Crystal structure of the complex of brominated diphenyl ethers from the marine sponge *Dysidea fragilis*

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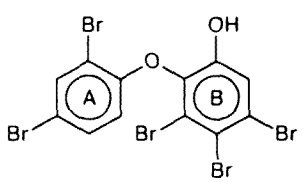
The spatial structures of 2-(2′,4′-dibromophenoxy)-3,4,5-tribromophenol (**1**) and 2-(2′-hydroxy-4′,6′-dibromophenoxy)-4,6-dibromoanisole (**2**) in crystals of the complex formed through two intermolecular O—H...O bonds were determined. The conformations of both molecules were found to be stabilized by intramolecular hydrogen bonds. The external hydrophobic surface of the complex of two molecules was shown to be occupied by nine bromine atoms.

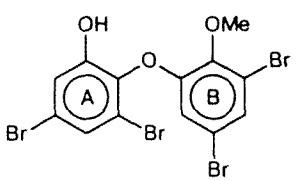
Key words: brominated diphenyl ethers, marine sponges, crystal and molecular structure.

A series of polyhalogenated oxyphenyl ethers with high antimicrobial activity was isolated from a small group of marine sponges belonging to the family *Dysideidae*.[1–5] Some of these substances are known to inhibit the enzymes of nucleic metabolism[6] and to possess antiinflammatory[7] and vasodilator[8] activities. The X-ray diffraction technique is used for structural identification of these substances.[9]

A study on the brominated diphenyl ethers from *Dysidea fragilis*[5] showed that chromatography on silica gel resulted in a fraction consisting of a mixture of compounds **1** and **2**. Compound **1** was hardly separated from **2** after repeated chromatography on Silufol-254. To explain such behavior, we performed an X-ray diffraction study of the single crystals obtained after crystallization of the mixture. The asymmetric part of the unit cell of the crystals was found to include two molecules, those of compounds **1** and **2**. The structures of **1** and **2** are shown on Fig. 1.



1



2

The molecules differ markedly in conformations. The angles between the planes of phenyl rings are 82° in **1** and 75° in **2**. The angles between the planes of phenyl rings and COC planes (including the ether oxygen and the ring carbon atoms linked with it) are −68° and 25° in **1** and 3° and 77° in **2**. The bond angles at the ether oxygen are 114(1)° in **1** and 119.7(1.3)° in **2**. The ether oxygen atom in **1** tips out of the plane of B ring for 0.17(2) Å. Deviations of ether oxygen atoms from the planes of other rings do not exceed the error of determination. Br(3), Br(4) and Br(5) atoms in **1** tip out of the plane of B ring for 0.14(2), −0.05(2), and 0.15(2) Å decreasing the steric tension in this part of the molecule. Deviation of bromine atoms from the planes of other rings do not exceed 0.05 Å.

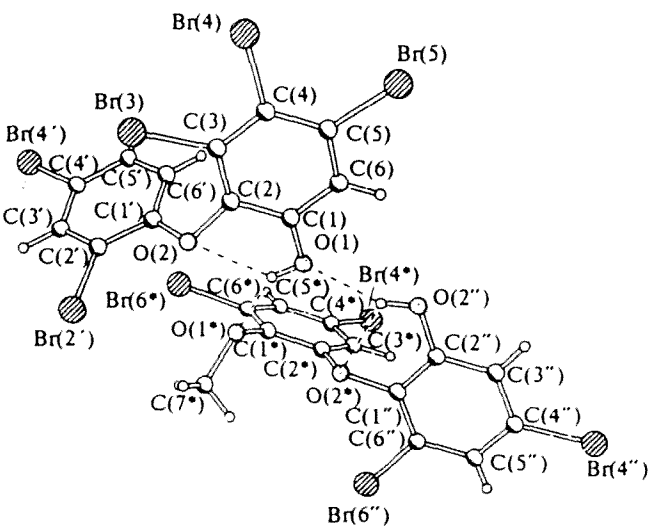


Fig. 1. Structures of **1** and **2** linked with hydrogen bonds in a crystal.

† Deceased

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Table 1. Contacts of Br atoms

A...B contacts	Position of B atom	Distance A...B/Å	Angle C—Br...Br maximum w_1/deg	Angle C—Br...Br minimum w_2/deg
Br(4')...Br(5)	$x,y-1,z-1$	3.730	163.6	126.2
Br(4")...Br(4)	$1-x,-y,-z$	3.483	164.3	113.5
Br(6")...Br(4*)	$1-x,-y,-z$	3.522	173.8	85.7
Br(6")...Br(6*)	$1-x,1-y,-z$	3.697	148.6	145.0
Br(4")...Br(4")	$1-x,-1-y,-1-z$	3.615	122.5	122.5

The intramolecular hydrogen bonds formed by hydroxyl groups and ether oxygen atoms (O...O and H...O distances are 2.74 Å and 2.27 Å; O—H...O angles are 114° (**1**) and 115° (**2**)) were found in both molecules. These bonds appear to play noticeable role in the stabilization of molecule conformations. The molecules **1** and **2** in crystal are linked by hydrogen bonds with the participation of the hydroxyl groups of each molecule. The hydroxyl group in **1** is linked to the oxygen atom of the methoxy group of **2** (O...O and H...O distances are 2.70 Å and 1.95 Å, O—H...O angle is 147°). The hydroxyl group in **2** is linked to the oxygen atom of the hydroxy group of **1** (O...O and H...O distances are 2.76 Å and 1.97 Å, O—H...O angle is 154°). Thus, the hydroxyl groups of both molecules participate in formation of intra- and intermolecular hydrogen bonds, the hydroxyl group in **1** being proton donor and proton acceptor the same time.

Alongside the hydrogen bonds the Br...Br contacts (Table 1) with the distances less than twice van der Waals radius of Br atom (3.94 Å) are observed. Five of them with the distances less than 3.79 Å can be conventionally referred to specific interactions including the two shortest ones (3.483(1) and 3.522(1) Å) classified as asymmetric ($w_1 \neq w_2$).[10]

The complex of brominated diphenyl ethers studied is formed through intermolecular OH...O hydrogen bonds of medium force and has a hydrophobic surface occupied by nine bromine atoms.

Experimental

Crystal data: $C_{12}H_5O_2Br_5 \cdot C_{13}H_8O_3Br_4$, M_1 = 531.84; M_2 = 580.72; a = 11.306(2), b = 11.390(1), c = 13.539(2) Å; α = 112.29(1), β = 102.99(1), g = 92.68(1)°; triclinic; space group $P\bar{1}$; V = 1554.9(3) Å^3; Z = 2; D_{calc} = 2.38 g·cm^{-3}; $F(000)$ = 1036; μ_{Mo} = 11.53 mm^{-1}.

Crystals were prepared from the solution in diethyl ether—hexane (1 : 2). Registration was performed at a Hilger & Watts four-circle diffractometer at room temperature by $\theta/2\theta$ mode to 2θ = 40° (graphite monochromator, Mo-Kα radiation, λ = 0.71069 Å); 2875 independent reflections were measured, 1639 of them with $I > 3\sigma(I)$ were used for refinement. The corrections for Lorentz factors, polarization, and absorption were made.[11] The structure was solved by direct methods and refined by full-matrix anisotropic approximation for non-hydrogen atoms using the weighting scheme $w = 1/\sigma^2(F)$. The benzene rings were refined as the rigid regular hexagons. The hydrogen atoms in hydroxyl groups were determined from difference syntheses and refined imposing the restrictions on O—H bond lengths and C—O—H angles. In other groups the hydrogen atoms were arranged according to geometry. The structure was refined to final divergence coefficients R = 0.075 and R_w = 0.041. Calculations were performed using SHELX-86 and SHELX-76 programs.[12,13]

Coordinates and equivalent anisotropic thermal parameters for non-hydrogen atoms are given in Table 2. Bond lengths and angles in molecules **1** and **2** are similar to the corresponding standard values.

Table 2. Atomic coordinates (×10^4) and equivalent isotropic thermal parameters (×10^3)

Atom	x	y	z	U/Å^2
Br(3)	9566(3)	3208(2)	3061(2)	61(1)
Br(4)	7828(2)	5299(3)	4257(2)	72(1)
Br(5)	8717(3)	8411(3)	4941(2)	70(1)
Br(2')	13014(3)	2309(3)	2273(2)	75(1)
Br(4')	9760(3)	288(3)	−2006(2)	77(1)
O(1)	12082(12)	7025(11)	2872(10)	61(2)
O(2)	11638(11)	4518(11)	2555(10)	42(2)
C(1)	11150(8)	6615(9)	3212(7)	33(2)
C(2)	10829(8)	5323(9)	2982(7)	41(2)
C(3)	9844(8)	4942(9)	3308(7)	36(2)
C(4)	9178(8)	5854(9)	3864(7)	32(2)
C(5)	9498(8)	7146(9)	4094(7)	45(2)
C(6)	10484(8)	7527(9)	3768(7)	50(2)
C(1')	11143(9)	3611(9)	1493(8)	36(2)
C(2')	11716(9)	2516(9)	1231(8)	50(2)
C(3')	11308(9)	1520(9)	185(8)	52(2)
C(4')	10327(9)	1619(9)	−601(8)	43(2)
C(5')	9754(9)	2714(9)	−339(8)	49(2)
C(6')	10161(9)	3710(9)	708(8)	46(2)
Br(4*)	6584(3)	1078(3)	1020(2)	68(1)
Br(6*)	7490(3)	5893(2)	837(2)	74(1)
Br(4")	4076(3)	−3870(2)	−5313(2)	67(1)
Br(6")	2999(3)	850(3)	−2545(2)	84(1)
O(1*)	6453(12)	4275(12)	−1647(10)	56(2)
O(2*)	5559(12)	1818(11)	−2674(9)	47(2)
O(2")	7028(12)	388(12)	−3869(11)	61(2)
C(1*)	6450(8)	3599(9)	−1014(8)	41(2)
C(2*)	6027(8)	2286(9)	−1547(8)	33(2)
C(3*)	6073(8)	1536(9)	−933(8)	57(2)
C(4*)	6542(8)	2100(9)	215(8)	47(2)
C(5*)	6964(8)	3414(9)	747(8)	22(2)
C(6*)	6918(8)	4163(9)	133(8)	50(2)
C(1")	5159(9)	518(9)	−3264(7)	47(2)
C(2")	5943(9)	−179(9)	−3849(7)	41(2)
C(3")	5610(9)	−1494(9)	−4479(7)	53(2)
C(4")	4492(9)	−2112(9)	−4524(7)	45(2)
C(5")	3708(9)	−1416(9)	−3940(7)	40(2)
C(6")	4041(9)	−102(9)	−3310(7)	49(2)
C(7*)	5335(18)	4825(18)	−1864(16)	85(2)

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