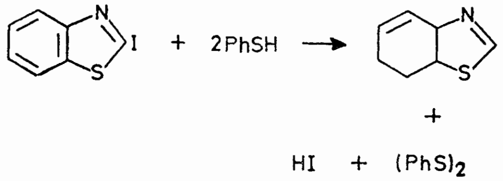
Reductive Dehalogenation of 2-Iodobenzothiazole with Alkanethiols

By **Giuseppe Bartoli, Leonardo Di Nunno,* Saverio Florio,** and **Michele Fiorentino,** Istituto di Chimica Organica, Università, 70126 Bari, Italy
Paolo E. Todesco, Istituto di Chimica Organica, Università, 40136 Bologna, Italy

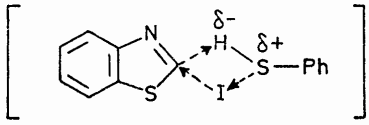
The reactions of 2-iodobenzothiazole with alkanethiols in methanol afford the unsubstituted benzothiazole as previously found for reactions with thiophenols. The reaction is autocatalytic, the hydroiodic acid produced being responsible for this phenomenon. A mechanism for the reaction is suggested.

THE reactions of 2-iodo- and 2-iodo-6-X-benzothiazoles with thiophenol or substituted thiophenols have been investigated previously.[1] In all cases 2-unsubstituted benzothiazoles were obtained, together with diaryl disulphides and hydroiodic acid. The reactions are sensitive to a change of substituent in thiophenol (ρ −0.7; σ^+ values used), while in 2-iodobenzothiazole the substituent effect was smaller and rather irregular. No sensitivity to the HI produced or added acid (perchloric) was observed, nor to potassium acetate or radical generators or inhibitors.



SCHEME 1

As a preliminary hypothesis a stepwise mechanism of reaction involving a ‘ four centre ’ intermediate (A) and affording benzothiazole and sulphenyl iodide was postulated. A fast reaction of sulphenyl iodide with a second molecule of thiophenol to give diphenyl disulphide and hydroiodic acid then occurs. More recently a similar reduction of 2-iodobenzothiazole has been observed with alkanethiols. However, these new reactions display different kinetic behaviour which cannot be interpreted on the basis of the previous mechanism. We have further defined the mechanism of this reaction.



(A)

RESULTS

The reaction of 2-iodobenzothiazole with ethanethiol in methanol afford benzothiazole in almost quantitative yield, as previously found for reactions with thiophenol. Contrary to observations for thiophenol, the reactions are autocatalytic (the second-order rate constants increase during the reaction). The autocatalysis may be attributed to the hydroiodic acid produced. In fact, by adding suitable amounts of pure methanesulphonic acid (some experiments were also carried out with 70% perchloric acid in water) the rate increases and the autocatalysis is suppressed. No effect on the rate was found by adding each of the other reaction products (*i.e.*, benzothiazole, diethyl disulphide or even I^- in the form of KI). The second-order rate constants are dependent on the concentration of added methanesulphonic acid (in excess with respect to 2-iodobenzothiazole and hence to overall HI). The relevant data are reported in Table 1.

TABLE 1

Second-order rate constants k ($\mathrm{l\ mol^{-1}\ s^{-1}}$)[a] for variable methanesulphonic acid concentrations in the reaction between 2-iodobenzothiazole and ethanethiol in methanol at 25°

$10^2[\mathrm{MeSO_3H}]/\mathrm{M}$	10^3k
0.0	1.2[b]
0.08	2.7[c]
0.11	3.1[c]
0.16	3.8[c]
0.22	4.7
0.30	5.7[c]
0.48	7.5[c]
0.87	10.5
1.40	13
2.50	16
4.0	20
7	24
8	23
9	24
39	24
74	24

[a] Followed titrimetrically: [2-iodobenzothiazole] $\leqslant 1.6 \times 10^{-2}\mathrm{M}$; [EtSH] $\geqslant 3 \times 10^{-2}\mathrm{M}$. For $[\mathrm{MeSO_3H}] < 1.6 \times 10^{-2}\mathrm{M}$, the kinetics were calculated as initial rate constants. [b] Extrapolated. [c] Followed spectrophotometrically: [2-iodobenzothiazole] $= 2 \times 10^{-4}\mathrm{M}$; [EtSH] $\geqslant 5 \times 10^{-2}\mathrm{M}$.

Some initial rate constants were also calculated from experiments carried out with comparable concentrations of 2-iodobenzothiazole and methanesulphonic acid. An increase of reactivity is observed for acid concentrations $\leqslant$ *ca.* 0.005M; above this concentration the reactivity becomes less sensitive to acid until a plateau is reached at *ca.* 0.07M. The reactivity of a series of alkanethiols for 0.39M-methanesulphonic acid (corresponding to the plateau for all the thiols considered) has also been investigated. The measured rate constants 10^3k ($\mathrm{l\ mol^{-1}\ s^{-1}}$) at 25° are 15, 24, 19, 23, 19, and 19 for MeSH, EtSH, $\mathrm{Pr^nSH}$, $\mathrm{Pr^iSH}$, $\mathrm{Bu^nSH}$, and $\mathrm{Bu^sSH}$, respectively.

On the other hand, the reaction of 2-iodobenzothiazole with thiophenol is insensitive to added acid. Autocatalysis (and hence sensitivity to acid addition) is also absent for the reactions in methanol of *p*-nitrophenylmethanethiol, while the reactions with phenylmethanethiol are autocatalytic (Table 2).

An increase in reactivity and the suppression of autocatalysis is observed upon addition of water (Table 3). In dioxan as solvent, the reactions with both ethanethiol and

---

[1] P. E. Todesco and P. Vivarelli, *Gazzetta*, 1964, **94**, 425; A. Picei, M. Foa, P. E. Todesco, and P. Vivarelli, *ibid.*, 1965, **95**, 465.

thiophenol are autocatalytic. The reactions cease to be autocatalytic upon addition of suitable amounts of water ($ca.$ 4M for EtSH) and the reactivity correspondingly increases. Furthermore the reaction with ethanethiol (in methanol) is also catalysed by pyridine ($\leqslant$0.3M; Table 4), the product being, for this concentration, benzothiazole (only traces of substitution product were detected). The dependence of the rate constants on the concentration of pyridine resembles that reported for acid addition (Table 1). However, in this case the plateau is not reached since at the required concentration (presumably >0.3M) competitive thioalkoxydeiodination occurs to a considerable extent.

TABLE 2

Second-order rate constants k (l mol^{-1} s^{-1}) for the reaction of thiophenol and phenylmethane- and p-nitrophenylmethane-thiol with 2-iodobenzothiazole in methanol at 25° and at variable concentrations of methanesulphonic acid

[MeSO$_3$H]/M	PhSH 10^3k	PhCH$_2$SH 10^3k	p-NO$_2$C$_6$H$_4$CH$_2$SH 10^3k
0.0	8.4	13^{a}	17
5 × 10^{-3}	8.3	16	17
1 × 10^{-2}	8.4	20	17
2 × 10^{-2}	8.4	24	17
4 × 10^{-2}		24	

^{a} Calculated as initial rate constant.

TABLE 3

Second-order rate constants k (l mol^{-1} s^{-1}) for the reaction of 2-iodobenzothiazole with ethanethiol in methanol at 25° and at variable concentrations of water and methanesulphonic acid

[H$_2$O]/M	10^2[MeSO$_3$H]/M	10^3k
4	1.3	17
4	2.6	18
4	4.3	20
4	13	24
28	0.15	24
28	0.29	24
28	0.73	23
28	1.5	25

TABLE 4

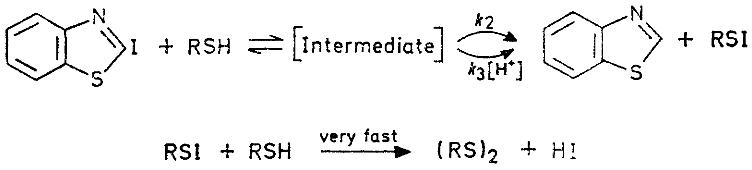
Second-order kinetic constants k (l mol^{-1} s^{-1}) for the reaction of 2-iodobenzothiazole with ethanethiol at 25° and at variable concentrations of pyridine

10^3[Py]/M	10^3k
2.5	1.4
6.2	1.9
18	2.8
27	3.4
100	6.7
230	11
300	12

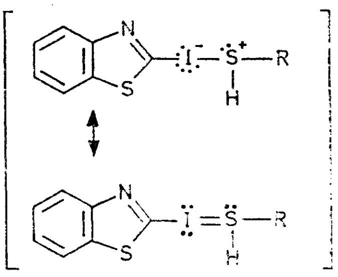
Finally, in methanol no sensitivity to light or to radical inhibitors was found.

DISCUSSION

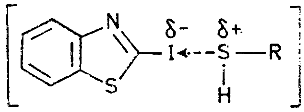
In the light of the results, the autocatalytic behaviour observed for the reactions in methanol of alkanethiols with 2-iodobenzothiazole can be related to their low acidity.[2] When the acid strength is increased (p-nitrophenylmethanethiol) autocatalysis is not observed; the amount of methanesulphonic acid required to suppress autocatalysis for the other alkanethiols increases with their basic character. The autocatalysis phenomenon cannot be explained adequately by the previously suggested mechanism. The new findings indicate a stepwise mechanism of the type depicted in Scheme 2. In this mechanism an intermediate of type (B) or (C) (charge transfer complex) is postulated instead of the 'four centre' intermediate previously hypothesized. Both (B) and (C) correspond to nucleophilic attack of the thiol sulphur atom on the iodine of 2-iodobenzothiazole. Some reported data [3,4] support the structures assigned to (B) and (C). No definitive choice between them can be made at the present, though in our view (C) seems more probable. From the intermediate, benzothiazole and sulphenyl iodide are formed by I$^+$ abstraction and proton transfer. At this stage the intervention of a zwitterionic species similar to that postulated by Breslow [5] is possible. Sulphenyl iodide in turn rapidly reacts with alkanethiol (as proposed previously),[1] affording dialkyl disulphide and hydroiodic acid.



SCHEME 2



(B)



(C)

---

[2] M. M. Kreevoy, E. T. Harper, R. E. Duvall, H. S. Wilgus, III, and L. T. Ditsh, *J. Amer. Chem. Soc.*, 1960, **82**, 4899; M. M. Kreevoy, B. E. Eichinger, F. E. Stary, E. A. Katz, and J. H. Sellstedt, *J. Org. Chem.*, 1964, **29**, 1641.

[3] G. Cilento, *Chem. Rev.*, 1960, **60**, 147; R. B. Sandin, *ibid.*, 1943, **32**, 249; D. F. Banks, *ibid.*, 1966, **66**, 243.

[4] O. Hassel and Chr. Rømming, *Quart. Rev.*, 1962, **16**, 1; G. Reichenbach, S. Santini, and U. Mazzucato, *J.C.S. Faraday I*, 1973, 143.

[5] R. Breslow, *J. Amer. Chem. Soc.*, 1957, **79**, 1762; *Chem. and Ind.*, 1957, 893.

This mechanism is consistent with the observed autocatalysis if the second stage ($k_2 + k_3[H^+]$) is assumed to be rate determining. This seems likely in the case of thiols because of their low acidic character. Thus, the increased proton availability of the medium,[6] due to the formation of hydroiodic acid during the reaction (or to the addition of methanesulphonic or perchloric acid, or even of water) may enhance the reactivity, as observed. This mechanism also agrees with the absence of autocatalysis and the substituent effect previously observed for thiophenols,[1] if the first step is regarded as rate determining in accord with the greater acidic and lesser nucleophilic character of thiophenol.[2]

On the other hand the rate determining step also depends on the conditions used, as confirmed by experiment. In dioxan the reactions with thiophenol are autocatalytic (*i.e.*, the second stage is rate determining) presumably because of the low polarity (and absence of proton availability) of the solvent which decreases the ($k_2 + k_3[H^+]$) term. On the contrary, if the polarity and/or proton availability of the medium are increased (*e.g.* by addition of a suitable amount of methanesulphonic acid) k_1 also becomes rate determining in the case of alkanethiols. This occurs on the plateau, where $k_2 + k_3[H^+] \gg k_1$ and k_{-1}. No definite trend is apparent on plotting such data for the alkanethiols against the respective σ^* values and this can be ascribed to experimental error and to the low ρ value (also suggested by the data obtained for substituted thiophenols).[1] However, from these data any appreciable steric effect can be excluded, in accord with the postulated nucleophilic attack on iodine (as opposed to attack on C-2; in thioalkoxydehalogenation of 2-halogenobenzothiazoles, considerable steric effects are observed).[7]

Finally, if the second stage (Scheme 2) is rate determining, base catalysis is also expected [6] since proton transfer from the thiol sulphur atom to the benzothiazole (probably initially to the aza-group) is involved. This can be verified by addition of pyridine ($\leqslant 0.3$M). For higher concentrations of pyridine the rate-determining step would be shifted towards nucleophilic attack of sulphur on iodine (*i.e.*, once more a plateau would be reached). Unfortunately, for concentrations >0.3M, competitive thioalkoxydeiodination occurs presumably due to formation of alkanethiolate ion arising from the equilibrium $RSH + Py \rightleftharpoons RS^- + PyH^+$.

In conclusion, the experimental results are in agreement with a stepwise mechanism. An alternative synchronous mechanism (stepwise and synchronous refer to the formation of benzothiazole and sulphenyl iodide) can be ruled out, since it does not explain the observed behaviour. Also a stepwise mechanism with proton transfer to the aza-group before nucleophilic attack of sulphur on iodine, even if worthy of consideration, is highly improbable in our case. In this case reactions with alkanethiols and thiophenol in methanol would be autocatalytic. A radical mechanism can also be excluded by the results.

EXPERIMENTAL

Materials.—Methanol and dioxan for kinetic experiments were commercial products (RP-ACS Carlo Erba) further purified by standard procedures.[8] Methanesulphonic and perchloric (70% in water) acid were commercial products (Fluka and C. Erba respectively). 2-Iodobenzothiazole, m.p. 79—80°, was synthesized from 2-aminobenzothiazole as previously described.[1] Methanethiol was synthesized according to the method of Backer and Stienstra.[9] Phenylmethanethiol [10] and *p*-nitrophenylmethanethiol [11] were synthesized as reported. The other alkanethiols and thiophenol were commercial products (Merck and Fluka) further purified by distillation before use. Benzothiazole [12] and dialkyl disulphides [13] (used as references in the product detection) were synthesized from 2-mercaptobenzothiazole and from the corresponding alkanethiols respectively.

Products.—The products detected (t.l.c. and g.l.c.) were benzothiazole and the dialkyl disulphides corresponding to the starting alkanethiols.

Kinetic Experiments.—These were performed in a thermostatted apparatus by mixing suitable amounts of thermostatted solutions of both 2-iodobenzothiazole (with or without methanesulphonic acid) and alkanethiol. Portions of the mixture were removed at suitable intervals, diluted by distilled water, and rapidly extracted with chloroform. The appearance of halide ion (aqueous layer) was then measured (Volhard) and from this, the rate constants were obtained using the appropriate kinetic equation. No appreciable effect on the accuracy of the results were observed by dilution in water.

This work was supported by a grant from the Consiglio Nazionale delle Ricerche, Rome.

[5/1238 *Received*, 23*rd June*, 1975]

---

[6] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' 2nd edn., Cornell University Press, Ithaca, 1969, p. 806.

[7] G. Bartoli, L. Di Nunno, and P. E. Todesco, *Tetrahedron Letters*, 1968, 2369.

[8] J. A. Riddick and W. B. Bunger, ' Techniques of Chemistry. Vol. II, Organic Solvents,' 3rd edn., Wiley-Interscience, New York, 1970.

[9] H. J. Backer and F. Stienstra, *Rec. Trav. chim.*, 1933, **52**, 1033.

[10] R. L. Frank and P. V. Smith, *J. Amer. Chem. Soc.*, 1946, **68**, 2103.

[11] T. S. Price and D. F. Twiss, *J. Chem. Soc.*, 1909, **95**, 1725.

[12] J. Čech, *Coll. Czech. Chem. Comm.*, 1949, **14**, 555.

[13] A. I. Vogel, ' Practical Organic Chemistry,' 3rd edn., Longman, Green, London, 1956, pp. 496—498.