Dehalogenation Reactions of Vicinal Dihalides. Part III.[1] Dehalogenations of 1-Chloro-2-iodo-1,2-diphenylethane induced by a Variety of Nucleophiles. The Nucleophilic Reactivity towards Iodine

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Dehalogenations of *erythro*-1-chloro-2-iodo-1,2-diphenylethane promoted by a variety of nucleophiles have been studied in methanol and, in the case of halide ions, also in *NN*-dimethylformamide. The susceptibility of iodine in this compound to undergo nucleophilic attack is extremely high and surpasses that of bromine by a factor larger than 10^6. An order of nucleophilic reactivity towards iodine bonded to a saturated carbon has been established. Dehalogenation rates follow approximately the Edwards equation with α and β values (2·13 and −0·12, respectively) indicating that polarizability and desolvation factors play a larger role than basicity in determining nucleophilic reactivity. The importance of the polarizability is also shown by the reactivity order of the halide ions in dimethylformamide which is $I^- > Br^- > Cl^-$. As an electrophilic centre, iodine appears to have a susceptibility to be attacked by polarizable nucleophiles which is larger than that of the saturated carbon atom.

DEHALOGENATIONS of vicinal dihalides have attracted renewed interest mainly with respect to the reaction mechanism and the factors determining halogen nucleophilicity.[1-4] However, these studies and previous ones have mostly dealt with reactions of dibromo-derivatives, whereas very few data have been reported on dehalogenations involving nucleophilic attack on an iodine atom. We have now investigated the kinetics of the reactions of *erythro*-1-chloro-2-iodo-1,2-diphenylethane with a variety of nucleophiles in methanol.

Reactivity data for the reactions of this substrate with halide ions in *NN*-dimethylformamide are also reported.

RESULTS

erythro-1-Chloro-2-iodo-1,2-diphenylethane reacts with several nucleophiles in both methanol and dimethylformamide according to equation (1). The kinetics have therefore been examined by following spectrophotometrically

$$(\textit{erythro})\text{-PhCHI·CHClPh} \xrightarrow{\text{Nu}} (\textit{trans})\text{-PhCH=CHPh} + \text{ICl} \quad (1)$$

at 320 nm the appearance of *trans*-stilbene, and of *trans*-stilbene and I_3^- when the reaction was that with I^- in dimethylformamide. The concentrations of the nucleophile and of the substrate were in the range 5×10^{-4}—0·5M and 2×10^{-5}—3×10^{-5}M, respectively. Thus, an excess of nucleophile was used. Good first-order plots were obtained for all the reactions. The second-order rate constant (k_2) values were practically unchanged by a 2—3-fold variation in the nucleophile concentration. The reaction rates were not influenced by the presence of 1% hydroquinone.

According to the optical densities, at the end of the reaction the yield in *trans*-stilbene was generally 80—90% in methanol. This is probably due to the reaction of 1-chloro-2-iodo-1,2-diphenylethane with the solvent. Such a reaction, however, should take place mainly during the preparation of the reaction solution which, owing to the difficulty in dissolving the slightly soluble dihalogeno-derivative, often takes longer than a kinetic run. In fact, the yield of *trans*-stilbene does not change appreciably on change either of the concentration or the nature of the nucleophile. Thus, the dehalogenation rate constants and, above all, their ratios should not be significantly influenced by this side-reaction of the substrate. In dimethylformamide the reactions were very fast and 1-chloro-2-iodo-1,2-diphenylethane undergoes a solvent-induced dehalogenation which somewhat influences the rate data obtained in this medium. Therefore, data for dimethylformamide are approximate.

All rate data are in the Table.

Kinetic data for the dehalogenations at 25 °C of 1-chloro-2-iodo-1,2-diphenylethane induced by a variety of nucleophiles

Nucleophile	$\dfrac{k_2}{\text{l mol}^{-1}\text{ s}^{-1}}$
In methanol	
$SeCN^-$	1·46
I^-	0·86 [a,b]
CN^-	0·40
$SC(NH_2)_2$	0·32
Piperidine	0·061
SCN^-	0·049
Br^-	0·022 [c]
Morpholine	0·015
Benzylamine	0·0048
Cl^-	0·0036 [d]
Hydrazine	0·0025
Imidazole	0·0005
Ammonia	0·0005
In dimethylformamide	
I^-	48 [d]
Br^-	9·5 [d]
Cl^-	6·8 [d]

[a] The source of I^- was KI. [b] k_2 = 0·88 In the presence of Cl^-. [c] The source of Br^- was NaBr. [d] The source of halide ions was a tetraethylammonium salt.

DISCUSSION

Reaction Mechanism.—Dehalogenations of vicinal dihalides are generally considered to occur by an *E*2-type mechanism of elimination.[5] Formation and breaking of bonds are concerted and the transition state should possess the general structure (I) (X = halogen, Nu = nucleophile, Y = leaving group).

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[1] Part II, E. Baciocchi and A. Schiroli, *J. Chem. Soc.* (*B*), 1969, 554.

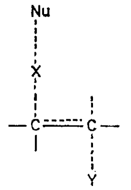
[2] E. Baciocchi and P. L. Bocca, *Ricerca sci.*, 1967, **37**, 1182.

[3] (*a*) C. S. T. Lee, I. M. Mathai, and S. I. Miller, *J. Amer. Chem. Soc.*, 1970, **92**, 4602; (*b*) W. K. Kwok and S. I. Miller, *ibid.*, p. 4599; (*c*) I. M. Mathai, K. Schug, and S. I. Miller, *J. Org. Chem.*, 1970, **35**, 1733; (*d*) I. M. Mathai and S. I. Miller, *ibid.*, p. 3416; (*e*) W. K. Kwok, I. M. Mathai, and S. I. Miller, *ibid.*, p. 3420; (*f*) W. K. Kwok and S. I. Miller, *ibid.*, p. 1034.

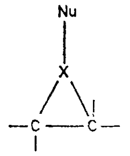
[4] F. Badea, I. Constantinescu, A. Juvana, and C. D. Nenitzescu, *Annalen*, 1967, **706**, 20.

[5] D. V. Banthorpe, 'Elimination Reactions,' Elsevier, New York, 1963, p. 140.

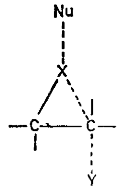
However, the possibility has also been suggested [6,7] of a multi-step mechanism involving a bridged intermediate (II) of the type postulated in the addition of halogens to olefins. Recently some evidence in this respect has been obtained by Miller and his co-workers with a careful study of the dehalogenations of (±)-1,2-dibromo-1,2-diphenylethane induced by I^- and Br^-.[3] However, for the corresponding reactions of *meso*-1,2-dibromo-1,2-diphenylethane the results were not conclusive and we feel that in such cases an *E*2 mechanism, which is favoured by conformational factors, should be the most probable one. As a first approximation it seems reasonable to extend this hypothesis, which is supported by a study of substituent effects,[1] to the reactions of *erythro*-1-chloro-2-iodo-1,2-diphenylethane; however, it must be considered that iodine is a much more effective neighbouring group than bromine [8] and that structures such as (II) should be much more stable when X is I rather than Br. Therefore, the possibility of a multi-step mechanism should be given careful consideration in the case of the reactions of *erythro*-1-chloro-2-iodo-1,2-diphenylethane. Unfortunately, at present it is not possible to make any clear choice between the concerted and the multi-step mechanism. The only indication is that, at least when $Nu = I^-$, intermediate (II), if formed, is not stable but rapidly decomposes to the products. In fact (Table) the reaction of 1-chloro-2-iodo-1,2-diphenylethane with I^- does not exhibit any mass-law effect when carried out in the presence of Cl^-. It follows that in the case of a multi-step mechanism the transition state of the rate-determining step should have structure (III).



(I)



(II)



(III)

In any case, whatever the details of the structure of the transition-state may be, there should be no doubt that in the dehalogenations of *erythro*-1-chloro-2-iodo-1,2-diphenylethane the nucleophilic attack occurs on the iodine atom. In fact, only a nucleophilic attack on the iodine atom can account for the much larger rates of these reactions than those of the corresponding reactions of *meso*-1,2-dibromo- and *erythro*-1-bromo-2-chloro-1,2-diphenylethane. Considerations relating to the factors determining nucleophilic reactivity on iodine are therefore possible.

Comparison between Iodine and Bromine as Electrophilic Centres.—Iodine is a stronger electron acceptor than bromine, as is shown by the better effectiveness of IBr than Br_2 in forming charge-transfer complexes with electron donors.[9] Therefore, it has to be expected that nucleophilic attack is significantly faster on iodine than on bromine. By comparing the reactivity data (Table) of *erythro*-1-chloro-2-iodo-1,2-diphenylethane with I^-, in methanol and dimethylformamide, and with Br^- in dimethylformamide, with the corresponding data,[1] $4{\cdot}16 \times 10^{-6}$ (I^-, MeOH), $5{\cdot}14 \times 10^{-5}$ (I^-, $Me_2N{\cdot}CHO$), $1{\cdot}45 \times 10^{-6}$ (Br^-, $Me_2N{\cdot}CHO$), for *erythro*-1-bromo-2-chloro-1,2-diphenylethane at 50 °C, we can estimate the relative susceptibility of I and Br, when bonded to a saturated carbon, of undergoing a nucleophilic attack.

With I^- the reactivity ratio is approximately 10^6 both in methanol and dimethylformamide. A still greater difference is observed with Br^- in dimethylformamide. These ratios are greater than that (less than 10^4) obtained by comparing the reactivities towards I^- in acetone of 1-bromo-2-iodoethane and 1,2-dibromoethane.[10] Such a difference could be explained, at least partially, by considering that in the 1,2-diphenylethane system there is more overcrowding than in the ethane system. Accordingly, in the former system an effect of steric relief can facilitate the elimination of ICl with respect to BrCl.

Nucleophilic Reactivity of Iodine.—The data in the Table for the reactions in methanol cover a reactivity range larger than 10^3 and represent the first scale of nucleophilic reactivity towards iodine bonded to a saturated carbon. Hydrazine does not appear to display any relevant α-effect, since its reactivity is less than that of morpholine, a reagent of comparable basicity.

The problem of correlating data of nucleophilic reactivity continues to receive attention. Among the equations suggested so far only that by Edwards [11] (2) uses the nucleophilic parameters *E* and *H* which are

$$\log k/k_0 = \alpha E + \beta H \qquad (2)$$

defined in an extra-kinetic way, *i.e.*, without reference to some standard substrate. *E* and *H* are the oxidative dimerization potential and the basicity of the nucleophile, respectively. Both parameters are normalized to 0 for the reference nucleophile, H_2O.

Since *E* is usually considered to be related to the polarizability (and solvation) of the nucleophile, the coefficients α and β should represent the sensitivity of the reaction to the polarizability (and solvation) and to the basicity of the nucleophile, respectively.

It seemed interesting to see if our kinetic data for those nucleophiles for which both *E* and *H* are known[12,13]

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[6] J. Hine and W. H. Brader, jun., *J. Amer. Chem. Soc.*, 1955, **77**, 361.

[7] J. Mulders and J. Nasielski, *Bull. Soc. chim. belges*, 1963, **72**, 322.

[8] E. S. Gould, ' Mechanism and Structure in Organic Chemistry,' Holt, Rinehart, and Winston, New York, 1959, pp. 574 and 575; S. Winstein and E. Grunwald, *J. Amer. Chem. Soc.*, 1948, **70**, 828.

[9] L. J. Andrews and R. M. Keefer, in ' Advances in Inorganic Chemistry and Radiochemistry,' eds. H. J. Emeléus and A. G. Sharpe, Academic Press, 1961, vol. 3, p. 107; see also G. G. Aloisi, G. Beggiato, and U. Mazzucato, *Trans. Faraday Soc.*, 1970, **66**, 3075.

[10] F. Declerck, J. Mulders, and J. Nasielski, *Bull. Soc. chim. belges*, 1972, **71**, 518.

[11] J. O. Edwards, *J. Amer. Chem. Soc.*, 1954, **76**, 1540.

[12] P. R. Wells, ' Linear Free Energy Relationships,' Academic Press, London and New York, 1968, p. 96.

[13] See G. Klopman, K. Tsuda, J. B. Louis, and R. E. Davis, *Tetrahedron*, 1970, **26**, 4549, for values for hydrazine.

could be correlated by equation (2). The only reservation is that dehalogenation data refer to a methanolic solution whereas the nucleophilic parameters are determined in H_2O.

Figure 1 shows that the plot of log $k/k_{Cl^-}/(E - E_{Cl^-})$ against $(H - H_{Cl^-})/(E - E_{Cl^-})$ is approximately linear.* From this plot values of 2·13 and −0·12 are calculated for α and β, respectively, which indicate that polarizability and desolvation factors play a larger role than basicity with respect to nucleophilic reactivity towards iodine. Despite the above reservation concerning the solvent, the indication appears very reasonable since iodine has a full set of outer electrons which can be excited easily and is an atom of low positive charge and large size.

Moreover, the role of polarizability which, in protic solvents, is difficult to separate from that of solvation, is clearly shown by the reactivity order of halide ions in dimethylformamide ($I^- > Br^- > Cl^-$) (Table). This order is the same as in methanol and parallels the polarizability order. Of course, solvation is also an important factor in determining nucleophilic reactivity towards iodine, as indicated by the larger reactivity spread observed in methanol than in dimethylformamide.

A similar reactivity order for halide ions in dimethylformamide has been found in corresponding nucleophilic reactions at bromine (dehalogenation of 1,2-dibromo-1,2-diphenylethane).[1] In such a case, however, halide ions covered a much larger interval of reactivity (520 against 7, for the $I^- : Cl^-$ reactivity ratio) than with 1-chloro-2-iodo-1,2-diphenylethane. The smaller discrimination between nucleophiles exhibited by the iodo-derivative is probably related to the much higher reactivity of this substrate than of the dibromo-derivative.

Very recently data of nucleophilic reactivity towards iodine bonded to an *sp* carbon atom have been obtained through a study of the reactions of nucleophiles towards 1-iodoalkynes.[14] In this case also the kinetic data are correlated by the Edwards equation. Interestingly, the values of α and β, 5·68 and 0·46 respectively, are higher than those found in the dehalogenation. Particularly significant is the change in the β value, which for the reaction of 1-iodoalkynes becomes relatively large and positive. This is probably due to the fact that when iodine is bonded to an *sp* carbon atom it has a more positive character than when it is bonded to an sp^3 carbon atom.[15]

Finally, further insight into the properties of the iodine atom as an electrophilic centre can be obtained by observing the plot of dehalogenation data against the nucleophilic constants n_{MeI} [16] (Figure 2).

Even if no linear correlation is found, as it is expected since n_{MeI} should correlate only for data concerning nucleophilic reactivity towards saturated carbon, this plot allows some interesting comparisons to be made between the properties of carbon and iodine as reaction centres.

Figure 1 shows that halide ions, $SeCN^-$, and thiourea display a relatively larger reactivity towards iodine than towards saturated carbon. In contrast, amines react relatively more rapidly with carbon than with iodine. Thus, iodine (in 1-chloro-2-iodo-1,2-diphenylethane) appears to have, as an electrophilic centre, a larger susceptibility than carbon (in MeI) to be attacked by the most polarizable nucleophiles. The reverse situation probably applies to the attack of the less polarizable, more basic nucleophiles. This conclusion is also supported by the observation that in dimethylformamide the reactivity order of halides towards the saturated carbon[17] is $Cl^- > Br^- > I^-$, whereas the reverse order applies for the reaction at the iodine atom.

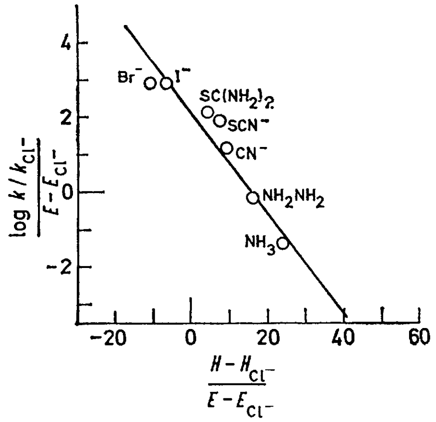

FIGURE 1 Plot of $k/k_{Cl^-}/(E - E_{Cl^-})$ against $(H - H_{Cl^-})/(E - E_{Cl^-})$ for the reactions of some nucleophiles with 1-chloro-2-iodo-1,2-diphenylethane

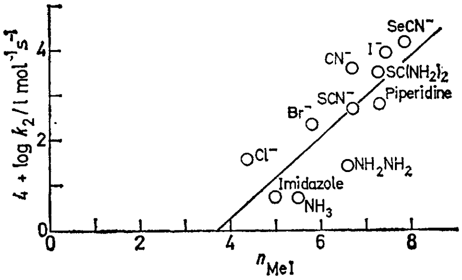

FIGURE 2 Rates of dehalogenation against n_{MeI}. The straight line has no significance except that of dividing the nucleophiles roughly into two groups

EXPERIMENTAL

Materials.—Dimethylformamide (Erba R.S.) was dried on molecular sieves and then carefully fractionated under vacuum; b.p. 50 °C/10 mmHg. Methanol was treated with Mg by standard procedures and then fractionated; b.p.

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* The Edwards equation can be written in the form log $(k/k_0)/E = \alpha + \beta H/E$; therefore, a plot of [log $(k/k_0)/E$] against H/E should result in a straight line whose intercept and slope give α and β, respectively. In our case, since k_0 (which is the reactivity constant in H_2O) is unknown, Cl^- has been taken as reference nucleophile.

[14] M. C. Verploegh, L. Donk, H. J. T. Boss, and W. Drenth, *Rec. Trav. chim.*, 1971, **90**, 765.

[15] R. E. Davis, *J. Amer. Chem. Soc.*, 1965, **87**, 3010.

[16] R. G. Pearson, H. Sobel, and J. Songstad, *J. Amer. Chem. Soc.*, 1968, **90**, 319.

[17] A. J. Parker, *Adv. Phys. Org. Chem.*, 1967, **5**, 173.

65 °C/760 mmHg. Potassium iodide (Erba, RP), sodium bromide (Erba, RP), and potassium thiocyanate (Merck) were dried at 120—150 °C. Tetraethylammonium iodide (Fluka, puriss.), bromide (Fluka, purum), and chloride (Schuchardt, 99%) were dried at 80—100 °C under vacuum. Thiourea (Erba, RP) was crystallized from water and dried, m.p. 176—178 °C. Piperidine (Erba, RP), morpholine (Erba, RP), and benzylamine (Erba, RP) were kept overnight over KOH pellets, then refluxed over sodium, and finally distilled. Imidazole (Fluka, purum), recrystallized twice from benzene, had m.p. 88—90 °C. Hydrazine hydrate (BDH, 99%), anhydrous ammonia, sodium selenocyanate (Schuchardt), and potassium cyanide (Erba, RP) were used without further purification.

erythro-1-Chloro-2-iodo-1,2-diphenylethane was prepared by adding ICl to *trans*-stilbene in chloroform at room temperature. The product (27% yield), recrystallized several times from benzene, had m.p. 126 °C (decomp.) (lit.,[18] 132 °C and [19] 122·5 °C) (Found: C, 49·0; I, 36·95; Cl, 10·2; H, 3·8. Calc. for $C_{14}H_{12}ClI$: C, 49·1; I, 37·05; Cl, 10·35; H, 3·55%). The i.r. spectrum shows the expected [18] peak at 504 cm^{-1} due to the stretching of the carbon–iodine bond. Surprisingly, the ^1H n.m.r. spectrum at 100 MHz in $CDCl_3$ and in benzene exhibits only one peak (τ 4·52 and 4·67, respectively) for the aliphatic protons in place of the expected two doublets. Measurements of ^1H n.m.r. spectrum at low temperatures and of the ^{13}C n.m.r. spectrum have so far been unsuccessful owing to the very low solubility and the instability of the compound.

Kinetics.—The appearance of *trans*-stilbene (or of *trans*-stilbene and I_3^- for the reaction with I^- in dimethyformamide) was followed at 320 nm. The solutions of the reactants were usually mixed directly in the absorption cell at 25 °C. The cells were then placed in the thermostatted compartment of a Beckman DU spectrophotometer and the optical densities measured at intervals. At the end of each experiment a complete u.v. spectrum of the mixture corresponded closely to that of a solution of *trans*-stilbene. In the case of the reactions with I^- in dimethylformamide and of I^-, Br^-, and SCN^- in methanol, the kinetic solutions were treated with a little $Na_2S_2O_3$ before the u.v. spectrum was recorded.

This work was supported by the Italian C.N.R. We thank Professor J. O. Edwards for discussions and comments.

[2/511 *Received*, 6*th March*, 1972]

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