



Short Note

2,8-Dibromo-6*H*,12*H*-6,12-epoxydibenzo[*b,f*][1,5]dioxocine

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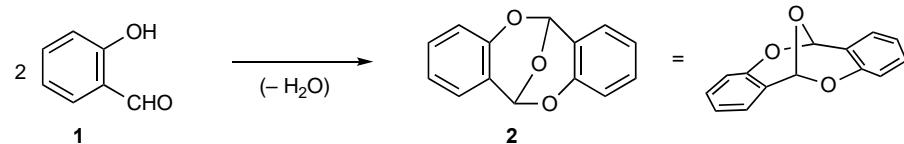
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Abstract: The title dibromodisalicylaldehyde, obtained as a by-product in the *m*-chloroperoxybenzoic acid oxidation of 5-bromo-2-(methoxymethoxy)benzaldehyde, has been characterised by IR and NMR spectroscopy and X-ray diffraction. The structure features two independent molecules with a π - π stacking interaction between them.

Keywords: X-ray structure; disalicylaldehyde; trioxabicyclo[3.3.1]nonadiene

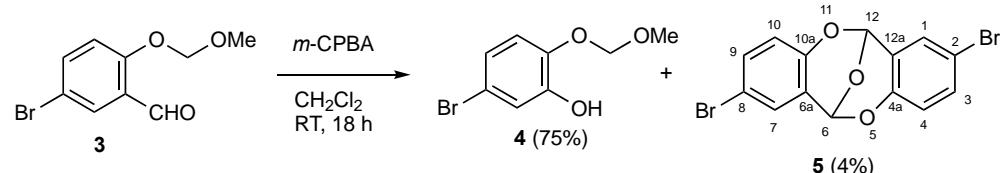
1. Introduction

Ever since salicylaldehyde **1** was first studied in the mid-19th century, it was observed to undergo dehydrative dimerisation, particularly under acidic conditions, to give a compound variously described as “parasalicyl” [1,2] and disalicylaldehyde [3]. There were various suggestions as to its structure and in a definitive paper of 1922 [4] this was finally shown by chemical methods to be the interesting dibenzo-fused trioxabicyclo[3.3.1]nonadiene **2** (Scheme 1). The activity of substituted derivatives of **2** as antimicrobial agents has been reported [5].



Scheme 1. Formation and structure of “disalicylaldehyde” **2**.

In the course of recent synthetic work, we were carrying out a Baeyer–Villiger oxidation of the methoxymethyl-ether-protected 5-bromosalicylaldehyde **3** to give the protected bromocatechol **4** and, in addition to the expected product, obtained a minor by-product in low yield which turned out to be the dibromo derivative of disalicylaldehyde **5** (Scheme 2). This has only been mentioned once before in a 1940 paper where it was obtained by direct bromination of **2** and only a melting point was given [6]. We describe here the full characterisation of this compound including its IR and NMR spectra and X-ray structure determination.



Scheme 2. Formation of compound **5**.

2. Results

The starting compound **3** was prepared according to a literature procedure [7] and subjected to *m*-chloroperoxybenzoic acid (*m*-CPBA) oxidation as described in a patent [8]. We faced significant difficulty in separating the desired product **4** from the *m*-chlorobenzoic



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acid and even after several washings had to subject the residue to column chromatography. This did give the required product **4** in 75% isolated yield after a further recrystallisation, but a fast-running minor component was also obtained which proved to be the unexpected dibromodisalicylaldehyde **5** (4%). In addition to NMR signals for a 1,2,4-trisubstituted benzene ring (see Supplementary Materials), this had a distinctive singlet at δ_H 6.28 and δ_C 89.4 ppm in agreement with expectation for a benzylic $\text{ArCH}(\text{OR})_2$ environment. The IR spectrum showed no significant signals above 1650 cm^{-1} confirming the absence of OH and C=O. The material failed to give any meaningful mass spectrometric data.

Recrystallisation from hexane gave colourless prisms suitable for X-ray diffraction and the resulting structure (Figure 1) shows two independent but closely similar molecules in the unit cell. At $1.888(8)$ – $1.892(8) \text{ \AA}$ the C–Br distances are rather short compared to the mean value of 1.899 \AA for $\text{ArC}-\text{Br}$ [9]. Two views of the molecule (Figure 2) show that the central trioxabicyclo[3.3.1] ring system is symmetrical and distinctly angular.

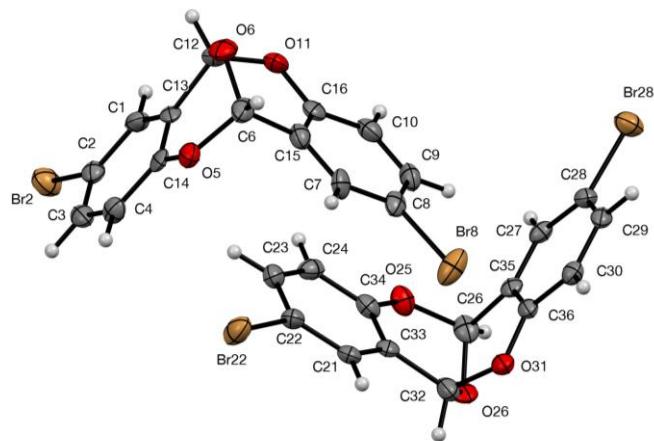


Figure 1. Molecular structure of **5** showing the two independent molecules with anisotropic displacement ellipsoids drawn at 50% probability level (hydrogen atoms are shown as grey spheres of arbitrary size) and the numbering system used.

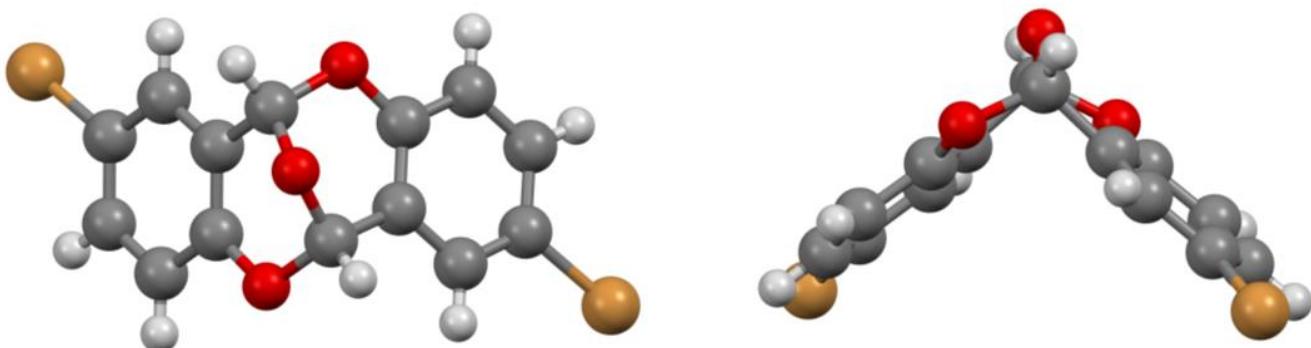


Figure 2. Two alternative views of **5** showing the symmetrical and distinctly angular shape of the molecule (carbon atoms—dark grey, hydrogen atoms—light grey, oxygen atoms—red, bromine atoms—brown).

As far as we are aware, only six compounds with this core structure have been previously characterised by X-ray diffraction (Figure 3) and the key geometric parameters for these are compared with **5** in Table 1. It can be seen that these form a relatively consistent pattern with the possible exception of the parent compound **2** which has longer bridging C–O bonds, a larger angle at the ring oxygens and a smaller angle between the mean planes. This last parameter is the angle between the planes defined by the five atoms making up each of the three-atom bridges in the bicyclo[3.3.1] system, i.e., $\text{CH}-\text{O}-\text{C}=\text{C}-\text{CH}$.

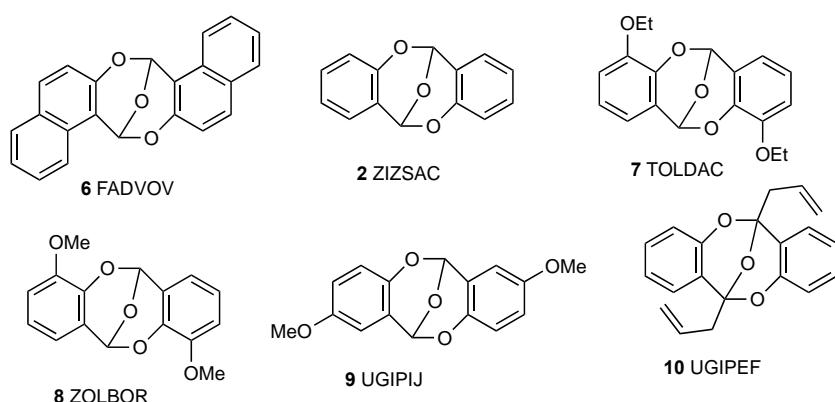


Figure 3. Crystallographically characterised disalicylaldehyde derivatives with CSD Ref Codes.

Table 1. Comparison of selected geometric parameters for **5** and related compounds (\AA , $^\circ$).

Compd	Bridging C–O Length (s)	Angle at Bridging O	Angle(s) at Ring Os	Angle between Mean Planes	Ref
5	1.404 (10), 1.410 (11)	109.6 (6)	111.6 (6), 112.4 (7)	72.9	This work
5	1.403 (11), 1.407 (11)	109.9 (6)	112.5 (6), 112.7 (6)	73.5	This work
6 FADVOV	1.418	108.6	112.3 (2)	71.7	[10]
2 ZIZSAC	1.549	106.5	117.9 (9)	65.9	[11]
7 TOLDAC	1.415(2), 1.417(2)	108.0(1)	111.4(1), 111.9(1)	73.5	[12]
8 ZOLBOR	1.411(3), 1.416(3)	107.8(2)	111.5(2), 111.7(2)	72.75	[13]
9 UGIPIJ	1.408(5), 1.414(5)	109.3(3)	112.2(2), 112.3(3)	72.75	[14]
10 UGIPEF	1.413(2), 1.417(2)	111.0(1)	112.6(1), 113.1(1)	73.6	[14]

The other main feature of the crystal structure of **5**, which is not evident in Figure 1, is the arrangement of adjacent pairs of independent molecules to allow a favourable π – π stacking interaction between them (Figure 4, distance between two mean planes 3.384 \AA , centroid···centroid distance 3.602(6) \AA). Among the six other structures of Figure 3 this feature only seems to occur for **2** (distance between two mean planes 3.264 \AA). We assume that the presence of bulky substituents in the other cases prevents this arrangement.

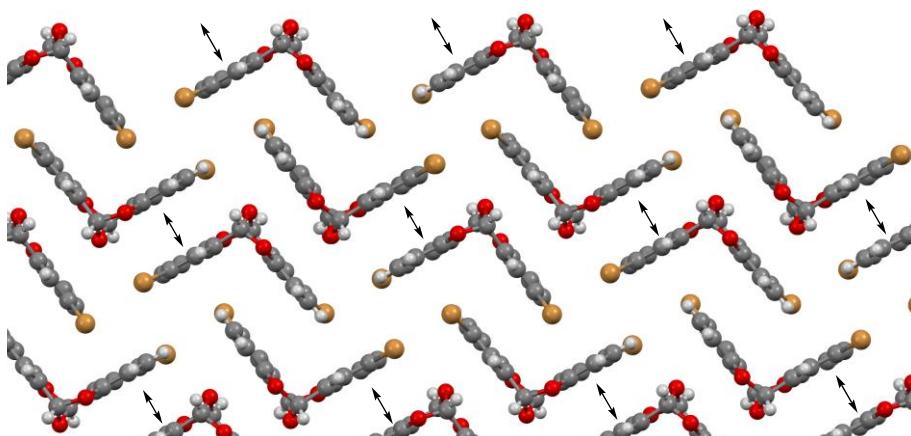


Figure 4. Crystal structure of **5** viewed along the crystallographic *a* axis showing π – π stacking interactions (arrows) between pairs of independent molecules.

In summary, the dibromodisalicylaldehyde **5** obtained as a minor by-product has been spectroscopically characterised for the first time and its X-ray crystal structure consist of pairs of independent molecules in a π – π stacking arrangement.

3. Experimental

Melting points were recorded on a Reichert hot-stage microscope (Reichert, Vienna, Austria) and are uncorrected. IR spectra were recorded using the ATR technique on a Shimadzu IRAffinity 1S instrument. NMR spectra were obtained using a Bruker AV300 instrument (Bruker, Billerica, MA, USA). Spectra were run with internal Me₄Si as the reference and chemical shifts are reported in ppm to high frequency of the reference.

3.1. Reaction Leading to Formation of 5

A solution of 5-bromo-2-methoxymethoxybenzaldehyde **3** [7] (20.0 g, 81.6 mmol) and *m*-chloroperoxybenzoic acid (28.8 g, 116.7 mmol) in CH₂Cl₂ (300 mL) was stirred at RT for 18 h. The mixture was filtered and the filtrate was stirred with 2 M aqueous Na₂S₂O₃ for 2 h. The organic layer was separated, dried and evaporated to give a solid (25.3 g). Column chromatography of this (SiO₂, hexane/EtOAc, 4:1) gave, as the first fraction, by-product **5** (0.66 g, 4%) followed by the desired product **4** (14.35 g, 75%) which had data in agreement with the published values [8].

Data for **5**: mp 157–159 °C (lit. [6] 168 °C); IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1607, 1477, 1412, 1265, 1221, 1184, 1132, 957, 881, 858, 814; ¹H NMR (300 MHz, CDCl₃, 25 °C): δ 6.28 (2H, s, OCHO, H-6,12), 6.79 (2H, d, *J* 6.6 Hz, H-4,10), 7.36 (2H, dd, *J* 6.6, 1.8 Hz, H-3,9), 7.42 (2H, d, *J* 1.8 Hz, H-1,7); ¹³C NMR (75 MHz, CDCl₃, 25 °C): δ 89.4 (2CH, OCHO, C-6,12), 113.9 (2C, C-2,8), 118.6 (2CH, C-4,10), 121.3 (2C, C-6a,12a), 130.1 (2CH, C-1,7), 134.2 (2CH, C-3,9), 149.4 (2C, C-4a,10a). ¹³C NMR assignments for CH confirmed by HSQC. Recrystallisation of **5** from hexane gave crystals suitable for X-ray diffraction.

3.2. X-ray Structure Determination of 5

X-ray diffraction data for compound **5** was collected at 173 K using a Rigaku FR-X Ultrahigh Brilliance Microfocus RA generator/confocal optics with XtaLAB P200 diffractometer [Mo Kα radiation ($\lambda = 0.71073 \text{ \AA}$)]. Data were collected and processed (including correction for Lorentz, polarization and absorption) using CrysAlisPro [15]. Structures were solved by dual-space methods (SHELXT) [16] and refined by full-matrix least-squares against F² (SHELXL-2019/3) [17]. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined using a riding model. All calculations were performed using the Olex2 [18] interface.

Crystal data for C₁₄H₈Br₂O₃, $M = 384.02 \text{ g mol}^{-1}$, colourless prism, crystal dimensions 0.09 × 0.08 × 0.06 mm, triclinic, space group P-1 (No. 2), $a = 6.9692(3)$, $b = 9.2930(4)$, $c = 21.4788(10) \text{ \AA}$, $\alpha = 97.000(4)$, $\beta = 97.013(4)$, $\gamma = 110.805(4)^\circ$, $V = 1270.00(10) \text{ \AA}^3$, $Z = 4$, $D_{\text{calc}} = 2.008 \text{ g cm}^{-3}$, $T = 173 \text{ K}$, $R_1 = 0.0798$, $wR_2 = 0.1442$ for 4246 reflections with $I > 2\sigma(I)$, and 343 variables, $R_{\text{int}} 0.0422$, Goodness of fit on F² 1.323. Data have been deposited at the Cambridge Crystallographic Data Centre as CCDC 2290326. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk/getstructures>.

Supplementary Materials: The following supporting information can be downloaded at: ¹H and ¹³C and HSQC NMR and IR data as well as cif and check-cif files for **5**.

Author Contributions: A.J.L. prepared the compound, D.B.C. and A.P.M. collected the X-ray data and solved the structure; R.A.A. designed the study, analysed the data, and wrote the paper. All authors have read and agreed to the published version of the manuscript.

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