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Synthesis and antimycotic properties of hydroxy sulfides derived from *exo*- and *endo*-4-phenyl-3,5,8-trioxabicyclo[5.1.0]octanes

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Both *exo*- and *endo*-isomers of 4-phenyl-3,5,8-trioxabicyclo[5.1.0]octane were reacted with thiophenol to afford individual diastereomers of hydroxy sulfides which were further processed in search for new antimycotic substances.

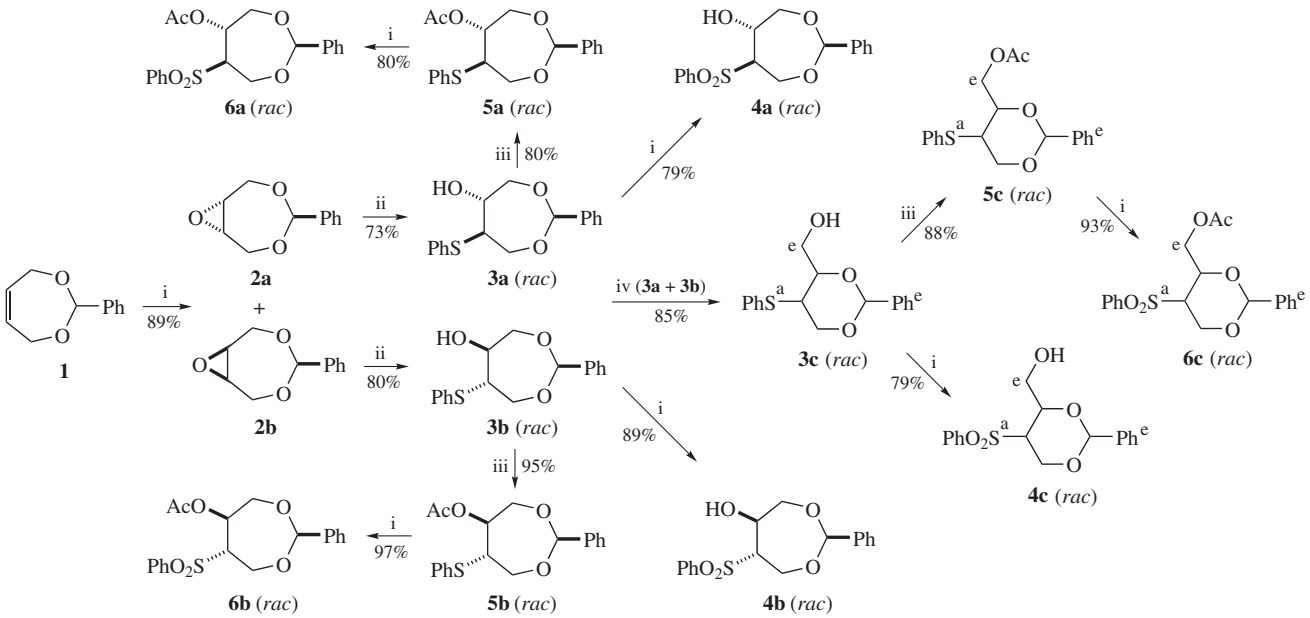
β-Hydroxy sulfides are used in the synthesis of allylic alcohols,[1] cyclic sulfides,[2] thioketones,[3] natural compounds and compounds with biological activity.[4,5] β-Hydroxy sulfones can be transformed into lactones,[6] 2,5-disubstituted tetrahydrofurans[7] and vinylsulfones.[8] Moreover, compounds containing phenylsulfonyl fragment are widely used in fine organic synthesis.[9]

In the continuation of our research,[10] we report herein the results on thiolysis of *exo*- and *endo*-isomers of 4-phenyl-3,5,8-trioxabicyclo[5.1.0]octane with thiophenols, leading to 1,3-dioxepane β-hydroxy sulfides as a result of oxirane ring opening. Isomerization of such hydroxy sulfides in the presence of *p*-toluenesulfonic acid was also studied (Scheme 1).†

Starting 2-phenyl-1,3-dioxacyclohept-5-ene **1** was obtained by acetalization of benzaldehyde with *cis*-but-2-ene-1,4-diol as described.[11] Epoxidation of compound **1** with oxone gave the corresponding epoxides **2a** and **2b**.[12] According to ^{1}H NMR data the ratio of these epoxy acetals is 2:1 in favour of the *endo*-isomer **2b**. Products **2a** and **2b** were separated by column chromatography on silica gel. Their neat reactions with thiophenol in the presence of K_2CO_3 afford β-hydroxy sulfides **3a** and **3b**, respectively, each of them being racemic individual diastereomer. The retention of the 7-membered dioxepane cycle was confirmed by 2D ^{1}H-^{1}H COSY NMR spectroscopy.

Hydroxy acetals **3a** and **3b** on keeping in chloroform in the presence of *p*-toluenesulfonic acid, completely isomerise to the 6-membered acetal **3c** as a result of intramolecular transacetalization. Structure of acetal **3c** was determined by means of 1D and 2D NMR spectroscopy, mass spectrometry and X-ray single crystal diffraction of its derivative **5c** (Figure 1).‡ To extend diversity of new compounds, the corresponding acetates **5a–c** and sulfones **4a–c**, **6a–c** were prepared.

The 1,3-dioxepanes herein obtained demonstrate antimycotic properties. To adequately study the influence of their structure on the biological activity, we tried to separate these racemic



Scheme 1 *Reagents and conditions*: i, Oxone, acetone, $NaHCO_3$, H_2O; ii, PhSH, K_2CO_3, heat; iii, Ac_2O, DMAP, Et_3N, CH_2Cl_2; iv, TsOH, $CHCl_3$.

† For syntheses and characteristics of compounds **2–6**, see Online Supplementary Materials.