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Novel Conversion of N,N-Dimethylformamide Dimethyl Acetal to Tetramethylammonium Salts by Its Reaction with 5-Methyl-4-Isoxazolecarboxylic Acid Derivatives

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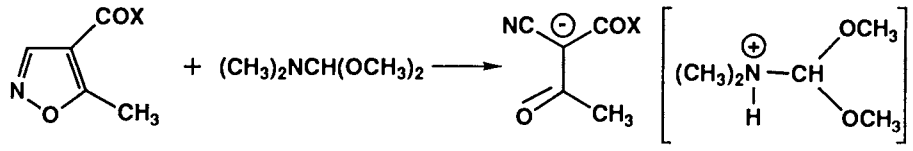
N,N-Dimethylformamide dimethyl acetal is converted to tetramethylammonium salts upon treatment with 5-methyl-4-isoxazolecarboxylic acid derivatives.

N,N-Dimethylformamide dimethyl acetal[1] is a versatile reagent in organic synthesis. It has been used in the conversion of carboxylic acids to methyl esters, phenols and enols to methyl ethers, and the introduction of a dimethylaminomethylene group into compounds bearing activated methyl or methylene groups. However, to our knowledge, there are no reports of its conversion to tetramethylammonium salts by the action of acidic compounds. In this report, we describe a novel reaction in which N,N-dimethylformamide dimethyl acetal is converted to tetramethylammonium salts during its reaction with 5-methyl-4-isoxazolecarboxylic acid derivatives. The first step is the base catalysed opening[2] of the isoxazole ring resulting in the formation of anions of 2-cyano-3-oxobutanoic acid derivatives[3,4] and cation **A** which is subsequently transformed to tetramethylammonium cation in four steps described in the flow chart (proposed mechanism).

To a stirred mixture of ethyl 5-methyl-4-isoxazolecarboxylate (**1**)[3] (31 g, 0.2 mol) and 1,4-dioxane (100 ml) was added N,N-dimethylformamide dimethyl acetal (66.5 ml, 0.5 mol) over a period of 2 h. The resulting yellow mixture was further stirred at ambient temperature for 72 h, heated at 65-75 °C for 1 h and then concentrated to dryness under reduced pressure. The orange solid was recrystallized from 1,4-dioxane to give 33.4 g (73%) of pale orange crystals of **3** : mp 132-134 °C; ^{1}H NMR ($CDCl_3$): δ 4.06 (q, 2H, $O\underline{CH}_2CH_3$), 3.35 (s, 12H, $\overset{+}{N}(CH_3)_4$), 2.26 (s, 3H, O=C-CH_3) and 1.22 (t, 3H, $OCH_2\underline{CH}_3$); ^{13}C-NMR ($CDCl_3$): δ 193.8 (O=$\underline{C}$-CH_3), 168.9 (-COO), 125.6 (C≡N), 73 (NC-$\underline{C}$-C-), 57.9 (OCH_2-), 55.4 ($\overset{+}{N}(CH_3)_4$), 28.1 ($\underline{C}H_3$-CO), and 14.6 ($\underline{C}H_3CH_2$); IR υ max (KBr) 2192 cm^{-1} (CN) and 1691 cm^{-1} ($COOC_2H_5$). Anal. Calcd for $C_{11}H_{20}N_2O_3$: C, 57.87; H, 8.87; N, 12.27. Found: C, 58.03; H, 8.80; N, 12.30.

Proposed Mechanism



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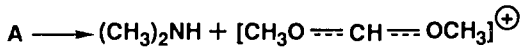

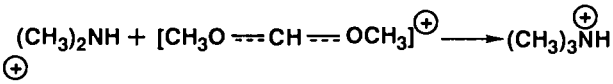

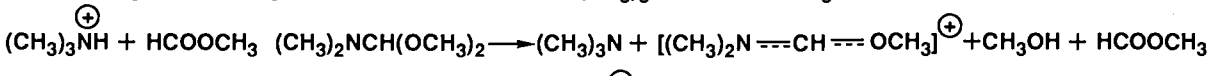

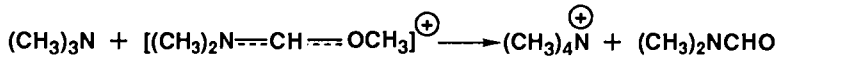

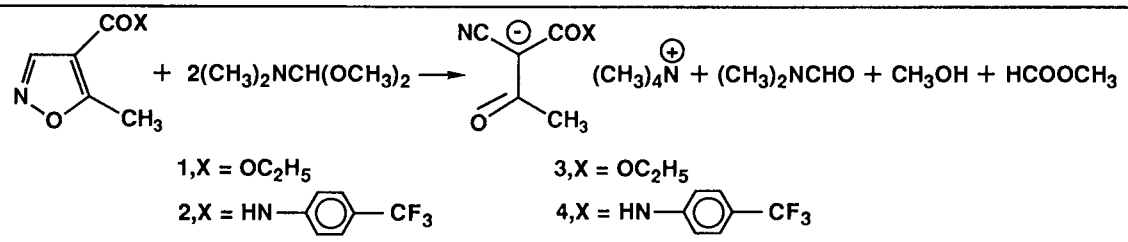

Following the procedure described for the preparation of **3**, **4** was obtained in a yield of 60%: mp 157-159 °C; ^{1}H NMR ($CDCl_3$); δ 12.32 (s, 1H, NH), 7.7, 7.45 (4H, J=6Hz, aromatic A_2B_2), 3.3 (s, 12H, $\overset{+}{N}(CH_3)_4$), and 2.26 (s, 3H, O=C-CH_3); ^{13}C-NMR ($CDCl_3$): δ 190.3 (O=$\underline{C}$-CH_3), 167.8 (O=C-NH-), 143.5 (C_1), 125.7 (C≡CN, C_2 and C_6), 124.2 (CF_3), 123. (C_4), 118.3 (C_3 and C_5), 77.3 (O=C-$\underline{C}$-CN), 55.8 ($\overset{+}{N}(CH_3)_4$) and 27.3 ($\underline{C}H_3C$=O); IR υ max (KBr) 2180.5 cm^{-1} (-CN) and 1642.3 cm^{-1} (-CONH-). Anal. Calcd for $C_{16}H_{20}F_3N_3O_2$: C, 55.97; H, 5.98; N, 12.23. Found: C, 56.11; H, 5.90; N, 12.28.

References

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