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ON THE STRUCTURES OF ALPHA-LITHIATED SULFOXIDE, SULFONE AND SULFONIUM SYSTEMS. IMPLICATIONS FOR THE STEREOCHEMISTRY OF FUNCTIONALIZATION OF CARBON ATOMS ADJACENT TO SULFUR

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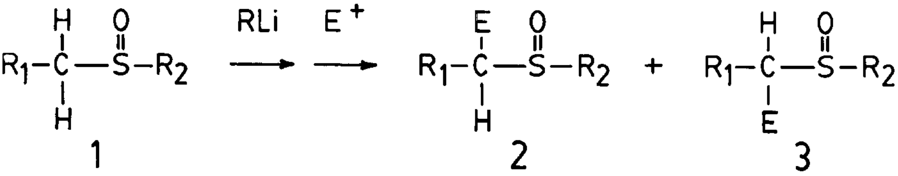
Summary: *The fully optimized geometries of C-S torsional isomers of* $LiCH_2SHO$, $LiCH_2SHO_2$ *and* $LiCH_2SH_2^+$ *have been computed at the 3-21G* level. The global minima of the sulfoxide and sulfone contain intramolecular Li-O bonds. In the presence of* Li^+, *intermolecular Li-O bonding alters the structure of the alpha-lithiated sulfoxide, and the C-Li bond is antiperiplanar to oxygen. The alpha-lithiated sulfonium cation exhibits no unusual conformational features, and a low barrier to C-S torsion. The implications of these results upon the stereochemistry of functionalization of a carbon atom adjacent to sulfur by a lithiation-quenching sequence are discussed.*

Alpha-lithiated sulfoxides are useful synthetic intermediates.[1] However, after extensive research on the formation and trapping of such species, it has become clear that the proportions of the diastereomers 2 and 3 that are produced from 1 depend, *inter alia*, upon the solvent, the nature and origin of the lithiating agent, the presence of added lithium salts, the presence of cation complexing agents, and the nature of the quenching reaction.



For example, protonation (deuteration) and hydroxyalkylation of alpha-lithiated sulfoxides proceed with retention of configuration,[2] but alkylation proceeds with inversion of configuration.[2] In tetrahydrofuran solvent, lithiation-deuteration of benzyl methyl sulfoxide leads to a 15:1 mixture of RR/SS and RS/SR alpha-deuteriobenzyl methyl sulfoxides *when* CH_3Cl*-derived* CH_3Li *is employed*; with CH_3Br-derived CH_3Li, a 3:1 mixture of RR/SS and RS/SR isomers is produced.[3] The same result is obtained upon addition of one equivalent of LiBr to the reaction mixture prior to lithiation with CH_3Cl-derived CH_3Li. Excess LiBr reverses the product ratio to 0.45:1.[3] The isomer ratio is also reversed by a change of solvent from tetrahydrofuran to dimethyl sulfoxide,[4] and it is 1:1 in hexamethylphorous triamide containing cryptate.[5]

In experiments with cyclic sulfoxides,[6,7] it has been determined that a salt-free lithiation-alkylation sequence leads to C-C bond formation *trans* to oxygen, but lithiation-deuteration leads to C-D bond formation *cis* to oxygen. Since the quenching reactions proceed with inversion and retention, respectively, it follows that lithium is *cis* to oxygen in an alpha-lithiated sulfoxide. The chelated structure 4 has been proposed,[6,8] with a planar configuration at the metallated carbon atom.

Recent theoretical studies on sulfur-containing carbanions $^-CH_2Sabc$, in which a, b and c represent combinations of lone pairs, oxygen atoms, and other ligands,[9] suggest that a 3-21G* basis set is appropriate for a study of the geometries of such species, and that hydrogen is an acceptable ligand for computational purposes. This Letter reports computations on $LiCH_2SHO$,

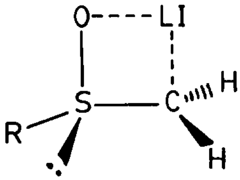
$LiCH_2SHO_2$ and $LiCH_2SH_2^+$, representing, respectively, alpha-lithiated sulfoxide, sulfone and sulfonium systems. In each case, the computations have been performed at the 3-21G* level,[10] with full optimization of all geometrical parameters[11] of several torsional isomers.

Structures 5 - 7 refer to torsional isomers of the alpha-lithiated sulfoxide. The global minimum 5 is 38.7 kcal/mole more stable than 6, and 40.7 kcal/mole more stable than 7. In 5, the $LiCH_1$ and $LiCH_2$ angles are 124.3° and 108.5°, respectively. The great stability of 5 relative to 6 and 7 suggests that only the chelated structure can be considered to exist under salt-free conditions. It is clear, therefore, that quenching of an alpha-lithiated sulfoxide with retention of configuration at carbon will place an alpha substituent *cis* to oxygen, and quenching with inversion of configuration at carbon will introduce an alpha substituent *trans* to oxygen.

On the other hand, as shown in 8, when Li^+ is added to the system, an *inter*molecular Li-O complex is preferred, and the C-Li bond is antiperiplanar to oxygen. In the presence of excess Li^+, the stereochemical behavior of an alpha-lithiated sulfoxide should, therefore, resemble that of an alpha-sulfinylcarbanion.[9] These results suggest that the lithiation of benzyl methyl sulfoxide under salt-free conditions should lead preferentially to 9;[12] deuteration of 9 with retention of configuration leads to the RR/SS diastereoisomer. When an intermolecular Li-O bond is present, the preferred structure will be 10; deuteration of 10 leads to the RS/SR isomer.

Structures 11 - 13 refer to torsional isomers of the alpha-lithiated sulfonium cation. No unusual geometrical features are seen in these structures. The gauche conformation 11 is the global minimum, but it is only 0.93 kcal/mole more stable than the antiperiplanar conformation 12, and 1.34 kcal/mole more stable than the eclipsed conformation 13. Since these energy differences would be smaller at a higher level of computation, little conformational preference is indicated for this species. Consequently, the stereochemistry of functionalization of a carbon atom adjacent to a sulfonium centre via an alpha-lithiated intermediate should exhibit no specific bias associated with the heteroatom, as is observed experimentally.[13]

In the case of the alpha-lithiated sulfone, only an unsymmetrically chelated structure 14 could be found computationally. A symmetrical structure has been suggested on the basis of vibrational spectroscopic data,[8] but this structure has higher energy, and its geometry could not be optimized. The similarity between 5 and 14 suggests that lithiation-quenching of a sulfone should be a highly stereoselective process. The very limited experimental data[14] are consistent with this conclusion.[15]



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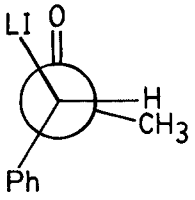

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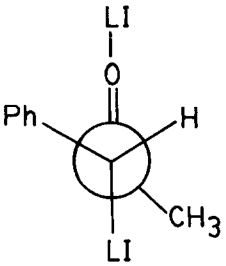

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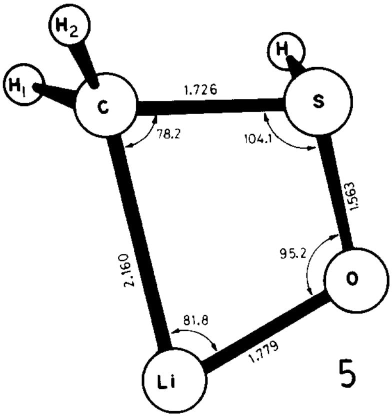
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H
H1
C
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S
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104.1
1.563
2.160
95.2
O
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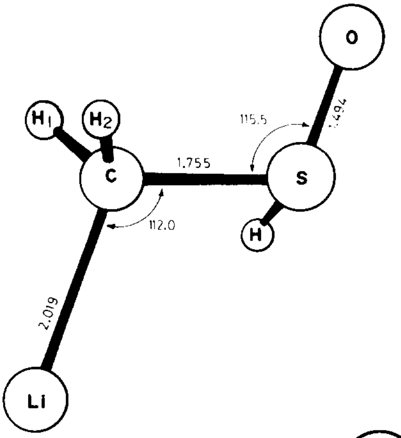
1.779
Li

5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H2
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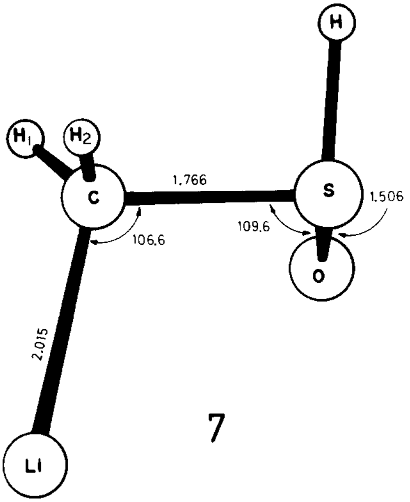
C
1.755
S
112.0
H
2.019
Li

6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H2
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S
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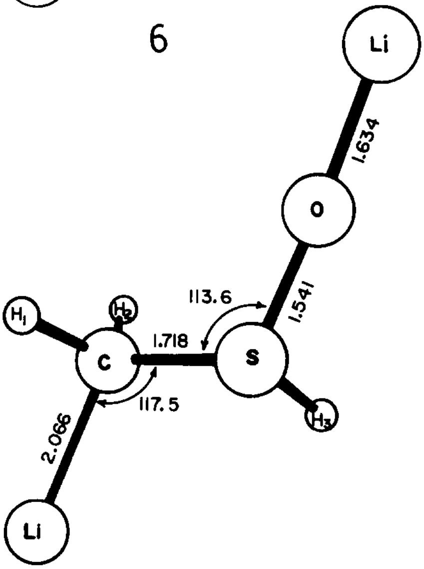
106.6
109.6
O
2.015
Li

7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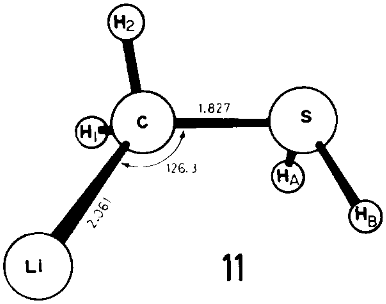
O
113.6
1.541
H1
H2
1.718
C
S
117.5
H3
2.066
Li

8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H1
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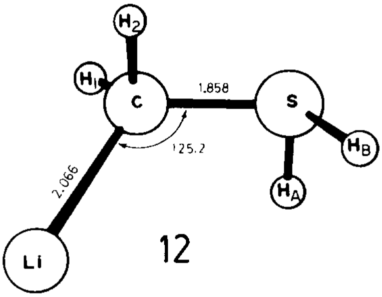
HA
2.061
HB
Li

11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C
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S
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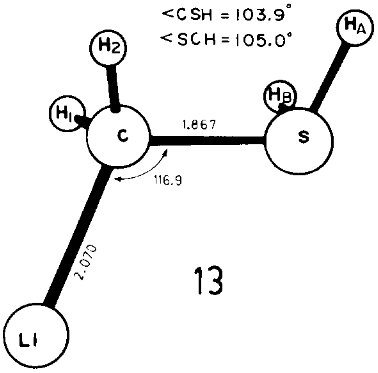
HB
2.066
HA
Li

12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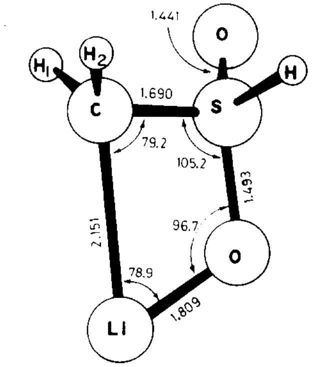
HA
H2
HB
H1
C
1.867
S
116.9
2.070
Li

13



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