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ISOLATION AND STRUCTURES OF NEW TANSHINONES

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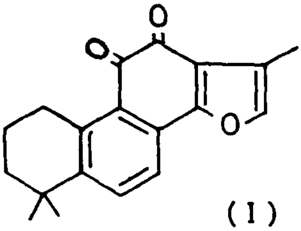
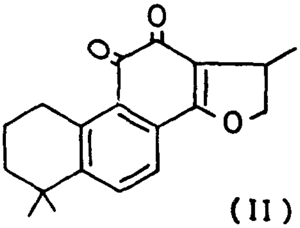
Three red crystalline pigments were isolated from Chinese drug "tan-shin", the dried red roots of Salvia miltiorrhiza Bunge, by Nakao in 1930 (1). The pigments were named tanshinone-I, -II and -III, and were characterized as *o*-quinones. Later Takiura found a new tanshinone, tanshinone-IIB(2), and showed that tanshinone-III was a mixture of tanshinone-II and another pigment which he named cryptotanshinone (3). The structures of tanshinone-I, -II(I), -IIB and cryptotanshinone(II) were determined by von Wessely(4), Kakisawa(5), Thomson(6) and Takiura(7), respectively. A possible biogenetic relationship of all these pigments to diterpenoids was discussed by Todd (8) and Wenkert (9). New tanshinones were isolated from "tan-shin" and we wish to report the structures of these new pigments in this communication.

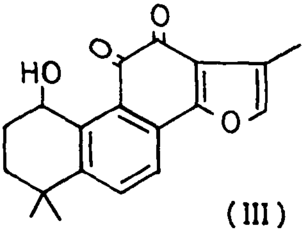
Two new quinones, hydroxytanshinone and methyl tanshinonate, were isolated in 0.005 and 0.002% yield, respectively, by repeated chromatography of the crude extracts. Spectral properties of these pigments, and tanshinone-II as a reference, are listed in the Table. The ultraviolet-visible absorption spectra of these pigments are all superimposable on that of tanshinone-II(I), and their IR spectra also exhibit similar absorption patterns to that of tanshinone-II in 3200-1500cm^{-1} region. These spectral properties showed that each of these compounds has the same furo-*o*-naphthoquinone chromophore.



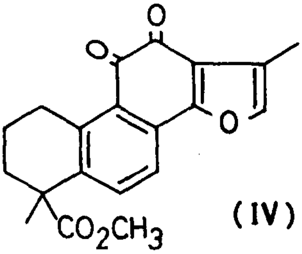
(I)



(II)



(III)



(IV)

TABLE

	λ_{max}^{EtOH} mμ	ν_{max}^{KBr} cm^{-1}	NMR δ^{CDCl_3} ppm	$[\alpha]_D$
Tanshinone-II	460 352 269 252 224	3150 1690 1670 1583 1535	1.30(s 6H) 1.7 (br m 4H) 2.25(d 3H) 3.15(br t 2H) 7.10(q 1H) 7.48(q 2H)	——
Hydroxy-tanshinone	462 348 273 252 222	3525 3150 1685 1670 1580 1535	1.28(s 3H) 1.40(s 3H) 2.04(br m 4H) 2.25(d 3H) 4.38(br s 1H) 4.98(br s 1H) 7.20(q 1H) 7.62(q 2H)	0°
Methyl tanshinonate	465 352 269 252 223	3150 1725 1690 1670 1580 1540	1.62(s 3H) 1.8 (br m 4H) 2.26(d 3H) 3.25(br t 2H) 3.66(s 3H) 7.25(q 1H) 7.52(q 2H)	−139°

Hydroxytanshinone, mp 187°, has the composition $C_{19}H_{18}O_4$(M^+310) and then it possesses one more oxygen atom than tanshinone-II. This was revealed as a hydroxy group by the absorption at 3525 cm^{-1} in its IR spectrum. The NMR spectrum of hydroxytanshinone shows a striking resemblance in many of its features to that of tanshinone-II and exhibits that the former possesses two ortho-benzenoid protons, a gem-dimethyl group bonded to a saturated carbon atom and a methyl group attached to a furan ring which is unsubstituted in the α-position. However, there are differences between the two spectra in two respects: the former lacks the 2-proton multiplet(3.15 ppm) of the benzylic methylene at C_1 of tanshinone-II but contains one-proton multiplet(4.38 ppm) characteristic of a benzyl alcohol. From these spectral properties the structure of hydroxytanshinone was deduced to 1-hydroxy-tanshinone-II(III) and it was confirmed by catalytic hydrogenation. Pd-catalyzed hydrogenation of hydroxytanshinone followed by air oxidation of the resultant leuco-compound afforded a mixture of two substances, one of which was identical with tanshinone-II(I) in all respects and another was identified as cryptotanshinone(II). Both compounds were produced by the hydrogenolytic removal of the benzylic hydroxy group.

Second new pigment, methyl tanshinonate, mp 175-176°, has also a furo-o-naphthoquinone chromophore, because the UV and IR(3500-1500cm^{-1}) spectra of the pigment are virtually identical with those of tanshinone-II. The pigment has the molecular formula $C_{20}H_{18}O_5$ (M^+ 338), therefore it possesses one carbon and two oxygen atoms more than tanshinone-II. They were revealed as a carbomethoxy group by an absorption at 1725 cm^{-1} in the IR spectrum and a sharp singlet at 3.66 ppm in the NMR spectrum. The position of the carbomethoxy group and the carbon skeleton were established from the NMR spectrum. The NMR spectrum of methyl tanshinonate is very similar to that of tanshinone-II, showing that former has two ortho-benzenoid protons, two benzylic protons adjacent to a methylene group, and a methyl group attached to a furan ring which is unsubstituted in the α-position. However, major differences are seen at high field where the 6-proton singlet at 1.30 ppm (gem-dimethyl group) in tanshinone-II is replaced by a 3-proton singlet at 1.62 ppm and an ester-methyl peak at 3.66 ppm in the spectrum of methyl tanshinonate. From these properties the structure (IV) was assigned to methyl tanshinonate.

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