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Facile, Regio and Stereoselective Diels-Alder Reactions of Allenic Trichloromethyl Sulfones and Sulfoxides.[1]

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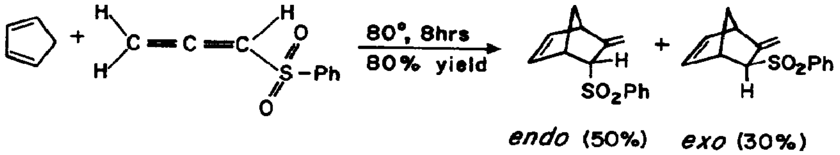
Abstract: *The dienophilic reactivity of allenes is drastically increased by the powerful electron withdrawing trichloromethylsulfonyl or sulfinyl substituents. The [4+2]-cycloadditions proceed smoothly with high regio- and stereoselectivity under mild conditions. Using an optically active allenyl sulfone, transfer of chirality has been observed.*

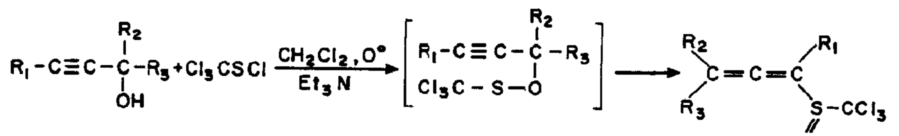
Because of its remarkable synthetic utility, the Diels-Alder reaction continues to attract wide attention.[2] The use of allenes as dienophiles provides an attractive approach to the synthesis of various methylenecyclohexanes which are useful building blocks of terpenoid natural products.[3] However, the use of allenes in the past was limited by the need of drastic conditions, due to their low dienophilic reactivity. Recent MNDO calculations for methanesulfonylpropadiene indicate that the introduction of a sulfonyl group causes a remarkable lowering of the LUMO energy level compared with allene ($\Delta E = 3.07$ ev), with the largest LUMO coefficients located at carbons α and β. Cycloaddition of allenic sulfones is thus expected to proceed in a highly regioselective fashion across the activated α,β-π bond.[4]



(1)

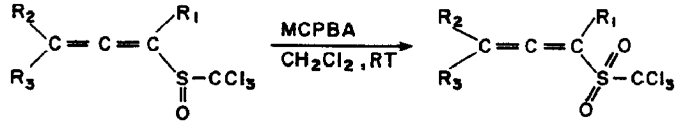
Based on such calculations, several attempts have been recently made to use allenic sulfones and sulfoxides as dienophiles.[4-6] For example, Kanematsu and coworkers[4] have shown that benzenesulfonylpropadiene reacted with various 1,3-dienes at relatively mild conditions. Thus, reaction with cyclopentadiene occurred already at 80° (eq. 1). Subsequently, Block and Putman[5] have described the application of the [4+2] cycloaddition of allenyl chloromethyl sulfone in a novel iterative ring-growing procedure for construction of linear fused carbocycles. More recently, Padwa and coworkers[6] succeeded in reacting (2-nitrobenzenesulfinyl)propadiene with cyclopentadiene at 11 kbar at room temperature. In view of our previous experience with allenes in general[7] and allenyl sulfones in particular,[8] we became interested in this reaction and wish to report that the dienophilic reactivity of allenes can be further increased by the use of trichloromethyl sulfone and sulfoxide derivatives.

All required starting materials are easily accessible even in multigram quantities. Thus, allenic trichloromethyl sulfoxides **2a-c** are obtained spontaneously by the well-known [2,3]-sigmatropic rearrangement of the appropriate propargyl trichloromethanesulfenate, during its preparation from propargyl alcohol and Cl_3CSCl at 0°C (eq 2).[9]



1a-c **2a-c** (2)

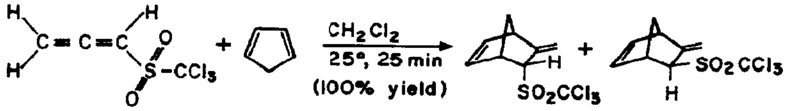
MCPBA oxidation of the allenic sulfoxides at room temperature affords the corresponding sulfones (**3a-c**) in practically quantitative yield (eq. 3).[10] Alternatively, the allenic sulfones **3a-c** can also be prepared by [2,3]-sigmatropic rearrangement of the appropriate propargyl trichloromethanesulfinate esters.[11] The latter were prepared by modification of a recently reported procedure.[12]



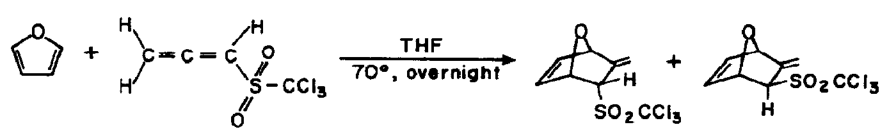
2a-c (3)

3 a, $R_1 = R_2 = R_3 = H$
b, $R_1 = R_2 = H, R_3 = CH_3$
c, $R_1 = H, R_2, R_3 = CH_3$

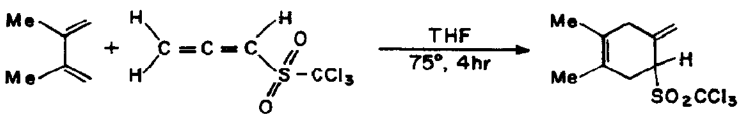
In contrast to the complete lack of reactivity of γ,γ-disubstituted allenyl *p*-tolyl sulfones, and the poor reactivity of the corresponding trichloromethyl sulfones towards cycloaddition to cyclopentadiene even at elevated temperatures in toluene, we have found that the unsubstituted allenyl trichloromethyl sulfone (**3a**) reacted completely at room temperature within half an hour in quantitative yield (eq. 4). The product was obtained as a mixture of the two expected *endo* and *exo*-cycloadducts, which were separated by column chromatography.[10] Furthermore, the same sulfone also reacted smoothly with the much less reactive furan when heated in refluxing THF solution for 2 hours, or even at room temperature, in the presence of a large excess of furan without any solvent. The reaction affords a mixture of both stereoisomers with a similar *endo-exo* ratio (eq. 5). Cycloaddition can also be observed with the poorly reactive 2,3-dimethyl butadiene, but the reaction proceeds to only 40% when refluxed overnight in THF solution (eq. 6).



3a **4a** *endo* (90%) **4b** *exo* (10%) (4)

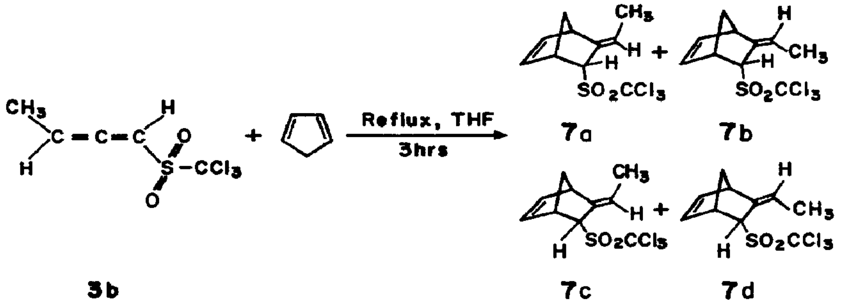


3a **5a** *endo*(91%) **5b** *exo* (9%) (5)



3a **6** (6)

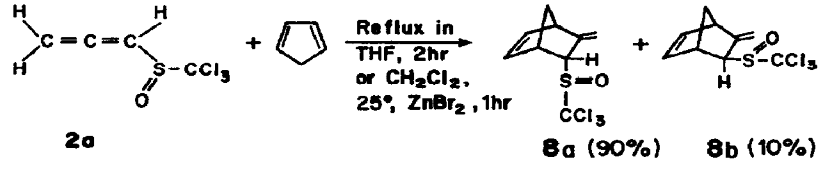
In continuation, we have found that γ-methylallenyl trichloromethyl sulfone (**3b**) also reacted smoothly with cyclopentadiene if heated in refluxing THF for 3 hours. In this case, a total of four different stereoisomers were produced (eq. 7). The ratio of *endo/exo* cycloadducts was about 3/2 and for the *exo* double bond, both E and Z isomers were formed in equal amounts. While the first type of isomers could be separated using column chromatography, we encountered enormous difficulty in separating the E/Z stereoisomers, probably because of their close polarities.



(7)

The decreased reactivity of the last sulfone (**3b**) compared with the unsubstituted allenyl dienophile **3a**, and the drastically reduced reactivity of the γ,γ-dialkylallenyl sulfones induced us to believe that a chiral optically active γ-alkylallenyl sulfone will react with a diene from the less hindered side (i.e. from the -H side) to give an optically active adduct. To investigate this question of π-facial diastereoselectivity and asymmetric Diels-Alder synthesis, optically active γ-methylallenyl trichloromethyl sulfone (**3b**, $[\alpha]_D$ +50°) was obtained by rearrangement of α-methylpropargyl trichloromethanesulfinate, $[\alpha]_D$ -55°. The latter was prepared by reaction of the corresponding alcohol ($[\alpha]_D$ -42°)[13] with $Cl_3CS(O)Cl$. Interestingly, if the same optically active alcohol is first treated with Cl_3CSCl and the optically active γ-methylallenyl trichloromethyl sulfoxide ($[\alpha]_D$ +25°) thus generated is next oxidized with MCPBA, optically active **3b** is obtained with exactly the same optical rotation. These results further demonstrate the concerted intramolecular and suprafacial nature of the [2,3]-sigmatropic sulfenate-sulfoxide and sulfinate-sulfone rearrangements.[14] Based on the Brewster-Loew rules,[15] the *S* absolute configuration was assigned for both the optically active sulfoxide and sulfone. To our delight, the optically active sulfone *S*-(+)-**3b** reacted smoothly with cyclopentadiene and furan and gave a mixture of optically active adducts with $[\alpha]_D$ +30° and +20° for the two dienes, respectively. However, these mixtures have not been separated, as yet.

Encouraged by our success in observing a facile and high yield cycloaddition of the allenic sulfones mentioned above, we investigated the analogous [4+2] cycloaddition of the corresponding allenic sulfoxides. Previous attempts by Padwa[6] to observe the cycloaddition of benzenesulfinylpropadiene at elevated temperature (150°) or under high pressure have failed. Interestingly, even the more reactive 2-nitrobenzenesulfinylpropadiene could only be reacted under high pressures with cyclopentadiene.



(8)

Interestingly, we have found that trichloromethanesulfinylpropadiene (2a) undergoes complete Diels-Alder reaction with cyclopentadiene in refluxing THF after 2 hours at atmospheric pressure (eq. 8). Furthermore, with the use of catalytic amounts of $ZnBr_2$ in dichloromethane, the reaction was completed after one hour at room temperature.

In conclusion, the trichloromethyl group is shown to be a highly activating moiety. Thus, the easily prepared trichloromethyl allenyl sulfones and sulfoxides can serve as reactive and efficient dienophiles. Furthermore, the various adducts possess allylic sulfones or sulfoxides moieties, whose synthetic usefulness has been documented.[16]

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10. All new compounds gave ir, nmr and mass spectral data in accord with the assigned structures; e.g. Sulfone **3a** Mp 30-31°, ^1H NMR ($CDCl_3$, 200 M Hz) δ 5.59 (d, J = 6.3 Hz, 2H), 6.44 (t, J = 6.3 Hz, 1H), 6.44 (t, J = 6.3 H, 1H). Sulfone **3b**. Mp 48-49°, ^1H NMR ($CDCl_3$) δ 1.93 (dd, J = 7.7 and 3.0 Hz, 3H), 6.10 (qd, J = 7.7 and 6.0 Hz, 1H), 6.32 (dq, J = 6.0 and 3.0 Hz, 1H); Sulfone **3c** Mp 75-77°, ^1H NMR ($CDCl_3$) δ 1.94 (d, J = 2.5 Hz, 6H), 6.20 (spt. J = 2.5 Hz, 1H).
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