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Reaction of Potassium Fluoride with Orgarnic Halogen Compound-Ⅱ.

Dimerization, Fluorination, and Decarboxylation of Organic Iodo acids, Iodides, and Polychlorinated Acid and Ester.

by

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有機할로겐化合物과 KF 과의 反應(第2報)

有機요-드酸, 沃化物 及 多鹽素化有機酸, 에스텔의 雙合, 弗化 及 脫炭酸 反應에 關하여

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要　約

아밀아이오다이드를 디메칠홀음아마이드 存在下에서 弗化加里와 低溫反應시켜 본 結果 弗化物과 데칸을 生成하였음. α, β,-디크로로-β-페닐-푸로피온酸과 같은 多鹽素化物은 α-크로로스타이렌, 弗化스타이렌 及 弗化酸을 生成하였음. 이 酸의 에칠에스텔은 弗化物을 生成하지 않고 各種 双合物의 混合物을 얻었음. 디부롬스타이렌은 부롬스타이렌과 弗化物을 生成하고 沃度를 含有한 有機酸, 메-타요드벤조익酸은 有機酸의 鹽과 微量의 双合物을 生成하였음. 메타요드토류엔 及 1-아미노-4-요-드-2-메칠벤젠과 같은 沃化物은 弗化加里에 對하여 反應을 나타내지 않았음. 本報에는 各 反應條件과 弗化反應, 脫炭酸反應 及 双合反應에 關하여 論議하였음.

Abstract

The reaction of potassium fluoride with amyl iodide in presence of dimethylformamide at low temperature gave a fluorination product together with decane. Polyhalogenated acid such as α, β, -dichloro-β-phenyl-propionic acid gave α-chlorostyrene, fluornated styrene, and fluorinated acid. The same reaction with the ethyl ester did not give the fluorination product and gave a mixture of various dimerized product. Dibromostyrene gave bromostyrene together with fluorination product. Iodo acid such as *m*-iodo acid gave the salt and a trace quantity of dimerized product. Iodides such as *m*-iodotoluene and 1-amino-4-iodo-2-methyl benzene did not show any appreciable reactivity towards potassim fluoride. The reaction condition was described, and fluorination, α-dehydrofluorination, decarboxylation, and dimerization were discussed.

Introduction

Reactions of potassium fluoride with organic halides, acids, and ester in presence dimethylformamide and their pyrolytic decarboxylation were previously investigated.[1] The reaction was proved to be a dimerization reaction in case of organo chlorine containing acids and to be a minute decarboxylative cyclization reaction in case of the reaction of *o*-chlorobenzoic acid at the elevated reaction temperature. Present investigation, a continuation of the previous research, was extended to the reaction system of organic iodo acids, iodides, and multiple halogenated acid, ester, and hydrocarbon in order to ascertain the reaction path in these compounds. Both a solvent reaction system such as dimethylformamide solvent and a pyrolytic reaction were investigated. The gas chromatographic technique was adopted for the elucidation of the reaction path.

Experimental*

Starting materials——The starting materials used in this experimental were partly obtained from commercial source. Amyl iodide (b. p. 156°, n_D^{20} 1.4955) and isoamyl iodide (b. p. 148°, n_D^{17} 1.4950) were prepared from the alcohol in presence of phosphorous and iodine. The α, β,-dichloro-β-phenyl-propionic acid (b. p. 163-4°, N. E. calc. 219, found 217) was prepared by the photochlorination of cinnamic acid, and the ester was prepared by Fisher esterification of the acid. (m. p. 29°) *o*-iodotoluene and *p*-iodotoluene were prepared by Sandmeyere's reaction of the corresponding toluidines. The dibromostyrene (m. p. 73°) was prepared by bromination of styrene. The *m*-iodo acid (m. p. 185-7°) was prepared by oxidation of the iodotoluene. The 2-methyl-4-iodoaniline (m. p. 85°) was prepared by iodination of the toluidine. Dimethylformamide (b. p. 152-3°, n_D^{20} 1.4250) was obtained from commercial source, and potassium fluoride (anhydrous, Riedel Haen product) was dried under reduced pressure prior to use.

Identification of product——The products in this experimental were mainly known compounds. The identification of the products were based on the gas chromatography and infrared spectrophotometry. An intergrator disc mounted on a Bristol recorder was used for the peak area calculation.

Reaction of amyl iodide with potassium fluoride——Into a 100 ml. three necked flask, equipped with a mercury sealed stirrer, condenser, and thermometer were placed 13.0 g. (0.065 mole) of amyliodide dissolved in 50 ml. of dimethylformamide and 4.8 g. of anhydrous potassium fluoride. The reaction mixture was heated under vigorous stirring for 8 hours at 130-100°. The reaction mixture was filtered and the filtrate was distilled to give a portion boiling below 120°, the solvent, and a brownish residue. The residue from the distillation was further distilled to give a portion boiling 165-180° (n_D^{14} 1.4366). Each fraction was examined by means of gas chromatography. The yield of each components of the distillate was calculated with an internal standard (adjacent eluate). There were 2.54g (43.5%) of amyl fluoride and 0.5g (6.5%) of decane. From the reaction mixture 2.4g. (50%) of patassium fluoride was recovered. From the distillation of the reaction mixture a formation of potassium iodide was observed.

In a separate reaction run 12.0 g (0.065 mol) of isoamyl iodide in 50 ml. of dimethylformamide were reacted with 3.6g of anhydrous potassium fluoride. The reaction mixture was heated under vigorous stirring for 4 hours at 80-100°. 2.9g (80.5%) of potassium fluoride were recovered. The reactivity of the iodide with potassium fluoride at lower temperature was slight. The product analysis was not carried out in this reaction run.

Reaction of *m*-iodo toluene with potassium fluoride.

Procedure A (a solvent system).——Into a 100 ml. three necked round bottomed flask were placed 11.0g (0.05 mole) of *m*-iodotoluene dissolved in 50 ml. of dimethylformamide and 2.9 g. of anhydrous potassium fluoride. The reaction mixture was refluxed under vigorous stirring for 5 hours. The reaction mixture was filtered and the filtrate was examined for inorganic iodide. There were no indication of the formation of inorganic iodide. There were no appericable reactivity of potassium fluoride in this reaction run.

Procedure B (a pyrolytic procedure).——Into a 100

* The melting point and boiling point listed in this experimental were not corrected. The infrared spectra and gas chromatograph were taken at this Institute by means of Beckmann IR-4 and G. C. -2 model, respectively.

ml. three necked round bottomed flask were placed 11.0 g (0.05 mole) of *m*-iodotoluene and 2.9 g of anhydrous potassium fluoride. The reaction mixture was well shaken and heated at 220-250° for 4 hours. The reaction mixture was filtrate, and the filtrate and the solid obtained were examined for inorganic iodide. There were no indication of inorganic iodide formatoin. There were no appreciable reactivity of potassium fluoride in this reaction run.

Reaction of α, β, dichloro-β-phenylpropionic acid with potassium fluoide. Procedure A (a solvent system). —— Into a 100 ml. three necked round bottomed flask were placed 21.9 g (0.1 mole) of the acid and 5.8 g (0.1 mole) of potassium fluoride in 50 ml of dimethylformamide. The reaction mixture were refluxed for 8 hours. The reaction mixture was filtered and the fitrate was distilled in order to remove the solvent. The sovent distillate was examined by means of gas chromatography to give a fraction other than the solvent itself. The solvent distillate was, therefore, redistilled to give a fraction boiling at 75-77°/17 mm., n_D^{16} 1.4570. The compound was aromatic and amounted 8.56 g. The compound was seemed to be 1, 2-difluoro-2-phenyl ethane. The residue from solvent distillation was washed with distilled water and the aqeous layer was extracted twice with ether. The ether extracts were dried over anhydrous calcium chloride and the ether was evaporated. The residue from ether evaporation was treated with carbon tetrachloride. From the carbon tetrachloride solution a brownish crystal (0.2 g.) was obtained, which contained chlorine, but no fluorine (m. p. 75°-80°). (I. R. 3080, 3050, 3000, 1690 (split), 1620, 1640 (doublet) 1300, 1210, 1190, 1100 (broad), 1070, 982, 975 (doublet) 925, 865, 848, 780, 745cm^{-1}.)

There were 0.1 g of yellowish solid which was various salts. The solid product was α-chlorocinnamic acid. (The yield was trace.) The acid was not recovered.

Procedure B (a pyrolytic procedure). —Into a 100ml round bottomed flask were placed 10.5g (0.48 mole) of the acid and 2.9 g. of anhydrous potassium fluoride. The mixture was well shaken and the resulting mixture was heated for 2 hours at 285°C until the reaction mixture ceased to reflux. The reaction mixture was then dissolved in alcohol and the alcoholic solution was distilled to remove the solvent. The residue from the solvent distillation was treated with distilled water. The water solution did not contain flluoride, which indicated that potassium fluoride was exhausted during the course of the reaction. The water insoluble solid amounted 1.3 g. was various acid salts, which contained chlorine and fluorine. The alcohol insoluble portion of the reaction mixture was treated with carbon tetrachloride. From the solution of carbon tetrachloride 3.9 g. of solid was obained, which was recrystallized from carbon tetrachloride melting 160-165° (2.1g). There were an insoluble solid in carbon tetrachloride treatment which contained chlorine, but no fluorine, and amounted 1.0 g. The melting point was 169-170°. It was the recovered acid. The carbon tetrachloride solution of the solid treatment was further distilled to give 2.3 g. of α-chlorostyrene boiling at 70°/84 mm (n_D^{17} 1.5627) which was examined by infrared spectroscopy. (I. R. 3050, 1090, 1070, 1030, 940, 860, 815, 740, 695cm^{-1}.) The yield of this reaction was 4.9 g. (45.6%) of the acid, 1.3 g of various salts mixture, and 2.3 g (16.9%) of α-chlorostyrene. There was trace amount of fluorinated products, which were not further characterized.

Reaction of ethyl 1, 2, -dichloro-2-phenyl-propionate with potassium fluoride.

Into a 500 ml. three necked round bottomed flask were placed 120 g. (0.466 mole) of the ester and 58.10 g. of potassium fluoride in 200 ml. of dimethylformamide. The reaction mixture was refluxed under vigorous stirring during the course of 16 hours. The reaction mixture was filtered and the solid from filtration gave a white precipitate by silver nitrate solution. The filtrate was distilled to remove the solvent, and the residue from the solvent distillation was further distilled under reduced pressure to give the following fractions.

B. Pt.	Amount, g	n_D^{20}
140-142°/16 mm	20.5	1.5708
144	8.8	1.5722
150	12.6	1.5732
150-48	5.4	1.5722
161	3.2	1.5822

solid residue, tarry materials

Each fraction was examined for the components by means of infrared spectrophtometry to give the ester, and the shifting of carboethoxy group to high frequency region wich is characterisitic for fluoro ester was not observed. The middle fraction contained chlorine, but no fluorine. Since the product was seemed to be a mixture of the dimerized product, it was exmeined by paper partition chromatography, which indicated the mixture did not contain the starting ester and no polychlorinated component. The gas chromatogram of the fraction gave a dull resolved peaks at the retention time of 13, 16, 25, 34, 37, (The peak at 13 and 37 minutes was a small sholder.) minutes respectively when the mixture was eluated through an apizeon L column (1.5 ft.) at 190°. The radioactivation analysis of the mixture indicated that it contained 13.46% of organically bound chlorine. Since there expected ten components of the dimerization reaction of the ester, further attempt of spearating the mixture was not considered, but the dimerization of the ester was apparent and it contained at least 5 components. (I.R. in CS_2 : 3000 (sholder), 3020 (sholder), 3000, 2900, 1750, 1725, 1630, 1400, 1390, 1315, [1305, 1290—1165, 1100, 1030 (broad), 990, 975, and 925 cm^{-1})

Reaction of *m*-iodo benzoic acid with potassium fluoride.

Procedure A (a solvent procedure). ——Into a 100 ml. three necked round bottomed flask were placed 3.0 g. (0.012 mole) of the acid in 50 ml. dimethylformamide and 0.7 g. of potassium fluoride. The reaction mixture was refluxed for 5 hours under vigorous stirring. The reaction mixture was filtered and the filtrate was distilled to remove the solvent. The distillation residue was washed with water and the insoluble solid was treated with ether. The ether insoluble solid (0.4 g. m.p. 155-160°) was a mixture and contained iodine, but no fluorine. The ether solution was evaporated to give 1.2 g. of a purple solid, which gave a paint pink crystal by means of washing it with alkali and acidifying. The solid melted at 185-188° and was the recovered acid. The water washing of the distillation residue gave 1.3 g. of the solid which was the salts of various acids. The yield of this run was 1.2 g. of the recovered acid (40%), 0.4 g. of the acid mixture, and 1.3 g. of salts. There were trace quantity of an unidentified material which was a purple paste. (I.R. The acid mixture: 1700, 1600 (broad) 745, 720, and 690 cm^{-1}.) From the infrared spectrum of the acid mixture it was confirmed that there obtained a slight quantity of the diacid. (*c.f.* The original acid has the carbonyl frequency at 1730 cm^{-1}.)

Procedure B (a pyrolytic reaction). ——Into a 100 ml. round bottomed flask were placed 2.7 g (0.01 mole) of *m*-iodo acid, 0.7 g. of anhydrous potassium fluoride. The mixture was well shaken and heated at 245° for an hour and at 350° for two hours. The reaction mixture was dissolved in alcohol and the insoluble solid was washed with water. The water washing contained inorganic iodide and fluoride. The water insoluble residue amounted 0.8 g., which contained inorganic fluoride, but no iodide (I.R. 1700 (dull), 1600 (broad), 740, 690, cm^{-1}) which was a mixture of the salt and acid. The alcoholic solution was distilled to give a faint brownish residue, which was recrystallized by alkaline and acid washing. It melted at 70°C. (I.R. 1700, 745, 725 cm^{-1}) The yield of this run was no recovery of the acid and 0.8 g. of the dimeized acid and acid salt. The sublimation of the acid was observed during the reaction.

Reaction of 2-methyl-4-iodo-aniline with potassium fluoride.

Into a three necked round bottomed flask were placed 7.0 g. (0.03 mole) of 2-methyl-4-iodo aniline dissolved in 50 ml. of dimethylformamide and 1.9 g. of anhydrous potassium fluoride. The reaction mixture was filtered and the residue from filtration was examined for inorganic iodide to give a negative test. The filtrate was distilled and the residue was treated with hydrochloric acid. The formed hydrochloride was examined and separated. It melted at 109-110°C and did not contain fluorine. The reactivity of the potassium fluoride in this reaction run was not observed.

Reaction of dibromostyrene with potassium fluoride.

Into a 100 ml. three necked round bottomed flask were placed 13.0 g (0.01 mole) of dibromostyrene and 2.9 g. of anhydrous potassium fluoride in 50 ml. of dimethylformamide. The reaction mixture was refluxed for 3 hours. The reaction mixture was filtered and the filtrate was examined by means of gas chromatography. There obtained two peaks other than the solvent itself.

The peak area comparison of the product was 1 ; 2. The distillation of the reaction mixture gave a fraction boiling at 65°/4mm, n_D^{17} 1.4505 (1.7g.), 75-82°/42mm, n_D^{17} 1.4704 (2.78g.), 75°/6mm, n_D^{17} 1.5415 of the fraction (1.1g), and tarry materials. There were crystallized residue after distillation amounted 5.3g. which dissolved in water and contained bromine and slight quantity of fluorine. The product was 1,2-difluoro styrene, 2-bromostyrene, and 1-bromo-2-fluorostyrene, and tarry materials. The solid obtained melted at 130°, and contained bromine and slight quantity fluorine. It was the mixture of potassium bromide contaminated by the product.

The yield of the reaction run was 1.8g of difluorostyrene (12.9%), 3.6 g. of bromostyrene (20.0%) and trace of bromofluorostyrene. The formation of tarry material was inherent to this reaction, because the prolonged reaction time in a separate reaction run gave exclusively tarry materials.

Results and discussion

The reaction of potassium fluoride with organic halides, acids, esters, and alcolhols were reported previously and proved to give a dimerization, decarboxylation, and decarboylative cyclization together with fluorination. Present investigation, a continuation of the previous one, gave a decarboxylation, dehydrofluorination, dimerization, and fluorination in case of organic iodides, iodo acids, bromostyrene, and polychlorinated acids and esters.

The solvent system adopted for the present research was dimethylformamide system, and a pyrolytic reaction of each reagents was conducted in parallel. Amyl iodide, a straight chaine iodide, was reacted with potasium fluoride at lower temperature in dimethylformamide solvent. The reaction gave a 40.0% yield of fluorination product and a 6.5% yield of decane (see (1)). The same reaction with isoamyl iodide at low reaction temperature did not show a good reactivity of potassium fluoride in this system and mainly the unreacted fluoride was recovered.

The polychlorinated acid such as α, β, -dichloro-β-phenyl-propionic acid and ester gave a different reaction path. The acid gave a dehydrofluorinated acid, α-chloro cinnamic acid in trace and a considerable amount of difluorinated styrene, a decarboxylation product, when it reacted in the solvent system. However, the same reaction carried under a pyrolytic condition gave dehydrofluorinated product, α-chlorostyrene, together with fluorination product (see (3)). The same reaction with the ester did not give any appreciable amount of fluorination, but gave a various dimerization product, which was difficult to separate (see 2). The formation of the product was, therefore, ascertained by means of mixture analysis using chlorine analysis, and gas chromatography.

These results indicated that the potassium fluoride, a strong fluorination reagent for halogen compounds [2] reacted with the present system giving various product. Thus, the iodide gave uausal fluorination, but a small yield of the dimerization product. The dihalo acid gave fluorination whereas the ester gave no fluorination and mainly showed the dimerization reaction. The iodide, a branched chain iodide, did not show much reactivity. These observations indicated that the fluorination by potassium fluoride suffered from a steric hindrance. The bulky compounds such as the ester did not give fluorination, but dimerization whereas the polychlorinated acid in previous research (dichloro acid and chloroacetate) [1] showed a remarkable reactivity.

The formation of the dehydrofluorinated product in the polychlorinated acid system was rather interesting. The fluorination was proceeded and the resulting fluoride was dehydrofluorinated to give the product. The dehydrofluorination during the reaction of silver fluoride was reported elsewhere [3]. However the reaction of this kind with potassium fluoride is rare except the present cases.

The yield of the product was also varied according to the reaction temperature. Thus, the dehydrofluorination of the fluorination product of the dichlorinated acid in the solvent system was small as compared to that of the reaction at the pyrolytic reaction condition. This result depends on the stability of the acid. That is, the unstable difluorinated acid formed in the low reaction temperature was mainly decarboxylated and gave a slight quantity of the dehydrofluorination product whereas the same reaction at the elevated reaction temperature gave the initial monofluorinated product and the product was decarboxylated prior to from the difluoro compounds because of the fluoro acid formed. In the solvent system, where a low reaction tempera-

ture(155-160°) was adopted, the decarboxylaton was not occured until the fluorination was completed because the monofluoro acid formed was stable enough at this reaction condition. The dibromostyrene was also gave a dehydrofluorinated product together with the mono and difluorinated(see (5)), but a considerable amount of a tarry material was accompanied to the product. This was due to the decomposition of the reaction system. Therefore, the reaction was further repeated using a short reaction time. The formation of the tarry materials was decreased in the amount, but it was inherently formed.

Since the decarboxylative cyclization was observed in the case of *o*-chloro acid sereies (1), *m*-iodobenzoic acid was reacted with potassium fluoride both in the solvent system and at a pyrolytic condition. In both cases the the formation of dimerization product was in trace with the acid salt, but there were no appreciable amount of the cyclized product(see (4)). This seemed to be due to the chemical structure of the starting material which will result a six membered polybenzonoid cyclic ketone, if the desired reaction is possible to be occured. On the other hand the reactivity of the iodine atom in the prementioned acid was also proved to be inert towards potassium fluoride, eventhough the electron attracting substituent in the meta position facilitate the halogen replacement considerably. In comparison, *m*-iodotoluene and 2-iodo-4-methylaniline were reacted with potassium fluoride both at the solvent system and pyrolytic reaction condition, but no appreciable reactivity was observed.

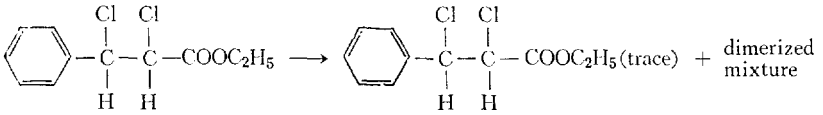
The iodide in these seires seemed to be inert reagents used. The reactivity of *o*-chlorobenzoic acid in the previous research is, therefore, due to the strong enhancing effect of the neighboring carboxylic substituent.

In conclusion the reaction of potassium fluoride with iodies and a sterically hindered ester suffers from the steric effect of the structure of the reactants and give a dimerized product. The polychlorinated acid, (a vicinal chlorine containing acid) give chloro olefine which is the dehydrofluorination product of the monofluorinated acid at the pyrolytic reaction, whereas the same reaction at low reaction temperature give a fluoro olefine in trace together with the decarboxylation product of the difluorinated acid.

This reaction path is in contrast to the gem.-dichloro acid system where an exclusive decomposition is introduced when it reacted at a pyrolytic reaction condition. Dibromostyrene give the same reaction as that of the acid and give fluoro, bromofluoro, and bromo-unsaturated styrene, respectively. *m*-iodo acid give a slight dimerization reaction with no fluorination, but phenyl iodides did not show any reactivity towards potassium fluoride. Even though further research is warranted for the elucidation of the reaction path, the present observation is resonably summarized as follows at least this instance.

Reaction path

$$CH_3CH_2CH_2CH_2CH_2I \longrightarrow CH_3CH_2CH_2CH_2CH_2F + CH_3(CH_2)_8CH_3 \qquad (1)$$



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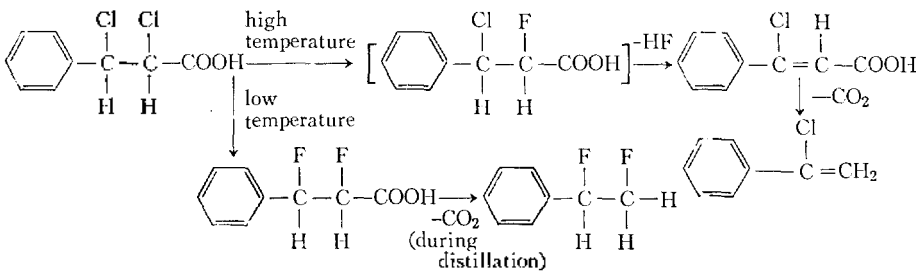

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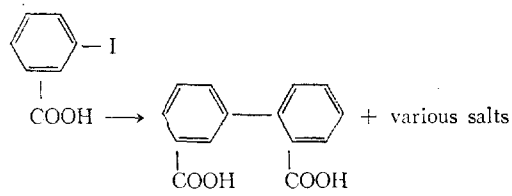

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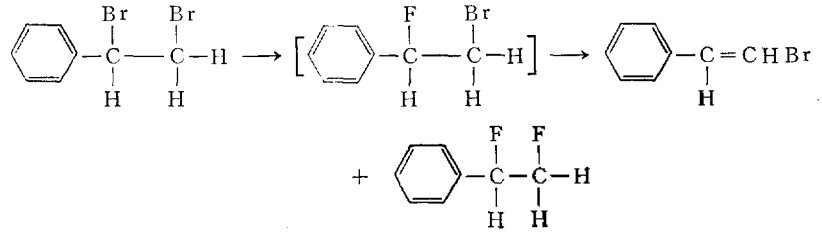

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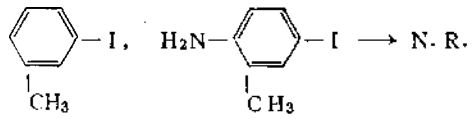

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