Darstellung chiraler heterocyclischer β-Aminosäureester

Preparation of Chiral Heterocyclic Esters of β-Amino Acids

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Chiral β-amino alcohols were successively prone to N-benzylation, O-allylation and oxidation of the resulting benzylamino group to give nitrones 3 which on hydrolysis afforded chiral hydroxylamines HO-NH-CH(R)-CH₂-O-CH₂-CH=CH₂ ((S)-4: R = Me, Bn, iPr, (R)-4: R = Et). Swern oxidation of methyl 2,2-dimethyl-3-hydroxypropionate (16) and treatment of the resulting aldehyde 17 with hydroxylamines (S)-4b (R = Bn) or (R)-4d (R = Et) provided nitrones 18 that underwent an intramolecular 1,3-dipolar cycloaddition on heating yielding the bicyclic β-amino-acid esters 19b and ent-19d, respectively. Reductive cleavage of the N,O-bond of compounds 19 afforded the eight-membered ring compounds 20b and ent-20d, respectively.

N-Benzylalaninol (22) was treated with β-bromo-methacrylate to give the amino alcohol 23. Swern oxidation and subsequent treatment with N-tert-butylhydroxylamine provided the bicyclic ester 26a (R = t-Bu) via the corresponding nitrone 24. Oxime 25 was prepared in an analogous way as 24 with unsubstituted hydroxylamine. It underwent an intramolecular 1,3-dipolar cycloaddition yielding 26b on heating in toluene. Reduction of 26a afforded the pyrrolidine-carboxylic ester 27a.

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