

Title (en)

METHOD FOR MAKING A PROLINEBORONATE ESTER.

Title (de)

Verfahren zur Herstellung von Prolineboronat ester.

Title (fr)

PROCEDE DE PRODUCTION D'UN ESTER DE PROLINEBORONATE.

Publication

**EP 0641347 A1 19950308 (EN)**

Application

**EP 92925238 A 19921119**

Priority

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Abstract (en)

[origin: WO9310127A1] A method for the preparation of esters of prolineboronic acid is described. An N-protected pyrrole (I) is lithiated at the 2-position. The lithiated species (II) is reacted with trialkylborate, to yield a protected pyrrole-2-boronic acid (III). This is reduced to form a protected prolineboronic acid (IV), which, in turn, is reacted with a diol to yield an ester (VI). With the boronic acid moiety protected by the ester group, the protecting group on the nitrogen is removed, yielding the desired prolineboronic acid ester (VII). In an alternative synthesis, a protected pyrrolidine (VIII) is lithiated at the 2-position to yield a protected 2-lithio-pyrrolidine (IX). This is reacted with trialkylborate to yield the intermediate IV. The prolineboronic acid esters so produced have a chiral center to the boron atom. Also disclosed are methods for resolving enantiomers. The final products can be coupled to activated carboxylic acids, to yield peptides having a prolineboronic acid ester, instead of an amino acid, at the C-terminus. These boronic acid peptide analogs are useful for inhibiting biologically important proteases. Several methods for removing pinanediol from pinanediol boronate esters are also disclosed.

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See references of WO 9310127A1

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WO2011127051A1; WO2012145603A1; EP2116235A1; WO2013055910A1; WO2012145604A1; WO2011005929A1; WO2014074668A1; US11253508B2; EP2253311A2; WO2012145361A1; WO2012170702A1; WO2012040279A1; WO2012135570A1; EP3323818A1; US10555929B2; US10772865B2; US11400072B2

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