

REACTIONS OF SOME α -ACYLIMMONIUM IONS

Jacek W. Morzycki* and Władysław J. Rodewald
 Department of Chemistry, University of Warsaw,
 02093 Warszawa, Poland

Abstract - The reactions of various hydroxylactams proceeding via α -acylimmonium ions are described.

The reductive N-cyclization of lactamoester 1 with LiAlH_4 at $-70^\circ\text{C}^{1)}$ or $\text{LiAlH}(\text{O}-t\text{-But})_3$ at room temperature resulted in the formation of two pairs of hydroxylactams 3a, 3b, 5a and 5b. The same result was obtained in the case of imide 2 reduction. The cyclic hydroxylactams have recently been found as a new class of precursors for the highly reactive α -acylimmonium ion and therefore have a variety of applications^{2,3)}. In the present communication we report the properties of some α -acylimmonium ions.

Compounds 3a or 3b in THF solution, treated with a drop of 60% HClO_4 at room temperature (30 min), afforded unsaturated lactam 4 (m.p. $133\text{-}135^\circ\text{C}$, $[\alpha]_D^{24} +154.6^\circ$; 65%) together with the starting materials 3a (5%) + 3b (15%). The reaction mixture composition was not significantly altered upon prolonging the reaction time for 3 h. It should be added that unsaturated lactam 4, treated with a drop of 60% HClO_4 in THF, resulted in the identical equilibration between the substrate and hydroxylactams 3a + 3b.

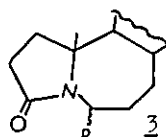
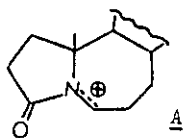
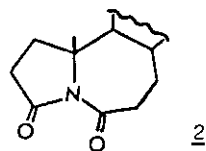
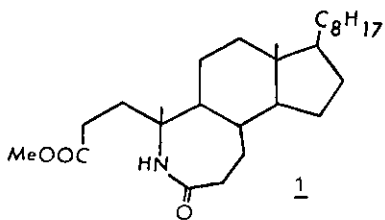
In the case of the reaction of hydroxylactams 5a or 5b with perchloric acid the corresponding dehydrated product 6 was not formed, but only the epimerization of hydroxylactams 5a \rightleftharpoons 5b (70% and 18%, respectively) was observed. It is likely, therefore, that the dehydration process of these hydroxylactams is unfavourable due to the comparatively high strain of the unsaturated five-membered ring system. However, unsaturated lactam 6 (m.p. $126\text{-}128^\circ\text{C}$, $[\alpha]_D^{24} +97.6^\circ$) was obtained by prolonged heating of hydroxylactams 5a or 5b in boiling pyridine. Under the same conditions hydroxylactams 3a or 3b also underwent almost quantitative dehydration to give

compound 4. Unsaturated lactam 6 in THF solution under acid conditions (HClO_4) was immediately transformed into the equilibrium mixture of hydroxylactams 5a and 5b in the ratio 4 : 1.

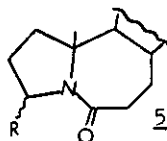
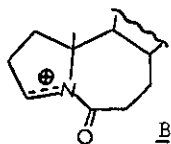
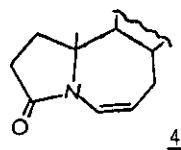
We suppose that all reactions of hydroxylactams with an acid have occurred via stabilized α -acylimmonium ion (A or B), which could lose a proton or to which a molecule of water could be added. This has been supported by methylation of hydroxylactams with methanol in the presence of small amounts of pyridine hydrochloride at room temperature. Under these conditions both hydroxylactams 5a and 5b formed one and the same product, α -methyl ether 5c (m.p. 115-117°C, $[\alpha]_d^{25} +67.0^\circ$). Hydroxylactams 3a and 3b, rather unexpectedly, afforded 6 β -methoxy-steroid 3c (an oil, $[\alpha]_D^{25} +96.0^\circ$) as the main product. In return the transformation OMe \rightarrow OH proved also to be possible. On treatment of 5c in THF with HClO_4 at room temperature a mixture of hydroxylactams 5a and 5b was obtained in almost quantitative yield. Under the same conditions methoxylactam 3c afforded unsaturated lactam 4 (65%) and hydroxylactams 3a + 3b.

Further evidence of the α -acylimmonium ion formation in acid medium was provided by reactions of lactamodiol 7⁴). Treatment of 7 with perchloric acid in THF solution afforded epoxy lactam 8 (m.p. 193-195°C, $[\alpha]_D^{17} +75.7^\circ$). The unusual closure to an oxirane ring from cis diol confirmed the formation of the well defined α -acylimmonium ion C in the first step of the reaction. The reaction of lactamodiol 7 with HClO_4 carried out in acetone solution afforded compound 9 (m.p. 89-90°C, $[\alpha]_D^{17} +45.1^\circ$) containing a dioxolane ring. The compound 9 was also formed from epoxy lactam 8 under acid conditions in acetone solution.

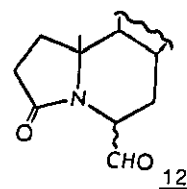
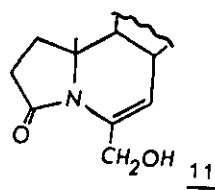
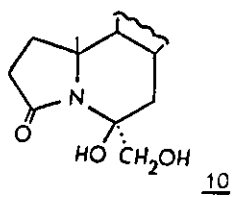
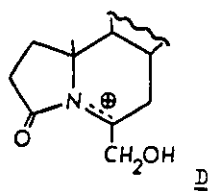
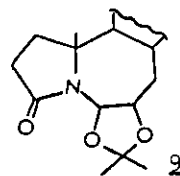
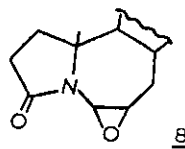
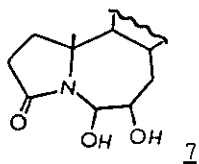
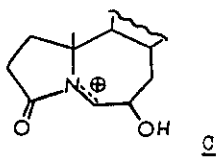
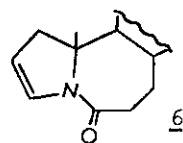
In the case of the reaction of isomeric lactamodiol 10⁴) with perchloric acid in THF the product was unsaturated alcohol 11 (138-142°C, $[\alpha]_D^{19} -23.4^\circ$). The corresponding epoxide was not detected. On the other hand, lactamodiol 10 treated in THF solution with hydrochloric acid (room temperature, 12 h) afforded aldehyde 12 (129-132°C, $[\alpha]_D^{17} -54.6^\circ$). The same product was obtained from compound 11 under the above conditions. The formation of aldehyde 12 from lactamodiol 10 probably proceeded via the intermediary unsaturated alcohol 11 which could be detected by TLC.



a: R=α-OH
b: R=β-OH
c: R=β-OMe



a: R=α-OH
b: R=β-OH
c: R=α-OMe



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