Formation of Δ^2-Oxazolines by Cyclization of *N*-Acyl-β-Hydroxy-amines on Zinc Acetate. An Oxazoline Complex of Zinc Acetate

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Summary Heating on solid zinc acetate converts *N*-acylated β-hydroxy-amines into Δ^2-oxazolines *via* a retention mechanism; a complex 1:1 of oxazoline and zinc acetate was isolated.

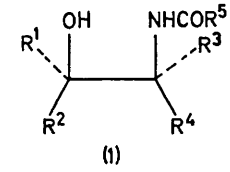
IT was previously assumed that rearrangements of 1,2-diol monoesters[1] and fragmentation of 1,3-diol monoesters[2] on Zn or $Zn(OAc)_2$ are promoted by co-ordination between the carbonyl group and the metal (or metal ion).

We now report that *N*-acyl-β-hydroxy-amines (**1**) are cyclized to Δ^2-oxazolines (**2**) when heated with solid zinc acetate and that this cyclization proceeds *via* a path which is in accordance with the above assumption. The oxazolines (see Table) were usually the only products formed (n.m.r. and t.l.c. evidence). Full retention of configuration was observed for the cyclization of all the compounds (**1d**—**j**) that allowed formation of isomers. The configuration of the oxazolines was determined by n.m.r. (shielding of a methyl *cis* to a phenyl group) and by non-identity with oxazolines formed (in lower yields) by an inversion mechanism when thionyl chloride was used as a cyclizing reagent.

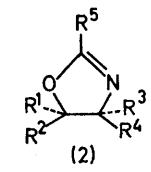
The retention mechanism was investigated by labelling with ^{18}O: (**1d**) labelled at the carbonyl group lost the isotope labelling during the reaction with zinc acetate, whereas (**1a**) and (**1c**), labelled at the OH group, afforded oxazolines with an unchanged content of ^{18}O. (m.sp.).

Hence the co-ordination of the amide carbonyl group with Zn^{II} induces sufficient polarization for OH attack.† The pathway leading to cyclization is thus different from the mechanism observed under other cyclizing conditions[3] (including pyrolysis[4]) which afford the most stable or inverted oxazolines due to the displacement of the hydroxy-group.‡

Direct filtration afforded, in a few cases, complexes which were decomposed into oxazolines by treatment with water or filtration through a Florisil column. The crystalline complex obtained from (**1i**) (plates, from ether) was stable in air and in anhydrous solvents. It was characterized as a 1:1 oxazoline:$Zn(OAc)_2$ complex by elemental analysis



(1)



(2)

and spectral data: n.m.r. ($CDCl_3$) δ 0·77 (3H, d, *J* 7 Hz, CH_3CH), 1·76 (3H, s) 2·32 (3H, d, *J* 2 Hz, $CH_3C{=}N$), and 2·05 (6H, s, OAc). Addition of water shifted the first three signals to positions superimposable with those of free oxazoline (δ 0·68, 1·68, and 2·08); the u.v. spectra of the complex and oxazoline showed identical λ_{max} at 252, 257, and 263 nm and the C=N band of oxazoline in the i.r. ($CHCl_3$) at 1664 cm^{-1} was shifted to lower frequency (1618 and 1647w) in the complex. The 1:1 ratio and the strong deshielding of the C-2 methyl group suggest that *N*- as well as *O*-co-ordination exists in this complex.

TABLE[a,b]

Cyclization of N-*acyl-β-hydroxy-amines on zinc acetate*

Compound (**1**)	Reaction time (min)	Temp. (°C)	Oxazoline (**2**) yield (%)[c]
(**1**) **a**; $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = R^5 = Ph$	120	160	94
b; $R^1 = R^2 = R^3 = R^4 = Me$, $R^5 = Ph$	120	145	90
c; $R^1 = R^2 = R^5 = Ph$, $R^3 = R^4 = H$	225	175	66
d; $R^1 = R^3 = R^5 = Ph$, $R^2 = Me$, $R^4 = H$	150	170	92
e; $R^1 = R^3 = Ph$, $R^2 = R^5 = Me$, $R^4 = H$	180	165	88
f; $R^1 = Me$, $R^2 = R^3 = R^5 = Ph$, $R^4 = H$	120	170	94
g; $R^1 = R^5 = Me$, $R^2 = R^3 = Ph$, $R^4 = H$	150	175	86
h; $R^1 = R^3 = R^5 = Me$, $R^2 = Ph$, $R^4 = H$	120	140	65
i; $R^1 = R^4 = R^5 = Me$, $R^2 = Ph$, $R^3 = H$	150	175	91
j; $R^1 = R^3 = H$, $R^2 = Me$, $R^4 = R^5 = Ph$	150	170	82

[a] Reactions were performed on up to 0·5 g reactant. Increase in the amount of reactant may require some increase in the reaction time. In absence of zinc acetate no reaction occurred under the given condition. [b] Satisfactory elemental analysis were obtained for all new compounds; i.r. and n.m.r. data were in agreement with the assigned structures. [c] Calculated on chromatographically purified products.

The reaction procedure involves heating of the reactant with a 10-fold excess of powdered anhydrous zinc acetate in a glass tube under nitrogen,[1] filtration of the mixture using ether and chloroform, and concentration of the filtrate.

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† The cyclization is not readily initiated by abstraction of the hydroxy-proton as was shown by the recovery of hydroxy-amides after prolonged treatment under reflux with sodium hydride in benzene.

‡ Cyclization by use of concentrated sulphuric acid was found to yield a mixture of 72% *trans*- and 28% *cis*-oxazoline starting either from the *erythro* -(**1e**) or *threo*-(**1g**) isomer. The retention mechanism of an acid-catalysed cyclization[5] was not clarified.

[1] E. Ghera, *J. Org. Chem.*, 1970, **35**, 660.
[2] E. Ghera, *Tetrahedron Letters*, 1970, 1539.
[3] See J. W. Cornforth in 'Heterocyclic Compounds', vol. 5, ed. R. C. Elderfield, Wiley, New York, 1957, pp. 377—390.
[4] T. Wagner-Jauregg and M. Roth, *Chem. Ber.*, 1960, **93**, 3036.
[5] G. Drefahl, M. Hartmann, and H. H. Hörhold, *Chem. Ber.*, 1958, **91**, 1092.