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An efficient method for the solid-phase synthesis of hydroxamic acids is described. The method comprises the nucleophilic displacement of esters immobilized on PEGA resins with hydroxylamine/sodium hydroxide in isopropanol. The hydroxyaminolysis protocol is compatible with a broad range of PEGA-supported peptide and peptidomimetic esters. The methodology was found to be compatible with two new strategies for the synthesis of solid-supported lactams and diketopiperazines, respectively, both relying on the high inter- and intramolecular reactivity of cyclic N-acyliminium ions with electron-rich aromatics and heteroaromatics, ultimately affording hydroxamic acid derivatives in high purities.

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