Synthesis of 17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluorene derivatives as chiral selectors for enantiomeric separation by HPLC on porous graphitised carbon

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The synthesis of the amides **2** which are designed to be selectors containing the chiral *N*-(3,5-dinitrobenzoyl)-α-phenylglycine covalently linked to tetrabenzo[*a*,*c*,*g*,*i*]fluorene is described. These amides are strongly adsorbed onto porous graphitised carbon, which affords chiral stationary phases that are able to resolve both racemic aromatic alcohols **3** and the methyl esters of Fmoc amino acids **4** on microgram quantities using high-pressure liquid chromatography. Two methods of preparation of these chiral phases from **2** and porous graphitised carbon are described and the stability of these phases to the chromatographic conditions and to water have also been investigated.

Introduction

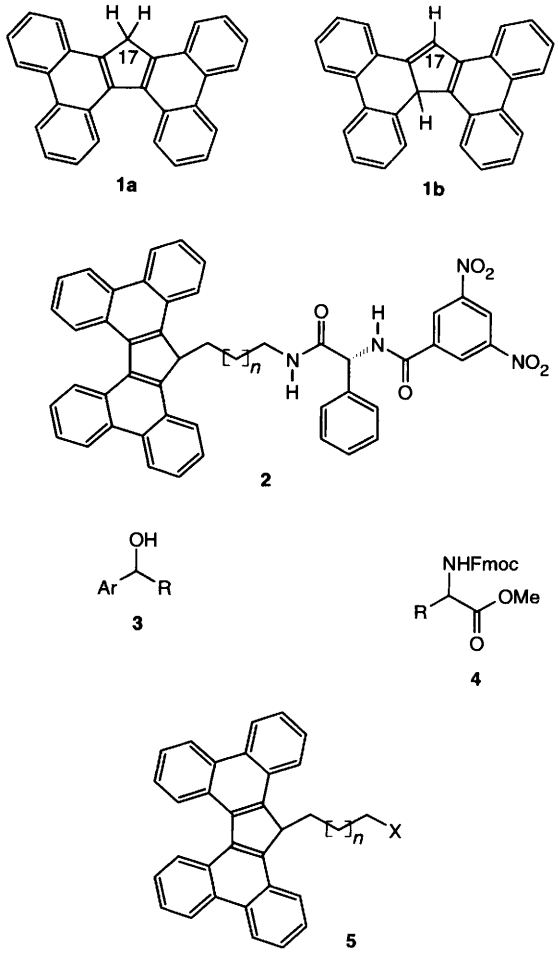
It is now almost mandatory in the pharmaceutical industry that the product of the organic synthesis of a chiral compound should be enantiomerically pure and hence it is essential to measure the enantiomeric purity of organic compounds. This has resulted in the development and use of chiral stationary phases (CSPs) in HPLC resolutions of racemic mixtures. Normally the CSP comprises a chiral selector immobilised on an inert support of which silica gel has been the most widely used.[1] It is important that such analytical separations should be capable of further development to the preparative scale.

Porous graphitised carbon (PGC) has recently been developed as a novel HPLC stationary phase and it has a number of unique properties[2] which make it potentially a better support than silica for the preparation of CSPs. These properties and advantages are: (i) high stereoselectivity since the surface of porous graphite is effectively flat; (ii) chemical inertness; (iii) uniform surface and high adsorptive capacity which enhances substrate loading.

Taking advantage of these features a number of resolutions of enantiomeric mixtures have been achieved using PGC when the chiral selector has been present in the mobile phase.[3]

Since PGC cannot form covalent bonds with organic compounds, the aim of the present research work was to design a compound which would be adsorbed strongly to the surface of PGC and also incorporate structural features which would allow a distinction to be made between the enantiomers of a racemic mixture. Therefore the compound must have one component which anchors it to PGC and another component that effects chiral separation *i.e.* a chiral selector.

Derivatives of 17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluorene (TBF) **1a** have been shown to be adsorbed strongly onto PGC from an appropriate solvent system[4] and can therefore act as the anchoring component. Therefore amides of the general type **2**, having the TBF system linked to the commercially available (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine chiral selector, developed by Pirkle,[5] have been prepared and adsorbed onto PGC. In appropriate solvent systems these CSPs have been shown to resolve alcohols **3**, bearing aromatic substituents, and protected Fmoc amino acids **4** (Tables 1 and 2).



Results and discussion

Synthesis

An efficient synthesis of the parent TBF system, **1b** has been developed in these laboratories,[6] however the preparation of

Table 1 Chiral resolution of racemic aryl alcohols **3** by chiral selectors **2** adsorbed on PGC

CSP amide **2**[a] value of *n*	Aryl alcohols[b,c]	Ar	R	Solvent[d]	α[e]	k'_1[e]
1	**3a**	9-Anthryl	Me	A	1.11	8.15
1	**3a**	9-Anthryl	Me	C	1.09	11.71
4	**3a**	9-Anthryl	Me	A	1.63	3.27
4	**3a**	9-Anthryl	Me	C	1.26	4.40
8	**3a**	9-Anthryl	Me	A	1.27	2.40
8	**3a**	9-Anthryl	Me	C	1.23	3.36
1	**3b**	9-Anthryl	Bu	A	1.08	7.15
1	**3b**	9-Anthryl	Bu	C	1.06	9.11
4	**3b**	9-Anthryl	Bu	A	1.87	2.83
4	**3b**	9-Anthryl	Bu	C	1.26	3.35
8	**3b**	9-Anthryl	Bu	A	1.41	2.05
8	**3b**	9-Anthryl	Bu	C	1.25	2.45
1	**3c**	9-Anthryl	Ph	A	1.19	3.92
1	**3c**	9-Anthryl	Ph	C	1.14	5.80
4	**3c**	9-Anthryl	Ph	A	1.47	1.81
4	**3c**	9-Anthryl	Ph	C	1.25	2.20
8	**3c**	9-Anthryl	Ph	A	1.49	1.32
8	**3c**	9-Anthryl	Ph	C	1.29	1.67
1	**3d***	9-Anthryl	CF_3	A	1.12	5.06
1	**3d***	9-Anthryl	CF_3	C	1.10	11.11
4	**3d***	9-Anthryl	CF_3	A	1.51	1.46
4	**3d***	9-Anthryl	CF_3	C	1.45	3.35
8	**3d***	9-Anthryl	CF_3	A	1.22	1.10
8	**3d***	9-Anthryl	CF_3	C	1.18	2.54
1	**3e**	1-Naphthyl	Me	D	1.05	2.19
8	**3f**	1-Naphthyl	Bu	B	1.17	0.60
4	**3f**	1-Naphthyl	Bu	D	1.08	1.26
4	**3g**	1-Naphthyl	Ph	B	1.10	1.10
4	**3g**	1-Naphthyl	Ph	D	1.05	1.85
4	**3h**	2-Naphthyl	Me	B	1.12	0.79
4	**3h**	2-Naphthyl	Me	D	1.18	1.52
8	**3h**	2-Naphthyl	Me	D	1.13	1.37
4	**3i**	2-Naphthyl	Bu	B	1.30	0.69
4	**3i**	2-Naphthyl	Bu	D	1.55	1.11
8	**3i**	2-Naphthyl	Bu	D	1.23	0.97
1	**3j**	2-Naphthyl	Ph	B	1.11	1.61
4	**3j**	2-Naphthyl	Ph	D	1.10	1.85

[a] *n* is the value of *n* in amide **2**. [b] Alcohols as in formula **3** with substituents shown in columns 3 and 4. [c] The *R* enantiomer elutes first for those entries marked with an asterisk. Elution orders of the remaining entries have not been established. [d] Solvents used: A, isopropyl alcohol–hexane (10:90, v/v); B, isopropyl alcohol–hexane (5:95, v/v); C, ethyl acetate–hexane (10:90, v/v); D, ethyl acetate–hexane (5:95, v/v). [e] See text for definition.

Table 2 Chiral resolution of racemic Fmoc amino acid methyl esters **4** by chiral selector **2** (where *n* = 4) on PGC

Fmoc amino acid[a,b]	R	Solvent[c]	α[d]	k'_1[d]
4a	Me	A	1.17	4.52
4a	Me	D	1.12	7.98
4b	$Bu^tO_2CCH_2$	A	1.12	3.80
4b	$Bu^tO_2CCH_2$	C	1.07	4.59
4c	Bu^i	A	1.17	2.58
4c*	Bu^i	D	1.17	5.28
4d	$BocNH(CH_2)_4$	B	1.06	14.58
4d*	$BocNH(CH_2)_4$	C	1.04	17.04
4e	Pr^i	A	1.15	3.24
4e	Pr^i	D	1.07	4.88

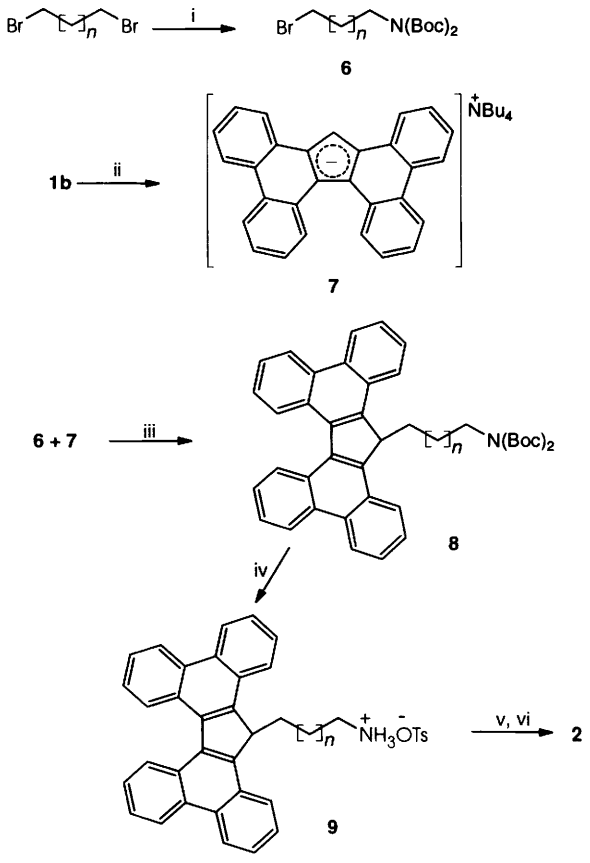
[a] Designation of aryl alcohols in text. [b] The L enantiomer was generally eluted first, with the exceptions being asterisked. [c] Solvents used: A, isopropyl alcohol–hexane (10:90, v/v); B, isopropyl alcohol–hexane (5:95, v/v); C, ethyl acetate–hexane (10:90, v/v); D, ethyl acetate–hexane (5:95, v/v). [d] See text for definition.

the series of amides **2** requires the synthesis of compounds of general structure **5**, where X is a group that can be easily transformed into a primary amine.

Prior to commencing this work **1b** had been lithiated with butyllithium, *cf.* fluorene,[7] and reacted to give the expected substitution products with allyl and benzyl halides,[8] although the desired reaction with alkyl halides gave predominantly the elimination products.[8] Accordingly a more general method of alkylation of **1b** was required which would give flexibility with respect to the length of the carbon chain and the nature of X.

It was found that lithiated TBF has more basic than nucleophilic properties, hence it was thought that a change of counter ion could reverse this characteristic. Earlier work on **1a** and **1b** had shown that, if these are suspended, and rapidly stirred, in THF in the presence of sodium hydroxide or sodium methoxide under aerobic conditions, the 17 position was oxidised to afford tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-one.[9] This result indicated that it is possible to deprotonate **1a** or **1b** with hydroxide ion. Since quaternary ammonium hydroxide bases have been used in alkylation reactions[10] an attempt was made to alkylate **1b** using this class of reagents as the base. Using 40% aqueous tetrabutylammonium hydroxide it proved possible to achieve the desired substitution reaction between **1b** and a number of commercially available alkyl halides.[11]

Since the problem of elimination had been overcome, attention was directed to the nature of the functional group X. A common protecting group for amines is *tert*-butoxycarbonyl (Boc)[12] and the scope for introducing this group by a substitution process has been facilitated with the development of di-*tert*-butyl iminodicarbonate.[13] Therefore a series of alkyl



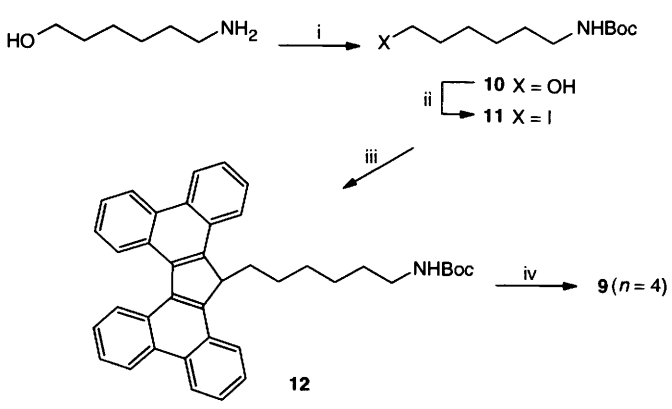
Scheme 1 *Reagents and conditions:* i, $(Boc)_2NNa$, DMF, THF, 65 °C; ii, Bu_4NOH, 1,4-dioxane, reflux; iii, 1,4-dioxane, reflux; iv, $C_7H_8O_3S{\cdot}H_2O$, DCM, reflux; v, NaOH, H_2O, DCM; vi, (*R*)(D)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine, EEDQ, THF

bromides **6** containing the ω-di-Boc amino group were prepared (Scheme 1) which were treated with **1b**, *via* the ammonium salt **7**. It was found that the reaction time was slowest when *n* is 1 and independent when *n* is 4 or 8. This gave the desired products **8** (Scheme 1), however the usual means of deprotection of the Boc group using trifluoroacetic acid[12] failed to give a clean reaction. Fortunately it proved possible to remove the Boc groups smoothly using toluene-*p*-sulfonic acid in refluxing dichloromethane. This gave the ammonium toluene-*p*-sulfonate salt **9** as a stable white solid (Scheme 1) from which the free amine could be liberated and treated with (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine to give the desired amides **2** using 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ)[14] as the coupling agent (Scheme 1).

After a series of such chiral selectors had been studied it was found that the six carbon chain subsequently gave the best chiral resolutions. A new route to the corresponding amine salt **9** ($n = 4$) was sought, which would not require chromatographic purification of synthetic intermediates and would be applicable to large scale synthesis. This new route is illustrated in Scheme 2 and starts with the commercially available 6-aminohexanol which can be protected exclusively as its mono *N*-Boc derivative **10** (Scheme 2).[15] The hydroxy group of **10** was then transformed into the corresponding iodide,[16] **11** which was then treated with **7** as described above, using degassed solvent, and the resulting mono *N*-Boc compound **12** was then converted into the salt **9** ($n = 4$) as above in Scheme 1.

Loading of TBF compounds onto PGC

Solutions of known concentrations of a TBF compound in acetonitrile were added to loose PGC and also to a prepacked



Scheme 2 *Reagents and conditions:* i, $(Boc)_2O$, THF; ii, I_2, PPH_3, imidazole, Et_2O, MeCN, 0 °C; iii, **7**, 1,4-dioxane, reflux; iv, $C_7H_8O_3S{\cdot}H_2O$, DCM, reflux

PGC column, with monitoring for breakthrough at 365 and 254 nm, respectively. The amounts adsorbed determined using these methods were *ca.* 4.5×10^{-5} mol g^{-1} and 5.5×10^{-5} mol g^{-1}, respectively. The values correspond approximately to monolayer coverage. With these results in hand, CSPs were prepared by adsorbing amides **2** onto prepacked columns or onto loose PGC prior to packing. Both methods worked well although the latter is more convenient due to the low solubility of amides **2** in acetonitrile and the latter method was used in the preparation of the CSPs whose results are reported herein. In general, preparation of a CSP involved dissolving the required amide **2** (0.06 mmol) in dichloromethane (DCM) (2 cm^3), MeCN (10 cm^3) and MeOH (35 cm^3). PGC (1.1 g) was then added and the mixture was allowed to stand with occasional stirring for 1 h whereupon the solvent was removed by pipette and the PGC was washed with MeOH (3×30 cm^3) and then packed into a 4.6×100 mm column.

Chromatography

Samples 2–5 mm^3† of approximately 0.001 (w/v) solutions of analytes were injected onto 100×4.6 mm columns packed with 7 μm porous graphite (Hypercarb^R). Capacity factors, *k'*, were determined using acetone as unretained marker. Selectivities, α, were calculated as $\alpha = k_2'/k_1'$, where k_1' and k_2' are the *k'*-values of the first- and second-eluting enantiomers.

The resolutions achieved by the CSPs prepared from the amides **2** adsorbed onto porous graphite are recorded for the aryl alcohols **3** in Table 1 and for the Fmoc amino acid methyl esters **4** in Table 2.

Table 1 shows that adsorbed amide **2** ($n = 4$) provides the highest selectivities for the separation of the aryl alcohols, and that isopropyl alcohol–hexane eluents give higher selectivities than with ethyl acetate–hexane eluents. Table 2 confirms that with amide **2** ($n = 4$), the best resolution of the Fmoc amino acid methyl esters is also obtained with the isopropyl alcohol containing eluents.

The stability of these phases to the eluent was tested using CSP **2** ($n = 8$) and 10% isopropyl alcohol–hexane was pumped through the column continuously for 20 days. In that time 30 dm^3 of solvent passed through the column, which corresponds to about 20 000 column volumes. Regular injections of **3c** (see Table 1 for identification) were made during this time, 90 in total, and it was found that the selectivity, retention and peak shape were retained throughout. Also the stability of this phase to protic solvents was tested using the CSP prepared from **2**

† 1 mm^3 ≡ 1 μl.

(n = 4). Isopropyl alcohol was passed through the column at 1 cm^3 min^{-1} for 20 min, followed by water (20 min), isopropyl alcohol (30 min) and hexane. After reequilibration with 10% isopropyl alcohol–hexane this column was able to separate, as before, **3b**, **3i** and **4a** (α = 1.83, 1.29 and 1.16, respectively) (see Tables 1 and 2 for comparison).

Experimental

General methods and equipment

All solvents applied as reaction media were HPLC or AnalaR grade. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. Ether refers to diethyl ether. Mps were determined on a Buchi 510 melting point apparatus and are uncorrected. TLC analyses were carried out on Merck Kieselgel $60F_{254}$ aluminium backed plates (0.2 mm). Visualisation of spots was accomplished with UV light, by dipping in either an ethanolic solution of *p*-anisaldehyde, which also contained sulfuric and acetic acid, or aqueous potassium permanganate, followed by heating. Crude products were purified by dry flash chromatography using Merck Kieselgel 60 H. Elemental analyses (CHN) were obtained using a Perkin-Elmer 2400 CHN Elemental Analyzer, at Edinburgh University. Optical rotations were measured on an Optical Activity AA1000 polarimeter, and are given in 10^{-1} deg cm^2 g^{-1}. UV spectra were recorded on a Varian Cary 210 from 400–235 nm and IR spectra on a BIO-RAD FTS-7 machine. NMR spectra were recorded using a Bruker AC 250 at 250 MHz for ^1H and 68.9 MHz for ^{13}C, unless indicated otherwise. Chemical shifts are reported in parts per million (δ) and J values are given in Hz. For ^{13}C NMR 1°, 2°, 3° and 4° denote methyl, methylene, methine and quaternary carbon, respectively. Mass spectra were obtained on a Kratos MS 50 TC mass spectrometer using fast atom bombardment (FAB). HPLC equipment combined a Gilson 305 and 302 pump, rheodyne Laboratory Data Control (LDC) 7125 injector valve, LDC 1204A detector, Hewlett Packard 3390A integrator, Kipp & Zonen recorder. Stainless steel columns 100 mm long and 4.6 mm bore were packed with 7 micron Hypercarb by Shandon HPLC.

Preparation of di-*tert*-butyl 3-bromopropylamine-*N*,*N*-dicarboxylate 6a

Di-*tert*-butyl iminodicarboxylate (969 mg, 4.46 mmol) was dissolved in tetrahydrofuran (THF) (20 cm^3) and *N*,*N*-dimethylformamide (DMF) (20 cm^3) under an atmosphere of nitrogen. Sodium hydride (80% dispersion in oil; 137 mg, 4.57 mmol) was added to it and the mixture heated at 65 °C for 2.5 h. 1,3-Dibromopropane (2.00 cm^3, 19.7 mmol) was added to it and the mixture heated at 65 °C for 3 h. On cooling to room temperature, ether (30 cm^3) and water (30 cm^3) were added to the mixture. The separated organic layer was washed with water (2 × 30 cm^3) and brine (20 cm^3), dried with $MgSO_4$, filtered and then the solvent was removed at reduced pressure to give a brown oil. The excess of dibromide was distilled from this oil at 0.8 mmHg. The residue after distillation was dry flash chromatographed eluting initially with 2% ether–hexane to give the title compound **6a** as a colourless oil (880 mg, 58%); ν_{max}(neat)/cm^{-1} 2980, 2935 (CH), 1791, 1744 and 1694 (C=O); δ_H(250 MHz; $CDCl_3$) 3.58 (2 H, t, J 6), 3.26 (2 H, t, J 6.5), 2.00 (2 H, quintet, J 7) and 1.37 [18 H, s, $C(CH_3)_3$]; δ_C(62.9 MHz; $CDCl_3$) 152.05 (2 × 4°, C=O), 82.11 [2 × 4°, $C(CH_3)_3$], 44.86 (2°), 31.83 (2°), 30.11 (2°) and 27.73 [6 × 1°, $C(CH_3)_3$]; *m*/*z* (FAB) 338 (MH^+, 30%), 282 (75), 222 (85), 146 (50) and 56 (100) (Found: MH^+, 338.096 33. $C_{13}H_{25}{}^{79}BrNO_4$ requires *M*, 338.096 69. Found: MH^+, 340.093 76. $C_{13}H_{25}{}^{81}BrNO_4$ requires *M*, 340.094 65).

Preparation of di-*tert*-butyl 6-bromohexylamine-*N*,*N*-dicarboxylate 6b

This compound was obtained by the above procedure using di-*tert*-butyl iminodicarboxylate (20.64 g, 95.1 mmol), sodium hydride (80% dispersion in oil; 3.30 g, 0.11 mol), 1,6-dibromohexane (78.85 g, 0.32 mol), THF (130 cm^3) and DMF (130 cm^3). After distillation the crude reaction mixture was dry flash chromatographed eluting initially with 4% ether–hexane. This gave the title compound **6b** as a colourless oil (14.82 g, 40%); ν_{max}(neat)/cm^{-1} 2980, 2930, 2865 (CH), 1780, 1746 and 1694 (C=O); δ_H(250 MHz; $CDCl_3$) 3.52 (2 H, t, J 7), 3.36 (2 H, t, J 7), 1.82 (2 H, q, J 7) and 1.57–1.24 [24 H, m, includes at 1.46, 18 H, s, $C(CH_3)_3$]; δ_C(62.9 MHz; $CDCl_3$) 152.24 (2 × 4°, C=O), 81.53 [2 × 4°, $C(CH_3)_3$], 45.80 (2°, CH_2N), 33.19 (2°), 32.28 (2°), 27.66 [6 × 1°, $C(CH_3)_3$], 27.42 (2°), 25.53 (2°) and 22.39 (2°); *m*/*z* (FAB) 382 (MH^+, 11.5%), 380 (MH^+, 22), 326 (18), 324 (32), 270 (100), 268 (100) and 56 (100) (Found: MH^+, 380.143 69. $C_{16}H_{31}{}^{79}BrNO_4$ requires *M*, 380.143 68. Found: MH^+, 382.141 74. $C_{16}H_{31}{}^{81}BrNO_4$ requires *M*, 382.141 71).

Preparation of di-*tert*-butyl 10-bromodecylamine-*N*,*N*-dicarboxylate 6c

This compound was obtained by the above procedure using di-*tert*-butyl iminodicarboxylate (4.44 g, 20.5 mmol), sodium hydride (80% dispersion in oil; 682 mg, 22.7 mmol), 1,10-dibromodecane (25.0 g, 83.3 mmol), THF (60 cm^3) and DMF (60 cm^3). After distillation the crude reaction mixture was dry flash chromatographed eluting initially with 2% ether–hexane. This gave the title compound **6c** as a colourless oil (3.35 g, 37%); ν_{max}(neat)/cm^{-1} 2980, 2932, 2855 (CH), 1789, 1748 and 1699 (C=O); δ_H(250 MHz; $CDCl_3$) 3.41 (2 H, t, J 7), 3.26 (2 H, t, J 7), 1.71 (2 H, quintet, J 7), 1.37 [18 H, s, $C(CH_3)_3$] and 1.35–1.10 (14 H, m); δ_C(62.9 MHz; $CDCl_3$) 152.34 (2 × 4°, C=O), 81.51 [2 × 4°, $C(CH_3)_3$], 46.11 (2°), 33.50 (2°), 32.49 (2°), 29.11 (2°), 29.00 (2°), 28.92 (2°), 28.68 (2°), 28.40 (2°), 27.86 [6 × 1°, $C(CH_3)_3$] and 26.44 (2°); *m*/*z* (FAB) 435 (M^+, 0.2%), 380 (10), 324 (67), 246 (65) and 56 (100) (Found: M^+, 435.198 44. $C_{20}H_{38}{}^{79}BrNO_4$ requires *M*, 435.198 45. Found: M^+, 437.196 49. $C_{20}H_{38}{}^{81}BrNO_4$ requires *M*, 437.196 48).

Preparation of *tert*-butyl 6-hydroxyhexylamine-*N*-carboxylate 10

6-Aminohexanol (24.93 g, 0.21 mol), was suspended in THF (170 cm^3) under nitrogen. Di-*tert*-butyl dicarbonate (44.11 g, 0.20 mol) was added to the suspension portion-wise at room temperature. After the final addition the mixture was stirred for 1 h. The mixture was filtered and the volume of THF reduced. Ether (150 cm^3) was added to it and the mixture washed with aq. HCl (2 mol dm^{-3}; 2 × 50 cm^3), water (50 cm^3) and brine (25 cm^3), dried with $MgSO_4$, filtered and then the solvent removed at reduced pressure to give an oil, which was dried at 0.8 mmHg. On cooling in a refrigerator the title compound **10** was obtained as a white solid (42.10 g, 96%), mp 35–36.5 °C (Found: C, 60.4; H, 11.0; N, 6.1. $C_{11}H_{23}NO_3$ requires C, 60.80; H, 10.67; N, 6.45%); ν_{max}(neat)/cm^{-1} 3355 (OH, NH) and 1693 (C=O); δ_H(250 MHz; $CDCl_3$) 4.58 (1 H, br s, NH), 3.58 (2 H, t, J 6.5, CH_2OH), 3.07 (2 H, q, J 6.5, CH_2N), 1.97 (1 H, s, exchanges with D_2O, OH) and 1.55–1.26 [17 H, m, includes at 1.40, 9 H, s, $C(CH_3)_3$]; δ_C(62.9 MHz; $CDCl_3$) 155.99 (4°, C=O), 78.70 [4°, $C(CH_3)_3$], 61.95 (2°, CH_2OH), 40.00 (2°, CH_2N), 32.23 (2°), 29.71 (2°), 28.14 [3 × 1°, $C(CH_3)_3$], 26.19 (2°) and 25.11 (2°); *m*/*z* (FAB) 218 (MH^+, 48%), 217 (M^+, 3.3), 162 (100), 154 (33.3), 144 (23.2), 138 (15.5), 137 (39) and 136 (24.1) (Found: MH^+, 218.175 31. $C_{11}H_{24}NO_3$ requires *M*, 218.175 62).

Preparation of *tert*-butyl 6-iodohexylamine-*N*-carboxylate 11

tert-Butyl 6-hydroxyhexylamine-*N*-carboxylate **10** (27.56 g, 0.127 mol), triphenylphosphine (40.30 g, 0.154 mol) and

imidazole (12.63 g, 0.186 mol) were dissolved in ether–acetonitrile (3:1) (1000 cm^3) with mechanical stirring under an atmosphere of nitrogen. This mixture was cooled to 0 °C with an ice–water bath. Iodine (41.94 g, 0.165 mol) was added to it and the mixture stirred at 0 °C for 1 h, and then water (900 cm^3) was added to it. The separated organic layer was washed with water (900 cm^3), saturated aq. $Na_2S_2O_3$ (250 cm^3), water (500 cm^3) and brine (200 cm^3), dried with Na_2SO_4, filtered and then the solvent was removed at reduced pressure to give an oil and a white solid. Hexane (5 × 50 cm^3) was added and decanted off the white solid. The hexane was removed to give a yellow oil which was filtered through silica using 10% ether–hexane to give the title compound **11** as a colourless oil, which was dried at 0.8 mmHg and solidified as a white solid in the refrigerator (37.03 g, 89%), mp 24–25 °C (Found: C, 40.25; H, 7.2: N, 4.25. $C_{11}H_{22}INO_2$ requires C, 40.37; H, 6.78; N, 4.28%); ν_{max}(neat)/cm^{-1} 3354 (NH) and 1696 (C=O); δ_H(250 MHz; $CDCl_3$) 4.52 (1 H, br s, NH), 3.15 (2 H, t, *J* 7, CH_2I), 3.07 (2 H, q, *J* 6.5, CH_2N), 1.81 (2 H, m) and 1.51–1.25 [15 H, m, includes at 1.41, 9 H, s, $C(CH_3)_3$]; δ_C(62.9 MHz; $CDCl_3$) 155.78 (4°, C=O), 78.71 [4°, $C(CH_3)_3$], 40.28 (2°, CH_2N), 33.13 (2°), 29.91 (2°), 29.68 (2°), 28.24 [3 × 1°, $C(CH_3)_3$], 25.44 (2°) and 6.83 (2°, CH_2I); *m/z* (FAB) 328 (M^+, 13.7%), 326 (10.5), 273 (37.5), 272 (100), 270 (25), 228 (53), 226 (35.4), 145 (17.5), 144 (44.4), 137 (22.5) and 136 (11.5) (Found: MH^+, 328.076 24. $C_{11}H_{23}INO_2$ requires *M*, 328.077 35).

Preparation of di-*tert*-butyl 3-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)propylamine-*N*,*N*-dicarboxylate 8a

TBF **1b** (286 mg, 0.78 mmol) was dissolved in refluxing 1,4-dioxane (12 cm^3) under an atmosphere of nitrogen. 40% aq. Bu_4NOH (0.5 cm^3, 0.75 mmol) in 1,4-dioxane (1.5 cm^3) was added to it and the mixture refluxed for 5 min. After cooling the yellow ammonium salt **7** was filtered off under nitrogen and washed with 1,4-dioxane (2 ×) and ether (2 ×). It was used in the next stage without further purification.

The ammonium salt **7** and di-*tert*-butyl 3-bromopropylamine-*N*,*N*-dicarboxylate **6a** (300 mg, 0.89 mmol) were mixed in 1,4-dioxane (15 cm^3) under nitrogen and the mixture refluxed for a further 14 h. On cooling to room temperature the mixture was filtered and the solvent removed at reduced pressure. Ether was added to it and the resulting precipitate filtered off, washed with hot ether and discarded. The ether was removed at reduced pressure to give a red oil, which was dry flash chromatographed using Kieselgel H, eluting initially with 50% DCM–hexane with 10% increments to give the product **8a** mixed with an unidentified product. The mixture was dry flash chromatographed using Kieselgel H, eluting initially with 20% ether–hexane to give the di-Boc compound **8a** as a yellow oily solid. The di-Boc compound was recrystallised from ether (−15 °C) overnight as a light brown solid (190 mg, 39%), mp 190–193 °C (Found: N, 2.5. $C_{42}H_{41}NO_4$ requires N, 2.25%); λ_{max}(DCM)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 17 686), 365 (18 256), 301 (44 487), 289 (36 526), 278 (sh), 260 (67 433), 254 (74 925) and 240 (56 662); ν_{max}(DCM mull)/cm^{-1} 2978, 2918 (CH), 1778 and 1742 (C=O); δ_H(250 MHz; $CDCl_3$) 8.78 (4 H, dm + d, *J* 8), 8.67 (2 H, dd, *J* 8 and 2), 8.23–8.12 (2 H, m), 7.72–7.41 (8 H, m), 5.04 (1 H, t, *J* 4), 3.06 (2 H, t, *J* 7.5), 2.62–2.54 (2 H, br m), 1.43 [18 H, s, $C(CH_3)_3$] and 0.67–0.46 (2 H, br m); δ_C(62.9 MHz; $CDCl_3$) 151.77 (2 × 4°, C=O), 143.59 (2 × 4°), 136.89 (2 × 4°), 131.31 (2 × 4°), 130.47 (2 × 4°), 128.57 (2 × 4°), 127.92 (2 × 4°), 127.47 (2 × 3°), 126.89 (2 × 3°), 125.95 (2 × 3°), 125.74 (2 × 3°), 125.09 (2 × 3°), 124.20 (2 × 3°), 123.49 (4 × 3°), 81.48 [2 × 4°, $C(CH_3)_3$], 46.47 (3°), 45.94 (2°), 30.62 (2°), 27.43 [6 × 1°, $C(CH_3)_3$] and 21.91 (2°); *m/z* (FAB) 623 (M^+, 38%), 468 (62), 365 (44) and 325 (100) (Found: M^+, 623.303 53. $C_{42}H_{41}NO_4$ requires *M*, 623.303 54).

Preparation of di-*tert*-butyl 6-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)hexylamine-*N*,*N*-dicarboxylate 8b

This compound was obtained by the above procedure using TBF **1b** (2.19 g, 5.98 mmol) in 1,4-dioxane (50 cm^3), 40% aq. Bu_4NOH (4.0 cm^3, 6.0 mmol) in 1,4-dioxane (12 cm^3) and di-*tert*-butyl 6-bromohexylamine-*N*,*N*-dicarboxylate **6b** in 1,4-dioxane (120 cm^3). The reaction was complete after 2 h at reflux. The crude reaction mixture was dry flash chromatographed eluting initially with 50% DCM–hexane to give the product **8b** as a pale yellow solid (1.48 g, 37%), mp 164–167 °C (Found: N, 2.2. $C_{45}H_{47}NO_4$ requires N, 2.10%); λ_{max}(DCM)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 17 829), 365 (18 312), 302 (41 442), 290 (34 696), 280 (32 286), 262 (62 645), 254 (68 428) and 240 (51 079); ν_{max}(DCM mull)/cm^{-1} 2980, 2930, 2860 (CH), 1776, 1738 and 1692 (C=O); δ_H(250 MHz; $CDCl_3$) 8.79 (4 H, m), 8.67 (2 H, dd, *J* 8 and 1), 8.22 (2 H, m), 7.75–7.6 (8 H, m), 4.97 (1 H, t, *J* 4.5), 3.20 (2 H, t, *J* 7, CH_2N), 2.58 (2 H, m), 1.35 [18 H, s, $C(CH_3)_3$], 1.13 (2 H, m), 0.77 (4 H, m) and 0.35 (2 H, m); δ_C(62.9 MHz; $CDCl_3$) 152.21 (2 × 4°, C=O), 144.01 (2 × 4°), 136.45 (2 × 4°), 131.02 (2 × 4°), 130.12 (2 × 4°), 128.48 (2 × 4°), 127.75 (2 × 4°), 127.19 (2 × 3°), 126.51 (2 × 3°), 125.51 (2 × 3°), 125.38 (2 × 3°), 124.74 (2 × 3°), 124.21 (2 × 3°), 123.28 (2 × 3°), 123.24 (2 × 3°), 81.50 [2 × 4°, $C(CH_3)_3$], 46.73 (3°), 45.88 (2°, CH_2N), 33.38 (2°), 29.05 (2°), 28.55 (2°), 27.73 [6 × 1°, $C(CH_3)_3$], 25.99 (2°) and 22.22 (2°); *m/z* (FAB) 665 (M^+, 46%), 510 (18.7), 466 (8), 365 (42) and 56 (100) (Found: M^+, 665.350 46. $C_{45}H_{47}NO_4$ requires *M*, 665.350 49).

Preparation of di-*tert*-butyl 10-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)decylamine-*N*,*N*-dicarboxylate 8c

This compound was obtained by the above procedure using TBF **1b** (2.8 g, 7.6 mmol) in 1,4-dioxane (50 cm^3), 40% aq. Bu_4NOH (5.0 cm^3, 7.5 mmol) in 1,4-dioxane (14 cm^3) and di-*tert*-butyl 10-bromodecylamine-*N*,*N*-dicarboxylate **6c** in 1,4-dioxane (120 cm^3). The reaction was complete after 2 h at reflux. The crude reaction mixture was dry flash chromatographed eluting initially with 50% DCM–hexane to give the product **8c** as a pale yellow solid (2.31 g, 53%), mp 53–56 °C (Found: N, 2.0. $C_{49}H_{55}NO_4$ requires N, 1.94%); λ_{max}(DCM)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 18 464), 365 (18 904), 301 (42 645), 289 (36 050), 278 (sh), 260 (65 066), 254 (71 220) and 240 (53 196); ν_{max}(DCM mull)/cm^{-1} 2981, 2932, 2857 (CH), 1782, 1742 and 1693 (C=O); δ_H(250 MHz; $CDCl_3$) 8.85–8.80 (4 H, m), 8.70 (2 H, dd, *J* 8 and 2), 8.21 (2 H, dd, *J* 8 and 2), 7.71–7.58 (8 H, m), 4.92 (1 H, t, *J* 4), 3.48 (2 H, t, *J* 7), 2.61–2.55 (2 H, br m), 1.49 [18 H, s, $C(CH_3)_3$], 1.24–0.72 (14 H, m) and 0.40–0.30 (2 H, br m); δ_C(62.9 MHz; $CDCl_3$) 152.59 (2 × 4°, C=O), 144.28 (2 × 4°), 136.68 (2 × 4°), 131.18 (2 × 4°), 130.29 (2 × 4°), 128.73 (2 × 4°), 127.96 (2 × 4°), 127.39 (2 × 3°), 126.68 (2 × 3°), 125.77 (2 × 3°), 125.53 (2 × 3°), 124.92 (2 × 3°), 124.10 (2 × 3°), 123.41 (4 × 3°), 81.81 [2 × 4°, $C(CH_3)_3$], 47.09 (3°), 46.38 (2°), 33.47 (2°), 29.37 (2°), 29.15 (2°), 29.04 (2°), 28.94 (2°), 28.85 (2°), 28.73 (2°), 27.98 [6 × 1°, $C(CH_3)_3$], 26.57 (2°) and 22.12 (2°); *m/z* (FAB) 721 (M^+, 50%), 566 (21), 522 (12), 365 (79) and 56 (100) (Found: M^+, 721.413 13. $C_{49}H_{55}NO_4$ requires *M*, 721.413 09).

Preparation of 3-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)propylammonium toluene-*p*-sulfonate 9a

Di-*tert*-butyl 3-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)propylamine-*N*-*N*-dicarboxylate **8a** (192 mg, 0.31 mmol) and toluene-*p*-sulfonic acid monohydrate (67 mg, 0.35 mmol) were dissolved in DCM (20 cm^3) under an atmosphere of nitrogen. The mixture was refluxed for 20 h. On cooling the solvent was removed at reduced pressure. DCM (2 cm^3) and ether (8 cm^3) were added to the white solid and the mixture centrifuged. The solvent was decanted off. The above was repeated until the

solvent was no longer red (3 ×) and the solid was dried to give the amine salt **9a** as a white solid (172 mg, 94%), mp 156–159 °C (Found: C, 78.0; H; 5.7; N, 2.5. $C_{39}H_{33}NO_3S$ requires C, 78.63; H, 5.58; N, 2.35%); λ_{max}[DCM–MeOH (1:1)]/nm 380 (ε/dm^3 mol^{-1} cm^{-1} 18 263), 365 (19 199), 301 (44 487), 289 (36 526), 278 (sh), 260 (67 433), 254 (74 925) and 240 (56 662); ν_{max}(bromoform mull)/cm^{-1} 3457, 3200–2900 (NH), 1608 and 1500; δ_H(360 MHz; [$^2H_6$]DMSO) 8.93 (4 H, t, *J* 8), 8.56 (2 H, d, *J* 8), 8.36 (2 H, d, *J* 8), 7.81–7.70 (8 H, m), 7.50 (2 H, d, *J* 8), 7.24 (3 H, br s, NH_3), 7.11 (2 H, d, *J* 8), 5.36 (1 H, t, *J* 4), 2.65–2.60 (2 H, br m), 2.28–2.20 (5 H, br m) and 0.56–0.46 (2 H, br m); δ_C(50.3 MHz; [$^2H_6$]DMSO) 145.62 (4°), 144.02 (2 × 4°), 137.93 (4°), 136.03 (2 × 4°), 131.10 (2 × 4°), 130.08 (2 × 4°), 128.26 (2 × 3°), 128.22 (2 × 4°), 127.59 (2 × 3°), 127.33 (2 × 3°), 126.86 (2 × 3°), 126.78 (2 × 4°), 126.35 (2 × 3°), 125.66 (4 × 3°), 124.83 (2 × 3°), 124.22 (2 × 3°), 123.95 (2 × 3°), 46.09 (3°), 38.76 (2°), 30.51 (2°), 20.94 (1°) and 20.63 (2°); *m*/*z* (FAB) 595 (M^+, 0.5%), 424 (100, $M^+ - C_7H_7SO_3$) and 365 (47) (Found: $M^+ - C_7H_7SO_3$, 424.206 55. $C_{32}H_{26}N$ requires *M*, 424.206 51).

Preparation of 6-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)hexylammonium toluene-*p*-sulfonate 9b

Method A: from 8b. This compound was obtained by the above procedure using di-*tert*-butyl 6-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]-fluorenyl)hexylamine-*N*,*N*-dicarboxylate **8b** (286 mg, 0.43 mmol), toluene-*p*-sulfonic acid monohydrate (83 mg, 0.44 mmol) and DCM (25 cm^3). The title compound **9b** was isolated as a white solid (277 mg, 98%), mp 153–155 °C.

Method B: from TBF 1b using iodide 11 as the alkylating agent. The ammonium salt **7** was prepared as above using TBF **1b** (20.24 g, 55.30 mmol), degassed 1,4-dioxane (500 cm^3) and 40% aq. Bu_4NOH (36.90 cm^3, 55.35 mmol) in degassed 1,4-dioxane (100 cm^3).

The iodide **11** (18.06 g, 55.23 mmol) in warm degassed 1,4-dioxane (250 cm^3) was added to the ammonium salt **7** prepared above under an atmosphere of nitrogen. The mixture was then brought to reflux and the mixture refluxed for 5 min after all the ammonium salt had dissolved. The total time at reflux was 12 min. The mixture was then stirred in an ice–water bath until precipitation of Bu_4NI was complete and then at room temperature for 5 min. The precipitate was filtered off and washed with ether. The solvent was then removed from the filtrate at reduced pressure to give a red oil, which was triturated with hexane (4 × 50 cm^3) and the oily residue then filtered through silica with 50% DCM–hexane. The solvent was removed from the column filtrate and then dried at 0.8 mmHg to give a foam (32.06 g, >100%). A small amount of this material was purified by chromatography for characterisation purposes. The major component isolated was the mono-Boc compound **12** as a yellow solid, mp 69–72 °C (Found: C, 79.6; H, 7.0; N, 2.4. $C_{40}H_{39}NO_2$ requires C, 84.96; H, 6.95; N, 2.48%); λ_{max}(DCM)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 17 152), 365 (17 656), 301 (45 401), 288 (43 384), 276 (sh), 262 (72 138) and 254 (75 670); ν_{max}(DCM mull)/cm^{-1} 3438, 3355 (NH) and 1711 (C=O); δ_H(250 MHz; $CDCl_3$) 8.80 (4 H, dt, *J* 8 and 2), 8.67 (2 H, dd, *J* 8 and 1.5), 8.23 (2 H, m), 7.72–7.58 (8 H, m), 5.00 (1 H, t, *J* 4.4), 3.70 (1 H, br s, NH), 2.65 (2 H, q, *J* 6.5), 2.61–2.55 (2 H, m), 1.36 [9 H, s, $C(CH_3)_3$], 0.95–0.85 (2 H, m), 0.8–0.65 (4 H, m) and 0.4–0.25 (2 H, m); δ_C(62.9 MHz; $CDCl_3$) 155.21 (4°, C=O), 144.07 (2 × 4°), 136.60 (2 × 4°), 131.20 (2 × 4°), 130.22 (2 × 4°), 128.59 (2 × 4°), 127.86 (2 × 4°), 127.30 (2 × 3°), 126.63 (2 × 3°), 125.74 (2 × 3°), 125.50 (2 × 3°), 124.87 (2 × 3°), 124.29 (2 × 3°), 123.37 (2 × 3°), 123.33 (2 × 3°), 78.62 [4°, $C(CH_3)_3$], 46.70 (3°), 40.07 (2°, CH_2N), 33.14 (2°), 29.23 (2°), 28.77 (2°), 28.27 [3 × 1°, $C(CH_3)_3$], 25.70 (2°) and 21.81 (2°); *m*/*z* (FAB) 565 (M^+, 100%), 510 (43.6), 466 (28.4), 366 (60.8), 365 (85.3), 364 (87.0), 363 (82.5), 58 (86.6) and 56 (40.9) (Found: M^+, 565.298 83. $C_{40}H_{39}NO_2$ requires *M*, 565.298 08).

The brown foam from above (31.76 g) was dissolved in DCM (250 cm^3) under nitrogen. Toluene-*p*-sulfonic acid monohydrate (8.5 g, 0.8 equiv.) was added to it and the mixture refluxed with stirring for 18 h. The mixture was then cooled in an ice–salt bath and the off-white solid filtered off from the red solution. The solid was dissolved in methanol (125 cm^3), filtered if necessary, and then the solvent removed at reduced pressure to give a light brown solid. DCM (60 cm^3) was added to the solid and the solution allowed to stand. The resulting white precipitate was filtered off and washed with DCM (2 ×), the DCM was removed and further DCM (30 cm^3) was added to the solid. The resulting white solid was filtered off and combined with the first crop. The combined first and second crops were dried at 0.8 mmHg for 3 h, to give the amine salt **9b** as a white solid (20.48 g, 58%), mp 152–155 °C. A third crop was also obtained (1.52 g), mp 145–149 °C.

The initial red filtrate was reduced in volume (50 cm^3) and toluene-*p*-sulfonic acid monohydrate (1.5 g) was added to it. The mixture was refluxed under nitrogen for 5 h and cooled in an ice–water bath. The resulting red precipitate was filtered off and washed with DCM (3 ×) to give a pink solid, which was dissolved in hot methanol (25 cm^3). The methanol was removed at reduced pressure and DCM (10 cm^3) was added to the solid and the solution allowed to stand for 1 h. The white precipitate was filtered off and DCM (20 cm^3) was added to it. The resulting white precipitate was then filtered off, washed with DCM and dried (0.8 mmHg) to give **9b** as a white solid (2.40 g), mp 152–155 °C.

The total amount of amine salt **9b** prepared from TBF **1b** (20.24 g, 55.30 mmol) was 22.72 g (64%), mp 152–155 °C (Found: C, 79.1; H, 6.6; N, 2.3. $C_{42}H_{39}NO_3S$ requires C, 79.09; H, 6.16; N, 2.20%). λ_{max}(DCM–MeOH, 1:1)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 15 532), 365 (15 700), 301 (35 887), 289 (30 504), 278 (sh), 260 (sh) and 254 (61 008); ν_{max}(DCM mull)/cm^{-1} 3250–2850 ($^+NH_3$); δ_H(250 MHz; $CDCl_3$) 8.75 (4 H, m), 8.63 (2 H, d, *J* 7), 8.15 (2 H, m), 7.62 (8 H, m), 7.39 (2 H, d, *J* 8, tosyl-H), 6.79 (2 H, d, *J* 8, tosyl-H), 4.97 (1 H, t, *J* 4), 2.47 (2 H, m), 2.20 (2 H, m), 1.96 (3 H, s), 0.86 (2 H, m), 0.45 (4 H, m) and 0.23 (2 H, m); *m*/*z* (FAB) 637 (M^+, 0.6%) and 466 (100, $M - C_7H_7SO_3$) (Found: MH^+, 638.272 88. $C_{42}H_{40}NO_3S$ requires *M*, 638.272 87).

Preparation of 10-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)decylammonium toluene-*p*-sulfonate 9c

This compound was obtained by the above procedure using di-*tert*-butyl 10-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)decylamine-*N*,*N*-dicarboxylate **8c** (351 mg, 0.48 mmol), toluene-*p*-sulfonic acid monohydrate (93 mg, 0.49 mmol) and DCM (25 cm^3). It proved impossible to purify **9c** using the above procedure and was used as isolated from the reaction mixture.

Preparation of *N*-{phenyl[3-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)propylcarbamoyl]methyl}-3,5-dinitrobenzamide 2a

The amine salt **9a** (146 mg, 0.25 mmol) was dissolved in methanol (4 cm^3) and DCM (20 cm^3). This mixture was then washed with aq. NaOH (0.4 mol dm^{-3}; 5 cm^3), water (10 cm^3) and brine (5 cm^3), dried with $MgSO_4$ and then filtered. The solvent was removed to give the free amine as a foam, which was used in the next stage of the reaction without further purification.

The free amine was dissolved in THF (5 cm^3) under an atmosphere of nitrogen (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine (93 mg, 0.27 mmol) was added to it followed by EEDQ (66 mg, 0.27 mmol). The mixture was stirred at room temperature for 18 h. The solvent was removed at reduced pressure to give an orange solid which was dissolved in DCM (2 cm^3) and then

hexane (10 cm^3) was added to the solution. The resulting orange precipitate was filtered off and washed with hexane. The above procedure was repeated. The orange solid was adsorbed onto silica and dry flash chromatographed using Kieselgel H, eluting initially with DCM then 0.2% MeOH–DCM upto 6%. This gave the amide **2a** as an orange solid (131 mg, 71%), mp 167–170 °C (Found: C, 75.2; H, 4.8; N, 7.6. $C_{47}H_{34}N_4O_6$ requires C, 75.19; H, 4.57; N, 7.46%); $[\alpha]_D^{24}$ −51.1 (*c* 4.85 × 10^{-3} in $CHCl_3$); λ_{max}(DCM)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 14 489), 365 (15 341), 301 (33 239), 289 (29 403), 260 (sh) and 254 (72 869); ν_{max}(DCM mull)/cm^{-1} 3394, 3301, 1644 (C=O) and 1540; δ_H(200 MHz; $CDCl_3$) 8.9 (1 H, t, *J* 2), 8.73–8.58 (8 H, m), 8.29 (1 H, d, *J* 6.5), 8.18–8.09 (2 H, m), 7.68–7.59 (8 H, m), 7.19–7.04 (5 H, m), 5.09 (1 H, d, *J* 6.5), 4.98 (1 H, t, *J* 4), 4.88 (1 H, t, *J* 6), 2.85–2.74 (1 H, m), 2.55–2.40 (3 H, br m) and 0.46–0.39 (2 H, br m); δ_C(90.6 MHz; $CDCl_3$) 169.35 (4°), 160.50 (4°), 147.29 (2 × 4°), 143.28 (4°), 142.94 (4°), 136.83 (4°), 136.44 (4°), 136.25 (4°), 135.43 (4°), 130.59 (2 × 4°), 129.76 (4°), 129.66 (4°), 128.58 (2 × 3°), 128.24 (3°), 127.92 (2 × 4°), 127.32 (2 × 4°), 127.23 (4 × 3°), 127.05 (3°), 126.77 (3°), 126.64 (3°), 126.23 (2 × 3°), 125.86 (3°), 125.76 (3°), 125.61 (3°), 124.93 (2 × 3°), 123.89 (2 × 3°), 122.96 (4 × 3°), 120.17 (3°), 56.95 (3°), 45.91 (3°), 39.30 (2°), 30.10 (2°) and 21.79 (2°); *m/z* (FAB) 751 (MH^+, 72%), 750 (M^+, 40), 433 (100) and 365 (62) (Found: MH^+, 751.255 65. $C_{47}H_{35}N_4O_6$ requires *M*, 751.255 64).

Preparation of *N*-{phenyl[6-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)hexylcarbamoyl]methyl}-3,5-dinitrobenzamide 2b

This compound was obtained as above using amine salt **9b** (136 mg, 0.21 mmol), (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine (83 mg, 0.24 mmol), EEDQ (58 mg, 0.24 mmol) and THF (5 cm^3). The product was isolated from the crude reaction mixture using dry flash chromatography eluting initially with DCM then 0.2% MeOH–DCM to give the amide **2b** as an orange solid (135 mg, 80%), mp 141–143 °C (Found: C, 75.4; H, 5.65; N, 7.0. $C_{50}H_{40}N_4O_6$ requires C, 75.74; H, 5.09; N, 7.07%); $[\alpha]_D^{25}$ −31.9 (*c* 6.4 × 10^{-3} in $CHCl_3$); λ_{max}($CHCl_3$)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 17 056), 365 (17 798), 302 (20 764), 289 (35 596), 278 (sh), 262 (sh), 254 (82 315) and 240 (70 449); ν_{max}(DCM)/cm^{-1} 3402, 3293, 3088 (NH), 1647 (C=O), 1540 and 1343 (NO_2); δ_H(250 MHz; $CDCl_3$) 8.96 (1 H, t, *J* 2), 8.76–8.70 (6 H, m), 8.61 (3 H, td, *J* 7 and 1), 8.19 (2 H, m), 7.62 (8 H, m), 7.20 (2 H, dd, *J* 7 and 2), 7.08–6.94 (3 H, m), 5.40 (1 H, d, *J* 6) 5.15 (1 H, t, *J* 6), 4.99 (1 H, t, *J* 4), 2.81–2.65 (2 H, m, AB system), 2.54 (2 H, m), 0.76 (2 H, quintet, *J* 7), 0.59 (2 H, q, *J* 7), 0.47 (2 H, q, *J* 7) and 0.20 (2 H, m); δ_C(62.9 MHz; $CDCl_3$) 169.58 (4°, C=O), 161.20 (4°, C=O), 147.84 (2 × 4°), 144.06 (4°), 144.02 (4°), 137.13 (4°), 136.56 (2 × 4°), 136.20 (4°), 130.98 (4°), 130.15 (4°), 130.07 (4°), 128.85 (3°), 128.52 (4°), 127.78 (4°), 127.72 (2 × 3°), 127.45 (2 × 3°), 127.28 (2 × 3°), 127.23 (2 × 3°), 126.93 (2 × 3°), 126.76 (2 × 3°), 125.87 (2 × 3°), 125.66 (4°), 125.03 (2 × 3°), 124.98 (4°), 124.34 (2 × 3°), 124.29 (4°), 123.34 (4 × 3°), 120.62 (3°), 57.35 (3°), 46.84 (3°), 39.57 (2°), 33.20 (2°), 28.82 (2°), 28.58 (2°), 25.73 (2°) and 21.85 (2°); *m/z* (FAB) 793 (MH^+, 9%), 466 (4) and 365 (10) (Found: M^+, 792.294 78. $C_{50}H_{40}N_4O_6$ requires *M*, 792.294 77).

Preparation of *N*-{phenyl[10-(17*H*-tetrabenzo[*a*,*c*,*g*,*i*]fluoren-17-yl)decylcarbamoyl]methyl}-3,5-dinitrobenzamide 2c

This compound was obtained as above using free amine (164 mg, 0.31 mmol), (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylglycine (117 mg, 0.34 mmol), EEDQ (83 mg, 0.34 mmol) and THF (6 cm^3). The product was isolated from the crude reaction mixture using dry flash chromatography eluting initially with DCM then 0.2% MeOH–DCM to give the amide **2c** as an orange solid (210 mg, 79%), mp 125–127.5 °C (Found: C, 76.3; H, 6.0; N, 6.6. $C_{54}H_{48}N_4O_6$ requires C, 76.40; H, 5.70; N, 6.60%); $[\alpha]_D^{23}$ −35.1 (*c* 6.8 × 10^{-3} in $CHCl_3$); λ_{max}($CHCl_3$)/nm 382 (ε/dm^3 mol^{-1} cm^{-1} 17 926), 365 (18 706), 302 (42 088), 290 (36 632), 260 (sh) and 254 (82 618); ν_{max}(DCM mull)/cm^{-1} 3398, 3306, 1639 (C=O) and 1542; δ_H(250 MHz; $CDCl_3$) 9.12 (1 H, d, *J* 7), 8.90 (1 H, t, *J* 2), 8.78–8.62 (8 H, m), 8.19 (2 H, t, *J* 6.5), 7.70–7.56 (8 H, m), 7.40–7.36 (2 H, m), 7.27–7.20 (3 H, m), 5.79 (1 H, t, *J* 6), 5.67 (1 H, d, *J* 7), 4.93 (1 H, t, *J* 4), 3.20–2.95 (2 H, m, AB system), 2.55–2.45 (2 H, br m), 1.28–1.17 (2 H, br m), 0.95–0.6 (12 H, m) and 0.28 (2 H, br s); δ_C(62.9 MHz; $CDCl_3$) 169.76 (4°), 161.37 (4°), 147.86 (2 × 4°), 144.23 (4°), 144.10 (4°), 137.21 (4°), 136.51 (4°), 136.45 (4°), 136.26 (4°), 130.93 (2 × 4°), 130.08 (4°), 130.03 (4°), 128.92 (2 × 3°), 128.51 (4° and 3°), 127.75 (4°), 127.72 (2 × 4°), 127.48 (2 × 3°), 127.21 (2 × 3°), 126.97 (2 × 3°), 126.61 (2 × 3°), 125.70 (2 × 3°), 125.46 (2 × 3°), 124.87 (2 × 3°), 124.32 (3°), 124.27 (3°), 123.27 (4 × 3°), 120.60 (3°), 57.52 (3°), 46.91 (3°), 39.88 (2°), 33.37 (2°), 29.23 (2°), 28.81 (3 × 2°), 28.59 (2 × 2°), 26.23 (2°) and 22.01 (2°); *m/z* (FAB) 849 (MH^+, 66%), 523 (28) and 365 (100) (Found: M^+, 848.357 37. $C_{54}H_{48}N_4O_6$ requires *M*, 848.357 37).

Acknowledgements

This research was funded by the DTI/SERC Link Programme in collaboration with Rhone-Poulenc-Rorer and Shandon. We are indebted to D. Dolphin and M. P. L. Caton and for discussions and K. T. Shaw for technical assistance.

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Paper 5/02808F
Received 2nd *May* 1995
Accepted 2nd *June* 1995