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STEREOSELECTIVITY IN THE ALKYLATION OF SULFONIUM SALTS

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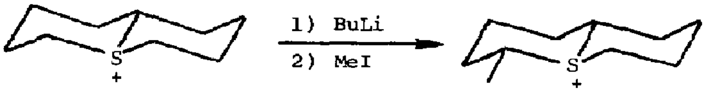
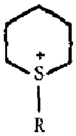
The stereoselectivity in the alkylation of sulfonium salts is attributed to the formation of an intermediate lithio-sulfonium salt rather than a free ylid.

In a recent paper[1] we presented a predictive model for the stereochemistry of proton-deuterc exchange α to sulfur in sulfonium salts. Other data have now appeared in the literature concerni the alkylation of sulfonium ylids[2] which seem inconsistent with that model. The pertinent exper imental data are summarized below and our theoretical model subsequently expanded to include thes recent results.

The first report of a stereoselective alkylation of a sulfonium salt came from this laboratory.[3] Thionia bicyclo[4.4.0]decane is stereoselectively methylated *trans* to the angular hydroge (equatorially) to provide 2. This result is consistent with the highly stereoselective deuteriur incorporation reaction in which the equatorial proton is exchanged some 30 times faster than the axial proton.[4] The S-phenyl thianium salt 3 is also methylated stereospecifically,[2] in distinct contrast to the stereorandom deuteration reaction[5] of methylthianium salt 4. This event is neatl accomodated by our initial model for deprotonation since the lack of stereochemistry was attribute to chair-chair interconversion of 4 such that both pairs of protons *cis* and *trans* to the sulfur substituent may attain a favorable geometry with respect to the sulfur lone pair. In the alkylati case conformational processes may be neglected since the activation barrier in the deprotonation reaction is small compared to the free energy required for a ring flip.[1]

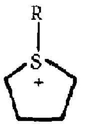


1 2



3: R = ϕ
4: R = CH_3

The simple model we developed breaks down, however in the case of the five-membered ring sal 5a and 6a:



5a: R = ϕ
5b: R = H

6a: R = ϕ
6b: R = H

In this case, the alkylation of 5a or 6a is nonstereoselective[2] while the deuterium incorporation reactions of the related 5b and 6b are highly stereospecific.[5]

It is known that when phosphonium salts are treated with an alkyllithium, a species is forme that differs markedly from that obtained under "salt free conditions".[6] On the basis of ^{13}C NMR data, the former has been described as a C-lithiated salt (ie., 7). Since the phosphorus ylids

$$R_3\overset{+}{P}-CH_2Li$$

7

used in the spectroscopic studies as well as those commonly encountered in synthesis are achiral, no stereochemical consequences result from the formation of such a species. The formation of a C-lithiated sulfonium salt on the other hand might have profound effects on the stereochemical outcome of reactions involving them as intermediates.

To address this question, the same technique employed in the assessment of conformational preference of sulfonium ylids was used. With the Gaussian 70 series of programs[7] a cross-section of the STO-3G potential energy surface for rotation about the unique C-S bond in $[(CH_3)_2SCH_2Li]^+$ (8) was calculated using a standard geometrical model[8] and a rigid rotor approximation. The dihedral angle ϕ is defined to be zero when the carbon-lithium bond axis is eclipsed with the sulfu lone pair axis. The calculated curve is presented in Figure 1 as is the curve for the free ylid described earlier.[1] The two curves are substantially different, and most important, the stereochemistry of alkylation is in good accord with the calculated stability of a C-lithiated sulfonium

Fig 1. Rigid rotor potential function for $[(CH_3)_2SCH_2Li]^+$ and $(CH_3)_2SCH_2$ (ref.1)

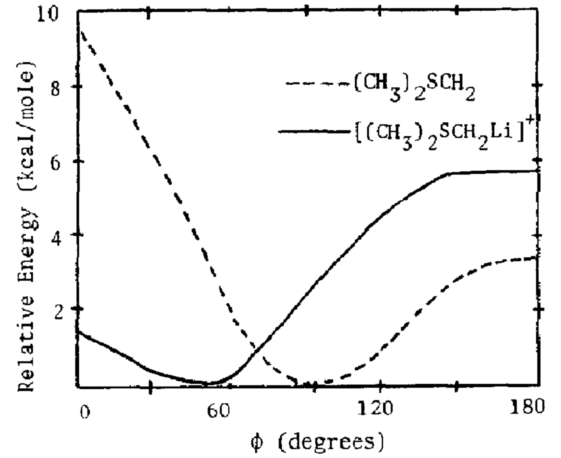
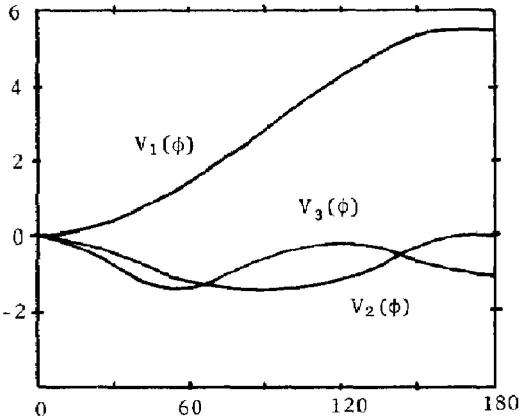
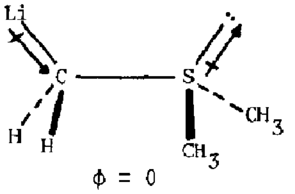


Fig 2. Fourier Decomposition of potential curve for $[(CH_3)_2SCH_2Li]^+$

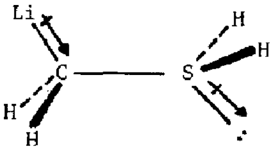


salt conformer assuming cleavage of the C-Li bond occurs with retention of configuration.[9] For example, the diastereotopic protons in 1 and 3 lie at dihedral angles of $H_{axial} = 180°$ and $H_{equatorial} = 60°$ in the most stable conformation. The lithiated salt derived from replacement of the equatorial proton is clearly favored. On the other hand in the case of thiolanium salts lithiation is predicted to enhance the acidiity of protons *syn* to the sulfur lone pair compared to a free ylid, again in accord with experiment. An exact numerical concordance between the *ab initio* results and the observed alkylation stereochemistry is not obtained. We have noted before that some correction to the shape of the calculated curve is required to account for solvation effects and achieve a good numerical correlation.[1] As an aid in interpreting the shape of the potential curve, a Fourier transformation of the curve is valuable.[1,10] The potential curv for 8 is well described by the three term series $V(\phi) = \frac{1}{2}V_1(1-\cos\phi) + \frac{1}{2}V_2(1-\cos 2\phi) + \frac{1}{2}V_3(1-\cos 3\phi)$ when $V_1 = 5.7$, $V_2 = -1.7$ and $V_3 = -1.5$ kcal/mole. The three-fold term V_3 is assigned its usual significance of torsional interactions: staggered conformations are preferred to eclipsed conformations. The two-fold term may be related to a destabilizing interaction between the sulfur lone pair and the C-Li bond pair in analogy to the lone pair-lone pair interaction which dominates the conformational equilibria in a free ylid.[1]

The dominant term in the Fourier series describing rotation in 8 is V_1. Two interactions may be envisioned that can lead to stabilization of the 0° conformation with respect to the 180° conformation. The first is a lone pair, bond pair dipole moment interaction illustrated below.



$\phi = 0$



$\phi = 180$

In the 180° conformation the dipole moments are aligned which should be less favorable energetical than the dipole interaction at $\phi = 0$. Another possibility is a direct through space interaction between sulfur and lithium such that the sulfur lone pair actually serves as a ligand for lithium We have not yet been able to establish the exact nature of this interaction by inspection of the calculated molecular orbitals or other means and so this question must await further study.

In conclusion, we propose that a dichotomy exists in the chemistry of carbanions derived from sulfonium salts. When an "ylid" is generated by treatment of the salt with an alkyllithium, the intermediate is probably a C-lithiated species, in analogy to the behavior of phosphonium salts under the same conditions. In aqueous media or presumably with other cations, coordination of the cation with the ylid carbon is disfavored such that the carbanion most closely resembles a free ylid. Experimental corroboration for this model is currently being sought.

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8) Geometrical parameters employed are described in ref. 1 except the C-Li bond which was assigned a value of 2.01 Å. It will be noted that in our earlier work the basis set 4-31G was employed. At that time we found that the STO-3G basis actually provides the same qualitative description of the rotational potential function, the magnitude of the barrier being some 15% smaller at STO-3G. With this knowledge it seems safe to assume that STO-3G is adequate for the present calculations.

9) This is certainly the case in the reactions of many configurationally stable alkyllithium derivatives such as vinyl and cyclopropyl. See D.J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York (1965).

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