(8) J. F. Coetzee and G. R. Padmanabhan, *J. Amer. Chem. Soc.*, **87**, 5005 (1965).
(9) I. M. Kolthoff and M. K. Chantooni, *J. Amer. Chem. Soc.*, **95**, 8539 (1973).
(10) On the other hand, acetonitrile has two (surmountable) disadvantages: anthrone tautomerizes spontaneously in this solvent and anthranol hydrogen bonds weakly to acetonitrile.
(11) See also P. W. Arana, C. W. Su, and J. W. Watson, *Chem. Commun.*, 363 (1970).
(12) No statistical correction for Dabco was made.
(13) F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, **93**, 511 (1971).
(14) P. Haake, R. D. Cook, and G. H. Hurst, *J. Amer. Chem. Soc.*, **89**, 2650 (1967).
(15) A qualitative explanation for the reactivity of weak oxygen bases in terms of Linnett theory may be found in the Ph.D. thesis of R. F. Williams (see footnote 7).
(16) The magnitude of 1.47 ppm may be gauged from the 2.57-ppm shift of *sym*-tetramethylguanidine relative to that of *N*,*N*-dimethylacetamide (the strongest and weakest bases recorded in ref 3).
(17) Phenoxide is a stronger base than triethylamine in acetonitrile by more than 8 pK_a units: J. F. Coetzee, *Progr. Phys. Org. Chem.*, **4**, 45 (1967).
(18) H. Baba, A. Matsuyama, and H. Kokubun, *Spectrochim. Acta*, **25A**, 1709 (1969), have found that *p*-nitrophenol and triethylamine form solvent-separated ion pairs in acetonitrile. However, anthranol (with a pK_a in acetonitrile probably six units greater than that of *p*-nitrophenol)[17] would not be expected to form ion pairs.
(19) F. M. Menger and A. C. Vitale, *J. Amer. Chem. Soc.*, **95**, 4931 (1973).
(20) Recipient of a Camille and Henry Dreyfus Foundation Teacher-Scholar Grant and a National Institutes of Health Research Career Development Award.

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Organoselenium Chemistry. Conversion of Cyclic Ketones and β-Dicarbonyl Compounds to Enones

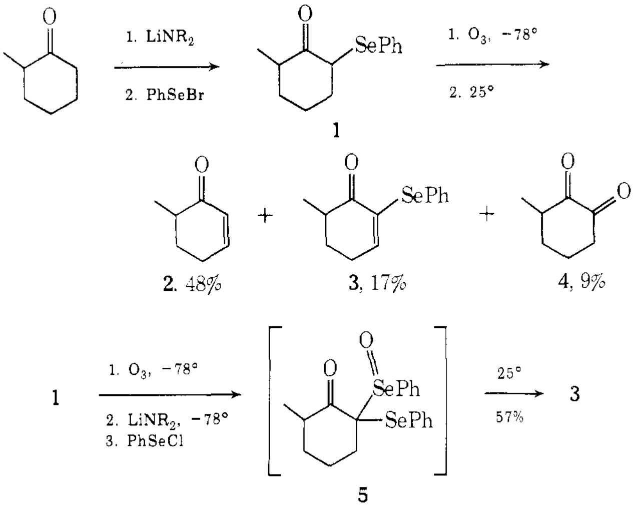
Summary: The selenoxide syn elimination method for the synthesis of enones has been extended to the preparation of β-dicarbonyl enones, cyclobutenones, and enone ketals; and an important limitation to the method has been found.

Sir: The syn elimination of selenoxides has been shown to be a convenient, mild, and high-yield method for the preparation of α,β-unsaturated carbonyl compounds.[1,2] The precursor α-phenylselenocarbonyl compounds can be prepared from ketones, aldehydes, and esters,[1,2] as well as from enol acetates[1b,2b] and acetylenes.[1b] We describe here some limitations of the method not heretofore recognized, as well as extensions to four-membered rings and β-dicarbonyl compounds.

The necessity for achieving a cyclic transition state in the selenoxide elimination[3] may impose conflicting conformational demands on cyclic systems, and in fact only a limited range of cyclic enones (five- and six-membered rings) have been prepared. Our inability to achieve a high yield transformation of 2-methyl-6-phenylselenocylohexanone (1) to the enone (2)[1a] led us to examine this reaction in more detail (Scheme I). The formation of by-products 3 and 4 can be rationalized as resulting from a Pummerer-like reaction of the ketoselenoxide. 2-Phenyl-6-phenylselenocyclohexanone[6] also gives only a fair yield of enone, but the isomeric 2-phenylseleno compound, in which the phenyl substituent prevents the Pummerer reaction, gives enone in high yield (Table I). Scheme I also presents an alternate synthesis of the vinyl selenide 3 by selenenylation of the ketoselenoxide.

Both 2-phenylselenocycloheptanone and -cyclooctanone give only small amounts of enone (5–15%) under all conditions we have tried. If the oxidation is carried out using sodium metaperiodate buffered with sodium bicarbonate, 33 and 48%, respectively, of the vinyl selenides analogous to 3 are formed.

Scheme I



The occurrence of a facile Pummerer reaction depends on the acidifying effect of the carbonyl group on the α proton. Hence it is not surprising that the ketal 6 undergoes oxidation[8a] and elimination[8b] to enone ketal 7 in good yield. 2-Phenylselenocycloheptanone can similarly be converted to the ethylene ketal of cycloheptenone in 68% yield.

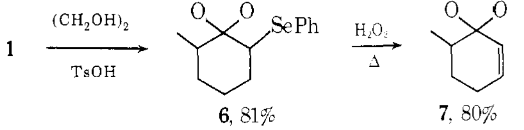
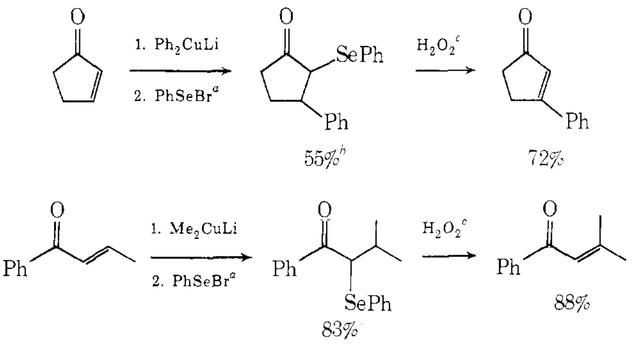


Table I shows several examples of the preparation of cyclopentenones[9a] and cyclobutenes. The great facility with which cyclobutanones undergo Baeyer–Villiger oxidation necessitates the use of ozone as oxidant[10] for the preparation of 3-phenyl-2-cyclobutenone.[11] Scheme II presents two examples which illustrate the ability to trap copper enolates with PhSeBr for the synthesis of β-substituted enones.

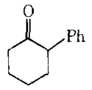
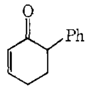
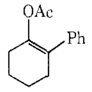
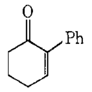
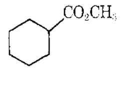
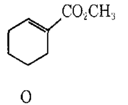
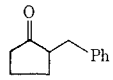
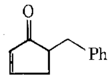
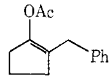
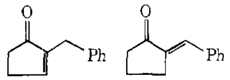
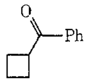
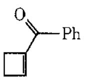
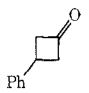
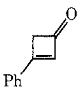
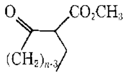
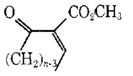
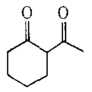
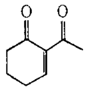
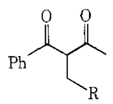
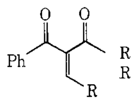
The extension of the selenoxide elimination to the synthesis of enediones from β-dicarbonyl compounds is an important one, since such transformations are difficult using classical methods.[12] The dehydrohalogenation in particular often fails because of instability of halodicar-

Scheme II



[a] Total quantity of PhSeBr used was 10% excess over RLi used in the preparation of the cuprate. A small amount of Ph_2Se_2 was added to suppress formation of α-halo ketones. [b] Both cis and trans isomers (1:4.5) appeared to give enone. [c] Reference 8a.

Table I
Preparation of α,β-Unsaturated Carbonyl Compounds

Compd	Olefin	Yield,[a] %	
		Selenide	Olefin
			60^{b-d}
		86^{e}	94^{d}
			$96^{b,c,f}$
			66^{b-d}
	 56:44	96^{g}	95^{d}
		87^{c}	83^{d}
		47^{c}	58^{h}
	 $n = 8$	96^{i}	93^{d}
	$n = 7$	90^{i}	93^{d}
	$n = 6$		$81^{b,h,i}$
	$n = 5$		$28^{b,h,i}$
		86^{i}	90^{h}
	 R = H	93^{i}	80^{d}
	R = *n*-Pr	96^{i}	$93^{d,j}$

[a] All compounds were fully characterized by spectral methods. [b] Overall yield. [c] Selenide was prepared by the reaction of lithium enolate (LiN-*i*-Pr_2) with PhSeBr or PhSeCl at −78°. [d] Oxidation of selenide with H_2O_2 in CH_2Cl_2; see ref 8a. [e] Selenide was prepared by reaction of lithium enolate (from cleavage of enol acetate with MeLi) with PhSeBr at −78°. [f] One pot procedure described in ref 1a. [g] Selenide prepared by reaction of enol acetate with $PhSeO_2CCF_3$; see ref 1b. [h] Oxidation by ozonolysis in CH_2Cl_2 at −78°, followed by warming to 25°. [i] Selenide prepared by the reaction of sodium enolate (NaH) in THF with PhSeCl or PhSeBr. [j] A 95:5 mixture of geometric isomers is formed.

bonyl compounds or enones under the reaction conditions. We have found the method to work superbly for the eight, seven and six-membered 2-carboethoxycloalkenones, a result which underscores the conclusions reached above that reactions involving the acidic α hydrogen, were responsible for the failure to achieve high yield syntheses of cylooctenone or cycloheptenone itself. Hydrogen peroxide cannot to be used as oxidant for the five-[13] and six-membered cyclic ketones, since rapid epoxide formation and further degradation occurs. Here ozonolysis at −78° followed by warming is the best procedure[10] (elimination occurs at or below −10°).

An important consequence of the mild reaction conditions is that in all cases exclusively nonenolized β-dicarbonyl enones are formed, even though a number of these systems are known to be significantly or even predominantly enolic at equilibrium.[12] Other synthetic methods invariably give a mixture of keto and enol forms.

The preparation of α-phenylseleno-β-dicarbonyl compounds is conveniently carried out at room temperature by the addition of ketone to a suspension of NaH (excess) in THF. When hydrogen evolution is complete (<15 min) a solution of 1.05 equiv of PhSeCl (or PhSeBr) in THF is added dropwise, and the reaction is immediately poured into ether and saturated $NaHCO_3$ solution. Completion of the work-up gives the selenide in quantitative yield. Oxidation is then carried out either by the H_2O_2–CH_2Cl_2 method[8a] or by ozonolysis.

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References and Notes

(1) (a) H. J. Reich, I. L. Reich, and J. M. Renga, *J. Amer. Chem. Soc.*, **95**, 5813 (1973); (b) H. J. Reich, *J. Org. Chem.*, **39**, 428 (1974).

(2) (a) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Amer. Chem. Soc.*, **95**, 6137 (1973); (b) D. L. J. Clive, *Chem. Commun.*, 695 (1973); (c) P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 120 (1974).

(3) The cyclic nature of the elimination can be inferred from differences in the elimination rates of diastereomeric steroidal selenoxides[4] and from the olefin stereochemistry in an acyclic system.[5]

(4) D. N. Jones, D. Mundy, and R. D. Whitehouse, *Chem. Commun.*, 86 (1970).

(5) K. B. Sharpless, M. W. Young, and R. F. Lauer, *Tetrahedron Lett.*, 1979 (1973).

(6) The deprotonation of 2-phenylcyclohexanone using LiN-*i*-Pr_2 in THF occurs 99:1 in favor of the secondary position (glc analysis of enol acetates). Acid-catalyzed ($HClO_4$) formation of enol acetates[7] gives a 90:10 mixture, with phenyl-substituted olefin predominating. See B. Miller and H. S. Wong [*Tetrahedron*, **28**, 2369 (1972)] for a study of the bromination and dehydrobromination of 2-phenylcyclohexanone.

(7) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 2502 (1965).

(8) (a) Oxidation was carried out by magnetically stirring a solution of the selenide in methylene chloride containing 2 equiv of pyridine with 5 to 10 equiv of 15% aqueous hydrogen peroxide for $\sim$10 min, when oxidation is usually complete (in a few cases the thermal elimination requires somewhat longer reaction times). We have found these conditions for oxidation and elimination to be superior in convenience and purity and yield of products to other methods for any selenide where the olefin product is not attacked rapidly by hydrogen peroxide. (b) Oxidation at room temperature as above gave selenoxide; elimination was completed by refluxing for 5 min in CCl_4 containing 2 equiv of pyridine. This is the only selenoxide among those described here which does not eliminate readily at or below room temperature.

(9) (a) Positional control during synthesis of enones by dehydrobromination of α-halo ketones has been achieved using a similar technique.[9b] (b) P. L. Stotter and K. A. Hill, *J. Org. Chem.*, **38**, 2576 (1973).

(10) Under these conditions $\frac{2}{3}$ of the selenium is recovered in the product as Ph_2Se_2; the remainder is removed as $PhSeO_2H$ in the work-up.

(11) S. L. Manatt, M. Vogel, D. Knutson, and J. D. Roberts, *J. Amer. Chem. Soc.*, **86**, 2645 (1964).

(12) (a) M. E. McEntee and A. R. Pinder, *J. Chem. Soc.*, 4419 (1957); (b) C. W. T. Hussey and A. R. Pinder, *ibid.*, 3525 (1961); (c) C. W. T. Hussey and A. R. Pinder, *ibid.*, 1517 (1962); (d) J. E. Brenner, *J. Org. Chem.*, **26**, 22 (1961); (e) D. Gorenstein and F. H. Westheimer, *J. Amer. Chem. Soc.*, **92**, 634 (1970).

(13) J. N. Marx, J. H. Cox, and L. R. Norman [*J. Org. Chem.*, **37**, 4489 (1972)] have dehydrogenated 2-carbomethoxycyclopentanone with SeO_2 in 48% yield. They also were unable to purify their reaction product.

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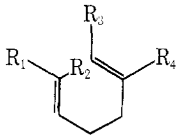
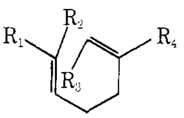
A General 1,5-Diene Synthesis. Application to the Synthesis of Squalene

Summary: A new method for the preparation of geometrically pure 1,5-dienes *via* coupling of allylic sulfones with allylic halides followed by reductive cleavage of the allylated sulfones is described.

Sir: The construction of 1,5-dienes of types I and II involving over-all allyl alcohol coupling with geometrical and positional control has recently received attention as a result of the importance and general utility of such systems for the synthesis of juvenile hormones and cyclic terpenoid or steroidal precursors. In conjunction with another project we required a method for carbon–carbon bond formation with formation of a 1,5-diene unit.[1]



I

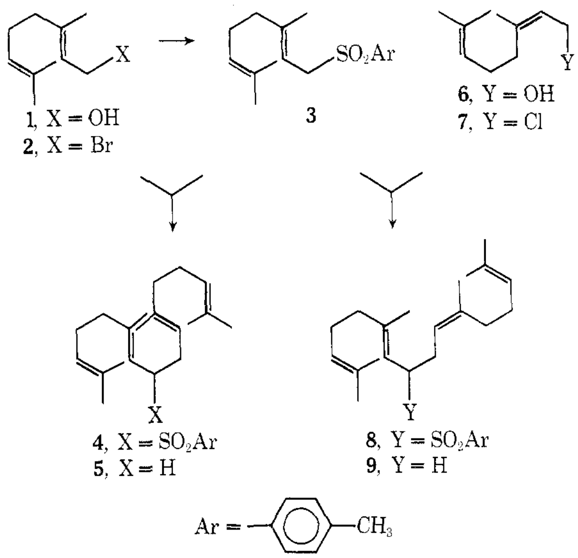


II

We wish to report a new method for the preparation of geometrically pure 1,5-dienes *via* coupling of allylic alcohol units which proceeds in good yields with essentially complete preservation of the geometry and position of the olefinic bonds.

The over-all synthetic sequence involves (1) conversion of the allylic alcohols to allylic bromides, (2) sulfone formation with one of the allylic bromides, (3) C-allylation of the desired stabilized allyl carbanion with another allylic bromide unit, and (4) reductive cleavage of the new sulfone. The complete process can be conveniently carried out in 60–70% yield with <1–2% isomerization, either positional or cis-trans.

Treatment of pure *trans*-geraniol (1) in anhydrous ether with PBr_3 at 0° afforded *trans*-geranyl bromide (2) in near-quantitative yield. Treatment of 2 with sodium *p*-toluenesulfinate in anhydrous DMF at ambient temperature for 18 hr gave *trans*-geranyl *p*-tolyl sulfone 3 in 98% yield. Metalation of sulfone 3 at $-20°$ with *n*-butyllithium in tetrahydrofuran–hexamethylphosphoramide (4:1) followed by cooling to $-78°$ and addition of *trans*-geranyl bromide resulted in formation of pure sulfone 4 (89% yield). Nmr analysis of the coupled sulfone revealed lack of aliphatic methyl resonance, a consequence of coupling at the γ position. In addition the nmr spectrum of 4 revealed no terminal vinyl resonance. Geometrical isomerization was rigorously ruled out by coupling of cis- and trans-allylic isomers and glpc comparison of the respective products derived from reduction cleavage of the sulfone moiety (*vide infra*).



The new sulfone 4 was purified and reduced at 0° with lithium in ethylamine under a nitrogen atmosphere. After stirring for 30 min the reaction mixture was worked up in the standard manner and the product chromatographed on silica gel to yield pure all-trans bisgeranyl 5[2] (77%) [the ratio of cis:trans allylic methyl groups at δ 1.58 and 1.67 was 2.0:1.0 as anticipated for pure trans,trans compound].

Coupling of *trans*-geranyl sulfone 3 with neryl chloride[1d] 7 as described gave sulfone 8 (71%). Reductive cleavage of the sulfone provided an 82% yield of *cis,trans*-nerylgeranyl 9 [nmr ratio of cis:trans allylic methyl groups was 1.0:1.0 as expected for pure cis,trans compounds]. Bisgeranyl 5 and nerylgeranyl 9 are readily separable by glpc and the products of the above couplings indicated <1–2% contamination.

Although the cleavage of the carbon–sulfur bond with lithium in ethylamine proved to be satisfactory, we had initially hoped to be able to perform the required cleavage reaction under milder reaction conditions. Dabby and coworkers[3] have reported that the C–S bond of sulfones can be cleaved with sodium amalgam. To investigate this carbon–sulfur cleavage reaction sulfone 4 was treated with 3% sodium amalgam[4] in ethanol for 1.5 hr. In addition to the expected all-trans tetraene 5 there was obtained the rearranged tetraene **10** in a ratio of 9:4 (90%), making this procedure unattractive from a synthetic viewpoint. Use of hexamethylphosphoramide in ethanol (6:1) resulted in an 11:6 mixture of 5 and **10**, respectively. In the case of 8, use of HMPA resulted in a 2:1 mixture of 9 and **11**.

In a similar fashion employing the procedures developed above, we have prepared *all-trans*-squalene **16** from pure *trans,trans*-farnesol **12**.[5]