmol) and dirhodium(II) acetate (10 mg) in chloroform (25 ml) was heated at reflux for 1.5 h. The reaction was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the intermediate **10a** (440 mg, 62%) as a yellow oil.

This was then immediately dissolved in toluene (15 ml) and Amberlyst® (110 mg) was then added and the mixture heated at reflux overnight. The reaction mixture was cooled, concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 5) to give the *title compound* (296 mg, 71%) as a colourless solid, mp 139–140 °C (from ethyl acetate–light petroleum) (Found: $[M + NH_4]^+$, 389.1532. $C_{20}H_{21}NO_4S + NH_4$ requires 389.1535); ν_{max} (KBr)/cm^{-1} 3446, 2954, 2918, 1691, 1259, 1146, 1126, 1084; δ_H (300 MHz; $CDCl_3$) 7.86 (2H, m, PhH), 7.66 (1H, m, PhH), 7.55 (2H, m, H-6,7), 7.39 (1H, ~s, H-4), 7.18 (2H, m, PhH), 4.82 (2H, t, *J* 7.4, NCH_2), 3.86 (3H, s, OMe), 3.60 (2H, t, *J* 7.4, NCH_2CH_2), 2.48 (3H, s, Me), 2.45 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 163.1, 139.0, 136.3, 133.8 (CH), 129.3 (CH), 128.0, 127.8 (CH), 127.5 (CH), 123.5, 121.9, 120.3, 109.5 (CH), 97.4 (CH), 55.6 (CH_2), 51.5 (Me), 38.9 (CH_2), 21.3 (Me), 10.7 (Me); *m*/*z* (EI) 371 (M^+, 17%), 229 (22), 198 (17), 170 (17), 142 (22), 115 (23), 77 (100), 51 (37), 42 (39).

Methyl 3-ethyl-5-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11b. A solution of 4-methyl-*N*-(2-phenylsulfonylethyl)aniline **9a** (623 mg, 2.26 mmol), diazo compound **2b** (530 mg, 3.39 mmol) and dirhodium(II) acetate (10 mg) in chloroform (25 ml) was heated at reflux for 1.5 h. The reaction mixture was concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 5) to give the intermediate **10b** (575 mg, 63%) as a yellow oil.

This was then immediately dissolved in toluene (15 ml) and Amberlyst® (110 mg) was added and the mixture heated at

reflux overnight. The reaction mixture was cooled, concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (361 mg, 66%) as a pink solid, mp 134–135 °C (ethyl acetate–light petroleum) (Found: MH^+, 386.1426. $C_{21}H_{23}NO_4S$ + H requires 386.1426); ν_{max} (KBr)/cm^{-1} 3435, 2968, 1695, 1540, 1437, 1363, 1151, 744; δ_H (300 MHz; $CDCl_3$) 7.90 (2H, m, PhH), 7.66 (1H, m, PhH), 7.55 (2H, m, PhH), 7.41 (2H, br, ArH), 7.18 (1H, br s, H-4), 4.81 (2H, t, *J* 7.4, NCH_2), 3.86 (3H, s, OMe), 3.62 (2H, t, *J* 7.4, NCH_2CH_2), 2.99 (2H, q, *J* 7.4, CH_2Me), 2.45 (3H, s, Me), 1.18 (3H, t, *J* 7.4, CH_2Me); δ_C (75 MHz; $CDCl_3$) 162.9, 139.2, 136.4, 133.8, 129.9 (CH), 129.3, 128.4, 127.9 (CH), 127.8, 127.8 (CH), 126.6 (CH), 120.2, 109.6 (CH), 55.6 (CH_2), 51.5 (Me), 38.9 (CH_2), 21.4 (Me), 18.6 (CH_2), 15.5 (Me); *m*/*z* (EI) 385 (M^+, 35%), 326 (63), 228 (34), 184 (28), 143 (25), 115 (26), 77 (100).

Methyl 5-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11c. A solution of 4-methoxy-*N*-(2-phenylsulfonylethyl)aniline **9c** (525 mg, 1.80 mmol), diazo compound **2a** (384 mg, 2.7 mmol, 1.5 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (10 ml) was heated at reflux for 1.5 h the reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 2) to give the intermediate **10c** (544 mg, 78%) as a pale yellow oil.

This was then dissolved in toluene (5 ml) and Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (365 mg, 49%) as a colourless solid, mp 118–119 °C (Found: $[M + NH_4]^+$, 405.1479. $C_{20}H_{21}NO_5S$ + NH_4 requires 405.1484); ν_{max} (KBr)/cm^{-1} 3427, 1707, 1444, 1209, 1146, 737; δ_H (300 MHz; $CDCl_3$) 7.85 (2H, m, PhH), 7.65 (1H, m, PhH), 7.53 (2H, m, PhH), 7.20 (1H, d, *J* 9.1, H-7), 7.03 (1H, dd, *J* 9.1, 2.2, H-6), 6.97 (1H, d, *J* 2.2, H-4), 4.82 (2H, m, NCH_2), 3.87 (6H, s, OMe), 3.61 (2H, m, NCH_2CH_2), 2.47 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 162.0, 154.6, 139.0, 133.8 (CH), 133.3, 129.3 (CH), 127.8, 127.5, 123.9, 121.6, 117.4 (CH), 110.8 (CH), 101.1 (CH), 55.8 (Me), 55.7 (CH_2), 51.5 (Me), 39.0 (CH_2), 10.9 (Me); *m*/*z* (ES) 410 (M^+Na, 100%), 405 (10), 388 (15), 269 (10), 215 (7), 161 (7), 129 (23), 97 (38).

Methyl 3,7-dimethyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11d. A solution of **9d** (150 mg, 0.55 mmol), diazo compound **2a** (200 mg, 1.4 mmol, 2.8 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (5 ml) was heated at reflux for 1.5 h. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the intermediate **10d** (156 mg, 73%) as a pale yellow oil.

This was then dissolved in toluene (5 ml) and Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the *title compound* (76 mg, 51%) as a colourless solid, mp 103–104 °C (Found: MH^+, 372.1266. $C_{20}H_{21}NO_4S$ + H requires 372.1270); ν_{max} (KBr)/cm^{-1} 3448, 2958, 1701, 1451, 1306, 1228, 1147, 741; δ_H (300 MHz; $CDCl_3$) 7.94 (2H, m, PhH), 7.68 (1H, m, PhH), 7.58 (2H, m, PhH), 7.47 (1H, m, ArH), 7.06 (2H, m, ArH), 5.07 (2H, m, NCH_2), 3.87 (3H, s, OMe), 3.58 (2H, m, NCH_2CH_2), 2.64 (3H, s, Me), 2.49 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 162.9, 139.1, 137.3, 133.9 (CH), 133.7, 129.3 (CH), 128.6, 128.0 (CH), 124.7, 123.3, 121.3 (CH), 20.5 (CH), 119.0 (CH), 56.8 (CH_2), 52.0 (Me), 40.2 (CH_2), 20.4 (Me), 10.9 (Me); *m*/*z* (EI) 371 (M^+, 80%), 229 (88), 216 (99), 198 (94), 170 (71), 142 (64), 115 (86), 77 (100).

Methyl 7-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11e. A solution of **9e** (150 mg, 0.52 mmol), diazo compound **2a** (200 mg, 1.4 mmol, 2.7 equiv.) and dirhodium(II) acetate (10 mg) in chloroform (5 ml) was heated at reflux for 1.5 h. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the intermediate **10e** (189 mg, 90%) as a yellow solid.

This was then dissolved in toluene (5 ml) and Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (88 mg, 48%) as a colourless oil (Found: MH^+, 388.1217. $C_{20}H_{21}NO_5S$ + H requires 388.1219); ν_{max} (film)/cm^{-1} 3448, 2951, 1733, 1701, 1350, 1306, 1232, 1159, 1087, 769, 534; δ_H (300 MHz; $CDCl_3$) 7.97 (2H, m, PhH), 7.70 (1H, m, PhH), 7.61 (2H, m, PhH), 7.20 (1H, d, *J* 8.0, ArH), 7.02 (1H, ~t, *J* 8.0, H-5), 6.70 (1H, d, *J* 8.0, ArH), 5.04 (2H, m, NCH_2), 3.86 (3H, s, Me), 3.84 (3H, s, Me), 3.73 (2H, m, NCH_2CH_2), 2.48 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 162.7, 147.3, 139.5, 133.7 (CH), 129.5, 129.3 (CH), 128.1 (CH), 124.8, 122.1, 120.6 (CH), 113.2 (CH), 105.6 (CH), 57.0 (Me), 55.2 (Me), 51.6 (CH_2), 41.4 (CH_2), 10.9 (Me); 1 C unobserved; *m*/*z* (EI) 387 (M^+, 15%), 248 (78), 220 (100), 186 (50), 125 (21), 94 (43), 78 (80), 44 (19).

Methyl 5-bromo-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11f. A solution of 4-bromo-*N*-(2-phenylsulfonylethyl)aniline **9f** (126 mg, 0.37 mmol), diazo compound **2a** (79 mg, 0.56 mmol, 1.5 equiv.) and dirhodium(II) acetate in chloroform (5 ml) was heated at reflux for 1.5 h. The reaction mixture was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the intermediate **10f** (61 mg, 36%) as a yellow oil.

The intermediate **10f** was then immediately dissolved in chloroform (5 ml), Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was then filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the *title compound* (44 mg, 79%) as a pale orange solid, mp 188–189 °C (Found: M^+, 435.0147. $C_{19}H_{18}{}^{79}BrNO_4S$ requires 435.0140); ν_{max} (KBr)/cm^{-1} 3411, 2927, 1697, 1145; δ_H (300 MHz; $CDCl_3$) 7.84 (2H, m, PhH), 7.74 (1H, d, *J* 1.9, H-4), 7.65 (1H, m, PhH), 7.52 (2H, m, PhH), 7.43 (1H, dd, *J* 8.9, 1.9, H-6), 7.21 (1H, d, *J* 8.9, H-7), 4.83 (2H, t, *J* 7.2, NCH_2), 3.88 (3H, s, OMe), 3.61 (2H, t, *J* 7.2, NCH_2CH_2), 2.44 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 162.7, 138.9, 136.4, 133.8 (CH), 133.1, 129.3 (CH), 128.9 (CH), 127.7 (CH), 124.4, 123.5 (CH), 121.5, 113.6, 111.5 (CH), 55.6 (CH_2), 51.7 (Me), 39.1 (CH_2), 10.7 (Me); *m*/*z* (EI) 437/435 (M^+, 97%), 295 (92), 294 (30), 293 (100), 281 (33), 279 (49), 261 (31), 236 (23), 234 (25), 233 (32), 77 (49).

Methyl 4-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11g[1] and methyl 6-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate 11g[2]. A solution of 3-methoxy *N*-(2-phenylsulfonylethyl)aniline **9g** (430 mg, 1.5 mmol) and diazo compound **2a** (315 mg, 2.2 mmol) and dirhodium(II) acetate (10 mg) in chloroform (7 ml) was heated at reflux for 1.5 h. The reaction was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the intermediate **10g** (383 mg, 63%) as a colourless solid. This was then dissolved in toluene (10 ml), Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 5) to give the *title compounds* methyl 4-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate (21 mg, 6%) and methyl 6-methoxy-3-methyl-1-(2-phenylsulfonylethyl)-indole-2-carboxylate (87 mg, 24%).

Methyl 4-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate ***11g[1]***. Mp 140–142 °C (ethyl acetate–light petroleum) (Found: M^+, 387.1139. $C_{20}H_{21}NO_5S$ requires 387.1140); ν_{max} (KBr)/cm^{-1} 3430, 2942, 1297, 1249, 1147, 736;

δ_H (400 MHz; $CDCl_3$) 7.90 (2H, m, PhH), 7.66 (1H, m, PhH), 7.55 (2H, m, PhH), 7.22 (1H, t, *J* 8.0, H-6), 6.83 (1H, d, *J* 8.0, ArH), 6.46 (1H, d, *J* 8.0, ArH), 4.77 (2H, m, NCH_2), 3.90 (3H, s, OMe), 3.84 (3H, s, OMe), 3.60 (2H, m, NCH_2CH_2), 2.69 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.0, 156.7, 139.5, 138.9, 133.8 (CH), 129.2 (CH), 127.8 (CH), 126.8 (CH), 123.6, 122.5, 117.5, 102.4 (CH), 100.0 (CH), 55.5 (CH_2), 55.2 (Me), 51.4 (Me), 39.2 (CH_2), 12.8 (Me); *m*/*z* (EI) 387 (M^+, 100), 328 (21), 245 (39), 232 (18), 230 (13), 214 (27), 187 (13), 186 (15), 149 (10), 77 (26).

Methyl 6-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate ***11g***[2]. Mp 122–123 °C (Found: M^+, 387.1138); ν_{max} 3431, 2950, 1697, 1309, 1222, 1162; δ_H (300 MHz; $CDCl_3$) 7.87 (2H, m, PhH), 7.64 (1H, m, PhH), 7.52 (2H, m, PhH), 7.47 (1H, d, *J* 8.8, H-4), 6.80 (1H, dd, *J* 8.8, 2.0, H-5), 6.72 (1H, d, *J* 2.0, H-7), 4.80 (2H, t, *J* 7.3, NCH_2), 3.87 (3H, s, OMe), 3.84 (3H, s, OMe), 3.62 (2H, t, *J* 7.3, NCH_2CH_2), 2,45 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 162.9, 159.5, 139.0, 138.9, 133.7 (CH), 129.2 (CH), 127.7 (CH), 123.1, 122.4, 121.9 (CH), 121.7, 111.9 (CH), 91.6 (CH), 55.6 (Me), 55.5 (CH_2), 51.3 (Me), 38.9 (CH_2), 10.9 (Me); *m*/*z* (EI) 387 (M^+, 100%), 328 (15), 246 (14), 245 (39), 232 (18), 214 (29), 187 (14), 186 (18), 77 (23).

Methyl 1-(2-benzylsulfonylethyl)-3,5-dimethylindole-2-carboxylate 11h. A solution of 4-methyl *N*-(2-benzylsulfonylethyl)-aniline **9h** (60 mg, 0.21 mmol), diazo compound **2a** (59 mg, 0.42 mmol) and dirhodium(II) acetate (4 mg) in chloroform (15 ml) was heated at reflux for 2 h. The same reaction can also be performed at room temperature for 6 h. The reaction mixture was then filtered, concentrated *in vacuo* and purified on a silica gel column eluting with ethyl acetate–light petroleum (1 : 3) to give the intermediate **10h** (55 mg, 65%) as a yellow oil. This was then immediately dissolved in dry toluene (10 ml) and Amberlyst® (30 mg) was added and the mixture heated at reflux for 12 h. The reaction mixture was cooled, filtered, concentrated under reduced pressure and purified on a silica gel column eluting with ethyl acetate–light petroleum (1 : 4) to obtain the *title compound* (33 mg, 62%) as a colourless solid, mp 160–162 °C (Found: M^+, 385.1345. $C_{21}H_{23}NO_4S$ requires 385.1348); ν_{max} (KBr)/cm^{-1} 2950, 2925, 1706, 1537, 1429, 1358, 1306, 1250, 1122, 784, 697; δ_H (300 MHz; $CDCl_3$) 7.45–7.22 (8H, m, ArH), 4.89 (2H, t, *J* 7.0, NCH_2), 4.07 (2H, s, CH_2Ph), 3.94 (3H, s, OMe), 3.39 (2H, t, *J* 7.0, NCH_2CH_2), 2.57 (3H, s, Me), 2.47 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 163.3, 136.5, 130.8 (CH), 130.0, 129.2, 129.0 (CH), 128.9 (CH), 128.2 (CH), 127.5, 123.7, 121.9, 120.4 (CH), 109.9 (CH), 60.0 (Me), 51.7 (CH_2), 51.6 (CH_2), 39.0 (CH_2), 21.4 (Me), 10.9 (Me); *m*/*z* (EI) 385 (M^+, 28%), 326 (7), 229 (28), 207 (73), 198 (27), 178 (30), 142 (15), 115 (35), 91 (100).

Methyl 1-(2-benzylsulfonylethyl)-5-methoxy-3-methylindole-2-carboxylate 11i. A solution of 4-methoxy-*N*-(2-benzylsulfonylethyl)aniline **9i** (133 mg, 0.44 mmol) and diazo compound **2a** (124 mg, 0.87 mmol) and dirhodium(II) acetate (10 mg) in chloroform (10 ml) was heated at reflux for 1.5 h. The reaction was then concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 3) to give the intermediate **10i** (181 mg, 98%) as a pale yellow oil.

This was dissolved in toluene (5 ml), Amberlyst® (110 mg) added and the mixture heated at reflux overnight. The reaction mixture was filtered, the filtrate concentrated *in vacuo* and then purified on silica eluting with ethyl acetate–light petroleum (1 : 3) and recrystallised (dichloromethane–hexane) to give the *title compound* (66 mg, 37%) as a colourless solid, mp 159–161 °C (Found: M^+, 401.1298. $C_{21}H_{23}NO_5S$ requires 401.1297); ν_{max} (KBr)/cm^{-1} 3853, 3750, 2949, 1700, 1436, 1218, 1120, 667; δ_H (300 MHz; $CDCl_3$) 7.41 (1H, d, *J* 9.0, H-7), 7.36 (3H, m, PhH), 7.24 (2H, m, PhH), 7.09 (1H, dd, *J* 9.0, 2.4, H-6), 7.03 (1H, d, *J* 2.4, H-4), 4.89 (2H, t, *J* 6.9, NCH_2), 4.05 (2H, s, CH_2), 3.94 (3H, s, OMe), 3.88 (3H, s, OMe), 3.39 (2H, t, *J* 6.9, NCH_2CH_2), 2.57 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 163.2, 154.7, 133.4, 130.8 (CH), 129.0 (CH), 128.9 (CH), 127.5, 127.4, 124.0, 121.7, 117.7 (CH), 111.2 (CH), 111.2 (CH), 101.2 (CH), 60.1 (CH_2), 55.8 (Me), 51.8 (CH_2), 51.6 (Me), 51.6 (Me), 39.2 (CH_2), 11.0 (Me); *m*/*z* (EI) 401 (M^+, 100%), 245 (57), 232 (30), 219 (13), 215 (9), 214 (48), 199 (7), 188 (16), 173 (8), 160 (8), 145 (13), 144 (12).

Methyl 3,7-dimethyl-1-(2-benzylsulfonylethyl)indole-2-carboxylate 11j. A solution of 2-methyl *N*-(2-benzylsulfonylethyl)-aniline **9j** (100 mg, 0.35 mmol), diazo compound **2a** (98 mg, 0.7 mmol) and dirhodium(II) acetate (6 mg) in chloroform (15 ml) was heated at reflux for 2 h. The same reaction can also be performed at room temperature for 6 h. The reaction mixture was then filtered, concentrated *in vacuo* and purified on a silica gel column eluting with ethyl acetate–light petroleum (1 : 3) to give the intermediate **10j** (84 mg, 60%) as a yellow oil.

This was then immediately dissolved in dry toluene (15 ml) and Amberlyst® (50 mg) was added and the mixture heated at reflux for 12 h. The reaction mixture was cooled, filtered, concentrated under reduced pressure and purified on a silica gel column eluting with ethyl acetate–light petroleum (1 : 4) to obtain the *title compound* (62 mg, 78%) as a colourless solid, mp 180–181 °C (Found: M^+, 385.1351. $C_{21}H_{23}NO_4S$ requires 385.1348); ν_{max} (KBr)/cm^{-1} 2945, 2920, 1706, 1455, 1450, 1301, 1224, 1107, 784, 743, 692, 523; δ_H (300 MHz; $CDCl_3$) 7.53–7.50 (1H, m, ArH), 7.39–7.37 (5H, m, PhH), 7.09–7.05 (2H, m, ArH), 5.17 (2H, t, *J* 7.7, NCH_2), 4.22 (2H, s, CH_2Ph), 3.95 (3H, s, OMe), 3.37 (2H, t, *J* 7.7, NCH_2CH_2), 2.72 (3H, s, Me), 2.54 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 163.3, 137.2, 130.9 (CH), 130.6, 129.5 (CH), 129.1 (CH), 129.0 (CH), 127.4, 124.6, 123.2, 121.5, 120.6 (CH), 119.1 (CH), 60.1 (Me), 52.8 (CH_2), 51.7 (CH_2), 39.7 (CH_2), 20.6 (Me), 11.0 (Me); *m*/*z* (EI) 385 (M^+, 27%), 354 (100), 232 (16), 204 (43), 200 (14), 183 (16), 172 (25).

Deprotection of 1-(2-ethoxycarbonylethyl)-, (2-phenylsulfonylethyl)- and (2-benzylsulfonylethyl)-indoles 11

Methyl 3,5-dimethylindole-2-carboxylate 12a. *(a) From methyl 1-(2-ethoxycarbonylethyl)-3,5-dimethylindole-2-carboxylate* ***8a***. Potassium *tert*-butoxide (55 mg, 0.49 mmol) was added to a stirred solution of indole **8a** (50 mg, 0.16 mmol) in DMF (5 ml) at room temperature under N_2 and the mixture stirred at this temperature overnight. Hydrochloric acid (1 M; 15 ml) was then added and the aqueous layer extracted with ethyl acetate (3 × 20 ml). The combined organic layers were then washed with hydrochloric acid (1 M; 2 × 20 ml), water (20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was then purified on silica eluting with ethyl acetate–light petroleum (1 : 11.5) to give the *title compound* (20 mg, 60%) as a colourless solid, mp 122–123 °C (Found: MH^+, 204.1021. $C_{12}H_{13}NO_2$ + H requires 204.1024); ν_{max} (KBr)/cm^{-1} 3431, 3319, 1683, 1469, 1263, 800, 779; δ_H (300 MHz; $CDCl_3$) 8.58 (1H, br s, NH), 7.44 (1H, m, H-4), 7.27 (1H, d, *J* 8.5, H-7), 7.16 (1H, dd, *J* 8.5, 1.7, H-6), 3.95 (3H, s, OMe), 2.59 (3H, s, Me), 2.47 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 163.1, 134.3, 129.2, 128.7, 127.6 (CH), 123.3, 120.1 (CH), 119.9, 111.3 (CH), 51.7 (Me), 21.5 (Me), 9.9 (Me); *m*/*z* (EI) 203 (M^+, 55), 171 (100), 143 (31), 142 (42), 115 (25).

(b) From methyl 3,5-dimethyl-1-(2-phenylsulfonylethyl)-indole-2-carboxylate ***11a***. (i) A solution of methyl 3,5-dimethyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate **11a** (80 mg, 0.22 mmol) and potassium *tert*-butoxide (73 mg, 0.65 mmol) in DMF (5 ml) was stirred for 17 h at room temperature. Work-up as above gave the *title compound* (39 mg, 87%) as a colourless solid.

(ii) To a stirred solution of methyl 3,5-dimethyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate **11a** (50 mg, 0.13 mmol) and triethylamine (0.19 ml, 1.35 mmol) in DMF (1 ml) was added DBN (0.10 ml, 0.77 mmol) and the resulting mixture was then heated at reflux for 2 h. The reaction mixture was then cooled and diluted with ether (20 ml), washed with water

(2 × 20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (9 : 1) to give the *title compound* (15 mg, 59%) as a colourless solid.

(iii) To a stirred solution of methyl 3,5-dimethyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate **11a** (50 mg, 0.13 mmol) and triethylamine (0.19 ml, 1.35 mmol) in DMF (3 ml) was added DBU (0.12 ml, 0.81 mmol) and the mixture heated at reflux for 2 h. The reaction mixture was then cooled, diluted with ether (20 ml), washed with water (2 × 30 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (11 mg, 42%) as a colourless solid.

*(c) From methyl 1-(2-benzylsulfonylethyl)-3,5-dimethylindole-2-carboxylate **11h**.* A solution of indole **11h** (70 mg, 0.18 mmol) and potassium *tert*-butoxide (41 mg, 0.36 mmol) in dry DMF (15 ml) was stirred for 15 min at room temperature. The reaction mixture was carefully acidified using dilute HCl (pH 5) and diluted with water (35 ml). The aqueous layer was extracted with ethyl acetate (3 × 15 ml). The combined organic layers were then washed with water, brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was then purified on silica gel column eluting with ethyl acetate–light petroleum (1 : 4) to obtain (i) the *title compound* (26 mg, 70%) as a colourless solid, and (ii) pyrrolo[1,2-*a*]indol-1-one **13a** (6 mg, 9%) as a colourless solid, mp 165–167 °C (data given below).

Methyl 5-methoxy-3-methylindole-2-carboxylate 12b. *(a) From methyl 1-(2-ethoxycarbonylethyl)-5-methoxy-3-methylindole-2-carboxylate **8b**.* A solution of indole **8b** (0.065 g, 0.20 mmol) and potassium *tert*-butoxide (0.68 g, 0.60 mmol) in DMF (5 ml) was stirred overnight. Hydrochloric acid (1 M; 15 ml) was added and the mixture extracted with ethyl acetate. The organic layer was washed twice with hydrochloric acid (1 M) and then with water. The organic layer was separated, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (dichloromethane–light petroleum) to yield the *title compound* as a colourless solid (0.34 g, 77%), mp 151–153 °C (lit.,[57] mp 156 °C) (Found: C, 65.2; H, 6.0; N, 6.0. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4%); ν_{max} (KBr)/cm^{-1} 3342, 2993, 2960, 2933, 1670, 1631; δ_H (300 MHz; $CDCl_3$) 8.56 (1H, br s, NH), 7.26 (1H, m, ArH), 7.00 (2H, m, ArH), 3.94 (3H, s, OMe), 3.88 (3H, s, OMe), 2.58 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.0, 154.3, 131.3, 128.7, 123.7, 119.7, 117.2 (CH), 122.6 (CH), 101.0 (CH), 55.8 (Me), 51.6 (Me), 10.0 (Me); *m*/*z* (EI) 219 (M^+, 15%), 188 (9), 187 (53), 172 (23), 144 (23), 89 (100).

*(b) From methyl 1-(2-benzylsulfonylethyl)-5-methoxy-3-methylindole-2-carboxylate **11i**.* A solution of methyl 1-(2-benzylsulfonylethyl)-5-methoxy-3-methylindole-2-carboxylate **11i** (30 mg, 0.07 mmol) and potassium *tert*-butoxide (25 mg, 0.22 mmol) in DMF (5 ml) was stirred at room temperature overnight under nitrogen. HCl (1 M; 5 ml) was then added and the aqueous layer extracted with ethyl acetate (3 × 15 ml). The combined organic layers were then washed with HCl (1 M; 2 × 20 ml), water (20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (15 mg, 91%) as a colourless solid.

Methyl 3-ethyl-5-methylindole-2-carboxylate 12c. A stirred solution of methyl 3-ethyl-5-methyl-1-(2-phenylsulfonylethyl)-indole-2-carboxylate **11b** (100 mg, 0.26 mmol) and DBN (0.3 ml, 2.59 mmol) in DMF (5 ml) was heated at reflux for 2 h. The reaction mixture was then diluted with ether (20 ml), washed with water (2 × 40 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the title compound (15 mg, 27%) as a colourless solid, mp 109–112 °C; ν_{max} (KBr)/cm^{-1} 3326, 2966, 2952, 1700, 1677, 1652, 1558, 1540, 1251, 667; δ_H (400 MHz; $CDCl_3$) 8.56 (1H, br s, NH), 7.47 (1H, br s, H-4), 7.27 (1H, d, *J* 8.4, H-7), 7.16 (1H, dd, *J* 8.4, 1.5, H-6), 3.95 (3H, s, OMe), 3.10 (2H, q, *J* 7.4, CH_2Me), 2.46 (3H, s, Me), 1.28 (3H, t, *J* 7.4, CH_2Me); δ_C (100 MHz; $CDCl_3$) 162.8, 134.3, 129.2, 127.7, 127.5 (CH), 126.6, 122.4, 120.0 (CH), 111.4 (CH), 51.6 (Me), 21.5 (Me), 18.0 (CH_2), 15.4 (Me). This compound could not be obtained completely pure.

Methyl 7-methoxy-3-methylindole-2-carboxylate 12d. Potassium *tert*-butoxide (44 mg, 0.39 mmol) was added to a stirred solution of indole **11e** (51 mg, 0.13 mmol) in DMF (5 ml) at room temperature under N_2 and the mixture stirred at this temperature overnight. Hydrochloric acid (1 M; 15 ml) was then added and the aqueous layer extracted with ethyl acetate (3 × 30 ml). The combined organic layers were then washed with hydrochloric acid (1 M; 2 × 20 ml), water (30 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was then purified on silica eluting with ethyl acetate–light petroleum (1 : 5) to give the *title compound* (31 mg, 55%) as a colourless solid: mp 143–144 °C (lit.,[57] mp 144–145 °C) (Found: MH^+, 220.0978. $C_{12}H_{13}NO_3$ + H requires 220.0974); δ_H (300 MHz; $CDCl_3$) 8.86 (1H, br s, NH), 7.26 (1H, d, *J* 8.2, H-6), 7.07 (1H, dd, *J* 8.2, 7.4, H-5), 6.74 (1H, d, *J* 7.4, H-4), 3.97 (3H, s, OMe), 3.95 (3H, s, OMe), 2.61 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 160.2, 147.3, 136.9, 135.8, 127.0, 120.7, 120.4 (CH), 113.1 (CH), 104.4 (CH), 55.4 (Me), 51.6 (Me), 10.2 (Me); *m*/*z* (EI) 219 (M^+, 16%), 158 (21), 100 (35), 98 (62), 52 (100).

Methyl 6-methoxy-3-methylindole-2-carboxylate 12e. To a stirred solution of methyl 6-methoxy-3-methyl-1-(2-phenylsulfonylethyl)indole-2-carboxylate **11g**[2] (30 mg, 0.08 mmol) in DMF (5 ml) at room temperature under nitrogen, was added potassium *tert*-butoxide (26 mg, 0.23 mmol) and stirring was continued overnight. HCl (1 M; 15 ml) was then added and the aqueous layer extracted with ethyl acetate (3 × 30 ml). The organic extracts were then combined, washed with HCl (1 M; 2 × 20 ml), water (30 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 4) to give the *title compound* (6 mg, 34%) as a colourless solid, mp 146–148 °C (Found: M^+, 219.0890. $C_{12}H_{13}NO_3$ requires 219.0895); ν_{max} (KBr)/cm^{-1} 3430 (br), 3336, 1674, 1540, 1471, 1257, 1216, 667; δ_H (300 MHz; $CDCl_3$) 8.56 (1H, br s, NH), 7.53 (1H, d, *J* 9.3, ArH), 6.81 (2H, m, ArH), 3.94 (3H, s, OMe), 3.87 (3H, s, OMe), 2.58 (3H, s, Me); δ_C (75 MHz; $CDCl_3$) 154.2, 148.9, 119.7(C), 117.2 (CH), 112.6 (CH), 100.9 (CH), 55.7 (Me), 51.6 (Me), 9.9 (Me); 3 C unobserved; *m*/*z* (ES) 219 (M^+, 100%), 60 (3).

Methyl 3,7-dimethylindole-2-carboxylate 12f. A solution of indole carboxylate **11j** (50 mg, 0.13 mmol) and potassium *tert*-butoxide (30 mg, 0.27 mmol) in dry DMF (8 ml) was stirred for 15 min at room temperature. Work-up as above gave *the title compound* (15 mg, 58%) as a colourless solid, mp 117–118 °C (Found: M^+ 203.0954. $C_{12}H_{13}NO_2$ requires 203.0946); ν_{max} (KBr)/cm^{-1} 3360, 2925, 1680, 1547, 1460, 1373, 1317, 1240, 1209, 784, 743, 615; δ_H (300 MHz; $CDCl_3$) 8.62 (1H, br, NH), 7.53 (1H, d, *J* 7.7, ArH), 7.14–7.05 (2H, m, ArH), 3.97 (3H, s, OMe), 2.62 (3H, s, Me), 2.51 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.2, 135.7, 128.1, 125.9 (CH), 123.0, 121.0, 120.9, 120.2 (CH), 118.4 (CH), 51.7 (Me), 16.6 (Me), 10.1 (Me); *m*/*z* (EI) 203 (M^+, 64%), 171 (100), 143 (46), 115 (35), and (ii) and pyrrolo-[1,2-*a*]indol-1-one **13b** (5 mg, 11%) as a colourless solid, mp 195–196 °C (data given below).

7,9-Dimethyl-2-benzylsulfonyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]-indol-1-one 13a. A solution of methyl 3,5-dimethyl-1-(2-benzylsulfonylethyl)indole-2-carboxylate **11h** (30 mg, 0.08 mmol) and potassium *tert*-butoxide (20 mg, 0.18 mmol) in freshly prepared dry THF (10 ml) was stirred for 20 min at

room temperature. The solvent was concentrated under reduced pressure and the residue was taken in water and carefully acidified (pH 5) using dilute HCl. The aqueous acidic solution was extracted with ethyl acetate (3 × 15 ml). The combined organic layers were washed with water, brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then purified on silica gel column eluting with ethyl acetate–light petroleum (1 : 4) to obtain the *title compound* (25 mg, 91%) as a colourless solid, mp 165–167 °C (Found: C, 67.8; H, 5.3; N, 3.8. $C_{20}H_{19}NO_3S$ requires C, 68.0; H, 5.4; N, 4.0); ν_{max} (KBr)/cm^{-1} 2925, 2848, 1696, 1573, 1301, 1132, 794, 697, 651, 518; δ_H (400 MHz; $CDCl_3$) 7.66–7.63 (2H, m, ArH), 7.47 (1H, d, *J* 8.5, H-5 or H-6), 7.43–7.42 (3H, m, ArH), 7.23–7.22 (2H, m, ArH), 5.05 (1H, d, *J* 14.1, C*H*HPh), 4.82 (1H, m, H-2), 4.52–4.41 (3H, m, H-3, including 1H, d, *J* 14.1, CH*H*Ph), 2.58 (3H, s, Me), 2.46 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 182.4, 134.5, 132.7, 131.4 (CH), 131.1, 130.9, 129.3 (CH), 129.2 (CH), 129.1 (CH), 127.6, 121.5 (CH), 115.8, 110.3 (CH), 65.8 (CH), 58.3 (CH_2), 38.9 (CH_2), 21.6 (Me), 9.0 (Me); *m*/*z* (EI) 353 (M^+, 57%), 198 (100), 170 (14), 154 (16), 142 (20), 115 (16), 91 (46).

5,9-Dimethyl-2-benzylsulfonyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]-indol-1-one 13b. A solution of methyl 3,7-dimethyl-1-(2-benzylsulfonylethyl)indole-2-carboxylate **11j** (50 mg, 0.08 mmol) and potassium *tert*-butoxide (30 mg, 0.27 mmol) in freshly prepared dry THF (10 ml) was stirred for 15 min at room temperature. Work-up as above gave *the title compound* (40 mg, 87%) as a colourless solid, mp 195–196 °C (Found: C, 67.8; H, 5.4; N, 3.9. $C_{20}H_{19}NO_3S$ requires C, 68.0; H, 5.4; N, 4.0); ν_{max} (KBr)/cm^{-1} 2914, 1701, 1562, 1342, 1317, 1291, 1153, 779; δ_H (400 MHz; $CDCl_3$) 7.65–7.63 (2H, m, ArH), 7.52 (1H, d, *J* 8.1, H-6 or H-8), 7.43–7.42 (3H, m, ArH), 7.09–7.03 (2H, m, ArH), 5.10 (1H, m), 5.05 (1H, d, *J* 14.0, C*H*HPh), 4.76 (1H, m), 4.48–4.43 (2H, m, including 1H, d, *J* 14.0, CH*H*Ph), 2.64 (3H, s, Me), 2.59 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 182.4, 136.0, 132.7, 131.3 (CH), 129.3 (CH), 129.2 (CH), 127.9 (CH), 127.6, 122.3, 121.5 (CH), 120.1 (CH), 116.7, 65.7 (CH), 58.3 (CH_2), 41.5 (CH_2), 17.9 (Me), 9.0 (Me); 1 C not observed; *m*/*z* (EI) 353 (M^+, 68%), 198 (100), 170 (17), 154 (14), 142 (18), 115 (22), 91 (55).

Protection and deprotection of indoles 14

5-Methoxy-(2-phenylsulfonylethyl)indole 15a. A solution of 5-methoxyindole **14a** (100 mg, 68 mmol) in dry DMF (1.0 ml) was added to a stirred solution of NaH (60% in oil, 30 mg, 1.23 mmol) in dry DMF (3 ml) at room temperature under a nitrogen atmosphere. When gas evolution had stopped, 2-phenylsulfonylethyl chloride (278 mg, 1.36 mmol) in dry DMF (2 ml) was added and stirring continued overnight. The reaction mixture was then diluted with ether (50 ml), washed with water (2 × 50 ml) and concentrated *in vacuo*. Ethyl acetate was then added to the residue, the mixture filtered and the filtrate concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 6) to give the *title compound* (157 mg, 73%) as a brown oil (Found: MH^+, 316.1011. $C_{17}H_{17}NO_3S$ + H requires 316.1007); ν_{max} (KBr)/cm^{-1} 3412, 2935, 2832, 1487, 1446, 1307, 1240, 1147, 728; δ_H (300 MHz; $CDCl_3$) 7.85 (2H, m, PhH), 7.64 (1H, m, PhH), 7.52 (2H, m, PhH), 7.05 (2H, m, ArH), 6.96 (1H, d, *J* 3.0, ArH), 6.85 (1H, dd, *J* 8.8, 2.7, H-6), 6.35 (1H, d, *J* 3.0, ArH), 4.53 (2H, t, *J* 7.4, NCH_2), 3.83 (3H, s, OMe), 3.53 (2H, t, *J* 7.4, NCH_2CH_2); δ_C (75 MHz; $CDCl_3$) 154.4, 138.8, 134.1 (CH), 130.6, 129.5 (CH), 129.3, 127.9 (CH), 127.7 (CH), 112.3 (CH), 109.4 (CH), 103.0 (CH), 102.2 (CH), 55.9 (Me), 55.5 (CH_2), 40.0 (CH_2); *m*/*z* (EI) 315 (M^+, 52%), 173 (100), 158 (46), 129 (45), 117 (26), 102 (57), 77 (43), 51 (30).

Ethyl 1-(2-phenylsulfonylethyl)indole-2-carboxylate 15b. A solution of ethyl indole-2-carboxylate **14b** (210 mg, 1.1 mmol) in dry DMF (4 ml) was added slowly to a stirred solution of NaH (60% in oil, 37 mg, 0.92 mmol) in DMF (5 ml) under a nitrogen atmosphere. After 10 min 2-phenylsulfonylethyl chloride (189 mg, 0.92 mmol) in DMF (5 ml) was added and the reaction mixture stirred at room temperature overnight. Ether (10 ml) was then added and the reaction mixture washed with water (2 × 50 ml). The combined aqueous layer was then extracted with ether (2 × 50 ml) and ethyl acetate (2 × 40 ml). The combined organic layers were then washed with brine (50 ml), dried ($MgSO_4$), concentrated *in vacuo* and purified on silica eluting with ethyl acetate–light petroleum (1 : 7) to give the *title compound* (219 mg, 67%) as a pale yellow solid, mp 109–111 °C (Found: $[M + NH_4]^+$, 375.1380. $C_{19}H_{19}NO_4S$ + NH_4 requires 375.1379); ν_{max} (KBr)/cm^{-1} 3431(b), 3049, 1701, 1448, 1308, 1147, 1085, 744, 702; δ_H (400 MHz; $CDCl_3$) 7.90 (2H, m, PhH), 7.64 (2H, m, PhH and ArH), 7.54 (2H, m, PhH), 7.36 (2H, m, ArH), 7.24 (1H, s, H-3), 7.17 (1H, m, ArH), 4.93 (2H, t, *J* 7.4, NCH_2), 4.33 (2H, q, *J* 7.0, OCH_2Me), 3.66 (2H, t, *J* 7.4, NCH_2CH_2), 1.39 (3H, t, *J* 7.1, OCH_2Me); δ_C (100 MHz; $CDCl_3$) 161.7, 138.9, 138.6, 133.8 (CH), 129.3 (CH), 127.7 (CH), 127.0, 126.0, 125.6 (CH), 122.7 (CH), 121.2 (CH), 111.5 (CH), 110.0 (CH), 60.8 (CH_2), 55.5 (CH_2), 38.5 (CH_2), 14.3 (Me); *m*/*z* (CI) 375 (M + NH_4, 4%), 358 (10), 218 (36), 188 (48), 186 (100), 143 (10), 125 (45), 95 (8), 94 (68), 78 (63), 44 (22).

5-Methoxyindole 14a. To a stirred solution of 5-methoxy-1-(2-phenylsulfonylethyl)indole **15a** (106 mg, 0.34 mmol) in DMF (5 ml) at room temperature under nitrogen was added potassium *tert*-butoxide (113 mg, 1.01 mmol), stirring was then continued overnight. Hydrochloric acid (1 M; 30 ml) was then added and the aqueous layer extracted with ethyl acetate (3 × 40 ml). The combined organic layers were then washed with hydrochloric acid (1 M; 2 × 40 ml), water (2 × 100 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 9) to give the title compound (46 mg, 91%) as a colourless solid, mp 54–56 °C, identical with an authentic sample.

Ethyl indole-2-carboxylate 14b. To a stirred solution of ethyl 1-(2-phenylsulfonylethyl)indole-2-carboxylate **15b** (55 mg, 0.15 mmol) in DMF (5 ml) at room temperature, under nitrogen was added potassium *tert*-butoxide (52 mg, 0.46 mmol) and stirring was continued overnight. Hydrochloric acid (1 M; 5 ml) was then added and the aqueous layer washed with ethyl acetate (3 × 15 ml). The combined organic layers were then washed with hydrochloric acid (1 M; 2 × 20 ml), water (20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. This was then purified on silica eluting with ethyl acetate–light petroleum (1 : 7) to give the title compound (28 mg, 100%) as a pale yellow solid, mp 121–123 °C, identical with an authentic sample.

Acknowledgements

We thank the EPSRC and Tripos Receptor Research Ltd for a CASE award (K.E.B.), the Cancer Research Campaign (now Cancer Research UK) for support of our work (E.S.), the Royal Society and the Indian National Science Academy for an international exchange grant (S.M.), and the EPSRC Mass Spectrometry Service at Swansea for mass spectra. We also thank Professor Richard Taylor (University of York) for details of the preparation of benzyl vinyl sulfone.

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