

RENIERONE, AN ANTIMICROBIAL METABOLITE FROM A MARINE SPONGE

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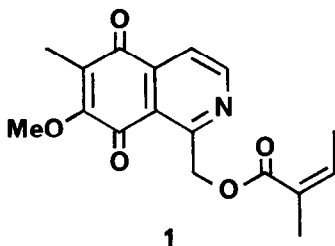
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Abstract: The major antibacterial metabolite in the sponge Reniera sp. was shown to be an isoquinoline quinone, renierone (1). The structure of renierone (1) was defined by X-ray crystallography.

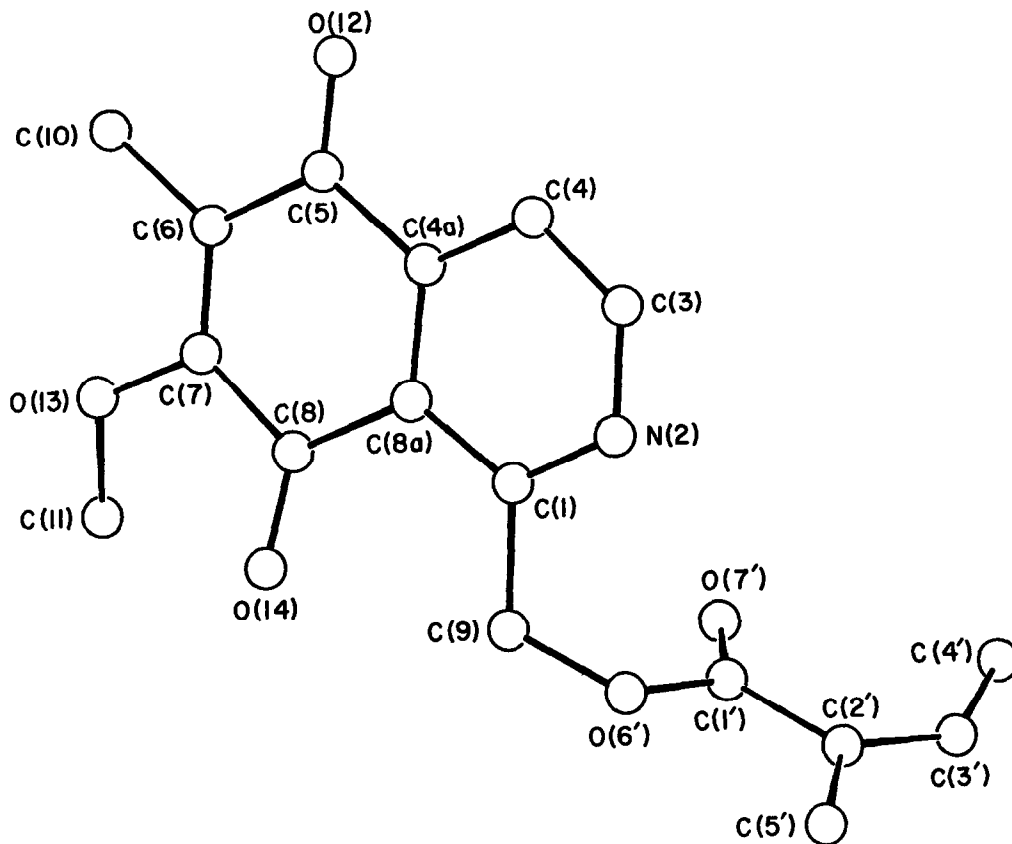
The dominant sponge in the vicinity of Isla Grande, Mexico was an intense blue sponge, identified as a Reniera species. Ethanolic extracts of the sponge exhibited strong antimicrobial activity against S. aureus, B. subtilis, and C. albicans. Silica gel chromatography of the chloroform soluble material gave three colored bands, each of which showed some antibacterial activity. We wish to report the structural assignment of renierone (1), the major antibacterial metabolite (0.03% dry weight).



Renierone (1), mp 91.5-92.5°C, had the molecular formula $C_{17}H_{17}NO_5$.¹ The infrared bands at 1705 and 1650 cm^{-1} could be assigned to an unsaturated ester and a quinone respectively while the ultraviolet absorptions at 312 nm (ϵ 4,000) and 214 nm (ϵ 20,000) indicated that the quinone must be further conjugated. The ^{13}C NMR spectrum¹ contained three carbonyl signals at δ 184.2, 181.4 and 167.6 which were again assigned to a quinone and an unsaturated ester. The signals at δ 65.0 (t) and 60.9 (q) could be assigned to a methylene bearing the ester and a methoxyl, respectively. The acid portion of the ester was recognized as angelic acid from the 1H NMR signals at δ 1.99 (d, 3H, $J = 1.5$ Hz), 2.04 (dd, 3H, $J = 7, 1.5$ Hz) and 6.10 (q, 1H, $J = 7$ Hz) and comparison of ^{13}C NMR signals with those of methyl angelate.² The remaining 1H NMR signals were assigned as follows: 2.09 (s, 3H) to a methyl on an aromatic ring, 4.15 (s, 3H) to a methoxyl, 5.78 (s, 2H) to a benzylic methylene bearing the ester, 7.87 (d, 1H, $J = 5$ Hz) and 8.91 (d, 1H, $J = 5$ Hz) to the β and α protons on a quinoline or isoquinoline ring system. Renierone (1) was therefore one of twelve possible isomers based on either a quinoline or an isoquinoline ring system having a *p*-quinone in the second ring. The structural elucidation was completed by a single crystal X-ray diffraction analysis.

Renierone (1) crystallized in the monoclinic crystal class with $a = 7.574(2)$ $b = 7.940(1)$ and $c = 25.624(4)$ Å and $\beta = 92.06(5)^\circ$. Systematic extinctions uniquely indicated space group $P2_1/c$ and a density of 1.36 g/cc suggested one molecule of $C_{17}H_{17}NO_5$ per asymmetric unit. All unique diffraction maxima were recorded on a four-circle diffractometer using graphite monochromated $MoK\alpha$ radiation (0.71069 Å) and a variable speed, 1° ω -scan. Of the 4344 reflections surveyed, 2201 (51%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) after correction for Lorentz, polarization and background effects. A phasing model was arrived at by a multiresolution sign determining procedure.³ The most consistent set of signs gave a plausible 10-atom fragment in the resultant E-synthesis. This fragment was used as a starting point for a tangent formula recycling procedure and the signs of 300 E's were determined in this way. The E-synthesis from

Figure 1. A computer-generated perspective drawing of renierone (1). Hydrogens are omitted for clarity.



this gave 17 nonhydrogen atoms and the remaining 6 nonhydrogen atoms were located in an F-synthesis. Full-matrix least-squares refinements with anisotropic temperature factors for nonhydrogen atoms and fixed, isotropic temperature factors for hydrogen atoms have converged to a standard crystallographic residual of 0.081 for the observed reflections.⁴

The result of the single crystal X-ray diffraction experiment is shown in Figure 1. The quinone nature is clearly shown by the C(5)-O(12) and C(8)-O(14) bond distances of $1.217(5) \text{ \AA}$. The aromatic portion of the molecule and attached atoms are planar within experimental error. The methyl carbon of the methoxy group, C(11), is $.72 \text{ \AA}$ removed from this plane. The angelate group is also planar and this plane makes an angle of 70° with the aromatic plane. In general,

bond distances and angles agree well with accepted values.

Renierone (1) is the first member of a unique class of sponge metabolites.⁵ The remaining colored bands contained inseparable mixtures of minor metabolites, which appeared from the ¹H NMR spectra and mass spectra to be related to renierone.⁶

Acknowledgments

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References and Notes

1. ¹³C NMR (CDCl₃) δ 184.2 (s), 181.4 (s), 167.6 (s), 158.2 (s), 156.6 (s), 153.7 (d), 138.6 (s), 137.6 (d), 130.1 (s), 127.6 (s), 122.4 (s), 118.0 (d), 65.0 (t), 60.9 (q), 20.3 (q), 15.4 (q), 8.7 (q); HRMS, found 315.111, C₁₇H₁₇NO₅ requires 315.111.
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3. J. P. Declercq, G. Germain and M. M. Woolfson, Acta Cryst., A31, 367 (1975).
4. All crystallographic calculations were done on a Prime 400 computer, operated by the Materials Science Center, Cornell University. The principal programs used were: REDUCE and UNIQUE, data reduction programs, M. E. Leonowicz, Cornell University, 1978; BLS, block diagonal least squares refinement, K. Hirotsu, Cornell University, 1978; ORFLS (modified), full matrix least squares, W. R. Busing, K. O. Martin and H. S. Levy, Oak Ridge, ORNL-TM305; ORTEP, crystallographic illustration program, C. Johnson, Oak Ridge, ORNL-3795; BOND, structural parameters and errors, K. Hirotsu, Cornell University, 1978; MULTAN-76, direct methods and fast fourier transform, G. Germain, P. Main and M. Woolfson, University of York. A table of fractional coordinates and temperature factors for renierone is available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, and from Prof. Clardy.
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