

## The Structure of Miltirone, a New Diterpenoid Quinone

By T. HAYASHI and H. KAKISAWA\*

(Department of Chemistry, Tokyo Kyoiku University, Otsuka, Tokyo, Japan)

and HONG-YEN HSŪ and YUH PAN CHEN

(Chinese Drugs Research Institute, College of Chinese Culture, Taipei, Taiwan)

**Summary** A new diterpenoid quinone has been isolated and characterized on the basis of the chemical and spectroscopic properties.

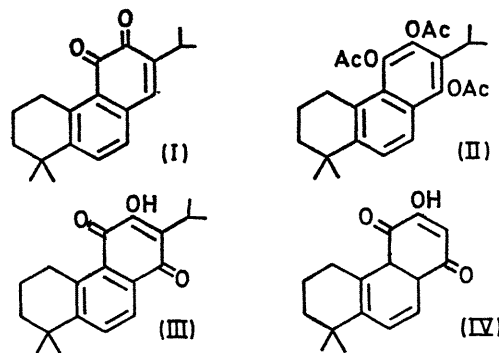
FROM the roots of *Salvia miltiorrhiza* Bunge, a new red crystalline pigment, designated miltirone (I),  $C_{19}H_{22}O_2$ , m.p.  $100^\circ$ ,  $M^+$  282.161 (calc. 282.162), was isolated, in addition to many tanshinones,<sup>1,2</sup> diterpenoid quinones having furonaphthaquinone chromophores.

The i.r. spectrum of miltirone (I) shows strong carbonyl absorptions at 1680(sh), 1660, and  $1635\text{ cm}^{-1}$  (KBr), characteristic of *ortho*-quinones, and the u.v. absorption maxima at 260 ( $\log \epsilon$  4.55), 362(3.36), and 436nm(3.52) (EtOH) indicate the presence of an alkyl-substituted 1,2-naphthaquinone chromophore.<sup>3</sup> The position of the alkyl groups and the carbon skeleton were deduced from the n.m.r. spectrum. The n.m.r. spectrum shows a *gem*-dimethyl group ( $\delta$  1.30) bonded to a saturated carbon atom, and an isopropyl group ( $\delta$  1.50, d, 6H,  $J$  7 Hz;  $\delta$  3.02, br. septet, 1H) attached to an aromatic ring. Two benzylic protons ( $\delta$  3.20 br t) adjacent to a methylene group ( $\delta$  1.7, m, 4H) appear at lower field as a result of the deshielding effect of the carbonyl group at C-11, the effect of which is typical of tanshinones.<sup>2</sup> In the aromatic region, one proton appears at  $\delta$  7.10 ( $J$  1 Hz) as a doublet which is coupled with a methine proton of the isopropyl group (as deduced from double-resonance studies), and two protons appear as an AB quartet centred at  $\delta$  7.34 ( $\Delta\delta$  0.4,  $J$  8 Hz), which shows the presence of two *ortho*-disposed benzenoid protons.

From these spectral properties, the structure (I) was assigned to miltirone, and this was confirmed by chemical evidence.

Miltirone was allowed to react with acetic anhydride and sulphuric acid to give the triacetate (II),  $\nu_{\max}$  ( $\text{CHCl}_3$ )  $1765\text{ cm}^{-1}$ . Hydrolysis of this acetate, followed by

chromic acid oxidation, afforded a hydroxy-1,4-naphthaquinone (III),  $\nu_{\max}$  ( $\text{CHCl}_3$ ) 3350 and  $1645\text{ cm}^{-1}$ . The n.m.r. spectrum of hydroxy-quinone (III) is very similar to that of (I), showing a *gem*-dimethyl group ( $\delta$  1.33), isopropyl group ( $\delta$  1.30, d, 6H,  $J$  7 Hz) attached to a double bond, and two benzylic protons ( $\delta$  3.30 br t) adjacent to a methylene group ( $\delta$  1.75, m, 4H). However, major differences are seen in the aromatic region, where 14-H doublet at  $\delta$  7.10 in miltirone (I) is replaced by a sharp singlet of a



hydroxy-proton ( $\delta$  7.82), which is exchangeable with  $\text{D}_2\text{O}$ , and the AB quartet of two benzenoid protons of (I) is shifted to low field (ABq centred at  $\delta$  7.95,  $\Delta\delta$  0.2,  $J$  8 Hz) in the spectrum of (III). The u.v. spectrum of (III), 250(sh), 256.5, 285—290, and 358 nm, is almost identical with that of a synthetic compound<sup>4</sup> (IV), thus establishing that (III) has a hydroxy-naphthaquinone moiety like that in (IV) and the full structure (III).

We thank Dr. Y. Yamada for the n.m.r. measurements.

(Received, January 13th, 1970; Com. 057.)

\* A. C. Baillie and R. H. Thomson, *J. Chem. Soc. (C)*, 1968, 48.

<sup>2</sup> H. Kakisawa, T. Hayashi, and T. Yamazaki, *Tetrahedron Letters*, 1969, 301.

<sup>3</sup> L. Mandell, *J. Amer. Chem. Soc.*, 1956, **78**, 3199.

<sup>4</sup> Y. Inouye and H. Kakisawa, *Bull. Chem. Soc. Japan*, 1969, **42**, 3318.