

**METHYL 3 α ,6 α -DIACETOXY-10-OXO-(7 α)-KEMP-11-EN-20-OATE:
THE REVISED STRUCTURE FOR THE KEMPANE DERIVATIVE
FROM THE FRONTAL GLAND SECRETION OF *Nasutitermes costalis*
SOLDIERS**

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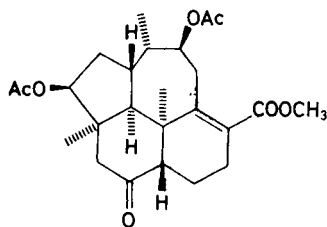
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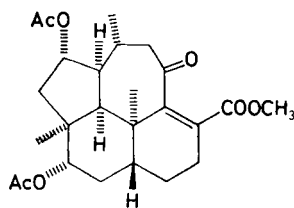
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The structure of methyl 3 α ,6 α -diacetoxy-10-oxo-(7 α)-kemp-11-en-20-oate (*II*) was established by X-ray analysis for a defense compound of termites *Nasutitermes costalis*. The previously suggested structure *I* with 7 β -kempane skeleton is revised.

On the basis of ¹H, ¹³C NMR, IR, UV, CD, and mass spectral data we have suggested¹ structure *I* for one of the components of the frontal gland secretion of soldiers of the *Nasutitermes costalis* species. By means of X-ray analysis we now have established that the compound in question possesses a modified skeleton which differs from that of kempane in configuration at C(7). The originally suggested structure *I*



I



II

should be therefore revised, and a new structure *II* is assigned to the defense compound. The present paper brings X-ray data establishing structure *II* and reinterpretes the NMR and mass spectral data on the basis of the revised structure.

X-Ray Analysis

Preliminary X-ray photographs showed that the crystals have orthorhombic symmetry. Systematic absences and approximate crystal density were consistent with the space group $P2_12_12_1$ and one molecule, $C_{25}H_{34}O_7$, $M = 446.540$, in the asymmetric unit. Accurate lattice constants

TABLE I
Positional parameters of atoms in II

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
O(1)	-0.2172(10)	0.0423(6)	0.9079(2)	H(1)	0.487	0.010	0.847
O(2)	0.4787(11)	-0.3441(6)	0.8945(2)	H(21)	0.577	0.009	0.768
O(3)	0.1615(12)	-0.1124(6)	0.7397(2)	H(22)	0.350	0.065	0.759
O(4)	0.8184(14)	-0.3425(7)	0.8933(3)	H(3)	0.461	-0.155	0.752
O(5)	0.3640(14)	-0.0627(7)	0.6841(2)	H(51)	0.541	-0.300	0.818
O(6)	0.0950(15)	0.1607(8)	0.9731(2)	H(52)	0.604	-0.172	0.820
O(7)	0.1893(13)	0.3274(6)	0.9435(2)	H(6)	0.577	-0.177	0.891
C(1)	0.3868(17)	0.0459(8)	0.8265(3)	H(7)	0.158	-0.261	0.892
C(2)	0.4177(15)	0.0047(9)	0.7783(3)	H(8)	0.339	-0.065	0.933
C(3)	0.3365(17)	-0.1169(9)	0.7683(3)	H(91)	-0.081	-0.144	0.937
C(4)	0.2855(18)	-0.1860(8)	0.8096(3)	H(92)	0.018	-0.058	0.970
C(5)	0.4952(20)	-0.2206(9)	0.8287(3)	H(131)	0.368	0.310	0.873
C(6)	0.4709(16)	-0.2289(7)	0.8794(3)	H(132)	0.527	0.213	0.892
C(7)	0.2545(14)	-0.1882(7)	0.8893(3)	H(141)	0.315	0.210	0.809
C(8)	0.2391(16)	-0.1294(9)	0.9338(3)	H(142)	0.560	0.203	0.819
C(9)	0.0222(16)	-0.0829(9)	0.9421(3)	H(16)	0.025	-0.138	0.844
C(10)	-0.0412(14)	0.0109(8)	0.9126(3)	H(171)	0.021	0.131	0.805
C(11)	0.1320(15)	0.0700(8)	0.8866(3)	H(172)	-0.007	0.004	0.785
C(12)	0.2222(14)	0.1651(7)	0.8994(3)	H(173)	-0.138	0.040	0.831
C(13)	0.3927(17)	0.2226(9)	0.8745(3)	H(181)	0.140	-0.342	0.823
C(14)	0.4176(16)	0.1759(8)	0.8279(3)	H(182)	0.037	-0.265	0.783
C(15)	0.1762(15)	0.0065(8)	0.8430(3)	H(183)	0.250	-0.341	0.775
C(16)	0.1689(13)	-0.1248(7)	0.8475(2)	H(191)	0.447	-0.235	0.970
C(17)	-0.0011(15)	0.0475(9)	0.8126(3)	H(192)	0.291	-0.162	0.997
C(18)	0.1709(22)	-0.2962(10)	0.7969(3)	H(193)	0.211	-0.273	0.969
C(19)	0.3041(23)	-0.2037(11)	0.9706(3)	H(211)	0.161	0.470	0.984
C(20)	0.1595(18)	0.2160(8)	0.9430(3)	H(212)	-0.024	0.378	0.990
C(21)	0.1272(23)	0.3849(11)	0.9846(4)	H(213)	0.208	0.346	1.008
C(22)	0.1940(20)	-0.0853(11)	0.6977(3)	H(231)	-0.122	-0.104	0.690
C(23)	0.0022(20)	-0.0882(9)	0.6713(3)	H(232)	-0.015	-0.008	0.654
C(24)	0.6622(16)	-0.3892(8)	0.9029(3)	H(233)	0.007	-0.151	0.549
C(25)	0.6456(23)	-0.5060(9)	0.9226(3)	H(251)	0.780	-0.544	0.929
				H(252)	0.562	-0.499	0.950
				H(253)	0.566	-0.555	0.901

$a = 6.540(1)$, $b = 11.743(2)$, $c = 30.504(6)$ Å were determined from a least-square fit of the angular setting of fifteen selected reflections. Unique intensity data with $2\theta \leq 110^\circ$ were measured on a computer controlled four-circle diffractometer, using variable $2\theta - \theta$ scans and graphite-monochromated $\text{CuK}\alpha$ radiation, $(\text{CuK}\alpha) = 7.6 \text{ cm}^{-1}$. Of the 1744 independent measured reflections, 1384 were considered significant ($I \geq \sigma(I)$) and used for the structure elucidation. The crystal structure was solved by the multiresolution direct method (SIR) (ref.²) using one-phase and two-phase semiinvariants to determine the starting set of phases, and negative quartets to discriminate the best set of refined phases. The positions of hydrogen atoms were found on difference Fourier synthesis ($\sin \theta/\lambda = 0.45 \text{ \AA}^{-1}$); block-diagonal least-squares calculations with anisotropic thermal parameters for non-hydrogen atoms and isotropic B values (equal to that of the carrier atoms) for hydrogens have converged to the residual $R = 0.077$ ($R_w = 0.114$) for the observed data. The calculations were carried out on the HP-1000 computer of the C.N.R. research Area of Rome, using the set of programs of the reference 3.

The results of the X-ray analysis (positional parameters for carbon, oxygen, and hydrogen atoms) of compound *II* are presented in Table I (for numbering of atoms see formula *IIa*)*. The stereochemistry is shown in Fig. 1. No attempt has been made to determine the absolute configuration by measurements of X-ray anomalous dispersion effects; the enantiomer depicted in Fig. 1 has configuration corresponding to that determined by CD measurements for kempene and trinervitane derivatives^{4,5}.

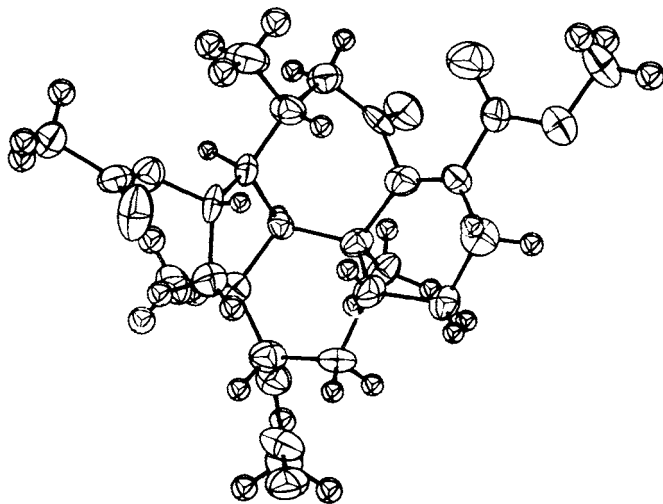


FIG. 1

Perspective drawing of molecule *II*

* Supplementary material containing side-chain torsion angles, bond distances and angles, anisotropic thermal parameters, observed and calculated structure factors and phases are deposited at the Cambridge Crystallographic Data Centre, U.K.

The conformation of the molecule is described by the torsion angles given in Table II. They allow us to assign a distorted twist form to the cyclohexane ring A, an envelope conformation to ring B with C_s -C(16) pseudosymmetry ($\Delta C_s = 6.4^\circ$), a half-chair conformation to the cyclohexene ring C with the pseudobinary axis

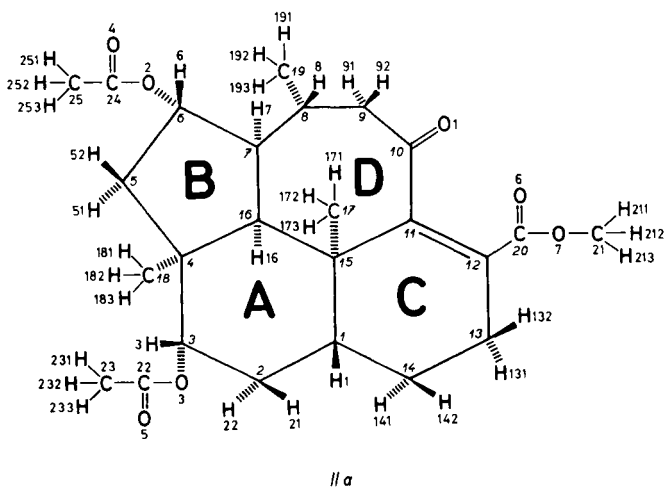


TABLE II
Skeleton torsion angles in compound II^a

Ring A (cyclohexane)		Ring B (cyclopentane)	
C(15)—C(1)—C(2)—C(3)	-39.5	C(16)—C(4)—C(5)—C(6)	23.7
C(1)—C(2)—C(3)—C(4)	-13.5	C(4)—C(5)—C(6)—C(7)	-5.2
C(2)—C(3)—C(4)—C(16)	43.2	C(5)—C(6)—C(7)—C(16)	-15.1
C(3)—C(4)—C(16)—C(15)	-16.4	C(6)—C(7)—C(16)—C(4)	29.0
C(4)—C(16)—C(15)—C(1)	-38.6	C(7)—C(16)—C(4)—C(5)	-31.6
C(16)—C(15)—C(1)—C(2)	67.4		
Ring C (cyclohexene)		Ring D (cycloheptanone)	
C(14)—C(1)—C(15)—C(11)	-46.6	C(16)—C(7)—C(8)—C(9)	48.8
C(1)—C(15)—C(11)—C(12)	20.1	C(7)—C(8)—C(9)—C(10)	-66.3
C(15)—C(11)—C(12)—C(13)	-3.9	C(8)—C(9)—C(10)—C(11)	-15.5
C(11)—C(12)—C(13)—C(14)	13.3	C(9)—C(10)—C(11)—C(15)	86.7
C(12)—C(13)—C(14)—C(1)	-39.0	C(10)—C(11)—C(15)—C(16)	-39.8
C(13)—C(14)—C(1)—C(15)	58.9	C(11)—C(15)—C(16)—C(7)	-38.4
		C(15)—C(16)—C(7)—C(8)	32.7

^a The e.s.d.'s range between 1.7 and 0.7°, with a mean value of 1.1°.

passing through the middle points of C(1)—C(14) and C(11)—C(12) bonds ($\Delta C_s = 6.3^\circ$), and boat conformation to the cycloheptanone ring D with pseudosymmetry C_s —C(16) ($\Delta C_s = 13.9^\circ$). The most characteristic feature of the tetracyclic system concerns the junction of the rings. Indeed, the junction is *cis* between rings A and B, A and D, and B and D, *trans* between rings A and C, and quasi-*trans* between rings C and D. It is worth noting that the A/B and A/D *cis* junctions are peculiar

TABLE III

^1H and ^{13}C NMR data of compound II in deuteriochloroform

Proton ^a	^1H NMR
C(8)—CH ₃	0.97 d (3 H), $J(19,8) = 5.1$
C(15)—CH ₃	1.19 s (3 H)
C(4)—CH ₃	1.27 s (3 H)
H(22)	1.44 dt (1 H), $J(22,1) = J(22,21) = 12.5$; $J(22,3) = 7.7$
H(21)	1.98 ddd (1 H), $J(21,1) = 4.0$; $J(21,3) = 6.3$; $J(21,22) = 12.5$
OAc	1.99 s
OAc	2.05 s
H(51), H(52), H(7), H(8)	2.22 m (4 H)
H(1), H(91)	2.40 m (2 H)
H(92)	2.89 d (1 H), $J(92,91) = 13.2$; $J(92,8) \cong 0$
COOCH ₃	3.69 s (3 H)
H(3)	4.79 dd (1 H), $J(3,21) = 6.3$; $J(3,22) = 7.7$
H(6)	5.05 m (1 H), $J(6,51) = 7.2$; $J(6,52) = 8.6$; $J(6,7) = 9.0$

Carbon (assign.)	^{13}C NMR	Carbon (assign.)	^{13}C NMR
C=O (10)	209.1	—CH ₂ —	43.9
C=O (22)	170.5	—C— (4)	41.0
C=O (24)	170.5	—CH—	36.2
C=O (20)	160.7	—CH—	31.8
—C= (11)	136.1	—CH ₂ —	30.6
—C= (12)	121.8	—CH ₃	26.2
—CH—O (6)	77.0	—CH ₂ —	24.5
—CH—O (3)	74.4	—CH ₃	23.6
—CH—	54.1	—CH ₂ —	23.2
—CH—	53.2	—CH ₃ (23)	21.3
—C— (15)	52.0	—CH ₃ (25)	21.3
—OCH ₃ (21)	52.0	—CH ₃	19.6
—CH ₂ —	44.3		

^a For numbering of protons see formula IIa.

for kempene derivatives which also have B/D junction of *trans*-type, while the B/D *cis* junction found in the present compound is characteristic of the trinervitane skeleton. The molecule *II* shows a dome-like shape in which most hydrogens and methyl substituents on the carbon skeleton protrude from the concave or convex face, while the oxygen-containing polar groups are located on the periphery.

Discussion of the Spectra

The revised structure requires that the previously suggested¹ mechanism of the mass spectral fragmentation of *II* be revised either. The spectrum shows an ion series $M^{+\cdot} \rightarrow C_{16}H_{21}O_4^+ \rightarrow C_{14}H_{17}O_2^+ \rightarrow C_{12}H_{13}^+$ arising by skeletal cleavage followed by loss of two molecules of acetic acid. The skeletal cleavage probably commences with opening of ring C, and requires a transfer of two hydrogen atoms onto the carbonyl-containing neutral fragment (Scheme 1).

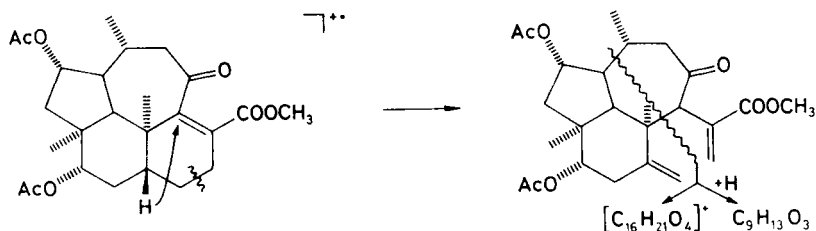
The UV and CD spectra provide the following parameters: UV: $\lambda_{sh} = 300$ nm ($\epsilon = 8$); $\lambda_{max} = 223.5$ nm ($\epsilon = 9180$). CD: $\Delta\epsilon_{297} = -6.16$; $\Delta\epsilon_{268} = 0$; $\Delta\epsilon_{252} = +4.40$; $\Delta\epsilon_{240} = 0$; $\Delta\epsilon_{212} = -17.32$ l mol⁻¹ cm⁻¹. The CD values $\Delta\epsilon_{212} = -17.32$ and $\Delta\epsilon_{252} = +4.40$ and the absorption band at 223.5 nm were assigned to the α,β -unsaturated ester group. The values corresponding to the keto group ($\Delta\epsilon_{297} = -6.16$ and $\lambda_{max} = 300$ nm) were erroneously interpreted in the previous paper as excluding the presence of an α,β - or β,γ -enone arrangement, and subse-

TABLE IV
Comparison of X-ray and ¹H NMR conformational data of compound *II*

Dihedral angle of protons H(<i>i</i>), H(<i>j</i>)	X-ray ^a $\Phi(i, j)$	¹ H NMR	
		<i>J</i> (<i>i, j</i>)	$\Phi(i, j)^b$
H(1)—C(1)—C(2)—H(21)	-49	4.0	55
H(1)—C(1)—C(2)—H(22)	-159	12.5	170
H(21)—C(2)—C(3)—H(3)	-5	6.3	40
H(22)—C(2)—C(3)—H(3)	109	7.7	145
H(51)—C(5)—C(6)—H(6)	115	7.2	140
H(52)—C(5)—C(6)—H(6)	2	8.6	25
H(6)—C(6)—C(7)—H(7)	-150	9.0	150
H(8)—C(8)—C(9)—H(92)	-71	0.0	90

^a Dihedral angles calculated with the coordinates of Table I for the hydrogen and carbon atoms; ^b determined from Karplus-like relation in ref.⁶; only absolute values of the angles are obtainable; where *J* value corresponds to two possible angles, only one, which is closer to $\Phi(i, j)$ from X-ray is given (rounded off to 5°).

quently led to the suggested structure *I*. With the knowledge of the molecular geometry of *II*, based on X-ray data, it now appears that these anomalous values correspond to the twisted α,β -enone group, where the torsion angle between the $C=O$ and $C=C$ bonds is about 90° (86.7° by X-ray analysis).



SCHEME 1

The ^1H and ^{13}C NMR spectra obtained at 200 MHz, and 50.3 MHz resp., were impossible to assign completely due to the very small amount of the compound isolated. A partial assignment, based on structure *II*, is given in Table III. The vicinal coupling constants that can be extracted from the ^1H NMR spectrum and that provide some information on the spatial arrangement of molecular fragments show, however, that the conformation of *II* in solution may be slightly different from that found by X-ray analysis in the crystal (see Table IV).

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