High yielding synthesis of oxazole-4-carboxylates from dehydroamino acid derivatives. Application as fluorescent markers for peptides

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Oxazoles are considered an important class of heterocyclic compounds since they are structural subunits of various biologically active natural products and are valuable synthetic precursors and pharmaceuticals. Oxazoles are associated with antibacterial, antifungal, anti-inflammatory and antitumoral activities and can be used as peptide mimetics or enzyme inhibitors[1], as efficient luminophores for liquid and plastic scintilators and as fluorescent probes for biological systems.[2] In our research group we have prepared oxazoles from *N*-acyl-β-hydroxyamino acids by a sequential dehydration reaction followed by an intramolecular cyclization promoted by iodine.[3] Continuing this work we have decided to investigate the possibility of obtaining substituted oxazoles from *N*-acyl-β-bromodehydroamino acids by treatment with a base. Thus, several β-halodehydroaminobutyric acids were treated with a 2% solution of DBU in acetonitrile to afford the corresponding oxazoles derivatives in high yields (84%-91%). The reaction was also applied to dehydrodipeptides having a β-bromodehydroaminobutyric acid as the C-terminal residue to give the corresponding oxazoles in good yields.

The absorption and fluorescence properties of some of the oxazoles prepared were studied in solvents of different polarity. The generally high fluorescence quantum yields of these oxazole derivatives and the moderate solvent sensitivity of their fluorescence emission make them good candidates to be used as fluorescence probes for peptides and proteins. To test this possibility, one of the oxazoles prepared was successfully introduced in two model peptides (H-Gly-Ala-OMe and H-Gly-Ala-Phe-OEt). The absorption and emission spectra of these peptides were obtained in ethanol and water, and the results obtained indicate that these oxazoles keep very reasonable fluorescence emission when linked to peptide chains, offering good possibilities to be used as fluorescent probes in peptides and proteins.

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