

New Brominated Diphenyl Ether from an Unidentified Species of *Dysidea* Sponge. ^{13}C NMR Data for Some Brominated Diphenyl Ethers

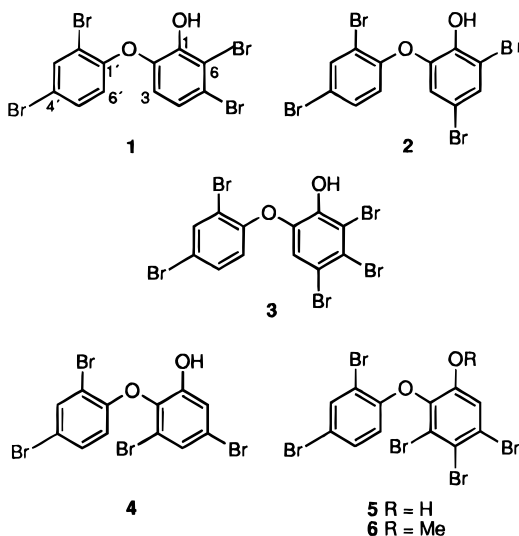
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The structure of a new brominated diphenyl ether, **1**, isolated from an unidentified species of *Dysidea* sponge, has been solved by spectroscopic analysis. ^{13}C NMR data of related diphenyl ethers were also assigned by analysis of their HMQC and HMBC spectra.

In an earlier paper,¹ we reported 14 polybrominated phenols and diphenyl ethers, six of them new, from four Indo-Pacific *Dysidea* sponges. Several of these compounds were inhibitors of inosine monophosphate dehydrogenase, guanosine monophosphate synthetase, or 15-lipoxygenase. From an undescribed *Dysidea* sp. (specimen 35T92) collected at Satawan Atoll, Chuuk State, Federated States of Micronesia, the four known compounds (**2**–**5**) had been isolated.¹ Further study of the fractions from an extract of this specimen has resulted in the isolation of an additional minor metabolite, which is a new diphenyl ether (**1**). In this paper, we report the structure elucidation of **1** and ^{13}C NMR data of compounds **1** and **3**–**6**.



Diphenyl ether **1** was obtained by further reversed-phase HPLC fractionation of mixtures remaining from our earlier work. The IR spectrum of phenol **1**, $\text{C}_{12}\text{H}_6\text{Br}_4\text{O}_2$ based on HREIMS, revealed the presence of a hydroxyl group (3480 cm^{-1}) and phenyl rings ($1580, 1455\text{ cm}^{-1}$). The ^1H NMR spectrum of **1** in CD_3OD contained signals at δ 7.83 (1H, d, $J = 2.4$ Hz), 7.46 (1H, dd, $J = 8.9, 2.4$ Hz), and 6.83 (1H, d, $J = 8.9$ Hz) assigned to the protons on the 2,4-dibromophenoxy ether ring and at δ 7.11 (1H, d, $J = 8.9$ Hz) and 6.65 (1H, d, $J = 8.9$ Hz) due to two ortho-situated aromatic protons on the phenolic ring. These assignments were confirmed by correlations observed in the COSY spec-

trum of **1**. It has been noted that the bromine substituent at C-3 affected the chemical shift of the C-6' proton significantly.² The chemical shift of the C-6' proton was at $\delta \sim 6.8$ in phenols **2** and **3**, which have no substituent at C-3 and at $\delta \sim 6.4$ in phenols **4** and **5**,² which have a bromine at C-3. The chemical shift at δ 6.83 for H-6' in compound **1** indicated that there is no bromine substituent at C-3. Therefore, phenol **1** was determined to be 5,6-dibromo-2-(2',4'-dibromophenoxy)phenol. Further support for this assignment was derived from observation of a NOESY correlation (CD_3OD) between H-6' (δ 6.83) and H-3 (δ 6.65). The structure was also confirmed by the observation that conversion of the phenol **1** to its sodium phenolate by adding one drop of 40% NaOD/ D_2O to a solution of **1** in $\text{DMSO}-d_6$ caused an upfield shifts of 0.15 ppm for H-3 and of 0.82 ppm for H-4, as expected for protons *meta* and *para* to a phenolic hydroxyl group.³

This work also gave us an opportunity to assign the ^{13}C NMR data for phenols **3**–**6** (see Table 1). To our knowledge, ^{13}C NMR data for compounds **3** and **6** have not been reported previously, and those for **4** and **5** have been reported but not assigned.^{1,4} A complete ^{13}C NMR chemical shift assignment for **4**–**6** was made with the aid of HMQC and HMBC experiments and literature analogies. The protonated carbons of **3** were assigned by HMQC data, but there was insufficient sample to obtain HMBC data to complete assignments of the quaternary carbons. Due to limited sample availability it was not possible to obtain a good broadband-decoupled ^{13}C spectrum of **1**, but from an HMQC spectrum assignments were made for the five protonated carbons in **1**, i.e., δ 137.5 (C-3'), 133.6 (C-5'), 122.5 (C-6'), 120.1 (C-3), 124.6 (C-4) ppm. It is worthwhile to note that the bromine substituent at C-3 also greatly affected the ^{13}C chemical shift of C-6', e.g., the chemical shift of C-6' was δ 122.5 and 121.3 in phenols **1** and **3** that have no substituent at C-3, while C-6' resonates at $\delta \sim 116$ in compounds **4**–**6** that have bromine at C-3.

Experimental Section

General Experimental Procedures. All NMR experiments were performed on a Varian VXR-500 spectrometer equipped with a 3 mm $^1\text{H}/^{13}\text{C}$ switchable gradient microprobe (MDG-500-3) and a pulsed field gradient driver. MS were measured with Hewlett-Packard 5985B (low resolution) and VG ZAB (high resolution) mass spectrometers. The IR spectrum was recorded on a Bio-Rad 3240-spc FT instrument.

Animal Material. This was described previously.¹

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Table 1. NMR Data of Compounds **3–6**^a

C no.	3^b			4^b		
	¹³ C	¹ H		¹³ C	¹ H	HMBC correln (C no.)
1	150.2 (s)			152.1 (s)		
2	143.8 (s)			138.4 (s)		
3	122.1 (d)	7.15 (s)		118.7 (s)		
4	121.8 (s)			125.1 (d)	7.36 (d, 2.0)	2, 3, 5
5	121.8 (s)			118.0 (s)		
6	116.5 (s)			119.6 (d)	7.17 (d, 2.0)	1, 2, 4, 5
1'	152.1 (s)			152.6 (s)		
2'	114.6 (s)			111.6 (s)		
3'	135.5 (d)	7.91 (d, 2.4)		135.1 (d)	7.85 (d, 2.5)	1', 2', 4'
4'	115.7 (s)			113.9 (s)		
5'	132.3 (d)	7.50 (dd, 8.6, 2.4)		131.5 (d)	7.38 (dd, 9.0, 2.5)	1', 3', 4', 6'
6'	121.3 (d)	6.87 (d, 8.6)		115.9 (d)	6.46 (d, 9.0)	1', 2', 4', 5'
OH					10.79 (brs)	

C no.	5^b			6^c		
	¹³ C	¹ H	HMBC correln (C no.)	¹³ C	¹ H	HMBC correln (C no.)
1	150.8 (s)			152.7 (s)		
2	139.5 (s)			141.2 (s)		
3	121.5 (s)			122.6 (s)		
4	115.9 (s)			119.2 (s)		
5	121.5 (s)			122.5 (s)		
6	120.7 (d)	7.43 (s)	1, 2, 4, 5	117.2 (d)	7.37 (s)	1, 2, 4, 5
1'	152.3 (s)			152.9 (s)		
2'	111.7 (s)			112.4 (s)		
3'	135.1 (d)	7.84 (d, 2.0)	1', 2', 4', 5'	136.2 (d)	7.83 (d, 2.4)	1', 2', 4', 5'
4'	114.1 (s)			115.2 (s)		
5'	131.5 (d)	7.35 (dd, 8.5, 2.0)	1', 3', 4'	131.5 (d)	7.27 (dd, 8.7, 2.4)	1', 3', 4'
6'	115.9 (d)	6.51 (d, 8.5)	1', 2', 4'	115.7 (d)	6.34 (d, 8.7)	1', 2', 4'
OH		10.92 (brs)				
OCH ₃				57.1 (q)	3.79 (s)	1

^a For proton signals: (mult, coupling in Hz). ^b DMSO-*d*₆. ^c CD₂Cl₂.

Extraction and Isolation. Polar minor eluates from our previous HPLC separation of extracts of this sponge were pooled and subjected to further purification by C18 reversed-phase HPLC using 16% H₂O in MeOH as eluent to yield ~0.1 mg of **1**.

5,6-Dibromo-2-(2',4'-dibromophenoxy)phenol (1): IR (neat) ν_{\max} 3480, 1580, 1455 cm⁻¹; ¹H NMR (CD₃OD) δ 7.83 (1H, d, *J* = 2.4 Hz, H-3'), 7.46 (1H, dd, *J* = 8.9, 2.4 Hz, H-5'), 7.11 (1H, d, *J* = 8.9 Hz, H-4), 6.83 (1H, d, *J* = 8.9 Hz, H-6'), 6.65 (1H, d, *J* = 8.9 Hz, H-3), (DMSO-*d*₆) δ 8.17 (1H, brs, OH), 7.89 (1H, d, *J* = 2.4 Hz, H-3'), 7.49 (1H, dd, *J* = 9.0, 2.4 Hz, H-5'), 7.00 (1H, d, *J* = 8.5 Hz, H-4), 6.81 (1H, d, *J* = 9.0 Hz, H-6'), 6.73 (1H, d, *J* = 8.5 Hz, H-3), (DMSO-*d*₆ + NaOD) δ 7.67 (1H, d, *J* = 2.4 Hz, H-3'), 7.29 (1H, dd, *J* = 9.0, 2.4 Hz, H-5'), 6.59 (1H, d, *J* = 8.5 Hz, H-3), 6.47 (1H, d, *J* = 9.0 Hz, H-6'), 6.18 (1H, d, *J* = 8.5 Hz, H-4) ppm; a correlation was observed in a NOESY spectrum in this solvent between δ 6.59 and 6.47; HREIMS (70 eV) *m/z* 499.7110, calcd for C₁₂H₆⁷⁹Br₃⁸¹BrO₂ 499.7081; 501.7039, calcd for C₁₂H₆⁷⁹Br₂⁸¹Br₂O₂ 501.7060; 503.7026, calcd for C₁₂H₆⁷⁹Br⁸¹Br₃O₂ 503.7040; LREIMS (70 eV) *m/z* 506

(11.6), 504 (47.2), 502 (68.9), 500 (50.2), 498 (12.5), 344 (51.3), 342 (100), 340 (53.8), 269 (3.1), 267 (6.1), 265 (4.2), 238 (16.4), 236 (28.2), 234 (16.3).

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References and Notes

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