J. Am. Chem. Soc. 1993, 115, 3776–3777

Peri- and Stereoselectivity Effects in the Intramolecular 2 + 2-Cycloaddition Reaction of Phenylsulfonyl-Substituted Allenes

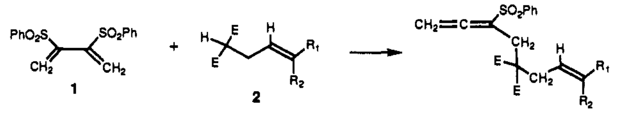
Albert Padwa,* Michelle A. Filipkowski, Michael Meske,
Scott H. Watterson, and Zhijie Ni

Department of Chemistry, Emory University
Atlanta, Georgia 30322

Received January 19, 1993

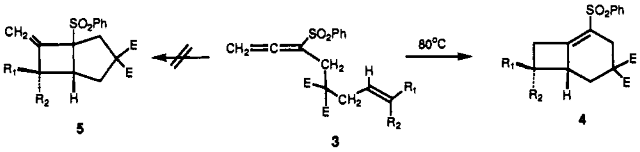
2 + 2-Cycloaddition reactions between allenes and alkenes have frequently been employed for the preparation of methylenecyclobutane derivatives.[1] Most of these addition reactions proceed by photochemical activation.[2,3] Thermal reactions,[4–8] including Lewis acid-promoted processes,[9–12] are restricted to a rather limited number of examples. The 2 + 2-thermal reaction is thought to proceed via a two-step, diradical intermediate mechanism.[13] Substitution on the allene not only enhances its reactivity but also allows for the formation of a mixture of regioisomers. The regiochemistry is generally determined by the initial carbon–carbon bond-forming step. Bond formation at C_2 of the allene gives a 1,4-diradical which can partition between two competitive paths to form regioisomeric products depending on which end of the allyl radical becomes incorporated into the cyclobutane ring. Intramolecular 2 + 2-cycloaddition of allenes has also been studied, and this process constitutes a particularly versatile method for the stereocontrolled synthesis of a variety of functionalized polycyclic compounds.[14] In connection with our efforts toward the development of new methodology using sulfonyl-substituted allenes,[15] we have uncovered a highly chemo- and stereospecific intramolecular 2 + 2-cycloaddition of a phenylsulfonyl-substituted allene. The results of this investigation are reported herein.[15]

Our interest in this area was initiated by a study of the reaction of 2,3-bis(phenylsulfonyl)-1,3-butadiene (**1**) with soft carbanions.[16] The reaction of **1** with a series of allylsubstituted bis(phenylsulfonyl)methanes (**2**) afforded allenes **3a–d** in 60–75% yield. An analogous process also occurred when substituted dimethyl malonates were treated with 1 equiv of NaH in THF at 0 °C in the presence of diene **1**. The reaction proceeds by initial attack of the carbanion onto the terminal position of the diene followed by elimination of $PhSO_2^-$ to give the phenylsulfonyl-substituted allene.



3a; $R_1=R_2=H$; $E=SO_2Ph$
3b; $R_1=R_2=Me$; $E=SO_2Ph$
3c; $R_1=Me$; $R_2=H$; $E=SO_2Ph$
3d; $R_1=H$, $R_2=Me$; $E=SO_2Ph$
3e; $R_1=R_2=H$; $E=CO_2Me$
3f; $R_1=R_2=Me$; $E=CO_2Me$

The thermal reactions of the easily available phenylsulfonyl allenes were performed by heating the reactants in benzene. The only products formed in all cases (ca. 80–98% yield) corresponded to the 2 + 2-cycloadducts **4** which were fully characterized by their ^1H and ^{13}C NMR spectra. The stereochemistry of cycloadduct **4c** was unequivocally established by X-ray crystallographic analysis. It is particularly interesting to note that only the C_1–C_2 double bond of the allene participates in the cycloaddition. In no case could any of the other regioisomer (i.e., **5**) be detected in the crude reaction mixture. This result is somewhat surprising since phenylsulfonyl-substituted allenes react with various 4π-systems in a highly chemoselective fashion undergoing cycloaddition across the C_2–C_3 activated π-bond.[17,18] MNDO calculations indicate that the introduction of a sulfonyl group on the allene backbone causes a significant lowering of the LUMO energy level compared with allene (ΔE = 1.3 eV). The largest LUMO coefficient resides on the central carbon and the next on the position bearing the sulfonyl group.[17,18] We believe that the high periselectivity observed is related to stereoelectronic factors. The primary spatial requirement for 2 + 2-cycloaddition is that the distance between the C_2 carbon of the allene and the olefinic π-bond should be sufficiently close that effective overlap of the π-systems can occur. Evidently, it is easier for stepwise bonding to occur in a 1,6-exo manner (leading to diradical **6**) than in a 1,7-endo fashion.[19]



slow rotation
fast closure

Another aspect of the cycloaddition worth noting is the complete stereospecificity of the process. Heating a sample of allene **3c**

---

(1) Schuster, H. E.; Coppola, G. M. *Allenes in Organic Synthesis*; Wiley-Interscience: New York, 1984. Landor, S. R. *The Chemistry of the Allene*; Academic Press: New York, 1982; Vol. 1–3.

(2) Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570. Eaton, P. E. *Tetrahedron Lett.* **1964**, 3695. Farwaha, R.; de Mayo, P.; Schauble, J. H.; Toong, Y. C. *J. Org. Chem.* **1985**, *50*, 245. Stenson, W.; Svendsen, J. S.; Hofer, O.; Sydnes, L. K. *Acta. Chem. Scan.* **1988**, *B42*, 259 and references cited therein.

(3) Becker, D.; Haddad, N. In *Organic Photochemistry*; Padwa, A., Ed., Dekker: New York, 1989; Vol. 10.

(4) Dolbier, W. R., Jr.; Weaver, S. L. *J. Org. Chem.* **1990**, *55*, 711. Dolbier, W. R., Jr.; Burkholder, C. R.; Wicks, G. E.; Palenik, G. J.; Gawron, M. *J. Am. Chem. Soc.* **1985**, *107*, 7183.

(5) Cripps, H. N.; Williams, J. K.; Sharkey, W. H. *J. Am. Chem. Soc.* **1959**, *81*, 2723.

(6) Baldwin, J. E.; Roy, U. V. *Chem. Commun.* **1969**, 1225.

(7) Kiefer, E. F.; Okamura, M. Y. *J. Am. Chem. Soc.* **1968**, *90*, 4187.

(8) Pasto, D. J.; Yang, S.-H. *J. Am. Chem. Soc.* **1984**, *106*, 152. Pasto, D. J.; Kong, W. *J. Org. Chem.* **1988**, *53*, 4807.

(9) Snider, B. B.; Spindell, D. K. *J. Org. Chem.* **1980**, *45*, 5017. Snider, B. B.; Ron, E. *J. Org. Chem.* **1986**, *51*, 3643.

(10) Hoffmann, H. M. R.; Ismail, Z. M.; Weber, A. *Tetrahedron Lett.* **1981**, 1953.

(11) Lukas, J. H.; Kouwenhaven, A. P.; Baardman, F. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 709.

(12) Komiya, Z.; Nishida, S. J. *J. Org. Chem.* **1983**, *48*, 1500.

(13) Dolbier, W. R.; Jr. *Acc. Chem. Res.* **1991**, *24*, 63.

(14) Hayakawa, K.; Ohsuki, S.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 4205. Hayakawa, K.; Aso, K.; Shiro, M.; Kanematsu, K. *J. Am. Chem. Soc.* **1989**, *111*, 5312. Yoshida, M.; Hiromatsu, M.; Kanematsu, K. *J. Chem. Soc. Chem. Commun.* **1986**, 1168. Yoshida, M.; Hidaka, Y.; Nawata, Y.; Rudzinki, J. M.; Osawa, E.; Kanematsu, K. *J. Am. Chem. Soc.* **1988**, *110*, 1232. Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1989**, 6559. Pirrung, M. C.; Thomson, S. A. *J. Org. Chem.* **1988**, *53*, 230. Dell, C. P.; Smith, E. H.; Warburton, D. *J. Chem. Soc., Perkin Trans. I* **1985**, 747. Skattebol, L.; Stenstrom, Y.; Uggerud, E. *Acta. Chem. Scan.* **1986**, *B40*, 363.

(15) Padwa, A.; Carter, S. P.; Chiacchio, U.; Kline, D. N. *Tetrahedron Lett.* **1986**, 2683. Padwa, A.; Kline, D. N.; Perumattam, J. *Tetrahedron Lett.* **1987**, 913. Padwa, A.; Yeske, P. E. *J. Org. Chem.* **1991**, *56*, 6386. Padwa, A.; Austin, D. J.; Ishida, M.; Muller, C. L.; Murphree, S. S.; Yeske, P. E. *J. Org. Chem.* **1992**, *57*, 1161.

(16) Padwa, A.; Filipkowski, M. A. *Tetrahedron Lett.* **1993**, 813.

(17) Padwa, A.; Craig, S. P.; Chiacchio, U.; Kline, D. N. *J. Org. Chem.* **1988**, *53*, 2232.

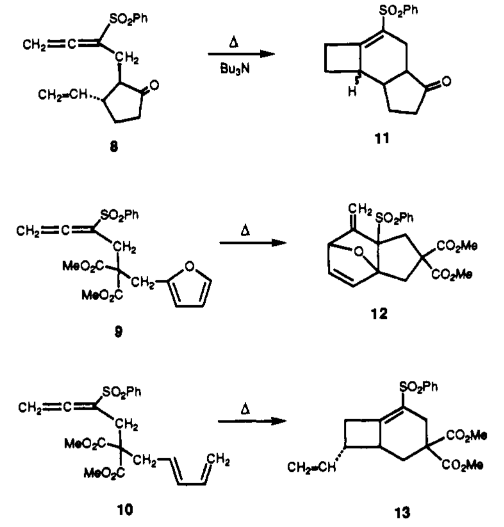
(18) Hayakawa, K.; Nishiyama, H.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 512. Hayakawa, K.; Takewaki, M.; Fujimoto, T.; Kanematsu, K. *J. Org. Chem.* **1986**, *51*, 5100.

(19) Related arguments to those used to rationalize exo and endo selectivity in the cyclization of 5-hexenyl or 6-heptenyl radicals can be invoked here, see: Beckwith, A. L. *J. Tetrahedron* **1981**, *37*, 3073. Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

0002-7863/93/1515-3776$04.00/0

in benzene for 7 h produced cycloadduct **4c** as the exclusive product. Thermolysis of **3d**, on the other hand, gave rise to diastereomer **4d** in 90% with no detectable signs of **4c**. One of the major problems in deciphering the mechanism of the bimolecular 2 + 2-cycloaddition of allenes has been to establish whether the reaction is concerted or involves diradical intermediates.[20] The antarafacial–suprafacial orbital interaction required for concertedness in this class of thermal reactions is quite reasonably achieved when an allenic linkage is involved, due to the sp hybridization of the central carbon. However, this same linkage may, in a stepwise mechanism, give rise to allylic stabilization of the intermediate diradical provided initial bond formation occurs at the central carbon. Calculations indicate that the two mechanisms are comparable energetically,[21] and, consequently, stereochemical arguments cannot distinguish between the two options.[6,7,22] The periselectivity encountered with the phenylsulfonyl-substituted allene **3** strongly suggests that the reaction proceeds in a stepwise manner, since a concerted cycloaddition should have been expected to occur preferentially across the more activated π-bond of the allene. Since the allene educt **6** contains two orthogonally twisted π-bonds, the initally formed *allyl radical* is also orthogonally twisted. Considering the lack of significant stabilization of the nonallylic part of the diradical intermediate, it might be expected to cyclize rapidly, thereby accounting for the high stereoselectivity observed. In fact, rotation of the allylic radical site might well be subject to considerable barriers. The regioselectivity is probably due to efficient radical stabilization by the $PhSO_2$ group, which, unlike ROCO, is free from anisotropic constraints of π-overlap.

To further illustrate the scope and synthetic utility of the intramolecular 2 + 2-process, we examined the thermal behavior of phenylsulfonyl allenes **8–10**. Heating a sample of **8** in toluene which contained several drops of tributylamine so as to epimerize the trans isomer gave cycloadduct **11** in 40% overall yield as a 4:1 mixture of diastereomers. In the reaction of **9** where there was potential competition between 2 + 2- and 4 + 2-processes, only the Diels–Alder adduct **12** (100%) was observed. In contrast to this observation, the structurally related allene **10** preferentially underwent 2 + 2-cycloaddition to give **13** (trans isomer, 64%). This is consistent with the general observation of Kanematsu that furanyl-substituted allenes readily undergo Diels–Alder chemistry, whereas the closely related butadienyl-substituted systems prefer 2 + 2-cycloaddition.[14a–e]


8 **11** **9** **12** **10** **13**

In conclusion, phenylsulfonyl alkenyl-substituted allenes are conveniently prepared reagents that can serve as substrates for intramolecular 2 + 2-cycloaddition chemistry. The resulting cycloadducts should find useful application in organic synthesis. Studies along these lines are in progress.

Acknowledgment. We gratefully acknowledge support of this work by the National Institutes of Health (CA-26750) and a scholarship to M.M. from the Deutschen Akademischen Austauschdienst.

Supplementary Material Available: Experimental details for the preparation and spectroscopic characterization of compounds **3**, **4**, **8–14**; an Ortep diagram and tables of X-ray data for cycloadduct **4c** (15 pages). This material is contained in many libraries on microfiche and immediately follows this article in the microfilm version of the journal. Alternatively, ordering information is given on any current masthead page.

---

[20] Levek, T. J.; Kiefer, E. F. *J. Am. Chem. Soc.* **1976**, *98*, 1875. Pasto, D. J.; Wassen, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3670.

[21] Lebedev, V. L.; Bagaturyants, A. A.; Taber, A. M.; Kalechits, I. V. *Zh. Fiz. Khim.* **1979**, *53*, 2745.

[22] Vogel, E.; Grimme, W.; Dinne, E. *Angew. Chem.* **1963**, *75*, 1103.