

BIS-METHYLENE ETHER PYRIDINIUM COMPOUND PREPARATION

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to antidotes for nerve agents and, more particularly, to a method for preparing bis-methylene ether pyridinium quaternary compounds using bis-mesylmethyl ether reactant, and the like.

2. Prior Disclosure

Antidotes for nerve gas, or nerve agents, are of unquestionable importance. Safe and inexpensive production methods for these antidotes are, of course, equally significant.

Three of the more common nerve agent antidotes, toxogonin, HI-6 and HGG-12 require, in their manufacture, the use of bis-chloromethyl ether (BCME). Recently, however, BCME has been found to be such a potent carcinogen that it is no longer commercially available. For safe handling, human beings simply must not be exposed to this substance in any concentration, no matter how slight it may be.

In addition to this zero BCME exposure requirement, and the lack of any satisfactory analytical technique for detecting this substance in concentrations of less than one part per billion, BCME also is undesirable for a number of other reasons. BCME, for example, is a relatively volatile material. The customary reaction to prepare bis-methylene ether pyridinium quaternary compounds usually occurs at higher temperatures, in the range of -60°C . Processing this dangerous and volatile material at these higher temperatures clearly is an hazardous undertaking.

Consequently, there is a need for a less volatile reagent for use in manufacturing nerve agent antidotes.

There is a further need to replace BCME in nerve agent antidote production with a non-carcinogenic material.

SUMMARY OF THE INVENTION

These and other difficulties that have characterized the prior art are overcome, to a great extent, through the practice of the invention. Illustratively, bis-mesylmethyl ether, which is non-carcinogenic, is substituted for the BCME in the production of bis-methylene ether pyridinium. A further advantage of the invention can be found in the fact that bis-mesylmethyl ether, when substituted for BCME in preparing bis-methylene ether pyridinium quaternary compounds, enjoys a low reaction temperature (0° - 5°C .) and is in solid form.

Thus, there is provided in accordance with the invention an improved and substantially safer method for producing antidotes to organophosphorus compound nerve gasses and other nerve agents.

It should be further noted that there are applications for the invention well beyond use in nerve agent antidote production. Insecticides, for instance, would make use of the reagents and methods that characterize this invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENT OF THE INVENTION

In accordance with the invention, bis-methylene ether pyridinium quaternary compounds are prepared using a specific sequence of reactions steps illustrated herein below, more specifically, the preparation of toxogonin, for example, in accordance with the principles

of the invention, a prescribed sequence of steps has been developed. In this sequence, the reactants are combined in the following order:

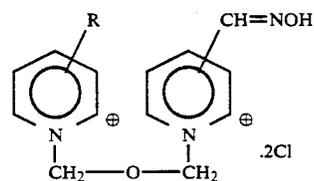
1. acetyl chloride + methanesulfonic acid yields acetyl methanesulfonate

2. acetylmethanesulfonate + S-trioxane yields bis-(acetoxy)methane + bis(methanesulfonoxymethyl) ether

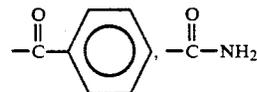
3. 4-pyridinealdoxime + bis(methanesulfonoxymethyl) ether yields 1,1'-[oxybis(methylene)]bis[4-(hydroxyimino) methyl]-pyridinium dimethanesulfonate

4. 1,140 [oxybis(methylene)]bis[4-(hydroxyimino)-methyl]pyridinium dimethanesulfonate is applied to a column of chloride ion exchange resin and separating the corresponding dichloride derivative referred to herein as toxogonin.

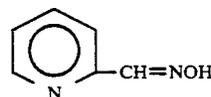
Applicants novel process is directed to the preparation of bis-methylene ether pyridinium quaternary composition 5 represented by the formula:



wherein R is selected from the group consisting essentially of

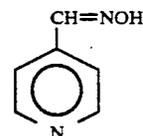


and $-\text{CH}=\text{NOH}$, comprising the steps of a. reacting bis(methanesulfonoxymethyl) ether with a pyridineal compound having the formula



at a temperature of about 0° to 5°C . and b. applying product of step a. to a column of chloride ion exchange resin and separating the said quaternary composition.

The preferred compositions prepared according to the process of this invention are made either when (1) the pyridineal compound of step a. is



or (2) the pyridineal compound of step a. is

