Perhydroazulenes – A New Class of Liquid Crystalline Materials

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Received 31 January 2011

Abstract: A new class of mesogenic compounds, the perhydroazulenes, carrying substituents in their *para* positions (HAZ derivatives), has been synthesized. The new liquid crystalline materials display a broad enantiotropic nemantic mesophase slightly above room temperature without any additional smectic phase. Their physical properties reveal that the perhydroazulene moiety can replace the currently often used cyclohexyl and biscyclohexyl units in liquid crystalline materials.

Key words: liquid crystals, perhydrogenated azulenes, nematic materials, electrooptical displays

The chemistry of tailor-made thermotropic nematic liquid crystalline (LC) materials for optoelectronic applications is at present largely focused on rod-like molecules possessing a core unit of six-membered cycloaliphatic and/or aromatic systems of two or three rings bearing polar and/ or nonpolar substituents R at the head or tail, as symbolized in the general structure **1**.



Figure 1 Classical thermotropic nematic LC materials 1, and the compounds reported herein (2)

The isotropic and anisotropic physical properties that determine the optoelectronic behavior of such molecules, viz. their chemical, optical, and thermal stability, their LC mesophases, nematic temperature range, dielectric and optical anisotropy, their viscous and elastic constants, are governed by linkage, ring combinations, and by longitudinal and lateral substituents with a single bond, an ethano group (-CH₂CH₂-), and a CF₂O moiety as the preferred linking group Z. Propyl, ethoxy, and fluorine-containing groups often serve as R groups. Furthermore, the properties of these LC materials depend on the ring size and length-to-width ratio of the core unit. We were therefore interested in the changes caused by a replacement of a cyclohexyl unit by the broader and longer perhydroazulene (HAZ) nucleus as illustrated by formula **2** (Figure 1).

SYNLETT 2011, No. 9, pp 1273–1276 Advanced online publication: 05.05.2011 DOI: 10.1055/s-0030-1260551; Art ID: B03011ST © Georg Thieme Verlag Stuttgart · New York Our preliminary investigations had indeed revealed that incorporation of the HAZ unit does lead to a novel class of LC materials with suitable properties for the preparation of novel multicomponent LC mixtures.¹ However, the extension of this concept called for a scalable, practical, and economic synthesis of a common advanced intermediate, which subsequently could be converted into a great variety of LC molecules. This intermediate is the *cis*-fused ketoacetal **9**, which was prepared as described in Scheme 1, and whose carbonyl groups at either end of the molecule could act as handles for further functionalization.



Scheme 1 Synthesis of the perhydroazulene dione derivative 9. *Reagents and conditions*: a) Mg, r.t., then HCO₂Et, 0 °C, Et₂O, 89%; b) Jones reagent (2.67 M), acetone, 0 °C, 98%; c) ethyleneglycol, PTSA·H₂O (cat.), benzene, reflux, 99%; d) Grubbs I (2 mol%), DCE, 40 °C, 30 h, 93%; e) MCPBA, CH₂Cl₂, 0 °C, 91%; f) allylmagnesium bromide, THF, 50 °C, 4 h, 82%; g) pyridinium chlorochromate, CH₂Cl₂, 0 °C, 91%; h) O₂, PdCl₂ (0.25 equiv), CuCl (1 equiv), DMF– H₂O (6:1), r.t., 81%; i) KOH, MeOH–H₂O, 65 °C, 90%; j) H₂, Pd/C, EtOAc, r.t., 99%.

Double addition of the Grignard reagent generated from 3^2 to ethyl formate afforded the dienol, which was oxidized with Jones reagent to furnish correspondent ketone in excellent yield.³ The ketone functionality was then converted into the dioxolane 4 under standard conditions, and the latter was then subjected to ring-closing metathesis using the Grubbs first-generation catalyst to afford the cycloheptenone derivative **5** in excellent yield. For the

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elaboration of 5 to the bicyclic system, an epoxidation reaction of the alkene was carried out first using m-chloroperbenzoic acid to furnish the epoxide 6.4 Nucleophilic ring opening of the epoxide by allylmagnesium bromide was employed for the introduction of the remaining carbon atoms that would be present in the target. The mixture of alcohols was subsequently oxidized in excellent yield to the corresponding ketone 7 using PCC as the oxidant. The allyl group was then converted into the methyl ketone 8 via a Wacker oxidation reaction. The stage was now set for an intramolecular aldol reaction, which was carried out by warming a solution of the bisketone in aqueous methanol in the presence of potassium hydroxide to furnish the bicyclic enone in excellent yield. Catalytic hydrogenation of the latter afforded the perhydroazulene derivative 9 in almost quantitative yield. Gratifyingly, hydrogenation of the enone double bond proceeded with complete stereoselectivity, generating only the required *cis*-isomer of 9.5 The stereoselectivity of the reduction is presumably the result of hydrogenation occurring from the more accessible convex face of the bicyclic enone. The structure and stereochemistry was confirmed by single-crystal X-ray analysis of 9 (see Figure 2). In summary, the perhydroazulene dione derivative 9 was synthesized from 4-bromobutene (3) in ten steps with an overall yield of 40% (Scheme 1).

Having generated sufficient quantities of 9, we set about synthesizing potentially LC derivatives by sequentially functionalizing the keto groups on both ends of 9. Our initial targets were HAZ derivatives that possessed an n-propyl chain on the five-membered ring and a fluorinated phenyl ring on the cycloheptane half of the molecule (Scheme 2). A highly efficient Wittig reaction of 9, employing the reagent generated from *n*-propyl bromide, furnished the semicyclic olefin. Catalytic hydrogenation next produced the ketal 13 in quantitative yield with complete stereoselectivity. As a result of the *cis* fusion of the rings, the perhydroazuelene system adopts a bent geometry, which favors the approach of the reducing agent from the more accessible convex face of the molecule. Similar instances of excellent stereochemical control resulting from the topology enforced by cis fusion of bicyclic systems



Figure 2 The stereochemistry of 9 as determined in the solid state

are well documented, especially in *cis*-decalin derivatives.⁶ The keto group of the seven-membered ring of **13** was then unmasked via acid hydrolysis to furnish the unprotected ketone.

Introduction of a fluorinated phenyl ring onto the cycloheptane half of the molecule required the generation of suitably functionalized aryllithium reagents. Commercially available phenol 10 was alkylated using dimethyl sulfate or diethyl sulfate (to 11 and 12, respectively), and a lithium-bromine exchange and subsequent addition of the corresponding aryllithium species to the ketone furnished the alcohols 14 and 15 in good yield. To complete the synthesis, an elimination-hydrogenation sequence was carried out on these benzylic alcohols. Acid-catalyzed dehydration resulted in the formation of corresponding styrenes, catalytic hydrogenation of which was finally carried out to furnish the target compound 16 in excellent yield. The reduction afforded a mixture of two epimeric compounds (ratio 3:2), which were separated by preparative HPLC. The structure and stereochemistry of the major product⁷ was confirmed by single-crystal X-ray analysis to be the *anti* derivative as shown in Figure 3. The structure of its syn isomer was also established by single-crystal X-ray crystallography. This derivative, however, did not display any mesogenic properties.

Today nematic LC are applied on a large scale in thin-film transistor-driven LC displays (TFT-LCD), which function as electrooptical shutters or light valves in flat TV screens, PC monitors, and numerous other types of information displays.⁸ The switching properties of these displays are mainly governed by the dielectric anisotropy $\Delta \varepsilon = \varepsilon_{\text{parallel}}$



Scheme 2 Synthesis of the LC compound 16. *Reagents and conditions*: a) *n*-PrPPh₃Br, KO*t*-Bu, THF, 0 °C, 99%; b) H₂, Pd/C, EtOAc, r.t., 99%; c) 2 M aq H₂SO₄, THF, 40 °C, 97%; d) 11 or 12, *n*-BuLi, Et₂O, -78 °C; e) PTSA·H₂O (cat.), benzene, reflux, 91% (R = Me), 94% (R = Et); f) H₂, Pd/C, EtOAc, r.t., 97%; g) preparative HPLC.

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Figure 3 The structure of *anti*-16 (R = Et) in the solid state

 $-\epsilon_{perpendicular}$, the birefringence $\Delta n = n_{parallel} - n_{perpendicular}$, and the anisotropic elastic and viscous constants of the LC used. In the case of technically applied nematic LC mixtures these parameters should be at room temperature in the range of $\Delta \varepsilon = +5$ to +6 and of $\Delta n = 0.09$ to 0.10 for twisted nematic displays (TN LCD), in the range of $\Delta \varepsilon = -3$ to -5 and of $\Delta n = 0.08$ to 0.12 for vertically and for polymer-stabilized vertically aligned displays (VA and PS-VA LCD), and in the range of $\Delta \varepsilon = +8$ to +12 and of $\Delta n = 0.08$ to 0.10 for in-plane-switching displays (IPS LCD).⁹ For all display types the elastic constants splay (k11), twist (k22), and bend (k33) of the molecules, which depend on the width-to-length ratio and on the substituents of the core as well as the viscosity v, or more precisely the three scalar viscosity coefficients η_1 , η_2 , and η_3 , and especially the rotational viscosity γ_1 , which shorten the turn-on and turn-off time of a LC display, should be small or at least as low as possible.¹⁰ Based on these considerations on structure-property correlations and on long stretched, potentially mesomorphic molecular structures, dielectrically 'neutral' ($\Delta \varepsilon = ca. \pm 0$), dielectrically 'positive' ($\Delta \varepsilon > 0$), and dielectrically 'negative' ($\Delta \varepsilon < 0$) hydroazulenes were synthesized from 9 based on the strategy summarized in Scheme 2. Some of them and their mesorange (melting and clearing points) are listed in Table 1 ($C_3 = 1$ -propyl; $C_5 = 1$ -pentyl).

 Table 1
 Structure and Mesorange Data of Selected para-Substituted Nematic Perhydroazulene Derivatives^{a,b}



$$C_5$$
 C_5 C_1 $C_7 = 63, N = 95, I$

$$\Delta \varepsilon > 0$$

$$C_3$$
 F $Cr = 35, N = 45, I$

$$C_3$$
 F $Cr = 6, N = 14, D$

$$C_3$$
 — $C_7 = 50,$
N = 99, I

Table 1 Structure and Mesorange Data of Selected *para*-Substitut-ed Nematic Perhydroazulene Derivatives^{a,b} (continued)

$$C_5$$
 — C_5 — C_7 — C_7

$$C_5$$
 — C_5 — C_7 = 43.5, $N = 154, I$

$$C_3$$
 — COO — CN $Cr = 80, N = 170, I$

$$C_5$$
 — COO – CN $Cr = 43, N = 154, I$

$$C_3$$
 — COO — CN $Cr = 95, N = 267, I$

 $\Delta \varepsilon < 0$







$$C_5$$
 C_5 $C_7 = 48,$
 $N = 70, I$

$$C_5$$
 OEt $Cr = 88, N = 121, I$

^a Cr: melting point = transition of solid to LC state or solid to isotropic liquid.

^b N: clearing point = transition from nematic LC to isotropic liquid phase (I) between N and I: nematic phase temperature range.

In Table 2 the (virtual) physical properties at room temperature (22 °C) of compound **16** are compared with data of two homologous phenylcyclohexane counterparts currently used in LC mixtures for VA-displays. $\Delta\epsilon$ -, Δ n-, and γ_1 -values – determined under identical conditions – are extrapolated from a solution of 10% of the compound in the nematic matrix ZLI-4792 (Merck). The measurement methods applied for the evaluation of the isotropic and anisotropic physical properties mentioned above are as described by Klasen and Götz, Tarumi and Heckmeier,¹⁰ and Goulding et al.¹¹

As these data demonstrate, *para*-disubstituted hydroazulenes (HAZ derivatives) are a new class of liquid crystals. The derivatives so far investigated exhibit a surprisingly broad enantiotropic nemantic mesophase slightly above room temperature without any additional smectic phase. Molecules with a phenylperhydroazulene core unit show

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Structure	OEt F C ₃ H ₇	OEt F C₃H ₇	PEt F C ₃ H ₇
Mesorange (°C)	Cr = 71, N = 114, I	Cr = 60, I	Cr = 79, SmB (78), N = 178
$\Delta\epsilon^{a}$	-6.6	-6.6	-6.4
$\Delta n^{\rm b}$	0.0968	0.0760	0.1108
$\gamma_1 [mPas]^c$	293	78	413

 Table 2
 Selected Physical Properties of Analogous LC Perhydorazulene, Cyclohexyl, and Biscyclohexyl Derivatives

^a $\Delta \varepsilon$ = dielectric anisotropy as defined in the text.

^b Δn = optical anisotropy or birefringence as defined in the text.

 $^{c} \gamma_{1}$ = rotational viscosity, an anisotropic viscosity parameter.

hexyl derivatives as well as three-ring derivatives with two cyclohexyl rings but with improved nematogenic behavior. Because of this combination of properties in only one molecular entity the new mesomorphic HAZ derivatives represent a real extension of the classes of LC materials presently known. Dielectrically 'neutral' LC molecules are generally substances with a relatively low viscosity. Therefore they are used as additives in dielectrically 'positive' as well as 'negative' multicomponent nematic mixtures to shorten the response times of LCD. In contrast to the enantiotropic purely nematic, low viscous, and low-melting dielectrically 'neutral' perhydroazulenes, the concentration of which is not restricted in a nematic LC mixture, the corresponding low-viscous and low-melting cyclohexyl derivatives used today, are often isotropic or monotropic nematic. Thereby they decrease the clearing point, that is, the upper temperature limit for technical applications of a LC mixture. In order to compensate for this effect, a high-clearing biscyclohexyl component is required to achieve a sufficiently broad nematic phase again. In contrast to their hydrazulene analogues such biscyclohexyl derivatives generally possess an additional smectic phase. As a consequence they show limited solubility in a nematic matrix and impair the electrooptical properties, mainly the response times at lower temperatures. These negative properties restrict the role of both in a mixture, requiring the addition of more singular components. This is one of the reasons why 'LC compositions' often consist of more than 15 substances to meet the physical and electrooptical display specifications. By our new class of thermally and light-stable, purely nematic, and relatively low-viscous LC hydrazulenes it may be possible to reduce this high compound complexity of actual LC mixtures for flat-screen information technology.

Further studies on anisotropic molecular parameters and structure–property correlations in the case of mesomorphic 2,6-disubstituted perhydroazulenes as well as a shorter synthetic route to the crucial intermediate **9** are under way.

Acknowledgment

We thank the Alexander von Humboldt Stiftung and the Fonds der Chemischen Industrie for support of this work and Prof. Dr. S. Laschat (University of Stuttgart) for DSC and POM measurements of our mesogenic materials and Prof. H. Finkelmann (University of Freiburg) for DSC measurements and phase assignments. Analytically pure compounds were isolated by Fischer Analytics (Bingen) using various HPLC techniques.

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