SYNTHESIS OF DERIVATIVES OF 4-SUBSTITUTED ISOXAZOLE-3,5-DICARBOXYLIC ACIDS

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Two procedures for the synthesis of derivatives of 4-substituted isoxazole-3,5-dicarboxylic acids (1) and a reaction mechanism are reported. One (i) is from 2-substituted-1,3-dinitroglutarates (2) and the other (ii) is from nitroacetate with n-alkyl halides. Method i: when a solution of 2 in alcohol with a primary amine (such as n-butylamine) is refluxed, 4-substituted-3,5-bis(n-butylcarbamoyl)-isoxazoles (3) are obtained in good yield. ii: A reaction mixture of nitroacetate with n-alkyl halides in a dipolar aprotic solvent, e.g. dimethylacetamide, in the presence of sodium methylate yields 4-n-alkyl-3,5-bis(methoxycarbonyl)isoxazoline-N-oxides (4) in reasonable yield. Furthermore, after heating the 4 with n-butylamine, the corresponding diamide is afforded.

Subsequently 3 leads to free acids of isoxazole (1) by alkali hydrolysis.