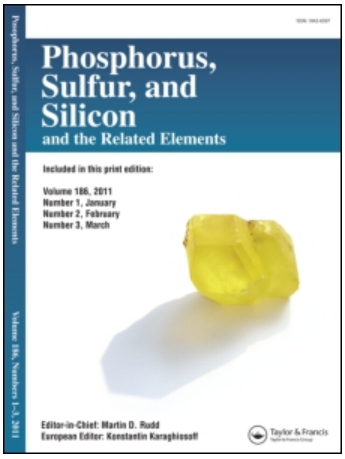

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The Synthesis of Diphenyl Phosphonate Analogues of α-Amino Acids as Enzyme Inhibitors

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The Synthesis of Diphenyl Phosphonate Analogues of α-Amino Acids as Enzyme Inhibitors

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α-Aminoalkylphosphonic acids are analogues of natural aminoacids and as such have been the subject of much research effort over past years[1]. The diphenyl esters of α-aminoalkylphosphonic acids are particularly potent and show high selectivity as irreversible inhibitors of serine proteinases. Thus far, α-aminoalkylphosphonic acid ester analogues of a number of aliphatic- and aromatic aminoacids have been prepared including valine, phenylalanine, tryptophan, and tyrosine[2], and the basic aminoacids ornithine, lysine, etc.[3]. We have now also prepared the α-diphenyl phosphonate analogues of the acidic aminoacids, aspartic and glutamic[4]. These have been examined as potential inactivators of serine proteinases exhibiting a P_1 specificity for aspartate and glutamate, e.g. *S. aureus* V8 protease and granzyme B.

Analogue	Apparent second-order rate constant (k_i/K_i)	
	S. aureus V8 protease	GranzymeB
Acetyl-Glu^P(OPh)$_2$	$5.3 \pm 0.5 \times 10^3$ $M^{-1}s^{-1}$	N.I.
Acetyl-Asp^P(OPh)$_2$	$5.0 \pm 0.5 \times 10^3$ $M^{-1}s^{-1}$	N.I.

Initial results show that they function as irreversible inactivators of *S. aureus* V8 proteinase but show no activity towards granzyme B.

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