A Novel Cycloaddition Reaction of Thermally Generated Sulfenes

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Abstract. The highly strained γ-sultine 4, resulting from the addition of SO₂ to benzobenzvalene, is shown to undergo a thermal cycloreversion which gives 1H-indene-1-thiocarbaldehyde dioxide (6) as an intermediate and subsequently 1H-indene-1-carbaldehyde (5). The sulfene can be intercepted with electron poor C=C bonds in a cycloaddition process leading to a five-membered ring. The structure of the fused heterocyclic product 8b resulting from addition of the sulfene 6 to N-phenylmaleimide was ascertained by X-ray analysis. Pent-4-enethial dioxide (12) produced by the interreaction of bis(trifluoromethyl)sulfene [2c] has been isolated during the eighties with structural determination coming from X-ray crystallography. Some of these amine complexes react with enamines or with enol ethers in the [2+2] fashion. With

Introduction

Sulfenes 1 have been invoked, by analogy to ketenes, for many decades as reactive intermediates of the tert-amino-promoted HCl elimination of αH-alkylsulfonyl chlorides or of the complex reaction of SO₂ with diazaalkanes. Formal [2+2] cycloadditions with enamines giving amino-substituted thietane-S,S-dioxides 2, or the addition of alcohols providing alkyl sulfonates, were purported to be characteristic sulfene reactions. The well-known formation of mesylates from mesyl chloride, the appropriate alcohol and a tert-amino normally follows this sulfene route rather than proceeding along an S₂ pathway [1b]. The direct observation of a free sulfene remains elusive despite of the considerable efforts made so far [1]. Recent work suggests that the reactive species resulting from the tert-amino-promoted HCl elimination of αH-alkylsulfonyl chlorides is an amine-stabilized sulfene [2]. In corroboration, several quinuclidine bound sulfenes, e.g. 3 the adduct of bis(trifluoromethyl)sulfene [2c], have been isolated during the eighties with structural determination coming from X-ray crystallography. Some of these amine complexes react with enamines or with enol ethers in the afore-mentioned [2+2] fashion.
The second most abundant adduct 8b was formed of 1,3-dipolar cycloversion reactions [7]. We attempted to intercept the intermediate 6 with dipolarophiles. Preference was given to π-electron deficient dipolarophiles due to the electronic nature of sulfenes (vide infra). When we heated the γ-sultine 4 in CH₂Cl₂ with excess methyl acrylate we obtained the stereoisomeric adducts 7(a–e) in 58% total yield. However, none of them crystallized, and structural proof was limited to standard spectroscopic methods. We have been more successful with N-phenylmaleimide (NPMI) as the trapping agent. Four stereoisomeric adducts 8a–d were obtained in 82% total yield (ratio a/b/c/d = 12:8:4:1). The second most abundant adduct 8b was readily crystallized (m.p. 189–190°), and its structure was determined by X-ray diffraction [8] (Fig. 1). This now provides definitive proof for the formation of the ring system and, in addition, it reveals the relative configuration at the S-atom for this particular adduct.

It can clearly be seen in Fig. 1, that the sulfene moiety has added to N-phenylmaleimide with the formation of a five-membered ring. Both, the indenyl group and the exocyclic oxygen at the S-atom are oriented trans with respect to the N-containing ring.

According to IR, ¹H-NMR, and ¹³C-NMR spectroscopy the isomeric adducts 8a, 8c, and 8d contain the same fused ring system as 8b, but their precise configuration is unknown at present.

Our hypothesis that the γ-sultine 4 undergoes a thermal cycloreversion to give the sulfene 6 gains additional support from the trapping reaction with acid-free EtOH. Heating 4 in CH₂Cl₂ with excess EtOH (sealed tube, 125°, 2 h) gives the sulfonate 9 in 87% isolated yield. It should be mentioned, however, that compound 4 reacts in a different manner with alcohols, if catalytic amounts of acid or base are present. As shown in Scheme 2, ring opening occurs by direct attack at the S-atom of 4. The reaction was found to be reversible when isolation of the ensuing sulfinate 10 by TLC on silica gel was attempted.

The thermal addition of a sulfene to an electron-deficient π-system in the previously discussed formal 1,3-dipolar fashion is to our knowledge without precedent, and so far it is an isolated case. The sulfene-type intermediates resulting from the HCl elimination of αH-alkylsulfonyl chlorides with tert-amines, which is normally performed at room temperature or below, are reported not to react with acroleine or acrylates [1c]. Attempts in our laboratory to utilise Blocks fluorodesilylation method [4] to intercept the sulfene with acrylate have not met with success, as dimerization and oligomerization reactions prevail. We, therefore, looked for an alternative method to generate a bona fide free sulfene at high temperature. The [3,3]sigmatropic rearrangement of allyl vinyl sulfone 11 was chosen for that purpose. King et al. [1b][9] have demonstrated that 11 undergoes a sulfo-Cope rearrangement when heated with EtOH/pyridine (sealed tube, 175°) to give, via 12, the pyridinium salt 13 (Scheme 3, path A). When we heated the compound 11 with a fivefold excess of N-phenylmaleimide (sealed tube, 175°, 6 h), we obtained the adduct 14 in 85% yield and virtually as a single stereoisomer (Scheme 3, path B). Compound 14 which is more sensitive to hydrolytic decomposition than the corresponding 8b was isolated by medium-pressure chromatography on a short silica-gel column (AcOEt/hexane 1:1) and was fully characterized by standard spectroscopic means. We tentatively assign trans-orientation to the but-3-enyl side chain of 14 with respect to the N-containing ring. The configuration at the S-atom is unknown as yet. Anyway, 14 has the same fused heterocyclic skeleton as the compounds 8a–d and certainly it has the same mechanistic provenance.
Discussion and MO Calculations

The electronic structure of the parent sulfene 15 (thioacetaldehyde dioxide; CH$_2$=SO$_2$) has been the object of semiempirical MO calculations at varying degrees of sophistication (CNDO [10a], CNDO/2 [10b], and CNDO/B [10c]). However, nowadays it is well established that the participation of the d-symmetry functions in the bonding of second-row atoms should be included in the computations [11]. Such polarized functions are capable of reproducing more accurately not only the geometries but also the charge distribution. Therefore, we performed ab initio MO calculations using the GAUSSIAN-88 [12] system of programs. Geometries of all structures were optimized at the Hartree-Fock level with the STO-3G* [13] and 3-21G* [14] polarization basis sets. Two stationary points were located on the parent sulfene potential energy surface, corresponding to the planar C$_{2v}$ structure and the perpendicular C$_{2v}$ rotamer. The vibrational frequencies analysis at the 3-21G* level permitted the characterization of the former as a global minimum, and the latter as a transition state for the rotation around the C–S bond (Table).

To assess the impact of alkyl substitution on the charge distribution in the sulfene, the ab initio computations have also been performed for the methyl sulfene 16 (thioacetaldehyde dioxide). The planar C$_{2v}$ structure has been found to be a minimum, whereas the twisted form is a transition state of C$_{2v}$ symmetry with the rotational barrier of 55 kcal/mol (Table). Optimized planar structures of 15 and 16 together with the atomic charges are depicted in Fig. 2. For both compounds, it is worthwhile noting, that fairly large positive and negative charges are located on the S- and the C-atom, respectively.

The addition reactions of the thermally released sulfenes 6 and 12 to the electron poor double bonds of acrylate or maleimide with formation of five-membered rings need not be via concerted cycloadditions. We actually prefer interpretation in terms of a multistep process which starts by conjugative addition of the nucleophilic C-centre of the sulfene to the Michael acceptor. The very large positive atomic charge on the S-atom accounts for the well-known electrophilic behaviour of sulfenes towards enamines and enol ethers, whereas the large negative charge on the C-atom and its concomitant nucleophilic features provide a good rationale for the cycloaddition described in the present work.

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