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Addition of a Reformatsky Reagent to *N*-Anthracene-9-sulfonyl and Related Imines: Synthesis of Protected β-Amino Acids

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Abstract: The Reformatsky reagent *tert*-butoxycarbonylmethylzinc bromide adds in high yields to *N*-sulfonylimines, *e.g.* **1a-1d**, derived by condensation of benzaldehyde dimethyl acetal with methanesulfonamide, toluene-4-sulfonamide, 4-(methoxycarbonyl)benzenesulfonamide and sulfamide: the products are protected β-amino acids **2a-2d**. *N*-Deprotection occurs reductively (Na-naphthalene; low yields) for **2b** and **2c** or hydrolytically (refluxing aq. pyridine; 76% yield of amino acid **3a** after acid hydrolysis of the *t*-butyl ester) for the sulfamide derivatives **2d**. Anthracene-9-sulfonamide (**6**) is readily available by sulfonation and chlorination of anthracene, and condenses with aldehydes [RCHO; R = Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-NCC_6H_4, 2-furyl, (*E*)-styryl], *e.g.* in the presence of $TiCl_4/Et_3N$, to yield imines **7a-7f**, which after addition of *tert*-butoxycarbonylmethylzinc bromide give protected amino acids **8a-8f**; however, **8f** cyclizes to the sultam **9** *via* a spontaneous intramolecular Diels-Alder reaction. Reductive cleavage of the *N*-anthracene-9-sulfonyl group is much easier than for traditional *N*-sulfonyl protecting groups, as demonstrated by the deprotection of **8a** and **8c** using aluminium amalgam.

Introduction

The addition of organometallic reagents to imines offers a route to the enantioselective synthesis of β-amino acids, β-lactams and other biologically important compounds, but is much less well explored than the corresponding addition reactions of aldehydes and ketones. The difficulties that have to be overcome stem from the low electrophilicity of unactivated imines, combined with the tendency of imines with α-hydrogen to deprotonate and to form enamines.

N-Arylimines are somewhat more electrophilic than their *N*-alkyl counterparts and react efficiently with such mild carbon nucleophiles as Reformatsky reagents.[1] If the aryl group is 4-methoxyphenyl then it may be cleaved oxidatively, *e.g.* using cerium (IV) ammonium nitrate (CAN), but it should be noted that this process generates highly reactive quinonoid intermediates which sometimes undergo side reactions.[2] Krzyzanowska has reported that $ZnBrCH_2CO_2Et$ adds to *N*-benzylidenediphenylphosphinamide (39 % yield);[3] although removal of the diphenylphosphinyl group was not attempted, it is reasonable to suppose that this would occur readily under acidic conditions.[4]

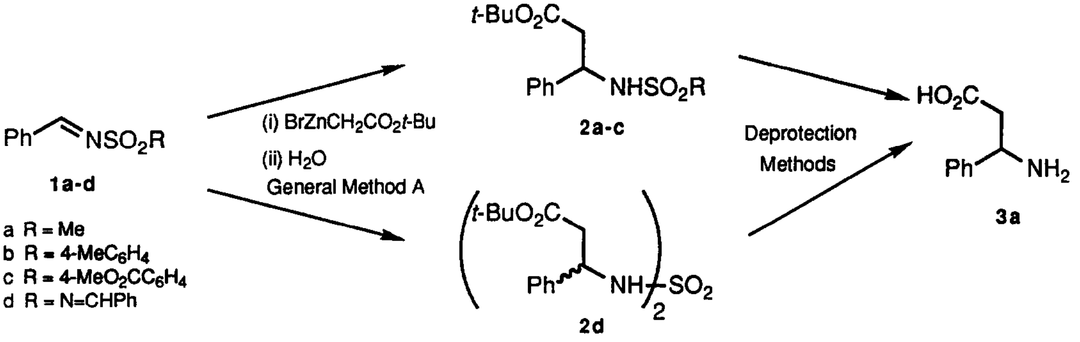
Reformatsky reactions of *N*-sulfonylimines have not previously been reported. However, the reactions of other carbon nucleophiles with such imines have been demonstrated, for example in the addition of the lactam enolate of a pyroglutamic acid derivative to *N*-benzylidenetoluene-4-sulfonamide,[5] in the Lewis acid-mediated reaction between *N*-(toluene-4-sulfonyl)imines and ketene silyl acetals,[6] and in the synthesis of protected α-amino acids by the reaction of *N*-mesitylenesulfonylimines with organolithium reagents.[7] It is notable that in none of the above examples[5-7] do the authors indicate how the *N*-arylsulfonyl activating groups might be removed when no longer required. Harsh conditions are normally needed for such deprotections, *e.g.* reduction with sodium naphthalenide[8] or heating with concentrated HBr.[9]

We now discuss the reaction of $ZnBrCH_2CO_2$*t*-Bu with a range of *N*-sulfonylimines and describe our search for an activating group which may easily be removed when required.

Results and Discussion

Preliminary investigations were conducted using imines derived from benzaldehyde. The sulfonylimines **1a-c** were obtained by heating benzaldehyde dimethyl acetal with methanesulfonamide, 4-toluenesulfonamide and 4-(methoxycarbonyl)benzenesulfonamide respectively, according to the method of Kresze.[10] We also prepared the dibenzylidenesulfamide **1d** which had been reported by Davis[11] to undergo addition of Grignard and organolithium reagents to yield *N,N*-disubstituted sulfamides.

All the above four *N*-benzylidenesulfonamides **1a-d** reacted with $BrZnCH_2CO_2$*t*-Bu (Scheme 1 and Table 1) to give the corresponding protected 3-amino-3-phenylpropanoate esters **2a-d**; in the case of the diimine **1d** the bis addition products **2d** were obtained in 86% yield as an inseparable, *ca* 1:1 mixture of the racemic and *meso-* diastereomers.



Scheme 1. Addition of $BrZnCH_2CO_2$*t*-Bu to benzaldimines other than 7a (which is included in Scheme 2).

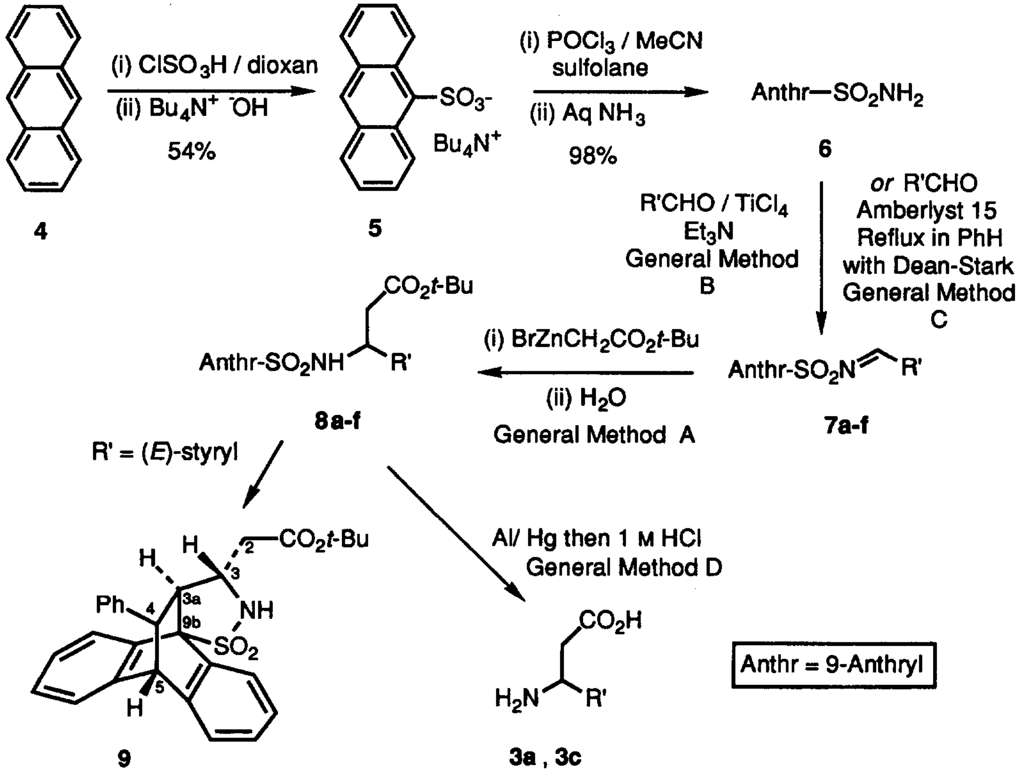
Table 1. Outcome of reactions depicted in Scheme 1.

Entry	Imine	Yield 1 to 2	Deprotection method 2 to 3	Yield 2 to 3
1	**1a**	79	Not attempted	–
2	**1b**	82	TFA then Na/ $C_{10}H_8$	11
3	**1c**	86	TFA then Na/ $C_{10}H_8$	14
4	**1d**	86	Pyridine-H_2O reflux, then 1 M HCl.	76

Since the *N*-methanesulfonyl group was expected to be very resistant to cleavage, deprotection of the derivative **2a** was not attempted. Deprotection of the *tert*-butyl esters of 4-toluenesulfonyl and 4-methoxycarbonylbenzenesulfonyl derivatives **2b** and **2c** by trifluoroacetic acid (TFA), followed by reductive cleavage of the sulfonyl groups using sodium naphthalenide[8] in 1,2-dimethoxyethane (DME), gave only low yields (11 and 14% respectively) of the amino acid **3a**. Deprotection of the diastereoisomeric sulfamide derivatives **2d** to racemic 3-amino-3-phenylacetic acid **3a** was accomplished in 76% yield by refluxing **2d** overnight in pyridine-water (19:1), followed by treatment with trifluoroacetic acid at 20 °C and then ion-exchange chromatography. Attempted deprotection of the sulfamide derivatives **2d** by refluxing overnight with concentrated hydrochloric acid brought about quantitative elimination to give cinnamic acid; a similar acid-induced elimination has been noted previously.[11]

Of the imines **1a-d** thus far examined, **1d** appeared to be the most suitable for our purposes, since deprotection to the β-amino acid **3a** could be achieved efficiently under relatively mild conditions. However, our attempts to extend this method to other diarylidenesulfamides were discontinued when we found that the reaction of sulfamide ($H_2NSO_2NH_2$) with 4-methoxybenzaldehyde or 4-cyanobenzaldehyde (benzene, Amberlyst® 15 acidic ion exchange resin, reflux with Dean-Stark trap) failed to give the corresponding diarylidenesulfamides, but instead stopped after the formation of the highly insoluble monoarylidenesulfamides ($ArCH=NSO_2NH_2$). This difficulty, together with the oily nature of the mixed addition product **2d**, prompted us to examine the reactivity of the novel *N*-(anthracene-9-sulfonyl)imines **7a-f** (Scheme 2 and Table 2).

Anthracene-9-sulfonyl chloride, which has been used to protect the side chain of arginine,[12] has previously been prepared in 34% overall yield by sulfonation of anthracene (SO_3, dioxan) to give anthracene-9-sulfonic acid, the sodium salt of which was then refluxed with phosphorus (III) chloride. Morley[13] has shown that anthracene-9-sulfonic acid is formed in the reaction of anthracene with chlorosulfonic acid in dioxan. We modified the latter appproach by precipitating the anthracene-9-sulfonic acid as its tetrabutylammonium salt **5**, which was converted into anthracene-9-sulfonyl chloride by analogy with the general procedure of Fujita[14] ($POCl_3$, sulfolane, acetonitrile) and thence into anthracene-9-sulfonamide (**6**) (53% overall yield from anthracene) using excess aqueous ammonia. Anthracene-9-sulfonamide (**6**) failed to react with benzaldehyde dimethyl acetal, but could be converted in 61% yield into the benzaldimine **7a** upon treatment with benzaldehyde, titanium (IV) chloride and triethylamine, according to the general method of Jennings[15] (General Method B). The analogous reactions of 4-fluorobenzaldehyde, 4-methoxybenzaldehyde, 4-cyanobenzaldehyde, furfural, and cinnamaldehyde gave the imines **7b-f** (26-66%). Since these imines decomposed on attempted chromatography using either silica or alumina, it was necessary to purify them by crystallisation, which may have led to some loss of product. Formation of the imine **7a** was found not to proceed to completion when the stoichiometric ratio of benzaldehyde to the sulfonamide **6** was employed, so 2.0 equivalents of aldehyde (1.3 equivalents in the case of 4-cyanobenzaldehyde, which is a solid) were normally used in these reactions in order to maximise the consumption of the relatively insoluble anthracene-9-sulfonamide (**6**) and thus to facilitate the isolation of the imines. Imines **7a** and **7e** were obtained in 70 and 72 % yields by simply refluxing **6** with the appropriate aldehyde (1 equivalent) and Amberlyst® 15 in benzene whilst removing water using a Dean and Stark trap. All the imines other than **7e**, which is derived from the somewhat acid-labile aldehyde furfural, could therefore be prepared in acceptable yields.



Scheme 2. Addition of $BrZnCH_2CO_2t$-Bu to *N*-anthracene-9-sulfonylimines.

Table 2. Outcome of reactions depicted in Scheme 2.

Entry	Imine	R'	Yield **6** to **7** (Method B)	Yield **6** to **7** (Method C)	Yield **7** to **8**	Yield **8** to **3**
1	**7a**	Ph	61	70	66	63[a]
2	**7b**	4-FC_6H_4	58		75	
3	**7c**	4-$MeOC_6H_4$	63		99	72
4	**7d**	4-NCC_6H_4	26	72	93	
5	**7e**	2-Furyl	29		18	
6	**7f**	(*E*)-Styryl	66		50[b]	

a. Conversion of **8a** to **3a** was also performed using 0.1 M CH_3SO_3H in TFA (40 °C, 7 d; 48% yield).

b. Isolated as **9**, the product of a spontaneous, intramolecular Diels-Alder reaction.

The imines **7a-e** underwent addition of $BrZnCH_2CO_2t$-Bu to give the corresponding protected amino acids **8a-e** (18-99% yields). The cinnamaldimine **7f** appeared to behave similarly, but in this case an intramolecular Diels-Alder reaction ensued to give the sultam **9** with the (3*R**, 3a*R**, 4*R**) relative configuration, as indicated by the ^1H NMR coupling constants ($J_{3,3a}$ = 10.7 Hz, $J_{3a,4}$ = 5.9 Hz) and by the presence of a nuclear Overhauser effect between 3-H and 4-H. Deprotection of the *N*-(anthracene-9-sulfonyl) amino esters **8a** and **8c** was performed by treatment with aluminium amalgam[12] in THF-H_2O followed by dilute hydrochloric acid (63 and 72% yields) to give the known amino acids **3a** and **3c**. *The* N-*anthracene-9-sulfonyl group therefore promises to have considerable synthetic utility, since it may be cleaved reductively under much milder reductive conditions than those required to remove traditional imine-activating groups such as toluene-4-sulfonyl.* However, since the removal of aluminium residues from the amino acids **3a** and **3c** required the use of ion-exchange chromatography, we are seeking other ways to cleave the anthracene-9-sulfonyl group. Deprotection of the sulfonamido ester **8a** to give the amino acid **3a** was performed in a single step by prolonged warming with 0.14 M methanesulfonic acid in TFA (48% yield).

Conclusion

The anthracene-9-sulfonyl group appears to be a useful activating group for imines and may easily be removed under mildly reductive conditions, complementary to those required to effect the oxidative cleavage of the 4-methoxyphenyl group. A further advantage is that since derivatives of anthracene-9-sulfonamide are often yellow or orange in colour and highly crystalline, they are easy to purify.

EXPERIMENTAL

Materials and General Procedures

The following starting materials were prepared by literature methods: *N*-(benzylidene)methanesulfonamide (**1a**),[10] *N*-(benzylidene)toluene-4-sulfonamide (**1b**),[10] and $(PhCH{=}N)_2SO_2$ (**1d**).[11] 4-(Methoxycarbonyl)benzenesulfonamide was prepared in 27% yield by treating a suspension of 4-carboxybenzenesulfonamide in dry methanol with thionyl chloride, then refluxing for 24 h and recrystallising from MeOH-H_2O; it had a mp in agreement with the literature value[16] Zinc-copper couple was prepared according to Schank and Shechter.[17] Methanol was distilled from magnesium methoxide. 'Petrol' refers to the light petroleum fraction bp 40-60 °C and was redistilled. THF and 1,2-dimethoxyethane (DME) were dried by distillation from sodium and benzophenone. All mass spectra were recorded in electron impact mode.

N-*(Benzylidene)-4-(methoxycarbonyl)benzenesulfonamide (1c)*. 4-(Methoxycarbonyl)benzenesulfonamide (3.23 g, 15 mmol) and benzaldehyde dimethyl acetal (3.75 mL, 3.81 g, 25 mmol) were heated together in a small still using a bunsen burner until distillation of methanol was complete (approx 10 min). The residue was extracted with a mixture of CH_2Cl_2 and petrol, and filtered to remove unreacted 4-(methoxycarbonyl)benzenesulfonamide. The solvents were evaporated and the residue was recrystallised from EtOAc-petrol to yield the *title compound* **1c** (3.35 g, 84 %) as white crystals, mp 133-135 °C. (Found: C, 59.4; H, 4.25; N, 4.5. $C_{15}H_{13}NO_4S$ requires C, 59.4; H, 4.3; N, 4.6 %); IR (KBr): ν = 1721 , 1571 , 1330 and 1158 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 3.97 (s, 3 H, CO_2Me), 7.42-7.56 (m, 2 H, *m*-Ph), 7.60-7.78 (m, 1 H, *p*-Ph), 7.92-7.98 (m, 2 H, *o*-Ph), 8.05-8.23 (AA'BB', 4 H, Ar-H_4), 9.10 (s, 1 H, CH=N); MS: *m/z* (%) = 303 (M^+, 36), 272 (8), 239 (11), 135 (100); HRMS: found 303.0589 (calc for $C_{15}H_{13}NO_4S$ 303.0565).

Addition of t-BuO_2CCH_2ZnBr to N-(Benzylidene)methanesulfonamide (1a). Example of General Method A. To Zn-Cu couple[17] (95% Zn; 111 mg, 1.6 mmol Zn) in hot anhydrous THF (1 mL) was added a solution of *t*-BuO_2CCH_2ZnBr (0.258 mL, 3 mmol) in THF (3 mL) over 5 min. The mixture was refluxed for

1 h, then a solution of the imine **1a** (147 mg, 0.8 mmol) in THF (3 mL) was added and refluxing was continued for 36 h. The mixture was then cooled, added to saturated aqueous $NaHCO_3$ (10 mL) and extracted into Et_2O (3 x 30 mL). Drying ($MgSO_4$) and evaporation of the Et_2O layer, then recrystallisation from CH_2Cl_2-petrol gave tert-*butyl 3-methanesulfonamido-3-phenylpropanoate* (**2a**) (190 mg, 79 %) as white crystals, m.p. 91-92 °C. (Found: C, 56.3; H, 7.4; N, 4.5. $C_{14}H_{21}NO_4S$ requires C, 56.2; H, 7.1; N, 4.7 %); IR: (KBr): ν = 3243, 1702 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, *t*-Bu), 2.67 (s, 3 H, Me), 2.77 (d, 2 H, *J* = 6 Hz, CH_2), 4.87 ('q', 1 H, *J* = 6 Hz, PhC*H*), 5.67 (d, 1 H, *J* = 7.5 Hz, NH), 7.27-7.45 (m, 5 H, Ph); MS: *m/z* (%) = 284 (M^+-Me, 0.2) 242 (0.1), 226 (5), 220 (17), 184 (100), 164 (67); HRMS: found 284.0944 [calc for $C_{13}H_{18}NO_4S$ (M^+-CH_3) 284.0957].

tert-*Butyl 3-(4-toluenesulfonamido)-3-phenylpropanoate (2b).* Imine **1b** (0.83 g, 3.2 mmol) was subjected to General Method A to yield the *title compound 2b* (0.99 g, 82 %) as white crystals, m.p. 110.5-112 °C (CH_2Cl_2-petrol). (Found: C, 63.9; H, 6.8; N, 3.6. $C_{20}H_{25}NO_4S$ requires C, 64.0; H, 6.7; N, 3.7 %); IR (KBr): ν = 3189, 1700 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (s, 9 H, *t*-Bu), 2.36 (s, 3 H, Me), 2.62 (dd, 1 H, *J* = 16, 7 Hz, 1/2 x CH_2), 2.74 (dd, 1 H, *J* = 16, 7 Hz, 1/2 x CH_2), 4.69 ('q', 1 H, *J* = 7 Hz, PhC*H*), 5.82 (d, 1 H, *J* = 8 Hz, NH), 7.07-7.19 (m, 7 H), 7.57-7.62 (m, 2 H); MS: *m/z (%)* = 318 (M^+-C_4H_9, 3), 302 (4), 260 (100), 220 (44), 164 (96), 155 (43); HRMS: found 318.0787 [calc for $C_{16}H_{16}NO_4S$ (M^+-C_4H_9) 318.0800].

tert-*Butyl 3-[4-(methoxycarbonyl)phenylsulfonamido]-3-phenylpropanoate (2c).* Imine **1c** (1.52 g, 5.0 mmol) was subjected to General Method A to yield the *title compound 2c* (1.80 g, 86 %) as white crystals, mp 141-142 °C ($CHCl_3$-petrol). (Found: C, 59.9; H, 6.3; N, 3.3. $C_{21}H_{25}NO_6S$ requires C, 60.1; H, 6.0; N, 3.3 %); IR (KBr): ν = 3201, 1731, 1708 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*-Bu), 2.67 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2), 2.72 (dd, 1 H, *J* = 16, 7 Hz, 1/2 x CH_2), 3.94 (s, 3 H, Me), 4.77 (q, 1 H, *J* = 7 Hz, PhC*H*), 6.20 (d, 1 H, *J* = 8 Hz, NH), 7.04-7.16 (m, 5 H, Ph), 7.71 ('d', 2 H, *J* = 7 Hz), 7.96 ('d', 2 H, *J* = 7 Hz); MS: *m/z* (%) = 346 (M^+-C_4H_9O, 2), 304 (85), 220 (36), 164 (100), 135 (36), 104 (30).

*Di-*tert-*butyl 3,3'-diphenyl-3,3'-sulfamyldiaminopropanoate (2d).* Diimine **1d** (272 mg, 1.0 mmol) was subjected to General Method A using $BrCH_2CO_2t$-Bu (4 mmol) and Zn (4 mmol). After the usual work up, purification by flash chromatography [CH_2Cl_2-petrol (1:1 to 1:0 gradient)] gave a *ca* 1:1 mixture of the (±)- and *meso* - forms of the title compound **2d** (436 mg, 86 %) as a colourless oil. IR (KBr): ν = 3280, 1734 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (s, 9 H, *t*-Bu), 1.31 (s, 9 H, *t*-Bu), 2.55 (dd, 1 H, *J* = 15, 6 Hz, 1/2 x CH_2CO), 2.63 (dd, 1 H, *J* = 15, 6 Hz, 1/2 x CH_2CO), 2.71 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2CO), 2.83 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2CO), 4.59-4.72 (m, 2 H, 2 x PhC*H*), 5.30 (d, 1 H, *J* = 7.5 Hz, NH), 5.47 (d, 1 H, *J* = 7.5 Hz, NH), 7.10-7.35 (m, 10 H, 2 x Ph).

3-Amino-3-phenylpropanoic acid (3a). Deprotection of tert-*Butyl 3-(4-toluenesulfonamido)-3-phenylpropanoate (2b) using TFA followed by sodium naphthalenide. tert-*Butyl 3-(4-toluenesulfonamido)-3-phenylpropanoate (**2b**) (380 mg, 1.0 mmol) was dissolved in TFA (1 mL) and stirred at 20 °C for 2 h. The solution was then evaporated and the residue was recrystallised from EtOAc-petrol to yield 3-phenyl-3-

(toluene-4-sulfonamido)propanoic acid (242 mg, 76%) as white crystals, mp 156-157 °C, with the following properties: IR (KBr): ν = 3253, 3180-2370, 1713 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, Me), 2.81 (dd, 1 H, *J* =16, 6 Hz, 1/2 x CH_2), 2.93 (dd, 1 H, *J* =16, 6 Hz, 1/2 x CH_2), 3.5 (br s, 1H, NH), 4.74 ('t', 1 H, *J*=6 Hz, C*H*Ph), 5.76 (br s, 1 H, CO_2H), 7.09-7.21 (m, 7 H, Ar-H_7), 7.60 (d, 2 H, *J*= 8 Hz, Ar-H_2); MS: *m/z* (%) = 319 (M^+, 1), 260 (81), 164 (94), 104 (42), 91 (100); HRMS: found 319.0855 [calc for $C_{16}H_{17}NO_4S$ 319.0878].

A solution of naphthalene (0.64 g, 5.0 mmol) in DME (10 mL) was stirred with Na (115 mg, 5.0 mmol) at 20 °C for 1 h. The resultant emerald green solution of $NaC_{10}H_8$ was gradually added to a solution of 3-phenyl-3-(toluene-4-sulfonamido)propanoic acid (160 mg, 0.5 mmol) in DME (3 mL) until a permanent reddish purple colour developed. The mixture was then acidified to pH 7 using 50 % aqueous AcOH and the bulk of the DME was evaporated. The residue was partitioned between Et_2O (20 mL) and H_2O (20 mL). The aqueous layer was washed with a further portion of Et_2O (25 mL), then the aqueous phase was concentrated and subjected to ion-exchange chromatography on a column of Dowex® 50x2-100 (H^+ form), eluting first with H_2O and then with 1 M aqueous NH_3. Pooling and evaporation of appropriate fractions gave 3-amino-3-phenylpropanoic acid (**3a**) (12 mg, 11 % from **2b**) as a white solid, mp 220-227 °C (decomp) [lit.[18] 216 °C, lit.[19] 222 °C (decomp)]. IR (KBr): ν = 2612, 2205, 1625, 1580 cm^{-1}; ^{1}H NMR (250 MHz, D_2O): δ = 2.88 (dd, 1 H, *J* = 16, 7 Hz, 1/2 x CH_2), 2.98 (dd, 1 H, *J* = 16, 8 Hz, 1/2 x CH_2), 4.69-4.85 (m, C*H*Ph and HOD), 7.48-7.61 (m, 5 H, Ph).

3-Amino-3-phenylpropanoic acid (3a). Deprotection of tert*-Butyl 3-(4-methoxycarbonylphenylsulfonamido)-3-phenylpropanoate (2c) using TFA followed by sodium naphthalenide:* A solution of *tert*-butyl 3-[4-(methoxycarbonyl)phenylsulfonamido]-3-phenylpropanoate (**2c**) (0.63 g, 1.5 mmol) in TFA (3 mL) was kept at 20 °C for 2 h. The mixture was then concentrated and the residue was thoroughly desiccated over NaOH pellets. The crude product was dissolved in DME and cooled to 0 °C. To this solution was added a solution of sodium naphthalenide prepared from naphthalene (0.64 g, 5 mmol), sodium (0.115 g, 5 mmol) and DME (10 mL) until a permanent change from colourless to reddish brown was observed. 50% Aqueous AcOH (2 mL) was added and the mixture was concentrated on a rotary evaporator. The residue was extracted with water (25 mL), which was washed with ether (2 x 25 mL). The aqueous layer was then concentrated *in vacuo* and purified by ion-exchange chromatography as in the preceding experiment to give 3-amino-3-phenylpropanoic acid (**3a**) (35 mg, 14 %), with identical properties to the sample described above.

3-Amino-3-phenylpropanoic acid (3a) from tert-Butyl 3,3'-diphenyl-3,3'-sulfamyldiaminopropanoate (2d). A solution of **2d** (75 mg, 0.15 mmol) in pyridine-H_2O (19:1 ; 10 mL) was refluxed for 15 h. The solvents were then evaporated *in vacuo* and the residue was dissolved in 1 M hydrochloric acid (30 mL) and washed with ether (2 x 25 mL). The aqueous layer was concentrated *in vacuo* and then the residue was purified by ion-exchange chromatography as in the preceding experiments. Pooling and evaporation of the appropriate ninhydrin-positive fractions gave 3-amino-3-phenylpropanoic acid (**3a**) (38 mg, 76 %) as a white solid, with identical properties to the samples described above.

Tetrabutylammonium anthracene-9-sulfonate (5). To ice-cooled dry dioxan (200 mL) was added chlorosulfonic acid (13.3 mL, 0.2 mol) at such a rate that the temperature remained below 20 °C. The mixture was cooled to 10 °C and anthracene (27.5 g, 0.15 mol) was added in portions over 5 min with stirring. The mixture was heated to 40 °C for 30 min, cooled, poured into stirred ice-water (300 g), filtered through Celite® to remove the yellow precipitate and brought to pH 9 using 4 M NaOH. Aqueous tetrabutylammonium hydroxide (40 wt%; 97.3 mL, 0.16 mol) was then added and the product was extracted into CH_2Cl_2 (3 x 100 mL). The CH_2Cl_2 phase was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give an orange oil, which was recrystallised from EtOAc-Et_2O to give *tetrabutylammonium anthracene-9-sulfonate* (40.7 g, 54%) as a yellow solid, mp 116-122°C; after further recrystallisations a sample had mp 123-127 °C. (Found: C, 71.6; H, 9.4; N, 2.9. $C_{30}H_{45}NO_3S$ requires C, 72.1; H, 9.1; N, 2.8 %); IR (KBr): ν = 1204 (SO_3^-) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, 12 H, J = 7.5 Hz, 4 x CH_3), 1.09 (sext, 8 H, J = 7.5 Hz, 4 x CH_2), 1.22-1.35 (m, 8 H, 4 x CH_2), 2.86-2.96 (br t, 8 H, 4 x NCH_2), 7.39-7.46 (m, 4 H, Ar 2-, 3-, 6-, 7-H), 7.88 ('d', 2 H, J = 7.5 Hz, 4-, 5-H), 8.38 (s, 1 H, Ar 10-H), 9.80 ('d', 2 H, J = 9 Hz, 1-, 8-H).

Anthracene-9-sulfonamide (6). A solution of tetrabutylammonium anthracene-9-sulfonate (5) (15.0 g, 30 mmol) in CH_3CN (30 mL) and sulfolane (15.2 mL) at 20 °C was treated with $POCl_3$ (11.2 mL, 120 mmol) dropwise over 5 min. The mixture was stirrred vigorously for 10 min and treated with water (150 mL) dropwise at <10 °C. The orange precipitate of crude anthracene-9-sulfonyl chloride was filtered off, washed with water, dried under vacuum and added to a mixture of aqueous NH_3 (d 0.880; 150 mL) and $CHCl_3$ (25 mL), which was stirred vigorously at 0 °C for 1 h and then at 20 °C for 1 h. The mixture was shaken with 2 M NaOH (300 mL) and the $CHCl_3$ phase was discarded. The remaining aqueous and solid phases were washed with further portions of $CHCl_3$ (2 x 100 cm^3), and then acidified with 6 M HCl to give *anthracene-9-sulfonamide* (6) (7.59 g, 98%) as a yellow solid, mp 200.5-202.5 °C. (Found: C, 65.0; H, 4.3; N, 5.35. $C_{14}H_{11}NO_2S$ requires C, 65.35; H, 4.3; N, 5.4 %); UV (MeOH): λ (ε) = 347sh, 364 (7300), 380 (7500 $dm^3mol^{-1}cm^{-1}$), 396 nm sh; IR (KBr): ν = 3409, 3300, 1312, 1144 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2CO$]: δ = 7.0 (br s, 2 H, NH_2), 7.56-7.72 (m, 4 H, 2-, 3-, 6-, 7-H), 8.19 ('d', 2 H, J = 9 Hz, 4-, 5- H), 8.91 (s, 1 H, 10-H), 9.37 ('d', 2 H, J = 9 Hz, 1-, 8-H); MS: m/z (%) = 257 (M^+, 100), 193 (45), 177 (37), 165 (20); HRMS: found 257.0502 [calc for $C_{14}H_{11}NO_2S$ (M^+) 257.0511].

N-*Benzylideneanthracene-9-sulfonamide (7a). Example of the preparation of an* N-*(anthracene-9-sulfonyl)imine by General Method B.* Anthracene-9-sulfonamide (6) (2.32 g, 9.0 mmol) was suspended in a solution of benzaldehyde (1.83 mL, 1.91 g, 18.0 mmol) and Et_3N (7.53 mL, 54 mmol) in CH_2Cl_2 (150 mL) under N_2. The mixture was cooled to 0 °C and $TiCl_4$ (1.47 mL, 13.5 mmol) was added dropwise with stirring. After 1 h the mixture was warmed to 20 °C and after a further 1 h it was filtered through Celite® and washed with saturated aqueous $NaHCO_3$ (3 x 50 mL). The organic phase was dried ($MgSO_4$), filtered, evaporated and the residue recrystallised from $CHCl_3$-petrol to give N-*(benzylidene)anthracenesulfonamide* (7a) (1.88 g 61%) as a bright yellow crystalline solid, mp 157-158.5 °C; IR (KBr): ν = 1573, 1315, 1146 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ = 7.43 (t, 2 H, J = 7.5 Hz, 3'-, 5'-H), 7.52-7.60 (m, 3 H, 3-, 6-, 4'-H), 7.71 (ddd, 2 H, J = 9, 7, 2 Hz, 2-, 7-H), 7.88 ('d', 2 H, J = 7 Hz, 2'-, 6'-H), 8.05 (d, 2 H, J = 8 Hz, 4-, 5-H), 8.74 (s, 1 H, 10-H), 9.18 (s, 1 H, CH=N), 9.45 ('d', 2 H, J = 8 Hz, 1-, 8-H); NMR assignments were supported by a COSY experiment; MS: *m/z* (%) 345 (M^+, 77), 281 (9), 241(2), 177 (100); HRMS: found 345.0848 [calc for $C_{21}H_{15}NO_2S$ (M^+) 345.0823].

N-*Benzylideneanthracene-9-sulfonamide (7a). Example of the preparation of an* N-*(anthracene-9-sulfonyl)imine by General Method C.* Anthracene-9-sulfonamide (**6**) (1.29 g, 5.0 mmol), benzaldehyde (0.508 mL, 5.0 mmol) and Amberlyst® 15 ion-exchange resin (350 mg) were refluxed in benzene (60 mL) for 36 h in an apparatus fitted with a Dean and Stark trap. The mixture was cooled, filtered and the residue was washed with CH_2Cl_2. The filtrate and washings were combined, concentrated and recrystallised to yield the title compound **7a** (1.61 g, 72 %) with physical properties which matched those of **7a** from the preceding preparation.

N-*(4-Fluorobenzylidene)anthracene-9-sulfonamide (7b).* Treatment of 4-fluorobenzaldehyde (1.93 mL, 2.23 g, 18 mmol) according to General Method B yielded the *title compound* **7b** (1.89 g, 58%) as a yellow solid, mp 204-205 °C. IR (KBr): ν = 1582, 1302, 1225, 1144 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 7.06-7.17 (m, 2 H, 3'-, 5'-H), 7.55 (ddd, 2 H, *J* = 11, 8, 1 Hz, 3-, 6-H), 7.70 (ddd, 2 H, *J* = 9, 7, 1.5 Hz, 2-, 7-H), 7.85-7.97 (m, 2 H, 2'-, 6'-H), 8.04-8.09 (m, 2 H, 4-, 5-H), 8.75 (s, 1 H, 10-H), 9.14 (s, 1 H, CH=N), 9.40-9.44 (m, 2 H, 1-, 8-H); MS: *m/z* (%) = 363 (M^+, 27), 299 (M^+-SO_2, 15), 178 (39), 177 (100); HRMS: found 363.0726 [calc for $C_{21}H_{14}FNO_2S$ (M^+) 363.0729].

N-*(4-Methoxybenzylidene)anthracene-9-sulfonamide (7c)*. Treatment of 4-methoxybenzaldehyde (2.45 g, 18 mmol) according to General Method B yielded the *title compound* **7c** (2.03 g, 63 %) as a yellow solid, mp 143-145 °C. IR (KBr): ν = 1588, 1315, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.83 (s, 3 H, Me), 6.87-6.95 (m, 2 H, 3'-, 5'-H), 7.48-8.09 (m, 8 H, Ar), 8.71 (s, 1 H, 10-H), 9.07 (s, 1 H, CH=N), 9.42-9.47 (m, 2 H, 1-, 8-H); MS: *m/z* (%) 311 (M^+- SO_2, 4), 257 (100), 193 (48), 177 (39); HRMS: found 311.1347 [calc for $C_{22}H_{17}NO$ (M^+-SO_2) 311.1310].

N-*(4-Cyanobenzylidene)anthracene-9-sulfonamide (7d) by General Method B.* Treatment of 4-cyanobenzaldehyde (1.56 g, 12 mmol) according to General Method B, but using 9 mmol of anthracene-9-sulfonamide (**6**), gave the *title compound* **7d** (0.47 g, 26 %) as a yellow solid, mp 196.5-198 °C. IR (KBr): ν = 2227, 1557, 1304, 1145 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 7.53-8.11 (m, 10 H, Ar), 8.79 (s, 1 H, 10-H), 9.21 (s, 1 H, CH=N), 9.37-9.42 (m, 2 H, 1-, 8-H); MS: *m/z* (%) 370 (M^+, 22), 257 (11), 193 (35), 177 (100); HRMS: found 370.0794 [calc for $C_{22}H_{14}N_2O_2S$ (M^+) 370.0776].

N-*(4-Cyanobenzylidene)anthracene-9-sulfonamide (7d) by General Method C.* Treatment of 4-cyanobenzaldehyde (0.79 g, 6.0 mmol) by General Method C (64 h reflux) yielded the title imine **7d** (1.61 g, 72 %) with physical properties which matched those of **7d** from the preceding preparation.

N-*(Furyl-2-methylene)anthracene-9-sulfonamide (7e).* Treatment of furan-2-carboxaldehyde (0.57 g, 6.0 mmol) according to General Method B yielded the *title compound* **7e** (0.29 g, 29 %) as a yellow-brown solid, mp 190-192 °C. IR (KBr): ν = 1581, 1314, 1148 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$]: δ = 6.59 (dd, 1 H, *J* = 3, 1.5 Hz, 4'-H), 7.30 (dd, 1 H, *J* = 4, 1 Hz, 3'-H), 7.50-7.74 (m, 5 H, 2-, 4-, 6-, 7-, 5'-H), 8.05 (dt, 2 H, *J* = 9, 1 Hz, 4-, 5-H), 8.74 (s, 1 H, 10-H), 8.98 (s, 1 H, CH=N), 9.40 (dd, 2 H, *J* = 9, 1 Hz, 1-, 8-H); MS: *m/z* (%) = 335 (M^+, 63), 271 (19), 270 (8), 177 (100); HRMS: found 335.0631 [calc for $C_{19}H_{13}NO_3S$ (M^+) 335.0616].

N-*(Cinnamylidene)anthracene-9-sulfonamide (7f)*. Treatment of cinnamaldehyde (2.38 g, 18.0 mmol) according to General Method B yielded the *title compound* **7f** (2.20 g, 66 %) as a bright orange solid, mp 195-197 °C. IR (KBr): ν = 1613, 1578, 1314, 1139 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 6.99 (dd, 1 H, *J* = 16, 9 Hz, C*H*-CH=N), 7.34-7.73 (m, 10 H), 8.06 (dt, 2 H, *J* = 8, 1 Hz, 4-, 5- H), 8.74 (s, 1 H, 10-H), 8.94 (d, 1 H, *J* = 9 Hz, CH=N), 9.36-9.42 (m, 2 H, 1-, 8-H); MS: *m/z* (%) = 371 (M^+, 0.3), 307 (1), 257 (16), 178 (100); HRMS: found 371.0997 [calc for $C_{23}H_{17}NO_2S$ (M^+) 371.0980].

tert-*Butyl 3-(anthracene-9-sulfonamido)-3-phenylpropanoate (8a)*. Treatment of the imine **7a** (1.10 g, 3.2 mmol) according to General Method A yielded the *title compound* **8a** (0.98 g, 66 %) as yellow crystals, mp 138.5-139.5 °C ($CHCl_3$-petrol). (Found: C, 69.9; H, 6.1; N, 3.0. $C_{27}H_{27}NO_4S$ requires C, 70.3; H, 5.9; N, 3.0 %). IR (KBr): ν = 3276, 1703 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (s, 9 H, *t*-Bu), 2.39 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2), 2.55 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2), 4.67 ('q', 1 H, *J* = 6 Hz, CHN), 6.32 (d, 1 H, *J* = 8 Hz, NH), 6.55-6.82 (m, 5 H, Ph), 7.47 ('t', 2 H, *J* = 7 Hz, 3-, 6- H), 7.62 (ddd, 2 H, *J* = 9, 7, 1.5 Hz, 2-, 7- H), 7.93 (d, 2 H, *J* = 8 Hz, 4-, 5- H), 8.49 (s, 1 H, 10-H), 9.23 (d, 2 H, *J* = 9 Hz, 1-, 8- H); MS: *m/z* (%) = 463 (M^++H_2, 5), 389 (1), 346 (12), 242 (3), 220 (1), 178 (100), 164 (35); HRMS: found 463.1792 [calc for $C_{27}H_{29}NO_4S$ (M^++H_2) 463.1817].

tert-*Butyl 3-(anthracene-9-sulfonamido)-3-(4-fluorophenyl)propanoate (8b)*. Treatment of the imine **7b** (1.09 g, 3.0 mmol) according to General Method A, then purification by flash chromatography [CH_2Cl_2-petrol (1:1) to CH_2Cl_2-Et_2O (9:1); gradient elution] followed by recrystallisation from CH_2Cl_2-petrol yielded the *title compound* **8b** (1.08 g, 75 %) as yellow crystals, m.p. 163-164 °C. IR (KBr): ν = 3251, 1703, 1222 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (s, 9 H, *t*-Bu), 2.40 (dd, 1 H, *J* = 16, 6 Hz, 1/2 x CH_2), 2.54 (dd, 1 H, *J* = 16, 6.5 Hz, 1/2 x CH_2), 4.65 ('q', 1 H, *J* = 7 Hz, CHN), 6.22-6.31 (m, 2 H, Ar-H_2), 6.34 (d, 1 H, *J* = 8 Hz, NH), 6.44-6.50 (m, 2 H, Ar-H_2), 7.49 (ddd, 2 H, *J* = 8, 7, 1-Hz, 3-, 6-H), 7.63 (ddd, 2 H, *J* 9, 7, 1.5 Hz, 2-, 7-H), 7.95 (dt, 2 H, *J* = 8, 1 Hz, 4-, 5-H), 8.52 (s, 1 H, 10-H), 9.21 (dd, 2 H, *J* = 9, 1 Hz, 1-, 8-H); MS: *m/z* (%) = 479 (M^+, 45), 423 (18), 364 (8), 257 (28), 182 (29), 178 (100); HRMS: found 479.1566 [calc for $C_{27}H_{26}FNO_4S$ (M^+) 479.1567].

tert-*Butyl 3-(anthracene-9-sulfonamido)-3-(4-methoxyphenyl)propanoate (8c)*. Treatment of the imine **7c** (1.08 g, 2.9 mmol) according to General Method A, then purification by flash chromatography (CH_2Cl_2-petrol 1:1) yielded the *title compound* **8c** (1.41 g, 99 %) as yellow crystals, mp 57.5-59 °C ($CHCl_3$-petrol). IR (KBr): ν = 3254, 1708 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (s, 9 H, *t*-Bu), 2.41 (dd, 1 H, *J* = 15, 6 Hz, 1/2 x CH_2), 2.56 (dd, 1 H, *J* = 15, 6 Hz, 1/2 x CH_2), 3.56 (3 H, s, CH_3), 4.63 ('q', 1 H, *J* = 7 Hz, CHN), 6.04-6.10 (m, 2 H, 3'-, 5'-H), 6.25 (d, 1 H, *J* = 8 Hz, NH), 6.37-6.43 (2 H, m, 2'-, 6'-H), 7.47 (2 H, ddd, *J* = 8, 7, 1-Hz, 3-, 6-H), 7.61 (ddd, 2 H, *J* 9, 7, 1.5 Hz, 2-, 7-H), 7.89-7.94 (2 H, m, 4-, 5-H), 8.48 (s, 1 H, 10-H), 9.21 (ddd, 2 H, *J* = 9, 2, 1 Hz, 1-, 8-H); MS: *m/z* (%) = 491 (M^+, 1), 476 (0.3), 314 (2), 257 (67), 193 (86), 178 (100); HRMS: found 491.1804 [calc for $C_{28}H_{29}NO_5S$ (M^+) 491.1766].

tert-*Butyl 3-(anthracene-9-sulfonamido)-3-(4-cyanophenyl)propanoate (8d).* Treatment of the imine **7d** (370 mg, 1.0 mmol) according to General Method A, then purification by flash chromatography [gradient from CH_2Cl_2-petrol (1:1) to CH_2Cl_2-Et_2O (9:1)] yielded the *title compound* **8d** (455 mg, 94 %) as yellow crystals, mp 139-142 °C. IR (KBr): ν = 3257, 2228, 1701 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ = 1.32 (s, 9 H, *t*-Bu), 2.20-2.83 (m, 2 H, CH_2CO), 4.72 ('q', 1 H, *J* = 7 Hz, CHN), 6.5-6.9 (m, 5 H, C_6H_4, NH), 7.3-8.1 (m, 6 H, 2-, 3-, 4-, 5-, 6-, 7-H), 8.53 (s, 1 H, 10-H), 9.1-9.3 (m, 2 H, 1-, 8-H); MS: *m/z* (%) = 486 (M^+, 0.3), 430 (0.2), 178 (100); HRMS: found 486.1612 [calc for $C_{28}H_{26}N_2O_4S$ (M^+) 486.1613].

tert-*Butyl 3-(anthracene-9-sulfonamido)-3-(2-furyl)-propanoate (8e).* Treatment of the imine **7e** (252 mg, 0.75 mmol) according to General Method A, followed by recrystallisation from EtOAc-petrol yielded the *title compound* **8e** (62 mg, 18 %) as air-sensitive yellow crystals. IR (KBr): ν = 3219, 1708 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$]: δ = 1.16 (s, 9 H, *t*-Bu), 2.46 (dd, 1 H, *J* = 15 and 8 Hz, 1/2 x CH_2CO), 2.59 (dd, 1 H, *J* = 15 and 8 Hz, 1/2 x CH_2CO), 4.73 ('q', 1 H, *J* = 8 Hz, CHN), 5.56 (d, 1 H, *J* = 3 Hz, 2'-H), 5.88 (dd, 1 H, *J* = 3, 2 Hz), 7.01 (dd, 1 H, *J* = 2, 1 Hz, 4'-H), 7.56-7.73 (m, 4 H, 2-, 3-, 6-, 7-H), 8.16 (d, 2 H, *J* = 8 Hz, 4-, 5-H), 8.81 (1 H, d, *J* 9 Hz, NH), 8.93 (s, 1 H, 10-H), 9.21 (d, 2 H, *J* = 9 Hz, 1-, 8-H); MS: *m/z* (%) = 451 (M^+, 5), 395 (1), 378 (1), 336 (1), 257 (100), 241 (1), 177 (51), 154 (8); HRMS: found 451.1452 [calc for $C_{25}H_{25}NO_5S$ (M^+) 451.1453].

(3R*,3aR*,4R*)*-3-(tert-butoxycarbonylmethyl)-3,3a,4,5-tetrahydro-4-phenyl-5,9b-*2H*-[1,2]-benzano-naphtho-[2,1-*d*][1,2]thiazole 1,1-dioxide (9).* Treatment of the imine **7f** (1.11 g, 3.0 mmol) according to General Method A yielded the *title compound* **9** (0.75 g, 50 %) as white crystals, m.p. 194-195 °C ($CHCl_3$-petrol). (Found: C, 70.1; H, 5.9; N, 2.7. $C_{29}H_{29}NO_4S$. 0.5 H_2O requires C, 70.1; H, 6.1; N, 2.8 %); IR (KBr): ν = 3315, 1719, 1158 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, *t*-Bu), 2.11 (dd, 1 H, *J* = 18, 2 Hz, 1/2 x CH_2), 2.25 (dd, 1 H, *J* = 18, 11 Hz, 1/2 x CH_2), 2.94 (dd, 1 H, *J* = 6, 2 Hz, 4-H), 3.02 (dd, 1 H, *J* = 11, 6 Hz, 3a-H), 3.19-3.26 (m, 1 H, 3-H), 4.20 (d, 1 H, *J* = 2 Hz, 5-H), 5.37 (d, 1 H, *J* = 6 Hz, NH), 6.66-6.71 (m, 2 H), 7.07 (d, 1 H, *J* = 6 Hz), 7.16-7.38 (8 H, m), 7.94 (d, 1 H, *J* = 7 Hz), 8.34-8.37 (m, 1 H); NMR assignments were supported by a COSY experiment; a NOESY experiment showed interactions between *inter alia* 3-H and 4-H; MS: *m/z* (%) = 488 (MH^+, 5), 431 (4), 372 (3), 308 (1), 280 (6), 257 (3), 202 (6), 178 (14), 41 (100); HRMS: found 488.1950 [calc for $C_{29}H_{30}NO_4S$ (MH^+) 488.1896].

3-Amino-3-phenylpropanoic acid (3a) from tert-*Butyl 3-(anthracene-9-sulfonamido)-3-phenylpropanoate (8a). Example of a Deprotection by Al/Hg then HCl (General Method D).* Aluminium foil (27 mg, 1.0 mmol) was stirred vigorously with 2.5 % (0.07 M) aqueous $HgCl_2$ solution for 20 s and then quickly washed with MeOH followed by Et_2O. The amalgamated aluminium was added to a solution of **8a** (115 mg, 0.25 mmol) in THF-H_2O (9:1; 5 mL) and the mixture was stirred for 1 h, whereupon the mixture was filtered through Celite®, which was rinsed with a further portion of THF-H_2O. Evaporation of the combined filtrates gave a yellow solid, which was stirred for 20 min with 1 M HCl (50 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was then concentrated to give a crude product, which after purification by ion-exchange chromatography as described in the deprotection of the sulfonamidoester

2b above gave 3-amino-3-phenylpropanoic acid (**3a**) (26 mg, 63%), with identical properties to the sample prepared from **2b**.

3-Amino-3-phenylpropanoic acid (3a) from tert-*Butyl 3-(anthracene-9-sulfonamido)-3-phenylpropanoate* (**8a**) *by means of CH_3SO_3H in TFA.* The protected amino acid **8a** (115 mg, 0.25 mmol) was dissolved in TFA (3 mL) and treated with methanesulfonic acid (40 mg, 0.42 mmol). The mixture was stirred at 40 °C for 7 d, then was concentrated and partitioned between EtOAc (20 mL) and H_2O (20 mL). The layers were separated and the EtOAc layer was washed with water (20 mL). The combined aqueous layers were washed with EtOAc (2 x 20 mL) and then concentrated to give a crude product, which after purification by ion-exchange chromatography as described in the deprotection of the sulfonamidoester **2b** above gave 3-amino-3-phenylpropanoic acid (**3a**) (20 mg, 48%), with identical properties to the sample prepared from **2b**.

3-Amino-3-(4-methoxyphenyl)propanoic acid (3c). tert-Butyl 3-(anthracene-9-sulfonamido)-3-(4-methoxyphenyl)propanoate (**8c**) (123 mg, 0.25 mmol) was deprotected by General Method D to yield 3-amino-3-(4-methoxyphenyl)propanoic acid (**3c**) (35 mg, 72%) as a white solid, mp 234.5-236 °C (decomp), [lit[18] 232 °C (decomp), lit[20] 240-241 °C]. ^{1}H NMR (80 MHz, D_2O): $\delta = 2.85\text{-}2.95$ (m, 2 H, CH_2CO), 3.93 (s, 3 H, Me), 4.6-5.0 (m, PhC*H* and HOD), 7.05-7.55 (m, 4 H, C_6H_4).

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REFERENCES

1. *e.g.* Gilman, H.; Speeter, M. *J. Am. Chem. Soc.* **1943**, *65*, 2255; Bose, A. K.; Gupta, K.; Manhas, M. S. *J. Chem. Soc., Chem. Commun.* **1984**, 86; Odriozola, J. M.; Cossio, F. P.; Palomo, C. *J. Chem. Soc., Chem. Commun.* **1988**, 809.
2. Fetter, J.; Keskeny, E.; Czuppon, T.; Lempert, K.; Kajtar-Peredy, M.; Tamas, J. *J. Chem. Soc., Perkin Trans.2* **1992**, 3061.
3. Krzyzanowska, B. *Z. Chem.* **1988**, *28*, 439.
4. Ramage, R.; Hopton, D.; Parrott, M. J.; Kenner, G. W.; Moore, G. A. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1357.
5. Bowler, A. N.; Doyle, P. M.; Hitchcock, P. B.; Young, D. W. *Tetrahedron Lett.* **1991**, *32*, 2679.
6. Shimada, S.; Saigo, K.; Abe, M.; Sudo, A.; Hasegawa, M. *Chem. Lett.* **1992**, 1445.
7. Braun, M.; Opdenbusch, K. *Angew. Chem., Int Ed. Engl.* **1993**, *32*, 578.
8. Ji, S.; Gortler, L. B.; Waring, A.; Battisti, A.; Bank, S.; Closson, W. D.; Wriede, P. *J. Am. Chem. Soc.* **1967**, *89*, 5311.
9. Snyder, H. R.; Heckert, R. E. *J. Am. Chem. Soc.* **1952**, *74*, 2006.
10. Albrecht, R.; Kresze, G.; Mlakar, B. *Chem. Ber.* **1964**, *97*, 483.
11. Davis, F. A.; Giangiordano, M. A.; Starner, W. E. *Tetrahedron Lett.* **1986**, *27*, 3957.
12. Arzeno, H. B.; Kemp, D. S. *Synthesis* **1988**, 33.
13. Morley, J. O. *J. Chem. Soc., Perkin Trans.* 2 **1976**, 1554.
14. Fujita, S. *Synthesis* **1982**, 423.
15. Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561.
16. Ash, A. S. F.; Challenger, F.; Greenwood, D. *J. Chem. Soc.* **1951**, 1877.
17. Shank, R. S.; Shechter, H. *J. Org. Chem.* **1959**, *24*, 1825.
18. Johnson, T. B.; Livak, J. E. *J. Am. Chem. Soc.* **1936**, *58*, 299.
19. Aldrich Catalogue Handbook of Fine Chemicals, 1992.
20. Kalvin, D. M.; Woodard, R. W. *J. Org. Chem.* **1985**, *50*, 2259.