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Cascade regioselective synthesis of pyrazoles from nitroallylic acetates and *N*-tosyl hydrazine

Nana Shao [a], Tong Chen [a], Taotao Zhang [a,b], Huajian Zhu [a], Qunxiong Zheng [b], Hongbin Zou [a,*]

[a] Institute of Materia Medica, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou 310058, PR China
[b] College of Food Science, Zhejiang Gongshang University, Hangzhou 310035, PR China

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ABSTRACT

A simple, practical, and regioselective synthetic protocol for the formation of pyrazoles was developed. Unlike all other previously reported reactions of nitroallylic acetates, this process was initiated by a S_N2 reaction at the electrophilic γ site. A plausible mechanism for the cascade S_N2-Michael synthesis is proposed.

1. Introduction

Pyrazoles represent an important class of heterocyclic compounds that possess a wide range of pharmaceutical activities,[1] such as inhibitors of cyclooxygenase-2,[1a] protein kinase,[1b] brain cannabinoid receptor,[1c] NS5B polymerase,[1d] metabotropic glutamate-5 receptor,[1e] and antimicrobial activities.[1f] In fact, some compounds with pyrazole motif are successfully commercialized agents, such as Celecoxib (nonsteroidal anti-inflammatory drug),[2a] Fipronil (insecticide),[2b] and Sildenafil (anti-erectile dysfunction drug)[2c] (Fig. 1). Moreover, some pyrazoles are widely used in agrochemical industries[3] as well as useful building blocks in the field of materials chemistry.[4]

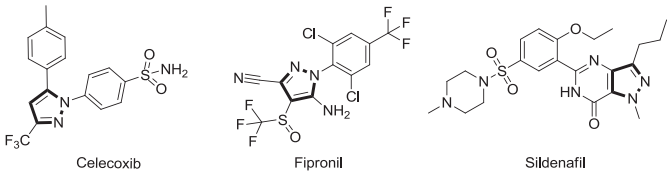

Fig. 1. Drugs containing pyrazole motif.

Due to the important applications of pyrazoles, significant effort has been put forth in developing approaches for their synthesis.[5] Among the many methodologies now available, cyclocondensation of 1,3-dielectrophilic compounds with hydrazines play a prominent role[6] of which 1,3-dicarbonyl compounds are the most prevalent synthons.[6e–i] 1,3-Dipolar cycloaddition is also widely used for the synthesis of pyrazoles, using diverse 1,3-dipoles, such as nitrilimines,[7a–c] diazoalkanes,[7d,e] and azomethine imines.[7f,g] Recently, progress has been made in the synthesis of pyrazoles through the use of transition metal-catalyzed reactions.[8] Despite significant advances in pyrazole synthesis, efficient and regioselective preparation of pyrazoles from readily available building blocks continues to be actively pursued.

Nitroallylic acetates, derived from Morita–Baylis–Hillman reaction of nitroethylene and aldehydes, are highly reactive synthetic Michael acceptors with four potential electrophilic sites (α, β, γ, δ, Scheme 1).[9] All four electrophilic sites are highly reactive and frequently used as efficient synthons to construct diversified functional organic molecules (**I-A**–**I-I**) as shown in Scheme 1.[9] Up to now, reactions of nitroallylic acetates were normally initiated by Michael addition at the electrophilic α site (**I**, Scheme 1).[9] Very recently, we reported the synthesis of 1,3,5-trisubstituted pyrazoles (**I-H**, Scheme 1) through cascade double Michael-elimination reactions in which the first Michael addition between phenylhydrazine and nitroallylic acetates also occurred at the electrophilic α site.[9j] Herein, for the first time, we report a regioselective

* Corresponding author. Tel./fax: +86 571 8820 8835; e-mail address: zouhb@zju.edu.cn (H. Zou).

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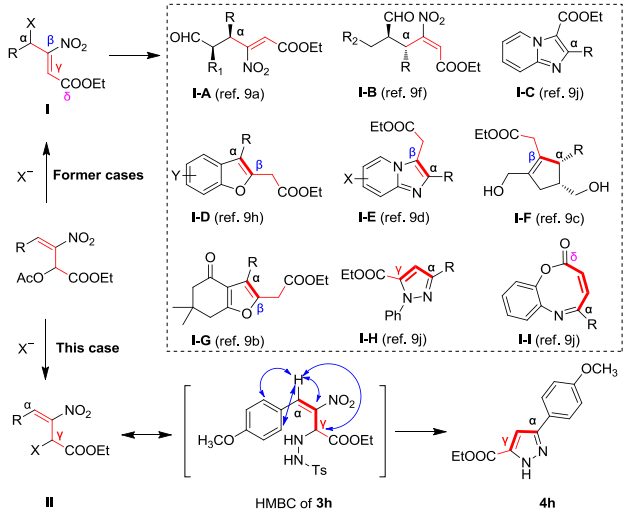
approach to the 3,5-disubstituted pyrazoles (**4h** as an example, Scheme 1) with cascade S_N2 (electrophilic γ site)-Michael (electrophilic α site) reactions of nitroallylic acetates and *N*-tosyl hydrazine.

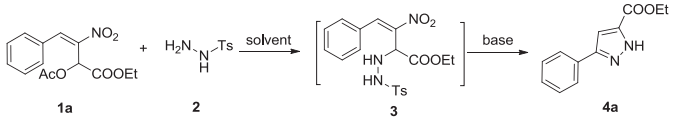


Scheme 1. New case of nitroallylic acetates reactions.

2. Results and discussion

Our initially initial experiments were performed with nitroallylic acetate **1a** and *N*-tosyl hydrazine[10] **2** under different conditions (Table 1). Two solvents employed in the literature,[9b,d] THF and methanol, were tested first at room temperature. Methanol was found to be much more efficient for the transformation. We were pleased to note the formation of a sole product, which was further purified and determined to be the reaction intermediate **3** (Table 1, **3h** of Scheme 1 as an example). Unexpectedly, the HMBC analysis of **3h** (Scheme 1) indicated that this process in our case was initiated for the first time by a S_N2 reaction at the electrophilic site γ (**II**, Scheme 1), which might due to the 'hard' nucleophilic nature of the nitrogen atom in tosyl hydrazine.

Table 1
Screening of reaction conditions[a]



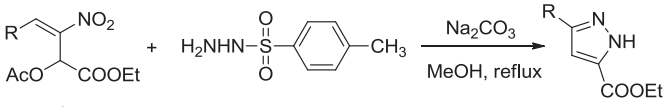
Entry	Base	Solvent	*T* (°C)	Yield[b] (%)
1	—	MeOH	25	0
2	—	MeOH	65	0
3[c]	Na_2CO_3	MeOH	65	49
4	Na_2CO_3	MeOH	25	0
5	**Na_2CO_3**	**MeOH**	**65**	**79**
6	Na_2CO_3	THF	65	66
7	Na_2CO_3	CH_3CN	81	60
8	Na_2CO_3	DMF	80	41
9	K_2CO_3	MeOH	65	71
10	DABCO	MeOH	65	19
11	DBU	MeOH	65	37
12	Et_3N	MeOH	65	11

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.1 mmol) in solvent (1 mL) were stirred at room temperature for 30 min. Then base (0.1 mmol) was added and the mixture was stirred for 2 h.
[b] Isolated yield of **4a**. The most successful entry is highlighted in bold.
[c] Reaction was directly stirred at 65 °C.

After the first S_N2 reaction, we tried to increase the reaction temperature and no further reaction occurred (entry 2, Table 1). Interestingly, addition of Na_2CO_3 initiated the reaction in situ to form pyrazole **4a** (entry 3, Table 1). Reaction temperature is also crucial for the synthesis of pyrazole since no reaction was observed when it was stirred at room temperature in the presence of Na_2CO_3 (entry 4). The preformation of the intermediate **3** was found to be very necessary (entries 3 and 5). Intrigued by the above results, we conducted a solvent and base screen using this protocol (unless otherwise specified entry 3) and monitored by HPLC analysis. The results are summarized in Table 1. Methanol was found to be the most favorable solvent for this cascade reaction (entries 5–8) and Na_2CO_3 was selected as the best base under this reaction condition, which substantially increased the yield (entries 5 and 9–12).

Using the optimized reaction condition, we investigated the scope of this unique one-pot pyrazole formation reaction and the results are summarized in Table 2. The pyrazole structures (**4a**–**r**) were established by HRMS, ^1H and ^{13}C NMR spectroscopic analysis and further confirmed by X-ray diffraction study of **4h** (Fig. 2).[11] As presented in Table 2, the reaction can tolerate various nitroallylic acetates with either aromatic or aliphatic substituents. Both electron-donating and -withdrawing groups on the phenyl ring afforded the desired product with good isolated yields. The nitroallylic acetates with electron withdrawing substituents on phenyl ring showed high isolated yields of pyrazoles **4** (entries 2–6 and 11). Further analysis of the results indicates that the efficiency of the *para* halide substituted phenyl ring (entries 2–4) ranks as F)Cl)Br. Among them, 4-fluoro phenyl substituted nitroallylic acetate afforded **4b** with an excellent isolated yield of 96% (entry 2).

Table 2
Pyrazoles from nitroallylic acetates and *N*-tosyl hydrazines



Entry	R	Product	Yield[a] (%)
1	Ph	**4a**	79
2	4-F–Ph	**4b**	96
3	4-Cl–Ph	**4c**	87
4	4-Br–Ph	**4d**	80
5	2-Br–Ph	**4e**	83
6	3-Br–Ph	**4f**	84
7	4-CH_3–Ph	**4g**	74
8	4-OCH_3–Ph	**4h**	70
9	4-N(CH_3)$_2$–Ph	**4i**	72
10	4-OAc–Ph	**4j**	77
11	3-CF_3vPh	**4k**	82
12	2-Furyl	**4l**	69
13	1-Naphthyl	**4m**	80
14	3-Cyclohexenyl	**4n**	70
15	Propyl	**4o**	70
16	Isopropyl	**4p**	81
17	Cyclopropyl	**4q**	87
18	Cyclohexyl	**4r**	61

[a] Isolated yield.

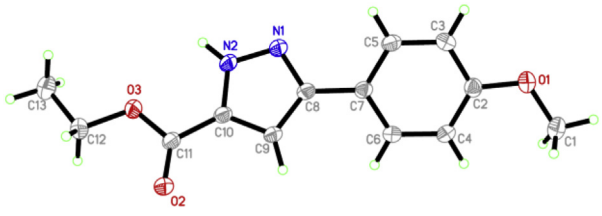
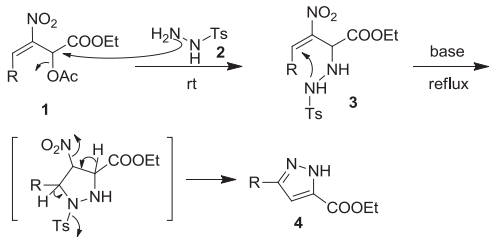


Fig. 2. Crystal structure of **4h**.

Based on these experimental results, we proposed the cascade S_N2-Michael reaction mechanism as shown in Scheme 2. In the absence of base, the electrophilic γ site of the nitroallylic acetate was attacked by the electron-rich nucleophilic nitrogen of *N*-tosyl hydrazine **2** to afford the intermediate **3**. The intermediate **3h**, as an example, was isolated and its structure was confirmed by NMR. Then the Michael addition at the electrophilic α site of **3** was initiated by addition of base to the reaction mixture and an increase of the reaction temperature to 65 °C. Subsequent elimination and aromatization of the intermediate provided the product **4**.



Scheme 2. Proposed mechanism.

3. Conclusions

In summary, starting from the nitroallylic acetates **1** and *N*-tosyl hydrazine **2**, a novel regioselective synthetic approach of 3,5-disubstituted pyrazoles has been described. This synthetic protocol appears to be useful and convenient due to the readily available starting materials, operational simplicity, mild conditions, and high isolated yields. Notably, the reactions of nitroallylic acetates were initiated for the first time by the S_N2 reaction at an electrophilic γ site. The results herein provide insights to the reactivity of nitroallylic acetates with bifunctional nucleophiles. Further investigation on transformation of nitroallylic acetates to a wider range of valuable heterocycles is underway.

4. Experimental section

4.1. General

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 spectral 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. The starting material nitroallylic acetates **1** were prepared according to the known methods.[12,13]

4.2. General procedure for the synthesis of 3,5-disubstituted pyrazoles 4

A mixture of 4-methylbenzenesulfonylhydrazide (**2**, 1.0 equiv) and nitroallylic acetate (**1**, 1.0 equiv) was dissolved in CH_3OH (1 mL) and stirred at room temperature for 30 min. Then Na_2CO_3 (0.1 mmol) was added and the mixture was refluxed at 65 °C for 2 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 pyrazole **4**.

*4.2.1. Ethyl 3-phenyl-1H-pyrazole-5-carboxylate (**4a**).* White solid. Mp: 107–108 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (2H, d, *J*=7.0 Hz), 7.39 (2H, t, *J*=7.5 Hz), 7.33 (1H, t, *J*=7.5 Hz), 7.03 (1H, s), 4.26 (2H, q, *J*=7.0 Hz), 1.27 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1, 148.4, 140.2, 130.4, 129.0, 128.7, 125.8, 105.4, 61.0, 14.2; HRMS calcd for $C_{12}H_{13}N_2O_2+H^+$: 217.0977, found: 217.0980.

*4.2.2. Ethyl 3-(4-fluorophenyl)-1H-pyrazole-5-carboxylate (**4b**).* White solid. Mp: 145–146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (2H, dd, *J*=8.5, 5.5 Hz), 7.09 (2H, t, *J*=8.5 Hz), 6.99 (1H, s), 4.30 (2H, q, *J*=7.0 Hz), 1.31 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9 (d, *J*=247 Hz), 160.5, 127.5 (d, *J*=8 Hz), 127.1, 115.9 (d, *J*=22 Hz), 105.2, 61.3, 14.2; HRMS calcd for $C_{12}H_{12}FN_2O_2+H^+$: 235.0883, found: 235.0887.

*4.2.3. Ethyl 3-(4-chlorophenyl)-1H-pyrazole-5-carboxylate (**4c**).* White solid. Mp: 146–147 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (2H, d, *J*=8.5 Hz), 7.36 (2H, d, *J*=8.0 Hz), 7.01 (1H, s), 4.31 (2H, q, *J*=7.0 Hz), 1.32 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.4, 134.4, 129.7, 129.1, 126.9, 105.4, 61.4, 14.2; HRMS calcd for $C_{12}H_{12}ClN_2O_2+H^+$: 251.0587, found: 251.0591.

*4.2.4. Ethyl 3-(4-bromophenyl)-1H-pyrazole-5-carboxylate (**4d**).* White solid. Mp: 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (2H, d, *J*=8.4 Hz), 7.54 (2H, d, *J*=8.4 Hz), 7.07 (1H, s), 4.37 (2H, q, *J*=6.8 Hz), 1.37 (3H, t, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 132.0, 130.3, 127.2, 122.5, 105.6, 61.5, 14.2; HRMS calcd for $C_{12}H_{12}BrN_2O_2+H^+$: 295.0082, found: 295.0088.

*4.2.5. Ethyl 3-(2-bromophenyl)-1H-pyrazole-5-carboxylate (**4e**).* Light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (1H, d, *J*=8.0 Hz), 7.61 (1H, dd, *J*=8.0, 1.5 Hz), 7.37 (1H, t, *J*=7.5 Hz), 7.24 (1H, td, *J*=7.5, 1.5 Hz), 7.23 (1H, s), 4.41 (2H, q, *J*=7.0 Hz), 1.40 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.8, 133.8, 131.7, 131.0, 130.0, 127.7, 121.8, 109.3, 61.4, 14.3; HRMS calcd for $C_{12}H_{12}BrN_2O_2+H^+$: 295.0082, found: 295.0088.

*4.2.6. Ethyl 3-(3-bromophenyl)-1H-pyrazole-5-carboxylate (**4f**).* Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (1H, s), 7.71 (1H, d, *J*=8.0 Hz), 7.47 (1H, d, *J*=8.0 Hz), 7.28 (1H, t, *J*=8.0 Hz), 7.10 (1H, s), 4.39 (2H, q, *J*=7.0 Hz), 1.38 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 133.5, 131.4, 130.4, 128.7, 124.2, 123.0, 105.9, 61.6, 14.2; HRMS calcd for $C_{12}H_{12}BrN_2O_2+H^+$: 295.0082, found: 295.0087.

*4.2.7. Ethyl 3-(p-tolyl)-1H-pyrazole-5-carboxylate (**4g**).* White solid. Mp: 145–146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (2H, d, *J*=8.0 Hz), 7.22 (2H, d, *J*=8.0 Hz), 7.05 (1H, s), 4.36 (2H, q, *J*=7.0 Hz), 2.38 (3H, s), 1.36 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.8, 138.6, 129.6, 127.9, 125.6, 105.2, 61.2, 29.7, 21.3, 14.2; HRMS calcd For $C_{13}H_{15}N_2O_2+H^+$: 231.1134, found: 231.1141.

*4.2.8. Ethyl 3-(4-methoxyphenyl)-1H-pyrazole-5-carboxylate (**4h**).* White solid. Mp: 152–153 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (2H, d, *J*=8.5 Hz), 6.93 (1H, s), 6.91 (2H, d, *J*=8.5 Hz), 4.25 (2H, q, *J*=7.0 Hz), 3.82 (3H, s), 1.26 (3H, t, *J*=7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1, 159.9, 148.0, 140.3, 127.0, 122.9, 114.3, 104.5, 61.1, 55.3, 14.1; HRMS calcd for $C_{13}H_{15}N_2O_3+H^+$: 247.1083, found: 247.1090.

*4.2.9. Ethyl 3-(4-(dimethylamino)phenyl)-1H-pyrazole-5-carboxylate (**4i**).* Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (2H, d, *J*=8.8 Hz), 6.95 (1H, s), 6.76 (2H, d, *J*=8.8 Hz), 4.36 (2H, q,

J=7.2 Hz), 2.99 (6H, s), 1.36 (3H, t, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 150.4, 148.4, 140.9, 126.7, 118.6, 112.7, 104.1, 61.1, 40.6, 14.3; HRMS calcd for $C_{14}H_{18}N_3O_2+H^+$: 260.1399, found: 260.1407.

*4.2.10. Ethyl 3-(4-acetoxyphenyl)-1H-pyrazole-5-carboxylate (**4j**).* Light yellow solid. Mp: 144–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (2H, d, *J*=7.6 Hz), 7.14 (2H, d, *J*=7.6 Hz), 7.07 (1H, s), 4.39 (2H, q, *J*=7.2 Hz), 2.32 (3H, s), 1.38 (3H, t, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 160.3, 150.8, 149.6, 138.3, 129.0, 126.9, 122.1, 105.6, 61.4, 21.1, 14.2; HRMS calcd for $C_{14}H_{15}N_2O_4+H^+$: 275.1032, found: 275.1027.

*4.2.11. Ethyl 3-(3-(trifluoromethyl)phenyl)-1H-pyrazole-5-carboxylate (**4k**).* White solid. Mp: 114–116 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (1H, s), 8.00 (1H, d, *J*=8.0 Hz), 7.60 (1H, d, *J*=7.5 Hz), 7.55 (1H, t, *J*=8.0 Hz), 7.18 (1H, s), 4.42 (2H, q, *J*=7.0 Hz), 1.40 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9, 150.2, 136.9, 132.6, 131.3 (q, *J*=32 Hz), 129.4, 128.9, 125.0 (q, *J*=4 Hz), 124.0 (d, *J*=271 Hz), 122.5 (q, *J*=4 Hz), 105.9, 61.7, 14.2; HRMS calcd for $C_{13}H_{12}F_3N_2O_2+H^+$: 285.0851, found: 285.0848.

*4.2.12. Ethyl 3-(furan-2-yl)-1H-pyrazole-5-carboxylate (**4l**).* Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (1H, d, *J*=1.6 Hz), 7.03 (1H, s), 6.74 (1H, d, *J*=3.2 Hz), 6.50 (1H, dd, *J*=3.2, 1.6 Hz), 4.41 (2H, q, *J*=7.2 Hz), 1.41 (3H, t, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 142.6, 129.5, 128.0, 122.2, 111.6, 107.2, 105.0, 61.5, 14.3; HRMS calcd for $C_{11}H_{10}N_2O_3+H^+$: 207.0770, found: 207.0777.

*4.2.13. Ethyl 3-(naphthalen-1-yl)-1H-pyrazole-5-carboxylate (**4m**).* Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (1H, d, *J*=7.5 Hz), 7.88 (2H, dd, *J*=8.5, 2.5 Hz), 7.57 (1H, d, *J*=7.0 Hz), 7.51–7.44 (3H, m), 7.12 (1H, s), 4.37 (2H, q, *J*=7.0 Hz), 1.36 (3H, t, *J*=7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 147.1, 140.3, 133.8, 131.1, 129.4, 128.4, 128.3, 127.3, 126.9, 126.2, 125.2, 125.2, 109.2, 61.3, 14.3; HRMS calcd for $C_{16}H_{15}N_2O_2+H^+$: 267.1134, found: 267.1129.

*4.2.14. Ethyl 3-(cyclohex-3-en-1-yl)-1H-pyrazole-5-carboxylate (**4n**).* White solid. Mp: 77–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (1H, s), 5.74 (2H, m), 4.37 (2H, q, *J*=7.2 Hz), 3.06–2.99 (1H, m), 2.45–2.35 (1H, m), 2.23–2.10 (3H, m), 2.07–2.00 (1H, m), 1.78–1.67 (1H, m), 1.38 (3H, t, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 127.2, 125.6, 105.3, 61.0, 31.8, 31.0, 28.4, 24.6, 14.3; HRMS calcd for $C_{12}H_{17}N_2O_2+H^+$: 221.1290, found: 221.1293.

*4.2.15. Ethyl 3-propyl-1H-pyrazole-5-carboxylate (**4o**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.60 (1H, s), 4.36 (2H, q, *J*=7.2 Hz), 2.66 (2H, t, *J*=7.6 Hz), 1.67 (2H, m), 1.37 (3H, t, *J*=7.2 Hz), 0.96 (3H, t, *J*=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 148.5, 140.8, 106.5, 60.9, 28.3, 22.4, 14.3, 13.6; HRMS calcd for $C_9H_{15}N_2O_2+H^+$: 183.1134, found: 183.1140.

*4.2.16. Ethyl 3-isopropyl-1H-pyrazole-5-carboxylate (**4p**).* Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.62 (1H, s), 4.37 (2H, t, *J*=7.2 Hz), 3.03 (1H, m), 1.37 (3H, t, *J*=7.2 Hz), 1.29 (6H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 153.8, 139.5, 103.8, 60.0, 25.5, 21.4, 13.3; HRMS calcd for $C_9H_{15}N_2O_2+H^+$: 183.1134, found: 183.1139.

*4.2.17. Ethyl 3-cyclopropyl-1H-pyrazole-5-carboxylate (**4q**).* White solid. Mp: 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.44 (1H, s), 4.35 (2H, q, *J*=7.2 Hz), 1.89 (1H, m), 1.35 (3H, t, *J*=7.2 Hz), 0.90 (2H, m), 0.67 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 151.4, 140.2, 104.3, 61.0, 14.3, 8.0, 7.5; HRMS calcd for $C_9H_{13}N_2O_2+H^+$: 181.0977, found: 181.0969.

*4.2.18. Ethyl 3-cyclohexyl-1H-pyrazole-5-carboxylate (**4r**).* White solid. Mp: 99–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.60 (1H, s), 4.36 (2H, q, *J*=7.2 Hz), 2.74–2.64 (1H, m), 2.04–1.95 (2H, m), 1.85–1.76 (2H, m), 1.76–1.67 (1H, m), 1.48–1.33 (4H, m), 1.37 (3H, t, *J*=7.2 Hz), 1.30–1.21 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 104.9, 60.9, 35.8, 32.7, 26.0, 25.8, 14.3; HRMS calcd for $C_{12}H_{19}N_2O_2+H^+$: 223.1447, found: 223.1486.

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Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra for all products. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.12.046. These data include MOL files and InChiKeys of the most important compounds described in this article.

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