

STUDIES ON THE SYNTHESIS AND REARRANGEMENT OF
INDAZOLYLPYRIDINIUM DERIVATIVES, PRECURSORS TO POTENTIAL
NEUROPROTECTIVE PRODRUGS BEARING A
1,2,3,6-TETRAHYDOPYRIDINYL CARRIER

By

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ABSTRACT

The neuronal nitric oxide synthase (nNOS) inhibitor 7-nitroindazole (7-NI) protects against the neurotoxicity of MPTP in a mouse model of neurodegeneration. Since 7-NI also inhibits the monoamine oxidase-B (MAO-B) catalyzed bioactivation of MPTP, the role of nNOS inhibition as a mediator of 7-NI's neuroprotective properties have been challenged. In order to examine in greater detail the neuroprotective effects of indazolyl derivatives, the synthesis of water soluble indazolyltetrahydropyridinyl derivatives as potential "prodrugs" that may undergo MAO bioactivation in the brain was undertaken. During the course of the studies on the synthesis of indazolylpyridinium derivatives, precursors to these "prodrugs", an interesting reaction involving the rearrangement of 4-(2*H*-indazolyl)-1-methylpyridinium iodide to the corresponding 1*H*-isomer was encountered. A detailed investigation of this rearrangement reaction is reported in this thesis.

The syntheses and interaction of nitroindazolyltetrahydropyridinyl "prodrugs" with MAO-B have been investigated previously. Molecular docking studies that attempt to explain the MAO-B substrate and inhibitor properties of members of this series of compounds are described. Finally, the MAO-A substrate properties of nitroindazolyltetrahydropyridinyl derivatives are reported.

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*dedicated to my parents,
biologic:*

İnci Işın and Dündar A.F. Işın

and academic:

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