

REACTION OF 1,2-DIHALIDES WITH THIOLATES

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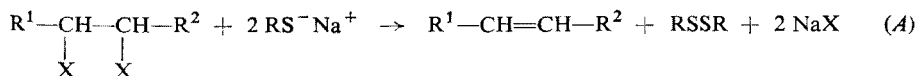
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Reaction of vicinal dihalides $R^1-CHBr-CHBr-R^2$ with thiolates in methanolic medium, which affords disulphides and unsaturated compounds, proceeds according to the kinetic equation $v = k[RS^-]^2$ [dihalide]. Reactions of dibromides $R-CHBr-CH_2Br$ with thiolates are accompanied by substitution with the ion $R-S^-$; the extent of this substitution decreases with increasing size of R. Alkyl groups exert only little influence upon the reaction whereas groups, capable of conjugation, have a great effect. The reactivity of thiols depends on the electron density on the sulphur atom. The ΔH^\ddagger and ΔS^\ddagger values of the reaction indicate a highly ordered transition state.

In the reaction of vicinal dihalides with various nucleophilic reagents, elimination of halogen takes place, besides substitution reaction and elimination of hydrogen halide¹. This reaction was studied *e.g.* in the reaction of 1,2-dihalides with halide ions²⁻⁴, thiolates^{5,6}, thiourea⁷, selenides⁸, derivatives of trivalent phosphorus^{9,10} and organometallic compounds¹. Alkenes can be obtained also by reaction with Cr^{2+} (ref.¹¹) or Fe^{2+} ions and with metals¹, this reaction being suitable for regeneration of alkenes from 1,2-dihalides used in the protection of double bonds. The stereochemistry of the dehalogenation varies extensively according to the reagent type and the reaction medium¹². The suggested mechanisms¹³ involve radicals, carbonium ions or synchronous fission of more bonds and differ mainly in the extent of the electron transfer in the first reaction step.

In the present work we investigate the reaction of thiolates with vicinal dihalides from the point of view of the relation between the structure of the both reaction components and the reaction rate. Dehalogenation of vicinal dihalides with thiolates proceeds according to the equation (A), where X = Cl, Br, or I.



This reaction was discovered by Otto^{6,14} and its mechanism was studied by other authors^{12,15}. Concerning its stereochemistry, it was found¹² that *meso*-1,2-dibromo-1,2-diphenylethane on treatment with sodium toluenethiolate in ethanol, dimethyl sulphoxide or dimethylformamide, affords 100% of *trans*-stilbene whereas the *DL*-isomer gives more than 75% *cis*-stilbene, the reaction thus being markedly stereospecific (*anti*-elimination). On the contrary, Eliel and Haber¹⁶ report that in the reaction of a mixture of *cis*- and *trans*-3,4-dibromo-1-*tert*-butylcyclohexane with benzenethiolate the reaction products of both isomers did not differ substantially.

The effect of the substituents R^1 and R^2 on the reaction rate was studied using the reaction of a series of dibromo and chlorobromo derivatives with sodium butane-thiolate in methanol, the effect of alkyls in the thiolate molecule was followed in the reaction with *trans*-1,2-dibromocyclohexane (Table I and II). The reaction rates were determined by alkalimetric titration of the thiolate as well as by gas-liquid chromatographic analysis of elimination products and of the formed disulphide. The rate constants were calculated and kinetic relations evaluated using an analogue computer.

The overall order of the reaction, as determined by the method of half-lives, is 2.9; the reaction is second order in thiolate and first order in dihalide and corresponds to the kinetic equation (1).

$$v = k[R - S^-]^2 [\text{dihalide}] \quad (1)$$

Kinetic measurements show that the reaction differs essentially from the reaction

TABLE I

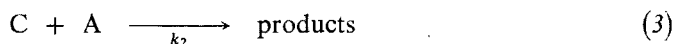
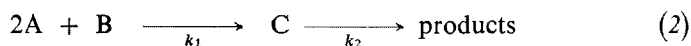
Rate Constants, k ($s^{-1} \text{ mol}^{-2} \text{ l}^2$), of the Reaction $R^1\text{-CHBr-CHBr-}R^2$ with Sodium Butane-thiolate in Methanol at 25°C and the Extent of Halogen Elimination, E (%)

R^1	R^2	k	E
H	C_2H_5	$8.5 \cdot 10^{-4}$	82
H	C_6H_{13}	$8.1 \cdot 10^{-4}$	98
H	C_2H_5	$8.5 \cdot 10^{-4}$	82
H	C_6H_{13}	$8.1 \cdot 10^{-4}$	98
H	$C(CH_3)_3$	$5.2 \cdot 10^{-4}$	99
H	$CH_2COOC_2H_5$	—	23
H	$COOC_2H_5$	—	52
H	$C_6H_5^a$	0.36	95
H	<i>p</i> - $C_6H_4NO_2$	12.2	96
CH_3^b	CH_3	$17.3 \cdot 10^{-4}$	96
CH_3^c	C_6H_5	1.92	92
$C_6H_5^d$	C_6H_5	100	91
$C_6H_5^e$	$COOCH_3$	$1 \cdot 10^4$	98
$COOC_2H_5^e$	$COOC_2H_5$	— ^e	100
	— $(CH_2)_4$ — ^f	$6.8 \cdot 10^{-4}$	98
	— $(CH_2)_3$ — ^g	$12.0 \cdot 10^{-4}$	96

^a k (E): 1-Chloro-2-bromo-1-phenylethane $7.6 \cdot 10^{-2}$ (92), 1-chloro-2-bromo-2-phenylethane $2.7 \cdot 10^{-2}$ (93); ^b a mixture of approximately 40% DL- and 60% *meso*-dibromo derivative; ^c *erythro*-isomer; ^d *meso*-isomer; ^e immeasurably fast reaction rate; ^f *trans*-1,2-dibromocyclohexane; ^g *trans*-1,2-dibromocyclopentane.

of dihalides with iodide ions^{4,17} which is first-order in the iodide ion. The reaction order determination can be influenced by ion association which, as shown by Závada and collaborators^{18,19}, has a great effect on the rate and stereochemistry of elimination reactions. We chose therefore efficiently solvating methanol as the reaction medium.

We investigated the validity of the kinetic pathways (2) and (3) (where C is an intermediate) because the equation (1) is in accord with the mechanism involving an intermediate (C) as well as with a one-step reaction. In all cases we found that Scheme (3) is not compatible with the results. This Scheme would be acceptable only if the first reaction step were reversible, an assumption which is not probable in this case.



Since it was experimentally not possible to measure the dependence of the concentration $[C]$ on time, we did not obtain directly the values k_2 but the values of the product $k_2[C]$ which were in all the studied cases very small. Since in any time the concentration of the formed disulphide corresponded within the accuracy of the method to the decrease in butanethiolate, the small $k_2[C]$ value can be explained only by a negligible concentration $[C]$ or by a reaction approaching to a one-step reaction.

TABLE II

Rate Constants, k ($s^{-1} \text{ mol}^{-2} \text{ l}^2$), of the Reaction of Thiolates $RSNa$ and Dithiolates $NaS \cdot (CH_2)_n SNa$ with *trans*-1,2-Dibromocyclohexane at 25°C

R	$RS^{(-)}$		$(^{-})S(CH_2)_nS^{(-) a}$		
	$k \cdot 10^4$	A^b	n	$k \cdot 10^4$	A^b
C_4H_9	6.80	86	2	9.9	98 ^c
$(CH_3)_2CH$	8.06	88	3	10.5	93
$(CH_3)_3C$	9.33	85	4	13.0	95
$C_6H_5CH_2$	6.33	85	5	13.5	96
C_6H_5	1.34	95	6	11.9	89
<i>p</i> -NO ₂ C ₆ H ₄	0.10	90	—	—	—

^a Concentration of the dithiolates was calculated with regard to the number of reacting groups; ^b $A = \%$ of the isolated disulphide; ^c a higher polymer, according to mass spectrometry.

It is seen from Table I that the alkyls R^1 and R^2 generally affect the reaction rate only little.

The reactions of 1,2-dibromoethane, 1,2-dibromopropane and 1,2-dibromobutane are accompanied to a greater extent by substitution with thiolate ion at both reaction centers; the extent of this side-reaction decreases with increasing chain length, in accord with the decrease in the rate of nucleophilic substitution²⁰ in the series $CH_3Br \rightarrow C_5H_{11}Br$. As a result, in the series $R-CHBr-CH_2Br$ the yield of substitution products decreases in the order $R = H > CH_3 > C_2H_5 > C_6H_{13}$ (72.7%, 55.2%, 18%, and 2%, respectively). Ethyl 2,3-dibromopropionate afforded by side-reactions four compounds in the approximate ratio 10.5 : 2.5 : 4.2 : 30, the principal part being oligomers of ethyl acrylate. Reaction of ethyl 3,4-dibromobutanoate gave, besides ethyl 3-butenate (20%), ethyl *trans*-4-butylthio-2-butenate (12%) and ethyl 3,4-bis(butylthio)butyrate (65%) as side-products.

Although alkyls have no significant effect on the rate of dehalogenation, all substituents capable of conjugation with the arising double bond affect strongly the reaction rate. Since no steric hindrance was observed in the elimination reaction, we may assume that the intermediate C, or the transition state in a synchronous process, contains a substantially developed multiple bond. It follows further from the experimental data that nucleophilic substitution (if occurring at all) is not the reaction determining step. Comparison of the reaction rates of 1,2-dibromo-1-phenylethane ($k = 36 \cdot 10^{-2} \text{ s}^{-1} \text{ mol}^{-2} \text{ l}^2$), 1-chloro-2-bromo-1-phenylethane ($k = 7.6 \cdot 10^{-2} \text{ s}^{-1} \cdot \text{mol}^{-2} \text{ l}^2$) and 1-chloro-2-bromo-2-phenylethane ($k = 2.7 \cdot 10^{-2} \text{ s}^{-1} \text{ mol}^{-2} \text{ l}^2$) shows that bromine reacts faster than chlorine; it is probable that stretching of the C-halogen bond participates in the transition state of the reaction.

Most of the mentioned dibromo derivatives are debrominated with sodium butanethiolate in high yields, only in cases when the dehalogenation would afford a thermodynamically less stable alkene with terminal double bond a substitution reaction takes place the extent of which decreases with increasing length of the alkyl.

The kinetic investigations of the effect of thiolate structure on the debromination rate of *trans*-1,2-dibromocyclohexane (Table II) have shown that the reaction rate depends on the electron density on the sulphur atom. All these reactions afforded only products of a *trans*-elimination of the halogen. In the reaction of dithiolates $^-S-(CH_2)_n-S^-$ where $n = 2$ and 6 we isolated the linear polysulphide $^-S-(CH_2)_n-S^-$; when $n = 3, 4, 5$ cyclic disulphides were obtained in yields higher than 92%. It is therefore possible to synthesise these compounds conveniently in this way.

For the reaction of sodium butanethiolate with *trans*-1,2-dibromocyclohexane following activation parameters were found: $\Delta H^\ddagger = 15.3 \text{ kcal/mol}$ and $\Delta S^\ddagger = -23.8 \text{ e.u.}$; these values indicate a high ordering of reactants in the transition state. A change in polarity due to transition from methanol to dioxane-methanol (9 : 1) mixture caused a 16 fold increase of the rate constant, $k(\text{s}^{-1} \text{ mol}^{-2} \text{ l}^2)$:

Dioxane-methanol	0	1 : 1	3 : 1	9 : 1
$k \cdot 10^{-4}$	6.8	15.2	58.6	108

Also the elimination : substitution ratio in the reaction of 1,2-dibromoethane with sodium butanethiolate is affected by the change in solvent polarity: in methanol there is 27%, whereas in dioxane-methanol (3 : 1) 78% of elimination. This is in accord with the observation of Weygand and Peine⁵ that a suspension of sodium ethanethiolate in ether reacted with diiodoethane to give 76% of ethylene. The formation of cyclic disulphides and polymers of ethyl acrylate indicates a one-electron transfer (a redox process) under formation of an R-S• radical which, however, is kinetically not independent. Weygand and Peine⁵ obtained in 36% yield tetracyanoethylene by treatment of dibromomalonodinitrile with thiolate; this also indicates the possibility of this course.

EXPERIMENTAL

Kinetic measurements. Methanolic solutions of the dihalides (1 equivalent) and sodium thiolate (2 equivalents) were mixed and allowed to stand at 25°C. The samples were withdrawn at appropriate time intervals and the reaction quenched by neutralisation with 0.1M-HCl. According to the reactivity, 1M–0.01M solutions were used. Product concentration was determined by gas-liquid chromatography (Chrom 3, Laboratorní přístroje, Prague), using a 2.4 m column, stationary phase SE-52 on Chromaton NAW-DMCS, carrier gas N₂. Dihalides, thiols and dithiols were prepared by the known procedures.

The reaction of *trans*-1,2-dibromocyclohexane with dithiolates was performed by mixing equivalent amounts of 1M solutions. After 20 hours the solvent was distilled off under diminished pressure and the residue was extracted with ether. The solvent was evaporated and the corresponding disulphide (polysulphide) was obtained by crystallisation. The reaction of ethanedithiolate with 1,2-dibromocyclohexane afforded in 98% yield, m.p. 147–8°C. This m.p. a compound corresponds to the value given for the dimer²¹. Mass spectral analysis showed that the product is a higher polymer. IR spectrum (cm⁻¹): 725, 1100, 1180, 1405. Analogously were obtained: 1,2-dithiolane, m.p. 73°C (chloroform-benzene; ref.²² reports m.p. 73°C), 93% yield; 1,2-dithiane, m.p. 31°C (hexane), 95% yield (ref.²³ reports m.p. 25–30°C); 1,2-dithiepane (96%), m.p. 56 to 58°C (ref.²⁴ states m.p. 41°C and ref.²³ m.p. 55–60°C).

REFERENCES

- King J. F., Pows R.: Can. J. Chem. 42, 1294 (1964).
- Tsai Lee C. S., Mathai I. M., Miller S. I.: J. Amer. Chem. Soc. 92, 4602 (1970).
- Baciocchi E., Schirotti A.: J. Chem. Soc. B 1969, 554.
- Badea F., Constantinescu T., Juvara A., Nenitzescu C. D.: Justus Liebigs Ann. Chem. 706, 20 (1967).
- Weygand F., Peine H. G.: Rev. Chim. Acad. Rep. Populaire Roumaine 7, 1379 (1962).
- Otto R.: J. Prakt. Chem. 51, 285 (1895).
- Ibne-Rasa K. M., Muhammad N., Hasibulah: Chem. Ind. (London) 1966, 1418.
- Prince M., Bremer B. W., Brenner W.: J. Org. Chem. 31, 4292 (1966).

9. Devlin C. J., Walker B. J.: *J. Chem. Soc., Perkin Trans. 1*, 1972, 1249.
10. Tung C. C., Speziale A. J.: *J. Org. Chem.* 28, 1521 (1963).
11. Kochi J. K., Singleton D. M., Andrews L. J.: *Tetrahedron* 24, 3503 (1968).
12. Mathai I. M., Schug K., Miller S. I.: *J. Org. Chem.* 35, 1733 (1970).
13. Csapila J.: *Chimia* 18, 37 (1964).
14. Otto R., Stoffel F.: *Chem. Ber.* 30, 1799 (1897).
15. Ko E. C. F., Parker A. J.: *J. Amer. Chem. Soc.* 90, 6447 (1968).
16. Eliel E., Haber R. G.: *J. Org. Chem.* 24, 143 (1959).
17. Mathai I. M., Miller S. I.: *J. Org. Chem.* 35, 1416 (1970).
18. Závada J., Svoboda M.: *Tetrahedron Lett.* 1972, 23.
19. Pánková M., Svoboda M., Závada J.: *Tetrahedron Lett.* 1972, 2465.
20. Dostrovsky I., Hughes E. D.: *J. Chem. Soc.* 1946, 157.
21. Fasbender H.: *Chem. Ber.* 21, 1470 (1888).
22. Bergson G., Claesson G.: *Acta Chem. Scand.* 11, 911 (1957).
23. Field L., Barbee R. B.: *J. Org. Chem.* 34, 36 (1969).
24. Schöberl A., Gräffe H.: *Justus Liebigs Ann. Chem.* 614, 66 (1958).

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