SYNLETT Spotlight 440

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

Compiled by Paweł Tokarz

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

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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.

(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

- (1) Wieland, H.; Schlichtung, O.; Langsdorf, W. *V. Z. Phys. Chem.* **1926**, *161*, 74.
- (2) (a) Whitney, T. A. U.S. Patent 4 085 138, **1978**. (b) Whitney, T. A. *J. Org. Chem.* **1980**, *45*, 4214.
- (3) Mucha, P.; Mlostoń, G.; Jasiński, M.; Linden, A.; Heimgartner, H. *Tetrahedron: Asymmetry* **2008**, *19*, 1600.
- (4) (a) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (b) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063.
- (5) Liu, Y.; Wang, J.; Sun, Q.; Li, R. *Tetrahedron Lett.* **2012**, *52*, 3584.
- (6) Fabio, R. D. et al. *J. Med. Chem.* **2008**, *51*, 7370.
- (7) Carril, M.; SanMartin, R.; Domínguez, E.; Tellitu, I. *Chem.–Eur. J.* **2007**, *13*, 5100.
- (8) Wang, J.; Qi, C.; Ge, Z.; Cheng, T.; Li, R. *Chem. Commun.* **2010**, *46*, 2124.
- (9) Skowronek, P.; Gawroński, J. *Org. Lett.* **2008**, *21*, 4755.
- (10) Tanaka, K.; Shimoura, R.; Caira, M. R. *Tetrahedron Lett.* **2012**, *51*, 449.
- (11) Tanaka, K.; Tsuchitani, T.; Fukuda, N.; Masumoto, A.; Arakawa, R. *Tetrahedron: Asymmetry* **2012**, *23*, 205.
- (12) Rivera, A.; Quiroga, D.; Jiménez-Cruz, L.; Fejfarová, K.; Dušek, M. *Tetrahedron Lett.* **2012**, *53*, 345.
- (13) Kwiatkowski, P.; Mucha, P.; Mlostoń, G.; Jurczak, J. *Synlett* **2009**, 1757.
- (14) Hou, W.; Zheng, B.; Chen, J.; Peng, Y. *Org. Lett.* **2012**, *14*, 2378.
- (15) Kapoor, I.; Schön, E. M.; Bachl, J.; Kühbeck, D.; Cativiela, D.; Saha, S.; Banerjee, R.; Roelens, 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.