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| Title: | Construction of Racemic and Enantiopure Biaryl Unnatural Amino Acid Derivatives via Pd(II)-Catalyzed Arylation of Unactivated Csp3−H Bonds |
| Authors: | Banga, Shefali (/jspui/browse?type=author&value=Banga%2C+Shefali)<br>Kaur, Ramandeep (/jspui/browse?type=author&value=Kaur%2C+Ramandeep)<br>Babu, Srinivasarao Arulananda (/jspui/browse?type=author&value=Babu%2C+Srinivasarao+Arulananda) |
| Keywords: | Pd(II)-Catalyzed<br>Csp3−H Bonds |
| Issue Date: | 2021 |
| Publisher: | Wiley |
| Citation: | European Journal of Organic Chemistry, 2021(25), 3641–3656. |
| Abstract: | We report the construction of racemic and enantiopure biaryl unnatural amino acid derivatives via the palladium-catalyzed stereoselective sp3 C−H activation and arylation of amino acid derivatives with iodobiaryls. The synthesis of biaryl motif installed (DL-), L- and D-amino acid derivatives including norvaline, phenylalanine, leucine, norleucine and 2-aminooctanoic acid with anti stereochemistry is reported. The synthesis of alanine derivatives with two biaryl motifs and aminoalkanoic acids with biaryl motifs is also shown. The C−H arylation of enantiopure carboxamides gave biaryl amino acid derivatives with good enantiopurity. Removal of the directing group 8-aminoquinoline, deprotection of the phthalimide moiety, and the preparation of biaryl amino acid derivatives containing free amino- and carboxylate groups are also reported. The stereochemistry (anti) of representative major diastereomers was unequivocally ascertained from X-ray structure analysis. Biaryl amino acids/peptides are important motifs in medicinal chemistry, and this work therefore represents a contribution towards enriching the library of biaryl amino acids. |
| Description: | Only IISER Mohali authors are available in the record. |
| URI: | https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejoc.202100683 (https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejoc.202100683)<br>http://hdl.handle.net/123456789/5151 (http://hdl.handle.net/123456789/5151) |
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