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Synthesis of substituted 1-trifluoromethyl and 1-perfluoroalkyl-3-(arylamino)prop-2-en-1-one: advances in the mechanism of Combes 2-trifluoromethyl and 2-perfluoroalkyl quinolines synthesis

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ABSTRACT

We report a new synthesis and our study of the mechanism of formation of substituted 1-trifluoromethyl and 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-one starting from 3-(R-phenoxy)-3-perfluoroalkyl-prop-2-enals and arylamines. Reactivity study of the intermediates confirmed that 3-perfluoroalkyl-*N*,*N*′-diphenyl-1,5-diazapentadienes are the synthetic intermediates of the synthesis of 2-perfluoroalkylquinolines. The mechanism of the reaction of 1-trifluoromethyl and 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-one with $POCl_3$ was studied. To our knowledge this is the first detection and isolation of *N*,*N*′-diaryldiazapentadiene derivatives as intermediates in the Combes F-alkyl substituted quinoline synthesis starting from enaminoketones. Finally, we succeeded isolating and identifying unsymmetrically substituted 2-perfluorolakyldiazapentadiene.

1. Introduction

Among the nitrogenous heterocycles, quinolines[1–6] and their derivatives represent an important class of organic molecules that attract the interest of both synthetic and medicinal chemists due to their broad spectrum of biological activities.[1–3] Quinoline derivatives have attracted considerable attention primarily due to their presence in many compounds, which have been isolated from natural substances and exhibit various biological activities.[4,5] As a heterocyclic moiety, quinolines also deserve special interest for chelation of various metal cations, including lanthanide ions.[6]

In addition, it has been recognized that attachment of a trifluoromethyl group into heterocycles can be used to modulate the physical, chemical and biological properties.[7,8] It is well documented that the influence of the trifluoromethyl substituent on physiological activity is due mainly to the increased lipophilicity of the molecules, causing greater cell permeability and resistance to enzyme degradation.[7] Consequently, synthetic methodology to incorporate fluorine and fluorous synthons must be improved in order to prepare sophisticated fluoroorganic molecules on a practical scale.

One of the most satisfactory methods for introducing a CF_3 group into heterocycles is via the trifluoromethylated building block approach. The fluoroalkyl-containing enaminoketones **1** proved to be a useful building block for the syntheses of many series of heterocyclic compounds.[9–15]

Several approaches to perfluoroalkylated quinolines are known, starting from enaminoketones **1** and typically providing access to 2-perfluoroalkyl or 2-trifluoromethyl substituted quinolines.[16–18] Linderman and Kirollos[17] reported the synthesis of 2-CF_3-substituted quinolines. In the same publication, another intramolecular cyclization route was also described, which allowed the synthesis of the 4-trifluoromethyl quinoline isomer. In some cases, the reactions resulted in mixtures of 2- and 4-trifluoromethylquinolines. Thus, the cyclization of adducts of acetylenic ketones (or 4-ethoxy-1,1,1-trifluoro-3-buten-2-one) with aromatic amines in methanol gives a 3-arylamino-substituted trifluoromethyl-enones, which cyclize on treatment with acids ($POCl_3$, $ZnCl_2$) giving rise to 2-trifluoromethyl or

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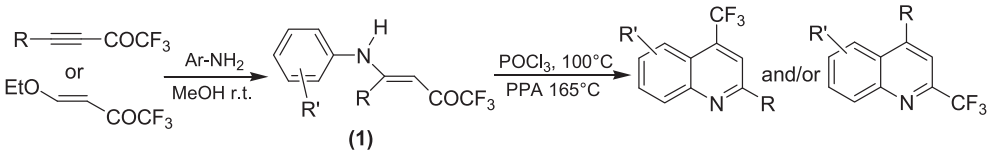
4-trifluoromethyl substituted quinolines in moderate yields (Scheme 1).[17] The ratio of the reaction products depends on the acidic catalyst used and the structure of the starting enones.

Moreover, related conjugated systems such as push–pull polyenes have become important in the study of nonlinear optical properties because these properties are enhanced by the large



Scheme 1. Synthesis of 2-trifluoromethyl and/or 4-trifluoromethyl quinolines. R′=Me, OH, OMe, Hal; R=H, alkyl, phenyl.

4-Trifluoromethylquinolines are the products of normal cyclization of **1** obtained by intramolecular electrophilic aromatic substitution. While the mechanism of formation of 2-trifluoromethylquinolines was investigated by Gerus et al.,[16] who noted that in the case of the aniline derivative only the 2-trifluoromethyl quinoline was obtained probably via retro-1,4 addition. However when R′=alkyl or aryl, 4-trifluoromethylquinolines are formed predominantly. The presence of electron-donating substituents in the *meta*-positions of the aromatic amine substantially facilitates cyclization and increases the total yield.[16]

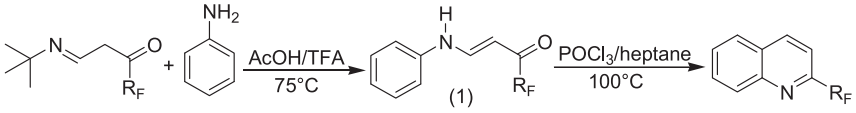
Schlosser et al.,[18] who have investigated the synthesis of 2- and 4-trifluoromethyl quinolines and quinolinones, demonstrated that 4-anilino-1,1,1-trifluoro-3-buten-2-ones can be readily obtained from 4-*tert*-butylamino-1,1,1-trifluorobut-3-en-2-one and aniline by simple trans-amination. Upon heating in the presence of phosphoryl oxychloride, they undergo ring closure to afford 2-trifluoromethyl quinolines rather than the expected 4-isomers in 50% average yield (Scheme 2).[18a]

changes in dipole moment and hence in charge distribution between the ground and excited states.[25]

Furthermore, β-enaminones **1** have attracted much attention due to the fact they are important synthons for the synthesis of many biologically active compounds[9b,26–31] such as dopamine auto-receptor agonists,[26] acetylcholinesterase inhibitors,[27] and anticonvulsants.[28] They are also useful intermediates for the preparation of several aminoacids,[29] aminols,[30] peptides and alkaloids.[9b]

In the present work, we report our study of the mechanism of formation of substituted 2-perfluoroalkylquinolines starting from 3-perfluoroalkyl-3-aryloxypropenals **3** and 1-perfluoroalkyl-3-(R_1-phenylamino)prop-2-en-1-ones **4a**–**o**.

In a first step, the synthesis and mechanism of formation of 1-trifluoromethyl and 1-perfluoroalkyl-3-(R_1-phenylamino)prop-2-en-1-ones **4a**–**o** are described, then NMR investigations of the reaction regioselectivity and tautomeric equilibrium in solution of compounds **4** are detailed.



Scheme 2. Synthesis of 2-trifluoromethylquinolines.[18] R_F=CF_3, C_2F_5, C_3F_7.

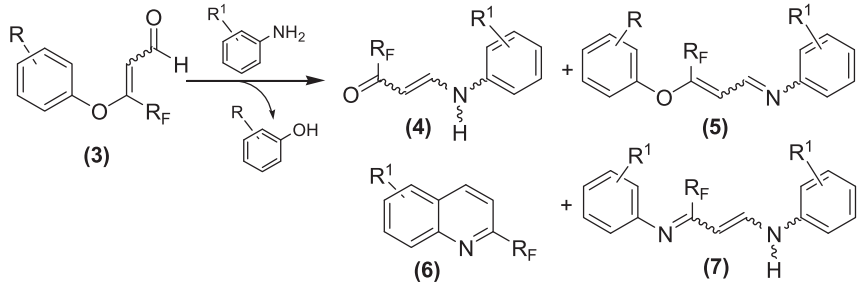
In subsequent experiments,[18b] these studies demonstrated that some perfluoroalkyl-substituted 3-aminoenones, when heated in the presence of phosphoryl chloride, cleaved hydrolytically, setting free the substituted anilines and the 1,3-dicarbonyl compounds. The authors postulated a non-proved recombination of these subunits through a vinylogous amidinium ion giving the unexpected 2-perfluoroalkylquinolines.[18b]

Furthermore, these 1,3-difunctional amino-derivatives **1** belong to the malonic class of compounds very important in the preparation of metal chelates,[13,19–24] thus, the development of a suitable volatile precursor for chemical vapour deposition (CVD)[19a] or atomic layer deposition (ALD)[20a] of thin metallic films is expected to revolutionize the manufacturing of electronic devices.[18]

2. Results and discussion

2.1. Synthesis of substituted 1-trifluoromethyl and 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-ones 4a–o

We found that 3-(R-phenoxy)-3-perfluoroalkyl-prop-2-enals **3a**–**e** react easily with aniline under acidic conditions and form 1-trifluoromethyl or 1-perfluoroalkyl-3-(R_1-phenylamino) prop-2-en-1-ones **4a**–**o**, phenyl-(3-perfluoroalkyl-3-phenoxyprop-2-enylidene)-amine **5**, 2-perfluoroalkyl-*N*,*N*′-diaryl-1,5-diazapentadienes **7** and 2-perfluoroalkylquinolines **6** (Scheme 3, Table 1). The starting compounds, enals **3**, can be easily prepared in a one pot reaction of substituted sodium phenoxides with 1-iodo-1-



Scheme 3. Reaction of 3-trifluoromethyl and 3-perfluoroalkyl-3-aryloxypropenals **3** with arylamines under acidic conditions (R=H, 4-OMe; R^1=H, 4-Me, 3-Me, 2-Me, 4-NO_2, 4-Cl, 2-Cl, 4-CO_2H, 3-CO_2H, 4-CN; R_F=CF_3, C_3F_7, C_5F_{11}).

Table 1
Reaction conditions and conversions observed for the reaction mixture at half time and at the end of the reaction of 3-trifluoromethyl-3-(phenoxy)propenal **3b** and aniline

Product **4a**	Conv[a] [%]									
	Time ½ (2 h)					Time (4 h)				
	4a	**5a**	**6a**	**7a**	**3b**	**4a**	**5a**	**6a**	**7a**	**3b**
Procedure A: 2% HCl/MeOH/65 °C	45	—	—	—	55	95	—	—	—	—
Procedure B: *p*-TsOH/toluene/111 °C	50	5	10	5	30	85	—	15		—

[a] Determined by ^{19}F NMR spectroscopic analysis of the reaction mixtures; NMR spectroscopic yields were based on consumed **3** and formed **4**, **5**, **6** and **7**.

acetoxy-2-perfluoroalkylethane derivatives as we reported earlier.[32–34]

The reaction of **3b** (R=H, R_F=CF_3, Scheme 3) with aniline was first tempted using *p*-toluenesulfonic acid in toluene as a solvent under reflux. The desired product **4a** was obtained in good yield with a mixture of phenyl-(3-perfluoroalkyl-3-phenoxyprop-2-enylidene)-amine **5a**, 2-perfluoroalkylquinolines **6a** and 2-perfluoroalkyl-*N*,*N*′-diaryl-1,5-diazapentadienes **7a** (Table 1).

However, we found that the reaction proceeds successfully when toluene was replaced by 2% hydrochloric acid in methanol as a solvent. Under these conditions, the expected compound **4a** was the only formed product and obtained in very good yield without side reactions (Table 1).

To further explore the structure–reactivity of this reaction, several starting arylamines were tested using conditions A as described previously. The enaminones **4a**–**o** were obtained in good to excellent yield (Table 2).

Table 2
Reaction conditions and conversions for the preparation of 1-trifluoromethyl and 1-perfluoroalkyl-3-(R^1-phenylamino)prop-2-en-1-ones **4a**–**o** using procedure A

Entry	Starting product		Enones	Arylamines	R_F	Time (h)	Conv[a] [%]
	3	R	**4**	R^1			
1	**3a**	4-OMe	**4a**	H	CF_{3a}	6	92
2	**3b**	H	**4a**	H	CF_3	4	95
3	**3c**	H	**4b**	H	C_3F_7	4	95
4	**3d**	4-OMe	**4c**	H	C_5F_{11}	6	90
5	**3e**	H	**4c**	H	C_5F_{11}	4	95
6	**3b**	H	**4d**	4-Me	CF_3	4	95
7	**3b**	H	**4e**	3-Me	CF_3	4	92
8	**3b**	H	**4f**	2-Me	CF_3	6	82
9	**3e**	H	**4g**	4-NO_2	C_5F_{11}	24	75
10	**3d**	4-OMe	**4g**	4-NO_2	C_5F_{11}	24	66
11	**3b**	H	**4h**	4-NO_2	CF_3	24	75
12	**3e**	H	**4i**	4-Cl	C_5F_{11}	12	80
13	**3b**	H	**4j**	4-Cl	CF_3	12	82
14	**3b**	H	**4k**	2-Cl	CF_3	24	66
15	**3b**	H	**4l**	4-CO_2H	CF_3	48	70
16	**3b**	H	**4m**	3-CO_2H	CF_3	48	70
17	**3e**	H	**4n**	4-CN	C_5F_{11}	24	66
18	**3b**	H	**4o**	4-CN	CF_3	24	70

[a] Determined by ^{19}F NMR spectroscopic analysis of the reaction mixtures; NMR spectroscopic yields were based on consumed **3** and formed **4**.

Slightly decreased yields were observed in the cases of arylamines substituted with moderately electron-withdrawing groups R^1=4-Cl, 2-Cl (Table 2, entries 12–14). In the case of strongly electron-withdrawing substituents like R^1=4-NO_2, 4-COOH, 3-COOH, 4-CN moderate yields of **4g**, **h** and **4l**–**o** were obtained (Table 2, entries 9–11 and 15–18).

Longer reaction times were required due to steric hindrance (R^1=2-Me, 2-Cl) (Table 2, entries 8 and 14) or to the presence of electron-withdrawing substituents (R^1=4-Cl, 2-Cl, 4-NO_2, 4-COOH, 3-COOH, 4-CN) (Table 2, entries 9–18).

2.2. Reaction mechanism

The mechanism of formation of compounds **4a**–**o** in acidic conditions could be explained by a substitution of the carbonyl group of **3a**–**e** and the formation of an *N*-arylimino enol-ether derivative **5**, which was isolated and identified. Then hydrolysis and elimination of the phenoxy group with subsequent tautomerization gives with total regioselectivity the corresponding 1-trifluoromethyl and 1-perfluoroalkyl-3-(R^1-phenylamino)prop-2-en-1-ones **4a**–**o** (Scheme 4).[16,35–37]

In our case, under acidic condition, steric factors could favour an 1,2-addition of arylamines then an acid catalyzed hydrolysis of the phenoxy group yielding compounds **4** in a total regiospecific manner.

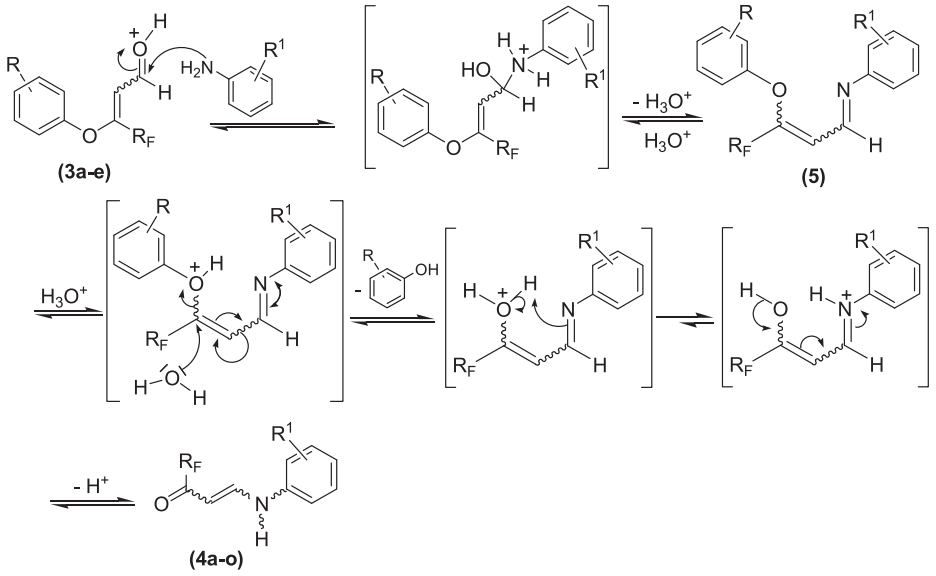
2.3. Structure determination of enaminoketones 4a–o

Similarly, the reaction of arylamines with **3** under acidic conditions (conditions A, Table 1), might give the 1,2- or/and the 1,4-addition products. However, close NMR spectral analyses of **4a**–**o** revealed that this reaction led to the regiospecific formation of single enaminoketone **4**β tautomer (Scheme 5). Structural assignments were accomplished without ambiguity using different ^1H, ^{13}C, ^{19}F, ^1H–^1H COSY and ^1H–^{13}C HETCOR spectral signals.

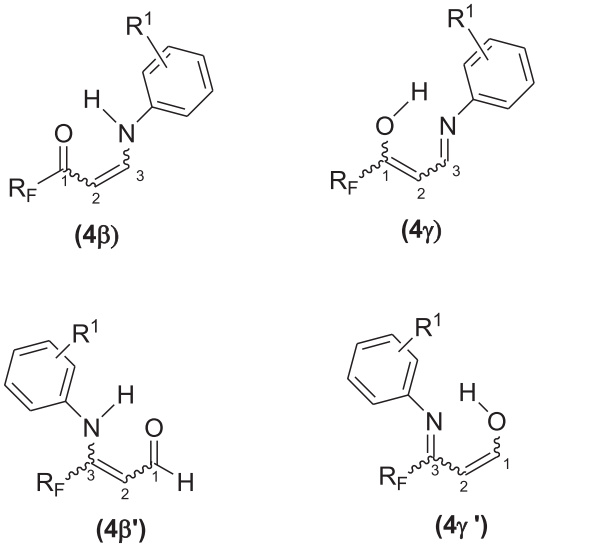
NMR spectral analysis confirms the structure of the obtained enaminoketones **4**β.

- The ^1H NMR and ^1H–^1H COSY spectra show a clear cross peak between consequently three vicinal protons, which exclude two possible regioisomers **4**γ and **4**β′ (Scheme 5, see Supplementary data).
- Then the presence of a carbonyl function is confirmed by ^{13}C NMR spectroscopy (in all cases the **C**=O carbon signal are observed around 175–180 ppm). As an experimental proof of the presence of C=O group, we compared with our previous results:[32a,34a] *N*,*N*′-diaryl-1,5-diazapentadiene compounds **7** (R=CF_3 or C_5F_{11}, R^1=H, *p*-Me, *m*-Me, *o*-Me, *p*-Cl, *m*-Cl, *o*-Cl, *p*-NO_2, *o*-OH, *p*-CN, *m*-COOH) and phenyl-(3-perfluoropenthyl-3-phenoxyprop-2-enylidene)-amine **5** (R_F=C_5F_{11}, R=R^1=H) (Scheme 3) their imine carbons showed ^{13}C NMR shifts around 153.2–154.5 and 152.9–154 ppm, respectively. Since there are no observable imine carbon signals, the regioisomer **4**γ′ is to be rejected.
- Furthermore, the $^2J_{CF}$ coupling constant observed between carbonyl carbon atoms C-1 and the fluorine atoms, which in all cases appears as a quartet or triplet around 175–180 ppm confirms the presence of a single stereochemically pure NH tautomer **4**β, excluding the presence of a tautomeric equilibrium for these derivatives[5c] (Scheme 5). This could be explained by the low basicity of the carbonyl group compared to imine function.

According to the literature, most of the studied cases corresponds to the stable **1**β tautomers of *N*-monosubstituted or *N*-unsubstituted enaminones **1** (R^2NH–CH=CH–COR^1 or NH_2–CH=CH–COR^1), very few works deals with the imino–enol or OH tautomers (R^2–N=CH–CHR^1–OH), which were considered to be unstable tautomers of enaminones **4**β[31] (Scheme 5). These works showed that the NH tautomers **4**β are more stable than the OH tautomers (by 2.93–3.54 kcal/mol) due to the higher proton affinity of the nitrogen atom as compared to the oxygen atom.[31]



Scheme 4. Mechanism of formation of 1-trifluoromethyl and 1-perfluoroalkyl-3-(R^1-phenylamino)prop-2-en-1-ones **4a**–**o** in acidic conditions.

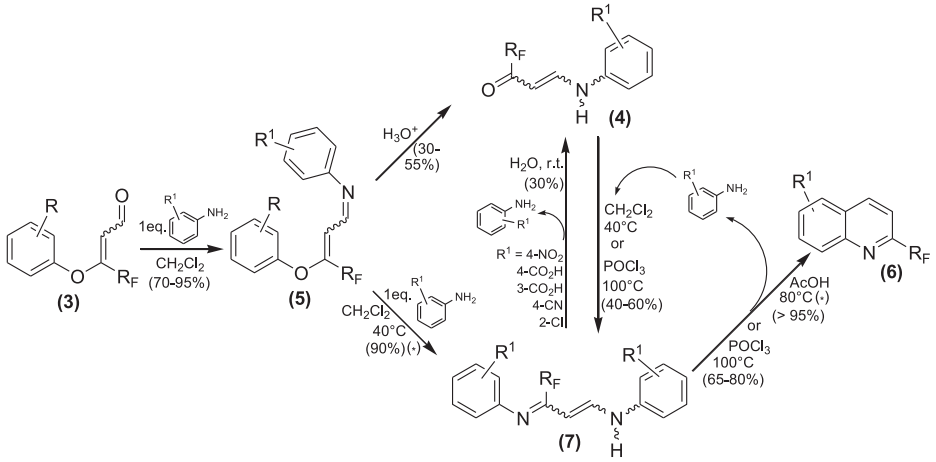


Scheme 5. Possible regioisomers and tautomers theoretically obtained from the reaction of **3** with arylamines.

3. Reactivity study of 4a–o: mechanism of formation of 2-trifluoromethyl and 2-perfluoroalkylquinolines 6

In order to study the mechanism of formation of 2-trifluoromethyl and 2-perfluoroalkylquinolines **6**, and to verify that the synthesis of quinolines **6** proceeds through intermediates of type 2-perfluoroalkyl-*N*,*N*′-diphenyl-1,5-diazapentadienes **7** or 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-one **4** and to reveal the reaction route as a whole,[32–34] we decided to study the intramolecular cyclization of **4a**–**o**, which leads to the 2-perfluoroalkylquinolines **6** (Scheme 6).

First we used different dehydrating reagents such as polyphosphoric acid (PPA) at 150 °C or *p*-toluenesulfonic acid in toluene under reflux. However, even when the reaction mixture where refluxed or heated for long time, the formation of the desired products **6** was not achieved, and complete degradation of the starting compounds **4** was observed by TLC. However, when **4** was heated in phosphorus oxychloride ($POCl_3$) at 100 °C, without any solvent, we obtained 2-trifluoromethyl or 2-perfluoroalkylquinolines **6** as the only formed products, through *N*,*N*′-diaryl-1,5-diazapentadienes **7** intermediates as detected by ^{19}F NMR spectroscopy of the reaction mixture (In DMSO-d_6 CF_3 signals



Scheme 6. Study and comparison of the reactivity of 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-ones **4a**–**o** and symmetrically substituted 2-perfluoroalkyl-*N*,*N*′-di(R^1-phenyl)-1,5-diazapentadienes **7** towards the synthesis of 2-perfluoroalkylquinolines **6**. *Published results[32a,34b] (R=H, 4-OMe; R^1=H, 4-Me, 3-Me, 2-Me, 4-NO_2, 4-Cl, 2-Cl, 4-CO_2H, 3-CO_2H, 4-CN; R_F=CF_3, C_3F_7, C_5F_{11}).

of **7** around −65 to −66 ppm or CF_2 signals at −109 ppm). Diazapentadienes **7** were isolated and identified. Elimination of 1 M equiv of arylamine by ring-closure cyclization of diazapentadienes **7** regenerates the starting arylamine (Scheme 6).

In comparison, previously,[32,34a,b] we reported the synthesis and reactivity of 2-trifluoromethyl and 2-perfluoroalkyl-*N*,*N*′-diphenyl-1,5-diazapentadienes **7**. We found that the formation of **7** starting from **3** proceed via intermediates of type phenyl-(3-perfluoroalkyl-3-(R^1-phenoxy)-prop-2-enylidene)-amine **5**, which by an aza-Michael addition–elimination mechanism of substituted arylamines affords the corresponding diazapentadienes **7** (Scheme 6).[32a] Then we investigated the structure and reactivity of enamino-imine compounds **7** having a trifluoromethyl or a perfluoroalkyl group and we showed that the reactivity of these push–pull systems strongly depends on the geometry of the conjugated unsaturated moiety.[32,34a] Thus the reactivity of push–pull enamino-imines can be controlled to some extent by equilibrium of stereoisomeric forms.[36] Moreover, the remarkable polarization of push–pull alkenes leads to special reactivity with nucleophile or electrophile reagents.[35a] From this point of view we investigate the stereochemistry and the mechanism of cyclization of compounds **7**.

Compounds **7** were found to cyclize in a total regiospecific manner under acidic conditions (AcOH/1,2-dichloroethane/reflux)[34b] or under basic conditions (arylamines/1,2-dichloroethane/reflux) by an electrophilic aromatic cyclization mechanism or by a push–pull cyclization mechanism, respectively, and gave the corresponding 2-perfluoroalkylquinolines **6** in high yields (Scheme 6).[34b]

We were the first to report the identification and isolation of 2-trifluoromethyl and 2-perfluoroalkyl-*N*,*N*′-diphenyl-1,5-diazatnqh_0009;pentadienes **7** as reactional intermediates of the synthesis of 2-trifluoromethyl and 2-perfluoroalkyl-quinolines starting from perfluoroalkylated malonic derivative.[33,34]

Following our previous studies,[32–34] in this work, we found, after its isolation and identification in the reaction mixture that phenyl-(3-perfluoroalkyl-3-(R^1-phenoxy)-prop-2-enylidene)-amine **5** could be the intermediate of the formation of enaminone **4** starting from **3**.

Moreover, while monitoring the reaction of **5** with arylamines by ^{19}F NMR spectroscopy, we observed the formation of both diazapentadienes **7** and enaminoketones **4** as intermediates. Both compounds **7** and **4** were isolated and identified. The ^{19}F NMR signals of **4** appear during the reaction and after few hours disappear completely to give **7** and new peak, which was assigned to quinolines **6**. At the end of the reaction only quinolines **6** where detected and isolated and compared with authentic samples synthesized in previous works.[33,34b]

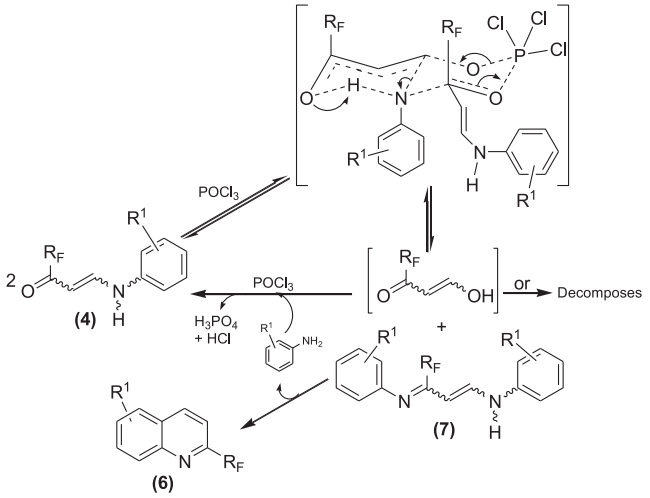
Moreover, in the course of our studies of the reactivity and stability of symmetrically substituted 2-perfluoroalkyl-*N*,*N*′-di(R^1-phenyl)-1,5-diazapentadienes **7**, we found that in the presence of highly electron-attracting substituents (such as R^1=4-NO_2, 4-CO_2H, 3-CO_2H, 4-CN) or when an *ortho*-chloro substituent was present on the phenyl group the corresponding diazapentadienes **7** were not indefinitely stable at room temperature, after varying periods of time (several days), they decompose and give 1-perfluoroalkyl-3-(phenylamino)prop-2-en-1-ones **4g**,**h**, and **4k**–**o** with elimination of 1 M equiv of arylamine (Scheme 6). This regioselective hydrolysis could be explained by the high electron-withdrawing effect of the perfluoroalkyl chain, which could activate the α-imino function towards a nucleophilic attack of water, with elimination of the corresponding arylamine.

These observations lead us to the conclusion that compounds **4** are formed from diazapentadienes **7** and these derivatives **7** are effectively the intermediate of the synthesis of quinolines **6**. Since diazapentadienes **7** are probably more basic than compounds **5**, hydrolysis of **7** occurs in the presence of trace of water to give enaminoketones **4** as detected in the course of the reaction (Scheme 6).

Additionally, enaminones **4** gave in the presence of arylamine in refluxing dichloromethane the corresponding symmetrically substituted 2-perfluoroalkyl-*N*,*N*′-di(R^1-phenyl)-1,5-diazapentatnqh_0009;dienes **7**. However, under acidic conditions the 1-phenylimino-3-phenoxy-3-perfluoroalkyl-prop-2-ene derivatives **5** cleaved hydrolytically its phenyl-enol-ether function, liberating 1 M equiv of substituted phenol and setting free the *N*-aryl enaminoketones **4** (Scheme 6).

3.1. Mechanism of the reaction of 4 with $POCl_3$

Since no reaction of **4** in the presence of polyphosphoric acid occurred it appears evident that protonation does not play a main role in this reaction. It is known that $POCl_3$ can substitute the oxygen atom of a carbonyl compound (Vilsmeier reaction).[38] Furthermore since we could detect the presence of diazapentadiene **7** in this reaction we propose the following Scheme 7 to explain this reaction.



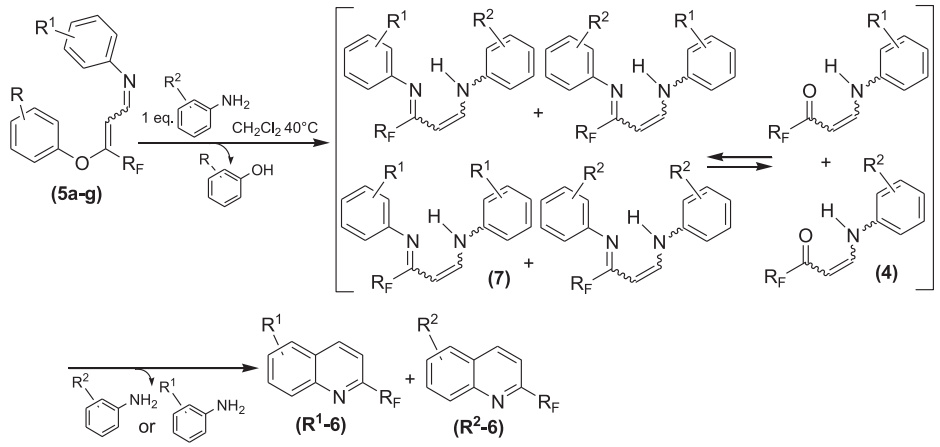
Scheme 7. Mechanism of the reaction of enaminoketones **4** with $POCl_3$ giving quinolines **6**.

$POCl_3$ complexes two molecules of **4** in a double six-centre heterobicyclic transition state having a trans-junction. The oxygen atoms can exchange through the coordination of the phosphorus atom leading to a molecule of **7** and a non-detectable ceto-enol, which probably decomposes or reacts spontaneously with a molecule of free arylamine to give **4** (Scheme 7).

To our knowledge until now this is the first detection and isolation of *N*,*N*′-diaryl-diazapenatadiene derivatives **7** as intermediates in the Combes F-alkyl substituted quinolines synthesis starting from enaminoketones. These results constitute a new advance in the comprehension of the quinoline synthesis using malonic compounds.

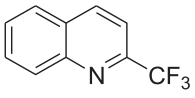
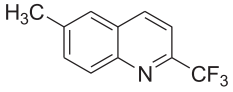
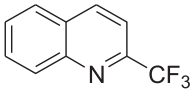
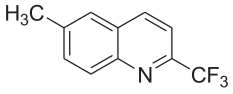
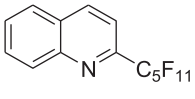
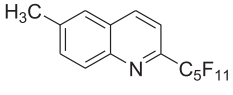
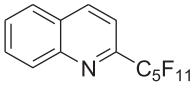
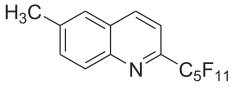
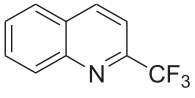
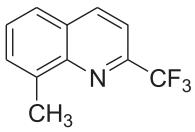
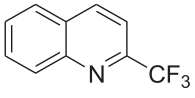
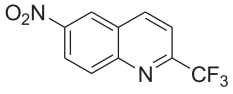
3.2. Unsymmetrically substituted diazapentadienes

We have carried out several experiments to check the reactivity of compounds **5a**–**g** towards arylamines (Scheme 8, Table 3). For example, we first heated imino enol-ether compound **5c** in dichloromethane at 40 °C, no trace of the expected diazapentadienes or quinolines was found. In a second step, **5c** was subjected to reaction carried out in the presence of 1 equiv of 4-methylaniline. After 1 h we were able to detect three sets of new



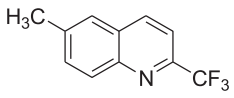
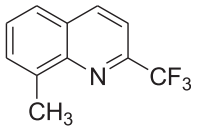
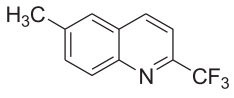
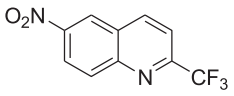
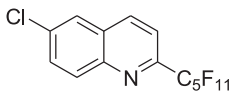
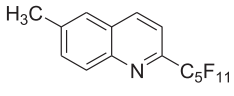
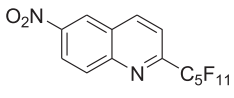
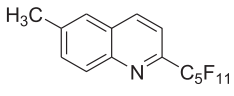
Scheme 8. Synthesis of quinolines **6a**–**h** under basic conditions starting from 1-phenylimino-3-aryloxy-3-perfluoropentylprop-2-enes **5a**–**g** (R=H, 4-OMe; R^1=H, 4-Me, 3-Me, 2-Me, 4-NO_2, 4-Cl, 2-Cl, 4-CO_2H, 3-CO_2H, 4-CN; R_F=CF_3, C_3F_7, C_5F_{11}).

Table 3
Results and yields obtained of reaction for the preparation of 2-trifluoromethyl and 2-perfluoroalkyl-quinolines **6a**–**h** and detection of their corresponding diazapentadiene intermediates **7**

5				Arylamines	MS analysis[a]		Conv[b] [%]		
	R	R^1	R_F	R^2	Time (h)	*m*/*z* (**7**)	Time (h)	R^1-(**6**) (%)	R^2-(**6**) (%)
5a	H	H	CF_3	—	—	—	24	0	0
5a	H	H	CF_3	4-Me	1.30	291, 319 and 305	6	 **6a** (14)	 **6b** (86)
5b	4-OMe	H	CF_3	4-Me	2.30	291, 319 and 305	6	 **6a** (15)	 **6b** (85)
5c	H	H	C_5F_{11}	4-Me	1.30	**7b** 491, **7c** 519 and **7d**, **7e** 505	6	 **6c** (15)	 **6d** (85)
5d	4-OMe	H	C_5F_{11}	4-Me	2.30	491, 519 and 505	6	 **6c** (15)	 **6d** (85)
5a	H	H	CF_3	2-Me	2	291, 319 and 305	6	 **6a** (30)	 **6e** (70)
5a	H	H	CF_3	4-NO_2	4	291, 381 and 336	12	 **6a** (90)	 **6f** (10)

(*continued on next page*)

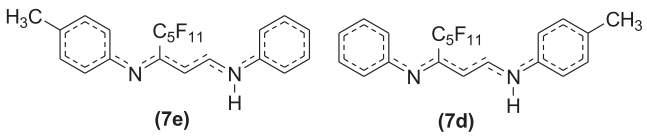
Table 3 (*continued*)

5				Arylamines	MS analysis[a]		Conv[b] [%]		
	R	R^1	R_F	R^2	Time (h)	*m*/*z* (**7**)	Time (h)	R^1-(**6**) (%)	R^2-(**6**) (%)
5e	H	4-Me	CF_3	2-Me	1.30	319	6	 **6b** (57)	 **6e** (43)
5e	H	4-Me	CF_3	4-NO_2	2	319, 381 and 350	12	 **6b** (95)	 **6f** (5)
5f	H	4-Cl	C_5F_{11}	4-Me	1.30	519, 559 and 539	6	 **6g** (25)	 **6d** (75)
5g	H	4-NO_2	C_5F_{11}	4-Me	2	519, 581 and 550	6	 **6h** (5)	 **6d** (95)

[a] measured *m*/*z* : formation of these diazapentadienes was detected by mass spectrometry showing three different picks corresponding to the molecular mass $[M+H]^+$ of **7**. Also all ^{19}F NMR spectroscopic analyses were consistent with the formation of four different diazapentadienes showing in DMSO-d_6 four CF_3 signals around −65 to − 66 ppm or four CF_2 signals at −109 ppm and two enaminones as deduced from ^{19}F NMR signals (in DMSO-d_6: CF_3 signal −75 to −76 ppm or CF_2 signals between −119 and −120 ppm).
[b] determined by ^{19}F NMR spectroscopic analysis of the reaction mixtures; NMR spectroscopic yields were based on consumed **5** and formed **6a** and **6b**.

signals in the ^{19}F NMR spectra of reaction mixtures. The first set of three signals around −109.6 to −109.8 ppm corresponds to four different symmetrically and unsymmetrically substituted diazapentadienes **7b**–**e**, the second set showed two signals around −120.3 to −120.4 assigned to two formed enaminoketones **4c** and **4p** and a signal at −114.3 attributed to the formed substituted 2-perfluoroalkylquinolines **6c** and **6d**. All these formed compounds were isolated and identified and compared to authentic samples synthesized in previous publications[33,34b] (Scheme 8) (see ^{19}F NMR spectra in Supplementary data II).

We succeeded to isolate directly these dissymmetric diazapentadienes as mixture of both regioisomers (2-perfluoro-tnqh_0009;pentyl-*N*-phenyl,*N*′-(4-Methylphenyl)-1,5-diazapentadiene **7d** and 2-perfluoropentyl-*N*-(4-Methylphenyl),*N*′-phenyl-1,5-diazapenta-tnqh_0009;diene **7e**) (Scheme 9) and to perform an NMR analyses quickly before degradation. The structure of these conjugated push–pull derivatives **7d** and **7e** is supported by ^1H, ^{13}C and ^{19}F NMR spectra. The ^1H NMR spectra of this vinamidine compound showed the appearance of three set of signals at 5.5; 7.4 and 9.8 ppm characteristic of the propene bridge of these conjugated push–pull compounds. The aromatic protons appearing between 6.6 and 7.3 ppm integrate for nine protons corresponding to the protons of the aromatic rings of an unsymmetrically substituted diazapentadienes. The ^{13}C spectra also showed for the propene carbons of these diazapentadienes characteristic signals around 90.8–91.6 and 140.6–141.7 ppm and



Scheme 9. Obtained dissymmetric push–pull diazapentadienes **7d** and **7e**.

triplets near 153 ppm attributed to the C_5F_{11}–C=N imine function (see Supplementary data).

Attempts to isolate the other unsymmetrically substituted diazapentadienes **7** were unsuccessful. However, the formation of these diazapentadienes was detected by mass spectrometry showing three different picks corresponding to the molecular mass of the formed intermediates (Table 3). Also all ^{19}F NMR spectroscopic analyses of reaction mixtures were consistent with the formation of four different diazapentadienes showing in DMSO-d_6 four CF_3 signals around −65 to −66 ppm or four CF_2 signals at −109 to −110 ppm, and two enaminones as deduced from ^{19}F NMR signals (in DMSO-d_6: CF_3 signal −75 to −77.5 ppm or CF_2 signals between −119 and −121.8 ppm).

The detection of symmetrically substituted 2-perfluoroalkyl-*N*,*N*′-di(R^2-phenyl)-1,5-diazapentadiene and unsymmetrically substituted 2-perfluoroalkyl-*N*-(R^1-phenyl),*N*′-(R^2-phenyl)-1,5-diazapentadienes **7** suggests that in the presence of arylamine (weak basic conditions) a trans-amination reaction occurred in derivatives **5a**–**g** and the expected cyclization products **6a**–**h** are obtained. The structure of the resulting quinolines was unequivocally assigned on the basis of a comparison of its physical data with those obtained before.[32a,34b] The trans-amination mechanism plays important roles in the biological area, specially during the pyridoxal mediated amino acids catabolism.[39]

Results shown in Table 3 show that in the presence of electron-donating substituent R_2 on the aromatic ring of the entering arylamine, R^2-substituted quinolines **6** are obtained as major products.

However, an electron-attracting substitution on the entering R^2-arylamine (R_2=4-NO_2) favours the trans-amination replacement of the existing R^1-aryl-imine function (R^1=H, 4-Me) and formation of R^1-substituted quinolines **6** is favoured (no 3-(aryloxy)-3-perfluoroalkyl-prop-2-enals **3** was detected during this reaction) (Scheme 8 and Table 3).

These results reported here showed an interesting comparison of the chemical behaviour for the mechanism of cyclization of these new enaminoketones and diazapentadienes, showing selective route of ring closure including direct regiospecific cyclization of 2-trifluoromethyl and 2-perfluoroalkyl-*N*,*N*′-diaryl-1,5-diazapentadienes **7** as the intermediates of the synthesis of 2-trifluoromethyl and 2-perfluoroalkylquinolines **6**.

4. Conclusion

In conclusion, we provided a new trifluoromethyl and perfluoroalkyl-containing 3-(phenylamino)-prop-2-en-1-ones **4a**–**o** in a one-step reaction starting from 3-perfluoroalkyl-3-aryloxypropenals **3a**–**e**. These compounds have been used as precursors for the synthesis of a variety of substituted five- and six-membered heterocycles.[1,5–8] Using ^{1}H, ^{13}C NMR and ^{1}H–^{1}H COSY NMR spectroscopy we were able to confirm the obtained **4**β regioisomer and to establish the structure of these unsaturated push–pull derivatives **4a**–**o** in solution (Scheme 5).

Then we explored the reactivity of **4**, we observed that enaminones **4a**–**o** react in the presence of $POCl_3$ and form regiospecifically 2-perfluoroalkylquinolines **6**, through diazapentadienes **7** as reactional intermediates. This confirms, our previous works according to which the 3-perfluoroalkyl-*N*,*N*′-diaryl-1,5-diazapentadienes **5** are the synthetic intermediates of the synthesis of 2-perfluoroalkylquinolines **6**. To our knowledge this is the first detection and isolation of *N*,*N*′-diaryl-diazapentadiene derivatives **7** as intermediates in the Combes F-alkyl substituted quinolines synthesis starting from enaminoketones.

5. Experimental section

5.1. General methods and spectroscopic measurements

All reaction solvents were distilled before use. All synthetic reactions were performed in oven-dried glassware, and their progress was monitored by thin layer chromatography (TLC), using silica gel plates, and by ^{19}F NMR spectroscopy. Chromatographic column purifications were performed on silica gel (40–63 μm). ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ or DMSO on 300 MHz and 400 MHz spectrometers. Chemical shifts are given in parts per million (ppm); the internal standard reference was trimethylsilane for ^{1}H and ^{13}C, and $CFCl_3$ for ^{19}F spectra. Abbreviations used in the description of NMR spectra: s: singlet, d: doublet, t: triplet, q: quadruplet, br s: broad signal, br d: broad doublet. The coupling constant (*J*) is given in hertz (Hz). High-resolution mass spectra were recorded in the FAB^{+} mode, using NBA as matrix with a Micromass Q-Tof Analyzer.

5.1.1. NMR measurements. The NMR spectra were run on a 300 MHz NMR spectrometer, operating at 300.13 MHz for ^{1}H observation, 75.46 MHz for ^{13}C analyses and at 282.40 MHz for ^{19}F acquisitions, in 5 mm sample tubes using 20–45 mg of the compounds in deuterated solvents. The ^{1}H, ^{13}C and ^{19}F NMR parameters were acquired from the same sample.

Due to *E*/*Z* isomerism about the push–pull system in **4a**–**o**, two sets of signals were observed for the resonance of these compounds, in both the ^{1}H and ^{13}C NMR spectra. In each case, the chemical shift differences were sufficient and signals were generally well dispersed and consequently, they were easily assigned. The corresponding ^{1}H and ^{13}C NMR spectra were then assigned by ^{1}H–^{1}H COSY and ^{1}H–^{13}C HMQC experiments. However, when having mixture of isomers in solutions of **4** the NMR signals of their phenyl groups were in some cases strongly overlapped and could not be differentiated.

5.2. General procedure B

To a mixture of 3-trifluoromethyl-3-phenoxypropenal **3b** (1 equiv) in toluene (10 mL/1 g of **3b**) was added *para*-toluenesulfonic acid (1 equiv) portion wise and stirred until complete dissolution. Then aniline (1 equiv) was added and the mixture was stirred under reflux (Table 1) until complete consumption of the starting material as judged by TLC and ^{19}F NMR spectroscopy (4 h). At the end of the reaction, the mixture was diluted, neutralized with a solution of 1% $NaHCO_3$ and washed with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. The resulting oil was purified by column chromatography over silica gel to afford compounds **4a** and **6**. In another procedure, we monitored the evolution of the reaction by ^{19}F NMR spectroscopy and at mid reaction time (2 h) we stopped heating and we added a solution of 1% $NaHCO_3$ into the mixture. Work up and washing as described previously permitted the isolation of compounds **4a**, **5a** and **6a** and **7a**.

5.3. Reaction of 3-trifluoromethyl-3-phenoxypropenal (3b) with aniline

Starting from 4.5 g (20.8 mmol) of **3b** and 1.93 g (20.8 mmol) of aniline, 2.2 g (10.2 mmol) of **4a** was obtained as yellow liquid (yield: 50%), 0.31 g (1.06 mmol) of **5a** was obtained as yellow liquid (yield: 5%), 0.4 g (2.03 mmol) of **6a** was obtained as amorphous white solid (yield: 10%) and 0.3 g (1.03 mmol) of **7a** was obtained as yellow amorphous solid (yield: 5%).

*5.3.1. 1-Trifluoromethyl-3-(phenylamino)prop-2-en-1-one (**4a**).* ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^{3}J_{H2H3}$=7.4 Hz, 1H, H-2), 6.4 (m, 2H, Ph–H), 6.6 (dd, $^{3}J_{H2H3}$=7.4 Hz and $^{3}J_{H3NH}$=13 Hz, 1H, H-3), 6.8–7 (m, 3H, Ph–H), 11.7 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 89.8 (s, =*C*–C=O), 117.1, 117.8 (q, *C*F_3, $^{1}J_{CF}$=289.2 Hz), 125.2, 129.6, 138.8, 149.1 (s, =*C*–NH), 179.2 (q, O=*C*–CF_3, $^{2}J_{CF}$=33.7 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −76.56 (s, 3F, CF_3); MS FAB^{+} *m*/*z* (%): 216 ($M+H^{+}$, 100), 215 (M^{+}, 45), 146 ($M^{+}-CF_3$, 40). Anal. Calcd for $C_{10}H_8F_3NO$: C, 55.82; H, 3.75; O, 7.44. Found: C, 55.89; H, 3.74; O, 7.44.

*5.3.2. 1-Phenylimino-3-(phenoxy)-3-trifluoromethyl-prop-2-ene (**5a**).* ^{1}H NMR (300.13 MHz, C_6D_6, *EE*) δ (ppm) 6.3 (d, $^{3}J_{HH}$=9.1 Hz, 1 H), 6.8–7.5 (m, 10 H), 8.8 (d, $^{3}J_{HH}$=9 Hz, 1H); ^{13}C NMR (100.61 MHz, C_6D_6, *EE*) δ (ppm) 117.1, 117.5, 121, 121.2, 127.1, 127.4, 130.3, 131.4, 151.6 (q, *C*$_3$–CF_3, $^{2}J_{CF}$=28.9 Hz), 153.1, 153.5, 156.2 (q, HC=N (*EE*), $^{4}J_{C1F}$=5.5 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *EE*) δ (ppm) 66.5 (s, 3F, CF_3); MS (*m*/*z*): 292 $[M+H]^{+}$; HRMS *m*/*z* $[M+H]^{+}$ calcd for $C_{16}H_{13}F_3NO$: 292.0949, found: 292.0955. Anal. Calcd for $C_{16}H_{12}F_3NO$: C, 65.98; H, 4.15; O, 5.49. Found: C, 65.99; H, 4.16; O, 5.51.

*5.3.3. 2-Trifluoromethylquinoline (**6a**).* ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 7.8 (m, 1H), 7.9 (m, 2H), 8.1 (d, *J*=7.5 Hz, 1H), 8.2 (d, *J*=8.6 Hz, 1H), 8.7 (d, *J*=8.6 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 117.6 (q, CH, $^{3}J_{CF}$=2.1 Hz), 122.6 (q, CF_3, $^{1}J_{CF}$=273.8 Hz), 127.4, 130, 130.2, 134.1, 138.5, 141, 146.8 (q, C–CF_3, $^{2}J_{CF}$=34.1 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −67.7 (s, 3F, CF_3); MS (*m*/*z*): 198 $[M+H]^{+}$; HRMS *m*/*z* $[M+H]^{+}$ calcd for $C_{10}H_7F_3N$, 198.0531, found 198.0536. Anal. Calcd for $C_{10}H_6F_3N$: C, 60.92; H, 3.07; N, 7.10. Found: C, 60.88; H, 3.12; N, 7.15.

*5.3.4. 2-Trifluoromethyl-1-phenylamino-3-phenyliminopropene (**7a**).* ^{1}H NMR (300 MHz, DMSO-d_6, *EEE*) δ (ppm) 5.6 (d, $^{3}J_{H2H3}$=13.7 Hz, H_2), 6.8 (d, *J*=7.5 Hz, 2H), 7 (m, 3H), 7.15 (t, *J*=7.4 Hz, 1H), 7.3 (t, *J*=7.8 Hz, 2H), 7.4 (t, *J*=7.7 Hz, 2H), 7.6 (t, *J*=13 Hz, H_3), 9.9 (d, $^{3}J_{H3NH}$=12.3 Hz, N*H*); ^{13}C NMR (75.4 MHz, DMSO-d_6, *EEE*)

δ (ppm) 90.8, 115.1, 119.2, 120.5 (q, CF_3, $^1J_{CF}$=279.2 Hz), 122.14, 123.5, 129.3, 129.7, 140.7, 140.9 (q, C_3H, $^4J_{C3F}$=2.9 Hz), 149.5, 153.3 (q, C–CF_3, $^2J_{C1F}$=31.2 Hz); ^{19}F NMR (282.4 MHz, DMSO-d_6, *EEE*) δ (ppm) −65.8 (s, 3F); MS (*m*/*z*): 291 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{14}F_3N_2$: 291.1109, found: 291.1088. Anal. Calcd for $C_{16}H_{13}F_3N_2$: C, 66.20; H, 4.51; N, 9.65. Found: C, 66.18; H, 4.50; N, 9.66.

5.4. General procedure for the preparation of 1-trifluoromethyl and 1-perfluoroalkyl-3-(R^1-phenylamino)prop-2-en-1-ones 4a–c (R^1=H), 4d–f (R^1=Me), 4i–k (R^1=Cl), and 4n–o (R^1=CN): procedure A

To a stirred solution of 3-perfluoroalkyl-3-aryloxypropenals **3** (1 equiv) in 2% hydrochloric methanolic solution (10 mL/1 g of **1**) was added 1 equiv of the corresponding arylamines. The resulting mixture was stirred under reflux and the reaction monitored by TLC and ^{19}F NMR spectroscopy. The terminal CF_3 or the CF_2 signals of compound **3** faded upon evolution of the reaction and new peaks appeared corresponding to the CF_3 or CF_2 signals of product **4** (4–24 h). On completion of the reaction, the mixture was diluted and extracted with diethyl ether (5×). The organic layers were washed with water and dried with sodium sulfate then concentrated in vacuum. The resulting yellow oils were purified by column chromatography on silica gel (EtOAc/petroleum ether 15:100) to afford **4**.

*5.4.1. 1-Trifluoromethyl-3-(phenylamino)prop-2-en-1-one (**4a**).* Same process as procedure A. Starting from 1.2 g (5.55 mmol) of **3b** and 0.51 g (5.55 mmol) of aniline, 1 g (5 mmol) of **4a** was obtained as yellow liquid (yield: 90%). Or starting from 1.1 g (4.47 mmol) of **3a** and 0.41 g (4.47 mmol) of aniline, 0.86 g (4 mmol) of **4a** were obtained as yellow liquid (yield: 90%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.4 Hz, 1H, H-2), 6.4 (m, 2H, Ph–H), 6.6 (dd, $^3J_{H2H3}$=7.4 Hz and $^3J_{H3NH}$=13 Hz, 1H, H-3), 6.8–7 (m, 3H, Ph–H), 11.7 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 89.8 (s, =*C*–C=O), 117.1, 117.8 (q, *C*F_3, $^1J_{CF}$=289.2 Hz), 125.2, 129.6, 138.8, 149.1 (s, =*C*–NH), 179.2 (q, O=*C*–CF_3, $^2J_{CF}$=33.7 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −76.56 (s, 3F, CF_3); MS FAB$^+$ *m*/*z* (%): 216 ($M+H^+$, 100), 215 (M^+, 45), 146 (M^+-CF_3, 40). Anal. Calcd for $C_{10}H_8F_3NO$: C, 55.82; H, 3.75; O, 7.44. Found: C, 55.89; H, 3.74; O, 7.44.

*5.4.2. 1-Perfluoropropyl-3-(phenylamino)prop-2-en-1-one (**4b**).* Same process as procedure A. Starting from 1 g (3.16 mmol) of **3c** and 0.29 g (3.16 mmol) of aniline, 0.89 g (2.8 mmol) of **4b** was obtained as yellow liquid (yield: 90%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.4 Hz, 1H, H-2), 6.3 (m, 2H, Ph–H), 6.7 (dd, $^3J_{H2H3}$=7.4 Hz and $^3J_{H3NH}$=13 Hz, 1H, H-3), 6.9–7 (m, 3H, Ph–H), 11.9 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 89.7 (s, =*C*–C=O), 117.2, 117.6, 125.2, 130, 138.8, 149.5 (s, =*C*–NH), 179.2 (t, O=*C*–CF_2, $^2J_{CF}$=25.6 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −80.4 (s, 3F), −119 (s, 2F), −126.7 (s, 2F); MS FAB$^+$ *m*/*z* (%): 316 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{12}H_9F_7NO$ 316.0572, found 316.0568. Anal. Calcd for $C_{12}H_8F_7NO$: C, 45.73; H, 2.56; O, 5.08. Found: C, 45.70; H, 2.55; O, 5.10.

*5.4.3. 1-Perfluoropenthyl-3-(phenylamino)prop-2-en-1-one (**4c**).* Same process as procedure A. Starting from 1.5 g (3.36 mmol) of **3d** and 0.31 g (3.36 mmol) of aniline, 1.25 g (3 mmol) of **4c** was obtained as yellow liquid (yield: 90%). Or starting from 1.5 g (3.6 mmol) of **3e** and 0.33 g (3.6 mmol) of aniline, 1.34 g (3.2 mmol) of **4c** was obtained as yellow liquid (yield: 90%); ^{1}H NMR (400 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.7 (d, $^3J_{H2H3}$=7.1 Hz, 1H, H-2), 6.6 (d, 2H, *J*=8 Hz, Ph–H), 6.9 (dd, $^3J_{H2H3}$=7.4 Hz and $^3J_{H3NH}$=13 Hz, 1H, H-3), 7.1–7.2 (m, 3H, Ph–H), 12.1 (br d, 1H, NH); ^{13}C NMR (100.6 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.4 (s, =*C*–C=O), 117.4, 125.5, 129.8, 138.8, 149.1 (s, =*C*–NH), 180.4 (t, O=*C*–CF_2, $^2J_{CF}$=24.8 Hz); ^{19}F NMR (235.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −81 (m, 3F), −120.3 (m, 2F), −122.5 (m, 4F), −126.5 (m, 2F); MS FAB$^+$ *m*/*z* (%): 416 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{14}H_9F_{11}NO$ 416.0508, found 416.0490. Anal. Calcd for $C_{14}H_8F_{11}NO$: C, 40.50; H, 1.94; O, 3.85. Found: C, 40.48; H, 1.95; O, 3.86.

*5.4.4. 1-Trifluoromethyl-3-(4-methylphenylamino)prop-2-en-1-one (**4d**).* Same process as procedure A. Starting from 1 g (4.62 mmol) of **3b** and 0.49 g (4.62 mmol) of 4-methylaniline, 0.93 g (4 mmol) of **4d** was obtained as yellow liquid (yield: 88%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 2.2 (s, 3H), 5.4 (d, $^3J_{H2H3}$=7.3 Hz, 1H, H-2), 6.7 (dd, *J*=7.3 Hz and 12.4 Hz, 1H, H-3), 6.9–7.3 (m, 4H, Ph–H), 11.9 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 16.9, 91.6 (s, =*C*–C=O), 117, 118.1 (q, *C*F_3, $^1J_{CF}$=288.3 Hz), 125.3, 127.1, 127.3, 131.3, 137.3, 149.1 (s, =*C*–NH), 180.1 (q, O=*C*–CF_3, $^2J_{CF}$=24.9 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −76.5 (s, 3F, CF_3); MS FAB$^+$ *m*/*z* (%): 230 ($M+H^+$, 100), 229 (M^+, 50), 160 (M^+-CF_3, 35); HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO$ 230.0793, found 230.0781. Anal. Calcd for $C_{11}H_{10}F_3NO$: C, 57.64; H, 4.40; O, 6.98. Found: C, 57.66; H, 4.40; O, 6.96.

*5.4.5. 1-Trifluoromethyl-3-(3-methylphenylamino)prop-2-en-1-one (**4e**).* Same process as procedure A. Starting from 1.1 g (5 mmol) of **3b** and 0.54 g (5 mmol) of 3-methylaniline, 0.99 g (4.3 mmol) of **4e** was obtained as yellow liquid (yield: 85%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 2 (s, 3H), 5.6 (d, $^3J_{H2H3}$=7.3 Hz, 1H, H-2), 6.5 (d, *J*=7.9 Hz, 1H, Ph–H), 6.8 (dd, $^3J_{H2H3}$=7.3 Hz and $^3J_{H3NH}$=13 Hz, 1H, H-3), 6.9–7.2 (m, 3H, Ph–H), 12.1 (br d, $^3J_{H3NH}$=11.6 Hz, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 16.9, 91.6 (s, =*C*–C=O), 115.1, 117.8 (q, *C*F_3, $^1J_{CF}$=289.4 Hz), 125.3, 127.2, 127.3, 131.3, 137.3, 149.1 (s, =*C*–NH), 180.1 (q, O=*C*–CF_3, $^2J_{CF}$=24.9 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) −76.5 (s, 3F, CF_3); MS FAB$^+$ *m*/*z* (%): 230 ($M+H^+$, 100), 229 (M^+, 50), 160 (M^+-CF_3, 35); HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO$ 230.0793, found 230.0795. Anal. Calcd for $C_{11}H_{10}F_3NO$: C, 57.64; H, 4.40; O, 6.98. Found: C, 57.68; H, 4.41; O, 6.94.

*5.4.6. 1-Trifluoromethyl-3-(2-methylphenylamino)prop-2-en-1-one (**4f**).* Same process as procedure A. Starting from 1.1 g (5 mmol) of **3b** and 0.54 g (5 mmol) of 2-methylaniline, 0.9 g (3.93 mmol) of **4f** was obtained as yellow liquid (yield: 78%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 2 (s, 3H), 5.8 (d, $^3J_{H2H3}$=7.2 Hz, 1H, H-2), 7.1 (t, *J*=7.5 Hz, 1H, Ph–H), 7.3 (m, 2H, Ph–H), 7.5 (d, *J*=8 Hz, 1H, Ph–H), 8.2 (dd, $^3J_{H2H3}$=7.4 Hz and $^3J_{H3NH}$=12.3 Hz, 1H, H-3), 12.1 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 16.7, 89.5 (s, =*C*–C=O), 115.5, 116.3 (q, *C*F_3, $^1J_{CF}$=294.5 Hz), 125, 126.9, 127, 131.2, 137.4, 151.5 (s, =*C*–NH), 177.9 (q, O=*C*–CF_3, $^2J_{CF}$=33.9 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −77.4 (s, 3F, CF_3); MS FAB$^+$ *m*/*z* (%): 230 ($M+H^+$, 100), 229 (M^+, 55), 160 (M^+-CF_3, 35); HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO$ 230.0793, found 230.0790. Anal. Calcd for $C_{11}H_{10}F_3NO$: C, 57.64; H, 4.40; O, 6.98. Found: C, 57.60; H, 4.40; O, 6.99.

*5.4.7. 1-Perfluoropentyl-3-(4-chlorophenylamino)prop-2-en-1-one (**4i**).* Same process as procedure A. Starting from 1.5 g (3.6 mmol) of **3e** and 0.45 g (3.6 mmol) of 4-chloroaniline, 1.16 g (2.59 mmol) of **4i** was obtained as yellow liquid (yield: 72%); ^{1}H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.5 Hz, 1H, H-2), 6.4 (d, *J*=8.2 Hz, 2H, Ph–H), 6.6 (dd, *J*=7.5 Hz and $^3J_{H3NH}$=13.1 Hz, 1H, H-3), 7.4 (d, *J*=8.2 Hz, 2H, Ph–H), 11.5 (br d, $^3J_{H3NH}$=13 Hz, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.3 (s, =*C*–C=O), 114.6, 123.7, 131.6, 132.2, 148.7 (s, =*C*–NH), 178.4 (t, O=*C*–CF_2, $^2J_{CF}$=23.6 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) −80.6 (m, 3F), −120.1 (m, 2F), −122.2 (m, 2F), −122.3 (m, 2F), −126 (m, 2F); MS FAB$^+$ *m*/*z*

(%): 450 ($M+H^+$, 55), 449 (M^+, 100); HRMS *m/z* $[M+H]^+$ calcd for $C_{14}H_8ClF_{11}NO$ 450.0119, found 450.0122. Anal. Calcd for $C_{14}H_7ClF_{11}NO$: C, 37.40; H, 1.57; O, 3.56. Found: C, 37.41; H, 1.57; O, 3.58.

*5.4.8. 1-Trifluoromethyl-3-(4-chlorophenylamino)prop-2-en-1-one (**4j**).* Same process as procedure A. Starting from 1 g (4.62 mmol) of **3b** and 0.58 g (4.62 mmol) of 4-chloroaniline, 0.84 g (3.37 mmol) of **4j** was obtained as yellow liquid (yield: 73%); ^1H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.5 (d, $^3J_{H2H3}$=7.7 Hz, 1H, H-2), 6.4 (d, *J*==8.8 Hz, 2H, Ph−H), 6.7 (dd, *J*=7.7 Hz and $^3J_{H3NH}$=12.8 Hz, 1H, H-3), 7.3 (d, *J*=8.8 Hz, 2H, Ph−H), 11.6 (d, $^3J_{H3NH}$=12.8 Hz, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.5 (s, =*C*−C=O), 115.5, 117.6 (q, *C*F_3, $^1J_{CF}$=292.6 Hz), 125.5, 127.2, 130.4, 135.2, 149 (s, =*C*−NH), 178.6 (q, O=*C*−CF_3, $^2J_{CF}$=33.4 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −77.5 (s, 3F); MS FAB$^+$ *m/z* (%): 250 ($M+H^+$, 80), 249 (M^+, 100), 180 (M^+-CF_3, 40); HRMS *m/z* $[M+H]^+$ calcd for $C_{10}H_8ClF_3NO$ 250.0247, found 250.0250. Anal. Calcd for $C_{10}H_7ClF_3NO$: C, 48.12; H, 2.83; O, 6.41. Found: C, 48.13; H, 2.83; O, 6.45.

*5.4.9. 1-Trifluoromethyl-3-(2-chlorophenylamino)prop-2-en-1-one (**4k**).* Same process as procedure A. Starting from 1.2 g (5.55 mmol) of **3b** and 0.7 g (5.55 mmol) of 2-chloroaniline, 0.83 g (3.33 mmol) of **4k** was obtained as yellow liquid (yield: 60%); ^1H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.5 Hz, 1H, H-2), 6.4 (d, *J*=8.2 Hz, 1H, Ph−H), 6.6 (m, 1H, H-3), 6.65 (m, 1H, Ph−H), 6.8 (t, *J*=8.4 Hz, 1H, Ph−H), 7 (d, *J*=8.5 Hz, 1H, Ph−H), 12.1 (br d, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.1 (s, =*C*−C=O), 115.4, 117.6 (q, *C*F_3, $^1J_{CF}$=289.76 Hz), 123.6, 125.3, 130.2, 136, 147.6 (s, =*C*−NH), 179.6 (q, O=*C*−CF_3, $^2J_{CF}$=34.7 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ −76.7 (s, 3F, CF_3); MS FAB$^+$ *m/z* (%): 250 ($M+H^+$, 80), 249 (M^+, 100), 180 (M^+-CF_3, 30); HRMS *m/z* $[M+H]^+$ calcd for $C_{10}H_8ClF_3NO$ 250.0247, found 250.0251. Anal. Calcd for $C_{10}H_7ClF_3NO$: C, 48.12; H, 2.83; O, 6.41. Found: C, 48.14; H, 2.80; O, 6.40.

*5.4.10. 1-Perfluoropentyl-3-(4-cyanophenylamino)prop-2-en-1-one (**4n**).* Same process as procedure A. Starting from 1.5 g (3.6 mmol) of **3e** and 0.42 g (3.6 mmol) of 4-cyanoaniline, 0.93 g (2.12 mmol) of **4n** was obtained as yellow liquid (yield: 59%); ^1H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.8 Hz, 1H, H-2), 6 (d, 2H, *J*=9.1 Hz, Ph−H), 6.2 (dd, $^3J_{H2H3}$=7.8 Hz and $^3J_{H3NH}$=12.9 Hz, 1H, H-3), 7.1 (d, 2H, *J*=9.1 Hz, Ph−H), 11.4 (d, $^3J_{H3NH}$=12.9 Hz, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.2 (s, =*C*−C=O), 113.9, 116.1, 123.6, 141.7, 142.7, 145.5 (s, =*C*−NH), 178.9 (t, O=*C*−CF_2, $^2J_{CF}$=25.1 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −80.8 (m, 3F), −119.8 (m, 2F), −122.1 (m, 2F), −122.2 (m, 2F), −126 (m, 2F); MS FAB$^+$ *m/z* (%): 441 ($M+H^+$, 100), 440 (M^+, 50); HRMS *m/z* $[M+H]^+$ calcd for $C_{15}H_8F_{11}N_2O$ 441.0461, found 441.0466. Anal. Calcd for $C_{15}H_7F_{11}N_2O$: C, 40.93; H, 1.60; O, 3.63. Found: C, 40.95; H, 1.62; O, 3.58.

*5.4.11. 1-Trifluoromethyl-3-(4-cyanophenylamino)prop-2-en-1-one (**4o**).* Same process as procedure A. Starting from 1.4 g (6.48 mmol) of **3b** and 0.76 g (6.48 mmol) of 4-cyanoaniline, 1 g (4.16 mmol) of **4o** was obtained as yellow liquid (yield: 66%); ^1H NMR (400 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.5 (d, $^3J_{H2H3}$=7.6 Hz, 1H, H-2), 6.1 (d, 2H, *J*=9 Hz, Ph−H), 6.3 (dd, $^3J_{H2H3}$=7.6 Hz and $^3J_{H3NH}$=13.1 Hz, 1H, H-3), 7.2 (d, 2H, *J*=9 Hz, Ph−H), 11.3 (br d, 1H, NH); ^{13}C NMR (100.6 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.1 (s, =*C*−C=O), 115.6, 116, 118.2 (q, *C*F_3, $^1J_{CF}$=291 Hz), 123.1, 127, 140.7, 141.3, 145.5 (s, =*C*−NH), 179.9 (q, O=*C*−CF_3, $^2J_{CF}$=33.1 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −77.1 (s, 3F); MS FAB$^+$ *m/z* (%): 241 ($M+H^+$, 100), 240 (M^+, 50), 171 (M^+-CF_3, 50); HRMS *m/z* $[M+H]^+$ calcd for $C_{11}H_8F_3N_2O$ 241.0589, found 241.0595. Anal. Calcd for $C_{11}H_7F_3N_2O$: C, 55.01; H, 2.94; O, 6.66. Found: C, 55.10; H, 2.94; O, 6.65.

5.5. General procedure for the preparation of 1-perfluoroalkyl-3-(R^1-phenylamino)prop-2-en-1-ones 4g,h ($R^1=NO_2$), 4l−m ($R^1=CO_2H$): procedure A

To a solution of 3-perfluoroalkyl-3-aryloxypropenals **3** (1 equiv) in 2% HCl methanol (5 mL/1 g of **1**) was added 1 equiv of the corresponding arylamines. The mixture was stirred under reflux until disappearance of ^{19}F NMR signals corresponding to the starting product **3** (24−48 h). At the end of the reaction, the solution was left at room temperature, a precipitate was formed. Then the reaction mixture was cooled to 0 °C and final pure derivatives **4** were isolated as yellow needles by direct crystallization on removal of solvent.

*5.5.1. 1-Perfluoropentyl-3-(4-nitrophenylamino)prop-2-en-1-one (**4g**).* Same process as procedure A. Starting from 2.5 g (6 mmol) of **3e** and 0.83 g (6 mmol) of 4-nitroaniline, 1.96 g (4.26 mmol) of **4g** was obtained as amorphous yellow solid (yield: 71%). Or starting from 2 g (4.48 mmol) of **3d** and 0.61 g (4.48 mmol) of 4-nitroaniline, 1.34 g (2.91 mmol) of **4g** was obtained as amorphous yellow solid (yield: 65%); ^1H NMR (300 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.5 (d, $^3J_{H2H3}$=7.5 Hz, 1H, H-2), 5.9 (d, 2H, *J*=8.8 Hz, Ph−H), 6.3 (dd, $^3J_{H2H3}$=7.8 Hz and $^3J_{H3NH}$=12.7 Hz, 1H, H-3), 7.8 (d, 2H, *J*=8.8 Hz, Ph−H), 11.4 (d, $^3J_{H3NH}$=11.7 Hz, 1H, NH); ^{13}C NMR (75.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.5 (s, =*C*−C=O), 114.7, 123.7, 141.5, 142.8, 145.7 (s, =*C*−NH), 179.9 (t, O=*C*−CF_2, $^2J_{CF}$=24.6 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −80.8 (m, 3F), −119.7 (m, 2F), −122 (m, 2F), −122.1 (m, 2F), −126 (m, 2F); MS FAB$^+$ *m/z* (%): 461 ($M+H^+$, 100), 460 (M^+, 55), 391 (M^+-CF_3, 30); HRMS *m/z* $[M+H]^+$ calcd for $C_{14}H_8F_{11}N_2O_3$ 461.0359, found 461.0355. Anal. Calcd for $C_{14}H_7F_{11}N_2O_3$: C, 36.54; H, 1.53; O, 10.43. Found: C, 36.55; H, 1.54; O, 10.46.

*5.5.2. 1-Trifluoromethyl-3-(4-nitrophenylamino)prop-2-en-1-one (**4h**).* Same process as **4g** procedure A. Starting from 1.5 g (6.94 mmol) of **3b** and 0.95 g (6.94 mmol) of 4-nitroaniline, 1.26 g (4.86 mmol) of **4h** was obtained as yellow amorphous solid (yield: 70%); ^1H NMR (400 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 5.4 (d, $^3J_{H2H3}$=7.7 Hz, 1H, H-2), 5.9 (d, 2H, *J*=9 Hz, Ph−H), 6.3 (dd, $^3J_{H2H3}$=7.7 Hz and $^3J_{H3NH}$=12.8 Hz, 1H, H-3), 7.8 (d, 2H, *J*=9 Hz, Ph−H), 11.2 (br d, 1H, NH); ^{13}C NMR (100.6 MHz, C_6D_6, *ZZE* 100%) δ (ppm) 91.6 (s, =*C*−C=O), 115.6, 118.2 (q, *C*F_3, $^1J_{CF}$=290.6 Hz), 125.4, 127.3, 140.3, 141.3, 145.5 (s, =*C*−NH), 179.7 (q, O=*C*−CF_3, $^2J_{CF}$=32.3 Hz); ^{19}F NMR (235.4 MHz, C_6D_6, *ZZE* 100%) δ (ppm) −77.4 (s, 3F); MS FAB$^+$ *m/z* (%): 261 ($M+H^+$, 100), 260 (M^+, 50), 191 (M^+-CF_3, 35); HRMS *m/z* $[M+H]^+$ calcd for $C_{10}H_8F_3N_2O_3$ 261.0487, found 261.0490. Anal. Calcd for $C_{10}H_7F_3N_2O_3$: C, 46.16; H, 2.71; O, 18.45. Found: C, 46.20; H, 2.70; O, 18.46.

*5.5.3. 1-Trifluoromethyl-3-(4-carboxylphenylamino)prop-2-en-1-one (**4l**).* Same process as **4g** procedure A. Starting from 2.1 g (9.72 mmol) of **3b** and 1.33 g (9.72 mmol) of 4-carboxyaniline, 1.51 g (5.83 mmol) of **4l** was obtained as yellow amorphous solid (yield: 60%); ^1H NMR (400 MHz, CD_3SOCD_3, *EEE*/*ZZE* 80:20) δ (ppm) (*ZZE*) 5.6 (d, $^3J_{H2H3}$=7.5 Hz, 1H, H-2), 7.5 (d, 2H, *J*=8.5 Hz, Ph−H), 7.9 (d, 2H, *J*=8.5 Hz, Ph−H), 8.2 (bdd, 1H, H-3), 11.6 (d, 1H, $^3J_{H3NH}$=12.8 Hz, NH); (*EEE*) 5.9 (d, $^3J_{H2H3}$=12.4 Hz, 1H, H-2), 7.3 (d, 2H, *J*=8.5 Hz, Ph−H), 7.9 (d, 2H, *J*=8.5 Hz, Ph−H), 8.4 (t, 1H, *J*=12.7 Hz, H-3), 11.2 (d, 1H, $^3J_{H3NH}$=13.1 Hz, NH); ^{13}C NMR (100.6 MHz, CD_3SOCD_3, *EEE*/*ZZE* 80:20) δ (ppm) 90.4 (s, =*C*−C=O, (*ZZE*)), 93.8 (s, =*C*−C=O, (*EEE*)), 113.2, 116.7, 117.6 (q, *C*F_3, $^1J_{CF}$=291.6 Hz), 117.9, 125.3, 126.5, 127.6, 131.4, 131.6, 143, 143.6, 149.9 (br d, =*C*−NH, (*EEE*)), 151.7 (s, =*C*−NH, (*ZZE*)), 166.2 (s, *C*O_2H), 167.2 (s, *C*O_2H), 176.7 (q, O=*C*−CF_3, $^2J_{CF}$=29.6 Hz), 177.5 (q, O=*C*−CF_3, $^2J_{CF}$=34.7 Hz); ^{19}F NMR

(282.4 MHz, CD_3SOCD_3, *EEE*/*ZZE* 80:20) δ (ppm) −76.1 (s, 3F, CF_3 (*ZZE*)), −76.2 (br s, 3F, CF_3 (*EEE*)); IR (cm^{-1}, KBr) 3429 (CO_2H); MS FAB$^+$ *m*/*z* (%): 260 ($M+H^+$, 50), 259 (M^+, 25), 242 (M^+-H_2O, 50), 190 (M^+-CF_3, 15); HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_9F_3NO_3$ 260.0535, found 260.0542. Anal. Calcd for $C_{11}H_8F_3NO_3$: C, 50.98; H, 3.11; O, 18.52. Found: C, 51.01; H, 3.10; O, 18.49.

*5.5.4. 1-Trifluoromethyl-3-(3-carboxylphenylamino)prop-2-en-1-one (**4m**).* Same process as **4g** procedure A. Starting from 2 g (9.25 mmol) of **3b** and 1.26 g (9.25 mmol) of 3-carboxyaniline, 1.43 g (5.55 mmol) of **4m** was obtained as amorphous yellow solid (yield: 60%); ^1H NMR (300 MHz, CD_3SOCD_3, *EEE*/*ZZE* 33:67) δ (ppm) (*ZZE*) 5.7 (d, $^3J_{H2H3}$=7.5 Hz, 1H, H-2), 7.6 (t, *J*=7.9 Hz, 1H, Ph−H), 7.7 (m, 1H, Ph−H), 7.9 (dd, *J*=7.6 and 2.5 Hz, 1H, Ph−H), 8 (d, *J*=3.6 Hz, 1H, Ph−H), 8.2 (dd, $^3J_{H2H3}$=7.5 Hz and $^3J_{H3NH}$=13.2 Hz, 1H, H-3), 11.8 (br d, 1H, $^3J_{H3NH}$=9.3 Hz, NH); (*EEE*) 6 (d, $^3J_{H2H3}$=12.4 Hz, 1H, H-2), 7.6 (t, *J*=7.9 Hz, 1H, Ph−H), 7.7 (m, 1H, Ph−H), 7.9 (dd, *J*=7.6 and 2.5 Hz, 1H, Ph−H), 8 (d, *J*=3.6 Hz, 1H, Ph−H), 8.5 (t, 1H, *J*=12.8 Hz, H-3), 10.1 (br d, 1H, $^3J_{H3NH}$=12.5 Hz, NH); ^{13}C NMR (100.6 MHz, CD_3SOCD_3, *EEE*/*ZZE* 33:67) δ (ppm) 90.4 (s, =*C*−C=O, (*ZZE*)), 94 (s, =*C*−C=O, (*EEE*)), 112.2, 116.4, 117.9 (q, *C*F_3, $^1J_{CF}$=289 Hz), 119.2, 120 (q, *C*F_3, $^1J_{CF}$=274.6 Hz), 122.8, 122.9, 123.6, 126.1, 127.1, 133.1, 133.2, 140.5, 149.4 (br d, =*C*−NH, (*EEE*)), 152.2 (s, =*C*−NH, (*ZZE*)), 166.92 (s, *C*O_2H), 167 (s, *C*O_2H), 179.4 (q, O=*C*−CF_3, $^2J_{CF}$=33.5 Hz), 179.5 (q, O=*C*−CF_3, $^2J_{CF}$=33.4 Hz); ^{19}F NMR (282.4 MHz, CD_3SOCD_3, *EEE*/*ZZE* 33:67) δ (ppm) −77.7 (s, 3F, CF_3 (*ZZE*), 67%), −77.9 (br s, 3F, CF_3 (*EEE*), 33%); IR (cm^{-1}, KBr) 3430 (CO_2H); MS FAB$^+$ *m*/*z* (%): 260 ($M+H^+$, 50), 259 (M^+, 20), 242 (M^+-H_2O, 50), 190 (M^+-CF_3, 20); HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_9F_3NO_3$ 260.0535, found 260.0539. Anal. Calcd for $C_{11}H_8F_3NO_3$: C, 50.98; H, 3.11; O, 18.52. Found: C, 50.99; H, 3.10; O, 18.56.

5.6. General procedure for the preparation of 1-(R^1-phenylimino)-3-(R-phenoxy)-3-perfluoroalkyl-prop-2-enes 5a−g

To a solution of 3-perfluoroalkyl-3-aryloxypropenals **3** (1 equiv) in anhydrous dichloromethane (5 mL/1 g of **3**) was added 1 equiv of the corresponding substituted aniline. The mixture was stirred at room temperature for 2 h. Molecular sieve (3 Å) was added when arylamines having electron-withdrawing substituents (R^1=NO_2, Cl) were put in reaction with **3**. At the end of the reaction, the reaction mixture was concentrated in vacuo. Petroleum ether was added to the resulting oil and the yellow mixture was cooled to 0 °C and the formed precipitate was immediately filtrated in a cooled Buchner funnel to afford **5** as a yellow amorphous solids. Synthesis of derivatives **5** could also be achieved as we reported in a previous publication.[32a]

*5.6.1. 1-Phenylimino-3-(phenoxy)-3-trifluoromethyl-prop-2-ene (**5a**).* Starting from 1.4 g (6.48 mmol) of **3b** and 0.6 g (6.48 mmol) of aniline, 1.79 g (6.15 mmol) of **5a** was obtained as yellow liquid (yield: 95%); ^1H NMR (300 MHz, C_6D_6, *EE* 100%) δ (ppm) 6.3 (d, $^3J_{HH}$=9 Hz, H_2), 6.8−7.5 (m, 10H), 8.8 (d, $^3J_{HH}$=9 Hz, H_1); ^{13}C NMR (100.6 MHz, C_6D_6, *EE* 100%) δ (ppm) 117.1, 117.5, 121.2, 121.3, 127.1, 127.5, 130.1, 131.5, 151.8 (q, C_3-CF_3, $^2J_{CF}$=29 Hz), 153.2, 153.8, 156.1 (q, *HC*=N (*EE*), $^4J_{C1F}$=5.7 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *EE* 100%) δ (ppm) 66.5 (s, 3F, CF_3); MS (*m*/*z*): 292 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{13}F_3NO$: 292.0949, found: 292.0952. Anal. Calcd for $C_{16}H_{12}F_3NO$: C, 65.98; H, 4.15; O, 5.49. Found: C, 65.98; H, 4.17; O, 5.54.

*5.6.2. 1-Phenylimino-3-(4-methoxyphenoxy)-3-trifluoromethyl-prop-2-ene (**5b**).* Starting from 1.1 g (4.47 mmol) of **3a** and 0.41 g (4.47 mmol) of aniline, 1.36 g (4.24 mmol) of **5b** was obtained as yellow liquid (yield: 95%); ^1H NMR (300 MHz, $CDCl_3$, *ZE*/*EE*: 74/26) δ (ppm) (*EE*): 3.8 (s, 3H, OMe), (*EE*): 6.1 (d, $^3J_{H1H2}$=9.3 Hz, 1H), 6.8−7.4 (m, 9 H, Ph−H), 8.4 (d, $^3J_{H1H2}$=9.3 Hz, 1H); (*ZE*): 6.8 (d, $^3J_{H1H2}$=9 Hz, 1H), 3.8−7.4 (m, 9 H, Ph−H), 8.2 (d, $^3J_{H1H2}$=9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, *ZE*/*EE* 74:26) δ (ppm) 55.5, 112.5, 114.2, 116.5, 119.6, 120.7, 121.9, 129.8, 136.7, 137.6, 145.1, 146.9 (q, C_3−CF_3, $^2J_{CF}$=25.7 Hz), 148.1, 151.5, 153.4 (q, *HC*=N (*EE*), $^4J_{C1F}$=5.9 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$, *ZE*/*EE* 74;26) δ (ppm) −66.2 (s, CF_3); MS (*m*/*z*): 322 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{17}H_{15}F_3NO_2$ 322.1055, found 322.1060. Anal. Calcd for $C_{17}H_{14}F_3NO_2$: C, 63.55; H, 4.39; O, 9.96. Found: C, 63.58; H, 4.40; O, 9.98.

*5.6.3. 1-Phenylimino-3-phenoxy-3-perfluoropentyl-prop-2-ene **5c**.* Starting from 1 g (2.4 mmol) of **3e** and 0.223 g (2.4 mmol) of aniline, 1.1 g (2.2 mmol) of **5c** was obtained as yellow liquid (yield: 94%); ^1H NMR (300 MHz, $CDCl_3$, *ZE*/*EE* 15:85) δ (ppm) (*EE*): 6.2 (d, $^3J_{H1H2}$=9 Hz, 1H), 7−7.5 (m, 10H), 8.5 (d, $^3J_{H1H2}$=9 Hz, 1H); (*ZE*): 6.9 (d, $^3J_{H1H2}$=8.9 Hz, 1H), 7−7.5 (m, 10H), 8.2 (d, $^3J_{H1H2}$=8.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, *ZE*/*EE* 15:85) δ (ppm) 115.1, 115.8, 120.8, 121, 123 (t, $^3J_{C2F}$=4.9 Hz, C_2, (*ZE*)), 126.4, 126.7, 127.4, 129.2, 129.3, 130.1, 130.5, 146.8 (t, C_3−CF_3, $^2J_{CF}$=25.8 Hz), 150.7, 151.4, 152.2 (t, C_3−CF_3, $^2J_{CF}$=27.3 Hz), 152.7, 153.2 (s, HC=N (*ZE*)), 154.6 (t, *HC*=N (*EE*), $^4J_{C1F}$=5.9 Hz), 157.7; ^{19}F NMR (282.4 MHz, $CDCl_3$, *ZE*/*EE* 15:85) δ (ppm) −80.8 (s, 3F), −111.7 (m, 2F, (*EE*), 85%), −114.9 (m, 2F, (*ZE*), 15%), −122.5 (m, 4F), −126.1 (s, 2F); MS (*m*/*z*): 492 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{13}F_{11}NO$ 492.0821, found 492.0822. Anal. Calcd for $C_{20}H_{12}F_{11}NO$: C, 48.89; H, 2.46; O, 3.26. Found: C, 48.90; H, 2.46; O, 3.28.

*5.6.4. 1-Phenylimino-3-(4-methoxyphenoxy)-3-perfluoropentyl-prop-2-ene **5d**.* Starting from 1.5 g (3.36 mmol) of **3d** and 0.31 g (3.36 mmol) of aniline, 1.66 g (3.19 mmol) of **5d** was obtained as yellow liquid (yield: 95%); ^1H NMR (300 MHz, $CDCl_3$, *ZE*/*EE* 75:25) δ (ppm) (*EE*): 3.8 (s, 3H, OMe), 6.2 (d, $^3J_{H1H2}$=9.3 Hz, 1H), 6.9−7.4 (m, 9H), 8.4 (d, $^3J_{H1H2}$=9.3 Hz, 1H); (*ZE*): 3.8 (s, 3H, OMe), 6.8 (d, $^3J_{H1H2}$=9 Hz, 1H), 6.9−7.4 (m, 9 H), 8.2 (d, $^3J_{H1H2}$=8.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, *ZE*/*EE* 75:25) δ (ppm) 55.6, 55.68, 114.5, 115.3, 115.5, 116.9, 117.3, 117.8, 122 (t, $^3J_{C2F}$=5 Hz, C_2, (*ZE*)), 122.9, 123, 126.1, 126.6, 127.1, 130.4, 131.5, 131.8, 146, 148.1 (t, C_3−CF_2, $^2J_{CF}$=25.5 Hz), 150.1, 151.1, 153 (t, C_3−CF_2, $^2J_{CF}$=25.8 Hz), 154.6 (s, HC=N (*ZE*)), 156 (t, *HC*=N (*EE*), $^4J_{C1F}$=5.9 Hz), 157.5. ^{19}F NMR (282.4 MHz, $CDCl_3$, *ZE*/*EE* 75:25) δ (ppm) −80.7 (s, 3F), −111.8 (m, 2F, (*EE*), 25%), −114.7 (m, 2F, (*ZE*), 75%), −122 (s, 2F), −122.5 (s, 2F), −126.1 (s, 2F); MS (*m*/*z*): 522 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{15}F_{11}NO_2$ 522.0927, found 522.0935. Anal. Calcd for $C_{21}H_{14}F_{11}NO_2$: C, 48.38; H, 2.71; O, 6.14. Found: C, 48.41; H, 2.72; O, 6.10.

*5.6.5. 1-(4-Methylphenylimino)-3-phenoxy-3-trifluoromethyl-prop-2-ene **5e**.* Starting from 1.1 g (5.09 mmol) of **3b** and 0.54 g (5.09 mmol) of 4-methylaniline, 1.39 g (4.58 mmol) of **5e** was obtained as yellow liquid (yield: 90%); ^1H NMR (300 MHz, $CDCl_3$, *ZE*/*EE* 62:38) δ (ppm) (*EE*): 2.4 (s, 3H, Me), 6.2 (d, $^3J_{H1H2}$=9.3 Hz, 1H), 6.7−7.3 (m, 9 H), 8.3 (d, $^3J_{H1H2}$=9.3 Hz, 1H); (*ZE*): 2.45 (s, 3H, Me), 6.5 (d, $^3J_{H1H2}$=8.9 Hz, 1H), 6.7−7.3 (m, 9 H), 8.1 (d, $^3J_{H1H2}$=8.9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, *ZE*/*EE* 62:38) δ (ppm) 17.7, 17.8, 114.4, 115.1, 115.4, 116.9, 117.2, 117.7, 122, 122.2, 126.1, 126.6, 126.7, 126.9, 130.4, 130.5, 131.5, 132.6, 145.9, 147.3 (q, C_3−CF_3, $^2J_{CF}$=25.5 Hz), 150.1, 151, 151.5, 153 (s, *HC*=N (*ZE*)), 154.6, 156 (q, *HC*=N (*EE*), $^4J_{C1F}$=5 Hz), 157.7; ^{19}F NMR (282.4 MHz, $CDCl_3$, *ZE*/*EE* 62:38) δ (ppm) −66.7 (m, 3F, (*EE*), 38%), −63.4 (m, 3F, (*ZE*), 62%); MS (*m*/*z*): 306 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{17}H_{15}F_3NO$ 306.1106, found 306.1112. Anal. Calcd for $C_{17}H_{14}F_3NO$: C, 66.88; H, 4.62; O, 5.24. Found: C, 66.90; H, 4.62; O, 5.22.

*5.6.6. 1-(4-Chlorophenylimino)-3-phenoxy-3-perfluoropentyl-prop-2-ene **5f**.* Starting from 1.6 g (3.84 mmol) of **3e** and 0.48 g (3.84 mmol) of 4-chloroaniline, 1.67 g (3.19 mmol) of **5f** was obtained as yellow liquid (yield: 83%); ^1H NMR (300 MHz, C_6D_6, *EE* 100%) δ (ppm) 6.2 (d, $^3J_{H1H2}$=9 Hz, H_2), 6.8−7.2 (m, 9 H), 8.8 (d,

$^3J_{H1H2}$=9 Hz, H_1); ^{13}C NMR (75.4 MHz, C_6D_6, *EE* 100%) δ (ppm) 117.1, 117.3, 121.7, 122, 127.2, 127.7, 130.7, 131.4, 151 (t, C_3–CF_2, $^2J_{CF}$=25.5 Hz), 152.9, 153.6, 155 (t, HC=N (*EE*), $^4J_{C1F}$=5.7 Hz); ^{19}F NMR (282.4 MHz, C_6D_6, *EE* 100%) δ (ppm) −80.7 (s, 3F), −111.4 (m, 2F, (*EE*)), −122.1 (s, 4F), −125.6 (s, 2F); MS (*m*/*z*): 526 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{12}ClF_{11}NO$ 526.0432, found 526.0440. Anal. Calcd for $C_{20}H_{11}ClF_{11}NO$: C, 45.69; H, 2.11; O, 3.04. Found: C, 45.75; H, 2.12; O, 3.08.

5.6.7. 1-(4-Nitrophenylimino)-3-phenoxy-3-perfluoropenthyl-prop-2-ene ***5g****.* Starting from 1.5 g (3.6 mmol) of **3e** and 0.49 g (3.6 mmol) of 4-nitroaniline, 1.35 g (2.52 mmol) of **5g** was obtained as yellow amorphous solid (yield: 70%); ^{1}H NMR (300 MHz, $CDCl_3$, *ZE*/*EE* 70:30) δ (ppm) (*EE*): 6.2 (d, $^3J_{H1H2}$=9.1 Hz, 1H), 6.9–7.3 (m, 9H), 8.5 (d, $^3J_{H1H2}$=9.1 Hz, 1H); (*ZE*): 6.8 (d, $^3J_{H1H2}$=9 Hz, 1H), 6.9–7.3 (m, 9H), 8.2 (d, $^3J_{H1H2}$=9 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, *ZE*/*EE* 70:30) δ (ppm) 112.2, 112.5, 114.5, 114.7, 115.6, 115.9, 117.2, 117.9, 120.1, 120.7, 121.5, 123.1, 123.3, 123.8, 130.1, 130.5, 136.7, 137.3, 146, 146.4 (q, C_3–CF_3, $^2J_{CF}$=24.3 Hz), 149, 151.9, 152.1, 153, 154.9 (s, HC=N (*ZE*)), 156.2 (q, HC=N (*EE*), $^4J_{C1F}$=5.1 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$, *ZE*/*EE*: 70/30) δ (ppm) −80.7 (s, 3F), −111.6 (m, 2F, (*EE*), 30%), −114.8 (m, 2F, (*ZE*), 70%), −122 (s, 2F), −122.4 (s, 2F), −126.1 (s, 2F); MS (*m*/*z*): 537 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{12}F_{11}N_2O_3$ 537.0672, found 537.0678. Anal. Calcd for $C_{20}H_{11}F_{11}N_2O_3$: C, 44.79; H, 2.07; O, 8.95. Found: C, 44.82; H, 2.07; O, 8.90.

5.7. Reactivity study of 5a–g: general procedure for the preparation of substituted 2-trifluoromethyl and 2-perfluoroalkylquinolines 6a–h

In a typical procedure, a mixture of the imino-enol-ether derivatives **5a**–**g** (1 equiv) and substituted arylamines (1 equiv) in dichloromethane (10 mL/1 g of **5**) was refluxed at 40 °C until disappearance of ^{19}F NMR signals corresponding to the starting products **5** (6–24 h). The reaction mixture was concentrated under reduced pressure to give brown oil. Chromatography on silica gel column (eluent: petroleum ether/ethyl acetate 98:2) left two yellow oils, which were precipitated from methanol/water to give pure samples of the corresponding substituted quinolines **6a**–**h** as amorphous white solids. Formation of the corresponding diazapentadiene intermediates was detected by mass spectrometry showing three different picks corresponding to the molecular mass $[M+H]^+$ of **7** after 2 h of heating.

5.7.1. Reaction of ***5a*** *with 4-methylaniline: synthesis of 2-trifluoromethylquinoline (****6a****) and 2-trifluoromethyl-6-methylquinoline (****6b****).* Starting with **5a** (1 g; 3.43 mmol) and 4-methylaniline (0.367 g; 3.43 mmol) in 10 mL of dichloromethane under reflux for 6 h, 75.8 mg of 2-trifluoromethylquinoline **6a** (14%) and 0.498 g of 2-trifluoromethyl-6-methylquinoline **6b** (86%) are obtained, total yield 80%.

5.7.2. Reaction of ***5b*** *with 4-methylaniline: synthesis of 2-trifluoromethylquinoline (****6a****) and 2-trifluoromethyl-6-methylquinoline (****6b****).* Starting with **5b** (1.1 g; 3.42 mmol) and 4-methylaniline (0.366 g; 3.42 mmol) in 10 mL of dichloromethane under reflux for 6 h, 81 mg of 2-trifluoromethylquinoline **6a** (15%) and 0.491 g of 2-trifluoromethyl-6-methylquinoline **6b** (85%) are obtained, total yield 80%.

5.7.2.1. 2-Trifluoromethylquinoline. See spectral description of (**6a**).

*5.7.2.2. 2-Trifluoromethyl-6-methylquinoline (****6b****).* 2-Trifluorometnqh_0009;thyl-6-methylquinoline (**6b**) also reported in our previous publication.[34b] ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 2.52 (s, 3H), 7.56 (d, *J*=8.6 Hz, 1H), 7.8 (m, 2H), 8.2 (d, *J*=8.6 Hz, 1H), 8.51 (d, *J*=8.5 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 21.65, 117.63 (q, CH, $^3J_{CF}$=2.2 Hz), 122.8 (q, CF_3, $^1J_{CF}$=273.9 Hz), 127.6, 130, 130.2, 134.2, 138.8, 140, 146.6, 147.4 (q, C–CF_3, $^2J_{CF}$=34.7 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −67.8 (s, 3F); MS (*m*/*z*): 212 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_9F_3N$: 212.0687, found: 212.0607. Anal. Calcd for $C_{11}H_8F_3N$: C, 62.56; H, 3.82; N, 6.63. Found: C, 62.45; H, 3.76; N, 6.68.

5.7.3. Reaction of ***5c*** *with 4-methylaniline: synthesis of 2-perfluoropentylquinoline (****6c****) and 2-perfluoropentyl-6-methylquinoline (****6d****).* Starting with **5c** (1 g; 2.03 mmol) and 4-methylaniline (0.217 g; 2.03 mmol) in 10 mL of dichloromethane under reflux for 6 h, 0.1 g of 2-perfluoropentylquinoline **6c** (15%) and 0.58 g of 2-perfluoropentyl-6-methylquinoline **6d** (85%) are obtained, total yield 82%.

5.7.4. Reaction of ***5d*** *with 4-methylaniline: synthesis of 2-perfluoropentylquinoline (****6c****) and 2-perfluoropentyl-6-methylquinoline (****6d****).* Starting with **5d** (1 g; 1.91 mmol) and 4-methylaniline (0.205 g; 1.91 mmol) in 10 mL of dichloromethane under reflux for 6 h, 91.4 mg of 2-perfluoropentylquinoline **6c** (15%) and 0.53 g 2-perfluoropentyl-6-methylquinoline **6d** (85%) are obtained, total yield 80%.

*5.7.4.1. 2-Perfluoropentylquinoline (****6c****).* ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.6 (t, J_{HH}=7.8 Hz, 1H), 7.65 (d, J_{HH}=8.5 Hz, 1H), 7.75 (t, J_{HH}=8.3 Hz, 1H), 7.8 (d, J_{HH}=8.3 Hz, 1H), 8.15 (d, J_{HH}=8.5 Hz, 1H), 8.25 (d, J_{HH}=8.5 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 117.2 (t, CH, $^3J_{CF}$=3.8 Hz), 126.6, 127.6, 127.7, 129.3, 129.7, 136.6, 146.3, 146.7 (t, C–CF_2, $^2J_{CF}$=25.2 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ (ppm) −81.3 (t, J_{FF}=7.8 Hz, 3F, CF_3), −114.3 (t, J_{FF}=13.1 Hz, 2F, CF_2), −122 (m, 2F, CF_2), −122.8 (m, 2F, CF_2), −126.5 (m, 2F, CF_2). MS (*m*/*z*): 398 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{14}H_7F_{11}N$ 398.0403, found 398.0400. Anal. Calcd for $C_{14}H_6F_{11}N$: C, 42.34; H, 1.52; N, 3.53. Found: C, 42.36; H, 1.51; N, 3.50.

*5.7.4.2. 2-Perfluoropentyl-6-methylquinoline (****6d****).* ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.5 (s, 3H), 7.4 (d, *J*=8.5 Hz, 1H), 7.7 (m, 2H), 8.1 (d, *J*=8.6 Hz, 1H), 8.5 (d, *J*=8.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.5, 117.5, 126.5, 130.5, 130.7, 135.2, 138.7, 139.8, 146.3, 147.7 (t, C–CF_2, $^2J_{CF}$=26.1 Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ (ppm) −81.3 (m, 3F, CF_3), −114.4 (m, 2F, CF_2), −122 (m, 2F, CF_2), −122.5 (m, 2F, CF_2), −126.5 (m, 2F, CF_2). MS (*m*/*z*): 412 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{15}H_9F_{11}N$ 412.0559, found 412.0565. Anal. Calcd for $C_{15}H_8F_{11}N$: C, 43.81; H, 1.96; N, 3.41. Found: C, 43.84; H, 1.98; N, 3.40.

5.7.5. Reaction of ***5a*** *with 2-methylaniline: synthesis of 2-trifluoromethylquinoline (****6a****) and 2-trifluoromethyl-8-methylquinoline (****6e****).* Starting with **5a** (1.1 g; 3.78 mmol) and 2-methylaniline (0.404 g; 3.78 mmol) in 10 mL of dichloromethane under reflux for 6 h, 0.189 g of 2-trifluoromethylquinoline **6a** (30%) and 0.47 g of 2-trifluoromethyl-8-methylquinoline **6e** (70%) are obtained, total yield 85%.

5.7.5.1. 2-Trifluoromethylquinoline. 2-Trifluoromethylquinoline see spectral description of (**6a**) and data also reported in our previous publication.[34b]

*5.7.5.2. 2-Trifluoromethyl-8-methylquinoline (****6e****).* 2-Trifluorometnqh_0009;thyl-8-methylquinoline (**6e**) also reported in our previous publication.[34b] ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 2.8 (s, 3H), 7.65 (m, 1H), 7.75 (d, *J*=6.8 Hz, 1H), 7.92 (m, 2H), 8.61 (d, *J*=8.5 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 17.6, 117.3 (q, CH, $^3J_{CF}$=2.1 Hz), 122.8 (q, CF_3, $^1J_{CF}$=274.2 Hz), 126.8, 129.5, 130, 131.8,

138.6, 139.8, 146.9, 147.1 (q, C–CF_3, $^2J_{CF}$=29 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −67.8 (s, 3F). MS (*m*/*z*): 212 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_9F_3N$: 212.0687, found: 212.0684. Anal. Calcd for $C_{11}H_8F_3N$: C, 62.56; H, 3.82; N, 6.63. Found: C, 62.45; H, 3.74; N, 6.61.

*5.7.6. Reaction of **5a** with 4-nitroaniline: synthesis of 2-trifluoromethylquinoline (**6a**) and 2-trifluoromethyl-6-nitroquinoline (**6f**).* Starting with **5a** (1 g; 3.43 mmol) and 4-nitroaniline (0.474 g; 3.43 mmol) in 10 mL of dichloromethane under reflux for 12 h, 0.456 g of 2-trifluoromethylquinoline **6a** (90%) and 62.37 mg of 2-trifluoromethyl-6-nitroquinoline **6f** (10%) are obtained, total yield 75%.

5.7.6.1. 2-Trifluoromethylquinoline. see spectral description of (**6a**) and data also reported in our previous publication.[34b]

*5.7.6.2. 2-Trifluoromethyl-6-nitroquinoline (**6f**).* 2-Trifluorometnqh_0009;thyl-6-nitroquinoline (**6f**) also reported in our previous publication.[34b] ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 8.2 (d, *J*=8.6 Hz, 1H), 8.4 (d, *J*=9.3 Hz, 1H), 8.6 (dd, *J*=2.5 and 9.3 Hz, 1H), 9.1 (d, *J*=8.6 Hz, 1H) 9.19 (d, *J*=2.5 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 119.5 (q, CH, $^3J_{CF}$=2.2 Hz), 122 (q, CF_3, $^1J_{CF}$=275.4 Hz), 127.5, 130.1, 132, 132.8, 134.5, 140.1, 145.2, 148 (q, C–CF_3, $^2J_{CF}$=34 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −68.5 (s, 3F). MS (*m*/*z*): 243 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{10}H_6F_3N_2O_2$: 243.0381, found: 243.0408. Anal. Calcd for $C_{10}H_5F_3N_2O_2$: C, 49.60; H, 2.08; N, 11.57. Found: C, 49.74; H, 2.12; N, 11.69.

*5.7.7. Reaction of **5e** with 2-methylaniline: synthesis of 2-trifluoromethyl-6-methylquinoline (**6b**) and 2-trifluoromethyl-8-methylquinoline (**6e**).* Starting with **5e** (1.5 g; 4.91 mmol) and 2-methylaniline (0.526 g; 4.91 mmol) in 15 mL of dichloromethane under reflux for 6 h, 0.532 g of 2-trifluoromethyl-6-methylquinoline **6b** (57%) and 0.4 g of 2-trifluoromethyl-8-methylquinoline **6e** (43%) are obtained, total yield 90%.

5.7.7.1. 2-Trifluoromethyl-6-methylquinoline and 2-trifluorometnqh_0009;thyl-8-methylquinoline. See spectral descriptions of **6b** and **6e** and data also reported in our previous publication.[34b]

*5.7.8. Reaction of **5e** with 4-nitroaniline: synthesis of 2-trifluoromethyl-6-methylquinoline (**6b**) and 2-trifluoromethyl-6-nitroquinoline (**6f**).* Starting with **5e** (1.6 g; 5.24 mmol) and 4-nitroaniline (0.723 g; 5.24 mmol) in 15 mL of dichloromethane under reflux for 12 h, 0.967 g of 2-trifluoromethyl-6-methylquinoline **6b** (95%) and 58.39 mg of 2-trifluoromethyl-6-nitroquinoline **6f** (5%) are obtained, total yield 92%.

5.7.8.1. 2-Trifluoromethyl-6-methylquinoline and 2-trifluorometnqh_0009;thyl-6-nitroquinoline. See spectral descriptions of **6b** and **6f** and data also reported in our previous publication.[34b]

*5.7.9. Reaction of **5f** with 4-methylaniline: synthesis of 2-perfluoropentyl-6-methylquinoline (**6d**) and 2- perfluoropentyl-6-chloroquinoline (**6g**).* Starting with **5f** (1 g; 1.90 mmol) and 4-nitroaniline (0.262 g; 1.90 mmol) in 10 mL of dichloromethane under reflux for 6 h, 0.184 g of 2-perfluoropentyl-6-chloroquinoline **6g** (25%) and 0.528 g of 2-perfluoropentyl-6-methylquinoline **6d** (75%) are obtained, total yield 90%.

5.7.9.1. 2-Perfluoropentyl-6-methylquinoline. See spectral description of (**6d**).

*5.7.9.2. 2-Perfluoropentyl-6-chloroquinoline (**6g**).* 2-Perfluorotnqh_0009;pentyl-6-chloroquinoline (**6g**) in acetone-d_6 also reported in our previous publication.[34b] ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 7.4 (d, *J*=9 Hz, 1H), 7.6 (d, *J*=8.5 Hz, 1H), 7.7 (d, *J*=9 Hz, 1H), 7.9 (s, 1H) 8.2 (d, *J*=8.6 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 118.5, 122.5, 127, 132.7, 133.1, 134.1, 140.5, 145.5, 147.9 (t, C–CF_2, $^2J_{CF}$=26 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −81.5 (m, 3F, CF_3), −114.2 (m, 2F, CF_2), −122 (m, 2F, CF_2), −122.5 (m, 2F, CF_2), −126 (m, 2F, CF_2). MS (*m*/*z*): 432 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{14}H_6ClF_{11}N$: 432.0013, found: 432.0020. Anal. Calcd for $C_{14}H_5ClF_{11}N$: C, 38.96; H, 1.17; N, 3.25. Found: C, 38.99; H, 1.17; N, 3.22.

*5.7.10. Reaction of **5g** with 4-methylaniline: synthesis of 2-perfluoropentyl-6-methylquinoline (**6d**) and 2-perfluoropentyl-6-nitroquinoline (**6h**).* Starting with **5g** (1.5 g; 2.79 mmol) and 4-methylaniline (0.299 g; 2.79 mmol) in 15 mL of dichloromethane under reflux for 6 h, 55.6 mg of 2-perfluoropentyl-6-nitroquinoline **6h** (5%) and 0.983 g 2-perfluoropentyl-6-methylquinoline **6d** (95%) are obtained, total yield 90%.

5.7.10.1. 2-Perfluoropentyl-6-methylquinoline. See spectral description of (**6d**).

*5.7.10.2. 2-Perfluoropenthyl-6-nitroquinoline (**6h**).* 2-Perfluorotnqh_0009;penthyl-6-nitroquinoline (**6h**) also reported in our previous publication.[34b] ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 8.2 (d, *J*=8.5 Hz, 1H), 8.4 (d, *J*=9 Hz, 1H), 8.6 (dd, *J*=2.1 and 9 Hz, 1H), 9 (d, *J*=8.5 Hz, 1H) 9.1 (d, *J*=2 Hz, 1H); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ (ppm) 120.1, 127.1, 130.1, 132.5, 132.8, 134.2, 141.5, 145.2, 148.5 (t, C–CF_2, $^2J_{CF}$=27.7 Hz); ^{19}F NMR (282.4 MHz, CD_3COCD_3) δ (ppm) −81 (m, 3F), −114 (m, 2F), −122.5 (m, 4F), −126.5 (m, 2F). MS (*m*/*z*): 443 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{14}H_6F_{11}N_2O_2$: 443.0254, found: 443.0264. Anal. Calcd for $C_{14}H_5F_{11}N_2O_2$: C, 38.03; H, 1.14; N, 6.34. Found: C, 38.08; H, 1.15; N, 6.35.

5.8. Synthesis and isolation of unsymmetrically substituted: 2-perfluoropentyl-*N*-phenyl,*N*′-(4-methylphenyl)-1,5-diazapentadiene (7d) and 2-perfluoropentyl-*N*-(4-methylphenyl),*N*′-phenyl-1,5-diazapentadiene (7e) (Scheme 8, Table 3).

A mixture of 5.5 g (11.2 mmol) of **5c** (1 equiv) and 1.19 g (11.2 mmol) of 4-methylaniline (1 equiv) in 110 mL of dichloromethane (20 mL/1 g of **5**) was refluxed at 40 °C. The evolution of the reaction was controlled by ^{19}F NMR spectroscopy and by CCM. After 1 h and a half, heating was stopped and the reaction mixture was diluted with dichloromethane and washed 5× with water. The organic layers were concentrated under reduced pressure to give yellow oil. Excess of petroleum ether was added and the yellow precipitate which had formed was filtered. ^{19}F NMR analysis of this precipitate showed the presence of a mixture of three different diazapentadienes. Chromatography on silica gel column (eluent: petroleum ether/ethyl acetate 95:5) permitted to separate three yellow amorphous solids corresponding to the corresponding symmetrically and unsymmetrically substituted **7c**, **7d**, and **7e** and unsubstituted diazapentadienes **7b** (22% of the formed products). Then the organic filtrate was concentrated giving a yellow liquid. Chromatography on silica gel column (eluent: petroleum ether/ethyl acetate 90:10) gave two enaminoketones **4c** and **4p** as amorphous yellow solids (26% of the formed products) and the corresponding quinolines **6c** and **6d** as white amorphous solids (22% of the formed products). Finally the unreacted starting product **5c** was recovered (1.15 g, 30% of the reaction mixture).

*5.8.1. 2-Perfluoropentyl-N,N′-diphenyl-1,5-diazapentadiene (**7b**).* 2-Perfluoropentyl-*N*,*N*′-diphenyl-1,5-diazapentadiene (**7b**) was

also reported in our previous publication.[32a] Yellow solid, 0.15 g (yield 4%); ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 5.5 (d, $^3J_{H2H3}$=13.7 Hz, H_2), 6.8 (t, J=8.7 Hz, 3H), 6.9 (t, J=7.4 Hz, 1H), 7.1 (t, J=7.4 Hz, 1H), 7.2 (t, J=8.1 Hz, 2H), 7.4 (t, J=7.8 Hz, 3H), 7.45 (m, 1H, H_3), 9.9 (d, $^3J_{H3NH}$=12.4 Hz, N*H*); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ (ppm) 91.4, 114.9, 118.4, 122.3, 123.6, 129.4, 129.5, 129.6, 140.5, 141.5 (t, C_3H, $^4J_{C3F}$=5.5 Hz), 149.9, 153.5 (t, C–CF_3, $^2J_{C1F}$=22.6 Hz); ^{19}F NMR (282.4 MHz, DMSO-d_6) δ (ppm) −80.2 (s, 3F), −109.6 (t, J=11.2 Hz, 2F), −120.4 (s, 2F), −121 (s, 2F), −125.8 (s, 2F); MS (*m*/*z*): 491 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{14}F_{11}N_2$ 491.0981, found 491.0983. Anal. Calcd for $C_{20}H_{13}F_{11}N_2$: C, 48.99; H, 2.67; N, 5.71. Found: C, 48.97; H, 2.66; N, 5.73.

*5.8.2. 2-Perfluoropentyl-N,N′-di-(4-methylphenyl)-1,5-diazapentadiene (**7c**).* Yellow solid, 0.56 g (yield 14%); ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.2 (s, 3H), 2.3 (s, 3H), 5.5 (d, J=13.6 Hz, 1H), 6.6 (d, J=8.1 Hz, 2H), 6.8 (d, J=8.2 Hz, 2H), 7 (d, J=8.2 Hz, 2H), 7.2 (d, J=8.1 Hz, 2H), 7.6 (t, J=12.8 Hz, 1H), 9.8 (br d, J=12.6 Hz, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ (ppm) 20, 20.2, 90.6, 115.2, 118.9, 129.5, 129.7, 129.8, 131, 131.1, 132.5, 138.1, 142.8 (t, CH, $^3J_{CF}$=3 Hz), 147.7, 153.1 (t, C–CF_2, $^2J_{CF}$=27.8 Hz); ^{19}F NMR (282.4 MHz, DMSO-d_6) δ (ppm) −80 (s, 3F), −109.8 (s, 2F), −120.5 (s, 2F), −121 (s, 2F), −125 (s, 2F); MS (*m*/*z*): 519 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{18}F_{11}N_2$: 519.1294, found: 519.1299. Anal. Calcd for $C_{22}H_{17}F_{11}N_2$: C, 50.97; H, 3.31; N, 5.40. Found: C, 50.99; H, 3.30; N, 5.38.

*5.8.3. 2-Perfluoropentyl-N-phenyl,N′-(4-methylphenyl)-1,5-diazapentadiene (**7d**) and 2-perfluoropentyl-N-(4-methylphenyl),N′-phenyl-1,5-diazapentadiene (**7e**).* Yellow solid, 0.15 g (yield 4%); ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.2 (3H, CH_3), 2.3 (3H, CH_3), 5.5 (dt, J=13.4 Hz and 4.4 Hz, 2H), 6.6–7.4 (m, 18 H), 7.5 (m, 2H), 9.8 (m, 2H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ (ppm) 20.1, 20.12, 90.9, 91.5, 114.8, 118.4, 121.9, 122, 123, 123.4, 129.4, 129.5, 129.8, 129.9, 131.1, 131.2, 132.5, 132.6, 138.2, 140.6, 141 (t, CH, $^3J_{CF}$=1 Hz), 141.4, 141.7, 147.5, 147.6, 150, 150.2, 153.6 (t, C–CF_2, $^2J_{CF}$=22 Hz); ^{19}F NMR (282.4 MHz, DMSO-d_6) δ (ppm) −80.5 (m, 3F), −80.8 (m, 3F), −109.7 (m, 4F), −120.5 (m, 4F), −121.2 (m, 4F), −126 (m, 2F), −126.2 (m, 2F); MS (*m*/*z*): 505 $[M+H]^+$: HRMS *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{16}F_{11}N_2$: 505.1138, found: 505.1145. Anal. Calcd for $C_{21}H_{15}F_{11}N_2$: C, 50.01; H, 3.00; N, 5.55. Found: C, 50.04; H, 3.01; N, 5.57.

*5.8.4. 1-Perfluoropenthyl-3-(phenylamino)prop-2-en-1-one (**4c**).* Yellow solid, 0.13 g (yield 4%); ^{1}H NMR (400 MHz, C_6D_6), *ZZE* 100%: δ (ppm) 5.7 (d, $^3J_{H2H3}$=7.1 Hz, 1H, H-2), 6.6 (d, 2H, J=8 Hz, Ph–H), 6.9 (dd, $^3J_{H2H3}$=7.4 Hz and $^3J_{H3NH}$=13 Hz, 1H, H-3), 7.1–7.2 (m, 3H, Ph–H), 12.1 (br d, 1H, NH); ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 91.4 (s, =*C*–C=O), 117.4, 125.5, 129.8, 138.8, 149.1 (s, =*C*––NH), 180.4 (t, O=*C*–CF_2, $^2J_{CF}$=24.8 Hz); ^{19}F NMR (282.4 MHz, C_6D_6) δ (ppm) −81 (m, 3F), −120.3 (m, 2F, *ZZE*), −122.5 (m, 4F), −126.5 (m, 2F); MS FAB$^+$ *m*/*z* (%): 416 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{14}H_9F_{11}NO$ 416.0508, found 416.0490. Anal. Calcd for $C_{14}H_8F_{11}NO$: C, 40.50; H, 1.94; O, 3.85. Found: C, 40.48; H, 1.95; O, 3.86.

*5.8.5. 1-Perfluoropentyl-3-(4-methylphenylamino)prop-2-en-1-one (**4p**).* Yellow solid, 0.74 g (yield 22%); ^{1}H NMR (400 MHz, C_6D_6), *ZZE* 100%: δ (ppm) 2.1 (s, 3H), 5.6 (d, $^3J_{H2H3}$=7 Hz, 1H, H-2), 6.6 (dd, $^3J_{H2H3}$=7.1 Hz and $^3J_{H3NH}$=12.2 Hz, 1H, H-3), 6.8–7.3 (m, 4H, Ph–H), 11.8 (br d, 1H, NH); ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 16.6, 91.4 (s, =*C*–C=O), 117.5, 125.5, 127.2, 128.1, 132.1, 138, 148.9 (s, =*C*–NH), 180 (t, O=*C*–CF_3, $^2J_{CF}$=24.1 Hz); ^{19}F NMR (282.4 MHz, C_6D_6) δ (ppm) −81.2 (m, 3F), −120.4 (m, 2F), −122.5 (m, 4F), −126 (m, 2F); MS FAB$^+$ *m*/*z*: 430 $[M+H]^+$; HRMS *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO$ 430.0665, found 430.0670. Anal. Calcd for $C_{11}H_{10}F_3NO$: C, 41.97; H, 2.35; O, 3.73. Found: C, 41.99; H, 2.38; O, 3.75.

5.8.6. 2-Perfluoropentylquinoline. White solid, 0.124 g (yield 4%); see spectral description of **6c**.

5.8.7. 2-Perfluoropentyl-6-methylquinoline. White solid, 0.58 g (yield 18%); see spectral description of **6d**.

5.9. Reaction of 4a–o with $POCl_3$, general procedure for the preparation of substituted 2-trifluoromethyl and 2-perfluoroal-tnqh_0009;kylquinolines 6 and isolation of the corresponding diazapentadiene intermediates 7

In a typical procedure, enaminones **4** were heated in excess of $POCl_3$ at 100 °C for 12 h until complete consumption of the starting material as judged by TLC and ^{19}F NMR spectroscopy (see ^{19}F NMR spectra of the reaction mixture in Supplementary data). The resulting brown dark mixture was stirred at room temperature then cooled using an ice bath. Water was added slowly. To the resulting mixture was added dichloromethane and then washed three times with a solution of 2% sodium hydrogenocarbonate. The organic layers were then dried over sodium sulfate and concentrated in vacuo. Chromatography on silica gel column (eluent: petroleum ether/ethyl acetate: 98:2) left yellow oil, which was crystallized from methanol/water to give pure samples of the corresponding substituted quinolines **6** (yield 65–80%).

*5.9.1. Isolation of diazapentadiene **7** intermediates.* 10–20 min of reaction at 100 °C was sufficient to identify and isolate the diazapentadiene intermediate **7** (as judged by TLC and ^{19}F NMR spectroscopy: see ^{19}F NMR spectra of the reaction mixture in Supplementary data). The brown mixture was stirred at room temperature then cooled using an ice bath. Water was added slowly. The resulting mixture was diluted with dichloromethane and washed with a solution of 2% sodium hydrogenocarbonate. The organic layers were then dried over sodium sulfate and concentrated in vacuo. Chromatography on silica gel column (eluent: petroleum ether/ethyl acetate 98;2) left yellow solid of **7** (yield 40–62%).

Spectral data of the obtained 2-perfluoroalkyl and 2-trifluoromethylquinolines or 2-perfluoroalkyl **6a**–**h** and 2-trifluoromethyl-*N*,*N*′-diaryl-1,5-diazapentadienes **7** are described in sections before or in previous publications.[32,34]

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Supplementary data

Copies of ^{1}H, ^{13}C, COSY ^{1}H–^{1}H, HMQC ^{13}C–^{1}H, ^{19}F NMR and IR spectra of **4a**–**o**, **5a**–**g**, **6a**–**h** and **7**. Copies of ^{19}F NMR spectra of reaction evolution of **4c** with $POCl_3$ and **5c** with 4-methylaniline.

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.12.073.

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