under vacuum at −10 °C, and aqueous THF was added. This mixture of cyclopentanone sulfoxide diastereomers (*S*)-(+)-**7a** and **7b** was reductively cleaved by aluminum amalgam; after preparative TLC and 0 °C rotary evaporation of most of the solvent, complete removal of solvent diethyl ether at 0.025 mmHg from the cold (−78 °C), crystalline product mixture reproducibly gave pure *trans*-(*S*)-(+)-**1a** [^{1}H NMR δ 1.08 (3 H, d, J = 9 Hz] and *cis*-(*S*)-(−)-**1b** [^{1}H NMR δ 0.98 (3 H, d, J = 9 Hz] in a 92:8 ratio ($[\alpha]^{24}_D$ +130°) in 55–61% overall yield from cyclopentenone sulfoxide (*S*)-(+)-**5** with *100% asymmetric induction*! If zinc bromide was not used to preform chelate **5a**, 1% copper bromide catalyzed vinylmagnesium bromide conjugate addition to cyclopentenone sulfoxide (*S*)-(+)-**5** proceeded with 80% asymmetric induction. In a separate experiment, the cyclopentanone sulfoxide diastereomers (*S*)-(+)-**7a** and **7b** from the zinc bromide mediated vinyl conjugate addition were treated with dimethylcopperlithium at −78 °C;[4,11] after reductive cleavage of the sulfinyl group had occurred (0 °C, 3 h), the regiospecifically formed enolate ion intermediate was added to a solution of trimethylsilyl chloride and triethylamine to form cyclopentenol silyl ether (*S*)-(+)-**2** in 54% yield by GLC calibration; preparative GLC provided (*S*)-(+)-**2**, $[\alpha]^{25}_D$ +55.4° (*c* 0.79, CCl_4).

Optically pure steroid intermediates (*S*)-**1** and (*S*)-(+)-**2**, available for the first time via a reliable, convenient, and *complete* asymmetric synthesis, will certainly be used for preparation of optically pure estrone and estrone derivatives. Furthermore, optically pure cyclopentenone sulfoxide (*S*)-(+)-**5** and related enone sulfoxides have many possible applications in synthesis of complex, enantiomerically pure compounds of broad interest and utility. We are actively pursuing such applications.

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Registry No. (2*S*,3*S*)-**1a**, 75917-46-3; (2*R*,3*S*)-**1b**, 75917-45-2; (*S*)-**2**, 74036-33-2; (*S*)-**5**, 79681-26-8; **6**, 79681-27-9; **7a**, 79681-28-0; **7b**, 79732-89-1; vinyl bromide, 593-60-2.

Supplementary Material Available: Experimental details for the **5** → **6** → **7a** + **7b** → **1a** + **1b** conversions and Tables I–III consisting of fractional coordinates, bond distances, bond angles, and observed and calculated structure factors for cyclopentane sulfoxide (*S*)-(+)-**7a** (6 pages). Ordering information is given on any current masthead page.

(11) For use of dimethylcopper–lithium in converting various α-heteroatom-substituted ketones into the corresponding enolate species, see: (a) Posner, G. H. "An Introduction to Synthesis Using Organocopper Reagents"; Wiley: New York, 1980; pp 22, 42. (b) Posner, G. H.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 3076. (c) Lansbury, P. T.; Erwin, R. W.; Jeffrey, D. A. *Ibid.* **1980**, *102*, 1602. (d) Deprés, J.-P.; Greene, A. E. *J. Org. Chem.* **1980**, *45*, 2036.

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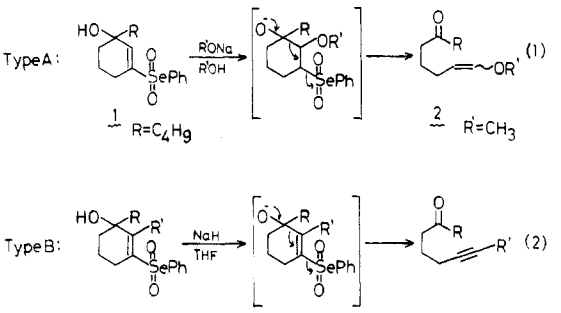
Highly Efficient Method for Ethylenic or Acetylenic Ketones via Fragmentation of Hydroxy Vinyl Selenones

Summary: Treatment of cyclic 3-hydroxyvinyl selenones with bases at room temperature leads to the formation of ethylenic or acetylenic ketones in good yields via 1,4-fragmentation, where phenylselenonyl group behaves as an excellent nucleofuge.

Sir: During our continuing study on the novel reactivity of aryl vinyl selenoxides[1] and/or selenones,[2] we have already demonstrated that an arylseleninyl or arylselenonyl group worked both as a very effective electronegative activator of olefinic bonds and as a good leaving group; e.g., some efficacy of these groups was shown in the cyclopropanation reaction[1] and the methoxyoxetane formation.[2]

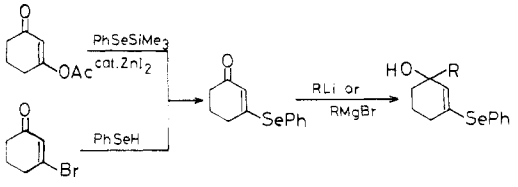
Further investigation has revealed that the phenylselenonyl group behaves quite effectively as a nucleofuge[3] in 1,4-fragmentation reactions[4] as outlined in eq 1 and 2.



When 1-butyl-3-(phenylselenonyl)-2-cyclohexen-1-ol (**1**) was treated with sodium methoxide in methanol at room temperature overnight and then at 45 °C for 3 h, 10-methoxy-9-decen-5-one (**2**) was obtained in 86% yield.[5] This reaction proceeds most probably via the conjugate addition of methoxide[6] to vinyl selenones followed by a 1,4-fragmentation reaction. This type of reaction (type A) was observed in the reaction of **1** with alkoxides (methoxide, ethoxide) and benzenethiolate to give 1,6-dicarbonyl derivatives in good to excellent yields. Results are summarized in Table I.

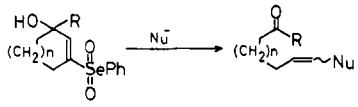
For the preparation of the starting hydroxy vinyl selenones it should be noted that the oxidation of hydroxy vinyl selenides to the corresponding vinyl selenones was quite difficult because of lability of allylic tertiary alcohols;[7] i.e., they underwent dehydration readily even on standing

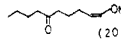
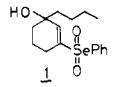
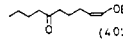
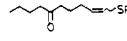
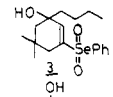
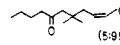
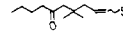
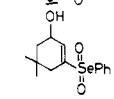
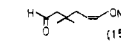
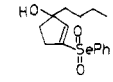
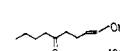
(1) Shimizu, M.; Kuwajima, I. *J. Org. Chem.* **1980**, *45*, 2921.
(2) Shimizu, M.; Kuwajima, I. *J. Org. Chem.* **1980**, *45*, 4063.
(3) For the use of this term, see ref 4.
(4) Grob, C. A.; Schiess, P. W. *Angew. Chem.* **1967**, *79*, 1. Grob, C. A. *Ibid.* **1969**, *81*, 543. Recent examples, see: Clark, D. A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567 and references cited therein.
(5) In contrast to the acyclic system, neither the oxetane nor the oxirane could be detected (see ref 2).
(6) The ability of the phenylselenonyl moiety as a leaving group has already been attested (see ref 2).
(7) Hydroxy vinyl selenides were usually prepared in the following manner:



0022-3263/81/1946-5246$01.25/0

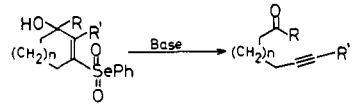
Table I. Fragmentation Reaction of Type A[a]

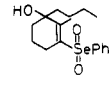
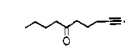
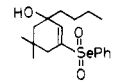
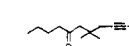
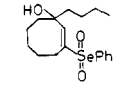
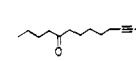


run	substrate	nucleophile	product[b] (olefin E/Z ratio[c])	% yield[d]
1		MeONa	 (20:80)	86
2	 1	EtONa	 (40:60)	84
3		PhSNa		68
4		MeONa	 (5:95 <)	78
5	3	PhSNa		43
6		MeONa	 (15:85)	68[c]
7		MeONa	 (80:20)	53

[a] Reactions were carried out on a 0.1–0.5-mmol scale. [b] All products were characterized by NMR, IR, and elemental analysis. [c] Determined by NMR. [d] Isolated yield.

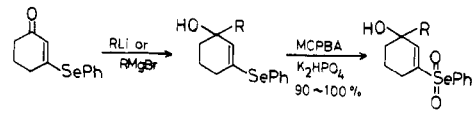
Table II. Fragmentation Reaction of Type B[a]



run	substrate	base	product[b]	% yield[c]
8		MeONa		40
9		NaH		84
10		NaH		59[d]
11		MeONa		43

[a] Reactions were carried out on a 0.08–0.5-mmol scale. [b] All products were characterized by NMR, IR, and elemental analysis. [c] Isolated yield. [d] When potassium *tert*-butoxide or LDA was used as a base, the acetylenic ketone was obtained in 39% or 20% yield, respectively.

Scheme I

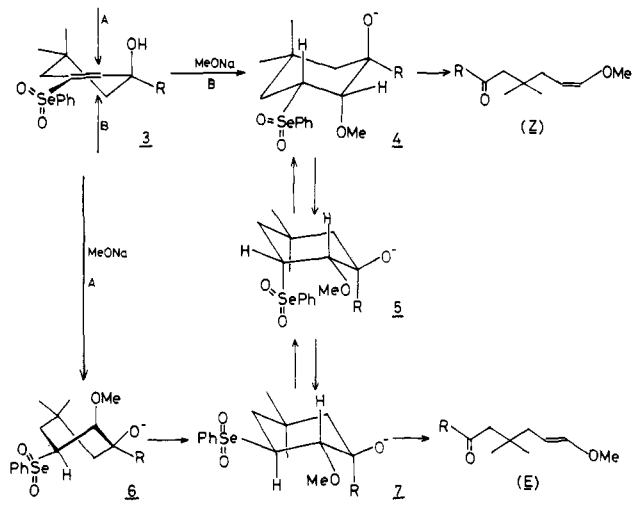


at −10 °C to give dienes. However, the transformation to selenones was successfully performed by the oxidation with MCPBA[8] in the presence of dipotassium hydrogen phosphate (6.0 equiv) in methanol at room temperature[9] (Scheme I).

Close examination of the olefin stereochemistry of the products has disclosed very interesting stereoselection; i.e.,

(8) Oxidation with peracetic acid was not successful.
(9) In the absence of dipotassium hydrogen phosphate, the desired hydroxy vinyl selenone was obtained in only 42% yield.

Scheme II



almost all of the product formed was one single compound in the case of the hydroxy vinyl selenone 3 (run 4, Table I). This selectivity may be explained in terms of the difference of the activation energies between the transition states 4 and 7 (Scheme II).[10] The attack of methoxide from the axial side (B) followed by protonation produces the intermediate 4 where the phenylselenonyl group is well situated for the 1,4-fragmentation mechanism, giving the *Z* olefin; whereas the conformational change of 4 gives the intermediate 5 which must undergo epimerization at the carbon bearing the phenylselenonyl group to 7 due to the antiperiplanar requirement of phenylselenonyl group. Since conformer 5 suffers from serious 1,3-diaxial repulsion between the R and methyl groups, this epimerization seems unlikely. The attack of methoxide from the equatorial side followed by protonation also leads to the intermediate 7 which fragments to the *E* olefin. However, this process is obviously unlikely due to the energetically unfavorable boat conformation 6. Thus, such high stereoselection was observed.

In the case of hydroxy vinyl selenones possessing tetrasubstituted olefins, the addition of alkoxide was quite slow, and the fragmentation reaction producing acetylenic ketones (type B)[11,12] predominated over the addition–fragmentation process. This type of fragmentation can be carried out selectively by using sodium hydride as a base. In contrast, vinyl selenoxides did not undergo fragmentation even on being heated but gave a complex mixture possibly through isomerization to allylic selenoxides.

In conclusion, considering the accessibility of vinyl selenones, we emphasize that the unique reactivity of the phenylselenonyl group will broaden the scope of the Grob-type fragmentation reactions, and it is expected that Se(VI)-containing species may be used widely in organic synthesis.

(10) Valls, J.; Toromanoff, E. *Bull. Soc. Chim. Fr.* **1961**, 758.
(11) Coke, J. L.; Williams, H. J.; Natarajan, S. *J. Org. Chem.* **1977**, *42*, 2380.
(12) For related fragmentation reaction of α,β-epoxy ketones, see: Eschenmoser, A.; Felix, D.; Ohloff, G. *Helv. Chim. Acta* **1967**, *50*, 708. Tanabe, M.; Crowe, D. F.; Dehn, R. L.; Detre, G. *Tetrahedron Lett.* **1967**, 3739. Schreiber, J.; Felix, D.; Eschenmoser, A.; Winter, M.; Gautschi, F.; Schulte-Elte, K. H.; Sundt, E.; Ohloff, G.; Kalvoda, J.; Kaufmann, H.; Wieland, P.; Anner, G. *Helv. Chim. Acta* **1967**, *50*, 2108. Tanabe, M.; Crowe, D. F.; Dehn, R. L. *Tetrahedron Lett.* **1967**, 3943. Muller, R. K.; Felix, D.; Schreiber, J.; Piers, K.; Horn, U.; Eschenmoser, A. *Helv. Chim. Acta* **1968**, *51*, 1461. Borrevang, P.; Hjort, J. Rapala, R. T.; Edie, R. *Tetrahedron Lett.* **1968**, 4905. Muller, R. K.; Felix, D.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1970**, *53*, 1479. Felix, D.; Schreiber, J.; Ohloff, G.; Eschenmoser, A. *Ibid.* **1971**, *54*, 2896. Felix, D.; Muller, R. K.; Horn, U.; Joos, R.; Shcreiber, J.; Eschenmoser, A. *Ibid.* **1972**, *55*, 1276. Corey, E. J.; Sachdev. H. S. *J. Org. Chem.* **1975**, *40*, 579.

These results are to be compared with those obtained from the fragmentation reaction of 3-halo-2-cycloalken-1-ols[11] where a high reaction temperature was required; i.e., the present reaction proceeds smoothly at around room temperature. Furthermore, although a fragmentation reaction using arenesulfonyl moiety as a nucleofuge has been successfully applied to the synthesis of *dl*-muscone,[13] simple cyclohexanol derivatives, for example, 3-(phenylsulfonyl)cyclohexanol, did not undergo the expected C–C bond cleavage even under rather drastic conditions, e.g., treament with potassium *tert*-butoxide in refluxing toluene. The high efficiency of the phenylselenonyl moiety as a leaving group is again pointed out.

However, the present fragmentation reaction has important limitations. Employment of other nucleophiles such as active methylene compounds did not meet with alkylative fragmentation.

Registry No. 1, 79681-30-4; (*E*)-2, 79681-31-5; (*Z*)-2, 79681-32-6; 3, 79681-33-7; 5,5-dimethyl-3-(phenylselenonyl)-2-cyclohexen-1-ol, 79681-34-8; 1-butyl-3-(phenylselenonyl)-2-cyclopenten-1-ol, 79681-35-9; (*E*)-10-ethoxy-9-decen-5-one, 79681-36-0; (*Z*)-10-ethoxy-9-decen-5-one, 79681-37-1; 10-(phenylthio)-9-decen-5-one, 79681-38-2; (*E*)-7,7-dimethyl-10-methoxy-9-decen-5-one, 79681-39-3; (*Z*)-7,7-dimethyl-10-methoxy-9-decen-5-one, 79681-40-6; 7,7-dimethyl-10-(phenylthio)-9-decen-5-one, 79681-41-7; (*E*)-3,3-dimethyl-6-methoxy-5-hexanal, 79681-42-8; (*Z*)-3,3-dimethyl-6-methoxy-5-hexenal, 79681-43-9; (*E*)-9-methoxy-8-nonan-5-one, 79681-44-0; (*Z*)-9-methoxy-8-nonen-5-one, 79681-45-1; 1-butyl-2-methyl-3-(phenylselenonyl)-2-cyclohexen-1-ol, 79681-46-2; 1-butyl-3-(phenylselenonyl)-2-cycloocten-1-ol, 79681-47-3; 9-undecyn-5-one, 79681-48-4; 7,7-dimethyl-9-decyn-5-one, 61882-83-5; 11-dodecyn-5-one, 79681-49-5; sodium methoxide, 124-41-4; sodium ethoxide, 141-52-6; sodium benzenethiolate, 930-69-8; sodium hydride, 7646-69-7.

(13) Fischli, A.; Branca, Q.; Daly, J. *Helv. Chim. Acta* **1976**, *59*, 2443.

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Intramolecular Nitrile Oxide Cycloaddition (INOC) Reactions in the Indole Series. 2. Total Synthesis of Racemic and Optically Active Paliclavine and 5-*epi*-Paliclavine

Summary: The first total synthesis of the ergot alkaloid paliclavine and the formal total synthesis of paspaclavine in optically active form are described.

Sir: We have reported previously a synthesis of the ergot alkaloid chanoclavine I via the intramolecular [3 + 2] dipolar cycloaddition reaction of a nitrile oxide.[1] We now describe the first *total* synthesis of the related ergot alkaloid paliclavine[2] and one of its isomers, 5-*epi*-paliclavine, through a variant of this strategy. This work further underscores the versatility and generality of the nitrile oxide approach to the ergot alkaloids. We had chosen paliclavine as our second target primarily from the standpoint that its synthesis would require the preparation of an intermediate that could be used *ideally* to construct no fewer than six other naturally occurring ergot products (agroclavine, costaclavine, fumigaclavine, lysergine, pyroclavine, festuclavine, etc.).[3]

Our work began with the Wittig reaction of *N*-tosylindole-4-carboxaldehyde (1)[4] and the γ-oxidophosphorane **2**. The phosphonium salt precursor to **2** was prepared in both racemic form from methyl β-bromomethacrylate and in optically active form [$[\alpha]^{25}_D$ +0.1° (*c* 0.102, Me_2SO)] from the known (*R*)-(−)-3-*tert*-butoxy-2-methyl-1-bromopropane.[5] In Scheme I, only the optically active series is depicted. The Wittig condensation produced predominantly the trans olefin **3** (ratio *E*/*Z* = 12:1) as ascertained from ^{1}H NMR [*J* = 16 Hz; $[\alpha]^{25}_D$ −22.1° (*c* 0.080, $CHCl_3$)].

Protection of the hydroxyl group as its tetrahydropyranyl ether [DHP, pyridinium *p*-toluenesulfonate, CH_2Cl_2, 99%; $[\alpha]^{25}_D$ −13.1° (*c* 0.128, $CHCl_3$)], N-detosylation [KOH, MeOH, 99%; $[\alpha]^{25}_D$ −15.0° (*c* 0.139, $CHCl_3$)], and reaction of the indole with excess nitroethylene in the dark at room temperature[6] gave the 3,4-disubstituted product **4** [$[\alpha]^{25}_D$ −12.1° (*c* 0.201, $CHCl_3$)] in 53% yield. A three-step sequence consisting of phenyl isocyanate/triethylamine treatment (91%), N-acetylation (85%),[7] and Dowex 50 W-X8 assisted cleavage of the tetrahydropyranyl group (84%)[8] served to convert **4** to the isoxazoline alcohols **5a** and **6a**. We had hoped that as a consequence of the suggested operation of the anti-periplanar effect in the addition of electrophiles to π systems[9] the nitrile oxide would exhibit some selectivity in its addition to the olefinic appendage (see structure **4** in Scheme I). Unfortunately, the ratio of diastereoisomers was approximately 1.1:1 in the dipolar cycloaddition reaction. These could, however, be conveniently separated at a latter stage (vide infra).

From our various attempts to dehydrate the alcohols **5** and **6**, we discovered that it was best to carry out the dehydration prior to reduction of the isoxazoline, since the more basic nitrogen atom of the isoxazolidine interfered with the preparation of the various derivatives required to activate the hydroxyl group toward elimination. Rather curiously, our first attempt to dehydrate the isoxazoline alcohols **5b** and **6b** (in the racemic series) through their corresponding mesylates led not to the desired product but rather to the fully aromatic isoxazole **7** instead. To avoid this presumably base-assisted aromatization reaction, we sought a milder method for accomplishing the dehydration

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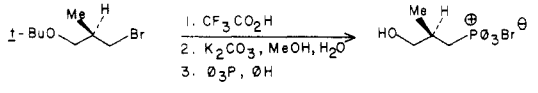
(2) (a) Tscherter, H.; Hauth, H. *Helv. Chim. Acta* **1974**, *57*, 113. (b) Fehr, T.; Stadler, P. A. *Ibid.* **1975**, *58*, 2484. (c) Acklin, W.; Fehr, T.; Stadler, P. A. *Ibid.* **1975**, *58*, 2492.
(3) For recent reviews on the ergot alkaloids, see: Kozikowski, A. P. *Heterocycles* **1981**, *16*, 267. Horwell, D. C. *Tetrahedron* **1980**, *36*, 3123. Floss, H. G. *Tetrahedron* **1976**, *32*, 873.
(4) Kozikowski, A. P.; Ishida, H.; Chen, Y. Y. *J. Org. Chem.* **1980**, *45*, 2236. The *N*-tosyl-protected indole was used in this reaction because it gave a higher yield of product than did the unprotected indole-4-carboxaldehyde.
(5) Cohen, N.; Eichel, W. F.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 3505. The *tert*-butyl ether was cleaved by trifluoroacetic acid to yield the corresponding trifluoroacetate [$[\alpha]^{25}_D$ −0.22° (*c* 0.188, $CHCl_3$)]. Cleavage of the trifluoroacetate (K_2CO_3, MeOH, H_2O) gave the bromo alcohol [$[\alpha]^{25}_D$ −8.13 (*c* 0.21, $CHCl_3$)] which was reacted with triphenylphosphine in benzene to furnish the phosphonium salt precursor to **2**.



(6) Ranganathan, D.; Rao, C. B.; Ranganathan, S.; Mehrotra, A. K.; Iyengur, R. *J. Org. Chem.* **1980**, *45*, 1185. Exposure of the reaction to the laboratory lighting or sunlight resulted in lower yields as a consequence of free radical induced side reactions.
(7) Nickisch, K.; Klose, W.; Bohlmann, F. *Chem. Ber.* **1980**, *113*, 2036.
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