SYNLETT Spotlight 354

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Diethyl Tartrate

Compiled by Christine Weiss

Christine Weiss was born in 1983 in Herten, Germany. She studied Chemistry at the Westfälische Wilhelms-University of Münster. After finishing her diploma thesis about chiral ion pair catalysis and asymmetric hydrogenation in the research group of Professor Dr. F. Glorius, Münster University, she is presently working towards her Ph.D. under the supervision of Professor Dr. N. Sewald at Bielefeld University. Her current research is focused on the synthesis of novel chemotherapeutics.

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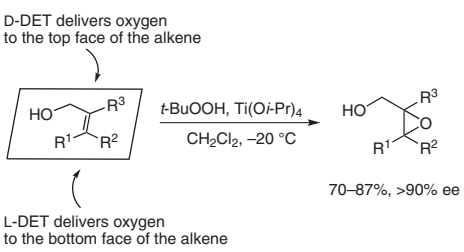
Introduction

Diethyl tartrate (DET) is a clear colorless slightly viscous liquid. It is the diethyl ester of tartaric acid, which is one of the most important α-hydroxy acids and originates from the *chiral pool*. L-DET (CAS: 87-91-2) and D-DET (CAS: 13811-71-7) are abundant and commercially available at low and moderate cost, respectively.

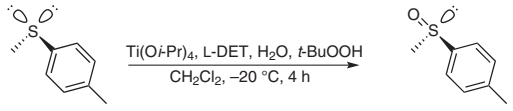
Diethyl tartrate has a wide range of applications in organic synthesis including precursors for chiral catalysts[1] and auxiliaries.[2] The desired stereoselectivity is tunable upon use of the corresponding enantiomer of diethyl tartrate. It was efficiently applied as a scaffold for the enantioselective synthesis of biomolecules.[3] In addition, it has been employed as a chiral resolving reagent.[4]

Abstracts

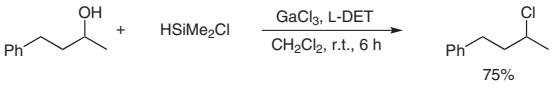
(A) *Asymmetric Epoxidation*:
Sharpless and co-workers developed a catalytic enantioselective epoxidation procedure for the transformation of primary and secondary allylic alcohols to α,β-epoxy alcohols.[5] The catalytic species is a titanium–tartrate complex.[6] The rate of epoxidation can be further improved by the addition of 3 Å or 4 Å molecular sieves.[7] Upon use of a given tartrate enantiomer, the epoxide oxygen is always delivered from the same enantioface of the olefin regardless of the substitution pattern.



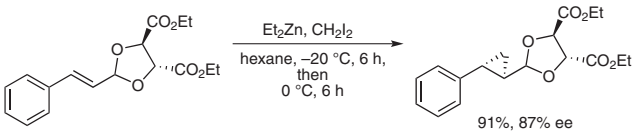
(B) *Asymmetric Oxidation of Sulfides*:
A slight modification of the Sharpless reagent can be used for the oxidation of sulfides to chiral monosulfoxides, which function as synthons for asymmetric C–C bond formation. The addition of one mol equivalent of water deactivates the Sharpless reagent for epoxidation. The new catalytic system is now active in the asymmetric oxidation of prochiral sulfides.[8]



(C) *Direct Chlorination of Alcohols*:
In case of acid-sensitive substrates chlorination of alcohols under neutral conditions is required. In the example shown, catalytic amounts of $GaCl_3$ and diethyl tartrate are used for the transformation of secondary alcohols with chlorodimethylsilane ($HSiMe_2Cl$) to the corresponding organic chlorides.[9]



(D) *Asymmetric Simmons–Smith Reaction*:
Many biologically active compounds exhibit a cyclopropyl unit. Therefore, methods for the stereoselective introduction of a cyclopropyl moiety are essential. In the asymmetric Simmons–Smith cyclopropanation, DET serves as a chiral protecting group and the cyclopropyl moiety is established with high diastereoselectivity. The asymmetric introduction is completely controlled by the auxiliary tartrate ligand.[2]



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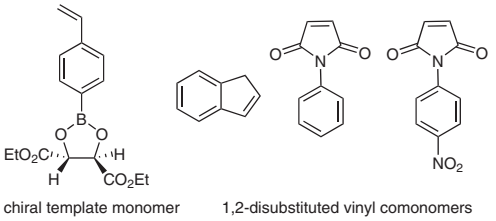
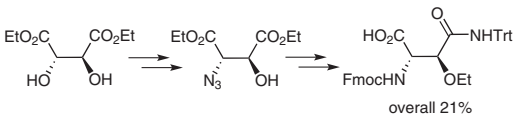
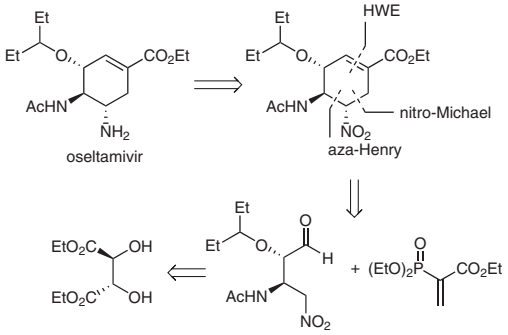
(E) *Chiral Template Mediated Polymerization*:
The synthesis of optical active polymers, which exhibit main-chain chirality, is challenging. 4-Vinylphenyl boronic acid was functionalized with L-DET as the chirality inducing agent. Radical copolymerization of this monomer with different 1,2-disubstituted vinyl monomers leads to the desired copolymers. Finally, the diethyl tartrate residues were removed quantitatively from the copolymer under mild conditions.[10]



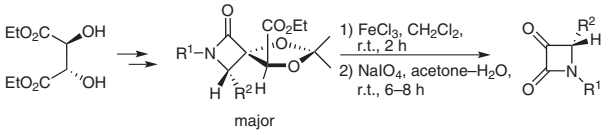
(F) *Synthesis of a Protected Non-Proteinogenic Amino Acid*:
L-*threo*-β-Ethoxyasparagine can be used as a building block for solid-phase peptide synthesis. This compound is the carboxy-protected form of L-*threo*-β-hydroxyasparagine, which is a non-proteogenic amino acid present in various antimicrobial peptides. Starting from D-DET, diethyl (2*S*,3*S*)-2-azido-3-hydroxysuccinate can be synthesized in two steps on a multi-gram scale. The final protected amino acid is obtained in further eight steps.[11]



(G) *Synthesis of Oseltamivir*:
Recently, a short and efficient synthesis of oseltamivir was reported.[12] Oseltamivir phosphate (Tamiflu) is the most used antiviral drug for the prevention and therapy of influenza.[13] In the presented route diethyl D-tartrate serves as starting material. An aza-Henry reaction and a domino nitro-Michael/Horner–Wadsworth–Emmons (HWE) reaction are the key steps for the construction of the cyclohexene ring. Beside the low cost, this approach features the advantages of an azide-free synthesis decreasing the operational hazard as well as prevention of heavy metals. Therefore, this synthetic route is a potential alternative for the industrial production of Tamiflu.



(H) *Scaffold for Azetidine-2,3-diones*:
A convenient synthesis of enantiopure azetidine-2,3-diones as building blocks[14] and precursors[15] for functionalized β-lactams was published.[16] Chiral ketene precursors prepared from commercially available diethyl L-tartrate were used in a Staudinger cycloaddition with different imines to generate diastereomers of spiro-β-lactams in a ratio of about 60:40. The final products were then obtained in a two-step procedure.



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