Liquid Crystalline Phases of Simple Polyene Schiff Bases

Mieng-Hua Wann and Gerard S. Harbison*

Department of Chemistry
State University of New York
Stony Brook, New York 11794
Received September 6, 1988

Thermotropic liquid crystals are materials of great scientific and technological importance.[1] Many diverse classes of molecules exhibit thermotropic mesophases;[2-5] these molecules share the properties of being highly anisotropic (and frequently rod shaped), polar, and rigid to a greater or lesser degree. As might be expected, therefore, the majority of synthetic liquid crystals have one or several aromatic rings and are of relatively high molecular weight (more than 200 Daltons). We have recently discovered that the Schiff bases of simple polyene aldehydes exhibit liquid crystalline phases at temperatures close to ambient; these have the lowest molecular weights of any simple monomeric organic liquid crystals yet reported.

The new liquid crystals are condensation products of the polyene aldehyde 2,4,6-octatrienal[6] and straight-chain aliphatic amines $C_nH_{(2n+1)}NH_2$. The Schiff bases were formed by combination of equimolar quantities of the aldehyde and amine in acetonitrile at room temperature; they precipitated from solution within 5 min. They were readily purified by vacuum sublimation, which if necessary was repeated until consistent and narrow (half-width less than 2°) phase transitions were obtained by differential scanning calorimetry (DSC). The compounds were also characterized by solution and solid-state NMR spectroscopy. In appearance the crystalline materials are white to off-white platelets, which tend to discolor on exposure to light and air but are stable for months under nitrogen at −20 °C.

The Schiff bases formed from propylamine up to at least nonylamine pass through viscous fluid anisotropic phases on heating, before clearing to isotropic liquids. Measurements of the phase transition temperatures were made by DSC and confirmed by optical microscopy through crossed polarizers on a microscope hot-stage melting point apparatus. The transition to the mesophase on raising the temperature is usually rather difficult to observe microscopically, since the microcrystalline aggregates retain their shape on a slide until pressure is applied to the cover slip, upon which viscous flow is observed. However, the expected endothermic crystalline-smectic transition is observed calorimetrically. On cooling from the clearing point on the microscope hot-stage, characteristic "palm frond", "fan", and occasional "Maltese-cross" textures are obtained. The observed textures are very similar for all of the C_4 to C_{10} amine Schiff bases and persist unaltered until crystallization commences; the mesophases often supercool up to 25 °C below the true melting point. Repeated heating and cooling result in some decomposition of the sample and was therefore avoided.

The phase transition temperatures for compounds of alkyl chain length C_1–C_{10} are plotted in Figure 1. The methylamine and ethylamine Schiff bases melt directly to an isotropic phase and no mesomorphism is observed. The propylamine Schiff base melts to a smectic phase with a very narrow temperature range, which is readily observed via DSC but is almost invisible microscopically. On cooling on a glass slide, a transition to a pseudoisotropic (homeotropic) presumably smectic liquid-crystalline phase (Figure 1) is observed; the texture of this phase is markedly different from those of the higher homologues of the series; the mesophase could usually be supercooled to at least 10 °C below its nominal transition temperature. For the higher homologs, the width of the

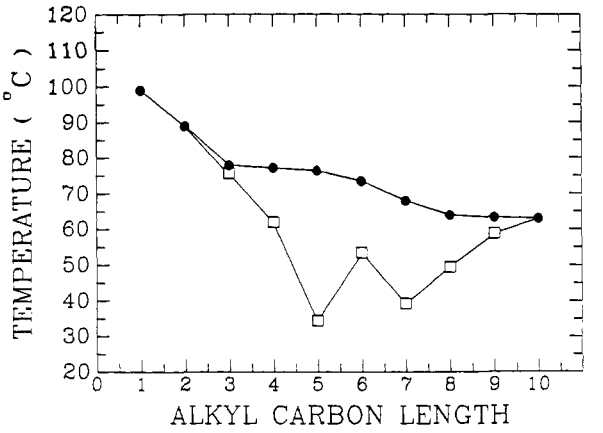

Figure 1. Melting and clearing points for the Schiff bases formed between 2,4,6-octatrienal and aliphatic amines and the phase transition temperatures being plotted against number of carbons in the aliphatic chain: (□) crystalline–smectic transition temperature and (●) crystalline/smectic–isotropic transition temperature.

liquid-crystalline phase at first increases with chain length (Figure 1) and then narrows again; the decylamine Schiff base melts directly to an isotropic phase but shows a monotropic smectic phase on cooling. The general dependence of the phase transition temperatures is reminiscent of that observed in the alkylbenzoic acids;[2] for example, a marked odd–even chain-length dependence is observed for the melting points but not for the clearing points. Both the textures and the viscosity of the materials are characteristically smectic and are consistent with a simple smectic A structure; no evidence for nematic phases or smectic–smectic phase transitions could be observed from the textures.

As part of our efforts to understand the structure of these materials, we have synthesized butylamine Schiff bases both specifically deuterated on the α position of the alkyl residue and perdeuterated on the alkyl chain. Solid-state NMR spectra have been obtained for both of these compounds as a function of temperature. Below the melting point we observe, for the 1,1′-d_2 derivative, a Pake doublet with a splitting of 117 kHz and a T_1 of approximately 5 s, consistent with an essentially immobile methylene residue. The perdeuterated compound shows two splittings of 38 and 121 kHz, attributed, respectively, to the three methyl and six methylene deuterons on the alkyl chain. Above the clearing point we observe the expected isotropic spectrum. The spectrum obtained for the 1,1′-d_2 Schiff base in the smectic phase at 63 °C is shown in Figure 2b. A Pake doublet splitting of 38.8 kHz is observed, reduced by about a factor of 3 from the rigid lattice value. The perdeuterated Schiff base (which was somewhat less pure) under the same conditions shows three splittings of 38.8, 16.6, and 11.9 kHz and a strong central line; we tentatively assign the two smaller splittings to the β and γ deuterons, respectively, and we believe the central peak is a combination of an unresolved methyl group splitting, presumably due to a very low-order parameter for the methyl group C_3 axis and isotropic impurities. The largest splitting (for the α position) is consistent with motional narrowing via rotation of the C–D bond axis approximately perpendicular to the molecule long axis, combined with some additional segmental mobility. The C-2 and C-3 splittings are probably further reduced by segmental mobility, presumably trans–gauche isomerization. These preliminary deductions are consistent with an expected molecular structure based on standard bond lengths and angles. The line shape indicates that the liquid crystalline domains do not spontaneously align in the magnetic field, at least on a time scale of hours; this is typical of smectic phases.

These compounds are among the simplest organic liquid crystals yet discovered. While nona-2,4-dienoic acid[7] and other dienoic acids have also been reported to exhibit a smectic phase, they actually exist as head-to-head dimers in the mesophase, and therefore their effective molecular weights are almost twice those of our compounds, which are almost certainly monomers. Because

(1) Review: *Liquid Crystals: The Fourth State of Matter*; Saeva, F. D., Ed.; Marcel Dekker: New York, 1979.
(2) Weygand, C.; Gabler, R. *J. Phys. Chem.* **1939**, *B46*, 270.
(3) Kelker, H.; Scheurle, B. *Angew. Chem.* **1969**, *81*, 903.
(4) Reinitzer, F. *Monatsch. Chem.* **1888**, *9*, 421.
(5) Chandrasekhar, S. *Mol. Cryst. Liq. Cryst.* **1981**, *63*, 171.
(6) Preparation: D'Amico, K. L.; Manos. C.; Christensen, L. *J. Am. Chem. Soc.* **1980**, *102*, 1777.

0002-7863/89/1511-7273$01.50/0

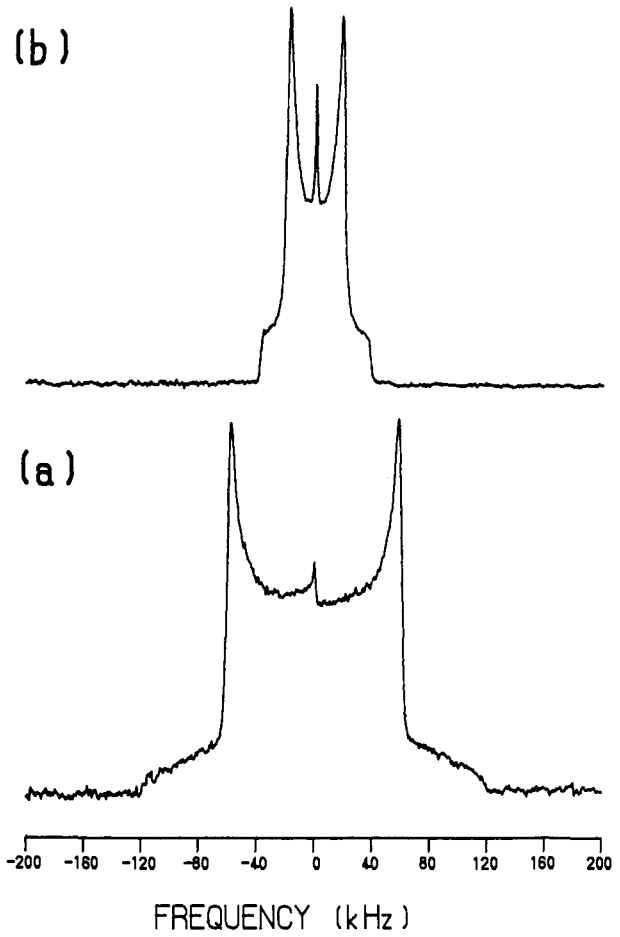

Figure 2. Deuterium NMR spectra of 200 mg of the Schiff base *N*-butyl-*1,1'-d*$_2$-2,4,6-octatrienylideneimine (a) in the crystalline phase at 30 °C and (b) in the smectic phase at 63 °C. Spectra were obtained at a field of 7.1 T (^{2}H frequency 46.3 MHz) by using a quadrupole echo pulse sequence with a 46-μs echo delay and a 2.5-μs $\pi/2$ pulse. Recycle delays were 20 s for the crystalline sample and 0.4 s for the liquid crystal. Line broadening of 1 kHz was applied to the former and 100 Hz to the latter spectrum; total transients accumulated were 1440 for (a) and 4096 for (b).

of their simple molecular structure, the polyene Schiff bases are therefore likely to be of some importance for the understanding of liquid crystalline phases in general. Polyenes and polyene Schiff bases are also of considerable theoretical interest in themselves, as oligomeric models for conjugated polymers, and are central to the mechanism of vision[8] and to the operation of the proton pump bacteriorhodopsin;[9] the existence of readily accessible anisotropic phases should facilitate the determination of the structures and the understanding of the spectroscopy of such compounds. Such studies are in progress.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, Grant number 19107G7, for partial support of this research. Support was also obtained from the National Institutes of Health (GM-39071) and the National Science Foundation Materials Research Initiative (DMR-8706432). We thank Wei-Jyun Chien for assistance with the spectroscopy, Pei Tang for her help with the figures, and P. J. Herley for assistance with the DSC.

Supplementary Material Available: DSC traces for the Schiff bases of 2,4,6-octatrienal with *n*-alkylamines of chain length 3–10, respectively (3 pages). Ordering information is given on any current masthead page.

(7) Weygand, C.; Gabler, R.; Hoffmann, J. *J. Phys. Chem.* **1941**, *B50*, 124.
(8) Wald, G. *Science (Washington, D.C.)* **1967**, *162*, 230.
(9) Schreckenbach, T.; Walckhoff, B.; Oesterhelt, D. *Eur. J. Biochem.* **1977**, *176*, 499.

Biosynthesis of the Antibiotic Thiostrepton. Methylation of Tryptophan in the Formation of the Quinaldic Acid Moiety by Transfer of the Methionine Methyl Group with Net Retention of Configuration

Pei Zhou,[†] David O'Hagan,[†] Ursula Mocek,[†,‡] Zhaopie Zeng,[†,‡] Lai-Duien Yuen,[†] Thomas Frenzel,[‡] Clifford J. Unkefer,[§] John M. Beale,[†,‡] and Heinz G. Floss*[,†,‡]

Department of Chemistry BG-10, University of Washington Seattle, Washington 98195
Department of Chemistry, The Ohio State University Columbus, Ohio 43210
Los Alamos Stable Isotope Resource Los Alamos National Laboratory Los Alamos, New Mexico 87545

Received March 24, 1989

Thiostrepton (**1**),[1] first isolated from *Streptomyces azureus*,[2] is the parent of a family of highly modified, sulfur-rich polypeptide antibiotics, which also includes the micrococcins,[3] the siomycins,[4] the thiopeptins,[5] and nosiheptide.[6] These compounds inhibit protein synthesis in gram-positive bacteria;[7] however, their limited solubility has so far prevented development for clinical use, although nosiheptide is used commercially as a growth promotant for poultry.[8] As part of our interest in this family of compounds,[9,10] we have examined the biosynthesis of **1**.

Following unequivocal assignment of all the signals in the ^{13}C NMR spectrum of **1**[11,12] (Tables I and II, Supplementary Material), feeding experiments with ^{13}C-labeled precursors in *S. laurentii* gave the results summarized in Figure 1 (see Tables I and II, Supplementary Material). As expected, based on precedent,[9,13] both the butyrine and the dehydroalanine moieties arise from the corresponding β-hydroxyamino acids, threonine and serine, the thiostreptine moiety is formed from isoleucine, and the thiazole rings each originate from a molecule of cysteine and the carboxyl group of an adjacent amino acid. Two molecules of serine, connected through their carbon atoms 3, and the carboxyl group of an adjacent cysteine give rise to the piperidine ring. Finally, the quinaldic acid moiety is formed from L-tryptophan. The latter accounts for all the carbon atoms except C12, which is contributed by methionine. The transformation of tryptophan may involve a ring expansion similar to that leading to the formation of the quinine type alkaloids.[14] The methyl group, C12, would thus be attached to the carbon originating from C2 of the indole ring of tryptophan, and the question arises whether tryptophan is first methylated at C2 and then transformed into the quinoline system or whether methylation is a later step in the biosynthesis.

We therefore synthesized D,L-2-methyl-[3'-^{13}C]tryptophan (99% ^{13}C) in analogy to the method of Weygand and Linden[15] and fed

[†] The Ohio State University.
[‡] University of Washington.
[§] Los Alamos National Laboratory.

(1) Anderson, B.; Crowfoot Hodgkin, D.; Viswamita, M. A. *Nature (London)* **1970**, *225*, 233.
(2) Pagano, J. F.; Weinstein, M. J.; Stout, M. A.; Donovick, R. *Antibiot. Ann.* **1956**, 554.
(3) Walker, J.; Olesker, A.; Valente, L.; Rabanal, R.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1977**, 706.
(4) Ebata, M.; Miyazaki, K.; Otsuka, H. *J. Antibiot.* **1969**, *22*, 434.
(5) Hensens, O.; Albers-Schönberg, G. *J. Antibiot.* **1983**, *36*, 814.
(6) Pascard, C.; Ducruix, A.; Lunel, J.; Prange, T. *J. Am. Chem. Soc.* **1977**, *99*, 6418.
(7) Pestka, S.; Bodley, J. W. In Antibiotics. *Mechanisms of Action*; Corcoran, J. W., Hahn, F. E., Eds.; Springer: New York, 1975; Vol. 3, pp 551–573.
(8) Keppens, L.; DeGrote, G. *Rev. Agric (Brussels)* **1979**, *32*, 159.
(9) Houck, D. R.; Chen, L.-C.; Keller, P. J.; Beale, J. M.; Floss, H. G. *J. Am. Chem. Soc.* **1988**, *110*, 5800.
(10) Dosch, D. C.; Strohl, W. R.; Floss, H. G. *Biochem. Biophys. Res. Commun.* **1988**, *156*, 517.
(11) Hensens, O. D.; Albers-Schönberg, G. *J. Antibiot.* **1983**, *36*, 832.
(12) Mocek, U.; Beale, J. M.; Floss, H. G. *J. Antibiot.*, in press.
(13) Pearce, C. D.; Rinehart, K. L. *J. Am. Chem. Soc.* **1979**, *101*, 5069.
(14) Leete, E.; Wemple, J. N. *J. Am. Chem. Soc.* **1969**, *91*, 2698.

0002-7863/89/1511-7274$01.50/0