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## Structural basis for superiority of quaternary N-triazynylammonium tetrafluoroborates as new coupling reagents in peptide synthesis

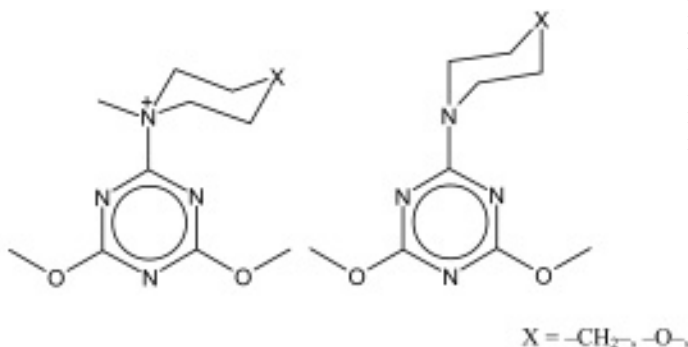
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Formation of the amide or ester bond is a crucial step in synthesis of numerous organic molecules, particularly peptides. The most valuable methods involve the coupling reagents activating carboxylic function directly in the reaction media. After two decades of domination of benzotriazole based chemistry, a new type of coupling reagents has been proposed [1, 2]. The latest development in so called molecular coupling reagents are N-triazynylammonium salts, especially those comprising quaternary morpholinium nitrogen atom [3]. Simple chlorides undergo substantial degradation during the storage.

To explain high stability and excellent performance of tetrafluoroborates as molecular coupling reagents, we have studied several N-triazynylammonium salts as well as their demethylated products by X-ray method. To our surprise no crystal structure of similar salt has been found in the literature.



X = -CH<sub>2</sub>-, -O-

The results enable to propose a mechanism of "superactive esters" formation reaction (i), explain side demethylation reaction (ii), explain higher stability of tetrafluoroborate salts over the chlorides (iii).

[1] Kaminski Z.J., *Tetrahedron Lett.*, 1985, 26, 2901.

[2] Kaminski Z.J., *Synthesis*, 1987, 917.

[3] Kaminski Z. J., Kolesinska B., Kolesinska J., Sabatino G., Chelli M., Rovero P., Blaszczyk M., Glowka M. L. and Papini A. M., *J. Am. Chem. Soc.*, 2005, 127, 16912.

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## Synthesis, crystallographic structure and semiempirical studies of N-[3-amino-5-methylisoxale]-3,5-di-tert-butylsalicylaldimine

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N-[3-amino-5-methylisoxale]-3,5-di-tert-butylsalicylaldimine (L<sub>1</sub>H) [C<sub>19</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub>] was synthesized by reaction 3,5-di-tert-butyl-hydroxybenzaldehyde in absolute ethanol and 3-amino-5-methylisoxale in ethanole. Its structure was determined by X-ray crystallography. These measurements were carried out using an Enraf-Nonius CAD-4 diffractometer with graphite monochromatised CuK<sub>α</sub> (λ = 1.54184 Å) radiation. It crystallizes in monoclinic system, space group P21/n, with lattice parameters a = 9.024(2) Å, b = 22.592(10) Å, c = 9.782(3) Å, β = 116.55(2)°, Z = 4, μ = 0.601 mm<sup>-1</sup>, S = 1.018, R = 0.053 and wR = 0.110 for 2949 observed reflections. The structures were solved by direct methods using the SHELX-97 program package and refined on F<sup>2</sup>. The data were treated and corrected for Lorentz-polarisation effects and for absorption using empirical psi-scans. The compound has four intramolecular and three intermolecular contacts. Also the dipole moments of the molecule is calculated for both X-ray and model starting geometry of molecule by MNDO, AM1, PM3 semiempirical and ab initio molecular orbital methods which are included in WinMopac.

