Axially chiral cyclopentadienyl ligands: stereoselective synthesis of 1-substituted-9-(1′-naphthyl)fluorenes and retention of axial chirality in the fluorenyl carbanions[1]

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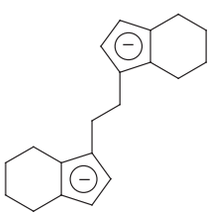
1-(*tert*-Butyl- or 1-(*p*-tolyl-sulfinyl)naphthalene-2-carboxylate esters undergo coupling reactions with fluorenyllithiums substituted at the 1-position, providing 1-(1′-substituted-fluoren-9′-yl)naphthalene-2-carboxylate esters as single rotamers where the naphthalene ester substituent is *syn* to the fluorene 9-H. The stereoselectivity of the coupling reaction, with respect to asymmetric induction at the fluorene 9-C, varies from 21–95% (ee or de) dependant on the sulfoxide, ester and fluorene substituents, and the reaction temperature. The stereomutation of +*ac*(*R*)-1-methyl-9-(2′-methoxymethyl-1′-naphthyl)fluorene 33 into *ent*-33 was achieved through thermal atropisomerisation of 33 to the −*sc*(*R*)-rotamer 34, followed by lithiation of 34 and then reprotonation of the resultant fluorenyllithium 35, demonstrating the retention of axial chirality in the fluorenyl carbanion.

Introduction

Chiral cyclopentadienylmetal complexes have been used, both stoichiometrically and catalytically, in a range of asymmetric transformations.[2] Some of the most widely studied complexes incorporate the ethylene-1,2-bis(tetrahydro-1-indenyl) ligand **1**.[3] C_2-Symmetric *ansa*-titanocene and -zirconocene complexes



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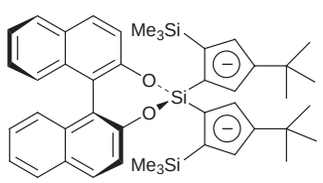

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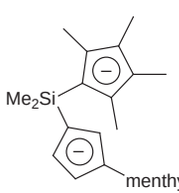

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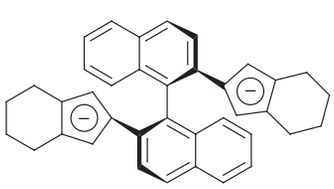

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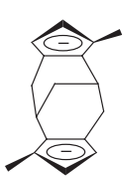

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incorporating **1** have been used in a number of catalytic reactions with high stereoselectivities often achieved. Examples of applications include α-olefin polymerisation,[4] hydrogenation of olefins[5] and imines,[6] hydrosilylation of ketones,[7] olefin carbomagnesiation[8] and Diels–Alder reactions.[9]

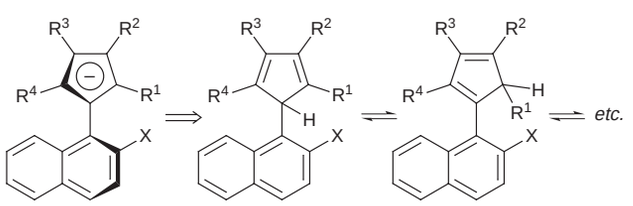
With ligands such as **1**, where the cyclopentadienyl ring is asymmetrically substituted, the faces of the cyclopentadienyl ring are enantiotopic (planarly prochiral) and metalation produces a racemic metal complex which must then be resolved (an additional separation of a *meso* isomer is also required in the preparation of complexes incorporating **1**[10]). By introduction of a stereogenic bridge or side-chain, the faces of an asymmetrically substituted cyclopentadienyl ring become diastereotopic and metalation can in principle be selective for the formation of a single stereochemically pure complex; such is the case for ligand **2**, which provides a single C_2-symmetric *ansa*-yttrocene complex.[11] In other cases separation of diastereoisomeric metal complexes may be necessary, for instance the silyl-bridged ligand **3**, where stereochemically pure lanthanide[12] and Group 4[13] metallocenes are obtained only after fractional crystallisation of diastereoisomeric mixtures initially formed on metalation. The racemisation or epimerisation of the planar chiral element of asymmetrically substituted cyclopentadienylmetal complexes under certain reaction conditions presents another potential drawback, as this may compromise the stereoselectivity of reactions mediated by the complex. Such stereolability has been reported for complexes involving the ligands **1**[14] and **3**.[12,15]

In order to avoid the problems associated with heterotopic ligand faces and still retain a helical chiral environment about the metal analogous to chiral complexes with ligand **1**, symmetrically substituted bis(cyclopentadienyl) ligands bridged by axially chiral biaryls have been prepared, for example ligand **4**.[16,17] Recently, Buchwald and co-workers[14] proposed another solution: the introduction of a stereogenic double-bridge between two asymmetrically substituted cyclopentadienyl groups. This approach was successfully demonstrated by preparation of an *ansa*-titanocene complex using ligand **5**, however, the highly constrained geometry of the bicyclic ligand precluded metalation with other Group 4 transition metals.

We were interested in an approach to chiral cyclopentadienyl ligands which addressed the problems of heterotopic ligand faces and incorporated a high degree of structural variability in the ligand design. The proposed ligands **6** (Scheme 1) would have a second metal coordination site X constrained to one face of an asymmetrically substituted cyclopentadienyl ring through hindered rotation about the bond between the cyclopentadienyl ring and a naphthalene moiety. The formation of chelating complexes using **6** would necessarily lead to the stereospecific generation of a planarly chiral cyclopentadienylmetal complex. The second metal coordination site could be another cyclo-

pentadienyl group, potentially leading to *ansa*-metallocene complexes, or a donor heteroatom such as N, O, P or S. While there has been increasing interest in cyclopentadienyl ligands containing pendant donor heteroatoms capable of internally coordinating to the metal,[18] to date there have been very few reports of chiral versions of these ligands.[19–21]

Strategies for the preparation of enantiopure cyclopentadienyl ligands **6** need to take into consideration that the precursor cyclopentadiene compounds can exist in tautomeric forms. While tautomers with an sp^2–sp^2 bond between the cyclopentadiene and naphthalene moieties, for example **7b**, might be anticipated to exist as stable atropisomers, the barrier to rotation would be expected to be much lower in tautomer **7a** with an sp^3–sp^2 linkage. There is, nonetheless, one system corresponding to **7a** in which stable atropisomers are known, *viz.* 9-arylfluorenes. Hindered rotation in 9-arylfluorenes was first reported by Chandross and Sheley in 1968,[22] and since then the properties and reactions of this system have been the subject of numerous investigations, particularly by Ōki and co-workers.[23,24] Asymmetric substitution of the fluorene nucleus of a 9-(1′-naphthyl)fluorene provides a system containing two stereogenic elements: a stereogenic centre at the fluorene 9-C and a stereogenic axis due to hindered rotation about the C_9–$C_{1'}$ (sp^3–sp^2) bond. Deprotonation of a non-racemic asymmetric 9-(1′-naphthyl)fluorene was expected to lead to a fluorenyl carbanion which remained non-racemic through hindered rotation about the C_9–$C_{1'}$ (now sp^2–sp^2) bond, as required in the proposed ligands **6**. However, contrary to this expectation, Ōki and co-workers have reported the stereomutation of 9-arylfluorene rotamers during reaction with butyllithium (BuLi),[25,26] and have interpreted the results to indicate that facile rotation about the aryl–fluorenyl bond occurs in the 9-arylfluorenyllithium intermediates.[26,27] Nevertheless, we believed the use of achiral compounds in these studies precluded an unambiguous determination of the mechanism of stereomutation. Here we describe the stereoselective synthesis of 1-substituted-9-(1′-naphthyl)fluorenes † and experiments demonstrating that fluorenyl carbanions obtained from these compounds do indeed retain an axial chiral element.



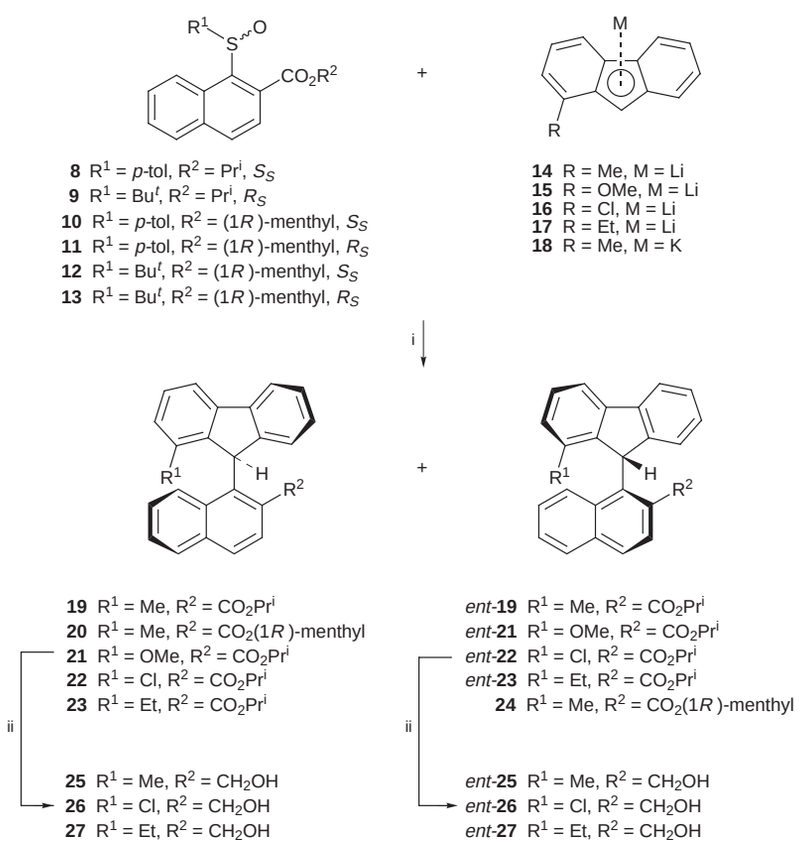
6 **7a** **7b**

Scheme 1

Results and discussion

We have recently described an enantioselective synthesis of 1,1′-binaphthyls through ligand coupling reactions of 1-(alkyl- or 1-(aryl-sulfinyl)naphthalenes, bearing electron-withdrawing 2-substituents, with 1-naphthyl Grignard reagents.[28] In adapting this reaction to the stereoselective synthesis of asymmetric 9-(1′-naphthyl)fluorenes, we chose to introduce substituents into the 1-position of the fluorenyl ligand, this position being seen as the most likely to influence the stereochemical course of the coupling reaction. Reaction of the (*S*)-*p*-tolyl sulfoxide **8**[28] (Scheme 2) with 1.5 mol equiv. of 1-methylfluorenyllithium **14** (generated by metalation of 1-methylfluorene with BuLi) in tetrahydrofuran (THF) at 0 °C for 30 min furnished the fluorene **19** in quantitative yield. The fluorene **19** was formed as a single rotamer, with none of the alternative rotamer evident by TLC analysis of the reaction mixture or inspection of the high field ^{1}H NMR spectrum of the isolated product. The relative configuration of **19**, with the naphthalene ester substituent *syn* to the fluorene 9-H, was determined by comparison of the ^{1}H NMR spectrum with the spectra of related compounds

† The fluorenes referred to here and elsewhere in this paper are 9*H*-fluorenes.



8 R^1 = *p*-tol, R^2 = Pr^i, S_S
9 R^1 = Bu^t, R^2 = Pr^i, R_S
10 R^1 = *p*-tol, R^2 = (1*R*)-menthyl, S_S
11 R^1 = *p*-tol, R^2 = (1*R*)-menthyl, R_S
12 R^1 = Bu^t, R^2 = (1*R*)-menthyl, S_S
13 R^1 = Bu^t, R^2 = (1*R*)-menthyl, R_S

14 R = Me, M = Li
15 R = OMe, M = Li
16 R = Cl, M = Li
17 R = Et, M = Li
18 R = Me, M = K

19 R^1 = Me, R^2 = CO_2Pr^i
20 R^1 = Me, R^2 = CO_2(1*R*)-menthyl
21 R^1 = OMe, R^2 = CO_2Pr^i
22 R^1 = Cl, R^2 = CO_2Pr^i
23 R^1 = Et, R^2 = CO_2Pr^i

ent-**19** R^1 = Me, R^2 = CO_2Pr^i
ent-**21** R^1 = OMe, R^2 = CO_2Pr^i
ent-**22** R^1 = Cl, R^2 = CO_2Pr^i
ent-**23** R^1 = Et, R^2 = CO_2Pr^i
24 R^1 = Me, R^2 = CO_2(1*R*)-menthyl

25 R^1 = Me, R^2 = CH_2OH
26 R^1 = Cl, R^2 = CH_2OH
27 R^1 = Et, R^2 = CH_2OH

ent-**25** R^1 = Me, R^2 = CH_2OH
ent-**26** R^1 = Cl, R^2 = CH_2OH
ent-**27** R^1 = Et, R^2 = CH_2OH

Scheme 2 *Reagents and conditions:* i, see Table 1; ii, $LiAlH_4$ (excess), diethyl ether, 25 °C, 30 min

Table 1 Reaction of 1-(*tert*-butyl- or 1-(*p*-tolyl-sulfinyl)naphthalene-2-carboxylate esters with 1-substituted-fluorenylmetals

Entry	Sulfoxide[a]	Fluorenylmetal[b]	Temp./°C (Time/h)	Product (Yield, %)	Product ee or de, %[c]
1	**8**	**14**	0 (0.5)	**19** (100)	57[d]
2	**9**	**14**	0 (0.5)	*ent*-**19** (100)	78[d]
3	**10**	**14**	0 (0.5)	**20** (93)	75
4	**11**	**14**	0 (0.5)	**24** (91)	70
5	**10**	**14**	−78 (20)	**20** (50)	86
6	**11**	**14**	−78 (20)	**24** (52)	84
7	**12**	**14**	0 (0.5)	**20** (98)	84
8	**13**	**14**	0 (0.5)	**24** (93)	82
9	**12**	**14**	−78 (20)	**20** (10)	95
10	**13**	**14**	−78 (20)	**24** (9)	86
11	**9**	**15**	0 (0.5)	**21**/*ent*-**21** (100)	21
12	**9**	**16**	0 (0.5)	**22**/*ent*-**22** (100)	36[d]
13	**9**	**17**	0 (0.5)	**23**/*ent*-**23** (100)	61[d]
14	**10**	**14**[e]	0 (1)	**20** (80)	72
15	**10**	**14**[f]	0 (0.5)	**20** (93)	68
16	**10**	**18**	0 (12)	no reaction	—
17	**10**	**18**[g]	0 (1)	**20** (70)	76
18	**10**	**18**[h]	0 (1)	**20** (82)	72
19	**10**	**14**[i]	0 (12)	no reaction	—

[a] Sulfoxides **8** and **9** were of >99% ee, sulfoxides **10** and **11** were of >98% de, sulfoxides **12** and **13** were of 97 and 98% de, respectively. [b] Excepting entries 14 and 15, reactions were conducted in THF. [c] Ee for entries 1, 2, 5, 6 and 7, de for all other entries. [d] Ee inferred from that of the corresponding naphthalene-2-methanol compounds. [e] Reaction conducted in diethyl ether. [f] Reaction conducted in DME. [g] In the presence of LiCl (1.1 equiv.). [h] In the presence of $MgCl_2$ (2 equiv.). [i] In the presence of $Me_2S{\cdot}CuBr$ (1 equiv.).

reported in the literature. In particular, the isopropoxy methine signal had a chemical shift typical for this group of δ_H 5.39 in $CDCl_3$ solution. For the alternative rotamer, with the ester substituent *anti* to the fluorene 9-H, a substantial shielding of this proton would be expected through the magnetic anisotropy of the fluorene ring. For example, Saito and Ōki reported[29] that in the ^{1}H NMR spectrum of methyl 1-(9′-fluorenyl)naphthalene-2-carboxylate the methyl signal appears at a typical chemical shift of δ_H 3.95 in $CDCl_3$ for the *sp* rotamer (ester substituent *syn* to the fluorene 9-H),‡ while for the *ap* rotamer (ester substituent *anti* to the fluorene 9-H) significant shielding to δ_H 2.83 occurs.

The enantiomeric purity of the ester **19** was unable to be determined directly. However, the enantiomeric excess (ee) of the alcohol **25** [obtained quantitatively on treatment of **19** with lithium aluminium hydride (LAH) in diethyl ether at room temperature (Scheme 2)], and by inference that of the ester **19**, was determined to be 57% by analysis of the benzoate derivative using a Chiralpak OT(+) chiral HPLC column (entry 1, Table 1). A higher level of enantioselectivity was observed in the reaction of the (*R*)-*tert*-butyl sulfoxide **9**[28] (Scheme 2). Treatment of **9** with 1.5 mol equiv. of **14** in THF at 0 °C for 30 min furnished the fluorene *ent*-**19** as a single rotamer in quantitative yield, which on reduction provided *ent*-**25** in 78% ee (entry 2, Table 1).

In order to determine the absolute configurations of the products of these reactions, the 2-lithio derivative of (*S*)-1-(*p*-tolylsulfinyl)naphthalene, obtained through metalation with 1.1 mol equiv. of lithium diisopropylamide (LDA) in THF at −78 °C for 20 min,[28] was caused to react with 1.1 mol equiv. of (1*R*)-menthyl chloroformate in THF at −78 °C for 5 h, furnishing the (1*R*)-menthyl ester **10** in 28% yield. Reaction of **10** (Scheme 2) with 1.5 mol equiv. of **14** in THF at 0 °C for 30 min furnished the fluorene **20** in 93% yield. The diastereomeric excess (de) of the fluorene **20** was determined to be 75% by HPLC analysis (entry 3, Table 1). Once again, only a single rotamer was evident by TLC analysis of the reaction mixture or inspection of the high field ^{1}H NMR spectrum of the isolated product, where the menthyloxy methine signals for the major and minor diastereoisomers had typical chemical shifts of δ_H 5.10 and 5.08, respectively, in $CDCl_3$ solution. Several recrystallisations from aqueous acetone furnished crystals of **20** (96% de) suitable for X-ray crystallographic analysis,[1] which allowed inference of the *R* absolute configuration at the fluorene 9-C and confirmed that the single rotamer formed in the reaction has the ester substituent *syn* to the fluorene 9-H; the configuration of the axial stereogenic element is, therefore, +*ac*. Reduction of +*ac*(*R*)-**20** of 75% de furnished **25** (quantitative yield) in 75% ee, establishing the absolute configurations of **19**, *ent*-**19**, **25** and *ent*-**25** as +*ac*(*R*), −*ac*(*S*), +*ac*(*R*) and −*ac*(*S*), respectively.

The epimeric *p*-tolyl sulfoxide **11** was obtained in 37% yield by reaction of the 2-lithio derivative of (*R*)-1-(*p*-tolylsulfinyl) naphthalene with 1.1 mol equiv. of (1*R*)-methyl chloroformate during 3.5 h in THF at −78 °C. Reaction of **11** (Scheme 2) with 1.5 mol equiv. of **14** in THF at 0 °C for 30 min furnished the −*ac*(*S*)-fluorene **24** in 91% yield and 70% de (entry 4, Table 1). The stereoselectivities of the reactions of **10** and **11** with **14** were increased on cooling to −78 °C, providing +*ac*(*R*)-**20** and −*ac*(*S*)-**24** in 86 and 84% de, respectively, but with the yields reduced to 50 and 52%, respectively, after a reaction time of 20 h (entries 5 and 6, Table 1).

With the results obtained thus far, it appeared that optimum stereoselectivity would be obtained from the reaction of **14** with a *tert*-butyl sulfoxide bearing a menthyl ester side-chain. Accordingly, (*S*)-1-(*tert*-butylsulfinyl)naphthalene of 90% ee was converted to the 2-lithio derivative through metalation with 1.1 mol equiv. of BuLi in THF at −78 °C for 10 min,[28] and this was then caused to react with 1.1 mol equiv. of (1*R*)-menthyl chloroformate in THF at −78 °C for 2 h, furnishing the (1*R*)-menthyl ester **12** in 32% yield and 90% de (HPLC analysis). The epimeric sulfoxide was obtained in a similar way through reaction of the 2-lithio derivative of (*R*)-1-(*tert*-butylsulfinyl)-naphthalene (90% ee) with 1.1 mol equiv. of (1*R*)-menthyl chloroformate in THF at −78 °C for 2 h, furnishing the (1*R*)-menthyl ester **13** in 40% yield and 90% de. Recrystallisation of **12** and **13** increased the stereochemical purity to 97 and 98% de, respectively. Reaction of the (*S*)-*tert*-butyl sulfoxide **12** (Scheme 2) with 1.5 mol equiv. of **14** in THF at 0 °C for 30 min furnished the +*ac*(*R*)-fluorene **20** in 98% yield and 84% de (entry 7, Table 1). Similar reaction of the (*R*)-*tert*-butyl sulfoxide **13** furnished the −*ac*(*S*)-fluorene **24** in 93% yield and 82% de (entry 8, Table 1). The stereoselectivities of the reactions of **12** and **13** with **14** were also increased on cooling to −78 °C, providing +*ac*(*R*)-**20** and −*ac*(*S*)-**24** in 95 and 86% de, respectively, but with the

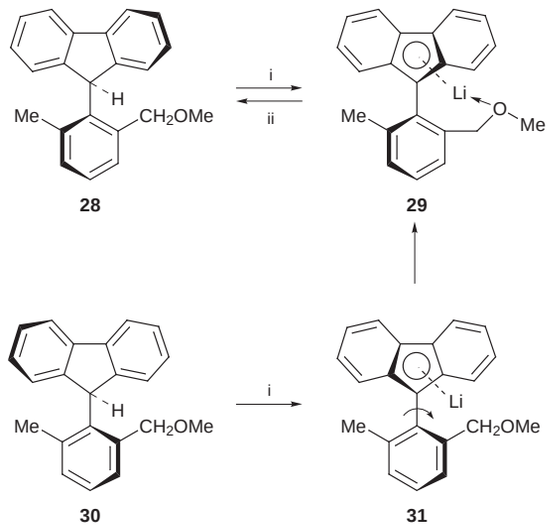
‡ The nomenclature for atropisomers about an sp^3–sp^2 bond is described in ref. 23

yields substantially reduced to 10 and 9%, respectively, after a reaction time of 20 h (entries 9 and 10, Table 1).

Our attention next turned to examination of other factors which may influence the stereoselectivity of the coupling reactions. Using the *tert*-butyl sulfoxide **9**, the influence of the 1-substituent of the fluorenyllithium on stereoselectivity was examined. Reaction of **9** with 1.2 mol equiv. of 1-methoxyfluorenyllithium **15**, 1-chlorofluorenyllithium **16** or 1-ethylfluorenyllithium **17** (generated through metalation of the fluorenes with BuLi) in THF at 0 °C for 30 min furnished the coupled products **21**, **22** and **23** (or their enantiomers), respectively, as single rotamers in quantitative yields (Scheme 2). In the ^{1}H NMR spectra of the products the isopropoxy methine signals appear at δ_H 5.37 to 5.40 in $CDCl_3$ solution, indicating that the ester substituent is *syn* to the fluorene 9-H in all cases. The absolute configurations of the major enantiomers formed in these coupling reactions have not been determined, although it is likely that the sense of asymmetric induction in the case of the reaction with **17** is the same as that determined for **14**, *i.e.* the major enantiomer is probably the −*ac*(*S*)-fluorene *ent*-**23**. The enantiomeric excess of **21**/*ent*-**21** was determined to be 21% (entry 11, Table 1) by ^{1}H NMR spectroscopy in the presence of tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]-europium(III) [Eu(hfc)$_3$]. Compounds **22**/*ent*-**22** and **23**/*ent*-**23** were quantitatively reduced to the corresponding alcohols **26**/*ent*-**26** and **27**/*ent*-**27**, respectively (Scheme 2), and the enantiomeric excesses determined to be 36 and 61%, respectively, by analysis of the benzoate derivatives using a Chiralpak OT(+) chiral HPLC column (entries 12 and 13, Table 1).

Using the *p*-tolyl sulfoxide **10**, the influence of reaction solvent and metal counterion was examined. The reaction of **10** with 1-methylfluorenyllithium **14** in diethyl ether or 1,2-dimethoxyethane (DME) had little impact on the stereoselectivity of the reaction, providing +*ac*(*R*)-**20** in yields of 80 and 93%, respectively, and in 72 and 68% de, respectively (entries 14 and 15, Table 1). Treatment of **10** with 1-methylfluorenylpotassium **18** (generated through reaction of 1-methylfluorene with potassium hydride) in THF at 0 °C for 12 h failed to produce any coupled products (entry 16, Table 1). However, the reaction using **18** did proceed with the inclusion of either LiCl (entry 17, Table 1) or $MgCl_2$ (entry 18, Table 1), providing +*ac*(*R*)-**20** in 70 and 82% yield, respectively, and in 76 and 72% de, respectively, suggesting that Lewis acid activation of the sulfoxide substrate by the fluorenylmetal counterion may be necessary for the coupling reaction to take place. Transmetalation of **14** with copper(I) bromide–dimethyl sulfide complex also resulted in the failure of the coupling reaction with **10** (entry 19, Table 1).

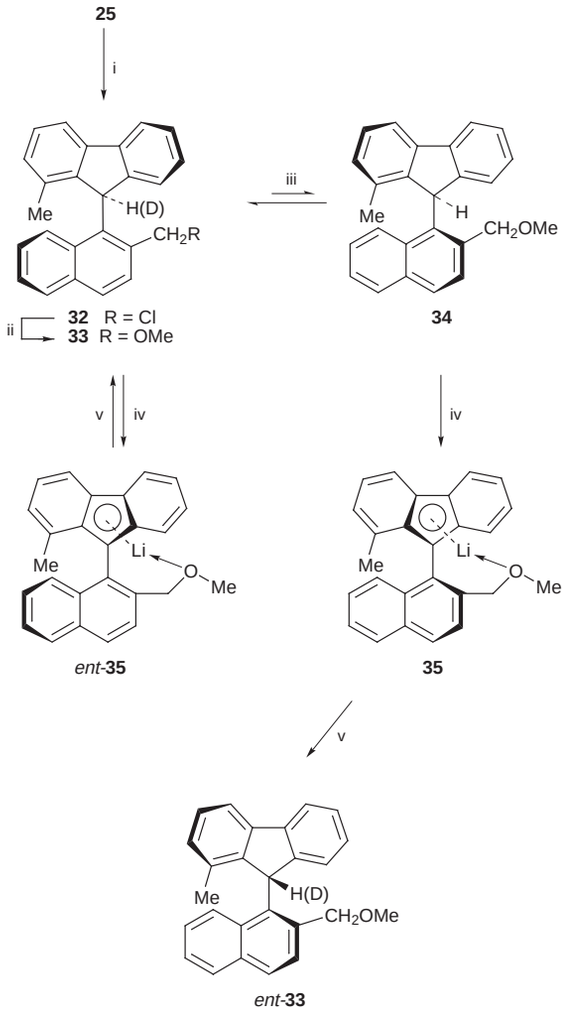
With optically active 9-(1′-naphthyl)fluorenes in hand we sought to resolve the mechanism of stereomutation of 9-arylfluorene rotamers during reaction with BuLi. Ōki and coworkers[26] have investigated the rates of deprotonation of 9-(2-methoxymethyl-6-methylphenyl)fluorene rotamers with a large excess of BuLi in benzene–hexane and determined that the *sp* rotamer **28** (Scheme 3) shows pseudo-first order kinetics, while the *ap* rotamer **30** shows pseudo-second order kinetics. The ^{1}H NMR spectra of both reactions indicated the formation of a common fluorenyllithium species, which on reprotonation gave exclusively the *sp* rotamer **28**. Since it can be expected[30] that in hydrocarbon solution protonation occurs on the same face of the fluorenyl carbanion with which the lithium cation is associated (as a contact ion pair[31]), the common fluorenyllithium species was assigned structure **29** where the lithium is internally coordinated to the methoxy group. In the case of the *sp* rotamer **28**, fluorenyllithium **29** can be formed intramolecularly following pre-coordination of BuLi to the methoxy group, hence the pseudo-first order kinetics. In the case of the *ap* rotamer **30**, the pseudo-second order kinetics suggested that a BuLi·**30** complex acts as the base for a second molecule of **30**. It was proposed that facile rotation about the fluorenyl–phenyl bond then



Scheme 3 *Reagents and conditions:* i, BuLi (excess), benzene–hexane; ii, HCl–H_2O

occurs in the initially formed fluorenyllithium **31**, allowing the favourable internal chelation present in fluorenyllithium **29**. On introduction of bulky substituents at the 9-position of 9-arylfluorenes, ground state destabilisation has been shown[23,24] to substantially reduce the barriers to rotation. Thus, unfavourable steric interactions between the carbanion and the lithium counterion were postulated to cause the low barrier to rotation in the fluorenyllithium **31**. The *ap* rotamer of 9-(2′-methoxy-1′-naphthyl)fluorene also undergoes conversion to the *sp* rotamer on treatment with BuLi followed by reprotonation.[25] Although this result has been interpreted to indicate facile rotation about the fluorenyl–naphthyl bond in the initial fluorenyllithium intermediate,[27] it has also been suggested[25] that stereomutation may occur through lithium migration to the internally chelating face of the fluorenyl carbanion through metal exchange reactions.

In order to determine whether these stereomutations do involve rotation about the fluorenyl–aryl bond in the fluorenyllithium intermediates, the alcohol **25** (75% ee) was, on treatment with thionyl chloride, converted to the +*ac*(*R*)-chloride **32** (Scheme 4) in 97% yield. Methanolysis of the chloride in the presence of CF_3SO_3Ag then furnished the +*ac*(*R*)-methyl ether **33** in 89% yield. The enantiomeric excess of **33** was determined to be 75% by integration of the ^{1}H NMR spectral signals due to the fluorene 1-methyl group in the presence of 5 equiv. of (*S*)-2,2,2-trifluoro-1-(9-anthryl)ethanol [(*S*)-TFAE] in C_6D_6 solution (*ca.* 0.6 mol dm^{-3}), which appeared at δ_H 1.66 and 1.68, respectively, for **33** and *ent*-**33** [Fig. 1(a)]. Heating **33** in a solution of xylenes under reflux for 20 h furnished a 2.2:1 mixture of **33** and the −*sc*(*R*)-fluorene **34**. The ^{1}H NMR spectrum of the reaction mixture in the presence of (*S*)-TFAE indicated that there was no loss in stereochemical purity at the fluorene 9-C during thermal isomerisation about the C_9–$C_{1'}$ bond, with the signals for the fluorene 1-methyl group of **34** and *ent*-**34** appearing at δ_H 1.59 and 1.56, respectively [Fig. 1(b)]. Consistent with the naphthalene 2-methoxymethyl group being *anti* to the fluorene 9-H in rotamer **34**, the methylene and methoxy signals in the ^{1}H NMR ($CDCl_3$) spectrum appeared as an AB pattern centred at δ_H 3.45 and as a singlet at δ_H 2.64, respectively, significantly shielded with respect to the corresponding signals for rotamer **33** at δ_H 5.08 and 3.60, respectively. The rotamers were separated by preparative HPLC, and a benzene solution of **34** (*ca.* 0.25 M) then treated with 2 equiv. of BuLi in hexane, resulting in the slow generation of the fluorenyl carbanion **35**. Quenching the reaction with acetic acid after 3 h at 25 °C gave a 1:1.1 mixture of **34** and *ent*-**33**. The ^{1}H NMR spectrum of the reaction mixture in the presence of (*S*)-TFAE revealed no loss in enantiomeric purity of *ent*-**33**,



Scheme 4 *Reagents and conditions:* i. $SOCl_2$ (5 equiv.), CH_2Cl_2, 25 °C, 23 h; ii, CF_3SO_3Ag (1.5 equiv.), MeOH, CH_2Cl_2, 25 °C, 4 d; iii, xylenes, reflux, 20 h; iv, BuLi (2 equiv.), benzene–hexane, 25 °C, 15 min or 3 h; v, CD_3CO_2D or CH_3CO_2H

consistent with the complete retention of axial chirality in the fluorenyl carbanion **35** [Fig. 1(c)]. Thus, formation of the internally chelated ion pair on lithiation of **34** does not involve rotation about the fluorenyl–naphthyl bond, which would be expected to return **33** on reprotonation. On quenching the reaction with [$^2H_4$]acetic acid, the ^{1}H NMR spectrum of the mixture revealed >98% incorporation of deuterium at C-9 of *ent*-**33** and no evidence of deuterium incorporation at C-9 of **34**. Recovered **34** had therefore not been lithiated and the reprotonation of the fluorenyl carbanion **35** stereospecifically affords *ent*-**33**.

In contrast to the behaviour of **34**, lithiation of **33** under the same conditions was complete within 15 min ([$^2H_4$]acetic acid quench, >98% deuterium incorporation at C-9 by ^{1}H NMR analysis), reprotonation of the fluorenyl carbanion *ent*-**35** returning **33** with no loss of enantiomeric purity evident by ^{1}H NMR analysis in the presence of (*S*)-TFAE.

With the viability of ligand design **6** now established, we are currently investigating the further elaboration of the 9-(1′-naphthyl)fluorene system and the preparation of metal complexes with the new ligands. This will involve conversion of the ester group at the naphthalene 2-position into various substituents capable of coordinating to a metal and the introduction of additional substituents on the fluorene in positions likely to influence the stereoselectivity of reactions mediated by coordinated metals. Approaches to other axially chiral cyclopentadienyl systems, for example 1-(3′-indenyl)naphthalenes,[32] are also being developed.

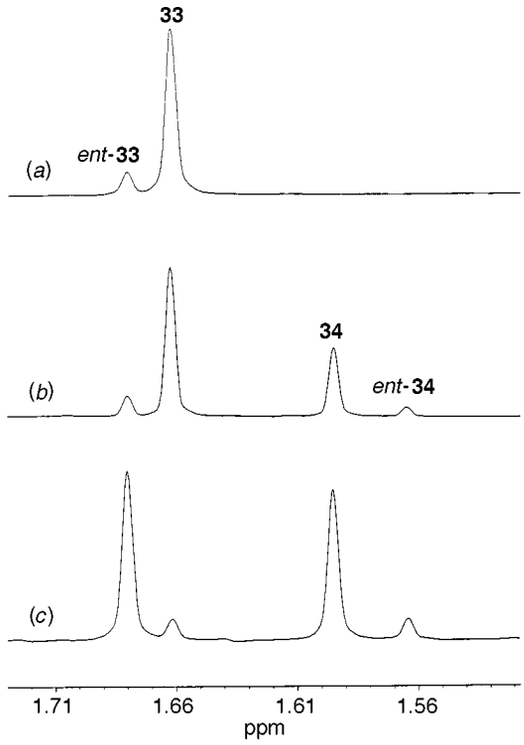


Fig. 1 Stereomutation of **33** into *ent*-**33** as followed by ^{1}H NMR spectroscopy in the presence of (*S*)-TFAE (see text for details)

Experimental

Mps were determined using a Reichert hot-stage microscope and are uncorrected. All experiments involving the use of organometallic species were conducted under dry nitrogen using the Schlenk technique. Anhydrous THF, DME, diethyl ether and benzene were distilled prior to use from sodium–benzophenone. Anhydrous dichloromethane (DCM) was distilled prior to use from CaH_2. Light petroleum was a hexane fraction. All organic extracts were dried over anhydrous sodium sulfate prior to evaporation under reduced pressure. Analytical TLC was carried out using Merck Kieselgel 60 PF_{254} precoated aluminium sheets visualised under UV light at 254 nm. Flash chromatography was carried out using Merck Kieselgel 60 (particle size 0.040–0.063 mm). Unless otherwise stated ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were determined for solutions in $CDCl_3$ on a Bruker AMX400 instrument, with *J* values given in Hz. ^{1}H NMR (200 MHz) spectra were obtained on a Bruker AC200 instrument.

Infrared spectra were recorded on a Perkin-Elmer 1600 Series FTIR. Mass spectra were recorded with a Kratos MS902 instrument using electron impact ionisation (70 eV) and a MSS MASPEC data system used to obtain high resolution spectra. Optical rotations were determined at ambient temperature with an Optical Activity PolAAr 2001 automatic polarimeter using a 0.25 dm microcell and are given in units of 10^{-1} deg cm^2 g^{-1}. Microanalyses were conducted by the Microanalytical Unit of the School of Chemistry at the University of New South Wales, Sydney, or by the Microanalytical Unit of the Research School of Chemistry at the Australian National University, Canberra.

Analytical HPLC was carried out using a Waters chromatography system consisting of a Model 6000A pump, U6K injector and Model 440 absorbance detector operating at 254 nm. Determinations of de were made using a 25 cm × 4.6 mm ID column (Zorbax 5 μm silica, Jones) eluting with the indicated mobile phase at a flow rate of 1.5 cm^3 min^{-1}. Determinations of ee were made using a 25 cm × 4.6 mm ID column [Chiralpak OT(+), Daicel] eluting with methanol at a flow rate of 0.5 cm^3 min^{-1} and a column temp. of 3 °C. Preparative HPLC was carried out using a Waters chromatography system

consisting of a Model 510EF pump, U6K injector, Model 481 absorbance detector operating at 280 nm, and Model R403 differential refractometer, using a 50 cm × 22 mm ID column (Whatman Partisil 10) eluted with the indicated mobile phase at a flow rate of 13.5 cm^3 min^{-1}.

(*R*)-1-(*p*-Tolylsulfinyl)naphthalene was prepared by the method of Andersen *et al.*[33] by treatment of (1*R*)-menthyl (*S*)-naphthalene-1-sulfinate[28] with *p*-tolylmagnesium bromide and the (*S*)-enantiomer prepared by treatment of (1*R*)-menthyl (*S*)-*p*-toluenesulfinate[34] with 1-naphthylmagnesium bromide. (*R*)-1-(*tert*-Butylsulfinyl)naphthalene was prepared by treatment of (1*R*)-menthyl (*S*)-naphthalene-1-sulfinate with *tert*-butylmagnesium chloride[28] and the (*S*)-enantiomer similarly prepared using (1*S*)-menthyl (*R*)-naphthalene-1-sulfinate. Sulfoxides **8** and **9**,[28] 1-methylfluorene,[35] 1-ethylfluorene,[36] 1-chlorofluorene[37] and 1-methoxyfluorene[38] were prepared by established procedures. Other reagents were obtained from commercial suppliers and used as received.

(1*R*)-Menthyl (*S*)-1-[(4-methylphenyl)sulfinyl]naphthalene-2-carboxylate 10

A solution of BuLi (2.62 mol dm^{-3}; 3.1 mmol) in hexane (1.2 cm^3) was added dropwise to a stirred solution of diisopropylamine (450 mm^3, 3.4 mmol) in anhydrous THF (25 cm^3) at 0 °C. After 15 min the solution was cooled to −78 °C and a solution of (*S*)-1-[(4-methylphenyl)sulfinyl]naphthalene (750 mg, 2.8 mmol) in anhydrous THF (10 cm^3) added dropwise *via* cannula. After 20 min the dark green solution was added rapidly *via* cannula to a stirred solution of (1*R*)-menthyl chloroformate (615 mm^3, 2.9 mmol) in anhydrous THF (5 cm^3) at −78 °C. The solution was stirred for 5 h longer and then an excess of 5% aq. ammonium chloride was added followed by DCM. The separated organic layer was washed with brine and the crude product purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *sulfoxide* **10** (358 mg, 28%) as an oil; $[a]_D$ −120 (*c* 1.8, toluene), >98% de (Found: C, 74.65; H, 7.25. $C_{28}H_{32}O_3S$ requires C, 74.95; H, 7.2%). The diastereoisomeric purity was determined by the ^1H NMR signals at $\delta_H(C_6D_6)$ 7.63 and 7.65 (each d, $J_{3,4}$ 8.4, 3-H), respectively, for **11** and **10**. δ_H 0.87 and 0.94 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.94 (3H, d, *J* 6.5, 5′-Me), 0.88–0.98 (1H, m, 4′ax-H), 1.07–1.21 (2H, m, 3′ax- and 6′ax-H), 1.52–1.64 (2H, m, 2′- and 5′-H), 1.69–1.78 (2H, m, 3′eq- and 4′eq-H), 2.11 (1H, d septet, *J* 2.7, 7.0, C*H*Me$_2$), 2.24–2.30 (1H, m, 6′eq-H), 2.33 (3H, s, tolyl Ar*Me*), 5.02 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H), 7.22 and 7.67 (4H, AA′BB′, tolyl ArH), 7.45 (1H, ddd, $J_{7,8}$ 8.6, $J_{7,6}$ 6.9, $J_{7,5}$ 1.4, 7-H), 7.51 (1H, ddd, $J_{6,5}$ 8.2, $J_{6,7}$ 6.9, $J_{6,8}$ 1.2, 6-H), 7.70 (1H, d, $J_{3,4}$ 8.5, 3-H), 7.86 (1H, br d, $J_{5,6}$ 8.2, 5-H), 7.99 (1H, d, $J_{4,3}$ 8.5, 4-H) and 8.80 (1H, br d, $J_{8,7}$ 8.6, 8-H);§ δ_C 166.8, 141.1, 140.1, 139.4, 135.5, 133.6 (each C), 132.6 (CH), 129.6 (2 × CH), 129.5 (C), 128.8, 127.9, 127.8, 125.7 (each CH), 125.1 (2 × CH), 123.7, 77.1, 47.0 (each CH), 40.7, 34.1 (each CH_2), 31.5, 26.4 (each CH), 23.2 (CH_2), 22.0, 21.2, 20.9 and 16.1 (each Me); ν_{max}(film)/cm^{-1} 1713 (C=O) and 1047 (S=O); *m*/*z* 448 (M^+, 7%), 431 (18), 311 (63), 293 (100), 262 (32), 234 (42), 203 (84), 202 (72), 108 (59) and 83 (48).

(1*R*)-Menthyl (*R*)-1-[(4-methylphenyl)sulfinyl]naphthalene-2-carboxylate 11

The 2-lithio derivative of (*R*)-1-[(4-methylphenyl)sulfinyl]-naphthalene (500 mg, 1.9 mmol) was treated with (1*R*)-menthyl chloroformate (410 mm^3, 1.9 mmol) during 3.5 h at −78 °C using the procedure described for the preparation of **10**. The crude product was purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *sulfoxide* **11** (312 mg, 37%) as an oil; $[a]_D$ +52 (*c* 2.3, toluene), >98% de (Found: C, 75.3; H, 7.3. $C_{28}H_{32}O_3S$ requires C, 74.95; H, 7.2%); δ_H 0.85 and 0.88 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.95 (3H, d, *J* 6.5, 5′-Me), 0.89–0.99 (1H, m, 4′ax-H), 1.06–1.23 (2H, m, 3′ax- and 6′ax-H), 1.41–1.49 (1H, m, 2′-H), 1.50–1.75 (3H, m, 3′eq-, 4′eq- and 5′-H), 1.99 (1H, d septet, *J* 2.7, 7.0, C*H*Me$_2$), 2.25–2.32 (1H, m, 6′eq-H), 2.34 (3H, s, tolyl Ar*Me*), 5.03 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H), 7.23 and 7.70 (4H, AA′BB′, tolyl Ar*H*), 7.45 (1H, ddd, $J_{7,8}$ 8.6, $J_{7,6}$ 6.9, $J_{7,5}$ 1.5, 7-H), 7.51 (1H, ddd, $J_{6,5}$ 8.1, $J_{6,7}$ 6.9, $J_{6,8}$ 1.2, 6-H), 7.73 (1H, d, $J_{3,4}$ 8.5, 3-H), 7.86 (1H, br d, $J_{5,6}$ 8.1, 5-H), 7.99 (1H, d, $J_{4,3}$ 8.5, 4-H) and 8.77 (1H, br d, $J_{8,7}$ 8.6, 8-H);§ δ_C 166.6, 141.2, 140.2, 139.4, 135.6, 133.2 (each C), 132.5 (CH), 129.6 (2 × CH), 129.3 (C), 128.8, 127.9, 127.7, 125.7 (each CH), 125.2 (2 × CH), 124.0, 77.1, 46.9 (each CH), 40.7, 34.1 (each CH_2), 31.5, 26.3 (each CH), 23.3 (CH_2), 22.0, 21.2, 20.7 and 16.2 (each Me); ν_{max}(film)/cm^{-1} 1714 (C=O) and 1047 (S=O); *m*/*z* 448 (M^+, 10%), 432 (18), 431 (17), 311 (96), 292 (59), 293 (94), 262 (31), 234 (42), 203 (84), 202 (70), 171 (31), 139 (45), 123 (37), 108 (93), 95 (47), 91 (37) and 83 (100).

(1*R*)-Menthyl (*S*)-1-(*tert*-butylsulfinyl)naphthalene-2-carboxylate 12

A solution of BuLi (2.64 mol dm^{-3}; 9.5 mmol) in hexane (3.6 cm^3) was added dropwise to a stirred solution of (*S*)-1-(*tert*-butylsulfinyl)naphthalene (2.00 g, 8.6 mmol, 90% ee) in anhydrous THF (50 cm^3) at −78 °C. After 10 min the dark orange solution was transferred rapidly *via* cannula to a stirred solution of (1*R*)-menthyl chloroformate (1.84 cm^3, 8.6 mmol) in anhydrous THF (20 cm^3) at −78 °C. The solution was stirred 2 h longer and then an excess of 5% aq. ammonium chloride was added followed by DCM. The separated organic layer was washed with brine and the crude product purified by flash chromatography with 15% ethyl acetate–light petroleum as eluent to afford the *sulfoxide* **12** (1.14 g, 32%) as an oil. Crystallisation from acetone–water furnished colourless prisms, mp 105–6 °C; $[a]_D$ −81 (*c* 1.7, toluene), 97% de (Found: C, 72.05; H, 8.5. $C_{25}H_{34}O_3S$ requires C, 72.4; H, 8.25%). The diastereoisomeric purity was determined by HPLC: mobile phase, 0.3% propan-2-ol–hexane; t_R 68 min for **12** and 78 min for **13**. The ^1H and ^{13}C NMR spectra of **12** contain signals for two rotameric forms[28] in a ratio of *ca.* 10:1 (* denotes signals for the minor rotamer); δ_H 0.83 and 0.90 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.96 (3H, d, *J* 6.5, 5′-Me), 0.87–0.98 (1H, m, 4′ax-H), 1.05–1.18 (2H, m, 3′ax- and 6′ax-H), 1.27 (9H, s, 3 × Me*), 1.30 (9H, s, 3 × Me), 1.49–1.62 (2H, m, 2′- and 5′-H), 1.68–1.76 (2H, m, 3′eq- and 4′eq-H), 1.95 (1H, d septet, *J* 2.7, 7.0, C*H*Me$_2$), 2.17–2.25 (1H, m, 6′eq-H), 2.44–2.50 (1H, m, 6′eq-H*), 4.96 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H), 5.03 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H*), 7.36 (1H, d, $J_{3,4}$ 8.4, 3-H*), 7.52–7.61 (3H, m, 3-, 6- and 7-H), 7.85–7.88 (1H, m, 5-H), 7.95 (1H, d, $J_{4,3}$ 8.4, 4-H), 8.15–8.18 (1H, m, 8-H*) and 9.55–9.58 (1H, m, 8-H);§ δ_C 169.0*, 167.4, 134.8, 134.6, 134.1, 133.6*, 133.0*, 132.6 (each C), 132.1 (CH), 131.1* (C), 130.8*, 128.3, 127.8 (each CH), 127.3 (C), 127.2, 127.1, 126.8*, 125.9*, 124.9*, 124.0, 76.5, 76.1* (each CH), 61.6*, 60.6 (each C), 47.1*, 46.9 (each CH), 40.4*, 40.3, 34.4*, 34.1 (each CH_2), 31.5, 26.3, 26.0* (each CH), 25.39, 25.32* (each 3 × Me), 23.4*, 23.3 (each CH_2), 22.1*, 22.0, 20.8*, 20.7, 16.2* and 16.1 (each Me); ν_{max}(film)/cm^{-1} 1711 (C=O) and 1053 (S=O); *m*/*z* 682 (5.4%), 650 (29), 328 (20), 313 (29), 284 (18), 205 (49), 204 (86), 203 (91), 202 (26), 188 (69), 187 (72), 186 (93), 158 (63), 155 (48), 138 (33), 127 (28), 115 (72), 97 (42), 95 (73), 83 (90), 81 (74) and 69 (100).¶

(1*R*)-Menthyl (*R*)-1-(*tert*-butylsulfinyl)naphthalene-2-carboxylate 13

The 2-lithio derivative of (*R*)-1-(*tert*-butylsulfinyl)naphthalene (2.00 g, 8.6 mmol, 90% ee) was treated with (1*R*)-menthyl

§ Primed numbers refer to the menthyl moiety.

¶ The ion at *m*/*z* 682 in the mass spectra of the *tert*-butyl sulfoxides **12** and **13** corresponds to a disulfide compound, presumably formed during volatilisation through thermal elimination of isobutene followed by disproportionation of the resulting sulfenic acid.[28]

chloroformate (1.84 cm^3, 8.6 mmol) during 2 h at −78 °C using the procedure described for the preparation of **12**. The crude product was purified by flash chromatography with 15% ethyl acetate–light petroleum as eluent to afford the *sulfoxide* **13** (1.43 g, 40%) as an oil. Crystallisation from acetone–water furnished colourless prisms, mp 122–3 °C; $[a]_D$ +54 (*c* 2.5, toluene), 98% de (Found: C, 72.3; H, 8.5. $C_{25}H_{34}O_3S$ requires C, 72.4; H, 8.25%). The ^1H and ^{13}C NMR spectra of **13** contain signals for two rotameric forms[28] in a ratio of *ca.* 4:1 (* denotes signals for the minor rotamer); δ_H 0.87 and 0.91 (each 3H, d, *J* 7.0, CH*Me*$_2$*), 0.87 and 0.93 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.96 (3H, d, *J* 6.5, 5′-Me and 5′-Me*), 0.89–1.00 (1H, m, 4′ax-H and 4′ax-H*), 1.07–1.20 (2H, m, 3′ax- and 6′ax-H; 3′ax- and 6′ax-H*), 1.28 (9H, s, 3 × Me*), 1.32 (9H, s, 3 × Me), 1.42–1.64 (2H, m, 2′- and 5′-H; 2′- and 5′-H*), 1.66–1.78 (2H, m, 3′eq- and 4′eq-H; 3′eq- and 4′eq-H*), 2.06 (1H, d, septet, *J* 2.7, 7.0, C*H*Me$_2$*), 2.15 (1H, d, septet, *J* 2.7, 7.0, C*H*Me$_2$), 2.17–2.23 (1H, m, 6′eq-H), 2.42–2.48 (1H, m, 6′eq-H*), 4.97 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H), 5.03 (1H, ddd, $J_{1',2'}$ 10.9, $J_{1',6'ax}$ 10.9, $J_{1',6'eq}$ 4.4, 1′-H*), 7.37 (1H, d, $J_{3,4}$ 8.4, 3-H*), 7.52–7.61 (3H, m, 3-, 6- and 7-H; 2H, m, 6- and 7-H*), 7.86–7.89 (1H, m, 5-H and 5-H*), 7.95 (1H, d, $J_{4,3}$ 8.4, 4-H), 7.96 (1H, d, $J_{4,3}$ 8.4, 4-H*), 8.16–8.19 (1H, m, 8-H*) and 9.53–9.56 (1H, m, 8-H);§ δ_C 169.4*, 167.2, 134.7, 134.5, 134.3, 133.7*, 133.6*, 132.9*, 132.4 (each C), 132.1, 131.1* (each CH), 131.0* (C), 128.3, 127.8 (each CH), 127.3 (C), 127.2, 127.14*, 127.09, 126.9*, 125.5*, 124.9*, 124.0, 76.6, 75.7* (each CH), 61.5*, 60.6 (each C), 47.1*, 47.0 (each CH), 40.8, 39.9*, 34.3*, 34.1 (each CH_2), 31.6*, 31.5, 26.3*, 26.0 (each CH), 25.5, 25.1* (each 3 × Me), 23.27*, 23.17 (each CH_2), 22.1*, 22.0, 20.8 and 15.9 (each Me); ν_{max}(film)/cm^{-1} 1720 (C=O) and 1043 (S=O); *m/z* 682 (0.8%), 650 (14), 313 (14), 204 (74), 203 (57), 188 (52), 187 (59), 186 (83), 172 (82), 155 (85), 138 (79), 127 (80), 123 (37), 115 (38), 95 (89), 83 (86), 81 (76), 69 (73), 64 (77), 57 (35), 55 (99), 43 (78) and 41 (100).¶

Isopropyl +*ac*(*R*)-1-(1′-methylfluoren-9′-yl)naphthalene-2-carboxylate 19

A solution of BuLi (2.65 mol dm^{-3}; 0.94 mmol) in hexane (355 mm^3) was added dropwise to a stirred solution of 1-methylfluorene (170 mg, 0.94 mmol) in anhydrous THF (5 cm^3) at 0 °C. A solution of the sulfoxide **8** (220 mg, 0.63 mmol) in anhydrous THF (5 cm^3) was then added dropwise. The solution was stirred 30 min longer and then an excess of 5% aq. ammonium chloride was added followed by DCM. The separated organic layer was washed with brine and the crude product purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **19** (244 mg, 100%) as a colourless solid, mp 140–144 °C; $[a]_D$ −73 (*c* 2.5, toluene) (Found: C, 85.9; H, 6.35. $C_{35}H_{36}O_2$ requires C, 85.7; H, 6.15%); δ_H 1.42 and 1.44 (each 3H, d, *J* 6.6, CH*Me*$_2$), 1.81 (3H, s, 1′-Me), 5.39 (1H, septet, *J* 6.6, C*H*Me$_2$), 6.19 (1H, s, 9′-H), 6.70 (1H, br d, $J_{8,7}$ 8.8, 8-H), 6.89 (1H, ddd, $J_{7,8}$ 8.8, $J_{7,6}$ 6.8, $J_{7,5}$ 1.3, 7-H), 6.98 (1H, br d, $J_{2',3'}$ 7.5, 2′-H), 7.21 (1H, ddd, $J_{7',8'}$ 7.4, $J_{7',6'}$ 7.4, $J_{7',5'}$ 1.0, 7′-H), 7.28 (1H, ddd, $J_{6,5}$ 8.0, $J_{6,7}$ 6.8, $J_{6,8}$ 1.1, 6-H), 7.34 (1H, br d, $J_{8',7'}$ 7.4, 8′-H), 7.35 (1H, dd, $J_{3',4'}$ 7.5, $J_{3',2'}$ 7.5, 3′-H), 7.40 (1H, br dd, $J_{6',7'}$ 7.4, $J_{6',5'}$ 7.6, 6′-H), 7.74 (1H, br d, $J_{5,6}$ 8.0, 5-H), 7.80–7.85 (3H, m, 3-, 4- and 4′-H) and 7.92 (1H, br d, $J_{5',6'}$ 7.6, 5′-H); δ_C 169.6, 147.9, 146.2, 140.4, 140.2, 136.6, 135.0, 134.7, 132.6, 131.4 (each C), 129.0, 128.3, 127.9, 127.34, 127.26, 127.0, 126.8, 126.2, 125.6, 125.0, 124.9, 120.1, 118.0, 69.3, 50.5 (each CH), 21.96, 21.93 and 18.7 (each Me); *m/z* 392 (M^+, 13%), 349 (73), 332 (100), 317 (23), 303 (25), 302 (24), 289 (22) and 149 (31).

Isopropyl −*ac*(*S*)-1-(1′-methylfluoren-9′-yl)naphthalene-2-carboxylate *ent*-19

The fluorenyllithium **14** from 1-methylfluorene (170 mg, 0.94 mmol) was treated with the sulfoxide **9** (200 mg, 0.63 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene ent*-**19** (245 mg, 100%) as a colourless solid, mp 123–125 °C (partially), then 142–144 °C; $[a]_D$ +96 (*c* 2.5, toluene). The spectroscopic properties were identical to those of **19**.

(1*R*)-Menthyl +*ac*(*R*)-1-(1′-methylfluoren-9′-yl)naphthalene-2-carboxylate 20

The fluorenyllithium **14** from 1-methylfluorene (277 mg, 1.54 mmol) was treated with sulfoxide **10** (460 mg, 1.03 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **20** (466 mg, 93%) as a colourless solid with 75% de. Several recrystallisations from acetone–water furnished **20** as colourless prisms, mp 137–139 °C; $[a]_D$ −137 (*c* 1.05, toluene), 96% de (Found: C, 86.05; H, 7.55. $C_{35}H_{36}O_2$ requires C, 86.05; H, 7.45%). The diastereoisomeric purity was determined by HPLC: mobile phase, 0.4% ethyl acetate–hexane; t_R 10.4 min for **20** and 11.6 min for **24**. δ_H 0.85 and 0.94 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.95 (3H, d, *J* 6.5, 5″-Me), 0.91–1.01 (1H, m, 4″ax-H), 1.11–1.25 (2H, m, 3″ax- and 6″ax-H), 1.55–1.67 (2H, m, 2″- and 5″-H), 1.72–1.81 (2H, m, 3″eq- and 4″eq-H), 1.86 (3H, s, 1′-Me), 2.16 (1H, d septet, *J* 2.6, 7.0, C*H*Me$_2$), 2.23–2.29 (1H, m, 6″eq-H), 5.10 (1H, ddd, $J_{1'',2''}$ 10.8, $J_{1'',6''ax}$ 10.8, $J_{1'',6''eq}$ 4.3, 1″-H), 6.27 (1H, s, 9′-H), 6.73 (1H, br d, $J_{8,7}$ 8-H), 6.90 (1H, br dd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.9, 7-H), 7.00 (1H, br d, $J_{2',3'}$ 7.4, 2′-H), 7.20 (1H, br dd, $J_{7',8'}$ 7.5, $J_{7',6'}$ 7.5, 7′-H), 7.29 (1H, br dd, $J_{6,5}$ 8.2, $J_{6,7}$ 6.9, 6-H), 7.32 (1H, br d, $J_{8',7'}$ 7.5, 8′-H), 7.37 (1H, dd, $J_{3',4'}$ 7.4, $J_{3',2'}$ 7.4, 3′-H), 7.40 (1H, br dd, $J_{6',7'}$ 7.5, $J_{6',5'}$ 7.5, 6′-H), 7.75 (1H, br d, $J_{5,6}$ 8.2, 5-H), 7.80–7.86 (3H, m, 3-,4- and 4′-H) and 7.92 (1H, br d, $J_{5',6'}$ 7.5, 5′-H);‖ δ_C 169.6, 148.0, 146.3, 140.4, 140.1, 136.8, 135.1, 134.6, 132.5, 131.4 (each C), 129.0, 128.3, 127.9, 127.3, 127.2, 127.0, 126.8, 126.2, 125.7, 124.9, 124.7, 120.1, 118.0, 75.7, 50.4, 47.1 (each CH), 41.0, 34.2 (each CH_2), 31.5, 26.4 (each CH), 23.2 (CH_2), 22.0, 20.8, 18.7 and 16.1 (each Me); *m/z* 488 (M^+, 2.7%), 350 (61), 349 (28), 333 (64), 332 (100), 317 (22), 303 (34), 302 (22), 289 (27) and 83 (65).

Variations in the procedure (Table 1, entries 5 and 14–19)

Entry 5. Using the procedure described for the preparation of **19**, the fluorenyllithium **14** from 1-methylfluorene (60 mg, 0.33 mmol) was treated with sulfoxide **10** (100 mg, 0.22 mmol) during 20 h at −78 °C to afford the *fluorene* **20** (54 mg, 50%) in 86% de.

Entry 14. Using the procedure described for the preparation of **19**, the fluorenyllithium **14** from 1-methylfluorene (60 mg, 0.33 mmol) was treated with sulfoxide **10** (100 mg, 0.22 mmol) during 1 h at 0 °C in diethyl ether to afford the *fluorene* **20** (87 mg, 80%) in 72% de.

Entry 15. Using the procedure described for the preparation of **19**, the fluorenyllithium **14** from 1-methylfluorene (60 mg, 0.33 mmol) was treated with sulfoxide **10** (100 mg, 0.22 mmol) during 30 min at 0 °C in DME to afford the *fluorene* **20** (101 mg, 93%) in 68% de.

Entry 16. A solution of 1-methylfluorene (200 mg, 1.11 mmol) in anhydrous THF (10 cm^3) was added dropwise to potassium hydride (45 mg, 1.12 mmol) and the mixture stirred at 25 °C for 1 h. The resulting solution of fluorenylpotassium **18** was cooled to 0 °C and a solution of the sulfoxide **10** (100 mg, 0.22 mmol) in anhydrous THF (5 cm^3) then added dropwise. The solution was stirred 12 h longer, with TLC analysis indicating that no coupled product had been produced.

Entry 17. A solution of lithium chloride (0.7 mol dm^{-3}; 0.77 mmol) in anhydrous THF (1.1 cm^3) was added to a solution of fluorenylpotassium **18** prepared from 1-methylfluorene (120 mg, 0.67 mmol) using the procedure described under entry 16.

‖ Double-primed numbers refer to the menthyl moiety.

The mixture was cooled to 0 °C and a solution of the sulfoxide **10** (100 mg, 0.22 mmol) in anhydrous THF (5 cm^3) then added dropwise. The solution was stirred 1 h longer and then worked-up using the procedure described under the preparation of **19**, to afford the *fluorene* **20** (76 mg, 70%) in 76% de.

Entry 18. A solution of magnesium chloride (0.2 mol dm^{-3}; 0.88 mmol) in anhydrous THF (4.4 cm^3) was added to a solution of fluorenylpotassium **18** prepared from 1-methylfluorene (80 mg, 0.44 mmol) using the procedure described under entry 16. The mixture was cooled to 0 °C and a solution of the sulfoxide **10** (100 mg, 0.22 mmol) in anhydrous THF (5 cm^3) then added dropwise. The solution was stirred 1 h longer and then worked-up using the procedure described under the preparation of **19**, to afford the *fluorene* **20** (89 mg, 82%) in 72% de.

Entry 19. A solution of fluorenyllithium **14** was prepared from 1-methylfluorene (60 mg, 0.33 mmol) in anhydrous THF (10 cm^3) using the procedure described under the preparation of **19**. The solution was added to $Me_2S{\cdot}CuBr$ (69 mg, 0.34 mmol) and the mixture stirred at −20 °C for 1 h. A solution of the sulfoxide **10** (100 mg, 0.22 mmol) in anhydrous THF (5 cm^3) was then added dropwise. The mixture was warmed to 0 °C and stirred 12 h longer, with TLC analysis indicating that no coupled product had been produced.

Preparation of fluorene 20 from sulfoxide 12 (Table 1, entries 7 and 9). The fluorenyllithium **14** from 1-methylfluorene (65 mg, 0.36 mmol) was treated with sulfoxide **12** (100 mg, 0.24 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **20** (116 mg, 98%) in 84% de. Carrying out the same reaction for 20 h at −78 °C afforded the *fluorene* **20** (12 mg, 10%) in 95% de.

(1*R*)-Menthyl −*ac*(*S*)-1-(1′-methylfluoren-9′-yl)naphthalene-2-carboxylate 24

The fluorenyllithium **14** from 1-methylfluorene (230 mg, 1.27 mmol) was treated with sulfoxide **11** (380 mg, 0.85 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **24** (377 mg, 91%) as a colourless solid with 70% de (Found: C, 86.45; H, 7.60. $C_{35}H_{36}O_2$ requires C, 86.05; H, 7.45%); δ_H 0.86 and 0.95 (each 3H, d, *J* 7.0, CH*Me*$_2$), 0.94 (3H, d, *J* 6.5, 5″-Me), 0.89–1.00 (1H, m, 4″ax-H), 1.11–1.23 (2H, m, 3″ax- and 6″ax-H), 1.55–1.67 (2H, m, 2″- and 5″-H), 1.71–1.81 (2H, m, 3″eq- and 4″eq-H), 1.81 (3H, s, 1′-Me), 2.12 (1H, d septet, *J* 2.6, 7.0, C*H*Me$_2$), 2.23–2.30 (1H, m, 6″eq-H), 5.08 (1H, ddd, $J_{1'',2''}$ 10.8, $J_{1'',6''ax}$ 10.8, $J_{1'',6''eq}$ 4.3, 1″-H), 6.26 (1H, s, 9′-H), 6.73 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.89 (1H, ddd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.9, $J_{7,5}$ 1.4, 7-H), 6.98 (1H, br d, $J_{2',3'}$ 7.4, 2′-H), 7.22 (1H, br dd, $J_{7',8'}$ 7.5, $J_{7',6'}$ 7.5, 7′-H), 7.29 (1H, br dd, $J_{6,5}$ 8.2, $J_{6,7}$ 6.9, 6-H), 7.36 (1H, dd, $J_{3',4'}$ 7.4, $J_{3',2'}$ 7.4, 3′-H), 7.38 (1H, br d, $J_{8',7'}$ 7.5, 8′-H), 7.41 (1H, br dd, $J_{6',7'}$ 7.5, $J_{6',5'}$ 7.5, 6′-H), 7.75 (1H, br d, $J_{5,6}$ 8.2, 5-H), 7.83 (1H, br d, $J_{4',3'}$ 7.4, 4′-H), 7.84 (2H, s, 3- and 4-H) and 7.93 (1H, br d, $J_{5',6'}$ 7.5, 5′-H);** δ_C 169.5, 148.0, 146.3, 140.5, 140.2, 137.0, 134.9, 134.7, 132.4, 131.4 (each C), 129.0, 128.3, 127.9, 127.31, 127.28, 127.0, 126.8, 126.2, 125.7, 125.1, 125.0, 120.1, 118.0, 75.9, 50.6, 47.0 (each CH), 40.8, 34.2 (each CH_2), 31.5, 26.4 (each CH), 23.4 (CH_2), 22.0, 20.8, 18.7 and 16.2 (each Me);** *m*/*z* 488 (M^+, 2.5%), 350 (61), 349 (28), 333 (61), 332 (100), 317 (20), 303 (22), 289 (23) and 83 (54).

Variation in the procedure (Table 1, entry 6). Using the procedure described for the preparation of **19**, the fluorenyllithium **14** from 1-methylfluorene (60 mg, 0.33 mmol) was treated with sulfoxide **11** (100 mg, 0.22 mmol) during 20 h at −78 °C to afford the *fluorene* **24** (57 mg, 52%) in 84% de.

** Signals for major diastereoisomer only.

Preparation of fluorene 24 from sulfoxide 13 (Table 1, entries 8 and 10). The fluorenyllithium **14** from 1-methylfluorene (65 mg, 0.36 mmol) was treated with sulfoxide **13** (100 mg, 0.24 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **24** (110 mg, 93%) in 82% de. Carrying out the same reaction for 20 h at −78 °C afforded the *fluorene* **24** (11 mg, 9%) in 86% de.

Isopropyl +*ac*(*R*)/−*ac*(*S*)-1-(1′-methoxyfluoren-9′-yl)-naphthalene-2-carboxylate 21/*ent*-21

The fluorenyllithium **15** from 1-methoxyfluorene (74 mg, 0.38 mmol) was treated with sulfoxide **9** (100 mg, 0.31 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **21**/*ent*-**21** (128 mg, 100%) as a colourless solid, mp 125–126 °C; $[\alpha]_D$ +11.9 (*c* 1.1, DCM), 21% ee (Found: C, 82.4; H, 6.05. $C_{28}H_{24}O_3$ requires C, 82.3; H, 5.9%). The enantiomeric purity was determined by the ^1H NMR (200 MHz) signals due to the fluorene 1-methoxy group in the presence of Eu(hfc)$_3$ (0.4 equiv., *ca.* 0.05 mol dm^{-3}); $\delta_H(C_6D_6)$ 3.07 and 3.12, respectively, for the minor and major enantiomers. δ_H 1.44 (6H, d, *J* 6.2, CH*Me*$_2$), 3.43 (3H, s, OMe), 5.40 (1H, septet, *J* 6.2, C*H*Me$_2$), 6.45 (1H, s, 9′-H), 6.69 (1H, br d, $J_{2',3'}$ 8.0, 2′-H), 6.76 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.88 (1H, ddd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.8, $J_{7,5}$ 1.4, 7-H), 7.25 (1H, ddd, $J_{7',8'}$ 7.5, $J_{7',6'}$ 7.5, $J_{7',5'}$ 1.1, 7′-H), 7.26 (1H, ddd, $J_{6,5}$ 8.2, $J_{6,7}$ 6.8, $J_{6,8}$ 1.1, 6-H), 7.35–7.43 (3H, m, 3′-, 6′- and 8′-H), 7.58 (1H, dd, $J_{4',3'}$ 7.6, $J_{4',2'}$ 0.6, 4′-H), 7.73 (1H, br d, $J_{5,6}$ 8.2, 5-H), 7.79 (1H, d, $J_{4,3}$ 8.5, 4-H), 7.86 (1H, d, $J_{3,4}$ 8.5, 3-H) and 7.93 (1H, br d, $J_{5',6'}$ 7.6, 5′-H); δ_C 169.5, 156.8, 148.6, 142.1, 140.2, 137.4, 135.5, 134.7, 132.1, 131.6 (each C), 128.7, 128.2, 127.4, 127.3, 126.9, 126.4, 125.80, 125.78, 125.3, 125.0, 120.4, 113.0, 109.9, 68.8 (each CH), 55.3 (Me), 48.7 (CH), 21.97 and 21.95 (each Me); *m*/*z* 408 (M^+, 6.8%), 365 (48), 349 (38), 348 (100), 305 (42), 298 (11), 276 (11) and 155 (19).

Isopropyl +*ac*(*R*)/−*ac*(*S*)-1-(1′-chlorofluoren-9′-yl)naphthalene-2-carboxylate 22/*ent*-22

The fluorenyllithium **16** from 1-chlorofluorene (201 mg, 1.00 mmol) was treated with sulfoxide **9** (266 mg, 0.84 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **22**/*ent*-**22** (344 mg, 100%) as a colourless solid, mp 158–9 °C; $[\alpha]_D$ +9.0 (*c* 1.0, DCM) (Found: M^+, 412.1214. $^{12}C_{27}{}^1H_{21}{}^{35}Cl^{16}O_2$ requires M^+, 412.1230); δ_H 1.41 and 1.42 (each 3H, d, *J* 6.2, CH*Me*$_2$), 5.38 (1H, septet, *J* 6.2, C*H*Me$_2$), 6.53 (1H, s, 9′-H), 6.64 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.87 (1H, ddd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.9, $J_{7,5}$ 1.4, 7-H), 7.11 (1H, br d, $J_{2',3'}$ 7.9, 2′-H), 7.22–7.29 (2H, m, 6- and 7′-H), 7.33–7.42 (3H, m, 3′-, 6′- and 8′-H), 7.73 (1H, br d, $J_{5,6}$ 8.1, 5-H), 7.82 (1H, d, $J_{4,3}$ 8.4, 4-H), 7.84 (1H, br d, $J_{4',3'}$ 7.5, 4′-H), 7.88 (1H, d, $J_{3,4}$ 8.4, 3-H) and 7.90 (1H, br d, $J_{5',6'}$ 7.5, 5′-H); δ_C 169.2, 147.8, 145.0, 142.8, 139.2, 136.2, 134.8, 132.6, 131.48, 131.40 (each C), 128.7, 128.5, 128.2, 128.0, 127.8, 127.3, 126.8, 126.2, 125.4, 125.3, 125.2, 120.5, 118.7, 69.1, 50.5 (each CH), 21.98 and 21.95 (each Me); *m*/*z* 414 (M^+, 0.7%), 412 (M^+, 2.2), 369 (7), 335 (8), 317 (10), 279 (13), 167 (34) and 149 (100).

Isopropyl +*ac*(*R*)/−*ac*(*S*)-1-(1′-ethylfluoren-9′-yl)-naphthalene-2-carboxylate 23/*ent*-23

The fluorenyllithium **17** from 1-ethylfluorene (136 mg, 0.70 mmol) was treated with sulfoxide **9** (186 mg, 0.58 mmol) during 30 min at 0 °C using the procedure described for the preparation of **19**. The crude product was purified by flash chromatography with 5% ethyl acetate–light petroleum as eluent to afford the *fluorene* **23**/*ent*-**23** (238 mg, 100%) as a colourless oil; $[\alpha]_D$ +84.5 (*c* 1.2, DCM) (Found: C, 85.75; H, 6.3. $C_{29}H_{26}O_2$

requires C, 85.7; H, 6.45%), δ_H 0.69 (3H, t, *J* 7.6, CH_2CH_3), 1.39 and 1.40 (each 3H, d, *J* 6.2, $CHMe_2$), 2.08 and 2.24 (2H, each dq, *J* 14.4, 7.6, CH_2CH_3), 5.37 (1H, septet, *J* 6.2, $CHMe_2$), 6.27 (1H, s, 9′-H), 6.71 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.85 (1H, br dd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.9, 7-H), 7.01 (1H, br d, $J_{2',3'}$ 7.4, 2′-H), 7.17 (1H, br dd, $J_{7',8'}$ 7.5, $J_{7',6'}$ 7.5, 7′-H), 7.24 (1H, br dd, $J_{6,7}$ 6.9, $J_{6,5}$ 8.1, 6-H), 7.32–7.39 (3H, m, 3′-, 6′- and 8′-H), 7.70 (1H, br d, $J_{5,6}$ 8.1, 5-H), 7.77–7.83 (3H, m, 3-, 4- and 4′-H) and 7.89 (1H, br d, $J_{5',6'}$ 7.5, 5′-H); δ_C 169.5, 147.9, 145.7, 141.1, 140.6, 140.2, 137.2, 134.8, 132.2, 131.5 (each C), 128.3, 127.9, 127.6, 127.3, 127.2, 127.0, 126.8, 126.2, 125.9, 125.2, 124.9, 120.0, 118.0, 69.2, 50.2 (each CH), 25.2 (CH_2), 21.9 (2 × Me) and 13.7 (Me); *m*/*z* 406 (M^+, 24%), 364 (26), 363 (64), 347 (39), 346 (91), 318 (35), 317 (100), 303 (22), 302 (35), 289 (24) and 191 (19).

+*ac*(*R*)-1-(1′-Methylfluoren-9′-yl)naphthalene-2-methanol 25

The ester **19** (120 mg, 0.31 mmol) was dissolved in anhydrous diethyl ether (10 cm^3) and lithium aluminium hydride (LAH) (50 mg, 1.32 mmol) added in one portion. The mixture was stirred at room temperature for 1 h then an excess of dilute hydrochloride acid (2 mol dm^{-3}) was cautiously added followed by DCM. The separated organic layer was washed with brine and the crude product purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *alcohol* **25** (103 mg, 100%) as a colourless oil; $[\alpha]_D$ −82 (*c* 1.2, toluene), 57% ee (Found: M^+, 336.1505. $^{12}C_{25}{}^1H_{20}{}^{16}O$ requires M^+, 336.1514). The enantiomeric purity was determined by HPLC analysis of the benzoate derivative (see below); t_R 33.5 min for **25**-benzoate and 42.2 min for *ent*-**25**-benzoate; δ_H 1.88 (3H, s, 1′-Me), 5.36 and 5.40 (2H, AB, *J* 12.2, CH_2), 5.93 (1H, s, 9′-H), 6.69 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.93 (1H, ddd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.8, $J_{7,5}$ 1.4, 7-H), 7.07 (1H, br d, $J_{2',3'}$ 7.6, 2′-H), 7.22–7.28 (2H, m, 7′- and 8′-H), 7.30 (1H, br dd, $J_{6,5}$ 8.2, $J_{6,7}$ 6.8, 6-H), 7.45 (1H, dd, $J_{3',4'}$ 7.6, $J_{3',2'}$ 7.6, 3′-H), 7.45–7.50 (1H, m, 6′-H), 7.74 (1H, d, $J_{3,4}$ 8.4, 3-H), 7.81 (1H, br d, $J_{5,6}$ 8.2, 5-H), 7.90 (1H, d, $J_{4,3}$ 8.4, 4-H), 7.91 (1H, br d, $J_{4',3'}$ 7.6, 4′-H) and 8.01 (1H, br d, $J_{5',6'}$ 7.6, 5′-H); δ_C 147.9, 146.2, 140.41, 140.36, 137.0, 134.9, 134.7, 133.9, 131.8 (each C), 129.0, 128.24, 128.20, 127.3, 127.2, 127.0, 126.9, 125.7, 125.5, 124.9, 124.3, 120.2, 118.1 (each CH), 64.9 (CH_2), 4.94 (CH) and 18.8 (Me); *m*/*z* 336 (M^+, 1.1%), 335 (1.1), 334 (1.6), 318 (35), 303 (100), 302 (28), 301 (16), 299 (14), 151 (18) and 150 (12).

Preparation of alcohol 25 from ester 20

The ester **20** (420 mg, 0.86 mmol, 75% de) was treated with LAH (50 mg, 1.32 mmol) during 1 h at room temperature using the procedure described above. The crude product was purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *alcohol* **25** (288 mg, 100%) as a colourless oil; $[\alpha]_D$ −103 (*c* 1.1, toluene), 75% ee.

−*ac*(*S*)-1-(1′-Methylfluoren-9′-yl)naphthalene-2-methanol *ent*-25

The ester *ent*-**19** (120 mg, 0.31 mmol) was treated with LAH (50 mg, 1.32 mmol) during 1 h at room temperature using the procedure described for the preparation of **25**. The crude product was purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *alcohol ent*-**25** (102 mg, 99%) as a colourless oil; $[\alpha]_D$ +108 (*c* 1.35, toluene), 78% ee. The spectroscopic properties were identical to those of **25**.

+*ac*(*R*)/−*ac*(*S*)-1-(1′-Chlorofluoren-9′-yl)naphthalene-2-methanol 26/*ent*-26

The ester **22**/*ent*-**22** (120 mg, 0.29 mmol) was treated with LAH (50 mg, 1.32 mmol) during 1 h at room temperature using the procedure described for the preparation of **25**. The crude product was purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *alcohol* **26**/*ent*-**26** (104 mg, 100%) as a colourless solid, mp 178–180 °C; $[\alpha]_D$ +0.4 (*c* 1.0, DCM), 36% ee (Found: C, 80.65; H, 5.15. $C_{24}H_{17}ClO$ requires C, 80.8; H, 4.8%). The enantiomeric purity was determined by HPLC analysis of the benzoate derivative (see below); t_R 32.5 min (minor) and 35.6 min (major); δ_H 5.26 and 5.35 (2H, AB, *J* 12.3, CH_2), 5.99 (1H, s, 9′-H), 6.53 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.84 (1H, ddd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.8, $J_{7,5}$ 1.4, 7-H), 7.14 (1H, dd, $J_{2',3'}$ 8.0, $J_{2',4'}$ 0.8, 2′-H), 7.16–7.23 (3H, m, 6-, 7′- and 8′-H), 7.36–7.42 (2H, m, 3′- and 6′-H), 7.64 (1H, d, $J_{3,4}$ 8.4, 3-H), 7.72 (1H, br d, $J_{5,6}$ 7.8, 5-H), 7.82 (1H, d, $J_{4,3}$ 8.4, 4-H), 7.86 (1H, dd, $J_{4',3'}$ 7.6, $J_{4',2'}$ 0.8, 4′-H) and 7.91 (1H, br d, $J_{5',6'}$ 7.7, 5′-H); δ_C 147.8, 144.8, 143.0, 139.3, 137.8, 134.0, 133.5, 131.7, 131.4 (each C), 128.8, 128.45, 128.43, 128.2, 127.9, 127.3, 127.1, 125.8, 125.3, 124.6, 124.5, 120.6, 118.9 (each CH), 65.2 (CH_2) and 49.8 (CH); *m*/*z* 358 (M^+, 0.8%), 356 (M^+, 2.8), 340 (11), 338 (31), 304 (25), 303 (100), 302 (42), 301 (20), 300 (22), 289 (12) and 151 (19).

+*ac*(*R*)/−*ac*(*S*)-1-(1′-Ethylfluoren-9′-yl)naphthalene-2-methanol 27/*ent*-27

The ester **23**/*ent*-**23** (60 mg, 0.15 mmol) was treated with LAH (50 mg, 1.32 mmol) during 1 h at room temperature using the procedure described for the preparation of **25**. The crude product was purified by flash chromatography with 20% ethyl acetate–light petroleum as eluent to afford the *alcohol* **27**/*ent*-**27** (52 mg, 100%) as a colourless solid, mp 168–169.5 °C; $[\alpha]_D$ +80 (*c* 1.7, DCM), 61% ee (Found: C, 88.8; H, 6.45. $C_{26}H_{22}O$ requires C, 89.1; H, 6.35%). The enantiomeric purity was determined by HPLC analysis of the benzoate derivative (see below); t_R 26.9 min (minor) and 37.6 min (major); δ_H 0.68 (3H, t, *J* 7.6, CH_2CH_3), 2.09 and 2.30 (2H, each dq, *J* 14.4, 7.6, CH_2CH_3), 5.26 and 5.35 (2H, AB, *J* 12.4, CH_2OH), 5.87 (1H, s, 9′-H), 6.64 (1H, br d, $J_{8,7}$ 8.7, 8-H), 6.85 (1H, br dd, $J_{7,8}$ 8.7, $J_{7,6}$ 6.8, 7-H), 7.07 (1H, br d, $J_{2',3'}$ 7.5, 2′-H), 7.13–7.19 (2H, m, 7′- and 8′-H), 7.21 (1H, br dd, $J_{6,5}$ 8.1, $J_{6,7}$ 6.8, 6-H), 7.35–7.41 (1H, m, 6′-H), 7.43 (1H, dd, $J_{3',4'}$ 7.5, $J_{3',2'}$ 7.5, 3′-H), 7.67 (1H, d, $J_{3,4}$ 8.4, 3-H), 7.71 (1H, br d, $J_{5,6}$ 8.1, 5-H), 7.81 (1H, d, $J_{4,3}$ 8.4, 4-H), 7.84 (1H, br d, $J_{4',3'}$ 7.5, 4′-H) and 7.93 (1H, br d, $J_{5',6'}$ 7.6, 5′-H); δ_C 147.8, 145.6, 141.0, 140.6, 140.4, 136.9, 135.2, 133.9, 131.8 (each C), 128.21, 128.18, 127.5, 127.2, 127.07, 127.02, 126.8, 125,7, 125.4, 125.1, 124.3, 120.1, 118.0 (each CH), 64.8 (CH_2), 49.1 (CH), 25.0 (CH_2) and 13.9 (Me); *m*/*z* 350 (M^+, 3.4), 349 (2.2), 333 (65), 318 (42), 317 (87), 304 (44), 303 (100), 301 (88), 289 (17), 178 (15) and 151 (28).

Preparation of the benzoate derivatives of alcohols 25/*ent*-25, 26/*ent*-26 and 27/*ent*-27

A solution of the alcohol (0.15 mmol), benzoyl chloride (35 mm^3, 0.30 mmol), pyridine (36 mm^3, 0.45 mmol) and 4-dimethylaminopyridine (1 mg, 0.01 mmol) in anhydrous DCM (5 cm^3) was stirred at room temperature for 48 h. Water (1 cm^3) was then added and the mixture stirred vigorously for 2 h. An excess of dilute hydrochloric acid (2 mol dm^{-3}) was then added followed by DCM. The separated organic layer was washed with brine and the crude product purified by flash chromatography with 30% DCM–light petroleum as eluent to afford the benzoate derivatives as colourless solids in 85–100% yields.

+*ac*(*R*)-1-Methyl-9-(2′-chloromethyl-1′-naphthyl)fluorene 32

A solution of the alcohol **25** (235 mg, 0.70 mmol, 75% ee) and thionyl chloride (0.3 cm^3, 4.1 mmol) in anhydrous DCM (15 cm^3) was stirred at room temperature for 23 h. The solution was then diluted with toluene (15 cm^3) and the solvent evaporated under reduced pressure. The crude product was purified by flash chromatography with 25% DCM–light petroleum as eluent to afford the *chloride* **32** (240 mg, 97%) as a colourless solid, mp 130–133 °C; $[\alpha]_D$ −101 (*c* 1.15, toluene) (Found: C, 84.35; H, 5.6. $C_{25}H_{19}Cl$ requires C, 84.6; H, 5.4%); δ_H 1.89 (3H, s, 1-Me), 5.24 and 5.31 (2H, AB, *J* 11.7, CH_2), 5.91 (1H, s, 9-H), 6.70 (1H, br d, $J_{8',7'}$ 8.7, 8′-H), 6.94 (1H, br dd, $J_{7',8'}$ 8.7, $J_{7',6'}$ 6.9, 7′-H), 7.07 (1H, br d, $J_{2,3}$ 7.5, 2-H), 7.24–7.34

(3H, m, 6′- and 7- and 8-H), 7.45 (1H, dd, $J_{3,4}$ 7.5, $J_{3,2}$ 7.5, 3-H), 7.48 (1H, br dd, $J_{6,7}$ 7.6, $J_{6,5}$ 7.6, 6-H), 7.68 (1H, d, $J_{3',4'}$ 8.4, 3′-H), 7.80 (1H, br d, $J_{5',6'}$ 8.0, 5′-H), 7.89 (1H, d, $J_{4',3'}$ 8.4, 4′-H), 7.91 (1H, br d, $J_{4,3}$ 7.5, 4-H) and 8.01 (1H, br d, $J_{5,6}$ 7.6, 5-H); δ_C 147.3, 145.9, 140.44, 140.38, 135.7, 135.0, 134.16, 134.11, 131.7 (each C), 129.2, 128.6, 128.3, 128.0, 127.5, 127.27, 127.24, 126.1, 126.0, 125.1, 124.5, 120.3, 118.2, 49.6 (each CH), 45.7 (CH_2) and 19.0 (Me); *m/z* 356 (M^+, 6.6%), 354 (M^+, 22), 319 (12), 318 (10), 303 (100), 302 (17), 301 (10), 300 (11) and 150 (16).

+*ac*(*R*)-1-Methyl-9-(2′-methoxymethyl-1′-naphthyl)fluorene 33

Methanol (10 cm^3) was added to a solution of the chloride **32** (225 mg, 0.63 mmol) in anhydrous DCM (10 cm^3) and a solution of silver trifluoromethanesulfonate (250 mg, 0.97 mmol) in methanol (1 cm^3) was then added in one portion. The mixture was stirred at room temperature, with protection from light, for 4 d, then diluted with DCM and filtered through a pad of Celite. The filtrate was washed with water, then brine, and the crude product purified by flash chromatography with 30% DCM–light petroleum as eluent to afford the *ether* **33** (198 mg, 89%) as a colourless solid, mp 167–170 °C; $[\alpha]_D$ −114 (*c* 1.4, toluene), 75% ee (Found: M^+, 350.1655. $^{12}C_{26}{}^{1}H_{22}{}^{16}O$ requires M^+, 350.1670). The enantiomeric purity was determined by the ^{1}H NMR (400 MHz) signals due to the fluorene 1-methyl group in the presence of (*S*)-TFAE (5 equiv., *ca.* 0.6 mol dm^{-3}); $\delta_H(C_6D_6)$ 1.66 and 1.68, respectively, for **33** and *ent*-**33**; δ_H 1.87 (3H, s, 1-Me), 3.60 (3H, s, OMe), 5.07 and 5.09 (2H, AB, *J* 11.4, CH_2), 5.89 (1H, s, 9-H), 6.68 (1H, br d, $J_{8',7'}$ 8.7, 8′-H), 6.94 (1H, ddd, $J_{7',8'}$ 8.7, $J_{7',6'}$ 6.8, $J_{7',5'}$ 1.4, 7′-H), 7.04 (1H, br d, $J_{2,3}$ 7.5, 2-H), 7.21–7.28 (3H, m, 6′-, 7- and 8-H), 7.42 (1H, dd, $J_{3,4}$ 7.5, $J_{3,2}$ 7.5, 3-H), 7.43–7.47 (1H, m, 6-H), 7.69 (1H, d, $J_{3',4'}$ 8.4, 3′-H), 7.83 (1H, br d, $J_{5',6'}$ 8.1, 5′-H), 7.86 (1H, d, $J_{4',3'}$ 8.4, 4′-H), 7.89 (1H, br d, $J_{4,3}$ 7.5, 4-H) and 7.99 (1H, br d, $J_{5,6}$ 7.6, 5-H); δ_C 148.0, 146.4, 140.4, 140.3, 135.4, 135.0, 134.8, 133.9, 131.7 (each C), 129.0, 128.2, 127.81, 127.76, 127.24, 127.16, 126.9, 125.6, 125.4, 124.8, 124.5, 120.2, 118.0 (each CH), 74.6 (CH_2), 58.6 (Me), 49.5 (CH) and 18.7 (Me); *m/z* 350 (M^+, 0.7%), 318 (64), 304 (48), 303 (100), 302 (42), 301 (18), 300 (19), 151 (25) and 150 (22).

−*sc*(*R*)-1-Methyl-9-(2′-methoxymethyl-1′-naphthyl)fluorene 34

A solution of the ether **33** (170 mg, 0.49 mmol) in xylenes (10 cm^3) was heated under reflux for 20 h. The solvent was evaporated under reduced pressure and a portion (160 mg) of the residue purified by preparative HPLC with 30% DCM–light petroleum as eluent. This gave, in addition to recovered **33** (109 mg, 68%), the isomeric *ether* **34** (49 mg, 30%) as a colourless solid, mp 135–137 °C; $[\alpha]_D$ −152 (*c* 1.5, toluene), 75% ee (Found: M^+, 350.1670. $^{12}C_{26}{}^{1}H_{22}{}^{16}O$ requires M^+, 350.1670). The enantiomeric purity was determined by the ^{1}H NMR (400 MHz) signals due to the fluorene 1-methyl group in the presence of (*S*)-TFAE (5 equiv., *ca*. 0.6 mol dm^{-3}); $\delta_H(C_6D_6)$ 1.59 and 1.56, respectively, for **34** and *ent*-**34**; δ_H 1.80 (3H, s, 1-Me), 2.64 (3H, s, OMe), 3.38 and 3.52 (2H, AB, *J* 12.9, CH_2), 6.16 (1H, s, 9-H), 7.07 (1H, br d, $J_{2,3}$ 7.6, 2-H), 7.13 (1H, br d, $J_{8,7}$ 7.5, 8-H), 7.20 (1H, br dd, $J_{7,8}$ 7.5, $J_{7,6}$ 7.4, 7-H), 7.39 (1H, dd, $J_{3,4}$ 7.6, $J_{3,2}$ 7.6, 3-H), 7.42 (1H, br dd, $J_{6,7}$ 7.4, $J_{6,5}$ 7.4, 6-H), 7.56 (1H, d, $J_{3',4'}$ 8.5, 3′-H), 7.60 (1H, br dd, $J_{6',5'}$ 8.2, $J_{6',7'}$ 6.9, 6′-H), 7.69 (1H, ddd, $J_{7',8'}$ 8.6, $J_{7',6'}$ 6.9, $J_{7',5'}$ 1.4, 7′-H), 7.79 (1H, br d, $J_{4,3}$ 7.6, 4-H), 7.88 (1H, d, $J_{4',3'}$ 8.5, 4′-H), 7.90 (1H, br d, $J_{5,6}$ 7.4, 5-H), 7.99 (1H, br d, $J_{5',6'}$ 8.2, 5′-H) and 8.64 (1H, br d, $J_{8',7'}$ 8.6, 8′-H); δ_C 147.3, 145.7, 140.77, 140.72, 135.7, 135.0, 133.7, 133.5, 132.4 (each C), 129.2, 128.8, 127.8, 127.4, 127.2, 127.1, 126.5, 126.0, 125.3, 124.5, 123.7, 120.1, 117.9 (each CH), 70.0 (CH_2), 57.3 (CH), 47.4 and 18.9 (each Me); *m/z* 350 (M^+, 41%), 321 (27), 320 (52), 319 (60), 318 (45), 306 (23), 305 (55), 304 (100), 303 (85), 302 (57), 301 (51), 291 (24), 290 (51), 151 (38) and 150 (25).

−*ac*(*S*)-1-Methyl-9-(2′-methoxymethyl-1′-naphthyl)fluorene *ent*-33

A solution of BuLi (2.65 mol dm^{-3}; 0.27 mmol) in hexane (100 mm^3) was added in one portion to a stirred solution of the ether **34** (45 mg, 0.13 mol) in anhydrous benzene (500 mm^3) at room temperature. The solution was stirred 3 h longer and then the reaction quenched by the addition of either acetic acid or [$^2H_4$]acetic acid (100 mm^3). The mixture was then diluted with DCM and washed in turn with saturated aq. sodium hydrogen carbonate, water, and finally brine. The crude product was purified by flash chromatography with 2% ethyl acetate–light petroleum as eluent to afford a colourless oil (32 mg, 70% recovery). The ^{1}H NMR spectrum of the product from the [$^2H_4$]acetic acid quenched reaction revealed a 1:1.1 mixture of **34** and *ent*-**33**, respectively, which by integration had >98% incorporation of deuterium at C-9 of *ent*-**33** and no evidence of deuterium incorporation at C-9 of **34**. The ^{1}H NMR spectrum of the product from the acetic acid quenched reaction in the presence of (*S*)-TFAE indicated the *ent*-**33** and unreacted **34** were both of 75% ee.

Lithiation and protonation of 33

The ether **33** (40 mg, 0.11 mmol) was treated with BuLi during 15 min at room temperature using the procedure described above. Quenching the reaction with either acetic acid or [$^2H_4$]acetic acid, followed by work-up as above and purification by flash chromatography with 2% ethyl acetate–light petroleum as eluent, afforded a colourless solid (38 mg, 95% recovery). The ^{1}H NMR spectrum of the product from the [$^2H_4$]acetic acid quenched reaction revealed the presence of **33** only, which by integration had >98% incorporation of deuterium at C-9. The ^{1}H NMR spectrum of the product from the acetic acid quenched reaction in the presence of (*S*)-TFAE indicated that **33** was of 75% ee.

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