SYNTHESIS OF SHIKALKIN AND CERTAIN RELATED COMPOUNDS*

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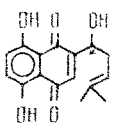
A successful total synthesis of a biologically active pigment from plants of the Boraginaceae family was carried out with naphthazarine as the starting material, and using the 1,4,5,8-tetramethoxynaphthalene, the corresponding 2-vinyl derivative and its epoxide or a cyclopropane adduct with diazoacetic ester at the key stages. In the course of developing the scheme of the synthesis of shikalkin, its three analogs were obtained, differing in the nature of the monoterpenoid side chain.

Keywords: *shikonin, alkannin, shikalkin, naphthazarine, tetramethoxynaphthalene, olefinization according to Wittig, cyclopropyl–carbinylic rearrangement, cerium–ammonium nitrate.*

Naphthoquinoid pigments shikalkin (**1**) and its enantiomers shikonin (*R*) — **1** and alkannin (*S*) — **1**, produced from the plant roots of the *Boraginaceae* family impart a wide spectrum of biological activities to preparation produced from these roots — an antimicrobial [3], antitumorigenic [4], antiburn, and wound-healing activities [5]. Although for medical requirements these compounds are prepared from natural sources or biotechnologically [6], the complexities of the cultivation of shikonin-containing plants and also the carrying out of the biosynthesis process in a callus culture of root cells has encouraged recent interest in the development of routes to its total synthesis [1, 7-11].

The present work, dealing with the synthesis of shikalkin **1**, two of its isomers **2** and **3** differing in the structure of the monoterpenoid side chain, and of cycloshikalkin **4**, follows this aim, showing that compound **1** can be obtained by two independent methods.

To accomplish our purposes we chose a strategy according to which the side chain of the above naphthazarine derivatives is produced by the direct introduction of a homopropenyl substituent into the molecule of a correspondingly functionalized naphthalene, or by successive propagation of this chain in this molecule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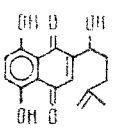
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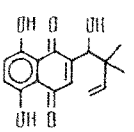
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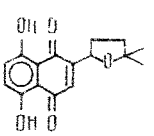
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In the approaches investigated, tetramethoxynaphthalene (**5**) was chosen as the base compound; it was obtained in an overall yield of 52% by successive methylation of naphthazarine with MeI in the presence of Ag_2O in accordance with [12], reduction of the 5,8-dimethoxy-1,4-naphthoquinone formed by $NaBH_4$, and culminating with the methylation of 5,8-dimethoxy-1,4-naphthalenedione with MeI in the presence of NaH.

*For preliminary report, see [1].

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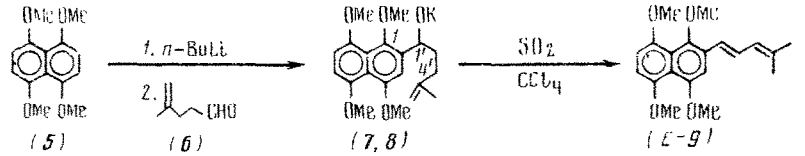
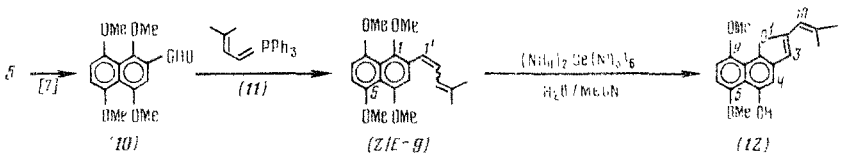


R=H (7); Ac (8).

The *n*-BuLi initiated deprotonation of **5** and the further treatment of the intermediate Li derivative with methylpentanal **6** leads to an oily carbinol **7** in a low yield, characterized in the form of a crystalline acetate **8**. The apparently logical transition from these compounds to the derivative of shikalkin **1** by the transformation of the isopropenyl fragment of the side chain of their molecules into the isopropenylidene fragment, however, proved to be unsuccessful. In particular, on using SO_2 for this purpose, the formation of a 1′*E*,3′-diene (**9**) was noted, in the PMR spectrum of which an SSCC $J_{1,2}$ = 16 Hz was recorded.

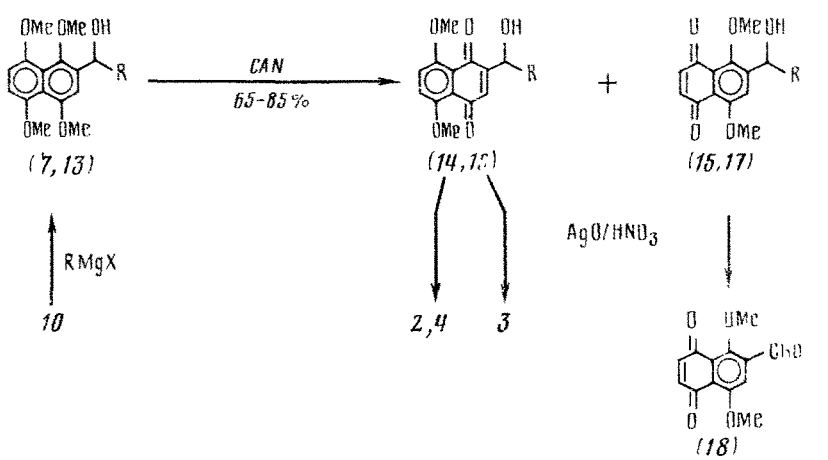
An independent approach to *E*-**9** and its 2′Z-stereoisomer was realized by Wittig-type olefinization of aldehyde **10** [7] obtained from **5** according to the Wilsmeier reaction, by means of phosphorane **11**.



As a result, a mixture of 1′,3′-dienes **9**, *Z*/*E* ≃ 5:2 was obtained, the analysis of the PMR spectrum of which confirms the correctness of the assignment made above for the 1′*E*-component. The two dienes are fairly labile compounds, the demethylation of which by cerium–ammonium nitrate (CAN) in an aqueous MeCN according to [13] leads to the naphthofuran derivative **12** in a moderate yield. The structure of this previously unknown product was confirmed by its elemental and structural analysis data.

Thus, in the IR spectrum of **12** there is a band at ~3195 cm^{-1} of the stretching vibration of the hydroxyl group included in the intramolecular interaction in systems with the methoxy group at C^6. In the PMR spectrum of **12** three signals of the H^3, H^4, and OH group protons at 6.50, 7.00, and 9.46 ppm, respectively, are observed, the last of which was subjected to deutero-exchange.

Considering the above-described difficulties in constructing the molecule of shikalkin **1** from tetramethoxynaphthalene **5** and C_6-aldehyde **6**, we have made a further detailed study of the synthetic possibilities of using aldehyde **10** for this purpose. Thus, its reaction with the Grignard reagent, prepared from isopentenyl bromide or prenyl chloride, gives carbinols **7** and **13**, respectively in high yields.



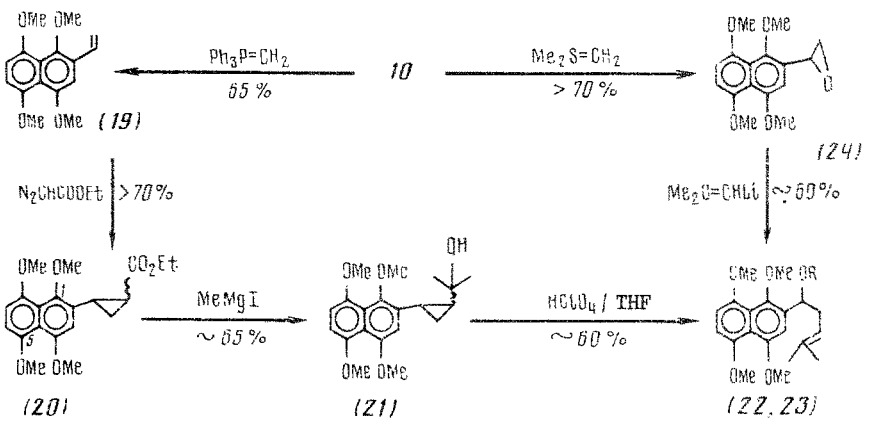
R=$(CH_2)_2CMe{=}CH_2$ (**7**, **14**, **15**); $CMe_2CH{=}CH_2$ (**13**, **16**, **17**).

The oxidative demethylation of tetraethers **7** and **13** by means of CAN under similar conditions to those described in [7, 9] leads, in addition to the expected substituted naphthoquinones **14** and **16**, to the formation of up to 40% of the corresponding structural isomers **15** and **17**, which can be readily separated by flash chromatography on SiO_2. It should be noted that in the case of the tetraether **7** by the action of CAN in addition to the formation of diethers **14** and **15**, an insubstantial amount (~4%) of isoshikalkin **2** is obtained.

The subsequent exhaustive demethylation of these two groups of naphthazarine derivatives carried out using the Corey reagent according to [14] was found to differ sharply in the end results. Thus, α-hydroxyalkenylnaphthoquinones **14** and **16** thus smoothly convert into the corresponding isoshikalkins **2** and **3**, the first of which contains ~25% of chromatographically readily separable known [15] cycloshikalkin **4**. At the same time, benzylcarbinols **15** and **17** under the same conditions undergo an oxidative degradation into aldehyde **18**, whereby the yield of the latter from dimethylvinyl derivative **17** was found to be ~5 times higher than from its regioisomer **15**, which correlates well with the ion-radical mechanism of this reaction [9, 13].

The above-described approach can be considered as fully preparative with respect to α-shikalkin **2**, the yield of which from aldehyde **10** was ~27% for the above-discussed considered three stages. However, in view of the unsuccessful attempts, as in the case of **7** and **8**, to isomerize **2** into shikalkin **1**, further modification of the accepted stagewise scheme of the total synthesis was eventually reduced to the introduction into the molecule of tetraether **5** of a two-carbon fragment, followed by propagation of the side chain into a chain of four atoms previously lacking. For this purpose, from aldehyde **10**, by Wittig-type olefinization, first styrene **19** was obtained, which was successively transformed into a mixture of cyclopropanecarboxylic esters **20** and alcohols **21**.

The cyclopropanylation of styrene **19** proceeds with the formation of a mixture of isomers **20** with a *trans/cis* ratio ≈5:2, which remains unchanged for carbinol **21** (PMR data).

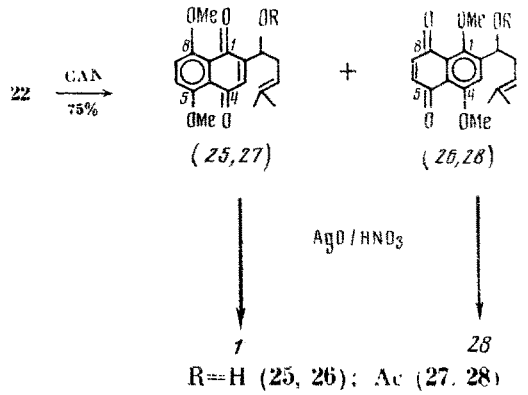


R=H (**22**); Ac (**23**).

The structure of all these previously unknown crystalline compounds was established from the data on their elemental and spectral analyses. In particular, in the PMR spectrum of mixture **21**, the signal of the benzyl-cyclopropane proton of the *trans* isomer appears at δ 2.48 ppm in the form of a doublet of triplets with ΣJ = 18.9 Hz, and of the *cis* isomer at δ 2.23 ppm in the form of a doublet of triplets with ΣJ = 23.8 Hz, which conforms well with the known features of the PMR spectra of cyclopropane derivatives [16].

Under the conditions of [17], $HClO_4$ catalyzed cyclopropyl–carbinyl rearrangement of mixture **21**, or of the individual stereoisomers obtained by chromatography on SiO_2, smoothly gives the homoallyl alcohol **22**, which was additionally characterized in the form of acetate **23**. The structure of these previously unknown compounds was confirmed spectrally, and also by an independent two-step synthesis from aldehyde **10**. Thus, the latter was converted by the action of dimethylsulfonium methylide according to Corey [18] into oxide **14**, which opens up regiospecifically by the action of isobutenyllithium into alcohol **22**, the overall yield of which did not exceed 40%. Demethylation of tetraether **22** by means of CAN leads smoothly, as in the case of **7** and **13**, to a chromatographically separable mixture of diethers **15/16** ≈3:2, which were converted into their acetates **17** and **18**.

It is interesting to note that the cyclopropyl–carbinyl rearrangement of alcohols **21** proceeding under mild conditions by the action of $HClO_4$, is accompanied by a partial (to the extent of ~15%) demethylation of tetraether **22** into derivatives of naphthoquinone **26**, clearly proceeding through the stage of formation of naphthalenediol, which is readily oxidized by atmospheric oxygen.



Similarly to benzylcarbinol **15** its β-regioisomer **26** is split by the action of the Corey reagent, only into dimethoxyaldehyde **18** in a low yield. Correspondingly, under the same conditions, diether **25**, similarly to **16**, smoothly converts into the desired shikalkin **1**, the physicochemical characteristics of which were found to be completely identical to those previously described for the natural product [7].

In the search for optimal conditions of preparation of shikalkin **1**, we also studied the two-step demethylation products of acetate **28**. Thus, from the products of the reaction with CAN, a mixture of acetoxy-diethers **27** and **28** was isolated in a ~75% yield having practically the same composition as recorded for the corresponding diethers **25** and **26** (~3:2; PMR data and flash chromatography on SiO_2). The similar use of MnO_2 impregnated with HNO_3 [19] results only in the formation of the acetoxy-diether **28** in a ~55% yield.

Thus, the eight-step sequence of transformations of naphthazarine → tetraether (**5**) → aldehyde (**10**) → epoxide (**24**) → tetraether (**24**) → diether (**25**) → shikalkin (**1**) was found to be the shortest and most effective of the known approaches [7-9] to a total synthesis of shikalkin. Its overall yield did not exceed 3.5% for the eight stages considered here, whereas in the twelve-step synthesis by Terada et al. it was only ~0.7%.

EXPERIMENTAL

The melting points were measured on a Koffler block. The IR spectra were run in $CHCl_3$ on an IR-75 spectrophotometer. The PMR spectra were measured on a Bruker WM-250 spectrometer in $CDCl_3$, relative to TMS. The mass spectra were obtained on an LKB 9000 spectrometer (70 eV). The R_f values are given for a stationary Silufol brand SiO_2 layer in a hexane–benzene–acetone (2:1:1) system.

5,8-Dimethoxynaphthalene-1,4-diol. A 56 mg portion (1.61 mmoles) of $NaBH_4$ was added to a stirred (Ar) solution of 0.16 g (0.73 mmole) of dimethyl ether of naphthazarine [12] in 32 ml of an ether–ethanol (3:1) mixture at ~25°C. After 2 h, the reaction mixture was decomposed by H_2O, extracted with ether, and the extract was evaporated under vacuum. Yield, 0.15 g (91%) of the desired end product in the form of light-orange needles, mp 168-170°C [from a hexane–acetone (1:1) mixture] (cf. [20]: mp 165.165.5°C]. IR spectrum (ν, cm^{-1}): 1035, 1540, 3520. PMR spectrum (δ, ppm): 3.90 s (6H, MeO), 6.53 s (2H, HC^2, HC^3), 6.76 s (2H, HC^6, HC^7).

1,4,5,8-Tetramethoxynaphthalene (5). A 5 ml portion of MeI (80.32 mmoles) was added to a stirred (Ar) solution of 0.44 g (2.0 mmoles) of the above-obtained diol in 25 ml of DMF at 10°C, and then 0.24 g (10.0 mmoles) of NaH was added in portions. The reaction mixture was stirred for 40 min at ~25°C, and then was decomposed with H_2O and neutralized with 10% HCl. After 3 h, the precipitate was separated and crystallized from hexane. Yield 0.34 g (68%) of **5** in the form of colorless plates, mp 169-170°C (cf. [21]: mp 170°C). IR spectrum (ν, cm^{-1}): 1035, 1550. PMR spectrum (δ, ppm): 3.81 s (12H, MeO), 6.58 s (4H, HC^2, HC^3, HC^6, HC^7).

2-(1′-Hydroxy-4′-methylpent-4′-en-1-yl)-1,4,5,8-tetramethoxynaphthalene (7). A 174 mg portion (1.5 mmoles) of tetramethylenediamine was added to a stirred (Ar) solution of 1.33 mmoles of *n*-BuLi in 1.7 ml of hexane at 25°C. The mixture was cooled to 0°C and treated in the course of 2 min with a solution of 0.31 g (1.25 mmoles) of **5** in 10 ml of ether. The reaction mixture was allowed to stand for 2 h at 0°C, then was treated in the course of 2 min with a solution of 137 mg (1.4 mmoles) of **6** [22] in 5 ml of hexane, and after 30 min was heated for 10 min to 25°C. After 16 h, the reaction mixture was decomposed with H_2O and extracted with ether. The usual treatment of the extract resulted in isolation of 0.36 g of a product,

which was chromatographed on 20 g of SiO_2. Elution with a hexane–acetone (5:1) mixture gave 50 mg (12%) of **7** in the form of a thick yellow oil. R_f 0.31. IR spectrum (ν, cm^{-1}): 1055, 1590, 3610. PMR spectrum (δ, ppm): 1.78 s (3H, CH_3), 2.13 m (4H, $HC^{2'}$, $HC^{3'}$), 3.78 s, 3.91 s, 3.95 s, and 3.96 s (12H, MeO), 4.76 s (2H, $HC^{5'}$), 5.25 m (1H, $HC^{1'}$), 6.83 s (2H, HC^6, HC^7), 7.00 s (1H, HC^3). Found, %: C 69.56; H 7.67. M^+ 346. $C_{20}H_{26}O_5$. Calculated, %: C 69.34; H 7.56; mol. wt. 346.4.

Acetate (8) — light-yellow crystals, mp 45-46°C [from a hexane–benzene (1:1) mixture]. IR spectrum (ν, cm^{-1}): 1070, 1080, 1367, 1630, 1740 (KBr). PMR spectrum (δ, ppm): 1.74 s (3H, CH_3), 2.05 m (4H, $HC^{2'}$, $HC^{3'}$), 2.13 s (3H, CH_3CO), 3.86 s, 3.90 s, 3.95 s and 3.96 s (12H, MeO), 4.75 s (2H, $HC^{5'}$), 6.33 m (1H, $HC^{1'}$), 6.84 s (2H, HC^6, HC^7), 6.87 s (1H, HC^3). Found, %: C 67.99; H 7.11; M^+ 388. $C_{22}H_{28}O_6$. Calculated, %: C 68.02; H 7.26; mol. wt. 388.4.

2-(4'-Methylpenta-1'*E*,3'-dien-1'-yl)-1,4,5,8-tetramethoxynaphthalene (9). A solution of 0.32 g (0.825 mmoles) of **8** in 3.5 ml of CCl_4 and 3.5 ml of SO_2 was held in a sealed tube (Ar) for 72 h at ~25°C, then was evaporated to dryness *in vacuo*, and the residue was chromatographed on 15 g of SiO_2. Elution with a hexane–acetone (10:1) mixture gave 40 mg (15%) of **9** in the form of light-yellow crystals, mp 79-81°C [from a hexane–benzene (1:1)mixture]. IR spectrum (ν, cm^{-1}): 1040, 1586, 1610, 1620. PMR spectrum (δ, ppm, J, Hz): 1.89 d and 1.93 d (6H, CH_3, J = 1.2), 3.75 s, 3.91 s, 3.94 s and 3.98 s (12H, MeO), 6.14 d. quint (1H, $HC^{3'}$, J = 1.2, 1.2 and 7.4), 6.81 d (1H, HC^6, J = 8.7), 6.85 d (1H, HC^7, J = 8.7), 7.01 s (1H, HC^3), 7.04 d.d (1H, HC^2, J = 7.4 and 16.0), 7.05 d (1H, $HC^{1'}$, J = 16.0). Mass spectrum (*m/z*, %): M^+ +1, 329 (13), M^+ 328 (100), 314 (6), 313 (22), 298 (7), 285 (12), 283 (8), 282 (9), 253 (11), 218 (13), 149 (20). Found, %: C 73.21; H 7.34. $C_{20}H_{24}O_4$. Calculated, %: C 73.15; H 7.37; mol. wt. 328.4.

1'*Z*,3'- and 1'*E*,3'-Dienes (9). A solution of 0.97 g (3.51 mmoles) of **10** in 50 ml of THF was added in the course of 20 min to a stirred solution of ylide **9** at −30°C (Ar), prepared at −40°C from 1.31 g (3.57 mmoles) of prenyltriphenylphosphonium chloride [23] in 40 ml of THF and 5 ml of a 0.86 *N* solution of BuLi in hexane (4.3 mmoles). The reaction mixture was stirred for 2 h at 0°C, and then for another 6 h at ~25°C, and after decomposition with H_2O was extracted with ether. Further usual treatment of the mixture gave 1.3 g of a product which was chromatographed on 50 g of SiO_2. Elution with a hexane–acetone (8:1) mixture gave 1.14 g (94%) of a mixture **9**, *Z*/*E* ≈ 5:2 (PMR data). PMR spectrum of 1'Z,3'-diene (**9**)* (δ, ppm, J, Hz): 1.82 d and 1.87 d (6H, CH_3, J = 1.2), 3.73 s, 3.92 s, and 3.94 s (12H, MeO), 6.35 d.quint (1H, $HC^{3'}$, J = 1.2; 1.2 and 11.2), 6.55 t (1H, $HC^{2'}$, J = 11.2), 6.71 d (1H, $HC^{1'}$, J = 11.2), 6.80 d (1H, HC^6, J = 8.7), 6.84 d (1H, HC^7, J = 8.7), 6.99 s (1H, HC^3).

2-(1-Isobutenyl)-6,9-dimethoxy-5-hydroxynaphtho[1,2-b]furan (12). A solution of 2.41 g (4.4 mmoles) of $(NH_4)_2Ce(NO_3)_6$ and 7 ml of H_2O cooled to 3°C was added to a stirred (Ar) solution of 328 mg (1.0 mmole) of *E*-**9** in a mixture of 8 ml of MeCN and 2 ml of H_2O at 0°C. The reaction mixture was stirred for 30 min at 0-3°C, and after diluting with water was extracted with $CHCl_3$. The usual treatment of the extract gave 0.2 g of a product which was chromatographed on 10 g of SiO_2. Elution with a hexane–acetone (8:1) mixture gave 68 mg (23%) of **12** in the form of a yellow oil. R_f 0.64. IR spectrum (ν, cm^{-1}): 1591, 1604, 3195. PMR spectrum (δ, ppm, J, Hz): 1.99 d and 2.28 d (6H, CH_3, J = 1.1), 4.02 s and 4.04 s (6H, MeO), 6.25 quint (1H, HC^{10}, J = 1.1), 6.50 s (1H, HC^3), 6.72 d and 6.80 d (2H, HC^7, HC^8, J = 8.5), 7.00 s (1H, HC^4), 9.46 s (1H, OH). Found, %: C 72.64; H 6.11; M^+ 298. $C_{18}H_{18}O_4$. Calculated, %: C 72.47; H 6.08; mol. wt. 298.3.

Preparation of Alcohol 7 from Aldehyde 10. A solution of 307 mg (1.11 mmoles) of **10** in 20 ml of THF was added in the course of 10 min to a stirred (Ar) solution of a Grignard reagent at −5°C, prepared from 120 mg (4.94 mg-atom) of Mg and 964 mg (6.47 mmoles) of 3-methylbut-3-en-1-yl bromide [24] in 30 ml Et_2O. The reaction mixture was stirred for 30 min at −5°C and for another 1 h at ~25°C, and then was decomposed with H_2O and extracted with ether. After the usual treatment of the extract, 370 mg of a product was obtained which was chromatographed on 15 g of SiO_2. Elution with a hexane–acetone (5:1) mixture gave 349 mg (91%) of **7**, which was identical (R_f, IR, PMR) with the above-described sample of this carbinol.

2-(1'-Hydroxy-2',2'-dimethylbut-3'-en-1'-yl)-1,4,5,8-tetramethoxynaphthalene (13). A solution of 135 mg (0.49 mmole) of **10** in 3 ml of THF was added in the course of 10 min to a stirred (Ar) solution of a Grignard reagent at 0°C, prepared from 45 mg (1.85 mg-atom) of Mg and 220 mg (2.08 mmoles) of prenyl chloride in 4 ml of Et_2O. The reaction mixture was allowed to stand for 3 h at ~25°C and then was subjected to the usual treatment. Yield 170 mg of a product which was chromatographed on 10 g of SiO_2. Elution with a hexane–acetone (4:1) mixture gave 138 mg (87%) of **13** in the form of a yellow oil. R_f 0.34. IR spectrum (ν, cm^{-1}): 1042, 1580, 3610. PMR spectrum (δ, ppm, J, Hz): 1.41 s (6H, CH_3),

*The above parameters were retrieved from the overall spectrum of a mixture of **9**., *Z*/*E* ≈ 5:2 (PMR data).

3.82 s, 3.90 s, 3.96 s and 3.98 s (12H, MeO) 5.04 d.d (1H, $HC^{4'}$, J = 2.0 and 17.4), 5.08 s (1H, $HC^{1'}$), 5.15 d.d (1H, $HC^{4'}$, J = 2.0 and 10.2), 5.31 d.d (1H, $HC^{3'}$, J = 10.2 and 17.4), 6.93 s (2H, HC^6, HC^7), 7.05 s (1H, HC^3). Mass spectrum, *m/z* (*I* %): M^+ 346 (20), 328 (3), 278 (21), 277 (100), 263 (11), 262 (58), 247 (22). Found, %: C 69.47; H 7.59. $C_{20}H_{26}O_5$. Calculated, %: C 69.34; H 7.56; mol. wt. 346.4.

2-(1'-Hydroxy-4'-methylpent-4'-en-1'-yl)-5,8-dimethoxy-1,4-naphthoquinone (14), 6-(1'-Hydroxy-4'-methylpent-4'-en-1'-yl)-5,8-dimethoxy-1,4-naphthoquinone (15), and 2-(1'-Hydroxy-4'-methylpent-4'-en-1'-yl)-5,8-dihydroxy-1,4-naphthoquinone (2). A solution of 1.5 g (2.74 mmoles) of $(NH_4)_2Ce(NO_3)_6$ in 4 ml of H_2O cooled to 0°C was added in the course of 15 min to a stirred solution of 0.37 g (1.07 mmoles) of **7** in 5 ml of MeCN and 2 ml of H_2O at 0°C. The reaction mixture was stirred for 30 min at 0-3°C, then was diluted with H_2O, extracted with ether, the extract was dried over Na_2SO_4, evaporated under vacuum, and the residue (0.39 g) was chromatographed on 15 g of SiO_2. Elution with a hexane–acetone (5:1 mixure gave 127 mg (38%) of **15** in the form of a yellow oil. R_f 0.40. IR spectrum (ν, cm^{-1}): 1060, 1470, 1660, 3620. PMR spectrum (δ, ppm): 1.74 s (3H, CH_3), 2.10 m (4H, $HC^{2'}$, $HC^{3'}$), 2.73 br.s (1H, OH), 3.84 s and 4.00 s (6H, MeO), 4.79 s (2H, HC^5), 5.13 d.d (1H, HC^1, J = 3.3 and 7.6 Hz), 6.78 s (1H, HC^2), 6.79 s (1H, HC^3), 7.55 s (1H, HC^7). Found, %: C 68.01; H 6.31. M^+ 316. $C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Elution with a hexane–acetone (3:1) mixture gave 162 mg (48%) of **14** in the form of an orange oil. R_f 0.36. IR spectrum (ν, cm^{-1}): 1060, 1570, 1660, 3617. PMR spectrum (δ, ppm): 1.74 s (3H, CH_3), 1.97 m (4H, $HC^{2'}$, $HC^{3'}$), 2.73 br.s (1H, OH), 3.95 s and 3.97 s (6H, MeO), 4.73 s (2H, $HC^{5'}$), 5.01 d.d (1H, $HC^{1'}$, J = 3.2 and 7.7 Hz), 6.79 s (1H, HC^3), 7.32 s (2H, HC^6, HC_7). Mass spectrum, *m/z* (*I*, %): M^+ +1 317 (14), M^+ 316 (65), 301 (18), 298 (17), 288 (12), 247 (57), 234 (53), 233 (100), 219 (38), 218 (25), 217 (27), 204 (31), 203 (32), 189 (40). Found, %: C 68.64; H 6.44. $C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Elution with a hexane–acetone (1:1) mixture gave 13 mg (4%) of **2** in the form of reddish-brown crystals, mp 136-138°C (from benzene). IR spectrum (ν, cm^{-1}): 1590, 1608, 2963, 3610. PMR spectrum (δ, ppm, *J*.Hz): 1.78 s (3H, CH_3), 2.04 m (4H, $HC^{2'}$), 2.23 t (2H, $HC^{3'}$, J = 6.0), 4.79 s (2H, $HC^{5'}$), 4.92 d.d (1H, $HC^{1'}$, J = 6.0 and 12.0), 7.16 s (1H, HC^3), 7.19 s (2H, HC^6, HC^7). Found, %: C 66.49; H 5.34; M^+ 288. $C_{16}H_{16}O_5$. Calculated, %: C 66.66; H 5.59; mol. wt. 288.3.

2-(1'-Hydroxy-2',2'-dimethylbut-3'-en-1'-yl)-5,8-dimethoxy-1,4-naphthoquinone (16) and 6-(1'-Hydroxy-2',2'-dimethylbut-3'-en-1'-yl)-5,8-dimethoxy-1,4-naphthoquinone (17). Under the above-described conditions, from 0.63 g (1.82 mmoles) of **18**, 0.12 g (21%) of **17** (eluent hexane–acetone, 6:1) and 0.25 g (44%) of **15** (eluent hexane–acetone, 4:1) were obtained.

Diether (16) — yellow oil, R_f 0.39. IR spectrum (ν, cm^{-1}): 1061, 1577, 1659, 3616. PMR spectrum (δ, ppm, *J*, Hz): 1.34 s (6H, CH_3), 3.96 s and 3.98 s (6H, MeO), 4.82 s (1H, $HC^{1'}$), 5.01 d.d (1H, $HC^{4'}$, J = 2.0 and 17.3 Hz), 5.12 d.d (1H, $HC^{4'}$, J = 2.0 and 10.2), 5.29 d.d (1H, $HC^{3'}$, J = 10.2 and 17.3), 6.74 s (1H, HC^3), 7.31 s (2H, HC^6, HC^7). Mass spectrum *m/z* (*I*, %): M^+ 316 (24), 301 (8), 299 (29), 287 (11), 283 (13), 249 (30), 248 (100), 247 (52), 233 (68). Found, %: C 68.40; H 6.35. $C_{18}H_{20}O_5$.Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Diether (17) — yellow oil, R_f 0.45. IR spectrum (ν, cm^{-1}): 1058, 1491, 1662, 3619. PMR spectrum (δ, ppm, *J*, Hz): 1.46 s (6H, CH_3), 3.86 s and 3.98 s (6H, MeO), 4.96 s (1H, $HC^{1'}$), 5.09 d.d (1H, $HC^{4'}$ J = 2.0 and 17.3), 5.20 d.d (1H, $HC^{4'}$, J = 2.0 and 10.2), 5.42 d.d (1H, $HC^{3'}$, J = 10.2 and 17.3), 6.80 s (2H, HC^2, HC^3), 7.46 s (1H, HC^7). Mass spectrum *m/z* (*I*, %): M^+ 316 (2), 249 (30), 248 (28), 247 (100), 246 (20), 234 (16), 233 (14), 219 (18), 204 (25). Found, %: C 68.20; H 6.32.$C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Isoshikonin (2) and 2-(5',5'-Dimethyltetrahydrofuran-2'-yl)-5,8-dihydroxy-1,4-naphthoquinone (4). A suspension of 0.32 g (1.01 mmoles) of **14** and 0.5 g (4.04 mmoles) of AgO [14] in 3 ml of dioxane was stirred for 30 min at ~25°C, and then was treated with 0.6 ml of 6 *M* HNO_3. The reaction mixture was stirred for 20 min at ~25°C and then was diluted with H_2O and extracted with benzene. The usual treatment of the extract gave 0.27 g of a product, which was chromatographed on 20 g of SiO_2. Elution with a hexane–acetone (9:1) mixture gave 0.18 g (62%) of **2**, which was identical (R_f, IR, PMR) with the above-described sample of this carbinol.

Elution with a hexane–acetone (8:1) mixture gave 42 mg (15%) of **4** in the form of dark-brown crystals, mp 160°C (dec.) [from a benzene–acetone (1:1) mixture] (cf. [15]: mp 158-159°C). IR spectrum (ν, cm^{-1}): 1564, 1607, 2980. PMR spectrum (δ, ppm): 1.36 s and 1.39 s (6H, CH_3), 1.85 m (2H, $HC^{4'}$), 2.64 m (2H, $HC^{3'}$), 5.15 t (1H, $HC^{2'}$, J = 7.6 Hz), 7.21 s (2H, HC^6, HC^7), 7.23 s (1H, HC^3), 12.55 s (2H, OH).

2-(1′-Hydroxy-2′,2′-dimethylbut-3′-en-1′-yl)-5,8-dihydroxy1,4-naphthoquinone (3). In a similar way, from 0.32 g (1.01 mmoles) of **16**, 235 mg (81%) of **3** was obtained in the form of reddish-brown crystals, mp 144-146°C (from dioxane). IR spectrum (ν, cm^{-1}): 1570, 1606, 1620, 2977. PMR spectrum (δ, ppm, J, Hz): 1.11 s (6H, CH_3), 4.94 s (1H, $HC^{1'}$), 5.09 d.d (1H, $HC^{4'}$, J = 1.9 and 17.1), 5.17 d.d (1H, $HC^{4'}$, J = 1.9 and 10.4), 5.45 d.d (1H, $HC^{3'}$, J = 10.4 and 17.1 Hz), 7.12 s (1H, HC^3), 7.20 s (1H, HC^6, HC^7), 12.47 s and 12.69 s (2H, OH). Found, %: C 66.56; H 5.60. M^+ 288. $C_{16}H_{16}O_5$. Calculated, %: C 66.66; H 5.59; mol. wt. 288.3.

6-Formyl-5,8-dimethoxy-1,4-naphthoquinone (18). As described above, starting from 0.16 g (0.505 mmole) of **15** and 0.25 g (2.02 mmoles) of AgO in 2 ml of dioxane at ~25°C in the course of 30 min, 0.09 g of a material was obtained which was chromatographed on 7 g of SiO_2. Elution with a hexane–acetone mixture (5:1) gave 19 mg (15%) of **18** in the form of light-yellow crystals, mp 168-170°C [from a hexane–benzene (1:1) mixture]. IR specrum (ν, cm^{-1}): 1637, 1660. PMR spectrum (δ, ppm): 4.00 s and 4.04 s (6H, MeO), 6.68 s (2H, HC^2, HC^3), 7.77 s (1H, HC^7), 10.55 s (1H, CHO). Found, %: C 63.31; H 4.15. M^+ 246. $C_{13}H_{10}O_5$. Calculated, %: C 63.42; H 4.09; mol. wt. 246.2. In a similar way, from 0.32 g (1.01 mmoles) of **17**, 182 mg (73%) of **18** was obtained, which was identical with the above-described sample of this compound.

2-Vinyl-1,4,5,8-tetramethoxynaphthalene (19). A solution of 2.0 g (7.25 mmoles) of aldehyde **10** in 30 ml of THF was added in the course of 20 min to a stirred (Ar) solution of phosphorane at −30°C, prepared at −40°C from 3.15 g (7.79 mmoles) of methyltriphenylphosphonium iodide in 150 ml of THF and 10 ml of a 0.86 *N* solution of BuLi in hexane (8.6 mmoles). The reaction mixture was stirred for 1 h at ~25°C, and then was decomposed with H_2O and extracted with $CHCl_3$. The usual treatment of the extract gave 2 g of a compund, which was chromatographed on 40 g of SiO_2. Elution with a hexane–acetone (6:1) mixture gave 1.3 g (65%) of **19**, in the form of light-yellow crystals, mp 98-99°C [from a hexane–benzene (1:1) mixture]. IR spectrum (ν, cm^{-1}): 1042, 1593, 1609. PMR spectrum (δ, ppm, J, Hz): 3.76 s, 3.91 s, 3.95 s and 3.97 s (12H, MeO), 5.38 d.d (1H, $HC^{2'}$, J = 1.0 and 10.8), 5.80 d.d (1H, $HC^{2'}$, J = 1.0 and 17.5), 6.83 s (2H, HC^6, HC^7), 7.06 s (1H, HC^3), 7.30 d.d (1H, $HC^{1'}$, J = 10.8 and 17.5). Mass spectrum, *m/z* (*I*, %): M^+ + 1 275 (20), M^+ 274 (100), 260 (17), 259 (88), 244 (25), 231 (16), 229 (19), 228 (40), 213 (26), 201 (20), 175 (48), 160 (85), 158 (30), 149 (87), 146 (98). Found, %: 70.20; H 6.63. $C_{16}H_{18}O_4$. Calculated, %: C 70.06; H 6.61; mol. wt. 274.3.

cis*–*trans*-1-(1,4,5,8-Tetramethoxynaphthyl-2)-2-ethoxycarbonylcyclopropane (20).** A 1.4 g portion (12.27 mmoles) of ethyl diazoacetate was added in the course of 2 h to a stirred (Ar) suspension of 40 mg (0.25 mmole) of anhydrus $CuSO_4$, 63 mg (1.0 mg-atom) of Cu wire, 0.75 g (2.73 mmoles) of **19** in 10 ml of boiling dichloroethane. The reaction mixture was cooled to ~25°C, then was diluted with dichloroethane, filtered, the filtrate was evaporated under vacuum, and the residue (0.85 g) was chromatographed on 25 g of SiO_2. Elution with a hexane–acetone (3:1) mixture gave 0.71 g (71%) of a mixture of *cis/trans*-**20** ≃ 5:2 (PMR data) in the form of a yellow oil, R_f 0.51. IR spectrum (ν, cm^{-1}): 1075, 1164, 1371, 1450, 1468, 1607, 1723. PMR spectrum of *trans*-**20 (δ, ppm, J, Hz): 1.27 t (3H, CH_3, J = 7.5), 1.67 m (3H, $HC^{3'}$, $HC^{2'}$), 1.92 m (1H, $HC^{1'}$, ΣJ = 19.1), 3.77 s, 3.87 s, and 3.93 s (12H, MeO), 4.19 q (2H, CH_2O, J = 7.5), 6.34 s (1H, HC^3), 6.78 d (1H, HC^6, J = 10.1), 6.8 d (1H, HC^7, J = 10.1). PMR spectrum of *cis*-**20*** (δ, ppm, J, Hz): 1.38 t (3H, CH_3, J = 7.5), 1.67 m (3H, $HC^{3'}$, $HC^{2'}$), 1.82 m (1H, $HC^{1'}$, ΣJ = 23.5), 3.77 s, 3.87 s, and 3.91 s (12H, MeO), 4.17 q (2H, CH_2O, J = 7.5), 6.37 s (1H, HC^3), 6.78 d (1H, HC^6, J = 10.1), 6.84 d (1H, HC^7, J = 10.1). Mass spectrum *m/z* (*I*, %): M^+ + 1 361 (23), M^+ 360 (100), 346 (5), 345 (20), 330 (9), 329 (8), 318 (6), 316 (6), 299 (11), 272 (22), 271 (53), 255 (37), 241 (25), 149 (24), 145 (32), 103 (67). Found, %: C 66.76; H 6.59. $C_{20}H_{24}O_6$. Calculated, %: C 66.65; H 6.71; mol. wt. 360.4.

cis-trans*-1-(1,4,5,8-Tetramethoxynaphthyl-2)-2-(2-hydroxypropyl-2)cyclopropane (21).** A solution of 0.36 g (1.0 mmole) of **20** was added to a stirred (Ar) solution of a Grignard reagent at 0°C, prepared from 219 mg (9.0 mg-atom) of Mg and 1.42 g (10.0 mmoles) of MeI in 25 ml of an Et_2O–THF (1:1) mixture. The reaction mixture was stirred for 3 h at ~25°C, and was then subjected to the usual treatment. The product obtained (~0.3 g) was chromatographed on 15 g of SiO_2. Elution with a hexane–acetone (3:1) mixture gave 228 mg (66%) of a mixture of *cis/trans*-**21** ~ 5:2 (PMR data) in the form of a viscous light-yellow oil, R_f 0.29. IR spectrum (ν, cm^{-1}): 1080, 1162, 1230, 1261, 1350, 1374, 1450, 1468, 1600, 3435. PMR spectrum of *trans*-**21 (δ, ppm, J, Hz): 0.9-1.1 m (2H, CH_2), 1.30 s and 1.34 s (6H, CH_3), 1.66 br.s (2H, $HC^{2'}$ and OH), 2.48 d.t (1H, $HC^{1'}$, ΣJ = 18.9), 3.83 s, 3.90 s, 3.91 s, and 3.94 s (12H, MeO), 6.38 s (1H, HC^3), 6.77 d (1H, HC^6, J = 10.2), 6.84 d (1H, HC^7, J = 10.2). PMR spectrum of *cis*-**21**† (δ, ppm, J, Hz): 0.9-1.1 m (2H, CH_2), 1.28 s and 1.34 s (6H, CH_3), 1.57 m (2H, $HC^{2'}$), 1.75 s (1H, OH), 2.23 d.t (1H, $HC^{1'}$, ΣJ = 23.8), 3.88 s, 3.89 s, 3.91s, and 3.94 s (12H,

*The parameters given were retrieved from an overall spectrum of mixture **20**.

†The parameters given were retrieved from an overall spectrum of mixture **21**.

MeO), 6.78 s (1H, HC^6, J = 10.2), 6.86 d (1H, HC^3), 6.88 d (1H, HC^7, J = 10.2). Mass spectrum m/z (I, %): M^+ +1 347 (7), M^+ 346 (100), 331 (5), 330 (5), 329 (6), 328 (22), 314 (5), 313 (13), 288 (7), 276 (10), 272 (15), 259 (14), 256 (17), 242 (19), 149 (26). Found, %: C 69.45; H 7.47. $C_{20}H_{26}O_5$. Calculated, %: C 69.34; H 7.56; mol wt. 346.4.

2(1′-Hydroxy-4′-methylpent-3′-en-1′-yl)-1,4,5,8-tetramethoxynaphthalene (22). A solution of 0.12 g (0.35 mmole) of **21** and two drops of 30% $HClO_4$ in 10 ml of THF was allowed to stand for 20 min at ~25°C, and then was diluted with 30 ml of Et_2O, washed with $NaHCO_3$, dried over Na_2SO_4, and the solvent was evaporated under vacuum. Yield ~0.1 g of a product, which was chromatographed on 10 g of SiO_2. Elution with a hexane–acetone (6:1) mixture gave 70 mg (58%) of **22** in the form of a thick light-yellow oil, R_f 0.33. IR spectrum (ν, cm^{-1}): 1080, 1260, 1368, 1452, 1459, 1604, 3420, 3600. PMR spectrum (δ, ppm, J, Hz): 1.64 d and 1.72 d (6H, CH_3, J = 1.1), 2.53 m (2H, CH_2), 3.75 s, 3.89 s, 3.93 s, and 3.95 s (12H, MeO), 5.23 t (1H, $HC^{1'}$, J = 8.1), 5.25 m (1H, $HC^{3'}$), 6.81 s (2H, HC^6, HC^7), 7.03 s (1H, HC^3). Mass spectrum m/z (I, %): M^+ 346 (31), 328 (11), 278 (20), 277 (60), 262 (49), 261 (18), 247 (29), 149 (100). Found, %: C 69.44; H 7.59. $C_{20}H_{26}O_5$. Calculated, %: C 69.34; H 7.56; mol. wt. 346.4. Elution with a hexane–acetone (5:1) mixture gave 14 mg (14%) of alcohol **26** (see below).

Acetate (23) — viscous light-yellow oil, R_f 0.49. IR spectrum (ν, cm^{-1}): 1070, 1360, 1597, 1620, 1735. PMR spectrum (δ, ppm, J, Hz): 1.57 s and 1.68 s (6H, CH_3), 2.12 s (3H, CH_3CO), 2.48 m (2H, CH_2), 3.78 s, 3.90 s, and 3.95 s (12H, MeO), 5.17 t (1H, $HC^{3'}$, J = 7.1), 6.36 t (1H, $HC^{1'}$, J = 6.6), 6.85 s (2H, HC^6, HC^7), 6.90 s (1H, HC^3). Found, %: C 68.12; H 7.20; M^+ 388. $C_{22}H_{28}O_6$. Calculated, %: C 68.02; H 7.26; mol. wt. 388.5.

(1,4,5,8-Tetramethoxynaphthyl-2)oxirane (24). A solution of 492 mg (2.0 mmoles) of Me_3SI in 10 ml of DMSO was added to a stirred (Ar) solution of sodium dimsyl at 0°C, prepared from 25 ml of DMSO and 48 mg (2.0 mmoles) of NaH in 25 ml of THF. The reaction mixture was stirred for 1 min at 0°C, and then was treated for 20 min with a solution of 552 mg (2.0 mmoles) of **10** in 5 ml of THF. Stirring was continued for an additional 1 h at 0°C, and for a further 1 h at ~25°C, and the mixtue was decomposed with H_2O, and extracted with ether. The usual treatment of the extract gave ~0.5 g of a product, which was chromatographed on 30 g of neutral Al_2O_3. Elution with a hexane–acetone (7:1) mixture gave 0.4 g (71%) of **24** in the form of colorless plates. Mp 80-82°C (from hexane). IR spectrum (ν, cm^{-1}): 1078, 1260, 1369, 1468, 1522, 1604. PMR spectrum (δ, ppm, J, Hz): 2.82 d.d (1H, $HC^{2'}$, J = 2.6 and 5.7), 3.25 d.d (1H, $HC^{2'}$, J = 4.4 and 5.7), 4.45 d.d (1H, $HC^{1'}$, J = 2.6 and 4.4), 3.84 s, 3.91 s, 3.93 s, and 3.97 s (12H, MeO), 6.64 s (1H, HC^3), 6.86 s (2H, HC^6, HC^7). Found, %:C 66.42; H 6.10; M^+ 290. $C_{16}H_{18}O_5$. Calculated, %: C 66.20; H 6.25; mol. wt. 290.3.

Alcohol (22). A solution of 0.41 g (1.4 mmoles) of **24** in 10 ml of THF was added in the course of 10 min to a stirred (Ar) solution of 2.2 moles of isobutenyllithium [25] in 15 ml of Et_2O at −10°C. The reactionmixture was stirred at −10°C for 1 h, and then for 15 h at ~25°C. It was then decomposed with H_2O and extracted with ether. By the usual treatment of the extract, ~0.35 g of a product was obtained, which was chromatographed on 20 g of SiO_2. Elution with a hexane–acetone (6:1) mixture gave 275 mg (57%) of **22**, which was identical (R_f, IR, PMR) to the above-described sample of this alcohol.

2-(1′-Hydroxy-4′-methylpent-3′-en-1′-yl)-5,8-dimethoxy-1,4-naphthoquinone (25) and 6-(1′-Hydroxy-4′-methylpent-3′-en-1′-yl)-5,8-dimethoxy-1,4-naphthoquinone (26). As described above for **7**, starting from 0.37 g (1.07 mmoles) of **22** and 1.5 g (2.74 mmoles) of $(NH_4)_2Ce(NO_3)_6$ in 5 ml of MeCN and 6 ml of H_2O, after chromatographic purification of the product on 15 g of SiO_2, 154 mg (47%) of **25** [elution with a hexane–acetone (3:1) mixture] and 92 mg (27%) of **26** [elution with a hexane–acetone (5:1) mixture] were obtained.

Alcohol (25) — thick orange oil, R_f 0.37 IR spectrum (ν, cm^{-1}): 1070, 1196, 1260, 1370, 1450, 1465, 1520, 1600, 1662, 3520, 3617. PMR spectrum (δ, ppm, J, Hz): 1.63 d and 1.72 d (6H, CH_3, J = 1.1), 2.38 m (2H, CH_2), 2.57 br.s (1H, OH), 3.96 s and 3.98 s (6H, MeO), 5.00 m (1H, $HC^{1'}$, J = 8.5; 4.2 and 1.0), 5.27 m (1H, $HC^{3'}$), 6.80 d (1H, HC^3, J = 1.0), 7.33 s (2H, HC^6, HC^7). Found, %: C 68.50; H 6.40; M^+ 316. $C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Alcohol (26) — thick light-yellow oil, R_f 0.39. IR spectrum (ν, cm^{-1}): 1065, 1250, 1340, 1370, 1398, 1468, 1654, 3500, 3635. PMR spectrum (δ, ppm, J, Hz): 1.66 d and 1.78 d (6H, CH_3, J = 1.2), 2.34 m (2H, CH_2), 2.60 br.s (1H, OH), 3.85 s and 4.01 s (6H, MeO), 5.12 d.d (1H, $HC^{1'}$, J = 8.6 and 4.3), 5.26 m (1H, $HC^{3'}$), 6.76 d (1H, HC^2, J = 10.0), 6.82 d (1H, HC^3, J = 10.0), 7.56 s (1H, HC^7). Found, %: C 68.22; H 6.39; M^+ 316. $C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37; mol. wt. 316.3.

Acetate (27) — viscous light-yellow oil, R_f 0.46. IR spectrum (ν, cm^{-1}): 1034, 1588, 1622, 1633, 1731. PMR spectrum (δ, ppm, J, Hz): 1.52 s and 1.78 s (6H, CH_3), 2.11 s (3H, CH_3CO), 2.50 m (2H, CH_2), 3.96 s and 3.97 s (6H,

MeO), 5.09 t (1H, $HC^{3'}$, J = 7.3), 5.91 d.d (1H, $HC^{1'}$, J = 5.4 and 7.5), 6.75 s (1H, HC^3), 7.30 s (2H, HC^6, HC^7). Found, %: C 67.24; H 6.25; M^+ 358. $C_{20}H_{22}O_6$. Calculated, %: C 67.03; H 6.19; mol. wt. 358.4.

Acetate (28) — thick light-yellow oil, R_f 0.43. IR spectrum (ν, cm^{-1}): 1037, 1585, 1631, 1657, 1735. PMR spectrum (δ, ppm, J, Hz): 1.53 s and 1.78 s (6H, CH_3), 2.13 s (3H, CH_3CO), 2.57 m (2H, CH_2), 3.90 s and 3.98 s (6H, MeO), 5.12 t (1H, $HC^{3'}$, J = 7.4), 6.14 d.d (1H, $HC^{1'}$, J = 5.5 and 7.7), 6.79 s (2H, HC^6, HC^7), 7.27 s (1H, HC^3). Found, %: C 67.30; H 6.20; M^+ 358. $C_{20}H_{22}O_6$. Calculated, %: C 67.03; H 6.19; mol. wt. 358.4.

Shikalkin (1). As described above for **14**, starting from 0.32 g (1.01 mmoles) of **15** and 0.5 g (4.04 mmoles) of AgO in 3 ml of dioxane, after the chromatographic purification of the product on 20 g of SiO_2, 113 mg (39%) of **1** was obtained [elution with a hexane–acetone (8:1) mixture] in the form of dark-brown crystals, mp 143-146°C (from dioxane) (comp. [7]: mp 145-147°C). IR spectrum (ν, cm^{-1}): 1583, 1608, 2962, 3527. PMR spectrum (δ, ppm, J, Hz): 1.67 s and 1.78 s (6H, CH_3), 2.55 m (3H, CH_2 and OH), 4.93 d.d (1H, $HC^{1'}$, J = 4.7 and 8.3), 5.23 t (1H, $HC^{3'}$, J = 7.3), 7.18 s (1H, HC^3), 7.20 s (2H, HC^6, HC^7), 12.46 s and 12.58 s (2H, OH).

Aldehyde (18). In a similar way, from 0.32 g (1.01 mmoles) of **26** and 0.5 g (4.04 mmoles) of AgO in 3 ml, of dioxane, 48 mg (19%) of **18** was obtained, which was identical (mp, R_f, IR, PMR) with an authentic sample of this compound.

Acetates (27) and (28). As described above for **7**, starting from 388 mg (1.0 mmole) of **23** and 1.5 g (2.74 mmoles) of $(NH_4)_2Ce(NO_3)_6$ in 5 ml of MeCN and 6 ml of H_2O, after chromatographic purification of the product on 15 g of SiO_2, 161 mg (45%) of **27** [elution with a hexane–acetone (8:1) mixture] and 104 mg (29%) of **28** [elution with a hexane–acetone (6:1) mixture] were obtained, which were identical (R_f, IR, PMR) with authentic samples of these triethers.

To a stirred solution of 388 mg (1.0 mmole) of **23** in 4 ml of CH_2Cl_2 at ~25°C, 0.87 g (10.0 mmoles) of MnO_2 impregnated with HNO_3 [19] was added in portions. The reaction mixture was stirred for 17 h, the precipitate was then separated, washed on the filter with $CHCl_3$, and the combined filtrates were evaporated under vacuum. Yield ~0.45 g of a product, which was chromatographed in 25 g of SiO_2. Elution with a hexane–acetone (8:1) mixture gave 193 mg (54%) of **28**, which was completely identical with the above-described sample of this compound

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