Synthesis of aminoalkylpyrazoles and -isoxazoles from cyclic β-(trifluoroacetyl) enamines

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A method for the synthesis of cyclic β-(trifluoroacetyl) enamines was proposed. Reactions of the latter with hydrazine and hydroxylamine gave pyrazoles and isoxazoles, respectively, containing trifluoromethyl and ω-aminoalkyl fragments. Addition of hydrazine (hydroxylamine) to the above amino enones was regiospecific, the regiochemistry of the heterocyclization of trifluoromethyl ketones being different from that for nonfluorinated analogs.

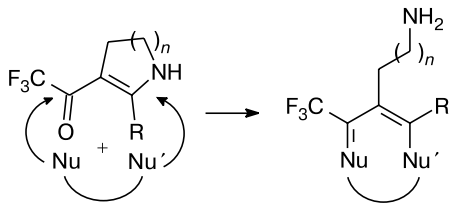
Key words: α,β-enones, enamines, pyrazoles, isoxazoles, hydrazines, hydroxylamine, organofluorine compounds, heterocyclization.

β-Aryl(hetaryl)alkylamines are important objects of organic and medicinal chemistry because of their high biological activities due to efficient interactions of such compounds with serotoninergic, adrenergic, and other types of receptors. Recently,[1,2] it has been confirmed that β-aryl(hetaryl)alkylamines take part in the operation of the cardiovascular system and regulate some processes, including the desynchronization of biological rhythms, the disruption of the sleep cycles, and the formation of mental disorders and depressive states.

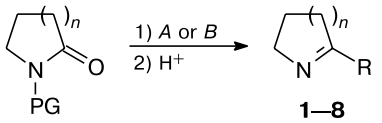
α,β-Unsaturated trifluoromethyl ketones are suitable building blocks for introduction of a trifluoromethyl group into various classes of acyclic, carbocyclic, and heterocyclic compounds; however, their properties have not been extensively studied hitherto.[3—5] The goal of the present work was to obtain β-aminosubstituted α,β-unsaturated trifluoromethyl ketones of cyclic series and investigate their reactions with polynucleophiles. These compounds feature the simultaneous presence of two fragments of synthetic interest: the trifluoroacetyl group and the cyclic enamine fragment. The latter is incorporated in the conjugated system of an α,β-unsaturated carbonyl compound and can participate in heterocyclization, converting itself to the ω-aminoalkyl group.[6] Thus, reactions of such compounds with binucleophiles can open up a concise and efficient route to heterocycles containing both trifluoromethyl and ω-aminoalkyl fragments (Scheme 1).

For the synthesis of the target trifluoroacetyl enamines, we used cyclic imines **1**—**8**, which were prepared in good yields from protected lactams by addition of organolithium compounds or by condensation with carboxylic acid esters followed by acid hydrolysis[7,8] (Scheme 2).

Scheme 1



Scheme 2



1—8

A. RLi; *B*. RCO_2Alk/NaH

Compound	*n*	R	PG	Method	Yield (%)
1	1	Ph	$CH=CH_2$	*A*	67
2	1	4-$Me_2NC_6H_4$	$CH=CH_2$	*A*	66
3	1	4-$MeOC_6H_4$	$CH=CH_2$	*A*	59
4	1	5-Methylthienyl	$CH=CH_2$	*A*	50
5	1	Bu^t	$CH=CH_2$	*B*	67
6	1	Me	$CH=CH_2$	*B*	38
7	2	Ph	$CH(OEt)_2$	*A*	83
8	3	Ph	$CH=CH_2$	*A*	59

Direct electrophilic trifluoroacetylation of alkenes is a convenient method for the synthesis of α,β-unsaturated trifluoromethyl ketones.[9] We initially chose this approach for trifluoroacetylation of cyclic imines. It is known[10] that *N*-alkenylsulfonamides can be acylated with trifluoro-

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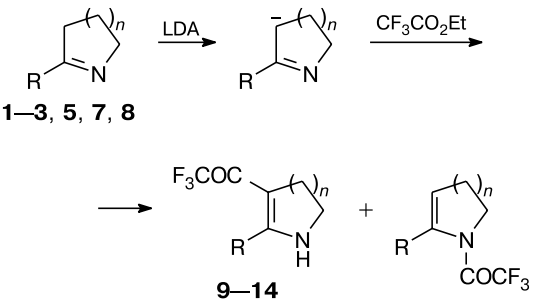
acetic anhydride in pyridine. Unexpectedly, treatment of cyclic imines with two equivalents of trifluoroacetic anhydride in pyridine gave *N*-trifluoroacetyl derivatives only.[11] Further *C*-trifluoroacetylation was probably prevented by the strong CF_3CO acceptor, which substantially lowers the nucleophilicity of the double bond. Variations in the solvent ($CHCl_3$, CH_2Cl_2, CH_2ClCH_2Cl, MeCN, and DMF), the reaction temperature, and the base, as well as conducting the reaction steps as separate processes, were unsuccessful.

Because of this, we employed an alternative one-step approach based on trifluoroacetylation of enamides of alkali metals. This approach has been once applied to the synthesis of trifluoroacetyl derivatives of cyclic imines.[12] Trifluoroacetylation of lithium enamide (prepared by treatment of an imine with lithium diisopropylamide (LDA) at 10 °C) gave a mixture of *C*- and *N*-trifluoroacetylation products in the ratio 9 : 1 (Scheme 3). The *N*-trifluoroacetyl derivative can be easily removed by washing with benzene. We found it indispensable to use at least two equivalents of a metalation agent; otherwise, the yield of the product did not exceed 35—40%. This is due to the protonation of the enamide by the resulting amino enone, which has a higher acidity than that of the starting imine, and elimination of the enamide from the reaction zone. The second equivalent of LDA converts the trifluoroacetylation product into the lithium salt, which keeps the imine deprotonated. The use of *N*,*N*-dimethyltrifluoroacetamide, as well as lithium hexamethyldisilazide as a metalation agent, did not increase the yields.

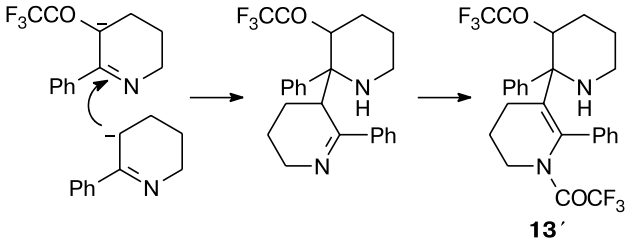
Scheme 3



Compound	*n*	R	Yield (%)
9	1	Ph	64
10	1	4-$Me_2NC_6H_4$	60
11	1	4-$MeOC_6H_4$	53
12	1	Bu^t	27
13	2	Ph	67
14	3	Ph	41

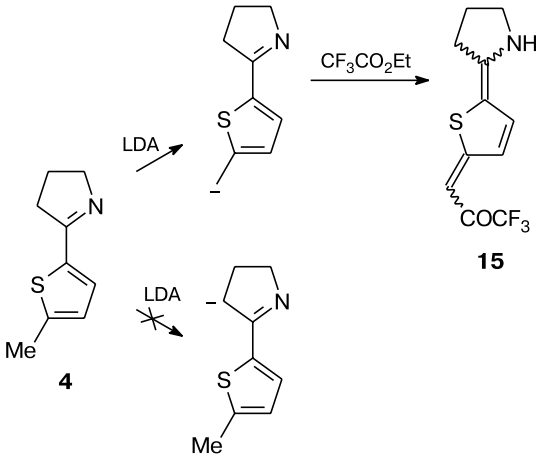
In the trifluoroacetylation of 6-phenyl-2,3,4,5-tetrahydropyridine (**7**), the yield of the target amino enone **13** was only 35% because of the formation of 25% by-product **13′** when the concentration of the starting imine in the reaction mixture was 0.2 mol L^{-1} (Scheme 4). The use of higher dilution increased the yield of product **13** to 67%.

Scheme 4



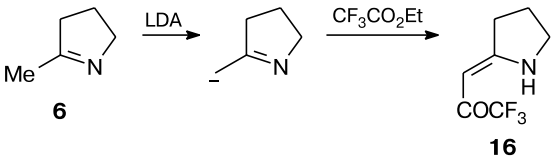
Interestingly, the trifluoroacetylation of 5-(5-methyl-2-thienyl)-3,4-dihydro-2*H*-pyrrole (**4**) occurred at the methyl group of the thiophene ring and was accompanied by migration of the double bonds to give compound **15** in 39% yield (Scheme 5).

Scheme 5



The trifluoroacetylation of 5-methyl-3,4-dihydro-2*H*-pyrrole (**6**) also involved the methyl group; the yield of the resulting exocyclic amino enone **16** was 78% (Scheme 6).

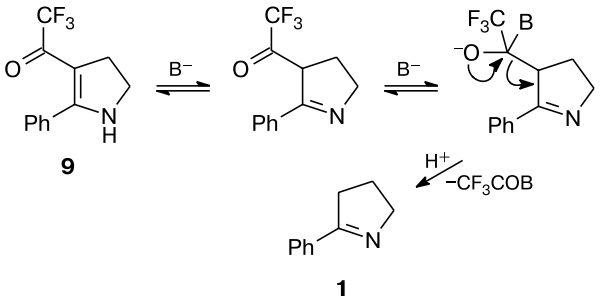
Scheme 6



First attempts to carry out reactions of the amino enones obtained with various binucleophiles (urea derivatives, semicarbazide, thiosemicarbazide, amidines, and 3-aminopyrazoles) resulted only in their *C*-deacylation to

the corresponding starting cyclic imines (^{1}H and ^{13}C NMR data). Such a behavior can be explained by the lability of these amino enones in the presence of bases. For instance, the room-temperature decomposition of compound **9** by sodium methoxide in methanol to imine **1** was completed in 1 h (Scheme 7).

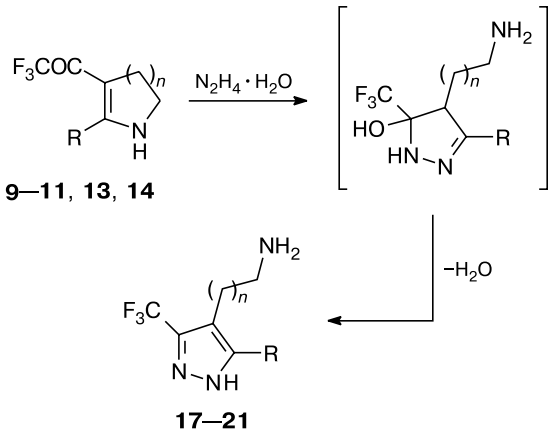
Scheme 7



B$^-$ is a base

We did manage to find the heterocyclization conditions. It turned out that the reaction pathway depends on both the particular polynucleophile and the starting amino enone. Reactions of compounds **9**—**11**, **13**, and **14** with hydrazine gave the corresponding pyrazoles (Scheme 8). The reaction conditions strongly depend on the ring size in the starting amino enone. For instance, for five-membered cycles, the reaction occurred in ethanol at room temperature. Subsequent acid treatment of the reaction mixture afforded the target pyrazoles in high yields as the sole product.

Scheme 8



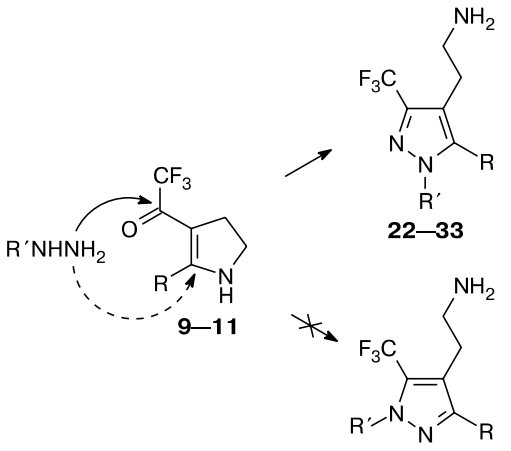
Compound	*n*	R	Yield (%)
17	1	Ph	91
18·2HCl	1	4-$Me_2NC_6H_4$	89
19·HCl	1	4-$MeOC_6H_4$	92
20·HCl	2	Ph	87
21	3	Ph	73

For compound **13** containing a six-membered ring, ~1-h refluxing was required. Under analogous conditions, a reaction with seven-membered amino enone **14** gave the corresponding cyclic imine as the result of deacylation. However, the reaction in boiling acetic acid in the presence of HCl afforded pyrazole **21** in 73% yield.

In a reaction of amino enone **9** (R = Ph) with hydrazine, intermediate hydroxypyrazoline was detected (^{1}H and ^{13}C NMR data). This compound is sufficiently stable at room temperature since the presence of the trifluoromethyl substituent stabilizes amino alcohol and *gem*-diol fragments.[4] However, we failed to isolate this hydroxypyrazoline in the individual state because of the presence of pyrazole **17**.

Reactions of ketones **9**—**11** with phenylhydrazine in ethanol yielded mixtures of products. Acetic acid as a solvent proved to ensure the best chemoselectivity of the reaction. The presence of two electrophilic centers in the amino enone molecule suggests that the reaction with phenylhydrazine can produce two regioisomers (Scheme 9). Nevertheless, only one of them was obtained in each case (compounds **22**, **29**, and **30**), *via* addition of phenylhydrazine to the trifluoroacetyl fragment of amino ketones **9**—**11**. Variation of the aryl substituent in arylhydrazine showed that the lowering of the nucleophilicity

Scheme 9



Compound	R	R′	Yield (%)
22	Ph	Ph	85
23·HCl	Ph	4-BrC_6H_4	90
24·HCl	Ph	3-ClC_6H_4	92
25·HCl	Ph	3-$CF_3C_6H_4$	60
26·HCl	Ph	2,4-$F_2C_6H_3$	82
27·HCl	Ph	4-$MeOC_6H_4$	91
28·HCl	Ph	Benzodioxan-6-yl	92
29·2HCl	4-$Me_2NC_6H_4$	Ph	90
30·HCl	4-$MeOC_6H_4$	Ph	88
31·HCl	Ph	Me	84
32·2HCl	4-$Me_2NC_6H_4$	Me	82
33·HCl	4-$MeOC_6H_4$	Me	77

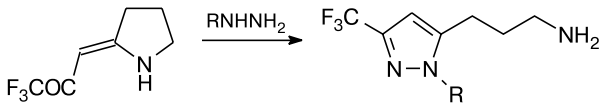
increases the reaction time and decreases the yield; however, the reaction keeps regiospecific (see Scheme 9, compounds **23**—**28**).

Heterocyclization with methylhydrazine required still more drastic conditions (CH_3COOH + conc. HCl); under less acidic conditions, amino enones decomposed only (two N atoms in methylhydrazine are known to differ in nucleophilicity much less than those in arylhydrazines). However, the reaction was also regiospecific (^1H and ^{13}C NMR data), giving the corresponding 1-methyl-3-trifluoromethylpyrazoles **31**—**33** as the sole products. Thus, the regiospecificity of heterocyclization of methyl- and arylhydrazines with the amino enones under study is of general character and allows one to obtain *N*-substituted pyrazoles containing the trifluoromethyl substituent in position 3.

In the ^{13}C NMR spectra of pyrazoles **22**—**33**, the signal for the C(3) atom appears at δ 139—140 as a quadruplet with $^2J_{C,F}$ = 34—37 Hz, which agrees well with the published data on the chemical shifts of the C(3) atom in 1-aryl-3-trifluoromethylpyrazoles (δ 140—143).[13—15] Note that the chemical shift of the C(3) atom in isomeric 1-aryl-5-trifluoromethylpyrazoles (see Scheme 9) was δ 129—134.[16,17] This allows unambiguous determination of the regiochemistry of heterocyclization from ^{13}C NMR spectra. An analogous pattern was observed for *N*-methylpyrazoles.

Reactions of exocyclic amino enone **16** with phenyl- and methylhydrazines gave pyrazoles **34** and **35** containing the 3-aminopropyl substituent in position 5 (Scheme 10).

Scheme 10

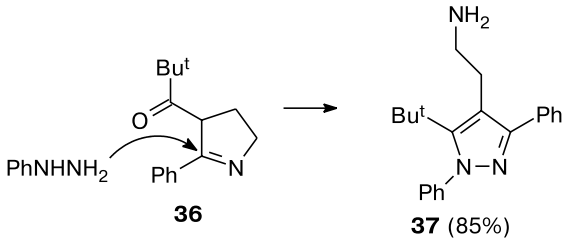


16

34: R = Ph (83%)
35: R = Me (71%)

The behavior of the trifluoromethyl derivatives in various reactions can often differ radically from the behavior of nonfluorinated analogs. For this reason, we compared the site of initial nucleophilic attack for a fluorinated compound and its nonfluorinated analog **36**, which has similar steric demands of the substituent[4] and was prepared analogously through lithium enamide. The reaction of compound **36** with phenylhydrazine proved to be regiospecific (Scheme 11), yielding pyrazole **37** with the *tert*-butyl group in position 5 (NOESY data). Therefore, phenylhydrazine adds to the imine fragment rather than the carbonyl group (*i.e.*, the regiochemistry of the heterocyclization is inverse with respect to trifluoromethyl derivatives). It should be noted that compound **36** exists as the oxo imine tautomer, in contrast to fluorinated analogs existing as the amino enone tautomer (^1H and ^{13}C NMR data).

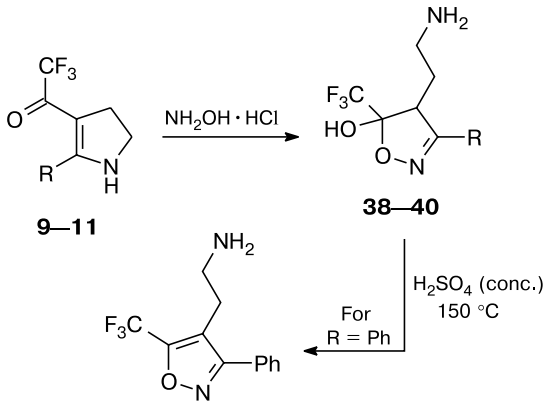
Scheme 11



36 **37** (85%)

Reactions of amino enones **9**—**11** with hydroxylamine hydrochloride in ethanol gave hydroxyisoxazolines **38**—**40** (Scheme 12). In this case, the substrate is initially attacked by the oxygen center of hydroxylamine (the chemical shift of the C(5) atom at δ 106—108). According to ^1H NMR data, only one diastereomer of isoxazolines **38**—**40** was obtained. These products are highly resistant to the action of dehydrating agents: the corresponding isoxazoles were not obtained on refluxing in toluene with *p*-toluenesulfonic acid, or on heating at 80 °C with conc. H_2SO_4, or in the presence of polyphosphoric acid. However, prolonged heating of compound **38** in conc. H_2SO_4 at 150 °C gave isoxazole derivative **41** in high yield.

Scheme 12



9—11

38—40

41 (93%)

Compound	R	Yield (%)
38	Ph	97
39	4-$Me_2NC_6H_4$	95
40	4-$MeOC_6H_4$	95

In conclusion, we discovered a route to cyclic β-(trifluoroacetyl) enamines *via* trifluoroacetylation of lithium enamides prepared from the corresponding cyclic imines. The reactions of β-(trifluoroacetyl) enamines with

hydrazines and hydroxylamine were found to be regiospecific; the regiochemistry of the heterocyclization of trifluoromethyl ketones differs from that for nonfluorinated analogs. We proved that the reaction proceeds through intermediate hemiaminals and hemiacetals; such isoxazole derivatives can be isolated in the individual state. We developed the method for the synthesis of pyrazoles and isoxazoles that simultaneously contain trifluoromethyl and ω-aminoalkyl fragments.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ and DMSO-d_6 with Me_4Si as the internal standard. IR spectra were recorded on a UR-20 spectrophotometer in thin films for liquids and in Nujol for solids. TLC analysis was carried out on Merck 60 F_{254} plates; spots were visualized with an acidified solution of $KMnO_4$ and the iodine vapor. For preparative chromatography, Merck 63-200 mesh silica gel was used.

5-Aryl-3,4-dihydro-2*H*-pyrroles were prepared according to known procedures.[7,8]

5-Phenyl-3,4-dihydro-2*H*-pyrrole (1). The yield was 67%, large reddish crystals, R_f 0.45 (hexane—ethyl acetate, 1 : 1), m.p. 43 °C, b.p. 85—95 °C (2 Torr) (*cf.* Ref. 18: m.p. 44 °C, b.p. 116—118 °C (8 Torr)).

5-(4-Dimethylaminophenyl)-3,4-dihydro-2*H*-pyrrole (2). The yield was 66%, colorless crystals, R_f 0.38 (MeCN—NH_3, 50 : 1), b.p. 130—145 °C (2 Torr), m.p. 140—141 °C. Found (%): C, 76.21; H, 8.39. $C_{12}H_{16}N_2$. Calculated (%): C, 76.55; H, 8.57. IR, ν/cm^{-1}: 1590 (C=N). ^{1}H NMR ($CDCl_3$), δ: 7.71 (d, 2 H, H arom., J = 8.0 Hz); 6.67 (d, 2 H, H arom., J = 8.9 Hz); 3.99 (m, 2 H, CH_2); 2.98 (s, 6 H, 2 Me); 2.87, 1.97 (both m, 2 H each, CH_2). ^{13}C NMR ($CDCl_3$), δ: 172.78 (CN); 151.63, 128.84, 122.56, 111.33 (C arom.); 60.99 (CH_2); 40.12 (2 Me); 34.56, 22.65 (both CH_2).

5-(4-Methoxyphenyl)-3,4-dihydro-2*H*-pyrrole (3). The yield was 59%, R_f 0.47 (hexane—ethyl acetate, 1 : 1), b.p. 121—125 °C (2 Torr), m.p. 75 °C (*cf.* Ref. 19: m.p. 74 °C).

5-(5-Methyl-2-thienyl)-3,4-dihydro-2*H*-pyrrole (4). The yield was 50%, R_f 0.52 (hexane—ethyl acetate, 1 : 1), b.p. 95—103 °C (2 Torr), m.p. 54—56 °C. Found (%): C, 64.92; H, 6.91. $C_9H_{11}NS$. Calculated (%): C, 65.41; H, 6.71. IR, ν/cm^{-1}: 1590 (C=N). ^{1}H NMR ($CDCl_3$), δ: 7.07 (m, 1 H, H of thiophene); 6.68 (d, 1 H, H of thiophene); 3.96, 2.85 (both m, 2 H each, CH_2); 2.46 (s, 3 H, Me); 1.98 (m, 2 H, CH_2). ^{13}C NMR ($CDCl_3$), δ: 167.69 (CN); 143.84, 137.19, 129.18, 125.57 (C arom.); 61.00, 35.06, 22.81 (all CH_2); 15.52 (Me).

5-*tert*-Butyl-3,4-dihydro-2*H*-pyrrole (5). The yield was 67%, R_f 0.28 (hexane—ethyl acetate, 1 : 1), b.p. 53 °C (15 Torr). ^{1}H NMR ($CDCl_3$), δ: 3.73, 2.46 (both t, 2 H each, CH_2, J = 7.4 Hz); 1.78 (m, 2 H, CH_2); 1.10 (s, 9 H, 3 Me). The ^{1}H NMR spectrum was identical with the earlier reported one.[20]

5-Methyl-3,4-dihydro-2*H*-pyrrole (6). The yield was 38%, R_f 0.25 (hexane—ethyl acetate, 1 : 1), b.p. 88—96 °C (760 Torr), n_D^{20} 1.4307 (*cf.* Ref. 21: b.p. 94 °C (760 Torr); *cf.* Ref. 22: n_D^{20} 1.4296).

6-Phenyl-2,3,4,5-tetrahydropyridine (7). The yield was 83%, R_f 0.55 (hexane—ethyl acetate, 1 : 1). ^{1}H NMR ($CDCl_3$), δ: 7.73—7.77 (m, 2 H, H arom.); 7.34—7.37 (m, 3 H, H arom.); 3.82, 2.61, 1.82, 1.66 (all m, 2 H each, CH_2). The ^{1}H NMR spectrum was identical with the earlier reported one.[23]

7-Phenyl-3,4,5,6-tetrahydro-2*H*-azepine (8). The yield was 59%, R_f 0.67 (hexane—ethyl acetate, 1 : 1), n_D^{20} 1.5660 (*cf.* Ref. 24: b.p. 139—141 °C (9 Torr), n_D^{20} 1.5650).

Acylation of cyclic imines (general procedure). A solution of imine **1**—**8** (0.025 mol) in anhydrous THF (20 mL) was added in one portion under argon at 0 °C to a stirred solution of LDA prepared from diisopropylamine (5.05 g, 0.05 mol) and a 2.5 *M* solution of Bu^{n}Li (20 mL, 0.05 mol) in anhydrous THF (100 mL). The reaction mixture was kept at 10 °C for 30 min and cooled to −80 °C, whereupon ethyl trifluoroacetate (0.0625 mol) was added in one portion. The solution was kept at −30 °C for several hours (monitoring by TLC) and quenched with a saturated solution of NH_4Cl. The organic phase was separated and the product was extracted from the aqueous phase with ether (2×50 mL). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator. The residue was triturated with a small amount of benzene. The resulting crystals were filtered off and dried *in vacuo*.

2,2,2-Trifluoro-1-(2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)ethanone (9). The yield was 64%, bright yellow crystals, R_f 0.42 (hexane—ethyl acetate, 1 : 1), m.p. 140—141 °C. Found (%): C, 58.97; H, 4.14. $C_{12}H_{10}F_3NO$. Calculated (%): C, 59.75; H, 4.18. IR, ν/cm^{-1}: 3210 (NH), 1600 (CO), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.36—7.52 (m, 5 H, H arom.); 5.37 (br.s, 1 H, NH); 3.79, 3.19 (both t, 2 H each, CH_2, J = 10.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 171.90 (q, CO, J = 32.3 Hz); 169.81 (quaternary C); 130.70, 128.40, 127.89 (C arom.); 118.07 (q, CF_3, J = 292.9 Hz); 100.30 (quaternary C); 46.54 (CH_2); 27.67 (q, CH_2, J = 3.2 Hz).

1-[2-(4-Dimethylaminophenyl)-4,5-dihydro-1*H*-pyrrol-3-yl]-2,2,2-trifluoroethanone (10). The yield was 60%, bright yellow crystals, R_f 0.75 (MeCN—NH_3, 50 : 1), m.p. 181—182 °C. Found (%): C, 58.57; H, 5.17. $C_{14}H_{15}F_3N_2O$. Calculated (%): C, 59.15; H, 5.32. IR, ν/cm^{-1}: 3200 (NH), 1610 (CO), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.71 (br.s, 1 H, NH); 7.49, 6.67 (both d, 2 H each, H arom., J = 8.9 Hz); 3.65 (t, 2 H, CH_2, J = 9.5 Hz); 2.97 (s, 6 H, 2 Me); 2.97 (t, 2 H, CH_2, J = 9.5 Hz). ^{13}C NMR (DMSO-d_6), δ: 170.19 (quaternary C); 167.98 (q, CO, J = 30 Hz); 152.16, 130.78 (C arom.); 118.80 (q, CF_3, J = 293.0 Hz); 116.56, 110.20 (C arom.); 96.62 (quaternary C); 45.51 (CH_2); 40.07 (2 Me); 27.35 (CH_2).

2,2,2-Trifluoro-1-[2-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrrol-3-yl]ethanone (11). The yield was 53%, bright yellow crystals, R_f 0.65 (hexane—ethyl acetate, 1 : 1), m.p. 161—162 °C. Found (%): C, 57.13; H, 4.64. $C_{13}H_{12}F_3NO_2$. Calculated (%): C, 57.57; H, 4.46. IR, ν/cm^{-1}: 3180 (NH), 1590 (CO), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.46, 6.83 (both d, 2 H each, H arom., J = 8.6 Hz); 6.00 (br.s, 1 H, NH); 3.80 (s, 3 H, Me); 3.67, 3.10 (both t, 2 H each, CH_2, J = 9.6 Hz). ^{13}C NMR (DMSO-d_6), δ: 169.71 (quaternary C); 168.70 (q, CO, J = 30.0 Hz); 161.27, 130.82, 122.55 (C arom.); 118.45 (q, CF_3, J = 292.6 Hz); 113.05 (C arom.); 97.81 (quaternary C); 55.34 (Me); 45.87, 27.18 (both CH_2).

1-(2-*tert*-Butyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2,2,2-trifluoroethanone (12). The yield was 27%, colorless crystals, R_f 0.8 (hexane—ethyl acetate, 1 : 1), m.p. 175—176 °C. Found (%):

C, 54.11; H, 6.52. $C_{10}H_{14}F_3NO$. Calculated (%): C, 54.29; H, 6.38. IR, ν/cm^{-1}: 3330 (NH), 1600 (CO), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.53 (br.s, 1 H, NH); 3.56, 2.89 (both t, 2 H each, CH_2, J = 9.5 Hz); 1.28 (s, 9 H, 3 Me). ^{13}C NMR (DMSO-d_6), δ: 182.11 (quaternary C); 166.69 (q, CO, J = 30.0 Hz); 118.97 (q, CF_3, J = 293.1 Hz); 97.03 (quaternary C); 45.66 (CH_2); 34.60 (quaternary C); 26.55 (q, CH_2, J = 4.3 Hz); 26.03 (3 Me).

2,2,2-Trifluoro-1-(2-phenyl-1,4,5,6-tetrahydropyridin-3-yl)ethanone (13). The reaction was carried out in anhydrous THF (500 mL). The yield was 67%, yellow crystals, R_f 0.48 (hexane—ethyl acetate, 1 : 1), m.p. 189—190 °C. Found (%): C, 61.47; H, 5.10. $C_{13}H_{12}F_3NO$. Calculated (%): C, 61.17; H, 4.74. IR, ν/cm^{-1}: 3270 (NH), 1620 (CO), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.40 (m, 3 H, H arom.); 7.27 (m, 2 H, H arom.); 5.13 (br.s, 1 H, NH); 3.42 (m, 2 H, CH_2); 2.68 (t, 2 H, CH_2, J = 6.0 Hz); 1.97 (m, 2 H, CH_2). ^{13}C NMR ($CDCl_3$), δ: 173.30 (q, CO, J = 30.0 Hz); 163.80 (quaternary C); 138.76, 129.19, 128.44, 128.20 (C arom.); 118.56 (q, CF_3, J = 293.0 Hz); 95.30 (quaternary C); 42.02 (CH_2); 22.10 (q, CH_2, J = 2.5 Hz); 21.16 (CH_2).

2,2,2-Trifluoro-1-[2-phenyl-2-(6-phenyl-1-trifluoroacetyl-1,2,3,4-tetrahydropyridin-5-yl)piperidin-3-yl]ethanone (13′). The reaction was carried out in anhydrous THF (100 mL). The yield was 35%, yellow crystals, R_f 0.75 (hexane—ethyl acetate, 1 : 1), m.p. 191—192 °C. Found (%): C, 60.94; H, 4.86. $C_{26}H_{24}F_6N_2O_2$. Calculated (%): C, 61.17; H, 4.74. IR, ν/cm^{-1}: 3390 (NH), 1690, 1650 (CO), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.25—7.43 (m, 8 H, H arom.); 7.02—7.04 (m, 2 H, H arom.); 5.59 (br.s, 1 H, NH); 4.79, 3.72, 3.12 (all m, 1 H each, H aliph.); 2.53 (m, 2 H, H aliph.); 2.34—2.40 (m, 1 H, H aliph.); 2.09—2.17 (m, 2 H, H aliph.); 1.92—1.67 (m, 5 H, H aliph.). ^{13}C NMR (DMSO-d_6), δ: 173.37 (q, CO, J = 30.0 Hz); 162.52; 157.07 (q, CO, J = 34.5 Hz); 138.34; 137.67; 128.85, 128.27, 128.05, 127.70, 127.38, 127.28 (C arom.); 117.72 (q, CF_3, J = 293.5 Hz); 116.40 (q, CF_3, J = 288.7 Hz); 96.12 (quaternary C); 70.96, 58.23, 43.41, 30.28, 23.56, 23.23, 21.23, 17.26 (C aliph.).

2,2,2-Trifluoro-1-(2-phenyl-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)ethanone (14). The yield was 41%, bright yellow crystals, R_f 0.31 (hexane—ethyl acetate, 1 : 1), m.p. 166—167 °C. Found (%): C, 62.46; H, 5.21. $C_{14}H_{14}F_3NO$. Calculated (%): C, 62.45; H, 5.24. IR, ν/cm^{-1}: 3280 (NH), 1610 (CO), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.47 (m, 1 H, H arom.); 7.37 (m, 4 H, H arom.); 5.25 (br.s, 1 H, NH); 3.63, 2.81 (both m, 2 H each, CH_2); 1.89 (m, 4 H, 2 CH_2). ^{13}C NMR ($CDCl_3$), δ: 178.73 (q, CO, J = 31.0 Hz); 169.23 (quaternary C); 138.95, 130.80, 129.11, 128.60 (C arom.); 117.79 (q, CF_3, J = 292.0 Hz); 103.39 (quaternary C); 46.89, 26.74, 26.60, 25.33 (all CH_2).

2-(Pyrrolidin-2-ylidene)-5-trifluoroacetylmethylidene-2,5-dihydrothiophene (15). The yield was 39%, bright red crystals, R_f 0.18 (hexane—ethyl acetate, 1 : 1), m.p. 260—262 °C (decomp.). Found (%): C, 49.97; H, 4.12. $C_{11}H_{10}F_3NOS$. Calculated (%): C, 50.57; H, 3.86. IR, ν/cm^{-1}: 2500—2800 (NH), 1630 (CO), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 10.63 (br.s, 1 H, NH); 7.75 (br.s, 1 H, H vinyl.); 6.77 (d, 1 H, H vinyl., J = 4.0 Hz); 6.16 (s, 1 H, H vinyl.); 3.75, 3.24 (both t, 2 H each, CH_2, J = 7.3 Hz); 2.12 (m, 2 H, CH_2). ^{13}C NMR (DMSO-d_6), δ: 167.28; 164.75 (q, CO, J = 26.4 Hz); 163.22; 140.82; 120.42; 119.45 (q, CF_3, J = 288.8 Hz); 113.85; 90.18; 50.04, 33.24, 21.15 (all CH_2).

(*Z*)-1,1,1-Trifluoro-3-(pyrrolidin-2-ylidene)propan-2-one (16). The yield was 78%, yellowish crystals, R_f 0.73 (hexane—ethyl acetate, 1 : 1), m.p. 90—92 °C. ^{1}H NMR ($CDCl_3$), δ: 10.18 (br.s, 1 H, NH); 5.43 (s, 1 H, H vinyl.); 3.70 (t, 2 H, CH_2, J = 7.1 Hz); 2.75 (t, 2 H, CH_2, J = 7.8 Hz); 2.08 (m, 2 H, CH_2) (*cf.* Ref. 12: m.p. 88—90 °C, identical ^{1}H NMR spectrum).

2,2-Dimethyl-1-(5-phenyl-3,4-dihydro-2*H*-pyrrol-4-yl)propan-1-one (36). The yield was 74%, brown crystals, R_f 0.68 (hexane—ethyl acetate, 1 : 1), m.p. 54—56 °C. Found (%): C, 78.60; H, 8.22. $C_{15}H_{19}NO$. Calculated (%): C, 78.56; H, 8.35. IR, ν/cm^{-1}: 1690 (CO), 1620 (CN). ^{1}H NMR ($CDCl_3$), δ: 7.65 (m, 2 H, H arom.); 7.33 (m, 3 H, H arom.); 4.67 (m, 1 H, CH); 4.14, 4.04, 2.38, 1.97 (all m, 1 H each, CH_2); 1.25 (s, 9 H, 3 Me). ^{13}C NMR ($CDCl_3$), δ: 213.50 (CO); 171.34 (CN); 134.06, 130.03, 128.25, 127.45 (C arom.); 60.42 (CH); 54.44 (CH_2); 44.53 (quaternary C); 30.52 (CH_2); 26.87 (3 Me).

Reactions of amino enones 9—11 and 13 with hydrazine (general procedure). Hydrazine hydrate (0.05 g, 0.001 mol) was added to a solution of an amino enone (0.001 mol) in ethanol (15 mL). The reaction mixture was kept at ~20 °C for 30 min (monitoring by TLC), treated with conc. HCl (0.3 mL), and evaporated to dryness *in vacuo*. The residue was triturated with ether—EtOH (5 : 1, 5 mL). The product was filtered off and dried *in vacuo*. To isolate the free base, aminopyrazole hydrochloride was dissolved in water (10 mL) and treated with 25% NH_3 (1 mL). The precipitate that formed was filtered off, washed with a small amount of water, and dried *in vacuo*.

4-(2-Aminoethyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole (17). The yield was 91%, gray crystals, R_f 0.55 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 97—98 °C. Found (%): C, 56.47; H, 4.92. $C_{12}H_{12}F_3N_3$. Calculated (%): C, 56.47; H, 4.74. IR, ν/cm^{-1}: 3370, 3310 (NH_2), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.59 (d, 2 H, H arom., J = 7.5 Hz); 7.49 (t, 2 H, H arom., J = 7.5 Hz); 7.45 (t, 1 H, H arom., J = 7.5 Hz); 2.65 (m, 4 H, 2 CH_2) ^{13}C NMR (DMSO-d_6), δ: 142.18 (C of pyrazole); 139.65 (q, C of pyrazole, J = 35.0 Hz); 128.93, 128.85, 128.70, 127.84 (C arom.); 122.39 (q, CF_3, J = 269.0 Hz); 113.94 (C of pyrazole); 42.91, 27.00 (both CH_2).

4-(2-Aminoethyl)-5-(4-dimethylaminophenyl)-3-trifluoromethyl-1*H*-pyrazole dihydrochloride (18·2HCl). The yield was 89%, gray crystals, R_f 0.42 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 249—250 °C. Found (%): C, 45.57; H, 5.50. $C_{14}H_{19}Cl_2F_3N_4$. Calculated (%): C, 45.30; H, 5.16. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 13.70 (br.s, 1 H, NH^+); 8.32 (br.s, 3 H, NH_3^+); 7.43, 6.82 (both d, 2 H each, H arom., J = 8.8 Hz); 2.92—2.99 (m, 2 H, CH_2); 2.95 (s, 6 H, 2 Me); 2.79 (m, 2 H, CH_2). ^{13}C NMR (DMSO-d_6), δ: 150.31 (C arom.); 142.99 (C of pyrazole); 139.76 (q, C of pyrazole, J = 36.7 Hz); 128.61 (C arom.); 122.32 (q, CF_3, J = 269.6 Hz); 115.64, 112.47 (C arom.); 109.59 (C of pyrazole); 39.96 (2 Me); 39.03, 20.92 (both CH_2).

4-(2-Aminoethyl)-5-(4-methoxyphenyl)-3-trifluoromethyl-1*H*-pyrazole hydrochloride (19·HCl). The yield was 92%, gray crystals, R_f 0.60 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 275—276 °C. Found (%): C, 40.88; H, 5.19. $C_{13}H_{15}ClF_3N_3O\cdot\cdot 3H_2O$. Calculated (%): C, 41.55; H, 5.63. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.37 (br.s, 3 H, NH_3^+); 7.54, 7.05 (both d, 2 H each, H arom., J = 8.6 Hz); 3.79 (s, 3 H, Me); 2.95, 2.77 (both m, 2 H each, CH_2). ^{13}C NMR (DMSO-d_6), δ: 159.85 (C arom.); 142.55 (C of pyrazole); 139.77 (q, C of pyrazole, J = 35.1 Hz); 129.52 (C arom.); 122.33 (q, CF_3,

J = 268.6 Hz); 120.42, 114.63 (C arom.); 110.47 (C of pyrazole); 55.42 (Me); 40.17, 20.87 (both CH_2).

4-(3-Aminopropyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (20 · HCl). The reaction mixture was refluxed for 1 h. The yield was 87%, colorless crystals, R_f 0.56 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 290—292 °C. Found (%): C, 50.05; H, 5.26. $C_{13}H_{15}ClF_3N_3 \cdot 1/3H_2O$. Calculated (%): C, 50.09; H, 5.07. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.00 (br.s, 3 H, NH_3^+); 7.52 (m, 5 H, H arom.); 2.72 (m, 2 H, CH_2); 2.65 (t, 2 H, CH_2, J = 7.9 Hz); 1.75 (m, 2 H, CH_2). ^{13}C NMR (DMSO-d_6), δ: 141.84 (C of pyrazole); 139.60 (q, C of pyrazole, J = 35.0 Hz); 128.93, 128.85, 128.70, 127.84 (C arom.); 122.37 (q, CF_3, J = 269.0 Hz); 114.78 (C of pyrazole); 38.55, 28.57, 19.77 (all CH_2).

Reactions of amino enone 14 with hydrazine and of amino enones 9—11 and 36 with aryl- and methylhydrazines (general procedure). A suspension of hydrazine hydrochloride in HCl was added to a boiling solution of an amino enone (0.001 mol) in a mixture of glacial acetic acid (10 mL) and conc. HCl (1 mL). The reaction mixture was refluxed for 30 min and concentrated in a rotary evaporator. The residue was triturated with ether—EtOH (5 : 1, 5 mL). The product was filtered off and dissolved in water (20 mL). The resulting solution was treated with 25% NH_3 (1 mL). The crystals that formed were filtered off, washed with a small amount of water, and dried *in vacuo*.

4-(4-Aminobutyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole (21). The yield was 73%, grayish crystals, R_f 0.65 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 122—123 °C. Found (%): C, 58.45; H, 5.51. $C_{14}H_{16}F_3N_3 \cdot 1/3H_2O$. Calculated (%): C, 58.12; H, 5.81. IR, ν/cm^{-1}: 3340, 3280 (NH_2), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.44 (m, 3 H, H arom.); 7.32 (m, 2 H, H arom.); 2.61 (t, 2 H, CH_2, J = 8.0 Hz); 2.59 (t, 2 H, CH_2, J = 7.0 Hz); 1.48, 1.35 (both m, 2 H each, CH_2). ^{13}C NMR (DMSO-d_6), δ: 141.84 (C of pyrazole); 139.40 (q, C of pyrazole, J = 34 Hz); 129.06, 129.01, 128.72, 127.76 (C arom.); 122.50 (q, CF_3, J = 269.0 Hz); 116.22 (C of pyrazole); 41.20, 33.02, 28.16, 22.25 (all CH_2).

4-(2-Aminoethyl)-1,5-diphenyl-3-trifluoromethyl-1*H*-pyrazole (22). The yield was 85%, a colorless oil, R_f 0.53 (MeCN—EtOH—NH_3, 80 : 12 : 8). Found (%): C, 65.80; H, 5.31. $C_{18}H_{16}F_3N_3$. Calculated (%): C, 65.25; H, 4.87. IR, ν/cm^{-1}: 3400—3300 (NH_2), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.18—7.42 (m, 10 H, H arom.); 2.81, 2.71 (both t, 2 H each, CH_2, J = 7.4 Hz); 1.19 (br.s, 2 H, NH_2). ^{13}C NMR ($CDCl_3$), δ: 142.86 (C of pyrazole); 140.13 (q, C of pyrazole, J = 36.0 Hz); 138.99, 129.84, 129.01, 128.89, 128.67, 128.65, 127.70, 124.78 (C arom.); 121.87 (q, CF_3, J = 269.0 Hz); 116.97 (C of pyrazole); 42.78, 27.38 (both CH_2).

4-(2-Aminoethyl)-1-(4-bromophenyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (23 · HCl). The yield was 90%, white crystals, R_f 0.55 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 205—206 °C. Found (%): C, 45.96; H, 3.38. $C_{18}H_{16}BrClF_3N_3 \cdot H_2O$. Calculated (%): C, 46.52; H, 3.90. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.29 (br.s, 3 H, NH_3^+); 7.58 (d, 2 H, H arom., J = 8.3 Hz); 7.44 (m, 3 H, H arom.); 7.34 (m, 2 H, H arom.); 7.19 (d, 2 H, H arom., J = 8.3 Hz); 2.81 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 143.88 (C of pyrazole); 139.88 (q, C of pyrazole, J = 35.8 Hz); 137.82, 132.08, 130.16, 129.61, 129.04, 127.57, 127.28 (C arom.); 121.75 (q, CF_3, J = 269.7 Hz); 121.55 (C arom.); 114.63 (C of pyrazole); 39.71, 20.89 (both CH_2).

4-(2-Aminoethyl)-1-(3-chlorophenyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (24 · HCl). The yield was 92%, white crystals, R_f 0.49 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 208—209 °C. Found (%): C, 49.84; H, 4.04. $C_{18}H_{16}Cl_2F_3N_3$. Calculated (%): C, 50.36; H, 4.46. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.26 (br.s, 3 H, NH_3^+); 7.52—7.33 (m, 8 H, H arom.); 7.20 (m, 1 H, H arom.); 2.82 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 144.00 (C of pyrazole); 139.75 (q, C of pyrazole, J = 36.0 Hz); 139.63, 133.14, 130.70, 130.14, 129.65, 129.00, 128.54, 127.47, 125.19, 123.97 (C arom.); 121.68 (q, CF_3, J = 269.5 Hz); 114.60 (C of pyrazole); 39.77, 20.83 (both CH_2).

4-(2-Aminoethyl)-5-phenyl-3-trifluoromethyl-1-(3-trifluoromethylphenyl)-1*H*-pyrazole hydrochloride (25 · HCl). The yield was 60%, white crystals, R_f 0.55 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 138—140 °C (decomp.). Found (%): C, 50.03; H, 3.85. $C_{19}H_{16}ClF_6N_3$. Calculated (%): C, 50.29; H, 4.00. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.29 (br.s, 3 H, NH_3^+); 7.73 (m, 1 H, H arom.); 7.32—7.68 (m, 8 H, H arom.); 2.83 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 144.16 (C of pyrazole); 140.16 (q, C of pyrazole, J = 36.4 Hz); 139.02, 130.55, 130.22, 129.72 (C arom.); 129.35 (q, C arom., J = 22.1 Hz); 129.09, 129.04, 127.45, 125.14 (C arom.); 123.33 (q, CF_3, J = 272.3 Hz); 121.85 (q, C arom., J = 3.7 Hz); 121.69 (q, CF_3, J = 270.0 Hz); 114.82 (C of pyrazole); 39.73, 20.84 (both CH_2).

4-(2-Aminoethyl)-1-(2,4-difluorophenyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (26 · HCl). The yield was 82%, white crystals, R_f 0.50 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 228—229 °C. Found (%): C, 48.94; H, 4.12. $C_{18}H_{15}ClF_5N_3 \cdot \cdot 2H_2O$. Calculated (%): C, 49.16; H, 4.35. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.27 (br.s, 3 H, NH_3^+); 7.69 (m, 1 H, H arom.); 7.37—7.45 (m, 4 H, H arom.); 7.31 (m, 2 H, H arom.); 7.21 (m, 1 H, H arom.); 2.73—2.93 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 162.46 (dd, C arom., J = 250.2 Hz, J = 11.5 Hz); 156.45 (dd, C arom., J = 252.3 Hz, J = 12.6 Hz); 145.65 (C of pyrazole); 140.40 (q, C of pyrazole, J = 35.8 Hz); 131.17 (d, C arom., J = 10.2 Hz); 129.68, 129.61, 128.86, 126.96 (C arom.); 123.04 (d, C arom., J = 16.9 Hz); 121.62 (q, CF_3, J = 269.5 Hz); 113.69 (C of pyrazole); 112.40 (d, C arom., J = 23.3 Hz); 105.10 (t, C arom., J = 23.5 Hz); 39.45, 20.68 (both CH_2).

4-(2-Aminoethyl)-1-(4-methoxyphenyl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (27 · HCl). The yield was 91%, grayish crystals, R_f 0.48 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 224—226 °C. Found (%): C, 57.30; H, 4.61. $C_{19}H_{19}ClF_3N_3O$. Calculated (%): C, 57.36; H, 4.81. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.24 (br.s, 3 H, NH_3^+); 7.42 (m, 3 H, H arom.); 7.31 (m, 2 H, H arom.); 7.17, 6.89 (both d, 2 H each, H arom., J = 8.7 Hz); 3.72 (s, 3 H, Me); 2.81 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 159.00 (C arom.); 143.85 (C of pyrazole); 139.15 (q, C of pyrazole, J = 36.0 Hz); 131.65, 130.16, 129.38, 128.89, 127.94, 126.90 (C arom.); 121.93 (q, CF_3, J = 270.5 Hz); 114.12 (C arom.); 113.96 (C of pyrazole); 39.93, 21.01 (both CH_2).

4-(2-Aminoethyl)-1-(2,3-dihydro-1,4-benzodioxan-6-yl)-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (28 · HCl). The yield was 92%, gray crystals, R_f 0.52 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 331—332 °C. Found (%): C, 56.12; H, 4.44. $C_{20}H_{19}ClF_3N_3O_2$. Calculated (%): C, 56.41; H, 4.50. IR, ν/cm^{-1}: 1300—1060 (CF_3).

^{1}H NMR (DMSO-d_6), δ: 8.25 (br.s, 3 H, NH_3^+); 7.51—7.28 (m, 5 H, H arom.); 6.80 (m, 2 H, H arom.); 6.68 (m, 1 H, H arom.); 4.20, 2.80 (both br.s, 4 H each, CH_2). ^{13}C NMR (DMSO-d_6), δ: 143.79; 143.48; 143.05; 139.17 (q, C of pyrazole, J = 35.0 Hz); 131.97, 130.13, 129.47, 128.93, 127.93 (C arom.); 121.89 (q, CF_3, J = 269.3 Hz); 118.48, 117.08, 114.47 (C arom.); 114.05 (C of pyrazole); 64.05 (2 CH_2); 40.15, 20.98 (both CH_2).

4-(2-Aminoethyl)-5-(4-dimethylaminophenyl)-1-phenyl-3-trifluoromethyl-1*H*-pyrazole dihydrochloride (29·2HCl). The yield was 90%, gray crystals, R_f 0.31 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 247—249 °C (decomp.). Found (%): C, 49.95; H, 5.34. $C_{20}H_{23}Cl_2F_3N_4 \cdot 2H_2O$. Calculated (%): C, 49.70; H, 5.63. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.19 (br.s, 3 H, NH_3^+); 7.35—7.41 (m, 3 H, H arom.); 7.25, 7.19 (both d, 2 H each, H arom., J = 8.3 Hz); 6.98 (m, 2 H, H arom.); 2.95 (s, 6 H, 2 Me); 2.81 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 172.04, 146.86 (C arom.); 143.42 (C of pyrazole); 139.62 (q, C of pyrazole, J = 36.1 Hz); 138.72, 131.49, 129.20, 128.66, 125.47 (C arom.); 121.92 (q, CF_3, J = 269.2 Hz); 117.55 (C arom.); 114.51 (C of pyrazole); 42.94 (2 Me); 39.09, 20.98 (both CH_2).

4-(2-Aminoethyl)-5-(4-methoxyphenyl)-1-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (30·HCl). The yield was 88%, gray crystals, R_f 0.53 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 182—183 °C. Found (%): C, 57.11; H, 4.88. $C_{19}H_{19}ClF_3N_3O$. Calculated (%): C, 57.36; H, 4.81. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.23 (br.s, 3 H, NH_3^+); 7.35—7.40 (m, 3 H, H arom.); 7.25 (m, 4 H, H arom.); 6.97 (d, 2 H, H arom., J = 8.8 Hz); 3.75 (s, 3 H, Me); 2.74—2.86 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 159.83 (C arom.); 143.79 (C of pyrazole); 139.47 (q, C of pyrazole, J = 35.9 Hz); 138.73, 131.59, 129.11, 128.51, 125.35 (C arom.); 121.92 (q, CF_3, J = 269.9 Hz); 119.78, 114.38 (C arom.); 114.22 (C of pyrazole); 55.22 (Me); 38.98, 20.99 (both CH_2).

4-(2-Aminoethyl)-1-methyl-5-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (31·HCl). The yield was 84%, gray crystals, R_f 0.62 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 113—115 °C. Found (%): C, 49.98; H, 5.33. $C_{13}H_{15}ClF_3N_3 \cdot 0.5H_2O$. Calculated (%): C, 49.61; H, 5.12. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.54—7.60 (m, 3 H, H arom.); 7.46—7.51 (m, 2 H, H arom.); 3.70 (s, 3 H, Me); 2.64—2.79 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 143.72 (C of pyrazole); 137.62 (q, C of pyrazole, J = 36.0 Hz); 129.92, 129.64, 129.18, 127.74 (C arom.); 122.01 (q, CF_3, J = 269.0 Hz); 113.09 (C of pyrazole); 39.48 (CH_2); 37.87 (Me); 21.01 (CH_2).

4-(2-Aminoethyl)-5-(4-dimethylaminophenyl)-1-methyl-3-trifluoromethyl-1*H*-pyrazole dihydrochloride (32·2HCl). The yield was 82%, gray crystals, R_f 0.60 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 281—282 °C (decomp.). Found (%): C, 45.57; H, 5.93. $C_{15}H_{21}Cl_2F_3N_4 \cdot 0.5H_2O$. Calculated (%): C, 45.70; H, 5.62. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.17 (br.s, 3 H, NH_3^+); 7.42 (d, 2 H, H arom., J = 8.2 Hz); 7.26 (br.s, 2 H, H arom.); 3.69 (s, 3 H, Me); 3.04 (s, 6 H, 2 Me); 2.64—2.78 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 147.60 (C arom.); 143.36 (C of pyrazole); 137.47 (q, C of pyrazole, J = 35.7 Hz); 131.16 (C arom.); 121.99 (q, CF_3, J = 269.6 Hz); 117.18 (C arom.); 113.07 (C of pyrazole); 42.62 (2 Me); 39.05 (CH_2); 37.82 (Me); 21.02 (CH_2).

4-(2-Aminoethyl)-5-(4-methoxyphenyl)-1-methyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (33·HCl). The yield was 77%, gray crystals, R_f 0.55 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 155—156 °C. Found (%): C, 47.13; H, 5.32. $C_{14}H_{17}ClF_3N_3O \cdot \cdot H_2O$. Calculated (%): C, 47.53; H, 5.41. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.23 (br.s, 3 H, NH_3^+); 7.41, 7.26 (both d, 2 H each, H arom., J = 8.3 Hz); 3.82, 3.68 (both s, 3 H each, Me); 2.64—2.77 (m, 4 H, 2 CH_2). ^{13}C NMR (DMSO-d_6), δ: 159.93 (C arom.); 143.51 (C of pyrazole); 137.27 (q, C of pyrazole, J = 35.2 Hz); 131.25 (C arom.); 121.90 (q, CF_3, J = 269.3 Hz); 119.55, 114.46 (C arom.); 112.79 (C of pyrazole); 55.27 (Me); 38.95 (CH_2); 37.64 (Me); 20.94 (CH_2).

5-(3-Aminopropyl)-1-phenyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (34·HCl). The yield was 83%, gray crystals, R_f 0.41 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 228—229 °C. Found (%): C, 47.91; H, 4.94. $C_{13}H_{15}ClF_3N_3$. Calculated (%): C, 48.23; H, 5.29. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.18 (br.s, 3 H, NH_3^+); 7.55 (m, 5 H, H arom.); 6.85 (s, 1 H, H of pyrazole); 2.77 (m, 4 H, 2 CH_2); 1.91 (m, 2 H, CH_2). ^{13}C NMR (DMSO-d_6), δ: 145.08 (C of pyrazole); 141.10 (q, C of pyrazole, J = 37.5 Hz); 138.36, 129.53, 129.12, 125.54 (C arom.); 121.59 (q, CF_3, J = 268.3 Hz); 103.71 (C of pyrazole); 37.91, 22.69, 18.59 (all CH_2).

5-(3-Aminopropyl)-1-methyl-3-trifluoromethyl-1*H*-pyrazole hydrochloride (35·HCl). The yield was 71%, gray crystals, R_f 0.57 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 178—179 °C. Found (%): C, 39.41; H, 5.11. $C_8H_{13}ClF_3N_3$. Calculated (%): C, 39.43; H, 5.38. IR, ν/cm^{-1}: 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 8.27 (br.s, 3 H, NH_3^+); 6.56 (s, 1 H, H of pyrazole); 3.81 (s, 3 H, Me); 2.78 (m, 4 H, 2 CH_2); 1.92 (m, 2 H, CH_2). ^{13}C NMR (DMSO-d_6), δ: 144.07 (C of pyrazole); 138.96 (q, C of pyrazole, J = 37.4 Hz); 121.65 (q, CF_3, J = 267.6 Hz); 102.62 (C of pyrazole); 37.91 (CH_2); 36.84 (Me); 21.65, 18.55 (both CH_2).

4-(2-Aminoethyl)-5-*tert*-butyl-1,3-diphenyl-1*H*-pyrazole (37). The yield was 85%, grayish crystals, R_f 0.46 (MeCN—NH_3, 50 : 1), m.p. 110—112 °C. Found (%): C, 75.01; H, 7.87. $C_{21}H_{25}N_3$. Calculated (%): C, 74.74; H, 8.06. IR, ν/cm^{-1}: 3360, 3300 (NH_2). ^{1}H NMR (DMSO-d_6), δ: 7.30—7.57 (m, 10 H, H arom.); 2.80, 2.64 (both m, 2 H each, CH_2); 1.22 (s, 9 H, 3 Me). ^{13}C NMR (DMSO-d_6), δ: 150.40; 148.20; 143.37; 134.24; 128.71; 128.50; 128.43; 128.22; 128.05; 127.28; 113.69 (C of pyrazole); 43.60 (CH_2); 33.17 (quaternary C); 31.36 (3 Me); 29.29 (CH_2).

Reactions of amino enones 9—11 with hydroxylamine (general procedure). Hydroxylamine hydrochloride (0.1 g, 0.0014 mol) was added to a solution of an amino enone (0.001 mol) in ethanol (15 mL). The reaction mixture was refluxed for 1 h. The solvent was removed in a rotary evaporator. The residue was dissolved in water (5 mL) and treated with 25% NH_3 (0.2 mL). The precipitate that formed was filtered off, washed with a small amount of water, and dried *in vacuo*.

4-(2-Aminoethyl)-5-hydroxy-3-phenyl-5-trifluoromethyl-4,5-dihydroisoxazole (38). The yield was 97%, white crystals, R_f 0.57 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 174—175 °C. Found (%): C, 52.52; H, 4.78. $C_{12}H_{13}F_3N_2O_2$. Calculated (%): C, 52.56; H, 4.78. IR, ν/cm^{-1}: 3500—3260 (NH_2, OH), 1620 (C=N), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.70—7.74 (m, 2 H, H arom.); 7.44—7.47 (m, 3 H, H arom.); 4.17 (dd, 1 H, CH, J = 6.6 Hz, J = 2.6 Hz); 2.59 (ddd, 1 H, CH_2, J = 13.1 Hz, J = 5.5 Hz, J = 2.0 Hz); 1.94—2.10 (m, 2 H, CH_2); 1.77 (ddt, 1 H, CH_2, J = 15.5 Hz, J = 11.2 Hz, J = 2.4 Hz). ^{13}C NMR

(DMSO-d_6), δ: 150.05 (C of isoxazoline); 130.21, 128.96, 128.90, 126.76 (C arom.); 123.73 (q, CF_3, J = 287.2 Hz); 107.50 (q, C of isoxazoline, J = 31.0 Hz); 48.57 (C of isoxazoline); 34.41 (Me); 26.68 (CH_2).

4-(2-Aminoethyl)-3-(4-dimethylaminophenyl)-5-hydroxy-5-trifluoromethyl-4,5-dihydroisoxazole (39). The yield was 95%, white crystals, R_f 0.42 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 180—181 °C. Found (%): C, 50.50; H, 5.91. $C_{14}H_{18}F_3N_3O_2 \cdot H_2O$. Calculated (%): C, 50.15; H, 6.01. IR, ν/cm^{-1}: 3620—3300 (NH_2, OH), 1600 (C=N), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.51, 6.72 (both d, 2 H each, H arom., J = 9.0 Hz); 4.08 (m, 1 H, CH); 2.94 (s, 6 H, 2 Me); 2.54—2.61 (m, 1 H, CH_2); 2.07, 1.96, 1.74 (all m, 1 H each, CH_2). ^{13}C NMR (DMSO-d_6), δ: 158.90 (C of isoxazoline); 151.34, 127.89 (C arom.); 123.85 (q, CF_3, J = 287.2 Hz); 115.67, 111.83 (C arom.); 106.30 (q, C of isoxazoline, J = 31.0 Hz); 48.88 (C of isoxazoline); 39.73 (CH_2); 34.36 (2 Me); 27.19 (CH_2).

4-(2-Aminoethyl)-5-hydroxy-3-(4-methoxyphenyl)-5-trifluoromethyl-4,5-dihydroisoxazole (40). The yield was 95%, white crystals, R_f 0.55 (MeCN—EtOH—NH_3, 80 : 12 : 8), m.p. 194—195 °C. Found (%): C, 50.93; H, 5.14. $C_{12}H_{13}F_3N_2O_2$. Calculated (%): C, 51.32; H, 4.97. IR, ν/cm^{-1}: 3600—3280 (NH_2, OH), 1610 (C=N), 1300—1060 (CF_3). ^{1}H NMR (DMSO-d_6), δ: 7.66, 7.00 (both d, 2 H each, H arom., J = 8.6 Hz); 4.15 (m, 1 H, CH); 3.78 (s, 3 H, Me); 2.56—2.61 (m, 1 H, CH_2); 2.06 (t, 1 H, CH_2, J = 11.9 Hz); 1.93—2.00 (m, 1 H, CH_2); 1.75 (d, 1 H, CH_2, J = 13.2 Hz). ^{13}C NMR (DMSO-d_6), δ: 160.74 (C arom.); 158.64 (C of isoxazoline); 128.42 (C arom.); 123.80 (q, CF_3, J = 287.2 Hz); 121.19, 114.44 (C arom.); 106.98 (q, C of isoxazoline, J = 30.9 Hz); 55.31 (Me); 48.74 (C of isoxazoline); 34.34, 26.87 (both CH_2).

4-(2-Aminoethyl)-3-phenyl-5-trifluoromethylisoxazole (41). A solution of hydroxyisoxazoline **38** (0.137 g, 0.0005 mol) in conc. H_2SO_4 (0.5 mL) was heated at 150 °C for 2 h. The reaction mixture was cooled, diluted with water (5 mL), and treated with 25% NH_3 (3 mL). The product was extracted from the resulting solution with CH_2Cl_2 (3×5 mL). The combined extracts were dried over Na_2SO_4, the solvent was removed, and the residue was dried *in vacuo*. The yield of compound **41** was 93%, a colorless oil, R_f 0.87 (MeCN—EtOH—NH_3, 80 : 12 : 8). Found (%): C, 56.01; H, 4.44. $C_{12}H_{11}F_3N_2O$. Calculated (%): C, 56.25; H, 4.33. IR, ν/cm^{-1}: 3400—3200 (NH_2), 1300—1060 (CF_3). ^{1}H NMR ($CDCl_3$), δ: 7.54—7.58 (m, 2 H, H arom.); 7.44—7.48 (m, 3 H, H arom.); 2.75 (s, 4 H, 2 CH_2); 1.52 (br.s, 2 H, NH_2). ^{13}C NMR ($CDCl_3$), δ: 163.59 (C of isoxazole); 154.90 (q, C of isoxazole, J = 40.4 Hz); 130.14, 128.96, 128.25, 127.64 (C arom.); 118.66 (q, CF_3, J = 270.9 Hz); 117.09 (C of isoxazole); 41.74, 25.79 (both CH_2).

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