3-Trifloxy-3-trifluoromethylpropeniminium Triflate: Reaction with Aromatic Amines – An Efficient Synthesis of 2-Trifluoromethylquinolines

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The reaction of iminium triflates **2** and **7** with various aromatic amines were investigated. The 2-R_f-substituted quinolines **3** and **8** were prepared in excellent yields by the reaction of **2** and **7**, respectively, with substituted anilines. The reactions of **2** and **7** with diarylamines proceeds, suprisingly, to afford the corresponding 3-R_f-substituted cinnamaldehydes **4** and **9**.

Introduction

Fluorinated compounds have been of great interest to synthetic and medicinal chemists due to the unique physical and biological properties imparted by fluorine.[1] Among these compounds, trifluoromethylated quinolines are the subject of considerable pharmacological attention as potent antimalarial agents; e.g., mefloquine {[2,8-bis(trifluoromethyl)-4-quinolinyl](2-piperidinyl)methanol} has been developed as an highly effective antimalarial drug.[2] The traditional methods for the preparation of 2-CF_3-substituted quinolines comprise two possible approaches, namely, fluorination of a suitable functional group [halogen exchange of $-CCl_3$ ($-CBr_3$)[3] and fluorination of $-CO_2H$[4]], and direct introduction by an Ullmann-type reaction of perfluoroalkyl iodides and arylhalides using copper powder.[5] In this way 2-R_f-substituted 4-quinolones have been easily obtained from anilines and R_f-substituted alkynyl esters or ethyl trifluoroacetoacetate.[6] Recently, several authors[7] have reported the regiospecific synthesis of 4-unsubstituted 2-trifluoromethylquinolines by intramolecular acid- (or $POCl_3$-)catalyzed ring closure of 4-anilino-1,1,1-trifluoro-but-3-en-2-ones, which are readily available from the corresponding anilines and trifluoroacetylacetylenes[7] or 4-alkylamino- or 4-alkoxy-enones.[7,8] However, the yields in these reactions are low.

Herein we report a simple and general one-pot synthesis of 2-trifluoromethylquinolines from anilines and 4-dimethylamino-1,1,1-trifluoro-3-buten-2-one (**1**). The starting compound enone **1** can be easily prepared in one pot by trifluoroacetylation of ethyl vinyl ether[8] followed by the addition of aqueous dimethylamine (Scheme 1). Treatment of **1** with triflic anhydride caused the formation of 3-trifloxy-3-trifluoromethylpropeniminium triflate (**2**) which was found to react with electron-rich aromatic compounds to give 3-trifluoromethylcinnamaldehydes in moderate to good yields.[9]

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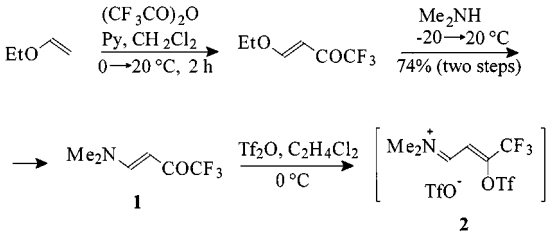
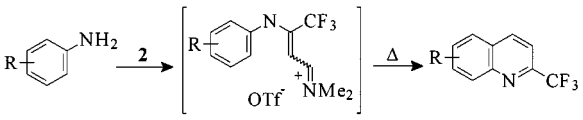


Scheme 1. Synthesis of iminium triflate **2**

It is known[10] that the treatment of trifloxypropeniminium salts with 2 equiv. of a secondary aliphatic amine results in the replacement of the OTf group by an amino moiety and the formation of vinamidinium salts. We envisioned the formation of similar compounds from the reaction of **2** with aromatic amines (Scheme 2). Subsequent intermolecular cyclization could lead to the 2-trifluoromethylquinolines.



Scheme 2. Reaction of trifloxypropeniminium triflate with aromatic amines

Thus, the successful implementation of Scheme 2 could lead to a new and synthetically very useful pathway to this type of fluorinated compounds. The reaction was first attempted using 1,2-dichloroethane as a solvent. However, the desired products were obtained only in the cases of anilines which have strong electron-donating substituents in *m*-position. In the case of unsubstituted aniline, even when the reaction mixture was refluxed for 15 h, the formation of 2-trifluoromethylquinoline was not achieved. It was found that the reaction proceeds successfully when dichloroethane was replaced by *o*-xylene as a solvent (this permits the reaction temperature to be raised from from 83°C to 144°C). Several anilines were subjected to this new reaction and the corresponding quinolines **3a**–**j** were obtained in excellent yields in the majority of cases (Scheme 3). However, the

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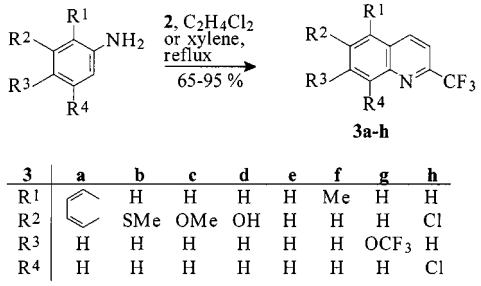
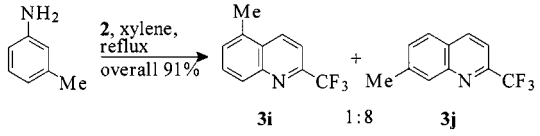
reaction failed when the *o*-substituent was a halogen or any electron-withdrawing group.



3	a	b	c	d	e	f	g	h
R1		H	H	H	H	Me	H	H
R2		SMe	OMe	OH	H	H	H	Cl
R3	H	H	H	H	H	H	OCF_3	H
R4	H	H	H	H	H	H	H	Cl

Scheme 3. Regioselective synthesis of 2-trifluoromehylquinolines

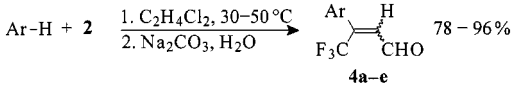
When the aniline carries only one substituent in *m*-position, the formation of 5- and 7-isomers can take place. The reaction of **2** with *m*-substituted anilines revealed the exceptionally strong preference for the 7-isomer; only in the case of *m*-toluidine was a mixture of regioisomers **3i** and **3j** (1:8) isolated (Scheme 4). The other 3-substituted anilines gave only the 7-isomers **3b**−**d** in good to excellent yields. These results are in agreement with the known empirical rule[7c,11] that strong +M substituents tend to discriminate against an attack of the electrophile in the *o*-position, and to favor attack at the *p*-position.



Scheme 4. Reaction of **2** with *m*-toluidine

In view of the simplicity of the experimental procedure compared with other existing methods the use of the iminium triflate **2** is an excellent preparative method for the synthesis of 2-CF_3-substituted quinolines. Anilines have been converted to 2-CF_3-substituted quinolines in a one-pot reaction and in excellent yields. Furthermore, target quinolines were obtained with 95% purity after aqueous workup, without the need for recrystallization or chromatographic purification.

We have also tested several secondary and tertiary aromatic amines in the reaction with **2**. Dimethylaniline reacted smoothly to afford the corresponding cinnamaldehyde **4a** in an almost quantitative yield (Scheme 5). It is surprising that very similar results were obtained from the reaction of **2** with a variety of diarylamines: in each case only *C*-acylation occurred giving the cinnamaldehydes **4b**−**e** as the sole products. It is known[12] that even the weak N-nucleophile carbazole is formylated by the classic Vilsmeier reagent (DMFA/$POCl_3$ complex) at the nitrogen atom. Probably steric factors are critical in the apparent difference in behavior between **2** and the Vilsmeier reagent in a reaction with diarylamines. Obviously, **2**, bearing at the electrophilic carbon atom two bulky substituents, CF_3 and TfO groups, is much sterically more demanding.

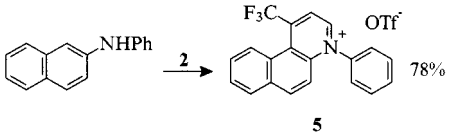


4	Ar	Yield (%)	*E*/*Z* ratio
a	Me_2N–	96	*E*
b		94	*E*
c		95	*E*
d		89	*E*
e		78	10:1

Scheme 5. Stereoselective synthesis of 3-CF_3-cinnamaldehydes

In all the cases investigated the formation of unsaturated aldehydes proceeds in a highly stereoselective manner to yield predominantly *E* isomers; only the carbazole derivative **4e** was found to contain a significant amount (nearly 9% from ^{1}H NMR) of (*Z*)-aldehyde. A similar stereochemistry was observed earlier[9][13] for the reaction of 3-trifloxypropeniminium triflates with electron-rich aromatic and hetaromatic compounds; *E* isomers of unsaturated aldehydes show in their ^{1}H-NMR spectra signals of an aldehyde proton at $\delta = 9.3-9.6$, whereas the corresponding proton signal of a *Z* isomers appear at lower field ($\delta = 9.95-10.31$).[9]

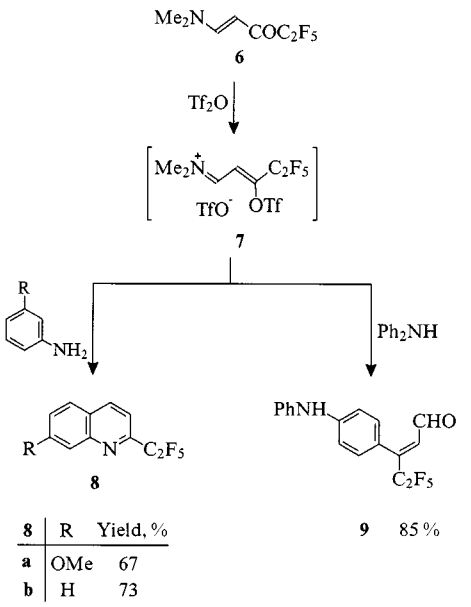
When 2-naphthylphenylamine was treated with **2**, the sole product proved to be the 4-trifluoromethylquinolinium salt **5** (Scheme 6) resulting from the initial attack at the 1-position of the naphthalene ring followed by cyclization at the nitrogen atom.



Scheme 6. Reaction of **2** with 2-naphthylphenylamine

In addition, we have found that the reaction may be extended to the preparation of other 2-R_f-containing quinolines and 3-R_f-substituted cinnamaldehydes. For example 1-(dimethylamino)-4,4,5,5,5-pentafluoro-1-penten-3-one (**6**) was prepared from ethyl vinyl ether and pentafluoropropionic anhydride in the same manner as **1**. Complex **7** (from **6** and Tf_2O) was found to react with aromatic amines under conditions similar to those by which CF_3 analogs were prepared to afford the C_2F_5-substituted quinolines **8** and cinnamaldehyde **9**, albeit in slightly lower yield (Scheme 7). It

would appear that the approach described is also applicable for the synthesis of quinolines with any R_f substituent in 2-position.



Scheme 7. Synthesis of C_2F_5-subtituted quinolines and cinnamaldehydes

Thus, the reaction of arylamines with iminium triflates **2** and **7** provide a useful method for the preparation of 2-R_f-substituted quinolines. The reaction of iminium triflates **2** and **7** with diarylamines gives rise to 3-R_f-substituted cinnamaldehydes in excellent yields. Taken in conjunction with our previous paper,[9] this new pathway represent a mild and effective route to some types of fluorinated compounds.

Experimental Section

General: M.p.: Uncorrected values. − NMR: Varian VXR-400, Bruker AM 400C (400 MHz and 100 MHz, for ^1H and ^{13}C, respectively), with TMS as an internal standard. − IR: UR-20, films. − Column chromatography: Silica gel 60 (63−200 mesh, Merck). − All solvents used were dried and distilled according to the standard procedure. Triflic anhydride was prepared according to a literature procedure[14] from trifluoromethanesulfonic acid (Merck).

(*E*)-4-(Dimethylamino)-1,1,1-trifluoro-3-buten-2-one (1): A solution of (*E*)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one in CH_2Cl_2 was prepared from ethyl vinyl ether (18.0 g, 0.25 mol) and trifluoroacetic anhydride (63.0 g, 0.30 mol) according to the Hojo protocol[8a] and cooled to −20°C. Then aqueous Me_2NH (70 mL of a 30% solution, 0.45 mol) was added dropwise over 10 min with vigorous stirring. The resulting mixture was allowed to warm to room temp., the aqueous layer extracted with CH_2Cl_2 (2 × 50 mL), combined organic layers washed with brine, dried with $MgSO_4$ and then concentrated under reduced pressure. The orange crystalline residue was purified by passing it through a short (7 cm) silica-gel column ($CHCl_3$) followed by recrystallization from hexane/benzene (5:1). Yield 31.0 g (74%) of colorless solid, m.p. 57−58°C (ref.[8d] m.p. 58°C).

(*E*)-1-(Dimethylamino)-4,4,5,5,5-pentafluoro-1-penten-3-one (6): This was prepared using the above procedure from ethyl vinyl ether (9.0 g, 0.125 mol), pentafluoropropionic anhydride (43 g, 0.15 mol) and aqueous Me_2NH (34 mL of a 30% solution, 0.22 mol), recrystallized from hexane. Yield 20.6 g (76%), colorless crystals, m.p. 49−50°C. − ^1H NMR ($CDCl_3$): δ = 2.97 (s, 3 H, CH_3), 3.23 (s, 3 H, CH_3), 5.35 (d, J = 12.2 Hz, 1 H, 2-H), 7.89 (d, J = 12.2 Hz, 1 H, 1-H). − ^{13}C NMR ($CDCl_3$): δ = 37.47, 45.50, 88.37, 108.32 (tq, J_F = 36.8 Hz, 264.3 Hz, CF_2), 118.43 (qt, J_F = 35.7 Hz, 286.7 Hz, CF_3), 156.56, 178.13 (t, J_F = 22.2 Hz, C=O). − $C_7H_8F_5NO$ (217.1): calcd. C 38.72, H 3.71; found C 38.82, H 3.82.

Preparation of 2-Trifluoromethylquinolines from Anilines Containing Strong Electron-Donating Substituents. − General Procedure I (GP I): A solution of 0.5 g (2.93 mmol) of **1** in anhydrous $C_2H_4Cl_2$ (10 mL) was cooled to 0°C. Over a period of 10 min, 0.83 g (2.93 mmol) of triflic anhydride in $C_2H_4Cl_2$ (10 mL) was added dropwise. The corresponding aniline (5.86 mmol) in $C_2H_4Cl_2$ (10 mL) was then added. The reaction mixture was refluxed for 1−6 h and then poured into aqueous Na_2CO_3. The organic layer was separated, washed with 1 N HCl (10 mL) and dried with $MgSO_4$. The organic solvents were removed in vacuo. The residue was purified by column chromatography [silica gel, hexane/diethyl ether (10:1)] to afford pure quinolines.

3-(Trifluoromethyl)benzo[*f*]quinoline (3a): According to GP I, yield 0.69 g (95%), colorless crystals, m.p. 113−114°C. − ^1H NMR ($CDCl_3$): δ = 7.65−7.71 (m, 2 H, 8-H, 9-H), 7.81 (d, J = 8.7 Hz, 1 H, 2-H), 7.85−7.89 (m, 1 H, 7-H), 7.97 (s, 2 H, 5-H, 6-H), 8.50−8.54 (m, 1 H, 10-H), 8.96 (d, J = 8.7 Hz, 1 H, 1-H). − ^{13}C NMR ($CDCl_3$): δ = 117.05, 121.82 (q, J_F = 273.6 Hz, CF_3), 122.91, 126.72, 127.56, 127.70, 128.31, 128.72, 128.79, 132.12, 132.22, 132.28, 147.18 (q, J_F = 34.7 Hz, 3-C), 147.48. − $C_{14}H_8F_3N$ (247.2): calcd. C 68.02, H 3.26; found C 68.13, H 3.34.

7-(Methylsulfanyl)-2-(trifluoromethyl)quinoline (3b): According to GP I, yield 0.63 g (89%), pale pink crystals, m.p. 90−91°C. − ^1H NMR ($CDCl_3$): δ = 2.58 (s, 3 H, CH_3), 7.32 (dd, J = 8.7 Hz, 1.8 Hz, 1 H, 6-H), 7.59 (d, J = 8.4 Hz, 1 H, 3-H), 7.66 (d, J = 8.7 Hz, 1 H, 5-H), 7.79 (d, J = 1.8 Hz, 1 H, 8-H), 8.18 (d, J = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 14.70, 115.59, 121.15 (q, J_F = 275.3 Hz, CF_3), 122.53, 126.22, 127.15, 127.74, 137.60, 143.64, 147.64, 147.98 (q, J_F = 34.4 Hz, 2-C). − $C_{11}H_8F_3NS$ (243.2): calcd. C 54.31, H 3.31; found C 54.49, H 3.30.

7-Methoxy-2-(trifluoromethyl)quinoline (3c): According to GP I, yield 0.62 g (93%), colorless crystals, m.p. 67−68°C. (ref.[7c] m.p. 65−66°C). − ^1H NMR ($CDCl_3$): δ = 3.93 (s, 3 H, CH_3), 7.27 (dd, J = 9.2 Hz, 2.4 Hz, 1 H, 6-H), 7.46 (d, J = 2.4 Hz, 1 H, 8-H), 7.56 (d, J = 8.4 Hz, 1 H, 3-H), 7.71 (d, J = 9.2 Hz, 1 H, 5-H), 8.19 (d, J = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 55.54, 107.31, 114.44, 121.45 (q, J_F = 274.2 Hz, CF_3), 122.13, 124.17, 128.46, 137.41, 147.87 (q, J_F = 33.7 Hz, 2-C), 148.99, 161.58. These spectral data are in good accord with those reported in ref.[7c]

2-(Trifluoromethyl)-7-quinolinol (3d): Crude product, obtained according to GP I (without chromatographic purification), was crystallized from $C_2H_4Cl_2$, yield 0.41 g (65%), pale-gray crystals, m.p. 250−255°C (dec.). − IR (nujol): $\tilde{\nu}$ = 3100 cm^{-1} (OH). − ^1H NMR ($CDCl_3$): δ = 7.38 (dd, J = 9.2 Hz, 2.4 Hz, 1 H, 6-H), 7.45 (d, J = 2.4 Hz, 1 H, 8-H,), 7.65 (d, J = 8.4 Hz, 1 H, 3-H), 7.96 (d, J = 9.2 Hz, 1 H, 5-H,), 8.48 (d, J = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 111.14, 114.65, 122.44, 122.85 (q, J_F = 272.8 Hz, CF_3), 124.65, 130.38, 139.02, 148.32 (q, J_F = 33.7 Hz, 2-C), 149.94, 160.63. − $C_{10}H_7F_3N$ (213.2): calcd. C 56.35, H 2.84; found C 56.11, H 2.93.

7-Methoxy-2-(1,1,2,2,2-pentafluoroethyl)quinoline (8a): Obtained according to GP I from **6** (0.64 g, 2.93 mmol), Tf_2O (0.83 g, 2.93 mmol) and *m*-anisidine (0.72 g, 5.86 mmol). Yield 0.54 g (67%), white crystals, m.p. 57−59°C. − ^{1}H NMR ($CDCl_3$): δ = 3.94 (s, 3 H, CH_3), 7.29 (dd, *J* = 9.0 Hz, 2.5 Hz, 1 H, 6-H), 7.50 (d, *J* = 2.5 Hz, 1 H, 8-H), 7.58 (d, *J* = 8.4 Hz, 1 H, 3-H), 7.73 (d, *J* = 9.0 Hz, 1 H, 5-H), 8.20 (d, *J* = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 55.63, 107.50, 112.24 (tq, J_F = 36.9 Hz, 253.7 Hz, CF_2), 115.72, 119.46 (qt, J_F = 37.2 Hz, 284.1 Hz, CF_3), 122.36, 124.11, 128.53, 137.24, 148.33 (t, J_F = 25.2 Hz, 2-C), 149.23, 161.63. − $C_{12}H_9F_5N$ (277.2): calcd. C 52.00, H 2.91; found C 51.73, H 2.77.

Preparation of 2-Trifluoromethylquinolines from Anilines without Strong Electron-Donating Substituents. − General Procedure II (GP II): The reaction mixture was prepared according to GP I from **1** (0.5 g, 2.93 mmol), Tf_2O (0.83 g, 2.93 mmol) and the corresponding aniline (5.86 mmol). Then, $C_2H_4Cl_2$ was evaporated, anhydrous *o*-xylene (15 mL) added and the reaction mixture was refluxed for 5−15 h. The products were isolated according to GP I.

2-(Trifluoromethyl)quinoline (3e): According to GP II, yield 0.50 g (83%), colorless crystals, m.p. 57−58°C. (ref.[7c] m.p. 57.0−57.5°C). − ^{1}H NMR ($CDCl_3$): δ = 7.65 (dd, *J* = 7.4 Hz, 8.4 Hz, 1 H, 6-H or 7-H), 7.71 (d, *J* = 8.4 Hz, 1 H, 3-H), 7.81 (dd, *J* = 8.5 Hz, 7.4 Hz, 1 H, 6-H or 7-H), 7.89 (d, *J* = 8.4 Hz, 1 H, 5-H), 8.21 (d, *J* = 8.5 Hz, 1 H, 8-H), 8.32 (d, *J* = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 116.51, 121.58 (q, J_F = 274.5 Hz, CF_3), 127.36, 128.36, 128.61, 129.84, 130.57, 137.87, 146.94, 147.75 (q, J_F = 34.3 Hz, 2-H). These spectral data are in good accord with those reported in ref.[7c]

8-Methyl-2-(trifluoromethyl)quinoline (3f): According to GP II, yield 0.55 g (90%), colorless oil, n_D^{16} = 1.5248 (ref.[7c] n_D^{20} = 1.5236). − ^{1}H NMR ($CDCl_3$): δ = 2.86 (s, 3 H, CH_3), 7.53 (dd, *J* = 8.6 Hz, 7.0 Hz, 1 H, 6-H), 7.62 (d, *J* = 7.0 Hz, 1 H, 7-H), 7.68 (d, *J* = 8.6 Hz, 1 H, 5-H), 7.71 (d, *J* = 8.4 Hz, 1 H, 3-H), 8.23 (d, *J* = 8.4 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 17.51, 116.27, 121.75 (q, J_F = 275.0 Hz, CF_3), 125.41, 128.22, 128.75, 130.57, 137.93, 138.27, 146.17, 146.54 (q, J_F = 34.1 Hz, 2-C). These spectral data are in good accord with those reported in ref.[7c]

6-(Trifluoromethoxy)-2-(trifluoromethyl)quinoline (3g): According to GP II, yield 0.59 g (72%), pale yellow crystals, m.p. 52−53°C. − ^{1}H NMR ($CDCl_3$): δ = 7.65 (dd, *J* = 9.2 Hz, 2.1 Hz, 1 H, 7-H), 7.71 (d, *J* = 2.1 Hz, 1 H, 5-H), 7.78 (d, *J* = 8.7 Hz, 1 H, 3-H), 8.25 (d, *J* = 9.2 Hz, 1 H, 8-H), 8.34 (d, *J* = 8.7 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 116.84, 117.47, 120.87 (q, J_F = 256.9 Hz, CF_3H), 121.95 (q, J_F = 273.0 Hz, CF_3C), 124.56, 128.82, 132.24, 137.70, 144.99, 148.05 (q, J_F = 34.1 Hz, 2-C), 148.17. − $C_{11}H_6F_6N$ (281.2): calcd. C 46.99, H 1.79; found C 46.58, H 1.97.

5,7-Dichloro-2-(trifluoromethyl)quinoline (3h): Obtained according to GP II, yield 0.73 g (94%), pale yellow crystals, m.p. 86−87°C. − ^{1}H NMR ($CDCl_3$): δ = 7.67 (d, *J* = 2.0 Hz, 1 H, 6-H), 7.79 (d, *J* = 8.8 Hz, 1 H, 3-H), 8.09 (d, *J* = 2.0 Hz, 1 H, 8-H), 8.66 (d, *J* = 8.8 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 117.62, 121.05 (q, J_F = 274.0 Hz, CF_3), 125.41, 128.15, 129.19, 132.21, 135.15, 136.17, 147.60, 149.62 (q, J_F = 34.8 Hz, 2-C). − $C_{10}H_4Cl_2F_3N$ (266.0): calcd. C 45.15, H 1.52; found C 44.79. H 1.65.

5-Methyl-2-(trifluoromethyl)quinoline (3i) and 7-Methyl-2-(trifluoromethyl)quinoline (3j). − Mixture 1:8 (^{1}H NMR): Obtained according to GP II, yield 0.56 g (91%), colorless crystals. − ^{1}H NMR ($CDCl_3$) of **3j**: δ = 2.51 (s, 3 H, CH_3), 7.40 (d, *J* = 8.6 Hz, 1 H, 6-H), 7.57 (d, *J* = 8.6 Hz, 1 H, 5-H), 7.68 (d, *J* = 8.4 Hz, 1 H, 3-H), 7.91 (s, 1 H, 8-H), 8.17 (d, *J* = 8.4 Hz, 1 H, 4-H). − ^{1}H NMR ($CDCl_3$) of **3i** δ = 2.62 (s, 3 H, CH_3), 7.65 (d, 1 H), 8.00 (d, 1 H), 8.38 (d, 1 H). Remaining signals covered by those of the major isomer. − ^{13}C NMR ($CDCl_3$) of **3j**: δ = 21.70, 121.60, 121.60 (q, J_F = 273.3 Hz, CF_3), 126.82, 127.14, 128.75, 130.76, 137.53, 141.27, 147.27, 147.64 (q, J_F 34.6 Hz, 2-C). − ^{13}C NMR ($CDCl_3$) of **3i**: δ = 18.37, 116.13, 128.11, 130.38, 134.40. Remaining signals coincide with those of the major isomer or are not detected. The spectral data for **3j** are in good accord with those reported in ref.[7c]

2-(1,1,2,2,2-Pentafluoroethyl)quinoline (8b): Obtained according to GP II from **6** (0.64 g, 2.93 mmol), Tf_2O (0.83 g, 2.93 mmol) and aniline (0.55 g, 5.86 mmol). Yield 0.53 g (73%), pale yellow oil, n_D^{16} = 1.4955. − ^{1}H NMR ($CDCl_3$): δ = 7.55 (dd, *J* = 7.5 Hz, 8.4 Hz, 1 H, 6-H or 7-H), 7.64 (d, *J* = 8.3 Hz, 1 H, 3-H), 7.70 (dd, *J* = 8.5 Hz, 7.5 Hz, 1 H, 6-H or 7-H), 7.77 (d, *J* = 8.4 Hz, 1 H, 5-H), 8.14 (d, *J* = 8.5 Hz, 1 H, 8-H), 8.22 (d, *J* = 8.3 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 111.35 (tq, J_F = 37.6 Hz, 255.1 Hz, CF_2), 117.70, 118.95 (qt, J_F = 37.5 Hz, 286.9 Hz, CF_3), 127.57, 128.26, 128.61, 130.14, 130.65, 137.75, 147.28, 147.42 (t, J_F = 25.2 Hz, 2-C). − $C_{11}H_6F_5N$ (247.2): calcd. C 53.45, H 2.45; found C 53.10, H 2.49.

Preparation of 3-Trifluoromethylcinnamaldehydes. − General Procedure III (GP III): The reaction mixture was prepared according to GP I from **1** (0.5 g, 2.93 mmol), Tf_2O (0.83 g, 2.93 mmol) and the corresponding arylamine (5.86 mmol). After stirring at 20−40°C for 2−4 h, the mixture was poured into aqueous Na_2CO_3 and the resulting mixture was stirred for 3−5 h. The organic layer was separated, the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel [benzene, hexane/diethyl ether (4:1)].

(*E*)-3-[4-(Dimethylamino)phenyl]-4,4,4-trifluoro-2-butenal (4a): Obtained according to GP III, yield 0.68 g (96%), yellow-orange viscous oil. − IR (Nujol): $\tilde{\nu}$ = 1660 cm^{-1} (C=H), 1590 (C=C). − ^{1}H NMR ($CDCl_3$): δ = 2.96 (s, 6 H, 2 CH_3), 6.47 (d, *J* = 7.4 Hz, 1 H, 2-H), 6.64 (d, *J* = 8.8 Hz, 2 H, 3′-H, 5′-H), 7.19 (d, *J* = 8.8 Hz, 2 H, 2′-H, 6′-H), 9.54 (d, *J* = 7.4 Hz, 1 H, CHO). − ^{13}C NMR ($CDCl_3$): δ = 40.04 (2 C), 111.50 (2 C), 123.30 (q, J_F = 276.1 Hz, CF_3), 125.69, 128.30 (q, J_F = 4.9 Hz, 2-C), 131.68 (2 C), 148.15 (q, J_F = 30.4 Hz, 3-C), 151.77, 192.55 (C=O). − $C_{12}H_{13}F_3N$ (243.2): calcd. C 59.26, H 4.97; found C 58.89, H 4.90.

(*E*)-3-(4-Anilinophenyl)-4,4,4-trifluoro-2-butenal (4b): Obtained according to GP III, yield 0.80 g (94%), yellow-orange crystals, m.p. 57−58°C. − IR (Nujol): $\tilde{\nu}$ = 3330 cm^{-1} (N−H), 1670 (C=H), 1600 (C=C). − ^{1}H NMR ($CDCl_3$): δ = 6.25 (br. s, 1 H, NH), 6.53 (dq, 1 H, *J* = 7.4 Hz, J_F = 1.1 Hz, H-2), 7.02−7.07 (m, 3 H), 7.17−7.21 (m, 2 H), 7.26 (d, *J* = 8.3 Hz, 2 H), 7.30 (dd, *J* = 7.9 Hz, 7.4 Hz, 2 H, 3′′-H, 5′′-H), 9.62 (d, *J* = 7.4 Hz, 1 H, CHO). − ^{13}C NMR ($CDCl_3$): δ = 115.24 (2 C), 119.40, 119.98 (2 C), 122.82, 123.05 (q, J_F = 275.6 Hz, CF_3), 129.18 (q, J_F = 4.9 Hz, 2-C), 129.38 (2 C), 131.49 (2 C), 140.85, 146.35, 147.78 (q, J_F = 30.9 Hz, 3-C), 192.18 (C=O). − $C_{16}H_{13}F_3N$ (291.3): calcd. C 65.98, H 4.15; found C 65.88, H 4.13.

(*E*)-3-(4-Anilino-1-naphthyl)-4,4,4-trifluoro-2-butenal (4c): Obtained according to GP III, yield 0.95 g (95%), bright yellow crystals, m.p. 105−107°C. − IR (Nujol): $\tilde{\nu}$ = 3350 cm^{-1} (N−H), 1680 (C=H), 1600 (C=C). − ^{1}H NMR ($CDCl_3$): δ = 6.25 (br. s, 1 H, NH), 6.83 (dq, *J* = 7.3 Hz, J_F 1.2 Hz, 1 H, 2-H), 7.04 (t, *J* = 7.8 Hz, 1 H, 4′′-H), 7.15 (d, *J* = 8.4 Hz, 2 H, 2′′-H, 6′′-H), 7.35−7.30 (m, 3 H), 7.58−7.48 (m, 3 H), 7.74 (d, *J* = 7.9 Hz, 1 H, 2′-H), 8.07 (m, 1 H, 8′-H), 9.31 (d, *J* = 7.7 Hz, 1 H, CHO). − ^{13}C NMR ($CDCl_3$): δ = 110.49, 119.14, 119.82 (2 C), 120.64, 121.46, 122.42, 122.49 (q, J_F = 274.7 Hz, CF_3), 125.47, 125.74, 126.08, 127.69, 128.90, 129.50

(2 C), 132.91 (q, J_F = 4.5 Hz, 2-C), 133.46, 141.17, 142.36, 147.17 (q, J_F = 32.1 Hz, 3-C), 192.01 (C=O). − $C_{20}H_{15}F_3N$ (341.3): calcd. C 70.38, H 4.13; found C 69.97, H 4.08.

(*E*)-3-(10,11-Dihydro-5*H*-dibenzo[*b,f*]azepin-2-yl)-4,4,4-trifluoro-2-butenal (4d): Obtained according to GP III, yield 0.83 g (89%), yellow-green crystals, m.p. 133−135°C (dec). − IR (Nujol): $\tilde{\nu}$ = 3350 cm^{-1} (N−H), 1670 (C=H), 1610 (C=C). − ^1H NMR ($CDCl_3$): δ = 3.00 (s, 4 H, 2 CH_2), 6.37 (br. s, 1 H, NH), 6.55 (d, *J* = 7.3 Hz, 1 H, 2-H), 6.76 (d, *J* = 8.2 Hz, 1 H, 4′-H or 6′-H), 6.79 (d, *J* = 8.0 Hz, 1 H, 4′-H or 6′-H), 6.85 (dd, *J* = 7.6 Hz, 7.2 Hz, 1 H, 8′-H), 7.14−7.04 (m, 4 H), 9.64 (d, *J* = 7.3 Hz, 1 H, CHO). − ^{13}C NMR ($CDCl_3$): δ = 34.59, 35.25, 117.95, 118.41, 118.92, 120.64, 123.06 (q, J_F = 274.8 Hz, CF_3), 127.02, 127.71, 128.84, 129.29, 129.38, 130.52, 133.06, 141.17, 144.73, 147.76 (q, J_F = 30.9 Hz, 3-C), 192.31 (C=O). − $C_{18}H_{15}F_3N$ (317.3): calcd. C 68.13, H 4.45; found C 68.20, H 4.51.

3-(9*H*-Carbazol-3-yl)-4,4,4-trifluoro-2-butenal (4e): According to GP III, yield 0.66 g (78%), *E*/*Z* = 10:1 (^1H NMR), pale yellow powder, m.p. 94−96°C. − IR (Nujol): $\tilde{\nu}$ = 3400 cm^{-1} (N−H), 1695 (C=H), 1610 (C=C). − ^1H NMR ($CDCl_3$) of *E*-**4e**: δ = 6.70 (d, *J* = 7.4 Hz, 1 H, 2-H), 7.26 (dd, *J* = 7.7 Hz, 7.0 Hz, 1 H, 6′-H), 7.49−7.35 (m, 4 H), 8.03 (d, *J* = 8.2 Hz, 1 H, 2′-H), 8.07 (s, 1 H, 4′-H), 8.34 (br. s, 1 H, NH), 9.60 (d, *J* = 7.4 Hz, 1 H, CHO). − ^1H NMR ($CDCl_3$) of *Z*-**4e**: δ = 6.49 (d, *J* = 7.8 Hz, 1 H, 2-H), 8.28 (br. s, 1 H, NH), 10.26 (d, *J* = 7.8 Hz, 1 H, CHO), remaining signals covered by those of the major isomer. − ^{13}C NMR ($CDCl_3$) for *E*-**4e**: δ = 110.86, 110.98, 119.61, 120.31, 120.56, 122.56, 122.62, 122.98 (q, J_F = 275.5 Hz, CF_3), 123.43, 126.92, 127.36, 130.09 (q, J_F 4.8 Hz, 2-C), 139.88, 140.47, 149.01 (q, J_F = 31.3 Hz, 3-C), 192.67 (C=O). − ^{13}C NMR ($CDCl_3$) for *Z*-**4e**: δ = 125.52, 126.78, 128.31, 131.85, 190.05 (C=H). Remaining signals coincide with those of the major isomer or are not detected. − $C_{16}H_{11}F_3N$ (289.3): calcd C 66.44, H 3.48; found C 66.23, H 3.49.

(*E*)-3-(4-Anilinophenyl)-4,4,5,5,5-pentafluoro-2-pentenal (9): Obtained according to GP III from **6** (0.64 g, 2.93 mmol), Tf_2O (0.83 g, 2.93 mmol) and diphenylamine (1.00 g, 5.86 mmol). Yield 0.85 g (85%), yellow-green crystals, m.p. 112°C. − IR (Nujol): $\tilde{\nu}$ = 3380 cm^{-1} (N−H), 1685 (C=H), 1600 (C=C). − ^1H NMR ($CDCl_3$): δ = 5.20 (br. s, 1 H, NH), 6.58 (d, 1 H, *J* = 7.3 Hz, H-2), 7.03−7.06 (m, 3 H), 7.30 (dd, *J* = 8.5 Hz, 1.1 Hz, 2 H), 7.26 (d, *J* = 8.6 Hz, 2 H), 7.30 (dd, *J* = 8.5 Hz, 8.4 Hz, 2 H, 3′′-H, 5′′-H), 9.57 (d, *J* = 7.3 Hz, 1 H, CHO). − ^{13}C NMR ($CDCl_3$): δ = 112.55 (tq, J_F = 36.7 Hz, 256.4 Hz, CF_2), 115.24 (2 C), 118.76 (qt, J_F = 37.7 Hz, 285.6 Hz, CF_3), 119.72, 120.1 (2 C), 122.98, 129.48 (2 C), 131.85 (2 C), 132.80, 140.86, 146.16, 147.62 (t, J_F = 22.0 Hz, 3-C), 191.85 (C=O). − $C_{17}H_{13}F_5N$ (341.3): calcd. C 59.83, H 3.54; found C 59.56, H 3.55.

4-Phenyl-1-(trifluoromethyl)-4-benzo[*f*]quinolinium Trifluoromethanesulfonate (5): A suspension of **2** was prepared according to GP I from **1** (0.5 g, 2.93 mmol) and Tf_2O (0.83 g, 2.93 mmol), then *N*-phenyl-2-naphthylamine (1.28 g, 5.86 mmol) was added and the reaction mixture was stirred at 40−60°C for 2 h. After quenching with water, the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Recrystallization from 1,2-dichloroethane gave 1.08 g (78%) of **5** as yellow powder, m.p. 229−231°C. − ^1H NMR {CD_3OD/[D_6]acetone (1:1)}: δ = 7.64 (d, *J* = 9.5 Hz, 1 H, 6-H,), 7.85−7.79 (m, 5 H), 7.96−8.00 (m, 2 H), 8.24−8.27 (m, 1 H), 8.52 (d, *J* = 9.5 Hz, 1 H, 5-H), 8.82−8.86 (m, 2 H), 9.65 (d, *J* = 6.4 Hz, 1 H, 3-H). − ^{13}C NMR {CD_3OD/[D_6]acetone (1:1)}: δ = 118.27, 121.63 (q, J_F = 319.1 Hz, CF_3S), 122.97 (q, J_F = 7.2 Hz), 123.93 (q, J_F = 274.6 Hz, CF_3C), 127.02, 127.47 (2 C), 129.25 (q, J_F = 33.2 Hz, 1-C), 129.53 (q, J_F = 7.2 Hz), 130.74, 131.00, 131.63 (2 C), 132.21, 133.04, 133.85, 140.61, 141.98, 145.12, 148.19. − $C_{21}H_{16}F_6NS$ (473.4): calcd. C 53.28, H 2.77; found C 53.00, H 2.44.

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