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USE OF 2,3-(DIPHENYLSULFONYL)-1-PROPENE AS AN ALLENE EQUIVALENT IN CYCLOADDITION CHEMISTRY

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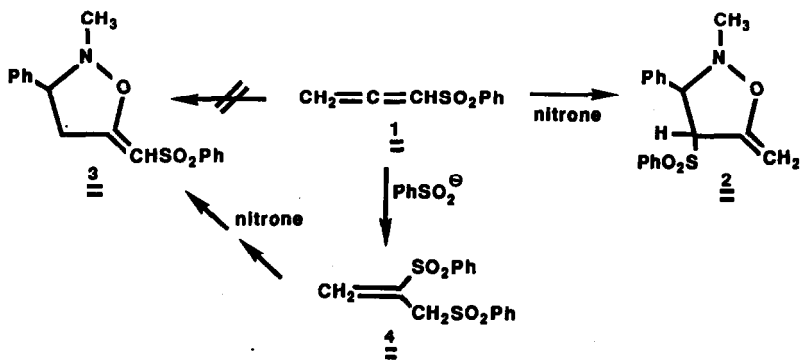
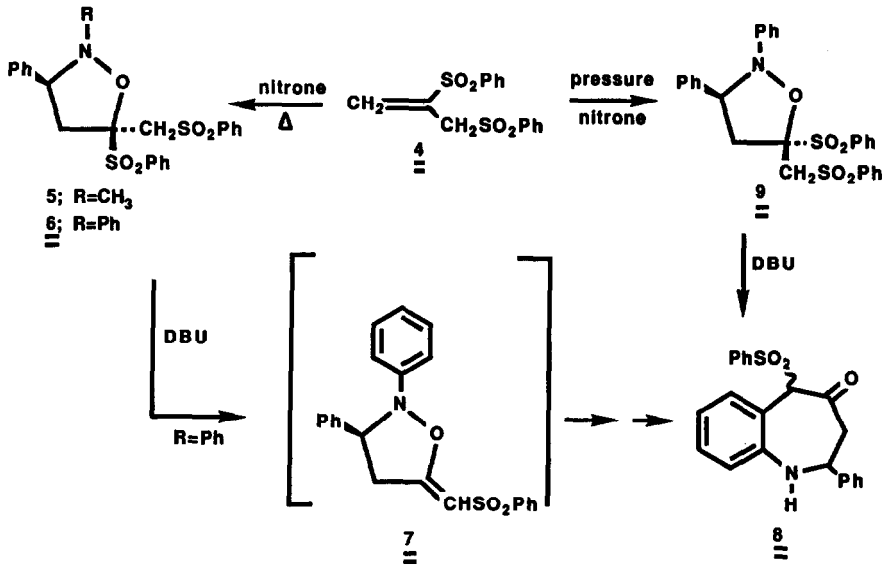
Abstract: The cycloaddition chemistry of 2,3-(diphenylsulfonyl)-1-propene with several nitrones has been investigated. The reagent formally corresponds to an allene equivalent.

Allenes are an interesting group of dipolarophiles since they contain two positions for attack.[1] Based on FMO theory,[2] allenes possessing electron-withdrawing substituents are expected to undergo dipolar cycloaddition across the more activated pi-bond.[3] This proved to be the case in the reaction of N-methyl-C-phenylnitrone with (phenylsulfonyl)-1,2-propadiene **1**.[4,5] No detectable quantities of the regioisomeric cycloadduct **3** could be found in the crude reaction mixture. In this communication, we wish to report on the use of 2,3-(diphenylsulfonyl)-1-propene (**4**) in cycloaddition chemistry.[6,7] This reagent corresponds to a formal "allene equivalent" and permits the indirect synthesis of the unfavorable cycloadduct **3**.



In order to establish the utility of **4** as a dipolarophile, we have investigated its cycloaddition behavior with several nitrones. Heating a solution of C-phenyl-N-methylnitrone with **4** at 80°C for 4 days gave cycloadduct **5** in 79% yield ($CDCl_3$, 360 MHz) δ 2.70 (s, 3H), 3.30 (dd, 1H, J=14.0 and 10.4 Hz), 3.98 (dd, 1H, J=14.0 and 6.9 Hz), 4.10 (d, 1H, J=14.6 Hz), 4.15 (d, 1H, J=14.6 Hz), 4.37 (dd, 1H, J=10.4 and 6.9 Hz) and 6.93-7.99 (m, 15H). Treatment of this material with DBU afforded 5-methylene isoxazolidine **3** in excellent yield[8] thereby providing an indirect synthesis of the previously unknown cycloadduct. It was also found that **4** undergoes clean 1,3-dipolar cycloaddition (80°C, 4 days) with C-phenyl-N-phenylnitrone to give isoxazolidine **6** as the exclusive cycloadduct in 85% isolated yield (NMR ($CDCl_3$, 360 MHz) δ 3.08 (dd, 1H, J=14.3 and

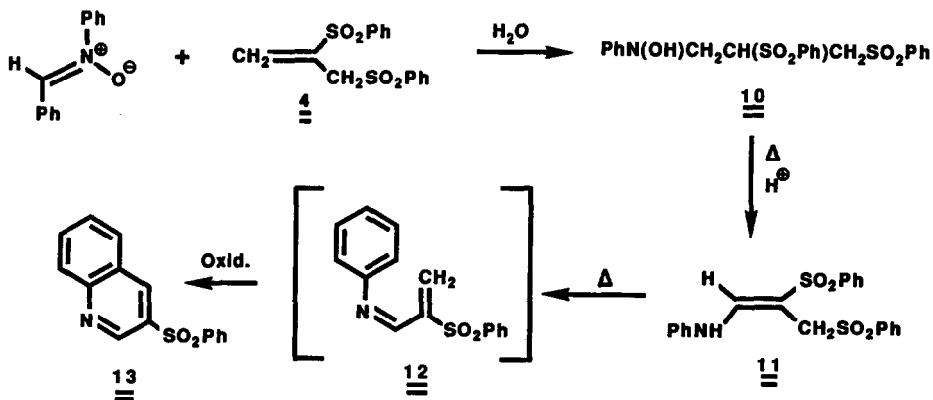
10.2 Hz), 3.92 (dd, 1H, J=14.3 and 7.2 Hz), 3.94 (d, 1H, J=14.9 Hz), 4.07 (d, 1H, J=14.9 Hz), 4.76 (dd, 1H, J=10.2 and 7.2 Hz), 6.77 (d, 2H, J=7.9 Hz), 6.84 (d, 2H, J=7.7 Hz) and 7.03-8.05 (m, 16H)). The stereochemical assignment of the phenylsulfonylmethyl group is based on NOE experiments. Treatment of **6** with DBU afforded a 1:2 mixture of *cis* and *trans*-1,2,3,5-tetrahydro-2-phenyl-5-phenylsulfonyl-4H-1-benzazepin-4-one (**8**) in 87% yield.[9] The formation of **8** most likely proceeds via the intermediacy of 5-methylene isoxazolidine **7** which rapidly undergoes a facile hetero-Cope rearrangement.[10]



Given the long periods of time to effect the dipolar cycloaddition of **4** with the above nitrones, we turned to the use of high pressures. High pressures are known to very markedly accelerate intermolecular cycloadditions with volumes of activation and reaction typically lying in the range of -30 to -40 cm^3 mol^{-1}.[11] Dipolar cycloadditions provide just one example of reactions available to the synthetic chemist which have negative volume of activation and therefore can be accelerated by application of pressure (*ca.* 3-15 kbar).[12] Other examples include Diels-Alder reactions,[13] Michael and Aldol reactions,[14] introduction of protecting groups[15] and formation of Wittig reagents.[16] The high pressure technique seems particularly rewarding in the case of nitrone cycloadditions due to the commonly encountered reversibility of the cycloadducts at high temperatures.[12] Most interestingly, we have found that the cycloaddition stereochemistry is distinctly dependent upon the reaction conditions employed. When a solution of **4** and N-phenyl-C-phenylnitrone were pressurized to 3 kbar at room temperature for 36 h, a 92% yield of cycloadduct **9** was obtained [NMR ($CDCl_3$, 360 MHz) δ 3.45 (dd, 1H, J=14.3 and 6.7 Hz), 3.83 (d, 1H, J=15.2 Hz), 3.87 (d, 1H, J=15.2 Hz), 4.02 (dd, 1H, J=14.3 and 11.2 Hz), 4.34 (dd, 1H, J=11.2 and 6.7 Hz) and 6.48-7.91 (m, 15H)]. No detectable signs of the thermal cycloadduct were found in the crude reaction mixture. Treatment of **9** with DBU afforded the same 1:2 mixture of diastereomeric benzazepinones (i.e. **8**) as that derived from **6**.

At first glance it would seem that one could rationalize the results by assuming that the thermolysis experiments give the thermodynamically more stable cycloadduct (i.e. **6**) while the high pressure reaction affords the kinetic product (i.e. **9**). Molecular mechanics calculations were carried out using the latest version of Still's Model program[17] so as to determine the total energy of the two diastereomers. These calculations reveal that an energy difference of 2.5 kcal (45.78 kcal/mole vs. 43.24 kcal/mole) exists between the lower energy thermal cycloadduct and the isoxazolidine derived from the high pressure experiments. We have subjected the pressure cycloadduct **9** to the thermolysis conditions and find, however, that it does not rearrange to cycloadduct **6**. The factors controlling the stereochemical outcome in these cycloadditions are not clearly defined and further experiments are needed to rationalize the results and to evaluate the potential of pressure as a means of influencing stereochemical control.[18]

During the course of these experiments we inadvertently carried out a pressurized reaction in the presence of some water and isolated a 70% yield of structure **10**. This material is probably derived by hydrolysis of the starting nitrone to benzaldehyde and phenylhydroxylamine followed by conjugate addition of the latter species to the activated sulfone. In fact, **10** could be independently synthesized in quantitative yield by stirring a mixture of **4** with phenylhydroxylamine at 25°C. Heating a sample of **10** in benzene at 80°C for 60 h with a trace of p-toluenesulfonic acid afforded 3-(phenylsulfonyl)quinoline **13** in 60% yield. A reasonable mechanism to rationalize the reaction involves initial dehydration of **10** to **11** followed by thermal elimination of phenyl sulfinic acid to give azadiene **12**. This transient intermediate undergoes a 6π-electrocyclization followed by an oxidation to give quinoline **13**. In support of the above suggestion we have been able to



isolate structure **11** (NMR ($CDCl_3$, 360 MHz) δ 4.20 (s, 2H) and 7.08-8.83 (m, 17H)) by carrying out the thermolysis of **10** for only 30 h. Further heating of **11** gave quinoline **13** in high yield.

In summary, 2,3-(diphenylsulfonyl)-1-propene is a useful synthetic reagent which formally corresponds to an allene equivalent and can also be used to prepare 3-sulfonyl substituted quinolines.

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References and Notes

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8. Structure **3**, mp 67-68°C, NMR ($CDCl_3$, 360 MHz) δ 2.78 (s, 3H), 3.32 (dd, 1H, J=17.1 and 11.0 Hz), 3.85 (dd, 1H, J=11.0 and 6.1 Hz), 4.07 (dd, 1H, J=17.1 and 6.1 Hz), 5.75 (s, 1H) and 7.36-7.85 (m, 10H).
9. *trans*-**8**: NMR ($CDCl_3$, 360 MHz) δ 2.92 (1H, J=16.2 and 4.0 Hz), 3.05 (dd, 1H, J=16.2 and 11.6 Hz), 3.90 (bs, 1H), 5.05 (s, 1H), 5.30 (dd, 1H, J=11.6 and 4.0 Hz) and 6.45-7.77 (m,14H).
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17. We wish to thank Professor Kosta Steliou of the University of Montreal for providing a copy of the extensively rewritten Still Model program (version 2.9).

18. The results described here complement those of DeShong[10] and Dicken who had previously found that the ratio of stereoisomeric isoxazolidines can vary as a function of pressure.

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