

Diastereoselective Addition of (*R*)-Methyl *p*-Tolyl Sulfoxide to Benzaldehyde

Manfred Braun* and Wilhelm Hild

Institut für Organische Chemie der Universität Karlsruhe,
Richard-Willstätter-Allee 2, D-7500 Karlsruhe

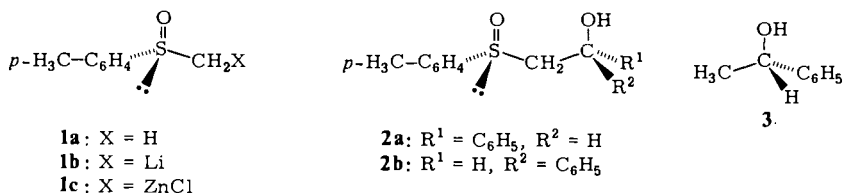
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Diastereoselektive Addition von (*R*)-Methyl-*p*-tolyl-sulfoxid an Benzaldehyd

(*R*)-Methyl-*p*-tolyl-sulfoxid (**1a**) läßt sich nach Umwandlung ins Zinkreagens **1c** diastereoselektiv an Benzaldehyd zu **2a/2b** addieren. Entschwefelung des durch Umkristallisation rein gewonnenen Überschußdiastereomeren **2a** liefert das (*S*)-Carbinol **3**.

Very poor stereoselectivity is observed in the addition of α -lithiated methyl aryl and methyl alkyl sulfoxides to aldehydes¹. As a typical example, the lithium reagent **1b**, available by deprotonation of (*R*)-methyl *p*-tolyl sulfoxide (**1a**), gives a 1 : 1 mixture of the diastereomers **2a** and **2b** by treatment with benzaldehyde².

We have been able to add the (*R*)-sulfoxide **1a** to benzaldehyde in a diastereoselective manner by using the zinc reagent **1c**, which is formed by transmetalation of the lithium compound **1b** with zinc chloride. Reaction of **1c** with benzaldehyde gives the adducts **2a/2b** in 80% diastereoselectivity³, according to the ¹H NMR spectra of the crude product. In view of the rather sluggish addition (see experimental part), an excess of the zinc reagent **1c** with regard to the aldehyde is used. The diastereomer **2a**, formed in excess, is easily isolated as pure isomer by simple recrystallization without any chromatography. Raney nickel desulfurization of **2a** gives the enantiomerically pure carbinol **3**.



Although the versatility of this diastereoselective sulfoxide addition seems to be limited by the fact that enolizable aldehydes give very poor chemical yields⁴, the transmetalation of **1b** to the zinc reagent **1c** opens an easy way for the preparation of enantiomerically pure arylmethylcarbinols.

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Experimental Part

M.p.'s were determined using a Büchi melting point apparatus. ^1H NMR spectra (solutions in deuteriochloroform with tetramethylsilane as internal standard) were recorded using a Bruker WH 250 spectrometer. A Perkin Elmer 141 polarimeter was used to determine specific rotations.

(R_C, R_S)- α -[(4-Methylphenyl)sulfinylmethyl]benzenemethanol (**2a**): A solution of 0.771 g (5.0 mmol) of (R)-(+)-methyl *p*-tolyl sulfoxide (**1a**)⁵⁾ ($[\alpha]_D^{25} = +145^\circ$; Lit.¹⁾ +168°, acetone) in 10 ml of tetrahydrofuran (THF) is added dropwise to a mixture of lithium diisopropylamide (prepared from 0.75 ml (5.0 mmol) of diisopropylamine and 3.4 ml of a 1.6 M solution of *n*-butyllithium in *n*-hexane) and 30 ml of THF at 0°C under nitrogen. After 2 h, a solution of 0.75 g (5.5 mmol) of anhydrous zinc chloride in 15 ml of THF is added. Stirring is continued for 30 min at 0°C. After addition of 0.27 g (2.5 mmol) of benzaldehyde, the solution is stirred for 30 h at 0°C. Ammonium chloride is added, and the mixture is extracted with chloroform (5 × 30 ml). The combined extracts are washed with water and dried with sodium sulfate. Evaporation of the solvent gives a crude product, which crystallizes when treated with ethanol. Filtration of the crystalline material affords 0.19 g (28%) of diastereomerically pure **2a**; m.p. 154°C (Lit.²⁾ 141–142°C); $[\alpha]_D^{25} = 88.2$ ($c = 0.41$; CHCl_3) (Lit.²⁾ $[\alpha]_D = +91.7^\circ$)⁶⁾. ^1H NMR: $\delta = 2.42$ (s, 3H, ar- CH_3), 2.30–3.24 (m, 2H, S(O)- CH_2), 4.27 (s, 1H, OH), 5.42 (dd, $J_1 = 10$, $J_2 = 1.5$ Hz, 1H, HO- CH), 7.28–7.72 (m, 9H, ar-H).

$\text{C}_{15}\text{H}_{16}\text{O}_2\text{S}$ (260.3) Calcd. C 69.20 H 6.19 Found C 69.28 H 6.26

In the crude product, the minor diastereomer **2b** (20%) can be detected by the ^1H NMR spectrum: $\delta = 5.23$ (dd, $J_1 = 10$, $J_2 = 1.5$ Hz, 1H, HO- CH).

(-)-(S)-1-Phenylethanol (**3**): The reduction of **2a** to **3** in the way described in Lit.²⁾ was found to occur with a considerable degree of racemization⁷⁾. This may be avoided, however, by treating a Raney nickel suspension (13.5 g) in methanol with hydrogen for 1 h before adding the sulfoxide **2a** (1.0 g; 3.6 mmol). Stirring the reaction mixture for 12 h at 0°C under hydrogen, filtration through a short column filled with silica gel (Merck, 0.2–0.3 mm), and evaporation of the solvent at room temperature gives an oil, which is dissolved in methylene chloride, washed with water, and dried with sodium sulfate. Evaporation of the solvent and distillation of the residue in a microdistillation apparatus, 100°C bath at 20 Torr, affords 0.13 g (30%) of **3**. $[\alpha]_D^{25} = -51^\circ$ ($c = 1.41$; ether) [Lit.²⁾ $[\alpha]_D = -42.6^\circ$ ($c = 0.27$; ether); authentic sample (EGA-Chemie): $[\alpha]_D^{25} = -55^\circ$ ($c = 1.88$; ether)].

¹⁾ G. Solladié, *Synthesis* **1981**, 185, and references cited therein. An exception was found in the case of lithiated sulfoxides having chiral centers in α - and β -position: D. R. Williams, J. G. Phillips, and J. C. Huffman, *J. Org. Chem.* **46**, 4101 (1981).

²⁾ G. Tsuchihashi, S. Iriuchijima, and M. Ishibashi, *Tetrahedron Lett.* **1972**, 4605.

³⁾ For a definition of the term "diastereoselectivity" (d.s.), see D. Seebach and R. Naef, *Helv. Chim. Acta* **64**, 2704 (1981).

⁴⁾ In the case of isobutyric aldehyde, the yield was less than 5%.

⁵⁾ K. K. Andersen, *J. Org. Chem.* **29**, 1953 (1964).

⁶⁾ This product may contain some of the (S_C, R_S)-diastereomer ($[\alpha]_D = +202.8^\circ$).

⁷⁾ C. Djerassi, M. Gorman, and J. A. Henry, *J. Am. Chem. Soc.* **77**, 4647 (1955).

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