A Highly Efficient Enzymic Route to Novel Chiral Liquid Crystals based on 3-Aryl-2-cycloalken-1-ones

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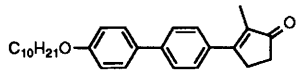
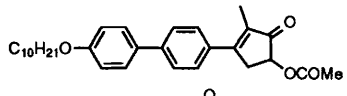
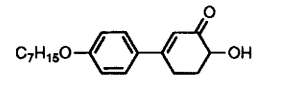
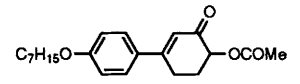
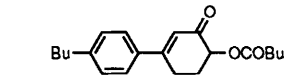
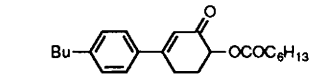
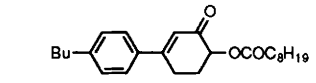
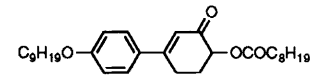
An enzymic route is used to produce novel chiral liquid crystals.

We recently described the synthesis of a number of novel racemic mesogens that incorporate a 2-cyclohexen-1-one ring in the core of each molecule.[1] The structure of this new core embodies a chiral centre and an adjacent carbonyl group, which confers a strong transverse dipole moment. Such structural features are of interest for use in new electrooptical applications based on chiral smectic liquid crystals.[2,3] Surface-stabilised ferroelectric liquid crystal displays and optical modulators are being developed as fast-switching devices.[4] They rely on the ferroelectric polarization that exists in tilted smectic C liquid crystals formed from chiral molecules. The symmetry-breaking due to molecular chirality introduces a polar axis perpendicular to the tilt plane of the smectic layers, which in turn leads to a preferred alignment direction for molecular dipole moments perpendicular to the long molecular axis. The magnitude and sign of the induced ferroelectric polarization depends on a number of factors, but in terms of molecular structure, rigid coupling between the transverse dipole moment and the origin of the symmetry-breaking chirality will maximise the local ferroelectric polarization.[5]

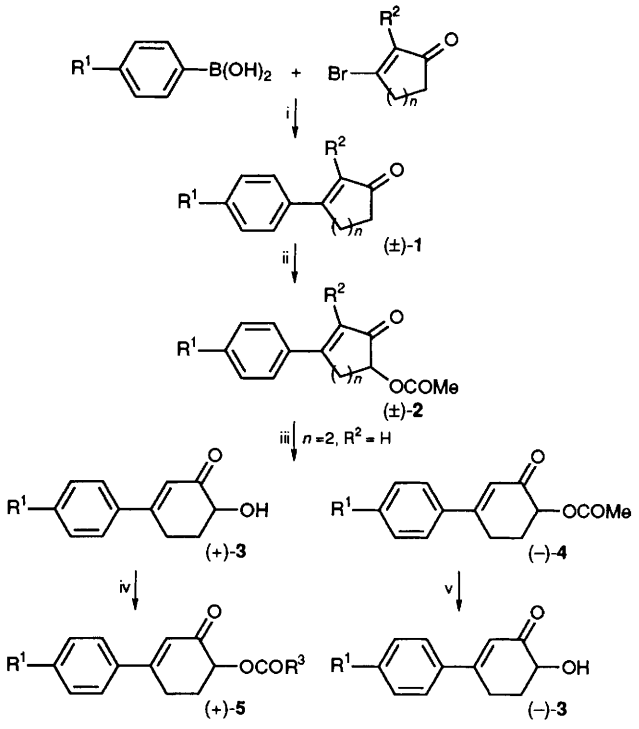
We now report new cyclic conjugated enone systems, which are also the first mesogens to feature the 2-cyclopenten-1-one and 2-cyclohexen-1-one ring systems as novel terminal groups.[6] The 2-cyclohexen-1-ones reported exhibit smectic phases, as do unsubstituted 2-cyclopenten-1-ones. Placement of a methyl group in the two position of the cyclopentenone ring results in the formation of a nematic phase stable over a short temperature range. The 3-aryl-2-cycloalken-1-ones were prepared by a particularly efficient Pd(0)-catalysed coupling. These cycloalkenones were subjected to acetoxylation α to the carbonyl group to give stable acetoxycyloalkenenes that underwent highly efficient enzymic resolution to give esters and their corresponding antipodal alcohols, both of high enantiomeric purity.

The palladium(0)-catalysed cross-coupling of a 3-bromo-2-cycloalken-1-one with the appropriate arylboronic acid afforded the corresponding 3-aryl-2-cyclopenten-1-one or 3-aryl-2-cyclohexen-1-ones **1** (Scheme).[6] The asymmetric hydrolysis of esters mediated by enzymes is well documented.[7] Since *Pseudomonas* lipases have been shown to hydrolyse acetates to give alcohols of high optical purity,[8] a route to optically active liquid crystals by enzymic resolution was investigated. The acetates **2** were obtained by reaction of the cyclic enones **1** with lead tetraacetate (1.0 mmol in benzene).[9] Enantioselective enyzmic hydrolysis† of the (±)-6-acetoxy-2-cyclohexen-1-ones **2** using lipase PS in aqueous acetone solution at pH 7.0 afforded the enantiomerically pure (+)-hydroxyenone **3** together with the unreacted acetate (−)-**4**.‡ Lastly, acylation of the hydroxyenones (+)-**3** under Schotten–Baumann conditions [R^3COCl (1.2 equiv.), pyridine (1.2 equiv.), CH_2Cl_2,

Table 1

Entry	Enone	$[\alpha]_D$	Yield (%)	e.e.(%)[a]	Transitions (°C)[b]
1a					K-63-N-69-I
2a					K-39-N-42-I
3a		+90.0	46[c]	>99	K-99-I
4a		−68.9	46[c]	95	K-109-I
5a		+85.3	81[d]	>99	K-79-S_A-81-I
5b		+67.0	50[d]	>99	K-73-S_A-83-I
5c		+56.6	76[d]	>99	K-76-S_A-84-I
5d		+51.9	75[d]	>99	K-74-S_A-120-I

[a] For the esters, enantiomeric excesses were determined by chiral HPLC (CHIRACEL OD; 4% propan-2-ol in light petroleum) using as a reference a sample of the racemic ester. The e.e.s of the alcohols were determined by conversion into the corresponding esters by acetylation (R^3COCl (1.2 equiv.), pyridine (1.2 equiv.), CH_2Cl_2, −15 to 0 °C, 10 min) which had been independently shown to proceed with little or no appreciable racemisation; comparison with a racemic sample was then made by using chiral HPLC. [b] K = crystalline; S_A = smectic A; N = nematic, I = isotropic. [c] Yield of alcohol or ester (max. 50%) obtained by enzymic resolution. [d] Yield of ester obtained by acylation of the corresponding alcohol.



Scheme 1 *Reagents*: i, $Pd(PPh_3)_4$, C_6H_6, EtOH, $Na_2CO_{3(aq)}$; ii, $Pb(OCOCH_3)_4$, C_6H_6; iii, lipase PS, phosphate buffer, acetone, pH 7.0; iv, R^3COCl, pyridine, CH_2Cl_2; v, Amberlite 400 (OH) resin, MeOH

−15 to 0 °C, 10 min) gave the desired 2-cyclohexen-1-one esters (+)-**5**. The (−)-enantiomers of **5** were prepared by the chemical hydrolysis of the acetate (−)-**4** [Amberlite IRA 400 (OH) resin, MeOH, 4 h] to give the hydroxyenone (−)-**3** which was then esterified [R^3COCl (1.2 equiv.), pyridine (1.2 equiv.) in CH_2Cl_2, −15 to 0 °C, 10 min).

The phase-transition temperatures of the enones observed by optical microscopy are given in Table 1. Phase types were identified by the optical textures, and phase transitions and temperatures were confirmed by differential scanning calorimetry (DSC). These materials have a strong tendency to form smectic A phases, which probably result from microphase separation of the aromatic and aliphatic parts of the mesogen. Increasing the breadth of the molecule by placement of a methyl group in the two-position of the cyclopentenone ring appears to cause a disruption of the smectic tendency, resulting in a substantial depression of the smectic–nematic transition temperature and the appearance of a short nematic phase. The convergent route outlined affords polyfunctionalised mesogenic enones of high enantiomeric purity and in multigram quantities.

The utility of these new chiral materials as components of ferroelectric smectic C* mixtures is being investigated with a view to developing improved materials for ferroelectric liquid crystal displays. Preliminary measurements of ferroelectric polarization have been carried out for some of the compounds listed in Table 1. Since none of the homologues prepared so far exhibits a smectic C phase, it has been necessary to make the measurements on mixtures of the test compounds in an achiral smectic C host H1 (Merck). Results for **5a** and **5b** for the ferroelectric polarization at a temperature $T = (T_{SA/SC} - 10)$ °C are 11.6 and 15.5 nC cm^{-2}, respectively, extrapolated to 100% concentration from measurements made on solutions of less than 10% concentration. Those relatively small values may be due to the poor compatibility of the test compounds with the H1 host which is composed of fluorobiphenyl esters.

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Footnotes

† Lipase SAM-2 from Amano Pharmaceutical Co., was used as supplied by Fluka.

‡ All compounds gave satisfactory spectral data (NMR, IR, MS), and combustion analyses. The enzymic resolution is described for (±)-**4a**. The acetoxyenone (±)-**4a** (0.50 g, 1.45 mmol) was added to a 0.1 mol dm^{-3} phosphate buffer (20 ml, pH 7, 20 °C) and acetone (*ca.* 10 ml) was added until the enone dissolved. The solution was then adjusted to pH 7 by dropwise addition of 1 mol dm^{-3} HCl, lipase PS (*ca.* 20 mg) was then added, and the mixture kept at 30 °C. After the hydrolysis had initiated, as detected by a rapidly decreasing pH, 0.1 mol dm^{-3} NaOH was added so as to maintain the solution at pH 7. The reaction was monitored by chiral HPLC [CHIRALCEL OD; 4% propan-2-ol in light petroleum (b.p. 40–60 °C)] until no further increase in the alcohol was observed (*ca.* 24 h). The mixture was then extracted with CH_2Cl_2, the solvent dried ($MgSO_4$) and evaporated to give an oil which was subjected to flash chromatography (SiO_2, 7:3 light petroleum–ethyl acetate) to give first (−)-**4a** (0.232 g; 46%) and then (+)-**3a** (0.192 g; 46%). **3a** was not found to exhibit mesophase behaviour.

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