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LUTEONE, A TWENTY THREE CARBON TERPENOID FROM THE DORID NUDIBRANCH *CADLINA LUTEOMARGINATA*

Jocelyne Hellou and Raymond J. Andersen*

Departments of Chemistry and Oceanography
University of British Columbia
Vancouver, B.C., Canada. V6T 1W5

Shahin Rafii, Edward Arnold and Jon Clardy*

Department of Chemistry
Cornell University
Ithaca, New York 14853, U.S.A.

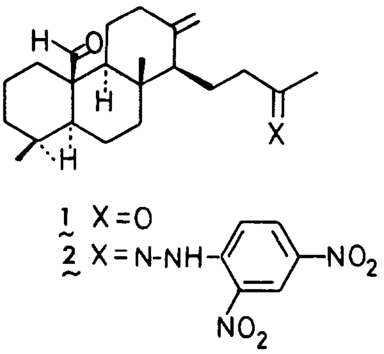
ABSTRACT: *The structure of luteone (1), a twenty three carbon terpenoid, has been solved by performing a single crystal x-ray analysis on a 2,4-dinitrophenylhydrazone derivative.*

Dorid nudibranchs are delicate, shell-less molluscs that feed mainly on marine sponges. *Cadlina luteomarginata*, one of the most abundant species in British Columbia waters, has a pleasant fruity odour. We have undertaken a study of the skin extracts of *C. luteomarginata* in an attempt to determine the origin of the fragrance. We report here the structure of luteone (1), a minor constituent of *C. luteomarginata* extracts, which may be the odiferous principle.

Specimens of *C. luteomarginata* were collected by hand using SCUBA (-5m to -18m) in Howe Sound and Barkley Sound, British Columbia. Freshly collected specimens were extracted whole in methanol at room temperature for 72 hours. The methanol was decanted and evaporated *in vacuo* to give a residue which was partitioned between water and chloroform. Silica gel column and preparative layer (PTLC) chromatography were used to fractionate the fragrant organic layer.

One PTLC band ($R_f \approx 0.3$, $CHC\ell_3$ eluent) retained the smell of *C. luteomarginata*. We were unable to chromatographically separate luteone, the major component of this fraction, from a persistent phthalate ester contaminent. Purification was ultimately achieved by preparation of a crystalline 2,4-dinitrophenylhydrazone derivative (2, mp 84-86°, CH_3OH).

A high resolution mass spectrum of the derivative 2 showed that it had a molecular formula of $C_{29}H_{40}N_4O_5$ (M^+ 524.3000, Calc'd 524.2988) indicating that underivatized luteone had a molecular formula of $C_{23}H_{36}O_2$. The ^1H NMR spectrum ($CDC\ell_3$, 270 MHz) of hydrazone 2 showed methyl singlets at 0.64, 0.76, 0.78 and 2.07 ppm, two exocyclic methylene protons at 4.56 and 4.89 ppm, and an aldehyde proton at 10.12 ppm[1]. We concluded from the spectral data of 2 that luteone was probably a terpenoid that contained a sterically hindered aldehyde, a methyl ketone, an olefin and three rings. A limited supply of luteone prevented further chemical studies and therefore the structure was solved by single crystal x-ray analysis.



Single crystal x-ray diffraction of luteone DNPH (2): Preliminary x-ray photographs showed orthorhombic symmetry and accurate lattice constants of a = 7.243(2), b = 18.471(3), c = 21.058(4)Å and were determined by a least squares fit of fifteen moderate, diffractometer measured, 2θ values. The pattern of systematic extinctions, the presence of chirality and density considerations were uniquely accommodated by the space group $P2_12_12_1$ with one molecule of $C_{29}H_{40}O_5N_4$ forming the asymmetric unit (ρ_c = 1.24 g/cm^3). All unique diffraction maxima with $2\theta \leq 114°$ were surveyed on a computer controlled, four-circle diffractometer using a variable speed, 1° ω-scan and graphite monochromated, CuKα radiation (1.54178Å). A total of 2006 reflections were surveyed in this fashion and after correction for Lorentz, polarization and background effects, 1736 (87%) were considered observed [$|F_o| \geq 3\sigma(F_o)$]. No corrections were deemed necessary for absorption or decomposition.

Numerous attempts to solve the phase problem using standard multi-solution techniques failed. The structure factors were normalized using a Wilson plot calculation which included a K curve and spherically averaged scattering factors for the dinitrophenyl group. The novel program YZARC78[2,3] was then used in conjunction with the MULTAN78 system to generate 200 sets of "random" phases for the 100 best-connected reflections out of the top 200 normalized structure factors (E's), and to refine each set of phases to consistency via a least squares phase refinement using a linear representation of the triple-phase relationship. Each of these phase sets was expanded to 200 phases and refined using the tangent formula. The E-synthesis calculated from the set with the highest combined figure of merit (CFOM = 2.27; ABS = 1.05, ψ_o = 1.21, R_k = 33.2) showed two plausible but unconnected molecular fragments. Eighteen of these atom positions were used to calculate phases for input into the tangent formula, and by means of successive tangent formula recycling the nonhydrogen framework was readily completed. Hydrogens were located on a ΔF synthesis following block-diagonal least squares refinement, and the final model with anisotropic nonhydrogen atoms and isotropic hydrogens has converged to a standard crystallographic residual of 0.059 for the observed data[4,5].

Luteone (1) appears to be a degraded terpenoid (Scheme 1). Degraded sesterterpenoids containing twenty one carbon atoms have been reported from marine sponges[6]; however, luteone is the first example of a degraded terpenoid containing twenty three carbon atoms.

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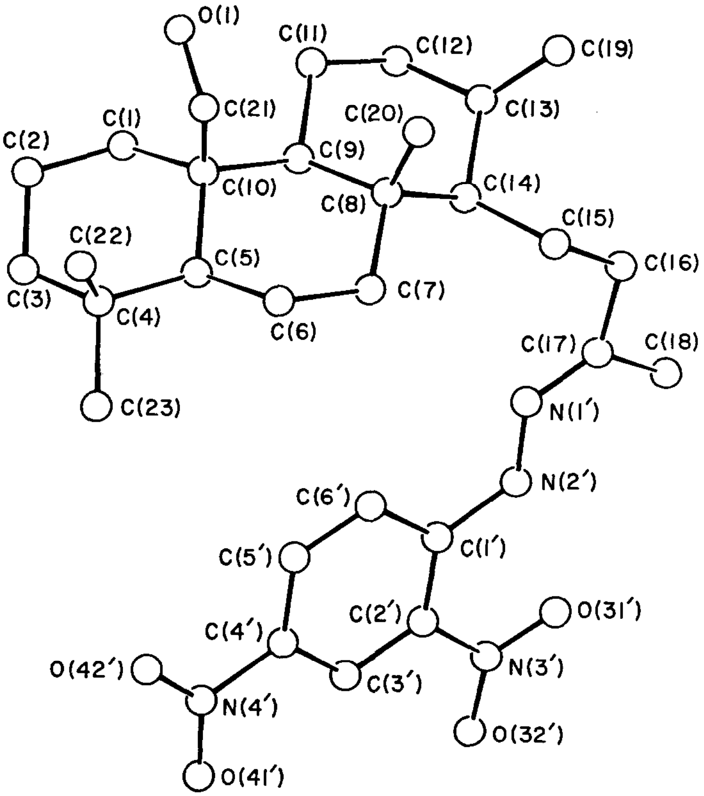
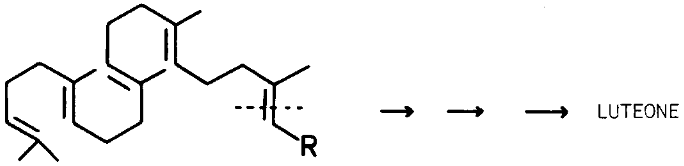


Figure 1. A computer generated perspective drawing of luteone DNPH. Hydrogens are omitted for clarity and no absolute configuration is implied.

Scheme 1.



Footnotes and References

1. Additional ^{1}H NMR signals were observed at: 7.96 (d, 1H, J=10 Hz), 8.32 (dd, 1H, J=2.5, 10 Hz) and 9.15 (d, 1H, J=2.5 Hz) ppm. Weak signals from the syn isomer of the hydrazone are also present. Mass spectrum (m/e, relative intensity) 524 (9), 495 (12), 449 (15), 327 (28), 326 (32), 161 (80), 135 (68), 123 (52), 121 (76), 109 (95), 107 (76), 95 (100), 93 (76), 81 (95), 55 (80).

2. Baggio, R., Woolfson, M.M., DeClercq, J.P., Germain, G., Acta Cryst. Sect. A, 1978, 31, 367-372.

3. For a more recent description of the use of the YZARC78 and MAGIC78 routines see: DeClercq, J.P., Germain, G., Woolfson, M.M., Acta Cryst. Sect. A, 1979, 35, 622-626.

4. Fractional coordinates and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.

5. All crystallographic calculations were done on a PRIME 400 computer operated by the Materials Science Center and the Department of Chemistry, Cornell University. The principal programs used were REDUCE and UNIQUE, data reduction programs, Leonowicz, M.E., Cornell University, 1978; BLS78A, anisotropic block-diagonal least squares refinement, Hirotsu, K. and Arnold, E., Cornell University, 1980; XRAY76, the X-ray System of Crystallographic Programs, edited by Stewart, J.M., University of Maryland, Technical Report TR-445, March, 1976; ORTEP, crystallographic illustration program, Johnson, C.K., Oak Ridge, ORNL-3794; BOND, molecular metrics program, Hirotsu, K., Cornell University, 1978; MULTAN-78, "A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data", University of York, England. Principal author, P. Main. For literature description of MULTAN see: Germain, G., Main, P., Woolfson, M.M., Acta Crystallogr., Sect. B, 1970, 26, 274-285 and Woolfson, M.M., Acta Crystallogr., Sect. A, 1977, 33, 219-225.

6. For example see: Fattorusso, E., Minale, L., Sodano, G., Trivellone, E., Tetrahedron, 1971, 27, 3909.

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