Electro-organic reactions. Part 42. The diastereoselective cathodic hydrodimerisation of cinnamate esters; preparative aspects[1]

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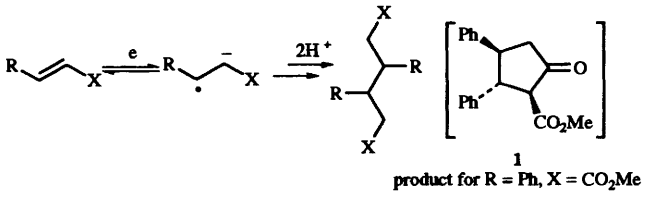
The cathodic reduction of cinnamate esters formed with chiral alcohols proceeds smoothly *via* coupling and intramolecular condensation, with high stereoselectivity, to give good yields of diastereoisomeric mixtures of the esters of the all-*trans* (±)-2-carboxy-3,4-diphenylcyclopentanone. Eight examples have been studied in detail and a diastereoisomeric excess of >95% is achieved using the bornyl ester. Choice of electrolyte cation (Li^+ or Et_4N^+) does not influence yield or stereoselectivity. In some other cases cleavage with loss of cinnamic acid is the preferred reaction. *meso* Isomers are not formed in the cyclic hydrodimerisation reaction. Pure diastereoisomers are easily isolated by fractional crystallisation and may be converted into (±)-3,4-diphenylcyclopentanone.

Electrohydrodimerisation (EHD) of alkenes is one of the most successful electrosynthetic methods. Essentially it involves the reaction of alkenes activated towards cathodic reduction by electron-withdrawing groups. The resulting radical anions may then undergo C–C bond formation by a variety of pathways including radical-ion–radical-ion coupling and Michael addition to the starting material of radical-anion or carbanions arising from protonation and further reduction. The overall EHD process is depicted in Scheme 1. The best known example is the production of adiponitrile from acrylonitrile (R = H, X = CN), pioneered by Baizer and Danly.[2]



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product for R = Ph, X = CO_2Me

Scheme 1

Another early example[3] was the EHD reaction of methyl cinnamate (R = Ph, X = CO_2Me). Klemm and Olson[3] observed that in this case it was difficult to obtain the expected linear hydrodimer but that the predominant product was that of subsequent Dieckmann reaction, (±)-2-(methoxycarbonyl)-3,4-diphenylcyclopentanone **1**; there was no trace of the corresponding *meso* isomer. The high stereoselectivity of this reaction and the original assignment of stereochemistry was confirmed later[4] by thorough analysis of the ^1H NMR spectrum and measurement of the coupling constants for the cyclopentanone ring protons. Furthermore it was shown[4] that very protic conditions, *e.g.* encapsulation in β-cyclodextrin, were required to form the linear hydrodimer. The reactions giving the cyclopentanones typically use aprotic solvent with tetraalkylammonium salts as electrolyte.

The formation only of the (±)-isomer suggests the possibility of reaction under control of a chiral auxiliary and an obvious starting point is to use chiral cinnamates, *i.e.* X = CO_2R^*, where R* is chiral. Preliminary results of successful experiments along these lines have been presented.[5] Kise *et al.* have recently reported success using oxazolidone derivatives of cinnamic acid.[6] We now present a full account of the preparative aspects of these reactions. Improvement in diastereoselectivities is likely to follow a more complete understanding of the mechanism and this has been the subject of a separate kinetic and stereochemical investigation.[7]

Results and discussion

The chiral cinnamates

For this study the requirements of the chiral auxiliary were that it should be readily available and electrochemically inactive. Consequently, commercially available optically active alcohols were used. In some cases they were modified by conversion of the functional groups into ones other than hydroxy which would otherwise interfere with esterification or with the intended electrochemical reaction.

In the above context: L-malic acid was first converted into diethyl and diisopropyl esters; (*R*)-(−)-mandelic acid into various esters; and the secondary amine group of (1*R*,2*S*)-(−)-ephedrine was protected through alkylation, acylation, tosylation and quaternisation.

The formation of the esters of cinnamic acid was straightforward and achieved by reaction of *trans*-cinnamoyl chloride with the alcohol either in dry benzene at room temperature or in chloroform containing pyridine and a small amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP). Details of the esters so prepared, together with key physical data, are presented in the experimental section. Not all of the esters proved to be amenable to convenient electrochemical conversion, but the formulae of those whose electroreductive reactions were explored are given below.

Electroanalytical experiments

Cyclic voltammetry and coulometry. These were used conveniently to give information on relevant reduction potentials and other conditions for preparative-scale electrolysis and the likelihood of hydrodimerisation (a 1 F process)† *vis-à-vis* hydrogenation or cleavage (usually 2 F reactions).

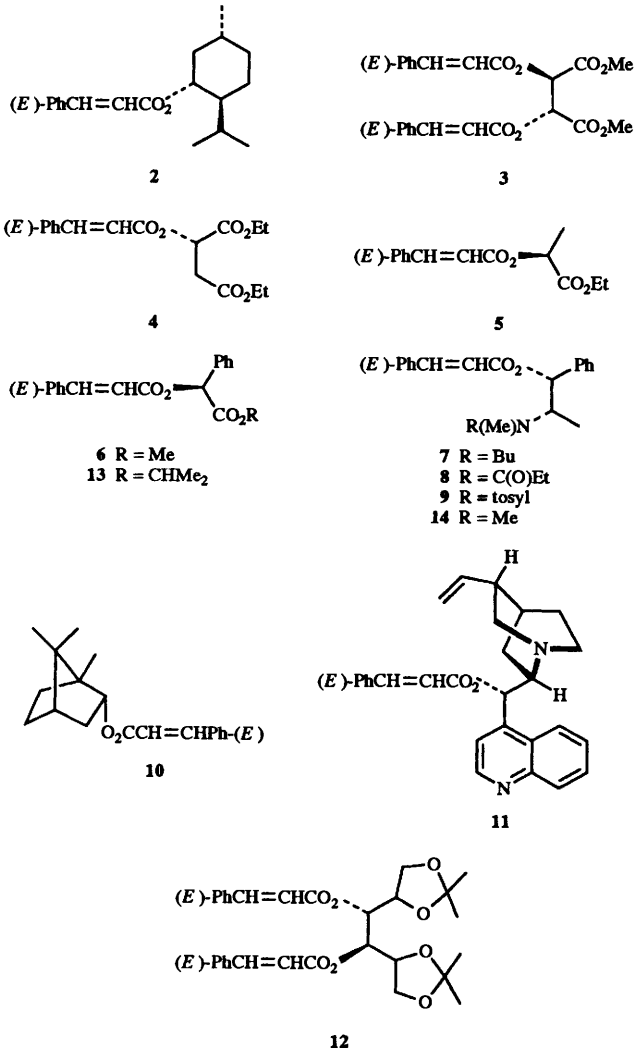
In cyclic voltammetry at modest sweep speeds (0.3 V s^{-1}) most of the cinnamate esters displayed two reduction peaks, the first of which was quasi-reversible and the second irreversible. The potentials so obtained (Table 1) are useful for defining conditions for preparative electrolysis and they are the basis of the reduction potentials listed in Table 2. The thermodynamically significant E^0 values have been measured by voltammetry

† 1 F = 9.649 × 10^4 C mol^{-1}.

Table 1 Voltammetric[a] and coulometric[b] experiments

Chiral cinnamate ester	$-E_{pc}(1)$[c]	$-E_{pc}(2)$[d]	n[e]
(−)-Menthyl cinnamate **2**	1.26	1.80	1
(−)-Dimethyl 2,3-di-*O*-cinnamoyltartrate **3**	1.24	1.48	2
(+)-Diethyl *O*-cinnamoylmalate **4**	1.42	1.76	1
(+)-Ethyl *O*-cinnamoyllactate **5**	1.20[f]	2.00	1
(−)-Methyl *O*-cinnamoylmandelate **6**	1.45[f]	1.74	1
(+)-*N*-Butyl *O*-cinnamoylephedrine **7**	1.35	1.92	1
(+)-*O*-Cinnamoyl-*N*-propionylephedrine **8**	1.46	2.04	1
(+)-*O*-Cinnamoyl-*N*-tosylephedrine **9**	1.40	2.08	1
(−)-*endo*-Bornyl cinnamate **10**	1.32	1.78	1
(−)-*O*-Cinnamoylcinchonine **11**	1.30	1.98	2
(+)-3,4-Di-*O*-cinnamoyl 1,2:5,6-di-*O*-isopropylidene-D-mannitol **12**	1.26	1.94	2

[a] Hg bead cathode, ester concentration 1–3 mmol dm^{-3}, DMF–Et_4NBr (0.1 mol dm^{-3}), 0.3 V s^{-1}. [b] At first reduction potential, Hg pool cathode, DMF–Et_4NBr (0.1 mol dm^{-3}). [c] V *vs.* Ag/AgBr, quasi-reversible unless otherwise indicated; pc = potential peak, cathodic. [d] V *vs.* Ag/AgBr, irreversible. [e] Charge consumed in Faradays; see footnote † on p. 1961. [f] Irreversible at 0.3 V s^{-1}.



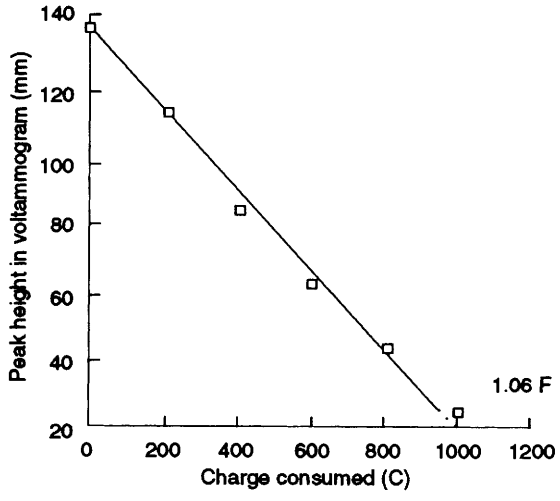


Fig. 1 Controlled potential coulometry; *O*-cinnamoyl-*N*-tosylephedrine **9** in DMF–TEAB, electrolysis at −1.42 V (*vs.* Ag/AgBr)

at higher scan rates together with key kinetic parameters. These data are presented elsewhere in the context of a full mechanistic analysis.[7] Furthermore, controlled potential coulometry gave in most cases clean 1 F conversion. A characteristic coulometric plot is given in Fig. 1 for *O*-cinnamoyl-*N*-tosylephedrine **9**.

In the cyclic voltammetric experiments the quasi-reversible reduction at the first wave indicates a relatively slow follow-up reaction; in most cases an increase in scan rate to as little as 0.9 V s^{-1} results in almost complete reversibility.[7] Irreversible behaviour is seen at 0.3 V s^{-1} for compounds **5** and **6**, possibly indicating faster reaction of the radical anions formed at the first reduction potential. However, it should be noted that cyclic voltammetry is a non-steady state method on a relatively short time-scale. On the much longer time-scale of preparative electrolysis, *i.e.* at steady state and much higher concentration, the follow-up reactions of the radical anions go smoothly to completion.

The clean electrolysis behaviour is for most cases presaged in the coulometric experiments. These were performed using a cell designed so that controlled potential electrolysis of a known weight of the ester could be interrupted at intervals of known charge consumption and the decrease in ester concentration followed by *in situ* cyclic voltammetry (*cf.* Fig. 1). Thus, the coulometric experiments are at steady state.

Coulometry shows a clear-cut difference between those esters which follow the 1 F reduction expected for electrohydrodimerisation and some which give 2 F electrolysis. These differences were also reflected in their behaviour in preparative-scale electrolysis. Because for preparative electrolysis it was convenient to use lithium perchlorate as electrolyte (not normally advised for reasons of safety) the influence of lithium salt on cyclic voltammetry was briefly examined. In contrast to the dramatic effects sometimes observed[8] there was for the few esters examined little effect on addition of lithium perchlorate until its concentration exceeded that of the substrate; at and after this point there was a *cathodic* shift of the first reduction

Table 2 Controlled potential preparative electrolyses[a]

Chiral ester	Medium[b]	$-E_{red}$[c]	Q[d]	Product[e] yield (%)
Menthyl cinnamate **2**	MeCN–TEAB	1.5	1.54	90
	DMF–$LiClO_4$	1.9	1.05	92
Dimethyl 2,3-di-*O*-cinnamoyltartrate **3**	MeCN–TEAB	1.26	—	—[f]
	DMF–$LiClO_4$	2.00	2.20	—[f]
Diethyl *O*-cinnamoylmalate **4**	DMF–TEAB	1.20	1.50	—[f]
Ethyl *O*-cinnamoyllactate **5**	DMF–TEAB	1.40	1.10	86
	DMF–$LiClO_4$	1.96	1.20	89
	DMF–$LiClO_4$	1.75	1.50	95
	DMF–$LiClO_4$	1.55	1.35	80
Methyl *O*-cinnamoylmandelate **6**	DMF–TEAB	1.20	1.00	99
	DMF–$LiClO_4$	1.65	1.68	73
Isopropyl *O*-cinnamoylmandelate **13**	DMF–TEAB	1.30	1.20	85
	DMF–$LiClO_4$	1.50	1.56	81
O-Cinnamoyl-*N*-methylephedrine **14**	DMF–TEAB	1.40	1.09	69
	DMF–$LiClO_4$	1.85	1.12	76
O-Cinnamoyl-*N*-butylephedrine **7**	DMF–TEAB	1.35	1.13	—[g]
	DMF–$LiClO_4$	1.80	1.20	—[g]
O-Cinnamoyl-*N*-propionylephedrine **8**	DMF–TEAB	1.45	1.00	95
O-Cinnamoyl-*N*-tosylephedrine **9**	DMF–$LiClO_4$	1.80	2.00	94
endo-Bornyl cinnamate **10**	DMF–$LiClO_4$	1.75	1.50	98
3,4-Di-*O*-cinnamoyl 1,2:5,6-di-*O*-isopropylidene-D-mannitol **12**	DMF–TEAB	1.40	2.16	—[h]
	DMF–$LiClO_4$	1.80	2.00	—[h]

[a] Hg pool cathode, divided cell. [b] Supporting electrolyte 0.1 mol dm^{-3}, TEAB = Et_4NBr. [c] V *vs.* Ag/AgBr. [d] Charge consumed in F. [e] The 3,4-diphenylcyclopentanone, *cf.* **15**. [f] Cinnamic acid isolated (70–75%) as major product. [g] Impure crude product although containing, by ^1H NMR, much cyclic hydrodimer. [h] Unidentified product, probably polymeric.

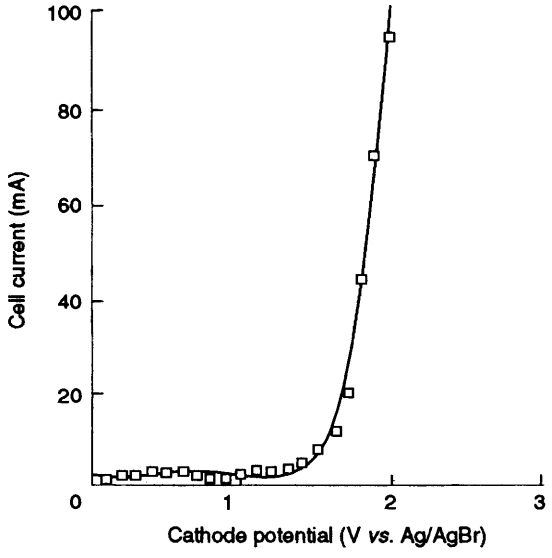


Fig. 2 Current–potential plot for 0.05 mol dm^{-3} methyl cinnamate **2** in DMF–lithium perchlorate (0.1 mol dm^{-3})

peak. In order to determine the potential for preparative-scale reduction in the presence of lithium perchlorate it was more convenient to plot steady-state current–potential curves using preparative concentrations of substrate. An example is given in Fig. 2 from which it is evident that a potential more cathodic than −1.8 V is required.

Preparative-scale electrolysis

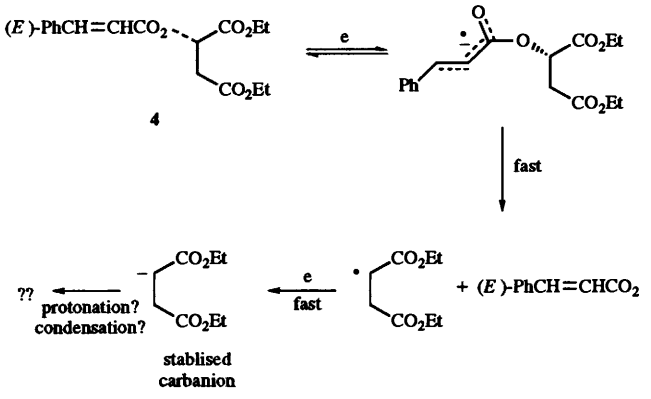
A divided cell of conventional design was used with a magnetically stirred mercury pool cathode as working electrode, a Ag/AgBr reference electrode and a graphite counter electrode (anode). The electrolyses were typically run at controlled potential until the current had fallen to a low background level. The solvent was DMF in most cases and either Et_4NBr or $LiClO_4$ were used as electrolyte; an aqueous work-up procedure was used in both types of electrolysis. The results of key preparative electrolyses are given in Table 2. At this stage no reference is made to the ratio of diastereoisomers observed and the assignment of stereochemistry of the cyclic hydrodimers is also dealt with later.

Many of the chiral cinnamates are smoothly converted in a 1 F process into the corresponding cyclic hydrodimer (the 3,4-cyclopentanone derivative) in excellent yields. This is achieved at relatively low cathodic potentials (*ca.* −1.40 V *vs.* Ag/AgBr) in DMF–Et_4NBr whereas a higher potential (*ca.* −1.80 V) is required when $LiClO_4$ is the electrolyte. In the latter system more than 1 F is often required for high conversion which suggests a somewhat lower current efficiency caused by a competing side reaction. Given that no special precautions were taken to dry the DMF, and the notorious ability of lithium cation to retain water of solvation, this reaction might well be hydrogen evolution at the rather negative potential used. This disadvantage is outweighed by the convenience of work-up with the alkali metal salt.

At this stage it is convenient to consider those substrates which are not converted into the hydrodimer. In particular, the electrolysis of compounds **3**, **4** and **12** departed from the expected pattern. The electrolyses of **3** and **4** each gave good yields (> 70%) of cinnamic acid as the only isolated product following aqueous work-up; for the tartrate ester **3** the experiment was performed using both DMF–TEAB and DMF–$LiClO_4$ electrolytes and similar results were obtained.

The loss of cinnamic acid from esters **3** and **4** is best understood as a reductive cleavage reaction with the cinnamate anion as leaving group. It is unlikely that the competing reaction is alkaline hydrolysis because there is no reason why these esters should hydrolyse and the others not. The driving force for cleavage of the C–O bond is postulated to be not only the stability of the carboxylate leaving group but also stabilisation by delocalisation of the departing radical. For reductive cleavages it is common for the departing radical

fragment to be rapidly reduced either at the cathode or homogeneously by the radical anion of the starting material. This results in 2 F reduction per cleaved group and this is not indicated by the coulometric measurements in Table 1. However, the actual charge consumption in the preparative electrolyses (Table 2) is more in line with the proposal. For **3** and **4** the yields of cinnamic acid were 70 and 75%, respectively, and adjusting the measured charge consumption (2.2 F and 1.5 F) gives reactions of 3.1 F for **3** (4 F required) and 2 F for **4** (2 F required). Thus, the most clear-cut case is that of **4** and a probable mechanism is given in Scheme 2. A possible competing



Scheme 2

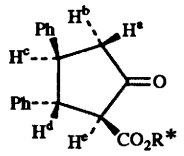
reaction in the reduction of **3** is intramolecular coupling but analysis of the residue after isolation of cinnamic acid was problematical.

Cleavage could occur in the opposite sense with the $PhCH^{\bullet}CHCO_2^{\bullet}$ radical leaving; this is not likely because decarboxylation of that species is likely to be rapid. These explanations are not, however, entirely satisfactory because α-carboxylate ester functions are also present in compounds **5**, **6** and **13** and yet these compounds give smooth EHD.

Intramolecular coupling is also possible for ester **12** and the likelihood of C–O cleavage is remote. But here also it did not prove possible to isolate and identify the product(s) satisfactorily. They appear to be polymeric and a plausible explanation is that the radical anions couple in a linear fashion with the bulky *O*-isopropylidine groups discouraging cyclic hydrodimerisation. Both coulometry (Table 1) and charge consumption during controlled potential electrolysis (Table 2) indicate clean 2 F reduction, *i.e.* 1e reduction for each cinnamoyl unit.

The cyclic hydrodimers

Structure and stereochemistry. The yields of products listed in the final column of Table 2 relate to crude yields of cyclic hydrodimers of the general structure **15** (see heading of Table 3). For the product from methyl cinnamate the all-*trans* stereochemistry was confirmed[4] by ^{1}H NMR spectroscopy; in particular it was found that neighbouring protons on the cyclopentanone ring had similar coupling constants, *ca.* 12.5 Hz. Reduction of the chiral cinnamates gives a mixture of diastereoisomers and analysis of the ^{1}H NMR spectra of mixtures was important for the determination of isomer ratios. This sometimes involved separation of the diastereoisomers and, *inter alia*, the all-*trans* stereochemistry was confirmed. As an example, the crude product from cathodic reduction of ethyl *O*-cinnamoyllactate **5** was crystallised and recrystallised several times from methanol to yield a single diastereoisomer. The product [**15**, R* = $CH(Me)CO_2Et$] is shown in Table 3 together with key NMR parameters. It is evident that, as in the other cases, the values of J = 12.5 Hz confirm the relative



15

Table 3 ^{1}H NMR data for **15** [R* = $CH(Me)CO_2Et$]

Proton	δ (ppm) (multiplicity)	Coupling constant (Hz)
H^a	2.72 (1 H, dd)	J_{ab} 19, J_{ac} 12.5
H^b	2.98 (1 H, dd)	J_{bc} 7.5
H^c	3.52 (1 H, dt)	J_{cd} 12.5, J_{cb} 7.5
H^d	3.92 (1 H, t)	J_{cd} 12.5, J_{de} 12.5
H^e	3.69 (1 H, d)	J_{de} 12.5

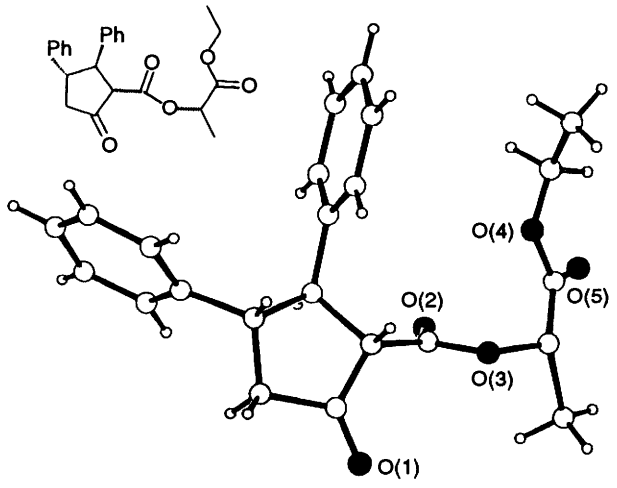


Fig. 3 X-Ray crystallographic structure of cyclic hydrodimer **15** [R* = $CH(Me)CO_2Et$]

stereochemistry. (Note that formula **15** depicts one enantiomer, not necessarily the correct one!)

Even more compelling is the confirmation of the structure of this product by X-ray crystallography (Fig. 3). An interesting feature of this structure is the alignment, at least in the crystal, of the two phenyl groups and the ethyl group. This linking of NMR data with an unambiguously determined structure gives confidence for the use of proton coupling constants in assigning the stereochemistry of the cyclic hydrodimers in the other cases.

Ratios of diastereoisomers

By ^{1}H NMR spectroscopy. The crude products listed in Table 2 gave relatively clean ^{1}H NMR spectra indicating a mixture of diastereoisomers. In most cases it was possible by fractional crystallisation to isolate one of the diastereoisomers and hence identify key chemical shifts to be used in the determination of isomer ratios in the crude product.

Even at 250 MHz resolution it was possible to distinguish clearly signals attributable to both diastereoisomers and, of course, the spectrum of one of the pure diastereoisomers was available. Taking the product depicted in Fig. 3, [**15**, R* = $CH(Me)CO_2Et$], and denoting the isomer isolated as D_a and the other as D_b, resolvable signals were: $COCH_2CH_3$, 1.07 (D_a), 1.21 (D_b); $CH(CH_3)CO_2Et$, 1.50 (D_a), 1.44 (D_b); H^a, 2.72 (D_a), 2.75 (D_b); H^e, 3.69 (D_a), 3.63 (D_b); $COCH_2CH_3$, 4.05 (D_a), 4.16 (D_b). In this case the relative integrals of the signals gave a ratio of D_a : D_b of 2 : 1, *i.e.* a diastereoisomeric excess of 33%.

HPLC measurements. The diastereoisomers were in most

Table 4 Diastereoisomeric excesses in EHD products[a] **15**

Starting chiral cinnamate	Diastereoisomeric excess (%)	
	By ^{1}H NMR	By HPLC
Menthyl cinnamate **2**	0	0.86
Ethyl *O*-cinnamoyllactate **5**	33	32
Methyl *O*-cinnamoylmandelate **6**	44	47
Isopropyl *O*-cinnamoylmandelate **13**	38; 40; 40; 41 (*i.e.* 39.8 ± 0.8)	41
O-Cinnamoyl-*N*-propionylephedrine **8**	—[b]	—[c]
O-Cinnamoyl-*N*-tosylephedrine **9**	34	36
O-Cinnamoyl-*N*-methylephedrine **14**	36[d]	—[c]
endo-Bornyl cinnamate **10**	(>95)[e]	(>95)[e]

[a] Electrolysis in DMF–$LiClO_4$ (0.1 mol dm^{-3}). [b] ^{1}H NMR signals not of sufficiently different chemical shift. [c] Not separable by HPLC. [d] Electrolysis in DMF–TEAB (0.1 mol dm^{-3}). [e] Only one diastereoisomer was isolated, in high yield (98%), see text.

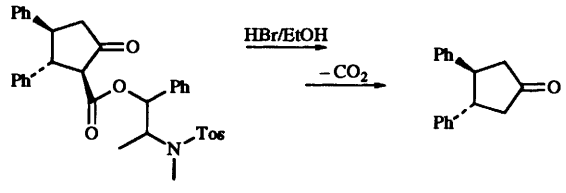
cases separable by HPLC with UV detection at 254 or 258 nm. ^{1}H NMR measurements on the crude product of electrolysis of the menthyl ester (**15**, R* = menthyl), showed clearly a 1:1 ratio of the diastereoisomers and they also gave baseline separation on HPLC analysis with relative peak areas of 49.56% (D_a) and 50.42% (D_b), a ratio of 0.98 and a de of 0.86%. The closeness of the results from the two methods suggests strongly that the extinction coefficients of the two isomers are the same at 258 nm. Consequently, where possible, diastereoisomeric excesses were determined by both NMR spectroscopy and by HPLC analysis. The results are combined in Table 4.

Other features of the results given in Tables 2 and 4 are: (i) electrolysis using either Et_4NBr or $LiClO_4$ as electrolyte give similar results both with regard to yield (Table 2) and diastereoisomeric excess (Table 4, entry for compound **14**); (ii) the reproducibility of the results is good—for compound **13** the results from separate electrolyses are listed. In one case, with the product from compound **8**, both analytical methods failed.

Electrolysis of the borneol ester **10** gave after aqueous work-up and extraction of the hydrodimer product with ethyl acetate a 98% yield of what appears to be a single diastereoisomer. The ^{1}H NMR spectrum showed sharp signals for the multiplets centred at δ 2.73 (H^a), 2.98 (H^b), 3.51 (H^c), 3.60 (H^e) and 3.88 (H^d) characteristic of the spectra of pure diastereoisomers and in contrast with those of the other crude product mixtures. Also, the product eluted in HPLC as a sharp peak with no evidence of separation. A similar result was obtained in a separate electrolysis after which the crude precipitate was filtered off and crystallised from methanol, with good recovery, rather than extracted. Consequently, it is assumed that in this case very high diastereoselectivity has been observed; allowing for possible errors in isolation a possibly conservative figure of 95% de is included in Table 4. For the other esters the de values are more modest, but given that the major diastereoisomer is easily obtained by fractional crystallisation even a de of 33% (2:1 ratio) is of practical value.

Hydrolysis of compounds 15 to 3,4-diphenylcyclopentanone 16. Attempted hydrolyses under alkaline conditions were complicated by side reactions, possibly condensation reactions as a result of acidic hydrogens adjacent to carbonyl groups although Kise *et al.*[6] used alkaline hydrolysis to convert the cyclopentanone esters into 3,4-diphenyladipates. In our cases, conditions for acidic hydrolysis were explored (*cf.* ref. 9) and the use of mixtures of 47% HBr or concentrated HCl with ethanol (3:5 v/v) was adopted for the hydrolyses with subsequent decarboxylation as shown in Scheme 3.

A published value for the optical rotation of the enantiomers of (±)-3,4-diphenylcyclopentanone **16** could not be found.



15 R* = CH(Ph)CH(Me)N(Me)Tos **16**

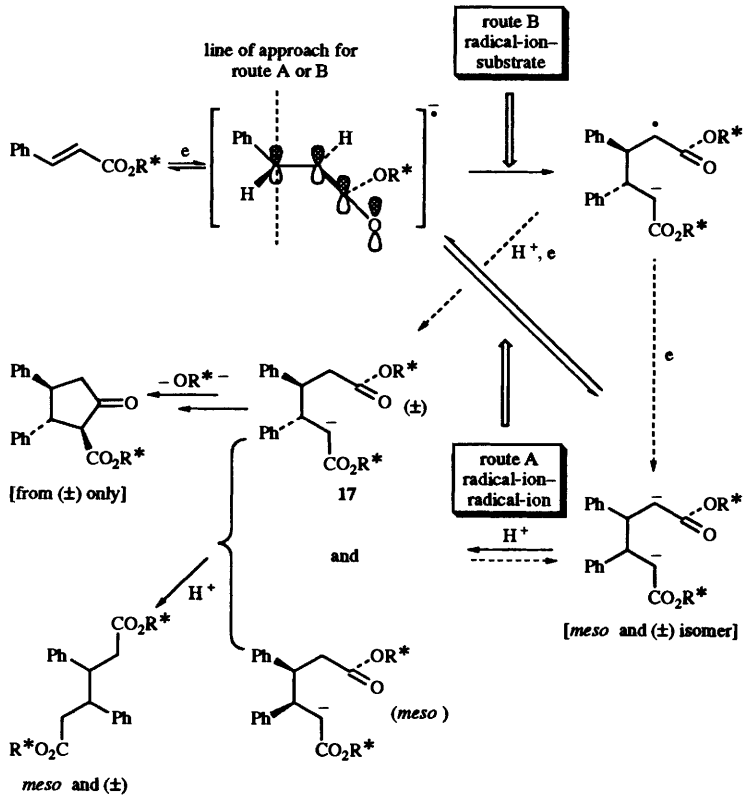
Scheme 3

Accordingly a sample of the pure, major, diastereoisomer of **15**, [R* = CH(Ph)CH(Me)N(Me)COEt] was hydrolysed using the HBr mixture to give in 53% yield what was assumed to be a single enantiomer of **16**. In chloroform solution this gave an $[\alpha]_D$ value of 219. However, no good match was found between the de values from the crude products and ee values determined by hydrolysis of the crude products and calculation from the $[\alpha]_D$ values of **16** so obtained. For example, hydrolysis of **15** [R* = $CH(Me)CO_2Et$] obtained with 33% de gave **16** in 40% yield with ostensibly 20% ee. The most likely origin of these discrepancies is the inefficient hydrolysis reaction. It is unlikely that under acidic conditions racemisation at the benzylic 3,4-positions occurs—**16** is of low, hydrocarbon, basicity. These points can be cleared up by checking the $[\alpha]_D$ value for the enantiomers, *e.g.* by resolution of **16**, and by improving the hydrolysis method to give near quantitative yields of **16**.

Mechanistic rationalisation

Pathways accounting for the overall reaction are given in Scheme 4. Route A is essentially that proposed[3] in earlier work, although on little evidence. It is difficult to see how the cyclopentanones could be formed by other than Dieckmann condensation and this argues for the intermediacy of the monoanion **17**. The dianion initially formed by coupling of the radical anions is unlikely to undergo intramolecular reaction because of coulombic repulsion. The mechanistic uncertainties are: (i) the nature of the coupling step (radical-ion–radical-ion or radical-ion–substrate); (ii) the reversibility or not of the coupling step; and (iii) why, for route A, is only one proton transferred?

It must be significant that the ester undergoing EHD with the highest de, *i.e.* **10**, is that bearing the bulkiest chiral auxiliary (bornyl). Both radical-ion–radical-ion and radical-ion–substrate coupling must proceed by orthogonal approach of the two species and when these mechanistic ambiguities are settled a detailed consideration of stereoelectronic factors may reveal the origin of the diastereoselectivity in these reactions. Such mechanistic work is at an advanced stage.[7]



Scheme 4

Experimental

Electrochemical experiments

The purification of solvents (for cyclic voltammetric and coulometric experiments), electrolytes, and the apparatus and methods used were as described in earlier papers in the series.[1] Conditions for the experiments are given as footnotes to the tables.

Coulometric experiments were carried out in a cell designed so that controlled potential electrolysis of a known amount of substrate could be interrupted at intervals of known charge consumption and its depletion monitored by *in situ* cyclic voltammetry (cv). A plot of substrate concentration (cv peak current) *vs.* charge passed is linear and extrapolation to zero substrate concentration gives charge consumption in coulombs. Preparative scale electrolyses were run in GPR grade DMF (Aldrich) and were performed using conventional glass divided cells with a magnetically stirred mercury pool cathode. The divider was either medium porosity sintered glass or microporous polypropylene (Hoechst-Celanese Celgard 2500); the secondary electrode was a carbon rod and the cathode compartment contained a reference electrode.

Instrumentation

The following instruments were used: ^{1}H NMR (Bruker AM250); FTIR (Perkin-Elmer 1600); mass spectroscopy (Kratos MS50RF/Kratos DS90 Data system). The X-ray crystallographic structure was determined by Mr Majid Motevalli using an Enraf-Nonius CAD 4-circle diffractometer in conjunction with a SHELXS-86 programme. Optical rotations were measured using an Optical Activity A4-1000 polarimeter at ambient temperature and are recorded in units of 10^{-1} deg cm^2 g^{-1}. HPLC experiments were carried out using a Spectra-Physics system (SP8700 solvent delivery/SP8750 pump) with a LC-871 UV/VIS detector and Jones JCL6000 data system.

Syntheses of chiral cinnamate esters

Some of the optically active alcohols were derivatised by the following method.

The hydroxy carboxylic acid (0.02 mol) was dissolved in the appropriate alcohol containing 5% HCl and the solution was refluxed for 5 h. The cooled final solution was poured into ice–water (10 g) and made faintly alkaline with saturated aqueous sodium hydrogen carbonate. The ester was extracted with diethyl ether, washed with water and dried (Na_2SO_4). The crude product recovered after evaporation of the solvent was checked by ^{1}H NMR and used directly in the esterification with cinnamoyl chloride. In an alternative method HCl gas was generated *in situ* by adding acetyl chloride (3 cm^3) to the alcohol (20 cm^3).

Chiral cinnamate esters were prepared by the general procedures described below.

Method A. A solution of cinnamoyl chloride (0.01 mol, 1.67 g) in dry benzene (5 cm^3) was added dropwise to a stirred solution of the chiral alcohol (0.01 mol) in dry benzene (5 cm^3) and the resulting solution was stirred for 2 days at room temperature. Benzene was removed under reduced pressure and the crude product was purified either by vacuum distillation or crystallisation from an appropriate solvent.

Method B. Cinnamoyl chloride (0.01 mol, 1.67 g) was dissolved in dry chloroform (5 cm^3) and added slowly to a solution of the optically active alcohol (0.01 mol) in dry pyridine (5 cm^3, dried over KOH) (sometimes a catalytic amount of DMAP was used as the catalyst). The final solution was stirred at room temperature (on a water bath). Evaporation of the solvents under reduced pressure gave an oily residue, which was dissolved in dichloromethane, washed with 1 mol dm^{-3} HCl, dilute aqueous $NaHCO_3$ and water, respectively, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product purified by distillation under reduced pressure or crystallisation from an appropriate solvent.

Physical data for these esters are displayed in Table 5.

Table 5 Physical data for chiral cinnamate esters

Compound	Method (% Yield)	Characterisation
(−)-Menthyl cinnamate **2**	A (87)	bp 180 °C/1 mmHg; $[\alpha]_D^{20}$ −59.29 (*c* 1.063, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3060, 2955, 2868, 1707 (C=O ester), 1638 (C=C alkene) and 1172; δ_H(80 MHz; $CDCl_3$) 0.8 (3 H, d, CH_3), 0.93 (6 H, d, 2 CH_3), 1.0–2.25 (9 H, m, menthyl ring H), 4.85 (1 H, dt, CO_2CH), 6.42 (1 H, d, *J* 16, =CH), 7.4 (5 H, m, Ph) and 7.7 (1 H, d, *J* 16, =CH); *m/z* 286.194 (M^+, 13.6%; $C_{19}H_{26}O_2$ requires 286.193), 138.1 (100), 131.1 (95.4), 123.1 (16.8), 103.1 (30.8), 95.1 (41.7), 81.1 (23.8) and 77.0 (18.5).
(−)-Dimethyl 2,3-di-*O*-cinnamoyltartrate **3**	A (97)	bp 200 °C/0.5 mmHg; $[\alpha]_D^{20}$ −145.67 (*c* 0.755, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3050, 2955, 1767 (C=O ester), 1729 (C=O α,β-unsaturated ester), 1633 (C=C alkene) and 1147; δ_H(80 MHz; $CDCl_3$) 3.8 (6 H, s, 2 CO_2CH_3), 5.95 (2 H, s, CO_2CH), 6.56 (2 H, d, *J* 16, =CH), 7.3–7.7 (10 H, m, Ph) and 7.83 (1 H, d, *J* 16, =CH); *m/z* 438.131 (M^+, 13.5%; $C_{24}H_{22}O_8$ requires 438.131), 260.1 (4.3%), 206.2 (4.3), 131.1 (92), 103.1 (100) and 77.0 (54.5).
(+)-Diethyl *O*-cinnamoylmalate **4**	B (90–95)	bp 190 °C/0.25 mmHg; $[\alpha]_D^{20}$ +9.92 (*c* 2.46, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 2983, 1745–1740 (C=O ester), 1713 (C=O α,β-unsaturated ester), 1633 (C=C alkene) and 1158; δ_H(80 MHz; $CDCl_3$) 1.2 (6 H, t, 2 CH_3), 2.95 (2 H, d, CH_2), 4.2 (4 H, q, CH_2), 5.6 (1 H, t, CO_2CH), 6.45 (1 H, d, *J* 16, =CH), 7.25–7.6 (5 H, m, Ph) and 7.75 (1 H, d, *J* 16, =CH); *m/z* 320.125 (M^+, 26.6%; $C_{17}H_{20}O_6$ requires 320.126), 275.1 (10), 148.1 (3.9), 131.1 (100), 103.1 (29.0) and 77.0 (17.2).
(+)-Ethyl *O*-cinnamoylactate **5**	A (93)	bp 150 °C/1 mmHg; $[\alpha]_D^{20}$ +29.15 (*c* 0.9125, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3061, 2987, 1730 (C=O ester), 1718 (C=O α,β-unsaturated ester), 1637 (C=C alkene), 1300 and 1100; δ_H(90 MHz; $CDCl_3$) 1.3 (3 H, t, CH_3), 1.57 (3 H, d, CH_3), 4.2 (2 H, q, CH_2), 5.2 (1 H, q, CO_2CH), 6.53 (1 H, d, *J* 16, =CH), 7.45 (5 H, m, Ph) and 7.78 (1 H, d, *J* 16, =CH); *m/z* 248.105 (M^+, 17.2%; $C_{14}H_{16}O_4$ requires 248.105), 131.1 (100), 103.1 (18.0) and 77.0 (11.7).
(−)-Methyl *O*-cinnamoylmandelate **6**	B (95)	bp 198–203 °C/0.5 mmHg; $[\alpha]_D^{20}$ −86.42 (*c* 1.21, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3060, 3030, 2952, 1755 (C=O ester), 1715 (C=O α,β-unsaturated ester), 1637 (C=C alkene), 1497, 1312, 1269 and 1160; δ_H(80 MHz; $CDCl_3$) 3.7 (3 H, s, CO_2CH_3) and 6.08 (1 H, d, *J* 16, =CH); *m/z* 296.108 (M^+, 22%; $C_{18}H_{16}O_4$ requires 296.105), 265.1 (0.7), 237.1 (1.3), 131.1 (100), 103.1 (23.2) and 77.0 (19.6).
(+)-*O*-Cinnamoyl-*N*-butylephedrine **7**	A (91)	bp 234 °C/0.5 mmHg; $[\alpha]_D^{20}$ +64.0 (*c* 1.325, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3061, 3030, 2956, 2795, 1711 (C=O α,β-unsaturated ester), 1637 (C=C alkene), 1450 and 1166; δ_H(80 MHz; $CDCl_3$) 0.9 (3 H, t, CH_3), 1.13 (3 H, d, CH_3), 1.1–1.5 (4 H, m, 2 CH_2), 2.25 (3 H, s, N–CH_3), 2.45 (2 H, t, N–CH_2 of butyl), 2.9–3.3 (1 H, m, CH–N), 6.04 (1 H, d, CO_2CH), 6.5 (1 H, d, *J* 16, =CH), 7.15–7.6 (10 H, 2 Ph) and 7.75 (1 H, d, *J* 16, =CH); *m/z* 351.219 (M^+, 0.01%; $C_{23}H_{29}NO_2$ requires 351.220), 308.2 (0.3), 204.2 (0.6), 131.1 (8.3), 114.1 (100) and 77.0 (5.4).
(+)-*O*-Cinnamoyl-*N*-propionylephedrine **8**	B (82)	mp 80–82 °C (EtOH); $[\alpha]_D^{20}$ +57.1 (*c* 3.93, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3061, 3033, 2979, 2934, 1709 (C=O α,β-unsaturated ester), 1636 (C=O amide and C=C alkene overlapped), 1496, 1449, 1402, 1371, 1282, 1203, 1163, 987, 767 and 701; δ_H(80 MHz; $CDCl_3$) 1.0 (3 H, t, CH_3), 1.28 (3 H, d, CH_3), 1.9–2.4 (2 H, m, CH_2 of ethyl), 2.8 (3 H, s, N–CH_3), 5.0–5.4 (1 H, m, CH–N), 6.0 (1 H, d, CO_2CH), 6.5 (1 H, d, *J* 16, =CH), 7.2–7.65 (10 H, 2 Ph) and 7.7 (1 H, d, *J* 16, =CH); *m/z* 351.183 (M^+, 0.9%; $C_{22}H_{25}NO_3$ requires 351.183, 203.1 (10.4), 147.0 (5.9), 114.0 (100) and 58.0 (75.0).
(+)-*O*-Cinnamoyl *N*-tosylephedrine **9**	B (70)	mp 138–140 °C (EtOH); $[\alpha]_D^{20}$ +54.61 (*c* 1.41, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3059, 3030, 2993, 2946, 1710 (C=O α,β-unsaturated ester), 1639 (C=C alkene), 1339 and 1164; δ_H(80 MHz; $CDCl_3$) 1.1 (3 H, t, CH_3), 2.4 (3 H, s, Ar–CH_3), 2.7 (3 H, s, N–CH_3), 4.3–4.75 (1 H, m, CH–N), 5.9 (1 H, d, CO_2CH), 6.5 (1 H, d, *J* 16, =CH), 7.1–7.65 (14 H, ArH) and 7.75 (1 H, d, *J* 16, =CH); *m/z* 449.230 (M^+, 0.7%; $C_{26}H_{27}NO_4S$ requires 449.194), 302.1 (0.5), 214.1 (22.5), 131.1 (68.6), 103.1 (42.3), 91.1 (100) and 77.0 (32.1).
(−)-Bornyl cinnamate **10**	A (81–85)	bp 214–218 °C/13–14 mmHg; $[\alpha]_D^{20}$ −27.30 (*c* 4.93, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3060, 3030, 2953, 2878, 1710 (C=O ester), 1638 (C=C alkene), 1451 and 1176; δ_H(80 MHz; $CDCl_3$) 0.85–1.0 (9 H, m, 3 CH_3), 1.0–2.65 (7 H, br, ring H), 5.0 (1 H, dq, *J* 10 and 2, CO_2CH), 6.5 (1 H, d, *J* 16, =CH), 7.3–7.6 (5 H, Ph) and 7.7 (1 H, d, *J* 16, =CH); *m/z* 184.177 (M^+, 17.6%; $C_{19}H_{24}O_2$ requires 284.178), 147.0 (9.1), 109.1 (33.8), 103.0 (89.7), 93.0 (10.8), 81.1 (18.5) and 77.0 (100).
(−)-*O*-Cinnamoylcinchonine **11**	B (61)	Purified by column chromatography, mp 45–48 °C; $[\alpha]_D^{20}$ −42.05 (*c* 2.54, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3061, 3030, 2936, 2870, 1714 (C=O ester), 1635 (C=C alkene) and 1162; δ_H(80 MHz; $CDCl_3$) 1.2–3.6 (13 H, br, aliphatic H), 5.0–5.25 (2 H, dd, vinylic CH_2), 5.8–6.3 (1 H, m, vinylic CH), 6.5 (1 H, d, *J* 16, =CH), 6.7 (1 H, d, CO_2CH), 7.2–7.9 (9 H, ArH and =CH), 8.05–8.4 (2 H, m, quinoline) and 8.9 (1 H, d, quinoline); *m/z* 424.215 (M^+, 0.7%; $C_{29}H_{30}N_2O_2$ requires 424.231), 277.2 (2.0), 234.1 (0.5), 136.1 (100), 103.1 (15.0) and 77.0 (10.3).

Table 5 (*continued*)

Compound	Method (% Yield)	Characterisation
(+)-3,4-Di-*O*-cinnamoyl 1,2:5,6-di-*O*-isopropylidene-D-mannitol **12**	B (88)	mp 123–125 °C (EtOH); $[\alpha]_D^{20}$ +76.03 (*c* 2.42, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3063, 2989, 2893, 1721–1708 (C=O ester), 1635 (C=C alkene), 1152 and 1065; δ_H(80 MHz; $CDCl_3$) 1.35 (12 H, d, *J* 6, two Pr^i), 4.0 (4 H, d, *J* 6, 2 CH_2), 4.3 (2 H, q, CH), 5.55 (2 H, d, CO_2CH), 6.5 (2 H, d, *J* 16, =CH), 7.3–7.65 (10 H, br, 2 Ph) and 7.78 (2 H, d, *J* 16, =CH); *m*/*z* 507.202 ($M^+ - CH_3$ (15.0236) 21.3%; $C_{30}H_{34}O_8$ requires 522.225), 321.0 (1.6), 273.1 (10.5), 131.0 (100), 101.1 (36.6) and 77.0 (14.0).
(−)-Isopropyl *O*-cinnamoylmandelate **13**	B (74)	bp 214–218 °C/1.2–1.4 mmHg; $[\alpha]_D^{20}$ −67.12 (*c* 0.787, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3060, 3030, 2981, 1730 (C=O ester), 1716 (C=O α,β-unsaturated ester), 1630 (C=C alkene) and 1160; δ_H(80 MHz; $CDCl_3$) 1.08–1.38 (6 H, dd, 2 CH_3), 4.8–5.4 (1 H, m, CH of Pr^i), 6.03 (1 H, s, CO_2CH), 6.58 (1 H, d, *J* 16, =CH), 7.3–7.68 (10 H, m, 2 Ph) and 7.8 (1 H, d, *J* 16, =CH); *m*/*z* 324.139 (M^+, 4.3%; $C_{20}H_{20}O_4$ requires 324.136), 265.1 (3.9), 238.1 (1.4), 193.1 (23), 131.1 (100), 103.1 (42.3) and 77.0 (31.2).
(+)-*O*-Cinnamoyl-*N*-methylephedrine **14**	A (97)	bp 202–204 °C/4 mmHg; $[\alpha]_D^{20}$ +103.44 (*c* 3.2, $CHCl_3$); ν_{max}(liq.)/cm^{-1} 3060, 3025, 2900, 2780, 1712 (C=O α,β-unsaturated ester), 1637 (C=C alkene) and 1166; δ_H(80 MHz; $CDCl_3$) 1.13 (3 H, d, CH_3), 2.33 (6 H, s, 2 N–CH_3), 2.8–3.15 (1 H, dt, CH–N), 6.1 (1 H, d, CO_2CH), 6.5 (1 H, d, *J* 16, =CH), 7.15–7.63 (10 H, 2 Ph), 7.73 (1 H, d, *J* 16, =CH); *m*/*z* 309.174 (M^+, 0.2%; $C_{20}H_{23}NO_2$ requires 309.173), 162.1 (2.5), 146.1 (1.5), 134.1 (20), 103.1 (21.1), 77.1 (21.1) and 72.1 (100).

Table 6 Physical data for cyclic hydrodimers (*cf.* Table 2)

	Cyclic hydrodimers **1**	
Cinnamate	Pure diastereoisomer	Crude product (mixture of diastereoisomers)
Menthyl **2**	ν_{max}(KBr)/cm^{-1} 3012, 2950, 2860, 1748 (C=O ester), 1710 (C=O ketone), 1450, 1272, 1252, 1120, 778 and 692; δ_H(250 MHz; $CDCl_3$) 0.7 (3 H, d, CH_3), 0.85 (6 H, dd, 2 CH_3), 0.8–2.1 (10 H, br, menthyl H), 2.73 (1 H, dd, *J* 19 and 12.5, 4-H), 2.97 (1 H, dd, *J* 19, *J* 7.5, 4-H), 3.48 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.58 (1 H, d, *J* 12.5, 1-H), 3.9 (1 H, t, *J* 12.5, 2-H), 4.7 (1 H, dt, CO_2CH) and 7.1–7.3 (10 H, 2 Ph) (Found: C, 80.3, H, 8.3. $C_{28}H_{34}O_3$ requires C, 80.38, H, 8.13%); *m*/*z* 418.250 (M^+, 14.2%; $C_{28}H_{34}O_3$ requires 418.251), 280.1 (100), 234.1 (40.5), 138.1 (67.6), 131 (34.4) and 104.1 (59.8).	δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 0.65 (3 H, d, CH_3, D_b), 0.69 (3 H, d, CH_3, D_a), 0.7–2.1 (32 H, menthyl H, D_a + D_b), 2.71 (2 H, 2 dd, 4-H, D_a + D_b), 1.96 (2 H, 2 dd, 4-H, D_a + D_b), 3.47 (2 H, dt, D_a + D_b), 3.52 (1 H, d, 1-H, D_b), 3.57 (1 H, d, D_a), 3.89 (2 H, dt, 2 2-H, D_a + D_b), 4.6 (1 H, dt, CO_2CH, D_b), 4.7 (1 H, dt, CO_2CH, D_a) and 7.1–7.3 (20 H, 4 Ph).
Ethyl lactate **5**	ν_{max}(KBr)/cm^{-1} 3030, 2982, 2926, 1751 (C=O ester-1), 1740 (C=O ester-2), 1718 (C=O ketone), 1458, 1376, 1346, 1273, 1249, 1144, 1099 and 1051; δ_H(250 MHz; $CDCl_3$) 1.08 (3 H, d, *J* 7.0, CH_3), 2.72 (1 H, dd, *J* 19 and 12.5, 4-H), 2.98 (1 H, dd, *J* 19, *J* 7.5, 4-H), 3.52 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.69 (1 H, d, *J* 12.5, 1-H), 3.92 (1 H, t, *J* 12.5, 2-H), 4.05 (2 H, q, CH_2 of ester), 5.12 (1 H, q, *J* 7.0, CO_2CH) and 7.1–7.3 (10 H, br, 2 Ph) (Found: C, 72.8, H, 6.3. $C_{23}H_{24}O_5$ requires C, 72.63, H, 6.31%); *m*/*z* 380.160 (M^+, 35.5%; $C_{23}H_{24}O_5$ requires 380.162), 235.1 (23.5), 131.0 (42.6), 104.1 (100) and 77.0 (12.1).	δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 1.07 (3 H, t, CH_3, D_a), 1.21 (3 H, t, CH_3, D_b), 1.44 (3 H, d, CH_3, D_b), 1.50 (3 H, d, CH_3, D_a), 2.72 (1 H, dd, *J* 19 and 12.5, 4-H, D_a), 2.75 (1 H, dd, *J* 19 and 12.5, 4-H, D_b), 1.98 (2 H, dd, 4-H, D_a + D_b), 3.52 (2 H, m, 3-H, D_a + D_b), 3.63 (1 H, d, *J* 12.5, 1-H, D_b), 3.69 (1 H, d, *J* 12.5, 1-H, D_a), 3.93 (1 H, 2-H, D_a + D_b), 4.05 (2 H, q, CH_2 of ester, D_a), 4.16 (2 H, 2, CH_2 of ester, D_b), 5.10 (2 H, m, CO_2CH, D_a + D_b) and 7.1–7.3 (20 H, br, 4 Ph).
Methyl mandelate **6**	ν_{max}(KBr)/cm^{-1} 3062, 2984, 2930, 1755 (C=O, 2 ester group bands are partly overlapped), 1718 (C=O ketone), 1496, 1438, 1219 and 1137; δ_H(250 MHz; $CDCl_3$) 2.74 (1 H, dd, *J* 19 and 12.5, 4-H), 2.99 (1 H, dd, *J* 19 and 7.5, 4-H), 3.53 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.59 (3 H, s, CO_2CH_3), 3.76 (1 H, d, *J* 12.5, 1-H), 3.95 (1 H, t, *J* 12.5, 2-H), 5.95 (1 H, s, CO_2CH), 7.05–7.3 (10 H, 2 Ph) and 7.35 (5 H, Ph) (Found: C, 75.3, H, 5.5. $C_{27}H_{24}O_5$ requires C, 75.70, H, 5.60%); *m*/*z* 428.162 (M^+, 5.7%; $C_{27}H_{24}O_5$ requires 428.162), 235.1 (19.5), 149.1 (27), 131.0 (49.1), 107.0 (100), 104.1 (76.2), 79.1 (39.3) and 77.0 (33.8).	δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 2.74 (1 H, 4-H, D_a), 1.76 (1 H, 4-H, D_b), 2.98 (2 H, dd, 4-H, D_a + D_b), 3.52 (2 H, m, 3-H, D_a + D_b), 3.59 (3 H, s, CO_2CH_3, D_a), 3.67 (3 H, s, CO_2CH_3, D_b), 3.76 (2 H, d, 1-H, D_a + D_b), 3.95 (1 H, t, 2-H, D_a), 3.96 (1 H, t, 2-H, D_b), 5.93 (1 H, q, CO_2CH, D_b), 5.96 (1 H, q, CO_2CH, D_a), 7.05–7.3 (20 H, 2 Ph) and 7.4 (10 H, Ph).

Table 6 (*continued*)

	Cyclic Hydrodimers **1**	
Cinnamate	Pure diastereoisomer	Crude product (mixture of diastereoisomers)
N-Propionylephedrine **8**	ν_{max}(KBr)/cm^{-1} 3031, 2972, 2922, 1750 (C=O ester), 1716 (C=O ketone), 1637 (C=O amide), 1490, 1455, 1408, 1375, 1248, 1135, 762 and 696; δ_H(250 MHz; $CDCl_3$) 1.02 (3 H, t, CH_3), 1.12 (3 H, d, CH_3), 2.20 (2 H, q, CH_2), 2.73 (1 H, dd, *J* 19 and 12.5, 4-H), 2.98 (1 H, dd, *J* 19 and 7.5, 4-H), 3.53 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.68 (1 H, d, *J* 12.5, 1-H), 3.88 (1 H, t, *J* 12.5, 2-H), 4.98 (1 H, m, CH–N), 5.9 (1 H, d, CO_2CH), 6.95–7.3 (15 H, 3 Ph) (Found: C, 77.0, H, 6.91, N, 2.83. $C_{31}H_{33}NO_4$ requires C, 77.02, H, 6.83, N, 2.90%); *m/z* 48.3.234 (M^+ 0.1%; $C_{31}H_{33}NO_4$ requires 483.240), 318.1 (0.6), 236.1 (30), 203.1 (14.6), 104.1 (100), 77.0 (78) and 58.1 (36.1).	
N-Tosylephedrine **9**	ν_{max}(KBr)/cm^{-1} 3030, 2920, 1752 (C=O ester), 1716 (C=O ketone), 1494, 1456, 1329, 1246, 1133, 1088, 961, 763 and 699; δ_H(250 MHz; $CDCl_3$) 1.0 (3 H, d, *J* 7.5, CH_3), 2.39 (3 H, s, Ar-CH_3), 2.7 (3 H, s, N–CH_3), 2.72 (1 H, dd, *J* 19 and 12.5, 4-H), 2.97 (1 H, dd, *J* 19 and 7.5, 4-H), 3.51 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.67 (1 H, d, *J* 12.5, 1-H), 3.87 (1 H, t, *J* 12.5, 2-H), 4.38 (1 H, dq, CH–N), 5.74 (1 H, d, CO_2CH), 7.0–7.3 (17 H, br, ArH) and 7.49 (2 H, d, 2 H of tosyl) (Found: C, 72.0, H, 5.9, N, 2.4. $C_{35}H_{35}NO_5S$ requires C, 72.28, H, 6.02, N, 2.41%); *m/z* (FAB) 582 (M^+ 1 1.8%; $C_{31}H_{33}NO_4$ requires 581.223), 460 (0.2), 426 (0.2), 399 (5.6), 302 (100), 263 (7.1), 235 (1.5) and 212 (94.1).	δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 0.90 (3 H, d, CH_3, D_b), 1.0 (3 H, d, CH_3, D_a), 2.40 (6 H, s, 2 Ar-CH_3 overlapped, D_a + D_b), 2.70 (6 H, s, 2 N–CH_3, D_a + D_b), 2.73 (2 H, dd, 4-H, D_a + D_b), 2.97 (2 H, dd, 4-H, D_a + D_b), 3.50 (2 H, m, 3-H, D_a + D_b), 3.65 (2 H, d, 1-H, D_a + D_b), 3.87 (1 H, t, 2-H, D_a), 3.94 (1 H, t, 2-H, D_b), 4.36 (2 H, m, 2 N–CH, D_a + D_b), 5.70 (1 H, d, *J* 5, CO_2CH, D_b) 5.74 (1 H, d, *J* 5, CO_2CH, D_a) and 7.0–7.6 (ArH).
endo-Bornyl **10**	ν_{max}(KBr)/cm^{-1} 3060, 3030, 2950, 2872, 1754 (C=O ester), 1715 (C=O ketone), 1490, 1450, 1386, 1125, 767 and 695; δ_H(250 MHz; $CDCl_3$) 0.62 (3 H, s, CH_3), 0.83 (3 H, s, CH_3), 0.86 (3 H, s, CH_3), 1.0–2.4 (7 H, bornyl ring H), 2.73 (1 H, dd, *J* 19 and 12.5, 4-H), 2.98 (1 H, dd, *J* 19 and 7.5, 4-H), 3.51 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.60 (1 H, d, *J* 12.5, 1-H), 3.88 (1 H, t, *J* 12.5, 2-H), 4.89 (1 H, dq, *J* 8 and 3, CO_2CH) and 7.1–7.3 (10 H, 2 Ph) (Found: C, 80.5, H, 7.7. $C_{28}H_{32}O_3$ requires C, 80.77, H, 7.69%); *m/z* 416.234 (M^+ 7.9%; $C_{28}H_{32}O_3$ requires 416.235), 280.1 (19.1), 137.1 (100), 95.1 (14.3) and 81.1 (30.5).	
Isopropyl mandelate **13**	ν_{max}(KBr)/cm^{-1} 3060, 2982, 2920, 1754 (C=O, 2 ester group bands are partly overlapped), 1730 (C=O ketone), 1270 and 1154; δ_H(250 MHz; $CDCl_3$) 0.98 (3 H, d, CH_3), 1.14 (3 H, d, CH_3), 2.74 (1 H, dd, *J* 19 and 12.5, 4-H), 2.98 (1 H, dd, *J* 19 and 7.5, 4-H), 3.50 (1 H, dt, *J* 12.5 and 7.5, 3-H), 3.78 (1 H, d, *J* 12.5, 1-H), 3.96 (1 H, t, *J* 12.5, 2-H), 4.9–5.05 (1 H, m, CH of Pr^i), 5.9 (1 H, q, CO_2CH) and 7.1–7.4 (15 H, 3 Ph) (Found: C, 76.4, H, 6.0. $C_{28}H_{28}O_5$ requires C, 76.31, H, 6.14%); *m/z* 457.196 (M + 1 1.7%; $C_{29}H_{28}O_5$ requires 456.194), 235.1 (17.6), 178.1 (10.1), 131.0 (31.3), 107.0 (100), 91.0 (25.2), 79.1 (32.6) and 77.0 (26).	δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 0.98 (3 H, d, CH_3, D_a), 1.09 (3 H, d, CH_3, D_b), 1.14 (3 H, d, CH_3, D_a), 1.23 (3 H, d, CH_3, D_b), 2.75 (1 H, dd, 4-H, D_a), 2.77 (1 H, dd, 4-H, D_b), 2.98 (1 H, dd, 4-H, D_a), 2.99 (1 H, dd, 4-H, D_b), 3.50 (2 H, m, 3-H, D_a + D_b), 3.72 (1 H, d, 1-H, D_b), 3.78 (1 H, d, 1-H, D_a), 3.96 (1 H, t, 2-H, D_a), 3.98 (1 H, t, 2-H, D_b), 4.9–5.05 (2 H, m, CH of Pr^i, D_a + D_b), 5.86 (1 H, q, CO_2CH, D_b), 5.9 (1 H, q, CO_2CH, D_a) and 7.1–7.4 (30 H, 4 Ph).
N-Methylephedrine **14**		ν_{max}(KBr)/cm^{-1} 3027, 2971, 2936, 1754 (C=O ester), 1725 (C=O ketone), 1640, 1494, 1452, 1254, 1125, 751 and 698; δ_H(250 MHz; $CDCl_3$) *inter alia* (D_a: diastereoisomer A, D_b: diastereoisomer B) 0.95 (3 H, d, CH_3, D_b), 1.02 (3 H, d, CH_3, D_a), 2.31 (6 H, s, $N(CH_3)_2$, D_a), 2.46 (6 H, s, $N(CH_3)_2$, D_b), 2.72 (2 H, dd, *J* 20 and 12.5, 4-H, D_a + D_b), 2.87 (2 H, m, N–CH, D_a + D_b), 2.98 (2 H, d, *J* 12.5, 1-H, D_a + D_b), 3.52 (2 H, m, *J* 12.5, 2-H, D_a), 3.91 (1 H, t, 2-H, D_b), 5.91 (1 H, d, *J* 5, CO_2CH, D_b), 5.95 (1 H, d, *J* 5, CO_2CH, D_a) and 7.0–7.36 (ArH); *m/z* 236.123 [(3,4-diphenylcyclopentanone) M – $C_{12}H_{15}NO_2$ 27%; $C_{29}H_{31}NO_3$ requires 441.230], 134.1 (14.8), 118.1 (19.2), 104.1 (98.4), 77.0 (17.8) and 72.1 (100).

Controlled potential electrolyses of chiral cinnamate esters

Optically active cinnamate esters were electrolysed, typically on a 2–3 mmole scale, at their first reduction potential (Table 1) in either DMF–TEABr (0.1 mol dm^{-3}) or DMF–$LiClO_4$ (0.1 mol dm^{-3}) solvent electrolyte systems in a divided cell with an Hg pool cathode, graphite rod anode and Ag/AgBr reference electrode. Electrolyses were carried out under nitrogen and continued until the current dropped to the background value (3–6 mA). Work-up involved quenching the catholyte in an excess of ice–water, neutralisation with dilute aqueous hydrochloric acid and, if the crude cyclic hydrodimer did not precipitate from the aqueous mixture, extraction with dichloromethane or ethyl acetate. Conditions employed for individual electrolyses are given in Table 2.

Physical data for the hydrodimers are summarised in Table 6.

Hydrolyses of cyclic hydrodimers

The general procedure as described below was applied for the removal of chiral auxiliaries from cyclic products under acidic conditions.

The cyclic hydrodimer (0.1 g) was refluxed in concentrated hydrobromic acid (3 cm^3, 47%) and ethanol (5 cm^3) solution for 5 h, during which time the solution turned to dark red. The cooled reaction mixture was concentrated to dryness under reduced pressure and the residue was dissolved in dichloromethane and filtered through silica gel to remove unchanged cyclic product and other impurities (low R_f values). Evaporation of dichloromethane under reduced pressure gave the (±)-3,4-diphenylcyclopentanone, which was recrystallised from ethanol, mp 180–183 °C (lit.,[9] mp 181–183 °C); ν_{max} (KBr)/cm^{-1} 3031, 1709 (C=OP ketone), 1496, 1419, 1296, 949, 776 and 700; δ_H(250 MHz; $CDCl_3$; Me_4Si) 2.90 (4 H, m, CH_2), 3.5 (2 H, m, CH) and 7.16 (10 H, 2 Ph); *m/z* 236.118 (M^+, 22.6%; $C_{17}H_{16}O$ requires 236.120), 137.0 (1.9), 115.1 (32), 104.1 (100), 91.1 (4.8) and 77.0 (7.7).

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