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# The Synthesis of Sultines from δ-Hydroxy Sulfoxides Revisited

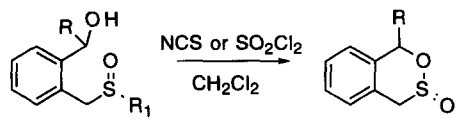
Terrence J. Connolly* and Tony Durst*

Department of Chemistry
University of Ottawa
Ottawa, Ontario
Canada
K1N 6N5

**Abstract**: A re-examination of a previously thought general synthesis of sultines from δ-hydroxy sulfoxides is shown to be more complicated than originally believed. The products obtained can be α,α'-dihaloxylenes or δ-halosulfones. The results are best interpreted based on carbocation stability of the key oxo-sulfoxonium salt intermediate. © 1997 Elsevier Science Ltd. All rights reserved.

The chemistry of sultines continues to attract considerable interest.[1] Much of this interest is due to the use of sultines as ortho-quinodimethane precursors.[2,3] There have been several advances recently in the use and synthesis of sultines. Most notable is the work of Dittmer who has developed a high-yield method for the conversion of α,α'-dihaloxylenes to sultines;[4,5] Chung who has prepared and characterized the reactivity of furan-, thiophene- and pyrrole-fused sultines;[6] and especially the work of Marson who has developed recently a synthesis of chiral sultines from unsaturated alcohols.[7]

A number of years ago, we were the first to generate ortho-quinodimethanes from sultines.[8] We showed that one of the main advantages of using sultines over sulfones was the lower thermolysis temperature required for the chelotropic elimination of $SO_2$. We also reported a general synthesis of sultines from δ-hydroxy sulfoxides.[8-10] As depicted in Equation [1], we had shown that S-benzyl (**1a**) and S-*t*-butyl (**1b**)-δ-hydroxy sulfoxides, when treated with chlorinating agents, underwent an intramolecular cyclization-fragmentation sequence and rapidly afforded sultines (**2**) in high yields. Recent results in our laboratory have caused us to re-examine the mechanism and generality of this reaction.

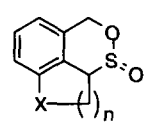



[1]

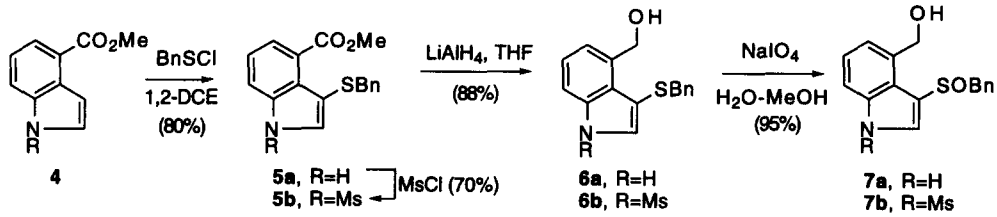
**1a**; $R_1$=Bn,
**1b**; $R_1$=t-Bu

**2**

One of the projects that has received considerable attention in our laboratory has been the synthesis of bicyclic sultines **3a-c**. In the hope of applying the synthetic method shown in [1] to this problem, we synthesized the desired hydroxy-sulfoxide **7a** as shown in Scheme 1.

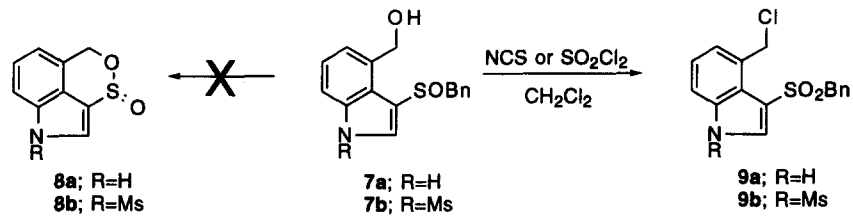



**3a**; X= NH, n=1
**3b**; X=$CH_2$, n=1
**3c**; X=$CH_2$, n=2



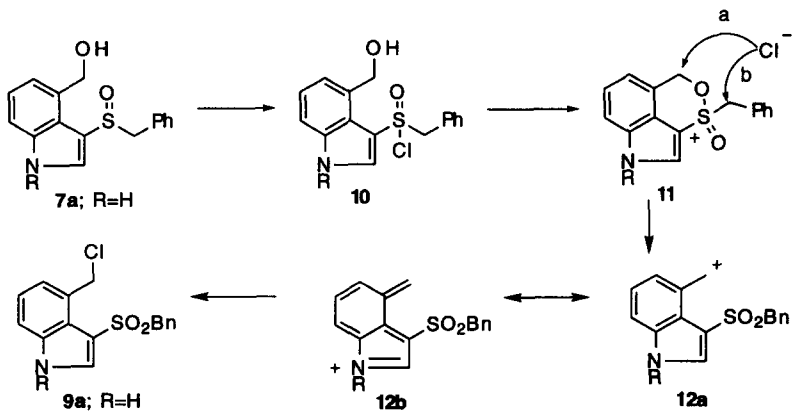

**Scheme 1**

Treatment of 4-carbomethoxyindole (**4**), readily available via the Leimgruber indole synthesis[11] with benzylsulfenyl chloride afforded indole **5a** in an 80% yield.[12] Reduction of the ester group with $LiAlH_4$ gave the benzylic alcohol **6a** in yields approaching 90%. Finally, $NaIO_4$ mediated oxidation of the sulfide provided the target hydroxy sulfoxide **7a** in near quantitative yield.




**Scheme 2**

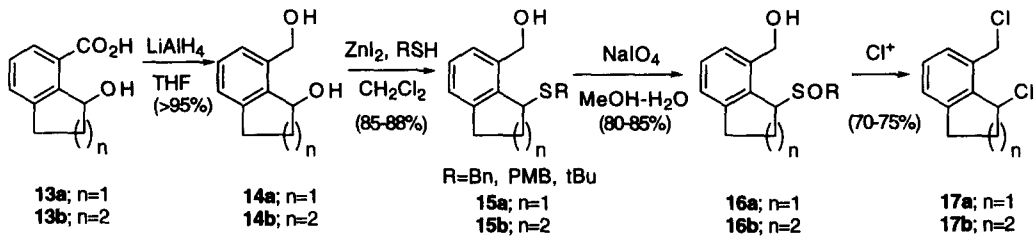
Treatment of a $CH_2Cl_2$ solution of **7a** with NCS or $SO_2Cl_2$ at room temperature afforded, instead of the desired sultine **8a**, chlorosulfone **9a** as the only detectable product in 57% yield (Scheme 2). The identity of **9a** was established by $^1$H-NMR, which showed two singlets for the benzylic methylene groups and an integration of the aromatic region that showed the benzyl group had not been cleaved. Additionally, the IR spectrum showed bands diagnostic of a sulfone (1119, 1334 $cm^{-1}$), and mass spectrometry supported the molecular formula. A detailed proposed mechanism to account for this result is shown in Scheme 3.




**Scheme 3**

Initial S-chlorination of sulfoxide **7a** to provide chloro sulfoxonium salt **10**, followed by intramolecular displacement of the halogen by the hydroxyl group affords the cyclic oxo-sulfoxonium salt **11**. At this point, the liberated halide may react at one of two sites. Although both pathways (route a and b) involve attack at benzylic centers, pathway a is favored, presumably due to the greater stability of the cation at this site (**12a**) due to the resonance available through the indole ring (**12b**). In an attempt to supress this, the synthesis shown in Scheme 1 was repeated with an electron-withdrawing group substituted on the nitrogen. Treatment of substrate **7b** (R = Ms) with NCS or $SO_2Cl_2$ also failed to afford the desired sultine **8b**, again furnishing the sulfone **9b** (R = Ms) as the only detectable product in a yield of 54%.

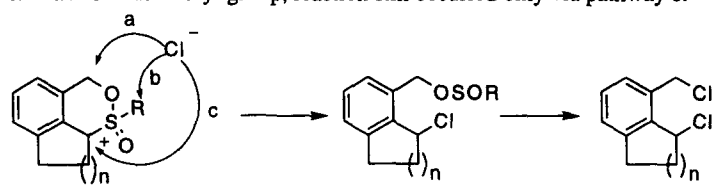
Other problems associated with the indole nucleus caused us to examine the use of our synthetic method in the synthesis of sultines **3b-c**. Starting with diols **14**, readily available via reduction of the corresponding hydroxy acids **13** [13,14] with $LiAlH_4$ and selective ionization of the secondary alcohol with $ZnI_2$ in the presence of various mercaptans allowed for the synthesis of several hydroxy sulfides **15**.[15] Oxidation with $NaIO_4$ afforded the hydroxy-sulfoxides **16**. Again, reaction with NCS or $SO_2Cl_2$ did not provide the desired sultines **3b-c**, instead the dichloroxylenes **17** were isolated (Scheme 4).[16]




**13a**; n=1 **13b**; n=2 — **14a**; n=1 **14b**; n=2 — **15a**; n=1 **15b**; n=2 — **16a**; n=1 **16b**; n=2 — **17a**; n=1 **17b**; n=2

**Scheme 4**

As shown in Scheme 5, examination of the key oxo-sulfoxonium salt intermediates (**18**) shows there are three possible sites for the chloride to attack. Only pathways b and c need be considered since the carbons adjacent to the charged sulfur will be more electrophilic than the benzylic center adjacent to the alcohol. In contrast to the indole case (Scheme 3), reaction via pathway a is not considered since there is no equivalent to the added stability of the benzylic cation offered by delocalization of the nitrogen electron density as shown by **12a-b**. Of the two pathways b and c, reaction via pathway c is favored since it occurs via a secondary benzylic carbocation. Even when R was t-butyl group, reaction still occurred only via pathway c.




**18a**; n=1 **18b**; n=2 — **19a**; n=1 **19b**; n=2 — **17a**; n=1 **17b**; n=2

**Scheme 5**

In summary, the reaction of δ-hydroxy sulfoxides with chlorinating agents to provide sultines is not as general as previously described. The cyclic oxo-sulfoxonium salt intermediate may react via a number of pathways to afford γ-chlorosulfones and α,α′-dichloroxylenes. The reaction products are best rationalized in terms of carbocation stability which seems to indicate that the reaction is occuring through an $S_N1$ pathway. Further work is underway in an attempt to suppress this pathway, as are alternative syntheses. This work will be reported in due course.[17]

**Acknowledgments**

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(16) Dittmer's route also failed to provide the desired sultines (**3a-b**) from the requisite dibromoxylenes (**17a-b**).

(17) All compounds showed satisfactory NMR, IR, MS and elemental analysis consistent with their proposed structures.

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