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TWO NEW TETRACYCLIC DITERPENES FROM THE DEFENSE SECRETION OF THE NEOTROPICAL TERMITE NASUTITERMES OCTOPILIS

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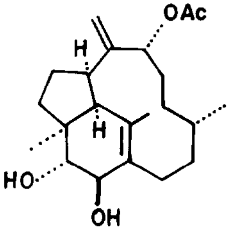
Abstract: Xray and spectral data are presented for two new tetracyclic diterpenes isolated from a termite soldier defensive secretion.

Chemical defense by the highly evolved nasute termite soldiers (Isoptera: Termitidae: Nasutitermitinae) is effected by squirting potential predators with an odorous sticky secretion.[1] This defense secretion, composed of monoterpene hydrocarbons and polyoxygenated cembrene-derived diterpenes, has been analyzed in detail for several species representing the genera Nasutitermes, Trinervitermes and Grallatotermes from Old and New World locations.[2-4] The diterpene components are dome-shaped, possessing either the tricyclic trinervitane (e.g., 1)[3] or the tetracyclic kempane (e.g., 2)[4] carbon skeletons. We now report the characterization of two novel β,γ-unsaturated ketones based on the kempane skeleton[5]: 3β-hydroxy-7β-kemp-8(9)-en-6-one (3) and 2β-acetoxy, 3β-hydroxy-7β -kemp-8(9)-en-6-one (4).



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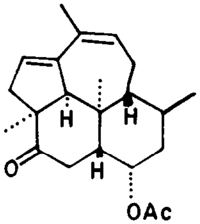

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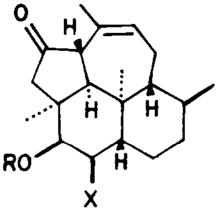


3, X=H, R=H
4, X=OAc, R=H
5, X=H, R=p-BrC_6H_4CO

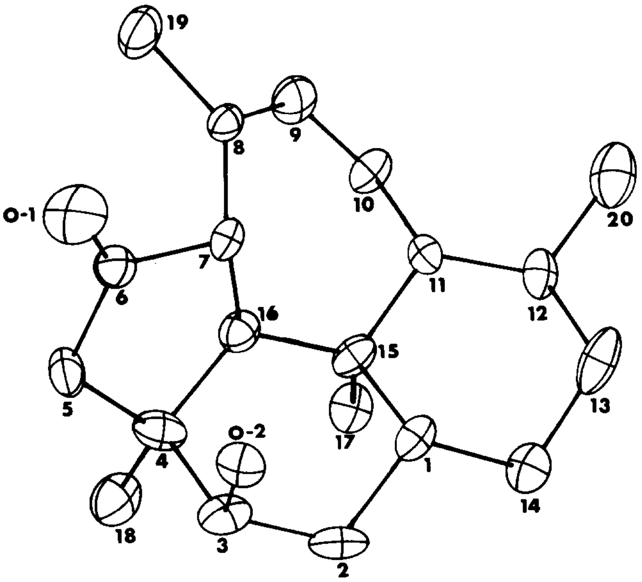
Kempenones 3 and 4 were isolated from the soldier defense secretion of Nasutitermes octopilis (Banks) by chromatography over Florisil.[6] The physical constants for 3 are: HRMS, m/e 302.2242 (M$^+$, $C_{20}H_{30}O_2$, 269.1911 (M$^+$-CH_3-H_2O, $C_{19}H_{25}O$), 242.2060 (M$^+$-H_2O-C_2H_2O); CD (MeOH), $\Delta\epsilon_{290}$ = -3.07 (ketone); IR (CCl_4) 3640 cm^{-1} (free-OH), 3450 (H-bonded OH), 1725, 1735 (cyclopentanone C=O). The 20 MHz ^{13}C-NMR showed signals at 216.8 ppm (C=O, five-membered ring ketone), 136.7 and 127.4 (trisubstituted olefin), 74.4 (HCR_2-O), and 16 aliphatic carbons.[7]

The 360 MHz ^{1}H-NMR ($CDCl_3$) showed signals at δ 5.40 ppm (br s, H-9), 3.67 (br s, H-3), 3.30 (br d, 10.8, H-7), 2.31 (dd, -16, 2, H-5β), 2.13 (d, 16, H-5α), 1.75 (br s, CH_3-19), 1.23 (s, CH_3-18), 1.00 (s, CH_3-17), 0.84 (d, 6.3, CH_3-20). The 5β proton is "W-coupled" to the allylic 7β proton (^4J = 2 Hz), which in turn shows long-range coupling to the C-19 methyl and ^3J = 10.8 Hz with H-16.

Compound 4 showed the following physical constants: HRMS, m/e 360.2297 (M^+, $C_{22}H_{32}O_4$), 300.2089 (M^+-CH_3CO_2H, $C_{20}H_{28}O_2$), 285.1833 (M^+-CH_3CO_2H -CH_3, $C_{19}H_{25}O_2$); CD (MeOH) $\Delta\varepsilon_{288}$ = -4.15; IR (CCl_4), 3620 cm^{-1} (free OH), 3400 (H-bonded OH), 1730 (acetate and ketone C=O overlapped). The ^{1}H-NMR and ^{13}C-NMR spectra of 4 were analogous to those of 3 with the addition of a secondary acetoxy group: δ 2.08 (s, CH_3CO_2-); δ 5.13 (dd, 12.6, 2.4, H-CR_2-OAc). The collapse of this signal to a doublet (J = 12 Hz) upon irradiation of the C-2 carbinyl proton unambiguously established both the position and stereochemistry of this substituent. The ^{13}C-NMR spectrum showed new acetate and carbinyl resonances at 170.6, 59.6, and 21.2 ppm.[7]

The structure of 3 was established by single-crystal xray diffraction using the p-bromobenzoate derivative. Alcohol 3 was converted (p-BrϕCOCl, Py, 5d, 55°C) in >90% yield[8] to the ester 5 (m/e 484, 486, M^+), which was purified by chromatography on Florisil. Crystallization from hexane-ethanol at -10°C gave small colorless prisms, mp 192-5°. The data crystal of 5 was mounted on an Enraf-Nonius CAD4A difractometer under the control of a PDP 11/45 computer system and subjected to Cu X-radiation (λ = 1.5418Å). The space group is $P2_12_12_1$ with a = 9.359(2)Å, b = 10.298(2)Å, c = 24.371(4)Å, and Z = 4. During data collection the intensities of 3 standard reflections were measured periodically and showed an anisotropic intensity decrease of about 25 percent. The data were reduced (p = 0.04) and corrected for the intensity decay and absorption.[9] Of the 1721 reflections measured ($0<2\theta\leq 90^\circ$) 1242 with $F_o^2>3\sigma(F_o^2)$ were used in the subsequent analysis. The structure was solved using Patterson and Fourier methods and refined with anisotropic temperature factors assigned to the heavy atoms. The H atoms were fixed with isotropic temperature factors. The refinement converged to values of 0.061 and 0.081 for R and R_w, respectively, for the 1242 reflections and 280 variables.[10] A similar refinement for the enantiomer of 5 was made yielding less satisfactory values 0.065 and 0.085 for R and R_w. The absolute stereochemistry shown below agrees both with these calculations and with biogenetic considerations.[3,4]

The figure shows a computer-generated perspective drawing (ORTEP) of 5, in which hydrogens and the bromobenzoate moiety have been omitted for clarity. The five-membered ring approximates an envelope conformation with C-16 lying 0.61Å below the least-squares plane of C-4, C-5, C-6, and C-7. A dihedral angle of 76° between the plane of the olefin (C-7, C-8, C-9, C-10, C-19) and the plane of the carbonyl (C-5, C-6, C-7, O-1) may account for the large ellipticity observed for the $n\rightarrow\pi^*$ transition.



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2. a) G.D. Prestwich, Insect Biochem. 7, 91 (1977); (b) G.D. Prestwich, Biochem. Syst. Ecol., in press (1979); (c) G.D. Prestwich, Insect Biochem., in press (1979); (d) G.D. Prestwich, Sociobiol., in press (1979); (e) G.D. Prestwich and J. Vrkoč, Sociobiol., in press (1979).

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5. Semisystematic nomenclature has been adopted for these diterpenoids according to IUPAC rules (see Ref. 2e).

6. Nasutitermes octopilis (Banks) colonies were collected from wet, rotten logs at Kartabo Point, Guyana and transported to Stony Brook; soldiers were removed, cooled to -10°C, and decapitated. The heads were crushed in 1:1 hexane-CH_2Cl_2, and the crude extract (84 mg from 500 soldiers) was chromatographed on 100/200 Mesh Florisil with 5% to 80% EtOAc-hexane mixtures. Diterpenes 3 (20 mg) and 4 (17 mg) had R_f values of 0.25 and 0.12, respectively (MN Polygram Sil UV, 25% EtOAc-hexane), and stained reddish-orange with the ethanolic vanillin-H_2SO_4 TLC visualization reagent. Identification of the remaining compounds will be reported later.

7. ^{13}C-NMR ($CDCl_3$) resonances for 3 (ppm from TMS=0): 216.8, 136.7, 127.4, 74.4., 60.3, 54.8, 52.6, 51.8, 41.2, 37.8, 36.3, 33.3, 33.2, 30.3, 28.3, 27.9, 25.9, 23.1, 20.9, 16.6; for compound 4: 215.7, 170.6, 136.6, 127.3, 73.4, 60.5, 59.6, 54.6, 52.5, 51.8, 41.7, 39.6,

37.4, 35.6, 30.1, 27.3, 25.8, 23.0, 22.7, 21.2, 20.8, 17.8. The ^{13}C-NMR data for natural and semisynthetic kempanes will be assigned in a full paper.

8. The low reactivity of the axial hydroxyl necessitated the severe acylation conditions. We feared that this might effect equilibration of 7α and 7β epimers of the β,γ-unsaturated system, thereby causing incorrect extrapolation from the xray structure to the original natural product. That this was not occurring is supported by two observations. First, acetylation of 3 (Py, Ac_2O, 5d, 55°) gave a single acetate (m/e 344) which had the same sign and magnitude for the Cotton effect ($\Delta\varepsilon_{288}$=-2.53). Dreiding models show this may only occur if the configuration at C-7 is unaltered; the cis-fused isomer shows the opposite dihedral helicity for the β,γ-unsaturated ketone chromophore (cf. P. Crabbé, Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry, Holden-Day (1965), pp. 222-237). Second, recovery of unreacted alcohol from the acetylation shows no change in shift or multiplicity in the ^{1}H-NMR resonances for C-5 and C-7.

9. The programs used were those of the Enraf-Nonius Structure Determination Package developed chiefly by Okaya and Frenz.

10. Tables of fractional coordinates, thermal parameters, bond distances, bond angles and their errors and values of 10 x F_{obs} and 10 x F_{calc} have been deposited with the Cambridge Crystallographic Data Center.

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