Remarkable Structural Effects in the Intramolecularly Assisted Hydrolysis of Aryl Chloroalkyl Ketones

Nagabushanam Kalyanam*† and M. A. Likhate

Research Centre, Hindustan Ciba-Geigy Limited, Goregaon East, Bombay 400 063, India

The carbonyl-assisted intramolecular hydrolysis of 4-chloro-1-(4′-hydroxyphenyl)butan-1-one and related compounds is sensitive to the substitutional pattern on the phenyl ring as well as to the number of methylene groups between the carbonyl carbon and the carbon joined to the chlorine.

We have observed a novel example of carbonyl-assisted intramolecular hydrolysis of 1-aryl-4-chlorobutan-1-ones (n = 3 in equation 1).

We find that the hydrolytic removal of chlorine in (**1**; $n = 3$) is controlled by the substituents on the aryl group, and that the ease of hydrolysis is uniquely dependent upon the value of n in equation (1).

Thus, the chloro-ketone (**1b**) underwent ready hydrolysis under experimental conditions A (see Table 1) to give the

$$\underset{(\mathbf{1})}{\mathrm{ArCO[CH_2]}_n\mathrm{Cl}} \xrightarrow[\mathrm{H_2O}]{\substack{\text{Conditions}\\ \text{A or B}}} \underset{(\mathbf{2})}{\mathrm{ArCO[CH_2]}_n\mathrm{OH}} \qquad (1)$$

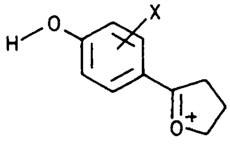
Table 1. Hydrolysis[a] of Ar–CO[CH_2]$_n$Cl (**1a**—**f**).

Compound	Ar	n	% Hydrolysis under Conditions A[b]	Conditions B[c]
(**1a**)	Ph	3	Nil	Nil
(**1b**)	4-HO-C_6H_4	3	100	100
(**1c**)	4-HO, 3-Me-C_6H_3	3	40	100
(**1d**)	4-HO; 3,5-di-Me-C_6H_2	3	Nil	100
(**1e**)	2-HO, 4-Me-C_6H_3	3	Nil	Nil
(**1f**)	4-HO-C_6H_4	4	Nil	Nil

[a] Satisfactory C, H analysis and spectroscopic data were obtained for all new compounds. [b] Conditions A: The chloro-ketone (1 g) was boiled in water (50 ml) for 1 h. [c] Conditions B: The chloro-ketone (1 g) was dissolved in nitrobenzene (50 ml) and steam (4 kg cm^{-2}) was passed through the solution till all the nitrobenzene had been distilled over (*ca.* 30 minutes).

---

† Correspondence to: Research & Development, Southern Petrochemical Industries Corporation Ltd., 92, G. N. Chetty Road, T. Nagar, Madras 600 017, India.



(3)

corresponding hydroxy-ketone. However, (**1a**) resisted hydrolysis under conditions A as well as under more forcing conditions B, indicating that a phenolic hydroxy-group is necessary for hydrolysis. Under conditions A, chloro-ketone (**1c**) underwent partial hydrolysis whereas (**1d**) was totally resistant to hydrolysis; but both of them were hydrolysed completely under more vigorous conditions B (See Table 1).

These facts could be rationalized by the intermediacy of the stabilized cation (**3**) in the hydrolysis reaction. The reactivity pattern observed for (**1c**) and (**1d**) could be then attributed to steric hindrance by methyl group(s) preventing the hydroxy-group from being planar with the aryl ring in (**3**).

In (**1e**), the keto-group is strongly hydrogen-bonded to the phenolic hydrogen (δ_{OH} 12.0) and is probably not sufficiently nucleophilic to displace the chlorine even under conditions B.

In the case of (**1b**), (**1c**), and (**1d**) which are hydrolysed *via* ion (**3**), the displacement of the chlorine is a 5-*exo-tet* ring closure.[1] A similar reaction with (**1f**) would be a 6-*exo-tet* process. Normally such 6-*exo-tet* ring closures are much disfavoured as illustrated by Baldwin.[2] Our results [see (**1f**) and (**1b**) in Table 1] thus remarkably reinforce the fact that 5-*exo-tet* ring closures occur more readily than the corresponding 6-*exo-tet* processes.[3]

Received, 19th January 1987; Com. 057

References

1 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734.

2 J. E. Baldwin and L. I. Kruse, *J. Chem. Soc., Chem. Commun.*, 1977, 233; see also S. Winstein and E. Grunwald, *J. Am. Chem. Soc.*, 1948, **70**, 828; S. Winstein, E. Allred, R. Heck, and R. Glick *Tetrahedron*, 1968, **3**, 1.

3 For carbonyl assisted reactions, see P. K. G. Hodgson and S. Warren, *J. Chem. Soc., Perkin Trans. 2*, 1975, 372; G. Chuchani and R. M. Dominguez, *Int. J. Chem. Kinet.*, 1983, **15**, 1275.