

where  $k_{-1}' = k_{-1}[\text{MeOH}]$ , but  $K$  is related to the  $pK_a$  of **1** and methanol by  $pK = pK_a^{\text{H}} - pK_a^{\text{MeOH}}$ . Using the values given in the text we calculate  $pK \approx 3.7$ . Then  $k_{-1}'$  can be calculated from  $pK = \log k_{-1}' - \log k_1 - \log [\text{MeOH}]$ . At 30 °C  $[\text{MeOH}] = 24.3 \text{ M}$ , and values of  $k_1$  are available from the data in Table I. The value of  $k_2$  can then be obtained from the ratios  $k_2/k_{-1}'$  in Table I.

- (23) Rate constants for electron transfer in the thermodynamically favored direction are at the diffusion-controlled limit: (a) P. S. Rao and E. Hayon, *J. Phys. Chem.*, **77**, 2753 (1973), and **79**, 397 (1975); (b) P. S. Rao and E. Hayon, *J. Am. Chem. Soc.*, **96**, 1287 (1974).

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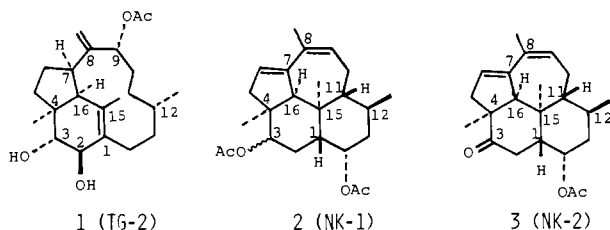
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## Kempene-1 and -2, Unusual Tetracyclic Diterpenes from *Nasutitermes* Termite Soldiers

Sir:

The glue-like secretions of nasute termite soldiers play a crucial role in the defense of these termite species against predacious ants.<sup>1</sup> Recently, we have described the structures<sup>2,3</sup> of the trinervitenes, e.g., **1** (TG-2), and the chemical composition of the secretion of the termite *Trinervitermes gratus* from which these compounds were first identified.<sup>4</sup> In this communication we reveal the structures of two new diterpenes, kempene-1 and -2, possessing novel tetracyclic cembrene-derived carbon skeletons.<sup>5</sup>



Kempene-1 (or NK-1, **2**) and kempene-2 (or NK-2, **3**) were isolated from the hexane extract of crushed heads of *Nasutitermes kempae* soldiers by chromatography over Florisil followed by HPLC on  $\mu$ -Porasil.<sup>6</sup> Kempene-2 was readily oxidized on standing under ambient conditions to give a substance containing one extra oxygen, a behavior which led to some confusion in the initial analysis of the spectral data.<sup>7</sup> The physical constants of **3** are as follows: mp 120.5–122.5 °C; mass spectrum  $m/e$  342 ( $M^+$ ) ( $C_{22}H_{30}O_3$ ), 282 ( $M^+ - \text{AcOH}$ ), 267 ( $M^+ - \text{AcOH} - \text{Me}$ ); UV (MeOH) 244 nm ( $\epsilon$  6330); CD (MeOH), 241 ( $\Delta\epsilon$  +0.025, diene), 289 nm ( $\Delta\epsilon$  +1.46, ketone); IR ( $\text{CCl}_4$ ) 1737 (OAc), 1702  $\text{cm}^{-1}$  (ketone). The nature of all 22 carbons was determined (see **4**, Figure 1) by the  $^{13}\text{C}$  NMR techniques of PND, selective decoupling, partially relaxed Fourier transform (PRFT), and combined PRFT/selective decoupling.<sup>8</sup>

The complex  $^1\text{H}$  NMR spectrum (see **5**, Figure 1) was analyzed in detail at 100 MHz and 220 MHz. With the aid of  $\text{Eu}(\text{fod})_3$ , it was possible to separate, at least in part, practically all proton signals (see **5**). Decoupling of the separate peaks, in conjunction with correlation of proton signals to carbon signals by selective heteronuclear decoupling, clarified most of the molecular structure (indicated by thick lines in **5**) except for the linkages between C-1 and C-15 and between C-12 and C-13 and those extending from C-11.<sup>8</sup> The chemical shifts of some overlapping peaks shown by approximate values in **5** were estimated by comparisons with the  $\text{Eu}(\text{fod})_3$ -shifted spectrum. Assignments of  $^1\text{H}$  NMR signals were also aided by comparisons with the signals of kempene-1. The ddd shape (each  $J$  being 3 Hz) of the 14-H peak defines the axial nature of OAc

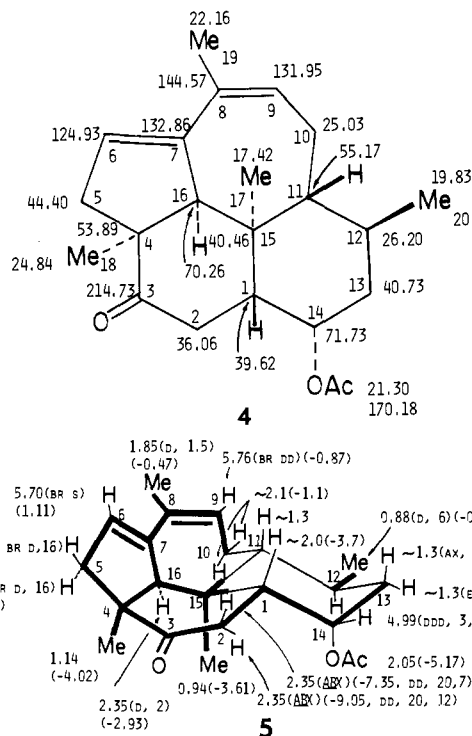


Figure 1.  $^{13}\text{C}$  NMR data (**4**), JEOL PS-100 with microprobe, and  $^1\text{H}$  NMR data (**5**), Varian HA-100 and HR-220, of NK-2 (**3**), both in  $\text{CDCl}_3$ . Negative  $^1\text{H}$  NMR values shown in brackets in **5** denote downfield shifts occurring upon addition of  $\text{Eu}(\text{fod})_3$ .

as well as the spatial relation between 14-H and the three adjacent protons. The large  $J_{\text{gem}}$  of the 2-H's (20 Hz) indicate the methylene to be adjacent to the ketone. The doublet nature ( $J = 2 \text{ Hz}$ ) of the isolated 16-H shows that it is long range coupled, probably to 5 $\alpha$ -H, through overlap of the 5-H and 16-h  $\sigma$  bonds with the 6-ene  $\pi$  bond.

Kempene-1 (**2**) had mass spectrum  $m/e$  386 ( $M^+$ ) ( $C_{24}H_{34}O_4$ ); UV (MeOH) 245 nm ( $\epsilon$  85),<sup>9</sup> CD (MeOH), 245 ( $\Delta\epsilon$  +0.058); IR ( $\text{CHCl}_3$ ) 1730  $\text{cm}^{-1}$  (OAc). The  $^{13}\text{C}$  NMR resonances for C-2 and C-4 of kempene-2 (**4**, 36.06 and 53.89 ppm) are shifted to the high fields of 28.75 and 44.96 ppm, respectively. In the  $^1\text{H}$  NMR spectrum, an additional carbonyl acetate proton (3-H) appears at 5.08 ppm (br d,  $J = 9 \text{ Hz}$ ), and hence the 3-one is replaced by a 3-acetate. Reduction of **4** mg of kempene-2 (**3**) with  $\text{LiAlH}_4$  followed by acetylation and HPLC separation ( $\mu$ -Porasil, 12% ether in hexane) afforded an  $\sim$ 1:1 mixture of **2** and its C-3 epimer: UV (MeOH) 243 nm ( $\epsilon$  85),<sup>9</sup> CD (MeOH) 244 nm ( $\Delta\epsilon$  +0.069);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 5.17 ppm (br d,  $J = 8 \text{ Hz}$ , 3-H). The 3-H signal of **2** and 3-epi-**2** merely indicated that in both compounds the 3-acetoxyl group is equatorially oriented (owing to conformational inversion), and hence it was not possible to assign configurations to this center either by NMR or other evidence.

The structure of **3** was solved by single-crystal x-ray diffraction experiments. Kempene-2 crystallized from olefin-free pentane under an argon atmosphere in the orthorhombic crystal class. Cell constants, determined by least-squares fitting of 15 high angle reflections, were  $a = 10.370$  (3),  $b = 9.671$  (2), and  $c = 19.817$  (7) Å. Systematic extinctions combined with the chirality of **3** indicated space group  $P2_12_12_1$  with one molecule of composition  $C_{22}H_{30}O_3$  per asymmetric unit ( $\rho = 1.14 \text{ g cm}^{-3}$ ). All unique data with  $2\theta \leq 114^\circ$  were collected on a computer-controlled four-circle diffractometer using graphite monochromated  $\text{Cu K}\alpha$  (1.54178 Å) x rays. Of the 1596 diffraction maxima surveyed, 1258 (79%) were considered to be observed ( $F_o^2 \geq 3\sigma(F_o^2)$ ) after correction for Lorentz, polarization, and background effects.

The angular dependence of the scattering was eliminated

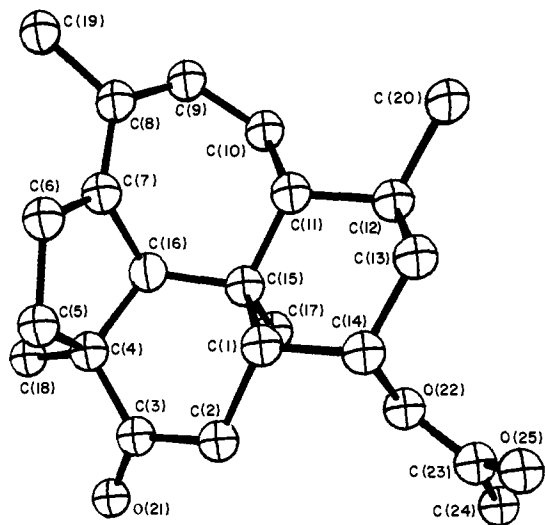


Figure 2. A computer-generated perspective drawing of kempene-2 (3). Hydrogens are omitted for clarity.

as the diffraction data were converted to normalized structure factors.<sup>10</sup> Phases were assigned to the 250 largest  $E$  values by a multiple-solution weighted tangent formula approach.<sup>11</sup> The resulting  $E$  synthesis showed most of the nonhydrogen atoms. The remaining atoms were located by tangent formula refinement with all  $|E| \geq 1.00$ . Hydrogens were located in difference electron density syntheses.<sup>12</sup> Full-matrix least-squares refinements with anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors for hydrogens have converged to a conventional crystallographic residual of 0.040 for the observed reflections. Tables of fractional coordinates, bond distances, bond angles, and observed and calculated structure factors can be found in the supplemental material.

A perspective drawing of the final x-ray model less hydrogens is given in Figure 2. The absolute configuration was not determined by the x-ray analysis (vide infra). Kempene-2 is a dome-like tetracyclic array of five-, six-, and seven-membered rings. Most of the substituents are on the convex surface, the exceptions being the hydrogens at C-1 and C-11. The bond distances and angles show no pronounced strain effects. The diene system is twisted  $\sim 20^\circ$  out of planarity.

The kempenes are closely related to the trinervitenes, e.g., TG-2 (1)<sup>2,3</sup> and hence the absolute configuration should be as drawn in 2 and 3. However, the configurations of the C-12 methyls are inverted. The absolute configuration shown is corroborated by the positive Cotton effects due to the positively twisted diene system<sup>13</sup> in the kempene skeleton (see stereostructure 5).

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**Supplemental Material Available:** Fractional coordinates (Table 1), important bond distances (Table 2), important bond angles (Table 3), and observed and calculated structure factors (Table 4) (9 pages). Ordering information is given on any current masthead page.

## References and Notes

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- (3) G. D. Prestwich, S. P. Tanis, F. G. Pilkwicz, I. Miura, and K. Nakanishi, *J. Am. Chem. Soc.*, **98**, 6062 (1976).
- (4) G. D. Prestwich, *Insect Biochem.*, **7**, 91 (1977).
- (5) We have recently learned of the presence of an as yet unidentified tetracyclic diterpene in the soldier secretions of the Cuban termite *Nasutitermes ripperti*: J. Vrkoc, M. Budesinsky, J. Krecek, and I. Hrdy, *Proc. Int. Congr. Int. Union Study Soc. Insects*, **8th**, in press.
- (6) *Nasutitermes kempae* Harris was collected from arboreal colonies in Kwale,

Kenya, East Africa. The termite soldiers were removed, cooled to  $0^\circ\text{C}$ , and decapitated, the heads were crushed under hexane, and the solvent was removed in vacuo. About 100 mg of crude secretion was obtained from 5000 individuals. Chromatography of this crude material over Florisil (100–200 mesh) with increasing percentages of ethyl acetate in benzene afforded two UV-active materials, kempene-1 ( $R_f$  0.41 on silica gel GF254 with 15% ethyl acetate in benzene) and kempene-2 ( $R_f$  0.37). Samples of 2 and 3 for spectroscopic studies ( $\sim 5$  mg each) were further purified by HPLC using a 30 cm  $\times$  4 mm  $\mu$ -Porasil column and eluting at 2 mL/min with 12 and 15% ether in hexane, respectively.

- (7) Neither the conditions leading to oxygenation nor the structure of the product were explored further. The EIMS and CIMS both led to a formula containing one extra oxygen.
- (8) Details of NMR structural studies will be published separately together with the corresponding data for the trinervitenes.
- (9) The very low intensities ( $\epsilon$  85) of the diene chromophores around 245 nm in 2 and its 3-*epi* acetate (see text) are anomalous. The CD  $\Delta\epsilon$  values of these two diacetates (+0.058 and +0.069) are slightly stronger than that of kempene-2 (3 or 5), and this implies that the diene in the two diacetates is slightly more positively twisted. However, this is hardly sufficient to account for the dramatic decrease in the UV peak heights. We tentatively attribute these low  $\epsilon$  values of the diacetates to the possibility that, when C-3 is  $sp^3$  hybridized as in 2, the ring strain of the bridged system is released so that the diene moiety approximates an allene-like orthogonality.
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- (15) Camille and Henry Dreyfus Award, 1972–1977.

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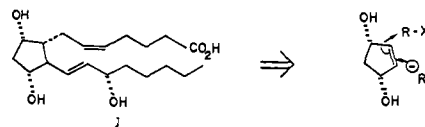
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## Prostaglandin Synthesis via Carbopalladation

Sir:

Synthesis of the primary prostaglandins has been a focal point for organic chemists for almost 10 years; during this time several elegant total syntheses have been achieved by a variety of workers.<sup>1</sup> We wish to report a different approach to this problem which has now led to the development of an exceptionally efficient and short conversion of cyclopentadiene into prostaglandin.

Our general strategy for synthesis of, for example, PGF<sub>2 $\alpha$</sub>  (1) initially involved the development of methods for the direct



attachment of two side-chain fragments R and R' to the unactivated double bond of an appropriately substituted cyclopentene derivative. To this end, preliminary studies in our