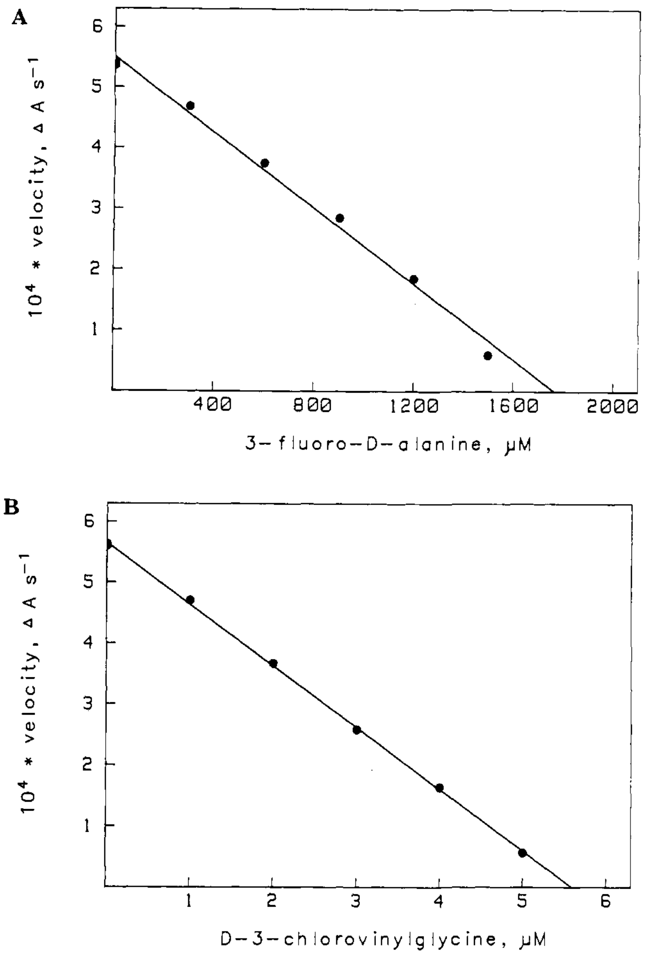

Figure 1. Comparison of partition ratios of D-fluoroalanine (A) and D-chlorovinylglycine (B). The two inhibitors were incubated with identical enzyme solutions in 0.1 M HEPES, pH 8.00 at 25 °C. Inactivation of the enzyme was allowed to proceed to >99% completion of the decomposition of the inhibitor, as calculated from the overall rate constants for inactivation determined under the experimental conditions. The remaining enzymatic activity was measured by using the coupled spectrophotometric assay (D-alanine to L-alanine direction) described by Wang and Walsh.[1] The plots show the residual activity as a function of total inhibitor concentration.

(16 ± 9) is slightly larger than that for the D-isomer.

The fluorovinylglycines are 100-fold less reactive than the chlorovinylglycines. Availability of enzyme has precluded an accurate determination of the partition ratio; an upper limit of 40 has been established for the racemate.

Consistent with the greater efficiency and more complex kinetics, there is physical evidence that the halovinylglycines follow a different mechanism of inhibition than established for their simpler homologues, the nonvinylic β-substituted alanines. Denaturation of the enzyme–inhibitor complex by heat gives quantitative release of free pyridoxal phosphate, as identified by its absorbance spectrum. This contrasts with the Schnackerz adduct of aminoacrylate and pyridoxal phosphate found for nonvinylic β-substituted alanines.[11] Consequently, irreversible inhibition must proceed by a different mechanism, which is currently under study.

Supplementary Material Available: The physical properties and analytical data for compounds [D]-**1a**-HCl, [L]-**1a**-HCl, [D,L]-**1a**-HCl, and [D,L]-**1b** and the separation of the latter into its diastereomers (1 page). Ordering information is given on any current masthead page.

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[11] (a) Roise, D.; Soda, K.; Yagi, T.; Walsh, C. T. *Biochemistry* **1984**, *23*, 5195. (b) Badet, B.; Roise, D.; Walsh, C. T. *Biochemistry* **1984**, *23*, 5188. This mechanism had been developed also by Metzler and colleagues for L-aspartate transaminase (Likos, J. J.; Ueno, H.; Feldhaus, R. W.; Metzler, D. E. *Biochemistry* **1982**, *21*, 4377) and for glutamate decarboxylase (Ueno, H.; Likos, J. J.; Metzler, D. E. *Biochemistry* **1982**, *21*, 4387).

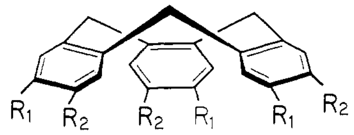
Inversion of the Cyclotribenzylene Cone in a Columnar Mesophase: A Potential Way to Ferroelectric Materials

Jacques Malthête* and André Collet*

Collège de France, Chimie des Interactions moléculaires
E.R. C.N.R.S. 285, 11, place Marcelin-Berthelot
75005 Paris, France

Received May 26, 1987

Certain hexaesters **3** of cyclotricatechylene (**1**) form thermotropic columnar mesophases,[1-4] in which the cone-shaped cyclotribenzylene units stack in parallel columns, at a distance of ~4.8 Å, like in the crystal structure of cyclotriveratrylene (**2**).[2] In a mesophase column, the cones are embedded into one another with the same orientation, making the column axis *polar*. Such mesophases might therefore be ferroelectric, if all the columns adopted the same polarization direction within a macroscopic domain, as sketched in Figure 1.[2,3] However, the high viscosity of these materials severely restricts the freedom of the molecules to turn upside down, and hence this mechanism would not easily allow orientation of the cones (e.g., in an electric field, since the cones may have a dipole moment along their axis).



1 $R_1 = R_2 = OH$
2 $R_1 = R_2 = OCH_3$
3 $R_1 = R_2 =$ O-CO-alkyl, O-CO-aryl
4 $R_1 = H$, $R_2 = OH$

An interesting property of the cyclotribenzylene structure is the possibility of *conformational inversion* of the nine-membered ring system, which takes place in solution over a barrier of ca. 27 kcal/mol;[5] it is therefore very slow at room temperature but may become fast on heating (the half-life of a given cone conformer is about 1 month at 20 °C, a few minutes at 100 °C, and less than 0.1 s at 200 °C). If the inversion process could still occur at a sufficient rate in a mesophase such as those of **3**, one would expect, by means of an external field, to polarize all the cones, hence the columns, in the same direction, *without need for any rotation of the molecules*; only an umbrellalike inversion of their cores is required.

A simple way to assess whether this process is feasible is to make use of optically active cyclotriveratrylenes; in effect inversion of a cone generates its mirror image structure, and the racemization rate therefore provides a direct measurement of the phenomenon. Such studies cannot be performed with hexaesters of type **3**, where $R_1 = R_2$, which are achiral (C_{3v}). In contrast, cyclotriveratrylenes

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[1] Malthête, J.; Collet, A. *Nouv. J. Chim.* **1985**, *9*, 151-153.
[2] Levelut, A.-M.; Malthête, J.; Collet, A. *J Physique* **1986**, *47*, 351-357.
[3] Zimmermann, H.; Poupko, R.; Luz, Z.; Billard, J. *Z. Naturforsch., A: Phys., Phys. Chem., Kosmophys.* **1985**, *40A*, 149-160.
[4] Zimmermann, H.; Poupko, R.; Luz, Z.; Billard, J. *Z. Naturforsch., A: Phys., Phys. Chem., Kosmophys.* **1986**, *41A*, 1137-1140.
[5] Canceill, J.; Collet, A.; Gottarelli, G. *J. Am. Chem. Soc.* **1984**, *106*, 5997-6003.

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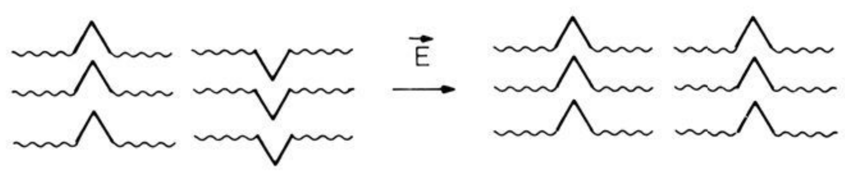


Figure 1. Antiferroelectric-to-ferroelectric transition in a columnar mesophase made of molecules with a cone-shaped core.

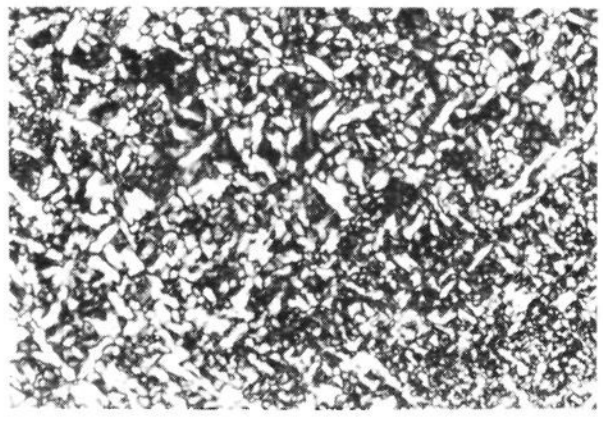
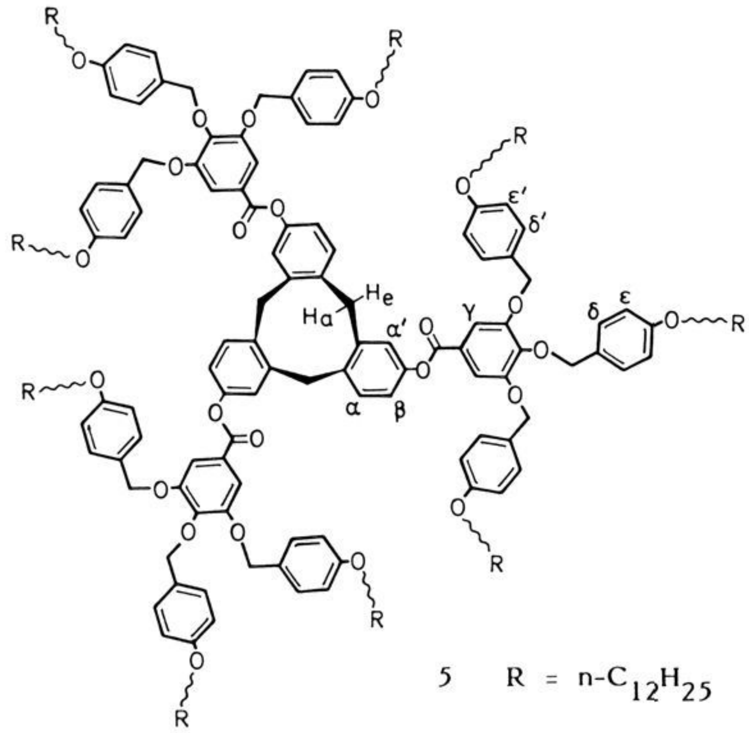


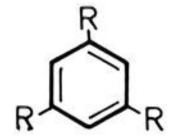
Figure 2. Optical texture of the mesophase of 5 at 146 °C, as observed between crossed Nicols, on cooling from the liquid phase.

with $R_1 \neq R_2$ are chiral (C_3), and some of them have been resolved, for instance **4** (cyclotriphenolene).[5] The aim of the present work was to synthesize a derivative of **4** that would form columnar mesophases. This has now been achieved, and we report here the synthesis of the mesogenic triester **5**, in racemic and optically active forms, and relevant data on the cone inversion rate in the mesophase and in the isotropic liquid.



5 R = n-$C_{12}H_{25}$

Only *three* phenol groups are available in **4** for grafting the mesogenic substituents, and three elongated chains, such as in **3**, would insufficiently fill the space around the core and therefore could not allow the existence of *columnar* mesophases. Mesogenic 1,3,5-trisubstituted benzenes have been described,[6] but they form classical (*nematic*, *smectic*) liquid crystals, presumably because they adopt an overall rodlike shape, with two parallel chains on one side, opposite to the one on the other side. In order to fill the space with only three substituents at 120° around a central unit, the substituents should have a *triangular* rather than elongated shape. The 3,4,5-tris(*p*-*n*-dodecyloxybenzyloxy)benzoyloxy group (DOBOB) is a good candidate for this purpose,[7] since, for instance, the trisubstituted benzene **6** effectively displays a columnar mesophase from room temperature up to 159 °C.[8]



6 R = DOBOB

Compound **5** was prepared in racemic and optically active forms by esterification of (±)-**4** and (+)-**4**[5] ($[\alpha]_D$ +179° (*c* 0.24, dioxane)), respectively, with the DOBOB acid[7] (3 equiv) in dichloromethane (25 °C, 67 h), in the presence of dicyclohexylcarbodiimide and *p*-(dimethylamino)pyridine. Purification was effected by TLC (silica gel, chloroform as the eluant, ca. 30% yield). The optically active **5** showed $[\alpha]_D$ +93° (chloroform).[9] The crown conformation of the cyclotribenzylene core in **5** is evidenced by the presence, in the NMR spectrum,[9] of the characteristic AX quartet of the CH_aH_e bridges.

Both (±)-**5** and (+)-**5** were obtained in mesomorphic state at room temperature. On heating the birefringent viscous mesophases, the isotropic liquid appears at 148–150 °C (ΔH = 12.7 ± 1 kcal/mol).[10] On cooling from the liquid, the mesophases were observed to grow with the texture shown in Figure 2, and X-ray diffraction measurements[11] indicated a hexagonal columnar structure, similar to the low-temperature mesophase of hexabenzoate **3** (with $R_1 = R_2$ = *p*-*n*-dodecyloxybenzoyloxy).[2]

The racemization of (+)-**5** was studied in the mesophase at 100 °C and 130 °C and in dioxane solution (isotropic) at 100 °C. In the latter case, (+)-**5** was almost completely racemized within 20 min; the first-order rate constant k of the (+) to (−) process was 1.3×10^{-3} s^{-1}, and the inversion barrier ($\Delta G^{\ddagger}$ (373 K) 26.9 kcal/mol) is thus the same as that measured so far for other chiral cyclotriveratrylenes in solution.[5] In the mesophase at 100 °C, the inversion rate was slower by two orders of magnitude, $k \sim 1.3 \times 10^{-5}$ s^{-1}, $\Delta G^{\ddagger}$ (373 K) 30.3 kcal/mol, and the half-life ($t_{1/2}$) of a given cone conformer was ~7 h 30 min, instead of 5 min in the isotropic solution. The racemization is faster at 130 °C, with $k \sim 3 \times 10^{-4}$ s^{-1}, and $t_{1/2} \sim 20$ min. Thus, the tight embedding of the cyclotribenzylene units, which is responsible, at least in part, for the high stability and viscosity of these mesophases, also increases the cone inversion barrier by 3.4 kcal/mol.

The estimated half-life of a cone, at 3° below the clearing temperature, is ca. 4 min, which seems fast enough to allow the mesophase columns to be oriented under the influence of an electric field, with all the cones eventually pointing in the same direction. Quenching the oriented mesophase to room temperature would then give a ferroelectric material in which the polarization of the columns might perhaps last several decades, since at 20 °C the mesophase is almost crystalline, and the estimated half-life of the cones is ~80 years. The next step of this work is to synthesize cyclotribenzylene mesogens with a strong dipole moment along the C_3 axis, in order to facilitate their orientation.

Acknowledgment. We are grateful to Dr. M.-J. Brienne and Dr. J. Canceill for helpful discussions and to Dr. A.-M. Levelut for the X-ray measurements.

Registry No. (±)-**4**, 89209-34-7; (+)-**4**, 89255-54-9; (±)-**5**, 110905-07-2; (+)-**5**, 110905-08-3; DOBOB acid, 110934-58-2.

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(7) Malthête, J.; Nguyen, H. T.; Levelut, A.-M. *J. Chem. Soc., Chem. Commun.* **1986**, 1548–1549; **1987**, 40.

(8) Malthête, J.; Levelut, A.-M., unpublished results.

(9) Satisfactory C,H elemental analyses were obtained for **5**: ^{1}H NMR (200.13 MHz, δ from internal Me_4Si in $CDCl_3$) 0.81 (t, CH_3), 1.19 (m, $(CH_2)_9$), 1.70 (m, OCH_2CH_2), 3.88 (m, $ArOCH_2$), 4.96 (s) and 4.99 (s) (OCH_2Ar), 3.75 (d, H_e) and 4.84 (d, H_a, J = 14 Hz), 6.69 (d, H_ϵ) and 7.18 (d, H_δ, J = 8.7 Hz), 6.81 (d, $H_{\epsilon'}$) and 7.26 (d, $H_{\delta'}$, J = 8.7 Hz), 6.92 (dd, H_β, J = 8.5 Hz and 2 Hz), 7.15 (overlapped d, $H_{\alpha'}$), 7.36 (d, H_α), and 7.42 (s, H_γ). The enantiomer (+)-**5** showed the following rotations (*c* 1.86 in chloroform, 25 °C): $[\alpha]_D$ +93°, $[\alpha]_{578}$ + 97°, $[\alpha]_{546}$ +113°, and $[\alpha]_{436}$ +223°.

(10) The transition temperature and enthalpy were measured on a Perkin-Elmer DSC2 microcalorimeter. No significant difference was found between racemic and optically active **5**. The unusually large ΔH value is due to the high molecular weight of this compound (M = 3245).

(11) The molecules stack in columns with a periodicity of ~4.7 Å (a very tight packing), and there is a further modulation along the column axis with a periodicity of 43 Å corresponding to about nine molecules, suggesting a helical structure like that of hexabenzoate **3** (for a pictorial representation, see ref 2); a projection along the column axis defines a 2D-hexagonal lattice, with a 35.2-Å separation between the columns. Details will be given in a forthcoming paper.