an equilibrium is rapidly attained between the imine, benzaldehyde (δ 9.97, CHO), and benzylamine (δ 4.08, CH_2). After 1.5 h, the equilibrium composition as indicated by the ^1H NMR spectrum is identical with that observed after 22 and 45 h, except that significant broadening of the methylene signal of benzylamine is seen owing to exchange of the NH_2 protons as they become more highly deuterated. No exchange of benzyl methylene protons is observed (the phenyl/CH_2 ratio remains constant at 2.5). In a parallel experiment the ^1H NMR spectrum of a solution of the imine (0.11 g) in CD_3CN (1.0 mL) and D_2O (0.11 g) and triethylamine (0.02 g) remained virtually unchanged during 24 h.

Acknowledgment. We are indebted to Dr. Richard S. Miller and the Office of Naval Research for support of this work.

Registry No. **2a**, 124782-15-6; **2a**·HCl, 124782-23-6; **2a**·HBr, 124782-24-7; **2b**, 124782-16-7; **2c**, 124782-17-8; **2d**, 124782-18-9; **2e**, 124782-19-0; **2f**, 124782-20-3; **2g**, 124782-21-4; **6**, 124782-22-5; **7**, 140-28-3; **13a**, 124782-25-8; **13b**, 124820-69-5; $PhCH_2NH_2$, 100-46-9; $(CHO)_2$, 107-22-2; $PhCH_2N{=}CHPh$, 780-25-6; 4-methylbenzylamine, 104-84-7; 4-isopropylbenzylamine, 4395-73-7; 4-methoxybenzylamine, 2393-23-9; 3,4-dimethoxybenzylamine, 5763-61-1; 2-chlorobenzylamine, 89-97-4; 4-chlorobenzylamine, 104-86-9; 4-(dimethylamino)benzylamine, 19293-58-4; dihydroxy-1,4-dioxane, 4845-50-5; benzylamine-*N*-d_2, 45579-94-0; benzaldehyde, 100-52-7; 4-(aminomethyl)pyridine, 3731-53-1.

Supplementary Material Available: Two figures showing full numbering used in X-ray analysis and the hydrogen atom locations and tables of (1) atom coordinates and equivalent isotropic thermal parameters for the non-hydrogen atoms, (2) anisotropic thermal parameters for non-hydrogen atoms, (3) hydrogen atom coordinates and thermal parameters, and (4) bond distances and valence angles (16 pages). Ordering information is given on any current masthead page.

Regiospecific and Highly Stereoselective Formation of Benzisochroman-6,9-quinones. Synthesis of (±)-Ventilagone and (±)-Ventiloquinone H

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An approach known to give regiospecific cycloadditions over a wide range of substrates has been applied to the synthesis of (±)-ventilagone and (±)-ventiloquinone H using a novel, electron-rich heterocyclic diene. The strategy provides for the sole formation of the natural, thermodynamically less stable diastereoisomer. As a basis for comparison of the spectral data, (±)-ventilagone 7-methyl ether was equilibrated and hydrolyzed to a mixture containing (±)-isoventilagone, a prototype of the heretofore unidentified trans series of compounds. Convenient substrates for eventual access to the more highly substituted natural products have also been obtained.

Although both cis and trans configurations are known in the case of naturally occurring benzisochroman-5,10-quinones (e.g., eleutherin and isoeleutherin), only the cis modification seems to far to have been attributed to the 6,9-isomers.[1,2] The structure of ventilagone (**1a**) is now well established from an X-ray crystallographic analysis,[3] and its NMR spectrum has been correlated to those of more recently isolated pigments.[2] However, no basis for comparison is available for isomeric materials, and this study shows that spectroscopic (mainly NMR) differences between the two diastereoisomeric series are indeed quite small in this area.

Many approaches have been proposed for the synthesis of natural benzisochroman-5,10-quinones[4a,b] but with the exception of one unsuccessful attempt[3] none has been devised for the 6,9-isomers such as ventilagone (**1a**) and ventiloquinones H (**18**) and I (**2**).[2] These juglone derivatives were nevertheless expected to be readily accessible by the Diels–Alder methodology involving halogenated quinones and electron-rich dienes[5] if an unusual heterocyclic reagent such as **7** were readily available.

A convenient route to a practical substrate is provided by two similar methods for the preparation of dihydro-γ-pyrones.[6,7] In a slight modification of the more recent of the two, methyl acetoacetate and crotonyl chloride were condensed in the presence of magnesium methylate to provide an 80% yield of 5,6-dihydro-3-(methoxycarbonyl)-2,6-dimethylpyran-4-one (**3**). Catalytic hydrogenation of a bicyclic product[6] analogous to the latter had previously shown that the 2,3 double bond was affected selectively albeit very slowly. However, when carried out on dihydropyrone **3** at 3 atm and in the presence of 10% palladized charcoal, the reaction was quite as satisfactory and far more rapid.

It was expected at this point that subsequent steps would either require a separation of isomers or have to be conducted on a mixture of substrates. However, only one product was isolated and corresponds to (±)-stereoisomer **4** in which, according to the NMR spectrum, all substituents show equatorial orientations, i.e., the methyl groups are cis to one another. Examination of the mother liquors does not reveal the presence of another epimeric product. This serendipitous result was particularly encouraging

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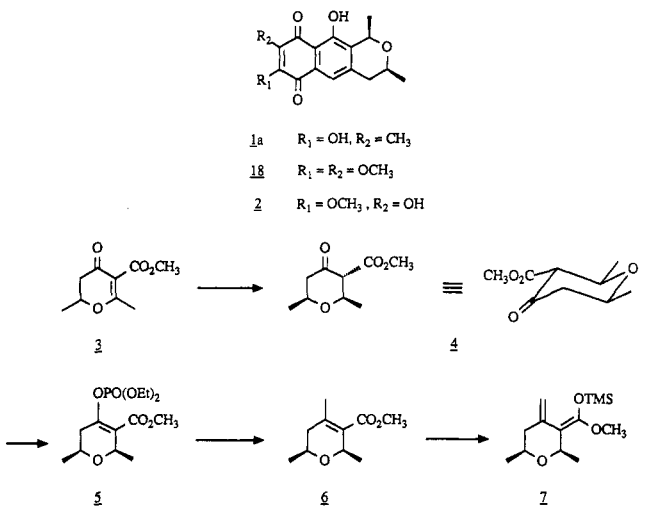
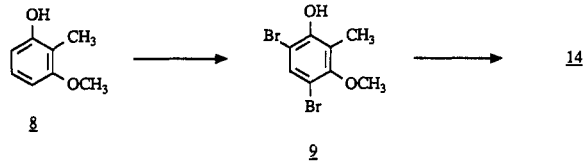
Scheme I



Scheme II

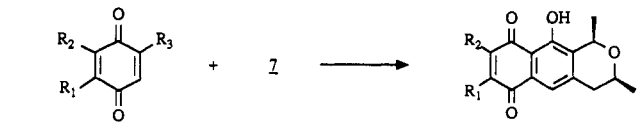


since to our knowledge only one other method of forming 1,3-disubstituted benzisochromanquinones solely affords the cis isomer.[4b]

Conversion of β-keto ester **4** to olefin **6** was advantageously realized by the coupling[8] of lithium dimethylcuprate with the corresponding enol phosphate **5** (a low yield, as yet unoptimized, of the 4-methylene isomer[9] has also been obtained directly from **4** by using a phase-transfer modification[10] of the Wittig reaction). Finally, a kinetically controlled enolsilylation[11] of unsaturated esters **6** provided the required heterocyclic diene **7** which, according to its 200-MHz NMR spectrum, consists of only one detectable isomer. This labile substance, having presumably the *E* configuration, rearranges slowly at room temperature to the C-silylated[12] compound and so cannot be purified by distillation. However, when freshly prepared, the diene contains about 8% of the rearranged product, is otherwise quite pure, and can be used directly since the contaminant does not interfere with the desired cycloaddition (Scheme I).

An eventual synthesis of ventilagone (**1a**) by this approach requires the use of 2-hydroxy (or methoxy)-3-methyl-5-bromo (or chloro)benzoquinone, e.g., **14**. Numerous attempts to oxidize 2-methyl-4,6-dibromoresorcinol or the dimethyl ether by ceric, ferric, periodate, or chromate ions under a variety of conditions either were unsuccessful or gave dimeric products. A Thiele reaction applied to 6-bromotoluquinone provided only the unwanted isomer, while a peroxide oxidation of toluhydroquinone failed to yield the expected 3,5-dihydroxytoluquinone. Although a somewhat inconvenient synthesis[13] of quinone **14** is available, an experimentally more simple modification was devised involving an improved preparation of monomethyl ether **8**, dibromination of the latter, and finally oxidation of phenol **9** with chromic acid in aqueous acetic acid[14] (an attempted monomethylation of 4,6-dibromo-2-methylresorcinol gave only 12% of the desired product). Other halogenated benzoquinones (**10–13**) are readily available by standard methods (see the Experimental Section; Scheme II).

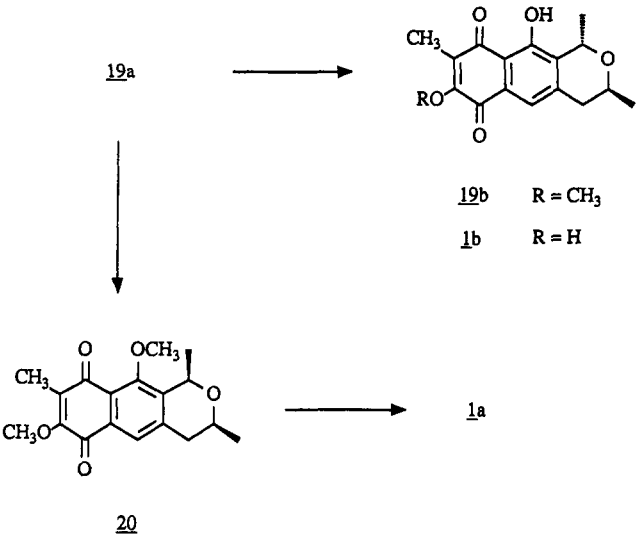
Scheme III



	R_1	R_2	R_3
10	H	OCH_3	Cl
11	OCH_3	H	Cl
12	H	CH_3	Cl
13	OCH_3	OCH_3	Cl
14	OCH_3	CH_3	Br

	R_1	R_2
15	H	OCH_3
16	OCH_3	H
17	H	CH_3
18	OCH_3	OCH_3
19a	OCH_3	CH_3

Scheme IV



Diene **7** reacts rapidly even at 0 °C in dichloromethane with a number of benzoquinones (**10–14**), and after aromatization of the adducts with concentrated HCl in THF the corresponding benzisochroman-6,9-quinones can generally be isolated in good-to-excellent yield. Only 5-chloro-2-methoxybenzoquinone (**11**) responded sluggishly and did not provide more than 41% of the desired product. Optimization will be required in this case since the product is one of the choice substrates for eventual syntheses of the more substituted members of this series.

In this way (±)-ventiloquinone H (**18**) is produced directly from the diene and benzoquinone **13**[15] with a 97% conversion (Scheme III). Treatment of this substance with concentrated HCl in ethanol as it was carried out for the natural product provided (±)-ventiloquinone I (**2**) in nearly quantitative yield. The 7-methyl ether (**19a**) of ventilagone was also obtained accordingly from benzoquinone **14** (75%), but cleavage of the latter to (±)-ventilagone proved unexpectedly difficult. Various procedures of basic hy-

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drolysis involving such reagents as 5% aqueous[16] and 1% methanolic NaOH produced the expected color changes (violet to red) but yielded only an intractable material (dimeric?) while from 10% aqueous Na_2CO_3[17] unchanged **19a** was recovered. When an unmethoxylated substrate (i.e., **17**) was subjected to strongly basic conditions to determine whether or not ventilagone could be an artifact (since the natural product was isolated from such a medium[18]), neither ventilagone nor the original quinone could be isolated. However, since the nor-analogue **16** could readily be demethylated in this way, a strong presumption occurs that reactive quinonemethides are formed in the other instances.

Hydrolysis of ventilagone 7-methyl ether (**19a**) in a 1:1 mixture of concentrated HCl and acetic acid at 90 °C[17] for 30 min was next attempted, although it is well established[19] that electronic effects render 2-methoxyjuglones particularly difficult to cleave under acidic conditions. Examination of the reaction mixture revealed that no demethylation had occurred but that about half of the substrate had assumed the more stable trans configuration, i.e., **1b** (Scheme IV).

The surest if not the simplest solution to the problem consisted in methylating the peri-hydroxyl group in position 10, responsible for the resistance to hydrolysis of the 7-methoxyl group. Acidic hydrolysis of this diether in the usual way[19] produced ventilagone (**1a**) and the 10-methyl ether in a 1:3.2 ratio without epimerization. Finally submitting this crude mixture directly to anhydrous $AlCl_3$ in CH_2Cl_2 at room temperature completed the demethylation but also induced a small amount of the isomerized product, isoventilagone (~4%), which could be eliminated by chromatography on deactivated silica gel (Scheme IV).

Since the characteristics of the trans isomers in this specific series do not seem to have been previously published, an attempt was made to obtain at least one representative for comparison purposes. By refluxing ventilagone 7-methyl ether (**19a**) in a 1:1 mixture of concentrated HCl and ethanol for 24 h, both pairs of epimers of **1** and **19** could be detected among the products in which **1b** (i.e., isoventilagone) predominated and could be readily isolated.

The spectral data for all synthetic benzisochroman-6,9-quinones are consistent with those published for the same or analogous natural products[2] (in the original paper some coupling constants had inadvertently been interchanged, i.e., in the case of ventiloquinone H).[20] The 400-MHz NMR spectra of compounds in the cis series, in conjunction with decoupling experiments, reveal a more detailed picture of the complex interactions than previously noted. Thus, both protons at C-4 are coupled with the one at C-5, while the axial hydrogens C-1 and C-3 also give rise to a small but difficultly evaluated coupling. In comparison, the iso series (i.e., **19b**), as expected, show smaller long-distance coupling constants that are not readily determined even by double irradiation. ^{13}C NMR data are also quite comparable to known values both for cis and analogous trans configurations[21] and confirm that differences between the two groups occur mainly at C-3. Mass spectroscopy reveals essentially the same decomposition patterns in both series with base peaks at M − 15, characteristic fragments a M − 14, M − 33, M − 43, and M − 57 and a common product of mass 115.

Experimental Section

All melting points were taken for samples in capillary tubes with a Thomas-Hoover apparatus and are not corrected. The UV spectra were determined on a Perkin-Elmer Lambda 5 spectrophotometer; the IR spectra on a Beckman Model IR-4250 instrument and calibrated with a film of polystyrene. NMR spectra were recorded with Varian XL-200 and Bruker WH-400 spectrometers using tetramethylsilane and, for C_6D_6 solutions, C_6HD_5 as standards. The 400-MHz spectra were provided by the Laboratoire régional de RMN à haut champ (Université de Montréal, Montréal). (Some coupling constants were verified by spin–spin decoupling.) For closely spaced ^{13}C NMR signals, assignments with an asterisk may be interchangeable. Mass spectra were obtained with a Hewlett-Packard 5995A spectrometer. Merck silica gel $60F_{254}$ for dry column chromatography and ICN SiliTech 32-63 60A for flash chromatography were used throughout in a product-to-adsorbent ratio of 1:50–100. A deactivated absorbent was obtained from silica gel (300 g) and 2% aqueous oxalic acid (800 mL). Elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, TN.

A. Preparation of Heterocyclic Diene 7. 3-Carbomethoxy-5,6-dihydro-2,6-dimethyl-4-pyrone (3). This compound was prepared from methyl acetoacetate (116.1 g, 1.00 mol), crotonyl chloride (115.0 g, 1.10 mol), magnesium (26.0 g, 1.10 mol), and methanol (105 mL), essentially according to the published procedure[7] but substituting a crystal of iodine for the CCl_4. Fractional distillation of the crude product gave pure dihydropyrone **3** (147.0 g, 80%): bp 90–92 °C/0.3 mmHg; IR ν_{max} (film) 2985, 2945, 1725, 1675, and 1600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.48 (3 H, d, J = 6.4 Hz, 6-CH_3), 2.23 (3 H, s, 2-CH_3), 2.49 (2 H, d, J = 8.2 Hz, 5-H), 3.82 (3 H, s, 3-CO_2CH_3), and 4.57 (1 H, qt, J = 6.4, 8.2 Hz, 6-H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.08 (C-6a), 20.36 (C-2a), 42.24 (C-5), 51.84 (MeO-3a), 75.51 (C-6), 111.67 (C-3), 165.77 (C-3a), 177.21 (C-2), and 187.74 (C-4); MS, m/z 184 (M^+).

***r*-3-Carbomethoxy-2,3,5,6-tetrahydro-*t*-2,*t*-6-dimethyl-4-pyrone (4).** Hydrogenation of dihydropyrone **3** (12.89 g, 70.0 mmol) in methanol (140 mL) over 10% palladized charcoal (400 mg) for 5 h at 40 psi gave the tetrahydro derivative **4** (16.30 g, 88%), mp 70.5–71.5 °C (hexane) as a single (±)-isomer; IR ν_{max} (KBr) 2965, 2880, 1745, and 1715 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.33 and 1.34 (2 × 3 H, 2d, J = 6.0 Hz, 2,6-CH_3), 2.20–2.51 (2 H, AB part of ABX system, J_{AB} = 14.3 Hz, $J_{AX,calcd}$ = 10.5 Hz, $J_{BX,calcd}$ = 3.2 Hz, 5-H), 3.20 (1 H, d, J = 10.6 Hz, 3-H), 3.78 (3 H, s, 3-CO_2CH_3), 3.86 (1 H, m, 6-H), and 4.02 (1 H, dq, J = 10.5, 6.0 Hz, 2-H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.72 (C-6a), 21.81 (C-2a), 48.19 (C-5), 51.95 (MeO-3a), 63.89 (C-3), 72.93 (C-6), 74.56 (C-2), 168.26 (C-3a), and 201.69 (C-4); MS, m/z 186 $(M)^+$. Anal. Calcd for $C_9H_{14}O_4$: C, 58.06; H, 7.53. Found: C, 57.86; H, 7.59.

Diethyl Enol Phosphate 5 of β-Keto Ester 4. Dihydropyran **5** was prepared from β-keto ester **4** (46.55 g, 0.250 mol) in dry ether (400 mL)—added (3 h) under nitrogen to NaH (6.60 g, 0.275 mol) in the same solvent (300 mL) at 0 °C—and diethyl chlorophosphate (47.75 g, 0.275 mol, 45 min) as described earlier in a general method.[8] The crude enol phosphate **5** (76.2 g, 95%) was used in the next step without further purification; IR ν_{max} (film) 2970, 1725, and 1025 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.28 and 1.29 (2 × 3 H, 2 d, J = 6.2 Hz, 2,6-CH_3), 1.36 (6 H, m, 4-OPO(OCH_2CH_3)$_2$), 2.43 (2 H, m, 5-H), 3.69 (1 H, m, 6-H), 3.76 (3 H, s, 3-CO_2CH_3), 4.20 (4 H, m, 4-OPO(OCH_2CH_3)$_2$), and 4.58 (1 H, m, 2-H); MS, m/z 322 $(M)^+$.

***cis*-3-Carbomethoxy-5,6-dihydro-2,4,6-trimethyl-2*H*-pyran (6).** To a solution of lithium dimethylcuprate (~0.165 mol) at −78 °C, prepared by addition of methyllithium (236 mL of a 1.4 M solution in ether, 0.330 mol) to a suspension of purified[22] CuI (31.42 g, 0.165 mol) in ether (330 mL) at −10 °C under nitrogen, was added dropwise (75 min) enol phosphate **5** (35.45 g, 0.110 mol) in the same solvent (150 mL). The reaction mixture, still under inert atmosphere, was stirred for 3 h at −78 °C, allowed to warm

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to 0 °C, and worked up as in the original procedure.[8] Fractional distillation of the crude residue gave unsaturated ester **6** (15.03 g, 74%): bp 103–105 °C/14 mmHg; IR ν_{max} (film) 2970, 1715, 1650, and 1240 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (6 H, d, J = 6.2 Hz, 2,6-CH_3), 1.84–2.25 (2 H, m, 5-H), 1.94 (3 H, br s, 4-CH_3), 3.62 (1 H, ddq, J = 9.9, 6.2, 3.3 Hz, 6-H), 3.74 (3 H, s, 3-CO_2CH_3), and 4.52 (1 H, m, 2-H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.36 (C-6a), 20.83 (C-4a), 21.14 (C-2a), 39.36 (C-5), 50.93 (MeO-3a), 68.78 (C-6), 71.29 (C-2), 128.75 (C-3), 140.25 (C-4), and 167.95 (C-3a); MS, m/z 184 (M)$^+$. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.22; H, 8.70. Found: C, 65.11; H, 8.53.

(*E*)-*cis*-3-(Methoxy(trimethylsiloxy)methylene)-2,6-dimethyl-4-methylenetetrahydropyran (7). To a solution of LDA prepared at 0 °C from *n*-butyllithium (39.0 mL of a 1.55 M solution of *n*-butyllithium in hexane, 60.0 mmol) and dry diisopropylamine (5.57 g, 55.0 mmol) in anhydrous THF (30 min) under nitrogen, cooled to −78 °C, was added chlorotrimethylsilane (8.15 g, 75.0 mmol) in the same solvent (10 mL, 30 min) and finally unsaturated ester **6** (9.21 g, 50.0 mmol) in THF (12.5 mL, 1.5 h). The reaction mixture was concentrated under vacuum at 20 °C, and the residue extracted with light petroleum ether (bp 35–60 °C, 250 mL). Upon evaporation of the extract, the residue was again taken in petroleum ether (130 mL). Filtration of the resultant suspension and evaporation of the filtrate yielded the crude diene as a very pale yellow oil (13.88 g): IR ν_{max} (film) 2965, 1650, 1250, 1065, 855, and 840 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.20 (9 H, s, =COTMS), 1.16 (3 H, d, J = 6.2 Hz, 6-CH_3), 1.22 (3 H, d, J = 6.2 Hz, 2-CH_3), 2.19 (1 H, ddt, J = 16.1, 11.0, 1.8 Hz, 5-H_a), 2.42 (1 H, ddt, J = 16.1, 2.2, 1.8 Hz, 5-H_e), 3.53 (3 H, s, =$COCH_3$), 3.56 (1 H, m, 6-H), 4.55 (1 H, q, J = 6.2 Hz, 2-H), 4.98 and 5.11 (2 × 1 H, 2 m, =CH_2); MS, m/z 256 (M)$^+$.

B. Preparation of 5-Bromo-2-methoxy-3-methyl-1,4-benzoquinone (14). 3-Methoxy-2-methylphenol (8). Of the several methods[23] available for the preparation of phenol **8**, the following modification of the Kirkemo and White[23c] procedure was found to be the most satisfactory. Dimethyl sulfate (12.80 g, 0.100 mol) was added dropwise over 30 min to a boiling aqueous solution of 2-methylresorcinol (12.40 g, 0.100 mol) and NaOH (4.00 g, 0.100 mol). After this was cooled, an additional portion of NaOH (6.00, 0.150 mol) was added, and the reaction mixture was extracted with chloroform (3 × 40 mL). Upon evaporation of the organic phase, the residue was found to contain some of phenol **8** and so was again partitioned between 2 N NaOH (200 mL) and chloroform (3 × 70 mL). The aqueous extracts were worked up as in the original method and provided 8.54 g (62%) of discolored but homogeneous phenol **8**. Purification of the latter by distillation give pure phenol **8** (5.92 g, 43%), bp 64–65 °C/0.2 mmHg.

4,6-Dibromo-3-methoxy-2-methylphenol (9). Addition of Br_2 (20.78 g, 0.130 mol) in CCl_4 (40 mL, 75 min) to phenol **8** (8.98 g, 0.065 mol) in the same solvent (20 mL) was carried out at room temperature. The reaction mixture was stirred for 2 h and evaporated, giving phenol **9** (16.85 g, 87%), mp 71.0–71.5 °C (petroleum ether, bp 65–110 °C) (lit.[13] mp 74 °C); IR ν_{max} (KBr) 3415, 1580, and 1455 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.27 (3 H, s, 2-CH_3), 3.78 (3 H, s, 3-OCH_3), 5.54 (1 H, s, 1-OH), and 7.50 (1 H, s, 5-H); MS, m/z 298/296/294 (M)$^+$.

5-Bromo-2-methoxy-3-methyl-1,4-benzoquinone (14). A solution of CrO_3 (5.80 g, 0.058 mol) in 60% aqueous acetic acid (35 mL) was added (25 min) at room temperature to dibromophenol **9** (5.92 g, 0.020 mol) in glacial acetic acid (30 mL). The mixture was stirred for 30 min, then kept at 50 °C for 90 min, and finally poured into water (300 mL) and extracted with $CHCl_3$ (4 × 140 mL). The organic phases were washed with water (7 × 200 mL), dried, and evaporated. Purification of the residue by chromatography (CH_2Cl_2) afforded benzoquinone **14** (2.03 g, 44%): mp 69.0–69.5 °C (aqueous methanol; (lit.[13] mp 65 °C); IR ν_{max} (KBr) 3050, 2960, 2860, 1665, 1625, and 1590 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.02 (3 H, s, 3-CH_3), 4.06 (3 H, s, 2-OCH_3), and 7.12 (1 H, s, 6-H); MS, m/z 232/230 (M)$^+$.

C. Preparation of Benzisochroman-6,9-quinones. General Method. A solution of diene **7** (769 mg, 3.00 mmol) in dry dichloromethane (6 mL) was added dropwise over 10 min to the benzoquinone (**10**–**14**) in the same solvent (14 mL) at 0 °C. The reaction mixture was stirred for 1 h under the same conditions and for an another hour at room temperature. Extra portions of the diene were then added at 30 min intervals if necessary until the presence of benzoquinone was no longer detected by TLC. After evaporation of the solvent at reduced pressure below 25 °C, the adduct was aromatized by stirring with a mixture of concentrated HCl (4 mL) and THF (20 mL) for 1 h at ambient temperature. The benzoisochromanquinone was then precipitated by addition of water (500 mL) and extracted with chloroform (2 × 200 mL).

(±)-*cis*-3,4,6,9-Tetrahydro-10-hydroxy-8-methoxy-1,3-dimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (15). Application of the foregoing method to 6-chloro-2-methoxybenzoquinone[24] (**10**, 345 mg, 2.00 mmol) and diene **7** (3.00 mmol) and purification of the crude product by dry column chromatography (ethyl acetate–petroleum ether, bp 35–60 °C, 1:3) gave quinone **15** (434 mg, 75%): mp 184–185 °C (toluene–petroleum ether, bp 65–110 °C); UV λ_{max} (MeOH) (log ϵ) 232 (4.50), 264 (4.19), 306 (4.18), and 430 (3.77) nm; IR ν_{max} (KBr) 1635 and 1595 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 5.9 Hz, 3-CH_3), 1.63 (3 H, d, J = 6.6 Hz, 1-CH_3), 2.73 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 3.91 (3 H, s, 8-OCH_3), 5.06 (1 H, qt, J = 6.6, ~2 Hz, 1-H), 6.11 (1 H, s, 7-H), 7.36 (1 H, s, 5-H), and 12.33 (1 H, s, 10-OH); ^{1}H NMR (200 MHz, C_6D_6) δ 1.15 (3 H, d, J = 5.9 Hz, 3-CH_3), 1.81 (3 H, d, J = 6.6 Hz, 1-CH_3), 2.08 (1 H, ddd, J = 16.5, 2.2, ~2 Hz, 4-H_e), 2.38 (1 H, ddd, J = 16.5, 10.3, ~2 Hz, 4-H_a), 2.88 (3 H, s, 8-OCH_3), 3.31 (1 H, qdd, J = 5.9, 10.3, 2.2 Hz, 3-H), 5.07 (1 H, qt, J = 6.6, ~2 Hz, 1-H), 5.66 (1 H, s, 7-H), 7.43 (1 H, s, 5-H), and 12.68 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.81 (C-3a), 21.30 (C-1a), 37.95 (C-4), 56.50 (MeO-8), 68.85 (C-3), 70.54 (C-1), 110.05 (C-7), 111.96 (C-9a), 119.18 (C-5), 129.26 (C-5a), 134.34 (C-10a), 145.50 (C-4a), 159.15 (C-10)*, 159.93 (C-8)*, 183.61 (C-6)*, and 184.40 (C-9)*; MS, m/z 288 (14) (M)$^+$, 273 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.31; H, 5.83.

(±)-*cis*-3,4,6,9-Tetrahydro-10-hydroxy-7-methoxy-1,3-dimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (16). In a reaction similar to the preceding one, 5-chloro-2-methoxybenzoquinone[24] (**11**, 345 mg, 2.00 mmol) and diene **7** (3.00 + 0.20 mmol), after separation by dry column chromatography (ethyl acetate–petroleum ether, bp 35–60 °C, 1:4) gave quinone **16** (238 mg, 41%): mp 175.0–175.5 °C (methanol); UV ν_{max} (MeOH) (log ϵ) 231 (4.51), 263 (4.20), 307 (4.11), and 438 (3.78) nm; IR ν_{max} (KBr) 1680, 1620, and 1585 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 5.9 Hz, 3-CH_3), 1.63 (3 H, d, J = 6.2 Hz, 1-CH_3), 2.72 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 3.91 (3 H, s, 7-OCH_3), 5.07 (1 H, qt, J = 6.2, ~2 Hz, 1-H), 6.06 (1 H, s, 8-H), 7.41 (1 H, s, 5-H), and 12.77 (1 H, s, 10-OH); ^{1}H NMR (200 MHz, C_6D_6) δ 1.16 (3 H, d, J = 5.9 Hz, 3-CH_3), 1.86 (3 H, d, J = 6.2 Hz, 1-CH_3), 2.07 (1 H, ddd, J = 16.5, 2.2, ~2 Hz, 4-H_e), 2.37 (1 H, ddd, J = 16.5, 10.3, ~2 Hz, 4-H_a), 2.87 (3 H, s, 7-OCH_3), 3.32 (1 H, qdd, J = 5.9, 10.3, 2.2 Hz, 3-H), 5.14 (1 H, qt, J = 6.2 Hz, ~2 Hz, 1-H), 5.50 (1 H, s, 8-H), 7.35 (1 H, s, 5-H), and 13.36 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.88 (C-3a), 21.39 (C-1a), 37.75 (C-4), 56.61 (MeO-7), 69.01 (C-3), 70.83 (C-1), 109.38 (C-8), 111.92 (C-9a), 119.86 (C-5), 128.42 (C-5a), 136.15 (C-10a), 143.52 (C-4a), 158.33 (C-10)*, 160.82 (C-7)*, 179.35 (C-6), and 190.56 (C-9); MS, m/z 288 (26) (M)$^+$, 273 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.77; H, 5.85.

(±)-*cis*-3,4,6,9-Tetrahydro-10-hydroxy-1,3,8-trimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (17). Cycloaddition of diene **7** (3.00 mmol) to 6-chloro-2-methylbenzoquinone[14] (**12**, 313 mg, 2.00 mmol) and aromatization of the resulting adduct gave quinone **17** directly (437 mg, 80%): mp 147–148 °C (methanol); UV λ_{max} (MeOH) (log ϵ) 2.19 (4.68), 260 (4.24), and 429 (3.81) nm; IR ν_{max} (KBr) 1660, 1630, and 1595 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 6.2 Hz, 3-CH_3), 1.63 (3 H, d, J = 6.6 Hz, 1-CH_3), 2.18 (3 H, d, J = 1.5 Hz, 8-CH_3), 2.72 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 5.07 (1 H, qt, J = 6.6, ~2 Hz, 1-H), 6.76 (1 H, q, J = 1.5 Hz, 7-H), 7.32 (1 H, s, 5-H), and 12.64 (1 H, s, 10-OH); ^{1}H NMR (200 MHz, C_6D_6) δ 1.15 (3 H, d,J = 6.2 Hz, 3-CH_3), 1.62 (3 H, d, J = 1.5 Hz, 8-CH_3), 1.84 (3 H, d, J = 6.6 Hz, 1-CH_3), 2.07

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(1 H, ddd, J = 16.5, 2.2, ~2 Hz, 4-H$_e$), 2.37 (1 H, ddd, J = 16.5, 10.3, ~2 Hz, 4-H$_a$), 3.29 (1 H, qdd, J = 6.2, 10.3, 2.2 Hz, 3-H), 5.11 (1 H, qt, J = 6.6, ~2 Hz, 1-H), 6.27 (1 H, q, J = 1.5 Hz, 7-H), 7.35 (1 H, s, 5-H), and 12.90 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 16.01 (C-8a), 20.87 (C-3a), 21.37 (C-1a), 37.87 (C-4), 68.94 (C-3), 70.69 (C-1), 112.74 (C-9a), 118.98 (C-5), 129.59 (C-5a), 134.77 (C-10a), 136.15 (C-7), 114.56 (C-4a), 147.92 (C-8), 158.75 (C-10), 183.96 (C-6), and 190.40 (C-9); MS, m/z 272 (13) $(M)^+$, 257 (100). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.66; H, 5.82.

(±)-*cis*-3,4,6,9-Tetrahydro-10-hydroxy-7,8-dimethoxy-1,3-dimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Ventiloquinone H] (18). A similar reaction mixture obtained from 5-chloro-2,3-dimethoxybenzoquinone[15] (**13**, 405 mg; 2.00 mmol) and diene **7** (3.00 + 0.20 mmol), upon purification by dry column chromatography (ethyl acetate–petroleum ether, bp 35–60 °C; 1:4) afforded quinone **18** (620 mg, 97%): mp 119–120 °C (petroleum ether, bp 65–110 °C) (lit.[2] mp (+)-isomer, 95–96 °C); UV λ_{max} (MeOH) (log ϵ) 223 (4.53), 272 (4.35), 315 (4.13), and 434 (3.82) nm; IR ν_{max} (KBr) 1655, 1630, and 1600 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.62 (3 H, d, J = 6.2 Hz, 1-CH$_3$), 2.70 (2 H, irregular m, 4-H), 3.66 (1 H, m, 3-H), 4.08, and 4.11 (2 × 3 H, 2 s, 7,8-OCH$_3$), 5.05 (1 H, qt, J = 6.2, ~2 Hz, 1-H), 7.34 (1 H, s, 5-H), and 12.47 (1 H, s, 10-OH); ^{1}H NMR (400 MHz, C_6D_6) δ 1.16 (3 H, d, J = 6.1 Hz, 3-CH$_3$), 1.84 (3 H, d, J = 6.4 Hz, 1-CH$_3$), 2.05 (1 H, dddd, J = 16.5, 2.2, 1.5, 0.4 Hz, 4-H$_e$), 2.35 (1 H, dddd, J = 16.5, 10.5, 2.1, 0.9 Hz, 4-H$_a$) 3.30 (1 H, qdd, J = 6.1, 10.5, 2.2 Hz, 3-H), 3.61, and 3.71 (2 × 3 H, 2 s, 7,8-OCH$_3$), 5.09 (1 H, qdd, J = 6.4, 2.1, 1.5 Hz, 1-H), 7.32 (1 H, br s, 5-H), and 12.87 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 20.83 (C-3a), 21.32 (C-1a), 37.75 (C-4), 61.27 (MeO-7)*, 61.56 (MeO-8)*, 68.91 (C-3), 70.63 (C-1), 110.94 (C-9a), 119.40 (C-5), 128.19 (C-5a), 135.19 (C-10a), 144.07 (C-4a), 146.43 (C-7)*, 147.80 (C-8)*, 158.42 (C-10), 180.87 (C-6), and 186.83 (C-9); MS, m/z 318 (50) $(M)^+$, 303 (100). Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.31; H, 5.67.

(±)-*cis*-3,4,6,9-Tetrahydro-10-hydroxy-7-methoxy-1,3,8-trimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Ventilagone 7-Methyl Ether] (19a). A similar reaction using 5-bromo-2-methoxy-3-methylbenzoquinone (**14**, 462 mg, 2.00 mmol) and diene **7** (3.00 + 0.20 + 0.20 mmol) according to the general method gave quinone **19a** directly (456 mg; 75%): mp 124.5–125.5 °C (methanol) (lit.[18] mp (+)-isomer, 115.5–116.5 °C); UV λ_{max} (MeOH) (log ϵ) 227 (4.51), 267 (4.25), 308 (4.09), and 441 (3.79) nm; IR ν_{max} (KBr) 1660 and 1620 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.62 (3 H, d, J = 6.2 Hz, 1-CH$_3$), 2.06 (3 H, s, 8-CH$_3$), 2.70 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 4.13 (3 H, s, 7-OCH$_3$), 5.06 (1 H, qt, J = 6.2, ~2 Hz, 1-H), 7.31 (1 H, s, 5-H), and 12.82 (1 H, s, 10-OH); ^{1}H NMR (400 MHz, C_6D_6) δ 1.16 (3 H, d, J = 6.1 Hz, 3-H), 1.87 (3 H, d, J = 6.4 Hz, 1-CH$_3$), 1.93 (3 H, s, 8-CH$_3$), 2.06 (1 H, dddd, J = 16.5, 2.2, 1.5, 0.4 Hz, 4-H$_e$), 2.38 (1 H, dddd, J = 16.5, 10.5, 2.1, 0.9 Hz, 4-H$_a$), 3.31 (1 H, qdd, J = 6.1, 10.5, 2.2 Hz, 3-H), 3.81 (3 H, s, 7-OCH$_3$), 5.13 (1 H, qdd, J = 6.4, 2.1, 1.5 Hz, 1-H), 7.30 (1 H, br s, 5-H), and 13.25 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 8.73 (C-8a), 20.96 (C-3a), 21.43 (C-1a), 37.80 (C-4), 61.08 (MeO-7), 69.05 (C-3), 70.83 (C-1), 112.07 (C-9a), 119.31 (C-5), 128.99 (C-5a), 130.88 (C-8), 135.30 (C-10a), 143.36 (C-4a), 158.08 (C-7)*, 158.20 (C-10)*, 180.50 (C-6), and 191.05 (C-9); MS, m/z 302(34) $(M)^+$, 287 (100). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.53; H, 6.17.

(±)-*cis*-3,4,6,9-Tetrahydro-8,10-dihydroxy-7-methoxy-1,3-dimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Ventiloquinone I] (2). A solution of (±)-ventiloquinone H (**18**, 64 mg, 0.20 mmol) in ethanol (60 mL) and concentrated HCl (60 mL) was heated to reflux for 30 min, cooled, and poured into water (150 mL). Extraction of the mixture with chloroform (3 × 100 mL) provided (±)-ventiloquinone I (**2**, 61 mg, 100%): mp 174–175 °C (methanol–petroleum ether, bp 65–110 °C) (lit.[2] mp (+)-isomer, 189 °C); UV λ_{max} (MeOH) (log ϵ) 260 (4.29), 301 (4.11), and 419 (3.78) nm; IR ν_{max} (KBr) 1660, 1640, and 1605 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.62 (3 H, d, J = 6.2 Hz, 1-CH$_3$), 2.70 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 4.19 (3 H, s, 7-OCH$_3$), 5.04 (1 H, qt, J = 6.2, ~2 Hz, 1-H), 6.78 (1 H, s, 8-OH), 7.38 (1 H, s, 5-H), and 11.70 (1 H, s, 10-OH); ^{1}H NMR (200 MHz, C_6D_6) δ 1.13 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.81 (3 H, d, J = 6.2 Hz, 1-CH$_3$), 1.99 (1 H, ddd, J = 16.5, 2.2 ~2 Hz, 4-H$_e$), 2.30 (1 H, ddd, J = 16.5, 10.3, ~2 Hz, 4-H$_a$), 3.26 (1 H, qdd, J = 6.2, 10.3, 2.2 Hz, 3-H), 3.84 (3 H, s, 7-OCH$_3$), 5.03 (1 H, qt, J = 6.2, ~2 Hz, 1-H), 6.26 (1 H, br s, 8-OH), 7.29 (1 H, s, 5-H), and 11.79 (1 H, s, 10-OH); MS, m/z 304 (27) $(M)^+$, 289 (00). Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.10; H, 5.53.

(±)-*cis*-3,4,6,9-Tetrahydro-7,10-dimethoxy-1,3,8-trimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Ventilagone 7,10-Dimethyl Ether] (20). (±)-Ventilagone 7-methyl ether (**19a**, 106 mg, 0.35 mmol) was methylated in the usual way with anhydrous K_2CO_3 (333 mg, 2.41 mmol) and dimethyl sulfate (293 mg, 2.32 mmol) in refluxing acetone (100 mL, 17 h). Purification of the crude product by dry column chromatography (ethyl acetate–petroleum ether, bp 35–60 °C, 1:4) gave quinone **20** (81 mg, 73%): mp 146.5–147.5 °c (petroleum ether, bp 65–110 °C); UV λ_{max} (MeOH) (log ϵ) 255 (4.36), 287 (4.04), and 356 (3.65) nm; IR ν_{max} (KBr) 1660, 1640, 1615, and 1585 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.37 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.60 (3 H, d, J = 6.6 Hz, 1-CH$_3$), 2.08 (3 H, s, 8-CH$_3$), 2.74 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 3.83 (3 H, s, 10-OCH$_3$), 4.06 (3 H, s, 7-OCH$_3$), 5.08 (1 H, qt, J = 6.6, ~2 Hz, 1-H), and 7.62 (1 H, s, 5-H); MS, m/z 316 (50), 301 (100). Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. found: C, 68.44; H, 6.48.

(±)-*cis*-3,4,6,9-Tetrahydro-7,10-dihydroxy-1,3,8-trimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Ventilagone] (1a). A solution of (±)-ventilagone 7,10-dimethyl ether (**20**, 380 mg, 1.20 mmol) in ethanol (175 mL) and concentrated HCl (175 mL) was heated to reflux for 30 min and treated as in the preparation of (±)-ventiloquinone I. The crude product consisted (by NMR) of a 3.2:1 mixture of (±)-ventilagone 10-methyl ether and (±)-ventilagone.

The latter was dissolved in a suspension of anhydrous $AlCl_3$ (2.08 g, 15.6 mmol) in dichloromethane (5 mL) at 0 °C. The mixture was then stirred at room temperature for 1 h and poured into ice (160 g) and concentrated HCl (75 mL). Stirring was continued for 17 h, and the product extracted with chloroform (3 × 100 mL). The residue consisted of a 26:1 mixture (94%) of (±)-ventilagone (**1a**) and (±)-isoventilagone (**1b**). Separation by flash chromatography on deactivated silica gel (ethyl acetate–dichloromethane, 1:99) gave pure quinone **19a**: mp 172.5–173.0 °C (toluene) (lit.[2] mp (+)-isomer, 205 °C); UV λ_{max} (MeOH) (log ϵ) 269 (4.23), 307 (4.07), and 422 (3.68) nm; IR ν_{max} (KBr) 1660, 1645, and 1600 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3 H, d, J = 6.2 Hz, 3-CH$_3$), 1.63 (3 H, d, J = 6.6 Hz, 1-CH$_3$), 2.07 (3 H, s,, 8-CH$_3$), 2.71 (2 H, irregular m, 4-H), 3.67 (1 H, m, 3-H), 5.07 (1 H, qt, J = 6.6, ~2 Hz, 1-H), 7.37 (1 H, s, 5-H), 7.39 (1 H, s, 7-OH), and 13.01 (1 H, s, 10-OH); ^{1}H NMR (400 MHz, C_6D_6) δ 1.15 (3 H, d, J = 6.1 Hz, 3-CH$_3$), 1.84 (3 H, d, J = 6.4 Hz, 1-CH$_3$), 1.93 (3 H, s, 8-CH$_3$), 2.02 (1 H, dddd, J = 16.5, 2.2, 1.5, 0.4 Hz, 4-H$_e$), 2.34 (H, dddd, J = 16.5, 10.5, 2.1, 0.9 Hz, 4-H$_a$), 3.28 (1 H, qdd, J = 6.1, 10.5, 2.2 Hz, 3-H), 5.10 (1 H, qdd, J = 6.4, 2.1, 1.5 Hz, 1-H, 7.13 (1 H, br s, 7-OH), 7.23 (1 H, m, 5-H), and 13.38 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 8.17 (C-8a), 20.98 (C-3a), 21.43 (C-1a), 37.69 (C-4), 69.05 (C-3), 70.96 (C-1), 112.07 (C-9a), 119.64 (C-5), 126.82 (C-8), 129.12 (C-5a), 137.23 (C-10a), 142.94 (C-4a), 153.51 (C-7), 158.75 (C-10), 180.27 (C-6), and 191.00 (C-9); MS, m/z 288 (26) $(M)^+$, 273 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.71; H, 5.76.

(±)-*trans*-3,4,6,9-Tetrahydro-7,10-dihydroxy-1,3,8-trimethyl-1*H*-naphtho[2,3-*c*]pyran-6,9-dione [(±)-Isoventilagone] (1b). After a solution of (±)-ventilagone 7-methyl ether (**19a**, 400 mg, 1.32 mmol) in ethanol (350 mL) and concentrated HCl (350 mL) was heated to reflux for 24 h, as indicated above, a 22:11:10:1 mixture (325 mg) of (±)-isoventilagone (**1b**), (±)-ventilagone (**1a**), (±)-isoventilagone 7-methyl ether (**19b**), and (±)-ventilagone 7-methyl ether was obtained. Separation by dry column chromatography on deactivated silica gel (ethyl acetate–dichloromethane, 1:99) provided (±)-isoventilagone (**1b**, 117 mg, 31%): mp 236.0–236.5 °C (toluene); UV λ_{max} (MeOH) (log ϵ) 255 (4.31), 298 (4.10), and 406 (3.72) nm; IR ν_{max} (KBr) 1655, 1640, and 1605 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 1.14 (3 H, d, J = 6.1 Hz, 3-CH$_3$), 1.59 (3 H, d, J = 6.7 Hz, 1-CH$_3$), 1.91 (3 H, s, 8-CH$_3$), 2.09 (1 H, dd, J = 17.1, 3.4 Hz, 4-H$_e$), 2.21 (1 H, ddt, J = 17.1, 10.4, 0.9 Hz, 4-H$_a$), 3.73 (1 H, qdd, J = 6.1, 10.4, 3.4 Hz, 3-H), 5.36 (1 H, br q, J = 6.7 Hz, 1-H), 7.22 and 7.23 (2 H, 2 br s, 5-H and 7-OH), and 13.21 (1 H, s, 10-OH); ^{13}C NMR (50.3 MHz,

$CDCl_3$) δ 8.15 (C-8a), 19.14 (C-3a), 21.63 (C-1a), 36.33 (C-4), 69.39 (C-3), 68.34 (C-1), 111.80 (C-9a), 119.77 (C-5), 126.99 (C-8), 137.19 (C-10a), 144.19 (C-4a), 153.58 (C-7), and 157.82 (C-10) (other signals were too weak); MS, m/z 288 (16) $(M)^+$, 273 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.61; H, 5.73.

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Registry No. **1a**, 124917-66-4; **1a** (10-methyl ester), 124821-11-0; **1b**, 124917-67-5; **2**, 124917-65-3; **3**, 124854-79-1; **4**, 124821-02-9; **5**, 124821-03-0; **6**, 124821-04-1; **7**, 124821-05-2; **8**, 6971-52-4; **9**, 88010-47-3; **10**, 54490-80-1; **11**, 24605-23-0; **12**, 1123-64-4; **13**, 30839-34-0; **14**, 84568-08-1; **15**, 124821-06-3; **16**, 124821-07-4; **17**, 124821-08-5; **18**, 124917-64-2; **19a**, 124821-09-6; **20**, 124821-10-9; $MeO_2CCH_2COCH_3$, 105-45-3; $CH_3CH{=}CHCOCl$, 10487-71-5; 2-methylresorcinol, 608-25-3.

Preparation of Novel 4-Substituted 6-Methoxy-, 6,7-Dimethoxy-, and 6,7-(Methylenedioxy)isochroman-3-ones. 2

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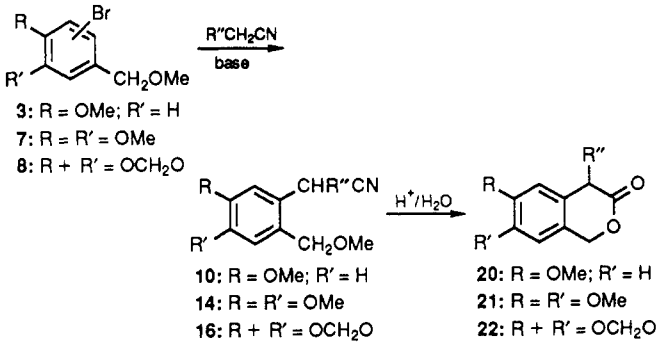
The titled compounds **20**, **21**, and **22** have been prepared in modest yields by a two-step reaction involving first the reaction of bromoarenes **3**, **7**, and **8** with lithioalkyl- and lithioarylacetonitriles under aryne-forming conditions. The cyano products **10**, **14**, and **16** so formed were then converted to the corresponding isochroman-3-ones by acidic hydrolysis.

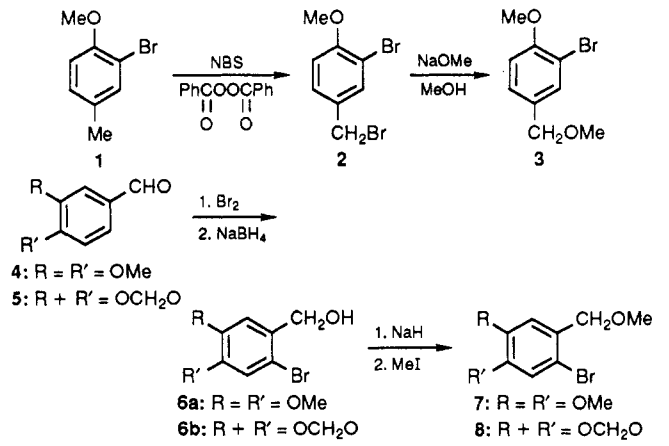
Introduction

Spangler[1] has shown that gas-phase pyrolysis of isochroman-3-ones furnishes synthetically useful *o*-quinodimethanes, several of which have served as valuable intermediates in natural product synthesis.[2] For example, the key step in the synthesis of deoxyisosikkimotoxin involves trapping the *o*-quinodimethane, obtained by the pyrolysis of the corresponding 6,7-dimethoxyisochroman-3-one, with *N*-phenylmaleimide.[3] 3-Isochromanones have also been converted by nonpyrolytic means to derivatives of isoquinoline,[4] thioisoquinoline,[5] and epoxyethanophenanthrene.[6]

Scheme I



Scheme II



We recently described[7] an efficient, two-step synthesis of novel 4-alkyl and 4-aryl derivatives of 6-(acetoxymethyl)isochroman-3-ones in which the key step involves the addition of a nitrile anion to 3,6-bis(methoxy-

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