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Articles

Conformations and Stereodynamics of Disulfide Radical Anions Generated by Photoreaction of Aliphatic Thiols

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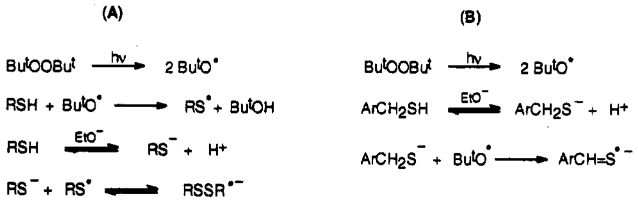
Photolysis of alkyl thiols (RSH) in alkaline solutions yields the corresponding disulfide radical anions ($RSSR^{\bullet-}$) whose EPR spectra can be detected over a large temperature range. When mixtures of two different thiols are photolyzed (RSH and R′SH) each of the three possible disulfide radical anions are observed, i.e., $RSSR^{\bullet-}$, $R'SSR^{\bullet-}$, and $R'SSR'^{\bullet-}$. In the case of the allylthiol ($CH_2=CHCH_2SH$) both the corresponding disulfide radical anion and the thioaldehyde radical anion ($CH_2=CHCH=S^{\bullet-}$) are simultaneously obtained, the latter exhibiting two rotational conformers due to the restricted rotation about the C–CS bond. Dilute solutions of dithiols yield the cyclic disulfide radical anions: line shape analysis of the EPR spectra of the 5- and 6-membered ring derivatives allowed us to measure the activation parameters for a ring reversal process corresponding to the exchange between the two possible conformational enantiomers ($\Delta G^* = 4.7_5$ and 5.8 kcal mol^{-1}, respectively). A detailed analysis of the EPR line width of the linear disulfides of the type $RCH_2SSCH_2R^{\bullet-}$ (R = Me, Bu^t) reveals the existence of diastereotopic methylene hydrogens, thus indicating that the CSSC dihedral angle is not planar. Accordingly, the linear radicals $RSSR^{\bullet-}$ must exist as racemic mixtures of pairs of conformational enantiomers.

Introduction

The reaction between oxygen-containing radicals and certain thiols of biological interest, such as glutathione, is a process which is used by cells as one way of obtaining protection against oxidative stress. Such a process is often referred to as "thiol pumping", and the key step is believed[2] to be the transformation of the thiol function into a transient disulfide radical anion. In a preliminary paper[3] we have reported that disulfide radical anions can be detected in the course of photochemical reactions. Low-temperature photolysis of alkaline solutions of simple aliphatic thiols, particularly in the presence of di-*tert*-butyl peroxide, yields intense signals when carried out in the cavity of an EPR spectrometer. Such a chemical process thus mimics the situation which is believed to occur in a biological environment. These experimental conditions only require minute amounts of reactants; thus, the method is more widely applicable than the flow technique previously employed[2,4] to detect a few selected disulfide radical anions. Furthermore, the radicals generated in this way can be studied in a relatively large temperature range, making possible the investigations of their temperature-dependent conformational behavior.

A few simple aliphatic thiols (RSH, with R = Me, Et, Pr^i, Bu^t) were investigated with this technique, and the spectral parameters of the resulting disulfide radical anions 1–4 ($RSSR^{\bullet-}$, with R = Me, Et, Pr^i, Bu^t, respectively) have been reported.[3] The values of the isotropic *g* factors lie in the range 2.0126–2.0134 and agree well with the anisotropic components ($g_x = g_y = 2.020$, $g_z = 2.002$) of the *g* factors reported by Symons *et al.*[5] for the solid-state EPR spectra of some disulfide radical anions generated by γ-irradiation of proteins containing S–S linkages.

Scheme I



In the case of thiols having an aromatic ring bonded to the α-carbon (i.e., $ArCH_2SH$, where Ar = phenyl, furyl, thienyl) the same general procedure yielded the radical anions of the corresponding thioaldehydes ($ArCH=S^{\bullet-}$).[6,7]

The proposed mechanisms for the formation of the disulfide radical anions (pathway A) and of the thioaldehyde radical anions (pathway B) are given in Scheme I.

In contrast to aliphatic thiols, which react according to pathway A of Scheme I, the arylmethanethiols ($ArCH_2SH$) undergo H-abstraction from the CH_2 group of thiolates (pathway B) more readily than from the SH moiety, thus yielding the corresponding aromatic thioaldehyde radical anions.

Indeed, Davies and Neville have shown[8] that also in the case of alkyl thiols RCH_2SH one obtains the corresponding

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[1] In partial fulfillment of the requirements for the Ph.D. Thesis in Chemical Sciences of the University of Bologna.

[2] Rao, D. N.; Fischer, V.; Mason, R. P. *J. Biol. Chem.* **1990**, *265*, 844.

[3] Cremonini, M. A.; Lunazzi, L.; Placucci, G. *J. Chem. Soc., Perkin Trans. 2* **1992**, 451.

[4] Gilbert, B. C.; Laue, H. A. H.; Norman, R. O. C.; Sealy, R. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 892.

[5] Rao, D. N. R.; Symons, M. C. R.; Stephenson, J. M. *J. Chem. Soc., Perkin Trans. 2* **1983**, 727.

[6] Casarini, D.; Lunazzi, L.; Placucci, G.; Ishida, T.; Ishii, A.; Okazaki, R. *J. Org. Chem.* **1988**, *53*, 1582.

[7] Borghi, R.; Cremonini, M. A.; Lunazzi, L.; Placucci, G.; Macciantelli, D. *J. Org. Chem.* **1991**, *56*, 6337.

[8] Davies, A. G.; Neville, A. G. *J. Chem. Soc., Perkin Trans. 2* **1992**, 171.

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aliphatic thioaldehyde radical anions, if all of the thiol is converted to thiolate (i.e., when the equilibrium in the third equation of Scheme IA is completely shifted to the right). By photolyzing pure alkyl thiolates ($RCH_2S^- Na^+$) they forced the reaction to follow pathway B.

It should also be mentioned that we could obtain both aliphatic disulfide and aromatic thioaldehyde radical anions also *without* the use of Bu^tOOBu^t, albeit in a much lower yield as judged from the lower intensity of the corresponding EPR spectra. In the absence of Bu^tOOBu^t, the hydrogen atom abstractor is probably the corresponding thiyl radical formed by direct photolysis[9,10] of the thiol. Since thiyl radicals are known[9-11] to be less active H-abstractors than $Bu^tO^\bullet$, the lower efficiency of radical formation is readily accounted for.

Results and Discussion

Diallyl Disulfide Radical Anion. The foregoing observations suggested to us that it should be interesting to explore the behavior of allyl thiol $CH_2{=}CHCH_2SH$, since the vinyl moiety has a conjugative ability lower than that of phenyl but higher than that of an alkyl group. As a consequence, allyl thiol might react by pathway A or by pathway B. In the event, it reacted by both routes, simultaneously yielding the EPR spectrum of $(CH_2{=}CHCH_2S)_2^{\bullet-}$, **5**, and of $CH_2{=}CHCH{=}S^{\bullet-}$, **6**, as shown in Figure 1 (the spectral parameters used for the computer simulations are collected in Table I). Radical **6** had also been reported by Davies and Neville,[8] using the thiolate. Under their conditions,[8] however, only one of the two possible rotamers (due to the restricted rotation around the C–CS bond) was observed,[12] whereas in our case, both are clearly visible (Figure 1).

When Bu^tOOBu^t is employed, the proportion of the two radicals, **5** and **6**, was 55:45. In the absence of this peroxide the disulfide radical **5** was essentially the only visible species. This is to be expected because thiyl radicals (here $CH_2{=}CHCH_2S^\bullet$) are less efficient[9-11] H-abstractors than $Bu^tO^\bullet$ and thus prefer to couple with the thiolate ($CH_2{=}CHCH_2S^-$) to yield radical **5** rather than abstract a hydrogen atom from the CH_2 group in the same thiolate to give the thioaldehyde radical anion **6**.

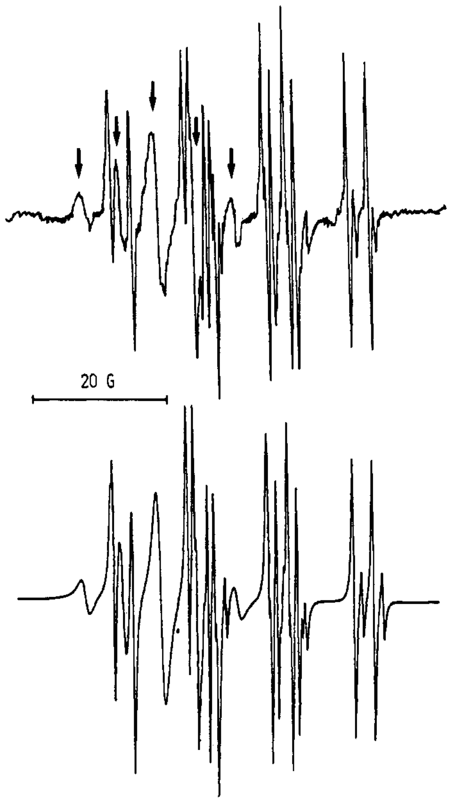

Figure 1. Experimental (top) and computer-simulated (bottom) EPR signals of the radicals obtained by photolysis of the allylthiol $CH_2{=}CHCH_2SH$. The five broader lines (marked by arrows) belong to the corresponding disulfide radical anion **5**. The sharper lines are those of the two *E,Z* rotational isomers (due to restricted C–CS rotation) of the corresponding thioaldehyde radical anion **6** ($CH_2{=}CHCH{=}S^{\bullet-}$).

Table I. EPR Parameters for Radicals 5 and 6 Obtained by Photolysis of Allyl Thiol at −30 °C. Radical 6 Displays Two Spectra for the Two Rotational Conformers (ratio 4:1) Due to Restricted C–CS Rotation

radical	proportion (%)	hyperfine splittings (a_H in G)	*g* factor
5	55	5.5 (4 H)	2.0126
6	36	12.0 (1H); 11.6 (1H); 10.7$_5$ (1H); 2.9 (1H)	2.0052$_5$
	9	13.5 (1H); 11.5 (1H); 11.0 (1H); 3.0 (1H)	2.0049$_5$

Table II. Hyperfine Splitting Constants (a_H) for Disulfide Radical Anions Obtained by Photolyzing Equimolecular Mixtures of the Thiols Indicated

reacting thiols	disulfide radical anions	rel amt (%)	a_H (G)
MeSH + EtSH	$MeSSMe^{\bullet-}$ (**1**)	45	5.25 (6H)
	$MeSSEt^{\bullet-}$ (**7**)	40	5.25 (3H); 6.0 (2H)
	$EtSSEt^{\bullet-}$ (**2**)	15	6.0 (4H)
EtSH + Pr^iSH	$EtSSEt^{\bullet-}$ (**2**)	60	6.0 (4H)
	$Pr^iSSEt^{\bullet-}$ (**8**)	35	6.25 (2H); 5.25 (1H)
	$Pr^iSSPr^{i\bullet-}$ (**3**)	5	5.25 (2H)
MeSH + Bu^tSH	$MeSSMe^{\bullet-}$ (**1**)	85	5.25 (6H)
	$Bu^tSSMe^{\bullet-}$ (**9**)	15	5.75 (3H)
Pr^iSH + Bu^tSH	$Pr^iSSPr^{i\bullet-}$ (**3**)	80	5.25 (2H)
	$Bu^tSSPr^{i\bullet-}$ (**10**)	20	5.75 (1H)

Nonsymmetric Disulfide Radical Anions. In order to confirm the occurrence of a coupling reaction between thiolates and thiyl radicals, we carried out the reaction starting with two different thiols, RSH and R′SH, which should yield all three possible radical anions, namely $RSSR^{\bullet-}$, $R'SSR^{\bullet-}$, and $R'SSR'^{\bullet-}$. Furthermore, if the group R′ is significantly bulkier than R, a lower proportion of $R'SSR'^{\bullet-}$ would be expected because of steric hindrance to coupling. This expectation was fulfilled. Thus, reaction of a 1:1 molar mixture of MeSH and EtSH gave the three radicals $MeSSMe^{\bullet-}$ (**1**), $MeSSEt^{\bullet-}$ (**7**), and $EtSSEt^{\bullet-}$ (**2**) in proportions of 45:40:15 (Table II). When EtSH was reacted with Pr^iSH (always in a 1:1 ratio) the difference in the relative amounts was even larger, with the bulkiest

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[9] (a) Pryor, W. A.; Golon, G.; Church, D. F. *J. Org. Chem.* **1978**, *43*, 793. (b) Lunazzi, L.; Placucci, G.; Grossi, L. *J. Chem. Soc., Chem. Commun.* **1979**, 573. (c) Lunazzi, L.; Placucci, G.; Grossi, L. *Tetrahedron* **1983**, *39*, 159. (d) Griller, D.; Simoes, J. A. M. In *Sulfur Centered Reactive Intermediates in Chemistry and Biology*; Chatgilialoglu, C., Asmus, K.-D., Eds.; Plenum Press: New York, 1990; p 327.

[10] (a) Von Sonntag, C.; Schuchmann, H.-P. In *The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Sulfur Analogues*; Patai, S., Ed.; J. Wiley and Sons: New York, 1980; Part 2, Suppl. E. p 923. (b) Von Sonntag, C. In *Sulfur Centered Reactive Intermediates in Chemistry and Biology*; Chatgilialoglu, C., Asmus, K.-D., Eds.; Plenum Press: New York, 1990; p 359.

[11] Grossi, L.; Lunazzi, L.; Placucci, G. *Tetrahedron Lett.* **1982**, *22*, 252.

[12] Also, the EPR parameters of ref 8 are different from ours, having a slightly lower value for the *g* factor and slightly higher values for the three large a_H splittings. This is due to the different environments employed, as proved by the fact that we could repeat the results of ref 8 using the same conditions.

Table III. Relative Amounts (Expressed as a Percent) of the Radical Anions 2, 8, and 3 Obtained on Varying the Molar Ratios of the Reacting Alkyl Thiols EtSH and Pr^iSH

EtSH:Pr^iSH	$EtSSEt^{\bullet-}$ (2)	$EtSSPr^{i\bullet-}$ (8)	$Pr^iSSPr^{i\bullet-}$ (3)
1:0.3	84	16	
1:1	60	35	5
1:5	24	43	33
1:10	9	27	64

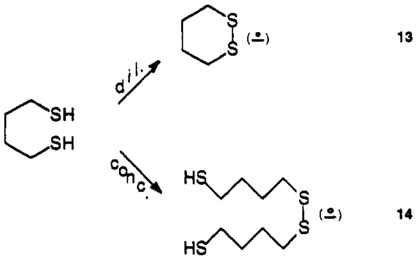
radical, $Pr^iSSPr^{i\bullet-}$ (3) now barely observable (5%) with respect to $EtSSPr^{i\bullet-}$ (8) and $EtSSEt^{\bullet-}$ (2) which were formed to the extent of 35% and 60%, respectively. It is the $EtSSEt^{\bullet-}$ radical, which was the bulkiest of the three possible radicals in the MeSH/EtSH reaction, that has now become the least hindered radical, and accordingly it is now formed in the largest rather than in the smallest amount.

The $Bu^tSSBu^{t\bullet-}$ radical (4) is quite short lived because it readily dissociates, shifting the equilibrium of the last equation of pathway A of Scheme I to the left. This is consistent with reports[13] that the strength of the S–S bond in 4 is lower than in radicals 3, 2, and 1, respectively. As a consequence, Bu^tSH is a most useful reactant to produce nonsymmetric disulfide radical anions, since the single EPR line[3] of radical 4 soon disappears and the EPR traces due to the superposition of the other two radicals are left behind. For instance, the reaction of a 1:1 molar mixture of Bu^tSH and Pr^iSH affords, in addition to the symmetric $Pr^iSSPr^{i\bullet-}$ radical 3, the nonsymmetric $Bu^tSSPr^{i\bullet-}$ radical 10 (Table II).

Experiments using different molar ratios of two reacting thiols (e.g., EtSH and Pr^iSH) allow a further check of the coupling reaction mechanism. For it is expected that an excess of EtSH will mainly yield the radical $EtSSEt^{\bullet-}$ (2), its proportion regularly decreasing on increasing the relative amount of Pr^iSH in the mixture. The opposite trend is expected for the radical $Pr^iSSPr^{i\bullet-}$ (3). Furthermore, it is also predictable that the radical resulting from the reaction of EtSH and Pr^iSH, i.e., $EtSSPr^{i\bullet-}$ (8), will initially increase its proportion on increasing the relative amount of Pr^iSH, until a certain maximum value is reached: once this maximum has been attained, further addition of Pr^iSH is expected, on the contrary, to reduce the proportion of $EtSSPr^{i\bullet-}$. These predictions have been fulfilled, as shown in Table III where the relative amount of the radical anions has been reported as function of the EtSH/Pr^iSH molar ratio, in the range 1:0.3–1:10. In particular, it has been found that the maximum amount (~45%) of $EtSSPr^{i\bullet-}$, 8, is obtained when a 1:5 EtSH/Pr^iSH ratio is employed.[14]

Conformation of Cyclic Disulfide Radical Anions. The results presented so far imply that dithiols should yield two different radical anions since the reaction can be either intra- or intermolecular to yield a cyclic or a linear radical, respectively. By varying the concentration of the dithiols it should be possible to favor one or other of the two possibilities. Indeed, when 1,4-butanedithiol $HS(CH_2)_4SH$ was photolyzed in concentrated solutions (see Experimental Section), the spectrum of the linear disulfide radical 14 was obtained, superimposed on that of the 6-membered cyclic radical 13 (1,2-dithiane radical anion). Dilute solutions (see Experimental Section) only gave the spectrum of 13 (Scheme II). The spectrum of 14 displays a quintet, due to four methylene hydrogens, with an a_H value (6.2 G) similar to that of $EtSSEt^{\bullet-}$ (2). On the contrary, when 1,3-propanedithiol $HS(CH_2)_3SH$ is employed, only the spectrum corresponding to the 5-membered cyclic (1,2-dithiolane) radical anion 11 could be observed, there being no trace of the linear disulfide radical 12, $HS(CH_2)_3SS(CH_2)_3SH^{\bullet-}$. Likewise, the 1,5-pentanedithiol yields the seven-membered ring radical[15] with a splitting $a(4H) = 6.4$ G.

Scheme II



On varying the temperature the EPR spectra of both the 5- and 6-membered disulfide radical anions (11 and 13, respectively) display line width alternation, a feature indicating the occurrence of a dynamic ring reversal process which allows the exchange between two conformational enantiomers. At −70 °C the spectra of these radicals show different a_H splittings (Table III) for the pair of pseudoaxial and pseudoequatorial methylene hydrogens of the SCH_2 moieties. In the case of the 6-membered radical 13, for instance, these values are 3.0 and 9.3 G; however, on raising the temperature to −5 °C a single averaged value (6.1 G.), corresponding to four equivalent hydrogens, is observed. Computer line shape simulation (Figure 2) yields the free energy of activation ($\Delta G^* = 5.8$ kcal mol^{-1}) and the other thermodynamic parameters (Table IV) for the ring reversal process. In an analogous way the corresponding parameters for the ring reversal process of the 5-membered radical 11 were obtained (Table IV): in the case of the latter the barrier is about 1 kcal mol^{-1} lower than for 13 ($\Delta G^* = 4.7_5$ kcal mol^{-1}).

In these radicals the a_H values for the pseudoaxial and pseudoequatorial hydrogens depend upon the dihedral angle θ made by the corresponding C–H bond and the direction of the orbital bearing the unpaired electron, according to the McConnell equation $a_H = A + B\cos^2\theta$ (where the term A is quite small and is usually neglected).[16] The radical anions of disulfides are believed[13,17,18] to have a three-electron S–S bond ($2\sigma/1\sigma^*$), analogous to that

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[13] (a) Goebl, M.; Bonifacic, M.; Asmus, K.-D. *J. Am. Chem. Soc.* **1984**, *106*, 5984. (b) Asmus, K.-D. In *Sulfur Centered Reactive Intermediates in Chemistry and Biology*; Chatgilialoglu, C., Asmus, K.-D., Eds.; Plenum Press: New York, 1990; p 155.

[14] One of the reviewers suggested the possibility that the observed radicals had the structure $RSOEt^{\bullet-}$, due to the reaction of $RS^\bullet$ with EtO^-. This possibility is, however, at variance with the observation that the radicals obtained using MeSH, Pr^iSH, or Bu^tSH (i.e, 1, 3, 4) do not display the spectral multiplicity corresponding to the a_H splitting due to the methylene hydrogens of the EtO moiety.

[15] A similar seven-membered cyclic disulfide radical anion has been recently reported by Gilbert *et al.* using conditions analogous to ours. See: Coates, R. J.; Gilbert, B. C.; Lee, T. C. P. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1387. On the contrary, all the attempts to obtain EPR spectra of disulfide radical anions by chemical (Li, Na, or K mirrors) or electrochemical reduction of the corresponding disulfides were unsuccessful in our hands.

[16] (a) Heller, C.; McConnell, H. M. *J. Chem. Phys.* **1960**, *32*, 1535. (b) Lunazzi, L.; Placucci, G.; Grossi, L. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1063. (c) Lunazzi, L.; Placucci, G.; Grossi, L.; Guerra, M. *J. Chem. Soc., Perkin Trans. 2* **1982**, *42*. (d) Guerra, M. *J. Am. Chem. Soc.* **1992**, *114*, 2077.

[17] (a) Naito, A.; Akasaka, K.; Hatano, H. *Chem. Phys. Lett.* **1975**, *32*, 247. (b) Symons, M. C. R. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1618. (c) Nelson, D. J.; Petersen, R. L.; Symons, M. C. R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 2005 and **1978**, 225.

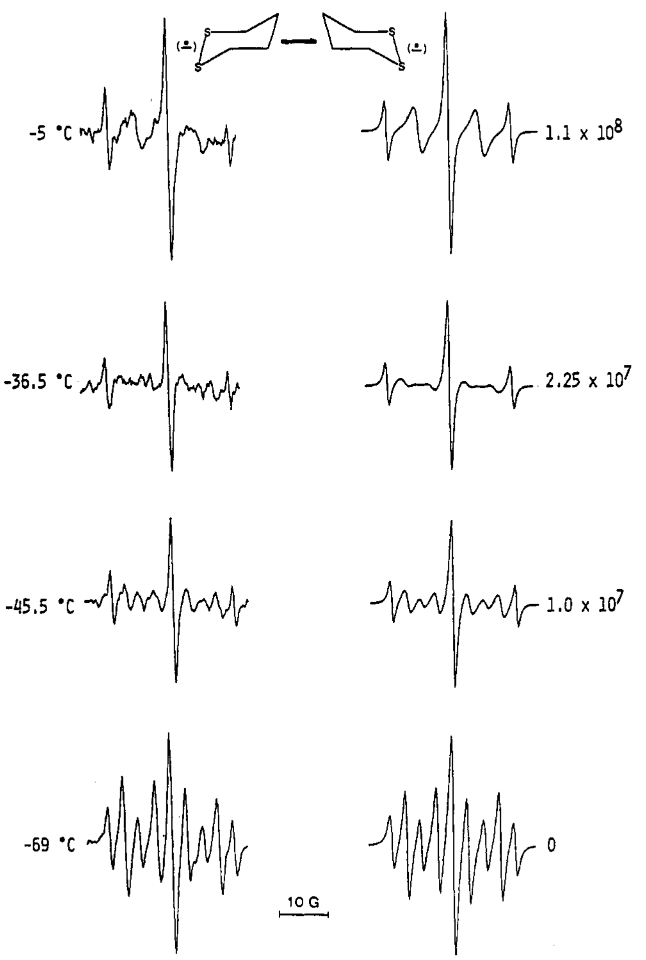


Figure 2. Experimental (left) EPR spectra of the radical anion of 1,2-dithiane **13** at various temperatures, showing the line broadening due to the exchange between the two conformational enantiomers indicated. On the right hand side are reported the spectra computed with the appropriate rate constants (k, in s^{-1}) yielding a ΔG^* value of 5.8 kcal mol^{-1}.

Table IV. Spectral and Activation Parametres for the Radical Anions 11 and 13 (EPR Spectroscopy) and for 1,2-Dithiane (NMR Spectroscopy)

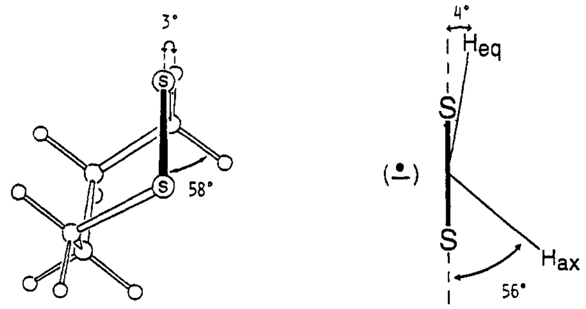
compd	a_H[a] (G)	ΔG^* (kcal mol^{-1})	ΔH^* (kcal mol^{-1})	ΔS^* (cal mol^{-1} T^{-1})
radical 11	12.4 (2H)$_{3.5\ eq}$ 0.65 (2H)$_{3.5\ ax}$ 1.25 (2H)$_4$	$4.7_5 \pm 0.1_5$	5.5 ± 0.7	3 ± 3
radical 13	9.35 (2H)$_{3.6\ eq}$ 3.0 (2H)$_{3.6\ ax}$	$5.8 \pm 0.1_5$	6.5 ± 0.7	3 ± 3

compd	$\Delta\nu$[b] (Hz)	ΔG^* (kcal mol^{-1})	ΔH^* (kcal mol^{-1})	ΔS^* (cal mol^{-1} T^{-1})
1,2-dithiane	57.5	11.9 ± 0.1	12.4 ± 0.6	2 ± 2

[a] EPR hyperfine splitting constants at −70 °C. [b] Chemical shift difference for axial and equatorial hydrogens in positions 3,6 at 200 MHz (−60 °C).

described[13,17-20] for the isostructural cation ($R_2SSR_2^{•+}$) and the neutral ($R_2SSR^•$) radicals. The unpaired electron thus resides in the $1\sigma^*$ antibonding orbital, whose direction is essentially parallel[17a] to that of the S–S bond. Since two experimental a_H values are available for both **11** and **13**, two independent McConnell equations can be used to simultaneously obtain the term B and the θ angle for the equatorial hydrogens (since for the axial hydrogen the relationship $\theta_{ax} = 60 - \theta_{eq}$ is obeyed[16b]). Solution of the two equations in the case of **13** yields[21] $B = 9.5$ G and $\theta_{eq} = 4°$ (thus $\theta_{ax} = 56°$) in excellent agreement with the results of molecular mechanics calculations[22] on the corresponding molecule (1,2-dithiane) which yield $\theta_{eq} = 3°$ and $\theta_{ax} = 58°$ (Scheme III). It seems quite evident that the chair conformation of the molecule has not been appreciably modified by the presence of the additional unpaired electron. The only variation which has to be expected in the radical is a lengthening[17a,23] of the SS bond, due to the fact that such a three-electron bond is weaker than a normal two-electron SS bond.[13] Accordingly, the 6-membered ring is expected to be more flexible in the radical anion **13** than in the corresponding molecule.

Scheme III. Conformation of 1,2-Dithiane (MM Calculations) Showing the Angles Made by the Axial and Equatorial α-CH Bonds with the Direction of the S–S Bond (Left). On the Right Hand Side the Same Angles, Obtained from the Experimental a_H Values of Radical 13, Are Reported.



A variable-temperature study of the line shape of the ^{1}H NMR spectrum of 1,2-dithiane yielded the ring reversal barrier for this molecule. In Figure 3 (left) the four protons in positions 3,6 display a single line spectrum above −28 °C (when the protons in positions 4,5 are decoupled), but an AB-type spectrum below −60 °C, due to the geminally coupled ($J = -11$ Hz) pseudoaxial and pseudoequatorial hydrogens. In Table IV the activation parameters, obtained by line shape simulation (Figure 3, right), indicate a negligible ΔS^* value, as in the case of the corresponding radical **13**. The two ΔG^* values, therefore, can be meaningfully compared, and as predicted, that for ring reversal of the radical (5.8 kcal mol^{-1}) is significantly lower than that for the corresponding molecule (11.9 kcal mol^{-1}).[24]

Conformation of Linear Disulfide Radical Anions.

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(18) Gilbert, B. C. In *Sulfur Centered Reactive Intermediates in Chemistry and Biology*; Chatgilialoglu, C., Asmus, K.-D., Eds.; Plenum Press: New York, 1990; p 135.

(19) (a) Gara, W. B.; Giles, J. R. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1444. (b) Giles, J. R. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1497.

(20) Lunazzi, L.; Pedulli, G. F. In *Organic Sulfur Chemistry*; Bernardi, F., Csizmadia, I. G., Mangini, A., Eds.; Elsevier: Amsterdam, 1985; p 484.

(21) The use of the McConnell relationship for radical **11** yields $\theta_{eq} = -12°$, $\theta_{ax} = 72°$, and $B = 13$ G. Thus, a B value of 11 ± 2 G seems to be the constant for the disulfide radical anions. Although the McConnell equation had been originally proposed for carbon radicals it is, apparently, applicable also to this type of radicals.

(22) The molecular mechanics calculations were performed using the MMX force field as implemented in Pc Model, Serena Software, Bloomington, IN.

(23) *Ab initio* calculations indicate that in the radical anion $MeSSMe^{•-}$ the SS bond length (2.62 Å) is about 25% longer than in the corresponding molecule MeSSMe (2.06 Å). See: Bonazzola, L.; Michaut, J. P.; Roncin, J. *J. Chem. Phys.* **1985**, *83*, 2727.

(24) The ΔG^* value obtained here for ring reversal of 1,2-dithiane is similar to the one that had been estimated, by means of the approximate coalescence method, in: Claeson, G.; Androus, G. M.; Calvin, M. *J. Am. Chem. Soc.* **1960**, *82*, 4428.

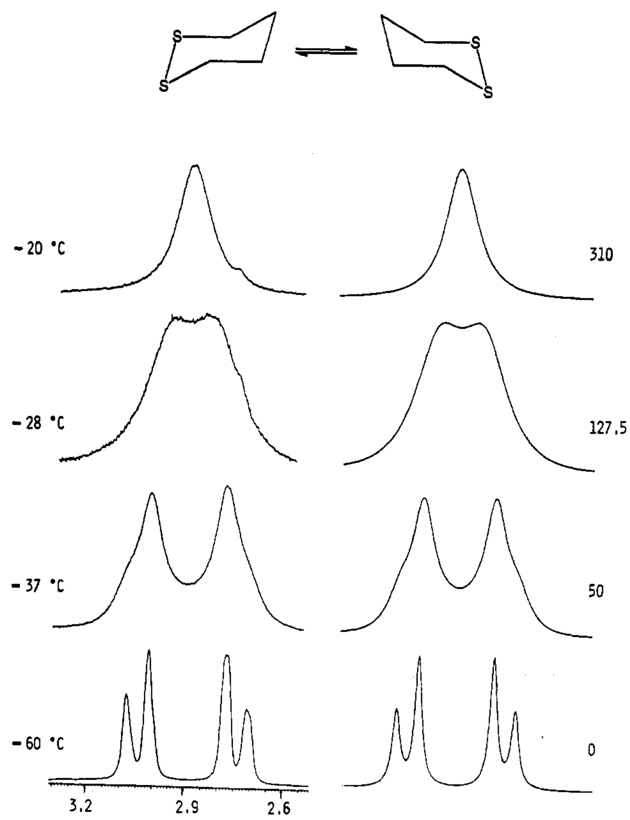

Figure 3. Experimental (left) ^{1}H NMR (200 MHz) signals of the methylene hydrogens in positions 3,6 (recorded whereas decoupling the hydrogens in positions 4,5) of 1,2-dithiane at various temperatures in CD_2Cl_2. On the right hand side are reported the spectra simulated with the rate constants (k, in s^{-1}) corresponding to the exchange between the two conformational enantiomers indicated ($\Delta G^* = 11.9$ kcal mol^{-1}).

Linear disulfide derivatives are known[25] to adopt a conformation having the CSSC dihedral angle twisted about 80° out of planarity. As a consequence, when the rotation about the S–S bond is slow at low temperature, the diastereotopic methylene hydrogens of compounds like RCH_2SSR yield anisochronous NMR signals that allow the S–S rotational barrier to be measured by line shape analysis at different temperatures.[26,27]

If the same nonplanar conformation is also adopted by the corresponding disulfide radical anions, different a_H splittings should be observable[28] at low temperature for the SCH_2 hydrogens in radicals like **2** ($MeCH_2SSCH_2Me^{\bullet-}$). Actually, on the basis of the equivalence of the x and y components of the anisotropic g factor, Symons *et al.*[5] concluded that the CSSC dihedral angle of disulfide radical anions is close to 90°, at least in the solid state. A difference in the methylene hydrogen splittings was not observed, however, in radical **2**, nor was it detected in $Bu^tCH_2SSCH_2Bu^{t\bullet-}$ (**15**), despite the sharper lines of **15** which was selected for study because it does not bear any γ-H atoms (which contribute to a broadening of the lines of **2**, by their unresolved long range splittings).

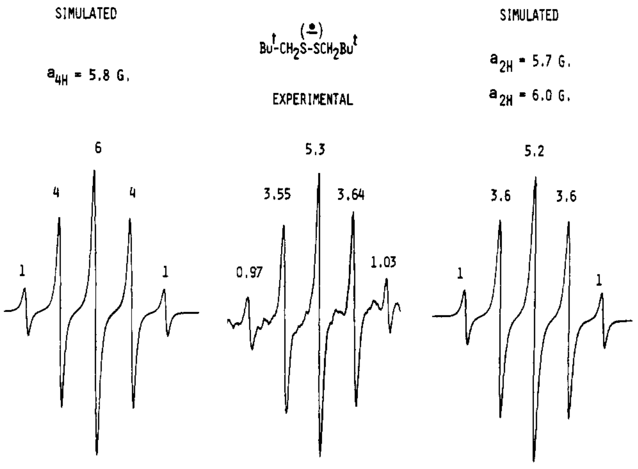

Figure 4. Experimental EPR spectrum of radical **15** (center) with the indication of the observed relative heights of the lines. On the left hand side is reported the spectrum computed assuming four equivalent hydrogens and on the right hand side that computed assuming a 0.3-G difference between the two a_H values (5.7 and 6.0 G) for the two diastereotopic hydrogens within each methylene group. Only the latter simulation matches well the experimental trend.

It has to be mentioned that the line width of the EPR spectra of disulfide radical anions decreases regularly with the increasing magnetic field.[29] Accordingly, when two lines correspond to the same absolute value of the total nuclear spin quantum number M_I, the signal at higher field appears to be slightly taller than its lower field companion (their integrated intensity remains, of course, equal). For the same reason the ratio between the heights of an upfield and a downfield line, corresponding to different $|M_I|$ values, slightly exceeds the expected binomial ratio (see, for instance, Figure 1 in ref 3). This linear dependence is a consequence of the anisotropy of the g factor, which is quite large, accompanied by a negligible effect of the anisotropy of the quite small a_H value: under these conditions the contribution of the quadratic term is almost irrelevant.[30] Such a linear dependence of peak height and magnetic field is also visible in radicals **2** and **15**, when lines with the same $|M_I|$ values are examined.[31] One might therefore expect that also in these radicals (as in those without the CH_2S moiety) the ratio between the heights of the high and low field lines with different $|M_I|$ values would exceed the binomial ratio. On the contrary in both **2** and **15** some of these ratios are much *lower* than the corresponding binomial ratios. This is clearly visible in Figure 4 (center) for the case of radical **15**, where the relative heights of the five lines (but not their integrated intensities) substantially differ from the trend expected for four equivalent hydrogens having a single a_H value (left hand side). This apparent discrepancy (which only occurs in the two radicals having the CH_2S moiety) can be accounted for by assuming that the two methylene hydrogens are diastereotopic and thus have nonresolved different splittings that broaden some of the lines. The computer simulation on the right hand side indicates in

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[25] (a) Lee, J. D.; Bryant, M. W. R. *Acta Crystallogr., Sect. B* **1969**, *25*, 2094. (b) Sacerdoti, M.; Gilli, G.; Damiano, P. *Acta Crystallogr., Sect. B* **1975**, *31*, 327.

[26] Fraser, R. R.; Boussard, G.; Saunders, J. K.; Lambert, J. B.; Mixon, C. E. *J. Am. Chem. Soc.* **1971**, *93*, 3822.

[27] Cremonini, M. A.; Lunazzi, L.; Placucci, G.; Okazaki, R.; Yamamoto, G. *J. Am. Chem. Soc.* **1990**, *112*, 2915.

[28] Casarini, D.; Lunazzi, L.; Placucci, G.; Macciantelli, D. *J. Org. Chem.* **1987**, *52*, 4721.

[29] For instance, the three lines of the spectrum of radical **3** ($Pr^iSSPr^{i\bullet-}$) have widths (2.15, 1.95, and 1.8 G) decreasing regularly with the increasing field.

[30] (a) Hudson, A.; Luckhurst, G. R. *Chem. Rev.* **1969**, *69*, 194. (b) Segal, B. C.; Reymond, A.; Fraenkel, G. K. *J. Chem. Phys.* **1969**, *51*, 1336.

[31] In the five line spectrum of **15** ($Bu^tCH_2SSCH_2Bu^{t\bullet-}$), for instance, the ratio between the heights of the fifth and first line is slightly larger than 1, as is the ratio between the fourth and second line (the experimental ratios being 1.06 and 1.02, respectively, as shown in Figure 4).

fact that the anomalous ratio can be well reproduced if these two splittings differ by 0.3 ± 0.05 G. On this basis two a_H values (5.7 and 6.0 G.) should be assigned to the two pairs of methylene hydrogens of radical **15** (and **2** as well). This experimental evidence proves that disulfide radical anions $RSSR^{\bullet-}$ have the CSSC dihedral angle twisted out of planarity[32] and, like the parent molecules are a racemic mixture of two conformational enantiomers.

Conclusions

Both the linear and cyclic disulfide radical anions were shown to adopt, in solution, conformations lacking planes of symmetry or a center of symmetry. They exist, therefore, as pairs of conformational enantiomers which were observed at low temperatures by the detection of diastereotopic methylene hydrogens in appropriate derivatives. In the linear radicals the interconversion between these enantiomers is achieved by means of a rotation about the S–S bond: the features of the EPR spectra were, however, unsuited for determining these rotational barriers. In the case of the 5- and 6-membered cyclic disulfide radical anions, on the other hand, the enantiomers exchange *via* ring-reversal processes whose barriers were amenable to EPR determinations (4.7_5 and 5.8 kcal mol^{-1}, respectively). The barrier for the 6-membered radical anion **13** was found lower than that (11.9 kcal mol^{-1}) measured by dynamic NMR for the corresponding molecule (1,2-dithiane).

Experimental Section

The compounds used in the present investigation were commercially available. 2,2-Dimethylpropane-1-thiol (Bu^tCH_2-SH) was prepared according to ref 33 and 1,4-dithiane according to ref 34. A typical sample contained 50 μL of the appropriate thiols and 50 μL of Bu^tOOBu^t in 500 μL of a ~1 M solution of EtOK/EtOH. To obtain the cyclic radical **13** a more diluted solution (containing ~5 μL of the appropriate dithiol) was necessary. More concentrated solutions (e.g., containing 50-100 μL of dithiol) yielded the noncyclic radical **14**, in addition to radical **13**. The EPR samples were degassed *in vacuo* in Suprasil quartz tubes and the *g* factors measured by comparison with a DPPH-containing capillary, inserted inside the tube itself. We noticed that the *g* factor was slightly solvent dependent so that addition, for instance, of cyclopropane to EtOK/EtOH solutions of **3** made the value to change from 2.0126 to 2.0133. Photolysis was achieved by means of a 500-W unfiltered high-pressure mercury lamp and the temperature measured by introducing a thermocouple within the cavity of the EPR spectrometer before and after each spectral determination.

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(32) The *ab initio* calculations of Bonazzola *et al.* (see ref 23) suggest for the radical anion $MeSSMe^{\bullet-}$ a CSSC dihedral angle of 81.4°, almost identical to that (82.8°) computed for the corresponding molecule MeSSMe. On the contrary, the same calculations predict a planar conformation (CSSC dihedral angle equal to 180°) for the corresponding radical cation $MeSSMe^{\bullet+}$.

(33) (a) Tanner, D.; Brownlee, B. G. *Can. J. Chem.* **1973**, *51*, 3366. (b) Vedejs, E.; Perry, A. D.; Wilde, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 2985.

(34) Brintzinger, H.; Schmahl, H. *Chem. Ber.* **1954**, *87*, 3121.