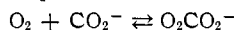
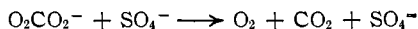


ion does not complex Ag^+ , which is similar in many respects to Cu^+ . Therefore it is unlikely that $\text{Cu}^+(\text{C}_2\text{O}_4)_2^{\ominus}$ is an important intermediate.

Inhibition by oxygen probably occurs through reaction with CO_2^- radicals to form a molecular complex or carbon peroxide^{10,12}



followed by chain termination



Reversibility of the first of these reactions is necessary for the rate law to have the same order with respect to peroxodisulfate and catalyst when oxygen is present.

The strong inhibition by Mn^{++} and MnO_4^- indicates that one or more manganese species derived from them is effective in terminating the reaction chains in this system. A related observation is the failure of manganic ion to catalyze the reaction of peroxodisulfate and oxalic acid.²⁵ Inhibition by $\text{S}_2\text{O}_3^{\ominus}$ and Cl^- probably also occurs through chain termination, while inhibition by NH_4OH is caused by transformation of the catalyst to the ammonia complex ion.

The proposed mechanism is consistent with the fact that the rate is independent of $p\text{H}$ over a wide range. It is not known why deviations from first-order kinetics occur at a $p\text{H}$ of ≤ 3.60 , but they may result from "bisulfate inhibition."²⁶ At sufficiently high values of the product $(\text{H}^+)(\text{SO}_4^{\ominus})$, the reverse of reaction 7 becomes important. If the chain-propagating steps are slower and the chain-terminating steps are faster for SO_4^- than for OH , then the result is inhibition of the over-all rate. In their study of the photolytic decomposition of peroxodisulfate, Tsao and

(25) H. Taube, *J. Am. Chem. Soc.*, **70**, 3928 (1948).

(26) M.-S. Tsao and W. K. Wilmarth, *J. Phys. Chem.*, **63**, 346 (1959).

Wilmarth observed inhibition only at much larger values of $(\text{H}^+)(\text{SO}_4^{\ominus})$. However, as the particular reactions involving SO_4^- and OH vary from one system to another, the region where bisulfate inhibition becomes important may also vary.

Application of the Brønsted equation to the rate law derived from the proposed mechanism shows that at low ionic strength, where the equation is valid, k should increase with increasing ionic strength. A graph of $\log k$ versus the square root of the ionic strength should be linear with a slope of 1.5. (For the alternative mechanism involving OH radicals, the slope should be 1.0.) Experimentally it was found that the rate constant was essentially independent of ionic strength over the range 0.05–0.54. However, the ionic strength in this range is too high for the Brønsted equation to be applicable. Another ionic reaction which behaves in this way is the reaction $\text{H}_2\text{O}_2 + \text{I}^- + \text{H}^+ \rightarrow \text{H}_2\text{O} + \text{HIO}$. The rate is approximately independent of ionic strength over the range 0.05–1.2, but at very low ionic strength the behavior expected from the Brønsted equation is approached.²⁷

From the relation between the experimental rate constant k and the rate constants for the separate steps in the mechanism, it follows that the experimental activation energy E is a composite of the individual activation energies: $E = \frac{1}{2}(E_1 + E_2 + E_5 - E_6)$. E is 32.2 kcal./mole, and E_1 is 33.5 kcal./mole.⁹ Therefore $E_2 + E_5 - E_6 = 30.9$ kcal./mole. It is estimated that E_5 is similar in magnitude to E_1 , while E_2 and E_6 are fairly small.

Acknowledgment.—We wish to express our appreciation to Professor R. M. Keefer for many helpful discussions.

(27) F. Bell, R. Gill, D. Holden and W. F. K. Wynne-Jones, *ibid.*, **55**, 874 (1951).

[CONTRIBUTION FROM THE LAWRENCE RADIATION LABORATORY AND DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY, CALIFORNIA]

The Activation Energy of Inversion in Substituted 1,2-Dithiane and 1,2-Dioxane Measured by the Nuclear Magnetic Resonance Technique¹

BY GORAN CLAESON,² GAYLORD ANDROES AND MELVIN CALVIN³

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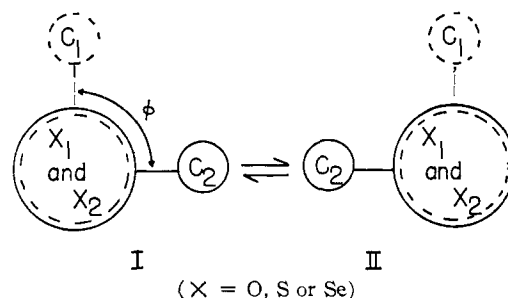
The activation energy, ΔE^\ddagger , and frequency factor, ν_0 , for inversion in 3,3,6,6-tetramethyl-1,2-dithiane (IV) and 3,3,6,6-tetramethyl-1,2-dioxane (V) have been measured by high resolution proton magnetic resonance methods. The results are $\Delta E^\ddagger = 16.1$ kcal./mole and $\nu_0 = 2 \times 10^{14}$ sec.⁻¹ for IV and $\Delta E^\ddagger = 18.5$ kcal./mole and $\nu_0 = 4.0 \times 10^{16}$ sec.⁻¹ for V. The difference in the values between the two compounds has been explained by means of a hypothesis of different pathways in the inversion of compounds IV and V.

An organic disulfide, R-S-S-R , or the corresponding oxygen or selenium analogs, consists of an equimolar mixture of I and II. These are optical antipodes, and their stability depends on the

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(3) Research Professor of Chemistry 1960–1961 in the Miller Institute for Basic Science, University of California, Berkeley.



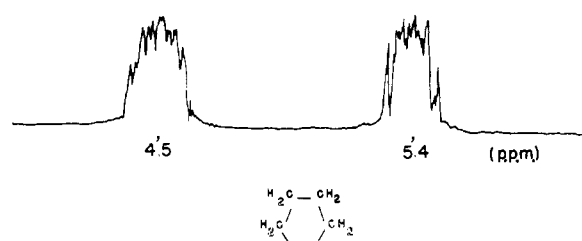


Fig. 1.—Proton magnetic resonance spectrum at 60 Mc./sec. of 1,2-dithiane at room temperature.

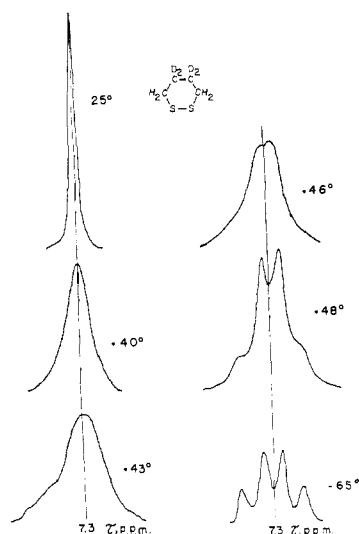
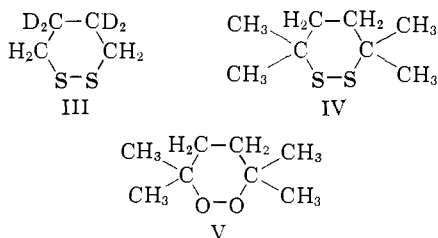


Fig. 2.—Proton magnetic resonance spectra at 60 Mc./sec. of 1,2-dithiane-4,5-D₂ at various temperatures.

height of the barrier hindering the free rotation about the disulfide bond.⁴ This barrier has a minimum when the dihedral angle (ϕ) has a value of about 90°.⁵

Cyclic disulfides, diselenides and peroxide are compounds suitable for a study of the interconversion between the antipodes by the nuclear magnetic resonance technique. In this paper, measurements of the inversion rate as a function of temperature for 1,2-dithiane-4,5-D⁴ (III), 3,3,6,6-tetramethyl-1,2-dithiane (IV), and the corresponding oxygen analog 3,3,6,6-tetramethyl-1,2-dioxane (V), are reported.



The n.m.r. spectrum of 1,2-dithiane itself is very complicated (Fig. 1). Its deuterium-substituted

derivative (III) was therefore synthesized to give a simpler spectrum. Preliminary results from the study of this compound were reported in an earlier communication.⁶

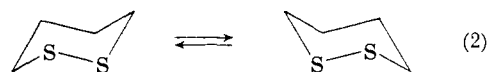
The n.m.r. spectra of compound III at different temperatures are shown in Fig. 2. At temperatures below -50° the spectrum consists of a quartet of the AB type.⁷ The four peaks are the result of spin-spin coupling between the two non-equivalent axial and equatorial α -hydrogens. The maximum separation of the two inner peaks is 10.4 c./sec., and the coupling constant is 13.0 c./sec. When the temperature is raised above -50° , the peaks in the quartet begin to converge, and at -43° the spectrum consists of one single broad peak, indicating that the interconversion now is so rapid that the two peaks are averaged out. As the temperature increases above -43° , the peak sharpens and remains constant up to the highest temperature studied (150°).

From the low temperature pattern, the chemical shift between the axial and equatorial hydrogens $\nu_a - \nu_e$ was calculated as 18.5 c./sec.⁸ We assumed that relation (1) for the rate of interconversion holds at -43° , the temperature where the peaks coalesce⁹

$$k = \pi(\nu_a - \nu_e)/\sqrt{2} \quad (1)$$

From this we calculated the rate constant $k = 41.1 \text{ sec.}^{-1}$. An exact value for k in this case may be calculated from quantum mechanical expressions given by Kaplan,¹⁰ but such a calculation probably would not change k significantly.

If the change from one isomer to the other



is treated as a typical rate process and the transmission coefficient (K) is equal to one, then Eyring's equation

$$k = \frac{RT}{Nh} \cdot e^{-\Delta F^\ddagger/RT} \quad (3)$$

gives $\Delta F^\ddagger = 11.6 \text{ kcal./mole}$. The activation energy (ΔE^\ddagger) cannot be evaluated from the free energy value (ΔF^\ddagger) because the entropy of activation (ΔS^\ddagger) for this reaction is not known.

A study of the temperature coefficient for a still simpler spectrum would, however, enable us to calculate the activation energy. Compounds IV and V give the desired type of simple spectra (Fig. 3 and 4). The methyl groups are not coupled to any other hydrogens, and at room temperature there is only one methyl peak. When the chair-chair interconversion is slowed down at lower temperatures, the methyl proton resonance is a doublet. This splitting is a chemical shift caused by the differently shielded axial and equatorial methyl groups. Thus a study of the temperature depen-

(6) G. Claeson, G. M. Androes and M. Calvin, *J. Am. Chem. Soc.*, **82**, 4428 (1960).

(7) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, New York, N. Y., 1959, p. 119.

(8) Ref. 7, p. 120.

(9) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

(10) (a) J. Kaplan, *ibid.*, **28**, 278 (1958). (b) M. Takeda and E. O. Stejskal, *J. Am. Chem. Soc.*, **82**, 25 (1960).

(4) D. W. Scott, H. L. Finke, M. E. Gross, G. R. Guthrie and H. M. Huffman, *J. Am. Chem. Soc.*, **72**, 2424 (1950). D. W. Scott, H. L. Finke, J. P. McCullough, M. E. Gross, R. E. Pennington and G. I. Waddington, *ibid.*, **74**, 2478 (1952). G. Bergson and L. Schotte, *Arkiv. Kemi*, **13**, 43 (1958). L. Pauling, "The Nature of the Chemical Bond," 2nd Ed., Cornell University Press, Ithaca, N. Y., 1960, p. 139.

(5) M. Calvin, *Federation Proc.*, **13**, 697 (1954). M. Calvin, in "Glutathione," Academic Press, Inc., New York, N. Y., 1954, p. 3.

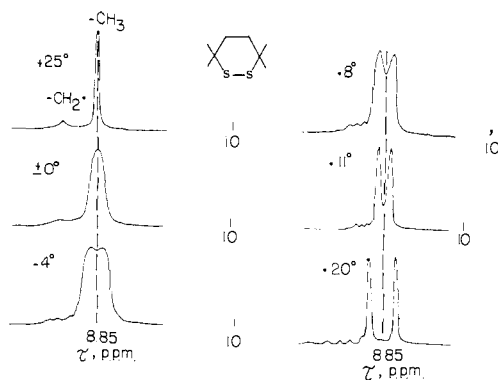


Fig. 3.—Proton magnetic resonance spectra at 60 Mc./sec. of 3,3,6,6-tetramethyl-1,2-dithiane at various temperatures.

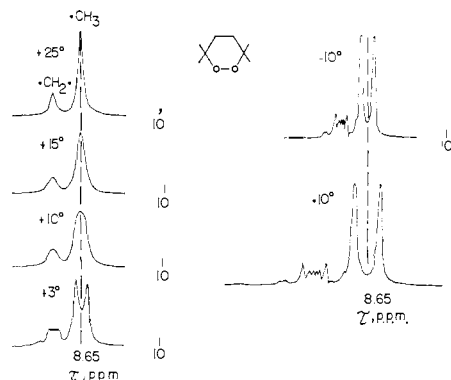


Fig. 4.—Proton magnetic resonance spectra at 60 Mc./sec. of 3,3,6,6-tetramethyl-1,2-dioxane at various temperatures.

dence of the line-separation in the methyl doublet gives us an opportunity to use the equations derived by Gutowsky and Holm⁹ for calculating the activation energy (ΔE^\ddagger) for the interconversion.

The temperature dependence of the rate constant for the interchange shown by equation 2 also may be expressed by

$$k = \nu_0 \cdot e^{-\Delta E^\ddagger / RT} \\ \left(\nu_0 = K \frac{RT}{Nh} e^{-\Delta S^\ddagger / R} \right) \quad (4)$$

where k is the rate constant, ν_0 the frequency factor and ΔE^\ddagger the activation energy for the interchange.

In our case we have equal populations and lifetimes of both forms (optical antipodes) and equation 4 can be rewritten⁹

$$\log \frac{1}{t\delta\omega} = \log \frac{2\nu_0}{\delta\omega} - \frac{\Delta E^\ddagger}{2.3R} \cdot \frac{1}{T} \quad (5)$$

where t is half of the lifetime of either form, and $\delta\omega$ is the true limiting separation of the two peaks when $t \rightarrow \infty$. ($\delta\omega$ is obtained from the observed separation of the components as $t \rightarrow \infty$ by using equation 8 in ref. 9), k and t are related by $k = 1/2t$. A plot of $\log 1/t\delta\omega$ versus $1/T$ gives us a straight line. ΔE^\ddagger is estimated from the slope of the line, and ν_0 is derived from the intersection with the Y-axis. Now we do not know t , but it is a function of $\delta\omega_e$ and T_2 . $\delta\omega_e$ is the experimentally observed separation of the peaks, and T_2 is the nuclear relaxation time. This function is quite complicated.

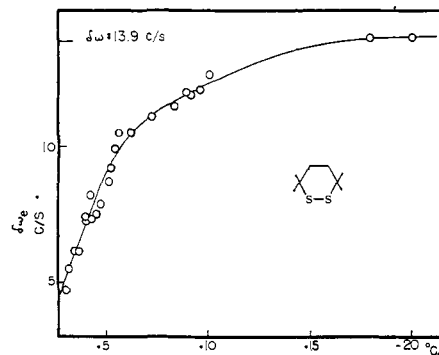


Fig. 5.—Plot of experimental separation of the methyl peaks ($\delta\omega_e$) versus temperature for 3,3,6,6-tetramethyl-1,2-dithiane.

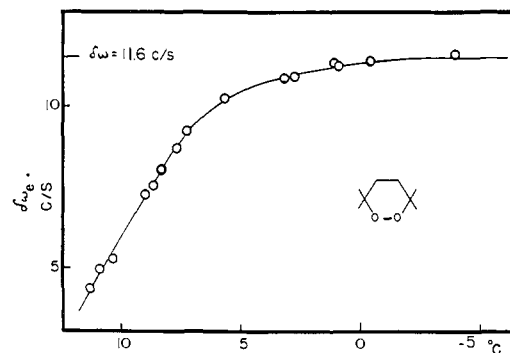


Fig. 6.—Plot of experimental separation of the methyl peaks ($\delta\omega_e$) versus temperature for 3,3,6,6-tetramethyl-1,2-dioxane.

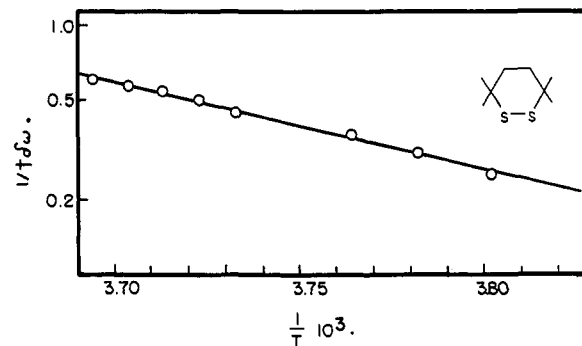


Fig. 7.—Temperature dependence of the inversion rate constant ($1/2t$) for 3,3,6,6-tetramethyl-1,2-dithiane.

Therefore $1/t\delta\omega$ is more readily obtained graphically from a plot of $1/T_2 \delta\omega$ as a function of $1/t \delta\omega$ for different values of $\delta\omega_e/\delta\omega$. Such a plot is given by Gutowsky and Holm (Fig. 3 in ref. 9).

Our observed $\delta\omega_e$ values were plotted against temperature. From these curves, Fig. 5 and 6, points were selected corresponding to the plotted values of $\delta\omega_e/\delta\omega$ in Fig. 3 in ref. 9, and the corresponding $1/t \delta\omega$ values were obtained from the latter diagram. This procedure gives a linear plot for the dithiane case (Fig. 7) but, for reasons which are not now understood, fails to do so in the dioxane case. The experimental points between 10 and 13° fall below a straight line extended from the lower temperature points. Thus, in the latter case (Fig. 8) data also were taken at temperatures above that at

TABLE I

Compound	T_2^a , sec.	$\frac{\delta\omega}{2\pi}$, c./sec.	Temp. ^c , °K.	ΔE^\ddagger , kcal./mole	ν_0 , sec. ⁻¹	ΔS^\ddagger , e.u.	ΔF^\ddagger , kcal./mole	ΔF^\ddagger , kcal./mole
1,2-Dithiane		18.5	230					11.6
Tetramethyldithiane	0.12	13.9	271	16.1	2.10×10^{14}	6.7	13.8	13.6
Tetramethyldioxane	0.14	11.6	285	18.5	4.0×10^{16}	14.4	14.6	14.5

^a T_2 is defined as $\frac{2}{\Delta\omega^{1/2}}$ where $\Delta\omega^{1/2}$ is the width of the peaks at half maximum at low temperature where the separation is complete. ^b Temp.^c is the temperature at which the doublet coalesces to a single line. ^c The value of ΔF^\ddagger calculated from equation 1.

which the two peaks coalesced. Values of $1/t \delta\omega$ were determined in this range from the temperature variation of the amplitude of the peak.^{10b} From the straight lines obtained (Fig. 7 and 8) we calculated the values of ΔE^\ddagger and ν_0 . Table I lists these values, and those derivable from them, together with those of T_2 and $\delta\omega/2\pi$.

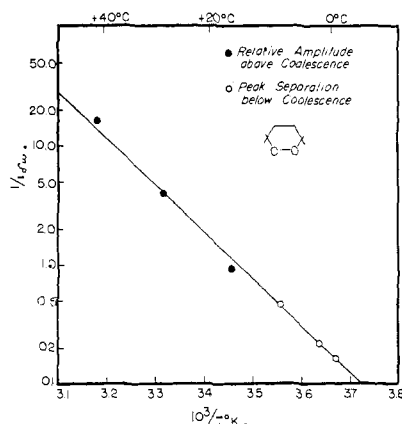


Fig. 8.—Temperature dependence of the inversion rate constant ($1/2t$) for 3,3,6,6-tetramethyl-1,2-dioxane.

Experimental

A Varian high-resolution n.m.r. spectrometer V-4311, operating at 60 Mc./s. was used to obtain the spectra. The Varian Model V-4340 variable temperature probe accessory and the Model V-4331-THR Dewar probe insert provided a means for controllable high- and low-temperature studies. The spectra were recorded by a Sanborn Model 151 recorder.

Cooling was achieved by a heater placed in a 25-liter metal Dewar of liquid nitrogen with an exit tube leading to the temperature probe. Temperature readings were made by the permanent thermocouple, previously calibrated against another thermocouple (copper-constantan) which was placed in the sample. The sample could be kept within $\pm 0.1^\circ$ of a given temperature during the measurements.

Samples used in these studies were about 25% solutions in carbon disulfide. Benzene was used as the internal standard for 1,2-dithiane and compound III, and tetramethylsilane was used for compounds IV and V. The samples were contained in 5 mm. o.d. Pyrex glass tubes; air was replaced with nitrogen and the tubes sealed.

The signal separations were measured by the side-band technique. The shielding values given in Figs. 1-4 are the τ -values introduced by Tiers¹¹ and defined by the equation

$$\tau_{(p.p.m.)} = 10 - \frac{\Delta(\text{Me}_2\text{Si}) \cdot 10^6}{\text{oscillator freq. (c./sec.)}}$$

We estimated the errors of ΔE^\ddagger by trial calculations with idealized data. These calculations showed that a small deviation in $\delta\omega$ introduces a large change in ΔE^\ddagger . Special care was therefore taken to measure $\delta\omega$ as accurately as possible. With the $\delta\omega$ values within ± 0.1 c./sec. ($\sim 1\%$) and the value of T_2 within $\pm 10\%$, we obtained an error in ΔE^\ddagger of less than $\pm 4\%$.

(11) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

3,3,6,6-Tetramethyl-1,2-dioxane was prepared by oxidizing 2,5-dimethyl-2,5-dihydroxyhexane with hydrogen peroxide according to the method of Criegee and Paulig.¹²

3,3,6,6-Tetramethyl-1,2-dithiane.—2,5-Dimethyl-2,5-dihydroxyhexane was converted to 2,5-dimethyl-2,5-dibromohexane with hydrobromic acid.¹³ The dibromo compound was treated with thiourea and hydrolyzed to give 2,5-dimethyl-2,5-dimercaptohexane, which was oxidized to the cyclic disulfide with iodine.¹⁴

1,4-Butanediol- d_2 .—2-Butyne-1,4-diol (Aldrich Chemical Co.) was recrystallized from ethyl acetate, m.p. 54–57°. 64.5 g. (0.75 mole) of this diol was dissolved in 60 ml. of D_2O (99.5%). The water was distilled off at reduced pressure. Benzene was added and distilled off to remove the last trace of water. The same procedure (dissolving in 60 ml. of D_2O and removing the water) was repeated twice.

1,4-Butanediol- d_2 -2,3- d_4 .—The resultant diol was dissolved in 150 ml. of hot ethyl acetate. The solution was cooled and approximately 0.2 g. of PtO_2 was added. The solution was deuterogenated by shaking in a 450 ml. bottle under a deuterium gas pressure of about 30 lb./sq. in. After 15 hr., the calculated amount of gas had been consumed. The PtO_2 was filtered off and the solvent distilled at reduced pressure. Fractionation gave 52.5 g. of a colorless liquid; b.p. 121–123° (10 mm.), n_D^{25} 1.449; yield, 73%.

1,4-Butanedithiol-2,3- d_4 .—In a 500 ml. three-necked round-bottom flask, fitted with a stirrer and reflux condenser, were placed 36.5 g. of 1,4-butanediol- d_2 -2,3- d_4 (0.38 mole), 60.8 g. of thiourea (0.8 mole) and 280 ml. of 47% hydrobromic acid (2.4 moles). The mixture was refluxed for 8 hr. with stirring. The flask was allowed to cool (the thiuronium salt was then precipitated as a fine crystalline solid), and a solution of 96 g. (2.4 moles) of sodium hydroxide in 200 ml. of water was added. The mixture was refluxed for 2 hr. while a stream of nitrogen was bubbled through the solution. The solution was cooled, and the two phases were separated. The acidified aqueous layer was extracted with three 100 ml. portions of ether. The combined organic layers were dried over calcium sulfate. The ether was removed at reduced pressure and the remaining oil fractionally distilled; b.p. 79–61° (17 mm.); yield, 21.6 g. (45%). (A forerun of 5 g. boiling at 31° (17 mm.) could be tetrahydrothiophene, b.p. 119°.)

1,2-Dithiane-4,5- d_4 .—1,4-Butanedithiol-2,3- d_4 (21.6 g., 0.171 mole) was dissolved in 2 liters of ethanol-water. A 5% alcoholic-iodine solution was added with stirring until a faint yellow color persisted. A few drops of 1% sodium thiosulfate solution was added to make the solution colorless. Water was added to a total volume of 5 liters and the solution extracted with two 150 ml. portions of petroleum ether. After the solution was dried over calcium sulfate, the solvent was removed by distillation. The remaining disulfide was distilled at 34 mm. and solidified in the condenser; b.p. 87–88° (34 mm.); yield, 18 g. (85%). The compound was sublimed easily to give crystals with m.p. 32–33°. The n.m.r. spectrum of the sublimed compound showed that it was about 99% isotopically pure.

Discussion

It is striking that the values of ΔE^\ddagger , ΔS^\ddagger and ν_0 for the oxygen compound (V) are so different from those of the analogous sulfur compound (IV). The high frequency factor and the correspondingly high entropy term for (V) show that this molecule passes through a flexible transition state. The sul-

(12) R. Criegee and G. Paulig, *Chem. Ber.*, **88**, 712 (1955).

(13) C. Harris, *Ann.*, **343**, 365 (1905).

(14) G. Claeson, *Svensk. Kem. Tidsskr.*, **69**, 395 (1957).

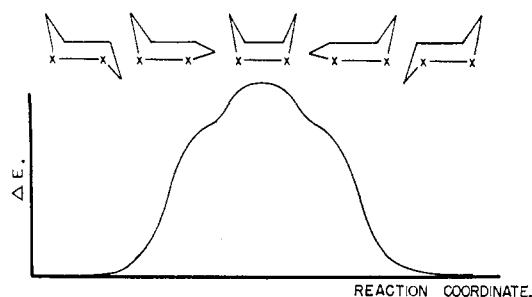


Fig. 9.—A reaction pathway and its energy barrier for inversion of 1,2-dithiane or 1,2-dioxane.

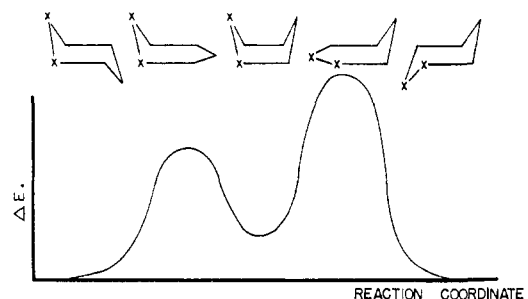


Fig. 10.—A reaction pathway and its energy barrier for inversion of 1,2-dithiane or 1,2-dioxane.

fur analog has normal values for a first order reaction. The difference between the kinetic constants of the two molecules might indicate different pathways for their chair-chair interconversions. Assuming that the molecule passes through an intermediate boat form, two different pathways of conversion can be drawn for the unsubstituted cyclic compounds (Fig. 9 and 10). In Fig. 9, the intermediate boat form of the molecule is symmetrical around the heteroatoms while in Fig. 10 it is unsymmetrical. The shapes of the energy barriers for these two pathways can be estimated roughly by considering the energies involved: (a) in the methylene oppositions, (b) in the change of the dihedral angles of the heteroatoms and (c) in the change of the ring valence angles. The pathway of Fig. 9 has a single maximum (transition state) and that of Fig. 10 has an unsymmetrical barrier with a minimum, which indicates a finite unstable intermediate state. (If the flipping in Fig. 10 is started from the other end of the molecule, the barrier would, of course, be a mirror image of the one shown.) We estimate the higher maximum in Fig. 10 to be higher than the one in Fig. 9 because of the extra valence angle distortion in the coplanar atoms (Fig. 10) beyond the single CH_2 opposition and the 0° dihedral angle common to both.

Applying the boat form conformation of Fig. 9 to compounds (IV) and (V) places the α -methyl groups very close together. Molecular models of the two compounds (IV and V) show that in the oxygen case it is not possible to build the symmetrical boat form (Fig. 9) due to a complete interference of two of the methyl groups. Thus, the

models indicate that this boat form of tetramethyldioxane (V) cannot exist. However, the space for the methyl groups in tetramethyldithiane (IV) seems to be sufficient to permit the existence of its symmetrical boat form. Therefore the sulfur compound (IV) probably inverts through the pathway shown in Fig. 9. The cyclic peroxide (V) is forced by these steric considerations to take the pathway over the higher barrier shown in Fig. 10. The transition states in the latter case are shown by a molecular model to be very flexible, in agreement with the higher entropy value found.

In the calculation of ΔF^\ddagger and ΔS^\ddagger the transmission coefficient (K) in equation 3 is equated to one for the sulfur compounds (III) and (IV), and to one-half for the oxygen compound (V).

From the ΔF^\ddagger value obtained for the inversion of 1,2-dithiane (III) and from the corresponding ΔF^\ddagger for cyclohexane,¹⁵ an estimation of the free energy barrier for the disulfide rotation alone was reported in an earlier communication.⁶ This energy difference (ΔF^\ddagger) between 0 and 90° dihedral angle was estimated to be 12.3 kcal./mole.

Further synthetic work and n.m.r. studies on deuterium and methyl-substituted 1,2-dioxane, 1,2-dithiane and 1,2-diselenane are now in progress. We hope by way of this work to estimate the barrier (ΔE^\ddagger) for rotation around the X-X bond (X = O, S or Se) and also to obtain more knowledge about the possible pathways for inversion of the molecules.

(15) F. R. Jensen, D. S. Noyce, C. H. Sederholm and A. J. Berlin, *J. Am. Chem. Soc.*, **82**, 1236 (1960).