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FUHALOLS AND DESHYDROXYFUHALOLS FROM THE BROWN ALGA *SARGASSUM SPINULIGERUM*

KARL-WERNER GLOMBITZA* and MICHAEL KEUSGEN†

Institut für Pharmazeutische Biologie, Nußallee 6, 53115 Bonn, Germany

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Key Word Index—*Sargassum spinuligerum*; Phaeophyceae; Sargassaceae; phlorotannins; fuhalols; deshydroxyfuhalols.

Abstract—Using a highly sophisticated HPLC method, 20 fuhalols and deshydroxyfuhalols were isolated from the ethanolic extract of the brown alga *Sargassum spinuligerum*. Because of their instability they were peracetylated before isolation. In addition to well known phlorotannins like deshydroxytetrafuhalol-A, tetrafuhalol-A, pentafuhalol-A, hexafuhalol-A, heptafuhalol-A, octafuhalol-A, nonafuhalol-A and undecafuhalol-A, the acetylated derivatives of deshydroxytetrafuhalol-C, deshydroxyhexafuhalol-A,-C and -D, deshydroxyoctafuhalol-C, octafuhalol-B, decafuhalol-A, dodecafuhalol-A, tetradecafuhalol-A, hexadecafuhalol-A, octadecafuhalol-A and eicosafuhalol-A are described for the first time. The last of them, containing twenty phloroglucinol units, is the largest phlorotannin isolated in purified form to date. The structural elucidation was carried out on the basis of ^1H, ^{13}C NMR and mass spectral data.

INTRODUCTION

Sargassum spinuligerum Sond. is a marine alga of New Zealand. The investigated specimen was collected at Wangaparoa Island, district Auckland. Brown algae very often contain a great number of phlorotannins based on phloroglucinol units [1]. Seventy-seven of these substances were obtained from the ethyl acetate fraction of the ethanolic extract of *S. spinuligerum*. The phlorotannins reported here are the fuhalols and deshydroxyfuhalols. The phloroglucinol units are linked exclusively by ether bonds and substituted by additional hydroxyl groups, but there are differences in the substitution pattern of these units. All main compounds belong to the fuhalol class.

RESULTS AND DISCUSSION

The aqueous residue of the ethanolic extract of the frozen alga was shaken with petrol, chloroform and ethyl acetate, respectively. Because of the instability of the phenols, the ethyl acetate fraction was immediately acetylated with acetic anhydride–pyridine. The higher polymeric phlorotannins consisting of more than 30 phloroglucinol units were removed by precipitation using a mixture of ether and petrol. All subsequent separations were made by a silica gel column.

The HPLC separation of the whole investigated fraction of peracetylated phlorotannins is shown in Fig. 1. The phloroglucinol oligomerization grade of the main compounds is expressed by roman numbers. This HPLC profile makes clear that the amount of oligomers decreases with the increase of the grade of oligomerization and that all main compounds have an even number of phloroglucinol units. The best results for this separation were acheived by a gradient solvent system consisting of chloroform and ethanol with a concentration increasing from 0.5 to 3.0% ethanol. For the following separations, solvent systems of *n*-hexane, chloroform and ethanol or alternatively chloroform, *n*-hexane and methyl cyanide were suitable.

All the main compounds identified in *S. spinuligerum* belonged to the fuhalol-A series. The peracetyl derivatives of tetrafuhalol-A, pentafuhalol-A, hexafuhalol-A, heptafuhalol-A, octafuhalol-A, nonafuhalol-A and undecafuhalol-A are described in previous papers [2–4].

The FAB- mass spectra of **1**–**6** showed $[M + Na]^+$ at m/z 2437.7 ($C_{112}H_{94}O_{61}$), m/z 2912.5 ($C_{134}H_{112}O_{73}$), m/z 3387.5 ($C_{156}H_{130}O_{85}$), m/z 3861.5 ($C_{178}H_{148}O_{97}$), m/z 4334.8 ($C_{200}H_{166}O_{109}$) and m/z 4810.3 ($C_{222}H_{184}O_{121}$), respectively. Because of the high M_r of these phlorotannins the peaks of the ions with at least one ^{13}C isotope gave a higher intensity than those of the molecules with only ^{12}C isotopes. The M_r of **3**, **4** and **6** were calculated by a distribution curve over the peak intensity. A reduced resolution was necessary to obtain clear signals. The structural element consisting of the rings IV and V has a M_r of 474. The multiplicity *n*

*Author to whom correspondence should be addressed.
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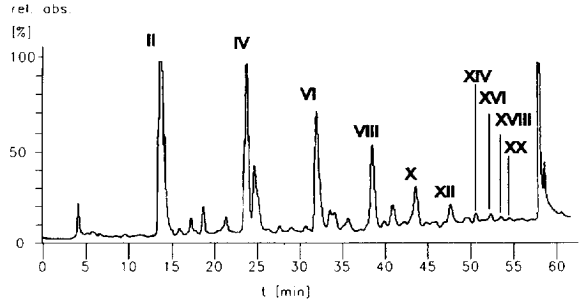
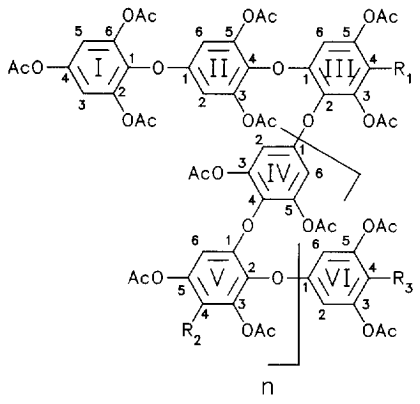


Fig. 1. HPLC-separation of the peracetylated phlorotannins from *Sargassum spinuligerum*, detected by UV 275 nm. II to XX: Oligomerization grade of the main compounds (e.g. oligomerization grade X: substance **1**, oligomerization grade XII: substance **2**, . . .).



Substance	n	R_1	R_2	R_3
1	1	OAc	OAc	OAc
2	2	OAc	OAc	OAc
3	3	OAc	OAc	OAc
4	4	OAc	OAc	OAc
5	5	OAc	OAc	OAc
6	6	OAc	OAc	OAc
7	1	H	OAc	OAc
8	1	OAc	H	OAc
9	0	OAc	---	H
10	1	OAc	OAc	H
11	2	OAc	OAc	H

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

of this element for each of these substances could be determined by mass spectrometry.

The structures of these substances were established by comparing the NMR data with each other and with the data of known fuhalols. All ^{1}H NMR spectra showed a singlet at δ6.94 in chloroform-*d* for two protons which was caused by the aromatic protons of ring I (Table 1). A singlet at δ2.28 for one and another at δ2.11 for two acetyl groups, respectively, were typical for ring I. Singlets at δ6.65 for two protons and at δ2.04 for two acetyl groups were caused by a 1,4-diphenoxylated 3,5-diacetoxybenzene ring (II). A signal at δ6.64 representing only one proton was recognizable in each spectrum of these substances. By spectra comparison with those of the deshydroxyfuhalols this singlet could be assigned to the ring III. The chemical shifts of the acetyl groups were similar to those of ring V. Independent of the M_r, the signals of the rings I, II, and III had the same relative intensity.

In contrast, the intensity of the signal groups caused by IV and V increased in correlation to the M_r. The aromatic protons of these rings induced a signal at *ca* δ6.66 (V) and at *ca* δ6.68 (IV). The signal for the aromatic proton of ring V, which was directly connected with ring VI, showed a downfield shift at δ6.70. The acetyl groups of rings IV gave a singlet at *ca* δ2.02; the chemical shifts for the acetyl groups of ring V were at *ca* δ2.18 (Ac at C-3), *ca* δ2.25 (Ac at C-4) and at *ca* δ2.19 (Ac at C-5), respectively.

All ^{1}H NMR spectra of **1–6** showed a singlet for two protons at δ6.72. This signal is typical for a 1-phenoxylated 3,4,5-triacetoxybenzene ring. This could be proved by spectra comparisons with those of **9–11** (Table 5), which differed only in the substitution pattern of this ring. The acetyl groups of ring VI produced a singlet at δ2.23 (Ac at C-3, C-5) and at δ2.25 (Ac at C-4). In addition, all substances were examined by ^{1}H NMR using acetone-d_6 as solvent. The aromatic ring protons are usually better resolved in acetone-d_6 than in chloroform-*d* [1], but the signals for the acetoxy groups are partially obscured by the solvent signal of acetone. Often it is easier to determine the ring types shown in Fig. 2 from the spectrum recorded in acetone-d_6. On the other hand, the spectrum measured in chloroform-*d* gave more detailed information about the exact positions of the protons in the particular molecule.* To allow a comparison with published results about fuhalols, whose structure elucidation is mainly based on spectra recorded in acetone-d_6 [1, 3, 5], Table 1 shows both data sets.

For the substances **1–3** and octafuhalol-A heneicosaacetate [2] (no ^{13}C NMR data published previously) a ^{13}C NMR spectrum was taken. Table 2 shows a good correlation between measured and calculated data. The calculation was based on a formula developed by Wegner–Hambloch and Glombitza [6]. The ring types A, B, C and D could be proved (Fig. 2).

Deshydroxyhexafuhalol-A pentadecaacetate **7** is a homologous phlorotannin to deshydroxytetrafuhalol-A decaacetate [7]. Compound **7** differs from hexafuhalol-A-hexadecaacetate only in the acetyl group at C-4 of ring

*For instance: signals for the aromatic protons of the ring type C can be obtained in the range between δ6.63 and 6.70 using chloroform-*d* as solvent. Also signals for the ring type B are visible in that range (δ6.64–6.68). The exact position of the signals depends on the relative position of the corresponding proton in the way described above. The spectra recoded in acetone-d_6 show signals for the aromatic protons of the ring type C in the range between δ6.66 and 6.70. The signals for those aromatic protons of the ring type B are visible in the range between δ6.75 and 6.79 and can be clearly distinguished from those of ring type C.

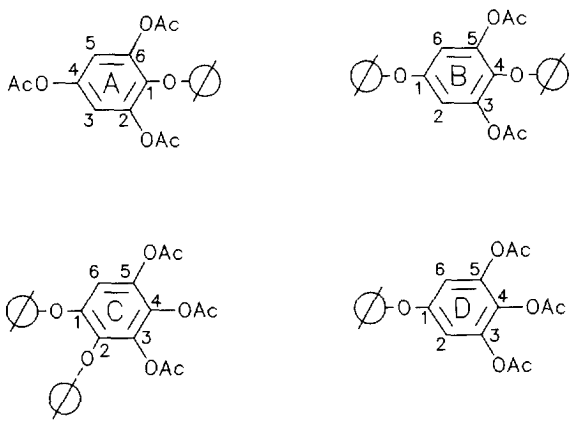


Fig. 2. Ring types A,B,C and D of the peracetylated phlorotannins of the fuhalol-A series. ø: Aryl rest.

III. The ^{1}H NMR spectrum of **7** (Table 3) showed for the aromatic proton of that ring an AB system in the region δ6.49–6.75 instead of a singlet at δ6.64. A coupling constant of 2.7 Hz is typical for aromatic protons in the *meta*-position. The $[M + H]^+$ of **7** at *m/z* 1409 ($C_{66}H_{38}O_{35}$) showed a difference of 58 in comparison to hexafuhalol-A-hexadecaacetate. So it is conceivable that **7** has one acetoxy group less than hexafuhalol-A-hexadecaacetate. A M_r of 1498 ($C_{66}H_{56}O_{55}$) could be deduced from the FAB-mass spectrum of **8**. Therefore, this phlorotannin has the same M_r as **7**. The ^{1}H NMR spectrum of **8** (Table 4) showed, in contrast to that of **7**, no singlet at δ6.69 (proton at C-6 of ring V, **7**), but a signal at δ6.65. Similarly to **7**, an AB system was visible at δ6.54–6.73. From these facts it could be deduced that ring III is 3,4,5-triacetoxylated and ring V is 3,5-diacetoxylated.

The EI-mass spectrum of **9** showed a $[M]^+$ at *m/z* 934 ($C_{44}H_{38}O_{23}$), from which a 10-fold ketene elimination series was observed down to *m/z* 514, the ion of the free phenol. For **10** and **11** M_r of 1408 and 1882, respectively, were determined from the FAB-mass spectra. In comparison to the M_r of the peracetylated fuhalols tetra-, hexa-, and octafuhalol-A with an equal number of phloroglucinol units, there was a difference of 58 a.m.u. according to one acetoxy group. Compared to the fuhalol-A series, the ^{1}H NMR spectra (Table 5) showed no singlet at δ6.72 but instead an AB_2 system at δ6.58–6.68. It is evident that **9**–**11** have a 1-phenoxylated 3,5-diacetoxybenzene ring instead of a 1-phenoxylated 3,4,5-triacetoxybenzene ring.

The FAB-mass spectrum of **12** showed a $[M + H]^+$ at *m/z* 1942 ($C_{90}H_{76}O_{49}$; highest intensity of the peak with ^{13}C isotope), according to the mass of octafuhalol-A heneicosaacetate. In comparison with this fuhalol, the ^{1}H NMR spectrum of **12** (Table 6) showed analogous signals for the rings I, II and III, but no singlet for one proton at δ6.69, which was visible in the spectrum of octafuhalol-A heneicosaacetate, and an additional signal at δ6.59. In the acetyl range of this spectrum two unusual signals at δ2.10 and 2.11, each for only one acetyl group, were obtained. Therefore, it is conceivable that two 1,2-diphenoxylated 3,4,5-triacetoxybenzene rings were directly connected by an ether bond. Probably ring V of **12** was linked with a 2-phenoxylated 3,4,5-triacetoxybenzene ring by an ether bridge. The chemical shifts for the protons of ring VII and VIII were similar to those of ring VIII and IX of nonafuhalol-A-tricosaacetate [3].

EXPERIMENTAL

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

Extraction and isolation. Frozen thalli of *Sargassum spinuligerum* (20 kg) were extracted within two portions with 20 l EtOH (96%) each, according to the method of ref. [8]. After concn the aq. soln was extracted with petrol, $CHCl_3$ and EtOAc, respectively by using a 4 l separating funnel. The EtOAc layer was dried over Na_2SO_4 and evapd under red. press., yield 6.37 g. The extract was subsequently acetylated with Ac_2O–pyridine. The crude acetylated phlorotannins (8.16 g) dissolved in 20 ml Me_2CO (soln A) were treated with a mixt. of 200 ml Et_2O and petrol (1:1, soln B). The polymeric phlorotannins were pptd almost completely and removed by filtration. This process was repeated several times with the newly formed ppt. but with stepwise reduced volume of soln **B** (up to ratio 1:1/soln A:soln B). The combined filtrates were evapd under red. press. To remove a small amount of remaining polymeric phlorotannins the combined filtrates were treated again in an analogous way as described above. The resulting soln contained low-M_r oligomers (6.54 g). Portions of 500 mg were separated by flash chromatography using a silica gel column (500 × 15 mm) with a gradient $CHCl_3$–*n*-hexane (1:1), $CHCl_3$–*n*-hexane (2:1), $CHCl_3$–n-hexane (4:1), $CHCl_3$–Me_2CO (49:1), $CHCl_3$–Me_2CO (4:1) and MeOH. This separation was monitored by a UV detector (Serva Chromatocord) and TLC (silica gel F_{254}, $CHCl_3$–Me_2CO, 9:1). Twelve frs were obtained. The last 5 frs contained partially desacetylated substances. They were acetylated once again. All frs were further sepd by HPLC (2 Knauer HPLC pumps, type 64, programmer 50) on LiChrosorb Si-60 (7 μm, 250 × 16 mm, or 5 μm, 250 × 8 mm) with a $CHCl_3$–EtOH gradient and were detected at UV 275 nm. For the sepn of related compounds solvent systems consisting of *n*-hexane–$CHCl_3$–EtOH, *n*-hexane–$CHCl_3$–MeCN or $CHCl_3$–MeCN were used.

*Compounds isloated.** Deshydroxytetrafuhalol-A decaacetate (3 mg), ^{1}H NMR data identical with ref. [7]. Tetrafuhalol-A undecaacetate (60 mg), ^{1}H NMR data identical with ref. [3]. Pentafuhalol-A tridecaacetate

*Yield from 20 kg frozen alga. After pre-sepn frs containing only known compounds and the fr. containing substance **1** were not entirely sepd.

Table 1. ^{1}H NMR spectral data of compounds **1–6**

	1		**2**		**3**		**4**		**5**		**6**	
H	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6
						Ring I						
3,5	6.93	7.05	6.94	7.05	6.94	7.05	6.94	7.05	6.94	7.05	6.94	7.05
Ac-2, Ac-6	2.11	2.10	2.11	2.10	2.11	2.10	2.11	2.10	2.11	2.10	2.11	2.10
Ac-4	2.27	2.27	2.28	2.27	2.28	2.26(5)*	2.28	2.26(5)	2.28	2.26(5)	2.28	2.26(5)
						Ring II						
2,6	6.64(5)	6.75(5)	6.64(7)	6.75	6.64(7)	6.75	6.64(7)	6.75	6.64(7)	6.75	6.64(7)	6.75
Ac-3, Ac-5[a]	2.03	2.06	2.04	2.06	2.04	2.06	2.04	2.06	2.04	2.06	2.04	2.06
						Ring III						
6	6.64	6.66	6.64	6.66	6.64	6.66	6.64	6.65(7)	6.64	6.65(5)	6.64	6.65(5)
Ac-3[b]	2.17(7)	2.19	2.18	2.18(7)	2.18	2.18(5)	2.18(3)	2.18(7)	2.18	2.19	2.18	2.19
Ac-4[c]	2.23(5)	2.24	2.24	2.24	2.24	2.24(3)	2.24	2.24	2.24	2.24	2.24(0)	2.25(7)
Ac-5[d]	2.21	2.22	2.21(5)	2.22	2.22	2.22	2.21(5)	2.22	2.21(5)	2.22	2.21(5)	2.22
						Ring IV						
2,6	6.66(5) (4H)	6.76(2H)	6.67(0) (2H)	6.76(2H)	6.67(2H)	6.76(2H)	6.67(0) (2H)	6.76(2H)	6.67(0) (2H)	6.75(5) (2H)	6.67(0) (2H)	6.75(5) (2H)
	6.68 (2H)	6.77(8) (2H)	6.67(3) (4H)	6.77(5) (2H)	6.67(5) (2H)	6.77(7) (2H)	6.75(5) (2H)	6.77(7) (2H)	6.67(5) (2H)	6.77 (2H)	6.67(5) (2H)	6.77 (2H)
		6.78 (2H)	6.67(9) (2H)	6.78 (4H)	6.68 (2H)	6.78(3) (4H)	6.67(7) (6H)	6.78(3) (2H)	6.67(7) (8H)	6.78(3) (2H)	6.67(7) (10H)	6.78(3) (2H)
						6.78(5) (2H)	6.68 (2H)	6.78(5) (6H)	6.68(3) (2H)	6.78(5) (8H)	6.68(3) (2H)	6.78(7) (10H)
Ac-3, Ac-5[a]	2.01 (6H)	2.04 (12H)	2.01 (6H)		2.01(3) (6H)		2.01(5) (6H)		2.01(5) (6H)		2.01(5) (6H)	
	2.02 (6H)	2.05 (6H)	2.02(0) (6H)	†	2.02 (24H)	†	2.02 (30H)	†	2.01(7) (6H)	†	2.02(0) (6H)	†
	2.02(5) (6H)		2.02(5) (12H)						2.02(5) (30H)		2.02(5) (36H)	

					Ring V							
6	6.65(3) (1H) 6.65(5) (1H) 6.69 (1H)	6.69 (2H) 6.70 (1H)	6.65(7) (2H) 6.65(8) (1H) 6.70 (1H)	6.69(0) (2H) 6.69(3) (1H) 6.70 (1H)	6.65(7) (2H) 6.66 (1H) 6.67 (1H) 6.69(5) (1H)	6.69(3) (4H) 6.67(0) (1H)	6.65(7) (4H) 6.66 (1H) 6.69(7) (1H)	6.69(3) (5H) 6.69(7) (1H)	6.65(7) (4H) 6.66 (1H) 6.66(3) (1H) 6.69(5) (1H)	6.69(3) (6H) 6.69(7) (1H)	6.65(5) (4H) 6.65(7) (3H) 6.69(7) (1H)	6.69(5) (7H) 6.70 (1H)
Ac-3[b]	2.16(7) (6H) 2.17(5) (3H)	2.16 (3H) 2.18 (3H) 2.18(5) (3H)	2.16(7) (3H) 2.17(5) (6H) 2.18 (3H)	2.16 (3H) 2.17(5) (3H) 2.18(0) (3H) 2.18(3) (3H)	2.16(5) (6H) 2.17 (6H) 2.18 (3H)	2.16 (3H) 2.17(0) (6H) 2.17(5) (3H) 2.18 (3H)	2.16(7) (9H) 2.17(3) (6H) 2.18(3) (3H)	2.16 (3H) 2.17(0) (9H) 2.17(5) (3H) 2.18 (3H)	2.16(5) (12H) 2.17 (6H) 2.18 (3H)	2.16 (3H) 2.17(0) (12H) 2.17(5) (3H) 2.18(3) (3H)	2.16(7) (15H) 2.17 (6H) 2.18 (3H)	2.16 (3H) 2.17(0) (12H) 2.17(5) (3H) 2.18(0) (3H) 2.18(7) (3H)
Ac-4[c]	2.24(0) (6H) 2.24(2) (3H)	2.25(5) (3H) 2.26 (6H)	2.24(0) (3H) 2.24(5) (9H)	2.25(3) (3H) 2.25(7) (3H) 2.26 (6H)	2.24(5) (12H) 2.24(7) (3H)	2.25(3) (3H) 2.25(5) (3H) 2.26 (9H)	2.24(5) (15H) 2.24(7) (3H)	2.25(3) (3H) 2.25(5) (3H) 2.26 (12H)	2.24(5) (18H) 2.24(7) (3H)	2.25(3) (3H) 2.25(5) (3H) 2.26 (15H)	2.24(5) (21H) 2.24(7) (3H)	2.25(7) (24H)
Ac-5[d]	2.18(3) (6H) 2.19(5) (3H)	2.19 (3H) 2.19(3) (6H)	2.18(5) (3H) 2.19 (6H) 2.20 (3H)	2.18(7) (3H) 2.19 (9H)	2.18(3) (6H) 2.18(5) (6H) 2.19(7) (3H)	2.18(5) (3H) 2.19 (12H)	2.18(3) (9H) 2.19 (6H) 2.20 (3H)	2.18(7) (18H)	2.18 (12H) 2.18(5) (6H) 2.19(5) (3H)	2.19 (21H)	2.18 (15H) 2.18(5) (6H) 2.19(5) (3H)	2.19 (24H)
					Ring VI							
2,6	6.72	6.79	6.72	6.79	6.72	6.78(7)	6.72	6.79	6.72	6.78(7)	6.72	6.79
Ac-3, Ac-5	2.23	2.23	2.23(5)	2.23	2.23(5)	2.23	2.23	2.23	2.23	2.22(7)	2.23(3)	2.23
Ac-4	2.24(5)	2.26	2.25	2.26	2.25(3)	2.26	2.25(3)	2.26	2.25(3)	2.26	2.25(5)	2.26(2)

[a–d]Assignments with the same letters may be interchanged (related to each compound).

*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.

†Hidden by solvent.

Table 2. ^{13}C NMR spectral data of octafuhalol-A heneicosaacetate and **1**–**3** (in $CDCl_3$)

	Measured				
C	*	**1**	**2**	**3**	Calculated [6]
			Ring type A		
1	136.3	136.4	136.4	136.4	136.8
2, 6	143.4(1)[a]	143.4(3)[d]	143.3(8)[g]	143.4(2)	143.6
3, 5	114.9	114.9	114.9	114.9	113.8
4	146.5	146.5	146.5	146.5	146.2
			Ring type B		
1	153.4	153.5	153.5	153.5	153.1
	153.8	153.9(5)	153.9(2)	153.9(7)	
	153.9	154.0(4)	153.9(8)	154.0(2)	
			154.0(2)	154.0(8)	
2, 6	108.9[b]	109.3[e]	109.2[h]	109.3[k]	108.3
	109.2[b]	109.6[e]	109.5[h]	109.5[k]	
	109.5[b]				
3, 5	143.3(4)[a]	143.5(1)[d]	143.4(6)[g]	143.5(0)[j]	142.5
	143.3(9)[a]	143.5(4)[d]	143.4(8)[g]	143.3(2)[j]	
	143.4(1)[a]				
4	133.9	133.9(7)	133.9(2)	133.9(6)	134.7
	134.0	134.0(4)	134.0(0)	134.0(5)	
	134.1[c]	134.2(2)[f]	134.1(8)[i]		
			Ring type C		
1	147.4(9)	147.5(8)	147.5(2)	147.5(7)	147.5
	147.5(6)	147.6(5)	147.6(0)	147.6(5)	
2	134.3(0)[c]	134.3(9)[f]	134.3(4)	134.3(8)[l]	134.4
	134.4(0)[c]	134.4(4)[f]	134.4(0)[i]	134.4(1)[l]	
	134.4(1)[c]	134.4(8)[f]	134.4(3)[i]	134.4(6)	
3	137.7	137.7	137.7	137.6(3)	136.6
				137.7(0)	
4	131.2	131.3	131.2	131.2(3)	131.2
5	139.8(7)	139.9(7)	139.9(2)	139.8(8)	139.2
	139.9(2)	139.9(9)	139.9(5)	139.9(5)	
	139.9(5)	140.0(3)	139.9(8)	140.0(0)	
6	109.0[b]	108.9(8)[e]	108.9[h]	108.8[k] to	109.0
		109.0(9)[e]	109.0[h]	108.9[k]	
			Ring type D		
1	154.6	154.7	154.7	154.7	155.2
2, 6	108.7[b]	108.8[e]	108.8[h]	108.8[k]	108.0
3, 5	143.4(6)[a]	143.4(7)[d]	143.4(1)[g]	143.4(5)[j]	144.4
4	130.1	130.2	130.2	130.3	130.2

*Octafuhalol-A heneicosaacetate.

[a–l]Assignments with the same letters may be interchanged.

†For some signals the chemical shift has been estimated to the approximate second decimal place (which is shown in parentheses). This is to distinguish between signals of very close value which could be differentiated by inspection of spectrum.

(23 mg), ^{1}H NMR data identical with ref. [3]. Hexafuhalol-A hexadecaacetate (33 mg), ^{1}H NMR data identical with ref. [3]. Heptafuhalol-A octadecaacetate (21 mg), ^{1}H NMR data identical with ref. [2]. Octafuhalol-A heneicosaacetate (118 mg), ^{1}H NMR data identical with ref. [3]. ^{13}C NMR data: see Table 2. Nonafuhalol-A tricosaacetate (28 mg), ^{1}H NMR data identical with ref. [3]. Undecafuhalol-A octacosaacetate (11 mg), ^{1}H NMR data identical with ref. [4].

Decafuhalol-A hexacosaacetate: 2,3,4,3′,5′-*pentaacetoxy*-6-{2,6-*diacetoxy*-4-[2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*)*phenoxy*]*phenoxy*}-4′-{3,4,5-*triacetoxy*-2-[3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*)*phenoxy*)*phenoxy*]*phenoxy*}-*diphenylether* (**1**). (40 mg), FAB-MS ketene elimination series: *m/z* 2453.7 $[M + K]^+$, 2437.7 $[M + Na]^+ \rightarrow$ 2312.7, 2415.8 $[M + H]^+ \rightarrow$ 2330.7. ^{1}H NMR data: see Table 1. ^{1}C NMR data: see Table 2.

Table 3. ^{1}H NMR spectra data of **7**

	7	
H	$CDCl_3$	Me_2CO-d_6
	Ring I	
3,5	6.94	7.05
Ac-2,Ac-6	2.12	2.11
Ac-4	2.28	2.26(5)*
	Ring II	
2,6[a]	6.66	6.75(5)
Ac-3, Ac-5	2.02	†
	Ring III	
4[d]	6.75	6.86
6[d]	6.49	6.49
Ac-3[b]	2.18	2.16
Ac-5	2.22	2.21
	Ring IV	
2,6[a]	6.64	6.75(5)
Ac-3, Ac-5	2.02	†
	Ring V	
6	6.69	6.70
Ac-3[b]	2.17	2.15
Ac-4[c]	2.25	2.25
Ac-5	2.20	2.20
	Ring VI	
2,6	6.72	6.76
Ac-3, Ac-5	2.24	2.23
Ac-4[c]	2.25(5)	2.26

[a–c]Assignments with the same letters may be interchanged.
[d]AB system, J = 2.8 Hz.
*See footnote to Table 1.
†Hidden by solvent.

Table 4. ^{1}H NMR spectral data of **8**

	8	
H	$CDCl_3$	Me_2CO-d_6
	Ring I	
3,5	6.94	7.05
Ac-2, Ac-6	2.11	2.10
Ac-4	2.28	2.26(5)*
	Ring II	
2,6	6.65	6.74
Ac-3, Ac-5[a]	2.04	†
	Ring III	
6	6.65	6.66
Ac-3	2.19(5)	2.18(5)
Ac-4[b]	2.25	2.24(5)
Ac-5[c]	2.21(5)	2.22
	Ring IV	
2,6	6.68	6.75
Ac-3, Ac-5[a]	2.00(5)	†
	Ring V	
4[d]	6.73	6.85
6[d]	6.54	6.53
Ac-3	2.16	2.13
Ac-5[c]	2.20(5)	2.18(7)
	Ring VI	
2,6	6.69	6.79
Ac-3, Ac-5	2.23(5)	2.23
Ac-4[b]	2.26	2.26

[a–c]Assignments with the same letters may be interchanged.
[d]AB system, J = 2.7/2.8 Hz ($CDCl_3$/Me_2CO-d_6).
*See footnote to Table 1.
†Hidden by solvent.

Dodecafuhalol-A hentriacontaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-4-{2,3,4-*triacetoxy*-6-[2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*) *phenoxy*] *phenoxy*}-2′{3,5-*diacetoxy*-4-[3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*] *phenoxy*}-*diphenylether* (**2**). (105 mg), FAB-MS ketene elimination series: m/z 2928.5 $[M + K]^+$, 2912.5 $[M + Na]^+ \rightarrow$ 2828.4. ^{1}H NMR data: see Table 1. ^{13}C NMR data: see Table 2.

Tetradecafuhalol-A hexatriacontaacetate: 2,3,4,3′,5′-*pentaacetoxy*-6- {2,6-*diacetoxy*-4-[2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4- (2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*)*phenoxy*)*phenoxy*)*phenoxy*]*phenoxy*}-4′-{3,4,5-*triacetoxy*-2-[3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*)*phenoxy*) *phenoxy*] *phenoxy*}-*diphenylether* (**3**). (58 mg), FAB-MS ketene elimination series:† m/z 3387.5 $[M + Na]^+ \rightarrow$ 3218.5. ^{1}H NMR data: see Table 1. ^{1}C NMR data: see Table 2.

†m/z were calculated by a distribution curve over the peak intensity.

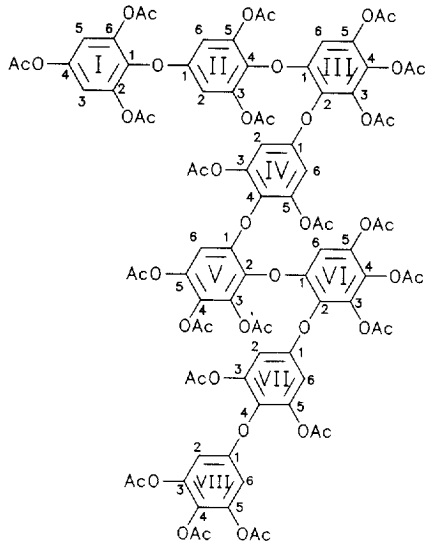
Hexadecafuhalol-A hentetracontaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-4-{2,3,4-*triacetoxy*-6-[2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxyl*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*}-2′-{3,5-*diacetoxy*-4-[3,4,5-*triacetoxy*-2-(3, 5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*) *phenoxy*) *phenoxy*)*phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*}-*diphenylether* (**4**). (28 mg), FAB-MS ketene elimination series:† m/z 3861.5 $[M + Na]^+ \rightarrow$ 3692.2. ^{1}H NMR data: see Table 1.

Octadecafuhalol-A hexatetracontaacetate: 2,3,4,3′,5′-*pentaacetoxy*-6-{2,6-*diacetoxy*-4-[2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2, 3, 4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*}-4′-{3,4,5-*triacetoxy*-2-[3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*}-*diphenylether* (**5**). (9 mg), FAB-MS ketene elimination series:† m/z 4334.8 $[M + Na]^+ \rightarrow$ 4040.7. ^{1}H NMR data: see Table 1.

Table 5. ^{1}H NMR spectral data of **9–11**

	9		**10**		**11**	
H	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6	$CDCl_3$	Me_2CO-d_6
			Ring I			
3, 5	6.94	7.05	6.94	7.05	6.94	7.05
Ac-2, Ac-6	2.12	2.10	2.11	2.10	2.11	2.10
Ac-4	2.28	2.26(5)*	2.28	2.26(5)	2.28	2.27
			Ring II			
2, 6	6.65(5)	6.75	6.64(5)	6.75	6.64(5)	6.75
Ac-3, Ac-5	2.04	†	2.03	†	2.03	2.05(5)
			Ring III			
6	6.66	6.66	6.64	6.66	6.64	6.66
Ac-3	2.15	2.15	2.19	2.18	2.19[f]	2.18(5)[j]
Ac-4	2.26	2.26	2.25(3)[b]	2.26[d]	2.25(3)[g]	2.26(3)[j]
Ac-5	2.22	2.22	2.21[c]	2.22[e]	2.22[h]	2.22[k]
			Ring IV			
2, 6			6.67(5)	6.79	6.66(5)	6.78
					6.67(5)	6.78(5)
Ac-3, Ac-5			2.03	†	2.01	2.00
					2.02(5)	2.04(5)
			Ring V			
6			6.67(7)	6.68	6.66	6.69
					6.68	6.69(3)
Ac-3			2.16	2.16	2.16	2.16
					2.18(7)[f]	2.18(3)[j]
Ac-4			2.25[b]	2.26[d]	2.25[g]	2.26[j]
					2.25[g]	2.26[j]
Ac-5			2.20[c]	2.20[e]	2.19[h]	2.18(5)[k]
					2.20[h]	2.19[k]
			Ring VI			
2,6	6.58[a]	6.61[a]	6.58[a]	6.61[a]	6.58[a]	6.61[a]
4	6.68[a]	6.72[a]	6.68[a]	6.73[a]	6.68[a]	6.73[a]
Ac-3, Ac-5	2.25	2.25(5)	2.24(5)	2.23	2.24	2.22(5)

[a]AB_2 system, J = 2.2 Hz.
[b–k]Assignments with the same letters may be interchanged.
*See footnote to Table 1.
†Hidden by solvent.



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Eicosafuhalol-A henpentacontaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-4-{2,3,4-*triacetoxy*-6-[2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,3,4-*triacetoxy*-6-(2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*}-2′-{3,5-*diacetoxy*-4-[3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,5-*diacetoxy*-4-(3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*) *phenoxy*)*phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*) *phenoxy*] *phenoxy*} *diphenylether* (**6**). (3 mg), FAB-MS ketene elimination series:† m/z 4810.3 $[M + Na]^+ \rightarrow$ 4686.3. ^{1}H NMR data: see Table 1.

Deshydroxyhexafuhalol-A pentadecaacetate: 2,4,3′,5′-*tetraacetoxy*-6-[2,6-*diacetoxy*-4-(2,4,6-*triacetoxy*-*phenoxy*) *phenoxy*]-4′-[3,4,5-*triacetoxy*-2-(3,4,5-*triacetoxyphenoxy*) *phenoxy*]-*diphenylether* (**7**). (2 mg), EIMS ketene elimination series: m/z 1060 → 640, 1058 → 638, 1042 → 622, 934 → 514, 894 → 516, 794 → 500, 792 → 498, 726 → 390, 724 → 388, 710 → 374, 624 → 372,

Table 6. ^{1}H NMR spectral data of **12**

H	**12**	
	$CDCl_3$	Me_2CO-d_6
	Ring I	
3, 5	6.94	7.05
Ac-2, Ac-6[a]	2.11(5)*	2.10
Ac-4[b]	2.28	2.31
	Ring II	
2, 6	6.64(7)	6.74
Ac-3, Ac-5	2.03	†
	Ring III	
6	6.64(5)	6.67
Ac-3[c]	2.18	2.18(5)
Ac-4[d]	2.26	2.26
Ac-5	2.21(5)	2.22
	Ring IV	
2, 6[e]	6.67	6.75
Ac-3, Ac-5	1.99	2.00
	Ring V, Ring VI	
6	6.59/6.66	6.65(2)/6.68(5)
Ac-3	2.10/2.11	2.11/2.11(5)
Ac-4[d]	2.24(5)/2.25(5)	2.25(5)
Ac-5[c]	2.19/2.23(3)	2.19/2.25(5)
	Ring VII	
2, 6[e]	6.67(5)	6.75(5)
Ac-3, Ac-5[a]	2.10	2.10(3)
	Ring VIII	
2, 6[e]	6.68(7)	6.78(5)
Ac-3, Ac-5	2.22	2.22
Ac-4[d]	2.28	2.27

[a–c]Assignments with the same letters may be interchanged.
*See footnote to Table 1.
†Hidden by solvent.

516 → 264, 434 → 266, 226 → 142, 210 → 126. FAB-MS ketene elimination series: *m/z* 1447 $[M + K]^+$, 1431 $[M + Na]^+ \rightarrow 1389$, 1409 $[M + H]^+ \rightarrow 1115$. ^{1}H NMR data: see Table 3.

Deshydroxyhexafuhalol-D pentadecaacetate: 2,3,4,3′,5′-*pentaacetoxy*-6-[2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*]-4′-[3,5-*diacetoxy*-2-(3,4,5-*triacetoxyphenoxy*)*phenoxy*]-*diphenylether* (**8**). (7 mg), EIMS ketene elimination series: *m/z* 726 → 390, 682 → 388, 624 → 372, 584 → 374, 376 → 250, 374 → 248, 226 → 142. FAB-MS ketene elimination series: *m/z* 1447 $[M + K]^+$, 1431 $[M + Na]^+ \rightarrow 1389$, 1409 $[M + H]^+ \rightarrow 1031$. ^{1}H NMR data: see Table 4.

Deshydroxytetrafuhalol-C decaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-4-(2, 4, 6-*triacetoxyphenoxy*)-2′-(3,5-*diacetoxyphenoxy*)-*diphenylether* (**9**). (2 mg), EIMS ketene elimination series: *m/z* 934 → 514, 876 → 498, 742 → 490, 684 → 390, 682 → 388, 666 → 372, 542 → 374, 434 → 266, 374 → 248, 226 → 142, 210 → 126. ^{1}H NMR data: see Table 5.

Deshydroxyhexafuhalol-C pentadecaacetate: 2,3,4, 3′,5′-*pentaacetoxy*-6-[2,6,-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*]-4′-[3,4,5-*triacetoxy*-2-(3,5-*diacetoxyphenoxy*)*phenoxy*]-*diphenylether* (**10**). (1 mg), EIMS ketene elimination series: *m/z* 724 → 514, 684 → 348, 682 → 388, 474 → 264, 434 → 266, 184 → 142, 210 → 126. FAB-MS ketene elimination series: *m/z* 1447 $[M + K]^+$, 1431 $[M + Na]^+ \rightarrow 1389$, 1409 $[M + H]^+ \rightarrow 1115$. ^{1}H NMR data: see Table 5.

Deshydroxyoctafuhalol-C eicosaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-4-{2,3,4-*triacetoxy*-6-[2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*)*phenoxy*}-2′-{3,5-*diacetoxy*-4-[3,4,5-*triacetoxy*-2-(3,5-*diacetoxyphenoxy*)*phenoxy*]*phenoxy*}-*diphenylether* (**11**). FAB-MS ketene elimination series: *m/z* 1921 $[M + K]^+$, 1905 $[M + Na]^+ \rightarrow 1821$, 1883 $[M + H]^+ \rightarrow 1563$. ^{1}H NMR data: see Table 5.

Octafuhalol-B heneicosaacetate: 2,6,3′,4′,5′-*pentaacetoxy*-6-{2,3,4-*triacetoxy*-4-[2,6-*diacetoxy*-4-(2,4,6-*triacetoxyphenoxy*)*phenoxy*]*phenoxy*}-2′-{3,4,5-*triacetoxy*-2-[3,5-*diacetoxy*-4-(3,4,5-*triacetoxyphenoxy*)*phenoxy*]*phenoxy*}-*diphenylether* (**12**). (1 mg), FAB-MS ketene elimination series: *m/z* 1964 $[M + Na]^+$, 1942 $[M + H]^+ \rightarrow 1873$. ^{1}H NMR data: see Table 6.

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