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# An update on the stereoselective synthesis of $\alpha$ -aminophosphonic acids and derivatives

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## ABSTRACT

This review describes the stereoselective synthesis of  $\alpha$ -aminophosphonic acids and their ester derivatives. The procedures have been classified in accordance with acyclic, carbocyclic and azacyclic nature of the products obtained, establishing in the first case an order related to the strategy used whereas in the cyclic and azacyclic the ring size is considered.

### Keywords:

$\alpha$ -aminophosphonic acids

$\alpha$ -aminophosphonates

stereoselective synthesis

Three component reaction

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**Abbreviations:** ABSA, 4-acetamidobenzenesulfonyl azide; Abu, aminobutyric acid; Ac, acetyl; ACE, angiotensin-converting enzyme; Ala, alanine; Ar, aryl; BINAP, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl; BINOL, 1,1'-bi-2-naphthol; Bn, benzyl; Boc, *tert*-butoxycarbonyl; BPE, 1,2-bis(2,5-diphenylphospholano)ethane; BH, benzotriazole; BuLi, butyllithium; Bz, benzoyl; CAN, cerium ammonium nitrate; catBH, catecholborane; Cbz, carboxybenzyl; CD, circular dichroism; COD, cyclooctadiene; CSA, camphorylsulfonic acid; DABCO, 1,4-diazabicyclo[5.4.0]undec-7-ene; DBU, 1,8-diaza-bicyclo[5.4.0]undec-7-ene; DDQ, 2,3-dichloro-5,6-dicyano-*para*-benzoquinone; DEAD, diethyl azodicarboxylate; DIAD, diisopropyl azodicarboxylate; DIBAL-H, diisobutylaluminium hydride; DMAP, 4-dimethylaminopyridine; DMF, *N,N*-dimethylformamide; DMSO, dimethyl sulfoxide; DPPA, diphenylphosphoryl azide; dr, diastereoisomeric ratio; ds, diastereoselectivity; ee, enantiomeric excess; EWG, electron withdrawing group; Gly, glycine; HIV, human immunodeficiency virus; HPLC, high-performance liquid chromatography; KHMDS, potassium bis(trimethylsilyl)amide; LDA, lithium diisopropylamide; L-DBTA, dibenzoyl-L-tartaric acid; Leu, leucine; LiHMDS, lithium bis(trimethyl-silyl)amide; LTMP, lithium tetramethyl piperidine; *m*-CPBA, *m*-chloroperbenzoic acid; Me, methyl; Mes, 2,4,6-trimethylphenyl; Ms, mesyl; MS, molecular sieves; MTBE, methyl *tert*-butyl ether; MW, microwave irradiation; NBS, *N*-bromosuccinimide; OAB, methyl oxazaborolidine; Ph, phenyl; Phe, phenylalanine; Phg, phenylglycine; PMB, *p*-methoxybenzyl; PMP, *p*-methoxyphenyl; PPTS, pyridinium *p*-toluenesulfonate; Pro, proline; PTC, phase-transfer catalysis; *p*-Tol, *p*-tolyl; Py, pyridine; RAMP, (*R*)-1-amino-2-(methoxy-methyl)pyrrolidine; SMS-Phos, 1,2-bis([*o*-RO-phenyl](phenyl)phosphino)ethane; TADDOL, 2,2-dimethyl- $\alpha,\alpha',\alpha'$ -tetraphenylidioxolane-4,5-dimethanol; TBox, tethered bis(8-quinolinato); TBS, *tert*-butyldimethylsilyl; *t*-Bu, *tert*-butyl; TCCA, trichloroisocyanuric acid; Tf, triflyl; TFA, trifluoroacetic acid; TFE, 2,2,2-trifluoroethanol; THF, tetrahydrofuran; THNAPhos, 1,2,3,4-tetrahydro-1-naphthylamine-derived phosphine-phosphoramidite; TMEDA, *N,N,N',N'*-tetramethylethylenediamine; TMS, trimethylsilyl; TMSBr, bromotrimethylsilane; Ts, Tosyl; Val, valine.

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