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α-Amino esters as nucleophiles in diastereoselective palladium catalysed allylic substitution reactions

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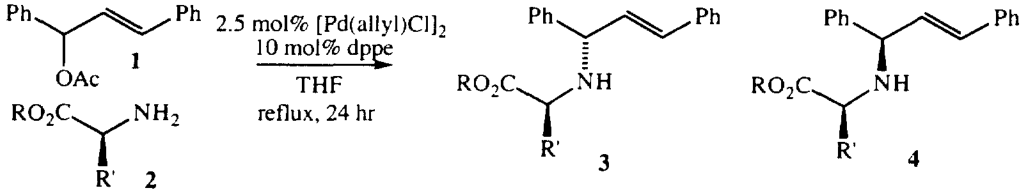
Abstract

Allylic acetates undergo palladium catalysed allylic substitution with amino ester nucleophiles. Using enantiomerically pure α-amino esters, the substitution products are obtained with moderate diastereoselectivity (up to 85:15: 70% d.e.). The reactions could also be performed using an enantiomerically pure ligand, which was found to exert a stronger influence over the stereochemical outcome. © 1998 Elsevier Science Ltd. All rights reserved.

Amines have previously been shown to be competent nucleophiles in palladium catalysed allylic substitution reactions.[1] Indeed, several research groups,[2] including this one have reported an enantioselective variant of this reaction.[3] In particular, we have an interest in using palladium catalysed allylic substitution reactions as a key transformation in the preparation of enantiomerically enriched α- and β-amino acids.[4]

Herein we report the use of enantiomerically pure amino esters as nucleophiles in palladium catalysed allylic substitution reactions. In the presence of an achiral palladium catalyst (allylpalladium chloride dimer/bisdiphenylphosphinoethane), 1,3-diphenylprop-2-en-1-yl acetate **1** was reacted with the amino esters **2** to afford the substitution products **3** and **4**. The best diastereoselectivities were obtained using the methyl esters, with up to 70% d.e. being achieved using L-leucine methyl ester as the nucleophile (Table 1).



Additionally, the use of other enantiomerically pure amines was considered. Both (S)-2-phenethylamine and L-valinol gave good yields of the substitution products (89% and 85%) but with low diastereoselectivities (8% and 6% d.e.).

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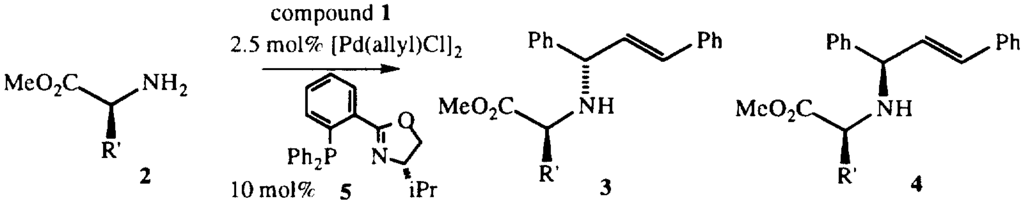
Table 1
Diastereoselective palladium catalysed allylic amination reactions

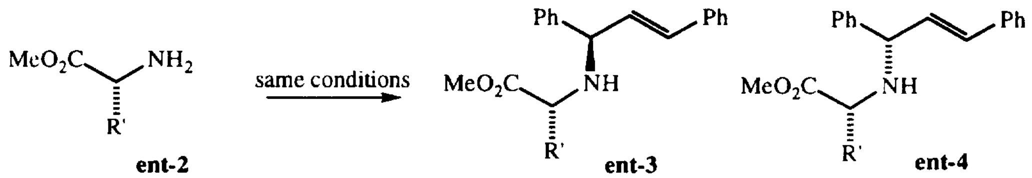
R	***R'***	***Diastereomer ratio (3:4)***[a]	***Yield***
Me	^{i}Bu	85 : 15	69
Me	^{i}Pr	80 : 20	72
Me	Ph	73 : 27	68
Me	CH_2Ph	60 : 40	74
Et	Me	61 : 39	56
Et	^{i}Bu	65 : 35	70
Et	^{i}Pr	60 : 40	70
Et	Ph	56 : 44	26
^{t}Bu	Me	58 : 42	45
^{t}Bu	iBu	57 : 43	79

[a] Diastereomer ratio determined by analysis of the ^{1}H nmr spectra

To date, we have been unable to separate by chromatography the diastereomeric products **3** and **4** (which are typically viscous oils). In order to gain more information about the relative stereochemistry of the major product, we have investigated the use of an enantiomerically pure ligand **5** in the allylic substitution reaction. The selectivity provided by ligand **5** overturns the normal diastereoselectivity of the reaction, affording diastereomer **4** as the major product. However, when D-amino esters **ent-2** were employed as the incoming nucleophiles, a matched pair results in an enhancement of the diastereoselectivity. Based on the known preference of ligand **5** to induce the stereochemistry indicated,[4] it is reasonable to suggest that the correct stereochemistry has been given throughout this communication.



R' = PhCH$_2$- **3** : **4** 22 : 78, 74% yield
^{i}Bu- **3** : **4** 16 : 84, 61% yield
Ph- **3** : **4** 42 : 58, 56% yield



R' = PhCH$_2$- **ent-3** : **ent-4** 91 : 9, 75% yield
^{i}Bu- **ent-3** : **ent-4** 91 : 9, 64% yield
Ph- **ent-3** : **ent-4** 74 : 26, 68% yield

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