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Regioselectivity of the protonation of captodative enamines bearing a CF_3 group

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ABSTRACT

Capodative enamines bearing a CF_3 group are protonated at the N- or β-C-atom depending on the structure of the initial base and the nature of protonating reagent.

1. Introduction

The regioselectivity of the protonation is an attractive and intricate problem underpinning the fascinating chemistry of enamines [1]. Understanding the relationships between structure and protonation site preference of enamine is a key-issue since their reactivity is directly related to their basicity [2,3]. In general, enamines are ambident conjugated systems in which the N- or C_β-atom of the enamine moiety as well as (in some cases) the heteroatom of the activating group serve as the nucleophilic center. All earliest studies of the proton affinity of enamines have shown that the nature of the product of the reaction depends on relatively trivial changes in reaction conditions or in the structure of the initial base [4]. Indeed, the simple enamines react with most acids to generate usually the stable iminium salts. The existence of the N-protonated forms as intermediates at the initial stages of the reaction was fully supported by NMR, IR, and UV data [4]. If the push–pull aminoenones are protonated predominantly at the oxygen atom [5], the regioselectivity of the electrophilic attack on the captodative ones dramatically depends on the nature of the protonating reagent [6]. The particular case of the captodative formyl(amino)alkenes deserves to be underlined since they react with both mineral and strong organic acids to give regiospecifically the enammonium salts which do not transform into the corresponding iminium ones, probably because of the stabilizing effect of the intramolecular hydrogen bond [7,8]. Captodative aminoalkenes bearing *gem*-cyano [9] or azomethine group [10] generally afford the corresponding enammonium salts which undergo a slow conversion into the C-protonated isomers. Finally, cyclic aminoenones add the proton at the heteroatom as well as at the β-carbon with subsequent enolization [11,12].

The chemistry of carbonyl bearing captodative aminoalkenes has appealed an increasing interest in the recent decades [13] while enamines having geminal trifluoromethyl group remained poorly studied so far. The introduction of fluorine atom into a molecule is known to often drastically perturb the properties of the parent compound [14,15]. Fluorine-containing enamines are versatile building blocks for the construction of new types of biologically active compounds and analogues of natural products. Attention has been recently paid to the synthesis of *gem*-amino(trifluoromethyl)alkenes [16]. Previously, it has been demonstrated that the protonation of such type of derivatives leads to the corresponding enammonium salts only because the presence of the CF_3 group favors their formation [17]. This observation raises an important question: whether the N-protonation of CF_3-substituted enamines is really regiospecific and enammonium salt can be stabilized by the trifluoromethyl group or do the structural changes in these compounds influence the site of electrophilic attack? This information is needed to better delineate the synthetic potential of these systems and their use in the organic synthesis. In the present communication, the protonation of α-trifluoromethylated enamines **1a–d** by both mineral and carboxylic acids is reported.

2. Results and discussion

The enamines **1a–d** were obtained as described previously [16] and exist as a mixture of geometric isomers. Their *Z*,*E*-configurations were established by the application of a ^1H–^1H 2D NOESY homonuclear experiments (Fig. 1). For example, the presence of a

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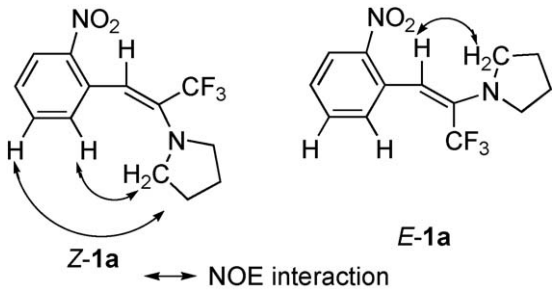


Fig. 1. Configurations of *Z*- and *E*-isomers of enamine **1a**.

quite intensive cross-peaks between the NCH_2 protons and both *ortho*- and *meta*-aromatic protons in the NOESY spectrum of the major isomer of the enamine **1a** confirms unambiguously its *Z*-configuration. In contrast, in the spectrum of the minor isomer there is one NOE peak between the resonance of the olefinic proton and the NCH_2 protons of the amine moiety, whereas no correlations are seen between the proton of the amine and aromatic moieties.

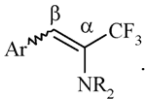
It should be noted that for each pair of isomers there is no significant difference in chemical shifts in both ^{13}C and ^{15}N NMR spectra while the chemical shift difference of olefinic protons achieves 0.5 ppm probably due to the anisotropic influence of substituents (Table 1).

The enamines **1a–d** are typical captodative olefins bearing attractive (CF_3) and donor (NR_2) substituents at the same carbon atom. The analysis of their NMR spectra showed that the enamine function is predominating in these compounds. In fact, the downfield chemical shifts of the α-carbon atom (δ 135–142 ppm) as well as upfield shifts of the β one (δ 101–116 ppm) in all enamines **1a–d** suggest a higher electron density on the latter carbon atom. The difference $\Delta\delta = \delta(C_\alpha) - \delta(C_\beta)$ reaches +35 ppm and is comparable to that observed for the simple enamines (30–45 ppm) [11]. These data are indicative of a high polarization of the double bond C=C and argue in favor of the iminium salts formation.

In fact, the treatment of enamine **1a** with an excess of trifluoromethanesulfonic acid **2a** in dichloromethane or chloroform resulted in the formation of iminium salt **3aa** only (the notation **3aa** means that this salt has been obtained from enamine **1a** and acid **2a**) (Scheme 1). It should be underlined that in all cases it proved impossible to isolate pure samples because of the highly reactive nature of the salts; hence characterisation is based solely upon 1D and 2D NMR spectroscopy data. The signals of the olefinic proton on the ^1H NMR spectrum of the two isomers **1a** disappear and a singlet assigned to the methylene protons appears at 4.84 ppm. A downfield shift of more than 1 ppm is observed for the α-methylene protons of the amino moiety with respect to the same signal of the initial enamine **1a**. In the ^{13}C NMR spectrum two resonance signals appear: a singlet at 40.17 ppm (a triplet ($^1J_{CH}$ = 135.2 Hz) in the coupling ^{13}C NMR spectrum) and quadruplet at 170.41 ppm which were assigned to carbon of CH_2 and $C{=}N^+$ groups, respectively. No significant shift of the resonance was observed in the ^{19}F NMR spectrum (from −64.9 (for *Z*-**1a**) and −58.7 (for *E*-**1a**) to −64.7 ppm) while a large downfield shift of the resonance of pyrrolidine moiety in ^{15}N NMR spectrum was noted (from −305.4 (for *E*-**1a**) and −312.5 (for *Z*-**1a**) to −146.9 ppm) when the initial base **1a** is transformed into the iminium salt **3aa**.

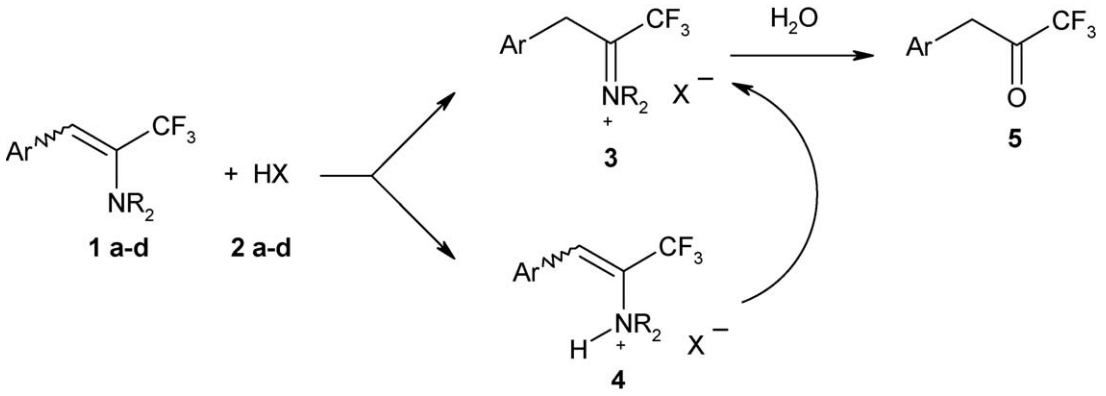
The similar alterations occur when the same enamine **1a** is treated with CF_3COOH in CD_2Cl_2 or when enamine **1b** reacts with CF_3SO_3H in $CDCl_3$. The formation of salts **3ab** and **3ba** is

Table 1
NMR Spectra of Enamines **1a–d**



1 a-d

	Enamine		^1H NMR, δ, ppm		^{13}C NMR, δ, ppm				^{15}N NMR, δ, ppm	
	Ar	NR_2	CH=		C_β		C_α		*Z*-	*E*-
			Z-	*E*-	*Z*-	*E*-	*Z*-	*E*-		
1a	2-$O_2NC_6H_4$	$N(CH_2)_4$	6.25	5.78	100.6	101.1	135.8	135.8	−312.5	−305.4
1b	2-BrC_6H_4	$N(CH_2)_4$	6.07	5.56	104.6	106.0	134.8	135.4	−315.5	−306.4
1c	2-BrC_6H_4	$N(CH_2)_5$	6.46	6.00	116.4	116.7	139.3	142.3	−326.8	−313.8
1d	4-$O_2NC_6H_4$	NEt_2	6.44	5.98	116.2	114.5	137.9	138.6	−323.7	−310.8



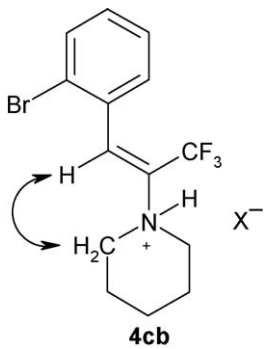
Scheme 1. 1: Ar = 2-$NO_2C_6H_4$, NR_2 = $N(CH_2)_4$ (**a**); Ar = 2-BrC_6H_4, NR_2 = $N(CH_2)_4$ (**b**); Ar = 2-BrC_6H_4, NR_2 = $N(CH_2)_5$ (**c**); Ar = 4-$NO_2C_6H_4$, NR_2 = NEt_2 (**d**). **2**: X = CF_3SO_3 (**a**), CF_3COO (**b**), and Cl (**c**).

accompanied by an appearance of small quantity of the hydrolysis products **5a** and **5b**, respectively. The ketone **5b** was obtained upon treatment of salts **3ba** and **3bb** with water and isolated by column chromatography.

Surprisingly, the trivial replacement of the pyrrolidine moiety in enamine **1b** by a piperidine triggers a significant change in the reaction route. Thus, when enamine **1c** was treated with trifluoroacetic or triflic acids, a mixture of iminium **3** and enammonium **4** salts was formed. The mixture obtained was examined by both 1D and 2D (^{1}H–^{13}C and ^{1}H–^{15}N) NMR spectroscopy. Thus, the structure of the salts **4ca** and **4cb** is easily confirmed by the presence, in the ^{1}H NMR spectra, of a singlet at ~4.5 ppm which characterised the C-protonated form. On the other hand, the retention of a singlet assigned to the CH= group in the same spectra confirms the formation of an enammonium salt. The olefin proton resonance is strongly shifted downfield and clearly displayed in the aromatic range, while the signal of the NH^+ proton appears at ~10.5 ppm. A downfield shift of the β-olefin carbon (~20 ppm) as well as the upfield shift of the α-carbon atom (~12 ppm) observed in the ^{13}C NMR spectra of enammonium salts **4ca** and **4cb** are in good agreement with the principal change in the conjugation of enamine moiety after protonation. Therefore, the N-protonation of the captodative trifluoromethylated enamines **1** results in the umpolung of the C=C bond since the electron density is shifted to the C_α atom bearing the electron withdrawing group CF_3.

Analysis of the 2D NOESY spectrum of salt **4cb** leads to the conclusion that the enammonium salt obtained has *E*-configuration. Its geometry was confirmed by the presence of an intensive cross-peak between the olefinic proton and the proton of the NCH_2 group of the piperidine moiety (Fig. 2). In contrast, no correlations is observed between the proton of the CH= group or the amine moiety and any of aromatic signals. Taking into account that the initial base **1b** consists of a mixture of geometrical isomers (*E*:*Z* = 1:3) one can conclude that the formation of the enammonium salt is accompanied by a partial isomerization of the double bond. The results obtained are in excellent agreement with the early described a Lewis acid-mediated conversion of push–pull *Z*-trifluoromethyl enamines into their *E*-isomers [18] Such ease *E*,*Z*-isomerization was also observed for captodative formyl(amino)alkenes and their azomethine analogues [6,7,10]. Similar transformations were observed on the initial steps of the reaction of enamine **1c** with trifluoroacetic acid (Fig. 3) as well as when the base **1c** was treated with a mild acid such as AcOH (Supporting Information). No N- or C-protonated forms are detected in the latter case.

It should be underlined that the cross-peaks originating from chemical exchange between the protons of initial enamine **1c**, enammonium and iminium salts **3cb** and **4cb**, as well as the acid proton appeared in the 2D NOESY spectrum during the reaction of these enamines with acids. Moreover, monitoring of the reaction of



4cb

Fig. 2. Relative stereochemistry of the salt **4cb**.

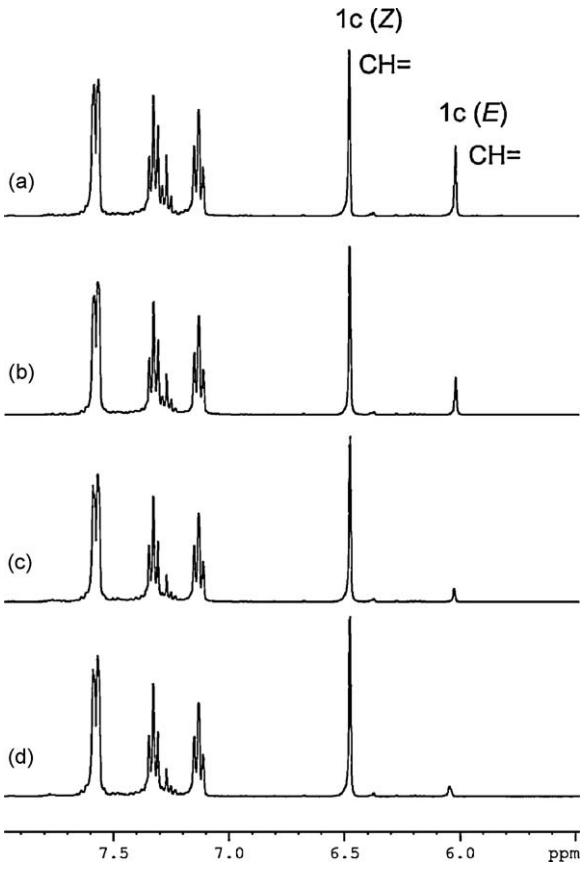


Fig. 3. *E*,*Z*-Isomerization of enamine **1c** at initial steps of the reaction with CF_3COOH. Initial enamine **1c** at rt (*Z*:*E* = 2:1) (a); the reaction mixture after addition of 0.05 (b), 0.10 (c) and 0.15 (d) eq of CF_3COOH at rt.

enamine **1d** with deuterated acid CF_3COOD in $CDCl_3$ showed fast disappearance of the signal of olefinic proton of *E*-**1d** caused by the H–D exchange and much more slow exchange process for its *Z*-isomer. In time, the signals of amine and aromatic moieties of the N- and C-protonated forms appeared.

The differences in the behavior of the enamines **1b** and **1c** is likely to be related to the higher *p*-character of the nitrogen lone-pair in the pyrrolidine appendage compared with the six-member ring of the piperidine. The particular properties of these heterocycles decrease the polarization of the double bond of the enamine **1c** [19]. Interestingly, the values of the chemical shift differences between the adjacent carbon atoms of the enamine **1c** are smaller than for its analogue **1b** (Table 1). Since the electron density at C_β atom of **1c** is decreased, the protonation of both N- and C-nucleophilic centers occurs.

The regioselectivity of protonation also depends not only on the nature of the acid but the geometry of the initial base. Thus, the treatment of enamine **1d** with an equimolar quantity of trifluoroacetic acid in CD_2Cl_2 at room temperature leads to the mixture of the initial base **1d** and the enammonium salt **4db** with a small quantity of hydrolysis product **5**. No signals of the corresponding iminium salt can be detected. While the *E*-isomer of the initial enamine **1d** undergoes the N-protonation immediately, more than 60% of the *Z*-isomer remains unreacted even at the presence of two equivalents of the acid! To our knowledge, it is a first example of the influence of the geometry of enamine on its protonation. The addition of an excess (~5 equiv.) of acid **2b** leads to the corresponding iminium salt **3db**. In contrast, if dry HCl is bubbled into a CD_2Cl_2 cooled solution of **1d**, the enammonium salt **4dc** is formed exclusively. This difference of behavior between the

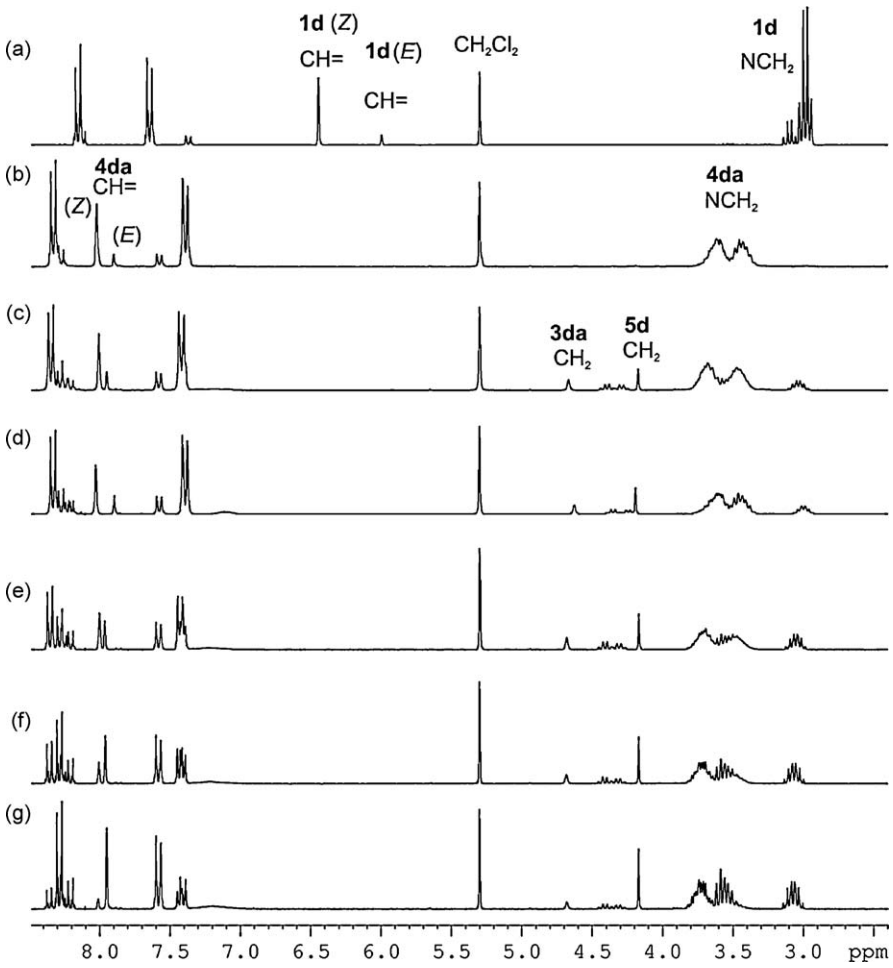


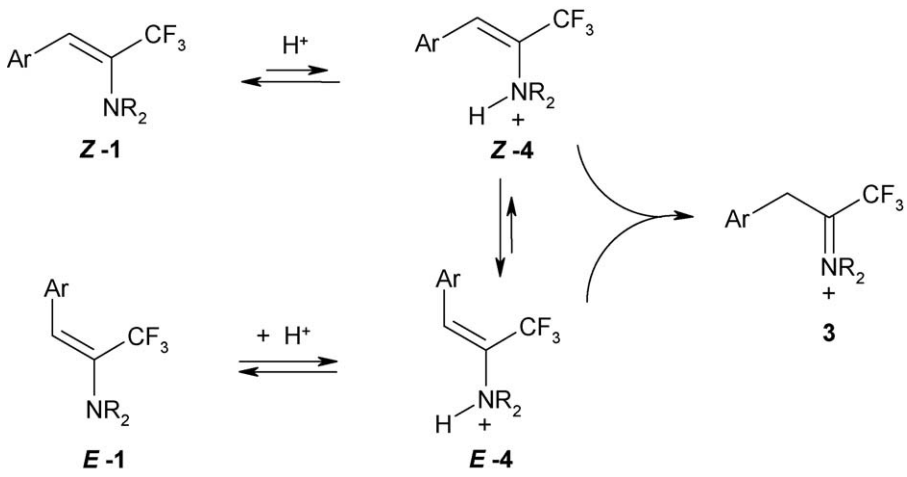
Fig. 4. ^{1}H NMR spectra of the protonation of enamine **1d** with CF_3SO_3H in CD_2Cl_2. Initial enamine **1d** at rt (a); the reaction mixture after protonation with CF_3SO_3H at −80 °C (b), +20 °C (c), −80 °C after a short heating cycle (d), and standing at +30 °C during 10 (e), 20 (f) and 30 (g) min.

mineral and strong carboxylic acids was attributed to the bifunctional catalysis of trifluoroacetic acid on the nitrogen-to-carbon transfer of the proton [20]. According to ^{1}H, ^{13}C and ^{15}N NMR spectra, compound **4dc** exists as a single isomer. The NOE experiments suggest that this salt has the *E*-configuration, that is opposite to the geometry of the initial enamine **1d** but is similar to that of the enammonium salt **4cb**. In contrast to the iminium salts formation, only a slight shielding of the resonance signal in ^{15}N NMR spectrum occurs in this case (from −310.8 and −323.7 for the initial base **1d** to −308.1 ppm for salt **4dc**). These data are in general agreement with the characteristic changes in ^{15}N spectra during the protonation of a lone electron pair of the nitrogen atom [21]. Note that the enammonium chloride **4dc** is quite stable: no iminium-type compounds were observed in the proton spectra after a day at room temperature in CD_2Cl_2 solution. But after a week a mixture of the enammonium salt **4dc** and initial base **1d** in a ratio 1.7:1 as well as a hydrolysis product **5** is detected by ^{1}H NMR spectroscopy. This fact support that the N-protonation is a reversible process.

One of the recurrent problems of enamine chemistry is to know whether the initial enamine **1** undergoes direct C-protonation or if the enammonium salt **4** is converted into the iminium **3** under acid conditions?

To answer this question, we monitored by NMR the reaction of the enamine **1d** with acid **2a** in CD_2Cl_2 at low temperature. In this case, the ^{1}H NMR spectrum recorded at −90 °C substantiates the sole existence of the pure triflate form **4da** together with the initial enamine **1d** (only *Z*-isomer). No traces of any other protonated forms in the reaction mixture were detected (Fig. 4). Varying the temperature from −90 °C to 0 °C did not show any change in this spectrum. Upon heating to +20 °C, the intensity of the olefinic proton signals of triflate **4da** was decreased and the singlets of the methylene group protons of the iminium salt **3da** (δ = 4.66) and the corresponding hydrolysis product **5d** (δ = 4.21) appeared progressively for the same quantity. Thus, we have received a strong evidence to support a nitrogen–carbon proton transfer by acid or solvent assisted process. The signals of these enammonium and iminium salts mixture were recorded while the temperature was decreased to −90 °C then increased to +30 °C. During this temperature cycle, the ^{1}H NMR singlet of the olefinic proton of one isomer of the salt **4da** (δ = 8.03) disappeared and, simultaneously, the singlet of the olefinic proton of the other isomer (δ = 7.98) appeared, suggesting that the a *Z*,*E*-isomerization of the enammonium salt taking place. The corresponding 2D NMR spectra (NOESY and HMBC) confirmed that the geometry of the major isomer **4da** finally obtained is actually opposite to the configuration of the initial enamine **1d**.

Therefore, we have shown that the first step of these transformations involves the formation of enammonium salt **4** exhibiting the same configuration that of the initial enamine **1** (Scheme 2). Its isomerization into the corresponding iminium salt



Scheme 2.

3 and the simultaneous *Z*,*E*-isomerization lead to the thermodynamically more stable *E*-isomer **4**. The same sequence of transformations has been recorded by NMR spectroscopy during the monitoring of the reaction of enamine **1d** with trifluoroacetic acid.

3. Conclusion

In conclusion, we have shown that *gem*-trifluoromethylated enamines can undergo both N- and C-protonations under the action of both strong carboxylic and hard mineral acids. The N-protonation N- *vs* C-protonation depends on both the structure of initial base and the nature of the protonating agent. We have thus successfully showed that the mechanistic course of the reaction suggests a $N \rightarrow C_\beta$ proton shift of the enammonium salt. Unfortunately, no convincing arguments for the direct C-protonation of the enamines **1** could be obtained in this research. The absence of the signals of the N-protonated forms in some cases is probably a result of the fast N → C-transformation. We found that the presence of acid could promote the rearrangement of *Z*-*gem*-trifluoro(amino)alkenes into their *E*-isomers at very mild conditions that allows to prepare these derivatives in high stereoselectivity. The results presented here are significant since showing a detail picture of the key transformations of the captodative trifluorinated enamines under the action of acids and will help to understand their behavior in organic synthesis. The theoretical studies on such enamines are in progress and will be published in due course.

4. Experimental

General remarks. Dynamic ^1H, ^{13}C, ^{19}F and ^{15}N NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400.16, 100.61, 376.5 and 40.55 MHz, respectively, for solution in CD_2Cl_2 or $CDCl_3$. Chemical shifts (δ) in parts per million (ppm) are reported using residual dichloromethane (5.32 for ^1H and 54.00 for ^{13}C) or chloroform (7.25 for ^1H and 77.20 for ^{13}C) as internal reference. The coupling constants (J) are given in Hertz. ^{19}F NMR chemical shifts are reported in ppm downfield to $CFCl_3$. ^{15}N NMR chemical shifts were obtained from 2D{^1H–^{15}N} spectra recorded by the use of a gradient probe working in the *hmbcgp* mode optimized to the long-range coupling constant J_{NH} of 9 Hz and reported in ppm downfield to CH_3NO_2. The concerted application of ^1H–^1H 2D homonuclear experiments COSY [22] and NOESY [23] as well as ^1H–^{13}C 2D heteronuclear experiments HSQC [24] and HMBC [25] were used for the distinction of the carbon and proton resonances in all cases. The IR spectrum was measured with a Specord IR-75 Instrument. The GC/MS analysis was performed on a Hewlett-Packard HP 5971A Instrument (EI, 70 eV). The silica gel used for flash chromatography was 230–400 mesh. All the solvents for NMR research were dried according to standard procedures and freshly distilled prior to use. The synthesis of *gem*-trifluoromethylated enamines **1a–d** was described in our previous paper [16].

4.1. The reaction of enamines 1a–d with acids

The reaction of protonation was carried out directly in tube of RMN. The following salts were obtained by this procedure.

4.2. Triflate 3aa

δ_H (400 MHz, CD_2Cl_2): 8.27 (dd, J = 8.0, 1.2 Hz, 1H), 7.81 (dt, J = 7.6, 1.2 Hz, 1H), 7.73–7.63 (m, 2H), 4.84 (s, 2H), 4.50–4.40 (m, 4H), 2.40–2.30 (m, 4H); δ_C (100.6 MHz, CD_2Cl_2): 23.76, 25.44 (CH_2 pyrrolidine), 40.17 (CH_2), 59.61, 60.28 ($N(CH_2)_2$), 117.45 (q, J = 284 Hz, CF_3), 125.08 (C-1), 125.96 (C-3), 130.89 (C-4), 134.97 (C-6), 135.76 (C-5), 147.25 (C-2), 170.41 (q, J = 42.7 Hz, C=N); δ_F (376.5 MHz, CD_2Cl_2): −64.7; δ_N (40.55 MHz, CD_2Cl_2): −10.3 (NO_2), −146.9 (=N^+).

4.3. Triflate 3ba

δ_H (400 MHz, $CDCl_3$): 7.47 (d, J = 7.8 Hz, 1H), 7.30–7.20 (m, 2H), 7.15–7.05 (m, 1H), 4.53 (s, 2H), 4.45–4.35 (m, 4H), 2.35–2.25 (m, 4H); δ_C (100.6 MHz, $CDCl_3$): 23.58, 24.04 (CH_2 pyrrolidine), 41.17 (CH_2), 59.53, 59.98 ($N(CH_2)_2$), 117.21 (q, J = 282 Hz, CF_3), 124.12 (C-2), 129.02 (C-5), 129.71 (C-1), 130.91 (C-4), 131.52 (C-6), 133.49 (C-3), 170.56 (q, J = 42.7 Hz, C=N).

4.4. Triflate 3ca

δ_H (400 MHz, $CDCl_3$): 7.65–7.50 (m, 2H), 7.45–7.15 (m, 2H), 4.59 (s, 2H), 4.45–4.25 (m, 4H), 2.20–1.70 (m, 6H); δ_F (376.5 MHz, $CDCl_3$): −61.7; δ_N (40.55 MHz, $CDCl_3$): −146.7 (=N^+).

4.5. Triflate 3da

δ_H (400 MHz, CD_2Cl_2): 8.30–8.20 (m, 2H), 7.45–7.35 (m, 2H), 4.70 (s, 2H), 4.43 (q, J = 7.3 Hz, 2H), 4.33 (q, J = 7.3 Hz, 2H), 1.68 (t,

J = 7.3 Hz, 3H), 1.59 (t, J = 7.3 Hz, 3H); δ_F (376.5 MHz, CD_2Cl_2): −62.1.

4.6. Trifluoroacetate **3ab**

δ_H (400 MHz, CD_2Cl_2): 8.29 (d, J = 8.0 Hz, 1H), 7.78 (dt, J = 7.6, 1.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 4.67 (s, 2H), 4.43–4.33 (m, 4H), 2.40–2.30 (m, 4H); δ_F (376.5 MHz, CD_2Cl_2): −64.5.

4.7. Trifluoroacetate **3cb**

δ_H (400 MHz, $CDCl_3$): 7.55–7.40 (m, 2H), 7.35–7.10 (m, 2H), 4.53 (s, 2H), 4.35–4.20 (m, 4H), 2.20–1.70 (m, 6H).

4.8. Trifluoroacetate **3db**

δ_H (400 MHz, CD_2Cl_2): 8.24 (d, J = 8.7 Hz, 2H), 7.38 (d, J = 8.7 Hz, 2H), 4.66 (s, 2H), 4.41 (q, J = 7.3 Hz, 2H), 4.34 (q, J = 7.3 Hz, 2H), 1.65 (t, J = 7.3 Hz, 3H), 1.58 (t, J = 7.3 Hz, 3H); δ_F (376.5 MHz, CD_2Cl_2): −63.6.

4.9. Triflate **4ca**

δ_H (400 MHz, $CDCl_3$): 10.40 (br.s., 1H), 7.88 (s, 1H), 7.65–7.50 (m, 2H), 7.45–7.15 (m, 2H), 3.90–3.70 (m, 2H), 3.70–3.50 (m, 2H), 2.20–1.70 (m, 6H); δ_C (100.6 MHz, $CDCl_3$): 20.70, 23.01 (CH_2 piperidine), 57.43 ($N(CH_2)_2$), 127.62 (=C–N), 122.11, 129.46, 131.62, 132.55, 133.86 (C_{ar}), 138.77 (CH=); δ_F (376.5 MHz, $CDCl_3$): −56.6; δ_N (40.55 MHz, $CDCl_3$): −317.4 ($=N^+$).

4.10. Trifluoroacetate **4cb**

δ_H (400 MHz, $CDCl_3$): 7.60 (s, 1H), 7.55–7.40 (m, 2H), 7.35–7.10 (m, 2H), 3.70–3.50 (m, 4H), 2.20–1.70 (m, 6H).

4.11. Chloride **4cc**

δ_H (400 MHz, $CDCl_3$): 9.44 (br.s., 1H), 8.57 (s, 1H), 7.55–7.45 (m, 2H), 7.30–7.15 (m, 2H), 3.60–3.40 (m, 4H), 2.40–2.20 (m, 4H), 1.80–1.60 (m, 2H).

4.12. Triflate **4da**

δ_H (400 MHz, CD_2Cl_2): *E*-isomer: 9.37 (br.s., 1H), 8.33 (d, J = 8.7 Hz, 2H), 8.06 (s, 1H), 7.40 (d, J = 8.7 Hz, 2H), 3.80–3.40 (m, 4H), 1.41 (t, J = 7.3 Hz, 6H); *Z*-isomer: 10.63 (br.s., 1H), 8.30 (d, J = 8.8 Hz, 2H), 7.98 (s, 1H), 7.54 (d, J = 8.8 Hz, 2H), 3.80–3.40 (m, 4H), 1.50 (t, J = 7.3 Hz, 6H); δ_C (100.6 MHz, CD_2Cl_2): *E*-isomer: 10.74 (CH_3), 55.20 ($N(CH_2)_2$), 125.35 (C-3,5), 125.17 (q, J = 35 Hz, =C–N), 129.02 (C-2,6), 132.60 (C-1), 139.17 (br.s., CH=), 149.20 (C-4); *Z*-isomer: 10.81 (CH_3), 54.55 ($N(CH_2)_2$), 119.77 (q, J = 277 Hz, CF_3), 124.12 (C-3,5), 125.17 (q, J = 35 Hz, =C–N), 129.94 (C-2,6), 135.01 (C-1), 140.14 (br.s., CH=), 149.07 (C-4); δ_F (376.5 MHz, CD_2Cl_2): *E*-isomer: −56.8; *Z*-isomer: −57.1; δ_N (40.55 MHz, CD_2Cl_2): *Z*-isomer: −14.4 (NO_2), −306.8 ($=N^+$).

4.13. Trifluoroacetate **4db**

δ_H (400 MHz, CD_2Cl_2): 8.30 (d, J = 8.7 Hz, 2H), 7.97 (s, 1H), 7.58 (d, J = 8.7 Hz, 2H), 3.62 (q, J = 7.3 Hz, 4H), 1.42 (t, J = 7.3 Hz, 6H); δ_C (100.6 MHz, CD_2Cl_2): 10.61 (CH_3), 53.20 ($N(CH_2)_2$), 123.80 (C-3,5), 126.39 (q, J = 35 Hz, =C–N), 129.60 (C-2,6), 136.10 (C-1), 139.42 (br.s., CH=), 148.7 (C-4); δ_F (376.5 MHz, CD_2Cl_2): −56.8; δ_N (40.55 MHz, CD_2Cl_2): −14.2 (NO_2), −307.5 ($=N^+$).

4.14. Chloride **4dc**

δ_H (400 MHz, CD_2Cl_2): *E*-isomer: 10.25 (br.s., 1H), 8.61 (s, 1H), 8.28 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 8.5 Hz, 2H), 3.51 (q, J = 7.3 Hz, 4H), 1.52 (t, J = 7.3 Hz, 6H); δ_C (100.6 MHz, CD_2Cl_2): 11.17 (CH_3), 52.66 ($N(CH_2)_2$), 120.77 (q, J = 277 Hz, CF_3), 124.29 (C-3,5), 126.18 (q, J = 34 Hz, =C–N), 130.02 (C-2,6), 137.03 (C-1), 141.78 (br.s., CH=), 149.15 (C-4); δ_F (376.5 MHz, CD_2Cl_2): −56.5; δ_N (40.55 MHz, CD_2Cl_2): −12.9 (NO_2), −308.1 ($=N^+$).

4.15. 3-(2-Bromophenyl)-1,1,1-trifluoroacetone **5b**

[Found: C, 40.47; H, 2.28. $C_9H_6BrF_3O$ requires C, 40.48; H, 2.26%]; δ_H (400 MHz, $CDCl_3$): 7.60 (d, J = 8.0 Hz, 1H), 7.35–7.25 (m, 1H), 7.27–7.18 (m, 2H), 4.19 (s, 2H); δ_C (100.6 MHz, $CDCl_3$): 43.81 (CH_2), 115.89 (q, J = 292 Hz, CF_3), 125.07 (C-2), 127.96 (C-5), 129.93 (C-4), 131.24 (C-1), 131.99 (C-6), 133.16 (C-3), 187.79 (q, J = 36 Hz, C=O); ν_{max} (film) 1769 (C=O) cm^{-1}; m/z (EI): 268 (M^++1, 55), 266 (M^+−1, 55), 187 (60), 169 (100).

4.16. 3-(4-Nitrophenyl)-1,1,1-trifluoroacetone **5d**

δ_H (400 MHz, $CDCl_3$): 8.21 (d, J = 8.8 Hz, 1H), 7.39 (d, J = 8.8 Hz, 1H), 4.13 (s, 2H); δ_C (100.6 MHz, $CDCl_3$): 43.29 (CH_2), 115.20 (q, J = 286 Hz, CF_3), 124.24 (C-3,5), 130.92 (C-2,6), 137.81 (C-1), 147.88 (C-4), 186.87 (q, J = 38 Hz, C=O).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2009.10.001.

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