Exceptionally long crystal formation from 4-(3-bromopropyloxy)salicylaldehyde. X-Ray crystallographic investigation

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Unusually long (> 14 cm) crystalline needles grow from 4-(3-bromopropyloxy)salicylaldehyde 1 presumably as a consequence of Br···Br interactions; the powdered form of 1 shows one order of magnitude greater SHG activity realtive to urea.

The phenomenon of crystal growth[1] is ubiquitous in nature. Thus manifestations of spontaneous crystallization are evident in diverse instances ranging from the common household to various scientific as well as industrial processes.[2] However, while the general approaches to crystal nucleation and engineering[3] are known, the exact manner in which one can control crystal growth direction remains largely elusive. Well grown crystals of predictable morphology find wide utility in the design of non-linear optical (NLO) materials[4] or in solid-state electronic devices.[5] However, very few materials that grow long crystals are of inorganic origin. Organic materials with controllable crystalline morphologies are very attractive because they are more amenable to structural modifications at the molecular level and could be functionalized with subunits having desirable properties.[6] But organic crystals with exceptional growing abilities are very rare.[7] Here, we report the unusual propensity of 4-(3-bromopropyloxy)salicylaldehyde **1** to grow very long crystals and its NLO activity. We also report its single-crystal structure based on X-ray diffraction.

During the preparation of salen (salicylidene ethylenediamine) based reagents[8] for DNA cleavage studies, we serendipitously discovered the formation of an unusually long crystal (> 14 cm) from 4-(3-bromopropyloxy)salicylaldehyde **1**.‡ While purifying compound **1** using column chromatography over silica gel (60–120 mesh) with 2–3% EtOAc in light petroleum (bp 60–80 °C), a few needle-shaped, optically transparent crystals started growing in the test tubes containing fractions corresponding to **1**. Within a week, the needle-like crystals outgrew the entire length of the test tube, limiting further possible crystalline propagation (Fig. 1). The aspect of crystal growth with **1** was verified by careful experimentation in a longer tube and indeed to our satisfaction we could reproduce the formation of even longer crystals under these circumstances. The length-to-diameter ratios for most of the crystals were > 150. Although most of the crystals were very long (width < 1 mm), they were found to be mechanically quite strong. Once grown they remained unscathed for over two years when kept in the refrigerator.

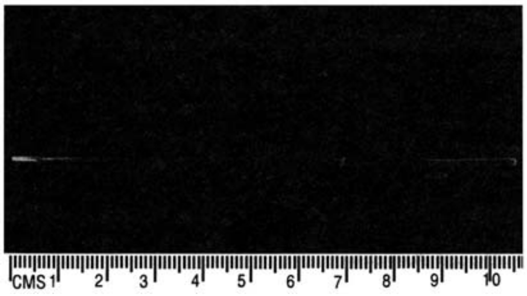


Fig. 1 Photograph of a representative specimen of the long single crystal of **1**. X-Ray diffraction patterns from five different fragments were checked before data collections were attempted; examination under polarized light of several sections along the length of the crystal showed extinctions indicating that the entire object is a single crystal.

To understand the factors that might be responsible for such crystal growth, we undertook a single-crystal X-ray diffraction study of **1**.§ This showed that the crystals were orthorhombic with space group $P2_12_12_1$. Oscillation photographs revealed that the crystal grew along the shortest axis of the crystal (*a* axis). Analysis of all the translated contacts of **1** showed that the majority of intermolecular interactions including C···Br were along the growth axis which most likely assisted in the nucleation as well as in the growth of the unusually long crystals. Closer scrutiny of the crystallographic environment around the Br centres indicate that 'nucleophilic–electrophilic' pairing (HOMO–LUMO interactions) exists between the bromines,[12,13] with a Br^{a}···Br^{b} distance of 3.88 Å (Fig. 2). The corresponding angles were C(10)^{a}–Br^{a}–Br^{b} (θ_1) 176.3° and C(10)^{b}–Br^{b}–Br^{a} (θ_2) 110.0° respectively. Ramasubbu *et al.* have earlier shown[12] that halogen–halogen interactions in θ_1, θ_2 space show preferred orientations. A concentration of points around θ_1 180° and θ_2 90° in θ_1, θ_2 space further indicates the existence of a nucleophilic–electrophilic pairing. In this scenario one of the halogen atoms would act as an electrophile while the other acts as a nucleophile so forming a nucleophilic–electrophilic pair.

We prepared a variety of analogues of **1**. It appears that the *n*-value in the O(CH$_2$)$_n$Br chain as well as the presence of the CHO group in **1** are important for the exceptional crystalline growth in **1**. Thus when we synthesized the corresponding compounds with pendant O(CH$_2$)$_2$Br or O(CH$_2$)$_4$Br chains

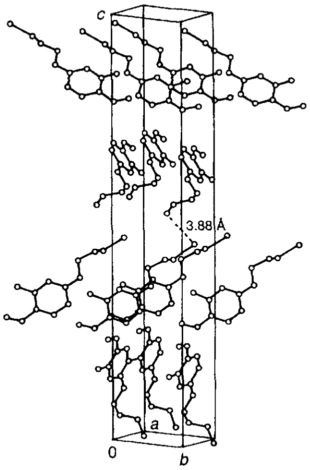
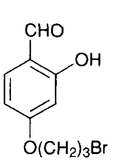


Fig. 2 Packing diagram of **1** viewed down the *y*-axis



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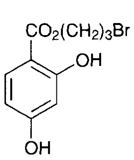

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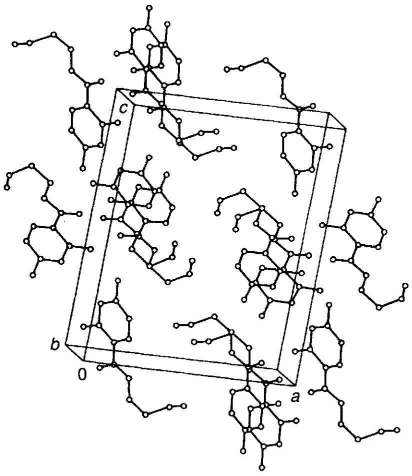

Fig. 3 Packing diagram of **2**

instead of $O(CH_2)_3Br$ in **1**, no such crystal formation with an unusual propensity for growth was detectable. With either of these derivatives of **1** only small, fragile, crystalline flakes could be seen under optimal crystallization conditions. Owing to the poor quality of these crystals, single-crystal X-ray diffraction studies were not undertaken. The replacement of CHO by CO_2H in **1** also led to poorly crystalline material.

We then synthesized a related analogue, **2**, in which the pendant $(CH_2)_3Br$ residue was linked through an ester, $C(O)O(CH_2)_3Br$, leaving the corresponding OH group on aromatic ring free. Transposition of $(CH_2)_3Br$ from an ethereal $[O(CH_2)_3Br]$ to an ester type of linkage $[C(O)O(CH_2)_3Br]$ gave a crystal of sufficient quality to be examined by single-crystal X-ray diffraction. This examination revealed that in **2**, an entirely altered crystalline arrangement was present which was not conducive for crystal growth along a particular crystallographic axis as seen with **1**. Calculations of the intermolecular contacts in **2** showed that there were no Br···Br interactions present within the lattice. In **2** the molecules packed into columnar structures across all the centres of symmetry in the unit cell (Fig. 3). The two rows in the column were held together by intermolecular hydrogen bonds [O(1)···O(2) 2.838 Å, H(1)···O(2) 2.020 Å and O(2)···O(3) 2.970 Å, H(2a)···O(3) 2.412 Å] in a 'head-to-tail' fashion. The existence of an intramolecular hydrogen bond between atoms O(2) and O(3) [O(2)···O(3) 2.606 Å, H(2a)···O(3) 1.950 Å] was also evident. The presence of such dimeric units across the centres of symmetry induced another short intermolecular interaction [O(3)···O(3) 2.842 Å] which most likely provided further stability to such a columnar mode of packing in the structure of **2**.

Owing to the non-centrosymmetric character of the space group in **1**, we examined its second harmonic generation (SHG) capacity. The SHG intensities of **1** were measured using the standard powder technique[14] on a polycrystalline sample ground to uniform grain size.¶ Although the sample melted upon prolonged exposure to the laser source (λ = 532 nm, Q-switched Nd:YAG laser, Quanta Ray, DCR-2A), powdered samples of **1** gave more than one order of magnitude greater SHG activity over that of urea. Consistent with the centrosymmetric nature of crystals of **2**, no SHG activity was detectable with **2**.

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Footnotes

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‡ **1** was prepared by refluxing 2,4-dihydroxybenzaldehyde with 1,3-dibromopropane in the presence of $KHCO_3$ in dry acetone for 60 h and was purified from the above mixture by column chromatography over silica gel with 2% EtOAc in light petroleum (bp 60–80 °C) (*ca.* 60% isolated yield).

2 was prepared by the reaction of 2,4-dihydroxybenzoic acid with 1,3-dibromopropane in the presence of $KHCO_3$ in dry acetone under reflux (2 days). After column chromatography over silica gel [$CHCl_3$–MeOH, (97:3)] (56% isolated yield) it was recrystallized from EtOAc–toluene to obtain crystals of diffraction quality. The ^1H NMR and IR spectral properties as well as the elemental analysis data for **1** and **2** were consistent with their given structures.

§ *Crystal data*: $C_{10}H_{11}BrO_3$ **1**, M = 259.089, orthorhombic, space group $P2_12_12_1$, a = 4.620(1), b = 6.569(1), c = 33.737(2) Å, U = 1024.1(2) Å^3, Z = 4, D_c = 1.681 g cm^{-3}, μ = 53.55 cm^{-1}, $F(000)$ = 520, crystal dimensions 0.13 × 0.15 × 0.5 mm, 969 reflections measured, 907 reflections observed. The symmetry operations for $C(10)^b$ and Br^b are: $C(10)^a$–Br^a (xyz)···Br^b–$C(10)^b$ ($x + 1/2, 3/2 - y, - z$).

$C_{10}H_{11}BrO_4$ **2**, M = 275.088, monoclinic, space group $P2_1/c$, a = 12.949(1), b = 5.337(1), c = 15.586(1) Å, β = 92.15(1)°, U = 1076.4(5) Å^3, Z = 4, D_c = 1.697 g cm^{-3}, μ = 52.03 cm^{-1}, $F(000)$ = 552, crystal dimensions 0.2 × 0.33 × 0.63 mm, 1878 reflections measured, 1506 reflections observed.

Crystal data for **1** and **2** were collected on an Enraf-Nonius CAD4 diffractometer at 293 K. Intensity data were collected using Ni-filtered Cu-Kα radiation (λ = 1.5418 Å). Cell dimension and the orientation matrix were obtained from least-squares refinement of the setting angles of 25 well defined reflections. No decay in the intensities of three standard reflections were observed during data collection. Corrections for Lorentz and polarization effects were applied and the structures solved using direct methods (SHELXS-86)[9] and refined by full-matrix least-squares analysis with anisotropic thermal parameters for all non-hydrogen atoms using SHELX-76[10] (**1**) and SHELXL-93[11] (**2**). Hydrogen atoms in **1** were located by difference Fourier synthesis and unrefined, and in **2** were fixed geometrically and treated as riding. The structure of **1** was refined to R = 0.060, R_w = 0.070 [$I > 3\sigma(I)$, 127 parameters] and that of **2** to R = 0.067 [$I > 4\sigma(I)$, 138 parameters], R = 0.075 (all data), R_w = 0.111 with a goodness of fit of 1.042 and 2.482 respectively. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/236.

¶ A pulsed Q-switched Nd:YAG laser (Quanta Ray, DCR-2A) (λ = 532 nm) with a pulse duration of 8 ns was used to generate second harmonic signals from the samples. The measured SHG intensities of the samples were normalized with respect to that of powdered urea. For further details, see ref. 6.

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