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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 $C_2$ 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 (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

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 (1R,2R)-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.

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.
(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 triglimine.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 alkylation 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

(15) Kapoor, I.; Schön, E. M.; Bachl, J.; Kühbeck, D.; Cativiela, D.; Saha, S.; Banerjee, R.; Roeleens, S.; Marrero-Tellado, J. J.; Díaz, D. Soft Matter 2012, 8, 3446. The image of the gel was provided and used under permission from Ms. Eva Maria Schön who is thanked for fruitful discussions.