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3d-ORBITAL RESONANCE IN DIVALENT SULPHIDES—VII

MECHANISM OF THE FORMATION OF 1,1-BIS (ETHYLMERCAPTO) PROPENE-1 BY REACTION OF 3-CHLORO-1,1-BIS (ETHYLMERCAPTO) PROPANE[1,2]

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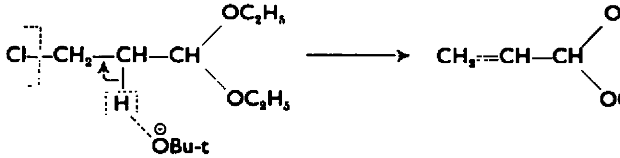
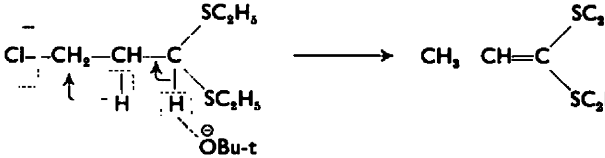
Abstract—The mechanism of the formation of1,1-bis(ethylmercapto)propane-1 (II) in the reaction of 3-chloro-1,1-bis(ethylmercapto)propane (I) with potassium t-butoxide in t-butanol has been investigated through the determination of the kinetic isotope effects of I and its oxygen analogue (III), both of which are *mono*-tritiated at β-positions. The magnitude of the kinetic isotope effects of the reaction of $k_H/k_T = 6{\cdot}20$, was found to be almost identical with that of 3-chloro-1,1-bis (ethoxy)propane-2-t_1 (III), $k_H/k_T = 6{\cdot}55$, and the rate of the formation of II from I was also found to be nearly the same as that of the elimination of hydrogen chloride in this reaction. Meanwhile, γ-hydrogens of the compound, II, were observed to exchange with those of solvent very rapidly, in the same reaction condition, owing to the participations of 3d-orbital resonance with two adjacent sulphur atoms and of allylic resonance. These facts imply that the reaction proceed through the prior 1,2-elimination, followed by immediate proton-transfer, as shown in equations (3) and (4).

Rothstein[4] found that 3-chloro-1,1-bis(ethylmercapto)-propane (I) gives 1,1-bis (ethylmercapto)propene-1 (II) on heating under reflux with potassium t-butoxide in t-butanol, whereas 3-chloro-1,1-bis(ethoxy)propane (III) produces acrolein diethylacetal (IV) in simple 1,2-elimination as shown in Equation (1). Based on the reasoning


(1)

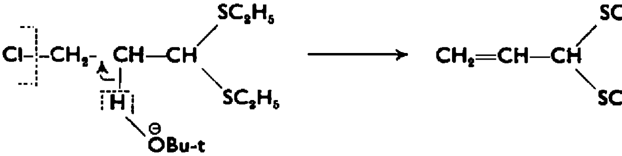
III IV

Mechanism I.


(2)

I II

Mechanism 2.


(3)

I V

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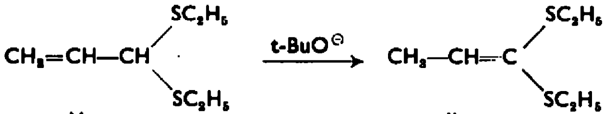
[1] Supported in part by Petroleum Research Fund, administered by American Chemical Society.

[2] Preliminary communication, see *Chem. & Ind.* 305 (1962).

[3] Present address, Department of Chemistry, Massachusetts Institute of Technology.

[4] E. Rothstein, *J. Chem. Soc.* 1558 (1940).



V II (4)

that an α-hydrogen adjacent to sulphur is easily displaced by alkali owing to the stabilization of the resulting anion by 3d-orbital resonance of sulphur, the author postulated that the reaction occurs as shown in Equation (2) which indicates initial proton removal followed by hydride shift. The alternative pathway as shown in Equations (3) and (4), was rejected as it was observed that 1,1-bis (ethylmercapto)-propene-2 (V) does not rearrange to II under the same reaction conditions.

Recently, Parham *et al.*[5] concluded that the structure of the compound V, suggested by Rothstein, is actually VI based on

$$C_2H_5S—CH_2—CH=CH—SC_2H_5$$

VI

observations that the characteristic absorption (900 and 995 cm^{-1}) of a terminal vinyl group that should be present in the compound V, was absent, and the presence of conjugated unsaturation was indicated by a band at 1608 cm^{-1} and also by several bands between 900 and 1100 $cm.^{-1}$ Furthermore, they suggested that all the chemical evidence employed by Rothstein for the structure V is consistent with structure VI and that, according, to recent mechanistic knowledge, both synthetic courses originally employed for the preparation of V undoubtedly lead to the formation of VI. All this has cast some doubt as to the validity of the Rothstein's mechanism, and it has become necessary to reconsider the possibility of the rejected mechanism 2.

According to the mechanism 1, the β-hydrogen atom transfers as a hydride intramolecularly immediately following the initial proton removal at α-position, while in mechanism 2 the β-proton is removed in 1,2-elimination simultaneously with the extrusion of γ-chloride in the initial step, as in the case of the oxygen analogue IV. One way to distinguish between mechanisms 1 and 2 is the determination of the kinetic isotope effects of both the sulphur and the oxygen compounds, by substituting the β-hydrogen atoms in each of the respective compounds either by deuterium or tritium.

Since the hydride transfer is known to give smaller values,[6] k_H/k_D usually ranging only from 1·8 to 2·6, a smaller kinetic isotope effect value is expected if the reaction of the sulphur compound proceeds through mechanism 1. On the other hand, the kinetic isotope effect would be substantially large in the 1,2-elimination of the sulphur compounds, k_H/k_D probably lying in the range of magnitude 3·6–6 and the value would be almost identical to that of the oxygen analogue, since the polar influences of two ethyl mercapto groups and of two ethoxy groups at an α-position to β-proton would not differ very much.

The kinetic isotope effects have been determined[7] for 3-chloro-1,1-bis-(ethylmercapto)propane-2-t_1 (VII) and 3-chloro-1,1-bis(ethoxy)propane-2-t_1 (VIII), both

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[5] W. E. Parham, J. H. Heberling and H. Wynberg, *J. Amer. Chem. Soc.* **77**, 1169 (1955).

[6a] C. G. Swain, R. A. Wiles and R. F. W. Bader, *J. Amer. Chem. Soc.* **83**, 1945 (1961);

[6b] C. G. Swain, R. F. W. Bader, R. M. Esteve, Jr. and R. N. Griffin, *Ibid*, **83**, 1951 (1961).

[7] A. Roe and M. Hellmann, *J. Chem. Phys.* **19**, 660 (1951).

of which were prepared[8] starting with acrolein and tritated hydrogen chloride. The data are shown in Table 1.

These almost identical values of isotope effects (4·4 for the sulphur and 4·5 for the oxygen analogue) for these two similar compounds, together with the fact that the magnitude of the isotope effect is a bit too high for the hydride transfer reaction but is just what one would expect for 1,2-elimination of less reactive chloro-compounds,[11,12] strongly suggests that the base-catalyzed reaction of I proceeds through 1,2-elimination followed by proton transfer, as shown in Equations (3) and (4).

TABLE 1. KINETIC ISOTOPE EFFECTS FOR THE REACTIONS OF CHLORO-ACETALS

	Activity, μc/mM			
X	$Cl—CH_2—CHT—CH(XC_2H_5)_2$	Product	k_H/k_T at 85°	k_H/k_D at 50°[a]
S	2·48	2·14	6·20	4·4
S	2·48	2·14	6·20	4·4
O	2·75	2·38	6·55	4·5
O	0·346	0·300	6·55	4·5

[a] Calculated using Equations (i)[9] and (ii).[10]

$$k_H/k_D = {}_e(h_H - h_D)/2RT \qquad (i)$$

$$k_Hk/_T = (k_H/k_D)\ 1{\cdot}442 \qquad (ii)$$

Now, the problem is to decide which step of the mechanism 2 is rate-determining. In order to clarify this point, the rates of formations of hydrogen chloride and of the compound II in the reaction of the compound I were determined using a large excess of potassium hydroxide. The rates of hydrogen chloride elimination from the compound I ($2{\cdot}98 \times 10^{-7}$) and of formation of the compound II ($2{\cdot}93 \times 10^{-7}$) indicate that the rate-determining slow step is the initial elimination step (3) and the dissociation of α-proton is substantially fast. This facile base-catalysed proton removal is quite understandable since the resulting carbanion is stabilized not only by the 3d-orbital resonance with two sulphur atoms of mercapto groups but also by the allylic resonance[13]. The substitution of an unsaturated group such as phenyl at α-carbon of thioacetals has been found to accelerate remarkably the of the rate base-catalysed hydrogen tritium exchange; thus benzaldehyde diethylthioacetal reacts about six powers of ten faster than ethyl thioethylal.[13]

Although even without the assistance of allylic resonance two mercapto groups on the α-carbon are capable of enhancing the acidity of the α-proton[14–16] through the 3d-orbital resonance with two sulphur atoms of mercapto groups, the effect is not large enough to lead to initial propon removal as suggested in mechansim 1 by Rothstein. Whereas in the oxygen analogue, having no available d-orbital for

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[8] A. H. Blatt, *Organic Syntheses*, Coll. Vol. II, p. 137, Jonh Wiley, New York (1949).

[9] K. B. Wiberg, *Chem. Revs.* **55**, 713 (1955).

[10] C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr. and L. L. Schaad, *J. Amer. Chem. Soc.* **80**, 5885 (1958).

[11] W. H. Saunders, Jr. and D. H. Edison, *J. Amer. Chem. Soc.* **82**, 138 (1960).

[12] F. H. Westheimer, *Chem. Revs.* **61**, 265 (1961).

[13] S. Oae, W. Tagaki and A. Ohno, *Tetrahedron* preceding papers.

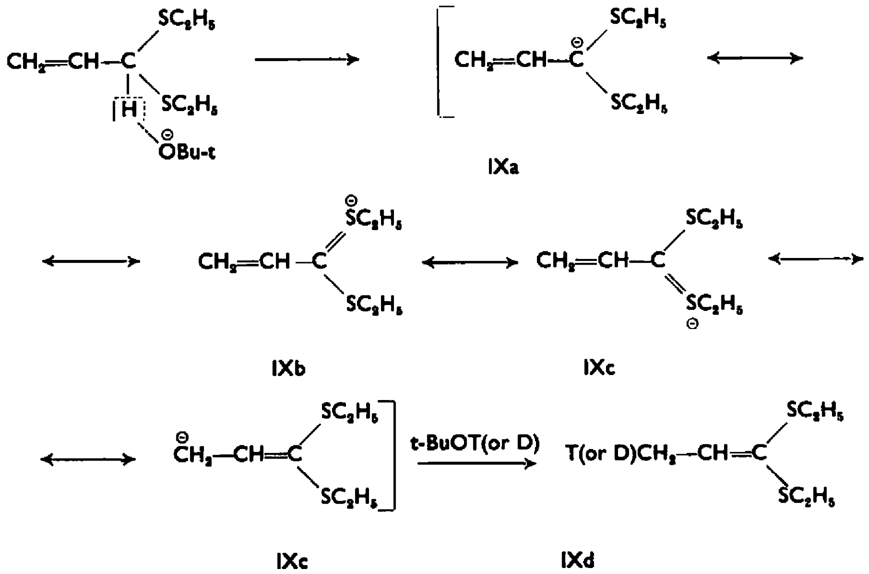
[14] J. F. Arens, M. Froling and A. Froling, *Rec. trav. Chim.* **78**, 663 (1959).

[15] J. F. Arens, Chapter 23, "*Some Aspects of the Chemistry of Organic Sulphur Compounds*" (Edited by N. Kharacsh) Vol. 1. Pergamon Press, (1961).

[16] J. Hine, R. P. Bayer and C. G. Hammer, *J. Amer. Chem. Soc.* **84**, 1751 (1962).

resonance, the allylic resonance alone appears incapable of enhancing the acidity of the α-proton in order to isomerize into 1,1-bis(ethoxy)propene-1.

Since the base-catalysed prototropy of V to II is very fast this intermediate, V, could not be isolated. However it is interesting to note that in the base-catalysed hydrogen exchange, II is presumed to form the same intermediate carbanion, IXa IXd, as V, and so the rate must be substantially fast.



IXa

IXb

IXc

IXc

IXd

Indeed, the hydrogen exchange of V is remarkably fast. On heating under reflux V with potassium t-butoxide in t-butanol, the tritium acitivity of the γ-tritiated compound V is almost completely lost within 12 hours. The reaction of I with potassium t-butoxide in both t-butanol-d_1 and t-butanol-t_1 have been carried out in order to determine the succeeding hydrogen exchange at the γ-position of the resulting compound V. The initial NMR peaks for the γ-methyl proton (doubly splitting, δ_{benzene}=7·17 p.p.m.) almost disappeared by deuterium exchange and the peaks for β-olefinic proton quadruply splitting, δ_{benzene}=0.57 p.p.m.) became a broad single peak, while ethyl protons were not affected. This fact clearly indicates that only the γ-methyl protons are exchangeable. Tritium exchange reaction also agrees with this deuterium exchange reaction, i.e., more than two protons were replaced by titrium but did not exceed three, as shown in Table 4.

EXPERIMENTAL

3-Chloro-1,1-bis(ethoxy) propane (III) *and 3-Chloro-1,1-bis(ethylmercapto)-propane* (I) were prepared following the same precedure as was used by Rothstein and the purified fractions b.p. 93° for III and b.p. 132°/18 mm Hg for I were used.

3-Chloro-1,1-bis(ethoxy)propane-2-t_1 (VIII) was prepared by an ordinary method[5], using instead of hydrogen chloride tritium chloride gas, made from phosphorus pentachloride and tritiated water. The distillate, b.p. 93°, 2·75 μc/mM, was used for the kinetic determination.

3-Chloro-1,1-bis(ethylmercapto)propane-2-t_1 (VII) was prepared from VIII by the method employed by Rothstein.[4] The oil, b.p. 130–132°/18 mm Hg, 2·75 μc/mM, was used for the kinetic experiment.

Kinetics of hydrogen chloride elimination from I. In 50 ml of 0·106N potassium t-butoxide in t-butanol, 500 mg of I was added and this solution was reacted under the atm of N_2 at 50·7°. At suitable time intervals, 5 ml aliquots were pipetted out, added into 10 ml degassed water and titrated with 0·0108N H_2SO_4 aq. using phenolphthalein as indicator. The result is shown in Table 2.

Kinetics for the formation of II. The same reaction conditions and techniques used in the former kinetic experiment were employed except for the analysis. Using Hitachi Photo-Electric Spectrophotometer Model EPU-2A kinetics were followed by measuring absorbancy at the maximum absorption band of 252 mμ after confirming that the absorbtion coefficient obeys Beer's law. The data are indicated in Table 2.

TABLE 2. FIRST-ORDER KINETIC RATE CONSTANTS OF HYDROGEN CHLORIDE ELIMINATION AND FORMATION OF 1,1-BIS(ETHYLMERCAPTO)PROPANE-1

		HCl–Elimination			Formation of II		
No.	Time, sec.	0·0108N—H_2SO_4 used, ml.	% reaction	$k_1 \times 10^7$	$-\log T$	% reaction	$k_1 \times 10^7$
1	0	58·775	—	—	0.070	—	—
2	7,200	58·650	0.21	2·91	·072	0·21	3·02
3	14,400	58·525	·43	2·98	·073	0·40	2·76
4	21,600	58·350	·72	(3·37)	·075	·64	3·02
5	25,200	58·325	·77	3·04	—	—	—
6	28,800	58·275	·85	2·97	—	—	—
			mean	2·98		mean	2·93

Measurement of kinetic isotope effects. Each 0·23 mole of VII or VIII was heated under reflux with 0·5 mole potassium t-butoxide in 30 ml t-butanol for 20 hours. After the solvent was distilled off, 10 ml water was added to the residue, the mixture extracted with ether and the ether layer dried (calc$_2$) The residual oil was distilled to give II or IV, respectively. b.p. 72°/9 mm Hg for II; 125°/760 mm Hg for IV.

The tritium activities were followed by Tri-carb liquid scintillation counter and the results are shown in Table 1.

Reaction of tritiated V *with potassium t-butoxide in t-butanol.* The reaction condition was the same as that mentioned above and the result is shown in Table 3.

TABLE 3. LOSS OF TRITIUM ACTIVITY IN THE REACTION OF 1,1-BIS (ETHYLMERCAPTO)-PROPANE-1 WITH BASE

Time, hr.	Activity of CH_3—CH=C(SC_2H_5)$_2$, μc/mM
0	3·20
12	0·10

Reaction of I *with t-butoxide in t-butanol-t_1 and/or-d_1.* The same reaction condition as mentioned above was employed and the results are shown in Table 4. To determine the position of isotopically substituted hydrogen, two techniques were employed: (1) 500 mg tritiated V was hydrolysed to propionic acid by 0·3N methanolic hydrogen chloride on heating under reflux for 6 hr, the solution was then neutralized with 5% Na_2CO_3 aq. and the solvent (methanol) distilled off. To this aq. propionic acid, 300 mg *p*-phenylphenacyl bromide was added and by repeated recrystallization, pure *p*-phenylphenacyl propionate mp. 106°, was obtained. By counting the activity of *p*-phenylphenacyl propionate, it was proved that hydrogen-tritium exchange reaction did not occur at methylmercapto groups: (2) the deuterated V was analysed by Varian NMR. Spectrometer Model V 4311. The NMR spectra of I showed characteristic bands at $\delta_{benzene}$ = 0·57 p.p.m. for —CH=, 5·93 p.p.m. for —CH_2— (ethyl), 7·17 p.p.m. for —CH_3 (γ-position), 8·23 p.p.m. for—CH_3 (ethyl).

TABLE 4. GAIN OF TRITIUM ACTIVITY IN THE REACTION OF 1,1-BIS(ETHYLMERCAPTO)-PROPENE-1 WITH BASE

Compound	Activity, μc/mM
t-BuOT	1·79
TCH_2—CH=C(SC_2H_5)$_2$	3·23
TCH_2—CH_2—COOH[a]	3·20

[a] Identified as *p*-phenyl phenacylate.