139975-79-4; 7, 126664-27-5; 7 (5-bromo), 139975-80-7; 8, 16935-04-9; 8 (5-bromo), 139975-81-8; 9, 13230-22-3; 9 (5-bromo), 72896-08-3; 10, 13230-06-3; 10 (5-bromo), 41604-61-9; 11, 139975-82-9; 11 (5-bromo), 139975-83-0; 12, 25459-12-5; 12 (5-bromo), 139975-84-1.

Supplementary Material Available: Elemental analyses for compounds 3-9, 11, and 12 (1 page). Ordering information is given on any current masthead page.

A Practical Preparation of Functionalized Alkylbenzoquinones: Synthesis of Maesanin and Irisquinone[1]

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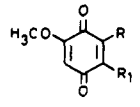
Natural products that contain the aromatic quinoid structure are of great medicinal importance.[2] Several highly functionalized quinones, for example, maesanin (**1a**),[3] irisquinone (**1b**),[4] irisoquin (**1c**),[5] rapanone (**1d**),[6] primine (**1e**),[7] among others,[8] which have alkyl chains of various lengths, have been isolated from natural sources and hold immense interest because of their biological activities. These molecules differ primarily in the presence



1a	Maesanin	R = $-(CH_2)_9-CH=CH-(CH_2)_3-CH_3$, R_1 = OH
1b	Irisquinone	R = $-(CH_2)_9-CH=CH-(CH_2)_5-CH_3$, R_1 = H
1c	Rapanone	R = $-(CH_2)_{12}-CH_3$, R_1 = OH
1d	Irisoquin	R = $-(CH_2)_{17}-CH_3$, R_1 = OH
1e	Primine	R = $-(CH_2)_4-CH_3$, R_1 = H

of an OH group at the C-5 position and in the type of side chain attached at the C-6 ring position, and these factors apparently determine their structure–activity relationships. The synthetic challenge of these molecules lies in the side chain attachment. This has been achieved in the past by circuitous routes, for instance, by the reaction of metallated aromatic rings with aldehydes followed by the deoxygenation of the resultant hydroxy group,[9] and by the Claisen rearrangement of a 3-phenoxy-1-alkene,[10] a method that often suffers from regiochemical problems. A conceivable convergent route to such molecules would be the direct alkylation of the aromatic nucleus with an alkyl halide. However, this method has not been utilized to synthesize any of these molecules, presumably due to the low yields of such alkylation reactions[11] with aliphatic halides. Our need for an efficient synthetic means to these alkylbenzoquinones for purposes of studying their structure–activity relationships prompted us to look for an alternative. The Heck-type reaction,[12] i.e. the palladium-mediated coupling of bromobenzene derivatives with terminal olefins, was investigated as a method for attaching a suitable side chain. The resultant molecule could then be transformed into the desired target, realizing an entry into this class of compounds. The effectiveness of this protocol has been successfully demonstrated in the syntheses of maesanin[3,13] and irisquinone.[4,14]

Maesanin is an active principle isolated from the berries of the East African *Maeses lanceolata* bush, the water extract of which is used as a preventive measure against cholera. Kubo and co-workers, who isolated this active principle on the basis of information provided by "Bwana Mganga", elucidated its structure and confirmed the structural assignment by synthesis. Maesanin is also a "host defensive stimulant" and has a direct activity against *Escherichia coli*, disrupting the enzyme KDO-transfrase, which is essential in cell-wall synthesis. In addition, maesanin has been shown to block 5-lipoxygenase and therefore may find use as an antiasthmatic drug.[15]

Results and Discussion

We began the synthesis of **1a** with the transformation of 3-bromo-4-hydroxy-5-methoxybenzaldehyde to the triacetyl compound **2** (in 54% overall yield) by a known procedure.[16] Since the acetyl groups did not survive the palladium-mediated coupling reaction, a better protecting group was sought. Methoxy methyl ether was chosen, keeping in mind that it must remain distinct from the ring methoxy group upon deprotection. Thus, the acetyl groups were removed by passing dry HCl gas through a methanolic solution of **2** at 0 °C to yield a rather unstable trihydroxy compound, which was immediately reprotected (K_2CO_3, MOM-Cl, acetone, 12 h) to obtain the tri-MOM ether **3a** in 62% yield. **3a** was subjected to a Heck-type coupling reaction with 9-decen-1-ol, mediated by palladium to furnish the alkylated product **4a**. Conversion of starting material to product was incomplete even after prolonged hours of heating, presumably because of the deposition of palladium metal. However, this problem was circumvented by the addition of excess catalyst along with Ph_3P at in-

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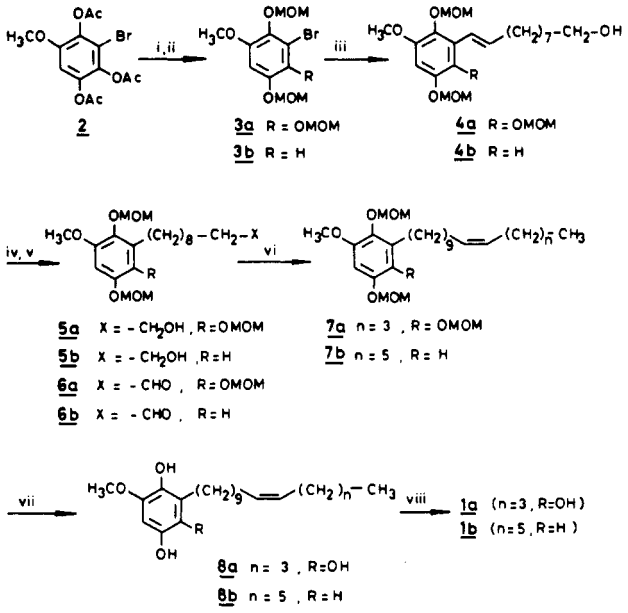
Scheme I[a]



[a] (i) Dry HCl gas, MeOH, 0 °C, 1 h; (ii) K_2CO_3, MOM chloride, acetone, rflux, 12 h; (iii) 9-decen-1-ol, $Pd(OAc)_2$, PPh_3, TEA, 80 °C; (iv) H_2, Pd/C, ethanol, 25 °C, 4 h; (v) DMSO, oxalyl chloride, TEA, CH_2Cl_2, −78 → 25 °C, 1 h; (vi) $NaNH_2$, $C_{n+2}H_{2n+5}P^+Ph_3Br^-$, THF −78 → 25 °C, 3 h; (vii) 47% HBr, ethanol, 25 °C, 1 h; (viii) Ag_2CO_3, benzene, 25 °C, 2 h.

tervals, and this afforded **4a** in better yield. The double bond in compound **4a** was easily hydrogenated over 10% palladized charcoal to give the saturated alcohol **5a**. Swern oxidation[17] [$(COCl)_2$, DMSO then Et_3N at −78 °C] of alcohol **5a** yielded aldehyde **6a**. Wittig olefination of aldehyde **6a** with *n*-pentylidenetriphenylphosphorane, which was generated in situ from the corresponding phosphonium bromide and $NaNH_2$, afforded exclusively the (*Z*)-olefin **7a**. Deprotection of the MOM ether of **7a** was effected[18] by the addition of a few drops of 48% HBr to the ethanolic solution of **7a**, which produced the required methoxyhydroquinone **8a** in 93% yield. Finally, hydroquinone **8a** was oxidized to maesanin **1a**, mp 69 °C (lit.[2] mp 70 °C) with Ag_2CO_3 in benzene in 91% yield. Spectral data was identical with reported values.

Likewise, the present strategy has been extended to the synthesis of irisquinone,[4,14] which is isolated from *Iris pallasii Fisch* and *Iris pseudacorus*. This compound is of interest in tumour radiotherapy as a potential radiosensitizer.[19] The synthesis of irisquinone was commenced with 2,5-dihydroxy-3-methoxybromobenzene,[20] which was protected as its methoxy methyl ether **3b**. Palladium-mediated coupling of compound **3b** with 9-decen-1-ol produced the alkylated product **4b** in 65% yield. It is noteworthy that this reaction was higher yielding and that the starting material disappeared in only 10 h, in contrast to the results with **3a**. **4b** was transformed to irisquinone by a set of reactions similar to that described for maesanin, except that in the Wittig olefination, *n*-heptyltriphenylphosphonium bromide was used. The overall yield from **4b** was 47%.

In conclusion, we have presented here a novel approach to the regiospecific and expedient synthesis of highly functionalized alkylbenzoquinones. The above strategy should thus find wide applicability to the syntheses of several other natural products belonging to this class of compounds.

Experimental Section

^1H nuclear magnetic resonance spectra were recorded at 80 MHz (FT-80A, Varian) or 200 MHz (Gemini, Varian) in $CDCl_3$. Chemical shifts of ^1H NMR are reported in parts per million relative to internal tetramethylsilane (0.0 ppm). *J* values are in hertz. Infrared spectra were obtained from neat liquids or solutions as capillary films between KBr plates on a Perkin-Elmer 683 or 1310 recording infrared spectrometer. Mass spectral data were obtained on either a Finnigan MAT 1020 B or a Micromass VG 70-70H spectrometer. Glass-support precoated (Merck silica gel 60 F 254, 0.25 mm) plates were employed for analytical TLC. Solvents were distilled before use, and petroleum ether refers to bp 60–80 °C. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium/benzophenone ketyl immediately prior to use.

2,3,6-Tris(methoxymethoxy)-5-methoxy-1-bromobenzene (3a). Triacetate **2**[16] (5 g, 14.8 mmol) was suspended in 25 mL of dry methanol and cooled to ice-bath temperature. Dry HCl gas was bubbled slowly into the solution for 1 h; following this the ice bath was removed and the reaction mixture was stirred for 1.5 h. The solvent was removed under reduced pressure to afford a solid residue of trihydroxy compound, which was dissolved in 20 mL of dry acetone under nitrogen atmosphere, and 8.6 g (62.3 mmol) of anhydrous potassium carbonate followed by 6.62 mL (87.16 mmol) of chloromethyl methyl ether were added. The reaction mixture was refluxed for 12 h. The resulting brown solution was filtered through celite, and the contents were concentrated. To this residue was added 25 mL of water, and the mixture was extracted with ether. The combined ethereal layers were washed with brine and dried (Na_2SO_4). Removal of the solvent furnished 3.37 g (62% yield) of **3a** as syrup. ^1H NMR ($CDCl_3$): δ 3.66 (s, 6 H, OCH_3 × 2), 3.85 (s, 6 H, OCH_3 × 2), 5.1 (s, 6 H, OCH_2OCH_3), 6.52 (s, 1 H, aromatic). IR (neat): ν 2950, 1590, 1020 cm^{-1}. Mass: *m/z* 368 (10, M^+ + 2), 366 (10, M^+), 181 (80), 45 (100). Anal. Calcd for $C_{13}H_{19}O_7Br$: C, 42.52; H, 5.22; Br, 21.76. Found: C, 42.46; H, 5.17; Br, 21.63.

2,5-Bis(methoxymethoxy)-3-methoxy-1-bromobenzene (3b). 2,5-Dihydroxy-3-methoxy-1-bromobenzene[20] (12.8 g, 58.5 mmol) was suspended in dry acetone (100 mL) to which was added anhydrous K_2CO_3 (24.2 g, 175.5 mmol) under a N_2 atmosphere followed by MOM chloride (14.2 mL, 175.5 mmol) after a short interval. The reaction mixture was refluxed for 10 h. After cooling, it was filtered through celite and solvent was removed. To this residue was added water, and the mixture was extracted with ether. The combined ethereal layers were washed with brine and dried (Na_2SO_4). Evaporation of the solvent yielded **3b** (14.3 g) as a liquid in 82% yield. ^1H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 5.08 (s, 2 H, OCH_2OCH_3), 5.11 (s, 2 H, OCH_2OCH_3), 6.58 (d, 1 H, *J* = 3 Hz, aromatic), 6.86 (d, 1 H, *J* = 3 Hz, aromatic). IR (neat): ν 2950, 1590 cm^{-1}. Mass: *m/z* 308 (38, M^+ + 2), 306 (38, M^+), 227 (44), 59 (60), 45 (100). Anal. Calcd for $C_{11}H_{15}O_5Br$: C, 43.01; H, 4.92; Br, 26.02. Found: C, 43.12; H, 4.84; Br, 26.14.

1-[2,3,6-Tris(methoxymethoxy)-5-methoxyphenyl]-1-decen-10-ol (4a). A mixture of **3a** (800 mg, 2.18 mmol) and 9-decen-1-ol (408 mg, 2.60 mmol) in 5 mL of triethylamine was taken in a round-bottom flask and flushed with nitrogen and the mixture was kept at 80 °C, while stirring. Palladium acetate (97 mg, 0.436 mmol) and triphenylphosphine (230 mg, 0.872 mmol) were divided into three equal portions and each portion was added to the reaction mixture at the interval of 3 h. After the addition of last portion, the reaction mixture was further stirred for 17 h at the same temperature. After cooling, the contents were diluted with ether (30 mL). The ethereal layer was washed with 10% hydrochloric acid (30 mL) and water followed by brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to

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leave an oily residue, which was purified to obtain 470 mg (49% yield, based on the recovery of **3a**) of **4a**. ^{1}H NMR ($CDCl_3$): δ 1.2–1.4 (m, 10 H, methylenes), 1.55 (m, 2 H, ArCH=CHCH$_2$CH$_2$), 2.18–2.4 (m, 2 H, allylic), 3.56 (t, 2 H, J = 6 Hz, CH$_2$OH), 3.58 (s, 6 H, OCH$_3$ × 2), 3.84 (s, 6 H, OCH$_3$ × 2), 5.04 (s, 6 H, OCH$_2$OCH$_3$ × 3), 5.3–5.65 (m, 1 H, ArCH=CH), 6.44 (s, 1 H, aromatic), 6.55 (dt, 1 H, J = 7 Hz, ArCH=CH). IR (neat): ν 3400, 2955, 1600, 1110, 950 cm^{-1}. Mass: m/z 442 (5, M$^+$), 426 (5), 380 (10), 336 (100), 305 (60). Anal. Calcd for $C_{23}H_{38}O_8$: C, 62.42; H, 8.66. Found: C, 62.93; H, 8.42.

1-[2,5-Bis(methoxymethoxy)-3-methoxyphenyl]-1-decen-10-ol (4b). Compound **4b** was prepared from **3b** (2.36 g, 7.69 mmol), adopting the same procedure as described for **4a**, except that the reaction mixture was heated at 80 °C only for 12 h, as it was found that starting material did not remain by then, 1.59 g (65% yield). ^{1}H NMR ($CDCl_3$): δ 1.2–1.4 (s, 12 H, methylenes), 2.0 (br s, 1 H, OH), 2.1–2.3 (m, 2 H, allylic), 3.5 (s, 3 H, OCH$_3$), 3.59 (s, 3 H, OCH$_3$), 3.65 (t, 2 H, J = 6 H, CH$_2$OH), 3.8 (s, 3 H, OCH$_3$), 5.0 (s, 2 H, OCH$_2$OCH$_3$), 5.18 (s, 2 H, OCH$_2$OCH$_3$), 5.52 (dt, 1 H, J_{trans} = 16 Hz, $J_{allylic}$ = 1.5 Hz, ArCH=CH), 6.2 (dt, 1 H, J = 7 Hz, ArCH=CH), 6.5 (d, 1 H, J = 2,8 Hz, aromatic), 6.76 (d, 1 H, J = 2.8 Hz, aromatic). IR (neat): ν 3400, 2955, 1600, 1110, 950 cm^{-1}. Mass: m/z 382 (18, M$^+$), 352 (10), 306 (5), 167 (10), 45 (100). Anal. Calcd for $C_{21}H_{34}O_6$: C, 65.94; H, 8.96. Found: C, 65.63; H, 9.01.

1-[2,3,6-Tris(methoxymethoxy)-5-methoxyphenyl]decan-10-ol (5a). Compound **4a** (224 mg, 0.507 mmol) was taken in ethanol (10 mL), and to this was added catalytic amount of palladized charcoal. This reaction mixture was stirred under hydrogen atmosphere for 4 h. The contents were filtered, and ethanol was removed at reduced pressure to produce 213 mg (95%) of **5a**, which was purified through column chromatography. ^{1}H NMR ($CDCl_3$): δ 1.22–1.44 (m, 14 H, methylenes), 1.55 (m, 2 H, ArCH$_2$CH$_2$), 1.92 (br s, 1 H, OH), 2.6–2.75 (m, 2 H, benzylic), 3.54 (s, 6 H, OCH$_3$ × 2), 3.6 (t, 2 H, J = 6 Hz, CH$_2$OH), 3.8 (s, 6 H, OCH$_3$ × 2), 5.0 (s, 6 H, OCH$_2$OCH$_3$ × 3), 6.39 (s, 1 H, aromatic). IR (neat): ν 3450, 2950, 1590 cm^{-1}. Mass: m/z 444 (2, M$^+$), 414 (10), 337 (60), 307 (100), 183 (70). Anal. Calcd for $C_{23}H_{40}O_8$: C, 62.13; H, 9.07. Found: C, 62.43;H, 8.93.

1-[2,5-Bis(methoxymethoxy)-3-methoxyphenyl]decan-10-ol (5b). Compound **5b** (955 mg) was prepared from **4b** (1 g, 2.62 mmol) in 95% yield, adopting the same procedure as described for **5a**. ^{1}H NMR ($CDCl_3$): δ 1.22–1.44 (m, 16 H, methylenes), 2.62 (t, 2 H, J = 6.5 Hz, benzylic), 3.48 (s, 3 H, OCH$_3$), 3.58 (s, 3 H, OCH$_3$), 3.65 (t, 2 H, J = 6.5 Hz, CH$_2$OH), 3.85 (s, 3 H, OCH$_3$), 5.0 (s, 2 H, OCH$_2$OCH$_3$), 5.12 (s, 2 H, OCH$_2$OCH$_3$), 6.46 (d, 1 H, J = 2.77 Hz, aromatic), 6.50 (d, 1 H, 2.77 Hz, aromatic). IR (neat): ν 3430, 2900, 1580 cm^{-1}. Mass: m/z 384 (5, M$^+$), 352 (35), 332 (95), 278 (95), 167 (60), 153 (95), 45 (100). Anal. Calcd for $C_{21}H_{36}O_6$: C, 65.59; H, 9.44. Found: C, 65.12; H, 9.63.

1-[2,3,6-Tris(methoxymethoxy)-5-methoxyphenyl]decan-10-al (6a). A mixture of dichloromethane (10 mL) and oxalyl chloride (1.0 mL, 11 mmol) was placed in a two-neck round-bottom flask. The dimethyl sulfoxide (1.7 mL, 22 mmol) was added to the stirred oxalyl chloride solution under a nitrogen atmosphere at −78 °C. The reaction mixture was stirred for 5 min, the alcohol **5a** (174 mg, 0.4 mmol) was added, and stirring was continued at the same temperature for an additional hour. Triethylamine (7.0 mL, 50 mmol) was added, and the reaction mixture was stirred for 5 min and then allowed to warm to room temperature. Water (10 mL) was added, and the aqueous layer was extracted with additional dichloromethane (10 mL). The organic layers were combined, washed with saturated sodium chloride solution (15 mL), and dried (Na_2SO_4). Concentration of the solvents at reduced pressure produced aldehyde **6a** in 86% yield (147 mg). ^{1}H NMR ($CDCl_3$): δ 1.2–1.4 (m, 14 H, methylenes), 2.4 (dt, 2 H, J_1 = 6.48 Hz, J_2 = 1.3 Hz, CH$_2$CHO), 2.7 (t, 2 H, J = 6.2 Hz, benzylic) 3.6 (s, 6 H, OCH$_3$ × 2), 3.84 (s, 6 H, OCH$_3$ × 2), 5.05 (s, 6 H, OCH$_2$OCH$_3$ × 3), 6.42 (s, 1 H, aromatic), 9.8 (t, 1 H, J = 1.3 Hz, CHO). IR (neat): ν 2905, 1720, 1590 cm^{-1}. Mass: m/z 442 (10, M$^+$), 412 (85), 367 (100), 336 (40). Anal. Calcd for $C_{23}H_{38}O_8$: C, 62.42; H, 8.66. Found: C, 62.23; H, 8.74.

1-[2,5-Bis(methoxymethoxy)-3-methoxyphenyl]decan-10-al (6b). Compound **6b** (250 mg) was prepared from **5b** (300 mg, 781 mmol) in 84% yield, adopting the same procedure as as described for **6a**. ^{1}H NMR ($CDCl_3$): δ 1.2–1.4 (m, 12 H, methylenes), 1.6 (m, 2 H, ArCH$_2$CH$_2$), 2.4 (dt, 2 H, J_1 = 5.78 Hz, J_2 = 1.4 Hz, CH$_2$CHO), 2.65 (t, 2 H, J = 6.5 Hz, benzylic), 3.48 (s, 3 H, OCH$_3$), 3.6 (s, 3 H, OCH$_3$), 3.82 (s, 3 H, OCH$_3$), 5.0 (s, 2 H, OCH$_2$OCH$_3$), 5.14 (s, 2 H, OCH$_2$OCH$_3$), 6.47 (d, 1 H, J = 2.6 Hz, aromatic), 6.51 (d, 1 H, J = 2.6 Hz, aromatic), 9.78 (t, 1 H, J = 1.4 Hz, CHO). IR (neat): ν 2905, 1720, 1590 cm^{-1}. Mass: m/z 382 (40, M$^+$), 352 (10), 337 (10), 167 (20), 45 (100). Anal. Calcd for $C_{21}H_{34}O_6$: C, 65.94; H, 8.96. Found: C, 66.23; H, 8.87.

(*Z*)-1-[2,3,6-Tris(methoxymethoxy)phenyl]-10-pentadecene (7a). A stirred suspension of pentyltriphosphonium bromide (187 mg, 0.452 mmol) in dry THF (5 mL) under a nitrogen atmosphere was treated with $NaNH_2$ (18 mg, 0.452 mmol) at room temperature. After 1 h, the reaction mixture was cooled (−78 °C), a THF (3 mL) solution of aldehyde **6a** (100 mg, 0.226 mmol) was added and allowed to stir for an additional 2 h. It was quenched with NH_4Cl solution and extracted with ether. The organic layer was washed with water and brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue of column chromatography afforded olefin **7a** (70 mg) in 63% yield, as a syrup. ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, J = 5.5 Hz, CH$_3$CH$_2$), 1.2–1.48 (m, 18 H, methylenes), 2.0 (m, 4 H, allylic), 2.7 (t, 2 H, J = 7 Hz, benzylic), 3.58 (s, 6 H, OCH$_3$ × 2), 3.80 (s, 6 H, OCH$_3$ × 2), 5.02 (s, 6 H, OCH$_2$OCH$_3$ × 3), 5.35 (t, 2 H, J = 5 Hz, CH=CH), 6.4 (s, 1 H, aromatic). IR (neat): ν 2900, 1600 cm^{-1}. Mass: m/z 466 (20, M$^+$ − 30), 421 (20), 390 (10), 183 (20), 45 (100). Anal. Calcd for $C_{28}H_{48}O_7$: C, 67.91; H, 9.74. Found: C, 67.43; H, 9.52.

(Z)-1-[2,5-Bis(methoxymethoxy)-3-methoxyphenyl]-10-heptadecene (7b). Compound **7b** (178 mg) was prepared from **6b** (224 mg, 0.588 mmol) and *n*-heptylphosphonium bromide (520 mg, 1.17 mmol) in 66% yield, adopting the same procedure as described for **7a**. ^{1}H NMR ($CDCl_3$): δ 0.9 (t, 3 H, J = 5.5 Hz, CH$_3$CH$_2$), 1.2–1.45 (m, 22 H, methylenes), 2.0 (m, 4 H, allylic), 2.62 (t, 2 H, J = 7 Hz, benzylic), 3.48 (s, 3 H, OCH$_3$), 3.59 (s, 3 H, OCH$_3$), 3.82 (s, 3 H, OCH$_3$), 5.0 (s, 2 H, OCH$_2$OCH$_3$), 5.12 (s, 2 H, OCH$_2$OCH$_3$), 5.35 (t, 2 H, J = 5 Hz, CH=CH), 6.47 (d, 1 H, J = 2.8 Hz, aromatic), 6.51 (d, 1 H, J = 2.8 Hz, aromatic). IR (neat): ν 2900, 1600 cm^{-1}. Mass: m/z 464 (20, M$^+$), 388 (20), 167 (40), 153 (50), 45 (100). Anal. Calcd for $C_{28}H_{48}O_5$: C, 72.37; H, 10.41. Found: C, 72.21; H, 10.67.

1-(2,3,6-Trihydroxy-5-methoxyphenyl)-10-pentadecene (8a). To a solution of **7a** (50 mg, 0.1 mmol) in 3 mL of ethanol was added few drops of 48% hydrobromic acid solution, and the mixture was stirred for 1 h. After the mixture had been diluted with ether, the solution was washed with saturated $NaHCO_3$ solution and brine, dried (Na_2SO_4), and evaporated to produce a syrup of **8a** (36 mg) in 93% yield. ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3 H, J = 5.5 Hz, CH$_2$CH$_3$), 1.19–1.45 (m, 18 H, methylenes), 2.0 (m, 4 H, allylic), 2.59 (t, 2 H, J = 6.5 Hz, benzylic), 3.82 (s, 3 H, OCH$_3$), 5.35 (t, 2 H, J = 5 Hz, CH=CH), 6.28 (s, 1 H, aromatic). IR (neat): ν 3410, 1610 cm^{-1}. Mass: m/z 364 (100, M$^+$), 168 (40). Anal. Calcd for $C_{22}H_{36}O_4$: C, 72.94; H, 9.96. Found: C, 72.23; H, 9.72.

1-(2,3-Dihydroxy-3-methoxyphenyl)-10-heptadecene (8b). Compound **8b** (36 mg) was obtained from **7b** (48 mg, 0.173 mmol) in 94% yield, adopting the same procedure as described for **8a**. ^{1}H NMR ($CDCl_3$): δ 0.8 (t, 3 H, J = 5.5 H, CH$_2$CH$_3$), 1.18–1.4 (m, 20 H, methylenes), 1.58 (m, 2 H, ArCH$_3$CH$_2$), 2.0 (m, 4 H, allylic), 2.55 (t, 2 H, J = 6.5 Hz, benzylic), 3.84 (s, 3 H, OCH$_3$), 5.25 (br s, 1 H, OH), 5.35 (t, 2 H, J = 5 Hz, CH=CH), 6.21 (d, 1 H, J = 3.5 Hz, aromatic), 6.31 (d, 1 H, J = 3.5 Hz, aromatic). IR (neat): ν 3410, 1610 cm^{-1}. Mass: m/z 376 (100, M$^+$), 154 (30). Anal. Calcd for $C_{24}H_{40}O_3$: C, 76.55; H, 10.71. Found: C, 76.43; H, 10.52.

Preparation of Maesanin (1a). Silver carbonate (33 mg, 0.12 mmol) was added to triphenolic compound **8a** (20 mg, 0.549 mmol) which was suspended in dry benzene (3 mL) and stirred for 2 h. After the disapperance of starting material was ensured, the contents were filtered through Celite and the solvent was removed under reduced pressure to leave a yellow solid substance. Purification through column chromatography furnished measanin (**1a**) (18 mg) in 91% yield as yellow crystalline solid: mp 69–70 °C (lit.[13] mp 69–69.5 °C). ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3 H, J = 5.5 Hz, CH$_3$CH$_2$), 1.2–1.45 (m, 18 H, methylenes), 1.99 (m, 4 H, allylic), 2.42 (t, 2 H, J = 7 Hz, benzylic), 3.84 (s, 3 H, OCH$_3$), 5.32 (t, 2 H, J_1 = 5 Hz, J_2 = 1.5 H, CH=CH), 5.82 (s, 1 H,

aromatic), 7.20 (s, 1 H, OH). IR (neat): ν 3410, 1650, 1620, 850 cm^{-1}. Mass: m/z 362 (100, M^+), 169 (40), 168 (55). HRMS: Calcd for $C_{22}H_{34}O_4$: 362.2457. Found: 362.2460.

Preparation of Irisquinone (1b). Irisquinone (23.3 mg) was obtained from **8b** (25 mg, 0.066 mmol) in 94% yield as yellow solid substance, mp 43 °C (lit.[4] mp 42.5–43.5 °C), adopting the same procedure as described for **1a**. ^1H NMR ($CDCl_3$): δ 0.9 (t, 3 H, J = 5.5 Hz, CH_2CH_2), 1.18–1.48 (m, 20 H, methylenes), 1.5 (m, 2 H, $ArCH_2CH_2$), 2.0 (m, 2 H, allylic), 2.42 (2 H, t, J_1 = 7 Hz, benzylic), 3.82 (s, 3 H, OCH_3), 5.34 (t, 2 H, J_1 = 2 Hz, CH=CH), 5.88 (d, 1 H, J = 3 Hz, aromatic), 6.46 (m, 1 H, aromatic). IR (neat): ν 1660, 1600, 845 cm^{-1}. Mass: m/z 374 (100, M^+), 167 (50), 153 (80), 55 (90). HRMS: Calcd for $C_{24}H_{38}O_3$: 374.2821. Found: 374.2828.

Registry No. **1a**, 82380-21-0; **1b**, 56495-82-0; **2**, 23030-48-0; **3a**, 139943-65-0; **3b**, 133099-84-0; **4a**, 139943-66-1; **4b**, 139943-67-2; **5a**, 139943-68-3; **5b**, 139943-69-4; **6a**, 139943-70-7; **6b**, 139943-71-8; **7a**, 139943-72-9; **7b**, 139943-73-0; **8a**, 139943-74-1; **8b**, 77285-25-7; 2,5-dihydroxy-3-methoxy-1-bromobenzene, 61654-67-9; 9-decen-1-ol, 13019-22-2; pentyltriphenylphosphonium bromide, 21406-61-1; *n*-heptyltriphenylphosphonium bromide, 13423-48-8.

Supplementary Material Available: ^1H NMR spectra of compounds **1a** and **1b** (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Determination of Configurations of *N*-Methoxy Imidoyl Halides via Catalytic Hydrogenation. Synthesis of Pure (*E*)-Aldoximes

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The chemistry of *N*-alkoxy imidoyl halides has not been investigated as fully as that of *N*-alkyl and *N*-aryl imidoyl halides.[1] We have found that *N*-alkoxyalkanimidoyl halides are more stable chemically and thermally than the corresponding alkyl imidoyl halides and can be useful as synthetic intermediates.[2] *N*-Hydroxy imidoyl halides, which are precursors of nitrile oxides, are well-known. However, the corresponding *N*-alkoxy compounds, especially *N*-alkoxyalkanimidoyl halides, appear rarely in the literature. Johnson et al. determined the configurations of *N*-methoxyarenecarboximidoyl chlorides by X-ray crystallographic analysis[3b,4] and dipole moment measurement[3b] and carried out studies of the mechanisms and stereochemistry of their substitution reactions with alkoxides and amines.[3a-d] On the other hand, configurations of *N*-methoxyalkanimidoyl halides have not been determined completely, and their chemistry has been scarcely investigated.[2]

We have synthesized *N*-methoxy-2-(2-naphthyl)ethanimidoyl bromide (**6a**) by a conventional method and have found the compound to have the *Z* configuration by X-ray crystallography. Catalytic reduction of **6a** leads to the pure (*E*)-*O*-methylaldoxime, showing that dehalogenation proceeds with retention of configuration. Configurations of other *N*-methoxy imidoyl halides, synthesized by the same methods, were determined to be *Z* by catalytic reduction and ^1H NMR analyses[5] of the resulting aldoximes.

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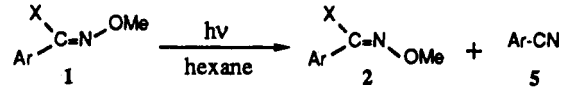
Table I. The *Z* → *E* Isomerization of *N*-Methoxy Imidoyl Halides by Irradiation



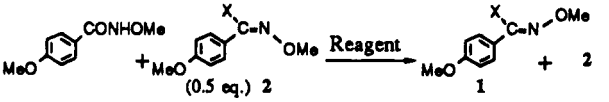
1 2 5

starting material	temp, °C	time, min	product (%)	recovery of 1 (%)
1a	0	10	**2a** (46), **5a** (18)	**1a** (28)
1b	0	18	**2b** (35), **5b** (21)	**1b** (32)
1d	25	120	**2d** (44), **5a** (8)	**1d** (15)

Table II. Chemical Shift Data for the *Z* and *E* Isomers of *N*-Methoxy Imidoyl Halides

compd	config	δ ($NOCH_3$)	$\Delta\delta$ ($Z - E$)
1a	*Z*	4.05	0.17
2a	*E*	3.88	
1b	*Z*	4.10	0.20
2b	*E*	3.90	
1d	*Z*	4.06	0.13
2d	*E*	3.93	

Table III. The *E* → *Z* Isomerization of *N*-Methoxy Imidoyl Halides 2 under Halogenation Conditions



run	reagent	temp, °C	time, h	X	yield 1 (%)	yield 2 (%)
1	PPh_3–CCl_4	reflux	2	Cl	**1d** (72)	**2d** (25)
2	PCl_5–$POCl_3$	100	0.5	Cl	**1d** (82)	**2d** (0)
3	$SOCl_2$	reflux	4	Cl	**1d** (38)	**2d** (0)
4	PPh_3–CBr_4	reflux	2	Br	**1a** (97)	**2a** (0)

Synthesis of (*E*)- and (*Z*)-*N*-Methoxy Imidoyl Halides. *N*-Methoxy imidoyl halides were synthesized from the corresponding *N*-methoxyamides with PCl_5, $POCl_3$, $SOCl_2$, PBr_3, or PPh_3–CX_4 (X = Cl, Br). In each case, the ^1H NMR spectrum and TLC of the crude product indicated that a single isomer had been formed. X-ray crystallographic studies of (*E*)- and (*Z*)-*N*-methoxy-4-nitrobenzenecarboximidoyl chlorides and subsequent dipole moment measurements proved that configurations of the single isomers obtained by above methods are *Z*.[3b,4] Johnson et al. synthesized nine pairs of *N*-alkoxybenzenecarboximidoyl chlorides by ultraviolet irradiation of hexane solutions of the corresponding *Z*-isomers and separation of the *E*/*Z* mixture by preparative gas chromatography; however, they could not obtain the corresponding *E*-bromides.[3e] By use of similar irradiation conditions and separation of the products by silica gel column chromatography, we have obtained the (*E*)-*N*-methoxybenzenecarboximidoyl bromides (**2b**), along with considerable amounts of the corresponding nitriles. The

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