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ISOLATION AND STRUCTURE ELUCIDATION OF THREE METABOLITES FROM *VERTICILLIUM INTERTEXTUM*: SORBICILLIN, DIHYDROSORBICILLIN AND BISVERTINOQUINOL†

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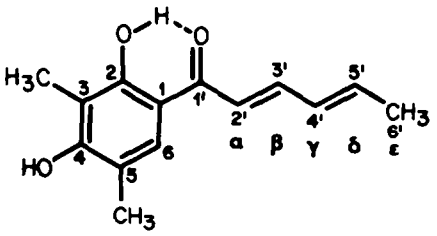
Abstract—From the culture medium of *Verticillium intertextum* three metabolites have been isolated, namely the hexaketides sorbicillin (**1**) and 2′3′-dihydrosorbicillin (**2**), and the dimeric hexaketide bisvertinoquinol (**3**). **1** has previously been isolated from *Penicillium chrysogenum* and also synthesised. Hydrogenation of **1** yielded tetrahydrosorbicillin (**8**), 2′5′-dihydrosorbicillin (**9**) and 2′,3′-dihydrosorbicillin (**2**). **2** was also obtained by a BF_3-catalysed condensation of 2,4-dimethyl-resorcinol (**5**) with (4R*, 5S*)-4,5-dibromo-hexanoic acid (**6**), followed by debromination with zinc and acetic acid. The structure of the dimeric hexaketide **3** (without absolute configuration) was obtained by X-ray structure analysis. It may be considered to be a Diels–Alder adduct of the quinols **11** and **12**, the latter being related to **1** and **2**, respectively, by simple hydroxylation at C(5). The ^1H and ^{13}C NMR signals of **3** and its mono-methyl ether **10** are interpreted and compared with the corresponding properties of **1**, **2**, vertinolide (**4**), 3-methoxy-2-methyl-2-cyclohexenone (**14**), and 2-[(E,E)-2,4-hexadienoyl)]-cyclohexanone (**13**). The latter was prepared by acylation of the lithium enolate of cyclohexanone with sorbyl chloride. From the spectra of the hexaketides from *V. intertextum* several patterns have been extracted which are characteristic for some common and some distinguishing substructures in these natural products.

In a recent note[1] we reported the isolation from the culture medium of *Verticillium intertextum* of four hexaketides, presumably related to each other by biosynthesis. In the present paper we describe the details of the isolation of three of them, namely sorbicillin (**1**), 2′,3′-dihydrosorbicillin (**2**) and bisvertinoquinol (**3**),[2] and present the arguments for their structures. The isolation and structural assignment of the fourth, namely vertinolide (**4**), has been published previously.[3] The absolute configuration of natural (−)-vertinolide had been suggested to be (S) by comparison of its CD curve (positive n-π^* and negative π-π^* Cotton effect) with those of tetronic acids with known absolute configuration.[4] A chiral total synthesis of (−)-vertinolide, achieved recently, established its absolute configuration to be (S).[5]



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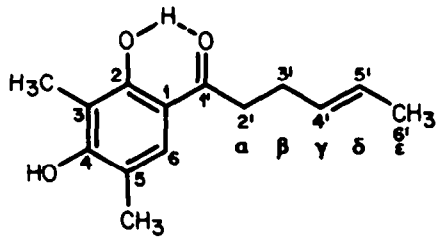
†Dedicated to Dr. Ulrich Weiss for his 75th birthday.



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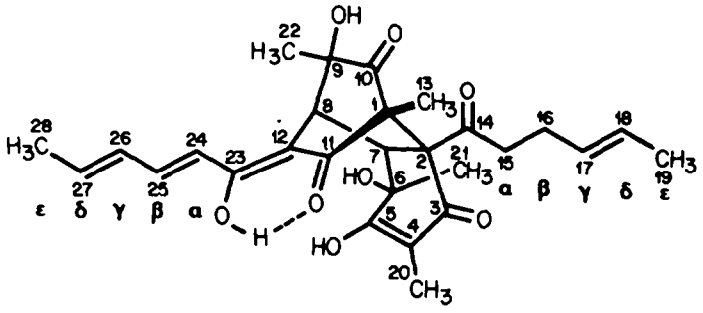
Isolation

The spent filtered culture medium of *V. intertextum* was acidified to pH 3.0 and extracted with chloroform. Chromatography of the extract on Sephadex LH-20 yielded three main fractions, a to c. From fraction b the main metabolite, vertinolide (**4**), was separated by crystallisation.[3] The three metabolites which are the subject of the present paper were isolated from the mother liquor of this crystallisation as follows:

The oily residue from the mother liquor of the crystallisation of vertinolide from fraction b, after standing for several weeks at −20°, deposited crystalline bisvertinoquinol (**3**, 1.4% of the chloroform extract), which was further purified by several recrystallisations. The combined residues of all the new mother liquors from fraction *b* were chromatographed twice on preparative silica gel plates



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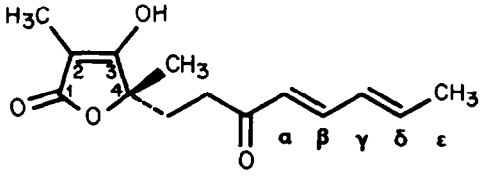
(formulated as 3a)[2]



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with different solvent systems to afford, after recrystallisation, pure sorbicillin (1, 0.11%) and 2′,3′-dihydrosorbicillin (2, 0.02% of the chloroform extract).

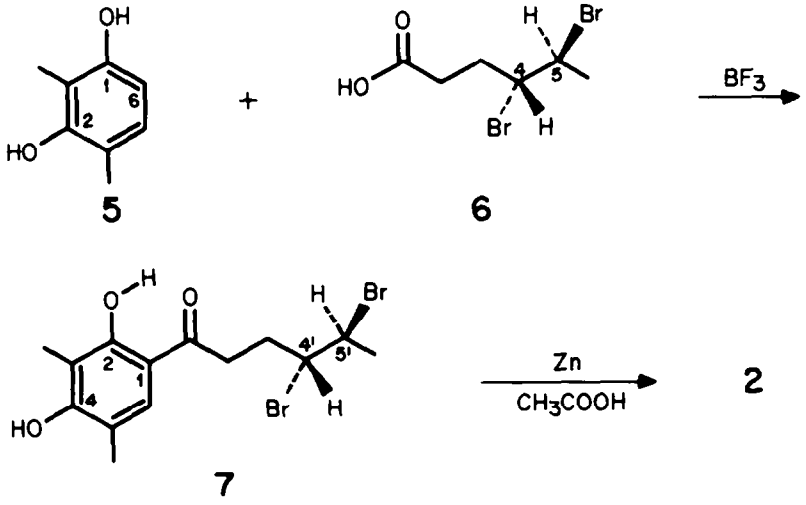
Sorbicillin (1)

The yellow pigment sorbicillin (1) had been observed previously as a natural product, namely as a minor metabolite of *Penicillium chrysogenum*[6,7] (formerly known as *P. notatum*). Its structure 1 was derived in 1948 on the basis of the UV spectrum and of certain degradations.[8] In 1954, a first synthesis of sorbicillin (1) was accomplished by Kuhn and Staab[9] and, in 1958, a practical one was published by McOmie and Tute.[10] According to the latter authors sorbicillin (1) exhibits crystal polymorphism, sometimes appearing as an orange (as in Ref. 6) and sometimes as a yellow solid (as in Ref. 9).

Our sample of sorbicillin (1) consisted of orange prisms, m.p. 122–125°. A sample of 1, synthesised by the method of McOmie and Tute,[10] was identical with our natural product sample. Its UV spectrum is the same as the one reported;[6] other spectroscopic data were not available in 1948. The IR and the mass spectrum are given in the Experimental. The ^1H and ^{13}C NMR data are collected in Tables 1 and 2, the first table showing the signals belonging to the (E,E)-2,4-hexadienoyl (sorbyl) side chain and the second those of the dimethyl resorcinol substructure. These NMR signals have diagnostic value for the presence of the corresponding substructures (see below). For comparison, the sorbyl signals of vertinolide (4)[3] and of the model compound 2-[(E,E)-2,4-hexadienoyl)]-cyclohexanone (13, see below) are included in Table 1.

2′,3′-*Dihydrosorbicillin* (2)

2′,3′-Dihydrosorbicillin (2) was isolated as colourless needles, m.p. 67–70°. Its NMR signals are listed in Table 1 (2,3-dihydrosorbyl side chain substructure) and in Table 2 (dimethylresorcinol substructure) and the other spectral properties (UV, IR and MS) are given in the Experimental. We also prepared 2 by a total synthesis (see Scheme 1). Boron trifluoride catalysed condensation[10] of 2,4-dimethylresorcinol (5)[11] and (4R*,5S*)-4,5-



Scheme 1.

Table 1. ^1H and ^{13}C NMR signals of the sorbyl, or the 2,3-dihydrosorbyl side chain substructure, or both, of sorbicillin (**1**), of 2',3'-dihydrosorbicillin (**2**), of vertinolide (**4**), of bisvertinoquinol (**3**), of bisvertinoquinol methyl ether (**10**) and of 2-[(E,E)-2,4-hexadienoyl]-cyclohexanone (**13**) [δ in ppm (J in Hz)]

Compound		^1H NMR [a]				^{13}C NMR [b]					
	side chain [c]	α	β	γ, δ	ε	C=O	α	β	γ	δ	ε
1	S'	6.92/d (15)	7.46/dxd (10,15)	6.4-6.2/m	1.88/d (6)	192.3/s	121.4/d	144.4/d	130.2/d	141.2/d	18.7/q
2	S"	2.97/t (7.5)	2.5-2.3/m	5.7-5.4/m	1.66/d (4)	204.3/s	37.5/t	27.2/t	129.2/d	125.9/d	17.7/q
4 [d]	S'	6.06/d (15)	7.19/dxd (10,15)	6.4-6.1/m	1.89/d (5)	199.1/s	128.6/d	143.5/d	131.4/d	140.7/d	18.7/q
3	S'	6.27/d (15)	7.22/dxdxd (10.5,15,2)	6.4-6.2/m 6.19/dxq (15,6.5)	1.87/d (6.5)						
	S"	2.65/d (18) 2.43/d (18) [e]	2.3-2.1/m	5.4-5.3/m	1.60/d (5)						
10	S'	6.28/d (15)	7.29/dxd (10,15)	6.3-6.1/m	1.90/d (6)	192.6/s [f]	118.7/d	142.7/d	131.0/d	140.6/d	19.2/q [g]
	S"	2.9-2.7/m 2.6-2.4/m	2.3-2.1/m	5.45-5.25/m	1.59/d (5)	205.9/s [h]	40.8/t	27.1/t	129.2/d	126.3/d	18.1/q [g]
13	S'	6.27/d (15)	7.30/dxd (10,15)	6.4-6.1/m	1.87/d (5.5)	192.4/s	121.5/d	141.9/d	131.1/d	138.8/d	18.7/q

[a] All spectra 200 MHz in $CDCl_3$, except that of **3**, which is 360 MHz in CD_3OD; the intensities of the signals correspond to the number of protons implied by the interpretation; [b] 25.1 MHz in $CDCl_3$ (except for **4**), chemical shifts from proton noise, multiplicities from off-resonance decoupled spectra; [c] S' = sorbyl, S" = 2',3'-dihydrosorbyl side chain; in the cases of **3** and **10**, the signal assignments to S' and S" are derived from comparisons with the other compounds; [d] data from[3]; the ^{13}C NMR spectrum in CD_3COCD_3; [e] upon irradiation at 2.20; [f] arbitrary choice of C(23) (and not C(11)) as belonging to the carbonyl group; [g] assignment might be interchanged; [h] assignment of this signal might be interchanged with that of C(10) (see Table 3).

Table 2. ^1H and ^{13}C NMR signals of the ring substructure of sorbicillin (1) and of 2′,3′-dihydrosorbicillin (2)

	sorbicillin (1)		2′,3′-dihydrosorbicillin (2)	
	^1H NMR [a]	^{13}C NMR [b]	^1H NMR [a]	^{13}C NMR [b]
C(1)	-	110.2/s [c]	-	110.1/s [d]
HO-C(2)	13.61/s	162.2/s [e]	12.97/s	161.5/s [f]
C(3)	-	113.0/s [c]	-	112.5/s [d]
CH_3-C(3)	2.13/s [g]	7.3/q	2.14/s [h]	7.2/q
HO-C(4)	5.30/s	158.8/s [e]	5.24/s	158.6/s [f]
C(5)	-	114.6/s [c]	-	114.5/s [d]
CH_3-C(5)	2.20/s [g]	15.5/q	2.21/s [h]	15.5/q
H-C(6)	7.43/s	128.5/d	7.40/s	128.8/d

[a] 200 MHz in $CDCl_3$; [b] 25.1 MHz in $CDCl_3$; [c-h] assignment of the signals carrying the same letter may be interchanged.

dibromohexanoic acid (6)[12] gave, presumably via a Fries rearrangement, 41% 1-[(4R*,5S*)-4,5 - dibromohexanoyl] - 2,4 - dihydroxy - 3,5 - dimethylbenzene (7), whose structure is fully supported by its spectroscopic properties (see Experimental). Debromination of 7 with zinc and acetic acid in ether[13] furnished 77% 2′,3′-dihydrosorbicillin (2), m.p. 68–70°. Attempts to synthesise 2 in a one step procedure, analogous to the synthesis of 1,[10] by reaction of 5 and (E)-4-hexenoic acid in presence of boron trifluoride failed, possibly due to double bond migration.

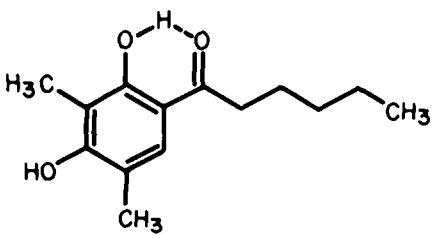
A dihydrosorbicillin, m.p. 146–147°, to which structure 2 had been assigned on the basis of its elemental composition and its UV spectrum[8] (the latter identical with that of our 2′,3′-dihydrosorbicillin (2)), had previously been isolated (10% yield) from a partial hydrogenation of sorbicillin (1),[8] but not from natural sources. The difference in m.p. of this sample (146–147°) and ours (68–70°) cannot be explained at present. The NMR spectra of our compound (see Tables 1 and 2 and Experimental) and its synthesis, however, leave no doubt as to its structure 2.

In our hands the hydrogenation of sorbicillin (1) gave the following results. When it was allowed to proceed until complete decolouration of the reaction mixture, only tetrahydrosorbicillin (8), m.p. 66–69°, was isolated in 21% yield, as had been reported previously.[8] Its IR and NMR spectra (see Experimental) confirm strcuture 8. When this hydrogenation of sorbicillin (1) was interrupted after the uptake of exactly 1 mole equivalent of hydrogen, a complex mixture of products resulted, from which (aside from 2% of recovered 1) 14% of 8 as well as 9% of a 2:3 mixture of 2′,3′-(2) and 2′,5′-dihydrosorbicillin (9) were isolated, along with a byproduct, which did not give a colour reaction with ferric chloride. Since we could not separate the two dihydrosorbicillins 2 and 9, the structure assignment of 9 is based on the spectra of the mixture; its UV spectrum is practically identical with that of 2 and the ^1H NMR spectrum, after subtraction of the signals of pure 2′,3′-dihydrosorbicillin (2), fits the 2′,5′-dihydrosorbicillin structure 9 (see Experimental).

Bisvertinoquinol (3)

The yellow bisvertinoquinol (3), m.p. 160–163°, is optically active, $[\alpha]_D^{20} = +329°$. Its structure 3 was obtained from an X-ray structure analysis, to be described in the last section. It was also converted to a mono-methyl ether 10 by brief treatment with diazomethane. Several properties of 3 and 10 are of general interest.

A comparison of the ^1H and ^{13}C NMR spectra of 10 and of the ^1H NMR spectrum of 3 (see below) with those of sorbicillin (1), 2′,3′-dihydrosorbicillin (2), vertinolide (4) and the model compound 13 manifests both the sorbyl and the 2,3-dihydrosorbyl substructure in bisvertinoquinol (3). The signals of these



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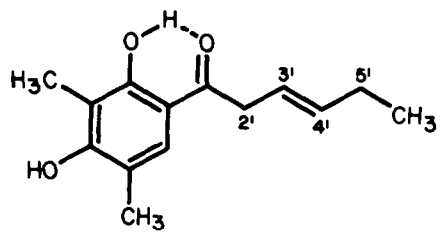

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substructures in the six compounds show much similarity (confirmed by decoupling), as can be seen in Table 1.

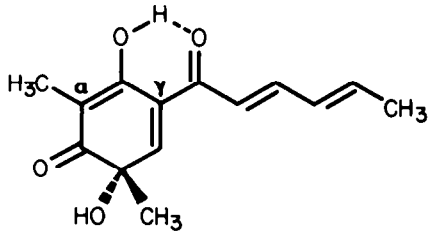
The mass spectra of **3** ($m/z = 498.2253$, $C_{28}H_{34}O_8$) showed that it readily dissociated into two parts; one interpretable as $C_{14}H_{18}O_4$ ($m/z = 250$) and the other as $C_{14}H_{16}O_4$ ($m/z = 248$). This NMR and MS evidence suggests that bisvertinoquinol (**3**) is a combination of sorbicillin (**1**, $C_{14}H_{16}O_3$) and 2',3'-dihydrosorbicillin (**2**, $C_{14}H_{18}O_3$), each of them enriched with an extra O-atom. Thus the natural pigment may be considered to be a Diels–Alder adduct of the quinol **11** and the quinol **12**, related to **1** and **2**, respectively, by simple oxidation of C(5). These quinols can exist in tautomeric forms, either as p- or as o-quinols. It is well known[14,15] that o-quinols readily dimerise, one molecule acting as diene, the other as dienophile, It has also been established[15] that such dimerisations occur with high regiospecificity, the a-position of the diene becoming attached to the y-position of the dienophile (head to tail addition), and also with high stereospecifities, the dimerisation occurring in an "endo-fashion" and with those sides of the cycloaddition partners facing each other which carry the hydroxyl group. The constitution and the relative configuration of **3** correspond exactly to what would be expected from the specificities of such a spontaneous dimerisation. Formula **3b** shows the result of a Diels–Alder reaction of **12** (as the dienophile) with **11** (as the diene).[2]

If both quinols **11** and **12** had been formed in the biological medium, one might have expected four Diels–Alder adducts, according to the four structural and positional variations of the two side chains, sorbyl and dihydrosorbyl. Since a careful TLC examination of the mother liquors of the crystallisation of **3** did not reveal the presence of any products similar to **3**, it appears more likely that the biosynthetic side chain differentiation (as found in **3**) occurs only after the Diels–Alder formation of the tricyclic skeleton, be it either by the addition of two H-atoms to C(15) and C(16) in the dimer of **11** or by the removal of two H-atoms from C(24) and C(25) in the dimer of **12**. This argument also suggests that the Diels–Alder reaction leading to **3** is a biosynthetic event and not an artifact of the isolation.

The molecule of **3** contains six centers of chirality, of which four are generated (specifically, see above) in the Diels–Alder reaction, while the other two (C(6) and C(9)) are carried over from the monomers. The relative configuration (R*,R*) at C(6) and C(9) (see Figs. 2 and 3) confirms that the monomers, **11** and/or **12**, have the "same" absolute configuration. The absolute configuration of **3**, however, is not available from the X-ray structure determination (see the last section). The CD spectra of **3** and of **10** in methanol are shown in Fig. 1. Because of the lack of appropriate models these spectra cannot be used at present to determine the absolute configuration of bisvertinoquinol (**3**).[16]

We can now discuss the NMR spectra. The signals obtained from $CDCl_3$ solutions of bisvertinoquinol (**3**) were not fully interpretable, perhaps due to the presence of several tautomeric forms. The ^1H NMR spectrum of **3** in CD_3OD, however, was informative, as were also the ^1H and ^{13}C NMR spectra in $CDCl_3$ of bisvertinoquinol methyl ether (**10**). The signals of these spectra are listed in Table 3.

First we consider the features due to tautomerism. Bisvertinoquinol (**3**) contains two enolized β-diketone substructures, one involving C(11), C(12) and C(23), the other C(3), C(4) and C(5). In the



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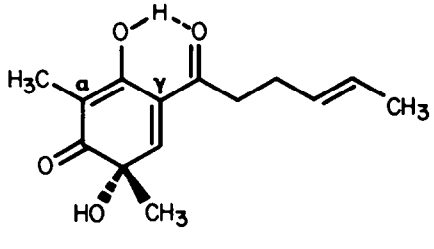

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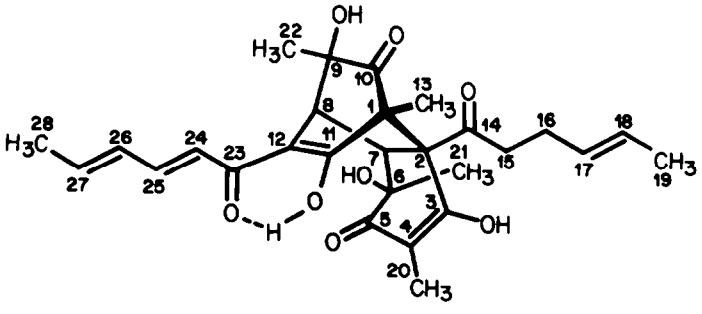

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(formulated as **3b**)[2]

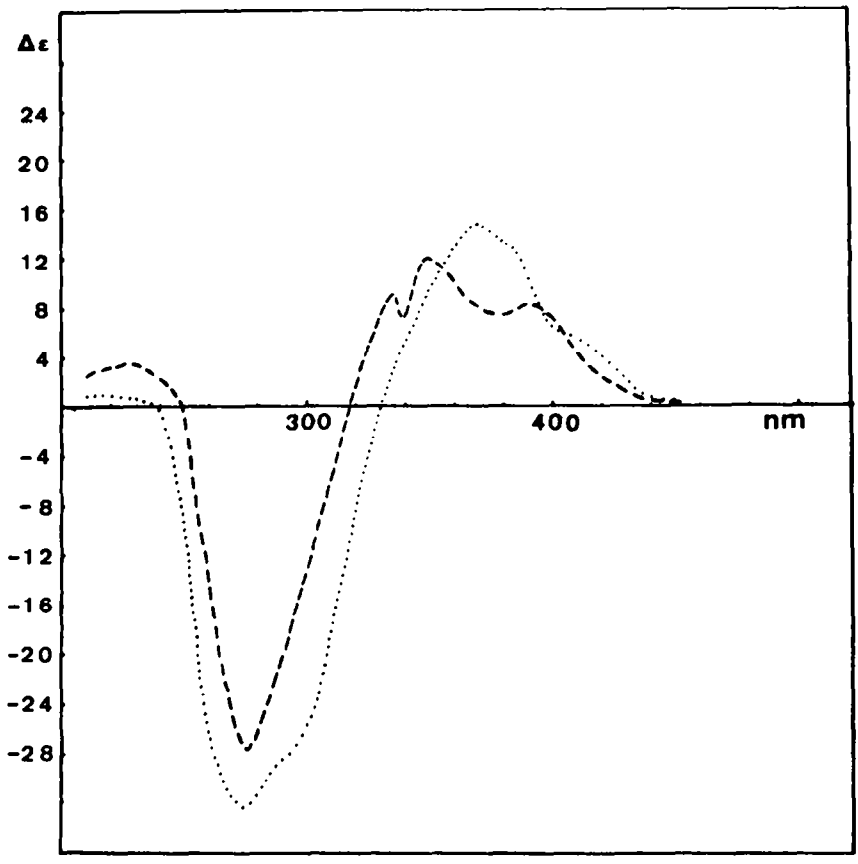


Fig. 1. CD spectra of bisvertinoquinol (3, -----) and of its methyl ether (10, ·····) in methanol.

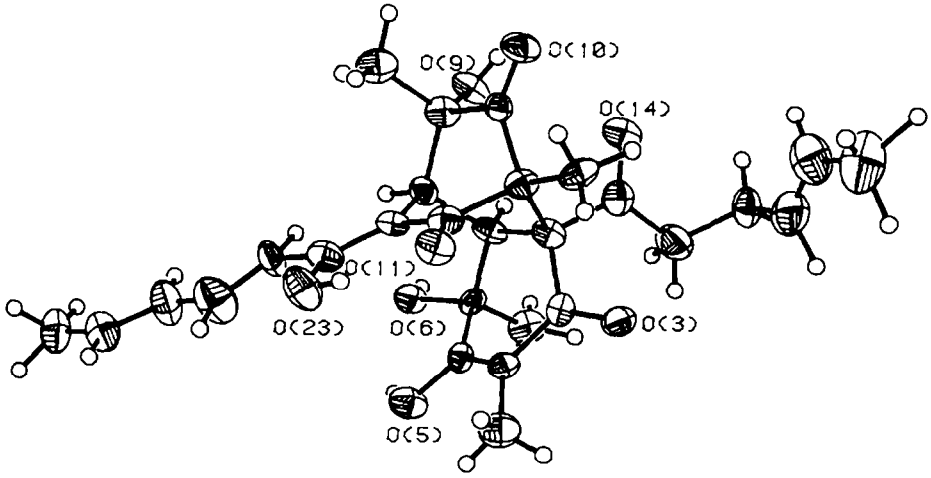
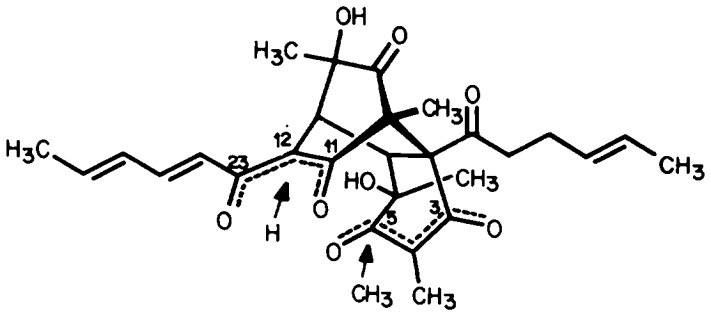


Fig. 2. Molecular drawing of bisvertinoquinol (3, formulated as 3a,[2] absolute configuration chosen arbitrarily). The H-atoms are drawn with an arbitrary radius, whereas the other atoms are represented by their 50% probability ellipsoids of vibration. The O-atoms are indexed with their numbers. For the numbering of the C-atoms see formula 3.



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crystal, both of these substructures are enolized in one direction only, the first in the direction of O–C(23) and the second in the direction of O–C(5). In methanolic solution, however, **3** appears to occur as a mixture of tautomers, fortunately mostly in a rapid equilibrium. Thus the formula of **3** in Table 3 shows the two enol substructures in a tautomerically non-committing manner.

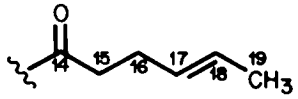
As far as the structure of bisvertinoquinol methyl ether (**10**) is concerned, we conclude that methylation of **3** has taken place at the β-diketo system involving C(3), C(4) and C(5) since diazomethane is known to react faster with non-chelated enols than with chelated ones[17] and since **10** gives the same colour with $FeCl_3$ as **3** and as the model compound **13** (see below). A definite conclusion as to whether the methylation took place at O–C(3) or O–C(5) is not possible at present. (Some preference may be given to the latter possibility since **10** does not fragment into two "halves" in the mass spectrum as does **3**.) Thus the position of the ether methyl group of **10** is also expressed non-committally in formula **10** and in Table 3.

On the basis of the above said we can now interpret the available NMR data of **3** and **10**. This interpretation is expressed in Table 3, where those alternative assignments of signals which are due to their similarity are indicated by wavy brackets and those which are due to difference in direction of enolization or place of methylation are mentioned explicitly.

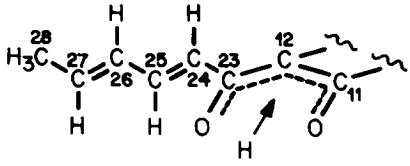
In the hope of facilitating the structure elucidation of other metabolites of *V. intertextum*, we summarize, in the following, some characteristic NMR spectral features of the substructures[19] of bisvertinoquinol **3** and its methyl ether **10**. They are the substructures A to H. Those signals which belong to one of these substructures are marked with the corresponding letters in Table 3, alternatively possible assignments again being indicated by wavy brackets.

Substructure A, the 2,3-dihydrosorbyl side chain, has already been discussed above and its NMR signals in **3** and **10** have been listed in Table 1.

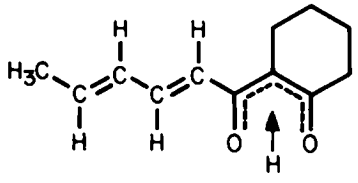
Substructure B contains the sorbyl side chain, already discussed above (see also Table 1), overlapping with one of the β-diketo substructures. As a



Substructure A of **3** and **10**



Substructure B of **3** and **10**



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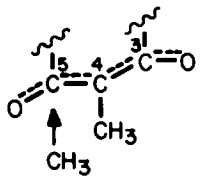
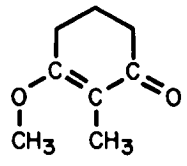
model we synthesised 2-[(E,E)-2,4-hexadienoyl]-cyclohexanone (**13**) by acylation of cyclohexanone with sorbyl chloride in the presence of LDA. The ^1H and the ^{13}C NMR signals of **13** and its yellow colour compare reasonable well with the corresponding properties of substructure B of **3** and **10**. In Table 3 corresponding signals are shown on the same line. Only one of the signals of **13** (181.4 ppm) is low-field shifted as compared to the corresponding signal of **10** (169.3 ppm), which might be attributed to a conformational difference around the chelate system. Substructure B must be responsible for the yellow colour of **3** and **10**.

Substructure C of **10** encompasses the methylated β-diketo system. Its ^{13}C and the ^1H NMR signals agree closely with the ones observed here and in Ref. 18 for the model compound **14**. The pertinent signals of **14** are shown in Table 3 on the same line as corresponding signals of **10**. The high field ^{13}C NMR absorption of the C-methyl group in substructure C and in **14** is characteristic for its α-position on an

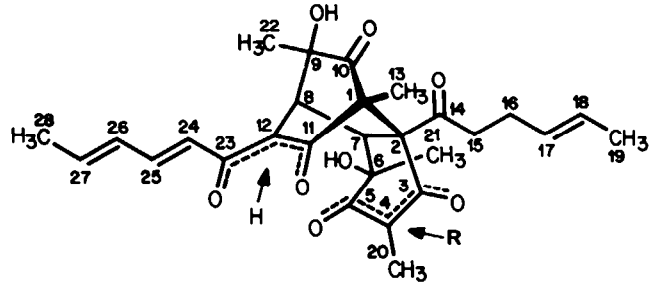




14

Substructure C of **10**

Table 3. ^{1}H and ^{13}C signals of bisvertinoquinol (**3**) and bisvertinoquinol methyl ether (**10**) with assignment to substructures A to H as well as of the model compounds **13** and **14**



3 (R = H, formulated as **3c**)[2]
10 (R = CH_3)

^{1}H NMR						^{13}C NMR			
H-atom[a]	**3**[b]	**10**[c]	sub-structure	model compounds[c]		C-atom	**10**[d]	sub-structure	model compounds[d]
O---H-O	-	13.92/s	B	16.79/s	**13**	C(10)	208.0/s	H	
H-C(25)	7.22/dxdxd (15, 10.5, 2)	7.29/dxd (15, 10)	B	7.30/dxd (15, 10)	**13**	C(14)	205.9/s	A	
						C(3) or C(5)[e]	196.2/s	C	201.2/s **14**
H-C(24)	6.27/d (15)	6.28/d (15)	B	6.27/d (15)	**13**	C(23) or C(11)[f]	192.6/s	B	192.4/s **13**
H-C(26)	6.4-6.2/m	6.3-6.1/m	B	6.4-6.1/m	**13**	C(5) or C(3)[e]	172.8/s	C	172.2/s **14**
H-C(27)	6.19/dxq (15, 6.5)					C(11) or C(23)[f]	169.3/s	B	181.4/s **13**
H-C(17)	5.4-5.3/m	5.45-5.25/m	A			C(25)	142.7/d	B	141.9/d **13**
H-C(18)						C(27)	140.6/d	B	138.8/d **13**
H_3CO	-	3.87/s	C	3.87/s	**14**[g]	C(26)	131.0/d	B	131.1/d **13**
H-C(7)	3.62/d (2.5)	3.75/d (3)	D			C(17)	129.2/d	A	
H-C(8)	3.38/d (2.5)	3.22/d (3)	D			C(18)	126.3/d	A	

HO-C(6)	-	3.01/s	E		C(24)	118.7/d	B	121.5/d **13**
HO-C(9)	-	2.95/s	E		C(4)	113.7/s	C	114.7/s **14**
H-C(15)	2.7-2.6/m	2.9-2.7/m	A		C(12)	108.6/s	B	106.9/s **13**
H'-C(15)	2.5-2.4/m	2.6-2.4/m	A		C(1)	74.0/s	G	
H_2-C(16)	2.3-2.1/m	2.3-2.1/m	A		C(2)	70.0/s	G	
H_3-C(28)	1.87/d (6.5)	1.90/d (6)	B	1.87/d (5.5) **13**	C(6)	69.0/s	E	
H_3-C(19)	1.60/d (5)	1.59/d (5)	A		C(9)	65.9/s	E	
H_3-C(20)	1.57/s	1.82/s	C	1.71/t (1.0) **14**[g]	CH_3O	61.8/q	C	55.2/q **14**
H_3-C(13)	1.45/s	1.45/s	F		C(7)	43.7/d	D	
H_3-C(21)	1.18/s	1.25/s	E		C(8)	41.3/d	D	
H_3-C(22)	1.13/s	1.13/s	E		C(15)	40.8/t	A	
					C(21)	35.5/q	E	
					C(16)	27.1/t	A	
					C(22)	24.3/q	E	
					C(28)	19.2/q	B	
					C(19)	18.1/q	A	18.7/q **13**
					C(13)	10.5/q	F	
					C(20)	9.6/q	C	7.3/q **14**

[a] the intensities of the signals correspond to the number of H-atoms shown in this column; [b] in CD_3OD, 360 MHz; [c] in $CDCl_3$, 200 MHz; [d] in $CDCl_3$, 25.1 MHz; [e] depending on whether methylation took place on O-C(3) or O-C(5); [f] depending on which tautomer is prevalent; [g] in $CDCl_3$, 60 MHz, taken from[18].

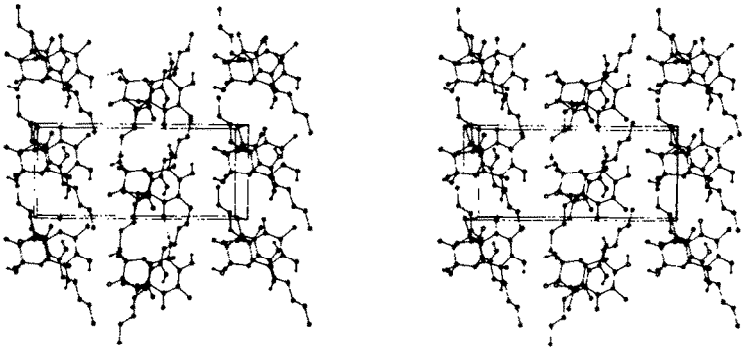


Fig. 3. Stereoscopic packing diagram of bisvertinoquinol (3, formulated as 3a[2]) viewing the a,b-plane. Intermolecular H-bonds are indicated by dotted lines. H-atoms attached to C-atoms are not shown.

enolised β-dicarbonyl system, as had been noted already for vertinolide (4).[3]

Substructure D consists of the two neighbouring methine groups (H–C(7) and H–C(8)). Close analogies to its ^{1}H NMR signals are found in two o-quinol Diels–Alder dimers ($\sim$2.8 and $\sim$3.1 ppm) whose structures are fully known.[15]

Substructure E is made up of the two isolated tertiary carbinol systems (HO–C(6)–CH_3 and HO–C(9)–CH_3) and substructure F consists of the methyl group on a quaternary C-atom H_3C(13). Of interest and, at the moment, not reliably interpretable is the high field ^{13}C NMR absorption of C(13) (9.6/q or 10.5/q). Substructure G contains two quaternary C-atoms (C(1) and C(2)). The saturated carbonyl group (aside from the one in substructure A) is substructure H, manifested also by the IR band at 1700 or 1732 cm^{-1} in **3** and at 1712 or 1732 cm^{-1} in **10**, respectively.

X-Ray diffraction analysis of bisvertinoquinol (**3**) *at ca* $-120°$

Bisvertinoquinol (**3**) crystallises from chloroform/ether as yellow triangular platelets, space group $P2_1$, a = 7.577(2), b = 17.120(4), c = 9.848(2) Å, β = 90.64(2)°, (from 25 automatically centered reflections of a hemisphere, $10° < 2\theta < 19°$), Z = 2. MoK$_\alpha$-Radiation was used to measure the intensities of 1746 symmetry independent reflections within 45° (2θ) on a Nicolet-R3 four circle diffractometer in the ω-scan mode. The intensities were conventionally corrected without absorption correction. The initial phases were determined by direct methods. The structure was solved and refined by application of the program SHELXTL.[20]

The identificatrion of the O- and C-atoms was based upon their bond distances and thermal parameters. The H-atoms were located by difference Fourier maps, but—due to the inferior quality of the crystal—some of them not very accurately. They were varied freely with isotropic temperature factors, while the other atoms were refined anisotropically. The 1414 structure factors with $F \geq 4\sigma(F)$ were used with unit weights to refine the 461 variables in a blocked cascade least squares refinement (*ca* 100 variables per block) to a conventional R-value of 0.047 (the conventional R_w, RG in SHELXTL,[20] is 0.048).

The coordinates of the C- and O-atoms and their equivalent isotropic temperature factors are listed in Table 4. Figure 2 shows a molecular drawing of **3** with the O-atoms numbered (for the C-atoms see Table 3). The absolute configuration was not determined.

Within the limited accuracy of data (average standard derivation of C–C bond lengths 0.01 Å), the bond lengths are in the range of usual values, except the bond between the quaternary C-atoms C(1) and C(2) (1.62 Å) and the essentially eclipsed bond between C(2) and C(7) (1.59 Å). In the side chains, some bonds are on the lower limit of their expected values. The conjugated system including the sorbyl side chain C(11), C(12), C(23) to C(27) and O(11) and it neighbour atoms C(1), C(8), C(28) and O(23) are approximately in a common plane, which includes a H-bridge from O(23) to O(11). The dihydrosorbyl side chain is coiled, the torsional angles C(14)C(15)C(16)C(17) and C(15)C(16)C(17)C(18) being 79° and $-113°$, respectively. The bicyclo [2.2.2]octane skeleton shows an almost perfectly eclipsed arrangement of the C–C bonds. The C(2), C(7)-ortho-fused cyclohexanedione ring exists in a boat-like conformation with C(4) folded towards C(11) (distance 3.08 Å) and C(5) towards C(12) (distance 3.05 Å). This conformation brings O(6) into a pseudo equatorial position so that an intramolecular H-bond from O(5) to O(6) is possible. Intermolecular H-bonds, from O(6) to O(3) and from O(9) to O(5), connect the molecules in the a, b-plane, as is shown by the dotted lines in Fig. 3.

The bond lengths of the two β-diketo-systems show that both systems exist in the crystal as just one enolic form. In one system these lengths are O(23)–C(23) 1.34 Å, C(23)–C(12) 1.37 Å, C(12)–C(11) 1.44 Å and C(11)–O(11) 1.25 Å, indicating enolisation in the direction of O(23) and in the other system they are O(5)–C(5) 1.35 Å, C(5)–C(4) 1.34 Å, C(4)–C(3) 1.45 Å and C(3)–O(3) 1.25 Å, showing enolisation in the direction of O(5), as is expressed in Fig. 2.

EXPERIMENTAL

CD spectra were measured on a Dichrograph II (Roussel-Jouan, Paris) and are reported as λ in nm ($\Delta\epsilon$). The 20 MHz ^{13}C NMR spectra were obtained on a Varian FT-80 A spectrometer, the high resolution (HR-MS) and the field desorption (FD-MS) mass spectra on a CEC 21-110 B instrument. The interpretations suggested in the non-high resolution are purely hypothetical. Preparative thin layer

Table 4. Fractional coordinates and equivalent isotropic temperature factors (Å²) of the C- and O-atoms of bisvertinoquinol (3) with e.s.d.s in units of the last significant digit

ATOM	X	Y	Z	U[a])
C(1)	.8113(7)	.4978(4)	.4170(6)	.032(2)
C(2)	.7257(7)	.5449(4)	.5424(6)	.031(2)
C(3)	.8326(7)	.6209(4)	.5498(6)	.029(2)
O(3)	.9841(5)	.6167(3)	.6007(4)	.036(1)
C(4)	.7670(8)	.6923(4)	.4875(6)	.032(2)
C(5)	.5915(7)	.7000(4)	.4747(5)	.028(2)
O(5)	.5184(5)	.7637(3)	.4153(5)	.043(2)
C(6)	.4600(7)	.6427(4)	.5352(6)	.029(2)
O(6)	.2967(5)	.6576(3)	.4663(4)	.037(1)
C(7)	.5217(8)	.5579(4)	.5103(7)	.031(2)
C(8)	.4756(8)	.5297(4)	.3661(6)	.031(2)
C(9)	.5009(7)	.4407(4)	.3585(6)	.034(2)
O(9)	.3906(5)	.4067(3)	.4573(4)	.043(1)
C(10)	.6963(8)	.4247(4)	.3876(5)	.029(2)
O(10)	.7589(5)	.3600(3)	.3772(4)	.042(2)
C(11)	.7800(8)	.5513(4)	.2929(6)	.033(2)
O(11)	.9070(5)	.5773(3)	.2269(4)	.038(1)
C(12)	.5970(7)	.5685(4)	.2654(6)	.029(2)
C(13)	1.0019(7)	.4750(4)	.4364(6)	.035(2)
C(14)	.7417(8)	.4916(4)	.6690(6)	.038(2)
O(14)	.7217(6)	.4219(3)	.6563(4)	.045(2)
C(15)	.7606(10)	.5268(4)	.8112(7)	.054(3)
C(16)	.8451(9)	.4711(4)	.9140(6)	.048(3)
C(17)	1.0382(12)	.4682(5)	.8987(7)	.065(3)
C(18)	1.1291(11)	.4083(6)	.8588(8)	.067(3)
C(19)	1.3281(10)	.4033(6)	.8442(8)	.077(4)
C(20)	.8980(8)	.7531(4)	.4445(7)	.046(2)
C(21)	.4368(8)	.6615(4)	.6850(7)	.043(2)
C(22)	.4536(8)	.4079(4)	.2186(7)	.047(2)
C(23)	.5502(8)	.6172(4)	.1603(6)	.039(2)
O(23)	.6727(6)	.6503(3)	.0815(4)	.052(2)
C(24)	.3651(8)	.6362(4)	.1216(6)	.040(2)
C(25)	.3233(10)	.6932(5)	.0395(8)	.068(3)
C(26)	.1413(10)	.7138(5)	.0007(8)	.063(3)
C(27)	.0949(10)	.7592(4)	-.1004(7)	.049(3)
C(28)	-.0859(10)	.7776(5)	-.1436(7)	.056(3)

[a]) The equivalent isotropic U is defined as one third of the trace of the orthogonalised U_{ij}-tensor

chromatography (prep TLC) was carried out with Merck silica gel $HF_{254+366}$ on hand coated, 20 × 20 cm plates (10 g per plate) and column chromatography with LiChroprep Si60 in Merck Lobar B columns. All other methods, instruments and abbreviations used here have already been described.[3]

Isolation of Bisvertinoquinol (3), *Sorbicillin* (1) *and 2',3'-Dihydrosorbicillin* (2)

The spent culture medium (841) of *Verticillium intertextum* ATCC 46284 (see Ref. 3) was extracted with $CHCl_3$ as described.[3] The crude extract weighing 8.44 g was chromatographed on 300 g Sephadex LH-20 in a 4.5 × 60 cm column with $CHCl_3$/pentane 2:1 at 4° in the dark using a flow rate of 1.67 ml/min. The solvent ratio was changed to 3:1 after 3700 ml solvent was collected. Three main fractions were collected after control by anal TLC ($CHCl_3/C_2H_5OH$ 94:6): Fraction a, 1700–2500 ml, 0.75 g yellow products; fraction b, 2500–4000 ml, 2.40 g containing all of 4; fraction c, 5100–7000 ml, 1.45 g yellow products. A first fraction preceding a and an intermediate fraction between b and c consist of several products, which were not isolated.

After separation of vertinolide (4) from fraction b by crystallisation, as has been described,[3] the mother liquor was concentrated. The brown-red oily residue was kept without solvent at −20° under argon for 30 days. Stirring with 2 ml cold ether at −15° for a short time, filtration and washing with cold ether left 280 mg of crude bisvertinoquinol (3) as a yellow powder, m.p. 155–159° (dec). Four recrystallisations from ether at room temp furnished 120 mg (1.4% of the crude extract) of pure bisvertinoquinol (3) as pale yellow triangular platelets, m.p. 160–163° (dec), intense green-brown colour with $FeCl_3$ in H_2O/C_2H_5OH. $[\alpha]_D^{20} = +329°$ (c = 0.2, $CHCl_3$). UV (CH_3OH): 250 sh (9000), 301 (18040), 370 (13430), 380 sh (13000), 400 sh (8000); UV after addition of one drop 0.1 N NaOH: 308

(22300), 367 (11500), 400 sh (7000); acidification regenerated the original spectrum. CD (CH_3OH): 230 (+3.6), 275 (−27.9), 336 (+9.2), 348 (+12.2), 389 (+8.3). IR ($CHCl_3$): 3550 m, 3400–3100 m, 2980 w, 2920 m, 2850 w, 1732 m, 1700 m, 1660 m, sh, 1628 s, 1605 m, sh, 1560 m. ^1H NMR see Table 3. Double resonance: Irradiation at 7.22 (H-C(25)) gave: 6.4–6.2/simplified m (H-C(26)) and 6.27/s (H–C(24)). Irrad. at 6.27 (H–C(24)) gave: 7.22/d × d, J = 10.5 & 2.0 (H–C(25)). Irrad. at 6.19 (H–C(27)) gave: 7.22/d × d, J = 15 & 10.5 (H–C(25)) and 6.4–6.2/simplified m (H–C(26)) and 1.87/s (H_3–C(28)). Irrad. at 5.40 (H–C(17) and H–C(18)) gave: 2.3–2.1/simplified m (H_2–C(16)) and 1.60/s (H_3–C(19)). Irrad. at 3.38 (H–C(7) or H–C(8)) gave: 3.62/s (H–C(8) or H–C(7)). Irrad. at 2.65 (H′–C(15)) gave: 2.5–2.4/simplified m (H–C(15)) and 2.3–2.1/simplified m (H_2–C(16)). Irrad. at 2.45 (H–C(15)) gave: 2.7–2.6/(simplified m (H′–C(15)) and 2.3–2.1/simplified m (H_2–C(16)). Irrad. at 2.20 (H_2–C(16)) gave: 2.65/d, J = 18 (H′–C(15) and 2.43/d, J = 18 (H–C(15)). MS: 498/1 (M^+); 480/1 (M^+–H_2O); 251/7; 250/27 ($C_{14}H_{18}H_4^+$); 248/19 ($C_{14}H_{16}O_4^+$); 233/12; 232/24; 231/7; 230/5; 222/5; 217/22; 216/16; 215/7; 209/5; 208/38; 207/31; 206/9; 205/28; 201/7; 194/6; 193/12; 192/6; 191/21; 190/7; 189/13; 182/12; 181/100; 180/33; 179/38; 178/13; 177/16; 175/11; 167/6; 166/10; 165/68; 164/6; 163/8; 161/10; 159/5; 155/9; 154/72; 153/28; 152/32; 151/22; 149/16; 139/28; 138/18; 137/33; 136/17; 135/23; 125/13; 124/18; 123/13; 121/15; 112/13; 111/16; 109/13; 107/13; 105/10; 97/18 ($COC_5H_9^+$); 96/14; 95/47 ($COC_5H_7^+$); 91/17; 85/14; 84/14; 83/40; 81/16; 79/19; 77/26; 69/42 ($C_5H_9^+$); 68/15; 67/35 ($C_5H_7^+$); 65/18; 57/14; 55/64; 53/27; 51/14. HR-MS: 498.2253 (M^+, Calc 498.2254). FD-MS: 498 (M^+). Found: C, 67.16; H, 7.06. Calc for $C_{28}H_{34}O_8$: C, 67.45; H, 6.87%.

The etheral mother liquor from the crystallisation of **3** was evaporated to dryness and the residue was chromatographed on eight plates (prep TLC (1)) using $CHCl_3/C_2H_5OH$ 94:6. The fraction of prep TLC (1) with R_f 0.63, containing sorbicillin (**1**) and 2′,3′-dihydrosorbicillin (**2**), was chromatographed on two plates (prep TLC (2)) with hexane/ether/CH_3OH 56:40:3. From a yellow band at R_f 0.44 of prep TLC (2), 9.3 mg (0.11% of the crude extract) of sorbicillin (**1**) was obtained as orange prisms, m.p. 122.5–125.0° (ether/pentane at −20°), (Ref. 6: m.p. 129–130°), black colour with $FeCl_3$ in H_2O/C_2H_5OH. UV (CH_3OH): 320 (22900), 380 sh (8000); UV after addition of one drop 0.1 N NaOH: 270 sh (12600), 275 (17800), 305 (14100), 410 (28800). The shape of this spectrum was identical with the published one.[6] IR ($CHCl_3$): 3580 m, 3440–3100 w, 2970 w, 2910 m, 2850 m, 1640 s, sh, 1616 s, 1561 s. ^1H and ^{13}C NMR see Tables 1 and 2. Double resonance: Irradiation at 7.46 (H–C(3′)) gave: 6.92/s (H–C(2′)) and 6.4–6.2/simplified m (H–C(4′) and H–C(5′). Irrad. at 1.88 (CH_3–C(5′)) gave: 6.4–6.2/simplified m (H–C(4′) and H–C(5′)). MS: 234/6; 233/13; 232/82 (M^+); 231/20; 218/15; 217/100 (M^+–CH_3); 216/6; 215/6; 203/5; 192/6; 191/38; 189/17; 175/18; 174/5; 166/8; 165/76 (M^+–C_5H_7); 164/34; 163/7; 161/5; 138/18; 136/59; 135/11; 109/10; 91/16; 83/21; 79/17; 77/19; 67/21 ($C_5H_7^+$), 65/19; 55/17; 53/16; 51/10; 43/26; 41/43.

From a colourless, but UV active band at R_f 0.50 of prep TLC (2) was obtained 1.7 mg (0.02% of the crude extract) of 2′,3′-dihydrosorbicillin (**2**) as colourless needles, m.p. 67.0–70.0° (ether/pentane), black colour with $FeCl_3$ in H_2O/C_2H_5OH. UV (CH_3OH): 238 sh (8000), 285 (14200), 330 (5700); UV after addition of 0.1 N NaOH: 256 (6000), 351 (33500); acidification regenerated the original spectrum. IR ($CHCl_3$); 3582 m, 3450–3100 w, 2980 w, sh, 2930 m, sh, 2910 m, 2850 w, 1620 s, 1480 m. ^1H and ^{13}C NMR: see Tables 1 and 2. Double resonance: Irradiation at 5.55 (H–C(4′) and H–C(5′)) gave: 2.39/t, J = 7.5 (H_2–C(3′)) and 1.66/s (CH_3–C(5′)). Irrad. at 2.40 (H_2–C(3′)) gave: 5.7–5.4/simplified m (H–C(4′) and H–C(5′)) and 2.97/s (H_2–C(2′)). MS: 234/16 (M^+): 217/4: 216/19: 215/3: 201/7; 191/4; 180/5; 175/4; 166/11; 165/100 (M^+–C_5H_9); 163/3; 151/4; 135/21; 107/13; 91/16; 79/10; 77/10; 71/11; 69/12 ($C_5H_9^+$); 57/21; 55/24; 53/10; 43/34; 41/36.

Hydrogenation of sorbicillin (**1**)

Hydrogenation according to the published procedure.[8] A solution of 70 mg (0.3 mmol) sorbicillin (**1**) in 15 ml 0.1 N NaOH was hydrogenated over Pt (10 mg PtO_2) at 1 atm until the deep orange solution had lost its colour (25 min). After filtration and acidification with 5% HCl, the product was extracted with ether and chromatographed on two prep TLC plates with hexane/ether/CH_3OH 56:40:3. The UV active zone was eluted with $CHCl_3$. Evaporation of the solvent afforded 15 mg (21%) crude tetrahydrosorbicillin (**8**) which was identical (^1H NMR) with the product isolated by the partial hydrogenation of sorbicillin (**1**; see below).

Partial hydrogenation of sorbicillin (**1**). A solution of 500 mg (2.16 mmol) sorbicillin (**1**) in 80 ml 0.1 N NaOH was hydrogenated over Pt (50 mg PtO_2) at 1 atm. After absorption of 2.16 mmol H_2 the hydrogenation was interrupted, the catalyst filtered off and the filtrate acidified with 5% HCl. Extraction with ether and removal of the solvent afforded a crude material, which was chormatographed on a Lobar B column with hexane/ether/CH_3OH 56:40:3 to give two fractions. The first fraction was further chromatographed on eight prep TLC plates impregnated with 6.7% $AgNO_3$ using the same solvent system. A first zone with R_f 0.56 gave 71 mg (14%) of tetrahydrosorbicillin (**8**), m.p. 66.0–69.0° (Ref. 8: m.p. 69–70°). The UV spectrum in abs. EtOH was identical with the one described.[8] IR ($CHCl_3$): 3580 m, 3450–3100 w, 2950 m, sh, 2920 m, 2850 m, 1620 s. ^1H NMR (200 MHz, $CDCl_3$): 12.95/s, 1H (HO–C(2)); 7.42/s, 1H (H–C(6)); 5.31/s, 1H (HO–C(4)); 2.90/t, J = 7.8, 2H (H_2–C(2′)); 2.22/s, 3H (CH_3–C(5)); 2.14/s, 3H (CH_3–C(3)); 1.80–1.60/m, 2H (H_2–C(5′)); 1.44–1.30/m, 4H (H_2–C(3′) and H_2–C(4′)); 0.92/t, J = 7.0, 3H (CH_3–C(5′)). MS: 237/2; 236/14 (M^+); 221/1; 219/1; 218/7; 203/2; 194/2; 193/15; 191/1; 189/1; 181/2; 180/19; 175/4; 166/10; 165/100 (M^+–C_5H_{11}); 55/10.

From a second zone with R_f 0.50 46 mg (9%) of a 2:3 mixture of 2′,3′-(**2**) and 2′,5′-dihydrosorbicillin (**9**) was isolated, an oil which was not amenable to further separation; it showed a black colour with ferric chloride in H_2O/C_2H_5OH. UV (CH_3OH): 238 sh (7300), 286 (16000), 328 (6000); UV after addition of 0.1 N NaOH: 255 (6450), 352 (31500); acidification regenerated the original spectrum. ^1H NMR (60 MHz, $CDCl_3$): 12.88/s, 0.4 H (HO–C(2) of **2**); 12.77/s, 0.6H (HO–C(2) of **9**); 7.31/s, 1H (H–C(6) of **2** and **9**); 5.70–5.30/m, 3H (H–C(4′), H–C(5′) and HO–C(4) of **2** and H–C(3′), H–C(4′) and HO–C(4) of **9**); 3.67–3.50/m, 1.2H (H_2–C(2′) of **9**); 2.98/t, J = 7.5, 0.8H (H_2–C(2′) of **2**); 2.20/s, 3H (CH_3–C(5) of **2** and **9**); 2.12/s, 3H (CH_3–C(3) of **2** and **9**); 2.55–1.85/m, 2H (H_2–C(3′) of **2** and H_2–C(5′) of **9**); 1.63/d, J = 4.0, 1.2H (CH_3–C(5′) of **2**); 0.99/t, J = 7.0, 1.8H (CH_3–C(5′) of **9**). MS: 235/1; 234/7 (M^+); 216/3; 201/2; 191/4; 180/2; 175/1; 167/1; 166/10; 165/100 (M^+–C_5H_9); 85/13; 69/5 ($C_5H_9^+$); 43/41; 41/16.

A third zone with R_f 0.44 yielded 12 mg (2%) of sorbicillin (**1**).

The second fraction from Lobar column chromatography was recrystallised three times from CH_3OH and twice from ether to give 44 mg of a product with unknown structure as colourless flakes, m.p. 160.0–162.0°. The product gave no colour reaction with ferric chloride.

Synthesis of 2′,3′-dihydrosorbicillin (**2**)

(4R*,5S*)-4,5-*Dibromohexanoic acid* (**6**). Prepared according to the described procedure[12] as colourless needles, m.p. 80.5–81.0° (Ref. 12: 84°). IR ($CHCl_3$): 3550–2500 m, 1710 s. ^1H NMR (200 MHz, $CDCl_3$): 11.62/s, 1H (COOH); 4.30–4.10/m, 2H (H–C(4) and H–C(5)); 2.85–2.50/m, 3H (H–C(3) and H_2–C(2)); 2.30–2.05/m, 1H(H–C(3)); 1.89/d, J = 6.2, 3H (CH_3). ^{13}C NMR (20.0 MHz, $CDCl_3$): 179.1/s (C(1)); 59.6/d and 51.9/d (C(4) and C(5)); 32.0/t and 31.8/t (C(2) and C(3)); 25.1/q (C(6)). MS: 195/8; 193/10 (M^+–HBr); 175/1; 150/2; 113/100 (M^+–HBr_2); 85/29; 71/55; 69/11; 67/18; 60/10; 57/11; 55/18; 53/10; 43/27; 41/49.

1 - [(4R*,5S*) - 4,5 - *Dibromohexanoyl*] - 2,4 - *dihydroxy*-3,5 - *dimethylbenzene* (**7**). A solution of 138 mg (1 mmol) of

2,4-dimethylresorcinol (**5**)[11] and 274 mg (1 mmol) of **6** in 2 ml BF_3–etherate was heated for 2.5 hr at 100°. After cooling, 5 g ice-water was added and the organic material extracted with 4 × 10 ml ether. The combined extract was evaporated to dryness and dissolved in 5 ml 80% CH_3OH. After keeping the solution at room temp for 15 min, the solvent was removed at reduced pressure and the residue chromatographed on four prep TLC plates with hexane/ether/CH_3OH 56:40:3. The UV active zone (254 nm: dark, 366 nm: yellow–orange) was extracted with $CHCl_3$ to give, after evaporation of the solvent and drying, 160 mg (41%) of **7** as colourless needles, m.p. 132.0–134.0° (dec) (ether/pentane). An analytical sampel had m.p. 136.8–138.0° (dec), black colour with ferric chloride in H_2O/C_2H_5OH. UV (CH_3OH): 285 (15200), 330 (6300); UV after addition of 0.1 N NaOH: 254 (5900), 292 sh (4000), 346 (26400); acidification regenerated the original spectrum. IR ($CHCl_3$): 3582 m, 3450–3150 w, 2970 w, 2920 m, 2850 w, 1627 s. ^1H NMR (200 MHz, $CDCl_3$): 12.78/s, 1H (HO–C(2)); 7.44/s, 1H (H–C(6)); 5.29/s, 1H (HO–C(4)); 4.40–4.20/m, 2H (H–C(4') and H–C(5')); 3.30–3.16/m, 2H (H_2–C(2')); 2.80–2.60/m, 1H (H–C(3')); 2.35–2.15/m, 1H (H–C(3')); 2.19/s, 3H (CH_3–C(5)); 2.14/s, 3H (CH_3–C(3)); 1.91/d, J = 6.4, 3H (CH_3–C(5')). ^{13}C NMR (25.1 MHz, CD_3COCD_3): 203.8/s (C(1')); 161.9/s and 161.0/s (C(4) and C(2)); 129.8/d (C(6)); 116.4/s, 112.9/s and 111.3/s (C(5), C(3) and C(1)); 62.2/d and 53.5/d (C(4') and C(5')); 36.0/t (C(2')); 32.2/t (C(3')); 24.5/q (CH_3–C(5')); 16.2/q (CH_3–C(5)); 8.0/q (CH_3–C(3)). MS: 396/3; 394/6 (M^+); 315/10 (M^+–Br); 313/10; 234/3; 233/8; 216/8; 201/3; 194/3; 193/26; 175/8; 166/11; 165/100 (M^+–$C_5H_9Br_2$). Found: C, 42.61; H, 4.41; Br, 40.25. Calc for $C_{14}H_{18}Br_2O_3$: C, 42.66; H, 4.60; Br, 40.55%.

2',3'-Dihydrosorbicillin (**2**). A mixture of 78.8 mg (0.2 mmol) **7**, 52 mg (0.8 mmol) Zn dust and 40 mg CH_3COOH was stirred in 4 ml ether at room temp for 2 hr. The inorganic material was filtered off and washed with ether. The combined filtrates were evaporated to dryness and the residue chromatographed on four prep TLC plates with hexane/ether/CH_3OH 56:40:3. The UV active zone was eluted with $CHCl_3$, the solvent evaporated and the residue recrystallised twice from ether/pentane at −20° to give 36 mg (77%) of **2** as colourless neeldes, m.p. 68.0–70.0°. The conventional spectra of this synthetic 2',3'-dihydrosorbicillin (**2**) were superimposable onto those of the natural sample, described above. Found: C, 71.61; H, 7.54. Calc for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74%.

Bisvertinoquinol methyl ether (**10**)

A solution of 80 mg (0.16 mmol) bisvertinoquinol (**3**) in ether was treated with 15 ml 1.4% diazomethane solution in ether at room temp. After 5 min the solvent was evaporated and the residue chromatographed on three plates with $CHCl_3/C_2H_5OH$ 97:3. The yellow zone was eluted with $CHCl_3$ to give, after evaporation of the solvent, 64 mg (78%) of **10** as a pale-yellow amorphous solid, m.p. 58–62°, anal TLC ($CHCl_3/C_2H_5OH$ 94:6) R_f 0.70. The product showed a dark green–brown colouring with ferric chloride in H_2O/C_2H_5OH. $[\alpha]_D^{25} = +77.2°$ (c = 0.96, $CHCl_3$). UV (CH_3OH): 259 (15500), 300 sh (11700, 308 (10600), 370 (22900), 380 (23300), 383 (23550), 405 sh (15000); UV after addition of one drop 0.1 N NaOH: 226 (12900), 274 (21000), 393 (16600); acidification regenerated the original spectrum. CD (CH_3OH): 274 (−32.4), 290 sh (−28.6), 369 (+14.3), 384 sh (+12.8), 404 sh (+6.0). IR ($CHCl_3$): 3570 m, 3500–3150 w, 3030 w, 2990 m, 2920 m, 2850 m, 1740 s, sh, 1732 s, 1712 m, 1688 m, sh, 1655 m, sh, 1620 s, 1560 s. ^1H and ^{13}C NMR see Table 3. MS: 513/3; 512/9 (M^+); 494/1 (M^+–H_2O), 327/7; 313/3; 275/4; 265/6; 249/4; 248/9; 247/14; 246/4; 243/3; 233/5; 231/3; 221/3; 219/4; 207/5; 206/22; 205/7; 203/4; 195/4; 193/8; 192/5; 191/4; 179/7; 177/4; 167/4; 165/4; 163/5/ 153/4; 97/14 ($COC_5H_9^+$); 95/100 ($COC_5H_7^+$); 69/36 ($C_5H_9^+$); 67/26 ($C_5H_7^+$); 57/17; 55/40; 45/23; 43/56; 41/40. HR-MS: 512.2401 (M^+, Calc for $C_{29}H_{36}O_8$ 512.2410). FD-MS: 512 (M^+).

2-[(E,E)-2,4-Hexadienoyl)]-cyclohexanone (**13**)

To a solution of LDA (30 mmol prepared from 4.08 g (30 mmol) diisopropylamine and 15 ml 2 M butyllithium (30 mmol) in hexane) in 20 ml THF cooled at −78° was added dropwise 2.30 g (23.5 mmol) cyclohexanone and then 3.9 g (30 mmol) sorbyl chloride within 10 min. After stirring at −78° for 15 min and at room temp. for 2 hr 15 ml 5% HCl and 25 ml ether were added. The organic layer was washed with water, dried with $MgSO_4$ and the solvent removed *in vacuo*. A solution of the residue in ether/hexane 4:1 was filtered through a short column of 50 g silica gel. The material from the yellow fraction was recrystallised twice from ether/hexane to give 2.75 g (61%) **13** as lemon yellow prisms, m.p. 93.0–95.0°, dark green colour with ferric chloride in H_2O/C_2H_5OH. UV (CH_3OH): 242 (3700), 296 (13800), 308 (14050), 354 (20200); UV after addition of one drop 0.1 N NaOH: 248 (4450), 295 (13500), 305 (13100), 353 (18700). IR ($CHCl_3$): 3600–3450 w, 3000 w, 2945 m, 2870 m, 1710 w, 1640 w, 1615 s, 1560–1500 s. ^1H NMR (200 MHz, $CDCl_3$); see Table 3 and 2.41/q, J = 6.5, 4H (H_2–C(3) and H_2–C(6)); 1.83–1.73/m, 4H (H_2–C(4) and H_2–C(5)). ^{13}C NMR (25.1 MHz in $CDCl_3$): see Table 3 and 34.1/t, 23.9/t, 23.2/t and 21.9/t (C(3) to C(6)). MS: 192/32 (M^+); 191/12; 178/8; 177/61; 174/15; 159/6; 151/25; 149/30; 135/14; 125/23; 123/11; 121/29; 107/22; 96/17; 95/100 ($COC_5H_7^+$); 91/13; 79/16; 77/13; 68/24; 67/64 ($C_5H_7^+$); 65/15; 55/26; 43/10; 41/51. Found: C, 75.22; H, 8.57. Calc for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%.

3-Methoxy-2-methyl-2-cyclohexenone (**14**)

The model compound **14** was obtained by treatment of 2 - methyl - 1,3 - cyclohexanedione with diazomethane as described.[21] ^1H NMR (60 MHz, $CDCl_3$) identical with the described[18] one, ^{13}C NMR (25.1 MHz, $CDCl_3$): see Table 3 and 36.3/t (C(6)); 24.8/t and 20.9/t (C(4) and C(5)).

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