Tetrahedron Letters No.13, pp. 1047-1048, 1969. Pergamon Press. Printed in Great Britain.

RING CONTRACTION OF 4-OXO-1,3-DIOXANES
A NEW ROUTE TO β-LACTONES

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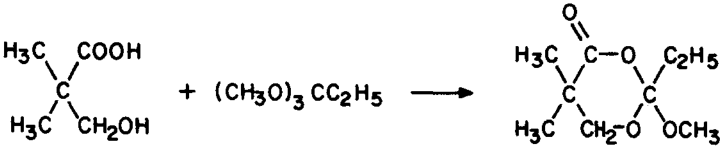
(Received in USA 7 February 1969; received in UK for publication 13 February 1969)

Several methods[1,2] are known for the preparation of β-lactones but most require intermediates less readily accessible than the β-hydroxyacids. In contrast to γ- and δ-hydroxyacids, β-hydroxyacids have been dehydrated to the lactone only in a few special cases involving particularly favorable steric circumstances.[3,4] Dehydration of β-hydroxyacids to β-lactones has now been effected by an exceptionally facile process involving reaction of the acid with an orthoester to yield a 4-oxo-1,3-dioxane which readily thermolyzes to a β-lactone. The new method appears applicable to a wide variety of β-hydroxyacids.

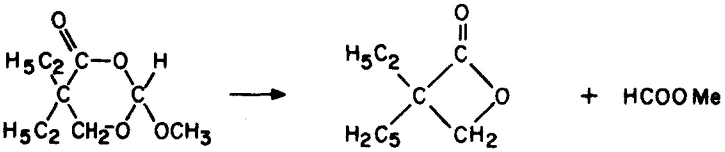
An initial survey of dehydrative reagents showed that pivalolactone was recovered in 72% yield by heating hydroxypivalic acid for ~2 hr at 130° in a 30% excess of methyl orthopropionate and an acidic ion exchange resin then distilling the mixture. Methanol was evolved early in the process in such quantities to suggest that the reaction involved the initial formation of a 4-oxo-1,3-dioxane:



It was then found that 4-oxo-1,3-dioxanes were formed by the uncatalyzed reaction of β-hydroxyacids and orthoesters at 50-100°. The reaction of hydroxypivalic acid and methyl orthoformate, for example, was carried out in benzene by distilling out the benzene—methanol azeotrope at 58°. When the methanol removal appeared complete, distillation gave 87% yield of 2-methoxy-5,5-dimethyl-4-oxo-1,3-dioxane (I) at 60-62°/0.4 mm n_D^{25} 1.4340. The nmr spectrum of I was particularly definitive. It showed signals at 5.95δ (s), 3.82δ (q, J_{AB} = 12.5 Hz), 3.15δ (s), and 1.30δ (s) in the ratio 1:2:3:6. Infrared absorption at 5.73μ (C=O) and a distinctive set of 11 bands in the 7.8-14μ region were noted. Anal. Calcd. for $C_7H_{12}O_3$: C, 52.49; H, 7.55; O, 39.96. Found: C, 52.43; H, 7.55; O, 39.89. Similarly 2-methoxy-5,5-diethyl-4-oxo-1,3-dioxane, II, b. 75°/0.25 mm, n_D^{25} 1.4464 was prepared in 84% yield. The structure of II was confirmed by ir, nmr and elemental analysis.

Both I and II produced β-lactones and methyl formate rapidly at 150-200° but II was selected for detailed study. Kinetics derived from observation of the rate of evolution of methyl formate from a solution of the compound in dioctyl phthalate indicated that the reaction was first order with $t_{1/2}$ = 73 min at 170° and $t_{1/2}$ = 28 min at 184° (E_{act} = 28 kcal/mole). The reaction was only mildly catalyzed by acids. Inclusion of 1.25% p-toluenesulfonic acid in the reaction mixture, for example, reduced $t_{1/2}$ to 18 min at 180°. Investigation of the effect of medium on the thermolysis showed that polar solvents, such as tetramethylenesulfone, increased rates little more than did the presence of acids.

There appears no doubt that the second step in this new synthesis of β-lactones is the ring contraction:



The lack of rate response to acids or increasing medium polarity suggests a concerted rather than an ionic mechanism.

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[3] N. J. Toivonen, P. Hirsjarvi, A. M., A. Kainulainen, A. Holonen and E. Pulkkinen, Acta Chim. Scand. 3,991 (1949).

[4] P. Hirsjarvi, Ann. Acad. Sci. Fennical Ser A II No.45, 7-44 via Chem.Abst. 48, 651, (1954).