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A convenient cross-metathesis approach to trisporins

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ABSTRACT

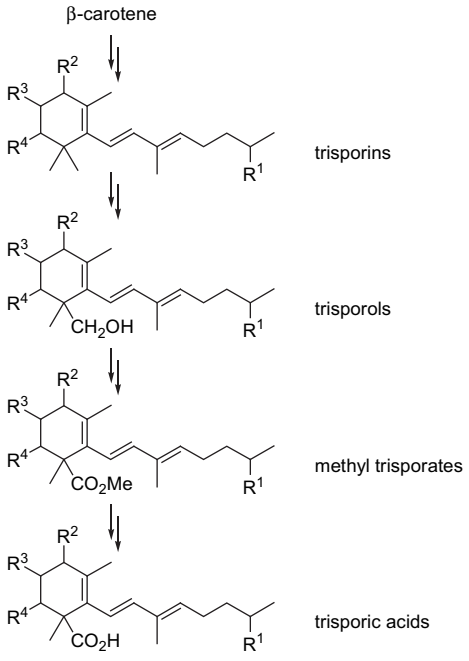
Three series of trisporins have been prepared using a strategy in which a cross-metathesis is the key step. This reaction has proved to be highly regioselective, allowing the combination of α- or β-ionone derivatives having a 1,1-disustituted olefin with trisubstituted alkenes. The stereochemistry of the newly formed olefins has been established by spectroscopic means.

1. Introduction

Trisporoids are a special group of natural products biosynthesized from β-carotene by several fungi of the order mucorales, like *Blakeslea trispora*,[1–3] *Phycomyces blakesleeanus*,[1,4] *Zygorhynchus moelleri*[3,5] and *Mucor mucedo*.[1,2,6] These fungi are able to reproduce sexually by zygospores followed by gametangial fusion. Their sexual development is mediated by hormones (trisporic acids), but simultaneous and cooperative metabolism in both mating-types is essential for hormone production: each mating-type produces prohormones (trisporins, trisporols and methyl trisporates), which the other can convert into the hormones (trisporic acids).[7] Thus, trisporoids are involved in the recognition of mating partners, induce the first steps of sexual differentiation and maintain the development of sexual structures. We are involved in a multidisciplinary project, which aims to clarify unknown aspects of the biosynthetic route of trisporic acids from β-carotene (Scheme 1).

Trisporins are located at the first stages of this route,[8–11] and are classified in series according to the functionalization of the side chain (A, B and C) or the ring (D and E). Natural trisporoids comprises both geometric isomers at the C9–C10 double bond,[12] while C7–C8 is always *trans*. These *E*/*Z* isomers show comparable levels of hormone activity on both the mating types of *M mucedo*.[13]

The total synthesis of trisporols and methyl trisporates has been achieved by different strategies, like the cyclization of a linear precursor,[14,15] a cyclization followed by chain extension through Wittig olefination,[16,17] by means of a lactol intermediate,[18–23] degradation of a enantiomerically pure α-hidroxydecalone[24,25] and through Meyer's chiral bicyclic lactams.[26] However only Boland and co-workers[27,28] have focused on the preparation of less functionalized type, the trisporins, using a strategy in which a Pd(0)-catalyzed cross-coupling with organozincates (Knochel coupling) is the key step.



Scheme 1. Biogenetic origin of trisporoids.

Here we present a convenient, high yielding divergent synthesis able to produce an entire library of trisporins (series A, B and C) to be screened for the appropriated biological properties (Table 1).

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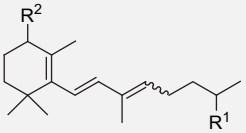
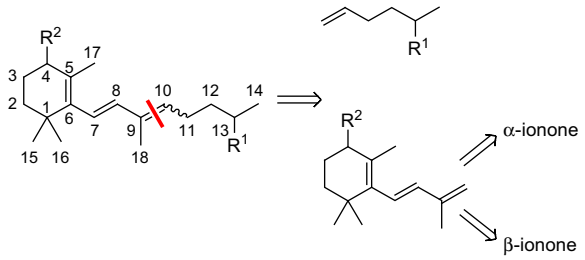
Table 1
Trisporins of series A, B and C

Structure	R_1	R_2	Compound	Name	Series
	–H	–OH	**1**	4-Dihydrotrisporin A	
	–H	=O	**2**	Trisporin A	**A**
	–H	–H	**3**	4-Desoxytrisporin A	
	=O	–OH	**4**	4-Dihydrotrisporin B	**B**
	=O	=O	**5**	Trisporin B	
	=O	–H	**6**	4-Desoxytrisporin B	
	–OH	–OH	**7**	4-Dihydrotrisporin C	**C**
	–OH	=O	**8**	Trisporin C	
	–OH	–H	**9**	4-Desoxytrisporin C	

2. Results and discussion

2.1. Strategy

Recently, it has been demonstrated that olefin metathesis has evolved to be a reliable tool in the synthesis of substituted olefins, due largely to the advent of powerful ruthenium catalysts that contain an *N*-heterocyclic carbene ligand.[29–31] Grubbs and co-workers have proved that the efficiency in olefin cross-metathesis reactions is affected by the steric bulk of *N*-heterocyclic carbene ligands of ruthenium-based catalysts, although for the formation of trisubstituted olefins the commercial *N*-mesityl containing catalyst (**25**) seems to be the most efficient.[31] However, the cross-metathesis methodology has not been much used in the field of isoprenoids synthesis, although an elegant work in the preparation of intermediates on the way to tocopherols (vitamin E) has been published.[32] It can also be used to obtain poly-unsaturated systems, with brilliant but scarce examples of application of this reaction to the chemo- and stereoselective synthesis of conjugated 1,3,5-triene moieties contained in bioactive natural products.[33,34] However, to the best of our knowledge, there are no examples of application to the preparation of conjugated trienes when both terminus olefins have a high degree of substitution. Here we present an application of this reaction to the preparation of the trisporin family of natural products. Our approach follows the retrosynthetic analysis depicted in Scheme 2.



Scheme 2. Retrosynthesis of trisporins from α- and β-ionone through cross-metathesis.

The disconnection of the Δ^9 double bond of the trisporin skeleton needs, if a cross-metathesis has to be performed, a simple olefin for the side chain terminus, and a triene, which can be readily prepared from α- or β-ionone, as simpler synthons.

2.2. Synthetic approach

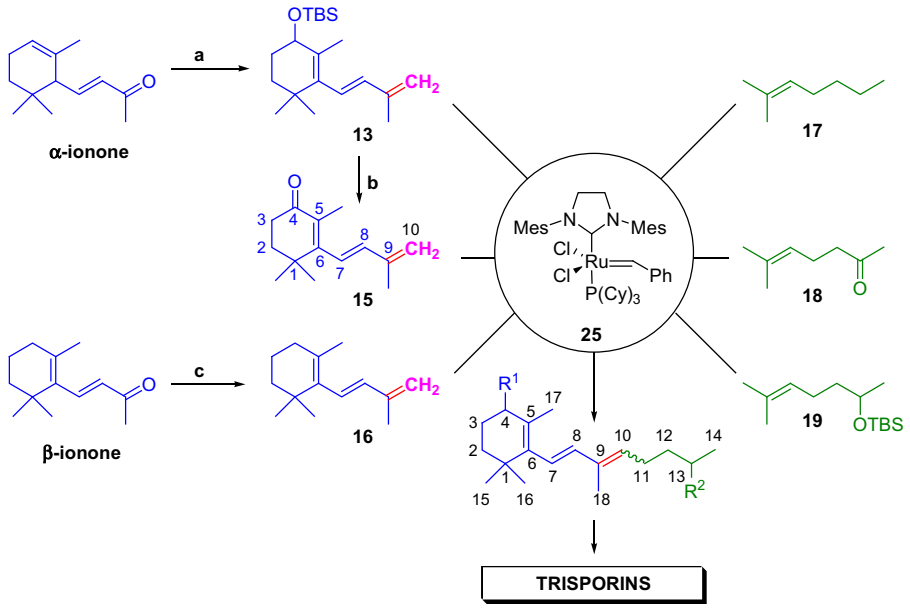
The preparation of the cross-metathesis reactants is summarized in Scheme 3. Ring side synthons were prepared from α- and β-ionone as commercial starting materials. α-Ionone was regioselectively epoxidised using *m*-chloroperbenzoic acid, and the resulting epoxide (**10**) was isomerised to the corresponding hydroxyionone derivative (**11**) by treatment with methanolic K_2CO_3.[35,36] The hydroxyl group was then protected as the *t*-butyldimethylsilyl ether (**12**).[37] Several methods were assayed for methylenation of the keto group in **12**, from which Wittig reaction with methylenetriphenyl phosphorane gave the best yield of synthon **13**. The second synthon, **15**, was prepared by deprotection of **13** with tetrabutylammonium fluoride and oxidation of the allylic alcohol (**14**)[38,39] with MnO_2. A similar Wittig olefination of β-ionone led to the formation of the third synthon **16**.[39] Chain side precursors are commercial (**17**, **18**) or readily accessible by standard procedures (**19**).[40]

We first tried to perform the cross-metathesis coupling between compound **13** and 1-hexene using Grubbs second generation catalyst (**25**), but only the dimerization product of the monosubstituted olefin (5-decene) was obtained. Fortunately, the use of the trisubstituted olefin **17**, much less reactive towards the ruthenium catalyst, avoided this problem, and **20** was formed in excellent yield as a 2.7:1 mixture of *E*:*Z* stereoisomers, which could not be separated by column chromatography. Deprotection of the TBS group using TBAF allowed us to obtain 4-dihydrotrisporin A, (**1**).[28] Table 2 shows the results obtained for all the other possible combinations, which behaved similarly in the cross-metathesis reaction, although the yields were significantly lower for those having a carbonyl group at C-4, specially when it is conjugated with the triene system (products formed from compound **15**). Despite of this, global yield of trisporins from commercial starting materials can be considered good or, in some cases, excellent, as a result of the synthetic design (Table 2).

Small amount of *E*:*Z* mixtures of **7**, **21** and **23** could be separated by meticulous column chromatography and both stereoisomers could be characterized spectroscopically in each case. Detailed analysis of the NOESY spectrum of the minor isomer of **21** allowed us to establish unambiguously the stereochemistry of the C9 double bond as *Z* (Fig. 1). The most significant differences between the ^{1}H NMR of the two isomers are the chemical shifts of the three olefinic protons. H7 and H8 signals are significantly deshielded in the *Z* isomer with respect to those in the *E* isomer. Thus, in the *Z* isomer H-8 appears as a doublet at 6.42 ppm (J=16.6 Hz) and H-7 at 6.10 ppm (J=16.6 Hz) while in the *E* isomer H-8 appears as a doublet at 6.02 ppm (J=16.6 Hz) and H-7 at 5.94 ppm (J=16.6 Hz). It is also interesting to highlight H-10, which appears as a broad triplet in both cases, but at lower field for the *E* isomer (*E*: δ=5.37 ppm, J=6.1 Hz; *Z*: δ=5.31 ppm, J=6.9 Hz). These data are in agreement with previous discussions on the stereochemistry of *cis* and *trans* isomers of trisporic acid C, proposed on the basis of the chemical shifts of their olefinic protons.[14] These results can be extended to the other trisporin mixtures prepared by us, and constitute a general method for a fast elucidation of the C9 double bond geometry in trisporoids. Tentative assignations previously published should be reconsidered at the light of this information.

3. Conclusion

Nine trisporins have been prepared through a divergent strategy in which the key step is a cross-metathesis catalyzed by the Grubbs



Scheme 3. Reagents and conditions: (a) i: m-CPBA, DCM, 0 °C, 78% of **10**; ii: K_2CO_3, MeOH, Δ, 95% of **11**; iii: TBSCl, DMF, 50 °C, 70% of **12**; iv: Ph_3PCH_3Br, *n*-BuLi, −35 °C, THF, 76% of **13**. (b) i: *n*-Bu_4NF, THF, 97% of **14**; ii: MnO_2, *n*-hexane, Δ, 95% of **15**. (c) Ph_3PCH_3Br, *n*-BuLi, −35 °C, THF, 65% of **16**.

second generation ruthenium complex (**25**). The process can be extended to the preparation of other trisporoids with different substitution patterns on the ring or chain. Although the stereoselectivity of the reaction was moderate to low, in some cases both *E* and *Z* isomers could be isolated and identified thoroughly using several NMR techniques.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 or Avance DRX 500 spectrometer. Chemical shifts are given in ppm relative to TMS. ^{13}C NMR peak assignments were made with the aid of 2D NMR (HMBC, HMQC and NOESY). Infrared spectra were recorded in liquid film between NaCl plates on an FTIR Mattson Genesis II spectrometer, and mass spectra were performed on a AutoSpec-Q VG-Analitical (Fisons) (HRMS) instrument, using the Fast Atom Bomb technique (FAB) with a 1% NaI doped matrix of thioglycerol or glycerol.

α- and β-ionone were purchased to Acros, [1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene]dichloro(phenylmethylene)(tricyclo-hexylphosphine)ruthenium (Grubbs second generation catalyst) (**25**), 2-methyl-2-heptene (**17**) and 6-methyl-5-hepten-2-one (**18**) were purchased to Sigma–Aldrich, and 6-methyl-5-hepten-2-ol[41] and its *t*-butyldimethylsilyl derivative (**19**)[40] were prepared following literature procedures.

4.2. Synthesis of compound 12

Imidazole (4.1 g, 60 mmol) and TBSCl (4.3 g, 29 mmol) were added to a solution of 4-(3-hydroxy-2,6,6-trimethylcyclohex-1-enyl)but-3-en-2-one (**11**)[35,36] (5 g, 24 mmol) in DMF (15 mL). The mixture was stirred for 6 h at 50 °C and then, was poured on cold hexane (23 mL). The layers were separated and the DMF one was washed with hexane (23 mL×2) and Et_2O (23 mL). The unified hexane and ether extracts were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (hexane:Et_2O, 98:2) and (*E*)-4-(3-(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylcyclohex-1-enyl)-but-3-en-2-one (**12**) (5.4 g, 16.8 mmol, 70% yield) was obtained. Spectral properties were in agreement with those previously reported.[37]

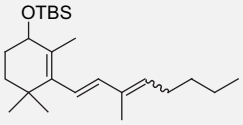
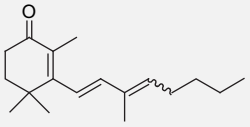
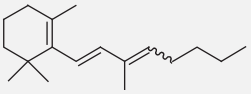
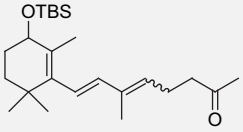
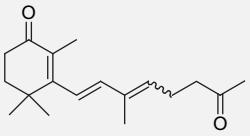
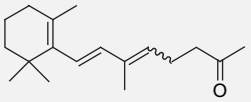
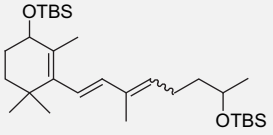
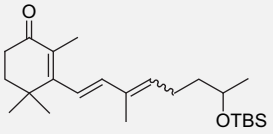
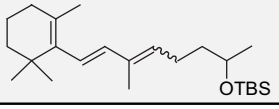
4.3. Methylenation of ketones

4.3.1. General Wittig reaction procedure. Methyl-triphenylphosphonium bromide (1.5 equiv) was suspended in dry THF (2 mL/mmol), under nitrogen, and cooled to −35 °C. *n*-BuLi (1.6 M in hexane, 1.5 equiv) was slowly added and the suspension was stirred until an orange colour appeared (30 min approx.). Then, a solution of the ketone (1 equiv) in dry THF (1 mL/mmol) was slowly added and the reaction mixture was allowed to warm to room temperature and stirred for 12 h. The solution was diluted with Et_2O and washed with brine. The organic layer was dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification was achieved on silica gel column chromatography using hexane:Et_2O (95:5) for elution.

*4.3.2. Compound **13**.* Following the general procedure, phosphonium salt (1.1 g, 3.2 mmol), *n*-BuLi (2 mL, 3.2 mmol), **12** (795 mg, 2.5 mmol) and THF (10 mL), afforded **13** (595 mg, 1.9 mmol, 76% yield). Oil, IR ν (cm^{-1}) 2954, 2931, 2856, 1468, 1359, 1253; 1081, 1048, 853, 773; *HRFABMS (m/z)*: calcd ($C_{20}H_{36}OSiNa$): 343.2433, found: 343.2428 $[M+Na]^+$; ^1H NMR (300 MHz, *CDCl*$_3$) δ (ppm) 6.16 (1H, d, *J*=16.5 Hz, H-8), 6.06 (1H, d, *J*=16.5 Hz, H-7), 4.96 (2H, bs, H-10), 4.05 (1H, t, *J*=5.3 Hz, H-4), 1.92 (3H, s, H-14)*, 1.83 (1H, m), 1.76 (**3H**, s, H-13)*, 1.67 (2H, m), 1.41 (1H, m), 1.06 (3H, s, H-11), 1.01 (3H, s, H-12), 0.94 (9H, s, $SiC(CH_3)_3$), 0.12 (6H, s, $Si(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 142.23 (C, C-6)#, 139.89 (C, C-9)#, 136.42 (CH, C-8), 130.99 (C, C-5), 127.15 (CH, C-7), 115.36 (CH_2, C-10), 71.16 (CH, C-4), 35.26 (C, C-1), 34.59 (CH_2, C-2), 29.25 (CH_2, C-3), 28.40 (CH_3, C-11), 28.30 (CH_3, C-12), 25.90 (CH_3, $SiC(CH_3)_3$), 18.35 (CH_3, C-14)*, 18.44 (CH_3, C-13)*, 18.14 (C, $SiC(CH_3)_3$), −4.66 (CH_3, $Si(CH_3)$), −4.25 (CH_3, $Si(CH_3)$). *,# may be interchanged.

*4.3.3. Compound **16**.* Following the general procedure, phosphonium salt (10 g, 28 mmol), *n*-BuLi (12 mL, 28 mmol,), β-ionone (3.6 g, 18.7 mmol) and THF (84 mL), afforded **16** (3 g, 15.8 mmol, 84% yield). Oil, IR ν (cm^{-1}) 2962, 2927, 2864, 1603, 1451, 967; HRFABMS (*m/z*): calcd ($C_{14}H_{22}Na$): 213.1619, found: 213.1601 $[M+Na]^+$; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.13 (2H, bs, H-7,

Table 2
Cross-metathesis and global yields in the synthesis of trisporins of series A, B and C

Series	Ring synthon	Chain synthon	Cross-metathesis product	Cross-metathesis[a] (%)	*E*:*Z*[b]	Trisporin[c] (%)
A	**13**	**17**		**20** (95%)	2.7:1	4-Dihydrotrisporin A, **1** (33%)
	15	**17**		**2** (69%)	3.4:1	Trisporin A, **2** (24%)
	16	**17**		**3** (95%)	1.8:1	4-Desoxytrisporin A, **3** (80%)
B	**13**	**18**		**21** (70%)	2.5:1	4-Dihydrotrisporin B, **4** (20%)
	15	**18**		**5** (57%)	1.8:1	Trisporin B, **5** (20%)
	16	**18**		**6** (75%)	1.2:1	4-Desoxytrisporin B, **6** (65%)
C	**13**	**19**		**22** (75%)	3.2:1	4-Dihydrotrisporin C, **7** (16%)
	15	**19**		**23** (89%)	3.2:1	Trisporin C, **8** (10%)
	16	**19**		**24** (75%)	1.8:1	4-Desoxytrisporin C, **9** (80%)

[a] Cross-metathesis yield.
[b] *E*:*Z* ratio determined by ^{1}H NMR analysis.
[c] Trisporin global yield from commercial starting materials.

H-8), 4.95 (2H, bs, H-10), 2.03 (2H, t, *J*=6.3 Hz, H-4), 1.93 (3H, s, H-14)*, 1.73 (3H, s, H-13)*, 1.65 (2H, m), 1.49 (2H, m), 1.04 (6H, s, H-11, H-12); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 142.44 (C, C-9), 137.43 (C, C-6), 135.76 (CH, C-8), 128.93 (C, C-5), 127.44 (CH, C-7), 114.81 (CH_2, C-10), 39.47 (CH_2, C-2), 34.11 (C, C-1), 32.85 (CH_2, C-3), 28.82 (CH_3, C-11, C-12), 21.56 (CH_3, C-13)*, 19.23 (CH_2, C-4), 18.49 (CH_3, C-14)*. * may be interchanged.

4.4. Synthesis of compound 15

MnO_2 (845 mg, 9.71 mmol) was added to a solution of (*E*)-2,4,4-trimethyl-3-(3-methylbuta-1,3-dienyl)-2-cyclohexen-ol (**14**) (500 mg, 2.43 mmol) in hexane (20 mL). The mixture was refluxed for 2 h, and then was filtered over Celite using CH_2Cl_2 for washing. After removal of the solvent, **15** was obtained as an oil (471 mg, 2.31 mmol, 95%). IR signals as previously reported.[39] HRFABMS (*m*/*z*): calcd ($C_{14}H_{20}ONa$): 227.1412, found: 227.1437 $[M+Na]^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.25 (1H, d, *J*=16.2 Hz, H-8), 6.12 (1H, d, *J*=16.2 Hz, H-7), 5.06 (1H, s, H-10a), 5.03 (1H, s, H-10b), 2.46 (2H, t, *J*=6.5 Hz, H-3), 1.89 (3H, s H-13), 1.82 (2H, t, *J*=6.5 Hz, H-2), 1.79 (3H, s, H-14), 1.14 (6H, s, H-11, H-12); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 199.14 (C, C-4), 160.90 (C, C-6), 141.34 (C, C-9), 138.65 (CH, C-8), 129.82 (C, C-5), 125.23 (CH, C-7), 118.49 (CH_2, C-10), 37.22 (CH_2, C-2), 35.53 (C, C-1), 34.19 (CH_2, C-3), 27.39 (CH_3, C-11, C-12), 18.15 (CH_3, C-14), 13.53 (CH_3, C-13).

4.5. Cross-metathesis

4.5.1. General cross metathesis procedure. To a solution of chain side synthon (**17**, **18** or **19**) (1.5 to 2 equiv) in dry CH_2Cl_2 (1 mL/mmol)

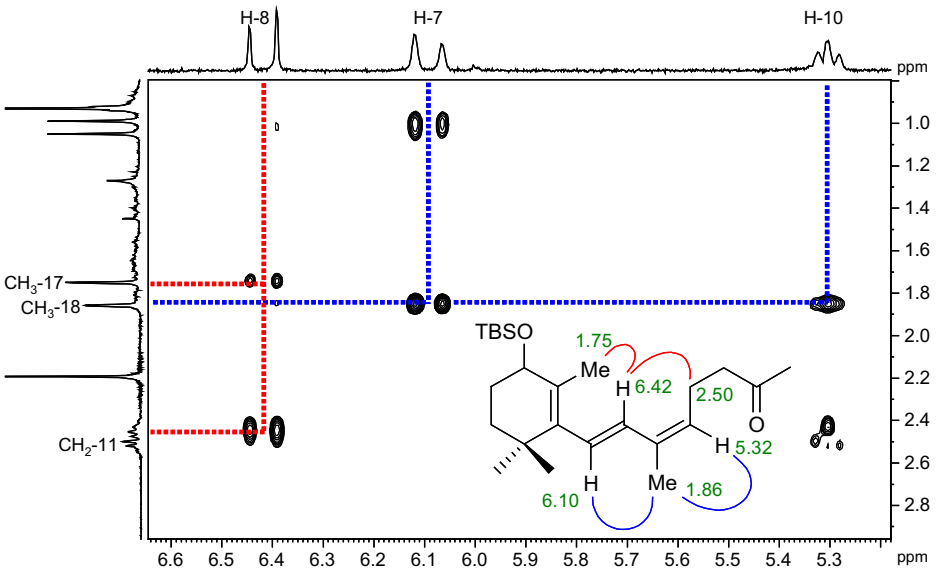


Figure 1. Diagnostic correlations originated by olefinic protons in the 2D-NOESY spectrum of *Z*-21.

under nitrogen atmosphere, Grubbs second generation catalyst (1/3 portion of a total of 5% mol) was added. The solution was heated to 35 °C and then, a solution of ring side synthon (**13**, **15** or **16**) (1 equiv) in dry CH_2Cl_2 (1 mL/mmol) was added. The mixture was heated to reflux for 6 h, and another portion (1/3) of the catalyst was added. After six more hours, the last portion of catalyst was added, and the mixture was heated to reflux for an additional period of 6 h. After cooling to room temperature, solvent was removed under reduced pressure, and the resulting crude oil was purified by silica gel column chromatography.

*4.5.2. Trisporin A (**2**).* Starting from **17** (0.3 mL, 2.06 mmol), ruthenium catalyst **25** (42 mg, 0.049 mmol), **15** (200 mg, 0.98 mmol), CH_2Cl_2 (3 mL) and following the general procedure (chromatography eluent hexane:Et_2O 95:5), **2** was obtained as an oil (176 mg, 0.68 mmol, 69% yield as a mixture *E*/*Z* 3.4:1). IR and HRMS signals as previously reported.[28] ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.22 (1H, d, *J*=16.2 Hz, H-8), 6.05 (1H, d, *J*=16.2 Hz, H-7), 5.57 (1H, t, *J*=7.3 Hz, H-10); (*signals due to the Z isomer*) δ (ppm) 6.63 (1H, d, *J*=16.2 Hz, H-8), 6.15 (1H, d, *J*=16.2 Hz, H-7), 5.52 (1H, t, *J*=7.3 Hz, H-10); (*common signals*) δ (ppm) 2.49 (2H, m, H-3), 2.16 (2H, m, H-11), 1.83 (3H, bs, H-17)*, 1.81 (3H, bs, H-18)*, 1.38 (6H, m, H-2, H-12, H-13), 1.16 (6H, s, H-15, H-16), 0.91 (3H, t, *J*=7.3 Hz, H-14); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 199.28 (C, C-4), 161.70 (C, C-6), 141.34 (CH, C-8), 135.82 (CH, C-10), 133.47 (C, C-9), 129.33 (C, C-5), 121.85 (CH, C-7), 27.47 (CH_3, C-15, C-16); (*signals due to the Z isomer*) δ (ppm) 140.24 (CH, C-8), 133.42 (CH, C-10), 124.45 (CH, C-7), 27.20 (CH_3, C-15, C-16); (*common signals*) δ (ppm) 37.23 (CH_2, C-2), 35.42 (C, C-1), 34.18 (CH_2, C-3), 31.50 (CH_2, C-12), 28.13 (CH_2, C-11), 22.34 (CH_2, C-13), 13.88 (CH_3, C-14), 13.64 (CH_3, C-17)*, 12.00 (CH_3, C-18)*. * may be interchanged.

*4.5.3. 4-Desoxytrisporin A (**3**).* Starting from **17** (0.3 mL, 2.21 mmol), ruthenium catalyst **25** (45 mg, 0.053 mmol), **16** (200 mg, 1.05 mmol), CH_2Cl_2 (3 mL) and following the general procedure (chromatography eluent hexane:Et_2O 98:2), **3** was obtained as an oil (245 mg, 0.99 mmol, 95% yield as a mixture *E*/*Z* 1.8:1). IR ν (cm^{-1}) 2958, 2926, 2862, 1455, 966; HRFABMS (*m*/*z*): calcd ($C_{18}H_{30}Na$): 269.2245, found: 269.2256 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.14–6.03 (2H, m, H-7, H-8), 5.46 (1H, t, *J*=6.5 Hz, H-10), 1.83 (3H, bs, H-17)*, 1.74 (3H, bs, H-18)*, 1.06 (6H, s, H-15, H-16); (*signals due to the Z isomer*) δ (ppm) 6.46 (1H, d, *J*=16.2 Hz, H-8), 6.14–6.03 (1H, m, H-7), 5.37 (1H, t, *J*=7.7 Hz, H-10), 1.90 (3H, bs, H-17)#, 1.76 (3H, bs, H-18)#, 1.07 (6H, s, H-15, H-16); (*common signals*) δ (ppm) 2.19 (2H, m, H-11), 2.04 (2H, t, *J*=6.1 Hz, H-4), 1.66 (2H, m), 1.51 (2H, m), 1.40 (4H, m), 0.95 (3H, m, H-14); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 138.04 (CH, C-8),137.86 (C, C-6), 133.82 (C, C-9), 131.47 (CH, C-10), 128.10 (C, C-5), 123.92 (CH, C-7), 34.09 (C, C-1), 32.88 (CH_2, C-12), 31.90 (CH_2, C-4), 28.00 (CH_2, C-11), 22.46 (CH_2, C-13), 21.62 (CH_3, C-17), 12.22 (CH_3, C-18); (*signals due to the Z isomer*) δ (ppm) 138.21 (C, C-6), 132.27 (C, C-9), 130.40 (CH, C-8), 129.70 (CH, C-10), 128.49 (C, C-5), 126.67 (CH, C-7), 34.16 (C, C-1), 32.92 (CH_2, C-12), 32.29 (CH_2, C-4), 27.04 (CH_2, C-11), 22.31 (CH_2, C-13), 21.65 (CH_3, C-17)*, 20.43 (CH_3, C-18)*; (*common signals*) δ (ppm) 39.55 (CH_2, C-2), 28.87 (CH_3, C-15, C-16), 19.31 (CH_2, C-3), 13.99 (CH_3, C-14). *,# may be interchanged.

*4.5.4. TBS-derivative of 4-dihydrotrisporin A (**20**).* Starting from 17 (0.1 mL, 0.66 mmol), ruthenium catalyst 25 (13 mg, 0.016 mmol), 13 (100 mg, 0.31 mmol), CH_2Cl_2 (1 mL) and following the general procedure (chromatography eluent hexane:Et_2O 98:2), 20 was obtained as an oil (111 mg, 0.29 mmol, 95% yield as a mixture *E*/*Z* 2.7:1). IR ν (cm^{-1}) 2957, 2931, 2858, 1719, 1672, 1463, 1361, 1256, 1083, 837, 777. HRFABMS (*m*/*z*): calcd ($C_{24}H_{44}OSiNa$): 399.3059, found: 399.3051 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.06 (1H, d, *J*=16.1 Hz, H-8), 5.96 (1H, d, *J*=16.1 Hz, H-7), 5.46 (1H, t, *J*=7.3 Hz, H-10), 1.80 (3H, s, H-17)*; 1.75 (3H, s, H-18)*, (*signals due to the Z isomer*) δ (ppm) 6.46 (1H, d, *J*=16.1 Hz, H-8), 6.06 (1H, d, *J*=16.1 Hz, H-7), 5.36 (1H, t, *J*=7.3 Hz, H-10), 1.87 (3H, s, H-17)#, 1.77 (3H, s, H-18)#, (*common signals*) δ (ppm) 4.06 (1H, t, *J*=5.6 Hz, H-4), 2.16 (2H, m, H-11), 1.67 (2H, m, H-3), 1.37 (6H, m, H-2, H-12, H-13), 1.05 (3H, s, H-15), 1.01 (3H, s, H-16), 0.95 (3H, t, *J*=6.1 Hz, H-14), 0.93 (9H, s, $SiC(CH_3)_3$), 0.10 (6H, s, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 140.35 (C, C-6), 138.65 (CH, C-8), 133.67 (C, C-9), 132.12 (CH, C-10), 130.66 (C, C-5), 123.59 (CH, C-7), 31.82 (CH_2, C-12), 28.36 (CH_2, C-11), 18.43 (CH_3, C-17)#, 12.21 (CH_3, C-18)#; (*signals due to the Z isomer*) δ (ppm) 131.01 (CH, C-8), 130.34 (CH, C-10), 126.40 (CH, C-7), 32.22 (CH_2, C-12), 27.99 (CH_2, C-11), 20.40 (CH_3, C-17)*, 13.98 (CH_3, C-18)*; (*common signals*) δ (ppm) 71.29 (CH, C-4), 35.28 (CH_2, C-2), 34.63 (C, C-1), 29.28 (CH_2, C-3), 28.43 (CH_3, C-15, C-16), 25.92 (CH_3, $(CH_3)_3CSi$), 22.42 (CH_2, C-13), 18.16 (C, $(CH_3)_3CSi$), 13.98 (CH_3,

C-14), −4.25 (CH_3, (CH_3)$_2$Si), −4.64 (CH_3, (CH_3)$_2$Si).*,# may be interchanged.

*4.5.5. Trisporin B (**5**).* Starting from 18 (0.10 mL, 0.84 mmol), ruthenium catalyst 25 (17 mg, 0.02 mmol), 15 (76 mg, 0.40 mmol), CH_2Cl_2 (2 mL) and following the general procedure (chromatography eluent hexane:Et_2O 8:2), 5 was obtained as an oil (59 mg, 0.22 mmol, 57% yield as a mixture *E*/*Z* 1.8:1). IR and HRMS signals as previously reported.[28] ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.15 (1H, d, *J*=16.3 Hz, H-8), 6.05 (1H, d, *J*=16.4 Hz, H-7), 5.47 (1H, t, *J*=7.2 Hz, H-10), 2.12 (3H, s, H-14), 1.12 (6H, s, H-15, H-16); (*signals due to the Z isomer*) δ (ppm) 6.58 (1H, d, *J*=16.2 Hz, H-8), 6.15 (1H, d, *J*=16.3 Hz, H-7), 5.41 (1H, t, *J*=7.2 Hz, H-10), 2.09 (3H, s, H-14), 1.14 (6H, s, H-15, H-16); (*common signals*) δ (ppm) 2.46 (6H, m, H-3, H-11, H-12), 1.82 (2H, m, H-2), 1.79 (3H, bs, H-18), 1.77 (3H, bs, H-17); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 207.79 (C, C-13), 199.20 (C, C-4), 161.46 (C, C-6), 140.67 (CH, C-8), 134.23 (C, C-9), 133.10 (CH, C-10), 129.48 (C, C-5), 122.68 (CH, C-7), 42.92 (CH_2, C-12), 35.58 (C, C-1), 29.85 (CH_3, C-14), 22.60 (CH_2, C-11), 13.63 (CH_3, C-17), 12.01 (CH_3, C-18); (*signals due to the Z isomer*) δ (ppm) 207.71 (C, C-13), 199.13 (C, C-4), 161.42 (C, C-6), 132.63 (CH, C-8), 132.45 (C, C-9), 130.88 (CH, C-10), 129.69 (C, C-5), 125.41 (CH, C-7), 43.45 (CH_2, C-12), 35.53 (C, C-1), 29.83 (CH_3, C-14), 21.67 (CH_2, C-11), 20.03 (CH_3, C-18)*, 13.59 (CH_3, C-17)*; (*common signals*) δ (ppm) 37.24 (CH_2, C-2), 34.18 (CH_2, C-3), 27.45 (CH_3, C-15, C-16). * may be interchanged.

*4.5.6. 4-Desoxytrisporin B (**6**).* Starting from **18** (0.3 mL, 2.21 mmol), ruthenium catalyst **25** (45 mg, 0.053 mmol), **16** (200 mg, 1.05 mmol), CH_2Cl_2 (3 mL) and following the general procedure (chromatography eluent hexane:Et_2O 85:15), **6** was obtained as an oil (75% yield as a mixture *E*/*Z* 1.2:1). IR ν (cm^{-1}) 2928, 2865, 1716, 1454, 1359, 968; HRFABMS (*m*/*z*): calcd ($C_{18}H_{28}ONa$): 283.2038, found: 283.2061 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 5.96 (2H, bs, H-7, H-8), 5.37 (1H, t, *J*=7.3 Hz, H-10), 2.13 (3H, s, H-14), 1.78 (3H, bs, H-18), 1.66 (3H, bs, H-17), 0.98 (6H, bs, H-15, H-16); (*signals due to the Z isomer*) δ (ppm) 6.36 (1H, d, *J*=16.2 Hz, H-8), 6.09 (1H, d, *J*=16.2 Hz, H-7), 5.24 (1H, t, *J*=7.2 Hz, H-10), 2.11 (3H, s, H-14), 1.82 (3H, bs, H-18), 1.69 (3H, bs, H-17), 0.99 (6H, bs, H-15, H-16); (*common signals*) δ (ppm) 2.49 (2H, m, H-12), 2.41 (2H, m, H-11), 1.99 (2H, m, H-4), 1.59 (2H, m, H-3), 1.44 (2H, m, H-2); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 208.18 (C, C-13), 137.63 (C, C-6), 137.44 (CH, C-8), 134.92 (C, C-9), 128.72 (CH, C-10), 128.30 (C, C-5), 124.76 (CH, C-7), 43.34 (CH_2, C-12), 39.40 (CH_2, C-2), 34.04 (C, C-1), 22.53 (CH_2, C-11), 21.55 (CH_3, C-17), 12.17 (CH_3, C-18); (*signals due to the Z isomer*) δ (ppm) 208.26 (C, C-13), 137.98 (C, C-6), 133.37 (C, C-9), 129.78 (CH, C-8), 128.77 (C, C-5), 127.63 (CH, C-7), 126.93 (CH, C-10), 43.85 (CH_2, C-12), 39.44 (CH_2, C-2), 34.08 (C, C-1), 21.68 (CH_2, C-11), 21.61 (CH_3, C-17), 20.33 (CH_3, C-18); (*common signals*) δ (ppm) 32.80 (CH_2, C-4), 29.84 (CH_3, C-14), 28.80 (CH_3, C-15, C-16), 19.21 (CH_2, C-3).

*4.5.7. TBS-derivative of 4-dihydrotrisporin B (**21**).* Starting from **18** (0.13 mL, 0.94 mmol), ruthenium catalyst **25** (26 mg, 0.031 mmol), **13** (200 mg, 0.62 mmol), CH_2Cl_2 (1.6 mL) and following the general procedure (chromatography eluent hexane:Et_2O 98:2), **21** was obtained as an oil (170 mg, 0.44 mmol, 70% yield as a mixture *E*/*Z* 2.5:1). IR ν (cm^{-1}) 2930, 2856, 1720, 1675, 1466, 1359, 1254, 1081, 1047, 835, 773. HRFABMS (*m*/*z*): calcd ($C_{24}H_{42}O_2SiNa$): 413.2852, found: 413.2821 $[M+Na]^+$; A small amount of this mixture was rechromatographied and both isomers were isolated.

4.5.7.1. (Z). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.42 (1H, d, *J*=16.6 Hz, H-8), 6.10 (1H, d, *J*=16.6 Hz, H-7), 5.31 (1H, t, *J*=6.9 Hz, H-10), 4.05 (1H, t, *J*=6.9 Hz, H-4), 2.48 (4H, m, H-11, H-12), 2.16 (3H, s, H-14), 1.85 (3H, s, H-18), 1.75 (3H, s, H-17); 1.42 (2H, m, H-2), 1.24 (2H, m, H-3), 1.05 (3H, s, H-15), 0.99 (3H, s, H-16), 0.93 (9H, s, $SiC(CH_3)_3$), 0.11 (6H, s, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 208.39 (C, C-13), 140.51 (C, C-6), 133.35 (C, C-9), 130.98 (C, C-5), 130.43 (CH, C-8), 127.57 (CH, C-7, C-10), 71.27 (CH, C-4), 43.95 (CH_2, C-12), 35.34 (CH_2, C-2), 34.63 (C, C-1), 30.90 (CH_3, C-14), 29.32 (CH_2, C-3), 28.45 (CH_3, C-15, C-16), 25.97 (CH_3, (CH_3)$_3$CSi), 21.81 (CH_2, C-11), 20.37 (CH_3, C-18), 18.41 (CH_3, C-17), 18.22 (CH_3, (CH_3)$_3$CSi), −4.21 (CH_3, (CH_3)$_2$Si), −4.59 (CH_3, (CH_3)$_2$Si).

4.5.7.2. (E). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.02 (1H, d, *J*=16.6 Hz, H-8), 5.94 (1H, d, *J*=16.6 Hz, H-7), 5.37 (1H, t, *J*=6.1 Hz, H-10), 4.03 (1H, m, H-4), 2.55–2.39 (4H, m, H-11, H-12), 2.16 (3H, s, H-14), 1.78 (3H, s, H-17)*, 1.72 (3H, s, H-18)*; 1.42 (4H, m, H-2, H-3), 1.04 (3H, s, H-15), 0.98 (3H, s, H-16), 0.97 (9H, s, $SiC(CH_3)_3$), 0.09 (6H, s, $Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 208.26 (C, C-13), 140.17 (C, C-6), 138.10 (CH, C-8), 134.82 (C, C-9), 130.54 (C, C-5), 129.37 (CH, C-10), 124.51 (CH, C-7), 71.22 (CH, C-4), 43.34 (CH_2, C-12), 35.24 (CH_2, C-2), 34.60 (C, C-1), 29.90 (CH_3, C-14), 29.24 (CH_2, C-3), 28.38 (CH_3, C-15, C-16), 25.90 (CH_3, (CH_3)$_3$CSi), 22.55 (CH_2, C-11), 18.39 (CH_3, C-17), 12.18 (CH_3, C-18), 18.13 (CH_3, (CH_3)$_3$CSi), −4.26 (CH_3, (CH_3)$_2$Si), −4.66 (CH_3, (CH_3)$_2$Si). * may be interchanged.

*4.5.8. TBS-derivative of 4-dihydrotrisporin C (**22**).* Starting from **19** (113 mg, 0.47 mmol), ruthenium catalyst **25** (13 mg, 0.016 mmol), **13** (100 mg, 0.31 mmol), CH_2Cl_2 (0.8 mL) and following the general procedure (chromatography eluent hexane:Et_2O 99:1), **22** was obtained as an oil (118 mg, 0.23 mmol, 75% yield as a mixture *E*/*Z* 3.2:1). HRFABMS (*m*/*z*): calcd ($C_{30}H_{58}O_2SiNa$): 529.3873, found: 529.3832 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 1.80 (3H, s, H-17)*, 1.74 (3H, s, H-18)*, 1.15 (3H, d, *J*=6.1 Hz, H-14); (*signals due to the Z isomer*) δ (ppm) 6.43 (1H, dd, *J*=16.2 Hz, *J*=4.0 Hz, H-8), 1.85 (3H, s, H-17)#, 1.84 (3H, s, H-18)#, 1.14 (3H, d, *J*=6.4 Hz, H-14); (*common signals*) δ (ppm) 6.09–5.93 (3H, m, H-7 (*Z*), H-7 (*E*), H-8 (*E*)), 5.14 (1H, m, H-10), 4.04 (1H, m, H-4), 3.86 (1H, m, H-13), 2.30 (2H, m), 2.20 (2H, m), 1.86 (2H, m), 1.45 (2H, m), 1.04 (3H, s, H-15), 1.00 (3H, s, H-16), 0.93 (9H, s, (CH_3)$_3$CSi), 0.09 (6H, s, (CH_3)$_2$Si). *,# may be interchanged.

*4.5.9. TBS-derivative of trisporin C (**23**).* Starting from **19** (249 mg, 1.03 mmol), ruthenium catalyst **25** (21 mg, 0.024 mmol), **15** (100 mg, 0.49 mmol), CH_2Cl_2 (1.5 mL) and following the general procedure (chromatography eluent hexane:Et_2O 95:5), **23** was obtained as an oil (170 mg, 0.44 mmol, 89% yield as a mixture *E*/*Z* 3.2:1). IR ν (cm^{-1}) 2958, 2928, 2857, 1728, 1670, 1462, 1375, 1256, 1031, 835, 774. HRFABMS (*m*/*z*): calcd ($C_{24}H_{42}O_2SiNa$): 413.2852, found: 413.2876 $[M+Na]^+$; A small amount of this mixture was rechromatographied and both isomers were isolated.

4.5.9.1. (Z). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.65 (1H, d, *J*=16.2 Hz, H-8), 6.18 (1H, d, *J*=16.3 Hz, H-7), 5.54 (1H, t, *J*=7.6 Hz, H-10), 3.81 (1H, sext, *J*=6.1 Hz, H-13), 2.53 (2H, t, *J*=6.6 Hz, H-3), 2.28 (1H, m, H-11a), 2.19 (1H, m, H-11b), 1.90 (3H, bs, H-18)*, 1.87 (3H, bs, H-17)*, 1.86 (2H, m, H-2), 1.46 (2H, m, H-12), 1.19 (6H, s, H-15, H-16), 1.14 (3H, d, *J*=6.1 Hz, H-14), 0.88 (9H, s, (CH_3)$_3$CSi), 0.05 (6H, s, (CH_3)$_2$Si); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 199.42 (C, C-4), 161.77 (C, C-6), 133.25 (CH, C-8, C-10), 131.54 (C, C-9), 129.66 (C, C-5), 124.72 (CH, C-7), 68.08 (CH, C-13), 39.91 (CH_2, C-12), 37.28 (CH_2, C-2), 35.59 (C, C-1), 34.26 (CH_2, C-3), 27.52 (CH_3, C-15, C-16), 25.82 (CH_3, (CH_3)$_3$CSi), 23.90 (CH_2, C-11), 23.71 (CH_3, C-14), 20.07 (CH_3, C-17)*, 18.06 (C, (CH_3)$_3$CSi), 13.75 (CH_3, C-18)*, −4.39 (CH_3, (CH_3)$_2$Si), −4.79 (CH_3, (CH_3)$_2$Si). * may be interchanged.

4.5.9.2. (E). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 6.23 (1H, d, *J*=16.2 Hz, H-8), 6.08 (1H, d, *J*=16.3 Hz, H-7), 5.60 (1H, t, *J*=7.6 Hz, H-10), 3.83 (1H, sext, *J*=6.1 Hz, H-13), 2.51 (2H, t, *J*=7.1 Hz, H-3), 2.28 (1H, m, H-10a), 2.19 (1H, m, H-10b), 1.87 (2H, m, H-2), 1.85 (3H,

bs, H-18)*, 1.83 (3H, bs, H-17)*, 1.46 (2H, m, H-12), 1.18 (6H, s, H-15, H-16), 1.16 (3H, d, J=6.1 Hz, H-14), 0.90 (18H, s, $(CH_3)_3CSi$), 0.06 (12H, s, $(CH_3)_2Si$). * may be interchanged.

*4.5.10. TBS-derivative of 4-desoxytrisporin C (**24**).* Starting from **19** (256 mg, 1.06 mmol), ruthenium catalyst **25** (22 mg, 0.026 mmol), **16** (100 mg, 0.53 mmol), CH_2Cl_2 (1.5 mL) and following the general procedure (chromatography eluent hexane:Et_2O 98:2), **24** was obtained as an oil (150 mg, 0.40 mmol, 75% yield as a mixture *E*/*Z* 1.8:1). IR ν (cm^{-1}) 2957, 2928, 2857, 1461, 1360, 1256, 1134, 1089, 1031, 966, 835, 773. HRFABMS (*m*/*z*): calcd ($C_{24}H_{44}OSiNa$): 399.3059, found: 399.3036 $[M+Na]^+$; ^1H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.02 (2H, bs, H-7, H-8), 5.45 (1H, t, J=7.3 Hz, H-10), 1.82 (3H, s, H-17)*, 1.73 (3H, s, H-18)*; (*signals due to the Z isomer*) δ (ppm) 6.45 (1H, d, J=16.1 Hz, H-8), 6.11 (1H, d, J=16.1 Hz, H-7), 5.38 (1H, d, J=8.1 Hz, H-10), 1.85 (3H, s, H-17)*, 1.74 (3H, s, H-18)*; (*common signals*) δ (ppm) 3.84 (1H, m, H-13), 2.25 (2H, m), 2.04 (2H, m), 1.55–1.45 (6H, m), 1.19 (3H, d, J=5.9 Hz, H-14), 1.05 (6H, s, H-15, H-16), 0.93 (9H, s, $(CH_3)_3CSi$), 0.09 (6H, s, $(CH_3)_2Si$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) (*signals due to the E isomer*) 137.96 (CH, C-8), 137.85 (C, C-6), 132.40 (C, C-9), 130.99 (CH, C-10), 128.06 (C, C-5), 124.02 (CH, C-7), 39.83 (CH_2, C-12), 24.63 (CH_2, C-11), 21.66 (CH_3, C-17)*, 12.14 (CH_3, C-18)*; (*signals due to the Z isomer*) 138.13 (C, C-6), 131.15 (C, C-9),130.28 (CH, C-8), 129.12 (CH, C-10), 128.50 (C, C-5), 126.85 (CH, C-7), 40.14 (CH_2, C-12), 24.38 (CH_2, C-11), 20.35 (CH_3, C-17)#, 17.55 (CH_3, C-18)#; (*common signals*) δ (ppm) 68.28 (CH, C-13), 39.53 (CH_2, C-2), 34.07 (C, C-1), 32.89 (CH_2, C-4), 28.85 (CH_3, C-15, C-16), 25.86 (CH_3, (CH_3)$_3$CSi), 23.72 (CH_3, C-14), 19.30 (CH_2, C-3), 18.07 (C, $(CH_3)_3CSi$), −4.43 (CH_3, (CH_3)$_2$Si), −4.80 (CH_3, (CH_3)$_2$Si).*,# may be interchanged.

4.6. TBS deprotection

4.6.1. General TBS-deprotection procedure. To a solution of the silylether in THF (5 mL/mmol), *n*-Bu_4NF (1 M in THF, 3 equiv) was added. The reaction mixture was stirred under reflux for 12 h. Then, the solvent was removed under reduced pressure and the residue was dissolved in Et_2O, washed with brine, dried over $MgSO_4$ and the solvent was removed again under reduced pressure. Purification was achieved on silica using hexane:Et_2O (1:1) for elution.

*4.6.2. Compound **14**.* Following the general procedure, **13** (1 g, 3.13 mmol), *n*-Bu_4NF (1 M in THF, 9.4 mL, 9.4 mmol) and THF (16 mL) yielded (*E*)-2,4,4-trimethyl-3-(3-methylbuta-1,3-dienyl)-2-cyclohexenol (**14**) (630 mg, 3.07 mmol, 95%). Oil, IR ν (cm^{-1}) 3335, 2960, 2935, 2862, 1602, 1602, 1449, 966; HRFABMS (*m*/*z*): calcd ($C_{14}H_{22}ONa$): 229.1568, found: 229.1595 $[M+Na]^+$; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.12 (1H, d, J=16.2 Hz, H-8), 6.03 (1H, d, J=16.5 Hz, H-7), 4.95 (1H, bs, H-10a), 4.93 (1H, bs, H-10b), 3.98 (1H, t, J=4.4 Hz, H-4), 1.89 (3H, s, H-13)*, 1.85 (1H, m), 1.81 (3H, s, H-14), 1.63 (2H, m), 1.41 (1H, m), 1.02 (3H, s, H-11), 0.99 (3H, s, H-12); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 142.00 (C, C-9), 141.33 (C, C-6), 136.66 (CH, C-8), 129.65 (C, C-5), 126.59 (CH, C-7), 115.75 (CH_2, C-10), 69.97 (CH, C-4), 34.61 (C, C-1), 34.47 (CH_2, C-2), 28.90 (CH_3, C-11), 28.41 (CH_2, C-3), 27.38 (CH_3, C-12), 18.47 (CH_3, C-13)*, 18.38 (CH_3, C-14)*. * may be interchanged.

*4.6.3. 4-Dihydrotrisporin A (**1**).* Following the general procedure, **20** (88 mg, 0.23 mmol), *n*-Bu_4NF (1 M in THF, 0.7 mL, 0.7 mmol) and THF (1.2 mL) yielded **1** as an oil (30 mg, 0.11 mmol, 50%). IR and HRMS signals as previously reported.[28] ^1H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.03 (1H, d, J=16.2 Hz, H-8), 5.90 (1H, d, J=16.2 Hz, H-7), 5.42 (1H, t, J=7.3 Hz, H-10), 1.81 (3H, s, H-17), 1.77 (3H, s, H-18), 1.02 (3H, s, H-15), 0.99 (3H, s, H-16); (*signals due to the Z isomer*) δ (ppm) 6.44 (1H, d, J=16.2 Hz, H-8), 6.03 (1H, d, J=16.2 Hz, H-7), 5.37 (1H, t, J=7.2 Hz, H-10), 1.84 (3H, s, H-17)*, 1.83 (3H, s, H-18)*, 1.03 (3H, s, H-15), 1.00 (3H, s, H-16); (*common signals*) δ (ppm) 3.98 (1H, m, H-4), 2.16 (2H, m, H-11), 1.68 (4H, m, H-3, H-2), 1.35 (4H, m, H-12, H-13), 0.90 (3H, t, J=6.1 Hz, H-14); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 141.84 (C, C-6), 138.91 (CH, C-8), 133.49 (C, C-9), 132.46 (CH, C-10), 128.98 (C, C-5), 123.03 (CH, C-7), 34.64 (C, C-1), 31.77 (CH_2, C-12), 27.97 (CH_2, C-11), 22.40 (CH_2, C-13), 18.57 (CH_3, C-17), 12.14 (CH_3, C-18); (*signals due to the Z isomer*) δ (ppm) 142.10 (C, C-6), 133.09 (C, C-9), 130.71 (CH, C-8), 129.39 (C, C-5), 127.92 (CH, C-10), 126.85 (CH, C-7), 34.58 (C, C-1), 32.18 (CH_2, C-12), 27.01 (CH_2, C-11), 22.24 (CH_2, C-13), 20.32 (CH_3, C-17)*, 18.57 (CH_3, C-18)*; (*common signals*) δ (ppm) 70.10 (CH, C-4), 34.48 (CH_2, C-2), 28.96 (CH_3, C-15), 28.43 (CH_2, C-3), 27.38 (CH_3, C-16), 13.94 (CH_3, C-14).* may be interchanged.

*4.6.4. 4-Dihydrotrisporin B (**4**).* Following the general procedure, **21** (100 mg, 0.26 mmol), *n*-Bu_4NF (1 M in THF, 0.78 mL, 0.78 mmol) and THF (1.3 mL) yielded **4** as an oil (50 mg, 0.18 mmol, 70%). IR and HRMS signals as previously reported.[28] ^1H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.09–5.98 (2H, m, H-7, H-8), 5.37 (1H, t, J=7.3 Hz, H-10), 2.16 (3H, s, H-14), 1.80 (6H, s, H-17, H-18), 1.02 (3H, s, H-15), 0.99 (3H, s, H-16); (*signals due to the Z isomer*) δ (ppm) 6.42 (1H, d, J=16.2 Hz, H-8), 6.09–5.98 (1H, m, H-7), 5.31 (1H, t, J=7.2 Hz, H-10), 2.14 (3H, s, H-14), 1.85 (3H, s, H-17)*, 1.83 (3H, s, H-18)*, 1.03 (3H, s, H-15), 1.00 (3H, s, H-16); (*common signals*) δ (ppm) 4.00 (1H, bs, H-4), 2.54–2.41 (4H, m, H-11, H-12), 1.67 (4H, m, H-2, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz) (*signals due to the E isomer*) δ (ppm) 141.84 (C, C-6), 138.40 (CH, C-8), 134.70 (C, C-9), 129.82 (CH, C-10), 129.11 (C, C-5), 123.95 (CH, C-7), 70.11 (CH, C-4), 43.30 (CH_2, C-12), 34.62 (C, C-1), 29.87 (CH_3, C-14), 22.55 (CH_2, C-11), 18.51 (CH_3, C-17), 12.17 (CH_3, C-18); (*signals due to the Z isomer*) δ (ppm) 142.10 (C, C-6), 133.09 (C, C-9), 130.71 (CH, C-8), 129.39 (C, C-5), 127.92 (CH, C-10), 126.85 (CH, C-7), 70.16 (CH, C-4), 43.80 (CH_2, C-12), 34.67 (C, C-1), 29.89 (CH_3, C-14), 21.69 (CH_2, C-11), 20.28 (CH_3, C-17)*, 18.56 (CH_3, C-18)*; (*common signals*) δ (ppm) 208.32 (C, C-13), 37.43 (CH_2, C-2), 28.43 (CH_2, C-3), 28.97 (CH_3, C-15), 27.35 (CH_3, C-s16). *,# may be interchanged.

*4.6.5. 4-Dihydrotrisporin C (**7**).* Following the general procedure, but at room temperature, **22** (97 mg, 0.19 mmol), *n*-Bu_4NF (1 M in THF, 1.1 mL, 1.1 mmol) and THF (1 mL) yielded **7** as an oil (28 mg, 0.10 mmol, 55%). IR and HRMS signals as previously reported.[28] A small amount of this mixture was rechromatographied and both isomers were isolated.

4.6.5.1. (Z). δ (ppm) 6.46 (1H, dd, J=16.2 Hz, J=4.0 Hz, H-8), 6.12 (1H, bd, J=16.2 Hz, H-7), 5.49 (1H, m, H-10), 4.02 (1H, m, H-4), 3.81 (1H, m, H-13), 1.85 (3H, s, H-17)*, 1.84 (3H, s, H-18)*, 1.20 (3H, d, J=6.4 Hz, H-14), 1.05 (3H, s, H-15), 1.02 (3H, s, H-16). * may be interchanged.

4.6.5.2. (E). ^1H NMR ($CDCl_3$, 300 MHz) *(E isomer)* δ (ppm) 6.03 (2H, m, H-7, H-8), 5.46 (1H, t, J=6.9 Hz, H-10), 4.01 (1H, m, H-4), 3.86 (1H, m, H-13), 2.30 (2H, m), 2.20 (2H, m), 1.86 (2H, m), 1.83 (6H, s, H-17, H-18), 1.45 (2H, m), 1.23 (3H, d, J=6.1 Hz, H-14), 1.05 (3H, s, H-15), 1.01 (3H, s, H-16).

*4.6.6. Trisporin C (**8**).* Following the general procedure, **23** (115 mg, 0.29 mmol), *n*-Bu_4NF (1 M in THF, 0.9 mL, 0.9 mmol) and THF (1.5 mL) yielded **8** as an oil (24 mg, 0.09 mmol, 30%). IR and HRMS signals as previously reported.[28] ^1H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 6.22 (1H, d, J=16.4 Hz, H-8), 6.09 (1H, d, J=16.3 Hz, H-7), 5.59 (1H, t, J=6.7 Hz, H-10); (*signals due to the Z isomer*) δ (ppm) 6.66 (1H, d, J=16.0 Hz, H-8), 6.22 (1H, d, J=16.0 Hz, H-7), 5.57 (1H, m, H-10); (*common signals*) δ (ppm) 3.84 (1H, m, H-13), 2.50 (2H, m, H-3), 2.29 (2H, m, H-11), 1.84 (6H, s, H-17, H-18),

1.74 (2H, m, H-2), 1.55 (2H, m, H-12), 1.23 (3H, d, J=6.2 Hz, H-14), 1.18 (3H, s, H-15), 1.16 (3H, s, H-16); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) (*signals due to the E isomer*) 198.74 (C, C-4), 163.40 (C, C-6), 141.06 (CH, C-8), 134.78 (CH, C-10), 133.77 (C, C-9), 129.49 (C, C-5), 122.33 (CH, C-7), 23.58 (CH_3, C-17)*, 13.70 (CH_3, C-18)*; (*signals due to the Z isomer*) 199.52 (C, C-4), 161.79 (C, C-6), 133.09 (CH, C-8), 132.63 (CH, C-10), 131.98 (C, C-9), 129.68 (C, C-5), 125.05 (CH, C-7), 20.12 (CH_3, C-17)#, 12.08 (CH_3, C-18)#; (*common signals*) δ (ppm) 67.64 (CH, C-13), 38.68 (CH_2, C-12), 37.25 (CH_2, C-2), 35.59 (C, C-1), 34.24 (CH_2, C-3), 27.52 (CH_3, C-15, C-16), 26.65 (CH_3, C-14), 23.99 (CH_2, C-11).*,# may be interchanged.

*4.6.7. 4-Desoxytrisporin C (**9**).* Following the general procedure, **24** (226 mg, 0.60 mmol), n-Bu_4NF (1 M in THF, 1.8 mL, 1.8 mmol) and THF (3 mL) yielded **9** (112 mg, 0.43 mmol, 71%). Oil, IR ν (cm^{-1}) 3350, 2963, 2926, 2864, 1455, 1359, 966; HRFABMS (m/z): calcd ($C_{18}H_{30}ONa$): 285.2194, found: 285.2215 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) (*signals due to the E isomer*) δ (ppm) 5.99 (2H, bs, H-7, H-8), 5.41 (1H, t, J=7.0 Hz, H-10), 1.86 (3H, s, H-17)*, 1.70 (3H, s, H-18)*; (*signals due to the Z isomer*) δ (ppm) 6.42 (1H, d, J=16.2 Hz, H-8), 6.10 (1H, d, J=16.2 Hz, H-7), 5.32 (1H, d, J=7.0 Hz, H-10), 1.80 (3H, s, H-17)#, 1.68 (3H, s, H-18)#; (*common signals*) δ (ppm) 3.80 (1H, m, H-13), 2.24 (2H, m), 1.99 (2H, m), 1.68–1.45 (6H, m), 1.20 (3H, d, J=5.9 Hz, H-14), 1.01 (6H, s, H-15, H-16); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) (*signals due to the E isomer*) 137.72 (C, C-6), 137.70 (CH, C-8), 134.38 (C, C-9), 130.39 (CH, C-10), 128.23 (C, C-5), 124.36 (CH, C-7), 24.64 (CH_2, C-11), 21.66 (CH_3, C-17)*, 12.24 (CH_3, C-18)*; (*signals due to the Z isomer*) 138.06 (C, C-6), 132.80 (C, C-9),129.99 (CH, C-8), 128.62 (CH, C-10), 128.41 (C, C-5), 127.28 (CH, C-7), 23.74 (CH_2, C-11), 21.60 (CH_3, C-17)#, 20.43 (CH_3, C-18)#; (*common signals*) δ (ppm) 67.66 (CH, C-13), 39.98 (CH_2, C-12), 39.48 (CH_2, C-2), 34.11 (C, C-1), 32.83 (CH_2, C-4), 28.84 (CH_3, C-15, C-16), 23.42 (CH_3, C-14), 19.25 (CH_2, C-3). *,# may be interchanged.

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