

Thespesenone and Dehydrooxoperezinone-6-methyl Ether, New Sesquiterpene Quinones from *Thespesia populnea*

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Thespesia populnea grows as a small tree or large shrub that occurs throughout Polynesia. We report the isolation of 7-hydroxycadalene (**6**), thesipesenone (**7**), and dehydrooxoperezinone-6-methyl ether (**8**) from its red heartwood. Compounds **7** and **8** are reported for the first time in nature. Several other sesquiterpene quinones were isolated including mansonone E (**4**), mansonone F (**3**), mansonone D (**1**), mansonone G (**9**), mansonone M (**10**), and thesipesone (**4**); the ^{13}C NMR spectra of these compounds are reported for the first time.

Cotton plants (*Gossypium hirsutum*) produce various sesquiterpenes when they are attacked by pathogens. These compounds are often toxic to the pathogen and thus help protect the plant from attack. *Thespesia populnea* (L.) Solander Correa (Malvaceae) (also called Milo or Portia tree) is a small tree that grows in Hawaii. The heartwood of *T. populnea* is a rich source of sesquiterpenoid quinones including mansonones C, D (**1**), E (**2**), and F (**3**), thesipesone (**4**), and thesipesone,¹ as well as mansonone H (**5**)² and 7-hydroxy-2,3,5,6-tetrahydro-3,6,9-trimethylnaphtho[1,8-*b*,*c*]pyran-4,8-dione.³ These compounds are similar to those produced in cotton; therefore, we are interested in determining the toxicity of the compounds in *T. populnea* to the pathogens that attack cotton. To obtain sufficient amounts of authentic compound for bioassay, CHCl_3 extracts from the dark heartwood of *T. populnea* were separated by chromatography techniques. Several known sesquiterpene quinones, 7-hydroxycadalene (**6**) and gossypol, were isolated along with two new sesquiterpenoid quinones, thesipesenone (**7**) and dehydrooxoperezinone-6-methyl ether (**8**), which we report on herein. The ^{13}C NMR spectra of mansonone D (**1**), mansonone G (**9**), mansonone M (**10**), and thesipesone (**4**) are also reported for the first time.

Thesipesenone (**7**) gave orange crystals with a melting point of 178–179 °C. MS provided a parent ion at m/z 256, while high-resolution TOF-ESI for the $M + 1$ ion indicated a molecular formula of $\text{C}_{15}\text{H}_{13}\text{O}_4$. The ^1H NMR was unusually simple with three methyl groups at δ 2.09 (singlet), 2.82 (singlet), and 2.51 (doublet) and two protons on sp^2 carbons at δ 7.48 (singlet) and 7.53 (quartet). This was consistent with the number of protons given in the high-resolution MS assuming one proton on a hydroxyl group. A COSY experiment and the proton–proton coupling constants showed that the quartet at δ 7.53 and the doublet at δ 2.51 were coupled, as were the broad singlets at δ 7.48 and 2.82. The ^{13}C NMR (Table 1) showed two quinone carbons at δ 182.5 and 186.4, which account for two additional oxygen atoms. An HMBC experiment was very informative. The first quinone carbon (δ 182.5) was weakly coupled to the methyl protons at δ 2.09 and 2.82, while the latter (δ 186.4) was weakly coupled to the methyl protons at δ 2.09. The methyl protons at δ 2.09 were also coupled to the carbon at δ 152.4, which is presumably the carbon to which an oxygen atom is attached, and to the carbon at δ 118.4. An additional aromatic carbon to which

Table 1. ^{13}C NMR Chemical Shifts (δ) for Mansonone D (**1**), Thesipesone (**4**), Thesipesenone (**7**), Dehydrooxoperezinone-6-methyl Ether (**8**), Mansonone G (**9**), and Mansonone M (**10**)

C#	1 ^a	4 ^a	7 ^a	8 ^a	9 ^b	10 ^a
1	178.8	180.5	182.5	178.1	180.9	180.5
2	182.6	153.8	152.4	180.5	182.9	181.0
3	136.7	117.7	118.4 ^c	109.1	136.8	116.6
4	137.4	186.3	186.4	169.1	138.7	161.6
4a	132.9	131.1	129.9	135.8	135.8	128.1
5	130.8	134.2	126.4	132.6	133.2	126.5
6	165.0	165.6	160.0	158.2	162.6	160.0
7	113.4	116.2	118.6	115.5	120.5	114.6
8	149.6	146.0	138.8	148.7	145.9	146.1
8a	122.5	120.7	123.7	117.4	123.5	120.7
9	34.6	37.1	118.3 ^c	96.9	27.5	26.1
10	79.9	80.4	146.4	25.8	21.3	71.7
11	22.0	19.7	13.5	25.8	21.3	17.4
12	23.8	23.9	23.9	21.0	23.2	23.5
13	15.8	8.4	8.6	7.9	15.7	7.9
OMe				56.3		55.9

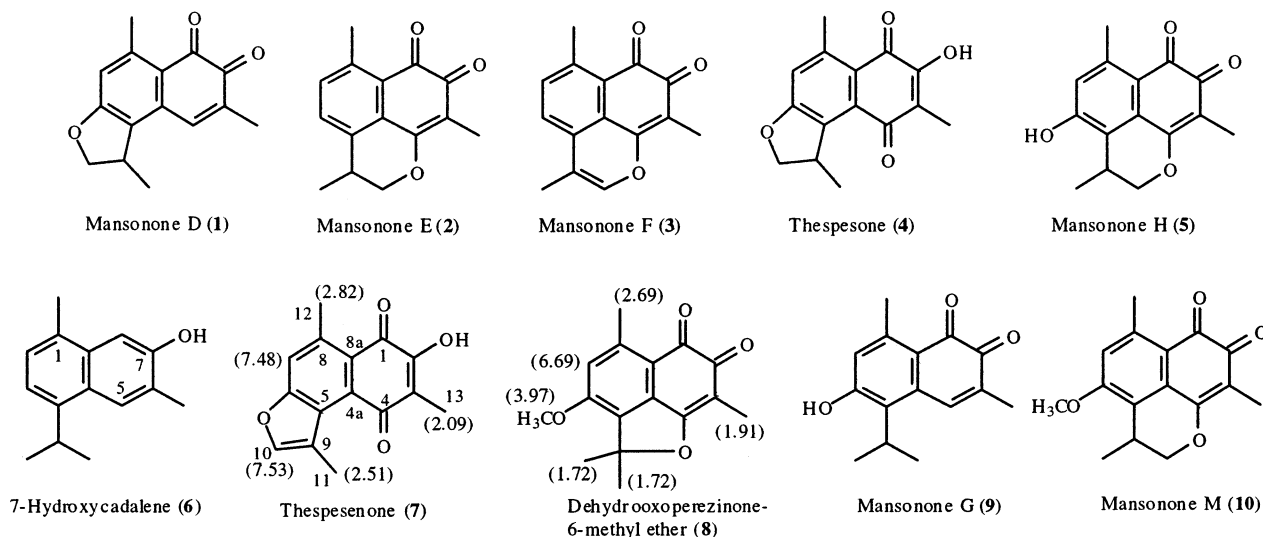
^a Solvent: CDCl_3 . ^b Solvent: acetone- d_6 . ^c Peaks so marked may be interchanged.

an oxygen is attached appeared at δ 160.0. This accounts for all oxygens in the molecule. The chemical shift (δ 146.4) of the carbon to which the proton at δ 7.53 was directly attached indicated this carbon was also oxygenated. Additionally, the δ 7.53 proton showed weak coupling to the oxygenated aromatic carbon at δ 160.0 and a second carbon at δ 126.4. The methyl group at δ 2.51 showed proton–carbon coupling to the carbons at δ 118.3, 146.4, and 126.4. These data are consistent with these carbons being part of a methyl-substituted furan ring. The aromatic proton at δ 7.48 showed *meta* coupling to carbons at δ 126.4 and 123.7 with additional coupling to the oxygenated carbon at δ 160.0 while being directly attached to the carbon at δ 118.6. Last, the aromatic methyl protons at δ 2.82 showed long-range coupling to the carbon to which the methyl group is attached (δ 138.8) and to the carbons *ortho* to this carbon (i.e., δ 118.6 and 123.7). Very weak coupling was also observed to the carbon at δ 129.9. An HMQC experiment showed that the methyl protons at δ 2.82, 2.51, and 2.09 were directly attached to carbons with chemical shifts at δ 23.9, 13.5, and 8.6, respectively. On the basis of these observations, we deduced its structure to be **7**.

The ^{13}C NMR of **4** is reported for the first time in Table 1. All assignments are based on HMBC and HMQC experiments. The similarity between the quinone carbons

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Chart 1



in **4** and those in **7** further confirms the structure of **7** as a *para*-quinone.

Dehydrooxoperezinone-6-methyl ether (**8**) was isolated as orange crystals with mp 249–253 °C. HRMS indicated the formula $\text{C}_{16}\text{H}_{16}\text{O}_4$. The ^1H NMR was uncomplicated, being composed of five singlets representing an aromatic proton at δ 6.69 and five methyl groups at δ 3.97 (O-CH₃), 2.69 (3H), 1.91 (3H), and 1.72 (6H). A COSY experiment showed only one proton–proton coupling, the proton on the aromatic ring (δ 6.69) being weakly coupled to the methyl group at δ 2.69. DEPT, HMBC, and HMQC experiments showed the following: two sp^2 carbon atoms attached to oxygens at δ 169.1 and at 158.2; quinone carbonyls at δ 180.5 and 178.1; a methoxy group at δ 56.3; a proton-substituted aromatic carbon at δ 115.5; and methyl carbons at δ 25.8 (2 each), 21.0, and 7.9. On the basis of the NMR spectra and molecular formula, structure **8** was proposed. The parent phenol of **8**, dehydrooxoperezinone, has previously been identified in the roots of *Aristolochia liukiuensis*.⁴ The ^{13}C NMR spectrum⁵ of the latter was in excellent agreement with **8** with the exception of the presence of an additional methoxy group at δ 56.3 in **8**. This is the first report of dehydrooxoperezinone-6-methyl ether (**8**) in nature, although it was synthesized in 1968.⁶ The synthetic product gave a UV spectrum with λ_{max} 204, 222, 226, 266, 291, 358, and 435 nm, which was in excellent agreement with the UV spectrum of **8**. Kazuhito et al.⁴ prepared the methyl ether of dehydrooxoperezinone and reported ^1H NMR and mass spectra plus a melting point of 252–253 °C that are in excellent agreement with our results.

Mansonone M (**10**) was prepared from isolated mansonone H (**5**).⁷ The structure of the synthesized mansonone M (**10**) along with those of isolated mansonone D (**1**), mansonone G (**9**), and thesipesone (**4**) were determined by comparison to spectral data reported in the literature^{1,7,8} and by detailed DEPT, HMBC, and HMQC experiments. The ^{13}C NMR chemical shifts for thesipesone (**4**) and mansonones D (**1**), G (**9**), and M (**10**) are reported for the first time in Table 1. The structure of 7-hydroxycadalene (**6**) was determined by comparison to an authentic synthetic sample.⁹ The structures of mansonones E (**2**) and F (**3**) were determined by comparison to published spectral data.¹⁰

Experimental Section

General Experimental Procedures. High-resolution MS were obtained on a Perkin-Elmer QStar TOF/MS using elec-

troscopy ionization. Other MS were obtained on a Thermo Finnigan Trace DSQ mass spectrometer. NMR spectra were obtained on Bruker Avance-300 or ARX-500 spectrometers. UV spectra were obtained on a Hewlett-Packard 8453 spectrometer in 95% ethanol.

Extraction and Isolation. Dark heartwood of *T. populnea* was purchased from Winkler Woods, Kurtistown, HI. Sawdust from the heartwood was generated via a power sander and then extracted with CHCl_3 . The individual mansonone- and thesipesone-type compounds were isolated from this extract using various chromatography procedures. Details on the extraction of the heartwood sawdust and purification of the individual compounds are provided in the Supporting Information.

Thespesone (7): orange solid; mp 178–179 °C; UV (EtOH) λ_{max} (log ϵ) 207 (4.20), 260 (4.16), 299 (3.94), 401 (3.35); ^1H NMR (CDCl_3) δ 7.48 (1H, bs, C-7), 7.53 (1H, q, $J = 1.26$ Hz, C-10), 2.51 (3H, d, $J = 1.26$ Hz, C-11), 2.82 (3H, bs, C-12), 2.09 (3H, s, C-13); ^{13}C NMR, see Table 1; EIMS m/z 256 [$\text{M}]^+$ (100), 228 (69), 227 (17), 200 (20), 199 (20), 185 (27), 173 (13), 172 (11), 171 (13), 157 (11), 152 (11), 145 (14), 129 (13), 128 (35), 127 (14), 115 (46), 90 (12), 76 (12), 63 (13); HRESTOF (MeOH) m/z 257.0829 [$\text{M} + 1]^+$ (calcd for $\text{C}_{15}\text{H}_{13}\text{O}_4$, 257.0813).

Dehydrooxoperezinone-6-methyl ether (8): orange solid; mp 249–253 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.32), 221 (4.24), 266 (4.29), 290 (4.15), 355 (3.85), 429 (3.45); ^1H NMR (CDCl_3) δ 6.69 (1H, s), 3.97 (3H, s), 2.69 (3H, s), 1.91 (3H, s), 1.72 (6H, s); ^{13}C NMR, see Table 1; EIMS m/z 272 (100), 257 (13), 245 (17), 244 (86), 229 (74), 216 (18), 215 (24), 202 (14), 201 (77), 185 (12), 173 (20), 158 (12), 157 (13), 129 (27), 128 (39), 127 (15), 115 (45), 83 (20), 77 (13); HRESTOF (EtOH) m/z 273.1136 [$\text{M} + 1]^+$ (calcd for $\text{C}_{16}\text{H}_{17}\text{O}_4$, 273.1127).

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Supporting Information Available: Details on the extraction of the compounds from the heartwood and their purification are available free of charge via the Internet at <http://pubs.acs.org>.

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