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A One-pot Approach to Ethyl 1,4,5-Triaryl-1*H*-pyrazole-3-carboxylates via an Improved Claisen Condensation-Knorr Reaction Sequence

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A one-pot approach to ethyl 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates has been developed in moderate to high yields. The *tert*-BuOLi-mediated Claisen condensation of 1,2-diarylethanones and ethyl oxalyl chloride efficiently provided the enolized lithium salts of ethyl 2,4-dioxo-3,4-diarylbutanoates, which in situ reacted with arylhydrazine hydrochlorides via a hydrochloric acid-promoted Knorr reaction to produce the exquisite triarylpyrazole-3-carboxylates. The procedure promises a convenient access to this highly crowded framework for drug discovery.

Keywords one-pot approach, 2,4-dioxo-3,4-diarylbutanoates, Claisen condensation, Knorr reaction, triarylpyrazole-3-carboxylates

Introduction

Pyrazoles and their derivatives have been frequently found in large numbers of biologically active molecules.[1] Among these compounds, monoaryl-1*H*-pyrazole-3-carboxylate[2] and diaryl-1*H*-pyrazole-3-carboxylate derivatives[3] generally possess widespread pharmacological activities acting as anti-inflammatory agents,[2a] antifungal agents,[2b] antimicrobials,[2c] *L*-2-hydroxy acid oxidase inhibitors,[2d] acrosin inhibitors,[2e] cannabinoid-1 (CB1) receptor antagonists,[3a-3e,3g] I$\kappa\beta$ kinase β (IKKβ or IKK-2) inhibitors[3f] and analgesics.[3h] Recently, it has been revealed that 1,4,5-triaryl-1*H*-pyrazole-3-carboxylic acids hold good anti-inflammatory and analgesic activities.[3h] In general, Knorr reaction and 1,3-dipolar cycloaddition as two prevalent strategies can be employed to prepare pyrazoles.[4] However, the synthesis of the highly crowded 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates is still scarce, and only two examples have been documented to date.[3h] In fact, the reported synthesis of triarylpyrazole-3-carboxylates was difficult to be reproduced (Scheme 1a).[3h] Hence, we realized that the development of an efficient approach to the special framework is imperative for drug discovery.

More recently, we reported the synthesis of 4-substituted 1,5-diaryl-1*H*-pyrazole-3-carboxylates,[5] however, the method generally presented a low efficiency for the synthesis of the overcrowded triarylpyrazole-3-carboxylates (Scheme 1b). A main reason is that the labile intermediates 2,4-dioxo-3,4-diaryl-butanoates are difficult to access via the previously developed Claisen condensation from diethyl oxalate and 1,2-diphenylethanones, due to larger steric effect of bulky phenyl groups.[5] Therefore, further improving the highly sterically hindered Claisen condensation reaction was needed for overcoming this encountered problem. The preliminary screening on counterparts of diethyl oxalate uncovered that ethyl oxalyl chloride was the most competent electrophile for preparing the desired 2,4-dioxo-3,4-diarylbutanoates (**2**), comparing with diethyl oxalate, dimethyl oxalate, di-*tert*-butyl oxalate and *tert*-butyl ethyl oxalate. Herein, we reported a one-pot approach to ethyl 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates (**4**) via a modified Claisen condensation-Knorr reaction sequence from readily available ethyl oxalyl chloride, 1,2-diarylethanones (**1**) and arylhydrazine hydrochlorides (**3**, Scheme 1c).

Results and Discussion

Further optimization for the model reaction of 1,2-diphenylethanone (**1a**) with ethyl oxalyl chloride was implemented as shown in Table 1. Initially, the condensation was highly effective to deliver ethyl 2,4-dioxo-3,4-diphenylbutanoate (**2a**) in 94% yield with

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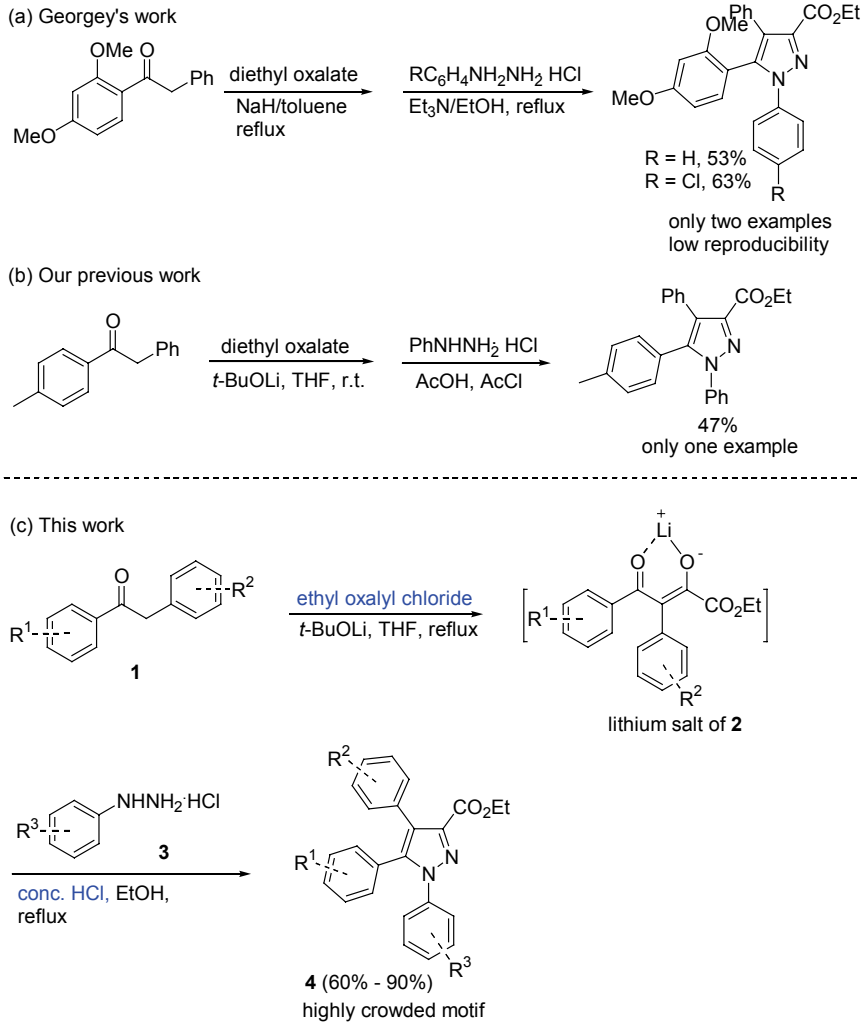
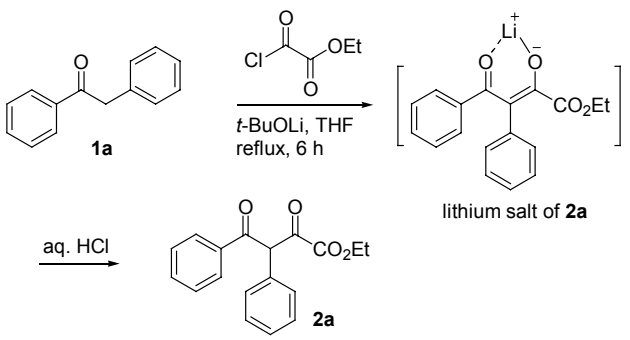
Scheme 1 Synthesis of triaryl-1*H*-pyrazole-3-carboxylates



1.5 equiv. of ethyl oxalyl chloride and 3.0 equiv. of *tert*-BuOLi under reflux for 6 h (Entry 1). Tentatively, the yield remarkably reduced to 74% under a lowered reaction temperature of 50 ℃ (Entry 2). Pleasingly, the reactions still worked well to afford an excellent yield of 94% in the presence of 1.4, 1.3 or 1.2 equiv. of ethyl oxalyl chloride with 3.0 equiv. of *tert*-BuOLi (Entries 3—5). When utilizing 1.1 equiv. of ethyl oxalyl chloride, the yield sharply dropped to 80% (Entry 6). On the other hand, it was observed that the use of 2.5 or 2.4 equiv. of *tert*-BuOLi proved to be equally effective for the condensation with 1.2 equiv. of ethyl oxalyl chloride (Entries 7 and 8). Besides, a lower yield of 87% was incurred with 2.3 equiv. of *tert*-BuOLi (Entry 9). Thus, the optimized conditions were established for the sterically hindered Claisen condensation (Entry 8).

The combination of the Claisen condensation and subsequent Knorr reaction into a one-pot procedure became a practical choice to avoid isolating unstable **2a**[6] (Table 2). Mechanistically, acid-mediated cyclization of the intermediate (*E/Z*)-**5aa**, produced from the initial reaction of **2a** and phenlhydrazine hydrochloride (**3a**), was crucial for the Knorr reaction.[1c,5,7] However, when using 4.0 equiv. of *para*-toluenesulfonic acid (*p*-TSA), AcOH, TFA or ethanolic HCl, the desired ethyl 1,4,5-triphenyl-1*H*-pyrazole-3-carboxylate (**4aa**) was afforded in low yields of 29%—56%, along with 37%—64% yields of uncyclized *N*-phenylhydrazones (*E/Z*)-**5aa** (Entries 1—4). In these cases, the concomitant generation of unknown precipitates possibly made negative impact on the cyclization of (*E/Z*)-**5aa** as well. To our surprise, switching to the use of 4.0 equiv. of concentrated hydrochloric acid, the procedure smoothly provided **4aa** in a high yield of 90% with trace of (*E/Z*)-**5aa** (Entry 5). In the case, the above detrimental precipitates were completely eliminated. It was reasonably inferred that the advantages of concentrated hydrochloric acid are based on: (i) neutralizing the residual *tert*-BuOLi, releasing free **2a** in situ from the enolized lithium salt, and avoiding the resulting precipitates; (ii) preferably promoting the cyclization of (*E/Z*)-**5aa** via isomerizing non-cyclizable (*Z*)-**5aa** into cyclizable (*E*)-**5aa** (Scheme2).[5] Considering the cheapness of concentrated hydrochloric acid, its dosage was not further optimized.

Table 1 Optimization of the Claisen condensation of **1a** with ethyl oxalyl chloride[a]

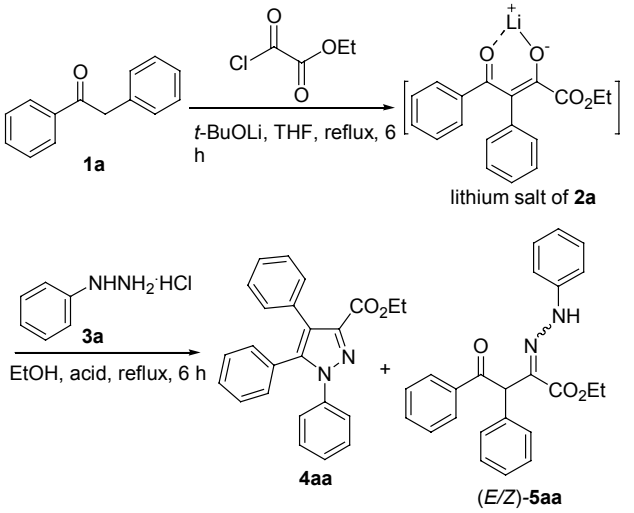


Entry	Ethyl oxalyl chloride (n_1 equiv.)	*t*-BuOLi (n_2 equiv.)	Yield[b]/%
1	1.5	3.0	94
2	1.5	3.0	76[c]
3	1.4	3.0	94
4	1.3	3.0	94
5	1.2	3.0	94
6	1.1	3.0	80
7	1.2	2.5	94
8	1.2	2.4	94
9	1.2	2.3	87

[a] Performed with **1a** (5.0 mmol), ethyl oxalyl chloride (n_1 equiv.) and *tert*-BuOLi (n_2 equiv.) in anhydrous THF (20 mL) for 6 h. The product **2a** was found to be extremely unstable on column chromatography, only purified via recrystallization. [b] Isolated yield via recrystallization from petroleum ether (25 mL). [c] Performed at 50 ℃.

With the improved Claisen condensation-Knorr reaction sequence in hand, we investigated the scope of substrates **1** and **3** for the synthesis of various 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates via the one-pot procedure (Table 3). Firstly, different 1,2-diarylethanones **1a**—**1k** were evaluated with **3a** (Entries 1—11). By varying substituent(s) R^1 at the benzoyl moiety, we found that, as for compound **1b** (R^1=*para*-methyl group), the procedure afforded the product **4ba** in a slightly low yield of 88% (Entry 2) in comparison with the unsubstituted **1a** (Entry 1). When the substrates **1c** (R^1=*ortho*, *para*-dimethyl groups) and **1d** (R^1=*ortho*, *ortho*, *para*-trimethyl groups) were used, the yields of the corresponding products **4ca** and **4da** dropped to

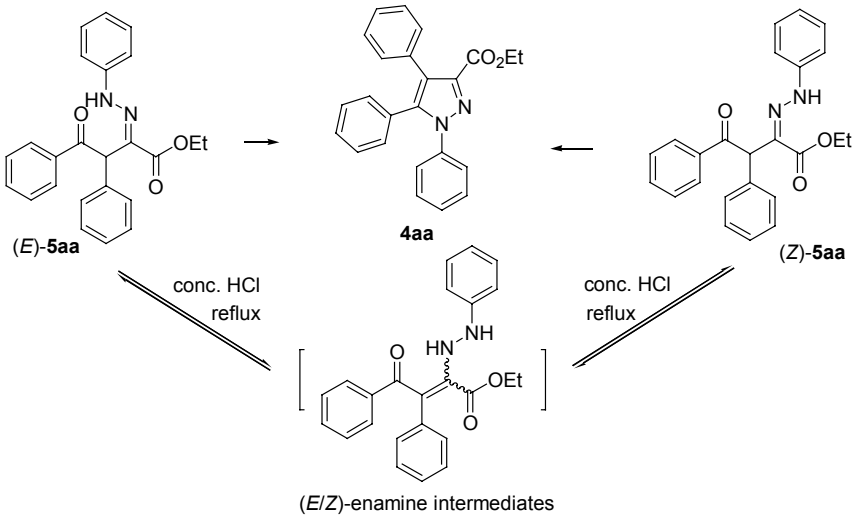
Table 2 Optimization of the one-pot procedure[a]



Entry	Acid	Yield[b]/% (**4aa**)	Yield[b]/% (**5aa**)
1	*p*-TSA	29	64
2	AcOH	36	55
3	TFA	41	51
4	Ethanolic HCl	56	37
5	Conc. HCl	90	trace

[a] A mixture of **1a** (5.0 mmol), ethyl oxalyl chloride (6.0 mmol) and *tert*-BuOLi (12.0 mmol) in anhydrous THF (20 mL) was refluxed for 6 h. After removal of THF, EtOH (20 mL), acid (4.0 equiv) and **3a** (5.0 mmol) were successively added to the residue and refluxed for another 6 h. [b] Isolated yield via column chromatography.

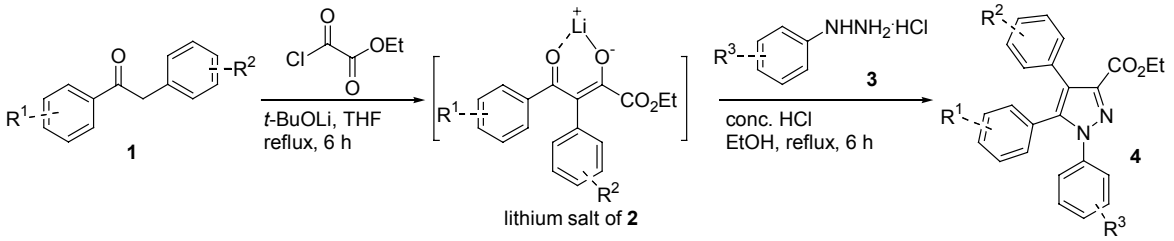
Scheme 2 Hydrochloric acid-promoted cyclization of **5aa**

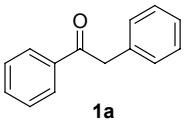
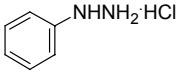
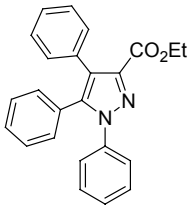
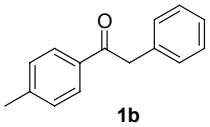
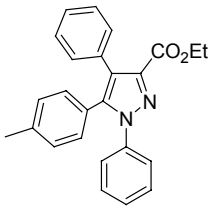
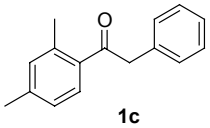
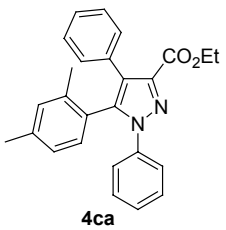
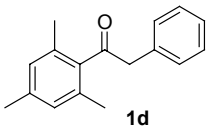
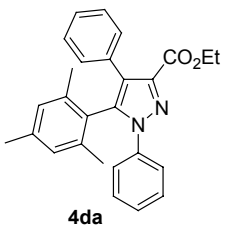


80% and 71%, respectively (Entries 3 and 4). The two results showed that the *ortho*-steric hindrance of the benzoyl moiety significantly affected the outcomes of the procedure. In addition, the influence of R^2 at the benzyl moiety was also examined (Entries 5—9). Regardless of electronic nature of R^2, for the substrates **1e** and **1f** (R^2=*para*-substitutent), the procedure delivered the products **4ea** and **4fa** in slightly low yields of 85% and 86%, respectively (Entries 5 and 6). With regard to the substrates **1g**—**1i** containing *ortho*-substituted benzyl moiety, the product yields distinctly decreased to 78%—81% (Entries 7—9). These results indicated an obvious *ortho*-steric hindrance in the benzyl moiety. Moreover, the one-pot approach smoothly proceeded to give more sterically crowded products **4ja** and **4ka** in the yields of 79% and 74%, respectively (Entries 10 and 11), clearly demonstrating the feasibility of the current procedure.

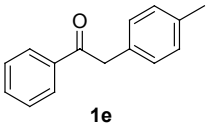
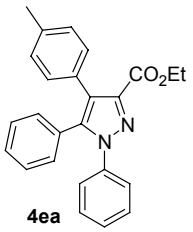
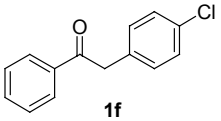
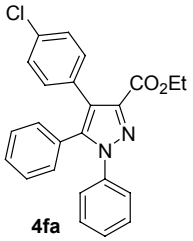
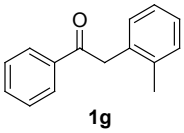
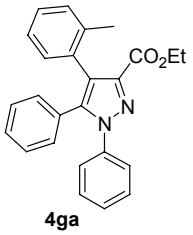
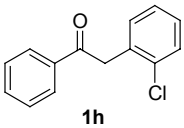
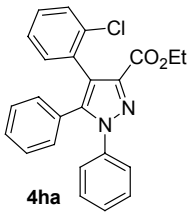
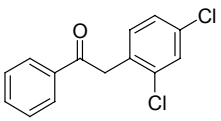
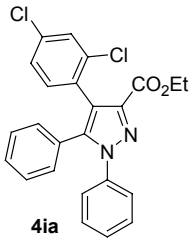
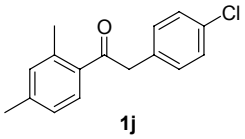
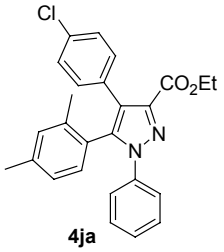
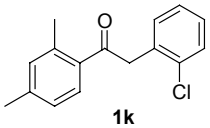
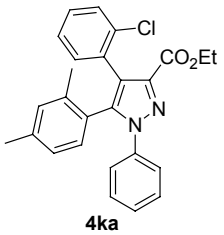
Next, arylhydrazine hydrochlorides **3** were also evaluated with **1a** (Entries 12—20). With respect to the substrates whether **3b**—**3d** bearing electron-donating groups or **3f**—**3h** bearing electron-withdrawing groups, the procedure gave their respective products **4ab**—**4ad** and **4af**—**4ah** in good yields of 81%—87% (Entries 12—14 and 16—18). In contrast, for the sterically crowded di-*ortho*-substituted substrates **3e** and **3i**, the procedure provided the products **4ae** and **4ai** in relatively low yields of 74% and 77%, respectively (Entries 15 and 19), irrespective of electronic nature of substituents. It was noteworthy that, for the substrate 4-phenyl-

Table 3 Synthesis of ethyl 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates **4** from **1** and **3**[a]



Entry	1	3	4	Yield[b]/%
1	 **1a**	 **3a**	 **4aa**	90
2	 **1b**	**3a**	 **4ba**	88
3	 **1c**	**3a**	 **4ca**	80
4	 **1d**	**3a**	 **4da**	71

Continued

Entry	1	3	4	Yield[b]/%
5	 **1e**	**3a**	 **4ea**	85
6	 **1f**	**3a**	 **4fa**	86
7	 **1g**	**3a**	 **4ga**	78
8	 **1h**	**3a**	 **4ha**	81
9	 **1i**	**3a**	 **4ia**	80
10	 **1j**	**3a**	 **4ja**	79
11	 **1k**	**3a**	 **4ka**	74

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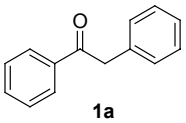
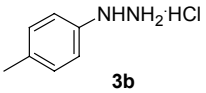
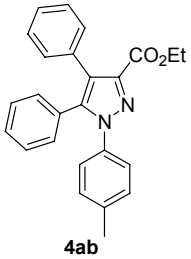
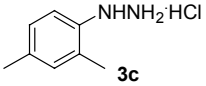
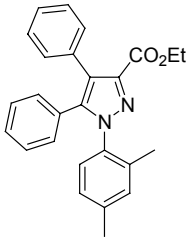
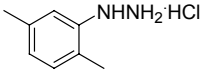
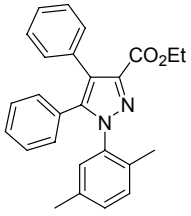
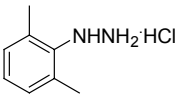
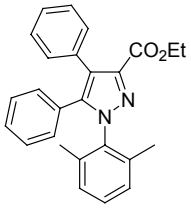
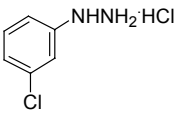
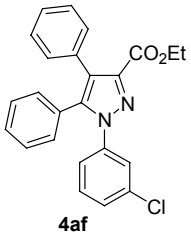
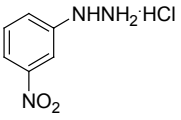
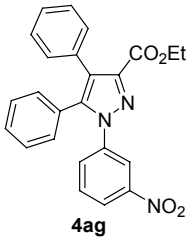
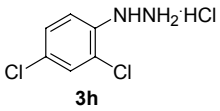
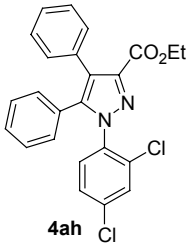
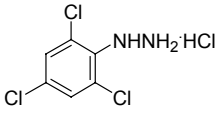
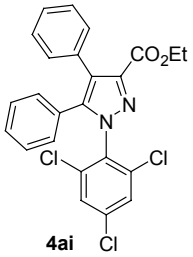
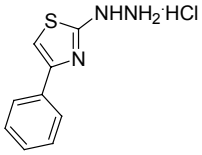
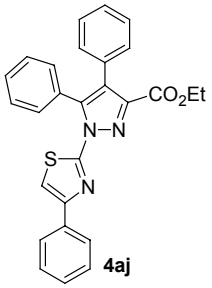
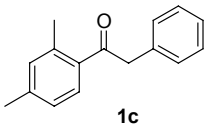
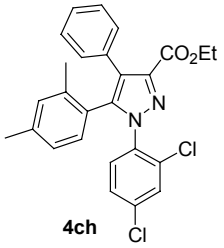
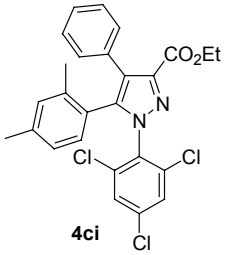
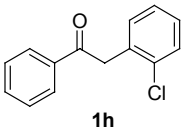
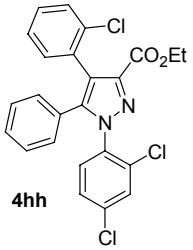
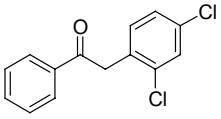
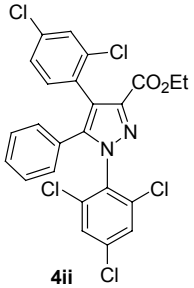
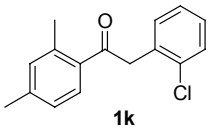
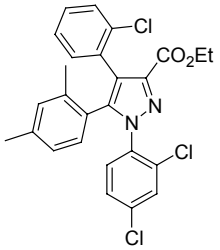
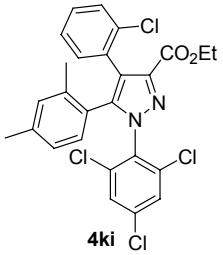
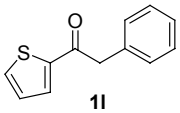
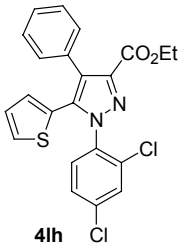
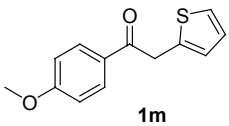
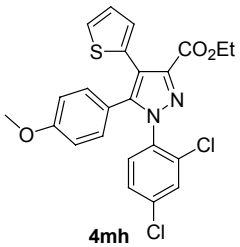
Entry	1	3	4	Yield[b]/%
12	 **1a**	 **3b**	 **4ab**	85
13	**1a**	 **3c**	 **4ac**	83
14	**1a**	 **3d**	 **4ad**	84
15	**1a**	 **3e**	 **4ae**	74
16	**1a**	 **3f**	 **4af**	86
17	**1a**	 **3g**	 **4ag**	87

Continued

Entry	1	3	4	Yield[b]/%
18	**1a**	 **3h**	 **4ah**	82
19	**1a**	 **3i**	 **4ai**	77
20	**1a**	 **3j**	 **4aj**	81
21	 **1c**	**3h**	 **4ch**	73
22	**1c**	**3i**	 **4ci**	66
23	 **1h**	**3h**	 **4hh**	75

Continued

Entry	1	3	4	Yield[b]/%
24	 **1i**	**3i**	 **4ii**	67
25	 **1k**	**3h**	 **4kh**	66
26	**1k**	**3i**	 **4ki**	60
27	 **1l**	**3h**	 **4lh**	82
28	 **1m**	**3h**	 **4mh**	83

[a] Performed with **1** (5.0 mmol), ethyl oxalyl chloride (6.0 mmol), *tert*-BuOLi (12.0 mmol), anhydrous THF (20 mL), EtOH (20 mL), concentrated hydrochloric acid (1.71 mL, 20.0 mmol) and **3** (5.0 mmol) following the general procedure. [b] Isolated yield via column chromatography.

thiazol-2-ylhydrazine hydrochloride (**3j**), the procedure favourably provided thiazolyl-substituted triarylpyrazoles **4aj** in 81% yield (Entry 20).

Afterwards, the substrates **1** and **3** were changed synchronously to further evaluate the viability of the procedure (Entries 21—28). The results showed that the sterically crowded triarylpyrazoles **4ch**, **4ci**, **4hh** and **4ii** were smoothly obtained in moderate yields of 66%—75% (Entries 21—24). Notably, the more sterically crowded triarylpyrazoles **4kh** and **4ki** were also accomplished in moderate yields of 66% and 60%, respectively (Entries 25 and 26). Impressively, as for thiophen-2-yl substituted ethanones **1l** and **1m**, the one-pot procedure efficiently delivered elegant heteroaryl-containing products **4lh** and **4mh** in high yields of 82% and 83%, respectively (Entries 27 and 28). The results meant that heteroaryl group can be flexibly installed at 1-, 4- or 5-position of the framework (Entries 20, 27 and

28). Besides, no isomers of 1,3,4-triaryl-1*H*-pyrazole-5-carboxylates were detected in the procedure.

Finally, the geometrical configuration of a representative product **4ka** was determined by single crystal X-ray crystallography (Figure 1, and see supporting information for details).[8] The crystal structural analysis exhibits that **4ka** molecule consists of three aryl rings and one central pyrazole ring, and these rings do not share a common plane. The phenyl and substituted phenyl rings lie in a propeller arrangement around the central pyrazole ring. The pyrazole ring makes dihedral angles of 45.4(3)°, 81.0(2)° and 76.3(3)° with the phenyl, the *ortho*,*para*-dimethylphenyl and *ortho*-chlorophenyl ring, respectively. There is an intermolecular C25—H25B···O1^{i} hydrogen bond involving the ethyl and carboxylate groups. The crystal structure is further stabilized by two kinds of intermolecular edge-to-face C—H···π interactions involving the *ortho*-chlorophenyl group and pyrazole ring as well as *ortho*, *para*-dimethylphenyl ring (Table S6 and Figure S1).

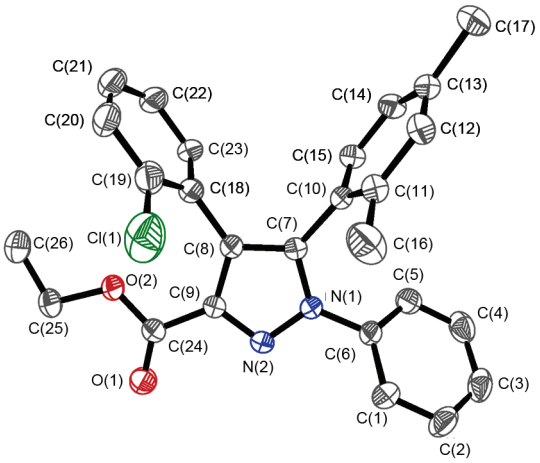


Figure 1 Single crystal structure of compound **4ka** (Table 3, Entry 11).

Conclusions

In summary, we have developed a one-pot approach to a variety of sterically crowded ethyl 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates in moderate to high yields from easily available ethyl oxalyl chloride, 1,2-diarylethanones and arylhydrazine hydrochlorides. The developed procedure involved an improved *tert*-BuOLi-mediated sterically hindered Claisen condensation and hydrochloric acid-promoted Knorr reaction, wherein ethyl oxalyl chloride and concentrated hydrochloric acid were identified as two key factors in the respective step to guarantee higher yields. Due to pharmaceutically potential importance of the triarylpyrazole-3-carboxylates, this methodology is of significant value in synthetic and medicinal chemistry.

Experimental

General information

Unless otherwise indicated, all reagents were obtained from commercial sources and used as received without further purification. All reactions were carried out in oven-dried glassware and monitored by thin layer chromatography (TLC, precoated silica gel plates containing HF_{254}). All solvents were only dried over 4 Å molecular sieves. Melting points were determined using an open capillaries and uncorrected. NMR spectra were determined on Bruker AV400 in $CDCl_3$ with TMS as internal standard for ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz), respectively. HRMS were carried out on a QSTAR Pulsar I LC/TOF MS mass spectrometer. Crystal data of **4ka** were collected on a Brüker Smart APEX II CCD diffractometer with monochromated Mo Kα radiation (λ=0.71073 Å) at 293 K, and operating in the *Ø*-*ω* scan mode. The structure was solved by direct methods and refined on F^2 by full matrix least-squares methods using SHELXTL.

Optimization of the Claisen condensation of 1a with ethyl oxalyl chloride (Table 1)

Ethyl oxalyl chloride (n_1 equiv.) was added to a solution of *t*-BuOLi (n_2 equiv.), **1a** (0.98 g, 5.0 mmol) in anhydrous THF (20 mL). The resulting mixture was stirred under reflux for 6 h unless otherwise indicated. Then, the mixture was concentrated in vacuo to remove THF giving a residual, to which were added water (10 mL), CH_2Cl_2 (15 mL) and 5% hydrochloric acid (*ca*. 5 mL) until pH 3—4 to make the solution partitioned into organic and aqueous layers. The aqueous layer was extracted with CH_2Cl_2 (10 mL×2). The combined organic phase was washed with water (20 mL×2), dried over anhydrous sodium sulfate, and concentrated to give a crude oil, which was recrystallized from petroleum ether (25 mL) to offer the desired **2a**.

Ethyl 2,4-dioxo-3,4-diphenylbutanoate (2a) Pale yellow solid, 1.39 g (94%, Entry 8), m.p. 74—75 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J=7.2 Hz, 3H), 4.32 (q, J=7.2 Hz, 2H), 6.35 (s, 1H), 7.28—7.38 (m, 5H), 7.43 (t, J=7.6 Hz, 2H), 7.55 (t, J=7.6 Hz, 1H), 7.97 (d, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 63.0, 63.1, 128.4, 128.8 (2C), 129.12 (2C), 129.15 (2C), 129.9 (2C), 131.2, 133.8, 135.3, 160.8, 188.4, 194.9; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{18}H_{17}O_4$: 297.1127, found 297.1122.

Optimization of the one-pot procedure (Table 2)

Ethyl oxalyl chloride (0.82 g, 6.0 mmol) was added to a solution of *t*-BuOLi (0.96 g, 12.0 mmol), **1a** (0.98 g, 5.0 mmol) in anhydrous THF (20 mL). The resulting mixture was stirred under reflux for 6 h. Then, the mixture was concentrated in vacuo to remove THF giving a residual. Afterwards, EtOH (20 mL), acid (4.0 equiv.) and phenylhydrazine hydrochloride (**3a**, 0.72 g, 5.0 mmol) were added to the residual at room temperature, and then the mixtures were refluxed for another 6 h. The reaction solution was concentrated in vacuo to remove EtOH affording a new residue, to which were added H_2O (15 mL) and CH_2Cl_2 (15 mL). The organic layer

was separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL×2). Finally, the combined organic phase was washed with brine (35 mL×2), dried over anhydrous sodium sulfate, and concentrated to provide a crude product, which was purified by column chromatography [*V*(petroleum ether)∶*V*(EtOAc)=1∶20] to give (*E*/*Z*)-**5aa** and **4aa**.

Ethyl 4-oxo-3,4-diphenyl-2-(2-phenylhydrazono)-butanoate (5aa) Pale yellow solid, 1.24 g (64%, Entry 1), m.p. 124−126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.18 (t, *J*=7.2 Hz, 3H), 4.14−4.29 (m, 2H), 5.97 (s, 1H), 6.89−6.92 (m, 3H), 7.19 (t, *J*=8.0 Hz, 2H), 7.24−7.36 (m, 5H), 7.41 (t, *J*=8.0 Hz, 2H), 7.49 (t, *J*=7.2 Hz, 1H), 7.99 (d, *J*=7.2 Hz, 2H), 12.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.0, 56.6, 61.0, 113.8 (2C), 122.2, 126.3, 127.3, 128.3 (2C), 128.57 (2C), 128.64 (2C), 129.2 (2C), 130.2 (2C), 132.7, 135.8, 136.8, 143.2, 162.7, 196.9; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{24}H_{23}N_2O_3$: 387.1709, found 387.1706.

Ethyl 1,4,5-triphenyl-1*H*-pyrazole-3-carboxylate (4aa) Pale yellow solid, 1.66 g (90%, Entry 5), m.p. 146−148 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.27 (t, *J*=7.2 Hz, 3H), 4.34 (q, *J*=7.2 Hz, 2 H), 6.98 (d, *J*=7.2 Hz, 2H), 7.16 (t, *J*=7.2 Hz, 2H), 7.21−7.24 (m, 3H), 7.26−7.31 (m, 6H), 7.37−7.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 60.9, 124.9, 125.7 (2C), 127.1, 127.7 (2C), 128.1, 128.3 (2C), 128.5, 128.8 (2C), 129.0, 130.4 (2C), 130.7 (2C), 131.8, 139.5, 141.6, 142.2, 162.5; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{24}H_{21}N_2O_2$: 369.1603, found 369.1594.

Synthesis of ethyl 1,4,5-triaryl-1*H*-pyrazole-3-carboxylates 4 from 1 and 3 (Table 3)

Ethyl oxalyl chloride (0.82 g, 6.0 mmol) was added to a solution of *t*-BuOLi (0.96 g, 12.0 mmol), 1,2-diarylethanones **1** (5.0 mmol) in anhydrous THF (20 mL). The resulting mixture was stirred under reflux for 6 h. Then, the mixture was concentrated in vacuo to remove THF giving a residual. Afterwards, EtOH (20 mL), concentrated hydrochloric acid (1.71 mL, 20.0 mmol) and arylhydrazine hydrochlorides **3** (5.0 mmol) were added to the residual at room temperature, and then the mixtures were refluxed for another 6 h. The reaction solution was concentrated in vacuo to remove EtOH affording a new residue, to which were added H_2O (15 mL) and CH_2Cl_2 (15 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL×2). Finally, the combined organic phase was washed with brine (35 mL×2), dried over anhydrous sodium sulfate, and concentrated to provide a crude product, which was purified by column chromatography [*V*(petroleum ether)∶*V*(EtOAc)=1∶20] to give the corresponding **4**.

Ethyl 1,4,5-triphenyl-1*H*-pyrazole-3-carboxylate (4aa) Pale yellow solid, 1.66 g (90%), m.p. 146−148 ℃. The spectral data were shown above.

Ethyl 1,4-diphenyl-5-*p*-tolyl-1*H*-pyrazole-3-carboxylate (4ba) Pale yellow solid, 1.68 g (88%), m.p. 128−132 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.26 (t, *J*=7.2 Hz, 3H), 2.26 (s, 3H), 4.33 (q, *J*=7.2 Hz, 2H), 6.86 (d, *J*=8.0 Hz, 2H), 6.96 (d, *J*=8.0 Hz, 2H), 7.21−7.31 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 21.3, 60.9, 124.7, 125.7 (2C), 126.0, 127.1, 127.7 (2C), 128.1, 128.8 (2C), 129.1 (2C), 130.2 (2C), 130.7 (2C), 132.0, 138.4, 139.6, 141.6, 142.4, 162.6; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{25}H_{23}N_2O_2$: 383.1760, found 383.1737.

Ethyl 5-(2,4-dimethylphenyl)-1,4-diphenyl-1*H*-pyrazole-3-carboxylate (4ca) Pale yellow solid, 1.59 g (80%), m.p. 126−128 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.29 (t, *J*=7.2 Hz, 3H), 1.78 (s, 3H), 2.24 (s, 3H), 4.35 (q, *J*=7.2 Hz, 2H), 6.85−6.99 (m, 4H), 7.16−7.26 (m, 7H), 7.30−7.36 (m, 1H), 7.40−7.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 19.6, 21.3, 60.9, 124.6 (2C), 125.3, 125.8, 126.7, 127.0, 127.6 (2C), 127.8, 128.7 (2C), 130.2 (2C), 131.1, 131.3, 131.9, 137.4, 139.1, 139.6, 141.3, 142.2, 162.7; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{26}H_{25}N_2O_2$: 397.1916, found 397.1921.

Ethyl 5-mesityl-1,4-diphenyl-1*H*-pyrazole-3-carboxylate (4da) Brown solid, 1.46 g (71%), m.p. 142−144 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.26 (t, *J*=7.2 Hz, 3H), 1.82 (s, 6H), 2.17 (s, 3H), 4.33 (q, *J*=7.2 Hz, 2H), 6.69 (s, 2H), 7.08−7.11 (m, 2H), 7.15−7.17 (m, 3H), 7.21 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 20.1 (2C), 21.2, 61.0, 123.8 (2C), 125.2, 125.5, 127.0, 127.6 (2C), 127.7, 128.5 (2C), 128.7 (2C), 129.6 (2C), 131.9, 137.8 (2C), 139.1, 139.6, 141.1, 141.4, 162.8; HRMS (ESI) *m*/*z*: [M + H$^+$] calcd for $C_{27}H_{27}N_2O_2$: 411.2073, found 411.2074.

Ethyl 1,5-diphenyl-4-*p*-tolyl-1*H*-pyrazole-3-carboxylate (4ea) White solid, 1.63 g (85%), m.p. 186−188 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.30 (t, *J*=7.2 Hz, 3H), 2.32 (s, 3H), 4.35 (q, *J*=7.2 Hz, 2H), 6.99 (d, *J*=8.4 Hz, 2H), 7.07 (d, *J*=8.4 Hz, 2H), 7.12 (d, *J*=8.4 Hz, 2H), 7.17 (t, *J*=7.2 Hz, 2H), 7.22 (d, *J*=7.2 Hz, 1H), 7.30−7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 21.3, 60.9, 123.4, 124.9, 125.7 (2C), 128.1, 128.3, 128.41, 128.44 (2C), 128.6, 128.8 (2C), 129.1, 130.4 (2C), 130.5 (2C), 136.7, 139.5, 142.1, 144.9, 162.5; HRMS (ESI) *m*/*z*: [M + H$^+$] calcd for $C_{25}H_{23}N_2O_2$: 383.1760, found 383.1768.

Ethyl 4-(4-chlorophenyl)-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (4fa) White solid, 1.73 g (86%), m.p. 160−162 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.30 (t, *J*=7.2 Hz, 3H), 4.35 (q, *J*=7.2 Hz, 2H), 6.97 (d, *J*=7.6 Hz, 2H), 7.15−7.22 (m, 4H), 7.23−7.35 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 61.1, 123.7, 125.7 (2C), 128.0 (2C), 128.3, 128.5 (2C), 128.7 (2C), 128.9 (2C), 130.3 (3C), 132.1 (2C), 133.2, 139.3, 141.4, 142.4, 162.4; HRMS (ESI) *m*/*z*: [M + H$^+$] calcd for $C_{24}H_{20}N_2O_2Cl$: 403.1213, found 403.1209.

Ethyl 1,5-diphenyl-4-*o*-tolyl-1*H*-pyrazole-3-carboxylate (4ga) Pale yellow solid, 1.49 g (78%), m.p. 106−108 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.19 (t, *J*=7.2 Hz, 3H), 2.06 (s, 3H), 4.27 (q, *J*=7.2 Hz, 2H),

6.94 (d, J=7.2 Hz, 2H), 7.09−7.22 (m, 7H), 7.31−7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 20.3, 60.8, 124.3, 125.2, 125.6 (2C), 127.7, 128.1, 128.3 (2C), 128.4, 128.9 (2C), 129.2, 129.5, 129.7 (2C), 131.0, 131.9, 137.4, 139.6, 142.06, 142.09, 162.3; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{25}H_{23}N_2O_2$: 383.1760, found 383.1736.

Ethyl 4-(2-chlorophenyl)-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ha) Brown oil, 1.63 g (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93 (t, J=7.2 Hz, 3H), 4.30 (q, J=7.2 Hz, 2H), 7.00 (d, J=8.0 Hz, 2H), 7.14−7.25 (m, 6H), 7.30−7.36 (m, 5H), 7.41 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 60.9, 122.1, 125.6 (2C), 126.2, 128.1, 128.3 (2C), 128.6, 128.79, 128.85 (2C), 128.9, 129.1, 129.8 (2C), 131.8, 132.2, 135.1, 139.4, 142.2, 142.6, 162.1; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{24}H_{20}N_2O_2Cl$: 403.1213, found 403.1217.

Ethyl 4-(2,4-dichlorophenyl)-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ia) Pale yellow solid, 1.75 g (80%), m.p. 144−146 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.24 (t, J=7.2 Hz, 3H), 4.31 (q, J=7.2 Hz, 2H), 6.98 (d, J=7.2 Hz, 2H), 7.08 (d, J=8.4 Hz, 1H), 7.14−7.25 (m, 4H), 7.30−7.35 (m, 5H), 7.43 (d, J=2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 61.0, 121.0, 125.6 (2C), 126.7, 128.3, 128.47 (2C), 128.53, 128.8, 128.9 (2C), 129.0, 129.8 (2C), 130.5, 133.0, 134.1, 135.8, 139.2, 142.1, 142.8, 161.9; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{24}H_{19}N_2O_2Cl_2$: 437.0824, found 437.0828.

Ethyl 4-(4-chlorophenyl)-5-(2,4-dimethylphenyl)-1-phenyl-1*H*-pyrazole-3-carboxylate (4ja) Brown solid, 1.70 g (79%), m.p. 158−160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J=7.2 Hz, 3H), 1.79 (s, 3H), 2.26 (s, 3H), 4.37 (q, J=7.2 Hz, 2H), 6.87−6.93 (m, 3H), 7.10 (d, J=8.4 Hz, 2H), 7.19 (d, J=8.4 Hz, 2H), 7.26−7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 19.6, 21.3, 61.1, 124.2, 124.6 (2C), 125.5, 126.8, 127.85 (2C), 127.90, 128.8 (2C), 130.4, 131.2 (2C), 131.5 (2C), 133.0, 137.3, 139.4, 139.5, 141.1, 142.3, 162.6; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{26}H_{24}N_2O_2Cl$: 431.1526, found 431.1521.

Ethyl 4-(2-chlorophenyl)-5-(2,4-dimethylphenyl)-1-phenyl-1*H*-pyrazole-3-carboxylate (4ka) Pale yellow solid, 1.59 g (74%), m.p. 110−112 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (t, J=7.2 Hz, 3H), 1.83 (s, 3H), 2.23 (s, 3H), 4.31 (q, J=7.2 Hz, 2H), 6.86 (t, J=7.6 Hz, 2H), 6.96−7.11 (m, 2H), 7.12−7.21 (m, 2H), 7.22−7.40 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.7, 21.2, 61.1, 124.6, 124.8, 126.4, 127.1, 127.4, 127.7 (2C), 130.05 (2C), 130.14, 130.6, 131.08, 131.12, 131.6, 133.3, 135.8, 135.9, 137.5, 139.3, 141.7, 144.0, 162.5; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{26}H_{24}N_2O_2Cl$: 431.1526, found 431.1530.

Ethyl 4,5-diphenyl-1-*p*-tolyl-1*H*-pyrazole-3-carboxylate (4ab) Gray solid, 1.63 g (85%), m.p. 138−140 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, J=7.2 Hz, 3H), 2.34 (s, 3H), 4.33 (q, J=7.2 Hz, 2H), 6.98 (d, J=7.6 Hz, 2H), 7.10 (d, J=8.0 Hz, 2H), 7.14−7.26 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 21.1, 60.9, 124.7, 125.5 (2C), 127.1, 127.7 (2C), 128.3 (2C), 128.4, 129.1, 129.4 (2C), 130.4 (2C), 130.7 (2C), 132.0, 137.0, 138.1, 141.4, 142.2, 162.6; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{25}H_{23}N_2O_2$: 383.1760, found 383.1786.

Ethyl 1-(2,4-dimethylphenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ac) Pale yellow solid, 1.65 g (83%), m.p. 104−106 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, J=7.2 Hz, 3H), 1.94 (s, 3H), 2.30 (s, 3H), 4.33 (q, J=7.2 Hz, 2H), 6.92 (d, J=8.0 Hz, 2H), 6.97 (d, J=8.0 Hz, 2H), 7.09 (t, J=7.6 Hz, 2H), 7.15 (t, J=7.6 Hz, 2H), 7.22−7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 17.6, 21.2, 60.8, 123.6, 127.0, 127.1, 127.7 (2C), 128.0, 128.1 (2C), 128.2, 128.8, 129.9 (2C), 130.7 (2C), 131.4, 132.1, 135.0, 136.2, 139.2, 141.1, 143.4, 162.6; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{26}H_{25}N_2O_2$: 397.1916, found 397.1931.

Ethyl 1-(2,5-dimethylphenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ad) White solid, 1.67 g (84%), m.p. 94−96 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, J=7.2 Hz, 3H), 1.88 (s, 3H), 2.30 (s, 3H), 4.33 (q, J=7.2 Hz, 2H), 6.93 (d, J=7.6 Hz, 2H), 7.02 (d, J=7.6 Hz, 1H), 7.10 (t, J=7.6 Hz, 3H), 7.14−7.19 (m, 2H), 7.23−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 17.2, 20.8, 60.8, 123.6, 127.1, 127.8 (2C), 128.1 (2C), 128.3, 128.8 (2C), 129.9 (2C), 130.2, 130.6, 130.8 (2C), 132.0, 132.1, 136.3, 138.5, 141.2, 143.3, 162.6; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{26}H_{25}N_2O_2$: 397.1916, found 397.1927.

Ethyl 1-(2,6-dimethylphenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ae) Pale yellow solid, 1.47 g (74%), m.p. 170−171 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, J=7.2 Hz, 3H), 2.01 (s, 6H), 4.34 (q, J=7.2 Hz, 2H), 6.90 (d, J=8.0 Hz, 2H), 7.03 (d, J=8.0 Hz, 2H), 7.08 (t, J=8.0 Hz, 2H), 7.17 (q, J=8.0 Hz, 2H), 7.26−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 17.9 (2C), 60.9, 123.6, 127.1, 127.8 (2C), 128.1 (2C), 128.2 (2C), 128.4, 128.6, 129.4 (4C), 130.8, 132.1, 136.2 (2C), 137.9, 141.4, 143.2, 162.6; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{26}H_{25}N_2O_2$: 397.1916, found 397.1927.

Ethyl 1-(3-chlorophenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4af) Pale yellow solid, 1.73 g (86%), m.p. 86−88 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, J=7.2 Hz, 3H), 4.34 (q, J=7.2 Hz, 2H), 6.99 (d, J=7.6 Hz, 2H), 7.06 (d, J=8.0 Hz, 1H), 7.16−7.25 (m, 5H), 7.26−7.29 (m, 2H), 7.33−7.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 61.0, 123.6, 125.1, 125.9, 127.3, 127.7 (2C), 128.3, 128.5 (2C), 128.6, 128.8, 129.7, 130.3 (2C), 130.6 (2C), 131.5, 134.6, 140.4, 142.1, 142.3, 162.3; HRMS (ESI) m/z: [M+H$^+$] calcd for $C_{24}H_{20}N_2O_2Cl$: 403.1213, found 403.1230.

Ethyl 1-(3-nitrophenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ag) Pale yellow solid, 1.80 g (87%), m.p. 130−132 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, J=7.2 Hz, 3H), 4.35 (q, J=7.2 Hz, 2H), 7.03 (d, J=8.0 Hz, 2H), 7.21−7.32 (m, 8H), 7.48 (t, J=8.0 Hz, 1H), 7.61 (d, J=8.0 Hz, 1H), 8.17 (d, J=8.0 Hz,

1H), 8.25 (d, *J*=1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.1, 61.2, 120.5, 122.6, 125.5, 127.4, 127.8 (2C), 128.3, 128.8 (2C), 129.2, 129.8, 130.3 (2C), 130.6 (2C), 130.9, 131.2, 140.3, 142.5, 142.7, 148.3, 162.1; HRMS (ESI) *m/z*: [M+Na$^+$] calcd for $C_{24}H_{19}N_3O_4Na$: 436.1273, found 436.1285.

Ethyl 1-(2,4-dichlorophenyl)-4,5-diphenyl-1*H*-pyrazole-3-carboxylate (4ah) Pale yellow solid, 1.79 g (82%), m.p. 124−126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.27 (t, *J*=7.2 Hz, 3H), 4.34 (q, *J*=7.2 Hz, 2H), 6.97 (d, *J*=7.6 Hz, 2H), 7.15 (t, *J*=7.6 Hz, 2H), 7.20 (d, *J*=7.2 Hz, 1H), 7.26−7.29 (m, 5H), 7.30 (d, *J*=2.0 Hz, 1H), 7.39−7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 61.1, 124.0, 127.3, 127.7, 127.8 (2C), 128.2, 128.3 (2C), 128.7, 129.9 (2C), 130.1, 130.7 (2C), 130.9, 131.5, 133.3, 136.0 (2C), 142.2, 144.1, 162.2; HRMS (ESI) *m/z*: [M + H$^+$] calcd for $C_{24}H_{19}N_2O_2Cl_2$: 437.0824, found 437.0818.

Ethyl 4,5-diphenyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-3-carboxylate (4ai) Yellow solid, 1.82 g (77%), m.p. 130−132 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.27 (t, *J*=7.2 Hz, 3H), 4.34 (q, *J*=7.2 Hz, 2H), 7.07 (d, *J*=8.0 Hz, 2H), 7.16 (t, *J*=7.6 Hz, 2H), 7.20−7.23 (m, 1H), 7.26−7.32 (m, 3H), 7.35 (s, 2H), 7.38−7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 61.1, 124.1, 127.3, 127.7 (2C), 128.0, 128.4 (2C), 128.6 (2C), 129.1, 129.5 (2C), 130.7 (2C), 131.3, 134.3, 135.8 (2C), 136.4, 142.9, 144.6, 162.1; HRMS (ESI) *m/z*: [M+H$^+$] calcd for $C_{24}H_{18}N_2O_2Cl_3$: 471.0434, found 471.0435.

Ethyl 4,5-diphenyl-1-(4-phenylthiazol-2-yl)-1*H*-pyrazole-3-carboxylate (4aj) Pale yellow solid, 1.83 g (81%), m.p. 181−183 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.27 (t, *J*=7.2 Hz, 3H), 4.34 (q, *J*=7.2 Hz, 2H), 7.24−7.38 (m, 14H), 7.47 (d, *J*=6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.1, 61.3, 111.1, 125.9 (2C), 126.2, 127.4, 127.7 (2C), 128.0 (2C), 128.3, 128.6 (2C), 128.8, 128.9, 130.5 (2C), 130.8, 130.9 (2C), 133.6, 143.1, 143.2, 152.4, 159.6, 161.9; HRMS (ESI) *m/z*: [M + H$^+$] calcd for $C_{27}H_{22}N_3O_2S$: 452.1433, found 452.1430.

Ethyl 1-(2,4-dichlorophenyl)-5-(2,4-dimethylphenyl)-4-phenyl-1*H*-pyrazole-3-carboxylate (4ch) Pale yellow solid, 1.70 g (73%), m.p. 62−64 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.31 (t, *J*=7.2 Hz, 3H), 1.82 (s, 3H), 2.22 (s, 3H), 4.38 (q, *J*=6.4 Hz, 2H), 6.83 (d, *J*=7.6 Hz, 2H), 6.95 (d, *J*=7.6 Hz, 1H), 7.21−7.23 (m, 6H), 7.31 (s, 1H), 7.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 19.6, 21.2, 61.1, 124.5, 124.7, 126.4, 127.1, 127.4, 127.7 (2C), 130.0 (2C), 130.1, 130.6, 131.05, 131.09, 131.6, 133.3, 135.8, 135.9, 137.5, 139.2, 141.7, 144.0, 162.4; HRMS (ESI) *m/z*: [M+Na$^+$] calcd for $C_{26}H_{22}N_2O_2NaCl_2$: 487.0956, found 487.0956.

Ethyl 5-(2,4-dimethylphenyl)-4-phenyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-3-carboxylate (4ci) Yellow solid, 1.65 g (66%), m.p. 134−136 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.32 (t, *J*=7.2 Hz, 3H), 1.75 (s, 3H), 2.23 (s, 3H), 4.38 (q, *J*=7.2 Hz, 2H), 6.84 (t, *J*=8.0 Hz, 2H), 7.10 (d, *J*=8.0 Hz, 1H), 7.22−7.25 (m, 6H), 7.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.2, 19.5, 21.2, 61.2, 124.0, 124.8, 126.4, 127.1, 127.7 (2C), 128.5, 128.6, 128.7, 129.8, 130.1 (2C), 131.4, 131.6, 135.3, 136.2, 136.4, 137.7, 139.4, 142.2, 144.1, 162.4; HRMS (ESI) *m/z*: [M + H$^+$] calcd for $C_{26}H_{22}N_2O_2Cl_3$: 499.0747, found 499.0747.

Ethyl 4-(2-chlorophenyl)-1-(2,4-dichlorophenyl)-5-phenyl-1*H*-pyrazole-3-carboxylate (4hh) Pale yellow solid, 1.77 g (75%), m.p. 72−74 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.11 (t, *J*=7.2 Hz, 3H), 4.20 (q, *J*=7.2 Hz, 2H), 6.91 (d, *J*=8.0 Hz, 2H), 7.05 (t, *J*=7.2 Hz, 2H), 7.10−7.24 (m, 6H), 7.34 (d, *J*=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.0, 61.0, 121.2, 126.3, 127.7, 128.0, 128.3 (2C), 128.5, 128.8, 129.07, 129.13, 129.3, (2C), 130.1, 130.8, 131.5, 132.2, 133.4, 136.0, 136.1, 142.9, 144.6, 161.8; HRMS (ESI) *m/z*: [M+H$^+$] calcd for $C_{24}H_{18}N_2O_2Cl_3$: 471.0434, found 471.0432.

Ethyl 4-(2,4-dichlorophenyl)-5-phenyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-3-carboxylate (4ii) Yellow solid, 1.81 g (67%), m.p. 60−62 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.25 (t, *J*=7.2 Hz, 3H), 4.33 (q, *J*=7.2 Hz, 2H), 7.07−7.10 (m, 2H), 7.13−7.28 (m, 5H), 7.33−7.37 (m, 1H), 7.42 (d, *J*=2.0 Hz, 1H), 7.45 (d, *J*=2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.1, 61.2, 120.2, 126.8, 127.4, 128.50 (2C), 128.55, 128.6, 128.9 (2C), 129.1, 129.4, 130.0, 132.9, 134.1, 134.3, 135.7, 135.86, 135.93, 136.6, 143.5, 145.3, 161.6; HRMS (ESI) *m/z*: [M+Na$^+$] calcd for $C_{24}H_{15}N_2OCl_{52}$-Na: 560.9474, found 560.9475.

Ethyl 4-(2-chlorophenyl)-1-(2,4-dichlorophenyl)-5-(2,4-dimethylphenyl)-1*H*-pyrazole-3-carboxylate (4kh) Orange oil, 1.65 g (66%); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.22 (t, *J*=7.2 Hz, 3H), 1.90 (s, 3H), 2.20 (s, 3H), 4.31 (q, *J*=7.2 Hz, 2H), 6.78−6.83 (m, 2H), 6.97 −7.41 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.0, 19.4, 21.2, 61.1, 124.0, 126.2, 126.3, 127.4, 128.8, 129.2, 130.1, 130.5, 131.0, 131.1, 131.3, 131.8, 133.2, 134.7, 135.76, 135.85, 137.7, 139.30, 139.35, 144.3, 148.7, 162.1; HRMS (ESI) *m/z*: [M+Na$^+$] calcd for $C_{26}H_{21}N_2O_2Cl_3Na$: 521.0566, found 521.0554.

Ethyl 4-(2-chlorophenyl)-5-(2,4-dimethylphenyl)-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-3-carboxylate (4ki) Pale yellow solid, 1.60 g (60%), m.p. 162−164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.24 (t, *J*=7.2 Hz, 3H), 1.87 (s, 2H), 2.05 (s, 1H), 2.20 (s, 1H), 2.21 (s, 2H), 4.32 (t, *J*=7.2 Hz, 2H), 6.78−6.91 (m, 3H), 7.03−7.29 (m, 4H), 7.39−7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 14.0, 19.2, 21.2, 61.2, 121.7, 123.4, 126.3, 126.4, 128.5 (2C), 128.7, 129.3, 129.8, 130.3, 131.3, 131.4, 131.6, 134.2, 134.7, 135.4, 136.2, 136.3, 139.4, 143.7, 144.4, 162.1; HRMS (ESI) *m/z*: [M+Na$^+$] calcd for $C_{26}H_{20}N_2O_2NaCl_4$: 555.0177, found 555.0173.

Ethyl 1-(2,4-dichlorophenyl)-4-phenyl-5-(thiophen-2-yl)-1*H*-pyrazole-3-carboxylate (4lh) Pale brown solid, 1.82 g (82%), m.p. 191−192 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.24 (t, *J*=7.2 Hz, 3H), 4.29 (q, *J*=7.2 Hz, 2H), 6.62 (d, *J*=2.8 Hz, 1H), 6.81 (t, *J*=4.0 Hz, 1H), 7.20 (d, *J*=5.2 Hz, 1H), 7.32−7.39 (m, 6H),

7.48—7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 61.1, 124.5, 126.9, 127.7, 127.88, 127.90, 127.95 (2C), 128.3, 129.0, 130.2, 130.7 (2C), 131.1, 131.5, 134.1, 135.9, 136.6, 138.1, 142.4, 161.9; HRMS (ESI) *m*/*z*: [M+Na$^+$] calcd for $C_{22}H_{16}N_2O_2NaSCl_2$: 465.0207, found 465.0214.

Ethyl 1-(2,4-dichlorophenyl)-5-(4-methoxyphenyl)-4-(thiophen-2-yl)-1*H*-pyrazole-3-carboxylate (4mh) Pale brown solid, 1.96 g (83%), m.p. 118—120 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J=7.1 Hz, 3H), 3.74 (s, 3H), 4.38 (q, J=7.2 Hz, 2H), 6.72 (d, J=8.4 Hz, 2H), 6.98—7.00 (m, 3H), 7.06 (d, J=3.2 Hz, 1H), 7.29 (d, J=8.4 Hz, 2H), 7.39 (d, J=12.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 55.1, 61.2, 113.9 (2C), 116.4, 120.0, 126.1, 126.6, 127.7, 128.9, 130.1, 130.9, 131.3 (2C), 131.9, 133.3, 135.9, 136.1, 142.5, 144.9, 160.0, 162.0; HRMS (ESI) *m*/*z*: [M+H$^+$] calcd for $C_{23}H_{19}N_2O_3SCl_2$: 473.0493, found 473.0490.

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[8] CCDC 949502 (**4ka**) contains the supplementary crystallographic data for this paper. There data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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