Removal of Fluorine from and Introduction of Fluorine into Polyhalopyridines: An Exercise in Nucleophilic Hetarenic Substitution

Carla Bobbio, Thierry Rausis, and Manfred Schlosser*[a]

Abstract: Starting from six industrially available fluorinated pyridines, an expedient access to all three tetrafluoropyridines (**2**–**4**), all six trifluoropyridines (**5**–**10**), and the five non-commercial difluoropyridines (**11**–**14** and **16**) was developed. The methods employed for the selective removal of fluorine from polyfluoropyridines were the reduction by metals or complex hydrides and the site-selective replacement by hydrazine followed by dehydrogenation–dediazotation or dehydrochlorination–dediazotation. To introduce an extra fluorine atom, a suitable precursor was metalated and chlorinated before being subjected to a chlorine/fluorine displacement process.

Keywords: fluorine · hydrazino compounds · hydrogenation · metalation · nucleophilic substitution

Introduction

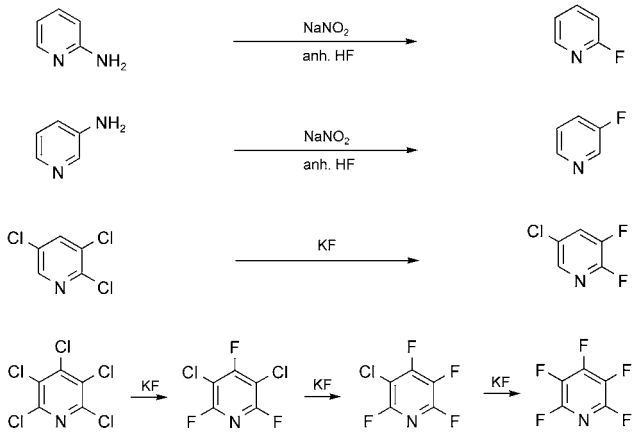
Fluorine is a marvelous tool for engineering biorelevant properties such as acidity, lipophilicity, and metabolic stability.[1] This creates a demand for novel fluorinated compounds equipped with suitable functionality, which can be incorporated as attractive building blocks into potential lead structures. Unlike the abundantly documented fluorinated benzoic acids, benzaldehydes, or areneboronic acids, heterocyclic analogues thereof are yet rather rare.

By using our toolbox methods,[2] we have functionalized 2-fluoropyridine,[3] 3-fluoropyridine,[4] and 2,6-difluoropyridine[5] in a regiochemically exhaustive fashion. This means each vacant position is selectively made amenable to substitution.

Since the key intermediates in the reaction sequences are polar organometallic species, they can be trapped by all kinds of electrophilic reagents. The choice is embarrassingly wide indeed. Virtually any imaginable functional entity can be attached to the core compound. Carboxylation, our standard derivatization method, represents just one out of dozens, if not hundreds, of possibilities.

When we began to extend our studies to 2,3-, 2,4-, and 2,5-difluoropyridines,[3,6] we faced a practical problem. As none of these new substrates is commercially supplied nor described in easily reproducible literature procedures, we set about convenient improved methods of preparation, and providing a suitable route to the missing difluoropyridines and, by extension, trifluoropyridines, and tetrafluoropyridines.

The most critical issue concerned the logistics. We decided to rely on just a few technically or commercially available substances as starting materials. Thus we selected 2- and 3-fluoropyridine which, like the unstable 4-isomer, can be readily prepared from the corresponding aminopyridines by fluorodediazotation (Scheme 1).[7–11] In addition, we picked



Scheme 1.

5-chloro-2,3-difluoropyridine,[12–14] which is made from 2,3,5-trichloropyridine (Scheme 1) and serves as an important industrial intermediate for the manufacture of a herbicide,

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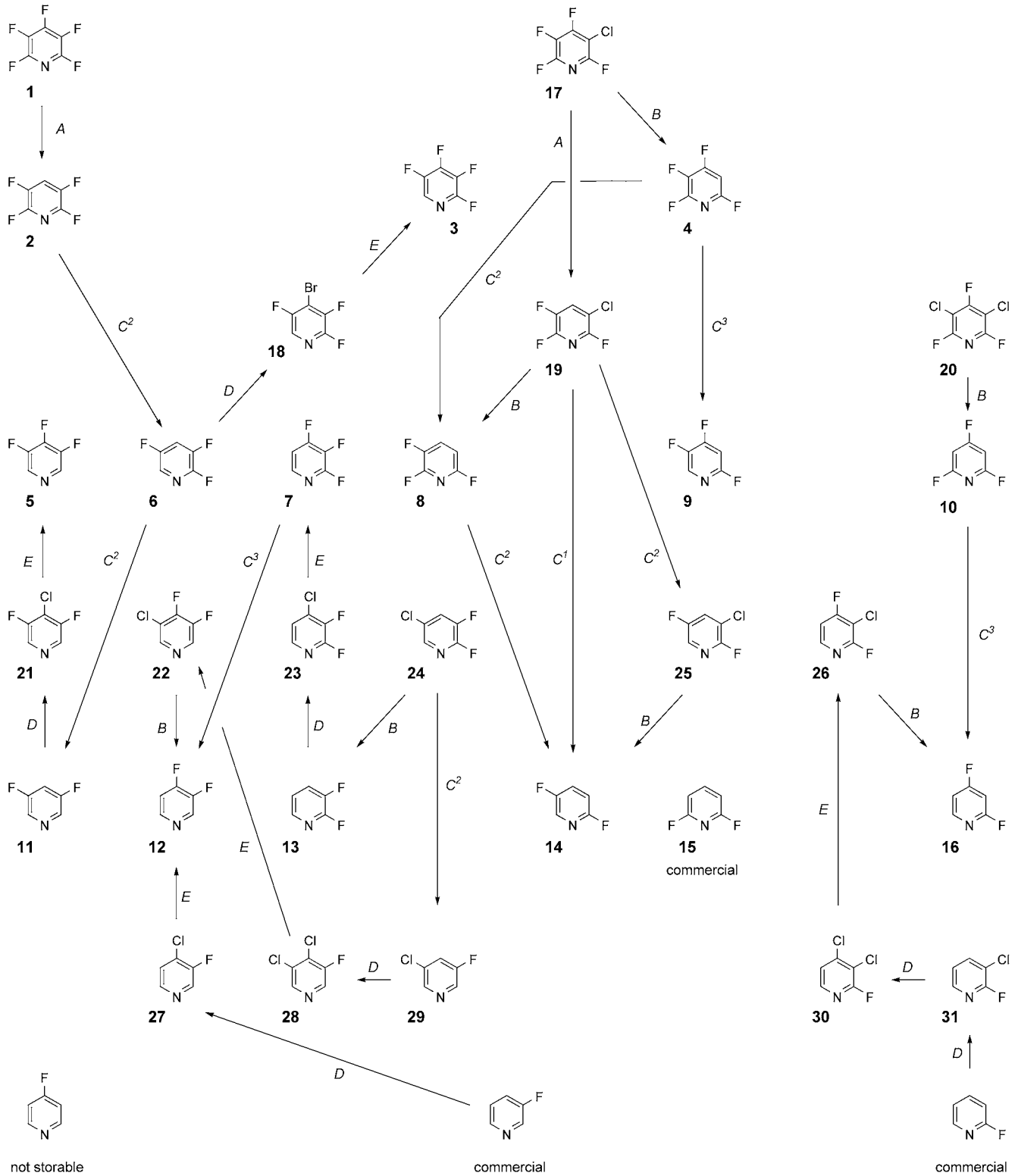


Scheme 2. Synopsis of the "downstream and upstream" modes of access to oligofluoropyridines. *A*: Defluorination using metals or complex metal hydrides; *B*: catalytic hydrogenation; C^1: reaction with hydrazine followed by dehydrochlorinative dediazotation; C^2: reaction with hydrazine followed by dehydrogenative dediazotation; C^3: like C^2 but preceded by metalation and trialkylsilylation and terminated by protodesilylation; *D*: metalation and chlorination (or bromination); *E*: chlorine(bromine)/fluorine displacement.

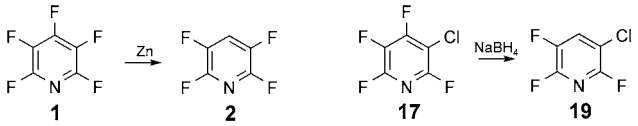
and finally we resorted to 3,5-dichlorotrifluoropyridine, 3-chlorotetrafluoropyridine, and pentafluoropyridine, the three latter being concomitantly produced by chlorine/fluorine displacement ("halex") from pentachloropyridine.[15,16]

2-Fluoropyridine is particularly inexpensive (50€ per mol) and the retail price of the other compounds is still moderate (150–250€ per mol).

Our results will be subdivided into work aimed at the introduction of one additional fluorine atom into insufficiently halogenated precursors and removal of one or several fluorine atoms from excessively halogenated precursors. As one can easily recognize, the "upstream" and "downstream" modes are complementary. Only by applying them conjointly, the fixed objectives could be attained (see Scheme 2).

Results and Discussion

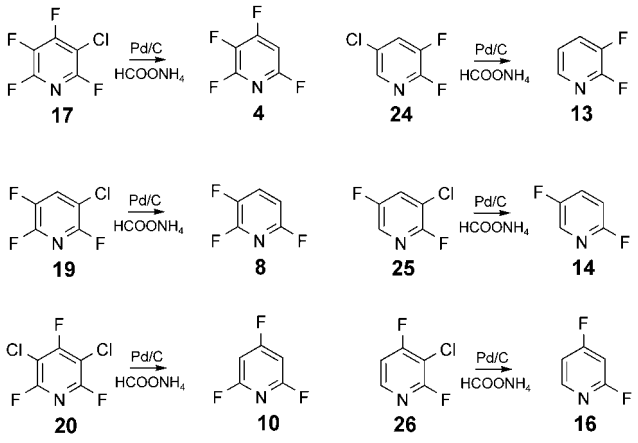
Removal of chlorine or fluorine from polyhalopyridines: The selective reduction of pentafluoropyridine (**1**) to 2,3,5,6-tetrafluoropyridine (**2**) by catalytic hydrogenation[17] or with lithium aluminum hydride[18] has been reported (Scheme 3).



Scheme 3.

We achieved a much higher yield (90% rather than 60%) under more convenient conditions when we used zinc powder in aqueous ammonia as the reagent at 0°C rather than at +25°C, as recommended.[19] The analogous removal of the fluorine atom from the 4-position of 3-chlorotetrafluoropyridine (**17**) proceeded most readily with sodium borohydride in ethanol affording 3-chloro-2,5,6-trifluoropyridine (**19**; 92%) as the sole product (Scheme 3).

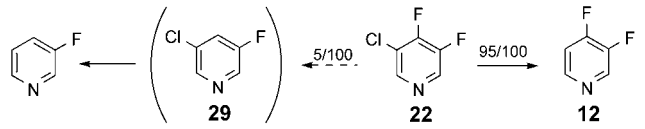
With one exception, the replacement of chlorine was always accomplished by transfer hydrogenation using palladium on charcoal as the catalyst and ammonium formate as the hydrogen source. The reaction temperature and time (generally 25°C for 6 h) and the solvent (mostly 1-octanol) were adapted to the situation when appropriate. In this way



Scheme 4.

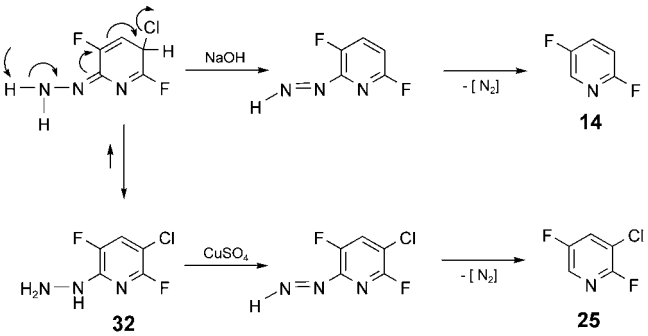
(see Scheme 4) 3-chlorotetrafluoropyridine (**17**) was cleanly converted into 2,3,4,6-tetrafluoropyridine (**4**; 89%), 3-chloro-2,5,6-trifluoropyridine (**19**) into 2,3,6-trifluoropyridine (**8**; 74%), 3,5-dichlorotrifluoropyridine (**20**) into 2,4,6-trifluoropyridine (**10**; 85%), 5-chloro-2,3-difluoropyridine (**24**) into 2,3-difluoropyridine (**13**; 75%), 3-chloro-2,5-difluoropyridine (**25**) into 2,5-difluoropyridine (**14**; 70%) and 3-chloro-2,4-difluoropyridine (**26**) into 2,4-difluoropyridine (**16**; 77%).

In a single instance the discrimination between the heavier and the lighter halogen proved imperfect. The catalytic hydrogenation of 3-chloro-4,5-difluoropyridine (**22**) provided a 5:95 mixture of 3-fluoropyridine (4%), evidently formed through 3-chloro-5-fluoropyridine (**29**), and 3,4-difluoropyridine (**12**; 75%; Scheme 5).



Scheme 5.

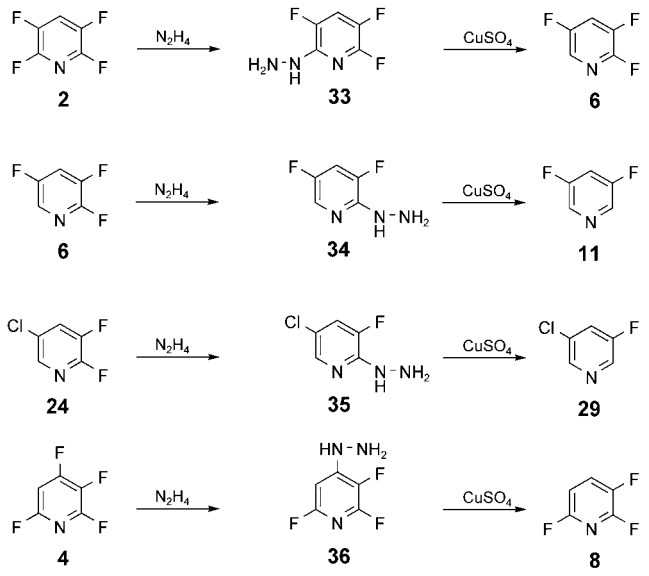
Our only case of a non-hydrogenolytic dechlorination concerns 3-chloro-2,5,6-trifluoropyridine (**20**) as the substrate. Hydrazine was found to displace with amazing selectivity the fluorine atom accommodated at the 6- rather than that at the 2-position. Arylhydrazines and hetarylhydrazines being extremely versatile intermediates, they can undergo dediazotation in various ways.[6,20] When the 3-chloro-2,5-difluoro-6-hydrazinopyridine (**32**) was heated with an aqueous solution of sodium hydroxide under reflux, the nitrogen and chlorine atoms were lost simultaneously thus giving rise to 2,5-difluoropyridine (**14**; 75%; Scheme 6). The dehydrohalo-



Scheme 6.

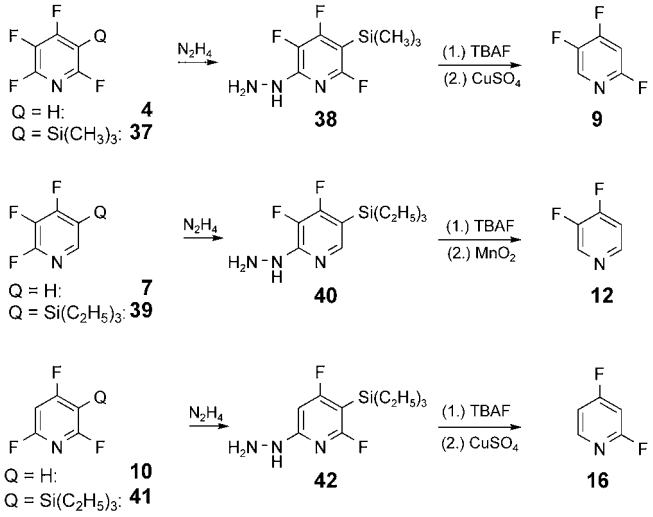
genation/dediazotation sequence obviously involves a (het)arylhydrazine tautomer[21,22] which suffers consecutive 1,6-elimination of hydrogen chloride and 1,2-elimination of dinitrogen. On the other hand, when the hydrazinopyridine **32** was treated with cupric sulfate, dehydrogenation generated directly a hetaryldiazene which collapsed to 3-chloro-2,5-difluoropyridine (**25**; 67%; Scheme 6).

The dehydrogenation/dediazotation method was applied to several other hydrazinopyridines (Scheme 7). Thus, 2,3,5-trifluoropyridine (**6**, 65%) was made from 2,3,5,6-tetrafluoropyridine (**2**) through the hydrazine derivative **33** (88%), 3,5-difluoropyridine (**11**; 79%) from 2,3,5-trifluoropyridine (**6**) through intermediate **34** (68%) and 3-chloro-5-fluoropyridine (**29**; 72%) from 5-chloro-2,3-difluoropyridine (**24**) through intermediate **35** (87%) and 2,3,6-trifluoropyridine (**8**; 73%) from 2,3,4,6-tetrafluoropyridine (**49**) through intermediate **36** (90%).



Scheme 7.

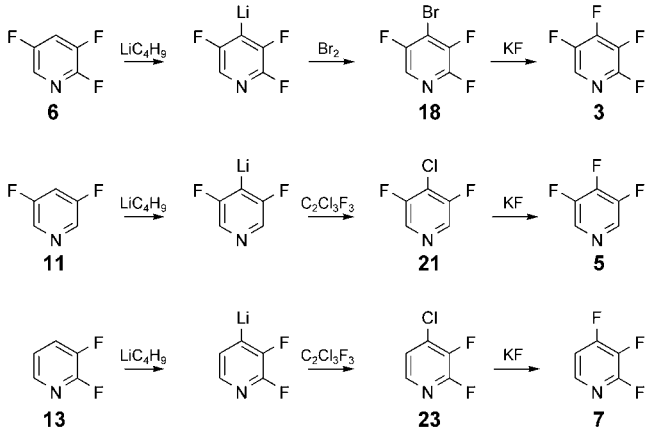
When both 2-(6-) and 4-positions of a pyridine bear fluorine atoms, hydrazine invariably attacks the latter site. However, the nucleophilic substitution can be redirected to the 2-(6-)position by screening the 4-halogen with a bulky trialkylsilyl group which can be readily attached to halopyridines such as **4**, **7**, and **10** by lithiation followed by condensation



Scheme 8.

with the respective chlorotrialkylsilane (Scheme 8).[19,20] In that way, the silanes **37**, **39**, and **41** (91, 82, and 91%) furnished a set of silylated 2-hydrazinopyridines **38**, **40**, and **42** (96, 96, and 98%) which were converted into the defluorinated pyridines **9**, **12**, and **16** (65, 60, and 51%) by protodesilylation performed with tetrabutylammonium fluoride hydrate (TBAF) and oxidation with cupric sulfate or manganese dioxide.

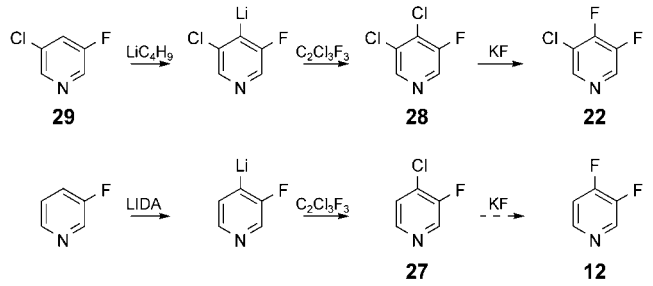
Introduction of chlorine into pyridines and its displacement by fluorine: The "upstream" strategy consists of the site-specific insertion of a heavier halogen, in particular chlorine, and its subsequent displacement by fluorine in a "halex" operation. As with the silylation described in the preceding paragraph, organometallic species generated by permutational hydrogen/metal interconversion acted as the crucial intermediates to which the extra halogen was delivered. Thus, 2,3,5-trifluoropyridine (**6**), 3,5-difluoropyridine (**11**), and 2,3-difluoropyridine (**13**) were all deprotonated by butyllithium at the 4-position. Treatment with molecular bromine and hexachloroethane or 1,1,2-trichloro-1,2,2-trifluoroethane provided 4-bromo-2,3,5-trifluoro-pyridine (**18**; 78%), 4-chloro-3,5-difluoropyridine (**21**; 73%) and 4-chloro-2,3-difluoropyridine (**23**; 81%; Scheme 9). These compounds re-



Scheme 9.

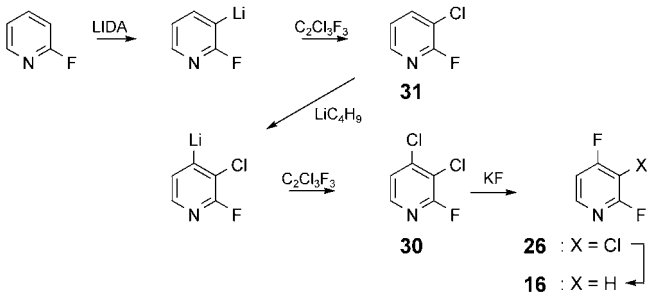
acted with spray-dried potassium fluoride in anhydrous dimethyl sulfoxide and in the presence of small amounts of tetramethylammonium chloride to give 2,3,4,5-tetrafluoropyridine (**3**; 70%), 3,4,5-trifluoropyridine (**5**; 51%) and 2,3,4-trifluoropyridine (**7**; 75%), respectively.

The access to 3,4-difluoropyridine (**12**) starting from 3-fluoropyridine (deprotonated by lithium diisopropylamide, LIDA) through 4-chloro-3-fluoropyridine (**27**; 68%) was hampered by very poor yields at the halogen exchange stage. A far superior route (Scheme 10) departs from 3-chloro-5-fluoropyridine (**29**; made from 5-chloro-2,3-difluoropyridine (**24**) by dehydrogenation–dediazotation of the 2-hydrazino derivative; see above) and passes through 3,4-dichloro-5-fluoropyridine (**28**; 78%) and 3-chloro-4,5-difluoropyridine (**22**; 71%) before being terminated with the catalytic hydrogenation of the latter intermediate (see above).



Scheme 10.

Catalytic hydrogenation was also the last step in the sequence leading from 2-fluoropyridine to 2,4-difluoropyridine (**16**; 77%; Scheme 11). This time the temporary help of even two chlorine atoms was required. The first one was introduced after prior metalation into the 3-position and the second analogously into the 4-position. The 3,4-dichloro-2-fluoropyridine (**28**; 78%) thus obtained was subjected to the standard "halex" procedure to afford the required 3-chloro-2,4-difluoropyridine (**26**; 79%).



Scheme 11.

Conclusion

Using inexpensive starting materials, we have developed simple and expedient protocols that make all non-commercial di-, tri-, and tetrafluoropyridines readily available. The synthetic approach is once more tributary to the intervention of selective organometallic methods. The results disclosed are of practical importance and, at the same time, mirror mechanistically fascinating facets.

Experimental Section

Generalities: Details concerning standard operations and abbreviations can be found in previous publications from this laboratory.[23–25] ^{1}H and (^{1}H-decoupled) ^{13}C NMR spectra were recorded at 400 and 101 MHz, respectively, samples having been dissolved in $CDCl_3$ or, if marked by an asterisk (*), in [D_6]acetone. Whenever possible and appropriate, yields and purities of products were determined, prior to isolation, by gas chromatographic comparison of their peak areas with that of a known amount of a reference substance ("internal standard") and correction of the ratios thus obtained by means of separately established calibration factors. The stationary phases employed are encoded as DB-23 (silicone type) and DB-WAX (polyethylene glycol type).

Defluorinations using metals or complex hydrides

2,3,5,6-Tetrafluoropyridine (2): Pentafluoropyridine (**1**; 55 mL, 85 g, 0.50 mol) and zinc powder (0.13 kg, 2.0 mol) were stirred in a 20% aqueous solution (0.50 L) of ammonia at 0°C. After 6 h, the mixture was diluted with water (1.0 L) and the product was purified by steam distillation. Distillation at atmospheric pressure afforded **2** as a colorless liquid (68.2 g; 90%) ; b.p. 101.5–102°C (ref. [18] 102°C). ^{1}H NMR: δ = 7.73 ppm (quint, J = 7.1 Hz, 1H).

3-Chloro-2,5,6-trifluoropyridine (19): 3-Chloro-2,4,5,6-tetrafluoropyridine (**17**; 93 g, 0.50 mol) was slowly added to sodium borohydride (29 g, 0.75 mol) in anhydrous ethanol (0.25 L) keeping the internal temperature between −10°C and 0°C, the first third of the reagent was added in the course of 1 h, the rest over about 15 min. At 0°C, the mixture was treated with 1.5% sulfuric acid (0.80 L). The lower phase was separated to afford **19** (68.1 g; 81%). An additional amount of **19** (9.1 g; 11%) was obtained by extraction of the aqueous phase with pentanes (3 × 40 mL); b.p. 134–135°C (ref. [26] 71°C/99 Torr). ^{1}H NMR: δ = 7.78 ppm (q, J = 7.3 Hz, 1H).

Catalytic hydrogenation of chlorofluoropyridines

2,3,4,6-Tetrafluoropyridine (4): The slurry containing 5-chloro-2,3,4,6-tetrafluoropyridine (**17**; 93 g, 0.50 mol), ammonium formate (32 g, 0.50 mol), 10% palladium on charcoal (13 g, 12 mmol), and octanol (0.25 L) was stirred at 25°C for 6 h. The product was directly flash distilled from the reaction mixture under reduced pressure and redistilled at atmospheric pressure; colorless liquid; b.p. 94–96°C (ref. [17] 89–90°C); yield: 67.2 g (89%). ^{1}H NMR: δ = 6.73 ppm (dddd, J = 8.0, 4.5, 2.9, 1.6 Hz, 1H).

2,3,6-Trifluoropyridine (8): Prepared analogously from 3-chloro-2,5,6-trifluoropyridine (**19**; 84 g, 0.50 mol); colorless liquid; b.p. 115–117°C (ref. [17] 115–116°C); yield: 49.2 g (74%). ^{1}H NMR: δ = 7.71 (tdd, J = 9.0, 8.0, 6.1 Hz, 1H), 6.84 ppm (ddd, J = 8.6, 3.2, 2.2 Hz, 1H).

2,4,6-Trifluoropyridine (10): Prepared analogously from 3,5-dichloro-2,4,6-trifluoropyridine (**20**; 0.10 kg, 0.50 mol) by using 63 g (1.0 mol) of ammonium formate; colorless liquid; b.p. 98°C (ref. [17] 94–95°C); yield: 56.6 g (85%). ^{1}H NMR: δ = 6.60 ppm (dt, J = 7.7, 1.0 Hz, 2H).

3,4-Difluoropyridine (12): Prepared analogously from 3-chloro-4,5-difluoropyridine (**22**; 22 g, 0.15 mol) using ammonium formate (9.5 g, 0.15 mol, added in three portions in 1 h intervals) under heating to 45°C for 6 h; colorless liquid; b.p. 101–103°C; yield: 13.6 g (79%). According to gas chromatography (30 m; DB-WAX; 35°C; DB-23; 35°C), the product contained 4% of 3-fluoropyridine. See later for analytical and spectral data of the pure compound.

2,3-Difluoropyridine (13): 5-Chloro-2,3-difluoropyridine (**23**; 75 g, 0.50 mol), ammonium formate (63 g, 1.0 mol) and 10% palladium on charcoal (27 g, 25 mmol) were stirred in 80% acetic acid (0.25 L) at 25°C for 6 h. After filtration and washing with water (0.25 L), the filtrate was neutralized before being steam distilled; colorless liquid; b.p. 119–121°C (ref. [27] 118°C); yield: 43.2 g (75%). ^{1}H NMR: δ = 7.99 (dt, J = 4.9, 1.5 Hz, 1H), 7.57 (dtd, J = 9.4, 8.1, 1.5 Hz, 1H), 7.19 ppm (ddd, J = 8.0, 4.9, 3.3 Hz, 1H).

2,5-Difluoropyridine (14): Prepared analogously starting from 3-chloro-2,5-difluoropyridine (**25**; 22 g, 0.15 mol) and stirring for 2 h at 25°C; colorless liquid; b.p. 113–115°C (ref. [28] 115–117°C); m.p. −35 to −33°C; n_D^{20} 1.4431; yield: 12.1 g (70%). ^{1}H NMR: δ = 8.06 (dd, J = 2.9, 1.6 Hz, 1H), 7.5 (symm. m, 1H), 6.93 ppm (dt, J = 9.0, 3.5 Hz); ^{13}C NMR: δ = 159.2 (d, J = 236 Hz), 157.4 (dd, J = 251, 5 Hz), 134.6 (dd, J = 28, 17 Hz), 128.2 (dd, J = 22, 9 Hz), 110.5 ppm (dd, J = 42, 5 Hz); elemental analysis calcd (%) for $C_5H_3F_2N$ (115.08): C 52.18, H 2.63; found: C 52.20, H 2.68.

2,4-Difluoropyridine (16): 3-Chloro-2,4-difluoropyridine (**26**; 22 g, 0.15 mol), 10% palladium on charcoal (8.0 g, 7.5 mmol) and ammonium formate (19 g, 0.30 mol, added in two portions in 2 h intervals), were heated at 75°C in octanol (75 mL) for 4 h. The product was flash-distilled from the reaction mixture under reduced pressure and redistilled at at-

mospheric pressure; colorless liquid; b.p. 105–106 °C (ref. [29] 107 °C); yield: 13.3 g (77 %). ^{1}H NMR: δ = 8.22 (dd, J = 8.6, 5.6 Hz, 1 H), 6.96 (dddd, J = 7.8, 5.9, 2.3, 0.6 Hz, 1 H), 6.67 ppm (dt, J = 8.6, 2.1 Hz, 1 H).

Dehalogenation through hydrazino derivatives

Fluoro(trialkylsilyl)pyridines:

2,3,4,6-Tetrafluoro-5-(trimethylsilyl)pyridine (37): Diisopropylamine (28 mL, 20 g, 0.20 mol), 2,3,4,6-tetrafluoropyridine (**4**; 30 g, 0.20 mol) and chlorotrimethylsilane (25 mL, 22 g, 0.20 mol) in tetrahydrofuran (0.10 L) were consecutively added to a solution containing butyllithium (0.20 mol) in tetrahydrofuran (0.25 L) and hexanes (0.15 L) cooled in a dry ice/methanol bath. After 45 min at −75 °C, the mixture was treated with water (0.10 L). Upon distillation, a colorless liquid (40.6 g; 91 %) was collected; b.p. 67–69 °C/20 Torr (reference [30] 71–73 °C/20 Torr).

2,3,4-Trifluoro-5-(triethylsilyl)pyridine (39): Diisopropylamine (28 mL, 20 g, 0.20 mol) and 2,3,4-trifluoropyridine (**7**; 27 g, 0.20 mol) were added consecutively to a solution of butyllithium (0.20 mol) in hexanes (0.15 L) and tetrahydrofuran (0.35 L) cooled in a dry ice/methanol bath. After 2 h at −75 °C, the mixture was treated with chlorotriethylsilane (33 mL, 30 g, 0.20 mol) and, 1 h later, with water (50 mL). The organic phase was washed with 5 % hydrochloric acid (4 × 70 mL) and dried. Upon distillation, a colorless liquid was collected (40.6 g; 82 %); b.p. 129–130 °C/30 Torr. ^{1}H NMR: δ = 7.88 (ddd, J = 6.7, 1.6, 0.9 Hz, 1 H), 0.9 ppm (m, 15 H); ^{13}C NMR: δ = 161.7 (dt, J = 258, 6 Hz), 154.4 (ddd, J = 238, 17, 5 Hz), 147.0 (m), 134.9 (ddd, J = 266, 29, 17 Hz), 120.7 (ddd, J = 27, 6, 4 Hz), 7.1, 3.3 ppm; elemental analysis calcd (%) for $C_{11}H_{16}F_3NSi$ (247.34): C 53.42, H 6.52; found: C 53.38, H 6.45.

2,4,6-Trifluoro-3-(triethylsilyl)pyridine (41): At −100 °C, butyllithium (0.20 mol) in hexanes (0.15 L) and, 45 min later, chlorotriethylsilane (34 mL, 30 g, 0.20 mol) were added to a solution of 2,4,6-trifluoropyridine (**10**; 27 g, 0.20 mol) in tetrahydrofuran (0.35 L). After 1 h at −75 °C, the mixture was poured into water (0.15 L). The organic phase was washed with brine (2 × 50 mL). Distillation afforded a colorless liquid (45.1 g; 91 %); b.p. 65–67 °C/1.6 Torr; n_D^{20} = 1.4630; ^{1}H NMR: δ = 6.50 (dd, J = 7.6, 1.9 Hz, 1 H), 0.9 ppm (m, 15 H); ^{13}C NMR: δ = 178.2 (ddd, J = 259, 16, 12 Hz), 166.5 (ddd, J = 243, 22, 18 Hz), 164.0 (ddd, J = 245, 20, 17 Hz), 102.3 (ddd, J = 50, 35, 6 Hz), 94.8 (ddd, J = 37, 30, 7 Hz), 7.1, 3.8 ppm (t, J = 2.1 Hz); elemental analysis calcd (%) for $C_{11}H_{16}F_3NSi$ (247.34): C 53.42, H 6.52; found: C 53.46, H 6.48.

Halo(hydrazino)pyridines:

5-Chloro-3,6-difluoro-2-hydrazinopyridine (32): Hydrazine monohydrate (39 mL, 40 g, 0.80 mol) was slowly added to a solution of 3-chloro-2,5,6-trifluoropyridine (**19**; 67 g, 0.40 mol) in ethanol (70 mL) kept at −5 °C. After 20 h, the mixture was poured into water (0.35 L). The precipitate, collected by filtration and dried, proved to be sufficiently pure for further transformations; yield: 58.9 g (82 %); yellow needles (from ethanol); m.p. 120–121 °C; ^{1}H NMR: δ = 7.34 (dd, J = 8.8, 6.8 Hz, 1 H), 6.2 (s, br., 1 H), 3.9 ppm (s, br., 2 H); ^{13}C NMR: δ = 153.6 (d, J = 233 Hz), 146.8 (t, J = 14 Hz), 142.4 (dd, J = 251, 5 Hz), 125.5 (d, J = 19 Hz), 101.2 ppm (dd, J = 38, 4 Hz); elemental analysis calcd (%) for $C_5H_4ClF_2N_3$ (179.56): C 33.45, H 2.24; found: C 33.65, H 2.20.

3,5,6-Trifluoro-2-hydrazinopyridine (33): 2,3,5,6-Tetrafluoropyridine (**2**; 30 g, 0.20 mol) and hydrazine monohydrate (20 mL, 20 g, 0.40 mol) in ethanol (70 mL) were heated under reflux for 2 h. Upon addition of water (0.20 L), a slightly yellow solid precipitated; yellow needles (from ethanol); m.p. 101–104 °C; yield: 28.7 g (88 %); ^{1}H NMR: δ = 7.23 (dd, J = 15.8, 8.7 Hz, 1 H), 5.9 (s, br., 1 H), 3.8 ppm (s, br., 2 H); ^{13}C NMR: δ = 145.7 (ddd, J = 234, 15, 3 Hz), 143.6 (ddd, J = 14, 13, 2 Hz), 141.3 (ddd, J = 252, 5, 3 Hz), 135.1 (ddd, J = 250, 30, 5 Hz), 114.8 ppm (td, J = 21, 4 Hz); elemental analysis calcd (%) for $C_5H_4F_3N_3$ (163.10): C 36.82, H 2.47; found: C 37.14, H 2.43.

3,5-Difluoro-2-hydrazinopyridine (34): Prepared analogously from 2,3,5-trifluoropyridine (**6**; 27 g, 0.20 mol) but heating under reflux in ethanol (0.20 L) for 6 h. At 25 °C, addition of water (0.40 L) and filtration afforded 19.7 g (68 %) of a white precipitate; colorless prisms (from ethanol); m.p. 146–148 °C; ^{1}H NMR: δ = 7.91 (d, J = 2.5 Hz, 1 H), 7.09 (ddd, J = 10.1, 7.7, 2.4 Hz, 1 H), 5.9 (s, br., 1 H), 3.9 ppm (s, br., 2 H); ^{13}C NMR: δ = 152.6 (dd, J = 249, 3 Hz), 146.9 (d, J = 11 Hz), 145.5 (dd, J = 260, 6 Hz), 128.9 (dd, J = 24, 6 Hz), 111.0 ppm (td, J = 25, 18 Hz); elemental analysis calcd (%) for $C_5H_5F_2N_3$ (145.11): C 41.39, H 3.47; found: C 41.69, H 3.27.

5-Chloro-3-fluoro-2-hydrazinopyridine (35): Prepared analogously from 5-chloro-2,3-difluoropyridine (**24**; 60 g, 0.40 mol) but heating under reflux for 20 h; colorless prisms (from ethanol); m.p. 173–174 °C; yield: 56.2 g (87 %); ^{1}H NMR: δ = 7.95 (d, J = 2.0 Hz, 1 H), 7.22 (dd, J = 10.4, 2.0 Hz, 1 H), 5.9 (s, br., 1 H), 3.9 ppm (s, br., 2 H); ^{13}C NMR: δ = 148.7 (d, J = 12 Hz), 145.7 (d, J = 259 Hz), 140.9 (d, J = 6 Hz), 121.4 (d, J = 18 Hz), 119.8 (d, J = 3 Hz); elemental analysis calcd (%) for $C_5H_5ClFN_3$ (161.57): C 37.17, H 3.12; found: C 37.43, H 3.13.

2,3,6-Trifluoro-4-hydrazinopyridine (36): Prepared analogously from 2,3,4,6-tetrafluoropyridine (**4**; 15 g, 0.10 mol) at 50 °C for 2 h; colorless platelets (from ethyl acetate); m.p. 149–151 °C; yield: 14.7 g (90 %); ^{1}H NMR: δ = 8.9 (s, br., 1 H), 6.89 (d, J = 4.2 Hz, 1 H), 3.0 ppm (s, br., 2 H); ^{13}C NMR: δ = 158.1 (ddd, J = 234, 17, 2 Hz), 150.5 (ddd, J = 233, 20, 13 Hz), 148.6 (ddd, J = 13, 8, 6 Hz), 131.2 (ddd, J = 244, 29, 6 Hz), 91.9 ppm (dd, J = 46, 5 Hz); elemental analysis calcd (%) for $C_5H_4F_3N_3$ (163.10): C 36.82, H 2.47; found: C 37.14, H 2.33.

3,4-Difluoro-2-hydrazinopyridine: Tetrabutylammonium fluoride trihydrate (63 g, 0.20 mol) and 3,4-difluoro-2-hydrazino-5-(triethylsilyl)pyridine (**40**; 52 g, 0.20 mol) in tetrahydrofuran (0.20 L) were kept for 2 h at 25 °C. The solvent was evaporated and the residue triturated with water (0.25 L). After filtration and washing with hexanes (3 × 20 mL), 20.9 g (72 %) of a pink solid were obtained; colorless cotton-like needles (from chloroform); m.p. 154–155 °C; ^{1}H NMR: δ = 7.89 (t, J = 6.3 Hz, 1 H), 6.54 (dt, J = 9.4, 5.6 Hz, 1 H), 6.0 (s, br., 1 H), 3.9 ppm (s, br., 2 H); ^{13}C NMR: δ = 154.5 (dd, J = 259, 8 Hz), 152.0 (dd, J = 8, 4 Hz), 143.6 (t, J = 8 Hz), 134.8 (dd, J = 254, 12 Hz), 104.3 ppm (dd, J = 16, 3 Hz); elemental analysis calcd (%) for $C_5H_5F_2N_3$ (145.11): C 41.39, H 3.47; found: C 41.58, H 3.46.

4,6-Difluoro-2-hydrazinopyridine: Prepared analogously from 4,6-difluoro-5-triethylsilyl-2-hydrazinopyridine (**42**; 52 g, 0.20 mol). After evaporation of the solvent, the residue was partitioned between water (50 mL) and diethyl ether (50 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL) and the combined organic layers were evaporated. Upon trituration from hexanes, an orange precipitate was collected by filtration; colorless cotton-like needles (from chloroform and hexanes); m.p. 101–103 °C; yield: 12.3 g (85 %). ^{1}H NMR: δ = 6.37 (dd, J = 10.0, 1.6 Hz, 1 H), 6.3 (s, br., 1 H), 5.98 (dt, J = 8.4, 1.7 Hz), 3.8 ppm (s, br., 2 H); ^{13}C NMR: δ = 172.6 (dd, J = 257, 14 Hz), 163.9 (dd, J = 236, 17 Hz), 162.0 (dd, J = 20, 14 Hz), 89.7 (dd, J = 24, 5 Hz), 86.5 ppm (dd, J = 41, 25 Hz); elemental analysis calcd (%) for $C_5H_5F_2N_3$ (145.11): C 41.39, H 3.47; found: C 41.69, H 3.27.

Fluorohydrazino(trialkylsilyl)pyridines:

3,4,6-Trifluoro-2-hydrazino-5-(trimethylsilyl)pyridine (38): A solution of 2,3,4,6-tetrafluoro-5-(trimethylsilyl)pyridine (**37**; 45 g, 0.20 mol) and hydrazine (0.40 mol) in tetrahydrofuran (0.40 L) was kept at 0 °C for 2 h. Filtration and evaporation afforded a yellow oil (45.2 g; 96 %) which proved to be sufficiently pure for further transformations.

3,4-Difluoro-2-hydrazino-5-(triethylsilyl)pyridine (40): 5-Triethylsilyl-2,3,4-trifluoropyridine (**39**; 50 g, 0.20 mol) and hydrazine monohydrate (19 mL, 20 g, 0.40 mol) in tetrahydrofuran (0.20 L) were heated at 50 °C for 20 h. After evaporation of the solvent, hexanes (70 mL) were added and the salt precipitated was filtered. The filtrate, after evaporation, afforded 49.8 g (96 %) of an orange oil which proved to be sufficiently pure for further transformations. ^{1}H NMR: δ = 7.82 (d, J = 6.4 Hz, 1 H), 0.9 ppm (m, 15 H); ^{13}C NMR: δ = 158.4 (dd, J = 253, 6 Hz), 152.7 (dd, J = 9, 4 Hz), 148.9 (dd, J = 14, 9 Hz), 134.6 (dd, J = 255, 16 Hz), 110.5 (dd, J = 27, 5 Hz), 7.2, 3.5 ppm.

4,6-Difluoro-2-hydrazino-5-(triethylsilyl)pyridine (42): Prepared analogously from 2,4,6-trifluoro-3-(triethylsilyl)pyridine (**41**; 50 g, 0.20 mol), but reducing the reaction time to 2 h; slightly yellow oil; yield: 50.8 g (98 %). ^{1}H NMR: δ = 6.30 (d, J = 10.0 Hz, 1 H), 6.3 (s, br., 1 H), 3.8 (s, br., 2 H), 0.9 ppm (m, 15 H); ^{13}C NMR: δ = 177.4 (dd, J = 255, 18 Hz), 167.6 (dd, J = 233, 22 Hz), 163.1 (dd, J = 20, 15 Hz), 90.7 (dd, J = 51, 36 Hz), 89.3 (dd, J = 30, 5 Hz), 7.5, 4.0 ppm (t, J = 2.0 Hz); elemental analysis

calcd (%) for $C_{11}H_{19}F_2N_3Si$ (259.37): C 50.94, H 7.38; found: C 51.21, H 7.31.

Reaction of a chlorohydrazinopyridine with sodium hydroxide:

2,5-Difluoropyridine (14): 5-Chloro-3,6-difluoro-2-hydrazinopyridine (**32**; 18 g, 0.10 mol) was heated in a 3.0 M aqueous solution (66 mL) of sodium hydroxide (8.0 g, 0.20 mol) under reflux for 45 min. Steam distillation gave **14** as a colorless liquid (8.63 g; 75%). For spectral and analytical data, see above.

Reactions of hydrazinopyridines with oxidants:

3-Chloro-2,5-difluoropyridine (25): 5-Chloro-3,6-difluoro-2-hydrazinopyridine (**32**; 18 g, 0.10 mol) and copper(II) sulfate pentahydrate (50 g, 0.20 mol) in water (0.20 L) were heated under reflux for some 2 h until the gas evolution ceased. Upon steam distillation a colorless liquid was collected; m.p. 10–12 °C; b.p. 136–137 °C; n_D^{20} = 1.4786; yield: 10.0 g (67%). ^{1}H NMR: δ = 7.98 (t, J = 2.3 Hz, 1H), 7.64 ppm (td, J = 6.9, 2.6 Hz, 1H); ^{13}C NMR: δ = 156.6 (dd, J = 256, 5 Hz), 154.8 (dd, J = 236, 2 Hz), 132.3 (dd, J = 27, 14 Hz), 128.3 (dd, J = 24, 2 Hz), 117.6 ppm (dd, J = 39, 6 Hz); elemental analysis calcd (%) for $C_5H_2ClF_2N$ (149.53): C 40.16, H 1.35; found: C 40.13, H 1.44.

2,3,5-Trifluoropyridine (6): Prepared analogously from 3,5,6-trifluoro-2-hydrazinopyridine (**33**; 25 g, 0.15 mol); colorless liquid; b.p. 101.5 °C (ref. [29] 101–102 °C); yield: 13.0 g (65%). ^{1}H NMR: δ = 7.89 (t, J = 2.5 Hz, 1H), 7.40 ppm (dtd, J = 9.8, 8.5, 2.6 Hz, 1H).

3,5-Difluoropyridine (11): Prepared analogously from 3,5-difluoro-2-hydrazinopyridine (**34**; 15 g, 0.10 mol); colorless liquid; b.p. 92–93 °C (ref.: [31] 92.5 °C); yield: 9.07 g (79%). ^{1}H NMR: δ = 8.36 (d, J = 2.4 Hz, 2H), 7.22 (tt, J = 8.6, 2.4 Hz, 1H) ppm.

3-Chloro-5-fluoropyridine (29): Prepared analogously from 5-chloro-3-fluoro-2-hydrazinopyridine (**35**; 49 g, 0.30 mol); colorless platelets (from methanol); m.p. 26–27 °C; b.p. 132–134 °C; yield: 28.4 g (72%); ^{1}H NMR: δ = 8.43 (s, br., 1H), 8.40 (d, J = 2.5 Hz, 1H), 7.47 ppm (dt, J = 8.1, 2.4 Hz, 1H); ^{13}C NMR: δ = 158.6 (d, J = 262 Hz), 144.6 (d, J = 4 Hz), 136.0 (d, J = 23 Hz), 131.8 (d, J = 4 Hz), 123.1 ppm (d, J = 21 Hz); elemental analysis calcd (%) for C_5H_3ClFN (131.54): C 45.65, H 2.30; found: C 45.69, H 2.22.

2,3,6-Trifluoropyridine (8): Prepared analogously starting from 2,3,6-trifluoro-4-hydrazinopyridine (**36**; 8.2 g, 50 mmol) under reflux for 45 min. A steam distillation followed by an ordinary distillation afforded a colorless liquid; yield: 4.86 g (73%). For the physical and spectral data of this compound, see above.

2,4,5-Trifluoropyridine (9): At 25 °C, 3,4,6-trifluoro-2-hydrazino-5-(trimethylsilyl)pyridine (**37**; 24 g, 0.10 mol) and tetrabutylammonium fluoride trihydrate (32 g, 0.10 mol) were dissolved in tetrahydrofuran (0.20 L). After 2 h, the mixture was evaporated and water (0.10 L) was added. The aqueous phase was extracted with diethyl ether (3 × 0.10 L), and the combined organic layers were evaporated. The residue, copper(II) sulfate pentahydrate (50 g, 0.20 mol) and water (0.20 L) were heated for 45 min under reflux. Upon steam distillation followed by an ordinary distillation, a colorless liquid was isolated; b.p. 99–101 °C; n_D^{20} = 1.4201; yield: 8.65 g (65%); ^{1}H NMR: δ = 8.15 (dt, J = 9.6, 1.3 Hz, 1H), 6.83 ppm (ddd, J = 8.0, 4.8, 2.9 Hz, 1H); ^{13}C NMR: δ = 159.2 (ddd, J = 237, 11, 2 Hz), 158.2 (dt, J = 267, 13 Hz), 146.7 (ddd, J = 254, 11, 6 Hz), 135.9 (ddd, J = 21, 19, 2 Hz), 99.3 ppm (dd, J = 46, 19 Hz); elemental analysis calcd (%) for $C_5H_2F_3N$ (133.07): C 45.13, H 1.51; found: C 45.27, H 1.61.

3,4-Difluoropyridine (12): 3,4-Difluoro-2-hydrazinopyridine (see above, 22 g, 0.15 mol) was added in three portions (at 15 min interval) to a mixture of manganese(IV) oxide (13 g, 0.15 mol) in octanol (75 mL) at 15 °C, and then the mixture was allowed to reach 25 °C. After flash distillation of the crude reaction mixture, the product was redistilled; colorless liquid; b.p. 102–103 °C; n_D^{20} = 1.4426; yield: 10.4 g (60%). ^{1}H NMR: δ = 8.59 (dd, J = 9.9, 2.3 Hz, 1H), 8.39 (t, J = 6.2 Hz, 1H), 7.17 ppm (dt, J = 10.0, 6.1 Hz, 1H); ^{13}C NMR: δ = 156.0 (dd, J = 265, 11 Hz), 148.6 (dd, J = 259, 10 Hz), 147.7 (t, J = 6 Hz), 140.8 (d, J = 19 Hz), 113.3 ppm (d, J = 13 Hz); elemental analysis calcd (%) for $C_5H_3F_2N$ (115.08): C 52.18, H 2.63; found: C 51.97, H 2.69.

2,4-Difluoropyridine (16): 4,6-Difluoro-2-hydrazinopyridine (see above, 10 g, 70 mmol) and copper(II) sulfate pentahydrate (35 g, 0.14 mol) in water (0.14 L) were heated under reflux for 25 min. Dilution with water and steam distillation afforded **16** (see above) as a colorless liquid (4.11 g; 51%).

Metalation and subsequent introduction of chlorine (or bromine)

4-Bromo-2,3,5-trifluoropyridine (18): At −75 °C, 2,3,5-trifluoropyridine (**6**; 27 g, 0.20 mol) was added to butyllithium (0.20 mol) in a mixture of hexanes (0.15 L) and tetrahydrofuran (0.25 L). After 2 h, the mixture was treated with bromine (10 mL, 32 g, 0.20 mol) and kept at −75 °C for 1 h, before being poured into a saturated solution (0.10 L) of sodium thiosulfate. The organic phase was dried and evaporated. Upon distillation, a colorless liquid was collected; b.p. 59–60 °C/27 Torr; yield: 33.1 g (78%). ^{1}H NMR: δ = 7.9 ppm (s, br., 1H); ^{13}C NMR: δ = 154.9 (ddd, J = 258, 5, 3 Hz), 148.1 (ddd, J = 239, 15, 3 Hz), 143.8 (dd, J = 267, 33 Hz), 128.2 (ddd, J = 28, 15, 7 Hz), 111.3 ppm (ddd, J = 24, 19, 5 Hz); elemental analysis calcd (%) for C_5HBrF_3N (211.97): C 28.33, H 0.48; found: C 28.01, H 0.49.

4-Chloro-3,5-difluoropyridine (21): Prepared analogously from 3,5-difluoropyridine (**11**; 23 g, 0.20 mol) by using hexachloroethane (47 g, 0.20 mol) instead of bromine. Distillation (b.p. 120–125 °C) afforded a colorless liquid containing compound **21** and tetrachloroethylene. The liquid was diluted in pentanes (0.15 L) and, at 0 °C, was treated with a saturated solution (65 mL) of 4.5 M hydrogen chloride in diethyl ether. The precipitate formed was collected by filtration, washed with pentanes (2 × 20 mL) and dissolved in water (30 mL). After neutralization at 0 °C and distillation of the organic phase, a colorless liquid was obtained; m.p. 7–9 °C; b.p. 129–131 °C; yield: 10.9 g (73%); n_D^{20} = 1.4794; ^{1}H NMR: δ = 8.4 ppm (s, br., 2H); ^{13}C NMR: δ = 155.6 (d, J = 263 Hz, 2 C), 134.3 (dd, J = 22, 5 Hz, 2 C), 118.6 ppm (t, J = 18 Hz); elemental analysis calcd (%) for $C_5H_2ClF_2N$ (149.53): C 40.16, H 1.35; found: C 40.16, H 1.18.

4-Chloro-2,3-difluoropyridine (22): Prepared as described in the preceding paragraph from 2,3-difluoropyridine (**13**; 23 g, 0.20 mol) but using 1,1,2-trichloro-2,2,1-trifluoroethane (48 mL, 75 g, 0.40 mol) instead of hexachloroethane. Distillation at atmospheric pressure afforded a colorless liquid; b.p. 139–141 °C; m.p. −23 to −25 °C; n_D^{20} = 1.4726; yield: 24.2 g (81%); ^{1}H NMR: δ = 7.91 (d, J = 5.4 Hz, 1H), 7.34 ppm (t, J = 4.9 Hz, 1H); ^{13}C NMR: δ = 152.8 (dd, J = 240, 14 Hz), 143.0 (dd, J = 263, 31 Hz), 141.6 (dd, J = 15, 8 Hz), 133.6 (d, J = 13 Hz), 124.0 ppm (t, J = 4 Hz); elemental analysis calcd (%) for $C_5H_2ClF_2N$ (149.53): C 40.16, H 1.35; found: C 40.25, H 1.36.

3,4-Dichloro-5-fluoropyridine (23): Prepared analogously from 3-chloro-5-fluoropyridine (**28**; 26 g, 0.20 mol); colorless liquid; m.p. −5 to −2 °C; b.p. 78–79 °C/29 Torr; n_D^{20} = 1.5292; yield: 23.3 g (78%); ^{1}H NMR: δ = 8.5 (s, br., 1H), 8.4 ppm (s, br., 1H); ^{13}C NMR: δ = 155.9 (d, J = 263 Hz), 145.8 (d, J = 5 Hz), 136.5 (d, J = 23 Hz), 131.7 (d, J = 3 Hz), 129.9 ppm (d, J = 17 Hz); elemental analysis calcd (%) for $C_5H_2Cl_2FN$ (165.98): C 36.18, H 1.21; found: C 35.99, 1.22.

4-Chloro-3-fluoropyridine (27): Diisopropylamine (28 mL, 20 g, 0.20 mol) and 3-fluoropyridine (19 g, 0.20 mol) were added consecutively to a solution of butyllithium (0.20 mol) in hexanes (0.15 L) and tetrahydrofuran (0.35 L) cooled in a dry ice/methanol bath. After 2 h at −75 °C, the mixture was treated with 1,1,2-trichloro-2,2,1-trifluoroethane (48 mL, 75 g, 0.40 mol) and, 1 h later, with water (80 mL). The organic phase was treated with 5% hydrochloric acid (4 × 30 mL), dried and concentrated. The residue was distilled affording a colorless liquid; m.p. −27 to −24 °C; b.p. 81–82 °C/97 Torr; n_D^{20} = 1.5033; yield: 17.9 g (68%). ^{1}H NMR: δ = 8.5 (s, br., 1H), 8.34 (d, J = 5.3 Hz, 1H), 7.39 ppm (dd, J = 6.5, 5.5 Hz, 1H); ^{13}C NMR: δ = 155.8 (d, J = 259 Hz), 146.2 (d, J = 6 Hz), 139.1 (d, J = 23 Hz), 130.5 (d, J = 15 Hz), 125.5 ppm; elemental analysis calcd (%) for C_5H_3ClFN (131.54): C 45.66, H 2.30; found: C 45.74, H 2.23.

3-Chloro-2-fluoropyridine (31): Prepared analogously from 2-fluoropyridine (17 mL, 19 g, 0.20 mol); colorless liquid; b.p. 68–70 °C/32 Torr (ref. [32] 94–95 °C/100 Torr); yield: 22.4 g (85%); ^{1}H NMR: δ = 8.12 (dd, J = 4.8, 1.4 Hz, 1H), 7.82 (ddd, J = 8.2, 7.6, 1.5 Hz, 1H), 7.17 ppm (ddd, J = 7.9, 4.8, 1.4 Hz, 1H).

3,4-Dichloro-2-fluoropyridine (30): At −75 °C, 3-chloro-2-fluoropyridine (**31**; 26 g, 0.20 mol) was added to butyllithium (0.20 mol) in a mixture of hexanes (0.15 L) and tetrahydrofuran (0.25 L). After 2 h, the mixture was

treated with 1,1,2-trichloro-2,2,1-trifluoroethane (48 mL, 75 g, 0.40 mol) and kept at −75 °C for 1 h. Upon distillation, a colorless liquid was collected; m.p. 17–19 °C; b.p. 62–63 °C/10 Torr; yield: 26.6 g (80 %); ^{1}H NMR: δ = 8.03 (dd, J = 5.5, 0.9 Hz, 1 H), 7.32 ppm (d, J = 5.5 Hz, 1 H); ^{13}C NMR: δ = 159.7 (d, J = 239 Hz), 145.7 (d, J = 3 Hz), 144.5 (d, J = 24 Hz), 123.4 (d, J = 5 Hz), 117.0 ppm (d, J = 36 Hz); elemental analysis calcd (%) for $C_5H_2Cl_2FN$ (165.98): C 36.18, H 1.21; found: C 36.54, H 0.93.

Halogen/fluorine displacement

2,3,4,5-Tetrafluoropyridine (3): 4-Bromo-2,3,5-trifluoropyridine (**18**; 21 g, 0.10 mol), potassium fluoride (12 g, 0.20 mol) and tetramethylammonium chloride (2.2 g, 20 mmol) were heated in dimethyl sulfoxide (0.20 L) at 150 °C for 2 h. Steam distillation followed by an ordinary distillation gave **3** as a colorless liquid (10.6 g; 70 %); b.p. 92–92.5 °C (ref. :[17] 87–88 °C). ^{1}H NMR: δ = 7.96 ppm (dt, J = 8.7, 2.1 Hz, 1 H).

3,4,5-Trifluoropyridine (5): Prepared analogously from 4-chloro-3,5-difluoropyridine (**21**; 15 g, 0.10 mol), but extending the reaction time to 6 h; colorless liquid; b.p. 85–87 °C; yield: 6.74 g (51 %); ^{1}H NMR: δ = 8.42 ppm (d, J = 7.4 Hz, 2 H); ^{13}C NMR: δ = 148.5 (dd, J = 263, 8 Hz, 2 C), 144.7 (dt, J = 268, 13 Hz), 136.0 ppm (symm. m, 2 C); elemental analysis calcd (%) for $C_5H_2F_3N$ (133.07): C 45.13, H 1.51; found: C 45.47, H 1.19.

2,3,4-Trifluoropyridine (7): As described for compound **3** starting from 4-chloro-2,3-difluoropyridine (**23**; 15 g, 0.10 mol); colorless liquid; b.p. 107–107.5 °C (ref. [28] 104.5–106 °C); yield: 9.95 g (75 %); ^{1}H NMR: δ = 7.95 (tm, J = 6.3 Hz, 1 H), 7.09 ppm (dt, J = 8.6, 5.3 Hz, 1 H).

3-Chloro-4,5-difluoropyridine (22): As described for compound **3** starting from 3,4-dichloro-5-fluoropyridine (**28**; 17 g, 0.10 mol) and heating at 125 °C for 6 h; colorless liquid; m.p. 4–6 °C; b.p. 70–72 °C/98 Torr; n_D^{20} = 1.4760; yield: 10.7 g (71 %); ^{1}H NMR: δ = 8.46 ppm (t, J = 8.0 Hz, 2 H); ^{13}C NMR: δ = 152.6 (dd, J = 267, 12 Hz), 148.7 (dd, J = 263, 10 Hz), 147.2 (d, J = 5 Hz), 138.8 (d, J = 19 Hz), 120.9 ppm (d, J = 12 Hz); elemental analysis calcd (%) for $C_5H_2ClF_2N$ (149.53): C 40.16, H 1.35; found: C 40.17, H 1.17.

3-Chloro-2,4-difluoropyridine (26): As described for compound **3** starting from 3,4-dichloro-2-fluoropyridine (**30**; 17 g, 0.10 mol); colorless liquid; m.p. 5–8 °C; b.p. 146–147 °C; n_D^{20}1.4782; yield: 11.8 g (79 %); ^{1}H NMR: δ = 8.10 (dd, J = 6.8, 5.8 Hz, 1 H), 7.07 ppm (dd, J = 7.4, 5.7 Hz, 1 H); ^{13}C NMR: δ = 166.5 (dd, J = 265, 5 Hz), 160.5 (dd, J = 237, 5 Hz), 146.1 (dd, J = 17, 10 Hz), 111.2 (dd, J = 18, 5 Hz), 106.0 ppm (dd, J = 38, 19 Hz); elemental analysis calcd (%) for $C_5H_2ClF_2N$ (149.53): C 40.16, H 1.35; found: C 40.37, H 1.28.

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