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# Development of a new cascade reaction for convergent synthesis of pyrazolo[1,5-*a*]quinoline derivatives under transition-metal-free conditions†

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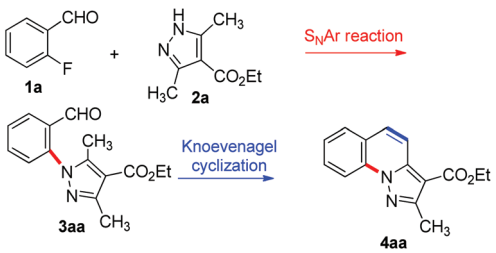
A novel method for the synthesis of pyrazolo[1,5-*a*]quinolines under the transition-metal-free conditions has been developed. This method involves a novel combination of aromatic nucleophilic substitution and Knoevenagel condensation reactions to give pyrazolo[1,5-*a*]quinolines.

## Introduction

Recently, the pyrazolo[1,5-*a*]quinoline subunit has been applied to useful compounds that display a biological and material function. In particular, 3-substituted pyrazolo[1,5-*a*]-quinoline derivatives have been developed for dopamine D4 antagonist agents,[1] GPR109a agonist agents,[2] and organic light-emitting device agents.[3] These reports suggest to us that the pyrazolo[1,5-*a*]quinoline skeleton may be a potentially useful privileged scaffold in the discovery of biologically and materially active compounds.[4] However, besides these examples, the pyrazolo[1,5-*a*]quinoline subunit has not been applied to seek further biologically and materially active compounds, which might be due to the lack of general methods for the synthesis of pyrazolo[1,5-*a*]quinoline derivatives.

Previous methods for the synthesis of pyrazolo[1,5-*a*]quinolones involve (1) a 1,3-dipolar cycloaddition reaction of *N*-iminoquinolines with acetylene esters;[5] (2) a nucleophilic reaction of *N*-iminoquinolines with ketene dithioacetals;[6] (3) an alkenylation/cyclization reaction of *N*-iminoquinolines with alkenyl iodides;[7] (4) a direct oxidative coupling reaction of phenylpyrazoles with internal alkynes;[8] and other approaches.[9] These methods require an inconvenient multi-step synthesis for the required substrates. Therefore, to develop medicinally and materially significant compounds possessing a pyrazolo[1,5-*a*]-quinoline subunit, a general and more facile approach to the synthesis of pyrazolo[1,5-*a*]quinolines and related compounds has become more desirable.




**Scheme 1** New cascade reaction for synthesis of pyrazolo[1,5-*a*]quinoline.

In this context, we envisaged a new cascade reaction as shown in Scheme 1. In this cascade reaction, the intermolecular aromatic nucleophilic substitution ($S_NAr$) of 2-fluorobenzaldehyde (**1a**) with 3,5-dimethyl-1*H*-pyrazole (**2a**) having a carboethoxy group at the 4-position is first conducted in the presence of a base to give the expected 1-substituted 3,5-dimethylpyrazole (**3aa**). In these intermediates, the 5-methyl group would be anionically more activated than the 3-methyl group under the conditions, since the trace anion generated at the 5-methyl group is favourably conjugated to the carboethoxy group.[10] The trace anions of **3aa** are successfully expected to proceed through the intramolecular Knoevenagel condensation reaction to give the desired pyrazolo[1,5-*a*]quinoline **4aa**. This $S_NAr$/Knoevenagel cyclization cascade reaction allows us to synthesize a variety of pyrazolo[1,5-*a*]quinolines without using any transition metal catalysts upon fine-tuning a combination of two substrates. In this paper, we describe the preliminary results of our studies.

## Results and discussion

### Optimization of the reaction conditions

First, we examined the $S_NAr$/Knoevenagel cyclization cascade reaction utilizing **1a** and **2a** as model substrates to optimize

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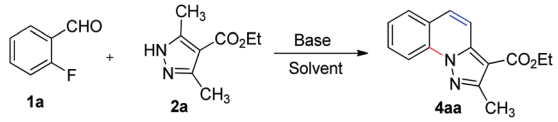
†Electronic supplementary information (ESI) available: Copies of $^1H$ and $^{13}C$ NMR spectra for all new compounds; X-ray analysis data for compound **9ca**. CCDC 900469. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob27050a

**Table 1** Optimization of the $S_NAr$/Knoevenagel cyclization cascade reaction[a]



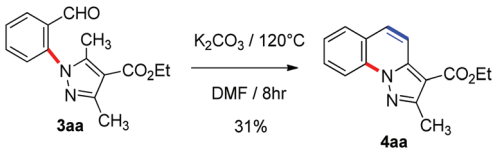

| Entry | Base | Solvent | Temp. (°C) | Yield[b] (%) of **4aa** |
|---|---|---|---|---|
| 1 | $K_2CO_3$ | DMF | 120 | 80 |
| 2 | $Na_2CO_3$ | DMF | 120 | Trace |
| 3 | $Cs_2CO_3$ | DMF | 120 | 64 |
| 4 | $K_3PO_4$ | DMF | 120 | 58 |
| 5 | KF | DMF | 120 | Not detected |
| 6 | $K_2CO_3$ | DMSO | 120 | 76 |
| 7 | $K_2CO_3$ | DMF | 100 | 59 |
| 8 | $K_2CO_3$ | DMF | 80 | Trace |
| 9 | $K_2CO_3$ | DMF | 120 | 37[c,d] |

[a] All reactions were carried out in the presence of pyrazole (**2a**) (1.2 mmol), 2-fluorobenzaldehyde (**1a**) (1.0 mmol), and base (3.0 mmol) in the indicated solvent (5 mL) for 8 h. [b] Isolated yield. [c] The reaction was carried out for 1 h. [d] The intermediate **3aa** was isolated in a 7% yield.

suitable bases and solvents. The results are shown in Table 1. When **1a** was treated with **2a** in the presence of an excess of $K_2CO_3$ (3 equiv.) in DMF at 120 °C for 8 h, the desired pyrazolo-[1,5-*a*]quinoline **4aa** was obtained with 80% yield as expected (Table 1, entry 1). Although a very slow reaction was observed when the reaction was carried out with $Na_2CO_3$ in place of $K_2CO_3$ (Table 1, entry 2), it was found that $Cs_2CO_3$ and $K_3PO_4$ are also effective bases for this cascade reaction in DMF at 120 °C to give **4aa** in slightly lower yields (Table 1, entries 3 and 4). It is noteworthy that organic bases such as $Et_3N$ and DBU were highly detrimental to this reaction and no desired products were detected for this reaction. No reaction occurred without a base in DMF at 120 °C.

Choice of the solvents is critical for this cascade reaction. When the reaction was carried out in the presence of $K_2CO_3$ at reflux upon switching the solvents from DMF to dioxane or toluene, no desired product was detected. However, DMSO was found to also be an efficient solvent to give **4aa** in a comparative yield (Table 1 entry 1 *vs.* 6). The cascade reaction was highly affected by the reaction temperature; the yield significantly decreased when the reaction was conducted below 120 °C (Table 1, entry 1 *vs.* 7, 8). Based on these results, at this stage, the optimal conditions for the cascade reaction were determined to be as conducted with 300 mol% of inexpensive $K_2CO_3$ in DMF at 120 °C for 8 h.

When the reaction was stopped within 1 h for the conditions of entry 1, **3aa** was isolated in a 7% yield along with 37% of **4aa** (Table 1, entry 9 and Scheme 1). The obtained **3aa** was resubmitted to the same conditions to entry 1 for 8 h to give **4aa** in a 31% isolated yield (Scheme 2). These experiments show that the proposed cascade reaction works well as expected (Scheme 1). We believe that the present cascade reaction is the first example in which the inactivated methyl group of the pyrazoles participates in the Knoevenagel cyclization




**Scheme 2** Knoevenagel condensation of **3aa**.

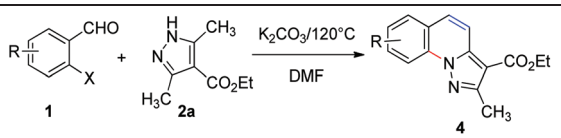
upon arylating at the nitrogen of the pyrazoles through the $S_NAr$ substitution.[11]

## Scope of 2-fluorobenzaldehydes

With the optimized conditions in hand, the scope and generality of the one-pot cascade reactions were investigated. First, **2a** was reacted with a variety of 2-fluorobenzaldehydes possessing a representative functional group on the aromatic ring. The results are shown in Table 2. Almost all of the tested combinations successfully produced the desired pyrazolo[1,5-*a*]quinolines **4ba–4na** with low to good isolated yields.

The results suggest that the electronic density of the corresponding 2-fluorobenzaldehydes might have some influence on this cascade reaction. 2-Fluorobenzaldehydes having an electron-withdrawing group were preferred substrates to those with an electron-donating group (Table 2, entries 1–13). Thus, when the cascade reaction was carried out with 2-fluorobenzaldehyde possessing a methoxy or methyl group under optimized conditions using $K_2CO_3$ as a base, the yield was significantly decreased (Table 2, entries 8–13). For instance, only 15% of the desired product was isolated upon reacting **1i** with **2a** using $K_2CO_3$ as a base (Table 2, entry 8). However, the

**Table 2** Scope of 2-fluorobenzaldehydes[a]

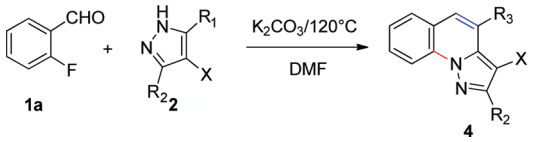



| | Aldehyde | | | Product | | |
|---|---|---|---|---|---|---|
| Entry | **1** | R | X | **4** | R | Yield[b] (%) |
| 1 | **1b** | 3-F | F | **4ba** | 9-F | 61 |
| 2 | **1c** | 5-F | F | **4ca** | 7-F | 64 |
| 3 | **1d** | 6-F | F | **4da** | 6-F | 12[c] |
| 4 | **1e** | 5-Br | F | **4ea** | 7-Br | 63 |
| 5 | **1f** | 6-Cl | Cl | **4fa** | 6-Cl | (24)[d] |
| 6 | **1g** | 5-CN | F | **4ga** | 7-CN | 47 |
| 7 | **1h** | 5-$CF_3$ | F | **4ha** | 7-$CF_3$ | 71 |
| 8 | **1i** | 5-$CH_3$ | F | **4ia** | 7-$CH_3$ | 15(50)[d] |
| 9 | **1j** | 3-$CH_3O$ | F | **4ja** | 9-$CH_3O$ | (52)[d] |
| 10 | **1k** | 4-$CH_3O$ | F | **4ka** | 8-$CH_3O$ | (61)[d] |
| 11 | **1l** | 5-$CH_3O$ | F | **4la** | 7-$CH_3O$ | (63)[d] |
| 12 | **1m** | 6-$CH_3O$ | F | **4ma** | 6-$CH_3O$ | (38)[d] |
| 13 | **1n** | 4,5-dimethoxy | F | **4na** | 7,8-dimethoxy | (36)[d] |

[a] All reactions were carried out in the presence of pyrazole (**2a**) (1.2 mmol), 2-fluorobenzaldehydes (1.0 mmol), and $K_2CO_3$ (3.0 mmol) in DMF (5 mL) for 8 h. [b] Isolated yields. [c] An adduct of **4da** with **2a** was obtained in a 36% yield (see Experimental section). [d] $Cs_2CO_3$ was used instead of $K_2CO_3$.

**Table 3** Scope of pyrazoles[a]




| Entry | Pyrazole **2** | | Product **4** | Yield[b] (%) |
|---|---|---|---|---|
| 1 | **2b** | X = H, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ab** $R_3$ = H | Not detected |
| 2 | **2c** | X = $CH_3$, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ac** $R_3$ = H | Not detected |
| 3 | **2d** | X = CN, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ad** $R_3$ = H | 34 |
| 4 | **2e** | X = F, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ae** $R_3$ = H | Not detected |
| 5 | **2f** | X = Cl, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4af** $R_3$ = H | 6[c] |
| 6 | **2g** | X = Br, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ag** $R_3$ = H | 58[c] |
| 7 | **2h** | X = I, $R_1$ = $CH_3$, $R_2$ = $CH_3$ | **4ah** $R_3$ = H | 12[c] |
| 8 | **2i** | X = $CO_2Et$, $R_1$ = $CH_3$, $R_2$ = H | **4ai** $R_3$ = H | 10 |
| 9 | **2j** | X = $CO_2Et$, $R_1$ = $CH_3$, $R_2$ = $SCH_3$ | **4aj** $R_3$ = H | 79 |
| 10 | **2k** | X = $CO_2Et$, $R_1$ = $CH_2CH_3$, $R_2$ = $SCH_3$ | **4ak** $R_3$ = $CH_3$ | 47[c] |
| 11 | **2l** | X = H, $R_1$ = $CH_3$, $R_2$ = $CF_3$ | **4al** $R_3$ = H | 71[c,d] |

[a] All reactions were carried out in the presence of pyrazoles (1.2 mmol), 2-fluorobenzaldehyde (**1a**) (1.0 mmol), and $K_2CO_3$ (3.0 mmol) in DMF (5 mL) for 8 h. [b] Isolated yields. [c] $Cs_2CO_3$ was used instead of $K_2CO_3$. [d] Reaction time was 4 days.

yield was significantly improved to 50% when $Cs_2CO_3$ was used instead of $K_2CO_2$.[12] Using $Cs_2CO_3$ as a base, 2-fluorobenzaldehyde possessing a methoxy functional group at either of the positions of the aromatic ring reacted with the pyrazole to give the desired compounds **4ja–4na** in modest yields (Table 2, entries 9–13). Although the less reactive 2-chlorobenzaldehyde could not react with **2a** (data not shown), the more electron-deficient 2,6-dichlorobenzaldehyde **1f** reacted with **2a** under the modified conditions using $Cs_2CO_3$ instead of $K_2CO_3$ to give the cascade product **4fa** in a low yield (Table 2, entry 5).

### Scope of pyrazoles

To extend the scope of the pyrazole substrates for the $S_NAr$/Knoevenagel cyclization cascade reaction, we next examined the reactions of 2-fluorobenzaldehyde **1a** with a variety of pyrazole derivatives **2b–l**. The results are shown in Table 3.

Although pyrazoles **2b** and **2c** bearing electron-rich or electron-neutral groups at the 4-position such as $–CH_3$ or –H could not react with **1a** (Table 3, entries 1 and 2), pyrazole **2d** bearing an electron-deficient cyano group (–CN) at the 4-position was able to react with **1a** to afford the desired products **4ad** with a moderate yield (Table 3, entry 3). We found that halogen atoms, except a fluorine atom, also function as available as an electron-deficient functional group at the 4-position (Table 3, entries 4–7). It is noteworthy that the cascade reaction with pyrazole **2g** substituted by a bromo group at the 4-position remarkably reacted with **1a** to give the desired product **4ag** with a good yield, though pyrazoles **2f** and **2h**, possessing other halogen atoms, did not react well (Table 3, entries 4–7).

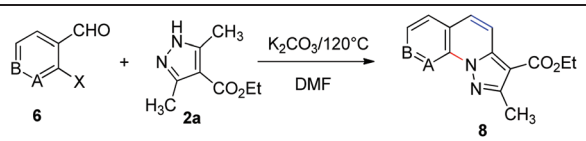
The substituent at the 3-position of the pyrazoles also strongly affected the present cascade reaction. When pyrazole **2i**, not having a methyl group at the 3-position, was used instead of **2a**, the corresponding cascade product **4ai** was obtained in a very low yield (Table 3, entry 8). However, pyrazoles **2j** and **2k** bearing $–SCH_3$ at the 3-position was able to react with **1a** to afford the desired product **4aj**[5] and **4ak** with a good yield (Table 3, entries 9 and 10). It should be pointed out that pyrazole **2l** bearing a $CF_3$ functional group at the 3-position reacts with **1a** to afford the desired product **4al** with a good yield (Table 3, entry 11). This experiment suggests to us that an electron-withdrawing group at the 4 position of the pyrazole is not necessary to induce the present cascade reaction.

### Application to synthesis of new heterocycles related to pyrazolo[1,5-*a*]quinolines

In an effort to apply the present cascade reaction to the synthesis of new heterocycles related to pyrazolo[1,5-*a*]quinolines, we finally examined the cascade reaction of **1a** with heteroaromatic aldehydes **6** and **7** (Tables 4 and 5).

As shown in Table 4, both 2-fluoro- and 2-chloropyridin-3-aldehydes **6a** and **6b** reacted with the pyrazole **2a** to give the expected adduct **8aa** in comparative yields (Table 4, entries 1 and 2). 3-Fluoropyridin-4-aldehyde **6c** reacted with the pyrazole

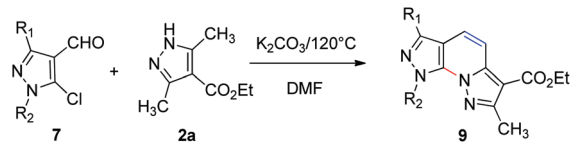
**Table 4** The cascade reaction of **2a** with pyridyl aldehydes **6** for synthesis of new heterocycles[a]




| Entry | Heteroaromatic aldehyde | | Product | Yield[b] (%) |
|---|---|---|---|---|
| 1 | **6a** | X = F, A = N, B = CH | **8aa** | 51 |
| 2 | **6b** | X = Cl, A = N, B = CH | **8aa** | 41[c] |
| 3 | **6c** | X = F, A = CH, B = N | **8ca** | 2 (30)[d] |

[a] All reactions were carried out in the presence of **2a** (1.2 mmol), **6** (1.0 mmol), and $K_2CO_3$ (3.0 mmol) in DMF (5 mL) for 8 h. [b] Isolated yields. [c] $Cs_2CO_3$ was used instead of $K_2CO_3$. [d] DMSO was used instead of DMF.

**Table 5** The cascade reaction of **2a** with pyrazolyl aldehydes **7** for synthesis of new heterocycles[a]




| Entry | Heteroaromatic aldehyde | | Product | Yield[b] (%) |
|---|---|---|---|---|
| 1 | **7a** | $R_1 = CH_3$, $R_2 = CH_3$ | **9aa** | 49[c] |
| 2 | **7b** | $R_1 = CH_3$, $R_2 = CH_2Ph$ | **9ba** | 27[c] |
| 3 | **7c** | $R_1 = CF_3$, $R_2 = CH_3$ | **9ca** | 64 |

[a] All reactions were carried out in the presence of **2a** (1.2 mmol), 7 (1.0 mmol), and $K_2CO_3$ (3.0 mmol) in DMF (5 mL) for 8 h. [b] Isolated yields. [c] $Cs_2CO_3$ was used instead of $K_2CO_3$.

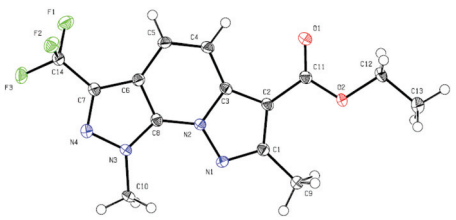


**Fig. 1** ORTEP drawing of **9ca**.

**2a** to give the expected adduct **8ca** in very low yields (Table 4, entry 3). However, the yield was significantly improved to 30% when DMSO was used instead of DMF.

5-Chloropyrazoles **7a–c** having a substituent at the 1-position also reacted with **2a** under these conditions to give new heterocycles **9aa–9ca** in varied yields. We wish to point out that pyrazole **8c** having an electron-withdrawing $CF_3$ group gave **9ca** in a good yield (Table 5).

All new heterocycles **9aa–9ca** were identified by conventional spectroscopic means. The structure of **9ca** was further confirmed by X-ray crystallographic analysis (Fig. 1).

## Conclusions

A convenient and general method for the synthesis of pyrazolo[1,5-*a*]quinolines and the related heterocycles has been developed. The method is based upon a cascade reaction through an aromatic nucleophilic substitution of 1*H*-pyrazoles with 2-fluorobenzaldehyde derivatives, followed by Knoevenagel cyclization of the resulting adducts. Our method potentially provides a variety of pyrazolo[1,5-*a*]quinolines and the related heterocycles without using any transition metal catalysts upon fine-tuning a combination of two readily available substrates.

## Experimental section

### General information

All reagents and solvents were pure analytical-grade materials purchased from commercial sources and were used without further purification except for 1*H*-pyrazoles **2d**, **2j** and **2k**. Compounds **2d**, **2j** and **2k** were synthesized by a known method.[13,14] All melting points were taken on a Yanagimoto micromelting point apparatus and were uncorrected. IR spectra were recorded on a JASCO FTIR-620. Mass spectra were measured on a JEOL GCmate by electron ionization and a Micromass Autospec by electrospray ionization. Elemental analysis was performed on an Elemental Vavio EL. NMR spectra were obtained on a JEOL JNM-ECP400 NMR spectrometer ($^1$H NMR: 400 MHz), a Bruker DPX400 NMR spectrometer ($^1$H NMR: 400 MHz) or a Bruker AVANCE III NMR spectrometer ($^1$H NMR: 400 MHz and $^{13}$C NMR: 100 MHz). The chemical shift data for each signal on $^1$H NMR were given in units of $\delta$ relative to $CHCl_3$ ($\delta$ = 7.26) for $CDCl_3$ solution. For $^{13}$C NMR spectra, the chemical shifts in $CDCl_3$ were relative to $CDCl_3$ ($\delta$ = 77.0) resonances. Column chromatography was carried out using 63–210 μm silica gel 60N (Kanto Chemical Co., Inc.). Analytical TLC was carried out with Merck plates precoated with silica gel $60F_{254}$ plates (0.25 mm). Crystallographic data (excluding structure factors) for the X-ray crystal structure analysis reported in this paper have been deposited with the Cambridge Crystallographic Data Center (CCDC) as supplementary publication No. CCDC 900469.

### Typical procedure for the preparation of pyrazolo[1,5-*a*] quinolone 4aa

A mixture of 2-fluorobenzaldehyde **1a** (202 mg, 1.0 mmol), 3,5-dimethyl-1*H*-4-pyrazolecarboxylate **2a** (125 mg, 1.2 mmol), and $K_2CO_3$ (420 mg, 3 mmol) in DMF (5 mL) was stirred at 120 °C for 8 h. After monitoring the end of the reaction on TLC, the mixture was cooled to room temperature and diluted with water. The resulting mixture was extracted with ethyl acetate twice. The combined organic layers were washed with water twice, dried over $MgSO_4$ and the solvent was removed *in vacuo* to afford a residue. The residue was purified by flash column chromatography (hexane : EtOAc = 5 : 1) on silica gel to afford pyrazolo[1,5-*a*]quinolone **4aa** (203 mg, 80% yield).

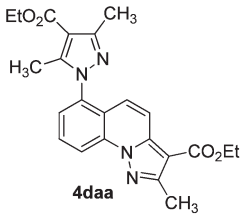



**Fig. 2** Structure of **4daa**.

### Reaction of 2,6-difluorobenzaldehyde (1d) with 2a (Table 2, entry 3)

Compound **1d** (143 mg, 1 mmol) was treated with **2a** (202 mg, 1 mmol) in the presence of $K_2CO_3$ (420 mg, 3 mmol) in DMF (5 mL) for 8 h at 120 °C in a similar manner for the preparation of **4aa**. The crude product was purified by silica gel column chromatography. Elution with a mixture of hexane : EtOAc = 5 gave **4da** (33 mg, 12.1%). Successive elution with EtOAc afforded the adduct **4daa** (149 mg, 35.5%). The structure of **4daa** is shown in Fig. 2.

**Ethyl 2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4aa).** Yield: 80%. Pale yellow solid. Mp. 84–85 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1698, 1617, 1561, 1549, 1272, 1124. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.56 (d, $J$ = 8.5 Hz, 1H), 8.03 (d, $J$ = 9.3 Hz, 1H), 7.79 (d, $J$ = 7.7 Hz, 1H), 7.72–7.67 (m, 1H), 7.63 (d, $J$ = 9.3 Hz, 1H), 7.49–7.45 (m, 1H), 4.40 (q, $J$ = 7.3 Hz, 2H), 2.74 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.31, 154.25, 140.25, 133.98, 129.99, 128.37, 127.84, 125.15, 123.42, 116.94, 115.85, 104.06, 59.85, 14.56, 14.51. MS (EI$^+$) $m/z$ 254 [M]$^+$, 209 [base]$^+$. HR-MS (ESI) calcd for $C_{15}H_{15}N_2O_2$ [M + H]$^+$ requires 255.1134, found 255.1134. Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.72; H, 5.62; N, 10.91.

**Ethyl 1-(2-formylphenyl)-3,5-dimethyl-1*H*-pyrazole-4-carboxylate (3aa).** Yield: 7%. Pale yellow solid. Mp. 100–102 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1701. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 9.64 (s, 1H), 8.07 (dd, $J$ = 7.7 Hz, 7.7 Hz, 1H), 7.74 (td, $J$ = 7.7 Hz, 1.5 Hz, 1H), 7.63 (t, $J$ = 7.7 Hz, 1H), 7.39 (d, $J$ = 7.7 Hz, 1H), 4.35 (q, $J$ = 7.1 Hz, 2H), 2.51 (s, 3H), 2.43 (s, 3H), 1.39 (t, $J$ = 7.1 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 188.89, 164.22, 152.11, 146.40, 140.38, 134.47, 132.51, 129.80, 128.87, 128.03, 111.13, 59.96, 14.39, 14.25, 12.26. HR-MS (ESI) calcd for $C_{15}H_{17}N_2O_3$ [M + H]$^+$ requires 273.1239, found 273.1234. Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.04; H, 5.98; N, 10.01.

**Ethyl 9-fluoro-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ba).** Yield: 61%. White solid. Mp. 121–126 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1696, 1571, 1551, 1324, 1272, 1228, 1105. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.13 (d, $J$ = 9.3 Hz, 1H), 7.63 (dd, $J$ = 1.9 Hz, 9.3 Hz, 1H), 7.59 (d, $J$ = 6.9 Hz, 1H), 7.49–7.46 (m, 1H), 7.44–7.38 (m, 1H), 4.41 (q, $J$ = 7.3 Hz, 2H), 2.76 (s, 3H), 1.45 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.09, 154.68 (d, $^3J_{CF}$ = 5.0 Hz), 152.20 (d, $^1J_{CF}$ = 256.6 Hz), 141.45, 127.46 (d, $^4J_{CF}$ = 2.0 Hz), 126.43, 125.01 (d, $^3J_{CF}$ = 7.6 Hz), 124.08 (d, $^4J_{CF}$ = 4.2 Hz), 123.39 (d, $^2J_{CF}$ = 7.9 Hz), 117.88, 116.97 (d, $^2J_{CF}$ = 20.5 Hz), 103.64, 59.99, 14.70, 14.45. MS (EI$^+$) $m/z$ 272 [M]$^+$, 227 [base]$^+$. HR-MS (ESI) calcd for $C_{15}H_{14}N_2O_2F$ [M + H]$^+$ requires 273.1039, found 273.1034. Anal. Calcd for $C_{15}H_{13}N_2O_2F$: C, 66.17; H, 4.81; N, 10.29. Found: C, 66.06; H, 4.92; N, 10.26.

**Ethyl 7-fluoro-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ca).** Yield: 64%. White solid. Mp. 145–146 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1700, 1566, 1436, 1241, 1123, 808. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.59 (dd, $J$ = 9.1 Hz, 4.8 Hz, 1H), 8.10 (d, $J$ = 9.5 Hz, 1H), 7.59 (d, $J$ = 9.5 Hz, 1H), 7.49–7.42 (m, 2H), 4.41 (q, $J$ = 7.1 Hz, 2H), 2.74 (s, 3H), 1.45 (t, $J$ = 7.1 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.17, 159.77 (d, $^1J_{CF}$ = 245.6 Hz), 154.26, 139.74, 130.66, 126.94 (d, $^4J_{CF}$ = 3.1 Hz), 124.56 (d, $^3J_{CF}$ = 8.9 Hz), 118.46 (d, $^2J_{CF}$ = 24.8 Hz), 118.30, 118.00 (d, $^3J_{CF}$ = 8.7 Hz), 112.88 (d, $^2J_{CF}$ = 22.6 Hz), 104.32, 59.93, 14.50, 14.47. HR-MS (ESI) calcd for $C_{15}H_{14}N_2O_2F$ [M + H]$^+$ requires 273.1039, found 273.1035. Anal. Calcd for $C_{15}H_{13}N_2O_2F$: C, 66.17; H, 4.81; N, 10.29. Found: C, 66.04; H, 5.06; N, 10.51.

**Ethyl 6-fluoro-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4da).** Yield: 12%. Pale yellow solid. Mp. 102–104 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1699, 1615, 1454, 1268, 1108, 791. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.35 (d, $J$ = 8.7 Hz, 1H), 8.09 (d, $J$ = 9.4 Hz, 1H), 7.89 (d, $J$ = 9.4 Hz, 1H), 7.66–7.61 (m, 1H), 7.18 (t, $J$ = 8.7 Hz, 1H), 4.41 (q, $J$ = 7.3 Hz, 2H), 2.73 (s, 3H), 1.45 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.12, 158.85 (d, $^1J_{CF}$ = 253 Hz), 154.66, 140.32, 134.85 (d, $^3J_{CF}$ = 6.2 Hz), 130.22 (d, $^3J_{CF}$ = 9.2 Hz), 120.14 (d, $^3J_{CF}$ = 5.4 Hz), 117.32 (d, $^4J_{CF}$ = 1.3 Hz), 113.66 (d, $^2J_{CF}$ = 19.3 Hz), 111.74 (d, $^3J_{CF}$ = 4.0 Hz), 110.14 (d, $^2J_{CF}$ = 19.9 Hz), 104.68, 60.00, 14.53, 14.50. MS (EI$^+$) $m/z$ 272 [M]$^+$, 227 [base]$^+$. HR-MS (ESI) calcd for $C_{15}H_{14}N_2O_2F$ (M + H)$^+$ requires 273.1039, found 273.1034. Anal. Calcd for $C_{15}H_{13}N_2O_2F$: C, 66.17; H, 4.81; N, 10.29. Found: C, 66.01; H, 5.00; N, 10.13.

**Ethyl 6-{4-(ethoxycarbonyl)-3,5-dimethyl-1*H*-pyrazol-1-yl}-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4daa, an adduct of 4da with 2a).** Yield: 36%. Pale yellow solid. Mp. 161–164 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1703, 1263, 1108. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.74 (d, $J$ = 8.5 Hz, 1H), 8.05 (d, $J$ = 9.6 Hz, 1H), 7.80 (t, $J$ = 8.5 Hz, 1H), 7.46–7.43 (m, 1H), 7.12 (d, $J$ = 9.6 Hz, 1H), 4.41–4.33 (m, 4H), 2.75 (s, 3H), 2.54 (s, 3H), 2.34 (s, 3H), 1.43–1.38 (m, 6H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.39, 164.00, 154.88, 152.06, 146.52, 140.02, 135.78, 134.67, 129.52, 124.46, 122.34, 121.18, 118.76, 117.49, 110.70, 104.79, 60.02, 59.94, 14.53, 14.45, 14.39, 12.09. MS (EI$^+$) $m/z$ 420 [M]$^+$. HR-MS (ESI) calcd for $C_{23}H_{25}N_4O_4$ [M + H]$^+$ requires 421.1876, found 421.1876. Anal. Calcd for $C_{23}H_{24}N_4O_4$: C, 65.70; H, 5.75; N, 13.33. Found: C, 65.75; H, 5.72; N, 13.05.

**Ethyl 7-bromo-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ea).** Yield: 63%. Pale yellow solid. Mp. 164–167 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1699, 1122, 813. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.46 (d, $J$ = 8.8 Hz, 1H), 8.08 (d, $J$ = 9.5 Hz, 1H), 7.95 (d, $J$ = 2.0 Hz, 1H), 7.79 (dd, $J$ = 8.8 Hz, 2.0 Hz, 1H), 7.55 (d, $J$ = 9.5 Hz, 1H), 4.41 (q, $J$ = 7.1 Hz, 2H), 2.73 (s, 3H), 1.45 (t, $J$ = 7.1 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.07, 154.54, 140.04, 132.94, 132.74, 130.51, 126.52, 124.81, 118.47, 118.23, 117.66, 104.54, 59.99, 14.51, 14.49. HR-MS (ESI) calcd for $C_{15}H_{14}N_2O_2Br$ [M + H]$^+$ requires 333.0239, found 333.0239. Anal. Calcd for $C_{15}H_{13}N_2O_2Br$: C, 54.07; H, 3.93; N, 8.41. Found: C, 54.19; H, 3.97; N, 8.61.

**Ethyl 6-chloro-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4fa).** Yield: 24%. White solid. Mp. 116–118 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1705, 1613, 1127, 1092, 791. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.54 (d, $J$ = 8.0 Hz, 1H), 8.14 (d, $J$ = 9.7 Hz, 1H), 8.07 (d, $J$ = 9.7 Hz, 1H), 7.62 (t, $J$ = 8.0 Hz, 1H), 7.56 (dd, $J$ = 8.0 Hz, 1.2 Hz, 1H), 4.42 (q, $J$ = 7.3 Hz, 2H), 2.74 (s, 3H), 1.46 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.05, 154.76, 140.03, 134.91, 132.65, 129.82, 125.60, 123.93, 121.45, 117.87, 114.84, 104.47, 59.98, 14.51, 14.48. HR-MS (ESI) calcd for $C_{15}H_{14}N_2O_2Cl$ $[M + H]^+$ requires 289.0744, found 289.0740.

**Ethyl 7-cyano-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ga).** Yield: 47%. Pale brown solid. Mp. 220–224 °C. IR (neat): $\nu_{max}/cm^{-1}$ 2227, 1697, 1613, 1542, 1431, 1324, 1270, 1159, 1124, 814. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.68 (d, $J$ = 8.8 Hz, 1H), 8.16 (d, $J$ = 9.4 Hz, 1H), 8.16 (d, $J$ = 1.8 Hz, 1H), 7.91 (dd, $J$ = 8.8 Hz, 1.8 Hz, 1H), 7.64 (d, $J$ = 9.4 Hz, 1H), 4.43 (q, $J$ = 7.2 Hz, 2H), 2.75 (s, 3H), 1.46 (t, $J$ = 7.2 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.81, 155.49, 140.83, 135.73, 133.36, 132.02, 126.55, 123.21, 119.13, 118.21, 117.22, 108.92, 105.47, 60.22, 14.57, 14.47. HR-MS (ESI) calcd for $C_{16}H_{14}N_3O_2$ $[M + H]^+$ requires 280.1086, found 280.1081. Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.79; H, 4.76; N, 15.09.

**Ethyl 2-methyl-7-(trifluoromethyl) pyrazolo[1,5-*a*]quinoline-3-carboxylate (4ha).** Yield: 71%. Yellow solid. Mp. 135–139 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1702, 1316, 1113. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.68 (d, $J$ = 8.5 Hz, 1H), 8.13 (d, $J$ = 9.4 Hz, 1H), 8.09 (s, 1H), 7.91 (dd, $J$ = 8.8 Hz, 1.5 Hz, 1H), 7.67 (d, $J$ = 9.4 Hz, 1H), 4.41 (q, $J$ = 7.3 Hz 2H), 2.75 (s, 3H), 1.45 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.95, 155.02, 140.67, 135.44, 127.32 (q, $^2J_{CF}$ = 33.0 Hz), 127.27, 126.17 (q, $^3J_{CF}$ = 3.2 Hz), 125.92 (q, $^3J_{CF}$ = 4.0 Hz), 125.23 (q, $^1J_{CF}$ = 272.0 Hz), 122.83, 118.52, 116.79, 104.97, 60.08, 14.54, 14.47. MS ($EI^+$) $m/z$ 322 $[M]^+$, 277 $[base]^+$. HR-MS (ESI) calcd for $C_{16}H_{14}N_2O_2F_3$ $[M + H]^+$ requires 323.1007, found 323.1007. Anal. Calcd for $C_{16}H_{13}N_2O_2F_3$: C, 59.63; H, 4.07; N, 8.09. Found: C, 59.66; H, 4.35; N, 8.28.

**Ethyl 2,7-dimethyl-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ia).** Yield: 15% (using $K_2CO_3$), 50% (using $Cs_2CO_3$). White solid. Mp. 103–104 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1697, 823. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.45 (d, $J$ = 8.5 Hz, 1H), 8.01 (d, $J$ = 9.2 Hz, 1H), 7.58 (d, $J$ = 9.2 Hz, 1H), 7.58 (s, 1H), 7.53 (dd, $J$ = 8.5 Hz, 1.5 Hz, 1H), 4.40 (q, $J$ = 7.3 Hz, 2H), 2.73 (s, 3H), 2.51 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.33, 154.01, 139.90, 134.90, 132.14, 131.46, 127.83, 127.62, 123.43, 116.80, 115.60, 103.75, 59.76, 21.12, 14.50, 14.49. MS ($EI^+$) $m/z$ 268 $[M]^+$, 223 $[base]^+$. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_2$ $(M + H)^+$ requires 285.1290, found 269.1292. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.41; H, 5.88; N, 10.42.

**Ethyl 9-methoxy-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ja).** Yield: 52%. White solid. Mp. 101–105 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1697, 1566, 1271, 1098. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.15 (d, $J$ = 9.2 Hz, 1H), 7.64 (d, $J$ = 9.2 Hz, 1H), 7.44–7.43 (m, 2H), 7.28–7.25 (m, 1H), 4.41 (q, $J$ = 7.2 Hz, 2H), 4.14 (s, 3H), 2.79 (s, 3H), 1.45 (t, $J$ = 7.2 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.35, 154.04, 150.34, 141.96, 128.39, 126.28, 125.30, 125.21, 121.07, 117.34, 112.82, 102.93, 59.87, 57.24, 15.02, 14.46. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_3$ $[M + H]^+$ requires 285.1239, found 285.1239. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.51; H, 5.58; N, 10.04.

**Ethyl 8-methoxy-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ka).** Yield: 61%. Pale yellow solid. Mp. 122–124 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1697, 1616, 1549, 1217, 1108. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.00 (d, $J$ = 2.5 Hz, 1H), 7.92 (d, $J$ = 9.2 Hz, 1H), 7.70 (d, $J$ = 8.7 Hz, 1H), 7.61 (d, $J$ = 9.2 Hz, 1H), 7.10 (dd, $J$ = 8.7 Hz, 2.5 Hz, 1H), 4.41 (q, $J$ = 7.1 Hz, 2H), 4.03 (s, 3H), 2.76 (s, 3H), 1.45 (t, $J$ = 7.1 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.33, 161.37, 154.33, 140.67, 135.25, 129.64, 127.61, 117.48, 115.93, 114.02, 103.55, 97.13, 59.75, 55.86, 14.57, 14.50. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_3$ $[M + H]^+$ requires 285.1239, found 285.1242. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.76; H, 5.46; N, 9.88.

**Ethyl 7-methoxy-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4la).** Yield: 63%. Pale yellow solid. Mp. 119–122 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1690, 1272, 1127, 806. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.49 (d, $J$ = 9.2 Hz, 1H), 8.03 (d, $J$ = 9.2 Hz, 1H), 7.58 (d, $J$ = 9.2 Hz, 1H), 7.32 (dd, $J$ = 8.9 Hz, 2.7 Hz, 1H), 7.18 (d, $J$ = 2.7 Hz, 1H), 4.40 (q, $J$ = 7.3 Hz, 2H), 3.92 (s, 3H), 2.72 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.33, 156.94, 153.86, 139.26, 128.88, 127.32, 124.43, 119.68, 117.35, 117.24, 108.78, 103.61, 59.74, 55.61, 14.50, 14.47. MS ($EI^+$) $m/z$ 284 $[M]^+$. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_3$ $[M + H]^+$ requires 285.1239, found 285.1238. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.69; H, 5.70; N, 9.83.

**Ethyl 6-methoxy-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4ma).** Yield: 38%. White solid. Mp. 132–133 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1701, 1617, 1105, 789. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.16 (d, $J$ = 8.2 Hz, 1H), 8.09 (d, $J$ = 9.6 Hz, 1H), 8.00 (d, $J$ = 9.6 Hz, 1H), 7.62 (t, $J$ = 8.2 Hz, 1H), 6.90 (d, $J$ = 8.2 Hz, 1H), 4.41 (q, $J$ = 7.4 Hz, 2H), 4.02 (s, 3H), 2.74 (s, 3H), 1.45 (t, $J$ = 7.4 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.49, 156.19, 154.45, 140.62, 134.87, 130.51, 122.43, 115.62, 114.82, 108.22, 104.87, 103.81, 59.90, 56.00, 14.67, 14.62. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_3$ $[M + H]^+$ requires 285.1239, found 285.1230.

**Ethyl 7,8-dimethoxy-2-methylpyrazolo[1,5-*a*]quinoline-3-carboxylate (4na).** Yield: 36%. White solid. Mp. 150–152 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1692, 1247, 1112. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.00 (s, 1H), 7.94 (d, $J$ = 9.2 Hz, 1H), 7.57 (d, $J$ = 9.2 Hz, 1H), 7.26 (s, 1H), 7.16 (s, 1H), 4.40 (q, $J$ = 7.2 Hz, 2H), 4.11 (s, 3H), 4.01 (s, 3H), 2.75 (s, 3H), 1.44 (t, $J$ = 7.2 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.41, 154.11, 152.09, 147.86, 139.77, 129.46, 127.01, 117.29, 114.67, 107.84, 103.10, 97.43, 59.69, 56.50, 56.12, 14.53. HR-MS (ESI) calcd for $C_{17}H_{19}N_2O_4$ $[M + H]^+$ requires 315.1345, found 315.1345. Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 64.71; H, 5.79; N, 8.74.

**3-Cyano-2-methylpyrazolo[1,5-*a*]quinoline (4ad).** Yield: 34%. White solid. Mp. 160–161 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1614, 1471,

1304, 804, 756, 744. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.55 (d, $J$ = 8.5 Hz, 1H), 7.84 (d, $J$ = 7.7 Hz, 1H), 7.78–7.73 (m, 1H), 7.71 (d, $J$ = 9.2 Hz, 1H), 7.56 (d, $J$ = 9.2 Hz, 1H), 7.56–7.51 (m, 1H), 2.64 (s, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 152.73, 139.75, 134.77, 129.61, 128.53, 125.84, 124.65, 123.23, 115.98, 114.81, 77.21, 54.96, 14.35. MS ($EI^+$) $m/z$ 207 $[M]^+$. HR-MS (ESI) calcd for $C_{13}H_{10}N_3$ $[M + H]^+$ requires 208.0875, found 208.0880.

**3-Chloro-2-methylpyrazolo[1,5-*a*]quinoline (4af).** Yield: 6%. White solid. Mp. 91–95 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1487, 1310, 801, 747. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.48 (d, $J$ = 8.5 Hz, 1H), 7.74 (d, $J$ = 7.7 Hz, 1H), 7.67–7.63 (m, 1H), 7.45–7.34 (m, 2H), 7.35 (d, $J$ = 9.2 Hz, 1H), 2.51 (s, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 147.82, 135.00, 134.55, 129.65, 128.55, 125.03, 124.66, 123.06, 114.75, 114.02, 102.13, 11.67. MS ($EI^+$) $m/z$ 216 $[M]^+$, 140 $[base]^+$. HR-MS (ESI) calcd for $C_{12}H_{10}N_2Cl$ $[M + H]^+$ requires 217.0533, found 217.0532.

**3-Bromo-2-methylpyrazolo[1,5-*a*]quinoline (4ag).** Yield: 58%. White solid. Mp. 116–118 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1478, 1305, 802, 743. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.49 (d, $J$ = 8.5 Hz, 1H), 7.74 (d, $J$ = 7.7 Hz, 1H), 7.67–7.63 (m, 1H), 7.45–7.40 (m, 2H), 7.33 (d, $J$ = 9.6 Hz, 1H), 2.51 (s, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 149.35, 136.59, 134.54, 129.61, 128.51, 125.35, 124.63, 123.07, 114.74, 114.62, 87.81, 12.60. MS ($EI^+$) $m/z$ 260 $[M - 1]^+$, 140 $[base]^+$. HR-MS (ESI) calcd for $C_{12}H_{10}N_2Br$ $[M + H]^+$ requires 261.0027, found 261.0032. Anal. Calcd for $C_{12}H_9N_2Br$: C, 55.20; H, 3.47; N, 10.73. Found: C, 55.28; H, 3.58; N, 10.74.

**3-Iodo-2-methylpyrazolo[1,5-*a*]quinoline (4ah).** Yield: 12%. White solid. Mp. 135–138 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1614, 1472, 1303, 803, 755, 743. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.50 (d, $J$ = 8.5 Hz, 1H), 7.75 (d, $J$ = 8.1 Hz, 1H), 7.67–7.62 (m, 1H), 7.46–7.39 (m, 2H), 7.29 (d, $J$ = 9.2 Hz, 1H), 2.53 (s, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 154.72, 141.61, 134.17, 130.69, 128.74, 128.71, 125.80, 123.37, 115.94, 114.16, 85.03, 13.14. MS ($EI^+$) $m/z$ 308 $[M]^+$. HR-MS (ESI) calcd for $C_{12}H_{10}N_2I$ $[M + H]^+$ requires 308.9889, found 308.9893. Anal. Calcd for $C_{12}H_9N_2I$: C, 46.78; H, 2.94; N, 9.09. Found: C, 46.63; H, 3.13; N, 9.11.

**Ethyl pyrazolo[1,5-*a*]quinoline-3-carboxylate (4ai).** Yield: 10%. Pale yellow solid. Mp. 101–102 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1703, 1244, 1218, 1097. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.62 (d, $J$ = 8.5 Hz, 1H), 8.44 (s, 1H), 8.10 (d, $J$ = 9.2 Hz, 1H), 7.84 (d, $J$ = 8.0 Hz, 1H), 7.76–7.72 (m, 1H), 7.70 (d, $J$ = 9.2 Hz, 1H), 7.53 (t, $J$ = 7.3 Hz, 1H), 4.41 (q, $J$ = 7.3 Hz, 2H), 1.43 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.57, 143.52, 139.08, 134.40, 130.15, 128.47, 128.13, 125.61, 123.60, 116.72, 116.01, 106.55, 60.12, 14.50. MS ($EI^+$) $m/z$ 240 $[M]^+$, 195 $[base]^+$; HR-MS (ESI) calcd for $C_{14}H_{13}N_2O_2$ $[M + H]^+$ requires 241.0977, found 241.0972. Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.96; H, 4.93; N, 11.73.

**Ethyl 2-(methylthio)pyrazolo[1,5-*a*]quinoline-3-carboxylate (4aj).** Yield: 79%. Pale yellow solid. Mp. 115–117 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1695, 1614, 1105. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.57 (d, $J$ = 8.5 Hz, 1H), 8.00 (d, $J$ = 9.4 Hz, 1H), 7.81 (d, $J$ = 7.7 Hz, 1H), 7.73–7.69 (m, 1H), 7.66 (d, $J$ = 9.4 Hz, 1H), 7.50–7.47 (m, 1H), 4.42 (q, $J$ = 7.3 Hz, 2H), 2.73 (s, 3H), 1.45 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.59, 154.87, 140.75, 133.81, 130.10, 128.38, 128.17, 125.12, 123.05, 116.34, 115.83, 103.25, 60.15, 14.52, 13.75. MS ($EI^+$) $m/z$ 286 $[M]^+$. HR-MS (ESI) calcd for $C_{15}H_{15}N_2O_2S$ $[M + H]^+$ requires 286.0864, found 287.0854. Anal. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78. Found: C, 62.73; H, 4.91; N, 9.87.

**Ethyl 2-(methylthio)-4-methyl-pyrazolo[1,5-*a*]quinoline-3-carboxylate (4ak).** Yield: 47%. Pale yellow solid. Mp. 112–114 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1713, 11525, 1078. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.56 (d, $J$ = 8.4 Hz, 1H), 7.70 (d, $J$ = 8.0 Hz, 1H), 7.64 (t, $J$ = 7.7 Hz, 1H), 7.47 (t, $J$ = 8.0 Hz, 1H), 7.40 (s, 1H), 4.41 (q, $J$ = 7.2 Hz, 2H), 2.77 (s, 3H), 2.72 (s, 3H), 1.45 (t, $J$ = 7.2 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.48, 154.91, 140.51, 132.73, 129.02, 127.85, 127.16, 126.73, 125.08, 122.98, 115.88, 105.07, 60.54, 21.85, 14.39, 14.26. HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_2S$ $[M + H]^+$ requires 301.1011, found 301.1012. Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33. Found: C, 63.91; H, 5.32; N, 9.35.

**Ethyl 2-trifluoromethyl-pyrazolo[1,5-*a*]quinoline-3-carboxylate (4al).** Yield: 71%. Pale yellow solid. Mp. 78–79 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1124, 811. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.63 (d, $J$ = 8.4 Hz, 1H), 7.80 (dd, $J$ = 7.9 Hz, 1.1 Hz, 1H), 7.73–7.69 (m, 1H), 7.547.25 (m, 3H), 6.86 (s, 1H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 143.89 (q, $^2J_{CF}$, 38.2 Hz), 138.63, 134.45, 129.80, 128.45, 125.98, 125.86, 123.66, 121.60 (q, $^1J_{CF}$, 272.0 Hz), 116.38, 116.00, 98.01 (q, $^3J_{CF}$, 2.0 Hz). HR-MS (ESI) calcd for $C_{12}H_8N_2F_3$ $[M + H]^+$ requires 237.0640, found 237.0643.

**Ethyl 2-methylpyrazolo[1,5-*a*][1,8]naphthyridine-3-carboxylate (8aa).** Yield: 51% (for **6a**), 41% (for **6b**). White solid. Mp. 125–129 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1700, 1619, 1550, 1414, 1109. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 8.88 (dd, $J$ = 4.6 Hz, 1.9 Hz, 1H), 8.18 (dd, $J$ = 7.7 Hz, 1.9 Hz, 1H), 8.15 (d, $J$ = 9.5 Hz, 1H), 7.61 (d, $J$ = 9.5 Hz, 1H), 7.51 (dd, $J$ = 9.4 Hz, 4.6 Hz, 1H), 4.42 (q, $J$ = 7.3 Hz, 2H), 2.79 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.98, 155.37, 150.58, 143.87, 142.03, 137.11, 126.55, 121.37, 118.38, 118.26, 105.37, 60.05, 14.63, 14.41. MS ($EI^+$) $m/z$ 255 $[M]^+$, 210 $[base]^+$. HR-MS (ESI) calcd for $C_{14}H_{13}N_3O_2Na$ $[M + H]^+$ requires 278.0905, found 278.0903.

**Ethyl 2-methylpyrazolo[1,5-*a*][1,7]naphthyridine-3-carboxylate (8ca).** Pale brown solid. Mp. 118–120 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1695, 1549, 1431, 1276, 1128. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 9.94 (s, 1H), 8.68 (d, $J$ = 5.4 Hz, 1H), 8.24 (d, $J$ = 9.3 Hz, 1H), 7.64 (d, $J$ = 5.4 Hz, 1H), 7.59 (d, $J$ = 9.3 Hz, 1H), 4.41 (q, $J$ = 7.3 2H), 2.75 (s, 3H), 1.45 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.82, 154.86, 144.47, 140.28, 139.68, 129.33, 127.81, 125.53, 121.89, 120.54, 105.34, 60.13, 14.46, 14.45; $EI^+$ $m/z$ 255 $[M]^+$, 210 $[base]^+$; HR-MS (ESI) calcd for $C_{14}H_{14}N_3O_2$ $(M + H)^+$ requires 256.1086, found 256.1085.

**Ethyl 1,3,7-trimethyl-1*H*-dipyrazolo[1,5-*a*:4′,3′-*e*]pyridine-6-carboxylate (9aa).** Yield: 49%. White solid. Mp. 140–142 °C. IR (neat): $\nu_{max}$/cm$^{-1}$ 1698, 1632, 1505, 1267, 1106. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 7.72 (d, $J$ = 9.3 Hz, 1H), 7.50 (d, $J$ = 9.3 Hz, 1H), 4.50 (s, 3H), 4.40 (q, $J$ = 7.3 Hz, 2H), 2.70 (s, 3H), 2.52 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.29, 155.08, 142.95, 142.50, 135.62, 121.51, 110.53, 110.08, 102.00, 64.00, 59.83, 38.05, 14.58, 14.49, 12.09. MS (EI+) $m/z$ 272 $[M]^+$. HR-MS (ESI) calcd for $C_{14}H_{17}N_4O_2$ $[M + H]^+$

requires 273.1352, found 273.1349. Anal. Calcd for $C_{14}H_{16}N_4O_2$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.73; H, 5.76; N, 20.54.

**Ethyl 1-benzyl-3,7-dimethyl-1*H*-dipyrazolo[1,5-*a*:4′,3′-*e*]pyridine-6-carboxylate (9ba).** Yield: 27%. White solid. Mp. 128–130 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1699, 1627, 1505, 1252, 1119, 1088. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 7.75 (d, $J$ = 9.2 Hz, 1H), 7.52(d, $J$ = 9.2 Hz, 1H), 7.40 (d, $J$ = 7.7 Hz, 2H), 7.30–7.21 (m, 3H), 6.13 (s, 2H), 4.40 (q, $J$ = 7.3 Hz, 2H), 2.71 (s, 3H), 2.52 (s, 3H), 1.43 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 164.35, 155.12, 143.80, 142.62, 137.31, 135.29, 128.55, 128.18, 127.73, 121.52, 110.74, 110.35, 102.74, 59.85, 53.85, 14.68, 14.52, 12.18. MS ($EI^+$) $m/z$ 348 $[M]^+$, 91 $[base]^+$; HR-MS (ESI) calcd for $C_{20}H_{21}N_4O_2$ $[M + H]^+$ requires 349.1665, found 349.1663. Anal. Calcd for $C_{20}H_{20}N_4O_2$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.03; H, 5.78; N, 16.08.

**Ethyl 1,7-dimethyl-3-(trifluoromethyl)-1*H*-dipyrazolo[1,5-*a*:4′,3′-*e*]pyridine-6-carboxylate (9ca).** Yield: 64%. White solid. Mp. 148–150 °C. IR (neat): $\nu_{max}/cm^{-1}$ 1702, 1509, 1266, 1180, 1120, 1091. $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 7.90 (d, $J$ = 9.6 Hz, 1H), 7.64 (d, $J$ = 9.6 Hz, 1H), 4.63 (s, 3H), 4.41 (q, $J$ = 7.3 Hz, 2H), 2.72 (s, 3H), 1.44 (t, $J$ = 7.3 Hz, 3H). $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 163.84, 155.60, 142.35, 135.64, 135.33 (q, $^2J_{CF}$ = 39.3 Hz), 121.05 (q, $^1J_{CF}$ = 269.3 Hz), 120.12, 113.92, 107.93, 103.86, 60.16, 39.47, 14.49, 14.42. MS ($EI^+$) $m/z$ 326 $[M]^+$, 281 $[base]^+$. HR-MS (ESI) calcd for $C_{14}H_{14}N_4O_2F_3$ $[M + H]^+$ requires 327.1069, found 327.1064. Anal. Calcd for $C_{14}H_{13}N_4O_2F_3$: C, 51.54; H, 4.02; N, 17.17. Found: C, 51.36; H, 4.28; N, 17.16.

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