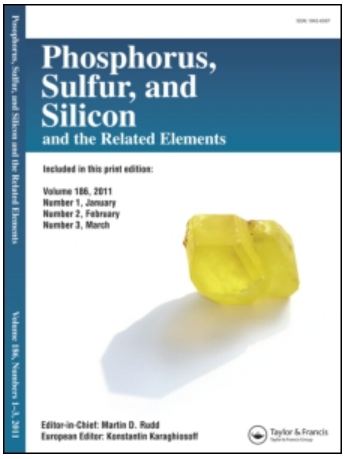

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Synthesis of New Potential NMDA Antagonist Based on Acylphosphonate Derivatives

Claudio Javier Salomon[a]; Eli Breuer[b]
[a] Department of Pharmacy, Faculty of Biochemical and Pharmaceutical Sciences, National University of Rosario, Rosario, Argentina [b] Department of Pharmaceutical Chemistry, School of Pharmacy, Hebrew University of Jerusalem, Jerusalem, Israel

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Synthesis of New Potential NMDA Antagonist Based on Acylphosphonate Derivatives

CLAUDIO JAVIER SALOMON[a] and ELI BREUER[b]

[a]*Department of Pharmacy, Faculty of Biochemical and Pharmaceutical Sciences, Suipacha 531, National University of Rosario, 2000 Rosario, Argentina and* [b]*Department of Pharmaceutical Chemistry, School of Pharmacy, POB 12065, Hebrew University of Jerusalem, Jerusalem, Israel*

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In recent years intensive pharmacological research is focused on the *N*-methyl-D-aspartate (**NMDA**) receptor, which has been implicated in normal neuronal functioning, including excitatory synaptic transmission, as well as in the pathologies of the central nervous system such epilepsy, Alzheimer and Parkinson's disease, and neurodegeneration following a stroke.

Phosphorus analogs of glutamic acid and its homologs have shown significant biological activity as antagonists of the **NMDA** receptor, emerging *AP5* and *AP7* as the lead compounds.

The acylphosphonic function is of particular interest, since it contains a novel structural variation of phosphonic acids, and may confer favorable properties on the molecules. To further explore the utility of acylphosphonate derivatives, we prepared a series of intermediates toward the synthesis of *AP5* analogs.

Starting from DL-glutamic acid, we studied the effects of different variables (e.g. phosphorus reagents, time, solvent, temperature) on the Arbuzov reaction. The acylphosphonate function was stabilized by reaction with hydroxylamine and semicarbazide to produce the phosphonohydroxyimino and semicarbazono amino acids as potential antagonists of the **NMDA** receptor.