The Synthesis of Salvinolone, Saprorthoquinone, and 4-Hydroxysapriparaquinone from (+)-Dehydroabietic Acid

Takashi MATSUMOTO,* Yasutaka TANAKA, Hiromitsu TERAO, Yoshio TAKEDA, and Makoto WADA
Faculty of Integrated Arts and Sciences, University of Tokushima,
Minamijosanjima, Tokushima 770

(Received May 24, 1993)

Salvinolone, saprorthoquinone, and 4-hydroxysapriparaquinone isolated from the roots of *Salvia prionitis* Hance. were synthesized starting from (+)-dehydroabietic acid via 11,12-dimethoxyabieta-8,11,13-trien-7-one and 12-methoxyabieta-8, 11,13-triene.

Recently, Cordell et al.[1] reported the isolation of salvinolone (**1**) and two rare 4,5-*seco*-5,10-*friedo*-abietane diterpenes, saprorthoquinone (**2**) and 4-hydroxysapriparaquinone (**3**), from the roots of *Salvia prionitis* Hance. Saprorthoquinone (**2**) was also obtained by an acidic treatment of 15-deoxyfuerstione (**4**), a component of the roots of *Salvia moorcraftiana*, by Simoes et al.[2] Among these natural diterpenes, salvinolone (**1**) and saprorthoquinone (**2**) showed cytotoxic activity against the P-388 assay and the KB lymphocytic leukemia test systems in vitro, respectively. In this paper, we describe the syntheses of salvinolone (**1**), saprorthoquinone (**2**), and 4-hydroxysapriparaquinone (**3**) starting from (+)-dehydroabietic acid (**5**), a component of pine rosin (Fig. 1).

11,12-Dimethoxyabieta-8,11,13-trien-7-one[3] (**6**), prepared from **5**, was refluxed with selenium dioxide in aqueous acetic acid to give salvinolone dimethyl ether (**7**) in 80.5% yield. Demethylation of **7** with anhydrous aluminum chloride and ethanethiol in dichloromethane afforded salvinolone (**1**: 72.5% yield).

Subsequently, the synthesis of saprorthoquinone (**2**) was carried out by the following two routes. Compound **1** was acetylated with acetic anhydride in pyridine to give diacetate (**8**) in 97.1% yield. The diacetate (**8**) was reduced with sodium borohydride in the presence of cerium (III) chloride heptahydrate[4] at room temperature and the resulting 7-hydroxy compound (**9**) was further treated with *p*-toluenesulfonic acid monohydrate in refluxing benzene to give a rearranged naphthalene derivative (**10**) in 61.3% yield from **8**. The mass spectrum of **10** gave a molecular ion peak at m/z 382.2160 (M^+) corresponding to the formula $C_{24}H_{30}O_4$. In the ^1H NMR spectrum, compound **10** exhibited the presence of two isopropyl methyl groups at $\delta=1.30$ (6H, d, $J=6.7$ Hz), two vinyl methyl groups at $\delta=1.59$ (3H, s) and 1.72 (3H, s), two phenolic acetoxyl groups at $\delta=2.35$ (6H, s), a methyl group on aryl ring at $\delta=2.47$ (3H, s), an olefinic proton at $\delta=5.23$ (1H, t, $J=6.2$ Hz), and three aromatic protons at $\delta=7.24$ (1H, d, $J=8.5$ Hz), 7.58 (1H, d, $J=8.5$ Hz), and 7.60 (1H, s). These spectral data suggested that the angular methyl group at the C-10 position in **9** migrated to the C-5 position and the ring-B was aromatized with an opening of the ring-A to form an unsaturated side chain. Thus, the structure of **10** was assigned as 4,5-*seco*-5,10-*friedo*-11, 12-diacetoxyabieta-3,5(10),6,8,11,13-hexaene. The reduction of **10** with lithium aluminum hydride afforded a phenolic compound (**11**), which was immediately oxidized with silver oxide in ether at room temperature to give saprorthoquinone (**2**) in 85.1% yield from **10**.

An alternative synthetic route for saprorthoquinone (**2**) was also developed as follows (Fig. 2). 12-Methoxyabieta-8,11,13-triene (**12**),[5] prepared from **5**, was oxidized with the Jones reagent in acetone to give a 7-oxo compound (**13**: 75.0% yield), which was converted into an enone derivative (**14**: 94.9% yield) by refluxing with selenium dioxide in aqueous acetic acid. The enone **14** was further converted into the corresponding acetate (**16**: 97.4% yield) by demethylation with anhydrous aluminum chloride and ethanethiol in dichloromethane (**14**→**15**), and subsequent acetylation with acetic anhydride in pyridine. The acetate **16** was reduced with sodium borohydride in the presence of cerium (III) chloride heptahydrate, and the resulting 7-hydroxy compound (**17**) was treated with *p*-toluenesulfonic acid monohydrate in benzene to give a 4,5-*seco* compound (**18**) in 58.9% yield from **16**. Treatment of **18** with lithium aluminum hydride produced a phenolic compound (**19**: 89.2% yield), which was oxidized with Fremy's salt and potassium dihydrogenphosphate in aqueous *N*,*N*-dimethylformamide to yield saprortho-

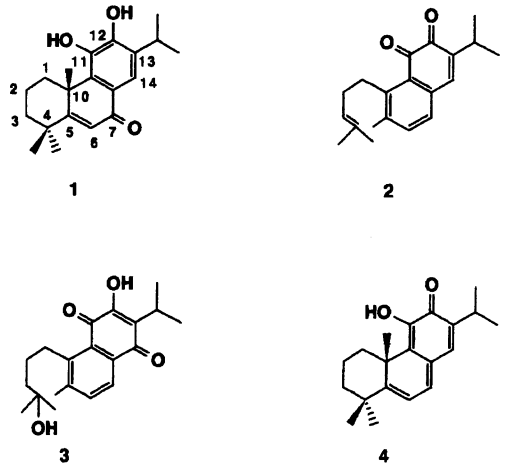

Fig. 1.

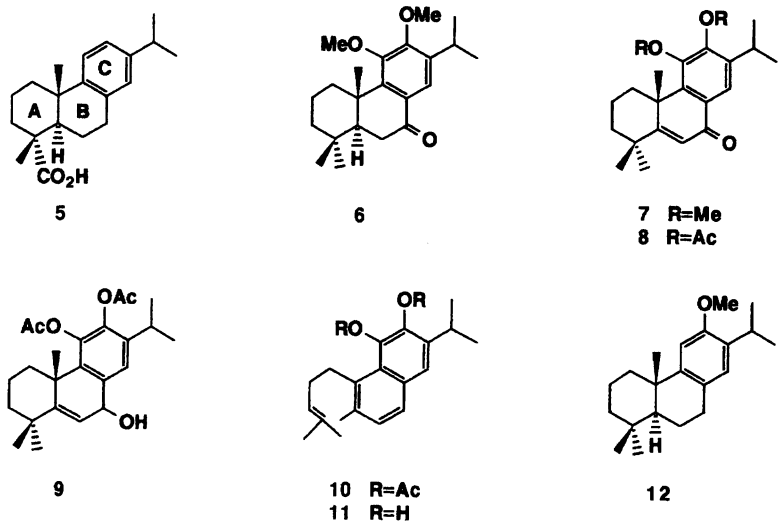

Fig. 2.

quinone (**2**) in 66.3% yield.

A comparison of the above two routes for the synthesis of saprorthoquinone (**2**) suggested that the latter route was superior to the former regarding the length of the reaction step and the overall yield from (+)-dehydroabietic acid (**5**).

Finally, the conversion of **18** into 4-hydroxysapriparaquinone (**3**) was also carried out as follows (Fig. 3). The trisubstituted double bond in **18** was oxidized with *m*-chloroperbenzoic acid in dichloromethane, and the resulting epoxide was immediately reduced with lithium aluminum hydride to give a phenolic tertiary alcohol (**20**) in 82.3% yield. To introduce an oxygen function at the C-11 position, the alcohol **20** was refluxed with benzoyl peroxide[6] in chloroform to give a mixture of 12-benzoyloxy-11-hydroxy compound (**21**) and its 11-benzoyloxy-12-hydroxy isomer (**22**). A mixture of **21** and **22** was further oxidized with the Jones reagent in acetone or *m*-chloroperbenzoic acid in the presence of *p*-toluenesulfonic acid monohydrate to give a benzoyloxy-*p*-quinone derivative (**23**) in 25.8 or 24.2% yield from **20**. The *p*-quinone **23** was then hydrolyzed with aqueous sodium hydrogencarbonate in refluxing methanol to give 4-hydroxysapriparaquinone (**3**) in 82.8% yield.

Experimental

All of melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform, and the ^{1}H NMR spectra in deuteriochloroform at 60 MHz with tetramethylsilane as an internal standard, unless otherwise stated; s: singlet, bs: broad singlet, d: doublet, t: triplet., m: multiplet. The column chromatography was performed using Merck silica gel (0.040—0.063 mm).

11,12-Dimethoxyabieta-5,8,11,13-tetraen-7-one (7). 11,12-Dimethoxyabieta-8,11,13-trien-7-one (**6**) was prepared from (+)-dehydroabietic acid (**5**) by the known procedure.[3] A mixture of **6** (387 mg) and selenium dioxide (1.548 g) in acetic acid (12 ml) and water (3.9 ml) was refluxed for 2.5 h. The cooled mixture was filtered and the filtrate was diluted with chloroform. The chloroform solution was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated in vacuo. The residue was chromatographed on silica gel (45 g), using benzene as an eluent, to give the starting **6** (43 mg: 11.1% yield). Further elution with the same solvent gave **7** (310 mg: 80.5% yield), which was recrystallized from hexane, mp 96—97 °C, $[\alpha]_D$ +64.3° (*c* 0.59). IR 1640 cm^{-1}. ^{1}H NMR (CCl_4) δ=1.22 and 1.27 (each 3H, d, *J*=6 Hz, –CH($C\underline{H}_3$)$_2$), 1.28 and 1.35 (each 3H, s, 4-(CH_3)$_2$), 1.58 (3H, s, 10-CH_3), 3.73 and 3.80 (each 3H, s, 11-OCH_3 and 12-OCH_3), 6.13 (1H, s, 6-H), and 7.54 (1H, s, 14-H). Found: C, 77.28; H, 8.74%. Calcd for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83%.

Salvinolone (1). Anhydrous aluminum chloride (462 mg) was added to a stirred solution of **7** (198 mg) and ethanethiol (0.44 ml) in dichloromethane (2.0 ml) at 3—5 °C with cooling in an ice-water bath over a 10-min period. After stirring at this temperature for 15 min and at room temperature for 4 h, the mixture was poured into ice-dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated in vacuo. The residue was recrystallized from acetone to give salvinolone (**1**) (132 mg: 72.5% yield) as pale yellow crystals, mp 252.5—253.5 °C, $[\alpha]_D$ +45.5° (MeOH, *c* 0.55). IR (KBr) 3421, 1636, and 1562 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ=1.14 and 1.17 (each 3H, d, *J*=6.5 Hz, –CH($C\underline{H}_3$)$_2$), 1.22 and 1.31 (each 3H, s, 4-(CH_3)$_2$), 1.58 (3H, s, 10-CH_3), 6.12 (1H, s, 6-H), and 7.31 (1H, s, 14-H). Found: C, 76.56; H, 8.41%. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34%. The synthetic **1** was identical with natural salvinolone (mp 253—254 °C, $[\alpha]_D$ +35.8° (MeOH, *c* 0.12))[1] on the basis of a mixed melting-point determination and direct comparisons of the spectral data (IR and ^{1}H NMR).

11,12-Diacetoxyabieta-5,8,11,13-tetraen-7-one (8). A mixture of the synthetic **1** (83 mg) and acetic anhydride (0.5 ml) in pyridine (0.5 ml) was allowed to stand at room temperature for 16.5 h. After the usual work-up, the crude product was chromatographed on silica gel (5 g), using ether–benzene (5 : 95) as an eluent, to give **8** (102 mg: 97.1%

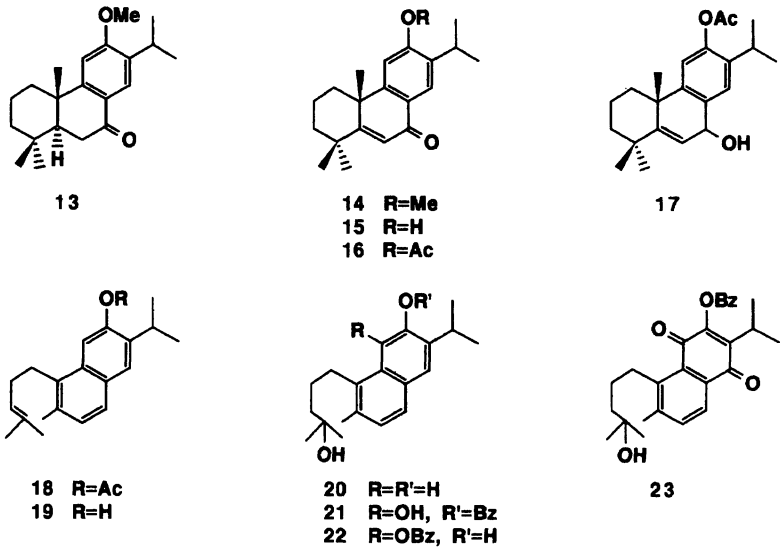

Fig. 3.

yield), which was recrystallized from methanol or a mixture of acetone and hexane, mp 159—160 °C, $[\alpha]_D$ +60.2° (*c* 1.05). IR 1770 and 1650 cm^{-1}. ^1H NMR δ=1.21 and 1.24 (each 3H, d, J=7.2 Hz, $-CH(C\underline{H}_3)_2$), 1.26 and 1.33 (each 3H, s, 4-$(CH_3)_2$), 1.54 (3H, s, 10-CH_3), 2.26 and 2.30 (each 3H, s, 11-OAc and 12-OAc), 6.36 (1H, s, 6-H), and 7.93 (1H, s, 14-H). Found: C, 72.24; H, 7.68%. Calcd for $C_{24}H_{30}O_5$: C, 72.33; H, 7.59%.

4,5-*seco*-5,10-*friedo*-11,12-Diacetoxyabieta-3,5(10),6,8,11,13-hexaene (10). Sodium borohydride (26 mg) was added to a stirred mixture of **8** (277 mg) and cerium (III) chloride heptahydrate (259 mg) in tetrahydrofuran (0.5 ml) and methanol (1.5 ml) at room temperature for 4 min. The mixture was further stirred at this temperature for 3 min, diluted with ether, washed with brine, dried over sodium sulfate, and evaporated in vacuo to give a crude alcohol (**9**) (285 mg).

A solution of the above-mentioned crude alcohol (**9**: 285 mg) and *p*-toluenesulfonic acid monohydrate (100 mg) in benzene (15 ml) was refluxed for 1.5 h. The solution was diluted with ether, washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated in vacuo. The residue was chromatographed on silica gel (25 g), using hexane–benzene (3 : 7) as an eluent, to give **10** (163 mg: 61.3% yield from **8**). IR 1765 cm^{-1}. ^1H NMR δ=1.30 (6H, d, J=6.7 Hz, $-CH(C\underline{H}_3)_2$), 1.59 and 1.72 (each 3H, s, 4-$(CH_3)_2$), 2.35 (6H, s, 11-OAc and 12-OAc), 2.47 (3H, s, 5-CH_3), 5.23 (1H, t, J=6.2 Hz, 3-H), 7.24 (1H, d, J=8.5 Hz, 6-H), 7.58 (1H, d, J=8.5 Hz, 7-H), and 7.60 (1H, s, 14-H). HRMS Found: m/z 382.2160 (M^+). Calcd for $C_{24}H_{30}O_4$: M, 382.2144.

12-Methoxyabieta-8,11,13-trien-7-one (13). 12-Methoxyabieta-8,11,13-triene (**12**) was prepared from (+)-dehydroabietic acid (**5**) by the known procedure.[5] Jones reagent (2.5 mol dm^{-3}, 21.3 ml) was added to a stirred solution of **12** (10.669 g) in acetone (142 ml) at 3—5 °C with cooling in an ice-water bath over a period of 10 min. After stirring at this temperature for 10 min and at room temperature for 2 h, the mixture was poured into water and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (200 g), using hexane–benzene (35 : 65) as an eluent, to give the starting **12** (1.863 g: 17.5% yield). Further elution with benzene afforded **13** (8.377 g: 75.0% yield) which was recrystallized from aqueous methanol, mp 137.5—138.5 °C, $[\alpha]_D$ +29.7° (MeOH *c* 0.82). IR 1660 cm^{-1}. ^1H NMR (CCl_4) δ=0.95 and 1.00 (each 3H, s, 4-$(CH_3)_2$), 1.19 and 1.21 (each 3H, d, J=7.0 Hz, $-CH(C\underline{H}_3)_2$), 1.23 (3H, s, 10-CH_3), 3.82 (3H, s, 12-OCH_3), 6.56 (1H, s, 11-H), and 7.62 (1H, s, 14-H). Found: C, 80.34; H, 9.76%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

12-Methoxyabieta-5,8,11,13-tetraen-7-one (14). A mixture of **13** (3.821 g) and selenium dioxide (15.284 g) in acetic acid (118 ml) and water (38 ml) was refluxed for 2 h. After the work-up as described for the preparation of **7**, the crude product was chromatographed on silica gel (50 g), using hexane–benzene (1 : 9) and then benzene as eluents, to give **14** (3.605 g: 94.9% yield) which was recrystallized from hexane, mp 157—158 °C (lit,[7] mp 155—156 °C), $[\alpha]_D$ +18.5° (*c* 1.76). IR 1640 cm^{-1}. ^1H NMR (CCl_4) δ=1.21 and 1.24 (each 3H, d, J=7.0 Hz, $-CH(C\underline{H}_3)_2$), 1.27 and 1.35 (each 3H, s, 4-$(CH_3)_2$), 1.52 (3H, s, 10-CH_3), 3.83 (3H, s, 12-OCH_3), 6.18 (1H, s, 6-H), 6.67 (1H, s, 11-H), and 7.73 (1H, s, 14-H). Found: C, 80.61; H, 9.26%. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03%.

12-Acetoxyabieta-5,8,11,13-tetraen-7-one (16). Anhydrous aluminum chloride (6.762 g) was added to a stirred solution of **14** (3.961 g) and ethanethiol (6.8 ml) in dichloromethane (40 ml) at 6—10 °C with cooling in an ice-water bath over a 20-min period. After stirring at this temperature for 10 min and at room temperature for 2 h, the mixture was treated as described for the preparation of **1** to give a crude phenolic compound (**15**) (3.761 g), a part of which was recrystallized from methanol, mp 292—293 °C (lit,[7] 283—284 °C). ^1H NMR δ=1.25 and 1.34 (each 3H, s, 4-$(CH_3)_2$), 1.30 (6H, d, J=5.6 Hz, $-CH(C\underline{H}_3)_2$), 1.51 (3H, s, 10-CH_3), 5.69 (1H, bs, 12-OH), 6.46 (1H, s, 6-H), 6.86 (1H, s, 11-H), and 8.02 (1H, s, 14-H).

The above crude **15** was acetylated with acetic anhydride (10 ml) in pyridine (20 ml) at room temperature for 14

h. After the usual work-up, the crude product was chromatographed on silica gel (50 g), using ether–benzene (2 : 98) as an eluent, to give **16** (4.203 g: 97.4% yield from **14**) which was recrystallized from methanol, mp 171—172 °C, $[\alpha]_D$ +17.1° (*c* 2.00). IR 1758 and 1650 cm^{-1}. ^1H NMR δ=1.26 and 1.28 (each 3H, d, J=8.8 Hz, $-CH(C\underline{H}_3)_2$), 1.27 and 1.29 (each 3H, s, 4-$(CH_3)_2$), 1.54 (3H, s, 10-CH_3), 2.35 (3H, s, 12-OAc), 6.49 (1H, s, 6-H), 7.15 (1H, s, 11-H), and 8.11 (1H, s, 14-H). Found: C, 77.54; H, 8.14%. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%.

4,5-*seco*-5,10-*friedo*-12-Acetoxyabieta-3,5(10),6,8,11,13-hexaene (18). Sodium borohydride (111 mg) was added to a stirred mixture of **16** (1.000 g) and cerium (III) chloride heptahydrate (1.094 g) in tetrahydrofuran (7.0 ml) and methanol (3.0 ml) at room temperature over a 5-min period. The mixture was further stirred at room temperature for 3 min, diluted with ether, washed with brine, dried, and evaporated in vacuo to give a crude alcohol (**17**) (1.073 g).

A solution of the above crude **17** (1.073 g) and *p*-toluenesulfonic acid monohydrate (107 mg) in benzene (27 ml) was stirred at room temperature for 1 h. After the work-up as described for the preparation of **10**, the crude product was repeatedly chromatographed on silica gel, using hexane–benzene (1 : 1) as an eluent, to give **18** (561 mg: 58.9% yield from **16**), IR 1750 cm^{-1}. ^1H NMR δ=1.31 (6H, d, J=6.7 Hz, $-CH(C\underline{H}_3)_2$), 1.58 and 1.71 (each 3H, s, 4-$(CH_3)_2$), 2.38 (3H, s, 12-OAc), 2.47 (3H, s, 5-CH_3), 5.30 (1H, t, J=7.0 Hz, 3-H), 7.22 (1H, d, J=8.5 Hz, 6-H), 7.58 (1H, d, J=8.5 Hz, 7-H) and 7.62 and 7.68 (each 1H, s, 11-H and 14-H). Found: C, 81.57; H, 8.81%. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70%.

4,5-*seco*-5,10-*friedo*-Abieta-3,5(10), 6,8,11,13-hexaen-12-ol (19). Lithium aluminum hydride (182 mg) was added to a stirred solution of **18** (1.040 g) in dry ether (35 ml) with cooling in an ice-water bath over a 10-min period. The mixture was stirred at room temperature for 45 min, poured into a mixture of ice and dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (30 g), using hexane–chloroform (3 : 2) as an eluent, to give an oily **19** (807 mg: 89.2% yield). IR 3620 and 3330 cm^{-1}. ^1H NMR δ=1.35 (6H, d, J=6.7 Hz, $-CH(C\underline{H}_3)_2$), 1.59 and 1.72 (each 3H, s, 4-$(CH_3)_2$), 2.45 (3H, s, 5-CH_3), 4.98 (1H, s, 12-OH), 5.32 (1H, t, J=7.0 Hz, 3-H), 7.11 (1H, d, J=8.5 Hz, 6-H), 7.52 (1H, d, J=8.5 Hz, 7-H), and 7.25 and 7.58 (each 1H, s, 11-H and 14-H). HRMS Found: m/z 282.1964 (M^+). Calcd for $C_{20}H_{26}O$: M, 282.1984.

Saprorthoquinone (2). a): A stirred solution of **19** (172 mg) in *N*,*N*-dimethylformamide (DMF: 20.6 ml) was protected from light with aluminum foil. After the addition of a solution of Fremy's salt (potassium nitrosodisulfonate) (817 mg) and potassium dihydrogenphosphate (315 mg) in water (31 ml), the mixture was stirred at room temperature under a stream of nitrogen for 1.5 h. The mixture was further treated as above with a solution of Fremy's salt (409 mg) and potassium dihydrogenphosphate (157 mg) in DMF (10 ml) and water (15 ml) for 1.5 h, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (20 g), using hexane–chloroform (1 : 1) as an eluent, to give an ortho-quinone (**2**) (120 mg: 66.3% yield) which was recrystallized from hexane to give red crystals, mp 96—97 °C. IR 1690, 1660, and 1635 cm^{-1}. ^1H NMR δ=1.17 (6H, d, J=6.7 Hz, $-CH(C\underline{H}_3)_2$), 1.62 and 1.70 (each 3H, s, 4-$(CH_3)_2$), 2.38 (3H, s, 5-CH_3), 5.30 (1H, t, J=7.9 Hz, 3-H), 7.03 (1H, d, J=7.6 Hz, 6-H), 7.09 (1H, s, 14-H), and 7.37 (1H, d, J=7.6 Hz, 7-H). HRMS Found: m/z 296.1758 (M^+). Calcd for $C_{20}H_{24}O_2$: M, 296.1776. The synthetic **2** was identical with natural saprorthoquinone (mp 97—98 °C).

b): A mixture of **10** (86 mg) and lithium aluminum hydride (21 mg) in dry ether (3.0 ml) was stirred at room temperature for 45 min. The mixture was poured into ice-dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo to give a crude phenolic compound (**11**: 68 mg) as an oil.

A mixture of silver oxide prepared from a solution of silver nitrate (340 mg) in water (2.0 ml) and aqueous sodium hydroxide (2.0 ml) containing sodium hydroxide (88 mg), anhydrous sodium sulfate (450 mg), and the crude **11** (68 mg) in dry ether (10 ml) was stirred at room temperature for 30 min. The mixture was filtered and the filtrate was evaporated in vacuo. The residue was chromatographed on silica gel (5 g), using hexane–chloroform (3 : 7) as an eluent, to give an ortho-quinone (**2**) (57 mg: 85.1% yield from **10**) which was shown to be identical with natural saprorthoquinone by spectral comparisons. Found: C, 81.22; H, 8.24%. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%.

4,5-*seco*-5,10-*friedo*-Abieta-5(10),6,8,11,13-pentaene-4,12-diol (20). A mixture of **18** (1.236 g) and *m*-chloroperbenzoic acid (85%, 789 mg) in dichloromethane (37 ml) was stirred at room temperature for 2 h. The mixture was diluted with ether and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo to give a crude epoxide (1.303 g).

Lithium aluminum hydride (436 mg) was added to a stirred solution of the above crude epoxide (1.303 g) in dry ether (26 ml) with cooling in an ice-water bath over an 8-min period. The mixture was further stirred at room temperature for 3.5 h, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residual solid was recrystallized from a mixture of acetone and hexane to give a diol (**20**) (911 mg: 79.6% yield), mp 140—142 °C. IR 3610 and 3320 cm^{-1}. ^1H NMR δ=1.23 (6H, s, 4-$(CH_3)_2$), 1.34 (6H, d, J=7.0 Hz, $-CH(C\underline{H}_3)_2$), 2.44 (3H, s, 5-CH_3), 7.09 (1H, d, J=8.5 Hz, 6-H), 7.26 and 7.57 (each 1H, s, 11-H and 14-H), and 7.52 (1H, d, J=8.5 Hz, 7-H). Found: C, 79.79; H, 9.28%. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39%. The mother liquor of the above recrystallization was evaporated in vacuo. The residue was chromatographed on silica gel (15 g), using ether–chloroform (1 : 1) as an eluent, to give an additional diol (**20**) (30 mg: 2.6% yield).

4,5-*seco*-5,10-*friedo*-12-Benzoyloxy-4-hydroxyabieta-5(10),6,8,12-tetraene-11,14-dione (23). A solution of **20** (741 mg) and benzoyl peroxide (717 mg) in chloroform (30 ml) was gently refluxed for 2 h. After the addition of ether (30 ml), acetic acid (0.3 ml), and aqueous potassium iodide (10%, 16 ml), the mixture was stirred at room temperature for 1 h and then washed successively with

water, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo to give a mixture (1.265 g) of 12-benzoyloxy-11-hydroxy compound (**21**) and its 11-benzoyloxy-12-hydroxy isomer (**22**).

a): The above mixture (466 mg) of **21** and **22** in acetone (23 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}, 0.93 ml) at 1—5 °C for 13 min. The mixture was diluted with ether, washed with brine, dried, and evaporated in vacuo. The residue was repeatedly chromatographed on silica gel (0.063 mm), using hexane–chloroform (3:7) as an eluent, to give a para-quinone (**23**) (116 mg: 25.8% yield from **20**). IR 3550, 1740, and 1660 cm^{-1}. ^1H NMR δ=1.19 (6H, s, 4-$(CH_3)_2$), 1.30 (6H, d, J=7.0 Hz, -CH($C\underline{H}_3)_2$), 2.45 (3H, s, 5-CH_3), 7.50 and 7.98 (each 1H, d, J=7.9 Hz, 6-H and 7-H), and 7.52—8.29 (5H, m, overlap, $-COC_6H_5$). Found: C, 74.81; H, 6.83%. Calcd for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96%.

b): The above mixture (526 mg) of **21** and **22** in dichloromethane (15 ml) was oxidized with *m*-chloroperbenzoic acid (85%, 648 mg) in the presence of *p*-toluenesulfonic acid monohydrate (50 mg) at room temperature for 22 h. The mixture was diluted with ether and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was repeatedly chromatographed on silica gel (0.063 mm), using hexane–chloroform (2:3) and then chloroform as eluents, to give a para-quinone (123 mg: 24.2% yield from **20**) which was shown to be identical with the above authentic **23** by spectral comparisons.

4-Hydroxysapriparaquinone (3). A mixture of **23** (76 mg) and aqueous sodium hydrogencarbonate (5%, 4.56 ml) in methanol (30 ml) was refluxed for 1 h. After removel of the methanol in vacuo, the residue was acidified with dilute hydrochloric acid, refluxed for 5 min, and then extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (5 g), using hexane–chloroform (1:1) as an eluent, to give a hydroxy-para-quinone (**3**) (48 mg: 82.8% yield) which was recrystallized from hexane to give brown crystals, mp 107—108 °C. IR 3525, 3345, and 1645 cm^{-1}. ^1H NMR δ=1.25 (6H, s, 4-$(CH_3)_2$), 1.30 (6H, d, J=6.5 Hz, -CH($C\underline{H}_3)_2$), 1.54 (1H, bs, 4-OH), 2.44 (3H, s, 5-CH_3), 7.50 and 7.98 (each 1H, d, J=7.9 Hz, 6-H and 7-H), and 7.78 (1H, s, 12-OH). Found: C, 72.78; H, 7.86%. Calcd for $C_{20}H_{26}O_4$: C, 72.20; H, 7.93%. The synthetic **3** was shown to be identical with natural 4-hydroxysapriparaquinone by spectral comparisons.

The authors are grateful to Professor G. A. Cordell, University of Illinois, for kindly supplying the natural samples.

References

1) L.-Z. Lin, G. Blasko, and G. A. Cordell, *Phytochemistry*, **28**, 177 (1989).
2) F. Simoes, A. Michavila, B. Rodriguez, M. C. Garcia-Alvarez, and M. Hasan, *Phytochemistry*, **25**, 755 (1986).
3) T. Matsumoto, Y. Ohsuga, S. Harada, and K. Fukui, *Bull. Chem. Soc. Jpn.*, **50**, 266 (1977).
4) J.-L. Luche, *J. Am. Chem. Soc.*, **100**, 2226 (1978).
5) T. Matsumoto, S. Imai, T. Yoshinari, and K. Tsuruta, *Bull. Chem. Soc. Jpn.*, **60**, 2401 (1987).
6) T. Matsumoto, S. Imai, S. Takeda, and M. Mitsuki, *Bull. Chem. Soc. Jpn.*, **56**, 2013 (1983), and references cited therein.
7) J. A. Hill, A. W. Johnson, T. J. King, S. Natori, and S. W. Tam, *J. Chem. Soc.*, **1965**, 361.