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Registry No. 1, 800-12-4; 2, 33624-92-9; hexamethylbenzene, 87-85-4.

Supplementary Material Available: Bond lengths and bond angles, with standard deviations, for 2 (Tables IV and V), final anisotropic thermal parameters for chlorine (Table VI), and atomic parameters for hydrogen (Table VII) (3 pages). [The structure factor table is available from the author.] Ordering information is given on any current masthead page.

Neighboring Group Participation in Radicals: Pulse Radiolysis Studies on Radicals with Sulfur–Oxygen Interaction

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Neighboring group participation by alcohol and carboxylate groups resulting in kinetic and thermodynamic stabilization of an oxidized sulfur atom in various organic sulfides is reported. The resulting radical intermediates of the general type $(-\overline{\mathrm{S}\leftrightarrow\mathrm{O}})^{\bullet}$ are characterized by an optical absorption in the 400-nm range and exhibit lifetimes of up to several hundred microseconds in aqueous solution under pulse radiolysis conditions. Significant sulfur–oxygen interaction seems to occur, however, only if both heteroatoms are separated by three or four carbon atoms in the unoxidized molecule which enables favorable five- or six-membered ring structures in the radical intermediates. This geometric effect can additionally be favored by minimizing the free rotation of the functional groups through rigid molecular structures, e.g., in norbornane derivatives, and introduction of particular substituents. A most suitable function for stabilization of an oxidized sulfur atom seems to be a carboxylate group where an overall neutral radical of the general structure $-\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{O}}\mathrm{OC}$ is formed. In these species stabilization can be envisaged to involve the carboxylate group as a whole rather than only an individual oxygen atom. The bond strength of the sulfur–carboxylate interaction is estimated to be of the order of 50 kJ mol^{-1} as deduced from the temperature dependence of its dissociation. Further evidence for net sulfur–carboxylate bonding is provided by rate constants of 10^5–10^7 M^{-1} s^{-1} for its proton-assisted decay. These rates are considerably lower than for the diffusion controlled protonation of free carboxylate functions. Oxidation of *endo*-2-(2-hydroxyisopropyl)-*endo*-6-(methylthio)bicyclo[2.2.1]heptane yields a transient where sulfur–oxygen interaction is associated with a strong acidification of the alcoholic hydroxyl group. A pK = 5.9 has been measured for the $(-\overline{\mathrm{S}\leftrightarrow\mathrm{O}}\mathrm{H})^{\bullet+} \rightleftarrows (-\overline{\mathrm{S}\leftrightarrow\mathrm{O}})^{\bullet} + \mathrm{H}^+$ equilibrium. All the results on these transient radical intermediates can be viewed in terms of neighboring group participation. Such participation is also clearly evidenced in the formation and properties of intermolecular radical cations, $(\mathrm{R_2S{\therefore}SR_2})^+$, derived from these sulfides, and in the kinetics of the primary oxidation process. Absolute rate constants for the one-electron oxidation of various sulfides by $\mathrm{CCl_3OO^{\bullet}}$ radicals, for example, have been found to range from 3×10^8 to $<10^{-6}$ M^{-1} s^{-1} depending on the nature of the oxygen containing functional groups. The present results are finally discussed in terms of the general possibility of stabilization of an oxidized sulfur function by other heteroatoms. Several electronic structures including the two-center-three $(2\sigma/1\sigma^*)$ electron bond can be advanced to describe the physicochemical properties of the radicals with sulfur–oxygen interaction.

Introduction

In previous studies[1-7] we have shown that radical cations of the general type $\mathrm{R_2S^{\bullet+}}$ can be generated in the radical-induced oxidation of organic sulfides. It has also been demonstrated that these sulfur-centered radical species exhibit a high tendency to stabilize themselves by reaction with an unoxidized sulfide molecule. This occurs within

$$\mathrm{R_2S^{\bullet+}} + \mathrm{R_2S} \rightleftharpoons (\mathrm{R_2S{\therefore}SR_2})^+ \qquad (1)$$

a thermodynamic equilibrium and leads to the formation of an intermolecular sulfur–sulfur bond containing a total of three electrons (eq 1). The latter results from interaction of the single p-electron in $\mathrm{R_2S^{\bullet+}}$ with the p-electron pair of the unoxidized $\mathrm{R_2S}$. The S∴S bond contains two electrons in a bonding σ-orbital and one electron in an antibonding σ^*-orbital.

Considering the nature of the three-electron bond it is not surprising to see such bonds also being formed intramolecularly, e.g., from dithia compounds,[2,4,7-12] or with participation of other heteroatoms.[9,13-26] Several recent

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Table I[a]

substr	$k(CCl_3OO^\bullet$ + substr), $M^{-1}\ s^{-1}$	$(\overline{S\leftrightarrow O})^\bullet$ interaction species			$(>S{\therefore}S<)^+$ ϵ, M^{-1} cm^{-1}
		k for decay reactions	thermodynamic data	ϵ, $M^{-1}\ cm^{-1}$	
1	7×10^7 (a)				7700
2	1×10^8 (b)	with H^+, $9.8 \times 10^5\ M^{-1}\ s^{-1}$	$E_a = 26$ kJ mol^{-1}	3200	
		with OH^-, $1.2 \times 10^7\ M^{-1}\ s^{-1}$	$D \approx 45$ kJ mol^{-1}		
		1st order, $3 \times 10^3\ s^{-1}$	$\Delta S^\ddagger = -90$ J $mol^{-1}\ K^{-1}$		
3				$\geq$1800	8500
4	$<10^6$ (b)				
5a	2×10^7 (a)				
5b	3×10^8 (b)	with H^+, $3.0 \times 10^7\ M^{-1}\ s^{-1}$	$E_a = 32$ kJ mol^{-1}	3900	
		with OH^-, $8.0 \times 10^6\ M^{-1}\ s^{-1}$	$D \approx 50$ kJ mol^{-1}		
		1st order: $1 \times 10^4\ s^{-1}$	$\Delta S^\ddagger = -60$ J $mol^{-1}\ K^{-1}$		
5c				2000 $(S\leftrightarrow O)^\bullet$	
				1200 $(S\leftrightarrow OH)^+$	

[a] Kinetic, thermodynamic, and optical data of radical species formed in the oxidation of various sulfides containing also oxygen containing functional groups. (Missing values could not be determined due to experimental limitations such as too slow reactions, overlapping absorptions, dominating competitive processes, or lack of sufficient amount of compound.) Estimated error limits: ±30% for rate constants in columns 1 and 2; ±5 kJ mol^{-1} for E_a, ±10 kJ mol^{-1} for D, and a factor of 2 and possibly more for $\Delta S^\ddagger$ (column 3); ±20% for extinction coefficients (columns 4 and 5). Rate constants have been measured via formation of $(R_2S{\therefore}SR_2)^+$ (species a) and of $(S^\bullet\leftrightarrow O)$ interaction (species b).

experimental and theoretical studies have demonstrated the establishment of σ/σ^{*1} interactions between a sulfur atom and nitrogen, oxygen, halide, or other atoms. The stability of such systems generally decreased with an increase in the difference between the electronegativities of the interacting atoms.[14] A number of time-resolved pulse radiolysis studies as well as ESR investigations have revealed, however, that such interactions can be favored by entropic parameters, i.e., suitably constrained geometries which facilitate p-orbital overlap.[19-22,24,25] These systems have been classified as 9-S-3 sulfuranyl radicals.[19] In such systems which can adopt a T-shaped geometry about the sulfur atom, two other bonding schemes are possible, namely, a σ-delocalized three-center-three-electron bond and a three-center-four-electron bond with the unpaired electron in a sulfur 3p orbital perpendicular to this bond.[19,27] These latter two bonding schemes are favored by electron-withdrawing groups attached to sulfur in the apical position albeit to different extents. The effects of the groups attached to sulfur on the bonding in 9-S-3 systems have been discussed.[19,27,28]

In the present paper we report on further evidence of sulfur-oxygen interaction with particular emphasis on oxidized sulfides which also carry carboxylate, alcohol, and ester functions. The investigation also includes information on the intermolecular S∴S interaction with such molecules. The methodology used has been the radiation chemical technique of pulse radiolysis which allows a direct and time-resolved observation of short-lived species. The choice of the experimental method has, in turn, determined the solvent in which these studies have been conducted, namely, water.

Experimental Section

All experiments were carried out at room temperature unless stated otherwise. The water for these aqueous solutions of the various sulfur containing compounds was especially purified by Millipore filtration and deionization.

Norbornane derivatives **5a–c**[29] and the open chain compound 3-(methylthio)propanoic acid[30] were synthesized and purified as described in the literature.[31] 4-(Methylthio)butanoic acid and 3,3′-thiodipropanoic acid were used as received from Aldrich Chemical Co. without further purification.

A detailed description of the radiation chemical technique of pulse radiolysis can be found in the literature.[32] Essential features of this technique are a radical generation and a radical detection system. The former is provided by a 1.55-MeV van de Graaff accelerator which delivers short pulses of high-energy electrons (typically of the order of 1-μs duration) into the aqueous solutions. The immediate chemical result is the generation of highly reactive radical species, mainly e_{aq}^- and $^\bullet OH$. Both are formed with about equal yield of $G = 2.8$ (species per 100 eV absorbed energy). This corresponds to concentrations of $(0.5\text{–}3) \times 10^{-6}$ M for the typically applied 2–10 Gy (J kg^{-1}) pulses. Whenever reactions of $^\bullet OH$ radicals were to be investigated the solutions were saturated with nitrous oxide. The latter converts hydrated electrons into hydroxyl radicals ($N_2O + e_{aq}^- \rightarrow N_2 + OH^- + {}^\bullet OH$) which essentially doubles the $^\bullet OH$ radical yield. Reactions initiated by hydrated electrons, on the other hand, could be studied selectively if the $^\bullet OH$ radicals were inactivated by reaction with added alcohols, generally *tert*-butyl alcohol. The latter system was generally applied to study oxidation reactions which were initiated by $CCl_3OO^\bullet$ radicals.[25,33] The experimental conditions for these investigations were air saturated solutions containing 1 vol % CCl_4 and 30 vol % *tert*-butyl alcohol. The underlying chemistry for the $CCl_3OO^\bullet$ formation is dissociative electron capture by the CCl_4 followed by fast oxygen addition to the $^\bullet CCl_3$ radical.[34]

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Error limits based on the application of radiation chemical techniques are generally within ±10%. Additional uncertainties are stated wherever necessary.

Results and Discussion

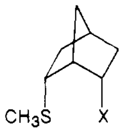
1. Formation and Lifetime of Bimolecular S∴S-Type Radical Cations. Various substrates containing sulfide as well as oxygen functions have been investigated with respect to their ability to form bimolecular S∴S-bonded radical cations. The compounds investigated are comprised of flexible open chain systems as well as of conformationally more restricted norbornane derivatives. $(R_2S\therefore SR_2)^+$-type radical cations could be observed whenever the solubility of the compounds allowed concentrations high enough to establish an equilibrium according to eq 1.

$CH_3SCH_2CH_2COOCH_3$ **1**

$CH_3SCH_2CH_2COOH$ **2**

$CH_3SCH_2CH_2CH_2COOH$ **3**

$S(CH_2CH_2COOH)_2$ **4**



5a, X = $COOCH_3$
b, X = $COOH$
c, X = $C(CH_3)_2OH$
d, X = $COCH_3$

The transient optical absorption spectra obtained upon pulse radiolysis of N_2O saturated solutions of these compounds exhibit maxima in the 460–500-nm range and thus correspond to those of simple aliphatic $(R_2S\therefore SR_2)^+$ radical cations.[1-3,35] Reasonably resolved spectra could be obtained in particular from **1** and **5a**, i.e., the ester derivatives. A spectral example is given in Figure 1a which shows the visible absorption recorded 20 μs after a 2-μs pulse in an N_2O saturated solution of 10^{-4} M **1** at pH 3. It is seen to peak at 490 ± 10 nm. Further evidence for the identity of the $(R_2S\therefore SR_2)^+$-type radical cation is provided by a time-resolved conductivity measurement (which identifies the positive charge of the transient; for details see section 5 and ref 1 and 36) and by the concentration dependence of both the yield and the lifetime of the three-electron-bonded species. The latter is demonstrated in Figure 1b,c, respectively. The observed characteristics in these curves are typical for the •OH radical induced oxidation of organic sulfides and essentially reflect the equilibrium shown in eq 1[1,37] and the fact that the S∴S bonded radical cation is kinetically more stable than the monomolecular $R_2S^{\bullet+}$-type radical cation.[1,5]

The yield of radical cations calculated from the observed change in conductivity in pulse irradiated N_2O saturated solutions of 5×10^{-3} M **1** corresponds to ca. 60% of the initial •OH radical yield ($G = 3.5$). From this and the measured change in optical density at 490 nm an extinction coefficient of $\epsilon = 7.7 \times 10^3$ M^{-1} cm^{-1} is calculated (see Table I). This value is in good agreement with that known for the $(R_2S\therefore SR_2)^+$ radical cations from simple aliphatic sulfides.[1,2]

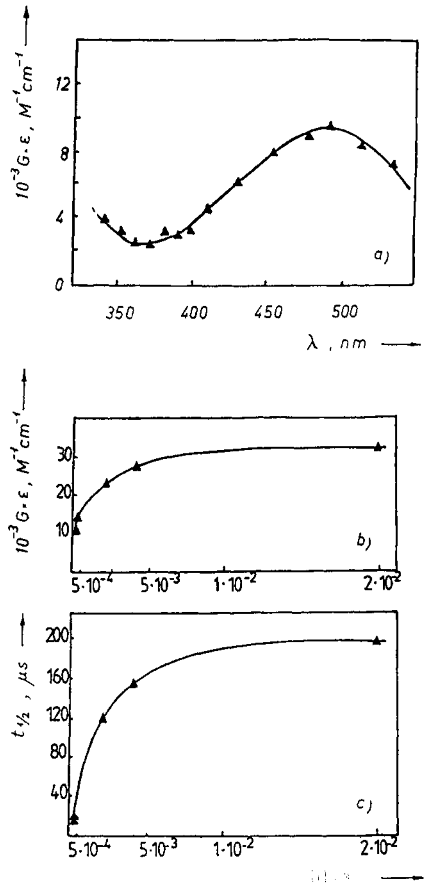


Figure 1. (a) Optical absorption in the 330–550-nm range recorded 20 μs after a 2-μs pulse in an N_2O-saturated, aqueous pH 3 solution of 10^{-4} M of compound **1**. (b) Yield of transient absorption at 480 nm in terms of G•ϵ as function of [**1**] (other conditions as in a). (c) First half-life of transient absorption at 480 nm as function of [**1**] (other conditions as in a).

There are a number of new and interesting aspects concerning the formation kinetics and the stability of these transients which emerge from the present data, in addition to features previously described. These merit the following evaluation.

An instructive set of experimental data are the solute concentrations at which formation of the $(R_2S\therefore SR_2)^+$-type radical cations commences for pulse-irradiated, N_2O saturated solutions of various norbornane derivatives **5a–d**. As can be seen, the optical absorption of the S∴S-bonded radical cation can be detected at concentrations as low as 10^{-4} M for the ester derivative **5a**. In case of the endo acid **5b** a five times higher concentration is required, and for the tertiary alcohol **5c** and the ketone **5d** a still higher concentration, considerably exceeding 5×10^{-4} M, is necessary. This finding is most remarkable in the sense that the oxidation and complexation takes place at the sulfide center and not at the substituents which seemingly cause these effects.

Several parameters can be envisaged to be reflected in the detectability of the $(R_2S\therefore SR_2)^+$-type species: the rate of the initial oxidation, the rate of the formation of the S∴S-bonded species from the primary oxidation product, possible competitive reactions to this process, and the kinetic stability of the $(R_2S\therefore SR_2)^+$ and $R_2S^{\bullet+}$ radical cations. The first of these parameters is probably not of significance for the •OH radical induced oxidations; the reaction of the hydroxyl radical with any sulfide seems to occur at a practically diffusion-controlled rate to yield an

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OH adduct at sulfur.[1,25] Similarly the reaction of the molecular radical cation with a second unattacked molecule to yield the three-electron bonded radical cation (forward reaction of eq 1) is probably also of lesser importance for the differences.[38] On the basis of the presently available data it is not possible to evaluate the relative contributions of the other parameters. In case of the $^{\bullet}$OH-induced oxidations these would also include the ionic dissociation of the OH adduct to the sulfur-centered $R_2S^{\bullet+}$ radical cation. It is nevertheless quite clear that the endo functional groups X in the norbornane structure **5** (and more generally as part of the substituent R) play a significant role in the formation and the stability of the sulfur-centered radical species. Considering the relatively rigid geometry of the norbornane derivatives all these effects may clearly be ascribed to neighboring group participation. This phenomenon has been deduced and well documented from a number of other studies, e.g., the bromide-catalyzed electrochemical oxidation of these compounds.[39]

The influence of structural effects is also reflected in the lifetimes of the $(R_2S\therefore SR_2)^+$ radical cations. They differ significantly as can be assessed from the first half-lives measured for N_2O-saturated, 5×10^{-3} M solutions at pH 3: $t_{1/2}$ = 109 μs for $(R_2S\therefore SR_2)^+$ from **1**, 163 μs **2**, 60 μs **3**, 162 μs **4**, and 23 μs **5b**. It is known that the $(R_2S\therefore SR_2)^+$ lifetimes primarily reflect both the stability of the sulfur–sulfur three-electron bond and the irreversible deprotonation of the $R_2S^{\bullet+}$ radical cation.[5] Small differences between similarly structured species should, of course, not be overemphasized, e.g., the ca. 50% lower lifetime of the radical cation derived from the ester **1** compared to that of the acids **2** and **4**. No simple explanation can, however, be given for the almost threefold decrease in $t_{1/2}$ for the respective radical cations from the substituted propanoic and butanoic acids **2** and **3**, respectively.

Differing data depending on the nature of the substituents were also obtained for the buildup kinetics of the $(R_2S\therefore SR_2)^+$-type species when the oxidation was initiated by $CCl_3OO^{\bullet}$ instead of $^{\bullet}$OH. Under such conditions the overall kinetics are only due to the direct one-electron oxidation of the sulfur function (eq 2) and the consecutive

$$R_2S + CCl_3OO^{\bullet} \rightarrow R_2S^{\bullet+} + CCl_3OO^- \qquad (2)$$

reaction of the radical cation via the forward reaction of eq 1.[25] The bimolecular rate constants derived from the dependence of the rate of formation of $(R_2S\therefore SR_2)^+$ as a function of the solute concentration (slope of $k = \ln 2/t_{1/2}$ vs. $[R_2S]$) amounted to 7×10^7 and 2×10^7 M^{-1} s^{-1} for the reaction of $CCl_3OO^{\bullet}$ with **1** and **5a**, respectively (listed in Table I). Since the process in eq 1 has, at least for simple open chain compounds, been found to be essentially diffusion controlled with $k \sim 10^9$ M^{-1} s^{-1}, the above lower rate constants are attributed to the initial oxidation, i.e., reaction 2 as the rate-determining step. Similar rate constants, significantly below the diffusion limit, have been observed for the reaction of $CCl_3OO^{\bullet}$ with other sulfides as well.[25]

No corresponding kinetic data could be evaluated for the oxidation of the acids **2**, **3**, **4**, and **5b**. Any possible formation of the $(R_2S\therefore SR_2)^+$ radical cations via initiation by $CCl_3OO^{\bullet}$ is either obscured since the primarily formed $R_2S^{\bullet+}$-type radical cation undergoes a fast intramolecular stabilization process which competes with the association reaction (see following section) or the primary oxidation process (reaction 2) is too slow ($k < 10^6$ M^{-1} s^{-1}) and thus escapes pulse radiolysis detection.

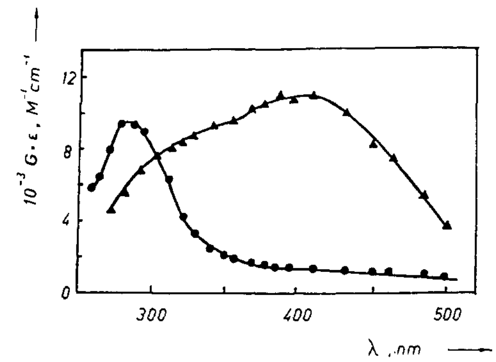
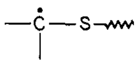


Figure 2. Optical absorption spectra recorded from a pulse irradiated, N_2O-saturated, aqueous pH 6.7 solution of 10^{-4} M **2** and 0.5 M NaH_2PO_4 at 30 (▲) and 200 μs (●) after the pulse.

2. Formation of Intramolecular S–O-Bonded Radicals from Acids. As indicated above, the oxidation of the acid derivatives may result in yet another stabilized radical different from the S∴S-bonded species. At low solute concentrations (typically $<10^{-4}$ M) a new transient optical absorption is observed which peaks around 400 nm.

A typical spectrum is shown in Figure 2 for an N_2O saturated neutral solution of 10^{-4} M of **2** recorded ca. 30 (▲) and 200 (●) μs after the pulse. A broad absorption band with λ_{max} = 410 nm is observed at the earlier recording time. As this absorption decreases a UV absorption with λ_{max} = 280 nm remains and, in fact, has increased. The latter directly emerges from the 410-nm species, and, in analogy with all other organic sulfides investigated so far, has to be attributed to a carbon-centered radical.[1,21,40] This results from deprotonation of the primary sulfur-centered radical cation $R_2S^{\bullet+}$ and to some extent also by direct abstraction of an α-hydrogen atom (relative to sulfur) by the $^{\bullet}$OH radical. The general structure of this species is



$$-\overset{\bullet}{\underset{|}{C}}-S\sim$$

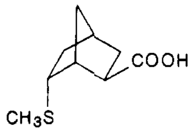
The 410-nm absorption must accordingly be associated (at least kinetically) with the immediate precursor of the 280-nm radical. By analogy to the previously described oxidation product of norbornane endo-acid **5b** (which absorbs at λ_{max} = 390 nm)[21,22] it is assigned to the absorption of the overall neutral radical in which the oxidized sulfur function associates intramolecularly with the carboxylate oxygen, denoted in its most general form as

$$\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$$

(a more detailed discussion on the possible electronic structures is given in the final section of this paper).

Several common features emerge from the investigations of these intramolecular complexes:

(a) They depend on the possibility of a direct interaction of the oxidized sulfur function with the carboxylate group. If, for example, the exo-acid



is oxidized, no such intermediate can be observed.[21,22]

(b) Their absorption maxima are located around 400 nm.

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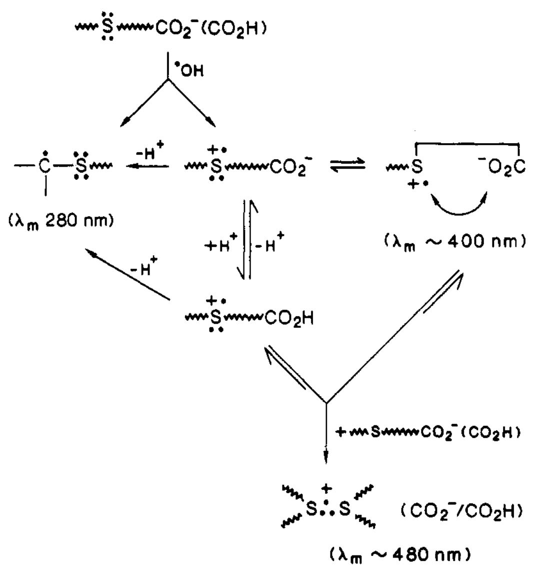
Scheme I



(c) Within the pH range accessible to conductivity measurements, i.e., pH 3–10, they are of overall neutral nature (see Figure 6 and ref 41).

(d) At high solute concentrations they may be converted into the bimolecular S∴S-bonded radical cation. The efficiency of this process differs depending on the inherent stability of the $\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{OOC}}$ interaction (see also Table I and related discussion).

(e) At low pH (<2) the $\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{OOC}}$ species is disfavored and the $(\mathrm{R_2S}\therefore\mathrm{SR_2})^+$ species forms at much lower solute concentrations, e.g., as low as 10^{-4} M. It is reasonable to assume that this change in properties is connected with a protonation process.

All these observations can be accommodated in the general reaction scheme in Scheme I.

Formation kinetics for the intramolecular radical species absorbing at around 400 nm have been evaluated for the reaction of **2**, **4**, and **5b** with $\mathrm{CCl_3OO^\bullet}$ radicals according to eq 2. The results are listed in Table I in terms of second-order rate constants. The observed linear dependence of the first-order rate constant $k = \ln(2/t_{1/2})$ as a function of solute concentration identifies the primary one-electron oxidation as the rate-determining step. The data are therefore directly comparable with the rate constants for the $\mathrm{CCl_3OO^\bullet}$-induced oxidation of the ester derivatives listed also in Table I. It is noted that the rate constants for the oxidation of **2** and **5b** are significantly higher than for the oxidation of **1** and **5a**. For the much slower reaction of **4** with $\mathrm{CCl_3OO^\bullet}$, on the other hand, only an upper limit of 10^6 $\mathrm{M^{-1}\ s^{-1}}$ can be given. Considering that oxidation of a sulfide generally takes place at the sulfur atom, the observed variation in the rate constants must be associated with the influence of the other substituents. The kinetics of the oxidation process therefore serve as another example for neighboring group participation.

The •OH radical induced processes are generally faster than those with $\mathrm{CCl_3OO^\bullet}$ radicals. However, the mechanism is more complex,[25] and assignment of rate constants to a particular step remains ambiguous and, therefore, has not been attempted.

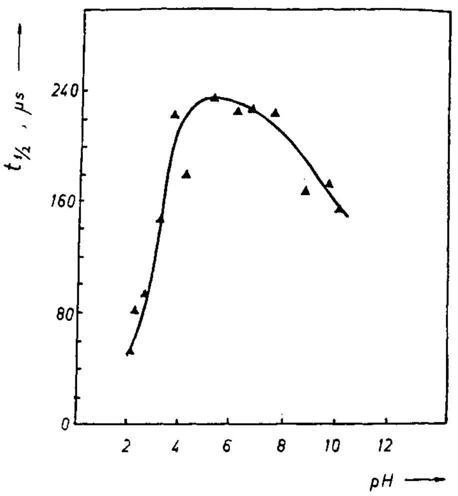


Figure 3. $t_{1/2}$ for the decay of the $(\mathrm{S}\leftrightarrow\mathrm{O})^\bullet$ interaction radical (measured at 390 nm) as a function of pH in pulse-irradiated, $\mathrm{N_2O}$-saturated, aqueous solutions of 10^{-4} M **2**.

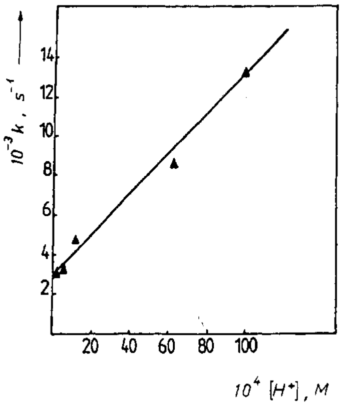


Figure 4. First-order rate constant $[k = \ln(2/t_{1/2})]$ for the decay of the $(\mathrm{S}\leftrightarrow\mathrm{O})^\bullet$ interaction radical (measured at 390 nm) as a function of $[\mathrm{H^+}]$ (conditions as in Figure 3).

3. Stability and Decay of the S–O-Bonded Species. The stabilities of the $\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{OOC}}$ radicals also vary significantly with the nature of the substrate. For example, the half-life for the first-order decay of the corresponding species from **2**, **3**, **4**, and **5b** in $\mathrm{N_2O}$-saturated, pH 3 solution of 10^{-4} M substrate was measured as 100, 5, 270, and 15 μs, respectively. It is not justified, however, to associate these lifetimes solely with the thermodynamic stabilities of the radicals with sulfur–oxygen interaction since kinetic parameters may contribute as well. The latter is in fact indicated by the stability as a function of pH. An example is given in Figure 3 which shows a plot of $t_{1/2}$ for the decay of the $\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{OOC}}$ absorption in pulse-irradiated solutions of 10^{-4} M **2** vs. pH. The decrease in $t_{1/2}$ on the acid side suggests a protonation process which is most likely to occur at the carboxyl group, as shown in eq 3.

$$-\overline{\mathrm{S}^{\bullet+}\leftrightarrow{}^{-}\mathrm{OOC}} + \mathrm{H^+} \rightarrow -\mathrm{S}^{\bullet+}\ \mathrm{COOH} \tag{3}$$

A quantitative assessment of this reaction can be evaluated from Figure 4, which exhibits a plot of $k = \ln 2/t_{1/2}$ vs. $[\mathrm{H^+}]$. From the slope of the straight line a bimolecular rate constant of 9.8×10^5 $\mathrm{M^{-1}\ s^{-1}}$ is derived for reaction 3. The intercept of 3×10^3 $\mathrm{s^{-1}}$ describes a pH-independent process. This could be a protonation by the solvent water although it seems highly unlikely to occur under neutral conditions where even a free carboxyl group is usually fully ionized (the pH of the unoxidized endo-acid is 5.5).[21] This slow process may also be attributed to a deprotonation at a carbon atom in an α-position to sulfur (eq 4), yielding the α-alkylthio radical (which absorbs in the 280-nm range). This may be more likely to occur,

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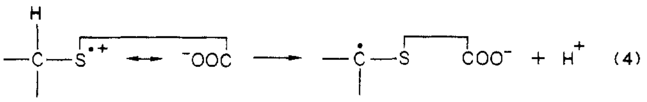
(41) Mahling, S. Ph.D. Thesis, Technical University Berlin, 1986.



$$-\overset{\overset{\text{H}}{|}}{\underset{|}{\text{C}}}-\overline{\text{S}^{\bullet+}\leftrightarrow{}^{-}\text{OOC}} \longrightarrow -\overset{\bullet}{\underset{|}{\text{C}}}-\overline{\text{S}\quad\text{COO}^{-}} + \text{H}^{+} \qquad (4)$$

however, from the open $R_2S^{\bullet+}$-type radical cation formed in reaction 3. Probably, a more reasonable alternative is the dissociation of the sulfur–carboxylate bond (eq 5). In this case the first order rate constant would then be a direct measure of the thermodynamic stability of the sulfur–carboxylate interaction.

$$-\overline{\text{S}^{\bullet+}\leftrightarrow{}^{-}\text{OOC}} \rightarrow -\overline{\text{S}^{\bullet+}\ \ \text{COO}^{-}} \qquad (5)$$

The observed slight decrease in $t_{1/2}$ on the basic side can be attributed to nucleophilic attack by hydroxide ions (eq 6). Either the oxidized sulfur center, or the carboxyl carbon or both may suffer such an attack. An example

$$-\overline{\text{S}^{\bullet+}\leftrightarrow{}^{-}\text{OOC}} + \text{OH}^{-} \xrightarrow{k_6} \text{products} \qquad (6)$$

for such reactions is hydrolysis of acyloxysulfonium salts, $R_2S^{+}OC(O)R$.[42] Whichever pathway is favored, a bimolecular rate constant of $k_6 = \{k(\text{pH } 10) - k(\text{pH } 7)\}/[\text{OH}^-] = [(4.2 - 3.0) \times 10^3]/10^{-4} = 1.2 \times 10^7\ \text{M}^{-1}\ \text{s}^{-1}$ is calculated for this process using the experimental value at pH 10.

A similar pH profile has also been obtained for the decay of the 390-nm absorption from the endo-acid **5b**. The rate constants calculated for this intermediate are $3.0 \times 10^7\ \text{M}^{-1}\ \text{s}^{-1}$ for the protonation of the carboxyl group according to reaction 3, $1 \times 10^4\ \text{s}^{-1}$ for the pH-independent process (reactions 4 or 5), and $0.8 \times 10^7\ \text{M}^{-1}\ \text{s}^{-1}$ for the OH^- induced decay (reaction 6). No such pronounced variations in the decay could be observed for the $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ species from **3** and **4**. The lifetimes of the 400-nm absorptions of these radical species remained more or less constant within the pH 3–10 range. The very high kinetic stability of the transient from the diacid **4** is certainly remarkable and would suggest that the stabilization is possibly caused by an additive Coulombic effect of both carboxylate groups.

It is noted that the rate constants for the proton-assisted decay of the 400-nm absorptions are several orders of magnitude below the diffusion-controlled rate constants for the protonation of a free carboxylate group. These kinetic data serve therefore as direct evidence for the existence of a net bonding between the oxidized sulfur center and the carboxylate group which has to be broken in the protonation process.

4. Temperature Dependence of the Decay Kinetics. The stability of the $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ species showed some temperature dependence which for experimental reasons could, however, only be studied in a limited range from 4 to 30 °C. For example, in N_2O-saturated, pH 8.9 solutions of 10^{-4} M **2** the half-life of the 410-nm transient increased from 232 μs at 18 °C to 397 μs at 5 °C. An Arrhenius plot for the first-order decay rate constant, ln k vs. $1/T$, shown in Figure 5, exhibits a good straight line from which an activation energy of $E_a = 26$ kJ mol^{-1}, and an activation entropy of $\Delta S^{\ddagger} = -90$ J mol^{-1} K^{-1} is calculated. Qualitatively similar data were obtained for the endo-acid **5b**, namely, $E_a = 32$ kJ mol^{-1} and $\Delta S^{\ddagger} = -60$ J mol^{-1} K^{-1}. Estimated error limits are ±20% for E_a and even higher ones for $\Delta S^{\ddagger}$, although the negative sign for the latter seems beyond doubt.

The E_a values may be compared with 59 and 19 kJ mol^{-1} which have been obtained for the dissociation of the $2\sigma/1\sigma^*$ three-electron bond in $(R_2S\therefore SR_2)^+$ radical cations with R = CH_3 and $(CH_3)_2CH$, respectively.[5] In view of the above kinetic discussion it seems reasonable to assign the E_a values for the solutes **2** and **5b** to the breakage of the $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ interaction forces. If one further considers that (a) the "free" oxidized sulfur atom associates with a molecule of water, as shown in eq 7, with a theoretically

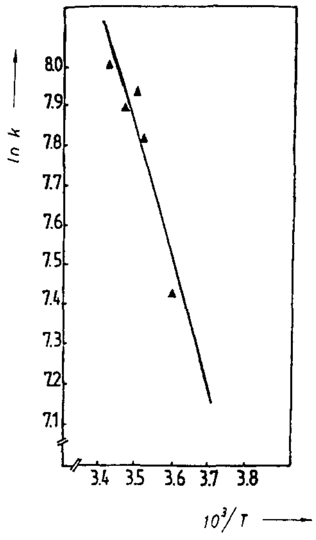


Figure 5. Arrhenius plot on the temperature dependence of the decay of the $(S\leftrightarrow O)^{\bullet}$ interaction radical (N_2O-saturated aqueous solution of 10^{-4} M **2**, pH 8.9; temperature range covered, 5–18 °C).

$$-\text{S}^{\bullet+}- + \text{H}_2\text{O} \rightarrow (>\text{S}^{\bullet}\leftrightarrow\text{OH}_2)^{+} \qquad (7)$$

estimated bond strength of ca. 20 kJ[38,43] and (b) the formation of $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ requires no extra activation energy once the sulfur has been oxidized (see also later discussion) the sum of E_a + 20 kJ mol^{-1} = D could be associated with the total strength of the $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ interaction. Numerically this amounts to $D \approx 45$ kJ mol^{-1} and 50 kJ mol^{-1} for the systems derived from **2** and **5b**, respectively. On the basis of the same considerations the strength of the $S\therefore S$ bond had been calculated to be $D \approx 80$ and 40 kJ mol^{-1} in the radical cations $(Me_2S\therefore SMe_2)^+$ and $(i\text{-}Pr_2S\therefore S\text{-}i\text{-}Pr_2)^+$, respectively.[5] This would mean that the sulfur–carboxylate interaction forces exceed those in $(>S^{\bullet}\leftrightarrow OH_2)^+$ by about a factor of two but are generally smaller than between two sulfur atoms in a three-electron bond unless the latter is substantially weakened by strong electron-releasing substituents (electron release increases the electron density in the antibonding σ^* orbital).

Despite the simlarity in the E_a values for $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ and $(S\therefore S)^+$ bonds a significant difference between these two systems exists with respect to $\Delta S^{\ddagger}$. While this is negative for the former a positive value of $\Delta S^{\ddagger} = +28$ J mol^{-1} K^{-1} had been measured for $(Me_2S\therefore SMe_2)^+$.[5] Thus the transition state in the decay of $\overline{S^{\bullet+}\leftrightarrow{}^{-}OOC}$ is characterized by a higher degree of order. This may be envisaged by a geometry in which the sulfur interacts with both the carboxylate as well as with a solvent water molecule. In addition, even if the sulfur–carboxylate bond were completely broken, both groups would still be linked via the norbornane backbone and lack the translational freedom the two constituents of a dissociated $(R_2S\therefore SR_2)^+$ would have.

It has not been possible to evaluate any such thermodynamic data for the oxidized system of **3**. The low sta-

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(43) Clark T. *J. Comput. Chem.* **1982**, *3*, 112; **1983**, *4*, 404; private communication.

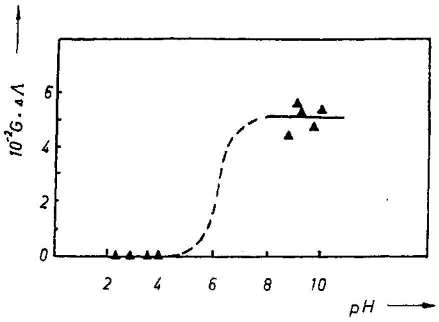


Figure 6. Changes of conductivity as function of pH in pulse-irradiated, N_2O-saturated solutions of N_2O-saturated, aqueous solutions of 10^{-4} M **2**.

bility of the corresponding $\overline{\mathrm{S^{\bullet+}\leftrightarrow{}^{-}OOC}}$ species and its ready conversion into the optically dominating $\mathrm{S\therefore S}$-type radical cation at even low solute concentrations prevents an unambiguous evaluation of meaningful data.

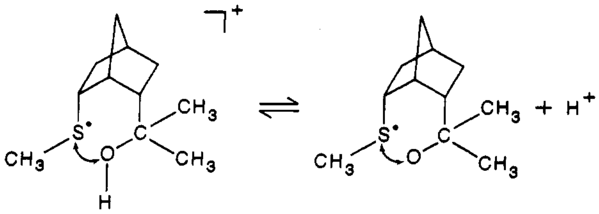
5. Extinction Coefficients. In several cases it has been possible to determine extinction coefficients for the various intra- and intermolecular radical species. The experimental basis has been conductivity measurements and shall briefly be discussed for the •OH induced oxidation of **2**. Figure 6 shows the observed changes in conductance in pulse irradiated N_2O saturated solutions of 10^{-4} M **2** at room temperature. In the acid pH range no net conductivity change occurs. This is compatible with the overall reaction shown in eq 8. The observed increase in conductance at high pH is based on the fact that the original acid is now ionized, as shown in eq 9, and the carboxylate anion ($\Lambda \sim 40\ \Omega^{-1}\ \mathrm{cm}^2$) is replaced by a highly conducting hydroxyl anion ($\Lambda = 180\ \Omega^{-1}\ \mathrm{cm}^{-2}$). As mentioned before, these results serve as evidence for the overall neutral character of the radical species irrespective of pH (any possible charge separation within the radical, i.e., zwitterionic nature does not show up in the conductivity measurements).

$$-\overline{\mathrm{S\ C}}\mathrm{OOH} + {}^{\bullet}\mathrm{OH} \longrightarrow -\overline{\mathrm{S^{+\bullet}\leftrightarrow{}^{-}OOC}} + \mathrm{H_2O} \qquad (8)$$

$$-\overline{\mathrm{S\ C}}\mathrm{OO^-} + {}^{\bullet}\mathrm{OH} \longrightarrow -\overline{\mathrm{S^{\bullet}\leftrightarrow{}^{-}OOC}} + \mathrm{OH^-} \qquad (9)$$

The yield of reaction 9 is calculated to be $G = 3.6$ (species per 100 eV absorbed energy) from the measured change in conductance at pH 9, $G\cdot\Delta\Omega = 505$, and $\Delta\Lambda = 180 - 40 = 140\ \Omega^{-1}\ \mathrm{cm}^2$. From the total optical absorption of $G\cdot\epsilon = 1.16 \times 10^4$ at 410 nm the extinction coefficient is then calculated as $\epsilon = 3220\ \mathrm{M^{-1}\ cm^{-1}}$. This and other extinction coefficients for $\overline{\mathrm{S^{\bullet+}\leftrightarrow{}^{-}OOC}}$ as well as $(\mathrm{R_2S\therefore SR_2})^+$-type species are listed in Table I. It is noted that ϵ for the $\mathrm{S\therefore S}$-bonded systems are higher than those for the sulfur–carboxylate species, with the former corresponding to previous findings on such species.[1,2]

6. Other Radicals with Sulfur–Oxygen Interaction. Intramolecular stabilization of an oxidized sulfur atom by an oxygen-containing function is not restricted to the latter being incorporated into a carboxylate group. As we have shown in previous publications[21,22] the oxidation of the tertiary alcohol **5c** leads to a radical species which exists in an acid base equilibrium, as shown in eq 10. The acidic form absorbs at 400 nm ($\epsilon = {\sim}1200\ \mathrm{M^{-1}\ cm^{-1}}$, $t_{1/2} \sim 40\ \mu$s) and the basic form at 420 nm ($\epsilon = 2000\ \mathrm{M^{-1}\ cm^{-1}}$, $t_{1/2} \sim 200\ \mu$s). In addition to these data we have now determined the dissociation constant for eq 10 to be $K = 1.26 \times 10^{-6}$ M, or pK = 5.9. The underlying pK curve, measured in terms of the optical absorption at 420 nm as a function of pH is shown in Figure 7.



(10)

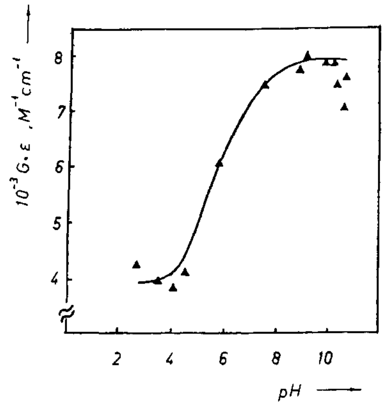
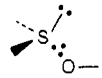


Figure 7. Optical density as function of pH measured at 420 nm in pulse-irradiated, N_2O-saturated, aqueous solutions of 10^{-4} M **5c**.

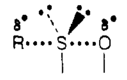
For the present discussion it is noteworthy that compound **5c** is the only one yielding a sulfur–oxygen interaction besides those where the oxidized sulfur is stabilized by a carboxylate group. In the case of the tertiary alcohol this is attributed to a most favorable geometric arrangement where the hydroxyl group is forced toward sulfur by the two bulky methyl groups.[30] The overall rigid norbornane structure is another necessary prerequisite.

It is further noted that the acidity of the hydroxyl group in the radical from **5c** is greatly enhanced over that of the unoxidized alcohol. This can be taken as direct evidence for the sulfur–oxygen interaction. By extrapolation to the corresponding sulfides with carboxylate functions it is now easily understood why the carboxylate group in the $\overline{\mathrm{S^{\bullet+}\leftrightarrow{}^{-}OOC}}$ radicals does not exist in its protonated form in even acid solutions (as shown in a previous section protonation occurs, but it is slow and leads to irreversible destruction of the sulfur–carboxylate interaction).

7. Bonding in Radicals with Sulfur–Oxygen Interaction. Various possibilities must be considered for the bonding in radicals with S–O interaction. These are shown in a–d. Structure a represents three-electron ($2\sigma/1\sigma^*$) two-center bonding between S and O.[2,6,54,55] Generally, relatively stable three-electron ($2\sigma/1\sigma^*$) two-center bonds are formed when the two centers (and perhaps their substituents) are the same and when the three-electron bond is further stabilized by a charge as in $(\mathrm{R_2S\therefore SR_2})^+$, $(\mathrm{R_3N\therefore NR_3})^+$, $(\mathrm{RI\therefore IR})^+$, $(\mathrm{RS\therefore SR})^-$, and $\mathrm{X\therefore X)^-}$ (X = Cl, Br, I, SCN, N_3, etc.).[3,50–53] Stabilization of corresponding electronic structures between two different hetero atoms seems to become increasingly effective the smaller the differences in electronegativity.[14,43] For example, a two-center three-electron (2c,3e) bond between



a



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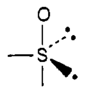

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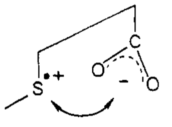

d

sulfur and iodine is very stable but not between sulfur and fluorine, and such a bond is of marginal stability between sulfur and chlorine.[14] On this basis oxygen is not a prime candidate for 2c,3e interaction with an oxidized sulfur atom unless a suitable steric arrangement facilitates p-orbital overlap. This is in accord with our results which have identified rigid five- and six-membered cyclic structures as a necessary prerequisite for an observable sulfur–oxygen stabilization. Structure b takes into account that the unpaired electron could be subject to easy delocalization depending on suitably located energy levels in the MO diagram and may resemble radicals with σ as well as with π character. An example which is probably best characterized by a three-center or perhaps better multicenter arrangement is found in the work of Perkins et al. on the photolysis of *tert*-butyl 2-(methylthio)peroxybenzoate.[19] Steric demands are, however, probably high for such an aligned system. Localization of the unpaired electron at sulfur, finally, is another realistic alternative. This may occur in the form of a typical sulfuranyl radical as depicted in c or in a system with more Coulombic interaction d which may specifically be envisaged for the oxidized thioether acids. The latter appears reasonable in view of the electron delocalization in the carboxylate group. A crude ESR experiment on a γ-irradiated sample of the endo-acid **5b** in a Freon matrix at 77 K indicated $g \sim 2.03$. This high value certainly points toward strong localization of the unpaired electron at sulfur.

Generally, it is probably realistic to view a–d as different geometric structures which may even exist in equilibrium. Which of these electronic situations prevails or describes best certain chemical properties will depend on structural parameters and substitution patterns. The nonspecific $S^{\bullet}\leftrightarrow O$ notation represents this.

Conclusion

From the results presented in this paper and some related earlier investigations a number of general conclusions can be drawn, but also some questions are raised. Our data provide further supporting evidence for the concept of neighboring group participation[22,39,44] and, in fact, clearly establish it now for radical species. The oxidation of the sulfur function in our compounds as well as the properties of the resulting radical species have been demonstrated to depend significantly on the influence of functional groups. However, the latter have to be located in a position suitable for interaction with the sulfur.

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Registry No. **1**, 13532-18-8; **2**, 646-01-5; **3**, 32391-97-2; **4**, 111-17-1; **5a**, 64887-94-1; **5b**, 64887-93-0; **5c**, 109216-48-0.

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A General Treatment of Nucleophilic Chemistry[†]

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A mechanistic model of nucleophilic chemistry has been developed and implemented in the computer program CAMEO. The program can make predictions on the outcome of nucleophilic processes by applying mechanistic reasoning and rules governing competing reactions that are based on literature precedents. The general procedure is divided into four steps: perception of reactive sites, recognition of applicable electron-push mechanisms, evaluation of the mechanisms for each nucleophilic site, and overall analysis of competing pathways. The model and the chemical rules used in these steps are described in this paper. The approach has general utility for synthetic analyses and allows the program to make sophisticated predictions on the outcome of a great variety of nucleophilic reactions.

I. Introduction

CAMEO is an interactive computer program designed to predict the products of organic reactions given starting materials and reaction conditions. It arrives at its predictions largely by mimicking the traditional mechanistic reasoning of chemists. The program is divided into modules which process different classes of reactions. These classes are distinguished primarily by the nature of the intermediates generated during the course of the reactions. They currently cover nucleophilic,[1-5] electrophilic,[6,7] rad-

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