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Obtaining the Ethers and Esters of Riccardin C, Potential NO Synthase Inhibitors

YU. S. KOSENKOVA, M. P. POLOVINKA, N. I. KOMAROVA, D. V. KORCHAGINA and N. F. SALAKHUTDINOV

Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Pr. Akademika Lavrentyeva 9, Novosibirsk 630090 (Russia)

E-mail: kosen@nioch.nsc.ru

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Abstract

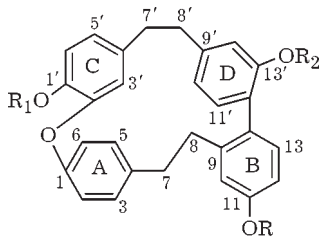
Riccardin C **1**, naturally occurring 18-membered macrocyclic bisbenzyl and NO synthase inhibitor has been isolated from *Primula macrocalyx* Bge in our experiments. A series of modifications is described for compound **1** *via* the interaction with various halogenides and chloroanhydrides of acids in the presence of bases with obtaining ethers and esters of riccardin C (**4**–**15**). The structure of the latter has been established with the use of spectral methods and a mass spectrometry technique.

Key words: *Primula macrocalyx* Bge., riccardin C, ethers and esters of riccardin C, NO synthase inhibitors

INTRODUCTION

In the course of studying the chemical composition of *Primula macrocalyx* Bge., we have for the first time isolated riccardin C 1 from higher plants, a phenolic compound with bisbenzyl skeleton [1]. Earlier, only liverworts were considered a phytogenous source of natural bisbenzyls such as marchantins [2], riccardins [3], pusilatins and others bisbenzyl macrocycles exhibiting a wide range of biological activity [4, 5]. Naturally occurring riccardins C, F, A (**1**–**3**, respectively) exhibit to some extent the properties of NO synthase inhibitors [6].

It is known, that an excess generation nitrogen dioxide, one of the universal regulators of cell metabolism, results in occurrence of various pathologies. In this connection, the inhibition of NO generation represents an important problem of biology and medicine [7]. Searching novel agents of natural origin those exhibit a NO inhibiting activity, and synthesizing the derivatives on their basis represents an actively developing field of bioorganic and medical chemistry. The analysis of the structure of naturally occurring riccardins **1**–**3** with respect to interrelation structure–NO inhibition activity demonstrates that the activity of monomethylated compounds is to a considerable extent higher than the activity of riccardin C [6].

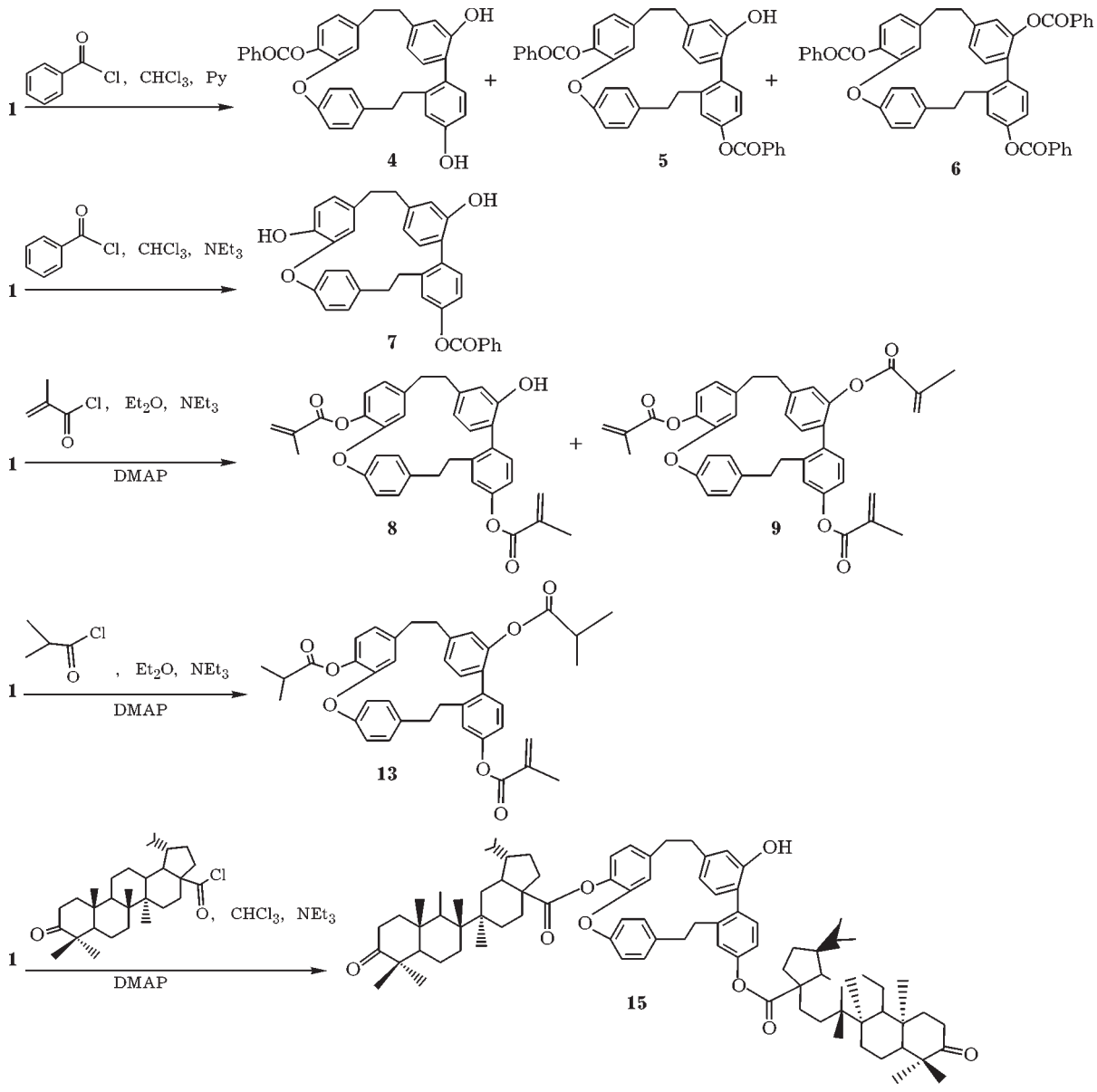


1 $R_1 = R_2 = R_3 = H$
2 $R_1 = Me$, $R_2 = R_3 = H$
3 $R_1 = R_2 = H$, $R_3 = Me$

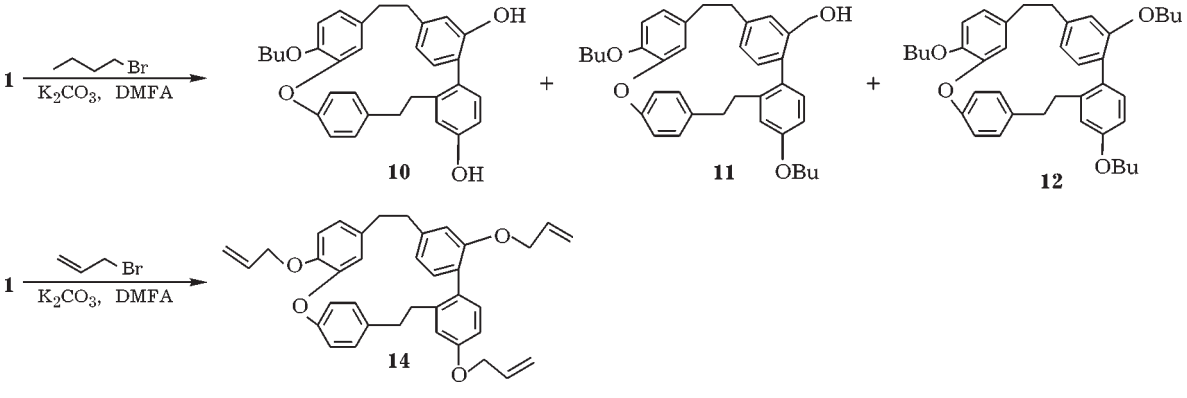
From riccardin C, researchers have synthetically obtained trimethyl derivative [3] and triacetyl derivative [8], whose biological activity was not studied. Such a scarce data set concerning chemical modification of compound **1** could be connected, to all appearance, with a low practical availability of initial bisbenzyls since they use to be isolated from liverworts in a very small amount, and their synthesis represents a multistage procedure [9].

RESULTS AND DISCUSSION

Earlier we have worked through a technique for isolating riccardin C **1** from *Primula macro-*



Scheme 1.



Scheme 2.

calyx Bge. [10]. Compound **1** was further entered into reactions for obtaining esters and ethers with respect to phenolic groups with various halogenides and halogenoanhydrides of acids in the presence of bases (Schemes 1, 2).

For the acylation of riccardin C **1** with benzoyl chloride (see Scheme 1) we used a technique described in [11]. The reaction was carried out in chloroform medium in the presence of pyridine. For obtaining compound **4** a mixture of compound **1** with pyridine and benzoyl chloride in a molar ratio 1 : 15.3 : 7.6 was held under stirring for 26 h at a room temperature. After the processing we obtained a reaction mixture containing compounds **4** and **5** with the prevalence of ester **4** (HPLC). After the chromatographic separation, we succeeded in isolating only ester **4** (the yield being of 16 %; hereinafter the yield after chromatography is presented). With holding the mixture compound **1** : pyridine : benzoyl chloride (molar ratio 1 : 15.3 : 7.3) during 36 h a reaction mixture containing ethers **4** and **5** is formed with the prevalence of the latter. The yield of compound **5** amounted to 6 %. Carrying out the reaction during 70 h with molar ratio substance **1** : pyridine : benzoyl chloride equal to 1 : 15.2 : 10 allowed us to obtain a reaction mixture containing mainly triester **6** (the yield being of 46 %).

Performing the reaction of acylation in the presence of triethylamine (molar ratio riccardin C : triethylamine : benzoyl chloride amounting to 1 : 3.5 : 2) under stirring and keeping at a room temperature during 24 h results in the formation of the reaction mixture containing mainly one product such as compound **7** (the yield being of 63.8 %). Thus, under these conditions there is a formation of monoether on phenolic group in the ring B of riccardin C observed.

The reactions of riccardin C with chloro anhydrides of methacrylic and isobutyric acids were carried out with triethylamine in the presence of catalytic amounts of dimethylaminepyridine (DMAP). It could be connected with the fact that the acylation in the presence of pyridine in these cases proceeds inefficiently, sophisticated reaction mixtures as well as unreacted compound **1** were produced. So, keeping a mixture of riccardin C **1** with methacryloyl chloride in air under stirring at a room temperature in the presence of triethylamine (molar ratio compound **1** : methacryloyl chloride : NEt_3 = 1 : 3 : 7) with the addition of a catalytic amount of DMAP, during 20 h results in the formation of the mixture of esters **8** and **9** (HPLC) with the yield amounting to 12 and 41 %, respectively.

Under the same conditions we have obtained triester **13** from riccardin C with chloro anhydride of isobutyric acid at a molar ratio compound **1** : chloro anhydride : NEt_3 = 1 : 12 : 18 (catalytic amounts of DMAP) and keeping at a room temperature during 20 h triester **13** (the yield being of 68 %).

The reaction with chloro anhydride of dihydrobethulonic acid was carried out reaction in chloroform medium due to better solubility of this chloroanhydride therein. A mixture of riccardin C, chloroanhydride of dihydrobethulonic acid and triethylamine with molar ratio 1 : 2 : 7 in chloroform medium with adding several crystals of DMAP was held under stirring at a room temperature during 24 h. After the separation of the reaction mixture with the help of a column chromatography on silica gel we isolated diester **15** (the yield being of 34 %).

Ethers **10**–**12**, **14** (see Scheme 2) obtained by a standard technique *via* the reaction between riccardin C **1** and corresponding alkyl and allyl bromides in acetone medium in the presence of potash with adding DMFA on boiling with a backflow condenser. The monitoring of the course of the reaction was carried out using TLC technique. We have obtained ethers **10**–**12** and **14** with the yield of 12, 5, 41 and 60 %, respectively.

As it is demonstrated by the analysis of the structure of products **4**–**15** (see Scheme 1), the greatest reactivity in the reactions of obtaining ethers is exhibited by the phenolic group in the ring C of riccardin C **1**: in the case of formation of monosubstituted ethers, just this group (compounds **4**, **10**) enters into the reaction. An exception is presented only by the reaction of compound **1** with benzoyl chloride in the presence of triethylamine when the only product formed is monoether with respect to the OH group in the ring B (ether **7**). A high activity of group OH–$C^{1'}$, to all appearance, could be caused by a positive mesomeric effect of oxygen located in the *ortho* position. A low reactivity of the phenolic group in the ring D (this group enters into the reactions of acyla-

tion and alkylation only in the case of a great excess of corresponding halogenide) could be exhplained by steric hindrance, since there are substituents in *ortho* and *meta* positions of the ring D. The greatest steric problems in this case, most likely, could be connected with the benzene ring in the ortho position.

The structure of the compounds **4**–**15** obtained has been established with the help of NMR method basing on the analysis ^{1}H NMR spectra with the attraction of ^{1}H–^{1}H double resonance spectra and two-dimensional proton-proton homonuclear correlation spectra, as well as the analysis ^{13}C NMR spectra with the use of two-dimentional heteronuclear ^{13}C–^{1}H correlation spectra for direct (^{13}C–^{1}H COSY) and long-range spin-spin coupling constants (COLOC). It should be noted that, as a rule, in ^{1}H NMR spectra of all the compounds **4**–**15** the signals resulting from protons of the aromatic ring A are exhibited as wide signals within the range of 6.6–6.9 ppm. A similar picture for the specified protons was observed in our studies earlier when registering ^{1}H NMR spec-

TABLE 1

Chemical shift values and the type of signals for C atoms in ^{13}C NMR spectra of riccardin C esters (**4**–**9**, **13**, **15**)

Atom	Compounds							
number	**4**	**5**	**6**	**7**	**8**	**9**	**13**	**15**
1	152.95 s	152.99 s	152.94 s	152.52 s	152.99 s	153.02 s	153.03 s	152.99 s
2	122.30 br d	122.33 br d	122.13[a] br d	122.27 br d	122.29 br d	122.11[a] br d	122.55[a] d	122.30 br d
3	129.16[a] br d	129.11 d	129.44[b] br d	129.23 br d	129.11 br d	129.40[b] br d	129.42[b] d	129.22[a] br d
4	139.76 s	139.71 s	139.42 s	139.58 s	139.59 s	139.44 s	139.49 s	139.25[b] s
5	128.98[a] br d	129.11 d	128.95[b] br d	129.23 br d	129.11 br d	128.96[b] br d	129.01[b] d	129.00[a] br d
6	122.30 br d	122.33 br d	122.53[a] br d	122.27 br d	122.29 br d	122.52[a] br d	122.00[a] d	122.30 br d
7	37.97 t	37.96 t	37.93 t	37.97 t	37.92 t	37.90 t	37.75 t	37.96 t
8	34.87 t	37.91 t	35.23 t	34.95 t	34.80 t	35.20 t	35.25 t	34.91 t
9	143.66 s	143.51 s	142.54 s	143.56 s	143.34 s	142.51 s	142.57 s	143.40 s
10	117.28 d	123.84 d	122.86 d	123.94 d	123.69 d	122.76 d	122.58 d	123.66 d
11	155.76 s	150.98 s	150.70 s	151.09 s	150.84 s	150.72 s	150.71 s	150.99 s
12	114.10 d	119.94 d	119.29 d	120.10 d	119.69 d	119.13 d	119.01 d	119.93 d
13	132.83 d	132.73 d	132.12 d	132.62 d	132.69 d	132.03 d	132.04 d	132.55 d
14	128.23 s	133.71 s	134.44 s	133.51 s	133.76 s	134.32 s	134.21 s	133.25 s
1′	137.84 s	137.86 s	137.94 s	143.28 s	137.80 s	137.97 s	138.01 s	137.66 s
2′	150.67 s	150.66 s	150.68 s	146.18 s	150.55 s	150.64 s	150.56 s	150.81 s
3′	117.90 d	117.96 d	117.74 d	115.92 d	118.00 d	117.73 d	117.69 d	117.63 d
4′	139.40 s	139.31 s	139.30 s	132.88 s	139.36 s	139.20 s	139.12 s	139.14[b] s
5′	121.78 d	121.79 d	121.82 d	122.07 d	121.72 d	121.77 d	121.74 d	121.63 d
6′	122.71 d	122.74 d	122.93 d	114.85 d	122.61 d	122.85 d	122.74 d	122.62 d
7′	37.25[b] t	37.28[a] t	37.21 t	36.90 t	37.31[a] t	37.16 t	37.13[c] t	37.27[c] t
8′	37.22[b] t	37.23[a] t	37.18 t	37.64 d	37.26[a] t	37.16 t	37.08[c] t	37.22[c] t
9′	141.42 s	141.76 s	141.34 s	142.29 s	141.59 s	141.25 s	141.27 s	141.81 s
10′	121.41 d	121.39 d	127.29 d	121.74 d	121.10 d	127.09 d	127.14 d	121.59 d
11′	131.50 d	131.44 d	132.24 d	131.22 d	131.39 d	132.07 d	131.94 d	131.42 d
12′	124.47 s	124.14 s	130.87 s	123.92 s	124.13 s	130.79 s	130.98 s	124.12 s
13′	151.89 s	151.94 s	147.40 s	151.68 s	152.05 s	147.39 s	147.34 s	151.80 s
14′	115.89 d	116.30 d	122.62 d	116.21 d	116.44 d	122.61 d	122.48 d	116.01 d

Note. Here and in Tables 2–4: the same letters (a, b, c, d) denote the chemical shift values, those, to all appearance, should be swapped within the same column.

tra for riccardin C at the temperature of 25–30 °C, which could be connected, to all appearance, with the rotation of the ring A around of C^1–C^4 axis. A comparative analysis of spin-spin coupling constants for protons of the aromatic rings B, C and D of the compounds under investigation with those for riccardin C demonstrates that the values of all the constants almost do not change with substituting a proton of the hydroxyl group by various substituents. Due to this, one could determine unequivocally in what of the rings of riccardin C there was the substitution. Chemical shifts for the signals of the protons of aromatic rings B, C and D of the compounds obtained exhibit a somewhat changing (as a rule, a signal shift towards weak field is observed), as one would expect, only for those rings where the substitution of OH group by OR is observed. The ^{1}H NMR spectral data for esters/ethers **4–15** are presented below, the ^{13}C NMR spectral data are presented in Tables 1–4.

TABLE 2

Chemical shift values and the type of signals for C atoms in ^{13}C NMR spectra of riccardin C ethers (**10–12**, **14**)

Atom	Compounds			
No.	**10**	**11**	**12**	**14**
1	153.18 s	153.19 s	152.95 s	152.66 s
2	122.48 br d	122.47 br d	122.18 d	122.11 d
3	129.08[a] br d	129.10[a] br d	129.20 br d	129.25[a] br d
4	138.97 s	139.04 s	139.46 s	139.39 s
5	128.87[a] br d	128.83[a] br d	129.20 br d	129.00[a] br d
6	122.48 br d	122.47 br d	122.18 d	122.11 d
7	38.01 t	38.07 t	38.16 t	38.09 t
8	34.91 t	35.05 t	35.60 t	35.55 t
9	143.85 s	143.47 s	143.05 s	142.96 s
10	117.41 d	116.76 d	115.73 d	115.95 d
11	155.80 s	159.37 s	158.43 s	157.88 s
12	114.17 d	112.99 d	11.53 d	111.75 d
13	132.68 d	132.34 d	132.38 d	132.35 d
14	128.12 s	127.73 s	130.87 s	130.92 s
1′	146.31 s	146.34 s	146.35 s	145.66 s
2′	149.10 s	149.15 s	149.26 s	149.02 s
3′	116.91 d	116.94 d	117.04 d	116.83 d
4′	133.81 s	133.83 s	133.88 s	134.03 s
5′	121.32 d	121.29 d	121.23 d	121.15 d
6′	114.00 d	114.07 d	114.18 d	114.32 d
7′	37.56[b] t	37.54[b] t	37.17 t	37.13 t
8′	36.92[b] t	36.89[b] t	37.92 t	37.79 t
9′	141.95 s	141.83 s	140.89 s	140.84 s
10′	121.50 d	121.39 d	121.42 d	121.69 d
11′	131.37 d	131.35 d	132.27 d	132.23 d
12′	124.30 s	124.48 s	127.98 s	127.78 s
13′	151.77 s	151.81 s	155.47 s	154.66 s
14′	115.83 d	115.79 d	112.71 d	112.68 d

Note. For designations see Table 1.

EXPERIMENTAL

High performance liquid chromatography (HPLC) analysis was performed employing a Milichrom A-02 microcolumn chromatograph (EcoNova Co., Novosibirsk, Russia) with the use of standard chromatographic columns (2 × 75 mm) packed with a reversed phase sorbent (ProntoSIL 120-5-C18, particle size 5 μm, Bischoff, Germany). We used a gradient elution mode with simultaneous multi-wavelength detection at six wavelength values (λ = 220, 240, 260, 280, 320, 360 nm) [12]. The eluent was methyl alcohol with 0.1 % of trifluoroacetic acid (TFA). The gradient amounted to 0–30 % of methanol, 0.1 % of TFA for 5 min, then 30–50 % of methanol, 0.1 % of TFA for 5 min, then 50–70, 70 %, 0.1 % of TFA for 10 min, 70–90, 90 %, 0.1 % of TFA for 10 and 5 min up to pure methanol. The temperature being of 35 °C, pressure 30–36 atm, the flow rate being 150 μL/min.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer (500.13 and 125.76 MHz, respectively) for substances dissolved in $CDCl_3$. As the internal standard we used the signals of chloroform (δ_H 7.24 ppm, δ_C 76.90 ppm).

High resolution mass spectra for compounds **4–14** were obtained on a Finnigan MAT 8200 mass spectrometer with the ionizing voltage of 70 eV. The registration of the mass spectrum for compound **15** was carried out with an Autoflex III MALDI-TOF mass spectrometer (Bruker Daltonics, Germany) in the reflectron mode with the generation of positively charged ions. For the ionization of molecules a nitrogen gas laser was employed (337.1 nm) with the frequency of 20 Hz and the energy of 3–4 mW (150–200 μJ/pulse). As a matrix we used satu-

TABLE 3

Chemical shift values and the type of signals for C atoms in ^{13}C NMR spectra for substituents in compounds **4**–**15**

Atom	Compounds								
No.	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
15	–	165.18[a] s	164.86 s	165.16 s	165.94[a] s	165.66[a] s	–	67.64 t	67.52 t
16	–	129.39 s	129.48 s	129.32 s	135.77[b] s	135.89[b] s	–	31.32[a] t	31.33[a] t
17	–	130.12 d	129.99 d	130.12 d	127.35[c] t	127.05[c] t	–	19.13[b] t	19.14[b] t
18	–	128.54 d	128.44 d	128.56 d	18.34[d] q	18.35[d] q	–	13.78[c] q	13.81 q
19	–	133.63 d	133.43 d	133.67 d	–	–	–	–	–
15′	164.95 s	164.98[a] s	164.72 s	–	165.80[a]s	165.48[a] s	69.35 t	69.25 t	69.34 t
16′	129.43 s	129.39 s	129.40 s	–	135.50[b] s	135.59[b] s	31.31 t	31.30[a] t	31.44[a] t
17′	130.24 d	130.24 d	130.18 d	–	127.24[c]	127.00[c] t	19.15 t	19.18[b] t	19.24[b] t
18′	128.38 d	128.38 d	128.32 d	–	18.28[d] q	18.28[d] q	13.81 q	13.76[c] q	13.78 q
19′	133.31 d	133.33 d	133.24 d	–	–	165.42[a] s	–	–	67.72 t
20′	–	–	164.67 s	–	–	135.59[b] s	–	–	31.35 t
21′	–	–	129.32 s	–	–	126.67 t	–	–	19.10 t
22′	–	–	129.75 d	–	–	18.13 q	–	–	13.69 q
23′	–	–	128.39 d	–	–	–	–	–	–
24′	–	–	133.27 d	–	–	–	–	–	–

Note. For designations see Table 1.

TABLE 4

Chemical shift values and the type of signals for C atoms of two substituents in keto derivatives dihydrobetulonic acid in ^{13}C NMR spectrum of compound **15**

Atom No.	**15**		Atom No.	**15**	
1″	39.50 t	39.50 t	16″	31.88 t	31.83 t
2″	34.01 t	34.01 t	17″	57.34 s	57.32 s
3″	218.08 s	217.90 s	18″	48.83 d	48.76 d
4″	47.22 s	47.18 s	19″	44.05 d	43.96 d
5″	54.86 d	54.82 d	20″	29.64 d	29.64 d
6″	19.53 t	19.53 t	21″	22.74 t	22.58 t
7″	33.65 t	33.61 t	22″	37.44 t	37.22 t
8″	40.72 s	40.59 s	23″	26.52 q	26.50 q
9″	49.60 d	49.60 d	24″	20.94 q	20.94 q
10″	36.79 s	36.73 s	25″	15.92[a] q	15.87[a] q
11″	21.36 t	21.36 t	26″	15.83[a] q	15.81[a] q
12″	26.91 t	26.84 t	27″	14.50 q	14.45 q
13″	38.31 d	38.16 d	28″		
14″	42.63 s	42.61 s	29″	14.59 q	14.59 q
15″	29.77 t	29.56 t	30″	22.87 q	22.86 q

Note. For designations see Table 1.

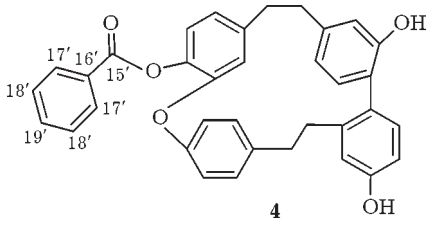
13	14	15
175.39[a] s	68.58 t	174.84[a] s
34.12[b] d	133.34 d	–
18.94[c] q	117.41 t	–
18.94[c] q	–	–
–	–	–
175.30[a] s	70.19 t	174.40[a] s
33.88[b] d	133.58 d	–
18.85[c] q	117.57 t	–
18.85[c] q	68.30 t	–
175.05[a] s	133.16 d	–
33.98 d	116.14 t	–
18.60[d]	–	–
18.48[d]	–	–
–	–	–
–	–	–

rated solution of 2,5-dihydroxybenzoic acid in acetonitrile. The mass spectrometer was calibrated according to external mass standard with the following composition: Angiotensin II (1046.5420), Angiotensin I (1296.6853), Substance P (1347.7361), Bombesin (1619.8230), ACTH clip 1-17 (2093.0868) (monoisotopic masses of ions were used).

Column chromatography was performed using Merck silica gel 60–200 μm. The analysis of fractions and monitoring the course of the reaction was carried out with the help of thin-layer chromatography technique on Sorbfil plates (PTSH-AF-V-UF, Krasnodar, Russia) in the system of chloroform–ethanol (2–5 % of EtOH). Chloroform, acetone and diethyl ether prior to the reaction were dried *via* passing through a column filled with calcined aluminium oxide. The monitoring of the course of the reaction was carried out a TLC technique.

Obtaining compounds 4–15

$O^{1'}$-benzoylriccardin C (4). Riccardin C (0.02 g, 0.047 mmol) was dissolved in chloroform (5 mL), to the solution was added pyridine (0.057 g, 0.72 mmol) at a room temperature under stirring, then benzoyl chloride being added (0.05 g, 0.36 mmol). The reaction mixture was held during 26 h, and then it was poured into a Petri dish. After the evaporation of solvent the mixture was treated by distilled water, then the organic part was extracted with chloroform and dried over $MgSO_4$. After chromatography the reaction mixture on SiO_2 (chloroform being an eluent; the ratio reaction mixture : SiO_2 = 1 : 86) as much as 4 mg of compound **4** (16 %) have been isolated.

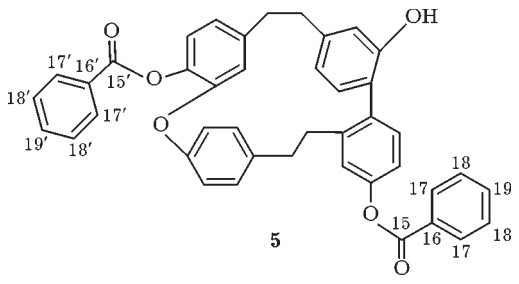


4

^{1}H NMR spectrum of monoether **4**, δ, ppm (J, Hz): 2.43–3.20 m ($4CH_2$), 4.88 and 5.00 both br s (2OH), 5.55 d ($H^{3'}$, $J_{3',5'}$ 1.9), 6.26 dd ($H^{10'}$, $J_{10',11'}$ 7.6, $J_{10',14'}$ 1.6), 6.39 d ($H^{14'}$, $J_{14',10'}$ 1.6), 6.77 dd (H^{12}, $J_{12,13}$ 8.3, $J_{12,10}$ 2.6), 6.79 d ($H^{11'}$, $J_{11',10'}$ 7.6), 6.86 d. d ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.93 d (H^{10}, $J_{10,12}$ 2.6), 7.04 d (H^{13}, $J_{13,12}$ 8.3), 7.12 d ($H^{6'}$, $J_{6',5'}$ 8.1), 7.47 dd ($2H^{18'}$, $J_{18',17}$ 7.8, $J_{18',19'}$ 7.5), 7.59 tt ($H^{19'}$, $J_{19',18'}$ 7.5, $J_{19',17'}$ 1.5), 8.22 dd ($2H^{17'}$, $J_{17',18'}$ 7.8, $J_{17',19'}$ 1.5). Protons H^2, H^3, and H^5, H^6 are exhibited as a very broad "hump" within the range of 6.66–6.90 ppm. $C_{35}H_{28}O_5$ m/z: 528.17 (33.69), 529.17 (11.72), 211.08 (22.30), 105.03 (100), 424.14 (8.36), 106.03 (6.61), 212.09 (5.80). Calculated value: m/z = 528.1931, measured value: m/z = 528.1930.

$O^{1'}$,O^{11}-dibenzoylriccardin C (5) was obtained in a similar manner as compound **4**. Riccardin C: 0.069 g (0.16 mmol); pyridine: 0.193 g (2.44 mmol); benzoyl chloride 0.169 g (1.2 mmol). The reaction mixture was held under stirring during 36 h. Monitoring the course of the reaction was carried out using a TLC technique. After chromatography the reaction mixture (hexane as an eluent with a gradient of chloroform; the ratio reaction mixture : SiO_2 = 1 : 80) we have isolated 7 mg of compound **5** (6.8 %).

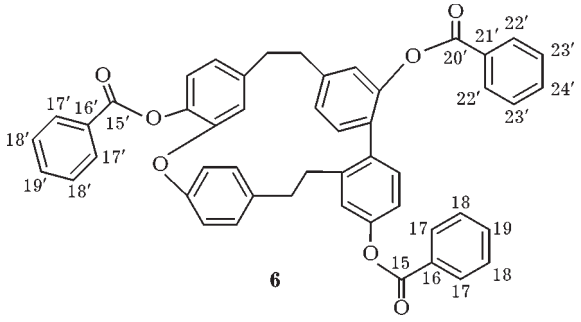
^{1}H NMR spectrum of diester **5**, δ, ppm (J, Hz): 2.62–2.85 m ($2H^{7'}$, $2H^{8'}$, H^{8a}), 2.83–2.98 m ($2H^7$), 3.10 m (H^{8b}), 5.17 br s (13′-OH), 5.56 d ($H^{3'}$, $J_{3',5'}$ 1.9), 6.30 dd ($H^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.5), 6.38 d ($H^{14'}$, $J_{14',10'}$ 1.5), 6.84 d ($H^{11'}$, $J_{11',10'}$ 7.7), 6.87 dd ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 7.13 d ($H^{6'}$,



5

$J_{6',5'}$ 8.1), 7.16 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 7.25 d (H^{13}, $J_{13,12}$ 8.4), 7.34 d (H^{10}, $J_{10,12}$ 2.4), 7.47 dd ($2H^{18'}$, $J_{18',17'}$ 7.8, $J_{18',19'}$ 7.5), 7.53 dd ($2H^{18}$, $J_{18,17}$7.8, $J_{18,19}$ 7.5), 7.59 br t ($H^{19'}$, $J_{19',18'}$ 7.5), 7.65 br t (H^{19}, $J_{19,18}$ 7.5), 8.23 m ($2H^{17}$, $2H^{17'}$). Protons H^2, H^3, H^5 and H^6 are exhibited as a very wide signal within the range of 6.68–6.86 ppm. $C_{42}H_{32}O_6$ *m/z*: 632.28 (21.53), 633.28 (9.78), 105.04 (100), 106.04 (6.76). Calculated value m/z = 632.2193, measured value m/z = 632.2186.

Tribenzoylriccardin C (6) was obtained in a similar manner as compound **4**. Riccardin C: 0.107 g (0.25 mmol); pyridine: 0.3 g (3.79 mmol); benzoyl chloride: 0.351 g (2.5 mmol). The reaction mixture was held under stirring during 70 h. After chromatography (hexane as an eluent with a gradient of chloroform; the ratio reaction mixture : SiO_2 = 1 : 39) we have isolated 0.086 g of compound **6** (46.2 %).

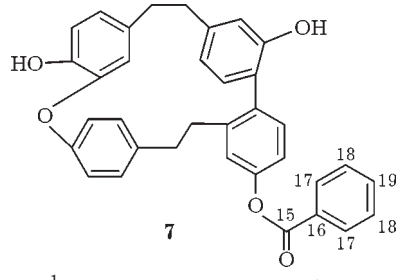


6

^{1}H NMR spectrum of triester **6**, δ, ppm (*J*, Hz): 2.65–2.78 m ($H^{7'a}$, $H^{8'a}$), 2.82–2.90 m (H^{7a}, H^{8a}), 2.90–2.97 m ($H^{7'b}$, $H^{8'b}$), 3.02 m (H^{7b}), 3.12 m (H^{8b}), 5.58 d ($H^{3'}$, $J_{3',5'}$ 1.9), 6.57 dd ($H^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.5), 6.72 br d and 7.00 br d (H^3, H^5, J ~ 8), 6.78 br d and 6.87 br d (H^2, H^6, J ~ 8), 6.88 d ($H^{14'}$, $J_{14',10'}$ 1.5), 6.90 dd ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 7.05 d ($H^{11'}$, $J_{11',10'}$ 7.7), 7.08 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.5), 7.17 d ($H^{6'}$, $J_{6',5'}$ 8.1), 7.19 d (H^{13}, $J_{13,12}$ 8.4), 7.25 d (H^{10}, $J_{10,12}$ 2.5), 7.44 dd ($2H^{23'}$, $J_{23',22'}$ 7.8, $J_{23',24'}$ 7.5), 7.48 dd ($2H^{18'}$, $J_{18',17'}$ 7.8, $J_{18',19'}$ 7.5), 7.50 dd ($2H^{18}$, $J_{18,17}$ 7.8, $J_{18,19}$ 7.5), 7.57 br t ($H^{24'}$, $J_{24',23'}$ 7.5), 7.59 br t ($H^{19'}$, $J_{19',18'}$ 7.5), 7.62 tt (H^{19}, $J_{19,18}$ 7.5, $J_{19,17}$ 1.5), 7.98 dd ($2H^{22'}$, $J_{22',23'}$ 7.8, $J_{22',24'}$ 1.5), 8.20 dd ($2H^{17}$, $J_{17,18}$ 7.8, $J_{17,19}$ 1.5), 8.24 dd ($2H^{17'}$, $J_{17',18'}$ 7.8, $J_{17',19'}$ 1.5). $C_{49}H_{36}O_7$ *m/z*: 736.37 (12.65), 737.38 (6.83), 105.0 (100), 106.0 (6.76).

Calculated value m/z = 736.2456, measured value m/z = 736.2441.

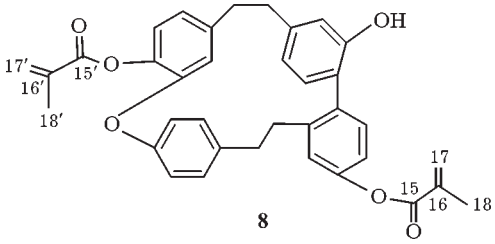
O^{11}-benzoylriccardin C (7). Riccardin C (0.024 g, 0.057 mmol) was dissolved in chloroform (5 mL), then were added 0.121 mmol (0.017 g) of benzoyl chloride, 0.2 mmol (0.02 g) of NEt_3, under stirring. The reaction was carried out at a room temperature and stirring during 24 h. Then to a reaction mixture were added 10 mL of $CHCl_3$, 15 mL of water. An aqueous part was decanted into a separating funnel and then extracted with $CHCl_3$, (3 × 15 mL). Organic layers were joined together, washed successively with 6 % HCl solution (3 × 15 mL), water, 15 % $NaHCO_3$ solution and with water again. The organic layer was dried over $MgSO_4$. After the filtration and solvent evaporation the reaction mixture was chromatographed on a column with SiO_2, thus 0.019 g of compounds **7** (63.8 %) was obtained.



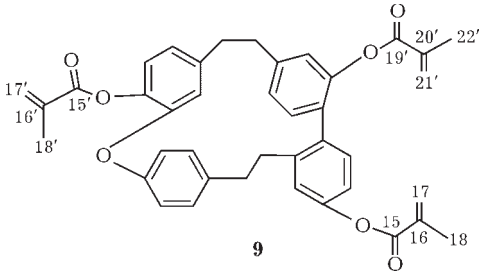
7

^{1}H NMR spectrum of monoester **7**, δ, ppm (*J*, Hz): 2.55–2.82 m ($2H^{7'}$, $2H^{8'}$, H^{8a}), 2.83–3.05 m ($2H^7$), 3.11 m (H^{8b}), 4.80 br s (13′-OH), 5.37 d ($H^{3'}$, $J_{3',5'}$ 1.9), 5.58 br s (1′-OH), 6.24 dd ($H^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.5), 6.41 d ($H^{14'}$, $J_{14',10'}$ 1.5), 6.73 dd ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.80 d ($H^{11'}$, $J_{11',10'}$ 7.7), 6.90 d ($H^{6'}$, $J_{6',5'}$ 8.1), 7.18 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 7.22 d (H^{13}, $J_{13,12}$ 8.4), 7.37 d (H^{10}, $J_{10,12}$ 2.4), 7.54 dd ($2H^{18}$, $J_{18,17}$ 7.9, $J_{18,19}$ 7.5), 7.66 tt (H^{19}, $J_{19,18}$ 7.5, $J_{19,17}$ 1.4), 8.24 dd ($2H^{17}$, $J_{17,18}$ 7.9, $J_{17,19}$ 1.4). The signals of protons H^2, H^3, H^5 and H^6 are exhibited as very broad signal within the range of 6.70–6.85 ppm. $C_{35}H_{28}O_5$ *m/z*: 528.2 (53.93), 529.2 (21.27), 424.1 (34.88), 425.1 (11.14), 211.1 (51.91), 212.1 (18.45), 213.1 (21.60). Calculated value m/z = 528.1931, measured value m/z = 528.1918.

$O^{1'}$,O^{11}-dimethacryloylriccardin C (8) and trimethacryloylriccardin C (9). Riccardin C (0.05 g, 0.12 mmol) was dissolved in diethyl ether (3.5 mL), then were added 0.35 mmol (0.037 g) of methacryloylchloride, 0.84 mmol (0.085 g) NEt_3 and three crystals of DMAP, under stirring. The reaction was carried out at a room temperature and stirring during 20 h. Then we added to the reaction mixture 10 mL of Et_2O, 15 mL of water. An aqueous part was decanted into a separating funnel and extracted with (3 × 10 mL) of Et_2O. Organic layers were joined together. The organic phase obtained was washed with 6 % HCl solution (3 × 15 mL), 6 % $NaHCO_3$ solution (3 × 15 mL), concentrated NaCl solution. The organic phase washed was dried over $MgSO_4$. After chromatography (hexane as an eluent with a gradient of diethyl ether the ratio reaction mixture : SiO_2 = 1 : 85) we have isolated 0.015 g of compounds **9** (41.9 %) and 0.0042 g of compounds **8** (12.7 %).



8

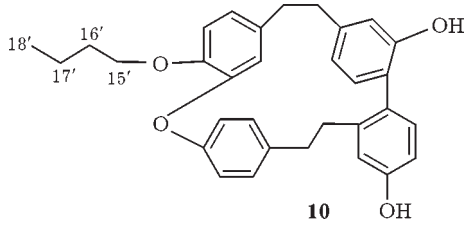


9

^{1}H NMR spectrum of diester **8**, δ, ppm (*J*, Hz): 2.05 br s and 2.08 br s ($C^{18}H_3$, $C^{18'}H_3$), 2.57–2.81 m ($2H^{7'}$, $2H^{8'}$, H^{8a}), 2.82–2.98 m ($2H^7$), 3.05 m (H^{8b}), 5.50 d ($H^{3'}$, $J_{3',5'}$ 1.9), 5.72 dq (*J* 1.7 and 1.5) and 6.37 br s ($2H^{17}$ or $2H^{17'}$), 5.78 dq (*J* 1.7 and 1.5) and 6.38 br s ($2H^{17}$ or $2H^{17'}$), 6.27 dd ($H^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.6), 6.30 d ($H^{14'}$, $J_{14',10'}$ 1.6), 6.80 d ($H^{11'}$, $J_{11',10'}$ 7.7), 6.82 dd ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 7.02 d ($H^{6'}$, $J_{6',5'}$ 8.1), 7.04 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 7.20 d (H^{13}, $J_{13,12}$ 8.4), 7.23 d (H^{10}, $J_{10,12}$ 2.4), 6.65–6.82 br m (H^2, H^3, H^5, H^6). $C_{36}H_{32}O_6$ *m/z*: 560.3 (51.03), 561.3 (22.35), 491.2 (18.55), 492.2 (23.30), 424.2 (6.09), 280.1 (7.92). Calculated value *m/z* = 560.2193, measured value *m/z* = 560.2190.

^{1}H NMR spectrum of triester **9**, δ, ppm (*J*, Hz): 1.85 br s ($C^{22'}H_3$), 2.05 br s and 2.08 br s ($C^{18}H_3$, $C^{18'}H_3$), 2.57–2.69 m and 2.83–2.92 m ($2H^{7'}$, $2H^{8'}$), 2.72 m (H^{8a}), 2.81 m and 2.95 m ($2H^7$), 3.04 m (H^{8b}), 5.48 d ($H^{3'}$, $J_{3',5'}$ 1.9), 5.55 dq (^2J 1.7, $J_{21',22'}$ 1.5) and 6.04 br s ($2H^{21'}$), 5.71 dq (*J* 1.7 and 1.5), 5.76 dq (*J* 1.7 and 1.5) and 6.36 m ($2H^{17}$, $2H^{17'}$), 6.47 dd ($H^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.6), 6.70 d ($H^{14'}$, $J_{14',10'}$ 1.6), 6.83 dd ($H^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.94 d ($H^{11'}$, $J_{11',10'}$ 7.7), 6.98 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 7.04 d ($H^{6'}$, $J_{6',5'}$ 8.1), 7.05 d (H^{13}, $J_{13,12}$ 8.4), 7.17 d (H^{10}, $J_{10,12}$ 2.4). The signals of the protons of the aromatic ring A are exhibited as very broad doublets. (*J* ~ 8): 6.66 and 6.90 ppm (H^3 and H^5), 6.71 and 6.79 ppm (H^2 and H^6). $C_{40}H_{36}O_7$ *m/z*: 628.31 (36.23), 629.31 (17.40), 560.24 (12.72), 559.24 (12.75), 211.09 (14.10). Calculated value *m/z* = 628.2456, measured value *m/z* = 628.2453.

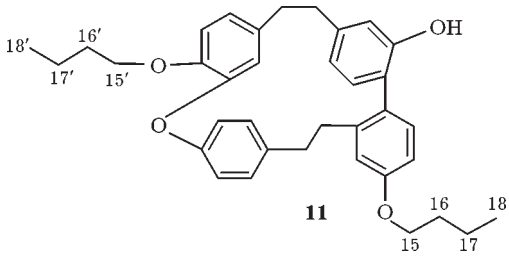
$O^{1'}$-butylriccardin C (10), $O^{1'}$,O^{11}-dibutylriccardin C (11), tributylriccardin C (12). Into a two-necked flask were loaded 0.072 g (0.171 mmol) of riccardin C, 5 mL of acetone and 0.72 mmol (0.1 g) of calcinated potassium carbonate, the reaction mixture was added with 1 mL of DMFA and stirred during 2 h. Then to the mixture was added 0.513 mmol (0.07 g) of butylbromide and with further boiling for 24 h under stirring. The reaction mixture was filtered to remove potassium carbonate, washed with acetone, and then the solvent was evaporated. To the residue obtained was added 15 mL of diethyl ether then the organic phase was successively washed with 6 % $NaHCO_3$ solution (3 × 15 mL) and concentrated NaCl solution (3 × 15 mL). The organic phase was dried over $MgSO_4$. After chromatography (hexane as an eluent with a gradient of chloroform; the ratio reaction mixture : SiO_2 = 1 : 78) we have isolated 0.042 g (41 %), 0.005 g (5 %) and 0.01 g (12 %) of compounds **12**, **11** and **10**, respectively.



10

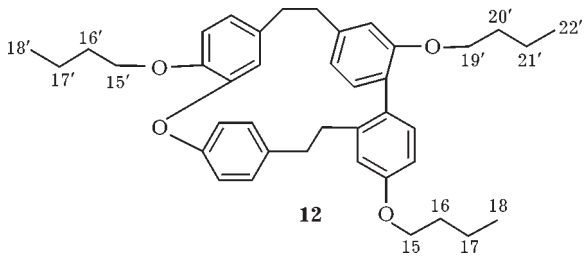
^{1}H NMR spectrum of monoether **10**, δ, ppm (*J*, Hz): 0.96 t ($C^{18'}H_3$, $J_{18',17'}$ 7.5), 1.51 m ($2H^{17'}$), 1.84 m ($2H^{16'}$), 2.55–2.80 m ($2H^{7'}$, $2H^{8'}$, H^{8a}),

2.81–2.96 m (2H^{7}), 3.02 m (H^{8b}), 4.08 t (2H$^{15'}$, $J_{15',16'}$ 6.8), 4.74 br s (13′-OH), 5.00 br s (11–OH), 5.42 d (H$^{3'}$, $J_{3',5'}$ 2.0), 6.25 dd (H$^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.6), 6.40 d (H$^{14'}$, $J_{14',10'}$ 1.6), 6.72 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 2.0), 6.770 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.5), 6.772 d (H$^{11'}$, $J_{11',10'}$ 7.7), 6.87 d (H$^{6'}$, $J_{6',5'}$ 8.1), 6.95 d (H^{10}, $J_{10,12}$ 2.5), 7.02 d (H^{13}, $J_{13,12}$ 8.4). Signals of protons H^{2}, H^{3}, H^{5} and H^{6} are exhibited as very broad signal within the range of 6.68–6.84 ppm. $C_{32}H_{32}O_4$ *m/z*: 480.2 (100), 481.2 (36.36), 424.2 (36.63), 425.2 (12.40), 225.1 (10.31), 226.1 (3.97), 211.1 (95.34), 212.1 (33.73), 213.1 (34.36), 197.1 (12.17), 105.0 (7.26), 107.0 (9.38). Calculated value *m/z* = 480.2295, measured value *m/z* = 480.2293.



11

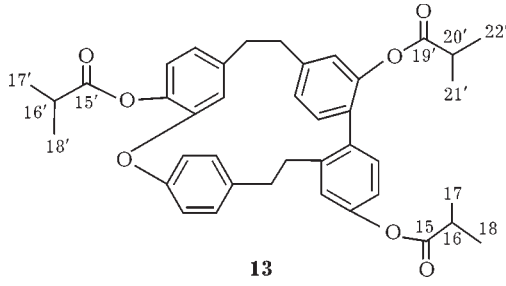
^{1}H NMR spectrum diether **11**, δ, ppm (*J*, Hz): 0.98 t (C$^{18'}$H$_3$, $J_{18',17'}$ 7.5), 1.01 t (C^{18}H$_3$, $J_{18,17}$ 7.4), 1.47–1.59 m (2H^{17}, 2H$^{17'}$) and 1.78–1.88 m (2H^{16}, 2H$^{16'}$), 2.56–2.81 m (2H$^{7'}$, 2H$^{8'}$, H^{8a}), 2.83–2.98 m (2H^{7}), 3.05 m (H^{8b}), 4.04 t (2H^{15}, $J_{15,16}$ 6.5), 4.08 t (2H$^{15'}$, $J_{15',16'}$ 6.8), 4.80 br s (13′-OH), 5.44 d (H$^{3'}$, $J_{3',5'}$ 2.0), 6.26 dd (H$^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.6), 6.40 d (H$^{14'}$, $J_{14',10'}$ 1.6), 6.73 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 2.0), 6.79 d (H$^{11'}$, $J_{11',10'}$ 7.7), 6.85 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.5), 6.87 d (H$^{6'}$, $J_{6',5'}$ 8.1), 7.01 d (H^{10}, $J_{10,12}$ 2.5), 7.07 d (H^{13}, $J_{13,12}$ 8.4). The protons of the ring A are exhibited as very broad signal within the range of 6.67–6.89 ppm. $C_{36}H_{40}O_4$ *m/z*: 537.33 (42.34), 536.32 (100), 480.22 (37.63), 323.20 (18.35), 267.14 (71.08), 213.09 (37.54), 211.07 (66.39). Calculated value *m/z* = 536.2921, measured value *m/z* = 536.2908.



12

^{1}H NMR spectrum triether **12**, δ, ppm (*J*, Hz): 0.87 t (C$^{22'}$H$_3$, $J_{22',21'}$ 7.5), 0.97 t (C$^{18'}$H$_3$, $J_{18',17'}$ 7.5), 1.01 t (C^{18}H$_3$, $J_{18,17}$ 7.4), 1.33 tq (2H$^{21'}$, $J_{21',20'}$ 7.5, $J_{21',22'}$ 7.5), 1.47–1.58 m (2H^{17}, 2H$^{17'}$), 1.59 m (2H$^{20'}$), 1.78–1.87 m (2H^{16}, 2H$^{16'}$), 2.56–2.82 m (2H$^{7'}$, 2H$^{8'}$, H^{8a}), 2.83–2.97 m (2H^{7}), 3.03 m (H^{8b}), 3.72 br s and 3.77 br s (2H$^{19'}$), 4.04 t (2H^{15}, $J_{15,16}$ 6.5), 4.08 t (2H$^{15'}$, $J_{15',16'}$ 6.8), 5.39 d (H$^{3'}$, $J_{3',5'}$ 2.0), 6.23 dd (H$^{10'}$, $J_{10',11'}$ 7.6, $J_{10',14'}$ 1.5), 6.39 d (H$^{14'}$, $J_{14',10'}$ 1.5), 6.69 br d (H^{2}, H^{6}, *J* ~ 8.0), 6.73 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 2.0), 6.77 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.5), 6.81 d (H$^{11'}$, $J_{11',10'}$ 7.6), 6.88 d (H$^{6'}$, $J_{6',5'}$ 8.1), 6.93 d (H^{10}, $J_{10,12}$ 2.5), 7.02 d (H^{13}, $J_{13,12}$ 8.4). Protons H^{3} and H^{5} are almost not visible at a room temperature because of a very broad signals; some eminence of the zero line is only observed. With a 10 °C increase in the temperature of registering the spectrum a very broad signal is observed within the range of 6.65–6.90 ppm. $C_{40}H_{48}O_4$ *m/z*: 592.40 (100), 593.40 (40.92), 536.30 (14.56), 537.31 (5.57), 324.22 (12.13), 323.21 (54.25), 268.16 (13.97), 267.15 (20.43), 240.13 (5.98), 213.11 (13.22), 211.10 (24.19), 107.06 (4.69). Calculated value *m/z* = 592.3547, measured value *m/z* = 592.3548.

Triisobutyrylriccardin C (13) was in a manner described for obtaining compounds **8** and **9**. Riccardin C: 0.02 g (0.047 mmol); chloro anhydride of isobutyric acid: 0.059 g (0.56 mmol); triethylamine: 0.09 g (0.89 mmol); three crystals of DMAP. The mixture was stirred during 20 h. The monitoring of the course of the reaction was carried out using a TCL technique. After the treatment of the reaction mixture and chromatographing (hexane as an eluent with a gradient of chloroform; the ratio reaction mixture : SiO_2 = 1 : 70) we have isolated 0.02 g of compound **13** (68.6 %).

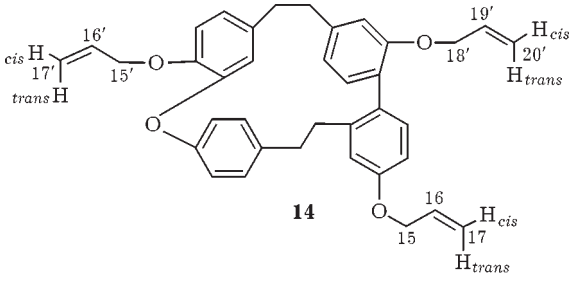


13

^{1}H NMR spectrum of triester **13**, δ, ppm (*J*, Hz): 0.98 br d and 1.04 br d (C$^{21'}$H$_3$, C$^{22'}$H$_3$, *J* 7.0), 1.30 d (*J* 7.0) and 1.34 d (*J* 7.0, 4CH$_3$), 2.50 septet (H$^{20'}$, *J* 7.0), 2.56–2.66 m and 2.75–2.90 m (2H$^{7'}$, 2H$^{8'}$, H^{7a}), 2.67 m and 3.04 m

(2H^{8}), 2.97 m (H^{7b}), 2.82 septet and 2.84 septet (H^{16}, H$^{16'}$, J 7.0), 5.47 d (H$^{3'}$, $J_{3',5'}$ 1.9), 6.43 dd (H$^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.6), 6.59 d (H$^{14'}$, $J_{14',10'}$ 1.6), 6.67 br d and 6.92 br d (H^{3}, H^{5}, J ~ 8), 6.70 br d and 6.79 br d (H^{2}, H^{6}, J ~ 8), 6.81 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.90 d (H$^{11'}$, $J_{11',10'}$ 7.7), 6.92 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 6.99 d (H$^{6'}$, $J_{6',5'}$ 8.1), 7.02 d (H^{13}, $J_{13,12}$ 8.4), 7.11 d (H^{10}, $J_{10,12}$ 2.4). $C_{40}H_{42}O_7$ m/z: 634.36 (2.15), 635.36 (0.88), 566.29 (5.82), 565.28 (24.75), 564.28 (67.46), 495.20 (19.61), 494.20 (57.18), 425.16 (27.32), 424.16 (100), 213.11 (11.05), 211.09 (34.20). Calculated value m/z = 634.2925, measured value m/z = 634.2931.

Triallylriccardin C (14) was obtained in a similar manner as ethers **10–12**. Riccardin C **1**: 0.105 g (0.25 mmol); K_2CO_3: 0.1 g (0.74 mmol); DMFA: 1 mL; allyl bromide: 0.089 g (0.74 mmol). The reaction was monitored using a TLC technique. After chromatography (hexane as an eluent with a gradient of diethyl ether; the ratio reaction mixture : SiO_2 = 1 : 37) we have isolated 0.081 g of compound **14** (60 %).

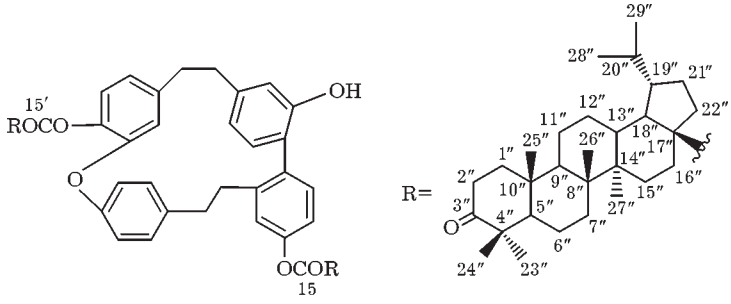


14

^{1}H NMR spectrum of triether **14**, δ, ppm (J, Hz): 2.56–2.66 m and 2.74–2.89 m (2H$^{7'}$, 2H$^{8'}$, H^{7a}), 2.70 m and 3.06 m (2H^{8}), 2.92 m (H^{7b}), 4.34 m (2H$^{18'}$), 4.61 br d (2H^{15}, $J_{15,16}$ 5.3), 4.68 br d (2H$^{15'}$, $J_{15',16'}$ 5.3), 5.14 br d (H$^{20'}_{cis}$, $J_{20'cis,19'}$ 10.5), 5.23 br d (H$^{20'}_{trans}$, $J_{20'transc,19'}$ 17.1), 5.29 br d and 5.32 br d (H$^{17}_{cis}$ and H$^{17'}_{cis}$, J 10.5), 5.40 d (H$^{3'}$, $J_{3',5'}$ 1.9), 5.45 br d and 5.48 br d (H$^{17}_{trans}$ and H$^{17'}_{trans}$, J 17.1), 5.90 ddt (H$^{19'}$, $J_{19',20'trans}$ 17.1, $J_{19',20'cis}$ 10.5, $J_{19',18'}$ 5.3), 6.08–6.18 m (H^{16}, H$^{16'}$), 6.27 dd (H$^{10'}$, $J_{10',11'}$ 7.7, $J_{10',14'}$ 1.5), 6.40 d (H$^{14'}$, $J_{14',10'}$ 1.5), 6.73 br d (H^{2}, H^{6}, J ~ 8), 6.74 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.82 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.5), 6.85 d (H$^{11'}$, $J_{11',10'}$ 7.7), 6.90 d (H$^{6''}$, $J_{6',5'}$ 8.1), 6.99 d (H^{10}, $J_{10,12}$ 2.5), 7.07 d (H^{13}, $J_{13,12}$ 8.4). Protons H^{3} and H^{5} are exhibited in the spectrum as broad signals at 6.70 and 6.87 ppm. $C_{37}H_{36}O_4$ m/z: 545.30 (37.52), 544.29 (100), 503.23 (28.44), 462.18 (8.20), 421.15 (13.86), 250.12 (11.40), 211.10 (27.94). Calculated value m/z = 544.2608, measured value m/z = 544.2605.

O$^{1'}$,O^{11}-didihydrobetulonoylriccardin C (15) was obtained in a similar manner as compounds **8** and **9**. Riccardin C: 0.047 g (0.11 mmol); chloroanhydride of dihydrobetulonic acid: 0.1 g (0.22 mmol) [13]; triethylamine: 0.07 g (0.7 mmol); DMAP: two crystals. The monitoring of the course of the reaction was carried out employing a TLC method. After treatment and chromatography (hexane as an eluent with a gradient of chloroform; the ratio reaction mixture : SiO_2 = 1 : 35) we have isolated 0.049 g of compound **15** (34 %) (Scheme 3).

^{1}H NMR spectrum of ester **15**, δ, ppm (J, Hz): 0.74, 0.79, 0.81, 0.87 all d (2C$^{28''}$H$_3$, 2C$^{29''}$H$_3$, J 6.8), 0.85 s, 0.93 s, 0.96 s, 0.98 s, 1.01 s (double intensity), 1.02 s, 1.03 s, 1.06 s, 1.07 s (10 CH$_3$ groups), 2.57–2.83 m (2H$^{7'}$, 2H$^{8'}$, H^{8a}), 2.87 m and 2.94 m (2H^{7}), 3.09 m (H^{8b}), 4.81 br s (13′-OH), 5.47 d (H$^{3'}$, $J_{3',5'}$ 1.9), 6.22 br s (H$^{10'}$), 6.40 br. s (H$^{14'}$), 6.78 d (H$^{11'}$, $J_{11',10'}$ 7.6), 6.80 dd (H$^{5'}$, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.9), 6.91 d (H$^{6''}$, $J_{6',5'}$ 8.1), 6.98 dd (H^{12}, $J_{12,13}$ 8.4, $J_{12,10}$ 2.4), 7.13 d (H^{10}, $J_{10,12}$ 2.4), 7.17 d (H^{13}, $J_{13,12}$ 8.4). Protons H^{2}, H^{3}, H^{5}



15

Scheme 3.

and H^6 are exhibited in the spectrum as very wide signals within the range of 6.65–6.93 ppm. The signals from protons of two residues of the derivatives of betulonic acid are exhibited as overlapped multiplets within the range of 0.88–2.55 ppm. $C_{88}H_{116}O_8$ *m/z* [M+Na] 1323.

CONCLUSION

In this work we have performed the chemical modifying of a naturally occurring phenolic compound riccardin C, isolated from *Primula macrocalyx* Bge. exhibiting the activity concerning the inhibition of NO synthase. Esters and ethers **4–15** are obtained *via* the interaction between initial compound **1** with various halogenides and halogenoanhydrides acids in the presence of bases. The structure of new compounds **4–15** has been confirmed by ^1H, ^{13}C NMR spectral data and mass spectrometry.

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