

Catalytic Acid Fluoride Synthesis via Carbonylation of Organic Bromides in the Presence Potassium Fluoride

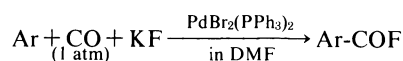
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Synopsis. Various aryl bromides were carbonylated under an atmospheric pressure of carbon monoxide in DMF in the presence of potassium fluoride to give aryl fluorides in excellent yields. The carbonylation was promoted by the addition of phase transfer catalysts, but the contamination with water reduced the selectivity.

Although acid fluorides are a versatile class of compounds, their preparation requires limited kinds of starting compounds¹⁾ and fluorinating agents which are hard to handle.²⁾ Recently a new synthetic method which is the carbonylation of aryl iodides in the presence of cesium fluoride as a stable fluorinating agent has been reported.¹⁾ However, either reaction using other aryl halides or other alkali metal fluorides does not give



aryl fluorides in satisfactory yields. Here we describe an improved method for the synthesis using both readily available organic bromides and potassium fluoride.

The carbonylation of iodobenzene in the presence of CsF in propionitrile which has been reported to be the best solvent proceeded smoothly to give benzoyl fluoride in a quantitative yield. However, neither the carbonylation of bromobenzene nor iodobenzene with potassium fluoride in propionitrile gave benzoyl fluoride in sufficient yields under the same conditions as above. One reason for the poor yield may be that potassium fluoride is far less soluble in organic solvents than cesium fluoride. The solvent effect was examined in detail, and summarized in Table 1. Among these

Table 1. Solvent Effect on the Carbonylation of Bromobenzene in the Presence of KF

| Solvent | Yield of PhCOF/% |
|---------------------|-----------------------|
| DMF | 66 |
| Pyridine | 59 |
| Diglyme | 59 |
| DMSO | 48 |
| Benzonitrile | 42 |
| Ethyl acetate | 41 |
| Methyl ethyl ketone | 39 |
| Acetonitrile | 31 |
| Propionitrile | 16 (53) ^{a)} |
| Toluene | 14 |
| Dioxane | 12 |
| Nitrobenzene | 0 |
| Chloroform | 0 |

Bromobenzene (5 mmol), spray dried KF (10 mmol), PdBr₂(PPh₃)₂ (0.1 mmol), PPh₃ (0.2 mmol), solvent (5 ml), CO (2 atm), 100 °C, 5 h. a) Iodobenzene (5 mmol) instead of PhBr was used.

solvents, the highly polar DMF was found to be the best. Pyridine and diglyme were also good solvents, though these solvents do not have high dielectric constants. The solvent effect seems to be related to not only the dielectric constant but also the donor number.

Using DMF as the solvent, some other factors were investigated. The catalytic activity of PdCl₂(PPh₃)₂ was almost equal to that of PdBr₂(PPh₃)₂. The addition of large excess of PPh₃ reduced the reactivity, while the absence of free phosphine brought about some deposit of metallic palladium. The types of phosphine ligand markedly influenced the catalytic activity. The complexes of PPh₃ and P(*p*-C₆H₄Cl)₃ showed high catalytic activity, but the activities of P(*p*-C₆H₄CH₃)₃ and PPh₂(*i*-Pr) complexes were poor. This fact suggests that the electron-withdrawing phosphines are desirable as auxiliary ligands. Bisphosphine complex, PdBr₂-

Table 2. Catalytic Activity of Palladium Phosphine Complexes in DMF

| Catalyst | Added phosphine/ mmol | Yield of PhCOF/% |
|---|--|---------------------|
| PdCl ₂ (PPh ₃) ₂ | PPh ₃ (0.2) | 61 |
| PdBr ₂ (PPh ₃) ₂ | PPh ₃ (0.2) | 65 |
| PdBr ₂ (PPh ₃) ₂ | None | 62 |
| PdBr ₂ (PPh ₃) ₂ | PPh ₃ (0.1) | 80 |
| PdBr ₂ (PPh ₃) ₂ | PPh ₃ (0.3) | 54 |
| PdBr ₂ (PPh ₃) ₂ | PPh ₃ (0.4) | 43 |
| PdBr ₂ [P(<i>p</i> -C ₆ H ₄ Cl) ₃] ₂ | P(<i>p</i> -C ₆ H ₄ Cl) ₃ (0.1) | 83 |
| PdBr ₂ [P(<i>p</i> -C ₆ H ₄ Me) ₃] ₂ | P(<i>p</i> -C ₆ H ₄ Me) ₃ (0.1) | 29 |
| PdBr ₂ [PPh ₂ (<i>i</i> -Pr)] ₂ | PPh ₂ (<i>i</i> -Pr)(0.1) | 6 |
| PdBr ₂ [Ph ₂ P(CH ₂) ₃ PPh ₂] | Ph ₂ P(CH ₂) ₃ PPh ₂ (0.05) | 38 |

Bromobenzene (5 mmol), spray dried KF (10 mmol), catalyst (0.1 mmol), DMF (5 ml), CO (1 atm), 100 °C, 5 h.

Table 3. Effects of Temperature, KF, and CO Pressure on the Carbonylation

| Temp/°C | KF/mmol ^{a)} | CO/atm | Yield of PhCOF/% |
|---------|-----------------------|--------|------------------|
| 80 | 10 | SD | 4 |
| 100 | 10 | SD | 65 |
| 110 | 10 | SD | 96 |
| 100 | 10 | BG | 62 |
| 100 | 10 | LM | 58 |
| 100 | 5 | SD | 61 |
| 100 | 15 | SD | 67 |
| 100 | 20 | SD | 69 |
| 100 | 10 | SD | 67 |
| 100 | 10 | SD | 63 |

Bromobenzene (5 mmol), PdBr₂(PPh₃)₂ (0.1 mmol), PPh₃ (0.2 mmol), DMF (5 ml), 5 h. a) SD; spray dried, BG; ball-mill ground, LM; large meshed.

Table 4. Effect of Some Additives on the Benzoyl Fluoride Synthesis

| Additive | mmol | Conversion/% | Selectivity/% |
|------------------|------|--------------|---------------|
| None | | 25 | 96 |
| H ₂ O | 1 | 62 | 65 |
| H ₂ O | 2 | 69 | 39 |
| H ₂ O | 6 | 77 | 0.1 |
| PhCOOH | 1 | 24 | 83 |
| HF ^{a)} | 1 | 28 | 89 |

Bromobenzene (5 mmol), spray dried KF (10 mmol), PdBr₂(PPh₃)₂ (0.1 mmol), PPh₃ (0.1 mmol), DMF (5 ml), CO (1 atm), 100 °C, 2 h. a) An HF in pyridine (HF 70 wt%) was used.

Table 5. Carbonylation of Bromobenzene in the Presence of Phase Transfer Catalysts

| Phase transfer catalyst | mmol | Yield/% |
|-------------------------|------|---------|
| None | | 80 |
| NBu ₄ I | 0.2 | 83 |
| NBu ₄ Br | 0.2 | 90 |
| NBu ₄ Br | 1.0 | 94 |
| Dibenzo-18-crown-6 | 1.0 | 92 |

Reaction time, 2 h; the other conditions were the same as in Table 4.

[Ph₂P(CH₂)₃PPh₂], was not so active as the PPh₃ complex.

The effect of carbon monoxide pressure was negligible in the range from 1 to 10 atm. The amount of potassium fluoride also had no influence on the yield. Additionally, there was substantially no difference in the reactivity between two kinds of potassium fluoride powder prepared by the spray-dry method and by the ball-mill grind method, though the use of large meshed potassium fluoride slightly decreased the reactivity. These results suggest that the reaction with dissolved potassium fluoride is predominant over that on the surface of solid potassium fluoride. The interpretation is supported by the unusual dependency on the reaction temperature. The yield of benzoyl fluoride was very low at 80 °C, but almost quantitative at 110 °C. This strong temperature dependency can be explained by an additional acceleration of reaction due to an elevation of the solubility of potassium fluoride at the high temperatures.

It is interesting to note that the addition of water markedly promoted the absorption rate of carbon monoxide. The conversion of bromobenzene increased by the addition of water, but the selectivity to benzoyl fluoride extremely decreased. The by-product was identified as benzoic acid. However, the addition of either benzoic acid or hydrogen fluoride (C₅H₅N · (HF)₉) had no effect on the reaction promotion. The unusual effect of water is still unclear.

Since the carbonylation is a type of two phase reaction, the use of phase transfer catalysts was studied. Tetrabutylammonium bromide and dibenzo-18-crown-6 proved to be contributory to the improvement of reactivity. Tetrabutylammonium iodide was less effective than the corresponding bromide. This may be due to a

Table 6. Acid Fluoride Synthesis from Various Organic Bromides and KF

| Substrate | Reaction time/h | Yield of acid fluoride/% |
|---|-----------------|--------------------------|
| <i>p</i> -NCC ₆ H ₄ Br | 3 | 97 |
| <i>p</i> -ClC ₆ H ₄ Br | 3 | 95 |
| <i>p</i> -BrC ₆ H ₄ Br ^{a)} | 3 | 98 |
| <i>p</i> -CH ₃ C ₆ H ₄ Br | 5 | 94 |
| <i>p</i> -CH ₃ OC ₆ H ₄ Br | 8 | 98 |
| <i>o</i> -ClC ₆ H ₄ Br | 8 | 2 |
| <i>o</i> -CH ₃ OC ₆ H ₄ Br | 8 | 12 |
| <i>p</i> -NCC ₆ H ₄ Cl ^{b)} | 8 | 18 |
| 1-Bromonaphthalene | 8 | 98 |
| 2-Bromonaphthalene | 3 | 95 |
| 3-Bromopyridine | 3 | 97 |
| 3-Bromothiophene | 5 | 85 |
| <i>trans</i> -PhCH=CHBr | 1 | 98 |
| PhCH ₂ Br | 8 | 13 |
| 1-Bromohexane | 8 | 0 |

Substrate (5 mmol), spray dried KF (10 mmol), PdBr₂(PPh₃)₂ (0.1 mmol), PPh₃ (0.2 mmol), DMF (5 ml), CO (1 atm), 110 °C a) 1,4-Benzenedicarbonyl difluoride was formed. b) *p*-NCC₆H₄COF was detected.

lower fluoride-ion extractability of the ammonium iodide than the bromide.³⁾ However, their effects on the organometallic phase transfer reaction were not so prominent as those on general organic two phase reactions. The insufficient effect may be mainly ascribed to the low concentrations of both palladium and phase transfer catalysts.⁴⁾

The carbonylation of various substrates was carried out in DMF at 110 °C in the absence of phase transfer catalysts. Aryl bromides were carbonylated within 8 h, and gave the corresponding aroyl fluorides in excellent yields, except for ortho-substituted bromobenzenes. The carbonylation of ortho-substituted bromobenzenes was slow, but no detectable by-products were formed. In the para-substituted bromobenzenes, electron-withdrawing substituents promoted their reactivities, while electron-donating substituents retarded the carbonylation. *p*-Cyanochlorobenzene, which is activated by the strong electron-withdrawing group, was carbonylated to the corresponding fluoride without by-product, though the reaction was slow under these conditions. The acid fluoride synthesis from β -bromostyrene was also successfully achieved. Unfortunately, the carbonylation of aliphatic bromides was unsuccessful except for benzyl bromide.

Experimental

Materials. All organic chemicals were purchased from chemical sources and purified by distillation or recrystallization before use. The spray-dried potassium fluoride and C₅H₅N · (HF)₉ were used without further purification. The crystalline cesium and potassium fluorides were ground to powder in a ball mill for 20 h and were vacuum-dried at 150 °C for 5 h prior to use. Carbon monoxide (99.9%) was obtained from Sumitomo Seiki Co. and used as received. Solvents were stored under argon after being distilled from appropriate drying agents. The palladium complexes, PdCl₂(PPh₃)₂, PdBr₂(PPh₃)₂, PdBr₂[P(*p*-C₆H₄Cl)₃]₂, PdBr₂[P(*p*-C₆H₄CH₃)₃]₂,

$\text{PdBr}_2[\text{P}(i\text{-Pr})\text{Ph}_2]_2$, and $\text{PdBr}_2[\text{Ph}_2\text{P}(\text{CH}_2)_3\text{PPh}_2]$ were prepared by treating $\text{PdCl}_2(\text{cod})^{5)}$ or $\text{PdBr}_2(\text{cod})^{5)}$ with the corresponding phosphines in CH_2Cl_2 .

Catalytic Carbonylation of Aryl Halides. Into a 25 ml glass autoclave or a 20 ml Schlenk tube attached with a gas buret were placed catalyst (0.1 mmol), phosphine (0.1 mmol) and KF (10 mmol) under an argon atmosphere. The reaction system was evacuated and flushed with CO, and then organic halide (5 mmol), solvent (5 ml) and CO were charged. The mixture was heated with vigorous stirring. After cooling the reaction mixture was analyzed by means of GC (Silicone DC-560, 2 m) using naphthalene or durene as an internal calibrant.

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