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Synthesis Development And Optimization Of Scopolamine

Shawn Blumberg Southwest Research Institute **Daniel Hinojosa** Southwest Research Institute **Paul Miguel** Southwest Research Institute

In the 1970's, the DOD developed the Mark 1 nerve agent antidote kit which contains atropine and 2□PAM. Atropine protects against the surge of acetylcholine by blocking the acetylcholine receptor sites in the synapse (called antagonism) while 2-PAM reactivates the inhibited AChE. Atropine primarily interacts with the muscarinic receptors (a receptor sub-type), which protects the heart and the lungs from the effects of the OPNA. However, atropine currently doesn't adequately treat many of the CNS effects of OP exposure, such as convulsions and memory/behavioral issues. Recent studies on (-)-scopolamine, however, have shown that it provides enhanced protection and survivability compared to atropine, making it an attractive candidate for improved protection against OPNA effects.

There are two obstacles, however, that could potentially impede both the utilization of scopolamine as a therapeutic as an OPNA antidote: its isolation from plants in the Solanaceae family and the lack of data on what structural features of scopolamine provide its beneficial pharmacological profile. To both remove the need for of both scopolamine and atropine from natural sources, and potentially explore the chemical space around these tropane alkaloids, Southwest Research Institute® (SwRI®) set out to develop an economical flexible synthesis of (-)-scopolamine and atropine using inexpensive starting materials. To that end, we developed the shortest (6 steps) and highest yielding synthesis of both tropane alkaloids. This route should enable the production of a domestic supply of synthetic scopolamine and atropine, which is currently sourced in farms outside the United states, as well as possible produce derivatives that provide improved protection against the effects of OPNA exposure.