NATURALLY OCCURRING NAPHTHAZARINS. SYNTHESIS OF (±)–VENTILOQUINONES C, D, E AND G.

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Abstract - The title compounds have been synthesized, some for the first time, from previously obtained (±)–1,3–dimethyl–10–hydroxybenzisochroman–6,9–quinones, by oxidation of the corresponding hydroquinone dimethyl ethers using ceric ammonium nitrate or better [bis(trifluoroacetoxy)iodo]benzene and, as required, selective demethylation.

The cycloaddition of electron-rich dienes to halogenated quinones, an effective annelating procedure, in particular for the synthesis of purpurins[1] and quinizarins,[2] remains disappointing for the preparation of naphthazarins.[1–3] A direct regioselective approach in this instance therefore remains one of the challenging objectives of quinone chemistry. Significant progress in this direction has however been realized in several areas (e.g. ref. 4) and in particular by the oxidation of partially protected polyhydroxynaphthalenes.[5] Thus, the recent syntheses[6] of naturally occurring juglones such as ventilagone (**1**) and ventiloquinone H (**3**) now provide convenient substrates for the elaboration of related naphthazarins,[7] i.e. ventiloquinones C, D, E and G.[8]

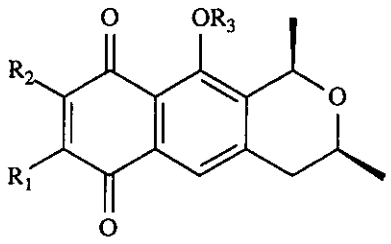
Although ventiloquinone H (**3**) was obtained in high yield, efficient access to the 7-methoxy analogue (**2**), after the usual cycloaddition to 2–chloro–5–methoxybenzoquinone, remained elusive. Attempts to optimize the formation of this substrate by modification of the usual parameters (reaction temperature, solvent, aromatization

procedure, sonication, etc.) did not improve the conversion beyond 41%. This threshold is probably determined, as in other well established cases, by a competitive addition of the diene to the carbonyl double bond.[1]

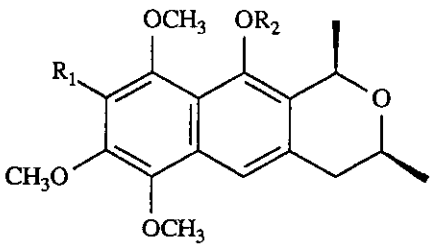
With these readily available substrates, the surest strategy seemed to require the preparation of selectively protected naphthols (such as **8, 9**) which were expected to yield the corresponding quinones by any of a variety of oxidizing agents. A convenient protection of the phenolic function as a MOM derivative was carried out easily and in high yield using NaH as base.[9] The resultant ethers (**4,5**), freed from a small amount of starting material, could then be reduced directly to the hydroquinone and methylated under phase transfer conditions[10] in an overall yield of 83-87% (from the hydroxyquinone).

Cleavage of the foregoing MOM ethers (**6,7**) to the corresponding phenols (**8,9**), as a prelude to oxidation, was not expected to cause difficulties but in fact, under standard conditions[11] (catalytic amount of conc. HCl in refluxing MeOH), considerable isomerization to the more stable trans form was observed. After evaluating a number of experimental conditions, it was found in the case of MOM ether (**6**), that reactions conducted at room temperature with small amounts of conc. H_2SO_4 and over fairly long periods of time produced quite satisfactory results with less than 5% of the isomerized product. Somewhat surprisingly, the use of other catalysts such as $ZnBr_2$ (for the analogous MEM ether),[12] TMSBr[13] and $BF_3{\cdot}Et_2O$ produced increasing proportions of the trans isomer (45%, 62% and 92% respectively).

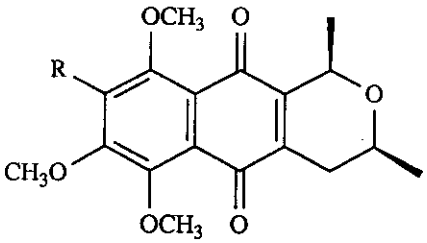
Finally, oxidation of hydroxy ethers (**8,9**) to the required naphthazarin derivatives (**10,11**) was attempted using either CAN, as prescribed by Laatsch,[5b] or [bis(trifluoroacetoxy)iodo]benzene,[14] a reagent that does not seem to have been applied previously in this particular area. Thus, naphthol (**8**) in the presence of $(CF_3COO)_2IC_6H_5$ provided ventiloquinone E (**10**) cleanly in 74% yield whilst CAN was slightly less efficient (64%) but also produced a small amount of the 6,9-demethylated species (**12**). From the racemic substance (**10**), the 6,7,9-trihydroxylated pigment, ventiloquinone G (**13**), became readily accessible in high yield by treatment with anhydrous $AlCl_3$ in CH_2Cl_2 at room temperature. However, under more selective conditions, i.e. using LiI in



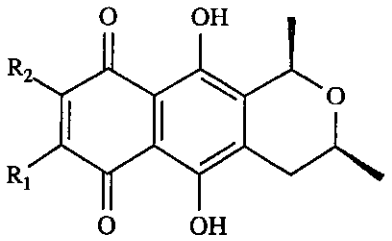
	R_1	R_2	R_3
1	OH	CH_3	H
2	OCH_3	H	H
3	OCH_3	OCH_3	H
4	OCH_3	H	MOM
5	OCH_3	OCH_3	MOM



	R_1	R_2
6	H	MOM
7	OCH_3	MOM
8	H	H
9	OCH_3	H



10	R = H
11	$R = OCH_3$



	R_1	R_2
12	OCH_3	H
13	OH	H
14	OCH_3	OCH_3
15	OH,OCH_3	
16	OH	OH

refluxing pinacolone,[5b] only the peri-demethylated products (**12**) was produced.

Similarly, phenol (**9**) and CAN afforded tetramethoxynaphthoquinone (**11**), this time, very efficiently (90%). Treatment of the latter with anhydrous $AlCl_3$ again reflected the ease of complexation by giving a mixture consisting mainly of the 7,8-demethylated product (**16**) and a small amount of the corresponding trans isomer along with ventiloquinones C (**15**) and D (**14**). In an attempt to refine the process, LiI in boiling pinacolone was again applied, but still produced a greater extent of demethylation than expected, resulting in an 80% yield of the mixture of monomethyl ethers known ventiloquinone C. One of these positional isomers, as yet unidentified, could be isolated by repeated trituration of the crude product in ether. Eventually, when the cleavage was conducted with the same reagent but at a lower temperature (50°C), a very selective process was achieved and ventiloquinone D (**14**) obtained, albeit in mediocre yield (45%). (All synthetic ventiloquinones showed spectroscopic properties in complete agreement with extensive published values).

EXPERIMENTAL

All melting points were taken for samples in capillary tubes with a Thomas-Hoover apparatus and are not corrected. The ir spectra were determined on a Beckman Model IR-4250 instrument and the nmr spectra were recorded with Varian XL-200 and Bruker WH-400 spectrometers using tetramethylsilane as internal standard. The 400 MHz spectra were provided by the Laboratoire régional de RMN à haut champ (Université de Montréal, Montréal). 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. Elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, TN.

(±)-*cis*-7-Methoxy-10-methoxymethoxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (4).

To a suspension obtained from 97% NaH (93mg; 3.8 mmol) in dry THF (150 ml) and benzisochroman (**2**)

(864 mg; 3.00 mmol) in the same solvent (60 ml), under N_2, then heated at 50°C (1 h), was added CH_3OCH_2Cl (0.30 ml; 3.8 mmol). The cooled mixture was poured into 1% aqueous Na_2CO_3 and the quite pure residue of a $CHCl_3$ extract (3 × 100 ml) was used as such in the next step; ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.34 (3H, d, J = 6.2 Hz, 3-CH_3), 1.62 (3H, d, J = 6.2 Hz, 1-CH_3), 2.70 (2H, irregular m, 4-H), 3.56 (3H, s, 10-OCH_2OCH_3), 3.65 (1H, m, 3-H), 3.84 (3H, s, 7-OCH_3), 4.78 (1H, d, J = 7.0 Hz, 10-OCH_2OCH_3), 5.15 (1H, q, J = 6.2 Hz, 1-H), 5.30 (1H, d, J = 7.0 Hz, 10-OCH_2OCH_3), 6.01 (1H, s, 8-H) and 7.68 (1H, s, 5-H); ms (m/z) 332 (1) $(M)^+$, 115 (100).

(±)-*cis*-7,8-Dimethoxy-10-methoxymethoxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (5).

In a procedure similar to the foregoing, (±)-ventiloquinone (**3**) (636 mg; 2.00 mmol) in THF (40 ml), 97% NaH (62 mg; 2.5 mmol) in the same solvent (100 ml) and CH_3OCH_2Cl (0.20 ml; 2.5 mmol) gave methoxymethyl ether (**5**); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.35 (3H, d, J = 5.9 Hz, 3-CH_3), 1.63 (3H, d, J = 6.2 Hz, 1-CH_3), 2.71 (2H, irregular m, 4-H), 3.58 (3H, s, 10-OCH_2OCH_3), 3.68 (1H, m, 3-H), 4.06 (6H, s, 7,8-OCH_3), 4.81 (1H, d, J = 7.0 Hz, 10-OCH_2OCH_3), 5.15 (1H, q, J = 6.2 Hz, 1-H), 5.33 (1H, d, J = 7.0 Hz, 10-OCH_2OCH_3) and 7.64 (1H, s, 5-H); ms (m/z) 362 (9) $(M)^+$, 330 (100).

(±)-*cis*-6,7,9-Trimethoxy-10-methoxymethoxy-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran (6).

To a solution of the crude methoxymethyl ether (**4**) obtained above and cetyltrimethylammonium bromide (143 mg; 0.375 mmol) in THF (40 ml) and H_2O (7 ml) was added, under N_2, $Na_2S_2O_4$ (3.3 g; 18 mmol) in H_2O (11.4 ml) with vigorous shaking. After the mixture had become colourless (~1 h), KOH (3.8 g; 68 mmol) in H_2O (9.6 ml) was introduced, followed after 15 min by dimethyl sulfate (4.2 g; 33 mmol). The reaction medium was stirred at room temperature (14 h) poured into H_2O (100 ml) and extracted with $CHCl_3$ (3 × 100 ml). Purification of the residue by chromatography (dry column) (AcOEt - petroleum ether, bp 35-60°C 1:3) gave *trimethyl ether* (**6**) (901 mg; 83%), mp 132.0-132.5°C (from petroleum ether, bp 65-110°C); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.35 (3H, d, J = 5.9 Hz, 3-CH_3), 1.69 (3H, d, J = 6.2 Hz, 1-CH_3), 2.80 (2H, irregular m, 4-H),

3.57 (3H, s, 10-$OCH_2OC\underline{H}_3$), 3.75 (1H, m, 3-H), 3.88, 3.92 and 3.96 (3 × 3H, 3s, 6,7,9-OCH_3), 4.86 (1H, d, J = 6.6 Hz, 10-$OC\underline{H}_2OCH_3$), 5.12 (1H, d, J = 6.6 Hz, 10-$OC\underline{H}_2OCH_3$), 5.32 (1H, q, J = 6.2 Hz, 1-H), 6.58 (1H, s, 8-H) and 7.58 (1H, s, 5-H); ms (m/z) 362 (100) $(M)^+$.

(±)-*cis*-6,7,8,9-Tetramethoxy-10-methoxymethoxy-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran (7). As in the preceding paragraph, crude ether (**5**), in the presence of cetyltrimethylammonium bromide (95 mg; 0.25 mmol), THF (25 ml) and H_2O (4.7 ml), was converted with $Na_2S_2O_4$ (2.2 g; 12 mmol) in H_2O (7.6 ml), KOH (2.5 g; 45 mmol) in H_2O (6.4 ml) and dimethyl sulfate (2.8 g; 22 mmol) into tetramethyl ether (**7**) (679 mg; 87%) mp 119.5-120.0°C (from petroleum ether, bp 65-110°C); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.37 (3H, d, J = 5.9 Hz, 3-CH_3), 1.70 (3H, d, J = 6.2 Hz, 1-CH_3), 2.80 (2H, irregular m, 4-H), 3.57 (3H, s, 10-$OCH_2OC\underline{H}_3$), 3.75 (1H, m, 3-H), 3.81, 3.97, 3.99 and 4.00 (4 × 3H, 4s, 6,7,8,9-OCH_3), 4.90 (1H, d, J = 6.6 Hz, 10-$OC\underline{H}_2OCH_3$), 5.11 (1H, d, J = 6.6 Hz, 10-$OC\underline{H}_2OCH_3$), 5.34 (1H, q, J = 6.2 Hz, 1-H) and 7.58 (1H, s, 5-H); ms (m/z) 392 (100) $(M)^+$. Anal. Calcd for $C_{21}H_{28}O_7$: C, 64.27; H, 7.19. Found: C, 64.36; H, 7.25.

(±)-*cis*-10-Hydroxy-6,7,9-trimethoxy-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran (8). A solution of methoxymethyl ether (**6**) (835 mg; 2.30 mmol) in methanol (200 ml) containing 2 drops (46 mg) of conc. H_2SO_4 was stirred at room temperature for 6.5 h, poured into H_2O (100 ml) and extracted with $CHCl_3$ (3 × 100 ml). Purification of the residue by chromatography (wet column) (CH_2Cl_2 - AcOEt 49:1) gave naphthol (**8**) (545 mg; 75%), mp 135.5-136.0°C (from MeOH) (a trace of the trans-isomer was also isolated); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.36 (3H, d, J = 6.2 Hz, 3-CH_3), 1.65 (3H, d, J = 6.2 Hz, 1-CH_3), 2.78 (2H, irregular m, 4-H), 3.71 (1H, m, 3-H), 3.89, 3.96 and 4.01 (3 × 3H, 3s, 6,7,9-OCH_3), 5.19 (1H, q, J = 6.2 Hz, 1-H), 6.51 (1H, s, 8-H), 7.28 (1H, s, 5-H) and 9.50 (1H, s, 10-H); ms (m/z) 318 (70) $(M)^+$, 303 (100). Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.90; H, 6.98. Found: C, 67.74; H, 6.89.

(±)-*cis*-10-Hydroxy-6,7,8,9-tetramethoxy-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran (9). Cleavage of methoxymethyl ether (**7**) (392 mg; 1.00 mmol) in methanol (100 ml) and conc. H_2SO_4 (46 mg)

(48 h) as in the preceding case afforded naphthol (**9**) (289 mg; 83%) mp 76.0-77.0°C (from MeOH) (along with a trace of the trans-isomer); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.36 (3H, d, J = 6.2 Hz, 3-CH_3), 1.65 (3H, d, J = 6.2 Hz, 1-CH_3), 2.77 (2H, irregular m, 4-H), 3.71 (1H, m, 3-H), 3.96, 4.00 and 4.09 (6H, 3H, 3H, 3s, 6,7,8,9-OCH_3), 5.20 (1H, q, J = 6.2 Hz, 1-H), 7.29 (1H, s, 5-H) and 9.86 (1H, s, 10-OH); ms (m/z) 348 (46) $(M)^+$, 333 (100).

(±)-*cis*-6,7,9-Trimethoxy-1,3-dimethyl-3,4,5,10-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-5,10-dione[(±)-ventiloquinone E] (10).

a) To a solution of naphthol (**8**) (64 mg; 0.20 mmol) in a 2:1 (v/v) mixture of MeCN and H_2O (18 ml) was added at 0°C [bis(trifluoroacetoxy)iodo]benzene (189 mg; 0.44 mmol) in the same solvent (18 ml). The reaction mixture was stirred at this temperature (2 h) and at room temperature (2 h) then diluted with H_2O (50 ml) and extracted with $CHCl_3$ (3 × 50 ml). Purification of the crude product by chromatography (wet column) (Et_2O - C_6H_6 1:1) gave ventiloquinone E (49 mg; 74%), mp 127.0-128.0°C (from ligroine) [lit.,[7] (+)-isomer, mp 119°C; [8](±)-isomer, mp 129-130°C].

b) Oxidation of the same substrate (**8**) (1.20 mmol) in MeCN (60 ml) with ceric ammonium nitrate (2.63 g; 4.80 mmol) in H_2O (27 ml), as for naphthol (**9**), provided the same product (**10**) (255 mg; 64%); ir ν_{max} (KBr) 1650, 1630 cm^{-1}; ^{1}H-nmr (400 MHz, $CDCl_3$) δ 1.34 (3H, d, J = 6.2 Hz, 3-CH_3), 1.50 (3H, d, J = 6.6 Hz, 1-CH_3), 2.11 (1H, ddd, J = 18.2; 10.3; 3.7 Hz, 4-Ha), 2.78 (1H, dt, J = 18.2; 2.6 Hz, 4-He), 3.50 (1H, ddq, J = 10.2; 6.2; 2.6 Hz, 3-H), 3.87, 3.97 (3H, 6H, 2s, 6,7,9-OCH_3), 4.80 (1H, ddq, J = 6.6; 3.7; 2.6 Hz, 1-H) and 6.73 (1H, s 8-H); ^{13}C-nmr (50.3 MHz, $CDCl_3$) δ 20.67 (3-CH_3), 21.34 (1-CH_3), 29.65 (4-C), 56.21, 56.77 and 61.32 (6,7, 9-OCH_3), 68.87 (3-C), 70.03 (1-C), 101.28 (8-C), 113.43 and 126.44 (5a, 9a-C), 140.54 (4a-C), 143.21 (10a-C), 147.45 (7-C), 157.44 (6-C), 159.20 (9-C), 182.30 and 183.52 (5, 10-C); ms (m/z) 332 (62) $(M)^+$, 317 (100). Anal. Calcd for $C_{18}H_{20}O_6$: C, 65.04; H, 6.08. Found: C, 64.71; H, 6.24.

(±)-*cis*-6,7,8,9-Tetramethoxy-1,3-dimethyl-3,4,5,10-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-5,10-dione (11).

A mixture obtained from naphthol (**9**) (261 mg; 0.750 mmol) in MeCN (30 ml) and ceric ammonium nitrate

(1.85 g; 3.30 mmol) in H_2O (18.5 ml) was stirred at room temperature for 30 min, diluted with H_2O (100 ml) and extracted with $CHCl_3$ (3 × 100 ml). The crude product, purified by chromatography (dry column) (AcOEt - petroleum ether, bp 35-60°C 1:4) afforded quinone (**11**) (244 mg; 90%), mp 88.0-89.0°C (from ligroine) [lit.,[7] (+)-isomer, mp 113°C]; ir ν_{max} (KBr) 1660, 1635 cm^{-1}; ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.31 (3H, d, J = 6.2 Hz, 3-CH_3), 1.45 (3H, d, J = 6.6 Hz, 1-CH_3), 2.06 (1H, ddd, J = 18.3; 10.3; 3.7 Hz, 4-Ha), 2.77 (1H, dt, J = 18.3; 2.6 Hz, 4-He), 3.51 (1H, ddq, J = 10.3; 6.2; 2.6 Hz, 3-H), 3.86 and 3.88 (2 × 3H, 2s, 7,8-OCH_3), 3.97 and 3.98 (2 × 3H, 2s, 6,9-OCH_3) and 4.78 (1H, ddq, J = 6.6; 3.7; 2.6 Hz, 1-H); ^{13}C-nmr (50.3 MHz, $CDCl_3$) δ 20.37 (3-CH_3), 21.34 (1-CH_3), 29.67 (4-C), 61.63 and 61.87 (6,7,8,9-OCH_3), 69.00 (3-C), 69.85 (1-C), 121.20 and 121.97 (5a, 9a-C), 141.41 (4a-C), 146.94 (10a-C), 150.65, 150.89, 152.29 and 152.51 (6,7,8,9-C), 182.30 and 183.23 (5,10-C); ms (m/z) 362 (78) $(M)^+$, 347 (100). Anal. Calcd for $C_{19}H_{22}O_7$: C, 62.96; H, 6.13. Found: C, 62.95; H, 6.12.

(±)-*cis*-5,10-Dihydroxy-7-methoxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-dione (12). A mixture of (±)-ventiloquinone E (**10**) (42 mg; 0.13 mmol), LiI (55 mg; 0.40 mmol) in dry *t*-butyl methyl ketone (10 ml) was heated to reflux (24 h), cooled, diluted with $CHCl_3$ and washed with H_2O. Chromatography (wet column) (CH_2Cl_2 - AcOEt 49:1) of the crude residue provided quinone (**12**) (28 mg; 75%), mp 186.0-187.0°C (from MeOH); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 1.38 (3H, d, J = 6.2 Hz, 3-CH_3), 1.62 (3H, d, J = 6.6 Hz, 1-CH_3), 2.38 (1H, ddd, J = 18.0; 10.3; 2.6 Hz, 4-Ha), 2.87 (1H, dt, J = 18.0; 2.2 Hz, 4-He), 3.60 (1H, m, 3-H), 3.93 (3H, s, 7-OCH_3), 5.01 (1H, m, 1-H), 6.19 (1H, s, 8-H), 12.74 and 13.34 (2 × 1H, 2s, 5, 10-OH); ms (m/z) 304 (100) $(M)^+$.

(±)-*cis*-5,7,10-Trihydroxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-dione[(±)-ventiloquinone G] (13).

(±)-Ventiloquinone E (33 mg; 0.10 mmol) in dry CH_2Cl_2 (10 ml) was added at 0°C to anhydrous $AlCl_3$ (133 mg, 1.00 mmol) in the same solvent (2 ml). The mixture was stirred at room temperature (48 h) then poured in ice (20 g), conc. HCl (5.5 ml) and $CHCl_3$ (50 ml). Vigorous agitation was maintained for 48 h, then

the aqueous solution was extracted with $CHCl_3$ (3 × 50 ml). Chromatography of the crude product (wet column) (AcOEt - petroleum ether, bp 35-60°C 1:3) allowed the elimination of a small amount of quinone (**12**) and elution with methanol gave (±)-ventiloquinone G (26 mg; 90%), mp 186.5-187.0°C (from MeOH-ligroine)[lit.,[7] (+)-isomer, mp 183°C; [8](±)-isomer, mp 183°C]; ir ν_{max} (KBr) 3200 (br), 1610, 1590 cm^{-1}; ^{1}H-nmr (400 MHz, $CDCl_3$) δ 1.40 (3H, d, J = 6.1 Hz, 3-CH_3), 1.65 (3H, d, J = 6.4 Hz, 1-CH_3), 2.42 (1H, ddd, J = 17.6; 10.4; 2.6 Hz, 4-Ha), 2.88 (1H, dt, J = 17.6; 2.1 Hz, 4-He), 3.63 (1H, ddq, J = 10.4; 6.2; 2.1 Hz, 3-H), 5.03 (1H, qt, J = 6.3; 2.3 Hz, 1-H), 6.35 (1H, s, 8-H), 7.40 (1H, br s, 7-OH), 11.95 and 13.47 (2 × 1H, 2s, 5,10-OH); ^{13}C-nmr (50.3 MHz, $CDCl_3$) δ 20.98 (3-CH_3), 21.26 (1-CH_3), 30.75 (4-C), 68.68 (3-C), 70.90 (1-C), 108.15 and 108.55 (5a, 9a-C), 111.19 (8-C), 135.55 (4a-C), 144.14 (10a-C), 156.93, 157.61 and 158.59 (5,7,10-C), 179.50 and 186.72 (6,9-C); ms (m/z) 290 (100) $(M)^+$. Anal. Calcd for $C_{15}H_{14}O_6$: C, 62.06; H, 4.87. Found: C, 61.68; H, 4.96.

(±)-*cis*-5,10-Dihydroxy-7,8-dimethoxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-dione[(±)-ventiloquinone D] (14).

A mixture of quinone (**11**) (181 mg; 0.500 mmol) and LiI (205 mg; 1.50 mmol) in dry t-butyl-methyl ketone (50 ml) was stirred at 50°C for 3 h. Treatment of the product as for compound (**12**) gave (±)-ventiloquinone D (75 mg; 45%), mp 121.0-121.5°C (from MeOH) [lit.,[7] (+)-isomer, mp 101°C]; ir ν_{max} (KBr) 1600 cm^{-1}; ^{1}H-nmr (400 MHz, $CDCl_3$) δ 1.39 (3H, d, J = 6.1 Hz, 3-CH_3), 1.63 (3H, d, J = 6.4 Hz, 1-CH_3), 2.40 (1H, ddd, J = 17.8; 10.4; 2.6 Hz, 4-Ha), 2.89 (1H, dt, J = 17.8; 2.1 Hz, 4-He), 3.62 (1H, ddq, J = 10.4; 6.1; 2.3 Hz, 3-H), 4.08 (6H, s, 7,8-OCH_3), 4.99 (1H, ddq, J = 6.4; 2.4; 2.1 Hz, 1-H), 12.80 and 13.05 (2 × 1H, 2s, 5,10-OH); ^{13}C-nmr (50.3 MHz, $CDCl_3$) δ 21.05 (3-CH_3), 21.39 (1-CH_3), 30.96 (4-C), 61.63 (7,8-OCH_3), 68.69 (3-C), 70.65 (1-C), 107.85 (5a, 9a-C), 137.59 and 140.87 (4a, 10a-C), 147.63 and 147.78 (7,8-C), 158.31 (5,10-C), 181.61 and 181.72 (6,9-C); ms (m/z) 334 (100) $(M)^+$. Anal. Calcd for $C_{17}H_{18}O_7$: C, 61.06; H, 5.44. Found: C, 60.93; H, 5.45.

(±)-*cis*-5,7 or 8,10-Trihydroxy-7- or 8-methoxy-1,3-dimethyl-3,4,6,9-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-6,9-

dione[(±)-ventiloquinone C] (15).

A mixture of quinone (**11**) (507 mg; 1.40 mmol) and LiI (600 mg; 4.20 mmol) in dry t-butyl methyl ketone (75 ml) was heated to reflux for 5 h and worked up as for compound (**12**). Chromatographic separation (wet column) (CH_2Cl_2 - AcOEt 49:1) isolated a small amount of ventiloquinone D (**14**) and elution with methanol afforded the mixture known as ventiloquinone C (218 mg; 49%). Repeated trituration of this product with ether gave a pure sample (54 mg) of one of the isomers, mp 214.0-215.0°C (from MeOH)[lit.,[7] (+)-mixture, mp 137°C]; ir ν_{max} (KBr) 3330, 1600 cm^{-1}; ^{1}H-nmr (400 MHz, $CDCl_3$) δ 1.39 (3H, d, J = 6.1 Hz, 3-CH_3), 1.63 (3H, d, J = 6.4 Hz, 1-CH_3), 2.42 (1H, ddd, J = 17.9; 10.5; 2.6 Hz, 4-Ha), 2.91 (1H, dt, J = 17.8; 2.1 Hz, 4-He), 3.62 (1H, ddq, J = 10.5; 6.2; 2.4 Hz, 3-H), 4.20 (3H, s, 7 or 8-OCH_3), 5.00 (1H, ddq, J = 6.4; 2.3; 2.1 Hz, 1-H), 6.92 (1H, s, 7 or 8-OH), 12.23 and 12.93 (2 × 1H, 2s, 5,10-OH); ^{13}C-nmr (50.3 MHz, $CDCl_3$) δ 20.89 (3-CH_3), 21.26 (1-CH_3), 31.06 (4-C), 60.68 (7 or 8-OCH_3), 68.65 (3-C), 70.51 (1-C), 106.84 and 107.22 (5a, 9a-C), 138.69 and 139.44 (7,8-C), 140.55 (10a-C), 143.06 (4a-C), 155.53 and 156.25 (5, 10-C), 182.26 and 183.82 (6,9-C); ms (m/z) 320 (100) $(M)^+$. Anal. Calcd for $C_{16}H_{17}O_7$: C, 60.00; H. 5.03. Found: C, 60.13; H, 4.97.

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