

Cyclodextrin Effect on Intramolecular Catalysis

A.M. Granados, G.O. Andres and R. Hoyos de Rossi

Instituto de Investigaciones en Físico Química de Córdoba (INFIQC), Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba. Ciudad Universitaria. 5000 Córdoba, Argentina

E-mail: ritah@dco.fcq.unc.edu.ar

Abstract: HPCD inhibits the hydrolysis reaction of monoamides and monoesters of phthalic and maleic acid at pH 2. The magnitude of inhibition depends on the leaving group. For some of the substrates, the reaction in the cavity is more than 100 times slower than that in solution.

Introduction

Cyclodextrins (CD) are doughnut-shaped, macrocyclic oligosaccharides constructed of glucose units linked by α - (1 \rightarrow 4) bonds. The compound with seven glucose units is known as β -cyclodextrin (β -CD)[1]. Hydroxypropyl- β -cyclodextrin is a derivative where several of the HO groups are substituted by hydroxypropyl groups and is more soluble in water than β -CD. Organic compounds included in CD form complexes with different properties from those of the free substrate [2]. Measuring the changes occurring in some of these properties, it is possible to determine the association constant, K_{as} .

The mechanism of hydrolysis of monoamides and monoesters of phthalic acid [3] maleic acid [4] is known to involve intramolecular catalysis by the neighboring carboxyl group. The formation of an inclusion complex with cyclodextrins may affect the efficiency of the catalysis by favoring or hindering the interaction of the hydroxyl group with the reactive center. This effect should result in modification of the hydrolysis rate. We report here results regarding the effect of HPCD on the hydrolysis of compounds **1-3**

Experimental

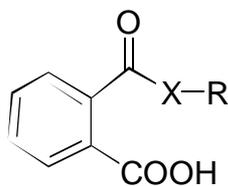
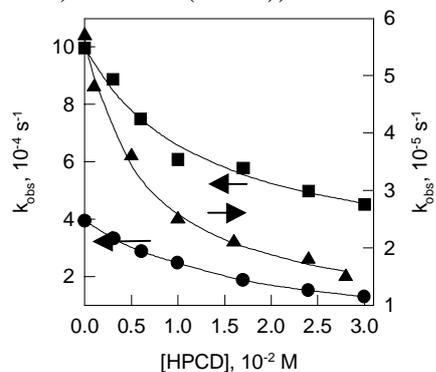
The substrates **1-3** were prepared by reaction of phthalic or maleic anhydride (sublimated) with aniline, 4-nitro-aniline, adamantylamine and phenol. All products were purified and characterized by MS and ^1H and ^{13}C NMR.

The rate constants were determined by measuring the absorption changes with time at 380 nm for **1a**, 276 nm for **1b** and **2b**, 225 nm for **1c**, and 300 nm for **3b**. The reaction conditions were: pH 2, 40°C for **1a,b,c** **2b** and 25°C for **3b**, ionic strength 0.5 M using NaCl as compensating electrolyte and

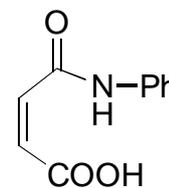
water as solvent with 4% of dioxane (for **1**) or acetonitrile (for **1b,c 2b** and **3b**).

Results and Discussion

The addition of HPCD decreased the hydrolysis rate of all the substrates. The Figure representative plot of the observed rateconstant as a function of the HPCD concentration (**1a** (triangles), **1b** (squares) and **2b** (cicles))



X=NH, R= p-NO₂-Ph, **1a** ;
Ph, **1b** ; adamantyl, **1c**
X= O, R= Ph ,**3b**



2b

These results are interpreted in terms of the formation of 1:1 complexes as shown in the following scheme:



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References and Notes

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