Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926090

A new family of carbohydrate liquid crystals. *N*-Alkylated 1-deoxynojirimycin derivatives [1]

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To cite this Article Blunk, Dirk , Praefcke, Klaus and Legler, Günter(1994) 'A new family of carbohydrate liquid crystals. *N*-Alkylated 1-deoxynojirimycin derivatives [1]', Liquid Crystals, 17: 6, 841 — 846
To link to this Article: DOI: 10.1080/02678299408035476
URL: http://dx.doi.org/10.1080/02678299408035476

LIQUID CRYSTALS, 1994, VOL. 17, NO. 6, 841–846

A new family of carbohydrate liquid crystals
N-Alkylated 1-deoxynojirimycin derivatives [1]

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(*Received 3 March 1994; in final form 22 July 1994; accepted 29 July 1994*)

The thermal properties of eight *N*-substituted 1-deoxynojirimycin (5-amino-1,5-dideoxy-D-glucopyranose, **1**) derivatives have been studied by means of polarizing microscopy, differential scanning calorimetry, and X-ray diffraction. It was thereby found for the first time that four of these biologically active compounds (**6**–**9**) exhibit the smectic A type of mesophase. Furthermore, in contact preparations of **6**–**9** with water lyomesogenic behaviour was also observed.

1. Introduction

Many carbohydrate derivatives with amphiphilic structures show biological activities or even occur in nature. Probably the most common examples of the latter are glycolipids which are found on the surface of all plasma membranes [2]. In addition, in recent times, such amphiphiles derived from natural products have provided interesting structures for liquid crystal research [3, 4]. Carbohydrate amphiphiles, as one of the fundamental groups of molecules of life, enjoy a steadily growing interest in various areas of science and are therefore synthesized and studied for manifold reasons.

Interesting hydrophilic head groups for such amphiphiles are given by 1-deoxy-1,5-iminohexitols and their 1,5-dideoxy analogues. These multiols formally belong to the family of piperidine alkaloids and possess remarkable biological activities [5, 6]. The first representative of these ‘heteroses’ discovered in nature, called nojirimycin, has the same stereochemical arrangement of its molecular functional groups as glucose [7].

Nojirimycin (5-amino-5-deoxy-D-glucopyranose) and 1-deoxynojirimycin (5-amino-1,5-dideoxy-D-glucopyranose, **1**) are both antibiotics and inhibit various glucosidases [8]. Thus, derivatives of **1** are of considerable importance today for the medical treatment of carbohydrate-dependent metabolic diseases [8]; several patents on antiviral effects of 1-deoxynojirimycin derivatives on HIV and other retroviruses have also been registered [9].

Despite this interest in, for example, 1-deoxynojirimycin derivatives with amphiphilic character, it has up to now never been considered whether such compounds could also exhibit liquid crystalline phases, although their molecular structure should actually have tempted one to do so. In view of the recent growth of literature [3, 4] on

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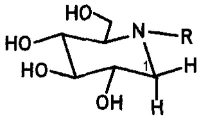

1 R = H
2 $R = CH_3$
3 $R = CH_2CH_3$
4 $R = CH_2CH_2$–phenyl
5 $R = CH_2–CH\overset{t}{=}CH$–phenyl
6 $R = CH_2(CH_2)_7CH_3$
7 $R = CH_2(CH_2)_8CH_3$
8 $R = CH_2(CH_2)_{10}CH_3$
9 $R = CH_2(CH_2)_{12}CH_3$

Figure 1. The molecular structure of the parent compound 1-deoxynojirimycin (**1**) and of the eight selected *N*-alkylated derivatives (**2–9**) investigated here.

the relationship between structure of carbohydrate derivatives and their possible mesogenic properties, this omission is surprising.

The *N*-alkyl-aminosugars **2–9** are perfectly suited to behave as self-organizing materials typical of carbohydrate derivatives forming hydrogen-bridge supported liquid crystalline phases [3, 4], at least if they possess one longer alkyl substituent as is the case with the members **6–9** of our new family of natural product liquid crystal materials. These latter compounds are rod-shaped and each can easily display an ideally stretched conformation. Consequently, their structural character engenders their mesogenic character, as is known for a great number of so-called single tailed carbohydrate liquid crystal materials [3, 4]. The partially unsaturated members **4** and **5** each possess a phenyl ring at the end of their lipophilic section. In these two cases, the lipophilic parts are broader and more rigid compared to **6–9** which carry flexible alkyl groups. However, the side chains of **4** and **5** are too short, rendering these *N*-alkylated derivatives non-liquid crystalline, as is also the case for **2** and **3**.

2. Results and discussion

2.1. *The characterization of the mesophases*

Our microscopic investigations of the four liquid crystalline tetrols **6–9** reveal that their mesophases show complete miscibility (contact method) with each other, as well as with 4-*O*-dodecyl-*myo*inositol [4(*e*)] or 1-*O*-octyl-β-D-glucopyranose [10], typical representatives of single-tailed carbohydrate mesogens exhibiting the smectic A type of phase.

On cooling from the isotropic liquid, the phase transition of each of the mesomorphic compounds leads to the formation of bâtonnets which turn into largely homeotropic domains with some oily streaks as the mesophase grows, a characteristic feature of single-tailed multihydroxy liquid crystal materials [4(c), (d), 11]. Using lipophilized slides and cover glasses, one may observe areas with birefringent textures, and in addition to domains that are still homeotropic, some fan-shaped regions become visible.

Without doubt, our miscibility studies and other microscopic observations clearly prove the existence of the smectic A type of phase in this series of multiols. Moreover, X-ray diffraction studies of the mesophases exhibited by the tetrols **6–9** confirm this assignment. For these four mesogens, the lamellar spacing (*d*) was examined by small angle X-ray scattering (SAXS) and its value calculated by Laue's law. The temperature dependence of the layer distance and a wide angle X-ray scattering (WAXS) pattern of the mesophase of the decyl derivative **7** were also determined.

The WAXS pattern of a non-oriented sample of **7** shows three concentric homogenous rings. The first one—very strong and sharp—located in the low angle area

The phase transition data and some X-ray results for eight selected *N*-alkyl derivatives (**2**–**9**) of 1-deoxynojirimycin (**1**); the type of thermotropic mesophase exhibited is always *smectic A* (S_A) = M see Results and Discussion. The temperatures for the melting and clearing processes (m.p. or cl.p., respectively) are given in °C and were obtained by polarizing microscopy/differential scanning calorimetry (ΔH = transition enthalpy in kJ mol^{-1}); d = calculated length in Å (UniChem 2·0, Cray Research Inc., method AM1) for the stretched molecular conformation; l = measured layer spacing in Å (SAXS) at 130°C; d/l = quotient of molecular length and layer spacing.

Tetrol	*R*	m.p.‡ (ΔH)	cl.p (ΔH)	*d*	*l*	*d/l*
2 [5]	Methyl	152·5/151·0 (27·5)	Not LC	—	—	—
3 [9 (b)]	Ethyl	155·9/153·4 (26·30)	Not LC	—	—	—
4 [9 (d)]	Phenylethyl (~ C_5)†	182·6/179·7 (39·9)	Not LC	—	—	—
5 [9 (e)]	Cinnamyl (~ C_6)†	164·7/161·4 (22·9)	Not LC	—	—	—
6 [9 (a), (b)]	Nonyl	106·8/105·6 (33·4)	150·0/149·5 (2·5)	25·1	16·1	1·56
7 [5]	Decyl	91·0/88·3 (34·5)	155·8/155·3 (2·2)	26·7	17·4	1·53
8 [5]	Dodecyl	99·1/98·1 (42·3)	166·1/164·6 (1·8)	29·7	19·9	1·49
9 [5]	Tetradecyl	102·1/101·9 (53·7)	167·7/166·7 (1·9)	32·7	22·5	1·45

† The approximate number of carbon atoms of an aliphatic chain of comparable length (using Dreiding models).

‡ Surprisingly, in earlier papers (cf. the respectively cited references) various *different melting temperatures* of these *N*-alkyl-1-deoxynojirimycin derivatives are given; however, the mesomorphic properties of these cyclic tetrols were *not* observed before.

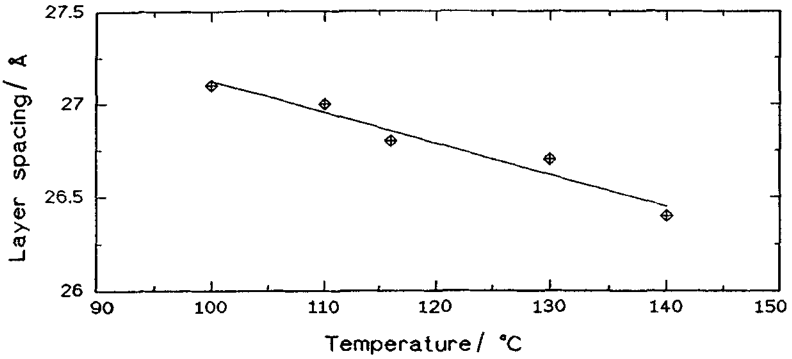

Figure 2. Temperature dependence of the layer distance of *N*-decyl-1-deoxynojirimycin (**7**).

corresponds to the layer distance, the second one, which is very weak, but nevertheless sharp, is the related second order signal. The outer ring in the wide angle region concerns the lipophilic chains and is broad and diffuse. This pattern clearly supports the characterization of this mesophase as smectic A. A smectic C phase would also show this pattern, but this can be excluded without doubt by the results from polarizing microscopy.

The layer distances of the four mesogens **6**–**9** were determined at the same temperature (130°C). The results obtained for the lamellar spacings and the calculated molecular lengths are compiled in the table. The ratio of the layer spacing (*d*) to the molecular length (*l*) decreases from 1·56 in the case of **6** to 1·45 in the case of **9**, indicating an interdigitated bilayer ordering of the molecules of **6**–**9** in their mesophases. This supramolecular architecture of the mesophase is typical for single-tailed carbohydrate mesogens [3].

In order to check the comparability of the results of the above measurements carried out at a single temperature of 130°C for the four derivatives **6–9**, the temperature dependence of the lamellar spacing was studied on the decyl example (**7**). With increasing temperature, the layer distance decreases only slightly, cf. figure 2. This behaviour is usually explained by the increasing entropy of the molecules [11, 12] and the higher flexibility of the partially folded alkyl chains [13]. Over nearly the entire temperature range of the mesophase, the magnitude of this decline is only about 0·5 Å, showing that the above choice of the fixed temperature (130°C) was valid. The smectic A phase is characteristic of the majority of carbohydrate based mesogens with *one* liphophilic chain [3, 4]. The temperature ranges of the mesophases observed in our cases are of the same order of magnitude as those for other monoalkyl-glucopyranosides [3 (*a*), 4, 10]; the phase transition data for our new liquid crystal materials are summarized in the table.

Furthermore, lyomesomorphism was found for the four long-chain tetrols **6–9**, i.e. in contact preparations with water surrounding the samples. Under these conditions, three mesophases are present: (i) the smectic A region (probably including some water) preserved in the centre of the preparation, encircled by (ii) a homeotropic (inner) belt of mesophase of higher viscosity upon which shearing attempts did not lead to any texture formation. Therefore, in accordance with studies of other monoalkyl-glycosides, we assume a cubic type of structure for this second mesophase [13]; (iii) in the outer belt, a fan-shaped texture exists which is most likely associated with a hexagonal columnar type of mesophase (cf. [13]). However, these interesting lyomesophases certainly have to be studied in more detail than we have done up to now.

3. Conclusions

The four mesomorphic compounds **6–9** exhibit an interdigitated smectic A liquid crystalline phase, as is expected for single-tailed rod-shaped amphiphiles. To the best of our knowledge, the 1-deoxynojirimycin derivatives **6–9** presented here constitute the first carbohydrate mesogens in which the pyranosidic oxygen is replaced by nitrogen, offering the possibility of derivatization at this special ring position. With reference to liquid crystallinity, nojirimycin and 1-deoxynojirimycin offer a new opportunity to synthesize a wide variety of interesting and novel materials, including amphiphiles and disc-shaped molecules. Finally, one might ask whether there could be a relationship for these compounds between their lyotropic liquid crystalline properties and their biological activities, a topic which in our opinion has not yet been tackled. In biochemistry, the vast majority of studies on phase transitions involving liquid crystals have centred on pure or mixed phospholipids in the form of bilayers [14]. Thus, single chained, mesogenic compounds of biological significance such as those investigated here should, much more than has hitherto been the case, stimulate studies of the effects of their phase transitions in biological membranes, where such transitions might affect enzyme activity and transmembrane transport of metabolites.

4. Experimental

The synthesis of the *N*-alkyl-1-deoxynojirimycin derivatives **2–9** is described elsewhere [5, 9]. Newly made NMR and MS measurements confirm their molecular structures.

The microscopic investigations were carried out with a Leitz Laborlux 12 Pol polarizing microscope equipped with a Mettler FP 82 hot stage. The DSC measurements were performed with a Mettler TA 3000/DSC 30 S with GraphWare TA 72. The heating/cooling rates applied in both methods were 5 K min^{-1}.

The lipophilized microscopic slides and cover glasses were prepared by treating the carefully cleaned glass plates in a sealed vessel with some drops of dichlorodimethylsilane for 2 hours.

X-ray diffraction patterns were recorded photographically (Polaroid XR-7 Land Diffraction Cassette No. 57-4, Polaroid type 57 sheet film, ASA 3000) using Ni-filtered CuK$_\alpha$ radiation collimated by a glass collimator (beam diameter 0·4 mm). The samples, about 1 mm thick, were placed freestanding in the circular hole (diameter 0·8 mm) of a stainless steel sample holder. Heating was achieved by a Bruker ER4111VT Variable Temperature Unit with an accuracy of ± 0·5 K. The specimen to film distance for the WAXS was 65 mm and typically about 265 mm for SAXS.

K. P. wishes to record his gratitude to the following organizations for their financial support of our liquid crystal work: Deutsche Forschungsgemeinschaft (Sonderforschungsbereich Sfb 335 'Anisotrope Fluide', project C3), Bonn, Fonds der Chemischen Industrie, Frankfurt/Main, Germany, Technische Universität Berlin, and Gesellschaft von Freunden der Technischen Universität (travelling funds to Dipl.-Chem. D. Blunk). The supply of samples of 1-deoxynojirimycin and of several of its *N*-alkyl derivatives by Dr B. Junge and Dr D. Schmidt, Bayer AG, Wuppertal, Germany, to both the Berlin and the Cologne group is also gratefully acknowledged. Furthermore, we thank Mr A. Eckert, technical assistant in our laboratory, for carrying out necessary synthetic work.

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