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SYNTHETIC STUDIES ON THE α-FLUORO-α-AMINO ACID DERIVATIVES

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Syntheses of α-fluoro-α-amino acid derivatives have been attempted from the viewpoints of their structural and biological interests.

α-Amino esters were diazotized with i-AmONO or $NaNO_2$ to produce the corresponding diazo esters, which were treated with NBS and HF/pyridine to yield the α-bromo-α-fluoro esters(R-CFBr-COOEt, 1a∼c). Introduction of nitrogenous functionality was undertaken by reaction of 1b(R=Me) and 1c ($R=CH_2Ph$) with potassium phthalimide to produce the undesired elimination products. Reaction of 1a(R=H) with the potassium salts of phthalimide or iminodicarboxylates gave the α-fluoroglycine derivatives(R'R''N-CHF-COOEt, 2a:R'–R''=phthalyl, 2b:R'=COOMe, R''=$COOBu^t$, 2c:R'=R''=$COOBu^t$). Removal of the phthalyl group of 2a under various conditions was unsuccessful. Acid treatment of 2b produced the unstable fluoro ester, MeOCONH-CHF-COOEt, which was easily hydrolyzed during workup to give the hydroxy derivative, MeOCONH-CH(OH)-COOEt. On the other hand, reaction of 2c with CF_3COOH resulted in complete decomposition, probably via the imine(HN=CH-COOEt) formation. Then, the alkaline hydrolysis of 2c was first carried out to yield successfully the N-protected fluoroglycine($(Bu^tOCO)_2N$-CHF-COOH, 3). However, the deprotection of the t-butoxycarbonyl group of 3 under acidic condition did not produce the 'free' α-fluoroglycine, presumably owing to the acid labile property of the α-fluoro-α-amino acid structure.

Reductions of the novel trifunctional carbon compounds, N_3-CHF-COOR and O_2N-CHF-$COOCH_2Ph$, under several kinds of neutral conditions, were also attempted.