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[4+1]-ANIONIC ANNULATION APPROACH TO PHENYLSULFONYL SUBSTITUTED CYCLOPENTENES

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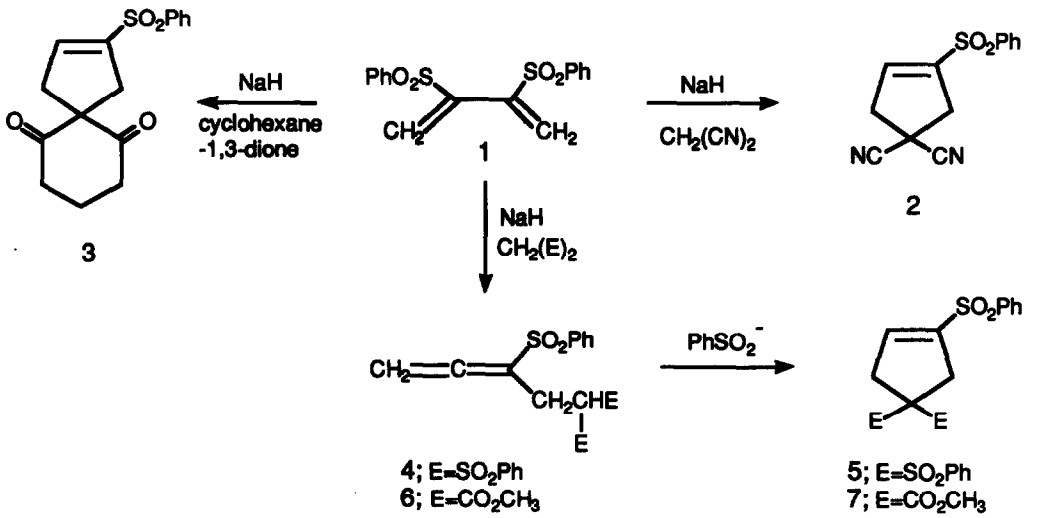
Abstract: *2,3-Bis(phenylsulfonyl)-1,3-butadiene undergoes a [4+1]-annulation reaction with a variety of soft carbanions to give phenylsulfonyl substituted cyclopentenes in good yield.*

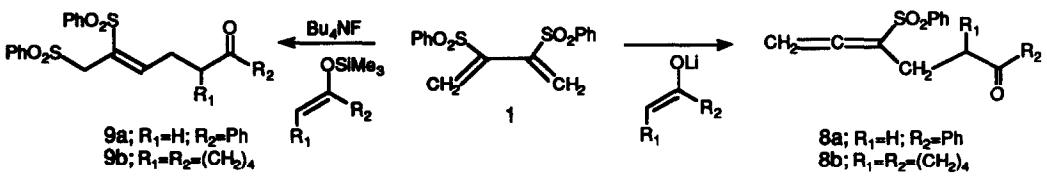
The chemistry of phenylsulfonyl substituted 1,3-butadienes is receiving increasing attention due to their synthetic versatility and the efficient π-bond activation by the sulfonyl group.[1-5] Recently, we demonstrated the use of *2,3-bis*(phenylsulfonyl)-1,3-butadiene (**1**) as a versatile building block in organic synthesis, particularly for [4+2]-cycloaddition chemistry.[5] This diene also played an important role in the successful outcome of our [4+1]-annulation strategy for pyrrolidine formation, since it is highly activated toward nucleophilic addition.[6] While the reaction of **1** with heteronucleophiles has been studied in some detail,[6] there have been no examples of carbon-carbon bond forming reactions of **1** with carbon-based nucleophiles. In the field of cyclopentanoid synthesis, a problem of continuing interest is the development of a general method for the conversion of conjugated dienes to cyclopentene derivatives.[7] Toward this end, we have used *2,3-bis*(phenylsulfonyl)-1,3-butadiene (**1**) as the key reagent for a novel 4+1-annulation approach to substituted cyclopentenes.

The pivotal step in our annulation strategy involves addition of a stabilized carbanion onto the highly activated π-bond of **1**. We began our studies by examining the reaction of **1** with malonitrile in the presence of a slight excess of NaH in THF at 25°C. The major product formed corresponded to cyclopentene **2** (60%). Similarly, treatment of diene **1** with cyclohexan-1,3-dione in the presence of NaH (THF) gave rise to the related spirocyclopentene **3** in 70% yield. Interestingly, the reaction of **1** with *bis*(phenylsulfonyl)methane (NaH/THF) afforded allene **4** as the exclusive product in 75% isolated yield. When **4** was allowed to stir for longer periods of time in the presence of a catalytic amount of sodium benzenesulfinate, it was quantitatively transformed into cyclopentene **5**. Since we were interested in the mechanism by which **4** was converted to **5**, we studied the analogous reaction of **1** with dimethyl malonate. Under conditions identical with those used above, allene **6** was initially formed and was subsequently converted to **7** upon further stirring at 25°C in the presence of $PhSO_2Na$.

Treatment of **1** with a variety of different lithium enolates results in the formation of several

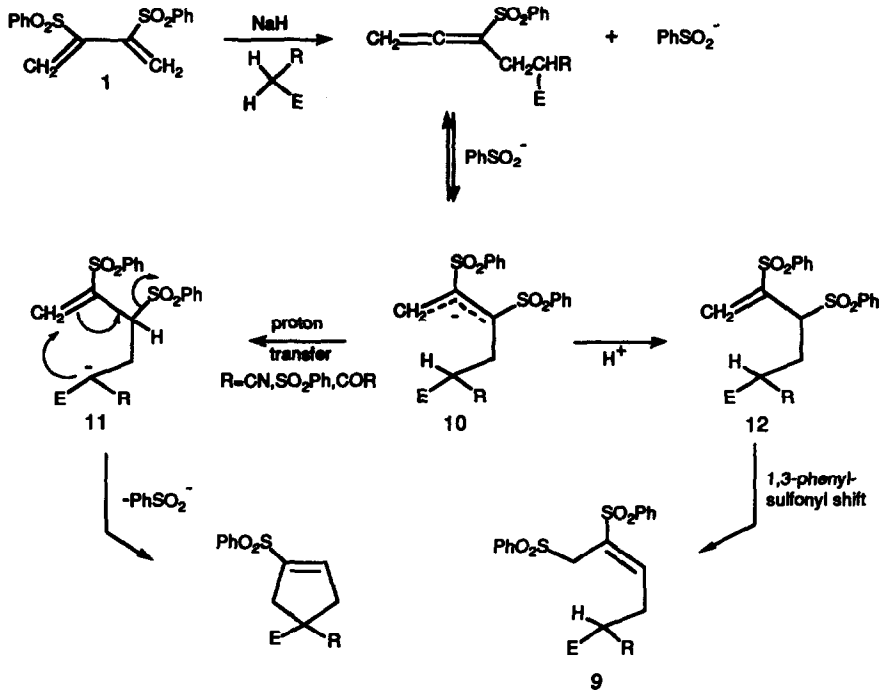


allenyl sulfones (*i.e.*, **8**) related to **4** in 60-70% yield. However, when the corresponding trimethylsilyl enol ethers were employed, the reaction with **1** in the presence of an equivalent of tetrabutylammonium fluoride afforded the rearranged adducts **9** in 75% yield.



A mechanism that is consistent with all the data is outlined in Scheme I. Initial attack of the carbanion onto the terminal position of diene **1** is followed by $PhSO_2^-$ elimination to give the phenylsulfonyl substituted allene (*i.e.*, **4** or **6**). This substrate is highly activated toward nucleophilic addition[8-11] because of its low lying LUMO energy level.[12,13] Further reaction of the allene with benzenesulfinate anion generates the allyl phenylsulfonyl stabilized carbanion **10**. A subsequent proton transfer (either *intra* or *intermolecular*) produces **11**, which is followed by a cyclization-elimination sequence providing the five-membered ring and an additional quantity of benzenesulfinate anion. This anion undergoes nucleophilic addition with another molecule of allene to regenerate **10** and continue the chain process.

Scheme I



The facility of the *5-endo trig* cyclization under such mild conditions (25°C) is worthy of note because it is generally considered to be a disfavored process.[14] There are, however, a number of closely related cyclizations reported in the literature, providing good precedence for the cyclization step[15-17]. When a lithium enolate is employed as the attacking nucleophile (*i.e.*, R=H or alkyl; E=COR_1), proton transfer from **10** to **11** is less likely to occur and ejection of $PhSO_2^-$ takes place with regeneration of the allenyl sulfone. Under the conditions used with trimethylsilyl enol ethers, carbanion **10** is protonated by some adventitious water producing **12** which undergoes a subsequent 1,3-phenylsulfonyl shift to give the thermodynamically more substituted isomer (*i.e.*, **9**).[18]

In summary, we have developed an efficient [4+1]-annulation sequence for the synthesis of phenylsulfonyl substituted cyclopentenes. This approach nicely complements the well known anionic [3+2]-cyclization route.[19] A number of useful addition reactions involving the vinyl sulfone functionality present in the ring can now be exploited so as to prepare a wide variety of cyclopentenes bearing functionalized appendages. Work along these lines is in progress and will be reported in due course.

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References and Notes

1. Bäckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396. Bäckvall, J. E.; Juntunen, S. K. *J. Org. Chem.* **1988**, *53*, 2398. Bäckvall, J. E.; Plobeck, N. A. *J. Org. Chem.* **1990**, *55*, 4528. Plobeck, N. A.; Bäckvall, J. E. *J. Org. Chem.* **1991**, *56*, 4508.
2. Masuyama, Y.; Yamazaki, H.; Toyoda, Y.; Kurusu, Y. *Synthesis* **1985**, 964.
3. Lee, S. J.; Lee, J. C.; Peng, M. L.; Chou, T-S. *J. Chem. Soc., Chem. Commun.* **1989**, 1020. Chou, T.; Hung, S. C. *J. Org. Chem.* **1988**, *53*, 3020.
4. Hardinger, S. A.; Fuchs, P. L. *J. Org. Chem.* **1987**, *52*, 2739.
5. Padwa, A.; Norman, B. H. *Tetrahedron Lett.* **1988**, *29*, 2417. Norman, B. H.; Gareau, Y.; Padwa, A. *J. Org. Chem.* **1991**, *56*, 2154. Padwa, A.; Harrison, B.; Norman, B. H. *Tetrahedron Lett.* **1989**, *30*, 3259. Padwa, A.; Gareau, Y.; Harrison, B. H. *J. Org. Chem.* **1991**, *56*, 2713. Padwa, A.; Gareau, Y.; Harrison, B.; Rodriguez, A. *J. Org. Chem.* **1992**, *57*, 3540.
6. Padwa, A.; Norman, B. H. *Tetrahedron Lett.* **1988**, *29*, 3041. Padwa, A.; Norman, B. H. *J. Org. Chem.* **1990**, *55*, 4801.
7. Hudlicky, T.; Fleming, A.; Radesca, L. *J. Am. Chem. Soc.* **1989**, *111*, 6691. Laabassi, M.; Gree, R. *Tetrahedron Lett.* **1988**, *29*, 611. Danheiser, R. L.; Bronson, J. J.; Okano, K. *J. Am. Chem. Soc.* **1985**, *107*, 4579. Barriere, F.; Barriere, J. C.; Barton, D. H. R.; Cleophax, J.; Gateau-Olesker, A.; Gero, S. D.; Tadj, F. *Tetrahedron Lett.* **1985**, *26*, 3121.
8. Appleyard, G. D.; Stirling, C. J. M. *J. Chem. Soc.* **1967**, 2686.
9. Denmark, S. E.; Harmata, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 4972.
10. Blechert, S. *Tetrahedron Lett.* **1984**, *25*, 1547.
11. Back, T. G.; Krishna, M. V. *J. Org. Chem.* **1987**, *52*, 4265.
12. Padwa, A.; Craig, S. P.; Chiacchio, U.; Kline, D. N. *J. Org. Chem.* **1988**, *53*, 2232.
13. Hayakawa, K.; Nishiyama, H.; Kanematsu, D. N. *J. Org. Chem.* **1985**, *50*, 512.
14. Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939 and references cited therein.
15. Beak, P.; Burg, D. A. *J. Org. Chem.* **1989**, *54*, 1647 and references cited therein.
16. Padwa, A.; Yeske, P. E. *J. Org. Chem.* **1991**, *56*, 6386.
17. An alternate possibility involves a prior conversion of **11** to **9** followed by cyclization *via* a 5-*exo-tet* pathway by displacement of the allylically-activated sulfone moiety.
18. Padwa, A.; Bullock, W. H.; Dyszlewski, A. D. *J. Org. Chem.* **1990**, *55*, 955. Lin, P.; Whitham, G. H. *J. Chem. Soc., Chem. Commun.* **1983**, 1102.
19. Kauffmann, T. *Top. Curr. Chem.* **1980**, *92*, 109 and references cited therein.

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