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Radical Cyclizations of Functionalized Allenes

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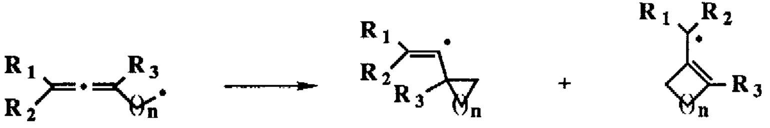
Abstract: *Substitution of* $P(O)Ph_2$, *SOPh, and* SO_2Ph *on an allene facilitates intramolecular radical addition to the central allene carbon to provide good yields of five-, six-, and seven-membered carbocycles.*

Much recent effort has been devoted to the development of free-radical methodology for organic synthesis.[1] Of particular concern are intramolecular processes of unsaturated radicals, especially olefinic and acetylenic species.[1] Relatively little attention has been directed to the chemistry of allenic radicals,[2,3] although we have demonstrated that cyclizations do proceed in favorable cases.[4,5,6] Thus, simple intermediates **2** and/or **3** are generated by cyclization of radicals of type **1** with n = 1 - 4. Reaction at the proximate sp^2 carbon to give **2** is seen with n = 1 and n = 4, and the alternate cyclization to **3** is observed exclusively when n = 2, whereas both cyclization modes operate with the n = 3 case. We now report on related systems bearing radical-stabilizing substituents[7] on the allene moiety, which markedly affect the efficiency, regiochemistry, and scope of the cyclization process.[1,8] The ready availability (*vide infra*) and potential for subsequent synthetic transformation directed our attention to radical precursors of type **4** with Z = $P(O)Ph_2$, SOPh, and SO_2Ph, which were converted to the reactive intermediates **5** using standard tin hydride methodology.[9,10]

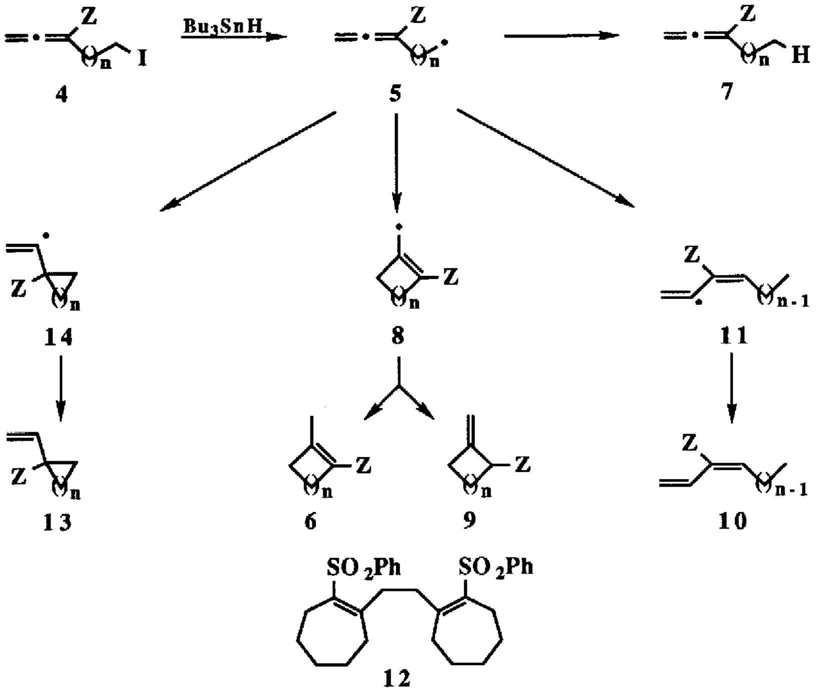


1 **2** **3**

All three of the n = 2 compounds were regioselectively converted to the cyclopentane derivatives **6** (n = 2) (See Scheme and Table). Like the analogous simple allene **1**,[5] these cyclizations were very efficient as indicated by the lack of acyclic allene **7** (n = 2). Interestingly, intermediate allylic radical **8** (n = 2) showed very high selectivity for hydrogen-abstraction at the unsubstituted exocyclic carbon, presumably for steric reasons. Nonetheless, a small amount of the isomeric phosphine oxide **9** was identified with the Z = $P(O)Ph_2$ precursor.

Similar behavior was observed with the n = 3 series, where good isolated yields of cyclohexenes **6** (n = 3) were generated as the only significant products in all cases. The exclusive formation of cyclohexenes in these instances is in striking contrast to the results with simple allenes **1** (n = 3), where five- and six-membered rings were produced competitively. Furthermore, uncyclized allenes **7** (n = 3) which were significant products with the simple allenes were not observed. These results indicate that the substituents Z accelerate cyclization and, moreover, promote radical attack at the central allene carbon. While these phenomena are mainly attributed to electronic effects of the Z groups in the cyclization step, addition to the near sp^2 carbon is also expected to be retarded sterically by substituents at this site.[8,11]

SCHEME



With an additional carbon unit intervening between the two reactive functions in **4** (n = 4), processes competitive with cyclization were seen for the first time. Nonetheless, cycloheptene **6** [n = 4, Z = $P(O)Ph_2$] was present in comparable amounts relative to reduced allene **7** (n = 4) under the usual cyclization conditions. Not only is the degree of cyclization higher than for the corresponding simple allene **1**, but the regiochemistry of addition has been completely changed. In fact, radical cyclizations to give seven-membered rings have only rarely been reported.[1,12] Gratifyingly, the use of a syringe pump to control the slow addition (Method B) of Bu_3SnH to iodide **4** [Z = $P(O)Ph_2$] substantially increased the proportion of cyclic product **6** (n = 4) (See Table). Also observed as products in the n = 4 series were conjugated acyclic dienes **10**,[13] undoubtedly the result of a 1,5-hydrogen shift (**5** → **8**), previously noted as an important process with the simple allenes.[5] Unfortunately, a radical-chain process under these very dilute conditions was not sustainable with the analogous sulfoxide **4** (n = 4, Z = SOPh). However, the corresponding sulfone **4** (n = 4, Z = SO_2Ph) is very efficiently cyclized, since acyclic allene **9** was not seen under dilute conditions, although conjugated diene **10** was detected in minor amounts. Surprisingly, the cyclization product in this case consisted of the two isomeric sulfones **6** and **9** derived from the intermediate allylic radical **8**, with the nonconjugated sulfone **9** being present in larger proportions than hitherto seen.[14] Another interesting minor component in this reaction was dimer **12**,[15] apparently derived from dimerization of radical **8** (n = 4) under the very dilute conditions. The above results are remarkable in that seven-membered carbocycles can be obtained in synthetically useful yields by a radical-cyclization process.[12]

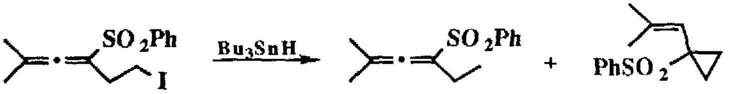
Table: Reduction of Allenyl Iodides 4 with Bu_3SnH

Iodide 4		Method[10]	Products[a,b]				
n	Z		7	13	6	9	10
1	$P(O)Ph_2$	A	50				
1	SO_2Ph	A		4			
2	$P(O)Ph_2$	A			79	3	
2	$S(O)Ph$	A			69		
2	SO_2Ph	A			70		
3	$P(O)Ph_2$	A			85		
3	$S(O)Ph$	A			72		
3	SO_2Ph	A			81		
4	$P(O)Ph_2$	A	(42)		39 (47)		(11)
4	$P(O)Ph_2$	B	7 (15)		49 (72)		(13)
4	SO_2Ph	B			30 (65)	4(20)	(8)[c]
5	$P(O)Ph_2$	B	51(95)				(5)
5	SO_2Ph	B	(83)		(7)		(10)

[a] ^1H NMR showed ≤ 5% of any other product. [b] Isolated yields; relative product distribution in parenthesis.
[c] Dimer **12** was 7% of the mixture.

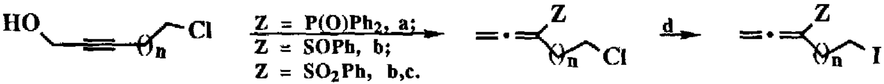
Several experiments with the n = 5 systems show that cyclization to provide eight-membered rings does not occur in a useful manner. Hence, no cyclic products were found with **4** [Z = $P(O)Ph_2$], which gave allene **7**, plus a few percent of acyclic diene **10** from 1,6-hydrogen transfer.[13] The sulfone analog gave similar products, but, in this case, a small amount (7%) of cyclic product was ascertained by comparison with an authentic sample of cyclooctene **6** (n = 5).[1]

Finally, a brief examination of the n = 1 case was conducted. With phosphine oxide **4** (n=1) the reduced allene **7** was the major material formed, along with uncharacterized tributyltin-containing products. The corresponding sulfone (**4**, Z = SO_2Ph) gave a 2:1 mixture of allene **7** and 1-vinylcyclopropylsulfone **13** (via intermediate radical **14**) in addition to a plethora of other products, some of which incorporate the tributyltin group. In order to minimize organotin products (presumably derived from free-radical addition to the products), the reduction of tetrasubstituted allene **15** was examined under similar conditions. In this case, a 2:1 mixture of allene **16** and cyclopropane **17** was formed in 71% yield. This cyclization parallels that found for the simple allene **1** (n = 1),[4] and provides the only instance in this work where radical attack was observed at the proximate sp^2 allene carbon. This result is not surprising considering the geometrical factors involved with this system, which favor three- over four-membered ring formation.[1,8]



15 **16** **17**

In conclusion, the substituents $P(O)Ph_2$, SOPh, and SO_2Ph facilitate the cyclization of allenyl radicals so that five-, six-, and even seven-membered rings are generated regioselectively with reasonable efficiency. Moreover, these substituents are of potential value in subsequent synthetic transformations of the cyclization products.



18 **19** **4**

(a) Ph_2PCl, Et_3N / CH_2Cl_2. (b) PhSCl, Et_3N / CH_2Cl_2. (c) MCPBA / CH_2Cl_2. (d) NaI / acetone.

In general, the starting materials for the cyclization studies were prepared from the readily available propargyl alcohols **18** by a 2,3-sigmatropic rearrangement process with Ph_2PCl[17] or PhSCl[18] in the presence of base. The sulfoxides were smoothly oxidized to sulfones with MCPBA.[19] Treatment of chlorides **19** with sodium iodide gave the desired allenes **4**.[20]

REFERENCES AND NOTES

1. (a) Curran, D. P. *Synthesis* **1988**, 417, 489. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, **1986**. (d) Surzur, J.-M. in *Reactive Intermediates*, Vol. 2; Abramovitch, A.R.; Ed.; Plenum Press, New York, **1982**.
2. For a leading reference to intermolecular radical additions to allenes, see: Pasto, D. J.; L'Hermine, G. *J. Org. Chem.* **1990**, *55*, 685.
3. (a) Burnett, D. A.; Choi, J.-K.; Hart, D. J.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1984**, *106*, 8201. (b) Arseniyadis, S.; Gore, J.; Laurent, A.; Roumestant, M.-L. *J. Chem. Res. (S)* **1978**, 416.
4. Crandall, J. K.; Tindell, G. L.; Manmade, A. *Tetrahedron Lett.* **1982**, *23*, 3769.
5. Apparu, M.; Crandall, J. K. *J. Org. Chem.* **1984**, *49*, 2125.
6. For related radical-anion cyclizations see (a) Crandall, J. K.; Mualla, M. *Tetrahedron Lett.* **1986**, *27*, 2243. (b) Pattenden, G.; Robertson, G. M. *Tetrahedron* **1985**, *41*, 4001. (c) Pattenden, G.; Robertson, G. M. *Tetrahedron Lett.* **1983**, *24*, 4617.
7. For recent examples where the sufonyl functionality is used as a radical-stabilizing substituent, see: (a) Sundberg, R. J.; Cherney, R. J. *J. Org. Chem.* **1990**, *55*, 6028. (b) Barton, D. H. R.; da Silva, E.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.* **1988**, 285.
8. For theoretical studies on the analogous 5-hexenyl radical cyclization, see (a) Park, S.-U.; Chung, S.-K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240. (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (c) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. (d) Beckwith, A. L. J.; Ingold, K. U. in *Rearrarrangements in Ground and Excited States*, Vol. 1; de Mayo, P.; Ed.; Academic Press, New York, **1980**, pp. 162-283.
9. (a) Kuilvila, H. G. *Adv. Organometallic Chem.* **1964**, *1*, 47. (b) Kuivila, H. G. *Synthesis* **1970**, 499.
10. Radicals **5** were generated by: Method A involved dropping-funnel addition of a 0.07 M solution of Bu_3SnH containing 10 mole-percent AIBN to a 0.07 M solution of iodide **4** in refluxing benzene over 1-3 hours; Method B involved the same concentrations of materials except a syringe pump was employed for slower Bu_3SnH addition (14-18 hours).
11. Placement of a methyl group at the near sp^2 carbon alters the regiochemistry of cyclization for simple allenes **1** (n = 3), analogously to the 5-hexenyl radical cyclization.[8] For example the ratio of five- to six-membered ring formation is 0.3 for $R_1 = R_2 = H$, $R_3 = CH_3$; 1.5 for $R_1 = R_2 = R_3 = H$; and 2.6 for $R_1 = R_2 = CH_3$, $R_3 = H$. (Ref. 5 and Krom, J.; Mennen, K. E. Unpublished results).
12. (a) Curran, D. P.; Chang, C.-T. *J. Org. Chem.* **1989**, *54*, 3140. (b) Sato, T.; Ishida, S.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. I* **1991**, 353. (c) Bachi, M. D.; Frolow, F.; Hoornaert, C. *J. Org. Chem.* **1983**, *48*, 1841.
13. Samples of dienes **10** [n = 4, Z = $P(O)Ph_2$ or SOPh] were synthesized using an adaptation of the known 2,3-sigmatropic rearrangement process[17,18] by treating 2,3-octadien-1-ol with Ph_2PCl or PhSCl in the presence of Et_3N. Oxidation of the sulfoxide to the sulfone was accomplished using MCPBA.[19] This synthesis provided a separable mixture of easily assignable *E*- and Z-isomers of **10**. Interestingly, only the *E*-isomer was observed in the Bu_3SnH reduction of **4** (n = 4 and 5). Dienes **10** (n = 5) were assigned by analogy to dienes **10** (n = 4).
14. In this instance, Curran's DBU procedure was employed for the removal of organotin residues.[12a]
15. Dimer **12** showed: ^1H NMR δ 7.87 (m, 4), 7.60-7.51 (m,6), 2.95 (s, 4), 2.55 (m, 8), 1.70 (m, 4), 1.54 (m, 4), 1.31 (m, 4); ^{13}C NMR δ 158.8, 141.7, 137.2, 132.8, 129.0 (2), 127.0 (2), 37.0, 34.5, 31.8, 29.8, 25.8, 25.2; FTIR ($CDCl_3$) 1620, 1296, 1144 cm^{-1}; MS m/z (rel. intensity) 498 (2), 357 (28), 249 (10), 216 (22), 215 (100).
16. Cyclooctene **6** (n = 5) was prepared by treating cyclooctanone with LDA and PhSSPh; followed by CH_3MgBr, MCPBA, and MsCl / Et_3N. A mixture of three isomeric olefins was obtained from which **6** was isolated. ^1H NMR δ 7.87 (m, 2), 7.56 (m, 1), 7.51 (m, 2), 2.59 (m, 2), 2.29 (m, 2), 2.19 (s, 3) 1.63 (m, 4), 1.45 (m, 4); ^{13}C NMR δ 151.8, 142.5, 135.8, 132.7, 128.9 (2), 127.2 (2), 36.7, 30.4, 28.5, 28.1, 26.3, 25.9, 20.6; FTIR ($CDCl_3$) 1623, 1299, 1153, 1084 cm^{-1}.
17. (a) Ayed, N.; Baccar, B. *Phosphorous and Sulfur* **1985**, *21*, 335. (b) Boisselle, A. P.; Meinhardt, N. A. *J. Org. Chem.* **1962**, *27*, 1828. (c) Khusainova, N. G.; Pudovik, A. N. *Russ. Chem. Rev.* **1987**, *56*, 564.
18. (a) Wu, K.-M.; Midland, M.; Okamura, W. H. *J. Org. Chem.* **1990**, *55*, 4381. (b) VanRheenen, V.; Shephard, K. P. *J. Org. Chem.* **1979**, *44*, 1582. (c) Smith, G.; Stirling, C. J. M. *J. Chem. Soc. C* **1971**, 1530. (d) Horner, L.; Binder, V. *Liebigs Ann. Chem.* **1972**, *757*, 33. (e) Evans, D.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.
19. Shen, G.-Y.; Tapia, R.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 7499.
20. All new compounds except where noted above were fully characterized after isolation by flash chromatography or HPLC by ^1H and ^{13}C NMR, IR, and mass-spectral or combustion analysis.

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