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Reaction of trifluoroacetyl acetylenes with β-amino alcohols. Synthesis of enaminoketones and unusual fragmentation

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1. Introduction

Since the 19th century, the efforts of organic chemists have mostly been directed towards creation of new carbon-carbon and carbon-heteroatom bonds. Despite this intense activity, there are still plenty of molecular frameworks that are extremely challenging to synthesize, and new and efficient approaches are constantly needed [1]. Although the approach to create new bonds has clearly dominated in organic chemistry, carbon-carbon bond cleavage is now seen as an alternative to the construction of unusual molecular skeletons (Beckmann fragmentation, the Grob/Eschenmoser fragmentation) [2]. Over the past few decades, significant progress has been made in C—C bond-cleavage reactions [3] and they can be categorized into two main approaches: 1) metal-involved carbon-carbon cleavage [4] and 2) nonmetal-involved carbon-carbon cleavage [5].

The triple bond of alkynes is known to be one of the strongest bonds in organic molecules. The cleavage of a triple bond is very difficult to perform owing to its rather high dissociation energy (>200 kcal/mol). Despite some rare reports about the cleavage of a triple C—C bond [6] cleavage of this bond without a metal catalyst remains a very challenging task [7]. On the other hand, new types of alkyne transformations are very attractive from synthetic point of view due to alkyne moiety is a recurring functional group in numerous natural products, bioactive compounds, and organic materials as well as versatile intermediates in synthesis [8]. Previously it has been shown that the reaction of acetylenic ketones with 1,2-diamines [7] and *pseudo*-ephedrine [9] resulted in total cleavage of triple bond of starting compounds. Similar transformation has been also observed in the reaction of trifluoromethylated halostyrenes with diamines, however trifluoromethylated acetylenes have been key intermediates of such fragmentation [10] (Scheme 1).

This study is devoted to the investigation of Michael addition of amino alcohols to acetylenic trifluoromethylated ketones as well as study of new fragmentation in the reaction conditions.

2. Results and discussion

In this paper we present the results of reaction of CF_3-ynones with amino alcohols. It should be noted that such ketones [11] have extremely polarized triple bond due to high EWG nature of CF_3CO fragment. On the other hand carbonyl group of these ketones is another rather electrophilic center for the attack of various nucleophiles.

First we studied the synthesis of the corresponding enaminoketones by aza-Michael addition of various amino alcohols. It was demonstrated that this transformation proceeds very cleanly under room temperature in ethanol to form target adducts in high yields (Table 1). The reaction is Z-diastereoselective in the case of amino alcohols having primary amino group, however a mixture of diastereomers was isolated in the case amino alcohols derived from secondary amines. These results are totally in agreement with literature data concerning configuration of trifluoromethylated enaminoketones. [11]

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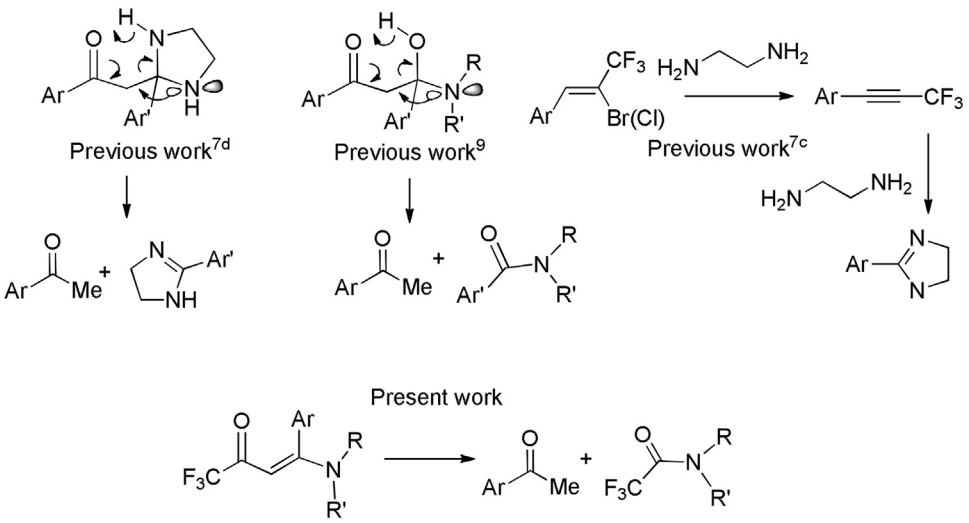
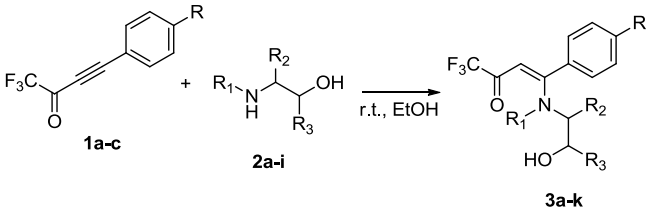


Scheme 1. Some examples of metal free fragmentation of acetylenes.

Table 1
Synthesis of trifluoromethylated enaminoketones.

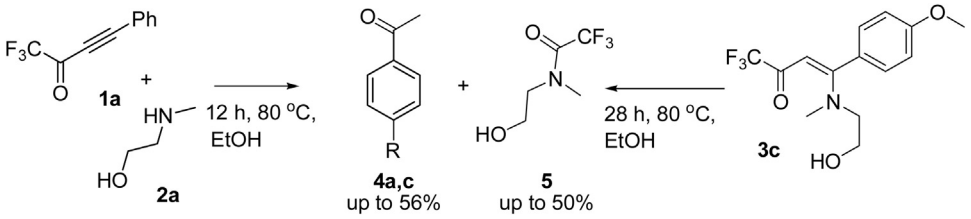
N	R	R_1	R_2	R_3	Reaction time, h	Yield, %
3a	H	Me	H	H	0.5	88
3b	Br	Me	H	H	1	90
3c	OMe	Me	H	H	1	93
3d	H	Me	Me	Ph	2	94
3e	H	H	H	H	8	83
3f	H	Bn	H	H	5	69
3g	H	H	Et	H	10	68
3h	H	H	H	CH_2OH	12	69
3i	H	H	*i*-Bu	H	20	92
3i	H	H	Ph	H	20	71
3k	H	H	Bn	H	20	85



As a rule the reaction proceeds during 1–2 h, however in the case of hindered amino alcohols the reaction was much slower to demand up to 20 h for completion. Unexpectedly, our attempts to accelerate the transformation by heating (up to 50 °C) or using excess of amino alcohol (1.5–2 equivalents) resulted in lower yields and formation of fragmentation products. The corresponding trifluoroacetamides derived from the amino alcohol used and acetophenones were detected in the reaction mixture.

This type of fragmentation is unknown in the literature. We believe that influence of trifluoromethyl group is very important in this case (see proposed mechanism below). Therefore, we decided to study the reaction more thoroughly to have deeper insight to the fragmentation process to understand the mechanism of this reaction. *N*-Methyl amino ethanol and trifluoroacetylated phenylacetylene were studied as a model system. Variation of solvents, reagents ratio and temperature shown that the fragmentation proceeded most efficiently in protic solvent (ethanol) under 80°C with double excess of the nucleophile. In these particular conditions we were able to isolate acetophenone and the corresponding trifluoroacetamide (due to small scale of experiments yields are not very high) (Scheme 2). This type of reaction was studied also for enaminoketone **3c** to demonstrate general character of the fragmentation. In both reactions the corresponding acetophenones **4** and amide **5** were isolated in good yield.

In addition we decided to perform ^{19}F NMR monitoring of fragmentation of enaminoketone **3a** in ethanol. For this aim starting material was heated at 80 °C during 12 h. Samples of reaction mixture were studied using ^{19}F NMR during 12 h. The results of this study are given on Fig. 1. The reaction proceeds very cleanly and we observed no formation of any intermediates under the reaction conditions. This monitoring gave the information about simultaneous fragmentation of starting ketone and appearance in the reaction mixture of *N*-methyl amino ethanol derived trifluoroacetamide **5**. At the beginning the reaction is very slow; however, after some period of time (approximately 30–50 min) significant acceleration of fragmentation is visible. After completion of the reaction acetophenone **4a** and amide **5** are formed in 1:1 ratio accordingly ^1H NMR data.



Scheme 2. Fragmentation of ynone **1a** and enaminoketone **3c**.

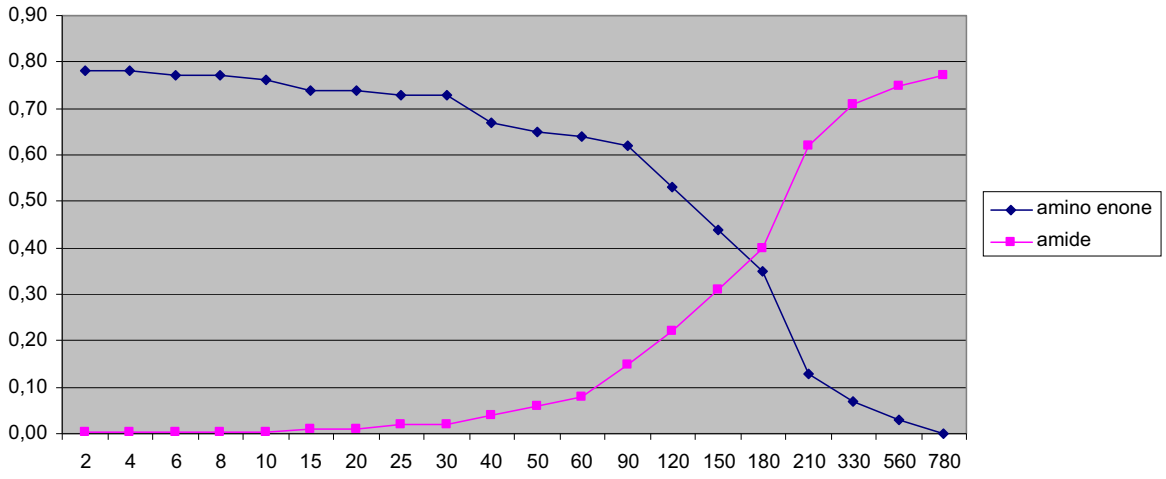
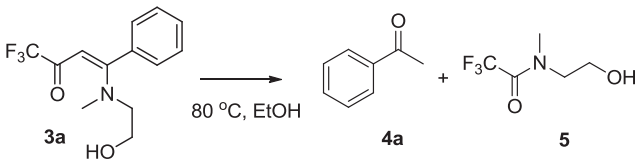


Fig. 1. Monitoring of fragmentation of enone **3a**.



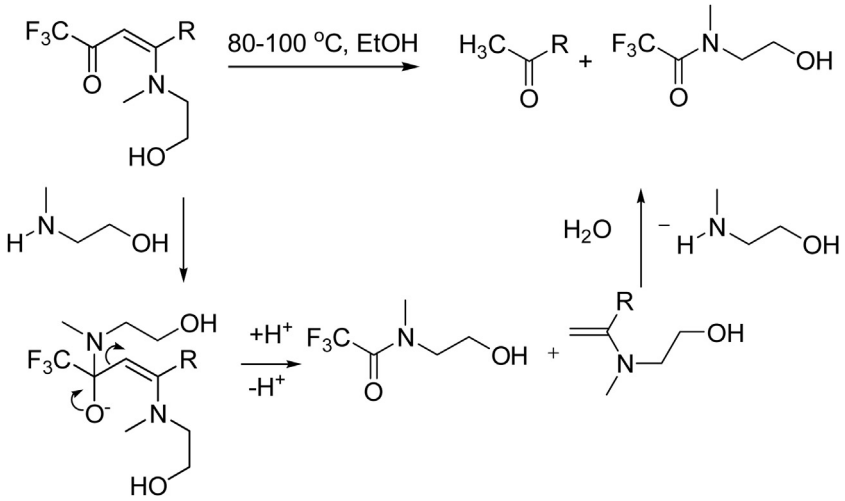
Very important question is the mechanism of the reaction. We proposed a possible scheme of this reaction based on literature data and our experimental observations. Most probably due to highly electrophilic nature of trifluoroacetyl fragment the nucleophilic attack of second molecule of amino alcohol at the carbonyl group takes place under the reaction conditions. We believe that EWG influence of CF_3-group is very important in this case to stabilize such intermediate. We confirmed that the fragmentation is accelerated by the use of excess of amino alcohol in protic solvents (ethanol was found solvent of choice). In the case of the fragmentation of pure enaminoketone first hydrolysis takes place with trace amounts of water (96% ethanol was used). After appearance of more nucleophilic amino alcohol in the reaction mixture the fragmentation is accelerated significantly (Scheme 3). Quite important moment is also the presence of hydroxyl in the structure of amino alcohols and enaminoketones **3**. Our attempt to use secondary amine without additional functionality at the same condition failed. We believe that hydroxyl group in the structure facilitates transfer of proton, which is necessary at the step of fragmentation to eliminate enamine. Finally, hydrolysis of enamine derived from amino alcohol makes the reaction scheme complete to give the corresponding trifluoroacetylated amide and acetophenone as products of the fragmentation.

3. Conclusions

We investigated the nucleophilic addition of aminoalcohols to trifluoroacetyl acetylenes. It was found that under room temperature this reaction provided efficient access to the corresponding enaminoketones. However, under higher temperature unusual fragmentation takes place to form the corresponding trifluoroacetylated amides and acetophenones. Possible reaction scheme was proposed.

4. General information

Column chromatography was performed on SiO_2 (Merck 60 (0.063–0.2 mm)). Analytical TLC was performed using Merck silica gel 60 F_{254} plates. The IR spectra were recorded using a UR-20 spectrometer. ^1H (400.1 MHz), ^{13}C (101.6 MHz), ^{19}F (376.5 MHz) NMR spectra were recorded on Bruker AVANCE 400 MHz spectrometer in $CDCl_3$, DMSO-d_6 The high-resolution ESI mass



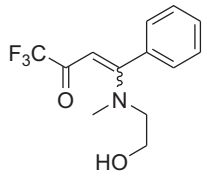
Scheme 3. Possible mechanism of fragmentation.

spectra were recorded using a Bruker micrOTOF II spectrometer. 2-Aminoethanol, 2-(methylamino)ethanol, (1R,2S)-2-(methylamino)-1-phenyl-1-propanol, 2-(benzylamino)ethanol, 2-amino-butan-1-ol, (S)-2-amino-4-methylpentan-1-ol, 3-aminopropane-1,2-diol, (R)-2-amino-2-phenylethanol, 2-amino-3-phenylpropan-1-ol were commercially available reactants. Starting acetylenic ketones **1a–c** were prepared and using literature approach [12].

5. General procedure. Synthesis of 3a–k

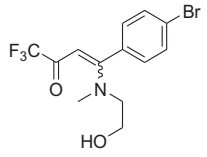
A mixture of ynone (**1a–c**) (0.5 mmol) and amino alcohols (**2a–i**) (0.5 mmol) was stirred in ethanol (0.5 mL) at room temperature for 0.5–20 h. The volatiles were evaporated *in vacuo*, the residues were purified on silica (ethyl acetate/hexane) to give **3a–k**.

6. (E,Z)-1,1,1-trifluoro-4-((2-hydroxyethyl)(methyl)amino)-4-phenylbut-3-en-2-one (3a)



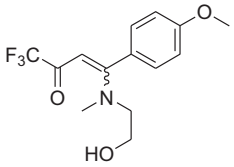
Yield 120 mg (88%), mp 123–125 °C. E-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.13–3.15 (m, 2H, CH_2), 3.18 (s, 3H, NCH_3), 3.40–3.43 (m, 2H, CH_2), 4.82 (br.s, 1H, OH), 5.34 (s, 1H, CH), 7.17-7.19 (m, 2H, CH_{Ar}), 7.42–7.43 (m, 3H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 38.7 (NCH_3), 54.5 (CH_2), 58.6 (CH_2), 86.5 (CH), 117.8 (q, *J* 292 Hz, CF_3), 127.6, 128.4, 128.8, 135.0, 168.6, 172.2. ^{19}F NMR (376 MHz, DMSO-d_6) −75.69. Z-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.78 (s, 3H, NCH_3), 3.62-3.65 (m, 2H, CH_2), 3.77 (m, 2H, CH_2), 5.07 (br.s, 1H, OH), 5.52 (s, 1H, CH), 7.18–7.19 (m, 2H, CH_{Ar}), 7.43–7.44 (m, 3H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.6 (NCH_3), 54.9 (CH_2), 57.1 (CH_2), 85.9 (CH), 117.8 (q, *J* 292 Hz, CF_3), 127.2, 128.6, 128.8, 135.7, 168.3, 172.2. ^{19}F NMR (376 MHz, DMSO-d_6) −75.62. IR (film, cm^{-1}) 1633 (C=O), 3406 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{13}H_{14}F_3NNaO_2$ $[M+Na]^+$ 296.0869, found, 296.0864.

7. (E,Z)-4-(4-bromophenyl)-1,1,1-trifluoro-4-((2-hydroxyethyl)(methyl)amino)but-3-en-2-one (3b)



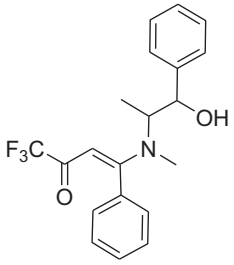
Yield 160 mg (90%), mp 153–155 °C. E-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.14–3.15 (m, 2H, CH_2), 3.17 (s, 3H, NCH_3), 3.42-3.43 (m, 2H, CH_2), 4.81 (br.s, 1H, OH), 5.34 (s, 1H, CH), 7.13-7.15 (d, 2H, *J* 8.22 Hz, CH_{Ar}), 7.62–7.64 (d, 2H, *J* 8.22 Hz, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 38.7 (NCH_3), 54.6 (CH_2), 58.4 (CH_2), 86.6 (CH), 117.7 (q, *J* 292 Hz, CF_3), 130.0, 131.5, 134.3, 167.4, 172.4. ^{19}F NMR (376 MHz, DMSO-d_6) −75.67. Z-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.80 (s, 3H, NCH_3), 3.62-3.64 (m, 2H, CH_2), 3.75 (m, 2H, CH_2), 5.06 (br.s, 1H, OH), 5.53 (s, 1H, CH), 7.15–7.18 (m, 2H, CH_{Ar}), 7.64–7.67 (m, 3H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.7 (NCH_3), 55.0 (CH_2), 57.1 (CH_2), 86.1 (CH), 117.7 (q, *J* 292 Hz, CF_3), 129.5, 131.8, 135.0, 167.4, 172.4. ^{19}F NMR (376 MHz, DMSO-d_6) −75.61. IR (film, cm^{-1}) 1630 (C=O), 3390 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{13}H_{13}BrF_3NNaO_2$ $[M+Na]^+$ 373.9974, found, 373.9984.

8. (E,Z)-1,1,1-trifluoro-4-((2-hydroxyethyl)(methyl)amino)-4-(4-methoxyphenyl)but-3-en-2-one (3c)



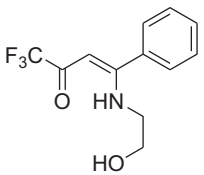
Yield 140 mg (93%), mp 134–135 °C. E-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.16 (s, 3H, NCH_3), 3.18–3.19 (m, 2H, CH_2), 3.42–3.43 (m, 2H, CH_2), 3.80 (s, 3H, OCH_3), 4.78 (br.s, 1H, OH), 5.31 (s, 1H, CH), 6.97–6.99 (m, 2H, CH_{Ar}), 7.10–7.12 (m, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 38.7 (NCH_3), 54.5 (CH_2), 55.1 (OCH_3), 58.6 (CH_2), 86.8 (CH), 113.9, 118.0 (q, *J* 292 Hz, CF_3), 126.9, 129.3, 159.6, 168.8, 172.2. ^{19}F NMR (376 MHz, DMSO-d_6) −75.58. Z-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.83 (s, 3H, NCH_3), 3.62 (m, 2H, CH_2), 3.75–3.76 (m, 2H, CH_2), 3.80 (s, 3H, OCH_3), 5.04 (br.s, 1H, OH), 5.49 (s, 1H, CH), 6.97–6.99 (m, 2H, CH_{Ar}), 7.10–7.12 (m, 3H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.5 (NCH_3), 54.3 (CH_2), 55.1 (OCH_3), 57.2 (CH_2), 86.2 (CH), 114.0, 118.0 (q, *J* 292 Hz, CF_3), 127.5, 131.5, 159.8, 168.8, 172.2. ^{19}F NMR (376 MHz, DMSO-d_6) −75.48. IR (film, cm^{-1}) 1628 (C=O), 3369 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{14}H_{16}F_3NNaO_3$ $[M+Na]^+$ 326.0974, found, 326.0968.

9. (E)-1,1,1-trifluoro-4-((1-hydroxy-1-phenylpropan-2-yl)(methyl)amino)-4-phenylbut-3-en-2-one (3d)



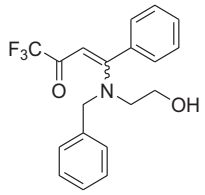
Yield 170 mg (94%), mp 165–168 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (d, 3H, *J* 6.65 Hz, CH_3), 3.12 (s, 3H, NCH_3), 4.61–4.64 (m, 1H, CH), 5.20 (s, 1H, CH), 5.65 (d, 1H, *J* 4.70 Hz, CH), 6.38 (d, 1H, *J* 7.43 Hz, OH), 7.01 (d, 2H, *J* 6.26 Hz, CH_{Ar}), 7.10–7.11 (m, 1H, CH_{Ar}), 7.27–7.41 (m, 7H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.7 (CH_3), 33.8 (NCH_3), 60.8, 73.8, 86.3, 117.6 (q, *J* 293 Hz, CF_3), 126.1, 126.4, 127.4, 127.9, 128.3, 128.5, 128.7, 134.9, 142.8, 168.2, 172.4. ^{19}F NMR (376 MHz, DMSO-d_6) −75.71. IR (film, cm^{-1}) 1624 (C=O), 3428 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{20}H_{20}F_3NNaO_2$ $[M+Na]^+$ 386.1338, found, 386.1335.

10. (Z)-1,1,1-trifluoro-4-(2-hydroxyethylamino)-4-phenylbut-3-en-2-one (3e)



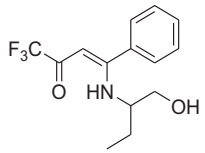
Yield 100 mg (83%), yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.34-3.35 (m, 2H, CH_2), 3.50–3.54 (m, 2H, CH_2), 5.07–5.09 (t, 1H *J* 4 Hz, OH), 5.30 (s, 1H, CH), 7.50–7.53 (m, 5H, CH_{Ar}), 11.25 (br.s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 47.5 (CH_2), 59.6 (CH), 88.9 (CH), 117.5 (q, *J* 278 Hz, CF_3), 127.6, 128.8, 130.5, 133.5, 170.5, 173.3. ^{19}F NMR (376 MHz, DMSO-d_6) −75.47. IR (film, cm^{-1}) 1608 (C=O), 3411 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{12}H_{12}F_3NNaO_2$ $[M+Na]^+$ 282.0718, found, 382.0724.

11. (E,Z)-4-(benzyl(2-hydroxyethyl)amino)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (3f)



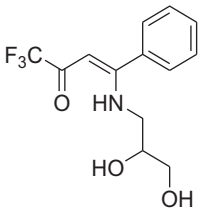
Yield 120 mg (69%), mp 123–125 °C. E-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.22–3.24 (m, 2H, CH_2), 3.43–3.47 (m, 2H, CH_2), 4.86–4.87 (m, 1H, OH), 4.89 (br.s, 2H, CH_2), 5.39 (s, 1H, CH), 7.11–7.47 (m, 10H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 53.9 (CH_2), 54.1 (CH_2), 59.4 (CH_2), 88.7 (CH), 118.3 (q, *J* 293 Hz, CF_3), 126.9, 127.4, 127.9, 128.9, 129.1, 129.2, 135.5, 135.9, 168.6, 172.9. ^{19}F NMR (376 MHz, DMSO-d_6) −76.09. Z-izomer. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.54–3.57 (m, 2H, CH_2), 3.70–3.74 (m, 2H, CH_2), 4.38 (br.s, 2H, CH_2), 5.08–5.11 (m, 1H, OH), 5.66 (s, 1H, CH), 7.11–7.47 (m, 10H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6) δ 51.8 (CH_2), 53.7 (CH_2), 56.8 (CH_2), 86.7 (CH), 118.1 (q, *J* 293 Hz, CF_3), 127.6, 127.7, 127.9, 129.0, 129.1, 129.2, 135.6, 136.7, 168.8, 172.9. ^{19}F NMR (376 MHz, DMSO-d_6) −75.76. IR (film, cm^{-1}) 1631 (C=O), 3385 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{19}H_{18}F_3NNaO_2$ $[M+Na]^+$ 372.1182, found, 372.1176.

12. (Z)-1,1,1-trifluoro-4-(1-hydroxybutan-2-ylamino)-4-phenylbut-3-en-2-one (3g)



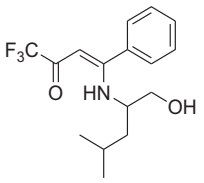
Yield 110 mg (68%), mp 78–80 °C (benzene). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.73–0.76 (m, 3H, CH_3), 1.44–1.57 (m, 2H, CH_2), 3.48–3.49 (m, 2H, CH_2), 5.16 (s, 1H, CH), 5.29 (s, 1H, CH), 7.50 (m, 5H, CH_{Ar}), 11.15 (d, 1H, *J* 9.00 Hz, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 10.0 (CH_3), 24.8 (CH_2), 58.4 (CH_2), 62.7 (CH), 89.0 (CH), 117.5 (q, *J* 288 Hz, CF_3), 127.5, 128.8, 130.3, 133.7, 170.9, 173.7. ^{19}F NMR (376 MHz, DMSO-d_6) −75.45. IR (film, cm^{-1}) 1602 (C=O), 3419 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{14}H_{16}F_3NNaO_2$ $[M+Na]^+$ 310.1025, found, 310.1024.

13. (Z)-4-(2,3-dihydroxypropylamino)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (3h)



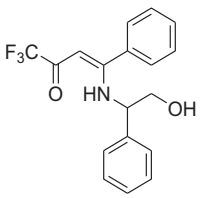
Yield 100 mg (69%), mp 102–105 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.19–3.29 (m, 2H, CH_2), 3.36–3.37 (m, 1H), 3.42–3.46 (m, 2H, CH_2), 4.71 (br.s, 1H, OH), 5.27–5.28 (m, 1H, OH), 5.31 (s, 1H, CH), 7.52–7.54 (m, 5H, CH_{Ar}), 11.30 (br.s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.3 (CH_2), 63.2 (CH_2), 69.6 (CH), 88.9 (CH), 117.7 (q, *J* 288 Hz, CF_3), 127.6, 128.8, 130.5, 133.5, 170.5, 173.2. ^{19}F NMR (376 MHz, DMSO-d_6) −75.40. IR (film, cm^{-1}) 1604 (C=O), 3403 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{13}H_{14}F_3NnaO_3$ $[M+Na]^+$ 312.0818, found, 312.0815.

14. (Z)-1,1,1-trifluoro-4-(1-hydroxy-4-methylpentan-2-ylamino)-4-phenylbut-3-en-2-one (3i)



Yield 145 mg (92%), mp 80–82 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.53 (d, 3H, J 6.26 Hz, CH_3), 0.71 (d, 3H, J 6.26 Hz, CH_3), 1.33–1.37 (m, 2H, CH_2), 1.41–1.46 (m, 1H, CH), 3.47–3.49 (m, 1H, CH), 3.52–3.55 (m, 2H, CH_2), 5.19-5.21 (t, 1H, J 4.30 Hz, OH), 5.27 (s, 1H, CH), 7.50–7.54 (m, 5H, CH_{Ar}), 11.11 (d, 1H, J 9.39 Hz, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.7 (CH_3), 22.6 (CH_3), 24.0 (CH), 41.1 (CH_2), 55.2 (CH_2), 63.4 (CH), 88.9 (CH), 117.4 (q, *J* 287 Hz, CF_3), 127.6, 128.8, 130.4, 133.6, 170.6, 173.4. ^{19}F NMR (376 MHz, DMSO-d_6) −75.45. IR (film, cm^{-1}) 1608 (C=O), 3434 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{16}H_{20}F_3NNaO_2$ $[M+Na]^+$ 338.1338, found, 338.1338.

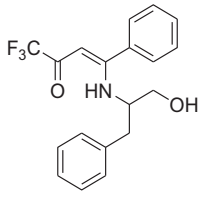
15. (Z)-1,1,1-trifluoro-4-(2-hydroxy-1-phenylethylamino)-4-phenylbut-3-en-2-one (3j)



Yield 120 mg (71%), yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.65–3.77 (m, 2H, CH_2), 4.67–4.72 (m, 1H, CH), 5.37–5.40 (m, 1H, OH), 5.38 (s, 1H, CH), 7.17 (d, 2H, *J* 7.04 Hz, CH_{Ar}), 7.26–7.29 (m, 1H, CH_{Ar}), 7.31–7.36 (m, 4H, CH_{Ar}), 7.43–7.47 (m, 2H, CH_{Ar}), 7.50–7.53 (m, 1H, CH_{Ar}), 11.74 (d, 1H, *J* 9.39 Hz, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 60.5 (CH_2), 64.9 (CH), 89.6 (CH), 117.5 (q, *J* 288 Hz, CF_3), 126.4, 127.3, 127.6, 128.7, 128.8, 130.6, 133.4, 139.2, 170.5, 174.4. ^{19}F NMR (376 MHz, DMSO-d_6) −75.44. IR (film, cm^{-1}) 1607 (C=O),

3401 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{18}H_{16}F_3NNaO_2$ $[M+Na]^+$ 358.1025, found, 358.1023.

16. (Z)-1,1,1-trifluoro-4-(1-hydroxy-3-phenylpropan-2-ylamino)-4-phenylbut-3-en-2-one (3k)



Yield 150 mg (85%), mp 128–130 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.70–2.88 (m, 2H, CH_2), 3.51–3.60 (m, 2H, CH), 3.61–3.64 (m, 1H, CH_2), 5.11 (s, 1H, CH), 5.28–5.30 (m, 1H, OH), 6.93-6.95 (m, 4H, CH_{Ar}), 7.21–7.22 (m, 3H, CH_{Ar}), 7.34–7.38 (m, 2H, CH_{Ar}), 7.44–7.47 (m, 1H, CH_{Ar}), 11.14 (d, 1H, *J* 9.78 Hz, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 38.1 (CH_2), 59.2 (CH_2), 62.7 (CH), 88.9 (CH), 117.5 (q, *J* 288 Hz, CF_3), 126.5, 127.1, 128.3, 128.5, 129.3, 130.1, 133.5, 137.54, 170.7, 173.8. ^{19}F NMR (376 MHz, DMSO-d_6) −75.43. IR (film, cm^{-1}) 1604 (C=O), 3398 (OH). HRMS (ESI) (*m*/*z*): calcd for $C_{19}H_{18}F_3NNaO_2$ $[M + Na]^+$ 372.1182, found, 372.1179.

17. Fragmentation of ynone (1a)

A mixture of ynone (**1a**) (0.5 mmol) and 2-(methylamino) ethanol (**2a**) (1 mmol) in ethanol (0.5 mL) was stirred at 80 °C for 8 h. Solvent was removed under reduced pressure, crude reaction mixture was purified by column chromatography (ethyl acetate/hexane) to give pure products.

18. Acetophenone (4a)

Yield 20 mg (33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (s, 3H), 7.46–7.49 (m, 2H), 7.96–7.98 (m, 2H), 7.57–7.59 (m, 1H) [13].

19. 2,2,2-Trifluoro-*N*-(2-hydroxyethyl)-*N*-methylacetamide (5)

Yield 40 mg (47%). Colorless oil which becomes pale yellow upon standing. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H), 3.10–3.13 (m, 2H), 3.84–3.86 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.5 (NCH_3), 51.7 (CH_2), 53.5 (CH_2), 116.5 (q, *J* 291 Hz, CF_3), 161.6 (C1). ^{19}F NMR (376 MHz, DMSO-d_6) −74.29 [14].

20. Fragmentation of amino enone 3c

The solution of amino enone **3c** (60 mg) (0.2 mmol) in ethanol (0.5 mL) was stirred at 100 °C for 28 h. Then solvents were removed *in vacuo* and crude reaction mixture was purified by column chromatography (ethyl acetate/hexane) to give pure products.

21. 1-(4-Methoxyphenyl)ethanone (4c)

Yield 17 mg (56%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.56 (s, 3 H), 3.83 (s, 3H, OCH_3), 7.02 (d, *J* 8 Hz, 2H), 7.92 (d, *J* 8 Hz, 2H) [15].

22. 2,2,2-Trifluoro-*N*-(2-hydroxyethyl)-*N*-methylacetamide (5)

Yield 16 mg (50%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.60 (s, 3H), 3.11–3.14 (m, 2H), 3.80–3.82 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 33.6 (NCH_3), 51.8 (CH_2), 53.7 (CH_2), 116.4 (q, *J* 291 Hz, CF_3), 161.6. ^{19}F NMR (376 MHz, DMSO-d_6) −74.32 [14].

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