Selenium-Stabilized Anions.[1] Preparation of α,β-Unsaturated Carbonyl Compounds Using Propargyl Selenides. Synthesis of (±)-7-Hydroxymyoporone[2]

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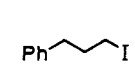
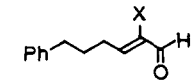
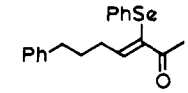
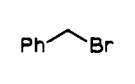
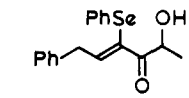
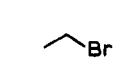
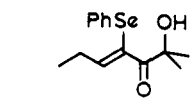
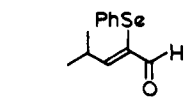
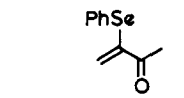
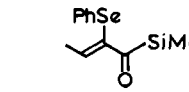
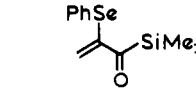
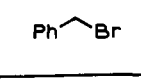
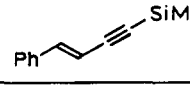
Abstract: The reaction of alkyl halides, carbonyl compounds, and trimethylsilyl chloride with the mono- and dianion (**1**) prepared by deprotonation of phenyl propargyl selenide with lithium diisopropylamide gives 1- or 3-monosubstituted or 1,3-disubstituted propargyl selenides (**3a**). Oxidation to selenoxides (**3b**) results in rearrangement to 2-(phenylseleno)-1,3-disubstituted propenones. The rate of rearrangement of propargyl selenoxides increases dramatically when the phenyl group is replaced by a 2-nitrophenyl group, and an intermediate allenyl selenate ester (**7c**) can be observed by low-temperature NMR. By appropriate modification of oxidation conditions, modest yields of 2-iodopropenones (e.g., **10**) or the selenium-free enones or enals can be obtained. A synthesis of (±)-7-hydroxymyoporone (**15**) and its epimer has been carried out by using the dianion **1** to assemble the carbon skeleton. The preparation of α-lithioallenyl phenyl selenide (**26**) has been accomplished, and its reaction with electrophiles has been studied.

Propargyl- and allenyllithium reagents have become increasingly important as synthetic reagents for the introduction of complex functionality. These include a variety of allenic and propargylic ethers[3] and thioethers.[3f,g,4]. Since many selenium-substituted carbanions can be conveniently prepared by deprotonation of selenides and selenoxides,[1,5] we undertook the study of lithium reagents from propargyl and allenyl selenides. It was anticipated that the products from reaction of such lithium reagents with electrophiles could be transformed to useful selenium-free materials by cleavage of the Se–C bond under oxidative or reductive conditions.[6]

Allylic selenoxides readily undergo [2.3] sigmatropic rearrangements,[1d,7] and adequate precedents exist in sulfur chemistry[8] that propargylic and allenic selenoxides will undergo similar rearrangements.

Table I. Oxidation Products of Mono- and Disubstituted Propargyl Selenides (Scheme I)

RUN NO.	RX	E	PRODUCT[a]	YIELD[b] %
		H_2O		
1			X = SePh	68[c]
2			X = H	38[d]
3		CH_3I[e]		59[f]
4				61[c]
5				59[f]
6		H_2O		60[f]
7	g	CH_3I[e]		61[f]
8	CH_3I	Me_3SiCl		42[f,h]
9	g	Me_3SiCl		56[f]
10		Me_3SiCl		38[f]

[a] Mixtures of cis-trans isomers were usually formed. [b] Yields are based on phenyl propargyl selenide. [c] Oxidant: ozone in CH_2Cl_2. [d] Oxidant: H_2O_2 in methanol. [e] Methylation in THF-HMPA (2 equiv) at 25 °C. [f] Oxidant: *m*-chloroperbenzoic acid in CH_2Cl_2. [g] The monoanion (**2**, R = H) of phenyl propargyl selenide (LiNH-*i*-Bu, THF, 78 °C). [h] 1-(Trimethylsilyl)but-3-en-1-yne was also formed.

(1) For previous papers in this series see: (a) H. J. Reich, S. K. Shah, and F. Chow, *J. Am. Chem. Soc.*, **101**, 6648 (1979); (b) *ibid.*, **101**, 6638 (1979); (c) H. J. Reich and S. K. Shah, *ibid.*, **97**, 3250 (1975); (d) H. J. Reich, *J. Org. Chem.* **40**, 2570 (1975); (e) H. J. Reich, J. M. Renga, and I. L. Reich, *ibid.*, **39**, 2133 (1974); (f) H. J. Reich and M. L. Cohen, *J. Am. Chem. Soc.*, **101**, 1307 (1979).

(2) These results were taken in part from the Ph.D. Thesis of S. K. Shah and were reported in preliminary form: (a) H. J. Reich and S. K. Shah, *J. Am. Chem. Soc.*, **99**, 263 (1977); (b) H. J. Reich, P. M. Gold, and F. Chow, *Tetrahedron Lett.*, 4433 (1979).

(3) (a) S. Hoff, L. Brandsma, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **87**, 916, 1179 (1968); (b) Y. Leroux and C. Roman, *Tetrahedron Lett.*, 2585 (1973); (c) M. Huche and P. Cresson, *ibid.*, 367 (1975); (d) F. Mercier, R. Epsztein, and S. Holand, *Bull. Soc. Chim. Fr.*, 690 (1972); (e) F. Mercier, N. LeGoff, and R. Epsztein, *C.R. Hebd. Seances Acad. Sci., Ser. C*, **279**, 525 (1974); (f) R. M. Carlson and J. L. Isidor, *Tetrahedron Lett.*, 4819 (1973); (g) R. M. Carlson, R. W. Jones, and A. S. Hatcher, *ibid.*, 1741 (1975); (h) E. J. Corey and S. Terashima, *ibid.*, 1815 (1972); (i) J. C. Clinet and G. Linstrumelle, *ibid.*, 1137 (1978); (j) D. Gange and P. Magnus, *J. Am. Chem. Soc.*, **100**, 7746 (1978); (k) Y. Leroux and R. Mantione, *Tetrahedron Lett.*, 591 (1971); *J. Organomet. Chem.*, **30**, 295 (1971).

(4) (a) L. Brandsma, C. Jonker, and M. H. Berg, *Recl. Trav. Chim. Pays-Bas*, **84**, 560 (1965); (b) A. Schaap, L. Brandsma, and J. F. Arens, *ibid.*, **86**, 393 (1967); (c) W. Kreiser and H. Wurziger, *Tetrahedron Lett.*, 1669 (1975).

(5) L. Christiaens, R. Dufour, and M. Renson, *Bull Soc. Chim. Belg.*, **79**, 143 (1970); J. Morel, C. Paulmier, D. Semard, and P. Pastour, *C.R. Hebd. Séances Acad. Sci., Ser. C*, **270**, 825 (1970); D. Seebach and N. Peleties, *Chem. Ber.*, **105**, 511 (1972); *Angew. Chem., Int. Ed. Engl.*, **8**, 450 (1969); K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973); R. H. Mitchell, *J. Chem. Soc., Chem. Commun.*, 990 (1975); P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 120 (1974); P. A. Grieco and Y. Yokoyama, *J. Am. Chem. Soc.*, **99**, 5210 (1977); P. A. Grieco, M. Nishizawa, T. Oguri, S. D. Burke, and N. Marinovic, *ibid.*, **99**, 5773 (1977); K. Sachdev and H. S. Sachdev, *Tetrahedron Lett.*, 4223 (1976); 814 (1977); S. Raucher and G. A. Koolpe, *J. Org. Chem.*, **43**, 3794 (1978); M. Sevrin, J. N. Denis, and A. Krief, *Angew. Chem.*, **90**, 550 (1978).

(6) For several review articles on synthetic applications of organoselenium reagents see: (a) H. J. Reich in "Oxidation of Organic Compounds", Part C, W. Trahanovsky, Ed., Academic Press, New York, 1978, p 1. (b) H. J. Reich, *Acc. Chem. Res.*, **12**, 22 (1979); (c) D. L. J. Clive, *Tetrahedron*, **34**, 1049 (1978).

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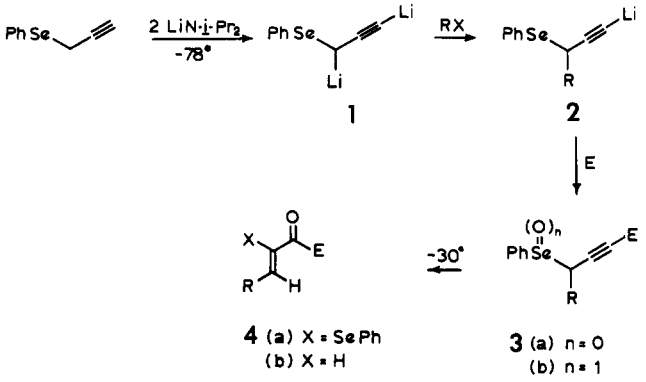
Scheme I



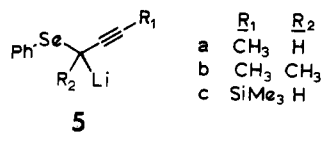
Results and Discussion

Deprotonation and Reactions of Phenyl Propargyl Selenide. Phenyl propargyl selenide is rapidly deprotonated by 1 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran or glyme at −78 °C to give the acetylenic anion **2** (R = H) and by 2 equiv of LDA to give a pale yellow solution of the dilithium reagent **1**. Polylithium reagents derived from a variety of acetylenes including alkoxy-[3k] and thio-substituted[4c] ones have been prepared previously.[9]

The dianion **1** is a powerful nucleophile as can be seen from the results in Table I. The reaction with primary bromides and iodides proceeds at −78 °C and with isopropyl iodide at −40 °C. Alkyl halides react with **1** at the α-position. Careful examination of the product from reaction of **1** with methyl iodide showed that greater than 99.5% of α-methylation results. Epoxides also react with **1** but higher temperatures and/or longer reaction times are necessary. The reactions of **1** with more reactive electrophiles like ketones and chlorosilanes are not as selective.

The monolithium reagents **2** which are the products of the alkylation of **1** can be treated with a second electrophile. Table I presents examples where **2** was alkylated, silylated, protonated, and hydroxyalkylated to give a variety of 1,3-disubstituted propargyl selenides **3a**. Although **2** can be sulfenylated with MeSSMe, it could not be cleanly sulfenylated with PhSSPh. More rapid base-catalyzed isomerization due to the greater acidifying effect of the phenylthio group might be responsible for this. Selective oxidation of selenium in the methylsulfenylated product could not be achieved.

The acetylenic lithium reagent **2** (R = H) can be prepared from phenyl propargyl selenide by treatment with 1 equiv of LDA or more conveniently with lithium isobutylamide at −78 °C. We have also prepared lithium reagents **5a**, **5b**, and **5c** by using LDA in



	R_1	R_2
a	CH_3	H
b	CH_3	CH_3
c	$SiMe_3$	H

5

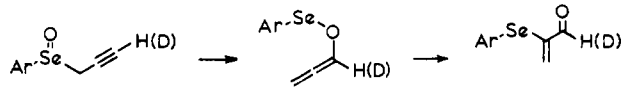
THF (−78 °C for 5–10 min). Methylation of **5a** occurs >97% α. Less regioselectivity is seen for **5b** although predominantly α-methylation occurs here also.

Oxidation of the propargyl selenides **3a** leads to selenoxides **3b**. When these are warmed above −30 °C, they rearrange to the α-(phenylseleno) enones **4a**. This isomerization will be discussed in more detail below. The initially formed product **4a** is a cis–trans mixture which can be converted into the pure *Z* isomer by stirring with pyridine in methanol.

A number of oxidizing conditions for the conversion of propargyl selenides (**3a**) to the selenoxides (**3b**) have been tried. *m*-Chloroperbenzoic acid and ozone have been the most useful. In neither case is oxidation of the acetylenic function a significant problem, provided oxidation is performed at low temperature and approximately stoichiometric amounts of reagents are used.

Table I summarizes the enones that have been prepared by using the method outlined in Scheme I. The unique capability of forming two bonds in a one-pot reaction can be used to assemble some unusual functional group combinations. The ability to easily prepare α′-hydroxy α,β-unsaturated ketones (runs 4 and 5) has been used as a key step in the synthesis of 7-hydroxymyoporone and its epimer below. Also noteworth is the ability to prepare vinyl silyl ketones (runs 8 and 9), for which few other routes have been reported.[3k,10] Unfortunately, the present procedure is flawed by the tendency of the silylated propargyl selenoxides to undergo syn elimination in competition with [2.3] sigmatropic rearrangement. This is because the trimethylsilyl substituent strongly retards the rearrangement. From approximate rate measurements on **3b** (R = H, E = $SiMe_3$) we estimate that it isomerizes at least a factor of 175 slower than the parent selenoxide **6a**. It is not known whether steric or electronic effects predominate, but the result is that compound **3b** (E = Me_3Si, R = CH_2Ph) gives enyne as the major product. Here, the syn elimination is especially favored by the conjugating phenyl substituent.[11a] For compound **3b** (E = Me_3Si, R = CH_3, run 8) approximately equal amounts of rearrangement (the silyl enone) and syn elimination product are observed. Competition between syn elimination and [2.3] sigmatropic rearrangement has also been reported for allyl selenoxides.[1d,7d,e]

Rearrangement of Phenyl Propargyl Selenoxide. Phenyl propargyl selenoxide (**6a**) like other allylic selenoxides is stable only



6 a Ar = C_6H_5
b Ar = m-$CF_3C_6H_4$
c Ar = o-$NO_2C_6H_4$

7 **8**

at low temperature. Ozonolysis of phenyl propargyl selenide at −78 °C cleanly gives the selenoxide, as shown by the presence of diastereomeric methylene protons in the NMR spectrum.[2a] Above −35 °C a clean isomerization to α-(phenylseleno)acrolein (**8a**) occurs. No intermediates or byproducts can be detected by NMR. The rearrangement was found to follow first-order kinetics with a rate constant $k_{obsd} = 6.2 \times 10^{-5}$ s^{-1} at −31 °C. The rate of formation of **8a** is the same as the rate of disappearance of **6a**. The transformation appears to be a slow [2.3] sigmatropic rearrangement to give **7a**, followed by a rapid isomerization of **7a** to **8a**. The *m*-(trifluoromethyl)phenyl-substituted selenoxide **6b** rearranges about 1.6 times as fast as **6a**. This can be compared to the rate acceleration (factor of 1.7) observed for the selenoxide syn elimination of *m*-(trifluoromethyl)phenyl alkyl selenoxides[11a] and the [2.3] sigmatropic rearrangement (factor of 3.26) of *p*-(trifluoromethyl)phenyl allyl sulfoxides[11b] compared to the phenyl analogues.

The isomerization is at least partially intermolecular as shown by a crossover experiment. When a mixture of **6b** and deuterated

(7) (a) K. B. Sharpless and R. F. Lauer, *J. Org. Chem.*, **37**, 3973 (1972); (b) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **94**, 7154 (1972); (c) K. B. Sharpless and R. F. Lauer, *ibid.*, **95**, 2697 (1973); (d) W. G. Salmond, M. A. Barta, A. M. Cain, and M. C. Sobala, *Tetrahedron Lett.*, 1683 (1977); (e) H. J. Reich, I. L. Reich, and S. Wollowitz, *J. Am. Chem. Soc.*, **100**, 5981 (1978).

(8) (a) K. C. Majumdar and B. S. Thyagarajan, *J. Chem. Soc., Chem. Commun.*, 83 (1972); Y. Makisumi and S. Takada, *ibid.*, 848 (1974); (b) M. Cinquini, S. Colonna, and C. J. M. Stirling, *ibid.*, 256 (1975); R. C. Cookson and P. J. Parsons, *ibid.*, 822 (1978).

(9) (a) J. Klein and S. Brenner, *Tetrahedron*, **26**, 2345 (1970); (b) T. L. Chwang and R. West, *J. Am. Chem. Soc.*, **95**, 3324 (1973); (c) L. Brandsma and E. Mugge, *Recl. Trav. Chim. Pays-Bas*, **92**, 628 (1973); (d) N. M. Libman, V. I. Zlobina, and S. G. Kuznestov, *Zh. Org. Khim.*, **10**, 2057 (1974); (e) A. J. Quillinan, E. A. Khan, and F. Scheinmann, *J. Chem. Soc., Chem. Commun.*, 1030 (1974); S. Bhanu and F. Scheinmann, *ibid.*, 817 (1975).

(10) A. Hassner and J. A. Soderquist, *J. Organomet. Chem.*, **131**, C1 (1977); J. A. Soderquist and A. Hassner, *J. Am. Chem. Soc.*, **102**, 1577 (1980). N. Minami, T. Abe, and I. Kuwajima, *J. Organomet. Chem.*, **145**, C1 (1978).

(11) (a) H. J. Reich, S. Wollowitz, J. E. Trend, F. Chow, and D. F. Wendelborn, *J. Org. Chem.*, **43**, 1697 (1978); (b) R. Tang and K. Mislow, *J. Am. Chem. Soc.*, **92**, 2100 (1970).

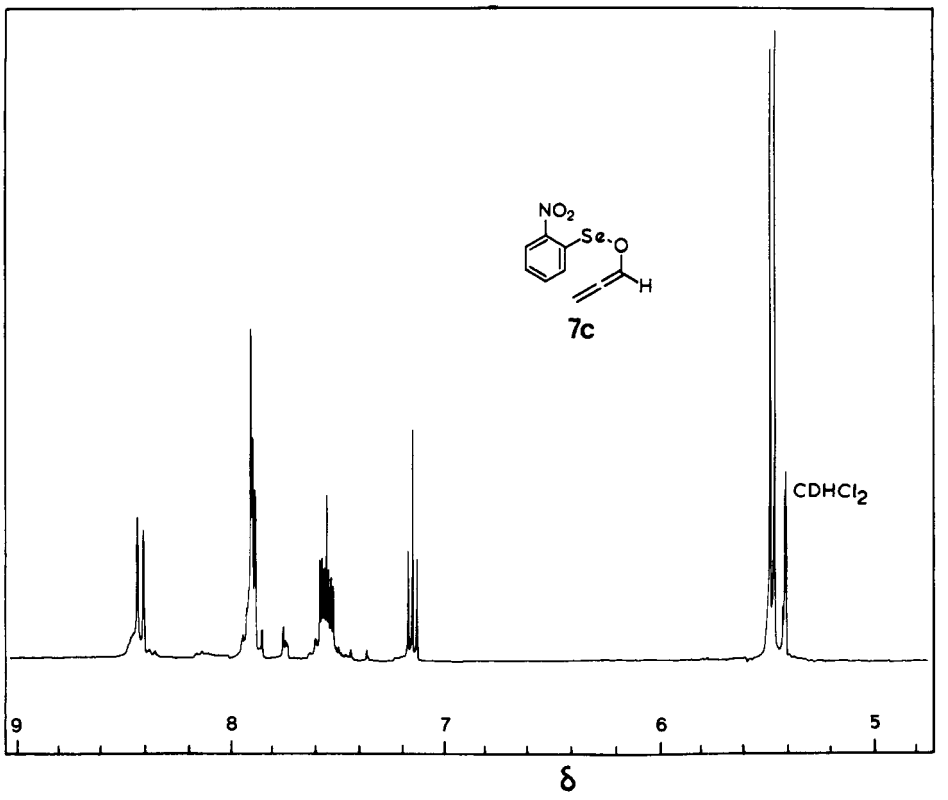


Figure 1. Proton NMR spectrum (270 MHz) of **7c** at −45 °C in CD_2Cl_2.

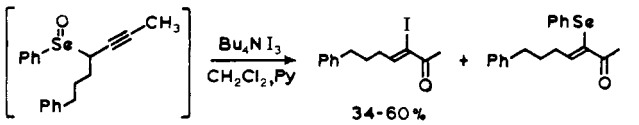
6a was allowed to rearrange, 30% of undeuterated **8a** was formed. Presumably the selenenate is hydrolyzed, and the allenol so formed is selenenylated. Powerful electrophilic selenium species are generated during selenoxide syn eliminations.[11a] A similar selenenylation of enols has been observed when some α-(phenylseleno) ketones are oxidized.[12]

Direct evidence for the intermediacy of allenol selenenate esters was provided by study of the *o*-nitrophenyl propargyl selenoxide (**6c**). This compound is much less stable than **6a** or **6b** ($t_{1/2} \approx$ 33 min at −50 °C) and isomerizes about 150 times as fast as does **6a**. This isomerization gives a new substance which has been identified as the allene **7c** from its low-temperature NMR spectrum (Figure 1) and characteristic IR absorption at 1950 cm^{-1} (compare 1956 cm^{-1} for alkyl allenyl ethers). The allene is stable to approximately −10 °C; at higher temperature it rearranges to an aldehyde **8c** identical with material prepared by reaction of allenyl 1-ethoxyethyl ether with *o*-nitrobenzeneselenenyl chloride. This aldehyde (**8c**) has some unusual NMR properties. At −45 °C the vinyl protons are at lower field (δ 7.33 and 7.40, compared with δ 5.81 and 6.44 for **8a**) than the aromatic proton ortho to selenium (δ 7.18). On being warmed to 25 °C these resonances exchange positions (vinyl at δ 7.17 and 7.19, aryl at δ 7.23).

The increased stability of the ortho–nitro-substituted selenenate ester is not unexpected. Selenenic acids and their alkyl esters[13] as well as sulfenic acid derivatives are very much stabilized toward disproportionation and hydrolysis by the introduction of *o*-nitro groups on the arylseleno or arylthio group.

Attempts To Trap Allenyl Selenenates with Electrophiles. The discovery that the phenylseleno group in **4a** was introduced by an intermolecular reaction suggested that it might be possible to trap the intermediate allenol with other electrophiles. We were encouraged in these efforts by the observation that when **6a** was allowed to rearrange in the presence of excess 3,3′-bis(trifluoromethyl)diphenyl diselenide, an 85:15 mixture of **8a** and **8b** was obtained. Although a number of other trapping reagents were tried, only two were somewhat successful—protonation and iodination.

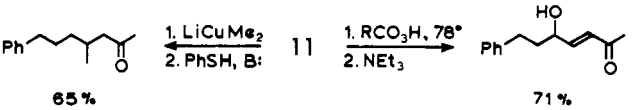
When several of the propargyl selenides were oxidized with hydrogen peroxide in methanol, moderate yields of selenium-free enones **4b** could be isolated (see Table I). Alternatively, if the selenoxide **9** was allowed to warm slowly from −50 to 0 °C in the



9 10 11

presence of pyridine and excess *n*-$Bu_4N^+I_3^-$ a cis–trans mixture of an α-iodoenone **10** is formed, together with lesser amounts of α-(phenylseleno) enone **11**. The iodination was somewhat capricious, and conditions which would reliably convert a variety of propargyl selenides could not be found. A more satisfactory synthesis of certain α-iodo enones using allenyl trimethylsilyl ethers has recently been developed.[14]

Transformations of α-(Phenylseleno) Enones. A number of further transformations of the easily available α-(phenylseleno) enones **4a** have been tried. Addition of dimethyl cuprate is



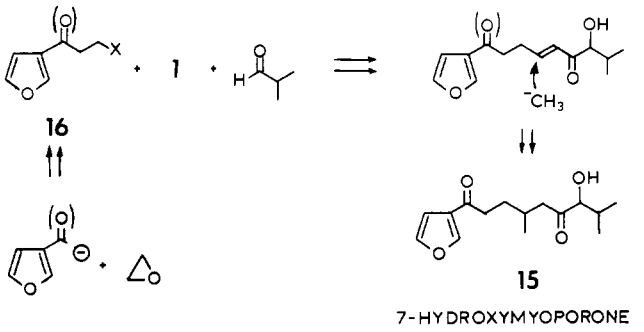
successful but some deselenation occurs. The deselenation can be completed by addition of benzenethiol or benzeneselenol. Oxidation of **11** to the selenoxide at low temperature followed by warming in the presence of triethylamine gives a γ-hydroxy enone. Presumably α,β- to β,γ-double bond isomerization followed by [2.3] sigmatropic shift occurs. Allylic selenoxides are reported to undergo a rapid [2.3] sigmatropic rearrangement.[1d,7] Similar

(12) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975).

(13) H. Rheinboldt and E. Giesbrecht, *Chem. Ber.*, **89**, 631 (1956); **88**, 666, 1037, 1974 (1955); G. Hölzle and W. Jenny, *Helv. Chim. Acta*, **41**, 331, 593 (1958). D. D. Lawson and N. Kharasch, *J. Org. Chem.*, **24**, 857 (1959).

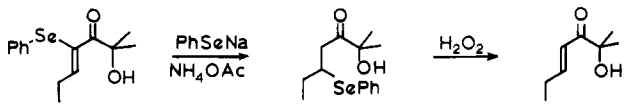
(14) (a) H. J. Reich, R. E. Olson, and M. C. Clark, *J. Am. Chem. Soc.*, **102**, 1423 (1980). R. E. Olson and M. C. Clark, unpublished results. (b) H. J. Reich, J. J. Rusek, and R. E. Olson, *J. Am. Chem. Soc.*, **101**, 2225 (1979).

Scheme II



γ-hydroxylations using the [2.3] sigmatropic rearrangement of a sulfoxide have been reported.[15]

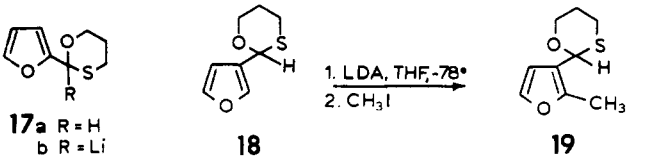
We have also converted α-(phenylseleno) enones **4a** to enones **4b** by a deselenation reaction.[12] Treatment of **12** by PhSeNa



buffered with ammonium acetate results in the formation of β-(phenylseleno) ketone **13**. Oxidation of **13** by H_2O_2 yields enone **14** via the selenoxide.

Synthesis of (±)-7-Hydroxymyoporone. To test the utility of the methodology described here in a somewhat more complex system, we undertook the preparation of 7-hydroxymyoporone (**15**), isolated and identified by Burka, Bowen, Wilson, and Harris.[16] The plan for the synthesis of **15** is presented in Scheme II.

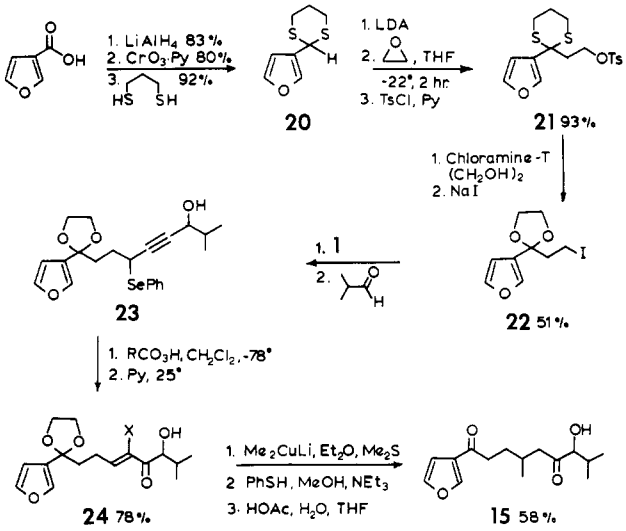
Initial model experiments were carried out by using the 2-furyl systems, since 3-substituted furans are much less readily available. The dithiane prepared from furfural did not prove usable, but oxathiane **17** was a suitable acyl anion equivalent.[17] Deproton-



ation with LDA and reaction with ethylene oxide gave a model system for **16**, which was used in a synthesis of a 7-hydroxymyoporone analogue with the side chain in the 2-position. Unfortunately the 3-furyl analogue **18** was deprotonated by LDA or *n*-BuLi predominantly on the furan ring, as shown by isolation of the methylated compound **19**. After several other approaches failed, the 3-substituted dithiane **20** was examined and found to react smoothly and in high yield with ethylene oxide giving compound **21** after tosylation. The preparation of **20** and subsequent reactions are summarized in Scheme III.

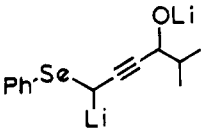
The dithiane tosylate **21** was resistant to S_N2 substitution both by the dianion **1** and even by iodide ion. A similar effect had been observed in the model 2-furyloxathiane tosylate derived from **17**. In each case the situation was much improved after a transketalization to the ethylene ketal had been performed. Two reagents were found suitable for this reaction in the sensitive furan

Scheme III



system: silver trifluoroacetate in ethylene glycol buffered with 2,6-di-*tert*-butylpyridine and chloramine-T in ethylene glycol.[18] The latter reagent was preferred since it is cheaper and gave better yields. The dioxolane tosylate could now be smoothly converted to the iodide **22**.

Assembly of the carbon skeleton could be carried out in three ways: (1) alkylation of the dianion **25** with **22**; (2) one pot



alkylation of dianion **1** followed by reaction with isobutyraldehyde as in Scheme III; (3) alkylation of **1** with **22** followed by a separate reaction in which the isobutyraldehyde was introduced. All three procedures proved viable, but (3) gave the highest yield on the basis of **22** since excess dianion **1** could be used in the crucial alkylation step.

Compound **23** was oxidized and allowed to rearrange under the usual conditions to give a cis–trans mixture of enones **24** (some deselenated enone was also formed), which was treated with lithium dimethyl cuprate. Deselenation and ketal hydrolysis completed the synthesis. The product was a 70:30 mixture of two diastereomers which could not be separated chromatographically. The major one was crystalline and could be obtained in pure form. Comparison of the 270-MHz NMR spectra of the synthetic material with that of the natural product[19] showed that the minor isomer was (±)-7-hydroxymyoporone, while the major was (±)-epi-7-hydroxymyoporone.

The stereochemistry is introduced during the cuprate addition. Since it did not seem unreasonable to assume that complexation between the incoming cuprate and the alkoxide group in **24** would provide some conformational control, it was considered that cis and trans enones **24** might give rise to different diastereomer ratios of **15**. While pure (*Z*)-**24** (X = H) did give a different diastereomer ratio (1:1) than did the mixture of *E*,*Z* isomers formed during the rearrangement, this approach did not seem promising enough to encourage more extensive studies of the cuprate addition.

α-Lithioallenyl Phenyl Selenide. We have developed three approaches to the lithium reagent **26** and have briefly studied its reactions with representative electrophiles. Alkylation and protonation occurs to give predominantly allenic products (CH_3I, >20:1; $PhCH_2Br$, 5:1 allenic–acetylenic). The allenyl selenide

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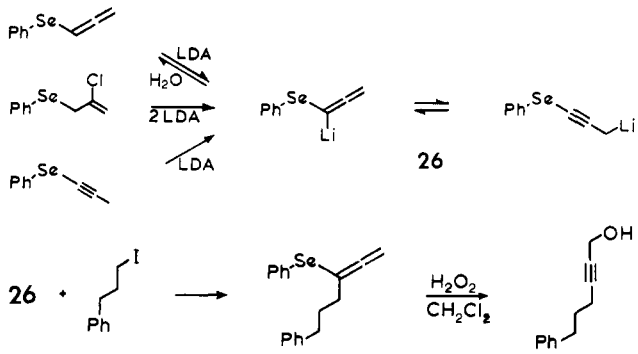
(16) L. T. Burka, R. M. Bowen, B. J. Wilson, and T. M. Harris, *J. Org. Chem.*, **39**, 3241 (1974).

(17) 2-Furylmethyllithium reagents readily undergo fragmentation: K. Atsumi and I. Kuwajima, *J. Am. Chem. Soc.*, **101**, 2208 (1979); M. J. Taschner and G. A. Kraus, *J. Org. Chem.*, **43**, 4235 (1978).

(18) Chloramine-T has been used to hydrolyze dithianes[14b] and oxo thioketals: D. W. Emerson and H. Wynberg, *Tetrahedron Lett.*, 3445 (1971).

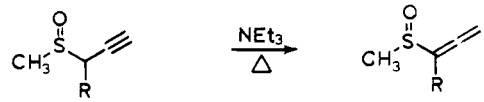
(19) We thank Professor Burka for providing us with a sample of 7-hydroxymyoporone.



is smoothly converted to 6-phenylhex-2-yn-1-ol on oxidation with excess hydrogen peroxide under conditions analogous to those used for allylic selenides.[1d] The allenic lithium reagent **26** does, however, have poorer nucleophilic properties than similar allyllithiums since reaction of **26** with 2-phenyl-1-bromoethane gives predominantly styrene, whereas the latter give substitution in good yield.

The reaction of **26** with benzaldehyde gives predominantly acetylenic product. Such reversal in regiochemistry when allenic and allylic lithium reagents react with carbonyl compounds and alkyl halides has been reported frequently.[20]

Rearrangement of Propargyl Sulfoxides. Aryl propargyl sulfoxides rearrange to benzothiophene derivatives at 80 °C.[8a] It has been proposed that the allenyl sulfenate ester formed by [2.3] sigmatropic rearrangement undergoes a thio-Claisen rearrangement. In order to avoid this process (which we have not observed in the selenium system), we chose the methyl sulfoxide **27**.

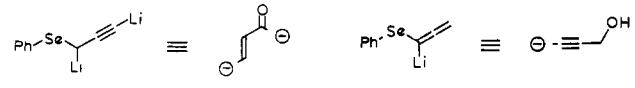


27 R = n-C_6H_{13} **28**

Alkylation of the dianion of methyl propargyl sulfide followed by oxidation gives the stable sulfoxide **27**. Compound **27** decomposes near 100 °C in the presence of HOAc or $(MeO)_3P$ to give ill-defined mixtures but no aldehydes. In the presence of triethylamine at 80 °C, allene **28** is formed in low yield presumably by a base-catalyzed proton migration. Thus although dianions of propargyl sulfides can be formed and alkylated,[4c] transformations analogous to the selenoxide rearrangement **3b** to **4** could not be achieved for sulfoxides.

The differences in the behavior of propargylic sulfoxides and selenoxides can be ascribed to two factors: the much greater rate of [2.3] sigmatropic rearrangement of selenoxides compared with sulfoxides (which has its parallel in the greater rate of selenoxide vs. sulfoxide syn elimination) and the greater ease of cleavage of the Se–O bond of selenenates when compared with the sulfenate esters.

Summary. The lithium reagents **1** and **26** which are the subject



1 **29** **26** **30**

of this paper are synthetic equivalents of acrolein dianion **29** and lithiopropargyl alcohol **30**, respectively. The two anionic centers of **29** can be utilized separately, although some restrictions on electrophiles do exist as a result of regiochemical and reactivity limitations. A number of acyl anion equivalents related to **29** have been developed.[21] These include lithium reagents derived from 1,3-bis(methylthio)propene and related compounds,[22] 3-chloro-but-2-enyl selenide[1d] and sulfide,[23] and methoxyallenes.[3b,i]

The anion **1** is the only one of the acrylyl anion equivalents which permits the formation of two C–C bonds in a one-pot reaction. It also has certain other advantages over many of the above in terms of convenience of preparation of the precursor (one step from commercially available materials), high regioselectivity, and mildness of the deprotection step. It suffers from the problems associated with the formation of α-(phenylseleno) enones **4a** rather than selenium-free materials (**4b**).

Sulfur analogues of **1** can be prepared and treated with electrophiles, but conversion to 1,3-disubstituted acrylyl compounds has not been reported.

Several synthetic equivalents of **30** are known. The simplest is an O-protected propargyl alcohol (the THP derivative has been frequently used[24]). Not enough work has been done with **25** to determine whether it has improved nucleophilic properties compared to the acetylenic anion.

Experimental Section

General Data. Nuclear magnetic resonance (NMR) spectra were obtained on JEOL MH-100 or FX-60 or Brucker WH-270 spectrometers. Infrared spectra (IR) were obtained on a Perkin-Elmer IR-267 spectrophotometer and mass spectra (MS) on an AEI MS-902 spectrometer. Unless specified otherwise NMR spectra were measured in CCl_4 solution, and IR spectra of neat liquid between salt plates were recorded. Elemental analyses were performed by Spang Microanalytical Laboratories. Melting and boiling points are uncorrected; all reaction temperatures are measured externally.

Starting materials were commercially available except for diphenyl diselenide,[12,25] 3,3′-bis(trifluoromethyl)diphenyl diselenide,[12] benzeneselenenyl chloride,[12,25] (2-nitro-4-methylphenyl)selenocyanate,[26] 2,2′-dinitrodiphenyl diselenide[27] and 3-phenyliodopropane,[28] which were prepared according to literature procedures. literature procedures.

Tetrahydrofuran (THF) was freshly distilled from $LiAlH_4$ or sodium benzophenone ketyl; 1,2-dimethoxyethane (DME) was freshly distilled from $LiAlH_4$. Hexamethylphosphoric triamide (HMPA) was distilled from CaH_2 in vacuum and stored under nitrogen. Diisopropylamine and isobutylamine were distilled from KOH and stored over 4A molecular sieves. Pyridine was stored over KOH. Stock solutions of lithium diisopropylamide (LDA), 1 M in THF–hexane, were prepared as in reference 12 and titrated with diphenylacetic acid.[29] *m*-Chloroperbenzoic acid (*m*-CPBA) obtained from various commercial sources was found to contain *m*-chlorobenzoic acid and water as major impurities. Recrystallization from hexane (3 g/65 mL) is recommended to remove these impurities. All reactions involving organolithium reagents, selenol, or selenolate anions were run under an atmosphere of dry nitrogen. Apparatus for anhydrous reactions was dried in a 110 °C oven for at least 3 h. Preparative thin-layer chromatography (TLC) was carried out by using Merck PF-254 silica gel and dry column chromatgraphy on MC and B 60 silica gel. Gas–liquid chromatographic (GLC) analysis was performed on a Varian 90-P3 gas chromatograph with a thermal conductivity detector. Bulb-to-bulb distillations were carried out with a Kugelrohr apparatus; bath temperatures are reported.

Normal Workup. The normal workup procedure involved dilution of the reaction mixture with 20 mL of 50% ether–pentane and addition of the solution to 30 mL of 7% $NaHCO_3$ solution. The aqueous layer was extracted with 2 × 25 mL of 50% ether–pentane. The combined organic portions were washed with 1.2 N HCl solution and with saturated NaCl solution and dried by filtering through a cone of Na_2SO_4. Solvent was removed on a rotary evaporator.

Caution! Selenium compounds are toxic and should be handled with due care.

Phenyl Propargyl Selenide. In a 250-mL 3-neck flask equipped with a reflux condenser, an addition funnel, and a gas inlet tube was placed

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(21) For recent reviews see: O. W. Lever, Jr., *Tetrahedron*, **32**, 1943 (1976); D. Seebach, *Angew Chem.*, **91**, 259 (1979).

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(23) P. T. Lansbury and R. W. Britt, *J. Am. Chem. Soc.*, **98**, 4577 (1976).

(24) A. I. Rachlin, N. Wasyliw, and M. W. Goldberg, *J. Org. Chem.*, **26**, 2688 (1961); E. J. Corey and H. S. Sachdev, *J. Am. Chem. Soc.*, **95**, 8483 (1973). S. Danishefsky, R. McKee, and R. K. Singh, *ibid.*, **99**, 4783 (1977).

(25) H. J. Reich, M. L. Cohen, and P. S. Clark, *Org. Synth.*, **59**, 141 (1979).

(26) H. Bauer, *Chem. Ber.*, **46**, 92 (1913).

(27) A modification of the prodedure of M. T. Bogert and A. Stull (*J. Am. Chem. Soc.*, **49**, 2012 (1927)) was used: Na_2Se_2 solution was prepared by reaction of Na_2Se (Se and $NaBH_4$) with Se in DMF; this was allowed to react with 2-nitrochlorobenzene for 3 h at 75 °C.

(28) 3-Phenylbromopropane was treated with NaI–acetone (J. v. Braun, *Chem. Ber.*, **43**, 2837 (1910).

(29) W. G. Kofron and L. M. Baclawski, *J. Org. Chem.*, **41**, 1879 (1976).

15 g (48 mmol) of Ph_2Se_2 dissolved in 120 mL of EtOH under a nitrogen atmosphere. Sodium formaldehyde sulfoxylate (7.5 g, 49 mmol) was added to this solution followed by NaOH (5.7 g) in 50 mL of water. The resulting solution was stirred for 15 min at 50 °C. The yellow color fades and a white precipitate forms. The oil bath was now replaced by an ice–salt bath. Propargyl bromide (7.95 mL, 100 mmol) was added to this cold solution and stirred for 3 h at 0 °C. The reaction mixture was poured into 200 mL of 10% HCl and extracted (3 × 100 mL) with ether–hexane. The combined organic extracts were washed with 50 mL of 5% $NaHCO_3$ and 50 mL of saturated salt solution and dried by filtering through a cone of Na_2SO_4. Distillation gave phenyl propargyl selenide[30] (18.2 g, 97% yield, bp 62–64 °C (0.07) mm)): NMR δ 2.10 (t, J = 2.5 Hz, 1 H), 3.38 (d, J = 2.5 Hz, 2 H), 7.1–7.6 (m, 5 H); IR 3300 (s), 3060 (m), 2150 (w), 1580 (m), 1479 (s), 1438 (s), 1407 (m), 1185 (m), 1074 (m), 1025 (s), 740 (s), 690 (s) cm^{-1}.

Anal. Calcd for C_9H_8Se: C, 55.40; H, 4.13. Found: C, 55.16; H, 4.03.

4-Methyl-2-nitrophenyl Propargyl Selenide. To a solution of 0.845 g (3.40 mmol) of (4-methyl-2-nitrophenyl)selenocyanate in 20 mL of absolute ethanol in a flask fitted with a reflux condenser and flushed with nitrogen was added 0.17 g (4.5 mmol) of $NaBH_4$. The solution became deep red. After 15 min, 0.27 mL (3.6 mmol) of propargyl bromide was added and a yellow-brown precipitate formed. The mixture was stirred overnight, and then 0.2 g (2 mmol) of chloroacetic acid was slowly added. The mixture was then poured into 40 mL of CH_2Cl_2, washed with 10% HCl, 3 × 50 mL of 5% Na_2CO_3, and saturated NaCl, dried (Na_2SO_4), and evaporated to give a yellow-orange solid. Recrystallization from ether–pentane (1:1) gave 0.724 g (81%) of yellow-orange crystals: mp 119–121 °C; NMR δ 2.30 (t, J = 2.5 Hz, 1 H), 2.48 (s, 3 H), 3.58 (d, J = 2.5 Hz, 2 H), 7.33–7.63 (m, 2 H), 8.18 (br s, 1 H); IR (CCl_4) 3310, 1525, 1345, 1260, 745, 652 cm^{-1}; MS M^+ 254.9799 (calcd for $C_{10}H_9NO_2Se$, 254.9799).

2-Nitrophenyl Propargyl Selenide was prepared by the same procedure as above, except that 2,2′-dinitrodiphenyl diselenide was used: mp 94–97 °C; NMR (270 MHz, CD_2Cl_2) δ 2.32 (t, J = 2.8 Hz, 1 H), 3.58 (d, J = 2.8 Hz, 2 H), 7.40 (ddd, J = 1.6, 7.0, 8.3 Hz, H_4), 7.6 (ddd, J = 1.5, 7.0, 8.3 Hz, H_5), 7.7 (br dd, J = 1.6, 7.0 Hz, H_6), 8.33 (ddd, J = 0.38, 1.5, 8.4 Hz, H_3); IR ($CHCl_3$) 3300, 1590, 1520, 1450, 1335, 1302, 1100, 1038, 852 cm^{-1}; MS M^+ 240.9642 (calcd for $C_9H_7NO_2Se$, 240.9643).

1-(Phenylseleno)-1-propyne. Into a N_2-flushed 3-neck flask cooled to −78 °C and equipped with an addition funnel and dry ice condenser and connected to a graduated cold trap was placed 60 mL of ether and 100 mL of ca. 1 M methyllithium. Propyne gas (11 mL of liquid) was condensed in the cold trap. The cold baths were removed, and propyne (8.5 mL, after which methane evolution stopped) was allowed to distill into the flask. The reaction mixture was cooled in an ice–salt bath, and a solution of 19.1 g (0.096 mol) of PhSeCl in 40 mL of THF and 40 mL of ether was dropped into the reaction mixture at a rate sufficient to maintain gentle reflux. The reaction mixture was stirred for 1 h at 25 °C after completion of addition and worked up. Distillation of the residue gave 14.78 g (76% yield) of 1-(phenylseleno)-1-propyne[30] (bp 72–74 °C (0.3 mm)); NMR δ 2.03 (s, 3 H), 7.1–7.6 (m, 5 H); IR 3060, 2920, 2180, 1580, 1481, 1443, 1067, 1022, 998, 733, 686 cm^{-1}.

Allenyl Phenyl Selenide. To a cooled (−78 °C) solution of 0.28 mL (2 mmol) of 1-(phenylseleno)-1-propyne in 4 mL of THF was added 2.05 mL of 1 M LDA. After 10 min, 1 mL of 10% aqueous THF was added to the reaction mixture and stirred for 5 min. The solution was quenched in saturated $NaHCO_3$ and worked up with ether–pentane. Distillation (Kugelrohr, bp 55 °C (0.05 mm)) gave 0.374 g (96% yield) of allenyl phenyl selenide:[30] NMR δ 4.72 (d, J = 6 Hz, 2 H), 5.97 (t, J = 6 Hz, 1 H), 7.0–7.6 (m, 5 H); IR 3050, 1940, 1577 cm^{-1}; MS M^+ 195.9791 (calcd for C_9H_8Se, 195.9791).

6-Phenyl-3-(phenylseleno)-1-hexyne (Run 1). To a solution of 0.98 g (0.7 mL, 5 mmol) of phenyl propargyl selenide in 15 mL of DME at −78 °C was added 12 mL of 1 M LDA solution. After 5 min, 1.32 g (0.75 mL, 5.35 mmol) of 3-phenyliodopropane was slowly added to this solution. After 25 min, H_2O (0.5 mL) was added and the solution was poured into 10% aqueous HCl and worked up. Purification by dry-column chromatography gave 1.47 g (93% yield): NMR δ 1.8 (m, 4 H), 2.19 (d, J = 2.5 Hz, 1 H), 2.54 (m, 2 H), 3.64 (m, 1 H), 7.0–7.7 (m, 10 H); IR 3290, 3060, 3030, 2940, 2100, 1602, 1580 cm^{-1}; MS$^+$ M^+ 314.0561 (calcd for $C_{18}H_{18}Se$, 314.0574).

6-Phenyl-2-(phenylseleno)hex-2-enal (Run 1). A solution of 0.504 g (1.61 mmol) of 6-phenyl-3-(phenylseleno)-1-hexyne in 10 mL of methanol was ozonized at −78 °C (blue endpoint). Pyridine (0.25 mL) was added, and the solution was slowly warmed to 25 °C. Normal workup followed by preparative TLC purification (10% ether–pentane) gave 449 mg of 85% pure product (73% yield): NMR δ 1.76 (quintet, J = 7 Hz, 2 H), 2.54 (q, J = 7 Hz, 2 H), 2.60 (t, J = 7 Hz, 2 H), 7.0–7.5 (m, 11 H), 9.25 (s, 1 H); IR 3080, 3030, 2930, 2740, 1690, 1598, 1577 cm^{-1}; MS M^+ 330.0525 (calcd for $C_{18}H_{18}OSe$, 330.0523).

6-Phenyl-2-hexenal (Run 2). A solution of 0.502 g (1.6 mmol) of 6-phenyl-3-(phenylseleno)-1-hexyne in 10 mL of methanol, 0.3 mL of H_2O, and 0.25 mL of pyridine was treated with 0.5 mL of 30% H_2O_2. The H_2O_2 solution was added dropwise, and the flask was kept in a cold water bath because the oxidation is very exothermic. The reaction mixture was stirred for 7 min, poured into 10% HCl, and worked up. Purification by preparative TLC (20% ether–pentane) gave 105 mg (38% yield) of 6-phenyl-2-hexenal:[31] NMR δ 1.79 (quintet, J = 7 Hz, 2 H), 2.29 (q, J = 7 Hz, 2 H), 2.63 (t, J = 7 Hz, 2 H), 6.03 (dd, J = 16, 7.5 Hz, 1 H), 6.71 (dt, J = 16, 7 Hz, 1 H), 7.1 (m, 5 H), 9.43 (d, J = 7.5 Hz, 1 H); IR 3070, 3030, 2940, 2740, 1680, 1630, 1600 cm^{-1}; MS M^+ 174.1041 (calcd for $C_{12}H_{14}O$, 174.1045).

7-Phenyl-4-(phenylseleno)-2-heptyne (Run 3). A solution of LDA (1 M, 11 mmol) was added dropwise to a cooled (dry ice–EtOH) solution of 0.7 mL (5 mmol) of phenyl propargyl selenide in 15 mL of DME. After 3 min 3-phenyliodopropane (0.75 mL, 5.7 mmol) was added, and the yellow solution was stirred for 0.5 h. Methyl iodide (0.5 mL, 8.2 mmol) was now added to the suspension followed by 1 mL of HMPA. The cold bath was removed, and the reaction mixture was allowed to warm to 25 °C. After 1 h this solution was poured into 1.2 N HCl, worked up, and chromatographed on a dry column (10% ether–pentane) to give 1.29 g (79% yield) of 7-phenyl-4-(phenylseleno)-2-heptyne: NMR δ 1.77 (d, J = 2.2 Hz, 3 H), 1.7 (m, 4 H), 2.59 (br t, J = 7 Hz, 2 H), 3.78 (m, 1 H), 7.0–7.6 (m, 10 H).

7-Phenyl-3-(phenylseleno)-3-hepten-2-one (11; Run 3). To a cold (−78 °C) solution of 7-phenyl-4-(phenylseleno)-2-heptyne in 6 mL of CH_2Cl_2 was added a solution of 0.605 g (3 mmol) of *m*-CPBA in 2 mL of CH_2Cl_2. After the mixture was stirred for 0.5 h, pyridine (0.6 mL) was added and the dry ice–EtOH bath was replaced by an ice bath. After 0.5 h this solution was poured into 5% Na_2CO_3 solution and worked up. The concentrated solution was chromatographed on a silica plate (10% ether–pentane) to give 0.768 g (74% yield) of 7-phenyl-3-(phenylseleno)-3-hepten-2-one (**11**) as a mixture of *E* and *Z* isomers: NMR (*Z* isomer) δ 1.75 (quintet, J = 7.5 Hz, 2 H), 2.18 (s, 3 H), 2.42 (q, J = 7.5 Hz, 2 H), 2.6 (t, J = 7.5 Hz, 2 H), 7.0–7.5 (m, 11 H); NMR (*E* isomer) δ 1.71 (quintet, J = 7 Hz, 2 H), 2.14 (s, 3 H), 2.33 (q, J = 7 Hz, 2 H), 2.56 (t, J = 7 Hz, 2 H), 6.25 (t, J = 7 Hz, 1 H), 7.04 (m, 10 H); IR 3060, 3030, 2930, 1690, 1605 cm^{-1}; MS M^+ 344.0680 (calcd for $C_{19}H_{20}OSe$, 344.0679).

2-Hydroxy-2-methyl-4-(phenylseleno)-4-hepten-3-one (12, Run 5). Following the procedure outlined for run 4, 0.28 mL (2 mmol) of phenyl propargyl selenide, 0.17 mL (2.2 mmol) of ethyl bromide and 0.15 mL (2.5 mmol) of acetone gave 0.45 g of 5-(phenylseleno)-3-heptyn-2-ol: NMR δ 1.05 (t, J = 7 Hz, 3 H), 1.36 (s, 6 H), 1.75 (quintet, J = 7 Hz, 2 H), 2.88 (br s, 1 H), 3.69 (t, J = 7 Hz, 1 H), 7.1–7.7 (m, 5 H).

Oxidation of crude 5-(phenylseleno)-3-heptyn-2-ol obtained above with 0.406 g (85%, 2 mmol) of *m*-CPBA, according to the procedure given for the preparation of **11** (run 3) furnished 0.351 g (59% yield) of **12** purified by preparative TLC: NMR δ 1.03 (t, J = 7 Hz, 3 H), 1.26 (s, 6 H), 2.12 (quintet, J = 7 Hz, 2 H), 3.3 (br s, 1 H), 6.25 (t, J = 7 Hz), 7.1–7.5 (m, 6 H); IR 3490, 3070, 2980, 1685, 1620, 1580 cm^{-1}; MS M^+ 298.0465 (calcd for $C_{14}H_{18}O_2Se$, 298.0427).

1-(Phenylseleno)-2-butyne (Run 7). *n*-Butyllithium (1.52 M in hexane, 6.7 mL) was slowly added to a magnetically stirred solution of 1.05 mL (10.5 mmol) of isobutylamine in 10 mL of THF maintained at −78 °C. After 5 min phenyl propargyl selenide (1.4 mL, 10 mmol) was added dropwise to this suspension, resulting in a pale yellow solution. After 3 min, 1 mL of methyl iodide was added followed by 1 mL of HMPA. The cold bath was removed, and the solution was stirred for 1 h and worked up. The concentrated filtrate on distillation (Kugelrohr, bp 63–66 °C (0.03 mm)) gave 1.93 g (92% yield) of 1-(phenylseleno)-2-butyne: NMR δ 2.78 (t, J = 2 Hz, 3 H), 3.36 (q, J = 2 Hz, 2 H), 7.0–7.7 (m, 5 H); IR 3060, 2920, 2230, 1580 cm^{-1}; MS M^+ 209.9948 (calcd for $C_{10}H_{10}Se$, 209.9947).

Anal. Calcd for $C_{10}H_{10}Se$: C, 57.47; H, 4.82. Found: C, 57.48; H, 4.94.

3-(Phenylseleno)-3-buten-2-one (Run 7). Ozone gas was passed through a CH_2Cl_2 (3 mL) solution of 0.418 g of 1-(phenylseleno)-2-butyne at −78 °C until the yellow color (due to contamination by traces of Ph_2Se_2) disappeared. This solution was warmed to 0 °C, stirred for 10 min, and worked up. This crude 3-(phenylseleno)-3-buten-2-one could be purified by preparative TLC but was usually without purification for further reaction. It is an unstable yellow oil: NMR δ 2.15 (s, 3 H), 5.4 (d, J = 1.6 Hz, 1 H), 6.36 (d, J = 1.6 Hz, 1 H), 7.0–7.7 (m, 5 H); IR

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3020, 1705, 1685, 1660, 1465, 1425 cm^{-1}; MS 225.9892 (calcd for $C_{10}H_{10}OSe$, 225.9889).

2-(Phenylseleno)-1-(trrimethylsilyl)propen-1-one (Run 9). To a solution of 5.0 mL (35 mmol) of phenyl propargyl selenide in 30 mL of THF at −78 °C was added 39.6 mL of a 0.93 M solution of LDA (37 mmol). After 10 min, 5.2 mL (41 mmol) of chlorotrimethylsilane was added, and after 10 min, the flask was warmed to 0 °C and stirred 45 min. The contents were poured into saturated aqueous NH_4Cl and extracted with 3 × 75 mL of ether–pentane (1:1). The combined organic layers were washed with saturated NaCl, dried (Na_2SO_4), evaporated, and distilled (Kugelrohr, 90–100 °C (0.6 mm)) to give 9.4 g (100%) of 3-(phenylseleno)-1-(trimethylsilyl)-1-propyne (about 86% pure): NMR δ 0.20 (s, 9 H), 2.52 (s, 2 H), 7.24–7.44 (m, 3 H), 7.60–7.80 (m, 2 H); IR 2940, 2160, 1885, 1570, 1470, 1245, 1035, 845 cm^{-1}; MS M^+ 268.0178 (calcd for $C_{12}H_{16}SeSi$, 268.01865).

This material was taken up in 30 mL of CH_2Cl_2 and treated at −78 °C with 7.7 g (38 mmol, 85% pure) of *m*-CPBA in 80 mL of CH_2Cl_2, followed in 20 min by 5.6 mL (40 mmol) of diisopropylamine. The flask was warmed to 0 °C, stirred 30 min, and then poured into 7% $NaHCO_3$. Extraction with 2 × 100 mL of ether–pentane (1:1) washing with saturated NaCl, drying (Na_2SO_4), and evaporation gave a yellow oil which was taken up in 25 mL of EtOH and cooled to −20 °C. After being left sitting overnight, the solution was filtered, giving (after vacuum drying) 5.57 g (56% yield) of 2-(phenylseleno)-1-(trimethylsilyl)propen-1-one as bright yellow crystals: mp 51–52.5 °C (discoloration); NMR δ 0.32 (s, 9 H), 5.64 (d, J = 2.0 Hz, 1 H), 6.44 (d, J = 2.0 Hz, 1 H), 7.28–7.44 (m, 3 H), 7.52–7.72 (m, 2 H); IR (CCl_4) 2960, 1610, 1580, 1256, 862, 568 cm^{-1}; MS M^+ 284.0314 (calcd for $C_{12}H_{16}OSeSi$, 284.0128). Two recrystallizations from 95% ethanol gave large yellow crystals, mp 53.5–54 °C (discoloration).

Anal. Calcd for $C_{12}H_{16}OSeSi$: C, 50.87; H, 5.70. Found: C, 50.92; H, 5.33.

Preparation and Rearrangement of 2-Nitrophenyl Propargyl Selenoxide (6c). An ozone–oxygen stream was calibrated by oxidizing Ph_2Se_2 to Ph_2SeO_3 at −78 °C (3 equiv of O_3/molecule). Dry ozone (0.13 mmol) was passed through a solution of 24 mg (0.1 mmol) of 2-nitrophenyl propargyl selenide in 0.5 mL of CD_2Cl_2 at −78 °C. Excess ozone was removed by a nitrogen stream (3 min), and the solution of selenoxide **6c** was transferred to a cold NMR tube by using a cold syringe: NMR (CD_2Cl_2, 270 MHz, −80 °C) δ 2.42 (br s, ≡CH), 3.72, 3.91 (ABq, J_{AB} = 14.7 Hz, CH_2), 7.79 (br t, J = 6 Hz), 8.02 (br t, $J \simeq$ 6 Hz), 8.19 (br d, J = 7 Hz), 8.35 (br d, J = 8 Hz).

This sample was kept at −45 °C for 1 h when rearrangement to the allenyl selenenate **7c** was complete: NMR (CD_2Cl_2, 270 MHz, −45 °C, Figure 1) δ 5.44 (d, J = 5.8 Hz, 2 H), 7.12 (t, J = 5.8 Hz, 1 H), 7.51 (m, 1 H), 7.87–7.90 (m, 2 H), 8.38 (dm, J = 8.1 Hz, 1 H). The IR spectrum of a similar solution prepared in CH_2Cl_2 showed an absorption at 1950 cm^{-1} which decayed during several minutes at room temperature, concurrent with the appearance of the aldehyde **8c** carbonyl absorption at 1700 cm^{-1}.

When the NMR sample prepared above was warmed to room temperature, **7c** rearranged to the aldehyde **8c**: NMR (270 MHz, CD_2Cl_2) δ 7.18 (s, 1 H), 7.19 (s, 1 H), 7.24 (dd, J = 7.9, 1.4 Hz, 1 H), 7.37 (ddd, J = 8.1, 7.1, 1.4 Hz, 1 H), 7.45 (ddd, J = 7.9, 7.1, 1.6 Hz, 1 H), 8.25 (dd, J = 8.1, 1.7 Hz, 1 H), 9.60 (s, 1 H); IR ($CHCl_3$) 3020, 2820, 1700, 1590, 1515, 1330, 1308, 1105, 1038, 926, 855 cm^{-1}; MS M^+ 256.9590 (calcd for $C_9H_7NO_3Se$, 256.9592).

A rate study was carried out on a solution of **6c** in CD_2Cl_2 prepared by oxidation of 2-nitrophenyl propargyl selenide with *m*-CPBA (−78 °C) followed by treatment with 1.5 equiv of NEt_3; $k_{6c} = 2.9 \times 10^{-4}$ s^{-1} at −50 °C.

Rearrangement of 6a to 8a. A solution of phenyl propargyl selenoxide (**6a**) in $CDCl_3$ was prepared as for **6c** above: NMR ($CDCl_3$, −39 °C) δ 2.51 (br t, J = 2.5 Hz, 1 H), 3.59, 3.74 (AB of ABX, J_{AB}, = 14.5, J_{AX} = 2.5 Hz, 2 H), 7.38 (m, 3 H), 7.6 (m, 2 H). The solution of **6a** was warmed to −31 °C, and the isomerization to **8a** was followed by spectral analyses: NMR δ 5.81 (s, 1 H), 6.44 (s, 1 H), 7.1–7.7 (m, 5 H), 9.4 (s, 1 H); IR 3070, 3060, 2915, 2905, 1720, 1690, 1580, 1480, 1440, 1220 cm^{-1}; MS M^+ 211.9744 (calcd for C_9H_8OSe, 211.9733).

Rearrangement of 6b to 8b. NMR of **6b** ($CDCl_3$, −31 °C): δ 2.56 (br t, J = 2.5 Hz, 1 H), 3.56, 3.80 (br ABq, J_{AB} = 15 Hz), 7.3–7.9 (m, 4 H). Warming of the solution of **6b** gave **8b**: NMR δ 5.94 (br s, 1 H), 6.58 (br s, 1 H), 7.3–8.0 (m, 4 H), 9.46 (s, 1 H); IR 3035, 2900, 2890, 1720, 1710, 1680, 1575, 1405, 1315 cm^{-1}; MS M^+ 279.9609 (calcd for $C_{10}H_7F_3OSe$, 279.9614). A 1:1 mixture of **6a** and **6b** was allowed to isomerize at −31 °C and observed by 270-MHz NMR. The rate followed first-order kinetics: $k_{6a} = 6.2 \times 10^{-5}$ and $k_{6b} = 10 \times 10^{-5}$ s^{-1}.

Rearrangement of Phenyl 3-(Trimethylsilyl)-2-propynyl Selenoxide to 2-(Phenylseleno)-1-(trimethylsilyl)propen-1-one. A solution of the selenoxide in $CDCl_3$ was prepared as for **6c** above: NMR (−25 °C) δ 0.14 (s), 3.49, 3.86 (ABq, J_{AB} = 14.3 Hz), 7.71 (m, 5 H). This solution showed less than 3% conversion to silyl ketone after 45 min of −25 °C ($k < 1.1 \times 10^{-5}$ s^{-1}); the selenoxide was briefly observable even at room temperature ($t_{1/2} \approx$ 3 min).

3-Iodo-7-phenyl-3-hepten-2-one (10). To a stirred cooled (−78 °C) solution of 0.323 g (1 mmol) of 7-phenyl-4-(phenylseleno)-2-heptyne in 5 mL of CH_2Cl_2 was added a CH_2Cl_2 (2 mL) solution of 0.203 g (1 mmol) of *m*-CPBA. Iodine (0.254 g 1 equiv) was dissolved in a solution of 0.37 g (1 mmol) of n-$Bu_4N^+I^-$ in 4 mL of CH_2Cl_2. This dark brown solution was added to the reaction mixture after 0.5 h. The reaction mixture was now warmed to −30 °C in 15 min and kept between −30 °C and −20 °C for 0.5 h. The solution was further warmed to 0 °C and then poured into 10% $Na_2S_2O_3$ solution, and the mixture was extracted with ether–hexane. The combined organic extracts were washed with 5% Na_2CO_3, 1.2 N HCl, and saturated NaCl solution, dried, concentrated, and purified by preparative TLC (20% ether–pentane) to give 0.176 g (56% yield) of **10** as a mixture of *E* and *Z* isomers: NMR (*Z* isomer) δ 1.82 (quintet, J = 7 Hz, 2 H), 2.36 (s, 3 H), 2.37 (q, J = 7 Hz, 2 H), 2.65 (t, J = 7 Hz, 2 H), 6.82 (t, J = 7 Hz, 1 H), 7.1 (m, 5 H); NMR (*E* isomer) δ 1.72 (quintet, J = 7 Hz, 2 H), 2.32 (q, J = 7 Hz, 2 H), 2.41 (s, 3 H), 2.61 (t, J = 7 Hz, 2 H), 6.5 (t, J = 8 Hz, 1 H), 7.1 (m, 5 H); IR 3070, 3030, 2930, 1682, 1598 cm^{-1}; MS M^+ 314.0169 (calcd for $C_{13}H_{15}IO$, 314.0167).

4-Methyl-7-phenyl-2-heptanone. Methyllithium (0.9 mL, 1.1 M) was added dropwise to a stirred suspension of 95 mg of CuI in 2 mL of ether at 0 °C until a clear solution resulted. This solution was cooled to −78 °C, and a solution of 0.137 g of enone **11** in 1 mL of ether was added slowly. Yellow precipitates (MeCu) appeared at this point. This solution was stirred for 5 min, and 0.1 mL of H_2O was added. The solution was warmed to 0 °C, poured into 1.2 N HCl, extracted, washed with saturated NH_4Cl, and dried. This crude product was chromatographed by using 20% ether–pentane to give 0.1 g of carbonyl product.

Ph_2Se_2 (60 mg) in 3 mL of EtOH was treated under N_2 with powdered $NaBH_4$ until the solution was clear. Acetone (0.03 mL) was added to remove excess $NaBH_4$. The carbonyl product obtained above in 1 mL of EtOH was added to this reaction mixture. After 1 h, 20 mg of chloroacetic acid was added to remove excess PhSeNa. The solution was stirred for 10 min, worked up, and purified by preparative TLC to give 53 mg (65% yield) of 4-methyl-7-phenyl-2-heptanone: NMR δ 0.86 (d, J = 7 Hz, 3 H), 1.26 (m, 2 H), 1.59 (q, J = 7 Hz, 2 H), 2.02 (s, 3 H), 2.19 (d, J = 8 Hz, 2 H), 2.1 (m, 1 H), 2.57 (br t, J = 8 Hz, 2 H), 7.0–7.4 (m, 5 H); IR 3030, 2940, 1710, 1603, 750, 698 cm^{-1}; MS M^+ 204.1515 (calcd for $C_{14}H_{20}O$, 204.1515).

5-Hydroxy-7-phenyl-3-hepten-2-one. To a cooled (−78 °C) solution of 0.343 g (1 mmol) of **11** in 4 mL of THF was added 0.203 g (1 mmol) of *m*-CPBA. After this solution was stirred for 0.5 h, 0.310 mL (2.2 mmol) of NEt_3 was added and the reaction mixture was allowed to warm to 0 °C during 30 min, poured into 5% Na_2CO_3 solution, and worked up. Preparative TLC (50% ether–pentane) gave 0.145 g (71% yield) of 5-hydroxy-7-phenyl-3-hepten-2-one: NMR δ 1.8 (q, J = 7.5 Hz, 2 H), 2.09 (s, 3 H), 2.7 (t, J = 7.5 Hz, 2 H), 3.86 (br s, 1 H), 4.18 (q, J = 7 Hz, 1 H), 6.12 (d, J = 16 Hz, 1 H), 6.68 (dd, J = 16, 15 Hz, 1 H), 7.1 (m, 5 H); IR 3440, 3040, 2935, 1677, 1630 cm^{-1}; MS M^+ 204.1136 (calcd for $C_{13}H_{16}O_2$, 204.1150).

2-Hydroxy-2-methyl-4-hepten-3-one (14). $NaBH_4$ was added to an EtOH (5 mL) solution of 0.5 g (1.6 mmol) of Ph_2Se_2 and 0.2 g (2.6 mmol) of NH_4OAc under N_2 until the solution was pale yellow. After 0.5 h, 10 mg of Ph_2Se_2 was added to remove excess $NaBH_4$. A solution of 0.276 g (0.93 mmol) of **12** in 1 mL of EtOH was added, and the solution was stirred for 2 h. The yellow color of Ph_2Se_2 developed after addition of **12**. The reaction mixture was added to 5% Na_2CO_3 solution and worked up.

The crude product (**13**) was dissolved in 10 mL of CH_2Cl_2. Pyridine (0.25 mL), H_2O (0.6 mL), and H_2O_2 (30%, 0.6 mL) were added. After the reaction mixture was stirred for 0.5 h, it was poured into a saturated $NaHCO_3$ solution and extracted with ether–pentane. The combined organic extracts were worked up and dried. The concentrated filtrate upon preparative TLC gave 96 mg (73% yield) of **14**: NMR δ 1.14 (t, J = 7 Hz, 3 H), 1.31 (s, 6 H), 2.33 (quintet, J = 7 Hz, 2 H), 3.66 (br s, 1 H), 6.40 (d, J = 14.5 Hz, 1 H), 7.12 (dt, J = 14.5 and 7 Hz, 1 H); IR 3480, 2980, 1685, 1625 cm^{-1}; MS M^+ 142.0989 (calcd for $C_8H_{14}O_2$, 142.0994).

Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.65; H, 10.04.

3-Furanmethanol. In a 500-mL three-neck flask was placed 2.3 g (60 mmol) of $LiAlH_4$ and 250 mL of freshly distilled THF. A solution of 3-furoic acid (4.28 g, 38.2 mmol) in 40 mL of THF was then dripped in cautiously, and the gray mixture was refluxed for 22 h. After being cooled to 25 °C, Glauber's Salt ($Na_2SO_4 \cdot H_2O$) was carefully added until the mixture became white. This was vacuum filtered and the granular

solid was washed twice with hot THF. The combined filtrates were concentrated under reduced pressure and the residue was distilled at 0.4 mm, maximum temperature 60 °C to give 3.12 g of clear liquid (83% yield): NMR ($CDCl_3$) δ 3.90 (t, J = 4 Hz, 1 H), 4.36 (d, J = 4 Hz, 2 H), 6.32 (s, 1 H), 7.28 (m, 2 H).

3-Furancarboxaldehyde.[32] In a 500-mL three-neck flask was placed 300 mL of CH_2Cl_2 and 19.5 mL (240 mmol) of pyridine. To this was added 12.0 g (120 mmol) of CrO_3, and the resulting dark green-brown solution was stirred for 15 min. Then 1.27 g (13 mmol) of 3-furanmethanol in 10 mL of CH_2Cl_2 was added while stirring was carefully continued and allowed to stir for 20 min. This crude mixture was decanted into a separatory funnel, the black residue washed twice with ether, and the combined organics were washed thrice with 5% NaOH and 10% HCl and once with saturated $NaHCO_3$ and brine. (An improved workup procedure has been developed wherein the crude reaction mixture is filtered through a short column of Florisil. The base extractions are then obviated, and the only contaminant remaining is pyridine.) The resulting organic layer was filtered through Na_2SO_4 and concentrated on the rotovap. The yellow oil was distilled at 0.5 mm, maximum temperature 50 °C, to afford 1.0 g of clear, sweet smelling liquid (80% yield): NMR ($CDCl_3$) δ 6.82 (s, 1 H), 7.56 (s, 1 H), 8.32 (s, 1 H), 10.02 (s, 1 H); IR ($CDCl_3$) 3150, 2850, 1720, 1690, 1570, 1520, 1415, 1385, 1285, 1170, 1160 cm^{-1}; MS M^+ 96.0209 (calcd for $C_5H_4O_2$, 96.0211).

2-(3-Furyl)-1,3-dithiane (20). In a 50-mL flask equipped with a Dean-Stark trap was placed 3-furancarboxaldehyde (1.0 g, 10.4 mmol), dissolved in 20 mL of dry benzene. To this solution was added 1.2 mL of propanedithiol (excess) and two crystals of toluenesulfonic acid, and the resulting mixture was heated to reflux for 4 h. The cooled mixture was decanted into 5% NaOH, and the layers were separated. The aqueous layer was extracted with 1:1 ether–pentane, and the combined organic extracts were washed with brine and filtered through Na_2SO_4. Solvent was removed under reduced pressure, and the resulting oil was distilled at 0.03 mm, maximum temperature 110 °C, giving a white, noxious smelling solid (1.75 g, 92% yield); mp 67–68 °C crude. An analytical sample, recrystallized from ether–pentane–CH_2Cl_2 (3:3:1) melted at 67.3–67.8 °C: NMR ($CDCl_3$) δ 2.08 (m, 4 H), 2.96 (m, 4 H), 5.12 (s, 1 H), 6.52 (s, 1 H), 7.40 (s, 1 H), 7.54 (s 1 H); IR ($CDCl_3$) 3150, 2950, 2920, 2840, 1590, 1575, 1508, 1430, 1278, 1190, 1160, 1080 cm^{-1}; MS M^+ 186.0174 (calcd for $C_8H_{10}O_2S_2$, 186.017 34).

Anal. Calcd for $C_8H_{10}O_2S_2$: C, 51.58; H, 5.41. Found: C, 51.54; H, 5.50.

2-(3-Furyl)-2-(2-hydroxyethyl)-1,3-dithiane. A 100-mL oven-dried flask was charged with 70 mL of THF and 2.42 g (13 mmol) of the dithiane **20**. After being flushed with N_2 for 5 min, the stirred solution was cooled to −78 °C and 13 mL of 1 M LDA was added. After 10 min 1.05 g of ethylene oxide (excess) was distilled into the mixture. The solution was then warmed to −22 °C for 2 h, and the reaction mixture was decanted into saturated NH_4Cl and worked up to give an oil which was distilled at 0.028 mm (bath temperature 120–140 °C). A colorless syrup, 2.85 g (12.4 mmol), was thus obtained (95% yield): NMR ($CDCl_3$) δ 2.00 (m, 2 H), 2.28 (t, J = 7 Hz, 2 H), 2.84 (m, 4 H), 3.0 (s, 1 H), 3.74 (t, 7 Hz, 2 H), 6.50 (s, 1 H), 7.44 (d, $J \approx 1$ Hz, 1 H), 7.56 (s, 1 H); IR 3385 (br), 2910, 2880, 1500, 1425, 1285, 1165, 1040, 1020, 880 cm^{-1}; MS M^+ 230.0433 (calcd for $C_{10}H_{14}O_2S_2$, 230.0435); major fragments 232 (10.5), 231 (13.2), 230 (100), 185 (44.5), 156 (82.5), 127 (40.0), 123 (42.1), 111 (48.8), 95 (54.2), 93 (83.1), 65 (28.1).

2-(3-Furyl)-2-(2-(tosyloxy)ethyl)-1,3-dithiane (21). In a 50-mL flask was placed 2.85 g (12.4 mmol) of alcohol dissolved in 20 dry mL pyridine. The solution was cooled to 0 °C and 3.40 g (17.9 mmol) of freshly recrystallized TsCl was added. This solid dissolved immediately, and the resulting solution was kept at 6 °C tightly stoppered for 40 h. The flask then contained long white needles (pyridine–HCl) and orange liquid. Addition of 30 mL of water and fourfold extraction with 1:1 ether–pentane gave an organic extract which was shaken vigorously with 10% HCl four times and once with saturated $NaHCO_3$ and brine. After filtration through Na_2SO_4 and removal of solvent under reduced pressure, a white solid remained: 4.72 g (12.3 mmol, 99% yield); mp 57–58 °C. After two recrystallizations from ether–pentane (50:50): mp 60.5–61.0 °C; NMR ($CDCl_3$) δ 1.96 (m, 2 H), 2.42 (t, J = 8 Hz, 2 H), 2.46 (s, 3 H), 2.78 (m, 4 H), 4.12 (t, J = 8 Hz, 2 H), 6.40 (s, 1 H), 7.32 (m, 4 H), 7.72 (d, J = 8 Hz, 2 H); IR ($CDCl_3$) 3120 (weak), 2885, 1600, 1500, 1360, 1195, 1180, 1025, 925 cm^{-1}; MS M^+ 384.0518 (calcd for $C_{17}H_{20}O_4S_3$, 384.0524); major fragments 384 (11.7), 219 (14.4), 212 (53.0), 185 (11.4), 172 (30.3), 155 (53.5), 138 (40.0), 111 (38.7).

Anal. Calcd for $C_{17}H_{20}O_4S_3$: C, 53.09; H, 5.24. Found: C, 53.17; H, 5.33.

1-(3-Furyl)-3-iodo-1-propanone, Ethylene Ketal (22). Anhydrous chloramine-T[33] (350 mg, 1.54 mmol) was dissolved in 3 mL of ethylene glycol, 1.2 mL of THF and 150 mg (0.39 mmol) of tosylate **21** were added, and the mixture was stirred until homogeneous and then for 1 h longer. The pale yellow solution was decanted into 5% NaOH and extracted three times with 1:1 ether–pentane. The organic extracts were combined, washed with brine, and dried by passing through Na_2SO_4, and the solvent was removed. The residue was nearly pure ethylene ketal tosylate (95% conversion), which was used directly in the next reaction: NMR ($CDCl_3$) δ 2.31 (t, J = 8 Hz, 2 H), 2.46 (s, 3 H), 3.90 (m, 4 H), 4.19 (t, J = 8 Hz, 2 H), 6.30 (m, 1 H), 7.35 (m, 4 H), 7.79 (d, J = 8 Hz, 2 H).

In 1.5 mL of reagent grade acetone was dissolved 190 mg of crude tosylate and 0.150 mL of 2,6-di-*tert*-butylpyridine. To this was added, under N_2, 270 mg of NaI (a yellow color developed immediately). When the solid had gone into solution, the reaction mixture was heated to 54 °C for 17.5 h. After the suspension of metallic appearing flakes was cooled to 25 °C and diluted with water until the solid had dissolved (and an oil separated), it was extracted four times with ether–pentane (1:1). The combined organic extracts were washed with concentrated $Na_2S_2O_3$ (color was discharged) and brine. Drying over Na_2SO_4 followed by preparative TLC (20% ether–pentane) gave two bands: 151 mg of iodide (R_f 0.48) and 100 mg of 2,6-di-*tert*-butylpyridine (R_f 0.85). The iodide **22** was obtained as a low-melting white solid in 51% overall yield from the dithiane tosylate **21**: NMR ($CDCl_3$) δ 2.55 (m, 2 H), 3.10 (m, 2 H), 3.90 (m, 4 H), 6.32 (s, 1 H), 7.38 (m, 2 H); IR 3150, 2960, 2890, 1585, 1500, 1470, 1435, 1375, 1325 cm^{-1}; MS M^+ 293.9762 (calcd for $C_9H_{11}IO_3$, 293.9752); major fragments 294 (1.0), 227 (1.2), 155 (4.4), 140 (11.2), 139 (100), 95 (83.8), 77 (5.0).

1-(3-Furyl)-4-(phenylseleno)-5-hexyn-1-one, Ethylene Ketal. A 25-mL flask was charged with 12 mL of DME and 0.250 mL (1.71 mmol) of phenyl propargyl selenide. This was flushed with N_2 and cooled to −78 °C, and 3.6 mL of 1 M LDA was added slowly. The resulting dark green solution was stirred for 12 min, and 300 mg (1 mmol) of iodide **22** was added in 2 mL of DME. This was stirred for 2 h at −78 °C (after 10 min a precipitate began to form and the reaction mixture lightened) and was then poured into dilute $NaHCO_3$. The layers were separated and the aqueous was washed three times with ether–pentane (1:1). The organic solutions were combined and shaken with brine and then filtered through Na_2SO_4. Solvent removal left an oil which was purified by preparative TLC (22% ether–pentane). At R_f 0.29 was centered a broad band, 327 mg of product (90% yield): NMR ($CDCl_3$) δ 1.96 (m, 2 H), 2.18 (m, 2 H), 2.40 (d, J = 2 Hz, 1 H), 3.92 (m, 5 H), 7.38 (m, 5 H), 7.64 (m, 2 H).

1-(3-Furyl)-4-(phenylseleno)-7-hydroxy-8-methyl-5-nonyn-1-one, Ethylene Ketal (23). In an oven-dried flask was placed the purified selenide prepared above (186 mg, 0.52 mmol) and 5 mL of DME. After being flushed with N_2, the solution was cooled to −78 °C and 0.52 mL of 1 M LDA was added. After 10 min, 0.06 mL of isobutyraldehyde (excess) was added by syringe, and the resulting mixture was warmed to 0 °C for 25 min. This reaction mixture was then decanted into dilute $NaHCO_3$ and worked up exactly as for the previous reaction. The solvent was removed. Small amounts of DME remained to contaminate the sample, though the NMR showed no other impurity (vide infra).

Alternatively, both of the previous reactions could be run in one pot. A typical experiment follows. In an oven-dried flask cooled to −78 °C was placed 8 mL of DME and 0.13 mL (0.89 mmol) of phenyl propargyl selenide and 1.76 mL of 1 M LDA was added. After 10 min, a solution of 238 mg (0.8 mmol) of iodide **23** in 1 mL of DME was added and allowed to react at −78 °C for 2 h. Then 0.140 mL of isobutyraldehyde (excess) was added, and the mixture was warmed to 0 °C for 25 min. After the solution was decanted into dilute $NaHCO_3$, the layers were separated and the water layer was extracted three times with 1:1 ether–pentane. The organic extracts were combined, washed with brine, and filtered through Na_2SO_4. The solvent was then stripped and the residue chromatographed (preparative TLC, 25% ether–pentane). Careful separation of the lower bands gave 230 mg of **23** at R_f 0.22 (65% yield): NMR ($CDCl_3$) δ 0.95 (d, J = 7 Hz, 6 H), 1.90 (m, 3 H), 2.18 (m, 2 H), 3.2 (m, 1 H), 3.90 (m, 5 H), 4.14 (dd, J = 8, 2 Hz, 1 H), 6.30 (s, 1 H), 7.30 (m, 5 H), 7.56 (m, 2 H); IR 3480, 3210, 3110, 3010, 2940, 1590, 1580, 1515, 1490, 1450 cm^{-1}; MS M^+ 434.0979 (calcd for $C_{22}H_{26}O_4Se$, 434.0996).

1-(3-Furyl)-5-(phenylseleno)-7-hydroxy-8-methyl-4-nonen-1,6-dione, 1-Ethylene Ketal (24, X = SePh). In 5 mL of CH_2Cl_2 was dissolved ca. 0.5 mmol of the crude seleno alcohol **23** from the two-pot sequence (see previous experiment) and the resulting solution was cooled to −78 °C. To this was added 0.5 mmol of *m*-CPBA. After 45 min 0.09 mL of pyridine was added and the now homogeneous solution was allowed to

(32) W. C. Still, *J. Am. Chem. Soc.*, **100**, 1481 (1978).

(33) For the preparation of anhydrous chloramine-T see: K. B. Sharpless, T. Hori, L. K. Truesdale, and C. O. Dietrich, *J. Am. Chem. Soc.*, **98**, 269 (1976).

warm to 25 °C during 1 h. Dilution with 1:1 ether-pentane (10 mL) followed by washing with 10% HCl, twice with saturated Na_2CO_3, once with brine, and filtration through Na_2SO_4 gave after removal of solvent and preparative TLC with 50% ether-pentane (R_f 0.05-0.53) 198 mg of a mixture of (*Z*)- and (*E*)-**24**, X = H and SePh (87% yield based on 1-(3-furyl)-4-(phenylseleno)-5-hexyn-1-one): IR 3580, 3100, 1765(sh), 1720, 1620, 1550, 1530, 1490 cm^{-1}.

A sample of stereochemically pure (*E*)-**24** (X = H) was prepared by deselenation of the mixture prepared above by using the same procedure as for the conversion of **12** to **14** (1 PhSeNa/NEt_3/MeOH; 2 H_2O_2): NMR ($CDCl_3$, 270 MHz) δ 0.69 (d, J = 6.9 Hz, 3 H), 1.11 (d, J = 6.9 Hz, 3 H), 2.1 (m, 3 H), 2.38 (br q, J = 7 Hz, 2 H), 3.95 (symm m, 4 H), 4.24 (d, J = 2.2 Hz, 1 H), 6.22 (dt, J = 15.6, 1.5 Hz, 1 H), 6.32 (m, 1 H), 7.05 (dt, J = 15.6, 7.0 Hz, 1 H), 7.4 (m, 2 H).

1-(3-Furyl)-4,8-dimethyl-7-hydroxy-1,6-nonandione, 1-Ethylene Ketal. An oven-dried flask was flushed with N_2, and 741 mg of CuI (3.88 mmol) was added, followed by 40 mL of ether and 0.29 mL of dimethyl sulfide. This was cooled to 0 °C, and MeLi (~1 M, 8 mL) was added until a clear yellow solution was obtained. After 15 min, the solution was cooled to -78 °C and 350 mg of enones **24** in 2.5 mL of ether was added. The reulting bright yellow solution was stirred at -78 °C for 2 h and then decanted into 15 mL of 10% HCl. The solid was removed by filtration (and washed with ether), and the acid layer was extracted three times with ether. The combined organic extracts were shaken with basic NH_4Cl-NaOH (pH 8.5) and brine. After filtration through Na_2SO_4, the ether was evaporated. The residue was taken up into 2.4 mL of MeOH and 0.3 mL of PhSH, and 0.4 mL of NEt_3 was added. After being stirred for 1.25 h, the reaction mixture was diluted with 5% NaOH and extracted four times with 1:1 ether-pentane. The extracts were combined, washed with brine, and dried over Na_2SO_4. Solvent removal followed by preparative TLC with 45% ether-pentane gave a broad band centered at R_f 0.30, containing 160 mg of the desired ketal (66% yield, ~2:1 mixture of diastereomers): NMR ($CDCl_3$) δ 0.5-1.45 (m, ~11 H including d, J = 7 Hz, at 0.70, 0.91, and 1.10), 1.6-2.5 (m, ~7 H), 3.43 (d, J = 6 Hz, 1 H), 3.9 (m, 5 H), 6.37 (m, 1 H), 7.43 (m, 2 H); IR 3480, 2960, 2880, 1705, 1500, 1420, 1385, 1365, 1175, 1115, 1050, 1020 cm^{-1}; MS M^+ 310.1780 (calcd for $C_{17}H_{26}O_5$, 310.1780); major fragments 310 (0.1), 210 (3.4), 195 (2.2), 149 (3.0) 147 (7.4), 139 (100), 123 (6.8), 95 (59.5), 83 (9.9), 73 (13.3), 71 (18.6), 55 (24.2).

1-(3-Furyl)-4,8-dimethyl-7-hydroxy-1,6-nonanedione ((±)-7-Hydroxymyoporone and Its Epimer). The ketal (220 mg, 0.71 mmol) was dissolved in 1.6 mL of THF, and 2.4 mL of 50% aqueous HOAc was added. The resulting solution was stirred at 21 °C for 7 h, diluted with 20 mL of saturated $NaHCO_3$, and extracted five times with ether-pentane (1:1). The extracts were washed with 1 mL of brine and filtered through Na_2SO_4. Solvent removal left 185 mg of semisolid crude material. Examination of the NMR showed that the ketal was >90% hydrolyzed (crude yield was 88%). Recrystallization from 50% ether in pentane (three times) gave small white crystals, mp 70.5-71.5 °C.

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.61; H, 8.30.

The proton and carbon NMR spectra of the crude product showed the presence of an ~70:30 mixture of isomers which could not be separated by TLC. The NMR spectra are summarized and compared with those of authentic 7-hydroxymyoporone in Table II (supplementary material). The synthetic mixture did not show any separate carbon resonances for the isomers in $CDCl_3$ solvent at 15.04 MHz, but in C_6D_6 at 25.16 MHz all except two of the aliphatic resonances showed peaks in approximately a 70:30 ratio. The 270-MHz proton spectra in benzene also showed a number of split signals. In each case the minor signal was identical with that of authentic (+)-7-hydroxymyoporone.

6-Phenyl-2-hexynol. LDA (2.05 mL, 1 M) was added to a cooled (-78 °C) THF (4 mL) solution of 0.28 mL (2 mmol) of 1-(phenylseleno)-1-propyne under N_2. After 10 min, 0.285 mL (2.02 mmol) of 3-phenylpropyl iodide was added and stirred for 1 h, and the reaction mixture was worked up. The crude 3-(phenylseleno)-6-phenyl-1,2-hexadiene (NMR δ 1.79 (quintet, J = 7 Hz, 2 H), 2.2 (m, 2 H), 2.56 (t, J = 7 Hz, 2 H), 4.57 (t, J = 2 Hz, 2 H), 7.0-7.7 (m, 10 H)) was oxidized without further purification. It was dissolved in 6 mL of CH_2Cl_2 and 0.2 mL of pyridine. Water (0.5 mL) and H_2O_2 (30%, 0.5 mL) were added to the solution, and it was vigorously stirred to initiate the reaction. Once the oxidation had started, the reaction mixture was stirred at moderate speed for 0.5 h and then worked up as usual. The concentrated filtrate gave 0.235 g (68% yield) of 6-phenyl-2-hexynol upon preparative TLC: NMR δ 1.78 (quintet, J = 7 Hz, 2 H), 2.16 (br t, J = 7 Hz, 2 H), 2.69 (t, J = 7 Hz, 2 H), 3.54 (s, 1 H), 4.15 (t, J = 1.5 Hz, 2 H), 7.1 (m, 5 H); IR 3380, 3030, 2940, 2220, 1602 cm^{-1}; MS M^+ 174.1041 (calcd for $C_{12}H_{14}O$, 174.1045.

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Supplementary Material Available: Experimental details for runs 4, 6, 8, and 10 (Table I), for the crossover experiment and the preparation of 3-(trifluoromethyl)phenyl propargyl selenide and deuterated phenyl propargyl selenide, for the determination of the regioselectivity for the methylation of **1** and **5a**, and for the preparation and reactions of 3-(methylthio)-1-nonyne and ^1H and ^{13}C spectral data for 7-hydroxymyoporone and epi-7-hydroxymyoporone (7 pages). Ordering information is given on any current masthead page.

Frontier-Controlled Pericyclic Reactions of Cyclooctatetraene with Cyclopentadienones. First Example of Exo [4 + 6]π Cycloadduct by Effective Secondary Orbital Control and Its Molecular Structure

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Abstract: Pericyclic reactions of cyclooctatetraene with 2,5-bis(methoxycarbonyl)-3,4-diphenylcyclopentadienone (**1a**), 2-oxo-1,3-bis(ethoxycarbonyl)-2*H*-cyclopenta[*i*]acenaphthylene (**1b**), and 2-oxo-1,3-diphenyl-2*H*-cyclopenta[*l*]phenanthrene (**1c**) were investigated. The cycloaddition reactions of cyclooctatetraene with **1a** and **1b** afforded the novel exo [4 + 6]π cycloadducts together with bis-Diels-Alder cycloadducts. The configuration of the exo [4 + 6]π cycloadduct was assigned by the spectral data and verified by X-ray crystallography. The reactions are discussed on the kinetic and molecular orbital calculation data together with X-ray structural determination of the exo [4 + 6]π and bis-Diels-Alder cycloadducts.

Cyclooctatetraene has played an outstanding role in many aspects of theoretical and synthetic chemistry. As a medium-ring polyene, it undergoes a wide variety of reactions which are often accompanied by skeletal transformations, and it is the progenitor

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