Connecting C_{19} Norditerpenoids to C_{20} Diterpenes: Total Syntheses of 6-Hydroxy-5,6-dehydrosugiol, 6-Hydroxysugiol, and Taiwaniaquinone H, and Formal Synthesis of Dichroanone

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Dedicated to Professor Dr. Rolf Huisgen on the occasion of his 90th birthday

Abstract: Oxidation of the B-ring of abietane derivatives by Sharpless dihydroxylation gave the natural products 6-hydroxy-5,6-dehydrosugiol and 6-hydroxysugiol. Moreover, further oxidation gave a hydroxy dione derivative that provides a synthetic entry into the C_{19} taiwaniaquinoid family of natural products. This route is based on biosynthetic considerations and involves a benzilic acid rearrangement followed by decarboxylation. On the basis of this approach, a total synthesis of (–)-taiwaniaquinone H and a formal synthesis of (–)-dichroanone have been achieved.

Key words: terpenoids, biomimetic synthesis, biosynthesis, oxidations, stereoselective synthesis, total synthesis

Synthetic routes that are based on biosynthetic considerations (biomimetic syntheses) have been shown to provide access to natural products with great efficiency and elegance.[1] In addition, these approaches can give rise to compounds that have not been isolated from nature. Therefore, a truly biomimetic synthesis can provide a general method for the preparation of both discovered and undiscovered natural products along a (postulated) biosynthetic pathway. This principle has been recognized by Skyler and Heathcock,[2] and was demonstrated in their general method for the preparation of pyridoacridine alkaloids.[2]

This interconnectivity of natural products by (bio)synthetic pathways can also provide a relationship between structurally different compounds, provided that truly biomimetic sequences are followed. Here, we expand on the hypothesis[3] that the C_{19} taiwaniaquinoid family of natural products[4,5]can be obtained by oxidative ring contraction from C_{20} abietane derivatives. In addition, we present a general synthetic route to both C_{19} norditerpenoids, such as dichroanone (**1**)[4b,5e] and taiwaniaquinone H (**2**),[4f,5n,k] and C_{20} oxidized diterpenes, such as 6-hydroxy-5,6-dehydrosugiol (**3**; HDHS)[6] and 6-hydoxysugiol (**4**).[6] The route is based on biosynthetic considerations, and it resulted in the first enantioselective synthesis of metabolites **3** and **4**, which have potential as anticancer agents.

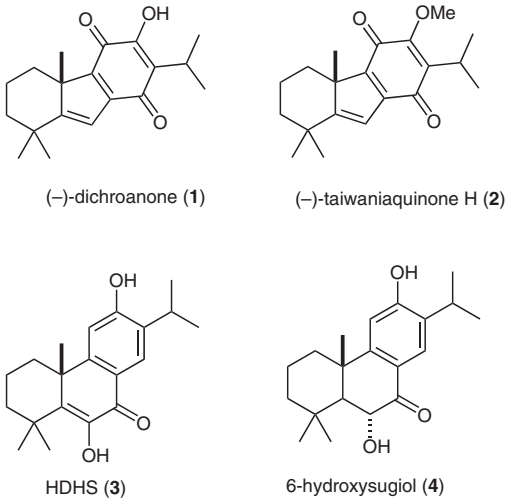

Figure 1 C_{19} norditerpenoids (**1** and **2**) and C_{20} oxidized diterpenes (**3** and **4**)

The synthesis began with the oxidation of the B ring of two C_{20} diterpenes derived from abietane and ferruginol, respectively. A two-step protocol was adopted for the oxidation of the B-ring. In the first oxidation step, 6,7-dehydroabietatrienes **5** and **6** were synthesized from abietic acid following known procedures.[7] In the second oxidation step, olefins **5** and **6** were treated with AD-mix-β and potassium osmate ($K_2OsO_4 \cdot 2H_2O$) at room temperature for 72 hours under Sharpless asymmetric dihydroxylation conditions.[8] However, the expected diols were not obtained, but instead the respective hydroxy diketones **7** and **8** were isolated as the major products in very good yields (90 and 91%, respectively) and excellent diastereoselectivities (Scheme 1). The relative configuration was confirmed by X-ray analysis.[3]

Thin-layer chromatography showed that the initial mixture of products formed after 24 hours converged to a major product after 72 hours. Moreover, a spot-to-spot conversion of the intermediate **9**[6b] (isolated from the initial mixture) into **8** was observed when **9** was treated under the same dihydroxylation conditions (Scheme 2). On the basis of these observations, a possible mechanistic path for this interesting transformation to achieve oxygen functionalization on three contiguous C atoms in the B

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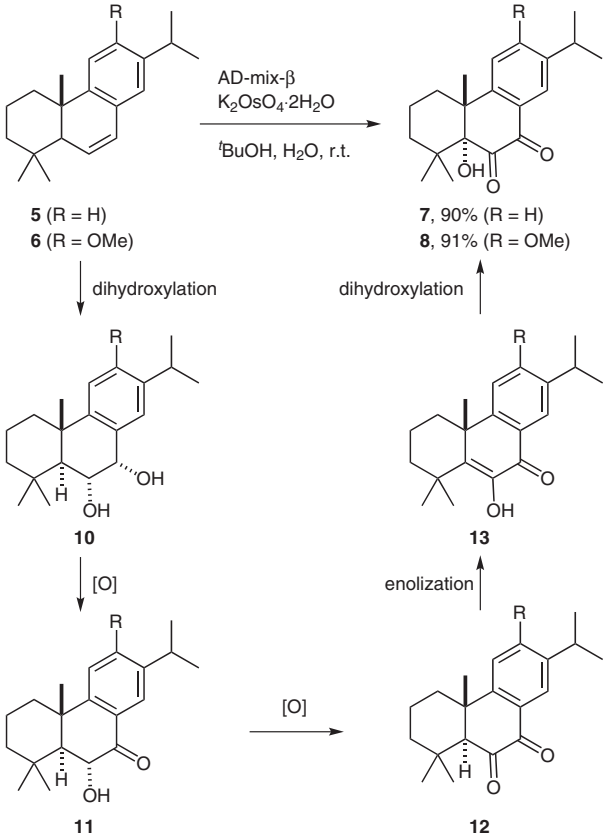
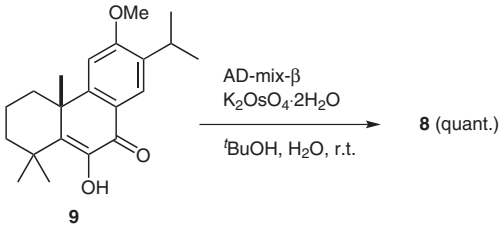


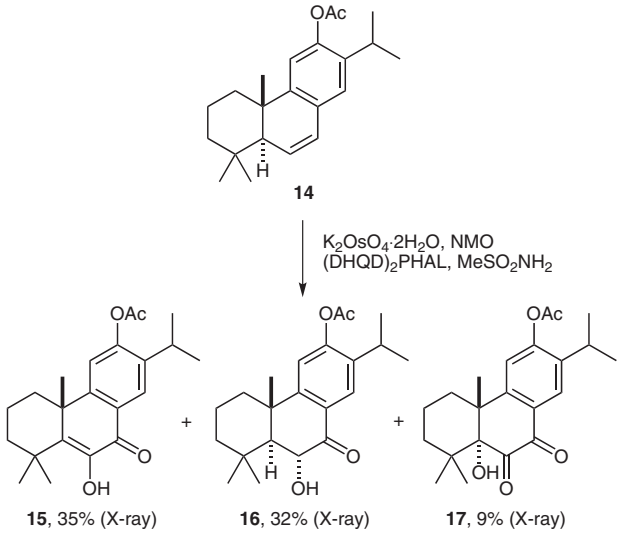
Scheme 1 B-ring oxidation of abietane derivatives

ring can be proposed. In the first step of this transformation, the olefin is diastereoselectively dihydroxylated to form the diol **10**. The facial selectivity of the dihydroxylation probably arises from the presence of the angular methyl group. The benzylic hydroxy group of **10** should then readily oxidize to give the corresponding hydroxy ketone **11** under the oxidative reaction conditions. However, an alternative mechanism for the formation of the hydroxy ketone **11** might also be possible.[9] Further oxidation could produce the diketone **12,** which can then enolize to **13** under basic conditions. A highly diastereoselective second dihydroxylation of enol **13** could then result in the hydroxy diketones **7** and **8**.



Scheme 2 Dihydroxylation of hydroxy ketone **9**

Interestingly, when the olefin **14**[10] was treated under various hydroxylation conditions {potassium osmate dihydroxide ($K_2OsO_4·2H_2O$), hydroquinidine 1,4-phthalazinediyl diether [$(DHQD)_2PHAL$], *N*-methylmorpholine *N*-oxide (NMO), and methanesulfonamide ($MeSO_2NH_2$)}, mixtures of products **15**, **16**, and **17** were isolated after 48 hours at room temperature (Scheme 3). The product distribution changed with the number of equivalents of the reagents that were used and the time of the reaction.



Scheme 3 Dihydroxylation of olefin **14**

The structures and the relative configurations of **15**, **16**, and **17** were confirmed by X-ray crystallography (Figure 2).

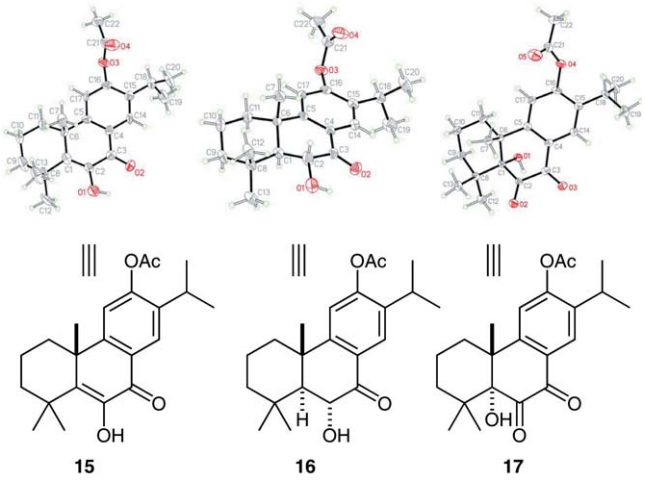
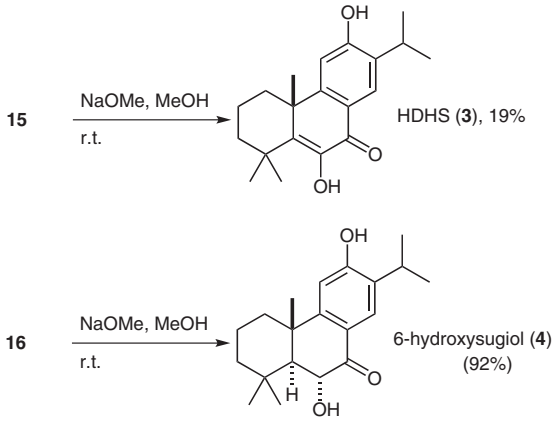


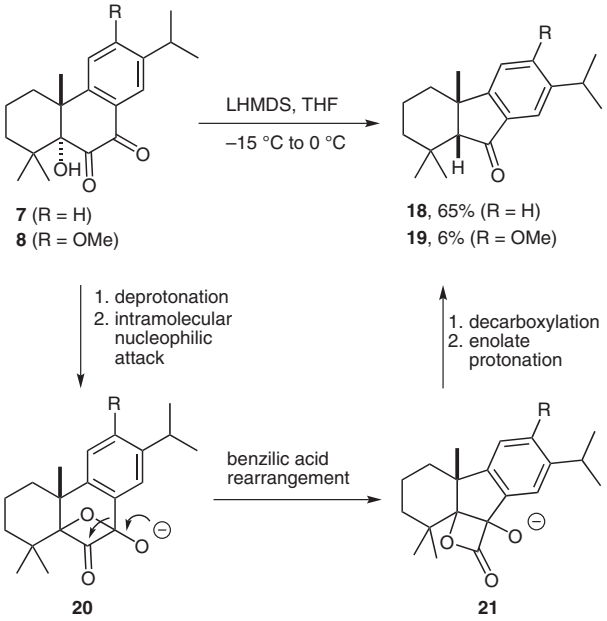
Figure 2 Crystal structures of **15**, **16**, and **17**

Removal of the protecting acetyl group from **15** and **16** gave the biologically relevant natural products HDHS (**3**) and 6-hydroxysugiol (**4**). Deacetylation of **15** was achieved through the standard transesterification procedure using sodium methoxide in methanol to provide the natural compound HDHS in 19% yield. By following a similar deacetylation protocol, 6-hydroxysugiol **4** was obtained from the acetate **16** in 92% yield (Scheme 4).



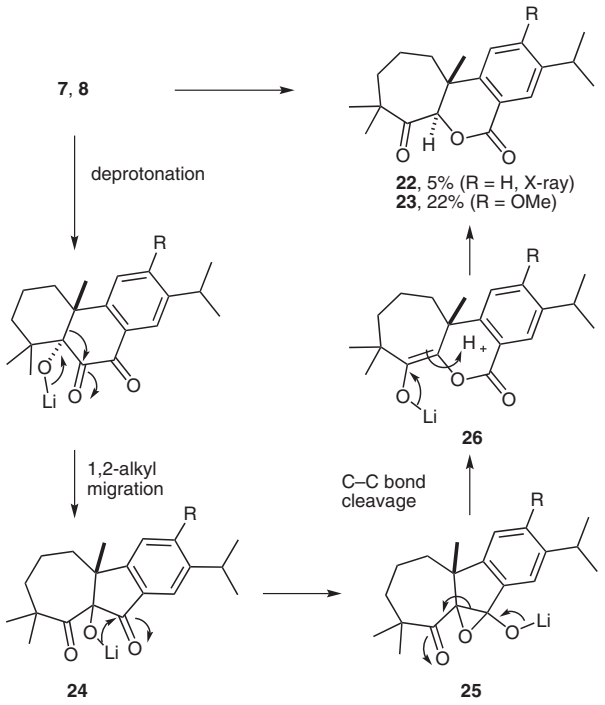
Scheme 4 Completion of the syntheses of HDHS (**3**) and 6-hydroxysugiol (**4**)

We speculated that the α-diketone functionality of the α-hydroxy diketone **7** or **8** could be utilized for contraction of the B-ring through a benzilic acid rearrangement to transform the abietane 6–6–6 skeleton into the 6–5–6 skeleton of a taiwaniaquinoid.[3] This proposal, which is based on biosynthetic considerations,[3] is supported by several reports on the biosynthesis of gibberellins.[11] However, reactions of the hydroxy diketone **8** reactions under a range of reaction conditions with a variety of bases were unsuccessful in producing the corresponding ring-contracted products in isolable yields. Surprisingly, however, the hydrofluorenone **18** was obtained in good yield (65%) from the hydroxy diketone **7** by treatment with lithium hexamethyldisilazide (LHMDS) under optimized conditions (Scheme 5). This ring contraction and loss of a ring carbon atom can be explained if we assume that the reaction proceeds by the sequence outlined in Scheme 5. An external base, such as LHMDS, removes the most acidic proton in **7** to form corresponding tertiary alkoxide, which then reacts intramolecularly with the benzylic carbonyl group to give the 3-oxetanone **20**.[12] The 3-oxetanone is converted into the β-lactone **21** through a ring-contractive process involving a benzilic acid-type rearrangement. Subsequent decarboxylation of β-lactone **21** causes it to collapse to the corresponding enolate, which is then diastereoselectively protonated during workup with saturated aqueous ammonium chloride to give the hydrofluorenone **18**. In support of this mechanism, a poor yield of fluorenone **19** was obtained when the electron-rich hydroxy diketone **8** was treated under the same conditions. This can be explained by the lower nucleophilicity of the benzylic keto group, which may disfavor the formation of the corresponding 3-oxetanone in comparison with other side reactions. The low tendency of **8** to undergo ring contraction provides support for a mechanism for ring contraction via a 3-oxetanone. Several other inorganic and organic bases, such as sodium hydride, calcium oxide, potassium hexamethyldilazide (KHMDS), or potassium hydroxide can be used as the external base to induce the ring contraction; however, amine bases, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) cannot be used. The Lewis acid titanium tetraisopropoxide [$Ti(OiPr)_4$] was also unable to initiate the ring contraction. Moreover, the product distribution for this reaction changed significantly depending on the nature of the base that was used, the temperature, and the time.



Scheme 5 Biomimetic ring-contraction reactions of hydroxy diketones **7** and **8**

In addition to the major product **18**, the minor product **22** was isolated (5%) and subsequently characterized by X-ray analysis (Figure 3), which showed it is a ring-expanded derivative (Scheme 6). The similar phenolic-ring-expanded derivative **23** was formed as the major product from the phenolic hydroxy diketone **8** on treatment with LHMDS or other bases. These compounds are formed through deprotonation of the tertiary alcohol moiety in **7** and **8** followed by ring expansion through (1,2)-alkyl migration to give the corresponding β-diketo alkoxide **24**. Many precedents for this transformation have been reported in the literature, and similar α-ketol rearrangements have been frequently used in organic synthesis.[13] The diketo alkoxide **24** reacts to form the oxirane **25**, which can be considered as the epoxide of a keto enolate. C–C bond fragmentation of oxirane **25** gives the corresponding enolate **26**. Diastereoselective protonation of enolate **26** finally gives the ring-expanded compounds **22** and **23**. A diketo alkoxide-to-keto lactone rearrangement was described by Karrer and co-workers in the context of epoxidized β-diketones,[14a] but subsequently this reaction has rarely been used in organic synthesis.[14] We believe that the presence of nonenolizable positions may favor this transformation. The rearrangements of **7** to **22** and of **8** to **23** represent interesting examples of a surprising skeletal transformation.



Scheme 6 Proposed mechanism for the formation of expanded derivatives **22** and **23**

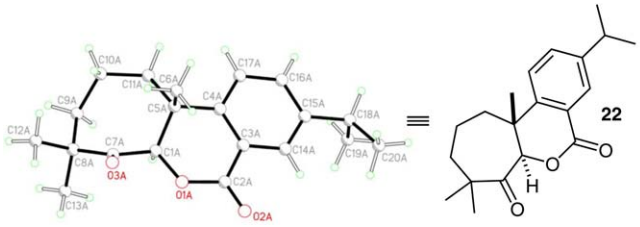
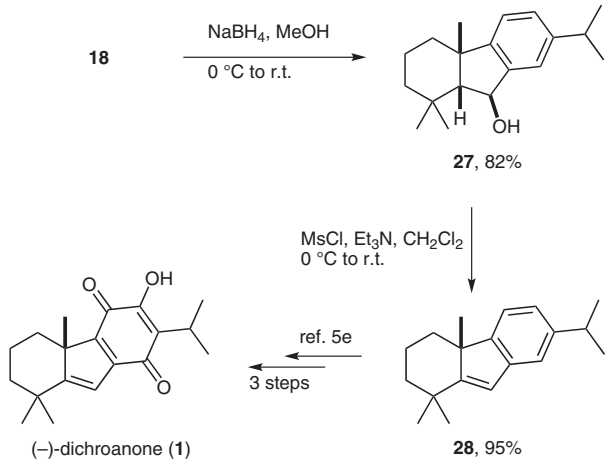


Figure 3 Crystal structure of **22**

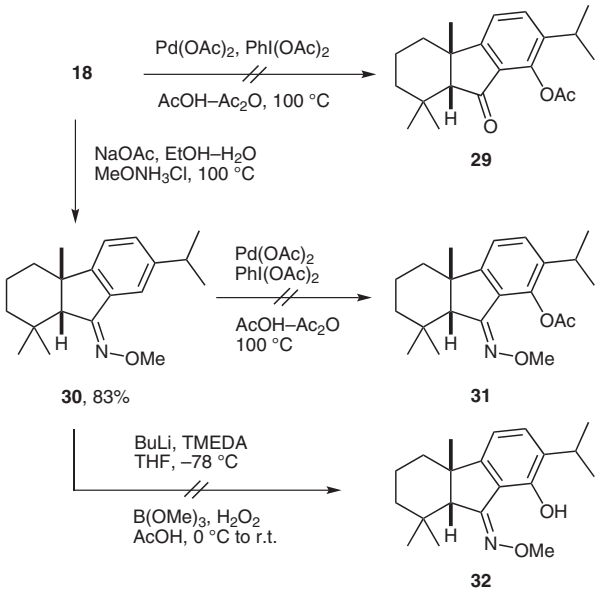
The diastereoselective reduction of hydroxy diketone **18** by sodium borohydride proceeded smoothly to give the benzylic alcohol **27** in 82% yield (Scheme 7). The relative configuration of **27** was identified from the molecular structure determined by single-crystal X-ray diffraction analysis.[3] To complete the formal synthesis of dichroanone (**1**), we then transformed the benzylic alcohol **27** into the olefin **28** by dehydration through treatment with mesyl chloride and triethylamine. The fluorene **28** was obtained in excellent yield (95%), and the spectroscopic data matched those of its enantiomer, as reported by Stoltz and McFadden in their dichroanone synthesis,[5e] except for the optical rotation{$([\alpha]_D^{23}$ +83 (*c* 0.29, $CHCl_3$); Lit.[5e] $[\alpha]_D^{24}$ –80.74 (*c* 0.320, $CHCl_3$)}. Dehydration of **27** also occurred in the presence of dilute hydrochloric acid in chloroform to provide **28**. As fluorene **28** can be transformed in three steps into the natural (–)-dichroanone,[5e] this constitutes a formal synthesis of this natural product.

After we had constructed the required carbon skeleton for C_{19} taiwaniaquinoids through a biomimetic ring contraction, our attention was drawn to finding a suitable and elegant protocol for the oxidation of the aromatic C ring in each of the tricyclic compounds **18**, **27**, and **28**. Modern palladium-mediated aromatic oxidation protocols were explored first. With the intention of making use of the benzylic keto group of **18** as a directing group for the aromatic palladation, we treated fluorenone **18** with palladium(II) acetate and diacetyl(phenyl)-λ^3-iodane [$PhI(OAc)_2$] in the presence of acetic acid and acetic anhydride, following the protocol developed by Sanford and co-workers[15] (Scheme 8). Unfortunately, no desired product **29** was obtained, and the starting material was isolated. Because it is known that *O*-methyl oximes are better directing group for aromatic *ortho*-metalation,[15,16] ketone **18** was treated with *O*-methylhydroxylamine in refluxing aqueous ethanol to give corresponding *O*-methyl oxime **30** in 83% yield. Treatment of oxime **30** under various oxidation conditions failed to provide the oxidized product **31**, so a one-pot lithiation–boration–oxidation sequence, widely used for aromatic oxidation,[17] was attempted. Various butyllithium-mediated conditions for *ortho*-lithiation were applied, but in all cases the desired lithiation to provide the phenol derivative **32** failed to occur.

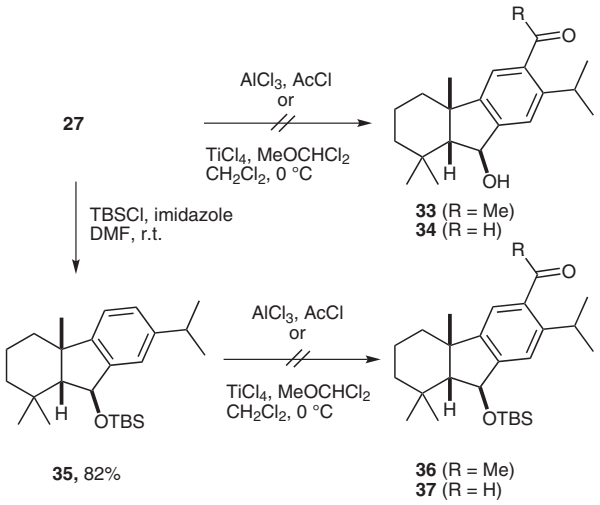


Scheme 7 Formal synthesis of (–)-dichroanone

We then decided to use alcohol **27** as a substrate for the aromatic oxidation. Both the classical Friedel–Crafts acylation (aluminum chloride, acetyl chloride)[18] and titanium tetrachloride-mediated formylation[19] reactions failed to produce the corresponding products **33** and **34** (Scheme 9). Mixtures of acylated or formylated products in which the hydroxy group was removed through dehydration were formed instead. To prevent this dehydration, we protected the hydroxy group as its *tert*-butydimethylsilyl (TBS) ether by silylation with *tert*-butyldimethylsilyl chloride in the presence of imidazole to provide **35** in very good yield (82%). Surprisingly, the expected products **36** and **37** were not obtained, and only deoxygenated products with acyl or formyl groups in the aromatic ring were formed when the TBS-ether **35** was treated under the acylation and formylation conditions described above.

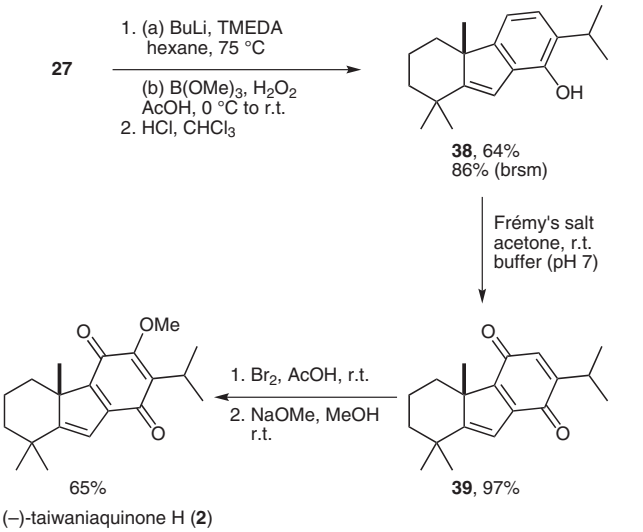


Scheme 8 Attempted functionalization of the C ring



Scheme 9 Failed attempts to functionalize **27** and **35**

Finally, the method for *ortho*-lithiation directed by the benzylic hydroxy group, as developed by Seebach and Meyer,[20] was successful in achieving aryl lithiation of compound **27**. When the benzylic alcohol **27** was treated with excess butyllithium in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine in refluxing hexane, the corresponding aryl lithium species was obtained (Scheme 10). The aryl lithium compound was then treated with trimethyl borate, and the resulting aryl borate was oxidized with hydrogen peroxide. The resulting phenol derivative was readily dehydrated under acidic conditions to provide **38** in 64% yield from **27** (86% based on recovered starting material). The phenol derivative **38** was cleanly oxidized by Frémy's salt to give the corresponding *para*-quinone **39** (97%). Electrophilic bromination of quinone **39** gave the corresponding vinylogous acid bromide, which was



Scheme 10 Completion of a total synthesis of (–)-taiwaniaquinones H

then reacted with sodium methoxide to provide (–)-taiwaniaquinone H (**2**) in 64% yield over the two steps.

In summary, we have reported surprising sequential oxidations of C_{20} abietane derivatives under Sharpless conditions: The hydroxy ketone **16** was converted into 6-hydroxysugiol (**4**), the enol ketone **15** was converted into HDHS (**3**), and the hydroxy ketone **17** possessed the correct oxidation pattern to provide access to C_{19} taiqaniaquinoids. On the basis of biosynthetic considerations, we demonstrated that such hydroxy ketones as **7** and **8** could be transformed by ring contraction into C_{19} derivatives with loss of a C atom. This synthetic route provides a connection between the C_{19} family of taiqaniaquinoids and C_{20} abietane diterpenes through a mechanistically interesting transformation. We postulate that a benzilic acid rearrangement could be involved in this contractive process, which was used in a total synthesis of (–)-taiwaniaquinone H (**2**) and a formal synthesis of dichroanone (**1**).

Unless otherwise stated, chemicals were purchased from Sigma-Aldrich, ABCR, Acros, or Lancaster, and weree used without further purification. Solvents for workup and chromatography were distilled from technical-quality materials. Solvents used for chemical transformations were either puriss quality or dried by filtration through activated alumina under argon or N_2 (H_2O content < 10 ppm by Karl Fischer titration). Reactions involving air- or moisture-sensitive reagents or intermediates were performed under argon or N_2 in glassware that had been dried by an oven or heat gun under a high vacuum. Concentrations under reduced pressure were performed by rotary evaporation at 40 °C, unless otherwise specified. Yields refer to dry spectroscopically pure compounds. Analytical TLC was performed on Merck silica gel 60 F254 plates (0.25 mm thick) precoated with a fluorescent indicator. The developed plates were examined under UV light after staining with ceric ammonium molybdate and heating. Flash chromatography was performed on silica gel 60 (Fluka 230–240 mesh) with forced-flow elution at 0.3–0.5 bar pressure. All ^1H and ^{13}C NMR spectra were recorded by using Bruker DPX 400 MHz (^1H) and 101 MHz (^{13}C) spectrometers at r.t. Chemical shifts (δ values) are reported in ppm relative to the solvent residual proton chemical shift ($CHCl_3$, δ = 7.26) or the sol-

vent residual carbon chemical shift ($CDCl_3$, δ = 77.16). IR spectra were recorded using a Varian 800 FT-IR ATR Spectrometer. Optical rotations were measured at the sodium D line using a 1-mL cell with a 1-dm path length on a Jasco P-2000 digital polarimeter, and the concentration *c* is given in g/100 mL. All mass spectra were recorded by the Mass Spectrometric Service of EPF Lausanne on a Micromass (ESI) Q-TOF Ultima API instrument. X-ray analyses were performed by Dr. R. Scopelliti at EPF Lausanne: data for both crystal structures were collected at a low temperature (140 K) using Mo K_α radiation on an Oxford Diffraction Sapphire/KM4 CCD kappa-geometry goniometer. Data were reduced by means of Crysalis PRO[21a] and then corrected for absorption.[21b] Solutions and refinements were performed by using SHELX.[21c] The structures were refined by full-matrix least-squares on F^2 with all nonhydrogen atoms anisotropically defined. Hydrogen atoms were placed in their calculated positions by means of the 'riding' model. Crystallographic data for compounds **15**–**17** and **22** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 776873, 776874, 776875, and 770126, respectively; copies can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or email: deposit@ccdc.cam.ac.uk].

(4a*R*,10a*R*)-10a-Hydroxy-7-isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,10a-hexahydrophenanthrene-9,10-dione (7)

AD-mix (β) (3.0 g) and $K_2OsO_4{\cdot}2H_2O$ (10 mg, 27 μmol) were added to a soln of olefin **5** (0.24 g, 0.89 mmol) in *t*-BuOH (4 mL) and H_2O (4 mL) at r.t., and the mixture was stirred for 3 days. Solid Na_2SO_3 (0.5 g) was added and the mixture was stirred for 1 h to quench the reaction. The mixture was then diluted with H_2O and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (5:1)] to give a yellow solid; yield: 0.25 g (0.81 mmol, 90%); mp: 160.7–161.5 °C; R_f = 0.2 (pentane–Et_2O, 5:1); $[\alpha]_D^{23}$ +334.1 (*c* 0.56, $CHCl_3$).

FT-IR (neat): 3487, 2959, 2932, 2874, 1740, 1686, 1609, 1462, 1385, 1300, 1246, 1045, 949, 910, 841, 733 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 2.0 Hz, 1 H), 7.50 (dd, *J* = 8.2, 2.1 Hz, 1 H), 7.33 (d, *J* = 8.2 Hz, 1 H), 2.95 (sept, *J* = 6.9 Hz, 1 H), 2.24 (s, 1 H), 2.21–2.07 (m, 3 H), 1.95–1.82 (m, 1 H), 1.75–1.68 (m, 2 H), 1.50 (s, 3 H), 1.37 (s, 3 H), 1.27 (s, 3 H), 1.25 (s, 3 H), 1.13 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.4, 185.8, 150.6, 148.1, 134.5, 131.3, 126.2, 125.0, 83.2, 46.3, 37.0, 37.0, 33.7, 31.8, 29.3, 27.8, 23.8, 23.7, 18.3.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{20}H_{27}O_3$: 315.1960; found: 315.1949.

(4a*R*,10a*R*)-10a-Hydroxy-7-isopropyl-6-methoxy-1,1,4a-trimethyl-1,2,3,4,4a,10a-hexahydrophenanthrene-9,10-dione (8)

AD-mix (β) (0.30g) and $K_2OsO_4{\cdot}2\ H_2O$ (2.0 mg, 5.4 μmol) were added to a soln of olefin **6** (24 mg, 0.08 mmol) in *t*-BuOH (0.40 mL) and H_2O (0.40 mL) at r.t., and the mixture was stirred for 3 days. Solid Na_2SO_3 (0.1 g) was added and the mixture was stirred for 1 h to quench the reaction. The mixture was then diluted with H_2O and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (5:1)] to give a yellow solid; yield: 25 mg (0.07 mmol, 91%): R_f = 0.2 (pentane–Et_2O, 5:1); $[\alpha]_D^{23}$ +181.9 (*c* 0.48, $CHCl_3$).

FT-IR (neat): 3462, 2920, 2880, 1733, 1665, 1589, 1497, 1461, 1275, 1252, 1040, 955, 843 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 6.78 (s, 1 H), 3.93 (s, 3 H), 3.25 (sept, *J* = 7.2 Hz, 1 H), 2.21 (s, 1 H), 2.18–2.14 (m, 2 H), 1.97–1.84 (m, 1 H), 1.78–1.71 (m, 2 H), 1.50 (s, 3 H), 1.39 (s, 3 H), 1.28–1.24 (m, 1 H), 1.23 (s, 3 H), 1.21 (s, 3 H), 1.15 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.0, 183.5, 163.4, 153.8, 136.9, 127.2, 124.6, 105.7, 83.2, 55.7, 46.6, 37.1, 37.0, 31.8, 29.2, 27.8, 26.8, 23.7, 22.5, 22.4, 18.3.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{21}H_{29}O_4$: 345.2066; found: 345.2061.

(4a*R*)-6-(Acetyloxy)-10-hydroxy-7-isopropyl-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-9(1*H*)-phenanthrenone (15), (4a*S*,10*R*,10a*S*)-6-(Acetyloxy)-10-hydroxy-7-isopropyl-1,1,4a-trimethyl-2,3,4,4a,10,10a-hexahydro-9(1*H*)-phenanthrenone (16), and (4a*S*,10a*S*)-6-(Acetyloxy)-7-isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,10a-hexahydro-9,10-phenanthrenedione (17)

NMO (19 mg, 0.14 mmol), $(DHQD)_2PHAL$ (2.0 mg, 2.5 μmol), $MeSO_2NH_2$ (7.0 mg, 73 μmol), and $K_2OsO_4{\cdot}2H_2O$ (2.5 mg, 6.7 μmol) were added successively to a soln of olefin **14** (23 mg, 70 μmol) in 3:1 acetone–H_2O (1.2 mL), and the mixture was stirred for 24 h at r.t. A portion of $K_2OsO_4{\cdot}2H_2O$ (2.5 mg) was added and the mixture was stirred for another 24 h. Solid Na_2SO_3 (200 mg) was then added, and the mixture was stirred for 15 min to quench the reaction. The mixture was diluted with brine (5 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated under vacuum. TLC of the crude mixture showed several products, including residual starting material. The residue was purified by flash column chromatography [pentane–Et_2O (gradient 20:1 to 10:1 to 5:1)] to give **15**, **16**, and **17**. The product composition and yields varied with the ratio of reagents used and the reaction times.

15

Colorless foam; yield: 8.5 mg (24 μmol, 35%); R_f = 0.8 (pentane–Et_2O, 2:1).

FT-IR (neat): 3373, 2963, 1764, 1640, 1607, 1369, 1197, 1168, 1045 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.17 (s, 1 H), 7.07 (s, 1 H), 3.03 (h, *J* = 7.2 Hz, 1 H), 2.36 (s, 3 H), 2.36–2.27 (m, 1 H), 1.98–1.68 (m, 5 H), 1.53 (s, 3 H), 1.43 (s, 6 H), 1.26 (d, *J* = 6.8 Hz, 3 H), 1.23 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 179.9, 169.3, 153.6, 152.2, 144.1, 142.6, 139.3, 125.7, 125.5, 119.6, 40.6, 37.9, 36.2, 35.3, 33.5, 28.3, 27.6, 27.5, 23.04, 22.9, 21.2, 17.6.

16

Colorless foam; yield: 8 mg (22 μmol, 32%) R_f = 0.7 (pentane–Et_2O, 2:1); $[\alpha]_D^{23}$ +16 (*c* 0.15, $CHCl_3$).

FT-IR (neat): 3474, 2932, 1767, 1679, 1611, 1370, 1195, 1111, 1044 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1 H), 7.02 (s, 1 H), 4.68 (dd, *J* = 12.8, 2.0 Hz, 1 H), 3.80 (d, *J* = 2.0 Hz, 1 H), 2.99 (h, *J* = 7.2 Hz, 1 H), 2.35 (s, 3 H), 2.22–2.20 (m, 1 H), 1.88 (d, *J* = 12.8 Hz, 1 H), 1.75 (tt, *J* = 13.6, 3.2 Hz, 1 H), 1.67–1.60 (m, 1 H), 1.53–1.48 (m, 2 H), 1.39 (s, 3 H), 1.33–1.29 (m, 1 H), 1.23 (s, 3 H), 1.231 (d, *J* = 6.8 Hz, 3 H), 1.22 (d, *J* = 6.8 Hz, 3 H), 1.20 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.4, 169.2, 155.4, 153.5, 139.2, 127.1, 126.4, 118.4, 74.3, 55.9, 43.0, 39.5, 38.9, 35.9, 34.3, 27.5, 24.9, 22.9, 22.8, 21.9, 21.1, 18.9.

17

Light-yellow foam; yield: 2 mg (6 μmol, 9%); R_f = 0.2 (pentane–Et_2O, 2:1); $[\alpha]_D^{23}$ +98.2 (*c* 0.18, $CHCl_3$).

FT-IR (neat): 3488, 2934, 1742, 1690, 1610, 1265, 1197, 1170, 1032, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1 H), 7.05 (s, 1 H), 3.03 (h, *J* = 6.8 Hz, 1 H), 2.36 (s, 3 H), 2.23 (s, 1 H), 2.12–2.08 (m, 2 H), 1.94–1.81 (m, 1 H), 1.74–1.67 (m, 2 H), 1.50 (s, 3 H), 1.40 (s, 3 H), 1.30–1.27 (m, 1 H), 1.24 (d, *J* = 6.8 Hz, 3 H), 1.238 (d, *J* = 6.8 Hz, 3 H), 1.13 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 193.2, 184.8, 169.0, 154.2, 152.2, 139.9, 129.4, 127.7, 119.3, 83.2, 46.3, 37.0, 36.9, 31.7, 29.2, 27.8, 27.5, 23.7, 22.9, 22.8, 21.2, 18.2.

6-Hydroxy-5,6-dehydrosugiol (3)

A soln of NaOMe (0.22 mL, 0.11 mmol) in MeOH was added to a soln of acetate **15** (18 mg, 51 μmol) in 2:1 MeOH–THF (4.5 mL) at r.t., and the mixture was stirred for 30 min. The solvents were removed in vacuo, and the residue was diluted with 1 M aq HCl (6 mL). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vaccum. The residue was purified by flash column chromatography [pentane–Et_2O (2:1)] to give a colorless oil; yield: 3.0 mg (9 μmol, 19%); R_f = 0.7 (pentane–Et_2O, 2:1). The ^{1}H NMR spectrum matched that reported in the literature.[6a]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (s, 1 H), 7.15 (s, 1 H), 6.84 (s, 1 H), 5.24 (s, 1 H), 3.17 (h, *J* = 6.8 Hz, 1 H), 2.33–2.27 (m, 1 H), 1.97–1.87 (m, 2 H), 1.81–1.70 (m, 2 H), 1.51 (s, 3 H), 1.43 (s, 3 H), 1.43 (s, 3 H), 1.31 (d, *J* = 6.8 Hz, 3 H), 1.28 (d, *J* = 6.8 Hz, 3 H), 1.25–1.23 (m, 1 H).

In addition to HDHS, 5-epixanthoperol[6a] [yield: 11 mg (35 μmol, 69%)] was isolated as a yellow foam that enolized to HDHS on standing in DMSO-d_6 for 10 h at r.t.

6-Hydroxysugiol (4)

A soln of NaOMe in MeOH (0.10 mL, 0.05 mmol) was added to a soln of acetate **16** (11 mg, 30 μmol) in 2:1 MeOH–THF (2.5 mL), and the mixture was stirred at r.t. for 30 min. The solvents were removed in vacuo, and the residue was acidified with 1 M aq HCl (3 mL). The mixture was extracted with Et_2O (3 × 10 mL), washed (brine), and dried ($MgSO_4$). The residue was purified by flash column chromatography [pentane–Et_2O (1:5)] to give a colorless foam; yield: 9.0 mg (28 μmol, 92%): R_f = 0.3 (pentane–Et_2O, 5:1); $[\alpha]_D^{23}$ +31.8 (*c* 0.42, $CHCl_3$) {Lit.[6a] $[\alpha]_D^{25}$ = +35.3 (*c* 0.5, $CHCl_3$)}. The ^{13}C NMR spectrum matched that reported in the literature.[6a]

FT-IR (neat): 3360, 2961, 2931, 2871, 1651, 1597, 1575, 1300, 1265, 1114, 757 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (s, 1 H), 6.70 (s, 1 H), 5.81 (s, 1 H), 4.63 (dd, *J* = 12.7, 2.0 Hz, 1 H), 3.94 (d, *J* = 2.0 Hz, 1 H), 3.15 (h, *J* = 6.5 Hz, 1 H), 2.18–2.16 (m, 1 H), 1.83 (d, *J* = 13 Hz, 1 H), 1.80–1.71 (m, 1 H), 1.64–1.59 (m, 1 H), 1.51–1.46 (m, 2 H), 1.35 (s, 3 H), 1.31–1.24 (m, 1 H), 1.26 (d, *J* = 7.0 Hz, 3 H), 1.25 (d, *J* = 7.0 Hz, 3 H), 1.22 (s, 3 H), 1.20 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 200.0, 159.2, 156.7, 133.6, 127.3, 121.8, 110.3, 74.0, 56.0, 43.0, 39.3, 38.9, 35.9, 34.3, 26.9, 24.8, 22.5, 22.4, 22.0, 19.0.

(4a*S*,9a*R*)-7-Isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,9a-hexahydro-9*H*-fluoren-9-one (18) and (6a*R*,11a*R*)-3-Isopropyl-8,8,11a-trimethyl-6a,8,9,10,11,11a-hexahydrocyclohepta[*c*]isochromene-5,7-dione (22)

LHMDS (0.19 mL, 0.19 mmol) was added dropwise to a soln of hydroxy diketone **7** (50 mg, 0.16 mmol) in THF (12 mL) at –15 °C, and the mixture was stirred for 15 min. The mixture was then warmed to 0 °C and stirred for 12 h. The reaction was quenched with sat. aq NH_4Cl, and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (20:1)] to give **18** and **22**.

18

Colorless oil; yield: 28 mg (0.10 mmol, 65%); R_f = 0.7 (pentane–Et_2O, 10:1); $[\alpha]_D^{25}$ –60.4 (*c* 0.47, $CHCl_3$).

FT-IR (neat): 2955, 2928, 2866, 2361, 1705, 1616, 1485, 1462, 1385, 1261, 1184, 833 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (m, 1 H), 7.44 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.33 (d, *J* = 8.0 Hz, 1 H), 2.96 (sept, *J* = 6.8 Hz, 1 H), 2.18 (s, 1 H), 2.08–2.01 (m, 1 H), 1.71–1.59 (m, 2 H), 1.50–1.42 (m, 1 H), 1.38–1.33 (m, 2 H), 1.28 (s, 6 H), 1.26 (br s, 3 H), 1.23 (s, 3 H), 0.68 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 208.6, 159.9, 148.3, 136.5, 133.3, 122.0, 120.7, 65.6, 41.6, 38.2, 33.9, 33.8, 33.8, 33.6, 32.4, 24.7, 24.0, 24.0, 18.3.

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{27}O$: 271.2062; found: 271.2054.

22

White foam; yield: 3 mg (9.6 μmol, 6%); R_f = 0.1 (pentane–Et_2O, 5:1).

FT-IR (neat): 2962, 2930, 2870, 2361, 2336, 1723, 1613, 1461, 1384, 1259, 1204, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 2.0 Hz, 1 H), 7.49 (dd, *J* = 8.0, 4.0 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 5.46 (s, 1 H), 2.96 (sept, *J* = 6.8 Hz, 1 H), 2.52–2.48 (m, 1 H), 1.94–1.78 (m, 3 H), 1.60–1.52 (m, 1 H), 1.43–1.32 (m, 1 H), 1.27 (d, *J* = 6.8 Hz, 3 H), 1.26 (d, *J* = 6.8 Hz, 3 H), 1.21 (s, 3 H), 1.16 (s, 3 H), 1.14 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 207.4, 164.6, 148.4, 146.3, 133.4, 132.8, 128.1, 124.3, 82.1, 47.3, 40.6, 39.0, 38.6, 33.8, 28.1, 23.9, 23.8, 23.5, 22.0, 20.4.

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{20}H_{27}O_3$: 315.1960; found: 315.1954.

(4a*S*,9a*R*)-7-Isopropyl-6-methoxy-1,1,4a-trimethyl-1,2,3,4,4a,9a-hexahydro-9*H*-fluoren-9-one (19)

LHMDS (69 μL, 69 μmol) was added dropwise to a soln of hydroxy diketone **8** (20 mg, 58 μmol) in THF (6 mL) at –15 °C. The mixture was stirred at –15 °C for 15 min then warmed to 0 °C and stirred for 12 h. The reaction was quenched with sat. aq NH_4Cl, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (10:1)] to give a yellow powder: yield: 1 mg (3 μmol, 5%); R_f = 0.5 (pentane–Et_2O, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (s, 1 H), 6.76 (s, 1 H), 3.92 (s, 3 H), 3.27 (sept, *J* = 6.8 Hz, 1 H), 2.14 (s, 1 H), 2.04–1.98 (m, 1 H), 1.72–1.60 (m, 2 H), 1.50–1.42 (m, 1 H), 1.39–1.35 (m, 2 H), 1.29 (s, 3 H), 1.24 (s, 3 H), 1.21 (br s, 3 H), 1.20 (br s, 3 H), 0.70 (s, 3 H).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{20}H_{29}O_2$: 301.2168; found: 301.2176.

(6a*R*,11a*R*)-3-Isopropyl-2-methoxy-8,8,11a-trimethyl-6a,8,9,10,11,11a-hexahydrocyclohepta[*c*]isochromene-5,7-dione (23)

LHMDS (38 μL, 38 μmol) was added dropwise to a soln of hydroxy diketone **8** (11 mg, 32 μmol) in THF (3.0 mL) at –15 °C. The reaction was stirred at –15 °C for 15 min then warmed to 0 °C and stirred for 12 h. The reaction was quenched with sat. aq NH_4Cl, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (5:1)] to give a colorless foam; yield: 2.4 mg (6.9 μmol, 22%): R_f = 0.2 (pentane–Et_2O, 3:1).

FT-IR (neat): 2963, 1720, 1609, 1461, 1257, 1038 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 6.73 (s, 1 H), 5.44 (s, 1 H), 3.90 (s, 3 H), 3.27 (h, *J* = 6.8 Hz, 1 H), 2.49–2.44 (m, 1 H), 1.95–1.81 (m, 3 H), 1.61–1.52 (m, 1 H), 1.41–1.36 (m, 1 H), 1.23 (d, *J* = 6, 8.0 Hz, 3 H), 1.21 (s, 3 H), 1.20 (d, *J* = 6, 8.0 Hz, 3 H), 1.16 (s, 3 H), 1.15 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 207.5, 164.4, 162.3, 148.7, 137.1, 128.6, 125.7, 105.0, 82.0, 55.7, 47.3, 40.7, 39.0, 38.9, 30.5, 28.1, 23.5, 22.6, 22.4, 21.9, 20.5.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{21}H_{29}O_4$: 345.2060; found: 345.2058.

(4a*S*,9*S*,9a*R*)-7-isopropyl-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydro-1*H*-fluoren-9-ol (27)

Solid $NaBH_4$ (36 mg, 0.94 mmol) was added to a soln of ketone **18** (23 mg, 85 μmol) in MeOH (1.5 mL) at 0 °C. After 15 min, the mixture was warmed to r.t. and stirred for 12 h. MeOH was removed under reduced pressure, and the mixture was diluted with H_2O. The mixture was acidified with 1 M aq HCl and extracted with Et_2O. The combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (20:1)] to give **27** a colorless foam; yield: 19 mg (70 μmol, 82%): R_f = 0.5 (pentane–Et_2O, 5:1); $[\alpha]_D^{23}$ +53.2 (*c* 0.40, $CHCl_3$).

FT-IR (neat): 3325, 2959, 2924, 2866, 2369, 1489, 1458, 1377, 1034, 822 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (s, 1 H), 7.15 (dd, *J* = 7.8, 1.1 Hz, 1 H), 7.07 (d, *J* = 7.8 Hz, 1 H), 5.04 (t, *J* = 8.4 Hz, 1 H), 2.94 (sept, *J* = 6.8 Hz, 1 H), 1.68–1.62 (m, 3 H), 1.60–1.56 (m, 1 H), 1.50 (s, 3 H), 1.47–1.38 (m, 3 H), 1.29 (s, 3 H), 1.27 (s, 3 H), 1.22 (s, 3 H), 1.18 (s, 3 H), 1.05–0.98 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.2, 147.7, 142.8, 126.5, 126.5, 121.9, 121.2, 76.3, 67.3, 43.8, 39.0, 36.5, 34.2, 32.4, 32.3, 30.0, 26.2, 24.4, 24.3, 18.8.

HRMS-ESI: *m/z* $[M + H]^+$ calcd for $C_{19}H_{27}$ ($[(M\text{-}H_2O)+H]^+$): 255.2113; found: 255.2104.

(4a*R*)-7-Isopropyl-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1*H*-fluorene (28)

MsCl (4.2 μL, 54 μmol) was added to a soln of alcohol **27** (9.8 mg, 36 μmol) and Et_3N (20 μL, 0.14 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C. The ice bath was removed after 15 min, and the mixture was stirred for overnight at r.t. The reaction was quenched with H_2O, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with sat. aq $NaHCO_3$, dried ($MgSO_4$), and concentrated under vacuum. The residue was purified by flash column chromatography (pentane) to give a colorless oil; yield: 8.6 mg (34 μmol, 95%): R_f = 0.5 (pentane); $[\alpha]_D^{23}$ +83.1 (*c* 0.29, $CHCl_3$).

FT-IR (neat): 2959, 2920, 2880, 1615, 1480, 1462, 1367, 1293, 886, 821 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.15 (m, 2 H), 7.00 (dd, *J* = 7.8, 1.2 Hz, 1 H), 6.35 (s, 1 H), 2.92 (sept, *J* = 6.8 Hz, 1 H), 2.15–2.12 (m, 1 H), 1.96 (qt, *J* = 14.0, 3.6 Hz, 1 H), 1.67–1.58 (m, 2 H), 1.37 (s, 3 H), 1.30 (s, 3 H), 1.28 (s, 3 H), 1.26 (s, 3 H), 1.24 (s, 3 H), 1.11 (td, *J* = 13, 4.4 Hz, 1 H), 1.00 (td, *J* = 13.2, 4.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.4, 152.9, 147.2, 142.4, 122.4, 120.9, 120.8, 118.5, 50.7, 42.8, 38.2, 35.7, 34.3, 31.4, 25.4, 24.5, 24.4, 23.7, 19.9.

(4a*S*,9*Z*,9a*R*)-7-Isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,9a-hexahydro-9*H*-fluoren-9-one *O*-methyloxime (30)

A soln of NaOAc (36 mg, 0.44 mmol) in H_2O (0.3 mL) and $MeONH_2$·HCl (64 mg, 0.77 mmol) were added to a soln of ketone **18** (12 mg, 44 μmol) in EtOH (0.5 mL). The mixture was refluxed at 90 °C until the starting material disappeared (TLC). The solvent was removed in vacuo, and the mixture was diluted with H_2O (5 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were washed (brine), dried ($MgSO_4$), and concentrated under vacuum. The residue was purified by flash column chromatography [pentane–Et_2O (50:1)] to give colorless oil; yield: 11 mg (37 μmol, 83%): R_f = 0.3 (pentane–Et_2O, 50:1).

FT-IR (neat): 2957, 2925, 2855, 1658, 1632, 1463, 1261, 1073, 1033, 899, 802 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 1.6 Hz, 1 H), 7.22 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.12 (d, *J* = 8 Hz, 1 H), 4.03 (s, 3 H), 2.92 (h, *J* = 6.8 Hz, 1 H), 2.32–2.27 (m, 1 H), 2.29 (s, 1 H), 1.54–1.45 (m, 2 H), 1.37–1.28 (m, 3 H), 1.26 (s, 3 H), 1.24 (s, 3 H), 1.11 (s, 3 H), 1.09 (s, 3 H), 0.30 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.1, 153.3, 147.7, 134.1, 128.8, 127.3, 120.6, 62.4, 60.6, 43.7, 40.1, 36.3, 34.2, 33.9, 33.5, 31.7, 24.4, 24.2, 23.9, 18.9.

(4a*S*,9*S*,9a*R*)-9-{[*tert*-Butyl(dimethyl)silyl]oxy}-7-isopropyl-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydrofluorene (35)

DBSCl (17 mg, 0.11 mmol) and imidazole (15 mg, 0.22 mmol) were added to a soln of alcohol **27** (20 mg, 73 μmol) in CH_2Cl_2 (0.5 mL) at r.t. The mixture was stirred for 36 h until the starting material was consumed, and then the reaction was quenched with sat. aq $NaHCO_3$ (5 mL). The mixture was extracted with Et_2O (3 × 15 mL), and the combined organic layers were washed (brine), dried ($MgSO_4$), and concentrated in vacuum. The residue was purified by flash column chromatography (pentane) to give a colorless oil; yield: 23 mg (60 μmol, 82%): R_f = 0.6 (pentane); $[\alpha]_D^{23}$ +31.1 (*c* 0.35, $CHCl_3$).

FT-IR (neat): 2955, 2928, 2858, 1462, 1253, 1082, 1058, 833, 772 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (br s, 1 H), 7.09–7.07 (m, 1 H), 6.99 (d, *J* = 7.6 Hz, 1 H), 5.08 (d, *J* = 5.2 Hz, 1 H), 2.89 (h, *J* = 6.8 Hz, 1 H), 1.81 (d, *J* = 5.2 Hz, 1 H), 1.54–1.45 (m, 3 H), 1.42 (s, 3 H), 1.31–1.27 (m, 3 H), 1.25 (s, 3 H), 1.23 (s, 3 H), 1.10 (s, 3 H), 0.91 (s, 9 H), 0.77 (s, 3 H), 0.13 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.0, 147.0, 143.8, 126.3, 123.2, 120.8, 77.9, 64.7, 44.3, 38.7, 37.6, 34.1, 32.1, 31.4, 30.91, 29.0, 26.3, 24.4, 24.3, 18.9, 18.4, –2.4, –3.0.

(4a*R*)-7-Isopropyl-1,1,4a-trimethyl-2,3,4,4a-tetrahydro-1*H*-fluoren-8-ol (38)

BuLi (0.14 mL, 0.22 mmol) was added to a soln of benzylic alcohol **27** (12 mg, 44 μmol) and TMEDA (33 μL, 0.22 mmol) in dry hexane (0.75 mL) at r.t., and the mixture was refluxed at 75 °C for 4 h.[20b] The mixture was allowed to cool to 0 °C, $B(OMe)_3$ (0.10 mL, 0.90 mmol) was added, and the mixture was stirred for 2 h at 0 °C. AcOH (83 μL) and 35% aq H_2O_2 (0.30 mL) were added and the mixture was stirred overnight. The reaction was quenched with sat. aq $Fe(NH_4)_2(SO_4)_2{\cdot}6H_2O$ and aq $NaHCO_3$, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed (aq $NaHCO_3$, brine), dried ($MgSO_4$), and concentrated in vacuo. A drop of 6 M HCl in dioxane was added to the soln of the crude product in $CHCl_3$ at r.t., and the mixture was stirred for 5 min. The mixture was then concentrated and the residue was purified by flash column chromatography [pentane–Et_2O (20:1)] to give the hydroxy compound **38** as a colorless oil; yield: 7.6 mg (28 μmol, 64%); R_f = 0.4 (pentane–Et_2O, 10:1); $[\alpha]_D^{23}$ +66.1 (*c* 0.28, $CHCl_3$). Some starting material **27** was also isolated; yield: 3.1 mg, (11 μmol, 26%).

FT-IR (neat): 3376, 2960, 2927, 2840, 1574, 1460, 1437, 1365, 1295, 1203, 1048, 976 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (d, *J* = 7.6 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 1 H), 6.44 (s, 1 H), 4.67 (s, 1 H), 3.21 (sept, *J* = 6.8 Hz, 1 H), 2.14–2.10 (m, 1 H), 2.01–1.89 (qt, *J* = 13.6, 3.2 Hz, 1 H), 1.67–1.58 (m, 2 H), 1.36 (s, 3 H), 1.31 (s, 3 H), 1.28 (d, *J* = 6.8 Hz, 3 H), 1.27 (d, *J* = 6.8 Hz, 3 H), 1.24 (s, 3 H), 1.11 (td, *J* = 13.0, 4.0 Hz, 1 H), 1.01 (td, *J* = 13.0, 4.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.4, 154.8, 145.7, 132.1, 128.5, 122.4, 115.4, 114.0, 51.5, 42.9, 38.3, 35.8, 31.4, 27.1, 25.5, 23.7, 23.1, 23.1, 19.9.

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{27}O$: 271.2062; found: 271.2085.

(4b*S*)-2-Isopropyl-4b,8,8-trimethyl-5,6,7,8-tetrahydro-1*H*-fluorene-1,4(4b*H*)-dione (39)

Frémy´s salt (20 mg, 75 μmol) was added to a soln of the hydroxy compound **38** (6.1 mg, 23 μmol) in a mixture of acetone (0.80 mL), H_2O (0.20 mL), and pH 7 phosphate buffer (0.12 mL),[51] and mixture was stirred at r.t. for 24 h. When the reaction was complete, the solvent was removed under vacuum and the mixture was extracted with Et_2O. The combined organic layer was washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash column chromatography [pentane–Et_2O (50:1)] to give a yellow oil; yield: 6.2 mg (22 μmol, 97%): R_f = 0.5 (pentane–Et_2O, 10:1); $[\alpha]_D^{23}$ –8.1 (*c* 0.21, $CHCl_3$).

FT-IR (neat): 2962, 2929, 1659, 1640, 1536, 1468, 1367, 1261, 1224, 1089, 1038, 800 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.39 (s, 1 H), 6.34 (d, *J* = 1.2 Hz, 1 H), 3.06 (sept d, *J* = 6.8, 1.2 Hz, 1 H), 2.43–2.38 (m, 1 H), 1.92 (qt, *J* = 14.0, 3.6 Hz, 1 H), 1.72–1.67 (m, 1 H), 1.65–1.58 (m, 1 H), 1.45 (s, 3 H), 1.28 (s, 3 H), 1.23 (s, 3 H), 1.14 (d, *J* = 6.8 Hz, 3 H), 1.13 (d, *J* = 6.8 Hz, 3 H), 1.11–1.03 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.8, 183.7, 175.1, 153.2, 152.8, 145.6, 132.0, 116.6, 55.7, 43.5, 37.3, 36.7, 31.1, 26.4, 24.9, 21.9, 21.8, 20.2, 19.2.

(–)-Taiwaniaquinone H (2)

A soln of **39** (7.0 mg, 25 μmol) in AcOH (0.50 mL) was treated with 36 μL of a stock soln of Br_2 (0.20 g) in AcOH (1.0 mL). The resulting mixture was stirred for 5 min at r.t. and then the reaction was quenched by the addition of 5% aq $NaHSO_3$ (20 μL). The mixture was stirred for another 5 min at r.t. then extracted with Et_2O (3 × 5 mL). The combined organic layers were washed sequentially with aq $NaHSO_3$ and brine then dried ($MgSO_4$) and concentrated in vacuo. The residue was passed through a short pad of silica [pentane–Et_2O (20:1)]. The resulting vinylic bromide was dissolved in 0.50 M NaOMe soln (0.50 mL), and the mixture was stirred for 45 min at r.t. The solvent was removed under vacuum, and the mixture was diluted (H_2O) and extracted with Et_2O (3 × 7 mL). The combined organic layer was washed (brine), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography [pentane–Et_2O (30:1)] to give an orange solid; yield: 5.0 mg (16 μmol, 65%); R_f = 0.6 (pentane–Et_2O, 10:1); $[\alpha]_D^{23}$ –95.7 (*c* 0.21, $CHCl_3$). The analytical data for **2** agreed with those reported in the literature,[4f,5d,n,k] except that the value of the optical rotation was higher than the reported values {lit.[5n] $[\alpha]_D^{21}$ –36.9 (*c* 0.30, $CHCl_3$); lit.[5k] $[\alpha]_D^{25}$ –11.9 (*c* 0.56, $CHCl_3$); lit.[4f] $[\alpha]_D^{25}$ –9.0 (*c* 0.29, $CHCl_3$)}.

FT-IR (neat): 2933, 1645, 1582, 1535, 1459, 1356, 1285, 1264, 1156, 1026, 757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.37 (s, 1 H), 3.98 (s, 3 H), 3.30 (sept, *J* = 6.8 Hz, 1 H), 2.42–2.37 (m, 1 H), 1.91 (qt, *J* = 14.0, 3.6 Hz, 1 H), 1.71–1.66 (m, 1 H), 1.64–1.57 (m, 1 H), 1.44 (s, 3 H), 1.27 (s, 3 H), 1.23 (d, *J* = 6.8 Hz, 3 H), 1.23–1.21 (d, *J* = 6.8 Hz, 3 H), 1.22 (s, 3 H), 1.13–1.04 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.5, 178.9, 175.9, 157.5, 150.7, 146.0, 136.1, 116.9, 61.5, 55.8, 43.5, 37.4, 36.8, 31.1, 25.0, 24.6, 20.8, 20.8, 20.3, 19.2.

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