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Cascade reaction for 3-pyrrolines and pyrroles from nitroallylic acetates and *N*-mesyl 2-aminoethanones

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ABSTRACT

Cascade reactions of nitroallylic acetates with methanesulfonyl 2-aminoethanones affords either the 3-pyrrolines or the pyrroles in one pot depending on reaction solvents and temperature. A possible mechanism for the entire sequence is proposed.

1. Introduction

Pyrroles and 3-pyrrolines are important five-membered heterocycles that constitute the core motif of many bioactive molecules.[1] Pyrroles display remarkable pharmacological—anti-inflammatory,[2a] antitumor,[2b] antimalarial,[2c] and anti-HIV[2d]—activities. Among them, many have been in first-line clinical use, such as Tolmetin and Atorvastatin (Fig. 1) for treatment of rheumatoid arthritis and dyslipidemia, respectively.[1c] Furthermore, they are widely used in materials science[3] and natural products synthesis.[4] 3-Pyrrolines, synthetic precursor to pyrroles, have been extensively used as building blocks in organic and materials chemistry.[5] They are contained in bioactive molecules,[6] such as the kinesin spindle protein inhibitor shown in Fig. 1.[6b]

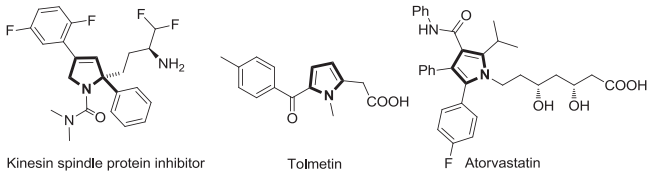

Fig. 1. Biologically active 3-pyrrolines and pyrroles.

Therefore, the development of efficient synthetic methodologies for these privileged heterocyclic scaffolds has received considerable attention over the years. The most frequently used synthetic methods for pyrroles include Hantzsch synthesis, Paal–Knorr synthesis and various cycloaddition strategies using 1,3-dicarbonyl compounds, isonitriles, nitroalkanes, nitroalkenes, and alkynes as starting materials.[1b] Recently, progress has been made in the synthesis of pyrroles through the use of transition-metal-catalyzed C–H bond functionalization. In fact this synthetic methodology is becoming increasingly popular.[7] Not surprisingly, various synthetic methods have been developed for the construction of 3-pyrrolines including Birch reduction of pyrroles,[8a] [3+2] cyclization[8b–e] as well as transition metal-catalyzed reactions.[8f–n] Herein we report a facile cascade reaction to provide 3-pyrrolines and pyrroles in one pot from nitroallylic acetates.

In 1973, Baylis and Hillman reported the synthesis of α-hydroxyethyl nitroethylenes via a MBH reaction[9a] between nitroethylene and aldehydes.[9b–c] After that Namboothiri and Chen made further investigation of this reaction emphasizing the use of electrophilic ethyl glyoxylate.[10] Further acetylation of the hydroxyl group of these conjugated nitroalkenes afforded the nitroallylic acetates as excellent synthetic Michael acceptors with four potential electrophilic sites (α, β, γ, δ, Scheme 1). Namboothiri and Chen demonstrated that the cycloaddition of the nitroallylic acetates predominantly occurred at the electrophilic α and β sites. This provided an efficient route for the synthesis of a number of functionalized products, such as furans,[11a] imidazolepyridines,[11b]

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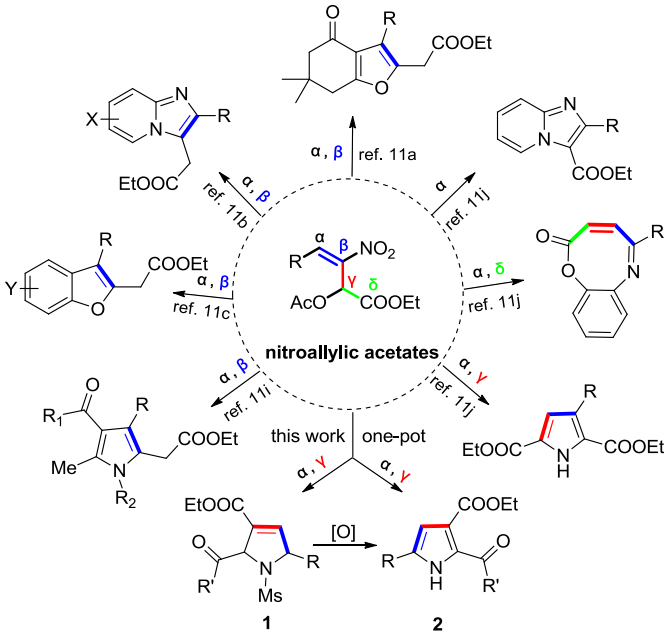


Scheme 1. Cascade reactions of nitroallylic acetates.

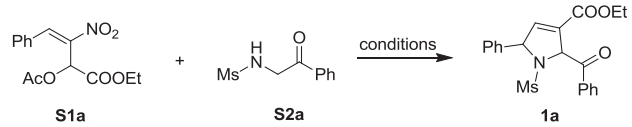
arenofurans,[11c] cyclopentenes,[11d] pyrans,[11a] pyrroles,[11i–j] and others[11e–h] (Scheme 1). Very recently, we have proved that all four potential electrophilic sites can be utilized in synthesizing diverse heterocycles through reaction with a broad range of bifunctional nucleophiles, such as imidazo[1,2-*a*]pyridines (electrophilic α site involved), indolizines (α/β),[11j] pyrroles (α/γ), and benzo[*b*][1,6]oxazocin-2-ones (α/δ) (Scheme 1).[11j] Inspired by this work, we investigated the reactions of nitroallylic acetates with *N*-mesyl 2-aminoethanones leading to the formation of 3-pyrrolines and pyrroles through a cascade Michael addition and elimination at the electrophilic α and γ sites. Generally, the transformation of 3-pyrrolines to pyrroles needs to go through an additional reaction step, such as a DDQ-mediated oxidation,[8d,12a–b] or redox isomerization.[12c] Notably, 3-pyrrolines in this reaction can easily be converted to pyrroles in one pot through the use of DMF/THF (1:1) as the solvent system and heated to 85 °C for 8 h under air.

2. Results and discussion

Initially, we investigated the synthesis of trisubstituted 3-pyrrolines from nitroallylic acetate **S1a** and methanesulfonyl 2-aminoethanone **S2a** as a model reaction. Different solvents were examined first, and the results showed that solvent selection is crucial for the success of the reaction (Table 1). In the presence of base, reaction of **S1a** and **S2a** in THF (entry 6) at rt showed a significant increase in the isolated yield. Optimization of bases revealed that base also plays a major role in a successful transformation and K_2CO_3 was identified as the most efficient base (entry 6, Table 1) in our study. No reaction was observed when the base was removed (entry 12). A slight decrease in the yield was observed when the reaction temperature was increased to the boiling point of THF (entry 7, Table 1).

With these optimal reaction conditions in hand, we examined the scope of this cyclization (Table 2). The 3-pyrrolines **1a**–**r** (Table 2) were isolated as single major enantiomers and the relative stereochemistry of the product was established by the NOESY analysis of **1c**. As shown in Fig. 2, the $^1H-^1H$ interactions between H_a and H_b was observed. The result suggests a *syn* configuration of the synthesized 3-pyrrolines.

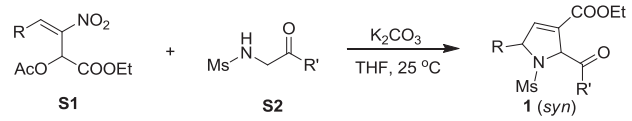
Table 1
Optimization of reaction conditions[a]



No.	Base	Solvent	Temp	Yield (%)[b]
1	K_2CO_3	DCM	25	71
2	K_2CO_3	MeOH	25	Trace
3	K_2CO_3	MeCN	25	75
4	K_2CO_3	DMF	25	Trace
5	K_2CO_3	Acetone	25	78
6	**K_2CO_3**	**THF**	**25**	**81**
7	K_2CO_3	THF	65	74
8	Na_2CO_3	THF	25	68
9	Et_3N	THF	25	24
10	DBU	THF	25	Trace
11	DABCO	THF	25	18
12	—	THF	25	0

[a] Reaction conditions: **S1a** (0.3 mmol, 1.5 equiv), **S2a** (0.2 mmol, 1.0 equiv), base (0.2 mmol, 1.0 equiv), solvent (2.0 mL) were stirred at rt for 10 h.
[b] Determined by high performance liquid chromatography, based on the disappearance of **S2a**. The most successful entry is highlighted in bold.

Table 2
Synthesis of 3-pyrrolines[a]



No.	R	R′	Product	Yield (%)[b]
1	Ph	Ph	**1a**	69
2	4-F–Ph	Ph	**1b**	80
3	4-Cl–Ph	Ph	**1c**	75
4	4-Br–Ph	Ph	**1d**	71
5	2-Br–Ph	Ph	**1e**	68
6	3-Br–Ph	Ph	**1f**	69
7	4-OCH_3–Ph	Ph	**1g**	64
8	4-CH_3–Ph	Ph	**1h**	68
9	4-CF_3–Ph	Ph	**1i**	76
10	1-Naphthyl	Ph	**1j**	71
11	2-Furyl	Ph	**1k**	45
12	Cyclopropyl	Ph	**1l**	47
13	Ph	4-CH_3–Ph	**1m**	72
14	Ph	4-OCH_3–Ph	**1n**	81
15	Ph	4-Br–Ph	**1o**	64
16	Ph	4-NO_2–Ph	**1p**	25
17	Ph	Cyclopropyl	**1q**	34
18	Ph	Isopropyl	**1r**	39

[a] Reactions were performed in 2.0 mL THF at 25 °C for 10 h in the presence of base.
[b] Isolated yield of major enantiomers.

As presented in Table 2, we found that a range of R-substituents of nitroallylic acetates **S1** and R′-substituents of mesylated 2-aminoethanones **S2** can be tolerated in this reaction. The results demonstrate that the reaction efficiency is affected by substituted

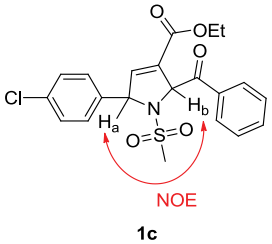
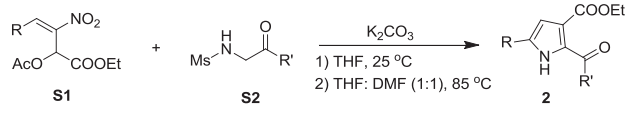


Fig. 2. NOESY analysis of 3-pyrroline **1c**.

S1 with various steric and electronic properties. The nitroallylic acetates with electron withdrawing substituents on phenyl ring showed higher isolated yields of 3-pyrrolines **1** (entries 2–6 and 9, Table 2). The influence of R′-substituents of **S2** in this reaction is illustrated in entries 1 and 13–18. The reverse trend was observed and the 4-methoxy phenyl substituted **S2** afforded 3-pyrroline **1n** with the highest isolated yield of 81% (entry 14, Table 2) under these reaction conditions. The aliphatic substituents at the nitroallylic acetates or methanesulfonyl 2-aminoethanones (entries 12, 17, and 18) gave lower yields than most aromatic substrates.

Upon formation of 3-pyrrolines, we added the same volume of DMF to the reaction and it was refluxed at 85 °C for another 8 h. In situ cascade aromatization and isomerization of 3-pyrrolines to pyrroles (**2a**–**r**) was observed and the results are summarized in Table 3. The functionalized trisubstituted pyrroles were fully characterized by HRMS, ^{1}H and ^{13}C NMR spectroscopic analysis and further confirmed by X-ray analysis of pyrrole **2g** (Fig. 3).[13] Interestingly, efficiency of the R- and R′-substituents on pyrroles' synthesis maintained the same trend as those of the 3-pyrrolines (entries 1–18, Table 2 and entries 1–18, Table 3). Another observation was that the isolated yields of some pyrroles were slightly higher than the corresponding 3-pyrrolines (entries 1–10, Table 2 and entries 1–10, Table 3 as examples). This might be ascribed to the instability of the pyrrolines[14] and the potential existence of a small amount of *anti* isomers of the 3-pyrrolines, which went through the subsequent elimination and rearrangements providing the pyrroles.

Table 3
Synthesis of pyrroles[a]



No.	R	R′	Product	Yield (%)[b]
1	Ph	Ph	**2a**	74
2	4-F–Ph	Ph	**2b**	85
3	4-Cl–Ph	Ph	**2c**	77
4	4-Br–Ph	Ph	**2d**	73
5	2-Br–Ph	Ph	**2e**	74
6	3-Br–Ph	Ph	**2f**	70
7	4-OCH_3–Ph	Ph	**2g**	68
8	4-CH_3–Ph	Ph	**2h**	69
9	4-CF_3–Ph	Ph	**2i**	79
10	1-Naphthyl	Ph	**2j**	72
11	2-Furyl	Ph	**2k**	42
12	Cyclopropyl	Ph	**2l**	52
13	Ph	4-CH_3–Ph	**2m**	75
14	Ph	4-OCH_3–Ph	**2n**	86
15	Ph	4-Br–Ph	**2o**	68
16	Ph	4-NO_2–Ph	**2p**	41
17	Ph	Cyclopropyl	**1q**	37
18	Ph	Isopropyl	**1r**	45

[a] Reaction were performed in 2.0 mL THF at 25 °C for 10 h in the presence of K_2CO_3 under air and then additional 2.0 mL of DMF was added to the reaction mixture. It was heated to 85 °C and further stirred for another 8 h.
[b] Isolated yield.

A proposed reaction mechanism for the synthesis of 3-pyrrolines and pyrroles is shown in Scheme 2. In the presence of base, the electrophilic α site of nitroallylic acetate was attacked by the nitrogen from the mesylated 2-aminoethanones as the nucleophile. Subsequently, another Michael addition occurred at the electrophilic γ site of the nitroallylic acetate followed by an automatic elimination and rearrangement to afford the mesylated 3-pyrrolines (**1**). When the reaction temperature increased to 85 °C with the mixed solvent system, the in situ elimination[15] and subsequent intramolecular rearrangement takes place to give the corresponding pyrroles (**2**).

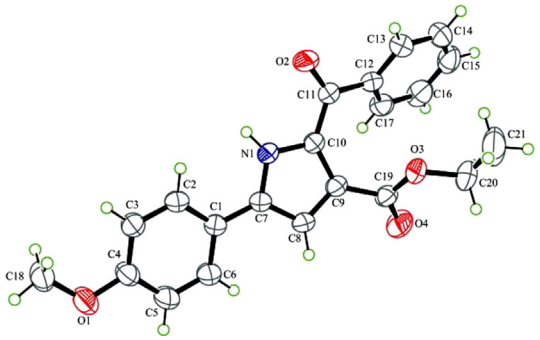
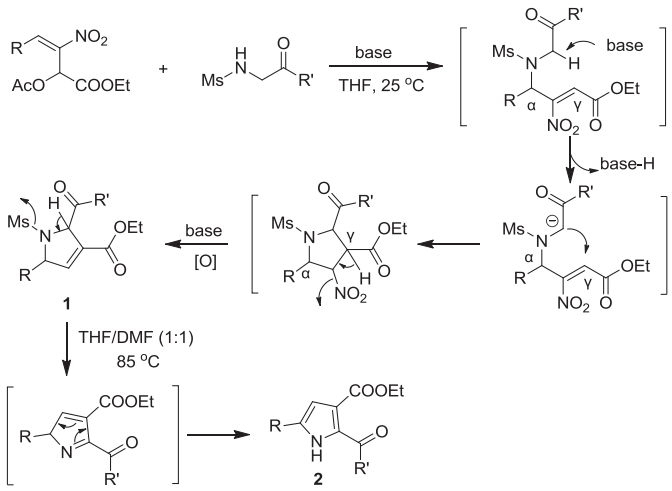


Fig. 3. ORTEP view of pyrrole **2g**.



Scheme 2. Proposed mechanism for the reaction sequence.

3. Conclusions

In summary, we have developed a new general and practical synthetic protocol for the efficient assembly of trisubstituted 3-pyrrolines and pyrroles from nitroallylic acetates and mesylated 2-aminoethanones as bifunctional nucleophiles. Cascade synthesis of these privileged heterocyclic scaffolds can be intentionally achieved depending on different reaction conditions in one pot. The results described herein provide insights to the property of nitroallylic acetates with four potential electrophilic sites and may find wider application in diversified heterocycles construction.

4. Experimental section

4.1. General

Reactions were carried out in anhydrous solvents under air. DMF was distilled from calcium hydride. Purifications of reaction products were carried out by chromatography using silica gel (200–300 mesh). Melting points were recorded on a BÜCHI B-540 melting point apparatus. NMR spectra were mostly recorded for ^{1}H NMR at 500 MHz and for ^{13}C NMR at 125 MHz while some of them were recorded for ^{1}H NMR at 400 MHz and for ^{13}C NMR at 100 MHz. For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ). The spectra data presented here are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), and coupling constant(s) in Hertz. For ^{13}C NMR TMS (δ=0) or $CDCl_3$ (δ=77.26) was used as internal standard and spectra were obtained with complete proton decoupling. HRMS were obtained using ESI ionization. A single-

crystal of compound **2g** was measured on a Rigaku RAXIS-RAPID single-crystal diffractometer. The starting material nitroallylic acetates **1** were prepared according to the known methods.[10c,16]

4.2. General procedure for the synthesis of 1

Nitroallylic acetate **S1a** (0.3 mmol, 1.5 equiv), methanesulfonyl 2-aminoethanone **S2a** (0.2 mmol, 1.0 equiv) and K_2CO_3 (0.2 mmol, 1.0 equiv) were mixed in THF (2.0 mL) and stirred at rt for 10 h. The reaction mixture was concentrated in vacuum and the crude was purified by flash column chromatography (petroleum ether/EtOAc) on silica gel to afford the desired 3-pyrrolines **1**.

*4.2.1. Ethyl 2-benzoyl-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1a**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (2H, d, J=7.5 Hz), 7.59 (1H, t, J=7.5 Hz), 7.50 (2H, t, J=7.5 Hz), 7.45–7.37 (5H, m), 6.89 (1H, t, J=2.0 Hz), 6.41 (1H, dd, J=6.0, 1.5 Hz), 6.02 (1H, dd, J=6.0, 2.0 Hz), 4.02 (2H, q, J=7.0 Hz), 2.45 (3H, s), 0.96 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 161.5, 143.4, 137.0, 136.4, 133.5, 132.2, 129.2, 129.1, 129.0, 128.5, 128.4, 70.5, 67.4, 61.3, 40.8, 13.6; HRMS calcd for $C_{21}H_{21}NO_5S+H^+$: 400.1219, found: 400.1214.

*4.2.2. Ethyl 2-benzoyl-5-(4-fluorophenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1b**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (2H, d, J=7.5 Hz), 7.60 (1H, t, J=7.5 Hz), 7.50 (2H, t, J=7.5 Hz), 7.39 (2H, dd, J=8.5, 5.5 Hz), 7.11 (2H, t, J=8.5 Hz), 6.86 (1H, s), 6.41 (1H, d, J=5.5 Hz), 6.01 (1H, dd, J=5.5, 1.5 Hz), 4.02 (2H, q, J=7.0 Hz), 2.51 (3H, s), 0.96 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.2, 164.5 (d, J=247 Hz), 162.9, 144.6, 137.8, 135.0, 134.5 (d, J=3 Hz), 133.8, 131.6 (d, J=8 Hz), 130.6, 130.0, 117.5 (d, J=22 Hz), 71.2, 68.8, 62.9, 42.2, 15.0; HRMS calcd for $C_{21}H_{20}FNO_5S+H^+$: 418.1124, found: 418.1119.

*4.2.3. Ethyl 2-benzoyl-5-(4-chlorophenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1c**).* Yellow solid; mp 208–210 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (2H, dd, J=8.0, 1.0 Hz), 7.61 (1H, t, J=7.5, 1.0 Hz), 7.50 (2H, t, J=8.0 Hz), 7.40 (2H, d, J=8.5 Hz), 7.35 (2H, d, J=8.5 Hz), 6.84 (1H, t, J=2.0 Hz), 6.43 (1H, dd, J=6.0, 1.5 Hz), 5.98 (1H, dd, J=6.0, 2.0 Hz), 4.01 (2H, q, J=7.0 Hz), 2.54 (3H, s), 0.95 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 161.4, 142.9, 136.3, 135.9, 135.1, 133.6, 132.5, 129.6, 129.3, 129.1, 128.6, 69.8, 67.4, 61.4, 40.7, 13.5; HRMS calcd for $C_{21}H_{20}ClNO_5S+H^+$: 434.0829, found: 434.0820.

*4.2.4. Ethyl 2-benzoyl-5-(4-bromophenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1d**).* Yellow solid; mp 215–217 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (2H, d, J=7.5 Hz), 7.62 (1H, t, J=7.5 Hz), 7.57 (2H, d, J=8.0 Hz), 7.52 (2H, t, J=7.5 Hz), 7.31 (2H, d, J=8.0 Hz), 6.85 (1H, t, J=1.5 Hz), 6.45 (1H, dd, J=6.0, 1.5 Hz), 5.98 (1H, dd, J=6.0, 1.5 Hz), 4.03 (2H, q, J=7.0 Hz), 2.56 (3H, s), 0.96 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 161.4, 142.9, 136.4, 136.3, 133.7, 132.5, 132.2, 129.9, 129.1, 128.6, 123.3, 69.8, 67.4, 61.4, 40.7, 13.5; HRMS calcd for $C_{21}H_{20}BrNO_5S+H^+$: 478.0324, found: 478.0321.

*4.2.5. Ethyl 2-benzoyl-5-(2-bromophenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1e**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (2H, d, J=7.5 Hz), 7.60 (2H, m), 7.51 (3H, m), 7.38 (1H, t, J=7.5 Hz), 7.20 (1H, td, J=7.5, 1.5 Hz), 6.88 (1H, t, J=2.0 Hz), 6.59 (1H, dd, J=6.0, 1.0 Hz), 6.41 (1H, dd, J=5.5, 1.0 Hz), 3.99 (2H, q, J=7.0 Hz), 2.87 (3H, s), 0.92 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.9, 161.4, 142.5, 141.1, 136.7, 133.8, 133.0, 130.2, 129.2, 128.8, 128.6, 128.4, 128.0, 122.6, 68.6, 68.2, 61.4, 39.1, 13.5; HRMS calcd for $C_{21}H_{20}BrNO_5S+H^+$: 478.0324, found: 478.0319.

*4.2.6. Ethyl 2-benzoyl-5-(3-bromophenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1f**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (2H, dd, J=7.5, 1.5 Hz), 7.61 (1H, t, J=7.5 Hz), 7.51 (4H, m), 7.36 (1H, dt, J=7.5, 1.5 Hz), 7.30 (1H, t, J=8.0 Hz), 6.84 (1H, t, J=2.0 Hz), 6.45 (1H, dd, J=5.5, 1.5 Hz), 5.94 (1H, dd, J=5.5, 2.0 Hz), 4.02 (2H, m), 2.58 (3H, s), 0.96 (3H, t, J=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.6, 161.3, 142.7, 139.8, 136.3, 133.7, 132.6, 132.3, 131.0, 130.5, 129.1, 128.6, 127.0, 123.1, 69.9, 67.4, 61.5, 40.6, 13.5; HRMS calcd for $C_{21}H_{20}BrNO_5S+H^+$: 478.0324, found: 478.0323.

*4.2.7. Ethyl 2-benzoyl-5-(4-methoxyphenyl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1g**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (2H, d, J=7.5 Hz), 7.58 (1H, t, J=7.5 Hz), 7.49 (2H, t, J=7.5 Hz), 7.32 (2H, d, J=8.5 Hz), 6.94 (2H, d, J=8.5 Hz), 6.87 (1H, s), 6.36 (1H, d, J=6.0 Hz), 6.00 (1H, dd, J=6.0, 1.5 Hz), 4.02 (2H, q, J=7.0 Hz), 3.82 (3H, s), 2.42 (3H, s), 0.96 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 161.6, 160.3, 143.6, 136.4, 133.4, 132.0, 129.8, 129.1, 128.7, 128.5, 114.4, 69.9, 67.1, 61.3, 55.4, 41.0, 13.6; HRMS calcd for $C_{22}H_{23}NO_6S+H^+$: 430.1324, found: 430.1318.

*4.2.8. Ethyl 2-benzoyl-1-(methylsulfonyl)-5-(p-tolyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1h**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (2H, d, J=7.5 Hz), 7.59 (1H, t, J=7.5 Hz), 7.49 (2H, t, J=7.5 Hz), 7.29 (2H, d, J=8.0 Hz), 7.22 (2H, d, J=8.0 Hz), 6.87 (1H, s), 6.39 (1H, d, J=5.5 Hz), 5.99 (1H, dd, J=5.5, 1.5 Hz), 4.02 (2H, q, J=7.0 Hz), 2.44 (3H, s), 2.37 (3H, s), 0.96 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.8, 161.6, 143.6, 139.2, 136.4, 133.9, 133.4, 132.0, 129.7, 129.1, 128.5, 128.4, 70.2, 67.3, 61.3, 40.8, 21.3, 13.6; HRMS calcd for $C_{22}H_{23}NO_5S+H^+$: 414.1375, found: 414.1371.

*4.2.9. Ethyl 2-benzoyl-1-(methylsulfonyl)-5-(4-(trifluoromethyl)-phenyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1i**).* Yellow solid; mp 164–166 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (2H, d, J=7.0 Hz), 7.68 (2H, d, J=8.0 Hz), 7.62 (1H, t, J=7.0 Hz), 7.52 (4H, m), 6.84 (1H, t, J=2.0 Hz), 6.50 (1H, dd, J=6.0, 1.5 Hz), 6.03 (1H, dd, J=6.0, 2.0 Hz), 4.02 (2H, q, J=7.0 Hz), 2.61 (3H, s), 0.93 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 161.3, 142.6, 141.6, 136.3, 133.8, 132.7, 131.3 (d, J=32 Hz), 129.2, 128.6, 128.4, 126.0 (q, J=3 Hz), 123.8 (d, J=271 Hz), 70.0, 67.6, 61.5, 40.3, 13.5; HRMS calcd for $C_{22}H_{20}F_3NO_5S+H^+$: 468.1093, found: 468.1089.

*4.2.10. Ethyl 2-benzoyl-1-(methylsulfonyl)-5-(naphthalen-1-yl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1j**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (1H, m), 8.10 (2H, m), 7.82 (2H, m), 7.60 (1H, d, J=6.4 Hz), 7.52 (2H, m), 7.45 (4H, m), 6.93 (1H, s), 6.65 (1H, dd, J=6.0, 1.2 Hz), 6.52 (1H, dd, J=5.6, 1.2 Hz), 3.92 (2H, q, J=7.2 Hz), 2.41 (3H, s), 0.86 (3H, t, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 161.6, 144.2, 136.5, 134.1, 133.9, 133.6, 131.7, 130.9, 129.8, 129.2, 128.8, 128.6, 127.4, 127.0, 126.1, 125.5, 122.6, 70.1, 67.7, 61.4, 40.6, 13.5; HRMS calcd for $C_{25}H_{23}NO_5S+H^+$: 450.1375, found: 450.1372.

*4.2.11. Ethyl 2-benzoyl-5-(furan-2-yl)-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1k**).* Brown solid; mp 158–160 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (2H, d, J=7.0 Hz), 7.58 (1H, t, J=7.0 Hz), 7.48 (3H, m), 6.89 (1H, t, J=2.0 Hz), 6.56 (1H, d, J=3.5 Hz), 6.44 (1H, dd, J=3.5, 1.5 Hz), 6.33 (1H, dd, J=5.5, 1.5 Hz), 6.10 (1H, dd, J=6.0, 2.0 Hz), 4.03 (2H, q, J=7.0 Hz), 2.48 (3H, s), 0.97 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.2, 161.3, 148.5, 143.5, 140.1, 136.3, 133.5, 133.4, 129.1, 128.5, 111.3, 111.2, 66.5, 63.2, 61.4, 39.8, 13.6; HRMS calcd for $C_{19}H_{19}NO_5S+H^+$: 390.1011, found: 390.1010.

*4.2.12. Ethyl 2-benzoyl-5-cyclopropyl-1-(methylsulfonyl)-2,5-dihydro-1H-pyrrole-3-carboxylate (**1l**).* Yellow solid; mp 96–98 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (2H, d, J=7.5 Hz), 7.62 (1H, t, J=7.5 Hz), 7.51 (2H, t, J=7.5 Hz), 6.93 (1H, d, J=2.0 Hz), 6.45 (1H, s),

4.12 (1H, d, *J*=9.5 Hz), 3.99 (2H, q, *J*=7.0 Hz), 2.89 (3H, s), 1.36–1.43 (1H, m), 0.94 (3H, t, *J*=7.0 Hz), 0.78–0.83 (1H, m), 0.67–0.76 (2H, m), 0.38–0.43 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.1, 161.7, 142.6, 136.5, 133.9, 131.7, 129.2, 128.8, 72.7, 66.2, 61.2, 42.4, 15.3, 13.5, 5.7, 2.1; HRMS calcd for $C_{18}H_{21}NO_5S+H^+$: 364.1219, found: 364.1212.

*4.2.13. Ethyl 2-(4-methylbenzoyl)-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1m**).* Yellow solid; mp 199–200 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (2H, d, *J*=8.0 Hz), 7.43–7.36 (5H, m), 7.29 (2H, d, *J*=8.0 Hz), 6.87 (1H, t, *J*=1.5 Hz), 6.40 (1H, dd, *J*=5.5, 1.0 Hz), 6.01 (1H, dd, *J*=6.0, 2.0 Hz), 4.04 (2H, q, *J*=7.0 Hz), 2.45 (3H, s), 2.42 (3H, s), 1.00 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.1, 161.6, 144.5, 143.3, 137.2, 133.8, 132.2, 129.3, 129.2, 129.2, 129.0, 128.4, 70.5, 67.3, 61.3, 40.7, 21.7, 13.6; HRMS calcd for $C_{22}H_{23}NO_5S+H^+$: 414.1375, found: 414.1374.

*4.2.14. Ethyl 2-(4-methoxybenzoyl)-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1n**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (2H, d, *J*=8.5 Hz), 7.40 (3H, m), 7.24 (2H, d, *J*=7.5 Hz), 6.91 (2H, d, *J*=9.0 Hz), 6.06 (1H, d, *J*=3.5 Hz), 5.95 (1H, d, *J*=4.0 Hz), 4.32 (2H, q, *J*=7.0 Hz), 3.96 (1H, t, *J*=4.0 Hz), 3.87 (3H, s), 3.41 (3H, s), 1.34 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 165.7, 162.0, 140.8, 138.1, 133.0, 132.4, 130.8, 129.7, 129.2, 125.7, 115.6, 73.7, 63.2, 57.0, 52.5, 44.9, 15.5; HRMS calcd for $C_{22}H_{23}NO_6S+H^+$: 430.1324, found: 430.1320.

*4.2.15. Ethyl 2-(4-bromobenzoyl)-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1o**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (2H, d, *J*=8.5 Hz), 7.64 (2H, d, *J*=9.0 Hz), 7.44–7.37 (5H, m), 6.89 (1H, t, *J*=2.0 Hz), 6.32 (1H, dd, *J*=5.5, 1.5 Hz), 6.02 (1H, dd, *J*=6.0, 2.0 Hz), 4.06 (2H, q, *J*=7.0 Hz), 2.41 (3H, s), 1.05 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.9, 161.6, 143.4, 136.8, 135.1, 132.0, 131.8, 130.6, 129.4, 129.1, 128.7, 128.5, 70.5, 67.2, 61.5, 40.9, 13.7; HRMS calcd for $C_{21}H_{20}BrNO_5S+H^+$: 478.0324, found: 478.0322.

*4.2.16. Ethyl 1-(methylsulfonyl)-2-(4-nitrobenzoyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1p**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (2H, d, *J*=9.0 Hz), 8.25 (2H, d, *J*=9.0 Hz), 7.42 (5H, m), 6.92 (1H, t, *J*=2.0 Hz), 6.32 (1H, dd, *J*=6.0, 1.5 Hz), 6.05 (1H, dd, *J*=5.5, 2.0 Hz), 4.09 (2H, q, *J*=7.0 Hz), 2.37 (3H, s), 1.09 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.8, 161.6, 150.3, 143.5, 141.1, 136.3, 132.0, 130.0, 129.6, 129.2, 128.6, 123.6, 70.5, 67.5, 61.7, 41.2, 13.8; HRMS calcd for $C_{21}H_{20}N_2O_7S+H^+$: 445.1069, found: 445.1065.

*4.2.17. Ethyl 2-(cyclopropanecarbonyl)-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1q**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (2H, m), 7.52 (3H, m), 6.92 (1H, t, *J*=2.0 Hz), 6.44 (1H, dd, *J*=6.0, 1.5 Hz), 6.05 (1H, dd, *J*=6.0, 2.0 Hz), 4.05 (2H, q, *J*=7.0 Hz), 3.10–3.16 (1H, m), 2.47 (3H, s), 1.09 (3H, t, *J*=7.0 Hz), 0.91–0.95 (2H, m), 0.73–0.77 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.9, 170.5, 147.9, 139.3, 131.1, 130.9, 129.8, 129.2, 70.8, 65.9, 63.0, 60.4, 40.9, 36.8, 20.3, 18.4, 14.0; HRMS calcd for $C_{18}H_{21}NO_5S+H^+$: 364.1219, found: 364.1214.

*4.2.18. Ethyl 2-isobutyryl-1-(methylsulfonyl)-5-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**1r**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (3H, m), 7.34 (2H, dd, *J*=8.0, 1.5 Hz), 6.81 (1H, t, *J*=1.5 Hz), 5.91 (1H, dd, *J*=6.0, 2.0 Hz), 5.50 (1H, dd, *J*=6.0, 2.0 Hz), 4.24 (2H, q, *J*=7.0 Hz), 3.21 (1H, m), 2.33 (3H, s), 1.30 (3H, t, *J*=7.0 Hz), 1.17 (6H, dd, *J*=12.0, 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 210.6, 161.8, 143.0, 136.5, 131.5, 129.4, 129.0, 128.7, 71.8, 70.3, 61.6, 40.7, 37.8, 20.0, 18.5, 14.0; HRMS calcd for $C_{18}H_{23}NO_5S+H^+$: 366.1375, found: 366.1373.

4.3. General procedure for the synthesis of 2

Nitroallylic acetate **S1a** (0.3 mmol, 1.5 equiv), methanesulfonyl 2-aminoethanone **S2a** (0.2 mmol, 1.0 equiv) and K_2CO_3 (0.2 mmol, 1.0 equiv) were mixed in THF (2.0 mL) and stirred at rt for 10 h. Then the same volume of DMF was added to the reaction mixture and it was refluxed for another 8 h under air. The reaction mixture was concentrated in vacuum and the crude was purified by flash column chromatography (petroleum ether/EtOAc) on silica gel to afford the desired pyrroles **2**.

*4.3.1. Ethyl 2-benzoyl-5-phenyl-1H-pyrrole-3-carboxylate (**2a**).* Yellow solid; mp 170–172 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.40 (1H, s), 7.81 (2H, dd, *J*=8.0, 1.0 Hz), 7.67 (2H, d, *J*=7.5 Hz), 7.56 (1H, t, *J*=7.5 Hz), 7.44 (4H, m), 7.36 (1H, t, *J*=7.5 Hz), 7.02 (1H, d, *J*=3.0 Hz), 3.76 (2H, q, *J*=7.0 Hz), 0.79 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.2, 164.6, 139.3, 136.3, 132.4, 130.7, 130.3, 129.1, 129.1, 128.4, 128.2, 125.1, 123.1, 110.5, 60.6, 13.4; HRMS calcd for $C_{20}H_{17}NO_3+H^+$: 320.1287, found: 320.1283.

*4.3.2. Ethyl 2-benzoyl-5-(4-fluorophenyl)-1H-pyrrole-3-carboxylate (**2b**).* Yellow solid; mp 165–167 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.56 (1H, s), 7.81 (2H, d, *J*=7.0 Hz), 7.66 (2H, m), 7.59 (1H, t, *J*=7.5 Hz), 7.47 (2H, t, *J*=8.0 Hz), 7.12 (2H, t, *J*=8.5 Hz), 6.97 (1H, d, *J*=3.0 Hz), 3.77 (2H, q, *J*=7.0 Hz), 0.81 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.4, 164.6, 162.8 (d, *J*=248 Hz), 139.2, 135.7, 132.5, 130.7, 129.1, 128.3, 127.1 (d, *J*=8 Hz), 126.7 (d, *J*=3 Hz), 123.3, 116.2 (d, *J*=22 Hz), 110.5, 60.7, 13.4; HRMS calcd for $C_{20}H_{16}FNO_3+H^+$: 338.1192, found: 338.1190.

*4.3.3. Ethyl 2-benzoyl-5-(4-chlorophenyl)-1H-pyrrole-3-carboxylate (**2c**).* Yellow solid; mp 185–187 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.34 (1H, s), 7.80 (2H, d, *J*=7.5 Hz), 7.58 (3H, m), 7.46 (2H, t, *J*=7.5 Hz), 7.40 (2H, d, *J*=7.0 Hz), 7.00 (1H, d, *J*=3.0 Hz), 3.77 (2H, q, *J*=7.0 Hz), 0.78 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.4, 164.5, 139.1, 135.3, 134.3, 132.6, 130.9, 129.4, 129.1, 128.8, 128.3, 126.4, 123.2, 110.8, 60.7, 13.4; HRMS calcd for $C_{20}H_{16}ClNO_3+H^+$: 354.0897, found: 354.0893.

*4.3.4. Ethyl 2-benzoyl-5-(4-bromophenyl)-1H-pyrrole-3-carboxylate (**2d**).* Yellow solid; mp 155–157 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.22 (1H, s), 7.79 (2H, dd, *J*=8.0, 1.0 Hz), 7.53 (5H, m), 7.46 (2H, t, *J*=7.5 Hz), 7.00 (1H, d, *J*=3.0 Hz), 3.76 (2H, q, *J*=7.0 Hz), 0.79 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.3, 164.4, 139.1, 135.1, 132.6, 132.3, 130.9, 129.2, 129.1, 128.3, 126.6, 123.1, 122.5, 110.8, 60.7, 13.4; HRMS calcd for $C_{20}H_{16}BrNO_3+H^+$: 398.0392, found: 398.0388.

*4.3.5. Ethyl 2-benzoyl-5-(2-bromophenyl)-1H-pyrrole-3-carboxylate (**2e**).* Yellow solid; mp 148–150 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.32 (1H, s), 7.80 (2H, dd, *J*=8.5, 1.5 Hz), 7.67 (1H, dd, *J*=8.0, 1.0 Hz), 7.56 (2H, m), 7.44 (2H, t, *J*=7.5 Hz), 7.37 (1H, td, *J*=7.5, 1.0 Hz), 7.23 (1H, td, *J*=8.0, 2.0 Hz), 7.05 (1H, d, *J*=3.0 Hz), 3.78 (2H, q, *J*=7.0 Hz), 0.78 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.0, 164.4, 139.0, 134.1, 134.1, 132.5, 131.3, 130.7, 130.6, 129.8, 129.2, 128.2, 127.9, 121.6, 121.1, 113.9, 60.6, 13.4; HRMS calcd for $C_{20}H_{16}BrNO_3+H^+$: 398.0392, found: 398.0390.

*4.3.6. Ethyl 2-benzoyl-5-(3-bromophenyl)-1H-pyrrole-3-carboxylate (**2f**).* Yellow solid; mp 112–113 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.89 (1H, s), 7.81 (2H, dd, *J*=8.0, 1.0 Hz), 7.79 (1H, t, *J*=7.0 Hz), 7.56 (2H, m), 7.49 (1H, ddd, *J*=8.5, 2.0, 1.0 Hz), 7.46 (2H, t, *J*=8.0 Hz), 7.31 (1H, t, *J*=8.0 Hz), 7.02 (1H, d, *J*=3.0 Hz), 3.78 (2H, q, *J*=7.0 Hz), 0.80 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.2, 164.3, 139.0, 134.4, 132.6, 132.3, 131.4, 131.1, 130.7, 129.1, 128.3, 128.1, 123.5, 123.4, 122.9, 111.1, 60.7, 13.4; HRMS calcd for $C_{20}H_{16}BrNO_3+H^+$: 398.0392, found: 398.0386.

*4.3.7. Ethyl 2-benzoyl-5-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate (**2g**).* Yellow solid; mp 148–150 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.25 (1H, s), 7.80 (2H, d, *J*=7.0 Hz), 7.60 (2H, d, *J*=8.5 Hz), 7.55 (1H,

t, J=7.0 Hz), 7.45 (2H, t, J=8.0 Hz), 6.95 (2H, d, J=9.0 Hz), 6.92 (1H, d, J=3.0 Hz), 3.85 (3H, s), 3.74 (2H, q, J=7.0 Hz), 0.79 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.0, 164.8, 159.9, 139.4, 136.7, 132.3, 130.1, 129.1, 128.2, 126.6, 123.5, 123.0, 114.6, 109.8, 60.7, 55.4, 13.4; HRMS calcd for $C_{21}H_{19}NO_4+H^+$: 350.1392, found: 350.1389.

*4.3.8. Ethyl 2-benzoyl-5-(p-tolyl)-1H-pyrrole-3-carboxylate (**2h**).* Yellow solid; mp 115–117 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.23 (1H, s), 7.80 (2H, dd, J=7.0, 1.5 Hz), 7.55 (3H, m), 7.44 (2H, t, J=8.0 Hz), 7.23 (2H, d, J=8.0 Hz), 6.97 (1H, d, J=3.0 Hz), 3.76 (2H, q, J=7.0 Hz), 2.39 (3H, s), 0.80 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.1, 164.7, 139.4, 138.6, 136.6, 132.3, 130.4, 129.8, 129.1, 128.2, 127.5, 125.1, 123.2, 110.2, 60.6, 21.3, 13.4; HRMS calcd for $C_{21}H_{19}NO_3+H^+$: 334.1443, found: 334.1440.

*4.3.9. Ethyl 2-benzoyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate (**2i**).* Yellow solid; mp 182–184 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.18 (1H, s), 7.81 (2H, dd, J=8.0, 1.0 Hz), 7.75 (2H, d, J=8.0 Hz), 7.69 (2H, d, J=8.0 Hz), 7.58 (1H, t, J=7.5 Hz), 7.47 (2H, t, J=8.0 Hz), 7.10 (1H, d, J=3.0 Hz), 3.79 (2H, q, J=7.0 Hz), 0.81 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.4, 164.2, 138.9, 134.4, 133.6, 132.7, 131.5, 130.3, 130.1, 129.1, 128.3, 126.2 (q, J=4 Hz), 125.2, 123.0, 111.6, 60.8, 13.4; HRMS calcd for $C_{21}H_{16}F_3NO_3+H^+$: 388.1161, found: 388.1160.

*4.3.10. Ethyl 2-benzoyl-5-(naphthalen-1-yl)-1H-pyrrole-3-carboxylate (**2j**).* Yellow solid; mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.47 (1H, s), 8.26 (1H, dd, J=6.0, 3.6 Hz), 7.91 (2H, m), 7.74 (2H, d, J=7.2 Hz), 7.61 (1H, dd, J=7.2, 1.2 Hz), 7.53 (4H, m), 7.41 (2H, t, J=7.6 Hz), 7.02 (1H, d, J=3.2 Hz), 3.78 (2H, q, J=7.2 Hz), 0.79 (3H, t, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 164.8, 139.2, 135.2, 133.9, 132.4, 131.1, 130.6, 129.3, 129.2, 128.9, 128.6, 128.2, 127.2, 127.0, 126.4, 125.3, 125.2, 122.5, 114.0, 60.7, 13.4; HRMS calcd for $C_{24}H_{19}NO_3+H^+$: 370.1443, found: 370.1439.

*4.3.11. Ethyl 2-benzoyl-5-(furan-2-yl)-1H-pyrrole-3-carboxylate (**2k**).* Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (1H, s), 7.68 (2H, dd, J=7.5, 1.5 Hz), 7.50 (1H, t, J=7.5 Hz), 7.37 (2H, t, J=7.5 Hz), 7.19 (1H, d, J=7.5 Hz), 7.17 (1H, d, J=1.5 Hz), 6.48 (1H, d, J=3.5 Hz), 6.28 (1H, dd, J=3.5, 2.0 Hz), 4.38 (2H, q, J=7.0 Hz), 1.40 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.7, 160.3, 147.8, 142.0, 137.8, 132.4, 128.9, 128.6, 128.4, 126.1, 122.2, 114.6, 111.4, 109.3, 61.4, 14.3; HRMS calcd for $C_{18}H_{15}NO_4+H^+$: 310.1079, found: 310.1070.

*4.3.12. Ethyl 2-benzoyl-5-cyclopropyl-1H-pyrrole-3-carboxylate (**2l**).* Yellow solid; mp 128–130 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.70 (1H, s), 7.75 (2H, dd, J=8.0, 1.0 Hz), 7.52 (1H, t, J=7.0 Hz), 7.42 (2H, t, J=7.5 Hz), 6.33 (1H, d, J=3.0 Hz), 3.70 (2H, q, J=7.0 Hz), 1.85–1.91 (1H, m), 0.96–1.01 (2H, m), 0.73–0.79 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.6, 164.9, 140.3, 139.5, 132.1, 129.0, 128.8, 128.1, 122.4, 109.0, 60.5, 13.4, 8.3, 7.8; HRMS calcd for $C_{17}H_{17}NO_3+H^+$: 284.1287, found: 284.1282.

*4.3.13. Ethyl 2-(4-methylbenzoyl)-5-phenyl-1H-pyrrole-3-carboxylate (**2m**).* Yellow solid; mp 179–180 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.50 (1H, s), 7.71 (2H, d, J=8.5 Hz), 7.67 (2H, d, J=7.5 Hz), 7.42 (2H, t, J=7.5 Hz), 7.34(1H, t, J=7.5 Hz), 7.24(2H, d, J=8.0 Hz), 7.01 (1H, d, J=3.0 Hz), 3.81 (2H, q, J=7.0 Hz), 2.42(3H, s), 0.83 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.2, 164.7, 143.3, 136.6, 136.2, 131.1, 130.4, 129.4, 129.1, 128.9, 128.3, 125.2, 122.8, 110.4, 60.6, 21.7, 13.5; HRMS calcd for $C_{21}H_{19}NO_3+H^+$: 334.1443, found: 334.1440.

*4.3.14. Ethyl 2-(4-methoxybenzoyl)-5-phenyl-1H-pyrrole-3-carboxylate (**2n**).* Yellow solid; mp 150–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.56 (1H, s), 7.81 (2H, d, J=8.5 Hz), 7.66 (2H, d, J=7.0 Hz), 7.41 (2H, t, J=7.5 Hz), 7.33 (1H, t, J=7.5 Hz), 7.01 (1H, d, J=3.0 Hz), 6.91 (2H, d, J=9.0 Hz), 3.87 (5H, m), 0.87 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.3, 164.7, 163.4, 135.9, 131.9, 131.7, 131.3, 130.5, 129.1, 128.2, 125.1, 122.2, 113.5, 110.2, 60.6, 55.5, 13.6; HRMS calcd for $C_{21}H_{19}NO_4+H^+$: 350.1392, found: 350.1390.

*4.3.15. Ethyl 2-(4-bromobenzoyl)-5-phenyl-1H-pyrrole-3-carboxylate (**2o**).* Yellow solid; mp 150–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.13 (1H, s), 7.67 (2H, d, J=8.5 Hz), 7.64 (2H, d, J=7.5 Hz), 7.58 (2H, d, J=8.5 Hz), 7.44 (2H, t, J=7.5 Hz), 7.37 (1H, t, J=7.5 Hz), 3.87 (2H, q, J=7.0 Hz), 0.90 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.0, 164.3, 138.0, 131.5, 130.6, 130.4, 130.1, 129.6, 129.2, 128.6, 128.1, 125.1, 123.0, 110.8, 60.8, 13.6; HRMS calcd for $C_{20}H_{16}BrNO_3+H^+$: 398.0392, found: 398.0388.

*4.3.16. Ethyl 2-(4-nitrobenzoyl)-5-phenyl-1H-pyrrole-3-carboxylate (**2p**).* Yellow solid; mp 163–165 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.78 (1H, s), 8.30 (2H, d, J=8.5 Hz), 7.93 (2H, d, J=9.0 Hz), 7.64 (2H, d, J=7.0 Hz), 7.48 (2H, t, J=7.5 Hz), 7.41 (1H, t, J=7.5 Hz), 7.05 (1H, d, J=3.0 Hz), 3.88 (2H, q, J=7.0 Hz), 0.97 (3H, t, J=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 184.9, 163.7, 149.7, 144.4, 137.2, 130.0, 129.8, 129.7, 129.4, 129.0, 125.1, 123.5, 123.4, 111.2, 60.9, 13.8; HRMS calcd for $C_{20}H_{16}N_2O_5+H^+$: 365.1137, found: 365.1134.

*4.3.17. Ethyl 2-(cyclopropanecarbonyl)-5-phenyl-1H-pyrrole-3-carboxylate (**2q**).* Yellow solid; mp 127–129 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.91 (1H, s), 7.58 (2H, dd, J=7.0, 1.5 Hz), 7.43 (2H, t, J=7.5 Hz), 7.34 (1H, t, J=7.5 Hz), 7.03 (1H, d, J=3.0 Hz), 4.37 (2H, q, J=7.0 Hz), 3.45 (1H, m), 1.41 (3H, t, J=7.0 Hz), 1.25 (2H, m), 1.07 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6, 164.5, 134.6, 132.7, 130.2, 128.4, 124.9, 120.3, 111.7, 60.8, 18.9, 14.3, 12.7; HRMS calcd for $C_{17}H_{17}NO_3+H^+$: 284.1287, found: 284.1281.

*4.3.18. Ethyl 2-isobutyryl-5-phenyl-1H-pyrrole-3-carboxylate (**2r**).* Yellow solid; mp 106–107 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.85 (1H, s), 7.58 (2H, d, J=7.5 Hz), 7.43 (2H, t, J=7.5 Hz), 7.35 (1H, t, J=7.5 Hz), 7.00 (1H, d, J=3.0 Hz), 4.37 (2H, q, J=7.0 Hz), 4.04 (1H, m), 1.41 (3H, t, J=7.0 Hz), 1.21 (6H, d, J=6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.1, 164.3, 135.1, 131.1, 130.2, 129.2, 128.4, 124.9, 120.1, 111.6, 60.8, 36.9, 19.3, 14.3; HRMS calcd for $C_{17}H_{19}NO_3+H^+$: 286.1443, found: 286.1440.

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Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra for all products and NOESY spectra of **1c**. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.10.045. These data include MOL files and InChiKeys of the most important compounds described in this article.

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