Synthesis of Optically Active 8-Hydroxy-1-tetralone Derivatives

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Starting from 8-aminonaphthalenesulfonic acid, 8-alkoxy-1-tetralone was synthesized in a four steps and was used as starting material for the preparation of racemic as well as optically active 8-hydroxy-1-tetralone derivatives.

Introduction

Deprotonated β-dicarbonyl compounds **1** are important ligands ("diketonates") for transition metal complexes.[1] For this reason, they play a considerable role in homogeneous catalysis. In order to access chiral "diketonato" complexes for asymmetric catalysis, we aim to prepare optically active β-dicarbonyl compounds. Actually, to prevent the ligand structure to undergo reactions as a nucleophile in the α-position, we propose that the title structure **2** could be a perfect substitute for a β-diketone. Therefore, we have developed a synthetic route to chiral derivatives of 8-hydroxy-1-tetralone.

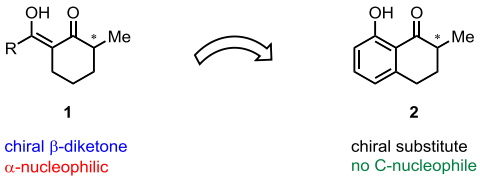
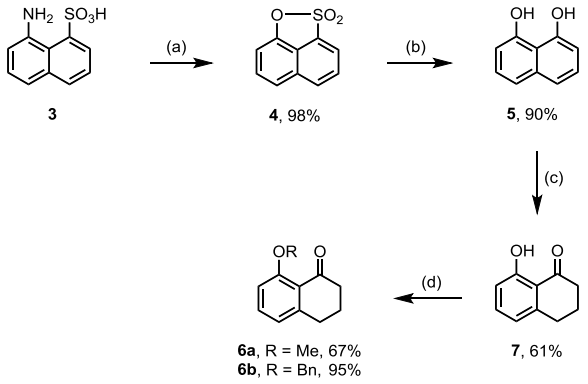


Figure 1: Hydroxytetralone **2** as a non-nucleophilic substitute for a chiral β-diketone **1**.

Preparation of 8-Alkoxy-1-tetralones

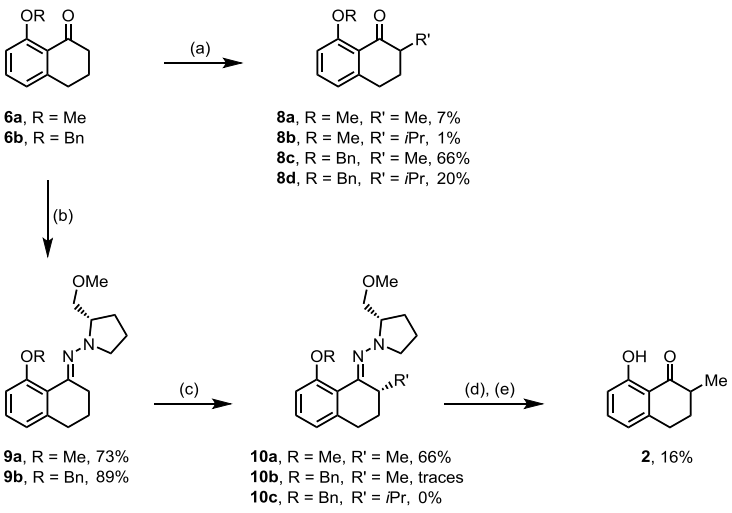
Starting from aminonaphthalenesulfonic acid **3**, sultone **4** was prepared in 98% yield by a diazotization reaction. 1,8-Dihydroxynaphthalene **5** could be obtained after subsequent treatment with an alkali metal hydroxide melt in yields up to 90%. After transfer hydrogenation with cyclohexane and $AlCl_3$ according to a literature procedure, 8-hydroxy-1-tetralone **7** was obtained in 61% yield.[2] Two alkyl halides MeI and BnBr were used to obtain the *O*-protected tetralones **6a-b** in 67–95% yield.



Scheme 1: Synthesis of the starting materials **6a-b**. (a) 2.5 eq. $NaNO_2$-H_2O, 13% HCl-H_2O, 100°C, 80 min; (b) 12.0 eq. KOH, 12.0 eq. NaOH, 220°C, 1 h; (c) 5.0 eq. $AlCl_3$, cyclohexane, 110°C, 1 h; (d) 6.0 eq. K_2CO_3, 4.4 eq. MeI / 4.0 eq. BnBr, acetone, 56°C, 23 h.

Synthesis of the 8-Hydroxy-1-tetralone Derivatives

Subsequently, to establish an enantiomeric analysis by means of GC on chiral phase, the tetralone derivatives **8a-d** were first prepared in racemic form. For this purpose, the four derivatives **8a-d** were synthesized starting from compounds **6a-b** with suitable alkylation methods. Access to optically active hydroxytetralone derivatives should also be carried out starting from the compounds **6a-b**. For that they were reacted with the chiral auxiliary (*S*)-(–)-1-amino-2-(methoxymethyl)pyrrolidine (SAMP) to obtain the hydrazones **9a-b** in yields of 73–89%. These should then be alkylated. Here, there was a problem that the hydrazone **9b**, which was benzyl-protected, decomposed under the reaction conditions. The compound **9a** could be alkylated in 66% yield. After cleavage of hydrazone **10a** and subsequent deprotection of the hydroxy group, compound **2** could be obtained in 16% yield over two steps, but the enantiomeric excess was 0% *ee*. The problem here could be due to the acidic workup. It is possible that acid-catalysis forms the enamine, which leads by epimerisation to the racemic product. In the future, this problem could be circumvented by other cleavage methods, such as the use of SmI_2 or the oxidative cleavage with SeO_2 and H_2O_2. Thus, the desired ligand could only be obtained in racemic form.



Scheme 2: Reagents and conditions. (a) LDA or KO*t*Bu, MeI or *i*PrI, THF; (b) 1.1 eq. SAMP, 0.1 eq. TosOH · H_2O, hexane, molecular sieve, 85°C, 16 h; (c) 1.4 eq. LDA, 2.3 eq. RI, –110°C → 23°C, 13 h, Et_2O; (d) oxalic acid, hexane, 23°C, 6 h; (e) 1.5 eq. $CeCl_3$ · 7 H_2O, 1.5 eq. NaI, 82°C, 3 h, MeCN.

[1] K. Binnemans, K. A. Gschneider Jr., J. C. G. Bünzli, V. K. Pecharsky, *Handbook on the Physics and Chemistry of Rare Earths*, *35*, Elsevier Verlag, Amsterdam, **2005**, 107–272.

[2] Z. Zhu, K. Y. Koltunov, *Mendeleev Comm.* **2016**, *26*, 79–80.