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STEREOCHEMISTRY OF THE SULFINYLNITRENE - SULFOXIDE REACTION. NUCLEOPHILIC SUBSTITUTION AT SULFUR WITH RETENTION OF CONFIGURATION.

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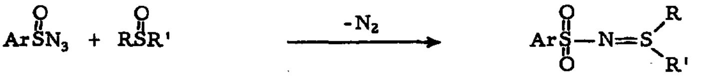
The stereochemical course of nucleophilic substitution reactions with sulfoxides and related compounds generally occurs with inversion of configuration at sulfur.[1] Three reported exceptions which occur with retention are the ^{18}O exchange of optically active methyl p-tolyl sulfoxide ((+)-(R)-2c) with dimethyl sulfoxide,[2] the conversion of methionine sulfoxide to methionine sulfimide,[3] and the reaction of N, N'-ditosyl-sulfodiimide with (+)-(R)-2c and (-)-(R)-methyl butyl sulfoxide in benzene.[4] We wish to report on the stereochemistry of the reaction of p-toluenesulfinylnitrene[5] with methyl p-tolyl sulfoxide ((+)-(R)-2c). Retention of configuration in the sulfimide product supports a four-membered cyclic sulfurane intermediate.

Treatment of (+)-(R)-methyl p-tolyl sulfoxide ((+)-(R)-2c) of 99% optical purity with p-toluenesulfinyl azide (1b) in acetonitrile at 50° gave a 42% yield of nonfractionally crystallized (+)-(R)-N-(p-tosyl)methyl-p-tolylsulfimide ((+)-(R)-3c) of 92.1% optical purity ($[\alpha]^{25}_{D}$ + 247.6, c 1.68, acetone).[6] p-Toluenesulfonamide (15.2%) and methyl p-tolyl sulfide (2.8%) were also isolated in addition to polymeric material and other minor components normally found in the absence of added sulfoxide.[5b]

The formation of sulfimide may be considered general, having been produced from the reaction of benzene- or p-toluenesulfinyl azide with dimethyl sulfoxide,[5a] methyl p-tolyl sulfoxide, and diphenyl sulfoxide. Reaction of 1a with diphenyl sulfoxide gave N-(benzenesulfonyl)-

diphenylsulfimide (26%), benzenesulfonamide (27%), and diphenyl sulfide (7%).



$\mathrm{ArS(O)N_3 + RS(O)R' \xrightarrow{-N_2} ArS(O)_2{-}N{=}SRR'}$

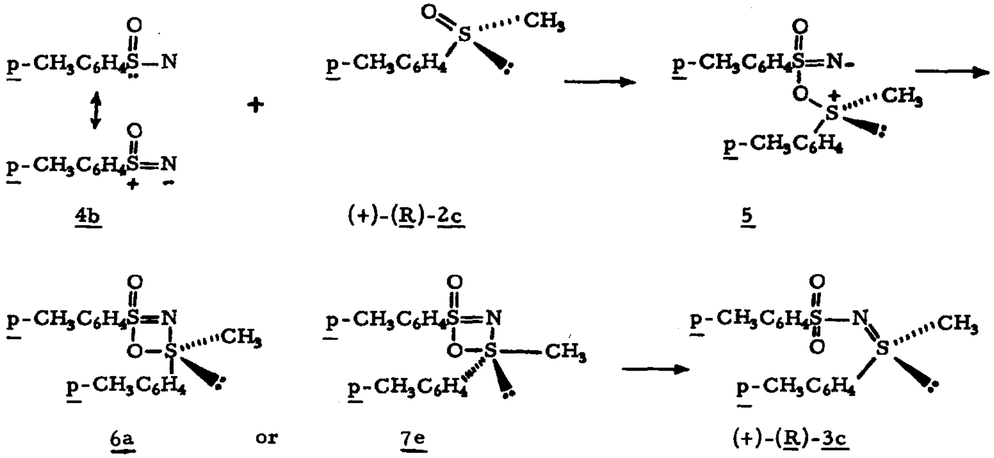
1 2 3

	Ar	R	R'
a	C_6H_5	CH_3	CH_3
b	*p*-$CH_3C_6H_4$	CH_3	CH_3
c	*p*-$CH_3C_6H_4$	CH_3	*p*-$CH_3C_6H_4$
d	C_6H_5	C_6H_5	C_6H_5

The transformation of sulfoxide to sulfimide with retention of configuration is consistent with a dipolar cycloaddition reaction of *p*-toluenesulfinylnitrene (4b) with sulfoxide (Scheme I). The first step of the reaction is proposed to be an attack of the sulfoxide oxygen on the positively charged sulfur of 4b to give a dipolar adduct 5. S-N cyclization followed by S-O ring opening would lead to the sulfimide (+)-(*R*)-3c.

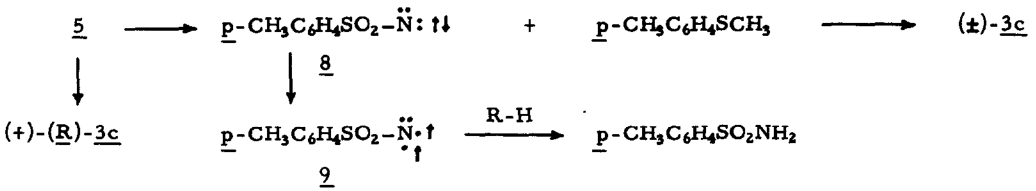
By analogy to the chemistry of phosphoranes[7] and other sulfuranes,[1,8] the cyclic intermediates (6 and 7) are assumed to possess trigonal bipyramidal geometry, having the four-membered ring in the axial-equatorial orientation and the electron pair in the most electronegative orbital (equatorial). Axial attack by the entering nitrogen and axial expulsion of the leaving oxygen group (aa mechanism) would be favored for electronic reasons. Such an aa mechanism would require pseudo-rotation[9] of 6a to 7e or of equivalent structures 7a to 6e (structures where the ring oxygen and nitrogen atoms of 6 and 7 are interchanged). The intermediates 6 and 7 are labeled a if formed from 5 by axial attack and e if formed by equatorial attack. However, if the pseudo-rotational processes are rate determining, axial attack and equatorial expulsion (ae mechanism or *vice versa*, ea) could occur[10] to form (+)-(*R*)-3c directly. Regardless of the actual mechanism (aa, ae, or ea) the same product, (+)-(*R*)-3c, would be expected.

Scheme I



Failure to obtain complete retention of configuration may be explained (Scheme II) by leakage from the dipolar adduct 5 through deoxygenation of the sulfoxide by sulfinyl nitrene 4b to give p-toluenesulfonylnitrene (8) and methyl p-tolyl sulfide. Recombination of the latter would most likely produce the racemic sulfimide from direct attack of the nitrene on sulfur.[11] Isolation of a sulfide from this reaction and from the diphenyl sulfoxide reaction supports this explanation. Furthermore, the formation of sulfonamides suggests that the singlet sulfonyl nitrene 8, which does not recombine with the sulfide, crosses over to the triplet state (9) and abstracts hydrogen from the medium.

Scheme II



The development of the sulfinyl azide reaction converting (+)-(R)-2c to (+)-(R)-3c provides a convenient route for the preparation of chiral sulfimides not readily available in high optical purity through other methods.[1-4] In particular, employing this reaction (retention) in conjunction with methanolic potassium hydroxide hydrolysis of the optically active sulfimide[1] (inversion), provides a two-step method for inverting the configuration of chiral sulfoxides.

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(11) A referee has suggested that all of 3c could be produced from rapid recombination of the sulfonylnitrene (8) and sulfide in a solvent cage. While possible, the extent of retention of configuration obtained is too high to be explained soley by that mechanism. Only a slight rotation of the sulfide would be necessary to invert the configuration and little steric hindrance exists to prevent that rotation.