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Organometalics free arylation and arylation/trifluoroacetylation of quinolines by their reaction with CF_3-ynones and base induced rearrangement

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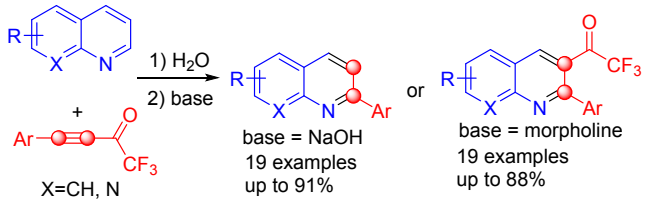


Abstract The reaction of quinolines with CF_3-ynones resulted in formation of 1,3-oxazinoquinolines. Subsequent treatment of the reaction mixture with a base initiated deep structural transformation of primary products. Both steps proceed in very high yield. As a result, unusual rearrangement of 1,3-oxazinoquinolines to form either 2-arylquinolines or 2-aryl-3-trifluoroacetylquinolines was discovered. The decisive role of base on the reaction direction was shown. Using these reactions, highly efficient pathways to 2-arylquinolines and 2-aryl-3-trifluoroacetylquinolines were elaborated to provide the corresponding compounds in high yields using simple one-pot procedure. The possible mechanism of rearrangement is discussed.

Introduction

Quinoline is one of the very first organic molecules known to organic chemists. It was discovered almost two centuries ago in 1834 by German chemist Friedlieb Ferdinand Runge in extracts of coal tar.[1] Nevertheless, chemistry of quinoline is a still intensively developing branch of the modern organic chemistry due to wide applications of quinoline derivatives.[2] Thus, this type of heterocycles has found application as sensors,[3] agrochemicals,[4] materials for phosphorescent organic light-emitting diodes,[5] ligands for transition metal complexes[6] and anti-foaming agents in refineries.[7] Quinoline scaffolds play

a significant role in drug discovery showing many types of biological activity such as antifungal,[8] anticancer,[9] anti-inflammatory,[10] and antileishmaniasis actions.[11] Almost 300 alkaloids, having quinoline moiety were listed in "The Dictionary of Alkaloids".[12] Nowadays, quinoline cinchona alkaloids and their derivatives are widely used in organic synthesis as key catalysts for asymmetric catalysis and organocatalysis (Figure 1).[13] Perhaps, probably the most important application of quinoline derivatives is their use as drugs. Quinolone antibiotics including the organofluorine compounds such as ofloxacin (Floxin), norfloxacin (Noroxin), ciprofloxacin (Cipro), and moxifloxacin (Avelox) are widely used worldwide for treatment a broad range of bacterial infections—such as pneumonia and tuberculosis (Figure 1).[14] In spite of big progress in treatment of tuberculosis, about 10 million people fell ill in 2018, 1.2 million lost their struggle with illness in 2018.[15] Quinoline alkaloid quinine was a first cure for treatment of malaria, known since the 17th century.[16] Malaria is the dangerous infective disease affected 228 million people in 2018, reaping nearly 0.4 million casualities that year.[17] There are a number of modern antimalarial quinoline derived drugs, for example Chloroquine, Hydroxychloroquine, Mefloquine.[18] In addition to the treatment or preventing malaria above mentioned drugs are currently tested as a possible cure for COVID-19.[19]

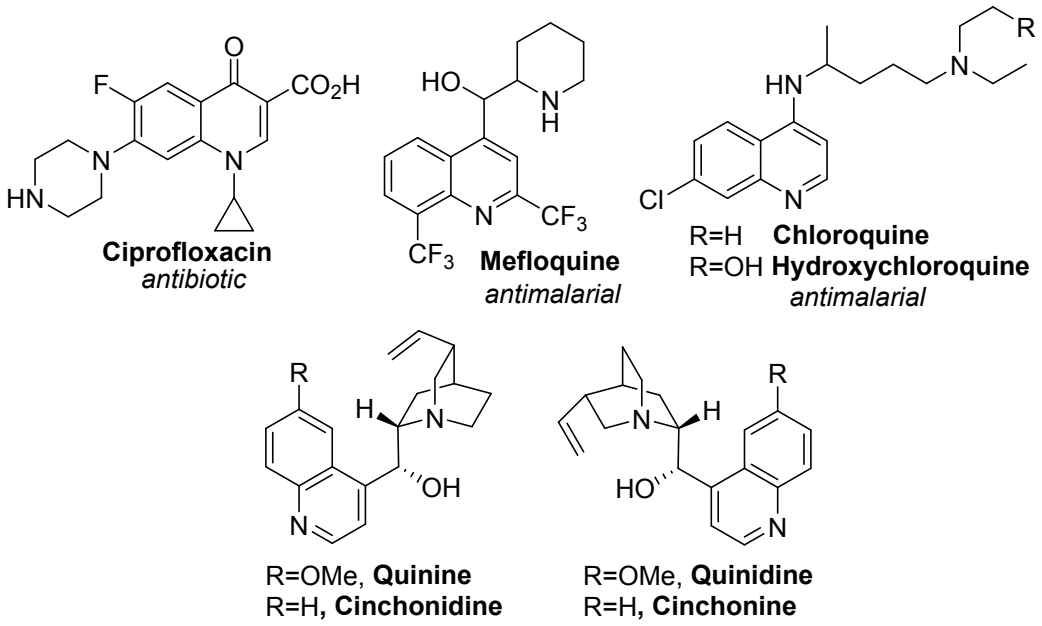
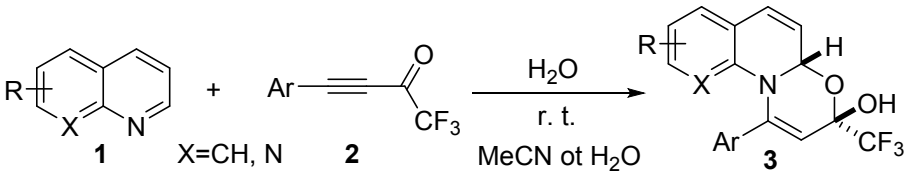


Figure 1. Selected examples of FDA approved drugs having quinoline moiety and cinchona alkaloids.

Nowadays, organofluorine compounds are in the focus of intensive investigation due to their unique physicochemical and biological properties.[20] These compounds are widely used as construction materials, components of liquid crystalline compositions, agrochemicals[21] and pharmaceuticals[22]. By recent estimation, about 20% (more than 300 compounds) of currently used drugs[23] contain at least one fluorine atom.[24] Moreover, last years show even higher shares of fluoropharmaceuticals among new small-molecule drugs (45% in 2018,[25] 41% in 2019[26]). Fluorinated heterocycles make a noticeable contribution into this group. In 2018 and 2019 FDA approved 11 drug bearing fluorinated heterocyclic motifs. As a result, a great attention has been paid for the development of novel effective methodologies for the synthesis of fluorinated heterocycles.[27]

Recently, we elaborated highly efficient stereoselective synthesis of CF_3-oxazinoquinolines using the reaction of CF_3-ynones[28] with quinolines (Scheme 1).[29] The synthetic utility of the prepared CF_3-oxazinoquinolines was demonstrated.[30] In this manuscript we report investigation of two intriguing rearrangements of **3** under treatment with NaOH in water at 80 °C and morpholine in MeCN at 80 °C. The first one leads to 2-phenylquinoline **4** while the second one affords 2-phenyl-3-trifluoroacetylquinoline **5**. The scope of the reactions and their mechanism is also reported.

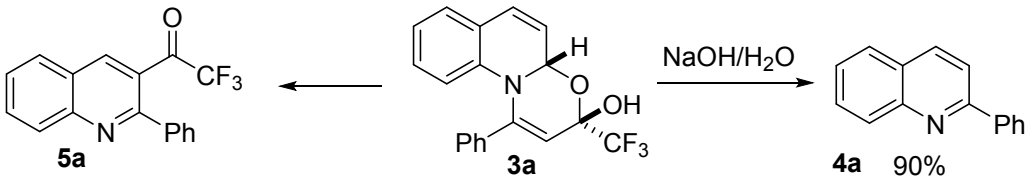


Scheme 1. Synthesis of **3a**.

Results and discussion

To start our investigation, optimization of the reaction conditions was performed using CF_3-oxazine **3a** as a model substrate (Scheme 2). Both nature of solvent and base were tested (for details see Tables S1 and S2 in SI). The main findings of this screening are following. Strong inorganic bases (t-BuOK, NaOH) favor formation of only 2-phenylquinoline in THF, MeCN or H_2O and aqueous NaOH is the

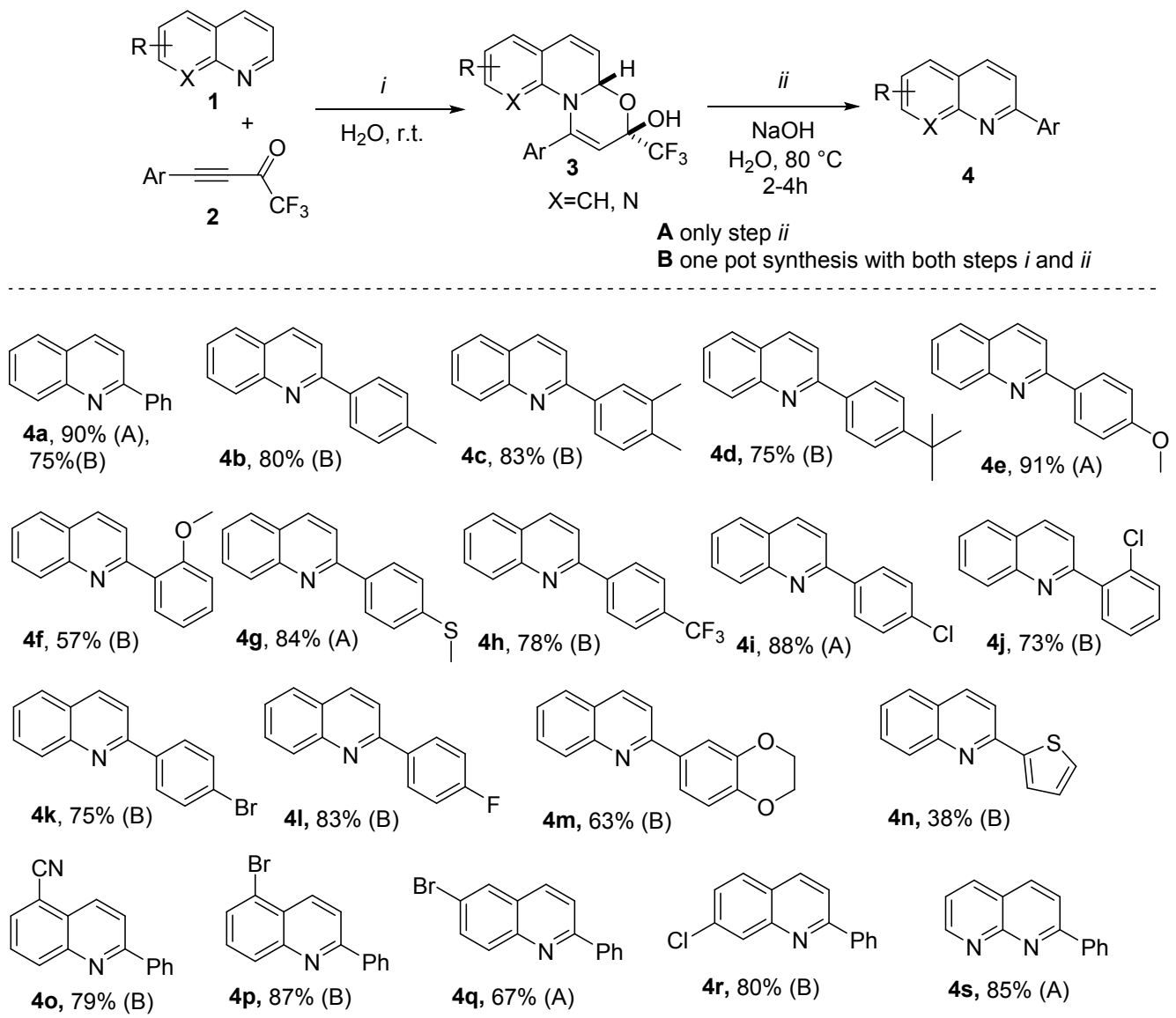
reagent of choice. In contrast, formation of trifluoroacetylquinoline **5a** is preferable under action of milder organic bases to give exclusively **5a** in case of morpholine and *N*-methylpiperidine in MeCN.



N-methylpiperidine/MeCN, 87%
morpholine/MeCN, 88%

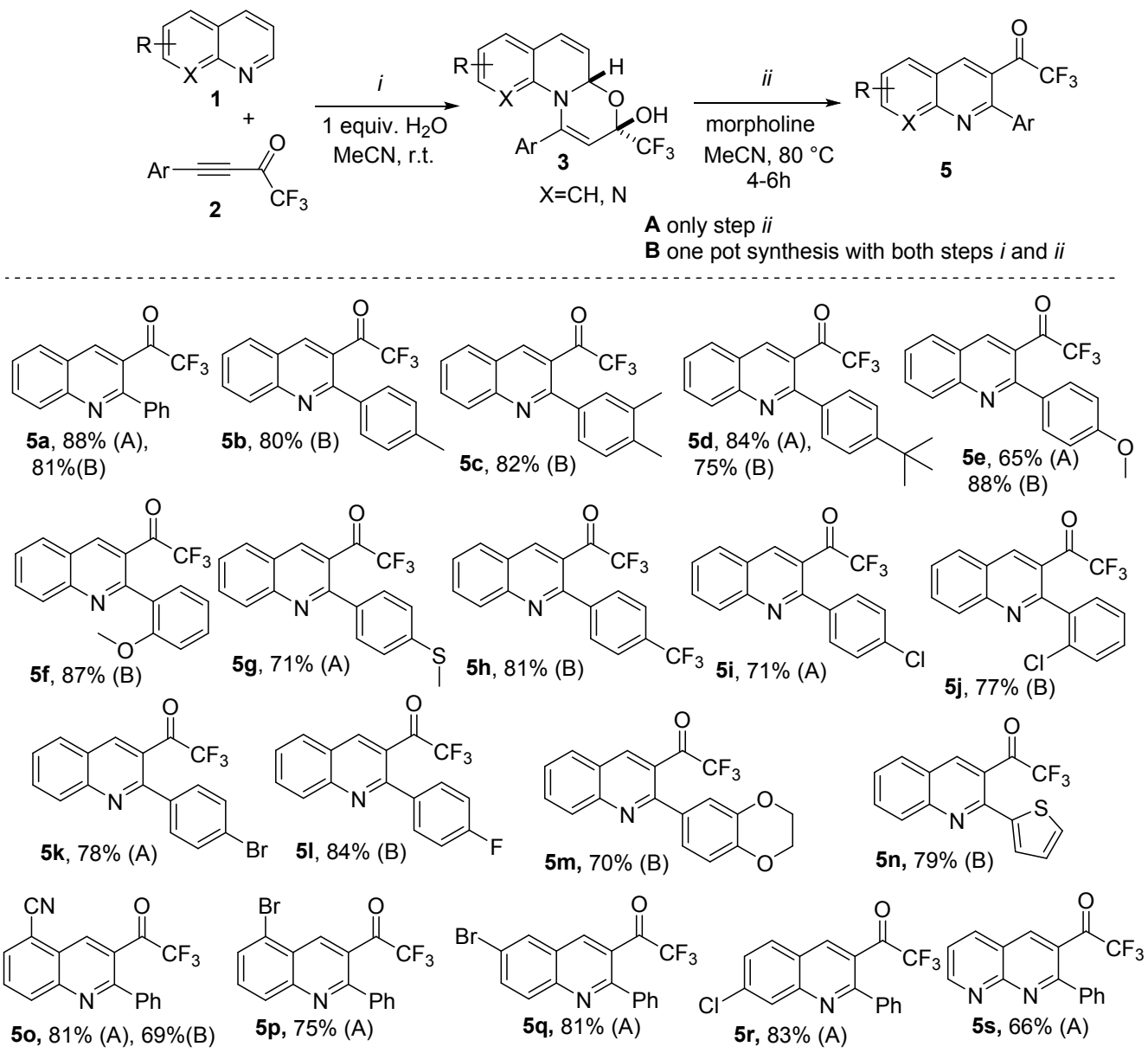
Scheme 2. Base induced transformation of oxazine **3a** into quinolines **4a** and **5a**.

Having optimal conditions in hand, we investigated the synthetic scope of both reactions. It was found, that various CF_3-oxazinoquinolines **3** can be easily transformed into the corresponding 2-arylquinolines in up to 91% yield (Scheme 3). One pot version was also used to prepare 2-arylquinolines in up to 83% yield. The reaction is very general, allowing construction of 2-arylquinolines having different substituents in the structure. No restrictions were found. As a rule, quinolines **4** bearing electron-donating and electron-withdrawing groups as well as bulky substituents in both quinoline and aryl moieties are formed in high yield. Somehow decreased yields were observed for ortho-substituted **4f** and electron rich **4m** prepared in 53% and 63% correspondingly (one pot synthesis). It was also found that the transformation can be used for the synthesis of other heterocyclic derivatives. Thus, 2-(2-thiophenyl)quinoline **4n** and 2-phenyl-1,8-naphtyridine **4s** were prepared successfully.



Scheme 3. Synthesis of 2-arylquinolines **4**.

The investigation of the second rearrangement revealed even better results. The reaction was appeared to be insensitive to the nature of the substituents in oxazines **3** to form 2-aryl-3-trifluoroacetylquinolines **5** in up to 88% yields (Scheme 4). High yields were observed for any derivatives. For example, 2-aryl-3-trifluoroacetylquinolines **5f** and **5m** were prepared in 87% and 70% in one pot variation of the synthesis. Thiophenyl- and 1,8-naphtyridine derivatives were also successfully synthesized. Notably, the yield of 2-thiophenyl derivative **5n** was almost twice better comparing to synthesis of **4n**.



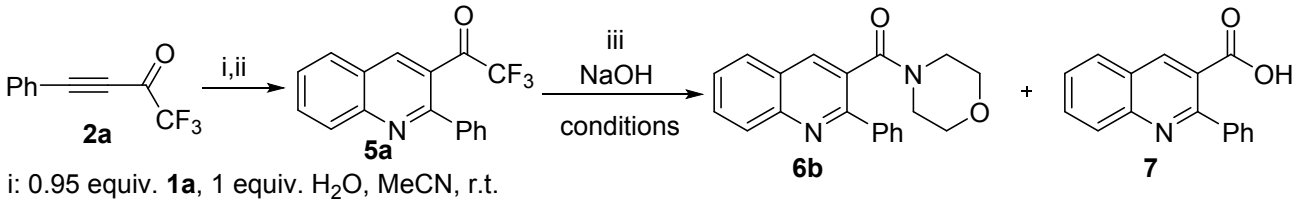
Scheme 4. Synthesis of 2-arylquinolines-3-trifluoroacetylquinoline **5**.

We have also carried out syntheses of 2-phenylquinoline **4a** and 2-phenyl-3-trifluoroacetylquinoline **5a** in sub gram scale. In both cases one pot procedures were used starting from 6 mmol of CF_3-ynone **2a**. As a result, the corresponding quinolines were prepared in high yield (**4a**, 0.722 g, 60% and **5a**, 1.432 g, 82%).

There are plenty methods for the synthesis of 2-arylquinolines or 3-trifluoroacetylquinolines. The most straightforward literature approaches to 2-arylquinolines are based on application of organometallic (lithium[31], magnesium[32], zinc[33], bismuth[34]) or organoelement (boron[35], silicon[36], tin[37]) derivatives.

Effective transformations of o-alkenylarylisonitriles into 2-arylquinolines by radical cascades were also reported[38]. 3-Trifluoroacetylquinolines have been prepared using trifluoroacetylating reagents[39] or by condensations of 2-aminobenzaldehyde[40] and 2-aminoaceto- and benzophenones[41] with carbonyl compounds. Obviously, these two groups of the methods are not compartible, in terms of starting materials and the reaction products. By each group of methods, either 2-diarylquinoline or 2-trifluoromethylquinoline can be obtained. In contrast, the proposed here approach allows preparation of both quinoline derivatives **4** and **5** using the same starting quinolines. Direction of transformation can be switched by choosing the base using for the rearrangement. As a result, formal arylation of starting quinoline at the C-2 position takes place or simultaneous arylation at C-2 and trifluoroacetylation at C-3 of quinoline. In addition, the proposed approaches are "orthogonal" to other methods. Thus, they are tolarate the Br substituents to open opportunities for further cross-couplings of the quinonine products obtained. To the best of our knowledge there are no such flexible methods known in the literature for modification of quinolines.

Next, some efforts were undertaken to investigate possible mechanisms of both rearrangements. First, we proposed possibility of transformation of trifluoroacetylquinoline **5** into quinoline **4** under action of NaOH in aqueous solution. However, heating of **5a** with NaOH led to formation of the corresponding quinoline-3-carboxylic acid **7** in 64% yield. No decarboxylation was observed under the reaction conditions. Similarly, formation of acid **7** was observed in MeCN. It was found, that addition of NaOH to the solution of trifluoroacetylquinoline **5a** obtained in situ by the treatment with morpholine afforded amide **6b** in moderate yield. Addition of water to the reaction mixture allowed to switch the reaction direction to form acid **7**. As a result, one pot three step synthesis of acid **7** was elaborated to give desired compound in 73% yield (Scheme 5). The obtained data permits to exclude transformation of compounds **5** into 2-arylquinolines **4** under the reaction conditions.



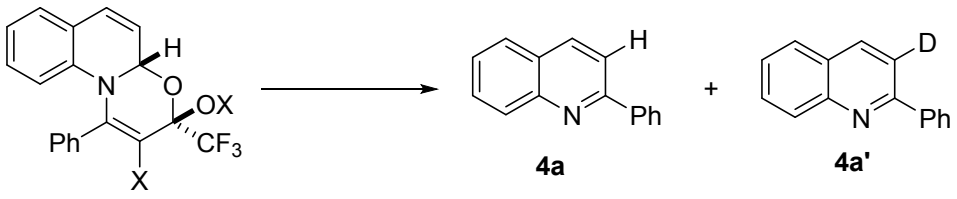
i: 0.95 equiv. **1a**, 1 equiv. H_2O, MeCN, r.t.
ii: morpholine, MeCN, 80 °C, 4-6h

B, C, D one pot

A only step *iii*, H_2O, 2 days, r.t.	-			64%
B *i,ii then iii,* 80 °C, 4-6h	43%	strong tarring		*traces*
C *i,ii then iii,* 10 equiv. H_2O, 80 °C, 4-6h	11%	strong tarring		46%
D *i,ii then iii,* 55 equiv. H_2O, 80 °C, 4-6h	traces			73%

Scheme 5. Transformation of 2-arylquinolines-3-trifluoroacetylquinoline **5a** under action of NaOH.

Next, additional experiments to study the reaction mechanism were performed. For this aim the reaction of **3a** with NaOH in D_2O was investigated. It was found, that no deuterium was incorporated into the structure of quinoline **4a** under these conditions. Next, deuterated oxazine **3a'** was prepared and their rearrangement to **4a** was studied. Treatment of **3a'** with NaOH in D_2O and H_2O resulted in transformation to quinoline **4a'** having position 3 deuterated. Small admixture of non-deuterated quinoline **4a** was formed as well. Monodeuterated product **4a'** was major product both in D_2O and H_2O. One the base of these results one can conclude, that proton adjacent to the third position of quinoline is originated from the enamine moiety of oxazine **3a'**. No significant exchange between substrate and the reaction media is observed during the rearrangement (Scheme 6).

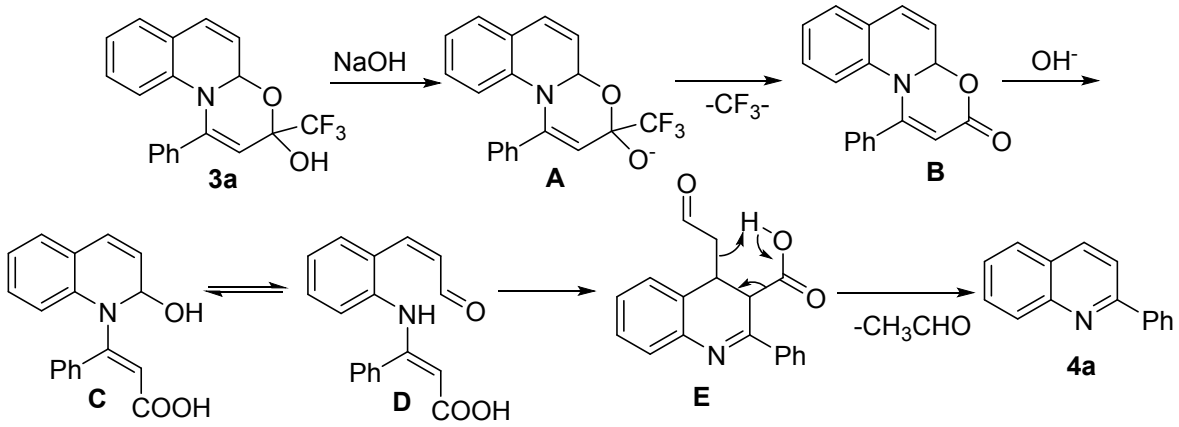


3a	X=H,	D_2O, NaOH, 80 °C, 4h (**4a+4a'**) 71%,	100	:	0
3a'	X=D,	D_2O, NaOH, 80 °C, 4h (**4a+4a'**) 80%,	6	:	94
3a'	X=D,	H_2O, NaOH, 80 °C, 4h (**4a+4a'**) 82%,	16	:	84

Scheme 6. Experiments with deuterium labeled compounds and in D_2O.

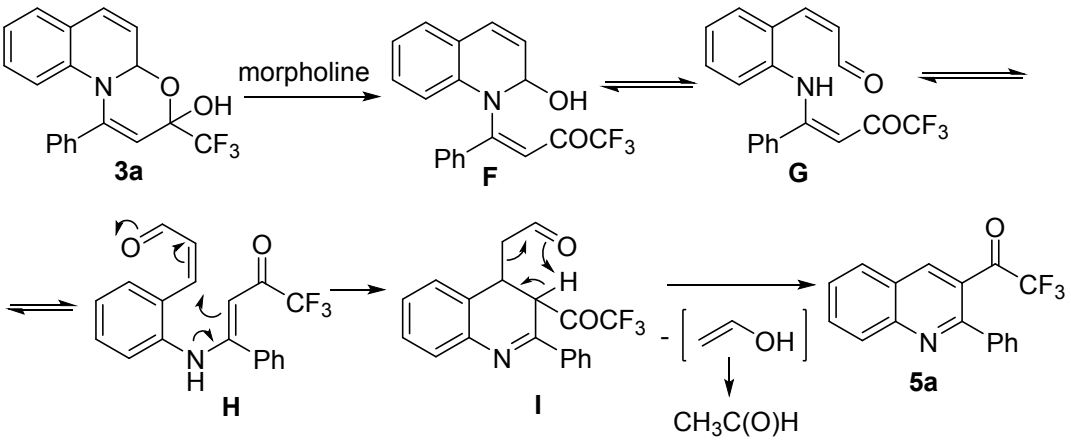
Taking into account the obtained results and literature data[42], we proposed following mechanism for the formation of **4a** (Scheme 7). Most probably the rearrangement proceeds through ANRORC type mechanism (**A**ddition of a **N**ucleophile, followed by the **R**ing **O**pening and **R**ing **C**losure during the

substitution)[43]. It is initiated by deprotonation of hydroxy group of **3a** to form intermediate **A** followed by elimination of trifluoromethyl fragment to give **B**. Subsequent NaOH induced ring opening resulted in formation of intermediate **C** which has semiaminal fragment and is in equilibrium with opened form **D**. This intermediate **D** has in the structure fragment of Michael acceptor (unsaturated aldehyde). On the other hand, it has enamine fragment in the structure as well. As a result new C-C bond is formed to give intermediate **E**. Finally, aromatization takes place by elimination of acetaldehyde and CO_2 to give target 2-substituted quinoline **4a**.



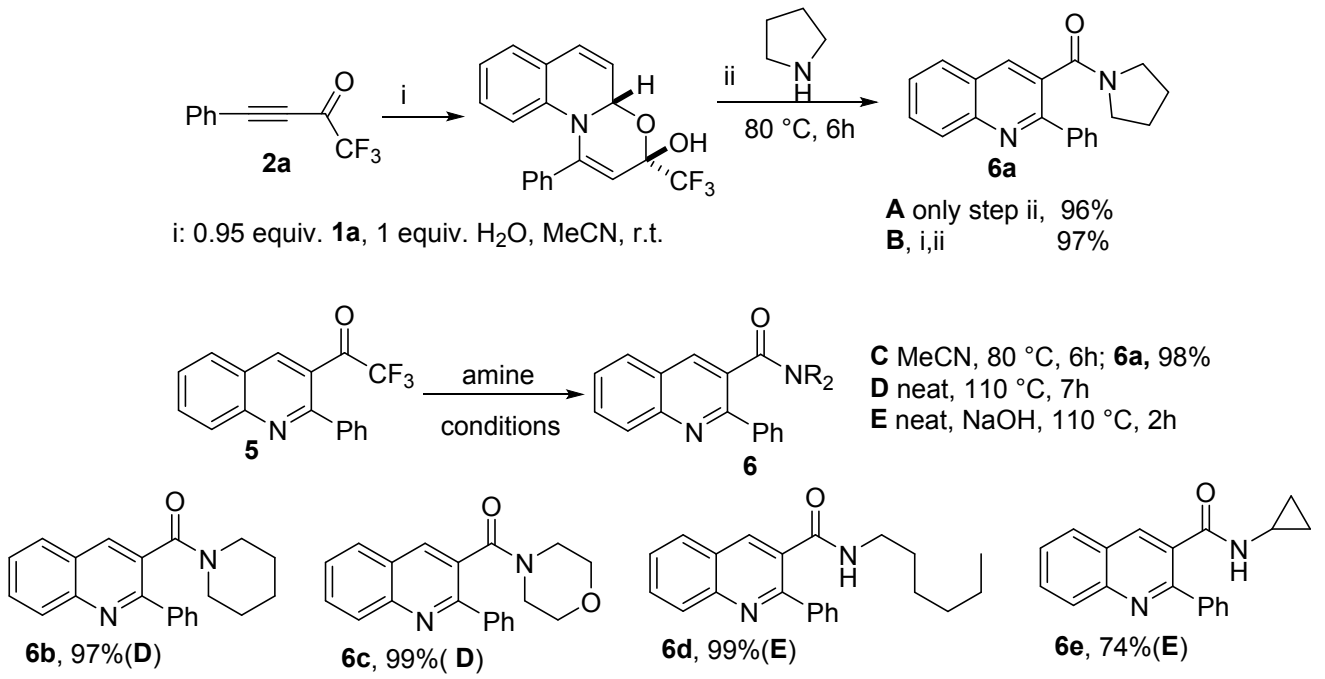
Scheme 7. Possible mechanism of formation of **4a**.

The proposed scheme of rearrangement of **3a** to **4a** can be simply adapted to the synthesis of trifluoroacetylated derivatives **5**. Significantly lower basicity of the reaction media (morpholine-CH_3CN) for this transformation should be taken into account. As a result, no elimination of trifluoromethyl anion takes place. In contract, base induced ring opening of **3a** gives semiaminal intermediate **F** which is in equilibrium with its opened form **G** (Scheme 8). E/Z isomerization of enaminoketone fragment and subsequent intramolecular Michael type reaction of enaminone **H** (or its more nucleophilic hemiaminal form) and unsaturated aldehyde resulted in cyclized intermediate **I**. Elimination of acetaldehyde from **I** ends up the transformation to form quinoline **5a**.



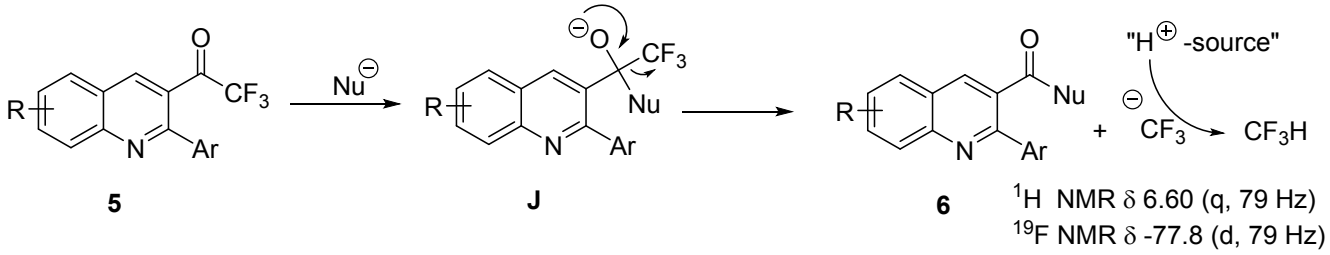
Scheme 8. Possible mechanism of formation of **5a**.

These two mechanisms are in perfect agreement with influence of nature of amine on the reaction (Table S2, SI). It was found, that rearrangement of oxazine **3a** under treatment of pyrrolidine in MeCN led surprisingly to amide **6a** after heating at 80 °C for 6 hours (Scheme 9). Most favorable explanation of this fact is a reaction of highly nucleophilic pyrrolidine with formed trifluoroacetylquinoline **5a**. Indeed, heating of **5a** with pyrrolidine afforded amide **6a** in high yield. We proposed, that various amines can be involved into the reaction to give efficient route to the corresponding amides. Less nucleophilic amines demanded to use elevated temperature. Thus, heating of **5a** in piperidine and morpholine at 110 °C for 7h afforded amides **6b** and **6c** in near quantitative yields. Heating of **5a** with primary amines did not lead to formation of the desired amides. However, addition of NaOH to the reaction mixture led to fast consumption of starting material to give the corresponding amides bearing cyclopropyl- and n-hexyl moieties **6d, 6e**.



Scheme 9. Synthesis of amides **6**.

It should be noted, that NMR investigation of the reaction mixtures revealed the formation of CF_3H in the reaction. Thus, presence of quadruplet at 6.60 ppm having very large H-F coupling constant (79 Hz) in ^1H NMR spectra as well as doublet at -77.8 (79 Hz) in ^{19}F NMR confirmed that fact.[44] Taking into account these results, the mechanism of the transformation of ketones **5** to amides can be rationalized as a two step process. Addition of a nucleophile to carbonyl group of **5** led to intermediate **J** which eliminates trifluoromethyl anion to afford final amide (Scheme 10).



Scheme 10.

In conclusion, we developed general and efficient pathways towards to 2-arylquinolines and 2-aryl-3-trifluoroacetylquinolines based on rearrangement of 1,3-oxazinoquinolines **3**. The reaction direction is orchestrated easily by choosing of the base. Thus, 2-arylquinolines **4** were prepared in high yields

under treatment of 1,3-oxazinoquinolines with NaOH in water. Alternatively, synthesis of 2-aryl-3-trifluoroacetylquinolines **5** can be performed using morpholine as a base. One pot versions of both syntheses were also elaborated starting from quinolines and CF_3-ynones. As a result, formal C-2 arylation and C-2 arylation/3-trifluoroacetylation of quinolines were developed. Possible mechanisms of all transformations are discussed. In addition, 2-aryl-3-trifluoroacetylquinolines **5** can be used as staring materials for novel efficient approaches to 2-phenylquinoline carboxylic acid and its amides.

Experimental section

General remarks. ^1H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker AVANCE 400 MHz spectrometer in CD_3CN and $CDCl_3$ at 400, 100 and 376 MHz respectively. Chemical shifts (δ) in ppm are reported with the use of the residual CHD_2CN and chloroform signals (1.94 and 7.25 for ^1H 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). ESI-MS spectra were measured with an Orbitrap Elite instrument. TLC analysis was performed on "Merck 60 F_{254}" plates. Column chromatography was performed on silica gel. All reagents were of reagent grade and were used as such or were distilled prior to use. CF_3-ynones **2**[28,45] and CF_3-oxazines **3**[30] were prepared as reported previously. Melting points were determined on an Electrothermal 9100 apparatus.

Synthesis of CF_3-ynones 2 from terminal acetylenes (general procedure): Preheated 500 mL three-necked round bottom flask equipped with thermometer, dropping funnel (with rubber septum) and argon inlet was purged with argon and then charged with 200 mL of dry THF and 0.1 mol of corresponding terminal acetylene. Thus obtained solution was cooled to -60°C and 0.11 mol of *n*-BuLi (44 mL, 2.5 M solution in hexane, 0.11 mol) was added dropwise. The reaction mixture was allowed to warm up to -20 °C and then was cooled to -60 °C. Next, CF_3CO_2Et was added slowly at temperature lower than -50 °C. The reaction mixture was allowed to warm up to room temperature (15-20 °C) and then quenched with ~100 mL of 2M HCl at 0-20 °C. Organic layer was separated and water phase was extracted with CH_2Cl_2 (3x30 mL). Combined extracts were washed with water (50 mL), dried over

Na_2SO_4 and volatiles were evaporated *in vacuo*. The residue was purified by vacuum distillation, recrystallization or by passing through short silica gel pad using appropriate hexane–CH_2Cl_2 mixtures as an eluent. Using this procedure CF_3-ynones **2a,c,k,m** (for structures see SI) were prepared. For characterization data of CF_3-ynones **2a,c,k,m** see[28].

4-(3,4-diMethylphenyl)-1,1,1-trifluorobut-3-yn-2-one (2c). Obtained from 4-ethynyl-1,2-dimethylbenzene (13.0 g, 0.1 mol). Yellow oil, yield 14.74 g (65%).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.41 (dd, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H), 7.19 (d, ^3J = 7.7 Hz, 1H), 2.32 (s, 3H, Me), 2.28 (s, 3H, Me) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -78.7 (CF_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 167.2 (q, $^2J_{CF}$ = 42.0 Hz, C=O), 142.7, 137.7, 134.9, 131.7, 130.3, 115.2, 114.9 (q, $^1J_{CF}$ = 288.6 Hz, CF_3), 102.0, 83.5, 20.1, 19.4 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{12}H_{10}F_3O^+$: 227.0678; found: 227.0691.

Synthesis of CF_3-ynones 2 from dichloroalkenes (general procedure): Preheated 500 mL three-necked round bottom flask equipped with thermometer, dropping funnel (with rubber septum) and argon inlet was purged with argon and then charged with dry THF (125 mL) and corresponding dichloroalkene (0.1 mol) or dibromoalkene (for **2n**). Thus obtained solution was cooled to -90°C and *n*-BuLi (0.205 mol, 82 mL, 2.5 M solution in hexane) was added dropwise keeping temperature below -70 to -60 °C. The reaction mixture was kept at -60 to -45 °C for 1h, cooling bath was removed and the reaction mixture was allowed to warm up to 0 to 5 °C. Then the reaction mixture was cooled to -90 °C and CF_3CO_2Et (15.6 g, 0.11 mol) was quite rapidly added for 1-2 minutes. Cooling bath was removed and the reaction mixture was allowed to warm up to 0 to 5 °C. Then the reaction mixture was cooled to -20 °C and HCl (0.25 mol, 125 mL, 2 M aqueous solution) was carefully added for 1 minute. After warming to room temperature (15-20 °C) organic layer was separated and water phase was extracted with CH_2Cl_2 (3x30 mL). Combined extracts were washed with water (50 mL), dried over Na_2SO_4 and volatiles were evaporated *in vacuo*. The residue was purified by vacuum distillation or by passing through short silica gel pad using hexane and appropriate hexane–CH_2Cl_2 mixtures as an eluents. Using

this procedure CF_3-ynones **2d,e,f,g,h,i,j,l** were prepared (for structures see SI). For characterization data of CF_3-ynones **2d,e,f,g,h,i,j,l** see.[45]

1,1,1-Trifluoro-4-(thiophen-2-yl)but-3-yn-2-one (2n). Obtained from 2-(2,2-dibromovinyl)thiophene (20.1 g, 0.075 mol). Yellow oil, yield 3.23 g (21%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.68 (pd, $^3J \sim 4.4$ Hz, 2H), 7.15 (d, $^3J \sim 4.4$ Hz, 1H), ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -78.6 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 166.7 (q, $^2J_{CF}$ = 42.0 Hz, C=O), 139.5, 134.8, 128.3, 117.8, 114.9 (q, $^1J_{CF}$ = 288.4 Hz, CF_3), 94.9, 88.8 ppm. The NMR data are in agreement with those in the literature.[46]

Synthesis of oxazines 3 by the reaction of CF_3-ynones and quinolines in water (general procedure): A 4 mL vial with a screw cap was charged with water (0.5 mL or D_2O for synthesis of **3a'**), quinoline **1** (0.475 mmol, 0.95 equiv.) and then CF_3-ynone **2** (0.5 mmol, 1 equiv.) was added at vigorous stirring. The reaction mixture was stirred at room temperature for 1-2 h and left overnight. Excess water was decanted; the solid residue was dissolved in ethyl acetate (0.5 mL) and dried over Na_2SO_4 (directly in the reaction vial). The solution was transferred into a round bottomed flask and the product crystallized by addition of appropriate amount of heptane (2-3 mL). The mother liquor was decanted, the crude product was dried under reduced pressure to give pure (3*R**,4a*R**)-isomer of **3**. Using this procedure oxazines **3a,d,e,g,i,k,o,p,q,r,s** were prepared (for structures see SI). For characterization data of these compounds see.[30]

Synthesis of 2-arylquinolines (4) (general procedure A). A 4 mL vial with a screw cap was charged with oxazine **3** (0.1 mmol), water (0.5 mL) and NaOH (0.012 g, 0.3 mmol, 3 equiv.). The reaction mixture was heated at 80 °C at stirring for 2 h using magnetic stirrer with heating. After cooling down to room temperature, the reaction mixture was extracted with EtOAc (2x0.5 mL), combined organic phase was passed through a short silica gel pad using hexane followed by hexane-CH_2Cl_2 (3:1) as eluents. Evaporation of volatiles afforded pure 2-arylquinoline **4**.

One pot synthesis of 2-arylquinolines(4) (procedure B). A 4 mL vial with a screw cap was charged with water (1 mL), quinoline **1** (0.475 mmol, 0.95 equiv.) and then CF_3-ynone **2** (0.5 mmol) was added

at vigorous stirring. The reaction mixture was stirred at room temperature overnight. After that NaOH (0.060 g, 1.5 mmol, 3 equiv.) was added and the reaction mixture was heated at 80 °C at stirring for 2 h using magnetic stirrer with heating. After cooling down to room temperature, the reaction mixture was extracted with CH_2Cl_2 (2x0.5 mL), combined organic phase was passed through a short silica gel pad using hexane followed by hexane-CH_2Cl_2 (3:1) as eluents. Evaporation of volatiles afforded pure 2-arylquinoline **4**.

2-Phenylquinoline (4a). Obtained from oxazine **3a** (0.030 g, 0.087 mmol) by procedure A or from quinoline **1a** (0.061 g, 0.473 mmol) and acetylene **2a** (0.099 g, 0.5 mmol) by procedure B Light brown powder, m.p. 81-83 °C (Lit. data[47]: 82-84 °C), yield 0.016 g (90%, A) or 0.073 g (75%, B). Sub gram scale synthesis was performed using procedure B from quinoline **1a** (0.756 g, 5.86 mmol) and acetylene **2a** (1.200 g, 6.061 mmol). Yield 0.722 g, (60%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.22 (d, ^3J = 8.6 Hz, 1H), 8.19-8.15 (m, 3H), 7.87 (d, ^3J = 8.6 Hz, 1H), 7.83 (dd, ^3J = 8.1 Hz, ^4J = 0.7 Hz, 1H), 7.75-7.70 (m, 1H), 7.54-7.51 (m, 3H), 7.48-7.44 (m, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.3, 148.2, 139.6, 136.7, 129.63, 129.61, 129.3, 128.8, 127.5, 127.4, 127.1, 126.2, 119.0 ppm. The NMR data are in agreement with those in the literature[47].

2-Phenylquinoline-3-d (4a'). Obtained from oxazine **3a'** (0.051 g, 0.147 mmol) by procedure A or from quinoline **1a** (0.129 g, 1 mmol) and acetylene **2a** (0.205 g, 1.035 mmol) by procedure B (D_2O was used instead of H_2O). Light brown viscous oil, yield 0.025 g (82%, A, 84:16 mixture with **3a**) or 0.165 g (80%, B, 94:6 mixture with **3a**). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.27 (d, ^3J = 8.6 Hz, 1H), 8.23-8.20 (m, 2H), 8.11 (s, 1H), 7.79-7.72 (m, 2H), 7.58-7.47 (m, 4H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.0, 148.1, 139.4, 136.4, 129.49, 129.43, 129.1, 128.6, 127.4, 127.3, 126.9, 126.0, 118.4 (t, $^1J_{CD}$ = 24.8 Hz) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{15}H_{11}DN^+$: 207.1027; found: 207.1020.

2-(p-Tolyl)quinoline (4b). Obtained from quinoline **1a** (0.030 g, 0.233 mmol) and acetylene **2b** (0.0556 g, 0.262 mmol) by procedure B. Yellow-orange crystals, m.p. 80-82 °C (Lit. data[47]: 79-81 °C),

yield 0.041 g (80%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.18 (d, ^3J = 8.5 Hz, 2H), 8.08 (d, ^3J = 8.1 Hz, 2H), 7.85 (d, ^3J = 8.6 Hz, 1H), 7.80 (dd, ^3J = 8.2 Hz, ^4J = 1.4 Hz, 1H), 7.72 (ptd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1H), 7.51 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.34 (d, ^3J = 8.1 Hz, 2H), 2.44 (s, 3H, Me) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.3, 148.2, 139.3, 136.8, 136.6, 129.6, 129.5, 127.4, 127.0, 126.0, 118.8, 21.3 ppm. The NMR data are in agreement with those in the literature[47].

2-(3,4-diMethylphenyl)quinoline (4c). Obtained from quinoline **1a** (0.0313 g, 0.242 mmol) and acetylene **2a** (0.0603 g, 0.267 mmol) by procedure B. Light yellow powder, m.p. 91-93 °C (Lit. data[48]: 89-91 °C), yield 0.047 g (83%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.18 (d, ^3J = 8.3 Hz, 1H), 8.17 (d, ^3J = 8.4 Hz, 1H), 7.99 (d, ^3J = 8.1 Hz, 1H), 7.87 (dd, ^3J = 8.3 Hz, ^4J = 1.8 Hz, 1H), 7.85 (d, ^3J = 8.6 Hz, 1H), 7.80 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1H), 7.72 (ptd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1H), 7.50 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.29 (d, ^3J = 7.8 Hz, 1H), 2.39 (s, 3H, Me), 2.34 (s, 3H, Me) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.5, 148.2, 138.1, 137.2, 137.0, 136.6, 130.1, 129.6, 129.5, 128.6, 127.4, 127.0, 126.0, 124.9, 118.9, 19.9, 19.7 ppm. The NMR data are in agreement with those in the literature[48].

2-(4-(tert-Butyl)phenyl)quinoline (4d). Obtained from quinoline **1a** (0.0305 g, 0.236 mmol) and acetylene **2d** (0.068 g, 0.268 mmol) by procedure B. Light brown solid, m.p. 62-64 °C (Lit. data[49]: 84-85 °C), yield 0.046 g (75%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.18 (d, ^3J = 8.6 Hz, 2H), 8.11 (d, ^3J = 8.6 Hz, 2H), 7.86 (d, ^3J = 8.6 Hz, 1H), 7.81 (dd, ^3J = 8.1 Hz, ^4J = 1.2 Hz, 1H), 7.72 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.56 (d, ^3J = 8.6 Hz, 2H), 7.51 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 1.39 (s, 9H, *t*-Bu) ppm. ^{13}C{^{1}H} (100.6 MHz, $CDCl_3$): δ 157.3, 152.5, 148.3, 136.9, 136.6, 129.6, 129.5, 127.4, 127.2, 127.0, 126.0, 125.8, 118.9, 34.7, 31.3 ppm. The NMR data are in agreement with those in the literature[49].

2-(4-Methoxyphenyl)quinoline (4e). Obtained from oxazine **3e** (0.081 g, 0.216 mmol) by procedure A. Light brown powder, m.p. 124-125 °C (Lit. data[47]: 119-121 °C), yield 0.046 g (91%). ^{1}H NMR (400.1

MHz, $CDCl_3$): δ 8.16-8.11 (m, 4H), 7.82-7.77 (m, 2H), 7.70 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.48 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.04 (d, ^3J = 8.9 Hz, 2H), 3.87 (s, 3H, MeO) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 160.7, 156.9, 148.2, 136.6, 132.2, 129.5, 129.4, 128.8, 127.4, 126.8, 125.9, 118.5, 114.2, 55.3 ppm. The NMR data are in agreement with those in the literature[47].

2-(2-Methoxyphenyl)quinoline (4f). Obtained from quinoline **1a** (0.061 g, 0.473 mmol) and acetylene **2f** (0.114 g, 0.5 mmol) by procedure B. Light yellow oil, yield 0.063 g (57%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.19 (d, ^3J = 8.5 Hz, 1H), 8.13 (d, ^3J = 8.6 Hz, 1H), 7.89 (d, ^3J = 8.6 Hz, 1H), 7.87 (dd, ^3J = 7.6 Hz, ^4J = 1.8 Hz, 1H), 7.82 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1H), 7.70 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.52 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.42 (ptd, ^3J = 7.4 Hz, ^4J = 1.8 Hz, 1H), 7.14 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.02 (d, ^3J = 8.3 Hz, 1H), 3.85 (s, 3H, MeO) ppm.

$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 157.1, 157.0, 148.2, 135.0, 131.4, 130.2, 129.6, 129.5, 129.1, 127.3, 126.9, 126.1, 123.4, 121.2, 111.3, 55.5 ppm. The NMR data are in agreement with those in the literature[50].

2-(4-(Methylthio)phenyl)quinoline (4g). Obtained from oxazine **3g** (0.0286 g, 0.0731 mmol) by procedure A. Light yellow powder, m.p. 146-148 °C (Lit. data[51]: 128-130 °C), yield 0.0154 g (84%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.19 (d, ^3J = 8.6 Hz, 1H), 8.14 (d, ^3J = 8.5 Hz, 1H), 8.09 (d, ^3J = 8.5 Hz, 2H), 7.84 (d, ^3J = 8.6 Hz, 1H), 7.81 (d, ^3J = 8.1 Hz, 1H), 7.71 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.51 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.38 (d, ^3J = 8.5 Hz, 2H), 2.54 (s, 3H, MeS) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 156.6, 148.3, 140.4, 136.8, 136.2, 129.7, 129.6, 127.8, 127.4, 127.1, 126.4, 126.2, 118.6, 15.5 ppm. The NMR data are in agreement with those in the literature[51].

2-(4-(Trifluoromethyl)phenyl)quinoline (4h). Obtained from quinoline **1a** (0.033 g, 0.256 mmol) and acetylene **2h** (0.070 g, 0.263 mmol) by procedure B. Light brown powder, m.p. 125-126 °C (Lit. data[50]: 122-124 °C), yield 0.0545 g (78%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.26 (d, ^3J = 8.1 Hz, 2H), 8.22 (d, ^3J = 8.6 Hz, 1H), 8.18 (d, ^3J = 8.5 Hz, 1H), 7.86-7.82 (m, 2H), 7.77-7.73 (m, 3H), 7.55 (ptd, ^3J = 7.5

Hz, ^4J = 1.1 Hz, 1H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -63.8 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 155.6, 148.2, 142.9 (q, $^4J_{CF}$ = 1.1 Hz), 137.1, 131.0 (q, $^2J_{CF}$ = 32.4 Hz, $\underline{C}$-CF_3), 130.0, 129.8, 127.8, 127.5, 127.4, 126.8, 125.7 (q, $^3J_{CF}$ = 3.7 Hz), 115.9 (q, $^1J_{CF}$ = 272.2 Hz, CF_3), 118.7 ppm. The NMR data are in agreement with those in the literature[50].

2-(4-Chlorophenyl)quinoline (4i). Obtained from oxazine **3i** (0.036 g, 0.0947 mmol) by procedure A. Light brown powder, m.p. 108-110 °C (Lit. data[47]: 114-116 °C), yield 0.020 g (88%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.21 (d, ^3J = 8.6 Hz, 1H), 8.15 (d, ^3J = 8.5 Hz, 1H), 8.11 (d, ^3J = 8.4 Hz, 2H), 7.82 (d, ^3J = 8.6 Hz, 2H), 7.73 (ptd, ^3J = 7.7 Hz, ^4J = 1.0 Hz, 1H), 7.53 (pt, ^3J = 7-8 Hz, 1H), 7.48 (d, ^3J = 8.4 Hz, 2H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 156.0, 148.2, 138.0, 137.0, 135.5, 129.8, 129.6, 129.0, 128.8, 127.5, 127.2, 126.5, 118.6 ppm. The NMR data are in agreement with those in the literature[47].

2-(2-Chlorophenyl)quinoline (4j). Obtained from quinoline **1a** (0.0313 g, 0.243 mmol) and acetylene **2j** (0.0605 g, 0.257 mmol) by procedure B. Light yellow-brown powder, m.p. 77-79 °C (Lit. data[52]: 72-75 °C), yield 0.0428 g (73%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.21 (d, ^3J = 8.7 Hz, 1H), 8.18 (d, ^3J = 8.7 Hz, 1H), 7.86 (dd, ^3J = 8.1 Hz, ^4J = 0.9 Hz, 1H), 7.75 (d, ^3J = 8.4 Hz, 1H), 7.74 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.69 (dd, ^3J = 7.4 Hz, ^4J = 2.1 Hz, 1H), 7.57 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.50 (dd, ^3J = 7.4 Hz, ^4J = 2.1 Hz, 1H), 7.43-7.35 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 157.4, 148.0, 139.6, 135.6, 132.3, 131.7, 130.0, 129.8, 129.7, 129.6, 127.5, 127.14, 127.07, 126.7, 122.7 ppm. The NMR data are in agreement with those in the literature[52].

2-(4-Bromophenyl)quinoline (4k). Obtained from quinoline **1a** (0.0305 g, 0.236 mmol) and acetylene **2k** (0.069 g, 0.249 mmol) by procedure B. Light brown powder, m.p. 114-115 °C (Lit. data[47]: 120-122 °C), yield 0.050 g (75%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.19-8.14 (m, 2H), 8.03 (d, ^3J = 8.5 Hz, 2H), 7.80 (d, ^3J = 8.1 Hz, 1H), 7.79 (d, ^3J = 8.6 Hz, 1H), 7.73 (ptd, ^3J = 7.6 Hz, ^4J = 1.3 Hz, 1H), 7.63 (d, ^3J = 8.5 Hz, 2H), 7.52 (ptd, ^3J = 7.5 Hz, ^4J = 0.9 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ

155.9, 148.1, 138.4, 136.9, 131.9, 129.8, 129.6, 129.0, 127.4, 127.2, 126.5, 123.9, 118.4 ppm. The NMR data are in agreement with those in the literature[47].

2-(4-Fluorophenyl)quinoline (4l). Obtained from quinoline **1a** (0.0301 g, 0.233 mmol) and acetylene **2l** (0.0612 g, 0.5 mmol) by procedure B. Light brown powder, m.p. 92-94 °C (Lit. data[47]: 90-91 °C), yield 0.043 g (83%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.19 (d, ^{3}J = 8.7 Hz, 1H), 8.18-8.13 (m, 3H), 7.81 (d, ^{3}J = 8.6 Hz, 2H), 7.72 (ptd, ^{3}J = 7.4 Hz, ^{4}J = 1.4 Hz, 1H), 7.52 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.0 Hz, 1H), 7.20 (pt, $^{3}J_{HH}$, $^{3}J_{HF}$ = 8.7 Hz, 2H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -113.67…-113.75 (m, Ar-F) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 163.7 (d, $^{1}J_{CF}$ = 249.0 Hz), 156.2, 148.2, 136.9, 135.8 (d, $^{4}J_{CF}$ = 3.1 Hz), 129.8, 129.6, 129.4 (d, $^{3}J_{CF}$ = 8.5 Hz), 127.4, 127.0, 126.3, 118.4, 115.7 (d, $^{2}J_{CF}$ = 21.6 Hz) ppm. The NMR data are in agreement with those in the literature[47].

2-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)quinoline (4m). Obtained from quinoline **1a** (0.0314 g, 0.243 mmol) and acetylene **2m** (0.063 g, 0.246 mmol) by procedure B. Light yellow powder, m.p. 115-117 °C (Lit. data[53]: 104 °C), yield 0.0405 g (63%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.14 (pt, ^{3}J = 8.3 Hz, 2H), 7.78 (d, ^{3}J = 8.6 Hz, 2H), 7.74 (d, ^{4}J = 2.1 Hz, 1H), 7.69 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.68 (dd, ^{3}J = 8.4 Hz, ^{4}J = 2.1 Hz, 1H), 7.48 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.1 Hz, 1H), 7.00 (d, ^{3}J = 8.4 Hz, 1H), 4.30 (s, 4H, $2CH_2$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 156.5, 148.1, 144.9, 143.8, 136.6, 133.2, 129.52, 129.50, 127.4, 126.9, 125.9, 120.8, 118.5, 117.5, 116.5, 64.5, 64.3 ppm. The NMR data are in agreement with those in the literature[53].

2-(Thiophen-2-yl)quinoline (4n). Obtained from quinoline **1a** (0.060 g, 0.465 mmol) and acetylene **2n** (0.101 g, 0.495 mmol) by procedure B. Light brown powder, m.p. 129-131 °C (Lit. data[50]: 124-127 °C), yield 0.0374 g (38%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.12 (d, ^{3}J = 8.8 Hz, 1H), 8.09 (d, ^{3}J = 8.6 Hz, 1H), 7.79-7.75 (m, 2H), 7.72 (dd, ^{3}J = 3.7 Hz, ^{4}J = 1.0 Hz, 1H), 7.69 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.50-7.45 (m, 2H), 7.15 (dd, ^{3}J = 5.0 Hz, ^{3}J = 3.7 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ

152.3, 148.1, 145.3, 136.6, 129.8, 129.2, 128.5, 128.0, 127.4, 127.1, 126.1, 125.8, 117.6 ppm. The NMR data are in agreement with those in the literature[50].

2-Phenylquinoline-5-carbonitrile (4o). Obtained from quinoline **1b** (0.037 g, 0.240 mmol) and acetylene **2a** (0.056 g, 0.281 mmol) by procedure B. Light yellow-green powder, m.p. 142-144 °C, yield 0.0436 g (79%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.54 (d, ^{3}J = 8.8 Hz, 1H), 8.37 (d, ^{3}J = 8.5 Hz, 1H), 8.18-8.15 (m, 2H), 8.04 (d, ^{3}J = 8.8 Hz, 1H), 7.92 (dd, ^{3}J = 7.3 Hz, ^{4}J = 0.9 Hz, 1H), 7.75 (dd, ^{3}J = 8.5 Hz, ^{3}J = 7.3 Hz, 1H), 7.56-7.48 (m, 3H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 158.8, 147.4, 138.4, 135.2, 133.9, 132.4, 130.1, 129.0, 128.8, 127.6, 126.8, 121.0, 116.8, 109.9 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{16}H_{11}N_2^+$: 231.0917; found: 231.0926.

5-Bromo-2-phenylquinoline (4p). Obtained from quinoline **1c** (0.0518 g, 0.249 mmol) and acetylene **2a** (0.0518 g, 0.262 mmol) by procedure B. Light brown powder, m.p. 80-82 °C, yield 0.0612 g (87%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.55 (d, ^{3}J = 8.8 Hz, 1H), 8.18-8.12 (m, 3H), 7.93 (d, ^{3}J = 8.8 Hz, 1H), 7.77 (d, ^{3}J = 7.3 Hz, 1H), 7.57-7.48 (m, 4H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.8, 148.9, 138.8, 136.1, 129.9, 129.8, 129.7, 129.6, 128.9, 127.6, 126.5, 121.7, 120.0 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{15}H_{11}{}^{79}BrN^+$: 284.0069; found: 284.0068; Calcd for $C_{15}H_{11}{}^{81}BrN^+$: 286.0049; found: 286.0049.

6-Bromo-2-phenylquinoline (4q). Obtained from oxazine **3q** (0.0626 g, 0.148 mmol) by procedure A. Light brown powder, m.p. 123-124 °C (Lit. data[49]: 123-124 °C), yield 0.0282 g (67%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.15-8.12 (m, 2H), 8.10 (d, ^{3}J = 8.7 Hz, 1H), 8.03 (d, ^{3}J = 9.0 Hz, 1H), 7.97 (d, ^{4}J = 2.2 Hz, 1H), 7.87 (d, ^{3}J = 8.7 Hz, 1H), 7.78 (dd, ^{3}J = 9.0 Hz, ^{4}J = 2.2 Hz, 1H), 7.55-7.45 (m, 3H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 157.6, 146.8, 139.1, 135.7, 133.1, 131.4, 129.6, 129.5, 128.9, 128.2, 127.4, 120.0, 119.7 ppm. The NMR data are in agreement with those in the literature[49].

7-Chloro-2-phenylquinoline (4r). Obtained from quinoline **1e** (0.0389 g, 0.239 mmol) and acetylene **2a** (0.057 g, 0.288 mmol) by procedure B. White powder, m.p. 114-115 °C (Lit. data[54]: 110-111 °C),

yield 0.046 g (80%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.17-8.14 (m, 4H), 7.85 (d, ^3J = 8.5 Hz, 1H), 7.73 (d, ^3J = 8.6 Hz, 1H), 7.55-7.44 (m, 4H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 158.2, 148.6, 139.1, 136.5, 135.4, 129.6, 128.9, 128.63, 128.62, 127.5, 127.2, 125.4, 119.1 ppm. The NMR data are in agreement with those in the literature[54].

2-Phenyl-1,8-naphthyridine (4s). Obtained from quinoline **1f** (0.027 g, 0.208 mmol) and acetylene **2a** (0.056 g, 0.288 mmol) by procedure B. White powder, m.p. 119-120 °C (Lit. data[55]: 120-121 °C), yield 0.0365 g (85%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 9.09 (dd, ^3J = 4.2 Hz, ^4J = 2.0 Hz, 1H), 8.30-8.27 (m, 2H), 8.19 (d, ^3J = 8.5 Hz, 1H), 8.14 (dd, ^3J = 8.1 Hz, ^4J = 2.0 Hz, 1H), 7.96 (d, ^3J = 8.5 Hz, 1H), 7.52-7.43 (m, 3H), 7.42 (dd, ^3J = 8.1 Hz, ^4J = 4.2 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 160.1, 156.0, 153.7, 138.4, 137.7, 136.7, 130.0, 128.7, 127.8, 121.7, 121.6, 119.6 ppm. The NMR data are in agreement with those in the literature[55].

Synthesis of 2,2,2-trifluoro-1-(2-arylquinolin-3-yl)ethanones (5) (procedure A). A 4 mL vial with a screw cap was charged with oxazine **3a** (0.1 mmol), MeCN (0.5 mL) and morpholine (0.0087 g, 0.1 mmol, 1 equiv.). The reaction mixture was heated at 80 °C for 4-6 h using magnetic stirrer with heating and then volatiles were evaporated in vacuo. The residue was passed through a short silica gel pad using hexane followed by hexane-CH_2Cl_2 (3:1) as eluents. Evaporation of volatiles afforded pure **5**.

One pot synthesis of 2,2,2-trifluoro-1-(2-arylquinolin-3-yl)ethanones (5) (procedure B). A 4 mL vial with a screw cap was charged with water (0.009 g, 0.5 mmol, 1 equiv.), quinoline **1** (0.475 mmol, 0.95 equiv.), MeCN (1.5 mL) and then CF_3-ynone **2** (0.5 mmol, 1 equiv.) was added at stirring. The clear solution thus obtained was left at room temperature for 24h. Next, morpholine (0.044 g, 0.5 mmol, 1 equiv.) was added and the reaction mixture was heated at 80 °C for 6 h using magnetic stirrer with heating. Volatiles were evaporated in vacuo, the residue was passed through a short silica gel pad using hexane followed by hexane-CH_2Cl_2 (3:1) as eluents. Evaporation of volatiles afforded pure **5**.

2,2,2-Trifluoro-1-(2-phenylquinolin-3-yl)ethanone (5a). Obtained from oxazine **3a** (0.030 g, 0.087 mmol) by procedure A or from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2a** (0.099 g, 0.5 mmol) by procedure B. Pale yellow powder, m.p. 86-87 °C, yield 0.023 g (88%, A) or 0.116 g (81%, B). Sub gram scale synthesis was performed using procedure B from quinoline **1a** (0.751 g, 5.821 mmol) and acetylene **2a** (1.167 g, 5.89 mmol). Yield 1.432 g, (82%). ^{1}H NMR (400.1 MHz, CD_3CN): δ 8.77 (s, 1H), 8.09 (m, 1H), 8.07 (m, 1H), 7.91 (m, 1H), 7.68 (m, 1H), 7.56 (m, 2H), 7.49 (m, 3H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, CD_3CN): δ 185.4 (q, $^{2}J_{CF}$ = 36.0 Hz, C=O), 158.4, 149.6, 140.8, 140.7 (q, $^{4}J_{CF}$ = 3.0 Hz, C-4), 134.3, 130.3, 130.2, 130.1, 129.6, 129.1, 126.4, 126.0, 117.1 (q, $^{1}J_{CF}$ = 291.7 Hz, CF_3) ppm. ^{19}F NMR (376.5 MHz, CD_3CN): δ -72.4 (CF_3) ppm. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.22 (d, ^{3}J = 8.5 Hz, 1H), 7.93 (d, ^{3}J = 8.1 Hz, 1H), 7.87 (ptd, ^{3}J = 8 Hz, ^{4}J = 1 Hz, 1H), 7.65-7.60 (m, 3H), 7.53-7.46 (m, 3H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 184.5 (q, $^{2}J_{CF}$ = 36.3 Hz, C=O), 157.6, 148.6, 139.3, 138.9 (q, $^{4}J_{CF}$ = 2.0 Hz, C-4), 132.9, 129.6, 129.3, 128.9, 128.7, 128.6, 127.8, 125.8, 124.8, 115.9 (q, $^{1}J_{CF}$ = 292.3 Hz, CF_3) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.7 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{11}F_3NO^+$: 302.0793; found: 302.0790.

2,2,2-Trifluoro-1-(2-(p-tolyl)quinolin-3-yl)ethan-1-one (5b). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2b** (0.106 g, 0.5 mmol) by procedure B. Pale yellow powder, m.p. 78-80 °C, yield 0.120 g (80%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.20 (d, ^{3}J = 8.5 Hz, 1H), 7.95 (d, ^{3}J = 8.3 Hz, 1H), 7.88 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.64 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.1 Hz, 1H), 7.48 (d, ^{3}J = 8.0 Hz, 2H), 7.30 (d, ^{3}J = 8.0 Hz, 2H), 2.42 (s, 3H, Me) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.8 (CF_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 184.9 (q, $^{2}J_{CF}$ = 36.1 Hz, C=O), 157.6, 148.8, 139.5, 138.9 (q, $^{4}J_{CF}$ = 2.0 Hz), 136.5, 132.8, 129.6, 129.5, 128.8, 128.7, 127.7, 126.0, 124.8, 115.9 (q, $^{1}J_{CF}$ = 292.5 Hz, CF_3), 21.4 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{13}F_3NO,^+$: 316.0944; found: 316.0941.

1-(2-(3,4-Dimethylphenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5c). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2c** (0.113 g, 0.5 mmol) by procedure B. White powder, m.p. 117-119 °C, yield 0.128 g (82%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.20 (d, ^3J = 8.4 Hz, 1H), 7.94 (d, ^3J = 8.1 Hz, 1H), 7.88 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.64 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.43 (s, 1H), 7.23 (s, 2H), 2.34 (s, 3H, Me), 2.32 (s, 3H, Me) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.8 (CF_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 185.1 (q, $^2J_{CF}$ = 36.1 Hz, C=O), 157.7, 148.8, 138.8 (q, $^4J_{CF}$ = 2.0 Hz), 138.2, 137.3, 136.9, 132.8, 130.0 (2C), 129.6, 128.6, 127.7, 126.4, 126.2, 124.8, 115.9 (q, $^1J_{CF}$ = 292.5 Hz, CF_3), 19.9, 19.7 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{19}H_{15}F_3NO^+$: 330.1100; found: 330.1100.

1-(2-(4-(*tert*-Butyl)phenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5d). Obtained from oxazine **3d** (0.060 g, 0.15 mmol) and morpholine (0.013 g, 0.150 mmol) by procedure A or from quinoline **1a** (0.017 g, 0.13 mmol) and acetylene **2d** (0.035 g, 0.138 mmol) by procedure B. Pale yellow powder, m.p. 109-111 °C, yield 0.045 g (84%, A) or 0.035 g (75%, B). IR (microlayer): 1615 (C=C), 1727 (C=O) cm^{-1}. ^{1}H NMR (400.1 MHz, CD_3CN): δ 8.74 (s, 1H), 8.06 (m, 2H), 7.89 (m, 1H), 7.65 (m, 1H), 7.54-7.48 (m, 4H,), 1.34 (s, 9H, *t*-Bu) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, CD_3CN): δ 185.4 (q, $^2J_{CF}$ = 34.7 Hz, C=O), 158.2, 153.4, 149.6, 140.5, 137.7, 134.1, 130.2, 130.1, 129.9, 128.9, 128.0, 126.5, 125.8, 117.1 (q, $^1J_{CF}$ = 291.6 Hz, CF_3), 35.4 (C from *t*-Bu), 31.5 (3Me from *t*-Bu) ppm. ^{19}F NMR (376.5 MHz, CD_3CN): δ -73.0 (CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{21}H_{19}F_3NO^+$: 358.1419; found: 358.1425.

2,2,2-Trifluoro-1-(2-(4-methoxyphenyl)quinolin-3-yl)ethan-1-one (5e). Obtained from oxazine **3e** (0.052 g, 0.138 mmol), morpholine (0.004 g, 0.046 mmol) by procedure A or from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2a** (0.114 g, 0.5 mmol) by procedure B. Pale yellow powder, m.p. 96-98 °C, yield 0.029 g (65%, A) or 0.139 g (88%, B). IR (microlayer): 1605 (C=C), 1725 (C=O) cm^{-1}. ^{1}H NMR (400.1 MHz, CD_3CN): δ 8.74 (s, 1H), 8.09 (m, 2H), 7.93 (m, 1H), 7.69 (m, 1H), 7.54 (m, 2H),

7.05 (m, 2H), 3.86 (s, 3H, OMe) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, CD_3CN): δ 185.6 (q, $^2J_{CF}$ = 35.5 Hz, C=O), 161.8, 157.8, 151.6, 149.7, 140.6, 136.9, 134.1, 133.0, 131.6, 130.1, 128.8, 125.8, 117.5 (q, $^1J_{CF}$ = 291.4 Hz, CF_3), 115.1, 56.1 (OMe) ppm. ^{19}F NMR (376.5 MHz, CD_3CN): δ -73.2 (CF_3) ppm. ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.17 (d, ^3J = 8.4 Hz, 1H), 7.89 (d, ^3J = 8.6 Hz, 1H), 7.85 (ptd, ^3J = 7.7 Hz, ^4J = 1.5 Hz, 1H), 7.59 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.56 (d, ^3J = 8.8 Hz, 2H), 7.02 (d, ^3J = 8.8 Hz, 2H), 3.84 (s, 3H, MeO) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.8 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 185.2 (q, $^2J_{CF}$ = 36.1 Hz, C=O), 160.6, 156.9, 148.7, 138.8 (q, $^4J_{CF}$ = 1.9 Hz), 132.7, 131.7, 130.4, 129.4, 128.6, 127.5, 125.9, 124.6, 115.8 (q, $^1J_{CF}$ = 292.5 Hz, CF_3), 114.2, 55.2 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{13}F_3NO_2^+$: 332.0893; found: 332.0901.

2,2,2-Trifluoro-1-(2-(2-methoxyphenyl)quinolin-3-yl)ethan-1-one (5f). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **5f** (0.114 g, 0.5 mmol) by procedure B. Light yellow powder, m.p. 152-154 °C, yield 0.136 g (87%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.20 (d, ^3J = 8.5 Hz, 1H), 7.91 (d, ^3J = 8.1 Hz, 1H), 7.85 (dd, ^3J = 7.5 Hz, ^4J = 1.7 Hz, 1H), 7.83 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.61 (ptd, ^3J = 7.5 Hz, ^4J = 0.9 Hz, 1H), 7.45 (ptd, ^3J = 7.9 Hz, ^4J = 1.7 Hz, 1H), 7.22 (ptd, ^3J = 7.5 Hz, ^4J = 0.8 Hz, 1H), 6.90 (d, ^3J = 8.2 Hz, 2H), 3.71 (s, 3H, MeO) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.5 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 182.2 (q, $^2J_{CF}$ = 35.6 Hz, C=O), 154.5, 154.4, 149.0, 135.5 (q, $^4J_{CF}$ = 2.4 Hz), 132.2, 130.99, 130.95, 129.6, 128.6, 127.64, 127.6, 126.5, 124.8, 122.0, 116.4 (q, $^1J_{CF}$ = 292.3 Hz, CF_3), 110.7, 54.8 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{13}F_3NO_2^+$: 332.0893; found: 332.0884.

2,2,2-Trifluoro-1-(2-(4-(methylthio)phenyl)quinolin-3-yl)ethan-1-one (5g). Obtained from oxazine **3g** (0.054 g, 0.138 mmol) by procedure A. Yellow brown powder, m.p. 105-107 °C, yield 0.034 g (71%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.19 (d, ^3J = 8.5 Hz, 1H), 7.95 (d, ^3J = 8.1 Hz, 1H), 7.89 (ptd, ^3J = 7.7 Hz, ^4J = 1.0 Hz, 1H), 7.65 (pt, ^3J = 7.4 Hz, 1H), 7.50 (d, ^3J = 8.3 Hz, 2H), 7.34 (d, ^3J = 8.3 Hz, 2H), 2.52 (s, 3H, MeS) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.7 (CF_3) ppm.

$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 184.6 (q, $^{2}J_{CF}$ = 36.1 Hz, C=O), 157.0, 148.8, 140.7, 139.1 (q, $^{4}J_{CF}$ = 2.2 Hz), 135.8, 133.0, 129.6, 129.3, 128.7, 127.9, 126.2, 125.7, 124.9, 115.9 (q, $^{1}J_{CF}$ = 292.5 Hz, CF_3), 15.4 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{13}F_3NOS^+$: 348.0664; found: 348.0665.

2,2,2-Trifluoro-1-(2-(4-(trifluoromethyl)phenyl)quinolin-3-yl)ethan-1-one (5h). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2h** (0.133 g, 0.5 mmol) by procedure B. White powder, m.p. 120-122 °C, yield 0.142 g (81%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.19 (d, ^{3}J = 8.5 Hz, 1H), 7.99 (d, ^{3}J = 8.1 Hz, 1H), 7.93 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.3 Hz, 1H), 7.76-7.66 (m, 5H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -63.8 (Ar-CF_3), -73.3 ($COCF_3$) ppm. $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 183.1 (q, $^{2}J_{CF}$ = 36.1 Hz, C=O), 156.7, 148.7, 142.9 (q, $^{4}J_{CF}$ = 1.1 Hz), 139.6 (q, $^{4}J_{CF}$ = 2.8 Hz), 133.5, 131.1 (q, $^{2}J_{CF}$ = 32.6 Hz), 129.7, 129.2, 128.9, 128.5, 125.6 (q, $^{3}J_{CF}$ = 3.7 Hz), 125.1, 124.8, 124.0 (q, $^{1}J_{CF}$ = 272.4 Hz, CF_3), 116.0 (q, $^{1}J_{CF}$ = 292.1 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{10}F_6NO^+$: 370.0661; found: 370.0650.

1-(2-(4-Chlorophenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5i). Obtained from oxazine **3i** (0.093 g, 0.245 mmol) by procedure A. Light yellow powder, m.p. 115-116 °C, yield 0.058 g (71%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.62 (s, 1H), 8.19 (d, ^{3}J = 8.5 Hz, 1H), 7.97 (d, ^{3}J = 8.2 Hz, 1H), 7.91 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.68 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.0 Hz, 1H), 7.51 (d, ^{3}J = 8.6 Hz, 2H), 7.46 (d, ^{3}J = 8.6 Hz, 2H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.6 (CF_3) ppm. $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 183.9 (q, $^{2}J_{CF}$ = 36.1 Hz, C=O), 156.6, 148.7, 139.3 (q, $^{4}J_{CF}$ = 2.2 Hz), 137.8, 135.6, 133.3, 130.2, 129.7, 129.0, 128.8, 128.2, 125.3, 125.0, 115.9 (q, $^{1}J_{CF}$ = 292.3 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}ClF_3NO^+$: 336.0398; found: 336.0395.

1-(2-(2-Chlorophenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5j). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2j** (0.116 g, 0.5 mmol) by procedure B. Yellow solid, m.p. 86-88 °C, yield 0.122 g (77%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.21 (d, ^{3}J = 8.5 Hz, 1H), 8.03 (d, ^{3}J = 8.1 Hz, 1H), 7.93 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.72 (ptd, ^{3}J = 7.6 Hz, ^{4}J = 1.0 Hz, 1H),

7.51 (pd, ^3J = 7-8 Hz, 2H), 7.48-7.41 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -72.3 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 180.7 (q, $^2J_{CF}$ = 35.4 Hz, C=O), 156.3, 148.9, 138.9 (q, $^4J_{CF}$ = 3.3 Hz), 138.4, 133.4, 131.3, 130.7, 130.2, 129.8, 129.5, 129.2, 128.5, 127.6, 125.3, 124.5, 116.3 (q, $^1J_{CF}$ = 292.5 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}ClF_3NO^+$: 336.0398; found: 336.0396.

1-(2-(4-Bromophenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5k). Obtained from oxazine **3k** (0.083 g, 0.196 mmol) by procedure A. Light yellow solid, m.p. 125-127 °C, yield 0.058 g (78%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.19 (d, ^3J = 8.4 Hz, 1H), 7.97 (d, ^3J = 8.1 Hz, 1H), 7.91 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.68 (ptd, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H), 7.62 (d, ^3J = 8.6 Hz, 2H), 7.44 (d, ^3J = 8.6 Hz, 2H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.6 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 183.8 (q, $^2J_{CF}$ = 36.3 Hz, C=O), 156.7, 148.7, 139.4 (q, $^4J_{CF}$ = 2.2 Hz), 138.2, 133.3, 131.9, 130.5, 129.7, 128.8, 128.2, 125.2, 125.0, 123.9, 115.9 (q, $^1J_{CF}$ = 292.5 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}{}^{79}BrF_3NO^+$: 379.9892; found: 379.9884; Calcd for $C_{17}H_{10}{}^{81}BrF_3NO^+$: 381.9873; found: 381.9865.

1-(2-(4-Fluorophenyl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5l). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2l** (0.113 g, 0.5 mmol) by procedure B. Light yellow powder, m.p. 94-95 °C, yield 0.127 g (84%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.19 (d, ^3J = 8.5 Hz, 1H), 7.95 (d, ^3J = 8.2 Hz, 1H), 7.90 (ptd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H), 7.66 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.57 (dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{HF}$ = 5.2 Hz, 2H), 7.18 (pt, $^3J_{HH}$, $^3J_{HF}$ = 8.7 Hz, 2H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.6 (s, 3F, CF_3), -112.88…-112.96 (m, 1F, Ar-F) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 184.2 (q, $^2J_{CF}$ = 36.3 Hz, C=O), 163.5 (d, $^1J_{CF}$ = 249.5 Hz), 156.6, 148.7, 139.2 (q, $^4J_{CF}$ = 2.4 Hz), 135.4 (d, $^4J_{CF}$ = 3.3 Hz), 133.1, 130.8 (d, $^3J_{CF}$ = 8.5 Hz), 129.6, 128.7, 128.0, 125.5, 124.9, 115.9 (q, $^1J_{CF}$ = 292.3 Hz, CF_3), 115.8 (d, $^2J_{CF}$ = 21.9 Hz) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}F_4NO^+$: 320.0693; found: 320.0685.

1-(2-(2,3-diHydrobenzo[b][1,4]dioxin-6-yl)quinolin-3-yl)-2,2,2-trifluoroethan-1-one (5m). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2m** (0.128 g, 0.5 mmol) by procedure B. Yellow brown solid, m.p. 84-85 °C, yield 0.120 g (70%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.18 (d, ^{3}J = 8.5 Hz, 1H), 7.93 (d, ^{3}J = 7.9 Hz, 1H), 7.87 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.3 Hz, 1H), 7.63 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.2 Hz, 1H), 7.21 (d, ^{4}J = 2.1 Hz, 1H), 7.00 (dd, ^{3}J = 8.3 Hz, ^{4}J = 2.1 Hz, 1H), 7.44 (d, ^{3}J = 8.3 Hz, 1H), 4.31-4.29 (m, 4H, $2CH_2$) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.8 (CF_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 185.1 (q, $^{2}J_{CF}$ = 36.7 Hz, C=O), 156.8, 148.7, 145.0, 143.9, 138.8, (q, $^{4}J_{CF}$ = 1.8 Hz), 132.8, 132.7, 129.6, 128.6, 127.7, 126.0, 124.8, 122.4, 118.0, 117.7, 115.9 (q, $^{1}J_{CF}$ = 290.3 Hz, CF_3), 64.5, 64.3 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{19}H_{13}F_3NO_3^+$: 360.0842; found: 360.0849.

2,2,2-Trifluoro-1-(2-(thiophen-2-yl)quinolin-3-yl)ethan-1-one (5n). Obtained from quinoline **1a** (0.061 g, 0.475 mmol) and acetylene **2n** (0.102 g, 0.5 mmol) by procedure B. White powder, m.p. 67-69 °C, yield 0.115 g (79%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.13 (dd, ^{3}J = 8.4 Hz, ^{4}J = 0.6 Hz, 1H), 7.86 (d, ^{3}J = 7.8 Hz, 1H), 7.83 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.4 Hz, 1H), 7.58 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.1 Hz, 1H), 7.54 (dd, ^{3}J = 5.1 Hz, ^{4}J = 1.0 Hz, 1H), 7.22 (dd, ^{3}J = 3.7 Hz, ^{4}J = 1.0 Hz, 1H), 7.11 (dd, ^{3}J = 5.1 Hz, ^{3}J = 3.7 Hz, 1H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -74.5 (CF_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 185.9 (q, $^{2}J_{CF}$ = 36.5 Hz, C=O), 149.5, 148.6, 142.5, 138.3 (q, $^{4}J_{CF}$ = 1.5 Hz), 132.7, 129.6, 129.3, 128.8, 128.4, 128.0, 127.7, 125.3, 124.7, 115.8 (q, $^{1}J_{CF}$ = 292.5 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{15}H_9F_3NOS^+$: 308.0351; found: 308.0353.

2-Phenyl-3-(2,2,2-trifluoroacetyl)quinoline-5-carbonitrile (5o). Obtained from oxazine **3a** (0.0392 g, 0.106 mmol) by procedure A or from quinoline **1b** (0.077 g, 0.5 mmol) and acetylene **2a** (0.104 g, 0.525 mmol) by procedure B. White powder, m.p. 107-109 °C, yield 0.028 g (81%, A) or 0.113 g (69%, B). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.84 (s, 1H), 8.46 (d, ^{3}J = 8.5 Hz, 1H), 8.08 (d, ^{3}J = 7.2 Hz, 1H), 7.95 (pt, ^{3}J = 7.9 Hz, 1H), 7.61-7.60 (m, 2H), 7.54-7.52 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ

-74.2 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 185.0 (q, $^2J_{CF}$ = 37.3 Hz, C=O), 159.0, 148.1, 138.4, 135.6, 135.1, 134.0, 131.6, 130.1, 129.0 (2C), 128.6, 124.8, 115.8, 115.6 (q, $^1J_{CF}$ = 292.0 Hz, CF_3), 111.3 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{18}H_{10}F_3N_2O^+$: 327.0740; found: 327.0739.

1-(5-Bromo-2-phenylquinolin-3-yl)-2,2,2-trifluoroethan-1-one (5p). Obtained from oxazine **3p** (0.091 g, 0.215 mmol) by procedure A. Light brown solid, m.p. 125-127 °C, yield 0.061 g (75%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.93 (s, 1H), 8.17 (d, ^3J = 8.4 Hz, 1H), 7.91 (dd, ^3J = 7.5 Hz, ^4J = 0.9 Hz, 1H), 7.72 (dd, ^3J = 8.4 Hz, ^3J = 7.5 Hz, 1H), 7.62-7.57 (m, 2H), 7.54-7.49 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.9 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 184.7 (q, $^2J_{CF}$ = 36.7 Hz, C=O), 158.2, 149.4, 138.6, 138.5 (q, $^4J_{CF}$ = 2.2 Hz), 132.9, 131.5, 129.7, 129.5, 129.0, 128.9, 127.1, 124.8, 122.8, 115.8 (q, $^1J_{CF}$ = 292.1 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}{}^{79}BrF_3NO^+$: 379.9892; found: 379.9899; Calcd for $C_{17}H_{10}{}^{81}BrF_3NO^+$: 381.9873; found: 381.9880.

1-(6-Bromo-2-phenylquinolin-3-yl)-2,2,2-trifluoroethan-1-one (5q). Obtained from oxazine **3q** (0.070 g, 0.165 mmol) by procedure A. Light yellow solid, m.p. 89-91 °C, yield 0.051 g (81%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.45 (s, 1H), 8.12 (d, ^4J = 1.5 Hz, 1H), 8.07 (d, ^3J = 8.9 Hz, 1H), 7.94 (dd, ^3J = 8.9 Hz, ^4J = 1.5 Hz, 1H), 7.58-7.56 (m, 2H), 7.49-7.48 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -74.0 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 184.6 (q, $^2J_{CF}$ = 36.7 Hz, C=O), 157.9, 147.3, 138.9, 137.6, 136.3, 131.4, 130.5, 129.6, 128.91, 128.85, 126.9, 126.0, 121.9, 115.8 (q, $^1J_{CF}$ = 292.3 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}{}^{79}BrF_3NO^+$: 379.9892; found: 379.9887; Calcd for $C_{17}H_{10}{}^{81}BrF_3NO^+$: 381.9873; found: 381.9867.

1-(7-Chloro-2-phenylquinolin-3-yl)-2,2,2-trifluoroethan-1-one (5r). Obtained from oxazine **3r** (0.065 g, 0.174 mmol) by procedure A. Light yellow oil, yield 0.048 g (83%). ^1H NMR (400.1 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.21 (d, ^4J = 1.9 Hz, 1H), 7.89 (d, ^3J = 8.7 Hz, 1H), 7.60 (dd, ^3J = 8.7 Hz, ^4J =

1.9 Hz, 1H), 7.58-7.55 (m, 2H), 7.52-7.48 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -73.8 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 184.4 (q, $^2J_{CF}$ = 36.5 Hz, C=O), 158.7, 149.0, 139.2, 138.9, 138.7 (q, $^4J_{CF}$ = 2.0 Hz), 129.8, 129.6, 129.1, 128.88, 128.83, 128.75, 126.1, 123.3, 115.8 (q, $^1J_{CF}$ = 292.3 Hz, CF_3) ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{17}H_{10}ClF_3NO^+$: 336.0398; found: 336.0395.

2,2,2-Trifluoro-1-(2-phenyl-1,8-naphthyridin-3-yl)ethan-1-one (5s). Obtained from oxazine **3s** (0.066 g, 0.191 mmol) by procedure A. Light brown powder, m.p. 74-76 °C, yield 0.038 g (66%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 9.28 (dd, ^3J = 4.2 Hz, ^4J = 2.0 Hz, 1H), 8.59 (s, 1H), 8.36 (dd, ^3J = 8.1 Hz, ^4J = 2.0 Hz, 1H), 7.70-7.68 (m, 2H), 7.63 (dd, ^3J = 8.1 Hz, ^3J = 4.2 Hz, 1H), 7.52-7.48 (m, 3H) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ -74.1 (CF_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, CD_3CN): δ 185.3 (q, $^2J_{CF}$ = 36.1 Hz, C=O), 161.4, 158.1, 157.0, 142.3 (q, $^4J_{CF}$ = 2.2 Hz), 140.1, 139.5, 130.6, 130.1, 129.7, 127.2, 124.5, 121.0, 116.8 (q, $^1J_{CF}$ = 291.7 Hz, CF_3) ppm.

HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{16}H_{10}F_3N_2O^+$: 303.0740; found: 303.0738.

Synthesis of (2-phenylquinolin-3-yl)(pyrrolidin-1-yl)methanone (6a) (procedure A). A 4 mL vial with a screw cap was charged with oxazine **3a** (0.025 g, 0.0724 mmol), MeCN (0.5 mL) and pyrrolidine (0.012 g, 0.169 mmol). The reaction mixture was heated at 80 °C for 6 h using magnetic stirrer with heating and then volatiles were evaporated in vacuo. The residue was passed through a short silica gel pad using hexane-CH_2Cl_2 (1:1) followed by CH_2Cl_2 and CH_2Cl_2 -MeOH (100:1) as eluents. Evaporation of volatiles afforded 0.021 g (96%) of pure **6a**. One pot synthesis of **6a** (procedure B). A 8 mL vial with a screw cap was charged with water (0.0188 g, 1.05 mmol), quinoline **1a** (0.1228 g, 0.952 mmol), MeCN (1 mL) and then CF_3-ynone **2a** (0.2035 g, 1.028 mmol) was added at stirring. The clear solution thus obtained was left at room temperature for 24h. Next, pyrrolidine (0.177 g, 2.49 mmol) was added and the reaction mixture was heated at 80 °C for 6 h. Volatiles were evaporated in vacuo, the residue was passed through a short silica gel pad using hexane-CH_2Cl_2 (1:1) followed by

CH_2Cl_2 and CH_2Cl_2 -MeOH (100:1) as eluents. Evaporation of volatiles afforded 0.280 g (97%) of pure **6a**. Synthesis of **6a** from **5a** (procedure C). A 4 mL vial with a screw cap was charged with **5a** (0.0285 g, 0.0947 mmol), MeCN (0.5 mL) and pyrrolidine (0.015 g, 0.21 mmol). The reaction mixture was heated at 80 °C for 6 h using magnetic stirrer with heating and then volatiles were evaporated in vacuo. The residue was passed through a short silica gel pad using hexane-CH_2Cl_2 (1:1) followed by CH_2Cl_2 and CH_2Cl_2 -MeOH (100:1) as eluents. Evaporation of volatiles afforded 0.0281 g (98%) of pure **6a**. Yellow brown viscous oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.22 (d, ^3J = 8.5 Hz, 1H), 7.90-7.87 (m, 2H, Ph), 7.85 (dd, ^3J = 8.2 Hz, ^4J = 1.0 Hz, 1H), 7.75 (ptd, ^3J = 7.7 Hz, ^4J = 1.5 Hz, 1H), 7.56 (ptd, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H), 7.48-7.40 (m, 3H, Ph), 3.48 (br s, 2H), 2.75 (br s, 2H), 1.68 (br s, 2H), 1.47 (br s, 2H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 168.0, 154.7, 147.8, 139.2, 135.5, 130.6, 130.3, 129.3, 129.0, 128.5, 128.2, 127.5, 126.8, 126.1, 47.4, 45.5, 25.3, 23.9 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{20}H_{19}N_2O^+$: 303.1492; found: 303.1504.

Synthesis of amides 6b-e (general procedures D,E). A 4 mL vial with a screw cap was charged with 2,2,2-trifluoro-1-(2-phenylquinolin-3-yl)ethanone **5a** (0.045-0.053 g, 0.150-0.176 mmol), corresponding amine (0.195-0.298 g, 0.169 mmol) and NaOH (0.020 g, 0.5 mmol for primary amines, procedure E). The reaction mixture was heated at 110 °C for 6-7 h (secondary amines, D) or 2 h (primary amines, E) using magnetic stirrer with heating and then volatiles were evaporated in vacuo. The residue was passed through a short silica gel pad using hexane-CH_2Cl_2 (1:1) followed by CH_2Cl_2 and CH_2Cl_2 -MeOH (100:1) as eluents. Evaporation of volatiles afforded corresponding pure amide **6**.

(2-Phenylquinolin-3-yl)(piperidin-1-yl)methanone (6b). Obtained from **5a** (0.053 g, 0.176 mmol) and piperidine (0.298, 3.506 mmol) by procedure D. White powder, m.p. 138-140 °C, yield 0.054 g (97%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.21 (s, 1H), 8.15 (d, ^{3}J = 8.4 Hz, 1H), 7.87-7.84 (m, 2H, Ph), 7.82 (d, ^{3}J = 8.1 Hz, 1H), 7.73 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.3 Hz, 1H), 7.54 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 0.9 Hz, 1H), 7.47-7.40 (m, 3H, Ph), 3.70-3.65 (m, 1H), 3.48-3.42 (m, 1H), 2.88-2.82 (m, 1H), 2.70-2.65 (m, 1H), 1.52-1.47 (m, 1H), 1.40-1.26 (m, 3H), 1.13-1.04 (m, 1H), 0.56-0.47 (m, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 168.2, 155.0, 147.8, 139.3, 135.9, 130.3, 129.9, 129.4, 129.1, 129.0, 128.4, 127.6, 127.0, 126.3, 47.6, 42.4, 25.1, 24.8, 23.9 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{21}H_{21}N_2O^+$: 317.1648; found: 317.1655.

Morpholino(2-phenylquinolin-3-yl)methanone (6c). Obtained from **5a** (0.047 g, 0.156 mmol) and morpholine (0.214, 2.460 mmol) by procedure D. White powder, m.p. 146-148 °C, yield 0.049 g (99%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.26 (s, 1H), 8.16 (d, ^{3}J = 8.5 Hz, 1H), 7.86-7.82 (m, 3H), 7.76 (ptd, ^{3}J = 7.7 Hz, ^{4}J = 1.5 Hz, 1H), 7.56 (ptd, ^{3}J = 7.5 Hz, ^{4}J = 1.1 Hz, 1H), 7.51-7.44 (m, 3H, Ph), 3.80-3.74 (m, 1H), 3.64-3.59 (m, 1H), 3.52-3.46 (m, 1H), 3.32-3.26 (m, 1H), 3.25-3.20 (m, 1H), 2.96-2.90 (m, 1H), 2.70-2.65 (m, 1H), 2.47-2.42 (m, 1H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 168.4, 154.8, 147.9, 139.0, 136.4, 130.6, 129.3, 128.9, 128.7, 128.5, 127.5, 127.1, 126.1, 65.8, 65.5, 46.7, 41.8 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{20}H_{19}N_2O_2^+$: 319.1441; found: 319.1446.

***N*-Hexyl-2-phenylquinoline-3-carboxamide (6d).** Obtained from **5a** (0.045 g, 0.1495 mmol) and n-hexyl amine (0.195, 1.931 mmol) by procedure E. Light yellow powder, m.p. 135-137 °C, yield 0.049 g (99%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.43 (s, 1H), 8.09 (d, ^{3}J = 8.5 Hz, 1H), 7.81 (d, ^{3}J = 8.0 Hz, 1H), 7.74-7.69 (m, 3H), 7.53 (pt, ^{3}J = 7.5 Hz, 1H), 7.47-7.43 (m, 3H, Ph), 5.64 (br s, 1H, NH), 3.16 (q, ^{3}J = 6.6 Hz, 2H, CH_2NH), 1.26-1.11 (m, 6H), 1.04-0.98 (m, 2H), 0.83 (t, ^{3}J = 7.1 Hz, 3H, Me) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 168.1, 156.0, 147.9, 139.5, 137.6, 130.3, 129.6, 129.3, 129.1,

128.9, 128.6, 127.9, 127.1, 126.1, 40.1, 31.3, 28.8, 26.3, 22.4, 13.9 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{22}H_{25}N_2O^+$: 333.1961; found: 333.1961.

N-Cyclopropyl-2-phenylquinoline-3-carboxamide (6e). Obtained from **5a** (0.0509 g, 0.169 mmol) and cyclopropylamine (0.270, 4.737 mmol) by procedure D. White powder, m.p. 185-187 °C, yield 0.036 g (74%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.14 (d, ^3J = 8.4 Hz, 1H), 7.89 (d, ^3J = 8.0 Hz, 1H), 7.78 (ptd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H), 7.71-7.68 (m, 2H), 7.58 (ptd, ^3J = 7.5 Hz, ^4J = 0.9 Hz, 1H), 7.50-7.46 (m, 3H, Ph), 5.41 (br s, 1H, NH), 2.70-2.64 (m, 1H), 0.69-0.65 (m, 2H), 0.19-0.15 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 169.4, 156.0, 148.0, 139.4, 137.8, 131.0, 129.3, 129.20, 129.18, 128.9, 128.6, 128.0, 127.2, 126.1, 22.8, 6.3 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{19}H_{17}N_2O^+$: 289.1335; found: 289.1343.

Synthesis of 2-phenylquinoline-3-carboxylic acid (**7**) from 2,2,2-trifluoro-1-(2-phenylquinolin-3-yl)ethanone **5a.** A 4 mL vial with a screw cap was charged with 2,2,2-trifluoro-1-(2-phenylquinolin-3-yl)ethanone **5a** (0.030 g, 0.0997 mmol), water (0.5 mL) and NaOH (0.020 g, 0.5 mmol). The reaction mixture was stirred for 2 days, and then pH was adjusted to slightly acidic (5-6) by carefull addition of 1M HCl. The precipitate formed was filtred off, washed with water (2x0.5 mL) and dried in vacuo to give pure **7**. Yield 0.016 g (64%).

One pot synthesis of 2-phenylquinoline-3-carboxylic acid (7) from quinoline 1a and CF_3-ynone 1a. A 8 mL vial with a screw cap was charged with water (0.0188 g, 1.05 mmol), quinoline **1a** (0.1228 g, 0.952 mmol), MeCN (1 mL) and then CF_3-ynone **2a** (0.2035 g, 1.028 mmol) was added at stirring. The clear solution thus obtained was left at room temperature for 24h. Next, morpoline (0.117 g, 1.345 mmol) was added and the reaction mixture was heated at 80 °C for 6 h using magnetic stirrer with heating. After that water (1 mL) and NaOH (0.131 g, 3.275 mmol) were added and the reaction mixture was heated at 80 °C for 1 h at stirring using magnetic stirrer with heating. Volatiles were evaporated in vacuo, to form slurry, which was acidified to slightly acidic medium (pH 5-6) by carefull addition of

1M HCl. The precipitate formed was filtred off, washed with water (2x0.5 mL) and dried in vacuo to give pure **7**. Yield 0.174 g (73%). Light beige powder, m.p. 232-234 °C (Lit. data[56]: 231 °C). ^{1}H NMR (400.1 MHz, DMSO-d_6): δ 8.76 (s, 1H), 8.12 (d, ^3J = 7.9 Hz, 1H), 8.07 (d, ^3J = 8.3 Hz, 1H), 7.86 (pt, ^3J = 7.2 Hz, 1H), 7.70-7.60 (m, 3H), 7.50-7.40 (m, 3H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d_6): δ 169.0, 156.8, 147.4, 140.2, 138.0, 131.5, 128.8, 128.7, 128.6, 128.0, 127.5, 127.3, 126.9, 125.6 ppm. ^{1}H NMR (400.1 MHz, D_2O+NaOH): δ 8.27 (s, 1H), 7.85 (d, ^3J = 8.6 Hz, 1H), 7.82 (d, ^3J = 8.1 Hz, 1H), 7.65 (pt, ^3J = 7.7 Hz, 1H), 7.61-7.54 (m, 2H), 7.51-7.39 (m, 4H) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, D_2O+NaOH): δ 176.1, 156.3, 145.6, 139.0, 135.4, 132.9, 130.4, 128.6, 128.0, 127.9, 127.7, 126.7, 126.6, 125.9 ppm. HRMS (ESI-TOF): m/z $[M+H]^+$ Calcd for $C_{16}H_{12}NO_2^+$: 250.0863; found: 250.0866.

ASSOCIATED CONTENT

Supporting Information. Structures of CF_3-ynones **2**, oxazines **3**, details of optimization of the reaction conditions, copies of all NMR spectra. The Supporting Information is available free of charge on the ACS Publications website.

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(1) Runge, F. F. Ueber einige Produkte der Steinkohlendestillation (On some products of coal distillation). *Ann. der Phys. u. Chem.* **1834**, *31*, 65-78 ; see especially p. 68: "*3. Leukol oder Weissöl*" (3. White oil [in Greek] or white oil [in German]). From p. 68: "Diese dritte Basis habe ich Leukol oder Weissöl genannt, weil sie keine farbigen Reactionen zeigt." (This third base I've named leukol or white oil because it shows no color reactions).

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