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STRUCTURE AND ABSOLUTE CONFIGURATION OF THE SESQUITERPENOID EMMOTINS*

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Key Word Index—*Emmotum nitens*; Icacinaceae; sesquiterpenoid tetralin; sesquiterpenoid naphthalenes; emmotin-F, -G, -H; emmotin-A, -B, -F; absolute configurations.

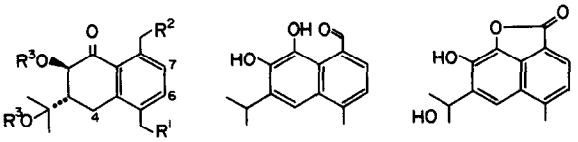
Abstract—The trunk wood of *Emmotum nitens* (Icacinaceae) contains the aromatic sesquiterpenes (2R,3S)-2-hydroxy-3-(2′-hydroxyisopropyl)-5,8-dimethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (emotin-F), 2-hydroxy-3-(2′-hydroxyisopropyl)-5,8-dimethylnaphthalene (emmotin-G) and 3-(2′-hydroxyisopropyl)-5,8-dimethyl-1,2-naphthoquinone (emmotin-H). The identity of the carbon skeletons of these emmotins was proved by conversion of all three into an identical quinoxaline derivative. The nature of this skeleton and the absolute configuration of emmotin-F, as well as of the previously described emmotins A and B, was established by conversion of emmotin-F into (+)-occidol.

RESULTS AND DISCUSSION

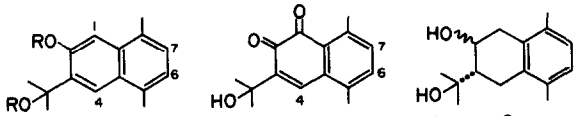
Emmotum nitens (Benth.) Miers, an arboreous Icacinaceae species, has a wide geographical distribution. A trunk wood sample from a specimen growing in the vicinity of Diamantina, Minas Gerais, contained two sesquiterpenoid tetralins, designated emmotin-A (**1a**) and -B (**1b**), and two sesquiterpenoid naphthalenes, designated emmotin-C (**2**) and -D (**3**). Their structural proposals were based mainly on PMR evidence, and, consequently, only the relative configurations for C-2 and C-3 of emmotin-A and -B were established. Allocation of the substituents to C-5, based on ^{13}C NMR evidence in the case of emmotin-A and -B, was considered a reasonable postulate also for emmotin-C and -D in the light of a probable biogenetic relationship [1].

The chemical investigation of another trunk wood sample, collected from a specimen growing in the Linhares Reserve, Rio Doce, Espirito Santo, where the species is known as "faia", revealed three different compounds. Elemental analysis and MS MW determination indicated their formulae to be $C_{15}H_{20}O_3$ (emmotin-F, **1c**), $C_{15}H_{18}O_2$ (emmotin-G, **4a**) and $C_{15}H_{16}O_3$ (emmotin-H, **5**).

Formation of a diacetate (**1d**) upon Ac_2O–C_5H_5N acetylation at reflux temp and of a triol on $NaBH_4$ reduction assigned the three oxygens of emmotin-F to two OH and one CO functions. The CO function must be substituted by a benzene ring and one of the carbinols. Evidence for conjugation with the benzene ring are UV (λ_{max} 259 nm, ϵ 11200) and IR (ν_{max} 1680 cm^{-1}) spectra, as well as ease of catalytic hydrogenolysis of emmotin-F to a diol (**6a**). Evidence for vicinality with a CHOH group was found in the formation of a red *o*-quinone (**7**) upon dehydrogenation of emmotin-F with Pd–C in refluxing xylene. Functionality and structural features of **7** were established by derivatization with *o*-phenylenediamine to a quinoxaline, $C_{21}H_{18}N_2$ (**8**). An isopropenyl group (τ 7.47, *t*, *J* 1.5 Hz [3H] and 4.53, *q*, *J* 1.5 Hz [2H]) is present in this compound (**8**), as well as in a derivative (**9**) obtained by heating emmotin-F or its diacetate (**1d**) in TsOH–Ac_2O, and shows the additional carbinol of emmotin-F to be part of a hydroxypropyl unit.



(**1a**) $R^1 = R^3 = H$, $R^2 = OMe$ (**2**) (**3**)
(**1b**) $R^1 = OH$, $R^2 = OMe$, $R^3 = H$
(**1c**) $R^1 = R^2 = R^3 = H$
(**1d**) $R^1 = R^2 = H$, $R^3 = Ac$
(**1e**) $R^1 = H$, $R^2 = OMe$, $R^3 = Ac$



(**4a**) R = H
(**4b**) R = Ac
(**5**)
(**6a**) R = βOH
(**6b**) R = αOH

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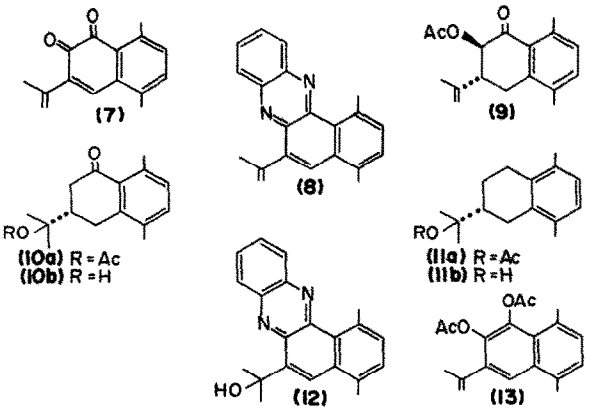

These facts, in conjunction with the interpretation of the PMR spectrum, which was very similar to those of emmotin-A (**1a**) and -B (**1b**) (Table 1), led to the tentative classification of emmotin-F as the tetralone emmotin **1c**. Both emmotin-A diacetate (**1e**) [1] and emmotin-F diacetate (**1d**) were deacetoxylated on reduction with Zn. The derivative (**10a**), submitted successively to catalytic hydrogenolysis and saponification, gave (+)-occidol (**11b**), characterized by mp, optical rotation [2] and direct UV, IR and PMR spectral comparison with a sample of synthetic (±)-occidol kindly supplied by Dr. Y. Hirose, Faculty of Agriculture, University of Tokyo, Japan. This correlation established not only the carbon skeleton and 3S-configuration, but also the 2R-configuration of emmotin-F, in view of the *trans*-diaxial relationship of H-2 and H-3, evidenced by PMR data (Table 1).

The ORD curve of emmotin-F is superimposable on those given by emmotins A (**1a**) and B (**1b**), compounds in which the substituents at C-2 and C-3 also are *trans*. All three tetralone emmotins, thus, possess identical absolute configurations. The constitution and absolute configuration of the previously mentioned diol can now be confidently formulated as **6a**. The racemates of **6a** and **10b** were prepared during a synthesis of (±)-rishitinol (**6b**) [3]. The published data on these products, however, are insufficient to validate comparisons with our compounds.

If it is admitted, as a working hypothesis, that the carbon skeleton of emmotin-F prevails in emmotin-G and -H, only the respective formulae **4a** and **5** can represent these compounds. Indeed, emmotin-G is a naphthol (λ_{max} 243 nm, ϵ 53900; λ_{max}^{NaOH} 254 nm, ϵ 55200) with a pair of *o*-related protons (τ 2.82 and 2.92, doublets, J 8 Hz) and a pair of *p*-related *peri*-protons (τ 2.27 and 2.58, singlets); and emmotin-H is an *ortho*-naphthoquinone (λ_{max} 265 nm, ϵ 40800; ν_{max} 1649 cm^{-1}; intense red colour slowly discharged by addition of aq. $Na_2S_2O_4$ to a $CHCl_3$ solution) with a pair of *o*-related protons (τ 2.64 and 2.87, doublets, J 8 Hz) and a single *peri*-proton (τ 2.14, singlet).

Table 1. PMR spectra (τ values) of emmotins (in $CDCl_3$)

	A* (1a)	B* (1b)	F (1c)	G (4a)	H (5)
H-1	—	—	—	2.60	—
H-2	5,57[a]	5.62[a]	5.60[a]	—	—
H-3	7.79[b]	7.99[b]	7.82[b]	—	—
CMe_2-3	8.55	8.59	8.58	8.22	8.43
	8.67	8.72	8.70	8.22	8.43
H-4	7.47[c]	7.41[c]	7.40[c]	2.25	2.12
H-4	6.98[d]	6.84[d]	6.90[d]	—	—
Me-5	7.68	—	7.75	7.41	7.46
H-6	2.46[e]	2.51	2.62[e]	2.92[e]	2.63[e]
H-7	2.54[e]	2.51	2.85[e]	2.82[e]	2.86[e]
Me-8	—	—	7.46	7.41	7.38

* For complete spectra of emmotins A to D see Ref. [1] a...d, J 12.5 Hz; *b*...*dt*, J 12.5, 12.5, 4.5 Hz; *c*...*dd*, J 16.5, 12.5 Hz; *d*...*dd*, J 16.5, 4.5 Hz, *e*...*d*, J 8.0 Hz.

As expected, acetylation of emmotin-G (to **4b**) caused a strong paramagnetic shift (Δ 0.59 ppm) of the H-1 singlet, and oxidation with Fremy's salt at room temperature yielded emmotin-H (**5**). Attempted direct acetylation of **5** under a variety of conditions led to mixtures. In contradistinction, either reductive acetylation in presence of zinc or acetylation of the quinoxaline derivative **12** gave good yields of isopropenyl compounds, **13** and **8** respectively. Since the dehydration product **8** is equally available from emmotin-F the initial hypothesis is correct, and also the emmotins G and H must possess the carbon skeleton of occidol (**11b**).

The 3S-configuration of the emmotins is typical of the natural eudesmane type sesquiterpenes. This fact suggests their biogenetic relationship with this class of compounds. It is, consequently, proposed that their biosynthesis, by analogy with that of occidol [4], should involve a one carbon shift by a dienol-benzene rearrangement of an eudesmane type precursor.

EXPERIMENTAL

Isolation of constituents. The C_6H_6-extract (175 g) of ground softwood (8 kg) was chromatographed on Si gel (1 kg). The indicated solvents eluted fractions (800 ml each) 1–72 (C_6H_6), 73–112 (C_6H_6–$CHCl_3$; (1:1), 113–162 ($CHCl_3$), 163–174 ($CHCl_3$–MeOH; 9:1), 175–186 (MeOH). Fraction 2 (90 mg), washed with hexane and crystallized from hexane–Et_2O (1:1), gave emmotin-E (47 mg). Fractions 9–17 (3.3 g) were rechromatographed on Si gel (200 g), C_6H_6–$CHCl_3$ (8:2) and (7:3) eluting emmotin-G (340 mg). Fractions 61–102 (40.7 g) were rechromatographed on Si gel (900 g), C_6H_6–$CHCl_3$ (1:1) and (2:8) eluting emmotin-F (17 g). Fractions 103–137 (16 g), washed with hexane and recrystallized from hexane–Et_2O (1:1), gave emmotin-H (3 g). Fractions 160–174 (46 g) were rechromatographed on Si gel (800 g), $CHCl_3$–MeOH (9:1) eluting a solid (1 g) which, by successive rechromatography on Sephadex LH-20 (20 g) in MeOH and PLC on Si gel C_6H_6–EtOAc–EtOH (50:43:7), gave emmotin-I (100 mg).

(2R,3S)-2-*Hydroxy*-3-(2′-*hydroxyisopropyl*)-5,8-*dimethyl*-1-*oxo*-1,2,3,4-*tetrahydronaphthalene* (emmotin-F, **1c**). mp 100–102° (EtOH) [Found: C, 72.84; H, 8.23. $C_{15}H_{20}O_3$ requires: C, 72.58; H, 8.06%]. ν_{max}^{KBr} (cm^{-1}): 3484, 3448, 1675, 1579, 1110, 1041, 912. λ_{max}^{EtOH} (nm): 259, 309 (ϵ 11200, 2800). PMR: Table. MS (*m/e*): 248 (4%) M^+, 247 (21), 229 (14), 200 (18), 189 (78), 186 (20), 173 (39), 172 (100), 171 (13), 160 (17), 159 (51), 157 (20), 146 (38), 145 (14), 144 (35), 143 (14), 129 (24), 128 (17), 119 (14), 118 (18), 117 (21), 115 (17), 91 (18), 59 (58), 55 (33), 43 (54). ORD (*c* 2 mg/100 ml, MeOH, 400–200 nm): $[\phi]_{360}$ 0, $[\phi]_{323}^{tr}$ −6100, $[\phi]_{310}$ 0, $[\phi]_{272}^{pk}$ +12400, $[\phi]_{255}$ 0, $[\phi]_{240}$ −9900. Acetylation (Ac_2O–C_5H_5N) at room temp was ineffective and at reflux temp gave, in 97% yield, the *diacetate* (**1d**), mp 98–99° (EtOH) [Found: C, 68.56; H, 7.31. $C_{19}H_{24}O_5$ requires: C, 68.67; H, 7.22%]. ν_{max}^{KBr} (cm^{-1}): 1760, 1721, 1697, 1272, 1248, 1148. λ_{max}^{EtOH} (nm): 259, 311 (ϵ 19600, 4700). PMR (100 MHz, $CDCl_3$, τ): 8.46 (*s*, Me), 8.39 (*s*, Me), 7.99 (*s*, MeCO), 7.74 (*s*, Me-8, MeCO), 7.45 (*s*, Me-5), 7.30 (*dd*, J 16.0, 12 Hz, H-4), 6.96 (*dd*, J 16 and 4 Hz, H-4), 6.80 (*dt*, J 12, 4 Hz, H-3), 4.56 (*d*, J 12 Hz, H-2), 3.00 (*d*, J 8 Hz, H-7), 2.78 (*d*, J 8 Hz, H-6). MS (*m/e*): 332 (2%) M^+, 272 (22), 231 (18), 230 (100), 213 (14), 212 (54), 201 (21), 189 (12), 187 (20),

184 (26), 172 (19), 171 (26), 149 (18), 146 (12), 91 (11), 59 (12), 43 (97).

(2R,3S)-2-*Acetoxy*-3-*isopropenyl*-5,8-*dimethyl*-1-*oxo*-1,2,3,4-*tetrahydronaphthalene* (**9**). Mixtures either of **1c** (100 mg) or of **1d** (100 mg) with TsOH (80 mg) in Ac_2O (15 ml) were freed of solvent by distillation, cooled, diluted with H_2O and extracted with Et_2O. The extract was washed with 10% NaOH and H_2O, dried and evaporated. The residue was chromatographed on alumina, and petrol eluted a chromatographically pure oil (yields from **1c** 51% and from **1d** 89%) [Found: M^+ 272. $C_{17}H_{20}O_3$ requires: 272]. ν_{max}^{film} (cm^{-1}): 1745, 1705, 1686, 1238, 1223, 1113, 1051, 902, 830. λ_{max}^{EtOH} (nm): 258, 308 (ϵ 19700, 5700). PMR (60 MHz, $CDCl_3$, τ): 8.19 (*t*, J 1.5 Hz, MeC=), 7.80 (*s*, MeCO), 7.75 (*s*, Me-5), 7.40 (*s*, Me-8), 7.05-6.84 (*m*, 2 H-4, H-3), 5.07 (*m*, CH_2), 4.50 (*d*, *J* 12 Hz, H-2), 2.94 (*d*, *J* 8 Hz, H-6), 2.77 (*d*, *J* 8 Hz, H-7). MS (*m/e*): 272 (34%) M^+, 213 (19), 212 (100), 197 (51), 184 (18), 171 (72), 169 (16), 159 (12), 146 (60), 118 (25), 117 (27), 115 (16), 103 (12), 91 (19), 43 (59), 41 (12), 28 (68). 1,2-*Dihydroxy*-3-(2′-*hydroxyisopropyl*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene*. An emmotin-F (240 mg) and $NaBH_4$ (500 mg) mixture in H_2O (5 ml) was stirred at room temp for 6 hr, acidified with conc HCl, diluted with H_2O (20 ml), concentrated under vacuum and extracted with $CHCl_3$. The extract was washed with 10% $NaHCO_3$ and H_2O, dried and evaporated. Residue (194 mg) was purified by Si gel chromatography to give a solid (120 mg; 62% yield), mp 230°. ν_{max}^{KBr} (cm^{-1}): 3470, 1410, 1302, 1282, 1211, 1136. PMR (60 MHz, $CDCl_3$, τ): 8.74 (*s*, Me), 8.64 (*s*, Me), 7.92 (*s*, Me-5), 7.59 (*s*, Me-8), 7.57–6.84 (*m*, 2 *H*-4, H-3), 6.17–5.67 (*m*, 3 OH), 3.09 (*m*, H-6, H-7).

2-*Hydroxy*-3-(2′-*hydroxyisopropyl*)-5,8-*dimethylnaphthalene* (emmotin-G, **4a**). mp 112–115° (EtOH) [Found: C, 78.44; H, 7.68. $C_{15}H_{18}O_2$ requires: C, 78.26; H, 7.83%]. ν_{max}^{KBr} (cm^{-1}) 3473, 3125, 1630, 1600, 1590, 1518, 1388, 1244, 1200, 1160, 950, 890, 860. λ_{max}^{EtOH} (nm): 233*i*, 243, 277i, 289, 301, 326i, 340 (ϵ 52500, 53900, 6000, 7400, 6500, 3200, 3700); $\lambda_{max}^{EtOH+NaOH}$ (nm): 230i, 254, 260i, 283, 290, 307, 360 (ϵ 25800, 55200, 48800, 6500, 7800, 5500, 5500). PMR (Table). MS (*m/e*): 230 (8%) M^+, 229 (45), 212 (100), 196 (38), 184 (25), 171 (12), 169 (35), 154 (10), 153 (15), 152 (12), 141 (12), 129 (10), 128 (17), 115 (11), 106 (12), 91 (10), 83 (11), 78 (14), 77 (18), 43 (26). Acetylation (Ac_2O–C_5H_5N) at room temp gave, in 81% yield, the *diacetate* (**4b**), mp 88–90° (EtOH) [Found: C, 72.51; H, 7.11. $C_{19}H_{22}O_4$ requires: C, 72.61; H, 7.01%]. ν_{max}^{KBr} (cm^{-1}): 1752, 1740, 1602, 1264, 1225, 1017, 918. λ_{max}^{EtOH} (nm): 242, 286i, 297 (ϵ 90400, 10100, 10700). PMR (60 MHz, $CDCl_3$, τ): 8.05 (*s*, 2 Me), 8.02 (*s*, MeCO), 7.62 (*s*, MeCO), 7.44 (*s*, ArMe), 7.35 (*s*, ArMe), 2.87 (*s*, H-6, H-7), 2.44 (*s*, H-4), 1.99 (*s*, H-1). MS (*m/e*): 314 (16%) M^+, 254 (91), 212 (37), 211 (100), 195 (14), 182 (12), 168 (15). A mixture of **4a** (10 mg) in MeOH (2 ml) and Fremy's salt (80 mg) in aq N NaOAc (2 ml) was stirred until the violet colour disappeared and extracted with EtOAc. The extract was washed, dried and evaporated under vacuum. The residue was purified on Si gel, giving red crystals (4 mg) identified by mp, mmp and spectral comparison with emmotin-H (**5**).

3-(2′-*Hydroxyisopropyl*)-5,8-*dimethyl*-1,2-*naphthoquinone* (emmotin-H, **5**) red crystals, mp 178–180° (hexane-Et_2O; 1:1) [Found: C, 73.90; H, 6.46. $C_{15}H_{16}O_3$ requires: C, 73.77; H, 6.55%]. ν_{max}^{KBr} (cm^{-1}): 3460, 1681, 1649, 1613, 1367, 1239, 1191, 1129. λ_{max}^{EtOH} (nm): 265, 437 (ϵ 40800, 6900). PMR (Table). MS (*m/e*): 244 (1%) M^+, 246 (1), 201 (10), 187 (20), 186 (100), 182 (17), 173 (35), 159 (13), 158 (64), 130 (14), 129 (27), 128 (27), 127 (14), 115 (24), 77 (11), 76 (10), 59 (50), 43 (18). A mixture of **5** (125 mg), anhydrous NaOAc (50 mg) and Zn powder (300 mg) in Ac_2O (4 ml) was refluxed for 5 min, cooled, filtered, poured into H_2O and extracted with $CHCl_3$. The extract was washed, dried and evaporated under vacuum. Residue was crystallized from EtOH to 1,2-*diacetoxy*-3-*isopropenyl*-5,8-*dimethylnaphthalene* (**13**) (115 mg, 25% yield), mp 141–143° [Found: C, 72.96; H, 6.41. $C_{19}H_{20}O_4$ requires: C, 73.06; H, 6.45%]. ν_{max}^{KBr} (cm^{-1}): 1768, 1445, 1373, 1346, 1205, 1161, 1150, 1028. λ_{max}^{EtOH} (nm): 243, 299 (ϵ 34300, 5700). PMR (60 MHz, $CDCl_3$, τ): 7.77 (*d*, *J* 1.5 Hz, MeC=), 7.68 (*s*, MeCO), 7.59 (*s*, MeCO), 7.33 (*s*, Me-5), 7.25 (*s*, Me-8), 4.6-4.9 (*m*, $=CH_2$), 2.82 (*s*, H-6, H-7), 2.13 (*s*, H-4). MS (*m/e*): 312 (11) M^+, 270 (19), 229 (20), 228 (100), 43 (60).

(2S,3S)-2-*Hydroxy*-3-(2′-*hydroxyisopropyl*)-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (**6a**). This was obtained by hydrogenation of emmotin-F (150 mg) in HOAc (10 ml) in presence of Pd/C (50 mg) in 86% yield, mp 140–142° (hexane) [Found: C, 77.05; H, 9.39. $C_{15}H_{22}O_2$ requires: C, 76.88; H, 9.46%]. ν_{max}^{KBr} (cm^{-1}): 3248, 1179, 1150, 1058, 1026, 819. λ_{max}^{EtOH} (nm): 223, 272 (ϵ 11200, 500). PMR (100 MHz, $CDCl_3$, τ): 8.66 (*s*, Me), 8.62 (*s*, Me), 8.30 (*s*, OH), 8.06 (*m*, *J* 12, 10, 5 Hz, H-3), 7.82 (*s*, ArMe), 7.80 (*s*, ArMe), 7.9–7.2 (*m*, H-1, H-4), 7.60 (*dd*, *J* 16, 5 Hz, H-4), 7.40 (*dd*, *J* 16, 6 Hz, H-1), 6.26 (broad, OH), 5.88 (*td*, *J* 10, 10, 6 Hz, H-2), 3.08 (*s*, H-6, H-7). MS (*m/e*): 234 (30%) M^+, 216 (11), 174 (28), 173 (100), 159 (13), 158 (54), 157 (31), 145 (18), 144 (41), 143 (59), 118 (13), 115 (13), 91 (14), 59 (57), 43 (26). (±)-**6a**, mp 127–128°, ν_{max}^{Nujol} (cm^{-1}): 3300, τ *ca* 6.5 (m, W_H 25 Hz, H_{ax}-2) [3].

6-*Isopropenyl*-1,4-*dimethylbenzo*[a]*phenazine* (**8**). (a) Preparation from emmotin F (**1c**). A mixture of **1c** (100 mg) and Pd/C (100 mg) in xylene (30 ml) was refluxed for 90 hr, cooled, filtered and evaporated under vacuum. Residue was chromatographed on Si gel to give 3-*isopropenyl*-5,8-*dimethyl*-1,2-*naphthoquinone* (**7**), a red solid (11 mg; 12% yield), ν_{max}^{KBr} (cm^{-1}): 1681, 1662, 1623, 1383, 1238. A mixture of **7** (5 mg) in EtOH (2 ml) and *o*-phenylenediamine (2 mg) was stirred at 100° for 45 min and evaporated under vacuum. The residue was chromatographed on Si gel to give the quinoxaline **8** (5 mg, 79% yield). (b) Preparation from emmotin-H (**5**). A mixture of **5** (122 mg) in EtOH (20 ml) and *o*-phenylenediamine (200 mg) was treated as described under a). The residue was crystallized from EtOH to give yellow crystals of 6-(2′-*hydroxyisopropyl*)-1,4-*dimethylbenzo*[a]*phenazine* (**12**) (121 mg, 82% yield), mp 190–192° [Found: C, 79.64; H, 6.39; N, 8.17. $C_{21}H_{20}N_2O$ requires: C, 79.74; H, 6.32; N, 8.86%]. ν_{max}^{KBr} (cm^{-1}): 3357, 1623, 1580, 1378, 1340, 1163, 1127, 933, 900, 818, 758. λ_{max}^{EtOH} (nm): 241, 263, 292, 406, 425 (ϵ 31100, 32900, 33200, 9500, 10100). PMR (60 MHz, $CDCl_3$, τ): 8.05 (*s*, 2 Me), 7.22 (*s*, Me-5), 6.64 (*s*, Me-8), 2.53 (*s*, H-6, H-7), 2.0–2.2 (*m*, BB′ part of AA′BB′ system), 1.83 (*s*, H-4), 1.8–2.0 (*m*, AA′ of AA′BB′). MS (*m/e*): 316 (15%) M^+, 302 (23), 301 (100), 283 (21), 273 (12). A mixture of **12** (87 mg), C_5H_5N (0.5 ml) and Ac_2O (5 ml) was refluxed for 16 hr. Standard work-up and crystallization of the product from EtOH gave the quinoxaline **8** (60 mg, 74% yield). (c) The samples of **8**, prepared according to (a) and (b), yellow crystals, mp and mixture mp 157–160° [Found: C, 84.41; H, 6.00; N, 9.54. $C_{21}H_{18}N_2$ requires: C, 84.53; H, 6.08; N, 9.39%] had superimposable spectra. ν_{max}^{KBr} (cm^{-1}): 1626, 1374, 1347, 1129, 1012, 875, 811, 754. λ_{max}^{EtOH} (nm): 249, 262, 291, 406, 425 (ϵ 28000, 29200, 27600, 9000, 12000). PMR (60 MHz, $CDCl_3$, τ): 7.47 (*t*, *J* 1.5 Hz, MeC=), 7.22 (*s*, Me-5), 6.58 (*s*, Me-8), 4.53 (*m*, $=CH_2$), 2.52 (*s*, H-6, H-7), 2.0–2.2 (*m*, BB′ part of AA′ BB′ system), 1.98 (*s*, H-4), 1.8–2.0 (*m*, AA′ of AA′BB′). MS (*m/e*): 298 (73%) M^+, 282 (100), 268 (21).

(2R)-2-(2′-*hydroxyisopropyl*)-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* [(+)-occidol, **11b**]. A mixture of emmotin-F diacetate (**1d**) (255 mg) and Zn powder (1 g) in HOAc (20 ml) was refluxed for 7 hr, cooled, filtered, diluted with Et_2O, washed with 5% aq NaOH and with H_2O, dried and evaporated. The oily residue (210 mg) was chromatographed on alumina, C_6H_6–$CHCl_3$ (1:1) eluting chromatographically pure 2-*dehydroxyemmotin*-F *acetate* (**10a**) as an oil (126 mg, 60%) [Found: M^+ 274. $C_{17}H_{22}O_3$ requires: 274]. ν_{max}^{film} (cm^{-1}): 1737, 1677, 1574, 1260, 1137, 1102, 1020, 842. λ_{max}^{EtOH} (nm): 258, 311 (ϵ 23000, 5500). PMR (60 MHz, $CDCl_3$, τ): 8.47 (*s*, 2 Me), 8.04 (*s*, MeCO), 7.75 (*s*, Me-5), 7.44 (*s*, Me-8), 6.7–7.6 (*m*, 2 H-4, 2 H-2, H-3), 3.04 (*d*, J 7.5 Hz, H-7), 2.82 (*d*, J 7.5 Hz, H-6). MS (*m/e*): 274 (2%) M^+, 215 (18), 214 (95), 199 (45), 173 (18), 172 (53), 171 (100), 159 (26), 158 (24), 157 (13), 129 (13), 128 (13), 115 (15), 91 (15), 59 (11), 57 (10), 55 (10), 43 (56). A soln of **10a** (100 mg) in EtOH (10 ml) was refluxed (7 hr) with 5% KOH in EtOH (15 ml). Standard work-up

gave **10b** (75 mg, 94% yield) [Found: M^+ 232. $C_{15}H_{20}O_2$ requires: 232] ν_{max}^{film} (cm^{-1}): 3448, 1667. PMR (60 MHz, $CDCl_3$, τ): 8.79 (*s*, 2 Me), 7.9–6.9 (*m*, 2 H-4, 2 H-2), 7.72 (*s*, Me-5), 7.40 (*s*, Me-8), 3.02 (*d*, *J* 7.5 Hz, *H*-7), 2.77 (*d*, *J* 7.5 Hz, H-6). A mixture of **10a** (200 mg) and Pd–C (200 mg) in HOAc (15 ml) was hydrogenated, filtered, neutralized with 10% $NaHCO_3$ and extracted. with $CHCl_3$. The extract was washed, dried and evaporated under vacuum, yielding chromatographically pure *occidol acetate* (**11a**) as an oil (122 mg, 65% yield) [Found: M^+260. $C_{17}H_{24}O_2$ requires: 260]. ν_{max}^{film} (cm^{-1}): 1730, 1370, 1256, 1136, 1020, 810. λ_{max}^{EtOH} (nm): 223i, 261 (ε 13100, 1300). PMR (60 MHz, $CDCl_3$, τ): 8.9–8.3 (*m*, 2 H-3), 8.40 (*s*, 2 Me), 7.95 (*s*, MeCO), 7.75 (*s*, Me-5), 7.7–7.1 (*m*, 2 H-1, 2 H-4, H-2), 3.03 (*s*, H-6, H-7). MS (*m/e*): 260 (5%) M^+, 201 (16), 200 (80), 186 (16), 185 (100), 159 (14), 158 (12), 157 (73), 145 (11), 144 (11), 143 (11), 142 (11), 129 (10), 59 (10), 43 (62), 28 (47). A mixture of **11a** (70 mg) in EtOH (10 ml) and ethanolic 5% KOH (20 ml) was refluxed for 5 hr, cooled, neutralized with dil HCl and extracted with $CHCl_3$. The extract was washed, dried and evaporated under vacuum. The residue was recrystallized from hexane, giving (+)-*occidol* (**11b**) (64 mg, 99% yield) mp 68–70°, $[\alpha]_D$ +120° (EtOH), lit. [2] mp 69–70°, $[\alpha]_D$ +163.7° ($CHCl_3$) [Found: C, 82.53; H, 10.20. $C_{15}H_{22}O$ requires: C, 82.51; H, 10.16%]. ν_{max}^{KBr} (cm^{-1}): 3360, 1600, 1463, 1376, 1357, 1130, 978, 923, 808. λ_{max}^{EtOH} (nm): 224i, 266 (ε 14400, 900). PMR (60 MHz, $CDCl_3$, τ): 8.61 (*s*, 2 Me), 8.1–8.6 (*m*, 2 H-3), 8.34 (*s*, OH, disappeared with D_2O), 7.70 (*s*, Me-5, Me-8), 7.0–7.9 (*m*, 2 H-1, 2 H-4, H-2), 3.00 (*s*, H-6, H-7). MS (*m/e*): 218 (39%) M^+, 211 (22), 210 (96), 190 (18), 189 (100), 165 (65), 164 (37), 163 (91), 162 (23), 151 (52), 150 (26), 149 (26), 138 (22), 135 (28), 125 (53), 58 (38).

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