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BACKBONE REARRANGEMENTS OF METHYL (-)-KAUR-9(11)-EN-19-OATE AND ITS EPOXIDE: STRUCTURES OF TWO DITERPENES OF A NEW SKELETAL TYPE

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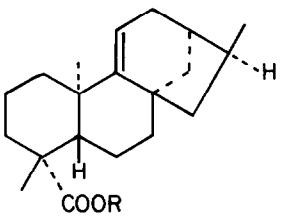
Abstract: Cleavage of the epoxide (2) of methyl (-)-kaur-9(11)-en-19-oate (1b) with boron trifluoride-ether in benzene and in acetic anhydride yielded (3a) and (3b), respectively. On epoxidation with m-chloroperbenzoic acid in the presence of N-nitrosomethyl urea, (1b) suffered a backbone rearrangement to form (6).

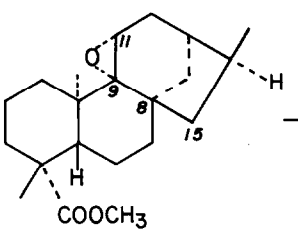
In an attempt to transform (-)-kaur-9,16-diene-19-oic acid to a derivative of zoapatline,[1] a diterpene lactone from the native Mexican shrub "zoapatle" (Montanoa tomentosa Cerv.), we have investigated the cleavage of α-epoxide (2) of its dihydro derivative (1b).[2] On treatment with boron trifluoride-ether in benzene, (2) yielded an aldehyde, $C_{21}H_{32}O_3$, m/e 332 (M^+). The ^1H n.m.r. spectrum showed signals for two tertiary methyls (δ 0.76 and 1.18, s), a secondary methyl (δ 0.78, d, J = 6 Hz), a methoxy group (δ 3.60, s), and an aldehyde proton (δ 9.75, t, J 1.8 Hz); the presence of an aldehyde function was confirmed by the i.r. spectrum [$\nu_{max.}$ 2720 (aldehyde CH) and 1736 (CO of ester and aldehyde) cm^{-1}]. It is apparent that an aldehyde group must have been generated from the rupture of ring C bearing the epoxide ring, and hence this compound is tricyclic with a tetrasubstituted double bond and is formulated as (3a). A possible mechanism for its formation may be as follows (see Scheme). Rupture of the epoxide ring with boron trifluoride-ether would take place with concomitant migration of the C(8)-C(15) bond to C(9) [formation of (4)]. Subsequent neutralization of the positive charge at C(8) by the breaking of the C(9)-C(11) bond would lead to (3a).

We assumed that in presence of acetic anhydride, any alcohol (4), if formed, might be esterified in situ and the resulting product might then be (5) rather than (3a). Therefore, we decided to conduct this epoxide ring cleavage in a medium of acetic anhydride. In this case, however, a nicely crystalline product [$C_{25}H_{38}O_6$, m/e 434 (M^+)], which showed three separate carbonyl bands ($\nu_{max.}$ 1770, 1750, and 1725 cm^{-1}) in its i.r. spectrum, was obtained.

The ^{1}H n.m.r. spectrum revealed that this compound contained two tertiary methyls (δ 0.70 and 1.14, s), a secondary methyl (δ 0.73, d, J 6 Hz), two acetoxy (δ 2.00, s), a methoxy (δ 3.56, s), and a CH_2-CH<O-/O- grouping (δ 6.65, t, J 5.4 Hz). This product is formulated as (3b) and its structure and stereochemistry were established unequivocally by a single-crystal X-ray analyis.[3] A view of the structure is provided in Figure 1.



1a ; R=H
1b ; R=CH_3



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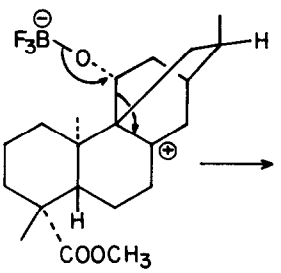

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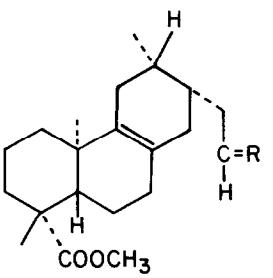
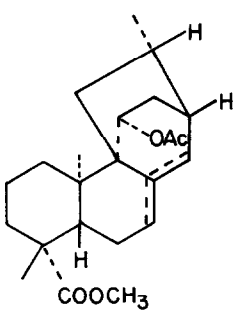


3a ; R = O
3b ; R = OAc / OAc



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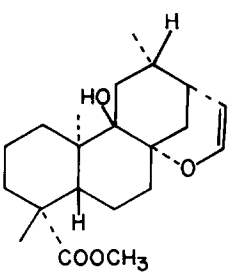

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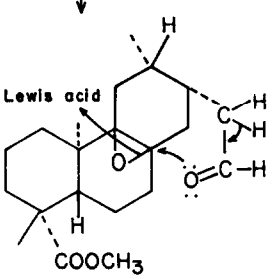

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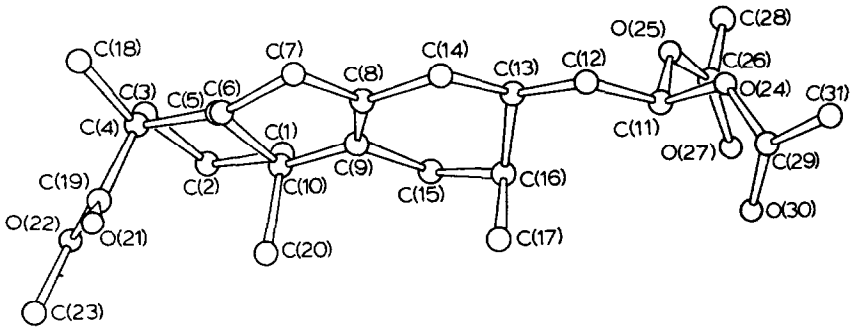

Figure 1. Structure and solid-state conformation of (3b)

During the epoxidation of (1b) we also observed that in the presence of N-nitrosomethyl urea,[6] the expected epoxide (2) was not obtained, but instead a compound, $C_{21}H_{32}O_4$, was isolated [^{1}H n.m.r.: δ 0.86 (3H, d, J 6 Hz, CH_3-CH), 0.95 (3H, s, CH_3), 1.23 (3H, s, CH_3), 3.87 (3H, s, CH_3O), 5.01 (1H, ddd, J 6.5, 6, and 3 Hz, O-CH=CH), and 6.86 (1H, d, J 6.5 Hz, O-CH=CH); i.r.: $\nu_{max.}$ 3550 (OH), 1740 (ester CO), 1650 (CH=CH), and 1247 (C-O) cm^{-1}; m/e 348 (M^+). A single-crystal X-ray analysis established the structure and stereochemistry of this product to be as represented by (6). A view of the structure is provided in Figure 2.

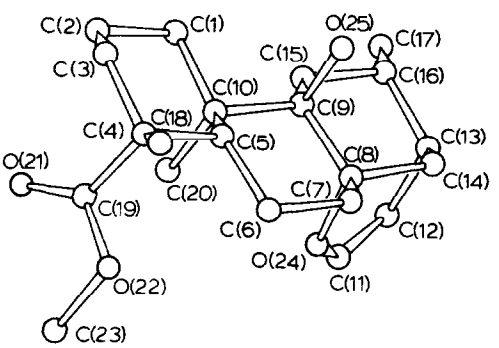

Figure 2. Structure and solid-state conformation of (6)

We postulated that an intermediate for formation of (6) is epoxide (2) and studied how the reaction proceeded. Immediately after (1b) (1 mol equiv.) was mixed in chloroform with N-nitrosomethyl urea (1 mol equiv.) and MCPBA (2 mol equiv.), the reaction was monitored by t.l.c. After 1 h, almost all of (1b) had disappeared, and a product (ca. 90%) of polarity identical with that of (2) appeared. When the reaction was discontinued at this point, (2) was obtained. However, when the above reaction was allowed to continue for an additional 3 h, (2) disappeared and two products, both of which are more polar than (2), appeared on t.l.c.

The more polar of these proved to be identical with (6), and the other, with (3a). A plausible mechanism may now be visualized as shown in the Scheme. The initially-formed epoxide (2) would suffer ring opening by the mixture of N-nitrosomethyl urea and MCPBA which would act in this case as a Lewis acid.[7] The aldehyde (3a) formed would react further with MCPBA to yield (7). Subsequent nucleophilic attack at C(8) by the aldehyde carbonyl and concurrent rupture of the epoxide ring would lead to (6). The foregoing postulated mechanistic pathway was further supported experimentally by preparing (6) from (3a) by epoxidation to (7), followed by an acid-catalyzed cleavage.

We thank Dr. H. O. House of Georgia Institute of Technology for helpful discussions.

REFERENCES AND NOTES

1. Y. Caballero and F. Walls, Bol. Inst. Quím. Univ. Nacl. Autón. México, 22, 79 (1970).
2. A. K. Banerjee, A. Martin, T. Nakano, and A. Usubillaga, J. Org. Chem., 38, 3807 (1973).
3. Crystal data: (3b), $C_{25}H_{38}O_6$, M = 434.6, monoclinic, space group $P2_1$, a = 11.247(5), b = 13.348(7), c = 8.243(4) Å, β = 99.80(5)°, U = 1219 Å³, Z = 2, D_c = 1.184 g cm^{-3}; (6), $C_{21}H_{32}O_4$, M = 348.5, orthorhombic, space group $P2_12_12_1$, a = 12.530(6), b = 17.149(9), c = 8.658(5) Å, U = 1860 Å³, Z = 4, D_c = 1.244 g cm^{-3}. Intensity data for all unique reflections, measured on an Enraf-Nonius CAD-3 automated diffractometer[4] (Ni-filtered Cu-K_α radiation, λ = 1.5418 Å; θ-2θ scans, $\theta_{max.}$ = 67°), yielded 1764 and 1212 reflections with $I > 2.0\sigma(I)$ for (3b) and (6), respectively. Both structures were solved by direct methods. Least-squares refinement of atomic positional[5] and thermal (anisotropic C, O; isotropic H) parameters converged to R = 0.052 for (3b) and R = 0.055 for (6).
4. For details, see; R. W. Miller and A. T. McPhail, J. Chem. Soc., Perkin Trans. 2, 1527, (1979).
5. Atomic coordinates for (3b) and (6) have been deposited with the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW.
6. Compound (1b) was prepared by methylation of (1a) with ethereal diazomethane. Diazomethane was generated in ether solution from N-nitrosomethyl urea and aqueous KOH, and was used without purification by distillation. In this case, some amount of N-nitrosomethyl urea was inevitably contaminated with (1b) and was not readily removed by recrystallization. The best way to eliminate the N-nitrosomethyl urea contaminant is to filter the methylated product in benzene solution over silica gel.
7. The epoxide (2) is stable in chloroform solution towards either N-nitrosomethyl urea or a mixture of MCPBA and m-chlorobenzoic acid. One reasonable guess, therefore, would be that N-nitrosomethyl urea in the presence of MCPBA may generate some amount of nitric acid (from oxidation and cleavage of the nitroso group).

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