

## A Novel Preparation of Quaternary 'Hexamminium' Salts

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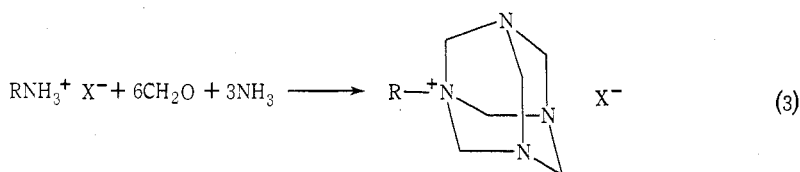
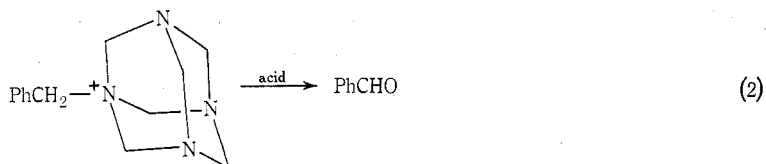
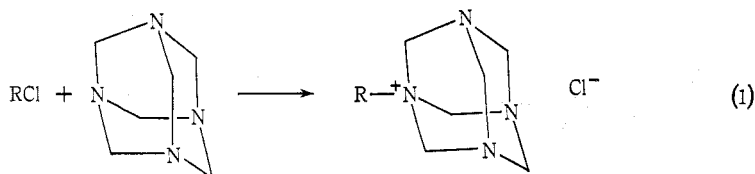
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### Abstract

Quaternary hexamminium salts (salts of *N*-alkyl-1,3,5,7-tetraazaadamantane cations) are readily prepared by condensation of the alkylammonium salt (most satisfactorily the perchlorate), ammonia and formaldehyde.

Quaternary 'hexamminium' salts (salts of 1-alkyl-3,5,7-triaza-1-azoniatricyclo-[3,3,1,1<sup>3,7</sup>]decane cations) have traditionally been prepared by reaction of hexamine\* with the appropriate alkyl halide, as in reaction (1).<sup>1,2</sup>



Quaternary hexamminium salts have been used to prepare aldehydes, particularly aryl formyl compounds, by the Sommelet reaction,<sup>3</sup> e.g. reaction (2). Many of the compounds are reported to show biological activity.<sup>1</sup>

\* 1,3,5,7-Tetraazatricyclo[3,3,1,1<sup>3,7</sup>]decane, 1,3,5,7-tetraazaadamantane, hexamethylenetetramine, urotropine.

<sup>1</sup> Blazević, N., Kolbah, D., Belin, B., Sunjić, V., and Kajfez, F., *Synthesis*, 1979, 161.

<sup>2</sup> Jacobs, W. A., and Heidelberger, M., *J. Biol. Chem.*, 1915, 20, 682.

<sup>3</sup> Angyal, S. J., *Org. React.*, 1954, 8, 197.

We find that salts of hexamminium ions can be prepared very readily by reaction of the appropriate amine, neutralized with some suitable acid, with formaldehyde and ammonia, as in reaction (3). Yields are negligible when the amine, formaldehyde and ammonia are mixed, and the acid then added.

With perchlorate or fluoroborate as the anion, the salts crystallize in about 80% yields from the reaction mixture, while with chloride and bromide the salts were isolated in about 60% yield by evaporation of the reaction mixture. The reaction has been applied to a number of primary alkylamines, including benzylamine, some diamines and some amino alcohols.

We find it surprising that this simple reaction has not previously been reported, but it is not mentioned in a recent review<sup>1</sup> on the chemistry of hexamine, and we have been unable to find any literature references to the reaction.

## Experimental

**Caution:** Amine hydroperchlorates may be explosive and should be handled with caution. However, attempts to induce any hexamminium perchlorate to detonate by shock or heating were unsuccessful.

The amine (c. 5 g) in methanol (20 ml) was neutralized by adding 72% perchlorate acid dropwise with stirring. Formaldehyde (40% in water, 6 mol propn) was added dropwise, with stirring, followed by ammonia (concentrated aqueous, in small excess, c. 6 mol propn). The products crystallized as the ammonia was added. These were filtered off and washed with propan-2-ol. Samples for analysis were recrystallized from hot methanol. The tetrafluoroborate salts were similarly prepared.

When this experimental procedure was followed, with hydrochloric or hydrobromic acids in place of the perchloric acid, the hexamminium salts did not crystallize, but were isolated by rotary evaporation of the reaction solution, leaving a white crystalline solid, which was transferred and washed with propan-2-ol. The resulting hexamminium salts were hygroscopic for the lower aliphatic amines.

Representative compounds were characterized by analysis, infrared spectroscopy, and <sup>1</sup>H n.m.r. spectroscopy.

### *1-Methyl-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>1,3,7</sup>]decane Perchlorate*

Prepared from methylamine (Found: C, 33.2; H, 5.6; N, 21.8. C<sub>7</sub>H<sub>15</sub>ClN<sub>4</sub>O<sub>4</sub> requires C, 33.0; H, 5.9; N, 22.0%). N.m.r.  $\delta$  (Me<sub>2</sub>SO): 2.42, s, 3H; 4.5, d, *J* 4 Hz, 6H; 5.0, s, 6H.

### *1-Ethyl-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>1,3,7</sup>]decane Perchlorate*

Prepared from ethylamine. N.m.r.  $\delta$  (Me<sub>2</sub>SO): 1.17, t, *J* 7 Hz, 3H; 2.80, q, *J* 7 Hz, 2H; 4.45, s, 6H; 4.92, s, 6H.

### *1-Benzyl-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>1,3,7</sup>]decane Perchlorate*

Prepared from benzylamine. N.m.r.  $\delta$  (Me<sub>2</sub>SO): 4.00, s, 4H; 4.45, s, 6H; 5.00, s, 6H; 7.42, s, 5H.

### *1-Benzyl-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>1,3,7</sup>]decane Chloride*

Prepared from benzylamine hydrochloride. N.m.r.  $\delta$  (D<sub>2</sub>O): 4.12, s, 2H; 4.62, s, 6H; 4.92, s, 6H; 7.47, s, 5H.

### *1,1'-Ethylenebis(3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>1,3,7</sup>]decane) Perchlorate*

Prepared from ethane-1,2-diamine. Yield lower at c. 40% (Found: C, 33.4; H, 5.6; N, 22.5. C<sub>14</sub>H<sub>28</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>8</sub> requires C, 33.1; H, 5.6; N, 22.1%). N.m.r.  $\delta$  (Me<sub>2</sub>SO): 3.28, s, 4H; 4.50, s, 12H; 5.12, s, 12H.

*1-(N-Acetylaminoethyl)-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>3,7</sup>]decane Perchlorate*

Prepared from *N*-acetyethane-1,2-diamine (Found: C, 37.2; H, 6.1; N, 21.5.  $C_{10}H_{20}ClN_5O_5$  requires C, 36.9; H, 6.2; N, 21.5%). N.m.r.  $\delta$  ( $Me_2SO$ ): 1.85, s, 3H; 2.80, t,  $J$  6 Hz, 2H; 3.35, t,  $J$  6 Hz, 2H; 4.5, s, 6H; 5.05, s, 6H.

*1-(2-Hydroxyethyl)-3,5,7-triaza-1-azoniatricyclo[3,3,1,<sup>3,7</sup>]decane Perchlorate*

Prepared from 2-aminoethanol (Found: C, 34.4; H, 6.2; N, 19.5.  $C_8H_{17}ClN_4O_5$  requires C, 33.7; H, 6.0; N, 19.7%). N.m.r.  $\delta$  ( $Me_2SO$ ): 2.85, t,  $J$  5 Hz, 2H; 3.75, t,  $J$  5 Hz, 2H; 4.5, s, 6H; 5.1, s, 6H.

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