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AN UNUSUAL REARRANGEMENT OF EUDESMANE SKELETON

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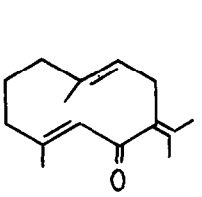
Summary: The lactone 5 was found to be a co-product of the BF_3 etherate induced cyclization of epoxyisogermacrone 2. The ketol 3 when treated with 100% HCOOH afforded the lactone 5 while under the same conditions the ketol 4 gave the corresponding ester 6. A mechanism is suggested for the rearrangements.

Recently, we reported the regio- and stereoselective cyclization of isogermacrone 1[1]. In continuing our interest in this area, we further examined the acid- and base-catalyzed cyclization of epoxyisogermacrone 2 leading mainly to formation of the eudesmane derivatives 3 and 4[2]. In the present paper, we wish to describe the unexpected obtaining of the lactone 5 when treated epoxyisogermacrone 2 with BF_3 etherate, as well as the unusual rearrangement of the eudesmane skeleton of the ketol 3 into the same lactone 5.

On treatment with BF_3 etherate (equimolar amounts) at 0° for 45 min epoxyisogermacrone 2 was converted into the ketol 3 and the lactone 5 in 80.5 and 8.2% yields, respectively. The structure of the latter product was unambiguously determined on the basis of its spectral data, as follows:



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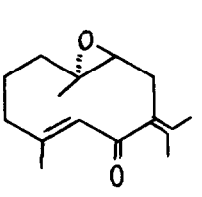

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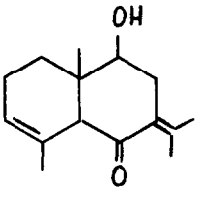

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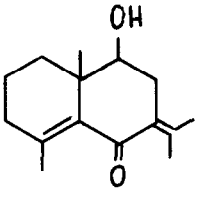

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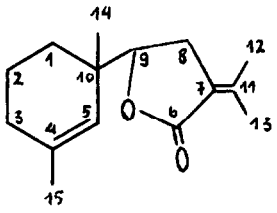
m.p. 72-74° (from ether/hexane); $C_{15}H_{22}O_2$ [m/e 235 $(M+H)^+$, 125 ($C_7H_9O_2$), 109 (C_8H_{13}), 97 ($C_7H_9O_2$- CO)]; ν_{max} (KBr): 1760, 1680, 1273, 1200 cm^{-1}; λ_{max} (EtOH): 230 nm (ε 15100); PMR (δ, $CDCl_3$): 1.00 (3H, s), 1.68 (3H, br s), 1.86 (3H, s), 2.25 (3H, t, J=2.2 Hz), 2.52-2.75 (2H, m), 4.21 (1H, t, J=7.7 Hz), 5.09 (1H, s).

CMR spectral data of the lactone 5

C-1	31.25	(t)*	C-9	81.93	(d)
C-2	18.86	(t)	C-10	38.71	(s)
C-3	30.20	(t)*	C-11	149.07	(s)
C-4	120.42	(s)	C-12	24.06	(q)
C-5	124.53	(d)	C-13	24.35	(q)
C-6	170.62	(s)	C-14	19.88	(q)
C-7	136.85	(s)	C-15	22.60	(q)
C-8	29.52	(t)*			

*These signals may be interchanged



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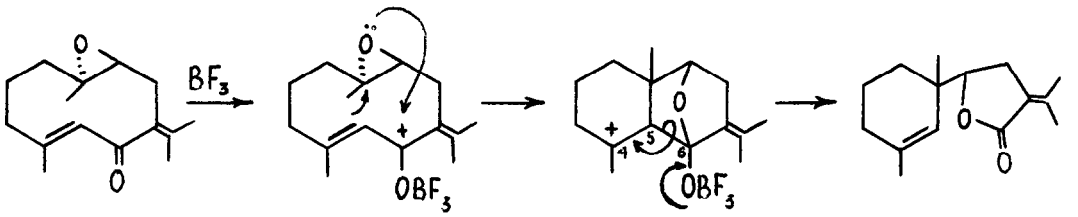
The UV and IR data (230 nm and 1760, 1680 cm^{-1}) showed the presence of an α,β-unsaturated-γ-lactone moiety. The chemical shift of C-6 (δ 170.62) also indicated that the carbonyl group is included in a lactone ring. Furthermore, the MS data confirmed not only the presence but also the location of the lactone ring - the two peaks at m/e 125 and 109 correspond to fragments obtained by cleavage of the C-9/C-10 bond. As judged from the PMR spectrum, the compound 5 has one tertiary (δ 1.00) and three olefinic (δ 1.68, 1.86 and 2.25) methyl groups. The broadening of the singlet at δ 1.68 and the splitting (2.2 Hz) of the signal at δ 2.25 is due to the homoallylic coupling between the isopropylidene methyl protons (C-12 and C-13) and the C-8 methylene protons (cisoid and transoid, respectively). The two C-8 protons appear in the region δ 2.52-2.75 as a complex multiplet because of their close chemical shift on one hand, and on the other the simultaneous geminal, vicinal (with H-9) and homoallylic (cisoid and transoid) coupling. However, after irradiation of the C-9 proton (δ 4.21) the C-8 protons appear as broad doublets (because of the homoallylic coupling) at δ 2.62 and 2.70 (each with J_{gem}= 16.3 Hz). Furthermore, irradiation of the C-13 methyl protons (δ 2.25) converted the C-8 protons multiplet into two broad doublets of doublets at δ 2.60 and 2.77 (each with J_{gem}= 16.3 Hz and J_{vic}= 7.7 Hz). The broadening of the signals is caused by the left cisoid homoallylic coupling with the C-12 methyl protons.

The formation of the lactone 5 from epoxyisogermacrone 2 can be rationalized as shown in Scheme 1. Clearly, the reaction must be initiated by attack of BF_3 etherate at the carbonyl group leading to the formation of the eudesmane hemi-

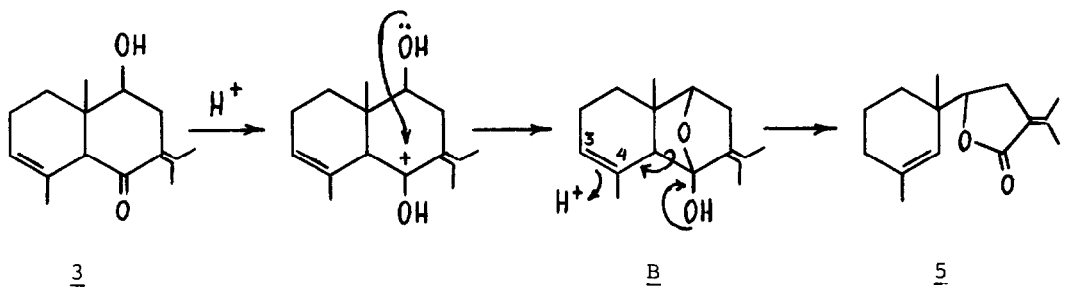
ketal intermediate A. The following cleavage of the C-5/C-6 bond afforded the lactone 5.



2 A 5

Scheme 1

The lactone 5 was also obtained from the ketol 3 when trying to carry out the acid-catalyzed isomerization[3] of the latter to the corresponding fully substituted $\alpha,\beta-\alpha',\beta'$-unsaturated ketone 4[4]. Thus, on treatment with 100% HCOOH at room temperature for 2 hrs the ketol 3 rearranges into the lactone 5 in 60% yield. The formation of 5 in this case may be considered, as shown in Scheme 2.



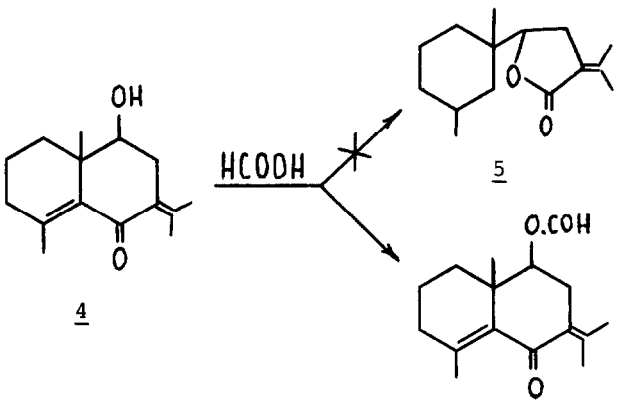
3 B 5

Scheme 2

According to the suggested mechanism, the rearrangement involves initial protonation of the carbonyl group followed by the oxygen bridging into the intermediate B. Subsequent protonation of the 3,4-double bond leads to cleavage of the C-5/C-6 bond and formation of the lactone 5.

As could be concluded from Scheme 1 and 2, the rearrangement of the eudesmane intermediates A and B requires the presence of a positive charge centered at C-4. An additional fact which supports such a mechanism is that the ketol 4 did not undergo this rearrangement. When treated with 100% HCOOH at room temperature for 3 hrs the ketol 4 was readily converted into the corresponding ester 6[5] in 95% yield. Obviously, the conjugated system in 4 prevents the formation of a B-like intermediate and a simple esterification of the hydroxyl

group takes place instead.



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References and Notes

1. E.Tsankova, I.Ognyanov and T.Norin, Tetrahedron, 36, 669 (1980)
2. Epoxidation of isogermacrone 1, cyclization under different conditions and the structures and stereochemistry of the products obtained will be discussed in details elswhere.
3. M.Niwa, M.Iguchi and S.Yamamura, Bull.Chem.Soc.Japan, 49, 3137 (1976)
4. The compound 4 was obtained by treatment of 3 with sodium ethoxide in ethanol.
5. Physical data of compound 6: colourless oil; $C_{16}H_{22}O_3$ m/e 262 (M+), 216 (M^+- HCOOH), 201 (M^+- HCOOH - CH_3) ; ν_{max}(film): 1764, 1713,1662,1213 cm^{-1}; λ_{max}(EtOH): 277 nm; PMR (, $CDCl_3$): 1.09 (3H, s), 1.80 (3H, br s), 1.89 (3H, s), 2.08 (3H, t, J=2.0 Hz), 2.50 (1H, dd, J=14.0 and 10.0 Hz), 2.98 (1H, dd, J=14.0 and 6.0 Hz), 5.07 (1H, dd, J=10.0 and 6.0 Hz), 8.14 (1H, s).

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