SYNTHESES OF 4-(C-GLYCOSYL)ISOXAZOLINE N-OXIDES AND RELATED SUBSTANCES

Eisuke Kaji, Hiromi Ichikawa, and Shonosuke Zen
School of Pharmaceutical Sciences, Kitasato University
Shirokane, Minato-ku, Tokyo 108

A new type of C-nucleoside; 4-(C-glycosyl)isoxazoline N-oxides and related substances were synthesized directly from aldehydo sugars by one-step cyclization with double moles of methyl nitroacetate in reasonable yield. The reaction of 2,3-O-isopropylidene-D-glyceraldehyde (1a) with two equivalents of methyl nitroacetate in the presence of an equivalent of diethylamine in N,N-dimethylacetamide afforded 3,5-bis(methoxycarbonyl)-4-(1,2-O-isopropylidene-D-glycero-dihydroxyethyl)isoxazoline N-oxide (2a) in 74 % yield. The same treatment of 2,3:4,5-di-O-isopropylidene-aldehydo-L-arabinose (1b) and aldehydo-D-glucose pentaacetate (1c) also gave the corresponding 4-(polyhydroxyalkyl)isoxazoline N-oxides (2b and 2c) which are considered to be promising precursors in the C-nucleoside synthesis.

Under similar reaction conditions 4-(aldofuranosyl)isoxazoline N-oxides; 3,5-bis(methoxycarbonyl)-4-(2,3-O-isopropylidene-β-D-erythrofuranosyl)isoxazoline N-oxide (2d), 3,5-bis(methoxycarbonyl)-4-(3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-tetrofuranos-4-yl)isoxazoline N-oxide (2e), 3,5-bis(methoxycarbonyl)-4-(2,3,5-tri-O-benzyl-β-D-ribofuranosyl)isoxazoline N-oxide (2f), and its 2,3,5-tri-O-benzoyl analogue (2g) were synthesized from corresponding cyclic aldehydo sugars. Carbamoylation of 2 was achieved by treatment with butylamine or methanolic ammonia, giving 3,5-bis(butylcarbamoyl) or 3,5-dicarbamoyl derivatives of 2. Attempted deprotection of sugar moieties of 2 was also examined.