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Spotlight 440

(1R,2R)-Diaminocyclohexane
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Introduction

trans-1,2-Diaminocyclohexane (1), denoted as trans-DACH, is a chiral molecule with C2 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 (1R,2R)-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

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 diastere- and enantioselective.

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(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.\(^\text{9}\)

(E) Similarly, \([3+3]\) cyclocondensation of 1 and 2,6-diformyl-4-methylphenol yields a macrocyclic triglimine.\(^\text{10}\) 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.\(^\text{11}\)

(F) 1 has been applied in the synthesis of tetracyclic amines by condensation with ammonia and paraformaldehyde under mild conditions.\(^\text{12}\)

(G) Interesting DACH-derived chiral bisimidazole \(N\)-oxides have recently been reported.\(^\text{13}\) 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.\(^\text{14}\)

(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.\(^\text{15}\)

References and Notes