JOC Article

A Very Efficient Route toward the 4a-Methyltetrahydrofluorene Skeleton: Short Synthesis of (±)-Dichroanone and (±)-Taiwaniaquinone H

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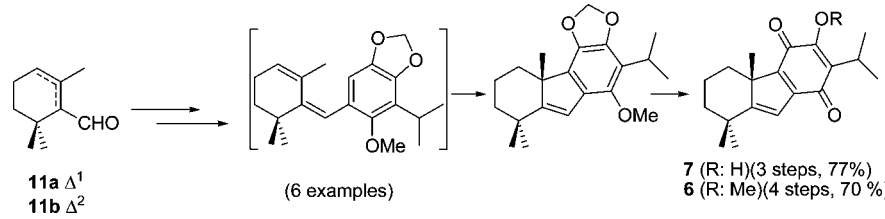

A very expedient and efficient new route toward taiwaniaquinoids, bearing the 4a-methyltetrahydrofluorene skeleton, is reported. Key steps are the intramolecular Friedel−Crafts alkylation of an aryldiene and the degradative oxidation of a methylenedioxy group; the latter process could also be utilized for building the 2-hydroxy-1,4-benzoquinone unit, which is frequently found in natural products. Utilizing this new methodology, (±)-dichroanone (**7**) (three steps, 77% overall yield) and (±)-taiwaniaquinone H (**6**) (four steps, 70% overall yield) have been synthesized from commercial α- (**11a**) or *β*-cyclocitral (**11b**).

Introduction

Taiwaniaquinoids are a family of tricyclic diterpenoids bearing an unusual 4a-methyltetra- (and hexa-)hydrofluorene skeleton, which were isolated during the past decade from different East Asian conifers, such as *Taiwania cryptomerioides*,[1] *Salvia dichroantha*,[2] and *Thuja standishii*.[3] They include taiwaniaquinol A (**1**), B (**2**),[1a] and C (**3**),[1c] taiwaniaquinone A (**4**),[1a] D (**5**),[1b] and H (**6**),[1d] dichroanone (**7**),[2] dichroanal B (**8**), and standishinal (**9**) (Figure 1).[3] Although only a few preliminary studies of the bioactivity of some of these compounds have been reported, taiwaniaquinols A (**1**) and C (**3**) and taiwaniaquinones A (**4**) and D (**5**) are known to exhibit potent cytotoxic activity against KB epidermoid carcinoma cancer cells;[1d] standishinal (**9**) shows aromatase inhibitory activity[4] and is therefore a promising candidate to be employed in the treatment of breast cancer.[5]

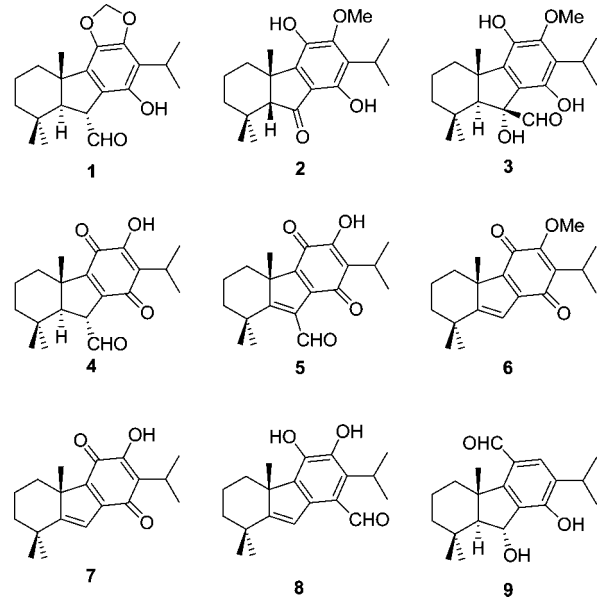

FIGURE 1. Some representative taiwaniaquinoids.

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(1) (a) Lin, W.-H.; Fang, J.-M.; Chang, Y.-S. *Phytochemistry* **1995**, *40*, 871–873. (b) Lin, W.-H.; Fang, J.-M.; Chang, Y.-S. *Phytochemistry* **1996**, *42*, 1657–1663. (c) Chang, C.-I.; Chien, S.-C.; Lee, S.-M.; Kuo, Y.-H. *Chem. Pharm. Bull.* **2003**, *51*, 1420–1422. (d) Chang, C.-I.; Chang, J.-Y.; Kuo, C.-C.; Pan, W.-Y.; Kuo, Y.-H. *Planta Med.* **2005**, *71*, 72–76.

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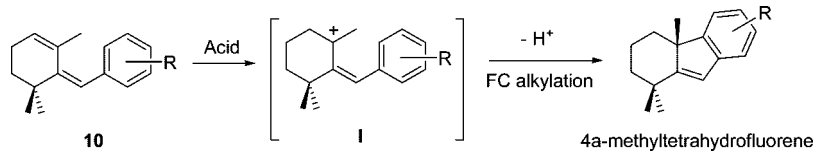
SCHEME 1. Direct Transformation of Aryldiene 10 into Taiwaniaquinoids



In addition to possessing promising biological activities, the unique carbotricyclic structure of this family of compounds has attracted varied synthetic approaches. Fillion reported a total synthesis of (±)-taiwaniaquinol B (**2**) based on an interesting domino acylation/alkylation step.[6] Dichroanone (**7**) was synthesized by Stoltz via a novel asymmetric palladium-catalyzed alkylation.[7] The most efficient processes toward this class of compounds utilize a monoterpene synthon, such as β-cyclocitral (**11a**) or cyclogeranic acid, together with a phenol derivative to construct the 4a-methyltetra- or (hexa-)hydrofluorene skeleton. The cyclopentane B ring of the target compounds has been elaborated through intramolecular Heck reactions, as Banerjee[8a,b] and Node[8c] used in their syntheses of dichroanone (**7**), or via Nazarov cyclizations, as Trauner reported in a synthetic approach to this family of compounds.[9] The synthesis of standishinal (**9**) has been achieved starting from *p*-formylanisol.[10] Recently, She reported the synthesis of taiwaniaquinol B (**2**) and dichroanone (**7**) featuring an interesting domino Friedel−Crafts acylation/alkylation step.[11] Very recently, our group has reported a new synthetic strategy toward these types of compounds based on a thermal 6π electrocyclization.[12]

Results and Discussion

As part of our research into the synthesis of taiwaniaquinoids we are exploring new routes toward these types of compounds, involving fewer steps and utilizing readily accessible synthons. Bearing this in mind, we planned a possible synthesis of taiwaniaquinoids (Scheme 1). The key intermediate would be the aryldiene **10**, which under acidic conditions would lead to the arylallyl cation **I**, which will undergo a fast intramolecular Friedel−Crafts alkylation, thus providing the 4a-methyltetrahydrofluorene skeleton.

The scheme in Table 1 shows the implementation of this synthetic proposal, utilizing different aromatic synthons with increasing electronic densities. The treatment of β-cyclocitral (**11a**) with the aryllithium derived from the corresponding bromobenzenes **12a**−**e** gave in excellent yield the allyl alcohols **13a**−**e**. These were quickly converted into the aryldienes **14a**−**e** after treatment with $SnCl_4$ in dichloromethane at 0 °C. Compounds **14a**−**e** were characterized as the *Z* stereoisomer on the basis of NOE experiments. The dienes **14a**−**e** were efficiently transformed into the 4a-methyltetrahydrofluorene derivatives **15a**−**e** by treating them with $SnCl_4$ in dichloromethane at room temperature. Compounds **14a**−**c** underwent cyclization even at low temperatures, and so these dienes are more suitably obtained for characterization purposes by treating the corresponding alcohols **13a**−**e** with cationic resin. This synthetic sequence constitutes the most efficient procedure yet reported for achieving the 4a-methyltetrahydrofluorene skeleton of taiwaniaquinoids.

We next applied this new methodology to the synthesis of dichroanone (**7**) and taiwaniaquinone H (**6**). The *O*-methyl derivative **20** of the commercially available sesamol (3,4-methylenedioxyphenol) was chosen as a suitable aromatic synthon for our purposes. Although achieving the rupture of the methylenedioxy group entails some difficulty, which has greatly limited its use as a protective group in organic synthesis, our previous studies on the degradative oxidation of methylenedioxybenzenes encouraged us to work to overcome this difficulty.[15] Scheme 2 shows the synthesis of compound **19**, an immediate precursor of the target compounds **6** and **7**, starting from the tricyclic derivative **15e**, obtained after a two-step sequence from β-cyclocitral (**11a**) (91% overall yield) (Table 1, entry 5).

When methyl ether **15e** was reacted with *n*-BuLi and then with acetone, the hydroxy derivative **17** resulted in 75% yield, and the starting material was partially recovered (17%). Alcohol **17** showed a considerable tendency to undergo dehydration under acidic conditions, leading to the isopropylene derivative **18**; the rapid transformation of alcohol **17** into compound **18** was observed in the NMR chloroform solutions. Compound **19** was obtained in high yield, after removal of the hydroxyl group by cationic reduction with ZnI_2 and $NaBH_3CN$. The carbon−carbon double bond was also reduced when Et_3SiH and trifluoroacetic acid were utilized.

Alternatively, the intermediate **19** was synthesized starting from the aryllithium derivative of bromide **23**. This compound was prepared from the methoxy derivative **20**, following the same procedure utilized for the methyl ether **15e**; finally, the treatment of the isopropyl derivative **22** with NBS afforded the bromide **23** (Scheme 3).

The condensation of aryllithium derived from bromide **23** with β-cyclocitral (**11a**) leads to alcohol **24a** and then to diene **25** and to the cyclized compound **19**, utilizing the above-described procedure (Scheme 4). Aryldienes **14a**−**e**, or **25**, were also expected to be formed after the condensation of α-cyclocitral (**11b**) and the corresponding aryllithium. This supposition was confirmed by utilizing the bromide **23** as the aromatic synthon; thus, the treatment of aldehyde **11b** with the aryllithium derived from **23** gave the homoallyl alcohol **24b** as a 1:1 mixture of diastereoisomers. This alcohol was converted into the diene **25** under the same conditions utilized for **24a**.

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(6) Fillion, E.; Fishlock, D. *J. Am. Chem. Soc.* **2005**, *127*, 13144–13145.
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(12) Alvarez-Manzaneda, E.; Chahboun, R.; Cabrera, E.; Alvarez, E.; Haidour, A.; Ramos, J. M.; Alvarez-Manzaneda, R.; Hmamouchi, M.; Es-Samti, H. *Chem. Commun.* **2009**, 592–594.
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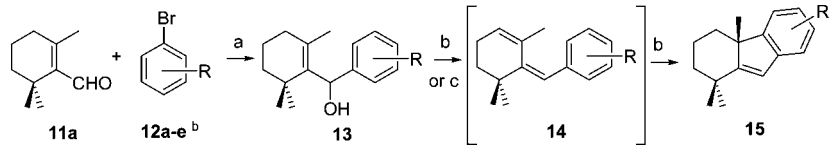
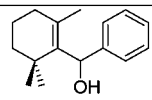
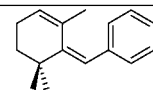
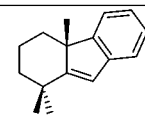
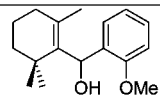
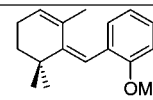
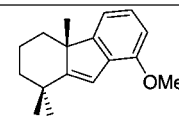
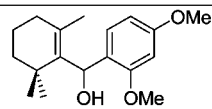
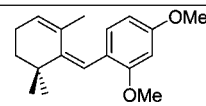
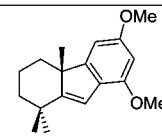
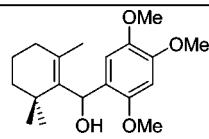
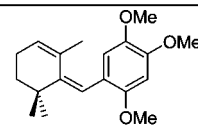
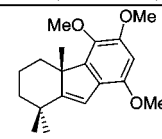
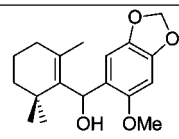
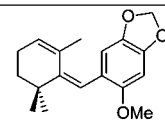
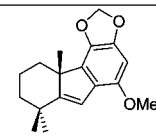
(15) Barrero, A. F.; Alvarez-Manzaneda, E. J.; Chahboun, R.; Cortés, M.; Armstrong, V. *Tetrahedron* **1999**, *55*, 15181–15208.

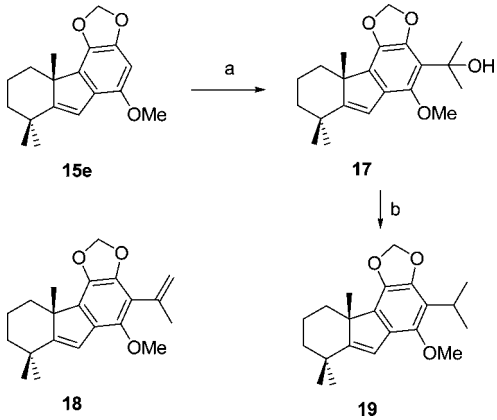
TABLE 1. Construction of the Core 6,5,6-ABC Tricyclic Skeleton of Taiwaniaquinoids[a]



Entry	Alcohol **13**	Diene **14**[c]	Compound **15**[d]
1	 **13a** (92%)	 **14a** (75 min, 90%)	 **15a** (1 h, 93%)
2	 **13b** (95%)	 **14b** (50 min, 91%)	 **15b** (70 min, 96%)
3	 **13c** (93%)	 **14c** (45 min, 94%)	 **15c** (85 min, 91%)
4	 **13d** (97%)	 **14d** (40 min, 95%)	 **15d** (90 min, 96%)
5	 **13e** (94%)	 **14e** (20 min, 92%)	 **15e** (110 min, 97%)

[a] Reagents and conditions: (a) **12**, *n*-BuLi, THF, −78 °C, 30 min; **11a**, 15 min; (b) $SnCl_4$, CH_2Cl_2, 0 °C to rt, 1−2 h; (c) Amberlyst A-15, CH_2Cl_2, rt, 20−75 min. [b] Bromobenzenes **12a**−**c** are commercially available. For compounds **12d** and **12e** see refs 13 and 14, respectively. [c] Yields obtained after treatment with cationic resin. [d] Yields from alcohols.

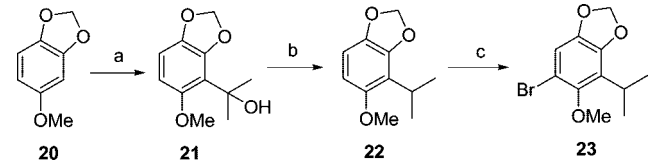
SCHEME 2. Synthesis of Intermediate 19[a]



[a] Reagents and conditions: (a) *n*-BuLi, THF, −20 °C, 20 min; acetone, HMPA, 0 °C, 4 h, 75%; (b) ZnI_2, $NaBH_3CN$, CH_2Cl_2, 0 °C to rt, 2 h, 98%.

Finally, the transformation of compound **19** into taiwaniaquinoids **6** and **7** was undertaken (Scheme 5). As indicated above, we had previously developed an oxidative process which

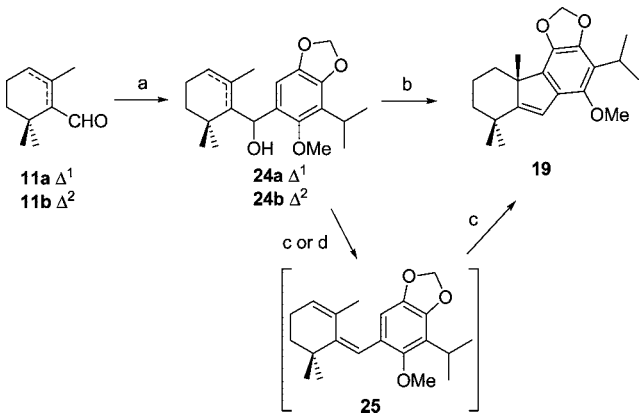
SCHEME 3. Synthesis of Aromatic Synthon 23[a]



[a] Reagents and conditions: (a) *n*-BuLi, TMEDA, THF, 0 °C, 30 min; acetone, 0 °C, 2 h, 72%; (b) ZnI_2, $NaBH_3CN$, CH_2Cl_2, 0 °C to rt, 2 h, 92%; (c) NBS, CH_2Cl_2, rt, 5 min, 94%.

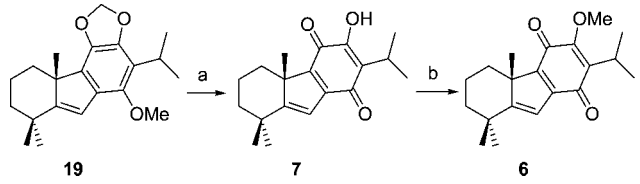
allows the efficient transformation of methylenedioxybenzenes into the corresponding *o*-quinones by treating them with DDQ and TsOH in refluxing dioxane. When methyl ether **19** was reacted under these conditions for 1 h 30 min, dichroanone (**7**) was obtained in high yield. Next, the transformation of this quinone into taiwaniaquinone H (**6**) was addressed. Methylation, utilizing MeI in basic medium, afforded a complex mixture; our objective was attained after treatment with Me_2SO_4 and K_2CO_3 in acetone under reflux.

SCHEME 4. Synthesis of Intermediate 19 Starting from the Aromatic Synthon 23[a]



[a] Reagents and conditions: (a) **23**, *n*-BuLi, THF, −78 °C, 60 min; **11a** or **11b**, 15 min (96% from **11a**; 98% from **11b**); (b) $SnCl_4$, CH_2Cl_2, 0 °C, 5 min; rt, 2 h, 94%; (c) $SnCl_4$, CH_2Cl_2, 0 °C to rt; (d) Amberlyst A-15, CH_2Cl_2, rt, 15 min, 92%.

SCHEME 5. Synthesis of Dichroanone (7) and Taiwaniaquinone H (6)[a]



[a] Reagents and conditions: (a) DDQ, TsOH, dioxane, reflux, 1 h 20 min, 84%; (b) Me_2SO_4, K_2CO_3, acetone, rt, 2 h, 90%.

Conclusion

A very expedient and efficient new route toward taiwaniaquinoids, starting from commercial α- (**11b**) or *β*-cyclocitral (**11a**), has been developed. Utilizing this methodology, (±)-dichroanone (**7**) (three steps, 77% overall yield) and (±)-taiwaniaquinone H (**6**) (four steps, 70% overall yield) have been synthesized. After construction of the tricyclic skeleton of the target compounds, via the intramolecular Friedel−Crafts alkylation of an aryldiene, the methylenedioxy benzene fragment of the resulting intermediate was directly converted into the 2-hydroxy-1,4-benzoquinone moiety through an oxidative degradation achieved by treatment with DDQ and TsOH in refluxing dioxane. The latter process could also be utilized for building the 2-hydroxy-1,4-benzoquinone unit, which is frequently found in natural products.

Experimental Section

General Procedure for the Preparation of Allyl Alcohols 13a−e. To a solution of bromobenzenes **12a−e** (1.2 mmol) in dry THF (10 mL) was added *n*-butyllithium (1.3 mmol) at −78 °C under an argon atmosphere, and the reaction mixture was stirred at this temperature for 30 min. Then a solution of α- (**11b**) or *β*-cyclocitral (**11a**) (1 mmol) in dry THF (10 mL) was added and the mixture stirred for a further 15 min (monitored by TLC). The reaction was quenched with water (1 mL), the solvent was removed under vacuum, and then the mixture was extracted with ether (2 × 15 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated under vacuum to yield a crude product which was directly purified by flash chromatography (hexanes/ether mixture) to yield the desired allyl alcohols **13a−e** (see Table 1).

Phenyl(2,6,6-trimethylcyclohex-1-enyl)methanol (13a). Colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.08 (s, 3H), 1.19 (s, 3H), 1.38 (s, 3H), 1.50−1.60 (m, 2H), 1.62−1.69 (m, 2H), 1.93 (br s, 1H), 1.99 (t, *J* = 6.2 Hz, 2H), 5.42 (s, 1H), 7.21 (ddd, *J* = 7.5, 7.5, 0.9 Hz, 2H), 7.32 (dd, *J* = 7.6, 7.5 Hz, 2H), 7.43 (dd, *J* = 7.6, 0.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 19.3 (CH_2), 21.6 (CH_3), 28.6 (CH_3), 28.9 (CH_3), 33.6 (CH_2), 34.8 (C), 39.7 (CH_2), 70.7 (CH), 125.9 (2CH), 126.1 (CH), 128.0 (2CH), 133.8 (C), 140.4 (C), 144.9 (C). IR (film): 3424, 1664, 1602, 1493, 1451, 1363, 1311, 1217, 1031, 974, 753 cm $^{-1}$. HRMS (FAB) *m*/*z*: calcd for $C_{16}H_{22}ONa$ ($M + Na^+$) 253.1568, found 253.1555.

General Procedure for the Preparation of Aryldienes 14a−e. To a solution of allyl alcohols **13a−e** (1 mmol) in dry CH_2Cl_2 (10 mL) was added Amberlyst 15 ion-exchange (0.5 g), and the reaction mixture was stirred for specified time (15−75 min), at which time TLC showed no starting material. The reaction mixture was filtered, and the solvent was removed under vacuum to yield the aryldienes **14a−e** (see Table 1).

(*Z*)-(2,6,6-Trimethylcyclohex-2-enylidenemethyl)benzene (14a). Colorless syrup. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.20 (s, 6H), 1.49 (br s, 3H), 1.60−1.70 (m, 2H), 2.26 (br s, 2H), 5.60 (br s, 1H), 6.48 (s, 1H), 7.18−7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 23.2 (CH_3), 23.9 (CH_2), 27.2 ($2CH_3$), 35.8 (C), 37.2 (CH_2), 121.3 (CH), 125.9 (CH), 127.6 (CH), 128.2 (C), 128.4 (C), 128.9 (CH), 129.2 (CH), 132.1 (C), 140.6 (C), 147.7 (C). IR (film): 1609, 1493, 1445, 1380, 1359, 1339, 1287, 1195, 1126, 1082, 1029, 979, 850, 821, 753, 719, 704 cm $^{-1}$. HRMS (FAB) *m*/*z*: calcd for $C_{16}H_{20}Na$ ($M + Na^+$) 235.1463, found 235.1458.

General Procedure for the Preparation of 4a-Methyltetrahydrofluorene Derivatives 15a−e. To a solution of allyl alcohols **13a−e** (1 mmol) in dry CH_2Cl_2 (10 mL) was added at 0 °C the Lewis acid (1.5 mmol), and the reaction mixture was stirred for 5 min and the cooling bath was removed. Then it was stirred at room temperature for a specified time (1−2 h), at which time TLC showed no starting material. The reaction mixture was cooled at 0 °C, water (1 mL) was added to quench the reaction, and the solvent was removed under vacuum. The crude was fractionated in water−ether (50 mL), extracted with ether (2 × 20 mL), and washed with water (2 × 10 mL), satd aqueous $NaHCO_3$ (2 × 10 mL), water (10 mL), and brine (10 mL). The dried organic layers were evaporated, and the residue was directly purified by flash chromatography (hexanes/ether mixture) to yield 4a-methyltetrahydrofluorene derivatives **15a−e** (see Table 1).

1,1,4a-Trimethyl-2,3,4,4a-tetrahydro-1*H*-fluorene (15a). Colorless syrup. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 0.99 (ddd, *J* = 13.1, 13.1, 3.8 Hz, 1H), 1.11 (ddd, *J* = 13.1, 13.1, 3.9 Hz, 1H), 1.25 (s, 3H), 1.30 (s, 3H), 1.37 (s, 3H), 1.54−1.70 (m, 2H), 1.97 (qt, *J* = 13.8, 3.4 Hz, 1H), 2.16 (d, *J* = 10.2 Hz, 1H), 6.36 (s, 1H), 7.12 (ddd, *J* = 7.3, 7.3, 1.2 Hz, 1H), 7.19 (ddd, *J* = 7.4, 7.4, 1.2 Hz, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 19.8 (CH_2), 23.4 (CH_3), 25.2 (CH_3), 31.2 (CH_3), 35.5 (C), 38.0 (CH_2), 42.6 (CH_2), 50.9 (C), 120.4 (CH_2), 120.7 (CH), 120.9 (CH), 123.9 (CH), 126.2 (CH), 142.1 (C), 155.2 (C), 164.1 (C). IR (film): 1606, 1467, 1370, 1290, 1187, 1014, 969, 873, 849, 747, 671 cm $^{-1}$. HRMS (FAB) *m*/*z*: calcd for $C_{16}H_{20}Na$ ($M + Na^+$) 235.1463, found 235.1471.

(3-Isopropyl-2-methoxy-4,5-methylenedioxyphenyl)(2,6,6-trimethylcyclohex-1-enyl)methanol (24a). Alcohol **24a** was synthesized following the general procedure described above for alcohols **13a−e** (reaction time: 1 h, 96%). White solid. Mp: 149−151 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) *δ*: 0.83 (s, 3H), 1.18 (s, 3H), 1.30 (d, *J* = 6.6 Hz, 3H), 1.36 (d, *J* = 6.6 Hz, 3H), 1.47 (ddd, *J* = 12.6, 11.4, 3.6 Hz, 1H), 1.52 (ddd, *J* = 9.1, 6.6, 3.1 Hz, 1H), 1.61−1.72 (m, 2H), 1.68 (s, 3H), 2.02−2.13 (m, 2H), 3.28 (h, *J* = 6.6 Hz, 1H), 3.48 (d, *J* = 1.8 Hz, 1H), 3.83 (s, 3H), 5.57 (d, *J* = 1.8 Hz, 1H), 5.91 (d, *J* = 5.2 Hz 2H), 6.59 (s, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz) *δ*: 19.4 (CH_2), 21.27 (CH_3), 21.34 (CH_3), 22.7 (CH_3), 25.4 (CH_3), 28.1 (CH), 28.9 (CH_3), 33.7 (CH_2), 34.7 (C), 39.8 (CH_2), 62.0 (CH_3), 68.7 (CH), 100.9 (CH_2), 106.3 (CH), 124.9 (C), 129.0

(C), 134.5 (C), 136.0 (C), 143.5 (C), 145.4 (C), 150.8 (C). IR (KBr): 2958, 2929, 2871, 2828, 1456, 1418, 1334, 1118, 1047 cm $^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{21}H_{30}O_4Na$ (M + Na^+) 369.2042, found 369.2031.

(Z)-3-Isopropyl-4-methoxy-1,2-methylenedioxy-5-(2,6,6-trimethylcyclohex-2-enylidenemethyl)benzene (25). Diene **25** was synthesized from **24a** or **24b** following the general procedure described above for dienes **14a**−**e** (reaction time: 15 min, 92%). Colorless syrup. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (s, 6H), 1.23 (d, J = 7.1 Hz, 6H), 1.48 (m, 2H), 1.50 (s, 3H), 2.12 (br s, 2H), 3.24 (h, J = 7.1 Hz, 1H), 3.58 (s, 3H), 5.48 (br s, 1H), 5.82 (s, 2H), 6.28 (s, 1H), 6.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.4 ($2CH_3$), 22.8 (CH_3), 23.9 (CH_2), 25.3 (CH_3), 27.3 (CH_3), 27.3 (CH), 35.8 (C), 37.1 (CH_2), 61.2 (CH_3), 100.6 (CH_2), 108.0 (CH), 117.6 (C), 123.9 (C), 126.0 (C), 128.7 (C), 131.8 (C), 143.1 (C), 144.5 (C), 146.7 (C), 149.8(C). IR (film): 1620, 1503, 1480, 1455, 1424, 1343, 1266, 1192, 1157, 1040, 1007, 937, 867, 811, 758 cm $^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{21}H_{28}O_3Na$ (M + Na^+) 351.1936, found 351.1928.

Synthesis of Compound 19 from Alcohols 24a,b. To a solution of **24a** or **24b** (235 mg, 0.68 mmol) in dry CH_2Cl_2 (10 mL) was added at 0 °C tin(IV) chloride (0.12 mL, 1.02 mmol), the reaction mixture was stirred for 5 min, and the cooling bath was removed. The mixture was stirred at room temperature for 2 h, at which time TLC showed no starting material. The reaction mixture was cooled at 0 °C, water (0.8 mL) was added to quench the reaction, and the solvent was removed under vacuum. The crude was fractionated into water−ether (40 mL) and extracted with ether (2 × 15 mL). The recombined organic phases were washed with water (2 × 10 mL), satd aqueous $NaHCO_3$ (2 × 10 mL), water (10 mL), and brine (10 mL). The dried organic layers were evaporated, and the residue was directly purified by flash chromatography (hexanes/ether, 95:5) to yield 209 mg of **19** (94%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.00−1.10 (m, 2H), 1.15 (s, 3H), 1.21 (s, 3H), 1.23 (d, J = 6.9 Hz, 3H), 1.24 (d, J = 6.9 Hz, 3H), 1.36 (s, 3H), 1.49−1.58 (m, 2H), 1.85 (qt, J = 13.7, 2.9 Hz, 1H), 2.21 (d, J = 12.7 Hz, 1H), 3.25 (h, J = 6.9 Hz, 1H), 3.71 (s, 3H), 5.82 (d, J = 7.8 Hz, 2H), 6.27 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.5 (CH_2), 21.4 (CH_3), 21.6 ($2CH_3$), 25.2 (CH), 25.6 (CH_3), 31.4 (CH_3), 35.6 (C), 36.8 (CH_2), 42.7 (CH_2), 50.8 (C), 63.7 (CH_3), 100.8 (CH_2), 117.3 (CH), 122.0 (C), 128.3 (C), 132.7 (C), 138.1 (C), 143.7 (C), 144.9 (C), 161.0 (C). IR (film): 1451, 1423, 1332, 1267, 1184, 1139, 1059, 962, 859, 772 cm $^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{21}H_{28}O_3Na$ (M + Na^+) 351.1936, found 351.1925.

Synthesis of Compound 19 from Diene 25. To a solution of **25** (310 mg, 0.94 mmol) in dry CH_2Cl_2 (10 mL) was added at 0 °C tin(IV) chloride (0.17 mL, 1.45 mmol), the reaction mixture was stirred for 5 min, and the cooling bath was removed. The mixture was stirred at room temperature for 2 h, at which time TLC showed no starting material. The reaction mixture was cooled at 0 °C, water (1 mL) was added to quench the reaction, and the solvent was removed under vacuum. The crude product was fractionated into water−ether (40 mL) and extracted with ether (2 × 20 mL). The combined organic phases were washed with water (2 × 10 mL), satd aqueous $NaHCO_3$ (2 × 10 mL), water (10 mL), and brine (10 mL). The dried organic layers were evaporated, and the residue was directly purified by flash chromatography (hexanes/ether, 95:5) to yield 289 mg of **19** (94%).

(±)-Dichroanone (7). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.415 g, 1.82 mmol) and *p*-toluensulfonic acid (0.3 g, 1.57 mmol) were added to a solution of **19** (0.5 g, 1.52 mmol) in 1,4-dioxane (15 mL), and the reaction mixture was stirred at reflux for 1 h 20 min, at which time TLC indicated no **19**. Then the reaction mixture was diluted with ether (40 mL) and washed with water (3 × 10 mL), satd aqueous $NaHCO_3$ (2 × 10 mL), water (10 mL), and brine (10 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield a crude product which was directly purified by flash chromatography (hexanes/ether, 9:1) to yield 383 mg of dichroanone (**7**) (84%) as red crystals. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.04−1.13 (m, 2H), 1.21 (s, 3H), 1.219 (d, J = 7.0 Hz, 3H), 1.222 (d, J = 7.0 Hz, 3H), 1.26 (s, 3H), 1.44 (s, 3H), 1.61 (m, 1H), 1.68 (ddd, J = 13.1, 5.4, 2.5 Hz, 1H), 1.91 (qt, J = 13.9, 3.4 Hz, 1H), 2.40 (ddd, J = 10.1, 4.9, 2.9 Hz, 1H), 3.24 (h, J = 7.0 Hz, 1H), 3.98 (s, 3H), 6.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.2 (CH_2), 20.2 (CH_3), 20.76 (CH_3), 20.78 (CH_3), 24.6 (CH_3), 24.9 (CH_3), 31.0 (CH), 36.8 (C), 37.3 (CH_2), 43.5 (CH_2), 55.7 (C), 61.4 (CH_3), 116.8 (CH), 136.1 (C), 145.9 (C), 150.7 (C), 157.4 (C), 175.7 (C), 178.9 (C), 186.4 (C). IR (film): 3348, 1638, 1527, 1367, 1317, 966 cm $^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{19}H_{24}O_3Na$ (M + Na^+) 323.1623, found 323.1614.

(±)-Taiwaniaquinone H (6). K_2CO_3 (200 mg, 1.45 mmol) was added to a solution of dichroanone (**7**) (150 mg, 0.5 mmol) in acetone (10 mL), and the reaction was kept stirring at room temperature for 5 min. Dimethyl sulfate (183 mg, 1.45 mmol) was added, and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under vacuum, and the crude reaction mixture was diluted with ether−water (20−5 mL), washed with water and brine, dried, and concentrated to give a crude product which was directly purified by flash column chromatography (hexanes/ether, 95:5) to yield taiwaniaquinone H (**6**) (141 mg, 90%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.04−1.15 (m, 2H), 1.232 (s, 3H), 1.234 (d, J = 7.0 Hz, 3H), 1.239 (d, J = 7.0 Hz, 3H), 1.25 (s, 3H), 1.45 (s, 3H), 1.63 (m, 2H), 1.71 (ddd, J = 13.2, 5.4, 2.4 Hz, 1H), 1.92 (qt, J = 13.9, 3.5 Hz, 1H), 2.37 (ddd, J = 12.4, 4.9, 2.1 Hz, 1H), 3.21 (h, J = 7.0 Hz, 1H), 6.44 (s, 1H), 7.30 (br s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.1 (CH_2), 20.09 (CH_3), 20.10 (CH_3), 20.19 (CH_3), 24.0 (CH_3), 24.8 (CH_3), 30.96 (CH), 37.06 (C), 37.4 (CH_2), 43.47 (CH_2), 55.4 (C), 118.1 (CH), 122.8 (C), 147.8 (C), 148.9 (C), 152.5 (C), 177.2 (C), 178.3 (C), 185.8 (C). IR (film): 1645, 1537, 1451, 1058 cm $^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{26}O_3Na$ (M + Na^+) 337.1780, found 337.1778.

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Supporting Information Available: . Experimental procedures and spectroscopic data for compounds **13b**−**e**, **14b**−**e**, **15b**−**e**, **16**−**19**, and **21**−**23** and copies of ^{1}H NMR and ^{13}C NMR spectra for compounds **6**, **7**, **13a**−**e**, **14a**−**e**, **15a**−**e**, **16**−**19**, **21**−**23**, **24a**,**b**, and **25**. This material is available free of charge via the Internet at http://pubs.acs.org.

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