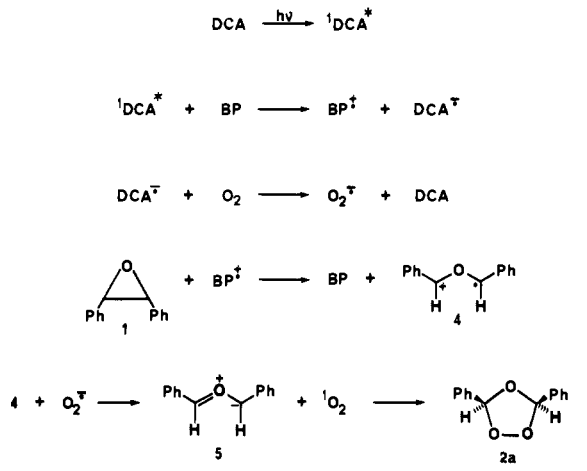
Scheme I



3.1 × 10^9 M^{-1} s^{-1}) to generate $DCA^{-\cdot}$ and $BP^{+\cdot}$. Although energetically unfavorable, a reversible electron transfer from epoxide **1** to $BP^{+\cdot}$ could generate the unopened epoxide radical cation. This step would be driven by the subsequent opening to **4** and irreversible formation of the ozonide (Scheme I).

Of present interest are the mechanistic implications of the exclusive formation of *cis*-ozonide **2a** from both epoxides **1a** and **1b**. These results are not consistent with a mechanism involving attack of $O_2^{-\cdot}$ on epoxide radical cation **4** to give long-lived biradical or zwitterion intermediates.[15] Such mechanisms would predict the formation of a mixture of isomeric ozonides. A plausible mechanism that is consistent with the stereoselective formation of ozonide **2a** involves (1) formation of the most stable *E,E* conformation of epoxide radical cation **4** from either **1a** or **1b**, (2) subsequent reduction of **4** by $O_2^{-\cdot}$ (or $DCA^{-\cdot}$) to yield the *E,E* isomer of carbonyl ylide **5**, and (3) 4 + 2 cycloaddition with $^1O_2$ acting as a dipolarophile. Santamaria[16] and Foote[17] have shown that $^1O_2$ can be formed in DCA-sensitized photooxygenations by energy transfer from singlet and triplet excited DCA to oxygen. Singlet oxygen could also be generated as a result of the electron transfer from $O_2^{-\cdot}$ to **4**.

The proposed intermediacy of carbonyl ylide **5** and its reaction with $^1O_2$ to form *cis*-ozonide **2a** is in accord with observations of several groups on the trapping of photogenerated carbonyl ylides.[13,18] For example, Griffin[18a] has recently shown that direct photolysis or thermolysis of 2,3-diaryloxiranes such as **1a** and **1b** generates carbonyl ylides that can be trapped by dipolarophiles to afford substituted tetrahydrofurans. As in the present study, the major products arise from a 4 + 2 cycloaddition of the dipolarophiles to the thermodynamically more stable *E,E* carbonyl ylides. In related work, Arnold[13] has utilized 1,4-dicyanonaphthalene as an electron-transfer sensitizer with epoxides **1** in the presence of dipolarophiles to yield substituted tetrahydrofurans in which the major products have a *cis*-diphenyl relationship. The proposed mechanism involves formation of the epoxide radical cation followed by back electron transfer from the sensitizer radical anion to give the carbonyl ylide.[19] Trozzolo and Griffin have used spectroscopic methods to characterize carbonyl ylides produced by the photochemical cleavage of epoxides.[20]

Experiments are continuing on the mechanism of the cosensitized electron-transfer photooxygenation of epoxides and other substrates. We have extended our investigations to the photooxygenation of substituted aziridines and have recently been able to isolate the first photochemically prepared 1,2,4-dioxazolidine.[21] The possibility that this reaction may involve azomethine ylides as intermediates is under study.

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Registry No. 1a, 1689-71-0; **1b**, 1439-07-2; **2a**, 21072-45-7; DCA, 1217-45-4; BP, 92-52-4.

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Syn and Anti Stereochemistry in Elimination Reactions Producing Acyclic Conjugated Thioesters

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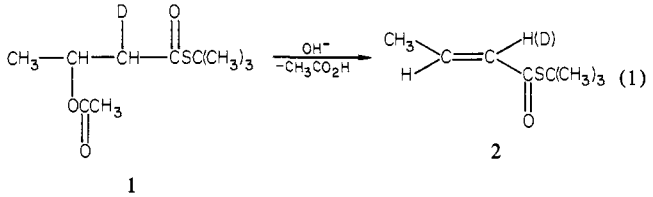
Although base-catalyzed addition–elimination reactions that involve the C=C—C=O moiety are important in organic chemistry, almost nothing has been reported on their innate stereochemistry. We now report the first stereochemical studies of a base-catalyzed 1,2-elimination reaction producing an alkene conjugated to a carbonyl group. Preliminary results show that syn and anti elimination pathways have comparable rates.

The dominant anti stereochemistry in 1,2-elimination reactions of acyclic compounds seemed secure until the work of Sicher and his colleagues on the syn–anti dichotomy.[1] The general importance of syn elimination pathways is accepted now, and factors that favor them have summarized.[2,3] Nevertheless, it was surprising when enzyme-catalyzed syn eliminations were observed.[4] Each of these involves a conjugated thioester or ketone product. No advantage for enzymic syn eliminations is apparent in the context of natural selection, other than the possible mechanistic efficiency due to the presence of relatively acidic protons α to the carbonyl group of each substrate. E1cB-like transition states may favor syn stereochemistry.[5]

Our substrate, (*R,R*)- and (*S,S*)-*S-tert*-butyl 3-acetoxy[2-$^2H_1$]butanethioate (**1**), was chosen because it provides an ap-



(1)

1 2

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propriate model for the substrate of enoyl-CoA hydratase (EC 4.2.1.17), one of the enzymes that catalyze syn eliminations. In addition, a thorough investigation on elimination reactions of the unlabeled 3-acetoxy thioester has been reported.[6] Fedor concluded that this base-catalyzed elimination of acetic acid is either E2 or E1cB with fast reaction of the carbanion.

NMR studies showed that our synthesis of **1** was stereospecific.[7] Later ^{1}H NMR investigations at 300 MHz, where the diastereotopic protons at C-2 were separated by 0.18 ppm, showed that the synthesis of **1** also produced 2.9% of the nondeuterated acetoxy thioester.

Our preliminary experiments on the stereochemistry of reaction 1 have shown some interesting results. Reaction of **1** at 25 °C in 3:1 EtOH/H_2O with 1.69 M KOH (10% excess) produced *S-tert*-butyl (*E*)-2-butenethioate (**2**) in 70–85% yield.[8] NMR analysis of nondeuterated **2** ($CDCl_3$) showed peaks at δ 6.8 (m, 1, C_3H), 5.97 (br d, 1, C_2H), 1.84 (dd, 3), and 1.5 (s, 9); UV_{max} was 262 nm (EtOH/H_2O, ϵ 6280). Compounds **1** and **2** did not undergo significant proton exchange with protonated or deuterated solvents under reaction conditions. The *Z*-alkene, synthesized by hydrogenation of tetrolic acid and esterification in the usual manner,[7] was formed in only 1% yield from reaction (1) and was stable under reaction conditions. A k_H/k_D value of 5.2 ± 0.1 was obtained through comparative (UV) second-order rate measurements on the diprotonated and dideuterated thioesters in EtOH/H_2O (3:1).[9]

Compound **2** was purified by preparative GC ($^3/_8$ in. × 8-ft 15% Carbowax 20 M column) and the vinyl protons were integrated by NMR. Multiple integrations in two separate experiments gave an average isotopic composition of 57.0 ± 1.2% ^{1}H and 43.0 ± 1.2% ^{2}H at C-2. After correction for the isotope effect, we find the stereochemical preference for the undeuterated substrate to be 86% anti and 14% syn elimination. The same results were obtained when the reaction was run to 50% completion. That this is the result of a definite stereochemical preference for anti elimination is demonstrated by the fact that the deuteron of **1** is eliminated 1.3 times faster than the proton. If a secondary isotope effect of 1.15 pertains in the rate of the dideuterated thioester,[10] the stereochemical preference is 85% anti/15% syn.

Reaction of **1** with LiOH, rather than KOH, in EtOH/H_2O gave virtually the same stereochemistry. However, reaction of **1** at 25 °C in hexane with lithium *tert*-butoxide (0.35 M, 20% excess) resulted in a much greater preference for syn elimination. The *t*-BuOLi/hexane reaction gave 85+% recovered yields of **2**. Control experiments showed that isomerization of the *Z*-alkene and proton exchange on **2** were negligible. Multiple NMR integrations on **2** from duplicate reactions gave an average isotopic composition of 13.0 ± 1.2% ^{1}H and 87.0 ± 1.3% ^{2}H at C-2. Kinetic isotope effects are relatively insensitive to base strength and association.[3,11] With correction for an isotope effect of 5.2, the values expected for the parent unlabeled β-acetoxy thioester are 44% anti and 56% syn elimination.

The 15% syn elimination from **1** in EtOH/H_2O is the largest deviation from the anti rule ever observed with base-catalyzed 1,2-elimination reactions on neutral acyclic compounds in a non-ion pairing medium. Such compounds rarely produce more than 5% syn elimination under ion-dissociating conditions; reaction of *t*-BuOK/Me_2SO with 5-fluoro[6-$^2H_1$]decane gave 12% syn elimination, the greatest amount observed heretofore.[12] Fluoride is a poor leaving group, and the transition state should have a good deal of carbanionic character. Most activated acyclic E2 eliminations for which stereochemical data are available have used phenyl or halogen activating groups. In contrast to our results, such compounds exhibit a diminished propensity for syn elimination.[3] In our reactions, which are at the E2–E1cB borderline, the transition states probably have a large amount of carbanion character and a small amount of C=C character. As expected, ion pairing with *t*-BuOLi/hexane favors a syn elimination pathway, so that syn and anti elimination occur with nearly equal facility.

That syn and anti stereochemistry compete effectively in base-catalyzed elimination reactions of the acetoxy thioester **1** may be of some biochemical significance. It now seems reasonable that enoyl-CoA hydratase and other enzymes catalyzing syn eliminations on acyclic substrates may do so for reasons of mechanistic efficiency. We are continuing to investigate the importance of substrate acidity, base strength, and leaving group on these reactions.

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Registry No. (*R,R*)-**1**, 86195-04-2; (*S,S*)-**1**, 86195-05-3; (*E*)-**2**, 86146-56-7; deuterium, 7782-39-0.

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Optical Resolution of 3-Methylcycloalkanones and 5-Methyl-γ-butyrolactone by Complexation with Optically Active 1,6-Bis(*o*-halophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol

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Optical resolution of guest molecules utilizing the inclusion phenomena in a host has been studied by several research groups.[1] Efficiency of the resolution, however, is not high except for some special cases involving the resolution of 2-chlorooctane by urea[1a] and of phosphinates[1d] and sulfinates[1e] by cyclodextrin. Recently, Cram and co-workers succeeded in resolving amino acids and amines as their salts quite efficiently by using the inclusion phenomena in optically active crown ethers.[1g-i] Nonetheless, an optically active host molecule that can resolve a neutral guest molecule efficiently has yet to be prepared. We now report optical resolution of 3-methylcyclohexanone (**3**), 3-methylcyclopentanone (**4**), and 5-methyl-γ-butyrolactone (**5**) by complexation with optically active 1,6-bis(*o*-halophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**2b–d**).

Previously, we have reported that 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (**2a**) forms 1:2 crystalline complexes with various guest molecules.[2a,c] It was also confirmed by an X-ray structural

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