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Cyclopropanoles as the Versatile Intermediates in the Synthesis of Polyring Liquid Crystalline Compounds

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New synthetic schemes for the preparation of liquid crystalline compounds which provide for the use of substituted 1-cyclopropanoles as the key intermediates are reported. Two main directions for the transformation of cyclopropanoles into LC compounds have been applied: a) the using of cyclopropanoles as the precursor of vinyl ketones in the "condensation building" of cyclohexenone ring which can be then converted into both laterally substituted and unsubstituted cyclohexyl or cyclohexenyl moiety; b) the opening of cyclopropane ring which allow to construct the functionally substituted terminal side chain.

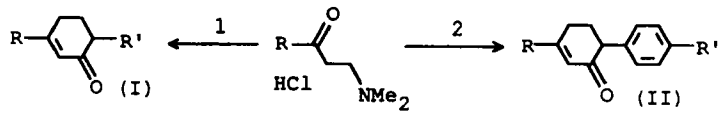
Keywords: cyclopropanoles; synthesis of liquid crystals; intermediates for liquid crystals

INTRODUCTION

Earlier we have reported the «condensation approach» for the synthesis of polyring liquid crystalline compounds which provides for the Michael type condensation of Mannich salts with 2-substituted acetoacetic esters or substituted benzyl methyl ketones leading to

3,6-disubstituted cyclohex-2-en-1-ones (I,II) (R = aryl or trans-4-aryl-cyclohexyl, R' = H, alkyl or any functional group) as a key intermediate[1-3].

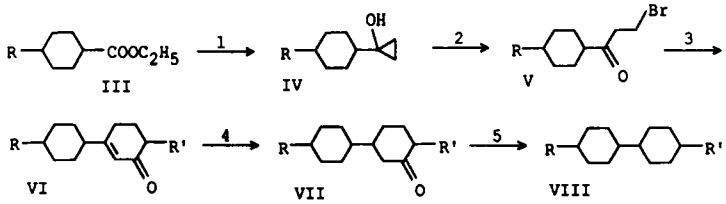
3,6-Disubstituted cyclohex-2-en-1-ones (I,II) are shown to be useful intermediates for the further chemical transformation into liquid crystalline derivatives possessing cyclohexane or cyclohexene or phenyl ring.



1. R'-CH($COCH_3$)$COOC_2H_5$; KOH; dioxane.
2. R'-C_6H_4-CH_2COCH_3; KOH; dioxane.

Recently we have proposed a new synthetic pathway for the preparation of liquid crystalline trans,trans-dicyclohexyl derivatives (VII,VIII) which are useful in LC mixtures because of their low viscosity and low birefringence[4]. Usually the synthesis of these compounds is being realised according to schemes which provide for catalytic cross-coupling reaction as a key stage or using of 4-(trans-4-alkylcyclohexyl)cyclohexanone as a main intermediate[5,6].

We have used 1-substituted cyclopropanoles (IV) as the key intermediates in the synthesis. It should be noted that substituted cyclopropanoles (IV) are easily available starting from ethyl trans-4-alkylcyclohexanecarboxylates (III) due to the new method for their preparation in reaction of Grignard reagents with esters (III) in the presence of tetraisopropoxytitanium[7].



R, R' = alkyl.

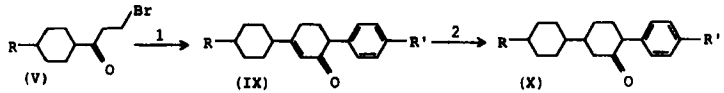
1. 2.5 eq. C_2H_5MgBr; 15 mol.% $Ti(Oi\text{-}C_3H_7)_4$; ether;
2. Br_2; CH_3OH/H_2O;
3. R'-$CH(COCH_3)COOC_2H_5$; 3 eq. KOH; dioxane;
4. H_2; Pd/C; KOH; ethanol;
5. N_2H_4; KOH; diethylene glycol;

RESULTS AND DISCUSSION

Here we have proposed and realised new synthetic possibilities for the preparation of polyring liquid crystals including dicyclohexyl derivatives. The key stage was recently discovered reaction of ethylmagnesium bromide with the corresponding esters in the presence of tetraisopropoxytitanium leading to 1-substituted cyclopropanoles with the high yields (more than 90%).

We have experimentally checked the new synthetic pathway to prepare three ring LC compounds possessing trans,trans-dicyclohexyl moiety. The condensation of β-bromoketones (V) with 4-substituted benzyl methyl ketones leads to the corresponding three ring cyclohexenones (IX) with the yield about 60% (melting points and phase transition temperatures are presented in Table 1).

Unsaturated cyclohexenones (IX) can be easily catalytically hydrogenated in the presence of palladium on carbon and potassium hydroxide in THF-methanol (10:1) like ketones (VI)[8]. The corresponding saturated cyclohexanones (X) were isolated with the quantitative yield as the mixture of trans,trans- and trans,cis-isomers. We were not studying the cis/trans ratio for the formed products because of easy interconversion.



R = alkyl; R' = F; OCH_3; alkyl.

1. CH_3COCH_2-C_6H_4-R' (R' = F; OCH_3; Cl; C_3H_7); 3 KOH; dioxane;
2. H_2; Pd/C; KOH; THF-ethanol;

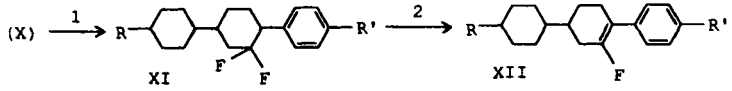
TABLE 1 Melting points and phase transition temperatures for the compounds IX.

No	R	R'	Phase transition temperatures, ^oC
IXa	C_3H_7	F	Cr 105 I
IXb	C_3H_7	OCH_3	Cr 95 (N 80) I
IXc	C_5H_{11}	F	Cr 107 I
IXd	C_5H_{11}	OCH_3	Cr 106 I
IXe	C_5H_{11}	C_3H_7	Cr 106 I

Some of the prepared saturated cyclohexanones (X) are liquid crystalline but first of all they are very useful as the excellent intermediates for the synthesis of other laterally substituted three ring LC compounds.

The most promising direction for the further chemical transformation of ketones (X) was interaction with diethylaminosulfur

trifluoride (DAST). This reaction leads to the corresponding liquid crystalline gem-difluoroderivatives (XI). gem-Difluoroderivatives (XI) are liquid crystalline compounds and can be also converted to monofluoroderivatives (XII) which are shown to be excellent LC compounds with relatively low melting points and possess a wide range of nematic phase, see Table 2. Earlier very complicated multistep method for the synthesis of compounds (XII) starting from 4-(trans-4-alkylcyclohexyl)cyclohexanone has been proposed by Merck[9].



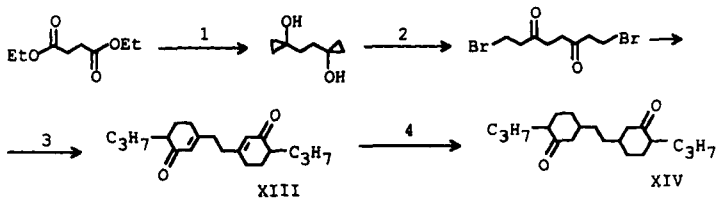
1. DAST; benzene;
2. KOH; ethylene glycol;

TABLE 2 Melting points and phase transition temperatures for the compounds (XI,XII).

No	R	R'	Phase transition temperatures, °C
XIa	C_3H_7	F	Cr 98 N 110 I
XIIa	C_3H_7	F	Cr 32 N 122 I
XIIb	C_3H_7	OCH_3	Cr 56 N 188 I
XIIc	C_5H_{11}	F	Cr 34 N 129 I
XIId	C_5H_{11}	OCH_3	Cr 54 N 101 I
XIIe	C_5H_{11}	C_3H_7	Cr 38 S_B 120 N 144 I

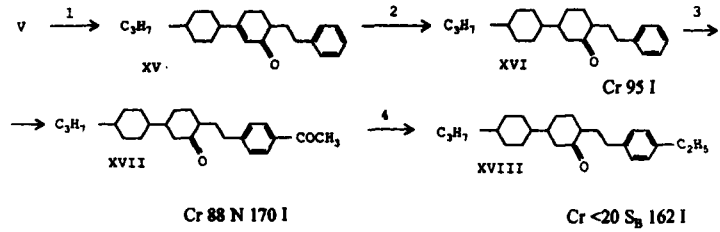
We have also made the attempt for the synthesis of polyring LC compounds having 1,2-ethylene bridge between cyclic moieties applying "cyclopropanol approach". Starting from diethyl succinate the corresponding bis-cyclopropanol has been prepared with almost quantitative yield. This compound was easily transformed into

corresponding bis-β-bromoketone which was used as the precursor of vinylketone in the condensation with 2-propylacetoacetic ester leading to bis-cyclohexenone (XIII). Unfortunately the ketone (XIII) has been prepared only with low yield (about 10%). The catalytic hydrogenation of (XIII) gave the saturated trans,trans-diketone (XIV) which has no liquid crystalline properties.



XIII XIV

The using of 2-substituted acetoacetic esters possessing substituents with ethylene bridge seems to be more promising for this purpose. Applying this approach liquid crystalline compounds (XV-XVIII) have been prepared. The carbonyl compound (XVIII) can be underwent to the further chemical transformations.



XV XVI XVII XVIII

Cr 95 I

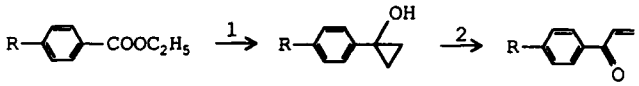
Cr 88 N 170 I Cr <20 S_B 162 I

1. $C_6H_5CH_2CH_2CH(COCH_3)COOC_2H_5$; 3 eq. KOH; dioxane;
2. H_2; Pd/C; KOH; ethanol;
3. CH_3COCl; $2AlCl_3$; methylene chloride;
4. H_2; Pd/C; CH_3COOH/THF;

It is known that cyclopropyl ring can be easily opened in reactions both with nucleophilic and electrophilic reagents. We believe that this can be applied for construction of the functionally substituted terminal side chain.

On the base of two ring esters (XIX,XX) the corresponding cyclopropanoles (XXI,XXII) have been prepared with a high yield. Bromination of (XIX,XX) followed dehydrobromination with a triethylamine gave the corresponding vinyl ketones (XXIII,XXIV) which can be underwent the further chemical transformation due to high reactivity of vinylcarbonyl moiety.

Now the investigations in this direction are in a progress.



(XIX,XX) (XXI,XXII) (XXIII,XXIV)

R = trans-4-$C_5H_{11}C_6H_{10}$- (XIX,XXI,XXIII);

R = 4-$C_5H_{11}C_6H_4$- (XX,XXII,XXIV);

EXPERIMENTAL

The structures of the prepared compounds are consistent with analytical data including H^1 NMR and mass spectra. Phase transfer temperatures were measured using a Linkam heating stage in conjugation with a polarising PZO microscope and also using a Setaram DSC 92.

1-(trans-4-Propylcyclohexyl)-1-cyclopropanol (IVa). The Grignard reagent prepared in the usual way from magnesium (6.0 g; 0.25 mole) and ethyl bromide (0.25 mole) was slowly added during 2 h

at room temperature to vigorously stirred solution of 0.1 mole of ethyl trans-4-propylcyclohexane-carboxylate and 0.02 mole (20 mol.%) of tetraisopropoxytitanium in 100 ml of dry ether. The reaction mixture having brown colour was then stirred additionally at room temperature during 1 h and decomposed with the cold 10% solution of sulphuric acid. After washing with water and drying over magnesium sulphate the solvent was removed. The prepared 1-(trans-4-propylcyclohexyl)-1-cyclopropanol just after removing of the solvent had the purity of about 95% and can be used in the next step without purification. The yield of cyclopropanol was almost quantitative.

1-(trans-4-Pentylcyclohexyl)-1-cyclopropanol (IVb) was prepared in the same way from the corresponding ester.

trans-4-Propylcyclohexyl-β-bromoethyl ketone (Va). 1-(trans-4-Propylcyclohexyl)-1-cyclopropanol prepared as described above was dissolved in 100 ml of methanol and approx. 5 ml of water was added. Then bromine (0.1 mole) was added dropwise during 15 min at room temperature. The bromine colour was disappearing continuously. Slightly coloured solution was diluted with water and the product was extracted twice with methylene chloride. The solvent was removed in vacuum and β-bromoketone was used without purification. The yield was more than 90%.

β-Bromoketones (V) should be prepared just before the further transformation. They take dark colour because of some decomposition when are stored.

3-(trans-4-Propylcyclohexyl)-6-(4-fluorophenyl)cyclohex-2-en-1-one (IXa). The prepared β-bromoketone was mixed with 4-fluorobenzyl methyl ketone (0.1 mole) and potassium hydroxide

(0.3 mole) in 150 ml of dioxane and the mixture was then refluxed under stirring during 5 h. After cooling and treatment with 10% solution of sulphuric acid (evolution of carbon dioxide takes place) the product was twice extracted with benzene. After drying over sodium sulphate and removing of the solvent the ketone was crystallised twice from ethanol. Yield 52% (isolated product); m.p. 104-105^{o}C.

The procedure used for the catalytic hydrogenation of cyclohexenones (IX) into cyclohexanones (X) was the same as already described[8].

trans-1,1-Difluoro-2-(4-fluorophenyl)-5-(trans-4-propylcyclohexyl)cyclohexane (XIa). 5-(trans-4-Propylcyclohexyl)-2-(4-fluorophenyl)cyclohexanone (6.4 g; 20 mmol) was dissolved in 100 ml of benzene and then DAST (4.8 g; 30 mmol) was added. The reaction mixture was refluxed during 10 h and after cooling was poured in aqueous solution of KOH. The organic layer was washed with water and dried over sodium sulphate. After removing of benzene the residue was dissolved in hexane and filtered through aluminium oxide layer to remove coloured impurities. The obtained crude product contained about 75% of gem-difluoroderivative (XI) and 25% of monofluoroderivative: 1-fluoro-2-(4-fluorophenyl)-5-(trans-4-propylcyclohexyl)cyclohex-1-ene. The pure analytical sample of gem-difluoroderivative was isolated by means of chromatography on silica gel using hexane as eluent. The main part of prepared product was used for the further dehydrofluorination.

1-Fluoro-2-(4-fluorophenyl)-5-(trans-4-propylcyclohexyl)-cyclohex-1-ene (XIIa). The product prepared as described above was mixed with ethylene glycol (75 ml) and KOH (1 g). The reaction

mixture was boiled under stirring and the solvent slowly distilled off (during 8-10 h). After removing of the part of solvent the residue was cooled, diluted with hexane and washed with diluted hydrochloric acid and then with water. The hexane solution was filtered through column filled with aluminium oxide or silica gel and after evaporating of solvent the residue was crystallised twice from ethanol. The yield was about 25% relating to starting saturated cyclohexanone (Xa).

3-(trans-4-Propylcyclohexyl)-6-(2-phenylethyl)cyclohex-2-en-1-one (XV). The β-bromoketone (Va) was mixed with 2-(2-phenylethyl)acetoacetic ester (0.1 mole) and potassium hydroxide (0.3 mole) in 150 ml of dioxane and the mixture was then refluxed under stirring during 5 h. After cooling and treatment with 10% solution of sulphuric acid (Take care! Evolution of carbon dioxide!) the product was extracted with benzene. After removing of solvent the ketone was crystallised from ethanol. Yield 19 g (58% after 3 stages); m.p. 57-58^{O}C.

trans-5-(trans-4-Propylcyclohexyl)-2-(2-phenylethyl)cyclohexanone (XVI). A solution of 3-(trans-4-propylcyclohexyl)-6-(2-phenylethyl)cyclohex-2-en-1-one (19 g) in 100 ml of ethanol containing potassium hydroxide (0.5 g) was hydrogenated under normal pressure in the presence of 0.4 g of 10 wt.% palladium on carbon at 30-40^{O}C with stirring until hydrogen was no longer absorbed. The catalyst was removed by filtration, the solvent was distilled off and the residue was dissolved in benzene. This solution was washed with water and dried over anhydrous magnesium sulphate. After evaporation of the solvent the residue was crystallised twice from ethanol to remove trans,cis-

isomer. The yield of trans,trans-isomer was 13.5 g (72%); m.p. 94-95°C.

trans-5-(trans-4-Propylcyclohexyl)-2-[2-(4-acetylphenyl) ethyl]cyclohexanone (XVII). trans-5-(trans-4-Propylcyclohexyl)-2-(2-phenylethyl)cyclohexanone (13.3 g, 41 mmol) in 50 ml of dry methylene chloride was added slowly to complex prepared from the acetyl chloride (45 mmol) and anhydrous aluminium chloride (86 mmol) in 100 ml of the same solvent. The temperature was not allowed to overcome 10-15°C. The reaction mixture was stirred during 2 h at 15-20°C and then was decomposed with the cold diluted hydrochloric acid. The organic layer was separated, washed with water and then dried over anhydrous magnesium sulphate. After removing of solvent the residue was dissolved in ethanol and boiled during 30 min with 1 g of charcoal and after filtering was crystallised twice from ethanol. The yield of ketone was 8.1 g (54%). This compound is liquid crystalline: Cr 88 N 170 I.

trans-5-(trans-4-Propylcyclohexyl)-2-[2-(4-ethylphenyl) ethyl]cyclohexanone (XVIII). A solution of trans-5-(trans-4-propylcyclohexyl)-2-[2-(4-acetyl-phenyl)ethyl]cyclohexanone (5 g) in 50 ml of acetic acid and THF (1:1 v/v) mixture was hydrogenated under normal pressure in the presence of 0.3 g of 10 wt.% palladium on carbon at 30-40°C with stirring until hydrogen was no longer absorbed. The catalyst was removed by filtration and the solvent was distilled off under reduced pressure. The residue was crystallised from ethanol. Yield 4.3 g (88%); Cr <20 S_B 162 I.

1-[4-(trans-4-Pentylcyclohexyl)phenyl]-1-cyclopropanol (XXI). Cyclopropanol (XXI) was prepared as described for IVa. THF

was used as the solvent instead of ether and equimolar quantity of tetraisopropoxytitanium was used. Yield 85%; m.p. 41-43 °C.

[4-(trans-4-Pentylcyclohexyl)phenyl] vinyl ketone (XXIII). Cyclopropanol (XXI) was brominated as described above for compound (V) and then treated with equimolar quantity of triethylamine in ether at room temperature. After usual procedure the ketone (XXIII) was isolated with the yield 65%; m.p. 65-66 °C.

4-Pentylbiphenyl-4'-yl vinyl ketone (XXIV) was prepared in the same way; yield 68%; m.p. 68-69 °C (from the literature m.p. 68 °C [10]).

Acknowledgments

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References

[1] V. Bezborodov, R. Dąbrowski and J. Dziaduszek, *SPIE Proc.*, **2372**, 242 (1994).
[2] V. Bezborodov, R. Dąbrowski, J. Dziaduszek, G. Sasnouski and V. Petrov, *Liq. Cryst.*, **24**, 647 (1998).
[3] G. Sasnouski, V. Bezborodov, R. Dąbrowski and J. Dziaduszek, *Mol. Cryst. Liq. Cryst.*, **303**, 313 (1997).
[4] G. Sasnouski, V. Bezborodov, R. Dąbrowski and J. Dziaduszek, *Mol. Cryst. Liq. Cryst.*, **332**, 227 (1999).
[5] Chisso Corp., EP. 120 627 (1984).
[6] K. Miyazawa and Y. Goto, *Mol. Cryst. Liq. Cryst.*, **260**, 277 (1995).
[7] O. Kulinkovich, S. Sviridov and D. Vasilevski, *Synthesis*, 1991, 234.
[8] V. Bezborodov, R. Dąbrowski, G. Sasnouski, J. Dziaduszek, J. Schirmer and P. Kohns, *Liq. Cryst.*, **21**, 237 (1996).
[9] Merck Patent GMBH, WO 95/04790.
[10] M.P. Burrow, G.W. Gray, D. Lacey, K.J. Toyne, *Liq. Cryst.*, **3**, 1643 (1988).