Highly Regioselective Reduction of Unsymmetrical Cyclic Carboxylic Acid Anhydrides to γ-Lactones

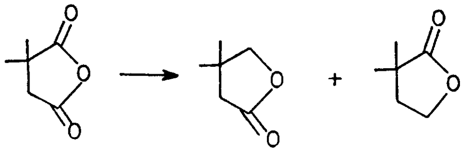
By PETER MORAND and MARGARET KAYSER

(*Department of Chemistry, University of Ottawa, Ottawa, Canada* K1N 6N5)

Summary The highly regioselective partial reduction of an unsymmetrical carboxylic acid anhydride to the corresponding γ-lactone with $LiAlH_4$ can be reversed by hydrogenation of the anhydride in the presence of $[RuCl_2(Ph_3P)_3]$ as catalyst.

IT is known[1] that the metal hydride reduction of unsymmetrical cyclic anhydrides to γ-lactones usually occurs at the more hindered carbonyl group. However, we are not aware of any efficient methods for the regioselective preparation of γ-lactones in good yield by direct reduction at the less hindered carbonyl group of the corresponding anhydride.

Blanc[2] has reported the isolation of the lactone (**3**) only, apart from a significant amount of the parent dicarboxylic acid, on reduction of 2,2-dimethylsuccinic anhydride (**1**). When this work was repeated in our laboratory the product obtained after removal of the dicarboxylic acid was found to be a mixture of lactones† (**2**) and (**3**) in a ratio of 11 : 9.



(1) (2) (3)

Recently, Lyons[3] found that symmetrical cyclic anhydrides could be converted in good yield into the corresponding lactones by hydrogenation catalysed with $[RuCl_2(Ph_3P)_3]$. When 2,2-dimethylsuccinic anhydride (**1**) was hydrogenated in toluene at 100 °C and *ca.* 300 lb in^{-2} pressure the lactones (**2**) and (**3**) were produced in a ratio of 1 : 9 (Table). Hydrogenations in progress with several other unsymmetrical cyclic anhydrides appear to proceed with comparable regioselectivity indicating that this may be a good general method for the direct conversion of cyclic anhydrides into lactones by reduction from the less hindered side.

TABLE

Reduction of 2,2-dimethylsuccinic anhydride (**1**)

Method	Yield (%) of isolated lactones	Ratio of (**2**) to (**3**)
$LiAlH_4$	70[a]	19 : 1
Na–EtOH	75	11 : 9
H_2–$[RuCl_2(Ph_3P)_3]$	72	1 : 9

[a] Using the method of Bloomfield and Lee (ref. 1b).

In the case of the metal hydride reduction of cyclic anhydrides, the highest degree of regioselectivity (attack from the more hindered side) seems to occur when there are two substituents on the hindered carbon atom adjacent to the carbonyl group. When there is only one substituent,[1b] even if it is a relatively large one, the regioselectivity is much less pronounced. In cases where each carbon atom adjacent to the carbonyl groups is fully substituted[4] it has been observed that reduction occurs from the less hindered side.

(*Received*, 18*th February* 1976; *Com.* 172.)

---

† Analyses were carried out with an Autoprep Model A-700 gas chromatograph and structures confirmed by n.m.r. spectroscopy.

[1] (a) R. Granger and H. Techer, *Compt. rend.*, 1960, **250**, 142; (b) J. J. Bloomfield and S. L. Lee, *J. Org. Chem.*, 1967, **32**, 3919; (c) D. M. Bailey and R. E. Johnson, *ibid.*, 1970, **35**, 3574.

[2] M. G. Blanc, *Bull. Soc. chim. France*, 1905, **33**, 879.

[3] J. E. Lyons, *J.C.S. Chem. Comm.*, 1975, 412.

[4] B. E. Cross and J. C. Stewart, *Tetrahedron Letters*, 1968, 3589.