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Chemoselective Synthesis of 1-Substituted 4-Amino-2-(trifluoromethyl)-1*H*-pyrroles through the Heterocyclization Reaction of 4-Methoxy-5-bromo-1,1,1-trifluoropent-3-en-2-ones with Amines

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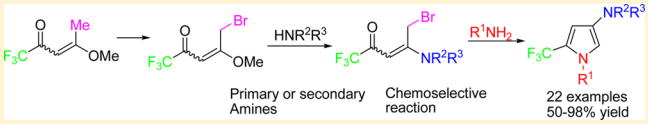
Supporting Information

ABSTRACT: A concise method to synthesize 1-substituted 4-amino-2-(trifluoromethyl)-1*H*-pyrroles from the heterocyclization reaction of 5-bromo-4-methoxy-1,1,1-trifluoropent-3-en-2-ones with amines is described. This method has the following advantages: it uses a wide range of primary amines, starting materials are easily available, it is simple to perform, the reaction conditions are mild, it is environmentally friendly, and it furnishes yields of up to 98%.



INTRODUCTION

The development of methodologies for the synthesis of pyrroles has received much attention recently, due to this class of compounds possessing one of the most important scaffolds among heterocyclic compounds, which are often found in many natural products, pharmaceuticals, and functional materials.[1] Pyrroles have been widely used as antitumor,[2] anti-inflammatory,[3] antibacterial,[3c,4] antioxidant,[5] and antifungal agents.[6]

The 2- or 5-substituted pyrroles are easily synthesized by electrophilic aromatic substitution; however, the 3- or 4-substituted species are less accessible and require special synthetic strategies in order to obtain them.[7] Additionally, pyrroles functionalized with electron-donating groups are not very stable and because of this they are relatively difficult to synthesize, isolate, and characterize, which explains the lack of citations in the literature.[8]

The synthesis of trifluoromethyl-substituted heterocycles has become important,[9] because the incorporation of a small and highly electronegative trifluoromethyl group can profoundly alter physical and chemical properties.[10] For example, the presence of a trifluoromethyl group can greatly influence the biological activity of a molecule, in terms of binding selectivity, lipophilicity, bioavailability, and metabolic stability.[11] In this context, pyrroles containing the CF_3 group have shown a variety of biological activities; for example, chlorfenapyr, used as an insecticide in agriculture,[12] 2-trifluoromethylmelatonin-MLTD, used as a general anesthesia inducer,[13] and pyrrolylmethyl chrysanthemate, used as an insecticide[14] (Figure 1).

One of the most satisfactory methods for introducing a CF_3 group in heterocycles is via the trifluoromethylated building block approach.[15] These building blocks, which are easily obtained from the trifluoroacetylation of enol ethers or acetals and give 4-alkoxy-1,1,1-trifluoroalk-3-en-2-ones in one step and in good yield,[16] have proved to be useful precursors for the synthesis of a series of heterocyclic compounds.[17,18]

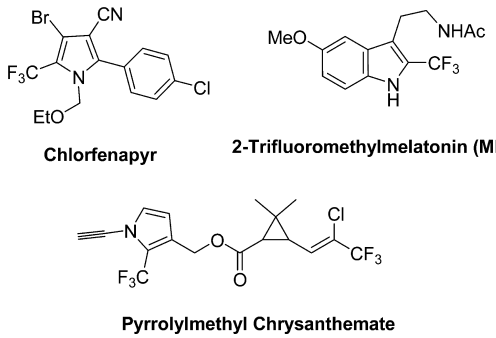


Figure 1. Examples of biologically important trifluoromethylated pyrrole derivatives.

In a search through the literature, very few methods were found for synthesizing 2-(trifluoromethyl)-4-aminopyrroles. In fact, only one method, which was reported by our research group in 2006, shows the preparation of a series of 2-(trifluoromethyl)-4-aminopyrroles from the Staudinger reaction of 5-azido-4-(dialkylamino)-1,1,1-trifluoropent-3-en-2-one with triphenyl- or trimethylphosphine, followed by an aza-Wittig intramolecular cyclization of the iminophosphorane intermediate, as shown in Scheme 1.[18]

This method, however, produces only 1-unsubstituted 4-amino-2-(trifluoromethyl)pyrroles. Another interesting method has been reported, in which N-substituted 3-(trifluoroacetyl)-pyrroles are generated from the reaction of 3-(trifluoroacetyl)-4,5-dihydrofuran and primary amines, followed by an in situ

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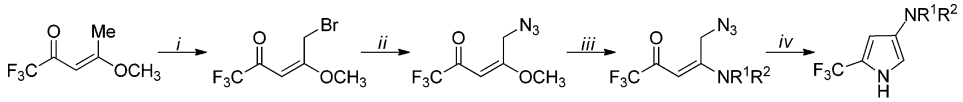
Scheme 1. Synthesis of 4-Amino-Substituted 2-Trifluoromethylpyrroles from the Staudinger Reaction Followed by an Aza-Wittig Intramolecular Cyclization[a]

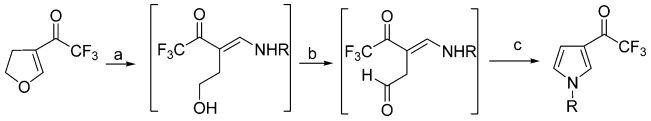


$R^1 = R^2$ = Me, Et, Bn, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_2-O-(CH_2)_2$

[a]Reaction conditions: (i) (1) Br_2, CH_2Cl_2, 0 °C to room temperature, 2 h, (2) Py, 0 °C to room temperature, 1 h, 95%; (ii) NaN_3, acetone, 0 °C to room temperature, 1 h, 90%; (iii) NHR^1R^2, acetonitrile, 0 °C to room temperature, 4 h, 76−92%; *(iv)* Ph_3P or Me_3P, THF, room temperature, 8 h, 61−81%.

oxidation with PCC[19a] or Swern oxidation[19b] and intramolecular cyclization, through an ANROC type of mechanism (Scheme 2).[20]

Scheme 2. Synthesis of N-Substituted 3-Trifluoroacetyl-1*H*-pyrroles through an ANROC Type of Mechanism[a]



[a]Reaction conditions: (a) RNH_2, CH_2Cl_2, 0.5 h, room temperature; (b) PCC, CH_2Cl_2; (c) reflux, 3 h.

In this study, we wish to report a new, simple, and chemoselective one-pot method to synthesize N-substituted 4-amino-3-(trifluoromethyl)pyrroles from the intramolecular cyclization reaction of the 5-bromo-4-(amino)-1,1,1-trifluoropent-3-en-2-one with primary amines.

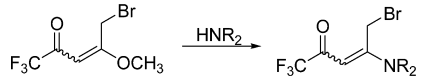
RESULTS AND DISCUSSION

The general method for the synthesis of N-substituted 4-amino-2-(trifluoromethyl)pyrroles is shown in Scheme 3. The enaminones **9**−**14** were prepared from the allylic bromination of the enone **1**,[21] followed by reaction with a primary or secondary amine.[22] The reaction of enaminones **9**−**14** with primary amines furnished the pyrroles **16**−**22**. To the best of our knowledge, no description of such a procedure has yet been reported for the synthesis of the title pyrroles.

This study was conducted using two strategies. The first strategy involved the reaction of brominated enone **2** with a secondary amine at low temperature in order to give the enaminones **9**−**14**, which were isolated. Six secondary amines were tested in order to obtain the most appropriate intermediate for the next step of the reaction—their yields are reported in Table 1. Among the series studied, it was found that diisobutylamine furnished the best reaction yield (entry 8, Table 1).

In the next step, the reaction of enaminones **9**−**14** with a series of primary amines furnished the pyrroles **19**−**21**. A comparative study was done in order to verify which of the six

Table 1. Optimized Reaction Conditions for the Synthesis of Enaminones 9−14



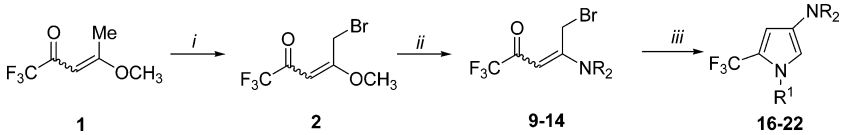
amine	R	product[a]	yield (%)[b]
3	$-(CH_2)_4-$	9	85
4	$-(CH_2)_2O(CH_2)_2-$	10	80
5	−Me	11	58
6	−Et	12	72
7	−Bu	13	86
8	−*i*-Bu	14	90

[a]Reaction conditions: NHR_2 (**3**−**8**), CH_2Cl_2, 0 °C to room temperature, 10 h. [b]Yields of isolated compounds.

enaminones (**9**−**14**) could give the best results for the cyclocondensation with a primary amine. For this study, two methods were tested. Method A employed a conventional reaction, and the optimization of its conditions is shown in Table 2. For this method, enaminone **14** (bearing the diisobutyl group) was used in a reaction with aniline, which was used as the primary amine. Enaminone **14** was used because, among the secondary amines tested, it was obtained in the best yield, and also because it is the only solid enaminone, which makes it easier to handle for the subsequent reaction step. One can see that the best reaction conditions were achieved when equimolar amounts of enaminone **14** and aniline were used, with the reaction done in THF as the solvent and sodium acetate as the base and refluxed for 3 h (entry 8, Table 2).

Method B was designed because, when 2-substituted anilines such as 2-fluoroaniline and 2-chloroaniline or 4-nitroaniline were used, method A gave a mixture of compounds, impurities, and/or low yields. Method B consists of reactions performed in a sealed tube in a solvent-free procedure. In order to find the best reaction conditions for method B, the reactions were performed using the enaminone **14** and aniline **15a** for the cyclization amine, as in method A. One can see that the best reaction conditions were achieved when equimolar amounts of

Scheme 3. General Method for the Synthesis of N-Substituted 4-Amino-2-(trifluoromethyl)pyrroles[a]



[a]Reaction conditions: (i) (a) Br_2, CH_2Cl_2, 0 °C to room temperature, 2 h, (b) Py, 0 °C to room temperature, 1 h; (ii) HNR_2 (**3**−**8**), CH_2Cl_2, 0 °C to room temperature, 8 h; (iii) H_2NR^1 (**15a-I**), 120 °C, 15 min.

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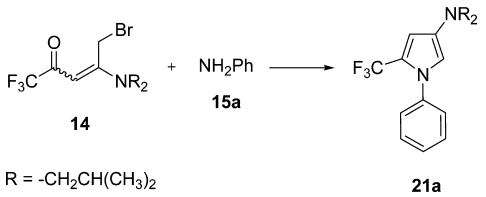
Table 2. Reaction Conditions Tested for Method A[a]



entry	amt of amine **15a** (mmol)	base	solvent	temp (°C)	time (h)	yield (%)[b]
1	1		ethyl ether	25	24	*c*
2	2		ethyl ether	25	24	*c*
3	1		ethyl ether	reflux	24	*c*
4	2		ethyl ether	reflux	6	60
5	1	Na_2CO_3	ethyl ether	reflux	6	*d*
6	1	Et_3N	ethyl ether	reflux	6	*d*
7	1	sodium acetate	ethyl ether	reflux	6	73
8	1	sodium acetate	THF	reflux	3	81

[a]Reaction conditions: enaminone **14** (1 mmol), aniline (1 mmol), solvent (5 mL), base (1 mmol). [b]Yields of isolated compounds. [c]Starting material. [d]The product was formed with many impurities.

the enaminone **14** and the aniline were used at 120 °C for 15 min (entry 3, Table 3).

Table 3. Reaction Conditions Tested for Method B

entry	time (min)[a]	temp (°C)[b]	yield (%)[c]
1	5	120	*d*
2	10	120	82
3	15	120	98
4	20	120	93
5	30	120	92
6	15	80	*d*
7	15	100	*d*
8	15	150	89
9[e]	15	120	79
10[f]	15	120	74

[a]Reaction conditions: enaminone **14** (1 mmol), aniline (1 mmol), solvent-free, sealed tube. [b]Temperature of the oil bath. [c]Yields of isolated compounds. [d]A mixture of product and starting material was obtained. [e]Reaction performed with the addition of sodium acetate (1 mmol). [f]Reaction performed with the addition of excess amine (2 mmol).

Once the best reaction conditions were found, for both methods A and B, these were applied to the synthesis of pyrroles using all of the enaminones **9**–**14** and a series of primary amines **15a**–**l**. The results of these reactions are shown in Table 4. This table shows that the cyclization reaction done with the enaminone **14** and the aniline **15a** furnished the best yields for both methods A and B. Thus, the cyclization was continued by using enaminone **14** with a series of alkyl-, aryl-, benzyl-, and phenethylamines (Table 4). One can observe that method B not only always gave better yields than method A but also allowed pyrroles to be obtained from 2-substituted anilines (entries 12 and 14, Table 4) and 4-nitroaniline (entry 13, Table 4) in a simple, fast, and solvent-free procedure.

The second strategy of this study was designed to obtain 1-substituted 4-amino-2-trifluoropyrroles from a three-component reaction, by reacting 1 equiv of the enone **2** with 2 equiv of the primary amines. However, the reaction only gave good results when 4 equiv of the arylamines was used. It is likely that 2 equiv of the amine is necessary to neutralize the protons eliminated during the course of the reaction. This suspicion was confirmed by performing the reaction with 1 equiv of the enone **2** with 2 equiv of the primary arylamine in the presence of 2 equiv of triethylamine, which also furnished the expected pyrrole in good yields. Method B was also chosen because it gave better yields in the previous study. The reactions between the brominated enone **2** with a series of arylamines (**15a,j**–**m**) furnished the pyrroles **22** in very good yields (Table 5).

All of the new compounds were fully analyzed by GC-MS, ^{1}H and ^{13}C NMR, and high-resolution mass spectrometry (HRMS).

A plausible reaction mechanism for the transformation of enone **2** into the pyrroles **16**–**22** starts with the nucleophilic addition of the secondary or primary amine to the *β*-carbon of enone **2**, followed by prototropism and the elimination of a methanol molecule to give the enaminones **9**–**14**, which undergo nucleophilic substitution of the bromine by a primary amine and furnish the intermediate **I** (Scheme 4). The *γ*-amino group of the intermediate **I** effects an intramolecular nucleophilic addition to the carbonyl carbon, which leads to the cyclic intermediate **II**, and through a prototropism this intermediate then furnishes the structure **III**, which subsequently furnishes the pyrroles **16**–**22** after elimination of a water molecule.

CONCLUSION

In conclusion, this study disclosed a novel, general procedure for the synthesis of a series of 1-substituted 4-amino-2-(trifluoromethyl)-1*H*-pyrroles from the heterocyclization reaction of 4-methoxy-5-bromo-1,1,1-trifluoropent-3-en-2-ones with amines, using easily available starting materials and a simple operation with mild reaction conditions that is environmentally friendly and furnishes very good yields. Additionally, a comparison study was done, which provided the isolation of the intermediate 5-bromo-4-(dialkylamino)-1,1,1-trifluoropent-3-en-2-one followed by a heterocyclization with a primary amine and a direct three-component reaction through reaction of 4-methoxy-5-bromo-1,1,1-trifluoropent-3-en-2-ones with 2 equiv of primary amines.

EXPERIMENTAL SECTION

General Information. Reagents were purchased and used without further purification. Flash chromatography was performed using silica gel (230–400 mesh) as the stationary phase. The procedure for obtaining 1,1,1-trifluoro-4-methoxy-3-penten-2-one (**1**) was described in ref 23. The bromination method for obtaining 5-bromo-1,1,1-trifluoro-4-methoxy-3-penten-2-one (**2**) was described in ref 21. Thin-layer chromatography (TLC) was performed using silica gel plates F-254, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light or stained with iodine vapor or acidic vanillin. Most reactions were monitored by TLC for disappearance of the starting material. ^{1}H NMR spectra were recorded at 400 and 200 MHz using TMS as the internal standard. Chemical shifts *δ* are quoted in parts per million (ppm), and coupling constants *J* are given in hertz (Hz). ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ solutions. High-resolution mass spectra (HRMS) were recorded on

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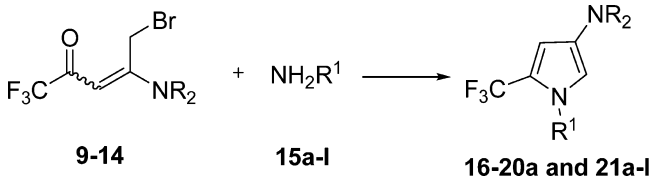
Table 4. Comparison of the Reaction Conditions and Yields Obtained for the Synthesis of Pyrroles 16−21 using Methods A and B

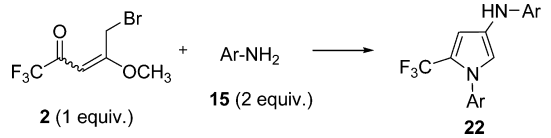


9-14 **15a-l** **16-20a and 21a-l**

entry	reagents	R	R^1	product	yield (%)[a] method A[b]	yield (%)[a] method B[c]
1	**9 + 15a**	$-(CH_2)_4-$	$-C_6H_5$	**16a**	70	85
2	**10 + 15a**	$-(CH_2)_2O(CH_2)_2-$	$-C_6H_5$	**17a**	77	86
3	**11 + 15a**	−Me	$-C_6H_5$	**18a**	70	90
4	**12 + 15a**	−Et	$-C_6H_5$	**19a**	69	97
5	**13 + 15a**	−Bu	$-C_6H_5$	**20a**	74	88
6	**14 + 15a**	−*i*-Bu	$-C_6H_5$	**21a**	81	98
7	**14 + 15b**	−*i*-Bu	−Bu	**21b**	76	93
8	**14 + 15c**	−*i*-Bu	−allyl	**21c**	88	94
9	**14 + 15d**	−*i*-Bu	$-(CH_2)_2-$	**21d**	80	89
10	**14 + 15e**	−*i*-Bu	$-CH_2-C_6H_5$	**21e**	69	89
11	**14 + 15f**	−*i*-Bu	$-(CH_2)_2-C_6H_5$	**21f**	60	95
12	**14 + 15g**	−*i*-Bu	$-2\text{-}ClC_6H_4$	**21g**		80
13	**14 + 15h**	−*i*-Bu	$-4\text{-}NO_2C_6H_4$	**21h**		50[d]
14	**14 + 15i**	−*i*-Bu	$-2\text{-}FC_6H_4$	**21i**		88
15	**14 + 15j**	−*i*-Bu	$-3\text{-}FC_6H_4$	**21j**	79	90
16	**14 + 15k**	−*i*-Bu	$-4\text{-}FC_6H_4$	**21k**	80	96
17	**14 + 15l**	−*i*-Bu	$-4\text{-}OMeC_6H_4$	**21l**	85	93

[a]Yields of isolated compounds. [b]Method A: enaminone (1 mmol), amine (1 mmol), sodium acetate (1 mmol), 5 mL of THF, reflux, 3 h. [c]Method B: enaminone (1 mmol), amine (1 mmol), sealed tube, 120 °C, 15 min. [d]Reaction time of 30 min.

Table 5. Yields of Pyrroles Obtained from the Three-Component Reaction



2 (1 equiv.) **15** (2 equiv.) **22**

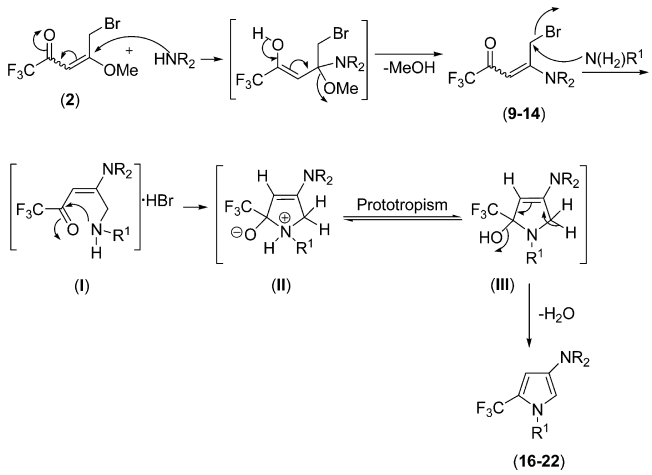
arylamine	Ar	product[a]	yield (%)[b]
15a	C_6H_5	**22a**	88
15j	$3\text{-}FC_6H_4$	**22j**	93
15k	$4\text{-}FC_6H_4$	**22k**	95
15l	$4\text{-}OMeC_6H_4$	**22l**	90
15m	$4\text{-}MeC_6H_4$	**22m**	86

[a]Reaction conditions: enone **2** (1 equiv), aryl amine (4 equiv), 120 °C, 15 min. [b]Yields of isolated compounds.

an ESI-TOF mass spectrometer, and the low-resolution mass spectra were recorded in EI mode (70 eV). Tetrahydrofuran and dichloromethane were dried and purified by distillation as described by Perrin procedures.[24] Temperatures above room temperature were maintained by use of a vegetable oil, and the reactions in a sealed tube used a sand bath.

General Procedure for the Synthesis of 5-Bromo-4-(amino)-1,1,1-trifluoropent-3-en-2-ones 9−14. A solution of amines **3**−**8** (5.0 mmol) in dry dichloromethane (10 mL) was slowly added to an ice bath cooled stirred solution of 5-bromo-1,1,1-trifluoro-4-methoxypent-3-en-2-one **2** (1.24 g, 5.0 mmol) in dry dichloromethane (10 mL). The mixture was stirred at room temperature for 10 h. The mixture was washed with water (3 × 15 mL) and the organic phase was dried with anhydrous sodium sulfate, filtered and the solvent removed under reduced pressure. When necessary the products were purified by column chromatography on silica gel using a 20:80 mixture of ethyl acetate and hexane.

Scheme 4. Plausible Mechanism for the Synthesis of 1-Substituted 4-Amino-2-trifluoromethylpyrroles



5-Bromo-1,1,1-trifluoro-4-(pyrrolidin-1-yl)pent-3-en-2-one ***(9)***. Yellow oil (1.37 g, 96% yield). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.11 (s, 1H), 4.79 (br s, 2H), 3.72 (t, J = 6.6 Hz, 2H), 3.35 (t, J = 6.6 Hz, 2H), 2.10 (qui, J = 6.6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9 (q, $^2J_{CF}$ = 31.2 Hz), 161.9, 117.61 (q, $^1J_{CF}$ = 292.0 Hz), 87.1, 49.7, 47.8, 25.1, 24.4, 24.4. HRMS (ESI$^+$): m/z calcd for $C_9H_{11}BrF_3NO$ $[M + H]^+$ 286.0054, found 286.0050.

5-Bromo-4-(dimethylamino)-1,1,1-trifluoropent-3-en-2-one ***(11)***. Yellow oil (1,04 g, 79% yield). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.19 (s, 1H), 4.84 (br s, 2H), 3.27 (s, 3H), 3.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2 (q, $^2J_{CF}$ = 31.6 Hz), 164.3, 117.5 (q, $^1J_{CF}$ = 292.0 Hz), 86.7, 41.2, 39.5, 22.9. HRMS (ESI$^+$): m/z calcd for $C_7H_9BrF_3NO$ $[M + H]^+$ 259.9898, found 259.9893.

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5-Bromo-4-(diethylamino)-1,1,1-trifluoropent-3-en-2-one (**12**). Orange oil (1.37 g, 95% yield). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.24 (s, 1H), 4.80 (br s, 2H), 3.55 (q, J = 7.1 Hz, 2H), 3.42 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2 (q, $^2J_{CF}$ = 31.5 Hz), 163.0, 117.7 (q, $^1J_{CF}$ = 292.2 Hz), 86.2, 45.2, 44.6, 22.9, 14.3, 10.5. HRMS (ESI$^+$): m/z calcd for $C_9H_{13}BrF_3NO$ [M + H]$^+$ 288.0211, found 288.0211.

5-Bromo-4-(dibutylamino)-1,1,1-trifluoropent-3-en-2-one (**13**). Brown oil (1.62 g, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (s, 1H), 4.80 (br s, 2H), 3.44 (t, J = 7.5 Hz, 2H), 3.30 (t, J = 7.5 Hz, 2H), 1.65 (qui, J = 7.9 Hz, 4H), 1.41−1.35 (m, 4H), 0.97 (t, J = 7.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9 (q, $^2J_{CF}$ = 31.5 Hz), 163.3, 117.7 (q, $^1J_{CF}$ = 292.1 Hz), 86.4, 50.9, 50.5, 31.3, 27.3, 22.9, 19.9, 13.6, 13.5. HRMS (ESI$^+$): m/z calcd for $C_{13}H_{21}BrF_3NO$ [M + H]$^+$ 344.0837, found 344.0823.

5-Bromo-4-(diisobutylamino)-1,1,1-trifluoropent-3-en-2-one (**14**). Brown solid (1.67 g, 97% yield). Mp: 79−82 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.26 (s, 1H), 4.86 (br s, 1H), 3.34 (d, 2H, J = 7.1 Hz), 3.18 (d, 2H, J = 7.1 Hz), 2.34−2.21 (m, 1H), 2.03−1.90 (m, 1H), 0.95 (d, 12H, J = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1 (q, $^2J_{CF}$ = 31.5 Hz), 163.9, 117.7 (q, $^1J_{CF}$ = 292.1 Hz), 87.9, 58.9, 29.0, 25.1, 23.1, 20.1, 20.0. HRMS (ESI$^+$): m/z calcd for $C_{13}H_{21}BrF_3NO$ [M + H]$^+$ 344.0837, found 344.0837.

General Procedure for the Synthesis of N-Substituted 4-Amino-2-trifluoromethylpyrroles 16−21. *Method A.* In a 25 mL round-bottom flask was placed 4-amino-5-bromo-1,1,1-trifluoro-3-penten-2-ones **9**−**14** (1.0 mmol), which was solubilized in 10 mL of anhydrous THF, and then sodium acetate (1 mmol) and primary amines **15a**−**l** (1 mmol) were added. A reflux condenser was adapted, and the reaction was conducted at a temperature of 80 °C with vigorous stirring for 3 h. After the reaction time, the THF was evaporated, the product was solubilized in chloroform and washed with acid water solution (3% HCl) (1 × 15 mL) and distilled water (2 × 15 mL). The aqueous phases were extracted with $CHCl_3$ (1 × 15 mL). The organic phase was dried with anhydrous sodium sulfate and filtered and the solvent removed with a rotary evaporator. When necessary, the products were purified by column chromatography on silica gel using a 10/90 mixture of chloroform and hexane.

Method B. In a screw-capped culture tube were placed 4-amino-5-bromo-1,1,1-trifluoro-3-penten-2-ones **9**−**14** (1.0 mmol) and primary amines **15a**−**l** (1.0 mmol). The tube was sealed and placed in a sand bath at 115 °C for 15 min with constant stirring (30 min for 4-nitroaniline). The reaction mixture was solubilized in chloroform (15 mL) and washed with a 3% solution of hydrochloric acid (1 × 15 mL) and distilled water (2 × 15 mL). The aqueous phases were extracted with chloroform (1 × 15 mL). The organic phase was dried with anhydrous sodium sulfate and filtered and the solvent removed under reduced pressure. When necessary, the products were purified by column chromatography on silica gel using a 10/90 mixture of chloroform and hexane.

1-Phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)-1H-pyrrole (**16a**). Brown oil (238 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.37 (m, 5H), 6.32 (d, 1H, J = 2.1 Hz), 6.27 (d, 1H, J = 2.1 Hz), 3.11 (t, 4H, J = 6.5 Hz), 1.98 (qui, 4H, J = 6.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6, 137.5, 128.9, 127.9, 126.4, 121.2 (q, $^1J_{CF}$ = 267.1 Hz), 120.4 (q, $^2J_{CF}$ = 38.0 Hz), 109.7 (q, $^4J_{CF}$ = 2.0 Hz), 102.2 (q, $^3J_{CF}$ = 3.4 Hz), 50.5, 24.9. GC-MS (EI, 70 eV): m/z (%) 280 (100) [M$^+$], 261 (6), 251 (13), 237 (19), 224 (9), 203 (9), 77 (9). HRMS (ESI$^+$): m/z calcd for $C_{15}H_{15}F_3N_2$ [M + H]$^+$ 281.1266, found 281.1251.

4-(1-Phenyl-5-(trifluoromethyl)-1H-pyrrol-3-yl)morpholine (**17a**). Brown oil (255 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.36 (m, 5H), 6.44 (d, 1H, J = 2.1 Hz), 6.39 (d, 1H, J = 2.2 Hz), 3.84 (t, 4H, J = 4.8 Hz), 2.96 (t, 4H, J = 4.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 139.2, 128.9, 128.2, 126.3, 120.9 (q, $^1J_{CF}$ = 267.0 Hz), 120.9 (q, $^2J_{CF}$ = 37.9 Hz), 111.9, 102.9 (q, $^3J_{CF}$ = 3.0 Hz), 66.5, 50.9. GC-MS (EI, 70 eV): m/z (%) 296 (100) [M$^+$], 281 (6), 238 (96), 217 (14), 77 (14). HRMS (ESI$^+$): m/z calcd for $C_{15}H_{15}F_3N_2O$ [M + H]$^+$ 297.1215, found 297.1194.

N,N-Dimethyl-1-phenyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**18a**). Brown oil (223 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.38 (m, 5H), 6.41 (d, 1H, J = 2.0 Hz), 6.32 (d, 1H, J = 2.1 Hz), 2.73 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 139.5, 128.9, 128.0, 126.4, 121.1 (q, $^1J_{CF}$ = 267.1 Hz), 120.7 (q, $^2J_{CF}$ = 38.0 Hz), 111.2 (q, $^4J_{CF}$ = 2.1 Hz), 102.9 (q, $^3J_{CF}$ = 3.5 Hz), 42.7. GC-MS (EI, 70 eV): m/z (%) 254 (100) [M$^+$], 239 (23), 224 (5), 170 (9), 77 (12). HRMS (ESI$^+$): m/z calcd for $C_{13}H_{13}F_3N_2$ [M + H]$^+$ 255.1109, found 255.1100.

N,N-Diethyl-1-phenyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**19a**). Brown oil (274 mg, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.37 (m, 5H), 6.39 (d, 1H, J = 2.1 Hz), 6.32 (d, 1H, J = 2.1 Hz), 3.11 (q, 4H, J = 7.1 Hz), 1.13 (t, 6H, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6, 137.1, 128.9, 127.9, 126.3, 121.2 (q, $^1J_{CF}$ = 267.1 Hz), 120.4 (q, $^2J_{CF}$ = 37.8 Hz), 111.9 (q, $^4J_{CF}$ = 2.1 Hz), 103.3 (q, $^3J_{CF}$ = 3.5 Hz), 45.5, 11.8. GC-MS (EI, 70 eV): m/z (%) 282 (46) [M$^+$], 267 (100), 237 (12). HRMS (ESI$^+$): m/z calcd for $C_{15}H_{17}F_3N_2$ [M + H]$^+$ 283.1423, found 283.1397.

N,N-Dibutyl-1-phenyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**20a**). Brown oil (297 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.36 (m, 5H), 6.35 (d, 1H, J = 2.1 Hz), 6.27 (d, 1H, J = 2.1 Hz), 3.02 (t, 4H, J = 7.6 Hz), 1.59−1.53 (m, 5H), 1.40−1.34 (m, 6H), 0.95 (t, 6H, J = 7.3 Hz).^{13}C NMR (100 MHz, $CDCl_3$) 139.7, 138.1, 128.9, 127.8, 126.3, 121.2 (q, $^1J_{CF}$ = 267.0 Hz), 120.2 (q, $^2J_{CF}$ = 38.0 Hz), 110.8 (q, $^4J_{CF}$ = 2.2 Hz), 102.7 (q, $^3J_{CF}$ = 3.4 Hz), 59.3, 29.2, 20.5, 13.9. GC-MS (EI, 70 eV): m/z (%) 338 (44) [M$^+$], 319 (6), 295 (94), 258 (100), 239 (28). HRMS (ESI$^+$): m/z calcd for $C_{19}H_{25}F_3N_2$ [M + H]$^+$ 339.2048, found 339.2033.

N,N-Diisobutyl-1-phenyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21a**). Brown oil (331 mg, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.37 (m, 5H), 6.33 (d, 1H, J = 1.9 Hz), 6.23 (d, 1H, J = 1.9 Hz), 2.86 (d, 4H, J = 7.2 Hz), 2.06−1.96 (m, 2H), 0.95 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.7, 138.7, 128.9, 127.8, 126.3, 121.2 (q, $^1J_{CF}$ = 266.8 Hz), 119.9 (q, $^2J_{CF}$ = 37.8 Hz), 110.3 (q, $^4J_{CF}$ = 2.3 Hz), 102.7 (q, $^3J_{CF}$ = 3.2 Hz), 62.6, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 238 (20) [M$^+$], 319 (13), 295 (100), 253 (9), 239 (52). HRMS (ESI$^+$): m/z calcd for $C_{19}H_{25}F_3N_2$ [M + H]$^+$ 339.2048, found 339.2033.

1-Butyl-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21b**). Yellow oil (293 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (d, 1H, J = 2.1 Hz), 6.07 (d, 1H, J = 1.8 Hz), 3.85 (t, 2H, J = 7.5 Hz), 2.75 (d, 4H, J = 7.2 Hz), 1.96−1.85 (m, 2H), 1.78−1.70 (m, 2H), 1.40−1.31 (m, 2H), 0.94 (t, 3H, J = 7.4 Hz), 0.89 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 121.7 (q, $^1J_{CF}$ = 266.4 Hz), 118.4 (q, $^2J_{CF}$ = 37.5 Hz), 109.2, 100.8 (q, $^3J_{CF}$ = 3.4 Hz), 62.9, 47.7, 33.4, 26.9, 20.6, 19.9, 13.6. GC-MS (EI, 70 eV): m/z (%) 318 (21) [M$^+$], 299 (4), 275 (100), 233 (13), 219 (51), 57 (9). HRMS (ESI$^+$): m/z calcd for $C_{17}H_{29}F_3N_2$ [M + H]$^+$ 319.2362, found 319.2347.

1-Allyl-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21c**). Yellow oil (284 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$)δ 6.09 (s, 1H), 6.06 (s, 1H), 5.99−5.89 (m, 1H), 5.20−5.08 (m, 2H), 4.46 (d, 2H, J = 5.6 Hz), 2.76 (d, 4H, J = 7.2 Hz), 1.96−1.86 (m, 2H), 0.88 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 133.9, 121.5 (q, $^1J_{CF}$ = 266.6 Hz), 118.6 (q, $^2J_{CF}$ = 37.7 Hz), 117.3, 108.8 (q, $^4J_{CF}$ = 2.5 Hz), 100.0 (q, $^3J_{CF}$ = 3.5 Hz), 62.7, 50.2, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 302 (24) [M$^+$], 283 (4), 259 (100), 217 (16), 203 (60), 57 (9). HRMS (ESI$^+$): m/z calcd for $C_{16}H_{25}F_3N_2$ [M + H]$^+$ 303.2049, found 303.2029.

1,1′-(Ethane-1,2-diyl)bis(N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine) (**21d**). Brown oil (490 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.09 (d, 1H, J = 2.0 Hz), 5.79 (d, 1H, J = 2.0 Hz), 4.14 (s, 2H), 2.72 (d, 4H, J = 7.2 Hz), 1.92−1.82 (m, 2H), 0.87 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 121.5 (q, $^1J_{CF}$ = 266.4 Hz), 118.5 (q, $^2J_{CF}$ = 37.7 Hz), 108.8, 101.7 (q, $^3J_{CF}$ = 2.7 Hz), 62.7, 48.5, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 550 (22) [M$^+$], 507 (100), 407 (11), 232 (28), 57 (22). HRMS (ESI$^+$): m/z calcd for $C_{28}H_{45}F_6N_4$ [M + H]$^+$ 551.3548, found 551.3559.

1-Benzyl-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21e**). Yellow oil (313 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.25 (m, 3H), 7.08−7.06 (m, 2H), 6.15 (d, 1H, J = 2.1 Hz),

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6.01 (d, 1H, J = 2.1 Hz), 5.05 (s, 2H), 2.74 (d, 4H, J = 7.2 Hz), 1.94−1.84 (m, 2H), 0.86 (d, 12H, J = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 137.7, 128.6, 127.6, 126.7, 121.6 (q, $^1J_{CF}$ = 266,8 Hz), 119.3 (q, $^2J_{CF}$ = 37.9 Hz), 109.5 (q, $^4J_{CF}$ = 2.4 Hz), 101.3 (q, $^3J_{CF}$ = 3.5 Hz), 62.6, 51.2, 26.9, 20.6. GC-MS (EI, 70 eV): m/z (%) 252 (39) [M^+], 333 (6), 309 (100), 287 (11), 273 (62), 237 (6). HRMS (ESI^+): m/z calcd for $C_{20}H_{27}F_3N_2$ [M + H]$^+$ 353.2205, found 353.2189.

*N,N-Diisobutyl-1-phenethyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21f**).* Yellow oil (348 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.20 (m, 3H), 7.12−7.09 (m, 2H), 6.09 (d, 1H, J = 2.0 Hz), 5.83 (d, 1H, J = 2.0 Hz), 4.07 (t, 2H, J = 7.4 Hz), 3.01 (t, 2H, J = 7.6 Hz), 2.69 (d, 4H, J = 7.2 Hz), 1.85−1.76 (m, 2H), 0.85 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 137.9, 128.8, 128.6, 126.6, 121.8 (q, $^1J_{CF}$ = 266.4 Hz), 118.2 (q, $^2J_{CF}$ = 37.5 Hz), 109.9 (q, $^4J_{CF}$ = 2.6 Hz), 101.5 (q, $^3J_{CF}$ = 3.5 Hz), 62.9, 49.6 (q, $^4J_{C-F}$ = 1.3 Hz), 38.1, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 366 (23) [M^+], 347 (3), 323 (100), 281 (12), 267 (32), 105 (22). HRMS (ESI^+): m/z calcd for $C_{21}H_{29}F_3N_2$ [M + H]$^+$ 367.2362, found 367.2349.

*1-(2-Chlorophenyl)-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21g**).* Brown oil (298 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.40 (m, 2H), 7.35−7.27 (m, 2H), 6.31 (s, 1H), 6.10 (s, 1H), 2.82 (t, 4H, J = 7.5 Hz), 2.02−1.92 (m, 2H), 0.90 (d, 12H, J = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 137.0, 133.4, 130.2, 129.9, 129.9, 126.9, 121.0 (q, $^1J_{CF}$ = 267.1 Hz), 120.3 (q, $^2J_{CF}$ = 37.8 Hz), 110.8, 102.4 (q, $^3J_{CF}$ = 3.1 Hz), 62.6, 26.9, 20.6. GC-MS (EI, 70 eV): m/z (%) 372 (17) [M^+], 353 (2), 329 (100), 287 (11), 273 (62), 237 (6). HRMS (ESI^+): m/z calcd for $C_{19}H_{24}ClF_3N_2$ [M + H]$^+$ 373.1658, found 373.1670.

*N,N-Diisobutyl-1-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21h**).* Red oil (192 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, 2H, J = 9.0 Hz), 7.54 (d, 2H, J = 8.9 Hz), 6.38 (d, 1H, J = 2.0 Hz), 6.19 (d, 1H, J = 2.0 Hz), 2.87 (d, 4H, J = 7.3 Hz), 2.04−1.95 (m, 2H), 0.91 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 144.9, 139.6, 126.0, 124.9, 120.9 (q, $^1J_{CF}$ = 267.0 Hz), 120.1 (q, $^2J_{CF}$ = 38.1 Hz,), 108.8, 105.1 (q, $^3J_{CF}$ = 3.3 Hz), 62.0, 26.8, 20.5. GC-MS (EI, 70 eV): m/z (%) 383 (14) [M^+], 364 (2), 340 (100), 284 (59), 238 (20), 57 (29). HRMS (ESI^+): m/z calcd for $C_{19}H_{24}F_3N_3O_2$ [M + H]$^+$ 384.1900, found 384.1884.

*1-(2-Fluorophenyl)-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21i**).* Brown oil (313 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.37 (m, 2H), 7.21−7.17 (m, 2H), 6.31 (d, 1H, J = 2.1 Hz), 6.13 (s, 1H), 2.82 (d, 4H, J = 7.2 Hz), 2.02−1.92 (m, 2H), 0.91 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9 (d, $^1J_{CF}$ = 252.3 Hz), 138.7, 130.1 (d, $^3J_{CF}$ = 7.6 Hz), 129.8, 127.2 (d, $^2J_{C-F}$ = 12.7 Hz), 124.1 (d, $^3J_{CF}$ = 4.1 Hz), 121.0 (q, $^1J_{CF}$ = 267.0 Hz), 120.5 (q, $^2J_{CF}$ = 38.0 Hz), 116.3 (d, $^2J_{CF}$ = 19.9 Hz), 110.6, 102.7 (q, $^3J_{CF}$ = 3.2 Hz), 62.6, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 356 (18) [M^+], 337 (4), 313 (100), 271 (12), 257 (78), 57 (8). HRMS (ESI^+): m/z calcd for $C_{19}H_{24}F_4N_2$ [M + H]$^+$ 357.1955, found 357.1938.

*1-(3-Fluorophenyl)-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21j**).* Brown oil (320 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.34 (m, 2H), 7.19−7.17 (m, 1H), 7.13−7.05 (m, 2H), 6.29 (d, 1H, J = 2.1 Hz), 6.17 (d, 1H, J = 1.9 Hz), 2.83 (d, 4H, J = 7.3 Hz), 2.00−1.93 (m, 2H), 0.91 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (d, $^1J_{CF}$ = 247.9 Hz), 140.9 (d, $^3J_{CF}$ = 9.9 Hz), 138.8, 130.0 (d, $^3J_{CF}$ = 9.3 Hz), 121.9, 121.1 (q, $^1J_{CF}$ = 266.9 Hz), 119.8 (q, $^2J_{CF}$ = 38.3 Hz), 114.7 (d, $^2J_{CF}$ = 20.7 Hz), 113.7 (d, $^2J_{CF}$ = 23.6 Hz), 109.7, 103.3 (q, $^3J_{CF}$ = 2.7 Hz, C3), 62.39 (C6), 26.80 (C7), 20.56(C8). GC-MS (EI, 70 eV): m/z (%) 356 (20) [M^+], 337 (4), 313 (100), 271 (14), 257 (65), 57 (8). HRMS (ESI^+): m/z calcd for $C_{19}H_{24}F_4N_2$ [M + H]$^+$ 357.1955, found 357.1940.

*1-(4-Fluorophenyl)-N,N-diisobutyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21k**).* Brown oil (342 mg, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.32 (m, 2H), 7.12−7.07 (m, 2H), 6.27 (d, 1H, J = 2.1 Hz), 6.14 (d, 1H, J = 2.0 Hz), 2.82 (d, 4H, J = 7.3 Hz), 2.00−1.93 (m, 2H), 0.91 (d, 12H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9 (d, $^1J_{CF}$ = 247.5 Hz), 138.7, 135.7 (d, $^4J_{CF}$ = 2.9 Hz), 128.2 (d, $^3J_{CF}$ = 8.5 Hz), 121.1 (q, $^1J_{CF}$ = 266.9 Hz), 120.1 (q, $^2J_{CF}$ = 37.7 Hz), 115.7 (d, $^2J_{CF}$ = 22.8 Hz), 110.3 (q, $^4J_{CF}$ = 1.7 Hz), 102.6 (q, $^3J_{CF}$ = 3.3 Hz), 62.5, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 356 (21) [M^+], 337 (4), 313 (100), 271 (13), 257 (66), 57 (11). HRMS (ESI^+): m/z calcd for $C_{19}H_{24}F_4N_2$ [M + H]$^+$ 357.1955, found 357.1938.

*N,N-Diisobutyl-1-(4-methoxyphenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**21l**).* Brown oil (342 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, 2H, J = 8.8 Hz), 6.94 (d, 2H, J = 8.9 Hz), 6.29 (d, 1H, J = 2.1 Hz), 6.19 (d, 1H, J = 2.1 Hz), 3.85 (s, 3H), 2.85 (d, 4H, J = 7.2 Hz), 2.05−1.95 (m, 2H), 0.94 (d, 12H, J = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 138.4, 132.6, 127.7, 121.2 (q, $^1J_{CF}$ = 266.9 Hz), 120.0 (q, $^2J_{CF}$ = 37.7 Hz), 113.9, 110.7 (q, $^4J_{CF}$ = 2.5 Hz), 102.1 (q, $^3J_{CF}$ = 3.3 Hz), 62.7, 55.4, 26.8, 20.6. GC-MS (EI, 70 eV): m/z (%) 368 (22) [M^+], 349 (2), 325 (100), 283 (12), 269 (56), 57 (6). HRMS (ESI^+): m/z calcd for $C_{20}H_{27}F_3N_2O$ [M + H]$^+$ 369.2154, found 369.2150.

General Procedure for the Synthesis of *N*-Aryl-4-amino-3-trifluoromethylpyrroles 22. In a sealed tube were placed 5-bromo-1,1,1-trifluoro-4-methoxy-3-penten-2-one (**2**; 0.124 g, 0.5 mmol) and arylamine (2 mmol). The reaction mixture was heated in a sand bath at 115 °C for a period of 15 min with constant agitation. The reaction mixture was solubilized in $CHCl_3$ (15 mL) and washed with acidic water solution (3% HCl) (1 × 15 mL) and distilled water (2 × 15 mL). The aqueous phases were extracted with $CHCl_3$ (1 × 15 mL). The organic phase was dried with anhydrous sodium sulfate and filtered and the solvent removed with a rotary evaporator.

*N,1-Diphenyl-5-(trifluoromethyl)-1H-pyrrol-3-amine (**22a**).* Brown oil (133 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.38 (m, 5H), 7.23−7.18 (m, 2H), 6.85 (d, J = 7.7 Hz, 2H), 6.80 (d, J = 7.2 Hz, 2H), 6.80 (d, J = 2.1 Hz, 1H), 6.62 (d, J = 1.5 Hz, 1H), 5.18 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 139.1, 129.4, 129.1, 128.5, 126.8, 126.5, 120.9 (q, $^1J_{CF}$ = 267.0 Hz), 120.9 (q, $^2J_{CF}$ = 38.4 Hz), 119.6 (q, $^4J_{CF}$ = 1.9 Hz), 118.9, 114.1, 108.9 (q, $^3J_{CF}$ = 3.4 Hz). GC- MS (EI, 70 eV): m/z (%) 302 (100) [M^+], 281 (7), 198 (18), 77 (18). HRMS (ESI^+): m/z calcd for $C_{17}H_{13}F_3N_2$ [M + H]$^+$ 303.1109, found 303.1110.

*N,1-Bis(3-fluorophenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**22j**).* Brown oil (157 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.40 (m, 1H), 7.21−7.12 (m, 4H), 6.81 (d, J = 2.1 Hz, 1H), 6.64 (d, J = 1.7 Hz, 1H), 6.60−6.52 (m, 2H), 6.50−6.45 (m, 2H), 5.28 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1 (d, $^1J_{CF}$ = 243.3 Hz), 162.6 (d, $^1J_{CF}$ = 248.7 Hz), 148.1 (d, $^3J_{CF}$ = 10.6 Hz), 140.2 (d, $^3J_{CF}$ = 9.9 Hz), 130.5 (d, $^3J_{CF}$ = 10.3 Hz), 130.4 (d, $^3J_{CF}$ = 9.5 Hz), 126.3, 122.3 (d, $^4J_{CF}$ = 1.9 Hz), 121.2 (q, $^2J_{CF}$ = 38.8 Hz), 120.7 (q, $^1J_{CF}$ = 267.6 Hz), 120.0 (q, $^4J_{CF}$ = 1.58 Hz), 115.8 (d, $^2J_{CF}$ = 20.9 Hz), 114.1 (d, $^2J_{CF}$ = 23.9 Hz), 109.7 (q, $^3J_{CF}$ = 3.2 Hz), 105.4 (d, $^2J_{CF}$ = 21.5 Hz), 100.8 (d, $^2J_{CF}$ = 25.7 Hz). GC-MS (EI, 70 eV): m/z (%) 338 (100) [M^+], 317 (8), 216 (16). HRMS (ESI^+): m/z calcd for $C_{17}H_{11}F_5N_2$ [M + H]$^+$ 339.0920, found 339.0925.

*N,1-Bis(4-fluorophenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**22k**).* Brown oil (161 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.34 (m, 2H), 7.14−7.10 (m, 2H), 6.93−6.89 (m, 2H), 6.81−6.79 (m, 2H), 6.72 (d, J = 2.1 Hz), 6.58 (d, J = 1.8 Hz), 5.1 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (d, $^1J_{CF}$ = 248.8 Hz), 156.7 (d, $^1J_{CF}$ = 236.9 Hz), 142.46 (d, $^4J_{CF}$ = 2.0 Hz), 134.9 (d, $^4J_{CF}$ = 3.1 Hz), 128.4 (d, $^3J_{CF}$ = 8.8 Hz), 127.6, 121.3 (q, $^2J_{CF}$ = 38.5 Hz), 120.8 (q, $^1J_{CF}$ = 267.4 Hz), 119.3 (q, $^4J_{CF}$ = 1.9 Hz), 116.0 (d, $^2J_{CF}$ = 21.2 Hz), 115.8 (d, $^2J_{CF}$ = 20.8 Hz), 115.5 (d, $^3J_{CF}$ = 7.6 Hz), 108.6 (q, $^3J_{CF}$ = 3.1 Hz). GC-MS (EI, 70 eV): m/z (%) 338 (100) [M^+], 317 (7), 216 (20). HRMS (ESI^+): m/z calcd for $C_{17}H_{11}F_5N_2$ [M + H]$^+$ 339.0920, found 339.0923.

*N,1-Bis(4-methoxyphenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**22l**).* Brown oil (163 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 6.85 (d, J = 9.2 Hz, 2H), 6.80 (d, J = 9.1 Hz, 2H), 6.69 (d, J = 2.1 Hz, 1H), 6.54 (d, J = 1,7 Hz, 1H), 4.99 (br s, 1H,), 3.85 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 153.3, 140.1, 131.9, 128.2, 127.8, 120.9 (q, $^1J_{CF}$ = 267.0 Hz), 120.9 (q, $^2J_{CF}$ = 38.2 Hz), 118.6 (q, $^4J_{CF}$ = 2.2 Hz), 116.2, 114.9, 114.1, 107.5 (q, $^3J_{CF}$ = 3.2 Hz), 55.8, 55.5. GC-MS (EI, 70 eV): m/z (%) 362 (100) [M^+], 347 (63), 181 (7). HRMS (ESI^+): m/z calcd for $C_{19}H_{17}F_3N_2O_2$ [M + H]$^+$ 363.1320, found 363.1322.

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*N,1-Bis(4-methylphenyl)-5-(trifluoromethyl)-1H-pyrrol-3-amine (**22m**).* Brown oil (142 mg, 86% yield). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (s, 4H), 7.02 (d, J = 8.0 Hz, 2H), 6.80−6.74 (m, 3H), 6.58 (d, J = 1.5 Hz, 1H), 5.01 (br s, 1H), 2.41 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 138.7, 136.6, 129.8, 129.6, 128.3, 127.5, 126.3, 121.0 (q, $^1J_{CF}$ = 267.2 Hz), 120.8 (q, $^2J_{CF}$ = 38.8 Hz), 119.1 (q, $^4J_{CF}$ = 1.9 Hz), 114.6, 108.3 (q, $^3J_{CF}$ = 3.4 Hz), 21.1, 20.5. GC-MS (EI, 70 eV): m/z (%) 330 (100) [M^+], 212 (9), 198 (6), 91 (10). HRMS (ESI$^+$): m/z calcd for $C_{19}H_{17}F_3N_2$ [M + H]$^+$ 331.1422, found 331.1427.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02320.

^{1}H and ^{13}C NMR spectra, GC-MS, and HRMS of compounds (PDF)

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Notes

The authors declare no competing financial interest.

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