New Synthetic Reactions. Sulfenylations and Dehydrosulfenylations of Esters and Ketones

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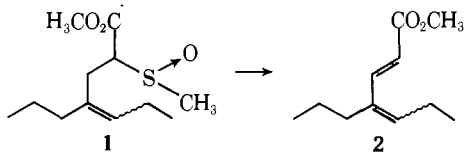
Abstract: Quenching the enolates of esters and ketones with dimethyl disulfide or diphenyl disulfide produces the corresponding α-sulfenylated products. The regio- and chemospecificity of these reactions are defined. Oxidation to the sulfoxide followed by thermolysis leads smoothly to the α,β-unsaturated systems. Temperatures for the elimination of the phenyl sulfoxides are normally around 50 °C, whereas those for the methyl sulfoxides are normally around 110 °C. In both cases, the presence of the carbonyl group significantly facilitates the elimination. Dipole–dipole effects account, in part, for this effect and rationalize the regioselectivity observed in cyclic cases. In some cases, the use of sulfenic acid traps, amines or trimethyl phosphite, is required for good yields. The synthesis of two bee pheromones demonstrates the utility of this approach for introduction of unsaturation. Conditions for mono- vs. disulfenylation are discussed. Use of the latter to effect conversion of an active methylene group into a carbonyl group is illustrated.

Introduction

The synthetic utility of α,β-unsaturated carbonyl compounds in the elaboration of complex organic structures is well established. The great synthetic value of these intermediates derives from the fact that the positions α, β, and γ to the carbonyl group can be activated and functionalized by various means. The most direct approach to such systems involves an oxidation of the corresponding saturated ester or ketone. In the case of ketones, the traditional approach to this oxidation has involved bromination and subsequent dehydrobromination.[2] Although recent advances have removed some of the difficulties formerly associated with this procedure, the use of reactive brominating agents, the instability of resulting bromo ketones, and the requirement for the use of strong bases at high temperatures to effect the dehydrobromination all greatly limit the general utility of the method, especially in highly functionalized systems. The extension of the above procedures to α-bromo esters has remained largely unexplored due mainly to the fact that the bromo esters themselves have only recently become readily available.[2g,3]

The other main general approach to the oxidation of saturated carbonyl compounds involves direct dehydrogenation by strong oxidizing agents. Reagents which have been employed to carry out this transformation include 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[4] selenium dioxide,[4b,5] palladium(II),[6] pyridine *N*-oxide-acetic anhydride,[7] periodic acid,[8] palladium on carbon,[9] and sulfur.[9,10] Although most of these methods have found utility in some cases, yields are often poor and reproducibility is frequently difficult.

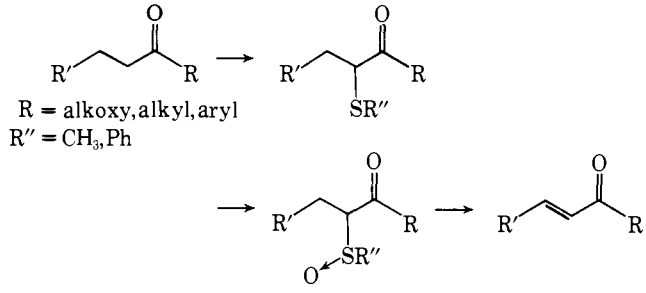
In connection with the exploration of various synthetic pathways directed toward the ultimate synthesis of steroidal natural products, we required a method to oxidize a carboxylic ester to the corresponding α,β-unsaturated ester in the presence of highly sensitive functionality. While the various methods discussed above did not appear to be compatible with this functionality, the observation that α-sulfinyl ester **1** underwent a facile elimination of methylsulfenic acid at 65 °C to yield diene **2**[11] resulted in the development of a general procedure



1 **2**

for the direct sulfenylation of ester and ketone enolates and the oxidation and thermal elimination of the resulting sulfides[12] (see Scheme I). Herein we report the details of this method as well as its application to the synthesis of pheromones of the honey bee.[12b]

Scheme I



Sulfenylation Reaction

At the time we initiated this work, several methods were known for the introduction of a thio group α to a ketone or a ketone derivative. These included (1) the reaction of a sulfenyl chloride with an enamine,[13a] a trimethylsilyl enol ether,[13b] or a simple ketone;[13o-q] (2) the reaction of thiolsulfonates with the anions of α-formyl ketones[13c-e] or malonates;[13f] (3) the reaction of various sulfenamides with active methylene compounds;[13g,h] (4) the reaction of α-chloro oximes with ethyl mercaptide;[13i-l] and (5) the reaction of aryl disulfides with malonate[13m] or dithiane anions.[13n] In addition, Grignard reagents,[14a] organolithiums,[14b] and phenols[15] could also be sulfenylated with diaryl disulfides. To our knowledge no examples of ester sulfenylations had been reported.

Since we desired a sulfenylating reagent which was readily available, easily purified, stable upon storage, and relatively inexpensive, we decided to employ dimethyl disulfide and diphenyl disulfide in our initial sulfenylation studies. Thus, the enolate of ethyl decanoate (Table I, entry 12) was prepared according to the general procedure of Rathke and Lindert[16] and quenched into a THF solution of dimethyl disulfide which was initially at −78 °C and subsequently allowed to warm to room temperature. The desired ethyl 2-(methylthio)decanoate was chromatographically isolated in 92% yield. No bis-sulfenylated material could be seen. Although this same procedure was employed for entry 15, Table I, it was determined that cooling the disulfide solution to −78 °C prior to the inverse quench was unnecessary, and therefore temperatures of 0–25 °C were employed in most instances. Whether an inverse quench procedure is necessary is questionable. In the case of α disubstituted esters where proton transfer from the initially formed sulfenylated material to the unreacted enolate was

Table I. Sulfenylation of Esters and Ketones

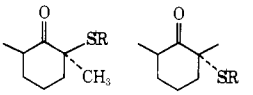
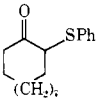
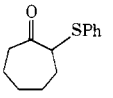
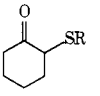
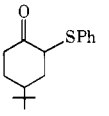
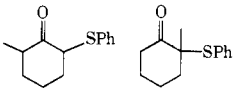
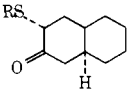
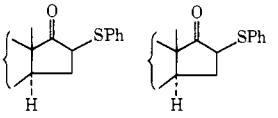
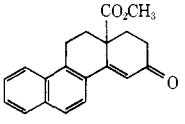
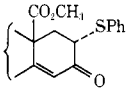
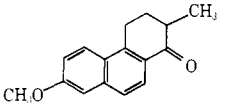
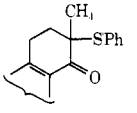
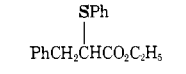
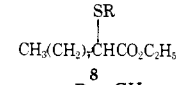
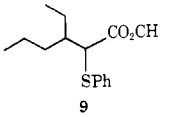
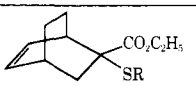
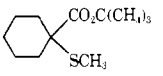
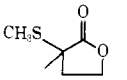
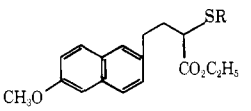
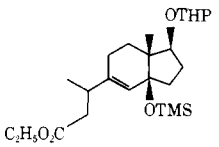
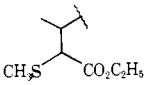
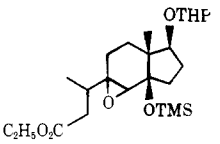
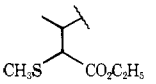
Entry	Ester or Ketone	Disulfide	Solvent	Product	% yield
			A. Ketones		
1	2,6-Dimethylcyclohexanone	(a) CH_3SSCH_3	THF	 3	0
		(b) CH_3SSCH_3	THF–HMPA	25 a, R = CH_3 75	52
		(c) PhSSPh	THF	22 b, R = Ph 78	94
2	Cyclododecanone	(a) PhSSPh	THF	 4	93
		(b) PhSSPh	THF–HMPA		85
3	Cycloheptanone	PhSSPh	THF	 5	87
4	Cyclohexanone	(a) CH_3SSCH_3	THF–HMPA	 R = CH_3	75
		(b) PhSSPh	THF–HMPA	R = Ph	83
5	4-*tert*-Butylcyclohexanone	PhSSPh	THF–HMPA		78
				 6	
6	2-Methylcyclohexanone	(a) PhSSPh	THF	80 20	87
		(b) $PhSSO_2Ph$	THF	>97 <3	85
7	Octahydro-4a-methyl-*trans*-2(1*H*)-naphthalenone				
		(a) CH_3SSCH_3	THF–HMPA	R = CH_3	85
		(b) PhSSPh	THF–HMPA	R = Ph	71
8	Estrone methyl ether	PhSSPh	THF–HMPA	 7	94
				75 25	
9		PhSSPh	THF–HMPA		47
10		PhSSPh	THF–HMPA		98
			B. Esters		
11	Ethyl 3-phenylpropanoate	PhSSPh	THF		90
12	Ethyl decanoate			 8	
		(a) CH_3SSCH_3	THF	a, R = CH_3	92
		(b) PhSSPh	THF	b, R = Ph	91
13	Methyl 3-ethylhexanoate	CH_3SSCH_3	THF	 9	88

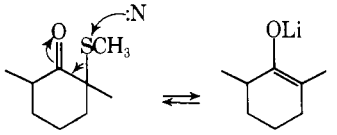
Table I (Continued)

Entry	Ester or Ketone	Disulfide	Solvent	Product	% yield
14	Ethyl bicyclo[2.2.2]oct-2-ene-5-carboxylate			 10	
		(a) CH_3SSCH_3	THF	a, R = CH_3	94
		(b) PhSSPh	THF	b, R = Ph	91
15	*tert*-Butyl cyclohexylcarboxylate	CH_3SSCH_3	THF	 11	98
16	2-Methyl-γ-butyrolactone	CH_3SSCH_3	THF	 12	79
17	Ethyl 4-(6'methoxy-1'-naphthyl)butyrate			 13	
		(a) CH_3SSCH_3	THF–HMPA	a, R = CH_3	89
		(b) PhSSPh	THF	b, R = Ph	87
18		CH_3SSCH_3	THF	 14	91
19		CH_3SSCH_3	THF	 15	82

impossible (see Table I, entry 14), direct quench was highly successful. Even for monosubstituted esters, direct quench with diphenyl disulfide leads to no complications due to proton transfer (Table I, entries 11 and 12b).

In certain cases, it was found that sulfenylation yields were decreased relative to the generally excellent yields in Table I, due apparently to a competitive thermal decomposition of the enolate (vide infra). In such cases, changing the solvent for the dimethyl disulfide reaction from THF to THF–HMPA mixtures or changing to diphenyl disulfide resulted in an enhanced rate of sulfenylation and improved product yield and purity (see Table I, entry 17 for an example in which this procedure was employed). The fact that the yield of sulfenylated product relative to unreacted starting material remains high indicates that the HMPA can increase the rate of sulfenylation without causing excessive proton transfer.

In an attempt to extend the above sulfenylation method to simple ketone enolates, 2,6-dimethylcyclohexanone was treated with 1 equiv of lithium cyclohexylisopropylamide in THF at −78 °C, allowed to reach room temperature, then quenched into a solution of dimethyl disulfide in THF. Upon workup, 2,6-dimethylcyclohexanone was isolated unchanged with no trace of sulfenylated product. There appeared to be two possible explanations for this apparent lack of reactivity. First, it was possible that an initial sulfenylation did occur, but that the sulfenylated product was subsequently desulfenylated by a nucleophile (CH_3S^- or R_1R_2NH) to regenerate the enolate according to eq 1. This reaction is well precedented in both sulfur and selenium chemistry.[17]



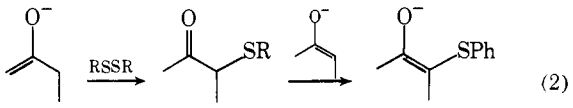
(1)

As opposed to the thermodynamic argument given above, the second explanation for the unreactivity of the ketone enolate with dimethyl disulfide is based on kinetics; i.e., the ketone enolate is simply not reactive enough as a nucleophile to cleave the alkyl disulfide bond in THF as solvent. Regardless of which of the above factors was actually determining the course of the reaction, it seemed apparent that a more reactive sulfenylating agent, i.e., one with a weaker sulfur–sulfur bond, would greatly facilitate the reaction. Diphenyl disulfide, which is commercially available as an essentially odorless crystalline solid, appeared to be the ideal substitute since it possessed all the required properties including a sulfur–sulfur bond strength which is reported to be approximately one-third that of simple dialkyl disulfides.[18]

In the event the enolate of 2,6-dimethylcyclohexanone, generated as above, was added to a solution of diphenyl disulfide at room temperature to give a 94% yield of the desired monosulfenylated material (see Table I, entry 1c). Furthermore, the enhanced reactivity of enolates in the presence of HMPA allows their sulfenylation with dimethyl disulfide. Quenching a solution of the enolate of 2,6-dimethylcyclohexanone in THF into a solution of dimethyl disulfide in HMPA at room temperature gave a 52% isolated yield of 2,6-dimethyl-2-(methylthio)cyclohexanone (see Table I, entry 1b). Alternatively, the addition of dimethyl disulfide to the enolate of cyclohexanone generated in a THF–HMPA mixture gave the desired sulfenylated product in 75% yield (Table I, entry 4a).

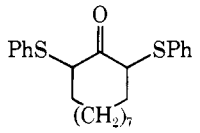
The ratio of ketone to base to disulfide (K:B:D) has varied from approximate ratios of 1:1:1 to 1:2:1 to 1:2:2. For sulfenylation at tertiary centers, such as 2,6-dimethylcyclohexanone, the 1:1:1 ratio is quite satisfactory. For α-methylene ketones, a 1:2:1 or 1:2:2 ratio appears preferable. The requirements of 2 equiv of base is presumably necessitated by the kinetic acidity

of the initial sulfenylated product (eq 2), a problem that did



(2)

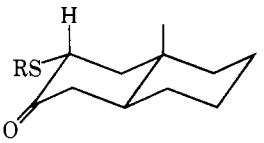
not arise in the case of esters. Heathcock has noted a similar problem in the direct sulfenylation of nitriles[19] and we in the case of imino ethers.[20] In some cases, especially in the presence of HMPA, there is sufficient competititon between the enolate and the amide base for diphenyl disulfide that a 1:2:2 ratio is sometimes preferred. However, the control of the reaction time under such conditions can become highly significant. For example, cyclododecanone sulfenylates in high yield (93%) utilizing the 1:2:1 ratio in THF *or* THF-HMPA (direct addition of disulfide), but polysulfenylation producing 2,12-diphenylthiocyclododecanone (**16**)[21] occurs in THF-HMPA with a



16

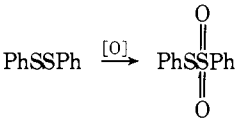
1:2:2 ratio. The NMR spectrum indicates it is a 2:1 mixture of isomers [dd at δ 3.96 (J = 10, 4 Hz) and 4.23 (J = 7, 6 Hz)]. On the other hand, cyclohexanone and 4-*tert*-butylcyclohexanone give 83% and 78% yields, respectively, of the desired monosulfenylated compounds. Estrone methyl ether sulfenylates in high yield with either ratio.

The regiospecificity of the sulfenylation of unsymmetrical ketones was briefly examined. A trans-fused decalone, which generates the 2,3 enolate preferentially,[22] sulfenylates at the 3 position with either dimethyl disulfide or diphenyl disulfide (K:B:D 1:2:2 in THF-HMPA) to give **17**. The structures are clearly supported by the appearance of the OCC*H*S as a dd (δ 3.43 for **17a** and δ 3.94 for **17b**) with J = 12, 6 Hz for **17a** and J = 11, 5 Hz for **17b**.



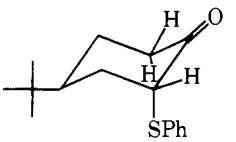
17a, R = CH_3
b, R = Ph

The case of 2-methylcyclohexanone was examined in more detail. Proton transfer occurs rapidly in this system and the alkylation of the kinetic enolate with reactive alkylating agents such as benzyl bromide gave about 10–15% of alkylation of the thermodynamically more stable enolate.[23] Sulfenylation of the kinetic enolate with diphenyl disulfide gave an 87% yield of a mixture of 80–85% **6** and 15–20% of 2-methyl-2-phenylthiocyclohexanone. This ratio approximates that found in simple alkylations. Increasing the reactivity of the sulfenylating agent by utilizing the readily available and stable phenyl phenylthiosulfonate[24] increases the regioselectivity to >95–97% of **6**, an amount that corresponds to the kinetic selectivity in enolate generation.

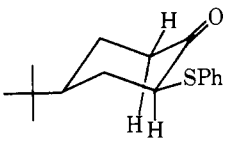


Use of such mild sulfenylating agents as the disulfides allows many functional groups to be present without complications. Thus, the enone ester (Table I, entry 9) sulfenylates at the α position. Most gratifying are entries 18 and 19 in Table I, where the compatibility of the reaction with an epoxide, olefin, acetal, and silyl ether is demonstrated. For the epoxide, entry 19, enolate instability requires the reaction to be performed at low temperatures. In these last two cases, ethyl esters gave significantly better results than methyl esters.

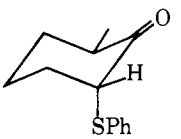
The stereochemistry of the resultant β-keto sulfides from cyclic ketones generally represents the thermodynamic stability of the products. Thus, in the conformationally rigid six-member ring systems (Table I, entries 7 and 9) the methine hydrogen adjacent to sulfur appears as a doublet of doublets with coupling constants demanding it to be an axial hydrogen, i.e., thio group equatorial. On the other hand, the case of 4-*tert*-butylcyclohexanone is most interesting since the ratio of **18a** to **18b** determined by integration of the methine α to sulfur at δ 3.64 (undefined m, $w_{1/2}$ 7 Hz) and δ 3.84 (dd, J = 12, 6 Hz), respectively, is 2:1. In **18a** axial hydrogen at C-6 (ddd, J = 13, 13, 6) also is strongly deshielded (δ 3.02) relative to the equatorial hydrogen. Integration of this signal relative to the aryl region confirms the ratio of **18a**:**18b**. A similar ratio of **6a** to **6b** is also seen. Since base treatment in the presence of a



18a



18b

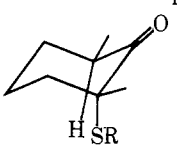


6a

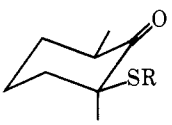
6b

proton source leads to the same isomer distribution, these ratios presumably reflect the thermodynamic stability of the two isomers. Thus, the thio substituent has a slight preference (~0.4 kcal/mol) for the axial position which parallels the α-halo effect.[25] For the condensed ring systems in entries 7 and 9, the severe 1,3-diaxial interactions of an axial thio substituent overwhelm the dipole effect so that the equatorial isomer is the only one seen.

A preference for axial attack in the sulfenylation is seen in the case of 2,6-dimethylcyclohexanone where subsequent equilibration is presumably precluded. The only reasonable conformations are those depicted. In both **3a** and **3b**, the NMR



(*E*)-**3a**,**b**

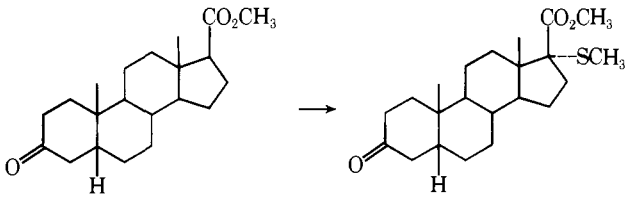


(*Z*)-**3a**,**b**

spectrum shows the absorption for the axial hydrogen at C-6 to be strongly deshielded (δ 3.32 for **3a** and δ 3.49 for **3b**) in the major isomer (3:1) relative to that (δ 2.40 for **3a** and ~δ 2.2 for **3b**) in the minor isomer. This deshielding may be associated with an axial thio substituent (vide supra). Thus, the preference for axial attack in sulfenylation, which is virtually identical for the diaryl and dialkyl disulfide, is approximately the same as that in alkylations.[26]

Chemospecific Sulfenylation

The observation that ketone and ester enolates possessed vastly different reactivities with dimethyl disulfide in THF solution led us to investigate the possibility of specifically reacting at only one site of a di- or polyfunctional molecule. Thus, the dienolate of 17β-carbomethoxy-5β-androstan-3-one (**19a**) was treated with 2 equiv of dimethyl disulfide in THF at room temperature for 1 h to give a quantitative yield of one isomer of the monosulfenylated product. The position of sulfenylation was assigned by a comparison of the chemical shifts of the



19a 19b

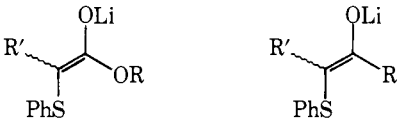
angular methyl groups in the starting material and sulfenylated product and by the subsequent formation of the unsaturated ester (vide infra). The stereochemistry of the newly introduced methylthio group is assigned as shown on the basis of the predicted attack of the disulfide molecule from the less sterically hindered α face of the enolate system.

The term "chemospecific" is introduced to define a reaction which is specific for a given structural unit even in the presence of other functionality that might have appeared to be as or more reactive. For example, the ability to brominate α to a ketone in the presence of a double bond (or vice versa) would also constitute a chemospecific reaction.

It should be noted that although the chemospecific reaction proceeds well in this case where the potential reacting centers are rigidly isolated, problems of apparent self-condensation have been encountered in an open chain system (vide infra).

Bis-Sulfenylation

In THF solutions, bis-sulfenylation of ketone enolates with diphenyl disulfide or of ester enolates with dimethyl disulfide were not observed regardless of the amount of excess base or disulfide. In THF-HMPA mixtures, bis-sulfenylation of ketone enolates can occur (vide supra). Such products can be observed with ester enolates and indeed be quite useful. *tert*-Butyl linoleate reacted with 2 equiv of base, followed by 2 equiv of diphenyl disulfide to give the α,α-bis-sulfenylated ester in 93% yield. This result points up the difference in reactivity between the corresponding ester and ketone enolates **20** and **21**.



20 21

The importance of the bis-sulfenylated ester derives from its potential to be converted into an α-keto ester. Since the linoleate system did not appear to be suitable for such studies, the bis(phenylthio) derivative of methyl 4-(6′-methoxy-1′-naphthyl)butanoate (Scheme I) was prepared as above in 79% recrystallized yield.

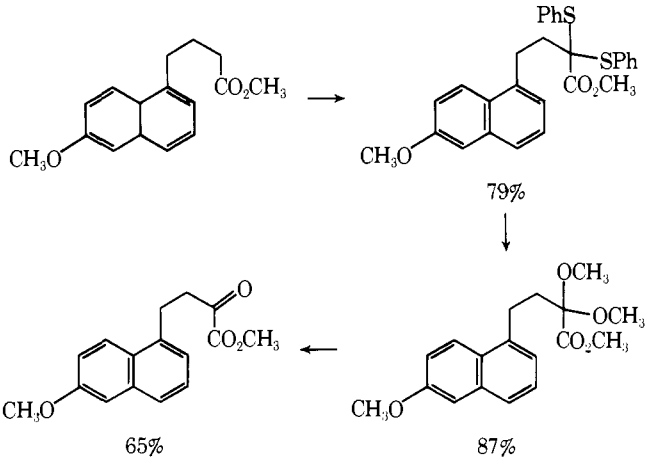
The most effective method for conversion of this material to the α-keto ester involved initial treatment of the thioketal with iodine in refluxing methanol to effect a transketalization, followed by hydrolysis of the resulting dimethyl ketal with perchloric acid in ether or with moist trifluoroacetic acid.

The sulfenylation of β-keto sulfides with highly reactive sulfenylating reagents like sulfenimides or arylthiosulfonates has been reported.[13] The combination of these methods serve as a mild way to convert (oxidize) an active methylene group of esters or ketones into a carbonyl group.

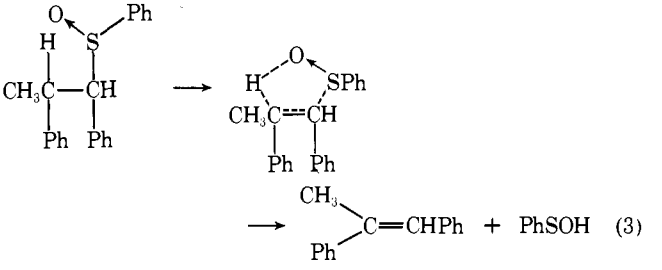
Dehydrosulfenylation. Introduction

The dehydrosulfenylation sequence involves first oxidation followed by thermolysis. The oxidation of sulfides to sulfoxides is a facile transformation for which many reagents have been employed. These include hydrogen peroxide,[27a] *tert*-butyl hydroperoxide,[27b] ozone,[27a] dinitrogen tetroxide,[27c] nitric acid,[27d] iodosobenzene,[27c] sodium metaperiodate,[27a,28] *tert*-butyl hypochlorite,[27f] chromic acid,[27g] *N*-chlorobenzotriazole[27h] and other positive halogen sources, and *m*-chloroperbenzoic acid[27a,i] and other peracids.

Scheme I. Bis-Sulfenylation–Hydrolysis



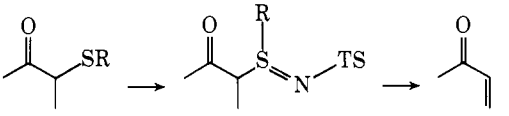
The thermal instability of sulfoxides has been recognized for a century,[29] but the exact mechanism of "decomposition" was not illucidated until 1960, when Cram and Kingbury demonstrated that the diastereomeric 1,2-diphenyl-1-propyl phenyl sulfoxides undergo facile elimination of the elements of benzenesulfenic acid to form the isomeric α-methylstilbenes.[30] The mechanism they proposed involves a stereospecific cis elimination as shown in the following equation:[31]



(3)

Subsequent work has shown that the sulfenic acid can be trapped and identified.[32] In the next 10 years, the generality of the sulfoxide elimination reaction was explored in more detail by several groups during which time conformational and electronic factors were more clearly elucidated.[33-44] Perhaps the most significant synthetic use of the sulfoxide elimination reaction was in the field of β-lactam antibiotic chemistry wherein Morin and co-workers[43] successfully converted phenoxymethyl penicillin sulfoxide methyl ester to the corresponding deacetoxycephalosporin by refluxing in xylene with a trace of acid catalyst. Trapping[32b-j,l] and deuterium labeling experiments[43] have shown the intermediacy of a sulfenic acid.

An alternative approach might involve converting the sulfide to the *N*-*p*-toluenesulfonylsulfilimines followed by pyrolysis.[45]



Since no advantages relative to the sulfoxide approach appeared evident and the formation of the sulfilimines appeared to be less attractive than simple oxidations, it has not been explored.

Dehydrosulfenylation. Results and Discussion

The oxidation method used for the large majority of sulfides listed herein involved the reaction of the sulfide substrate with 1 equiv of sodium metaperiodate in aqueous methanol at room temperature.[27a,28] The ease of workup and high degree of

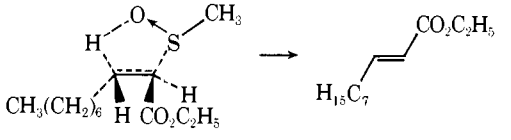
purity of the resulting sulfoxides allowed for the carrying of material directly to the elimination reaction without further purification. In cases where separation of the sulfenylated product from unreacted starting material proves difficult or inconvenient, purification can be postponed until after the oxidation when a very simple chromatographic separation is possible due to the high polarity of the resultant sulfoxide.

In three of the examples listed (Table II, entries 6, 15, and 16), the above reaction proved unsatisfactory. In the last two cases, the slightly acidic, aqueous reaction mixtures resulted in hydrolysis of the trimethylsilyl ether. If a buffered solution was employed, the oxidation reaction was essentially completely suppressed. In the first case, solubility considerations made the aqueous methanol reaction impossible.

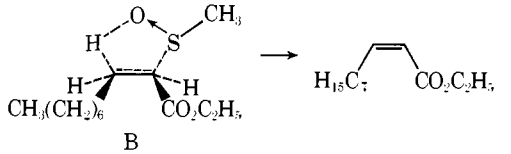
In these cases, it was determined that smooth oxidation to the sulfoxide could be effected by treatment of a methylene chloride solution of the corresponding sulfide with 1 equiv of *m*-chloroperbenzoic acid at −78 °C.[27a,i] Chromatographic analysis indicated that even at this low temperature, oxidation was extremely rapid, and no starting material could be detected even immediately after the dropwise addition of the peracid solution was completed. Sulfone formation did not appear to be occurring, and other functionality which might have been expected to react in competition for the peracid proved to be inert under these very mild conditions.

Other oxidation reagents which were investigated briefly include *N*-chlorobenzotriazole,[27h] hydrogen peroxide,[27a] and *tert*-butyl hydroperoxide in the presence of vanadylacetonyl acetonoate;[27b,46] however, these reagents did not appear to provide the generally high yields and selectivities as well as the previously discussed reactions.

Our initial studies of the sulfoxide elimination to form α,β-unsaturated carbonyl compounds were performed on ethyl 2-(methylsulfinyl)decanoate (Table II, entry 7). This material was heated neat in an NMR tube starting at 60 °C, with periodic NMR monitoring to determine whether reaction was occurring. When no reaction occurred at 60 °C, the temperature was gradually raised in ~10 °C increments until a relatively rapid rate of reaction was attained (~120 °C). NMR analysis indicated that within 5 h at this temperature complete reaction had taken place as evidenced by the disappearance of the two diastereomeric sulfoxide methyl groups of the starting material. The olefinic product, ethyl dec-(*E*)-2-enoate, was chromatographically isolated in 98% yield. Essentially the same result could be obtained by refluxing the sulfoxide in toluene for 14 h. The exclusive formation of the *E* isomer is readily explained by an analysis of the two possible transition-state geometries which would lead to the *E* and *Z* isomers. In A, steric interactions between the ester and *n*-heptyl groups are greatly minimized relative to the severe interactions in **B**.



A

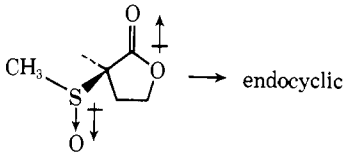


B

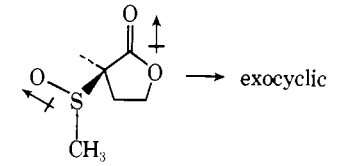
Assuming the argument presented above was correct, it could be predicted that, in the case of a β,β-disubstituted sulfinyl ester, elimination would give a mixture of trisubstituted olefins. In fact, when methyl 2-(methylsulfinyl)-3-ethylhexanoate (Table II, 8) was thermalized neat at 120 °C for 6 h, a 92% yield of an approximate 1:1 mixture of *E* and *Z* methyl 3-ethyl-2-hexenoate was isolated.

In an attempt to determine the feasibility of using the sulfoxide elimination method to gain access to simple α-methylene-γ-lactones,[47] α-methyl-α-(methylsulfinyl)-γ-butyrolactone (Table II, 12) was thermalized as above. NMR analysis of the crude reaction mixture indicated an 87:13 ratio of endo to exo double bond isomers. Indeed, the reaction generally favors endocyclic vs. exocyclic double bond formation.

One attractive explanation for the regiospecificity of the above elimination is based on an analysis of the conformations required for elimination, i.e., C and D. Thus, it would be predicted that the C=O bond of the carbonyl and the S→O bond of the sulfoxide, both of which are strong dipoles, would tend to align themselves so as to minimize dipole–dipole repulsions. In the case at hand, a conformation such as C would be favored leading to preference for formation of the endocyclic double bond isomer. In predicting the regioselectivity of elimination, such dipole–dipole interactions must be considered along with other factors such as steric interactions, double bond stability, acidity of the hydrogen being abstracted, etc. The observed regiospecificity results from a blend of all factors.

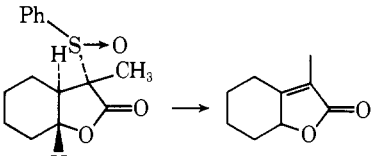


C

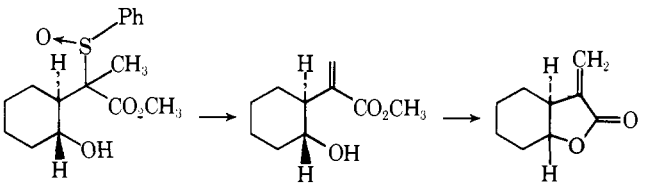


D

Support for the importance of such dipole–dipole effects in the conformationally rigid cyclic cases can be seen in the totally different regiospecificity observed for lactone **22**[47a] relative to its acyclic counterpart **23**.[48] In the absence of conformational constraints, the intrinsic order of $CH_3 > CH_2 > CH$ is reflected in the elimination. Thus, α-methylene lactones are available by this reaction *without the need to resort to stereochemical control* by the simple expedient of pyrolyzing the hydrolyzed lactone.



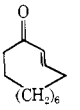
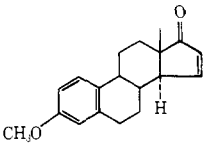
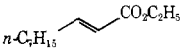
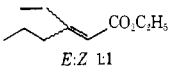
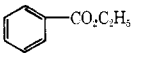
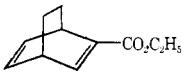
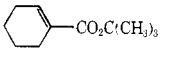
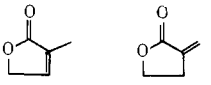
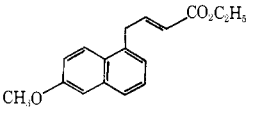
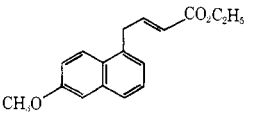
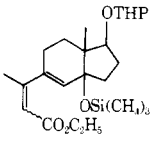
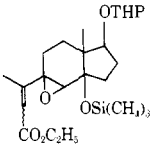
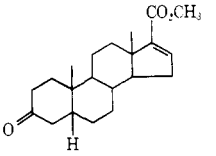
22



23

The thermolyses of all but one of the remaining methyl sulfinyl esters proceeded very smoothly to yield the corresponding α,β-unsaturated esters. Many of the reactions, especially entries 15 and 16 in Table II, serve to demonstrate the mildness of the overall oxidation sequence with respect to the various functionality that can be present during the elimination. Thus, *tert*-butyl esters, acetals, olefins, epoxides, ketones, and silyl ethers are all uneffected. The positional in-

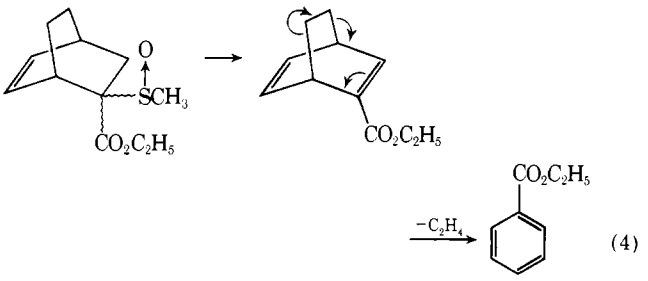
Table II. Dehydrosulfenylation

Entry	Sulfide	Oxidation method[a]	Sulfoxide yield	Olefin	Olefin yield	Overall yield
1	3a	A	100	 100	84	84
2	3b	B	93	 94 6	90	84
3	4	A or B	95		93	88
4	5	A	100		81	81
5	6	A	98		83	81
6	7	B	100		88	88
7	8a	A	97		86	83
8	9	A	92	 E:Z 1:1	92	85
9	10a	A	100		96	96
10	10b	A	98		86	84
11	11	A	93		88	82
12	12	A	94	 87 13	95	89
13	13a	A	95		90	86
14	13b	A	100			
15	14	B	98		93	91
16	15	B	85		79	67
17	19b	A	100		92	92

[a] Method A, sodium metaperiodate; method B, *m*-chloroperbenzoic acid.

tegrity of the newly introduced olefin is also demonstrated in entries 6 and 13, where no migration of the double bond into the thermodynamically more stable position could be detected. It should be noted that better yields were obtained in the thermolysis of examples 15 and 16 when the elimination reaction was carried out in xylene (~140 °C) rather than in toluene (~110 °C).

Only in the thermolysis of ethyl 2-(methylsulfinyl)bicyclo[2.2.2]oct-5-ene-2-carboxylate (entry 9) was a spurious result obtained. When this material was heated neat at 120 °C substantial evolution of gas was noted and upon workup a 96% yield of ethyl benzoate was obtained. This product undoubtedly arose from further thermal reaction of the initially formed diene ester as illustrated in the following equation



(4)

Lowering the reaction temperature in an effort to stop the undesired retro-cycloaddition reaction also essentially halted the elimination reaction. The problem could be completely solved by thermalyzing the phenylsulfinyl ester (entry 10) which eliminates at 50 °C in 17 h to give ethyl bicyclo[2.2.2]-octa-2,5-diene-2-carboxylate in 86% yield.

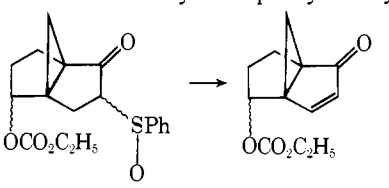
The fact that the phenylsulfinyl ester undergoes the elimination reaction at a temperature 70 °C lower than the corresponding methyl compound can be explained by a number of related factors. Emerson[37] has determined that in the transition state for the elimination, partial negative charge resides on the sulfur-containing moiety. The phenyl ring would be expected to be better able to stabilize this charge than would the methyl. The predicted lower strength of the carbon–sulfur bond in the phenylsulfinyl compound relative to the methyl would also be expected to contribute to the lower elimination temperature since it is one of the two bonds that must break during the reaction. The mesomeric effect of the benzene ring would be predicted to increase the polarization of the sulfur–oxygen bond. This increase should have two related effects on the elimination reaction. First, the aforementioned dipole–dipole induced conformational preference should be enhanced, and second, the basicity of the sulfoxide oxygen should be increased.

The thermolysis of the sulfinyl ketones in entries 2 and 3 in Table II were carried out by heating in carbon tetrachloride at 50 °C. 2,6-Dimethyl-2-(phenylsulfinyl)cyclohexanone completely eliminated within 3 h to give a 94:6 ratio of endo to exo double bond isomers and eliminated slowly (about 50% complete in 36 h) at room temperature. The explanation for the great predominance of the endo product parallels that given previously for the lactone. The corresponding methylsulfinyl compound (entry 1) eliminates in refluxing toluene to given an 84% yield of 2,6-dimethylcyclohex-2-enone, with no trace of the exocyclic methylene compound; however, it is not clear as to whether the alternate isomer never formed, or whether at the higher temperature for elimination it simply decomposed prior to isolation. Once again, the vast difference in elimination temperatures between the phenyl and methyl derivatives should be noted.

The thermolysis of 2-(phenylsulfinyl)cyclododecanone at 50 °C was allowed to proceed overnight and gave a 93% yield of exclusively the *E* isomer of 2-cyclododecenone. Previous arguments pertaining to the stereochemistry of olefin products in acyclic systems seem to be applicable to this large ring compound.

The attempted eliminations of 2-(phenylsulfinyl)cycloheptanone in carbon tetrachloride at 50 or 76 °C led to extensive decomposition of the starting material with little or no trace of the desired unsaturated ketone. Although the products of these reactions were not analyzed fully, it seemed probable that the sulfoxide starting material was undergoing some sort of decomposition which was being catalyzed by the initially formed sulfenic acid. While attempts to buffer the reaction medium met with little success, it was determined that promoting a very rapid elimination reaction by heating at 110 °C in toluene containing a trace of calcium carbonate minimized the decomposition pathway and allowed for the isolation of an 81% yield of cyclohept-2-enone. It is interesting to note that when cycloheptanone is subjected to the usual selenylation–selenoxide elimination conditions, less than 10% of the desired enone can be isolated.[12d] Although this yield can be improved to 55% by oxidation with ozone and subsequent addition of the cold (−78 °C) selenoxide to a refluxing solution of diethylamine in carbon tetrachloride, the sulfoxide route seems to be superior in this case. Similar results to the above were obtained in the synthesis of 6-methylcyclohex-2-en-1-one by the two elimination procedures. It appears that, in general, for the synthesis of cycloenones in which the α position of the newly introduced double bond is unsubstituted, the sulfoxide route is less prone to side reactions.

The thermolysis of 16-(phenylsulfinyl)estrone methyl ether (Table II, entry 6) in refluxing toluene or xylene containing a small amount of powdered calcium carbonate resulted in extensive decomposition of the starting sulfoxide with only a trace of the desired eliminated material in the NMR. An attempt to trap the initially formed sulfenic acid with succinic anhydride[49] also had no effect; however, the addition of 1 equiv of pyridine to the reaction mixture gave a 34% yield of $\Delta^{15,16}$-estrone methyl ether. This yield jumped to 88% when trimethyl phosphite (2 equiv) was used as the sulfenic acid trap. Again, the success of this reaction may be contrasted with the selenoxide approach in which none of the desired enone was obtained.[12g] It should be noted that the low yields obtained for the thermolysis of the estrone sulfoxide in the absence of appropriate traps does not appear to reflect a general trend for cyclopentanones since the tricyclic α-phenylsulfinyl ketone **24**



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eliminates readily in >90% yield upon refluxing for 16 h in carbon tetrachloride.[50]

In connection with the use of various sulfenic acid traps in the thermolysis reaction, it should be pointed out that although the thermolysis of ethyl 2-(phenylsulfinyl)-4-(6′-methoxy-1′-naphthyl)butyrate (entry 14, Table II) appeared to proceed smoothly and the desired unsaturated ester could be detected by NMR spectroscopy, it was difficult to successfully remove some of the sulfur-containing by-products by the standard chromatographic procedures. Although in this case the problem was solved by utilizing the methylthio compound which produces elimination by-products which are either volatile or water soluble, a more general approach, which we and others[47b] have subsequently employed, involves the use of trapping agents such as trimethyl phosphite and 2-mercaptobenzothiazole[47b,51] which transform the initially formed sulfenic acids into materials which are easily removed by extractive or chromatographic procedures.

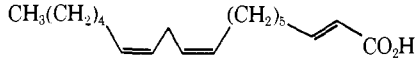
Table III. Sulfenylation of Linoleic Esters

Ester	Solvent	Yield of sulfide, %
CH_3	THF	61
CH_2CH_3	THF	75
	THF–HMPA	92
$(CH_3)_3C$	THF	84

It is important to note that all the elimination reactions discussed herein proceed at temperatures substantially lower than would be expected if the adjacent carbonyl group was to be replaced by a simple alkyl group. This trend, which has also been observed in the α-carbonyl selenoxide elimination,[12d] can be accounted for by several factors. The effect of dipole–dipole interactions on the energy and the conformation of the ground state of the sulfoxide can be invoked to explain the general facilitation caused by the adjacent carbonyl group even in acyclic systems. The conjugative stabilization of the newly introduced double bond also seems to be an important factor in the lowering of the reaction temperature. One recent example illustrates that when an aromatic system with extended conjugation can be formed, the elimination of *p*-toluenesulfenic acid can occur rapidly even at 0 °C.[52] It should be noted that this conjugative stabilization can also be rendered by other polar groups.[30,53]

Synthesis of Pheromones of the Honey Bee

The sulfenylation–dehydrosulfenylation approach to the synthesis of α,β-unsaturated esters appeared to offer a very attractive approach to the synthesis of two important pheromones of the honey bee—the pollen attractant of honey bees,[54] **25**, and the queen substance,[55] **26**, since both these materials possess the *E* α,β-unsaturated carboxylate moiety.



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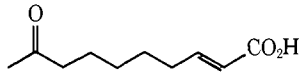

26

The precursor for the synthesis of **25** is the readily available linoleic acid (9,12-octadecadienoic acid, **27**). The known

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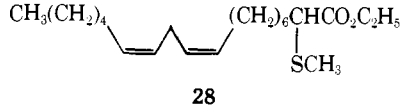
methyl, ethyl, and *tert*-butyl esters of this material, all readily available by standard methods, were sulfenylated with dimethyl disulfide in THF using minor modifications of the previously discussed methods. The yields of the resulting α-(methylthio) compounds are listed in Table III. The order of yields and purity of the resulting α-(methylthio) compounds appears to parallel the predicted general order of enolate stability;[56] i.e., the more thermally stable *tert*-butyl enolate gave both higher yield and cleaner product. Since *tert*-butyl esters are not always readily accessible in highly functionalized systems, we sought to modify the reaction conditions used for the methyl or ethyl esters in such a way as to minimize any pathway other than the desired sulfenylation. Quenching a solution of the enolate of ethyl linoleate at −78 °C into a solution of dimethyl disulfide (10% excess) in HMPA at room temperature gave a 92% yield of the sulfenylated material **28**. When this same procedure was applied to the methyl ester, and



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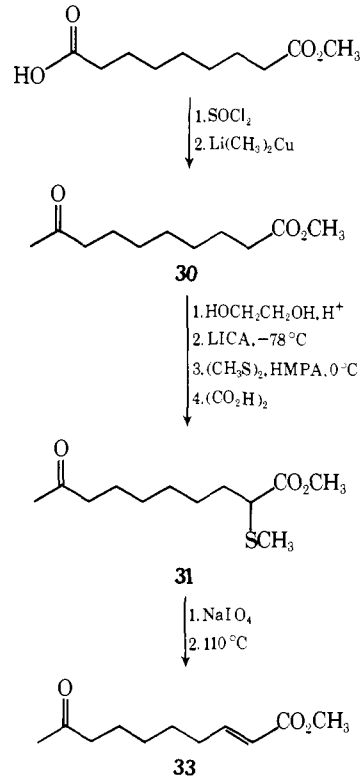
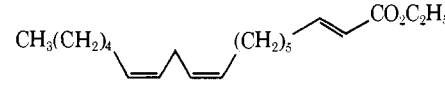
Scheme II



reaction times >1 h at room temperature were employed, several by-products could be isolated in addition to the desired sulfenylated material. Although these by-products were not fully characterized they appeared to arise from nucleophilic desulfenylation and/or dealkylative ester hydrolysis.[57] Oxidation with 1 equiv of *m*-chloroperbenzoic acid followed by the normal thermolysis gave an 81% yield of the desired octadeca-(*E*)-2-(*Z*,*Z*)-9,12-trienoate (**29**).[58] A similar sequence based upon organoselenium reagents has been reported.[12e]



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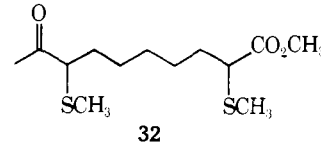
The queen substance, 9-oxo-(*E*)-2-decenoic acid (**26**), in addition to being an important sex attractant of the queen bee,[55] has also recently been implicated as a pheromone of termites.[59] The interest in this substance is reflected in the large number of syntheses which have appeared.[60] Unfortunately, the overall yields of these syntheses are uniformly very low, and nonreadily available starting materials are often required. Our initial approach involved a proposed chemospecific sulfenylation of methyl 9-oxodecanoate[61] (**30**), which was readily prepared in 81% yield[62] from commercially available azelaic acid monomethyl ester (Scheme II). Although many permutations of conditions were explored involving changes in temperature, solvent, amide base, ester alkyl, and stoichiometry, in no case was >30% of the desired sulfenylated material **31** present as determined by NMR spectroscopy. In one reaction wherein HMPA was used as a cosolvent, a 25% yield of methyl 2,8-di(methylthio)-9-oxodecanoate (**32**) was isolated.



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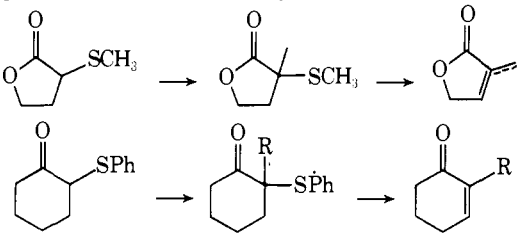
Since the problem in all the above reactions was apparently caused by inter- and intramolecular decomposition of the dienolate, the ketone of **30** was protected as the ethylene ketal,

and this material was successfully sulfenylated with dimethyl disulfide (2 equiv) in THF-HMPA in 86% yield. The sulfenylated ketal ester was hydrolyzed in aqueous oxalic acid to give a 69% overall yield of methyl 2-(methylthio)-9-oxodecanoate (**31**). Oxidation to the sulfoxide and elimination gave the methyl ester of the queen substance, **33**, in 86% yield for an overall yield of 47% from azeleic acid monomethyl ester.

Conclusion

Since our initial communication on the sulfenylation-dehydrosulfenylation method for the introduction of unsaturation, many interesting applications have evolved. A main thrust of much of this work has been directed toward the preparation of substituted butenolides and α-methylene-γ-butyrolactones from the corresponding saturated precursors.[47,63] The alkylation of dianions derived from α-sulfinyl ketones has provided new synthetic approaches to both cyclic and acyclic substituted vinyl ketones.[64] One pot alkylation-elimination reactions involving the alkylation and subsequent thermolysis of the anions of methyl phenylsulfinylacetate allow for a facile olefination of alkyl halides or π-allyl palladium substrates.[48,54,65] The synthesis and elimination of sulfoxides β to a carbonyl group have been employed to prepare α-methylene ketones, acids, and lactones.[66] A new ketone synthesis based upon the pyrolysis of β-hydroxy sulfides appears promising.[67] The direct sulfinylation of ketone enolates with methyl arylsulfinates has also recently been reported.[68] In addition to the oxidation-elimination sequence previously discussed, it is important to note that the α-thio esters and ketones which are readily available by direct sulfenylation are valuable synthetic intermediates in and of themselves.[13d,13l,69] Since sulfur serves to activate the adjacent carbon toward alkylation, combining this reaction with the desulfenylation procedure serves as an alkylative elimination.



ref 69f

ref 69a

The demonstrated versatility of sulfenylated esters and ketones has led to the investigation of other possible substrates for direct sulfenylation among which are pyridines,[70] nitriles,[19] aldimines,[69a] imino ethers,[20] allylic sulfoxides,[71] allylic ethers,[72] vinyllithiums,[73] etc.

The sulfenylation-dehydrosulfenylation method described above provides a generally applicable, high yield route for the oxidation of esters and ketones to the corresponding unsaturated systems. The ready availability and long term stability of the sulfenylating reagents—dimethyl disulfide, diphenyl disulfide, and phenyl phenylthiolsulfonate—greatly enhances their utility. The range of reactivity which is demonstrated by these reagents allows for a useful latitude in the design of reactions and can be exploited in order to obtain chemospecific sulfenylation at one end of the reactivity scale and regiospecific sulfenylation at the other. Although these reagents should provide direct access to α-thio carbonyl compounds in any case where the corresponding enolate is easily available and relatively stable, in compounds where this is not the case, one of the alternate sulfenylation methods discussed previously could be employed instead.

In cases where the sulfenylation-dehydrosulfenylation method can be directly compared with the selenylation-dehydroselenylation sequence developed by Reich,[12d] Sharpless,[12e] Clive,[12f] and their co-workers, yields are generally found to be similar except in the case of α-methylene ring ketones where the sulfoxide elimination appears to be less prone to side reactions. The sulfenylation of α-methylene esters also appears to be cleaner than the corresponding selenylation reaction.[12d] The selenoxide elimination occurs at temperatures substantially lower than the sulfoxide elimination, and this might prove to be advantageous in the preparation of certain thermally labile enones; however, we have found that no functional group that survived the initial sulfenylation reaction was adversely affected by the elimination conditions. The fact that the yields of unsaturated carbonyl products actually increased with increasing thermolysis temperature in several cases and the wide range of functionality that has been demonstrated to be stable under the sulfoxide elimination conditions should be noted. Other advantages of the sulfur-based scheme include lower toxicity and expense of the sulfenylating reagents as well as the ability to easily remove unreacted carbonyl starting materials by postponing purification until after the oxidation to the polar sulfoxide. Sharpless describes the direct selenylation of ketones under slightly acidic conditions with selenyl halides in analogy to the sulfur counterpart.[12e,13] Such a procedure, which avoids the need for enolate formation, provides additional versatility and should have special promise with base sensitive molecules.

Experimental Section

General. All reactions were run under a positive pressure of dry nitrogen. Infrared spectra were obtained as solutions in the indicated solvent on a Beckman IR-8 or a Perkin-Elmer 267 spectrophotometer and are given in cm^{-1}. NMR spectra were determined in the indicated solvent on a Varian A60A or a Jeolco MH-100 spectrometer at 60 and 100 MHz, respectively; chemical shifts are given in ppm from Me_4Si. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants are given in hertz. Mass spectra were taken on an AEI MS-902 high resolution mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 100 mA unless otherwise indicated. Melting points were obtained on a Thomas-Hoover apparatus, in open capillary tubes, and are uncorrected. Boiling points are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. VPC analyses were performed on a Varian Aerograph Model 90P. Thin layer or preparative thick layer (1.5 mm) plates were made of E. Merck AG Darmstadt silica gel PF-254 activated by drying at 140 °C for 2 h. Eluting solvents are indicated in the text. Removal of material from the silica gel was accomplished by successive washings with ether. In experiments requiring dry solvents, ether and tetrahydrofuran were distilled from sodium benzophenone. Benzene, toluene, and xylene were distilled from calcium hydride. Apparatus for experiments requiring anhydrous conditions was dried by flaming in a stream of dry nitrogen. Dimethyl disulfide (Aldrich) was distilled from calcium hydride. Diphenyl disulfide (Eastman) was used without further purification. Isopropylcyclohexylamine was distilled from potassium hydroxide. During workup of reactions, routine drying was performed over anhydrous magnesium sulfate unless otherwise indicated.

"Usual" preparation of lithium isopropylcyclohexylamide or lithium diisopropylamide involves the addition by syringe of 1 equiv of *n*-butyllithium (Foote Mineral Co.) to a solution of 1 equiv of isopropylcyclohexylamine or diisopropylamine in THF at −78 °C. This solution is ready for use after stirring at −78 °C for 15 min.

"Standard" workup of the sulfenylation reactions consists of pouring the reaction mixture into a separatory funnel containing ether or ethyl acetate and 10% aqueous hydrochloric acid. The aqueous layer is separated, and the organic phase is washed with another portion of acid and with one portion of saturated aqueous sodium bicarbonate solution. The organic phase is dried over anhydrous magnesium sulfate and concentrated in vacuo.

Standard workup of a sodium metaperiodate oxidation consists of filtering the reaction mixture and washing the filter cake with several portions of methanol. The filtrate is concentrated in vacuo, and the residue is dissolved in ether and dried over magnesium sulfate. Removal of the ether in vacuo yields the crude sulfoxide.

In cases where conditions of "reflux" are described, the flask con-

Table IV. Experimental Details for Additional Sulfenylations of Esters and Lactone

Ester (wt, mmol)	Amine (wt, mmol)	Disulfide (wt, mmol)	Method	Product, wt (% yield)	R_f (solvent)
Ethyl 3-phenylpropanoate (712 mg, 4.0)	(620 mg, 4.4)	PhSSPh (959 mg, 4.4)	B	1.03 g (90)	0.49 (5% C_2H_5OAc/hex)
Ethyl decanoate (2.00 g, 10)	(1.41 g, 10.0)	CH_3SSCH_3 (1.13 g, 12)	A	2.26 g (92)	0.7 ($CHCl_3$)
Ethyl decanoate (60 mg, 3.0 mmol)	(465 mg, 3.3)	PhSSPh (719 mg, 3.3)	B	840 mg (91)	0.64 (5% C_2H_5OAc/hex)
Methyl 3-ethylhexanoate (2.00 g, 12.7)	(1.79 g, 12.7)	CH_3SSCH_3 (2.38 g, 25.4)	A	2.28 g (88)	0.60 ($CHCl_3$)
Ethyl bicyclo[2.2.2]oct-5-ene-2-carboxylate (1.00 g, 5.56)	(1.41 g, 10.0)	CH_3SSCH_3 (940 mg, 10.0)	B	1.17 g (94)	0.75 ($CHCl_3$)
tert-Butyl cyclohexylcarboxylate (1.84 g, 10.0)	(1.41 g, 10.0)	CH_3SSCH_3 (1.13 g, 12.0)	A	2.25 g (98)	0.6 ($CHCl_3$)
2-Methyl-γ-butyrolactone (1.50 g, 15.0)	(2.12 g, 15.0)	CH_3SSCH_3 (3.38 g, 22.5)	A	1.73 g (79)	0.7 ($CHCl_3$)
Ethyl 4-(6′-methoxy-1′-naphthyl)butyrate (1.00 g, 3.68)	(519 mg, 3.68)	CH_3SSCH_3 (514 mg, 4.42) (in 5 ml HMPA)	A	1.03 g (89)	0.6 (3:2 ether–hexane, 2 elutions)
6,7,7a,7b-Tetrahydro-5-(2′-ethoxycarbonyl-1′-methylethano)-7αβ-methyl-1β-tetrahydropyranyloxy-7b-trimethylsiloxyindan (1.72 g, 3.93)	(609 mg, 4.32)	CH_3SSCH_3 (444 mg, 4.72)	A	1.73 g (91)	0.8 (3:2 ether–hexane)
6,7,7a,7b-Tetrahydro-5-(2′-ethoxycarbonyl-1′-methylethano)-7αβ-methyl-4,5β-oxa-1β-tetrahydropyranyloxy-7bβ-trimethylsiloxyindan (488 mg, 1.075)	(166 mg, 1.18)	CH_3SSCH_3 (122 mg, 1.30)	A	438 g (82)	0.7 (3:2 ether–hexane)

taining the reaction mixture is placed in a preheated oil bath unless otherwise indicated.

Sulfenylations of Enolates of Esters and Lactones. Method A. Methyl 2-(Phenylthio)-4-(6′-methoxy-1′-naphthyl)butanoate. The amide (4.27 mmol) was prepared as usual in 10 ml of THF. A solution of methyl 4-(6′-methoxy-1′-naphthyl)butanoate (1.00 g, 3.88 mmol) in 5 ml of THF was added dropwise by syringe, and the resulting reaction mixture was stirred at −78 °C for 30 min. The enolate solution was then siphoned through a Teflon tube into a solution of diphenyl disulfide (931 mg, 4.27 mmol) in 5 ml of THF at room temperature. Alternatively, the enolate solution was added via syringe to the disulfide. The resulting solution was stirred at room temperature for 45 min, then worked up as usual to yield a yellow oil. This material was absorbed onto 3 g of silica gel and chromatographed on a 2 in. × 10 in. silica gel dry column (10% ether in hexane) to yield 1.23 g (87%) of the desired product at R_f = 0.3: ir (CCl_4) 1739, 1625, 1595; NMR (CCl_4) δ 6.7–7.9 (11 H, m), 3.80 (3 H, s), 3.60 (3 H, s), 3.3–3.8 (1 H, obscured by the methyl singlets), 3.05 (2 H, br t, J = 8), 2.15 (2 H, m); mass spectrum (*m/e*, %) 368 (3), 367 (8), 366 (33), 259 (13), 258 (25), 256 (14), 197 (38), 184 (23), 172 (36), 171 (100), 153 (23), 141 (17), 129 (17), 128 (100), 115 (20), 109 (26), 77 (15), 67 (21). Calcd for $C_{22}H_{22}O_3S$: 366.1289. Found: 366.1287.

Method B. Ethyl 2-(Phenylthio)bicyclo[2.2.2]oct-5-en-2-carboxylate. The amide (10.0 mmol) was prepared as usual in 15 ml of THF. Ethyl bicyclo[2.2.2]oct-5-en-2-carboxylate (1.00 g, 5.56 mmol) was added dropwise by syringe at −78 °C. After addition was complete, the dry ice-2-propanol bath was replaced by a dry ice–carbon tetrachloride bath (~−25 °C) (preferred method) or the reaction mixture was allowed to warm to room temperature prior to the dropwise addition of diphenyl disulfide (2.19 g, 10.0 mmol) in 5 ml of THF. After stirring at room temperature for 1 h, the reaction mixture was diluted with 100 ml of ether and worked up as usual to yield a yellow oil which was absorbed on 6 g of silica gel and chromatographed on a 200 g silica gel column (5% ether in hexane) to yield 1.48 g (91%) of a pale yellow oil, R_f 0.35: ir (CCl_4) 1724; NMR (CCl_4) mixture of isomers δ 7.1–7.6 (5 H, m), 6.0–6.5 (2 H, m), 3.6–4.3 (2 H, m), 2.8–3.1 (1 H, m), 2.3–2.8 (3 H, m), 0.8–1.8 (7 H, m); mass spectrum (*m/e*, %) 200 (2), 280 (4), 288 (19), 218 (12), 209 (11), 208 (51), 180 (25), 176 (28), 166 (25), 163 (41), 150 (23), 149 (20), 137 (20), 135 (100), 130 (20), 129 (35), 124 (50), 123 (57), 120 (35), 108 (15), 107 (21), 105 (45), 101 (45), 95 (34), 91 (50), 87 (20), 84 (30), 83 (24), 80 (50), 79 (50), 78 (25), 77 (38), 73 (21). Calcd for $C_{17}H_{20}O_2S$: 288.1184. Found: 288.1187. The specific reaction parameters for the additional samples are summarized in Table IV.

Spectral Properties. Ethyl 2-phenylthio-3-phenylpropanoate: ir ($CHCl_3$) 1732, 1608, 1589, 1497 cm^{-1}; NMR δ 7.0–7.6 (10 H, m), 3.95 (2 H, q, J = 7 Hz), 3.77 (1 H, X part of ABX, J_{AX} = 6 Hz, J_{BX} = 7 Hz), 3.18 and 3.00 (2 H, AB part of ABX, J_{AB} = 14 Hz), 1.00 (3 H, t, J = 7 Hz); mass spectrum (*m/e*, %) 286 (48), 213 (17), 195 (24), 177 (96), 149 (73), 135 (100), 131 (46), 121 (83), 110 (50), 109 (51), 105 (56), 104 (37), 103 (44), 91 (84), 78 (39), 77 (85), 65 (44), 51 (46). Calcd for $C_{17}H_{18}O_2S$: 286.1028. Found: 286.1022.

8a: ir (CCl_4) 1730; NMR (CCl_4) δ 4.13 (2 H, q, J = 7 Hz), 2.98 (1 H, d of d, J = 8.0, 7.5 Hz), 2.06 (3 H, s), 1.0–2.0 (17 H, m), 0.7–1.0 (3 H, unresolved t); mass spectrum (*m/e*, %) 248 (5), 247 (13), 246 (70), 201 (9), 200 (52), 199 (22), 174 (15), 173 (100), 172 (15), 157 (47), 134 (40), 88 (19). Calcd for $C_{13}H_{26}O_2S$: 246.1653. Found: 246.1653.

8b: ir ($CHCl_3$) 1725, 1600, 1581 cm^{-1}; NMR (CCl_4) δ 7.1–7.6 (5 H, m), 4.08 (2 H, t, J = 7 Hz), 3.57 (1 H, t, J = 7 Hz), 1.1–2.0 (14, m), 0.9 (3 H, unresolved t, J = 7 Hz); mass spectrum (*m/e*, %) 308 (93), 235 (100), 213 (75), 143 (73), 122 (69), 110 (72), 109 (32), 83 (46), 69 (80), 57 (34), 55 (68). Calcd for $C_{18}H_{28}O_2S$: 308.1810. Found: 308.1783.

9: ir (CCl_4) 1730; NMR (CCl_4) δ 3.75 (3 H, s), 3.05 (1 H, d, J = 9 Hz), 2.08 (3 H, s), 1.0–2.0 (7 H, m), 0.7–1.0 (6 H, m); mass spectrum (*m/e*, %) 206 (2), 205 (4), 204 (21), 201 (18), 157 (17), 145 (24), 129 (14), 127 (85), 120 (100), 116 (38), 115 (14), 101 (22), 97 (23), 88 (46), 83 (16), 61 (23), 57 (87), 55 (55). Calcd for $C_{10}H_{20}O_2S$: 204.1184. Found: 204.1184.

10a: ir (CCl_4) 1720; NMR (CCl_4, ext. Me_4Si) mixture of isomers δ 6.1–6.4 (2 H, m), 4.13 (2 H, q, J = 7.3 Hz), 3.0 (1 H, m), 2.17–2.72 (3 H, m), 2.05 (3 H, s), 1.0–1.7 (4 H, m), 1.27 (3 H, t, J = 7.3 Hz); mass spectrum (*m/e*, %) 228 (1), 227 (2), 226 (12), 148 (11), 147 (100), 146 (19), 125 (35), 106 (16), 105 (55), 102 (17), 101 (75), 81 (26), 80 (95), 79 (85), 78 (28), 77 (51), 73 (37), 51 (17). Calcd for $C_{12}H_{18}O_2S$: 226.102743. Found: 226.10274.

11: ir (CCl_4) 1721; NMR (CCl_4) δ 1.8–2.2 (2 H, m), 1.97 (3 H, s), 1.0–1.8 (8 H, m), 1.46 (9 H, s); mass spectrum (*m/e*, %, 20 eV) 232 (2), 231 (4), 230 (26), 131 (5), 130 (10), 129 (100), 111 (23), 110 (36), 83 (24), 81 (24), 57 (18), 56 (10). Calcd for $C_{12}H_{22}O_2S$: 230.1340. Found: 230.1342.

12: ir (CCl_4) 1773; NMR (CCl_4, ext. Me_4Si) δ 4.36 (2 H, m), 2.1–2.7 (2 H, m), 2.16 (3 H, s), 1.55 (3 H, s); Mass spectrum (*m/e*, %) 146 (35), 101 (6), 100 (100), 87 (20), 69 (18), 56 (12), 55 (47). Calcd for $C_6H_{10}O_2S$: 146.0405. Found: 146.0401.

13a: ir (CCl_4) 1726, 1625, 1598; NMR (CCl_4) δ 6.9–8.1 (6 H, m), 3.9–4.3 (2 H, overlapping quartets), 3.77 (3 H, s), 2.8–3.3 (3 H, m), 1.8–2.5 (2 H, m), 2.04 (3 H, s), 1.22 (3 H, t, J = 7 Hz); mass spectrum (*m/e*, %) 320 (2), 319 (5), 318 (25), 274 (2), 273 (20), 272 (100), 249 (10), 227 (23), 198 (7), 197 (15), 185 (29), 184 (98), 183 (7), 172 (38), 171 (89), 141 (23), 129 (21), 128 (33), 127 (10), 115 (10), 93 (12), 67 (14). Calcd for $C_{18}H_{22}O_3S$: 318.1290. Found: 318.1288.

14: ir (CCl_4) 2930, 2860, 2838, 1725, 1247, 896; NMR (CCl_4, silyl

ether = 0.00) mixture of diastereomers δ 4.39 (1 H, br s), 3.8–4.2 (2 H, m), 3.1–3.8 (3 H, m), 2.2–2.9 (1 H, m), 2.57 (1 H, br s), 1.97 and 1.88 (total 3 H, 2 singlets, ratio 1:2.5), 0.8–2.1 (20 H, m), 0.64 (3 H, s), 0.00 (9 H, s); mass spectrum (*m/e*, %) 15 eV 10x [502 (5), 501 (10), 500 (30), 417 (4), 416 (12), 399 (10), 398 (11), 370 (11), 369 (11)], 3x [353 (10), 352 (13), 341 (13), 326 (15), 324 (10), 291 (10), 280 (10)], 262 (20), 168 (10), 147 (15), 132 (10), 120 (14), 105 (20), 94 (38), 86 (10), 85 (100), 84 (40), 75 (25). Calcd for $C_{25}H_{44}O_6SiS$: 500.2528. Found: 500.2528.

15: ir (CCl_4) 2930, 2860, 2835, 1726, 1245; NMR (CCl_4, silyl ether = 0.00) δ 5.26 (1 H, br s), 4.42 (1 H, br s), 3.83–4.25 (2 H, m), 3.2–3.8 (3 H, m), 2.8–3.2 (1 H, m), 2.1–2.8 (2 H, m), 1.98 (3 H, s with shoulder), 0.91–2.1 (19 H, m), 0.76 (3 H, narrow m), 0.00 (9 H, s); mass spectrum (*m/e*, %) 15 eV 486 (3), 485 (5), 484 (11), 427 (18), 426 (60), 384 (17), 382 (21), 380 (15), 353 (38), 352 (42), 351 (86), 346 (19), 342 (22), 341 (15), 340 (28), 311 (16), 310 (86), 309 (35), 308 (100), 262 (15), 243 (15), 207 (38), 175 (38), 134 (31). Calcd for $C_{25}H_{44}O_5SiS$: 484.2579. Found: 484.2597.

Bis-sulfenylation of *tert*-Butyl Linoleate. Utilizing method B of the sulfenylations of esters (except the disulfide was added at −78 °C and then the reaction allowed to warm), 1.50 g (4.47 mmol) of *tert*-butyl linoleate was converted to its enolate with 8.94 mmol of amide base and quenched with 1.95 g (8.94 mmol) of diphenyl disulfide. Isolation by dry column chromatography eluting with hexane gave 2.3 g of colorless oil: ir (CCl_4) 1724, 1658, 1577 cm^{-1}; NMR (CCl_4) δ 7.1–7.7 (10 H, m), 5.1–5.4 (4 H, m), 2.70 (2 H, bt, J = 5 Hz), 1.7–2.1 (4 H, m), 1.28 (9 H, s), 0.7–1.7 (19 H, m).

Bis-sulfenylation of Methyl 4-(6′-Methoy-1′-naphthyl)butanoates. Utilizing method A of the sulfenylations of esters, 516 mg (2.00 mmol) of ester was converted to its enolate with 4.20 mmol of amide base and quenched with 915 mg (4.20 mmol) of diphenyl disulfide. Isolation by dry column chromatography eluting with 5% ether in hexane gave 750 mg (79% yield) of white crystals, mp 114–115 °C, after recrystallization from methanol: ir (CCl_4) 1735, 1628, 1603; NMR (CCl_4) δ 6.9–7.9 (16 H, m), 3.87 (3 H, s), 3.68 (3 H, s), 2.2–3.4 (4 H, AA′BB′); mass spectrum (*m/e*, %) 10x [476 (2), 475 (5), 474 (19)], 376 (8), 268 (15), 267 (87), 184 (23), 183 (100), 140 (18). Calcd for $C_{28}H_{26}O_3S_2$: 474.1321. Found: 474.1321.

Preparation of Methyl 4-(6′-Methoxy-1′-naphthyl)-2-oxobutanoate. Methyl 2,2-bis(phenylthio)-4-(6′-methoxy-1′-naphthyl)butanoate (474 mg, 1.00 mmol) was heated in 15 ml of methanol until dissolution was complete. Iodine (508 mg, 2.00 mmol) was added, and the reaction mixture was heated at reflux for 2 h, then cooled, diluted with ether, and washed successively with saturated aqueous sodium thiosulfate solution, saturated aqueous sodium bicarbonate solution, and several portions of water. The organic phase was dried and concentrated in vacuo to yield 577 mg of a yellow oil which was chromatographed on two 20 × 40 cm TLC plates (2:1 ether–hexane) to yield 276 mg (87%) of the desired methyl ketal as a pale yellow gum at R_f 0.5: ir (CCl_4) 1750, 1625, 1600, 1586 cm^{-1}; NMR ($CDCl_3$) δ 7.1–8.0 (6 H, m), 3.85 (3 H, s), 3.80 (3 H, s), 3.31 (6 H, s), 2.1–3.2 (4 H, AA′BB′).

Perchloric acid (5 drops of 60% aqueous solution) was added to a solution of methyl 2,2-dimethoxyl-4-(6′-methoxy-1′-naphthyl)butanoate (200 mg, 0.63 mmol) in 5 ml of ether, and the resulting solution was stirred at room temperature for 16 h, then diluted with ether and washed with saturated aqueous sodium bicarbonate solution. The ether phase was dried and concentrated in vacuo to yield a yellow oil which was triturated with hexane to yield 109 mg (65%) of white crystals: mp 72.5–73.5 °C; ir (CCl_4) 1764, 1733, 1627, 1601; NMR (CCl_4) δ 6.9–7.9 (6 H, m), 3.88 (3 H, s), 3.79 (3 H, s), 3.0–3.5 (4 H, m). Calcd for $C_{16}H_{16}O_4$: 272.1048. Found: 272.1039.

Sulfenylation of Ketones. Method A. 2-Phenylthiocycloheptanone. The amide (20.0 mmol) was prepared as usual in 30 ml of THF. Cycloheptanone (1.12 g, 10.0 mmol) was added dropwise by syringe, and the resulting solution was stirred at −78 °C for 30 min prior to being siphoned via a Teflon tube (or syringed) into a room temperature solution of diphenyl disulfide (2.62 g, 12.0 mmol) in 10 ml of HMPA. After stirring at 25 °C for 1 h, the reaction was worked up as usual to give a yellow oil which was chromatographed on a 20 cm silica gel dry column (5% ether in hexane) to yield 1.92 g (87%) of an almost colorless oil at R_f = 0.3: ir (CCl_4) 1702, 1582; NMR ($CDCl_3$) δ 6.8–7.8 (5 H, m), 3.79 (1 H, d of d, J = 10 Hz, 5.5 Hz), 2.6–3.0 (1 H, m), 1.0–2.6 (9 H, m); mass spectrum (*m/e*, %) 222 (3), 221 (8), 220 (51), 113 (20), 110 (100), 109 (16), 55 (29). Calcd for $C_{13}H_{16}OS$: 220.0922. Found: 220.0931.

Method B. 2,6-Dimethyl-2-phenylthiocyclohexanone. The amide (15.9 mmol) was prepared as usual in 15 ml of THF. 2,6-Dimethylcyclohexanone (2.00 g, 15.9 mmol) was added dropwise by syringe, and the resulting solution was stirred at −78 °C for 1 h. The cold enolate solution was then added by syringe (or by siphon) to a room temperature solution of diphenyl disulfide (4.14 g, 19.0 mmol) in 5 ml of THF. (In several runs, the disulfide was added to the enolate solution.) The resulting reaction mixture was stirred at 25 °C for 1.5 h, then worked up as usual to yield a yellow oil. This material was chromatographed on six 20 × 20 cm TLC plates (1% ether in hexane) to yield 3.50 g (94%) of an almost colorless oil at R_f 0.25: ir (CCl_4) 1706, 1587; NMR (CCl_4) mixture of isomers δ 7.21 (5 H, s), 3.48 (0.65 H, m), 1.0–2.4 (6.35 H, m), 1.16 (3 H, s), 0.97 (3 H, d, J = 7 Hz); mass spectrum (*m/e*, %) 236 (3), 235 (8), 234 (40), 125 (50), 110 (77), 109 (16), 97 (77), 96 (74), 82 (17), 81 (35), 55 (100). Calcd for $C_{14}H_{18}OS$: 234.1078. Found: 234.1079.

Method C. Octahydro-4a-methyl-3-methylthio-2(1*H*)-naphthalenone. The amide (4.80 mmol) was prepared as usual in 4 ml of dry THF at −25 °C. After 30 min, a solution of 322 mg (2.00 mmol) of octahydro-4a-methyl-2(1*H*)-naphthalenone in 0.5 ml of THF and 3 ml of HMPA was added over a period of 5 min. After stirring at −25 °C for 30 min, 0 °C for 30 min, and finally room temperature for 40 min, 451 mg (4.80 mmol) of dimethyl disulfide was added. Preferably the disulfide was added at 0 °C and then the reaction allowed to warm to room temperature. (When diphenyl disulfide is employed, it is added as a solution in THF or HMPA.) The reaction mixture was stirred at room temperature for 1 h and worked up as usual. Purification by preparative TLC (PhH) gave 360 mg (85%) of colorless oil: ir ($CHCl_3$) 1712; NMR (CCl_4) 3.43 (dd, J = 12, 6 Hz), 2.04 (3 H, s), and 1.11 (3 H, s) superimposed upon 1.0–2.2 (13 H, m); mass spectrum (*m/e*, %) 212 (5), 180 (100), 165 (42), 109 (90), 96 (42), 95 (80), 81 (70), 79 (37), 68 (35), 67 (90), 55 (60), 53 (37). Calcd for $C_{12}H_{20}OS$: 212.1235. Found: 212.1227. The reaction details for the additional examples are summarized in Table V.

Spectral Properties. 2,6-Dimethyl-2-methylthiocyclohexanone. Ir (CCl_4) 1699; NMR ($CDCl_3$) δ 3.32 (0.65 H, m), 1.4–2.5 (6.35 H, m), 1.83 (3 H, s), 1.34 (3 H, s), 1.02 (3 H, d, J = 7 Hz); mass spectrum (*m/e*, %) 174 (2), 172 (5), 172 (40), 129 (30), 126 (25), 125 (44), 124 (19), 101 (25), 97 (100), 96 (27), 82 (16), 81 (26), 69 (19), 55 (98). Calcd for $C_9H_{16}OS$: 172.1922. Found: 172.1921.

2-Phenylthiocyclododecanone. Mp 94–98 °C; ir (CCl_4) 1704; NMR (CCl_4) δ 7.35 (5 H, m), 3.92 (1 H, dd, J = 12.0 Hz, 3.6 Hz), 2.3–3.0 (2 H, m), 1.0–2.3 (16 H, m); mass spectrum (*m/e*, %) 292 (3), 291 (10), 290 (45), 263 (3), 262 (14), 218 (6), 149 (15), 137 (5), 136 (7), 135 (8), 123 (26), 112 (5), 111 (10), 109 (21), 101 (28), 97 (25), 96 (11), 95 (23), 91 (10), 85 (17), 83 (37), 82 (19), 81 (30), 77 (11), 71 (16), 69 (37), 68 (16), 67 (29), 66 (10), 65 (10), 57 (11), 56 (10), 55 (66), 54 (11), 53 (10). Calcd for $C_{18}H_{26}OS$: 290.170425. Found: 290.17043.

2-Methylthiocyclohexanone.[74] Ir ($CHCl_3$) 1703; NMR (CCl_4) δ 3.16 (1 H, t, J = 5 Hz), 2.76 (1 H, m), 2.00 (3 H, s), 1.2–3.0 (7 H, m); mass spectrum (*m/e*, %) 144 (4), 128 (18), 119 (35), 112 (50), 55 (100), 43 (38), 41 (51). Calcd for $C_7H_{12}OS$: 144.0609. Found: 144.0602.

2-Phenylthiocyclohexanone.[75] Ir ($CHCl_3$) 1708, 1585; NMR δ 7.1–7.4 (5 H, m), 3.68 (1 H, t, J = 5 Hz), 2.8 (1 H, m), 1.4–2.4 (7 H, m); mass spectrum (*m/e*, %) 206 (67), 110 (100), 69 (23), 41 (38). Calcd for $C_{12}H_{14}OS$: 206.0765. Found: 206.0760.

4-*tert*-Butyl-2-phenylthiocyclohexanone. Ir ($CHCl_3$) 1717, 1582; NMR δ 7.1–7.5 (5 H, m), 3.84 (dd, J = 12, 6 Hz), and 3.64 (m) for total 1 H, 3.02 (0.66 H, td, J = 13, 6 Hz), 2.1–3.0 (6.33 H, m), 1.04 (9 H, s); mass spectrum (*m/e*, %) 262 (23), 110 (70), 109 (21), 96 (24), 69 (31), 67 (26), 66 (23), 57 (100), 55 (27), 41 (60). Calcd for $C_{16}H_{22}OS$: 262.1416. Found: 262.1391.

2-Methyl-6-phenylthiocyclohexanone. Ir (CCl_4) 1710, 1581; NMR (CCl_4) 66:34 mixture of trans:cis 2-methyl-6-phenylthiocyclohexanones contaminated by <5% 2-methyl-2-phenylthiocyclohexanone:[13b] δ 6.8–7.6 (5 H, m), 3.84 (0.34 H, dd, J = 11, 5 Hz), 3.69 (0.66 H, m), 2.9–3.4 (0.7 H, m), 1.2–2.6 (6.3 H, m), 1.02 (0.9 H, d, J = 6 Hz), 0.96 (2.1 H, d, J = 8 Hz); mass spectrum (*m/e*, %) 222 (3), 221 (6), 220 (48), 162 (13), 135 (20), 111 (30), 110 (100), 109 (24), 91 (20), 83 (54), 82 (20), 77 (25), 68 (33), 67 (36), 66 (21), 65 (30), 55 (26), 52 (26). Calcd for $C_{13}H_{16}OS$: 220.0922. Found: 220.0917.

Octahydro-4a-methyl-3-phenylthio-2(1*H*)-naphthalenone. Mp 83 °C; ir ($CHCl_3$) 1713, 1585; NMR (CCl_4) δ 7.1–7.5 (5 H, m), 4.00 (1 H, dd, J = 13, 6 Hz), 2.2 (2 H, d, J = 8 Hz), 1.94 (1 H, dd, J = 13

Table V. Experimental Details for Additional Sulfenylations of Ketones

Ketone (wt, mmol)	Amine (wt, mmol)	Disulfide (wt, mmol)	Method	Product wt (% yield)	R_f (solvent)
2,6-Dimethylcyclohexanone (500 mg, 3.97)	(560 mg, 3.97)	CH_3SSCH_3 (448 mg, 4.77)	A	352 mg, 52%	0.5 ($CHCl_3$)
Cyclododecanone					
a (1.00 g, 5.49)	(1.55 g, 11.0)	PhSSPh (1.44 g, 6.60)	B[a]	1.48 g, 93%[b]	0.3 (5% ether in
b (546 mg, 3.00)	(846 mg, 6.0)	PhSSPh (785 mg, 3.6)	C	743 mg, 85%	hexane)
Cyclohexanone					
a (980 mg, 10.0)	(2.121 g, 21.0)	CH_3SSCH_3 (1.974 g, 21.0)	C	1.075 g, 75%	0.55 (20% ethyl acetate in hexane)
b (490 mg, 5.0)	(1.622 g, 11.5)	PhSSPh (2.507 g, 11.5)	C	860 mg, 83%	0.3 (PhH)
4-*tert*-Butylcyclohexenone (456 mg, 2.96)	(917 mg, 6.50)	PhSSPh (1.417 g, 6.50)	C	603 mg, 78%	0.3 (20% ethyl acetate in hexane)
2-Methylcyclohexanone					
a 336 mg (3.00)	(423 mg, 3.00)	PhSSPh (785 mg, 3.60)	B	575 mg, 87%	0.2–0.4 (10% ether in hexane)
b 433 mg (3.86)	(571 mg, 4.05)	$PhSSO_2Ph$ (972 mg, 4.05)	B[c]	726 mg, 85%	
Octahydro-4a-methyl-*trans*-2(1*H*)-naphthalenone (210 mg, 1.27)	(410 mg, 2.91)	PhSSPh (634 mg, 2.91)	C	246 mg, 71%[d]	0.4 (PhH)
Estrone methyl ether (230 mg, 0.81)	(286 mg, 2.03)	PhSSPh (212 mg, 0.97)	A	298 mg, 94%	0.3 (3:2 ether–hexane)
Methyl 1,2,3,11,12,12a-hexahydro-3-oxobenzo[*a*]-phenanthrene-12a-carboxylate (612 mg, 2.00)	(649 mg, 4.60)	PhSSPh (1.003 g, 4.60)	C	390 mg, 47%[e]	(30% ethyl acetate in hexane
7-Methoxy-2-methyl-1,2,3,4-tetrahydro-1-phenanthrone (600 mg, 2.50)	(441 mg, 3.13)	PhSSPh (682 mg, 3.13)	C	855 mg, 98%[f]	0.53 (30% ethyl acetate in hexane)

[a] Disulfide added directly to the enolate and stirring for 90 min. [b] Mp 94–98 °C. [c] The quench solution containing the sulfenylating agent as well as the reaction after adding the enolate solution was kept at 0 °C. [d] Mp 83 °C from *n*-hexane. [e] Mp 175–176 °C from carbon tetrachloride as pale yellow prisms. [f] Mp 125–126 °C from ethanol as colorless prisms.

Hz), 1.1–1.8 (10 H, m), 1.06 (3 H, s); mass spectrum (*m/e*, %) 274 (21), 197 (23), 155 (25), 137 (23), 110 (26), 109 (40), 95 (100), 81 (39), 67 (42), 55 (38), 41 (49). Calcd for $C_{17}H_{22}OS$: 274.1391. Found: 274.1389.

16-(Phenylthio)estrone Methyl Ether. Ir (CCl_4) 1746, 1610, 1500; NMR ($CDCl_3$) mixture of isomers δ 6.3–7.6 (8 H, m), 3.94 (0.25 H, unresolved t), 3.69 (3 H, s), 3.48 (0.75 H, unresolved t), 2.8 (2 H, m), 1.0–2.6 (11 H, m), 0.90 (0.75 H, s), 0.73 (2.25 H, s); mass spectrum (*m/e*, %) 394 (5), 393 (17), 392 (80), 229 (14), 228 (100), 218 (15), 186 (25), 173 (21), 160 (14), 136 (16), 120 (40), 119 (31), 77 (16), 65 (16). Calcd for $C_{25}H_{28}O_2S$: 392.1810. Found: 392.1834.

7-Methoxy-2-methyl-2-phenylthio-1,2,3,4-tetrahydro-1-phenanthrone. Mp 125–126 °C; ir ($CHCl_3$) 1663, 1618, 1574; NMR ($CDCl_3$) δ 8.13 (1 H, d, J = 9 Hz), 7.84 (1 H, d, J = 9 Hz), 7.58 (1 H, d, J = 9 Hz), 7.0–7.4 (7 H, m), 3.80 (3 H, s), 3.1–3.5 (2 H, m), 2.2–2.4 (2 H, m), 1.44 (3 H, s); mass spectrum (*m/e*, %) 348 (1), 240 (16), 239 (26), 238 (100), 211 (24), 198 (28), 195 (40), 170 (16), 110 (63), 109 (16), 66 (23). Calcd for $C_{22}H_{20}O_2S$: 348.1184. Found: 348.1172.

Methyl 1,2,3,11,12,12a-Hexahydro-3-oxo-2-phenylthiobenzo[*a*]-phenanthrene-12a-carboxylate. Mp 175–176 °C; ir ($CHCl_3$) 1735, 1668, 1597; NMR (7.2–8.1 (11 H, m), 6.88 (1 H, s), 4.14 (1 H, dd, J = 15, 5 Hz), 3.60 (3 H, s), 3.00–3.40 (2 H, m), 2.48–2.90 (2 H, m), 1.68–2.30 (2 H, m); mass spectrum (*m/e*, %) 414 (1), 121 (33), 119 (100), 117 (100), 84 (17), 82 (25), 47 (22). Calcd for $C_{26}H_{22}O_3S$: 414.1290. Found: 414.1294.

Chemospecific Sulfenylation of 17β-Carbomethoxy-17α-(methylthio)-5β-androstan-3-one. The amide (5.76 mmol) was prepared as usual in 7 ml of THF. A solution of 17β-carbomethoxy-5β-androstan-3-one (870 mg, 2.63 mmol) in 5 ml of THF was added dropwise by syringe, and the reaction was allowed to warm to room temperature. As warming occurred, the dienolate precipitated as a white solid. When the mixture reached room temperature, dimethyl disulfide (4.92 mg, 5.24 mmol) was added by syringe. After stirring for an additional 1 h at 25 °C, the reaction mixture was diluted with ether and worked up as usual to yield a yellow oil. This material was chromatographed on three 20 × 20 cm TLC plates (chloroform) to yield 910 mg (100%) of a white foam, R_f 0.8: ir (CCl_4) 1727, 1721; NMR ($CDCl_3$) δ 3.77 (3 H, s), 2.03 (3 H, s), 1.0–2.9 (22 H, m), 1.03 (3 H, s), 0.85 (3 H, s); mass spectrum (*m/e*, %) 380 (6), 379 (15), 578 (55), 347 (16), 346 (62), 308 (15), 246 (53), 244 (29), 231 (15), 145 (15), 133 (17), 132 (100). Calcd for $C_{22}H_{34}O_2S$: 378.2228. Found: 378.2228.

Preparation of 2,12-Bis(phenylthio)cyclododecanone. Following method C for the sulfenylation of ketones, 546 mg (3.00 mmol) of cyclododecanone was converted to its enolate (7.20 mmol of base) and sulfenylated with 1.570 g (7.20 mmol) of diphenyl disulfide. Purification by preparative TLC (1:1 hexane–benzene) gave 955 mg (80%) of colorless needles: mp 120 °C (recrystallized from *n*-hexane); ir ($CHCl_3$) 1700; NMR δ 7.0–7.4 (10 H, m), 4.23 (0.67 H, dd, J = 7, 6 Hz), 3.96 (0.33 H, dd, J = 10, 4 Hz), 1.0–2.0 (18 H, m); mass spectrum (*m/e*, %) 398 (57), 261 (92), 123 (84), 110 (42), 109 (57), 95 (61), 91 (41), 81 (50), 69 (42), 67 (45), 55 (100), 41 (73). Calcd for $C_{24}H_{30}OS_2$: 398.1738. Found: 398.1732.

Oxidation of Sulfides. Method A. Preparation of Ethyl 2-Methylsulfinyldecanoate. Ethyl 2-methylthiodecanoate (1.53 g, 6.22 mmol) was dissolved in 20 ml of methanol and cooled in an ice bath prior to the dropwise addition of a solution of sodium metaperiodate (1.33 g, 6.22 mmol) in a minimum amount of water. When addition was complete, the ice bath was removed, and the reaction was stirred at room temperature. TLC analysis (chloroform) showed complete disappearance of the starting material spot at R_f 0.7 after 24 h. (Reaction times of 2–24 h were required.) The reaction mixture was filtered, and the precipitate was washed several times with methanol. The combined filtrate and washings were concentrated in vacuo to yield a pale yellow oil which was dissolved in ether and dried. Concentration of the organic layer in vacuo gave 1.58 g (97%) of an almost colorless oil which showed one spot on TLC (chloroform) at R_f 0.2: ir (CCl_4) 1730, 1063; NMR (neat, external Me_4Si) mixture of diastereomers δ 4.12 (2 H, overlapping quartets), 3.13 (1 H, m), 2.47 and 2.43 (3 H, two singlets), 0.95–2.2 (17 H, m), 0.65–0.95 (3 H, m). Generally, the crude sulfoxide was utilized directly in the elimination step. Table VI summarizes the additional examples.

Method B. Preparation of 16-(Phenylsulfinyl)estrone Methyl Ether. A solution of 16-(phenylthio)estrone methyl ether (575 mg, 1.47 mmol) in 30 ml of methylene chloride was cooled to −78 °C, and a solution of *m*-chloroperbenzoic acid (298 mg of 85% mixture, 1.47 mmol) in 10 ml of methylene chloride was added dropwise by syringe over a 5-min period. Upon completion of the addition, TLC analysis (3:2 ether–hexane) showed complete loss of the starting material spot at R_f 0.8. The cold reaction mixture was poured into a separatory funnel containing 100 ml of ether and 100 ml of 10% aqueous sodium sulfite solution. The organic layer was separated, washed twice with saturated aqueous sodium bicarbonate solution, dried and concentrated in vacuo to yield 600 mg (100%) of a white foam: ir ($CHCl_3$)

Table VI. Experimental Details for Additional Desulfenylations

Compd	Oxidation (wt, mmol)	Oxidation (wt, mmol)	Oxidation Time (h)	Elimination Method	Elimination Solvent	Elimination Time (h)	Elimination Temp (°C)	Elimination Product wt (% yield)	R_f (solvent)	Ref
3a	(172 mg, 1.00)	A (214 mg, 1.00)	16	B	$PhCH_3(CaCO_3)$	16	110	105 mg (84)	0.6 (5% ether/hexane)	77
3b	(1.60 g, 6.84)	A (1.41 g, 6.84)	16	See detailed examples						77
4	(1.08 g, 3.70)	A (795 mg, 3.70)	16	C	CCl_4	16	50	(93)[a]	0.6 (10% ether/hexane)	78
5	(522 mg, 2.37)	A (507 mg, 2.37)	14	B	$PhCH_3(CaCO_3)$	1.5	110	210 mg (81)	0.4 ($CHCl_3$)	2e, 79
6	(500 mg, 2.27)	A (486 mg, 2.27)	16	B	$PhH(CaCO_3)$	2	80	202 mg (81)	0.5 (1:1 ether/hexane)	80
7	(575 mg, 1.47)	See detailed examples		(1) B	$PhCH_3$ (pyridine, 79 mg)	50	110	(34)[b]	(3:2 ether/hexane)	81
				(2) B	$PhCH_3$ ($(CH_3O)_3P$, 95 mg)	55	110	(88)[c]	(3:2 ether/hexane)	81
9	(1.05 g, 5.14)	A (1.10 g, 5.14)	2	See detailed examples						
8		See detailed examples		(1) B	See detailed examples					
				(2) A	None	5	120	(98)[d]	0.7 ($CHCl_3$)	76
10a	(775 mg, 3.44)	A (734 mg, 3.44)	2	A	None	6	120	(96)[e]	($CHCl_3$)	
10b	(840 mg, 2.92)	A (625 mg, 2.92)	16	A	None	17	50	(86)[f]	0.6 (10% ether/hexane)	12d
11	(1.15 g, 5.00)	A (1.065 g, 5.00)	2	B	$PhCH_3$ ($CaCO_3$)	12	110	(88)[g]	0.7 ($CHCl_3$)	
12	(1.15 g, 7.88)	A (1.68 g, 7.88)	2	A	None	1.3	120	(77)[h]	0.7 ($CHCl_3$)	82
13a	(318 mg, 1.00)	A (428 mg, 2.00)	2	B	Xylene ($CaCO_3$)	3	130	229 mg (85)	0.6 (3:2 ether/hexane)	
14	(635 mg, 1.31)	B (204 mg, 1.18)	0.1	B	Xylene ($CaCO_3$)	1	130	470 mg (93)	0.7 (4:1 ether/hexane)	
15	(430 mg, 0.86)	B (141 mg, 0.82)	0.1	B	Xylene ($CaCO_3$)	2	130	(79)[i]	0.8 (4:1 ether/hexane)	
19b	(871 mg, 2.38)	A (506 mg, 2.38)	3	B	$PhCH_3$	16	110	(92)[j]	0.6 (4:1 ether/hexane)	

[a] A 800-mg aliquot of the crude sulfoxide was thermolyzed to give 438 mg of enone. [b] A 408-mg aliquot of the crude sulfoxide was thermolyzed to give 95 mg of enone, mp 175–177 °C (lit. mp 181 °C). [c] A 157-mg aliquot of the crude sulfoxide was thermolyzed to give 98 mg of enone, mp 178–179 °C (lit. mp 181 °C). [d] A 138-mg aliquot of the crude sulfoxide was thermolyzed to give 102 mg of enoate. [e] A 550-mg aliquot of the crude sulfoxide was thermolyzed to give 323 mg of ethyl benzoate. [f] A 644-mg aliquot of the crude sulfoxide was thermolyzed to give 325 mg of enoate. [g] A 660-mg aliquot of the crude sulfoxide was thermolyzed to give 431 mg of enoate. [h] A 600-mg aliquot of the crude sulfoxide was thermolyzed to give 280 mg of product as a 65:35 mixture of endo:exo double bond isomers as determined by the integral ratio of the NMR absorption at δ 5.93 or 5.54 for the exocyclic isomer compared with δ 7.20 for the endocyclic isomer. [i] A 198-mg aliquot of the crude sulfoxide was thermolyzed to give 137 mg of product. [j] A 800-mg aliquot of the crude sulfoxide was thermolyzed to give 616 mg of product, mp 170.5–171.5 °C.

1740, 1610, 1500, 1040; NMR ($CDCl_3$) mixture of isomers and diastereomers δ 6.3–8.1 (8 H, m), 3.73 (3 H, s), 3.1–4.3 (1 H, several multiplets), 2.8 (2 H, m), 1.0–2.6 (11 H, m), 0.6–1.0 (3 H, several singlets). Generally the crude sulfoxide was employed directly in the elimination step. Table VI summarizes the additional examples.

Eliminations of Sulfoxides. Method A. Preparation of Methyl 3-Ethyl-2-hexenoate. Methyl 2-methylsulfinyl-3-ethylhexanoate (650 mg, 2.95 mmol) was placed in an NMR tube under a positive pressure of dry nitrogen and heated in an oil bath at 120 °C with periodic NMR monitoring. After 6 h, no starting material remained, and the product mixture was diluted with carbon tetrachloride and chromatographed on two 20 × 40 cm TLC plates (chloroform) to yield 425 mg (92%) of a colorless oil, R_f 0.7. Analysis of this material on several VPC columns (10 ft, 20% SE-30 on Chromosorb P, 150 °C; 23 ft, 20% SE-30 on Chromosorb W, 150 °C; 8 ft, 20% DEGS on Chromosorb W, 130 °C, retention time = 12.2 and 12.8 min) indicated an approximate 1:1 mixture of *E* and *Z* isomers. Ir (CCl_4) 1721, 1642; NMR (CCl_4, ext. Me_4Si) δ 5.50 (1 H, narrow m), 3.52 (3 H, s), 2.3–2.7 (2 H, m), 1.9–2.3 (2 H, m), 1.1–1.6 (2 H, m), 0.8–1.1 (6 H, m); mass spectrum (*m/e*, %) 158 (5), 157 (9), 156 (29), 136 (15), 127 (100), 125 (26), 120 (20), 116 (29), 95 (25), 85 (19), 85 (25), 69 (38), 67 (19), 57 (80), 56 (16), 55 (55), 54 (16), 53 (31). Calcd for $C_9H_{16}O_2$: 156.1150. Found: 156.1150.

Method B. Preparation of Ethyl (*E*)-2-Decenoate. Crude ethyl 2-methylsulfinyldecanoate (680 mg, 2.59 mmol) was dissolved in 20 ml of toluene, and the resulting solution was heated to reflux. In many cases the thermolysis is carried out in the presence of added solid calcium carbonate. After 14 h, TLC analysis (chloroform) showed no remaining starting material at R_f 0.25, and the reaction mixture was concentrated in vacuo to yield a yellow oil which was chromatographed utilizing chloroform to yield 403 mg (96%) of an oil R_f 0.7 whose spectral properties (ir, NMR, mass spectrum) are identical with an authentic sample.[76]

Method C. Preparation of 2,6-Dimethylcyclohex-2-enone. 2,6-Dimethyl-2-phenylsulfinylcyclohexanone (642 mg, 2.50 mmol) was dissolved in 5 ml of carbon tetrachloride and heated to 50 °C. TLC monitoring (5% ether in hexane) indicated complete disappearance of the starting material (R_f 0.15) after 3 h. The reaction mixture was concentrated in vacuo and chromatographed on three 20 × 20 cm TLC plates (5% ether in hexane) to yield 283 mg (90%) of an oil at R_f 0.6. VPC analysis of this material [10 ft, 20% SE-30 on Chromosorb P, 160 °C, retention time = 5.0 (exo) and 7.7 (endo) min] showed it to contain 6% of the exocyclic olefin:[77] ir (CCl_4) 1675; NMR (CCl_4) endo isomer δ 6.58 (1 H, m), 1.6–2.6 (5 H, m), 1.73 (3 H, narrow m), 1.10 (3 H, d, J = 8 Hz); mass spectrum (*m/e*, %) 125 (5), 124 (38), 82 (100), 54 (31). Anal. ($C_8H_{12}O$): C, H.

Properties of Enones and Enoates. For all known compounds, references are given in Table VI, last column, for literature comparisons. For compounds not reported in the literature, the properties are listed below.

Methyl 3-ethyl-2-hexenoate: see detailed procedures. *tert*-Butyl cyclohex-1-en-1-carboxylate: ir (CCl_4) 1706, 1647; NMR (CCl_4) δ 6.73 (1 H, m), 2.13 (4 H, m), 1.4–1.8 (4 H, m), 1.46 (9 H, s); mass spectrum (*m/e*, %, 40 eV) 182 (3), 127 (30), 126 (15), 111 (32), 110 (100), 109 (27), 83 (55), 81 (19), 57 (36). Calcd for $C_{11}H_{18}O_2$: 182.1307. Found: 182.1311.

Ethyl 4-(6-methoxy-1-naphthyl)but-(*E*)-2-enoate: mp 37–38 °C; ir (CCl_4) 1720, 1650, 1624, 1599; NMR (CCl_4) δ 6.9–7.8 (7 H, m), 5.68 (1 H, d of t, J = 16, 2 Hz), 4.04 (2 H, q, J = 7 Hz), 3.76 (3 H, s), 3.70 (2 H, br s), 1.12 (3 H, t, J = 7 Hz); mass spectrum (*m/e*, %) 274 (4), 273 (19), 272 (100), 225 (20), 197 (42), 196 (27), 195 (22), 165 (24), 128 (17), 45 (23). Calcd for $C_{17}H_{18}O_3$: 270.1256. Found: 270.1256.

6,7,7a,7b-Tetrahydro-5-(1′-carbomethoxy-2′-propenyl)-7aβ-methyl-4,5β,oxa-1β-tetrahydropyranyloxy-7bβ-trimethylsiloxyindan: ir (CCl_4) 2930, 2855, 1715, 1645; NMR (CCl_4, silyl ether = 0.00) mixture of isomers and diastereomers δ 6.84, 6.73, 6.52 (total 0.15 H, 3 s), 6.00, 5.68, 5.48, 5.44 (0.85 H, 4 s), 4.42 (1 H, br s), 3.80–4.25 (2 H, m), 3.1–3.8 (3 H, m), 2.3–2.8 (2 H, m), 2.00 and 1.87 (3 H, 2 s, ratio 2:3), 0.9–2.2 (18 H, m), 0.64 (3 H, narrow m), 0.00 (9 H, s). Calcd for $C_{24}H_{40}O_6Si$: 452.2594. Found: 452.2594.

6,7,7a,7b-Tetrahydro-5-(1′-carbomethoxy-2′-propenyl)-7aβ-methyl-1β-tetrahydropyranyloxy-7bβ-trimethylsiloxyindan: ir (CCl_4) 2935, 2865, 2845, 1723, 1630, 1612; NMR (CCl_4, silyl ether = 0.00) mixture of isomers and diastereomers δ 5.87 and 5.75 (0.5 H, 2 s), 5.48 and 5.16 (1.5 H, 2 a), 4.52 (1 H, m), 3.9–4.3 (2 H, m), 3.2–3.9 (3 H, m), 2.22 and 1.85 (3 H, 2 s, ratio 1:3), 1.0–2.5 (17 H, m), 0.80 (3 H, narrow m), 0.00 (9 H, s); mass spectrum (*m/e*, %) 15 eV, 438 (2), 451 (6), 436 (16), 377 (15), 353 (18), 352 (66), 294 (15), 293 (15), 292 (18), 85 (100). Calcd for $C_{24}H_{40}O_5Si$: 436.2645. Found: 436.2645.

17-Carbomethoxy-5β-androst-16(17)-en-3-one: mp 170.5–171.5 °C (ether–pentane); ir (CCl_4) 1710, 1600; NMR ($CDCl_3$) δ 6.78 (1 H, unresolved t), 3.73 (3 H, s), 1.2–3.0 (20 H, m), 1.07 (3 H, s), 0.95 (3 H, s); mass spectrum (*m/e*, %) 329 (4), 328 (10), 313 (38), 283 (40), 271 (58), 270 (76), 255 (29), 159 (15), 145 (25), 133 (20), 131 (35), 129 (21), 123 (15), 121 (16), 119 (33), 117 (26), 115 (18), 109 (15), 107 (31), 105 (55), 95 (22), 93 (55), 92 (20), 91 (100), 81 (44), 79 (65), 78 (19), 77 (58), 69 (15), 67 (48), 65 (22), 59 (35), 55 (56), 53 (33). Anal. ($C_{21}H_{32}O_3$): C, H.

Methyl 9-Oxodecanoate. Azelaic acid monomethyl ester (Aldrich, 3.00 g, 14.8 mmol) and thionyl chloride (3.52 g, 29.6 mmol) were stirred together in the neat for 19 h. Excess thionyl chloride was removed in vacuo to yield 3.1 g (95%) of the crude acid chloride: NMR (CCl_4, ext. Me_4Si) δ 3.50 (3 H, s), 2.80 (2 H, t, J = 6.8 Hz), 2.13 (2 H, t, J = 7.6 Hz), 1.4–1.9 (4 H, m), 1.25 (10 H, br s).

Methyllithium (52.2 ml of 1.7 M solution in ether, 88.8 mmol) was added by syringe to a suspension of cuprous iodide (8.42 g, 44.4 mmol) in 120 ml of anhydrous ether at 0 °C, and the resulting mixture was stirred at 0 °C for 10 min, then cooled to −78 °C. A solution of the crude acid chloride (3.1 g) in ether at 0 °C was added by syringe to the cuprate solution, and the resulting reaction mixture was stirred at −78 °C for 20 min, then quenched by the addition of 6.6 ml of methanol and allowed to warm to room temperature. The resulting reaction mixture was extracted with two volumes of saturated aqueous ammonium chloride solution, and the organic phase was dried and concentrated in vacuo to yield 3.1 g of a yellow oil which was distilled

[73 °C (0.2 mm)] to yield 2.43 g (81% overall) of methyl 9-oxodecanoate,[61] which had spectra identical with those reported previously.

Methyl 2-Methylthio-9-oxodecanoate. To a solution of methyl 9-oxodecanoate (700 mg, 3.50 mmol) and ethylene glycol (406 mg, 7.00 mmol) in 12 ml of dry benzene was added a trace of *p*-toluenesulfonic acid, and the resulting solution was heated at reflux in a flask equipped with a Dean–Stark trap. After 16 h, the reaction mixture was cooled, diluted with ether, washed with saturated aqueous sodium bicarbonate solution, dried, and concentrated in vacuo to yield 900 mg of a colorless oil which was chromatographed on a 20 × 40 cm TLC plate (2:1 ether–hexane) to yield 865 mg (100%) of the desired ketal at R_f 0.6: ir (CCl_4) 1739; NMR (CCl_4, ext. Me_4Si) δ 3.81 (4 H, s), 3.57 (3 H, s), 2.19 (2 H, t, J = 7.2 Hz), 1.1–1.8 (12 H, m), 1.15 (3 H, s).

The amide (1.98 mmol) was prepared as usual in 10 ml of THF. Methyl 9-oxodecanoate ethylene ketal (440 mg, 1.80 mmol) was added dropwise by syringe, and the resulting solution was stirred at −78 °C for 1 h. The enolate solution was then added to a solution of dimethyl disulfide (845 mg, 9.00 mmol) in 5 ml of HMPA at 0 °C, and the resulting solution was stirred for 30 min. Standard workup gave 600 mg of a yellow oil which was chromatographed on a 20 × 40 cm TLC plate (2:1 ether–hexane) to yield 449 mg (86%) of the sulfenylate material at R_f 0.7: NMR (CCl_4) δ 3.86 (4 H, s), 3.73 (3 H, s), 3.09 (1 H, t, J = 8 Hz), 2.08 (3 H, s), 1.00–2.00 (12 H, m), 1.22 (3 H, s).

Methyl 2-(methylthio)-9-oxodecanoate ethylene ketal (610 mg, 2.10 mmol) in 20 ml of methanol was treated with a solution of oxalic acid (378 mg, 4.20 mmol) in 15 ml of water. The resulting reaction mixture was stirred at room temperature for 4 h, then diluted with brine and extracted with ether. The ether extract was washed with water and saturated aqueous sodium bicarbonate solution, dried and concentrated in vacuo to yield a pale yellow oil which was chromatographed on a 20 × 40 cm TLC plate (2:1 ether–hexane) to yield 404 mg (80%) of methyl 2-methylthio-9-oxodecanoate: ir (CCl_4) 1720, 1656; NMR (CCl_4) δ 3.70 (3 H, s), 3.06 (1 H, t, J = 8 Hz), 2.36 (2 H, t, J = 8 Hz), 2.07 (3 H, s), 2.04 (2 H, s), 1.0–2.0 (10 H, br m); mass spectrum (*m/e*, %) 246 (6), 214 (100), 189 (14), 187 (39), 143 (46), 142 (14), 120 (45), 111 (46), 98 (15), 97 (16), 95 (21), 88 (17), 87 (47), 83 (41), 81 (75), 74 (29), 71 (26), 69 (28), 67 (20), 61 (63), 59 (20), 58 (46), 55 (54). Calcd for $C_{12}H_{22}O_3S$: 246.1298. Found: 246.1289.

Methyl 9-Oxodec-(*E*)-2-enoate. Methyl 2-methylthio-9-oxodecanoate (400 mg, 1.64 mmol) in 20 ml of methanol was treated with a solution of sodium metaperiodate (351 mg, 1.64 mmol) in a minimum volume of water, and the resulting reaction mixture was stirred at room temperature for 20 h. Standard workup gave 443 mg (104%) of a yellow oil: NMR (CCl_4) mixture of diastereomers δ 3.75 (3 H, s), 3.48 (1 H, m), 2.56–2.51 (total 3 H, 2 s), 2.39 (2 H, t, J = 7 Hz), 1.0–2.0 (10 H, br m).

Methyl 2-methylsulfinyl-9-oxodecanoate (426 mg, 1.64 mmol) was dissolved in 5 ml of toluene containing a small amount of powdered calcium carbonate, and the resulting mixture was heated at reflux for 16 h, then diluted with ether, filtered, and concentrated in vacuo to yield a yellow oil. This material was chromatographed on a 20 × 40 cm TLC plate (2:1 ether–hexane) to yield 277 mg (86% overall) of methyl 9-oxodec-(*E*)-2-enoate at R_f 0.6, identical with that reported previously.[55,60]

Methyl 2,8-Dimethylthio-9-oxodecanoate. The amide (6.00 mmol) solution was prepared as usual in 8 ml of THF and 2 ml of HMPA. A solution of methyl 9-oxodecanoate (400 mg, 2.00 mmol) in 2 ml of THF was added dropwise. Dimethyl disulfide (195 mg, 2.20 mmol) was added by syringe, and the resulting solution was stirred at −78 °C for 30 min, then allowed to warm to −20 °C for an additional 1 h. Standard workup gave 482 mg of a yellow oil which was chromatographed on two 20 × 10 cm TLC plates (2:1 ether–hexane) to give 122 mg (25%) of a pale yellow oil at R_f 0.5: ir (CCl_4) 1733, 1708; NMR (CCl_4) δ 3.70 (3 H, s), 3.02 (2 H, t, J = 8 Hz), 2.20 (3 H, s), 2.07 (3 H, s), 1.88 (3 H, s), 1.2–2.0 (10 H, m); mass spectrum (*m/e*, %) 10x [294 (3), 293 (4), 292 (15)], 246 (35), 215 (19), 203 (100), 171 (65), 123 (50), 95 (60), 87 (51), 83 (15), 81 (56), 74 (23), 71 (20), 69 (21), 67 (21), 61 (75), 59 (66), 55 (51). Calcd for $C_{13}H_{24}O_3S_2$: 292.1167. Found: 292.1166.

Sulfenylations of Linoleates. Procedure 1. Utilizing method A of the sulfenylations of esters, 1.00 g (3.24 mmol) of ethyl linoleate after conversion to its enolate with 3.24 mmol of amide base was quenched with 609 mg (6.48 mmol) of dimethyl disulfide. Isolation by preparative TLC eluting with chloroform (R_f 0.5) gave 865 mg (75%) of product: ir (CCl_4) 1733; NMR (CCl_4) δ 5.2–5.6 (4 H, m), 4.17 (2 H, q, J = 8 Hz), 3.13 (1 H, t, J = 8 Hz), 2.75 (2 H, unresolved t), 2.07 (3 H, s), 1.8–2.4 (4 H, m), 0.8–1.8 (22 H, br m); mass spectrum (*m/e*, %) 10x [356 (6), 355 (6), 354 (15), 293 (20), 267 (30), 265 (19), 257 (33), 241 (21), 171 (17), 157 (15), 155 (16), 147 (21), 147 (19), 143 (16), 137 (16), 136 (20), 135 (40), 134 (60), 133 (24), 129 (25), 123 (32), 122 (21), 121 (57), 119 (28), 117 (18), 115 (27), 113 (16), 111 (20)], 95 (31), 93 (21), 91 (15), 86 (22), 83 (15), 81 (57), 80 (18), 79 (42), 77 (16), 73 (20), 69 (35), 68 (19), 67 (93), 61 (45), 57 (25), 56 (16), 55 (100), 54 (25), 53 (21). Calcd for $C_{21}H_{38}O_2S$: 354.2592. Found: 354.2592.

Similar procedures to the above were used for the sulfenylations of methyl and *tert*-butyl linoleate in 61 and 84% yields, respectively.

Procedure 2. The amide (3.24 mmol) was prepared as usual in 12 ml of THF. Ethyl octadec-(*Z,Z*)-9,12-dienoate (1.00 g, 3.24 mmol) was added dropwise by syringe, and the resulting reaction mixture was stirred at −78 °C for 1 h, then siphoned through a Teflon tube into a solution of dimethyl disulfide (534 mg, 3.56 mmol) in 5 ml of HMPA at room temperature. This solution was stirred at room temperature for 30 min, then worked up as usual to give a yellow oil which was chromatographed on five 20 × 20 cm TLC plates to yield 1.06 g (92%) of product identical with that prepared above.

Preparation of Ethyl Octa-(*E*)-2-(*Z,Z*)-9,12-trienoate. Utilizing method B for the oxidation of sulfides 238 mg (0.673 mmol) of ethyl 2-methylthiooctadeca-(*Z,Z*)-9,12-dienoate was oxidized with 137 mg of an 85% pure (0.673 mmol) sample of *m*-chloroperbenzoic acid. After purification by preparative TLC eluting with chloroform (R_f 0.2), 2.10 mg (85%) of sulfoxide was obtained: ir (CCl_4) 1724 cm^{-1}; NMR ($CDCl_3$) mixture of diastereomers δ 5.2–5.6 (4 H, m), 4.1–4.4 (2 H, m), 3.52 (1 H, m), 2.75 (2 H, m), 2.63 and 2.60 (3 H, 2 singlets, 2:1), 1.7–2.3 (4 H, br m), 0.7–1.7 (22 H, m).

Following method B for eliminations ($PhCH_3$, $CaCO_3$, 110 °C, 24 h), the above sulfoxide generated after TLC purification eluting with chloroform 140 mg (81%) of product whose structure was confirmed by comparison of its properties to those reported in the literature.[58]

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