

SYNLETT Spotlight 283

Glyceraldehyde Acetonide – Recent Applications of this Chiron in Organic Synthesis

Compiled by Evanoel Crizanto de Lima

Evanoel Crizanto de Lima was born in Rio de Janeiro, Brazil. He studied chemistry at UERJ and obtained his M.Sc. at Universidade Federal do Rio de Janeiro in 2005, where he worked the greater part of his Ph.D. thesis under the supervision of Paulo R. R. Costa and Ayres G. Dias. Evanoel is currently finishing his experiments at the Universidad de Alicante, Spain, under the supervision of Carmen Nájera and José M. Sansano with a doctoral fellowship from CNPq, Brazil. His research interests focus on the stereoselective synthesis of bioactive pyrrolidines, pyrrolidones and amino acids.

Laboratório de Química Bioorgânica (LQB), NPPN, BI H, Centro de Ciências da Saúde, Universidade Federal do Rio de Janeiro, Cidade Universitária, CEP: 21941-590, Rio de Janeiro, Brazil
E-mail: evanoel.crizanto@gmail.com

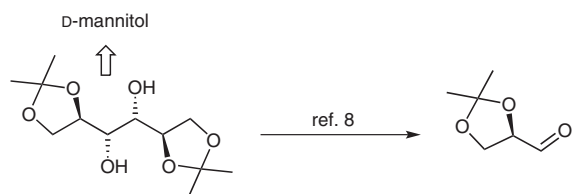


This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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

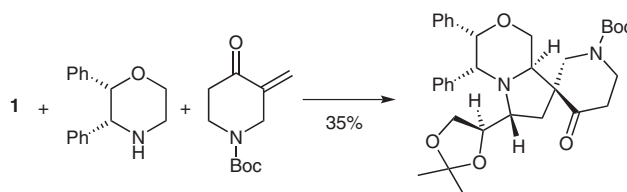
its enantiomer can be obtained from vitamin C.⁹ The present Spotlight emphasises recent applications of this chiron in organic synthesis in its *R* and *S* enantiomeric forms.



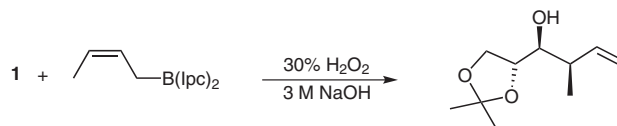
Scheme 1

Abstracts

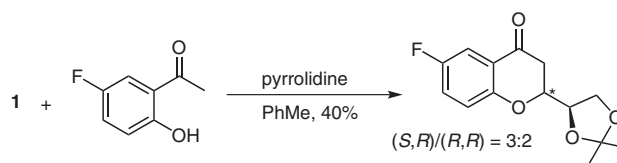
(A) Ahrendt and Williams reported the synthesis of the ADE fragment of nakadomarin A by a stereoselective three-component 1,3-dipolar cycloaddition with azomethine ylide obtained from **1**. The formation of the 2,5-*trans*-cycloadduct resulted in a single diastereomer.³



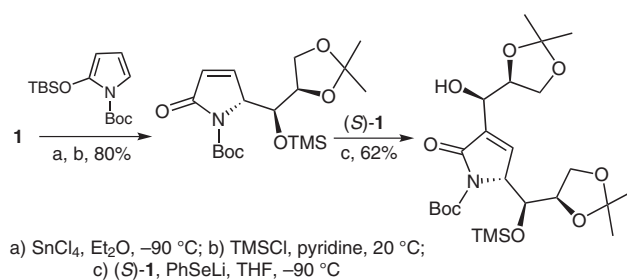
(B) The construction of C1–C21 linear skeleton of tartrolon B was reported by Kim and Lee. The synthesis started with the asymmetric crotylation of aldehyde **1** to yield the *syn*-crotyl adduct.¹⁰



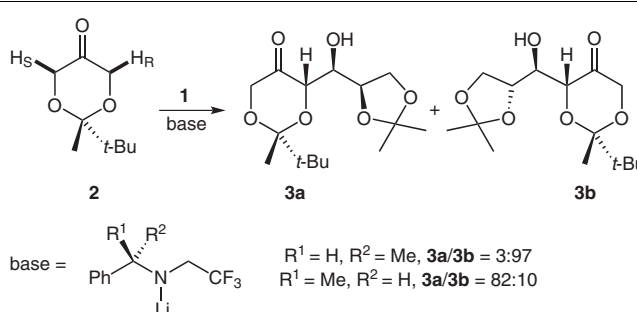
(C) Wang's group synthesized the β -adrenergic antagonist (*S,R,R,R*)-neбиволol using the pyrrolidine-catalyzed cyclization between **1** and 2-acetyl-4-fluorophenol. This key step gave a diastereomeric mixture of products (*S,R*)/(*R,R*) (60:40) in 40% yield, which could be easily separated by chromatography.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



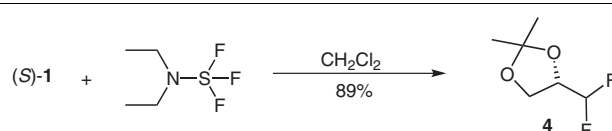
(D) Both enantiomers of **1** were used by Casiraghi's group to prepare amino acids polyols via a vinylogous Mukaiyama aldol reaction, standard protection of the resulting alcohol as a TMS ether, and a variant of the Morita–Baylis–Hillman reaction using a pyrrole as starting material and exploiting the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



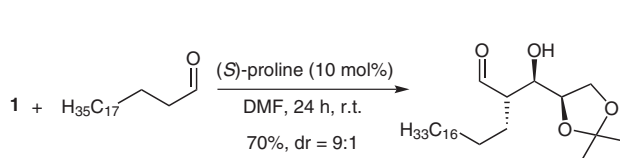
(E) Treatment of a prochiral symmetrical ketone **2** with chiral lithium amides leads to the formation of non-racemic lithium enolates. The base discriminates between two enantiotopic protons H_R and H_S and the resulting enolate could be trapped with electrophiles as **1**, exhibiting a double stereoselection.¹²



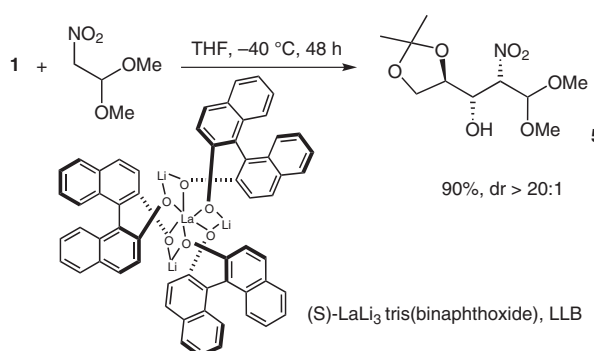
(F) Diethylaminosulfur trifluoride (DAST) was used on fluorination of $(S)\text{-1}$ for the preparation of difluorated ketal **4** used to prepare b-difluoroalanine and g-difluorothreonine as useful building blocks for the preparation of biologically active peptides and peptidomimetics.¹³



(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 $(S)\text{-LLB}$ was employed as catalyst to prepare nitroadduct **5** from **1** in good yields and diastereoselectivity.



References

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