

Addition of Carboxylic Acids Using Chiral Lithium Amides as Auxiliaries

Category

Metal-Mediated
Synthesis

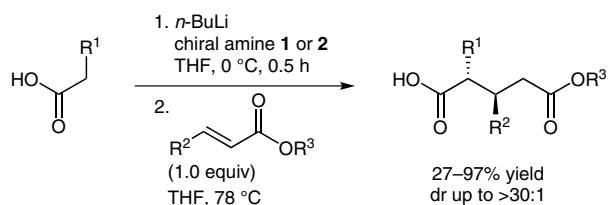
Key words

lithium

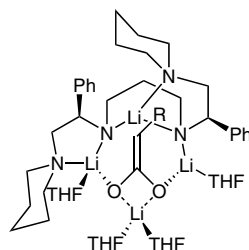
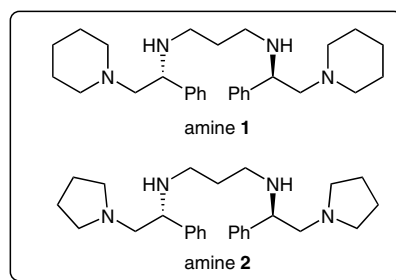
amides

Michael addition

Synfact
of the month

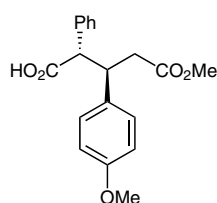


R¹ = Ph, (Het)Ar, CH₂Bn
 R² = Ph, (Het)Ar, Alk, CF₃
 R³ = Me, *t*-Bu

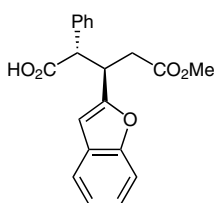


aggregate formation
of the carboxylic acid and chiral amine 1

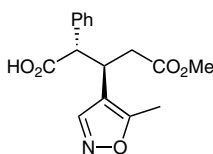
Selected examples:



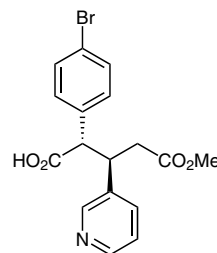
74% yield
dr = 30:1, 75% ee
(amine 1)



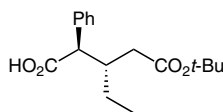
89% yield
dr > 30:1, 73% ee
(amine 1)



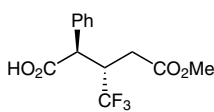
54% yield
dr > 30:1, 86% ee
(amine 1)



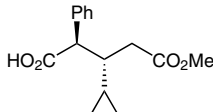
63% yield
dr = 8:1, 763% ee
(amine 1)



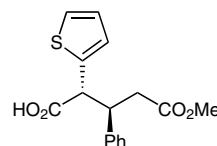
72% yield
dr = 5:1, 84% ee
(amine 2)



87% yield
dr > 30:1, 58% ee
(amine 1)



78% yield
dr = 5:1, 85% ee
(amine 2)



83% yield
dr > 30:1, 94% ee
(amine 1)

Significance: Zakarian and co-workers report the direct enantioselective Michael addition of carboxylic acids to α,β -unsaturated esters using chiral lithium amides as traceless auxiliaries.

Comment: The chiral reagents can be readily recovered in 99% yield by extraction with aqueous acid. Additionally, this protocol has been applied to the enantioselective total synthesis of the presumed structure of pulveraven B.