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Asymmetric allylic alkylation catalyzed by Pd/Al_2O_3 modified with chiral phosphines

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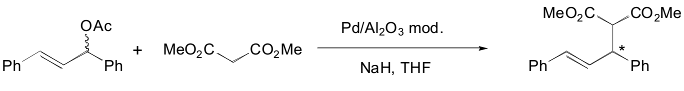
Soluble chiral Pd complexes afford excellent yields and enantioselectivities in asymmetric allylic alkylation reactions. Recently, the method has been extended to colloidal Pd modified by a chiral xylofuranoside diphosphite. This catalyst system affords up to 97% *ee* at medium conversions [1], and is one of the very few examples on highly enantioselective reactions on heterogeneous catalysts apart from the thoroughly investigated hydrogenation reactions. Here we report an extension of the method to other catalyst-modifier systems, using the same model reaction, the transformation of racemic **1** to **2**.



rac-**1** **2**

Allylic alkylation of **1** has been carried out on Pd/Al_2O_3 modified with various P-containing compounds such as (*S*,*S*)-chiraphos or (*R*)-BINAP. Several reaction parameters like the catalyst pretreatment, the reaction temperature and the concentrations of both the nucleophile and modifier have been studied. Under optimized reaction conditions high conversion and good chemo- and enantioselectivity were achieved at reasonably low catalyst/substrate and modifier/substrate ratios. Interestingly, the enantioselectivity of the homogeneous system with (*R*)-BINAP as ligand depends strongly on the reaction temperature, whereas the opposite holds for the heterogeneous system.

[1] S. Jansat, M. Gomez, K. Philippot, G. Muller, E. Guiu, C. Claver, S. Castillon, B. Chaudret, *J. Am. Chem. Soc.* **2004**, *126*, 1592.

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Strand Invasion by α-tricyclo-DNA

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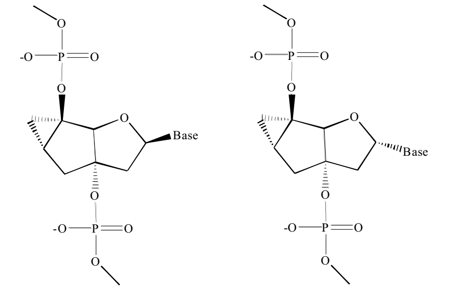
β-tricyclo (tc) DNA is a third generation antisense oligonucleotide that has been extensively studied in our lab [1]. We recently became interested in the pairing properties of the α-anomeric form and observed parallel orientation in the duplexes with natural DNA and RNA complements [2]. Interrestingly, within its own backbone series α-tc-DNA exhibits poor thermal stability which makes it a candidate for strand invasion applications. We present recent results on the triplex forming and strand invasion properties of α-tc DNA.



β-tricyclo DNA α-tricyclo DNA

[1] D. Ittig, S. Liu, D. Renneberg, D. Schümperli, and C. J. Leumann, *Nucleic Acids Research*, **2004**, *32*, 346–353

[2] S. P. Scheidegger, C. J. Leumann, *Chem. Eur. J.,* **2006**, *12*, 8014-8023

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Catalytic Electrophilic Amination of ß-Keto Ester

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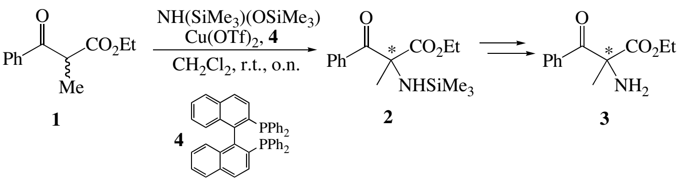
Very few catalytic asymmetric syntheses of α-amino acid involving carbon-nitrogen bond forming reactions have been described in literature.[1] Our group recently reported an efficient electrophilic amination of ß-keto esters catalyzed by chiral copper(II)-bisoxazoline.[2] However, this method gives α-hydrazino ß-keto esters, which are difficult to convert to the desired amino acids.



We present now a new direct α-amination of ß-keto ester **1** catalyzed by a copper(II)-binap (**4**) complex with bis(trimethylsilyl)-hydroxylamine as the nitrogen source. The reaction gives ß-keto-ester **2**, which is a convenient precursor of the corresponding α-amino acid **3**. Our efforts are currently directed toward the optimization of the reaction conditions and the full characterization of the products.

[1] Marigo, M.; Juhl, K.; Jørgensen, K.A.; *Angew. Chem. Int. Ed.*, **2003**, *42*, 1367.
[2] Huber, D.P.; Stamek, K.; Togni, A., *Tetrahedron: Asym.*, **2006**, *17*, 658.

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A target assembled tandem oligonucleotide probe assay based on excimer formation

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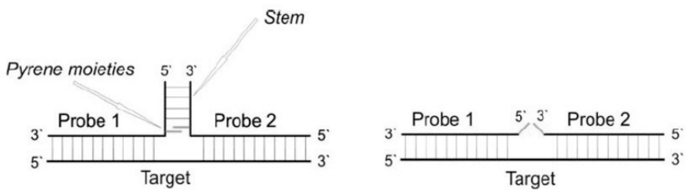
The tetracyclic hydrocarbon pyrene is well known for its ability to form an excimer emission band and has been studied extensively as a reporter fluorophore[1]. This dual probe assay based on excimer formation of incorporated pyrene moieties with an additional stem is able to discriminate a single-base insertion much better than does the assay with the pyrene moieties terminally attached.
We have studied the use of non-nucleosidic pyrene building block in the context of a dual probe assay. Of particular interest was the discrimination of single base mismatches. The results will be presented.



[1] F.M. Mannik, *Chem. Revs.* **1993**, *93*, 587-614.