

## Synthesis of a Cyclic Chiral Axially Disymmetric Tetramethylethylenediamine-like but Non Chelating 1,2-Diamine

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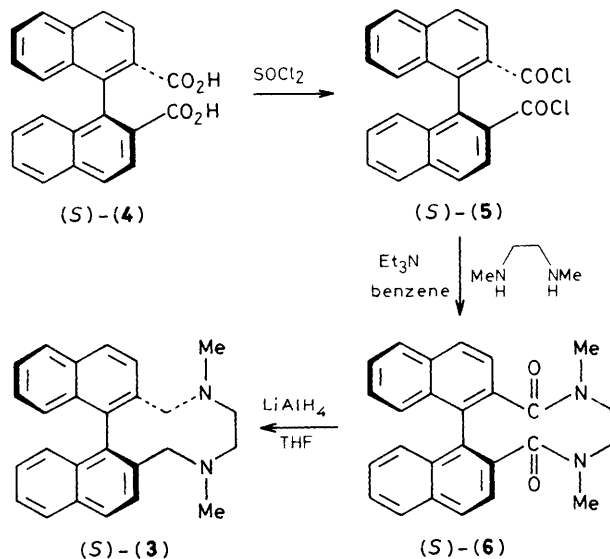
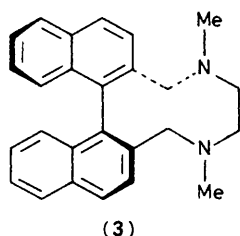
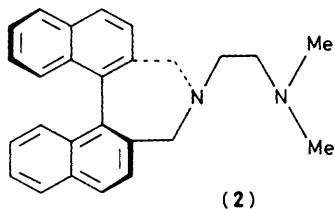
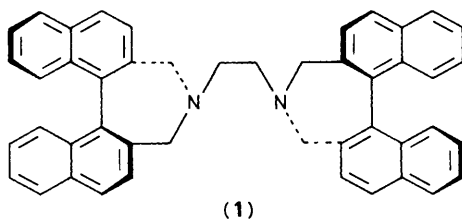
The diamine (*S*)-(3), obtained by treatment of (*S*)-1,1'-binaphthyl-2,2'-dicarboxylic acid chloride with *N,N'*-dimethylethylene-1,2-diamine, is evaluated as a chiral catalyst for addition of *n*-butyl-lithium to benzaldehyde, but leads to racemic 1-phenylpentan-1-ol, which is interpreted as a failure to complex the Bu<sup>n</sup>Li.

The well known activation of organometallic reagents by complexation with tetramethylethylenediamine, TMEDA,<sup>1</sup> and the high efficiency of the 1,1'-binaphthyl unit for chiral recognition,<sup>2</sup> suggested that compounds (1), (2), and (3) might serve as chiral catalysts for asymmetric induction in reactions of organometallic reagents. Hosts (1) and (2) have already been shown to be highly efficient stoichiometric

catalysts in the addition of organolithium reagents to aldehydes.<sup>3</sup>

In this communication we report synthesis and preliminary evaluation of the cyclic, C<sub>2</sub>-symmetric diamine (*S*)-(3) which, like (1) and (2), is a 1,1'-binaphthyl-substituted TMEDA.

Treatment of optically pure (*S*)-1,1'-binaphthyl-2,2'-dicarboxylic acid (4)<sup>4</sup> with thionyl chloride led to the



corresponding acid chloride (S)-(5),<sup>5</sup> which was condensed with *N,N'*-dimethylethylenediamine in high dilution conditions,<sup>6†</sup> to give the diamide (S)-(6)‡ in 26% yield after chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>-MeOH 95:5) followed by crystallization from dichloromethane-ethyl acetate. Reduction of (S)-(6) with lithium aluminium hydride in refluxing tetrahydrofuran, THF, for 6 h led to the desired diamine (S)-(3)‡ in 64% yield after chromatography (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>-MeOH 85:15).

The diamine (S)-(3) was evaluated as a chiral catalyst in the addition of *n*-butyl-lithium to benzaldehyde: a solution of (S)-(3) (0.914 g; 2.5 mmol) in 100 cm<sup>3</sup> Et<sub>2</sub>O was cooled to -50 °C and Bu<sup>n</sup>Li (1.4 cm<sup>3</sup>; 1.70 M), in hexane was added.§ The

solution was stirred under an argon atmosphere for 1 h, and cooled to -120 °C. A solution of benzaldehyde (0.120 g; 1.13 mmol) in *ca.* 3 cm<sup>3</sup> Et<sub>2</sub>O was then added slowly by syringe. The reaction mixture was stirred at -120 °C for 1 h and quenched with 20% HCl. Acid-base extraction gave recovered diamine (S)-(3) (0.895 g; 98%) in the basic extract and 1-phenylpentan-1-ol in the neutral extract. After purification by preparative t.l.c. (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>), the alcohol (0.129 g; 70%) had zero optical rotation at all wavelengths, therefore no asymmetric induction had occurred in the reaction.

Considering the high enantiomeric excess (e.e.) previously obtained in the same reaction with diamines (1) or (2) (respectively 95% and 58% e.e.<sup>3</sup>), this lack of asymmetric induction strongly suggests that unchelated Bu<sup>n</sup>Li is involved in the present case. That Bu<sup>n</sup>Li is not complexed by the diamine (3) but is by TMEDA is certainly not due to the inductive effect of the two benzylic type groups since they also are present in compounds (1) and (2), but is more likely to be related to conformational hindrance: the structure of the ten-membered cyclic diamine (3) is apparently too rigid to allow readily bond distortions which are necessary for the lone pairs of the nitrogen atoms to adopt the *syn* conformation required for chelation.

† A solution of the crude acid chloride (S)-(5) (9 mmol) in 400 cm<sup>3</sup> benzene and a solution of *sym*-dimethylethylenediamine (9 mmol) and triethylamine (50 mmol) in 400 cm<sup>3</sup> benzene were simultaneously added dropwise over a period of 7 h at room temperature with mechanical stirring, into a round bottomed flask containing 1.8 dm<sup>3</sup> benzene. No special vessel or stirring equipment<sup>6</sup> was used.

‡ (S)-(6): M.p. 355–360 °C; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>): δ 8.1–7.2, (m, 12H, ArH), 3.44 (m, 4H, NCH<sub>2</sub>), 2.70, (s, 6H, NMe); [α]<sub>D</sub><sup>23</sup> (c 1, CHCl<sub>3</sub>) -292° (589 nm), -306° (578), -352° (546), -635° (436), -1165° (365); mass spectrum: *m/z* 394 (*M*<sup>+</sup>). (S)-(3): Solid foam; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>): δ 7.5–6.3, (m, 12H, ArH), 2.97 and 2.70 (dd, 4H, ArCH<sub>2</sub>N *J* 12 Hz), 2.02 (m, 4H, NCH<sub>2</sub>), 1.73 (s, 6H, NMe); [α]<sub>D</sub><sup>23</sup> (c 1, CHCl<sub>3</sub>) -7.5° (589 nm), -7.8° (578), -8.5° (546), -8.7° (436), -62.4° (365); mass spectrum: 366 *m/z* (*M*<sup>+</sup>). Satisfactory elemental analysis was obtained.

§ No colour change of the solution was observed upon addition of *n*-butyl-lithium, in contrast to what usually occurred with compounds (1) or (2), for which development of a yellow or yellow-brown colour was attributed to chelation of Bu<sup>n</sup>Li.

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