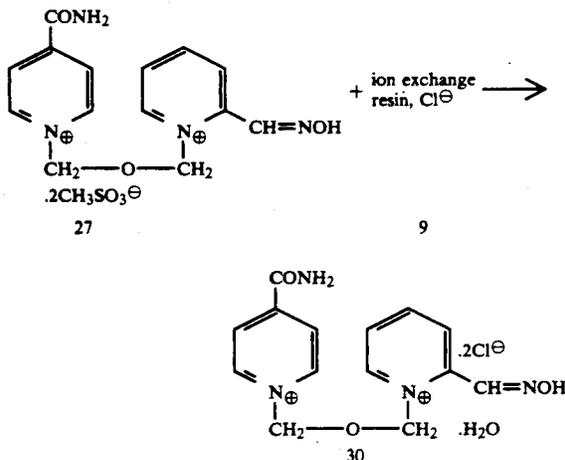


1-(2-Hydroxyiminomethyl-1-pyridino)-3-(4-carbamoyl-1-pyridino)-(2-oxapropane dichloride monohydrate (30)



A solution of 1,1'-oxybis(methylene) bis 2-hydroxyimino)methyl pyridinium dimethanesulfonate (25.1 g) (27) in 40 mL of water was applied to an ion exchange column (300 mL of Dowex 1×2, Cl[⊖]form). The solution was held on the column for 45 minutes then eluted with water. The fractions containing the product were combined, and concentrated in vacuo. The residue was dried azeotropically with ethanol (100 mL), triturated with 150 mL of EtOH, and the solid was collected and dried in vacuo to give 16.6 g. This material was dissolved in a solution of methanol (1000 mL) and water (30 mL) and water (30 mL), treated with decolorizing charcoal, then filtered. The filtrate was cooled, and the precipitate (2.2 g) which formed was removed by filtration. The filtrate was concentrated to about 50 mL then cooled. The white solid (13 g), recovered from the solution, was recrystallized from water (20 mL) and ethanol (75 mL) to give 7.9 g of pure product; mp 145°-147° (d).

Anal.	C	H	N	Cl	O
Calc'd. for C ₁₄ H ₁₆ N ₄ O ₃ Cl ₂ ·H ₂ O	44.58	4.81	14.85	18.80	16.97
Found	44.59	4.78	14.87	18.98	16.77

Spectral Data:

Infrared (Nujol)

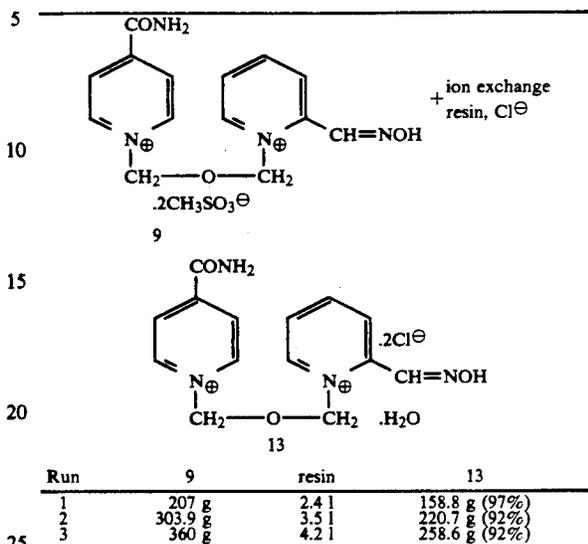
Major bands: 3320, 3260, 3180, 3080, 3030, 2960, 2920, 2860, 2780, 1680, 1640, 1625, 1570, 1490, 1460, 1440, 1395, 1380, 1330, 1260, 1240, 1190, 1160, 1140, 1120, 1095, 1080, 1070, 1010, 960, 860, 810, 780, 710 cm⁻¹

Ultraviolet (H₂O): λ_{max} 350 nm (log_ε 3.093); 300 nm (4.018); 270 nm (3.966); 218 nm (4.181).

Nuclear Magnetic Resonance: δ 9.40-7.70 (m, 9H, aromatic and methine); 6.45 (s, 2h, -CH₂-); 6.32 (s, 2H, -CH₂-).

This process was repeated:

1-(2-Hydroxyiminomethyl-1-pyridino)-3-(4-carbamoyl-1-pyridino)-2-oxapropane dichloride monohydrate (13) (HI-6)



Run	9	resin	13
1	207 g	2.4 l	158.8 g (97%)
2	303.9 g	3.5 l	220.7 g (92%)
3	360 g	4.2 l	258.6 g (92%)

A solution of 1,1'-[oxybis(methylene)]bis [bis(2-hydroxyimino)-methyl]pyridinium dimethanesulfonate (303.0 g, 0.635 mol) in 520 mL of water was applied to an ion exchange column (3.5 L of Dowex 1×2, Cl[⊖]form). The solution was held on the column for 45 minutes then eluted with water. The fractions containing the product was combined, then concentrated in vacuo. The residue was dried azeotropically with ethanol (100 mL) then triturated with 150 mL of EtOH. The insoluble solid was collected and dried in vacuo to give 220.7 g (92%). The total yield was 638 g of HI-6.

Thus, the invention provide a safe procedure for the manufacture of nerve agent antidotes without using carcinogenic raw materials. Some minor variations to the procedure and materials described above render the invention adaptable to insecticide production. These variations, being within the ability of a skilled artisan, also are within the scope of the claimed invention.

Utility

The bis-methylene ether pyridinium quaternary compounds prepared according to the process of this invention are useful as nerve agent antidotes. More specifically, evidence indicates that these compounds demonstrate activity against nerve gases or nerve agents.

We claim:

1. A method for producing 1-(2-Hydroxyiminomethyl-1-pyridino)-3-(4-carbamoyl-1-pyridino)-2-oxapropane dichloride mono hydrate comprising the steps of

a. reacting bis(methylsulfonoxymethyl)ether with pyridino-2-aldoxime at a temperature of about 0° to 5° C.;

b. adding isonicotinamide with the reaction product of step a.; and

c. applying the product of step b. to a column of chloride ion exchange resin and separating the said quaternary composition.

2. The composition prepared according to the process of claim 1.

3. A method for producing 1-(2-Hydroxyiminomethyl-1-pyridino)-3-(3-benzoyl-1-pyridino)-2-oxapropane dichloride comprising the steps of

a. reacting bis(methylsulfonoxymethyl)ether with 3-benzoylpyridine at about -35° C.;

b. reacting the reaction product of step a. with pyridine-2-aldoximine; and

c. applying the product of step b. to a column of chloride ion exchange resin and separating the said 2-oxapropane.

4. The composition prepared according to the process of claim 3.

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