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THE STEREOCHEMISTRY OF THE REARRANGEMENT OF ALLYLIC SULPHONIUM YLIDS: A NEW METHOD FOR THE STEREOSELECTIVE FORMATION OF ASYMMETRY AT QUATERNARY CARBON

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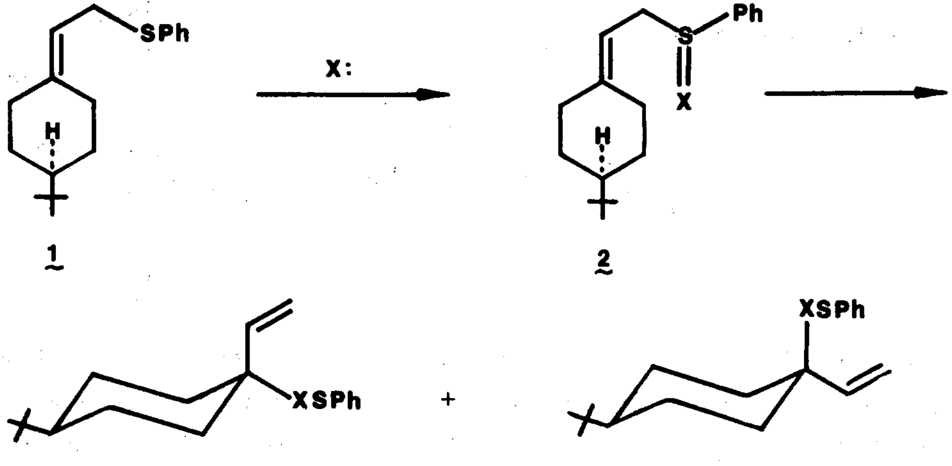
As part of our general interest in the development of the synthetic potential of [2,3] sigmatropic rearrangements, we have examined the stereochemical result of the rearrangement of ylids of structure **2** in a conformationally biased cyclohexylidene ring system. The overall process depicted in Scheme I offers a potentially versatile method for the stereoselective synthesis of quaternary centers flanked by functionality which complements existing procedures.[2,3]

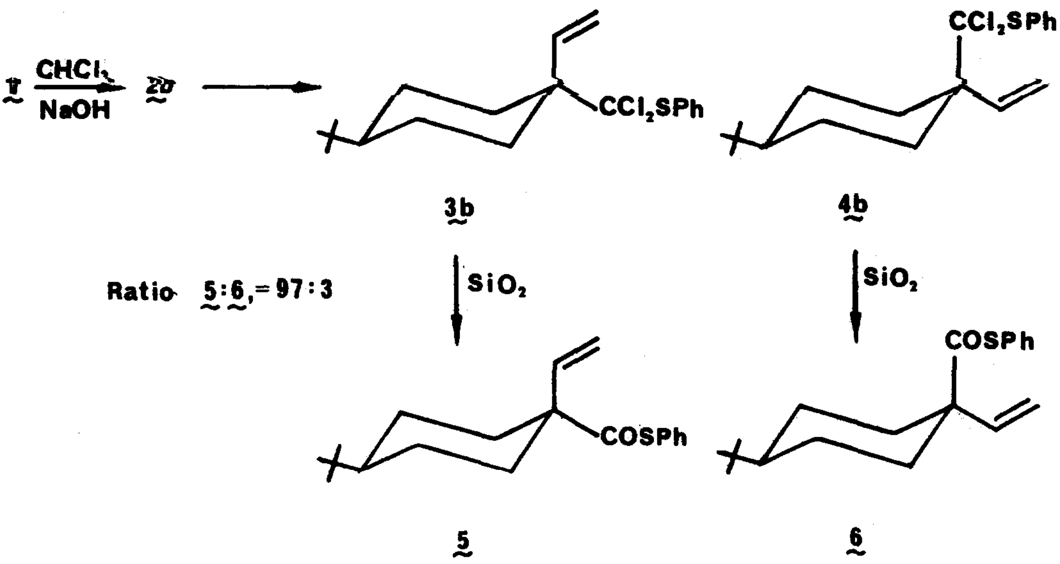
Scheme I



a, $X = CHCO_2Et$, **b**, $X = CCl_2$, **c**, $X = O$

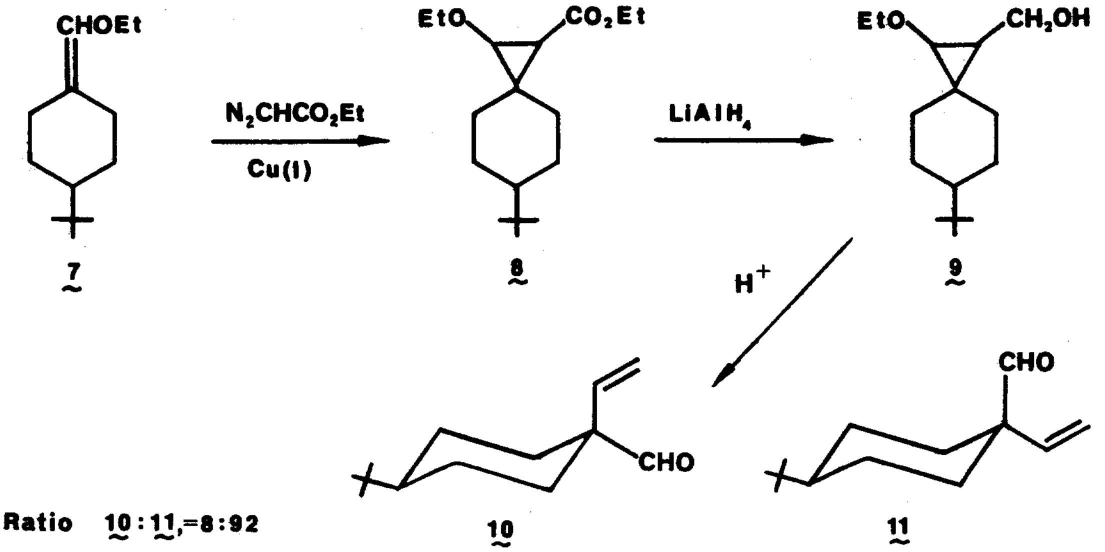
While allylic sulphonium ylids have been formed both by the action of base on allylic sulphonium salts[4] and the addition of carbenes to allylic sulphides,[5] we have found the latter procedure to be of more general utility. Indeed, the addition of ethyl diazoacetate to a homogenous solution of allylic sulphide 1[6,7] in the presence of a catalytic amount of (triethylphosphite)-copper(I) chloride[8] in hexane at 25° results in a 91:9 mixture of the unsaturated sulphide esters 3a and 4a (molecular dist. 60°, 0.05 mm)[6] in 59% yield,[9] presumably *via* the ylid 2a.

Scheme II



Similarly, the micellular addition of dichlorocarbene[10,11] at room temperature to sulfide 1 (Scheme II) afforded, after chromatography on silica gel, a 97:3 mixture of β,γ-unsaturated thiophenylate esters 5 and 6 in 53% isolated yield. This overall transformation proceeds *via* ylid 2b to the dichlorosulfides 3b and 4b[5a] which are hydrolyzed to the thioesters 5 and 6 upon chromatography.[6] Products derived from carbene insertion into the C-C double bond were not observed. In order to unambiguously determine the stereochemistry of the rearrangement products 5 and 6 the complementary stereoselective route illustrated in Scheme III was investigated.[2] It was felt that the addition of copper(I)-carbenoids across the equatorial face of the cyclohexylidene enol ether 7 should be preferred resulting in a preponderance of the axial formyl isomer 11 upon reduction of 8 followed by acid-catalyzed ring cleavage.

Scheme III



Treatment of enol ether 7[12] with ethyl diazoacetate in the presence of (triethylphosphite)-copper(I) chloride catalyst at 25° afforded a complex mixture of the four possible cyclopropanes 8. Lithium aluminium hydride reduction followed by acid catalyzed rearrangement with 10% aqueous hydrochloric acid gave a mixture of aldehydes 10 and 11 in a ratio of 8:92. The mixture of aldehydes 10 and 11 was correlated by glpc[13] to the 97:3 mixture of aldehydes obtained by sequential lithium aluminium hydride reduction and chromium trioxide-pyridine oxidation of thiophenylate esters 5 and 6. The stereochemistry of both 10 and 11, and thus 5 and 6, was determined by nmr. The formyl proton resonance ($CDCl_3$) of the axial isomer 11 (9.26 δ) as compared to 10 (9.30 δ) showed the expected upfield shift of the axial formyl group.[15]

The highly stereoselective formation of isomers 5 and 6 is consistent with the previously observed entrapment of allylic sulfenate esters 3c and 4c (3c:4c, 92:8 at 25°).[16] The results summarized in Table I suggest that the extreme sensitivity of these [2,3] sigmatropic processes to steric environment may be a general attribute of this varied class of reactions.[17] The utility of [2,3] sigmatropic rearrangements as a method of generating molecular asymmetry in natural products synthesis is currently being explored.

Table I - [2,3] Sigmatropic Rearrangements in Cyclohexylidene Ring System

[2,3] Sigmatropic Process	Temperature	Conditions	Equat. Axial Ratios, 3:4
2a ⟶ 3a + 4b	25°	C_6H_{14}	91:9
2b ⟶ 3b + 4b	25°	$CHCl_3$-NaOH	97:3
2c ⟶ 3c + 4c[16]	25°	CH_3OH-$(MeO)_3P$	92:8

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6. Consistent spectral data and combustion analysis were obtained on all compounds reported.
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11. Generated by the addition of 1.5 equiv of ethanol-free chloroform to a dispersion of sulphide 1 in 20% aqueous sodium hydroxide with a catalytic amount of Triton B.
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