The Structures of Cassumunaquinones 1 and 2 from *Zingiber cassumunar*

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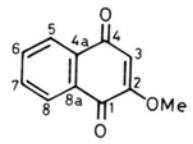
Z. Naturforsch. **35 c,** 154–155 (1980);
received September 17, 1979

Zingiber cassumunar Roxb. Zingiberaceae, Phenyl-Substituted Naphthaquinones, ^{13}C N.M.R. Spectroscopy

Two novel pigments have been isolated from the lyophilised rhizomes of *Zingiber cassumunar*, wild ginger from Thailand. Their structures have been established by spectroscopic means as 2-methoxy-8(3,4-dimethoxyphenyl)-1,4-naphthaquinone (cassumunaquinone 1) and 2-methoxy-8(2,4,5-trimethoxyphenyl)-1,4-naphthaquinone (cassumunaquinone 2).

Wild ginger (rhizome of *Zingiber cassumunar* (Roxb)) has been used in folklore medicine throughout tropical parts of East Asia *e.g.* in Thailand, as a remedy against thrombophlebitis. Preliminary tlc-experiments of the lipophilic extractives revealed the presence of two red spots (silica gel; toluene-$CHCl_3$ [2 : 8]; $R_f = 0.20$ and 0.18). The fractionation of a toluene-extract from lyophilized rhizomes led to the isolation of both these pigments, which were named cassumunaquinones 1 and 2. The isolation procedure [1] comprises firstly chromatography on silica gel columns using toluene-$CHCl_3$ [2 : 8] followed by re-chromatography on SC (using toluene-$CHCl_3$ [2 : 8], toluene-acetone [9 : 1] and cyclohexane-ethyl acetate [9 : 1], as eluents) and finally chromatography on thick-layer-plates. Although the pigments are rather unstable against oxidation and light and are present in only small concentration (10^{-3}% of the dried drug) we were able to obtain them in a crystalline state.

Cassumunaquinone 1 (CQ 1), m. p. 183.5–185 °C had the molecular formula $^{12}C_{19}H_{16}O_5$ (M^+ 324.0998) and cassumunaquinone 2 (CQ 2) had m. p. 163.5–165 °C and formula $^{12}C_{20}H_{19}O_6$ (M^+ 354.1086). Cassumunaquinone 1 (CQ 1) had λ_{max}($CHCl_3$), 241 (4.33), 275 (4.27), 279 (4.29) and 346 nm (3.39) and cassumunaquinone 2 (CQ 2) absorbed at 242 (4.34), 275 (4.24), 280 (4.24) and 325 nm (3.69). The UV spectra of the two compounds showed that they were closely related, and moreover were extremely similar to lawson methyl ether (**1**) which absorbs at 241 (4.23), 247 (4.24), 276 (4.17) and 333 nm (3.45). All three compounds also showed the same peaks at 1668, 1615 and 1600 cm^{-1} in the carbonyl region of the IR (KBr) spectrum. The ^1H NMR supports the hypothesis that both compounds are 2-methoxynaphthaquinones as CQ 1 has signals due to H-3 at 6.15 s * (1 H) and the 2-OMe at 3.83 s (3 H), and CQ 2 has the corresponding signal at 6.07 s (1 H) and 3.83 s (3 H). These compare with similar signals from **1** at 6.15 and 3.86.



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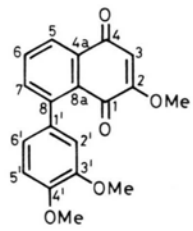

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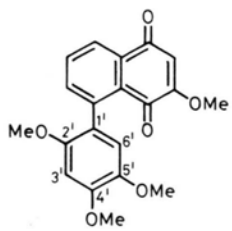

3

The ^1H NMR spectrum of CQ 1 differed from that of **1** in that **1** shows a four proton multiplet between δ7.6–8.2, whereas in that region the ^1H NMR spectrum of CQ 1 has signals at 8.15 d, J 7 (1 H) due to H-5 (see structure **2**), 7.8 d.d. J_{65}, 7, J_{67}, 7, (1 H) due to H-6 and at 7.6 d. J 7 (1 H) due to H-7. CQ 2 similarly has signals at 8.05 d, J 6 (1 H), 7.65 d.d., $J_1$6, $J_2$6 (1 H) and 7.4 d, J 6 (1 H). Hence both compounds are 2-methoxynaphthaquinones substituted at either the 5- or 8-positions.

CQ 1 exhibits peaks due to three aromatic protons as a multiplet from 7.15–6.75, together with peaks due to two aromatic methoxyl groups at 3.94 s (3 H) and 3.89 s (3 H). Hence the 5- or 8-substituent of CQ 1 is a dimethoxyphenyl residue.

CQ 2 shows two aromatic protons at 6.6 s (1 H) and 6.46 s (1 H) together with three methoxyl signals at 3.94 s (3 H), 3.89 (3 H) and 3.88 s (3 H). Thus

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* All ^1H NMR values in δ.

Table I. ^{13}C NMR of cassumumaquinones 1 and 2 [a, b, c].

Carbon atom	1	2	Calcd. Value	3	Calcd. Value
C-1	179.5	179.9		179.8	
C-2	168.6	161.1		161.2	
C-3	103.0	108.0		108.4	
C-4	179.3	184.6		184.9	
C-4 a	132.0	133.0		133.2	
C-5	129.0	126.0		125.8	
C-6	135.0 *	137.1 *		137.2 *	
C-7	131.5 *	133.0 *		133.2 *	
C-8	125.0	133.0		149.5	
C-8 a	130.0	128.3		129.5	
C-1′		133.0	134.8	121.5	120.4
C-2′		111.1	114.1	150.6	152.2
C-3′		143.9	145.9	97.8	101.1
C-4′		148.7	144.5	143.3	145.5
C-5′		111.9	115.5	139.6	138.2
C-6′		120.5	120.8	113.5	115.1

[a] All spectra run in DMSO. Chemical shifts given in ppm. downfield from TMS. [b] All assignments supported by the multiplicity of signals in the off-resonance spectra. [c] Identical superscripts indicate interchangeable assignment, in any one column.

CQ2 is a 2-methoxynaphthaquinone substituted at C-5 or C-8 by a trimethoxyphenyl residue, of which the substitution pattern is such that the aromatic protons are *para*.

That CQ1 and CQ2 are indeed 2-methoxynaphthaquinones is emphasised by comparison of the ^{13}C NMR spectra of these compounds with **1** (Table I).

The ^{13}C NMR spectra of CQ1 and CQ2 also enables the aryl residues to be defined as 3,4-dimethoxyphenyl- and 2,4,5-trimethoxyphenyl-respectively. Whilst the correspondence between these signals and those calculated for simple aromatic compounds is by no means exact, they are the best that can be obtained from calculations of all possible substitution patterns. The calculations were done by using increments for simple phenyl residues [3] and clearly suffer from some limitations when applied to the highly hindered systems present in CQ1 and CQ2.

It remained to define the position of the aryl substituent as being at C-5 or C-8. This was done by examining the C-H coupling constants of C-1 and C-4. For CQ1 having an 8-aryl substituent (structure **2**), C-1 can couple only with H-3, with a large coupling constant, and C-4 can couple with a medium coupling constant with H-5 and a small one with H-3. This was indeed the pattern found for CQ1. C-1 had only a one proton coupling of 7.5 Hz, whilst C-4 had two coupling constants of 4.5 and 1.2 Hz. If the aryl substituent had been at C-5, then C-1 would have a large and a medium coupling constant (7.5 and 4.5 Hz) whilst C-4 would have had a single small coupling of $\sim$ 1 Hz.

The pattern found can only be explained by structure **2** which is accordingly assigned to cassumunaquinone 1. By analogy, and in view of the great similarities of the IR, UV and ^1H and ^{13}C NMR spectra between CQ1 and CQ2, cassumunaquinone 2 is assigned structure **3***.

The possible biosynthetic relationships between CQ1 and CQ2 and the 3-aryl-4-styrylcyclohexenes also isolated from *Z. cassumunar* are delineated in the following communication. Briefly, it seems likely that the cassumunaquinones arise by Diels-Alder reaction between 2-methoxyquinone and 1-arylbutadiene, followed by oxidation. The 8-substitution pattern is exactly as expected from such a reaction.

* Following completion of the draft of this m. s. it became known to us that CQ2 had very recently been isolated and characterised by X-ray crystallography [2]. Our structure agrees fully with that found by X-ray analysis and our methology complements that used in the X-ray study.

[1] H. Dinter, Thesis, Free University Berlin 1979 (where details on the isolation procedure are given).
[2] T. Amatayakul *et al.*, Austral. J. Chem. **32,** 71 (1979).
[3] F. W. Wehrli and T. Wirthlin, Interpretations of C^{13} NMR Spectra, Heyden and Sons, London 1978.