

Photooxidation of Methionine and Related Compounds

Sir:

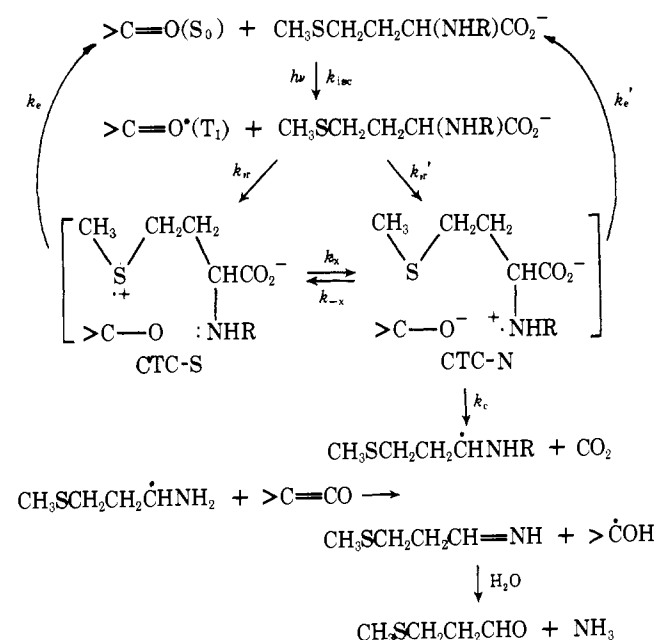
We wish to report on the mechanism of light-induced oxidation of methionine, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$, inferred from a study of the kinetics, quantum yields, and products of photoreduction of 4-carboxybenzophenone by methionine and related compounds. Such reactions proceed via rapid charge transfer interaction at a heteroatom, k_{ir} , followed by quenching, k_e , or by proton transfer, reduction, k_h .¹ Quantum yields for reduction are determined by the k_h/k_e ratios and are generally high for amines and low for thioethers,² which act as efficient quenchers.

Solutions were degassed by the freeze-thaw method and irradiated in Pyrex under argon. Values of k_{ir} were obtained from quenching of emission at 450 nm, excitation at 350 nm, of 0.008 *M* 4-carboxybenzophenone, by 5×10^{-5} to 1×10^{-4} *M* sulfur compound, or 10^{-4} *M* amino compound at pH 12, and up to 0.1 *M* amino compound at pH 7, and application of the expression: $I_0/I = 1 + \tau_0 k_{ir}(Q)$. Values of τ_0 were 5.1×10^{-6} sec at pH 12, 8.1×10^{-6} sec at pH 7. Quantum yields, ϕ , for reduction to ketyl radical were obtained from rate of decrease of carbonyl absorption at 340 and 350 nm, on the basis that two ketyls combine to form pinacol at pH 7, and disproportionate to hydrol and ketone at pH 12.³ Reduction by triethylamine, irradiated concurrently with the samples on a turntable, was used as a secondary actinometer, $\phi = 1.4$ at 334 nm, determined by ferrioxalate actinometry.⁴ Results are summarized in Table I.

For the sulfur compounds I-V, values of k_{ir} are high and similar, $1-2 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$, independent of pH and the presence or absence of amino, acetamido, ammonium, and carboxylate groups, and characteristic of thioethers in a polar solvent.² For the amino compounds VI and IX, which lack S, values of k_{ir} at pH 12 are an order of magnitude smaller;⁴ at pH 7 the low residual concentrations of free amine lead to apparently low values of k_{ir} , since the calculation is based on the total concentration, including inert ammonium compound. The acetamido compounds VII and VIII show quite low values of k_{ir} , apparently lower at pH 7 than at pH 12.

The quantum yield for reduction to ketyl is high for methionine at pH 12, $\phi = 0.9$, and lower at pH 7 where the amino group is largely protonated, $\phi = 0.55$. The quantum yield with II, in which the amino group is acetylated, is decreased to 0.43 at pH 12 and becomes quite low at pH 7, $\phi = 0.12$. The amino group alone with S assists in photoreduction at pH 12 by III, $\phi = 0.28$; the ammonium ion makes little contribution at pH 7, in contrast to the effect in photoreduction by hydrazinium ion in which it protonates the ketyl radical anion.⁵ The acetamido group, alone or in the presence of S or carboxylate separately, compounds VIII, V, and VII, leads to little reduction. The carboxylate

Scheme I



also does not assist reduction after interaction at S, compound IV. This may be in contrast to carbonyl sensitized decarboxylation of some compounds of type $\text{RXCH}_2\text{CO}_2\text{H}$, in which proton transfer from carboxyl to ketyl radical anion is postulated.⁶ In the absence of S, the free amino groups of compounds VI and IX show normal efficient reduction, which is enhanced by carboxylate.

In the photoreduction by methionine at pH 7, methional, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CHO}$, was the oxidation product, 100% yield, 1 mol per 2 mol of ketone reduced; the benzpinacol was the reduction product. At pH 12 the hydrol was obtained and the methional was degraded. In photoreduction by *N*-acetylmethionine at pH 12, acetamide was obtained, 1 mol per 2 mol of ketone reduced, 50% yield, while at pH 7 the yield was quite low. The reactions of the excited ketone with methionine and *N*-acetylmethionine at pH 12 may be formulated as shown in Scheme I, $\text{R} = \text{H}, \text{CH}_3\text{CO}$.

The initial charge transfer interactions with I and III are 90% at S, k_{ir} , 10% at N, k_{ir}' , and with II, >99.9% at S. The quantum yield for reduction at S may be ≤ 0.09 ;² the increase due to presence of N in III supports electron transfer within the charge transfer complex, k_x , and two forms, CTC-S and CTC-N. The low quantum yield with IV may indicate little, if any, electron transfer from $-\text{CO}_2^-$ to S^+ , such as has been proposed.⁷ The CTC-N zwitterion may lose CO_2 directly and efficiently, k_c , to form the α -amino radical, and not require electron transfer from $-\text{CO}_2^-$ to $>\text{N}^+$. Both forms of the CTC may undergo quenching by spin inversion and charge destruction, k_e and k_e' , but the

Table I. Photoreduction of 0.003 *M* 4-Carboxybenzophenone by 0.04 *M* Methionine and Related Compounds, pH 12 and 7

Reducing agent	pH 12		pH 7	
	ϕ_{ketyl}	$k_{ir}, \text{M}^{-1} \text{sec}^{-1}$	ϕ_{ketyl}	$k_{ir}, \text{M}^{-1} \text{sec}^{-1}$
I	0.90	1.6×10^9	0.55	1.2×10^9
II	0.43	1.5×10^9	0.12	1.5×10^9
III	0.28	2.0×10^9	0.11	1.7×10^9
IV	0.09	1.3×10^9	0.13	1.1×10^9
V	0.09	1.3×10^9	0.07	1.1×10^9
VI	0.93	1.6×10^8	0.26	$\sim 2 \times 10^5$
VII	0.03	2.1×10^6	0.05	$\sim 2 \times 10^5$
VIII	0.07	1.0×10^6	0.05	$\sim 3 \times 10^5$
IX	0.67	1.8×10^8	0.21	1.1×10^6
X	1.4	1.9×10^9	0.35	7.2×10^5

process k_x , k_c competes favorably. The oxidation of an amino acid may take a similar course, loss of CO_2 from a radical zwitterion, and differ from that of an amine, loss of α -proton from a radical cation. The importance of alkali in reduction by *N*-acetylmethionine indicates that alkali may remove the amide proton in the CTC-S, facilitating electron transfer from N to S, and then loss of CO_2 . The α -acetamido radicals may be ionized at pH 12,⁸ and dispropionate rather than reduce ground state ketone efficiently.

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References and Notes

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Stereochemical Course of an Associative Nucleophilic Displacement at Tetracoordinate Sulfur(IV). An Optically Active Trigonal Bipyramidal Molecule, a Chlorosulfurane¹

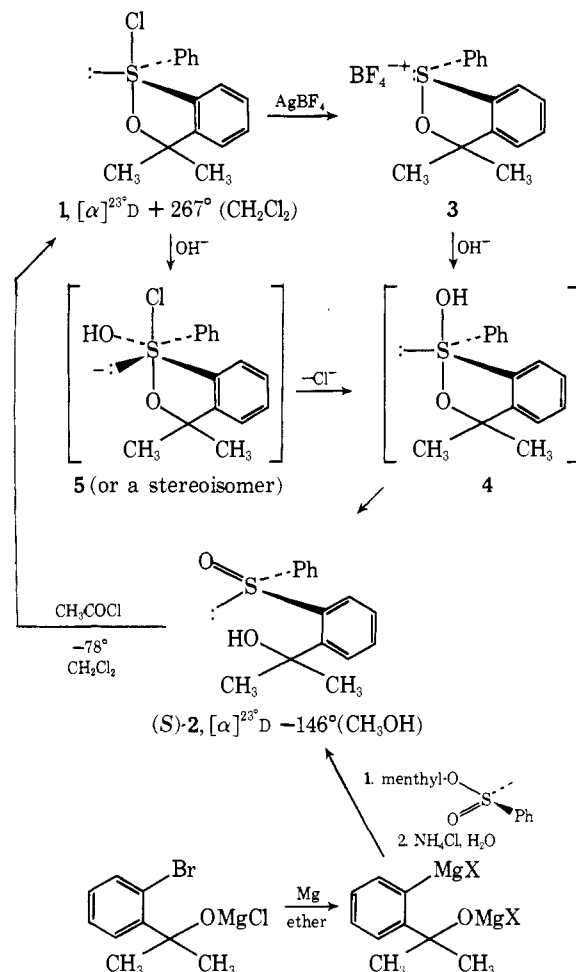
Sir:

We report the synthesis of optically active chlorosulfurane **1** in 95% enantiomeric purity by the route indicated in Scheme I, the first example of an optically active tetracoordinate sulfur(IV) species. It is hydrolyzed in base by an associative mechanism to give sulfoxide **2** with retention of configuration about sulfur.

The stability of fluorosulfuranes is sufficiently high that many examples of this class of compound have been isolated and studied.² The chlorosulfuranes, in contrast, are much less stable. Several have been observed, without isolation, as reaction intermediates.³ Those which have been isolated^{4a-d} have usually been thermally unstable^{4e} and easily hydrolyzed. Chlorosulfurane **1**, which includes one oxygen ligand and one carbon ligand to sulfur in a five-membered ring,^{4a} is stable in crystalline form indefinitely at room temperature. Racemic **1** (mp 125–126°) is only slightly decomposed after two melting-cooling cycles (ca. 1° lowering in melting point). Less than 15% hydrolysis was noted by NMR after overnight exposure of crystalline **1** to air.

Racemic **1** and its substituted analogs, **6a–e**, are easily formed from the corresponding sulfoxides in chloroform by treatment with acetyl chloride or anhydrous HCl or from the corresponding sulfides by treatment with *tert*-butyl hypochlorite. Removal of the solvent from a chloroform solution of acetyl chloride and **2** gave **1** in 100% isolated yield: NMR (CDCl_3) δ 1.26 (s, 3), 1.68 (s, 3), 7.44 (s, 7), 7.70 (m, 2), 9.33 (m, 1); ir (CHCl_3) 2980 (s), 1448 (m), 1240 (m), 1150 (m), 997 (s) cm^{-1} . This compound, and all oth-

Scheme I



ers isolated in this study, gave satisfactory elemental analyses. Addition of 1 equiv of H_2O to a chloroform solution of **1** gives no hydrolysis detectable by NMR. Further addition of 1 equiv of diisopropylethylamine or *N,N*-dimethylaniline results in complete hydrolysis. Competitive rates of hydrolyses of binary mixtures of the above chlorosulfuranes (**1** and **6a–e**) were followed using limited H_2O in the presence of an equivalent amount of one of the named amines, analyzing for products and unreacted starting material by ^1H NMR.

