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Preferential Geminal Bis-silylation of 3,4-Benzothiophane Is Caused by the Dominance of Electron Withdrawal by R₃Si over Steric Shielding Effects

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ABSTRACT: Benzylic C–H lithiation of 3,4-benzothiophane and subsequent treatment with triphenyl- or trimethylchlorosilane under a variety of conditions leads to α,α- rather than α,α'-bis-silylation products as a consequence of anion stabilization by R₃Si and very fast deprotonation of the intermediate monosilylated product, even with a sterically bulky base such as lithium diisopropylamide.

The origin of the research reported herein was the question of whether chiral cyclic sulfides of general structure 1 (or enantiomers) might be useful for catalytic enantioselective methylene transfer to C–Co or C–O from methylene precursors such as Et₂Zn/ICH₂Cl or Zn/CH₂I₂, following a process in which 1 serves as a carrier to provide chiral ylide 2. Initial studies were directed toward the synthesis of α,α'-bis-silanes such as 1, R = Me₃Si, Ph₃Si, and t-BuMe₂Si, from the readily available starting material 3 (Figure 1). It seemed reasonable that rapid access to the series of silyl ligands 1 might be secured simply by sequential, one-flask silylation of monoanions derived from 3 or by one-step bis-silylation of the α,α'-dianion of 3, a 12-π-electron (non-Hückel stabilized) system. Surprisingly, however, access to the desired 2,5-bis-silylated 3,4-benzothiophane structure proved to be difficult because the behavior of anions desired from 3 was strongly influenced by the electronic and steric effects of silyl substituents.

Reaction of 3 in THF at −78 °C with 1.0 equiv of n-BuLi (2.5 M in hexanes) for 3 h followed by slow addition of Ph₃SiCl (in THF at −78 °C) afforded as major product (along with unreacted 3) the crystalline gem-bis-silane 4 in 31% yield. The structure of 4 was established by X-ray crystallographic analysis (Figure 2).

The formation of 4 likely occurs via the C(2)-monosilylation product 5 by further deprotonation at C(2) (either by monolithiated 3 or residual BuLi) followed by a second silylation (Scheme 1). The putative intermediate 5 could be obtained by the gradual addition of a cold (−78 °C) solution of lithium diisopropyl amide (LDA) in THF to a mixture of 3 and 1.0 equiv of Ph₃SiCl in THF at −78 °C, which gave 5 in 42% yield along with recovered 3 (40%).

Consistent with these observations was the finding that the addition of 1.0 equiv of LDA in THF (at −78 °C) to a solution of 5 and Ph₃SiCl in THF at −78 °C afforded 4 (76%) as major product, without the formation of a detectable amount of the α,α'-silylated product 1, R = Ph (Scheme 2). Evidently even with the use of the very bulky base LDA, the acidifying effect of an C(2) Ph₃Si group is sufficiently great to override its steric shielding of the geminal C(2)-H proton. An α-triphenylsilyl group has been found to increase the acidity of the C(9)-proton of fluorene by about 10⁴ in previous work.

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extensive experimentation, no conditions could be found to convert 3 to the \( \alpha\alpha'-\)bis-silylated derivative 1, \( R = Ph \).

The same preference for the formation of \( \text{gem-bis-silylated} \) product was demonstrated using Me\(_3\)SiCl as the silylation reagent. Thus, the addition of 3 to a mixture of 2.0 equiv of LDA and 6.0 equiv of TMSCl at \(-78^\circ\text{C}\) produced the \( \text{gem-bis-silylation} \) product 7 in 64% yield with no measurable amount of the isomeric \( \alpha\alpha'-\)bis-TMS compound (Figure 3).

At this point, it should be mentioned that all of the above silylation reactions must be carried out at low temperatures because the intermediate 6 is unstable above \(-60^\circ\text{C}\). There is considerable precedent for decomposition via the cycloelimination pathway shown in Scheme 3.\(^7\)

Although the reaction of monolithium intermediate 6 with triphenylchlorosilane occurs readily at \(-78^\circ\text{C}\) to form 5, NMR studies showed that proton transfer from 5 to 6 is even faster to form the silyl stabilized lithio-anion 9. Further, NMR measurements also revealed that the reaction of 9 with Ph\(_3\)SiCl (Scheme 4) is slower than expected and requires several hours at \(-78^\circ\text{C}\). The slower rate of the silylation 9 to 4 appears to be a consequence of the anion-stabilizing effect (electron withdrawal) of Ph\(_3\)Si combined with the steric shielding by Ph\(_3\)Si in both 9 and Ph\(_3\)SiCl.

The research described above has revealed significant nuances in the behavior of lithiation products derived from 3,4-benzothophane involving surprising rates of C–H lithiation and C–Li silylation.

\section*{ASSOCIATED CONTENT}

\section*{Supporting Information}

Experimental procedures and characterization data for all reactions and products, including copies of \( ^1\text{H} \) NMR and \( ^{13}\text{C} \) NMR spectra and single-crystal X-ray diffraction analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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\section*{REFERENCES}


(3) All organolithium reactions reported herein were carried out under an atmosphere of \( \text{N}_2 \) at \(-78^\circ\text{C}\).

(4) See the Supporting Information for details.


(6) For data on stabilization of carbanions by \( \text{R}_3\text{Si} \) in the gas phase, see: Wetzel, D. M.; Braman, J. I. J. Am. Chem. Soc. 1988, 110, 8333–8336.