SYNLETT
Spotlight 283

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

Glyceraldehyde Acetonide – Recent Applications of this Chiron in Organic Synthesis

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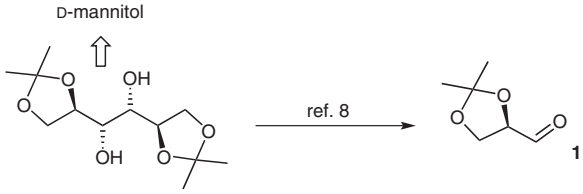
Introduction

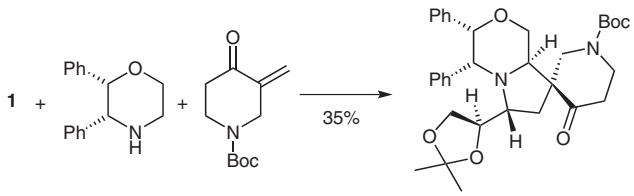
Glyceraldehyde acetonide (2,3-*O*-isopropylidene-D-glyceraldehyde, **1**) it is a well-known chiron which has been used in organic synthesis for multiple purposes.[1] It has been applied on the synthesis of a β-adrenergic antagonist,[2] on multicomponent reaction in the synthesis of nakadomarin A precursor,[3] and reacts with several organometallics to afford chiral alcohols used as precursors in total syntheses.[4–7] Its *R* isomer is easily prepared from selective protection and oxidative cleavage of inexpensive and available commercially D-mannitol (Scheme 1)[8] and its enantiomer can be obtained from vitamin C.[9] The present Spotlight emphasises recent applications of this chiron in organic synthesis in its *R* and *S* enantiomeric forms.



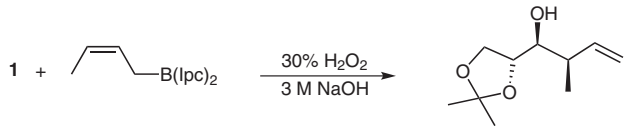
Scheme 1

Abstracts

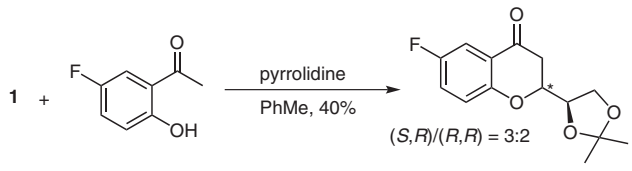
(A) Ahrendt and Williams reported the synthesis of the ADE fragment of nakadomarin A by a stereoselective three-component 1,3-dipolar cycloaddition with azomethine ylide obtained from **1**. The formation of the 2,5-*trans*-cycloadduct resulted in a single diastereomer.[3]



(B) The construction of C1–C21 linear skeleton of tartrolon B was reported by Kim and Lee. The synthesis started with the asymmetric crotylation of aldehyde **1** to yield the *syn*-crotyl adduct.[10]



(C) Wang's group synthesized the β-adrenergic antagonist (*S*,*R*,*R*,*R*)-nebivolol using the pyrrolidine-catalyzed cyclization between **1** and 2-acetyl-4-fluorophenol. This key step gave a diastereomeric mixture of products (*S*,*R*)/(*R*,*R*) (60:40) in 40% yield, which could be easily separated by chromatography. Both isomers were used to prepare (*S*,*R*,*R*,*R*)-nebivolol.[2]



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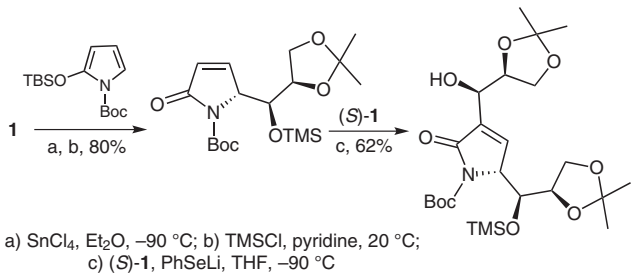
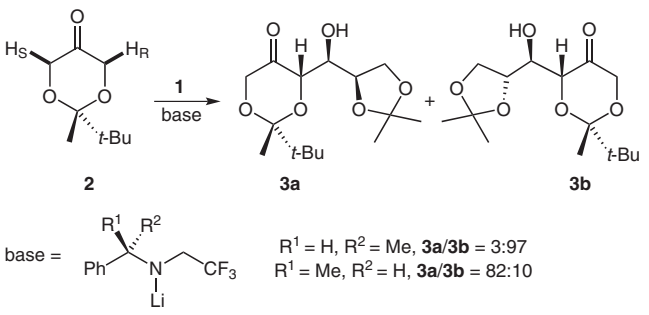
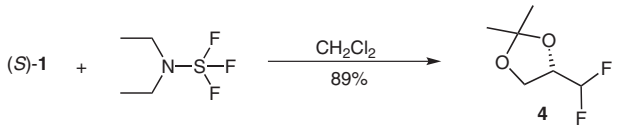
(D) Both enantiomers of **1** were used by Casiraghi's group to prepare amino acids polyols via a vinylogous Mukaiyama aldol reaction, standard protection of the resulting alcohol as a TMS ether, and a variant of the Morita–Baylis–Hillman reaction using a pyrrole as starting material and exploiting the configuration of **1**.[11]



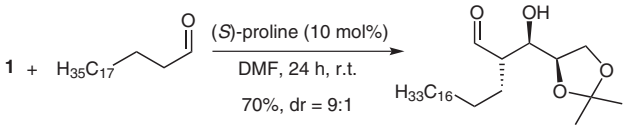
(E) Treatment of a prochiral symmetrical ketone **2** with chiral lithium amides leads to the formation of non-racemic lithium enolates. The base discriminates between two enantiotopic protons H_R and H_S and the resulting enolate could be trapped with electrophiles as **1**, exhibiting a double stereoselection.[12]



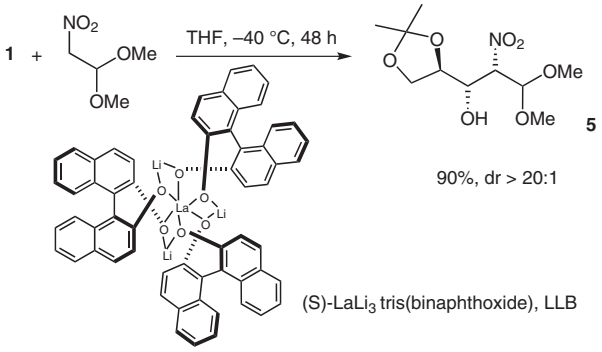
(F) Diethylaminosulfur trifluoride (DAST) was used on fluorination of (*S*)-**1** for the preparation of difluorated ketal **4** used to prepare b-difluoroalanine and g-difluorothreonine as useful building blocks for the preparation of biologically active peptides and peptidomimetics.[13]



(G) Kumaraswamy and Markondaiah synthesized stereoselectively the natural and unnatural nocardiolactone using **1** as starting material.[14] They indicated the synthesis accomplishing a (*S*)-proline-catalyzed crossed aldol reaction between eicosanal and aldehyde **1**. They changed (*S*)- to (*R*)-proline under otherwise identical conditions, but the results indicated that there is a negligible matched or mismatched effect on the diastereoselectivity of the product.



(H) Shibasaki's group related the stereodivergent construction of three contiguous stereocenters in catalytic doubly diastereoselective nitroaldol reactions of α-chiral aldehydes with nitroacetaldehyde dimethyl acetal using heterobimetallic catalysts.[15] (*S*)-LLB was employed as catalyst to prepare nitroadduct **5** from **1** in good yields and diastereoselectivity.



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