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THE ACYLOIN REARRANGEMENT IN α,β-UNSATURATED α´-KETOLS

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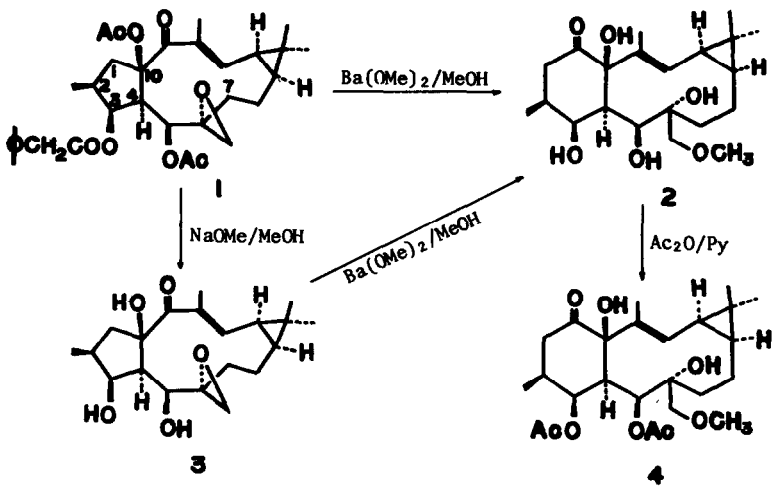
The acyloin rearrangement of the bridehead α-ketols under basic catalysis has been known to proceed *via* the delocalized intermediate[1]. In this rearrangement, the counterpart metal ion was assumed to uninfluence a mode of reaction mechanism[2].

We would now like to report, for the first time, an anionic rearrangement of α,β-unsaturated α´-ketols in which the major product has been shown to depend upon the sorts of the metal ion.

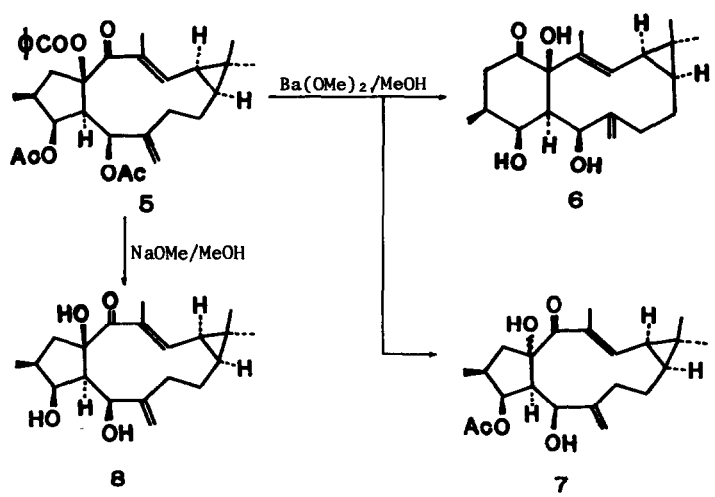
Treatment of epoxylathyrol (1) with barium methoxide (nine molar equivalents) in methanol at room temperature for 8 hr, followed by careful chromatography of the mixture on a silica gel column, gave colorless needles (2) in 45% yield. The compound 2, m.p. 230-233°, had the molecular formular $C_{21}H_{34}O_6$ on the basis of elemental analysis[3] and mass spectral (M^+ m/e 382) results The compound 2 showed the presence of a hydroxyl (3350 and 3250 cm^{-1}) and a six membered ketone (1710 cm^{-1}) in the ir spectrum (in Nujol). The uv spectrum was significantly different from 1 in that it showed no absorption of the conjugated chromophor above 210 nm. The nmr spectrum[4] (in $CDCl_3$) of 2 displayed the absence of acyl group and newly appeared a methoxy group (δ 3.53), an olefinic proton (δ 4.63, d, J=12 Hz), and further, two tertiary methyls (δ 0.96 and 1.03), a secondary methyl (δ 1.10, d, J≈6 Hz), and two methin protons bound the hydroxy group (δ 3.66, d, J=10 Hz; δ 3.88, t, J=4 Hz). Acetylation of 2 with acetic anhydride in pyridine yielded the diacetate (4) as an amorphous powder, $C_{25}H_{38}O_8 \cdot 1/2\ H_2O$, mol. wt. 466 (mass spectrum). The spectral results of 4 were shown as follows; ir (Nujol) ν_{max}, 3420 (OH), 1725 (OAc), 1737 cm^{-1} (OAc), nmr ($CDCl_3$) ppm, δ 0.95 (3H, d, J=6 Hz), 0.96 (3H, s), 1.03 (3H, s), 1.93 (3H, d, J≈1 Hz), 2.03 (3H, s), 2.06 (3H, s), 3.40 (3H, s), 3.81 (1H, d, J=2 Hz), 3.93 (1H, d, J=2 Hz), 4.08 (1H, d, J=8 Hz), 4.46 (1H, t, J=8 Hz), 4.75 (1H, dd, J_1=9 Hz, J_2≈1 Hz). These results are expected for the skeletal rearrangement of 1 to 2. On the other hand, when either potassium or sodium methoxide was employed in this reaction instead of barium methoxide 1 gave the normal hydrolysed triol (3)[5], m.p. 207-209°, $C_{20}H_{30}O_5$, uv (EtOH) λ_{max} 274.5 nm (ε 15800). Treatment of the triol 3 with barium methoxide under the identical conditions gave the compound 2 as the

sole product (Scheme 1).



Scheme 1

As expected, treatment of ester L_3 (5)[6,7], having the same α-acylated hydroxy keto moiety as that of epoxylathyrol, with barium methoxide in methanol gave the rearranged compound (6), m.p. 204-205°, $C_{20}H_{30}O_4$, mol. wt 334 (mass spectrum) besides the partially deacylated product (7) (Scheme 2). The spectral results of 6 and 7 were shown as follows; 6, ir (Nujol) ν_{max}, 3500 and 3440 (OH), 1718 cm^{-1} (six membered ketone), nmr (CD_3OD) ppm, δ 0.96 (3H, s), 1.00 (3H, d, J=6 Hz), 1.06 (3H, s), 1.91 (3H, s), 4.23 (1H, t, J=3 Hz), 4.46 (1H, d, J=10 Hz), 4.63 (1H,

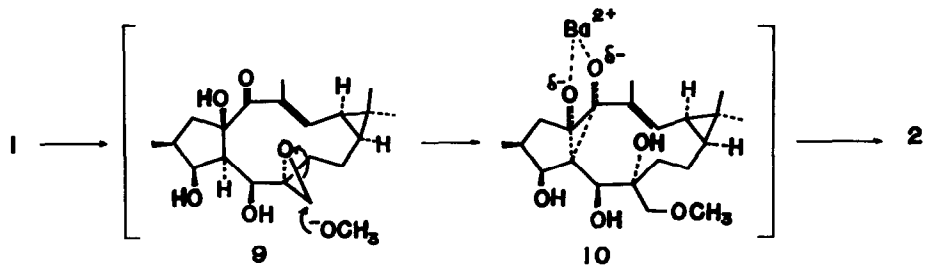


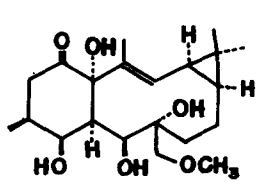
Scheme 2

d, J=9 Hz), 4.81 (1H, br. s), 5.15 (1H, br. s); 7, ir (film) ν_{max}, 3480 (OH), 1742 (OAc), 1685 and 1632 cm^{-1} (α,β-unsaturated ketone), nmr ($CDCl_3$) ppm, δ 0.86 (3H, s), 1.06 (3H, s), 1.16 (3H, d, J=6 Hz), 1.81 (3H, s), 2.15 (3H, s), 4.80 (1H, d, J=8 Hz), 5.96 (1H, br. s), 6.00 (1H, q, J_1=3 Hz, J_2=10 Hz), 6.18 (1H, br. s), 6.83 (1H, d, J=10 Hz). When the reaction was run in the presence of sodium methoxide in methanol the normal deacylated product (8), m.p. 167-169°, $C_{20}H_{30}O_4$, mol. wt. 334 (mass spectrum) was obtained. The spectral results were shown as follows; uv (EtOH) λ_{max}, 279 nm (ε 11900), ir (Nujol) ν_{max}, 3350 and 3210 (OH), 1640 and 1620 (α,β-unsaturated ketone), 908 cm^{-1} (vinylidene), nmr ($CDCl_3$) ppm, δ 1.13 (3H, d, J=6 Hz), 1.16 (6H, s), 1.91 (3H, br. s), 3.30 (1H, d, J=6 Hz), 3.38 (1H, d, J=6 Hz), 4.26 (1H, t, J=4.5 Hz), 4.38 (1H, d, J=5 Hz), 4.40 (1H, br. s), 5.03 (1H, br. s), 6.04 (1H, br. d, J=11 Hz).

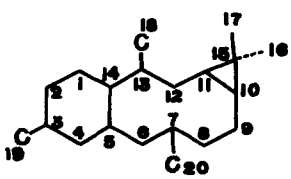
While isomerization of the bridehead α-ketols can often be induced by acidic and basic reagents, to our knowledge no such precedent has been described for the α,β-unsaturated α′-ketols. This skeletal rearrangement 1 → 2 or 5 → 6 might be formally analogous to the acyloin rearrangement which proceeded the migration of the C_{4-10} bond to the carbonyl carbone. However, no formation of another thermodynamic isomer 11 which was expected from a common intermediate 10 was observed. Assignment of β-configuration to the 14-hydroxyl group in 2 and 6 was in favor of no intramolecular hydrogen bonding in their ir spectra.

Although the influence of various metal ions on the mechanism of the acyloin rearrangement





11



is not so clear, we posturated to explain that the barium ion have greater coordinating power than those of the potassium and the sodium ions.

REFERENCES AND NOTES

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2) P. Y. Johnson and M. A. Priest, *J. Am. Chem. Soc.*, *96*, *5618 (1974)*.

3) All new compounds gave satisfactory elemental analyses.

4) Nmr spectra were taken on Varian T-60 and Hitachi R-20 spectrometers. The chemical shifts (δ) were calculated on the basis of TMS as internal standard.

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7) We confirmed the structure and the absolute configuration of ester L_3 by correlation with epoxylathyrol. In preparation.