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Periselectivity in the Base-Catalyzed Intramolecular [2+2]-Cycloaddition Reaction of 3-Phenylsulfonyl-Substituted Propynes

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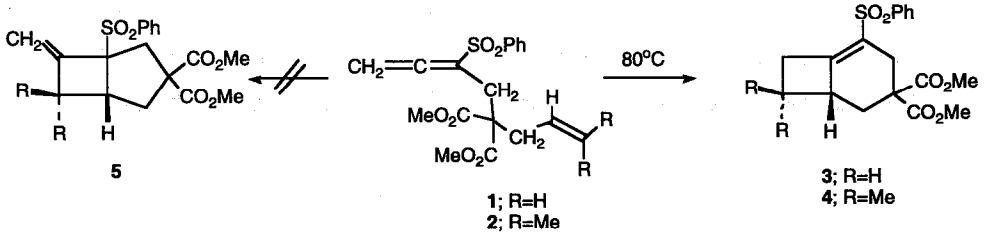
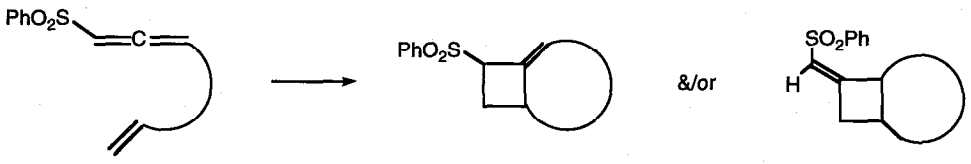
Abstract: Phenylsulfonyl-substituted allenes containining a tethered π-bond are conveniently prepared reagents that can serve as substrates for intramolecular [2+2]-cycloaddition chemistry.

[2+2]-Cycloaddition reactions between allenes and ethylene derivatives have frequently been employed for the preparation of methylene cyclobutane derivatives.[1,2] Many of these reactions proceed by way of photochemical initiation, in which case the mechanistic pathway involves stepwise ring closure *via* diradical or dipolar intermediates.[3] Not only is there considerable regiochemical regularity in the [2+2]-photoaddition, but the products are also easily transformed into useful ring systems by one of several general methods[4-7] making this a very synthetically useful reaction. While well represented in the literature, these photochemical protocols are not the sole choice for allenic [2+2]-cycloadditions. Certain examples involve Lewis acid catalysis, where ionic intermediates are clearly involved.[8] Still others proceed under strictly thermal conditions.[9-13] The mechanistic details associated with these [2+2]-reactions constitute a topic of much study and debate.[14] Substitution on the allene not only enhances its reactivity but also allows for the formation of a mixture of regioisomers.

In connection with our efforts toward the development of new methodologies using sulfonyl substituted allenes,[15] we uncovered a highly chemo- and stereospecific intramolecular [2+2]-cycloaddition of phenylsulfonyl allenes **1** and **2**.[16] The only products formed in both cases corresponded to the [2+2]-cycloadducts **3** and **4** in 90 and 85% yield, respectively. It is particularly interesting to note that only the C_1-C_2 double bond of the allene participates in the cycloaddition. This result was quite puzzling since phenylsulfonyl-substituted allenes react with various 4π-systems in a highly chemoselective fashion undergoing cycloaddition across the more activated C_2-C_3 π-bond.[17] Our ongoing interest dealing with intramolecular cycloaddition reactions inspired us to take a more detailed look at the scope and synthetic ramifications of these [2+2]-allene cycloadditions.



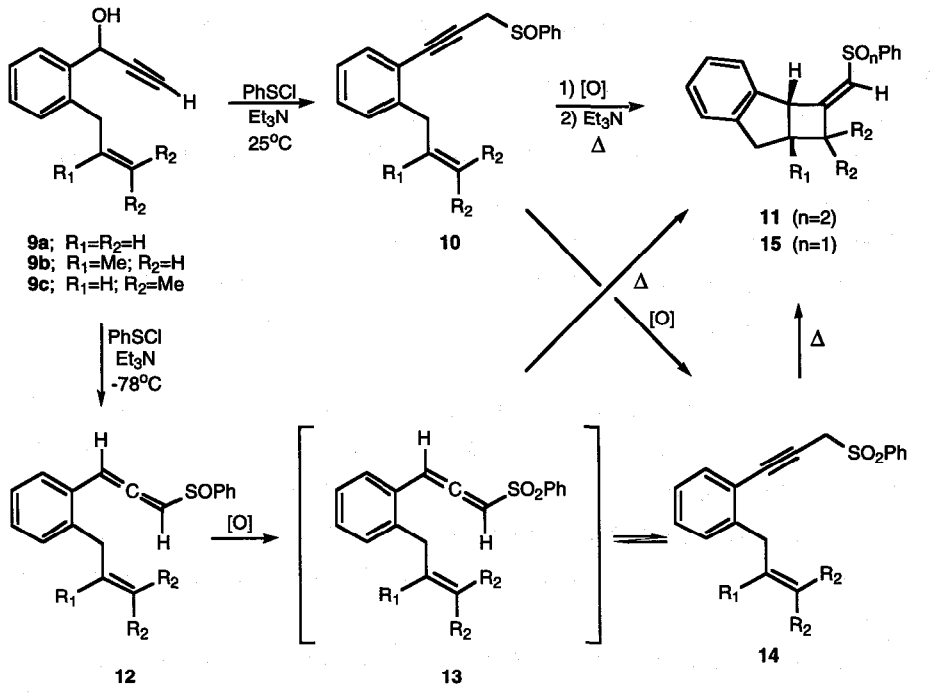
Two basic structural variations can be achieved by altering the point of attachment of the alkenyl tether on the allenyl π-bond. We refer to these two modes as *type I* (*i.e.*, **1**→**3**) and *type II* (*i.e.*, **6**→**7** or **8**) *internal cycloaddition modes*. Since chemical reactivity and regiochemistry can be modified by choice of substituent and geometry, we have undertaken an investigation of the chemistry of several alkenyl phenylsulfonyl-substituted allenes of *type II*. In particular, we were interested in probing the regioselectivity of the process as a function of the nature of the π-bond. The results reported below summarize various aspects of this effort.



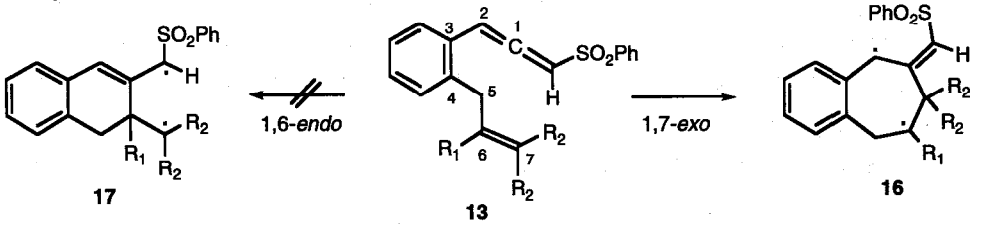
6 **7** **8**

Our strategy for the synthesis of a type II allenyl sulfone such as **6** relies on the well precedented 2,3-sigmatropic shift of propargylic sulfenates to α-allenic sulfoxides.[18] The first system we examined involved the reaction of carbinol **9a** with benzenesulfenyl chloride in the presence of 2 equiv of triethylamine. When this reaction was carried out at 25°C, only the acetylenic sulfoxide **10a** was isolated in 80% yield. Oxidation of **10a** with Oxone gave the corresponding sulfone **14a** which was readily converted to methylene cyclobutane **11a** on stirring with a trace of NEt_3 at 80°C. We believe that this unusual reaction proceeds by a partial isomerization of **14a** to allenyl sulfone **13a** which, in turn, undergoes intramolecular [2+2]-cycloaddition across the allyl π-bond. Support for this proposal was obtained by carrying out the reaction of **9a** with $PhSCl/NEt_3$ at -78°C and isolating the labile allenic sulfoxide **12a**. Oxidation of **12a** using Oxone gave cycloadduct **11a** in 71% isolated yield. As was the case with *type I* allenes, only the less activated C_1-C_2 double bond of **12** was found to participate in the cycloaddition.

A related set of reactions also occurred using carbinols **9b** and **9c**. In both cases the cycloaddition proceeded with total regioselectivity giving rise to cycloadducts **11b** and **11c** in 95% and 98% yield, starting from the acetylenic sulfones **14b** and **14c**. The stereochemistry about the olefinic π-bond was unequivocally established by X-ray crystallographic analysis. Heating sulfoxide **12b** at 40°C also resulted in [2+2]-cycloaddition producing a 3:2-diastereomeric mixture of **15b**. We believe that the high peri-selectivity observed is related to stereoelectronic factors. Evidently, it is easier for stepwise bonding to occur in a 1,7-*exo* manner (leading to diradical **16**) rather than in a 1,6-*endo* fashion. The exclusive formation of the *Z*-sulfonyl substituted alkene present in **11** is readily understandable in terms of steric



considerations. In the transition state leading to the Z-isomer, the tethered alkenyl group can avoid interacting with the bulky phenylsulfonyl group thereby avoiding the unfavorable steric interaction which occurs in the formation of the *E*-diastereomer. Interestingly, incorporation of two methyl substituents at the terminal π-bond does not alter the regioselectivity of the [2+2]-cycloaddition. The added stability of the tertiary radical (*i.e.*, **17**; R_2=Me) is apparently not enough to tip the balance toward the 1,6-*endo trig* mode of cyclization.



In conclusion, phenylsulfonyl substituted alkynes are conveniently prepared reagents that can serve as substrates for intramolecular [2+2]-cycloaddition chemistry by base catalyzed isomerization to a transient allene. The cycloaddition process occurs by a mechanism involving stepwise bonding *via* a 1,7-*exo trig* cyclization. Further studies are in progress and will be reported at a later date.

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