

The AlCl₃-L Reagent and its Application to the Regioselective Carbon-Carbon Bond Formation

Alejandra G. Suárez

Instituto de Química Orgánica de Síntesis - IQUIOS, CONICET. Facultad de Ciencias Bioquímicas y Farmacéuticas - Universidad Nacional de Rosario. Suipacha 531, 2000 Rosario, Argentina
E-mail: asuarez@agatha.unr.edu.ar

Abstract: Use of the AlCl₃-L reagent in the regioselective acylation of benzodioxinic derivatives. Spectroscopic studies show the presence of coordination compounds as reaction intermediates, being the responsible of the observed regioselectivity.

Introduction

Carbon-carbon bond forming reactions are one of the most important processes in organic synthesis. Many of these transformations are promoted by ordinary Lewis acids, which activates a wide variety of functional groups. The reactions usually proceed efficiently but with low chemo- and regioselectivities. For this reason, it is of great interest the development of new methodologies to perform these organic transformations in a selective form.

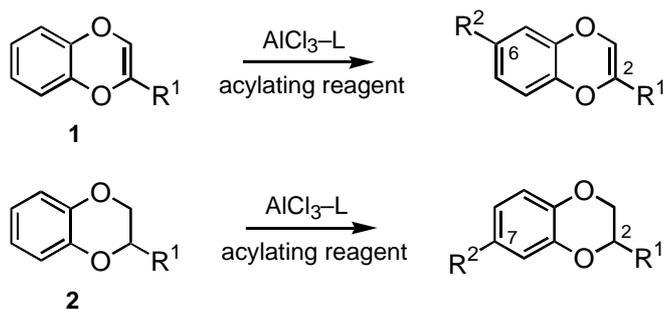
We have demonstrated that the combination of AlCl₃ with an organic donor ligand is an excellent reagent for the acylation reaction of benzodioxin derivatives, which is carried out in the absence of added solvent [1,2]. Derivatives of this nucleus bearing an acyl group in position 6 or 7 are key intermediates in the preparation of therapeutically valuable benzodioxin compounds [3].

Results and Discussion

The use of AlCl₃ in conjunction with DMF, DMSO or DMA and acyl halides or anhydrides produce the regioselective functionalization of benzodioxin derivatives in excellent yields.

Both the 6- and 7- position of the aromatic ring are activated towards the electrophilic attack. However, acylation of 2-substituted-1,4-benzodioxin derivative **1** provides the 6-acyl compound as the major or unique product, and the same reaction with the saturated analogs **2** affords the 7-acyl compound as the main product, whatever the nature of the R¹ group.

The experimental results demonstrate that the nature of the reacting electrophile and the donor ligand employed have almost no influence on the isomeric distribution which is function exclusively on the substrate structure.



$R^1 = \text{CO}_2\text{Me}, \text{CH}_2\text{OMe}, \text{CH}_2\text{OAc}$

$R^1 = \text{COMe}, \text{COPh}$

$L = \text{DMF}, \text{DMSO}, \text{DMA}$

Spectroscopic studies reveal the presence of coordination compounds as reaction intermediates. The NMR ^1H and ^{13}C spectra of reaction mixtures show a complexed entity between the $\text{AlCl}_3\text{-L}$ reagent and the polar functionality of the aromatic substrate. The formation of this complex seems to be responsible for the inversion of the regioselectivity between the saturated and unsaturated benzodioxinic compounds.

Acknowledgements: Financial support from Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Universidad Nacional de Rosario and Agencia Nacional de Promoción Científica y Tecnológica is gratefully acknowledged.

References and Notes

1. Suárez, A.G. *Tetrahedron Lett.* **1999**, *40*, 3523.
2. Mata, E.G.; Suárez, A. G. *Synthetic Comm.* **1997**, *27*, 1291.
3. Campbell, S. F.; Davey, M. J.; Hardstone, J. D.; Lewis, B. N.; Palmer, M. J. *J. Med. Chem.* **1987**, *30*, 49.