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On the Reaction of the Sulfite Radical Anions with Thioureas

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We have shown previously[2] that the sulfite radical anions, SO_3^-, are formed during the reaction of sodium bisulfite with Ce^{4+} in an aqueous solution probably by

$$HSO_3^- + Ce^{4+} \longrightarrow SO_3^- + H^+ + Ce^{3+} \qquad (1)$$

The detection of the radical anions has been made by a rapid-mixing flow technique coupled with electron spin resonance (ESR) measurements.[3,4] The method also enables us to detect secondary radicals formed if suitable reactants are present in the solution and react with the primary radicals. Thus, we were able to show the formation of secondary radicals, for example, when methacrylic, crotonic and fumaric acids were respectively added to the solution which was generating the sulfite radical anions.[5]

In view of the biological importance of the reaction of bisulfite, in particular, with 4-thiouridine,[6] we have made further investigations on the reaction of the SO_3^- radical anions with thioureas by the method quoted above. As the result we found that some new intermediate radicals are formed during the reactions. The present communication concerns with such investigations.

Experimental

ESR measurements were carried out on a JEOL-PE-1X ESR spectrometer (X-band) with 100 kHz field modulation in conjunction with a JEOL mixing chamber. This apparatus enabled us to detect radicals having the life-time 5—100 msec.

The hyperfine (hf) coupling constants and g-values were calibrated by comparison with an aqueous solution of Fremy's salt ($g=2.0055$, $a^N=13.0$ G)[7] kept in a capillary tube attached to the sample.

For the generation of the SO_3^- radicals, commercial samples of $Ce(NO_3)_4 \cdot 2NH_4NO_3$ and $NaHSO_3$ were used without further purification. Two solutions were prepared: one contained 0.01 M Ce^{4+} acidified with sulfuric acid (a) and the other 0.1 M $NaHSO_3$ (b).

To investigate the reactions of the SO_3^- radicals with thioureas, the latter chemical was added usually to the solution (b) at 0.1 M concentration.

Thioureas used in the present study were commercial thiourea, ethylenethiourea(2-imidazolidinethiourea), 1-allyl-2-thiourea (thiosinamine), and tetramethylthiourea.

Result and Discussion

When the two solutions (a) and (b) were mixed, in the absence of thioureas, in the cavity of the ESR spectrometer, a singlet absorption line was observed, as expectedly, at $g=2.0022$ (Fig. 1) which has been assigned by us as the SO_3^- radical.[2] When thiourea was added to the solution (b) and allowed to react with the solution (a), the absorption line was reduced considerably along with the appearance of another singlet line at $g=2.0051$.

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[1] Location: *Hongo, Bunkyoku, Tokyo.*

[2] T. Ozawa, M. Setaka and T. Kwan, *Bull. Chem. Soc. Japan*, **44**, 3473 (1971).

[3] See, *e.g.*, W.T. Dixon and R.O.C. Norman, *J. Chem. Soc.*, **1963**, 3119.

[4] M. Setaka, T. Ozawa and T. Kwan, *Chem. Pharm. Bull.* (Tokyo), **20**, 1061 (1972).

[5] T. Ozawa, M. Sato and T. Kwan, Chemistry Letters, 591 (1972).

[6] H. Hayatsu and M. Inoue, *J. Am. Chem. Soc.*, **93**, 2301 (1971).

[7] J.Q. Adams, S.W. Nicksic, and J.R. Thomas, *J. Chem. Phys.*, **45**, 654 (1966).

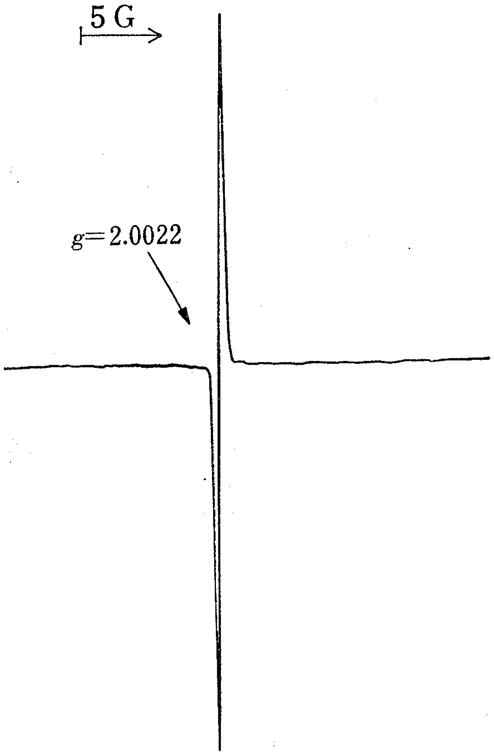
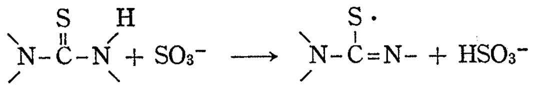


Fig. 1. ESR Spectrum of SO_3^- Radical Anions

Quite similarly, when ethylenethiourea or 1-allyl-2-thiourea was added to the system, a new resonance line was found to appear at g=2.0049 or g=2.0052, respectively. These spectra are shown in Fig. 2a—c. They were not detectable in the absence of either Ce^{4+} ion or $NaHSO_3$, suggesting that the SO_3^- radicals participate in the formation of secondary radicals.

Since the g factors (2.0049—2.0052) of the newly formed radicals are somewhat higher than those of carbon radicals, they would imply that the spectra are not due to carbon radicals. Also, in the ESR spectra of these radicals, any symptom of hyperfine structures due to N nucleus and/or protons were not observed in accordance with the supposition. On this ground, it is suggested that the newly formed spectra are due to sulfur radicals.

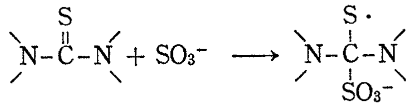
The mechanism of the formation of sulfur radicals should now be discussed. First, the SO_3^- radical might abstract a hydrogen atom from the amino group of thioureas followed by the formation of sulfur radicals as



$$\rangle N-\overset{\displaystyle S}{\overset{\|}{C}}-N\langle^{H} + SO_3^- \longrightarrow \rangle N-\overset{\displaystyle S\cdot}{\overset{|}{C}}=N- + HSO_3^- \qquad (2)$$

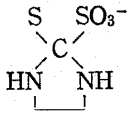
This mechanism seems unlikely, however, because the SO_3^- radical was rather inactive toward a hydrogen atom abstraction as previously reported by us.⁵⁾ Moreover, tetramethylthiourea also gave rise to secondary radicals as will be mentioned later.

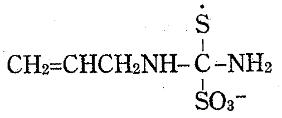
On the other hand, it seems likely that the SO_3^- adds to the carbon atom of thioureas leading to the formation of a new sulfur radical by



$$\rangle N-\overset{\displaystyle S}{\overset{\|}{C}}-N\langle + SO_3^- \longrightarrow \rangle N-\underset{\displaystyle SO_3^-}{\underset{|}{\overset{\displaystyle S\cdot}{\overset{|}{C}}}}-N\langle \qquad (3)$$

In accordance with (3) we assigned the radicals formed during the reaction of the SO_3^- radical with ethylenethiourea, and 1-allyl-2-thiourea as shown below,





$$CH_2{=}CHCH_2NH-\underset{\displaystyle SO_3^-}{\underset{|}{\overset{\displaystyle \dot{S}}{\overset{|}{C}}}}-NH_2$$

If the sulfur radicals are formed by the direct attack of the SO_3^- radical to the carbon atom of thioureas, tetramethylthiourea should also give rise to a new radical adduct. This was appealed to experiments, and a new singlet line was found to appear at g=2.0054. Thus, all the secondary radicals mentioned above are considered to appear by the direct addition of the SO_3^- radicals to the C=S bond of thioureas.

We have also investigated the interaction of the SO_3^- radicals with urea, dimethylurea, formic acid, acetic acid and acetone with the same technique. Neither the formation of secondary radicals nor the decay of primary radicals SO_3^- was observed, suggesting that the

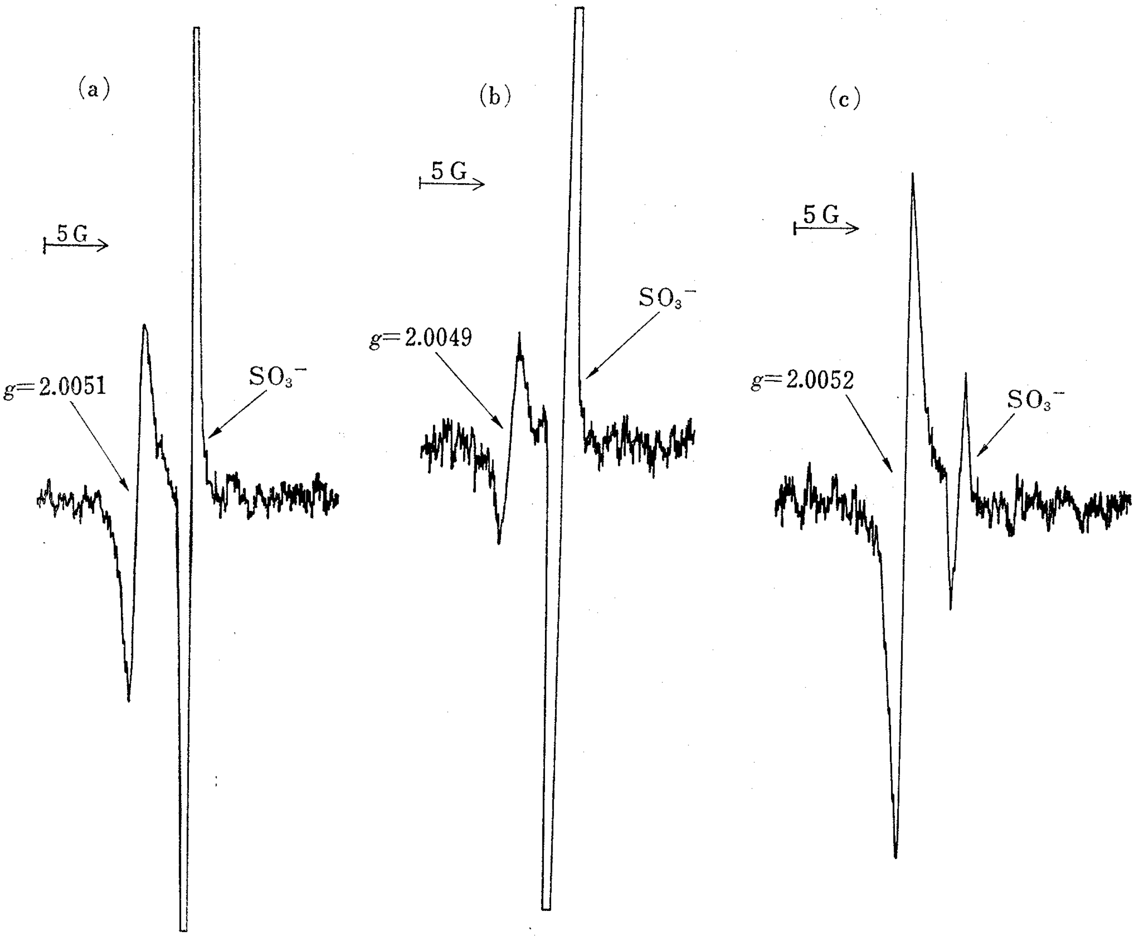
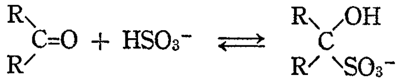


Fig. 2. ESR Spectra of Secondary Radicals formed with thiourea (a), ethylenethiourea (b) and 1-allyl-2-thiourea (c)

SO_3^- radical can not react on the C=O bond contrary to the C=S bond. We have not sufficient grounds for explaining the difference.

Sodium bisulfite is known to form an adduct with some carbonyl compounds,[8] in terms of the equilibrium reaction (4).



$$\begin{matrix}R \\ R'\end{matrix}\!\!>C{=}O + HSO_3^- \rightleftarrows \begin{matrix}R \\ R'\end{matrix}\!\!>C<\!\!\begin{matrix}OH \\ SO_3^-\end{matrix} \qquad (4)$$

The equilibrium data on acetone-bisulfite system shows that both ketone and adduct exist in the same order under the reaction condition. However, urea or thiourea seems unable to form such an adduct on the basis of the data of literatures.[8] Hydrolysis of thiourea in sodium bisulfite solution was not observed in infrared spectrum of chloroform extract from the solution. These facts may support that the above mentioned new ESR signals originate from the adduct radicals to the >C=S in thioureas.

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[8] J. Zabicky, "The Chemistry of the Carbonyl Group", John Wiley & Sons, London, II, 1970, p. 33.