Chemical Modifications of 1,2,5-Oxadiazole N-Oxide System Searching for Cytotoxic Selective Hypoxic Drugs

M. Boiani², H. Cerecetto¹, M. González¹,², M. Risso¹, G. Seoane¹, G. Sagrera², O. Ezpeleta³, A. López de Cerán³ and A. Monge³

¹Cátedra de Química Orgánica, Facultad de Química
²Laboratorio de Química Orgánica, Facultad de Ciencias, Universidad de la República, CC 1157, CP 11800, Montevideo, Uruguay
E-mail: mrisso@bilbo.edu.uy
³C.I.F.A., Universidad de Navarra, Pamplona, España

Abstract: New analogues of 3-Formyl-4-phenyl-1,2,5-oxadiazole N-oxide (1) are prepared and evaluated as cytotoxic selective agents in hypoxia.

Introduction

As part of our research project on biorreducible drugs in hypoxia conditions, we have developed a series of compound derivatives of N-oxide of 1,2,5-oxadiazoles system. They were evaluated as cytotoxic agents against V79 cells in oxia and hypoxic conditions. None of them showed selectivity in hypoxic conditions, but the derivative 1 presented a good profile of Cytotoxicity (Figure 1). In order to gain insight the mechanism of action and to obtain a selective compound, we designed the following modifications.

![Figure 1](image-url)

Experimental

Following, we showed the modifications outlined.
All the products were characterized by $^1$H RMN, $^{13}$C RMN, (1D, 2D), EM, IR and in some cases elemental microanalysis. The cytotoxicity of the synthesized products was tested against V79 cells in oxia and hipoxia conditions at a concentration of 20 µM, following a protocol previously described [1].

**Results and Discussion**

All the synthetic procedures conducted to the products of interest with variable yields. As the drug-modulations previously described [2], the new ones may asseverate that the substituent at the 3 position of the 1,2,5-oxadiazol N-oxide plays an important role in the cytotoxic activity of this kind of compounds.

**Acknowledgment:** C.H.L.C.C., CYTED, PEDECIBA.

**References and Notes**


2. Cerecetto, H.; González, M.; Risso, M.; Seoane, G.; Ezpeleta, O.; López de Cérrain; Monge, A. *Derivados del Sistema N-Óxido de 1,2,5-oxadia