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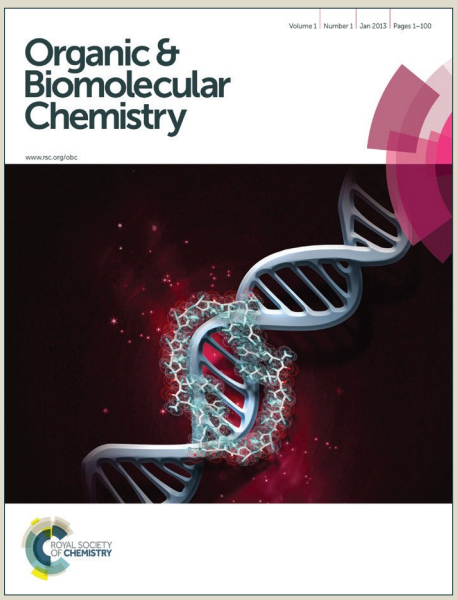

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ARTICLE

One-pot preparation of trifluoromethylated homoallylic *N*-acylhydrazines or *α*-methylene-*γ*-lactams from acylhydrazines, trifluoroacetaldehyde methyl hemiacetal, allylic bromide and tin†

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An efficient and convenient one-pot method for preparation of trifluoromethylated homoallylic *N*-acylhydrazines or *α*-methylene-*γ*-lactams has been described. In this processes, allylic bromide and metal tin are used instead of toxic stannanes, and commercially available aqueous trifluoroacetaldehyde methyl hemiacetal was used as a trifluoromethyl source.

Introduction

Fluorine-containing organic compounds have been increasingly applied in pharmaceuticals, agrochemicals, and material sciences due to the unique physicochemical features brought about by the introduction of fluorine atoms in organic molecules.[1] Trifluoromethyl group is indisputablely the most prevalent fluorine-containing group appeared in the organofluorine compounds. Thus, many strategies to incorporate trifluoromethyl group into organic molecules have been developed these days.[2] In general, there are two main ways of introducing trifluoromethyl group into complex organic molecules. The first strategy for the introduction of the trifluoromethyl group is to use trifluoromethylating reagents such as nucleophilic,[3] electrophilic[4] or radical agents.[5] Alternatively, trifluoromethylated compounds could be prepared by the use of trifluoromethylated synthetic building blocks. Although trifluoromethylating reagents have provided powerful and effective ways for the introduction of trifluoromethyl group into organic molecules, there are still some drawbacks for these reagents, such as tedious preparation procedures, high prices and difficult control for asymmetric trifluoromethylation. Hence, incorporation of trifluoromethyl group into organic molecules by trifluoromethylated building blocks also provides another important way to construct trifluoromethylated organic molecules, and has gained many attentions,[6] especially in asymmetric trifluoromethylation.[6m,6n] On the other hand, *N*-acylhydrazines are a class of important organic compounds, which are not only relatively new scaffolds found in a wide variety of biologically active molecules,[7] but also show potential applications in material science such as electroluminescence and liquid crystals.[8] *N*-*tert*-butyl-*N*,*N*′-diacylhydrazines, such as RH-5849 , RH-5992 , RH0345 and so on, have been widely used as pesticides since 1980s.[9] Some *N*-acylhydrazines are reported to be medicinal candidates for anticancer agents,[10] anti-inflammatory,[11] or other bioactivities.[12] In particular, trifluoromethylated *N*-acylhydrazines were proved to be anticancer agents in 2009.[13] Besides, *N*-acylhydrazines also act as versatile synthetic building blocks for preparation of nitrogen-containing compounds.[14] Traditionally, the methods for preparation of *N*-acylhydrazines include reaction of hydrazines with carboxylic acids or their derivatives such as esters, acyl chlorides and anhydrides. Nucleophilic reactions of *N*-acylhydrazones with various nucleophiles provide another important way for the synthesis of *N*-acylhydrazines.[15] In view of the potential application of trifluoromethylated *N*-acylhydrazines in drugs, agrochemicals and materials, we chose cheap and commercially available aqueous trifluoroacetaldehyde methyl hemiacetal as a trifluoromethyl source to react with *N*-acylhydrazines, tin powder, allylic bromide or ethyl 2-(bromomethyl)acrylate in simple one-pot procedure for producing trifluoromethylated homoallylic hydrazides or *α*-methylene-*γ*-lactams in high yields (Scheme 1). Compared to traditional allylic tributyltin reagents, combination of allylic bromide and tin powder avoids the use of toxic organotin reagent and make the reactions proceed in water.[16] In this paper, we would like to report our results for the synthesis of trifluoromethylated homoallylic hydrazides and *α*-methylene-*γ*-lactams.

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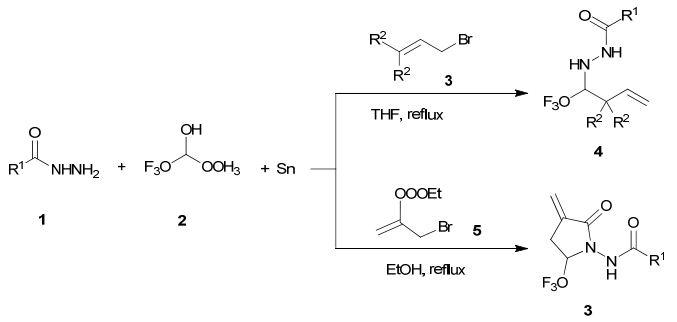


Scheme 1 One-pot preparation of compounds **4** and **6** promoted by Sn powder.

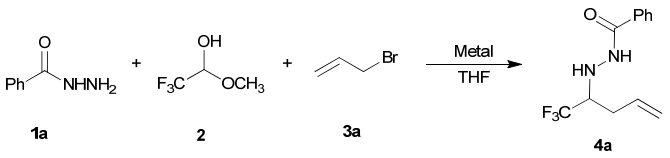
Results and discussion

As an initial investigation, benzoylhydrazine (**1a**) was reacted with aqueous trifluoroacetaldehyde methyl hemiacetal (**2**), allylic bromide (**3a**) and tin powder in THF at room temperature, but there was no product formed at all (Table 1, Entry 1). Interestingly, when the temperature reached to 55°C, the product **4a** was really produced in 44% yield (Table 1, Entry 3). Performing the reaction at reflux increased the yield of **4a** to 78% (Table 1, Entry 4). When other metals such as In, Zn and Mg were used under the same reaction conditions, the yields of **4a** were lower than using Sn powder (Table 1, Entries 4-7).

In order to further improve the yield, the other reaction conditions were optimized using Sn as promoter and the results were listed in Table 2. As reported in literature, some Bronsted acids or Lewis acids were usually used to activate the tin powder promoted reaction.[16b,16d-16f] Thus, the effects of different acids on the reaction were studied firstly. It was found that both of Bronsted acids and Lewis acids were not beneficial for this reaction (Table 2, Entries 1-6). Then, a variety of solvents were screened. THF was found to be the best solvent for the preparation of trifluoromethylated homoallylic hydrazides (Table 2, Entries 1 and 7-13). Other solvents such as ethanol, 1,4-dioxane, $CHCl_3$, CH_2Cl_2, toluene, ethyl ether and water gave the products in lower yields. Finally, the investigation of the influence of reactants' ratio proved that 85% yield could be achieved when the ratio of **1a**/**2**/**3a**/Sn was 1/1.5/2/2.5 (Table 2, Entries 14-21).

With the optimized reaction conditions in hand, the generality of the reaction for different *N*-acylhydrazines and allylic bromides has been studied (Table 3). In general, most *N*-acylhydrazine reacted with allylic bromide to afford the trifluoromethylated homoallylic hydrazides in good to excellent yields. Electronic properties of the substituents on the phenyl ring of *N*-acylhydrazines did not affect the reaction results too much. *N*-acylhydrazines with both electron withdrawing and donating groups on their phenyl ring could give the products in good yields (Table 3, **4b**, **4e**-**4g**). However, the positions of the substituents on the phenyl ring greatly affected the reaction results. For example, when the methyl group was in the *para*- or *meta*-position, the corresponding products could be obtained in good yields (Table 3, **4d** and **4e**), but the yield of the product would decrease to 43% when the methyl group was in the *ortho*-position (Table 3, **4c**). This method could also be applied to heteroaromatic *N*-acylhydrazines to produce the products in good yield (Table 3, **4j**, **4q**). However, aliphatic *N*-acylhydrazines were not suitable for the reaction. For instance, when acetylhydrazine and long-chained stearoyl hydrazine were used, the corresponding products could not be obtained (Table 3, **4r** and **4s**).

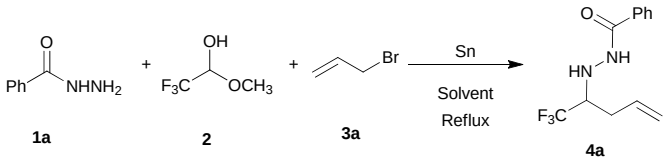
Table 1 The effects of different metals on the yields of compound **4a**[a]



Entry	Metal	Temp (°C)	Time (h)	Isolated yield (%)
1	Sn	r.t.	36	0
2	Sn	40	36	0
3	Sn	55	20	44
4	Sn	reflux	18	78
5	In	reflux	36	54
6	Zn	reflux	28	52
7	Mg	reflux	36	7

[a]Reaction conditions: benzoylhydrazine (**1a**, 0.36 mmol), trifluoroacetaldehyde methyl hemiacetal (**2**, 0.54 mmol), allylic bromide (**3a**, 0.54 mmol), metal (0.54 mmol), THF (5.0 mL).

Table 2 Optimization of reaction conditions[a]

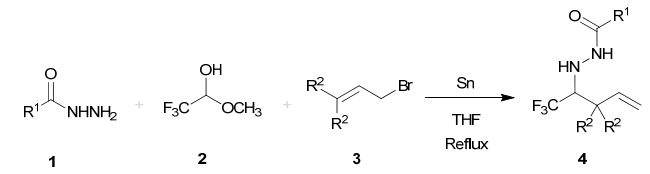


Entry	Mole Ratio of **1**/**2**/**3**/Sn	Solvent	Additive (10 mol%)	Time (h)	Isolated yield (%)
1	1/1.5/1.5/1.5	THF	--	18	78
2	1/1.5/1.5/1.5	THF	T_fOH	20	63
3	1/1.5/1.5/1.5	THF	$AlCl_3$	20	28
4	1/1.5/1.5/1.5	THF	TMSCl	21	24
5	1/1.5/1.5/1.5	THF	$Ni(ClO_4)_4{\cdot}6H_2O$	22	23
6	1/1.5/1.5/1.5	THF	HCl	19	23
7	1/1.5/1.5/1.5	EtOH	--	22	50
8	1/1.5/1.5/1.5	1,4-Dioxane	--	20	66
9	1/1.5/1.5/1.5	$CHCl_3$	--	20	40
10	1/1.5/1.5/1.5	CH_2Cl_2	--	20	25
11	1/1.5/1.5/1.5	Toluene	--	20	57
12	1/1.5/1.5/1.5	Ether	--	20	10
13	1/1.5/1.5/1.5	H_2O		18	37
14	1/1/1/1	THF	--	22	47
15	1/1.5/1/1	THF	--	22	54
16	1/1.5/1/1.5	THF	--	22	50

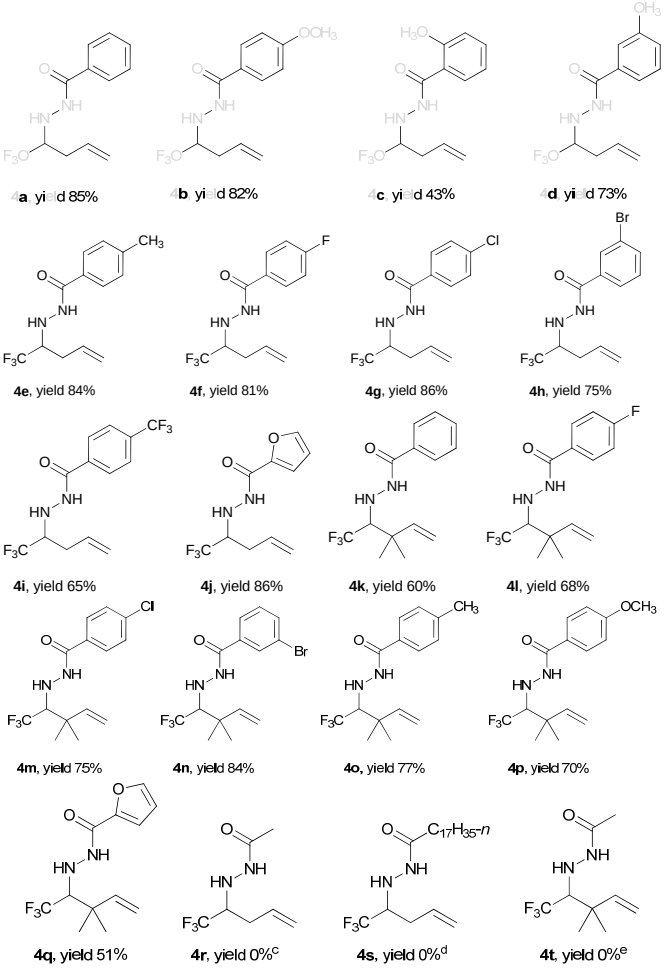
17	1/1.5/1.5/1.5	THF	--	18	78
18	1/1.5/2/1.5	THF	--	15	80
19	1/1.5/2/2	THF	--	14	82
20	1/1.5/2/2.5	THF	--	14	85
21	1/1.5/2.5/2.5	THF	--	14	83

[a]Reaction conditions: acylhydrazine (**1a**, 0.36 mmol), trifluoroacetaldehyde methyl hemiacetal (**2**, 0.36-0.54 mmol), allylic bromide (**3a**, 0.36-0.9 mmol), Sn (0.36-0.9 mmol), solvent (5.0 mL).

Table 3 Reaction of different acylhydrazines with allylic bromides[a, b]

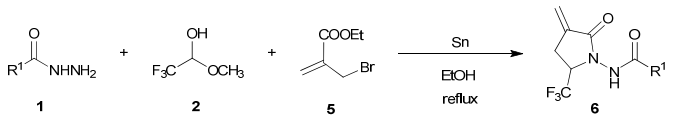


1 2 3 4

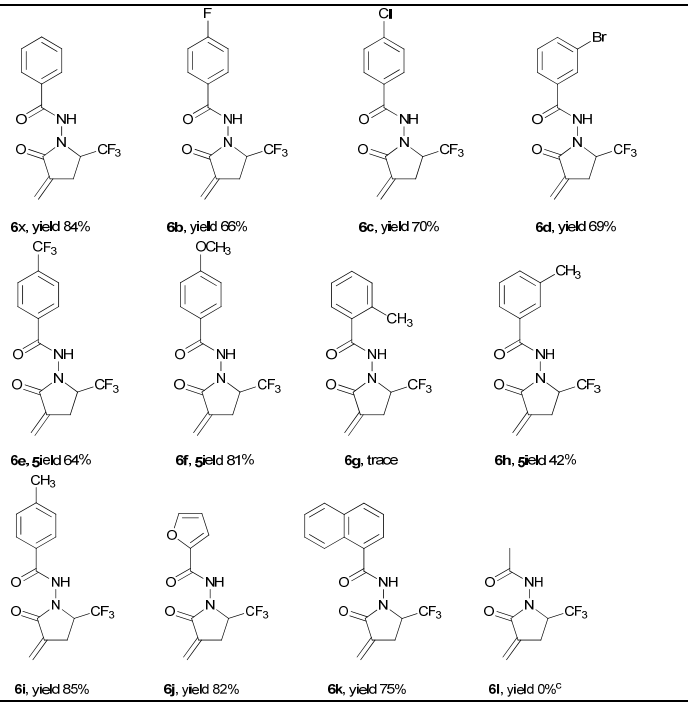


[a]Reaction conditions: acylhydrazines (**1**, 0.36 mmol), trifluoroacetaldehyde methyl hemiacetal (**2**, 0.54 mmol), allylic bromide(**3**, 0.72 mmol), and Sn powder (0.9 mmol) were stirred at reflux for 13-18 h in THF (5.0 mL). [b]Isolated yields. [c,d,e]Trifluoromethyl acylhydrazone was obtained in 85%, 87%, 90% yield, respectively.

Table 4 Reaction of different acylhydrazines with ethyl 2-(bromomethyl)acrylate[a,b]



1 2 5 6



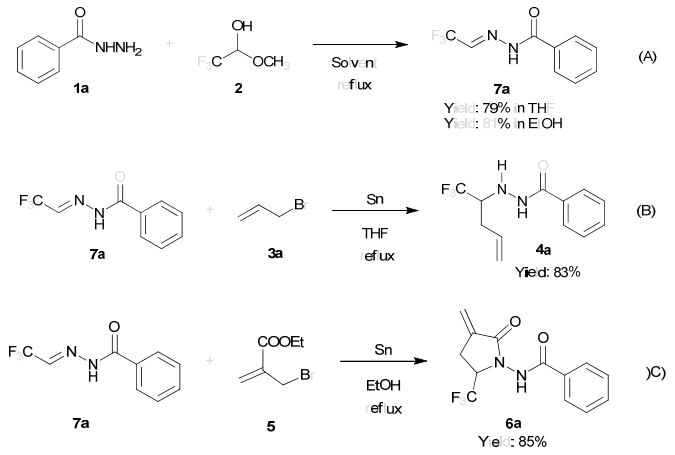
[a]Reaction conditions: acylhydrazine (**1**, 0.36 mmol), trifluoroacetaldehyde methyl hemiacetal (**2**, 0.54 mmol), ethyl 2-(bromomethyl)acrylate (**5**, 1.08 mmol), and Sn powder (1.26 mmol) were stirred at reflux for 15-18 h in EtOH (5.0 mL). [b]Isolated yields. [c]Trifluoromethyl acylhydrazone was obtained in 85% yield.

Next, allylic bromide was replaced by prenyl bromide to perform the reaction. The reaction could smoothly occur with aromatic *N*-acylhydrazines to produce the corresponding products, but not with aliphatic *N*-acylhydrazines (Table 3, **4k**-**4q** and **4t**). Futhermore, the *γ*–addtion products were obtained. This result is consistent with the tendency of prenyl bromide to add to carbonyl compounds and imines at the most substituted allylic terminus.[17]

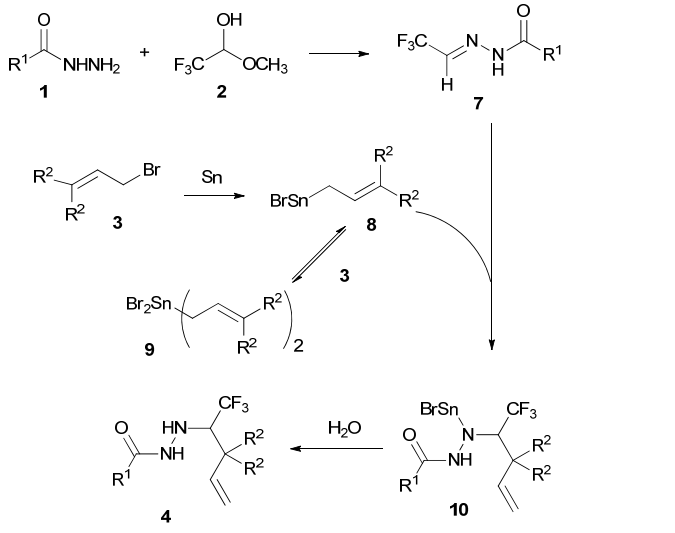
Finally, allylic substrates were extended to ethyl 2-(bromomethyl)acrylate (**5**). When benzoylhydrazine was reacted with trifluoroacetaldehyde methyl hemiacetal and ethyl 2-(bromomethyl)acrylate in the presence of tin powder using THF as solvent under the above reaction conditions, *α*-methylene-*γ*-lactam **6a** was obtained in only 45% yield. After brief optimization of the reaction conditions, the yield of **6a** could be improved to 84% when ethanol was used as solvent. Then, the reactions of ethyl 2-(bromomethyl)acrylate with different *N*-acylhydrazines and trifluoroacetaldehyde methyl hemiacetal were investigated. Most of the reactions could occur smoothly to give the corresponding *α*-methylene-*γ*-lactams **6**, an important units found in many biologically active molecules.[18] As showed in Table 4, most of the aromatic *N*-acylhydrazines could be used in the reaction to produce the products in good yields (Table 4, **6a**-**6k**), but aliphatic *N*-

acylhydrazines could not give the products (Table 4, **6l**). In addition, *ortho*-substituted aromatic *N*-acylhydrazine did not give product (Table 4, **6g**).

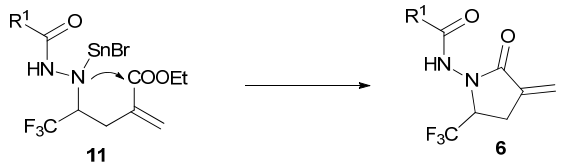
In order to investigate the mechanism, some control experiments have been explored (Scheme 2). Benzoylhydrazine was reacted firstly with aqueous trifluoroacetaldehyde methyl hemiacetal to afford the *N′*-(2,2,2-trifluoroethylidene)-benzohydrazide (**7a**) in 79% yield in THF or in 81% yield in ethanol after 8 hours (Scheme 2, A). Compound **7a** was stable at room temperature under air atmosphere. Refluxing of **7a** with allylic bromide and tin powder in THF afforded compound **4a** in 83% yield, or with ethyl 2-(bromomethyl)acrylate in ethanol gave product **6a** in 85% yield (Scheme 2, B and C). All of these results proved that trifluoromethylated *N*-acylhydrazones were formed firstly from *N*-acylhydrazines and trifluoroacetaldehyde methyl hemiacetal, and then reacted with in-situ formed allylic tin species to give the products.



Scheme 2 Control experiments.



Scheme 3 Proposed mechanism for formation of **4**.



Scheme 4 Formation of *α*-methylene-*γ*-lactams **6.**

Based on experimental results and literature,[16b,16c] a possible mechanism is tentatively proposed in scheme 3. Trifluoromethylated *N*-acylhydrazones **7** were produced firstly from condensation of *N*-acylhydrazines and trifluoroacetaldehyde methyl hemiacetal, and then reacted with allylic tin bromide **8** to give the intermediate **10**, which is then hydrolyzed to afford products **4** (Scheme 3). When the allylic bromides were replaced by ethyl 2-(bromomethyl)acrylate, intermidate **11** was formed and then cyclized to give trifluoromrthylated *α*-methylene-γ-lactams **6** (Scheme 4).

Conclusions

In conclusion, an efficient and convienient one-pot method has been developed for preparation of trifluoromethylated homoallylic *N*-acylhydrazines or *α*-methylene-*γ*-lactams, which provide an opportunity for the test of their bioactivity as drugs or pesticides. In this method, allylic bromide and metal tin were used instead of toxic stannanes. Cheap and commercially available aqueous trifluoroacetaldehyde methyl hemiacetal was used as a trifluoromethyl source.

Experimental Section

General procedures for synthesis of trifluoromethylated homoallylic *N*-acylhydrazines 4

A solution of acylhydrazine **1** (0.36 mmol), trifluoroacetaldehyde methyl hemiacetal **2** (0.54 mmol), allylic bromide **3** (0.72 mmol) and tin powder (0.9 mmol) in THF (5 mL) was stirred at reflux for 12-18 h (monitored by TLC). After completion, the reaction mixture was cooled to room temperature, saturated NH_4Cl solution (10 mL) was added into the mixture and stirred for 10 min, and then the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuum. Purification of the residue by silica gel column chromatography using petroleum ether: acetone (6:1-4:1) as eluent furnished the products **4**.

***N′*-(1,1,1-Trifluoropent-4-en-2-yl)benzohydrazide (4a).** White solid; 79.1 mg, 85% yield; mp 96-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.72 (m, 3H), 7.55 (s, 1H), 7.46 (d, J = 6.8 Hz, 2H), 6.02-6.00 (m, 1H), 5.33 (d, J = 14.8 Hz, 2H), 4.94 (s, 1H), 3.50 (s, 1H), 2.64-2.61 (m, 1H), 2.39-2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 132.1, 132.0, 131.91, 128.63, 126.79, 125.9 (q, J_{C-F} = 279.4 Hz),119.9, 60.5 (q, J_{C-F} = 26.8 Hz), 31.4 (d, J_{C-F} = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, J_{F-H} = 6.8 Hz); HRMS (ESI) m/z $C_{12}H_{14}F_3N_2O$ [M + H]$^+$ calcd. 259.1053, found: 259.1051.

4-Methoxy-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4b). White solid; 85.4 mg, 82% yield; mp 99-100 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.69 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 6.02-5.95 (m, 1H), 5.31-5.28 (m, 2H), 4.92 (d, J = 6.0 Hz, 1H), 3.84 (s, 3H), 3.49-3.44 (m, 1H), 2.61-2.58 (m, 1H), 2.36-2.30 (m,1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 162.7, 132.1, 128.7, 126.1 (q, $J_{C\text{-}F}$ = 279.6 Hz), 124.4, 119.9, 113.9, 60.7 (q, $J_{C\text{-}F}$ = 26.7 Hz), 55.4, 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{13}H_{16}F_3N_2O_2$ $[M + H]^+$ calcd 289.1158, found: 289.1157.

2-Methyl-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4c). White solid; 42.1 mg, 43% yield; mp 79-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.36-7.31 (m, 2H), 7.23-7.18 (m, 2H), 6.06-5.95 (m, 1H), 5.35-5.30 (m, 2H), 4.91 (d, J = 6.4 Hz, 1H), 3.57-3.48 (m, 1H), 2.65-2.59 (m, 1H), 2.43 (s, 3H), 2.39-2.31 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 136.8, 133.3, 131.9, 131.2, 130.6, 127.0, 126.0 (q, $J_{C\text{-}F}$ = 279.6 Hz), 125.8, 120.1, 60.6 (q, J = 26.7 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz), 19.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.3 (d, $J_{F\text{-}H}$ = 6.8 Hz,); HRMS (ESI) m/z $C_{13}H_{16}F_3N_2O$ $[M + H]^+$ calcd 273.1209, found: 273.1216.

3-Methyl-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4d). White solid; 71.5 mg, 73% yield; mp 75-77 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, J = 6.0 Hz, 1H), 7.54 (s, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.33 (d, J = 7.2 Hz, 1H), 7.32-7.30 (m, 1H), 6.02-5.95 (m, 1H), 5.32-5.28 (m, 2H), 4.92 (d, J = 6.0 Hz, 1H), 3.51-3.45 (m, 1H), 2.60 (d, J = 14.4 Hz, 1H), 2.38 (s, 3H), 2.36-2.31 (m,1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 138.6, 132.9, 132.1, 132.1, 128.6, 127.6, 126.1 (q, $J_{C\text{-}F}$ = 279.6 Hz), 123.8, 119.9, 60.6 (q, $J_{C\text{-}F}$ = 26.7 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz), 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{13}H_{16}F_3N_2O$ $[M + H]^+$ calcd 273.1209, found: 273.1215.

4-Methyl-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4e). White solid; 81.5 mg, 84% yield; mp 100-101 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (br, 1H), 7.62 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 6.02-5.95 (m, 1H), 5.31-5.28 (m, 2H), 4.92 (d, J = 5.4 Hz, 1H), 3.47 (s, 1H), 2.59 (d, J = 15.0 Hz, 1H), 2.39 (s, 3H), 2.36-2.30 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.4, 142.8, 132.0, 129.4, 129.3, 126.9, 126.0 (q, $J_{C\text{-}F}$ = 279.4 Hz), 119.9, 60.6 (q, $J_{C\text{-}F}$ = 26.7 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz), 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{13}H_{16}F_3N_2O$ $[M + H]^+$ calcd 273.1209, found: 273.1214.

4-Fluoro-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4f). White solid; 80.0 mg, 81% yield; mp 81-82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.74-7.73 (m, 2H), 7.12 (t, J = 8.4 Hz, 2H), 6.01-5.96 (m, 1H), 5.32-5.30 (m, 2H), 4.91 (d, J = 6.0 Hz, 1H), 3.50-3.45 (m, 1H), 2.61 (d, J = 14.4 Hz, 1H), 2.36-2.30 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 165.1 (d, $J_{C\text{-}F}$ = 251.9 Hz), 131.9, 129.3 (d, $J_{C\text{-}F}$ = 9.0 Hz), 128.3 (d, $J_{C\text{-}F}$ = 3.2 Hz), 126.0 (q, $J_{C\text{-}F}$ = 279.6 Hz), 120.1, 115.9 (d, $J_{C\text{-}F}$ = 22.0 Hz), 60.6 (q, $J_{C\text{-}F}$ = 26.5 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz), -107.1 (m); HRMS (ESI) m/z $C_{12}H_{12}NaF_4N_2O$ $[M + Na]^+$ calcd 299.0778, found: 299.0783.

4-Chloro-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4g). White solid; 90.1 mg, 86% yield; mp 114-115 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.67 (d, J = 12.0 Hz, 2H), 7.42 (d, J = 12.0 Hz, 2H), 6.01-5.95 (m, 1H), 5.33-5.30 (m, 2H), 4.92 (d, J = 6.0 Hz, 1H), 3.51-3.46 (m, 1H), 2.63-2.59 (m, 1H), 2.36-2.31 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 138.6, 131.9, 130.5, 129.1, 128.3, 126.0 (q, $J_{C\text{-}F}$ = 279.5 Hz), 120.1, 60.6 (q, $J_{C\text{-}F}$ = 26.5 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz);^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{12}H_{13}ClF_3N_2O$ $[M + H]^+$ calcd 293.0663, found: 293.0662.

3-Bromo-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4h). White solid; 90.1 mg, 75% yield; mp 80-82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.85 (m, 2H), 7.67-7.63 (m, 2H), 7.33-7.31 (m, 1H), 6.01-5.95 (m, 1H), 5.33-5.30 (m, 2H), 4.91 (d, J = 6.0 Hz, 1H), 3.51-3.46 (m, 1H), 2.64-2.60 (m, 1H), 2.37-2.31 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 135.2, 134.1, 131.9, 130.3, 130.2, 126.0 (q, $J_{C\text{-}F}$ = 279.6 Hz), 125.4, 122.9, 120.2, 60.6 (q, $J_{C\text{-}F}$ = 27.0 Hz), 31.5 (d, $J_{C\text{-}F}$ = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.4 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{12}H_{13}BrF_3N_2O$ $[M + H]^+$ calcd 337.0158, found: 337.0159.

4-(Trifluoromethyl)-*N*′-(1,1,1-trifluoropent-4-en-2-yl)benzohydrazide (4i). White solid; 75.8 mg, 65% yield; mp 87-89 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.83 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 6.01-5.94 (m, 1H), 5.33-5.29 (m, 2H), 4.93 (d, J = 6.0 Hz, 1H), 3.53-3.47 (m, 1H), 2.63-2.60 (m, 1H), 2.36-2.28 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2, 135.4, 133.9 (q, $J_{C\text{-}F}$ = 32.5 Hz), 131.8, 127.4, 126.0 (q, $J_{C\text{-}F}$ = 279.6 Hz), 125.8 (d, $J_{C\text{-}F}$ = 3.5 Hz), 123.4 (q, $J_{C\text{-}F}$ = 271.2 Hz), 120.3, 60.5 (q, $J_{C\text{-}F}$ = 27.1 Hz), 31.4 (d, $J_{C\text{-}F}$ = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.6 (d, $J_{F\text{-}H}$ = 5.3 Hz), -75.5 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{13}H_{13}F_6N_2O$ $[M + H]^+$ calcd 327.0927, found: 327.0926.

***N*′-(1,1,1-Trifluoropent-4-en-2-yl)furan-2-carbohydrazide (4j)**. White solid; 76.1 mg, 86% yield; mp 65-67 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.46 (s, 1H), 7.15 (d, J = 3.6 Hz, 1H), 6.52 (t, J = 1.8 Hz, 1H), 6.02-5.96 (m, 1H), 5.33-5.29 (m, 2H), 4.82 (d, J = 6.0 Hz, 1H), 3.49-3.47 (m, 1H), 2.62-2.59 (m, 1H), 2.36-2.31 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.1, 146.2, 144.6, 132.0, 126.0 (q, $J_{C\text{-}F}$ = 279.6 Hz), 120.1, 115.3, 112.1, 60.8 (q, $J_{C\text{-}F}$ = 27.0 Hz), 31.4 (d, $J_{C\text{-}F}$ = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, $J_{F\text{-}H}$ = 6.8 Hz); HRMS (ESI) m/z $C_{10}H_{12}F_3N_2O_2$ $[M + H]^+$ calcd 249.0845, found: 249.0842.

***N*′-(1,1,1-Trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4k)**. Colourless oil; 61.8 mg, 60% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71-7.70 (m, 2H), 7.69 (d, J = 1.2 Hz, 1H), 7.52-7.50 (m, 1H), 7.43-7.40 (m, 2H), 6.08 (dd, J = 17.4, 10.8 Hz, 1H), 5.22-5.18 (m, 2H), 5.00 (d, J = 6.0 Hz, 1H), 3.21 (q, J = 8.4 Hz, 1H), 1.31 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 143.7, 132.3, 132.1, 128.7, 126.8, 126.7 (q, $J_{C\text{-}F}$ = 282.4 Hz), 114.0, 68.3 (q, $J_{C\text{-}F}$ = 24.2 Hz), 39.0, 25.8, 22.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, $J_{F\text{-}H}$ = 7.8 Hz); HRMS (ESI) m/z $C_{14}H_{18}F_3N_2O$ $[M + H]^+$ calcd 287.1366, found: 287.1363.

4-Fluoro-*N*′-(1,1,1-trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4l). White solid; 73.8 mg, 68% yield; mp

85-86 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74-7.73(m, 2H), 7.72 (s, 1H), 7.13-7.10 (m, 2H), 6.08 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.23-5.19 (m, 2H), 5.00 (d, *J* = 6.0 Hz, 1H), 3.22 (q, *J* = 7.8 Hz, 1H), 1.32 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 165.1 (d, J_{C-F} = 236.7 Hz), 143.6, 129.2 (d, J_{C-F} = 9.0 Hz), 128.5 (d, J_{C-F} = 3.0 Hz), 126.7 (q, J_{C-F} = 282.6 Hz), 115.9 (d, J_{C-F} = 21.9 Hz), 114.0, 68.3 (q, J_{C-F} = 24.4 Hz), 39.0, 25.8, 22.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, J_{F-H} = 7.8 Hz), -107.2 (m); HRMS (ESI) m/z $C_{14}H_{16}NaF_4N_2O$ $[M + Na]^+$ calcd 327.1091, found: 327.1096.

4-Chloro-*N′*-(1,1,1-trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4m). White solid; 86.1 mg, 75% yield; mp 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 6.0 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 6.07 (dd, *J* =17.2, 10.8 Hz, 1H), 5.24-5.19 (m, 2H), 4.99 (d, *J* = 6.0 Hz, 1H), 3.21 (q, *J* = 8.0 Hz, 1H), 1.32 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 143.6, 138.4, 130.7, 129.0, 128.3, 126.7 (q, J_{C-F} = 282.6 Hz), 114.1, 68.2 (q, J_{C-F} = 24.3 Hz), 39.0, 25.8, 22.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, J_{F-H} = 7.8 Hz); HRMS (ESI) m/z $C_{14}H_{17}ClF_3N_2O$ $[M + H]^+$ calcd 321.0976, found: 321.0975.

3-Bromo-*N′*-(1,1,1-trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4n). White solid; 109.8 mg, 84% yield; mp 70-72 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.72 (d, *J* = 6.0 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 6.07 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.23-5.19 (m, 2H), 4.98 (d, *J* = 6.0 Hz, 1H), 3.20 (q, *J* = 8.4 Hz, 1H), 1.31 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 143.6, 135.0, 134.3, 130.3, 130.2, 126.6 (q, J_{C-F} = 282.6 Hz), 125.4, 122.9, 114.1, 68.2 (q, J_{C-F} = 24.3 Hz), 39.0, 25.8, 22.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, J_{F-H} = 7.6 Hz); HRMS (ESI) m/z $C_{14}H_{17}BrF_3N_2O$ $[M + H]^+$ calcd 365.0471, found: 365.0470.

4-Methyl-*N′*-(1,1,1-trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4o). White solid; 83.1 mg, 77% yield; mp 129-130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, *J* = 6.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.10 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.24-5.20 (m, 2H), 5.01 (d, *J* = 6.0 Hz, 1H), 3.21 (q, *J* = 8.4 Hz, 1H), 2.39 (s, 3H), 1.33 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 143.7, 142.6, 129.5, 129.4, 126.8, 126.7 (q, J_{C-F} = 282.6 Hz), 113.9, 68.3 (q, J_{C-F} = 24.0 Hz), 39.0, 25.8 (d, J_{C-F} = 1.7 Hz), 22.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, J_{F-H} = 7.8 Hz); HRMS (ESI) m/z $C_{15}H_{20}F_3N_2O$ $[M + H]^+$ calcd 301.1522, found: 301.1521.

4-Methoxy-*N′*-(1,1,1-trifluoro-3,3-dimethylpent-4-en-2-yl)benzohydrazide (4p). White solid; 79.4 mg, 70% yield; mp 80-82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 6.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.09 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.23-5.19 (m, 2H), 5.01 (d, *J* = 6.0 Hz, 1H), 3.84 (s, 3H), 3.20 (q, *J* = 7.8 Hz, 1H), 1.32 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 162.6, 143.7, 128.7, 126.8 (q, J_{C-F} = 282.7 Hz), 124.5, 114.0, 113.9, 68.4 (q, J_{C-F} = 24.0 Hz), 55.4, 39.0, 25.8, 22.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.9 (d, J_{F-H} = 7.9 Hz); HRMS (ESI) m/z $C_{15}H_{20}F_3N_2O_2$ $[M + H]^+$ calcd 317.1471, found: 317.1479.

***N′*-(1,1,1-Trifluoro-3,3-dimethylpent-4-en-2-yl)furan-2-carbohydrazide (4q)**. Colourless oil; 50.3 mg, 51% yield; mp 99-100 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.4 Hz, 1H), 7.45 (s, 1H), 7.26 (s, 1H), 7.13 (d, *J* = 1.8 Hz, 1H), 6.50 (d, *J* = 1.2 Hz, 1H), 6.08 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.23-5.19 (m, 1H), 4.87 (d, *J* = 6.6 Hz, 1H), 3.19 (q, *J* = 7.8 Hz, 1H), 1.32 (s, 1H), 1.24 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.7, 146.3, 144.5, 143.6, 126.7 (q, J_{C-F} = 282.6 Hz), 115.1, 114.1, 112.1, 68.4 (q, J_{C-F} = 24.4 Hz), 39.0, 25.8, 22.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.1 (d, J_{F-H} = 7.9 Hz); HRMS (ESI) m/z $C_{12}H_{15}NaF_3N_2O_2$ $[M + Na]^+$ calcd 299.0978, found: 299.0993.

General procedures for synthesis of trifluoromethylated *α*-methylene-*γ*-lactams 6

A solution of acylhydrazine **1** (0.36 mmol), trifluoroacetaldehyde methyl hemiacetal **2** (0.54 mmol), ethyl 2-(bromomethyl)acrylate **5** (1.08 mmol) and tin powder (1.26 mmol) in EtOH (5 mL) was stirred at reflux for 15-18 h (monitored by TLC). After completion, the reaction mixture was cooled to room temperature, saturated NH_4Cl solution (10 mL) was added into the mixture and stirred for 10 min, then the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuum. Purification of the residue by silica gel column chromatography using petroleum ether : acetone (5:1-4:1) as eluent furnished the products **6**.

***N*-(3-Methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6a)**. White solid; 86.0 mg, 84% yield; mp 177-178 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.42 (s, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 6.23 (s, 1H), 5.59 (s, 1H), 4.50-4.48 (m, 1H), 3.25-3.20 (m, 1H), 2.89 (d, *J* = 18.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 165.5, 132.9, 132.4, 130.5, 128.5, 127.5, 124.6 (q, J_{C-F} = 280.0 Hz), 120.6, 56.7 (q, J_{C-F} = 31.5 Hz), 24.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, J_{F-H} = 6.4 Hz); HRMS (ESI) m/z $C_{13}H_{12}F_3N_2O_2$ $[M + H]^+$ calcd 285.0845, found: 285.0842.

4-Fluoro-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6b). White solid; 71.2 mg, 66% yield; mp 154-156 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.82-7.79 (m, 2H), 6.96 (t, *J* = 8.4 Hz, 2H), 6.24 (s, 1H), 5.61 (s, 1H), 4.46 (s, 1H), 3.25-3.21 (m, 1H), 2.90 (d, *J* = 18.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.3, 165.2 (d, *J* = 252.5 Hz), 164.2, 132.8, 130.0 (d, *J* = 9.2 Hz), 126.6 (d, *J* = 2.8 Hz), 124.5 (q, J_{C-F} = 280.0 Hz), 120.8, 115.6 (d, *J* = 22.0 Hz), 56.8 (q, J_{C-F} = 32.0 Hz), 24.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.0 (d, J_{F-H} = 6.4 Hz), 106.5 (m); HRMS (ESI) m/z $C_{13}H_{10}NaF_4N_2O_2$ $[M + Na]^+$ calcd 325.0571, found: 325.0577.

4-Chloro-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6c). White solid; 79.9 mg, 70% yield; mp 160-162 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.22 (s, 1H), 5.60 (s, 1H), 4.45-4.42 (m, 1H), 3.23-3.19 (m, 1H), 2.90-2.86 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.3, 164.3, 138.9, 132.7, 128.8, 128.7, 128.6, 124.4 (q, J_{C-F} = 280.0 Hz), 120.9, 56.8 (q, J_{C-F} = 32.0 Hz), 24.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.0 (d, J_{F-H} = 6.4 Hz); HRMS (ESI) m/z $C_{13}H_{14}ClF_3N_3O_2$ $[M + NH_4]^+$ calcd 336.0721, found: 336.0723.

3-Bromo-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6d). White solid; 90.9 mg, 69% yield; mp 122-124 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.89 (s, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.19-7.16 (m, 1H), 6.23 (t, J = 2.4 Hz, 1H), 5.60 (s, 1H), 4.47-4.44 (m, 1H), 3.25-3.20 (m, 1H), 2.90 (dd, J = 17.4, 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 163.9, 135.5, 132.7, 132.2, 130.9, 130.1, 125.6, 124.4 (q, $J_{C\text{-}F}$ = 280.2 Hz), 122.8, 120.9, 56.8 (q, $J_{C\text{-}F}$ = 31.6 Hz), 24.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, $J_{F\text{-}H}$ = 6.1 Hz); HRMS (ESI) m/z $C_{13}H_{10}NaBrF_3N_2O_2$ $[M + Na]^+$ calcd 384.9770, found: 384.9777.

***N*-(3-Methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)-4-(trifluoromethyl)benzamide (6e)**. White solid; 81.1 mg, 64% yield; mp 137-138 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.16 (s, 1H), 7.84 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 6.27 (t, J = 2.4 Hz, 1H), 5.64 (s, 1H), 4.49-4.46 (m, 1H), 3.28-3.23 (m, 1H), 2.93 (dd, J = 17.4, 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 163.9, 134.0 (q, $J_{C\text{-}F}$ = 32.4 Hz), 133.5, 132.5, 127.8, 125.6 (q, J = 3.6 Hz), 124.4 (q, $J_{C\text{-}F}$ = 280.0 Hz), 123.4 (q, $J_{C\text{-}F}$ = 270.7 Hz), 121.1, 56.9 (q, $J_{C\text{-}F}$ = 32.0 Hz), 24.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.8 (s), -81.0 (d, $J_{F\text{-}H}$ = 6.0 Hz); HRMS (ESI) m/z $C_{14}H_{10}NaF_6N_2O_2$ $[M + Na]^+$ calcd 375.0539, found: 375.0544.

4-Methoxy-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6f). White solid; 91.9 mg, 81% yield; mp 158-160 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.94 (br, 1H), 7.77 (d, J = 8.4 Hz, 2H), 6.76-6.75 (m, 2H), 6.22 (s, 1H), 5.58 (s, 1H), 4.47 (s, 1H), 3.79 (s, 3H), 3.24-3.20 (m, 1H), 2.88 (d, J = 17.4 Hz, 1H), ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 165.1, 162.9, 133.0, 129.5, 124.6 (q, $J_{C\text{-}F}$ = 279.9 Hz), 122.9, 120.4, 113.7, 56.9 (q, $J_{C\text{-}F}$ = 31.6 Hz), 55.3, 24.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, $J_{F\text{-}H}$ = 6.2 Hz); HRMS (ESI) m/z $C_{14}H_{13}NaF_3N_2O_3$ $[M + Na]^+$ calcd 337.0770, found: 337.0778.

3-Methyl-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6h). White solid; 45.0 mg, 42% yield; mp 141-143 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.61 (d, J = 6.0 Hz, 2H), 7.23 (d, J = 7.8 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 6.22 (t, J = 2.4 Hz, 1H), 5.58 (t, J = 2.4 Hz, 1H), 4.52-4.48 (m, 1H), 3.25-3.20 (m, 1H), 2.91-2.87 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 165.6, 138.3, 133.1, 133.0, 130.5, 128.4, 128.12, 124.5, 124.6 (q, $J_{C\text{-}F}$ = 279.9 Hz), 120.4, 56.7 (q, $J_{C\text{-}F}$ = 31.6 Hz), 24.8, 21.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, $J_{F\text{-}H}$ = 6.2 Hz); HRMS (ESI) m/z $C_{14}H_{13}NaF_3N_2O_2$ $[M + Na]^+$ calcd 321.0821, found: 321.0826.

4-Methyl-*N*-(3-methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)benzamide (6i). White solid; 91.2mg, 85% yield; mp 140-142 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.92 (s, 1H), 7.67 (d, J = 7.8 Hz, 2H), 7.06 (d, J = 7.8 Hz, 2H), 6.20 (s, 1H), 5.56 (s, 1H), 4.47 (s, 1H), 3.22-3.18 (m, 1H), 2.87 (d, J = 17.4 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 165.5, 143.0, 133.0, 129.1, 127.8, 127.5, 124.6 (q, $J_{C\text{-}F}$ = 280.1 Hz), 120.4, 56.8 (q, $J_{C\text{-}F}$ = 31.6 Hz), 24.8, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, $J_{F\text{-}H}$ = 6.2 Hz); HRMS (ESI) m/z $C_{14}H_{13}NaF_3N_2O_2$ $[M + Na]^+$ calcd 321.0821, found: 321.0828.

***N*-(3-Methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)furan-2-carboxamide (6j)**. White solid; 80.2 mg, 82% yield; mp 154-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (br, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.14 (d, J = 3.2 Hz, 1H), 6.42 (dd, J = 4.0, 2.0 Hz, 1H), 6.23 (t, J = 2.4 Hz, 1H), 5.59 (t, J = 2.4 Hz, 1H), 4.50-4.44 (m, 1H), 3.23 (dd, J = 17.6, 9.2 Hz, 1H), 2.93-2.88 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.3, 156.5, 145.4, 145.2, 132.8, 124.6 (q, $J_{C\text{-}F}$ = 280.0 Hz), 120.5, 116.4, 112.0, 56.9 (q, $J_{C\text{-}F}$ = 31.6 Hz), 24.8 (d, J = 1.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.9 (d, $J_{F\text{-}H}$ = 6.4 Hz); HRMS (ESI) m/z $C_{11}H_9NaF_3N_2O_3$ $[M + Na]^+$ calcd 297.0457, found: 297.0461.

***N*-(3-Methylene-2-oxo-5-(trifluoromethyl)pyrrolidin-1-yl)-2-naphthamide (6k)**. White solid; 90.2 mg, 75% yield; mp 187-189 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.35 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 6.6 Hz, 1H), 7.55-7.50 (m, 2H), 7.36-7.34 (m, 1H), 6.18 (d, J = 1.8 Hz, 1H), 5.55 (d, J = 1.2 Hz, 1H), 4.59 (s, 1H), 3.21 (dd, J = 16.2, 9.6 Hz, 1H), 2.88 (d, J = 17.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 167.2, 133.5, 132.7, 131.9, 130.2, 129.9, 128.3, 127.6, 126.6, 126.1, 125.1, 124.5, 124.7 (q, $J_{C\text{-}F}$ = 279.6 Hz), 120.6, 56.7 (q, $J_{C\text{-}F}$ = 31.6 Hz), 24.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.7 (d, $J_{F\text{-}H}$ = 6.0 Hz); HRMS (ESI) m/z $C_{17}H_{13}NaF_3N_2O_2$ $[M + Na]^+$ calcd 357.0821, found: 357.0826.

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One-pot preparation of trifluoromethylated homoallylic *N*-acylhydrazines or *α*-methylene-*γ*-lactams from acylhydrazines, trifluoroacetaldehyde methyl hemiacetal, allylic bromide and tin

Ganggang Du, Danfeng Huang,* Ke-Hu Wang, Xiaowei Chen, Yanli Xu, Junyan Ma, Yingpeng Su, Ying Fu, and Yulai Hu*

Tin promoted one-pot preparation of trifluoromethylated homoallylic *N*-acylhydrazines or *α*-methylene-*γ*-lactams has been developed instead of using toxic stannanes.