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Synthesis of 2-trifluoromethylated quinolines from CF_3-alkenes†

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α-CF_3-enamines can be prepared by the reaction of pyrrolidine with the corresponding haloalkenes. The prepared enamines react with 2-nitrobenzaldehydes to give *ortho*-nitro-substituted α,β-diaryl-CF_3-enones highly stereoselectively in up to 88% yield. Subsequent reduction of the nitro-group by an Fe–AcOH system promotes intramolecular cyclization to afford 2-CF_3-3-arylquinolines in up to 99% isolated yield. High synthetic utility of all synthetic steps of the sequence was shown. A one-pot procedure was developed to give the target trifluoromethylated quinolines directly from enamines or haloalkenes.

Introduction

Quinoline was discovered by F. Runge in 1834.[1] Two centuries of investigations have afforded many approaches to the synthesis of the quinoline core. The Skraup,[2] Doebner–von Miller,[3] Combes,[4] Friedländer,[5] Pfitzinger,[6] and Conrad–Limpach[7] syntheses have become classics of heterocyclic chemistry known to students from textbooks. Modern approaches to quinoline synthesis often employ transition metal-catalyzed reactions.[8] Green and clean syntheses using microwaves, clay, or some other catalyst which could be recycled and reused, one-pot reactions, solvent-free reaction conditions, ionic liquids, ultrasound promoted synthesis, and photocatalytic synthesis (UV radiation) have also been developed.[9] Nevertheless, novel approaches to quinolines are in great demand because quinoline chemistry is still at the top of the modern organic chemistry agenda. The high biological activity of quinolines makes them very attractive scaffolds in drug discovery. For example, antifungal,[10] anticancer,[11] anti-inflammatory,[12] and antileishmanial actions[13] have been documented. A number of quinoline derivatives are used as important drugs. Thus, quinolone antibiotics such as ofloxacin (Floxin), norfloxacin (Noroxin), ciprofloxacin (Cipro), and moxifloxacin (Avelox) are widely used worldwide for treating a broad range of bacterial infections—such as pneumonia and tuberculosis.[14] The quinoline alkaloid quinine[15] and a number of modern quinoline derived drugs, for example, Chloroquine, Hydroxychloroquine, and Mefloquine,[16] are used to treat malaria, which is a dangerous infective disease that affected 228 million people in 2018, leading to nearly 0.4 million casualties that year.[17] Proflavine is used as a topical antiseptic. Pitavastatin is a representative of statins used for lowering lipid levels in the blood. Bosutinib possesses antineoplastic activity and is used for the treatment of chronic myelogenous leukemia (Fig. 1).

One of the defining trends of modern science is concern about the applicability of the obtained results in everyday life. A lot of attention has been paid to organofluorine chemistry due to organofluorine compounds having unique physicochemical and biological properties.[18] As a result these compounds have found applications as construction materials, components of liquid crystalline compositions, agrochemicals[19] and pharmaceuticals.[20] About 20% (more than 300 compounds) of currently used drugs[21] contain at least one fluorine atom.[22] Recent analysis revealed sustainable growth of the fluoropharmaceuticals share among new small-molecule drugs, which has doubled in the last two years (45% in 2018,[23] 41% in 2019[24]). Obviously, the combination of fluorine or fluorinated substituents with heterocyclic moieties is a fruitful strategy in drug design. Indeed, 11 drugs bearing fluorinated heterocyclic motifs and 19 drugs with both fluorine and heterocyclic moieties in the molecule were approved by the FDA in 2018 and 2019. Novel effective methodologies for the synthesis of fluorinated heterocycles are in great demand.[25]

It should be pointed out that fluorinated quinolines are hot topic compounds. A lot of effort has been made in this field due to the high importance of fluoroquinolone antibiotics. 2-CF_3-quinolines are highly attractive molecules as well. A lot of reports devoted to their synthesis have appeared in the literature during the last 2 decades.[25] For example, for only the last 10 years, more than 9000 hits can be found in the Reaxys

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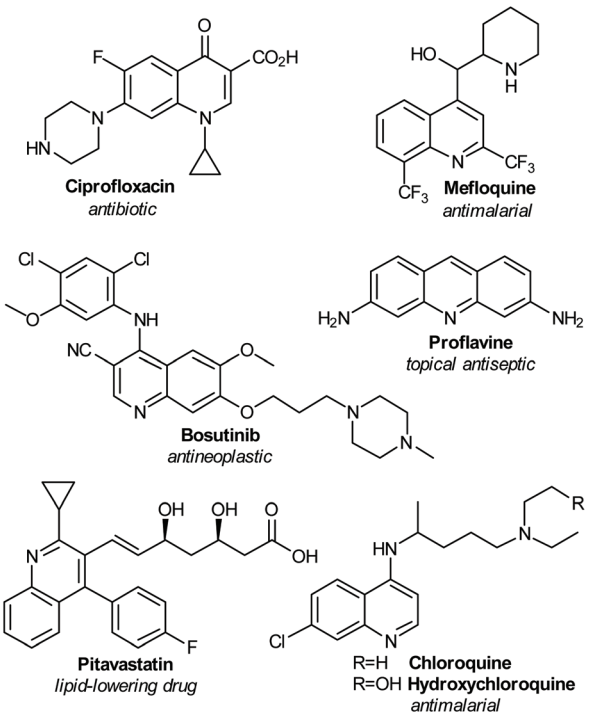


Fig. 1 Selected examples of drugs with quinoline moieties.

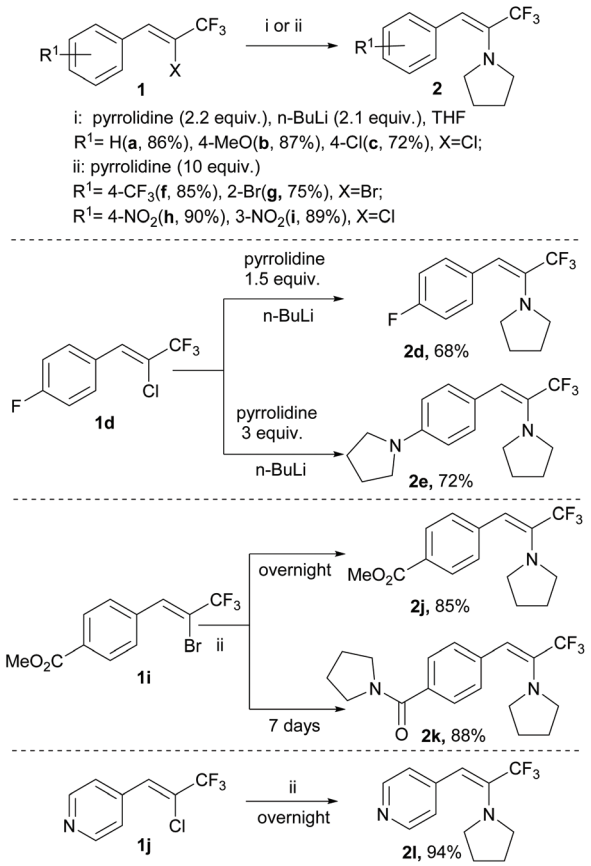
data base. The most popular methods are based on trifluoromethylation of quinoline derivatives,[26] 2-haloquinolines[27] or isocyanides.[28] Various cyclizations using anilines[29] or isatines[30] as precursors have also been reported.

In this article, we report the synthesis of *ortho*-nitro-substituted α,β-diaryl-α′-CF_3-enones based on the condensation of α-CF_3-β-aryl enamines with 2-nitrobenzaldehydes. Subsequent conversion of these ketones into 2-CF_3-quinolines can be performed by reduction of the nitro-group followed by intramolecular cyclization.

Results and discussion

To start our investigation, a set of enamines **2** with both electron-withdrawing and electron-donating groups was prepared (Scheme 1). Depending on the quantity of pyrrolidine used, the reaction of 4-fluoro-substituted styrene **1d** afforded enamine **2d** (1.5 equiv.) or enamine **2e** with a additional pyrrolidine moiety in the *para*-position of the aryl ring (3 equiv.). Similarly, styrene **1i** can be converted into either enamine **2j** or enamine **2k** by controlling the reaction time. Performing the reaction overnight is enough to create the enamine functional group to give enamine **2j**. Conversion of the ester to the amide can be performed by carrying out the reaction for 7 days to give enamine **2k**. Enamine **2l** with a heterocyclic moiety was also successfully prepared in 94% yield (Scheme 1).

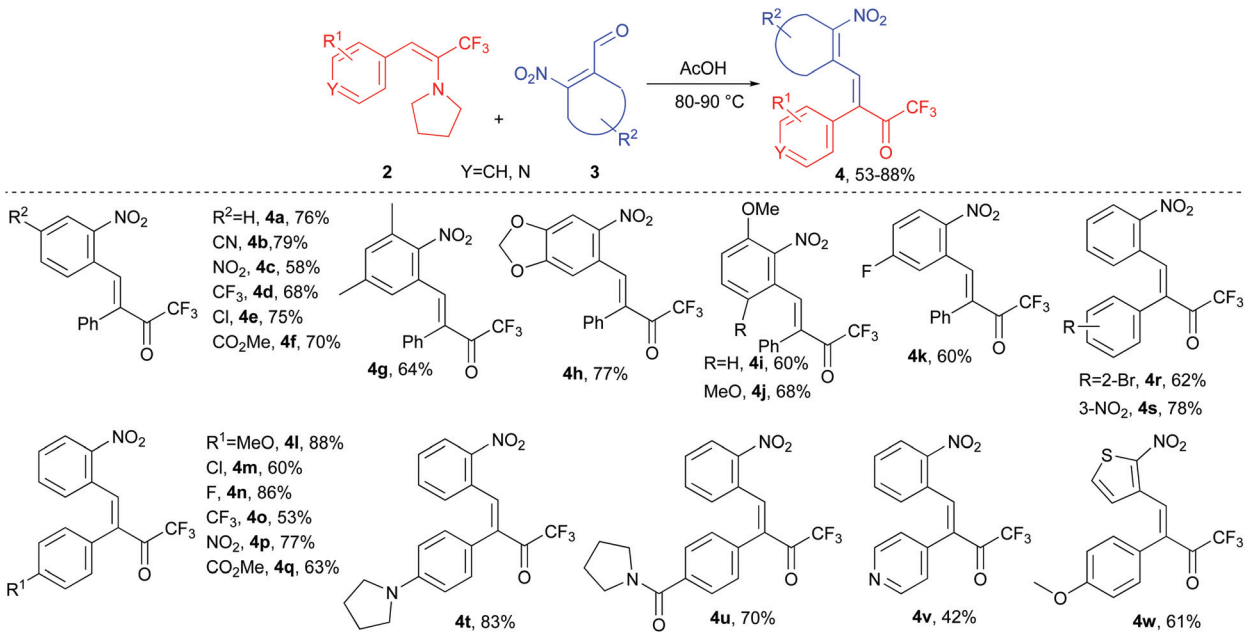
With a set of trifluromethylated enamines **2** in hand, their reaction with *ortho*-nitro-substituted benzaldehydes was investigated. The model reaction of enamine **2a** with 2-nitrobenzaldehyde was performed in acetic acid at 80–90 °C. To our delight, the reaction gave the desired ketone **4a** in 76% yield after 6 h heating at 80–90 °C (Scheme 2).



Scheme 1 Synthesis of starting enamines **2**.

Next, the scope of 2-nitrobenzaldehydes **3** was studied using **2a** as a model enamine. It was found that the reaction is very general. All target ketones **4b–k** were prepared in good to high yields. Further, we varied the enamine moiety and conducted the reaction with 2-nitrobenzaldehyde. Again, a set of ketones **4l–u** was successfully prepared in up to 86% yield. We also attempted to involve enamine **2l** with a heterocyclic motif in the reaction. As a result, the corresponding ketone **4v** bearing a 4-pyridyl substituent was synthesized in good yield. To have a heterocyclic ring adjacent to the other side of the double bond of ketone **4**, we performed the reaction of enamine **2b** with 2-nitro-3-thiophenecarbaldehyde. The reaction afforded the thiophene derived ketone **4w** in 61% yield. Summarizing the results obtained, one can point out the high synthetic utility of the reaction, allowing us to prepare the desired ketones with various combinations of electron-donating and electron-withdrawing groups on both aryl rings. Aldehydes and enamines with various functional groups, as well as bulky substituents and heterocyclic moieties, can be involved in the reaction.

Another outstanding feature of the reaction is its very high stereoselectivity. Thus, the *E*-isomer with *cis*-arranged aryl sub-



Scheme 2 Scope of the synthesis of *o*-nitrophenyl-substituted enones.

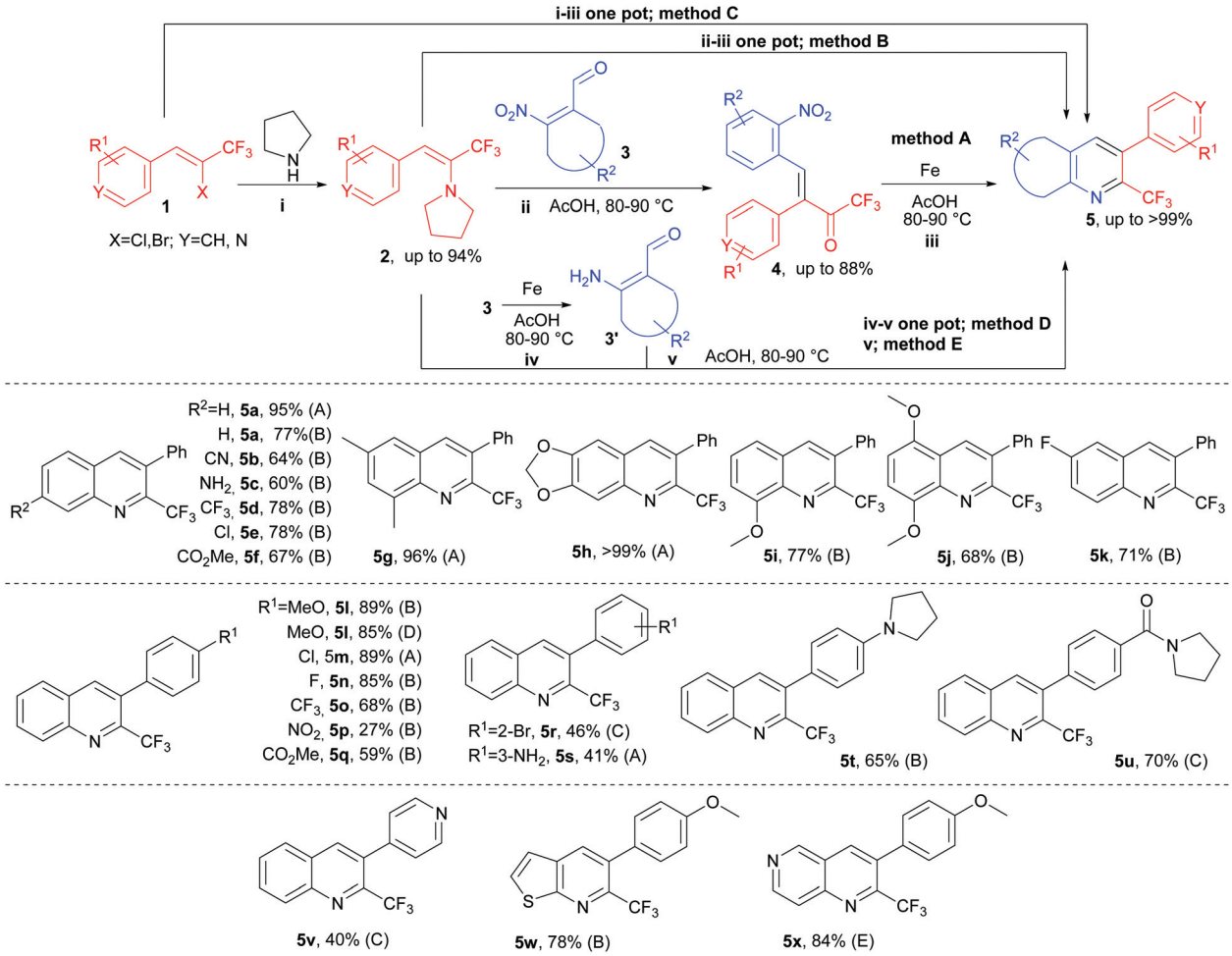
stituents is the major product of the reaction. As a rule, the fraction of the minor *Z*-isomer does not exceed 1–6%. Moreover, in many cases formation of the *Z*-isomer was not detected at all. Only in the case of **4b**, about 14% *Z*-isomer was formed. The stereochemical outcome of the reaction can be explained by the formation of a Zimmerman–Traxler like transition state.[31]

Next, the possibility of transformation of the *ortho*-nitro-substituted ketones **4** into the corresponding CF_3-quinolines was studied. It was found that ketone **4a** can be converted into the desired quinoline **5a** in 95% yield using an Fe–AcOH system. A very clean reduction–heterocyclization sequence takes place when these classical conditions for the reduction of the nitro-group are used. No formation of any organic by-products was observed during the reaction (Scheme 3, method A). As a result, the isolation of the target product can be performed just by separation of the target product from the inorganic products of iron oxidation.

On the other hand, one can mention that the synthesis of the starting ketone was carried out in the same solvent (acetic acid). Therefore, we decided to use a more attractive one-pot protocol (Scheme 3, method B). To our delight, quinoline **5a** was obtained in 77% yield using a two-step one-pot procedure without intermediate isolation of ketone **4a**. Some other reductive systems were studied as well. However, catalytic reduction using hydrogen and palladium on carbon in methanol led to the formation of a complex mixture of products. Most probably, deeper reduction occurred as well. All our attempts to halt over-reduction to obtain pure quinoline **5a** or force the reaction to isolate the corresponding tetrahydroquinoline failed. An ammonium formate–Pd/C system in methanol at room temperature works much more selectively, leading to the target quinoline **5a** in 90% yield. An attempt to carry out the reaction in one pot in acetic acid showed that no reduction occurs at room temperature. When heated, the reaction proceeds successfully, however, formation of a minor amount of impurities decreases the yield of the target quinoline **5a** by about 10%.

Thus, the Fe–AcOH system appears to be optimal for this transformation. Using these conditions, a set of 2-CF_3-3-arylquinolines **5** with various combinations of substituents was prepared from the corresponding enones (Scheme 3, method B). The reaction tolerates both electron-donating and electron-withdrawing groups, and cyano, amide and ester functional groups to give the target quinolines in nearly quantitative yields for the 1-step transformation from ketones (**5a,g,h,m,s**), or in good to high yields for the one-pot 2-step transformation from enamines (**5a,b–f,i–l,n–t**). The reaction is not sensitive to steric demands, allowing us to involve ketones with *ortho*-substituents on both aryl rings (**5g,i,j,r**). When the starting ketone has an additional nitro-group in the structure (enones **4c,s,p**), reduction of both NO_2 groups takes place to give the corresponding quinolines **5c,s,p** with aminoaryl fragments. This functionality can be used to create a library of 2-CF_3-quinolines for subsequent study of their biological activity (Scheme 3).

We also found that all 3 steps of this approach can be performed in one pot starting from the CF_3-alkenes **1**. We demonstrated the synthesis of quinolines directly from styrenes **1**, bypassing the purification of the intermediate enamines **2** and the isolation of ketones **4**. In this case, the yields of quinolines **5r,u** reached a respectable 70%, allowing us to simplify the procedure and avoid purification of the intermediate products (Scheme 3, method C).



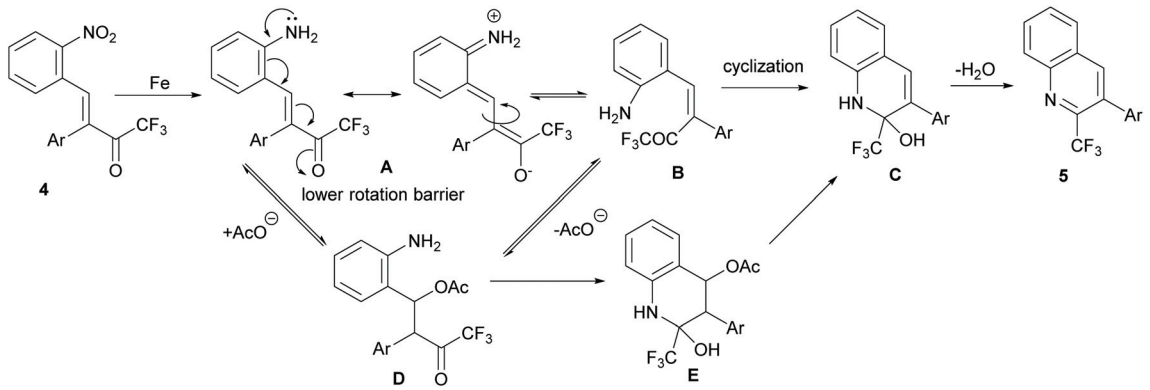
Scheme 3 Synthesis of quinolines **5** from enamines **2**.

As a proof of principle, we examined the possibility of shifting the reduction step to the beginning of the sequence. For that purpose, 2-nitrobenzaldehyde was treated with Fe powder in AcOH to form 2-aminobenzaldehyde in about 1 h. Subsequent addition of enamine **2b** followed by heating for several hours afforded quinoline **5l** in high yield (method D).

We have also shown that this approach is applicable for the preparation of quinolines with heterocyclic substituents. Thus, the 4-pyridyl derived quinoline **5v** was synthesized in 40% yield (method C). In addition, the approach can be expanded to the synthesis of other heterocyclic cores. Starting from 2-nitrothiophene-3-carbaldehyde, 6-(trifluoromethyl)thieno[2,3-*b*]pyridine **5w** was obtained in good yield. Using 4-amino-3-pyridinecarbaldehyde, the corresponding trifluoromethylated 1,6-naphthyridine **5x** was prepared in 84% yield using method E.

The possible mechanism of the reaction should be discussed due to the fact that the enones are formed exclusively or preferentially as *E*-isomers. The transformation can be rationalized as follows. In the first step, reduction of the nitro-group takes place to form the *E*-configured aniline **A** (Scheme 4). Cyclization of this intermediate into quinoline **5** is not possible due to geometrical reasons. However, isomerization of the double bond of *E*-aniline **A** can occur very easily due to the low rotation barrier for the double bond. Such isomerization is typical for CF_3-substituted aminoenones.[9d] It can be explained by the corresponding resonance form of **A** (Scheme 4). Cyclization of *Z*-aniline **B** thus formed leads to intermediate **C**, which eliminates water to finally give **5**.

It should be noted that similar isomerization of non-fluorinated analogs of 2-aminostyryl ketones does not proceed spontaneously in contrast to CF_3-derived **A**. Thus, isomerization of non-fluorinated 2-aminostyryl ketones requires catalysis by phosphoric acid derivatives,[32] benzylamine[33] or iodide.[34] Taking into account these data, an alternative explanation for the isomerization of **A** can be proposed, using the participation of acetate in the reaction. Reversible Michael addition of AcO^- to the activated double bond of **A** leads to intermediate **D**. Subsequent elimination of acetate results in the desired *Z*-aniline **B**. Alternatively, cyclization of **D** can afford the tetrahydroquinoline intermediate **E**, which eliminates acetate to give **C** (Scheme 4).



Scheme 4 Possible mechanism of the reduction–heterocyclization sequence.

Conclusions

In conclusion, we developed a novel approach to 2-CF_3-3-aryl-quinolines **5**. The target trifluoromethylated derivatives **5** were prepared in up to quantitative yield by reduction of nitro-substituted α,β-diaryl-CF_3-enones by an Fe–AcOH system. Key nitro-substituted α,β-diaryl-CF_3-enones can be prepared by condensation of α-CF_3-enamines with 2-nitrobenzaldehydes. Efficient one-pot 2-step (from enamines) and 3-step (from styrenes) protocols for the synthesis of the target trifluoromethylated quinolines were also developed. The high yields and broad scope of all synthetic transformations are distinct advantages of the method.

Experimental

General remarks

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker AVANCE 400.1 MHz spectrometer in $CDCl_3$ at 400.1, 100.6 and 376.5 MHz respectively. Chemical shifts (δ) in ppm are reported with use of the residual chloroform signals (7.25 for ^{1}H and 77.0 for ^{13}C) as internal reference. The ^{19}F chemical shifts were referenced to C_6F_6 (−162.9 ppm). The coupling constants (J) are given in Hertz (Hz). The following abbreviations are used in reporting NMR data: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; ddd, doublet of doublets of doublets; td, triplet of doublets; pt, pseudo-triplet; ptd, pseudo-triplet of doublets; m, multiplet. ESI-MS spectra were recorded with an Orbitrap Elite instrument. TLC analysis was performed on "Merck 60 F_{254}" plates. Column chromatography was performed on silica gel. Melting points were determined on an Electrothermal 9100 apparatus. All reagents were of reagent grade and were used as received or distilled prior to use. The starting α-CF_3-β-aryl enamines **2** were synthesized by the reaction of β-halogeno-β-trifluoromethylstyrenes with 2.2 equivalents of lithium pyrrolidide (generated by the reaction of pyrrolidine and *n*-BuLi, **2a–e**) in THF (method A) or by the reaction with 10 equivalents of neat pyrrolidine (**2f–k**, method B), using previously reported procedures.[35] The NMR data of compounds **2a–c** and **2g–j** are in agreement with those in the literature.[35] 2-Nitrothiophene-3-carbaldehyde[36] and 4-aminonicotinaldehyde[37] were prepared as previously reported.

(*Z*)-4-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)pyridine (1j)

Obtained from isonicotinaldehyde (16.07 g, 150 mmol) by a catalytic olefination reaction using the procedure used for olefination of picolinaldehyde.[38] Burgundy oil, yield 16.51 g (53%). Mixture of *Z*- and *E*-isomers: 82 : 18. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.23 (s, 1H, CH═C), 7.46–7.54 (m, 2H, Py), 8.64–8.74 (m, 2H, Py). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 120.1 (q, $^1J_{CF}$ = 272.4 Hz, CF_3), 123.3, 123.7 (q, $^2J_{CF}$ = 37.4 Hz, C–CF_3), 128.4 (q, $^3J_{CF}$ = 4.4 Hz, CH═CCF_3), 138.7, 150.2. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −70.4 (d, ^4J = 0.7 Hz, 3F, CF_3). *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.09–7.15 (m, 2H, Py), 7.17 (s, 1H, CH═C), 8.58–8.64 (m, 2H, Py). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 119.8 (q, $^1J_{CF}$ = 274.4 Hz, CF_3), 122.4 (q, $^3J_{CF}$ = 2.0 Hz), 124.2 (q, $^2J_{CF}$ = 38.4 Hz, C–CF_3), 133.9 (q, $^3J_{CF}$ = 2.4 Hz, CH═CCF_3), 140.1, 149.8. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.9. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_8H_6ClF_3N^+$: 208.0135; found: 208.0130.

Synthesis of enamines 2 by the reaction of styrenes 1 with lithium pyrrolidide (method A)

A preheated three neck 250 mL round bottomed flask was flushed with argon, charged with dry THF (75 mL) and dry pyrrolidine (6.72 mL, 82 mmol), and cooled down to −70 °C. Next, *n*-BuLi (32 mL, 80 mmol, 2.5 M solution of *n*-BuLi in hexane) was added dropwise over 5 min. The cooling bath was removed and the reaction mixture was allowed to warm to −5–0 °C. After that the reaction mixture was cooled down to −70 °C and the corresponding styrene **1** (40 mmol) was slowly added. The reaction mixture was allowed to warm to room temperature and quenched with water (80 mL). The organic phase was separated and the water phase was extracted with ether (3 × 20 mL). The combined extracts were washed with water (50 mL) and brine (50 mL), and dried over Na_2SO_4. Volatiles were removed *in vacuo*, and the residue was filtered

through a short silica gel pad using hexane followed by hexane–CH_2Cl_2 (3 : 1).

(*Z*)-1-(3,3,3-Trifluoro-1-phenylprop-1-en-2-yl)pyrrolidine (2a)

Obtained from (*Z*)-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl) benzene **1a** (8.26 g, 40 mmol) by method A. Pale brown oil, yield 8.26 g (86%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.85–1.93 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.11–3.18 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 6.24 (s, 1H, C$\underline{H}$=C), 7.23–7.29 (m, 1H, Ph), 7.35–7.39 (m, 4H, Ph). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.5, 50.2, 110.0 (q, $^3J_{CF}$ = 5.9 Hz, $\underline{C}$H=CCF_3), 122.5 (q, $^1J_{CF}$ = 278.8 Hz, CF_3), 136.6 (q, $^2J_{CF}$ = 28.5 Hz, $\underline{C}$–CF_3), 126.5, 127.8, 129.3, 135.8. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.7.

(*Z*)-1-(3,3,3-Trifluoro-1-(4-methoxyphenyl)prop-1-en-2-yl) pyrrolidine (2b)

Obtained from (*Z*)-1-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-4-methoxybenzene **1b** (9.46 g, 40 mmol) by method A. Slightly brown oil, yield 9.41 g (87%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.81–1.89 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.04–3.11 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 3.84 (s, 3H, OCH_3), 6.21 (s, 1H, C$\underline{H}$=C), 6.88 (d, ^3J = 8.7 Hz, 2H, Ar), 7.34 (d, ^3J = 8.7 Hz, 2H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.4, 49.9, 55.1, 112.9 (q, $^3J_{CF}$ = 5.1 Hz, $\underline{C}$H=CCF_3), 122.8 (q, $^1J_{CF}$ = 279.6 Hz, CF_3), 132.2 (q, $^2J_{CF}$ = 27.8 Hz, $\underline{C}$–CF_3), 113.4, 127.9, 130.6, 158.6. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.4.

(*Z*)-1-(1-(4-Chlorophenyl)-3,3,3-trifluoroprop-1-en-2-yl) pyrrolidine (2c)

Obtained from (*Z*)-1-chloro-4-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)benzene **1c** (9.64 g, 40 mmol) by method A. Slightly brown oil, yield 7.97 g (72%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.76–1.85 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.00–3.07 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 6.06 (s, 1H, C$\underline{H}$=C), 7.19 (d, ^3J = 8.6 Hz, 2H, Ar), 7.25 (d, ^3J = 8.6 Hz, 2H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.5, 50.2, 108.2 (q, $^3J_{CF}$ = 5.9 Hz, $\underline{C}$H=CCF_3), 122.2 (q, $^1J_{CF}$ = 278.8 Hz, CF_3), 134.1 (q, $^2J_{CF}$ = 28.5 Hz, $\underline{C}$–CF_3), 127.9, 130.3, 131.8, 134.2. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −64.6.

(*Z*)-1-(3,3,3-Trifluoro-1-(4-fluorophenyl)prop-1-en-2-yl) pyrrolidine (2d)

Obtained from (*Z*)-1-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-4-fluorobenzene **1d** (2.240 g, 10 mmol), pyrrolidine (1.23 mL, 15 mmol, 1.5 equiv.) and *n*-BuLi (6 mL, 15 mmol, 1.5 equiv.) by method A. Slightly brown oil, yield 1.760 g (68%). Mixture of *Z*- and *E*-isomers: 95 : 5. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.76–1.87 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.02–3.05 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 6.11 (s, 1H, C$\underline{H}$=C), 6.96–7.03 (m, 2H, Ar), 7.25–7.30 (m, 2H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.4, 50.1 (q, $^4J_{CF}$ = 1.1 Hz, N($\underline{C}H_2CH_2$)$_2$), 109.5 (q, $^3J_{CF}$ = 5.9 Hz, $\underline{C}$H=CCF_3), 114.7 (d, $^2J_{CF}$ = 21.4 Hz), 122.4 (q, $^1J_{CF}$ = 279.0 Hz, CF_3), 130.7 (d, $^3J_{CF}$ = 7.7 Hz), 131.6 (d, $^4J_{CF}$ = 3.5 Hz), 133.5 (dq, $^2J_{CF}$ = 26.7 Hz, $\underline{C}$–CF_3), 161.3 (d, $^1J_{CF}$ = 246.5 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.5 (s, 3F, CF_3), −115.50, −116.15 (m, 1F, 4-FC_6H_4). HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}F_4N^+$: 260.1057; found: 260.1060. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 2.00–2.04 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.16–3.19 (m, 4H, N($C\underline{H}_2CH_2$)$_2$) 5.59 (s, 1H, C$\underline{H}$=C), 6.91–6.96 (m, 2H, Ar). Other signals are overlapped with those of the major isomer. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 24.7, 49.4 (q, $^4J_{CF}$ = 1.9 Hz, N($\underline{C}H_2CH_2$)$_2$). Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.5 (s, 3F, CF_3), −117.72, −117.97 (m, 1F, 4-FC_6H_4).

(*Z*)-1-(3,3,3-Trifluoro-1-(4-(pyrrolidin-1-yl)phenyl)prop-1-en-2-yl)pyrrolidine (2e)

Obtained from (*Z*)-1-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-4-fluorobenzene **1d** (5.78 g, 18 mmol), pyrrolidine (4.42 mL, 54 mmol, 3 equiv.) and *n*-BuLi (22 mL, 55 mmol, 3 equiv.) by method A. Slightly beige solid, m.p. 57–58 °C, yield 4.035 g (72%). Mixture of *Z*- and *E*-isomers: 97 : 3. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.82–1.90 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 1.98–2.06 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.07–3.11 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 3.31–3.34 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 6.29 (s, 1H, C$\underline{H}$=C), 6.53 (d, ^3J = 8.8 Hz, 2H, Ar), 7.38 (d, ^3J = 8.8 Hz, 2H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.3, 25.5, 47.5, 49.5, 111.0, 117.3 (q, $^3J_{CF}$ = 6.1 Hz, $\underline{C}$H=CCF_3), 122.0, 123.3 (q, $^1J_{CF}$ = 280.0 Hz, CF_3), 129.8 (q, $^2J_{CF}$ = 27.5 Hz, $\underline{C}$–CF_3), 130.7, 147.0. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −64.7. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.92–1.95 (m, 4H, N($CH_2C\underline{H}_2$)$_2$), 3.13–3.16 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 3.28–3.31 (m, 4H, N($C\underline{H}_2CH_2$)$_2$), 5.79 (s, 1H, C$\underline{H}$=C), 6.51 (d, ^3J = 8.6 Hz, 2H, Ar), 7.11 (d, ^3J = 8.6 Hz, 2H, Ar). Other signals are overlapped with those of the major isomer. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 24.36, 24.42, 45.0, 49.8, 110.9, 130.5 (q, $^2J_{CF}$ = 29.4 Hz, $\underline{C}$–CF_3), 130.9. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.8. HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}F_3N_2^+$: 311.1730; found: 311.1723.

Synthesis of α-CF_3-β-arylenamines by the reaction with neat pyrrolidine (general procedure, method B)

A one neck 25 mL round bottomed flask was charged with dry pyrrolidine (8.5 mL, 100 mmol) and cooled down to −18 °C, and the corresponding styrene **1** (10 mmol) was added in one portion with vigorous stirring. The reaction mixture was stirred at room temperature for 1–3 h until all starting styrene was consumed (TLC monitoring). The excess pyrrolidine was evaporated *in vacuo*, and the viscous residue was dissolved in CH_2Cl_2 (50 mL), washed with water (3 × 50 mL) and dried over Na_2SO_4. CH_2Cl_2 was removed *in vacuo*, and the residue was filtered through a short silica gel pad using hexane or appropriate mixtures of hexane and CH_2Cl_2. The *Z*/*E*-isomers of enamines **2** could not be separated by column chromatography.

1-[(1*Z*)-3,3,3-Trifluoro-1-(4-trifluoromethylphenyl)prop-1-en-2yl]pyrrolidine (2f)

Obtained from (*Z*)-1-(2-bromo-3,3,3-trifluoroprop-1-en-1-yl)-4-(trifluoromethyl)benzene **1e** (3.962 g, 12.420 mmol) by method

B. Colourless oil, yield 3.257 g (85%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.80–1.87 (m, 4H, N($CH_2C\underline{H}_2)_2$), 3.04–3.08 (m, 4H, N($C\underline{H}_2CH_2)_2$), 6.07 (s, 1H, CH=C), 7.30 (d, ^3J = 8.3 Hz, 2H, Ar), 7.54 (d, ^3J = 8.3 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 25.5, 50.6 (q, $^4J_{CF}$ = 1.7 Hz, N($\underline{C}H_2CH_2)_2$), 105.9 (q, $^3J_{CF}$ = 6.1 Hz, $\underline{C}H{=}CCF_3$), 122.0 (q, $^1J_{CF}$ = 278.6 Hz, CF_3), 124.2 (q, $^1J_{CF}$ = 271.6 Hz, CF_3), 124.6 (q, $^3J_{CF}$ = 3.7 Hz), 127.8 (q, $^2J_{CF}$ = 32.4 Hz, $\underline{C}{-}CF_3$) 129.1, 135.3 (q, $^2J_{CF}$ = 28.4 Hz, $\underline{C}{-}CF_3$(Ar)), 139.7 (d, $^4J_{CF}$ = 1.3 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.8 (CF_3), −63.5 (4-$CF_3C_6H_4$). HRMS (ESI-TOF): m/z [M] calcd for $C_{14}H_{13}F_6N$: 309.0947; found: 309.0943; m/z [M + H]$^+$ calcd for $C_{14}H_{13}F_6N^+$: 310.1025; found: 310.1020.

(*Z*)-1-(1-(2-Bromophenyl)-3,3,3-trifluoroprop-1-en-2-yl) pyrrolidine (2g)

Obtained from (*Z*)-1-bromo-2-(2-bromo-3,3,3-trifluoroprop-1-en-1-yl)benzene **1f** (3.3001 g, 10.005 mmol) by method B. Colorless oil, yield 2.402 g (75%). Mixture of *Z*- and *E*-isomers: 90 : 10. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.70–1.75 (m, 4H, N($CH_2C\underline{H}_2)_2$), 2.93–2.97 (m, 4H, N($C\underline{H}_2CH_2)_2$), 5.93 (s, 1H, $C\underline{H}$=C), 6.98 (td, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, Ar), 7.13 (dd, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 1H, Ar), 7.16–7.22 (m, 1H, Ar), 7.47 (dd, ^3J = 7.9 Hz, ^4J = 0.6 Hz, 1H, Ar). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.9. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.88–1.92 (m, 4H, N($CH_2C\underline{H}_2)_2$), 3.19–3.22 (m, 4H, N($C\underline{H}_2CH_2)_2$), 5.43 (s, 1H, CH=C). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −60.3.

(*Z*)-1-(3,3,3-Trifluoro-1-(4-nitrophenyl)prop-1-en-2-yl) pyrrolidine (2h)

Obtained from (*Z*)-1-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-4-nitrobenzene **1g** (2.516 g, 10.000 mmol) by method B. Orange-yellow crystals, m.p. 74–77 °C, yield 2.576 g (90%). Mixture of *Z*- and *E*-isomers: 96 : 4. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.81–1.91 (m, 4H, N($CH_2C\underline{H}_2)_2$), 3.07–3.10 (m, 4H, N($C\underline{H}_2CH_2)_2$), 6.03 (s, 1H, CH=C), 7.26 (d, ^3J = 8.7 Hz, 2H, Ar), 8.14 (d, ^3J = 8.7 Hz, 2H, Ar). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.9. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.37 (s, 1H, CH=C), 7.86 (d, ^3J = 8.8 Hz, 2H, Ar), 8.29 (d, ^3J = 8.8 Hz, 2H, Ar). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.8.

(*Z*)-1-(3,3,3-Trifluoro-1-(3-nitrophenyl)prop-1-en-2-yl) pyrrolidine (2i)

Obtained from (*Z*)-1-(2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-3-nitrobenzene **1h** (6.780 g, 26.949 mmol) by method B. Yellow oil, yield 6.865 g (89%). Mixture of *Z*- and *E*-isomers: 97 : 3. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.81–1.90 (m, 4H, N($CH_2C\underline{H}_2)_2$), 3.05–3.08 (m, 4H, N($C\underline{H}_2CH_2)_2$), 6.08 (s, 1H, CH=C), 7.46 (td, ^3J = 15.7 Hz, ^3J = 7.8 Hz, 2H, Ar), 8.00 (d, ^3J = 8.0 Hz, 1H, Ar), 8.06 (s, 1H, Ar). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −66.0. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.94–1.98 (m, 4H, 2N$CH_2C\underline{H}_2$), 3.22–3.26 (m, 4H, 2N$C\underline{H}_2CH_2$), 5.50 (s, 1H, CH=C). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.7.

Methyl 4-[(1*Z*)-3,3,3-trifluoro-2-pyrrolidin-1-ylprop-1-enyl] benzoate (2j)

Obtained from methyl (*Z*)-4-(2-bromo-3,3,3-trifluoroprop-1-en-1-yl)benzoate **1i** (3090 mg, 10 mmol) by method B by performing the reaction overnight. Yield 2542 mg (85%); colorless oil; IR (nujol) 1610 (C=C), 1720 (C=O, CO_2Me) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82–1.89 (m, 4H, 2N$CH_2C\underline{H}_2$), 3.04–3.11 (m, 4H, 2N$C\underline{H}_2CH_2$), 3.93 (s, 3H, $CO_2C\underline{H}_3$), 6.10 (s, 1H, $C\underline{H}{=}CCF_3$), 7.27 (d, J = 8.2 Hz, 2H, Ar), 7.98 (d, J = 8.2 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5 (2N$CH_2\underline{C}H_2$), 50.6 (2N$\underline{C}H_2CH_2$), 52.0 ($CO_2\underline{C}H_3$), 106.4 (q, J = 5.9 Hz, $\underline{C}H{=}CCF_3$), 122.0 (q, J = 278.8 Hz, CF_3), 135.2 (q, J = 28.5 Hz, $\underline{C}{-}CF_3$), 127.4, 128.8, 129.0, 140.9 (Ar), 166.9 ($\underline{C}O_2CH_3$).

(*Z*)-Pyrrolidin-1-yl(4-(3,3,3-trifluoro-2-(pyrrolidin-1-yl)prop-1-en-1-yl)phenyl)methanone (2k)

Obtained from methyl (*Z*)-4-(2-bromo-3,3,3-trifluoroprop-1-en-1-yl)benzoate **1i** (3.092 g, 10 mmol) by method B by performing the reaction for 7 days. Yellow oil, yield 2.970 g (88%). Mixture of *Z*- and *E*-isomers: 76 : 24. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.75–2.02 (m, 8H, 2N($CH_2C\underline{H}_2)_2$), 3.03–3.06 (m, 4H, N($C\underline{H}_2CH_2)_2$), 3.43–3.46 (m, 2H, N($C\underline{H}_2CH_2)_2$), 3.61–3.65 (m, 2H, N($C\underline{H}_2CH_2)_2$), 6.07 (s, 1H, CH=C), 7.24 (d, ^3J = 8.3 Hz, 2H, Ar), 7.45 (d, ^3J = 8.3 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 24.2, 25.3, 26.2, 46.02, 49.4, 50.2 (q, $^4J_{CF}$ = 1.3 Hz), 107.5 (q, $^3J_{CF}$ = 6.1 Hz, $\underline{C}H{=}CCF_3$), 122.0 (q, $^1J_{CF}$ = 278.8 Hz, CF_3), 126.50, 128.5, 134.2 (q, $^2J_{CF}$ = 28.3 Hz, $\underline{C}{-}CF_3$), 134.5, 137.3, 169.2. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.8. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.19–3.22 (m, 4H, N($C\underline{H}_2CH_2)_2$), 5.59 (s, 1H, $C\underline{H}$=C), 7.18 (d, ^3J = 8.2 Hz, 2H, Ar), 7.41 (d, ^3J = 8.2 Hz, 2H, Ar). Other signals are overlapped with those of the major isomer. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 24.5, 45.98, 49.2 (q, $^4J_{CF}$ = 1.9 Hz), 105.6 (q, $^3J_{CF}$ = 3.1 Hz, $\underline{C}H$=C), 121.8 (q, $^1J_{CF}$ = 277.9 Hz, CF_3), 126.47, 128.6 (q, $^3J_{CF}$ = 2.3 Hz), 134.3, 135.3 (q, $^2J_{CF}$ = 30.1 Hz, $\underline{C}{-}CF_3$), 138.3, 169.4. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.7. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{22}F_3N_2O^+$: 339.1679; found: 339.1681; [M + Na]$^+$ calcd for $C_{18}H_{21}F_3N_2NaO^+$: 361.1498; found: 361.1496.

4-(3,3,3-Trifluoro-2-(pyrrolidin-1-yl)prop-1-en-2-yl)pyridine (2l)

Obtained from 4-[2-chloro-3,3,3-trifluoro-1-propenyl]pyridine **1j** (1.07 g, 4.8 mmol) by method B. Pale brown oil, yield 1.09 g (94%). Mixture of *Z*- and *E*-isomers: 74 : 26. For the mixture of isomers: *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.76–1.84 (m, 4H, N($CH_2C\underline{H}_2)_2$), 3.02–3.05 (m, 4H, N($C\underline{H}_2CH_2)_2$), 5.87 (s, 1H, CH=C), 6.97 (d, ^3J = 5.9 Hz, 2H, Py), 8.45 (d, ^3J = 4.9 Hz, 2H, Py). $^{13}C\{1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 25.4, 50.9 (q, $^4J_{CF}$ = 1.7 Hz), 102.9 (q, $^3J_{CF}$ = 6.3 Hz, $\underline{C}H{=}CCF_3$), 121.6 (q, $^1J_{CF}$ = 278.8 Hz, CF_3), 123.3, 136.5 (q, $^2J_{CF}$ = 28.8 Hz, $\underline{C}{-}CF_3$), 143.7,

149.0. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −65.9. *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.87–1.93 (m, 4H, $N(CH_2\underline{C}H_2)_2$), 3.19–3.23 (m, 4H, $N(\underline{C}H_2CH_2)_2$), 5.33 (s, 1H, CH═C), 7.01 (d, ^3J = 5.4 Hz, 2H, Py), 8.40 (d, ^3J = 4.5 Hz, 2H, Py). ^{13}C{1H} NMR (100.6 MHz, $CDCl_3$): δ 24.8, 49.3 (q, $^4J_{CF}$ = 2.7 Hz), 102.0 (q, $^3J_{CF}$ = 3.0 Hz, $\underline{C}H$═CCF_3), 121.7 (q, $^1J_{CF}$ = 277.9 Hz, CF_3), 123.9, 136.4 (q, $^2J_{CF}$ = 30.2 Hz, $\underline{C}$–CF_3), 144.9. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −59.8. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{14}F_3N_2^+$: 243.1104; found: 243.1106.

Synthesis of α,β-diaryl-CF_3-enones 4 by the reactions of α-CF_3-β-aryl enamines 2 with aromatic aldehydes 3 (general procedure)

A one-necked 50 mL round bottom flask (or 12 mL vial) was charged with enamine **2** (5 mmol), aromatic aldehyde **3** (5.75 mmol) and glacial acetic acid (10 mL or 5 mL for reaction in a vial). The reaction mixture was kept at 80–90 °C under stirring for 6–12 hours until the aldehyde was consumed and the corresponding benzyl ketone formed by hydrolysis of the enamine (monitored by ^{1}H NMR). Volatiles were evaporated *in vacuo*, and the residue was dissolved in CH_2Cl_2 (50 mL), washed with water (2 × 20 mL) and dried over Na_2SO_4. Volatiles were evaporated *in vacuo*, and the residue was purified by column chromatography, using appropriate mixtures of hexane and CH_2Cl_2 or CH_2Cl_2 as eluents.

(*E*)-1,1,1-Trifluoro-4-(2-nitrophenyl)-3-phenylbut-3-en-2-one (4a)

Obtained from enamine **2a** (1.206 g, 5.0 mmol) and 2-nitrobenzaldehyde (0.869 g, 5.75 mmol). Yellow oil, yield 1.225 g (76%). Mixture of *E*- and *Z*-isomers: 97 : 3. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.93 (d, ^3J = 7.8 Hz, 1H, 2-$NO_2C_6H_4$), 7.02–7.10 (m, 2H, Ph), 7.21–7.30 (m, 3H, Ph), 7.34 (td, ^3J = 7.8 Hz, ^4J = 1.2 Hz, 1H, 2-$NO_2C_6H_4$), 7.41 (td, ^3J = 7.8 Hz, ^4J = 1.2 Hz, 1H, 2-$NO_2C_6H_4$), 8.14 (dd, ^3J = 7.8 Hz, ^4J = 1.2 Hz, 1H, 2-$NO_2C_6H_4$), 8.19 (s, 1H, CH═C). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 116.5 (q, $^1J_{CF}$ = 292.1 Hz, CF_3), 124.8, 128.4, 128.7, 129.9, 130.1, 130.7, 131.6, 132.1, 133.4, 136.2, 143.3 (q, $^4J_{CF}$ = 3.3 Hz, $\underline{C}$═C–C═O), 147.7, 181.1 (q, $^2J_{CF}$ = 34.5, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.3. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.55 (td, ^3J = 8.2 Hz, ^4J = 1.1 Hz, 1H, 2-$NO_2C_6H_4$), 7.61–7.67 (m, 2H, 2-$NO_2C_6H_4$ and CH═C), 8.22 (dd, ^3J = 8.2 Hz, ^4J = 1.1 Hz, 2-$NO_2C_6H_4$). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.3. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{11}F_3NO_3^+$: 322.0686; found: 322.0679.

(*E*)-3-Nitro-4-(4,4,4-trifluoro-3-oxo-2-phenylbut-1-en-1-yl) benzonitrile (4b)

Obtained from enamine **2a** (1.206 g, 5.0 mmol) and 4-formyl-3-nitrobenzonitrile (1.013 g, 5.75 mmol). Dark orange viscous liquid, yield 1.368 g (79%). Mixture of *E*- and *Z*-isomers: 86 : 14. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.02–7.05 (m, 2H, Ph), 7.07 (d, ^3J = 8.1 Hz, 1H, Ar), 7.26–7.35 (m, 3H, Ph), 7.58 (dd, ^3J = 8.1 Hz, ^4J = 1.5 Hz, 1H, Ar), 8.10 (s, 1H, CH═C), 8.43 (d, ^4J = 1.5 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 113.9, 115.9, 116.3 (q, $^1J_{CF}$ = 292.0 Hz, CF_3), 128.5, 128.8, 129.4, 130.0, 131.2, 132.9, 135.2, 135.9, 137.9, 140.4 (q, $^4J_{CF}$ = 3.2 Hz, $\underline{C}$═C–C═O), 147.7, 180.8 (q, $^2J_{CF}$ = 34.0 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.6. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.39–7.47 (m, 5H, Ph), 7.53 (d, ^3J = 8.0 Hz, 1H, Ar), 7.92 (dd, ^3J = 8.0 Hz, ^4J = 1.5 Hz, 1H, Ar), 8.47 (d, ^4J = 1.5 Hz, 1H, Ar). Other signals are overlapped with those of the major isomer. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 113.8, 115.9, 127.1, 128.7, 129.1, 132.4, 133.26, 134.9, 136.6, 139.4, 147.2. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −75.9. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{10}F_3N_2O_3^+$: 347.0638; found: 347.0633.

(*E*)-4-(2,4-Dinitrophenyl)-1,1,1-trifluoro-3-phenylbut-3-en-2-one (4c)

Obtained from enamine **2a** (1.206 g, 5.0 mmol) and 2,4-dinitrobenzaldehyde (1.127 g, 5.75 mmol). Dark orange viscous liquid, yield 1.061 g (58%). Mixture of *E*- and *Z*-isomers: 94 : 6. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.03–7.08 (m, 2H, Ph), 7.17 (d, ^3J = 8.6 Hz, 1H, Ar), 7.25–7.35 (m, 3H, Ph), 8.13 (s, 1H, CH═C), 8.16 (dd, ^3J = 8.6 Hz, ^4J = 2.3 Hz, 1H, Ar), 8.96 (d, ^4J = 2.3 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 116.3 (q, $^1J_{CF}$ = 291.9 Hz, CF_3), 120.3, 127.3, 128.8, 129.4, 130.0, 131.2, 133.3, 136.8, 138.1, 140.1 (q, $^4J_{CF}$ = 3.2 Hz, $\underline{C}$═C–C═O), 147.5, 147.8, 180.8 (q, $^2J_{CF}$ = 35.2 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.8. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.41–7.48 (m, 4H), 7.62 (t, ^4J = 4.0 Hz, 2H, Ph), 8.47 (dd, ^3J = 8.5 Hz, ^4J = 2.3 Hz, 1H, Ar), 8.98 (d, ^4J = 2.3 Hz, 1H, Ar). Other signals are overlapped with those of the major isomer. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 115.0 (q, $^1J_{CF}$ = 292.7 Hz, CF_3), 120.5, 120.6, 127.1, 127.9, 128.9, 129.1, 129.4, 132.3, 132.7, 136.6, 139.7, 147.3, 186.0 (q, $^2J_{CF}$ = 36.8 Hz, $\underline{C}$═O). Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −75.7. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{10}F_3N_2O_5^+$: 367.0536; found: 367.0523.

(*E*)-1,1,1-Trifluoro-4-(2-nitro-4-(trifluoromethyl)phenyl)-3-phenylbut-3-en-2-one (4d)

Obtained from enamine **2a** (0.482 g, 2 mmol) and 2-nitro-4-(trifluoromethyl)benzaldehyde (0.460 g, 2.100 mmol). Orange viscous liquid, yield 0.529 g (68%). Mixture of *E*- and *Z*-isomers: 99 : 1. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.06–7.08 (m, 2H, Ph), 7.12 (d, ^3J = 8.2 Hz, 1H, Ar), 7.24–7.33 (m, 3H, Ph), 7.57–7.62 (m, 1H, Ar), 8.16 (s, 1H, CH═C), 8.41 (d, ^4J = 0.6 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 116.5 (q, $^1J_{CF}$ = 291.9 Hz, CF_3), 122.2 (q, $^4J_{CF}$ = 3.8 Hz, Ar–CF_3), 122.4 (q, $^1J_{CF}$ = 272.9 Hz, Ar–CF_3), 128.7, 129.2, 129.8 (q, $^4J_{CF}$ = 3.2 Hz, Ar–CF_3), 130.0, 131.5, 132.1 (q, $^2J_{CF}$ = 34.5 Hz, Ar–CF_3), 132.8, 134.3, 137.5, 141.1 (q, $^4J_{CF}$ = 3.3 Hz, $\underline{C}$═C–

C═O), 147.7, 181.0 (q, $^{2}J_{CF}$ = 34.9 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.4 ($COCF_3$), −64.2 (Ar–CF_3). For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.43–7.48 (m, 5H, Ph), 7.54 (d, ^{3}J = 8.0 Hz, 1H, Ar–CF_3), 7.91 (dd, ^{3}J = 8.0 Hz, ^{4}J = 0.9 Hz, 1H, Ar–CF_3), 8.47 (br s, 1H, Ar–CF_3). Other signals are overlapped with those of the major isomer. $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 127.2, 129.9, 132.4, 132.70, 132.71. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.0 ($COCF_3$), −64.1 (Ar–CF_3). HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_9F_6NO_3Na^+$: 412.0379; found: 412.0391.

(*E*)-4-(4-Chloro-2-nitrophenyl)-1,1,1-trifluoro-3-phenylbut-3-en-2-one (4e)

Obtained from enamine **2a** (1.205 g, 5 mmol) and 4-chloro-2-nitrobenzaldehyde (0.978 g, 5.26 mmol). Pale yellow viscous liquid, yield 1.336 g (75%). Mixture of *E*- and *Z*-isomers: 97 : 3. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.87 (d, ^{3}J = 8.4 Hz, 1H, Ar), 7.05–7.07 (m, 2H, Ph), 7.24–7.35 (m, 3H, Ph and 1H, Ar), 8.10 (s, 1H, CH═C), 8.13 (d, ^{4}J = 2.0 Hz, 1H, Ar). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.5 (q, $^{1}J_{CF}$ = 291.9 Hz, CF_3), 125.1, 128.7, 129.0, 129.1, 130.1, 131.8, 132.8, 133.5, 135.9, 136.8, 141.6 (q, $^{4}J_{CF}$ = 3.5 Hz, C═C–C═O), 148.1, 181.0 (q, $^{2}J_{CF}$ = 34.8 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.4. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.42–7.50 (m, 5H, Ph), 7.56 (s, 1H, CH═C), 7.64 (dd, ^{3}J = 8.2 Hz, ^{4}J = 2.0 Hz, 1H, Ar), 8.22 (d, ^{4}J = 2.0 Hz, 1H, Ar). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.1. HRMS (ESI-TOF): *m*/*z* $[M + NH_4]^+$ calcd for $C_{16}H_{13}ClF_3N_2O_3^+$: 373.0561; found: 373.0566.

Methyl-3-nitro-4-[(1*E*)-4,4,4-trifluoro-3-oxo-2-phenylbut-1-en-1-yl]benzoate (4f)

Obtained from enamine **2a** (1.205 g, 5 mmol) and methyl 4-formyl-3-nitrobenzoate (1.097 g, 2.25 mmol). Yellow viscous liquid, yield 1.321 g (70%). Mixture of *E*- and *Z*-isomers: 96 : 4. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.94 (s, 3H, CH_3), 7.02–7.07 (m, 3H, Ar, Ph), 7.24–7.31 (m, 3H, Ph), 7.98 (dd, ^{3}J = 8.1 Hz, ^{4}J = 1.3 Hz, 1H, Ar), 8.17 (s, 1H, CH═C), 8.77 (d, ^{4}J = 1.3 Hz, 1H, Ar). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 52.9, 116.5 (q, $^{1}J_{CF}$ = 291.9 Hz, CF_3), 125.9, 128.6, 129.1, 130.1, 131.7, 131.8, 132.1, 133.7, 134.8, 137.2, 141.9 (q, $^{4}J_{CF}$ = 3.1 Hz, C═C–C═O), 147.8, 164.3, 181.0 (q, $^{2}J_{CF}$ = 34.7 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.5. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.44–7.49 (m, 5H, Ph), 7.63 (s, 1H, CH═C), 8.29 (dd, ^{3}J = 7.9 Hz, ^{4}J = 1.4 Hz, 1H, Ar), 8.85 (d, ^{4}J = 1.3 Hz, 1H, Ar). Other signals are overlapped with those of the major isomer. $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 127.2, 129.2, 129.8. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.2. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{13}F_3NO_5^+$: 380.0740; found: 380.0731.

(*E*)-4-(3,5-Dimethyl-2-nitrophenyl)-1,1,1-trifluoro-3-phenylbut-3-en-2-one (4g)

Obtained from enamine **2a** (1.222 g, 5.065 mmol) and 3,5-dimethyl-2-nitrobenzaldehyde (1.043 g, 5.821 mmol). Light beige solid, m.p. 56–59 °C, yield 1.132 g (64%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 6.46 (s, 1H, Ar), 7.00 (s, 1H, Ar), 7.10–7.15 (m, 2H, Ph), 7.27–7.34 (m, 3H, Ph), 7.74 (s, 1H, CH═C). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 18.3, 20.9, 116.5 (q, $^{1}J_{CF}$ = 292.1 Hz, CF_3), 127.8, 128.5, 128.8, 129.1, 130.0, 131.2, 132.3, 133.3, 137.7, 140.2 (q, $^{4}J_{CF}$ = 2.8 Hz, C═C–C═O), 140.9, 148.6, 181.2 (q, $^{2}J_{CF}$ = 34.4 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.4. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{15}F_3NO_3^+$: 350.0999; found: 350.1009.

(*E*)-1,1,1-Trifluoro-4-(6-nitrobenzo[*d*][1,3]dioxol-5-yl)-3-phenylbut-3-en-2-one (4h)

Obtained from enamine **2a** (1.257 g, 5.210 mmol) and 6-nitrobenzo[*d*][1,3]dioxole-5-carbaldehyde (1.169 g, 5.992 mmol). Yellow solid, m.p. 99–101 °C, yield 1.903 g (77%). Mixture of *E*- and *Z*-isomers: 94 : 6. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 5.97 (s, 2H, CH_2), 6.28 (s, 1H, Ar), 7.06–7.14 (m, 2H, Ph), 7.25–7.33 (m, 3H, Ph), 7.57 (s, 1H, Ar), 8.14 (s, 1H, CH═C). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 103.4, 105.1, 109.6, 116.5 (q, $^{1}J_{CF}$ = 292.2 Hz, CF_3), 127.2, 128.4, 128.7, 130.0, 132.0, 135.2, 142.3, 143.8 (q, $^{4}J_{CF}$ = 3.1 Hz, C═C–C═O), 148.6, 151.8, 180.9 (q, $^{2}J_{CF}$ = 34.3 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.3. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.03 (s, 2H, 4,5-$O_2C\underline{H}_2$-2-$NO_2C_6H_2$-), 6.25 (s, 1H, 4,5-O_2CH_2-2-$NO_2C_6\underline{H}_2$-), 7.07–7.10 (m, 2H, Ph), 7.28–7.33 (m, 3H, Ph), 7.61 (s, 1H, 4,5-O_2CH_2-2-$NO_2C_6\underline{H}_2$-), 8.12 (s, 1H, C$\underline{H}$═C). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 103.5, 105.8, 109.9, 116.8 (q, $^{1}J_{CF}$ = 292.0 Hz, CF_3), 127.2, 128.4, 128.9, 129.6, 133.4, 134.6, 141.5, 146.2 (q, $^{4}J_{CF}$ = 2.8 Hz, C═C–C═O), 148.5, 152.2, 181.2 (q, $^{2}J_{CF}$ = 33.6 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.2. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}F_3NO_5^+$: 366.0584; found: 366.0595.

(*E*)-1,1,1-Trifluoro-4-(3-methoxy-2-nitrophenyl)-3-phenylbut-3-en-2-one (4i)

Obtained from enamine **2a** (1.206 g, 5.0 mmol) and 3-methoxy-2-nitrobenzaldehyde (1.042 g, 5.75 mmol). Beige viscous liquid, yield 1.054 g (60%). Mixture of *E*- and *Z*-isomers: 98 : 2. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.88 (s, 3H, CH_3), 6.38 (d, ^{3}J = 8.2 Hz, 1H, Ar), 6.95 (d, ^{3}J = 8.2 Hz, 1H, Ar), 7.09 (d, ^{3}J = 8.2 Hz, 1H, Ar), 7.12–7.14 (m, 2H, Ph), 7.28–7.35 (m, 3H, Ph), 7.67 (s, 1H, CH═C). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 56.5, 113.6, 116.4 (q, $^{1}J_{CF}$ = 292.1 Hz, CF_3), 121.8, 128.2, 128.6, 129.0, 129.9, 130.9, 132.0, 138.2 (q, $^{4}J_{CF}$ = 2.9 Hz, C═C–C═O), 138.9, 141.0, 151.1, 181.1 (q, $^{2}J_{CF}$ = 34.4 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.4. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.89 (s, 3H, CH_3), 6.85 (d, ^{3}J = 7.7 Hz, 1H, Ar), 7.38–7.44 (m, 3H, Ph and 1H, CH═C). Other signals are overlapped with those of the major isomer. $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 113.6, 115.1 (q, $^{1}J_{CF}$ = 292.8 Hz, CF_3), 121.0, 126.9, 129.1, 129.7,

131.7, 133.9, 140.0, 140.8, 151.3, 187.5 (q, $^2J_{CF}$ = 37.0 Hz, C═O). Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.0. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{17}H_{13}F_3NO_4^+$: 352.0791; found: 352.0791.

(*E*)-4-(3,6-Dimethoxy-2-nitrophenyl)-1,1,1-trifluoro-3-phenylbut-3-en-2-one (4j)

Obtained from enamine **2a** (0.455 g, 1.887 mmol) and 3,6-dimethoxy-2-nitrobenzaldehyde (0.458 g, 2.170 mmol). Yellow solid, m.p. 92–94 °C, yield 0.489 g (68%). Mixture of *E*- and *Z*-isomers: 94 : 6. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.44 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 6.76 (d, ^3J = 9.2 Hz, 1H, Ar), 6.92 (d, ^3J = 9.2 Hz, 1H, Ar), 7.02–7.07 (m, 2H, Ph), 7.19–7.27 (m, 3H, Ph), 7.58 (s, 1H, CH═C). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.7, 56.7, 113.6, 114.2, 116.4 (q, $^1J_{CF}$ = 292.1 Hz, CF_3), 117.9, 127.8, 128.7, 129.2 132.8, 136.2 (q, $^4J_{CF}$ = 2.9 Hz, C═C–C═O), 140.3, 140.4, 144.8, 149.3, 180.8 (q, $^2J_{CF}$ = 34.7 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.3. For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.97 (d, ^3J = 7.5 Hz, 1H, Ar), 7.42–7.38 (m, 3H, Ph). Other signals are overlapped with those of the major isomer. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 113.7, 127.7, 128.8, 129.4, 140.3, 144.9. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −74.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{15}F_3NO_5^+$: 382.0897; found: 382.0897.

(*E*)-1,1,1-Trifluoro-4-(5-fluoro-2-nitrophenyl)-3-phenylbut-3-en-2-one (4k)

Obtained from enamine **2a** (1.206 g, 5.0 mmol) and 5-fluoro-2-nitrobenzaldehyde (0.972 g, 5.75 mmol). Beige crystals, m.p. 44–45 °C, yield 1.018 g (60%). Mixture of *E*- and *Z*-isomers: 99 : 1. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.64 (dd, ^3J = 8.7 Hz, ^4J = 2.7 Hz, 1H, Ar), 7.07–7.11 (m, 2H, Ph and 1H, Ar), 7.26–7.33 (m, 3H, Ph), 8.17 (s, 1H, CH═C), 8.27 (dd, ^3J = 9.2 Hz, ^3J = 5.0 Hz, 1H, Ar). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 116.4 (q, $^1J_{CF}$ = 292.0 Hz, CF_3), 116.9 (d, $^2J_{CF}$ = 23.4 Hz, Ar), 118.5 (d, $^2J_{CF}$ = 25.3 Hz, Ar), 127.7 (d, $^3J_{CF}$ = 10.2 Hz, Ar), 128.6, 129.0, 129.9, 131.5, 133.8 (d, $^3J_{CF}$ = 9.8 Hz, Ar), 136.7, 141.9 (q, $^4J_{CF}$ = 2.8 Hz, C═C–C═O), 143.8 (d, $^4J_{CF}$ = 2.8 Hz, Ar), 164.4 (d, $^1J_{CF}$ = 258.9 Hz, Ar), 181.0 (q, $^2J_{CF}$ = 34.7 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.6 (CF_3), −103.04 to −103.11 (Ar–F). For the *Z*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.43 (br s, 5H, Ph), 7.58 (s, 1H, CH═C), 8.25 (dd, ^3J = 9.1 Hz, ^3J = 5.0 Hz, 1H, Ar). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.0 (CF_3), −102.41, −102.48 (Ar–F). HRMS (ESI-TOF): m/z [M + MeOH + NH_4]$^+$ calcd for $C_{17}H_{17}F_4N_2O_4^+$: 389.1119; found: 389.1113.

(*E*)-1,1,1-Trifluoro-3-(4-methoxyphenyl)-4-(2-nitrophenyl)but-3-en-2-one (4l)

Obtained from enamine **2b** (1.355 g, 5 mmol) and 2-nitrobenzaldehyde (0.801 g, 5.305 mmol). Light yellow solid, m.p. 86–88 °C, yield 1.482 g (88%). Mixture of *E*- and *Z*-isomers: 97 : 3. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.75 (s, 3H, CH_3), 6.77 (d, ^3J = 8.8 Hz, 2H, 4-$MeOC_6H_4$), 6.94–7.01 (m, 2H, 4-$MeOC_6H_4$ and 1H, 2-$NO_2C_6H_4$), 7.37 (td, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1H, 2-$NO_2C_6H_4$), 7.42 (td, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1H, 2-$NO_2C_6H_4$), 8.11 (s, 1H, CH═C), 8.14 (dd, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1H, 2-$NO_2C_6H_4$). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.1, 113.9, 116.6 (q, $^1J_{CF}$ = 292.3 Hz, CF_3), 124.1, 124.8, 129.7, 131.0, 131.5, 131.7, 133.4, 136.0, 142.4 (q, $^4J_{CF}$ = 2.6 Hz, C═C–C═O), 147.8, 159.8, 181.6 (q, $^2J_{CF}$ = 34.3 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −70.2. For the *Z*-isomer: ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −75.2. HRMS (ESI-TOF): m/z [M + NH_4]$^+$ calcd for $C_{17}H_{16}F_3N_2O_4^+$: 369.1057; found: 369.1052.

(*E*)-3-(4-Chlorophenyl)-1,1,1-trifluoro-4-(2-nitrophenyl)but-3-en-2-one (4m)

Obtained from enamine **2c** (1.375 g, 5 mmol) and 2-nitrobenzaldehyde (0.808 g, 5.35 mmol). Pale brown solid, m.p. 48–50 °C, yield 1.072 g (60%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.93 (d, ^3J = 7.8 Hz, 1H, 2-$NO_2C_6H_4$), 7.01 (d, ^3J = 8.5 Hz, 2H, 4-ClC_6H_4), 7.22 (d, ^3J = 8.5 Hz, 2H, 4-ClC_6H_4), 7.40 (td, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H, 2-$NO_2C_6H_4$), 7.46 (td, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H, 2-$NO_2C_6H_4$), 8.16 (dd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H, 2-$NO_2C_6H_4$), 8.22 (s, 1H, CH═C). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 116.5 (q, $^1J_{CF}$ = 291.9 Hz, CF_3), 124.9, 128.8, 130.2, 130.5, 130.6, 131.5, 131.6, 133.7, 134.9, 135.1, 144.0, 147.7, 180.8 (q, $^2J_{CF}$ = 34.6 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −70.2. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_9ClF_3NO_3Na^+$: 378.0115; found: 378.0109.

(*E*)-1,1,1-Trifluoro-3-(4-fluorophenyl)-4-(2-nitrophenyl)-but-3-en-2-one (4n)

Obtained from enamine **2d** (1.036 g, 4 mmol) and 2-nitrobenzaldehyde (0.635 g, 4.205 mmol). Yellow-red viscous oil, yield 1.165 g (86%). Mixture of *E*- and *Z*-isomers: 99 : 1. For the *E*-isomer: ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.90–6.97 (m, 1H, 2-$NO_2C_6H_4$ and 2H, 4-FC_6H_4), 7.02–7.08 (m, 2H, 4-FC_6H_4), 7.36–7.48 (m, 2H, 2-$NO_2C_6H_4$), 8.15 (d, ^3J = 8.1 Hz, 1H, 2-$NO_2C_6H_4$), 8.21 (s, 1H, CH═C). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 115.6 (d, $^2J_{CF}$ = 21.7 Hz, 4-FC_6H_4), 116.5 (q, $^1J_{CF}$ = 292.1 Hz, CF_3), 124.9, 128.1 (d, $^4J_{CF}$ = 3.5 Hz, 4-FC_6H_4), 130.0, 130.6, 131.5, 132.1 (d, $^3J_{CF}$ = 8.3 Hz, 4-FC_6H_4), 133.6, 135.2, 143.9 (q, $^4J_{CF}$ = 3.3 Hz, C═C–C═O), 147.7, 162.7 (d, $^1J_{CF}$ = 249.3 Hz, C–F), 181.0 (q, $^2J_{CF}$ = 34.6 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.2 (CF_3), −112.67 to −113.15 (4-FC_6H_4). For the *Z*-isomer: ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.1 (CF_3), −112.10 to −112.24 (4-F-C_6H_3). HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_9F_4NO_3Na^+$: 362.0411; found: 362.0414.

(*E*)-1,1,1-Trifluoro-4-(2-nitrophenyl)-3-(4-trifluoromethylphenyl)but-3-en-2-one (4o)

Obtained from enamine **2f** (0.473 g, 1.53 mmol) and 2-nitrobenzaldehyde (0.266 g, 1.759 mmol). Beige viscous liquid, yield 0.316 g (53%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 6.89 (d, ^3J

= 7.7 Hz, 1H, 2-$NO_2C_6H_4$), 7.20 (d, ^3J = 8.1 Hz, 2H, 4-$CF_3C_6H_4$), 7.39 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, 2-$NO_2C_6H_4$), 7.43–7.50 (m, 1H, 2-$NO_2C_6H_4$), 7.52 (d, ^3J = 8.1 Hz, 2H, 4-$CF_3C_6H_4$), 8.19 (dd, ^3J = 8.2 Hz, ^4J = 1.2 Hz, 1H, 2-$NO_2C_6H_4$), 8.30 (s, 1H, CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.5 (q, $^1J_{CF}$ = 291.8 Hz, CF_3), 123.7 (q, $^1J_{CF}$ = 272.3 Hz, 4-$\underline{C}F_3C_6H_4$), 125.0, 125.4 (q, $^4J_{CF}$ = 3.7 Hz, 4-$CF_3\underline{C}_6H_4$), 130.2, 130.4, 130.68 (q, $^2J_{CF}$ = 32.8 Hz, $\underline{C}$–CF_3), 130.74, 131.4, 133.8, 134.8, 136.0, 145.1 (q, $^4J_{CF}$ = 3.2 Hz, $\underline{C}$═C–C═O), 147.6, 180.5 (q, $^2J_{CF}$ = 35.0 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.1 ($COCF_3$), −63.8 (4-$CF_3C_6H_4$). HRMS (ESI-TOF): m/z $[M + K]^+$ calcd for $C_{17}H_9F_6NO_3K^+$: 428.0118; found: 428.0124.

(*E*)-1,1,1-Trifluoro-3-(4-nitrophenyl)-4-(2-nitrophenyl)but-3-en-2-one (4p)

Obtained from enamine **2h** (0.286 g, 1.0 mmol) and 2-nitrobenzaldehyde (0.174 g, 1.15 mmol). White crystals, m.p. 129–132 °C, yield 0.282 g (77%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 6.88 (d, ^3J = 7.6 Hz, 1H, 2-$NO_2C_6H_4$), 7.27 (d, ^3J = 8.7 Hz, 2H, 4-$NO_2C_6H_4$), 7.41 (t, ^3J = 7.6 Hz, 1H, 2-$NO_2C_6H_4$), 7.50 (t, ^3J = 7.8 Hz, 1H, 2-$NO_2C_6H_4$), 8.12 (d, ^3J = 8.7 Hz, 2H, 4-$NO_2C_6H_4$), 8.22 (d, ^3J = 8.2 Hz, 1H, 2-$NO_2C_6H_4$), 8.35 (s, 1H, CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.4 (q, $^1J_{CF}$ = 291.8 Hz, CF_3), 123.6, 125.2, 129.9, 130.7, 131.2, 131.4, 133.9, 134.1, 139.0, 145.8 (q, $^4J_{CF}$ = 3.4 Hz, $\underline{C}$═C–C═O), 147.5, 147.8, 180.1 (q, $^2J_{CF}$ = 35.3 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.2. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{10}F_3N_2O_5^+$: 367.0536; found: 367.0547.

(3*E*)-Methyl 4-(4,4,4-trifluoro-1-(2-nitrophenyl)-3-oxobut-1-en-2-yl)benzoate (4q)

Obtained from enamine **2j** (0.748 g, 2.5 mmol) and 2-nitrobenzaldehyde (0.408 g, 2.702 mmol). Light yellow crystals, m.p. 152–153 °C, yield 0.597 g (63%). Mixture of *E*- and *Z*-isomers: 99.6 : 0.4. For the *E*-isomer: ^1H NMR (400.1 MHz, $CDCl_3$): δ 3.85 (s, 3H, CH_3), 6.89 (d, ^3J = 7.7 Hz, 1H, 2-$NO_2C_6H_4$), 7.14 (d, ^3J = 8.3 Hz, 2H, 4-$CO_2MeC_6H_4$), 7.34 (td, ^3J = 7.6 Hz, ^4J = 1.1 Hz, 1H, 2-$NO_2C_6H_4$), 7.39–7.45 (m, 1H, 2-$NO_2C_6H_4$), 7.89 (d, ^3J = 8.3 Hz, 2H, 4-$CO_2MeC_6H_4$), 8.14 (dd, ^3J = 8.2 Hz, ^4J = 1.0 Hz, 1H, 2-$NO_2C_6H_4$), 8.26 (s, 1H, CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 52.1, 116.4 (q, $^1J_{CF}$ = 291.9 Hz, CF_3), 124.9, 129.5, 130.21, 130.25, 130.3, 131.4, 133.6, 135.2, 136.8, 144.5 (q, $^4J_{CF}$ = 3.3 Hz, $\underline{C}$═C–C═O), 147.5, 166.3, 180.5 (q, $^2J_{CF}$ = 34.9 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.2 (d, ^4J = 0.9 Hz, 3F, CF_3). For the *Z*-isomer: ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.2. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{13}F_3NO_5^+$: 380.0740; found: 380.0744.

(3*E*)-3-(2-Bromophenyl)-1,1,1-trifluoro-4-(2-nitrophenyl)but-3-en-2-one (4r)

Obtained from enamine **2g** (2.401 g, 7.5 mmol) and 2-nitrobenzaldehyde (1.139 g, 7.537 mmol). Light yellow viscous liquid, yield 1.861 g (62%). Mixture of *E*- and *Z*-isomers: 96 : 4. For the *E*-isomer: ^1H NMR (400.1 MHz, $CDCl_3$): δ 6.92–6.97 (m, 1H, Ar), 7.08 (dd, ^3J = 7.3 Hz, ^4J = 1.2 Hz, 1H, Ar), 7.11–7.18 (m, 2H, Ar), 7.36–7.49 (m, 2H, Ar), 7.50–7.59 (m, 1H, Ar), 8.15 (dd, ^3J = 8.0 Hz, ^4J = 1.5 Hz, 1H, Ar), 8.31 (s, 1H, CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.4 (q, $^1J_{CF}$ = 291.8 Hz, CF_3), 124.3, 124.8, 127.7, 130.2, 130.3, 130.45, 130.51, 131.8, 132.6, 133.7, 134.2, 136.1, 144.0 (q, $^4J_{CF}$ = 3.1 Hz, $\underline{C}$═C–C═O), 147.1, 180.0 (q, $^2J_{CF}$ = 34.9 Hz, $\underline{C}$═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.9. For the *Z*-isomer: ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.19–7.23 (m, 1H), 7.28–7.35 (m, 2H), 7.60–7.65 (m, 1H), 7.65–7.72 (m, 1H), 8.25 (dd, ^3J = 8.3 Hz, ^4J = 1.1 Hz, 1H, 2-$NO_2C_6H_4$). Other signals are overlapped with those of the major isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −75.3. HRMS (ESI-TOF): m/z $[M + NH_4]^+$ calcd for $C_{16}H_{13}BrF_3N_2O_3^+$: 417.0056, 419.00361; found: 417.0046, 419.0031.

(3*E*)-1,1,1-Trifluoro-3-(3-nitrophenyl)-4-(2-nitrophenyl)-but-3-en-2-one (4s)

Obtained from enamine **2i** (0.98 g, 3.423 mmol) and 2-nitrobenzaldehyde (0.595 g, 3.936 mmol). Light beige crystals, m.p. 92–93 °C, yield 0.98 g (78%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 6.92 (d, ^3J = 7.7 Hz, 1H, 2-$NO_2C_6H_4$), 7.35–7.52 (m, 2H, 2-$NO_2C_6H_4$ and 2H, 3-$NO_2C_6H_4$), 7.99 (pt, $^4J \sim 1.9$ Hz, 1H, 3-$NO_2C_6H_4$), 8.14 (ddd, ^3J = 8.2 Hz, ^4J = 2.1 Hz, ^4J = 1.1 Hz, 1H, 3-$NO_2C_6H_4$), 8.20 (dd, ^3J = 8.1 Hz, ^4J = 1.0 Hz, 1H, 2-$NO_2C_6H_4$), 8.37 (s, 1H, CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.4 (q, $^1J_{CF}$ = 291.7 Hz, CF_3), 123.7, 125.2, 125.3, 129.6, 129.9, 130.7, 131.3, 133.7, 133.8, 133.9, 136.4, 145.8 (q, $^4J_{CF}$ = 3.5 Hz, $\underline{C}$═C–C═O), 147.5, 148.0, 180.2 (q, $^2J_{CF}$ = 35.3 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.14. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{10}F_3N_2O_5^+$: 367.0536; found: 367.0546.

(*E*)-1,1,1-Trifluoro-4-(2-nitrophenyl)-3-(4-(pyrrolidin-1-yl)phenyl)but-3-en-2-one (4t)

Obtained from enamine **2e** (1.24 g, 4 mmol) and 2-nitrobenzaldehyde (0.653 g, 4.32 mmol). Dark red viscous oil, yield 1.291 g (83%). Mixture of *E*- and *Z*-isomers: 98 : 2. ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.93–2.01 (m, 4H, $N(CH_2C\underline{H}_2)_2$), 3.22–3.25 (m, 4H, $N(C\underline{H}_2CH_2)_2$), 6.39 (d, ^3J = 8.7 Hz, 2H, Ar), 6.88 (d, ^3J = 8.7 Hz, 2H, Ar), 7.02–7.07 (m, 1H, 2-$NO_2C_6H_4$), 7.34–7.41 (m, 2H, 2-$NO_2C_6H_4$), 7.93 (s, 1H, CH═C), 8.10–8.15 (m, 1H, 2-$NO_2C_6H_4$). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 25.4, 47.4, 111.3, 116.7 (q, $^1J_{CF}$ = 292.3 Hz, CF_3), 118.2, 124.7, 129.3, 131.4, 131.8, 132.0, 133.3, 136.9, 139.7 (q, $^4J_{CF}$ = 3.5 Hz, $\underline{C}$═C–C═O), 147.9, 148.0, 182.6 (q, $^2J_{CF}$ = 33.9 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.4 (d, ^4J = 0.6 Hz, 3F, CF_3). For the *Z*-isomer: ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.5. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{18}F_3N_2O_3^+$: 391.1264; found: 391.1255.

(*E*)-1,1,1-Trifluoro-4-(2-nitrophenyl)-3-(4-(pyrrolidine-1-carbonyl)phenyl)but-3-en-2-one (4u)

Obtained from enamine **2k** (1.698 g, 5 mmol) and 2-nitrobenzaldehyde (0.757 g, 5.01 mmol). Beige viscous liquid, yield 1.464 g (70%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.95–2.14 (m, 4H, $2NCH_2C\underline{H}_2$), 3.52 (br s, 2H, $N(C\underline{H}_2CH_2)_2$), 3.74 (br s, 2H, $N(C\underline{H}_2CH_2)_2$), 6.88 (d, J = 7.6 Hz, 1H, 2-$NO_2C_6H_4$), 7.22 (d, J = 8.2 Hz, 2H, Ar), 7.36–7.51 (m, 2H, 2-$NO_2C_6H_4$ and 2H, Ar), 8.19 (dd, J = 8.2 Hz, J = 0.8 Hz, 1H, 2-$NO_2C_6H_4$), 8.35 (s, 1H,

CH═C). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 24.1, 26.1, 46.0, 49.3, 116.3 (q, $^1J_{CF}$ = 292.1 Hz, CF_3), 124.6, 127.0, 129.95, 129.99, 130.1, 131.3, 133.4, 133.5, 135.1, 137.0, 144.0 (q, $^4J_{CF}$ = 3.0 Hz, C═C–C═O), 147.3, 168.5, 180.6 (q, $^2J_{CF}$ = 34.7 Hz, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.2. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{18}F_3N_2O_4^+$: 419.1213; found: 419.1219.

(*E*)-1,1,1-Trifluoro-4-(2-nitrophenyl)-3-(pyridine-4-yl)but-3-en-2-one (4v)

Obtained from enamine **2l** (1.017 g, 4.2 mmol) and 2-nitrobenzaldehyde (0.728 g, 4.82 mmol). Dark orange viscous liquid, yield 0.568 g (42%). The compound is quite unstable and forms black tar upon standing for several days. ^1H NMR (400.1 MHz, $CDCl_3$): δ 6.90 (d, ^3J = 7.7 Hz, 1H, 2-$NO_2C_6H_4$), 6.97–7.03 (m, 2H, Py), 7.40 (td, ^3J = 7.6 Hz, ^4J = 1.1 Hz, 1H, 2-$NO_2C_6H_4$), 7.49 (td, ^3J = 8.0 Hz, ^4J = 0.9 Hz, 1H, 2-$NO_2C_6H_4$), 8.21 (dd, ^3J = 8.2 Hz, ^4J = 1.1 Hz, 1H, 2-$NO_2C_6H_4$), 8.33 (s, 1H, CH═C), 8.47–8.55 (m, 2H, Py). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 116.4 (q, $^1J_{CF}$ = 291.9 Hz, CF_3), 125.0, 125.1, 129.9, 130.6, 131.2, 133.7, 133.9, 140.5, 145.5 (q, $^4J_{CF}$ = 3.3 Hz, C═C–C═O), 147.5, 150.0, 180.0 (q, $^2J_{CF}$ = 35.3, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.3 (d, ^4J = 0.8 Hz, 3F, CF_3). HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{10}F_3N_2O_3^+$: 323.0638; found: 323.0645.

(*E*)-1,1,1-Trifluoro-3-(4-methoxyphenyl)-4-(2-nitrothiophen-3-yl)but-3-en-2-one (4w)

Obtained from enamine **2b** (0.140 g, 0.516 mmol) and 2-nitrothiophene-3-carbaldehyde (0.092 g, 0.59 mmol). Yellow-brown solid, m.p. 125–127 °C, yield 0.103 g (61%). Mixture of *E*- and *Z*-isomers: 87 : 13. For the *E*-isomer: ^1H NMR (400.1 MHz, $CDCl_3$): δ 3.82 (s, 3H, CH_3), 6.26 (d, ^3J = 5.7 Hz, 1H, 2-$NO_2SC_4H_2$), 6.90 (d, ^3J = 8.7 Hz, 2H, 4-$MeOC_6H_4$), 7.06 (d, ^3J = 8.7 Hz, 2H, 4-$MeOC_6H_4$), 7.19 (d, ^3J = 5.7 Hz, 1H, 2-$NO_2SC_4H_2$), 8.37 (s, 1H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 55.3, 114.4, 116.6 (q, $^1J_{CF}$ = 292.1 Hz, CF_3), 124.5, 128.5, 129.1, 129.5, 131.2, 135.3 (q, $^4J_{CF}$ = 3.1 Hz, C═C–C═O), 135.8, 138.2, 160.5, 181.7 (q, $^2J_{CF}$ = 34.5, C═O). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −71.3 (d, ^4J = 0.7 Hz, 3F, CF_3). For the *Z*-isomer: ^1H NMR (400.1 MHz, $CDCl_3$): δ 3.85 (s, 3H, CH_3), 6.96 (d, ^3J = 8.8 Hz, 2H, 4-$MeOC_6H_4$), 7.34 (d, ^3J = 8.8 Hz, 2H, 4-$MeOC_6H_4$), 7.47 (d, ^3J = 5.6 Hz, 1H, 2-$NO_2SC_4H_2$), 7.62 (s, 1H). Other signals are overlapped with those of the major isomer. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 55.4, 114.7, 124.8, 128.7, 130.8, 136.0, 139.8, 150.8, 161.1. Other signals are overlapped with those of the major isomer or cannot be seen in the spectrum due to the low concentration of the minor isomer. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −76.0. HRMS (ESI-TOF): *m*/*z* $[M + MeOH + NH_4]^+$ calcd for $C_{16}H_{18}F_3N_2O_5S^+$: 407.0883; found: 407.0832.

Synthesis of quinolines 5 by the reduction of nitro-substituted CF_3-enones 4 (general procedure A)

A 12 mL vial with a screw cap was charged with ketone **4** (0.5 mmol), glacial acetic acid (1 mL), water (0.1 mL) and Fe powder (0.084 g, 1.5 mmol). The reaction mixture was kept at 80 °C under stirring for 0.5–1 hours until the Fe powder dissolved (after 10–15 min the gas pressure must be released!) and the vigorous reaction finished. Volatiles were evaporated *in vacuo*, and the residue was dispersed between CH_2Cl_2 (5–10 mL) and 6 M HCl (1 mL). The organic phase was separated, washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated *in vacuo*, to give pure quinoline **5**.

One pot synthesis of quinolines 5 by the reduction of nitro-substituted CF_3-enones 4 starting from enamines 2 (general procedure B from pure enamine; procedure C from crude enamine)

An aliquot of the reaction mixture for the synthesis of ketone **4** (~0.5 mmol, 1 mL) was placed into a 12 mL vial with a screw cap, and water (0.1 mL) and Fe powder (0.084 g, 1.5 mmol) were then added. The reaction mixture was kept at 80 °C under stirring for 0.5–1 hours until the Fe powder dissolved (after 10–15 min the gas pressure must be released!) and the vigorous reaction finished. Volatiles were evaporated *in vacuo*, and the residue was dispersed between CH_2Cl_2 (5–10 mL) and 6 M HCl (1 mL). The organic phase was separated, washed with water (10 mL) and dried over Na_2SO_4. Volatiles were evaporated *in vacuo*, and the residue was purified by column chromatography, using appropriate mixtures of hexane and CH_2Cl_2 or CH_2Cl_2 as eluents.

3-Phenyl-2-(trifluoromethyl)quinoline (5a)

Obtained from ketone **4a** (0.160 g, 0.5 mmol) by procedure A or by procedure B (2 mmol). Pale brown solid, m.p. 71–73 °C, yield 0.130 g (95%, A) or 0.420 g (77%, B). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.40–7.48 (m, 5H), 7.67 (ptd, ^3J = 7.6 Hz, ^4J = 1.0 Hz, 1H), 7.81 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.86 (d, ^3J = 8.2 Hz, 1H), 8.15 (s, 1H), 8.27 (d, ^3J = 8.6 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 121.8 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 127.4, 128.0, 128.1, 128.3, 129.0, 129.2 (q, $^4J_{CF}$ = 1.5 Hz), 129.8, 130.6, 133.4, 137.4, 139.7, 145.4 (q, $^2J_{CF}$ = 32.4 Hz), 145.6 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.4 (CF_3) ppm. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{11}F_3N^+$: 274.0838; found: 274.0836.

3-Phenyl-2-(trifluoromethyl)quinoline-7-carbonitrile (5b)

Obtained from ketone **4b** by procedure B (0.5 mmol). Pale green solid, m.p. 145–147 °C, yield 0.096 g (64%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.39–7.41 (m, 2H), 7.45–7.50 (m, 3H), 7.82 (dd, ^3J = 8.4 Hz, ^4J = 1.5 Hz, 1H), 8.01 (d, ^3J = 8.4 Hz, 1H), 8.25 (s, 1H), 8.61 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 114.0, 117.8, 121.2 (q, $^1J_{CF}$ = 277.0 Hz, CF_3), 128.2, 128.7, 128.96 (q, $^4J_{CF}$ = 1.3 Hz), 129.0, 129.4, 130.1, 135.7, 136.17, 136.25, 139.7, 144.3, 147.4 (q, $^2J_{CF}$ = 33.2 Hz) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −63.0 (CF_3) ppm. HRMS (ESI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{10}F_3N_2^+$: 299.0791; found: 299.0789.

3-Phenyl-2-(trifluoromethyl)quinolin-7-amine (5c)

Obtained from ketone **4c** by procedure B (0.5 mmol). Light yellow powder, m.p. 174–175 °C, yield 0.087 g (60%). ^1H NMR

(400.1 MHz, $CDCl_3$): δ 4.22 (s, 2H, NH_2), 7.09 (dd, ^3J = 8.7 Hz, ^4J = 2.0 Hz, 1H), 7.32 (d, ^4J = 2.0 Hz, 1H), 7.37–7.46 (m, 5H), 7.65 (d, ^3J = 8.7 Hz, 1H), 7.96 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 108.8, 121.2, 121.9 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 122.3, 127.7, 127.9, 128.6, 129.3, 129.8, 137.9, 139.3, 145.4 (q, $^2J_{CF}$ = 31.9 Hz), 147.6, 148.7 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.5 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{12}F_3N_2^+$: 289.0947; found: 289.0952.

3-Phenyl-2,7-bis(trifluoromethyl)quinoline (5d)

Obtained from ketone **4d** by procedure B (0.5 mmol). White solid, m.p. 88–90 °C, yield 0.133 g (78%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.40–7.44 (m, 2H), 7.47–7.50 (m, 3H), 7.85 (dd, ^3J = 8.6 Hz, ^4J = 1.5 Hz, 1H), 8.02 (d, ^3J = 8.6 Hz, 1H), 8.25 (s, 1H), 8.59 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 121.5 (q, $^1J_{CF}$ = 277.0 Hz, CF_3), 123.6 (q, $^1J_{CF}$ = 272.6 Hz, CF_3), 124.6 (q, $^3J_{CF}$ = 3.0 Hz), 127.9 (q, $^3J_{CF}$ = 4.4 Hz), 128.2, 128.5, 128.8, 129.1 (q, $^4J_{CF}$ = 1.5 Hz), 129.7, 132.3 (q, $^2J_{CF}$ = 33.0 Hz), 135.6, 136.6, 139.7, 144.6, 147.0 (q, $^2J_{CF}$ = 33.0 Hz) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.9 (s, 3F, CF_3), −64.1 (s, 3F, CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{10}F_6N^+$: 342.0712; found: 342.0722.

7-Chloro-3-phenyl-2-(trifluoromethyl)quinoline (5e)

Obtained from ketone **4e** by procedure B (0.5 mmol). Brown oil, yield 0.120 g (78%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.38–7.42 (m, 2H), 7.44–7.48 (m, 3H), 7.62 (dd, ^3J = 8.8 Hz, ^4J = 1.9 Hz, 1H), 7.81 (d, ^3J = 8.8 Hz, 1H), 8.14 (s, 1H), 8.25 (d, ^4J = 1.9 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 121.5 (q, $^1J_{CF}$ = 276.7 Hz, CF_3), 126.6, 128.1, 128.3, 128.6, 128.8, 129.1 (q, $^4J_{CF}$ = 1.5 Hz), 130.1, 133.7, 136.5, 136.9, 139.6, 145.8, 146.3 (q, $^2J_{CF}$ = 32.6 Hz) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.7 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{10}ClF_3N^+$: 308.0448; found: 308.0450.

Methyl 3-phenyl-2-(trifluoromethyl)quinoline-7-carboxylate (5f)

Obtained from ketone **4f** by procedure B (1 mmol). Pale brown solid, m.p. 92–94 °C, yield 0.221 g (67%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.40–7.43 (m, 2H), 7.46–7.49 (m, 3H), 7.94 (d, ^3J = 8.8 Hz, 1H), 8.21 (s, 1H), 8.28 (dd, ^3J = 8.6 Hz, ^4J = 1.6 Hz, 1H), 8.99 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 52.4, 121.5 (q, $^1J_{CF}$ = 276.5 Hz, CF_3), 127.7, 128.0, 128.27, 128.34, 129.0, 130.4, 131.9, 132.4, 135.2, 136.8, 139.4, 144.8, 146.4 (q, $^2J_{CF}$ = 33.3 Hz), 166.1 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.8 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{13}F_3NO_2^+$: 332.0893; found: 332.0898.

6,8-Dimethyl-3-phenyl-2-(trifluoromethyl)quinoline (5g)

Obtained from ketone **4g** (0.366 g, 1.049 mmol) by procedure A. White powder, m.p. 70–72 °C, yield 0.302 g (96%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 2.55 (s, 3H, Me), 2.89 (s, 3H, Me), 7.44–7.54 (m, 7H), 8.01 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 17.4, 21.7, 122.1 (q, $^1J_{CF}$ = 276.2 Hz, CF_3), 123.9, 127.9, 127.9, 128.4, 129.2 (q, $^4J_{CF}$ = 1.5 Hz), 132.8, 133.1, 137.8, 137.8, 138.8, 138.9, 143.2 (q, $^2J_{CF}$ = 32.4 Hz), 143.4 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.4 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{15}F_3N^+$: 302.1151; found: 302.1154.

7-Phenyl-6-(trifluoromethyl)-[1,3]dioxolo[4,5-*g*]quinoline (5h)

Obtained from ketone **4h** (0.183 g, 0.5 mmol) by procedure A. Yellow-brown solid, m.p. 104–107 °C, yield 0.158 g (>99%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 6.17 (s, 2H, CH_2), 7.08 (s, 1H), 7.36–7.40 (m, 2H), 7.41–7.45 (m, 3H), 7.50 (s, 1H), 7.94 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 101.9, 102.1, 105.7, 122.0 (q, $^1J_{CF}$ = 276.2 Hz, CF_3), 126.0, 127.9, 129.1, 131.9, 137.5, 138.1, 142.8 (q, $^2J_{CF}$ = 32.4 Hz), 144.0, 149.8, 151.7. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{11}F_3NO_2^+$: 318.0736; found: 318.0738.

8-Methoxy-3-phenyl-2-(trifluoromethyl)quinoline (5i)

Obtained from ketone **4i** by procedure B (0.5 mmol). Yellow-brown solid, m.p. 93–95 °C, yield 0.117 g (77%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.12 (d, ^3J = 7.7 Hz, 1H), 7.38–7.45 (m, 6H), 7.58 (t, ^3J = 7.7 Hz, 1H), 8.12 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 56.2, 118.9, 121.7 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 127.9, 128.1, 129.1 (q, $^4J_{CF}$ = 1.3 Hz), 129.47, 129.54, 134.0, 137.2, 137.5, 139.6, 144.0 (q, $^2J_{CF}$ = 32.8 Hz), 155.7 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.2 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{17}H_{13}F_3NO^+$: 304.0944; found: 304.0936.

5,8-Dimethoxy-3-phenyl-2-(trifluoromethyl)quinoline (5j)

Obtained from ketone **4j** by procedure B (0.189 mmol). Pale brown solid, m.p. 149–152 °C, yield 0.043 g (68%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 3.94 (s, 3H, MeO), 4.07 (s, 3H, MeO), 6.87 (d, ^3J = 8.5 Hz, 1H), 7.02 (d, ^3J = 8.5 Hz, 1H), 7.39–7.47 (m, 5H), 8.56 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 55.8, 56.4, 106.0, 108.1, 121.8 (q, $^1J_{CF}$ = 276.4 Hz, CF_3), 121.9, 127.9, 128.0, 129.3 (q, $^4J_{CF}$ = 1.3 Hz), 133.3, 135.1, 137.6, 137.9, 144.5 (q, $^2J_{CF}$ = 32.8 Hz), 148.3, 149.6 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.3 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{15}F_3NO_2^+$: 334.1049; found: 334.1049.

6-Fluoro-3-phenyl-2-(trifluoromethyl)quinoline (5k)

Obtained from ketone **4k** by procedure B (0.5 mmol). Pale beige powder, m.p. 120–123 °C, yield 0.103 g (71%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 7.39–7.42 (m, 2H), 7.44–7.49 (m, 4H), 7.56–7.61 (m, 1H), 8.10 (s, 1H), 8.27 (dd, ^3J = 9.3 Hz, ^3J = 5.3 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 110.4 (d, $^2J_{CF}$ = 22.1 Hz), 121.2 (d, $^2J_{CF}$ = 26.2 Hz), 121.7 (q, $^1J_{CF}$ = 276.5 Hz, CF_3), 128.1, 128.3, 129.1 (q, $^4J_{CF}$ = 1.5 Hz), 129.2 (dq, J_{CF} = 10.6 Hz, J_{CF} = 0.6 Hz), 132.7 (d, J_{CF} = 9.6 Hz), 134.3, 137.0, 139.0 (d, J_{CF} = 5.7 Hz), 142.7, 145.9 (qd, $^2J_{CF}$ = 32.6 Hz, $^6J_{CF}$ = 3.0 Hz), 161.9 (d, $^1J_{CF}$ = 252.3 Hz, CF_3) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.6 (s, 3F, CF_3), −110.15, −110.21 (m, 1F, F) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{10}F_4N^+$: 292.0744; found: 292.0746.

3-(4-Methoxyphenyl)-2-(trifluoromethyl)quinoline (5l)

Obtained from ketone **4l** by procedure B (0.5 mmol). Pale beige powder, m.p. 127–128 °C, yield 0.135 g (89%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.86 (s, 3H, MeO), 6.98 (d, ^3J = 8.6 Hz, 2H), 7.33 (d, ^3J = 8.6 Hz, 2H), 7.66 (pt, ^3J = 7.5 Hz, 1H), 7.80 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.85 (d, ^3J = 8.1 Hz, 1H), 8.13 (s, 1H), 8.24 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.2, 113.4, 121.8 (q, $^1J_{CF}$ = 276.8 Hz, CF_3), 127.3, 128.3, 128.9, 129.6, 129.8, 130.38 (q, $^4J_{CF}$ = 1.5 Hz), 130.40, 133.2, 139.8, 145.4, 145.6 (q, $^2J_{CF}$ = 32.1 Hz), 159.5 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.7 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{17}H_{12}F_3NONa^+$: 326.0763; found: 326.0753.

3-(4-Chlorophenyl)-2-(trifluoromethyl)quinoline (5m)

Obtained from ketone **4m** (0.178 g, 0.5 mmol) by procedure A. Pale brown solid, m.p. 134–136 °C, yield 0.137 g (89%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.33 (d, ^3J = 8.3 Hz, 2H), 7.43 (d, ^3J = 8.3 Hz, 2H), 7.69 (pt, ^3J = 7.5 Hz, 1H), 7.83 (pt, ^3J = 7.7 Hz, 1H), 7.88 (d, ^3J = 8.1 Hz, 1H), 8.13 (s, 1H), 8.25 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 121.7 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 127.4, 128.2, 128.3, 129.2, 130.0, 130.6 (q, $^4J_{CF}$ = 1.5 Hz), 130.8, 132.2, 134.4, 135.8, 139.7, 145.2 (q, $^2J_{CF}$ = 32.4 Hz), 145.7 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.5 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{10}ClF_3N^+$: 308.0448; found: 308.0460.

3-(4-Fluorophenyl)-2-(trifluoromethyl)quinoline (5n)

Obtained from ketone **4n** by procedure B (0.5 mmol). Pale brown solid, m.p. 103–105 °C, yield 0.124 g (85%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.14 (pt, ^3J = 8.6 Hz, 2H), 7.37 (dd, ^3J = 8.4 Hz, ^4J = 5.4 Hz, 2H), 7.69 (pt, ^3J = 7.5 Hz, 1H), 7.83 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.88 (d, ^3J = 8.2 Hz, 1H), 8.15 (s, 1H), 8.26 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 115.1 (d, $^2J_{CF}$ = 21.8 Hz), 121.7 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 127.4, 128.3, 129.1, 130.0, 130.8, 131.0 (dq, $^4J_{CF}$ = 8.3 Hz, $^5J_{CF}$ = 1.5 Hz), 132.4, 133.3 (d, $^4J_{CF}$ = 3.5 Hz), 139.8, 145.4 (q, $^2J_{CF}$ = 32.6 Hz), 145.7, 162.7 (d, $^1J_{CF}$ = 247.7 Hz) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.7 (s, 3F, CF_3), −114.90, −114.98 (m, 1F, F) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{10}F_4N^+$: 292.0744; found: 292.0752.

2-(Trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)quinoline (5o)

Obtained from ketone **4o** by procedure B (0.5 mmol). White powder, m.p. 135–138 °C, yield 0.116 g (68%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.54 (d, ^3J = 8.2 Hz, 2H), 7.71–7.75 (m, 3H), 7.87 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.92 (d, ^3J = 8.2 Hz, 1H), 8.18 (s, 1H), 8.28 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 121.6 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 124.0 (q, $^1J_{CF}$ = 272.2 Hz, CF_3), 125.0 (q, $^3J_{CF}$ = 3.7 Hz), 127.5, 128.1, 129.3, 129.7 (q, $^4J_{CF}$ = 1.1 Hz), 130.0, 130.4 (q, $^2J_{CF}$ = 32.8 Hz), 131.1, 131.9, 139.7, 141.1, 145.0 (q, $^2J_{CF}$ = 32.6 Hz), 145.9 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −61.4 (CF_3), −62.7 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{17}H_{10}F_6N^+$: 342.0712; found: 342.0709.

4-(2-(Trifluoromethyl)quinolin-3-yl)aniline (5p)

Obtained from ketone **4p** by procedure B (0.5 mmol). Light yellow powder, m.p. 115–117 °C, yield 0.039 g (27%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.81 (s, 2H, NH_2), 6.76 (d, ^3J = 8.3 Hz, 2H), 7.20 (d, ^3J = 8.3 Hz, 2H), 7.66 (pt, ^3J = 7.5 Hz, 1H), 7.79 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.85 (d, ^3J = 8.2 Hz, 1H), 8.14 (s, 1H), 8.24 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 114.5, 121.9 (q, $^1J_{CF}$ = 276.8 Hz, CF_3), 127.3, 127.4, 128.5, 128.8, 129.9, 130.23, 130.25, 133.7, 139.8, 145.4, 145.8 (q, $^2J_{CF}$ = 32.3 Hz), 146.4 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.7 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{12}F_3N_2^+$: 289.0947; found: 289.0952.

Methyl 4-(2-(trifluoromethyl)quinolin-3-yl)benzoate (5q)

Obtained from ketone **4q** by procedure B (0.5 mmol). Bright yellow crystals, m.p. 136–139 °C, yield 0.098 g (59%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.95 (s, 3H, CO_2Me), 7.48 (d, ^3J = 8.3 Hz, 2H), 7.70 (ptd, ^3J = 7.5 Hz, ^4J = 0.9 Hz, 1H), 7.84 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.89 (d, ^3J = 8.1 Hz, 1H), 8.12 (d, ^3J = 8.5 Hz, 2H), 8.16 (s, 1H), 8.26 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 52.2, 121.6 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 127.5, 128.1, 129.2, 129.3, 129.4 (q, $^4J_{CF}$ = 1.5 Hz), 129.9, 130.0, 130.9, 132.4, 139.5, 142.0, 145.0 (q, $^2J_{CF}$ = 32.8 Hz), 145.8, 166.7 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.5 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{13}F_3NO_2^+$: 332.0893; found: 332.0889.

3-(2-Bromophenyl)-2-(trifluoromethyl)quinoline (5r)

Obtained from ketone **4r** by procedure C (2.5 mmol). Pale yellow oil, yield 0.403 g (46%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.29–7.34 (m, 2H), 7.38–7.42 (m, 1H), 7.68–7.71 (m, 2H), 7.85 (ptd, ^3J = 7.7 Hz, ^4J = 1.0 Hz, 1H), 7.89 (d, ^3J = 8.2 Hz, 1H), 8.14 (s, 1H), 8.28 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 121.5 (q, $^1J_{CF}$ = 276.8 Hz, CF_3), 123.9, 126.8, 127.6, 128.1, 129.1, 130.0, 130.9, 131.2 (q, $^4J_{CF}$ = 1.1 Hz), 131.9, 132.5, 137.7, 140.1, 145.3 (q, $^2J_{CF}$ = 32.6 Hz), 146.0 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −64.4 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{10}BrF_3N^+$: 351.9943, 353.9923; found: 351.9941, 353.9922.

3-(2-(Trifluoromethyl)quinolin-3-yl)aniline (5s)

Obtained from ketone **4s** (0.195 g, 0.53 mmol) by procedure A. Light yellow powder, m.p. 70–72 °C, yield 0.062 g (41%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.77 (s, 2H, NH_2), 6.71 (br s, 1H), 6.75–6.79 (m, 2H), 7.21 (d, ^3J = 7.8 Hz, 1H), 7.68 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.81 (ptd, ^3J = 7.7 Hz, ^4J = 1.5 Hz, 1H), 7.87 (d, ^3J = 8.3 Hz, 1H), 8.16 (s, 1H), 8.25 (d, ^3J = 8.6 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 114.8, 115.9 (q, $^4J_{CF}$ = 1.1 Hz), 119.7 (q, $^4J_{CF}$ = 1.5 Hz), 121.8 (q, $^1J_{CF}$ = 276.8 Hz, CF_3), 127.4, 128.3, 128.9, 129.0, 129.9, 130.5, 133.7, 138.5, 139.5, 145.4 (q, $^2J_{CF}$ = 32.8 Hz), 145.6, 146.0 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.6 (CF_3) ppm. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{12}F_3N_2^+$: 289.0947; found: 289.0954.

3-(4-(Pyrrolidin-1-yl)phenyl)-2-(trifluoromethyl)quinoline (5t)

Obtained from ketone **4t** by procedure B (0.5 mmol). Light brown powder, m.p. 212–214 °C, yield 0.112 g (65%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 2.02–2.07 (m, 4H, CH_2), 3.33–3.37 (m, 4H, NCH_2), 6.63 (d, ^3J = 8.5 Hz, 2H), 7.28 (d, ^3J = 8.5 Hz, 2H), 7.65 (pt, ^3J = 7.5 Hz, 1H), 7.78 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.85 (d, ^3J = 8.0 Hz, 1H), 8.14 (s, 1H), 8.23 (d, ^3J = 8.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 25.5, 47.5, 111.0, 122.0 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 123.3, 127.3, 128.6, 128.7, 129.8, 130.0, 130.1 (q, $^4J_{CF}$ = 1.5 Hz), 134.2, 139.7, 145.2, 145.9 (q, $^2J_{CF}$ = 31.9 Hz), 147.5 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.7 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{18}F_3N_2^+$: 343.1417; found: 343.1423.

Pyrrolidin-1-yl(4-(2-(trifluoromethyl)quinolin-3-yl)phenyl) methanone (5u)

Obtained from ketone **4u** by procedure C (0.758 mmol). Yellow-brown solid, m.p. 132–134 °C, yield 0.195 g (70%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.80–1.94 (m, 4H, CH_2), 3.42–3.45 (m, 2H, NCH_2), 3.60–3.63 (m, 2H, NCH_2), 7.37 (d, ^3J = 8.2 Hz, 2H), 7.56 (d, ^3J = 8.2 Hz, 2H), 7.60 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.74 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.80 (d, ^3J = 7.9 Hz, 1H), 8.08 (s, 1H), 8.15 (d, ^3J = 8.6 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 24.2, 26.2, 46.1, 49.5, 121.5 (q, $^1J_{CF}$ = 276.6 Hz, CF_3), 126.7, 127.3, 128.0, 129.0, 129.6, 130.6, 132.4, 136.6, 138.7, 139.5, 144.8 (q, $^2J_{CF}$ = 32.6 Hz), 145.4, 169.0 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.5 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{21}H_{18}F_3N_2O^+$: 371.1366; found: 371.1361.

3-(Pyridin-4-yl)-2-(trifluoromethyl)quinoline (5v)

Obtained from ketone **4v** by procedure C (~0.87 mmol). Pale brown powder, m.p. 137–139 °C, yield 0.096 g (40%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.36 (d, ^3J = 6.0 Hz, 2H, Py), 7.69–7.78 (m, 1H), 7.84–7.90 (m, 1H), 7.92 (d, ^3J = 8.2 Hz, 1H), 8.16 (s, 1H), 8.28 (d, ^3J = 8.5 Hz, 1H), 8.72 (d, ^3J = 6.0 Hz, 2H, Py) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 121.5 (q, $^1J_{CF}$ = 276.4 Hz, CF_3), 124.1 (d, $^4J_{CF}$ = 1.5 Hz), 127.5, 128.0, 129.4, 130.0, 130.5, 131.3, 139.4, 144.6 (q, $^2J_{CF}$ = 33.2 Hz), 145.4, 146.0, 149.6 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −62.4 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{15}H_{10}F_3N_2^+$: 275.0791; found: 275.0802.

5-(4-Methoxyphenyl)-6-(trifluoromethyl)thieno[2,3-*b*]pyridine (5w)

Obtained from ketone **4w** by procedure B (~0.26 mmol). White powder, m.p. 81–82 °C, yield 0.063 g (78%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.86 (s, 3H, CH_3), 6.97 (d, ^3J = 8.7 Hz, 2H, 4-$MeOC_6H_4$), 7.29 (d, ^3J = 8.7 Hz, 2H, 4-$MeOC_6H_4$), 7.32 (d, ^3J = 6.0 Hz, 1H), 7.74 (d, ^3J = 6.0 Hz, 1H), 8.03 (s, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.3, 113.5, 121.0, 122.1 (q, $^1J_{CF}$ = 275.7 Hz, CF_3), 129.7, 130.4 (q, $^4J_{CF}$ = 1.5 Hz), 131.3, 132.8, 134.2, 134.8, 142.1 (q, $^2J_{CF}$ = 32.6 Hz), 159.0, 159.5 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −61.5 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{15}H_{11}F_3NOS^+$: 310.0508; found: 310.0515.

Synthesis of quinoline 5l by the reaction of enamine 2b with 2-aminobenzaldehyde 3′a generated *in situ* (procedure D)

A 12 mL vial with a screw cap was charged with 2-nitrobenzaldehyde (0.075 g, 0.5 mmol), glacial acetic acid (2 mL), water (0.1 mL) and Fe powder (0.084 g, 1.5 mmol). The reaction mixture was kept at 80 °C under stirring for 0.5–1 hours until the Fe powder dissolved (after 10–15 min the gas pressure must be released!) and the vigorous reaction finished. Next, enamine **2b** (0.088 g, 0.325 mmol) was added and the reaction mixture was heated at 80–90 °C under stirring for 8 hours. Volatiles were evaporated *in vacuo*, and the residue was dispersed between CH_2Cl_2 (5–10 mL) and 6 M HCl (1 mL). Volatiles were evaporated *in vacuo*, and the residue was purified by column chromatography, using a mixture of hexane and CH_2Cl_2 (1 : 1) as eluent. Quinoline **5l** was obtained as a pale beige powder, yield 0.084 g (85%). For characterization date see above.

Synthesis of 3-(4-methoxyphenyl)-2-(trifluoromethyl)-1,6-naphthyridine (5x) by the reaction of enamine 2b with 4-aminonicotinaldehyde

A 12 mL vial with a screw cap was charged with enamine **2b** (0.086 g, 0.32 mmol), 4-aminonicotinaldehyde (0.039 g, 0.32 mmol) and glacial acetic acid (2 mL). The reaction mixture was kept at 80–90 °C under stirring for 12 hours (monitored by ^{1}H NMR). Volatiles were evaporated *in vacuo*, and the residue was purified by column chromatography, using a mixture of CH_2Cl_2 and MeOH (100 : 1) as eluent. Pale brown oil, yield 0.082 g (84%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.98 (d, ^3J = 8.7 Hz, 2H), 7.31 (d, ^3J = 8.7 Hz, 2H), 8.04 (d, ^3J = 6.0 Hz, 1H), 8.28 (s, 1H), 8.83 (d, ^3J = 6.0 Hz, 1H), 9.34 (d, ^3J = 0.8 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.3, 113.7, 121.2 (q, $^1J_{CF}$ = 277.4 Hz, CF_3), 122.1, 123.4, 128.5, 130.3 (q, $^4J_{CF}$ = 1.7 Hz), 135.1, 139.6, 147.5, 147.6, 150.0 (q, $^2J_{CF}$ = 32.8 Hz), 152.7, 159.8 ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −63.2 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{16}H_{12}F_3N_2O^+$: 305.0896; found: 305.0896.

Conflicts of interest

There are no conflicts to declare.

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