gem-Dimethyl-substituted Cyclic Anhydrides

GERD BORGEN

*Kjemisk Institutt, Universitetet i Oslo,
Oslo 3, Norway*

Because of their instability few medium-ring cyclic anhydrides are known. Hill and Carothers have described the synthesis of cyclic anhydrides from suberic and azelaic acid.[1] The corresponding cyclic anhydrides with two *gem*-dimethyl groups have now been prepared for conformational studies. Treatment of the tetramethyl-substituted dicarboxylic acids with acetic anhydride gave a mixture of polymeric anhydrides which by distillation were transformed into the cyclic monomer, dimer, and higher cyclic homologs. From 3,3,6,6-tetramethyl suberic acid the 9- and 18-membered ring anhydrides were prepared, and from 3,3,7,7-tetramethyl azelaic acid the 10-membered ring anhydride was synthesized.

The course of the reaction as well as the properties of the products are strikingly different when *gem*-dimethyl substituted suberic and azelaic acids are used compared with the unsubstituted dicarboxylic acids. The anhydrides which Hill and Carothers obtained by the action of acetic anhydride on the unsubstituted dicarboxylic acids were linear, solid polymers. From these linear polymeric anhydrides they got the cyclic anhydrides by slow sublimation under high vacuum.

With *gem*-dimethyl substituted dicarboxylic acids the primary reaction products seem to be cyclic anhydrides, and the monomers can be distilled off. The residues, after distillation up to 200°, are liquids and probably consist of cyclic anhydrides of moderate molecular weight; no solid, linear high polymers are isolated.

The chemical stabilities of tetramethyl-substituted and unsubstituted cyclic monomers are also very different. Hill and Carothers found no cyclic monomer from suberic acid, and with azelaic acid the cyclic monomer polymerized so rapidly even at very low temperatures (liquid air in the condenser), that a special technique was needed to demonstrate its temporary existence.

With *gem*-dimethyl substituted suberic and azelaic acid, however, the 9- and 10-membered ring anhydrides are formed in

reasonable yields; they are crystalline and stable at room temperature when not contaminated. They polymerize slowly to higher cyclic homologs in chloroform solution an by melting.

The increased tendency to cyclization when *gem*-dimethyl groups are present in the chain of dicarboxylic acids represent examples of a positive *gem*-dimethyl effect.[2] The dimethyl groups increase the probability of *gauche* bonds and cause a bending of the chain whereby the chances for cyclization are increased. In addition they also seem to stabilize the cyclic anhydrides formed against polymerization.

In a previous paper,[3] differences in yields with *gem*-dimethyl groups in 1,4 and 1,5 positions by Dieckmann cyclizations have been reported. No such tendency could be observed by the cyclization to anhydrides.

The physical properties of the cyclic anhydrides and the conformational problems will be the subject of a later publication.

Experimental. 3,3,6,6-Tetramethyl anhydride. 3,3,6,6-Tetramethyl suberic acid (25 g)[4] was dissolved in acetic acid anhydride (200 ml) and refluxed for 6 h. Acetic acid and acetic anhydride were distilled off at atmospheric pressure until 142°. The rest was refluxed for 2 h with acetic anhydride (200 ml) followed by distillation to 142°. The rest was vacuum distilled. The fraction b.p. 75 − 140°/0.05 mm was partly crystalline. The crystals were separated and sublimed at 35°/0.1 mm to give monomeric 3,3,6,6-tetramethyl suberic anhydride (1 g = 4 %), m.p. 71°. (Found: C 67.89; H 9.39; mol.wt. 212 (by osmometry in chloroform). Calc. for $C_{12}H_{20}O_3$: C 67.89; H 9.50; mol wt. 216). Mass spectrometry: mol.ion + 1 = 213. IR anhydride group absorptions in CCl_4: 1758 and 1790 cm⁻¹. ¹H chemical shifts: 1.0, 1.4, 2.4 ppm.

The non-crystalline part of the fraction b.p. 75 − 140°/0.05 mm was extracted with pentane. The pentane was evaporated partly until precipitation of an oil which was shown by IR and NMR spectroscopy to be a cyclic anhydride and by osmometry in chloroform to be the *dimeric 3,3,6,6-tetramethyl suberic anhydride.* Mol.wt: Calc. 424. Found: 405 (osmometry). IR absorptions in CCl_4: 1735 and 1810 cm⁻¹. ¹H chemical shifts: 1.0, 1.3, 2.3 ppm. The pentane solution was found by NMR spectroscopy to contain at least three other cyclic anhydrides. The residue after vacuum distillation to 200°/0.05 mm consisted of cyclic

anhydrides of molecular weight 854 (by osmometry).

3,3,7,7-Tetramethyl azelaic anhydride. 3,3,7,7-Tetramethyl azelaic acid was treated as described above. Vacuum distillation gave a partly crystalline fraction, b.p. 70−160°/0.05 mm. The crystals were dried on filter paper and sublimed at 40−42°/0.05 mm to give *monomeric 3,3,7,7-tetramethyl azelaic anhydride* (1.5 g=3.5 %), m.p. 59°. (Found: C 68.69; H 9.79. Mol.wt. 221 (by osmometry in chloroform). Calc. for $C_{13}H_{22}O_3$: C 68.99; H 9.80. Mol.wt. 226). IR absorptions in CCl_4: 1745 and 1790 cm^{-1}. ^1H chemical shifts: 1.0, 2.4 ppm (methyl and α-methylene). Neither the dimer nor other cyclic anhydrides from tetramethyl azelaic acid were found in the fraction.

1. Hill, J. W. and Carothers, W. H. *J. Am. Chem. Soc.* **55** (1933) 5023.
2. Eliel, E. L., Allinger, N. L., Angyal, S. J. and Morrison, G. A. *Conformational Analysis*, Wiley-Interscience, New York 1965, p. 191.
3. Borgen, G. and Dale, J. *Acta Chem. Scand.* **26** (1972) 952.
4. Birch, S. F., Grippe, V. E., McAllan, D. T. and Nathan, W. S. *J. Chem. Soc.* **1952** 1363.
5. Blomquist, A. T. and Miller, G. A. *J. Am. Chem. Soc.* **83** (1961) 243.

Received June 8, 1973.

Kinetics of the Hydrolysis of α-Chlorobenzyl Esters

NILS J. CLEVE and ERKKI K. EURANTO

Department of Chemistry, University of Turku, 20500 Turku 50, Finland

The uncatalysed hydrolysis of α-haloalkyl carboxylates has been investigated previously. It was found to proceed either by the mechanism of the neutral ester hydrolysis (*e.g.* chloromethyl formate,[1] chloromethyl chloroacetate,[2] and chloromethyl dichloroacetate[3]), by the

S_N1 mechanism (*e.g.* α-chloroethyl acetate,[1] α,β-dichloro-*sec.*-propyl acetate,[4] and α-chloro-*sec.*-propyl acetate[5]), or by the $S_N1,2$ mechanism (*e.g.* chloromethyl acetate[1] and chloromethyl benzoate[6]). These reactions may also occur concurrently, as was found to be the case in the hydrolysis of bromomethyl chloroacetate.[7] The aim of this work was to enlarge the knowledge of the hydrolysis of the α-haloalkyl esters of carboxylic acids so as to embrace also those esters in which the α-carbon carries a phenyl or a hexachlorocyclohexyl group.

Materials. The α-chlorobenzyl esters of formic, acetic, trichloroacetic, and trifluoroacetic acids as well as hexachlorocyclohexylchloromethyl trifluoroacetate were prepared by chlorinating the corresponding benzyl esters.[8] When solvent mixtures were prepared, acetone (E. Merck A. G., guaranteed reagent) was used as received but dioxane (BDH) was purified using the method described by Hess and Frahm.[9] The symbol *p* vol. "%" employed in the following denotes 100 ml of the solvent mixture containing $(100-p)$ g of water.

Determination of rate coefficients. The rate coefficients of the hydrolysis of the α-chlorobenzyl and of the hexachlorocyclohexylchloromethyl trifluoroacetate were determined by a conductometric method employing a Philips PR 9501 conductometer. The dependence of conductance on concentration was not linear, and was therefore determined experimentally. The fraction of α-chlorobenzyl acetate used in the kinetic experiments contained benzoyl chloride as an active impurity.[8] The rates of hydrolysis of this impurity were determined separately under the same experimental conditions and taken into account when calculating the rate coefficients for α-chlorobenzyl acetate. The low hydrolysis rates of benzyl trifluoroacetate were determined by a gas chromatographic method. The rate coefficients for the hydrolysis of these esters and the derived activation parameters are collected in Tables 1 and 2.

The values of the thermodynamic functions of activation presented in Table 1 show that in the hydrolysis of the α-chlorobenzyl esters of trifluoro- and trichloroacetic acids the enthalpy of activation is about 10 kcal mol^{-1} and the entropy of activation 30−40 cal mol^{-1}K^{-1} lower than the corresponding values for the hydrolysis of the α-chlorobenzyl esters of formic and acetic acids. It is evident that the reaction of the former esters proceeds by the mechanism of a neutral ester