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STEPWISE ADDITION OF CHLOROSULFONYL ISOCYANATE TO CYCLOPROPENES

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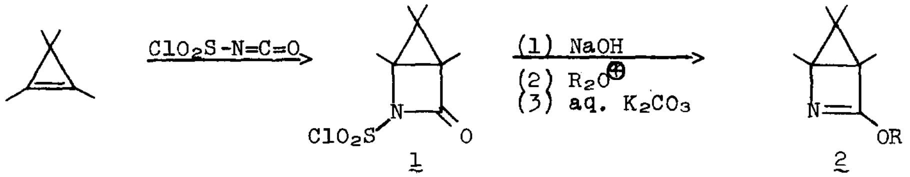
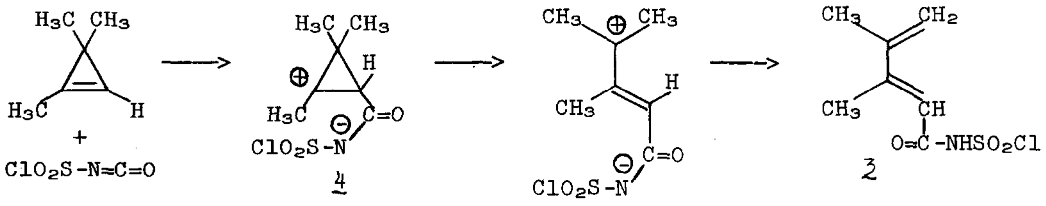
The cycloaddition reactions of chlorosulfonyl isocyanate (CSI) with olefins have provided the most facile and direct route to β-lactams (azetidinones) (1-4). It would therefore appear that the reaction of CSI with a cyclopropene could result in a one step synthesis of the azabicyclo[2.1.0]pentane system (1) and through treatment with a trialkyloxonium salt afford the azabicyclo[2.1.0]pentene ring system (2).



Initial attempts to react CSI with cyclopropene resulted in the formation of uncharacterized dark tars. Due largely to synthetic availability, our attention turned then to the more stable derivative, 1,3,3-trimethylcyclopropene (5). Dropwise addition of an equimolar solution of CSI in ether to a cooled (Dry Ice/acetone) ether solution of the cyclopropene afforded, upon workup, a white, crystalline solid, mp 93-6°, in good yield (6). The infrared spectrum revealed a carbonyl stretch at 1670 cm^{-1}, clearly eliminating a β-lactam (1) from consideration. The nmr spectrum ($CDCl_3$) showed two methyl singlets at δ 1.97 and 2.40 (each 3 H), three singlets in the olefinic region 5.39, 5.67, and 6.06 (each 1 H), and broad N-H absorption at 9.05 (1 H). The mass spectrum contained a parent ion at m/e 223 and a P+2 peak of 39% correctly corresponding to a molecular formula of $C_7H_{10}ClNO_2S$. Fragment ions of m/e 187 (-HCl) and 124 ($-CO_2Cl$) were prominent. An empirical formula of $C_7H_{10}ClNO_2S$ was confirmed by high resolution mass spectroscopy with an exact mass of the parent ion found to be 223.0068 (calculated 223.00697). This information leads to the conclusion that the product is structure 3. A proposed pathway for the formation of 3 is given below.



A two-step mechanism for the reaction of CSI with olefins leading to a dipolar intermediate such as 4 was originally proposed by Graf (1-3) largely on the basis of product analysis. Later kinetic evidence (7) and, perhaps prematurely viewed, orbital symmetry restrictions (8) appeared to confirm this interpretation. Both the 1,4-addition of CSI to cycloöctatetraene (9) and the totally rearranged products of hexamethyldewarbenzene and CSI have been rationalized as arising from an electrophilic addition leading to a "free" carbonium ion (10). However evidence is currently accruing that in certain cases the addition of CSI to olefins is a near-synchronous process (8). The exclusive formation of 3 provides excellent evidence of considerable carbonium ion character in this reaction. Both relief of strain and the formation of a more stable cationic center supply the impetus for cyclopropane ring opening (11).

In an effort to decrease the possibility of ring opening of the intermediate cyclopropyl cation, the isocyanate reaction was run with 1-methylcyclopropene (12). Analogous ring opening would afford a primary rather than a tertiary carbonium ion and ring closure to the β-lactam might then be favored. However, addition of 1-methylcyclopropene to a stirred ether solution of CSI at 0° produced a white, crystalline compound (mp 121.0-2.5°) whose mass spectrum and elemental analysis clearly showed it to be a 2:1 (CSI:cyclopropene) adduct. The infrared spectrum revealed two overlapping carbonyl bands at 1730 and 1760 cm^{-1} and the nmr spectrum consisted of a two-proton apparent triplet at δ 5.44, a one-proton apparent singlet at 5.19 and a three-proton apparent doublet at 1.88. Since this spectral information did not appear to allow unambiguous assignment, the structure determination by x-ray crystallography was undertaken.

Weissenberg photographs indicated the monoclinic crystal system with *a*=8.473±.001 Å, *b*=9.020±.001 Å, *c*=9.624±.001 Å, and β=58.95±.02°. Systematic extinctions (0k0, k=2n+1) and approximate density measurements indicated two molecules per unit cell and space group $P2_1$ (no molecular symmetry) or $P2_1/m$ (i or *m* molecular symmetry). Intensity data for the unique reflections with $2\theta \le 110°$ were collected on a fully automated four circle diffractometer using the stationary crystal stationary counter method. After correction for background and LP factors 826 reflections were judged observed. A sharpened three-dimensional Patterson synthesis showed the correct space group was $P2_1$ and a consistent set of heavy atoms (2 Cl's and 2 S's) was found. The remaining non-hydrogen atoms were located in subsequent electron density syntheses. Full-matrix least-squares refinements with anisotropic temperature factors for all atoms reduced the conventional R-factor to 8.1% for the observed reflections.

The least-squares estimated standard deviations of bond lengths is ±0.01 Å and bond angles, ±1.0°. A drawing with the final bond lengths is given below. The N-S-Cl plane is orthogonal to the plane of the hydantoin ring in both instances. Compound 5 spontaneously resolved on crystallization either throughout the entire crystal or in small crystalline domains.

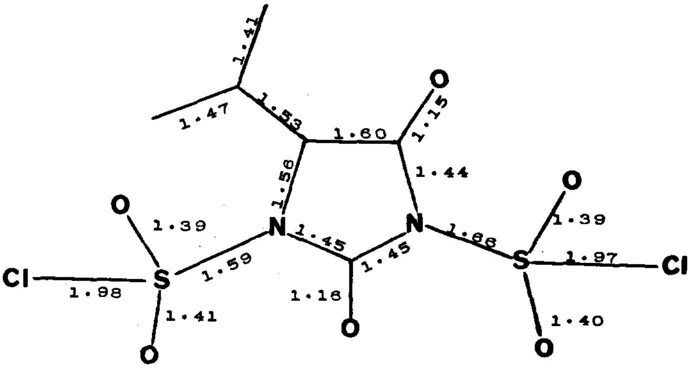
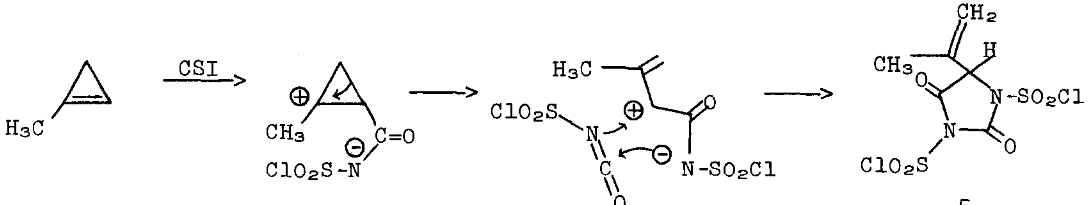


Figure 1. Bond Lengths of Adduct 5

1,3-Dichlorosulfonyl-5-isopropenylhydantoin (5) most logically arises from the pathway illustrated below.



5

Of particular interest is the opening of the cyclopropyl cation to provide an allyl cationic portion of the intermediate, which may be thought of as either a 1,5- or 1,3-dipole. The reaction with a second molecule of CSI to afford 5 may then be considered as a 1,3-dipolar cycloaddition where the 1,3-dipole is simply a zwitterionic form of an α-lactam. In addition to clearly establishing the polar mechanism in the reaction of CSI with cyclopropenes, with concomitant intriguing mechanistic findings, this work unfortunately shows the impossibility of azabicyclo[2.1.0]pentane synthesis through this route.

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