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Thermochemistry of Perthiyl Radicals[1]

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Abstract: Mass spectrometry was used to measure appearance energies for the reaction RSS–*t*-Bu → RSS· + *t*-Bu$^+$ for R = Me, Et, *i*-Pr, and *t*-Bu. The data lead to the heats of formation of perthiyl radicals, RSS·, and hence to S–C bond dissociation energies in disulfides (ca. 54 kcal mol^{-1}) and to S–S bond dissociation energies for the central bonds of tetrasulfides (32.3 ± 1.0 kcal mol^{-1}). The appearance energy method was also used to measure the ionization energy of *t*-BuSS· (8.25 ± 0.08 eV) and the heat of formation of the ion *t*-BuSS$^+$ (195 ± 2 kcal mol^{-1}).

Perthiyl radicals are encountered more often than is generally supposed. In optical absorption and in electron paramagnetic resonance spectroscopy, they have often been misidentified as thiyl radicals[3] and they appear to be important intermediates in the radiolysis and photolysis of disulfide bridges in proteins.[3]

Despite their chemical significance, there is little information on their thermochemistry. That which exists[4] has been assembled by indirect methods involving a number of assumptions. This gives some cause for concern since, as Benson has pointed out,[4] accurate thermochemical data on sulfur-containing radicals are required for a thorough understanding of their involvement in other areas of chemistry, such as those involving coal, oil, and atmospheric pollution.

To combat this problem, we have carried out experiments in mass spectrometry to measure heats of formation and, in one case, the ionization energy of perthiyl radicals. The data obtained lead directly to bond strengths for the sulfur–carbon bonds in disulfides and for the central sulfur–sulfur bond in tetrasulfides.

Experimental Section

Materials. Di-*tert*-butyl disulfide was commercially available and was purified by preparative GC.

Mixed disulfides were prepared following the method of Alonso and Aragona.[5] They were obtained in ca. 98% purity by distillation. The disulfides were characterized as follows: *tert*-butyl methyl disulfide, bp 48–50 °C (18 mm) (yield 83%); mass spectrum m^+/e 134 (p$^+$); NMR ($CDCl_3$) δ 1.34 (9 H, s, *t*-Bu), 2.34 (3 H, s, Me), *tert*-butyl isopropyl disulfide, bp, 60 °C (18 mm) (78%); mass spectrum m^+/e 164 (p$^+$); NMR δ 1.33 (9 H, s, *t*-Bu), 1.32 (6 H, d, Me), 2.97 (1 H, septet, CH); *tert*-butyl ethyl disulfide, bp 50–55 °C (18 mm) (72%); mass spectrum m^+/e 150 (p$^+$); NMR δ 1.40 (9 H, s, *t*-Bu), 2.36 (3 H, t, Me), 2.73 (2 H, q, CH_2).

Di-*tert*-butyl tetrasulfide was prepared by the reported procedure[6] and diethyl tetrasulfide was prepared by a similar route.[6] Thus, a solution of sulfur monochloride (16 g, 0.12 mol), which had been freshly distilled from sulfur, was added dropwise with stirring at 23 °C, under nitrogen, to a solution of ethanethiol (15.5 g, 0.25 mol) in carbon tetrachloride (100 mL). Occasional cooling was required during the addition. The reaction mixture was stirred for a further 12 h. The carbon tetrachloride was evaporated and the residual yellow oil was quickly distilled (bp 76–79 °C (0.5 mm)): yield 37%; mass spectrum m^+/e 186 (p$^+$); NMR (CCl_4) δ 1.6 (3 H, t, Me), 2.9 (2 H, q, CH_2).

All of the materials used in this work were further refined to >99% purity by preparative GC (Varian Aerograph Model 920, 10 ft, $^3/_8$ in. aluminum columns containing SE-30 on 60–80 mesh Chromasorb G support).

Apparatus for Mass Spectrometry. Disulfides were ionized in the gas phase (ca. 10^{-6} torr) by the impact of an electron beam that had been energy resolved (dispersion 0.08 eV) by an electrostatic electron monochromator. The ions were detected by a quadrupole mass spectrometer coupled with a microprocessor data system. The technique has been described in detail elsewhere.[7,8]

Table I. Energies for Reactions 1 and 2 and Heats of Formation of Mixed Disulfides and of Perthiayl Radicals

RSS*t*-Bu	IE(I),[a] eV	AE(2),[a] eV	ΔH_f(RSS*t*-Bu), kcal mol^{-1}	ΔH_f(RSS·),[b] kcal mol^{-1}
MeSS*t*-Bu	8.40	9.08	−26.8	16.4
EtSS*t*-Bu	8.16	9.05	−32.8	10.4
i-PrSS*t*-Bu	8.12	9.08	−39.9	3.3
t-BuSS*t*-Bu	*c*	9.12	−47.8	−4.6

[a] Error ±0.8 eV; 1 eV = 23.069 kcal mol^{-1}. [b] Based on the average value of AE(2) = 9.08 ± 0.04 eV. Relative error ±1.0 kcal mol^{-1}; absolue error ±2.0 kcal mol^{-1}. [c] Parent ion too small to be detected.

Results and Discussion

The thermochemistry of perthiyl radicals was investigated with an appearance energy, AE, technique. A series of disulfides, each containing *tert*-butyl as one of the alkyl groups, was ionized in a mass spectrometer using an energy-resolved electron beam. The minimum energy required for formation of a given ion was determined by detecting the threshold for an ion current at the mass of that ion.

The ionization requiring the lowest energy led to formation of the parent ions of the disulfides, eq 1. The ionization energies for reaction 1, IE(1), are reported in Table I.

$$\text{RSS–}t\text{-Bu} + e \xrightarrow{\text{IE(1)}} \text{RSS–}t\text{-Bu}^+ + 2e \qquad (1)$$

Following ionization to form the parent ion, the most facile fragmentation, as judged by the magnitude of the ion currents, was loss of *tert*-butyl as the carbonium ion, eq 2. This left a

$$\text{RSS–}t\text{-Bu} + e \xrightarrow{\text{AE(2)}} \text{RSS}\cdot + t\text{-Bu}^+ + 2e \qquad (2)$$

perthiyl radical as a second reaction product and thereby formed the basis of a method for the heats of formation of these radicals.

In a typical experiment, the mass spectrometer was set to monitor the current due to the *tert*-butyl carbonium ion (m^+/e 57) and the energy of the ionizing beam was swept repetitively (120 times) in 0.02-eV steps over a 0.8-eV range in the vicinity of ion current onset. These sweeps were stored and analyzed by the microcomputer to evaluate the point of onset. The appearance energy at this threshold, AE(2), is related to the other thermodynamic parameters of interest via eq 3.[9]

$$\text{AE(2)} = \Delta H_f(t\text{-Bu}^+) + \Delta H_f(\text{RSS}\cdot) - \Delta H_f(\text{RSS–}t\text{-Bu}) \qquad (3)$$

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(9) The appearance energy is, in principle, greater than or equal to the terms on the right-hand side of the equation. However, since the lowest energy fragmentation pathway for the disulfide is that described in eq 1, the magnitude of any inequality is almost certainly less than the experimental error involved in the measurement of AE.[10,11]

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Table II. Bond Dissociation Energies for MeSS–R′[a]

R′	ΔH_f(MeSSR′), kcal mol^{-1}	ΔH_f(R′·),[b] kcal mol^{-1}	BDE(MeSS–R′),[c] kcal mol^{-1}
Me	−5.8	34.4	56.6
Et	−11.8	28.0	56.2
i-Pr	−18.9	19.2	54.5
t-Bu	−26.8	9.4	52.6

[a] ΔH_f(MeSS·) = 16.4 kcal mol^{-1}, Table I. [b] Data from ref 14. [c] Relative error ±1 kcal mol^{-1}; absolute error ±2 kcal mol^{-1}.

The values of the appearance energies are reported in Table I. It is immediately clear that the energy required to achieve the fragmentation described in reaction 2 is, within error, the same for all of the disulfides. This implies that the nature of R has no measurable effect on the strength of the S–*t*-Bu bond. The appearance energy for reaction 2 can therefore best be represented by the average of the measurements, i.e., 9.08 ± 0.04 eV.

BDE(RSS–*t*-Bu). With the above information to hand, the homolytic dissociation energy for the S–*t*-Bu bond is easily calculated by introducing the minimum of additional experimental data, eq 3–5. Taking $\Delta H_f(t\text{-Bu}^+)$ = 166.2 kcal mol^{-1} [12] and $\Delta H_f(t\text{-Bu}\cdot)$ = 9.4 kcal mol^{-1} [13] leads to a value of BDE(RSS–*t*-Bu) = 52.6 ± 2.0 kcal mol^{-1}.

$$\text{BDE(RSS–}t\text{-Bu)} = \Delta H_f(\text{RSS}\cdot) + \Delta H_f(t\text{-Bu}\cdot) - \Delta H_f(\text{RSS–}t\text{-Bu}) \quad (4)$$

$$\text{BDE(RSS–}t\text{-Bu)} = \text{AE(2)} - \Delta H_f(t\text{-Bu}^+) + \Delta H_f(t\text{-Bu}\cdot) \quad (5)$$

ΔH_f(RSS·). Heats of formation of the perthiyl radicals themselves were obtained by using the above value of BDE(RSS–*t*-Bu) in eq 4. Clearly, in addition to this piece of data, heats of formation of the mixed disulfides are required. These data can be readily obtained from the heats of formation of the symmetric disulfides, eq 6. The approach used in this equation

$$2\Delta H_f(\text{RSS–}t\text{-Bu}) = \Delta H_f(\text{RSSR}) + \Delta H_f(t\text{-Bu–SS–}t\text{-Bu}) \quad (6)$$

is based on the group additivity method in thermochemistry[17] and is equivalent to assuming that the strength of the S–S bond in the disulfides is independent of the nature of the alkyl groups. Fortunately, three of the required heats of formation of the required symmetric disulfides have been determined experimentally.[18] The remaining value ΔH_f(*i*-Pr–SS–*i*-Pr) was determined from group contributions to be −32.0 kcal mol^{-1}.[17] Substitution of these values into eq 6 and 4 leads to the heats of formation of the mixed disulfides and of the perthiyl radicals, Table I. The value obtained for ΔH_f(MeSS·) is in good agreement with that of 17.3 ± 1.0 kcal mol^{-1} estimated by Benson.[4]

Table III. Bond Dissociation Energies for RSS–SSR[a]

R′	ΔH_f(RS$_4$R),[b] kcal mol^{-1}	BDE(RSS–SSR),[c] kcal mol^{-1}
Me	+0.10	32.9
Et	−11.0	31.8
i-Pr	−25.4	32.0
t-Bu	−41.6	32.4

[a] Values for ΔH_f(RSS·) taken from Table I. [b] From group contributions, ref 4 and 17. [c] Relative error ±1 kcal mol^{-1}; absolute error ±2 kcal mol^{-1}.

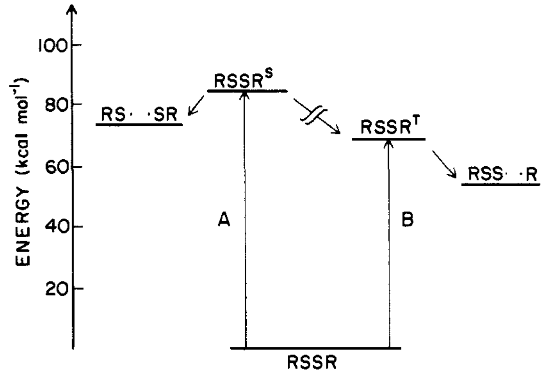

Figure 1. Photochemistry of disulfides: (A) direct photolysis; (B) sensitized photolysis by triplet benzophenone.

BDE(RSS–R′). The constancy of the appearance energies for the fragmentation of the mixed disulfides, eq 2, led to the conclusion that the nature of R had essentially no influence on BDE(RSS–R′). However, it is reasonable to expect that this bond dissociation energy will depend upon the nature of the group, R′, which is linked directly to the bond being broken. We have calculated the effect of substitution using eq 7 for R = Me and

$$\text{BDE(RSS–R}') = \Delta H_f(\text{RSS}\cdot) + \Delta H_f(\text{R}'\cdot) - \Delta H_f(\text{RSSR}') \quad (7)$$

R′ = Me, Et, *i*-Pr, and *t*-Bu. The results are given in Table II. Despite the fact that the combined error limits are large, compared to the differences in bond dissociation energies, there appears to be a trend in the expected direction, i.e., that the bond becomes weaker in the direction R′ ≡ primary to R′ ≡ tertiary.

BDE(RSS–SSR). Heats of formation of the perthiyl radicals can be combined with those of the corresponding tetrasulfides to yield BDE(RSS–SSR). The values, reported in Table III, are nearly identical and are close to the value of 33.6 ± 2 kcal mol^{-1} recommended by Benson[4] who reassessed the measured 36.6 kcal mol^{-1} obtained in a study of the thermolysis of dimethyl sulfide.[19] The basis for the reassessment was that the value reported for the *A* factor of the reaction was unreasonably high. The interpretation would seen to be justified in the light of our own measurements.

To confirm the above conclusion that the strength of the central S–S bond in the tetrasulfides is quite independent of the nature of R, we measured the rate constants for thermolysis of di-*tert*-butyl and diethyl tetrasulfides in carefully matched experiments.

Deoxygenated solutions of the tetrasulfides (0.12 M) in toluene containing di-*tert*-butyl nitroxide (0.014 M) were heated at 100 °C. The nitroxide functioned as a radical trap,[19] eq 8 and 9, and

$$\text{RSS–SSR} \xrightarrow{\Delta} 2\text{RSS}\cdot \quad (8)$$

$$\text{RSS}\cdot + (t\text{-Bu})_2\text{NO}\cdot \rightarrow \text{RSS–ON}(t\text{-Bu})_2 \quad (9)$$

the rate of tetrasulfide thermolysis was monitored by the disappearance of the nitroxide spectrophotometrically at 458 nm. The observed rate constants are equal to $2kf$, where f is the fraction of radical pairs that excape the solvent cage after S–S bond homolysis.[19] The observed values of $2k_8f$ were (1.7 ± 0.3) × 10^{-4} s^{-1} (t-BuS$_4t$-Bu) and (2.0 ± 0.3) × 10^{-4} s^{-1} (EtS$_4$Et). They are clearly the same, within experimental error, but were slightly different to the value of 4.5 × 10^{-4} s^{-1} (100 °C) previously reported for MeS$_4$Me.[19] The results support the conclusion, drawn from the appearance energy measurements, that the strength of the S–S bond in tetrasulfides is independent of the nature of R.

IE(*t*-BuSS·). The ionization potential of the *tert*-butyl perthiyl radical was measured by thermolyzing a sample of the tetrasulfide in a quartz furnace attached to the mass spectrometry apparatus, reaction 8. The RSS· radicals were ionized to give RSS$^+$, and the appearance energy for this process, which is equivalent to the

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ionization energy, IE, of the radical was found to be 8.25 ± 0.08 eV, eq 10 and 11. Taking $\Delta H_f(t\text{-BuSS}\cdot) = -4.6$ kcal mol^{-1} (Table I) leads to $\Delta H_f(t\text{-BuSS}^+) = 195 \pm 2$ kcal mol^{-1}.

$$\text{RSS}\cdot + e \xrightarrow{\text{IE}(10)} \text{RSS}^+ + 2e \qquad (10)$$

$$\text{AE}(10) = \Delta H_f(\text{RSS}^+) - \Delta H_f(\text{RSS}\cdot) = \text{IE}(\text{RSS}\cdot) \qquad (11)$$

Disulfide Photochemistry. One of the most interesting photochemical properities of dialkyl disulfides is that direct irradiation predominantly cleaves the S–S bond (BDE = 74 ± 2 kcal mol^{-1})[4] even though it is some 20 kcal mol^{-1} stronger than the S–C bond (Table II). By contrast, triplet-sensitized photolysis cleaves the weaker S–C bond.[3,20,21] Presumably, the singlet excited states of dialkyl disulfides are dissociative so that fragmentation to give two alkylthiyl radicals is faster than intersystem crossing to the triplet state. The latter must be lower lying than the singlet since it can be accessed by sensitization using benzophenone, for which the triplet energy (69 kcal mol^{-1})[22] is less than the S–S bond strength (Figure 1).

Summary

The energy required to fragment a series of mixed disulfides (RSS–*t*-Bu) to give RSS· and *t*-Bu$^+$ was found to be independent of the nature of R. Measurements of these appearance energies led to data for the heats of formation of perthiyl radicals, S–C bond dissociation energies in disulfides, and S–S bond dissociation energies for the central bond in tetrasulfides. Thermolysis of di-*tert*-butyl tetrasulfide in the mass spectrometer provided a source of *t*-BuSS· perthiyl radical, allowing measurement of its ionization energy.

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Cyclodextrin Inclusion Complexes of 1-Pyrenebutyrate: The Role of Coinclusion of Amphiphiles

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Abstract: Several inclusion complexes with various stoichiometries are formed from 1-pyrenebutyrate ion (P) and the different cyclodextrins (α-, β-, and γ-CD). With α- and β-CD, the initially formed 1:1 complexes lead to the formation of 1:2 complexes ($\text{P}\cdot\alpha_2$ and $\text{P}\cdot\beta_2$). As P can be only partially included in the small cavity of α-CD, the equilibrium constants for the formation of both complexes of α-CD are about an order of magnitude smaller than those of β-CD. For the same reason, $\text{P}\cdot\beta_2$, to which we assign a "barrel" configuration, is also an order of magnitude more effective than $\text{P}\cdot\alpha_2$ in protecting singlet-excited P against quenching by triethanolamine. We had shown earlier that with γ-CD the 1:1 complex ($\text{P}\cdot\gamma$) dimerizes to a 2:2 complex ($\text{P}_2\cdot\gamma_2$), to which we also assigned a barrel configuration. The lack of efficient 1:2 complex formation in this case is attributed to the large size of the "barrel" enclosed by two γ-CD molecules. The extra space next to a single P molecule in such a cavity would have to be filled with water. However, the formation of a 1:2 inclusion complex between P and γ-CD can be induced by the coinclusion of a molecule with a hydrophobic moiety such as sodium hexanesulfonate (X). This replaces the water within the cavity and leads to the formation of $\text{P}\cdot\text{X}\cdot\gamma_2$. This complex provides the highest degree of protection against quenching of excited P in these inclusion complexes.

Cyclodextrins (CD's) are cyclic oligosaccharides that form inclusion complexes with appropriate guest molecules. The smallest of these molecules, α-CD, consists of six glucose units and has a cavity diameter of 5.7 Å. The next higher homologues, β-CD with seven glucose units and γ-CD with eight glucose units, have cavity diameters of 7.8 and 9.5 Å, respectively.[1] Because all hydroxyl groups are on the exterior of these nearly cylindrical molecules, their cavities present hydrophobic environments. It is this property that enables CD's to extract, hold, and protect hydrophobic molecules from aqueous solutions.

The alteration of photophysical properties through CD inclusion is the subject of much current research. Because of its long fluorescence lifetime, we find the pyrene moiety to be an attractive probe for such studies. A number of studies have been based on molecular pyrene, but consistency of results among different investigators is lacking.[2-4] For example, one study of the pyrene/β-CD system reports both 1:1 and 2:2 complexes together with time-dependent shifts ("aging" effects),[2] whereas two other studies report only 1:1 complexes.[3,4] For the weakly interacting combination of pyrene and α-CD, the source of disagreement was whether pyrene or a pyrene dimer undergoes hydrophobic interactions with the exterior surface of α-CD.[3,4] Most likely many of these inconsistencies are traceable to the low solubility limit (1.6×10^{-6} M) of pyrene in water; even at an intended concentration of 5×10^{-7} M in water, excimer fluorescence, attributed to pyrene microcrystals, is observed.[2] As shown recently, unless special precautions are taken in sample preparation, attempted dissolution of pyrene in water even below the solubility limit may lead to microcrystal formation or adherence to glass surfaces, with consequent unreliable solution concentrations of pyrene.[5]

Even with the water-soluble 1-pyrenesulfonate, several investigators report inconsistent results.[3,6,7] We chose to work instead with water-soluble sodium 1-pyrenebutyrate (P), because it has

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