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Orthogonal Synthesis of Fluorinated Acridones and Acridines from Perfluorobenzophenone

Paola Del Buttero,[b] Ramona Gironda,[a] Massimo Moret,[a] Antonio Papagni,[a] Matteo Parravicini,[a] Silvia Rizzato,[c] and Luciano Miozzo*[a,d]

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The reaction between perfluorobenzophenone and aromatic amines proceeds with the substitution of one or more fluorine atoms. The regiochemistry of this substitution is controlled by solvent polarity, temperature, and nucleophilic character of the amine. *o*-Anilinononafluorobenzophenone can be selectively transformed into acridines or acridones by using acid or base catalysis through electrocyclization or aromatic nucleophilic substitution.

Introduction

Known since the 19th century, acridines and acridones are versatile heteroaromatic compounds. Acridine derivatives show broad biological activities and have been extensively used for their chemotherapeutic properties, having a wide range of applications against bacteria[1] and protozoa.[2] In the 1970s, the antitumoral effects of acridines was discovered.[3] Because of their high DNA binding affinity, acridines have been used also as vectors to direct different drugs (e.g., *cis*-platinum, aziridin) to specific DNA sites.[4] Acridones as well form a well-known class of drugs with antileishmanial, antifungal, antitumor, and anticancer properties.[5] Beyond these classical applications as drugs and as ligands (both η^4 and η^6 ligands[6] or through aza coordination[7]), they have also been used as fluorescent probes and chemosensors.[8] Common methods for the synthesis of acridines are based on the substitution of *o*-halogenobenzoic acid derivatives with functionalized anilines through reduction of acridone intermediates,[9] the Bernthsen reaction (condensation of a diarylamine heated with a carboxylic acid or an acid anhydride),[10] the cyclization of diphenylamine-2-carboxaldehyde,[11] or a modified Pfitzinger reaction used for quinoline synthesis.[12] Recently, a benzannulation reaction was used to prepare substituted acridines through a 6-*endo*-*dig* cyclization process catalyzed by a Rh^I complex.[13] Acridones are often prepared by some of the aforementioned methods or others, such as the acid-induced ring closure of *N*-phenylanthranilic acids, which can be obtained from Ullmann condensation of anilines with *ortho*-halogen-substituted benzoic acids. Recently, a new approach based on an annulation reaction utilizing salicylates and silylaryl triflates plus CsF has been presented.[14] However, harsh reaction conditions and multistep procedures are generally required.[15] Within this frame, fluorinated acridines and acridones form an interesting group of compounds with applications as fluorophores for biological probes and in materials science.[16] Among different synthetic approaches, the reaction of anilines with pentafluorobenzaldehyde has proven to be one of more simple methods to access fluorinated acridines.[17] While the reaction of aromatic amines with pentafluorobenzaldehyde to afford tetrafluoroacridines has been thoroughly analyzed, the same reaction on decafluorobenzophenone (**1**) has received less attention. Decafluorobenzophenone (**1**) shows different reactivity from that of pentafluorobenzaldehyde: for instance whereas that latter produces the corresponding imines with anilines at room temperature without an acid catalyst, the formation of the corresponding imines of **1** requires the presence of $AlCl_3$ and forced conditions.[18] Because the formation of the corresponding imines is the first step in the well-established synthesis of tetrafluoroacridines from pentafluorobenzaldehyde,[17] that protocol cannot be extended to the synthesis of fluorinated acridines starting from **1**. On the contrary, when **1** is treated with anilines, fluorine aromatic nucleophilic substitution is always observed. On the other side, *ortho*-substituted nonafluorobenzophenones obtained in that way could be useful reagents, for instance, for the synthesis of *N*-arylocta-

[a] Dipartimento di Scienza dei Materiali,
Università di Milano Bicocca,
Via R.Cozzi, 53 Milano, Italy
Fax: +39-0264485400
E-mail: luciano.miozzo@mater.unimib.it
[b] Dipartimento di Chimica Organica e Industriale,
Università degli Studi di Milano,
Via Venezian, 21 Milano, Italy
[c] Dipartimento di Chimica Strutturale e Stereochimica Inorganica and Facoltà di Farmacia,
Università degli Studi di Milano,
Via Venezian, 21Milano, Italy
[d] ITODYS, Université Paris Diderot,
15, Jean Antoine de Baïf, 75205 Paris, France
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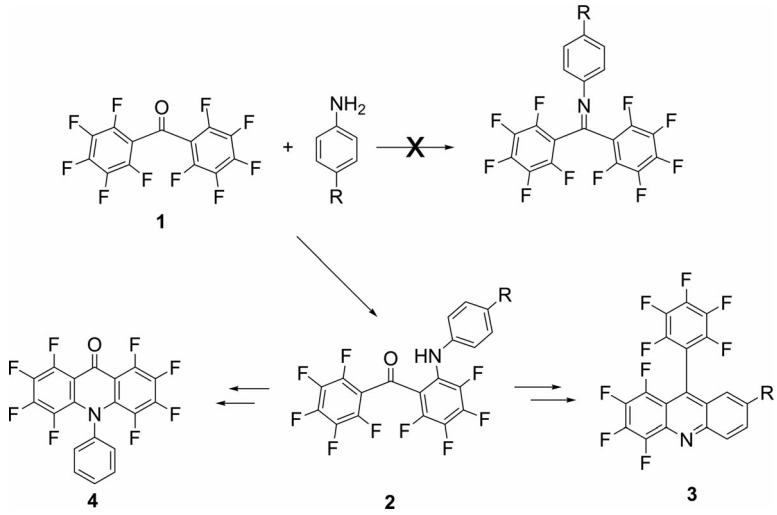
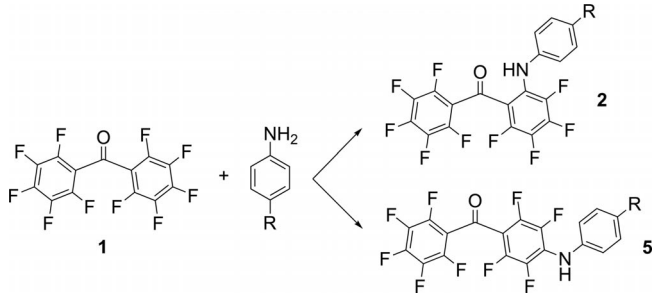


Scheme 1. Synthetic pathway to acridone and acridine starting from decafluorobenzophenone. The imine can be prepared only in the presence of an acid catalyst ($AlCl_3$).

fluoroacridones by an intramolecular aromatic nucleophilic reaction; unfortunately, that approach is strongly hindered by haloform-type degradation that this ketone undergoes under basic conditions, producing pentafluorobenzene and pentafluorobenzoic acid.[19] Here we have investigated in more detail the reactivity of **1** with aromatic amines and we report on the possibility to exploit *o*-anilino-substituted nonafluorobenzophenones **2** as starting materials for the orthogonal synthesis of 9-pentafluorophenyl-1,2,3,4-tetrafluoroacridines (**3**) and octafluoroacridones (**4**) just acting on experimental conditions (Scheme 1).

Results and Discussion

The reaction of decafluorobenzophenone with anilines produces mainly two isomers, that is, *ortho*- and *para*-anilino-substituted derivatives **2** and **5** (Scheme 2). We found that the regiochemistry and the yield of this reaction are strongly dependent on the nature of the solvent, the temperature, and the nucleophilic character of the aniline. Using *p*-anisidine as a reference aniline, we carried out a detailed study on the solvent effects of the aromatic nucleophilic substitution reaction, focusing our attention on *ortho*-substituted isomer **2**. We always observed the formation of *ortho*-**2** and *para*-**5** isomers, and we found also that polysubstitution products can sometimes contaminate *para* substitution products. We found that the yield of isomer **2** has a good correlation with donor number (DN)[20a] (Table 1). Because Lewis basicity (expressed by DN) of the solvent plays an important role in determining the yield of **2**, this fact indicates that the formation of isomer **2** is favored by the formation of a hydrogen bond between the amine hydrogen atoms of the incoming aniline and the carbonyl unit of **1**. In fact, when carrying out the reaction in decaline or toluene (at 87 °C), with a DN similar to that of 1,2-dichloroethane, the yield of isomer **2** was approximately the same (Table 1). Solvents able to form H-bonds with the amino group of the amine perturb or hinder the C=O···H–N interaction, decreasing the yield of isomer **2**.[21] This is particularly evident in the case of 1,4-dioxane, which shows the highest DN value between the solvent used, even though it has a dielectric constant similar to that of decaline or toluene. When we carried out the reaction in DMSO, which has an even higher DN, the yield of **2** fell to zero and other substitution products were obtained. Also, high temperatures negatively affected the formation of isomer **2**, and this is reasonable due destabilization of the C=O···H–N interaction, as shown in the test carried out in toluene and 1,4-dioxane at reflux.



Scheme 2. Synthesis of anilino-substituted benzophenones.

Table 1. Solvent effects on the yield of **2**.

Solvent	DN[a] (ε)	Time [h]	Temp. [°C]	Yield of **2** [%]
Decaline	0 (2.2)	22	87	76
1,2-Dichloroethane	0 (10.4)	14	87	76
Toluene	0.1 (2.38)	22	87	61
Toluene	0.1 (2.38)	10	111	51
1,4-Dioxane	14 (2.3)	11	87	42
1,4-Dioxane	14 (2.3)	2	101	25
DMSO	29.8 (46.7)	4	87	0

[a] See ref.[20b]

Under optimized experimental conditions (1,2-dichloroethane) the reaction was extended to other anilines with the aim of comparing their reactivity and to prepare a pool of compounds. As expected, the highest yield in substitution products was obtained with electron-rich anilines (Table 2). Reaction with *p*-(*N*,*N*)-dimethylaminoaniline afforded isomer **2** in a lower yield, but the reaction was also much more rapid, as the reagent was completely consumed after 4 h of heating. At the basis of higher reactivity and lower selectivity is the higher nucleophilicity of incoming NH_2, preventing effective stereocontrol through the formation of the C=O···H–N hydrogen bond.

Table 2. Substituent effects on the yield of **2**.

R	Time [h]	Yield of **2** [%]
2a: OCH_3	14	76
2b: $N(CH_3)_2$	4	52
2c: Br	25	31
2d: H	22	43
2e: NH–Ph	18	43

The formation of an intramolecular hydrogen bond between the C=O and N–H moieties in the *ortho* derivatives is clearly evident in both the ^{1}H NMR and IR spectra. In fact, in the ^{1}H NMR spectra, the N–H resonances in the *ortho* derivatives fall in the 8–9 ppm region. The presence of hydrogen bonding is also confirmed by IR spectroscopy (see the Supporting Information). The strongest hydrogen bond is present in **2b**, where the electron-donating dimethylamino fragment causes the highest low-field shift of the N–H ^{1}H NMR signal and the highest low-frequency shift of the stretching signal of the N–H bond. In analogy with the reaction of anilines with pentafluorobenzaldehyde, *ortho*-substituted nonafluorobenzophenones allow access to the corresponding 9-pentafluorophenyltetrafluoroacridines. Indeed, during purification by column chromatography of compound **2a** over Al_2O_3, we noticed the formation of a fluorescent compound, which was found to be the corresponding 9-pentafluorophenyltetrafluoroacridine. The Lewis acid properties of Al_2O_3 suggest that the transformation of **2** into **3** requires acid catalysis. This is also confirmed by reports in the literature,[19] where concentrated H_2SO_4 is used for the transformation of 2-aminobenzophenones into the corresponding acridines. Thus, *ortho*-substituted derivatives **2a**–**e** were firstly treated with concentrated H_2SO_4. As expected, these where transformed into the corresponding acridines in excellent or nearly quantitative yield by stirring a H_2SO_4 solution of **2a**–**e** at room temperature. The structures of compounds **3a** and **3b** were also confirmed by single-crystal X-ray diffraction. Figures 1 and 2 show the molecular structure of **3a** and **3b** together with selected bond parameters.

It is reasonable that the cyclization of **2** to acridine **3** proceeds by 6π-electrocyclization involving the enolic form of the carbonyl group favored by protonation of the carbonyl in the strong acid media, followed by H_2O elimination.[22] We have also tried another strong acid such as trifluoroacetic acid (TFA), but it proved to be less effective

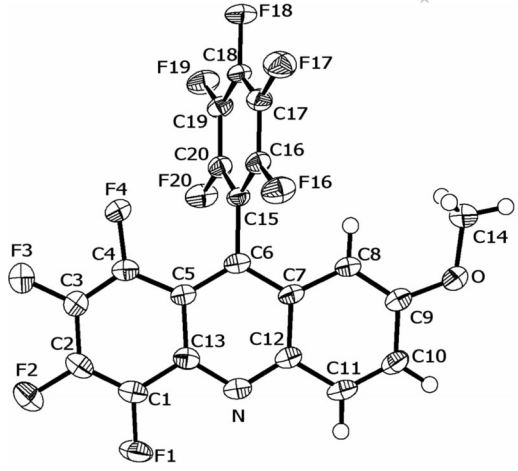


Figure 1. Molecular structure of **3a**.[23] Selected bond lengths [pm] and angles [°]: O–C9 135.3(4), O–C14 142.7(4), C9–O–C14 118.0(3), O–C9–C8 125.7(3), O–C9–C10 113.9(3), C5–C6–C15–C16 110.0(4), C5–C6–C15–C20 –69.5(4).

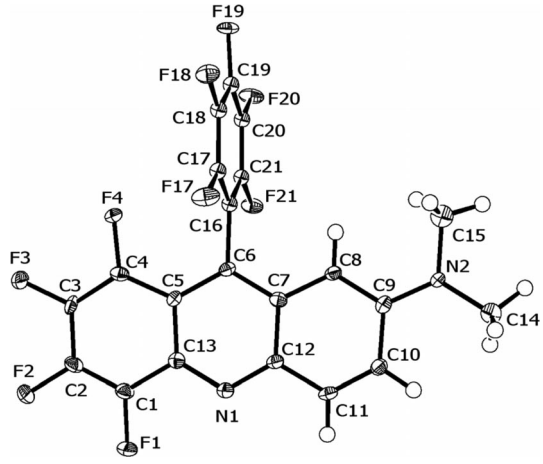


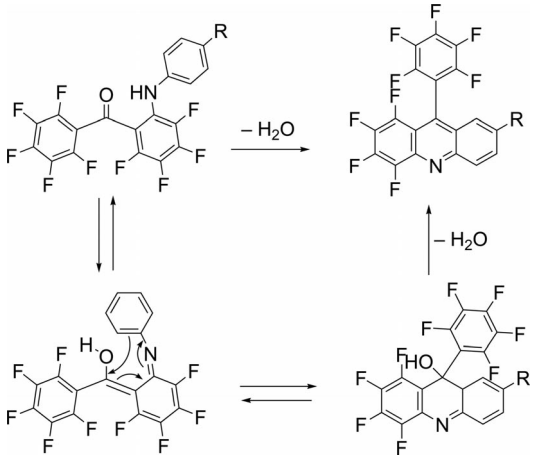
Figure 2. Molecular structure of **3b**.[23] Selected bond lengths [pm] and angles [°]: N2–C9 137.2(7), N2–C14 143.7(8), N2–C15 146.5(6), C9–N2–C14 122.7(4), C9–N2–C15 118.2(5), C14–N2–C15 117.9(4), N2–C9–C8 123.3(4), N2–C9–C10 118.9(5), C5–C6–C16–C17 79.9(4), C5–C6–C16–C21 –98.4(4).

than sulfuric acid (Table 3). We did not observe any reaction of **2b** [R = $N(CH_3)_2$] even after 22 h of heating at reflux in TFA. The use of concentrated H_2SO_4, which has better dehydrating properties than TFA, could be important in the evolution of **2** in **3** by shifting all the equilibria towards the

Table 3. Substituent effects on the yield of **3**.

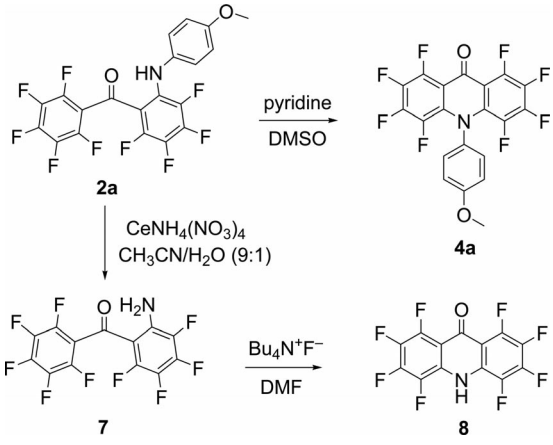
R	H_2SO_4			CF_3COOH		
	Yield [%]	Time [h]	*T* [°C]	Yield [%]	Time [h]	*T* [°C]
3a:OCH_3	89	24	25	99	72	25
3b: $N(CH_3)_2$	90	88	25	0	72	25
3c: Br	93	64	25	93	72	25
3d: H	90	80	25	–	–	–
3e: NH-Ph	43	80	25	–	–	–

formation of acridine. This could be particularly true in the case of **2b**, considering the fact that in this case the reaction occurs on its the protonated form (Scheme 3).



Scheme 3. Mechanism of acridine formation.

Later on, our attention was focused on the conversion of *ortho* derivatives **2** into *N*-aryloctafluoroacridones **4**, because in principle this could be possible by deprotonation of the NH group by a base, followed by intramolecular nucleophilic aromatic substitution of fluorine. However, the selection of the base and the experimental conditions were not trivial, given that nucleophilic attack to the carbonyl function by the base catalyst is in competition with the deprotonation at nitrogen. Indeed it is reported that nucleophilic attack to the carbonyl function causes haloform-type degradation of the ketone, affording pentafluorobenzene and perfluorinated aromatic carboxylic acids.[19] We performed a detailed study on **2a** to optimize the experimental conditions for its transformation into the corresponding acridone. We obtained the best results when using 1 equiv. of pyridine in DMSO, allowing **4a** (64% yield) to be collected after 19 h at room temperature (Scheme 4). It is noteworthy that, when R = $N(CH_3)_2$, owing to the strong nucleophilic character of the amino group, the cyclization to the corresponding octafluoroacridone partially occurs during the synthesis of **2b**. Finally, we undertook the synthesis of *N*-H-octafluoroacridone. Starting from **2a**, the *p*-methoxyphenyl group was removed by oxidation with $CeNH_4(NO_3)_4$ to obtain the corresponding 2-aminononafluorobenzophenone **7** in 70% chemical yield and 40% from the starting decafluorobenzophenone (Scheme 4). The obtained overall yield is ten times better than that reported in the literature, where the synthesis of **7** was carried out from 3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone by a multistep procedure. We transformed compound **7** into the corresponding octafluoroacridone **8** by treating it with tetrabutylammonium fluoride in DMF at 120 °C (51% yield, comparable to that reported in the literature;[23] Scheme 4).



Scheme 4. Synthesis of octafluoroacridones.

Conclusions

In conclusion, we explored the reactivity of perfluorobenzophenone with aromatic amines, showing how the reaction yield depends on the nature of the amine and on the reaction conditions. *ortho*-Derivatives are interesting intermediates for the synthesis of *N*-aryloctafluoroacridones and fluorinated acridines. Whereas the formation of acridines proceeds very well in pure H_2SO_4, the optimization of the synthesis of octafluoroacridones proved to be more difficult. Finally, *o*-aminononafluorobenzophenone can be readily prepared by an original approach. This latter compound allow access to another compound, namely, octafluoroacridone, but other transformations of this group can be also envisaged.

Experimental Section

General Experimental Procedures: Solvents of analytical grade were used without further purification. Reagents were purchased from Sigma–Aldrich and used without further purification. Melting points were measured with an Electrothermal 9100 melting point instrument. UV spectra were recorded with a Perkin–Elmer Lambda 900 spectrophotometer. Fluorescence spectra were measured with an Aminco Bowman AB2 spectrofluorimeter. IR spectra were obtained with a Spectrum 100, FTIR Spectrometer Perkin–Elmer. NMR spectra were recorded in $CDCl_3$ with a Varian Mercury 400 Spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz, ^{19}F 376 MHz). Molecular structures and purity were analyzed by GC–MS (GCD 1800C; Hewlett–Packard) with a 50-m DB-5MS column (J&W Scientific, Folsom, Calif.). Silica gel (230–400 mesh) was used for column chromatography.

General Procedure for the Synthesis of *o*-Anilinononafluorobenzophenones 2a–e: To a solution of decafluorobenzophenone (**1**: 250 mg, 0.691 mmol) in the appropriate solvent (30 mL, see Table 1) was added the appropriate aniline (2 equiv.), and the solution was heated at 87 °C (or at reflux temperature, depending of the experimental conditions; see Table 1 for details). The reaction was monitored by TLC (SiO_2; *n*-hexane/CH_2Cl_2, 7:3). Then the solvent was removed under reduced pressure. The crude was purified by silica gel column chromatography, affording the desired product.

2-(4-Methoxyanilino)-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (2a): The crude was purified by column chromatography (silica gel; *n*-hexane/CH_2Cl_2, 1:1). Yield: 76%. Orange solid. M.p. 92 °C. ^{1}H NMR ($CDCl_3$): δ = 9.48 (s, 1 H, NH), 6.99–7.02 (d, J = 8.7 Hz, 2 H), 6.85–6.87 (d, J = 8.8 Hz, 2 H), 3.81 (s, 3 H) ppm. ^{19}F NMR

($CDCl_3$): δ = –137.77 (m, 1 F), –142.80/–142.85 (d, J = 17.2 Hz, 2 F), –144.13 (m,1 F), –145.80 (m, 1 F), –149.7 (t, J = 22, 44 Hz, 1 F), –160.38 (m, 2 F), –169.92 (t, J = 46, 23 Hz, 1 F) ppm. $C_{20}H_8F_9NO_2$ (465.04): calcd. C 51.63, H 1.73, N 3.01; found C 51.21, H 1.70, N 2.95.

2-(4-*N*,*N*-Dimethylamino)-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (2b): The crude was purified by column chromatography (silica gel, CH_2Cl_2). Yield: 52%. Red solid. M.p. 120 °C. ^{1}H NMR ($CDCl_3$): δ = 9.61 (s, 1 H, NH), 6.99–6.97 (d, J = 8 Hz, 2 H), 6.69–6.67 (d, J = 8 Hz, 2 H), 3.95 (s, 6 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –138.16 (s, 1 F), –142.90/–142.95 (d, J = 18.4 Hz, 2 F), –144.53 (s, 1 F), –147.02 (s, 1 F), –150.25 (s, 1 F), –160.57 (s, 2 F), –171.23 (s, 1 F) ppm. $C_{21}H_{11}F_9N_2O$ (478.07): calcd. C 52.73, H 2.32, N 5.86; found C 52.44, H 2.20, N 5.77.

2-(4-Bromoanilino)-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (2c): The crude was purified by column chromatography (silica gel; *n*-hexane/CH_2Cl_2, 3:7). Yield: 31%. White solid. M.p. 90 °C. ^{1}H NMR ($CDCl_3$): δ = 9.09 (s, 1 H, NH), 7.41–7.43 (d, J = 8.7 Hz, 2 H), 6.88–6.85 (dd, J = 8.8, 2.5 Hz, 2 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –137.11/–137.22 (m, 1 F), –142.40/–142.44 (d, J = 18.4 Hz, 3 F), –143.68/–143.82 (m, 1 F), –148.45/–148.56 (t, J = 44.4, 22.4 Hz, 1 F), –160.01 (m, 1 F), –166.50/–166.67 (m, 1 F) ppm. $C_{19}H_5BrF_9NO$ (512.94): calcd. C 44.39, H 0.98, N 2.72; found C 44.22, H 0.85, N 2.65.

2-Anilino-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (2d): The crude was purified by column chromatography (silica gel; *n*-hexane/CH_2Cl_2, 3:7). Yield: 43%. Yellow solid. M.p. 124 °C. ^{1}H NMR ($CDCl_3$): δ = 9.17 (s, 1 H, NH), 7.30–7.34 (dd, J = 7.5, 8.1 Hz, 2 H), 7.09–7.13 (dd, J = 7.9, 7.3 Hz, 1 H), 6.99–7.00 (d, J = 7.5 Hz, 2 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –137.67 (m, 1 F), –142.48/–142.55 (m, 2 F), –142.89 (m, 1 F), –144.29 (m, 1 F), –148.98 (t, J = 44, 22 Hz, 1 F), –160.22 (m, 2 F), –167.61 (t, J = 48.4, 24 Hz, 1 F) ppm. $C_{19}H_6F_9NO$ (435.03): calcd. C 52.43, H 1.39, N 3.22; found C 52.30, H 1.22, N 3.25.

2-(4-Phenylamino-anilino)-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (2e): The crude was purified by column chromatography (silica gel; *n*-hexane/CH_2Cl_2, 1:1). Yield: 43%. Red solid. M.p. 159 °C. ^{1}H NMR ($CDCl_3$): δ = 9.41 (s, 1 H), 7.24–6.93 (m, 9 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –137.5/–137.7 (m, 1 F), –142.6/–142.7 (d, J = 26 Hz, 2 F), –144.1 (m, 1 F), –145.0 (m, 1 F), –149.4 (t, J = 49, 25 Hz, 1 F), –160.2/–160.3 (m, 2 F), –169.5 (m, 1 F) ppm. $C_{25}H_{11}F_9N_2O$ (526.07): calcd. C 57.05, H 2.11, N 5.32; found C 56.90, H 2.15, N 5.20.

General Procedure for the Synthesis of 1,2,3,4-Tetrafluoro-9-pentafluorophenylacridines 3a–c: *o*-Anilinononafluorobenzophenone (0.2 mmol) was dissolved in H_2SO_4 (4 mL) at room temperature under a nitrogen atmosphere. The reaction was monitored by TLC (see Table 3 for the total reaction time). The 1,2,3,4-tetrafluoroacridines were easily detected, as they are fluorescent. The solution was then poured into an excess amount of water and then neutralized; the pH of the solution was initially increased with NaOH and then adjusted to pH 7 with $NaHCO_3$. The solution was then extracted with CH_2Cl_2. The organic phase was washed with water and then dried with Na_2SO_4; the solvent was removed under reduced pressure, affording the expected product with the desired purity.

1,2,3,4-Tetrafluoro-7-methoxy-9-pentafluorophenylacridine (3a): The reaction was monitored by TLC (silica gel; *n*-hexane/CH_2Cl_2, 1:1). Yield: 89%. Yellow solid. M.p. 235 °C. ^{1}H NMR ($CDCl_3$): δ = 8.32–8.29 (d, J = 9.5 Hz, 1 H), 7.62–7.59 (dd, J = 9.5, 2.8 Hz, 1 H), 6.58 (s, 1 H), 3.85 (s, 3 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –139.42 (dd, J = 23, 7 Hz, 1 F), –148.44 (t, J = 35, 17.5 Hz, 1 F), –150.26 (t, J = 35, 17.5 Hz, 1 F), –151.62 (t, J = 44.4, 22 Hz, 1 F), –154.44 (t, J = 36.8, 18.4 Hz, 1 F), –155.22 (t, J = 18.4, 36.8 Hz, 1 F), –161.01 (m, 2 F) ppm. $C_{20}H_6F_9NO$ (447.03): calcd. C 53.71, H 1.35, N 3.13; found C 53.56, H 1.23, N 3.16.

1,2,3,4-Tetrafluoro-7-*N*,*N*-dimethylamino-9-pentafluorophenylacridine (3b): The reaction was monitored by TLC (silica gel; *n*-hexane/CH_2Cl_2, 1:1). Yield: 90%. Red purple solid. M.p. 246 °C. ^{1}H NMR ($CDCl_3$): δ = 8.21–8.24 (d, J = 9.8 Hz, 1 H), 7.64–7.65/7.67–7.68 (dd, J = 9.7, 2.7 Hz, 1 H), 6.14 (s, 1 H), 3.07 (s, 6 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –139.66 (dd, J = 23.6, 8 Hz, 2 F), –149.47 (t, J = 34.4, 17.2 Hz, 1 F), –151.27 (t, J = 34.4, 17.2 Hz, 1 F), –152.72 (t, J = 44, 22 Hz, 1 F), –156.71 (t, J = 37.2, 18.4 Hz, 1 F), –157.36 (t, J = 40, 20 Hz, 1 F), –161.66 (m, 2 F) ppm. $C_{21}H_9F_9N_2$ (460.06): calcd. C 54.80, H 1.97, N 6.09; found C 54.55, H 1.81, N 6.15.

1,2,3,4-Tetrafluoro-7-bromo-9-pentafluorophenylacridine (3c): The reaction was monitored by TLC (silica gel; *n*-hexane/CH_2Cl_2, 7:3). Yield: 93%. White solid. M.p. 191 °C. ^{1}H NMR ($CDCl_3$): δ = 8.28–8.3 (d, J = 9.2 Hz, 1 H), 7.96–7.99 (dd, J = 9.2, 1.4 Hz, 1 H), 7.68 (s, 1 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –139.23 (dd, J = 20, 4 Hz, 2 F), –147.04 (t, J = 36, 16 Hz, 1 F), –149.25 (t, J = 36, 16 Hz, 1 F), –150.57 (t, J = 44, 24 Hz, 1 F), –151.11 (t, J = 36, 16 Hz, 1 F), –153.43 (t, J = 36, 16 Hz, 1 F), –160.37 (m, 2 F) ppm. $C_{19}H_3BrF_9N$ (494.93): calcd. C 46.00, H 0.61, N 2.82; found C 45.78, H 0.59, N 2.91.

1,2,3,4-Tetrafluoro-9-pentafluorophenylacridine (3d): The reaction was monitored by TLC (silica gel; *n*-hexane/CH_2Cl_2, 7:3). Yield: 90%. Bright yellow solid. M.p. 156 °C. ^{1}H NMR ($CDCl_3$): δ = 8.44–8.41 (d, J = 9.2 Hz, 1 H), 7.96–7.92 (dd, J = 8, 16 Hz, 1 H), 7.68–7.65 (dd, J = 15, 8.4 Hz, 1 H), 7.57–7.55 (d, J = 8.8 Hz, 1 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –139.36/–139.39 (dd, J = 24, 8 Hz, 2 F), –147.25 (t, J = 36, 20 Hz, 1 F), –149.82 (t, J = 36, 20 Hz, 1 F), –151.48 (t, J = 48, 24 Hz, 1 F), –152.01 (t, J = 40, 20 Hz, 1 F), –154.88 (t, J = 40, 20 Hz, 1 F), –160.940/–161.094 (m, 1 F) ppm. $C_{19}H_4F_9N$ (417.02): calcd. C 54.70, H 0.97, N 3.36; found C 54.65, H 0.92, N 3.39.

1,2,3,4-Tetrafluoro-7-phenylamino-9-pentafluorophenylacridine (3e): The reaction was monitored by TLC (silica gel; *n*-hexane/CH_2Cl_2, 7:3). Yield: 43%. Red solid. M.p. 192 °C. ^{1}H NMR ($CDCl_3$): δ = 8.26–8.24 (d, J = 9.2 Hz, 1 H), 7.63–7.60 (dd, J = 9.2, 2.0 Hz, 1 H), 7.34 (m, 2 H, arom.), 7.17 (m, 2 H, arom.), 7.11 (m, 1 H, arom.), 6.81 (d, J = 2.0 Hz, 1 H), 6.34 (br. s, 1 H, NH) ppm. ^{19}F NMR ($CDCl_3$): δ = –139.4 (dd, J = 24, 8 Hz, 2 F), –148.5 (t, J = 40, 20 Hz, 1 F), –150.5 (t, J = 36, 16 Hz, 1 F), –152.2 (t, J = 48, 24 Hz, 1 F), –155.6 (t, J = 40, 20 Hz, 1 F), –161.6 (m, 2 F) ppm. $C_{25}H_9F_9N_2$ (508.06): calcd. C 59.07, H 1.78, N 5.51; found C 59.01, H 1.66, N 5.53.

General Procedure for the Synthesis of 1,2,3,4,5,6,7,8-Octafluoro-*N*-arylacridones: *o*-Anilinononafluorobenzophenone (0.5 mmol) was dissolved in xylene (15 mL) at room temperature under a nitrogen atmosphere. A solution of pyridine (0.093 mg) in xylene (7 mL) was added. The reaction was stirred under reflux for 48 h under a nitrogen atmosphere. After evaporation of the solvent under reduced pressure, the product was purified by silica gel chromatography (*n*-hexane/CH_2Cl_2, 3:7), affording the desired product and unreacted *o*-anilinononafluorobenzophenones.

1,2,3,4,5,6,7,8-Octafluoro-*N*-*p*-anisidinoacridone (4a): Yield: 66%. Pale grey solid. M.p. 199 °C. ^{1}H NMR ($CDCl_3$): δ = 7.28–7.26 (d, J = 8.7 Hz, 2 H), 6.89–6.87 (d, J = 8.7 Hz, 2 H), 3.81 (s, 3 H) ppm. ^{19}F NMR ($CDCl_3$): δ = –142.2 (m, 2 F), –143.4 (t, J = 36, 16 Hz, 2 F), –145.7 (m, 2 F), –161.1 (t, J = 44, 20 Hz, 2 F) ppm.

$C_{20}H_7F_8NO_2$ (445.03): calcd. C 53.95, H 1.58, N 3.15; found C 53.81, H 1.55, N 3.12.

Synthesis of 2-Amininonafluorobenzophenone (7): 2-(4-Methoxyanilino)-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (0.3 mmol) was dissolved in CH_3CN/H_2O (9:1, 20 mL). The solution was cooled to 0 °C, and a solution of ammoniumcerium(IV) nitrate (0.391 g) in CH_3CN/H_2O (9:1, 20 mL) was dropped under a nitrogen atmosphere. The mixture was warmed to room temperature. The reaction was monitored by TLC (*n*-hexane/CH_2Cl_2, 7:3; silica gel). After 48 h the solvent was removed under reduce pressure. The solid was taken up with CH_2Cl_2, and the solution was washed with water. The organic solution was dried with Na_2SO_4, and then the solvent was removed under reduced pressure, affording the expected product with the desired purity.

2-Amino-3,4,5,6,2′,3′,4′,5′,6′-nonafluorobenzophenone (7): Yield: 67%. Yellow solid. ^{1}H NMR ($CDCl_3$): δ = 6.54 (s, 2 H) ppm. M.p. and ^{19}F NMR spectroscopy data in accordance with literature data.[23]

Synthesis of *N*-H-Octafluoroacridone (8): To a solution of *o*-aminoperfluorobenzophenone (0.3 mmol) in dry DMF (5 mL) was added tetrabutylammonium fluoride trihydrate (315 mg), and the mixture was heated for 3 h at 120 °C. The reaction was monitored by TLC (CH_2Cl_2, silica gel). The formation of the product could be easily detected by TLC, because of its fluorescence. The solution was poured into water and then extracted with CH_2Cl_2. The red mixture was sublimated at 120 °C to give octafluoroacridone, as a yellow solid. Yield: 51%. M.p. and NMR spectroscopy data in accordance with literature data.[23]

Crystal Structure Analysis of 1,2,3,4-Tetrafluoro-7-methoxy-9-pentafluorophenyl-acridine (3a):[24] $C_{20}H_6F_9NO$, molecular weight 447.26, crystal system triclinic, space group $P\bar{1}$, a = 7.365(1) Å, b = 10.021(1) Å, c = 12.574(2) Å, α = 105.986(2)°, β = 102.199(2)°, γ = 102.818(2)°, V = 832.4(2) Å^3, Z = 2, $d_{calcd.}$ = 1.784 g/cm^3, F(000) = 444, μ = 0.180 mm^{-1}, crystal color yellow, crystal size 0.08 × 0.08 × 0.03 mm^3, Bruker SMART-APEX CCD (area detector) diffractometer, T = 298(2) K, λ(Mo-K_α) = 0.71073 Å, θ_{min} = 2.21°, θ_{max} = 25.66°, $-8 \le h \le 8$, $-12 \le k \le 12$, $-15 \le l \le 15$, empirical absorption correction (SADABS), 12486 reflections collected, 3138 unique reflections [R(int) = 0.0523], refinement program SHELXL-97, refinement by full-matrix least-squares on F^2, S = 0.983, R indices [$I > 2\sigma(I)$]: R_1 = 0.0488, wR_2 = 0.1076, R indices [all data]: R_1 = 0.1172, wR_2 = 0.1389, min./max. Residual electron density: –0.180/0.239, completeness of data 99.9%.

Crystal Structure Analysis of 1,2,3,4-Tetrafluoro-7-*N*,*N*-dimethylamino-9-pentafluorophenylacridine (3b):[24] $C_{21}H_9F_9N_2$, molecular weight 460.30, crystal system orthorhombic, space group $P2_12_12_1$, a = 7.235(1) Å, b = 12.028(2) Å, c = 20.281(2) Å, V = 1765.0(4) Å^3, Z = 4, $d_{calcd.}$ = 1.732 g/cm^3, F(000) = 920, μ = 0.170 mm^{-1}, crystal color orange, crystal size 0.22 × 0.08 × 0.04 mm^3, Bruker SMART-APEX CCD (area detector) diffractometer, T = 150(2) K, λ(Mo-K_α) = 0.71073 Å, θ_{min} = 2.63°, θ_{max} = 24.47°, $-2 \le h \le 8$, $-13 \le k \le 9$, $-23 \le l \le 8$, empirical absorption correction (SADABS), 2556 reflections collected, 1419 unique reflections [R(int) = 0.0518], refinement program SHELXL-97, refinement by full-matrix least-squares on F^2, S = 0.936, R indices [$I > 2\sigma(I)$]: R_1 = 0.0395, wR_2 = 0.0922, R indices [all data]: R_1 = 0.0506, wR_2 = 0.0977, min./max. Residual electron density: –0.347/0.307, completeness of data 83.0%.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{19}F NMR spectra, GC–MS and MS spectra, UV/Vis absorption and fluorescence spectra of selected compounds, and intramolecular NH–CO hydrogen bond analysis of compounds **2a**–**e** by IR and NMR spectroscopy.

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