The Synthesis and Transition Temperatures of Some Difluoro-substituted Cyclohexanes

Michael Hird,*[a] Kenneth J. Toyne,[a] Andrew J. Slaney,[a] John W. Goodby[a] and George W. Gray[b]
[a] *School of Chemistry, The University, Hull, UK HU6 7RX*
[b] *Merck Ltd., Broom Road, Poole, Dorset, UK BH12 4NN*

A range of *trans*-1,4-disubstituted cyclohexane materials has been prepared that incorporates a difluoromethylene unit as part of the cyclohexane ring. These compounds illustrate the great difference in mesogenic behaviour between compounds with fluoro-substituents in an alicyclic environment and those with fluoro-substituents in aromatic rings. An improved fluorination method, which involves the use of hydrogen fluoride–pyridine, has been developed and provides high yields of fluorinated materials. Highly efficient palladium-catalysed cross-coupling reactions involving arylboronic acids have been used to provide the final liquid crystal materials. The important issue of the *cis* and *trans* isomers of these compounds is discussed and the structures of the fluorinated materials are discussed with reference to their interesting ^1H and ^{13}C NMR spectra.

In recent years the effect of aromatic lateral fluoro-substitution in liquid-crystal materials has been extensively studied.[1–5] It is now well established that fluoro-substituents can improve certain characteristics of a material or may completely change its nature. One notable area involving the successful use of fluoro-substitution is in terphenyl materials.[1,3,4] Unsubstituted terphenyl systems have high melting points and exhibit crystal smectic and smectic mesophases;[3] the introduction of one lateral fluoro-substituent drastically reduces melting points and confers tilted mesophase character (*e.g.*, G, J, S_I and S_C) upon the materials.[3] A second lateral fluoro-substituent *ortho* to the first has the effect of eliminating all mesophases which underlie the S_C phase, thus creating materials with low melting points and wide S_C ranges that are useful host materials for ferroelectric mixtures.[1,6,7] Other arrangements of difluoro-substituents so far reported tend to eliminate all smectic phases to give compounds with wide nematic ranges.[4]

The work reported here represents initial investigations into the effect of fluoro-substituents in cyclohexane systems in order to evaluate the potential of those materials for use in both nematic and S_C* devices. The effect of fluoro-substitution on sp^3 carbons cannot be extrapolated from the extensive data available for its effect in aromatic systems. The purpose of the work was to evaluate the effect of fluoro-substitution in cyclohexane systems and to make comparisons with fluoro-substituted aromatic systems. The number and variety of fluoro-substitutions it is possible to make in cyclohexanes is much greater than in benzene systems and the synthetic problems are immense. This work initiates a systematic study of fluorinated cyclohexanes.

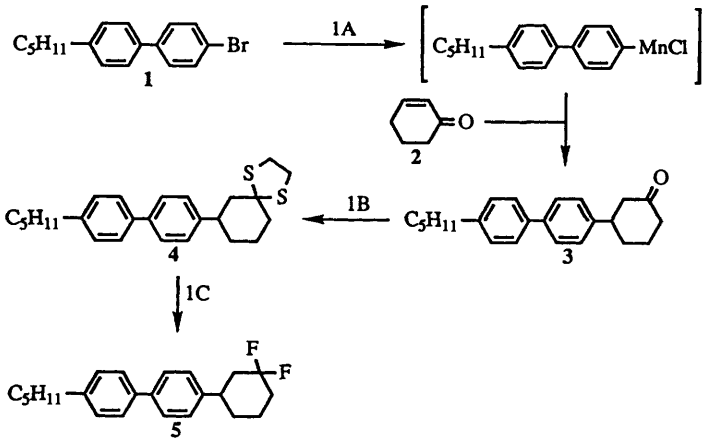
When considering the use of liquid crystals for displays, material that incorporate a *trans*-1,4-disubstituted cyclohexane ring in their structures have been found to be superior, in many respects, to their phenyl-ring analogues.[8–12] The cyclohexane ring can undergo many different conformational deformations which make it possible for compounds to absorb thermal energy, and so allow higher clearing points. Compounds which contain cyclohexane rings and phenyl rings tend to have low melting points and reduced smectic character because of the incompatibility in the packing of the two rings, and this provides materials with a combination of broad nematic ranges and low viscosities.[9]

Materials that contain *trans*-1,4-disubstituted cyclohexane rings are dominated by orthogonal smectic phases and are not very conducive to the formation of the S_C mesophase. Even when used in conjunction with moieties which are normally highly conducive to S_C-phase formation, it is usually the B or S_A phases which dominate,[5–7] although we have recently prepared some dimethylene linked cyclohexyl-2,3-difluorobiphenyl materials of low melting points and moderate S_C phase stabilities (up to 70 °C).[5] It was therefore decided to place a small polar substituent (*i.e.*, fluoro) on a cyclohexane ring in cyclohexane-substituted biphenyls, to determine whether or not tilted smectic phases (*e.g.*, S_C) would be generated analogously to the effect of lateral fluoro-substitution in aromatic systems. Initially, in order to avoid the greater complexity of specific axial and equatorial fluoro-substituents, we have prepared difluoro-substituted materials.

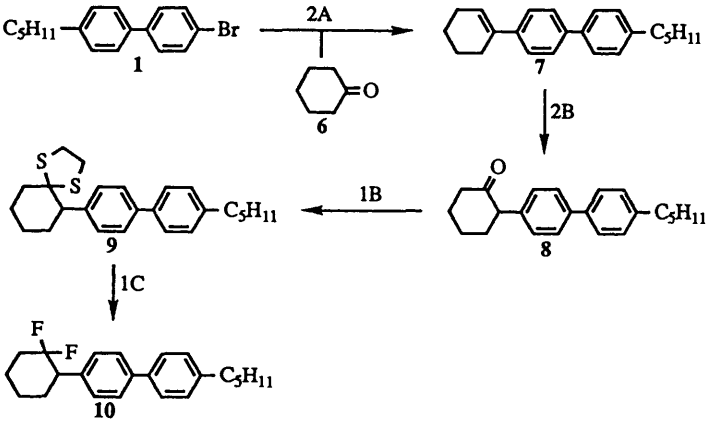
Synthesis.—Most fluoro-substituted aromatic compounds can be prepared from commercially available fluoro-substituted starting materials. However, the synthesis of fluoro-substituted alicyclic systems is more difficult, and since suitable fluoro-substituted starting materials are not commercially available, it is necessary to use fluorination reactions. There are many fluorination methods available,[13–16] however, most of these methods involve the use of expensive and/or toxic reagents and experimental procedures can be complex and the reported yields are often low. Fortunately, the difluoromethylene unit can be readily obtained by treating a ketone with a fluorinating agent such as DAST (diethylaminosulfur trifluoride).[15] However, an even more attractive fluorination route was to use hydrogen fluoride–pyridine which is relatively inexpensive. The substrates used in the reaction with hydrogen fluoride–pyridine are dithiolanes which are prepared from ketones in near-quantitative yields.[16] Ketone **3** (Scheme 1) was prepared by the 1,4-conjugate addition of an organomanganese derivative (prepared *in situ* from compound **1**) to cyclohex-1-enone (**2**);[17] all other ketones required were prepared from appropriate cyclohexene compounds.

The intermediate cyclohexenes (Schemes 2, 3 and 4) were prepared by treatment of the appropriate Grignard reagent with the cyclohexanone [compound **6** (Scheme 2) and compound **12** (Schemes 3 and 4)] followed by dehydration (conc. sulfuric acid in THF) of the resulting tertiary, benzylic alcohols.

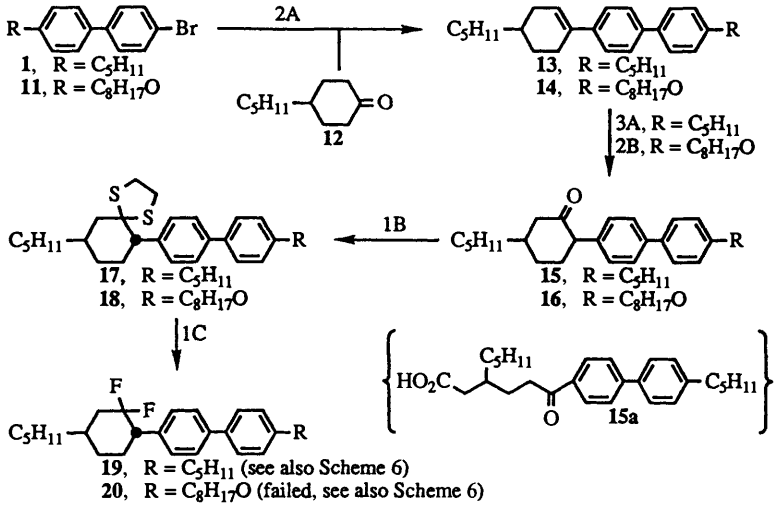
The initial method chosen for the conversion of the cyclohexenes into the desired cyclohexanones involved hydroboration followed by oxidation with aqueous chromic acid.[18]



Scheme 1 1A: i, Mg, THF; ii, $MnCl_2$, $CuCl_2$, THF; 1B: ethane-1,2-dithiol, BF_3·2HOAc; 1C: HF–pyridine, 1,3-dibromo-5,5-dimethylhydantoin, CH_2Cl_2



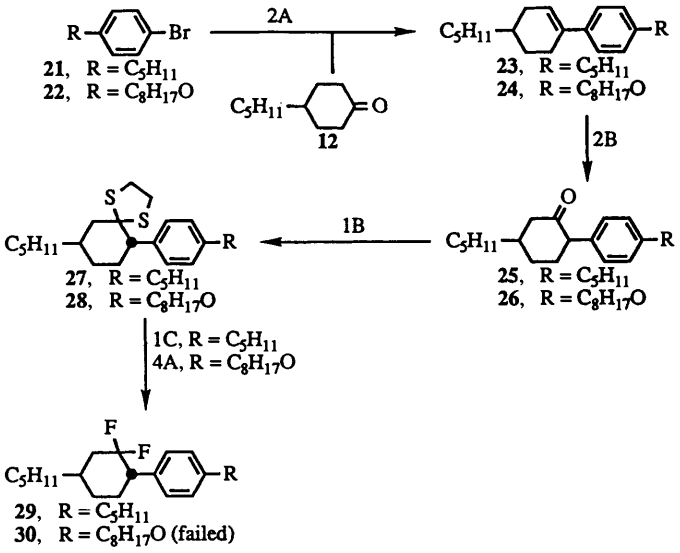
Scheme 2 2A: i, Mg, THF; ii, a cyclohexanone, THF; iii, c.H_2SO_4, THF; 2B: H_2O_2, HCO_2H



Scheme 3 3A: i, $LiBH_4$, BF_3·Et_2O; ii, $Na_2Cr_2O_7$·$2H_2O$, H_2SO_4, H_2O

Hydroboration of the cyclohexene **13** (Scheme 3) was carried out using lithium borohydride and boron trifluoride etherate (which provides borane *in situ*) and when followed by the *in situ* oxidation with aqueous chromic acid it gave, in most attempts, the ring-opened product (compound **15a**). On a single occasion, however, we obtained a good yield of the desired cyclohexanone **15**, containing *ca.* 10% of compound **15a**. Clearly, this approach was unsatisfactory and subsequently another method was used, involving the treatment of the cyclohexene with hydrogen peroxide in formic acid.[19] This gave reasonable results with variable yields [compound **8** (Scheme 2), compound **16** (Scheme 3) and compounds **25** and **26** (Scheme 4)]. Except for ketones **3** and **8** (Schemes 1 and 2), all of the cyclohexanones with both 2- and 5-substituents were mixtures of *cis* and *trans* isomers (GLC analysis revealed a ratio of between 1:2 and 1:3, which fortunately, by ^1H NMR spectroscopy was found to be in favour of the *trans* isomer).

The cyclohexanones were converted into their dithiolane derivatives by treatment with ethane-1,2-dithiol and boron trifluoride acetic acid[16] in near-quantitative yields. It was at this stage that the pure *trans* isomers were isolated by column

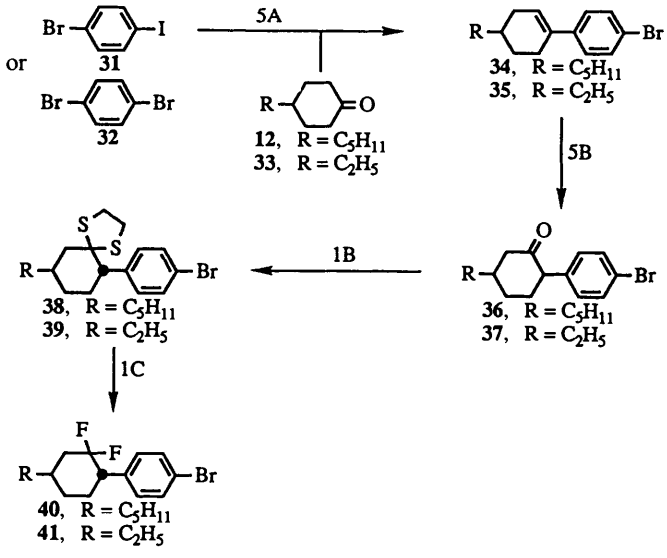


Scheme 4 4A: HF–pyridine, *N*-iodosuccinimide, CH_2Cl_2

chromatography (it would have been possible to isolate the *trans* isomers at the ketone stage, but the separation proved much easier for the dithiolane products) and therefore the yields for compounds **17** and **18** (Scheme 3) and compounds **27** and **28** (Scheme 4) appear relatively low.

The dithiolane products were then treated with hydrogen fluoride–pyridine in the presence of 1,3-dibromo-5,5-dimethylhydantoin in dry dichloromethane at −78 °C[16] to give the desired difluoro-substituted cyclohexane compounds [compound **5** (Scheme 1), compound **10** (Scheme 2), compound **19** (Scheme 3) and compound **29** (Scheme 4)] in very consistent yields of *ca.* 35% (see later for the optimization of this procedure). However, this procedure was not as simple as it appears because 1,3-dibromo-5,5-dimethylhydantoin is a brominating agent and if aromatic rings are present with 'activating' substitutuents (as is often the case for liquid-crystal compounds) then aromatic bromination can occur. For the alkyl-substituted derivatives, mono-bromination of the aromatic ring only occurred (30% by GC–MS analysis) in compound **10** (Scheme 2). This material was purified by treatment with *n*-butyllithium in THF at −78 °C followed by quenching with wet THF. In the case of the two alkoxy-substituted compounds, the attempted preparation of compound **20** (Scheme 3) led to the formation of a monobromo-substituted compound and a dibromo-substituted compound. The use of *N*-iodosuccinimide is reported[16] to circumvent this ring halogenation problem, but on attempting this approach in the preparation of compound **30** (Scheme 4), GC–MS analysis revealed the presence of a small amount of iodinated product and the presence of both *cis* and *trans* ketones (compound **26**). The mechanism requires the presence of a halogen donor because the fluorination reaction involves Br^+ which opens up the dithiolane and provides a carbocation which is attacked by F^-; this sequence occurs at both points of dithiolane attachment to give the difluoromethylene unit.

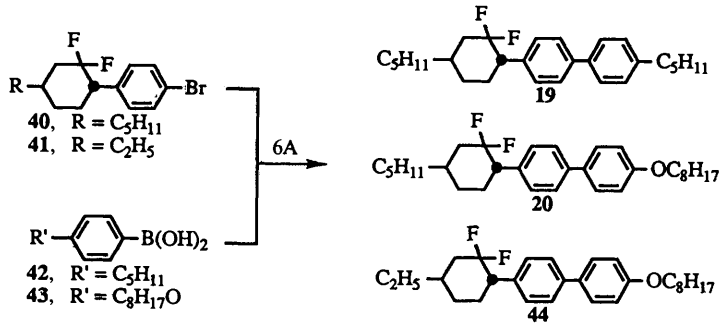
In order to produce a completely general method for the synthesis of liquid crystal difluorocyclohexane compounds, intermediate cyclohexene materials were prepared with a bromo-substituent in the aromatic ring (compounds **34** and **35**, Scheme 5). However, the conversion into the cyclohexanones (compounds **36** and **37**) using hydrogen peroxide and formic acid produced only a trace of product materials. Therefore, the method of hydroboration followed by oxidation was again attempted, but this time borane tetrahydrofuran was used for hydroboration and pyridinium chlorochromate in dry di-



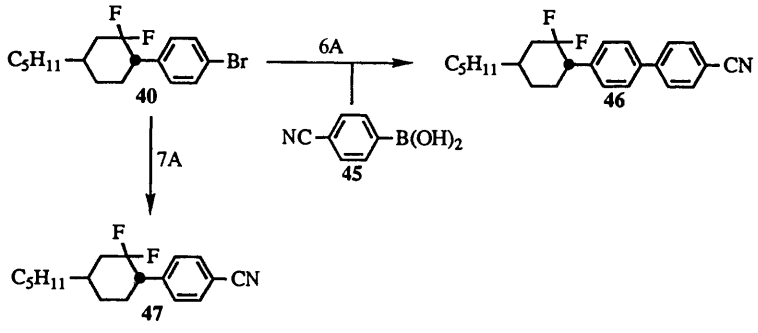
Scheme 5 5A: i, Bu^{n}Li, THF; ii, a cyclohexanone, THF; iii, PTSA, toluene; 5B: i, BH_3-THF, THF; ii, pyridinium chlorochromate, CH_2Cl_2

chloromethane under anhydrous conditions was used for the oxidation.[20,21] This procedure proved to be very efficient in giving the desired cyclohexanones in good yields as a mixture of *cis* and *trans* isomers (1:3 by GLC analysis and also by ^1H NMR analysis, see later). The conversion[16] into dithiolane materials (compounds **38** and **39**) gave the usual high yields and allowed the efficient isolation of the *trans* isomer.

Although the bromo-substituent is deactivating and ring bromination during the fluorination reaction cannot occur, the opportunity was taken to optimize the fluorination procedure. The literature procedure[16] involves stirring the reaction mixture at −78 °C for 10 min followed by filtration through a short alumina column. When this exact method was followed, yields of *ca.* 35% were obtained for compounds **40** and **41**. However, in the course of this optimization, compound **41** was obtained in 48% yield. Best results were obtained when the reaction mixture was allowed slowly to warm over *ca.* 2 h to *ca.* −10 °C, then quickly cooled to −78 °C again and then poured into a stirred, cooled (−78 °C) slurry of basic alumina in dry dichloromethane. The use of the fully optimized method led to compound **40** being consistently obtained in greater than 70% yield (double the yields from the original method).



Scheme 6 6A: $Pd(PPh_3)_4$, DME, 2 mol dm^{-3} Na_2CO_3



Scheme 7 7A: CuCN, DMF

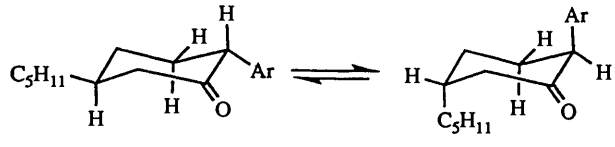
In addition to the deactivating effect of the bromo-substituent circumventing ring bromination during the fluorination step, the use of the bromo-substituted intermediate has other advantages. The intermediate can be prepared in large quantities and converted into a large range of final compounds for liquid-crystal applications. Schemes 6 and 7 show the initial uses of these intermediates (compounds **40** and **41**) in palladium-catalysed cross-coupling procedures which have been so successfully developed for the synthesis of liquid-crystal compounds;[22] compound **19** was also prepared less efficiently by the alternative route (Scheme 3). The terminal cyano-substituted compound (**46**) was prepared by a coupling reaction with 4-cyanophenylboronic acid[23] (compound **45**), whereas compound **47** was prepared by a cyanation reaction.

Analysis of the Cyclohexane Materials by NMR Spectroscopy.—There were two main issues of concern when preparing the difluoro-substituted cyclohexane materials. Firstly, there was the requirement to obtain pure *trans* isomers at some stage of the synthetic route (as mentioned previously the *cis–trans* separations were carried out at the dithiolane stage). Secondly, the possibility of elimination of hydrogen fluoride to give fluoro-substituted cyclohexenes in conjugation with the aromatic core needed to be ruled out.

The *cis–trans* issue arose in all of the synthetic schemes except Schemes 1 and 2 and *cis–trans* mixtures first appeared at the substituted cyclohexanone stage. The relative amounts of the *cis* and *trans* isomers in the cyclohexanones (compounds **15**, **16**, **25**, **26**, **36** and **37**) were first determined by GLC analysis and in all cases a ratio of *ca.* 1 : 2 or *ca.* 1 : 3 was indicated and ^1H NMR spectroscopy of the cyclohexanone mixtures revealed the nature of each component.

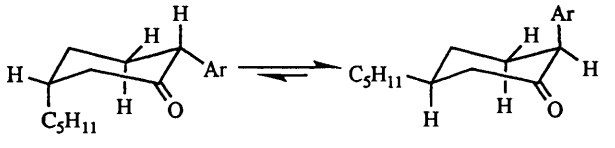
The multiplicity and chemical shift value of the signal for the benzylic methine proton of the cyclohexanone ring enabled the assignment of *cis* and *trans* isomers and the relative integration values provided, in each case, the same relative amounts as GLC analysis.

Molecular modelling (Quanta/Charm software on a Silicon Graphics Indigo Workstation) was used to determine the dihedral angles formed between benzylic methine proton and



Conformer A Conformer B

Fig. 1 The *trans* cyclohexanones where the diaxial conformer (**B**) is more favourable than the diequatorial conformer (**A**)

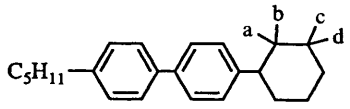


Conformer C Conformer D

Fig. 2 The *cis* cyclohexanones where conformer **D** (axial aryl group) is preferred to conformer **C** (axial alkyl chain)

the adjacent methylene protons for the significant conformers of each cyclohexanone isomer. This molecular modelling system was also used to determine the most stable conformation of each cyclohexanone isomer and each cyclohexane analogue by overall minimizations of energies and by considering rotations about the bonds connecting the pentyl and aryl substituents to the alicyclic moiety. For the *trans* cyclohexane material, the diequatorial conformer is, as expected, greatly preferred over the diaxial conformer. However, the change from cyclohexane to cyclohexanone has a very large effect on the axial–equatorial equilibrium for a substituent. Compared with the situation in cyclohexanes, substituents at the 2-position in cyclohexanones have a greater tendency to give axial conformations[24] (because of the interaction of the equatorial group with the adjacent carbonyl bond). Substituents at the 3- or 5-positions have a greater proportion of axial conformer because one of the 1,3-diaxial interactions is lost with the introduction of the carbonyl group.[25] With the *trans* cyclohexanones (compounds **15**, **16**, **25**, **26**, **36** and **37**) there are therefore two factors which favour an increase in the diaxial arrangement (see Fig. 1, conformer **B**). In the case of the *trans* isomer (Fig. 1), the energy difference

Table 1 Transition temperatures (°C) for two difluorocyclohexylbiphenyls without a terminal substituent in the cyclohexane (**5** and **10**)



Compound					*T*/°C		
No.	a	b	c	d	C	N	I
5	H	H	F	F	• 57.0	[• 5]	•
10	F	F	H	H	• 76.5	[• 28]	•

obtained from the molecular modelling is fairly small (0.34 kcal mol^{-1}) but there is a preference for the diaxial conformer (**B**). Conformer **A** has both substituent groups (alkyl and aryl) equatorial and hence both methine protons are axial. The dihedral angles formed between the benzylic proton and the adjacent methylene protons are different (62.0° and 178.5°) and although the corresponding dihedral angles for the slightly more preferred conformer (**B**) are similar (44.5° and 69.7°) the overall effect on the ^1H NMR signal of the benzylic methine proton would be to produce different coupling constants and hence a double doublet would be seen. Indeed the larger methine signal occurs at around δ 3.0 and is seen as a clear, well defined double doublet with coupling constants of 12.5 Hz and 5.5 Hz; this indicates that the larger component is the *trans* isomer. For the *cis* compounds (Fig. 2) there are also two significantly stable conformers (**C** and **D**). Again, expectations based on cyclohexane systems were that the bulkier aryl group would take up the equatorial position in preference to the alkyl group. However, these sytems are cyclohexanones with the carbonyl group next to the aryl moiety. The results from the molecular modelling show that conformer **D** with the aryl group in the axial position is the preferred conformer to a much greater extent (2.40 kcal mol^{-1}) than was the case for the *trans* isomer conformations. In a separate molecular-modelling exercise based on an analogous *cis* cyclohexane system it was seen, as expected, that the conformer with the equatorial aryl group is the most stable. Conformer **D** is more stable because there is considerable steric interaction between the bulky aryl group and the adjacent carbonyl group when the aryl group is equatorial; such severe steric interference is avoided when the aryl group is axial. Additionally, conformer **D** has an equatorial pentyl chain which precludes steric interference with the axial proton on the next but one carbon atom. Conformer **D** has the aryl group axial and the alkyl group equatorial and therefore the benzylic methine proton should give approximately equal angles with the adjacent methylene protons. Approximately equal coupling constants would be produced and an apparent triplet, as opposed to a double doublet, would result. From the molecular modelling, it was found that the dihedral angle with the adjacent equatorial proton was 67.7° and that the dihedral angle with the adjacent axial proton was 46.8° for conformer **D**. Although clearly different, the magnitude is not sufficient to confer a clear double doublet in the ^1H NMR spectrum. Conformer **C** has the aryl group equatorial and the dihedral angles of the axial benzylic methine proton with the adjacent methylene protons were found to be 60.4° and 176.6°. This suggests that the coupling constants would be different and therefore that the signal in the ^1H NMR would appear predominantly as a double doublet but because conformer **C** is much less preferred the ^1H NMR signal relating to the benzylic proton of the *cis* isomers of compounds **15**, **16**, **25**, **26**, **36** and **37** would be expected to tend towards an apparent triplet. The recorded ^1H NMR spectra of the *cis* and *trans* mixtures of compounds **15**, **16**, **25**, **26**, **36** and **37** all supported the findings of the molecular-modelling work. The larger *trans* component was revealed by a double doublet signal due to the benzylic methine proton at *ca.* δ 3.0 with coupling constants of 12.5 Hz and 5.5 Hz. The ^1H NMR signal (at *ca.* δ 3.3) relating to the *cis* isomer (minor component) was an apparent triplet because of approximately equal coupling constants (5.5 Hz). Another explanation for the ^1H NMR signals of the benzylic protons is that in the *trans* isomers the two adjacent protons are chemically and magnetically different, whereas, by coincidence they could be chemically and magnetically equivalent in the *cis* isomers. The NMR data for ketones **15**, **16**, **25**, **26**, **36** and **37** have not been included in the experimental section because all of these compounds were present as *cis*/*trans* mixtures and the only useful information to be conveyed is the difference in the benzylic methine proton for the *cis* and the *trans* isomers (see the discussion above). The aromatic protons were clearly assignable and those nearest to the cyclohexanone unit showed slightly different chemical shift values between the *cis* and the *trans* isomers but this difference was not as clear as for the benzylic methine proton. All of the other signals in the ^1H NMR spectrum were, as expected, ill-defined multiplets that provided no information regarding the identification of the *cis* and *trans* isomers.

The *trans* isomers were isolated at the dithiolane stage (compounds **17**, **18**, **27**, **28**, **38** and **39**) of the synthetic routes by careful column chromatography. The ^1H NMR spectra for the benzylic protons all revealed a very clear double doublet at *ca.* δ 2.80–2.90. However, a multiplet signal from a proton of the ethylenedisulfanyl group occurred next to the signal for the benzylic proton and so both have been documented as a two-proton multiplet in the experimental data.

The ^1H NMR spectra of the benzylic protons for the *trans* difluoro-substituted cyclohexanes (compounds **19**, **20**, **29**, **40**, **41**, **44**, **46** and **47**) each consist of four distinct multiplets (a double doublet of multiplets) at *ca.* δ 2.80–2.90. These are caused by a large coupling constant with one of the fluoro-substituents in combination with a smaller coupling constant from the other fluoro-substituent and significantly smaller coupling constants from the two neighbouring protons.

Carbon 13 NMR spectra were also obtained for all of the difluoro-substituted cyclohexanes (compounds **19**, **20**, **29**, **40**, **46** and **47**) except the ethyl-substituted homologues (compounds **41** and **44**) and interesting results were obtained. The spectra obtained were proton-decoupled but, of course, couplings with the fluoro-substituents were still present. The most remarkable feature was the precessional frequency of the CF_2 carbon. These signals were found in the aromatic region and close to typical nitrile carbon signals (*ca.* δ 121). As can be seen from the data provided in the experimental, this signal appears as a triplet because of the similar magnitudes of the spin–spin coupling from both of the fluoro-substituents (in some cases, however, the signal is slightly resolved into a double doublet signal). The coupling constants involved are both very large, as would be expected from fluoro-substituents attached to the carbon in question giving one-bond couplings.

Another interesting feature of the ^{13}C NMR is that the signals for the two carbons next to the CF_2 carbon are also subject to spin–spin couplings. However, the coupling constants involved ($J_{C\text{-}C\text{-}F}$) are significantly smaller. Most of these signals appear as triplets but many on close examination are revealed as double doublet signals (see the data provided in the Experimental section). Occasionally, three-bond ($J_{C\text{-}C\text{-}C\text{-}F}$) couplings are revealed but these simply appear as slight distortions or doublings of the single-line signals.

Transition Temperatures.—The effect on the transition temperatures of compounds by lateral fluoro-substitution in aromatic rings is well documented[1-7,26,27] and often confers remarkable changes in mesophase types and transition

Table 2 Transition temperatures (°C) for a range of reference compounds for comparison with the novel compounds

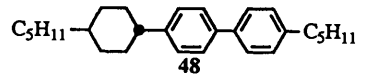
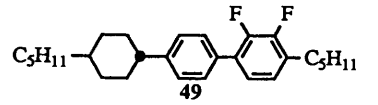
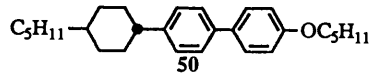
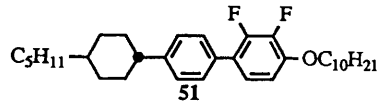
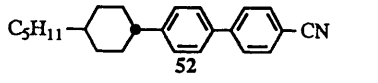
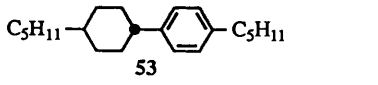
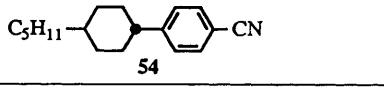
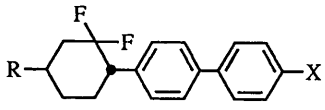
Compound	*T*/°C
 **48**	C 13.0 B 164.0 N 166.0 I[28]
 **49**	C 33.0 S_A 96.5 N 123.0 I[29]
 **50**	C 42.0 B 183.0 I[28]
 **51**	C 52.0 S_C 58.5 S_A 126.5 N 137.0 I[29]
 **52**	C 96.0 N 222.0 I[30]
 **53**	C −1.0 (S −8.0 N −5.0) I[31]
 **54**	C 31.0 N 55.0 I[8]

Table 3 Transition temperatures (°C) for some 4-alkyl-1-(4′-X-biphenyl-4-yl)-2,2-difluorocyclohexanes (**19**, **20**, **44** and **46**)



Compound			*T*/°C							
No.	R	X	C		E		B	N		I
19	C_5H_{11}	C_5H_{11}	•	68.5	—		• 70.5 •	122.0		•
20	C_5H_{11}	$C_8H_{17}O$	•	95.0	—		• 99.0 •	147.0		•
44	C_2H_5	$C_8H_{17}O$	•	80.0	(• 70.0	•	79.0) •	124.0		•
46	C_5H_{11}	CN	•	103.0	—		—	• 173.0		•

temperatures. Generally, melting points are depressed, often quite substantially. Smectic phases (especially high-order smectic phases) are usually much more depressed than the nematic phase, although smectic phases are upheld by the presence of a fluoro-substituent on the outer edge of the core. Fluoro-substitution has, therefore, been successfully used to produce low-melting, wide-range nematic materials with a very low smectic tendency.[4,26]

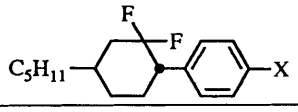
However, in some other systems (notably terphenyls) the slight steric and strong polar effect of lateral fluoro-substituents can provide low-melting materials with wide S_C ranges. So lateral fluoro-substitution has also been used to generate host materials for ferroelectric (S_C*) mixtures.[1,3,6,7]

The transition temperatures for the difluoro-substituted cyclohexanes without terminal chain substituents (Table 1) show that these compounds are not mesogenic. This was, of course not unexpected, but they were prepared initially because there is not a *cis–trans* issue in these cases and they provided simpler model systems on which to test the synthetic methods. Melting points are moderate (57.0 °C for compound **5** and 76.5 °C for compound **10**). Virtual T_{N-I} values were obtained by extrapolation of mixtures (up to 20 wt%) in E7 and were found to be quite low. A higher melting point and a higher T_{N-I} value have been obtained where the fluoro-substituents are closer to the aromatic core.

The parent, unfluorinated compound **48**[28] (Table 2) has a remarkably low melting point and a high T_{N-I} value. However, B-phase stability is also high and this gives a very wide B range and only a narrow nematic range. The effect of lateral fluoro-substitution in the aromatic core is illustrated by comparison with compound **49**[29] and the effects shown here are typical of certain other systems. The melting point has actually been increased by virtue of the increased polarity but overall smectic tendency has been reduced by 67.5 °C and the B phase of compound **48** has been replaced by the less ordered S_A mesophase. Nematic phase stability has been less affected by lateral fluoro-substitution (a reduction of 43.0 °C is revealed).

The effect of lateral fluoro-substitution in the cyclohexane ring (compound **19**, Table 3) was difficult to predict, however, increased polarity is probably responsible for the increase in melting point (by 55.5 °C). The same mesophase types are exhibited in the difluorocyclohexane system (compound **19**) and

Table 4 Transition temperatures (°C) for two 4-alkyl-1-(4-X-phenyl)-2,2-difluorocyclohexanes (**29** and **47**)



Compound		T/°C		
No.	X	C	N	I
29	C_5H_{11}	• 40.0	[• −45]	•
47	CN	• 75.0	[• −10]	•

the parent system (compound **48**) and the B-phase stability has been reduced quite substantially (by 93.5 °C), but nevertheless it is still quite high. As expected, the nematic-phase stability has been less affected (reduced by 44.0 °C) and this has led to a much increased nematic range. Thus compound **19** is similar in mesogenic behaviour to its parent system, whereas compound **49** is different but has, by coincidence, a similar T_{N-I} value.

The parent system (compound **50**)[28] for comparison with the alkoxy-substituted difluorocyclohexane system (compound **20**) does not provide a true comparison, but it is reasonably similar and the trends are still clear. It was thought to be possible that the two fluoro-substituents at one end of the molecule in the cyclohexane ring would combine with the polarity from the alkoxy-substituent at the other end of the molecule and tend to produce a tilted S_C mesophase. However, as was the case in the previous comparison, mesophase types have not been altered (except that the related parent system does not show a nematic phase in this case). The melting point has been increased by 53.0 °C and the B-phase stability has been reduced by 84.0 °C which is similar to the changes found in the previous comparison. This reduction in B-phase stability has allowed the nematic phase to be seen in compound **20**.

In complete contrast, fluoro-substitution in the aromatic core has totally changed the mesophase types exhibited by compound **51**.[27] This compound is still low melting and, as for compound **49**, the S_A phase is dominant. However, for this decyloxy-substituted homologue, a short range S_C phase is exhibited. Shorter alkoxy-substituted materials do not show an S_C phase (*e.g.*, the ethoxy-substituted homologue exhibits K 68.0 S_A 87.0 N 172.0 I).[6]

The ethyl-substituted homologue (compound **44**) was prepared in the expectation of providing a lower melting point and a lower B-phase stability than for the longer pentyl-substituted homologue (compound **20**). These effects might be expected to reveal any tendency towards S_C character if it were at all possible. A lower melting point (by 15 °C) and a lower B-phase stability (by 20 °C) have been obtained but this has simply allowed an E phase to be exhibited (both E and B phases are monotropic). Therefore, it is fairly apparent that these difluoro-substituted materials have little tendency towards the S_C phase.

As expected, the difluoro-substituted cyclohexane material with a terminal cyano-substituent (compound **46**, Table 3) is nematogenic, however, in comparison with its non-fluorinated parent system[30] (compound **52**) the melting point has increased by 7.0 °C and the T_{N-I} value has been reduced by 49.0 °C. This represents no real difference to the typical effect of fluoro-substitution in an aromatic core except that melting points are usually reduced; however, fluoro-substitution in a polar parent compound (*e.g.*, terminal cyano) is known to lead to higher melting points.

The compounds shown in Table 4 are simple two-ring systems that were thought to be potentially important low-melting materials of very low $\Delta\varepsilon$ in the case of the terminal alkyl-substituted compound (**29**) or very high positive $\Delta\varepsilon$ in the case of compound **47**. The results show that the two fluoro-substituents in the cyclohexane ring (compounds **29** and **47**) have increased melting points substantially (by 41.0 °C and 44.0 °C for the pentyl- and cyano-substituted materials, respectively) compared with compounds **53** and **54**, respectively. The virtual T_{N-I} values for both compounds were measured by extrapolation from mixtures in E7 (up to 23% for compound **29** and up to 43% for compound **47**). When compared with their parent systems (compounds **53**[31] and **54**,[8] respectively) the T_{N-I} values have been reduced by 40 °C for compound **29** and by 65 °C for compound **47**. The reduction in T_{N-I} for compound **29** is typical of the reductions already seen for the compounds in Table 3. However, the reduction in T_{N-I} for compound **47** is significantly more; this could be due to a reduction of antiparallel associations in the difluoro-substituted material.

Attention is drawn to the mesogenic behaviour of several of the intermediate materials (compounds **7**, **13**, **14**, **18** and **24**). The transition temperatures for these compounds are shown with the experimental details and will not be fully discussed. All except compound **18** are aromatic-substituted cyclohexenes with the double bond conjugated with the aromatic unit and as such their mesogenic behaviour (orthogonal smectic phases) was expected. An interesting range of related cyclohexene compounds which we have been preparing will be reported later. Compound **18** (Scheme 3) is a *trans*-1,4-disubstituted cyclohexane compound with a 2,2-ethylenedisulfanyl substituent. This bulky protecting group moiety would perhaps be expected to depress any mesogenic behaviour, however, the polarity from the two sulfur atoms would certainly go towards stabilizing mesophases. These two factors combined with the low melting point (caused by the disruption in packing due to the bulky protecting group) lead to the monotropic S_A and nematic phases.

Conclusions

The synthesis of alicyclic fluoro-substituted mesogens requires a totally different approach to that previously used in the synthesis of compounds with fluoro-substituents in the aromatic rings. Many interesting points have emerged from the synthetic route used.

(*a*) An improved method of fluorination has been demonstrated which, in this case, has doubled the isolated yields.

(*b*) The *cis–trans* separation issue was efficiently achieved at the dithiolane stage by column chromatography which produced pure *trans* isomers.

(*c*) Palladium-catalysed cross-coupling procedures continue to prove essential in the efficient synthesis of novel liquid-crystal materials.

(*d*) Molecular modelling (Quanta/Charm software on a Silicon Graphics Indigo workstation) has been used to show the relative stabilities of the conformers of the *cis* and *trans* isomers of the cyclohexanones (compounds **15**, **16**, **25**, **26**, **36** and **37**). The appropriate dihedral angles between the benzylic methine proton and the two adjacent methylene protons were obtained for the significant conformers of the *cis* and *trans* isomers and the ^1H NMR spectra were interpreted.

(*e*) The successful use of NMR spectroscopy in the determination of the structure and stereochemistry of the materials has been discussed.

There is obviously no close similarity in the mesogenic behaviour of compounds with fluoro-substitution in the aromatic system and those with fluoro-substitution in the cyclohexane moiety. It has been shown that difluoro-substitution in the cyclohexane ring increases melting points, reduces B-phase stability more than nematic phase stability and does not alter mesophase type. These effects are very different from

the effect of fluoro-substitution in the aromatic rings of mesogens where melting points are greatly depressed and tilted smectic (*e.g.*, S_C) phases are generated. Quite apart from transition temperatures, these materials were prepared to investigate the effect of such alicyclic fluoro-substitution on physical properties generally and these results will be published later by our collaborators at DRA (Malvern). The synthetic routes which have been developed in the course of this work are very useful in the future synthesis of fluoro-substituted alicyclic systems.

Experimental

Confirmation of the structures of intermediates and products was obtained by ^1H and ^{13}C NMR spectroscopy (JEOL JNM-GX270 spectrometer), infrared spectroscopy (Perkin-Elmer 457 grating spectrophotometer) and mass spectrometry (Finnigan-MAT 1020 GC/MS spectrometer). High resolution mass spectrometry (Kratos MS 25 spectrometer) data were obtained for each final compound prepared (**5**, **10**, **19**, **20**, **29**, **44**, **46** and **47**). The progress of reactions was frequently monitored using a Perkin-Elmer 8320 capillary gas chromatograph fitted with a 12 m QC2/BP1-1.0 SGE column. Transition temperatures were measured using a Mettler FP5 hot-stage and control unit in conjunction with an Olympus BH2 polarising microscope and these were confirmed using differential scanning calorimetry (Perkin-Elmer DSC-7 and IBM data station). The purities of intermediates **17**, **18**, **27**, **28** and **38**–**41** and each of the final compounds in Tables 1, 3 and 4 were checked by GLC analysis (see above) and by HPLC analysis (Microsorb C18 80-215-C5 RP column) and were found to be > 99% pure.

Compounds **1**, **11** and **12** were kindly supplied by our collaborators at Merck (UK) Ltd., Poole, Dorset. The preparations of intermediates **21**,[1] **22**,[1] **42**,[3] **43**[3] and **45**[23] have been previously reported. Tetrakis(triphenylphosphine)palladium(0) was prepared according to the literature procedure.[32] Compounds **2**, **6** and **31**–**33** were purchased from Aldrich.

3-(4′-*Pentylbiphenyl*-4-*yl*)*cyclohexanone* (**3**).—A solution of the Grignard reagent prepared in the usual way from magnesium (1.00 g, 0.041 mol) and compound **1** (10.72 g, 0.035 mol) in dry THF (90 cm^3) under dry nitrogen, was added dropwise to a stirred, cooled (−5 °C) suspension of dry manganese(II) chloride (4.65 g, 0.037 mol) in dry THF (60 cm^3). The mixture was stirred at room temperature for 3 h, cooled (0 °C) and copper(I) chloride (0.17 g, 1.72 mmol) was added. After 5 min at 0 °C a solution of compound **2** (3.07 g, 0.032 mol) in dry THF (30 cm^3) was added dropwise at 0 °C. The mixture was stirred at room temperature for 2 h (GLC analysis revealed a complete reaction), cooled to 0 °C and 10% hydrochloric acid was added. The product was extracted into ether (×2), the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel; dichloromethane) to give a colourless solid which was recrystallized from ethanol to yield a colourless powder.

Yield 5.60 g (55%); m.p. 91 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.32–1.40 (4 H, m), 1.60–1.70 (2 H, m), 1.80–1.90 (1 H, m), 2.10–2.20 (2 H, m), 2.38–2.55 (2 H, m), 2.60–2.70 (5 H, m), 3.00–3.12 (1 H, m), 7.24 (2 H, d), 7.28 (2 H, d), 7.49 (2 H, d) and 7.55 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1705, 1500, 820 and 795; *m/z* 320 (M^+) and 263.

1,1-*Ethylenedisulfanyl*-3-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**4**).—Boron trifluoride–acetic acid (1.18 g, 6.25 mmol) was added to a stirred suspension of compound **3** (2.00 g, 6.25 mmol) and ethane-1,2-dithiol (1.18 g, 0.0126 mol) under dry nitrogen. The resulting paste was stirred at room temperature for 30 min and ether and water were added. The aqueous layer was washed with ether and the combined ethereal extracts were washed with saturated sodium hydrogen carbonate, 10% sodium hydroxide and brine and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C)–dichloromethane, 5:1] to give a colourless solid.

Yield 2.42 g (98%); m.p. 67–68 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.30–1.40 (6 H, m), 1.60–1.70 (2 H, m), 1.94 (2 H, m), 2.00–2.14 (2 H, m), 2.22 (1 H, m), 2.35 (1 H, m), 2.63 (2 H, t), 2.87 (1 H, m), 3.32 (4 H, s), 7.22 (2 H, d), 7.27 (2 H, d), 7.48 (2 H, d) and 7.51 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1500, 1280 and 805; *m/z* 396 (M^+), 368, 353, 335 and 303.

1,1-*Difluoro*-3-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**5**).—Hydrogen fluoride–pyridine (70%) (3.00 cm^3) was added dropwise to a stirred, cooled (−78 °C) solution of 1,3-dibromo-5,5-dimethylhydantoin (1.78 g, 6.22 mmol) in dry dichloromethane (30 cm^3) under dry nitrogen. A solution of compound **4** (2.35 g, 5.93 mmol) in dry dichloromethane (20 cm^3) was added dropwise at −78 °C to −60 °C. The solution was stirred at −70 °C for 30 min and filtered through a short column of basic alumina (care!). The solvent was removed *in vacuo* and the residue was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of dichloromethane] to give a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 0.75 g (37%); transitions (°C) C 57.0 [N 5.0] I; $\delta_H(CDCl_3)$ 0.90 (3 H, t), 1.35 (5 H, m), 1.55–2.00 (7 H, m), 2.20 (1 H, m), 2.35 (1 H, m), 2.65 (2 H, t), 2.90 (1 H, t), 7.23 (2 H, d), 7.27 (2 H, d), 7.49 (2 H, d) and 7.53 (2 H, d); $\delta_C(CDCl_3)$ 14.14 (s), 22.53 (s), 22.65 (s), 31.28 (s), 31.66 (s), 32.59–32.63 (d), 33.31–34.01 (dd), 35.66 (s), 40.50–40.64 (d), 40.84–41.52 (dd), 120.26–126.93 (dd, CF_2), 126.93 (s), 127.16 (s), 127.25 (s), 129.91 (s), 138.21 (s), 139.65 (s), 142.13 (s) and 143.26 (s); $\nu_{max}(KBr)/cm^{-1}$ 2940, 2860, 1500, 1365, 1085, 985, 810 and 795; *m/z* 342 (M^+), 313, 299 and 285 (Found: M^+, 342.4735. $C_{23}H_{28}F_2$ requires *M*, 342.4738).

1-(4′-*Pentylbiphenyl*-4-*yl*)*cyclohexene* (**7**).—A solution of compound **6** (2.30 g, 0.023 mol) in dry THF (10 cm^3) was added to a solution of the Grignard reagent, prepared in the usual way from compound **1** (8.18 g, 0.027 mol) and magnesium (0.75 g, 0.031 mol) in dry THF (150 cm^3) under dry nitrogen. The mixture was heated under reflux for 2 h, cooled and aqueous ammonium chloride was added. The product was extracted into ether (×2) and the combined ethereal extracts were washed with brine and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of ethyl acetate] and the resulting alcohol was stirred with dry THF (50 cm^3) and 98% sulfuric acid (10 cm^3) for 15 min (GLC analysis revealed a complete reaction). Water was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the slight introduction of dichloromethane] to give a colourless solid. A small sample was recrystallized from ethanol.

Yield 5.98 g (86%); transitions (°C) C 77.5 B 113.0 I; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.32–1.38 (4 H, m), 1.60–1.72 (4 H, m), 1.75–1.85 (2 H, m), 2.18–2.28 (2 H, m), 2.42–2.48 (2 H, m), 2.65 (2 H, t), 6.18 (1 H, m), 7.23 (2 H, d), 7.43 (2 H, d), 7.51 (2 H, d) and 7.54 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1515, 1480, 1260, 1090, 850 and 810; *m/z* 304 (M^+) and 247.

2-(4′-*Pentylbiphenyl*-4-*yl*)*cyclohexanone* (**8**).—Hydrogen peroxide (3 cm^3) was added dropwise to a stirred mixture of compound **7** (5.45 g, 0.018 mol) in formic acid (25 cm^3) at room temperature. The mixture was warmed at 40 °C for 2 h and then heated under reflux for 3 h (GLC analysis revealed a complete reaction). The mixture was cooled and poured into water and the product was extracted into ether (×2). The combined ethereal extracts were washed with 10% sodium hydroxide, water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of dichloromethane] to give an off-white solid.

Yield 3.72 g (64%); m.p. 97.5 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.30–1.40 (4 H, m), 1.65 (2 H, quintet), 1.85 (2 H, m), 2.00–2.20 (3 H, m), 2.30 (1 H, m), 2.45–2.55 (2 H, m), 2.65 (2 H, t), 3.65 (1 H, q), 7.19 (2 H, d), 7.23 (2 H, d), 7.49 (2 H, d) and 7.55 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1700, 1495, 1120 and 800; *m/z* 320 (M^+), 292, 276, 263 and 235.

1,1-*Ethylenedisulfanyl*-2-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**9**).—Quantities: compound **8** (3.35 g, 0.010 mol), ethane-1,2-dithiol (1.90 g, 0.020 mol), boron trifluoride–acetic acid (1.90 g, 0.010 mol). The experimental procedure was as described for the preparation of compound **4** to give colourless solid.

Yield 3.83 g (97%); m.p. 81.0 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.25–1.40 (6 H, m), 1.65 (2 H, quintet), 1.80–2.05 (5 H, m), 2.15 (1 H, m), 2.35 (1 H, d), 2.65 (2 H, t), 2.70 (1 H, m), 2.80–3.05 (3 H, m), 7.23 (2 H, d) and 7.48–7.55 (6 H, m); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1505, 1450, 1010 and 815; *m/z* 396 (M^+), 368, 353, 335 and 303.

1,1-*Difluoro*-2-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**10**).—Quantities: compound **9** (3.65 g, 9.22 mmol), 1,3-dibromo-5,5-dimethylhydantoin (2.90 g, 0.010 mol), hydrogen fluoride–pyridine (6 cm^3, 70%).

The experimental procedure was as described for the preparation of compound **5** and gave a colourless solid (GC–MS analysis revealed 30% of a ring brominated product). The material was dissolved in dry THF (50 cm^3) and cooled to −78 °C, *n*-butyllithium (5.00 cm^3, 2.5 mol dm^{-3} in hexanes, 0.013 mol) was added dropwise and the mixture was stirred at −78 °C for 30 min then quenched with wet THF (GLC analysis revealed a complete reaction). Water was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of dichloromethane] to give a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 1.09 g (35%); transitions (°C) C 76.5 [N 28.0] I; $\delta_H(CDCl_3)$ 0.90 (3 H, t), 1.30–1.40 (4 H, m), 1.45 (1 H, m), 1.60–1.75 (3 H, m), 1.85–2.05 (5 H, m), 2.25 (1 H, m), 2.65 (2 H, t), 2.85–3.05 (1 H, m), 7.23 (2 H, d), 7.37 (2 H, d), 7.49 (2 H, d) and 7.54 (2 H, d); $\delta_C(CDCl_3)$ 14.15 (s), 22.67 (s), 23.09–23.23 (d), 25.21 (s), 30.22–30.33 (d), 31.28 (s), 31.67 (s), 34.75–35.47 (dd), 35.68 (s), 49.79–50.42 (t), 119.51–126.79 (t, CF_2), 126.79 (s), 127.02 (s), 128.85 (s), 129.71 (s), 136.67 (s), 138.38 (s), 140.24 (s) and 142.08 (s); $\nu_{max}(KBr)/cm^{-1}$ 2940, 2860, 1500, 1455, 1170, 1100, 965 and 800; *m/z* 342 (M^+), 313, 299 and 285 (Found: M^+, 342.4734. $C_{23}H_{28}F_2$ requires *M*, 342.4738).

4-*Pentyl*-1-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexene* (**13**).—Quantities: compound **1** (9.10 g, 0.030 mol), magnesium (0.83 g, 0.034 mol), compound **12** (4.50 g, 0.027 mol). The experimental procedure was as described for the preparation of compound **7** and yielded a colourless solid.

Yield 7.71 g (76%); transitions (°C) C 101.5 B 180.0 S_A 194.0 I; $\delta(CDCl_3)$ 0.90 (6 H, t), 1.35 (13 H, m), 1.60 (3 H, m), 1.90 (2 H, m), 2.30–2.50 (3 H, m), 2.65 (2 H, t), 6.16 (1 H, m), 7.24 (2 H, d), 7.44 (2 H, d), 7.51 (2 H, d) and 7.53 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1500 and 805; *m/z* 374 (M^+), 345, 317 and 303.

1-(4′-*Octyloxybiphenyl*-4-*yl*)-4-*pentylcyclohexene* (**14**). Quantities: compound **11** (7.48 g, 0.021 mol), magnesium (0.60 g, 0.025 mol), compound **12** (3.10 g, 0.018 mol). The experimental procedure was as described for the preparation of compound **7** and yielded a colourless solid.

Yield 3.80 g (49%); transitions (°C) C 133.0 B 182.0 S_A 206.0 I; $\delta(CDCl_3)$ 0.90 (6 H, m), 1.25–1.60 (20 H, m), 1.70–2.00 (4 H, m), 2.30–2.40 (1 H, m), 2.50 (2 H, m), 4.00 (2 H, t), 6.15 (1 H, m), 6.95 (2 H, d), 7.43 (2 H, d), 7.49 (2 H, d) and 7.51 (2 H, d); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1495, 1245 and 800; *m/z* 432 (M^+), 417, 403 and 389.

5-*Pentyl*-2-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexanone* (**15**).—A solution of boron trifluoride–diethyl ether (0.35 g, 2.46 mmol) in dry THF (10 cm^3) was added dropwise to a stirred solution of compound **13** (5.80 g, 0.016 mol) and lithium borohydride (0.16 g, 7.27 mmol) in dry THF (40 cm^3) at between 30 and 40 °C under dry nitrogen. The mixture was stirred at 35 °C for 3.5 h, cooled and water was added. A solution of chromic acid, prepared from sodium dichromate(VI) (4.40 g, 0.015 mol), conc. sulfuric acid (3.5 cm^3) and water (14.5 cm^3), was added dropwise at room temperature. The mixture was heated under reflux for 16 h (GLC analysis revealed a complete reaction with two product peaks corresponding to the *cis* and *trans* isomers in a 1:2 ratio). The mixture was cooled and water was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of ethyl acetate] to give a pale-yellow solid [contains 10% ring-opened material (compound **15a**)].

Yield 6.00 g (96%); ^1H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:2); $\nu_{max}(film)/cm^{-1}$ 2960, 2940, 2860, 1710, 1610, 1500, 1460, 1010 and 815; *m/z* 390 (M^+), 362, 346, 334, 305 and 193.

2-(4′-*Octyloxybiphenyl*-4-*yl*)-5-*pentylcyclohexanone* (**16**).—Quantities: compound **14** (3.50 g, 8.10 mmol), formic acid (40 cm^3), hydrogen peroxide (2 cm^3). The experimental procedure was as described for the preparation of compound **8** and yielded an off-white solid.

Yield 1.58 g (44%); ^1H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:3); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1700, 1605, 1500, 1250 and 820; *m/z* 448 (M^+), 436 and 419.

trans-2,2-*Ethylenedisulfanyl*-4-*pentyl*-1-(4′-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**17**).—Quantities: compound **15** (6.00 g, 0.015 mol), ethane-1,2-dithiol (2.91 g, 0.031 mol), boron trifluoride acetic acid (2.91 g, 0.015 mol). The experimental procedure was as described for the preparation of compound **4**. The crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of dichloromethane] to give the isolated *trans* isomer as a colourless solid followed by a colourless oil (1.47 g, 21%, the *cis* isomer).

Yield 3.64 g (52%); m.p. 60.0 °C; $\delta(CDCl_3)$ 0.90 (6 H, t), 1.00–1.10 (1 H, m), 1.20–1.40 (12 H, m), 1.65 (3 H, m), 1.80–2.10 (5 H, m), 2.35 (1 H, d), 2.60–2.68 (3 H, m), 2.82–2.92 (2 H, m), 2.98–3.07 (1 H, m), 7.24 (2 H, d), and 7.50–7.55 (6 H, m); $\nu_{max}(KBr)/cm^{-1}$ 2960, 2940, 2860, 1495, 1005 and 805; *m/z* 466 (M^+), 395, 277, 237 and 201.

trans-2,2-*Ethylenedisulfanyl*-1-(4'-*octyloxybiphenyl*-4-*yl*)*pentylcyclohexane* (**18**).—Quantities: compound **16** (1.40 g, 3.13 mmol), ethane-1,2-dithiol (0.60 g, 6.38 mmol), boron trifluoride–acetic acid (0.60 g, 3.19 mmol). The experimental procedure was as described for the preparation of compound **17** and gave a colourless solid (pure *trans* isomer).

Yield 0.77 g (47%); transitions (°C) C 76.5 (S_A 43.5 N 53.5) I; δ($CDCl_3$) 0.90 (6 H, m), 0.95–1.10 (1 H, m), 1.20–1.40 (16 H, m), 1.45 (2 H, m), 1.60 (1 H, m), 1.70–2.00 (7 H, m), 2.33 (1 H, d), 2.65 (1 H, q), 2.80–2.90 (2 H, m), 2.95–3.05 (1 H, m), 3.98 (2 H, t), 6.94 (2 H, d), 7.44 (2 H, d), 7.50 (2 H, d) and 7.53 (2 H, d); ν_{max}(KBr)/cm^{-1} 2940, 2860, 1610, 1500, 1255, 830 and 810; *m/z* 524 (M^+), 453 and 335.

trans-2,2-*Difluoro*-4-*pentyl*-1-(4'-*pentylbiphenyl*-4-*yl*)*cyclohexane* (**19**).—*Method A*. Quantities: compound **17** (3.40 g, 7.30 mmol), 1,3-dibromo-5,5-dimethylhydantoin (2.30 g, 8.04 mmol), hydrogen fluoride–pyridine (4 cm^3, 70%). The experimental procedure was as described for the preparation of compound **5** and gave a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 0.98 g (33%); transitions (°C) C 66.0 B 66.0 N 118.0 I; δ_H($CDCl_3$) 0.90 (6 H, t), 1.08–1.18 (1 H, m), 1.22–1.50 (12 H, m), 1.40–1.50 (1 H, m), 1.65 (2 H, quintet), 1.72–1.82 (1 H, m), 1.90–2.10 (3 H, m), 2.20–2.36 (1 H, m), 2.64 (2 H, t), 2.84–3.02 (1 H, m), 7.24 (2 H, d), 7.36 (2 H, d), 7.49 (2 H, d) and 7.54 (2 H, d); δ_C($CDCl_3$) 14.15 (2 C, s), 22.65 (s), 22.73 (s), 26.50 (s), 29.5–29.68 (d), 31.26 (s), 31.67 (s), 31.96 (s), 32.03 (s), 34.93–35.07 (d), 35.68 (s), 36.36 (s), 41.07–41.74 (t), 49.61–50.29 (t), 119.71–126.79 (t, CF_2), 126.79 (s), 127.02 (s), 128.85 (s), 129.71 (s), 136.54 (s), 138.38 (s), 140.24 (s) and 142.08 (s); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1505, 1390, 1170, 960 and 815; *m/z* 412 (M^+), 392, 355 and 335 (Found: M^+, 412.6084. $C_{28}H_{38}F_2$ requires *M*, 412.6088).

Method B. Tetrakis(triphenylphosphine)palladium(0) (0.03 g, 0.026 mmol) and compound **42** (0.20 g, 1.04 mmol) were added sequentially to a stirred solution of compound **40** (0.28 g, 0.81 mmol) in 1,2-dimethoxyethane (20 cm) and 2 mol dm^{-3} sodium carbonate (20 cm^3) under dry nitrogen. The mixture was heated under reflux (100°C) for 16 h (GLC/TLC analysis revealed a complete reaction) and cooled. Water was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with brine and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of dichloromethane] to give a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 0.20 g (60%); transitions (°C) C 68.5 B 70.5 N 122.0 I; spectroscopy data is as shown previously for compound **19** (Method A).

The attempted preparation of trans-2,2-*Difluoro*-1-(4'-*octyloxybiphenyl*-4-*yl*)-4-*pentylcyclohexane* (**20**).—*Method A*. Quantities: compound **18** (0.70 g, 1.34 mmol), 1,3-dibromo-5,5-dimethylhydantoin (0.42 g, 1.47 mmol), hydrogen fluoride–pyridine (1 cm^3, 70%). The experimental procedure was as described for the preparation of compound **5** and gave a mixture of the desired product and a substantial amount of mono- and di-brominated materials (GC–MS analysis).

Method B. Quantities: compound **40** (1.20 g, 3.48 mmol), compound **43** (1.05 g, 4.20 mmol). The experimental procedure was as described for the preparation of compound **19** (Method B) except that the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C)–dichloromethane 5:1] to yield colourless crystals.

Yield 1.27 g (78%); transitions (°C) C 95.0 B 99.0 N 147.0 I; δ_H($CDCl_3$) 0.90 (6 H, 2 × t), 1.05–1.20 (1 H, m), 1.22–1.40 (16 H, m), 1.40–1.55 (3 H, m), 1.75–1.85 (3 H, m), 1.90–2.10 (3 H, m), 2.20–2.35 (1 H, m), 2.80–3.00 (1 H, m), 3.98 (2 H, t), 6.95 (2 H, d), 7.35 (2 H, d) and 7.52 (4 H, 2 × d); δ_C($CDCl_3$) 14.15 (s), 14.19 (s), 22.73 (s), 26.16 (s), 26.50 (s), 29.34 (2 C, s), 29.39 (2 C, s), 29.46 (2 C, s), 29.67–29.66 (d), 31.91 (s), 32.03 (s), 34.91–35.05 (d), 36.35 (s), 41.04–41.72 (dd), 49.61–50.25 (t), 114.78 (s), 119.69–126.89 (t, CF_2), 126.50 (s), 128.13 (s), 129.71 (s), 133.34 (s), 136.34 (s), 139.94 (s) and 158.72 (s); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1605, 1500, 1250, 1160 and 820; *m/z* 470 (M^+), 358 (Found: M^+, 470.6892. $C_{31}H_{44}F_2O$ requires *M*, 470.6892).

4-*Pentyl*-1-(4-*pentylphenyl*)*cyclohexene* (**23**).—Quantities: compound **21** (5.72 g, 0.025 mol), magnesium (0.70 g, 0.029 mol), compound **12** (3.50 g, 0.021 mol). The experimental procedure was as described for the preparation of compound **7** and yielded a colourless oil.

Yield 4.10 g (66%); δ($CDCl_3$) 0.85–0.95 (6 H, m), 1.20–1.40 (12 H, m), 1.55–1.65 (4 H, m), 1.75–1.95 (2 H, m), 2.25–2.35 (1 H, m), 2.40–2.50 (2 H, m), 2.57 (2 H, t), 6.07 (1 H, s), 7.12 (2 H, d) and 7.32 (2 H, d); ν_{max}(film)/cm^{-1} 2960, 2940, 2860, 1470, 810 and 770; *m/z* 298 (M^+), 283, 269, 241 and 227.

1-(4-*Octyloxyphenyl*)-4-*pentylcyclohexene* (**24**).—Quantities: compound **22** (7.54 g, 0.026 mol), magnesium (0.73 g, 0.030 mol), compound **12** (3.78 g, 0.023 mol). The experimental procedure was as described for the preparation of compound **7** and yielded a colourless solid.

Yield 6.67 g (81%); transitions (°C) C 50.0 B 70.0 S_A 82.0 I; δ($CDCl_3$) 0.90 (6 H, m), 1.20–1.60 (20 H, m), 1.70–1.90 (4 H, m), 2.25–2.45 (3 H, m), 3.95 (2 H, t), 6.00 (1 H, m), 6.83 (2 H, d) and 7.31 (2 H, d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1605, 1510, 1250 and 805; *m/z* 356 (M^+), 341, 327, 313 and 299.

5-*Pentyl*-2-(4-*pentylphenyl*)*cyclohexanone* (**25**).—Quantities: compound **23** (3.80 g, 0.013 mol), hydrogen peroxide (2 cm^3), formic acid (10 cm^3). The experimental procedure was as described for the preparation of compound **8** and gave a pale-yellow solid.

Yield 2.90 g (71%); ^1H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:3); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1720, 1520, 1470, 1390, 1310, 1190, 1135 and 840; *m/z* 314 (M^+), 300, 285, 270 and 257.

2-(4-*Octyloxyphenyl*)-5-*pentylcyclohexanone* (**26**).—Quantities: compound **24** (5.90 g, 0.017 mol), formic acid (40 cm^3), hydrogen peroxide (4 cm^3). The experimental procedure was as described for the preparation of **8** and yielded an off-white solid.

Yield 3.35 g (53%); ^1H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:3); ν_{max}(film)/cm^{-1} 2960, 2940, 2860, 1705, 1510, 1460, 1240 and 1175; *m/z* 372 (M^+), 359, 344, 328 and 315.

trans-2,2-*Ethylenedisulfanyl*-4-*pentyl*-1-(4-*pentylphenyl*)*cyclohexane* (**27**).—Quantities: compound **25** (2.75 g, 8.76 mmol), ethane-1,2-dithiol (1.65 g, 0.018 mol), boron trifluoride–acetic acid (1.65 g, 8.78 mmol). The experimental procedure was as described for the preparation of compound **17** and yielded the *trans* isomer as a colourless oil.

Yield 2.12 g (62%); δ($CDCl_3$) 0.85 (6 H, m), 0.97–1.14 (1 H, m), 1.20–1.40 (12 H, m), 1.60 (3 H, m), 1.75–2.00 (5 H, m), 2.32 (1 H, d), 2.57 (3 H, m), 2.78–2.87 (2 H, m), 2.96–3.06 (1 H, m), 7.05 (2 H, d) and 7.35 (2 H, d); ν_{max}(film)/cm^{-1} 2960, 2940, 2860, 1510, 1460, 1275 and 825; *m/z* 390 (M^+), 362, 329, 319 and 297.

trans-2,2-*Ethylenedisulfanyl*-1-(4-*octyloxyphenyl*)-4-*pentylcyclohexane* (**28**).—Quantities: compound **26** (3.10 g, 8.33 mmol), ethane-1,2-dithiol (1.60 g, 0.017 mol), boron trifluoride–acetic acid (1.60 g, 8.51 mmol). The experimental procedure was as described for the preparation of compound **17** and gave the *trans* isomer as a colourless oil.

Yield 2.25 g (60%); $\delta(CDCl_3)$ 0.90 (6 H, m), 0.95–1.10 (1 H, m), 1.20–1.40 (17 H, m), 1.45 (2 H, m), 1.60 (1 H, m), 1.70–2.00 (6 H, m), 2.33 (1 H, d), 2.62 (1 H, quintet), 2.76–2.88 (2 H, m), 2.96–3.05 (1 H, m), 3.92 (2 H, t), 6.78 (2 H, d) and 7.35 (2 H, d); ν_{max}(film)/cm^{-1} 2960, 2940, 2860, 1610, 1510, 1470, 1240, 1175 and 825; *m/z* 448 (M^+), 420 and 405.

trans-2,2-*Difluoro*-4-*pentyl*-1-(4-*pentylphenyl*)*cyclohexane* (**29**).—Quantities: compound **27** (1.95 g, 5.00 mmol), 1,3-dibromo-5,5-dimethylhydantoin (1.60 g, 5.59 mmol), hydrogen fluoride–pyridine (3 cm^3, 70%). The experimental procedure was as described for the preparation of compound **5** and gave a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 0.55 g (33%); transitions (°C) C 40.0 [N – 45.0] I; $\delta_H(CDCl_3)$ 0.90 (6 H, t), 1.08–1.18 (1 H, m), 1.22–1.40 (12 H, m), 1.40–1.50 (1 H, m), 1.60 (2 H, quintet), 1.70–1.80 (1 H, m), 1.85–2.05 (3 H, m), 2.20–2.30 (1 H, m), 2.58 (2 H, t), 2.75–2.95 (1 H, m), 7.12 (2 H, d) and 7.22 (2 H, d); $\delta_C(CDCl_3)$ 14.14 (2 C, s), 22.65 (s), 22.73 (s), 26.50 (s), 29.57–29.68 (d), 31.19 (s), 31.71 (s), 32.03 (2 C, s), 34.93–35.05 (d), 35.66 (s), 36.36 (s), 41.07–41.76 (dd), 49.59–50.22 (t), 119.69–126.87 (t, CF_2), 128.20 (s), 129.19 (s), 134.94 (s) and 141.97; ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1520, 1475, 1170, 960 and 835; *m/z* 336 (M^+), 307, 293 and 279 (Found: M^+, 336.5105. $C_{22}H_{34}F_2$ requires *M*, 336.5108).

The Attempted Preparation of trans-2,2-*Difluoro*-1-(4-*octyloxyphenyl*)-4-*pentylcyclohexane* (**30**).—Quantities: compound **28** (2.05 g, 4.58 mmol), *N*-iodosuccinimide (4.13 g, 0.018 mol), hydrogen fluoride–pyridine (3 cm^3, 70%). The experimental procedure was as described for the preparation of compound **5** except that *N*-iodosuccinimide replaced 1,3-dibromo-5,5-dimethylhydantoin to give a mixture of the desired product, compound **26** and iodinated products (GC–MS analysis).

1-(4-*Bromophenyl*)-4-*pentylcyclohexene* **34**).—A solution of *n*-butyllithium (7.70 cm^3, 10.0 mol dm^{-3} in hexanes, 0.077 mol) was added dropwise to a stirred, cooled (−78 °C) solution of compound **31** (20.00 g, 0.071 mol) in dry THF (180 cm^3) under dry nitrogen. The mixture was stirred at −78 °C for 30 min and a solution of compound **12** (11.36 g, 0.068 mol) in dry THF (20 cm^3) was added dropwise and the mixture was allowed to warm to room temperature overnight. Saturated ammonium chloride was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was dissolved in toluene (150 cm^3), toluene-4-sulfonic acid (2.40 g) was added and the mixture was heated under reflux in a Dean–Stark apparatus for 1.5 h (GLC analysis revealed a complete reaction). Saturated sodium hydrogen carbonate was added and the product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was distilled to give a colourless solid.

Yield 13.74 g (66%); m.p. 69.0 °C; b.p. 140–145 °C at 0.1 mmHg; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.25–1.40 (9 H, m), 1.50–1.65 (1 H, m), 1.75–1.95 (2 H, m), 2.25–2.45 (3 H, m), 6.10 (1 H, m), 7.23 (2 H, d) and 7.40 (2 H, d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1485, 1465, 1005, 830 and 800; *m/z* 308 (M^+), 306 (M^+), 279, 277, 237, 223 and 235.

1-(4-*Bromophenyl*)-4-*ethylcyclohexene* (**35**).—Quantities: compound **32** (24.80 g, 0.105 mol), *n*-butyllithium (10.5 cm^3, 10.0 mol dm^{-3} in hexanes, 0.105 mol), compound **33** (12.60 g, 0.100 mol). The experimental procedure was as described for the preparation of compound **34** and yielded a pale yellow, low-melting solid.

Yield 25.80 g (97%); m.p. 25 °C; b.p. 120–125 °C at 0.01 mmHg; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.25–1.40 (3 H, m), 1.40–1.55 (1 H, m), 1.70–1.90 (2 H, m), 2.25–2.30 (1 H, m), 1.30–2.45 (2 H, m), 6.10 (1 H, m), 7.24 (2 H, d), 7.41 (2 H, d); ν_{max}(film)/cm^{-1} 2960, 2940, 2860, 1485, 1005, 815 and 800; *m/z* 266 (M^+), 264 (M^+), 237, 235, 223 and 221.

2-(4-*Bromophenyl*)-5-*pentylcyclohexanone* (**36**).—A solution of borane–THF (29.00 cm^3, 1.0 mol dm^{-3} in THF, 0.029 mol) was added to a stirred, cooled (0 °C) solution of compound **34** (8.00 g, 0.026 mol) in dry THF (100 cm^3) under dry nitrogen. The mixture was heated under reflux for 1.5 h, cooled and ice–water was added carefully. The product was extracted into ether (×2) and the combined ethereal extracts were dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was dried (P_2O_5 at 0.05 mmHg). The product was dissolved in dry dichloromethane (120 cm^3) and molecular sieves (0.1 g) and pyridinium chlorochromate (19.62 g, 0.091 mol) were added. The mixture was heated under reflux for 3 h (GLC/TLC analysis revealed a complete reaction), cooled and filtered through Hyflo Supercel. Brine was added to the filtrate and the aqueous layer was washed with dichloromethane and the combined organic extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the gradual introduction of ethyl acetate] to give a pale-yellow solid (GLC analysis revealed a *cis–trans* mixture, *ca.* 1:3).

Yield 6.24 g (74%); ^{1}H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:3); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1705, 1470, 1060, 1005 and 800; *m/z* 324 (M^+), 322 (M^+), 280 and 278.

2-(4-*Bromophenyl*)-5-*ethylcyclohexanone* (**37**).—Quantities: compound **35** (10.15 g, 0.38 mol), borane–THF (43.00 cm^3, 1.0 mol dm^{-3} in THF, 0.042 mol), pyridinium chlorochromate (29.00 g, 0.134 mol). The experimental procedure was as described for the preparation of compound **36** and yielded a pale-yellow solid (GLC analysis revealed a *cis–trans* mixture, *ca.* 1:2).

Yield 8.14 g (76%); ^{1}H NMR ($CDCl_3$) revealed a *cis–trans* mixture (1:2); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1705, 1470, 1060, 1005 and 800; *m/z* 282 (M^+), 280 (M^+), 238 and 236.

trans-1-(4-*Bromophenyl*)-2,2-*ethylenedisulfanyl*-4-*pentylcyclohexane* (**38**).—Quantities: compound **36** (5.85 g, 0.018 mol), ethane-1,2-dithiol (3.40 g, 0.036 mol), boron trifluoride acetic acid (3.40 g, 0.018 mol). The experimental procedure was as described for the preparation of compound **17** and gave a colourless solid (pure *trans* isomer).

Yield 4.85 g (68%); m.p. 78 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.02 (1 H, m), 1.20–1.40 (8 H, m), 1.60 (1 H, m), 1.74–2.05 (5 H, m), 2.33 (1 H, d), 2.58–2.66 (1 H, quintet), 2.77–2.91 (2 H, m), 2.98–3.06 (1 H, m), 7.34 (2 H, d) and 7.39 (2 H, d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1490, 1275, 1010 and 820; *m/z* 400 (M^+), 398 (M^+), 372, 370, 329 and 327.

trans-1-(4-*Bromophenyl*)-4-*ethyl*-2,2-*ethylenedisulfanylcyclohexane* (**39**).—Quantities: compound **37** (6.82 g, 0.025 mol), ethane-1,2-dithiol (4.58 g, 0.049 mol), boron trifluoride–acetic acid (4.57 g, 0.025 mol). The experimental procedure was as described for the preparation of compound **17** and gave a colourless solid (pure *trans* isomer).

Yield 3.58 g (41%); m.p. 60 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.02 (1 H, m), 1.25–1.35 (2 H, m), 1.50–1.60 (1 H, m), 1.74–2.05 (5 H, m), 2.33 (1 H, d), 2.58–2.66 (1 H, quintet), 2.77–2.91 (2 H, m), 2.98–3.06 (1 H, m), 7.34 (2 H, d) and 7.39 (2 H, d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1490, 1275, 1010 and 820; *m/z* 358 (M^+), 356 (M^+), 329 and 327.

trans-1-(4-*Bromophenyl*)-2,2-*difluoro*-4-*pentylcyclohexane* (**40**).—Hydrogen fluoride–pyridine (7 cm^3, 70%) was added dropwise to a stirred, cooled (−78 °C) solution of 1,3-dibromo-5,5-dimethylhydantoin (3.75 g, 0.013 mol) in dry dichloromethane (50 cm^3) under dry nitrogen. Then a solution of compound **38** (4.75 g, 0.012 mol) in dry dichloromethane (50 cm^3) was added dropwise at −78 °C and the mixture was stirred at −78 °C for 1 h and allowed to warm to *ca.* −10 °C. The mixture was immediately cooled again to −78 °C and then poured into a stirred, cooled (−78 °C) slurry of basic alumina in dry dichloromethane and allowed to warm to room temperature and filtered. The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C) with the very gradual introduction of dichloromethane] to give a colourless solid.

Yield 3.06 g (74%); m.p. 56–57 °C; $\delta_H(CDCl_3)$ 0.90 (3 H, t), 1.00–1.15 (1 H, m), 1.20–1.40 (8 H, m), 1.40–1.45 (1 H, m), 1.65–1.80 (1 H, m), 1.85–2.00 (3 H, m), 2.20–2.35 (1 H, m), 2.75–2.95 (1 H, m), 7.18 (2 H, d) and 7.44 (2 H, d); $\delta_C(CDCl_3)$ 14.15 (s), 22.71 (s), 26.46 (s), 29.45–29.54 (d), 31.80–32.02 (d), 34.86 (s), 34.98 (s), 36.29 (s), 40.91–41.59 (dd), 49.46–50.09 (t), 119.35–126.55 (t, CF_2), 122.96 (s), 131.10 (s), 131.30 (s) and 136.79 (s); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1485, 1160, 1010, 950 and 820; *m/z* 346 (M^+), 344 (M^+), 266, 197 and 195.

trans-1-(4-*Bromophenyl*)-4-*ethyl*-2,2-*difluorocyclohexane* (**41**).—Quantities: compound **39** (3.58 g, 0.010 mol). The experimental procedure was as described for the preparation of compound **40**.

Yield 1.46 g (48%); m.p. 50 °C; $\delta(CDCl_3)$ 0.90 (3 H, t), 1.00–1.15 (1 H, m), 1.20–1.40 (2 H, m), 1.40–1.45 (1 H, m), 1.65–1.80 (1 H, m), 1.85–2.00 (3 H, m), 2.20–2.35 (1 H, m), 2.75–2.95 (1 H, m), 7.18 (2 H, d) and 7.44 (2 H, d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1485, 1160, 1010, 950 and 820; *m/z* 304 (M^+) and 302 (M^+).

trans-4-*Ethyl*-2,2-*difluoro*-1-(4′-*octyloxybiphenyl*-4-*yl*)-*cyclohexane* (**44**).—Quantities: compound **41** (0.65 g, 2.20 mmol), compound **43** (0.65 g, 2.60 mmol). The experimental procedure was as described for the preparation of compound **20** (Method B) to yield colourless crystals.

Yield 0.30 g (32%); transitions (°C) C 80.0 (E 70.0 B 79.0) N 124.0 I; $\delta(CDCl_3)$ 0.90 (6 H, 2 × t), 1.05–1.20 (1 H, m), 1.22–1.40 (10 H, m), 1.40–1.55 (3 H, m), 1.75–1.85 (3 H, m), 1.90–2.10 (3 H, m), 2.20–2.35 (1 H, m), 2.80–3.00 (1 H, m), 3.98 (2 H, t), 6.95 (2 H, d), 7.35 (2 H, d) and 7.52 (4 H, 2 × d); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 1605, 1500, 1250, 1160 and 820; *m/z* 428 (M^+) and 316 (Found: M^+, 428.6082. $C_{28}H_{38}F_2O$ requires *M*, 428.6082).

trans-1-(4′-*Cyanobiphenyl*-4-*yl*)-2,2-*difluoro*-4-*pentylcyclohexane* (**46**).—Quantities: compound **40** (1.20 g, 3.48 mmol), compound **45** (0.62 g, 4.22 mmol). The experimental procedure was as described for the preparation of compound **19** (Method B) except that the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C)–dichloromethane 2:1] to yield colourless crystals.

Yield 0.70 g (55%); transitions (°C) C 103.0 N 173.0 I; $\delta_H(CDCl_3)$ 0.90 (3 H, t), 1.05–1.20 (1 H, m), 1.22–1.38 (8 H, m), 1.40–1.55 (1 H, m), 1.70–1.85 (1 H, m), 1.90–2.05 (3 H, m), 2.20–2.35 (1 H, m), 2.85–3.05 (1 H, m), 7.43 (2 H, d), 7.55 (2 H, d), 7.67 (2 H, d) and 7.72 (2 H, d); $\delta_C(CDCl_3)$ 14.15 (s), 22.71 (s), 26.46 (s), 29.46–29.57 (d), 31.84 (s), 32.00 (s), 34.87–35.02 (d), 36.29 (s), 40.96–41.63 (dd), 49.68–50.31 (t), 110.86 (s), 119.08 (s), 119.58–126.80 (t, CF_2), 127.02 (s), 127.70 (s), 130.16 (s), 132.66 (s), 138.16 (s), 138.54 (s) and 145.47 (s); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2860, 2240, 1620, 1500, 1165, 955 and 825; *m/z* 367 (M^+), 310, 296 and 218 (Found: M^+, 367.4831. $C_{24}H_{27}F_2N$ requires *M*, 367.4835).

trans-1-(4-*Cyanophenyl*)-2,2-*difluoro*-5-*pentylcyclohexane* (**47**).—A mixture of compound **40** (1.50 g, 4.35 mmol) and copper(I) cyanide (0.50 g, 5.59 mmol) in dry DMF (15 cm^3) was heated under reflux under dry nitrogen for 16 h (GLC/TLC analysis revealed a complete reaction) and the mixture was cooled and poured into 10% hydrochloric acid. The product was extracted into ether (×2) and the combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product was purified by column chromatography [silica gel; petroleum fraction (b.p. 40–60 °C)–dichloromethane 2:1] to give a colourless solid which was recrystallized from ethanol to yield colourless crystals.

Yield 0.80 g (63%); transitions (°C) C 75.0 [N − 10.0] I; $\delta_H(CDCl_3)$ 0.90 (3 H, t), 1.00–1.20 (1 H, m), 1.20–1.35 (8 H, m), 1.40–1.55 (1 H, m), 1.65–1.75 (1 H, m), 1.80–2.05 (3 H, m), 2.20–2.35 (1 H, m), 2.85–3.00 (1 H, m), 7.42 (2 H, d) and 7.62 (2 H, d); $\delta_C(CDCl_3)$ 14.14 (s), 22.69 (s), 26.43 (s), 29.23–29.32 (d), 31.60 (s), 31.32 (s), 34.78–34.91 (d), 36.20 (s), 40.82–41.49 (t), 50.07–50.70 (t), 111.28 (s), 118.97 (s), 119.26–126.46 (t, CF_2), 130.24 (s), 131.94 (s) and 143.28 (s); ν_{max}(KBr)/cm^{-1} 2960, 2940, 2240, 1610, 1460, 1515, 1185, 1165, 1150, 955 and 825; *m/z* 291 (M^+), 263 and 235 (Found: M^+, 291.3853. $C_{18}H_{23}F_2N$ requires *M*, 291.3855).

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