SYNLETT
Spotlight 440

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

(1*R*,2*R*)-Diaminocyclohexane

Compiled by Paweł Tokarz

Paweł Tokarz was born in Łask, Poland, in 1986. He received his M.Sc. in inorganic chemistry from the University of Łódź in 2010. Currently, he is a Ph.D. student in the Department of Organic Chemistry at the same university under the supervision of Professor Jarosław Lewkowski. His research focuses on the diastereoselective synthesis of phosphonic derivatives of ligands based on (1*R*,2*R*)-diaminocyclohexane (so called salen-like compounds).

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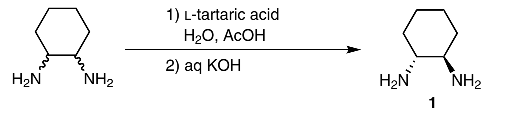
Introduction

trans-1,2-Diaminocyclohexane (**1**), denoted as *trans*-DACH, is a chiral molecule with C_2 symmetry. It was synthesized for the first time in 1926 from hexahydrophthalic acid by Wieland.[1] A convenient way for the resolution of the enantiomers was introduced by Whitney in 1980.[2] An aqueous solution of racemic *trans*-DACH and enantiomerically pure L-(–)-tartaric acid was treated with glacial acetic acid and the resulting white precipitate of enantiomerically pure (1*R*,2*R*)-diaminocyclohexane tartarate was subsequently treated with an aqueous solution of KOH yielding **1** (Scheme 1). Recently, it was demonstrated that the second enantiomer can be recovered from the resulting filtrate with another portion of L-(–)-tartaric acid.[3]

In the early 1990s, Jacobsen and co-workers published two subsequent papers on the enantioselective oxidation of olefins catalyzed by an imine complex derived from (1*R*,2*R*)-diaminocyclohexane.[4] Since then, the interest in DACH-based compounds in chiral synthesis has been growing. Although many derivatives of the compound have been applied in chiral catalysis, recent years brought catalytic and synthetic applications of *trans*-DACH itself.

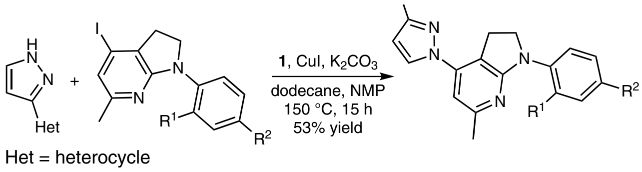


Scheme 1

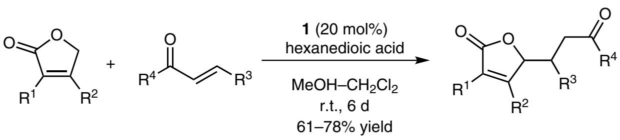
Abstracts

(A) **1** has been confirmed as a cheap and good organocatalyst for enantioselective aldol reactions. Various organic acids were tested as co-catalysts. The model reaction of 4-nitrobenzaldehyde with cyclohexanone, which was studied by Liu and co-workers,[5] proceeds with good yield (75%) and enantioselectivity (93% ee).

(B) **1** can be used as a cheap and simple chiral ligand for N-arylation, the reaction of an aryl halide with amines. This reaction was applied in the synthesis of possible novel corticotropin-releasing factor antagonists.[6] By analogy, **1** can catalyze S-arylations in which thioethers are formed.[7]

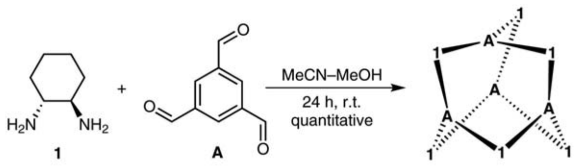


(C) As reported by the group of Ge,[8] **1** works as an organocatalyst in the asymmetric vinylogous Michael addition. This reaction proceeds through a bis-iminium intermediate and is highly diastereo- and enantioselective.

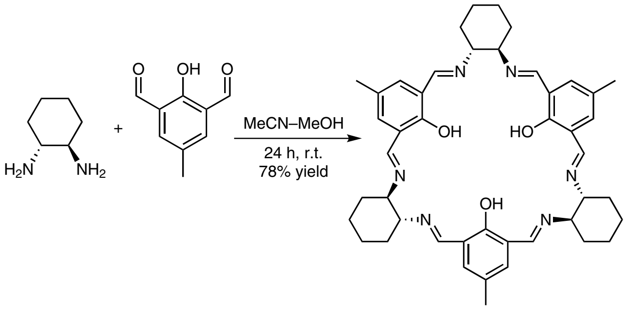


SYNLETT 2013, 24, 1597–1598
Advanced online publication: 26.06.2013
DOI: 10.1055/s-0033-1339302; Art ID: ST-2013-V0447-V

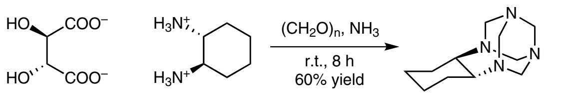
(D) Apart from having catalytic properties, **1** is a skeleton for many high symmetry chiral molecules. One of the most spectacular examples is a spherand prepared by thermodynamically driven [4+6] cyclocondensation of **1** and benzene-1,3,5-tricarboxaldehyde.[9]



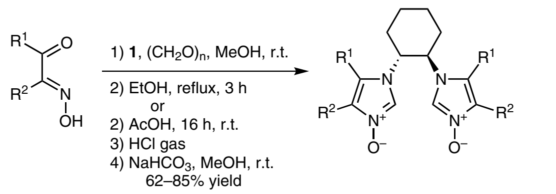
(E) Similarly, [3+3] cyclocondensation of **1** and 2,6-diformyl-4-methylphenol yields a macrocyclic trianglimine.[10] Crystallization of the enantiomerically pure compound gives a yellow solid with photochromic properties. Noteworthy, racemic crystals do not show the same behavior. This class of macrocycles has been used in a highly enantioselective fluorescent recognition of mandelic acid derivatives.[11]



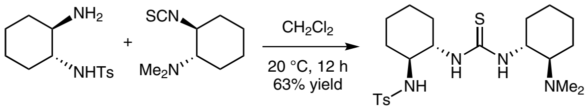
(F) **1** has been applied in the synthesis of tetracyclic amines by condensation with ammonia and paraformaldehyde under mild conditions.[12]



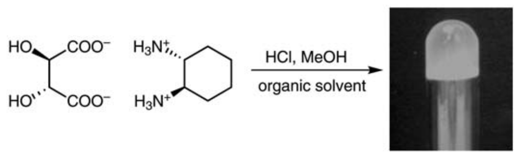
(G) Interesting DACH-derived chiral bisimidazole *N*-oxides have recently been reported.[13] They were prepared in a multistep reaction starting from oximes. The compounds were tested as organocatalysts in the enantioselective allylation of aromatic aldehydes.



(H) By addition of the mono-tosylated intermediate to **1**-based thiocyanate, a chiral thiocyanate derivative was synthesized. The product was subsequently applied as a catalyst for the asymmetric synthesis of biologically active 4-aminochromanes.[14]



(I) Beyond synthetic chemistry, the tartrate of **1** was used as a main ingredient of a novel multicomponent (organo)gelator solution (MGS). Concentrations of the MGS as low as 0.06 M allowed for the preparation of gels from various solvents with moderate polarity. The gelation relies on an ionic dissociation–exchange process.[15]



References and Notes

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