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The Synthesis and Transition Temperatures of Novel Low Molar Mass Cholesteric Materials Derived from (R—(4-Hydroxyphenoxy)propanoic Acid

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The Synthesis and Transition Temperatures of Novel Low Molar Mass Cholesteric Materials Derived from (*R*)-2-(4-Hydroxyphenoxy)propanoic Acid†

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A comprehensive series of (*R*)-2-(4-substituted-phenoxy)propanoates and (*R*)-2-(4-substituted-phenoxy)propanonitriles have been prepared. A wide variety of 4-substituents and ester functions have been examined to determine how the position of the chiral centre affects the cholesteric phase formation in these classes of materials; the synthesis of these novel materials, their transition temperatures and a procedure for assessing their optical purity are described and discussed. Mesogenicity is significantly depressed if the chiral centre is placed centrally within the molecule.

Keywords: cholesterics, 2-substituted propanoates, 2-substituted propanonitriles, enantiomeric excess, chiral shift reagent

Chiral liquid crystals find extensive use as thermochromic materials,[1] and are important for ferroelectric and related applications.[2] The necessary chirality of the organic molecules can be achieved in a variety of ways, e.g., (i) with an asymmetric carbon atom or atoms (usually denoted as C*)[3]; (ii) with compounds containing other quadrivalent asymmetric atoms such as sulphur[4]; (iii) with compounds containing asymmetric atoms such as nitrogen or phosphorus[5]; (iv) by the presence of orthogonal perpendicular dissymmetric planes about a chiral axis produced either by restricted rotation (e.g. with ortho-disubstituted biphenyls)[6] or by molecular structure (e.g. with allenes or cycloalkylidenes)[7,8]; (v) by generating asymmetry of the molecule through helicity to give a right- or left-handed helix (examples include

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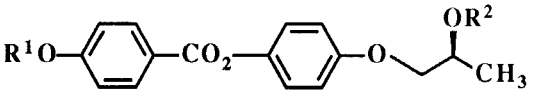
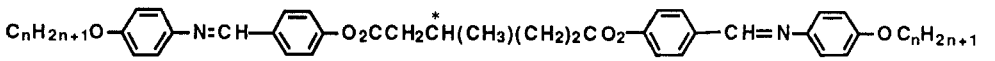
helicenes[9–11] and twistanes)[12]; (vi) by producing molecular asymmetry due to other types of restricted rotation, e.g. with substituted paracyclophanes[13] and substituted metallocenes.[14]

Although many of these methods have been used to generate chirality in liquid crystals (as given in some of the references above), most chiral liquid crystals owe their chirality to the fact that they contain asymmetric carbon atoms. In such materials, the chirality is usually introduced by using a suitable, commercially available chiral material directly or by preparing compounds stereospecifically from readily available chiral precursors. A most essential requirement of the final product and of any intermediate compound is that they are stable towards racemization processes (thermal, chemical and photochemical) so that optical activity is not lost during synthesis or during the lifetime of the ultimate application.

Most of the work carried out so far with chiral liquid crystals has utilized core systems in which the chiral centre is incorporated into a terminal unit (e.g. **I**)[15] and only recently has an example (**II**) of a chiral unit within a core system been reported.[16]

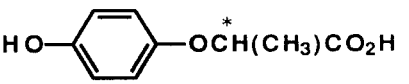


I



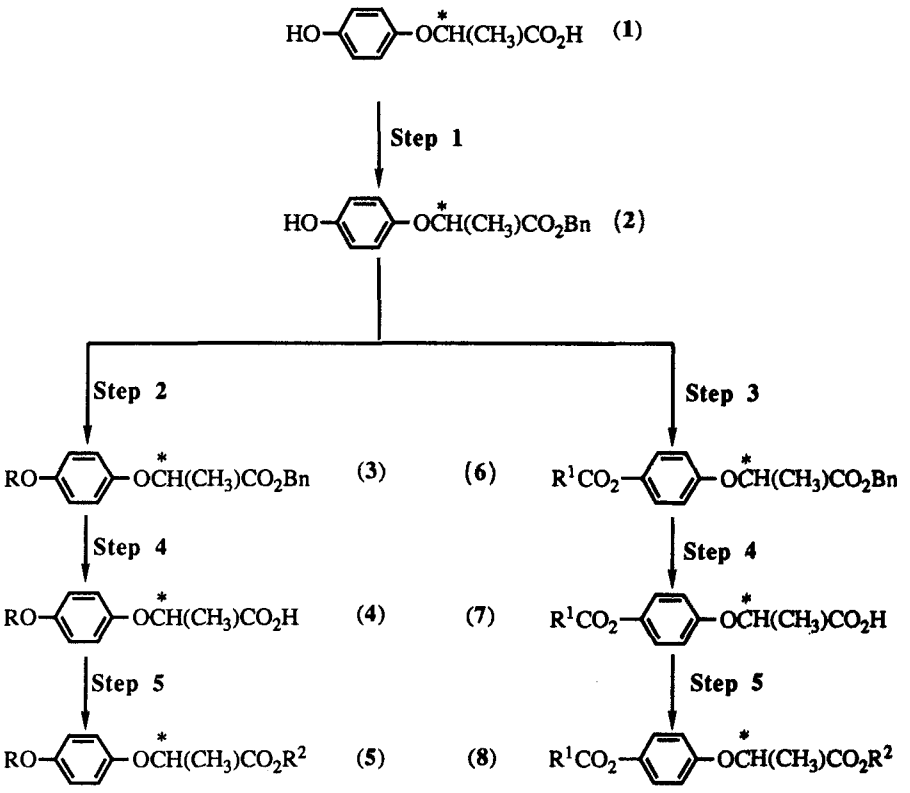
II

We report here our work based upon the compound (*R*)-2-(4-hydroxyphenoxy)propanoic acid (**III**), which was chosen because its bifunctionality allows either extension of the molecule at the phenolic site to give a system in which the chiral unit is in a terminal position, or extension at the carboxylic acid moiety to result in a more centrally placed chiral unit. By making examples of both series of derivatives of compound **III** it was hoped to illustrate how the generation of cholesteric (chiral nematic) phases is influenced by the position of the chiral centre in the molecule.



III

Using compound **III**, the synthesis of both the propanoate esters and the propanonitriles were carried out with careful attention at all times to the following two points: (a) compound **III** has an acidic hydrogen atom α to the electron withdrawing carboxylic group and the formation of the carbanion, or the enolate anion, which would occur in the presence of certain bases, would lead to racemization and therefore mild reaction conditions were used to ensure that products of high



Bn = benzyl, $PhCH_2$

Step 1...(i) K_2CO_3, MeOH, H_2O, pH=7.00, (ii) BnBr, DMF, RT.

Step 2....RBr, K_2CO_3, acetone, reflux.

Step 3....R^1CO_2H, dicyclohexylcarbodiimide, 4-*N*,*N*-dimethylaminopyridine or 4-(*N*-pyrrolidino)pyridine, CH_2Cl_2, RT.

Step 4....H_2, 5% Pd-C, ethyl acetate, RT.

Step 5....R^2OH, dicyclohexylcarbodiimide, 4-*N*,*N*-dimethylaminopyridine or 4-(*N*-pyrrolidino)pyridine, CH_2Cl_2, RT or (i) $(COCl)_2$, DMF, C_6H_6, RT, (ii) NH_3 (aq), RT, (iii) R^2OH, Et_3N, CH_2Cl_2, RT.

R and R^1CO = X, and R^2 = Y in Table I

a..R=C_8H_{17}, **b**..R^1=C_5H_{11}Ch, **c**..R^1=C_5H_{11}ChCh, **d**..R^1=C_5H_{11}ChPh, **e**..R^1=C_5H_{11}Bco, **f**..R^1=C_5H_{11}PhPh

Routes Used for the Synthesis of Chiral Propanoates

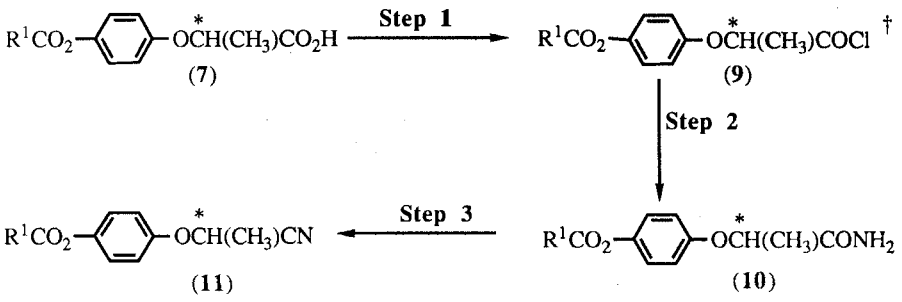
SCHEME I

optical purity were obtained; (b) compound **III** is bifunctional, and therefore a high degree of selectivity is required in further modifying either reactive moiety. The use of a protection-deprotection technique is necessary and the ideal protecting group is one that fulfills points (a) and (b).

The routes used for the synthesis of the chiral propanoate esters are shown in Scheme **I**. The carboxyl moiety of compound **1** was protected with a benzyl group which was easily introduced using very mild conditions and was readily removed by catalytic hydrogenolysis. Wang's method for selective benzylation of peptides[17] was easily adapted for compound **1** and by use of a suitable base, the more acidic carboxylic acid group was esterified in preference to the less acidic phenol group to give high yields of compound **2** in high purity.

Once the acid moiety had been protected, the group at the phenolic site was introduced in one of two ways, either by alkylation, using 1-bromooctane and potassium carbonate, or by esterification using a carboxylic acid (R^1CO_2H) and dicyclohexylcarbodiimide (DCC) and a pyridine based catalyst.[18,19] The benzyl ester was then hydrogenolysed at room temperature by using palladium-on-charcoal catalyst to yield the appropriate (*R*)-2-(4-substituted-phenoxy)propanoic acids (**4** and **7**). These acids were then esterified to give the various target compounds. Two methods of esterification were employed for this step, and one of these, the previous DCC process, worked well for reactions involving 4-substituted-phenols, secondary or tertiary alicyclic alcohols. However, it resulted in extremely poor yields of alkyl esters from primary aliphatic alcohols and an alternative procedure, using oxalyl chloride to give the acid chloride, which was then treated with the alcohol in the presence of a suitable amine base, gave the desired alkyl ester in improved yield.

The chiral propanonitriles were prepared as shown in Scheme **II**, which follows



† Not isolated.

Step 1....$(COCl)_2$, DMF, C_6H_6, RT.
Step 2....NH_3 (aq), RT.
Step 3....$SOCl_2$, DMF, RT.

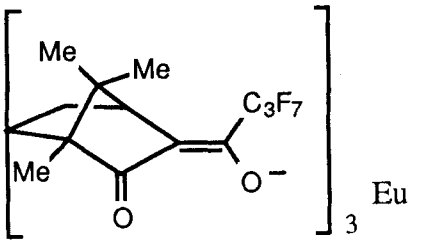
R^1CO = X in Table II

Route Used for the Synthesis of Chiral Propanonitriles

SCHEME II

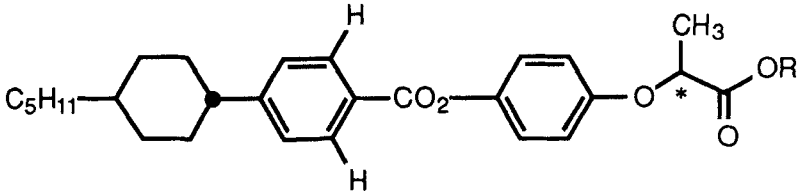
a similar route to that reported previously.[20] The appropriate (*R*)-2-(4-substituted-phenoxy)propanoic acids were converted into their amides *via* the acid chlorides and the amides were easily dehydrated in the presence of an excess of thionyl chloride in dry *N*,*N*-dimethylformamide to give the propanonitriles (**11**).

The optical purity of selected compounds (propyl and butyl esters, **A27** and **A28**) was determined by ^{1}H Nmr spectroscopy using the chiral shift reagent (+)-europium tris-(3-heptafluorobutyrylcamphorate) (**IV**). The method developed was tested using racemic modifications of these compounds which were prepared as shown in Scheme **III**. As the chiral centre in these esters carries a proton and a methyl group



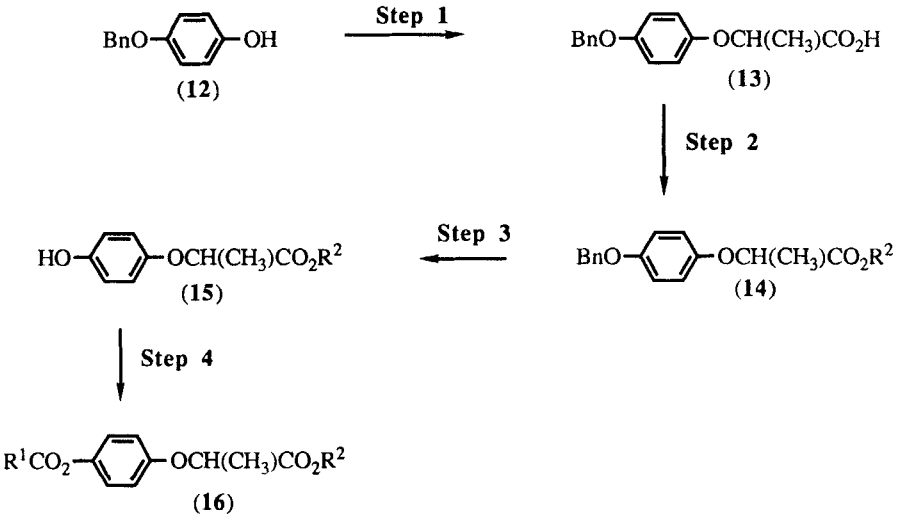
IV

as substituents, it was hoped that the signals corresponding to these units would show the major change in chemical shift. However, the chiral shift reagent caused line broadening and high background noise for these particular resonances; fortunately noticeable downfield shifts were observed for the protons *ortho* to the core acids' carboxyl group, (**V**). These protons resonate at δ 8.10 ppm, and appear as doublets, coupled to the neighbouring aromatic protons. In the case of the racemic modification of propyl ester **16a**, this doublet separated in the presence of the shift reagent into virtually identical doublets at δ 8.37 and 8.33 ppm corresponding to both the (*R*)- and (*S*)-isomers of the racemic mixture.

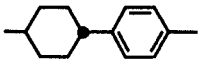


V

In the similar analysis of **A27**, two signals were resolved, one being a doublet centered on δ 8.30 ppm and the other being a smaller shoulder centered at 8.27 ppm. Integration reveals 84.3% and 15.7% of each enantiomer, giving an overall enantiomeric excess of 68.6%. However, in the case of the butyl ester (**A28**), the proton needed to be decoupled from its neighbour, so that only two singlets at δ 8.38 and 8.34 ppm were observed. Integration reveals 87.3% and 12.7% of either enantiomer, giving an enantiomeric excess of 74.6% in this case. By using the methods described previously, compound **III** was modified to give molecules in



Bn = benzyl, $PhCH_2$

R^1 = C_5H_{11} 

a...R^2 = C_3H_7, b...R^2 = C_4H_9.

Step 1....$CH_3CHBrCO_2H$, NaOH, EtOH, H_2O, 50-60 °C.
Step 2...(i) $(COCl)_2$, C_6H_6, DMF, RT, (ii) R^2OH, Et_3N, CH_2Cl_2, RT.
Step 3....H_2, 5% Pd-C, ethyl acetate, RT.
Step 4.... R^1COCl, Et_3N, CH_2Cl_2, RT.

Routes Used for the Synthesis of Racemic Compounds

SCHEME III

which the point of chirality is located either terminally or centrally. The full range of propanoate esters prepared is listed in Table I along with their melting points, transition temperatures and specific optical rotations.

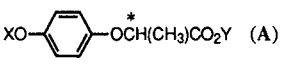
Four major divisions of compounds are given for the phenyl ring of **III** substituted with an alkoxy group (compounds **A1–A8**), a *trans*-4-pentylcyclohexylcarbonyloxy group (compounds **A9–A13**), a *trans*-4-(*trans*-4-pentylcyclohexyl)cyclo-

hexylcarbonyloxy group (CCH type, compounds **A14–A24**) and a 4-(*trans*-4-pentylcyclohexyl)benzoyloxy group (PCH type, compounds **A25–A29**). In each of the first three sets the propanoate ester had one- or two-ring substituents (and, in one instance, an alkyl group) and the final PCH set is confined to the more successful single ring and alkyl chain derivatives. The most apparent point from the table is that the majority of the compounds are not mesogenic and in the first three sets no enantiotropic phases were seen and only two examples of monotropic phases occur in the CCH set (cyclohexyl systems are widely recognized as strong promoters of the S_B phase).[21] In order to make some assessment of the mesogenic character of these compounds, virtual Ch-I values were determined by extrapolation from mixtures in E7, usually using mixtures of at least 20% wt/wt composition.

The melting points of the compounds are classified remarkably consistently by the number of ring systems present e.g., for a fixed X group, the two-ring systems always have higher melting points than the single-ring compounds and for a fixed Y group the melting points always increase as the first and then the second cyclohexyl rings are introduced.

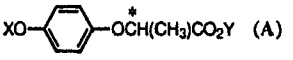
TABLE I

Melting points and transition temperatures (°C) for (*R*)-2-(4-substituted-phenoxy)propanoate esters (**A**)

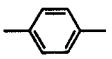
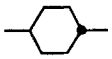


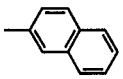
Compound Number	X	Y	K	S_B	S_A	Ch	I	$[\alpha]_D^a$
A1	C_8H_{17}	PhC_3H_7	. 24.5			[. -63]	.	+55.7
A2	"	PhC_7H_{15}	. 32.0			[. -13]	.	+38.4
A3	"	$PhPhC_5H_{11}$	. 84.6			[. -26]	.	+51.9
A4	"	$BcoC_5H_{11}$	. 25.7			[. -60]	.	+30.9
A5	"	$ChChC_5H_{11}$	. 70.7			[. 26]	.	+25.2
A6	"	ChC_5H_{11}	. 27.8			[. -48]	.	+30.3
A7	"	PhPhCN	. 67.8			[. -40]	.	+59.7
A8	"	2-Naph	. 54.0				.	+63.4
A9	$C_5H_{11}ChCO$	PhC_3H_7	. 55.4			[. -40]	.	+56.0
A10	"	PhC_7H_{15}	. 54.4			[. -38]	.	+46.8
A11	"	$PhPhC_5H_{11}$	. 122.5			[. -12]	.	+45.4
A12	"	$BcoC_5H_{11}$	. 67.9			[. -28]	.	+28.1
A13	"	$ChChC_5H_{11}$	. 114.3			[. 28]	.	+23.8
A14	$C_5H_{11}ChChCO$	PhC_3H_7	. 99.8			[. 50]	.	+42.3
A15	"	PhC_7H_{15}	. 92.6			[. 39]	.	+35.8
A16	"	$PhPhC_5H_{11}$	. 152.1				.	+40.6

TABLE I (*continued*)



Compound Number	X	Y	K	S_B	S_A	Ch	I	$[\alpha]_D^a$
A17	"	$BcoC_5H_{11}$	. 97.1			[. 46]	.	+18.9
A18	"	ChC_5H_{11}	. 106.6			[. 57]	.	+19.8
A19	"	ChH	. 109.8	(.70.3)			.	+19.8
A20	"	PhPhCN	. 137.6			[. 49]	.	+33.6
A21	"	C_4H_9	. 109.2	(. 44.6)			.	+19.7
A22	"	$PhOC_2H_5$	. 127.8			[. 48]	.	+45.4
A23	"	$PhOC_6H_{13}$	. 104.6			[. 42]	.	+29.8
A24	"	PhH	. 126.8				.	+45.2
A25	$C_5H_{11}ChPhCO$	PhC_3H_7	. 104.3			[. 25]	.	+48.7
A26	"	ChH	. 86.4			[. 56]	.	+20.8
A27	"	C_3H_7	. 67.2		(. 60.5)	. 77.9	.	+19.3
A28	"	C_4H_9	. 58.1		(. 46.2)	. 67.3	.	+20.5
A29	"	C_5H_{11}	. 59.1			. 60.8	.	+25.2

Ph is  , Ch is 

2-Naph is  , Bco is 

[a]...measured at ambient temperature (22-24 °C) in $CHCl_3$.

( )...monotropic transition.

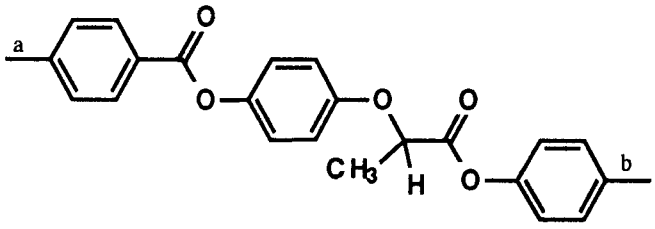
[ ]...virtual transition; determined from mixtures in E7 (BDH) up to 20 % wt/wt.

Although the substituents X and Y had been varied in type and in length of core unit in an attempt to induce mesophases, it is clear that most of the molecular structures are very poor at promoting liquid crystal behavior. For those cases were X = C_8H_{17} or $C_5H_{11}ChCO$-, the virtual Ch-I values are low and even a two-ring system in place of Y does not promote mesophase stability very markedly.

Lengthening the substituent X in the CCH series does give a pronounced increase in [Ch-I] values (cf **A9**, **A14**; **A10**, **A15**; **A12**, **A17**) at the expense of increased melting points but it is only when substituent Y is small (i.e. for **A19** and **A21**) that a monotropic mesophase arises. The most favourable situation occurs, therefore,

when the chiral point (arising from the methyl substituent) is not placed between two effective core units but is at one end of the molecule. The methyl group on the chiral carbon atom is a substituent which will inevitably protrude from the general molecular cylinder and when this site is at the end of a molecule, intermolecular associations of the rest of the core are still possible but when the protrusion is placed more centrally it will be much more effective in preventing intermolecular associations.

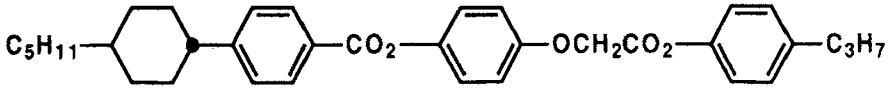
An attempt has been made, using molecular modelling, to determine whether the centrally located methyl substituent, causes this pronounced depression in mesogenicity by distorting molecular shape so that the terminal substituents are rendered less collinear than the analogous phenoxyethanoic derivative or by a steric effect which keeps the adjacent molecules apart. The Alchemy II molecular modelling package (Tripos Associates, Inc) was used and the energy of compound **VI**, which represents part of the central region of compound **A25**, was minimized starting from a variety of initial structures. The transposed angle between the bonds



VI

a and b then reveals how far the bonds a and b are from collinearity and an optimum transposed angle of 180° would show that the axes of bonds a and b are in the same direction. The angles determined for the methyl compound lie within the range 155.5–166.0° and for the methylene system within the range 156.8–171.6°. We believe that the reasonable similarity of these values indicates that the poor mesogenicity of such propanoic acid derivatives is not a consequence of a molecular deformation arising from the presence of the methyl substituents but it is more likely that the effect is predominantly steric in that the lateral methyl group in the centre of the molecule prevents the effective association of molecules.

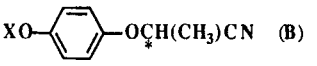
It is also interesting to note that the achiral compound **VII**, without the methyl substituent, has a nematic phase which clears almost 150°C above the virtual Ch-I value of 25°C determined for the non-mesogenic compound **A25** to which it is related (The synthesis of **VII** *via* intermediates **17–20** is given in the Experimental section). The PCH series of compounds (**A25–A29**) were therefore restricted to those with small Y substituents and in this series enantiotropic cholesteric phases were generated for compounds **A27–A29**. The propyl and butyl derivatives show



VII

TABLE II

Melting points and transition temperatures (°C) for (*R*)-2-(4-substituted-phenoxy)propanonitriles (**B**)†



Compound Number	X	K	S_A	Ch	I	$[\alpha]_D$[a]
B1	$C_5H_{11}ChCO$	. 44.7	———		.	+62.0
B2	$C_5H_{11}BcoCO$	. 46.6	———	(. 25.7)	.	+66.7
B3	$C_5H_{11}ChChCO$	. 82.5	. 146.9	. 179.6	.	+34.9
B4	$C_5H_{11}ChPhCO$	.122.3	(. 92.9)	. 151.6	.	+40.6
B5	$C_5H_{11}PhPhCO$	.120.7	.155.4	. 166.6	.	+42.2

† Footnotes as footnotes as in Table I.

monotropic S_A phases and on cooling from the Ch phase these compounds give brilliant iridescent colour play as the cholesteric helix is unwound.[22] Blue phases were observed by optical microscopy for all of these compounds.

The propanonitriles shown in Table II provide another illustration of the desirability of having the chiral centre in a terminal chain rather than in a core system. Even the single ring substituent for X (compound **B2**) gives a monotropic Ch phase and all the two ring core units (compounds **B3–B5**) give enantiotropic Ch phases with thermal stabilities vastly increased (see compounds **B3** and **B4** respectively) by comparison with the CCH and PCH alkyl esters.

The conclusions to be drawn from these results with the (*R*)-2-(4-substituted-phenoxy)propanoic acid units are that: (a) when Y is either aryl or cyclohexyl, the propanoate effectively has two "core" units which suppress liquid crystallinity by competition with each other, (b) even a two-ring system will permit the generation of a cholesteric phase, if both rings are to the left of the chiral centre in a terminal chain, (c) the compound is best used with Y as simple alkyl esters or with the carboxylic group converted into a nitrile so that two competing 'cores' are avoided.

EXPERIMENTAL

Confirmation of the structures of intermediates and products was obtained by ^1H Nmr spectroscopy (Jeol GX NM270 FT-Nmr spectrometer, using tetramethylsilane as the internal standard), mass spectrometry (Finnigan 1020 GC-MS spectrometer) and Ir spectroscopy (Perkin Elmer 783 spectrometer). Specific optical rotations, $[\alpha]_D$, were determined at ambient temperature (22–24°C) in chloroform using a Bendix-NPL Automatic Polarimeter Type 143A optical unit and control unit.

Thin-layer chromatographic analyses were performed using preformed aluminium backed silica gel plates (60 F254 Merck). Gravity column chromatography was carried out using Fisons 60–120 mesh silica gel and flash chromatography was performed using Merck fine mesh silica gel 60 (230–400 mesh).

(*R*)-2-(4-Hydroxyphenoxy)propanoic acid (**1**) was supplied by ICI Organics Division, Huddersfield, as a crude material which was purified by repeated recrystallization from ethanol.

All phase transitions were recorded using a Mettler FP52 hot-stage, Mettler FP5 temperature controller and an Olympus model BH-2 polarizing microscope.

(R)-Benzyl 2-(4-hydroxyphenoxy)propanoate (**2**). (*R*)-2-(4-Hydroxyphenoxy)propanoic acid (**1**) (50.00 g, 0.28 mol) was dissolved in methanol-water (500 ml, 9:1) with stirring. The pH was then adjusted to 7.00 (pH meter) using aqueous potassium carbonate (20% solution). Most of the solvent was removed under reduced pressure (water pump, water-bath temp <50°C) and the final traces were removed azeotropically using dichloromethane (500 ml) to give a viscous brown oil. This was dissolved in dry DMF (100 ml) and benzyl bromide (47.12 g, 0.28 mol) in dry DMF (65 ml) was added dropwise during 30 min with stirring at room temperature. After 48 h, analysis by thin layer chromatography showed that the reaction had reached completion and the excess of DMF was then removed under reduced pressure (water pump, water-bath at 40–50°C) and water (200 ml) was added with stirring. The product was extracted into diethyl ether (5 × 40 ml), the extracts were combined and washed with water (3 × 50 ml), dried (Na_2SO_4), filtered and the filtrate was evaporated under reduced pressure to give a brown oil. This oil was then purified by column chromatography [silica gel; gradient elution with 9:1 dichloromethane-petrol (bp 40–60°C) and finally with 9:1 dichloromethane-ethyl acetate] to give an oil which crystallized on standing.

Yield = 61.61 g (82%) mp 49.3–50.9°C

^{1}H Nmr ($CDCl_3$) δ 1.56 (3H, d), 4.57 (1H, q), 4.58 (1H, s), 5.20 (2H, s), 6.69 (4H, 2xd), 7.30 (5H, m).

Ir ν_{max} (KCl) 3420, 3020, 3000, 1740, 1512, 1459, 1215, 830, 750, 700 cm^{-1}.

$[\alpha]_D^{24} = +31.7°$.

(R)-Benzyl 2-(4-octoxyphenoxy)propanoate (**3a**). Compound **2** (13.12 g, 0.050 mol), potassium carbonate (13.36 g, 0.100 mol), 1-bromo-octane (9.25 g, 0.050 mol) and dry acetone (65 ml) were heated under reflux with continuous stirring for 48 h (analysis by thin layer chromatography showed complete reaction). The mixture was allowed to cool, the potassium bromide and the excess of potassium carbonate were filtered off and the acetone was evaporated off under reduced pressure to give a brown-yellow oil. The oil was purified by column chromatography [silica gel; dichloromethane] to give a colourless liquid.

Yield = 12.93 g (75%)

^{1}H Nmr ($CDCl_3$) δ 0.89 (3H, t), 1.30 (10H, m), 1.58 (3H, d), 1.75 (2H, quintet), 3.90 (2H, t), 4.70 (1H, q), 5.18 (2H, s), 6.77 (4H, 2xd), 7.50 (5H, m).

Ir ν_{max} (film) 2930, 2870, 1760, 1310, 1230, 1135, 825, 750, 700 cm^{-1}.

(R)-Benzyl 2-(4-substituted-phenoxy)propanoates (**6**). Dicyclohexylcarbodiimide (1.15 mol equivalents) in dry dichloromethane (50 ml) was added dropwise during 10 min to a stirred solution of the appropriate carboxylic acid (1.00 mol equivalent), compound **2** (1.00 mol equivalent), 4-(*N*-pyrrolidino)pyridine (0.30 mol equivalent) in dry dichloromethane (150 ml). The reaction mixture was stirred for 18 h, before removal of the precipitated *N,N'*-disubstituted urea by filtration through 'Hyflo supercel'. The dichloromethane solution was then successively washed with water (1x), 5% (v/v) acetic acid solution (2x) and water (1x) and dried ($MgSO_4$). Filtration and evaporation of the solvents gave a solid in each case which was purified by column chromatography [silica gel; dichloromethane as eluant, unless otherwise stated].

The following compounds were prepared using this procedure.

(R)-Benzyl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**6b**).
Yield = 11.76 g (69%) mp 58.4–60.9°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (5H, m), 1.25 (9H, m), 1.53 (2H, d), 1.60 (4H, d), 1.87 (2H, d), 2.11 (2H, d), 2.44 (1H, sextet), 4.65 (1H, q), 5.16 (2H, s), 6.83 (2H, d), 6.93 (2H, d), 7.27 (2H, d), 7.33 (2H, d).
Ir ν_{max} (KCl) 2930, 2850, 1750, 1600, 1505, 1455, 1245, 705, 525 cm^{-1}.

(R)-Benzyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**6c**).
Yield = 13.18 g (67%) mp 108.7–109.4°C
^{1}H Nmr ($CDCl_3$) δ 0.88 (5H, t), 1.08 (9H, m), 1.25 (6H, m), 1.52 (2H, d), 1.61 (3H, d), 1.76 (6H, d), 2.13 (2H, d), 2.42 (1H, sextet), 4.75 (1H, q), 5.20 (2H, s), 6.82 (2H, d), 6.92 (2H, d), 7.30 (5H, m).
Ir ν_{max} (KCl) 2930, 2850, 1750, 1600, 1505, 1250, 765, 705, 605, 520 cm^{-1}.

(R)-Benzyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxyl}propanoate (**6d**).
Yield = 9.68 g (72%) mp 147.3–150.7°C
^{1}H Nmr ($CDCl_3$) δ 0.89 (3H, d), 1.09 (2H, q), 1.29 (10H, m), 1.49 (2H, q), 1.63 (3H, d), 1.90 (4H, d), 2.56 (1H, sextet), 4.77 (1H, q), 5.19 (2H, s), 6.88 (2H, d), 7.02 (2H, d), 7.31 (6H, m), 8.10 (2H, d).
Ir ν_{max} (KCl) 2930, 2850, 1750, 1735, 1610, 1505, 1260, 1245, 1195, 1180, 1145, 1105, 1075, 1015, 750, 710 cm^{-1}.

(R)-Benzyl 2-{4-(4-pentylbicyclo[2.2.2]octane-1-carbonyloxy)phenoxy}propanoate (**6e**). Purified by flash chromatography [silica gel; 9:1 dichloromethane-petrol (bp 40–60 °C)].
Yield = 6.95 g (65%) mp 56.6°C
^{1}H Nmr ($CDCl_3$) δ 0.88 (3H, t), 1.22 (8H, m), 1.43 (6H, t), 1.61 (3H, d), 1.90 (6H, t), 4.74 (1H, q), 5.17 (2H, s), 6.82 (2H, d), 6.90 (2H, d), 7.26 (2H, d) and 7.34 (3H, m).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1740, 1505, 1270, 1195, 1130, 1055, 970, 750, 700, 595, 545 and 480 cm^{-1}.
m/z 478 (M^+, 2%), 179 (100%), 137 (10%), 123 (35%) and 109 (55%).

(R)-Benzyl 2-{4-[4-(4-pentylphenyl)benzoyloxy]phenoxy}propanoate (**6f**). Purified by flash chromatography [silica gel; 1:1 dichloromethane-petrol (bp 40–60°C)].
Yield = 15.79 g (67.5%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (4H, t), 1.35 (5H, m), 1.65 (6H, m), 2.65 (2H, t), 4.77 (1H, q), 5.20 (2H, s), 6.90 (2H, d), 7.15 (2H, d), 7.35 (4H, m), 7.58 (2H, d), 7.72 (2H, d) and 8.24 (2H, d).
Ir ν_{max} (KCl) 2930, 2870, 1770, 1755, 1730, 1610, 1510, 1455, 1405, 1385, 1315, 1275, 1245, 1195, 1120, 1080, 1005, 880, 870, 850, 815, 770, 750, 745, 725, 695 and 550 cm^{-1}.

Debenzylation of the (R)-Benzyl 2-(4-substituted-phenoxy)propanoates. The appropriate benzyl 2-(4-substituted-phenoxy)propanoate (**6**) was dissolved in ethyl acetate and a slurry of 5% palladium-on-charcoal in ethyl acetate was added with stirring. The mixture was then stirred under a hydrogen atmosphere for 18 h. The catalyst was removed by filtration through 'Hyflo supercel', the solution was dried ($MgSO_4$), refiltered and the solvent removed to leave a white solid.

The following compounds were prepared using this procedure.

(R)-2-(4-Octoxyphenoxy)propanoic acid (**4a**).
Yield = 7.95 g (76%) mp 80.8–82.3°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.30 (10H, m), 1.62 (3H, d), 1.75 (2H, quintet), 3.90 (2H, t), 4.60 (1H, q), 6.88 (4H, 2xd), (carboxylic acid H not detected).
Ir ν_{max} (KCl) 3160, 2930, 2860, 1730, 1679, 1515, 1225, 1041, 829, 765 cm^{-1}.

(R)-2-[4-(trans-4-Pentylcyclohexylcarbonyloxy)phenoxy]propanoic acid (**7b**).
Yield = 8.63 g (91%)
^{1}H Nmr ($CDCl_3$) δ 0.95 (5H, m), 1.33 (9H, m), 1.58 (2H, d), 1.70 (3H, d), 1.91 (2H, d), 2.16 (2H, d), 2.49 (1H, sextet), 4.80 (1H, q), 6.93 (2H, d), 7.03 (2H, d), (carboxylic acid H not detected).
Ir ν_{max} (KCl) 3420, 2930, 2860, 1745, 1715, 1512, 1245, 1200, 1140, 850, 520 cm^{-1}.

(R)-2-{4-[trans-4-(trans-4-Pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoic acid (**7c**).
Yield = 11.40 g (79%) mp 196.2–199.9°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (5H, m), 1.05 (9H, m), 1.25 (6H, m), 1.52 (2H, q), 1.75 (9H, m), 2.13 (2H, d), 2.43 (1H, sextet), 4.75 (1H, q), 6.85 (2H, d), 6.98 (2H, d), (carboxylic acid H not detected).
Ir ν_{max} (KCl) 3420, 2930, 2860, 1750, 1715, 1515, 1245, 1205, 1040, 855, 525 cm^{-1}.

(R)-2-{4-[4-(trans-4-Pentylcyclohexyl)benzoyloxy]phenoxy}propanoic acid (**7d**).
Yield = 7.23 g (90%) mp 158.3–160.7°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, m), 1.10 (2H, q), 1.30 (10H, m), 1.50 (2H, q), 1.70 (3H, d), 1.90 (3H, d), 2.55 (1H, t), 4.80 (1H, q), 6.95 (2H, d), 7.15 (2H, d), 7.33 (2H, d), 8.10 (2H, d), (carboxylic acid H not detected).
Ir ν_{max} (KCl) 3440, 2920, 2850, 1735, 1615, 1505, 1270, 1245, 1195, 1180, 1075, 705 cm^{-1}.

(R)-2-{4-(4-Pentylbicyclo[2.2.2]octane-1-carbonyloxy)phenoxy}propanoic acid (**7e**).
Yield = 5.08 g (91%) mp 97.1–98.5°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, m), 1.20 (8H, m), 1.45 (6H, t), 1.60 (3H, d), 1.85 (6H, t), 4.73 (1H, q), 6.85 (2H, d), 6.95 (2H, d) and 10.30 (1H, s, broad).
Ir ν_{max} (KBr) 3200, 2930, 2860, 2840, 1750, 1740, 1505, 1225, 1190, 1130, 1050, 980, 840, 800 and 520 cm^{-1}.
m/z 388 (M^+), 207 (10%), 179 (100%), 137 (10%), 123 (40%) and 109 (75%).
$[\alpha]_D^{24}$ = +4.3°

(R)-2-{4-[4-(4-Pentylphenyl)benzoyloxy]phenoxy}propanoic acid (**7f**).
Yield = 12.58 g (97%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.35 (5H, m), 1.70 (6H, m), 2.65 (2H, t), 4.80 (1H, q), 6.97 (2H, d), 7.17 (2H, d), 7.29 (2H, d), 7.57 (2H, d), 7.71 (2H, d) and 8.23 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1730, 1610, 1505, 1455, 1425, 1400, 1380, 1275, 1250, 1190, 1135, 1100, 1075, 1015, 1005, 935, 875, 815, 765, 750, 695, 630, 580, 555, and 525 cm^{-1}.

(R)-2-(4-Substituted-phenoxy)propanamides (**10**). Oxalyl chloride (5.75–11.50 mmol, 2 mol equivalents) in dry benzene (20 ml) was added dropwise to a stirred suspension of the appropriate acid (**7**) (2.69–4.45 mmol, 1 mol equivalent) in dry benzene (20 ml) containing 5 drops of dry DMF. The suspension was left to stir overnight before removing the excess of benzene and oxalyl chloride under reduced pressure (water pump) to give the crude acid chloride. The residue was dissolved in dry diglyme (25 ml) and was added slowly to a stirred solution of ammonia (35% solution, 70 ml). The mixture was cooled (ice bath, 0°C) and the precipitated amide was filtered off, washed with water, dried (P_2O_5) to give an off-white powder in each case.

The following amides were prepared using this procedure and were used in the next step without further purification.

(R)-2-[4-(trans-4-Pentylcyclohexylcarbonyloxy)phenoxy]propanamide(**10b**).
Yield = 1.46g (91%).

(R)-2-{4-[trans-4-(trans-4-Pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanamide (**10c**).
Yield = 1.06 g (88%)

(R)-2-{4-[4-(trans-4-Pentylcyclohexyl)benzoyloxy]phenoxy}propanamide (**10d**).
Yield = 1.18 g (100%).

(R)-2-{4-(4-Pentylbicyclo[2.2.2]octane-1-carbonyloxy)phenoxy}propanamide (**10e**).
Yield = 1.31 g (94%).

(R)-2-{4-[4-(4-Pentylphenyl)benzoyloxy]phenoxy}propanamide (**10f**).
Yield = 1.51 g (100%)

(R)-2-(4-Substituted-phenoxy)propanonitriles (**11**). Thionyl chloride (23.50–41.36 mmol, 10 mol equivalents) in dry DMF (5 ml) was added dropwise to a stirred suspension of the appropriate (*R*)-2-(4-substituted-phenoxy)propanamide (**10**) (2.35–4.04 mmol, 1 mol equivalent) in dry DMF (10 ml). The reaction mixture was stirred for 24 h and then poured on to ice (50 g) and water (50 ml) with vigorous stirring. The product was extracted into dichloromethane (3 × 20 ml) and the combined extracts were washed successively with water (10 ml), saturated aqueous sodium hydrogen carbonate (3 × 20 ml) and water (10 ml). The extracts were dried ($MgSO_4$), filtered and the filtrate was evaporated under reduced pressure (water pump) to give an oil or a solid. The crude products were purified by column chromatography [silica gel] and dried using a vacuum drying pistol (P_2O_5, 40°C, 0.5 mmHg for 4 to 6 h).

The following compounds were prepared using this procedure.

(R)-2-[4-(trans-4-Pentylcyclohexylcarbonyloxy)phenoxy]propanonitrile (**11b, B1**). Flash chromatography, eluant 2:1 dichloromethane-petrol (bp 40–60°C); recrystallized (ethyl acetate).
Yield = 0.21 g (15%).
^{1}H Nmr ($CDCl_3$) δ 0.89 (3H, m), 1.27 (10H, m), 1.53 (3H, m), 1.78 (3H, d), 1.87 (2H, d), 2.12 (2H, d), 2.46 (1H, sextet), 4.84 (1H, q), 7.20 (4H, 2xd).
Ir ν_{max} (KCl) 2920, 2850, 1750, 1510, 1455, 1200, 1130, 1050, 980, 845, 830, 525 cm^{-1}.
m/z 343 (M^+, 20%), 180 (30%), 163 (45%), 109 (50%), 97 (100%), 83 (70%), 55 (65%).

(R)-2-{4-(4-Pentylbicyclo[2.2.2]octane-1-carbonyloxy)phenoxy}propanonitrile (**11e, B2**). Flash chromatography, eluant 2:1 dichloromethane-petrol (bp 40–60°C); recrystallized (ethyl acetate-petrol (bp 60–80°C)).
Yield = 0.47 g (37%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (3H, t), 1.22 (8H, m), 1.44 (6H, t), 1.78 (3H, d), 1.90 (6H, t), 4.80 (1H, q) and 7.00 (4H, s).
Ir ν_{max} (film) 2930, 2870, 1750, 1600, 1505, 1455, 1380, 1350, 1225, 1195, 1130, 1100, 1045, 980, 875, 795 and 525 cm^{-1}.
m/z 369 (M^+), 267 (15%), 179 (100%), 123 (35%) and 109 (60%).

(R)-2-{4-[trans-4-(trans-4-Pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanonitrile (**11c, B3**). Flash chromatography, eluant 9:1 dichloromethane-petrol (bp 40–60°C); recrystallized (ethyl acetate).
Yield = 0.47 g (47%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (5H, t), 1.00 (3H, d), 1.11 (7H, m), 1.25 (3H, m), 1.55 (3H, t), 1.79 (10H, m), 2.14 (2H, d), 2.44 (1H, sextet), 4.84 (1H, q), 7.02 (4H, 2xd).
Ir ν_{max} (KCl) 2960, 2920, 1850, 1745, 1505, 1235, 1200, 1140, 525 cm^{-1}.
m/z 425 (M^+, 15%), 262 (53%), 235 (23%), 210 (25%), 163 (38%).

(R)-2-{4-[4-(trans-4-Pentylcyclohexyl)benzoyloxy]phenoxy}propanonitrile (**11d, B4**). Flash chromatography, eluant 1:1 dichloromethane-petrol (bp 40–60°C); recrystallized (ethyl acetate).
Yield = 0.63 g (56%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.09 (2H, t), 1.27 (9H, m), 1.51 (3H, m), 1.81 (3H, d), 1.91 (3H, d), 2.56 (1H, sextet), 4.87 (1H, q), 7.06 (2H, d), 7.18 (2H, d), 7.34 (2H, d), 8.11 (2H, d).
Ir ν_{max} (KCl) 2970, 2920, 2850, 1740, 1505, 1265, 1190, 1180, 1075, 1015, 770, 705 cm^{-1}.
m/z 419 (M^+), 257 (100%), 131 (5%), 91 (5%).

(R)-2-{4-[4-(4-Pentylphenyl)benzoyloxy]phenoxy}propanonitrile (**11f, B5**). Flash chromatography, eluant 2:1 dichloromethane-petrol (bp 40–60°C); recrystallized (ethyl acetate).
Yield = 0.61 g (44%)
^{1}H Nmr ($CDCl_3$) δ 0.91 (3H, t), 1.35 (4H, m), 1.54 (1H, s), 1.67 (1H, quint), 1.82 (3H, d), 2.67 (2H, t), 4.99 (1H, q), 7.08 (2H, d), 7.22 (2H, d), 7.30 (2H, d), 7.58 (2H, d), 7.73 (2H, d) and 8.24 (2H, d).
Ir ν_{max} (KCl) 2970, 2920, 2880, 2850, 1730, 1610, 1505, 1400, 1385, 1290, 1235, 1180, 1100, 1075, 1045, 1015, 930, 850, 820, 770 and 750 cm^{-1}.
m/z 413 (M^+), 350, 251, 165, 152 and 109.

(R)-4-Propylphenyl 2-(4-octoxyphenoxy)propanoate (**A1**). Dicyclohexylcarbodiimide [DCC] (0.45 g, 2.18 mmol), compound **4a** (0.60 g, 2.04 mmol), 4-propylphenol (0.28 g, 2.07 mmol) and 4-(*N*-pyrrolidino)pyridine (0.05 g, 0.34 mmol) were dissolved in dry dichloromethane (60 ml) and stirred for 18 h (unless stated otherwise) at room temperature. The precipitated *N,N'*-dicyclohexylurea was filtered off through 'Hyflo supercel' and the dichloromethane solution was washed successively with water (10 ml), 5% (v/v) aqueous acetic acid (2 × 15 ml), water (10 ml) before being dried ($MgSO_4$); filtration and evaporation of the filtrate gave a white solid which was purified by column chromatography [silica gel; dichloromethane].
Yield = 0.57 g (68%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (6H, m), 1.30 (9H, m), 1.60 (3H, m), 1.75 (5H, m), 2.55 (2H, t), 3.90 (2H, t), 4.85 (1H, q), 6.85 (2H, d), 6.93 (4H, 2xd), 7.15 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1780, 1505, 1470, 1380, 1230, 1195, 1165, 1120, 1100, 890, 825, 525 cm^{-1}.
m/z 412 (M^+, 31%), 249 (28%), 222 (75%), 110 (63%).

The following compounds were prepared using a procedure similar to that described for the preparation of **A1**.

(R)-4-Heptylphenyl 2-(4-octoxyphenoxy)propanoate (**A2**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 1.56 g (69%)
^{1}H Nmr (DMSO-d_6) δ 0.88 (6H, m), 1.30 (18H, m), 1.60 (2H, m), 1.75 (5H, m), 2.60 (2H, t), 3.93 (2H, t), 4.88 (1H, q), 6.83 (2H, d), 6.93 (4H, 2xd), 7.15 (2H, d).

Ir ν_{max} (KCl) 2960, 2930, 2860, 1765, 1510, 1230, 1200, 1170, 1120, 1100, 820 cm^{-1}.
m/z 468 (M^+, 60%), 249 (42%), 222 (100%), 110 (89%).

(R)-4-Pentylbiphenyl-4-yl 2-(4-octoxyphenoxy)propanoate (**A3**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 0.77 g (22%)
^1H Nmr ($CDCl_3$) δ 0.90 (6H, m), 1.35 (14H, m), 1.65 (2H, t), 1.75 (5H, m), 2.65 (2H, t), 3.93 (2H, t), 4.90 (1H, q), 6.85 (2H, d), 6.95 (2H, d), 7.18 (2H, d), 7.25 (2H, d), 7.45 (2H, d), 7.58 (2H, d).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1765, 1515, 1230, 1170, 1080, 1050, 1005, 890, 830, 800, 765 cm^{-1}.
m/z 516 (M^+, 36%), 266 (100%), 248 (40%), 240 (82%), 222 (49%), 183 (66%).

(R)-4-Pentylbicyclo[2.2.2]oct-1-yl 2-(4-octoxyphenoxy)propanoate (**A4**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 1.00 g (31%)
^1H Nmr ($CDCl_3$) δ 0.88 (6H, m), 1.18 (4H, m), 1.30 (11H, m), 1.50 (12H, m), 1.75 (2H, quintet), 1.95 (6H, t), 3.90 (2H, t), 4.50 (1H, q), 6.80 (4H, 2xd).
Ir ν_{max} (KCl) 2930, 2860, 1755, 1730, 1450, 1285, 1230, 1135, 1100, 1050, 1030, 825 cm^{-1}.
m/z 472 (M^+, 100%), 249 (24%), 109 (28%).

(R)-trans-4-(trans-4-Pentylcyclohexyl)cyclohexyl 2-(4-octoxyphenoxy)propanoate (**A5**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 1.20 g (36%)
^1H Nmr ($CDCl_3$) δ 0.88 (9H, m), 1.05 (9H, m), 1.30 (19H, m), 1.55 (3H, d), 1.75 (4H, m), 1.90 (2H, d), 2.00 (2H, d), 3.90 (2H, t), 4.60 (1H, q), 4.70 (1H, sextet), 6.80 (4H, 2xd).
Ir ν_{max} (KCl) 2930, 2850, 1745, 1515, 1240, 1200, 1145, 825 cm^{-1}.
m/z 528 (M^+, 100%), 416 (5%), 294 (10%), 249 (15%), 182 (20%), 137 (17%), 110 (31%).

(R)-trans-4-Pentylcyclohexyl 2-(4-octoxyphenoxy)propanoate (**A6**). Column chromatography [fine mesh silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 0.70 g (30%)
^1H Nmr ($CDCl_3$) δ 0.88 (6H, m), 1.25 (23H, m), 1.57 (3H, d), 1.75 (4H, sextet), 1.88 (1H, d), 1.95 (1H, d), 3.88 (2H, s), 4.60 (1H, q), 4.72 (1H, septet), 6.80 (4H, d).
Ir ν_{max} (KCl) 2930, 2860, 1755, 1735, 1510, 1280, 1230, 1190, 1135, 1050, 825 cm^{-1}.
m/z 446 (M^+, 100%), 406 (13%), 334 (5%), 294 (6%), 182 (21%), 137 (26%), 110 (40%).

(R)-4-Cyanobiphenyl-4'-yl 2-(4-octoxyphenoxy)propanoate (**A7**). Column chromatography [fine mesh silica gel; 5:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethyl acetate).

Yield = 1.62 g (56%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.30 (10H, d), 1.78 (5H, m), 3.93 (2H, t), 4.93 (1H, q), 6.85 (2H, d), 6.94 (2H, d), 7.15 (2H, d), 7.57 (2H, d), 7.64 (2H, d), 7.73 (2H, d).
Ir ν_{max} (KCl) 2930, 2860, 2240, 1765, 1515, 1235, 1170, 1130, 830, 765, 535 cm^{-1}.
m/z 471 (M^+, 58%), 249 (69%), 222 (92%), 110 (100%).

(R)-Naphth-2-yl 2-(4-octoxyphenoxy)propanoate (**A8**). Column chromatography [fine mesh silica gel; 1:1 dichloromethane-petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.12 g (5%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.30 (6H, m), 1.83 (3H, m), 3.93 (2H, t), 4.95 (1H, q), 6.86 (2H, d), 7.05 (2H, d), 7.16 (1H, d), 7.47 (3H, m), 7.81 (6H, m).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1765, 1515, 1295, 1230, 1210, 1175, 1100, 1050, 830, 815, 775, 490 cm^{-1}.
m/z 420 (M^+, 52%), 222 (100%), 171 (32%), 144 (43%), 136 (35%), 115 (40%), 110 (93%).

(R)-4-Propylphenyl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**A9**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 1.40 g (70%)
^{1}H Nmr ($CDCl_3$) δ 0.91 (7H, m), 1.27 (10H, m), 1.60 (4H, septet), 1.77 (3H, d), 1.87 (2H, d), 2.12 (2H, d), 2.45 (1H, sextet), 2.56 (2H, t), 4.92 (1H, q), 6.90 (2H, d), 6.97 (4H, 2xd), 7.15 (2H, d).
Ir ν_{max} (KCl) 2930, 2860, 1775, 1750, 1505, 1245, 1125, 530 cm^{-1}.
m/z 480 (M^+, 5%), 300 (100%), 163 (43%), 136 (43%), 110 (65%).

(R)-4-Heptylphenyl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**A10**). Column chromatography [silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 0.69 g (31%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (7H, m), 1.25 (17H, m), 1.56 (5H, q), 1.77 (3H, d), 1.87 (2H, d), 2.12 (2H, d), 2.45 (1H, sextet), 2.57 (2H, t), 4.92 (1H, q), 6.90 2H, d), 6.95 (4H, 2xd), 7.15 (2H, d).
Ir ν_{max} (KCl) 2970, 2930, 2860, 1765, 1745, 1510, 1250, 1195, 1180, 1110 cm^{-1}
m/z 536 (M^+, 5%), 356 (100%), 317 (17%), 218 (100%), 136 (63%), 107 (89%).

(R)-4'-Pentylbiphenyl-4-yl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**A11**). Column chromatography [fine mesh silica gel; 19:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethyl acetate).
Yield = 0.50 g (15%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (10H, m), 1.30 (11H, m), 1.60 (4H, m), 1.80 (3H, d), 1.87 (2H, d), 2.12 (2H, d), 2.46 (1H, sextet), 2.63 (2H, t), 4.95 (1H, q), 6.97 (2H, d), 7.02 (2H, d), 7.08 (2H, d), 7.24 (2H, d), 7.46 (2H, d), 7.55 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1750, 1505, 1265, 1200, 1165, 1130 cm^{-1}.
m/z 584 (M^+, 4%), 404 (20%), 266 (22%), 240 (100%), 183 (27%).

(R)-4-Pentylbicyclo[2.2.2]oct-1-yl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**A12**). Column chromatography [fine mesh silica gel; 19:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethyl acetate).
Yield = 1.02 g (46%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (8H, m), 1.25 (17H, m), 1.50 (11H, m), 1.90 (8H, q), 2.10 (2H, d), 2.45 (1H, sextet), 4.55 (1H, q), 6.85 (2H, d), 6.95 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1765, 1730, 1505, 1280, 1240, 1195, 1120, 1050, 985, 850 cm^{-1}.
m/z 540 (M^+), 360 (100%).

(R)-trans-4-(trans-4-Pentylcyclohexyl)cyclohexyl 2-[4-(trans-4-pentylcyclohexylcarbonyloxy)phenoxy]propanoate (**A13**). Column chromatography [fine mesh silica gel; 24:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethanol).
Yield = 2.15 g (71%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (8H, m), 1.05 (8H, m), 1.26 (21H, m), 1.59 (4H, m), 1.71 (6H, t), 1.86 (3H, d), 1.95 (1H, d), 2.10 (2H, d), 2.44 (1H, sextet), 4.65 (1H, q), 4.70 (1H, sextet), 6.85 (2H, d), 6.95 (2H, d).
Ir ν_{max} (KCl) 2930, 2850, 1745, 1510, 1250, 1200, 1165, 1130 cm^{-1}.
m/z 596 (M^+), 416 (100%).

(R)-4-Propylphenyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A14**). Column chromatography [fine mesh silica gel; 7% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethanol).
Yield = 0.18 g (14%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (8H, m), 1.09 (6H, m), 1.25 (7H, m), 1.60 (5H, septet), 1.76 (10H, m), 2.14 (2H, d), 2.43 (1H, sextet), 2.56 (2H, t), 4.93 (1H, q), 6.95 (6H, 3xd), 7.15 (2H, d).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1770, 1745, 1510, 1245, 1200, 1165, 1140, 1125, 1095, 850, 520 cm^{-1}.
m/z 562 (M^+), 300 (100%), 162 (47%), 136 (35%), 110 (62%).

(R)-4-Heptylphenyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A15**). Column chromatography [fine mesh silica gel; 7% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethanol).
Yield = 0.77 g (55%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (8H, m), 1.08 (8H, m), 1.26 (15H, m), 1.55 (7H, m), 1.77 (6H, m), 2.14 (2H, d), 2.43 (1H, sextet), 2.58 (2H, t), 4.93 (1H, q), 6.90 (2H, d), 6.95 (4H, 2xd), 7.15 (2H, d).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1765, 1745, 1510, 1245, 1210, 1200, 1165, 1145, 1125, 850, 520 cm^{-1}.
m/z 618 (M^+), 218 (80%), 136 (49%), 110 (73%).

(R)-4'-Pentylbiphenyl-4-yl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A16**). Column chromatography [fine mesh silica gel; 6% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).

Yield = 0.34 g (19%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (13H, m), 1.30 (18H, m), 1.80 (8H, m), 2.14 (3H, d), 2.44 (1H, sextet), 2.63 (2H, t), 4.95 (1H, q), 6.95 (4H, 2xd), 7.07 (2H, d), 7.24 (2H, d), 7.46 (2H, d), 7.55 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2850, 1765, 1745, 1510, 1250, 1200, 1175, 1165, 1140, 1125, 850, 525 cm^{-1}.
m/z 666 (M^+), 404 (12%), 266 (25%), 240 (100%), 183 (28%).

(R)-4-Pentylbicyclo[2.2.2]oct-1-yl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A17**). Column chromatography [fine mesh silica gel; 9:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethyl acetate).
Yield = 0.60 g (41%)
^{1}H Nmr ($CDCl_3$) δ 0.87 (9H, q), 1.10 (12H, m), 1.24 (10H, m), 1.51 (10H, m), 1.82 (13H, m), 2.13 (2H, d), 2.42 (1H, sextet), 4.55 (1H, q), 6.83 (2H, d), 6.93 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2850, 1745, 1510, 1245, 1215, 1200, 1135, 1125, 845, 750, 525 cm^{-1}.
m/z 622 (M^+), 360 (100%).

(R)-trans-4-Pentylcyclohexyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A18**). Column chromatography [fine mesh silica gel; 9:1 petrol (bp 40–60°C)-ethyl acetate]; recrystallized (ethyl acetate).
Yield = 1.15 g (56%)
^{1}H Nmr ($CDCl_3$) δ 0.87 (8H, q), 1.11 (13H, m), 1.25 (12H, m), 1.57 (8H, m), 1.78 (10H, m), 2.13 (2H, d), 2.42 (1H, sextet), 4.65 (1H, q), 4.92 (1H, sextet), 6.84 (2H, d), 6.95 (2H, d).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1745, 1505, 1450, 1250, 1200, 1165, 1140, 990, 845, 525 cm^{-1}.
m/z 596 (M^+), 334 (100%), 137 (30%).

(R)-Cyclohexyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A19**). Column chromatography [fine mesh silica gel; chloroform]; recrystallized (ethyl acetate).
Yield = 0.70 g (60%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (6H, t), 1.08 (9H, m), 1.26 (9H, m), 1.57 (8H, m), 1.71 (5H, d), 1.82 (4H, t), 2.13 (2H, d), 2.44 (1H, sextet), 4.67 (1H, q), 4.83 (1H, sextet), 6.85 (2H, d), 6.95 (2H, d).
Ir ν_{max} (KCl) 2930, 2860, 1755, 1510, 1245, 1210, 1195, 1160, 1140 cm^{-1}.
m/z 526 (M^+), 264 (100%).

(R)-4-Cyanobiphenyl-4'-yl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A20**). Column chromatography [fine mesh silica gel; 10% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (acetonitrile).
Yield = 0.27 g (16%)
^{1}H Nmr ($CDCl_3$) δ 0.88 (3H, m), 1.10 (2H, m), 1.25 (10H, m), 1.55 (6H, m), 1.80 (9H, m), 2.15 (2H, d), 2.44 (1H, sextet), 4.97 (1H, q), 6.96 (2H, d), 7.20 (2H, d), 7.24 (2H, d), 7.57 (2H, d), 7.64 (2H, d), 7.73 (2H, d).

Ir ν_{max} (KCl) 2960, 2920, 2850, 2240, 1765, 1745, 1650, 1505, 1495, 1245, 1200, 1155, 1140, 1125, 850, 835, 815 cm^{-1}.
m/z 621 (M^+, 3%), 359 (100%), 235 (11%), 222 (21%), 195 (35%), 137 (40%), 110 (89%).

(R)-Butyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A21**). Column chromatography [fine mesh silica gel; chloroform]; recrystallized (ethanol).
Yield = 0.67 g (59%)
^{1}H Nmr ($CDCl_3$) δ 0.89 (8H, m), 1.08 (8H, m), 1.30 (8H, quintet), 1.58 (8H, m), 1.71 (3H, d), 1.82 (3H, t), 2.13 (2H, d), 2.45 (1H, sextet), 4.15 (2H, t), 4.70 (1H, q), 6.85 (2H, d), 6.95 (2H, d).
Ir ν_{max} (KCl) 2970, 2930, 2860, 1745, 1515, 1250, 1200, 1145, 850, 525 cm^{-1}.
m/z 500 (M^+), 238 (100%), 137 (31%), 81 (47%), 55 (65%).

(R)-4-Ethoxyphenyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A22**). Column chromatography [fine mesh silica gel; dichloromethane]; recrystallized (ethyl acetate).
Yield = 0.40 g (31%).
^{1}H Nmr ($CDCl_3$) δ 0.88 (5H, t), 1.10 (8H, m), 1.25 (6H, m), 1.55 (5H, s), 1.77 (10H, m), 2.14 (2H, d), 2.43 (1H, sextet), 4.00 (2H, q), 4.55 (1H, q), 6.85 (2H, d), 6.92 (2H, d), 6.94 (2H, d), 7.00 (2H, d).
Ir ν_{max} (KCl) 2990, 2920, 2850, 1765, 1755, 1510, 1255, 1195, 1165, 1125, 1100, 820, 525 cm^{-1}.
m/z 564 (M^+), 302 (5%), 164 (11%), 138 (100%).

(R)-4-Hexoxyphenyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A23**). Column chromatography [fine mesh silica gel; dichloromethane]; recrystallized twice (ethyl acetate and then ethanol).
Yield = 0.60 g (45%)
^{1}H Nmr ($CDCl_3$) δ 0.89 (9H, m), 1.09 (11H, m), 1.29 (4H, m), 1.50 (6H, m), 1.76 (12H, m), 2.14 (2H, d), 2.43 (1H, sextet), 3.91 (2H, t), 4.91 (1H, q), 6.84 (2H, d), 6.91 (2H, d), 6.94 (2H, d), 7.00 (2H, d).
Ir ν_{max} (KCl) 2960, 2920, 2850, 1765, 1745, 1510, 1250, 1200, 1175, 1165, 1140, 1125, 850, 525 cm^{-1}.
m/z 620 (M^+, 2%), 194 (100%), 110 (69%).

(R)-Phenyl 2-{4-[trans-4-(trans-4-pentylcyclohexyl)cyclohexylcarbonyloxy]phenoxy}propanoate (**A24**). Column chromatography [fine mesh silica gel, 5% v/v ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.16 g (57%)
^{1}H Nmr ($CDCl_3$) δ 0.89 (5H, m), 1.09 (9H, m), 1.26 (5H, m), 1.52 (3H, q), 1.78 (9H, m), 2.14 (2H, d), 2.44 (1H, sextet), 4.96 (1H, q), 6.95 (5H, m), 7.23 (2H, d) and 7.37 (2H, d).
Ir ν_{max} (KCl) 3000, 2930, 2860, 1780, 1750, 1605, 1595, 1505, 1450, 1380, 1325, 1245, 1200, 1165, 1140, 1130, 1100, 1010, 990, 920, 850, 760, 690 and 530 cm^{-1}.
m/z 520 (M^+), 258 (90%), 137 (20%), 121 (20%) and 110 (100%).

(R)-4-Propylphenyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**A25**). Column chromatography [fine mesh silica gel; 5% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.60 g (31%)
^{1}H Nmr ($CDCl_3$) δ 0.91 (7H, m), 1.09 (2H, t), 1.27 (12H, m), 1.78 (3H, d), 1.91 (4H, d), 2.57 (3H, t), 4.95 (1H, q), 6.94 (2H, d), 7.01 (2H, d), 7.14 (2H, d), 7.16 (2H, d), 7.34 (2H, d), 8.10 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1780, 1735, 1610, 1500, 1270, 1245, 1180, 1165, 1110, 1060, 1020, 880, 505 cm^{-1}.
m/z 556 (M^+, 22%), 257 (100%).

(R)-Cyclohexyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**A26**). Column chromatography [fine mesh silica gel; 6% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.41 g (35%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (4H, m), 1.08 (2H, m), 1.30 (16H, m), 1.62 (6H, m), 1.91 (5H, d), 2.61 (1H, sextet), 4.71 (1H, q), 4.89 (1H, septet), 6.92 (2H, d), 7.09 (2H, d), 7.33 (2H, d), 8.10 (2H, d).
Ir ν_{max} (KCl) 2920, 2850, 1740, 1730, 1505, 1275, 1200, 1130, 1090, 1075, 1015, 845, 765, 700, 535 cm^{-1}.
m/z 520 (M^+, 4%), 257 (100%), 91 (31%), 55 (71%).

(R)-Propyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**A27**). Column chromatography [fine mesh silica gel; 5% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.57 g (43%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (6H, t), 1.09 (2H, t), 1.27 (9H, m), 1.63 (7H, m), 1.90 (4H, d), 2.56 (1H, sextet), 4.13 (2H, 3xd), 4.74 (1H, q), 6.91 (2H, d), 7.10 (2H, d), 7.33 (2H, d), 8.09 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2860, 1740, 1505, 1260, 1245, 1190, 1175, 1070, 880, 710 cm^{-1}.
m/z 480 (M^+, 15%), 257 (100%).

(R)-Butyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**A28**). Column chromatography [fine mesh silica gel; 5% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).
Yield = 0.58 g (51%)
^{1}H Nmr ($CDCL_3$) δ 0.91 (6H, m), 1.09 (2H, t), 1.30 (10H, m), 1.60 (8H, m), 1.91 (4H, d), 2.56 (1H, sextet), 4.17 (2H, t), 4.73 (1H, q), 6.91 (2H, d), 7.10 (2H, d), 7.33 (2H, d), 8.10 (2H, d).
Ir ν_{max} (KCl) 2965, 2930, 2860, 1735, 1615, 1505, 1275, 1195, 1180, 1135, 1075, 1015, 850, 815, 770, 705 cm^{-1}.
m/z 494 (M^+, 3%), 257 (100%).

(R)-Pentyl 2-{4-[4-(trans-4-pentylcyclohexyl)benzoyl]phenoxy}propanoate (**A29**). Column chromatography [fine mesh silica gel; 5% (v/v) ethyl acetate in petrol (bp 40–60°C)]; recrystallized (ethyl acetate).

Yield = 0.24 g (17%)
^{1}H Nmr ($CDCl_3$) δ 0.89 (6H, m), 1.09 (2H, q), 1.28 (12H, m), 1.51 (3H, m), 1.63 (5H, m), 1.91 (4H, d), 2.56 (1H, sextet), 4.16 (2H, sextet), 4.73 (1H, q), 6.91 (2H, d), 7.10 (2H, d), 7.33 (2H, d), 8.09 (2H, d).
Ir ν_{max} (KCl) 2960, 2930, 2850, 1755, 1740, 1505, 1275, 1245, 1180, 1175, 1120, 1075, 1020, 1015, 880, 705 cm^{-1}.
m/z 508 (M^+, 7%), 257 (100%).

(R,S)-2-[4-(Benzyloxy)phenoxy]propanoic Acid (**13**). 4-(Benzyloxy)phenol (**12**) (9.44 g, 47.14 mmol) was added to a stirred solution of 2-bromopropanoic acid (10.00 g, 65.37 mmol), sodium hydroxide (5.91 g, mmol), ethanol (130 ml) and water (13 ml) at 0°C. The mixture was then allowed to warm to room temperature before being heated to between 55° and 60°C for four hours. The reaction was then allowed to cool overnight, and a white precipitate formed. This was redissolved by the addition of water (50 ml), and the solution was then acidified to pH = 1.00 using concentrated hydrochloric acid. The product was then extracted with ethyl acetate (3 × 100 ml), the combined extracts were then dried ($MgSO_4$), filtered and evaporated to give a white solid. The product was recrystallized from ethyl acetate-petrol (bp 60–80°C), filtered and dried in a vacuum (P_2O_5, 0.2 mmHg, RT, 18 h).
Yield = 8.54 g (66%) mp = 129.8–131.7°C
^{1}H Nmr ($CDCl_3$/DMSO-d_6) δ 1.60 (3H, d), 4.60 (1H, q), 5.00 (2H, s), 6.85 (4H, m), 7.40 (5H, m), (carboxylic acid proton not detected).
Ir ν_{max} (KBr) 3440, 3060, 3020, 3005, 2960, 2920, 2880, 1740, 1510, 1455, 1385, 1290, 1140, 1100, 1025, 930, 830, 740, 735 and 700 cm^{-1}.
m/z 272 (M^+, 25%), 200 (1%), 181 (5%), 109 (23%) and 91 (100%).

Propyl (R,S)-2-[4-(benzyloxy)phenoxy]propanoate (**14a**). Oxalyl chloride (18.67 g, 147.1 mmol) in dry benzene (20 ml) were added dropwise at room temperature to a stirred suspension of **13** (4.00 g, 14.7 mmol) in dry benzene (50 ml) containing 10 drops of dry dimethylformamide. The reaction was left to stir for a further 24 h before the benzene and excess of oxalyl chloride were removed under reduced pressure to give a yellow oil. The oil was immediately redissolved in dry dichloromethane (50 ml) and a few crystals of 4-*N*,*N*-dimethylaminopyridine were added and cooled to 0°C with stirring. Triethylamine (1.80 g, 14.8 mmol), and propanol 1.02 g, 17 mmol) in dry dichloromethane (50 ml) were added dropwise at 0°C. After one hour at 0°C the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was washed successively with water (20 ml), 10% (v/v) hydrochloric acid (2 × 20 ml), water (20 ml) before being dried ($MgSO_4$), filtered and evaporated to give an orange oil. The oil was purified by flash chromatography [5% ethyl acetate-petrol (bp 40–60°C)] and a colourless liquid was obtained.
Yield = 2.57 g (55%).
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.60 (5H, m), 4.20 (2h, m), 4.67 (1H, q), 5.00 (2H, s), 6.82 (2H, d), 6.89 (2H, d) and 7.40 (5H, m).

Ir ν_{max} (KBr, thin film) 3070, 3040, 2970, 2935, 1755, 1735, 1510, 1455, 1380, 1230, 1135, 1100, 825, 740 and 700 cm^{-1}.
m/z 314 (M^+, 100%), 223 (30%), 91 (85%).

Butyl (R,S)-2-[4-(benzyloxy)phenoxy]propanoate (**14b**). This compound was prepared by a procedure similar to that described for compound **14a**.
Yield = 3.74 g (77%).
^{1}N Nmr ($CDCl_3$) δ 0.89 (3H, t), 1.31 (2H, m), 1.60 (5H, m), 4.15 (2H, m), 4.66 (1H, q), 5.00 (2H, s), 6.82 (2H, d), 6.88 (2H, d) and 7.37 (5H, m).
Ir ν_{max} (KBr, thin film) 3070, 3040, 2970, 2940, 1755, 1740, 1510, 1460, 1385, 1285, 1240, 1200, 1050, 1030, 950, 830, 780, 740 and 700 cm^{-1}.
m/z 328 (M^+, 38%), 237 (12%), 91 (100%).

Propyl (R,S)-2-(4-hydroxyphenoxy)propanoate (**15a**). Compound **14a** (2.45 g, 7.80 mmol), 5% palladium-on-charcoal (0.19 g) and ethyl acetate (100 ml) were degassed under vacuum and then stirred at room temperature under hydrogen for 24 h. The catalyst was removed by filtration through 'Hyflo supercel', the filtrate was dried ($MgSO_4$), filtered and evaporated to give an oil. The residue was purified by column chromatography [silica gel, dichloromethane] to give a pale brown oil which was dried under vacuum ($CaCl_2$, 0.4 mmHg, RT, 3 h).
Yield = 1.37 g (78%).
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.60 (5H, m), 4.10 (2H, m), 4.65 (1H, q), 6.75 (4H, 2xd), (phenolic proton was not detected).
Ir ν_{max} (KBr, thin film) 3430, 3040, 2980, 2950, 2890, 1735, 1515, 1450, 1220, 1140, 1110, 960, 835, 765 and 755 cm^{-1}.
m/z 224 (M^+, 100%), 137 (78%), 110 (60%).

Butyl (R,S)-2-(4-hydroxyphenoxy)propanoate (**15b**). This compound was prepared by a procedure similar to that described for compound **15a**.
Yield = 1.64 g (62%)
^{1}H Nmr ($CDCl_3$) δ 0.89 (3H, t), 1.31 (2H, m), 1.59 (5H, m), 4.15 (2H, m), 4.65 (1H, q), 5.40 (1H, s, broad) and 6.73 (4H, m).
Ir ν_{max} (KBr, thin film) 3420, 3040, 2970, 2940, 2880, 1735, 1515, 1455, 1210, 1140, 1100, 1050, 955, 830, and 765 cm^{-1}.
m/z 238 (M^+, 65%), 137 (83%) and 109 (100%).

Propyl (R,S)-2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**16a**). Oxalyl chloride (7.25 g, 57.32 mmol) in dry benzene (20 ml) was added dropwise at room temperature to a stirred suspension of 4-(*trans*-4-pentylcyclohexyl)benzoic acid (1.65 g, 6.02 mmol) in dry benzene (20 ml) containing 5 drops of dry *N,N*-dimethylformamide. This was left to stir for 18 h before the benzene and excess of oxalyl chloride were removed under reduced pressure to give an orange oil. The oil was immediately redissolved in dry dichloromethane (20 ml), cooled to 0°C with stirring and compound **15a** (1.34 g, 5.98 mmol), triethylamine (0.61 g, 6.03 mmol) and dry dichloromethane (20 ml) were then added dropwise at 0°C. The reaction was left to stir at 0°C for 1 hour before being allowed to warm

to room temperature over 18 h. The product was obtained as described for compound **14a** and the residual oil was purified by flash chromatography [fine mesh silica gel, 4% ethyl acetate-petrol (bp 40–60°C)]; recrystallized [ethyl acetate-petrol (bp 60–80°C)], dried in a vacuum (P_2O_5, 0.4 mmHg, 40°C, 6 h) to give the racemic form of compound **A27**.
Yield = 1.18 g (41%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (6H, m), 1.09 (2H, m), 1.27 (11H, m), 1.63 (5H, m), 1.91 (4H, d), 2.56 (1H, 3xt), 4.13 (2H, sextet), 4.74 (1H, q), 6.91 (2H, d), 7.10 (2H, d), 7.33 (2H, d) and 8.10 (2H, d).
Ir ν_{max} (KBr) 2970, 2930, 2860, 1750, 1735, 1510, 1275, 1190, 1135, 1080, 880, 850, 770 and 705 cm^{-1}.
m/z 480 (M^+, 10%), 257 (100%), 131 (5%).

Butyl (R,S)-2-{4-[4-(trans-4-pentylcyclohexyl)benzoyloxy]phenoxy}propanoate (**16b**). This compound was prepared using a procedure similar to that used for compound **16a** and gave the racemic form of compound **A28**.
Yield = 1.45 g (43%)
^{1}H Nmr ($CDCl_3$) δ 0.90 (6H, m), 1.10 (3H, m), 1.30 (9H, m), 1.65 (8H, m), 1.90 (4H, d), 2.56 (1H, m), 4.17 (2H, t), 4.74 (1H, q), 6.90 (2H, d), 7.10 (2H, d), 7.32 (2H, d) and 8.10 (2H, d).
Ir ν_{max} (KBr) 2960, 2930, 2960, 1735, 1615, 1505, 1280, 1240, 1195, 1185, 1135, 1075, 1040, 1025, 1015, 880, 855, 770 and 710 cm^{-1}.
m/z 494 (M^+, 2%), 257 (100%), 131 (17%).

Ethyl 2-(4-benzyloxyphenoxy)ethanoate (**17**). 4-Benzyloxyphenol (**12**) (20.38 g, 0.102 mol), ethyl bromoacetate (17.06 g, 0.102 mol), potassium carbonate (15.29 g, 0.111 mol) and butanone (220 ml) were heated under reflux with stirring for 24 h (TLC analysis showed the reaction to be complete). The inorganic precipitates were filtered off, and the filtrate was evaporated under reduced pressure to give a white solid. This was recrystallized (ethanol) and dried.
Yield = 26.96 g (92%) mp 76.7–77.7°C
^{1}H Nmr ($CDCl_3$) δ 1.30 (3H, t), 4.25 (2H, q), 4.57 (2H, s), 5.00 (2H, s), 6.90 (4H, q), 7.40 (5H, m).
Ir ν_{max} (KCl) 2040, 3020, 2990, 2940, 2920, 1760, 1510, 1435, 1385, 1290, 1240, 1200, 1165, 1085, 1015, 830, 780, 750 and 700 cm^{-1}.
m/z 286 (M^+, 12%), 195 (9%), 91 (100%).

2-(4-Benzyloxyphenoxy)ethanoic Acid (**18**). Compound **17** (25.56 g, 0.090 mol), potassium hydroxide (14.47 g, 0.260 mol), 2-methoxyethanol (373 ml) and water (28 ml) were heated at ~100°C for 1.75 h (TLC analysis of the reaction mixture showed the reaction to be complete). The reaction mixture was cooled to 0°C and conc hydrochloric acid was added dropwise with stirring to give pH = 1. The precipitated acid was filtered off and dried *in vacuo* ($CaCl_2$).
Yield = 19.9 g (90%) mp 142.4–146.3°C
^{1}H Nmr ($CDCl_3$/DMSO-d_6) δ 4.55 (2H, s), 5.02 (2H, s), 6.88 (4H, m), 7.36 (5H, m); carboxylic acid proton was not detected.

Ir ν_{max} (KCl) 3430, 3040, 2910, 2970, 1735, 1715, 1510, 1430, 1290, 1235, 1090, 825, 785, 750 and 705 cm^{-1}.

4-Propylphenyl 2-(4-benzyloxyphenoxy)ethanoate (**19**). Compound **18** (2.13 g, 8.26 mmol),4-propylphenol (1.12 g, 8.24 mmol), dicyclohexylcarbodiimide (2.08 g, 10.08 mmol), 4-*N*,*N*-dimethylaminopyridine (0.30 g, 2.46 mmol) and dichloromethane (100 ml) were reacted as described for compound **6**. The crude product was purified by column chromatography [fine mesh silica gel; 5% v/v ethyl acetate in petrol (bp 40–60°C). The solid obtained was recrystallized (ethyl acetate).
Yield = 1.09 g (35%)
Ir ν_{max} (KCl) 2960, 2930, 2880, 1780, 1510, 1390, 1290, 1235, 1180, 1020, 830, 755 and 700 cm^{-1}.

4-Propylphenyl 2-(4-hydroxyphenoxy)ethanoate (**20**). Compound **19** (1.07 g, 2.85 mmol), 5% palladium-on-charcoal (0.18 g) and ethyl acetate (50 ml) were used as described for compound **7b**.
Yield = 0.72 g (88%) mp 128.9–132.0°C
^{1}H Nmr ($CDCl_3$) δ 0.90 (3H, t), 1.63 (2H, sextet), 2.58 (2H, t), 4.80 (2H, s), 6.82 (4H, 2xd), 7.00 (2H, d), 7.18 (2H, d); the phenolic proton was not detected.
Ir ν_{max} (KBr) 3430, 3020, 2960, 2930, 2860, 1755, 1510, 1440, 1215, 1100, 1080, 860, 830, 810 and 785 cm^{-1}.
m/z 286 (M^+, 30%), 149 (100%), 132 (55%), 107 (40%).

4-Propylphenyl 2-[4-(trans-4-pentylcyclohexyl)benzoyloxyphenoxy]ethanoate (**VII**). Oxalyl chloride (1.46 g, 11.50 mmol) in dry benzene (10 ml) was added dropwise at room temperature to a stirred suspension of 4-(*trans*-4-pentylcyclohexyl)benzoic acid (0.29 g, 1.06 mmol) in dry benzene (10 ml) containing 3-drops of dry *N*,*N*-dimethylformamide. The reaction mixture was stirred at room temperature for a further 24 h, before the benzene and the excess of oxalyl chloride were removed under reduced pressure to give a yellow oil. This was redissolved in dry dichloromethane (10 ml) and triethylamine (0.12 g, 1.19 mmol) and cooled to 0°C; compound **20** (0.20 g, 1.05 mmol) in dry dichloromethane was then added dropwise with stirring. The reaction mixture was allowed to warm to room temperature overnight, (TLC analysis showed the reaction to have proceeded with several side reactions). The reaction mixture was washed successively with water (20 ml), 10% hydrochloric acid (2 × 20 ml), water (20 ml) and then dried ($MgSO_4$) and evaporated under reduced pressure to give a brown solid. This was purified by column chromatography [fine mesh silica gel; 1:1 dichloromethane-petrol (bp 40–60°C)], and the solid so obtained was recrystallized (ethyl acetate) and dried (P_2O_5, 0.2 mmHg, 50°C, 5 h).
Yield = 0.08 g (13%) K 137.2°C N 173.4°C I
^{1}H Nmr ($CDCl_3$) δ 0.92 (6H, m), 1.09 (2H, m), 1.29 (9H, m), 1.62 (4H, m), 1.92 (4H, d), 2.58 (3H, t), 4.85 (2H, s), 7.03 (4H, m), 7.16 (4H, m), 7.34 (2H, d) and 8.11 (2H, d).
Ir ν_{max} (KBr) 2960, 2930, 2860, 1780, 1735, 1610, 1500, 1445, 1270, 1250, 1175, 1165, 1105, 1070, 1020, 1010, 980 and 905 cm^{-1}.
m/z 542 (M^+), 257 (100%), 107 (10%), 91 (12%).

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