Stereospecific synthesis of *endo-endo*-3,7-dioxabicyclo[3.3.0]octane lignans using 1,6-bis(dipropylboryl)-2,4-hexadiene*

*A. N. Anfimov,[a] S. Yu. Erdyakov,[a]† M. E. Gurskii,[a] and Yu. N. Bubnov[a,b]**

[a]*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5328. E-mail: bor@ioc.ac.ru*
[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5085. E-mail: bubnov@ineos.ac.ru*

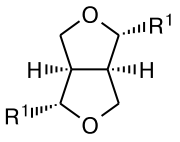
A general methodology for the stereoselective synthesis of compounds of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane series was developed. The strategy includes allylboration of aromatic aldehydes with 1,6-bis(dialkylboryl)-2,4-hexadiene, ozonolysis of the thus obtained 1,4-diaryl-2,3-divinyl-1,4-diols, and subsequent intramolecular cyclization. This methodology was used for obtaining the naturally occurring lignans of the furofuran series, *viz.*, diaeudesmin, diayangambin, epiasarinin, epieudesmin, epiyangambin, and asarinin.

Key words: allylboration, diallyl diboranes, ozonolysis, furofuran lignans.

3,7-Dioxabicyclo[3.3.0]octane compounds are the basic structural fragments of naturally occurring lignans of the furofuran series,[1] one of the main classes of phytoestrogenes produced by many plants.

Due to the wide range of biological activity,[2] antitumor, antiviral, antioxidant, immunosuppressant, antiinflammatory, hypotensive effect, *etc.*, they attract attention of chemists and biologists,[3—5] and their directed synthesis presented a challenging task.[6—8]

The purpose of the present work was to use the products of allylboration reaction (with compounds containing two boronallyl fragments in the molecule) as the starting compounds for the synthesis of 3,7-dioxabicyclo-[3.3.0]octanes.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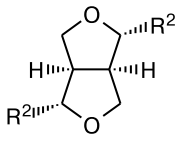
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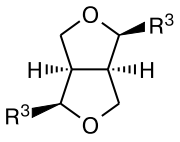
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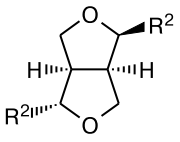
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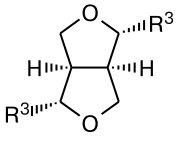
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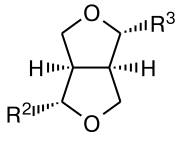
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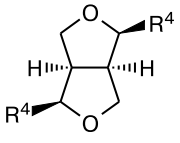
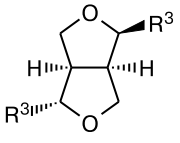
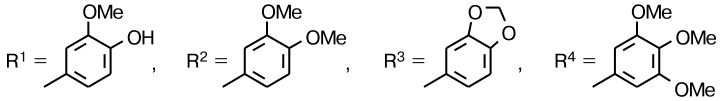

Diayangambin


Asarinin



* Dedicated to Academician of the Russian Academy of Sciences O. M. Nefedov on the occasion of his 80th birthday.
† Deceased.

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Results and Discussion

We have recently found[9] that the reaction of 1,6-bis-(dipropylboryl)-2,4-hexadiene (**1**) with aromatic aldehydes readily proceeds at −78 °C and after oxidative deboration (H_2O_2/OH^-) leads to a mixture of diastereomeric 1,4-diaryl-*d,l*-2,3-divinyl-1,4-butanediols **2** and **3** in total 70—80% yields (Scheme 1), which are easy separated by column chromatography. Using NMR spectroscopy and X-ray crystallography we established that one of the products (**2**) contains two *anti*-homoallyl fragments, whereas another one (**3**) has both the *anti*- and the *syn*-homoallyl fragments.

We also showed that the reaction of 1,6-bis(dipropylboryl)-2,4-hexadiene **1** with 3,4-dimethoxybenzaldehyde in the ratio 1 : 1 proceeds diastereoselectively, quantitatively leading (after oxidation) to only a single diastereomer (**2**) of the (1*R**,2*S**,3*S**,4*R**)-configuration.

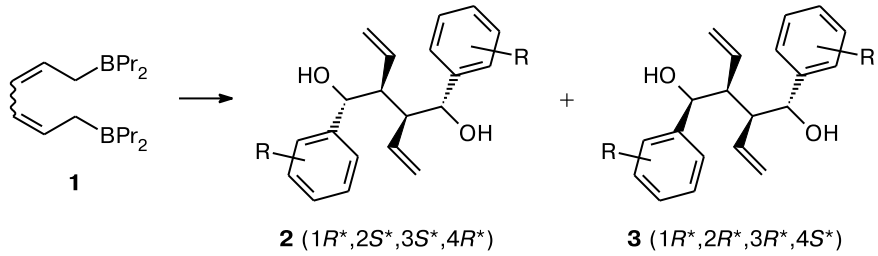
This paper describes methodology for the synthesis of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane systems with the *endo-endo*- and *endo-exo*-arrangement of aryl substituents with respect to the furofuran ring. Unsaturated diols **2** with the relative (1*R**,2*S**,3*S**,4*R**)-configuration were used as the starting compounds for the synthesis.

Scheme 2 shows a retro-synthetic analysis of the approach to the construction of a furofuran core.

To create the 3,7-dioxabicyclo[3.3.0]octane system, we suggested to use a reaction of electrophilic halocyclization (in particular, iodocyclization). As it has been shown previously, this reaction smoothly proceeds for the products of allylboration of aliphatic ketones with 1,6-bis-(dipropylboryl)-2,4-hexadiene.[10] The cyclization stereospecifically leads to 3,7-dioxabicyclo[3.3.0]octane derivatives with the *endo*-arrangement of the iodomethyl groups and the *cis*-annulation of the rings.

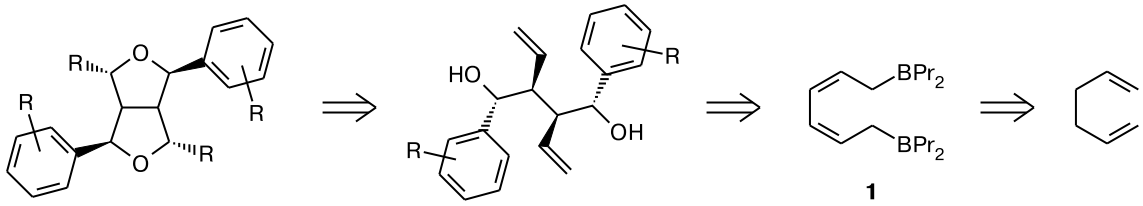
However, we did not succeed in carrying out this reaction with aromatic bis-homoallylic alcohols **2a**—**e** (Scheme 3).

Scheme 1

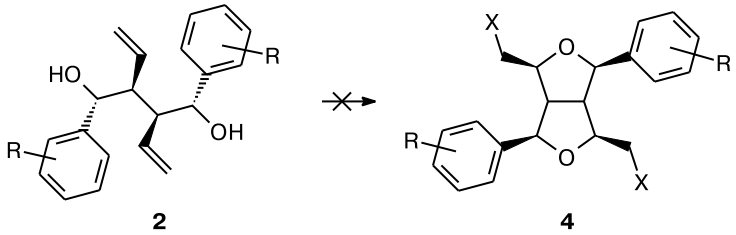


Reagents and conditions: 1) ArCOH, −78—20 °C; 2) H_2O_2, OH^-, 5 °C.

Scheme 2



Scheme 3



X = I, Br

Reagents: I_2, $NaHCO_3$ or NBS.

By all accounts, the failure seems to be caused by steric hindrance for the second ring closure to occur. Therefore, we developed an alternative synthetic strategy based on the direct ozonolysis of unsaturated diols **2**.

Ozonolysis was performed under conditions standard for such reactions: ozone was bubbled through the solution of unsaturated diol dissolved in CH_2Cl_2 at −78 °C. The reaction progress was monitored by TLC. After the reaction reached completion, the system was purged with argon and treated with Me_2S or PPh_3. Bislactols (4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octanes) **6a—f** were isolated by flash-chromatography on SiO_2 in total 30—50% yields (Scheme 4).

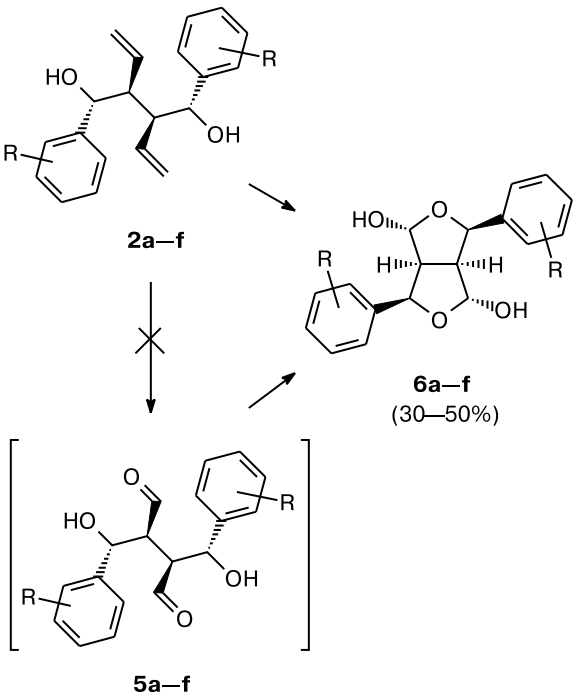
The structures of compounds **6a—f** were confirmed by elemental analysis and ^1H and ^{13}C NMR spectroscopy (Tables 1 and 2). It should be noted that this is the first example of obtaining furofuran systems using an ozonolysis reaction.

Initially we suggested that dicarbonyldihydroxy derivatives **5a—f** were formed in the process of ozonolysis, which further spontaneously undergo intramolecular cyclization to the corresponding bislactols due to the higher stability of the cyclic product.[11,12] Such a type of the ring-chain tautomerism is well known for γ-hydroxycarbonyl compounds.[13] However, analysis of the IR and NMR spectra showed that no tautomerism is observed for compounds **6a—f** either on heating, or on the solvent change. Moreover, ozonolysis of **2a** using $NaBH_4$ as a reducing agent did not lead to tetraol **7**, the compound **6a** was obtained instead, likewise on the reduction with PPh_3 and Me_2S (Scheme 5).

Results obtained for different conditions of ozonolysis and for different reducing agents allowed us to suggest the following mechanism of formation of bislactols **6a—f** (Scheme 6). It seems that the "molecular diozonide" **8** is formed initially, which is transformed to dihydroperoxide compound **10** *via* the intermediate **9**.

This reaction sequence is based on the mechanism concept for the reaction of ozone with olefins in the presence of alcohols and carboxylic acids,[14,15] which leads to alkoxy- and acyloxyhydroperoxides. Reduction of the peroxide compounds **10** gives 4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octanes **6**.

Scheme 4



R = 4-Br (**a**), 3,4-$(MeO)_2$ (**b**), 3-NO_2 (**c**), 3,5-$(MeO)_2$ (**d**), 3,4,5-$(MeO)_3$ (**e**), 3,4-(OCH_2O) (**f**)

Reagents and conditions: 1) O_3, CH_2Cl_2, −78 °C; 2) Me_2S or PPh_3, −78—20 °C.

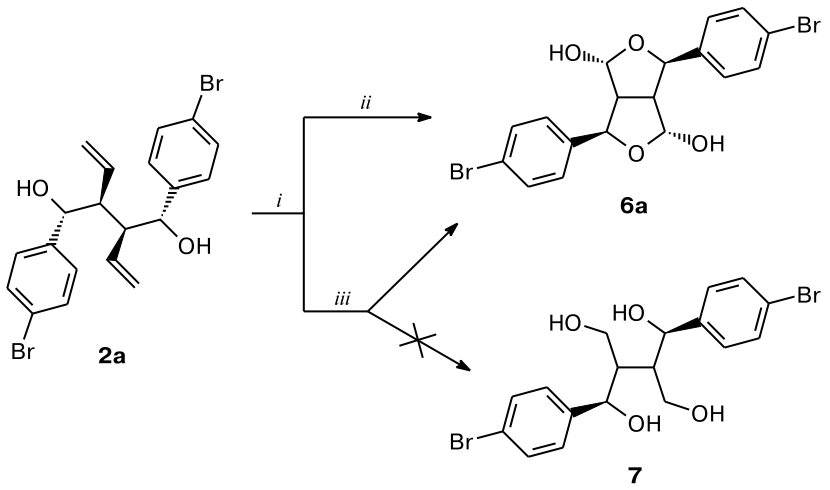
The aryl substituents in lactols **6** are in the *endo-endo*-positions with respect to the furofuran ring, whereas the hydroxy groups are in the *exo*-positions.

Using a standard procedure[16,17] (treatment with triethylsilane in the presence of boron trifluoride diethyl etherate), bislactols **6b**, **6e** and **6f** were converted to the corresponding naturally occurring lignans diaeudesmin, diayangambin, and epiasarinin (Scheme 7). Diayangambin, for example, was isolated[18] from leaves of the

Table 1. ^1H NMR chemical shifts for lactols **6a—f**

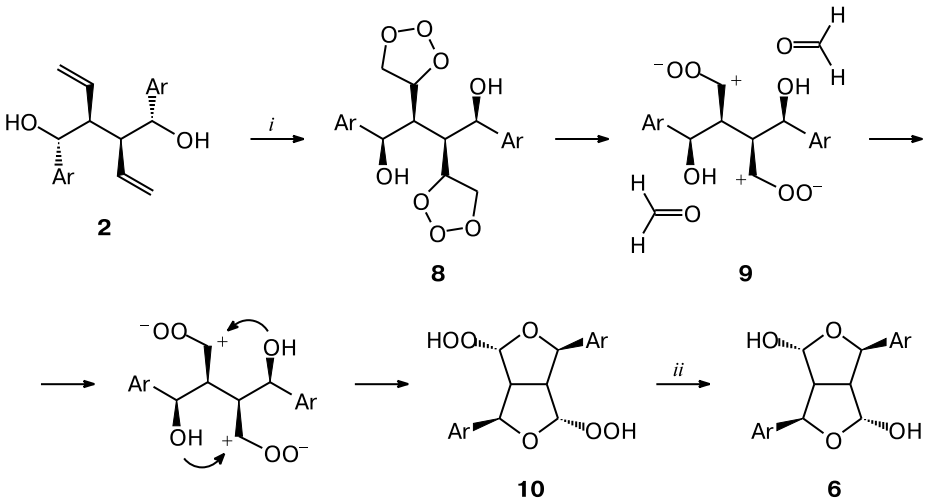
Compound		δ				Yield (%)
		H(1), H(5) (m)	H(2), H(6) (br.s)	H(4), H(8) (m)	Other	
6a	CD_3OD	3.15	4.81	5.4	7.27, 7.48	45
6b	CD_3OD	2.47	5.1	5.5	3.9, 6.9	43
6c	$(CD_3)_2SO$	3.32	4.77	5.56	6.32, 7.80, 7.91, 8.24, 8.28	54
6d	$CDCl_3$	3.24	5.1	5.48	3.8, 6.39, 6.52	39
6e	$CDCl_3$	3.20	5.05	5.45	3.83, 3.86, 6.61	40
6f	$CDCl_3$	3.00	4.76	5.28	6.03, 6.83—6.96	29

Scheme 5



Reagents and conditions: *i*. O_3, CH_2Cl_2, −78 °C; *ii*. Me_2S or PPh_3, −78—20 °C; *iii*. $NaBH_4$, −78—20 °C.

Scheme 6

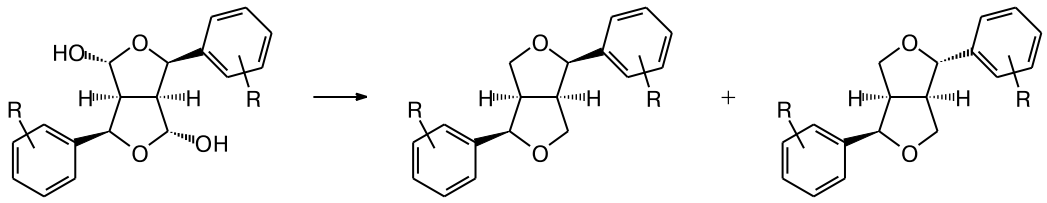


Reagents and conditions: *i*. O_3, CH_2Cl_2, −78 °C; *ii*. Me_2S (PPh_3, $NaBH_4$), −78—0 °C.

Table 2. ^{13}C NMR chemical shifts for lactols **6a—f**

Compound	Solvent	δ				Yield (%)
		C(1), C(5)	C(2), C(6)	C(4), C(8)	Other	
6a	CD_3OD	57.3	80.7	99.6	121.2, 129.1, 132.5, 139.4	45
6b	CD_3OD	55.8	80.2	98.0	55.7, 55.9, 109.2, 111.1, 118.3, 130.6, 148.3, 148.9	43
6c	$(CD_3)_2SO$	60.9	83.4	103.1	125.8, 127.6, 135.3, 138.0, 146.6, 153.1	52
6d	$CDCl_3$	68.1	80.3	99.0	99.6, 104.0, 140.7, 161.0	39
6e	$CDCl_3$	61.0	80.2	98.7	103.6, 134.2, 145.6, 153.3	52
6f	$CDCl_3$	55.7	80.1	98.4	101.4, 106.9, 108.3, 119.4, 132.1, 146.8, 147.8	29

Scheme 7



6b,e,f **11b,e,f** **12b,e,f**

Compound	R	Products	Total yield of products (%)	Ratio **11** : **12**
b	3,4-$(MeO)_2$	(±)-Diaeudesmin (**11b**) (±)-Epieudesmin (**12b**)	73	65 : 35
e	3,4,5-$(MeO)_3$	(±)-Diayangambin (**11e**) (±)-Epiyangambin (**12e**)	68	70 : 30
f	3,4-$(OCH_2O)_2$	(±)-Epiasarinin (**11f**) (±)-Asarinin (**12f**)	75	68 : 32

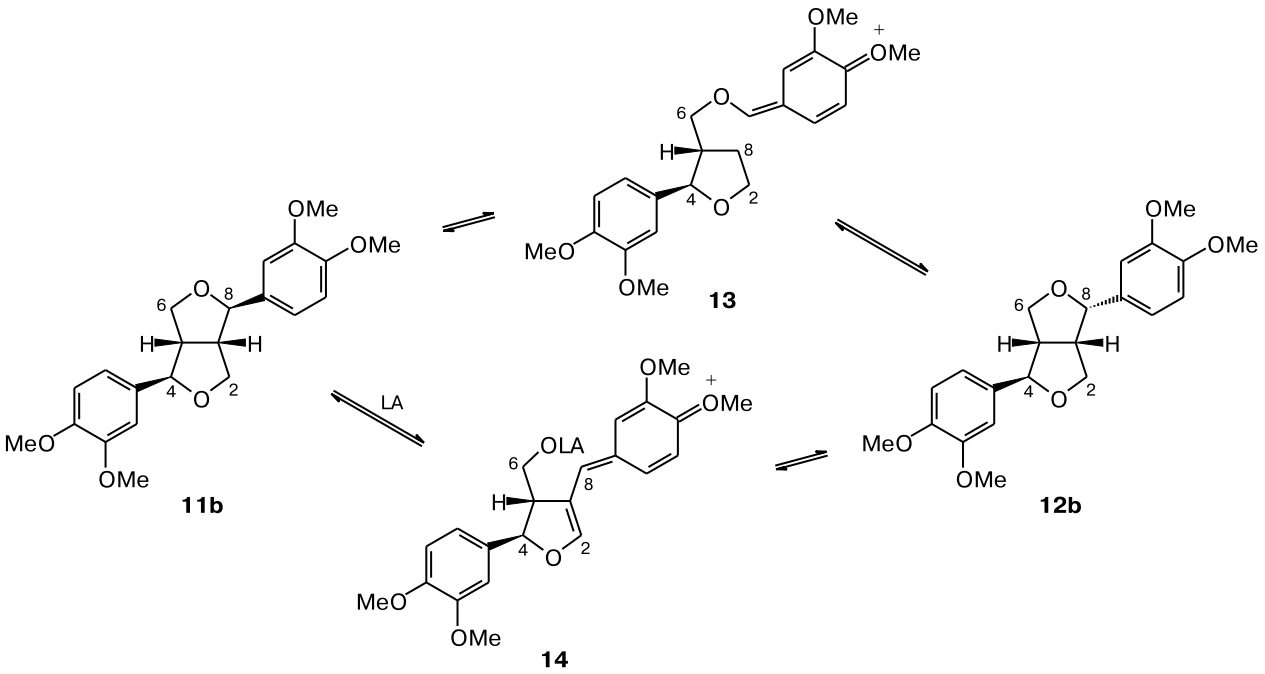
Reagents and conditions: 1)Et_3SiH_2, −78 °C; 2) $Et_2O \cdot BF_3$, −40 °C.

Pepper family plant, *Piper fimbriulatum C.DC.,* growing in Panama; this compound possesses immunosuppressant and antiinflammatory effects.[19] The ^1H and ^{13}C NMR spectral data of the synthesized natural compounds are identical to those given in the literature.[20]

The reduction of lactols of the *endo-endo*-series is accompanied by a partial epimerization of one of the C—Ar chiral centers, giving rise to the lignans of the *endo-exo*-series **12**: epiyangambin, epieudesmin, and asarinin, the compounds produced by different plants. The epimerization seems to occur by means of the C(1)—C(8) or C(4)—C(5) bond cleavage with the formation of the intermediate oxonium cation **13**, which undergoes recyclization to more stable isomer of the *endo-exo*-series.[21] The epimerization can also take place through the compound **14**, whose formaztion is facilitated by the electron-donating groups on the phenyl rings. This high-energy process takes place only at temperatures higher −78 °C (Scheme 8).

In conclusion, we have developed an efficient approach to the furofuran structures based on simple reagents, such as aromatic aldehydes and 1,6-bis(dipropylboryl)-2,4-hexadiene, easy generated from diallyl. At the present, the

Scheme 8



11b **13** **12b** **14**

LA is the Lewis acid

enantioselective version of this reaction using optically active organoboron compounds is underway.

Experimental

^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AC-200 spectrometer (200.13 MHz for ^1H, 50.32 MHz for ^{13}C, and 188.31 MHz for ^{19}F) in $CDCl_3$ and CD_3OD. Mass spectra were recorded on a Finnigan LC instrument (EI-MS). Thin-layer chromatography was performed on Silufol UV-254 plates. Ozonolysis was performed by bubbling the oxygen—ozone gas mixture (3 mL min^{-1}, 0.775 mmol min^{-1} of ozone).

Allylboration of carbonyl compounds (general procedure for the preparation of compounds 2a—e). An anhydrous carbonyl compound (2.2 mol-equiv.) was added to a solution of diallyl diboron compound **1** (1 mol-equiv.) in anhydrous diethyl ether at −78 °C. After the mixture warmed-up to room temperature, it was sequentially treated with 10% aqueous NaOH (4.2 mol-equiv.) and 30% aq. H_2O_2 (4.5 mol-equiv.) at 5—10 °C and refluxed for 3 h. After extraction with diethyl ether, drying with Na_2SO_4, and evaporation of the solvent at reduced pressure, a dry residue was obtained, which was a mixture of two diastereomers, in total 65—85% yields. The diastereomers obtained were separated by column chromatography (ethyl acetate — hexane).

Ozonolysis (general procedure for the preparation of compounds 6a—e). Ozone was bubbled through the solution of γ,δ-unsaturated diol dissolved in CH_2Cl_2 at −78 °C. The reaction progress was monitored by TLC. The ozone bubbling was stopped when TLC analysis showed the absence of the starting compound in the system, then the system was purged with argon for 60 min and treated with Me_2S. The reaction mixture was further stirred at −78 °C for 60 min and at −50 °C for 120 min and then was let to warm-up to room temperature. The solvent was evaporated *in vacuo*, a precipitate formed was dissolved in CH_2Cl_2, washed with water, and dried with Na_2SO_4. Flash-chromatography on SiO_2 gave products in total 30—50% yields.

2,6-Bis(4-bromophenyl)-4,8-dihydroxy-3,7-dioxabicyclo-[3.3.0]octane (6a). The yield was 45%. White crystalline compound. Found (%): C, 53.25; H, 4.31. $C_{20}H_{20}O_2Br_2$. Calculated (%): C, 53.12; H, 4.46. ^1H NMR (200.13 MHz, $CDCl_3$), δ: 3.15 (m, 2 H, H(1), H(5)); 5.03 (br.s, 2 H, H(2), H(6)); 5.45—5.55 (m, 2 H, H(4), H(8)); 7.26 (d, 4 H, H(2′), H(2″), H(6′), H(6″), arom., J = 8.1 Hz); 7.48 (d, 4 H, H(3′), H(3″), H(5′), H(5″) arom., J = 8.1 Hz). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 57.3 (C(1), C(5)); 80.7 (C(2), C(6)); 99.6 (C(4), C(8)); 122.1 (C(4′), C(4″) arom.); 129.1 (C(2′), C(2″), C(6′), C(6″), arom.); 132.5 (C(3′), C(3″), C(5′), C(5″), arom.); 139.4 (C(1′), C(1″), arom.).

2,6-Bis(3,4-dimethoxyphenyl)-4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octane (6b). The yield was 43%. White crystalline compound, m.p. 168—170 °C. Found (%): C, 69.60; H, 7.50. $C_{24}H_{30}O_6$. Calculated (%): C, 69.54; H, 7.30. ^1H NMR (200.13 MHz, $CDCl_3$), δ: 2.47 (br.s, 2 H, OH); 3.15—3.30 (m, 2 H, H(1), H(5)); 3.88, 3.90 (both s, 12 H, OMe); 5.10 (br.s, 2 H, H(2), H(6)); 5.45—5.55 (m, 2 H, H(4), H(8)); 6.80—7.05 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 55.7, 55.9 (OMe); 55.8 (C(1), C(5)); 80.2 (C(2), C(6)); 98.0 (C(4), C(8)); 109.2 (C(2′), C(2″), arom.); 111.1 (C(3′), C(3″), arom.); 118.3 (C(6′), C(6″), arom.); 160.6 (C(1′), C(1″), arom.); 148.3, 148.9 (C(4′), C(4″), C(5′), C(5″), arom.).

2,6-Bis(3-nitrophenyl)-4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]-octane (6c). The yield was 54%. Light yellow crystalline compound, m.p. 208—209 °C. Found (%): C, 62.62; H, 5.30; N, 7.13. $C_{20}H_{20}O_2N_2$. Calculated (%): C, 62.49; H, 5.24; N, 7.29. ^1H NMR (200.13 MHz, $(CD_3)_2SO$), δ: 3.27—3.37 (m, 2 H, H(1), H(5)); 4.72—4.83 (m, 2 H, H(2), H(6)); 5.51—5.61 (m, 2 H, H(4), H(8)); 6.32 (d, 2 H, OH, J = 4.3 Hz); 7.80—8.28 (m, 8 H, arom.). ^{13}C NMR (50.32 MHz, $(CD_3)_2SO$), δ: 60.9 (C(1), C(5)); 83.4 (C(2), C(6)); 103.1 (C(4), C(8)); 125.8, 127.6, 135.3, 138.0, 146.6, 153.1 (arom).

2,6-Bis(3,5-dimethoxyphenyl)-4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octane (6d). The yield was 39%. White oil. Found (%): C, 76.30; H, 7.00. $C_{24}H_{26}O_4$. Calculated (%): C, 76.17; H, 6.92. ^1H NMR (200.13 MHz, $CDCl_3$), δ: 3.19—3.29 (m, 2 H, H(1), H(5)); 3.80, 3.81 (both s, 12 H, OMe); 5.1 (br.s, 2 H, H(2), H(6)); 5.43—5.53 (m, 2 H, H(4), H(8)); 6.39, 6.55 (both s, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3OD), δ: 55.5 (OMe); 68.1 (C(1), C(5)); 80.3 (C(2), C(6)); 99.0, 99.6 (C(4), C(8), C(4′), C(4″), arom.); 104.0 (C(2′), C(2″), arom.); 140.7 (C(1′), C(1″), arom.); 161.0 (C(3′), C(3″), C(5′), C(5″), arom.).

2,6-Bis(3,4,5-trimethoxyphenyl)-4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octane (6e). The yield was 40%. White crystalline compound. Found (%): C, 66.00; H, 7.02. $C_{26}H_{34}O_8$. Calculated (%): C, 65.81; H, 7.22. ^1H NMR (200.13 MHz, $CDCl_3$), δ: 2.47 (br.s, 2 H, OH); 3.20 (m, 2 H, H(1), H(5)); 3.83, 3.86 (both s, 18 H, OMe); 5.05 (br.s, 2 H, H(2), H(6)); 5.45 (m, 2 H, H(4), H(8)); 6.61 (s, 4 H, arom.). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 55.8, 56.1 (OMe); 61.0 (C(1), C(5)); 80.2 (C(2), C(6)); 98.7 (C(4), C(8)); 103.6 (C(2′), C(2″), C(6′), C(6″), arom.); 134.2 (C(1′), C(1″), arom.); 145.6 (C(4′), C(4″), arom.); 153.3 (C(3′), C(3″), C(5′), C(5″), arom.).

2,6-Bis(3,4-methylenedioxyphenyl)-4,8-dihydroxy-3,7-dioxabicyclo[3.3.0]octane (6f). The yield was 29%. White oil. Found (%): C, 62.00; H, 4.80. $C_{20}H_{22}O_2$. Calculated (%): C, 62.17; H, 4.70. ^1H NMR (200.13 MHz, $CDCl_3$), δ: 3.25—3.35 (m, 2 H, H(1), H(5)); 4.76 (br.s, 2 H, H(2), H(6)); 5.23—5.33 (m, 2 H, H(4), H(8)); 6.03 (s, 4 H, OCH_2O, arom.); 6.83—6.96 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, $CDCl_3$), δ: 55.7 (C(1), C(5)); 80.1 (C(2), C(6)); 98.4 (C(4), C(8)); 101.4 (OCH_2O, arom.); 106.9, 108.3 (C(2′), C(2″), C(5′), C(5″), arom.); 119.4 (C(6′), C(6″), arom.); 132.1 (C(1′), C(1″), arom.); 146.8, 147.7 (C(3′), C(3″), C(4′), C(4″), arom.).

Preparation of compounds 11 and 12 (dehydroxylation, general procedure). Triethylsilane (8 mol-equiv.) was slowly added to a solution of lactol in dichloromethane at −78 °C under argon. The solution that obtained was stirred for 10 min at the same temperature, followed by slow addition of boron trifluoride diethyl etherate (10 mol-equiv.) and stirring the thus obtained solution for 30 min. Then, the mixture was treated with saturated aq. $NaHCO_3$ at −20 °C. After extraction with EtOAc, drying with Na_2SO_4, and evaporation of the solvent at reduced pressure, a dry residue was obtained, which was purified by flash-chromatography on SiO_2 (diethyl ether—hexane—triethylamine, 25 : 75 : 1).

2,6-Bis(3,4-dimethoxyphenyl)-3,7-dioxabicyclo[3.3.0]-octane, diaeudesmin (11b). Colorless oil. Found (%): C, 68.60; H, 6.90. $C_{22}H_{26}O_6$. Calculated (%): C, 68.38; H, 6.78. ^1H NMR (200.13 MHz, CD_3Cl), δ: 3.10—3.25 (m, 2 H, H(1), H(5)); 3.45—3.51, 3.70—3.80 (both m, 4 H, H(4), H(8)); 3.90, 3.95 (both s, 12 H, OMe); 4.92 (d, 2 H, H(2), H(6), J = 5.0 Hz); 6.85—7.00 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 49.4 (C(1), C(5)); 55.84 (OCH_3); 68.7 (C(4), C(8)); 83.9 (C(2),

C(6)); 109.6 (C(2′), C(2″), arom.); 110.9 (C(5′), C(5″), arom.); 118.4 (C(6′), C(6″), arom.); 131.4 (C(1′), C(1″), arom.); 148.0 (C(3′), C(3″), arom.); 148.7 (C(4′), C(4″), arom.).

2,6-Bis(3,4,5-trimethoxyphenyl)-3,7-dioxabicyclo[3.3.0]-octane, diayangambin (11e). Colorless oil. Found (%): C, 64.35; H, 6.94. $C_{24}H_{30}O_8$. Calculated (%): C, 64.56; H, 6.77. ^{1}H NMR (200.13 MHz, CD_3Cl), δ: 3.16—3.26 (m, 2 H, H(1), H(5)); 3.45—3.60, 3.75—3.83 (both m, 4 H, H(4), H(8)); 3.85, 3.89 (both s, 12 H, OMe); 4.92 (d, 2 H, H(2), H(6), J = 4.9 Hz); 6.61 (s, 4 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 49.4 (C(1), H(5)); 56.00, 60.1 (OCH_3); 68.8 (C(4), C(8)); 84.0 (C(2), C(6)); 103.0 (C(2′), C(2″), C(6′), C(6″), arom.); 134.5 (C(1′), C(1″), arom.); 136.9 (C(4′), C(4″), arom.); 153.2 (C(3′), C(3″), C(5′), C(5″), arom.).

2,6-Bis(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]-octane, epiasarinin (11f). Colorless oil. Found (%): C, 75.34; H, 6.44. $C_{22}H_{22}O_4$. Calculated (%): C, 75.41; H, 6.33. ^{1}H NMR (200.13 MHz, CD_3Cl), δ: 3.08—3.16 (m, 2 H, H(1), H(5)); 3.47—3.57, 3.67—3.77 (both m, 4 H, H(4), H(8)); 4.87 (d, 2 H, H(2), H(6), J = 5.0 Hz); 5.97 (s, 4 H, OCH_2O, arom.); 6.82—6.89 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 49.5 (C(1), C(5)); 68.7 (C(4), C(8)); 84.1 (C(2), C(6)); 100.9 (OCH_2O, arom.); 107.1, 108,1 (C(2′), C(2″), C(4′), C(4″), arom.); 119.5 (C(6′), C(6″), arom.); 132.1 (C(1′), C(1″), arom.); 146.7, 146.7 (C(3′), C(3″), C(4′), C(4″), arom.).

2,6-Bis(3,4-dimethoxyphenyl)-3,7-dioxabicyclo[3.3.0]oct-ane, epieudesmin (12b). Colorless oil. Found (%): C, 68.70; H, 6.60. $C_{22}H_{26}O_6$. Calculated (%): C, 68.38; H, 6.78. ^{1}H NMR (200.13 MHz, CD_3Cl), δ: 2.85—3.00 (m, 1 H, H(1)); 3.30—3.45 (m, 2 H, H(5), $H(4_{ax})$); 3.75—3.95 (m, 2 H, $H(4_{eq})$, $H(8_{ax})$); 3.85—3.97 (m, 12 H, OCH_3); 4.14 (m, 1 H, $H(8_{eq})$); 4.46 (d, 1 H, H(2), J = 7.0 Hz); 4.89 (d, 1 H, H(6), J = 5.6 Hz); 6.92—7.00 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 50.4 (C(5)); 54.7 (C(1)); 56.1 (OCH_3); 70.0 (C(4)); 71.2 (C(8)); 82.3 (C(6)); 87.9 (C(2)); 109.2, 109.4, 111.2, 117.9, 118.7, 131.2, 133.9, 148.2, 149.0, 149.1, 149.5, arom.

2,6-Bis(3,4,5-trimethoxyphenyl)-3,7-dioxabicyclo[3.3.0]oct-ane, epiyangambin (12e). Colorless oil. Found (%): C, 64.85; H, 6.34. $C_{24}H_{30}O_8$. Calculated (%): C, 64.56; H, 6.77. ^{1}H NMR (200.13 MHz, CD_3Cl), δ: 2.90—3.00 (m, 1 H, H(1)); 3.27—3.37 (m, 2 H, $H(4_{eq})$, H(5)); 3.87—3.89 (m, 18 H, OCH_3); 3.90—4.00 (m, 2 H, $H(4_{ax})$, $H(8_{eq})$); 4.12—4.22 (m, 1 H, $H(8_{ax})$); 4.45 (d, 1 H, H(2), J = 7.0 Hz); 4.84 (d, 1 H, H(6), J = 5.0 Hz); 6.52—6.62 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 49.5 (C(5)); 54.4 (C(1)); 56.2 (4 OCH_3); 60.2 (OCH_3); 69.2 (C(4)); 71.0 (C(8)); 82.1 (C(6)); 87.6 (C(2)); 102.7, 103.0, 137.0, 137.6, 153.1, 153.3 (arom.).

2,6-Bis(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]-octane, asarinin (12f). Colorless oil. Found (%): C, 75.30; H, 6.34. $C_{22}H_{22}O_4$. Calculated (%): C, 75.41; H, 6.33. ^{1}H NMR (200.13 MHz, CD_3Cl), δ: 2.80—2.90 (m, 1 H, H(1)); 3.25—3.35 (m, 2 H, $H(4_{eq})$, H(5)); 3.78—3.88 (m, 2 H, $H(4_{ax})$, $H(8_{eq})$); 4.02—4.14 (m, 1 H, $H(8_{ax})$); 4.39 (d, 1 H, H(6), J = 6.8 Hz); 4.83 (d, 1 H, H(2), J = 5.2 Hz); 5.95, 5.96 (both s, 4 H, OCH_2O, arom.); 6.75—6.85 (m, 6 H, arom.). ^{13}C NMR (50.32 MHz, CD_3Cl), δ: 50.1 (C(5)); 54.6 (C(1)); 69.7 (C(8)); 70.9 (C(4)); 82.0 (C(6)); 87.6 (C(2)); 100.9, 101.0 (OCH_2O, arom.); 106.4, 106.5, 108.5, 118.7, 119.6, 132.2, 135.0, 146.5, 147.9 (arom.).

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References

1. R. S. Ward, *Nat. Prod. Rep*. 1995, **12**, 183.
2. W. D. MacRae, G. H. N. Towers, *Phytochemistry*, 1984, **23**, 1207.
3. S. Iwakami, Jin-Bin Wu, Y. Ebizuka, U. Sankawa, *Chem. Pharm. Bull.*, 1992, **40** (5), 1196.
4. M. W. Biavatti, P. C. Vieira, M. Fa´tima G. F. da Silva, J. B. Fernandes, Ana L. G. Degani, Q. B. Cass, A. B. Schefer, A. G. Ferreira, *Phytochem. Anal.*, 2001, 12, 64.
5. (a) A. Pelter, R. S. Ward, D. J. Watson, P. Collins, I. T. Kay, *J. Chem. Soc., Perkin Trans.*, 1982, **1**, 175; (b) R. C. D. Brown, J. D. Hinks, *Chem. Commun*. 1998, **17**, 1895; (c) R. C. D. Brown, C. J. R. Bataille, G. Bruton, J. D. Hinks, N. A. Swain, *J. Org. Chem*, 2001, **66**, 6719.
6. R. C. D. Brown, C. J. R. Bataille, G. Bruton, J. D. Hinks, N. A. Swain, *J. Org. Chem*., 2001, **66**, 6719.
7. D. J. Aldous, A. J. Dalencüon, P. G. Steel, *Org. Lett.*, 2002, **4**, 1159.
8. M. Pohmakotr, A. Pinsa, T. Mophuang, P. Tuchinda, S. Prabpai, P. Kongsaeree, V. Reutrakul, *J. Org. Chem*., 2006, **71**, 386.
9. A. N. Anfimov, S. Yu. Erdyakov, M. E. Gurskii, A. V. Ignatenko, K. A. Lyssenko, Yu. N. Bubnov, *Mendeleev Commun.*, 2011, **21**, 1.
10. M. E. Gurskii, A. V. Geiderikh, A. V. Ignatenko, Yu. N. Bubnov, *Izv. Akad. Nauk, Ser. Khim*., 1993, 160 [*Russ. Chem. Bull.* (*Engl. Transl.*), 1993, **42**, 144.
11. R. E. Valters, F. Fulop, D. Korbonits, *Advances Heterocyclic Chem.*, 1995, **64**, 251.
12. G. A. Molander, C. Kenny, *J. Org. Chem*., 1988, **53**, 2134.
13. M. Watanabe, N. Harada, *J. Org. Chem*., 1995, **60**, 7372.
14. S. G. Van Ornum, R. M. Champeau, R. Pariza, *Chem. Rev*., 2006, **106**, 2990.
15. (a) S. D. Razumovskii, Yu. Z. Yur´ev, *Neftekhimiya* [*Petrochemistry*], 1966, **6**, 737 (in Russian); (b) S. D. Razumovskii, G. A. Zaikov, *Ozon i ego reaktsii s organicheskimi soedineniyami* [*Ozone and Its Reactions with Organic Compounds*], Nauka, Moscow, 1974, 322 pp. (in Russian).
16. A. Pelter, R. S. Ward, P. Collins, R. Venkateswarlu, I. T. Kay, *J. Chem. Soc., Perkin Trans. 1*, 1985, 587.
17. A. Pelter, R. S. Ward, R. Venkateswarlu, C. Kamakshi, *Tetrahedron*, 1992, **48**, 7209.
18. D. A. Olmedo, N. Nakamura, M. Hattori, M. D. Correa, P. N. Solis, M. P. Gupta, *Lignanos anti-Aedes aegupti de Productos Naturales y sus Aplicaciones* (Chile, 1998, 1—4 de Deciembre).
19. E. J. De Leon, D. A. Olmedo, P. N. Solis, M. P. Gupta, M. C. Terencio, *Planta Med.*, 2002, **68**, 1128.
20. A. Pelter, R. S. Ward, *Tetrahedron*, 1976, **32**, 2783.
21. A. Pelter, R. S. Ward, *Chemistry of Lignans*, Ed. C. B. S. Rao, Andhra University Press, 1978, Ch. 7.

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