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NEW FURANONAPHTHOQUINONE FROM
STREPTOMYCES CINNAMONENSIS

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ABSTRACT.—Structure **1** was assigned to a metabolite isolated from *Streptomyces cinnamonensis* on the basis of spectroscopic analyses.

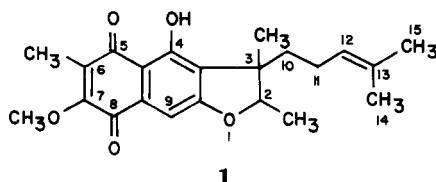
While re-investigating the phenazine fraction from *Streptomyces cinnamonensis* ATCC 15413 (1,2), we isolated an orange compound of molecular formula $C_{22}H_{26}O_5$ (hrms and ^{13}C nmr). This paper deals with structure elucidation of this metabolite.

Hydrogens bonded to carbons ($6 \times Me$, $2 \times CH_2$, $3 \times CH$) account for 25 atoms; the remaining hydrogen is present as a OH group (broad singlet at 6.958 ppm, ir ν_{OH} 3405 cm^{-1}). COSY and delayed-COSY experiments revealed two partial structures: $MeCHO-$ and $-CH_2CH_2CH=C(Me)_2$. These moieties contain three methyls. The fourth methyl (δ_H 1.272, δ_C 19.58) exhibiting a coupling to a quaternary carbon at 46.83 ppm represents an $Me-C_{\text{qu}}-$ group. The fifth methyl (δ_H 2.076, δ_C 9.42) is coupled to a carbon δ_C 134.05 and therefore belongs to the $Me-C_{\text{qu}}=$ type. The last methyl (δ_H 3.993, δ_C 60.67) was assigned to an aromatic methoxyl on the basis of its coupling to the carbon δ_C 156.92. The methine (δ_H 7.214, δ_C 109.44) belongs to an isolated aromatic type.

Ten of the eleven quaternary carbon atoms are sp^2 -hybridized. According to their chemical shifts, five of them are attached to oxygen. Because the chemical shifts of the oxymethine atoms (a part of the $MeC_{\text{qu}}CHO$ group) point to its ether character, the presence of an oxygen bridge joining this group and one $=C_{\text{qu}}-O-$ atom could be inferred. The nature of three oxygen atoms from the total five is now accounted for: a methoxyl, a

phenolic hydroxyl, and an ether oxygen. The remaining two represent two carbonyl groups (δ_C 181.33 and 184.19) of a *p*-quinone system (3). Chemical shifts of the downfield carbonyl and phenolic OH indicate hydrogen bonding between these groups.

Combination of the above-mentioned fragments into the final structure was aided by proton-coupled ^{13}C -nmr spectra, H,C-COSY, and H,C-COSY optimized for the detection of small coupling constants (4). Both quinone carbonyls exhibit a fine structure in proton-coupled ^{13}C -nmr spectra (5): that involved in hydrogen bonding gives a quartet, the other one a doublet. The olefinic methyl δ_H 2.076 is responsible for the above-mentioned quartet splitting so it is located ortho to this carbonyl. The same methyl is also coupled to the carbon at 156.92 ppm that carries a methoxyl (see above). That completes the first ring, as the fourth member has to be the second carbonyl. Its doublet splitting is caused by the isolated aromatic proton that is therefore placed at the peri position. This proton is further coupled to carbons resonating at 109.17 and 127.89 ppm. The chemical shift of the former carbon atom corresponds to that of a quaternary carbon located between the $=C_{\text{qu}}-OH$ and $-C_{\text{qu}}=O$ groups



(6). The latter carbon is also coupled to the aliphatic quaternary methyl that has to be three bonds away. Other coupling partners of this methyl (Figure 1) are

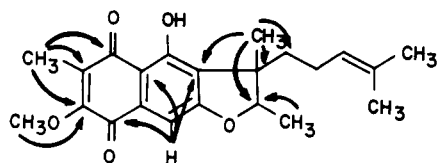


FIGURE 1. Experimentally found (^1H , ^{13}C)-couplings used in structure elucidation of Compound 1.

quaternary carbon (δ_{C} 46.83, 2J), oxymethine (88.06 ppm, 3J), and aliphatic side chain methylene (37.77 ppm, 3J). Accumulated evidence allows us to assign the structure **1**. Four carbon signals devoid of fine structure (Table 1) are associated with the isolated aromatic CH and the quaternary carbons located ortho and para to it. The mass spectrum supports the structure **1**: the $[M + 2]^+$ peak

m/z 372 is typical for quinones (7); elimination of C_6H_{11} (side chain) from the $[\text{M}]^+$ ion gives the base peak m/z 287 that then loses CO to produce the ion m/z 259.

Compound **1** is related to droserone (8) and to the recently described furaquinocin antibiotics (9); the similarity of uv spectra is especially noteworthy. However, the later compounds have the furan ring closed to 4-OH, and their side chain is hydroxylated.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The melting point (uncorrected) was determined on a Kofler hot-stage apparatus. Optical rotation was determined with a Bendix-Ericsson 143 A polarimeter. The uv spectrum was measured with a Cary 118 C spectrophotometer. The ir spectrum was measured in KBr discs on a Perkin-Elmer 580 A spectrophotometer. Mass spectra were measured using a Finnigan MAT-90 spectrometer. ^1H - and ^{13}C -nmr spectra (400 and 100 MHz) were measured with a Varian VXR-400 spectrometer in CDCl_3 at 25° (internal TMS). All 2D

TABLE 1. Nmr Data of Compound 1.

Atom	δ_{C}	m	J [Hz]	δ_{H}	m	n_{H}	J [Hz]
2	88.06	dqq	147.9, 5.4, 2.0	4.847	q	1	6.6
3	46.83	mt	—	—	—	—	—
3a	127.89	dq	6.1, 4.2	—	—	—	—
4	161.20	s	—	—	—	—	—
4a	109.17	d	5.9	—	—	—	—
5	184.19	q	3.7	—	—	—	—
6	134.05	q	6.8	—	—	—	—
7	156.92	mt	n.d.	—	—	—	—
8	181.33	d	4.2	—	—	—	—
8a	133.18	s	—	—	—	—	—
9	109.44	d	163.5	7.214	s	1	—
9a	157.59	s	—	—	—	—	—
10	37.77	tmt	125.5	1.713	mt	1	—
				1.983	mt	1	—
11	23.68	rdd	124.8, 6.4, 2.0	1.845	mt	1	—
				1.962	mt	1	—
12	123.84	dmt	150.4	5.055	mt	1	6.8, 6.8 1.2, 0.9
13	131.91	mt	n.d.	—	—	—	—
14	17.57	qdt	127.8	1.537	mt	3	1.2
15	25.62	qmt	128.2	1.649	mt	3	0.9
2-Me	15.38	q	127.4	1.447	d	3	6.6
3-Me	19.58	qmt	128.2	1.272	s	3	—
6-Me	9.42	q	129.9	2.076	s	3	—
7-OMe	60.67	q	146.1	3.993	s	3	—
4-OH	—	—	—	6.958	s	1	—

experiments were performed using standard manufacturer's software.

CULTIVATION.—*S. cinnamomensis* ATCC 15413 was cultivated on a rotary shaker (70 flasks, each containing 60 ml of the medium (soya flour 1.5%, NaCl 0.5%, CaCO₃ 0.3%, FeSO₄·7H₂O 0.03%, glycerol 5%), at 28° for 120 h.

ISOLATION.—Mycelium was filtered off and extracted with MeOH; the extract was diluted with H₂O and extracted with CHCl₃. Solvent was removed and the residue was subjected to cc on Si gel in the system CHCl₃-MeOH (95:5). The product was then purified by preparative tlc on Si gel in the system heptane-EtOAc-MeOH (25:65:10) or (5:4:1); (*R_f* 0.46). Compound **1** (35 mg): mp 288–290° (MeOH), [α]²⁰_D -129.6° (*c* = 0.1, CHCl₃); no marked reaction with FeCl₃; decolorizes upon dithionite treatment and regains the orange color when exposed to air; uv λ max nm, ϵ (MeOH) 222 (27, 100), 252 (14, 500), 266 (15, 100), 301 (8600), 414 (5100); ir ν max cm⁻¹ (KBr) 1298, 1310, 1568, 1615 sh, 1630, 1670 (quinone), 2940, 3260, 3405 (ν_{OH}); eims *m/z* (rel. int.) 372 (12), 371 (17), 370 (57), 368 (4), 301 (27), 288 (59), 287 (100), 273 (18), 272 (4), 259 (22), 244 (7), 231 (4), 189 (15), 161 (2), 109 (2), 83 (3), 69 (4), 55 (8), 41 (9); hreims

370.1759 (C₂₂H₂₆O₅ requires 370.1780), 287.0879 (C₁₆H₁₅O₅ requires 287.0919), 259.0978 (C₁₅H₁₅O₄ requires 259.0970).

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