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N-Acetylation as a Means to Activate Polyfluoroarylamines for Selective *ortho*-Hydrodefluorination by Zinc in Aqueous Ammonia: A Concise Route to Polyfluorobenzo Azaheterocycles

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Dedicated to Professor J. Grobe on the occasion of his 75th birthday

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N-Acetylation of polyfluoroarylamines is proposed as a means to remove the amino group blocking effect of their hydrodefluorination by zinc in aqueous ammonia. With pentafluoroacetanilide, the Zn ion specific effect has been demonstrated to be responsible for *ortho* hydrodefluorination. This regiochemistry is accompanied by the removal of a fluorine atom from the *para* position, which occurs predominantly in the initial phase of the process in the absence of deliberately added zinc salt. The $CuCl_2$ additive has been found to accelerate the reaction and to propel it to double defluorination. Quantum chemical calculations suggest a diminished electron affinity of pentafluoroaniline, which is responsible for its inertness in relation to the hydrodefluorination reaction. The pentafluoroaniline radical anion, which essentially has a nonplanar structure, is prone to easy fragmentation to give an aminotetrafluorophenyl radical. For pentafluoroacetanilide, CVA experiments and quantum chemical calculations predict that the pentafluorophenyl moiety serves as the electron receptor and that the acetamido group is twisted out of coplanarity with the benzene ring; thus, together with the electron-withdrawing effect of the acetyl group, the amino group blocking effect is suppressed. On this ground, the selective *ortho* hydrodefluorination of polyfluoroacetanilides is developed as an important protocol for the expeditious and general synthesis of polyfluorobenzo azaheterocycles via readily accessible polyfluoroarylamines from base polyfluoroarenes. Its applicability has been illustrated by preparing quinolines that possess a polyfluorinated benzene moiety by the Skraup synthesis utilizing crude polyfluoroacetanilide hydrodefluorination products as starting materials.

Introduction

Fluorine-containing nitrogen heterocyclic compounds, in particular quinoline derivatives, are among the actually and potentially bioactive substances and efficient medicines.[1] One of the general synthetic strategies used to construct polyfluorobenzo azaheterocycles uses polyfluorinated aromatic amines with a nonsubstituted position *ortho* to the amino group as the universal building blocks. This opens an opportunity to fuse the polyfluorinated benzene ring with an azaheterocycle by means of some kind of heterocyclization.[2] Within this approach, however, the main obstacle that must be overcome is the low accessibility of the partially fluorinated amines, the syntheses of which tend to be multistep, laborious processes.[2b,3a,3b] At the same time, highly fluorinated arylamines are easily available and can be obtained by direct ammonolysis of base polyfluoroarenes, such as hexafluorobenzene, octafluorotoluene, and decafluorobiphenyl. In view of this, a novel and concise route to less accessible heterocyclizable partially fluorinated amines from highly fluorinated arylamines, and more generally from aromatic raw materials, to polyfluorobenzo azaheterocycles can be envisaged if these arylamines could undergo selective *ortho* hydrodefluorination.

Earlier,[4–6] zinc in aqueous ammonia was established to be, apparently, the simplest of all reductive systems which were previously utilized for the selective hydrodefluorination of polyfloroarenes and some of their functional derivatives under mild conditions (room temperature). In this connection, it seems appropriate to assay this system in the synthesis of partially fluorinated arylamines, of special interest are those with an unsubstituted position *ortho* to the amino group. However, the placement of the amino group on the polyfluoroarene ring blocks the reaction.[6] Because the most probable reason for this can be ascribed

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to the electron-donating effect of the amino group, its acylation could be anticipated to renew the ability of the substrate to be hydrodefluorinated by zinc in aqueous ammonia.

In a view of the above-mentioned facts, in the given article: (1) The reduction by zinc in aqueous ammonia (for preliminary results see ref.[7]) is investigated in detail as a method for the selective removal of a fluorine atom from the *ortho* position of polyfluoroarylamine *N*-acetyl derivatives. (2) By using the pentafluoroaniline *N*-acetyl derivative as an example, zinc ions are revealed to accelerate the hydrodefluorination reaction and to be a crucial factor promoting its *ortho* orientation. (3) The effect of a copper salt additive is revealed as a means to reach, in some cases, the double hydrodefluorination product; thus, the variety of accessible building blocks for the construction of polyfluorobenzo azaheterocycles is increased. (4) Mechanistic aspects of (a) blocking the polyfluoroarene hydrodefluorination by an amino substituent, (b) suppressing this effect by polyfluoroarylamine *N*-acetylation, and (c) the zinc ion influence on the rate and regioselectivity of hydrodefluorination of *N*-acetylpolyfluoroarylamine are considered. (5) Examples of syntheses and further transformations of some fluorinated quinoline derivatives serve to develop the methodology of polyfluoroacetanilide hydrodefluorination and this process is demonstrated to be applicable to the synthesis of benzoazaheterocycles with a polyfluorinated benzene ring and to their functional derivatives.

Results and Discussion

Hydrodefluorination of Polyfluorinated *N*-Acetylarylamines by Zinc in Aqueous Ammonia and the Effects of the Zinc Ion and a Copper Salt Additive

The results of the reduction of the *N*-acetyl derivatives of polyfluoroarylamines by zinc in 30% aqueous ammonia at room temperature are given in Table 1. The ratio of the products resulting from the monodefluorination of the acetamido group of pentafluoroacetanilide (**1**) at the *ortho*- and *para* positions, 2,3,4,5-tetrafluoroacetanilide (**2**, major product) and 2,3,5,6-tetrafluoroacetanilide (**3**, minor product), respectively (Scheme 1), was revealed to change over the course of the reaction. In the initial stage of the reaction, which corresponds to no more than 10% transformation of the starting material (≈ 1.2 h), *para* hydrodefluorinaton mainly occurs to give anilide **3** (Table 1, Entry 1). However, after ≈ 30% transformation (≈ 3 h), *ortho* defluorinated anilide **2** becomes predominant and a minor amount of the twice-defluorinated product, 2,4,5-trifluoroacetanilide (**4**), is discerned in the ^{19}F NMR spectrum (Table 1, Entries 3, 4) of the reaction mixture.

It was reasonable to account for such a change in the product ratio by the accumulation of zinc ions in the reaction mixture. In support of this, the primary addition of $ZnCl_2$ into the reaction system led to a prevalence of the *ortho* defluorination product from the very start of the reaction. Additionally, the transformation of the starting compound was accelerated (Table 1, compare Entries 1 and 5, 4 and 6). At the maximum point of transformation, compound **2** was obtained in 47% isolated yield (Table 1, Entry 7) and this entry exhibits the efficiency of the present method as compared with the previous multistep syntheses of 2,3,4,5-tetrafluoroaniline.[2b,3]

Under similar conditions, only the fluorine atom in the position *ortho* to the acetamido group of 4-acetoamidotetrafluorobenzotrifluoride (**5**) is removed to afford 4-acetamido-2,3,6-trifluorobenzotrifluoride (**6**) (Scheme 2), irrespective of the $ZnCl_2$ additive. However, in addition to what was previously reported, we demonstrate that the $ZnCl_2$ additive somewhat accelerates the process (Table 1, Entries 8, 9). Despite the fact that the isolation of the principal product is complicated by a small admixture of its hydrolysis product, 4-amino-2,3,6-trifluorobenzotrifluoride, anilide **6** was obtained by processing the mixture with acetic anhydride in 72% yield.

Reduction of 4-acetamidononafluorobiphenyl (**7**) without the $ZnCl_2$ additive afforded a 50–70% transformation of the starting compound into the *para*-monodefluorination product of the pentafluorophenyl ring, 4-acetamido-2,2′,3,3′,5,5′,6,6′-octafluorobiphenyl (**8**), Scheme 3 (Table 1, Entries 19, 20). Analysis of the ^{19}F NMR spectrum of the product mixture revealed that the $ZnCl_2$ additive does not significantly change the result. Thus, in this case, the strongest reactivity of the *para* position of the pentafluorophenyl ring displays itself, even in the presence of zinc ions.

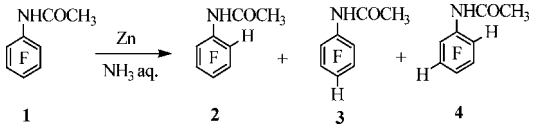
Thus, the experimental data presented reveal zinc ions to accelerate the hydrodefluorination of polyfluoroacetanilides and, in case of **1**, to provide its *ortho* regioselectivity to an acetamido group. However, the latter effect generally competes with other orienting factors, which can prevail in certain situations. At the same time, despite the accelerating effect of the zinc ions, the reaction time for the transformation into the monodefluorination products is rather long, and twice defluorinated products, which are also potentially valuable precursors to polyfluorobenzo azaheterocycles, are formed, if any, only in minor amounts.

Additional possibilities to intensify the process were sough and we explored a copper salt additive, taking into account that the Zn–Cu couple was found to be efficient as a polyfluoroarene hydrodefluorinaton reagent.[11] The $CuCl_2$ additive of 20% upon Zn was found to pronouncedly accelerate the reduction of **1** in 30% aqueous ammonia (Table 1, Entries 3 and 10) so that a mixture of approximately equal amounts of the primary and secondary defluorination products, anilides **2** and **4**, was formed after 6 h. Moreover, 2,3,5-trifluoroacetanilide (**9**) appeared in the reaction mixture, likely from further defluorination of **3**, which remained intact under the same conditions without the $CuCl_2$ additive (Table 1, Entry 18). The twofold increased copper salt additive furnished proportionally increased quantities of anilides **4** and **9** (Table 1, Entries 10 and 11). Together with the process elongation this provides some more amount of defluorination (Table 1, Entries 12–

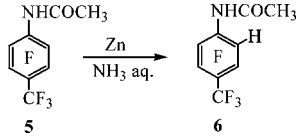
Table 1. Reactions of polyfluoroacetanilides with zinc.

Entry	Reagents					Time	Isolated mixture composition[a] [mol-%]		
	Starting compound	[mmol]	Zn [mmol]	Additive	[mmol]	[h]	Starting compound	Defluorination products	Double defluorination products
1	**1**	3.5	30	–	–	1.2	89	**2** 4; **3** 7	
2	**1**	3.5	30	–	–	3	77	**2** 11; **3** 12	
3	**1**	3.5	30	–	–	5	57	**2** 25; **3** 16	**4** ≈ 1
4	**1**	3.5	30	–	–	13	29	**2** 51; **3** 16	**4** 3
5	**1**	3.5	30	$ZnCl_2$	10	1.2	76	**2** 21; **3** 3	
6	**1**	3.5	30	$ZnCl_2$	10	13	13	**2** 71; **3** 11	**4** 4
7	**1**	24	150	$ZnCl_2$	50	23	≈ 1	**2** 78; **3** 13	**4** 7
8	**5**	6.2	60	–	–	40	14	**6** 50; **6a**[b] 36	
9	**5**	6.2	60	$ZnCl_2$	20	40	≈ 1	**6** 85; **6a** 13	
10	**1**	0.9	10.7	$CuCl_2$	1.8	6		**2** 47; **3** 10	**4** 34; **9** 3
11	**1**	0.9	13.4	$CuCl_2$	4.4	6		**2** 31; **3** 9	**4** 51; **9** 6
12	**1**	0.9	10.7	$CuCl_2$	1.8	24		**2** 14; **3** 3	**4** 73; **9** 8
13	**1**	0.9	13.4	$CuCl_2$	4.4	84		**3** 7	**4**[c] 77; **9a**[d] 5
14	**1**	8.9	107	$CuSO_4$	44.5	72		**2** 10; **3** 5	**4** 63; **9** 3[e]
15	**2**[f]	0.8	13.4	$CuCl_2$	4.4	84	50	**4** 84; **9** 3	
16	**3**	1.0	14.6	$CuCl_2$	4.8	72	60	**9** 33	
17	**3**[g]	1.0	14.6	$CuCl_2$	4.8	84	25	**9**[h] 58; **9a** 15	
18	**3**	1.0	9.7	$ZnCl_2$	9.7	72	95	**9** 3	
19	**7**	0.3	4.5	–	–	25	50	**8** 50	
20	**7**	2.6	7.1	–	–	26	30	**8** 70	
21	**7**	0.3	4.5	$CuCl_2$	1.5	25	22	**8** 45	**X**[j] 33
22	**7**[i]	0.3	4.5	$CuCl_2$	1.5	25		**8** 72	**X**[j] 22
23	**7**[i]	3.0	45	$CuCl_2$	15	25		**8** 78	**X**[j] 20

[a] In all cases when the total percentage does not reach 100%, all respective anilines are present in trace quantities. [b] ^{19}F NMR spectroscopic characteristics accord with the literature data.[7] [c] Previously reported in ref.[7] ^{19}F NMR (188.3 MHz, [D$_6$]acetone, $CFCl_3$ int. std): δ = 141.9 [m, $J(F^5,F^4)$ = 20 Hz, $J(F^5,H^6)$ ≈ 12 Hz, $J(F^5,F^2)$ ≈ 12 Hz, $J(F^5,H^3)$ = 7 Hz, 1 F, F^5], 141.1 [dm, $J(F^4,F^5)$ = 20 Hz, 1 F, F^4], 129.2 (m, 1F, F^2) ppm; ^1H NMR (200.1 MHz, [D$_6$]acetone): δ = 2.16 (s, 3 H, CH_3), 7.27 [td, $J(H^3,F^4)$ = 10 Hz, $J(H^3,F^2)$ = 11 Hz, $J(H^3,F^5)$ = 7 Hz, $J(H^3,H^6)$ <1.5 Hz, 1 H, H^3], 8.28 [dt, $J(H^6,F^5)$ = 13 Hz, $J(H^6,F^2)$, $J(H^6,F^4)$ = 7–9 Hz, $J(H^6,H^3)$ < 1.5 Hz, 1 H, H^6], 9.11 (br. s, 1 H, NH) ppm. [d] ^{19}F NMR spectroscopic characteristics accord with literature data.[9] [e] The presence of 3,4,5-trifluoroacetanilide (11%) is also indicated by the ^{19}F NMR spectrum. [f] 86% **2** content in a mixture with **3** and **4**. [g] Product mixture from Entry 16 was used as the starting material. [h] Previously reported in ref.[10] ^{19}F NMR (188.3 MHz, [D$_6$]acetone, $CFCl_3$ int. std): δ = 158.0 [m, $J(F^2,F^3)$ = 20 Hz, $J(F^2,F^5)$ = 9 Hz, 1 F, F^2], 135.2 [ddt, $J(F^3,F^2)$ = 20 Hz, $J(F^3,H^4)$ = 11 Hz, $J(F^3,H^6)$, $J(F^3,F^5)$ = 2 Hz, 1 F, F^3], 114.4 [m, $J(F^5,H^6)$, $J(F^5,H^4)$ = 11 Hz, $J(F^5,F^2)$ = 9 Hz, $J(F^5,F^3)$ = 2 Hz, 1 F, F^5] ppm; ^1H NMR (200.1 MHz, [D$_6$]acetone): δ = 2.19 (s, 3 H, CH_3) 6.94 (m, 1 H, H^4), 8.00 (m, 1 H, H^6), 9.34 (br. s, 1 H, NHAc) ppm. [i] Ethanol (20 mL) was added. [j] 4-Acetamido-2,2′,3,3′,5′,6,6′-heptafluorobiphenyl according to ^{19}F NMR (188.3 MHz, [D$_6$]acetone, $CFCl_3$ int. std): δ = 135.0 (m, 1 F, F^2), 156.4 (m, 1 F, F^3), 114.7 (m, 1 F, F^6), 139.0 (m, 2 F, $F^{2',6'}$), 138.6 (m, 2 F, $F^{3',5'}$) ppm, and its corresponding amine.



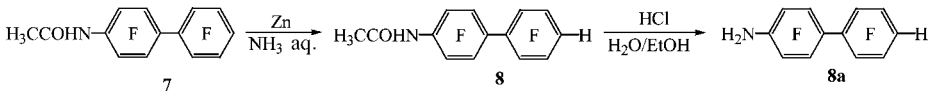
Scheme 1.



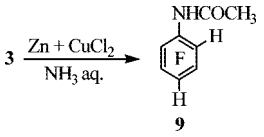
Scheme 2.

14). According to the NMR and CMS data, the respective free amines appeared as a result of partial hydrolysis of their acetyl derivatives.

The interaction of **2** with a 10-fold amount of zinc in aqueous ammonia and the $CuCl_2$ additive (50% upon Zn) during an 84 h reaction period afforded a mixture containing, according to the NMR spectroscopic data, more than 80% of anilide **4** (Table 1, Entry 15). Similarly, after two sequential reduction operations, a mixture was obtained from **3** with a ≈ 70% total content of anilide **9** and 2,3,5-trifluoroaniline (**9a**) (Table 1, Entries 16 and 17) (Scheme 4). In the presence of $ZnCl_2$, the reduction of **3** by zinc practically does not occur for 72 h (Table 1, Entry 17).



Scheme 3.



Scheme 4.

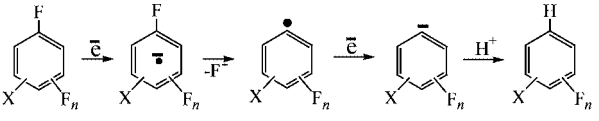
In both cases, doubly defluorinated products **4** and **9** thus formed are the *N*-acetyl derivatives of trifluoroanilines, prepared earlier by the significantly longer methods, taking into account a low accessibility of their immediate precursors.[8,10]

The reduction of anilide **7** with the $CuCl_2$ additive gave no increase in the yield of anilide **8** which was isolated in 53% yield and transformed into 4-amino-2,2′,3,3′,5,5′,6,6′-octafluorobiphenyl (**8a**) by hydrolysis in 55% yield (Scheme 3). However, the degree of transformation was noticeably enhanced and, from the analysis of the ^{19}F NMR spectrum of the product mixture, twice defluorinated product 4-acetamido-2,2′,3,3′,5′,6,6′-heptafluorobiphenyl appeared (Table 1, Entries 19–21). Moreover, hydrodefluorination was found to be further driven by adding ethanol, obviously because of the increase in its solubility, up until the starting compound was fully consumed (Table 1, Entries 22 and 23). However, the attempted complete conversion of **7** into the doubly defluorinated compound by a longer reaction time failed.

Mechanistic Consideration

Amino Group Blocking Effect

By considering the influence of the amino group as a substituent on the rate of polyfluoroarene hydrodefluorinaton, we relied on the conventional mechanism for the process[12] as a sequence of steps. These steps include electron capture by a substrate, fragmentation of the derived radical anion (RA) to give a fluoride anion and a polyfluoroaryl radical, reduction of the latter, and, at last, protonation of an arising polyfluoroaryl anion (Scheme 5).



Scheme 5.

The propensity of the polyfluoroarene to undergo reductive hydrodefluorinaton is believed to be determined by the influence of the substituent X on the rate of one or on both of the first two steps depicted in Scheme 5. A priori, the observed irreducibility of pentafluoroaniline seems likely to be brought about by the π-electron-donating ability of the amino group in the first step. However, the possibility that this is, at least partially, due to a substituent influence on the rate of RA fragmentation (the second step in Scheme 5) cannot be completely ignored. To examine the probability of both situations, we performed the quantum chemical study of the energetics of electron capture by a pentafluoroaniline molecule, a potential energy surface (PES) of pentafluoroaniline RA thus derived, ($C_6F_5NH_2^{-\cdot}$) and the relative energies of the products of its competing fragmentations – the isomeric aminotetrafluorophenyl radicals ($NH_2C_6F_4^{\cdot}$).

Because the amino group is pyramidal, the $C_6F_5NH_2$ molecule has lower symmetry compared with C_6F_5H and, by neglecting the NH_2 group rotation, belongs to the C_s symmetry group. Nevertheless, this insignificantly perturbs the MO's of the aromatic system and, despite the formal lack of a molecular symmetry plane coincident with the benzene ring, allows an unequivocal assignment of the MO's to the π- or σ-type. The CIS/6-31G*//B3LYP/6-31+G* results (Table 2) predict the vertical electron capture to occur onto a π(*a*′′)-MO (EA^{vert} = –0.57 eV). Previously,[13] the PES character of the fluorobenzene RA's was shown to occur from the presence of low-lying excited π*- and σ*-states. The analogous states of $C_6F_5NH_2^{-\cdot}$ belong to the same irreducible representation of the C_s group *a*′, the lowest π*-state lying above the ground state on about 2 eV and the σ*-state lying above the ground state on about 3 eV (Table 2).

Table 2. CIS/6-31G*//B3LYP/6-31+G* relative energies of low lying anionic states of pentafluoroaniline and anilide **1** appearing from the vertical electron capture.

State	$C_6F_5NH_2^{-\cdot}$ (C_s) [eV]		**1**$^{-\cdot}$ (C_1) [eV]	
π-state (b_1-type)	$^2A'$	1.88	^2A	0.
π-state (a_2-type)	$^2A''$	0.	^2A	1.32
σ-state	$^2A'$	3.13	^2A	3.02

The calculated energy closeness of these states implies a strong vibronic interaction that causes out-of-plane distortion of RA and a complicated PES structure. The B3LYP/6-31+G* study (Table 3) reveals the PES to be a pseudorotation surface (similar to that of RA's of other fluorinated benzenes[13]). The overall PES minimum corresponds to a_2-type deformed structure **A** (Figure 1), which determines the adiabatic electron affinity (EA_{ad}) of $C_6F_5NH_2$. The RB3LYP results predict EA_{ad} to be positive and to have a value of 0.13 eV. This is markedly lower than EA_{ad} = 0.60 eV, which was calculated for C_6F_6 in the same approximation with the latter being in compliance with the experimental values of 0.5–0.9 eV.[12]

Table 3. RB3LYP/6-31+G* stationary PES structures of $C_6F_5NH_2^{-\cdot}$.

Structure	E_{tot} [a.u.][a]	E_{rel} [kcal mol^{-1}]	EA_{ad} [eV]
A (C_1)	–783.454080 (minimum)	0	0.13
B (~C_s)	–783.452660 (minimum)	0.89	0.10
(C_1)	–783.452575 (saddle)	0.94	0.09

[a] For $C_6F_5NH_2$ E_{tot} = –783.449123 a.u.

There is a second minimum on the PES of $C_6F_5NH_2^{-\cdot}$ that corresponds to b_1-type deformed structure **B**. As a result, the PES embraces, in view of its mirror symmetry, four

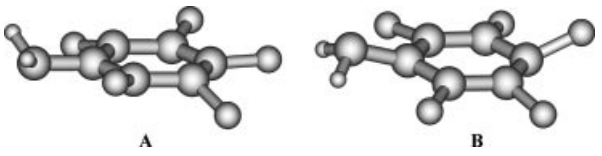


Figure 1. Stationary structures of $C_6F_5NH_2^{-\cdot}$ corresponding to the PES minima.

minima equivalent in pairs and separated by equivalent saddle points that are in pairs, mirror images of each other. The energy difference between the structures of **A** and **B** does not exceed ca. 1 kcal/mol and the energy barrier separating them is negligibly small. All of the RA stationary structures are essentially nonplanar and cannot be unambiguously qualified as pseudo-π- or σ-type. Thus, in this case, a RA fragmentation is not symmetry forbidden, unlike what takes place for planar RA's.[14]

Thus, according to the computational results, $C_6F_5NH_2^{-\cdot}$ is structurally flexible and easily alters its electronic state with the concomitant redistribution of the electronic density between all of the C–F fragments; thus, all of its possible competitive fragmentations are rendered. The calculated energies of the isomeric aminotetrafluorophenyl radicals ($NH_2C_6F_4^{\cdot}$) (Table 4) predict the *para*-fragmentation to be the most thermodynamically preferred fragmentation for $C_6F_5NH_2^{-\cdot}$. Comparison of the calculated energies of the gas-phase fragmentations of $C_6F_6^{-\cdot}$ and of the *para*-position of $C_6F_5NH_2^{-\cdot}$ (Figure 2) reveals that the latter undergoes decay more readily. In turn, this means that the inertness of $C_6F_5NH_2$ under the present defluorination conditions is most likely caused by its low electron affinity.

Table 4. Total and relative energies of isomeric $NH_2C_6F_4$.

Isomer	E_{tot} [a.u.]	E_{rel} [kcal mol^{-1}]
para	–683.561263	0.
ortho	–683.560692	0.36
meta	–683.558827	1.53

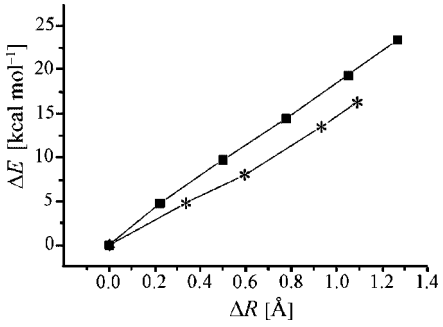


Figure 2. Energy dependence on the C–F bond stretching: (■) for $C_6F_6^{-\cdot}$, (*) for the *para* position of $C_6F_5NH_2^{-\cdot}$.

N-Acetylation Deblocking Effect

As specified above, acylation of the amino group eliminates the substituent blocking effect so that polyfluoroacetanilides, unlike their corresponding amines, are reduced by zinc in aqueous ammonia at room temperature. This dramatic change is most likely caused by the fact that *N*-acylation minimizes the substituent electron-donating effect towards a benzene ring.

To shed some light on the nature of the above effect of the acetylation of the amino group, electrochemical reduction potentials of hexafluorobenzene, pentafluoroaniline, and anilide **1** were measured by means of cyclic voltammetry (CVA) in DMF on a platinum electrode with Et_4NClO_4 as the supporting electrolyte. One irreversible reduction peak was detected for C_6F_6 and $C_6F_5NH_2$ with an E_p value of –2.10 and –2.04 V, respectively. Thus, the observed larger reducibility of C_6F_6 compared with that of $C_6F_5NH_2$ is not reproduced in the electrochemical reduction. The reason for this disparity is not definitely clear but can probably be caused by the various correlations of the effective E values of C_6F_6 and $C_6F_5NH_2$ operating in the conditions of chemical and electrochemical experiments because of the different medium influences on both the respective E^o values and the rates of the subsequent decay of initially formed radical anions. The reduction of anilide **1** exhibited a spread peak with an approximate E_p value of –1.6 V, which corresponds to a diffusionally controlled process that is reflected by a linear current dependence on the depolarizer concentration and a square root of the potential sweep rate. It is not excluded that such a peak character is caused by the existence of **1** as a mixture of conformers that differ by a rotation angle around the N–$COCH_3$ bond (cf.[15]) and reduced at somewhat different potential values. From the analysis of the potential values, the pentafluorophenyl moiety is most likely the electron receptor, rather than the acetyl group. For example, under the same conditions, acetanilide $C_6H_5NHCOCH_3$ is not reduced up to E = –2.6 V. The easier electrochemical reducibility of anilide **1** compared with that of C_6F_6 is in compliance with its calculated (RB3LYP/6-31+G*) EA_{ad} value of 0.74 eV.

The calculated electronic and spatial structures reveal the LUMO of anilide **1** (Figure 3) and the SOMO of its RA (**1**$^{-\cdot}$) (Figure 4) to be almost completely located in the benzene ring. The acetamido group is out of coplanarity with the benzene ring both in anilide **1** (the dihedral angle value φ = 63°) and in RA **1**$^{-\cdot}$ ($\varphi \approx 90°$). The ring parts of the LUMO in **1** and of the SOMO in **1**$^{-\cdot}$ are of the b_1-type (Figures 3 4), which indicates that the acetamido group does not exert an appreciable π-donating effect. The significant deviation of the acetamido group from the ring plane suggests that the suppression of this effect is caused both by an electronic influence of the acetyl group and by its steric interaction with the neighboring fluorine atoms (cf.[16]).

Indicatively, **1** is reduced easier compared with both $C_6F_5NH_2$ and C_6F_6. This is in line with a suppression of the acetamido nitrogen electron-donating resonance effect that occurs towards the benzene ring, whereas the fluorine substituent in C_6F_6, as well as an amino group in $C_6F_5NH_2$, is able to exert such an effect. According to the data,[17] in the TS of polyfluoroarene RA fragmentation, the dissociating C–F bond is considerably deviated out-of-plane,

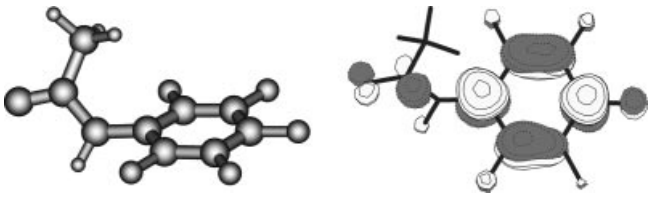


Figure 3. Spatial structure and LUMO of anilide **1**.

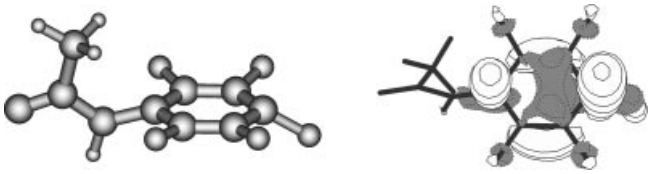
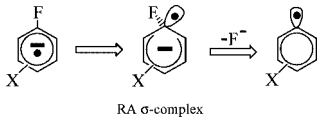


Figure 4. Spatial structure and SOMO of RA $\mathbf{1}^{-\cdot}$.

whereas other C–F bonds are closer to the ring plane than in a starting RA, which approaches their spatial orientation in a planar polyfluorophenyl radical that will be formed. All of these TS features resemble an anionic cyclohexadienyl structure with an odd electron located on the carbon atom of the out-of-plane deviated C–F bond. This structure is similar to that of a conventional intermediate of the aromatic nucleophilic substitution reaction (S_NAr), where the odd electron mimics an added nucleophile (cf.[18]) (the RA σ complex depicted in Scheme 6).



Scheme 6.

Since in the actually occurring RA fragmentation, the C–F bond out-of-plane deviation is synchronous with its stretching, the fragmentation mechanism is believed to be akin to the hypothetical one-step S_NAr mechanism, whose TS is modeled after the RA σ complex described above. Within such an assumption, the regioselectivity of the process is expected to be similar to that which occurs in S_NAr reactions of respective RA polyfloroarene precursors and caused mostly by the relative stability of intermediate anionic σ complexes.[19] By implying that the acetamido group, neighbored by two fluorine atoms, does not exert a significant π-donating effect, one may anticipate, by analogy with S_NAr reactions of C_6F_5X compounds,[20] that the *para* hydrodefluorinaton of **1** does occur, and this is exactly what is observed at the initial phase of the reduction of **1** by zinc in aqueous ammonia, as well as in the reductive hydrodefluorinatons of other C_6F_5X compounds.[4–6,17] By taking into account the above-mentioned similarity of the TS to the RA σ complex, the b_1-type of SOMO in RA $\mathbf{1}^{-\cdot}$ is believed to crucially favor its transformation into the TS of the *para*-C–F-bond cleavage, since it is the bond that is out-of-plane deviated to the greatest degree (Figure 4) and the HOMO's of $\mathbf{1}^{-\cdot}$ and the corresponding RA σ complex ideally fit each other by symmetry (Figure 5).

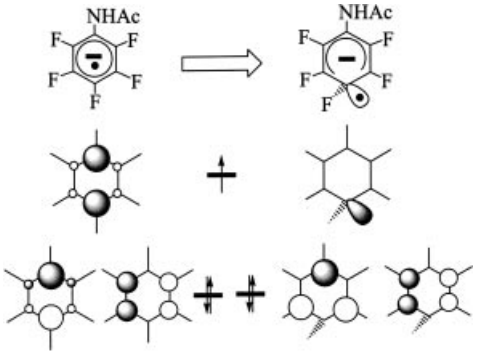
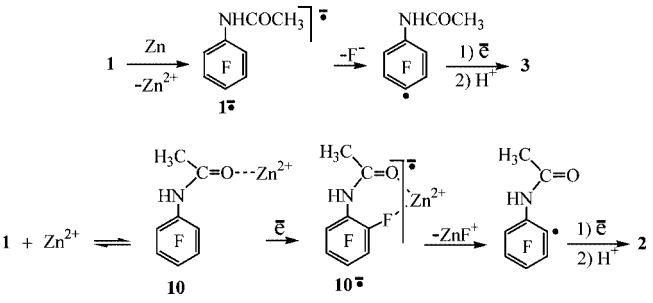


Figure 5. HOMO's of RA $\mathbf{1}^{-\cdot}$ and the corresponding RA σ complex (the MO images are simplified by omitting the minor lobes associated with the fluorine atoms and the acetamido group).

Zinc Cation Effect

The acceleration of hydrodefluorinaton by adding the zinc salt (see above) is apparently caused by formation of a complex of **1** with a zinc ion (Scheme 7, complex **10**), which is present in a small but kinetically significant concentration. One may believe complex **10** to be a stronger electron acceptor and, respectively, be reduced more readily than the starting anilide that brings about the process acceleration with zinc ions accumulation. Both in this complex and in the respective complex $\mathbf{10}^{-\cdot}$ formed by RA $\mathbf{1}^{-\cdot}$, the zinc ion is, apparently, coordinated to the oxygen atom of the acetyl group (cf.[21]), that is, it is located in close proximity to the fluorine atom *ortho* to the acetamido group. Because the capability of organically bound fluorine atoms to coordinate with electron-deficient entities is amply documented and characterized,[22] one may suggest the Zn(II)–F coordination to occur in $\mathbf{10}^{-\cdot}$, which is favored by an anionic nature of the chelating ligand. Obviously, the aggregate of the above reasons causes the change of the first observable *para* defluorinaton of **1** by its *ortho* defluorination with the zinc ions accumulation. In so doing, $\mathbf{10}^{-\cdot}$ is apparently formed through the sequence outlined in Scheme 7, rather than as a result of zinc ion interaction with originally formed free $\mathbf{1}^{-\cdot}$. Likely, the latter is a short-lived species (cf.[17,23]) and hardly has time to form the complex with a zinc ion before the fragmentation occurs.

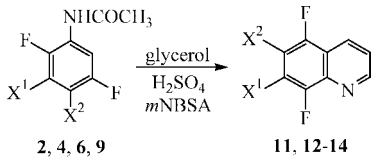


Scheme 7.

As outlined above, the hydrodefluorinaton regioselectivity of **2** and obviously that of **7** is *para* to an unsubstituted position rather than *ortho* to the acetamido group. This is suggested to be due to two factors. In the case of **2**, it is probable that the Zn–RA complexes of primary defluorination products with one unsubstituted position *ortho* to the $NHCOCH_3$ group sterically prefer the *transoid* arrangement of this group with respect to the *ortho* fluorine atom, thus, there is no possibility for Zn–F coordination to occur and no promotion for further *ortho* defluorination. Moreover, the actual regioselectivity is also obviously favored by the tendency to remove a fluorine atom from the middle position in a group of neighboring electron-accepting fragments, the position *para* to this fluorine atom is not occupied by a substituent that exerts a significant π-electron-donating effect.[19,20] This is the tendency which obviously also dominates in the regioselectivity of the primary hydrodefluorinaton of biphenyl **7** and is strengthened by an electronic effect of the *para*-located polyfluorinated phenyl substituent. This group stabilizes the cyclohexadienyl anion type TS (vide supra), whereas the Zn chelation operates only in the secondary hydrodefluorinaton.

Synthesis of Polyfluorinated Quinolines

The efficiency of the developed *ortho* defluorination of polyfluoroacetoanilides as a first stage of the general approach to quinolines with polyfluorinated benzene moiety is additionally illustrated by the opportunity to directly employ the crude defluorination product mixtures as starting materials in the Skraup syntheses. Earlier,[2a] 5,6,7,8-tetrafluoroquinoline (**11**) was prepared from 2,3,4,5-tetrafluoroaniline by this reaction with the use of As_2O_5 as an oxidant. In the present work, **11** was obtained in a 63% isolated yield by utilizing the crude mixture of **2**, **3**, and **4**, obtained from the reduction of **1** by Zn in aqueous NH_3 (see above), as a starting material and, by analogy with,[2c] *meta*-nitrobenzenesulfonic acid as an oxidant (Scheme 8). From product mixtures derived by the $CuCl_2$-promoted hydrodefluorination of **1** and **3** and containing anilides **4** and **9**, respectively, as main components, quinolines **12** and **13** were obtained both in 30% isolated yield. Similarly, from crude **6** containing a small admixture of its respective amine **6a**, obtained was 6-trifluoromethyl-5,7,8-trifluoroquinoline (**14**) in 58% yield (Scheme 8).

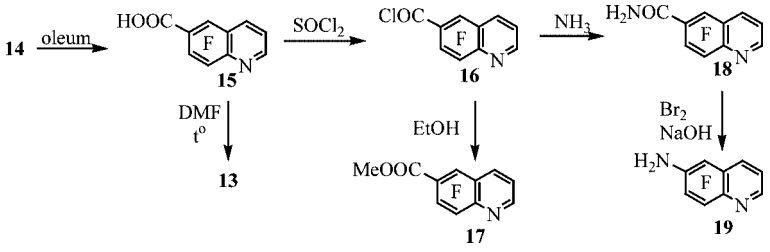


2, **11** X^1, X^2 = F; **4**, **12** X^1 = H, X^2 = F; **9**, **13** X^1 = F, X^2 = H; **6**, **14** X^1 = F, X^2 = CF_3

Scheme 8.

The hydrolysis of the trifluoromethyl group of quinoline **14** with oleum and upon heating afforded 6-carboxy-5,7,8-trifluoroquinoline (**15**), which was further easily decarboxylated by heating in DMF to give quinoline **13**. Acid **15** also was converted into acyl chloride **16** from which methyl ester **17** and amide **18** were obtained. The latter was subjected to a Hoffman rearrangement to yield 6-amino-5,7,8-trifluoroquinoline (**19**) (Scheme 9). These transformations illustrate the possibility that **15** can serve as a base building block for a wide variety of fluorinated quinolines that are functionalized at the 6-position. In this respect, indicative is the preparation of amine **19** since the direct ammonolysis of **11** by aqueous ammonia was reported to afford 7-amino-5,6,8-trifluoroquinoline.[2a]

In the ^1H NMR spectra of polyfluorinated quinolines, the sets of signals typical of the pyridine ring[24a] are observed: $\delta(H^2)$ = 8.6–9.2 ppm, $\delta(H^3)$ = 7.5–7.7 ppm, $\delta(H^4)$ = 8.4–8.5 ppm [$J(H^3,H^4)$ = 8.2–8.6 Hz; $J(H^2,H^3)$ = 3.8–4.0 Hz]. The ^{19}F NMR chemical shifts of polyfluorinated quinolines are collected in Table 5. The ^{19}F NMR spectrum of **11** contains four signals, each having two doublet splittings with close $J(F,F)_{ortho}$ and $J(F,F)_{para}$ values of 18–20 Hz (by analogy with polyfluorinated naphthalenes[25,26]). The low-field signal in the ^{19}F NMR spectrum of octafluoronaphthalene is known[26] to belong to the α-F atoms. On this basis and in the case of **11**, two low-field signals should be attributed to F^5 and F^8. On the other hand, because of the conjugation of F^5 and F^7 with the pyridine nitrogen, their signals should be shifted to a lower field relative to the F^8 and F^6 signals. The superposition of these arguments does not allow the ^{19}F NMR spectrum of **11** to be unequivocally interpreted. Therefore, the ^{19}F NMR spectrum of **11** was recorded with the addition of $Eu(fod)_3$ as a chemical shift reagent. Appreciably low-field shifted signals turned out only as a signal initially located at δ = 152.8 ppm. By implying that a Eu^{III} ion is bound to the nitrogen atom,



Scheme 9.

Table 5. 400.1 MHz ^{19}F NMR spectroscopic data for polyfluorinated quinolines in $CDCl_3$ with $CFCl_3$ as an internal standard.

Compound	δ [ppm]	J(F,X) [Hz]
11	F^5 = –152.0, F^7 = –155.1, F^8 = –152.8, F^6 = –158.2	F^5,F^6 = 19; F^5,F^8, F^7,F^8 = 17; F^7,F^6 = 18; F^8H^4 = 1[a]
12[b]	F^5 = –154.2, F^6 = –137.7, F^8 = –126.6	F^5,F^6, F^5,F^8 = 18; F^7,F^8, F^5H^7 = 1.5; F^6,H^7, F^8,H^7 = 9; F^8,H^4 = 1[c]
13[d]	F^5 = –125.3, F^7 = –134.6, F^8 = –156.9	F^5,F^7 = 2.5; F^5,F^8, F^7,F^8 = 18; F^5,H^6 9; F^7,H^6 = 10; F^8,H^6 = 4.5; F^8,H^4 = 1.5[c]
14[e]	F^5 = –123.3, F^7 = –140.4, F^8 = –153.9, F^{CF_3} = –56.6	F^5,F^8 = 18; F^7,F^8 = 19; F^5,F^{CF_3} = 26, F^7,F^{CF_3} = 20; F^8,H^4 = 1.5[a]
15[f]	F^5 = –122.6, F^7 = –137.8, F^8 = –154.5	F^5,F^8 = 19; F^7,F^8 = 17; F^8,H^4 = 1.5[a]
16[g]	F^5 = –120.1, F^7 = –135.8, F^8 = –151.7	F^5,F^8, F^7,F^8 = 18
17[f,h]	F^5 = –122.1, F^7 = –138.1, F^8 = –154.3	F^5,F^8 = 18; F^7,F^8 = 17; F^8,H^4 = 1[a]
18[i,j]	F^5 = –126.3, F^7 = –139.3, F^8 = –155.6	F^5,F^8 = 18; F^7,F^8 = 19; F^8,H^4 = 1.5[a]
19[k]	F^5, F^7 = –152.8, –153.2, F^8 = –157.4	F^5,F^7 = 7; F^5,F^8 = 17; F^7,F^8 = 16; F^8,H^4 = 1.5[a]

[a] Observed only in the ^1H NMR spectrum and is obscured in the ^{19}F NMR spectrum. [b] **12**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.36 [$J(F^5,H^7)$ = 1.5 Hz, $J(F^6,H^7)$, $J(F^8,H^7)$ = 9 Hz, H^7] ppm. [c] Observed in both the ^1H- and ^{19}F NMR spectra. [d] **13**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.17 [$J(F^5,H^6)$ = 9 Hz, $J(F^7,H^6)$ = 10 Hz, $J(F^8,H^6)$ = 4.5 Hz, H^6] ppm. [e] In CH_2Cl_2. [f] In [D_6]acetone. [g] In $SOCl_2$. [h] **17**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 4.02 ppm (s, 3 H, CH_3). [i] In [D_7]DMF. [j] **18**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.27 (br. s 1 H, NH_2), 8.55 (br. s 1 H, NH_2) ppm. [k] **19**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 5.48 ppm (br. s, 1 H, NH_2).

this signal was assigned to the F^8 atom as the nearest one to the coordination site. This assignment and the spin coupling pattern were a clue for the full interpretation of the ^{19}F NMR spectrum of **11** (Table 5).

The δ_F values for quinolines **12**–**19** (Table 5) are in accordance with the above signal assignment for **11**, with the respective non-fluorine substituent increments (SCS) taken into account.[24b] When passing from **11** to these compounds, the signals for the fluorine atoms neighbored by a non-fluorine substituent and located in the quinoline α-position (α-F) undergo a somewhat larger low-field chemical shift and the β-F signals undergo a somewhat smaller low-field shift, than that observed for the *ortho* fluorine atoms in the respective C_6F_5X compounds (cf.[27]). The similar "disproportion" was previously observed for β-X-heptafluoronaphthalenes[26] as well as for β-X-substituted trifluoroquinolines that were derived from nucleophilic fluorine substitution in **11**,[28] and it was explained by the fact that the distance from a substituent to the adjacent α- and β-F is somewhat shorter than and somewhat longer than, respectively, that which is realized for the *ortho* fluorine atoms in the respective benzene counterpart.

Experimental Section

General: Melting points are uncorrected. ^1H- and ^{19}F NMR spectra were recorded in [D_6]acetone and $CDCl_3$ with $CHCl_3$ and $CFCl_3$ as internal standards, respectively, with a Bruker WP-200 spectrometer or a Bruker AM-400 spectrometer. HRMS data were obtained with a Finnigan MAT-8200 high resolution mass spectrometer. The GC–MS analyses were performed with a Hewlett–Packard 5890 apparatus by using a 30 m capillary column coated with HP-5 oil. Aqueous ammonia was "Pure" grade, zinc powder was "ZP-2". Solvents and reagents were reagent quality.

Compounds **1**, **3**, **5**, and **7** were prepared according to the literature procedures from the respective amines.[7,29–32] Anilide **3**: ^1H NMR (200.1 MHz, [D_6]acetone): δ = 2.17 (s, 3 H, CH_3); 7.44 [tt, $J(H^4,F^5)$, $J(H^4,F^3)$ = 11 Hz, $J(H^4,F^6)$, $J(H^4,F^2)$ = 7 Hz, 1 H, H^4]; 9.18 (br. s, 1 H, NH) ppm. ^{19}F NMR (188.3 MHz, [D_6]acetone, $CFCl_3$ int. std): δ = 145.5 (m, 2 F, $F^{2,6}$), 140.4 (m, 2 F, $F^{3,5}$) [$J(F^2,F^3)$, $J(F^6,F^5)$ = 20 Hz, $J(F^2,F^5)$, $J(F^3,H^4)$ = 11 Hz, $J(F^2,H^4)$ = 7 Hz] ppm. Anilide **7**: M.p. 205–207 °C (from ethanol/water, 1:1). $C_{14}H_4F_9NO$ (373.01): calcd. C 45.06, H 1.09, F 45.82; found C 45.10, H 1.37, F 45.60. ^{19}F NMR spectroscopic data are presented in Table 6.

Table 6. 188.3 MHz ^{19}F NMR spectroscopic data for polyfluorinated biphenyl derivatives in [D_6]acetone with $CFCl_3$ as an intenal standard.

Compound	δ [ppm]				
	$F^{2,6}$	$F^{2',6'}$	$F^{3,5}$	$F^{3',5'}$	$F^{4'}$
7a[a]	142.5	138.6	161.7	162.2	153.0
calculated[b]	141.6	138.2	160.3	160.8	150.3
7[c]	139.8[d]	138.1[d]	144.0	161.5	151.2
calculated[b]	139.4	138.2	143.1	160.8	150.3
8[e]	138.7[d]	139.9[d]	144.1	138.1[d]	–
calculated[b]	139.9	141.3	144.0	135.6	
8a[f]	142.5	139.0[d]	161.8	138.7[d]	–
calculated[b]	141.3	139.9	161.8	138.1	

[a] **7a**: ^1H NMR (200.1 MHz, [D_6]acetone): δ = 5.96 ppm (bs, 2 H, NH_2). [b] Increments taken from[24b] were used. [c] **7**: ^1H NMR (200.1 MHz, [D_6]acetone): δ = 2.21 (s, 3 H, CH_3), 9.51 (bs, 1 H, NH) ppm. [d] The assignment of these signals to certain fluorine atoms is conditional. [e] **8**: ^1H NMR (200.1 MHz, [D_6]acetone): δ = 2.23 (s, 3 H, CH_3), 9.41 (bs, 1 H, NH), 7.84 (m, 1 H, H^4) ppm. [f] **8a**: ^1H NMR (200.1 MHz, [D_6]acetone): δ = 7.75 (m, 1 H, H^4), 5.95 (bs, 2 H, NH_2) ppm.

Reactions of Fluorinated Acetanilides with Zinc: A mixture of an anilide, zinc powder, and if necessary an additive was stirred in 30% aqueous ammonia at room temperature (for reagent ratios and reaction conditions see Table 1). The solid was separated and washed with water and diethyl ether. The aqueous solution was extracted with diethyl ether or dichloromethane (3 × 60 mL). The combined extract was dried with $MgSO_4$, and the solvent was distilled off. In case of the reaction with a cupric salt additive, it was dissolved in ice-cooled 30% aqueous ammonia (50 mL), then zinc was added. The obtained mixture was stirred for 20 min, the cooling bath was removed, and a substrate was added. The mixture was stirred for a necessary time and worked up as mentioned above. When necessary, ethanol was added after the addition of the substrate for solubilization, the reaction mixture was then stirred for the specified time, the liquid was decanted from zinc and diluted with water (150 mL), the solid was filtered out, washed with water, and dissolved in CH_2Cl_2 (80 mL). Zinc was washed with CH_2Cl_2 and water and the filtrate was extracted with CH_2Cl_2 (4 × 20 mL).

The combined CH_2Cl_2 layers were dried with $MgSO_4$ and worked up as mentioned above. The crude products were used as starting materials in the Skraup synthesis of a certain polyfluoroquinoline (see below).

Anilide 2: The product was isolated by threefold crystallization (ethanol/water, 1:1 by volume, 47% yield) of a crude product obtained from **1** and was identical to that described in ref.[3b] By using the $CuCl_2$ additive, a mixture was obtained from **1** (Table 1, Entry 13) and was found to contain previously reported[8] anilide **4** as the main component (77%).

Anilide 6: The crude product that was obtained from anilide **5** (Table 1, Entry 9) was processed with acetic anhydride, and the reaction mixture was worked up as describe above to give anilide **6** (72%). M.p. 126.5–128 °C (ref.[7] 126–128 °C).

Anilide 8: The product was isolated from the crude defluorination product obtained from anilide **7** (Table 1, Entry 20) by crystallization from benzene. Yield: 53%. M.p. 203–205 °C. $C_{14}H_5F_8NO$ (355.02): calcd. C 47.34, H 1.43, F 42.79; found C 46.63, H 1.92, F 42.20. ^{19}F NMR spectroscopic data are presented in Table 6.

4-Amino-2,3,5,6,2′,3′,5′,6′-octafluorobiphenyl (8a): The mixture of anilide **8** (0.5 g), conc. HCl (5 mL), and ethanol (10 mL) was boiled for 2 h, The mixture was then cooled and neutralized by NaOH (2.5 g in 10 mL of water). The solid was filtered off, dissolved in CH_2Cl_2 (30 mL), and dried with $MgSO_4$. The solvent was removed under vacuum to give a yellow solid (0.26 g) containing 93% (CMS) of amine **8a**. M.p. 131–132 °C (after fourfold crystallization from hexane). $C_{12}H_3F_8N$ (313.01): calcd. C 46.03, H 0.96, N 4.47; found C 46.21, H 0.86, N 4.08. ^{19}F NMR spectroscopic data are presented in Table 6.

Reaction of Polyfluoroacetanilide Defluorination Products with Glycerol: Quinoline **11**: To a stirred mixture of the crude defluorination product (4.70 g) containing anilide **2** (17.7 mmol) (obtained from **1**;Table 1, entry 7), glycerol (11.00 g), boric acid (1.80 g), and iron(II) sulfate (1.00 g), was added *m*-nitrobenzenesulfonic acid (1 M, 22.00 mL, 22 mmol) in sulfuric acid. The mixture was heated at 130 °C for 5 h, cooled to room temperature, and neutralized with 30% aqueous sodium hydroxide. Steam-distillation gave crude **11** (2.64 g, 92% content) with an admixture of **12** (8%) (^{19}F NMR spectroscopic data). Crystallization from hexane gave **11** (2.23 g, 63% yield). M.p. 92.5–93.5 °C (ref.[2a]93–93.5 °C).

Quinoline 14: Following the procedure described above, from the mixture of **6** and 4-amino-2,3,6-trifluorobenzotrifluoride [1.30 g, 5.1 mmol in total, obtained from **5** (Table 1, Entry 9)], quinoline **14** (0.74 g, 58% yield) was prepared. M.p. 40.5–42.0 °C (from hexane). $C_{10}H_3F_6N$ (251.02): calcd. C 47.82, H 1.21, F 45.39, N 5.58; found C 47.84, H 1.35, F 45.47, N 5.29.

Quinoline 12: Following the procedure described above, from the crude product (0.2) of the reduction of anilide **1** (Table 1, Entry 14) containing anilide **4** (63%), a mixture (0.05 g) was obtained containing quinoline **12** as the principal component (75%, for ^{19}F NMR spectroscopic data see Table 5).

Quinoline 13: Following the procedure described above, from the crude product (0.12) of the reduction of anilide **3** (Table 1, Entry 17) containing anilide **9** and 2,3,5-trifluoroaniline (73% in total) (Table 1, Entry 17), quinoline **13** (0.03 g) was obtained identical to the specimen characterized below.

6-Carboxy-5,7,8-trifluoroquinoline (15): Quinoline **14** (0.70 g, 2.8 mmol) and boric anhydride (0.1 g) in 20% oleum (5 mL) were heated at 140 °C for 6 h. After cooling, the reaction mixture was poured into water (75 mL). The aqueous solution was extracted with diethyl ether (3 × 30 mL). The combined ether extract was dried with $MgSO_4$, and the solvent was removed by distillation. The crude product (0.42 g) was crystallized from heptane to give acid **15** (0.38 g, 60% yield). M.p. 234–235 °C. HRMS: calcd. for $C_{10}H_4F_3NO_2$ [M^+] 227.0194; found 227.0211.

5,7,8-Trifluoroquinoline (13): Acid **15** (0.34 g, 1.5 mmol) in DMF (3 mL) was heated at 140 °C for 2 h. Steam-distillation gave a crude product (0.23 g) which was crystallized from hexane to obtain quinoline **13** (0.19 g, 69% yield). M.p. 141.5–143 °C. HRMS: calcd. for $C_9H_4F_3N$ 183.0296; found 183.0291.

6-Methylcarboxy-5,7,8-trifluoroquinoline (17): Acid **15** (0.50 g) was heated at reflux with thionyl chloride (10 mL) for 3.5 h. The excess thionyl chloride was distilled off and absolute methanol (10 mL) was added. The mixture was refluxed with a small amount of charcoal for 10 min and then filtered. The resulting solution was diluted with water (40 mL), the precipitate was filtered off, and dissolved in diethyl ether (20 mL). The solution was dried with $MgSO_4$, and the solvent was evaporated to afford ester **17** (0.30 g, 56% yield). M.p. 101–102 °C (from hexane). $C_{11}H_6F_3NO_2$ (241.04): calcd. C 54.79, H 2.51, F 23.63, N 5.81; found C 54.62, H 2.71, F 23.49, N 5.40.

6-Amidocarboxy-5,7,8-trifluoroquinoline (18): Method a: Acid **15** (0.30 g) was treated with thionyl chloride as described above. The residue was dissolved in diethyl ether (10 mL) and gaseous ammonia was bubbled through the solution for 15 min while cooling with an ice–salt bath. The white solid was filtered off, washed with water, and dried in air to give amide **18** (0.25 g, 84% yield) identical to the specimen described below.

Method b: Ester **17** (0.26 g) and 30% aqueous ammonia (20 mL) were stirred at ambient temperature for 24 h. The solid was filtered off, washed with water, and dried in air to afford amide **18** (0.14 g, 57% yield). M.p. 250.5–252 °C (from ethanol). $C_{10}H_5F_3N_2O$ (226.04): calcd. C 53.09, H 2.23, F 25.22; found C 53.46, H 2.09, F 24.98.

6-Amino-5,7,8-trifluoroquinoline (19): Amide **18** (0.25 g) was added to the ice-cooled mixture of NaOH (0.27 g), Br_2 (0.22 g), and water (5 mL). The reaction mixture was kept at 5 °C for 5 min and then stirred at 80–85 °C for 1 h. The solution was cooled to room temperature, the solid was filtered off, washed with water (3 × 3 mL), and dried in air to afford quinoline **19** (0.13 g, 60% yield). M.p. 171–172 °C (ethanol/water, 1:1). $C_9H_5F_3N_2$ (198.04): calcd. C 54.55, H 2.55, F 28.76, N 14.14; found C 54.66, H 2.36, F 29.00, N 14.24.

CVA Measurements: Cyclic voltammograms were measured with an SVA_1BM electrochemical system (Bulgaria) equipped with a LAB_MASTER polyfunctional interface (Institute of Nuclear Physics, Novosibirsk, Russia), which enables one complete digital control of the system. Measurements were carried out in triangular pulse potential sweep in the sweep rates 0.1 $V s^{-1}$. A standard electrochemical cell with a working volume of 5 mL switched to the system by the three electrode scheme and equipped with a salt bridge filling with a supporting electrolyte solution in DMF to connect the working volume and reference electrode. The working electrode was a stationary needle Pt electrode with a surface area of 9 mm^2, a Pt spiral was the auxiliary electrode, and a saturated aqueous calomel electrode (SCE) served as the reference electrode. Because of pollution of the electrode surface, the electrode was calcinated in a flame. The supporting electrolyte was Et_4NClO_4 (0.1 $mol L^{-1}$). Oxygen was removed by passing argon through the working solution. The concentration of depolarizers was $2 \cdot 10^{-3}$ $mol L^{-1}$.

Quantum Chemical Calculations: Quantum chemical calculations were performed with the GAMESS program suit.[34] The geometry of neutral and anionic species was optimized at the RB3LYP/6-31+G* level of theory. When calculating the energy dependence on the C–F bond stretching (Figure 2), the length of this C–F bond was frozen for each point whereas all other geometrical parameters were varied. The excited state energies were obtained by a configurational interaction method involving only single excitations (CIS). To avoid nonbonded solutions, a basic set that did not include diffusional functions (6-31G*) was used. The structure images and MO plots were made by the MOLDEN program.[35]

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