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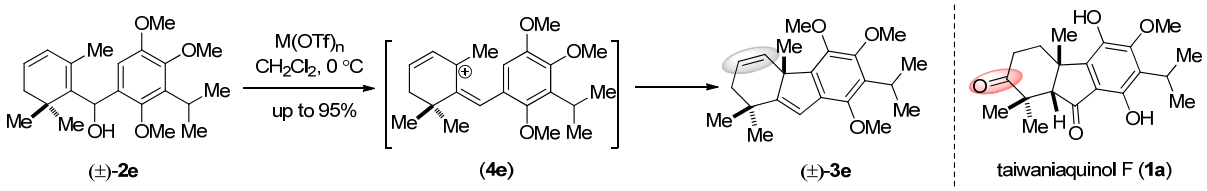


ABSTRACT

First total synthesis of (±)-taiwaniaquinol F (**1a**) has been accomplished *via* an efficient Lewis acid catalyzed Nazarov type cyclization of aryldiallylcarbinols (±)-**2a** derived from safranal **7**. The methodology works under mild conditions using only 2 mol% metal triflate as catalyst to afford a previously unknown carbotricyclic core sharing an olefin functionality in excellent yields. The aforementioned methodology also offers enough flexibility to complete the total syntheses of various taiwaniaquinoids, (±)-taiwaniaquinone H (**1d**), (±)-dichroanone (**1e**), (±)-5-*epi*-taiwaniaquinone G (*ent*-**1h**), and (±)-taiwaniaquinol B (**1b**).

INTRODUCTION

The taiwaniaquinoids (**1a-k**, Figure 1)[1] are a family of unusual diterpenoids possessing a [6,5,6]-*abeo*-abietane skeleton sharing an all-carbon quaternary stereocenter at the pseudobenzylic position. Most of these diterpenoids have been isolated since 1995 from *Taiwania cryptomerioides* Hayata (Taxodiaceae) of the central mountains of Taiwan independently by Cheng[2] and Kuo,[3] from *Salvia dichroantha* Stapf (Lamiaceae) a Turkish flowering sage by Kawazoe,[4] and from *Thuja standishii* (Cupressaceae) a Japanese conifer by Tanaka.[5] Reportedly, a few members of taiwaniaquinoids are found to exhibit potent cytotoxic activity against KB epidermoid carcinoma cancer cells[3b] and one of the members standishinal (**1i**) has shown aromatase inhibitory activity.[6] Because of their diverse biological profiles and uncommon structural features, the taiwaniaquinoids have gained extensive attention from the synthetic community leading to numerous efficient approaches.

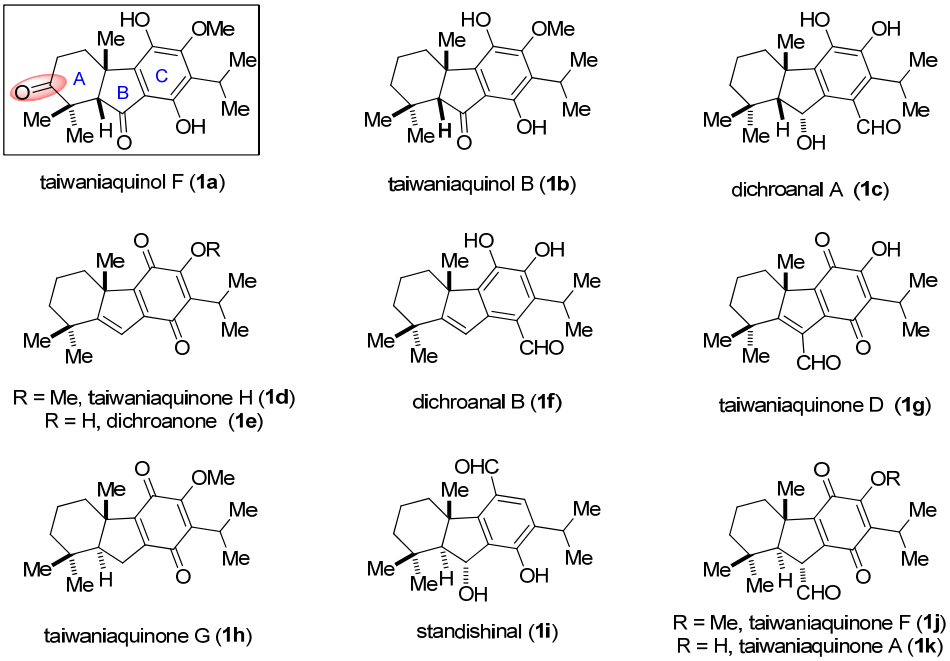
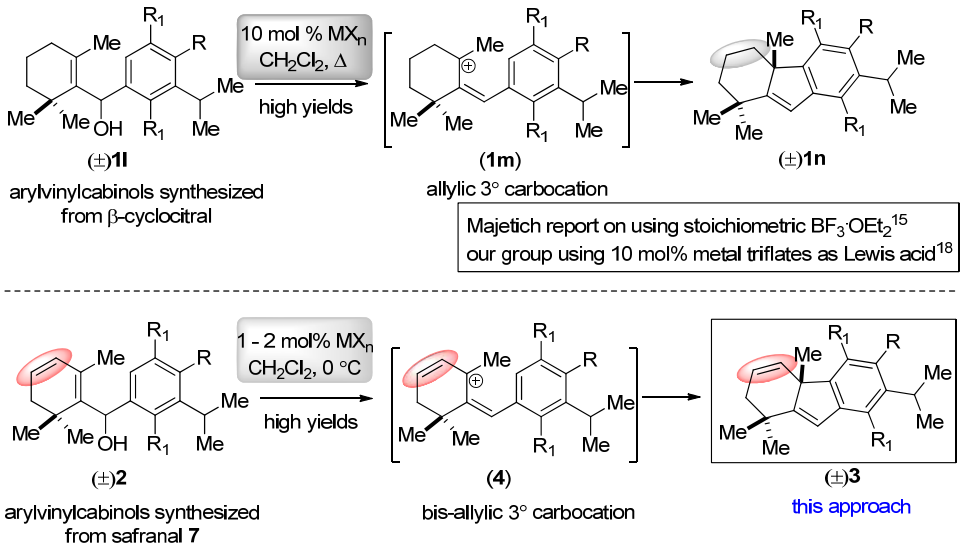


Figure 1: Selected taiwaniaquinoids (**1a-k**).

The approaches to taiwaniaquinoids include, Pd(0)-catalyzed intramolecular reductive cyclization by Banerjee,[7] domino intramolecular acylation carbonyl α-*tert*-alkylation reaction by Fillion,[8] intramolecular Heck cyclization by Node,[9] Nazarov cyclization by Trauner,[10] tandem acylation-Nazarov cyclization reaction by Chiu,[11] acid promoted Friedel−Crafts acylation/alkylation approach independently by She[12] and Cheng,[13] intramolecular cyclization of aryldienes independently by Balme,[14] Alvarez-Manzaneda[15] and Majetich (Scheme 1),[16] ring contraction from abietane diterpenoids by Li,[17] our Friedel-Crafts alkylations to set all-carbon quaternary center (Scheme 1),[18] and thermal ring expansion/4π-electrocyclization by Hu,[19] and other approaches.[20] Asymmetric syntheses include, enantioselective decarboxylative allylation by Stoltz,[21] enantiospecific thermal 6π-electrocyclization by Alvarez-Manzaneda,[22] enantioselective Heck reaction by Node,[23] ring contraction of abietane diterpenoids by Gademann,[24] semisynthesis involving cleavage of the C7−C8 double bond of abietane diterpenes by Alvarez-Manzaneda,[25] iridium catalyzed borylation and palladium-catalyzed asymmetric α-arylation by Hartwig,[26] and recent Pd(0)-catalyzed enantioselective conjugate addition of arylboronic acid by Stoltz.[27-28] All these above syntheses mainly concentrate on taiwaniaquinoids comprising a saturated *gem*-dimethyl cyclohexane ring system (A ring of **1a-k**). However, there is no report on taiwaniaquinoids with various oxidation pattern of A-ring, such as (±)-taiwaniaquinol F (**1a**) till date, mainly due to difficulty of functionalization of A-ring.

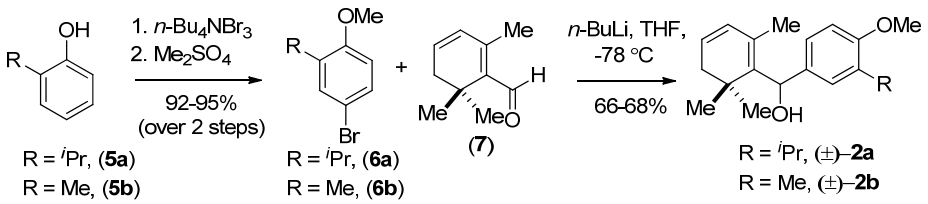


Scheme 1: Our approach to taiwaniaquinoids.

We envisioned that, carbotricyclic core of type (±)-**3** (Scheme 1) having an olefin functionality at A-ring could be advanced intermediate to access various oxidized variants of taiwaniaquinoids (**1a**). Herein, we report synthesis of carbotricycle (±)-**3** by Lewis acid-catalyzed Nazarov type cyclization and its application to a protecting-group-free first total synthesis of (±)-taiwaniaquinol F (**1a**).

RESULTS AND DISCUSSION

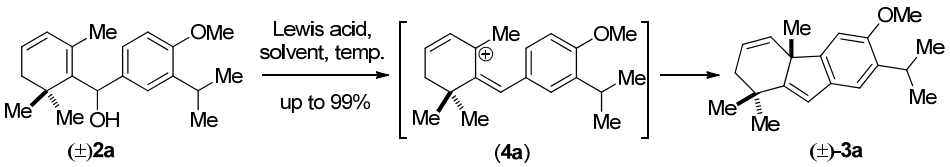
For our study, arylvinyl carbinol (±)-**2a-b** was synthesized by 1,2-addition of the aryllithium corresponding to arylbromides **6a** or **6b** to safranal **7** (Scheme 2). Having the key intermediate aryldivinylcarbinol (±)-**2a** in hand, the stage was set for cyclization to **3a**. At the outset, we examined Nazarov type cyclization of (±)-**2a** using various Lewis acids in different solvents to affect the synthesis of carbotricyclic structure (±)-**3a** (Table 1).



Scheme 2: Synthesis of arylvinylcarbinol (±)-**2a**.

Initially, the Nazarov type cyclization of (±)-**2a** was carried out using 5 mol% of $Bi(OTf)_3$ using different solvents (entries 1-6, table 1) and it was found that dichloromethane was preferred, and afforded (±)-**3a** in 99% isolated yield at 0 ºC in just 5 min (entry 5). This is important to note that, inert atmosphere is not required for efficient reaction. The use of 5 Mol% of metal triflates such as $Cu(OTf)_2$, $In(OTf)_3$, $Yb(OTf)_3$, $Zn(OTf)_2$, $Sc(OTf)_3$, $La(OTf)_3$, $Nd(OTf)_3$, or $Sn(OTf)_2$ afforded (±)-**3a** in 87%, 71%, 62%, 64%, 74%, 55%, 67%, and 98% isolated yields, respectively (entries 7-14). Interestingly, we found that 2 mol% of $Bi(OTf)_3$ and $Sn(OTf)_2$ (entries 16-17) are equally efficient to furnish carbotricycle (±)-**3a** in 98% and 93% isolated yields, respectively. The high reactivity of (±)-**2a** is presumably due the formation of the tertiary bis-allyic carbocation **4a** during the course of the reaction. Gratifyingly, 1 mol% of $Bi(OTf)_3$ and $Sn(OTf)_2$ also afforded cyclization products in 94% and 62% isolated yields, respectively (entries 18-19). Significantly, the reaction is highly regioselective involving only the aryl carbon *para* to the *i*-Pr group and affording only (±)-**3a** presumably involvement of the aryl carbon *ortho* to *i*-Pr group is disfavored due to severe steric crowding. Based on our optimization studies, we further choose 2 mol% of each $Bi(OTf)_3$ (condition **A**) and $Sn(OTf)_2$ (condition **B**) for further substrate scope.

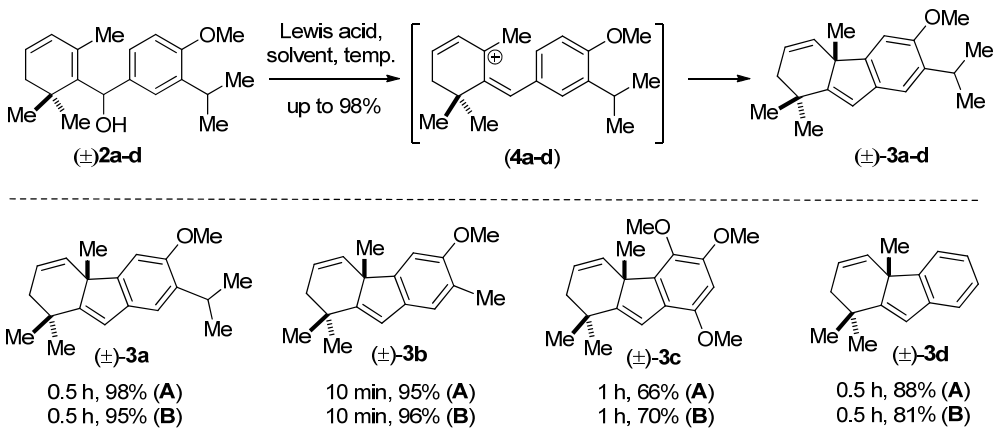
Table 1: Selected optimization of Nazarov type reaction of **2a**.



S. No.	Lewis acid (mol%)	solvent	temp	time	% yield (**3**)[a,b]
1.	5 mol% $Bi(OTf)_3$	Et_2O	25 ºC	3 h	51%[c]
2.	5 mol% $Bi(OTf)_3$	$CHCl_3$	25 ºC	2.5 h	80%[c]
3.	5 mol% $Bi(OTf)_3$	$(CH_2Cl)_2$	25 ºC	20 min	85%
4.	5 mol% $Bi(OTf)_3$	CH_2Cl_2	25 ºC	5 min	82%[c]
5.	5 mol% $Bi(OTf)_3$	CH_2Cl_2	0 ºC	5 min	99%
6.	5 mol% $Bi(OTf)_3$	CH_3CN	0 ºC	10 min	86%
7.	5 mol% $Cu(OTf)_2$	CH_2Cl_2	25 ºC	30 min	87%
8.	5 mol% $In(OTf)_3$	CH_2Cl_2	0 ºC	20 min	71%[c]
9.	5 mol% $Yb(OTf)_3$	CH_2Cl_2	25 ºC	12 h	62%[c]
10.	5 mol% $Zn(OTf)_2$	CH_2Cl_2	25 ºC	2 h	64%[c]
11.	5 mol% $Sc(OTf)_3$	CH_2Cl_2	0 ºC	20 min	74%[c]
12.	5 mol% $La(OTf)_3$	CH_2Cl_2	25 ºC	12 h	55%[c]
13.	5 mol% $Nd(OTf)_3$	CH_2Cl_2	0 ºC	12 h	67%[c]
14.	5 mol% $Sn(OTf)_2$	CH_2Cl_2	0 ºC	5 min	98%
15.	2 mol% $Cu(OTf)_2$	CH_2Cl_2	25 ºC	1 h	79%
16.	2 mol% $Bi(OTf)_3$	CH_2Cl_2	0 ºC	10 min	98%[d]
17.	2 mol% $Sn(OTf)_2$	CH_2Cl_2	0 ºC	10 min	93%[e]
18.	1 mol% $Bi(OTf)_3$	CH_2Cl_2	0 ºC	10 min	94%
19.	1 mol% $Sn(OTf)_2$	CH_2Cl_2	0 ºC	10 min	62%

[a]all the reactions were performed using 0.3 mmol of (±)-**2a**. [b]isolated yields after column chromatography. [c]decomposition of the rest of the mass balance. [d]2 mol% of $Bi(OTf)_3$ (condition **A**). [e]2 mol% of $Sn(OTf)_2$ (condition **B**).

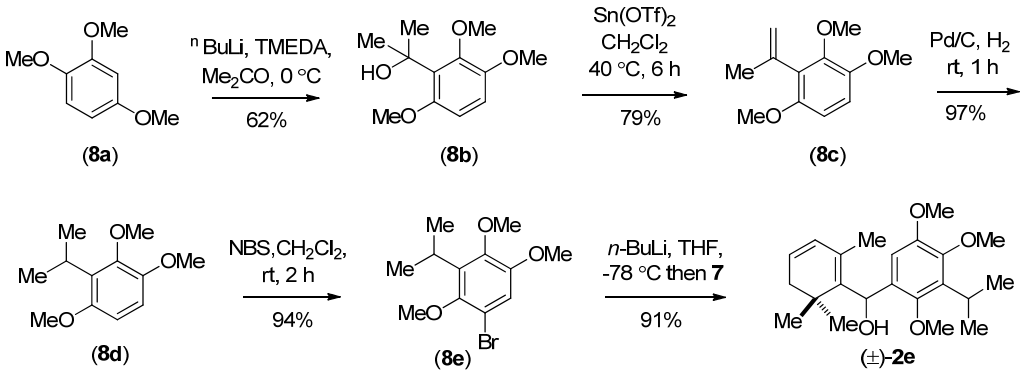
Aryldivinyl carbinols (±)-**2b-d** were then subjected to our optimized conditions to access carbotricyclic cores (±)-**3b-d** and the results are shown in Scheme 3. We found that the arylvinyl carbinols (±)-**2a-c** containing electron-donating group/s were good starting materials for this process, which afforded products **3b-c** in good to excellent yields (Scheme 3). Interestingly, we also observed that arylvinylcarbinols (±)-**2d** with no aromatic ring substituent also afforded (±)-**3d** in high yields (Scheme 3).



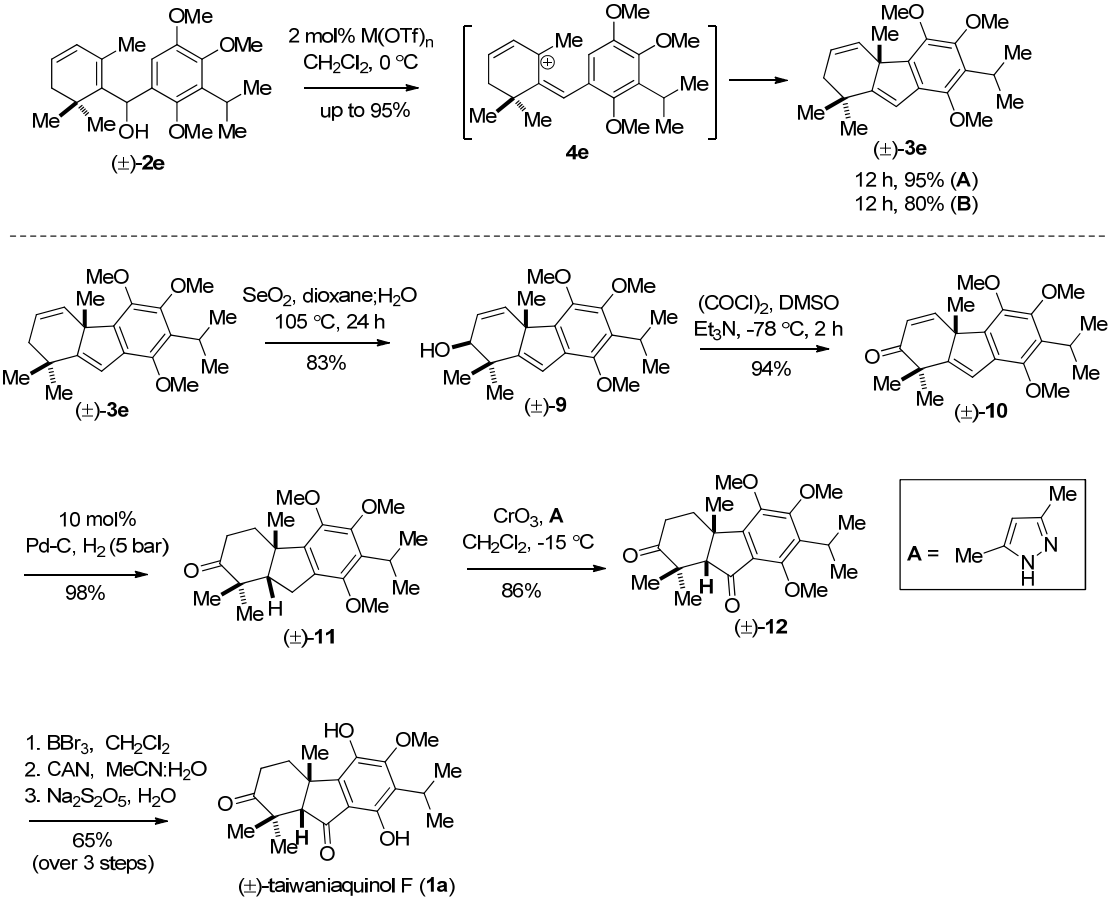
2 mol% of $Bi(OTf)_3$ (**condition A**); 2 mol% of $Sn(OTf)_2$ (**condition B**)

Scheme 3: Substrate scope of Nazarov type cyclization of (±)-**2a-d**.

Targeting carbotricyclic core (±)-**3e** having additional olefin functionality (Scheme 5), we synthesized aryldivinyl carbinol (±)-**2e** (Scheme 4). 1,2,4-Trimethoxybenzene (**8a**) was reacted with acetone in presence of *n*-BuLi and TMEDA at 0˚C to afford benzylalcohols **8b** in 62% yield, which was then reacted in presence of $Sn(OTf)_2$ to fºurnish α-methylstyrenes **8c** 79% yield. The later was hydrogenated in presence of Pd-C at 1 atm. pressure to afford cumene derivative **8d** in 97% yield, which was then reacted with *N*-bromo succinimide (NBS) to afford bromoarene **8e** in 94% yield. From this bromoarene **8e**, aryldivinyl carbinols (±)-**2e** was synthesized in 91% yield (Scheme 4). We found that, when (±)-**2e** was reacted under our optimized conditions **A** and **B**, it afforded product (±)-**3e** in 80-95% (Scheme 5).



Scheme 4: Synthesis of arylvinylcarbinol (±)-**2e**.



Scheme 5: Total synthesis of (±)-taiwaniaquinol F (**1a**).

With carbotricyclic core (±)-**3e** in hand, we were positioned to complete the total synthesis of (±)-taiwaniaquinol F (**1a**). Thus, allylic oxidation of (±)-**3e** with SeO_2 in dioxane:water afforded allylalcohol (±)-**9** as single diastereomer in 83% yield (Scheme 5). The excellent diastereoselectivity observed in this allylic oxidation was attributed to approach of the oxidant SeO_2 from less hindered convex face of substrate (±)-**3e**.[29] In fact energy minimization (MM2) calculation of diene **3e** (Figure 2) also supports our observed selectivity.

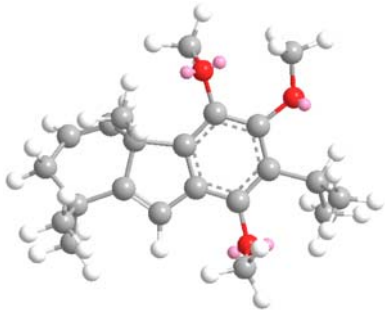


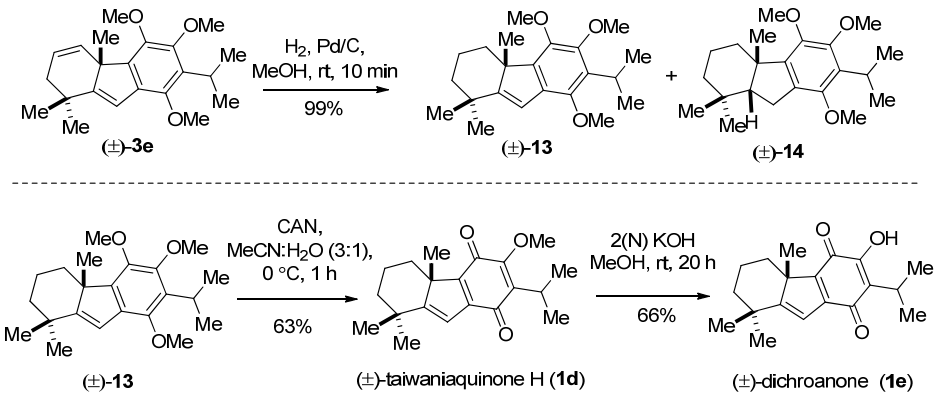
Figure 2. Energy-minimized representation of **3e**.[29]

Neopentyl alcohol (±)-**9** was oxidized to obtain α,β-unsaturated ketone (±)-**10** in 94% yield under Swern oxidation conditions. Enone (±)-**10** was then hydrogenated in the presence of 10% Pd-C at 5 bar pressure of H_2 in MeOH to afford tricyclic ketone (±)-**11** in 98% yield. Later, (±)-**11** was reacted with CrO_3 in presence of 3,5-dimethylpyrazole to effect benzylic oxidation[30] to furnish diketone (±)-**12** in 86% yield, the structure of which was confirmed from X-ray crystallography (CCDC: 1405987). From intermediate (±)-**12**, total synthesis of (±)-taiwaniaquinol F **1a** was completed in 3 steps in 65% overall yield by the treatment with BBr_3 followed by oxidation using ceric(IV) ammonium nitrate (CAN) and finally reduction with $Na_2S_2O_5$. The X-ray structure of (±)-**1a** (CCDC: 1405985) unambiguously proved the structure of (±)-taiwaniaquinol F **1a**.

Further, we turned our attention to pursue total syntheses of (±)-taiwaniaquinone H (**1d**) and (±)-dichronanone (**1e**) from a common precursor (±)-**3e**. For this purpose, we synthesized carbotricyclic core (±)-**13** from (±)-**3e** via selective hydrogenation of the more exposed disubstituted olefin (A-ring) over trisubstituted styrene olefin (B-ring) in presence of 10% Pd-C under 1 atm. pressure of H_2 in MeOH (Scheme 6). This reaction led to the formation of required carbotricycle (±)-**13** in 50% isolated consistently produced the over reduced *cis*-fused (±)-**14** in 48% yield. This is probably due to the preferential hydrogenation

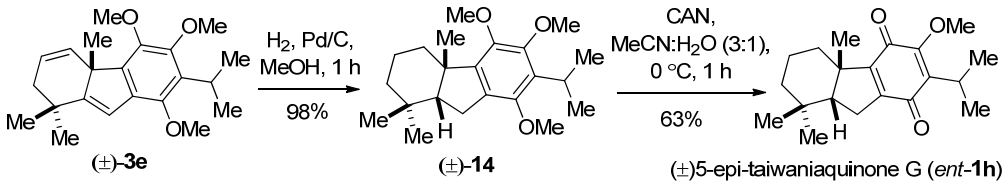
from less hindered convex face (Figure 2) leading to the formation of highly stereoselective *cis*-fused (±)-**14**.

With (±)-**13** in hand, we then performed ceric(IV) ammonium nitrate (CAN) mediated oxidative transformation of (±)-**13** to *p*-quinone, thus completing total synthesis of (±)-taiwaniaquinone H (**1d**) in 63% yield. The later was then demethylated using 2(*N*) KOH in MeOH to complete total synthesis of (±)-dichroanone (**1e**) (Scheme 6).



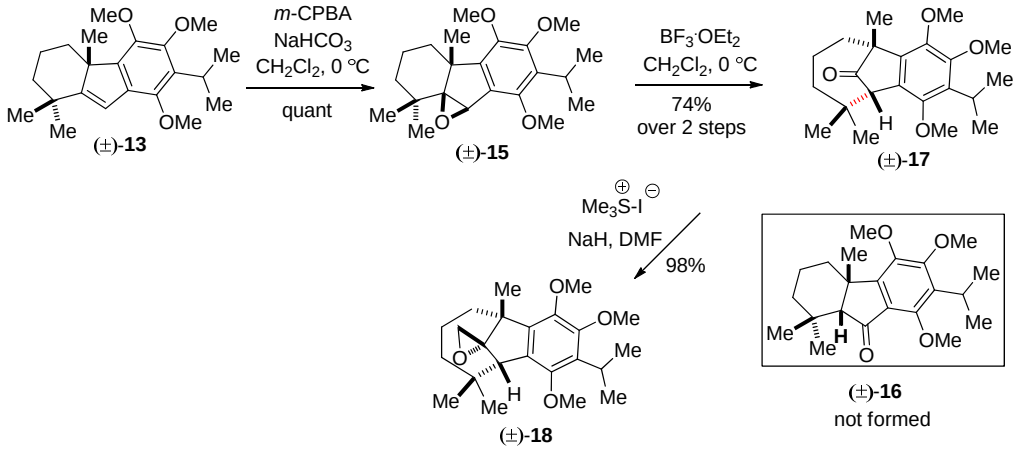
Scheme 6: Total syntheses of (±)-taiwaniaquinone H (**1d**) and (±)-dichroanone (**1e**).

For further synthetic elaboration, carbotricyclic core (±)-**3e** was completely hydrogenated in presence of 10% Pd-C under 1 atm. pressure of H_2 in MeOH for 1 h to furnish (±)-**14** in 98% yield, which was then followed by an oxidative quinone formation in presence of CAN to accomplish total synthesis of (±)-5-*epi*-taiwaniaquinone G (**1c**) in 63% overall yield from (±)-**3e** (Scheme 7). To our delight, it was found that oxidative quinone formation of carbotricyclic cores (±)-**13** and (±)-**14** having electron-rich systems work fine only in the presence of CAN (Schemes 6 and 7).



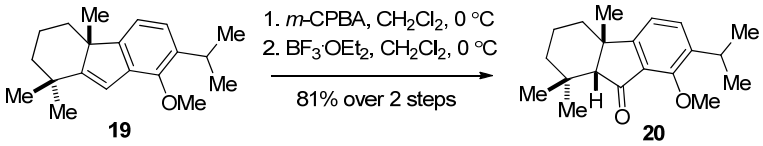
Scheme 7: Total synthesis of (±)-5-*epi*-taiwaniaquinone G (*ent*-**1h**).

Next, we were interested to complete total synthesis of (±)-taiwaniaquinol B (**1b**) from dimethylether of (±)-**16**. We thought that tricyclic ketone (±)-**16** can be synthesized from a $BF_3{\cdot}OEt_2$-mediated rearrangement of epoxide (±)-**15** (Scheme 8),[22b] which in turn can be accesses from olefin (±)-**13** via a reaction with *m*-chloroperbenzoic acid (*m*-CPBA). In forward direction, we oxidized olefin (±)-**13** in the presence of *m*-CPBA to furnish epoxide (±)-**15** in quantitative yield. However, as per literature shown in Scheme 9, $BF_3{\cdot}OEt_2$ treatment of (±)-**15** didn't afford even trace amount of the expected tricyclic ketone (±)-**16**.[22b]



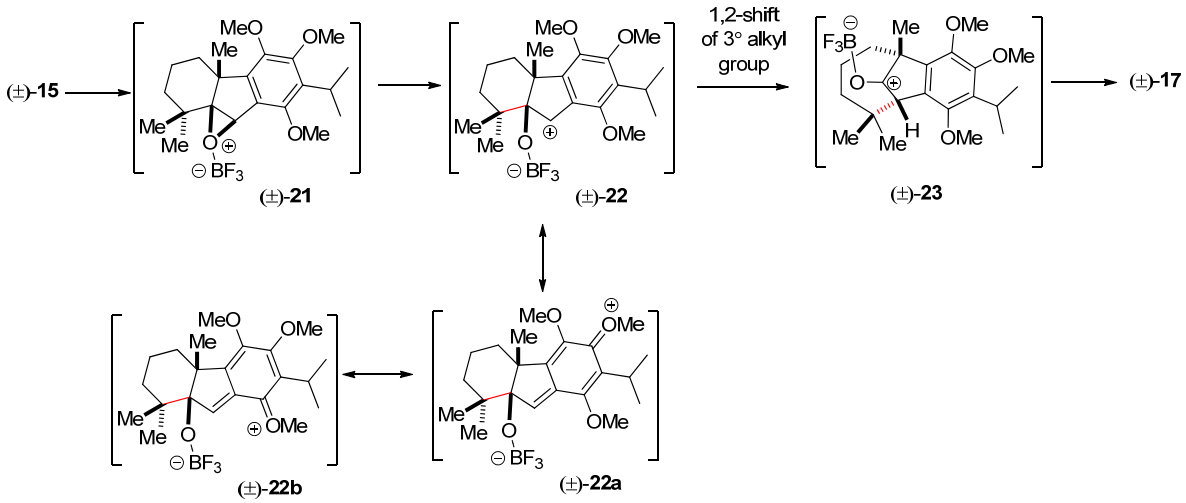
Scheme 8: Unexpected formation of (±)-**17**.

In fact**,** from this reaction, we could only isolate unexpected ring expansion ketone (±)-**17** as the sole product in 74% yield. Reaction of ketone (±)-**17** with trimethylsulfonium iodide in the presence of sodium hydride afforded product (±)-**18**, which was unambiguously confirmed from X-ray structure (CCDC: 1405989).



Scheme 9: Synthesis of tricyclic ketone **20** by Alvarez-Manzaneda.[22b]

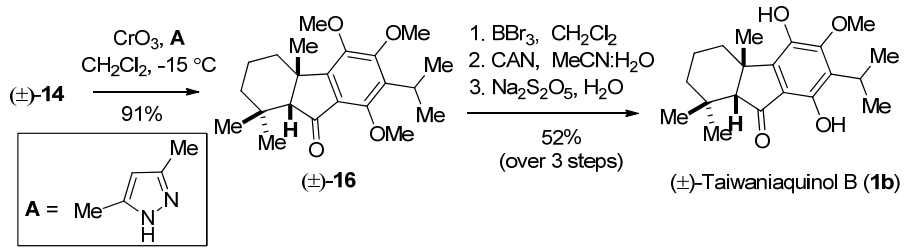
A plausible mechanism of the formation of cycloheptane ring of (±)-**17** shown in Scheme 10. In presence of $BF_3{\cdot}OEt_2$, (±)-**15** forms intermediate **21** which forms a benzylic carbocation **22**, from where a 1,2-migration of 3º alkyl group leads to the formation of ketone (±)-**17** via a carbocation **23**. The stability of carbocation **22** is attributed because of highly electron-rich aromatic ring, which stabilizes **22** via intermediates **22a-b** (Scheme 10).



Scheme 10: Unexpected formation of 7-membered (±)-**17**.

Thus, we adopted an alternate route, in which carbotricyclic core (±)-**14** was reacted with CrO_3 in the presence of 3,5-dimethylpyrazole to effect benzylic oxidation to furnish ketone (±)-**16** in 91% yield. From this intermediate, total synthesis of (±)-taiwaniaquinol B was accomplished in a three step sequence in 52% overall yield via demethylation using

BBr_3, oxidation in presence of CAN followed by reduction with $Na_2S_2O_5$ (Scheme 11). It was observed that oxidative quinone formation of carbotricyclic cores (±)-**12** and (±)-**16** with electron-deficient systems with CAN was unsuccessful and, hence, a three-step sequence was used (Scheme 11).



Scheme 11: Total synthesis of (±)-taiwaniaquinol B (**1b**).

CONCLUSIONS

In summary, we have demonstrated an operationally simple, inexpensive, yet efficient process for the synthesis of a variety of taiwaniaquinoids via a Nazarov type cyclization of aryldivinyl carbinols in the presence of a catalytic amount of a metal triflate as Lewis acid. The methodology affords a variety of carbotricyclic structures in excellent yields. This methodology has been applied to first total synthesis of (±)-taiwaniaquinol F (**1a**) by using minimum protecting groups in 36.4% overall yield starting from safranal (**7**) over 8 steps. In addition, we have also accomplished concise and straightforward total syntheses of (±)-taiwaniaquinone H (**1d**), (±)-dichronanone (**1e**), (±)-5-*epi*-taiwaniaquinone G (*ent*-**1h**) and (±)-taiwaniaquinol B (**1b**). Further exploration of this strategy towards the synthesis of *trans*-fused taiwaniaquinoids is currently under active investigations in our laboratory.

EXPERIMENTAL SECTION

EXPERIMENTAL SECTION

Materials. Unless otherwise stated, reactions were performed in oven-dried glassware fitted with rubber septa under a nitrogen atmosphere and were stirred with Teflon-coated magnetic stirring bars. Liquid reagents and solvents were transferred via syringe using standard Schlenk techniques. Tetrahydrofuran (THF), diethyl ether (Et_2O) was distilled over sodium/benzophenone ketyl. Dichloromethane (CH_2Cl_2) and toluene were distilled over calcium hydride. All other solvents such as acetonitrile, chloroform, methanol, 1,2-dichloroethane and reagents were used as received. Thin layer chromatography was performed using silicagel 60 F-254 precoated plates (0.25 mm) and visualized by UV irradiation, anisaldehyde stain and other stains. Silicagel of particle size 100-200 mesh was used for flash chromatography. ^1H and ^{13}C NMR spectra were recorded on 400 MHz, 500 MHz and 500 MHz spectrometers with ^{13}C operating frequencies of 100, 125 MHz, respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent ($CDCl_3$ and DMSO-d_6) signal (δ = 7.26 for ^1H NMR and δ = 77.0 for ^{13}C NMR). Data for ^1H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). IR spectra were recorded on a FT-IR system (Spectrum BX) and are reported in frequency of absorption (cm^{-1}). Only selected IR absorption bands are reported. High-Resolution Mass Spectrometry (HRMS) data were recorded on MicrOTOF-Q-II mass spectrometer using methanol as solvent.

General procedure for the synthesis of arylvinylcarbinol ±(2a-c and **2e):** A flame-dried round-bottom flask was charged with substituted bromoarene (13.56 mmol; 1.1 equiv) under

nitrogen atmosphere in dry THF (30 mL). To this solution was added 7.5 mL of 2.0 M solution of *n*-BuLi in cyclohexane (14.92 mmol; 1.2 equiv) dropwise *via* syringe over a period of 5 min at −78 ºC. After 5 min. of stirring at this temperature, safranal **7** (1.8 mL, 11.30 mmol; 1.0 equiv) (dissolved in 10 mL THF) was added dropwise *via* syringe over a period of 5 min. The mixture was treated with saturated aq. solution of NH_4Cl over a period of 5 min. Then, it was transferred to the separatory funnel and shaken vigorously. An aqueous layer was extracted with EtOAc (50 mL X 2). The combined EtOAc extracts were dried over anhydrous Na_2SO_4 and concentrated in rotary evaporator under vacuum. The crude product was finally purified by column chromatography with EtOAc/hexane (1:9) to afford pure compound (±)-**2.**

(3-Isopropyl-4-methoxyphenyl)(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methanol ±(**2a**): The product was obtained as colorless viscous oil (2.3 g, 68%), R_f = 0.5 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 1.6 Hz, 1H), 7.22 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 5.78-5.77 (m, 2H), 5.69 (d, *J* = 4.6 Hz, 1H, CH-OH), 3.81 (s, 3H), 3.30 (septet, *J* = 6.9 Hz, 1H), 2.08-2.07 (m, 2H), 1.88-1.87 (m, 1H), 1.74 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 3H), 0.99 (s, 3H); **^{13}C NMR** (100 MHz, , $CDCl_3$) δ 155.6, 140.9, 136.6, 135.2, 130.1, 128.8, 125.5, 124.23, 124.2, 109.9, 71.5, 55.4, 40.7, 34.2, 27.0, 26.8, 26.5, 22.8, 22.7, 19.6; **IR** (film) υ_{max} 3460, 3033, 2959, 1498, 1465, 1245, 1089, 1035, 734 cm^{-1}. **HRMS** (ESI) m/z 323.1998 $[(M + Na)]^+$; calculated for $[C_{20}H_{28}O_2 + Na]^+$: 323.1982.

(4-Methoxy-3-methylphenyl)(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methanol ±(**2b**): The product was obtained as colorless viscous oil (2.0 g, 66%), R_f = 0.6 (10% EtOAc in hexane). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23-7.21 (m, 2H), 6.77 (d, *J* = 8.1 Hz, 1H), 5.81-

5.73 (m, 2H),5.66 (d, *J* = 2.6 Hz, 1H), 3.82 (s, 3H), 2.22 (s, 3H), 2.10-2.07 (m, 1H), 1.83-1.82 (m, 1H), 1.74 (s, 3H), 1.04 (s, 3H), 1.00 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.6, 139.9, 135.1, 130.1, 128.8, 128.7, 126.2, 125.5, 124.5, 73.3, 55.3, 40.6, 34.2, 27.1, 26.5, 19.6, 16.4; **IR** (film) υ_{max} 3500, 3433, 2956, 2918, 1503, 1463, 1250, 1127, 1110, 1036, 814, 700 cm^{-1}; **HRMS** (ESI) m/z 295.1673 $[(M + Na)]^+$; calculated for $[C_{18}H_{24}O_2 + Na]^+$: 295.1669.

(2,4,5-Trimethoxyphenyl)(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methanol ±(**2c**): The product was obtained as colorless viscous oil (2.76 g, 77%), R_f = 0.45 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$+DMSO-D_6) δ 7.0 (s, 1H), 6.46 (s, 1H), 5.70-5.56 (m, 3H), 3.91 (s, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.66 (s, 3H), 1.98 (d, ***J*** = 17.0 Hz, 1H), 1.86 (dd, *J* = 17.0, 4.5 Hz, 1H), 1.76 (s, 3H), 0.87 (s, 3H), 0.81 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$+DMSO-D_6) δ 151.7, 148.8, 142.3, 138.4, 130.6, 128.3, 124.6, 123.3, 113.5, 97.6, 67.1, 56.7, 56.2, 56.1, 40.6, 34.4, 26.7, 25.7, 20.0; **IR** (film) υ_{max} 3500, 2934, 2360, 1609, 1506, 1466, 1309, 1206, 1105, 1035, 861, 768 cm^{-1}; **HRMS** (ESI) m/z 317.1739 $[(M - H)]^+$; calculated for $[C_{19}H_{26}O_4 - H]^+$: 317.1747.

(3-Isopropyl-2,4,5-trimethoxyphenyl)(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methanol ±(**2e**): The product was obtained as colorless solid (3.7 g, 91%), R_f = 0.5 (10% EtOAc in hexane).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 5.81-5.82 (m, 2H), 5.77-5.73 (m, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.73 (s, 3H), 3.36 (septet, *J* = 7.0 Hz, 1H), 3.32 (d, *J* = 1.6 Hz, 1H), 2.13-2.00 (m, 2H), 1.83 (s, 3H), 1.36 (d, *J* = 7.1 Hz, 3H), 1.32 (d, *J* = 7.0 Hz, 3H), 1.10 (s, 3H), 0.93 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.1, 149.1, 148.6, 137.3, 135.0, 130.3, 130.26, 129.8, 125.0, 110.5, 69.0, 62.0, 60.6, 55.9, 40.3, 34.3, 26.8, 26.0, 25.6, 21.9, 20.3; **IR** (film) υ_{max} 3472, 2957, 1589, 1455, 1235, 1105, 1041, 855 cm^{-1}; **MP** 105-108 °C.

Procedure for synthesis of (±)-**2d:** A flame-dried round-bottom flask was charged with safranal **7** (3.21 mmol; 1.0 equiv) under nitrogen atmosphere in dry THF (10 mL). The reaction mixture was cooled to 0 °C. To this solution was added 1.0 M solution of phenylmagnesium bromide in THF (3.86 mmol; 1.2 equiv) drop wise *via* a syringe over a period of 5 min and stirring was continued for additional 1 h. The mixture was treated with saturated aq. solution of NH_4Cl for 5 min. It was transferred to the separatory funnel and shaken vigorously. An aqueous layer was extracted with EtOAc. The combined EtOAc extracts were dried over anhyd. Na_2SO_4 and concentrated using rotator evaporator under vacuum. The crude product was finally purified by column chromatography with EtOAc/hexane to afford pure compound (±)-**2d.**

Phenyl(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methanol±(2d): The product was obtained as colorless viscous oil (734 mg, 94%), R_f = 0.5 (5% EtOAc in hexane). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.52-7.50 (m, 2H), 7.38-7.35 (m, 2H), 5.29-7.25 (m, 1H), 5.84 (s, 1H), 5.83-5.80 (m, 2H), 2.13 (m, 1H), 2.04 (d, *J* = 4.8 Hz, 1H), 1.75 (s, 3H), 1.14 (s, 3H), 1.03 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 143.8, 139.9, 129.9, 128.1, 126.5, 125.9, 125.8, 71.45, 40.8, 34.3, 27.1, 26.7, 19.5; **IR** (film) υ_{max} 3438, 2955, 2914, 1445, 1359, 1168, 1004, 984, 837, 721, 703 cm^{-1}; **HRMS** (ESI) m/z 251.1384[(M + Na)]$^+$; calculated for $[C_{16}H_{20}O + Na]^+$: 251.1406.

General procedure for metal triflate-catalyzed cyclization of arylvinylcarbinols: In an oven-dried round-bottom flask, aryldivinyl carbinols (0.3 mmol; 1.0 equiv.) was dissolved in dichloromethane (3 mL) and cooled to 0 ºC. To this solution solid $Bi(OTf)_3$ (2 mol%) [**Condition A**] or $Sn(OTf)_2$ (2 mol%) [**Condition B**] was added. The reaction mixture was stirred at 0 ºC for indicated time (5-10 min). Upon complete consumption of starting material

(TLC) the reaction mixture was quenched with saturated $NaHCO_3$ solution. The whole reaction mixture was transferred to a separatory funnel and extracted with 5 mL of EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The crude products were purified by flash chromatography (10:1 hexanes/EtOAc) to afford cyclization products.

7-Isopropyl-6-methoxy-1,1,4a-trimethyl-2,4a-dihydro-1H-fluorene ±(**3a**): The product was obtained as colorless viscous oil (83 mg, 98%), R_f = 0.5 (2% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11 (s, 1H), 6.86 (s, 1H), 6.36 (s, 1H), 6.0 (d, *J* = 9.4 Hz, 1H), 5.58-5.54 (m, 1H), 3.85 (s, 3H), 3.34-3.28 (m, 1H), 2.18 (dd, *J* = 17.2, 5.0 Hz, 1H), 1.96 (bd, *J* = 17.2 Hz, 1H), 1.44 (s, 3H), 1.35 (s, 6H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.18 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.1, 154.8, 150.1, 135.3, 134.7, 131.8, 125.1, 120.8, 118.1, 104.9, 56.0, 53.3, 45.4, 34.9, 29.3, 27.1, 27.0, 26.7, 23.2, 22.9; **IR** (film) υ_{max} 2960, 2931, 1464, 1419, 1256, 1044, 888 cm^{-1}; **HRMS** (ESI) m/z 283.2076 $[(M + H)]^+$; calculated for $[C_{20}H_{26}O + H]^+$: 283.2056.

6-Methoxy-1,1,4a,7-tetramethyl-2,4a-dihydro-1H-fluorene ±(**3b**)**:** The product was obtained as colorless viscous oil (73 mg, 96%), R_f = 0.5 (2.5% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.85 (s, 1H), 6.32 (s, 1H), 6.02-6.00 (m, 1H), 5.59-5.54 (m, 1H), 3.86 (s, 3H), 2.21 (s, 3H), 2.17-2.15 (m, 1H), 1.98-1.94 (m, 1H), 1.44 (s, 3H), 1.35 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 155.7, 151.6, 134.5, 131.7, 125.1, 124.7, 122.7, 120.5, 104.5, 55.8, 53.3, 45.4, 35.0, 29.2, 27.0, 26.97, 16.4; **IR** (film) υ_{max} 3024, 2915, 1482, 1463, 1292, 1195, 1042, 880, 701 cm^{-1}; **HRMS** (ESI) m/z 255.1730 $[(M + H)]^+$; calculated for $[C_{18}H_{22}O + H]^+$: 255.1743.

5,6,8-trimethoxy-1,1,4a-trimethyl-2,4a-dihydro-1H-fluorene ±(**3c**): The product was obtained as colorless viscous oil (63 mg, 70%), R_f = 0.55 (10% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.41 (s, 1H), 6.40 (s, 1H), 6.28 (dd, *J* = 9.7, 2.2 Hz, 1H), 5.58-5.54 (m, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 2.17-2.11 (dd, *J* = 17.1, 5.1 Hz, 1H), 2.0-1.92 (d, *J* = 17.1 Hz, 1H), 1.50 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.3, 151.2, 148.3, 145.3, 139.7, 131.1, 125.1, 123.8, 116.3, 97.0, 61.0, 56.5, 56.2, 45.1, 35.0, 29.3, 27.0, 24.6; **IR** (film) υ_{max} 2958, 2835, 1614, 1468, 1314, 1269, 1125, 1045, 987, 735 cm^{-1}; **HRMS** (ESI) m/z 301.1798 $[(M + H)]^+$; calculated for $[C_{19}H_{24}O_3 + H]^+$: 301.1798.

1,1,4a-trimethyl-2,4a-dihydro-1H-fluorene ±**(3d)**: The product was obtained as colorless viscous oil (55 mg, 88%), R_f = 0.5 (in hexane). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.31 (d, *J* = 7.2 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 6.28 (td, *J* = 7.4, 1.1 Hz, 1H), 7.13 (td, *J* = 7.4, 1.2 Hz, 1H), 6.43 (s, 1H), 6.06-6.04 (m, 1H), 5.59-5.56 (m, 1H), 2.23-2.18 (m, 1H), 2.00-1.96 (m, 1H), 1.45 (s, 3H), 1.37 (s, 3H), 1.37 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 163.3, 152.6, 142.2, 131.5, 126.5, 125.0, 124.3, 121.1, 121.06, 120.6, 53.2, 45.2, 35.0, 29.3, 26.9, 26.7; **IR** (film) υ_{max} 3017, 2960, 2916, 1465, 1363, 1256, 1048, 987, 872, 848, 792, 746, 712 cm^{-1}; **HRMS** (ESI) m/z 211.1482 $[(M + H)]^+$; calculated for $[C_{16}H_{18} + H]^+$: 211.1481.

7-Isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-2,4a-dihydro-1H-fluorene ±(**3e**): The product was obtained as colorless solid (992 mg, 95%, (in 3.05 mmol)), R_f = 0.6 (5% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.4 (s, 1H), 6.28 (dd, *J* = 9.7, 2.1 Hz, 1H), 5.59-5.54 (m, 1H), 3.90 (s, 3H), 3.81 (s,3H), 3.80 (s, 3H), 3.47-3.39 (m, 1H), 2.17 (dd, *J* = 17.0, 4.7 Hz, 1H), 1.99-1.95 (m, 1H), 1.52 (s, 3H), 1.34-1.33 (m, 9H), 1.31 (d, *J* = 2.2 Hz, 3H) ;**^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.0, 149.5, 147.5, 145.5, 142.4, 132.2, 131.3, 130.2, 124.9,

117.2, 62.0, 60.5, 60.2, 54.5, 45.2, 35.1, 29.3, 27.0, 24.8, 22.22, 22.21; **IR** (film) υ_{max} 2960, 1455, 1415, 1120, 1051 cm^{-1}; **HRMS** (ESI) m/z 343.2296 $[(M + H)]^+$; calculated for $[C_{22}H_{30}O_3 + H]^+$: 343.2268; **MP** 71-74 °C.

Synthesis of (2,4a)-7-isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-2,4a-dihydro-1H-fluoren-2-ol ±(**9**): In a sealed tube, compound **3e** (910 mg, 2.66 mmol; 1.0 equiv) was taken in mixture of dioxane (12 mL) and water (3 mL) (4:1 ratio). To this solution was added SeO_2 (354 mg, 3.19 mmol; 1.2 equiv) at room temperature. Then, the reaction mixture was hedted to reflux at 105 °C and stirring was continued for 22 h. After full consumption of starting material (judged by TLC) the reaction mixture was extracted with ethyl acetate and purified by column chromatography (9:1 hexanes/EtOAc) to furnish 790 mg (83% yield) of (±)-**9** as white solid. $\mathbf{R_f}$ 0.5 (20% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.56 (s, 1H), 6.44 (d, *J* = 9.6 Hz, 1H), 5.81 (dd, *J* = 9.6, 5.1 Hz, 1H), 3.91 (s, 3H), 3.83 (s,3H), 3.82 (s, 3H), 3.73 (dd, *J* = 10.9, 5.1 Hz, 1H), 3.44 (septet, *J* = 7.1 Hz, 1H), 1.51 (s, 3H), 1.36 (s, 3H), 1.338 (d, *J* = 7.0 Hz, 3H), 1.332 (s, 3H), 1.331 (d, *J* = 7.1 Hz, 3H), 0.86 (d, *J* = 11.1 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.1, 149.9, 147.4, 145.5, 141.5, 134.8, 133.6, 129.6, 127.1, 121.1, 76.6, 62.1, 60.5, 60.2, 54.7, 40.9, 25.7, 25.4, 23.6, 23.5, 22.18, 22.16; **IR** (film) υ_{max} 3472, 3019, 2918, 1445, 1414, 1333, 1272, 1121, 1050, 989, 701 cm^{-1}; **HRMS** (ESI) m/z 359.2232 $[(M + H)]^+$; calculated for $[C_{22}H_{30}O_4 + H]^+$: 359.2217; **MP** 69-71 °C.

Synthesis of 7-isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-1H-fluoren-2(4aH)-one ±(**10**): To a stirred solution of dry DMSO (0.53 mL, 7.97 mmol; 4.5 equiv.) in CH_2Cl_2 (20 mL) at -78 °C was added oxalyl chloride (0.3 mL, 3.55 mmol; 2.0 equiv.) carefully. Then the mixture was stirred for 20 min. at -78 °C followed by drop wise addition of compound (±)-**9** (635 mg, 1.77 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL). The reaction mixture was stirred for 1 h at

-78 °C followed by addition of Et_3N (1.23 mL, 8.88 mmol; 5.0 equiv.) at same temperature. Later, the reaction was slowly brought to room temperature. Upon completion of starting material (monitored by TLC) the reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (20 X 2 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude material was purified in flash chromatography (15:1 hexanes/EtOAc) to give 593 mg (94% yield) of (±)-**10** as white solid. $\mathbf{R_f}$ = 0.6 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 9.7 Hz, 1H), 6.57 (s, 1H), 5.97 (d, *J* = 9.8 Hz, 1H), 3.96 (s, 3H), 3.82 (s, 3H), 3.45 (septet, *J* = 7.0 Hz, 1H), 1.69 (s, 3H), 1.50 (s, 3H), 1.48 (s, 3H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.33 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 202.7, 155.9, 150.6, 150.1, 147.8, 145.7, 139.0, 134.5, 129.8, 127.3, 121.0, 62.2, 60.5, 60.2, 54.3, 47.8, 26.5, 25.7, 24.8, 23.7, 20.1; **IR** (film) υ_{max} 2982, 2923, 1681, 1462, 1450, 1415, 1338, 1272, 1122, 1048, 1019, 826 cm^{-1}; **HRMS** (ESI) m/z 357.2067 $[M+H]^+$; calculated for $[C_{22}H_{28}O_4 + H]^+$: 357.2060; **MP** 104-106 °C.

Synthesis of (4a)-7-isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-4,4a,9,9a-tetrahydro-1H-fluoren-2(3H)-one ±(**11**): In an oven-dried pear shaped round bottom flask compound (±)-**10** (500 mg, 1.40 mmol) was dissolved in HPLC grade methanol (70 mL). This solution was passed through H-Cube Hydrogenator having 10% Pd/C cartridge at 34 °C and 5 bar pressure having 0.3 mL/min flow of solution. Then the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography (10:1 hexanes/EtOAc) to afford 495 mg (98% yield) of (±)-**11** as a white solid. $\mathbf{R_f}$ = 0.5 (10% EtOAc in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.84 (s, 3H), 3.80 (s, 3H), 3.69 (s, 3H), 3.39 (septet, *J* = 7.1 Hz, 1H), 3.10 (dd, *J* = 16.5, 9.1 Hz, 1H), 2.53 (dd, *J* = 16.5, 7.7 Hz, 1H), 2.49-2.43 (m, 1H), 2.27 (dd, *J* = 9.0, 7.7 Hz, 1H), 2.24-2.21 (m, 2H), 2.17-2.11 (m, 1H), 1.60 (s, 3H), 1.316 (d, *J* = 7.1 Hz, 3H), 1.314 (d, *J* = 7.1 Hz, 3H), 1.29 (s, 3H), 1.06 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 217.3, 151.5, 149.7, 146.2, 141.6, 133.6, 128.9, 60.4, 60.2, 60.0, 55.8, 47.3, 47.28, 36.4, 33.5, 33.4, 28.9, 26.7, 25.7, 23.7, 22.1; **IR** (film) υ_{max} 2969, 2909, 1712, 1463, 1449, 1412, 1337, 1268, 1118, 1047, 976, 741 cm^{-1}; **HRMS** (ESI) m/z 361.2348 $[M+H]^+$; calculated for $[C_{22}H_{32}O_4 + H]^+$: 361.2373; **MP** 79-81 °C.

Synthesis of (4a)-7-isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-4,4a-dihydro-1H-fluorene-2,9(3H,9aH)-dione ±(**12**): To a stirred solution of 3,5-dimethylpyrazole (4.16 g, 43.31 mmol; 17.93 equiv) in CH_2Cl_2 (10 mL) was added CrO_3 (4.3 g, 43.31 mmol; 17.93 equiv) at -15 ºC. Then the reaction mixture was stirred for 15 min. at same temperature before a solution of tricyclic compound (±)-**11** (870 mg, 2.41 mmol; 1.0 equiv) in CH_2Cl_2 (5 mL) was added drop wise. This dark mixture was stirred for 1 h at -10 ºC and it was directly purified by flash chromatography (10:1 hexanes/EtOAc) to furnish 777 mg (86% yield) of (±)-**12** as a white solid. $\mathbf{R_f}$ = 0.55 (20% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.46 (septet, *J* = 7.1 Hz, 1H), 2.52-2.43 (m, 3H), 2.33-2.26 (m, 1H), 2.26 (s, 1H), 1.45 (s, 3H), 1.38 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H), 1.00 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.3, 201.8, 159.1, 152.8, 152.4, 146.0, 135.7, 124.1, 63.2, 62.2, 60.2, 60.0, 46.7, 41.1, 34.8, 30.3, 28.3, 25.3, 25.2, 22.3, 21.7; **IR** (film) υ_{max} 2962, 2925, 1704, 1579, 1469, 1449, 1415, 1316, 1272, 1129, 1045, 958, 701 cm^{-1}; **HRMS** (ESI) m/z 375.2192 $[M+H]^+$; calculated for $[C_{22}H_{30}O_5 + H]^+$: 375.2166; **MP** 112-114 °C.

Synthesis of (±)**-taiwaniaquinol F (1a)**: To a stirred solution of compound (±)-**12** (166 mg, 0.444 mmol; 1.0 equiv) in dry CH_2Cl_2 (6 mL) was added BBr_3 (147 µL, 1.55 mmol; 3.5 equiv) at -78 ºC. Then the reaction mixture was stirred for 1.5 h. After complete consumption of starting material (judged by running tlc), the reaction mixture was quenched with water

and extracted with ethyl acetate (10 X 2 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*.

The crude product was taken in 20 mL of MeCN:H_2O (3:1) at 0 ºC. To this reaction mixture, a solution of ammonium ceric nitrate (CAN) (1217 mg, 2.22 mmol; 5.0 equiv) in water (7 mL) was added and it was stirred for 20 minutes at 0 ºC. After complete consumption of starting material, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_5$ and kept on stirring for 20 min. Upon completion of the reaction (judged by running tlc), it was diluted by water (10 mL) and extracted with EtOAc (25 mL) by using a separatory funnel. The organic filtrate was dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The crude was purified by flash chromatography (4:1 hexanes/EtOAc) to afford 99 mg (overall 65% yield in two steps) of (±)-taiwaniaquinol F (**1a**) as crystalline solid. $\mathbf{R_f}$ = 0.45 (20% EtOAc/hexanes); **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.41 (s, 1H), 5.48 (s, 1H), 3.81 (s, 3H), 3.28 (septet, *J* = 7.1 Hz, 1H), 2.50-2.39 (m, 4H), 2.38 (s, 1H), 1.51 (s, 3H), 1.41 (s, 3H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.37 (d, *J* = 7.1 Hz, 3H), 1.13 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 214.9, 208.3, 152.9, 151.0, 141.4, 138.5, 127.0, 118.0, 63.2, 62.1, 46.8, 42.0, 34.6, 29.4, 26.7, 26.0, 25.8, 22.2, 20.53, 20.52; **IR** (film) υ_{max} 3418 (br), 2997, 2967, 2915, 1708, 1660, 1425, 1328, 1112, 1021, 932, 891, 739, 701 cm^{-1}; **HRMS** (ESI) m/z 347.1832 $[M+H]^+$; calculated for $[C_{20}H_{26}O_5 + H]^+$: 347.1853; **MP** 119-121 °C. [Lit. Chang, C.–I.; Chang, J. –Y; Kuo, C.–C.; Pan, W.–Y.; Kuo, Y.–H. *Planta. Med.* **2005**, *71*, 72.]

Synthesis of (±)-7-Isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1H-fluorene ±(13): A flame-dried round-bottom flask was charged with compound (±)-**3e** (85 mg, 0.30 mmol; 1.0 equiv) under nitrogen atmosphere in MeOH (5 mL) The solution was purged under nitrogen atmosphere for 20 min. To this solution was added Pd on activated

charcoal (1.6 mg) and purged with hydrogen balloon for the period of 10 min. The reaction mixture was filtered through celite and concentrated using rotary evaporator under vaccum. The crude was finally purified by flash chromatography (10:1 hexanes/EtOAc) to furnich 52 mg in 50% yield of (±)-**13** as colorless solid. $\mathbf{R_f}$ = 0.6 (5% EtOAc/hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 6.33 (s, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.47-3.40 (m,1H), 2.44-2.40 (m, 1H), 2.0-1.87 (m, 1H), 1.62-1.58 (m, 2H), 1.43 (s, 3H), 1.33 (d, *J* = 1.7 Hz, 3H), 1.31 (d, *J* = 1.3 Hz, 3H), 1.26 (s, 3H), 1.22 (s, 3H), 1.15-1.06 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 162.9, 149.3, 147.2, 145.7, 145.0, 132.7, 130.3, 116.8, 61.9, 60.5, 60.2, 52.3, 36.8, 35.5, 31.4, 29.7, 25.7, 25.5, 22.3, 22.2, 21.6, 19.5; **IR** (film) υ_{max} 2935, 1455, 1414, 1119, 1053 cm^{-1}; **HRMS** (ESI) m/z 367.2236 $[(M + Na)]^+$; calculated for $[C_{22}H_{32}O_3 + Na]^+$: 367.2244; **MP** 79-83 °C.

Synthesis of (±)-taiwaniaquinone H ±(1d): A oven dried round-bottom flask was charged with compound (±)-(**13**) (270 mg, 0.783 mmol; 1 equiv) in MeCN:H_2O (3:1) (30 mL). To this solution was added a solution of ceric ammonium nitrate (CAN) (1288 mg, 2.35 mmol; 3.0 equiv) in water (12 mL) at 0 ºC. The reaction mixture was stirred at that temperature for 10 min. and then diluted with water (20 mL) and extracted with EtOAc (20 mL X 2). The combined organic phase washed with brine and dried over Na_2SO_4 and concentrated using rotator evaporator under vaccum. The crude product was finally purified by flash chromatography (20:1 hexanes/EtOAc) to afford 167 mg (63% yield) of (±)-taiwaniaquinone H (**1d**) as a red syrup. R_f = 0.4 (5% EtOAc in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.34 (s, 1H), 4.0 (s, 3H), 3.24 (septet, *J* = 7.1 Hz, 1H), 2.40-2.35 (m, 1H), 1.89 (qt, *J* = 13.8, 3.5 Hz, 1H), 1.68-1.64 (m, 1H), 1.61-1.60 (m, 1H), 1.42 (s, 3H), 1.24 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.21 (s, 3H), 1.09-1.03 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 186.3, 178.8, 175.5, 157.3, 150.6, 145.8, 136.0, 116.7, 61.4, 55.6, 43.4, 37.2, 36.7, 31.0,

24.8, 24.5, 20.7, 20.67, 20.1, 19.1; **IR** (film) υ_{max} 2922, 1646, 1560, 1536, 1354, 1290, 1265, 1152, 1025, 930 cm^{-1}; **HRMS** (ESI) m/z 315.1941 $[(M + H)]^+$; calculated for $[C_{20}H_{26}O_3 + H]^+$: 315.1955. [Lit.: Liang, G.; Xu, Y.; Seiple, I. B.; Trauner, D. *J. Am. Chem. Soc*. **2006**, *128*, 11022.

Synthesis of (±)-dichroanone ±(1e): An oven dried round-bottom flask was charged with (±)-taiwaniaquinone H (60 mg, 0.19 mmol; 1.0 equiv) in MeOH (5 mL). To this solution was added a solution of 2M KOH solution in MeOH (3 mL) at room temprature. The reaction mixture was stirred at room temperature for 24 h. Then, 2N HCL (1.5 mL) was added slowly and the mixture was diluted with dichloromethane (15 mL). The combined organic phase washed with brine and dried over Na_2SO_4 and concentrated using rotator evaporator under vaccum. The crude product was purified by flash chromatography (20:1 hexanes/EtOAc) to give 35 mg (66% yield) of (±)-dichroanone **(1e)** as a red syrup. R_f = 0.4 (2.5% EtOAc in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.30 (brs, 1H), 6.45 (s, 1H), 3.21 (septet, *J* = 7.0 Hz, 1H), 2.39-2.35 (m, 1H), 1.93 (qt, *J* = 14.1, 3.4 Hz, 1H), 1.73-1.69 (m, 1H), 1.65-1.60 (m, 1H), 1.45 (s, 3H), 1.28 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.234 (s, 3H), 1.14-1.06 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 186.3, 178.8, 175.5, 157.3, 150.6, 145.8, 136.0, 116.7, 61.4, 55.6, 43.4, 37.2, 36.7, 31.0, 24.8, 24.5, 20.7, 20.67, 20.1, 19.1; **IR** (film) υ_{max} 3354, 2912, 1643, 1633, 1527, 1372, 1360, 1319, 1170, 965, 919, 871cm^{-1}; **HRMS** (ESI) m/z 301.1776$[(M + H)]^+$; calculated for $[C_{19}H_{24}O_3 + H]^+$: 301.1798. [Lit.: Kawazoe, K.; Yamamato, M.; Takaishi, Y.; Honda, G.; Fujita, T.; Sezik, E.; Yesilada, E. *Phytochemistry* **1999**, *50*, 493]

Synthesis of (4a,9a)-7-Isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydro-1H-fluorene ±(14): A flame-dried round-bottom flask was charged with

compound (±)-**3e** (630 mg, 1.83 mmol; 1.0 equiv) under nitrogen atmosphere in MeOH (5 mL) and purged with nitrogen gas. To this reaction mixture was added Pd on activated charcoal (19 mg, 0.18 mmol; 0.1 equiv) and placed with a hydrogen balloon for the period of 1 h. The reaction mixture was filtered through celite and concentrated using rotary evaporator under vaccum. The crude products were purified by flash chromatography (9:1 hexanes/EtOAc) to afford 618 mg of compound ±-(**14**) in 98% yield as colorless viscous oil, R_f = 0.55 (5% EtOAc and hexane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.77 (s, 3H), 3.70 (s, 3H), 3.40-3.31 (m, 1H), 2.85-2.79 (m, 1H), 2.63-2.56 (m, 1H), 1.82-1.73 (m, 2H), 1.59 (s, 3H), 1.43-1.40 (m, 1H), 1.39-1.35 (m, 2H), 1.32 (m, 2H), 1.30 (s, 3H), 1.29 (s, 3H), 1.10 (s, 3H), 0.91 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.0, 150.3, 146.3, 144.3, 132.3, 128.9, 60.5, 60.3, 60.2, 56.6, 47.1, 35.2, 35.0, 32.2, 31.2, 31.1, 29.9, 25.6, 25.5, 22.24, 22.23, 18.7; **IR** (film) υ_{max} 2919, 1452, 1413, 1338, 1255, 1154, 1042 cm^{-1}; **HRMS** (ESI) m/z 369.2425$[(M + Na)]^+$; calculated for $[C_{22}H_{34}O_3 + Na]^+$: 369.2400.

Symthesis of (±)-5-*epi*-taiwaniaquinone G (*ent*-1h): A oven dried round-bottom flask was charged with compound **14** (187 mg, 0.30 mmol; 1.0 equiv) in MeCN:H_2O (3:1) (25 mL). To this solution was added a solution of ceric ammonium nitrate (CAN) (1480 mg, 2.69 mmol; 5.0 equiv) in water (8 mL) at 0 ˚C. Reaction mixture was stirred at that temperature for 1 h and then diluted with water (20 mL) and extracted with EtOAc (20 mL X 2). The combined organic phase washed with brine and dried over Na_2SO_4 and concentrated using rotary evaporator under vaccum. The crude products were purified by flash chromatography (20:1 hexanes/EtOAc) to furnish 116 mg (68% yield) of (±)-5-*epi*-taiwaniaquinone G as a red color viscous oil. R_f = 0.5 (5% EtOAc and hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.91 (s, 3H), 3.18 (septet, *J* = 7.1 Hz, 1H), 2.65 (dd, J = 18.0, 8.1 Hz, 1H), 2.34 (dd, *J* = 18.0, 11.5 Hz, 1H), 1.90 (dt, *J* = 13.5, 3.4 Hz, 1H), 1.73 (dd, *J* = 11.5, 8.1 Hz, 1H), 1.61-1.52 (m, 1H), 1.50

(s, 3H), 1.41 (dt, J = 13.9, 3.9 Hz, 1H), 1.29-1.26 (m, 2H), 1.22-1.20 (m, 1H), 1.19 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.10 (s, 3H), 0.91 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 187.3, 182.6, 156.5, 152.4, 146.2, 136.7, 61.1, 54.9, 47.9, 34.9, 34.2, 31.7, 31.1, 31.0, 29.4, 24.5, 24.2, 20.6, 20.5, 17.9; **IR** (film) υ_{max} 2984, 2964, 2919, 2845, 1658, 1651, 1596, 1449, 1262, 1162 cm^{-1}; **HRMS** (ESI) m/z 339.1935 $[(M + nNa)]^+$; calculated for $[C_{20}H_{28}O_3 + nNa]^+$: 339.1931. [Lit. ref.: Tapia, R.; Guardia, J. J.; Alvarez, E.; Haidöur, A.; Ramos, J. M.; Alvarez-Manzaneda, R.; Chahboun, R.; Alvarez-Manzaneda, E. *J. Org. Chem.* **2012**, *77*, 573.]

Synthesis of (4a,9a)-7-Isopropyl-5,6,8-trimethoxy-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1H-fluoren-9(9aH)-one (±)-16: To a stirred solution of 3,5-dimethylpyrazole (1.5 g, 15.55 mmol; 17.93 equiv) in CH_2Cl_2 (5 mL) was added CrO_3 (1555 mg, 15.55 mmol; 17.93 equiv) at -15 ºC. Then the reaction mixture was stirred for 15 min. at same temperature before solution of tricyclic compound ±(**14**) (300 mg, 0.867 mmol; 1.0 equiv) in CH_2Cl_2 (3 mL) was added. This dark mixture was stirred at -10 ºC till the tlc showed complete consumption of starting material (1 h). Then, it was directly purified by flash chromatography (15:1 hexanes/EtOAc) to afford 284 mg (91% yield) of (±)-**16** as a colorless solid. R_f = 0.6 (10% EtOAc in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.87 (s, 3H), 3.86 (s, 3H), 3.82 (s, 3H), 3.47 (septet, *J* = 7.0 Hz, 1H), 2.28-2.23 (m, 1H), 2.01 (s, 1H), 1.86-1.81 (m, 1H), 1.70-1.63 (m, 1H), 1.59-1.50 (m, 1H), 1.36 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 6H), 1.23 (s, 3H), 0.77 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 204.8, 158.6, 152.9, 152.7, 146.2, 134.8, 124.8, 65.6, 62.1, 60.3, 59.9, 41.9, 124.8, 65.6, 62.1, 60.3, 59.9, 41.9, 37.5, 34.2, 32.7, 31.5, 25.3, 24.6, 21.9, 18.1; **IR** (film) υ_{max} 2934, 1743, 1454, 1413, 1340, 1294, 1259, 1187, 1116 cm^{-1}; **HRMS** (ESI) m/z 383.2204 $[(M + Na)]^+$; calculated for $[C_{22}H_{32}O_4 + Na]^+$: 383.2193; **MP** 87-89 ˚C.

Synthesis of (±)-taiwaniaquinol B (1b): To a stirred solution of compound (±)-**16** (270 mg, 0.75 mmol; 1.0 equiv) in dry CH_2Cl_2 (3 mL) was added BBr_3 (180 µL, 1.87 mmol; 2.5 equiv) at −78 ºC. Then the reaction mixture was stirred for 1.5 h at −78 ºC. After complete consumption of starting material (judged by running tlc), the reaction mixture was quenched with water and extracted with ethyl acetate (10 X 2 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*.

The crude product was taken in 20 mL of MeCN:H_2O (3:1) at 0 ºC. To this reaction mixture, a solution of ammonium ceric nitrate (CAN) (2.1 g, 3.75 mmol; 5.0 equiv) in water (8 mL) was added and it was stirred for 20 minutes at 0 ºC. After complete consumption of starting material, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_5$ and kept on stirring for additional 20 min. Upon completion of the reaction (monitored by running tlc), it was diluted by water (5 mL) and extracted with EtOAc (10 X 2 mL) by using a separatory funnel. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The crude was purified by flash chromatography (10:1 hexanes/EtOAc) to afford 130 mg (overall 52% yield in two steps) of (±)-taiwaniaquinol B as crystalline solid. R_f = 0.6 (10% EtOAc in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.54 (s, 1H), 5.31 (brs, 1H), 3.80 (s, 3H), 3.27 (septet, *J* = 7.1 Hz, 1H), 2.12 (s, 1H), 2.08-1.96 (m, 2H), 1.75-1.67 (m, 1H), 1.63-1.55 (m, 1H), 1.44 (s, 3H), 1.42-1.40 (m, 2H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.25 (s, 3H), 0.88 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 211.1, 152.3, 151.1, 142.7, 138.4, 126.1, 118.3, 65.1, 62.1, 42.7, 36.5, 34.3, 33.0, 30.3, 28.8, 25.9, 24.3, 20.6, 17.5; **IR** (film) υ_{max} 2945, 2927, 2850, 1720, 1450, 1426, 1286, 1256, 1187, 1125 cm^{-1}; **HRMS** (ESI) m/z 333.2040 $[(M + H)]^+$; calculated for $[C_{22}H_{28}O_4 + H]^+$: 333.2060; **MP** 143-145 °C. [Lit.: MP 142-144 °C, see ref.: Lin, W. -H.; Fang, J.-M.; Cheng, Y.-S. *Phytochemistry* **1995**, *40*, 871.]

3-isopropyl-1,2,4-trimethoxy-5,6,6-trimethyl-6,7,8,9-tetrahydro-5H-5,9-methanobenzo[7]-annulen-10-one ±(**17**): A oven dried round-bottom flask was charged with compound **13** (104 mg, 0.302 mmol; 1.0 equiv) in CH_2Cl_2 (15 mL) was added *m*-CPBA (115 mg, 0.453 mmol; 1.5 equiv) at 0 °C. Then, solid $NaHCO_3$ (76 mg, 0.908 mmol; 3.0 equiv) was added to reaction mixture at same tempature and reaction mixture was allowed to stir for 1 h. The reaction mixture was treated with aq. saturated solution of Na_2SO_3 (2 mL) and stirred for an additional 10 min. It was poured into a mixture of CH_2Cl_2 (15 mL) and ice water (3 mL) and the mixture was shaken and separated. The organic phase was washed with saturated aq. $NaHCO_3$ solution and dried over Na_2SO_4 and concentrated using rotary evaporator under vacuum.

Crude product (95 mg) was taken in CH_2Cl_2 (8 mL) and $BF_3{\cdot}Et_2O$ (0.205 mL, 0.65 mmol; 2.1 equiv) was added at 0 °C. After 30 min of stirring, water (1 mL) was added to this mixture and stirring continued for additional 15 min. Then saturated aq. solution of $NaHCO_3$ (8 mL) was added to the reaction mixture and it was extracted with CH_2Cl_2 (8 mL). The organic layer was dried over Na_2SO_4 and concentrated using rotary evaporator under vacuum. The crude compound was finally purified by column chromatography (9:1 hexanes/EtOAc) to afford compound **17** in 74% overall yield as colorless viscous oil, R_f = 0.4 (5% EtOAc in hexane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.82 (s, 3H), 3.80 (s, 3H), 3.61 (s, 3H), 3.42-3.37 (m, 1H), 3.25 (s, 1H), 1.97 (dt, *J* = 13.4, 4.4 Hz, 1H), 1.59-1.48 (m, 1H), 1.46 (s, 3H), 1.40-1.36 (m, 1H), 1.33 (d, *J* = 7.2 Hz, 3H), 1.30 (d, *J* = 7.1 Hz, 3H), 1.26-1.23 (m, 1H), 1.17 (s, 3H), 1.15-1.05 (m, 2H), 0.97 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 217.6, 152.1, 151.3, 140.2, 136.4, 134.1, 127.6, 60.5, 60.1, 59.8, 54.5, 42.1, 41.6, 35.7, 30.8, 26.9, 25.8, 22.3, 21.9, 20.4, 20.3; **IR** (film) υ_{max} 2934, 1743, 1454, 1413, 1340, 1294, 1259, 1187, 1116 cm^{-1}. [Lit. ref.: Alvarez-Manzaneda, E.; Chahboun, R.; Cabrera, E.; Alvarez, E.; Haidöur, A.;

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Synthesis of 3-isopropyl-1,2,4-trimethoxy-5,6,6-trimethyl-6,7,8,9-tetrahydro-5H-spiro[5,9-methanobenzo[7]annulene-10,2'-oxirane] ±(18): NaH (60% in mineral oil) (28 mg, 0.706 mmol; 1.2 equiv) was taken in dimethylsulfoxide (2 mL) at room temperature. To this solution was added trimethylsulphonium Iodide (144 mg, 0.706 mmol; 1.2 equiv) and stirred for 30 min. A solution of compound **17** (212 mg, 0.588 mmol; 1.0 equiv) in THF (1 mL) was added to this reaction mixture and stirring continued for overnight. The reaction mixture was diluted with EtOAc (10 mL) and water (10 mL) at room temperature and the layers were separated. The combined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was evaporated in rotatory evaporator under reduced pressure to furnish compound **18** in 98% yield as colorless solid, R_f = 0.5 (5% EtOAc in hexane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.83 (s, 3H), 3.78 (s, 3H), 3.64 (s, 3H), 3.46-3.37 (m, 1H), 2.91 (d, *J* = 5.3 Hz, 1H), 2.83 (s, 1H), 2.54 (d, *J* = 5.3 Hz, 1H), 1.87-1.80 (m, 2H), 1.71-1.64 (m, 1H), 1.43-1.37 (m, 1H), 1.34 (d, J = 7.1 Hz, 3H), 1.31 (d, J = 7.1 Hz, 3H), 1.28-1.23 (m, 1H), 1.20 (s, 3H), 1.10 (s, 3H), 1.06-0.96 (m, 1H), 0.88 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 151.9, 151.1, 146.2, 137.9, 133.4, 130.4, 70.0, 60.4, ,60.2, 60.0, 53.0, 52.9, 47.1, 42.4, 40.9, 37.7, 33.0, 27.2, 25.8, 22.4, 22.0, 21.8, 20.7; **IR** (film) υ_{max} 2928, 2916, 2837, 1448, 1450, 1408, 1338, 1257, 1114 cm^{-1}; **HRMS** (ESI) m/z 397.2360 $[(M + Na)]^+$; calculated for $[C_{23}H_{34}O_4+ Na]^+$: 397.2349.

ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H, and ^{13}C NMR spectra for all new compounds and CIF files of (±)-**1a**, (±)-**12**, and (±)-**18**. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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