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The four aldol condensation products of methylcyclohexanone isomers and 4-(4-hexyloxy-benzoyloxy)benzaldehyde have been prepared. These chiral products were either obtained with high enantiomeric excess or the enantiomers were separated by means of chiral HPLC. In all cases only the *E*-isomer was obtained. UV irradiation was used to isomerize the *E*-isomers to the *Z*-isomers. Comparison of the helical twisting powers (HTP) of the *E*-isomers revealed that the derivative in which the methyl group is directly next to the double bond exhibits the highest value. Although the other three *E*-isomers have lower HTP values, they show large HTP changes and reversal of the helical twist sense upon irradiation. Of these compounds, the one derived from the commercially available (*R*)-3-methylcyclohexanone is an interesting candidate for use as an alternative to compounds derived from menthone for realizing photochemically induced twist changes in twisted nematic and cholesteric materials.

1. Introduction

Cholesteric liquid crystalline materials have received much attention due to their capability of reflecting circularly polarized light. On the basis of this property several applications have been explored, ranging from paints to organic broadband mirrors [1, 2]. The reflection colour can be chosen by the ratio of nematic and chiral material. The colour can be changed after applying such a mixture by making use of the thermochromic effect [3] or diffusion techniques [4]. In both cases it is possible to make materials which reflect different colours in different areas after polymerization of the mixture. Another way of making patterned colour reflectors is by using photochromic systems in which the helical twisting power of the chiral component can be tuned by means of ultraviolet irradiation. On the basis of this process, Shibaev *et al.* [5] and van de Witte *et al.* [6, 7] prepared polymers whose reflection wavelengths can be changed from UV to infrared simply by changing the UV dose. The chiral component of these polymers is **1b** (see scheme 1), which is derived from menthone. It undergoes an *E* to *Z* isomerization under UV irradiation, and this is accompanied by a large drop in helical twisting power (HTP). Several applications of these

polymers have meanwhile been explored [7, 8], the most promising example being the formation of cholesteric colour filters for use in LCDs [9].

In a previous publication the HTP of compounds **1a** and **1b** derived from menthone was investigated [10] (see scheme 1). The effect of the isopropyl and methyl groups attached to carbon atoms 3 and 6, respectively, was investigated by preparing compounds **1c** and **1d**, which contain only one chiral centre. Comparison of diastereomers **1a** and **1b** revealed that the configuration at C3 plays a minor role in the HTP of these compounds relative to that of the methyl group at position 6. No major difference in HTP was observed between the two diastereomers either before or after photoisomerization to compounds **2a** and **2b**. Comparison of the HTP of compounds **1c** and **1d** confirmed that the methyl group at position 6 plays a major role in the HTP of the menthone derivatives. The fact that all *Z*-isomers **2a**–**d** exhibit a lower HTP than the *E*-isomers **1a**–**d** suggests that the conformation of the methylmethylene styrene moiety in compounds **1a**, **1b** and **1d** is responsible for the relatively high HTP of these compounds [11].

In order to test whether this methylmethylene styrene moiety represents the only way of obtaining a high HTP in these types of compound, we decided to study several isomers of **1d**. We here present the preparation of compounds **1e**, **1f** and **1g**, in which the methyl group is linked

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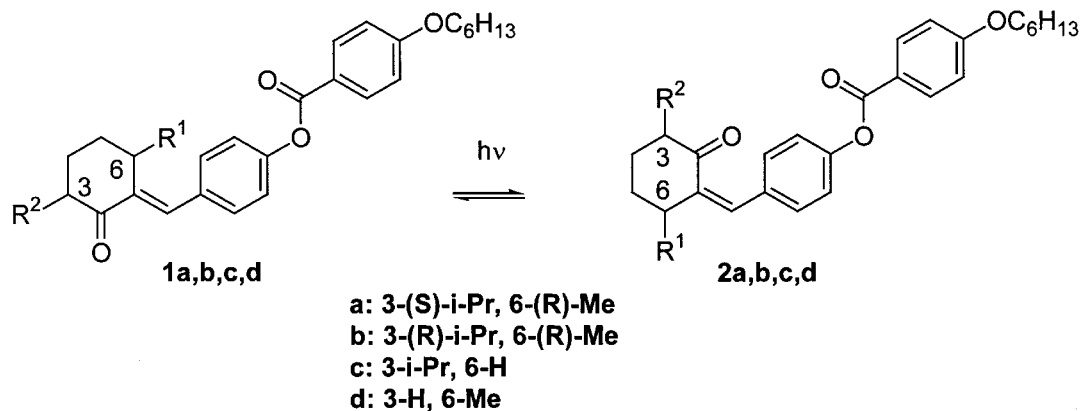
Scheme 1.   Structures of compounds **1a–d** and **2a–d**.

at positions 5, 4 and 3, respectively, of the cyclohexane ring (see scheme 2). We also studied photoisomerization to their respective *Z*-isomers **2e**, **2f** and **2g**.

2.   Experimental
2.1.   *Materials and methods*

E7 (a mixture of nematic liquid crystals derived mainly from cyanobiphenyl) and S811 ((*S*)-1-methylheptyl 4-(4-hexyloxybenzoyloxy)benzoate) were obtained from Merck. 4-(1-Ethoxyethoxy)benzaldehyde was prepared in a similar manner to that described for 4-(tetrahydropyran-2-yloxy)benzaldehyde [8]. All the other chemicals were obtained from Aldrich.

UV spectra were recorded with the aid of a Unicam UV2-100 spectrometer and using acetonitrile as solvent. NMR spectra were recorded with the aid of a Bruker DP300 spectrometer on solutions in deuterated dichloromethane. The ^{1}H spectra were interpreted with the aid of ^{1}H–^{13}C correlation spectra. The ^{1}H and ^{13}C NMR data were fully consistent with the required structures and confirmed the purity of all the final products.

The enantiomeric excess of compound **1f** was determined with the aid of chiral HPLC—column: Chiralcel

OD (250×4.6 mm) Daicel, mobile phase: heptane/ethanol ($95:5$).

The helical twisting power was determined using the Grandjean–Cano method [12]. Wedge cells (EHC Japan, $\tan \alpha = 0.0083$) were filled with solutions of compounds **1e–g** in E7 and solutions of compounds **1e–g** with S811 in E7 (in order to determine the sign of the HTP). The total amount of chiral compounds never exceeded 1 wt %. The clearing points of these mixtures before and after irradiation varied less than 1°C compared with pure E7. The distance between the disclination lines was measured before and after irradiation with 365 nm light.

2.2.   *Synthesis*
2.2.1.   *4-(5-Methyl-2-oxo-cyclohexylidenemethyl)phenol (5e)*

Coarsely powdered potassium hydroxide (6.0 g) was added to a magnetically stirred mixture of 17 g of 4-methylcyclohexanone, 26 g of 4-(1-ethoxyethoxy)-benzaldehyde and 60 ml of DMSO. The mixture was stirred for 4 h at room temperature. 150 ml of water was added and the organic material was extracted into 100 ml
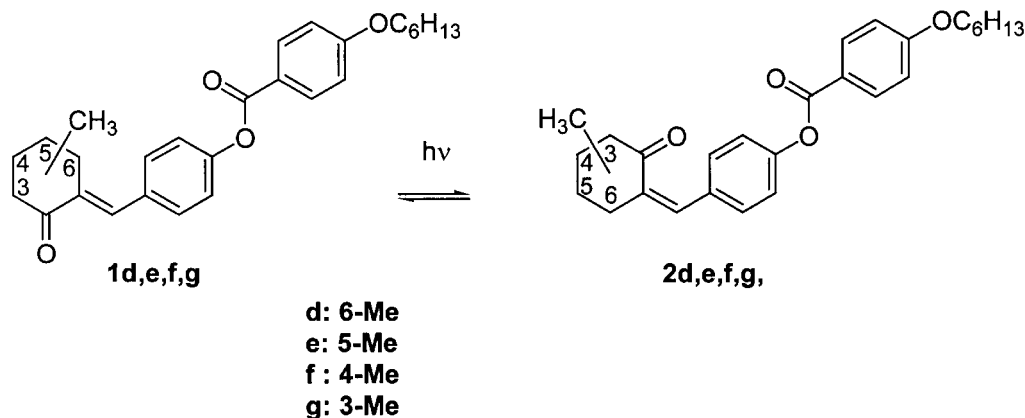
Scheme 2.   Structures of compounds **1d–g** and **2d–g**.

of toluene. The crude intermediate **4e** was obtained after washing with 100 ml of water, drying over potassium carbonate and evaporation. It was boiled for 90 min with 100 ml of methanol, 1 ml of water and 0.60 g of pyridinium 4-toluenesulphonate. After evaporation of the methanol, 100 ml of water was added to the residue and the mixture shaken twice with 80 ml of toluene. The product was obtained after evaporation of the toluene extract and elution with toluene over silica; 0.6 g of a white powder (2%) was obtained.

2.2.2. *4-(4-Methyl-2-oxo-cyclohexylidenemethyl)phenol (5f)*

(*R*)-3-methylcyclohexanone (7.54 g) was added to a solution of 8.5 g of lithium di-isopropylamide in 35 ml of tetrahydrofuran, cooled to −50°C. After stirring for 20 min, a solution of 14.0 g of 4-(1-ethoxyethoxy)-benzaldehyde in 10 ml of tetrahydrofuran was added dropwise. After stirring for another 90 min at −50°C, 50 ml of saturated aqueous ammonium chloride was added at once. After addition of more water, the mixture was shaken with toluene. After washing the extract with water and evaporation of the toluene, the crude intermediate **4f** was obtained. It was heated under reflux for 90 min with 29 g of oxalic acid dihydrate in 70 ml of water. After cooling, the aqueous layer was decanted and 25 ml of a 33 wt % sodium hydroxide solution added to the residue. This solution was washed with 50 ml of toluene and then acidified with acetic acid. The crude product was extracted into 50 ml of dichloromethane and purified by means of Kugelrohr distillation; 2.27 g (16%) of a white powder was obtained after precipitation from an ethanolic solution into water.

2.2.3. *4-(3-Methyl-2-oxo-cyclohexylidenemethyl)phenol (5g)*

This compound was obtained in 10% yield starting from racemic 2-methylcyclohexanone in the same way as that described for the synthesis of 4-(5-methyl-2-oxo-cyclohexylidenemethyl)phenol (**5e**).

2.2.4. *Synthesis of the final products 1e–g*

These products were obtained in 60–75% yield in the same manner as that described for the synthesis of 4-(3-isopropyl-2-oxo-cyclohexylidenemethyl)phenyl 4-hexyloxybenzoate (**1c**) and 4-(6-methyl-2-oxo-cyclo-hexylidenemethyl)phenyl 4-hexyloxybenzoate (**1d**) [10]. 4-(4-Methyl-2-oxo-cyclohexylidenemethyl)phenyl 4-hexyl-oxybenzoate (**1f**) was recrystallized from methanol; it had an enantiomeric excess of more than 99% measured by means of chiral HPLC.

2.2.5. *Separation of the enantiomers of 1e and 1g*

100 mg samples of both enantiomers of 4-(5-methyl-2-oxo-cyclohexylidenemethyl)phenyl 4-hexyloxybenzoate (**1e**) were obtained with a 99% enantiomeric excess after preparative chiral HPLC of about 250 mg of the racemic mixture—column: Chiralpak AD (250 × 4.6 mm) Daicel, mobile phase: heptane/2-propanol (90:10). In the same way, both enantiomers of 4-(3-methyl-2-oxo-cyclo-hexylidenemethyl)phenyl 4-hexyloxybenzoate (**1g**) were obtained—column: Chiralpak AD (250 × 4.6 mm) Daicel, mobile phase: heptane/2-propanol (99:1).

## 3. Results and discussion
3.1. *Synthesis*

The synthesis of compound **1d** is described in our previous publication [10]. Compounds **1e** and **1g** were obtained from 4-methylcyclohexanone and race-mic 2-methylcyclohexanone, respectively, according to scheme 3. The synthesis is similar to that of menthone compound **1a** [8] and compound **1c**, which is derived from 2-isopropylcyclohexanone [10]. The intermediate phenolic derivatives **5e** and **5g** were obtained in low yields (of 2 and 10%, respectively) compared with the yields of this type of intermediate in the synthesis of **1a**–**c**. Thus, these reaction conditions are probably not optimal and it is possible that other reaction conditions will increase the yield considerably.

Racemic mixtures of the final products **1e** and **1g** were obtained after aldol condensation with protected 4-hydroxybenzaldehyde, deprotection and esterification with 4-hexyloxybenzoic acid. Both enantiomers were then separated by means of preparative chiral HPLC. The absolute configuration of these enantiomers is unknown. Compound **1f** was obtained from the commercially available (*R*)-3-methylcyclohexanone. For that reason, the resulting end product **1f** has the (*R*)-configuration. In order to increase the yield of the intermediate phenolic compound **5f**, the aldol condensation reaction was performed using lithium di-isopropylamide instead of potassium hydroxide. In this way a yield of 16% was obtained. Only condensation at the 6 position of (*R*)-3-methylcyclohexanone was observed.

3.2. *Characterization of compounds 1d–g and their isomerization products 2d–g*

In order to characterize whether these compounds were indeed obtained as *E*-isomers, NOESY ^{1}H NMR spectra were recorded. The aromatic protons in the *ortho*-position to the vinyl group are observed at 7.4 ppm. In all cases interaction between these aromatic protons and the protons linked to C6 of the cyclohexane ring was observed. These protons linked to C6 were observed at 3.4 ppm, at 3.0 and 2.2 ppm, at 3.0 and 2.6 ppm and
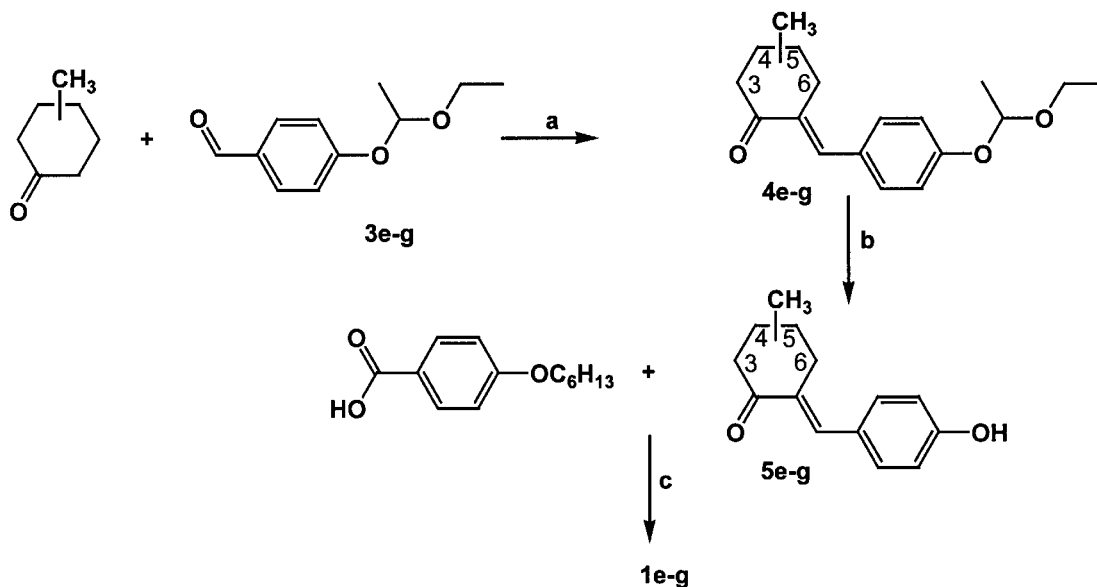
Scheme 3. Synthetic route to **1e**–**g**. *a*: KOH in DMSO or LDA in THF; *b*: PPTS in MeOH or $C_2H_2O_4$ in H_2O; *c*: DCC, DMAP in CH_2Cl_2.

at 3.0 and 2.6 ppm in the case of compounds **1d**, **1e**, **1f** and **1g**, respectively. In the case of compound **1d**, interaction between the aromatic signals at 7.4 ppm and signals at 1.2 ppm from the methyl group was also observed. In none of these cases was interaction observed between the olefinic proton and any other proton in the molecule. This clearly reflects the *E*-structure of compounds **1d**–**g**. This is also apparent from the spectral position of the olefinic proton, which is approximately 7.3 ppm. Upon irradiation, this signal shifts to approximately 6.3 ppm, which is a typical value of the *Z*-structure of compounds **2d**–**g**.

After irradiation, the aromatic protons in the *ortho*-position to the vinyl group of **2d**–**g** were observed at 7.3 ppm. This signal did not show interaction with any other proton in the molecule. On the other hand, these isomers showed typical interactions between the olefinic proton and the protons linked to C6 of the cyclohexane ring, as expected for the *Z*-isomer. These protons linked to C6 were observed at 2.7, 2.5, 2.7 and 2.6 ppm in the case of compounds **2d**, **2e**, **2f** and **2g**, respectively. Furthermore, the protons of the methyl group linked to C6 observed at 1.1 ppm showed interaction with the olefinic proton in the case of **2d**.

Some of the properties of the compounds are shown in table 1. Only in the case of compounds **1f** and **1g** was liquid crystalline behaviour observed. Apparently methyl groups closer to the aromatic moiety, as in **1d** and **1e**, have a suppressing effect on the formation of liquid crystalline phases. This effect was also observed when the menthone derivatives **1a** and **1b** were compared

with derivative **1c**. Only **1c** showed liquid crystalline behaviour and also lacked the methyl group near the aromatic moiety [10].

The UV spectra of compounds **1e**–**g** are almost identical. Compound **1d** exhibited a blue shift of 4 nm relative to the other three compounds (see table 1). The chromophore of these compounds consists of the cinnamoyl system whose maximum absorption is determined by the torsion angle of the carbonyl and double bond and by the torsion angle of the double bond and aromatic ring. The repulsion between the methyl group and the aromatic ring in compound **1d** will increase both angles and therefore decrease the maximum absorption wavelength relative to that of compounds **1e**–**g**. For the same reason a blue shift was observed in the spectra of the menthone derivatives **1a** and **1b** relative to the spectrum of compound **1c**, which lacks this methyl group [10]. The UV spectra of the *Z*-isomers **2a**–**g** were obtained from the spectra in the photostationary state and the spectra of **1a**–**g** by calculation. The composition of the photostationary state was obtained from the NMR experiments. All the compounds **2a**–**g** show a λ_{max} of 268 nm. This means that interaction between the methyl group at any position and the phenyl group has no effect on the torsion angles in the cinnamoyl moiety.

3.3. *The HTP values before and after irradiation*

Table 1 shows the HTP values of the four compounds **1d**–**g**. Because the absolute configuration of **1d**, **1e** and **1g** is unknown, the relation between the absolute configuration and the sign of the HTP cannot be determined.

Table 1. Physical data for compounds **1d**–**g** before and after irradiation and of **2d**–**g** obtained by calculation.

Compound	Phase transitions	Configuration	UV data (in CH_3CN)		HTP/μm^{-1} (in E7)	
			λ_{max}/nm	ε_{max}	Before irradiation	After irradiation
E-isomer						
1d	$T_{Cr-I} = 66°C$		277	32×10^3	-16	$-4.0 \ (22)^a$
1e	$T_{Cr-I} = 91°C$		281	31×10^3	-5.0	$+15 \ (15)$
1f	$T_{Cr-I} = 102°C$	$4R$	281	32×10^3	-9.0	$+12 \ (21)$
	$(T_{N^*-I} = 91°C)$					
1g	$T_{Cr-N^*} = 107°C$		281	34×10^3	-8.0	$+8.1 \ (9)$
	$T_{N^*-I} = 111°C$					
Z-isomer			(Calculated)		(Calculated)	
2d			268	30×10^3	-0.6	
2e			268	30×10^3	$+18$	
2f		$4R$	268	30×10^3	$+18$	
2g			268	32×10^3	$+9.7$	

[a] Figures in parentheses denote % *E*-isomer (NMR).

The highest absolute value was observed for **1d**. It was suggested that the interaction of the methyl group with the aromatic ring in compound **1d** and also in menthone derivatives **1a** and **1b** is responsible for a high HTP. Due to this interaction, the molecule exhibits a spiral form, which has a strong twisting effect on the interaction with nematic molecules [11]. Compound **1f** is the only compound with a defined stereochemistry, namely *R*; its HTP has a negative value. A negative HTP was also observed in menthone derivatives **1a** and **1b**. In these molecules the HTP is determined mainly by the chiral group at position 6, which also has the *R*-configuration. The absolute configurations of at least compounds **1e** and **1g** should be determined to find out whether there is indeed any correlation between the *R*-configuration of this type of compound and a negative HTP.

The highest degree of conversion in the photo-stationary state was observed in the case of compound **1g**. Likewise, the menthone derivatives **1a** and **1b** and also **1c** showed a higher degree of conversion upon photo-isomerization than **1d**. This suggests that the formation of the *Z*-isomers under the irradiation conditions employed is favoured by substitution at position 3 of the cyclo-hexane ring. Compounds **1e**, **1f** and **1g** showed inversion of the sign of the HTP upon isomerization. This was also observed in the case of compound **1c**. All these compounds lack a substituent at C6. This shows that substituents at positions other than C6 contribute to the HTP of the *E*-isomer as well as of the *Z*-isomer. It is however difficult to rationalize the relation between the observed conformational changes upon isomerization and the inversion of the HTP. Comparison of **1d** and **1g** reveals that they show a similar HTP change upon irradiation. Much higher HTP changes were observed in the case of compounds **1e** and **1f**. The *Z*-isomers **2e**

and **2f** of these compounds exhibit relatively large HTP values. Apparently, to obtain high values for the HTP of *Z*-isomers, the chiral centre(s) should preferably be far away from the double bonds of the cinnamoyl system as in **2e** and **2f**, instead of close to these bonds as in **2d** and **2g**.

4. Conclusions and prospects

Of the four *E*-isomers **1d**–**g**, **1d**, in which the methyl group is linked to carbon 6, exhibits the highest HTP. This is probably due to a strong twisting effect in the molecule as a result of repulsion between the methyl group and the aromatic ring. **2e**, **2f** and **2g** have HTPs with opposite signs relative to their *E*-isomers, whereas isomer **2d** has an HTP of almost zero. This means that the chiral centre in **2d** plays an unimportant role. When the methyl groups are further away from the double bond as in **2e** and **2f**, high HTP values are observed. Although the initial HTPs of compounds **1e** and **1f** are not as high as that of **1d**, due to the high HTP of the *Z*-isomers a higher HTP change upon irradiation was observed for these compounds than for **1d**. For practical applications, compound **1g** is less useful than the others due to its low HTP values before and after irradiation. Furthermore, this compound and also compounds **1d** and **1e** have the disadvantage that they are relatively difficult to synthesize, and enantiomer separations have to be effected to obtain enantiomerically pure samples. For this reason, compound **1f** is the most interesting compound for practical applications. Its synthesis is more convenient, mainly because no enantiomer separation needs to be effected. It is more or less complementary to the commonly used menthone derivatives such as **1b** (see table 2). The sign of the HTP of **2f** is opposite to

Table 2. Comparison of the HTP values before and after irradiation of compounds **1a** and **1f**, and of **2a** and **2f** obtained through calculation.

Compound	Configuration	HTP/μm^{-1}		
		Before irradiation (in E7)	After irradiation (in E7)	Calculated
1b	3*R*, 6*R*	−19	−3.0 (3)[a]	
1f	4*R*	−9.0	+12 (21)	
2b				−3.0
2f				+18

[a] Figures in parentheses denote % *E*-isomer (NMR/HPLC).

that of **2b**, which makes it possible to invert the handedness of the helix of a cholesteric film which then reflects light of the opposite circular polarization state. Furthermore, for **1f** the absolute value of the HTP in the photostationary state is higher than before irradiation, whereas for **1b** the HTP in the photostationary state is almost zero and less than that of pure **1b** (see table 2). This may broaden the application area of these types of photoactive compounds.

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