Templated polar order of a guest in a quasiracemic organic host[†]

Tia Jacobs,^{*a*} Martin W. Bredenkamp,^{*a*} Pieter H. Neethling,^{*b*} Erich G. Rohwer^{*b*} and Leonard J. Barbour^{*a}

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A quasiracemic mixture of Dianin's compound and its thiol derivative enforces additional anisotropy of the guest-accessible space, thus facilitating a net polar arrangement of guest molecules; guest alignment is rationalized in terms of van der Waals volume considerations.

Even-order non-linear optical (NLO) materials are capable of second harmonic generation (SHG) and can thus be used to double the frequency of laser light. Net polar alignment of molecules is an important phenomenon for NLO properties¹ and significant effort has thus been devoted to engineer polar order in crystals. Although several studies have expanded upon serendipitous observations of polar-ordered guest molecules in host systems with persistent packing arrangements,² very few of these architectures have been specifically tailored with a view to enforce guest alignment. In such systems, guest molecules with high molecular hyperpolarizabilities would be preferred, but these often form side-by-side dimers in a centrosymmetric arrangement. This can be counteracted by utilizing narrow channels that facilitate in-line head-to-tail dipolar arrangements, but this favorable mode of packing could still be negated if neighboring channels, though individually polar, would align in an antiparallel fashion to afford an overall non-polar material.

The well-known Dianin's compound (1, Scheme 1) host system has been adapted³ to produce a chiral guest-accessible space for enantiomeric separation of guest molecules. However, to date this robust framework type has not been targeted for



Scheme 1 Dianin's compound.

guest polar ordering in the context of second harmonic generation. Here we describe a crystal engineering strategy that exploits the well-known tendency for racemic Dianin's compound and its close analogs to form centrosymmetric and isoskeletal⁴ columnar inclusion compounds. We have modified the host synthetically in order to produce a new quasiracemic mixture,³ thus enforcing anisotropy of the guest-accessible space to yield SHG activity.

Dianin's compound was first isolated in 1914 and is one of the most recognized organic hosts in inclusion chemistry. In its pure form, or in the presence of a wide variety of guests (usually solvent molecules), the as-synthesized racemic mixture assembles such that six host molecules position themselves about a site of $\overline{3}$ symmetry. A cyclic up-down arrangement of alternating *R* and *S* isomers is formed, and successive molecules are linked to each other by OH···O hydrogen bonds between their phenolic moieties. The hexamers stack in columns such that successive units interdigitate to enclose hourglass-shaped guest-accessible cavities of approximately 240 Å.³ Owing to the trigonal symmetry of the host packing motif, it is usually not possible to model guest molecules that do not also possess threefold symmetry.

In the absence of suitable guest molecules, the thiol derivative (2) of Dianin's compound spontaneously resolves upon crystallization, separately forming crystals of both R and S enantiomerically pure host. However, when forming inclusion compound crystals, 2 packs in a manner analogous to 1, with SH···S hydrogen bonds tethering the enantiomers together. We therefore postulated that an equimolar mixture of (R)-1 and (S)-2 would also assemble in an analogous manner by forming a quasiracemic hexa-adduct held together by an $(\cdots OH \cdots SH)_3$ hydrogen bonded ring.

The resolution of racemic **1** was achieved by esterification with (1S)-(-)-camphanic chloride, fractional crystallization of the diastereomeric mixture from 2-methoxyethanol and subsequent hydrolysis of the appropriate diastereomer to afford (S)-**1**.⁵ The opposite enantiomer of **1** was obtained in an analogous manner using (1R)-(+)-camphanic chloride as the resolving agent. Enantiomerically pure (S)-**1** was then converted to the thiol-derivative (S)-**2** via a thiocarbamate intermediate.⁶

Equimolar amounts of (R)-1 and (S)-2 (hereafter this mixture is designated as 3) were dissolved in CCl₄ and clathrate crystals suitable for single-crystal diffraction studies were obtained by slow evaporation of the solvent. The corresponding clathrates of compounds 1 and 2 were also grown from CCl₄ and the three different inclusion compounds will be referred to as 1a, 2a and 3a.[‡] The structure–property relationships of these related but subtly different crystals are rationalized below. However, it is important to note that the discussion assumes each crystal to be defect-free.

^a Department of Chemistry, University of Stellenbosch, 7602, South Africa. E-mail: ljb@sun.ac.za; Fax: +27 21 808 3849; Tel: +27 21 808 3335

^b Department of Physics, University of Stellenbosch, 7602, South Africa

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Structure **1a** crystallizes in the centrosymmetric trigonal space group $R\bar{3}$ with lattice parameters a = b = 26.8078(12) and c = 10.8706(10) Å. Each guest-accessible cavity is occupied by only one CCl₄ guest molecule, which is disordered over two crystallographically equivalent positions (Fig. 1a) across a site of $\bar{3}$ symmetry. From a space-filling model, it can be inferred that the orientation of the guest in one cavity does not influence that in the adjacent cavity along [001]. Therefore the guest molecules are most likely statistically (*i.e.* 50 : 50) disordered throughout the structure such that no localized polar alignment exists.

The structure of **2a** is analogous to that of **1a**, with lattice parameters a = b = 26.632(2) and c = 12.0349(17) Å. In contrast to **1a**, elongation of the cavity by *ca*. 1.2 Å along [001] allows enclathration of two guest molecules per void in **2a**; both guests are 50 : 50 disordered over two positions in accordance with the $\bar{3}$ site symmetry of the guest-accessible space (Fig. 1b). Based on space-filling models, it follows that the two CCl₄ molecules situated within any cavity must both be oriented with a C–Cl bond aligned in the same direction along the crystallographic threefold axis. Furthermore, the larger aperture between adjacent cavities in 2a allows one of the chlorine atoms to protrude slightly into the adjacent cavity. This can only occur if the two guest molecules in the adjacent cavity are also aligned in the same direction along [001]. Thus, from purely spatial considerations it can be deduced that each column contains guest molecules that are all aligned in a polar fashion along the crystallographic c axis. Although the orientation of any given guest molecule enforces the same orientation on its cavity partner, and indeed also on the rest of the guest molecules within the same column, there is most likely no communication between neighboring columns with regard to the direction of the polar axis along c. Therefore the disorder of the crystallographic model implies that, while individual columns of guest molecules might be polar, the bulk material consists of a random 50:50 distribution in terms of the alignment of these columns along either [001] or [00-1].

Structure **3a** crystallizes in the polar and chiral space group R3 (note the reduction in symmetry from the centrosymmetric space group $R\overline{3}$ obtained for **1a** and **2a**) with lattice parameters a = b = 26.6670(16) and c = 11.7710(14) Å. The anticipated quasiracemic crystal structure (Fig. 1c) is a hybrid of **1a** and **2a**. In addition to being chiral, the arrangement of the host molecules is also polar—throughout the structure, the hydroxyl moieties of **1** are all directed towards one end of the crystal along its trigonal axis, and the thiol extremities of **2** are facing the opposite end. Each cavity is bounded by two $(\cdots O-H\cdots S-H)_3$ hydrogen bonded rings $(O_{donor} \cdots S_{acceptor} and S_{donor} \cdots O_{acceptor} = 3.428(3)$ and 3.522(3) Å, respectively)





Fig. 1 Columnar stacking of CCl_4 clathrates of Dianin's compound and its analogs. (a) **1a**, (b) **2a** and (c) **3a**. All projections are perpendicular to [001]. Molecules of **1** and **2** are shown in red and purple, respectively (capped-stick representation). In each case the CCl_4 guest molecules are disordered over two possible positions (yellow and green, ball-and-stick representation). Guest-accessible volume is shown as semitransparent grey surfaces. All hydrogen atoms, except those of the hydroxyl- and thiol-moieties have been omitted for clarity.

Fig. 2 Perspective view of 3 along [00-1] illustrating the trigonal symmetry of the host–guest adduct. Only hydrogen atoms belonging to the hydroxyl and thiol groups are shown. Host carbon atoms are represented as capped-sticks while oxygen and sulfur atoms are shown in ball-and-stick mode. The two CCl₄ guest molecules within the guest-accessible cavity that are present in the 85% occupancy state are shown in space filling representation (dark green in the foreground and light green in the background). The alternating $(\cdots O-H \cdots S-H)_3$ ring is indicated using dashed red cylinders to represent hydrogen bonds.



Fig. 3 Plot of the relationship between the input power of the fundamental wave (800 nm) and the measured intensity of the second harmonic wave (400 nm) for **1a** to **3a**.

and contains a total of two disordered CCl₄ guest molecules (see Fig. 2). In this case, the two components of the disordered model are not related to each other by the crystallographic symmetry, although the rationalization of the alignment of the guest molecules in **3a** is similar to that for **2a**. That is, owing to spatial constraints, all of the guest molecules in any given column are aligned such that they have the same orientation along [001]. However, the enforced asymmetry of the cavity introduces a bias such that the disorder no longer represents a 50 : 50 distribution of the overall direction of the polar alignment of the guest molecules. Refinement against intensity data yielded a model for CCl₄ that is biased 85 : 15 in favor of alignment of the host phenolic moiety (the green guest molecules in Fig. 1c).

It is interesting to note that desolvation of 2a results in the formation of a polycrystalline powder comprising a mixture of resolved (*R*)-2 and (*S*)-2 (see ESI[†]). Similarly, 3a desolvates to yield resolved (*R*)-1 and (*S*)-2. These experiments imply that the presence of guest is essential for the formation of the racemic or quasiracemic host framework.

Since 3a is noncentrosymmetric in terms of the arrangement of both host and guest, the crystals were expected to exhibit bulk SHG properties. Optical measurements were carried out on single crystals of 1a, 2a and 3a. Indeed, only 3a exhibited intense SHG for incident light of wavelength 800 nm (red laser), whereas 1a and 2a produced no significant second harmonic response (Fig. 3), even for incident intensities up to 88 GW cm⁻².

In summary, we have expanded upon the concept of utilizing quasiracemates⁷ in order to sculpt the topology of the guest-accessible space of a noncentrosymmetric inclusion compound. Our approach has been to exploit the notion that, although quasiracemates mimic the structural patterns of their racemic counterparts, they are devoid of inversion symmetry in a rigorous sense, owing to stereochemical restrictions. Thus a rational design strategy has been devised and implemented to control guest alignment within the well-known Dianin's host system by introducing asymmetry. In this contribution we have rationalized the lack of polar order in the two related racemic host frameworks **1a** and **2a**, and have shown that these materials exhibit no NLO activity. The quasiracemic

hybrid system **3a** was specifically constructed to increase the anisotropy of the crystal, resulting in a dramatic alteration of the optical properties of a well-known type of material. The presence of the guest molecules is essential for "gluing" the host molecules together and the overall acentricity of the system is derived from multiple sources—*i.e.* both components of the host framework, as well as the guest molecules exhibit polar alignment. The guest templates the formation of the host framework, which in turn templates the polar alignment of the guest.

Notes and references

‡ Crystal data for **1a**: $C_{109}H_{120}Cl_4O_{12}$, M = 1763.96, colorless block, $0.38 \times 0.23 \times 0.11 \text{ mm}^3$, trigonal, space group $R\bar{3}$ (No. 148), a = b =26.8078(12), c = 10.8706(10) Å, V = 6765.6(8) Å³, Z = 18, $D_c = 1.299$ g cm⁻³, $F_{000} = 2814$, MoK α radiation, $\lambda = 0.71073$ Å, T = 100(2) K, $2\theta_{max} = 56.5^{\circ}$, 14 393 reflections collected, 3588 unique $(R_{\text{int}} = 0.0569)$. Final GooF = 1.037, $R_1 = 0.0515$, w $R_2 = 0.1288$, R indices based on 2853 reflections with $I > 2\sigma(I)$ (refinement on F^2) 200 parameters, 2 restraints. Lp and absorption corrections applied, $\mu = 0.196 \text{ mm}^{-1}$. Crystal data for **2a**: C₁₁₀H₁₂₀Cl₈O₆S₆, M = 2014.08, light yellow block, $0.30 \times 0.27 \times 0.21$ mm³, trigonal, space group $R\bar{3}$ (No. 148), a = b = 26.6320(19), c = 12.0349(17) Å, V = 7392.3(13)Å³, Z = 3, $D_c = 1.357$ g cm⁻³, $F_{000} = 3180$, MoK α radiation, $\lambda = 0.71073$ Å, T = 100(2) K, $2\theta_{\text{max}} = 56.6^{\circ}$, 15611 reflections collected, 3863 unique ($R_{int} = 0.0602$). Final GooF = 1.063, $R_1 = 0.0651$, $wR_2 = 0.1855$, *R* indices based on 3220 reflections with $I > 2\sigma(I)$ (refinement on F^2), 215 parameters, 6 restraints. Lp and absorption corrections applied, $\mu = 0.412$ mm⁻¹. Crystal data for **3a**: $C_{110}H_{120}Cl_8O_9S_3, M = 1965.87$, colorless block, $0.25 \times 0.21 \times 0.21$ 0.18 mm³, trigonal, space group *R*₃ (No. 146), *a* = *b* = 26.6670(16), *c* = 11.7710(14) Å, *V* = 7249.2(11) Å³, *Z* = 3, *D_c* = 1.351 g cm⁻³, *F*₀₀₀ = 3108, MoKα radiation, λ = 0.71073 Å, T = 100(2) K, $2\theta_{\text{max}} = 56.5^{\circ}$, 15661 reflections collected, 7407 unique $(R_{\text{int}} = 0.0346)$. Final GooF = 0.976, $R_1 = 0.0593$, w $R_2 = 0.1375$, Rindices based on 5469 reflections with $I > 2\sigma(I)$ (refinement on F^2), 410 parameters, 35 restraints. Lp and absorption corrections applied, $\mu = 0.358 \text{ mm}^{-1}$. Absolute structure parameter⁸ = 0.06(7).

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