Synthesis and Mesomorphic Properties
of New Liquid Crystalline Cyclohexyl-phenyl- and Dicyclohexyl-pyrimidines

Alois Villiger*, Arthur Boller, and Martin Schadt
Central Research Units, F. Hoffmann-La Roche & Co., Ltd. CH-4002 Basel, Switzerland
Z. Naturforsch. 84b, 1535-1541 (1979); received April 28, 1979

Lithium Crystals, Cyclohexyl-phenyl-pyrimidines, Dicyclohexyl-pyrimidines

The synthesis and mesomorphic properties of three new classes of cyano-substituted cyclohexyl-phenyl- and dicyclohexyl-pyrimidines are reported. The compounds are colourless, chemically and photochemically stable and have wide nematic mesophases. The thermal compatibility of the new compounds with other nematic liquid crystals is excellent. The large static positive dielectric anisotropics are shown to depend strongly on the position and number of hydrogenated rings as well as on the alkyl chain lengths within a homologous series. The reported bulk viscosities vary considerably among homologues. Hydrogenating the ring adjacent to the cyano end group causes $\eta$ to increase, whereas a considerable viscosity reduction compared to nonhydrogenated homologues was found by hydrogenating the ring adjacent to the alkyl end group. The measured refractive indices of the new compounds are comparable to those of biphenyls.

The use of 2,5-disubstituted pyrimidine rings as a structural element in liquid crystals is well known. Mono- and disubstituted diphenyl pyrimidines have been studied mainly by Schubert et al. [1] and various phenyl pyrimidines have been prepared by Zaschke [2].

We have shown that in cyano-alkylphenyl- and alkyl-cyanophenyl-pyrimidines [3] as well as in diphenyl- and biphenyl-pyrimidines [4] the relative position of the permanent dipole moments of the pyrimidine and the cyano group is very important in determining the size of the dielectric constants and the mesomorphic properties. A large positive dielectric anisotropy is obtained if the contributions are additive and in this case the tendency of forming smectic mesophases is least (Type 6).

In the meantime the use of colourless liquid crystalline compounds and mixtures with lower viscosities and increased UV-stability has become more and more important. Both goals are achieved replacing p-disubstituted benzene rings by trans-1,4-cyclohexylene rings. Representatives with positive dielectric anisotropy are for example the trans-phenyl-, trans-diphenyl- and trans-biphenyl-cyclohexanes (1–3) [5] and the cyanophenyl cyclohexane-carboxylates (4) [6].

In general compounds with the cyano group attached to the cyclohexane ring show thermally less stable mesophases than those with the alkyl group bound to the cyclohexane ring. Substance 5 does not show a mesophase down to room temperature (by mixing with liquid crystalline biphenyls one can extrapolate a virtual clp. of $-25 \degree C$) [7] whereas the analogous compound 1 (R = pentyl, m = 1) has a clp. of 55 $\degree C$ [5].

Compounds of type 6 [4]* are used in commercial mixtures. We therefore synthesized the corresponding substances with hydrogenated benzene rings (classes 7, 8 and 9).

* The diphenylpyrimidines 6 are subsequently called terpyrimidines.

* Reprint requests to Dr. A. Villiger. 0340-5087/79/1100-1535/$ 01.00/0
The syntheses are outlined in Schemes 1-3. As before [3, 4] suitably substituted amidines were used as the nitrogen containing units for the construction of the pyrimidine ring, for compounds 8 and 9 starting with methyl trans-4-cyano-cyclohexanecarboxylate. They were condensed with substituted β-alkoxy acroleins yielding the tricyclic amides which in turn were dehydrated to the corresponding nitriles.

The β-alkoxy acroleins used were described earlier [4] or were built from trans-4-n-alkyl cyclohexanecarboxylic acids. In this case owing to slightly different reactivities of the compounds involved the conditions of the reactions and the reagents had to be modified in most instances. The colourless nitriles obtained showed in all classes pure nematic mesophases. No other transitions between melting and clearing point could be observed (Table I).

<table>
<thead>
<tr>
<th>R -</th>
<th>mp.°C</th>
<th>clp.°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃-</td>
<td>150.5</td>
<td>213.5</td>
</tr>
<tr>
<td>C₄H₉-</td>
<td>118</td>
<td>225</td>
</tr>
<tr>
<td>C₆H₁₃-</td>
<td>118</td>
<td>234</td>
</tr>
<tr>
<td>C₇H₁₅-</td>
<td>100.5</td>
<td>231</td>
</tr>
<tr>
<td>C₆H₁₃-</td>
<td>91.5</td>
<td>224.5</td>
</tr>
<tr>
<td>Clp.°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>150.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>119</td>
<td></td>
<td></td>
</tr>
<tr>
<td>105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Experimental

All compounds were recrystallized to constant melting point and identified by their mass, NMR and infrared spectra. Elemental analysis for C, H and N always gave satisfactory values. The given transition temperatures were determined microscopically in polarized light with a Mettler hot stage FP52 and a Mettler FP5 electronic recording apparatus. Transition temperatures were also measured with a Mettler TA2000 thermoanalyzer system which was used for the determination of the purity by the cryoscopic method. It was found that all compounds listed in Table I were at least 99.5% pure. Mass spectra were recorded on a MS9 (AEI, Manchester) spectrometer (ionizing voltage: 70 V; ion source temperature approx. 250 °C). For NMR spectra, a Varian EM 360 spectrometer (CDCl₃, TMS) was used.

trans-p-[5-(4-Pentyl-cyclohexyl)-2-pyrimidinyl]benzonitrile (7, R = C₅H₁₁, Scheme 1)

A solution of 63.9 g of trans-4-pentylcyclohexanecarboxylic acid [8] in 250 ml of dry ether is added dropwise to a stirred suspension of 12.2 g of lithium aluminium hydride in such a manner that there is gentle refluxing. After 1 h of stirring 80 ml of ethyl acetate and then 100 ml of water are added dropwise with caution. The reaction mixture is then poured on cool dilute hydrochloric acid (congored), the organic phase separated, washed successively with water, sodium hydrogen carbonate solution and dried. The trans-4-pentylcyclohexanecarbinol so obtained is used directly for the next step.

To a stirred suspension of 125 g of pyridinium chlorochromate [9] in 900 ml of methylene chloride is added a solution of 59.0 g of trans-4-pentylcyclohexanecarbinol in 100 ml of ether. After 2 h at
room temperature the mixture is diluted with 400 ml of ether, stirred for 15 min and decanted from a tarry precipitate (rinsed with ether). Filtration of the solution through a column of florisil and evaporation of the eluate gives trans-4-pentylcyclohexanecarboxaldehyde, used without further purification for the next step.

To a stirred suspension of 223.1 g of (methoxy-methyl)triphenylphosphonium chloride in 1,600 ml of ether are added 76.2 g of potassium tert-butylate. 45 min later a solution of 51.4 g of trans-4-pentylcyclohexanecarboxaldehyde in 300 ml of ether is added dropwise. After 2 h at room temperature the reaction mixture is poured in ice-water. The organic layer is separated, washed with water and dried. The crude 2-(trans-4-pentylcyclohexyl)vinylmethyl-ether is distilled at 92–96 °C/0.7 mm.

38.7 g of 2-(trans-4-pentylcyclohexyl)vinylmethyl-ether are added dropwise to a solution of 13.1 g of boron trifluoride etherate in 700 ml of distilled ethyl orthoformate, cooled in an ice bath and the reaction mixture is stirred at room temperature overnight. After dilution with 1,000 ml of toluene, washing with sodium hydrogen carbonate solution and water, drying and evaporating the solvent crude trans-4-pentylcyclohexyl malonic tetraacetal is obtained.

A stirred mixture of 57.4 g of crude trans-4-pentylcyclohexyl malonic tetraacetal, 3.5 ml of water and 150 mg of p-toluene sulfonic acid is kept 3 h at 80–85 °C. After cooling 1.6 g of sodium hydrogen carbonate are added, the reaction mixture stirred for 1½ h, diluted with ether, extracted 3 times with cold 3 N sodium hydroxide solution, washed with water and dried. The crude 3-ethoxy-2-(trans-4-pentylcyclohexyl)acrolein obtained after evaporation of the solvent is used immediately in the next step.

17.8 g of this 3-ethoxy-acrolein and 16.2 g of 4-amidinobenzoic acid amide hydrochloride are stirred in a solution of 4.8 g of sodium metal in 175 ml of methanol at 50 °C overnight under nitrogen. After cooling the yellow suspension is treated with 55 ml of 3 N hydrochloric acid, filtered, washed with water and dried. The crude brownish trans-p-[5-(4-pentylcyclohexyl)-2-pyrimidinyl]benzamide is used in the next step.

A stirred suspension of 17.2 g of crude amide in 150 ml of pyridine is treated with 9.5 ml of benzene sulfonic acid and kept at 55 °C for 6 h. The reaction mixture is poured on cold diluted hydrochloric acid, extracted with methylene chloride and the organic layer washed successively with hydrochloric acid, sodium hydrogen carbonate solution and water. After drying and evaporating the solvent the crude trans-p-[5-(4-pentylcyclohexyl)-2-pyrimidinyl]benzonitrile is chromatographed on a column of 600 g of silica gel with toluene/5% acetone. The pure fractions are combined, dissolved in hexane, treated with charcoal and recrystallized from hexane (yield 11.8 g); m.p. 100.5 °C, clp. 231 °C.

UV (EtOH) $\lambda_{\max}$ (ε): 268 sh (31,900),
276 (33,300),
288 sh (20,500).

NMR:
$\delta$ 8.71 (2, s),
8.56 (2, d, $J = 8.5$ Hz),
2.85–2.2 (1, m),
2.2–0.7 (20, m),
7.78 (2, d, $J = 8.5$ Hz).

MS m/e (%):
333 (M+, 100),
304 (11),
290 (7),
271 (14),
221 (23),
207 (33),
194 (32),
128 (34).

C$_{22}$H$_{27}$N$_{3}$

<table>
<thead>
<tr>
<th>Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 79.24</td>
<td>79.28</td>
</tr>
<tr>
<td>H 8.16</td>
<td>8.06</td>
</tr>
<tr>
<td>N 12.60</td>
<td>12.75</td>
</tr>
</tbody>
</table>

trans-4-[5-(p-Heptylphenyl)-2-pyrimidinyl]cyclohexanecarbonitrile (8, $R = C_7H_{15}$, Scheme 2)

Dry hydrogen chloride is passed into a solution of 96.6 g of methyl trans-4-cyanocyclohexanecarboxy-
cooling to room temperature and removal of the ammonia the reaction mixture is evaporated, the residue suspended in ether, filtered and washed with ether. The crude trans-4-carbamoylcylohexane-carboxamidinehydrochloride is recrystallized from methanol (yield 68.3 g).

12.6 g of crude 3-ethoxy-2-(trans-4-heptylphenyl)-acrolein [4] and 9.9 g of trans-4-carbamoylcylohexane-carboxamidine hydrochloride are stirred in a solution of 3.2 g of sodium metal in 125 ml of methanol overnight at 50 °C under nitrogen. After cooling the yellow suspension is treated with diluted hydrochloric acid, filtered, washed with water and dried. For purification the sparingly soluble trans-4-[5-(p-heptylphenyl)-2-pyrimidinyl]cylohexancarboxamide is refluxed with ether.

A stirred suspension of 10.8 g of the amide in 150 ml of pyridine is treated with 6.0 ml of benzene sulfochloride and kept 2 h at 55 °C. The reaction mixture is poured on ice water, extracted with methylene chloride and the organic layer washed with hydrochloric acid, sodium hydrogen carbonate solution and water. After drying and evaporating the solvent the crude trans-4-[5-(p-heptylphenyl)-2-pyrimidinyl]cylohexancarbonitrile is chromatographed on a column of 300 g of silica gel with toluene/5% acetone. The pure fractions are combined, dissolved in hexane, treated with charcoal and recrystallized from hexane (yield 9.3 g); m.p. 83.5 °C, clp. 160 °C.

UV (EtOH) \( \lambda_{\text{max}}(\epsilon) \): 258 (21,100).

NMR:
\[
\begin{align*}
\delta & \quad \text{8.86 (2, s),} \\
& \quad 7.65-7.15 (4, m), \\
& \quad 3.0 (1, br m), \\
& \quad 2.68 (2, br t, J = 7 Hz), \\
& \quad 2.5-0.7 (22, m).
\end{align*}
\]

MS \( m/e \) (%):
361 (M+, 100),
307 (21),
295 (27),
281 (61),
268 (26),
196 (13),
115 (14).

C\(_{24}\)H\(_{31}\)N\(_3\)
Calcd C 79.73 H 8.64 N 11.62,
Found C 79.63 H 8.63 N 11.42.

Dielectric Constants
The measuring apparatus used to determine the static dielectric constants (at \( f = 1592 \text{ Hz} \)) was described earlier. Figures 1-4 show the dependence of the dielectric constants \( \epsilon_{||} \) and \( \epsilon_{\perp} \) measured parallel and perpendicular to the long molecular axis respectively on reduced temperature \( T/T_c \). The
measurements depicted in Fig. 1 were made within the homologous series of hydrogenated terpyrimidines \( (8) \), denominated TP\(_3\)H\(_1\)X. (The index in \( H_1 \) indicates the position of the hydrogenated ring with respect to the cyano end group (Fig. 1), whereas the index in \( P_3 \) refers to the position of the pyrimidine nitrogens with respect to the cyano end group.) Measurements made within the homologous series \( 7 \), denominated TP\(_3\)H\(_3\)X, where the third ring is hydrogenated, are shown in Fig. 2. Due to the large nematic-isotropic transition temperatures \( T_c \) (Table I) of this series the measurements could not be extended into the isotropic phase. The measurements of Fig. 3 were made with dicyclohexylpyrimidines \( (9) \), denominated DCHP\(_3\)X.

Comparing Figs. 1–3 shows that \( \varepsilon_\perp \) does not vary much within the homologous series as well as between the three classes of compounds (\( \varepsilon_\perp \approx 5 \approx \varepsilon_\parallel \) constant). However, \( \varepsilon_\parallel \) was found to depend strongly on the length of the alkyl chains and to a lesser extent also on the position and number of hydrogenated rings. The dependence of \( \varepsilon_\parallel \) on chain length at a given reduced temperature is largest in short chain representatives of the type TP\(_3\)H\(_1\)X (Fig. 1), followed by TP\(_3\)H\(_3\)X and DCHP\(_3\)X (Figs. 2, 3). The dielectric anisotropy \( \Delta \varepsilon = (\varepsilon_\parallel - \varepsilon_\perp) \) of TP\(_3\)H\(_1\)X for \( X \leq 4 \) is 20–30\% larger than the corresponding values of \( \Delta \varepsilon \) of the other two series. \( \Delta \varepsilon \) (TP\(_3\)H\(_3\)X) is comparable to \( \Delta \varepsilon \) (DCHP\(_3\)X).

For comparison Fig. 4 shows measurements of the temperature dependence of \( \varepsilon_\parallel \) and \( \varepsilon_\perp \) of the nonhydrogenated terpyrimidine TP\(_3\)4 (\( R = C_4H_9 \)) and the terphenyl T15 respectively. The data show
that $\Delta \varepsilon$ of TP$_4$ is $\sim$15\% lower than $\Delta \varepsilon$(TP$_3$H$_4$) (Figs. 1, 4). $\Delta \varepsilon$(T15) < $\Delta \varepsilon$(TP$_3$H$_4$) < $\Delta \varepsilon$(TP$_4$) was found for the dielectric anisotropy of TP$_3$H$_4$. However, short chain molecules of the homologous series TP$_3$H$_X$ with their large dielectric anisotropies have – in contrast to the terpyrimidine or terphenyl series – still large mesomorphic ranges. Thus TP$_3$H$_2$ whose $\Delta \varepsilon$ is comparable to $\Delta \varepsilon$(TP$_4$) (Figs. 2, 4) can be used instead of TP$_4$ in applications requiring large dielectric anisotropies, whereas at the other end of the series the dielectric properties of TP$_3$H$_7$ are comparable to those of T15.

**Viscous and birefringence properties**

The dependence of the bulk viscosity $\eta$ of single components on temperature could not be measured with our rotating cone Brookfield microviscometer because of their high melting temperatures. To lower the melting temperatures towards room temperatures, where viscosity data of other liquid crystal classes are available [11] for comparison, binary mixtures were made. The binary mixtures A = (TP$_3$H$_5$, TP$_3$H$_7$), B = (TP$_3$H$_5$, TP$_3$H$_7$), and C = (DCHP$_5$, TP$_3$H$_7$) contained each a pentyl and a heptyl component in molar proportions 40\%, 60\%. For comparison with known three-ring compounds the viscosities of the binary mixtures (TP$_4$, TP$_3$H$_7$), E = (TP$_3$H$_2$, TP$_3$) and F = (T15, TP$_3$H$_7$) in the same molar proportions, i.e. (40\%, 60\%) were also investigated. The measured temperature dependences $\eta$(T) of the mixtures are depicted in Fig. 5. Comparing graphs B and F in Fig. 5 shows that the bulk viscosity of TP$_3$H$_5$ is comparable to the viscosity of T15. As viscosity decreases with decreasing alkyl chain length $\eta$(TP$_3$H$_2$) < $\eta$(T15) can be assumed. Fig. 5 indicates that the viscosity of compounds TP$_3$H$_2$X is lowest among the three new LC-classes (A, B and C in Fig. 5). This shows that the viscosity of hydrogenated compounds depends strongly on the position and the number of the hydrogenated rings in the molecule. The measurements indicate that hydrogenation the ring adjacent to the cyano end-group increases the viscosity considerably, whereas hydrogenation of the ring adjacent to the alkyl end-group lowers $\eta$ compared to nonhydrogenated homologues (cf. A, B, C, D in Fig. 5). This finding is in agreement with $\eta$(DCHP$_3$X) for which $\eta$(TP$_3$H$_3$X) < $\eta$(DCHP$_3$X) < $\eta$(TP$_3$H$_1$X) was found. A comparison between graphs B, D and E in Fig. 5 shows that the viscosity of TP$_4$ is considerably larger than $\eta$ of TP$_3$H$_3$X compounds. Table II gives a summary of the viscous and dielectric data of mixtures A till F measured or extrapolated from Figs. 1–5 to T = 60 °C. Table II also shows the melting and clearing temperatures $T_m$, $T_c$ of the binary mixtures A–F made at T = 60 °C = constant.

<table>
<thead>
<tr>
<th>LC</th>
<th>$\varepsilon_1$</th>
<th>$\Delta \varepsilon$</th>
<th>$\eta$ (cp)</th>
<th>$T_m$ [°C]</th>
<th>$T_c$ [°C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4.80</td>
<td>19.80</td>
<td>84.0</td>
<td>63</td>
<td>165</td>
</tr>
<tr>
<td>B</td>
<td>4.20</td>
<td>17.20</td>
<td>30.6</td>
<td>67</td>
<td>222</td>
</tr>
<tr>
<td>C</td>
<td>4.20</td>
<td>16.90</td>
<td>38.5</td>
<td>57</td>
<td>198</td>
</tr>
<tr>
<td>D</td>
<td>4.05</td>
<td>19.20</td>
<td>38.5</td>
<td>86</td>
<td>228</td>
</tr>
<tr>
<td>E</td>
<td>3.74</td>
<td>15.26</td>
<td>55.0</td>
<td>70</td>
<td>236</td>
</tr>
<tr>
<td>F</td>
<td>3.74</td>
<td>15.26</td>
<td>28.6</td>
<td>43</td>
<td>219</td>
</tr>
</tbody>
</table>

Table II. Measurements of the static dielectric constants $\varepsilon_1$, $\Delta \varepsilon = (\varepsilon_\parallel — \varepsilon_\perp)$, the bulk viscosity $\eta$ and the melting and clearing temperatures $T_m$, $T_c$ of the binary mixtures A–F made at T = 60 °C = constant.

Fig. 5. Temperature dependence of the bulk viscosity of the binary mixtures.

A = (TP$_3$H$_5$, TP$_3$H$_7$), D = (TP$_4$, TP$_3$H$_7$), B = (TP$_3$H$_5$, TP$_3$H$_7$), E = (TP$_3$H$_2$, TP$_3$), C = (DCHP$_5$, TP$_3$H$_7$), F = (T15, TP$_3$H$_7$), having molar ratios (40\%, 60\%).
The values found for $\Delta n$ are comparable to those of biphenyls [11] as expected from the two conjugated aromatic rings in each class which primarily determine the birefringence properties.

The authors would like to thank H. R. Saladin, R. Mory, A. Germann and G. Daub, who carried out the experimental chemical work. We also thank R. Ayer and B. Blöchliger for the performance of the dielectric measurements. We are greatful to B. Halm and F. Wild for the measurements of the thermoanalytical data. We thank W. Meister, W. Vetter and W. Arnold for the discussion of the NMR and mass spectra. Microanalyses have been carried out under the supervision of A. Dirscherl.


