



PHLORETHOLS, FUHALOLS AND THEIR DERIVATIVES FROM THE BROWN ALGA *SARGASSUM SPINULIGERUM**

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Key Word Index—*Sargassum spinuligerum*; Phaeophyceae; Sargassaceae; phlorotannins; fuhalols; phloretols; hydroxyphloretols; deshydroxyfuhalols; hydroxyfuhalols; structural elucidation.

Abstract—The structural elucidation of 14 new phloroglucinol derivatives isolated from the ethanolic extract of the brown alga *Sargassum spinuligerum* is described. To protect them from rapid oxidation they were peracetylated before isolation. These phlorotannins belong to the classes of phloretols, hydroxyphloretols, deshydroxyfuhalols, fuhalols and hydroxyfuhalols. By means of spectral analysis, the following compounds were identified: hydroxytrifuhalol-A and -B nonaacetate, dihydroxytetraphloretol-A and -B undecaacetate, deshydroxytetrafuhalol-B decaacetate, pentaphloretol-A undecaacetate, pentafuhalol-B tridecaacetate, hydroxypentafuhalol-B tetradecaacetate, deshydroxyhexafuhalol-B pentadecaacetate, heptafulhalol-B octadecaacetate, hydroxyheptafulhalol-A and -B nonadecaacetate and nonafuhalol-B tricosacetate. In addition, the following 14 well known substances were identified: phloroglucinoltriacetate, diphloretolpentaacetate, bifuhalolhexaacetate, triphloretol-A and -B heptaacetate, trifuhalol-B octaacetate, tetraphloretol-C nonaacetate, tetrafuhalol-B undecaacetate, hydroxypentafuhalol-A tetradecaacetate, hexafuhalol-B hexadecaacetate, trifuhalol-A octaacetate, hydroxytetraphloretol-A decaacetate, pentafuhalol-A tridecaacetate and heptafulhalol-A octadecaacetate. An accurate assignment of ¹H NMR chemical shifts was carried out for the last four of these.

INTRODUCTION

Recently we reported [1] on the isolation and structural elucidation of 20 fuhalols and deshydroxyfuhalols from *Sargassum spinuligerum* Sond. As with these phlorotannins the substances described below contain phloroglucinol units exclusively linked by aryl ether bonds. However, the substitution patterns of these isolated compounds are very varied.

RESULTS AND DISCUSSION

After extraction of the frozen thallus with ethanol the fraction containing phenols was obtained by shaking with ethyl acetate. It was immediately acetylated with acetic anhydride-pyridine. The higher polymeric acetylated phenols were removed by precipitation with a mixture of diethyl ether and petrol. The low-*M*_n fraction was fractionated by flash chromatography on silica gel and afterwards purified in several HPLC steps [1].

By means of ¹H NMR spectra (CDCl₃) and comparison with published data phloroglucinoltriacetate [2], diphloretolpentaacetate [3], bifuhalolhexaacetate [4],

triphloretol-A and -B heptaacetate [5, 6], trifuhalol-A (10) and -B octaacetate [7, 8], tetraphloretol-C nonaacetate [5], hydroxytetraphloretol-A decaacetate (12) [9], tetrafuhalol-B undecaacetate [10], pentafulhalol-A tridecaacetate (15) [11], hydroxypentafuhalol-A tetradecaacetate (2) [12], hexafuhalol-B hexadecaacetate [12] and heptafulhalol-A octadecaacetate (17) [13] were identified. For 10, 12, 15 and 17 the chemical shift for nearly all protons could be assigned by comparing the NMR data with all known and newly discovered fuhalols [1, 12, 14] (see Tables 1-4).

Recently we reported fuhalols belonging to the A-series [1]. Hydroxytrifuhalol-B nonaacetate (1), 2 and hydroxyheptafulhalol-B nonadecaacetate (3) belong to a very similar series. The only difference to the fuhalol-A series (e.g. 15 and 17) is that ring I is connected with a 1,2-phenoxylated phloroglucinol unit instead of a 1,4-phenoxylated ring. In comparison with the aromatic protons of ring I of the fuhalol-A series (typical δ6.94) the corresponding protons of 1-3 are shifted to a higher field (typically δ6.91, measured in CDCl₃). Also the signals for the acetyl groups of ring I are shifted upfield (δ2.05 for 1 and δ2.03 for 3, respectively; chemical shifts for 2 are reported in ref. [12]). The proton at C6 of ring II is shifted downfield in comparison to the proton at C6 of ring III of the fuhalol-A series (from a typical δ6.64 for the fuhalol-A series to δ6.70 and 6.66 for 1 and 3, respectively). All other chemical shifts of both series are very

*Dedicated to Prof. Dr F.-C. Cygan, Würzburg, on his sixtieth birthday.

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Table 1. ^1H NMR spectral data of **10** and **11**

H	10		11
	CDCl_3	CDCl_3	$d_6\text{-Me}_2\text{CO}$
3, 5	6.96	6.96	7.07
Ac-2, Ac-6	2.10	2.11	2.12
Ac-4	2.27	2.27 ^a	2.26 ^b
	Ring II		
2, 6	6.69	6.70	6.80
Ac-3, Ac-5	2.05	2.09	2.08
	Ring III		
2	6.69		
6	6.69	6.53	6.56
Ac-2		2.18	2.20
Ac-3	2.22	2.27 ^a	2.30 ^c
Ac-4	2.24	2.25 ^a	2.25(5) ^{b, c*}
Ac-5	2.22	2.23	2.25

^{a-c} Assignments with the same letter may be interchanged.

*For some signals the chemical shift has been estimated to the approximated third decimal place (shown in parentheses). This is to distinguish between signals of very close value but which could nevertheless be clearly differentiated by visual inspection of the spectra.

similar. For **1** and **2** the ring types A, B, C and D (Fig. 1) were established by ^{13}C NMR. Also the measured data match the calculated data very well (Table 5).

The EI-mass spectrum of **1** showed the molecular ion $[\text{M}]^+$ at m/z 784 ($\text{C}_{36}\text{H}_{32}\text{O}_{20}$) and a ketene elimination series 784 \rightarrow 406, down to the free phenol, corresponding

to nine acetoxy groups. A M_r of 1732 ($\text{C}_{80}\text{H}_{68}\text{O}_{44}$) for **3** could be deduced from a FAB-mass spectrum. Also a five-fold ketene elimination series starting with the ion at m/z 474 could be observed in the EI-mass spectra of **1** and **3**. These series are characteristic for dioxin fragments and also confirm the linkage of ring I, II and III [14].

For structural elucidation, a ^1H NMR spectrum measured in d_6 -acetone is useful [14]. This spectrum allows a clear determination of ring types independent of the position of a single ring in the total molecule [1]. For instance: the rings II, IV and VI of **3** belong to the ring type B (see Fig. 1). Consequently, the chemical shifts for the aromatic protons of these rings are very similar when measured in d_6 -acetone: δ 6.68(5), δ 6.69(2) and δ 6.69(5), respectively. For this reason a ^1H NMR spectrum was recorded in chloroform-*d* and in d_6 -acetone for all new compounds.

The separation of these fuhalols was possible by HPLC using the method described in ref. [1]. The R_f are significantly different from those of the fuhalols of the A series with the same number of rings. In our previous paper we showed the HPLC elution profile of the total peracetylated phlorotannin fraction [1]. The R_f of the tetrafuhalol-A undecaacetate and pentafuhalol-A undecaacetate are close together. The same was found for hexafuhalol-A hexadecaacetate and hepta fuhalol-A octadecaacetate. But the first pair of fuhalols can be easily separated from the second. The number of 1,4-diphenoxylated benzene units has an obviously smaller influence on the R_f than the number of 1,2-diphenoxylated benzene units per molecule.

The same was established for the fuhalol series containing **1-3** and hexafuhalol-B hexadecaacetate. Compound

Table 2. ^1H NMR spectral data of **12-14**

H	12		13		14	
	CDCl_3	$d_6\text{-Me}_2\text{CO}$	CDCl_3	$d_6\text{-Me}_2\text{CO}$	CDCl_3	$d_6\text{-Me}_2\text{CO}$
3, 5	6.95	7.05	6.95	7.06	6.94	7.04
Ac-2, Ac-6	2.10	2.08	2.14	2.11(3)	2.12	2.11
Ac-4	2.27	2.25	2.29 ^a	2.26(7) ^b	2.28 ^c	2.27 ^d
	Ring I					
2	6.66	6.77			6.65	6.73
6	6.66	6.77	6.50	6.57	6.65	6.73
Ac-2			2.27 ^a	2.25(5)		
Ac-3	2.05	*	2.18	2.14	2.04	2.01
Ac-5	2.05	*	2.03	2.02	2.04	2.01
	Ring II					
2	6.69	6.80	6.69	6.73		
6	6.69	6.80	6.69	6.73	6.47	6.53
Ac-2					2.29 ^c	2.32 ^d
Ac-3	2.09	2.07	2.13	2.11	2.27(5) ^c	2.26(5) ^d
Ac-5	2.09	2.07	2.13	2.11	2.12	2.14
	Ring III					
2	6.69	6.80	6.69	6.73		
6	6.69	6.80	6.69	6.73	6.47	6.53
Ac-2					2.29 ^c	2.32 ^d
Ac-3	2.09	2.07	2.13	2.11	2.27(5) ^c	2.26(5) ^d
Ac-5	2.09	2.07	2.13	2.11	2.12	2.14
	Ring IV					
2, 6	6.70	6.82	6.71	6.78	6.71	6.79
Ac-3, Ac-5	2.22	2.21	2.25	2.24	2.23(5)	2.23
Ac-4	2.24	2.24	2.26 ^a	2.26(3) ^b	2.25 ^c	2.25(5) ^d

^{a-d} Assignments with the same letter may be interchanged.

*Hidden by solvent.

Table 3. ^1H NMR spectral data of **15** and **16**

H	15		16
	CDCl_3	CDCl_3	$d_6\text{-Me}_2\text{CO}$
Ring I			
3, 5	6.94	6.94	7.05
Ac-2, Ac-6	2.12	2.12	2.10
Ac-4	2.28	2.28 ^b	2.27 ^c
Ring II			
2, 6	6.65	6.65	6.76
Ac-3, Ac-5	2.06	2.06	2.07
Ring III			
6	6.64(5)	6.64(5)	6.66
Ac-3	2.21	2.20	2.20
Ac-4	2.25 ^a	2.25(7) ^b	2.25
Ac-5	2.22	2.22	2.23(5)
Ring IV			
2, 6	6.69(5)	6.71	6.81
Ac-3, Ac-5	2.07	2.10	2.08
Ring V			
2	6.70		
6	6.70	6.56	6.59
Ac-2		2.18	2.17
Ac-3	2.23	2.28 ^b	2.30 ^c
Ac-4	2.26 ^a	2.26 ^b	2.26 ^c
Ac-5	2.23	2.24	2.24

^{a-c} Assignments with the same letter may be interchanged.

Table 4. ^1H NMR spectral data of **17** and **18**

H	17		18
	CDCl_3	CDCl_3	$d_6\text{-Me}_2\text{CO}$
Ring I			
3, 5	6.94	6.94	7.05
Ac-2, Ac-6	2.11	2.11	2.10
Ac-4	2.28	2.28 ^d	2.26(5) ^h
Ring II			
2, 6	6.65	6.65	6.75
Ac-3, Ac-5	2.04 ^a	2.05 ^e	2.06(5) ⁱ
Ring III			
6	6.64	6.64	6.66
Ac-3	2.19 ^b	2.20 ^f	2.19(5) ^j
Ac-4	2.25(5) ^c	2.26 ^d	2.26 ^h
Ac-5	2.21	2.22 ^g	2.22 ^k
Ring IV			
2, 6	6.67(5)	6.67(5)	6.79
Ac-3, Ac-5	2.03 ^a	2.04 ^e	* ⁱ
Ring V			
6	6.67	6.67	6.70
Ac-3	2.19 ^b	2.19 ^f	2.19 ^j
Ac-4	2.25 ^c	2.26 ^d	2.26(5) ^h
Ac-5	2.21	2.21 ^g	2.20 ^k
Ring VI			
2, 6	6.70(5)	6.71	6.81
Ac-3, Ac-5	2.07	2.10	2.07 ⁱ
Ring VII			
2	6.71		
6	6.71	6.57	6.60
Ac-2		2.17	2.16
Ac-3	2.22	2.28 ^d	2.30 ^h
Ac-4	2.25(7) ^c	2.26 ^d	2.25 ^h
Ac-5	2.22	2.24	2.23

*Hidden by solvent.

^{a-k} Assignments with the same letter may be interchanged.

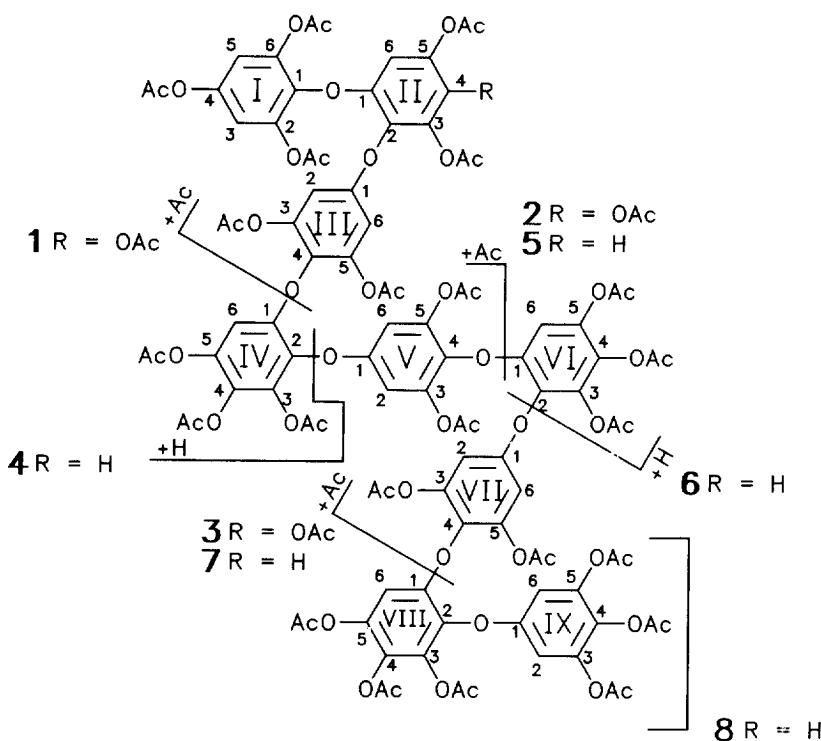
2 and hexafuhalol-B hexadecaacetate have a similar R_f . Both substances have the same number of 1,2-diphenoxylated benzene units but a different number of 1,4-diphenoxylated benzene units. The R_f of these fuhalols was found to be between those of penta fuhalol-A tridecaacetate and hexafuhalol-A hexadecaacetate. The R_f of the fuhalols described below follows similar rules.

The homologous phlorotannin series, consisting of the substances deshydroxytetra fuhalol-B decaacetate (**4**), penta fuhalol-B tridecaacetate (**5**), hexafuhalol-B hexadecaacetate (**6**), hepta fuhalol-B octadecaacetate (**7**) and nonafuhalol-B tricosaacetate (**8**), differs from the fuhalol series described above (**1-3**) only in position 4 of ring II. Consequently for the protons at C-4 and C-6 the ^1H NMR spectra (CDCl_3) of **4-8** showed an AB-system at typically δ 6.74 and 6.52. The resulting coupling constant of $ca J_{AB} = 2.7$ Hz indicates aromatic protons in the *meta* position. These chemical shifts for the AB system are comparable to those of deshydroxytetra fuhalol-A decaacetate [9] and deshydroxyhexafuhalol-A pentadecaacetate [1], described in the previous paper [1]. All other chemical shifts of **4-8** are very similar to the homologous series, consisting of **1-3**.

The ^{13}C NMR spectra of **5** and **7** showed a chemical shift of δ 112.0 and 108.5 for C-4 and C-6 of ring II, respectively. Analogously to ring type C, ring II is 1,2-diphenoxylated and is given the type indication 'C'. The presence of the ring types A to D could be proven. Table 6 shows a good correlation between measured and calculated data.

In the EI-mass spectra of **4-6** a four-fold ketene elimination series from m/z 416 down to m/z 248 is visible, produced by the benzodioxin fragment consisting of rings I and II [8]. The EI-mass spectrum of **4** showed a $[\text{M}]^+$ at m/z 934 ($\text{C}_{44}\text{H}_{38}\text{O}_{23}$), from which a 10-fold ketene elimination series was observed down to the free phenol. The M_r of 1200 ($\text{C}_{56}\text{H}_{48}\text{O}_{30}$) for **5**, 1408 ($\text{C}_{66}\text{H}_{56}\text{O}_{35}$) for **6**, 1674 ($\text{C}_{78}\text{H}_{66}\text{O}_{42}$) for **7** and 2148 ($\text{C}_{100}\text{H}_{84}\text{O}_{54}$) could be derived from the FAB-mass spectra.

The $[\text{M}]^+$ of pentaphloretol-A undecaacetate (**9**) at m/z 1084 ($\text{C}_{52}\text{H}_{44}\text{O}_{26}$) showed a difference of 116 to the M_r of **5**. Consequently, **9** has two acetoxy groups less than **5**. The ^1H NMR spectrum (CDCl_3) showed two AB-systems at δ 6.53/6.75 and δ 6.53/6.74, with a coupling constant of $J_{AB} = 2.1$ Hz and an AB_2 -system at δ 6.56/6.66 with $J_{AB} = 2.7$ Hz. This means that **9** contains two 1,2-diphenoxylated 3,5-diacetoxybenzene units and one 1-phenoxy 3,5-diacetoxybenzene unit as well. According to **5** in the EI-mass spectrum of **9** a ketene elimination series for a dioxin fragment could be obtained (m/z 416 \rightarrow 248). In conclusion, the two 1,2-diphenoxylated rings (II and IV) are linked by a 1,4-diphenoxylated



The numbering of the carbons in the figure is not in accordance with IUPAC-rules.

Table 5. ^{13}C NMR spectral data of **1** and **2** (in CDCl_3)

C	Measured		Calculated [15]
	1	2	
Ring Type A			
1	136.1	136.1	136.8
2, 6	143.0 ^a	143.1 ^b	143.6
3, 5	114.8	114.8	113.8
4	146.5	146.5	146.2
Ring Type B			
1	153.9	153.1	
2, 6	109.2(9)	108.3	
3, 5	143.5 ^b	142.5	
4	134.1	134.7	
Ring Type C			
1	147.5	147.5/147.8	147.5
2	134.6	134.5/134.6	134.4
3	137.9	137.8/137.9	136.6
4	131.5	131.3/131.5	131.2
5	140.1	140.0(9)/140.1(2)	139.2
6	109.4	109.1(8)/109.3(2)	109.0
Ring Type D			
1	154.8	154.8	155.2
2, 6	108.9	108.9	108.0
3, 5	143.6 ^a	143.6 ^b	144.4
4	130.3	130.3	130.2

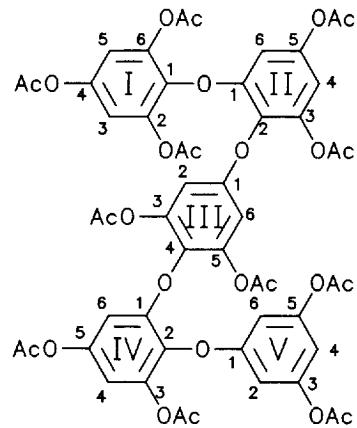
^{a, b}Assignments with the same letters may be interchanged.

ring (III). The AB_2 -system belongs to the aromatic protons of ring V and is typical for phloretols [5, 6].

A M_r 784 ($\text{C}_{36}\text{H}_{32}\text{O}_{20}$) could be deduced from the EI-mass spectrum of hydroxytrifulhalol-A nonaacetate (**11**).

The difference to the M_r of trifulhalol-A octaacetate (M_r , 726 [7]) is 58 corresponding to one acetoxy group. The position of that additional acetoxy group could be determined by ^1H NMR.

The resonances of the protons of ring I and II of **10** and **11** are very similar (Table 1). Only the signal of one acetyl group of ring II is shifted from δ 2.05 (**10**) to δ 2.09 (**11**, CDCl_3). Consequently, ring III carries the additional acetoxy group and there is only one singlet for one aromatic proton at ring III of **11** visible (δ 6.53, CDCl_3). Also the signal at δ 2.22 (**10**) for six protons, according to the acetyl groups at C-3 and C-5 of ring III was not detected in the spectrum of **11**. Instead of that signal the NMR spectrum of **11** showed additional signals at δ 2.18, 2.27 and 2.23 (CDCl_3), each for one acetoxy group. In the spectrum recorded in d_6 -acetone, one of these signals is



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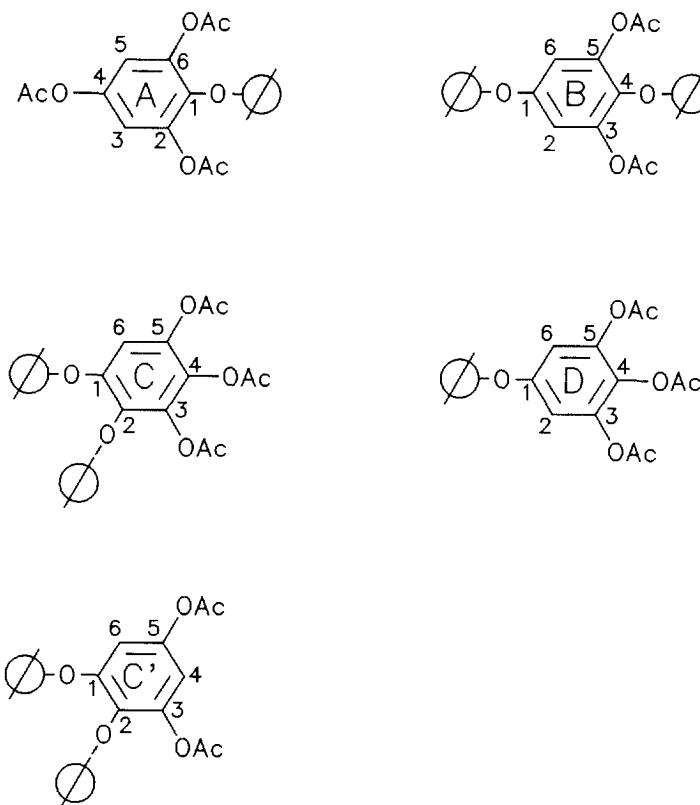


Fig. 1. Ring types A, B, C, C' and D of peracetoxylated phlorotannins. \emptyset : Aryl ester.

shifted significantly downfield (δ 2.30). This indicates that C-2, C-3, C-4 and C-5 of ring III (**11**) are substituted with acetoxy groups. The acetoxy groups with the largest downfield shift are assigned to C-3 and C-4.

Dihydroxytetraphlorethol-A undecaacetate (**13**) and dihydroxytetraphlorethol-B undecaacetate (**14**) have the same M_r (7992) and the same molecular formula ($C_{46}H_{40}O_{25}$). The difference to the M_r of hydroxytetraphlorethol-A decaacetate (**12**, m/z 934, [9]) corresponds to one acetoxy group.

In previous investigations it was shown that the chemical shift from approximately δ 6.9 ($CDCl_3$) is characteristic for the aromatic protons of a 1-phenoxyated 2,4,6-triacetoxybenzene [14] and the chemical shifts in the range of δ 6.69–6.72 are typical for the aromatic protons of a 1-phenoxyated 3,4,5-triacetoxybenzene [1]. Both NMR spectra of **13** and **14** showed these signals (Table 2). Consequently, the rings I and IV of **13** and **14** have the same substitution pattern as those of **12**.

To provide the position of the additional acetoxy group of **13** and **14** it was necessary to confirm the chemical shifts for all protons of **12** exactly. It is nearly impossible to do this by means of ^{13}C NMR techniques, because there is no proton–carbon coupling from one ring over the ether bridge to another one. Also there is no NOE effect between the acetoxy groups of two rings connected by an ether bridge. One possible way seems to be a comparison of the proton chemical shifts of **12** with

related phlorotannins, e.g. with the fuhalols of the A-series [1]. Only the fuhalols with an odd number of rings (e.g. pentafulhalol-A tridecaacetate **15** and heptafulhalol-A octadecaacetate **17**, see Tables 3 and 4) have a singlet at δ 6.70 \pm 0.01 for two protons and a signal for six protons at δ 2.07 ($CDCl_3$). The only difference between these fuhalols and the fuhalols of the A series with an even number of rings is an additional 1,4-phenoxyated 3,5-diacetoxybenzene unit (e.g. ring IV of **15**), which is connected with a 1-phenoxyated 3,4,5-triacetoxybenzene unit (e.g. ring V of **15**). Consequently, the signal at δ 6.70 \pm 0.01 belongs to the aromatic protons at C-2 and C-6, and the signal at δ 2.07 belongs to the acetyl groups of the 1,4-phenoxyated 3,5-diacetoxybenzene unit. Analogously, **12** contains the same 1,4-diphenoxylated 3,5-diacetoxybenzene unit (ring III) as described above. Therefore, the chemical shifts for the two aromatic protons of ring III of **12** are δ 6.69 and for the two acetoxy groups δ 2.09 ($CDCl_3$).

The resonances caused by the protons of ring II (**12**) are similar to the resonances of ring II of **15** and **17**. For the aromatic protons and the acetoxy groups of ring II (**12**) a chemical shift of δ 6.66 and 2.05 ($CDCl_3$) was obtained. Table 2 shows the whole proton assignment of **12**.

The 1H NMR spectrum of **13** showed no singlets at δ 6.66 and 2.05 in comparison to **12**. Instead a singlet for one proton at δ 6.50 and three additional signals in the range between δ 2.03 and 2.30 ($CDCl_3$) could be obtained.

Table 6. ^{13}C NMR spectral data of **5** and **7** (in CDCl_3)

C	Measured		Calculated [15]
	5	7	
Ring Type A			
1	136.1	136.1	136.8
2, 6	143.3	143.3	143.6
3, 5	114.8	114.8	113.8
4	146.6	146.7	146.2
Ring Type B			
1	154.3	154.1/154.3	153.1
2, 6	109.0 ^a	109.1/109.3 ^c	108.3
3, 5	143.5 ^b	143.5/143.7 ^d	142.5
4	133.9	133.9/134.1	134.7
Ring Type C			
1	147.3	147.4/147.8	147.5
2	134.5	134.5/134.6	134.4
3	137.8	137.8	136.6
4	131.3	131.3	131.2
5	140.1	140.0(8)/140.1(4)	139.2
6	109.1	109.0/109.2 ^c	109.0
Ring Type C'			
1	150.6	150.6	150.6
2	133.5	133.5	133.7
3	144.3	144.3	143.9
4	112.0	112.0	111.8
5	147.3	147.3	147.8
6	108.5	108.5	108.3
Ring Type D			
1	154.9	154.9	155.2
2, 6	108.8 ^a	108.9 ^c	108.0
3, 5	143.6 ^b	143.6 ^d	144.4
4	130.3	130.3	130.2

^{a-d}Assignments with the same letters may be interchanged.

This means that ring II carries an additional acetoxy group. The acetoxy groups at C-3 and C-5 could be assigned to δ 2.18 and 2.03, respectively. The chemical shift of δ 2.27 for the acetoxy group at C-2 is similar to the

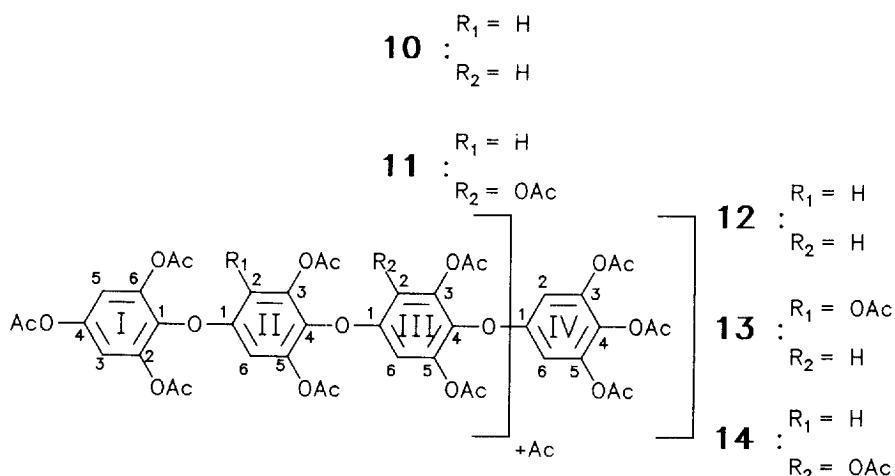
shift of the acetoxy groups at C-4 of ring I and IV, respectively.

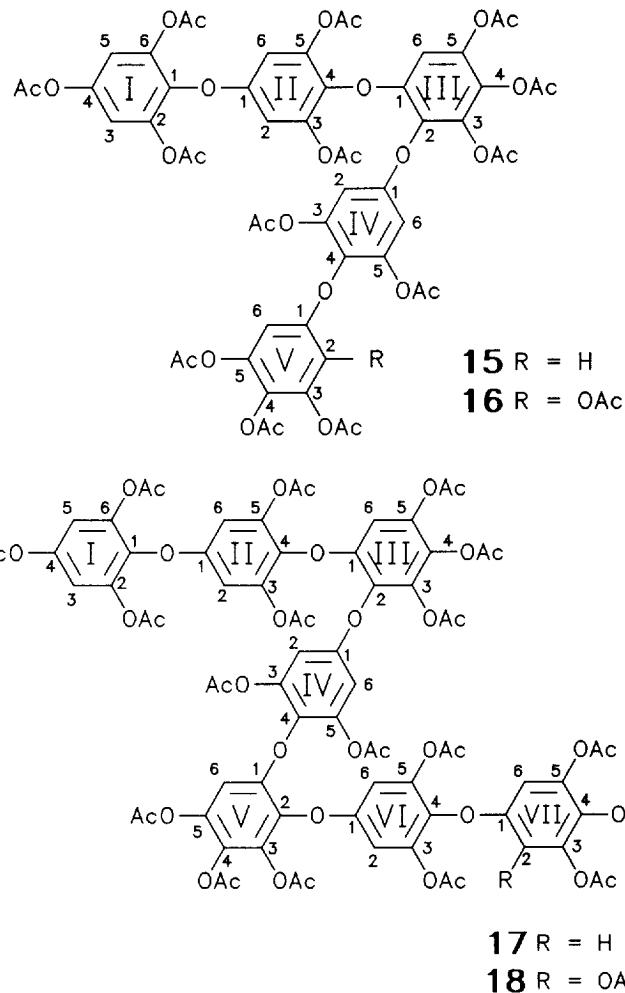
The ^1H NMR spectrum of **14** showed no signal at δ 6.69 and 2.09 in contrast to **12**. Compound **14** is similar to **13** in that a signal for one proton at δ 6.47 and three additional signals for acetyl groups in the range from δ 2.12 to 2.29 (CDCl_3) could be obtained. Consequently, ring III of **14** carries an additional acetoxy group.

Molecular modelling calculations (computer programm Sybil using the TRYPOS field) showed for ring II and III of **14** that the acetoxy group at C-2, ring III, can be arranged without any interaction with the other acetoxy groups.

The $[\text{M} + \text{H}]^+$ in the FAB-mass spectrum of hydroxy-pentafuhalol-B tetradecaacetate (**16**) was found at m/z 1259 [$\text{C}_{58}\text{H}_{50}\text{O}_{32} + \text{H}]^+$. This means that **16** has one acetoxy group more than **15** (M_r 1200 [11]). The ^1H NMR spectra of **15** and **16** showed significant differences in the chemical shifts for ring V (Table 3). Instead of a signal for two aromatic protons at δ 6.70 (CDCl_3) only a signal for one proton at δ 6.56 could be obtained in the spectrum of **16**. Therefore, ring V of **16** carries four acetoxy groups with a chemical shift of δ 2.18 (Ac at C-2), δ 2.24 (Ac at C-5) and δ 2.26/2.28 (Ac at C-3 and C-4). Similarly to **11** the signals for the acetoxy groups of the phloroglucinol unit linked with the tetraacetylated ring are shifted slightly downfield.

The FAB-mass spectrum of hydroxyheptafulhalol-A nonadecaacetate (**18**) showed the molecular ion at m/z 1733 for $[\text{M} + \text{H}]^+$ ($\text{C}_{80}\text{H}_{68}\text{O}_{44} + \text{H}^+$). Consequently, **18** has one acetoxy group more than **17** and is homologous to **16**. Ring VII is tetraacetylated. The chemical shift for the aromatic proton at C-6 of this ring could be obtained at δ 6.57, the shifts for the acetyl groups at δ 2.17 (Ac at C-2), 2.24 (Ac at C-5) and δ 2.26/2.28 (Ac at C-4 and C-3). In conclusion the chemical shifts for the 1-phenoxy-2,3,4,5-tetraacetoxybenzene in **11**, **16** and **18** are very similar. This is the first time that a phlorotannin with such a substitution pattern has been isolated and described. Also, a 1,4-phenoxy-2,3,5-triacetoxybenzene ring (**13**, **14**) has not been obtained before.





EXPERIMENTAL

EIMS operation: 70 eV, 200–300°; positive ion FAB-MS: Xe gun, 3-nitrobenzylalcohol as matrix. ^1H NMR spectra (90 and 300 MHz) and ^{13}C NMR (75 MHz) were recorded using solvents as int. standards.

Extraction and isolation. Extraction and sepn are described in ref. [1].

Isolated compounds. Phloroglucinoltriacetate: 10 mg, ^1H NMR data (CDCl_3): δ 6.84 (s, 3H), δ 2.24 (s, 9H). Diphloretolpentaacetate: 8 mg, ^1H NMR data identical with ref. [3]. Bifuhalolhexaacetate: 11 mg, ^1H NMR data identical with ref. [4]. Triphloretol-A heptaacetate: 1 mg, ^1H NMR data identical with ref. [5]. Triphloretol-B heptaacetate: 1 mg, ^1H NMR data identical with ref. [6]. Trifuhalol-B octaacetate: 8 mg, ^1H NMR data identical with ref. [8]. Tetraphloretol-C nonaacetate: 1 mg, ^1H NMR data identical with ref. [5]. Tetrafuhalol-B undecaacetate: 3 mg, ^1H NMR data identical with ref. [10]. Hexafuhalol-B hexadecaacetate: 2 mg, ^1H NMR data identical with ref. [12].

Hydroxytrifuhalol-B nonaacetate: 3,4,5-triacetoxyl-(2,4,6-triacetoxypheoxy)-2-(3,4,5-triacetoxypheoxy)

benzene (**1**). 16 mg, EIMS ketene elimination series: m/z 784 → 406, 726 → 390, 682 → 388, 476 → 266, 474 → 264, 226 → 142. ^1H NMR: Table 7, ^{13}C NMR: Table 5.

Hydroxypentafuhalol-A tetradecaacetate (**2**). 18 mg, ^1H NMR data identical with ref. [12], ^{13}C NMR: Table 5.

Hydroxyheptafuhalol-B nonadecaacetate: 3,4,5-triacetoxyl-1-(2,6-diacetoxyl-4-[2,3,4-triacetoxyl-6-(2,4,6-triacetoxypheoxy)phenoxy]phenoxy)-2-[3,5-diacetoxyl-4-[3,4,5-triacetoxyl-2-(3,4,5-triacetoxypheoxy)phenoxy]phenoxy]benzene (**3**). 6 mg, FAB-MS ketene elimination series: m/z 1771 [$\text{M} + \text{K}$] $^+$, 1755 [$\text{M} + \text{Na}$] $^+$ → 1713, 1733 [$\text{M} + \text{H}$] $^+$ → 1523. EIMS ketene elimination series: m/z 950 → 530, 948 → 528, 892 → 514, 890 → 512, 742 → 406, 740 → 404, 684 → 390, 682 → 388, 534 → 282, 476 → 266, 474 → 264, 226 → 142, 168 → 126. ^1H NMR: Table 7, ^{13}C NMR: Table 5.

Deshydroxytetrafuhalol-B decaacetate: 2,4,3'5'-tetraacetoxyl-6-(2,4,6-triacetoxypheoxy)-4'-(3,4,5-triacetoxypheoxy)diphenylether (**4**). 4 mg, EIMS ketene elimination series: m/z 934 → 514, 916 → 496, 516 → 390, 514 → 388, 500 → 374, 416 → 248, 392 → 266, 334 → 250, 226 → 142, 210 → 126. ^1H NMR: Table 8.

Table 7. ^1H NMR spectral data of **1** and **3**

H	1		3	
	CDCl_3	$d_6\text{-Me}_2\text{CO}$	CDCl_3	$d_6\text{-Me}_2\text{CO}$
Ring I				
3, 5	6.91	7.01	6.91	7.02
Ac-2, Ac-6	2.05	2.06	2.03	2.06
Ac-4	2.26(5)	2.26(5)	2.26(3)	2.27
Ring II				
6	6.70	6.69	6.66	6.68(5)
Ac-3	2.18	2.16	2.20 ^c	2.19 ^g
Ac-4	2.25 ^a	2.25 ^b	2.24 ^d	2.24(5) ^h
Ac-5	2.23	2.22	2.22 ^e	2.22 ⁱ
Ring III				
2, 6	6.71	6.75	6.66(3)	6.75(7)
Ac-3, Ac-5	2.24(5)	2.23(5)	2.02 ^f	* ^j
Ac-4	2.26 ^a	2.25(5) ^b		
Ring IV				
6		6.66	6.69(2)	
Ac-3		2.17(5) ^e	2.18(5) ^g	
Ac-4		2.24(5) ^d	2.25(7) ^h	
Ac-5		2.20(5) ^e	2.21 ⁱ	
Ring V				
2, 6		6.68	6.76(5)	
Ac-3, Ac-5		2.02(2) ^f	2.03(5) ^j	
Ring VI				
6		6.69	6.69(5)	
Ac-3		2.17	2.16	
Ac-4		2.25 ^d	2.25(3) ^h	
Ac-5		2.20 ^e	2.19 ⁱ	
Ring VII				
2, 6		6.72	6.78	
Ac-3, Ac-5		2.23(5)	2.23	
Ac-4		2.25(5) ^d	2.26(3) ^h	

^{a-j}Assignments with the same letter may be interchanged.^{*}Hidden by solvent.

Pentafuhalol-B tridecaacetate: 1,3-diacetoxy-2-[3,4,5-triacetoxy-2-(3,4,5-triacetoxyphenoxy)phenoxy]-5-[2,4-diacetoxy-6-(2,4,6-triacetoxyphenoxy)phenoxy]benzene (**5**). 20 mg, FAB-MS ketene elimination series: m/z 1239 [$\text{M} + \text{K}$]⁺, 1223 [$\text{M} + \text{Na}$]⁺ → 1139, 1201 [$\text{M} + \text{H}$]⁺ → 907. EIMS ketene elimination series: m/z 1158 → 696, 1056 → 888, 1042 → 874, 1016 → 638, 892 → 514, 890 → 512, 832 → 538, 750 → 540, 724 → 388, 684 → 390, 584 → 374, 434 → 266, 416 → 248, 226 → 142, 210 → 126. ^1H NMR: Table 8, ^{13}C NMR: Table 6.

Deshydroxyhexafuhalol-B pentadecaacetate: 2,6,3',4',5'-pentaacetox-4-[2,4-diacetoxy-6-(2,4,6-triacetoxyphenoxy)phenoxy]-2'-[3,5-diacetoxy-4-(3,4,5-triacetoxyphenoxy)phenoxy]diphenylether (**6**). 4 mg, FAB-MS ketene elimination series: m/z 1447 [$\text{M} + \text{K}$]⁺, 1431 [$\text{M} + \text{Na}$]⁺ → 1345, 1409 [$\text{M} + \text{H}$]⁺ → 863. EIMS ketene elimination series: m/z 892 → 514, 890 → 512, 708 → 540, 684 → 390, 476 → 266, 416 → 248, 226 → 142, 210 → 126. ^1H NMR: Table 8.

Heptafulhalol-B octadecaacetate: 3,4,5-triacetoxy-1-{2,6-diacetoxy-4-[2,4-diacetoxy-6-(2,4,6-triacetoxyphenoxy)phenoxy]-2-[3,5-diacetoxy-4-(2,3,4,5-tetraacetoxyphe-

oxy)phenoxy]phenoxy}-2-[3,5-diacetoxy-4-[3,4,5-triacetoxy-2-(3,4,5-triacetoxyphenoxy)phenoxy]phenoxy]benzene (**7**). 20 mg, FAB-MS ketene elimination series: m/z 1713 [$\text{M} + \text{K}$]⁺, 1697 [$\text{M} + \text{Na}$]⁺ → 1655, 1675 [$\text{M} + \text{H}$]⁺ → 1213. ^1H NMR: Table 8, ^{13}C NMR: Table 6.

Nonafuhalol-B tricosaacetate: 1,3-diacetoxy-2-[3,4,5-triacetoxy-2-[3,5-diacetoxy-4-(3,4,5-triacetoxy-2-(3,4,5-triacetoxyphenoxy)phenoxy)phenoxy]-5-[2,3,4-triacetoxy-6-[2,6-diacetoxy-4-(2,4-diacetoxy-6-(2,4,6-triacetoxyphenoxy)phenoxy)phenoxy]phenoxy]benzene (**8**). 13 mg, FAB-MS ketene elimination series: m/z 2188 [$\text{M} + \text{K}$]⁺, 2172 [$\text{M} + \text{Na}$]⁺ → 2045, 2150 [$\text{M} + \text{H}$]⁺. ^1H NMR: Table 8.

Pentaphlorethol-A undecaacetate: 1,3-diacetoxy-2-[3,5-diacetoxy-2-(3,5-diacetoxyphenoxy)phenoxy]-5-[2,4-diacetoxy-6-(2,4,6-triacetoxyphenoxy)phenoxy]benzene (**9**). 1 mg, FAB-MS ketene elimination series: m/z 1107 [$\text{M} + \text{Na}$]⁺, 1085 [$\text{M} + \text{H}$]⁺ → 809. EIMS ketene elimination series: m/z 1084 → 622, 892 → 514, 834 → 498, 700 → 406, 684 → 390, 584 → 374, 434 → 266, 376 → 250, 416 → 248, 318 → 234, 226 → 142, 168 → 126. ^1H NMR: Table 9.

Trifuhalol-A octaacetate (**10**). 31 mg, ^1H NMR data: Table 1.

Hydroxytrifuhalol-A nonaacetate: 1,3-diacetoxy-2-(2,3,4,5-tetraacetoxyphe-
oxy)-5-(2,4,6-triacetoxyphenoxy)benzene (**11**). 6 mg, EIMS ketene elimination series: m/z 784 → 406, 724 → 472, 684 → 390, 476 → 266, 460 → 250, 184 → 142. ^1H NMR: Table 1.

Hydroxytetraphlorethol-A decaacetate (**12**). 4 mg, ^1H NMR: Table 2.

Dihydroxytetraphlorethol-A undecaacetate: 2,3,6,3',5'-pentaacetox-4-(2,4,6-triacetoxyphenoxy)-4'-(3,4,5-triacetoxyphenoxy)diphenylether (**13**). 1 mg, FAB-MS ketene elimination series: m/z 993 [$\text{M} + \text{H}$]⁺ → 741. EIMS ketene elimination series: m/z 992 → 530, 892 → 514, 876 → 498, 708 → 372, 684 → 390, 682 → 388, 476 → 266, 416 → 248, 376 → 250, 226 → 142, 168 → 126. ^1H NMR: Table 2.

Dihydroxytetraphlorethol-B undecaacetate: 2,6,2',3',5'-pentaacetox-4-(2,4,6-triacetoxyphenoxy)-4'-(3,4,5-triacetoxyphenoxy)diphenylether (**14**). 2 mg, FAB-MS ketene elimination series: m/z 1031 [$\text{M} + \text{K}$]⁺, 1015 [$\text{M} + \text{Na}$]⁺ → 931, 993 [$\text{M} + \text{H}$]⁺ → 699. ^1H NMR: Table 2.

Pentafulhalol-A tridecaacetate (**15**). 23 mg, ^1H NMR: Table 3.

Hydroxypentafulhalol-B tetradecaacetate: 3,4,5-triacetoxy-1-[2,6-diacetoxy-4-(2,4,6-triacetoxyphenoxy)phenoxy]-2-[3,5-diacetoxy-4-(2,3,4,5-tetraacetoxyphe-
oxy)phenoxy]benzene (**16**). 6 mg, FAB-MS ketene elimination series: m/z 1297 [$\text{M} + \text{K}$]⁺, 1281 [$\text{M} + \text{Na}$]⁺ → 1239, 1259 [$\text{M} + \text{H}$]⁺ → 797. EIMS ketene elimination series: m/z 1216 → 712, 1116 → 654, 1100 → 638, 1084 → 622, 992 → 530, 834 → 498, 700 → 406, 698 → 456, 684 → 390, 682 → 388, 626 → 374, 624 → 372, 492 → 282, 434 → 266, 432 → 264, 418 → 250, 416 → 248, 226 → 142, 168 → 126. ^1H NMR: Table 3.

Heptafulhalol-A octadecaacetate (**17**). 21 mg, ^1H NMR: Table 4.

Table 8. ^1H NMR spectral data of 4-8

H	4			5			6			7			8		
	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	CDCl ₃	<i>d</i> ₆ -Me ₂ CO	
3, 5 Ac-2, Ac-6	6.92 2.05	7.04 *	6.92 2.03	7.03 2.06	6.91 2.02	7.03 *	6.92 2.02(1) ^b	7.03 2.27	6.91 2.27	7.03 2.06	6.91 2.02	7.03 2.27	6.91 2.06	7.03 2.26(5)	
Ac-4	2.28	2.25	2.27	2.26	2.27	2.26(5)									
4	6.75 ^f	6.89 ^f	6.74 ^f	6.88 ^f	6.74 ^f	6.88 ^f	6.74 ^f	6.88 ^f	6.74 ^f	6.88 ^f	6.74 ^f	6.88 ^f	6.74 ^f	6.88 ^f	
6	6.53 ^f	6.53 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.52 ^f	6.51 ^f	6.52 ^f	6.51 ^f	6.52 ^f	
Ac-3	2.20	2.15	2.19	2.16 ^c	2.21	2.21	2.21	2.21	2.16 ^c	2.16 ^c	2.16 ^c	2.16 ^c	2.16 ^c	2.16 ^c	2.16 ^c
Ac-5	2.24 ^a	2.19	2.23	2.21 ^d	2.23	2.23	2.23	2.23	2.20(5)	2.23 ^j	2.23 ^j	2.22(7)	2.22(7)	2.22(7)	2.22(7)
2, 6 Ac-3, Ac-5	6.67 2.08	6.75 *	6.64 2.03	6.75 2.04	6.64 2.03	6.73 2.05	6.64 *	6.73 *	6.64 2.01(7) ^b	6.75(2) ^b	6.64 2.04(2) ^m	6.75(7) ^b	6.64 2.01(7) ^p	6.75(7) ^b	6.75(7) ^b
2	6.70	6.78	6.69	6.69	6.66	6.69	6.66	6.66	6.66	6.68(5) ^y	6.65	6.68(5) ^y	6.65	6.68(5) ^y	6.65
6	6.70	6.78	2.21	2.17	2.15 ^e	2.19	2.20	2.18 ^t	2.18 ^t	2.18(5)	2.18 ^t	2.17(7) ^w	2.18 ^t	2.17(7) ^w	2.18 ^t
Ac-3	2.24	2.21	2.23	2.24(5) ^b	2.24(5) ^e	2.25 ^f	2.24(5) ^s	2.24(5) ^s	2.24(5) ^s	2.24(5) ^y	2.24(5) ^y	2.24(5) ^y	2.24(5) ^y	2.24(5) ^y	2.24(5) ^y
Ac-4	2.26 ^a	2.21	2.21	2.20(7) ^a	2.20(7) ^a	2.22	2.20(5)	2.20(5)	2.20(2)	2.20(5) ^l	2.20(5) ^l	2.20(7) ^v	2.20(7) ^v	2.20(7) ^v	2.20(7) ^v
Ac-5	2.24														
2, 6 Ac-3, Ac-5 Ac-4	6.72 2.24 2.25 ^b	6.70 2.23 2.25 ^e	6.76 2.23 2.25 ^s	6.70 2.07	6.76 *	6.76 *	6.69 2.02(1) ^b	6.69 2.02(1) ^b	6.69 2.02(1) ^b	6.75(7) ^b	6.67(3) ^b	6.76 2.01(7) ^p	6.76 2.01(7) ^p	6.76 2.04(2) ^u	6.76 2.04(2) ^u

Table 8. *Continued*

H	4		5		6		7		8	
	CDCl ₃	d ₆ -Me ₂ CO	CDCl ₃	d ₆ -Me ₂ CO	CDCl ₃	d ₆ -Me ₂ CO	CDCl ₃	d ₆ -Me ₂ CO	CDCl ₃	d ₆ -Me ₂ CO
2										
6	6.71	6.80	6.70	6.69(3)	6.65(7)	6.69 ^v				
Ac-3	6.71	6.80	2.17	2.15(5) ^y	2.17 ^r					
Ac-4	2.22(3)	2.21(5)	2.24(8) ^j	2.25(5) ⁿ	2.25(5) ⁿ	2.24(5) ^q	2.18 ^w			
Ac-5	2.26 ^f	2.25(5) ^g					2.25(5) ^g	2.25(5) ^g		
	2.22(3)	2.21(5)	2.20	2.18(5)	2.20 ^r	2.20 ^r				
2,6										
Ac-3, Ac-5			6.72	6.78	6.67(7)	6.78				
Ac-4			2.23(5)	2.23	2.01 ^p	2.03(5) ^u				
			2.25 ^j	2.25(5) ⁿ						
6										
Ac-3							6.69	6.69(7)		
Ac-4							2.16(5) ^o	2.15 ^s		
Ac-5							2.24(8) ^q	2.24(8) ^q		
							2.19 ^r	2.25(5) ^j		
								2.18(7) ^w		
2,6										
Ac-3, Ac-5								6.72	6.78(5)	
Ac-4								2.23	2.23	
Ac-5								2.25 ^q	2.25 ^q	
								2.26 ^r	2.26 ^r	

^{*} Hidden by solvent.[†] AB system, *J* = 2.7 Hz.[‡] AB system, *J* = 3.0 Hz.^{a-x} Assignments with the same letters may be interchanged.

Table 9. ^1H NMR spectral data of **9**

H	9	
	CDCl_3	$d_6\text{-Me}_2\text{CO}$
Ring I		
3, 5	6.92	7.03
Ac-2, Ac-6	2.03	2.06
Ac-4	2.28	2.26
Ring II		
4	6.75*	6.85†
6	6.53*	6.52†
Ac-3	2.19	2.15
Ac-5	2.23(5)	2.21
Ring III		
2, 6	6.65	6.76
Ac-3, Ac-5	2.02	2.03(5)
Ring IV		
4	6.74*	6.88†
6	6.53*	6.52†
Ac-3	2.15	2.12
Ac-5	2.22	2.20
Ring V		
2, 6	6.56‡	6.59§
4	6.66	6.70§
Ac-3, Ac-5	2.24(5)	2.23

*AB system, $J = 2.1$ Hz.†AB system, $J = 2.8$ Hz.‡AB system, $J = 2.7$ Hz.§AB system, $J = 2.1$ Hz.

Hydroxyheptafulhalol-A nonadecaacetate: 1,3-diacetoxy-2-{3,4,5-triacetoxy-2-[3,5-diacetoxy-4-(2,3,4,5-tetraacetoxyphenoxy)phenoxy]-5-{2,3,4-triacetoxy-6-[2,6-diacetoxy-4-(2,4,6-triacetoxyphenoxy)phenoxy]phenoxy}benzene (18). 1 mg, FAB-MS ketene elimination series: m/z 1771 [$\text{M} + \text{K}$] $^+$, 1755 [$\text{M} + \text{Na}$] $^+ \rightarrow$ 1713, 1733 [$\text{M} + \text{H}$] $^+ \rightarrow$ 1271. ^1H NMR: Table 4.

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REFERENCES

1. Glombitza, K.-W. and Keusgen, M. (1995) *Phytochemistry* (in press).
2. Glombitza, K.-W., Rösener, H.-U., Vilter, H. and Rauwald, W. (1973) *Planta Med.* **24**, 301.
3. Glombitza, K.-W., Rösener, H.-U. and Müller, D. (1975) *Phytochemistry* **14**, 1115.
4. Glombitza, K.-W. and Rösener, H.-U. (1974) *Phytochemistry* **13**, 1245.
5. Koch, M. and Gregson, R. P. (1984) *Phytochemistry* **23**, 2633.
6. Glombitza, K.-W., Schnabel, C. and Koch, M. (1981) *Arch. Pharm. (Weinheim)* **314**, 602.
7. Glombitza, K.-W. and Sattler, E. (1973) *Tetrahedron Letters* **14**, 4277.
8. Glombitza, K.-W., Forster, M. and Eckhardt, G. (1978) *Phytochemistry* **17**, 579.
9. Everth, G. (1986) Dissertation. University of Bonn.
10. Koch, M., Glombitza, K.-W. and Rösener, H.-U. (1980) *Bot. Mar.* **23**, 735.
11. Glombitza, K.-W., Rösener, H.-U. and Koch, M. (1976) *Phytochemistry* **15**, 1279.
12. Glombitza, K.-W. and Li, S.-M. (1991) *Phytochemistry* **30**, 2741.
13. Sattler, E., Glombitza, K.-W., Wehrli, F.-W. and Eckhardt, G. (1977) *Tetrahedron* **33**, 1239.
14. Ragan, M. A. and Glombitza, K.-W. (1986) in *Progress in Phycological Research*, Vol. 4 (Round, F. E. and Chapman, D. J., eds), p. 129. Biopress, Bristol.
15. Wegner-Hambloch, S. and Glombitza, K.-W. (1985) *Chem. Mag. Res.* **23**, 358.