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# Halex reactions of aromatic compounds catalysed by 2-azaallenium, carbophosphazenium, aminophosphonium and diphosphazenium salts: a comparative study

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**Abstract**

An increasing number of biologically active compounds in the pharma and agro-chemical sector contain carbon fluorine bonds. One of the most common methods to introduce fluorine into intermediates is the well-investigated halogen-exchange reaction, in which chloro- and bromoaromatics activated towards nucleophilic substitution, react with a fluoride source to yield the corresponding fluoroarenes. In general, the reaction is supported by phase-transfer catalysts. The use of a new class of very active phase-transfer catalysts gives the possibility of substituting even halogens with weak activation giving a convenient access to interesting compounds that are not available so far and opening up new synthetic routes in Halex chemistry. Our new classes of catalysts, $CNC^+$ (**1a**), $PNC^+$ (**2a**) and several different approaches presented by other groups are described and experimental results discussed.


*Keywords:* Phase-transfer catalyst; Halex reaction; Fluorination

## 1. Introduction

Fluorine atoms incorporated into biologically active molecules are known to have major effects on bioavailability and metabolism caused by changes in the lipophilicity and the oxidative stability. Only minor changes in molecular dimension are observed.

One of the most important techniques for introducing fluorine atoms into aromatic rings besides the Baltz–Schiemann reaction, is the halogen-exchange reaction (Halex) [1]. Halogens (mostly chlorine, rarely bromine) that are activated towards nucleophilic substitution by electron-withdrawing groups are exchanged against fluoride at temperatures above 200 °C. The fluoride source usually is an alkaline metal salt.

In the 1930s, the first Halex reactions were performed with strongly electron-deficient chloroarenes. Using alkaline metal fluorides, moderate to good yields were achieved [2]. The need for strong electron-deficiency limited the starting materials to the class of dinitrohalo and nitro compounds with further electron-withdrawing substituents.

The drawback of the alkaline metal fluorides is their low solubility in aromatic substrates as also in aprotic solvents. High temperatures of 240–300 °C were needed to increase the concentration of fluoride in solution and to extend the reaction zone beyond the liquid–solid phase barrier. Therefore, long reaction times were needed which led to side reactions and decomposition. Since the fluoride salts are very hygroscopic careful drying of all reaction components is necessary. The role of water in the Halex reaction is discussed by Sasson et al. [3].

Over the last decades, enormous improvements have been made by variation of additives and changes in the overall process. The use of spray-dried potassium fluoride and high-boiling dipolar aprotic solvents like sulpholane or NMP enables the substitution of less activated halogen atoms, for example, in benzonitriles and benzotrifluorides. Taking advantage of the fact that the fluorinated product always has a lower boiling point than the starting material, the

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overall yield of fluorinated products may be increased by distilling off the product from the vessel continuously, so less decomposition and side-product formation occur.

The formation of dehalogenated species as side products, especially at temperatures above 225 °C, can be reduced by addition of radical scavengers like nitrobenzene, 4-fluoronitrobenzene, $Me_2SO$ or methylphenylsulphoxide [4].

## 2. Results and discussion

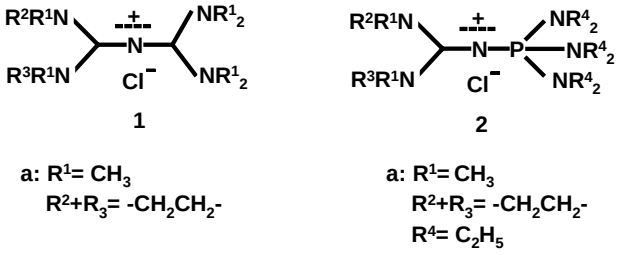
The main breakthrough in the Halex chemistry was achieved by using phase-transfer catalysts. Increased solubility of the fluoride salt improves the reaction rates in an homogeneous phase. Due to a drop in the reaction temperature and time, which leads to less side products and decomposition, the yields are improved. Despite these promising results the early generation phase-transfer catalysts exhibited an inherent problem due to their limited temperature stability. In 1986, a general correlation between molar weight and thermostability was found [5]. Catalysts with at least 16 carbon atoms keep their catalytic activity up to temperatures of 215 °C.

So far, tetraphenylphosphonium bromide and tetra-*n*-butylphosphonium bromide have been the most widely used, patent-free catalysts. Both start to decompose above 200 and 180 °C, respectively. The corresponding ammonium salts decompose at even lower temperature. So there was a need of new catalysts that are active and stable above 200 °C.

Although large improvements were made in the light of all these facts, the limited solubility of fluoride salts and the strong hygroscopicity still are major issues for all catalytic systems. To overcome those, hydrogendifluorides of the type $Ph_4P^+HF_2^-$ were used. These exhibit good solubility in polar solvents and acceptable thermal stability, but two equivalents are needed to achieve full conversion [6]. Due to the high costs this is unfavourable for technical uses.

The goal of the latest Halex research is to improve space–time yield by using little or even no solvent. Therefore, catalysts are needed that do not have to be activated by the solvent. Over the last years, several concepts and catalysts have been presented. A common goal of all these concepts is to find a temperature stable phase-transfer catalyst, which can be produced easily at low cost and which is not toxic but recyclable. Further, the catalyst must be stable at the strongly basic conditions in the Halex reaction.

One class of compounds presented by Berris and Cheng [7] and Kolomeitsev and Pasenok [8] are aminophosphonium compounds of the type $(R_2N)_4PX$ which show their best activity between 200 and 240 °C. All catalysts of the PN-type exhibit potential dermal toxicity due to traces of hexaalkylphosphoramide (for example, HEPA from $(Et_2N)_4PBr$) or analogues. Therefore, the PN-type catalysts are not the best choice for technical purposes. PN-type catalysts containing cyclic amine residues exhibit an improved biological profile [9].




Scheme 1.

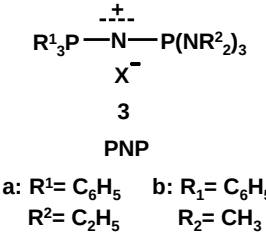
Higher yields were observed, when mixing this type of catalysts with a co-catalyst like trimethyl(ethoxypolypropoxypropyl)ammonium chloride or polyethylene glycol [10]. The improvement is limited to rather strongly activated compounds, since the additives are not stable enough at the temperatures required for weakly activated substrates, though. Schach et al. followed a similar approach when using quaternary ammonium salts with at least one alkoxypolyoxy-alkyl residue [11].

We chose a different approach when looking for a highly delocalised, chemically and temperature stable salt. Our new classes of catalysts that are useful in the Halex reaction derived from the substructures shown in Scheme 1 [12].

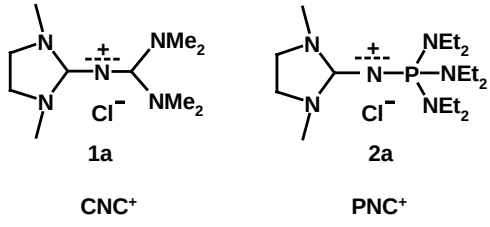
The substructures (**1**) are known in the literature [13], but were never used in Halex reactions. The carbophosphazenium salts (**2**) containing substituted dialkylamino groups at the C–N–$P^+$ backbone were co-developed at Bayer and the University of Bremen [12]. A very similar approach has been chosen by Schanen et al. [14] with their PNP catalysts (**3**) (Scheme 2).

For this study we decided to show the outstanding catalytic activity of our catalysts **1a** and **2a** shown in Scheme 3.

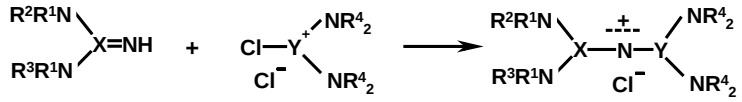
$CNC^+$ (**1a**) can easily be synthesised from dimethylimidazolinone and tetramethylguanidine. $PNC^+$ (**2a**) is acces-




Scheme 2.




Scheme 3.




**1a**: X, Y = C
$R^1$,$R^4$: $CH_3$
$R^2$+$R^3$: $-CH_2CH_2-$

**2a**: X = C, Y = $P(NR^4_2)$
$R^1$: $CH_3$,
$R^2$+$R^3$: $-CH_2CH_2-$
$R^4$: $C_2H_5$

Scheme 4.

sible via the analogous tris(diethylamino)phosphazene (Scheme 4).

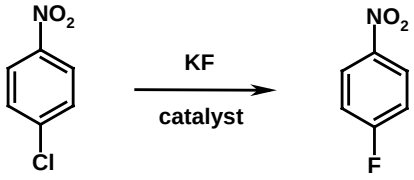
These catalysts are compared with the following:

1. $Ph_4PBr$,
2. $(Et_2N)_4PBr$,
3. $(R^1_2N)_3$–$PNPPh_3Br$ (**3a**, $R^1$ = Et) and (**3b**, $R^1$ = Me).

The complexity of running Halex reactions with high yields increases with the number of halogen atoms to be substituted and with the decrease in activation by electron-withdrawing substituents. Therefore, we chose five examples starting with a strongly activated nitro compound, moving to medium activated aldehydes, benzoyl chlorides and benzotrifluorides and finally a non-activated chloroarene.

The fluorination of strongly activated chloroarenes was pursued for a long time. 4-Fluoronitrobenzene (**5**) can be produced either by the fluorination of 4-chloronitrobenzene (**4**) or by the nitration of fluorobenzene. To establish a competitive Halex process, the catalysts have to work at moderate temperatures to prevent side reactions and decomposition (Scheme 5).

The reaction of 4-chloronitrobenzene (**4**) was performed in sulpholane, $Me_2SO$ or dimethylimidazolidine (DMI). Furthermore, some of the catalysts were tested in the absence of a solvent or with only catalytic amounts of $Me_2SO$. A temperature of 170–190 °C was chosen for the reactions. Compared with the non-catalysed process this means a drop in reaction temperature of 30–60 °C (Table 1).




**4** **5**

Scheme 5.

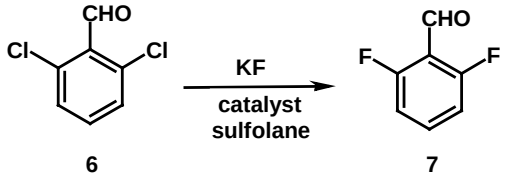
Conversion and yield are strongly dependent on the dilution of the reaction mixture. Adding only catalytic amounts of solvent does not give satisfactory results. Although it is unfavourable due to health and safety reasons $Me_2SO$ proved to be the best solvent for this reaction. $CNC^+$ (**1a**) furnishes nearly quantitative yields after 5 h at 170 °C, with $(Et_2N)_4PBr$ and $Ph_4PBr$ being slightly worse under these conditions.

The fluorination of 2,6-dichlorobenzaldehyde (**6**) to 2,6-difluorobenzaldehyde (**7**) is more challenging due to less activated halogen atoms and the fact that two chlorine atoms have to be substituted (Scheme 6).

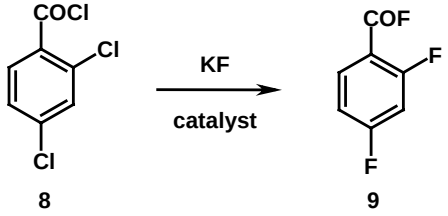
As with chloronitrobenzene (**4**), acceptable reaction rates can only be achieved, when the reactions are performed in a solvent. Because of the lower activation, the reaction temperature and reaction time have to be increased. Therefore, $Me_2SO$ cannot be used due to its decomposition under these conditions. We found that sulpholane is a good compromise

Table 1
4-Fluoronitrobenzene (**5**) from 4-chloronitrobenzene (**4**)

| Entry | Solvent (wt.%) | Catalyst (mol%) | Temperature (°C) | Time (h) | Yield (conversion) (%) |
|---|---|---|---|---|---|
| 1 | – | $Ph_4PBr$ (1.3) | 190 | 10 | (∼30) |
| 2 | – | $(Et_2N)_4PBr$ (1)/PEG500 (8) [10] | 180 | 20 | 88 |
| 3 | – | $(Et_2N)_4PBr$ (1.3) | 190 | 10 | (∼30) |
| 4 | Sulpholane (70) | $Ph_4PBr$ (1.6) | 180 | 5 | (40) |
| 5 | Sulpholane (130) | $Ph_4PBr$ (1.6) | 180 | 6 | 60 (71) |
| 6 | Sulpholane (250) | $Ph_4PBr$ (1.6) | 180 | 4 | 80 (94) |
| 7 | $Me_2SO$ (130) | $CNC^+$ (**1a**) (1.0) | 170 | 5 | 96 |
| 8 | $Me_2SO$ (130) | $(Et_2N)_4PBr$ (1.0) | 170 | 6 | 93 |
| 9 | $Me_2SO$ (130) | $Ph_4PBr$ (1.0) | 170 | 6 | 89 |




Scheme 6.




Scheme 7.

between good thermal stability and acceptable reaction rates (Table 2).

For the fluorination of 2,6-dichlorobenzaldehyde (**6**), $PPh_4Br$ is a very good catalyst even better than the $CNC^+$ (**1a**) and the $PNP^+$ (**3a**) catalyst. Obviously, both catalysts favour the decomposition of the aldehydes.

The activation of the halogens by a chlorocarbonyl group is comparable to that of an aldehyde group, but the fluorination of chlorobenzoyl chlorides shows the improved catalytic activity of $CNC^+$ (**1a**) in the field of medium activated chloroaromatics. Fluorinated acid chlorides/fluorides are produced on the technical scale from the chlorinated precursors as they are intermediates for antibiotics, like Avelox® (Bayer), Clinafloxacin® (Warner-Lambert) and Fandofloxacin® (Dong Wha Pharma) (Scheme 7).

Low yields are observed in the fluorination of 2,4-dichlorobenzoyl chloride (**8**) in the presence of only co-catalytic amounts of $Me_2SO$ or sulpholane. The yield is increased by performing the reaction in sulpholane (Table 3).

The best results are achieved when **1a** is used in dimethylimidazolinone, delivering a 75% yield. Due to the boiling point of 2,4-difluorobenzoyl fluoride (**9**), the reaction temperature is limited to 180 °C. As decomposition occurs at higher temperatures the yield cannot be improved by running the reaction in an autoclave at 200 °C.

The interpretation of the results from the fluorination of dichlorobenzaldehyde (**6**) and the dichlorobenzoyl chloride (**8**) clearly shows that there are no universal rules for running successful Halex reactions. Although activation of the halogen atoms is comparable in both molecules, the results strongly depend on the catalyst system. Each of these systems has its own strengths and the reaction conditions have to be chosen for each substrate individually.

The next level of complexity is the fluorination of medium activated polychloroarenes. Since several chlorine atoms are to be substituted, a large amount of fluoride is needed. In general, this would lead to bad space–time yields if the corresponding amount of solvent was used in a one-step process. On the other hand, problems in stirring would arise if the amount of solvent is reduced drastically. Therefore, the process is split into two sequential reaction steps.

Tetrafluorobenzotrifluoride (**11**) is an intermediate in the synthesis of Avelox®, an antibiotic by Bayer that is produced on a multi-ton scale (Scheme 8).

No solvent is needed for the fluorination of tetrachlorobenzotrifluoride (**10**), which therefore leads to excellent space–time yields. The catalyst is activated by catalytic amounts of dichloromethane.

In the first reaction step approximately two chlorine atoms are substituted for fluorine and the resulting product mixture is then reacted again with fluoride in the second step to yield the desired tetrafluorobenzotrifluoride (**11**) (Table 4).

**1a** shows the best activity with these reaction conditions and yields the desired tetrafluorobenzotrifluoride (**11**) as main product. With the commonly used $PPh_4Br$ the reaction stops at the dichlorodifluorobenzotrifluorides (**13**).

On a technical scale the mixture of the chlorotrifluorobenzotrifluorides (**12** and **13**) is separated by fractional distillation and fed back in to the next batch, which leads to economic and ecological improvements.

The ultimate challenge in Halex reactions is the fluorination of non-activated polychloroarenes. For a long time this type of reaction was thought to be a dream reaction. Due to the weak activation of the chlorine atoms, high temperatures are needed to find acceptable reaction rates and good conversion. The limited thermostability of $PPh_4Br$ and other early generation catalysts would make it impossible to run this type of reaction. We chose 1,3,5-trichlorobenzene (**15**) to show the quality of our catalysts (Scheme 9).

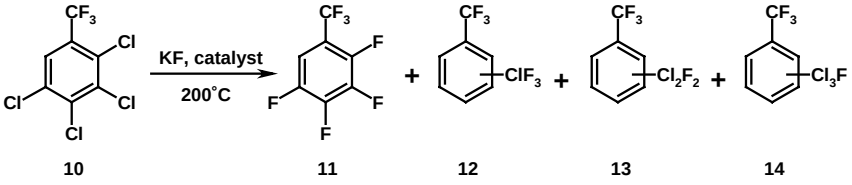
Because of the large amount of fluoride this reaction is also performed stepwise. Although forcing conditions

Table 2
2,6-Difluorobenzaldehyde (**7**) from 2,6-dichlorobenzaldehyde (**6**)

| Entry | Catalyst (mol%) | Temperature (°C) | Time (h) | Yield, $F_2$-benzaldehyde (**7**) (%) |
|---|---|---|---|---|
| 1 | $PPh_4Br$ (2.5) | 180 | 24 | 72 (100% conversion); 0 F,Cl-benzaldehyde |
| 2 | $CNC^+$ (**1a**) (2.5) | 180 | 24 | 63 (100% conversion); 8 F,Cl-benzaldehyde |
| 3 | $(NEt_2)_3PNPPh_3Br$ (**3a**) (2.5) | 180 | 24 | 54 (100% conversion); 0 F,Cl-benzaldehyde |
| 4 | $(Et_2N)_4PBr$ (2)/$(C_2H_5O(C_2H_4O)_n)NMe_3Cl$ (6) [10] | 165 | 20 | 69 (88% conversion) |

Table 3
2,4-Difluorobenzoylfluoride (**9**) from 2,4-dichlorobenzoylchloride (**8**)

| Entry | Solvent (wt.%) | Catalyst (mol%) | Temperature (°C) | Time (h) | Yield (conversion) (%) |
|---|---|---|---|---|---|
| 1 | Sulpholane (150) | – | 200 | 9 | 30 |
| 2 | Sulpholane (150) | $Ph_4PBr$ (2.0) | 180 | 7 | (~5) |
| 3 | Sulpholane (10) | $CNC^+$ (**1a**) (1.5) | 175 | 24 | 5 |
| 4 | $Me_2SO$ (10) | $CNC^+$ (**1a**) (1.5) | 175 | 24 | 20 |
| 5 | Sulpholane (100) | $CNC^+$ (**1a**) (1.5) | 175 | 24 | 54 |
| 6 | Sulpholane (100) | $CNC^+$ (**1a**) (1.5) | 190 | 15 | 49 |
| 7 | DMI (100) | $CNC^+$ (**1a**) (1.5) | 180 | 24 | 75 |
| 8 | DMI (100) | $(NEt_2)_3PNPPh_3Br$ (**3a**) (1.5) | 180 | 24 | (30) |




Scheme 8.

Table 4
Tetrafluorobenzotrifluoride (**11**) from tetrachlorobenzotrifluoride (**10**)

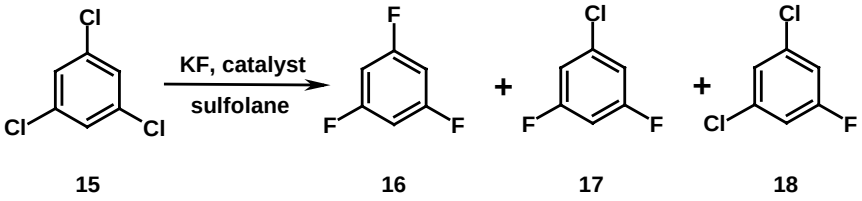
| | GC area (%) | | | | | |
|---|---|---|---|---|---|---|
| | Temperature (°C) | $Cl_4$-BTF (**10**) | $Cl_3F$-BTF (**14**) | $Cl_2F_2$-BTF (**13**) | $ClF_3$-BTF (**12**) | $F_4$-BTF (**11**) |
| First step | | | | | | |
| $CNC^+$ (**1a**) (1.5 mol%) | 200 | 0 | 29 | 66 | 5 | 0 |
| $PNC^+$ (**2a**) (1.5 mol%) | 200 | 0 | 5 | 70 | 24 | 1 |
| $PPh_4Br$ (1.5 mol%) | 200 | 19 | 62 | 19 | 0 | 0 |
| $(NEt_2)_3PNPPh_3Br$ (**3a**) (1.5 mol%) | 200 | 4 | 38 | 54 | 4 | 0 |
| Second step | | | | | | |
| $CNC^+$ (**1a**) (1.9 mol%) | 200 | 0 | 0 | 0 | 17 | 84 |
| $PNC^+$ (**2a**) (1.9 mol%) | 200 | 0 | 0 | 0 | 33 | 67 |
| $PPh_4Br$ (1.9 mol%) | 200 | 0 | 14 | 78 | 6 | 1 |
| $(NEt_2)_3PNPPh_3Br$ (**3a**) (1.9 mol%) | 200 | 0 | 0 | 40 | 51 | 9 |

are applied, the catalyst has to be activated by adding a solvent. Preliminary trials were performed using sulpholane. Since a temperature of 230 °C increases by-product formation of dehalogenated side products 1 mol% of nitrobenzene is added as a radical scavenger (Table 5).

After 36 h at 230 °C in sulpholane, **1a** delivers the trifluorobenzene (**16**) as the main product. On a technical scale the chlorofluorobenzenes (**17** and **18**) would be collected by fractional distillation and fed-back in the next batch. $PNP^+$ (**3b**) delivers a 1:1 mixture of the trifluorobenzene (**16**) and chlorodifluorobenzene (**17**).

Table 5
Trifluorobenzene (**16**) from trichlorobenzene (**15**)

| | GC area (%) | | | | | |
|---|---|---|---|---|---|---|
| | Temperature (°C) | $Cl_3$-benzene (**15**) | $Cl_2F$-benzene (**18**) | $ClF_2$-benzene (**17**) | $F_3$-benzene (**16**) | Rest (side reactions, decomposition) |
| First step (12 h) | | | | | | |
| $CNC^+$ (**1a**) (5 mol%) | 230 | 1 | 20 | 61 | 18 | 1 |
| $(NMe_2)_3PNPPh_3Br$ (**3b**) (5 mol%) | 230 | 1 | 20 | 60 | 15 | 5 |
| Second step (24 h) | | | | | | |
| $CNC^+$ (**1a**) (5 mol%) | 230 | 0 | 1 | 8 | 87 | 4 |
| $(NMe_2)_3PNPPh_3Br$ (**3b**) (5 mol%) | 230 | 0 | 2 | 46 | 46 | 6 |




Scheme 9.

## 3. Concluding remarks

These five examples, from strongly activated to non-activated substrates, show the proof of principle for the new generation of Halex catalysts of the $CNC^+$ (**1a**) and $PNC^+$ (**2a**) types.

With $CNC^+$ (**1a**), we have found a very active catalyst for running even challenging reactions with good yields and reasonable space–time yields. Furthermore, **1a** is easily accessible from commercially available starting materials.

Interpretation of all the results show that there are no universal rules for running successful Halex reactions. Fine-tuning regarding solvent or its absence, dilution, temperature, additives and process has to be carried out each substrate individually in a series of trials, to find the optimum combination of reaction parameters. Only then the combination of the system and optimised reaction conditions leads to a cost-effective and economic process.

The core competence of Bayer Chemicals in the field of fluorinated intermediates is substantially strengthened by the catalytic abilities of these two catalysts. $CNC^+$ (**1a**), in particular, can be produced via a cost-effective process and exhibits good thermal stability in combination with good catalytic activity over a wide temperature range.

Compared with the commonly used phosphonium salts like $PPh_4Br$, dramatic improvement has been achieved, especially in the substitution of low or non-activated chlorine atoms. In comparison with $(Et_2N)_4PBr$ and $(R^1_2N)_3PNPPh_3Br$ (**3a** and **3b**), the activity is equal or slightly better, so $CNC^+$ (**1a**) is competitive in the modern Halex processes, especially since there is no risk of hexaalkylphosphoramide formation.

The adaptation of these promising results for the production of fluorinated heterocycles (pyrimidines, pyridines) is under investigation.

## 4. Experimental

### 4.1. General experimental procedures

All $^1H$ NMR spectra were recorded at 400 MHz, $^{13}C$ NMR spectra at 100 MHz on Bruker or Varian NMR spectrometers. The chemical shifts of $^1H$ signals are reported in ppm down field relative to tetramethylsilane (TMS) (=0.00) in $CDCl_3$. $^{13}C$ signals are expressed in ppm using the central peak of the $CDCl_3$ signal as internal standard (=77.00). Mass spectroscopy data were recorded on a ThermoFinnigan MAT95. GC analysis was performed on a Hewlett Packard HP6890. Melting points are uncorrected.

All the reagents and solvents were obtained from Aldrich, Merck or Lancaster and were used as purchased. Reactions requiring anhydrous conditions were carried out under nitrogen.

### 4.2. $CNC^+$: (N,N-dimethylimidazolidino)-tetramethylguanidinium chloride (*1a*)

A vessel was charged with 600 ml of toluene and 360 g of phosgene was added within 3.5 h at room temperature. 1,3-Dimethylimidazolindione of 344 g (3.00 mol) in 450 ml toluene was added slowly within 1.5 h. The temperature was kept at 40 °C. When the gas evolution stopped, the excess of phosgene was removed by a stream of nitrogen and the suspension was filtered (nitrogen atmosphere). (*N*,*N*-dimethylimidazolidino)-chloride of 438 g (2.56 mol) was collected as a colourless solid with yield = 85% and mp = 156–158 °C.

A vessel was charged with 600 ml dichloromethane and 400 g (2.34 mol) (*N*,*N*-dimethylimidazolidino)-chloride. Within 2 h, 552 g tetramethylguanidine (2 equiv, 4.8 mol) was added while cooling with an ice bath.

The solvent was removed and 600 ml of methanol was added to the solid residue. 432 g (2.4 mol) 30% sodium methylate in methanol was added to the suspension with ice cooling. Stirring was continued at room temperature for 1 h. Solvents were removed via distillation and 200 ml of dichloromethane was added. The precipitate is filtered off. The filtrate was concentrated to dryness to yield 449 g (1.80 mol) (*N*,*N*-dimethylimidazolidino)-tetramethylguanidinium chloride (**1a**) with yield = 94% and mp = 145–147 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 2.88$ (s, 6H, $CH_3N$), 2.99 (s, 12H, $CH_3N$), 3.83 (s, 4H, $CH_2CH_2$). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 32.2$ ($CH_3$, $CH_3N$), 39.5 ($CH_3$, $CH_3N$), 47.0 ($CH_2CH_2$), 160.3, 162.8 (C=N). FAB (glycerine, +/−): 214 (90) and 35 (30, Cl).

### 4.3. 4-Fluoronitrobenzene (*5*)

A vessel was charged with 200 g dimethylsulphoxide, 62.7 g (1.08 mol) potassium fluoride and 2.49 g (*N*,*N*-dimethylimidazolidino)-tetramethylguanidinium chloride

(**1a**) (0.01 mol) and 157 g (1 mol) 4-chloronitrobenzene. The mixture was heated to 170 °C with stirring for 5 h. The reaction mixture was cooled to room temperature and 300 ml of water are added. After phase separation 4-fluoronitrobenzene was isolated via fractional distillation of the organic phase. Yield = 135 g liquid (0.96 mol), 96%.

For entries 8 and 9 in Table 1 $(Et_2N)_4PBr$ and $Ph_4PBr$ were used in the same process with 0.01 mol of each catalyst. The yield was 93 and 89%, respectively.

### 4.4. 2,6-Difluorobenzaldehyde (*7*)

A vessel was charged with 600 g sulpholane and 211 g KF. Sulpholane of 80 g was removed in vacuum. (*N*,*N*-dimethylimidazolidino)-tetramethylguanidinium chloride (**1a**) of 9.7 g and 265 g 2,6-dichlorobenzaldehyde were added and the mixture was heated to 180 °C for 24 h with stirring. 2,6-Difluorobenzaldehyde was isolated from the reaction mixture by fractional distillation under reduced pressure.

For entries 1 and 3 in Table 2, $(NEt_2)_3PNPPh_3Br$ (**3a**) and $Ph_4PBr$ were used in the same process with the same equimolar ratios of each catalyst compared to $CNC^+$ (**1a**).

### 4.5. 2,4-Difluorobenzoyl fluoride (*9*)

A vessel was charged with 100 g (0.48 mol) 2,4-dichlorobenzoyl chloride, 1.78 g **1a**, 100 g of dimethylimidazolindione and 94.3 g (1.62 mol) potassium fluoride. The mixture was stirred under nitrogen at 190 °C for 24 h. The product was distilled off from the reaction mixture under reduced pressure. Yield = 75% (0.36 mol). For entry 8 in Table 3 $(NEt_2)_3PNPPh_3Br$ (**3a**) was used in the same process with the same equimolar ratio compared to **1a**.

### 4.6. 2,3,4,5-Tetrafluorobenzotrifluoride (*11*) with $CNC^+$ (*1a*)

(a) A stainless steel autoclave was charged with 400 g tetrachlorobenzotrifluoride, 212 g potassium fluoride, 5 g (*N*,*N*-dimethylimidazolidino)-tetramethyl-guanidinium chloride (**1a**) and 2 g dichloromethane was stirred for 8 h at 200 °C. The vessel was cooled to room temperature. The solids were removed by filtration. The product mixture was analysed by GC and used in the next step without further purification.
(b) A stainless steel autoclave was charged with the crude product from step (a), 6.3 g (*N*,*N*-dimethylimidazolidino)-tetramethylguanidinium chloride (**1a**) and 193.5 g potassium fluoride. The mixture was stirred at 200 °C for 32 h. The vessel is then cooled to room temperature and the crude product is distilled.

#### 4.6.1. With $PNC^+$(*2a*)

6.6 g *N*-(*N*,*N*-dimethylimidazolidino)-tris-(diethylamino)-phophazenium chloride (**2a**) instead of $CNC^+$ (**1a**) and 28 g of sulpholane instead of dichloromethane were used. The reaction mixture was stirred for 24 h (instead of 32 h) in step (b).

#### 4.6.2. With $PPh_4Br$

Tetraphenylphosphonium bromide of 8.38 g was used. The reaction mixture was stirred for 28 h (instead of 32 h) in step (b).

#### 4.6.3. With $(NEt_2)_3PNPPh_3Br$ (*3a*)

$(NEt_2)_3PNPPh_3Br$ of 12.75 g was used in the first step and 16.15 g in the second step, respectively.

### 4.7. 1,3,5-Trifluorobenzene (*16*)

(a) A stainless steel autoclave was charged with 500 g trichlorobenzene, 3 ml dichloromethane, 2.8 ml nitrobenzene, 520 g potassium fluoride, 34.72 g **1a** and 1100 ml sulpholane. The vessel was pressurised with 1 bar of nitrogen and the mixture was stirred at 230 °C for 12 h. The vessel was cooled to room temperature and the crude product mixture was distilled off, analysed by GC and used in the next step without further purification.
(b) A stainless steel autoclave was charged with the crude product from step (a), 2 ml dichloromethane, 2.8 ml nitrobenzene, 292 g potassium fluoride, 34.72 g **1a** and 620 ml sulpholane. The vessel was pressurised with 1 bar of nitrogen and the mixture was stirred at 230 °C for 24 h. The vessel was cooled to room temperature and the crude product mixture was distilled off and analysed by GC.

#### 4.7.1. With $(NMe_2)_3PNPPh_3Br$ (*3b*)

$(NMe_2)_3PNPPh_3Br$ (**3b**) of 35.8 g in each step was used for the same process with half the amounts of all other materials.

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