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cis–trans Enantiomerism in the Diels–Alder cycloadducts of 6-arylfulvenes with maleic anhydride: resolution of the *exo* adducts via the *N*-((1*S*)-1-(naphth-1-yl)ethyl)imide derivatives: assignment of the absolute configurations based on the crystal structure of an imide diastereomer

Sosale Chandrasekhar* and Suresh Kumar Gorla

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

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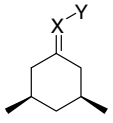
Abstract—A new case of the uncommon *cis–trans* enantiomerism is presented. The titled anhydride adducts were prepared in good yields by the known reaction of three 6-arylfulvenes with maleic anhydride (aryl = phenyl, *p*-tolyl and *p*-anisyl). The *exo* adducts were converted to the corresponding imides by reaction with (1*S*)-1-(naphth-1-yl)ethylamine in ~80% yields, and the resulting diastereomeric imides separated by silica gel column chromatography. They were hydrolysed and recyclised to the chiral anhydrides, in 'one-pot' with 10% NaOH–EtOH, followed by treatment with 2 M HCl, in ~40% yields. The titled anhydrides were thus obtained in homochiral form, in enantiomeric purities (generally) of ~90% as indicated by chiral HPLC. The chiral anhydrides were also converted to the corresponding imides (presumably stereospecifically), by treatment with ammonia solution in excellent yields. The crystal structure of one of the above diastereomeric imides (derived from 6-phenylfulvene) was determined, and based on the known (*S*)-configuration of the naphthylethylamine moiety, the 'configurations' of the original anhydride adducts were assigned.

1. Introduction

That molecules may be chiral even though they possess no stereogenic centres is well known, and also well-demonstrated in allenes, biphenyls, spiranes, etc.[1] Appropriately substituted derivatives of these may be chiral by virtue of possessing a chiral axis. A somewhat related and fascinating case is that of the alkylidenecycloalkanes, which may possess stereogenic centres when appropriately substituted, but by virtue of *cis–trans* isomerism at the alkylidene moiety. Thus, for instance, *cis*-3,5-dimethylcyclohexanone **1a** is achiral, while the corresponding oxime **1b** can exist in chiral forms (Scheme 1), essentially because the oxime moiety can exist in both *cis* and *trans* forms. However, this is with respect to the C_3 and C_5 stereogenic centres: intriguingly, thus, the *cis* and *trans* forms are indistinguishable in an achiral environment. Interestingly also, the alkylidenecycloalkanes apparently represent a transition from axial to *cis–trans* chirality, as either property may be exhibited by an appropriately substituted derivative.[1]



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1	X	Y
a	O	-
b	N	OH
c	CH	Me

Scheme 1. The possibility of *cis–trans* enantiomerism in certain derivatives of the *meso* compound *cis*-3,5-dimethylcyclohexanone **1a**, which is effectively desymmetrised in its oxime **1b** and ethylidene **1c** derivatives.

The above dependence of the overall molecular chirality on *cis–trans* isomerism has been termed as '*cis–trans* enantiomerism',[1] and is not merely of theoretical interest. In fact, an interesting practical consequence is that the inversion of the geometry around the double bond (say) in an appropriate alkylidenecyclohexane (e.g., **1c**),

* Corresponding author. Tel.: +91 80 2293 2689; fax: +91 80 23600 529; e-mail: sosale@orgchem.iisc.ernet.in

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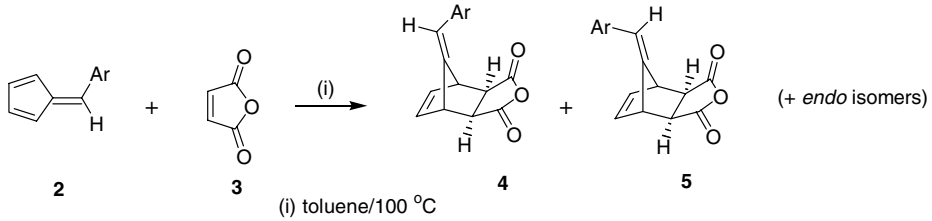
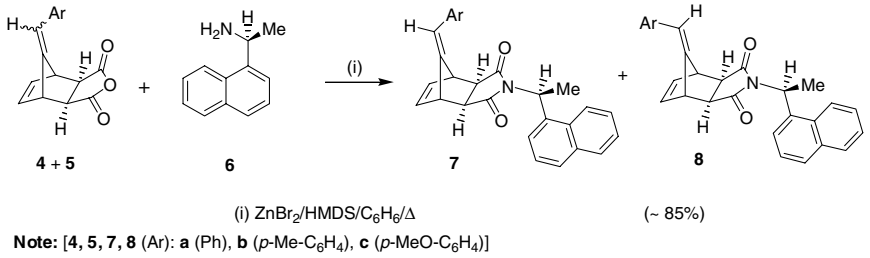


Scheme 2. Cycloaddition of the 6-arylfulvenes **2a**–**2c** with maleic anhydride **3** to form the corresponding enantiomeric *exo* adducts **4** and **5** (as a racemic mixture, cf. Table 1).



Scheme 3. Conversion of the racemic mixture of adducts **4a**–**4c** and **5a**–**5c** to the corresponding diastereomeric *N*-(naphth-1-yl)ethylimides **7** and **8**, via reaction with (1*S*)-(naphth-1-yl)ethylamine **6** in the presence of $ZnBr_2$ and hexamethyldisilazane (HMDS; cf. Table 1).

would result in the inversion of the overall molecular chirality. In order to appreciate the significance and potential of such a process, one needs to consider the fact that the inversion of the overall chirality of a complex molecule possessing several stereogenic centres, by a single inversion operation is very rarely possible. The inversion of the overall chirality would be most useful if it followed a resolution step, as it would convert all of the original racemate into one chiral form.[2] Several methods exist for the inversion of olefin geometry.[3] These considerations indicate the desirability of exploring the concept of *cis–trans* enantiomerism, and possibly discovering practically useful examples, which would function as chiral synthons for further elaboration.

Over the course of a study on the cycloaddition reactions of the fulvenes,[4] we were struck by the fact that products **4** of the Diels–Alder reaction between 6-arylfulvenes **2** and maleic anhydride **3** displayed *cis–trans* enantiomerism (Scheme 2). Adducts **4**, notably, possessed four stereogenic centres. As a result we embarked on a program of isolating and resolving the adducts, essentially via their conversion to diastereomeric imide derivatives (cf. Scheme 3), with the results obtained reported in detail herein.

2. Results and discussion

Cycloadducts **4** and **5** were obtained in satisfactory yields (Table 1), via the reaction of the appropriate fulvene **2** and a moderate excess of maleic anhydride **3** in refluxing toluene.[4] The enantiomeric pair **4** and **5** are shown separately in Scheme 2 in order to clarify the discussion below. The *exo* and *endo* cycloadducts were separated by fractional crystallization or chromatography, with the *exo* generally predominating. The crystal structure of the *endo* *p*-anisyl adduct [corresponding to (**4c**+**5c**), structure not shown] was also determined by X-ray diffraction[5] and this aided the spectroscopic structure assignments of the other derivatives.

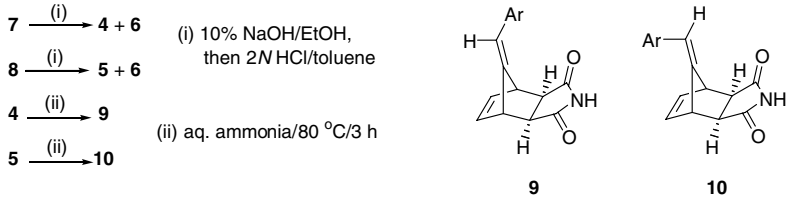
The *exo* adducts **4** and **5** were reacted with (1*S*)-1-(naphth-1-yl)ethylamine **6** in benzene at 70 °C, employing a mixture of zinc bromide and hexamethyldisilazane (HMDS),[6] to obtain the corresponding diastereomeric imides **7** and **8** in high yields (Scheme 1, Table 1), as indicated by chromatographic and spectral evidence.

Thus, silica gel column chromatography yielded the pure diastereomers **7** and **8** in nearly equal amounts, which possessed the following (typical) spectral

Table 1. Percentage yields of the *exo* cycloadducts **4** and **5** and the diastereomeric *N*-(naphthylethyl)imides **7** and **8**,[a] cf. Schemes 2 and 3

Item	Compound (**4**, **5**, **7**, **8**)	Ar	Yield (%)		
			(**4**+**5**)[a]	**7**	**8**
1	**a**	Ph	70 (1.5)	40	40
2	**b**	*p*-Me–(C_6H_4)–	70 (0.8)	41	41
3	**c**	*p*-MeO–(C_6H_4)–	65 (2.7)	43	43

[a] The numbers in parentheses represent the ratio (*exo*/*endo*).



Scheme 4. Hydrolysis and recyclisation of the diastereomeric naphthylethylimides **7a**–**7c** and **8a**–**8c** to the enantiomeric anhydrides **4a**–**4c** and **5a**–**5c**, respectively, and the conversion of these to the corresponding imides **9a**–**9c** and **10a**–**10c**, respectively (cf. Table 2).

Table 2. Percentage yields and ees of the homochiral anhydrides (*E*)-**4** and (*Z*)-**5** (from the hydrolysis and recyclisation of the (naphthylethyl)imides **7** and **8**), cf. Scheme 4

Item	Compound (**4**, **5**, **9**, **10**)	Ar	Yield[a] (%)	
			(*E*)-**4**	(*Z*)-**5**
1	**a**	Ph	40 (94)	38 (70)
2	**b**	*p*-Me–(C_6H_4)–	38 (91)	36 (91)
3	**c**	*p*-MeO–(C_6H_4)–	42 (30)	40 (94)

[a] Relative to a maximum of 100% for each enantiomer; the values in parentheses refer to the ee values determined by chiral HPLC.

characteristics.[7] In the IR spectra, the imide moiety displayed two bands at 1768 and 1697 cm^{-1}. In the 300 MHz ^1H NMR spectra, the amino(naphthyl)methine proton resonated at δ 6.05 as a quartet, in both the diastereomers; the key exocyclic arylidene methine proton resonated as a singlet at δ 5.92 and 5.57 in the different diastereomers, this difference in chemical shift being around 0.3 δ in all the three cases studied.

Diastereomeric imides **7** and **8** were also hydrolysed and recyclised to the corresponding homochiral anhydrides **4** and **5**, by successive treatment with 10% ethanolic NaOH and 2 N HCl in toluene,[8] in yields of around 40% (Scheme 4 and Table 2). Homochiral **4** and **5** were identical spectroscopically to the original racemate mixture, which was thus deemed to be resolved. The optical rotations for the enantiomers were found to be identical in magnitude within experimental error, with the enantiomeric purities being determined with the aid of chiral HPLC (on a Chiralcel® column). Circular dichroism (CD) spectra and optical rotations also confirmed these results, the CD curves being of opposite signs for the enantiomers (cf. Fig. 1).

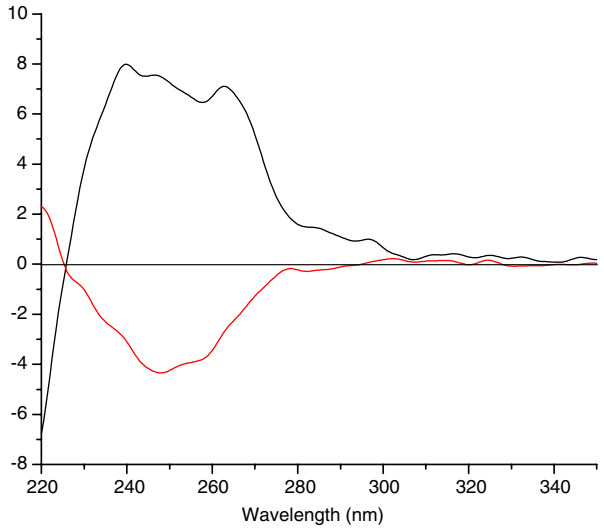


Figure 1. Circular dichroism (CD) spectra of the resolved enantiomers of the *cis–trans* enantiomeric bicyclic anhydrides **4b** (in red) and **5b** (in black), derived originally from 6-(*p*-tolyl)fulvene **2b**, cf. Schemes 2–4 (the CD is represented on the *y* axis in units of millidegrees).

Furthermore, we were able to determine the crystal structure of the 6-phenylfulvene derived imide **7a**.[9] The ORTEP diagram of **7a** (Fig. 2) shows that, in a conformation in which the naphthyl group points towards the *endo* side (i.e., away from the benzylidene moiety, essentially as shown in Scheme 3), the phenyl ring is on the same side as the amino(naphthyl)methine hydrogen atom (C_{17}–H). This is with reference to a plane passing through C_{17}, N_1, C_7, C_8 and the mid-points of the C_2–C_3 and C_5–C_6 bonds, employing crystallographic numbering, cf. Scheme 5. Since the configuration of the naphthylethylamine moiety is known to be *S*, this enabled us to assign the configuration of the arylalkylidene moiety in **7a**, and also of the resolved anhydrides **4** and **5.** Thus, inspection indicated that **7a** derives from

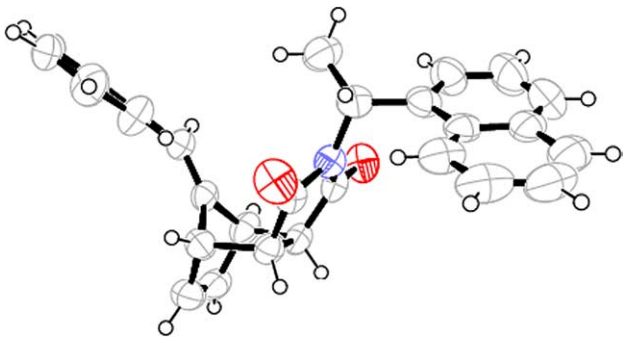
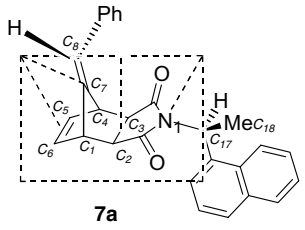


Figure 2. ORTEP diagram of the *N*-(naphthylethyl)imide diastereomer **7a**, derived originally from 6-phenylfulvene **2a**, cf. Schemes 2 and 3.



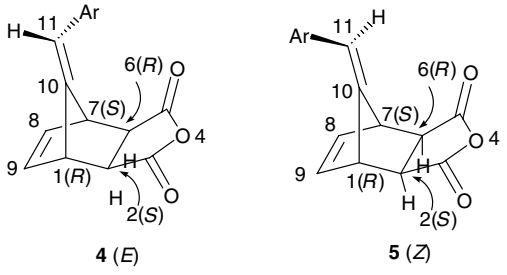
7a

Scheme 5. The orientation of the benzylidene moiety (at C_7) relative to the orientations of the substituents at C_{17}, as seen in the X-ray diffraction crystal structure of the imide **7a** (cf. Fig. 2: note that the crystallographic numbering has been retained here). The dashed rectangle represents a plane that includes C_7, C_8, C_{17}, N_1, and the mid-points of C_2–C_3 and C_5=C_6; the four dashed lines within the rectangle lie within this plane, and serve to indicate that C_7, N_1, and the mid-points of C_2–C_3 and C_5=C_6 lie in this plane. It is thus seen that the C_8–Ph group and the C_{17}–H atom are on the same side of this plane. Also, as the stereogenic C_{17} centre is known to be of an (*S*)-configuration (as indicated above), the 'configuration' around the C_7–C_8 double bond may be assigned (cf. Scheme 6 and the discussion below).

4a, which was also determined to be dextrorotatory via the hydrolysis of **7a** (cf. Scheme 4).

The configurational nomenclature for *cis–trans* enantiomerism employs the *E*,*Z* system rather than the *R*,*S*, as the chirality derives from the *cis–trans* isomerism.[1] Thus, the configuration of **4** would be *E*, as the higher priority aryl (Ar) group is *cis* to the C_7 centre which is of an (*S*)-configuration (cf. Scheme 6). Accordingly, the configuration of **5** is *Z*. It should be noted that in this analysis, the C_1 and C_7 centres have been taken into consideration, rather than the C_2 and C_6 centres, which are also stereogenic. This establishes an arbitrary preference for stereogenic centres closest to the double bond that gives rise to the enantiomerism, but this is reasonable and also necessary in the case of molecules possessing more than two stereogenic centres. This, of course, needs to be consistently employed. Note that, were the C_2 and C_6 centres to be considered then the above assignments would be inverted (cf. Scheme 6).

The diastereomeric imides **7** and **8** can then be denoted as (*E*,*S*) and (*Z*,*S*), respectively, '*E*' and '*Z*' referring to the configuration at the exocyclic C_7–C_8 double bond, and '*S*' to the configuration at the C_{17} naphthylethyl centre (cf. Scheme 5). A clearly discernible upfield shift of the exocyclic C_8–H proton (cf. Scheme 5) of 0.34 ppm was observed in the case of **7a**, relative to the diastereomeric **8a**, in the NMR. Similar shifts in the case of **7b**/**8b** (0.26 ppm) and **7c**/**8c** (0.30 ppm) enabled the structural assignments of the diastereomeric pairs (the other resonances were largely unchanged in these diastereomeric pairs). Interestingly, the C_2–H and C_3–H protons (cf. Scheme 5) in **7** and **8** were clearly distinguished in the NMR: in contrast, the corresponding (diastereotopic) protons in the anhydrides **4** and **5** resonated together (at 300 MHz).



Scheme 6. Assignment of the 'configurations' of the *cis–trans* enantiomeric adducts **4** and **5**, based on the orientation of the higher priority group (Ar) on the C_{10}–C_{11} double bond. As 'Ar' is *trans* to the higher priority *R* centre (C_1) in **4**, this is assigned the *E* 'configuration'; and as 'Ar' is *cis* to C_1 in **5**, this is assigned the *Z* 'configuration'.

The resolved anhydrides **4** and **5** were converted in ~80% yields to the corresponding imides **9** and **10** by heating with aqueous ammonia (Scheme 4). The products were characterised spectrally, but the stereoselectivity of the transformation is currently under investigation, and full details will be published in a further paper.

It is noteworthy that the *endo*-isomers of adducts **4** and **5** could not be resolved as above, as the corresponding imides (*endo* **7** and **8**) were not separable by chromatography. This is presumably because in these, the two chiral moieties are relatively far apart, so that the diastereomers may not differ much in energy. Also, the hydrolysis and recyclisation of diastereomeric imides **7** and **8** presumably occurs *via* the ring-opened succinic monoamide derivatives, as indicated by spectral evidence prior to the treatment with 2 M HCl, and by literature precedent.[8]

3. Conclusions

A new case of *cis–trans* enantiomerism has been demonstrated in a system of general interest, namely the (*exo*) Diels–Alder adducts from three 6-arylfulvenes and maleic anhydride. The resolution of the *cis–trans* enantiomers was accomplished via the formation of diastereomeric imides with (1*S*)-(naphth-1-yl)ethylamine, and their subsequent hydrolysis and recyclisation. The enantiomers were characterised spectrally, polarimetrically (including CD) and by chiral HPLC. The configuration of one of the enantiomeric pairs was assigned on the basis of the X-ray crystal structure of its *N*-(naphth-1-yl)ethylimide.

4. Experimental

Melting points are uncorrected. Evaporations were performed under reduced pressure in a rotary evaporator. The following instruments were employed: Carlo Erba elemental analyser, JASCO FT/IR-410 (IR), JEOL JNM-LA 300 (300 MHz ^{1}H NMR), Micromass Q-TOF (mass spectra), Bruker AXS SMART APEX CCD (X-ray diffraction), JASCO DIP-370 (digital polarimeter), JASCO J-715 Spectropolarimeter (CD), Shimadzu LC-10AS/Chiralcel AD-H column (chiral HPLC on an amylose carbamate stationary phase). Naphthylethylamine

6 (98%) was purchased from the Aldrich Chemical Co. IR spectra were generally recorded on Nujol mulls (reported as ν_{max} in cm^{-1}); NMR spectra were recorded in $CDCl_3$ solution [^1H at 300 MHz and ^{13}C at 75 MHz, reported as δ_H and (^1H-decoupled) δ_C, respectively, relative to internal TMS].

4.1. Cycloadducts 4 and 5

The 6-arylfulvenes **2** were prepared by standard procedures and characterised spectrally;[4] they were then reacted with maleic anhydride **3** (1.2 equiv) in refluxing dry toluene (0.4 M in fulvene) for 6 h. After removal of toluene in vacuo, the residue was fractionally crystallised in EtOAc to separate the *exo* and *endo* isomers (alternatively silica gel column chromatography, eluting with EtOAc–hexane, was employed). The yields of the adducts and the *exo*/*endo* ratios are shown in Table 1. The crystal structure of the *endo* adduct derived from 6-(*p*-methoxyphenyl)fulvene **2c** was determined by X-ray diffraction,[5] and this aided the *exo*/*endo* assignments by NMR of **4** and **5**. ^1H NMR features were similar to those reported for related adducts,[4b] with the signals for the *exo* isomers generally being deshielded relative to the corresponding signals of the *endo* isomers. Thus, the exocyclic arylidene C_{11}–*H* signal (cf. Scheme 6 for the numbering), was relatively deshielded by 0.14–0.17 δ in all the above *exo* adducts.

4.2. Phenyl derivatives 4a and 5a

Mp 133–135 °C. Found (calcd for $C_{16}H_{12}O_3$) C 75.99 (76.18), H 5.02 (4.79). ν_{max} 1856, 1780 (C=O). δ_H 7.34–7.17 (5H, m, Ar–*H*), 6.58–6.46 (2H, m, endocyclic C=C–*H*), 6.08 (1H, s, exocyclic C=C(Ar)–*H*), 4.25 (1H, d, *J* 2.7 Hz, C=C–C–*H*), 3.73 (1H, d, *J* 3.0 Hz, C=C–C–*H*), 3.18 (2H, s, CO–C–*H*). δ_C 170.71, 170.62, 146.75, 137.78, 137.72, 135.13, 128.57, 127.96, 127.45, 114.92, 51.09, 48.99, 48.95, 45.83.

4.3. Tolyl derivatives 4b and 5b

Mp 146–147 °C. Found (calcd for $C_{17}H_{14}O_3$) C 76.49 (76.69), H 5.59 (5.26). ν_{max} 1857, 1780 (C=O). δ_H 7.12 (2H, d, *J* 8.4 Hz, Ar–*H*), 7.07 (2H, d, *J* 8.4 Hz, Ar–*H*), 6.54–6.51 (2H, m, endocyclic C=C–*H*), 6.02 (1H, s, exocyclic C=C(Ar)–*H*), 4.25 (1H, d, *J* 2.4 Hz, C=C–C–*H*), 3.71 (1H, d, *J* 2.4 Hz, C=C–C–*H*), 3.16 (2H, s, CO–C–*H*), 2.32 (3H, s, Ar–*Me*). δ_C 170.80, 170.63, 145.91, 137.90, 137.80, 137.27, 132.24, 129.26, 127.86, 114.83, 51.12, 50.78, 49.02, 45.83.

4.4. Anisyl derivative 4c and 5c

Mp 150–151 °C. Found (calcd for $C_{17}H_{14}O_4$) C 72.24 (72.33), H 5.27 (5.00). ν_{max} 1853, 1782 (C=O). δ_H 7.11 (2H, d, *J* 8.7 Hz, Ar–*H*), 6.83 (2H, d, *J* 8.7 Hz, Ar–*H*), 6.53–6.46 (2H, m, endocyclic C=C–*H*), 5.98 (1H, s, exocyclic C=C(Ar)–*H*), 4.22 (1H, s, C=C–C–*H*), 3.78 (3H, s, O*Me*), 3.67 (1H, s, C=C–C–*H*), 3.14 (2H, s, CO–C–*H*). δ_C 170.85, 170.78, 158.84, 145.02, 137.86, 137.70, 114.23, 113.95, 55.17, 51.12, 48.99, 48.94, 45.70.

4.5. Diastereomeric imides 7 and 8

A stirred mixture of the adducts **4** and **5** in dry benzene (0.12 M) at 25 °C, was treated dropwise with a solution of naphthylethylamine **6** in benzene (0.36 M, 1.0 equiv). The mixture was heated at 70 °C for 1.5–2.0 h, cooled and treated with $ZnBr_2$ (1.0 equiv) in one portion.[6] The resulting mixture was heated at 70 °C, and treated dropwise with a solution of HMDS in dry benzene (0.55 M, 1.5 equiv) over 30 min. The mixture was refluxed for 2 h, cooled and poured into 0.5 M HCl (50 ml), and worked up with EtOAc. The crude product was chromatographed on a silica gel column eluting with toluene–EtOAc, to obtain the pure diastereomeric imides **7** and **8**; the salient spectral features have been indicated in the discussion, and the crystal structure of **7a** has been determined.[9]

4.6. Phenyl derivative (*E*,*S*)-7a

Mp 157–159 °C. $[\alpha]_D^{24} = +112$ (*c* 2.5, $CHCl_3$). ν_{max} 1697 (strong), 1768 (weak) (C=O); δ_H 8.02 (1H, d, '*J* 9.0 Hz, naphthyl Ar–*H*), 7.84 (1H, d, '*J* 7.5 Hz, naphthyl Ar–*H*), 7.60–7.51 (2H, m, Ar–*H*), 7.47–7.41 (1H, m, Ar– *H*), 7.34–7.28 (2H, m, Ar–*H*), 7.11–7.07 (3H, m, Ar–*H*), 6.73–6.70 (2H, m, Ar–*H*), 6.44–6.35 (2H, m endocyclic C=C–*H*), 6.05 (1H, q, *J*7.5 Hz, N–C(naphthyl)–*H*), 5.57 (1H, s, exocyclic C=C(Ar)–*H*), 3.99 (1H, d, *J* 3 Hz, –C=C–C–*H*), 3.48 (1H, d, *J* 2.7 Hz, –C=C–C–*H*), 2.78 (1H, d, *J* 7.5Hz, –CO–C–*H*), 2.69 (1H, d, *J* 7.5Hz, –CO–C–*H*), 1.77 (3H, d, *J* 7.5 Hz, –N–C(naphthyl)–*Me*). δ_C 177.0, 176.8, 147.4, 137.9, 137.4, 135.3, 133.5, 133.1, 131.2, 128.7, 128.6, 128.1, 127.5, 126.6, 126.5, 126.2, 125.1, 124.5, 122.9, 114.1, 50.3, 47.5, 47.3, 45.9, 44.8, 16.8. HRMS: *m*/*z* 428.1614 ($MNa^+ \cdot C_{28}H_{23}NO_2$ requires 428.1626).

4.7. Phenyl derivative (*Z*,*S*)-8a

Mp 135–137 °C. $[\alpha]_D^{24} = -114$ (*c* 1.6, $CHCl_3$). ν_{max} 1697, 1776 (C=O). δ_H 8.07 (1H, m, naphthyl Ar–*H*), 7.86–7.75 (3H, m, naphthyl Ar–*H*), 7.47–7.37 (3H, m, naphthyl Ar–*H*), 7.31–7.15 (5H, m, Ar–*H*), 6.51–6.38 (2H, m, endocyclic C=C–*H*), 6.05 (1H, q, *J* 7.0 Hz, N–C(naphthyl)–*H*), 5.91 (1H, s, exocyclic C=C(Ar)–*H*), 4.12 (1H, dd, J_1 2.1 Hz, J_2 0.6 Hz, –C=C–C–*H*), 3.61 (1H, d, *J* 2.1 Hz, –C=C–C–*H*), 2.82 (1H, dd, J_1 7.3 Hz, J_2 1.2 Hz, –CO–C–*H*), 2.65 (1H, dd, J_1 7.3 Hz, J_2 0.9 Hz, –CO–C–*H*), 1.65 (3H, d, *J* 7.0 Hz, –N–C(naphthyl)–*Me*). δ_C 177.2, 176.9, 148.3, 137.8, 137.5, 135.6, 133.7, 133.5, 131.2, 128.8, 128.5, 128.4, 127.8, 126.9, 126.6, 126.5, 125.4, 124.8, 122.8, 113.9, 50.8, 50.6, 47.3, 46.2, 44.8, 17.2. HRMS: *m*/*z* 428.1607 ($MNa^+ \cdot C_{28}H_{23}NO_2$ requires 428.1626).

4.8. Tolyl derivative (*E*,*S*)-7b

Mp 105–107 °C. $[\alpha]_D^{26} = +73$ (*c* 5.0, $CHCl_3$); ν_{max} 1699 (strong), 1767 (C=O). δ_H 8.02 (1H, d, '*J* 8.4 Hz, naphthyl Ar–*H*), 7.84 (1H, d, '*J* 6.9 Hz, naphthyl Ar–*H*), 7.65–7.59 (2H, m, naphthyl Ar–*H*), 7.47–7.05 (3H, m, naphthyl Ar–*H*), 6.94 (2H, d, '*J* 7.8 Hz, Ar–*H*), 6.70 (2H, d, '*J* 7.8 Hz, Ar–*H*), 6.45–6.37 (2H, m, endocyclic

C=C–*H*), 6.03 (1H, q, *J* 7.0 Hz, N–C(naphthyl)–*H*), 5.61 (1H, s, –C=C(Ar)–*H*), 4.03 (1H, br s, C=C–C–*H*), 3.48 (1H, br s, –C=C–C–*H*), 2.78 (1H, d, *J* 7.5 Hz, –CO–C–*H*), 2.67 (1H, d, *J* 7.5 Hz, –CO–C–*H*), 2.03 (3H, s, Ar–*Me*), 1.75 (3H, d, *J* 7.0 Hz, N–C(naphthyl)–*Me*). δ_C 177.1, 176.9, 146.8, 137.9, 137.5, 136.3, 133.6, 133.3, 132.5, 131.3, 128.9, 128.5, 128.1, 127.5, 126.7, 126.3, 125.2, 124.7, 122.0, 114.4, 50.4, 47.5, 47.3, 46.0, 44.9, 44.8, 16.9. HRMS: *m*/*z* 458.1508 ($MK^+ \cdot C_{29}H_{25}NO_2$ requires 458.1522).

4.9. Tolyl derivative (*Z*,*S*)-8b

Mp 128–130 °C. $[\alpha]_D^{25} = -104$ (*c* 2.0, $CHCl_3$). ν_{max} 1698 (strong), 1767 (C=O). δ_H 8.04–8.01 (1H, m, naphthyl Ar–*H*), 7.85–7.73 (3H, m, naphthyl Ar–*H*), 7.47–7.39 (3H, m, naphthyl Ar–*H*), 7.29–7.02 (4H, m, Ar–*H*), 6.49–6.39 (2H, m, endocyclic C=C–*H*), 6.04 (1H, q, *J* 7.0 Hz, N–C(naphthyl)–*H*), 5.87 (1H, s, exocyclic C=C(Ar)–*H*), 4.10 (1H, br s, –C=C–C–*H*), 3.58 (1H, br s, –C=C–C–*H*), 2.79 (1H, d, *J* 7.5 Hz, –CO–C–*H*), 2.62 (1 H, d, *J* 7.5 Hz, –CO–C–*H*), 2.34 (3H, s, Ar–*Me*), 1.64 (3H, d, *J* 7.0 Hz, N–C(naphthyl)–*Me*). δ_C 177.1, 176.9, 147.4, 137.8, 137.6, 136.7, 133.8, 133.6, 132.8, 131.2, 129.1, 128.8, 128.5, 127.8, 126.6, 126.5, 125.3, 124.9, 122.8, 113.8, 50.6, 47.3, 46.2, 44.9, 44.8, 21.1, 17.2. HRMS: *m*/*z* 442.1782 ($MNa^+ \cdot C_{29}H_{25}NO_2$ requires 442.1783).

4.10. Anisyl derivative (*E*,*S*)-7c

Mp 147–149 °C. $[\alpha]_D^{24} = +90$ (*c* 3.8, $CHCl_3$). ν_{max} 1698 (strong), 1769 (C=O); δ_H 8.02 (1H, d, '*J* 8.4 Hz, naphthyl Ar–*H*), 7.84 (1H, d, '*J* 7.2 Hz, naphthyl Ar–*H*), 7.64–7.58 (2H, m, naphthyl Ar–*H*), 7.48–7.06 (3H, m, Ar–*H*), 6.70–6.63 (4H, m, anisyl Ar–*H*), 6.46–6.37 (2H, m, endocyclic C=C–*H*), 6.04 (1H, q, *J* 7.0 Hz, N–C(naphthyl)–*H*), 5.53 (1H, s, exocyclic C=C(Ar)–*H*), 4.00 (1H, d, *J* 2.7 Hz, C=C–C–*H*), 3.78 (3H, s, anisyl O*Me*), 3.48 (1H, d, *J* 2.7 Hz, C=C–C–*H*), 2.78 (1H, dd, J_1 7.3 Hz, J_2 0.6 Hz, –CO–C–*H*), 2.69 (1H, dd, J_1 7.3 Hz, J_2 1.2 Hz, –CO–C–*H*), 1.76 (3H, d, *J* 7.0 Hz, N–C(naphthyl)–*Me*). δ_C 177.2, 176.9, 158.3, 145.7, 137.9, 137.5, 133.5, 133.2, 131.3, 128.7, 128.5, 128.0, 127.6, 126.7, 126.2, 125.6, 125.1, 124.6, 122.9, 113.6, 55.2, 50.8, 50.4, 47.6, 45.9, 44.8, 16.9. HRMS: *m*/*z* 474.1496 ($MK^+ \cdot C_{29}H_{25}NO_3$ requires 474.1472).

4.11. Anisyl derivative (*Z*,*S*)-8c

Mp 125–127 °C. $[\alpha]_D^{25} = -114$ (*c* 3.5, $CHCl_3$). ν_{max} 1698 (strong), 1769 (C=O); δ_H 8.05–8.02 (1H, m, naphthyl Ar–*H*), 7.85–7.72 (3H, m, naphthyl Ar–*H*), 7.47–7.39 (3H, m, naphthyl Ar–*H*), 7.07 (2H, d, '*J* 8.4 Hz, Ar–*H*), 6.79 (2H, d, '*J* 8.4 Hz, anisyl Ar–*H*), 6.44–6.34 (2H, m, endocyclic C=C–*H*), 6.04 (1H, quartet, *J* 7.0 Hz, N–C(naphthyl)–*H*), 5.83 (1H, s, exocyclic C=C(Ar)–*H*), 4.07 (1H, d, *J* 1.8 Hz, C=C–C–*H*), 3.79 (3H, s, anisyl O*Me*), 3.55 (1H, d, *J* 1.8 Hz, –C=C–C–*H*), 2.75 (1H, dd, J_1 7.2 Hz, J_2 0.9 Hz, –CO–C–*H*), 2.62 (1H, dd, J_1 7.2 Hz, J_2 0.9 Hz, –CO–C–*H*), 1.63 (3H, d, *J* 7.0 Hz, N–C(naphthyl)–*Me*). δ_C 177.2, 177.0, 158.5, 146.4, 137.8, 137.6, 133.8, 133.5, 131.2, 129.0, 128.8, 128.5, 128.2, 128.0, 126.5, 126.4, 125.3, 124.8, 122.8, 113.8, 55.1, 50.7, 50.6, 47.4, 46.2, 44.7, 17.2. HRMS: *m*/*z* 458.1730 ($MNa^+ \cdot C_{29}H_{25}NO_3$ requires 458.1732).

4.12. Resolved (optically active) anhydrides 4 and 5

(Naphthylethyl)imide **7** or **8** in EtOH was treated with 10% aqueous NaOH (1 equiv), and the mixture refluxed for 2 h.[8] The mixture was cooled, concentrated in vacuo and worked up by acidifying with 2 M HCl and extraction with CH_2Cl_2, etc. Removal of the volatiles thoroughly in vacuo furnished a dry residue, which was dissolved in the minimum quantity of dry toluene, and the solution stirred at 25 °C for 4–6 h. The toluene was removed in vacuo, and the residue purified by column chromatography on silica gel eluting with EtOAc–hexane. This gave pure **4** or **5**, along with some uncyclised intermediate diacid (~10%), which was redissolved in toluene for cyclisation as above.

The resolved **4** and **5** were spectroscopically identical to the original racemate, but differed in melting point and rotations as noted below. They were then subjected to chiral HPLC eluting with 9:1 hexane–isopropanol (flow rate: 0.6 ml/min, detector: 254 nm) to determine the purities and ees. The ees were calculated from the peak areas (*a* and *b*), by the relation % ee = $(a - b) \cdot 100/(a + b)$. The reported specific rotations have been corrected for the ee values from HPLC, which are generally 91–94%, except for **5a** (70%) and **4c** (30%). The correlation of configuration and rotational sign in the case of **4a** and **5a** is made on the basis of the crystal structure of imide **7a**, but assumed analogously in the other cases.

4.13. Phenyl derivatives (*E*)-4a and (*Z*)-5a

Compound (*E*)-**4a**: mp 106 °C. $[\alpha]_D^{25} = +80.9$ (*c* 1.0, $CHCl_3$). Found (calcd for $C_{16}H_{12}O_3$) C 76.34 (76.18), H 4.86 (4.79).

Compound (*Z*)-**5a**: mp 111 °C. $[\alpha]_D^{25} = -76.6$ (*c* 1.6, $CHCl_3$). Found (calcd for $C_{16}H_{12}O_3$) C 75.91 (76.18), H 4.92 (4.79).

4.14. Tolyl derivatives (*E*)-4b and (*Z*)-5b

Compound (*E*)-**4b**: mp 119.5 °C. $[\alpha]_D^{25} = +192.8$ (*c* 1.1, $CHCl_3$). Found (calcd for $C_{17}H_{14}O_3$) C 76.63 (76.69), H 5.33 (5.26).

Compound (*Z*)-**5b**: mp 121 °C, $[\alpha]_D^{25} = -176.4$ (*c* 1.4, $CHCl_3$). Found (calcd for $C_{17}H_{14}O_3$) C 76.45 (76.69), H 5.41 (5.26).

4.15. Anisyl derivatives (*E*)-4c and (*Z*)-5c

Compound (*E*)-**4c**: mp 133 °C. $[\alpha]_D^{24} = +284.1$ (*c* 0.9, $CHCl_3$). Found (calcd for $C_{17}H_{14}O_4$) C 71.23 (72.33), H 5.27 (5.00).

Compound (*Z*)-**5c**: mp 129.5 °C. $[\alpha]_D^{24} = -169.4$ (*c* 1.0, $CHCl_3$). Found (calcd for $C_{17}H_{14}O_4$) C 71.99 (72.33), H 5.23 (5.00).

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References

1. Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley: New York, 1994, Chapter 14, pp 1137–1138.
2. Chandrasekhar, S.; Kulkarni, G. *Tetrahedron: Asymmetry* **2002**, *13*, 615–619, and references cited therein.
3. Ref. 1, pp 584–590, and references cited therein.
4. (a) Neuenschwander, M. In *Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; John Wiley: Chichester, 1989, Chapter 16, pp 1131–1268, and references cited therein; (b) Yates, P. In *Advances in Alicyclic Chemistry*; Hart, H., Ed.; Academic Press: New York, 1968; Vol. 2, pp 146–151.
5. Details of the crystal structure may be obtained from: Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk), quoting the depository number CCDC 282717.
6. Reddy, P. Y.; Kondo, S.; Toru, T.; Ueno, Y. *J. Org. Chem.* **1997**, *62*, 2652–2654.
7. Kemp, W. *Organic Spectroscopy*, 3rd ed.; MacMillan: London, 1991; Chapters 2 and 3.
8. Starr, J. T.; Koch, G.; Carreira, E. M. *J. Am. Chem. Soc.* **2002**, *122*, 8793–8794.
9. Details of the crystal structure may be obtained from: Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk), quoting the depository number CCDC 273700.