Pergamon

*Tetrahedron: Asymmetry*, Vol. 7, No. 4, pp. 1189-1198, 1996

0957-4166/96 $15.00 + 0.00

S0957-4166(96)00125-5

# Novel 2-Chrysenyl- and 1-Pyrenyl-tartaramide Derivatives as Liquid Chromatographic Chiral Phases for Enantiomeric Separation on Porous Graphitic Carbon.

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**Abstract:** Four new chiral stationary phases have been obtained by coupling 2-chrysenyl-amine and 1-pyrenylamine to chiral selector groups based on (R,R)-tartaric acid diamide. The compounds (R,R)-*N*-isopropyl-*N'*-(1-pyrenyl)tartaramide, (R,R)-*N*-(2-chrysenyl)-*N'*-isopropyltartaramide and (R,R)-*N*-(2-chrysenyl)-*N'*-(3-nitrophenyl)tartaramide are strongly adsorbed on to porous graphitic carbon to produce a novel type of carbon-based chiral stationary phase. These new materials were evaluated by HPLC and were found to exhibit excellent enantioselectivity for various types of compound including aromatic alcohols, binaphthyl derivatives, β-blocking agents and anti-inflammatory agents. These new chiral phases are very stable showing negligible tendency for phase loss or degradation.


## INTRODUCTION

The use of a chiral stationary phase (CSP) for liquid chromatographic separation of enantiomers has gained general acceptance as a resolution method. The popularity of this technique is due to the ease of operation and chromatographic stability of such systems and from the recent development of new, highly selective stationary phases for chiral chromatography. Usually a CSP comprises of a chiral selector (CS) chemically linked to a support phase, the most common being silica gel.[1,2] A common disadvantage of this type of column is its relatively low efficiency and limited column life due to racemisation or chemical degradation of the chiral phase. Furthermore, this type of CSP is less tolerant of polar solvents especially if the phase is ionically bonded where elution of the ionic ligand is a problem.[3] For these reasons the search for more robust alternatives continues.

Porous graphitic carbon[4,5] (PGC) has been introduced as a novel high performance liquid chromatography (HPLC) packing material which has the advantages of a flat uniform surface with high adsorptive capacity (high affinity for planar molecules) and chemical inertness. These characteristics make PGC potentially a better support than silica for the preparation of a chiral chromatography column with a CSP. Since PGC has no functional groups on the surface, it cannot form covalent bonds with organic compounds. The objective of the present work was to design compounds which would be adsorbed strongly to the surface of PGC and also incorporate a chiral group to effect enantiomer separation. Thus new compounds were required with a large planar aromatic component (to provide the anchor to PGC) linked to another component that can provide the chiral environment (the CS group). The relationship of this type of CSP to the support phase is modeled in Fig 1.

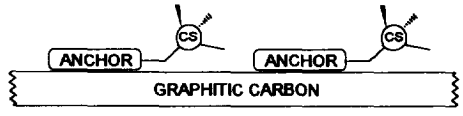



**Fig. 1** Schematic representation of a Chiral Stationary Phase on Porous Graphitic Carbon

Both pyrene and chrysene have been shown[6,7] to be adsorbed strongly on to PGC from an appropriate solvent system and therefore can be used as the anchor components. The easy accessibility of tartarates has made them common starting materials for the preparation of both immobilised and dynamic chiral selectors for liquid chromatography.[8-10] We report here the synthesis of 1-pyrenyl and 2-chrysenyl derivatives of (R,R)-*N*-isopropyltartaramide and (R,R)-*N*-(3-nitrophenyl)tartaramide and the preparation of chiral columns by the adsorption on to PGC of four types of CSP.

## RESULTS AND DISCUSSION

*Synthesis.* The four new chiral compounds are shown in Fig. 2 and the synthetic route is shown in Scheme 1. (R,R)-Tartaric acid **1** was converted to diacetyltartaric acid anhydride **2** and then the half amide formed by aminolysis with either isopropylamine in $CH_2Cl_2$ or 3-nitroaniline in THF giving **3a** and **3b** respectively. The half amides were condensed with 2-aminochrysene or 1-aminopyrene using *N*-methylmorpholine and ethyl chloroformate in THF[11] to give the diamides **4a** - **4c**. Hydrolysis with methanolic ammonia removed the protecting acetyl groups to give compounds **5a** - **5c**. It is assumed that all chemical transformations were accomplished without significant loss in stereochemical integrity since there

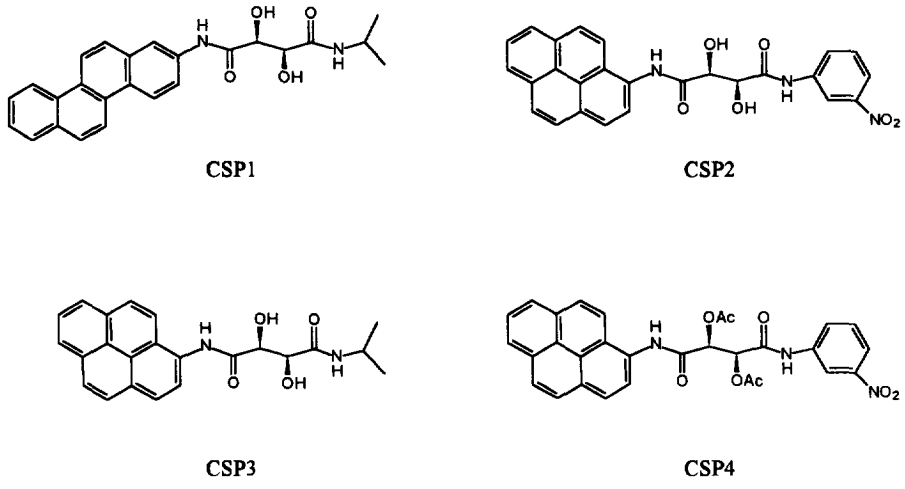
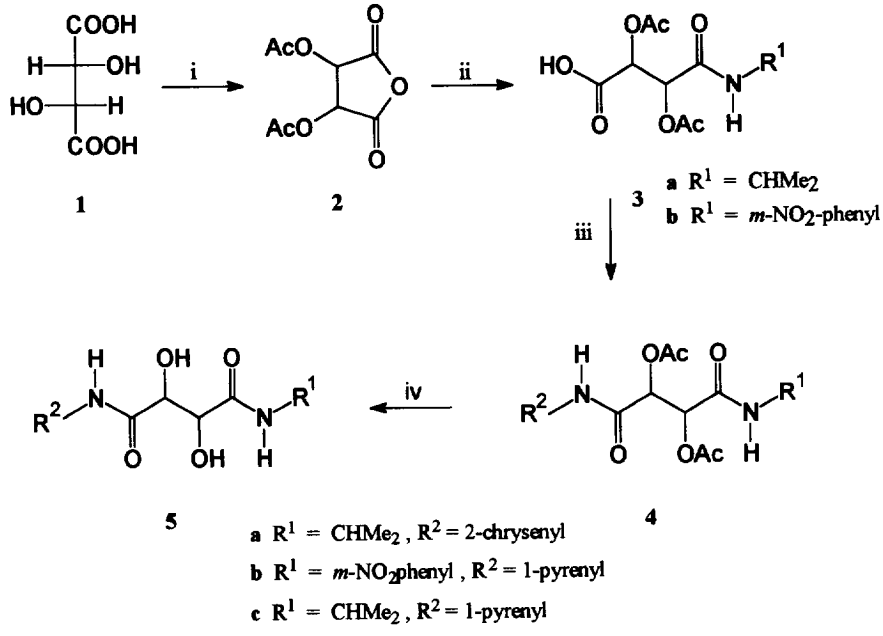



**Fig. 2 New chiral stationary phases**

was no evidence, in the NMR spectra of the crystallised products, for the (R,S) diastereoisomer. It is very unlikely that synchronous inversion of both stereogenic centres can occur.

*Column coating.* A solution of CSP1, CSP2, CSP3 or CSP4 (0.5 mg $ml^{-1}$ in tetrahydrofuran) was cycled at a flow rate of 1 ml $min^{-1}$ through a column (50 x 4.6 mm or 100 x 4.6 mm) packed with 7 μm porous graphitic carbon ("Hypercarb"). Progressive adsorption of the CSP was monitored on-line by measuring the change in the retention time of test solutes until a constant retention time was obtained and this was further confirmed off-line by UV-spectrophotometry until no further uptake appeared to occur. The amount adsorbed was *ca.* 26 mg of CSP1 on a 100 mm column and 16 mg of CSP2 on a 50 mm column (2.6 - 3.0% by weight of PGC). These values correspond approximately to monolayer coverage indicating that the surface density of the chiral selector is comparable to that of chemically bonded phases. It is clear from Fig. 1 that analyte–CSP interaction will involve specific molecular association between analyte and chiral selector rather than a general 'chiral surface' interaction.

*Chromatography.* Analyte solutions (*ca.* 5 μg $ml^{-1}$) were introduced via an autosampler with a 5 μl loop on to a column prepared as above with CSP1 and standard chromatographic parameters were determined (Table 1) for the pair of enantiomers of several chiral compounds, using various different mobile phases. These test compounds were selected to contain functional groups (amino, hydroxy, carbonyl) which were likely to interact with the chiral selector groups under investigation, and to derive their dissymmetry either from the presence of one or more stereogenic centres or from the presence of a binaphthyl moiety. The results show that for the ten test systems studied excellent chiral discrimination was

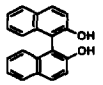
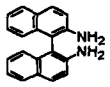
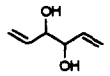
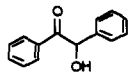
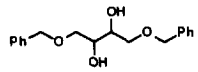
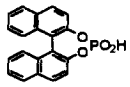
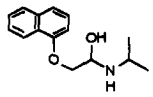
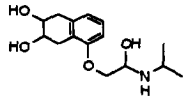
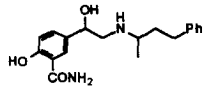
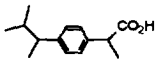



**Scheme 1** *Reagents:* (i) HOAc, $H_2SO_4$; (ii) *either* isopropylamine *or* *m*-nitroanaline; (iii) N-methylmorpholine, $ClCO_2Et$ and *either* 1-aminopyrene *or* 2-aminochrysene; (iv) 0.6M $NH_3$ in MeOH

found in all cases. The intrinsic selectivity lies between 1.10 and 1.31 and is highest for the β-blocker compounds (*eg* entry IX in Table 1) which have similar chemical structure to the chiral selector in CSP1. The resolution showed a slightly greater range, 0.8 - 2.1, the largest values again being found for the β-blockers (*eg* VIII). The detailed nature of the mode of chiral recognition which is exercised by CSP1 will be discussed elsewhere but is evident that the new type of chiral HPLC column described here has excellent potential.

The chromatographic results for CSP3 are not shown since these were very similar to those for CSP1. Not surprisingly the structural change made to the anchor group (chrysenyl to pyrenyl) made little difference to the chiral selectivity. In contrast the results for CSP2 given in Table 2, show significant differences when compared to those for CSP1 and clearly the changed structure of the chiral selector (replacement of the isopropyl N-substituent by a *m*-nitrophenyl group ) alters the enantioselectivity in a subtle way. Some compounds show better enantiomeric separation but other compounds such as hexadien-3,4-diol (III) and propranolol (VII) are unresolved. It is noteworthy that where resolution is achieved with both phases the elution order of enantiomers is the same (where that is known), indicating that the

**Table 1.** Chromatographic parameters for enantiomeric separations on PGC with the chrysene-based chiral phase CSP1.[a]

| No | Chiral analyte[b] | $k_1'$ [c] | $k_2'$ | α | $R_S$ | Mobile phase[d] |
|---|---|---|---|---|---|---|
| I |  | 1.22(S) | 1.40(R) | 1.16 | 0.86 | A |
| II |  | 4.01(R) | 4.39(S) | 1.10 | 1.05 | B |
| III |  | 0.86 | 1.05 | 1.22 | 0.80 | A |
| IV |  | 2.69 | 2.98 | 1.11 | 1.18 | B |
| V |  | 10.10(R,R) | 11.20(S,S) | 1.12 | 1.05 | A |
| VI |  | 1.19(S) | 1.40(R) | 1.18 | 1.02 | C |
| VII |  | 11.98 | 15.05 | 1.26 | 2.10 | D |
| VIII |  | 2.40 | 2.91 | 1.20 | 1.20 | E |
| IX |  | 5.74 | 7.90 | 1.31 | 1.66 | D |
| X |  | 10.6 | 11.6 | 1.09 | 0.78 | A |

[a] PGC is porous graphitic carbon and CSP1 is the compound shown in Scheme 1. [b] Compound names are given in the Experimental section. [c] Elution order of enantiomers (R and S) is only given where this was established unequivocally with pure enantiomers. [d] Mobile phase: A = hexane–2-propanol (95:5); B = hexane–dichloromethane (98:2); C = ammonium acetate in methanol (1 mM); D = ammonium acetate in methanol (100 mM); E = ammonium acetate in methanol (10 mM).

**Table 2.** Chromatographic parameters for enantiomeric separations on PGC with the chiral phases CSP2 and CSP4.[a]

| | CSP2 | | | | CSP4 | | | |
|---|---|---|---|---|---|---|---|---|
| Analyte[a] | $k'_1$ | $k'_2$ | α | MP | $k'_1$ | $k'_2$ | α | MP |
| I | 2.40(S) | 3.10(R) | 1.29 | A | 2.60 | 2.60 | 1.00 | B |
| II | 8.40(R) | 10.20(S) | 1.21 | B | 2.08(R) | 2.17(S) | 1.04 | B |
| III | 4.50 | 4.50 | 1.00 | C | | | | |
| IV | 1.86 | 2.12 | 1.14 | A | 2.03 | 2.93 | 1.45 | B |
| V | 12.90(R,R) | 13.50(S,S) | 1.05 | B | | | | |
| VI | 1.20 | 1.20 | 1.00 | C | 1.00(S) | 1.35(R) | 1.35 | H |
| VII | 13.50 | 13.50 | 1.00 | D | | | | |
| VIII | 4.70 | 5.20 | 1.14 | F | | | | |
| IX | 7.10 | 8.83 | 1.24 | G | 9.70 | 13.50 | 1.40 | I |
| X | 5.90 | 6.60 | 1.12 | D | | | | |

[a] See footnotes to Table 1. The structure of the phases CSP2 and CSP4 are shown in Fig.2. [b] Mobile phase: A = hexane-2-propanol (98:2); B = hexane-dichloromethane (98:2); C = hexane-THF (99:1); D = hexane-THF (95:5); E = ammoniöum acetate in methanol (2.5 mM); F = ammonium acetate in methanol (0.5 mM); G = ammonium acetate in methanol (0.1 mM); H = ammonium acetate in methanol (25 mM); I = ammonium acetate in methanol (50 mM).

underlying chiral recognition mechanism must be similar.

It might be supposed that hydrogen bonding makes a crucial contribution to the interaction between chiral selector and chiral analyte and that blocking the tartarate hydroxy groups would seriously effect the enantiomeric selectivity. Some results using CSP4 (identical to CSP2 except for retention of the acetyl groups) are also shown in Table 2. Surprisingly, for several chiral substrates the selectivity is *increased*, although that is not observed in every case. Evidently the manifold of interactions which contributes to chiral recognition is not easily modeled and further investigation is required.

All of the above results demonstrate that chiral chromatography based on PGC with appropriate adsorbed phases has exciting potential, provide that such columns are stable and have reproducible performance. To test the stationary phase stability, the performance of each column type was monitored periodically with pure test compounds I and III during the passage of *ca.* 4000 ml of mobile phase (2-propanol–hexane, 5:95). Over a range of about 800 injections, retention, selectivity and peak shape were unchanged. If impure analytes are used there can be a build up of strongly retained material which

effectively reduces the active area of the surface with consequent effects on the retention time of test analytes.[7] However flushing the column with a suitable mobile phase (hexane–tetrahydrofuran, 85:15) restores the performance to its original level. Thus it can be concluded that a CSP based on chrysene or pyrene has such a strong affinity for the surface of PGC that bleeding of the stationary phase is completely negligible under the conditions indicated above and in the Tables.

The columns were further tested by the extended passage of mobile phase consisting of water or methanol or mixtures of these, with the pH adjusted between 3 and 12. The performance of all columns was unaffected by such treatment.. This confirms that this type of CSP must be chemically stable under these conditions and that degradation of the stationary phase is unlikely under all normal conditions. Thus a long lifetime can be expected for columns of this type.

## EXPERIMENTAL

A gradient modular HPLC system (Gilson Medical Electronics Inc., Middleton USA) was used for the work with a variable wavelength UV detector. The detector wavelength was set at 210, 225 or 254 nm as required by different analytes. The columns, 50 x 4.6 mm and 100 x 4.6 mm, were packed with 7μm "Hypercarb" porous graphitic carbon ( Shandon Scientific, Runcorn, Cheshire, UK). New compounds were characterised by elemental analysis (Fisons Instruments, EA1108 CHN), nuclear magnetic resonance spectroscopy (JEOL, JNM GX270 FTNMR), infrared spectroscopy (Perkin-Elmer PE983G), optical rotation (Optical Activity, AA-10 automatic polarimeter) and mass spectrometery (Finnigan 1020GC/MS).

2-Aminochrysene was obtained from Lancaster (Lancashire, UK), 1-aminopyrene, *N*-methylmorpholine, ethylchloroformate and isopropylamine from Fluka (Dorset, UK) and (R,R)-tartaric acid and acetic anhydride from BDH Laboratory Supplies (Poole, UK). The enantiomeric compounds are I: (R)-(+)- and (S)-(-)-1,1'-bi(2-naphthol) (Fluka); II: (R)-(+)- and (S)-(-)-1,1'-bi(2-naphthylamine) (Fluka); III: (±)-1,5-hexadiene-3,4-diol (Sigma); IV: (±)-benzoin (Fluka); V: (R,R)-(+)- and (S,S)-(-)-1,4-di-*O*-benzylthreitol (Fluka); VI: (R)-(-)- and (S)-(+)-1,1'-binaphthylene-2,2'-diyl hydrogen phosphate (Aldrich); VII: (±)-propranolol (Sigma); VIII: (±)-nadolol (Sigma); IX: (±)-labetolol (ICI); X: (±)-ibuprofen (Sigma). These and all other chemicals were of analytical grade and were used without any further purification.

(R,R)-*Diacetyltartaric acid anhydride* **2.**—Concentrated sulphuric acid (0.4 ml) was added to a mixture of (R,R)-tartaric acid (11.0 g, 73.3 mmol) in acetic acid anhydride (24 ml) with stirring at room temperature. Following the exothermic reaction the solution was gently refluxed for 10 min and then cooled to 0°C. The crystalline precipitate was collected, washed with benzene (30 ml) and diethyl ether (30

ml) and to afford compound **2** (11.7 g, 54.2 mmol, 74%). m.p. 131-132°C, IR (KBr) $\nu_{max}/cm^{-1}$ 2940 (C-H), 1895, 1825 (anhydride), 1755, 1380 (C=O). This material was used immediately for the next step.

(R,R)-N-*Isopropyl*-O,O-*diacetyltartaric acid monoamide* **3a**.—Isopropylamine (4.7 g, 79.5 mmol) was added dropwise at 0°C under argon to (R,R)-diacetyltartaric acid anhydride (8.0 g, 37 mmol) in dichloromethane (40 ml) and the mixture stirred for 20 min. The solvent was removed under reduced pressure, the residue taken up in ethyl acetate (550 ml) and the solution washed with hydrochloric acid (5M, 70 ml) saturated with NaCl then with brine (3 x 40 ml) and dried ($MgSO_4$). Evaporation of the solvent gave a crude material which recrystallized (2-propanol–hexane) to give compound **3a** as colourless crystals (9.2 g, 33.4 mmol, 90%), m.p. 176°C (Found: C, 48.1; H, 6.2; N, 5.0. Calc. for $C_{11}H_{17}O_7N$: C, 48.4; H, 6.4; N, 5.0); $[\alpha]_D^{22}$ -25.2 (*c* 0.19, DMSO); $\nu_{max}/cm^{-1}$ 3335 (N-H), 2975 (O-H), 1750 (C=O ester), 1635 (C=O amide), 1555 (amide); $\delta_H$ (DMSO-$d_6$, 270 MHz) 1.01 (d, 3H, *J* = 6.6 Hz, CH*Me*$_2$), 1.05 (d, 3H, *J* = 6.6 Hz, CH*Me*$_2$), 2.02 (s, 3H, OCOMe), 2.07 (s, 3H, OCOMe), 3.89 (m, 1H, C*H*Me$_2$), 5.44 (d, 1H, *J* = 3.7 Hz, C*H*CH), 5.52 (d, 1H, *J* = 3.7 Hz, CHC*H*), 7.64 (br d, 1H, *J* = 7.4 Hz NH), 11.1 (br s, 1H, OH); m/z 275 ($MH^+$).

(R,R)-N-(2-*Chrysenyl*)-N'-*isopropyl*-*O,O-diacetyltartaramide* **4a**.—Compound **3a** (0.71 g, 2.0 mmol) in dry THF (10 ml) was cooled to -21°C with stirring and *N*-methylmorpholine (0.22g, 2.0 mmol) added dropwise followed by ethylchloroformate (0.2g, 2.0 mmol). After 20 min at -21°C, 2-amino-chrysene (0.40g, 1.7 mmol ) in THF (2.5 ml) was added dropwise and the mixture stirred for a further 24 h at 0°C. The solvent was evaporated and the residue taken up in EtAc (100 ml) and the solution washed with a 10% v/v hydrochloric acid solution (3 x 10 ml), saturated sodium bicarbonate (3 x 10 ml) and brine (3 x 10 ml) and dried. The solvent was removed under vacuum and the residue triturated with diethylether to afford **4a** as pale brown powder (0.45g, 0.90 mmol, 53%). m.p. 235-236°C (Found: C, 68.6; H, 5.55; N, 5.5. Calc. for $C_{29}H_{28}O_6N_2.1/2\ H_2O$: C, 68.3; H, 5.7; N, 5.5); $[\alpha]_D^{26}$ +50 (*c* 0.85, THF); $\nu_{max}/cm^{-1}$ 3260 (N-H), 1740 (C=O ester), 1660 (C=O amide); $\delta_H$ (DMSO-$d_6$) 1.06 (d, 3H, *J* = 6.5 Hz, CH*Me*$_2$), 1.12 (d, 3H, *J* = 6.5 Hz, CH*Me*$_2$), 2.21 (s, 3H, OCOMe), 2.23 (s, 3H, OCOMe), 3.94 (m, 1H, C*H*Me$_2$), 5.70 (d, 1H, *J* = 2.4 Hz, C*H*CH), 5.93 (d, 1H, *J* = 2.4 Hz, CHC*H*), 7.69-9.02 (m, 12H, aromatic, NH), 10.47 (br s, 1H, NH); m/z 500 ($MH^+$)

(R,R)-N-(2-*Chrysenyl*)-N'-*isopropyltartaramide* **5a**.—To compound **4a** (0.25g, 0.5 mmol) in methanol (2 ml) at 0 °C, methanolic ammonia (0.6 M, 4 ml) was added and the mixture stirred for 4h. The precipitate was collected, washed (methanol) and recrystallized ($HCONMe_2$) to give **5a** as a cream solid (0.20g, 0.48 mmol, 96%), m.p. 259°C (Found: C, 72.2; H, 5.85; N, 6.7. Calc for $C_{25}H_{24}O_4N_2$: C,72.1; H, 5.8; N, 6.7); $[\alpha]_D^{24}$ +119 (*c* 0.28, DMSO); $\nu_{max}/cm^{-1}$ 3320, 3265 (br, N-H, OH), 1660 (C=O), 1540

(amide); $\delta_H$ (DMSO-$d_6$) 1.13 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$), 1.16 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$ ), 4.0 (m, 1H, C*H*Me$_2$), 4.40, 4.64 (2 dd, 2H, $J_{AX}$ = 1.5 Hz, $J_{OH}$ = 7.5 Hz, CHCH), 5.95, 6.24 (2 d, 2H, 2 x OH), 7.56 (d, 1H, $J$ = 8.0 Hz, NH), 7.68-9.16 (m, 11H, aromatic), 9.96 (s, 1H, NH); m/z 416 ($MH^+$)

(R,R)-N-(3-*Nitrophenyl*)-O,O-*diacetyltartaric acid monoamide* **3b**.—3-Nitroaniline (7.3 g, 53 mmol) in THF (10 ml) was added dropwise under argon to (R,R)-diacetyltartaric acid anhydride (11.5 g, 53 mmol) in THF (75 ml) and the mixture stirred for a 24 h. The solvent was removed under reduced pressure, the residue was taken up in ethyl acetate (50 ml) and the solution extracted with saturated $NaHCO_3$ solution (4 x 10 ml). This aqueous extract was taken to pH 1.0 (conc. HCl), sodium chloride was added and mixture extracted with EtAc (40 ml). This extract was worked up to give compound **3b** as pale brown powder (14.2 g, 40.1 mmol, 76%), m.p. 144°C (Found: C, 47.6; H, 3.9; N, 7.75; Calc for $C_{14}H_{14}O_9N_2$; C, 47.5; H, 3.9; N, 7.9); $[\alpha]_D^{26}$ +8.4 (*c* 2.4, THF); $\nu_{max}/cm^{-1}$ 3330 (N-H), 2600-3100 (O-H), 1750 (C=O), 1600 (C=C aromatic), 1530 and 1350 ($NO_2$); $\delta_H$ (DMSO-$d_6$) δ 2.06 (s, 3H, OCOMe), 2.16 (s, 3H, OCOMe), 5.61 (d, 1H, $J$ = 3.2 Hz, C*H*CH), 5.68 (d, 1H, $J$ = 3.2 Hz, CHC*H*), 7.63-8.55 (m, 4H, aromatic), 10.7 (s, 1H, NH), 13.7 (br s, 1H, OH); m/z ;354 ($MH^+$).

(R,R)-N-(3-*Nitrophenyl*)-N'-(1-*pyrenyl*)-O,O-*diacetyltartaramide* **4b**.—Using the method described above for **4a**, 1-aminopyrene and **3b** were condensed to give **4b,** obtained as a green solid (0.76 g, 1.38 mmol, 55%), m.p. 258°C (Found: C, 64.4; H, 4.0; N, 7.5; Calc. for $C_{30}H_{23}O_8N_3.1/2H_2O$, C, 64.1; H, 4.3; N, 7.5); $[\alpha]_D^{24}$ -5.9 (*c* 0.41, DMSO$\nu_{max}/cm^{-1}$ 3250 (N-H), 1740 (C=O ester), 1680 (C=O amide), 1600 (C=C aromatic), 1535, 1350 ($NO_2$) and 735 (C-H aromatic); $\delta_H$ (DMSO-$d_6$) 2.21 (s, 3H, OCOMe), 2.30 (s, 3H, OCOMe), 5.86 (d, 1H, $J$ = 3.0 Hz, C*H*CH), 6.03 (d, 1H, $J$ = 3.0 Hz, CHC*H*), 7.63-8.55 (m, 13H, aromatic), 10.69, 10.82 (2 br s, 2H, 2 x NH); m/z ; 553 ($MH^+$).

(R,R)-N-(3-*Nitrophenyl*)-N'-(1-*pyrenyl*)*tartaramide* **5b**.—Compound **4b** was hydrolysed as described above and the product recrystallized (acetone-water) to give **5b** (0.34 g, 0.72 mmol, 95%) as a yellow-green solid, m.p. 215-216°C (Found: C, 64.4; H, 4.1; N, 8.6; calc. for $C_{26}H_{19}O_6N_3.H_2O$: C, 64.1; H, 4.3; N, 8.6); $[\alpha]_D^{26}$ +125 (*c* 0.0118, THF); $\nu_{max}/cm^{-1}$ 3410, 3340 (br, N-H, OH), 1665 (C=O), 1600 (C=C aromatic),1530, 1335 ($NO_2$), 735 (C-H aromatic); $\delta_H$ (DMSO-$d_6$) 4.67, 4.75 (2 dd, 2H, $J_{AX}$ = 1.8 Hz, $J_{OH}$ = 6.8 Hz, CHCH), 6.38 (d, 2H, $J$ = 6.8 Hz, 2 x OH), 7.65-8.94 (m, 13H, aromatic), 10.20, 10.40 (2 s, 2H, 2 x NH); m/z ; 469 ($MH^+$).

(R,R)-N-*Isopropyl*-N'-(1-*pyrenyl*)-O,O-*diacetyltartaramide* **4c**.—Using the method described above for **4a**, 1-aminopyrene and compound **3a** were condensed to give **4c** (0.79 g, 1.67 mmol, 72%) as dark cream solid, m.p. 235-236°C (Found: C, 68.3; H, 5.5; N, 5.9; Calc. for $C_{27}H_{26}O_6N_2$: C, 68.3; H, 5.5; N, 5.7); $[\alpha]_D^{22}$ <2 (*c* 0.72, DMSO); $\nu_{max}/cm^{-1}$ 3260 (N-H), 1740 (C=O ester), 1660 (C=O amide); $\delta_H$

(DMSO-$d_6$) 1.07 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$), 1.13 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$), 2.21 (s, 3H, OCOMe), 2.23 (s, 3H, OCOMe), 3.94 (m, 1H, C*H*Me$_2$), 5.70 (d, 1H, $J$ = 2.4 Hz, C*H*CH), 5.89 (d, 1H, $J$ = 2.4 Hz, CHC*H*), 7.96-8.33 (m, 10H, aromatic, NH), 10.6 (br s, 1H, NH); m/z ; 474 ($MH^+$).

(R,R)-N-*Isopropyl*-N'-(1-*pyrenyl*)*tartaramide* **5c**.—Compound **4b** was hydrolysed as described above and the product recrystallized (acetone-water) to give **5c** (0.45 g, 1.15 mmol, 96%) as a pale grey crystals, m.p. 229°C (Found: C, 70.8; H, 5.5; N, 7.1. Calc. for $C_{23}H_{22}O_4N_2$: C, 70.8; H, 5.7; N, 7.2); $[\alpha]_D^{22}$ +78.4 (*c* 0.85, DMSO); $\nu_{max}/cm^{-1}$ 3380, 3240 (br, N-H, O-H), 1660 (C=O), 1550 (amide); $\delta_H$ (DMSO-$d_6$) 1.13 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$), 1.15 (d, 3H, $J$ = 6.5 Hz, CH*Me*$_2$ ), 4.0 (m, 1H, C*H*Me$_2$), 4.39, 4.63 (2 dd, 2H, $J_{AX}$ = 1.5 Hz, $J_{OH}$ = 7.5 Hz, CHCH), 5.90, 6.19 (2 d, 2H, 2 x OH), 7.56 (d, 1H, $J$ = 8.0 Hz, NH), 8.05-8.36 (m, 9H, aromatic), 10.10 (br s, 1H, NH); m/z ; 390 ($MH^+$)

## REFERENCES

1. Taylor, D. R.; Maher, K. M., *J. Chromatogr. Sci.*, **1992**, 30, 67
2. Pirkle, W. H.; Pochapsky, T. C., *Chem. Rev.*, **1989**, 89, 347.
3. Poole, C. F.; Poole, S. K., *Chromatography Today*, Elsevier, Amsterdam, 1991.
4. Gilbert, M. T.; Knox, J. H.; Kaur, B., *Chromatographia*, **1982**, 16, 138.
5. Knox, J. H.; Kaur, B.; Millward, G.R., *J. Chromatogr.*,**1986**, 352, 3.
6. Monser, L. I.; Greenway, G. M., unpublished work.
7. Monser, L. I.; Greenway, G. M., *Anal. Commun.*, **1996**, in press.
8. Dobashi, Y.; Hara, H., *J. Org. Chem.*, **1987**, 52, 2490.
9. Heldin, E.; Huynh, N.; Petersson, C., *J. Chromatogr.*, **1991**, 585, 35.
10. Wilkins, S.; Taylor, D.; Smith, R., *J. Chromatogr. A*, **1995**, 697, 587.
11. Bridger, G., *Ph.D. Thesis*, UMIST, Manchester, 1987.

(*Received in UK* 4 *February* 1996)