influence of substituents on k_r/k_s in TFE indicates identical transition states for both reactions in that solvent.

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Synthesis of β-Acylacrylic Esters and α,β-Butenolides via β-Keto Sulfoxide Alkylation

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Abstract: Alkylation of the anions derived from (methylsulfinyl)methyl ketones (**1**) with methyl bromoacetate proceeds readily to afford the 3-(methylsulfinyl)-4-oxobutanoates (**2**). These intermediates are converted to the corresponding unsaturated keto esters (**3**) in excellent overall yield (Table I) by thermal elimination of methylsulfenic acid. Alternatively, the γ-substituted-α,β-butenolides (**5**) are obtained on sodium borohydride reduction of the alkylated intermediates (**2**), followed by lactonization and loss of CH_3SOH. These sequences have been applied to aliphatic and aromatic β-keto sulfoxides and used to prepare the isocardenolide 3β-acetoxy-20-hydroxy-21-nor-5,22-choladien-24-oic acid γ-lactone in excellent yield. The relative configurations of the diastereomeric intermediates **2** have been deduced from their thermal stabilities, and the absolute configurations of the diastereomeric steroidal sulfoxides **1c** have been determined from their circular dichroism spectra.

We have embarked on a program directed toward the synthesis of medium- and large-ring natural products. Several of these compounds incorporate a γ-oxidized α,β-unsaturated lactone moiety,[1] and we sought an efficient method for the construction of this functional array. While a variety of methods are available for the synthesis of β-acylacrylic esters,[2] none appeared to meet our needs of simplicity and efficiency. Many routes involve condensation steps which are capricious or low-yield reactions, or which require relatively inaccessible starting materials. The most generally efficient synthesis of β-acylacrylates is that of Bestmann,[2d] using an alkylation–elimination sequence involving stabilized phosphoranes. This method, however, requires relatively vigorous conditions and a twofold excess of the ylide component.

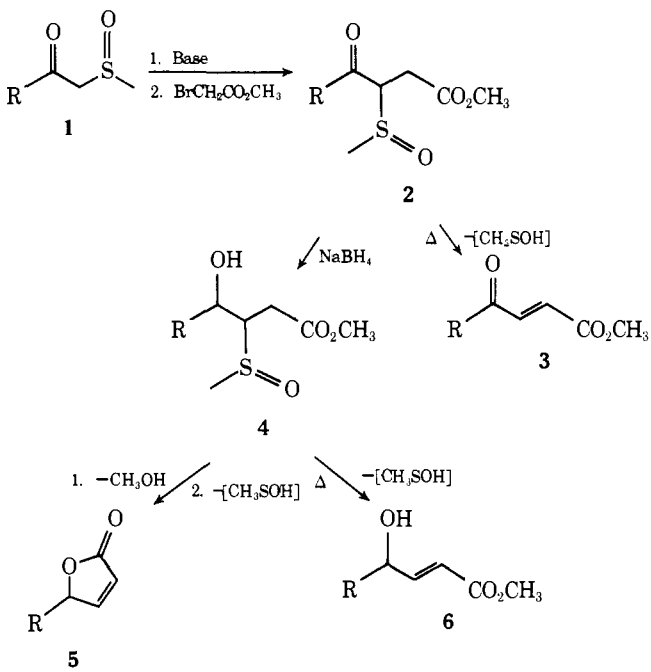
The sulfinyl group has received attention in organic synthesis by virtue of its ability to stabilize carbanions[3] and to function as an alkene precursor.[3f-1,4] The anions derived from α-sulfinyl ketones and esters may be alkylated under favorable conditions,[3] and, on heating, sulfoxides with hydrogens in the β position which can adopt a syn conformation readily eliminate a sulfenic acid with introduction of a double bond.[3f-1,4] Trost has recently taken advantage of these properties for the synthesis of α,β-unsaturated esters[3i,k] and other conjugated alkenes.[3j] α-Sulfinyl carbonyl compounds are accessible by a variety of methods, including oxidation of the corresponding sulfides,[3f,4] enolate sulfinylation,[5a,b] and sulfinyl anion acylation.[3b,5c-e] In view of the ready availability of β-keto sulfoxides from the corresponding carboxylic esters,[3b,5c-e] the pos-

sibility of their conversion to α,β-unsaturated ketones via an alkylation–elimination sequence was attractive. We have investigated this route for the synthesis of β-acylacrylates, as shown in Scheme I. Additionally, it was anticipated that the intermediates in this sequence would prove to be versatile precursors to γ-substituted-α,β-butenolides and γ-hydroxycrotonic acid derivatives, if reduction of the ketonic carbonyl were effected prior to elimination.

α,β-Butenolides have been synthesized in a variety of ways,[6] and several syntheses based on the thermal fragmentation of α-seleninyl- and α-sulfinyl-γ-butyrolactones have been reported.[3g-k,4a,6b-d] However, the conversion of a carboxyl carbon into the γ-carbon of a butenolide has not been straightforward, in spite of the simplicity of this functional group. In addition, such a sequence, in combination with the reduction of butenolides to furan derivatives,[6c,7] would enable the elaboration of a carboxyl group into an α-furyl substituent.

The application of these transformations (Scheme I) to a

Scheme I



1 2 3 4 5 6

a, R = cyclohexyl
b, R = 10-acetoxydecyl
c, R = 3β-acetoxyandrost-5-en-17β-yl
d, R = *p*-methoxyphenyl
e, R = *p*-bromophenyl

variety of aliphatic and aromatic β-keto sulfoxides constitutes the subject of this report.

Synthesis of β-Keto Sulfoxides. The β-keto sulfoxides used for this study (**1a–1e**) were prepared from the corresponding methyl esters using the method of Corey,[5d] with the minor modification that potassium hydride was used for the generation of dimsyl anion in a THF–Me_2SO mixture. This is procedurally simpler, since the reaction is rapid at room temperature, and it also allows a reduction in the proportion of Me_2SO to substrate in the acylation reaction, thereby facilitating purification of the often significantly water-soluble product.[5d]

The acetoxy derivatives **1b** and **1c** were prepared by condensation of dimsyl anion with appropriate hydroxy esters, followed by esterification of the hydroxy keto sulfoxides with acetic anhydride in pyridine. The steroidal derivative **1** (R = 3β-hydroxyandrost-5-en-17β-yl) was isolated as a mixture of diastereomers which were readily separable by recrystallization. The stereochemistry of these compounds will be discussed below.

Alkylation of β-Keto Sulfoxides with Methyl Bromoacetate. Alkylation of carbonyl-stabilized sulfoxide anions with alkyl halides is often plagued by the low reactivity of these anions and the low solubility of their alkali metal salts in ethereal solvents.[3a-c] With the highly reactive methyl bromoacetate, no difficulty was encountered in the alkylation of the potassium salts of the β-keto sulfoxides **1a–1e,** and the reactions were typically complete within a few hours at 0° in THF solvent. Although no rigorous comparisons were made, it was soon clear that the potassium salts are alkylated significantly more rapidly than are the sodium salts; consequently, potassium hydride was used throughout for the preparation of the stabilized carbanions. Only in the case of ω-methylsulfinyl-*p*-bromoacetophenone was any difficulty encountered with the solubility of the salt. In this case HMPA (10% v/v) was added to the reaction mixture to facilitate the alkylation.

Each of the alkylation products **2a–e** was obtained as a mixture of diastereomers, readily distinguishable by NMR and, in some cases, by TLC. Since both chiral centers of **2** are lost in subsequent transformations, no attempt was made to purify the crude alkylation products and separate the isomers when material was to be carried on in subsequent reactions. For this reason, yields reported below for the sulfur-free products (**3, 5,** and **6**) are based on the β-keto sulfoxide **1** as starting material.

Fragmentation of Alkylated Intermediates: Synthesis of β-Acylacrylates. Formation of the β-acylacrylates **3a–e** via thermal elimination of methylsulfenic acid from the crude alkylated intermediates **2a–e** was accomplished in two ways: simple bulb-to-bulb distillation at reduced pressure or, more generally, by refluxing in dioxane solution for 1 h, followed by washing with aqueous alkali (Table I). For those reactions carried out in refluxing dioxane, an equivalent of methyl bromoacetate and excess sodium bicarbonate were included in the reaction mixture. In the absence of these reagents, the products were isolated in a lower state of purity, although the nature of the malodorous contaminant was not determined. It was envisaged that this combination would be an effective scavenger for methylsulfenic acid[8] via alkylation to give the alkali-soluble methyl methylsulfinylacetate.

As indicated in Table I, all the β-acylacrylates **3** were isolated directly from the reaction in excellent overall yield from the β-keto sulfoxides **1.** In every instance the more stable *E* isomer was obtained; there was no evidence for the *Z* isomers in the NMR spectra of the products. In view of the availability of carboxylic esters and the ease with which this reaction sequence can be carried out, it constitutes a very efficient and practical synthesis of β-acylacrylates.

Reduction of Alkylated Intermediates: Synthesis of α,β-Butenolides. A. Aliphatic Derivatives. Reduction of the aliphatic alkylated intermediates **2a–c** with sodium borohydride (1 mol/mol) in cold methanol, followed by dilution of the reaction mixture with ethyl acetate and washing with aqueous alkali, afforded the corresponding α,β-butenolides **5a–c** directly, again in high overall yield (Table I). Of particular interest is the synthesis of the isocardenolide **5c,** previously available in less than 35% yield from 3β-acetoxy-21-iodopregn-5-en-20-one.[6g]

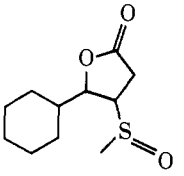
The direct isolation of the unsaturated lactones in lieu of the sulfoxide precursors was not unexpected. Lactonization of the initially formed hydroxy ester **4** affords an intermediate in which the methylsulfinyl substituent and a hydrogen atom β to it are held in an eclipsed relationship, ideally disposed for concerted elimination. Further experiments, however, have modified our view of the actual mechanism. When the reduction of **2a** (mixture of isomers) was carried out under nonalkaline conditions, namely with 1% acetic acid/methanol as solvent and saturated ammonium chloride instead of alkali as the aqueous wash, no α,β-butenolide was formed. However,

Table I. Conversion of **2** to β-Acylacrylates **3** and α,β-Butenolides **5**

R–	% yield of 3[a,b]	Yield of 5[a,b]
Cyclohexyl	96 (A)	94 (C)
10-Acetoxydecyl	98 (B)	82 (C)
3β-Acetoxyandrost-5-en-17β-yl	99 (B)	95 (C)
p-Methoxyphenyl	96 (A)	81 (D)
p-Bromophenyl	85 (B)	33 (D) 37[c] (C)

[a] Isolated yield overall from β-ketosulfoxide. [b] Method of conversion: A, bulb-to-bulb distillation (175°/0.1 mm); B, $NaHCO_3$ and $BrCH_2CO_2CH_3$ in refluxing dioxane; C, $NaBH_4$/methanol with 2 N NaOH workup; D, $NaBH_4$/methanol with 5% Na_2CO_3 workup. [c] Yield of β,γ-isomer.

the ir spectrum indicated that a significant amount of saturated lactone (ν_{CO} 1780 cm^{-1}) was present in the crude product. From this mixture, a crystalline compound was isolated and shown to be the β-sulfinylbutyrolactone **7** (ir ($CDCl_3$) 1780 (C=O), 1055 cm^{-1} (S=O), no O-H; NMR ($CDCl_3$) δ 2.54 (s, 3 H, SCH_3), 4.5 (br t, 1 H, J = 5 Hz, H_γ)). This material was surprisingly stable in comparison with the keto ester **2a**, undergoing less than 50% fragmentation to the α,β-butenolide **5a** after 1 h at 70° in $CDCl_3$, conditions which converted both diastereomers of **2a** almost completely to the β-acylacrylate **3a**. The lactone **7** also underwent elimination to the α,β-butenolide when subjected to the routine reduction conditions and workup, or simply on dissolution in ethyl acetate and washing with aqueous alkali.



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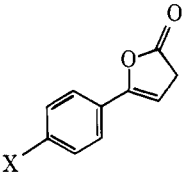
When the reduction was carried out in pure methanol and worked up with a saturated ammonium chloride solution, the product was still predominantly the butenolide **5a**, indicating that the elimination is not solely due to an alkaline workup. The fact that no butenolide is formed in the absence of alkali, even under conditions in which the lactones are formed, implies that the elimination observed in the synthesis of the α,β-butenolides **5a–c** is not a thermal fragmentation. In further support of the conclusion that the elimination is base-catalyzed and occurs under the very mildly alkaline conditions of borohydride in cold methanol is the fact that the lactone **7** was converted to the α,β-butenolide **5a** when subjected to these conditions for 10 min and worked up with saturated NH_4Cl.

B. Aromatic Derivatives. Although reduction of the aliphatic compounds **2a–c** followed by alkaline workup afforded excellent yields of the α,β-butenolides, when the aromatic derivatives **2d** and **2e** were treated in the same way, only small amounts of impure products were isolated. The essential difference between the two series of compounds was shown to be the ease with which the hydroxy esters **4** lactonize under the conditions of the reduction. Whereas reduction of **2a** in pure methanol at 0° (nonalkaline workup) afforded almost entirely the α,β-butenolide **5a**, compounds **2d** and **2e** gave only the hydroxy esters **4d** and **4e** (ir ($CHCl_3$) 3300 (O-H), 1735–1740 cm^{-1} (C=O)) under the same conditions. Bulb-to-bulb distillation (175° (0.1 mm)) of these compounds effected elimination of methylsulfenic acid without lactonization and afforded the allylic alcohols **6d** and **6e** in 80 and 90% yield, respectively, based on β-keto sulfoxides **1d** and **1e**.

When solutions of the hydroxy esters **4d** and **4e** in ethyl acetate or ether were washed with 2 N sodium hydroxide, they lactonized with loss of methylsulfenic acid and formation of the α,β-butenolides. However, because of the enhanced acidity of these butenolides due to the aryl substitution, extensive isomerization and hydrolysis occurred under the alkaline conditions. Identified by NMR were the α,β- and β,γ-butenolides **8**, the ketones **9**, and the allylic alcohols **6** (R = aryl).



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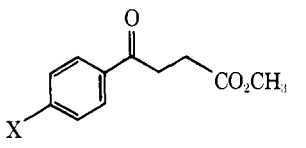

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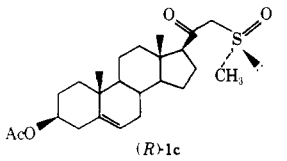
From the bromo derivative, the β,γ-butenolide **8** (X = Br) was isolated in 37% yield after bulb-to-bulb distillation. When 5% sodium carbonate was used instead, reextraction of the methoxyarylbutenolide **5d** into the organic phase competed favorably with isomerization, and a good yield of this previously unknown material (see below) was isolated after bulb-to-bulb distillation. A similar workup applied to the bromo derivative **4e** was less successful, and only a poor yield of the α,β-butenolide was obtained after column chromatography.

Attempts to generate the bromoarylbutenolide **5e** from the hydroxy ester under homogeneous conditions more alkaline than sodium borohydride in methanol (e.g., triethylamine in methanol or acetonitrile) were also unsuccessful, for the only products identified by NMR were the ketone **9** (X = Br) and the allylic alcohol **6** (R = p-BrC_6H_4). The allylic alcohol was stable under these conditions, demonstrating that the ketone arose by methanolysis of the β,γ-butenolide. Apparently the bromoaryl substituent facilitates base-catalyzed isomerization and hydrolysis reactions of the α,β-butenolide to such an extent that conditions sufficiently alkaline to generate the lactone result in its rapid destruction. Although the less electron-withdrawing methoxyaryl group also facilitates base-catalyzed side reactions, it does so to a lesser extent and the α,β-butenolide can be generated in good yield.

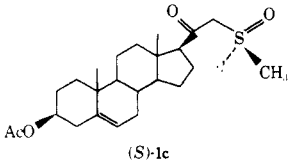
For monosubstituted butenolides of the general formula **5**, the position of the double bond equilibrium favors the conjugated α,β isomer when R = alkyl.[6a] When R = aryl, the situation is reversed: the only previously reported γ-aryl-α,β-butenolide, the phenyl derivative **5** (R = C_6H_5), isomerizes readily to the β,γ isomer **8** (X = H) in the presence of acid or base.[9] The α,β-butenolide structure **5d** has been assigned to the high-melting (184 °C) product obtained on treatment of the β,γ isomer **8** (X = CH_3O) with hot *tert*-butylamine.[10] This assignment is incorrect, for we have fully characterized the α,β-butenolide **5d** (mp 56.5–58 °C; ir ($CHCl_3$) 1793, 1758 cm^{-1} (α,β-butenolide[11]); NMR ($CDCl_3$) δ 7.5 (dd, 1 H, J = 2 and 6 Hz, H_β), 6.2 (dd, 1 H, J = 2 and 6 Hz, H_α), 5.95 (t, 1 H, J = 2 Hz, H_γ)) and shown that it rearranges rapidly to the β,γ isomer[13] in chloroform at 25° with triethylamine as catalyst.

Stereochemistry of Diastereomeric Intermediates. A. Absolute Configuration of 1c. As noted above, the steroidal β-keto sulfoxides **1c** (HO- instead of AcO-) were formed as a mixture of diastereomers by virtue of the asymmetric steroid nucleus. Although one isomer (mp 167–168 °C) was obtained in pure form by recrystallization of the mixture from ethyl acetate or methanol, a satisfactory solvent was not found for recrystallization of the more soluble diastereomer (mp 145–149 °C). Therefore, both isomers were converted to their more readily purified acetates for spectroscopic comparison. The distinctive AB quartet patterns of the C-20 methylene protons in the NMR spectrum of each isomer were unaltered by this treatment, indicating that no epimerization had taken place during the acetylation reactions. The relevant NMR and circular dichroism data for the two isomers are presented in Table II.

Table II. Spectroscopic Comparison of the Diastereomeric Steroidal Sulfoxides 1c



(R)-1c



(S)-1c

Mp, °C	175.5–176	153–154°
(Mp: HO– instead of AcO–)	(167–168)	(145–149°)[a]
NMR ($CHCl_3$),	3.69, 3.79	3.61, 3.93
δ $COCH_2SO$, ppm	(J = 15 Hz)	(J = 14 Hz)
CD (MeOH), λ_{nm} ([θ])[b]	215 (–2 000)	215 (7 000)
	224 (–10 200)	224 (10 400)
	254 (0)	254 (2 400)
	294 (14 800)	294 (13 000)

[a] Contaminated with approximately 10% of the other diastereomer. [b] Deg cm²/dmol.

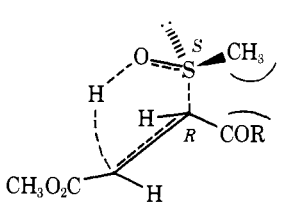
It is quite clear from the CD spectra that the isomers differ only in their configuration at the sulfur atom. A positive Cotton effect centered near the weak n → π* ketone absorption band around 300 nm is characteristic of 17β-acyl steroids[14] and present in both compounds, indicating that the carbonyl groups are subject to similar asymmetric perturbation. A comparable band, at slightly shorter wavelength, is present in the CD spectrum of pregnenolone acetate ($[\theta]_{MeOH}$ = 13 700 at 286 nm). At shorter wavelengths, near the n → π* sulfoxide absorption band around 225 nm, the two diastereomers display opposite Cotton effects, reflecting their epimeric relationship at sulfur. Pregnenolone acetate shows no circular dichroism in this region.

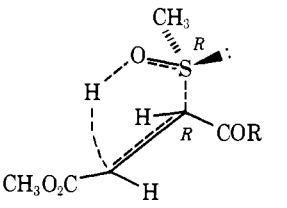
For dialkyl sulfoxides, Mislow and Jones have shown that a negative Cotton effect for the short wavelength, n → π* sulfoxide transition in the optical rotatory dispersion spectrum is indicative of the *R* configuration.[15] This rule is not applicable in cases where a strongly perturbing chromophore or restricted rotation of the sulfinyl moiety relative to an asymmetric substituent is present.[15a,d] That the sulfoxide and ketone absorptions are not strongly coupled in the diastereomers of **1b** is clear from the independence of their circular dichroic bands, and the *R* configuration is assigned to the higher melting isomer because it exhibits a negative Cotton effect for the sulfoxide n → π* absorption.

B. Relative Stereochemistry of the Alkylation Products 2. In the NMR spectra ($CDCl_3$) of the crude alkylation products **2,** separate resonances could be discerned for the methine protons and the *S*-methyl protons of the two diastereomers, which were present in comparable amounts in each instance. Chemical shift differences for the methine protons ranged from 0.15 to 0.28 ppm, and for the *S*-methyl resonances from 0.07 to 0.14 ppm. With the exception of the methoxyaryl derivative **2d,** which was not obtained in crystalline form, crystallization afforded a single diastereomer from each of the alkylation products. This diastereomer, designated isomer A, in each case proved to be that with the downfield *S*-methyl resonance and the upfield methine resonance.

The thermal fragmentation of these isomers was readily followed by NMR, for the reaction proceeded at a convenient rate at 70° in chloroform. Two points bear consideration. First, in each case the crystalline diastereomer, isomer A, underwent elimination at a significantly faster rate than did isomer B. For instance, a mixture of the two diastereomers of **2a** (ratio of A/B = 2.3) was heated in $CDCl_3$ at 70° for 10 min., at which point only 25 ± 5% of isomer A and 90 ± 5% of isomer B remained (ratio of A/B = 0.7). The isomers are interconverted to a small extent (less than 5%) during the course of the reaction, presumably via readdition of methylsulfenic acid to the alkene.[16] Because the interconversion of these diastereomers is slow compared to fragmentation, their rates of disappearance reflect primarily the ease with which they decompose to the β-acylacrylates.

In the transition state for cyclic elimination,[17] illustrated below for one enantiomer of each diastereomer of **2,** the *R,S*

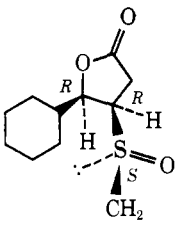




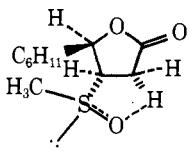
isomer experiences a significant eclipsing interaction between the *S*-methyl and the acyl group, an interaction which destabilizes this transition state and impedes the elimination reaction. Therefore the (*R,R*)-(*S,S*) stereochemistry is assigned to the more thermally labile diastereomer A. The rates of thermal elimination of amine oxides[18] and of other sulfoxides[17a,19] show a similar dependence on relative configurations and eclipsing interactions. In a similar study, Kingsbury and Cram[17a] showed that the diastereomeric 2-methylsulfinyl-3-phenylbutanes underwent stereospecific syn elimination at differing rates. They assigned the configuration at the sulfur atom by considering the stability of the most favored ground state conformations.

Second, the only olefins observed from the fragmentations of **2a–e** have the *E* geometry; none of the *Z* isomers were detected by NMR at any stage in the elimination. However, although it is a reasonable assumption that the *E* isomer is the initially formed product, this could not be shown conclusively because isomerization of the *Z* isomer is more rapid than thermal fragmentation of **2** under the conditions of the elimination. A sample of methyl (*E*)-4-cyclohexyl-4-oxo-2-butenoate (**3a**) was irradiated in an NMR tube in $CDCl_3$ with a medium-pressure mercury arc lamp until conversion to the *Z* isomer was essentially complete (>95%). This material isomerized back to the *E* isomer with a half-life on the order of 8 min in $CDCl_3$ at 70°. However, when a portion of the *Z* isomer was added to a mixture of the diastereomers of **2a,** and heated at 70° for 15 min in $CDCl_3$, none of the *Z* isomer was detected by NMR, although a significant amount of **2a** remained.

C. Tentative Assignment of the Relative Stereochemistry of Lactone 7. The lactone isolated from reduction of **2a** in acidic methanol is presumably only one of four diastereomeric *dl* pairs with the covalent structure indicated by **7.** A sharp melting point is observed, as well as a single sharp resonance for the *S*-methyl protons in the NMR. In view of the thermal stability of this compound mentioned above, it is attractive to assign the relative stereochemistry as depicted in **7a.** In the transition state (**10**) for concerted syn elimination of methyl-



7a



10

sulfenic acid from **7a**, a severe steric crowding between the cyclohexyl and the *S*-methyl groups would occur. We were initially reluctant to make this assignment because the lactone **7** can be obtained by reduction of a pure sample of isomer A of **2a**, to which we have assigned the (*R,R*)-(*S,S*) configuration. However, starting material isolated after incomplete reduction of **2a** (isomer A) in acidic methanol at 0° consisted of comparable amounts of both diastereomers. This indicates that isomerization took place under these conditions and removes any correlation between the relative stereochemistries of **7** and the starting keto sulfoxide **2a**.

One would expect the diastereomer with the opposite configuration at sulfur to eliminate far more readily than **7a** because of the much smaller steric demand of the sulfur lone-pair electrons. Similar arguments apply for the diastereomers with the trans disposition of substituents about the lactone ring, although in this case the dichotomy between the sulfoxide epimers would be greatly reduced. Unfortunately, the conformational ambiguity of five-membered rings in general precludes stereochemical assignments based on vicinal coupling constants[20] in the systems at hand, and, in the absence of other diastereomers for direct comparison, the assignment of structure **7a** must remain tentative.

Experimental Section[21]

Unless otherwise indicated, the organic layer in the workup of each reaction was ultimately washed with saturated NaCl, dried over $MgSO_4$, and filtered, and the product was obtained by removal of the solvent at room temperature, first at aspirator pressure and finally at 0.1 mm. Distillations were evaporative bulb-to-bulb distillations, using a Büchi Kugelrohrofen at the pressure and oven temperature indicated.

Methyl 4-Cyclohexyl-3-methylsulfinyl-4-oxobutanoate (2a). A 5.6-mmol sample of potassium hydride/oil was washed four times with hexane and dried under a stream of dry nitrogen. The hydride was stirred at 25° while 8 ml of THF and 500 mg (2.7 mmol) of cyclohexyl (methylsulfinyl)methyl ketone (**1a**)[5d] were added. After hydrogen evolution ceased, the mixture was cooled to 0° and 0.43 ml (4.6 mmol) of methyl bromoacetate was added. After stirring 5 hr at 0°, the mixture was partitioned between ethyl acetate and saturated NH_4Cl. The aqueous phase was separated and extracted once with ethyl acetate, and the organic layers were combined to give 737 mg of semisolid product (theoretical yield, 691 mg). The product from a similar preparation was recrystallized from ether to give an analytical sample of the (*R,R*)-(*S,S*) isomer: mp 96–97 °C; ir (CCl_4) 1742, 1705 (C=O), 1070 cm^{-1} (S=O); NMR δ 2.48 (s, 3 H, SCH_3), 3.70 (s, 3 H, CH_3O), 4.53 (dd, 1 H, J = 5 and 8.5 Hz, COCHSO). The NMR spectrum of the crude mixture of diastereomers showed resonances at δ 2.42 (s, SCH_3) and 4.72 (dd, J = 5 and 7.5 Hz, COCHSO)) for the other diastereomer.

Anal. ($C_{12}H_{20}O_4S$) C, H, S.

Methyl (*E*)-4-Cyclohexyl-4-oxo-2-butenoate (3a). A 120-mg portion (≤0.43 mmol) of the crude alkylation product (**2a**) described above was distilled (160° (0.01 mm)) to give 82 mg (0.42 mmol, 96% yield) of the unsaturated keto ester **3a**: mp 53–56 °C; ir ($CHCl_3$) 1695, 1665 (C=O), 1600 cm^{-1} (C=C); NMR δ 3.83 (s, 3 H, CH_3O), 6.67 and 7.17 (ABq, 2 H, J = 15.5 Hz, CH=CH). After recrystallization from hexane, mp 57–58 °C (lit.[2d] mp 56–57 °C).

5-Cyclohexyl-2(5*H*)-furanone (5a). A slurry of 177 mg (≤0.64 mmol) of the crude alkylation product (**2a**) described above in 1.5 ml of methanol was stirred at 0°, while 26 mg (0.69 mmol) of sodium borohydride was added. After 10 min the mixture was diluted with ether and washed twice with 2 N NaOH to give 100 mg (0.60 mmol, 94% yield) of the α,β-butenolide, **5a**, mp 72–73 °C. Recrystallization from isopropyl ether afforded an analytical sample: mp 73.5–75 °C; ir ($CHCl_3$) 1755 cm^{-1} (C=O); NMR δ 4.9 (m, 1 H, H_γ), 6.01 (dd, 1 H, $J_{\alpha,\beta}$ = 6.0 Hz, $J_{\alpha\gamma}$ = 2.2 Hz, H_α), 7.44 (dd, 1 H, $J_{\alpha\beta}$ = 6.0 Hz, $J_{\beta\gamma}$ = 1.5 Hz, H_β).

Anal. ($C_{10}H_{14}O_2$) C, H.

5-Cyclohexyl-4-methylsulfinyl-3,4-dihydro-2(5*H*)-furanone (7). A solution of 0.49 mmol of the crude alkylation product (**2a**) in 1.5 ml of methanol and 15 μl of acetic acid was stirred at 0°, and 37 mg (0.97 mmol) of sodium borohydride was added slowly. After 0.5 h, the mixture was diluted with ethyl acetate and washed with saturated NH_4Cl to give 110 mg of semisolid product. This material was triturated with cold ether to give 21 mg (19% yield) of **7** as a white solid, mp 101–102 °C after recrystallization from ether: ir ($CDCl_3$) 1780 (C=O), 1055 cm^{-1} (S=O); NMR δ 2.52 (s, 3 H, SCH_3), 4.50 (br t, 2 H, J = 5 Hz, >CHO—).

Anal. ($C_{11}H_{18}O_3S$) C, H, S.

12-Hydroxy-1-methylsulfinyl-2-dodecanone (1, R = $HO(CH_2)_{10}$). A 22.4-mmol sample of potassium hydride/oil was washed three times with hexane, dried under a stream of dry nitrogen, and stirred in 10 ml of THF at 25° while 4 ml of Me_2SO was added. After hydrogen evolution ceased, another 10 ml of THF and 1.5 ml of Me_2SO were added, and the solution was cooled to 0° with stirring. To this solution was added 1.21 g (5.6 mmol) of methyl 11-hydroxyundecanoate in 7 ml of THF, and the mixture was allowed to warm to 25°. After 2 h, the reaction was quenched with acetic acid and the mixture was concentrated at reduced pressure. The residue was diluted with ethyl acetate and washed with water and saturated $NaHCO_3$ to give 1.15 g (78% yield) of the β-keto sulfoxide as a white solid. Recrystallization from ether afforded an analytical sample: mp 84–86 °C; ir ($CHCl_3$) 3450, 3625 (OH), 1715 (C=O), 1020 (S=O); NMR δ 1.33 (broad, 16 H, $-(CH_2)_8-$), 2.35 (s, 1 H, OH), 2.61 (t, 2 H, J = 6.5 Hz, CH_2C=O), 2.73 (s, 3 H, SCH_3), 3.62 (br t, 2 H, OCH_2), 3.82 (s, 2 H, $COCH_2SO$).

Anal. ($C_{13}H_{20}O_3S$) C, H, S.

12-Acetoxy-1-methylsulfinyl-2-dodecanone (1b). A 1.11-g sample (4.2 mmol) of the alcohol **1** (R = $HO(CH_2)_{10}$) and 0.8 ml of acetic anhydride were dissolved in pyridine and kept at 25° for 24 h. The mixture was diluted with ethyl acetate and washed twice each with 2 N HCl and saturated $NaHCO_3$ to give 1.23 g (96% yield) of the acetate **1b** as a cream-colored solid. Recrystallization from isopropyl ether afforded an analytical sample: mp 63–63.5 °C; ir ($CHCl_3$) 1725 (C=O), 1040 cm^{-1} (S=O); NMR δ 1.3 (br, 16 H, $-(CH_2)_8-$), 2.0 (s, 3 H, CH_3CO_2), 2.58 (t, 2 H, J = 6.5 Hz, CH_2C=O), 2.63 (s, 3 H, SCH_3), 3.80 (br s, 2 H, $COCH_2SO$), 4.03 (br t, 2 H, OCH_2).

Anal. ($C_{15}H_{28}O_4S$) C, H, S.

Methyl 14-Acetoxy-3-methylsulfinyl-4-oxotetradecanoate (2b). To a stirred suspension of 2.9 mmol of potassium hydride in 3 ml of THF under nitrogen at 25° was added 460 mg (1.4 mmol) of the β-keto sulfoxide (**1b**). After hydrogen evolution ceased, the mixture was cooled to 0° and 0.2 ml (2.1 mmol) of methyl bromoacetate was added. After 1 h, the viscous slurry was partitioned between ethyl acetate and saturated $NaHCO_3$. The aqueous phase was separated and extracted once with ethyl acetate, and the organic phases were combined to give 535 mg of semisolid product (theoretical yield, 508 mg). The analytical sample was obtained by recrystallization from ether: mp 79–80 °C; ir ($CHCl_3$) 1730 (C=O), 1060 cm^{-1} (S=O); NMR δ 1.31 (br, 16 H $-(CH_2)_8-$), 2.04 (s, 3 H, CH_3CO_2), 2.49 (s, 3 H, SCH_3), 2.6–3.0 (m, 2 H, CH_2CO_2), 3.71 (s, 3 H, CH_3O), 4.07 (t, 3 H, J = 6.5 Hz, OCH_2), 4.32 (dd, 2 H, J = 4.5 and 8.5 Hz, COCHSO). The NMR spectrum of the crude mixture of diastereomers showed resonances at δ 2.47 (s, SCH_3) and 4.40 (dd, J = 4.5 and 7 Hz, COCHSO) for the other isomer.

Anal. ($C_{18}H_{32}O_6S$) C, H, S.

Methyl (*E*)-14-Acetoxy-4-oxo-2-tetradecenoate (3b). A mixture of 161 mg (≤0.41 mmol) of the crude alkylation product **2b** described above, 80 mg (0.95 mmol) of sodium bicarbonate, 40 μl (0.43 mmol) of methyl bromoacetate, and 1.5 ml of dioxane was stirred at reflux for 1 h. The mixture was diluted with ether and washed twice with dilute potassium hydroxide and with water to give 127 mg (0.41 mmol, 98% yield) of the unsaturated ester, mp 56–60 °C. An analytical sample was obtained by recrystallization from hexane: mp 65–66 °C; ir (CCl_4) 1740, 1707 (C=O), 1650 cm^{-1} (w, C=C); NMR δ 1.3 (br, 16 H, $-(CH_2)_8-$), 2.02 (s, 3 H, CH_3CO_2), 2.67 (br t, 2 H, CH_2C=O), 3.83 (s, 3 H, CH_3O), 4.10 (br t, 2 H, J = 6 Hz, OCH_2), 6.73, 7.13

(ABq, 2 H, J = 15.5 Hz, CH=CH).

Anal. ($C_{17}H_{28}O_5$) C, H.

5-(10-Acetoxydecyl)-2(5*H*)-furanone (5b). A 187-mg sample (≤0.47 mmol) of the crude alkylation product **2b** described above was dissolved in 2 ml of methanol and stirred at 0° with 19 mg (0.5 mmol) of sodium borohydride. After 20 min, the mixture was diluted with ethyl acetate and washed twice with dilute KOH to give 139 mg of semisolid product. Distillation (175° (0.3 mm)) gave 111 mg (0.39 mmol, 82% yield) of the butenolide **5b**, mp 25 °C. This material was recrystallized from hexane/isopropyl ether to give an analytical sample: mp 32.5–33.5 °C; ir ($CHCl_3$) 1750 cm^{-1} (C=O); NMR δ 1.3 (br, 16 H, $-(CH_2)_8-$), 2.05 (s, 3 H, CH_3CO_2), 4.10 (br t, 2 H, OCH_2), 5.1 (m, 1 H, H_γ), 6.14 (dd, 1 H, J = 2 and 6 Hz, H_α), 7.57 (dd, 1 H, J = 1.5 and 6 Hz, H_β).

Anal. ($C_{16}H_{26}O_4$) C, H.

3β-Hydroxy-20-methylsulfinylpregn-5-en-20-one. A solution of 3.32 g (10 mmol) of methyl 3β-hydroxyetienate[22] in 30 ml of THF was added slowly to a vigorously stirred solution of dimsylpotassium prepared from 35 mmol of potassium hydride, 30 ml of THF, and 18 ml of Me_2SO. After 0.5 h, the gray-green slurry was poured into water and neutralized with solid NH_4Cl, and the aqueous suspension was extracted twice with methylene chloride. The combined organic layers were washed with water to give a crude product which was recrystallized from 150 ml of ethyl acetate, yielding 1.86 g of the *R* diastereomer, mp 167–168 °C. Recrystallization from methanol afforded an analytical sample: mp 171–172 °C; $[\alpha]^{25}D$ 83° (c 0.019); ir ($CHCl_3$) 3600, 3400 (OH), 1710 (C=O), 1050 cm^{-1} (S=O); NMR δ 0.69 (s, 3 H, 18-CH_3), 1.01 (s, 3 H, 19-CH_3), 2.1 (s, 1 H, OH), 2.71 (s, 3 H, SCH_3), 3.75 and 3.85 (ABq, 2 H, J = 15 Hz, $COCH_2SO$), 5.2 (m, 1 H, vinyl H).

Anal. ($C_{22}H_{34}O_3S$) C, H, S.

On concentration of the mother liquor and crystallization from 10 ml of methanol, a further 300 mg of the *R* diastereomer was obtained (total yield, 57%). The mother liquor residue from this recrystallization (1.5 g (40% crude yield), mp 145–149 °C; $[\alpha]^{25}D$ 45° (c 0.019)) was predominantly the *S* diastereomer as determined by NMR: δ 0.66 (s, 3 H, 18-CH_3), 1.01 (s, 3 H, 19-CH_3), 2.72 (s, 3 H, SCH_3), 3.69 and 3.99 (ABq, 2 H, J = 14 Hz, $COCH_2SO$), 5.2 (m, 1 H, vinyl H).

S-(*R*)-3β-Acetoxy-20-methylsulfinylpregn-5-en-20-one. A solution of 1.14 g (3.0 mmol) of the *R* isomer and 0.65 ml (7 mmol) of acetic anhydride in 10 ml of pyridine was kept at 25° for 18 h, then poured into water and extracted with ethyl acetate. The organic layer was washed with water, saturated $NaHCO_3$, and 2 N H_2SO_4 to give 1.23 g (97% yield) of (*R*)-**1c.** Recrystallization from ethanol afforded an analytical sample: mp 176.5–177 °C; $[\alpha]^{25}D$ 72° (c 0.031); ir ($CHCl_3$) 1720, 1710 (C=O), 1250 (C-O), 1040 cm^{-1} (S=O); NMR δ 0.67 (s, 3 H, 18-CH_3), 1.00 (s, 3 H, 19-CH_3), 1.99 (s, 3 H, CH_3CO_2), 2.64 (s, 3 H, SCH_3), 3.69 and 3.79 (ABq, 2 H, J = 15 Hz, $COCH_2SO$); ORD (MeOH) λ_{nm}([θ]deg cm^2/dmol): 215 (−2000), 224 (−10 200), 254 (0), 294 (14 800).

Anal. ($C_{24}H_{36}O_4S$) C, H, S.

S-(*S*)-3β-Acetoxy-20-methylsulfinylpregn-5-en-20-one. A sample of the crude *S* isomer described above was acetylated in a similar manner to afford (*S*)-**1c,** mp 153–154 °C after recrystallization from methanol: $[\alpha]^{25}D$ 38° (c 0.029); NMR δ 0.66 (s, 3 H, 18-CH_3), 1.00 (s, 3 H, 19-CH_3), 1.99 (s, 3 H, CH_3CO_2), 2.66 (s, 3 H, SCH_3), 3.61 and 3.93 (ABq, 2 H, J = 14 Hz, $COCH_2SO$); ORD (MeOH) λ_{nm} ([θ] deg cm^2/dmol); 215 (7000), 224 (10 400), 254 (2400), 294 (13 000).

Anal. ($C_{24}H_{36}O_4S{\cdot}CH_3OH$) C, H, S.

Methyl 3β-Acetoxy-22-methylsulfinyl-20-oxo-21-norchol-5-en-24-oate (2d). To a stirred suspension of 1.5 mmol of potassium hydride in 3 ml of THF under nitrogen at 25° was added 300 mg (0.71 mmol) of (*R*)-**1d** and 2 ml of THF. After hydrogen evolution had ceased, the solution was cooled in an ice bath and 83 μl (1.1 mmol) of methyl bromoacetate was added. After 2 h, the thick slurry was poured into a rapidly stirred mixture of ethyl acetate and saturated NH_4Cl, and the organic layer was separated to give 367 mg (theoretical yield, 350 mg) of semicrystalline material. An analytical sample was obtained by recrystallization from methanol: mp 89–91 °C; ir ($CHCl_3$) 1725 (C=O), 1695 (shoulder), 1250 (CO), 1050 cm^{-1} (S=O); NMR δ 0.66 (s, 3 H, 18-CH_3), 1.00 (s, 3 H, 19-CH_3), 1.99 (s, 3 H, CH_3CO_2), 2.37 (s, 3 H, SCH_3), 3.64 (s, 3 H, CH_3O), 4.34 (dd, 1 H, J = 4 and 9 Hz, COCHSO). The SCH_3 of the diastereomeric product resonates at δ 2.26.

Anal. ($C_{27}H_{40}O_6S$) C, H, S.

Methyl 3β-Acetoxy-20-oxo-21-norchola-5,22(*E*)-dien-24-oate (3c). A mixture of 122 mg (≤0.24 mmol) of the crude alkylation product **2c** described above, 50 mg of sodium bicarbonate, 23 μl (0.25 mmol) of methyl bromoacetate, and 0.5 ml of dioxane was stirred at reflux for 1 h. The mixture was diluted with ethyl acetate and washed twice with 2 N NaOH and with water to give 101 mg (99% yield) of **3c,** mp 154–159 °C. Recrystallization from methanol (75% recovery) gave yellow plates: mp 156–159 °C (lit.[6g] mp 156–158 °C); ir ($CHCl_3$) 1730 (shoulder), 1723, 1694 (C=O), 1640 (w, C=C), 1250 cm^{-1} (C-O); NMR δ 0.60 (s, 3 H, 18-CH_3), 1.02 (s, 3 H, 19-CH_3), 1.99 (s, 3 H, CH_3CO_2), 3.70 (s, 3 H, CH_3O), 6.53 and 7.01 (ABq, 2 H, J = 16 Hz, CH=CH).

3β-Acetoxy-20-hydroxy-21-norchola-5,22-dien-24-oic Acid γ-Lactone (24 → 20) (5c). A solution of 244 mg (≤0.47 mmol) of the crude alkylation product **2c** described above in 2 ml of methanol and 0.4 ml of methylene chloride was stirred at 0° with 20 mg (0.5 mmol) of sodium borohydride for 20 min. At this point, another 20 mg of $NaBH_4$ was added and stirring was continued at 0° for 2 h more. The mixture was diluted with ethyl acetate and washed twice with 2 N NaOH and with saturated NH_4Cl to give 178 mg (95% yield) of the isocardenolide **5c** as a mixture of isomers, mp 217–222 °C (sealed tube). Several recrystallizations from methanol gave colorless plates: mp 227–230 °C (sealed tube) (lit.[6g] mp 225–227 °C); ir ($CHCl_3$) 1795, 1753 (α,β-butenolide), 1727 cm^{-1} (C=O); NMR δ 0.84 (s, 3 H, 18-CH_3), 1.04 (s, 3 H, 19-CH_3), 2.00 (s, 3 H, CH_3CO_2), 5.3 (m, 2 H, CHO and 6-H) 6.03 (dd, 1 H, J = 2 and 5.5 Hz, H_α), 7.44 (dd, 1 H, J = 1.5 and 5.5 Hz, H_β).

Methyl 3-Methylsulfinyl-4-*p*-methoxyphenyl-4-oxobutanoate (2d). To a stirred suspension of 3.1 mmol of potassium hydride in 8 ml of THF under nitrogen at 25° was added 315 mg (1.5 mmol) of ω-methylsulfinyl-*p*-methoxyacetophenone.[5c] After hydrogen evolution had ceased, the mixture was cooled to 0° and 0.21 ml (2.3 mmol) of methyl bromoacetate was added. After 2 h, the slurry was partitioned between ethyl acetate and saturated NH_4Cl, and the phases were separated. The aqueous layer was extracted with ethyl acetate, and the organic layers were combined to give 465 mg (theoretical yield, 422 mg) of crude product as a thick syrup. This material could not be crystallized, and an analytical specimen was not obtained: ir ($CHCl_3$) 1735 (ester C=O), 1660 (ketone C=O), 1600 (aryl), 1050 cm^{-1} (S=O); NMR δ 2.30 and 2.37 (s, 3 H, SCH_3), 3.66 (s, 3 H, CO_2CH_3), 3.87 (s, 3 H, CH_3O-aryl), 5.08 and 5.37 (dd, 1 H, J = 5 and 8 Hz, COCHSO), 6.95 and 8.01 (ABq, 4 H, J = 9 Hz, aryl).

Methyl (*E*)-4-*p*-Methoxyphenyl-4-oxo-2-butenoate (3d). 46 mg (≤0.15 mmol) of the crude alkylation product **2d** described above was distilled (170° (0.1 mm)) to give 31 mg (96% yield) of **3d** as a yellow solid, mp 65–68 °C. Recrystallization from isopropyl ether afforded yellow prisms: mp 69–70 °C (lit.[2d] mp 64–65 °C); ir ($CHCl_3$) 1720 (ester), 1665 (ketone), 1600 cm^{-1} (C=C); NMR δ 3.83 (s, 3 H, CH_3O), 3.88 (s, 3 H, CH_3O), 6.86 and 7.91 (ABq, 2 H, J = 16 Hz, CH=CH), 6.98 and 8.00 (ABq, 2 H, J = 8 Hz, aryl).

Methyl 4-Hydroxy-4-(*p*-methoxyphenyl)-3-methylsulfinylbutanoate (4d). A solution of 1.3 mmol of the crude alkylation product **2d** described above in 4.5 ml of methanol was stirred at 0° with 55 mg (1.4 mmol) of sodium borohydride for 5 min. The mixture was partitioned between ethyl acetate and saturated NH_4Cl, the aqueous phase was separated and extracted with ethyl acetate, and the organic layers were combined to give 359 mg (95% crude yield) of the hydroxy compound **4d** as a colorless syrup. This material was not obtained in crystalline form, and an analytical sample was not prepared: ir (neat) 3300 (OH), 1735 (C=O), 1030 cm^{-1} (S=O); NMR δ 2.48, 2.60, 2.83 (3 H, SCH_3), 3.1 (s, 1 H, OH), 3.63 (s, 3 H, CO_2CH_3), 3.78 (s, 3 H, CH_3O), 4.8–5.6 (m, 1 H, CHO), 7.1 (ABq, 4 H, aryl).

Methyl (*E*)-4-Hydroxy-4-(*p*-methoxyphenyl)-2-butenoate (6d). A 73-mg (≤0.25 mmol) sample of the crude reduction product **4d** described above was distilled (175° (0.1 mm)) to give 48 mg (80% overall) of the unsaturated ester **6d** as a pale yellow oil: ir (neat) 3350 (OH), 1712 (C=O), 1660 cm^{-1} (C=C); NMR δ 2.9 (s, 1 H, OH), 3.68 (s, 3 H, CO_2CH_3), 3.75 (s, 3 H, CH_3O), 5.27 (dd, 1 H, J = 2 and 5 Hz, H_γ), 6.07 (dd, 1 H, J = 2 and 16 Hz, H_α), 6.95 (dd, 1 H, J = 5 and 16 Hz, H_β), 7.0 (ABq, 4 H, aryl). The analytical sample was purified by column chromatography.

Anal. ($C_{12}H_{14}O_3$) C, H.

5-(*p*-Methoxyphenyl)-2(5*H*)-furanone (5d). To a solution of 0.39 mmol of the crude alkylation product **2d,** prepared as described above, in 1.5 ml of methanol at 0° was added 18 mg (0.5 mmol) of sodium borohydride. After 5 min, the mixture was diluted with 10 ml of ethyl

acetate and shaken vigorously for 2 min with two 15-ml portions of 5% sodium carbonate. The aqueous layers were extracted with 10 ml of ethyl acetate, and the organic layers were combined to give 61 mg (81% yield) of **5d** after distillation (170° (0.1 mm)), mp 40–47 °C. Recrystallization from isopropyl ether afforded an analytical sample: mp 56.5–58 °C; ir (neat) 1793, 1758 cm^{-1} (α,β-butenolide[12]); NMR δ 3.79 (s, 3 H, CH_3O), 5.98 (br t, 1 H, J = 2 Hz, H_γ), 6.23 (dd, 1 H, J = 2 and 6 Hz, H_α), 7.07 (ABq, 4 H, aryl), 7.53 (dd, 1 H, J = 2 and 5 Hz, H_β).

Anal. ($C_{11}H_{10}O_3$) C, H.

5-(*p*-Methoxyphenyl)-2(3*H*)-furanone (8d). A sample of the α,β-butenolide **5d** was dissolved in $CDCl_3$ with 2% triethylamine. Within 10 min no resonances were visible in the NMR except those attributable to the β,γ-butenolide. Concentration of the sample and recrystallization from methanol gave material: mp 110–110.5 °C (lit.[13] 110–111 °C); ir ($CHCl_3$) 1800 cm^{-1} (C=O); NMR δ 3.37 (d, 2 H, J = 2.5 Hz, CH_2), 3.83 (s, 3 H, CH_3O), 5.62 (t, 1 H, =CH), 6.93 and 7.53 (ABq, J = 9 Hz, aryl).

Methyl 4-(*p*-Bromophenyl)-3-methylsulfinyl-4-oxobutanoate (2e). To a stirred suspension of 8.1 mmol of potassium hydride in 20 ml of THF at 25° under dry nitrogen was added 1.06 g (4.05 mmol) of ω-(methylsulfinyl)-*p*-bromoacetophenone.[5c] After hydrogen evolution ceased, the slurry was cooled to 0° and 0.57 ml (6.1 mmol) of methyl bromoacetate was added. After 2 h 10 ml of THF and 2 ml of HMPA were added, and stirring was continued for 5 h more. The mixture was diluted with ethyl acetate and washed with saturated $NaHCO_3$ and water to give 1.39 g of semicrystalline material (theoretical yield, 1.35 g). Two recrystallizations from ether afforded an analytical sample of the (*R,R*)-(*S,S*) isomer: mp 99–100 °C; ir ($CHCl_3$) 1730 (ester C=O), 1670 (ketone C=O), 1060 cm^{-1} (S=O); NMR δ 2.43 (s, 3 H, SCH_3), 2.92 (dd, 1 H, J = 5 and 17 Hz, *H*CH), 3.14 (dd, 1 H, J = 9 and 17 Hz, HC*H*), 5.01 (dd, 1 H, J = 5 and 9 Hz, COCHSO), 7.75 (ABq, 4 H, aryl). The NMR spectrum of the crude product showed resonances at δ 2.33 (s, SCH_3) and 5.34 (dd, J = 5 and 8 Hz, COCHSO) for the other diastereomer.

Anal. ($C_{12}H_{13}BrO_4S$) C, H, Br, S.

Methyl (*E*)-4-(*p*-Bromophenyl)-4-oxo-2-butenoate (3e). A mixture of 0.67 mmol of the crude alkylation product **2e**, prepared as described above, 150 mg of sodium bicarbonate, 64 μl (0.69 mmol) of methyl bromoacetate, and 2 ml of dioxane was stirred at reflux for 1 h. The mixture was diluted with ether and washed with 2 N NaOH and water to give 154 mg (85% yield) of pale yellow needles, mp 72–74 °C. After recrystallization from isopropyl ether: mp 75–77 °C (lit.[25] mp 77 °C); ir ($CHCl_3$) 1717 (ester C=O), 1673 (ketone C=O), 1635 cm^{-1} (w, C=C); NMR δ 3.83 (s, 3 H, CH_3), 6.87 (d, 1 H, J = 16 Hz, $CHCO_2$), 7.83 (d, 1 H, J = 16 Hz, aryl CH), 7.73 (ABq, 4 H, aryl).

Methyl 4-(*p*-Bromophenyl)-4-hydroxy-3-methylsulfinylbutanoate (4e). To a solution of 0.56 mmol of the crude alkylated product **2e**, prepared as described above, in 2 ml of methanol was added 23 mg (0.6 mmol) of sodium borohydride. After 5 min, the mixture was diluted with ethyl acetate and washed with saturated NH_4Cl. The aqueous phase was separated and extracted with ethyl acetate, and the organic layers were combined to give 188 mg (100% yield) of the hydroxy ester **4e** as a colorless gum: ir (neat) 3300 (OH), 1740 (C=O), 1050 cm^{-1} (S=O); NMR δ 2.49, 2.53, 2.66, 2.70 (singlets, 3 H, SCH_3), 3.57 (s, 3 H, CO_2CH_3), 5.0 (m, 2 H, CH and OH), 7.38 (ABq, 4 H, aryl). When a pure sample of the (*R,R*)-(*S,S*) isomer of **2e** was reduced in this manner, an analytical sample was obtained by recrystallization from ether: mp 114–115 °C.

Anal. ($C_{12}H_{15}BrO_4S$) C, H, Br, S.

Methyl (*E*)-4-(*p*-Bromophenyl)-4-hydroxy-2-butenoate (6e). The crude reduction product **4e** (≤0.56 mmol) described above was distilled (175° (0.1 mm)) to give 137 mg (90% yield) of the unsaturated ester as a pale yellow oil: ir (neat) 3400 (OH), 1705 (C=O), 1640 cm^{-1} (C=C); NMR δ 3.70 (s, 3 H, CO_2CH_3), 5.27 (dd, 1 H, J = 1.5 and 5 Hz, H_γ), 6.08 (dd, 1 H, J = 1.5 and 16 Hz, H_α), 6.98 (dd, 1 H, J = 5 and 16 Hz, Hβ), 7.37 (ABq, 4 H, aryl). The analytical sample was purified by column chromatography.

Anal. ($C_{11}H_{11}BrO_3$) C, H, Br.

5-(*p*-Bromophenyl)-2(5*H*)-furanone (5e). To a solution of 1.4 mmol of the crude alkylation product **2e**, prepared as described above, in 5 ml of methanol was added 70 mg (1.8 mmol) of sodium borohydride at 0°. After 15 min, the mixture was diluted with ethyl acetate and washed twice with 5% potassium carbonate to give a brown, oily product. This material was chromatographed to give 110 mg (33% yield) of the α,β-butenolide **5e**. An analytical sample was obtained by recrystallization from carbon tetrachloride: mp 91–92 °C; ir ($CHCl_3$) 1793, 1760 cm^{-1} (α,β-butenolide[12]); NMR δ 5.97 (t, 1 H, J = 2 Hz, H_γ), 6.20 (dd, 1 H, J = 2 and 5.5 Hz, H_α), 7.35 (ABq, 4 H, aryl), 7.5 (dd, 1 H, J = 2 and 5.5 Hz, H_β).

Anal. ($C_{10}H_7BrO_2$) C, H, Br.

5-(*p*-Bromophenyl)-2(3*H*)-furanone (8e). An ethyl acetate solution of 1.14 mmol of the crude reduction product **4e**, prepared as described above, was shaken with 2 N NaOH to give an immediate green color. The mixture was quickly neutralized by shaking with saturated NH_4Cl, and after separation of the phases, the organic layer gave a red-brown solid on workup. This material was distilled (175° (0.1 mm)), affording 100 mg (37% yield) of the β,γ-butenolide **8e** as a yellow solid. Recrystallization from methanol gave orange prisms: mp 126–133 °C (lit.[13] mp 115–130 °C); ir ($CHCl_3$) 1805 cm^{-1} (C=O); NMR δ 3.38 (d, 2 H, J = 3 Hz, CH_2), 5.78 (t, 1 H, J = 3 Hz, =CH), 7.50 (s, 4 H, aryl).

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Organic Sulfur Mechanisms. 18. The Sulfo-Cope Rearrangement and Other Thermal Reactions of Unsaturated Sulfonyl Species[1,2]

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Abstract: The first examples of sulfene formation by thermal rearrangement of allyl vinyl sulfones—the "sulfo-Cope" rearrangement—are described. In ethanol-pyridine solution the *N*-ethylpyridinium salt of the corresponding sulfonic acid is obtained in good yields (70–95%); the reaction is therefore a potentially useful process for making a new carbon-carbon bond. The rearrangement takes place also on flash thermolysis to give a poor yield of the aldehyde, resulting from thermal desulfinylation of the sulfene. Deuterium labeling shows the sulfo-Cope rearrangement to be clearly of the order [3,3] either in the gas or the liquid phase. Flash thermolysis of a series of alkenesulfonyl chlorides has given a new rearrangement to a sulfene and a new desulfonylation rearrangement, as well as an elimination of sulfur dioxide and hydrogen chloride; the origins of this diversity of reaction are discussed.

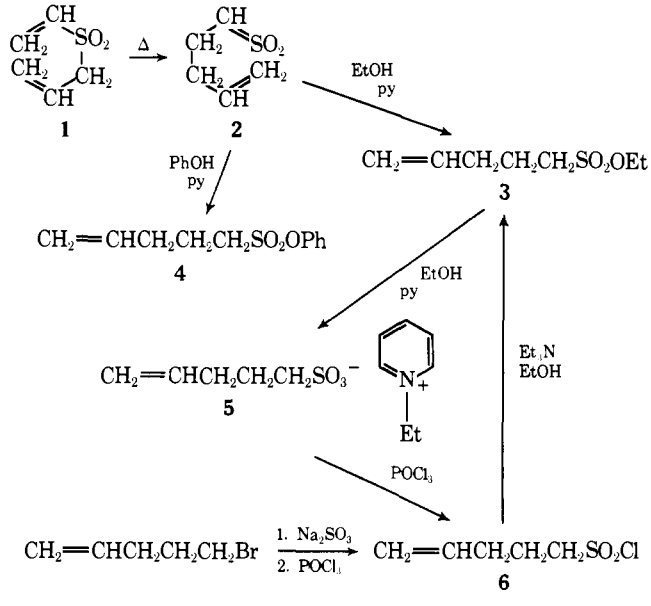
As part of a systematic study of sulfenes,[3] we wished to see if they could be formed by rearrangement of an allyl vinyl sulfone, e.g., **1** → **2**. Such a process would be one of the family of "hetero-Cope" rearrangements[4] and might be conveniently labeled the "sulfo-Cope" rearrangement. Cope, Morrison, and Field[5] actually explored the possibility of such a reaction in 1950, but they obtained no identified products. We describe herein our observation that allyl vinyl sulfones, either in the liquid phase or upon flash thermolysis,[6] do, in fact, undergo a rearrangement similar to that of 1,5-hexadienes; we report also some related reactions observed on flash thermolysis of unsaturated sulfonyl chlorides.

Results

Sulfo-Cope Rearrangement in the Liquid Phase. Allyl vinyl sulfone (3-ethenesulfonylpropene, **1**), on heating in a pyridine-ethanol solution in a sealed tube at 165–175 °C for 2 h, gave *N*-ethylpyridinium 4-pentene-1-sulfonate (**5**) in about 70% yield. The structure of this product was shown by (a) elemental analysis and spectroscopy and (b) conversion of **5** to 4-pentene-1-sulfonyl chloride (**6**) and comparison of **6** with a specimen synthesized from 5-bromo-1-pentene (Scheme I). Under the conditions of the above rearrangement, authentic ethyl 4-pentene-1-sulfonate (**3**) is converted to **5** in 93% yield. Both this and the formation of **4** (in only 14% yield, however) on heating **1** in phenol-pyridine, are in accord with the pathways shown in Scheme I. A number of other reaction media were tried (see Experimental Section), but gave little or no identified product.

Similar heating of **7a** and **7b** gave the rearranged products **8a** and **8b** in 96 and 81% yields, respectively. The rearrangement of **7b** proceeds also at lower temperatures, a 64% yield of **8b** being obtained after 2 h at 125°. The assignment of structures **8a** and **8b** follows not only from the analogy with

Scheme I



5, but also from the agreement of analytical and spectroscopic data obtained both from **8a** and **8b** themselves and from the further transformation products shown in Scheme II.

In order to determine if this rearrangement is of the order [3,3] or [1,3] (or both), allyl-α,α-d_2 vinyl sulfone (**11**) was prepared by base-catalyzed deuteration[7] of **1** and rearranged in pyridine-ethanol-*d*. The product (**12**) obtained after reaction with phosphorus oxychloride was exactly that expected for a [3,3] rearrangement: the CD_2 was, within the limits of NMR detection, entirely at the terminal carbon and, in addi-