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Liquid Crystals

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Substitution pattern and stereochemistry versus liquid crystalline behaviour [1]

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Novel inositol ethers

Substitution pattern and stereochemistry versus liquid crystalline behaviour [1]

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Selectively *O*-alkylated inositols of *myo*-, *scyllo*- and *chiro*-configuration allow detailed studies of the relationship between the substitution pattern in the cyclohexane ring and the liquid crystalline properties observed to be made for these mainly novel cyclic compounds containing hydroxyl functions. The types of thermotropic mesophase formed and containing hydrogen bonds are strongly influenced by the number and the stereochemical arrangement of both the hydroxyl groups and the alkyloxy chains, as well as by their positions on the cyclohexane ring.

The mesophases of the various new inositol ethers have been studied by polarizing optical microscopy and differential scanning calorimetry, and are discussed here in comparison with known systems, as a function of the above-mentioned structural factors.

1. Introduction

Steric and electronic interactions between molecules of suitable constitutions may result in the occurrence of liquid crystal phenomena. Also the spontaneous build-up of hydrogen bridges, in particular of dynamic intermolecular hydrogen bonding networks, can be very important for mesophase formation.

As hydrogen bonds are directed interactions, properties of mesophases supported in this way are strongly influenced by structural factors of the pro-mesogenic molecules, for example by the substitution pattern and stereochemical arrangement of the units giving rise to the hydrogen bridges.

Studies on the functional and configurational conditions for the formation of liquid crystal phases based on molecular multimerizations are of current interest [2–17]. In our opinion, inositol (1,2,3,4,5,6-hexahydroxycyclohexane) derivatives are the materials of choice for this project; some results are presented here.

2. Results and discussion

Nine of the new inositol ethers were derived in multistep syntheses [18] starting from *myo*-inositol, or in the case of **10**, from quebrachitol, 2-O-methyl-(−)-inositol. All ethers are racemic, only the *chiro*-inositol derivative **10** is enantiomericly pure. Their structures were verified by ^{1}H, ^{13}C NMR and mass spectroscopy, as well as by combustion analyses.

The mesomorphic properties were studied by polarizing optical microscopy and differential scanning calorimetry using a Leitz Laborlux 12 Pol microscope equipped with a Mettler hot stage FP 82 or a Mettler TA 3000/DSC 30 S with GraphWare TA 72, respectively; the heating rates were 5 K min^{-1} for both methods. The properties of the inositol ethers are discussed below in the order of increasing number of ether functions at their cyclohexane cores.

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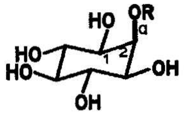
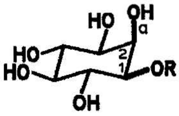
2.1. *Inositol monoethers/pentols*

After three mono(*thio*)ethers of *scyllo*-thioinositol were prepared and found to be liquid crystalline [12], in this paper we present four more cyclohexane pentols which are the first examples of (*myo*- or *scyllo*-)inositol mono-dodecyl ethers. The structural formulae **1**–**4a** depict the differences in position and stereochemical situation of their five hydroxyl functions and the one dodecyloxy group relative to each other. These hitherto unknown [2, 17] compounds having only one long alkoxy chain are of special interest for comparisons of their thermo-mesomorphic properties with those of the thio-derivative **4b** [12] and analogous monoethers recently [16] derived from D-glucopyranose.



1



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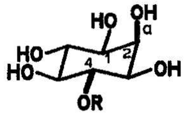
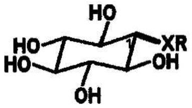


3

R = dodecyl



4a (X=O)
b (X=S)

The thermal behaviour of the new inositol monoethers **1**–**4a** is as follows. The axial ether **1** shows a monotropic mesophase (cf. table 1) which could not be studied in detail due to very rapid crystallization. Unlike **1**, each of the two equatorial *myo*-inositol ethers **2** and **3** form an enantiotropic smectic A phase, identified by their typical texture and by miscibility studies (contact method) with the known S_A phase of the tetrol diethers **5** [12]. Due to its very high melting temperature (cf. table 1), however, no mesophase could be observed for the *scyllo*-inositol mono-ether **4a**. Thus, as is known from the behaviour of other mesogenic amphiphiles consisting of a hydrophilic head and one lipophilic chain (see, for example, [2, 3, 9, 12, 14–17]), our inositol monoethers **1**–**3** also form smectic supramolecular structures. Mounted between normal glass plates, the ethers **1**–**3** tend to align fully homeotropically; the use, however, of lipophilic glass plates [19] gives rise to fan shaped textures with large homeotropic areas.

Table 1. Phase transition data for the five inositol or thioinositol mono-(*O* or *S*)dodecyl ethers **1**–**4**.

Inositol/ thioinositol ether	C		M		I
1†	●	220·5 /223·5 (48·8)	{M_1	215·2 /216·7 (6·6)}	●
2	●	124·4 /127·6 (32·0)	S_A	221·1 /221·7 (1·8)	●
3	●	147·6 /150·2 (29·1)	S_A	216·0 /216·3 (1·8)	●
4a ($X=O$)‡	●	241·9 /240·0 (35·4)	—		●
4b ($X=S$) [12]	●	216·9§/217·6 (39·6)§	S_A	231·0§/229·6 (2·1)§	●

Temperatures in °C; polarizing microscopy/differential scanning calorimetry: PM/DSC; enthalpies (kJ mol^{-1}) in brackets; heating rate 5 K min^{-1}.

† The clearing temperature was determined on cooling from the isotropic liquid.

‡ Heating rate: 10 K min^{-1}.

§ A new value not yet published in [12].

{ } A monotropic mesophase; C, crystalline; M the type of mesophase; I isotropic liquid; S_A, smectic A; M_1, a mesophase most probably of a smectic type.

The phase transition data for the four inositol monoethers or pentols **1–4a** in table 1 reveal a strong dependence of their melting temperatures on the position in each of the one dodecyl ether function and on the fixed stereochemistry in the inositol unit. On the other hand, their clearing temperatures are very similar—close to 220°C. We feel that this conspicuous behaviour is in full accordance with the criteria [20, 21] of a revised model for the molecular arrangement in the smectic A phase of carbohydrate-derived amphiphiles with one alkyl chain. Our findings on the inositol derivatives **1–4a** carrying identical alkyl chains nicely complete the picture of that model [20, 21], on the basis here of the differently structured hydrophilic moieties.

Apparently, due to their comparatively disturbed molecular symmetry **2** and **3** in this group of natural product liquid crystals exhibit the widest smectic A phase range, starting from below 150°C. Most probably, this idea could also be discussed for, for example, the dodecyl ether series of D glucopyranose [16] in which the 2- and 6-ethers have the widest smectic A phase range with the highest clearing points, whereas the 3- and 4-ethers give the narrowest ranges with the lowest clearing temperatures. Finally, at present due to insufficient data, we leave the dramatic difference in the thermotropic behaviour between the ether **4a** and the thioether **4b** of identical stereochemistry without any comment.

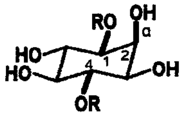
2.2. *Inositol diethers/tetrols*

The substitution patterns of the ten inositol derivatives **5** to **11** produce three different types of molecules geometries:

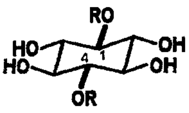
(i) rod-shaped and linear in examples **5** and **6**, having their two ether functions in opposite positions in the cyclohexane ring,
(ii) peg-shaped and tripodal in the vicinal diethers **7** to **10**, or
(iii) angled in the case of **11**, with its two ether chains in this third possible arrangement in the ring.

Because of their linear molecular shape the two *myo*-inositol diethers **5a** and **b** (R = hexyl or octyl, respectively) [12] exhibit the smectic A phase on heating, cf. a sketch of its monolayer type in the figure (*d*). However, the *scyllo*-isomer **6** (R = hexyl) [12], also rod-shaped in structure, melts at too high a temperature to exhibit a mesophase; it is the highest melting compound discussed in this paper.

Rod-shaped

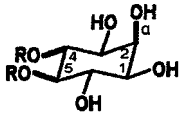


5 a,b

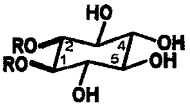


6

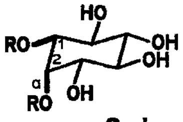
Peg-shaped



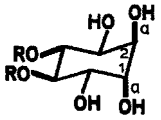
7a,b



8

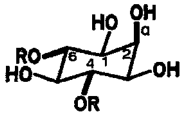


9a,b



10

Angled



11

Table 2. Phase transition data for the ten (*chiro*-, *myo*-, and *scyllo*-)inositol diethers **5** to **11**†.

Inositol ether‡			C		M		I
5a	[12]	(6)	●	144·4/144·8 (27·9)	S_A	176·1/176·9 (9·3)	●
5b	[12]	(8)	●	139·5/141·2 (28·8)	S_A	168·1/170·1 (10·5)	●
6	[12]	(6)	●	258·3/265·2 (40·5)	—		●
7a		(6)	●	112·7/112·9	H_x	125·1/125·2 (1·2)	●
7b		(8)	●	111·2/112·7 (18·6)	H_x	148·1/147·2 (1·6)	●
8	[11, 13]	(6)	●	— /111·5 (16·0)	H_x	— /167·1 (1·8)	●
9a	[11, 13]	(6)	●	110·0/110·2 (21·9)	—		●
9b	[11, 13]	(8)	●	102·0/101·8 (20·8)	H_x	131·5/131·7 (1·2)	●
10		(6)	●	69·0/ 70·1 (10·7)	S_A	82·3/ 80·9 1·1)	●
11		(8)	●	48·4/ 49·2 (10·6)	—		●

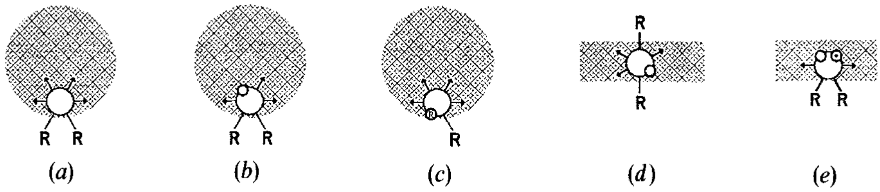
† See the footnotes to table 1; H_x, hexagonal columnar mesophase, cf. [5].

‡ The numbers of carbon atoms in the alkyl chains in **5**–**11** are given in brackets.

Mostly, mesogenic molecules of the second type of geometry, for example, **7a, b, 8,** and **9b,** aggregate into columns which are arranged in a hexagonal lattice; the corresponding transition data are summarized in table 2. The tendency of tripodal molecules to form a so-called H_x type thermotropic mesophase is discussed elsewhere [13, 22] in more detail.

At least one of the hydroxy functions of these compounds has to be in a configuration such that it can point toward the centre of the column, cf. the figures (*a*) and (*b*); inside the columns three dimensional, dynamic networks of hydrogen bridges are formed. In this connection deuterium NMR studies are planned. Comparisons of the transition data for the diethers **7**–**10** of three (*myo*-, *scyllo*-, and *chiro*-) stereoisomeric inositols now to hand reveal interesting stereochemical effects [11, 23] upon the formation and stability of mesophases, cf. the figure and table 2.

By taking the flat *scyllo*-inositol diether **8** of this series—an example for the case in the figure (*a*)—as the compound of reference, both *myo*-analogues **7a** and **b** (cf. the figure (*b*)) with equal or even longer alkyl chains, but one hydroxyl function opposite to an alkoxy group R axial are less good and less stable thermo-mesogens. If one more spacious alkoxy group, instead of a hydroxyl function, is transformed into an axial



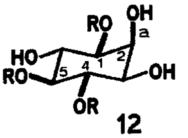
Sketches of cuts through hexagonal columnar or layered arrays of selected inositol derivatives, for instance diethers, in their hydrogen bridge containing thermotropic mesophases, (i) of the H_x type of phase ((*a*), (*b*) and (*c*) top views, in each case with only one of the maximum of five possible [13, 22] molecules shown in a stylized manner), (ii) of smectic A phases ((*d*) a monolayer, (*e*) part of a bilayer). The larger open disc inside each hydrophilic area (shaded) symbolizes the cyclohexane ring; the little discs denote axial hydroxyl functions (○, ⊙) or an axial alkoxy group (Ⓡ) attached to it and pointing perpendicular (opposite in (*e*)) to the plane of these cuts. Arrows on the larger circles typify equatorial hydroxyl functions pointing in the directions shown in the plane of the cuts. *R* = hetero-aliphatic side chains.

position (**9a**, cf. the figure (*c*)), no thermotropic mesophase is observed, but, a prolongation of the alkyl chains (cf. **9b**) improves this situation. It seems important to note that these stereochemical modifications at only one ring position do not change the types of mesophase; here, all are or remain hexagonal columnar (H_x)! This point is proved by texture and miscibility studies (contact method) using glucosedioctyldithioacetal [4, 5].

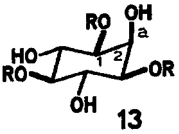
On the other hand (cf. situations (*b*) and (*e*) in the figure), the change in the type of mesophase from columnar to a layered array of the molecules in the case of the frog-shaped molecules of **10** (see (*e*) in the figure), with two axial hydroxyl functions each opposite to alkoxy groups R, is unique and completely unexpected! The steep drop in mesophase stability of **10** in comparison to **8** and **7a,** however, is plausible and a consequence of the stronger, mesophase weakening stereochemical effect of these two axial hydroxyl functions. With this particular configuration, the molecules of **10** in their thermotropic mesophase favour a multimerization, in such a way that a supramolecular self-assembly process giving layers takes place. The mesophase of **10** was identified as smectic A by microscopic studies of its texture and by miscibility investigations (contact method) using **5b** as the material of reference. Finally, the *myo*-inositol diether **11** seems not to fit into any of the classes of multiols known so far, as derived from carbohydrates. This particular diether is not liquid crystalline, although alkyl 6-*O*-acyl-glycopyranosides [24] with a comparable substitution pattern, but differently functionalized (with an acetal and ester group), exhibit columnar mesophases.

2.3. *Inositol triethers/triols*

We think it is interesting to note that the triether **12,** which can be regarded as a relatively spacious derivative of **5a**, but troubled by a bulky group at position 5 of the cyclohexane ring, is still smectic (type A, proved in the usual way), although with a marked loss of phase stability; the phase is now monotropic, but remains of identical type—cf. the corresponding data in tables 2 and 3. In other words, the tetrol, **5a**, a double vicinal diol, has been transformed into the triol **12,** having one equatorial hydroxyl group less available for the formation of an intermolecular, dynamic, hydrogen bonding network. Most probably both types of compound (**5** and **12**) behave as rod-shaped multiols because the vicinal alkoxy chains in **12** lie parallel in the smectic monolayer phase (see (*d*) in the figure).



12



13

Table 3. Phase transition data for the two *myo*-inositol triethers **12** and **13**†.

Inositol ether‡		C		M		I
12	(6)	●	111·7/113·1 (38·1)	{S_A	97·1/—	●}
13	(8)	●	47·2/49·2 (13·6)	—		●

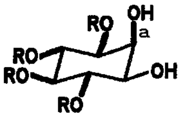
† See the footnotes to table 1.

‡ The numbers of carbon atoms in the alkyl chains in both ethers are given in brackets.

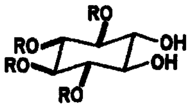
In contrast to the vicinal, peg-shaped diether **7a**, formation of an H_x phase by **12** is impossible, because the alkoxy chain at ring position 1 would stay inside the hydrophilic section and hinder the construction of a hexagonal columnar ordering of molecules. As pointed out previously [5], this description is along the same lines of an inhibiting effect on the formation of columnar aggregates caused by another non-polar group (methyl) in carbohydrate moieties [25]. Thus, the peg-shaped half of the molecule **12** does not control the kind of molecular aggregation. Rather, the rod-shape (although disturbed in its symmetry, see above) of the whole molecule dominates this process and no change in mesophase takes place: $S_A \nrightarrow H_x$. But, the formal transformation of **7a** into **12** by etherification at position 1 does result in a change of mesophase from hexagonal columnar to smectic: $H_x \rightarrow S_A$. The symmetric triether **13** is not liquid crystalline, most probably due to insufficient space filling [23] in the periphery of the saturated core and/or the inability to aggregate.

2.4. *Inositol tetra- and pentaethers/diols and mono-ols*

Representatives of the two vicinal diol series **14** and **15** have already been studied in great detail [11, 13, 22]; they exhibit columnar mesophases which are built up from hydrogen-bridged dimers of **14** or **15**. The stability of the mesophases is determined by the configuration of the diol groups: *trans*-diequatorial (in **15**) is better than the *cis*-situation (**14**). Moreover, depending on the length of the alkoxy chains, members of the series of type **15** show a rich multi-thermo-mesomorphism [11, 13, 22]. The corresponding pentaethers/mono-ols derived from **14** and **15** and having their remaining one hydroxyl function either axial or equatorial, were found to be either not liquid crystalline or to give only monotropic columnar discotic properties, respectively; in the latter case, this occurrence at temperatures far below the melting point of −4·2°C [26].



14



15

3. Concluding remarks

From this report on about twenty—half of them new—ether derivatives of three stereoisomers of inositol (1,2,3,4,5,6-hexahydroxycyclohexane), it emerges that the occurrence, type, and stability of the mesophases are determined by the number, the position, and the stereochemical arrangement of both the hydroxyl groups and the alkoxy chains on the cyclohexane ring.

In general, axial groups weaken a mesophase. Also, too high molecular symmetry in these systems appears to be disadvantageous to the formation of mesophases. The change of mesophases from the hexagonal columnar to the smectic type occasioned by a purely stereochemical effect of two vicinal hydroxyl functions (cf. **8** and **10**) deserves attention and the study of further examples. In our opinion, the same seems to hold for the influence of disturbing substituents on the change in type and stability of the mesophases (cf. **7a** and **12** or **5a** and **12** respectively).

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[18] The syntheses of the ten new inositol ethers **1**–**4a**, **7a**, **b**, **10**–**13** will be published elsewhere; the inositol ethers **1**, **2**, **4a**, and **10** were prepared by B. Bilgin, J. Hempel, and A. Humke, members of our group.

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[25] *Note added in proof*.— The same is true in cases of methyl glycosides, private communication (4 December 1992) by R. Miethchen, Institute of Organic Chemistry, The University, Rostock, Germany; cf. MIETHCHEN, R., HOLZ, J., and PRADE, H., 1993, *Colloid, Polym. Sci.*, **271** (in the press).

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