Tetrahedron 65 (2009) 6991–7000

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Selective synthesis of α-trifluoromethyl-β-aryl enamines or vinylogous guanidinium salts by treatment of β-halo-β-trifluoromethylstyrenes with secondary amines under different conditions

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ARTICLE INFO

Article history:
Received 7 April 2009
Received in revised form 5 June 2009
Accepted 12 June 2009
Available online 18 June 2009

Keywords:
Defluorination
β-Halo-β-trifluoromethylstyrenes
Secondary amines
Vinylic nucleophilic substitution
α-Trifluoromethyl-β-aryl enamines
Vinylogous guanidinium salts

ABSTRACT

Unprecedented selective reactions of β-halo-β-trifluoromethylstyrenes with secondary amines under different conditions were discovered. Depending on the electronic properties of the starting styrenes and the reaction parameters, two pathways were found. With neat secondary amines a series of α-trifluoromethyl-β-aryl enamines were prepared in high yields. In contrast, the reactions of the mentioned styrenes with the same amines in polar solvents by substitution of all halogen atoms gave vinylogous guanidinium salts. Possible reaction mechanisms are discussed.

1. Introduction

Organofluorine compounds were intensively investigated in recent decades.[1] The remarkable interest on these compounds is due to their unique physical and biological properties caused by the presence of fluorine substituents in the molecules.[2] Numerous publications were dedicated to the elaboration of new synthetic approaches to fluorine-containing organic compounds, which resulted in an enormous progress in this field.[3]

Recently, a new catalytic olefination reaction of aldehydes and ketones was discovered by our research group.[4] This reaction was found to be a new general approach to construct carbon–carbon double bonds. A number of convenient and simple methods for the synthesis of various alkenes including fluorinated ones were developed using that reaction.[5] Also, the ease of β-halogen atom substitution by *C*-, *S*- and *O*-nucleophiles in β-chloro- and β-bromo-β-(trifluoromethyl)styrenes or β-bromo-β-fluorostyrenes was demonstrated in a series of publications. Treatment of these compounds with copper cyanide, sodium 4-methylphenylsulfinate, alkylthiolates, arylthiolates and alkoxides resulted in a number of novel convenient approaches to α-fluoro- and α-trifluoromethylacrylonitriles,[6] α-fluoro-β-arylvinyl sulfones,[7] trifluoromethyl(vinylsulfides),[8] and alkoxy-β-(trifluoromethyl)styrenes.[9]

Having such encouraging results, we decided to continue our investigations on the synthetic utility of β-halo-β-(trifluoromethyl)styrenes examining their reactions with *N*-nucleophiles. Initially, secondary amines were chosen since the substitution of the β-halogen atom might lead to 1-trifluoromethyl-2-aryl enamines. Such compounds have been shown to be promising building blocks for the synthesis of various new fluorine-containing compounds and natural product analogues.[10] Several methods for the preparation of such enamines have been described in the literature already. Most important among them are the Wittig reaction with trifluoroacetamides,[11,12] the reaction of amines with perfluoroalkylketones,[13] the addition of amines to trifluromethyl-

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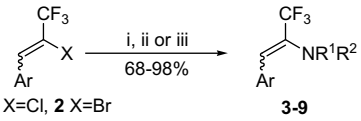
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.06.048

acetylenes,[10c] the direct trifluoromethylation of pyrrolidinones[10d] and nucleophilic substitutions of trifluoromethylated vinyl halides. The latter method itself provides one of the most general pathways towards capto-dative alkenes, especially for systems bearing halogen or another leaving group in *gem*-position to a strong electron-withdrawing substituent.[14] Accordingly, 1-perfluoroalkyl enamines were prepared by substitution of fluorine in fluorostyrenes using lithium alkylamides.[15] Generally, this reaction is not stereoselective and formation of two regioisomers was observed in many cases. Nevertheless, in some particular alkenes nucleophilic substitution of the vinylic leaving group with lithium alkylamides proceeded regio- and stereoselectively. Substitution of an ethoxy group in β-ethoxy-β-trifluoromethylstyrenes[10g] and of the chlorine atom in β-chloro-β-trifluoromethylstyrenes[16] by treatment with two equivalents of lithium alkylamides gave the corresponding enamines in high yields as single regio- and stereoisomers. We considered, that β-bromostyrenes would be more reactive than β-chlorostyrene. Furthermore, electron withdrawing groups in the aromatic ring should increase the reactivity and the corresponding enamines might be available under milder conditions without application of organometallic reagents.

2. Results and discussion

Initially, we investigated the most reactive styrene **1a**, bearing a nitro group in *para*-position of the aryl ring. The reaction of an 88:12 *Z*/*E*-mixture of **1a** with excess of pyrrolidine without solvent proceeded very fast accompanied by remarkable heat evolution. The starting material was consumed within a minute and the desired enamine **3a** was obtained regio- and stereoselectively as pure *Z*-isomer in almost quantitative yield (Scheme 1, Table 1).



Scheme 1. Reactions of β-chloro- and β-bromo-β-trifluoromethylstyrenes **1** and **2** with pyrrolidine. *Conditions*: (i) 10 equiv HNR^1R^2, rt (**3a**–**3h**); (ii) 10 equiv HNR^1R^2, heating in a sealed tube (**4a**, **5**–**8**); (iii) 7.5 equiv HNR^1R^2, EtOH, reflux (**3a**, **9**).

In case of less active secondary amines the reactions proceeded much slower under the same conditions. For example, piperidine gave the corresponding enamine **4a** only after 3 days of standing at room temperature. Nevertheless, the reactions with less reactive secondary amines were successfully performed at heating, giving the desired enamines **4a** and **5**–**8** as single regioisomers in high yields (Table 1). However, the reaction was found to be less stereoselective and the enamines **4a** and **5**–**8** were isolated as *Z*/*E*-mixtures (70:30 to 95:5).

The synthetic scope and limitations of the method were investigated using the most reactive secondary amine, pyrrolidine, as a model in reactions with a series of styrenes, containing either electron-withdrawing or electron-donating substituents in the aryl ring. The reactions of the styrenes **1** and **2** bearing electron-withdrawing groups proceeded smoothly and within minutes at room temperature giving the desired enamines **3** regio- and stereoselectively in high yields. Although the styrenes **1** and **2** were used as mixtures of *Z*/*E*-isomers (see Table 1 and Refs. 5b and e), the corresponding enamines **3** were generally obtained as single *Z*-isomers. Only in case of the enamines **3f** and **3h** with *ortho*-substituents admixture of the *E*-isomer was found. The *Z*/*E*-ratio was 92:8 and 88:12, respectively. The configuration of the 1-trifluoromethyl enamines was determined spectroscopically. The proton decoupled ^{13}C NMR spectra of compounds **3** were recorded and the spin–spin coupling constants $^3J_{H,C}$ between the trifluoromethyl carbon atom and the proton at the double bond were determined to range between 4.4 and 4.7 Hz. Consequently, this proton and the trifluoromethyl group are in *cis*-position and the compounds have *Z*-configuration.[17] Configurations of both *Z*- and *E*-isomers of compound **3h** were confirmed unambiguously by NOESY experiments (Fig. 1). Additionally, ^1H and ^{13}C spectra of compound **3c** are in good agreement with literature data for the previously described *Z*-isomer.[10g]

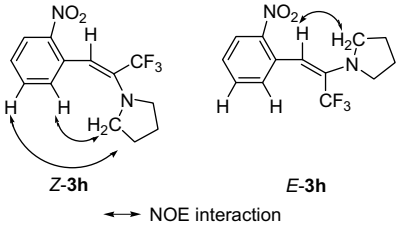


Figure 1. Configurations of *Z*- and *E*-isomers of compound **3h** according to NOESY.

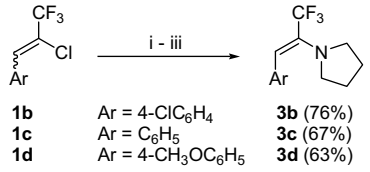
We found that the nature of the halogen atom is not important in case of styrenes with electron-withdrawing groups such as nitro and methoxycarbonyl functions. High yields of enamines were observed starting either from chloro-**1a**, **1g** and **1h** or bromostyrenes **2e**. In case of less electron withdrawing halogen substituents in the aromatic ring the yields dropped dramatically from bromo to chlorostyrenes (**1b** and **2b**). For the unsubstituted or the 4-methoxy styrenes **2c** and **2d**, the reaction rate decreased significantly and only traces of the desired enamines **3c** and **3d** were observed

Table 1
Synthesis of α-trifluoromethyl-β-aryl enamines **3**–**9**

Styrene	*Z*/*E* ratio[a]	Ar	R^1–R^2	*T* (°C)	Enamine	*Z*/*E* ratio[a]	Yield (%)
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_4-$	rt	**3a**	100:0	95
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_4-$	Reflux[b]	**3a**	96:4	69[b]
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_5-$	85	**4a**	83:17	89
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_6-$	125	**5**	96:4	78
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_2O(CH_2)_2-$	125	**6**	71:29	84
1a	88:12	4-$NO_2C_6H_4$	$-(CH_2)_2NH(CH_2)_2-$	125	**7**	95:5	92
1a	88:12	4-$NO_2C_6H_4$	Et	85	**8**	88:12	82
1b	75:25	4-ClC_6H_4	$-(CH_2)_4-$	rt	**3b**	100:0	31
2b	89:11	4-ClC_6H_4	$-(CH_2)_4-$	rt	**3b**	100:0	68
2c	86:14	Ph	$-(CH_2)_4-$	rt	**3c**	—	Traces
2d	89:11	4-$MeOC_6H_4$	$-(CH_2)_4-$	rt	**3d**	—	Traces
2e	83:17	4-$MeCO_2C_6H_4$	$-(CH_2)_4-$	rt	**3e**	100:0	85
2f	66:34	2-BrC_6H_4	$-(CH_2)_4-$	rt	**3f**	92:8	75
1g	75:25	3-$NO_2C_6H_4$	$-(CH_2)_4-$	rt	**3g**	100:0	78
1h	83:17	2-$NO_2C_6H_4$	$-(CH_2)_4-$	rt	**3h**	88:12	98
1h	83:17	2-$NO_2C_6H_4$	*n*-Pr	Reflux[b]	**9**	92:8	53[b]

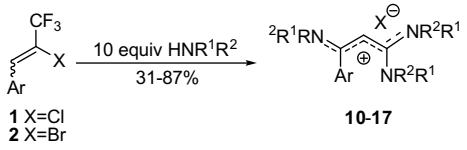
[a] Determined by ^1H NMR spectroscopy.
[b] The reactions were carried out in ethanol.

within complex mixtures of other products. However, the *Z*-configurated enamines **3b**–**3d** were synthesized in high yields by reaction of the styrenes **1b**–**1d** with two equivalents of lithiated pyrrolidine (Scheme 2).



Scheme 2. Reactions of β-chloro-β-trifluoromethylstyrenes **1** with lithium pyrrolidide. *Conditions*: (i) 2 equiv pyrrolidine, 2.2 equiv BuLi, THF, −78 °C; (ii) −78 °C to 0 °C, 2 h; (iii) NH_4Cl.

Unexpected results were obtained when the reactions of styrenes **1** and **2** with secondary amines were performed in polar solvents. The most reactive styrene **1a** showed dramatic drop of the reaction rate with pyrrolidine in dry ethanol giving acceptable yield of **3a** only at reflux (Table 1, line 2). This might be attributed to the formation of hydrogen bonds between ethanol and pyrrolidine and hence drop of its reactivity. It should also be noted, that the reaction was less stereoselective in refluxing ethanol providing **3a** as a 96:4 mixture of *Z*- and *E*-isomers in 69% yield. Much more surprising results were obtained for less electron deficient styrenes. Refluxing the styrene **2b** with 10 equiv of pyrrolidine in ethanol led to the *E*-isomer of the vinylogous guanidinium salt **10b** in 86% yield as the main product (Scheme 3, Table 2). Thus, all halogen atoms were replaced by the nucleophile. This is another of the quite rare examples of substitution of all three fluorine atoms of a trifluorometyl group by a nitrogen nucleophile. While the activation of aliphatic C–F bonds in saturated compounds by use of transition metals as reducing agents is well documented,[18] only a few papers reported the substitution of aliphatic C–F bonds by means of the nucleophilic attack of sulfur-, oxygen- or nitrogen compounds without metal catalysis.[19]



Scheme 3. Reactions of β-chloro- and β-bromo-β-trifluoromethylstyrenes **1** and **2** with secondary amines in the presence of solvents.

The structure of the salt **10b** was determined by NMR-spectroscopy, mass spectrometry, elemental analysis and was doubtlessly confirmed by X-ray analysis (Fig 2).

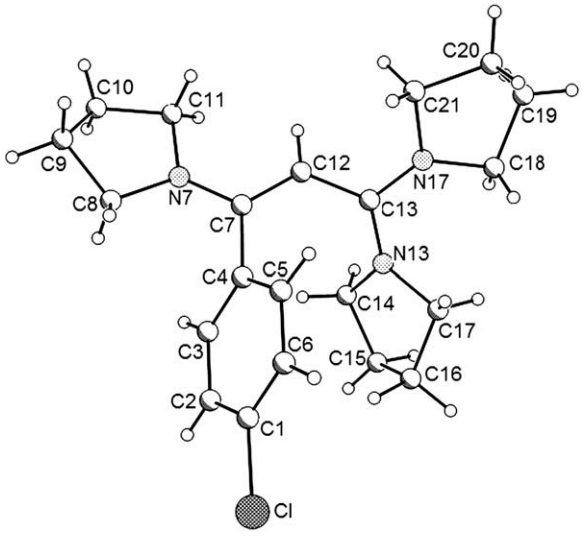


Figure 2. X-ray structure of compound **10b**.

The analyzed crystal of **10b** was found to be a hydrate, **10b**·H_2O. The pyrrolidine rings have envelope conformation with 0.55–0.60 Å deviation from the plane. Generally, C–N bond lengths vary between 1.466(4) and 1.494(4) Å, whereas the C(7)–N(7), C(13)–N(13) and C(13)–N(17) bonds are significantly shorter (1.338(4)–1.359(4) Å) in **10b**. The carbon–carbon bond lengths C(12)–C(7) and C(12)–C(13) are different, 1.377(4) and 1.445(4) Å, respectively, but both are between a single and a double bond indicating the conjugated system. Bromide and the water molecules are connected by hydrogen bonds. Weak van-der-Waals interactions were found between neighboring ions.

The NMR signals of the pyrrolidine ring protons connected to the double bond are significantly broadened at room temperature due to hindered rotation of the C–N bond. Low temperature experiments provided a rotation barrier of about 14 kcal/mol. In the ^1H and ^{13}C NMR spectra two sets of signals of amino moieties were found in 2:1 ratio. The coalescence point of their signals lays as low as approximately 230–240 K. The chemical shifts of ^{15}N atoms in

Table 2
Synthesis of vinylogous guanidinium salts **10**–**17**

Styrene	Ar	R^1–R^2	Solvent	*T* (°C)	Time (h)	Product	Yield (%)
2b	4-ClC_6H_4	–$(CH_2)_4$–	EtOH	Reflux	6	**10b**	86
2d	4-$MeOC_6H_4$	–$(CH_2)_4$–	EtOH	Reflux	6	**10d**	76
1b	4-ClC_6H_4	–$(CH_2)_4$–	EtOH	85–88	17	**11b**	19[a]
1b	4-ClC_6H_4	–$(CH_2)_4$–	THF	85–88	17	**11b**	74
1d	4-$MeOC_6H_4$	–$(CH_2)_4$–	Neat	85–88	16	**11d**	87
1i	4-BrC_6H_4	–$(CH_2)_4$–	EtOH	Reflux	6	**11i**	13[b]
1j	2-Pyridinyl	–$(CH_2)_4$–	THF	85–88	16	**11j**	74
2b	4-ClC_6H_4	–$(CH_2)_5$–	EtOH	120	16	**12b**	66
2d	4-$MeOC_6H_4$	–$(CH_2)_5$–	EtOH	120	16	**12d**	42
2f	2-BrC_6H_4	–$(CH_2)_5$–	Dioxane	Reflux	13	**12f**	35[c]
1i	4-BrC_6H_4	–$(CH_2)_5$–	EtOH	110	13	**13i**	59
2k	4-MeC_6H_4	–$(CH_2)_5$–	EtOH	110	9	**12k**	39
2b	4-ClC_6H_4	–$(CH_2)_6$–	Neat	130	75	**14**	75
2b	4-ClC_6H_4	–$(CH_2)_2O(CH_2)_2$–	Neat	130	75	**15**	32[d]
2b	4-ClC_6H_4	–$(CH_2)_2NH(CH_2)_2$–	EtOH	120	16	**16**	0
2b	4-ClC_6H_4	Et	Neat	130	75	**17**	66

[a] 70% of starting material was recovered.
[b] 47% of starting material was recovered.
[c] 52% of enamine **4f** was isolated as a 70:30 mixture of *Z*- and *E*-isomers.
[d] Substitution of bromine atom in aryl ring by morpholine was observed.

10b were measured using the 2D HMBC $^{1}H–^{15}N$ method. For the nitrogen neighboring the double bond −258.3 ppm was determined, while the nitrogen atoms connected to the positively charged carbon atom are shifted downfield to −269.4 ppm. Nevertheless, the quite similar chemical shift values of all three nitrogen atoms prove the significant charge delocalization.

Although the loss of fluorine is observed in that case, the reaction is interesting since it provides a novel pathway to vinylogous guanidinium salts, which were used, for example, for the synthesis of 1,1,3-tris-(dialkylamino)propadiene derivatives.[20] In order to investigate thoroughly this unusual reaction pathway, we reacted several styrenes **1** and **2** with pyrrolidine and a number of other secondary amines both neat and in solvents. In this way a series of vinylogous guanidinium salts **10**–**17** was synthesized in moderate to high yields. Electron deficient as well as electron rich styrenes do react in this way. The reaction of the *p*-chlorostyrene **1b** with pyrrolidine proceeded considerably faster in THF providing **11b** in 74% yield after 17 h at 85–88 °C, while the reaction in EtOH at the same temperature gave only 19% of **11b** after 17 h. The nature of β-halogen is not very important and both bromo- and chlorostyrenes gave the salts **10**–**17** in comparable yields (Table 2). Piperidine, morpholine, dimethyl- and diethylamine also gave the expected salts when reacted with **2b**, while the reaction of this styrene with piperazine led to a complex mixture of products. In all other cases vinylogous guanidinium salts were found as the sole products and only the styrene **2f** with an *ortho*-bromine substituent gave a mixture of the salt **12f** and the enamine **4f** by reaction with piperidine in dioxane.

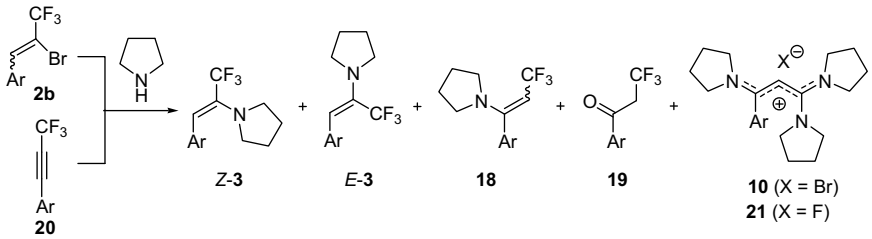
In order to clear up the possible reaction mechanism we followed the progress of some reactions by ^{1}H and ^{19}F NMR spectroscopy. According to these experiments the reaction of bromostyrene **2b** with pyrrolidine in EtOH proceeded quite rapidly even at room temperature and the starting material was completely consumed after less then 4 h. The reaction in EtOH as well as in neat pyrrolidine afforded a mixture of five products. In addition to *Z*-**3b** and *E*-**3b**, one of its regioisomers **18b**, the corresponding ketone **19b** and the vinylogous guanidinium salt **10b** were observed in the reaction mixture by ^{1}H and ^{19}F NMR spectroscopy (Scheme 4, Table 3).

It should be noted that both the quantity and the ratio of stereoisomers **3b** did not change with time and remained constant even after heating for several hours. The share of compounds **18b** and **19b** in the reaction mixture decreased with time and both compounds disappeared after reflux. Simultaneously, the relative amount of the salt **10b** increased on the expense of compounds **18b** and **19b**. On the other hand compound **3b** did not participate in the formation of the salt **10b**. Another proof is the experimental fact, that enamines **3b** and **9** did not show any reactions with neat pyrrolidine or in ethanol at reflux. Thus, the formation of **18b** can be considered as the initial step in the reaction cascade leading to the salt **10b** (Scheme 5).

After formation of **18**, the unshared electron pair on nitrogen kicks out fluoride to give the difluoroalkene derivative **22**, which easily gives the enamine **23** by nucleophilic addition of amine to the activated double bond. One more fluoride extrusion/amine addition continues the reaction leading to the monofluoro compound **25** via **24**. The reaction is completed by the last fluoride extrusion to form the final vinylogous guanidinium salts **10**–**17** or **21** (Scheme 5).

The reasons for the significant change in the position of nucleophilic attack depending on the reaction conditions are not completely understood yet. Kinetic or thermodynamic control of the reaction pathways is the most reasonable explanation. Since the share of enamines **3b** decreased by increasing reaction temperature both in neat pyrrolidine and EtOH, one can conclude, that the enamines **3b** are the kinetically favored primary products, while compounds **18b** (which in turn are transformed to **10**) are favored thermodynamically. This supposition is in a good agreement with quantum chemical calculations [B3LYP/6-311+G(2d,2p)] of the heat of formation of enamines **3b** and **18b**. *E*-**18b** is the thermodynamically most stable compound, followed by *Z*-**18b**, *Z*-**3b** and *E*-**3b** (2.14, 4.39 and 7.16 kcal/mol, respectively). However, the position of the nucleophilic attack is also significantly determined by the *p*-substituent in the aromatic ring. While only **3a** was formed in the reaction of the *p*-nitro compound **1a** with pyrrolidine, the *p*-chloro compound **2b** gave a mixture of **3b** and **18** (and its consecutive products), and the *p*-methoxy derivative **2d** gave only traces of **3d**.

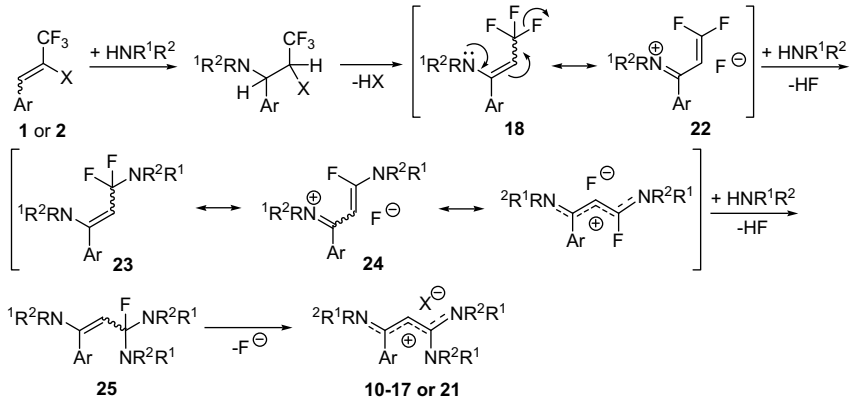
In the case of the reactions in solvents, also solvatation of the amine must be taken into the account. As a consequence, the



Scheme 4. Reaction of styrene **2b** and alkyne **20** with pyrrolidine.

Table 3
Time and temperature dependent product ratio of the reaction of styrene **2b** and alkynes **20a**, **20b** and **20d** with pyrrolidine

Compound	Ar	Solvent	*T* (°C)	Time (h)	*Z*-**3**	*E*-**3**	**18**	**19**	**10** or **21**
2b	4-ClC_6H_4	EtOH	rt	4	37	2	10	36	15
2b	4-ClC_6H_4	EtOH	rt	24	41	2	8	12	36
2b	4-ClC_6H_4	EtOH	rt, then reflux	72, then 8	45	2	—	—	53
2b	4-ClC_6H_4	EtOH	Reflux	5	29	3	—	—	68
2b	4-ClC_6H_4	Neat	rt	14	51	3	11	23	12
2b	4-ClC_6H_4	Neat	rt, then 80	14, then 5	57	4	—	—	39
2b	4-ClC_6H_4	Neat	rt, then 80	72, then 30	59	3	—	—	38
2b	4-ClC_6H_4	Neat	80	5	32	8	—	—	60
20a	4-$NO_2C_6H_4$	Neat	rt	Overnight	71	29	—	—	—
20b	4-ClC_6H_4	Neat	rt	Overnight	55	4	35	2	2
20d	4-$MeOC_6H_4$	Neat	rt	Overnight	—	—	87	9	4



Scheme 5. Possible pathway of formation of salts **10**–**17** and **21**.

sterically more demanding solvated amine attacks the less hindered α-position of the styrene preferentially to give the regioisomers **18**, which in turn are transformed to consecutive products. However, more detailed experimental investigations of the solvent effect and higher-level calculations of activation barriers considering the solvent are necessary to get detailed information on the reaction pathway. Results of these ongoing investigations will be published in due course.

Furthermore, there is the question of the mechanism of the nucleophilic substitution of the vinylic halogen atoms. A number of mechanisms were discussed in literature.[21] Most frequently the addition–elimination mechanism was postulated, starting with a nucleophilic addition to the double bond to yield a carbanion, followed by elimination of the leaving group. This pathway is facilitated by electron-withdrawing groups at the double bond and by reactive anionic nucleophiles. Alternatively, strongly basic anions can cause elimination of hydrogen halide followed by nucleophilic addition towards a formed intermediate.

Earlier, an elimination–addition mechanism was suggested for the reaction of β-chlorostyrenes **1** with secondary lithium amides.[16] It was shown that aryltrifluoromethylalkynes **20** reacted with lithium amide of secondary amines to give *Z*-isomers of the enamine regio- and stereoselectively. We prepared the aryltrifluoromethylalkynes **20a**, **20b**, and **20d** and examined their reactions with pyrrolidine. In our hands these alkynes reacted rapidly and smoothly with neat pyrrolidine at room temperature, affording a mixture of products (Scheme 4, Table 3).

The reaction of the alkyne **20a** with pyrrolidine led exclusively to a mixture of *Z*- and *E*-isomers of **3a**, while **1a** (88:12 mixture of *Z*/*E*-isomers) gave pure *Z*-**3a** under the same conditions. The less electron deficient alkyne **20b** afforded mainly *Z*-**3b** and minor amounts of *E*-**3b**. The second major product was the enamine **18**, while only very small amounts of the vinylogous guanidinium salt **21** were formed. In the case of the electron rich alkyne **20c** the regioselectivity was completely opposite to the reaction of **20a** forming compound **18** almost exclusively. The enamines **3c** were not found and only 4% of **21** were detected.

Summarizing these data, we can conclude that reactions of β-halostyrenes such as **1** and **2** with pyrrolidine do not occur via an elimination–addition sequence in contrast to its reactions with secondary lithium amides. The addition–elimination mechanism is most probable for its reactions with secondary amines affording enamines.

3. Conclusions

According to the experimental data, we can conclude that the reaction pathway of β-halo-β-trifluoromethylstyrenes with secondary amines strongly depends on the electronic properties of the aromatic ring and the reactivity of the applied secondary amine. Two different reaction pathways were observed. In case of very reactive styrenes such as **1a**, bearing the very strong electron-withdrawing nitro group in the aromatic ring, the reactions always proceeded as nucleophilic vinylic substitutions forming the corresponding *Z*/*E*-isomeric enamines **3** with all used secondary amines. Moreover, the most reactive secondary amine, pyrrolidine, gave the enamines **3a** from styrenes **1a** both in a polar solvent and under solvent free (neat) conditions. These reactions proceed via an addition–elimination mechanism. Less electron deficient styrenes such as **2b**, bearing a halogen atom in the aromatic ring, gave enamines only with neat secondary amines. With neat amines at elevated temperature or in solvents such as ethanol at reflux, the reaction pathway changed significantly and a cascade of reactions led to the vinylogous guanidinium salts **10**–**17** as the major reaction products. Kinetic or thermodynamic control of the initial substitution step seems to be the reason for the different reaction pathways.

4. Experimental

4.1. General

^{1}H-, ^{13}C- and ^{19}F NMR spectra were recorded on Bruker ARX 300 and Bruker AMX 400 spectrometers in $CDCl_3$, CD_3CN with TMS, $CDCl_3$ and CCl_3F as internal standards. IR spectra were obtained as films. Column and TLC chromatography were performed using silica gel Merck 60 or Merck $60F_{254}$ plates, respectively. Mass spectra were measured on a MicroTof Bruker Daltonics (ESI-MS) and a Hewlett–Packard HP 5971A instrument (EI, 70 eV). The alkynes **20**, β-chloro-**1** and β-bromo-β-trifluoromethylstyrenes **2** were synthesized according to our previously reported procedures.[5b,e,9]

4.2. Reactions of β-chloro- and β-bromo-β-trifluoromethylstyrenes 1 and 2 with pyrrolidine

4.2.1. Reactions with neat secondary amines

A one neck 25 mL round bottomed flask was charged with dry pyrrolidine (8.5 mL, 100 mmol), cooled down to −18 °C and the corresponding styrene (**1** or **2**, 10 mmol) was added in one portion with vigorous stirring. The reaction mixture was stirred at room temperature for 1–3 h until all starting styrene was consumed (TLC monitoring). The excess of pyrrolidine was evaporated in vacuum, the viscous residue was dissolved in CH_2Cl_2 (50 mL), washed with water (3×50 mL) and dried over Na_2SO_4. CH_2Cl_2 was removed in vacuo, and the residue was filtered through a short silica gel pad using hexane or appropriate mixtures of hexane and CH_2Cl_2. The *Z*/

E-isomers of enamines **3** could not be separated by column chromatography.

*4.2.1.1. 1-[(1Z)-2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3a**).* Obtained from styrene **1a** (2501 mg, 10 mmol). Yield 2717 mg (95%); yellow-orange crystals; mp 81–82 °C; IR (Nujol) 1330, 1510 (NO_2), 1615 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.86–1.91 (m, 4H, $2NCH_2CH_2$), 3.08–3.14 (m, 4H, $2NCH_2CH_2$), 6.06 (s, 1H, C*H*=CCF_3), 7.29 (d, *J*=8.7 Hz, 2H, Ar), 8.16 (d, *J*=8.7 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −64.7; ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6 ($2NCH_2CH_2$), 51.2 ($2NCH_2CH_2$), 103.9 (q, *J*=5.9 Hz, *C*H=CCF_3), 121.7 (q, *J*=278.8 Hz, CF_3), 136.6 (q, *J*=29.3 Hz, *C*–CF_3), 123.1, 129.2, 143.2, 145.3 (Ar); ESI-MS (*m*/*z*): calcd for $C_{13}H_{13}F_3N_2O_2Na$ [M^+] 309.0824, found 309.0821. Anal. Calcd for $C_{13}H_{13}F_3N_2O_2$: C 54.55; H 4.58. Found: C 54.81; H 4.61.

*4.2.1.2. 1-[(1Z)-2-(4-Chlorophenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3b**).* Obtained from styrene **2b** (2860 mg, 10 mmol). Yield 1877 mg (68%); colorless oil; IR (Nujol) 1620 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.76–1.85 (m, 4H, $2NCH_2CH_2$), 3.00–3.07 (m, 4H, $2NCH_2CH_2$), 6.06 (s, 1H, C*H*=CCF_3), 7.19 (d, *J*=8.6 Hz, 2H, Ar), 7.25 (d, *J*=8.6 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −64.6; ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 ($2NCH_2CH_2$), 50.2 ($2NCH_2CH_2$), 108.2 (q, *J*=5.9 Hz, *C*H=CCF_3), 122.2 (q, *J*=278.8 Hz, CF_3), 134.1 (q, *J*=28.5 Hz, *C*–CF_3), 127.9, 130.3, 131.8, 134.2 (Ar). Anal. Calcd for $C_{13}H_{13}ClF_3N$: C 56.63; H 4.75. Found: C 56.43; H 4.88.

*4.2.1.3. Methyl 4-[(1Z)-3,3,3-trifluoro-2-pyrrolidin-1-ylprop-1-enil]-benzoate (**3e**).* Obtained from styrene **2e** (3090 mg, 10 mmol). Yield 2542 mg (85%); colorless oil; IR (Nujol) 1610 (C=C), 1720 (C=O, CO_2Me) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.82–1.89 (m, 4H, $2NCH_2CH_2$), 3.04–3.11 (m, 4H, $2NCH_2CH_2$), 3.93 (s, 3H, CO_2CH_3), 6.10 (s, 1H, C*H*=CCF_3), 7.27 (d, *J*=8.2 Hz, 2H, Ar), 7.98 (d, *J*=8.2 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 ($2NCH_2CH_2$), 50.6 ($2NCH_2CH_2$), 52.0 (CO_2CH_3), 106.4 (q, *J*=5.9 Hz, *C*H=CCF_3), 122.0 (q, *J*=278.8 Hz, CF_3), 135.2 (q, *J*=28.5 Hz, *C*–CF_3), 127.4, 128.8, 129.0, 140.9 (Ar), 166.9 (CO_2CH_3). Anal. Calcd for $C_{15}H_{16}F_3NO_2$: C 60.20; H 5.39. Found: C 60.51; H 5.49.

*4.2.1.4. 1-[2-(2-Bromophenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3f**).* Obtained as a 92:8 mixture of *Z*/*E*-isomers from styrene **2f** (3300 mg, 10 mmol). Yield 2400 mg (75%); colorless oil; IR (Nujol) 1610 (C=C) cm^{-1}; *Z*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 1.79–1.86 (m, 4H, $2NCH_2CH_2$), 3.04–3.11 (m, 4H, $2NCH_2CH_2$), 6.07 (s, 1H, C*H*=CCF_3), 7.06 (td, *J*=7.6 Hz, *J*=1.5 Hz, 1H, Ar), 7.23–7.27 (m, 1H, Ar), 7.29 (d, *J*=7.6 Hz, 1H, Ar), 7.58 (dd, *J*=7.8 Hz, *J*=0.9 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.6 ($2NCH_2CH_2$), 50.5 ($2NCH_2CH_2$), 104.6 (q, *J*=6.6 Hz, *C*H=CCF_3), 122.2 (q, *J*=278.2 Hz, CF_3), 134.8 (q, *J*=28.5 Hz, *C*–CF_3), 124.5, 126.4, 127.6, 131.1, 132.1, 136.8 (Ar); *E*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 1.98–2.02 (m, 4H, $2NCH_2CH_2$), 3.29–3.33 (m, 4H, $2NCH_2CH_2$), 5.56 (s, 1H, C*H*=CCF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 ($2NCH_2CH_2$), 49.3 ($2NCH_2CH_2$), 126.7, 127.8, 137.4 (Ar); the other signals are identical to those of the *Z*-isomer. Anal. Calcd for $C_{13}H_{13}BrF_3N$: C 48.77; H 4.09. Found: C 48.47; H 4.30.

*4.2.1.5. 1-[(1Z)-2-(3-Nitrophenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3g**).* Obtained from styrene **1g** (2510 mg, 10 mmol). Yield 2231 mg (78%); yellow oil; IR (Nujol) 1330, 1510 (NO_2), 1620 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.84–1.91 (m, 4H, $2NCH_2CH_2$), 3.05–3.12 (m, 4H, $2NCH_2CH_2$), 6.09 (s, 1H, C*H*=CCF_3), 7.44–7.54 (m, 2H, Ar), 8.01 (d, *J*=8.1 Hz, 1H, Ar), 8.07 (br s, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 ($2NCH_2CH_2$), 50.7 ($2NCH_2CH_2$), 105.0 (q, *J*=6.6 Hz, *C*H=CCF_3), 121.9 (q, *J*=278.8 Hz, CF_3), 135.7 (q, *J*=29.3 Hz, *C*–CF_3), 120.8, 123.2, 128.5, 134.7, 137.6, 147.9 (Ar). Anal. Calcd for $C_{13}H_{13}F_3N_2O_2$: C 54.55; H 4.58. Found: C 54.67; H 4.66.

*4.2.1.6. 1-[2-(2-Nitrophenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3h**).* Obtained as a 88:12 mixture of *Z*/*E*-isomers from styrene **1h** (2510 mg, 10 mmol). Yield 2802 mg (98%); yellow oil; IR (Nujol) 1340, 1530 (NO_2), 1620 (C=C) cm^{-1}; *Z*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 1.76–1.83 (m, 4H, $2NCH_2CH_2$), 2.99–3.06 (m, 4H, $2NCH_2CH_2$), 6.25 (s, 1H, C*H*=CCF_3), 7.29–7.35 (m, 2H, Ar), 7.55 (td, *J*=8.6 Hz, *J*=1.0 Hz, 1H, Ar), 7.96 (dd, *J*=8.3 Hz, *J*=1.0 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 ($2NCH_2CH_2$), 50.9 ($2NCH_2CH_2$), 100.1 (q, *J*=6.6 Hz, *C*H=CCF_3), 121.6 (q, *J*=278.1 Hz, CF_3), 135.8 (q, *J*=28.5 Hz, *C*–CF_3), 124.3, 126.8, 131.8, 132.0, 137.0, 147.8 (Ar). *E*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 1.95–2.01 (m, 4H, $2NCH_2CH_2$), 3.17–3.31 (m, 4H, $2NCH_2CH_2$), 5.78 (s, 1H, C*H*=CCF_3), 7.51 (td, *J*=7.6 Hz, *J*=1.0 Hz, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 ($2NCH_2CH_2$), 49.3 ($2NCH_2CH_2$), 132.9 (q, *J*=2.9 Hz, *C*H=CCF_3), 124.1, 127.1, 133.8, 148.2 (Ar);the other signals are identical to those of the *Z*-isomer. Anal. Calcd for $C_{13}H_{13}F_3N_2O_2$: C 54.55; H 4.58. Found: C 54.72; H 4.68.

4.2.2. Reaction in THF with lithium amide of pyrrolidine

A previously heated one neck 25 mL round bottomed flask was flushed with argon, charged with dry THF (50 mL), dry pyrrolidine (1.67 mL, 20 mmol) and cooled down to −40 °C. Next, 2.5 M solution of *n*-BuLi in hexane (8.8 mL, 22 mmol) was added dropwise during 5 min. The reaction mixture was stirred another 30 min at −30 to −40 °C, cooled down to −78 °C and the corresponding styrenes (**1**) (10 mmol) were added dropwise at this temperature. The reaction mixture was allowed to warm to room temperature and quenched with saturated solution of NH_4Cl. The organic phase was separated and the water phase was extracted with ether (3×20 mL). The combined extracts were washed with water (2×50 mL) and dried over Na_2SO_4. The volatiles were removed in vacuo, and the residue was filtered through a short silica gel pad using hexane.

*4.2.2.1. 1-[(1Z)-2-Phenyl-1-(trifluoromethyl)vinyl]pyrrolidine (**3c**).* Obtained from styrene **1c** (2070 mg, 10 mmol). Yield 1615 mg (67%); colorless oil; IR (Nujol) 1610 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.85–1.93 (m, 4H, $2NCH_2CH_2$), 3.11–3.18 (m, 4H, $2NCH_2CH_2$), 6.24 (s, 1H, C*H*=CCF_3), 7.23–7.29 (m, 1H, Ar), 7.35–7.39 (m, 4H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 ($2NCH_2CH_2$), 50.2 ($2NCH_2CH_2$), 110.0 (q, *J*=5.9 Hz, *C*H=CCF_3), 122.5 (q, *J*=278.8 Hz, CF_3), 136.6 (q, *J*=28.5 Hz, *C*–CF_3), 126.5, 127.8, 129.3, 135.8 (Ar). ^1H NMR and ^{13}C NMR spectra are in agreement with literature.[10g]

*4.2.2.2. 1-[(1Z)-2-(4-Methoxyphenyl)-1-(trifluoromethyl)vinyl]pyrrolidine (**3d**).* Obtained from styrene **1d** (2810 mg, 10 mmol). Yield 1707 mg (63%); colorless oil; IR (Nujol) 1620 (C=C) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.81–1.89 (m, 4H, $2NCH_2CH_2$), 3.04–3.11 (m, 4H, $2NCH_2CH_2$), 3.84 (s, 3H, OCH_3), 6.21 (s, 1H, C*H*=CCF_3), 6.88 (d, *J*=8.7 Hz, 2H, Ar), 7.34 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.4 ($2NCH_2CH_2$), 49.9 ($2NCH_2CH_2$), 55.1 (OCH_3), 112.9 (q, *J*=5.1 Hz, *C*H=CCF_3), 122.8 (q, *J*=279.6 Hz, CF_3), 132.2 (q, *J*=27.8 Hz, *C*–CF_3), 113.4, 127.9, 130.6, 158.6 (Ar). Anal. Calcd for $C_{14}H_{16}F_3NO$: C 61.98; H 5.94. Found: C 61.85; H 5.88.

4.3. Reactions of styrene 1a with other secondary amines

The styrene **1a** (500 mg, 2 mmol) and the corresponding secondary amine (20 mmol) were heated in a sealed glass tube with a Young-tap. The excess of secondary amine was evaporated at reduced pressure and the residue was purified by column chromatography on silica gel (CH_3OH/CH_2Cl_2 1:10 for piperazine and pentane/CH_2Cl_2 2:1 for others). The *Z*- and *E*-isomers of enamines **4**–**8** could not be separated by column chromatography.

*4.3.1. 1-[2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]piperidine(**4a**)*

Obtained as a 83:17 mixture of *Z*/*E*-isomers by heating with piperidine at 85 °C for 2 h. Yield 534 mg (89%); yellow oil; *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51–1.67 (m, 6H), 2.86–2.98 (m, 4H, 2NCH_2), 6.36 (s, 1H, CH=CCF_3), 7.72 (d, *J*=8.9 Hz, 2H, Ar), 8.21 (d, *J*=8.9 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.4; ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7 ($NCH_2CH_2CH_2$), 26.1 ($NCH_2CH_2CH_2$), 51.5 (NCH_2), 115.2 (q, *J*=5.5 Hz, CH=CCF_3), 122.5 (q, *J*=281.3 Hz, CF_3), 140.6 (q, *J*=27.9 Hz, C–CF_3), 123.4 (CH), 129.7 (CH), 141.5, 146.5 (Ar); *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.67–1.76 (m, 6H), 6.05 (s, 1H, CH=CCF_3), 7.39 (d, *J*=8.8 Hz, 2H, Ar), 8.14 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.1; ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8 ($NCH_2CH_2CH_2$), 25.7 ($NCH_2CH_2CH_2$), 51.7 (NCH_2), 113.7 (q, *J*=2.4 Hz, CH=CCF_3), 142.4 (q, *J*=30.1 Hz, C–CF_3), 123.1 (CH), 129.6 (q, *J*=2.4 Hz, CH), 142.6 (Ar); the other signals are identical to those of the *Z*-isomer. ESI-MS (*m*/*z*): calcd for $C_{14}H_{15}F_3N_2O_2Na$ [M^+] 323.0983, found 323.0978. Anal. Calcd for $C_{14}H_{15}F_3N_2O_2$: C 56.00; H 5.04; N 9.33. Found: C 55.48; H 4.96; N 9.53.

*4.3.2. 1-[2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]azepane (**5**)*

Obtained as a 96:4 mixture of *Z*/*E*-isomers by heating with hexamethylenamin at 125 °C for 8 h. Yield 490 mg (78%); yellow-orange crystals; mp 64–67 °C; *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.57–1.72 (m, 8H), 3.01–3.13 (m, 4H, 2NCH_2), 6.33 (s, 1H, CH=CCF_3), 7.48 (d, *J*=8.8 Hz, 2H, Ar), 8.20 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −64.4; ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.2 ($NCH_2CH_2CH_2$), 29.1 ($NCH_2CH_2CH_2$), 53.6 (NCH_2), 113.6 (q, *J*=5.0 Hz, CH=CCF_3), 122.5 (q, *J*=280.5 Hz, CF_3), 141.1 (q, *J*=29.0 Hz, C–CF_3), 123.6 (CH), 129.4 (CH), 142.2, 146.3 (Ar); *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74–1.84 (m, 6H), 3.25–3.33 (m, 4H, 2NCH_2), 5.80 (s, 1H, CH=CCF_3), 7.32 (d, *J*=8.8 Hz, 2H, Ar), 8.11 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −56.9; ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.1 ($NCH_2CH_2CH_2$), 28.8 ($NCH_2CH_2CH_2$), 53.5 (NCH_2), 143.0 (q, *J*=31.6 Hz, C–CF_3), 123.1 (CH), 129.8 (q, *J*=2.6 Hz, CH), 144.2, 145.9 (Ar); the other signals are identical to those of the *Z*-isomer. ESI-MS (*m*/*z*): calcd for $C_{15}H_{17}F_3N_2O_2Na$ [M^+] 337.1140, found 337.1134. Anal. Calcd for $C_{15}H_{17}F_3N_2O_2$: C 57.32; H 5.45; N 8.91. Found: C 57.64; H 5.47; N 8.91.

*4.3.3. 1-[2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]morpholine (**6**)*

Obtained as a 71:29 mixture of *Z*/*E*-isomers by heating with morpholine at 125 °C for 8 h. Yield 509 mg (84%); yellow crystals; mp 87–90 °C; *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.95–3.04 (m, 4H, NCH_2CH_2O), 3.71–3.78 (m, 4H, NCH_2CH_2O), 6.50 (s, 1H, CH=CCF_3), 7.80 (d, *J*=8.9 Hz, 2H, Ar), 8.23 (d, *J*=8.9 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.5; ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.4 (NCH_2), 66.8 (OCH_2), 117.4 (q, *J*=5.5 Hz, CH=CCF_3), 122.2 (q, *J*=280.8 Hz, CF_3), 139.2 (q, *J*=28.1 Hz, C–CF_3), 123.6 (CH), 129.9 (CH), 140.7, 146.9 (Ar); *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81–3.86 (m, 4H, NCH_2CH_2O), 6.10 (s, 1H, CH=CCF_3), 7.40 (d, *J*=8.8 Hz, 2H, Ar), 8.17 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.0; ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.8 (NCH_2), 66.5 (OCH_2), 114.5 (q, *J*=2.4 Hz, CH=CCF_3), 141.4 (q, *J*=30.5 Hz, C–CF_3), 123.2 (CH), 129.6 (q, *J*=2.4 Hz, CH), 141.9, 146.7 (Ar); the other signals are identical to those of the *Z*-isomer. ESI-MS (*m*/*z*): calcd for $C_{13}H_{13}F_3N_2O_3Na$ [M^+] 325.0776, found 325.0771. Anal. Calcd for $C_{13}H_{13}F_3N_2O_3$: C 51.66; H 4.34; N 9.27. Found: C 51.84; H 4.12; N 9.41.

*4.3.4. 1-[2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]piperazine (**7**)*

Obtained as a 95:5 mixture of *Z*/*E*-isomers by heating with piperazine at 125 °C for 8 h. Yield 550 mg (92%); yellow-orange crystals; mp 72–76 °C; *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.51–2.63 (br s, 3H), 2.91–3.11 (br s, 3H), 6.43 (s, 1H, CH=CCF_3), 7.76 (d, *J*=8.8 Hz, 2H, Ar), 8.21 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.5; ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.3 (NCH_2), 51.4 (NCH_2), 116.0 (q, *J*=5.5 Hz, CH=CCF_3), 122.3 (q, *J*=280.8 Hz, CF_3), 139.6 (q, *J*=27.9 Hz, C–CF_3), 123.5 (CH), 129.9 (CH), 141.1, 146.6 (Ar); *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.08 (s, 1H, CH=CCF_3), 7.40 (d, *J*=8.7 Hz, 2H, Ar), 8.15 (d, *J*=8.7 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.0; ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.5 (NCH_2), 51.0 (OCH_2), 114.0 (q, *J*=2.0 Hz, CH=CCF_3), 123.2 (CH), 129.7 (q, *J*=2.0 Hz, CH), 142.3, 146.8 (Ar); the other signals are identical to those of the *Z*-isomer. ESI-MS (*m*/*z*): calcd for $C_{13}H_{14}F_3N_3O_2H$ [M^+] 302.1116, found 302.1111. Anal. Calcd for $C_{13}H_{14}F_3N_3O_2 \times H_2O$: C 48.90; H 5.05; N 13.16. Found: C 49.12; H 4.68; N 13.35.

*4.3.5. N,N-Diethyl-N-[2-(4-nitrophenyl)-1-(trifluoromethyl)-vinyl]amine (**8**)*

Obtained as a 88:12 mixture of *Z*/*E*-isomers by heating with diethylamine at 85 °C for 15 h. Yield 472 mg (82%); yellow-orange crystals; mp 34–37 °C; *Z*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.08 (t, *J*=7.1 Hz, 6H, CH_2CH_3), 3.02 (t, *J*=7.1 Hz, 4H, CH_2CH_3), 6.44 (s, 1H, CH=CCF_3), 7.67 (d, *J*=8.8 Hz, 2H, Ar), 8.20 (d, *J*=8.8 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.7; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.5 (CH_3), 46.2 (CH_2), 116.2 (q, *J*=5.1 Hz, CH=CCF_3), 122.5 (q, *J*=281.6 Hz, CF_3), 138.2 (q, *J*=28.5 Hz, C–CF_3), 123.6 (CH), 129.5 (CH), 141.8, 146.5 (Ar); *E*-isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (t, *J*=7.0 Hz, 6H, CH_2CH_3), 3.14 (t, *J*=7.0 Hz, 4H, CH_2CH_3), 5.98 (s, 1H, CH=CCF_3), 7.39 (d, *J*=8.7 Hz, 2H, Ar), 8.15 (d, *J*=8.7 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.6; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.6 (CH_3), 45.3 (CH_2), 114.5 (q, *J*=2.6 Hz, CH=CCF_3), 123.2 (CH), 129.6 (d, *J*=2.6 Hz, CH), 143.1, 146.4 (Ar); the other signals are identical to those of the *Z*-isomer. ESI-MS (*m*/*z*): calcd for $C_{13}H_{15}F_3N_2O_2Na$ [M^+] 311.0983, found 311.0980. Anal. Calcd for $C_{13}H_{15}F_3N_2O_2$: C 54.17; H 5.24; N 9.72. Found: C 54.29; H 5.33; N 9.57.

*4.3.6. 3,3,3-Trifluoro-1-(2-nitrophenyl)-N,N-dipropyl-1-propen-2-amine (**9**)*

A one neck 25 mL round bottomed flask was charged with *N*,*N*-dipropylamine (1010 mg, 10 mmol), EtOH (2.5 mL) and the styrene **1h** (377 mg, 1.5 mmol). The reaction mixture was stirred at reflux for 5 h until all starting materials were consumed (TLC monitoring). The volatiles were evaporated in vacuum and the residue was purified by column chromatography on silica gel using (hexane/ether, 1:3) to yield the enamine **9** as a mixture (88:12) of *Z*/*E*-isomers. Yield 334 mg (53%); yellow-orange oil; IR (film) 1623 (C=C) cm^{-1}; *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (t, *J*=7.4 Hz, 6H), 1.30–1.50 (m, 4H), 2.72 (t, *J*=7.4 Hz, 4H), 6.57 (s, 1H), 7.35–7.40 (m, 1H), 7.42–7.50 (m, 1H), 7.52–7.60 (m, 1H), 7.95–7.85 (m, 1H); ^{19}F NMR (377 MHz, $CDCl_3$): δ −63.9; ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.5 (CH_3), 21.5 (CH_2), 54.4 (NCH_2), 112.4 (q, *J*=5.4 Hz, =CH), 122.7 (q, *J*=280.3 Hz, CF_3), 124.8 (C-3), 128.2 (C-4), 131.5 (C-1), 131.6 (C-6), 132.7 (C-5), 140.0 (q, *J*=28.4 Hz, C–N), 147.0 (C-2); *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, *J*=7.4 Hz, 6H), 1.55–1.65 (m, 4H), 2.97 (t, *J*=7.4 Hz, 4H), 6.26 (s, 1H), 7.35–7.40 (m, 1H), 7.42–7.50 (m, 1H), 7.52–7.60 (m, 1H), 7.95–7.85 (m, 1H); ^{19}F NMR (377 MHz, $CDCl_3$): δ −58.3; ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7 (CH_3), 20.0 (CH_2), 53.9 (NCH_2), 112.4 (q, *J*=5.4 Hz, =CH), 122.7 (q, *J*=280.3 Hz, CF_3), 124.6 (C-3), 128.2 (C-4), 131.5 (C-1), 131.6 (C-6), 132.4 (C-5), 140.0 (q, *J*=28.4 Hz, C–N), 147.0 (C-2); mass spectrum (*m*/*z*, %): 316 (14), 287 (57), 198 (53), 43 (100). Anal. Calcd for $C_{15}H_{19}F_3N_2O_2$: C 56.96; H 6.05; N 8.86. Found: C 56.86; H 6.22, N 9.01.

4.4. 1-[(1*Z*)-2-(2-Bromophenyl)-1-(trifluoromethyl)-vinyl]piperidine (4f)

The styrene **2f** (330 mg, 1 mmol) and piperidine (850 mg, 10 mmol) were refluxed in dioxane (2 mL) for 10 h. The volatiles were evaporated in vacuum and the residue was purified by column chromatography on silica gel. Gradient elution by ether/hexane 1:1 and $CHCl_3$/CH_3OH 9:1 mixtures afforded enamine **4f** (173 mg, 52%)

and salt **12f** (182 mg, 35%). Spectroscopic data of compound **12f** see below.

Obtained as a 70:30 mixture of *Z*/*E*-isomers. Yellow-orange oil; IR (Nujol) 1636 (C=C) cm^{-1}; *Z*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 1.40–1.75 (m, 6H), 2.75–2.85 (m, 4H, 2NCH_2), 6.46 (s, 1H, C*H*=CCF_3), 7.05–7.15 (m, 1H), 7.25–7.35 (m, 1H), 7.50–7.60 (m, 2H); ^{19}F NMR (377 MHz, $CDCl_3$): δ −63.8; ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1 ($NCH_2CH_2CH_2$), 26.3 ($NCH_2CH_2CH_2$), 51.7 (NCH_2), 116.4 (q, *J*=5.1 Hz, *C*H=CCF_3), 123.0 (q, *J*=280.0 Hz, CF_3), 139.3 (q, *J*=28.4 Hz, *C*–CF_3), 124.5, 126.9 (CH), 129.0 (CH), 131.1 (CH), 132.6 (CH), 135.7 (Ar); *E*-isomer: ^1H NMR (400 MHz, $CDCl_3$): δ 2.90–3.00 (m, 4H, 2NCH_2), 6.00 (s, 1H, C*H*=CCF_3); ^{19}F NMR (377 MHz, $CDCl_3$): δ −58.4; ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0 ($NCH_2CH_2CH_2$), 51.9 (NCH_2), 116.7 (q, *J*=2.1 Hz, *C*H=CCF_3), 122.3 (q, *J*=278.0 Hz, CF_3), 142.3 (q, *J*=29.6 Hz, *C*–CF_3), 125.0, 127.0 (CH), 128.8 (CH), 130.9 (CH), 132.1 (CH), 136.2 (Ar); the other signals are identical to those of the *Z*-isomer. Mass spectrum (*m*/*z*, %): 335 (M^++1, 63), 333 (M^+−1, 63), 254 (100), 178 (84). Anal. Calcd for $C_{14}H_{15}BrF_3N$: C 50.32; H 4.52; N 4.19. Found: C 50.06; H 4.35; N 4.21.

4.5. Synthesis of vinylogous guanidinium salts 10–17

The corresponding styrene **1**, **2** (0.5–2 mmol), the secondary amine (5–20 mmol) and the solvent[†] (1.5–5 mL of EtOH, THF or dioxane) were heated in a sealed glass tube with a Young-tap. The excess of secondary amine was evaporated at reduced pressure and the residue was purified by column chromatography on silica gel ($CHCl_3$/CH_3OH 9:1).

*4.5.1. 1-[(2E)-3-(4-Chlorophenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium bromide (**10b**)*

Obtained from styrene **2b** (143 mg, 0.5 mmol) and pyrrolidine (365 mg, 5 mmol) by reflux in EtOH (1.5 mL) for 6 h. Yield 283 mg (86%); colorless crystals, mp 41 °C; IR (Nujol) 1549, 1573 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.55–1.70 (br s, 8H), 1.80–2.05 (br s, 4H), 3.10–3.30 (br s, 4H), 3.30–3.50 (br s, 8H), 4.61 (s, 1H), 7.30 (d, *J*=8.5 Hz, 2H), 7.43 (d, *J*=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 25.4 (CH_2), 51.4, 52.0 (NCH_2), 86.1 (=CH), 129.2 (C-3,5), 130.4 (C-2,6), 133.8 (C-1), 136.6 (C-4), 158.1 (=C–N), 163.0 (N–C–N); ^1H NMR (400 MHz, CD_3CN): δ 1.55–1.65 (br s, 8H), 1.85–2.05 (br s, 4H), 3.15–3.30 (br s, 4H), 3.30–3.45 (br s, 8H), 4.60 (s, 1H), 7.37 (d, *J*=8.5 Hz, 2H), 7.49 (d, *J*=8.5 Hz, 2H); ^{13}C NMR (100 MHz, CD_3CN): δ 26.1, 26.5 (CH_2), 51.3, 52.7 (NCH_2), 86.7 (=CH), 130.0 (C-3,5), 132.1 (C-2,6), 135.9 (C-1), 137.0 (C-4), 159.5 (=C–N), 164.5 (N–C–N); mass spectrum (*m*/*z*, %): 286 (100), 185 (72), 169 (50), 75 (39). Anal. Calcd for $C_{21}H_{29}BrClN_3$: C 57.48; H 6.66; Br 18.21; Cl 8.08; N 9.58. Found: C 57.54; H 6.58; Br 17.89; Cl 7.85; N 9.35.

*4.5.2. 1-[(2E)-3-(4-Methoxyphenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium bromide (**10d**)*

Obtained from styrene **2d** (211 mg, 0.75 mmol) and pyrrolidine (550 mg, 7.5 mmol) by reflux in EtOH (2 mL) for 6 h. Yield 167 mg (76%); colorless crystals, mp 213 °C; IR (KBr) 1534 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.35–1.60 (br s, 8H), 1.65–1.90 (br s, 4H), 3.00–3.15 (br s, 4H), 3.15–3.35 (br s, 8H), 3.61 (s, 3H), 4.43 (s, 1H), 6.77 (d, *J*=8.2 Hz, 2H), 7.06 (d, *J*=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.4, 24.7 (CH_2), 50.9 (NCH_2), 54.8 (CH_3O), 84.9 (=CH), 113.5 (C-3,5), 126.7 (C-1), 129.6 (C-2,6), 158.4 (=C–N), 160.5 (N–C–N), 162.6 (C-4). Anal. Calcd for $C_{22}H_{32}BrN_3O$: C 60.83; H 7.42; N 9.67. Found: C 60.47; H 7.22, N 9.49.

*4.5.3. 1-[(2E)-3-(4-Chlorophenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium chloride (**11b**)*

Obtained from styrene **1b** (482 mg, 2 mmol) and pyrrolidine by heating in THF (5 mL) at 85–88 °C for 17 h. Yield 583 mg (74%); white crystals, mp 110–112 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.61–1.80 (br s, 8H), 1.91–2.07 (br s, 4H), 3.23–3.42 (br s, 4H), 3.42–3.55 (br s, 8H), 4.79 (s, 1H, Ar–C=C*H*), 7.39 (d, *J*=8.4 Hz, 2H, Ar), 7.51 (d, *J*=8.4 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9 (NCH_2CH_2), 25.2 (NCH_2CH_2), 50.3 (NCH_2CH_2), 85.4 (Ar–C=*C*H), 158.0 (Ar–*C*=CH), 162.8 (N–C=N), 129.0 (CH), 130.0 (CH), 133.6, 136.4 (Ar); ESI-MS (*m*/*z*) calcd for $C_{21}H_{29}ClN_3^+$ [M^+]: 358.2045, found 358.2045. Anal. Calcd for $C_{21}H_{29}ClN_3\times H_2O$: C 61.16; H 7.58; N 10.19. Found: C 61.08; H 7.53; N 10.09.

*4.5.4. 1-[(2E)-3-(4-Methoxyphenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium chloride (**11d**)*

Obtained from styrene **1d** (474 mg, 2 mmol) and neat pyrrolidine by heating at 85–88 °C for 16 h. Yield 679 mg (87%); pale brown crystals, mp 98–99 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.62–1.77 (br s, 8H), 1.85–2.16 (br s, 4H), 3.20–3.36 (br s, 4H), 3.36–3.48 (br s, 8H), 3.87 (s, 3H, MeO), 4.57 (s, 1H, Ar–C=C*H*), 7.01 (d, *J*=8.8 Hz, 2H, Ar), 7.25 (d, *J*=8.8 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.0 (NCH_2CH_2), 25.3 (NCH_2CH_2), 51.5 (NCH_2CH_2), 55.6 (MeO), 84.8 (Ar–C=*C*H), 159.6 (Ar–*C*=CH), 161.3 (N–C=N), 114.1 (CH), 127.3, 130.0 (CH), 163.4 (Ar); ESI-MS (*m*/*z*) calcd for $C_{22}H_{32}N_3O^+$ [M^+]: 354.2540, found 354.2540. Anal. Calcd for $C_{22}H_{32}ClN_3O\times H_2O$: C 64.77; H 8.40; N 10.30. Found: C 64.36; H 8.32; N 10.09.

*4.5.5. 1-[(2E)-3-(4-Bromophenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium chloride (**11i**)*

Obtained from styrene **1i** (285 mg, 1 mmol) and pyrrolidine (355 mg, 5 mmol) by reflux in EtOH (5 mL) for 6 h. Yield 57 mg (13%); ^1H NMR (400 MHz, $CDCl_3$): δ 1.55–1.75 (br s, 8H), 1.85–2.05 (br s, 4H), 3.15–3.35 (br s, 4H), 3.35–3.50 (br s, 8H), 4.66 (s, 1H), 7.24 (d, *J*=8.2 Hz, 2H), 7.61 (d, *J*=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 25.5 (CH_2), 52.0 (NCH_2), 86.1 (=CH), 124.9 (C-4), 130.5 (C-3,5), 132.3 (C-2,6), 134.4 (C-1), 158.2 (=C–N), 163.2 (N–C–N). Anal. Calcd for $C_{21}H_{29}BrClN_3$: C 57.48; H 6.66; N 9.58. Found: C 57.09; H 7.01; N 9.28.

*4.5.6. 1-[(2E)-3-Pyridin-2-yl-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium chloride (**11j**)*

Obtained from styrene **1j** (416 mg, 2 mmol) and pyrrolidine by heating in THF (5 mL) at 85–88 °C for 16 h. Yield 533 mg (74%); green-gray crystals, mp 117–119 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.62–1.74 (br s, 8H), 1.96–2.04 (br s, 4H), 3.27–3.38 (br s, 4H), 3.43–3.53 (br s, 8H), 4.70 (s, 1H, –C=C*H*), 7.46 (ddd, *J*=7.8 Hz, *J*=4.8 Hz, *J*=0.9 Hz, 1H, Py), 7.71 (d, *J*=7.8 Hz, 1H, Py), 8.14 (td, *J*=7.8 Hz, *J*=1.8 Hz, 1H, Py), 8.66 (ddd, *J*=4.8 Hz, *J*=1.8 Hz, *J*=0.9 Hz, 1H, Py); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9 (NCH_2CH_2), 25.0 (NCH_2CH_2), 49.8 (NCH_2CH_2), 51.5 (NCH_2CH_2), 85.4 (Ar–C=*C*H), 156.8 (Ar–*C*=CH), 162.7 (N–C=N), 124.8 (CH), 124.9 (CH), 137.6 (CH), 149.2 (CH), 153.4 (Ar); ESI-MS (*m*/*z*) calcd for $C_{20}H_{29}N_4^+$ [M^+]: 325.2387, found 325.2387.

*4.5.7. 1-[(2E)-3-(4-Chlorophenyl)-1,3-dipiperidin-1-ylprop-2-enylidene]piperidinium bromide (**12b**)*

Obtained from styrene **2b** (572 mg, 2 mmol) and piperidine by heating in EtOH (5 mL) at 120 °C for 16 h. Yield 632 mg (66%); yellow powder, mp 123–125 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.46–1.84 (m, 18H), 2.99–3.65 (br s, 12H), 4.89 (s, 1H, Ar–C=C*H*), 7.33 (d, *J*=8.5 Hz, 2H, Ar), 7.57 (d, *J*=8.5 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 23.7, 25.5, 25.7, 50.9 (NCH_2), 52.1 (NCH_2), 88.4 (Ar–C=*C*H), 165.1 (Ar–*C*=CH), 169.0 (N–C=N), 129.6 (CH), 130.7 (CH), 133.1, 137.1 (Ar); ESI-MS (*m*/*z*) calcd for $C_{24}H_{35}ClN_3^+$ [M^+]: 400.2514, found 400.2514.

[†] In the case of salts **11d**, **14**, **15**, and **17** the reactions were carried out without solvent.

*4.5.8. 1-[(2E)-3-(4-Methoxyphenyl)-1,3-dipiperidin-1-ylprop-2-enylidene]piperidinium bromide (**12d**)*

Obtained from styrene **2b** (562 mg, 2 mmol) and piperidine by heating in EtOH (5 mL) at 120 °C for 16 h. Yield 400 mg (42%); yellow-brown viscous oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43–1.84 (m, 18H), 3.10–3.66 (br s, 12H), 3.89 (s, 3H, MeO), 4.72 (s, 1H, Ar–C=C*H*), 7.08 (d, *J*=9.0 Hz, 2H, Ar), 7.25 (d, *J*=9.0 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 23.8, 25.5, 25.8, 51.0 (N*C*H$_2$), 51.8 (NCH$_2$), 55.7 (MeO), 87.0 (Ar–C=*C*H), 166.8 (Ar–*C*=CH), 169.7 (N–C=N), 114.7 (CH), 126.4 (CH), 130.8, 161.7 (Ar); ESI-MS (*m*/*z*) calcd for $C_{25}H_{38}N_3O^+$ [M^+]: 396.3009, found 396.3009.

*4.5.9. 1-[(2E)-3-(2-Bromophenyl)-1,3-dipiperidin-1-ylprop-2-enylidene]piperidinium bromide (**12f**)*

Obtained from styrene **2f** (330 mg, 1 mmol) and piperidine (850 mg, 10 mmol) as a mixture with *1-[2-(2-bromophenyl)-1-(trifluoromethyl)vinyl]piperidine* (***4f***) by reflux in dioxane (2 mL) for 10 h. Yield 182 mg (35%); viscous oil; IR (KBr) 1535 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30–1.80 (br s, 18H), 2.70–3.70 (br s, 12H), 4.79 (s, 1H), 7.15–7.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 23.6, 25.3 (CH$_2$), 52.0 (NCH$_2$), 88.2 (=CH), 122.0 (C-2), 128.6 (C-4), 131.8 (C-6), 131.9 (C-5), 133.9 (C-3), 134.3 (C-1), 162.5 (=C–N), 167.9 (N–C–N). Anal. Calcd for $C_{24}H_{35}Br_2N_3$,: C 54.87; H 6.72; N 8.00. Found: C 54.74; H 6.59; N 8.25.

*4.5.10. 1-[(2E)-3-(4-Methylphenyl)-1,3-dipiperidin-1-ylprop-2-enylidene]piperidinium bromide (**12k**)*

Obtained from styrene **2k** (265 mg, 1 mmol) and piperidine by heating in EtOH (2 mL) at 110 °C for 9 h. Yield 180 mg (39%); colorless crystals, mp 118–119 °C; IR (KBr) 1512, 1534 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10–1.40 (br s, 18H), 1.98 (s, 3H), 2.65–3.20 (br s, 12H), 4.28 (s, 1H), 6.65 (br s, 2H), 6.90 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (CH$_3$), 23.3, 23.5, 25.3, 25.5 (CH$_2$), 50.7, 51.7 (NCH$_2$), 87.3 (=CH), 128.8 (C-3,5), 129.6 (C-2,6), 131.5 (C-1), 141.4 (C-4), 165.6 (=C–N), 169.4 (N–C–N). Anal. Calcd for $C_{25}H_{38}BrN_3$: C 65.21; H 8.32; Br 17.35; N 9.12. Found: C 64.93; H 8.70; Br 17.02; N 8.80.

*4.5.11. 1-[(2E)-3-(4-Bromophenyl)-1,3-dipiperidin-1-ylprop-2-enylidene]piperidinium chloride (**13**)*

Obtained from styrene **1j** (285 mg, 1 mmol) and piperidine by heating in EtOH (2 mL) at 110 °C for 13 h. Yield 283 mg (59%); colorless crystals, mp 135 °C; IR (KBr) 1536 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–1.65 (br s, 18H), 2.80–3.50 (br s, 12H), 4.55 (s, 1H), 6.95–7.05 (br s, 2H), 7.49 (d, *J*=7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.3, 23.5, 25.3, 25.5 (CH$_2$), 50.7, 51.8 (NCH$_2$), 88.1 (=CH), 125.2 (C-4), 130.6 (C-3,5), 132.3 (C-2,6), 133.4 (C-1), 165.0 (=C–N), 168.8 (N–C–N). Anal. Calcd for $C_{24}H_{35}BrClN_3$: C 59.94; H 7.34; N 8.74. Found: C 59.81; H 7.12; N 8.78.

*4.5.12. 1-[(2E)-1,3-Diazepan-1-yl-3-(4-chlorophenyl)prop-2-enylidene]azepanium bromide (**14**)*

Obtained from styrene **2b** (572 mg, 2 mmol) and hexamethylenediamine by heating in neat at 130 °C for 75 h. Yield 785 mg (75%); viscous yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39–1.82 (br s, 24H), 3.13–3.55 (br s, 12H), 4.82 (s, 1H, Ar–C=C*H*), 7.39 (d, *J*=8.6 Hz, 2H, Ar), 7.56 (d, *J*=8.6 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.7, 26.9, 27.2, 28.3 (CH$_2$), 53.0, 54.1 (NCH$_2$), 86.4 (Ar–C=*C*H), 164.1 (Ar–*C*=CH), 170.6 (N–C=N), 129.4 (CH), 130.6 (CH), 133.0, 136.9 (Ar); ESI-MS (*m*/*z*) calcd for $C_{27}H_{41}N_3Cl^+$ [M^+]: 442.2984, found 442.2984.

*4.5.13. 4-[(2E)-1,3-Dimorpholin-4-yl-3-(4-morpholin-4-ylphenyl)-prop-2-enylidene]morpholin-4-ium bromide (**15**)*

Obtained from styrene **2b** (572 mg, 2 mmol) and morpholine by heating in neat at 130 °C for 75 h. Yield 344 mg (32%); yellowish crystals, mp 223–225 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.13–3.51 (m, 16H), 3.61–3.73 (br s, 8H), 3.74–3.84 (br s, 4H), 3.86 (t, *J*=4.8 Hz, 4H), 4.76 (s, 1H, Ar–C=C*H*), 7.00 (d, *J*=8.6 Hz, 2H, Ar), 7.18 (d, *J*=8.6 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.4 (NCH$_2$CH$_2$O), 51.1 (NCH$_2$CH$_2$O), 66.0 (NCH$_2$CH$_2$O), 66.5 (NCH$_2$CH$_2$O), 88.0 (Ar–C=CH), 167.7 (Ar–*C*=CH), 170.3 (N–C=N), 114.6 (CH), 122.8 (CH), 131.0, 153.3 (Ar); ESI-MS (*m*/*z*) calcd for $C_{25}H_{37}N_4O_4^+$ [M^+]: 457.2809, found 457.2809. Anal. Calcd for $C_{25}H_{37}BrN_4O_4$: C 55.86; H 6.94; N 10.42. Found: C 55.70; H 7.19; N 9.56.

*4.5.14. N-[(2E)-3-(4-Chlorophenyl)-1,3-bis(diethylamino)prop-2-enylidene]-N,N-diethylammonium bromide (**17**)*

Obtained from styrene **2b** (572 mg, 2 mmol) and diethylamine by heating in neat at 130 °C for 75 h. Yield 590 mg (66%); pale brown crystals, mp 135–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79–1.18 (m, 15H, CH$_3$), 1.27–1.52 (br s, 3H, CH$_3$), 2.97–3.18 (br s, 2H, CH$_2$), 3.18–3.42 (br s, 8H, CH$_2$), 3.54–3.74 (br s, 2H, CH$_2$), 4.77 (s, 1H, Ar–C=C*H*), 7.34 (d, *J*=8.4 Hz, 2H, Ar), 7.55 (d, *J*=8.4 Hz, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5 (CH$_3$), 12.4 (CH$_3$), 13.9 (CH$_3$), 44.8 (CH$_2$), 45.3 (CH$_2$), 45.6 (CH$_2$), 86.2 (Ar–C=*C*H), 163.8 (Ar–*C*=CH), 169.8 (N–C=N), 129.2 (CH), 129.5 (CH), 133.1, 136.3 (Ar); ESI-MS (*m*/*z*) calcd for $C_{21}H_{35}ClN_3^+$ [M^+]: 364.2514, found 364.2514. Anal. Calcd for $C_{21}H_{35}BrClN_3 \times CHCl_3$: C 46.79; H 6.51; N 7.44. Found: C 47.10; H 6.45; N 7.38.

4.6. Reactions of acetylenes 20 with pyrrolidine

The corresponding acetylene **20** (0.5 mmol) and pyrrolidine (0.43 mL, 5 mmol) were mixed and allowed to stay for 2 h at room temperature. The volatiles were evaporated in vacuum and the residue was investigated by NMR spectroscopy.

*4.6.1. 1-[(1E)-2-(4-Nitrophenyl)-1-(trifluoromethyl)vinyl]-pyrrolidine (**3a**)*

Obtained from acetylene **20a** as a mixture with *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.95–2.00 (m, 4H, 2NCH$_2$*C*H$_2$), 3.28–3.32 (m, 4H, 2N*C*H$_2$CH$_2$), 5.48 (s, 1H, C*H*=CCF$_3$), 7.28 (d, *J*=8.6 Hz, 2H, Ar), 8.11 (d, *J*=8.6 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.59; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.0 (2NCH$_2$*C*H$_2$), 49.5 (2N*C*H$_2$CH$_2$), 102.5 (q, *J*=3.2 Hz, *C*H=CCF$_3$), 144.0 (q, *J*=32.9 Hz, *C*–CF$_3$), 129.6 (q, *J*=2.6 Hz, CH), 144.4 (Ar); the other signals are identical to those of the *Z*-isomer.

*4.6.2. 1-[1-(4-Methoxyphenyl)-2-(trifluoromethyl)vinyl]-pyrrolidine (**18d**)*

Obtained from acetylene **20c** as a mixture with 3,3,3-trifluoro-1-(4-methoxyphenyl)propan-1-one (**19d**) and 1-[(2*E*)-3-(4-methoxyphenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium fluoride (**21d**). **18d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.80–1.94 (m, 4H, 2N*C*H$_2$CH$_2$), 2.94–3.07 (m, 4H, 2NCH$_2$*C*H$_2$), 3.81 (s, 3H, OCH$_3$), 4.27 (q, *J*=7.9 Hz, 1H, C=C*H*CF$_3$), 6.90 (d, *J*=8.7 Hz, 2H, Ar), 7.20 (d, *J*=8.7 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −48.0 (d, *J*=7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.4 (2NCH$_2$*C*H$_2$), 48.4 (2N*C*H$_2$CH$_2$), 55.2 (OCH$_3$), 83.4 (q, *J*=35.2 Hz, C=*C*HCF$_3$), 126.6 (q, *J*=265.3 Hz, CF$_3$), 154.6 (q, *J*=4.7 Hz, *C*=CHCF$_3$), 113.4 (CH), 129.7 (CH), 128.3, 159.6 (Ar); **19d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (q, *J*=10.2 Hz, 2H, C*H*$_2$CF$_3$), 3.88 (s, 3H, OCH$_3$), 6.96 (d, *J*=9.0 Hz, 2H, Ar), 7.92 (d, *J*=9.0 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.0 (t, *J*=10.2 Hz). ^{1}H NMR and ^{13}C NMR spectra of compound **19d** are in agreement with literature.[22]

*4.6.3. 1-[(1E)-2-(4-Chlorophenyl)-1-(trifluoromethyl)vinyl]-pyrrolidine (**3b**)*

Obtained from acetylene **20b** as a mixture with *Z*-isomer, 1-[1-(4-chlorophenyl)-2-(trifluoromethyl)vinyl]pyrrolidine (**18b**), 3,3,3-trifluoro-1-(4-chlorophenyl)propan-1-one **19b** and 1-[(2*E*)-3-(4-chlorophenyl)-1,3-dipyrrolidin-1-ylprop-2-enylidene]pyrrolidinium fluoride (**21b**). **3b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90–1.98 (m, 4H, 2NCH$_2$*C*H$_2$), 3.15–3.22 (m, 4H, 2N*C*H$_2$CH$_2$), 5.55 (s, 1H,

C*H*=CCF$_3$); ^{19}F NMR (282 MHz, $CDCl_3$): δ −58.5; **18b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84–1.90 (m, 4H, 2NCH_2CH$_2$), 2.93–3.02 (m, 4H, 2NCH$_2$CH_2), 4.30 (q, J=7.9 Hz, 1H, C=C*H*CF$_3$), 7.21 (d, J=8.5 Hz, 2H, Ar), 7.36 (d, J=8.5 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −48.2 (d, J=7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3 (2NCH$_2$*C*H$_2$), 48.5 (2N*C*H$_2$CH$_2$), 84.0 (q, J=35.4 Hz, C=*C*HCF$_3$), 128.4 (CH), 129.8 (q, J=1.3 Hz, CH), 133.9 (Ar); **19b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (q, J=9.9 Hz, 2H, CH_2CF$_3$), 7.49 (d, J=8.7 Hz, 2H, Ar), 7.89 (d, J=8.7 Hz, 2H, Ar); ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.0 (t, J=9.9 Hz). NMR spectra of compound **19b** are in agreement with literature.[23]

4.7. X-ray structure analysis

The single crystal diffraction data for compound **10b** were collected on a SMART APEX CCD (Bruker AXS) automatic diffractometer (Mo Kα, λ=0.71073 Å). The structure was solved by direct methods and refined by the full-matrix least-squares method in an anisotropic approximation for non-hydrogen atoms. The positions of the H atoms were mostly calculated. The methyl H atoms were refined with isotropic thermal parameters. Structure solution and refinement calculations were carried out with SHELX-97 and Bruker SHELXTL Version 6.12 program packages.

10b·H$_2$O: $C_{21}H_{31}BrClN_3O$; FW=456.85; T=240 K; Monoclinic, $P2_1/c$; a=12.8773(19); b=8.7456(13); c=19.939(3) Å; β=93.492(2)°; V=2241.3(6) Å^3; Z=4, D_C=1.354 g/cm^3; μ=1.969 mm^{-1}; $2.51<\theta<23.35°$; 16,736 collected, 3259 unique, R_{int}=0.1217; 369 parameters; *Goof*=0.946; R indices for $I>2\sigma R_1$=0.0448, wR_2=0.1084; R indices (all data) R_1=0.0551, wR_2=0.1120.

Crystallographic data (excluding structure factors) for the structure of **10b**·H$_2$O have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC-725313. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk.

Acknowledgements

This project was supported by the Deutsche Forschungsgemeinschaft (DFG) through grant Gz: 436 RUS 113/858/0-1 and the Russian Foundation for Basic Research (grants no. 08-03-00736-a, RFBR-DFG 07-03-91562-NNIO_a and 08-03-00067-a). The authors are grateful to Oliver Mimkes and Jakub Grajewski, Münster, for preliminary quantum chemical calculations.

References and notes

1. (a) *Organofluorine Chemistry. Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, NY, 1994; (b) Howe-Grant, M. *Fluorine Chemistry: A Comprehensive Treatment*; John Wiley & Sons: New York, NY, 1995; (c) Hiyama, T. *Organofluorine Compounds. Chemistry and Applications*; Springer: Berlin, 2000; (d) Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell: Oxford, 2004; (e) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, 2004; (f) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, 2006.
2. (a) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley & Sons: Chichester, UK, 1991; (b) *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Filler, R., Kobayashi, Y., Yagupolskii, L. M., Eds.; Elsevier: Amsterdam, 1993; (c) *Fluorine-Containing Amino Acids. Synthesis and Properties*; Kukhar, V. P., Soloshonok, V. A., Eds.; Wiley & Sons: Chichester, UK, 1995; (d) *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; ACS Symposium Series 639; American Chemical Society: Washington, DC, 1996; (e) Fluorine in the Life Sciences, Multiauthor Special Issue *ChemBioChem* **2004**, *5*, 559–722; (f) Fluorine in the Life Science Industry, Multiauthor Special Issue *Chimia* **2004**, *58*, 92–162; (g) Theodoridis, G. Fluorine-Containing Agrochemicals: An Overview of Recent Developments. In *Advances in Fluorine Science*; Tressaud, A., Ed.; Elsevier: Amsterdam, 2006; Vol. 2, pp 121–175; (h) Bégué, J. P.; Bonnet-Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*; John Wiley & Sons: Hoboken, 2008; (i) *Fluorine and Health. Molecular Imaging, Biomedical Materials and Pharmaceuticals*; Tressaud, A., Haufe, G., Eds.; Elsevier: Amsterdam, 2008; pp 553–778.
3. (a) Hudlický, M.; Pavlath, A. P. *Chemistry of Organic Fluorine Compounds II*. ACS Symposium Series 187; American Chemical Society: Washington, DC, 1995; *Enantiocontrolled Synthesis of Fluoro-Organic Compounds*; Soloshonok, V. A., Ed.; Wiley & Sons: Chichester, UK, 1999; (b) *Asymmetric Fluoroorganic Chemistry. Synthesis, Applications, and Future Directions*; Ramachandran, P. V., Ed.; ACS Symposium Series 746; American Chemical Society: Washington, DC, 2000; (c) *Fluorine-Containing Synthons*; Soloshonok, V. A., Ed.; ACS Symposium Series 911; American Chemical Society: Washington, DC, 2005; (d) *Science of Synthesis*; Percy, J. M., Ed.; Fluorine; Thieme: Stuttgart, 2006; Vol. 34; (e) *Current Fluoroorganic Chemistry. New Synthetic Directions, Technologies, Materials, and Biological Applications*; Soloshonok, V. A., Mikami, K., Yamazaki, T., Welch, J. T., Honek, J. F., Eds.; ACS Symposium Series 949; American Chemical Society: Washington, DC, 2006.
4. (a) Shastin, A. V.; Korotchenko, V. N.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **2000**, *56*, 6557–6563; (b) Korotchenko, V. N.; Shastin, A. V.; Nenajdenko, V. G.; Balenkova, E. S. *Synthesis* **2001**, 2081–2084; (c) Korotchenko, V. N.; Shastin, A. V.; Nenajdenko, V. G.; Balenkova, E. S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 883–887; (d) Shastin, A. V.; Nenajdenko, V. G.; Korotchenko, V. N.; Balenkova, E. S. *Russ. Chem. Bull.* **2001**, *50*, 1401–1405; (e) Korotchenko, V. N.; Nenajdenko, V. G.; Shastin, A. V.; Balenkova, E. S. *Org. Biomol. Chem.* **2003**, 1906–1908; (f) Nenajdenko, V. G.; Korotchenko, V. N.; Shastin, A. V.; Balenkova, E. S. *Russ. Chem. Bull.* **2004**, *53*, 1034–1064.
5. (a) Nenajdenko, V. G.; Shastin, A. V.; Korotchenko, V. N.; Varseev, G. N.; Balenkova, E. S. *Eur. J. Org. Chem.* **2003**, 302–308; (b) Korotchenko, V. N.; Shastin, A. V.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **2001**, *57*, 7519–7527; (c) Nenajdenko, V. G.; Varseev, G. N.; Korotchenko, V. N.; Shastin, A. V.; Balenkova, E. S. *J. Fluorine Chem.* **2003**, *124*, 115–118; (d) Nenajdenko, V. G.; Varseev, G. N.; Korotchenko, V. N.; Shastin, A. V.; Balenkova, E. S. *J. Fluorine Chem.* **2004**, *125*, 1339–1345; (e) Nenajdenko, V. G.; Varseev, G. N.; Shastin, A. V.; Balenkova, E. S. *J. Fluorine Chem.* **2005**, *126*, 907–913; (f) Shastin, A. V.; Muzalevsky, V. M.; Balenkova, E. S.; Nenajdenko, V. G. *Mendeleev Commun.* **2006**, *16*, 179–180.
6. Nenajdenko, V. G.; Muzalevskiy, V. M.; Shastin, A. V.; Balenkova, E. S.; Haufe, G. *J. Fluorine Chem.* **2007**, *128*, 818–826.
7. Shastin, A. V.; Muzalevskiy, V. M.; Balenkova, E. S.; Nenajdenko, V. G.; Fröhlich, R.; Haufe, G. *Tetrahedron* **2008**, *64*, 9725–9732.
8. Muzalevskiy, V. M.; Shastin, A. V.; Balenkova, E. S.; Nenajdenko, V. G. *Russ. Chem. Bull.* **2007**, *56*, 1526–1533.
9. Muzalevskiy, V. M.; Nenajdenko, V. G.; Shastin, A. V.; Balenkova, E. S.; Haufe, G. *Synthesis* **2009**, 2249–2259.
10. (a) Uneyama, K.; Morimoto, O.; Yamashita, F. *Tetrahedron Lett.* **1989**, *30*, 4821–4824; (b) Gerus, I. I.; Gorbunova, M. G.; Kukhar, V. P. *J. Fluorine Chem.* **1994**, *69*, 195–198; (c) Cen, W.; Ni, Y.; Shen, V. *J. Fluorine Chem.* **1995**, *73*, 161–164; (d) Bürger, H.; Dittmar, T.; Pawelke, G. *J. Fluorine Chem.* **1995**, *70*, 89–93; (e) Kurykia, M. A.; Volpin, I. M.; German, L. S. *J. Fluorine Chem.* **1996**, *80*, 9–12; (f) Sanin, A. V.; Nenajdenko, V. G.; Smolko, K. I.; Denisenko, D. I.; Balenkova, E. S. *Synthesis* **1998**, 842–846; (g) Bégué, J. P.; Bonnet-Delpon, D.; Bouvet, D.; Rock, M. H. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1797–1800; (h) Moon Park, H.; Uegaki, T.; Konno, T.; Ishihara, T.; Yamanaka, H. *Tetrahedron Lett.* **1999**, *40*, 2985–2988.
11. Bégué, J. P.; Bonnet-Delpon, D.; Mesureur, D.; Née, G.; Wu, S. W. *J. Org. Chem.* **1992**, *57*, 3807–3814.
12. Bégué, J. P.; Mesureur, D. *Synthesis* **1989**, 309–312.
13. (a) Soloshonok, V. A.; Ono, T. *Synlett* **1996**, 919–921; (b) Bravo, P.; Crucianelli, M.; Zanda, M. *Tetrahedron Lett.* **1995**, *36*, 3043–3046.
14. Rulev, A. Yu. *Usp. Khim.* **2002**, *71*, 225–254; *Russ. Chem. Rev.* **2002**, *71*, 195–221.
15. Dmowski, W. *J. Fluorine Chem.* **1984**, *26*, 379–394.
16. Jiang, B.; Zhang, F. J.; Xiong, W. N. *Tetrahedron* **2002**, *58*, 261–264.
17. Hansen, P. E. *Prog. Nucl. Magn. Reson. Spectrosc.* **1981**, *14*, 175–296.
18. (a) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373–431; (b) Burdeniuc, J.; Jedlicka, B.; Crabtree, R. H. *Chem. Ber./Recueil* **1997**, *130*, 145–154; (c) Richmond, T. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3241–3244; (d) Richmond, T. G. *Top. Organomet. Chem.* **1999**, *3*, 243–269; (e) Kiplinger, J. L.; Richmond, T. G. *J. Am. Chem. Soc.* **1996**, *118*, 1805–1806; (f) Burdeniuc, J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 2525–2526; (g) Hughes, R. P.; Smith, J. M. *J. Am. Chem. Soc.* **1999**, *121*, 6084–6085; (h) Deacon, G. B.; Meyer, G.; Stellfeldt, D. *Eur. J. Inorg. Chem.* **2000**, 1061–1071; (i) Kraft, B. M.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **2000**, *122*, 8559–8560; (j) Kraft, B. M.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **2001**, *123*, 10973–10979; (k) Jones, W. D. *Dalton Trans.* **2003**, 3991–3995; (l) Nova, A.; Mas-Balleste, R.; Ujaque, G.; Gonzalez-Duarte, P.; Lledos, A. *Chem. Commun.* **2008**, 3130–3132; (m) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119–2183.
19. (a) MacNicol, D. D.; Robertson, C. D. *Nature* **1988**, *332*, 59–61; (b) Welch, J. T. In *Methods of Organic Chemistry (Houben–Weyl)*; Baasner, B., Hagemann, H., Tatlow, J. C., Eds.; Georg Thieme: Stuttgart, 2000; Vol. E10b/2, pp 382–459; (c) Yamanaka, H.; Ishihara, T. *J. Fluorine Chem.* **2000**, *105*, 295–303; (d) Liddle, B. J.; Gardinier, J. R. *J. Org. Chem.* **2007**, *72*, 9794–9797.
20. Gompper, R.; Schneider, C. S. *Synthesis* **1979**, 213–215.
21. For reviews on the S$_N$V mechanism see: (a) Rappoport, Z. *Adv. Phys. Org. Chem.* **1969**, *7*, 1–114; (b) Modena, G. *Acc. Chem. Res.* **1971**, *4*, 73–80; (c) Miller, S. I. *Tetrahedron* **1977**, *33*, 1211–1218; (d) Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7–15; (e) Rappoport, Z. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 309–349; (f) Shainyan, B. A. *Usp. Khim.* **1986**, *55*, 942–973; *Russ. Chem. Rev.* **1986**, *55*, 511–530; (g) Rulev, A. Yu. *Usp. Khim.* **1998**, *67*, 317–332; *Russ. Chem. Rev.* **1998**, *67*, 279–293; (h) Okuyama, T.; Lodder, G. *Adv. Phys. Org. Chem.* **2002**, *37*, 1–56.
22. Kamitori, Y.; Hojo, M.; Masuda, R.; Ohara, S.; Kawamura, Y.; Ebisu, T. *Synthesis* **1989**, 43–45.
23. Kamigata, N.; Udodaira, K.; Shimizu, T. *Phosphorus, Sulfur Silicon Relat. Elem.* **1997**, *129*, 155–168.