The Solid-State Substitution Reaction between Halogenoacetates and Metal Halides

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Halogenoacetates react with metal halides in the solid state *via* halogen exchange. This was studied in detail for the reaction between sodium chloroacetate and sodium iodide to sodium iodoacetate and sodium chloride. The reaction was followed at 50, 70, and 90°C by discontinuous proton NMR spectroscopy and at 90°C by *in situ* high-temperature X-ray powder diffractometry (TXRD). The reaction leads to an incorporation of iodoacetate into the chloroacetate lattice. This destabilizes the lattice and accelerates the thermal decomposition of the sodium halogenoacetates. © 1996 Academic Press, Inc.

INTRODUCTION

Many investigations of solid-state reactions of organic compounds deal with photochemically induced reactions (1–4). Especially well studied are photopolymerizations in the solid state (5, 6). In these reaction types, we have single-phase reactions. In favorable cases, a single-crystal-to-single-crystal reaction can be monitored (7–10). A very interesting feature is the possibility to carry out enantioselective photoreactions of prochiral guest compounds in an inclusion crystal with an optically active host (see Refs. (11–12) and references therein).

Thermally induced organic reactions between two solid reactants are studied to a much lesser extent. Some typical examples include the reduction of ketones with $NaBH_4$ (13–15), the Baeyer–Villiger oxidation of ketones with *m*-chlorperbenzoic acid (16, 17), and the reaction between *p*-substituted anilines and *p*-benzoquinone (18). A considerable number of organic solid-state reactions was found and studied by Toda *et al.* (see Refs. (11–12) for recent reviews). These reactions are of general interest because a solvent is not needed and because the stereoselectivity in the solid state can sometimes be better controlled (2, 11, 17, 19). The first point can be important for a practical application (20). The explosion and health hazards and cost of organic solvents (purchase and disposal) are high.

We here report about a halogen exchange between an organic and an inorganic phase, both being solids. Such a substitution reaction is well known for a pair of solid metal halides and in organic solution chemistry, but—to our knowledge—unknown so far for solid organic compounds. It was the aim of our work to explore the potential of this reaction type in the solid state. As organic reactants we used alkali halogenoactates. These are advantageous for such a study because they are all solid, nonvolatile and easily accessible. The inorganic phases were alkali metal halides.

EXPERIMENTAL

^{1}H NMR spectroscopy was carried out with a Bruker WP-80 instrument at 80 MHz. Sample aliquots were dissolved in D_2O and immediately examined. The integral ratio of the methylene protons of chloroacetate (4.03 ppm) and iodoacetate (3.63 ppm) gives the degree of reaction. By measuring defined mixtures of sodium chloroacetate and sodium iodoacetate, we confirmed the linearity of the integral ratio. The accuracy of this method was determined to 1–2% of each compound. It was assured in advance that the substitution reaction in solution during the time needed for recording the NMR spectrum was negligible.

For high-temperature X-ray powder diffractometry (TXRD) we used a Philips XPERT diffractometer with a Paar HTK 10 camera and a steel heating strip. Cu$K\alpha$ radiation ($\lambda = 1.54178$ Å, secondary monochromator) was used. The temperature signal was calibrated with the II → I phase transition of KNO_3 at 128°C.

DSC experiments were carried out with a calibrated Mettler DSC 27HP/TA 4000/TC 11-system at ambient pressure.

All substances were of analytical grade. Halogenoacetates were recrystallized from ethanol before use and their purity checked by ^{1}H NMR, DSC, and elemental analysis (especially for the absence of halogenoacetic acid).

RESULTS AND DISCUSSION

The thermodynamic feasibility of the exchange reaction

TABLE 1
Results of Solid-State Substitution Reactions

Organic reactant	Inorganic reactant	Reaction	Organic reactant	Inorganic reactant	Reaction
Cl–CH$_2$CO$_2$Na	NaBr	yes	Br–CH$_2$CO$_2$Na	NaI	yes
Cl–CH$_2$CO$_2$Na	LiI	no	I–CH$_2$CO$_2$Na	NaCl	no
Cl–CH$_2$CO$_2$Na	NaI	yes	Cl–CH$_2$CO$_2$K	NaI	yes
Cl–CH$_2$CO$_2$Na	KI	no	Cl–CH$_2$CO$_2$K	KI	no
Cl–CH$_2$CO$_2$Na	CsI	no			

Note. Some systems for the solid-state substitution reaction show reactivity, some do not. Whether the reason is of thermodynamic or kinetic origin is not known. Reaction times were 7–14 days at room temperature.

$$X–CH_2–CO_2M(s) + M'Y(s) \rightleftharpoons \qquad [1]$$
$$Y–CH_2–CO_2M(s) + M'X(s)$$
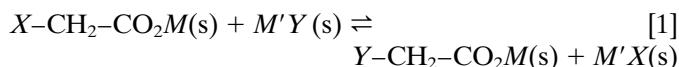
(M, M′ = metal; X, Y = halogen is difficult to estimate in advance because the enthalpy of formation of the solid organic reactants is usually not known. Therefore we had to carry out a number of test experiments to see if a reaction occurred. The direction of such a reaction in the solid state may be different from that in solution because the reaction enthalpy is the small difference of the large enthalpies of crystallization and of solution. This can be easily shown by setting up a Born–Haber cycle.

The results of a number of experiments are displayed in Table 1. All reactions were carried out between $1:2 = n(\text{organic}):n(\text{inorganic})$ powder mixtures of organic and inorganic compound under air in closed Schlenk tubes. Crystal hydrate water of the inorganic salts was not explictly excluded. The mixtures were stored for 7–14 days at room temperature. The degree of reaction α was determined by ^{1}H NMR spectroscopy. In cases where a reaction occurred, the degree of reaction was in the range 5–15%. The detection limit for a reaction product is estimated to 0.5–1%.

What we observe is a halogen exchange between some combinations of alkali halogenoacetates and alkali halides, with NaBr and NaI being effective. No crystal structure of a halogenoacetate has been reported so far. Consequently, no structural reason for the different reactivity in Table 1 can be given. It is not possible at this stage to discriminate between thermodynamic and kinetic feasibility.[1]

A dependence of the reaction rate from the kind of metal ion was also reported in Ref. (21). The hydroxide-catalyzed benzylic acid rearrangement in the solid state was studied. This reaction occurs upon thoroughly mixing benzil C$_6$H$_5$–C(O)–C(O)–C$_6$H$_5$ and a metal hydroxide and heating to 80°C. In some cases, the reaction rate is higher in the solid state than in solution. The authors varied the kind of solid hydroxide and used alkali and earth alkali hydroxides, Cu(OH)$_2$, and Al(OH)$_3$. Some proved effective in the solid-state reaction, some did not. For the row of alkali hydroxides Li–Na–K–Rb–Cs, the reactivity peaked with KOH. The reason is not known, but it may be assumed that the rate of diffusion of the hydroxide ion plays an important role. In Ref. (21) the substituents on the benzil aromatic rings were also varied. A notable change in reactivity was found depending on the electron donor/acceptor properties of the substituents.

In detail, we studied the halogen exchange between dry sodium iodide (no crystal water present) and sodium chloroacetate ($1:1 = n:n$):
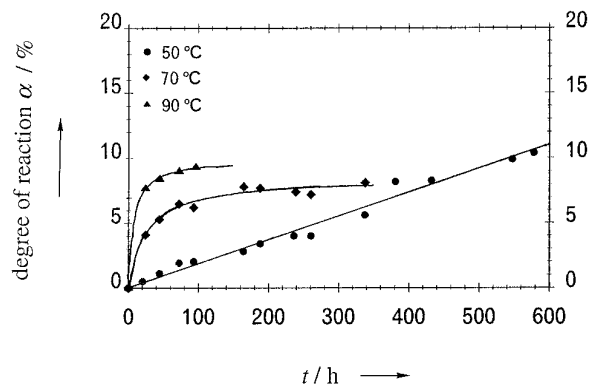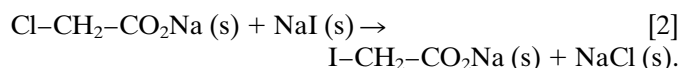
$$Cl–CH_2–CO_2Na\ (s) + NaI\ (s) \rightarrow \qquad [2]$$
$$I–CH_2–CO_2Na\ (s) + NaCl\ (s).$$

FIG. 1. Degree of reaction α vs time for $1:1 = n:n$ powder mixtures of sodium iodide and sodium chloroactate. The degree of reaction was measured by ^{1}H NMR spectroscopy on aliquots. The reaction was carried out at 50, 70, and 90°C. At $\alpha \approx 10\%$, the reaction product iodoacetic acid undergoes decomposition.

[1] In this context it is interesting that the halogenoacetic acids themselves do not react with inorganic halides. We carried out reactions between chloroacetic acid, iodoacetic acid, and a number of alkali and earth alkali halides with $1:2 = n(\text{organic}):n(\text{inorganic})$. Neither at room temperature nor at 50°C we observed a reaction after 7 days. We assume that the reason is the small diffusion coefficient of halide ions in the organic lattice and vice versa.
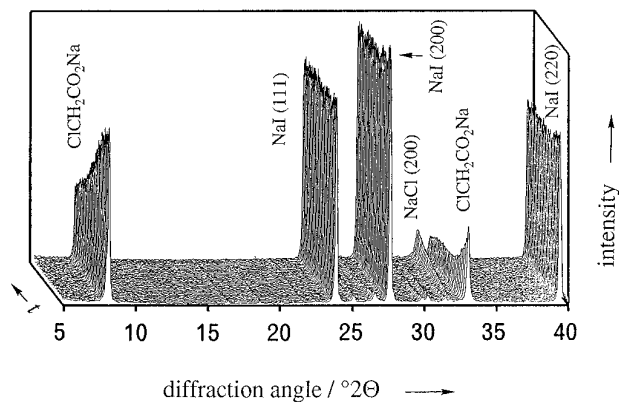
FIG. 2. High-temperature X-ray powder diffractometry on a reaction mixture. The reaction was carried out under air at 90°C for 108 hr. Sodium chloroacetate peaks (8.2°2Θ and 33.1°2Θ) shrink and a sodium chloride peak (31.7°2Θ) is forming.

To enhance the reaction, we carried out the reaction at higher temperature (50, 70, 90°C). The samples were thoroughly ground and mixed in an agate mortar in a nitrogen-filled glove box. They were stored under dry nitrogen in Schlenk tubes. Care was given when taking aliquots that no air or moisture contacted the sample. With samples containing crystal water of NaI, undefined decomposition to red-brown slurries occurred. The degree of reaction was determined by ^{1}H NMR.

The results of these experiments are shown in Fig. 1. The reaction rate increases with rising temperature, but the reaction ceases at $\alpha \approx 10\%$. For times greater than displayed, an insoluble residue remains. Obviously, a decomposition had occurred.

The decomposition of a halogenoacetate at such low temperatures is unusual. DSC experiments (both isothermal and nonisothermal) showed that decomposition of the pure chloro- and iodo-compounds occurs only above $\sim130°C$ within days. This points to a catalysis of the decomposition by sodium iodide.

To gain more insight into the reaction, we carried out high-temperature X-ray powder diffractometry (TXRD) (22). Mixtures ($1:1 = n:n$) of sodium iodide and sodium chloroacetate were annealed at 90°C for 108 hr at ambient pressure under air.

In this X-ray experiment, however, no product peaks of sodium iodoacetate occur (Fig. 2). The diffraction peaks of sodium chloroacetate at 8.2°2Θ and 33.1°2Θ decrease. The peaks of sodium iodide at 23.9°2Θ (111), 27.7°2Θ (200), and 39.5°2Θ (220) remain constant. The only detectable product peak is the one at 31.7°2Θ. This was identified as the (200) peak of sodium chloride. These findings are interpreted that reaction [2] occurs but that the formed sodium iodoacetate rapidly decomposes under the continu-

ous X radiation. The decomposition reaction leads to NaCl and probably a polymer (polyglycolide):

$$I-CH_2-CO_2Na \text{ (s)} \rightarrow NaI \text{ (s)} \qquad [3]$$
$$+ 1/n \text{ }\textbf{+}CH_2CO_2\textbf{+}_n \text{ (amorphous).}$$
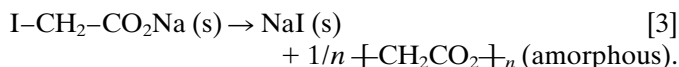
Such a reaction was already postulated by Bischoff and Walden in 1894 for the thermal decomposition of sodium chloroacetate (23–26). The polymer is X-ray amorphous. After the experiment, the reaction mixture was partially insoluble in water, acetone, and chloroform. ^{1}H NMR in D_2O showed only the presence of sodium chloroacetate. Sodium iodide is consumed by reaction [2], but regenerated by reaction [3], so that the peak intensities remain constant. The decrease in the sodium chloroacetate peaks and the formation of a sodium chloride peak confirm the occurrence of reaction [2].

By additional isothermal X-ray experiments at 90°C it was assured that neither pure sodium chloroacetate nor pure sodium iodoacetate decompose under these conditions. Only partial amorphization takes place, but no formation of NaCl or NaI or of an insoluble residue could be observed.

The peak of sodium chloroacetate at 33.1°2Θ shows an interesting behavior (Fig. 3). The peak width doubles within 35 hr, and then decreases to 1.5 times of its initial value. The intensity halves during the reaction. The peak position goes from 33.00°2Θ to 32.64°2Θ. This corresponds to an increase of the lattice d-spacing of approximately 1.1%.

We assume that during the reaction iodide ions diffuse into the sodium chloroacetate lattice. After reaction [2], the lattice of sodium chloroacetate is expanded due to the larger iodide ions. This deformation destabilizes the structure, and eventually leads to destruction by X rays. At no time did we have enough sodium iodoacetate present
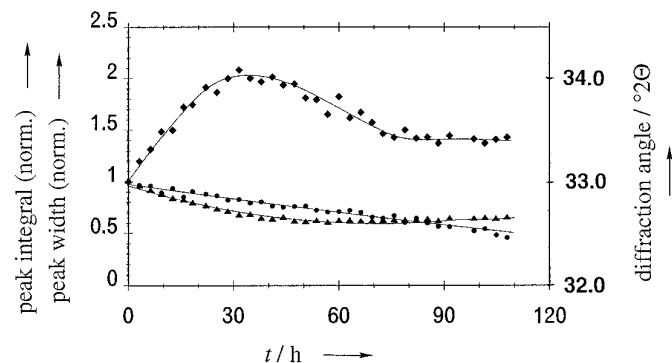

FIG. 3. Change of parameters of the sodium chloroacetate peak at 33.1°2Θ during the reaction at 90°C. Same data as in Fig. 2. ● normalized intensity (as integral), ◆ normalized width (FWHM; $t = 0$: 0.202°2Θ), ▲ position in °2Θ.

that domains large enough to coherently scatter the X rays were formed. The solubility of the product in the educt lattice was never exceeded. A high product solubility was frequently observed for organic solid-state reactions (27).

Crystal structures are known neither for sodium chloroacetate nor for sodium iodoacetate. All our attempts to obtain single crystals resulted in extremely thin platelets with obvious stacking disorder. Very slow crystallization by the diffusion method led to hydrolysis and NaCl crystals after 2 months. However, we took X-ray powder diffractograms of both compounds which point to a similar lattice symmetry of the two compounds. The strongest peak of sodium chloroacetate at small angles is found at 8.1°2Θ ($d = 10.78$ Å) that of sodium iodoacetate at 7.4°2Θ ($d = 11.95$ Å). These peaks likely correspond to the same set of *hkl* values. This indicates a larger lattice constant of sodium iodoacetate, corroborating the above interpretation.

To learn more about the mobility of the reacting species, we carried out a reaction at room temperature between two tablets consisting of sodium iodide and sodium chloroacetate. The tablets were brought in contact under slight pressure and stored for 90 days in a dry box ($CaCl_2$). After this time, the tablets were separated and both contact area and backside were investigated by X-ray powder diffractometry.

The contact side of the NaI tablet showed the presence of NaI and NaCl, and the backside only showed that of NaI. On the contact side of the sodium chloroacetate tablet we found sodium chloroacetate and sodium iodoacetate and on the backside only sodium chloroacetate. This indicates that Cl⁻ ions diffuse into the NaI lattice, and that I⁻ ions diffuse into the sodium chloroacetate lattice to react to sodium iodoacetate. This is in accordance to the above mentioned lattice expansion of the sodium chloroacetate by iodide ions.

The direction of the diffusion underlines the well-known difficulties in diffusion of bulky organic molecules in the solid state (27, 28). Only the smaller halide anions seem to be able to diffuse.

CONCLUSION

To summarize, it can be said that metal halogenoacetates do react with metal halides in some cases. The reaction is controlled both by thermodynamics and by kinetics. In the thermodynamically feasible case of the reaction between sodium iodide and sodium chloroacetate (reaction [2]), the slow diffusion restricts the reaction rate. If the temperature

is elevated to speed up the reaction, decomposition of the product occurs. However, with both suitable conditions and systems, such a halogen exchange reaction could be of interest for synthesis. Applications could be the reversal of the reaction as compared to a solution reaction or a better stereochemical control of the reaction.

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