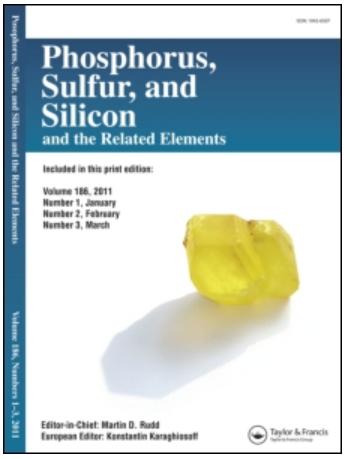


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthetic and Mechanistic Aspects of Some Free-Radical and Electrophilic Organoselenium Reactions

Thomas G. Back[a]
[a] Department of Chemistry, University of Calgary, Calgary, Alberta, Canada

To cite this Article Back, Thomas G.(1992) 'Synthetic and Mechanistic Aspects of Some Free-Radical and Electrophilic Organoselenium Reactions', Phosphorus, Sulfur, and Silicon and the Related Elements, 67: 1, 203 — 218
To link to this Article: DOI: 10.1080/10426509208045838
URL: http://dx.doi.org/10.1080/10426509208045838

Phosphorus, Sulfur, and Silicon, 1992, Vol. 67, pp. 203–218 Reprints available directly from the publisher Photocopying permitted by license only

SYNTHETIC AND MECHANISTIC ASPECTS OF SOME FREE-RADICAL AND ELECTROPHILIC ORGANOSELENIUM REACTIONS

THOMAS G. BACK
Department of Chemistry, University of Calgary, Calgary, Alberta, Canada T2N 1N4

Abstract Selenenic derivatives such as selenosulfonates ($PhSeSO_2Ar$) and selenenyl sulfonates ($PhSeOSO_2Ar$) undergo free-radical and electrophilic additions to unsaturated organic substrates, often with high regio- and stereoselectivity. These processes can be employed in tandem with selenoxide eliminations, [2,3]-sigmatropic rearrangements and various types of substitution and reduction reactions of the selenium moiety. Applications include preparations of various types of synthetically useful unsaturated sulfones and a new protocol for the synthesis of sterol side chains, such as that of the plant growth-promoter brassinolide.

INTRODUCTION

The electrophilic additions of various selenenyl halides and pseudohalides (ArSeX) to olefins and acetylenes have been widely studied.[1] These processes permit the vicinal introduction of the arylseleno group and the moiety X into an unsaturated substrate (Scheme 1). Further transformations of the adducts can be achieved by selenoxide elimination, by reduction or substitution of the arylseleno residue, and by [2,3] sigmatropic rearrangement when the selenide is allylic. Other synthetically useful products are accessible through appropriate manipulation of the halide or pseudohalide function. Free-radical additions of species ArSeX are encountered less frequently,[2] but in some cases can be performed efficiently and may lead to products of complementary regiochemistry to those obtained under electrophilic conditions.

Scheme 1

The selenosulfonates ($ArSO_2SePh$) are stable, odourless, crystalline solids that were first reported by Foss[3] in 1947, but were then ignored until recently. They are

readily available by the oxidation of sulfonhydrazides[4] or sulfinic acids[5] with benzeneseleninic acid, as shown below, and undergo both electrophilic and free-radical additions called selenosulfonations to various unsaturated substrates.

$$ArSO_2NHNH_2 + PhSeO_2H \longrightarrow ArSO_2SePh + N_2 + 2\,H_2O$$

$$2\,ArSO_2H + PhSeO_2H \longrightarrow ArSO_2SePh + ArSO_3H + H_2O$$

On the other hand, selenenyl sulfonates ($ArSO_2OSePh$) are unstable compounds that must be generated in situ. We recently observed that the p-tolyl derivative undergoes efficient electrophilic additions to acetylenes.[6] Independent studies of the triflate[7] and m-nitrophenyl sulfonate[8] analogues by other groups have also been reported recently.

SELENOSULFONATION

Olefins and allenes

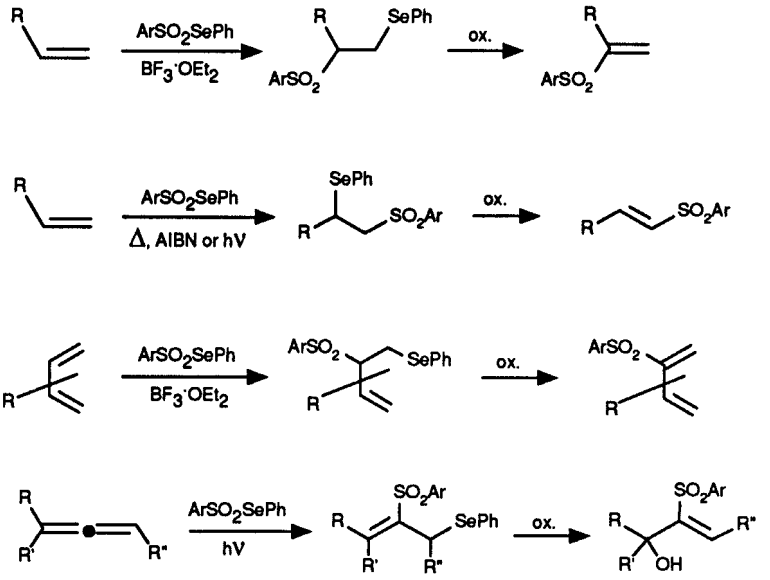
Early work by our group[9] and by Kice and coworkers[5] demonstrated that selenosulfonates add to olefins under either Lewis acid-catalyzed electrophilic conditions, or via a free-radical chain mechanism initiated photolytically or by thermolysis with AIBN. The adducts are complementary regioisomers that afford the respective vinyl sulfones in high yield when subjected to selenoxide elimination. The electrophilic reactions[9] are stereospecific (anti) and presumably involve bridged seleniranium ion intermediates. Conjugated dienes afford chiefly the products of 1,2-addition in the presence of Lewis acids and similarly produce dienyl sulfones upon oxidation.[9,10] The free-radical selenosulfonation of allenes results in the regioselective incorporation of the sulfonyl group at the central allene carbon atom and the adducts afford 2-sulfonyl allylic alcohols after oxidation and [2,3] sigmatropic rearrangement.[11] These processes are shown in Scheme 2.

Acetylenes

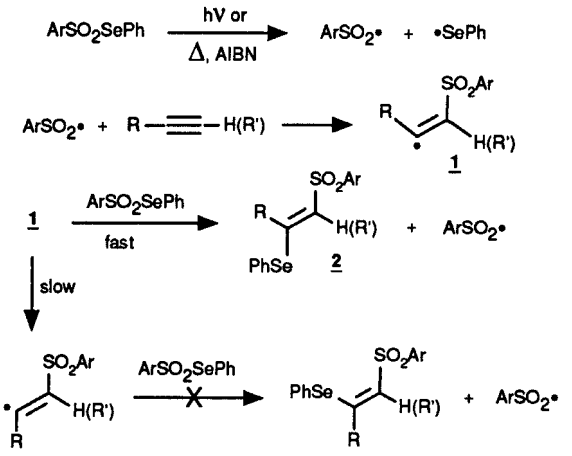
Acetylenes undergo free-radical, but not electrophilic, selenosulfonation.[12] The corresponding β-(phenylseleno)vinyl sulfones 2 are formed in high yield (usually >80%) from terminal acetylenes, and somewhat less efficiently from disubstituted ones. The additions are generally highly stereoselective (anti) and, in the case of terminal acetylenes, are also highly regioselective, as shown in Scheme 3. The observed stereochemistry is consistent with rapid chain-transfer compared to slower inversion of the vinyl radical intermediate 1 in Scheme 3, while the regiochemistry

reflects the formation of the more substituted vinyl radical.

Scheme 2



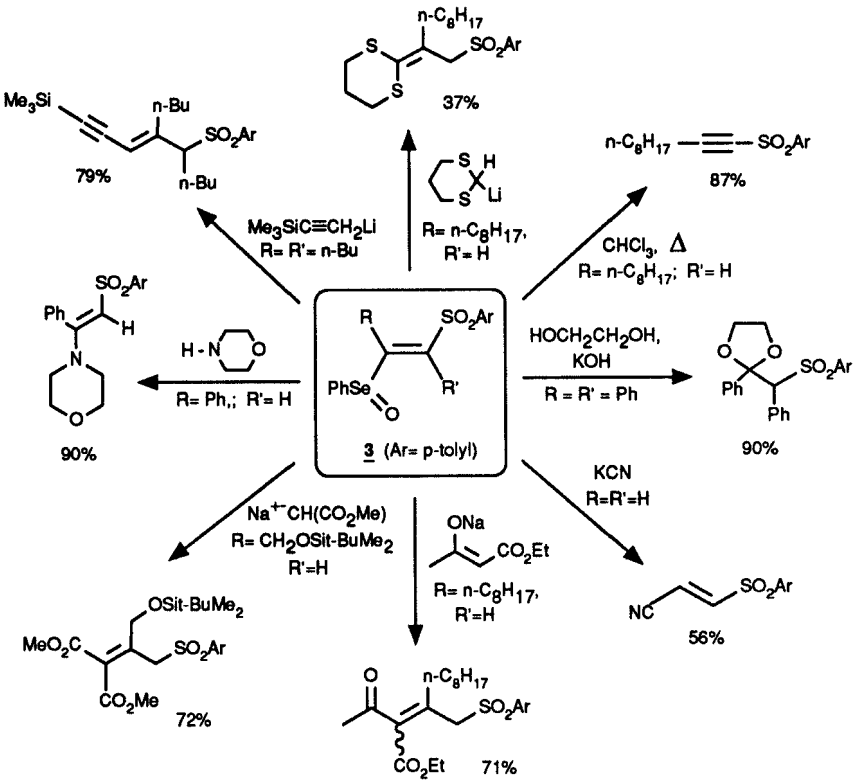
Scheme 3



The adducts 2 can be employed in a number of useful transformations by oxidation to the corresponding selenoxides 3. When refluxed in chloroform, smooth syn-elimination of 3 occurs to afford acetylenic sulfones in excellent yield.[12] The selenoxides also react with a variety of nucleophiles to afford the products of overall

substitution of the selenium moiety via either addition-elimination or elimination-addition mechanisms.[12a,13] Illustrative examples are shown in Scheme 4.

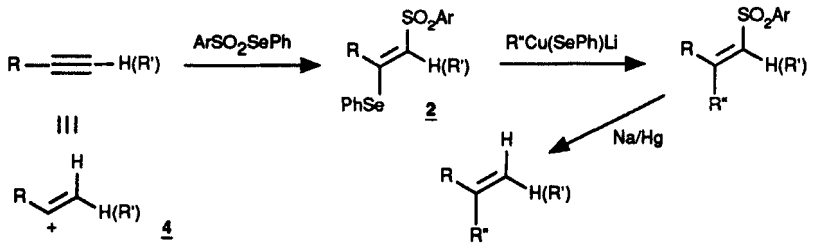
Scheme 4



When adducts 2 were treated with organocuprates, substitution of the phenylseleno group occurred with retention of configuration.[14] Subsequent reductive desulfonylation permits the overall conversion of acetylenes into di- or trisubstituted olefins (Scheme 5), and enables the acetylenes to be employed as synthetic equivalents of the vinyl cation 4. This method has been applied to the synthesis of sterol side chains containing 24-methylene groups.[15]

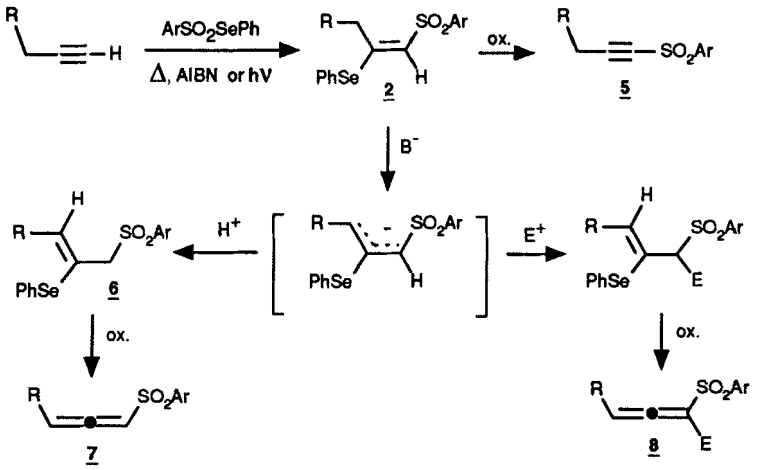
The selenosulfonation of acetylenes provides a clean route to either acetylenic or allenic sulfones. Direct oxidation and selenoxide elimination of the adducts proceeds with high regioselectivity towards the hydrogen at the sulfone-substituted vinylic position, rather than towards the allylic hydrogen, to afford acetylenic sulfones 5 in high yield (Scheme 6). However, the original adducts 2 can first be isomerized to the corresponding allylic sulfones 6 by treatment with bases ranging

Scheme 5



in strength from triethylamine to LDA.[16] When compounds 6 are oxidized to their selenoxides, elimination affords the corresponding allenic sulfones 7 by abstraction of one of the more acidic hydrogens from the sulfone-substituted carbon.[17] Furthermore, the isomerization step favours the Z-isomers of 6, thereby precluding syn-elimination towards the vinylic hydrogen. The highly selective formation of either acetylenic or allenic sulfones is therefore possible by either omitting or including the base-catalyzed isomerization step. It is also possible to prepare allenic sulfones 8, containing an additional substituent in the α-position, by deprotonation of the original adduct with LDA, followed by the addition of electrophiles such as alkyl iodides, trimethylsilyl chloride or D_2O (Scheme 6).[17]

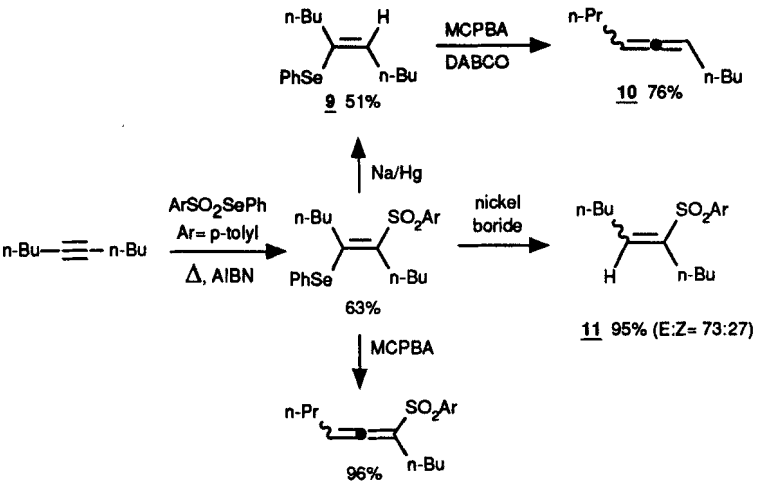
Scheme 6



The reductive desulfonylation of the allenic sulfones produced in Scheme 6 would make possible the overall synthesis of allenes from acetylenes. Unfortunately, all attempts at such desulfonylations with conventional reagents failed in our hands.

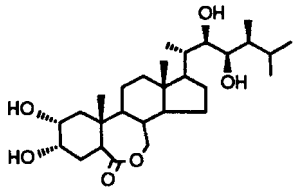
We therefore desulfonylated the selenosulfonate adducts, or their allylic isomers, prior to oxidation to afford vinyl selenides (e.g. 9 in Scheme 7). Subsequent oxidation-elimination then provided the desired allenes (e.g. 10) as the principal products.[17] In some cases, however, these were accompanied by significant amounts of acetylenic byproducts. Alternatively, deselenization of the adducts with nickel boride gave either vinyl or saturated sulfone products (e.g. 11).[18]

Scheme 7

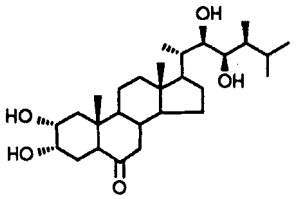


Synthesis of Castasterone and Brassinolide

Brassinolide (12) is a plant-growth promoter that was first isolated in minute quantities from *Brassica napus* L. pollen in 1979.[19] The low abundance, potent biological properties and unusual structure of 12 make it, and related sterols such as castasterone (13), interesting synthetic objectives.



Brassinolide (12)

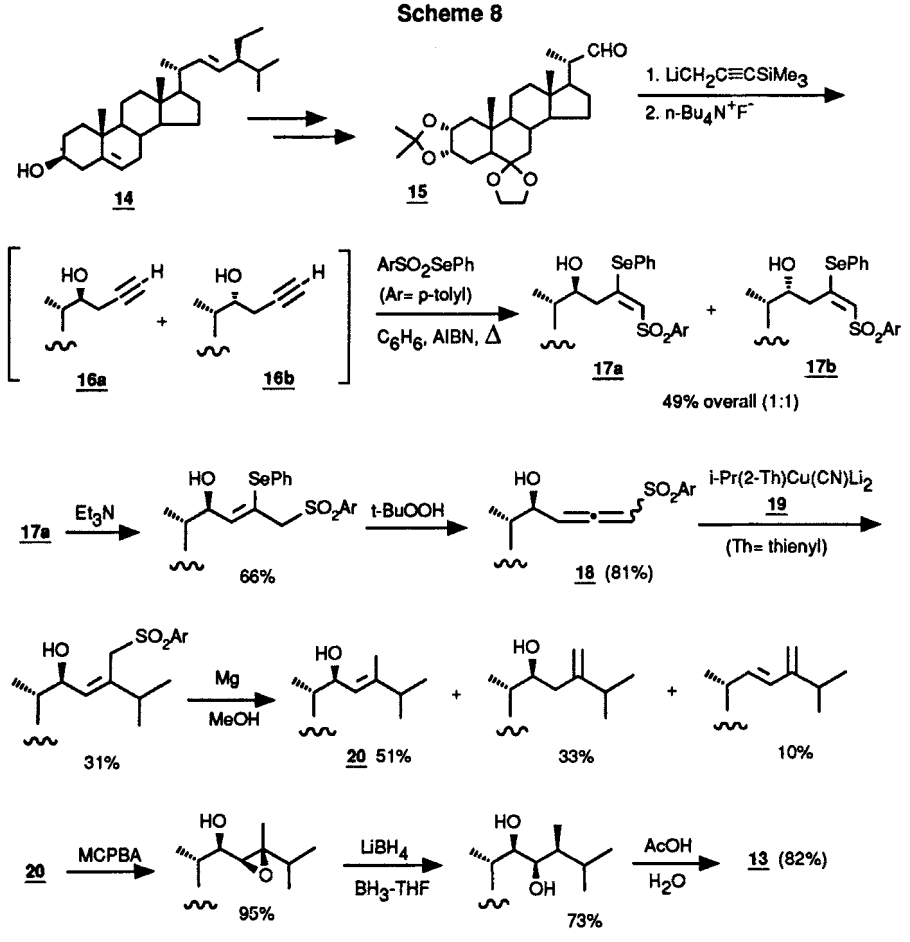


Castasterone (13)

Our approach[20] to these compounds is shown in Scheme 8 and employed the allenic sulfone 18, obtained by the selenosulfonation methodology described above, as a key intermediate. The aldehyde 15 was prepared from commercially available stigmasterol (14) by standard methods.[21] It was treated with 3-lithio-1-(trimethyl-

silyl)propyne, followed by terabutylammonium fluoride, to afford the epimeric alcohols 16a and 16b. These were subjected to selenosulfonation, giving the easily separable stereoisomers 17a and 17b. Isomerization and selenoxide elimination of 17a provided the required allenic sulfone 18. Treatment of 18 with the cuprate reagent 19[22] produced the corresponding sulfonyl-substituted Z-allylic alcohol in modest yield, but with excellent stereoselectivity. Desulfonylation of the latter was attempted with a variety of literature reagents, but the best results were obtained with magnesium in methanol.[23] The further conversion of the product 20 into castasterone (13) was based on literature precedents.[24] Since the transformation of 13 into brassinolide (12) has been previously reported,[21,24b,25] this also constitutes a formal synthesis of the latter sterol.

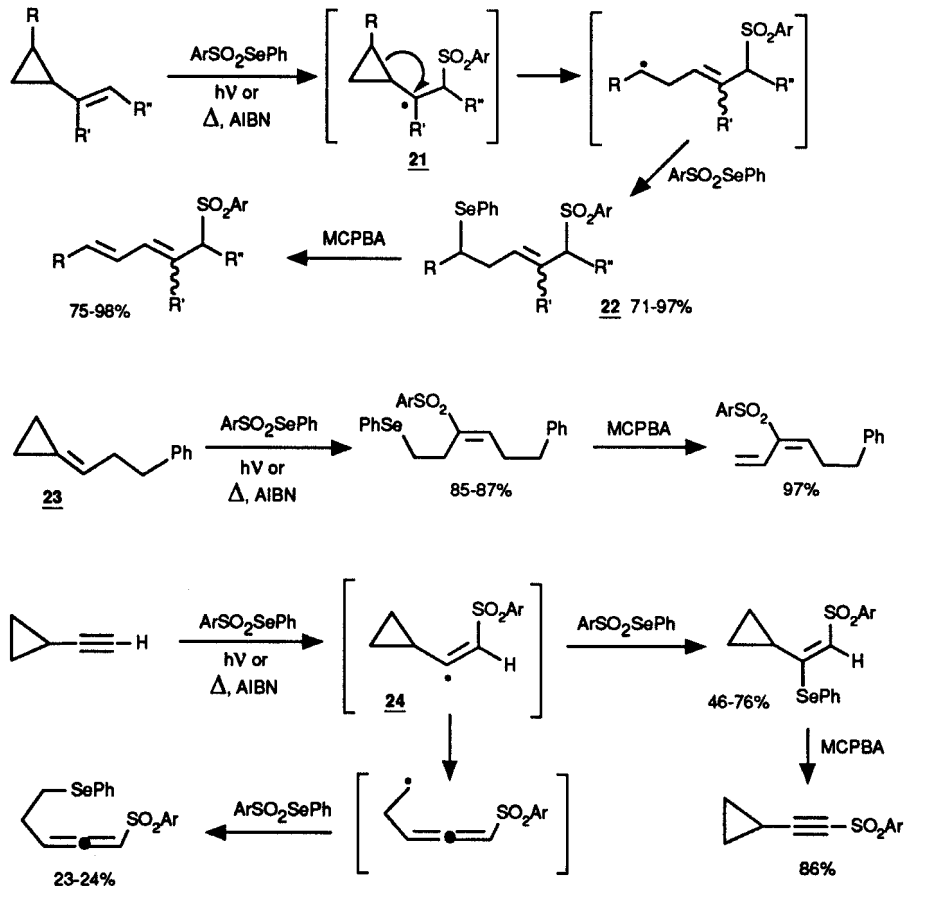
Scheme 8



Selenosulfonation of Vinyl Cyclopropanes

The free-radical selenosulfonation of vinyl cyclopropanes proceeds via cyclopropylcarbinyl radical intermediates 21.[26] These species undergo ring-opening to afford the 1,5-adducts 22 in high yield (Scheme 9). Subsequent selenoxide elimination produces dienyl sulfones that are synthetically useful in Julia olefinations.[27] The rate of ring-opening of cyclopropylcarbinyl radicals has been measured[28] (ca. 1.3×10^8 s^{-1} at 25 °C)[28a] and can be used as a "free-radical clock" against which competing reaction rates can be compared. Since the present reaction affords exclusively 1,5-adducts and not the usual 1,2-adducts, it can be concluded that the rate of chain-transfer is considerably slower than that of ring-opening under the conditions employed.

Scheme 9

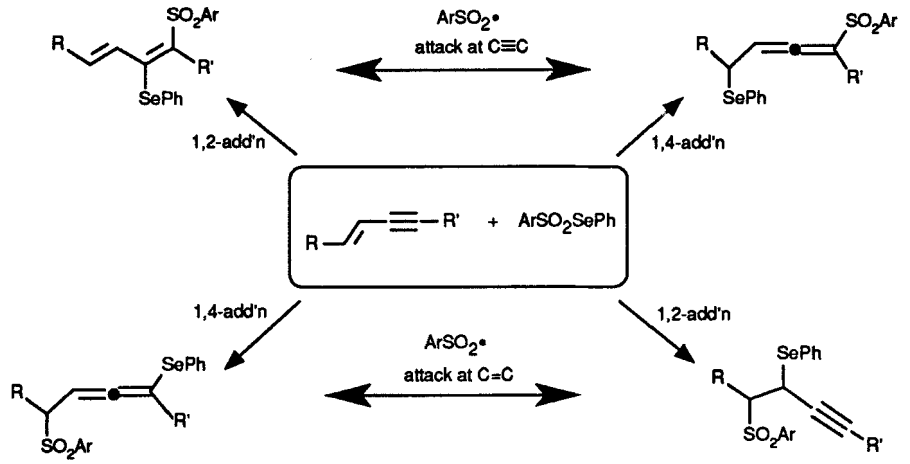


Cyclopropylidene 23 behaved similarly. In contrast, 1,2-addition competed favourably with 1,5-addition in the case of cyclopropylacetylene, with the ratio of the two products dependent upon the concentrations of the reactants. This suggests that either cyclopropylvinyl radicals 24 undergo faster chain-transfer than do cyclopropylcarbinyl radicals 21, or that ring-opening is less facile in 24.

Selenosulfonation of Enynes and Enyne Equivalents

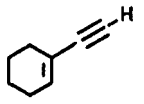
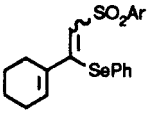
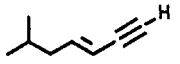
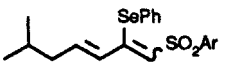
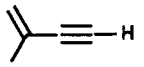
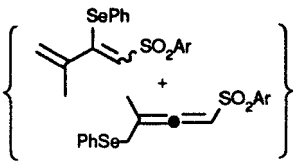
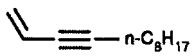
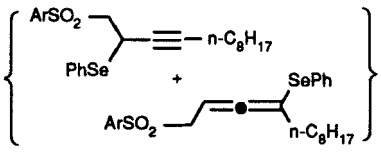
In principle, a conjugated enyne can undergo free-radical selenosulfonation by attack of the sulfonyl radical at the terminus of either the double or triple bond, by either 1,2- or 1,4-addition (Scheme 10). The results of several examples[29] displayed in Table 1 show that addition to enynes with monosubstituted triple bonds results in incorporation of the sulfone moiety exclusively at that terminus, via either 1,2- or 1,4-addition. The reactions are less stereoselective than in the case of simple acetylenes, but still favour anti addition. On the other hand, enynes with terminal double bonds afforded more complex mixtures that included the products of 1,2- and 1,4-addition to the olefin moiety.

Scheme 10

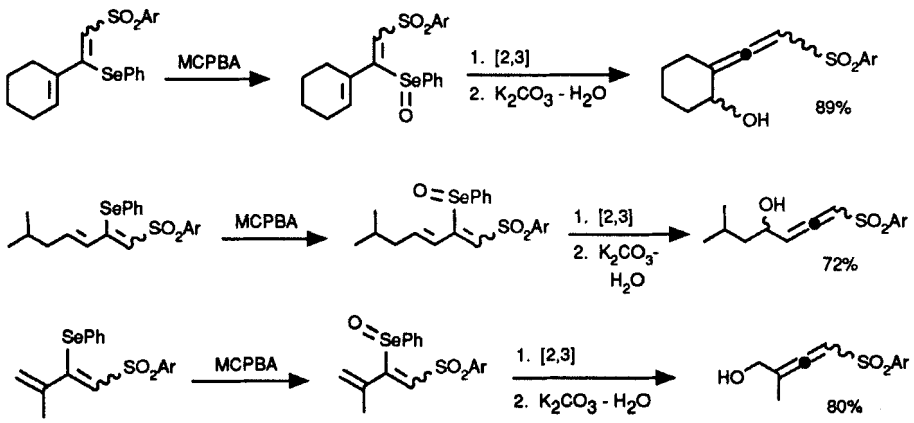


The adducts derived from terminal acetylenes by 1,2-addition are allylic selenides that undergo facile [2,3] sigmatropic rearrangement[30] of the corresponding selenoxides to afford allenic alcohols (Scheme 11). The further elaboration of the products through Diels-Alder reactions of the sulfone-substituted π-bond is an attractive method for preparing highly functionalized cycloadducts.

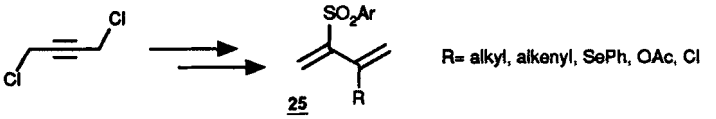
Table 1. Selenosulfonation of Enynes

Enyne	Conditions	Product(s) (Ar= p-tolyl)	Yield % (E:Z ratio)
	C_6H_6, hv		83 (3.8:1)
	$CHCl_3$, AIBN, Δ		92 (8:1)
	$CHCl_3$, AIBN, Δ		22 (1.8:1) 53
	$CHCl_3$, hv		37 10

Scheme 11



1,4-Dichloro-2-butyne acts as the synthetic equivalent of an enyne, since reductive dehalogenation can be used to generate an additional unit of unsaturation. Moreover, selenosulfonation of this internal acetylene should result in the incorporation of the sulfone moiety at the 2-position, rather than at the 1- or 4-positions, as occurred in the case of enynes. We were thus able to devise a protocol for the preparation of a series of 3-substituted 2-(arylsulfonyl)-1,3-dienes 25,[29] a class of compounds of considerable current interest as dienes in Diels-Alder reactions with inverse electron demand.[31]



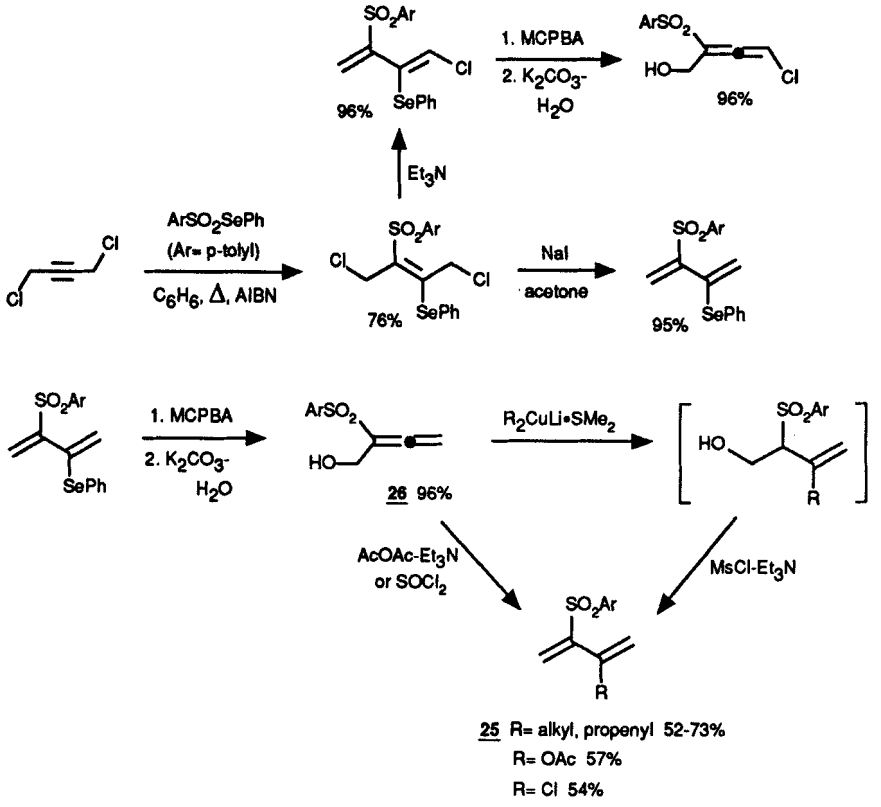
25

The selenosulfonation and further transformations of 1,4-dichloro-2-butyne are shown in Scheme 12. In particular, the allenic alcohol 26 is readily available by this route and affords variously substituted dienes 25 in high yield by the addition of organocuprates to 26, followed by dehydration. Alternatively, the reaction of 26 with acetic anhydride-pyridine or with thionyl chloride produced 25 with R= OAc and Cl, respectively.

REACTIONS OF BENZENESELENENYL p-TOLUENESULFONATE

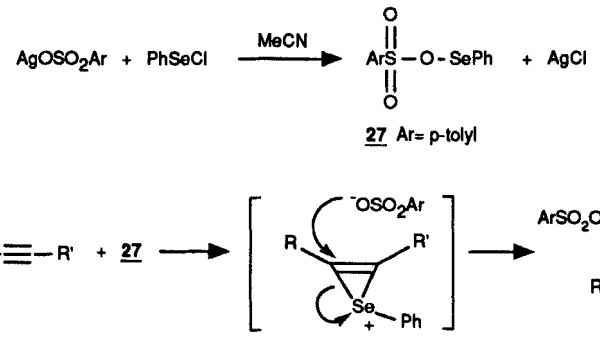
The electrophile 27 was conveniently generated by the reaction of silver tosylate with benzeneselenenyl chloride in acetonitrile. It undergoes anti addition to acetylenes in a highly stereospecific manner, but displays poor regioselectivity, unless a strongly orienting group (e.g. phenyl) is present (Scheme 13; Table 2). The resulting adducts proved remarkably stable towards acids and bases. However, treatment of the mixture of regioisomers 28 and 29 with potassium t-butoxide in THF at 0°C rapidly produced the acetylenic selenide 30, which isomerized to an equilibrium mixture of the propargylic and allenic isomers 31 and 32, formed in the ratio of 6:1. Compound 29 presumably reacts via an ordinary base-catalyzed syn-elimination, while 28 undergoes migration of the PhSe group in a manner reminiscent of the Fritsch-Buttenberg-Wiechell rearrangement[32] (Scheme 14). The selenoxides of these adducts were quite stable, even at elevated temperatures, although the one derived from 28 slowly produced a small amount (ca. 20%) of the corresponding allenic sulfone 33 upon pyrolysis at 85-100°C.

Scheme 12



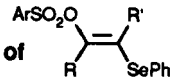
25 R= alkyl, propenyl 52-73%
R= OAc 57%
R= Cl 54%

Scheme 13



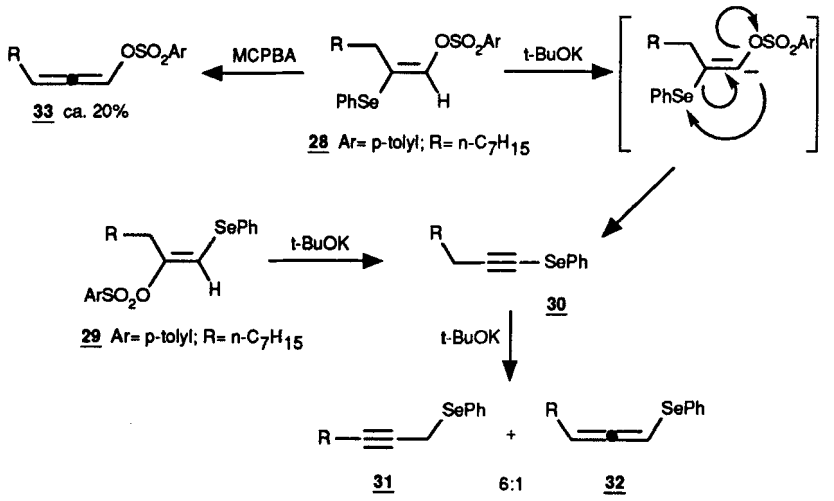
27 Ar= p-tolyl

The selenenyl sulfonate 27 does not form stable adducts with olefins, but is an effective reagent for "cyclofunctionalization" reactions,[33] as illustrated by the examples in Scheme 15.

Table 2. Preparation of  **from R-C≡C-R'**

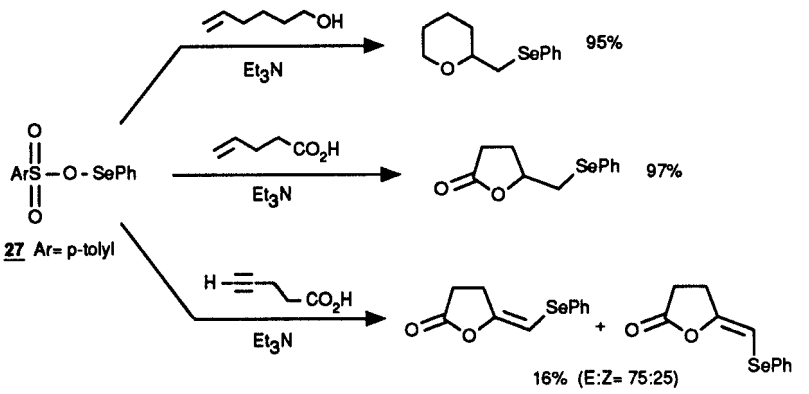
R	R'	Yield (%)
H	H	51
$\left\{\begin{matrix} n\text{-}C_8H_{17} \\ H \end{matrix}\right.$	$\left.\begin{matrix} H \\ n\text{-}C_8H_{17} \end{matrix}\right\}$	81 (57:43)
Ph	H	62
Ph	Me	75
Ph	n-Bu	65
Ph	Ph	60
n-Bu	n-Bu	84
$ClCH_2$	CH_2Cl	80
H	CO_2Me	42
MeO_2C	CO_2Me	25

Scheme 14

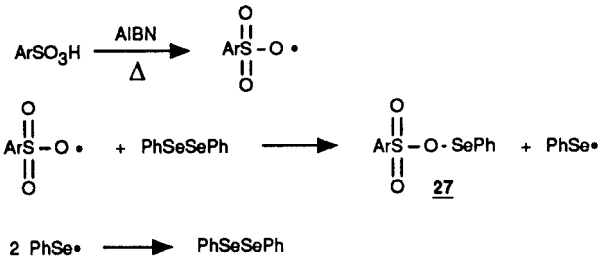


Finally, it is interesting to note that the selenenyl sulfonate 27 was also produced in situ when p-toluenesulfonic acid, diphenyl diselenide and AIBN were refluxed in benzene, or when the sulfinyl sulfone 34 was pyrolyzed in the presence of the diselenide. Evidence for the formation of 27 under these conditions stems

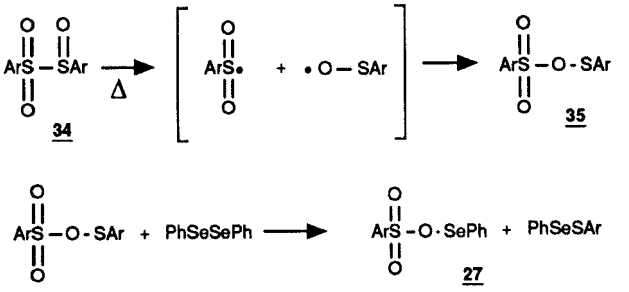
Scheme 15



Scheme 16



Scheme 17



from trapping experiments where the same adducts as shown in Table 2, with essentially identical regioisomer distributions, were produced when these reactions were performed in the presence of acetylenes. In the first case, we postulate that sulfonate radicals ($ArSO_3$•) are produced by hydrogen abstraction from the sulfonic acid by pyrolysis products of AIBN. The sulfonate radicals then react with the

diselenide to produce 27, as shown in Scheme 16. In the second case, the known[34] isomerization of 34 to 35, followed by disproportionation with the diselenide again produces 27, as shown in Scheme 17.

CONCLUSION

Selenosulfonates are readily available and convenient reagents for electrophilic or free-radical additions to olefins, allenes, acetylenes, unsaturated cyclopropanes and enynes. Further manipulation of the selenide moiety of the resulting adducts by elimination, substitution, reduction or rearrangement provides facile access to a host of synthetically useful unsaturated sulfones, including vinyl, dienyl, acetylenic, allenic, and other species. The less known selenenyl sulfonate 27 is easily generated in situ by several methods. It produces 1,2-adducts with acetylenes by electrophilic addition and efficiently induces a variety of "cyclofunctionalization" processes.

I am indebted to the many talented coworkers whose efforts made this work possible. Their names are given in the list of references. We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial support.

REFERENCES

1. For a review of electrophilic selenium reactions, see: T.G. Back, in "Organoselenium Chemistry", edited by D. Liotta (Wiley, New York, 1987), Chap. 1.
2. For a review of free-radical selenium reactions, see: T.G. Back, Ibid., Chap. 7.
3. O. Foss, J. Am. Chem. Soc., 69, 2236 (1947).
4. T.G. Back, S. Collins and M.V. Krishna, Can. J. Chem., 65, 38 (1987).
5. R.A. Gancarz and J.L. Kice, J. Org. Chem., 46, 4899 (1981).
6. T.G. Back and K.R. Muralidharan, J. Org. Chem., 56, 2781 (1991).
7. (a) S. Murata and T. Suzuki, Chem. Lett., 849 (1987). (b) S. Murata and T. Suzuki, Tetrahedron Lett., 28, 4297 and 4415 (1987). (c) R. Okazaki and Y. Itoh, Chem. Lett., 1575 (1987). (d) Y. Ito and T. Ogawa, Tetrahedron Lett., 29, 1061 (1988).
8. M. Yoshida, N. Satoh and N. Kamigata, Chem. Lett., 1433 (1989).
9. T.G. Back and S. Collins, J. Org. Chem., 46, 3249 (1981).
10. J.-E. Bäckvall, C. Nájera and M. Yus, Tetrahedron Lett., 29, 1445 (1988).
11. J.L. Kice and Y.-H. Kang, Tetrahedron, 41, 4739 (1985).
12. (a) T.G. Back, S. Collins and R.G. Kerr, J. Org. Chem., 48, 3077 (1983). (b) T.G. Back, S. Collins, U. Gokhale and K.-W. Law, J. Org. Chem., 48, 4776 (1983). (c) T. Miura and M. Kobayashi, J. Chem. Soc., Chem. Commun., 438 (1982).
13. (a) T.G. Back, S. Collins and K.-W. Law, Can. J. Chem., 63, 2313 (1985). (b) T.G. Back and M.V. Krishna, J. Org. Chem., 52, 4265 (1987).
14. T.G. Back, S. Collins, M.V. Krishna and K.-W. Law, J. Org. Chem., 52, 4258 (1987).
15. T.G. Back, J.R. Proudfoot and C. Djerassi, Tetrahedron Lett., 27, 2187 (1986).

16. For previous examples, see: (a) E. Block and M. Aslam, J. Am. Chem. Soc., 105, 6164 (1983). (b) J.J. Eisch and J.E. Galle, J. Org. Chem., 44, 3279 (1979). (c) V. Sváta, M. Procházka and V. Bakos, Coll. Czech. Chem. Commun., 43, 2619 (1978). (d) D.E. O'Connor and W.I. Lyness, J. Am. Chem. Soc., 86, 3840 (1964). (e) C.D. Broaddus, J. Am. Chem. Soc., 90, 5504 (1968).
17. T.G. Back, M.V. Krishna and K.R. Muralidharan, J. Org. Chem., 54, 4146 (1989).
18. T.G. Back, V.I. Birss, M. Edwards and M.V. Krishna J. Org. Chem., 53, 3815 (1988).
19. M.D. Grove, G.F. Spencer, W.K. Rohwedder, N. Mandava, J.F. Worley, J.D. Warthen, Jr., G.L. Steffens, J.L. Flippen-Anderson and J.C. Cook, Jr., Nature, 281, 216 (1979).
20. T.G. Back and M.V. Krishna, J. Org. Chem., 56, 454 (1991).
21. K. Mori, M. Sakakibara, Y. Ichikawa, H. Ueda, K. Okada, T. Umemura, G. Yabuta, S. Kuwahara, M. Kondo, M. Minobe and A. Sogabe, Tetrahedron, 38, 2099 (1982).
22. B.H. Lipshutz, M. Koerner and D.A. Parker, Tetrahedron Lett., 28, 945 (1987).
23. A.C. Brown and L.A. Carpino, J. Org. Chem., 50, 1749 (1985).
24. (a) K. Mori, M. Sakakibara and K. Okada, Tetrahedron, 40, 1767 (1984). (b) S. Fung and J.B. Siddall, J. Am. Chem. Soc., 102, 6580 (1980).
25. S. Takatsuto, N. Yazawa, M. Ishiguro, M. Morisaki and N. Ikekawa, J. Chem. Soc., Perkin Trans. 1, 139 (1984).
26. T.G. Back and K.R. Muralidharan, J. Org. Chem., 54, 121 (1989).
27. For examples, see: (a) M. Julia and J.-M. Paris, Tetrahedron Lett., 4833 (1973). (b) D. Arnould, P. Chabardes, G. Farge and M. Julia, Bull. Soc. Chim. Fr., 130 (1985).
28. (a) D. Griller and K.U. Ingold, Acc. Chem. Res., 13, 317 (1980). (b) L. Mathew and J. Warkentin, J. Am. Chem. Soc., 108, 7981 (1986).
29. T.G. Back, E.K.Y. Lai and K.R. Muralidharan, J. Org. Chem., 55, 4595 (1990).
30. For a review, see: H.J. Reich in ""Organoselenium Chemistry", edited by D. Liotta (Wiley, New York, 1987), Chap. 8.
31. For examples, see: (a) J.-E. Bäckvall and S.K. Juntunen, J. Am. Chem. Soc., 109, 6396 (1987). (b) J.-E. Bäckvall and F. Rise, Tetrahedron Lett., 30, 5347 (1989). For other cycloaddition reactions of sulfonyl dienes, see: (c) T. Cuvigny, C. Hervé du Penhoat and M. Julia, Tetrahedron, 42, 5329 (1986). (d) T. Chou and S.-C. Hung, J. Org. Chem., 53, 3020 (1988). (e) A. Padwa, B. Harrison, S.S. Murphree, and P.E. Yeske, J. Org. Chem., 54, 4232 (1989).
32. For a review, see: G. Köbrich and P. Buck in "Chemistry of Acetylenes", edited by H.G. Viehe, (Dekker, New York, 1969), Chap. 2, pp. 117-134.
33. (a) D.L.J. Clive, G. Chittattu, N.J. Curtis, W.A. Kiel and C.K. Wong, J. Chem. Soc., Chem. Commun., 725 (1977). (b) D.L.J. Clive, C.G. Russell, G. Chittattu and A. Singh, Tetrahedron, 36, 1399 (1980). For a review, see: (c) K.C. Nicolaou, N.A. Petasis, and D.A. Claremon in "Organoselenium Chemistry", edited by D. Liotta (Wiley, New York, 1987), Chap. 2.
34. J.L. Kice and N.E. Pawlowski, J. Am. Chem. Soc., 86, 4898 (1964).