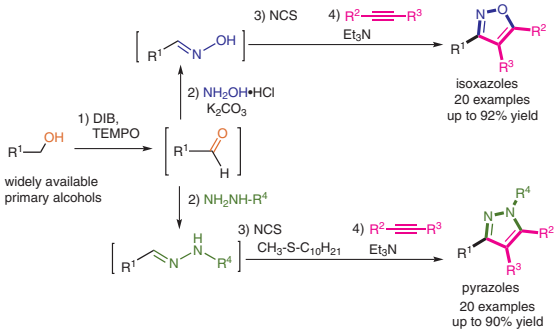
Synthesis E. Kobayashi, H. Togo Paper

Facile One-Pot Transformation of Primary Alcohols into 3-Aryl- and 3-Alkyl-isoxazoles and -pyrazoles

Eiji Kobayashi
Hideo Togo*

Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan
togo@faculty.chiba-u.jp



Received: 09.05.2019
Accepted after revision: 06.06.2019
Published online: 18.06.2019
DOI: 10.1055/s-0039-1690102; Art ID: ss-2019-f0261-op

Abstract Various primary alcohols were smoothly transformed into 3-aryl- and 3-alkylisoxazoles in good yields in one pot by successive treatment with $PhI(OAc)_2$ in the presence of TEMPO, NH_2OH, and then NCS, followed by reaction with alkynes in the presence of Et_3N. Similarly, various primary alcohols were smoothly transformed into 3-aryl- and 3-alkylpyrazoles in good yields in one pot by successive treatment with $PhI(OAc)_2$ in the presence of TEMPO, $PhNHNH_2$, and then NCS and decyl methyl sulfide, followed by reaction with alkynes in the presence of Et_3N. Thus, both 3-aryl- and 3-alkylisoxazoles, and 3-aryl- and 3-alkylpyrazoles could be prepared from readily available primary alcohols in one pot under transition-metal-free conditions.

Key words isoxazole, pyrazole, alcohol, oxime, hydrazone, cycloaddition

Nitrogen-containing heterocyclic compounds are very important and attractive due to their potent biological activities.[1] Among them, isoxazoles[2] and pyrazoles[3] are the most important nitrogen-containing five-membered heteroaromatics, and they serve as units or cores of many pharmaceuticals and agrochemicals. For example, Valdecoxib,[2d,f] a 3-phenylisoxazole derivative, and Celecoxib,[2e,f,3b] a 3-arylpyrazole derivative, are nonsteroidal anti-inflammatory drugs (Figure 1).

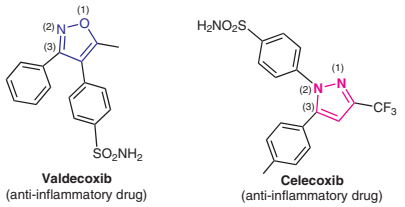


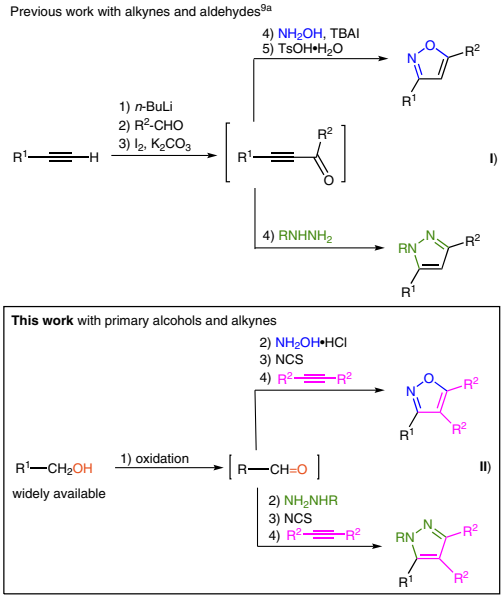
Figure 1 Typical pharmaceuticals bearing 3-arylisoxazole or 3-arylpyrazole units

Numerous synthetic studies of isoxazoles and pyrazoles have been carried out. The most typical and useful method for the preparation of isoxazoles is the 1,3-dipolar cycloaddition reaction of nitrile *N*-oxides with alkynes. Recent synthetic studies of isoxazoles via nitrile *N*-oxides are:[4] (1) The preparation of 3-isopropylisoxazoles from isopropyloxime, alkynes, NaCl, and Oxone®;[4a] (2) 3-(*p*-Phenylbenzyl)isoxazoles from *p*-phenylbenzyl hydroximoyl fluorides, alkynes, EtONa, and Ag_2CO_3;[4b] (3) 3-Substituted isoxazoles bearing a phosphate group at the 4- or 5-position from halogenoximes, bromovinyl phosphates, and $NaHCO_3$;[4c] (4) 3-(Difluoromethyl)isoxazoles from difluoromethyl nitrile *N*-oxides and alkynes;[4d] (5) 3-(α-Amino)alkylisoxazoles from chloroximes derived from α-amino acids and alkynes;[4e] (6) 3,4,5-Trisubstituted isoxazoles from β-ketoamides and chloroximes with *N*,*N*,*N*′,*N*′-tetramethylguanidine and Et_3N;[4f] (7) 3-(Trifluoromethyl)isoxazoles from (trifluoromethyl)hydroximoyl bromide and alkynes with Et_3N;[4g] (8) 3,4,5-Trisubstituted isoxazoles from aldoximes, alkynes, and (diacetoxyiodo)benzene ($PhI(OAc)_2$, DIB);[4h] and (9) 3,5-Disubstituted isoxazoles from aldoximes, alkynes, and 3,5-(dimethyl)iodobenzene, and Oxone®.[4i] The preparation of isoxazoles with transition metals was also reported recently, as follows:[5] (1) The preparation of 3,5-disubstituted isoxazoles from ynone *O*-methyl oximes in the presence of $Pd(O_2CCF_3)_2$ and $CuCl_2$;[5a,b] (2) 3-(Difluoromethyl)- and 3-(trifluoromethyl)isoxazoles from arylacetylenes, $CHF_2CH_2NH_2$ or $CF_3CH_2NH_2$, and *tert*-butyl nitrite in the presence of $ZnBr_2$ and CuI;[5c] (3) 3,5-Disubstituted isoxazoles from arylacetylenes and *tert*-butyl nitrite in the presence of $Sc(OTf)_3$;[5d] (4) 3,5-Diarylisoxazoles from enone oximes in the presence of $Cu(OAc)_2$;[5e] and (5) 4-Borylated 3-arylisoxazoles from ynone oximes and $HB(OR)_2$ in the presence of $^{i}PrAuTFA$.[5f] Under transition-metal-free conditions, the preparation of 3,5-disubstituted isoxazoles from ynones and $TMSN_3$ was also reported.[6]

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

On the other hand, recent synthetic studies on the preparation of pyrazoles with hydrazines include:[7] (1) The preparation of 4-borylated pyrazoles from hydrazone with *B*-chlorocatecolborane, Et_3N, and $Cu(OTf)_2$;[7a] (2) 3-Aryl-5-(arylmethyl)pyrazoles from arylacetylenes and hydrazine in the presence of CuI and $Ru(bpy)_3Cl_2$ under irradiation with blue LED;[7b] (3) 5-Amino-1-aryl-3-methylpyrazoles from arylhydrazines and β-aminocrotononitrile under microwave irradiation;[7c] (4) 5-Aryl-4-iodo-3-(trifluoromethyl)pyrazoles from hydrazones derived from CF_3-ynones with I_2;[7d] (5) 5-Aryl-3-(trifluoromethyl)pyrazoles from ynones and arylhydrazines in the presence of AgOTf;[7e] (6) 4-Benzeneselenyl-3,5-diarylpyrazoles from chalcones, arylhydrazines, and PhSeSePh in the presence of CuBr;[7f] (7) 3,4,5-Trisubstituted pyrazoles from arylhydrazines and 1,3-diketones in the presence of $Cu(NO_3)_2$;[7g] and (8) 3-Arylpyrazole-5-tetrafluoroborates from ynone trifluoroborates and hydrazines.[7h] Moreover, the preparation of pyrazoles bearing ester groups from alkenes and α-diazoesters;[8a,b] pyrazoles bearing amide groups from β-ketoamides, hydrazonyl chlorides, and DMAP;[8c] and pyrazoles bearing 1,5-cyclic group from hydrazones and α-bromomalonate esters in the presence of $[Ir(ppy)_2dtbbpy]PF_6$ under blue LED irradiation[8d] was also reported.

We reported the one-pot preparation of 3,5-disubstituted isoxazoles through the reaction with terminal alkynes and *n*-BuLi, and then with aldehydes and molecular iodine, followed by the reaction with hydroxylamine; we also reported the reaction of 3,5-disubstituted pyrazoles with terminal alkynes and *n*-BuLi, and then with aldehydes and molecular iodine, followed by the reaction with hydrazine, respectively, by a successive treatment, as shown in Scheme 1 (**I**).[9a]

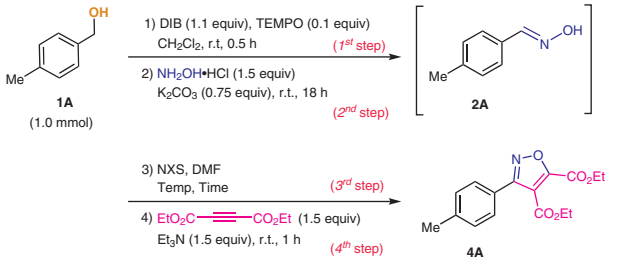


Scheme 1 One-pot preparation of isoxazoles and pyrazoles

Here, as part of our continuing synthetic studies on nitrogen-containing heteroaromatics, such as isoxazoles, pyrazoles, oxazoles, quinolines,[9] we would like to report a facile one-pot transformation of primary alcohols into 3-aryl- and 3-alkylisoxazoles and -pyrazoles, as shown in Scheme 1 (**II**).

One of the most efficient precursors for the preparation of both isoxazoles and pyrazoles are aldehydes, and one of the most useful, safe, and promising methods for the preparation of aldehydes from widely available primary alcohols is DIB oxidation in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as catalyst.[10] Thi is because most primary alcohols can be smoothly oxidized to aldehydes in good yields at room temperature with a TEMPO-DIB system, and the oxidation can be carried out without bad smell, as is the case using the Swern oxidation, and without using explosive reagents, such as Dess–Martin reagent. Based on these considerations, first, the optimum reaction conditions for the preparation of diethyl 3-(*p*-methylphenyl)isoxazole-4,5-dicarboxylate (**4A**) from *p*-methylbenzyl alcohol (**1A**) were examined (Table 1). *p*-Methylbenzyl alcohol **1A** (1.0 mmol) was treated with DIB (1.1 equiv) in the presence of TEMPO (0.1 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 0.5 h (first step), and then with $NH_2OH{\cdot}HCl$ (1.5 equiv) and K_2CO_3 (0.75 equiv) at room temperature for 18 h to form oxime **2A** (second step). Under

Table 1 Transformation of 4-Methylbenzyl Alcohol (**1A**) into 3-(4′-Methylphenyl)isoxazole (**4A**)



Entry	NXS (equiv)	Temp, time	Yield **4A** (%)
1[a]	NCS (1.2)	r.t., 1 h → 40 °C, 1 h	55 (16)[b]
2[c]	NCS (1.2)	r.t., 1 h → 40 °C, 1 h	62 (8)[b]
3[c]	NCS (1.2)	0 °C, 1 h → r.t., 3 h	73 (10)[b]
4[c]	NCS (1.2)	–78 °C, 1 h → r.t., 3 h	72 (10)[b]
5[d]	NCS (1.2)	0 °C, 1 h → r.t., 3 h	78
6[d]	NCS (1.5)	0°C, 1 h → r.t., 3 h	88
7[d]	NBS (1.5)	0 °C, 1 h → r.t., 3 h	0
8[c]	NIS (1.5)	0 °C, 1 h → r.t., 3 h	0

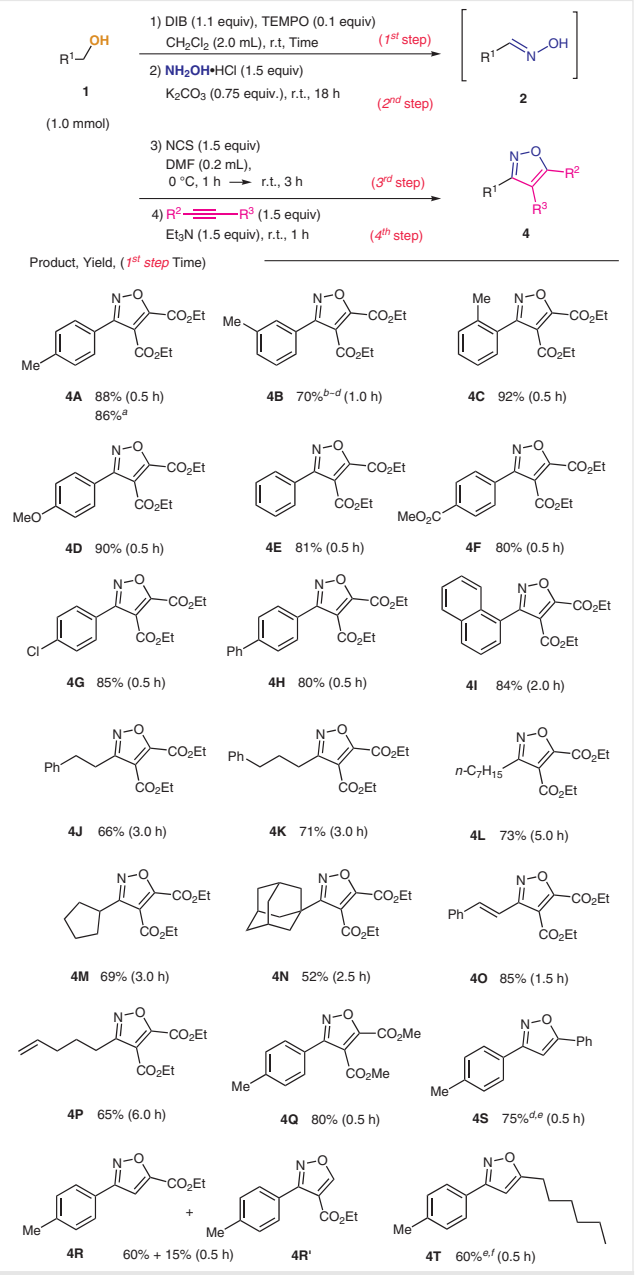
[a] DMF (0.1 mL) was not used in the third step of the reaction.
[b] Yield of oxime **2A**.
[c] CH_2Cl_2 (1.0 mL) in the first step of the reaction and DMF (0.1 mL) in the third step were used.
[d] CH_2Cl_2 (2.0 mL) in the first step of the reaction and DMF (0.2 mL) in the third step were used.

the present reaction procedure and conditions, oxime **2A** was obtained from *p*-methylbenzyl alcohol **1A** in one pot, quantitatively. The mixture was treated with NCS (1.2 equiv) in the absence or presence of DMF (0.1 mL) at room temperature for 1 h, and then warmed to 40 °C for 1 h to form the precursor of nitrile *N*-oxide (third step). This mixture was further treated with diethyl acetylenedicarboxylate (1.5 equiv) and Et_3N (1.5 equiv) at room temperature for 1 h (fourth step) to form isoxazole **4A** in 55% and 62% yields, respectively, together with oxime **2A** in low yields (entries 1 and 2). Here, the addition of DMF was effective to increase the solubility of oxime **2A**. When NCS was added to the mixture at 0 °C and –78 °C, and both reaction mixtures were warmed to room temperature (third step), respectively, under the same procedure and conditions, the yields of isoxazole **4A** were increased to 73% and 72%, together with oxime **2A** in 10% yield, respectively (entries 3 and 4).

Moreover, when the amounts of CH_2Cl_2 and DMF were increased to 2.0 and 0.2 mL using 1.2 and 1.5 equiv of NCS under the same procedure and conditions, the yields of isoxazole **4A** were increased to 78 and 88%, respectively (Table 1, entries 5 and 6 in entries 3–6). Thus, entry 6 summarizes the best result. When a gram-scale experiment with 8.0 mmol of *p*-methylbenzyl alcohol **1A** was carried out under the same procedure and conditions as those detailed in entry 6, isoxazole **4A** was obtained in 86% yield, as shown in Scheme 2.

On the other hand, when NBS and NIS instead of NCS were used in the third reaction step under the same procedure and conditions, no isoxazole **4A** was obtained (Table 1, entries 7 and 8, respectively). Thus, NCS played an important role in the formation of isoxazole **4A**.[11]

Based on those results, various benzylic alcohols (1.0 mmol), such as *m*-methylbenzyl alcohol (**1B**), *o*-methylbenzyl alcohol (**1C**), *p*-methoxybenzyl alcohol (**1D**), benzyl alcohol (**1E**), *p*-(methoxycarbonyl)benzyl alcohol (**1F**), *p*-chlorobenzyl alcohol (**1G**), *p*-phenylbenzyl alcohol (**1H**), and 1-naphthalenemethanol (**1I**), were treated with DIB (1.1 equiv) in the presence of TEMPO (0.1 equiv) in CH_2Cl_2 (2.0 mL) at room temperature for 0.5–2.0 h (first step), and then with $NH_2OH{\cdot}H_2O$ (1.5 equiv) and K_2CO_3 (0.75 equiv) at room temperature for 18 h to form oxime **2** (second step). The mixtures were then treated with NCS (1.5 equiv) in the presence of DMF (0.2 mL) at 0 °C for 1 h, and then warmed to room temperature for 3 h (third step). The mixtures were further treated with diethyl acetylenedicarboxylate (1.5 equiv) and Et_3N (1.5 equiv) at room temperature for 1 h (fourth step) to form diethyl 3-arylisoxazole-4,5-dicarboxylates **4B–I** in good yields, respectively, as shown in Scheme 2. Aliphatic primary alcohols, such as 3-phenylpropanol (**1J**), 4-phenylbutanol (**1K**), 1-octanol (**1L**), cyclopentanemethanol (**1M**), and 1-adamantanemethanol (**1N**), were also smoothly transformed into the corresponding 3-alkylisoxazole-4,5-dicarboxylates **4J–M** in good yields, respectively, and into diethyl 3-(1′-adamantyl)isoxazole-4,5-dicarboxylate (**4N**) in moderate yield, under the same procedure and conditions. Moreover, primary alcohols bearing an olefinic group, such as cinnamyl alcohol **1O** and 5-hexen-1-ol **1P**, could be successfully converted into the corresponding 3-alkenylisoxazoles **4O** and **4P** in good yields,



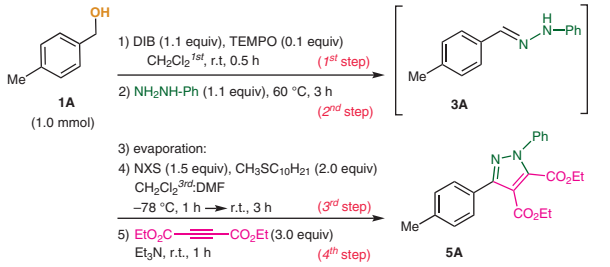
Scheme 2 Transformation of primary alcohols **1** into isoxazoles **4**. [a] Substrate **1A** (8.0 mmol) was used. [b] NH_2OH (2.0 equiv) and K_2CO_3 (1.0 equiv) were added at second step of the reaction. [c] Reaction was carried out at 0 °C for 10 h at third step of the reaction and at 0 °C for 16 h at fourth step of the reaction. [d] After evaporation, CH_2Cl_2 (2.0 mL) and DMF (0.2 mL) were added at the third step of the reaction. [e] Reaction time at the fourth step of the reaction was 3 h. [f] 1-Octyne (10.0 equiv) was added at the fourth step of the reaction.

keeping their olefinic groups. Other alkynes, such as dimethyl acetylenedicarboxylate, ethyl propiolate, phenylacetylene, and 1-octyne, instead of diethyl acetylenedicarboxylate could be also used under the same procedure and conditions to form 3-(*p*-methylphenyl)isoxazole derivatives **4Q–T** in good to moderate yields, respectively, together with regioisomer **4R′** in 15% yield using ethyl propiolate.

The one-pot preparation of 1-phenyl-3-arylpyrazoles was then studied. The optimum reaction conditions for the preparation of diethyl 3-(*p*-methylphenyl)-1-phenylpyrazole-4,5-dicarboxylate (**5A**) from *p*-methylbenzyl alcohol (**1A**) were studied. *p*-Methylbenzyl alcohol (**1A**; 1.0 mmol) was treated with DIB (1.1 equiv) in the presence of TEMPO (0.1 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 0.5 h (first step), and then with NH_2NHPh (1.1 equiv) at 60 °C for 3 h to form hydrazone **3A** (second step). After the second reaction step, the mixture was treated with NCS (1.5 equiv) and dodecyl methyl sulfide (2.0 equiv) in CH_2Cl_2 (4.0 mL) and DMF (0.5 mL) at –78 °C for 1 h and then warmed to room temperature for 3 h to form hydrazonyl chloride (third step),[12] a precursor of nitrilimine. The mixture was further treated with diethyl acetylenedicarboxylate (3.0 equiv) and Et_3N (3.0 equiv) at room temperature for 1 h (fourth step) to form diethyl 3-(*p*-methylphenyl)-1-phenylpyrazole-4,5-dicarboxylate (**5A**) in 48% yield, as shown in Table 2 (entry 1). When the solvent was removed after the second reaction step, and the residue was treated in CH_2Cl_2 (5.0 mL) without or with DMF (0.5 mL) in the third reaction step under the same procedure and conditions, pyrazole **5A** was generated in 72% and 82% yields, respectively (entries 2 and 3). Thus, the removal of the solvent after the second reaction step and the addition of DMF in the third reaction step are important to promote the formation of hydrazonyl chloride and, therefore, to improve the yield of pyrazole **5A**. After optimizing the experimental conditions by changing the amounts of CH_2Cl_2 and Et_3N, it was found that the addition of CH_2Cl_2 (5.0 mL) in the third reaction step and Et_3N (1.5 equiv) in the fourth reaction step was best, giving pyrazole **5A** in 82% yield (entry 5). When dodecyl methyl sulfide was not used in the third reaction step under the same procedure and conditions as those summarized in entry 5, the yield of pyrazole **5A** decreased to 50% (entry 6). When a gram-scale experiment with 8.0 mmol of *p*-methylbenzyl alcohol **1A** was carried out under the same procedure and conditions as those of entry 5, pyrazole **5A** was obtained in 83% yield, as shown in Scheme 3. When NBS and NIS instead of NCS were used in the third reaction step under the same procedure and conditions, pyrazole **5A** was not obtained at all (entries 7 and 8, respectively). Again, NCS played an important role in the formation of pyrazole **5A**.

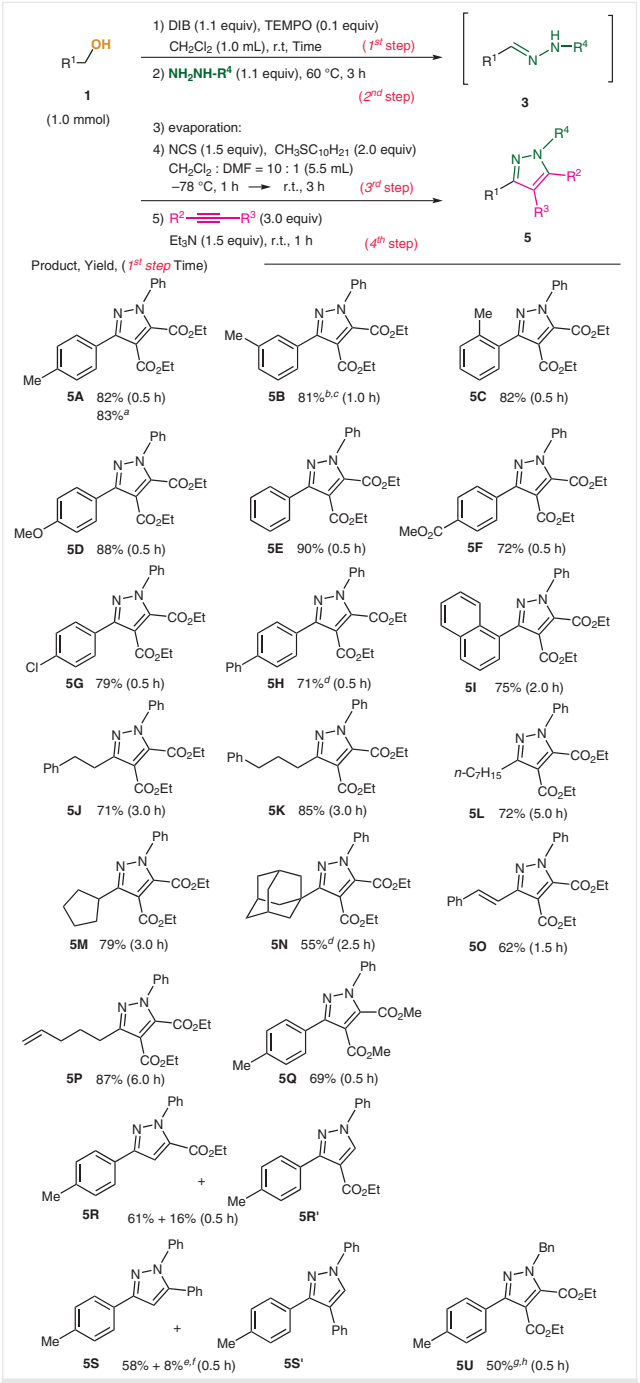
Based on those results, benzylic alcohols **1B–I** were treated with DIB (1.1 equiv) in the presence of TEMPO (0.1 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 0.5–2.0 h (first step), and then with NH_2NHPh (1.1 equiv) at 60 °C for 3 h to form hydrazones **3** (second step). After the removal of the solvent, CH_2Cl_2 (5.0 mL) and DMF (0.5 mL) were added to the residue, and the mixtures were treated with NCS (1.5 equiv) at –78 °C for 1 h, and then warmed to room temperature for 3 h (third step). The mixtures were then further treated with diethyl acetylenedicarboxylate (3.0 equiv) and Et_3N (1.5 equiv) at room temperature for 1 h (fourth step) to form diethyl 3-aryl-1-phenylpyrazole-4,5-dicarboxylates **5B–I** in good yields, respectively, as shown in Scheme 3. Aliphatic primary alcohols **1J–N** were also smoothly transformed into the corresponding diethyl 3-alkyl-1-phenylpyrazole-4,5-dicarboxylates **5J–M** in good yields, and into diethyl 3-(1′-adamantyl)-1-phenylpyrazole-4,5-dicarboxylate (**5N**) in moderate yield, under the same procedure and conditions. Furthermore, primary alcohols bearing an olefinic group, such as cinnamyl alcohol **1O** and 5-hexen-1-ol **1P**, could be also successfully transformed into the corresponding 3-alkenylpyrazoles **5O** and **5P** in good yields, keeping their olefinic groups. Other alkynes, such as dimethyl acetylenedicarboxylate, ethyl propiolate, and phenylacetylene, instead of diethyl acetylenedicarboxylate could be also used under the same procedure and conditions to form 3-(*p*-methylphenyl)-1-phenylpyrazole derivatives **5Q–S** in good to moderate yields, together with regioisomers **5R′** and **5S′** in 16% and 8% yields using ethyl propiolate and phenylacetylene, respectively. When benzylhydrazine was used instead of phenylhydrazine in the second reaction step under the same procedure and conditions, diethyl 1-benzyl-3-(*p*-methylphenyl)pyrazole-

Table 2 Transformation of 4-Methylbenzyl Alcohol **1A** into 3-(4′-Methylphenyl)pyrazole **5A**



Entry	CH_2Cl_2 1st (mL)	CH_2Cl_2 3rd/DMF (mL)	NXS	Et_3N (equiv)	Yield **5A** (%)
1[a]	1.0	4.0:0.5	NCS	3.0	48
2	1.0	5.0:0	NCS	3.0	72
3	1.0	5.0:0.5	NCS	3.0	82
4	1.0	4.0:0.5	NCS	3.0	76
5	**1.0**	**5.0:0.5**	**NCS**	**1.5**	**82**
6[b]	1.0	5.0:0.5	NCS	1.5	50
7	1.0	5.0:0.5	NBS	1.5	0
8	1.0	5.0:0.5	NIS	1.5	0

[a] After the second step of the reaction, solvent was not removed.
[b] Without CH_3-S-$C_{10}H_{21}$ in the third step of the reaction.

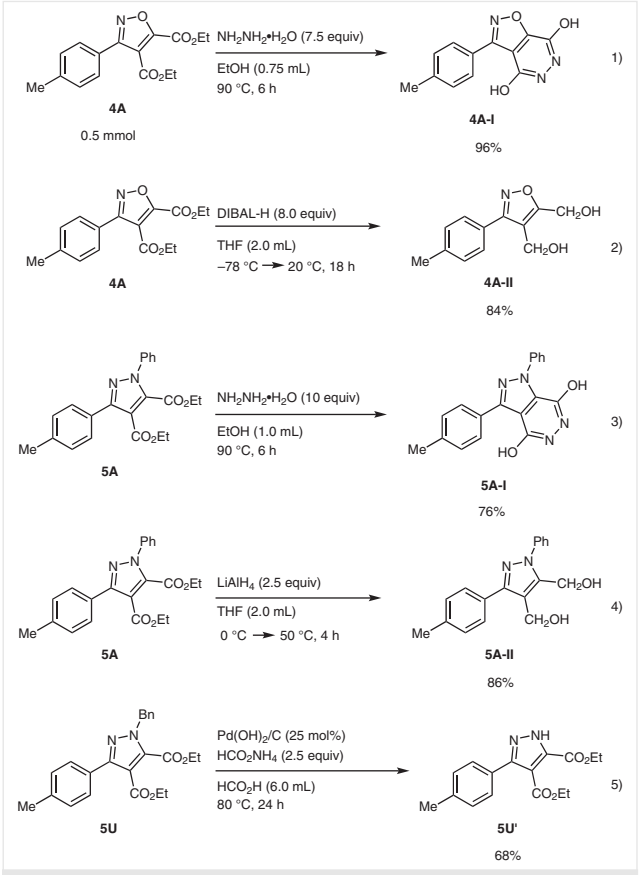


Scheme 3 Transformation of primary alcohols **1** into pyrazoles **5**.
[a] Substrate **1A** (8.0 mmol) was used. [b] NH_2NHPh (1.5 equiv) was added in the second step of the reaction. [c] Reaction was carried out at –78 °C for 1 h and at 0 °C for 12 h in the third step of the reaction, and at 0 °C for 24 h in the fourth step of the reaction. [d] CH_2Cl_2 (2.0 mL) was used as a solvent in the first step of the reaction. [e] Reaction time for the fourth step of the reaction was 3 h. [f] After evaporation, alkyne (15.0 equiv) was added. [g] $NH_2NHBn{\cdot}HCl$ (1.1 equiv) and Et_3N (1.1 equiv) were added instead of NH_2NHPh in the second step of the reaction. [h] After addition of Et_3N (1.5 equiv) at r.t., NaH (3.0 equiv) was added in the fourth step of the reaction.

4,5-dicarboxylate (**5U**) was obtained in 50% yield. However, when methylhydrazine and hydrazine were used instead of phenylhydrazine under the same procedure and conditions, diethyl 1-methyl-3-(*p*-methylphenyl)pyrazole-4,5-dicarboxylate and diethyl 3-(*p*-methylphenyl)pyrazole-4,5-dicarboxylate, respectively, were not formed at all.

Unfortunately, the present methods could not be applied to *N*-Boc-protected L-prolinol due to the occurrence of deprotection mediated by HCl formed with NCS in the third reaction step. Additionally, the standard treatment of 3-hydroxymethyl-1-methylindole, 3-(hydroxymethyl)benzothiophene, and 3-(hydroxymethyl)benzofuran gave the corresponding 3-heteroarylisoxazoles and -pyrazoles together with their monochlorination products at the 2-position of the heteroaryl groups by NCS, as mixtures in the range of 32–40% yields.

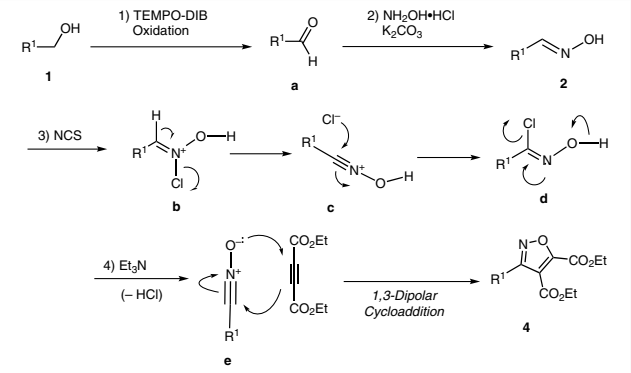
Once diethyl 3-arylisoxazole-4,5-dicarboxylates and diethyl 3-arylpyrazole-4,5-dicarboxylates were formed, they could be further transformed into other 3-arylisoxazole and 3-arylpyrazole derivatives. Thus, treatment of isoxazole derivative **4A** with hydrazine in ethanol at 90 °C for 6 h gave bicyclic pyridazine derivative **4A–I** in 96% yield, as shown in Scheme 4, Equation 1. Treatment of isoxazole derivative **4A** with DIBAL in THF at temperatures from –78 to 20 °C gave compound **4A–II** in 84% yield (Eq. 2).



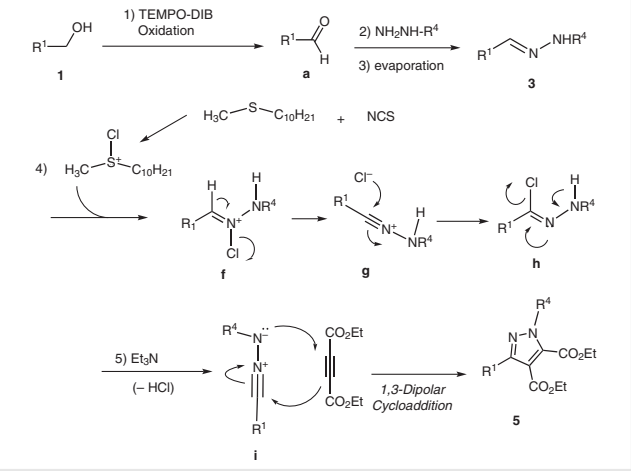
Scheme 4 Derivatization of isoxazole **4** and pyrazoles **5**

The reactions of pyrazole derivative **5A** with hydrazine in ethanol at 90 °C for 6 h, and with $LiAlH_4$ in THF at temperatures from 0 to 50 °C also gave pyridazine derivative **5A–I** and compound **5A–II** in 76 and 86% yields, respectively (Eq. 3 and 4). Debenzylation of pyrazole derivative **5U** with $Pd(OH)_2$ and HCO_2NH_4 in HCO_2H at 80 °C generated diethyl *N*-free pyrazole **5U′** in 68% yield (Eq. 5).

The reaction pathways for the preparation of 3-aryl- and 3-alkylisoxazoles and -pyrazoles from primary alcohols are shown in Scheme 5 and Scheme 6, respectively.



Scheme 5 Reaction pathway for isoxazoles



Scheme 6 Reaction pathway for pyrazoles

Primary alcohol **1** is smoothly oxidized to aldehyde **a**, and this further reacts with hydroxylamine to form oxime **2**. Oxime **2** reacts with NCS to form nitrile *N*-oxide **e** via the dehydrochlorination of hydroximoyl chloride **d**. Once nitrile *N*-oxide **e** is formed, it smoothly reacts with diethyl acetylenedicarboxylate via a 1,3-dipolar cycloaddition to form diethyl 3-aryl- and 3-alkylisoxazole-4,5-dicarboxylate **4**, as shown in Scheme 5. Similarly, formed aldehyde **a** reacts with hydrazine to give hydrazone **3**. The latter reacts with NCS in the presence of decyl methyl sulfide to form nitrilimine **i** through dehydrochlorination of hydrazonyl chloride **h**. Once nitrilimine **i** is formed, it reacts with diethyl acetylenedicarboxylate via a 1,3-dipolar cycloaddition to form diethyl 3-aryl- and 3-alkylpyrazole-4,5-dicarboxylate **5**, as shown in Scheme 6.

In conclusion, 3-aryl- and 3-alkylisoxazoles could be obtained efficiently from primary alcohols by successive treatment with DIB in the presence of TEMPO, hydroxylamine, and then NCS, followed by the reaction with alkynes in the presence of Et_3N. 3-Aryl- and 3-alkyl-1-phenylpyrazoles could be also obtained efficiently from primary alcohols by successive treatment with DIB in the presence of TEMPO, phenylhydrazine, and then NCS in the presence of decyl methyl sulfide, followed by reaction with alkynes in the presence of Et_3N. The chlorine atom derived from NCS plays an important role in the formation of 1,3-dipolar precursors, nitrile *N*-oxide and nitrilimine, from oximes and hydrazones, respectively. The present successive operations will be useful for the one-pot preparation of 3-aryl- and 3-alkylisoxazoles and -pyrazoles from readily available primary alcohols.

^1H NMR spectra were measured with 400 MHz spectrometers. Chemical shifts were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sext = sextet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured with 100 MHz spectrometers. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard ($CDCl_3$ at δ = 77.0 ppm, or DMSO-d_6 at δ = 39.5 ppm). Characteristic peaks in the infrared (IR) spectra are given in wavenumber (cm^{-1}). High-resolution mass spectra (HRMS) were recorded with Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Melting points are uncorrected. Thin-layer chromatography (TLC) was performed using 0.25 mm silica gel plates (60F254). The products were purified by column chromatography on neutral silica gel 60N (63–200 mesh).

Transformation of Primary Alcohols 1 into Diethyl 3-Aryl- or 3-Alkylisoxazole-4,5-dicarboxylates 4; Typical Procedure

DIB (354.0 mg, 1.1 mmol) was added to a solution of *p*-methylbenzyl alcohol **1A** (122.2 mg, 1.0 mmol) and TEMPO (15.6 mg, 0.1 mmol) in CH_2Cl_2 (2.0 mL). The mixture was stirred at r.t. under Ar atmosphere. After 30 min, $NH_2OH{\cdot}HCl$ (104.2 mg, 1.5 mmol) and K_2CO_3 (103.7 mg, 0.75 mmol) were added and the obtained mixture was stirred for 18 h at r.t. Then, DMF (0.2 mL) and NCS (200.1 mg, 1.5 mmol) were added to the solution at 0 °C. After 1 h, the reaction mixture was stirred for 3 h at r.t., then Et_3N (209.1 μL, 1.5 mmol) and diethyl acetylenedicarboxylate (238.5 μL, 1.5 mmol) were added to the solution and the obtained mixture was stirred for 1 h at r.t. The mixture was quenched with sat. aq. $NaHCO_3$ and extracted with $CHCl_3$ (3 × 10.0 mL), and the organic layer was dried over Na_2SO_4. After removal of the solvent, purification by short column chromatography on silica gel (hexane/EtOAc, 8:1) gave diethyl 3-(*p*-methylphenyl)isoxazole-4,5-dicarboxylate **4A** (266.9 mg, 88%).

Diethyl 3-(*p*-Methylphenyl)isoxazole-4,5-dicarboxylate (4A)

Yield: 266.9 mg (88%); white solid; mp 45–46 °C (44–46 °C).[9g,h]

IR (neat): 2923, 1737, 1447, 1274, 826 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.0 Hz, 3 H), 1.43 (t, *J* = 7.0 Hz, 3 H), 2.41 (s, 3 H), 4.38 (q, *J* = 7.0 Hz, 2 H), 4.47 (q, *J* = 7.0 Hz, 2 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 7.60 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 13.7, 21.1, 62.1, 62.6, 115.9, 123.9, 127.7 (2C), 129.3 (2C), 140.7, 155.9, 159.1, 160.1, 161.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}O_5N$: 304.1179; found: 304.1176.

Diethyl 3-(*m*-Methylphenyl)isoxazole-4,5-dicarboxylate (4B)

Yield: 212.3 mg (70%); colorless oil.

IR (neat): 2984, 1734, 1445, 1304, 1069 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.2 Hz, 3 H), 1.43 (t, *J* = 7.2 Hz, 3 H), 2.41 (s, 3 H), 4.38 (q, *J* = 7.0 Hz, 2 H), 4.47 (q, *J* = 7.0 Hz, 2 H), 7.31 (d, *J* = 7.4 Hz, 1 H), 7.36 (t, *J* = 7.4 Hz, 1 H), 7.48 (d, *J* = 7.4 Hz, 1 H), 7.53 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 21.3, 62.3, 62.8, 116.2, 125.2, 126.9, 128.7, 128.7, 131.4, 138.6, 156.1, 159.3, 161.2, 161.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}O_5N$: 304.1179; found: 304.1177.

Diethyl 3-(*o*-Methylphenyl)isoxazole-4,5-dicarboxylate (4C)

Yield: 279.0 mg (92%); colorless oil.

IR (neat): 2984, 1733, 1463, 1304, 1065, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.2 Hz, 3 H), 1.44 (t, *J* = 7.2 Hz, 3 H), 2.28 (s, 3 H), 4.2 (q, *J* = 7.2 Hz, 2 H), 4.50 (q, *J* = 7.2 Hz, 2 H), 7.24–7.31 (m, 3 H), 7.38 (dt, *J* = 8.2, 1.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 14.0, 19.9, 61.8, 62.9, 116.4, 125.6, 126.6, 129.6, 130.0, 130.3, 137.3, 156.3, 160.0, 160.3, 162.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}O_5N$: 304.1179; found: 304.1178.

Diethyl 3-(*p*-Methoxyphenyl)isoxazole-4,5-dicarboxylate (4D)

Yield: 287.4 mg (90%); yellow oil.

IR (neat): 2985, 1610, 1455, 1254, 1066, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, 3 H, *J* = 7.3 Hz), 1.43 (t, 3 H, *J* = 7.3 Hz), 3.86 (s, 3 H), 4.38 (q, 2 H, *J* = 7.3 Hz), 4.47 (q, 2 H, *J* = 7.3 Hz), 6.98 (d, 2 H, *J* = 8.8 Hz), 7.66 (d, 2 H, *J* = 8.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 55.3, 62.4, 62.8, 114.2 (2C), 115.9, 119.2, 129.6 (2C), 156.1, 159.2, 160.7, 161.4, 161.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}O_6N$: 320.1129; found: 320.1127.

Diethyl 3-Phenylisoxazole-4,5-dicarboxylate (4E)

Yield: 234.3 mg (81%); colorless oil.

IR (neat): 2985, 1733, 1443, 1302, 1273, 1066, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.3 Hz, 3 H), 1.43 (t, *J* = 7.3 Hz, 3 H), 4.37 (q, *J* = 7.3 Hz, 2 H), 4.48 (q, *J* = 7.3 Hz, 2 H), 7.45–7.53 (m, 3 H), 7.69–7.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.0, 62.4, 62.8, 116.1, 127.0, 128.1 (2C), 128.8 (2C), 130.5, 156.0, 159.3, 161.1, 161.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{16}O_5N$: 290.1023; found: 290.1019.

Diethyl 3-[*p*-(Methoxycarbonyl)phenyl]isoxazole-4,5-dicarboxylate (4F)

Yield: 277.9 mg (80%); colorless oil.

IR (neat): 2985, 1724, 1436, 1250, 1273, 1065, 720 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.3 Hz, 3 H), 1.44 (t, *J* = 7.3 Hz, 3 H), 3.96 (s, 3 H), 4.38 (q, *J* = 7.3 Hz, 2 H), 4.49 (q, *J* = 7.3 Hz, 2 H), 7.79 (d, *J* = 8.4 Hz, 2 H), 8.14 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.0, 52.4, 62.5, 63.0, 116.0, 128.3 (2C), 129.9 (2C), 131.2, 132.0, 156.0, 160.0, 160.5, 161.0, 166.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}O_7N$: 348.1077; found: 348.1078.

Diethyl 3-(*p*-Chlorophenyl)isoxazole-4,5-dicarboxylate (4G)

Yield: 275.2 mg (85%); yellow oil.

IR (neat): 2985, 1732, 1272, 1065, 731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.2 Hz, 3 H), 1.43 (t, *J* = 7.2 Hz, 3 H), 4.38 (q, *J* = 7.2 Hz, 2 H), 4.48 (q, *J* = 7.2 Hz, 2 H), 7.46 (d, *J* = 8.5 Hz, 2 H), 7.66 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.0, 62.5, 62.9, 115.7, 125.4, 129.1 (2C), 129.5 (2C), 136.9, 156.0, 159.9, 160.2, 161.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}O_5NCl$: 324.0633; found: 324.0628.

Diethyl 3-(*p*-Biphenyl)isoxazole-4,5-dicarboxylate (4H)

Yield: 292.3 mg (80%); white solid; mp 79–80 °C (78–79 °C).[9g,h]

IR (neat): 2965, 1726, 1283, 1070, 733, 510 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, *J* = 7.0 Hz, 3 H), 1.44 (t, *J* = 7.0 Hz, 3 H), 4.41 (q, *J* = 7.0 Hz, 2 H), 4.49 (q, *J* = 7.0 Hz, 2 H), 7.40 (t, *J* = 7.3 Hz, 1 H), 7.48 (t, *J* = 7.0 Hz, 2 H), 7.63 (d, *J* = 7.3 Hz, 2 H), 7.70 (d, *J* = 8.4 Hz, 2 H), 7.80 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 62.5, 62.9, 125.8, 127.1 (2C), 127.5 (2C), 127.9, 128.6 (2C), 128.9 (2C), 140.0, 143.4, 156.1, 159.5, 160.9, 161.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}O_5N$: 366.1336; found: 366.1335.

Diethyl 3-(Naphthalen-1′-yl)isoxazole-4,5-dicarboxylate (4I)

Yield: 285.1 mg (84%); colorless oil.

IR (neat): 2983, 1732, 1300, 1095, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.3 Hz, 3 H), 1.46 (t, *J* = 7.3 Hz, 3 H), 4.04 (q, *J* = 7.3 Hz, 2 H), 4.53 (q, *J* = 7.3 Hz, 2 H), 7.48–7.57 (m, 3 H), 7.61 (d, *J* = 7.7 Hz, 1 H), 7.79 (d, *J* = 7.7 Hz, 1 H), 7.92 (d, *J* = 7.7 Hz, 1 H), 7.99 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 14.0, 61.8, 63.0, 117.2, 124.5, 124.8, 124.9, 126.3, 127.0, 128.2, 128.4, 130.6, 133.4, 133.3, 156.3, 160.1, 160.2, 161.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}O_5N$: 340.1179; found: 340.1177.

Diethyl 2-(Phenethyl)isoxazole-4,5-dicarboxylate (4J)

Yield: 209.5 mg (66%); colorless oil.

IR (neat): 2983, 1726, 1269, 1196, 1098, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.3 Hz, 3 H), 1.42 (t, *J* = 7.3 Hz, 3 H), 3.00–3.04 (m, 2 H), 3.16–3.20 (m, 2 H), 4.35 (q, *J* = 7.3 Hz, 2 H), 4.46 (q, *J* = 7.3 Hz, 2 H), 7.20–7.24 (m, 3 H), 7.28–7.32 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.95, 14.00, 27.4, 33.9, 61.8, 62.9, 113.9, 126.3, 128.4 (2C), 128.5 (2C), 140.3, 156.8, 160.5, 161.2, 162.7.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}O_5N$: 318.1335; found: 318.1336.

Diethyl 3-(3′-Phenylpropyl)isoxazole-4,5-dicarboxylate (4K)

Yield: 235.3 mg (71%); colorless oil.

IR (neat): 2983, 1728, 1269, 1196, 1098, 1030, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.3 Hz, 3 H), 1.41 (t, *J* = 7.3 Hz, 3 H), 2.04 (quint, *J* = 7.3 Hz, 2 H), 2.71 (t, *J* = 7.3 Hz, 2 H), 2.90 (t, *J* = 7.3 Hz, 2 H), 4.33 (q, *J* = 7.3 Hz, 2 H), 4.45 (q, *J* = 7.3 Hz, 2 H), 7.18–7.21 (m, 3 H), 7.29 (q, *J* = 7.5 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (2C), 25.0, 29.2, 35.2, 61.7, 62.9, 114.0, 126.0, 128.4 (2C), 128.5 (2C), 141.3, 156.9, 160.6, 161.1, 163.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}O_5N$: 332.1492; found: 332.1490.

Diethyl 3-(Heptyl)isoxazole-4,5-dicarboxylate (4L)

Yield: 227.3 mg (73%); yellow oil.

IR (neat): 2930, 1730, 1467, 1272, 1196, 1097, 1196, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.5 Hz, 3 H), 1.26–1.40 (m, 8 H), 1.37 (t, *J* = 7.3 Hz, 3 H), 1.41 (t, *J* = 7.3 Hz, 3 H), 1.69 (quint, *J* = 7.5 Hz, 2 H), 2.85 (t, *J* = 7.5 Hz, 2 H), 4.36 (q, *J* = 7.3 Hz, 2 H), 4.45 (q, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (3C), 22.6, 25.4, 27.7, 28.8, 29.1, 31.6, 61.7, 62.9, 114.0, 156.9, 160.7, 161.0, 163.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{26}O_5N$: 312.1805; found: 312.1801.

Diethyl 3-(Cyclopentyl)isoxazole-4,5-dicarboxylate (4M)

Yield: 194.1 mg (69%); colorless oil.

IR (neat): 2963, 1730, 1267, 1098 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.3 Hz, 3 H), 1.41 (t, *J* = 7.3 Hz, 3 H), 1.62–1.73 (m, 2 H), 1.73–1.89 (m, 4 H), 2.02–2.11 (m, 2 H), 3.39 (quint, *J* = 7.7 Hz, 1 H), 4.36 (q, *J* = 7.3 Hz, 2 H), 4.44 (q, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (2C), 25.3 (2C), 31.2 (2C), 36.7, 61.7, 62.7, 114.4, 156.8, 160.6, 161.0, 166.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}O_5N$: 282.1336; found: 282.1333.

Diethyl 3-(Adamantan-1′-yl)isoxazole-4,5-dicarboxylate (4N)

Yield: 180.7 mg (52%); white solid; mp 42–45 °C.

IR (neat): 2922, 2854, 1724, 1289, 1097, 1059, 848 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.3 Hz, 3 H), 1.39 (t, *J* = 7.3 Hz, 3 H), 1.73–1.80 (m, 6 H), 2.05–2.07 (m, 9 H), 4.40 (q, *J* = 7.3 Hz, 2 H), 4.41 (q, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 28.0 (3C), 35.7, 36.3 (3C), 40.2 (3C), 62.3, 62.5, 116.4, 156.3, 158.4, 162.8, 168.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{26}O_5N$: 348.1806; found: 348.1805.

Diethyl (*E*)-3-(Styryl)isoxazole-4,5-dicarboxylate (4O)

Yield: 268.1 mg (85%); yellow oil.

IR (neat): 2984, 1728, 1274, 1101, 752 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, *J* = 7.0 Hz, 3 H), 1.43 (t, *J* = 7.0 Hz, 3 H), 4.42 (q, *J* = 7.0 Hz, 2 H), 4.48 (q, *J* = 7.0 Hz, 2 H), 7.19 (d, *J* = 14.6 Hz, 1 H), 7.33–7.42 (m, 3 H), 7.55 (d, *J* = 6.5 Hz, 2 H), 7.58 (d, *J* = 14.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (2C), 62.0, 63.0, 112.8, 113.9, 127.4 (2C), 128.8 (2C), 129.4, 135.5, 137.6, 156.6, 159.4, 160.8, 160.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}O_5N$: 316.1179; found: 316.1179.

Diethyl 3-(4′-Penten-1′-yl)isoxazole-4,5-dicarboxylate (4P)

Yield: 182.9 mg (65%); yellow oil.

IR (neat): 3469, 2983, 1728, 1269, 1197, 1098, 1031 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.0 Hz, 3 H), 1.42 (t, *J* = 7.0 Hz, 3 H), 1.81 (quint, *J* = 7.7 Hz, 2 H), 2.15 (q, *J* = 7.7 Hz, 2 H), 2.87 (t, *J* = 7.7 Hz, 2 H), 4.36 (q, *J* = 7.0 Hz, 2 H), 4.46 (q, *J* = 7.0 Hz, 2 H), 4.99–5.08 (m, 2 H), 5.76–5.86 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (2C), 24.9, 26.8, 33.1, 61.7, 62.9, 114.0, 115.4, 137.5, 156.9, 160.6, 161.1, 163.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}O_5N$: 282.1336; found: 282.1334.

Dimethyl 3-(*p*-Methylphenyl)isoxazole-4,5-dicarboxylate (4Q)

Yield: 220.2 mg (80%); white solid; mp 66–68 °C.

IR (neat): 2959, 1731, 1448, 1280, 1218, 1068, 820, 806 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 3.91 (s, 3 H), 4.02 (s, 3 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 7.58 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 53.1, 53.3, 116.0, 123.9, 128.0 (2C), 129.6 (2C), 141.0, 156.5, 159.1, 161.2, 161.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{14}O_5N$: 276.0866; found: 276.0863.

Ethyl 3-(*p*-Methylphenyl)isoxazole-5-carboxylate (4R)[9g,9h,13]

Yield: 138.8 mg (60%); white solid; mp 46–48 °C.

IR (neat): 2980, 1729, 1445, 1278, 821, 509 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, *J* = 7.0 Hz, 3 H), 2.41 (s, 3 H), 4.46 (q, *J* = 7.3 Hz, 2 H), 7.23 (s, 1 H), 7.29 (d, *J* = 8.2 Hz, 2 H), 7.73 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.4, 62.3, 107.3, 125.1, 126.7 (2C), 129.7 (2C), 140.8, 156.9, 160.7, 162.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}O_5$: 232.0968; found: 232.0969.

3-(*p*-Methylphenyl)-5-phenylisoxazole (4S)[9g,9h]

Yield: 176.5 mg (75%); white solid; mp 125–128 °C.

IR (neat): 2915, 1445, 813, 761, 688, 528 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 6.81 (s, 1 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.43–7.52 (m, 3 H), 7.77 (d, *J* = 8.0 Hz, 2 H), 7.84 (d, *J* = 6.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 97.4, 125.8 (2C), 126.3, 126.7 (2C), 127.5, 129.0 (2C), 129.6 (2C), 130.1, 140.1, 162.9, 170.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}ON$: 236.1070; found: 236.1070.

5-Hexyl-3-(*p*-methylphenyl)isoxazole (4T)

Yield: 146.1 mg (60%); yellow oil.

IR (neat): 3122, 2958, 2918, 1601, 1430, 911, 813, 723 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.3 Hz, 3 H), 1.30–1.44 (m, 6 H), 1.74 (quint, *J* = 7.3 Hz, 2 H), 2.40 (s, 3 H), 2.78 (t, *J* = 7.3 Hz, 2 H), 6.25 (s, 3 H), 7.25 (d, *J* = 8.2 Hz, 2 H), 7.68 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.3 (2C), 22.5, 26.7, 27.5, 28.7, 31.4, 98.6, 126.6 (2C), 129.5 (2C), 139.8, 162.2, 174.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{22}ON$: 244.1696; found: 244.1694.

Transformation of Primary Alcohols 1 into 3-Aryl- and 3-Alkyl-1-phenylpyrazole-4,5-dicarboxylates 5; Typical Procedure

DIB (354.0 mg, 1.1 mmol) was added to a solution of *p*-methylbenzyl alcohol **1A** (122.2 mg, 1.0 mmol) and TEMPO (15.6 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL). The mixture was stirred at r.t. under Ar atomosphere. After 30 min, phenylhydrazine (108.1 μL, 1.1 mmol) was added and the obtained mixture was stirred at 60 °C for 3 h. After removal of the solvent under reduced pressure, CH_2Cl_2 (5.0 mL), DMF (0.5 mL), decyl methyl sulfide (445.9 μL, 2.0 mmol), and NCS (200.1 mg, 1.5 mmol) were added at –78 °C. After being stirred for 1 h, the reaction mixture was stirred at r.t. for 3 h, then Et_3N (209.1 μL, 1.5 mmol) and diethyl acetylenedicarboxylate (477.0 μL, 3.0 mmol) were added to the solution and the obtained mixture was stirred for 1 h at r.t. The reaction was quenched with sat. aq. $NaHCO_3$ and extracted with $CHCl_3$ (3 × 10.0 mL), and the organic layer was dried over Na_2SO_4. After removal of the solvent, purification by short column chromatography on silica gel (hexane/EtOAc, 8:1) gave diethyl 3-(*p*-methylphenyl)-1-phenylpyrazole-4,5-dicarboxylate **5A** (310.3 mg, 82%).

Diethyl 3-(*p*-Methylphenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5A)

Yield: 310.3 mg (82%); yellow solid; mp 50–53 °C (210–212 °C).[13]

IR (neat): 2982, 1714, 1498, 1231, 1111, 757, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.3 Hz, 3 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 2.39 (s, 3 H), 4.30 (q, *J* = 7.3 Hz, 4 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 7.42–7.50 (m, 3 H), 7.52–7.55 (m, 2 H), 7.65 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.0, 21.3, 61.1, 62.4, 114.2, 124.8 (2C), 128.5, 128.7 (2C), 128.8 (2C), 129.0, 129.1 (2C), 136.9, 138.7, 139.2, 152.0, 160.2, 163.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{23}O_4N_2$: 379.1652; found: 379.1649.

Diethyl 3-(*m*-Methylphenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5B)

Yield: 306.5 mg (81%); yellow oil.

IR (neat): 2983, 1727, 1498, 1221, 752 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.3 Hz, 3 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 2.40 (s, 3 H), 4.31 (q, *J* = 7.3 Hz, 4 H), 7.22 (d, *J* = 8.2 Hz, 1 H), 7.31 (t, *J* = 7.7 Hz, 1 H), 7.43–7.57 (m, 7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 13.9, 21.4, 61.1, 62.3, 114.4, 124.8 (2C), 125.9, 128.0, 129.0, 129.1 (2C), 129.3, 129.6, 131.2, 136.8, 137.7, 139.1, 151.9, 160.1, 163.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{23}O_4N_2$: 379.1652; found: 379.1652.

Diethyl 3-(*o*-Methylphenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5C)

Yield: 310.3 mg (82%); yellow solid; mp 75–77 °C.

IR (neat): 2984, 1726, 1498, 1259, 1223, 756 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.0 Hz, 3 H), 1.27 (t, *J* = 7.0 Hz, 3 H), 2.30 (s, 3 H), 4.16 (q, *J* = 7.0 Hz, 2 H), 4.36 (q, *J* = 7.0 Hz, 2 H), 7.19–7.27 (m, 2 H), 7.30 (d, *J* = 6.8 Hz, 1 H), 7.33 (t, *J* = 6.8 Hz, 1 H), 7.41–7.50 (m, 3 H), 7.57 (d, *J* = 6.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7 (2C), 20.1, 60.6, 62.6, 114.5, 124.0 (2C), 125.1 (2C), 128.7, 128.8, 129.2, 129.7 (2C), 130.2, 131.5, 137.3, 138.9, 153.0, 160.9, 162.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{23}O_4N_2$: 379.1652; found: 379.1652.

Diethyl 3-(*p*-Methoxyphenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5D)

Yield: 347.1 mg (88%); white solid; mp 78–80 °C.

IR (neat): 2979, 1729, 1715, 1498, 1234, 1111, 845, 763 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.0 Hz, 3 H), 1.29 (t, *J* = 7.0 Hz, 3 H), 3.85 (s, 3 H), 4.30 (q, *J* = 7.3 Hz, 4 H), 6.96 (d, *J* = 8.4 Hz, 2 H), 7.42–7.55 (m, 5 H), 7.72 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.0, 55.3, 61.1, 62.4, 113.5 (2C), 113.8, 123.9, 124.7 (2C), 129.0, 129.1 (2C), 130.2 (2C), 137.1, 139.1, 151.8, 160.1, 160.3, 163.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{23}O_5N_2$: 395.1601; found: 395.1601.

Diethyl 1,3-Diphenyl-(1*H*)-pyrazole-4,5-dicarboxylate (5E)

Yield: 328.0 mg (90%); yellow solid; mp 51–54 °C (52–53 °C).[13]

IR (neat): 2987, 1717, 1497, 1262, 1230, 762, 630 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 4.30 (q, *J* = 7.2 Hz, 2 H), 4.31 (q, *J* = 7.2 Hz, 2 H), 7.38–7.56 (m, 8 H), 7.73–7.77 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 13.9, 61.1, 62.4, 114.2, 124.7 (2C), 128.0 (2C), 128.8 (2C), 129.0, 129.1 (2C), 131.4, 137.0, 139.1 (2C), 151.9, 160.1, 162.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{21}O_4N_2$: 395.1495; found: 395.1495.

Diethyl 3-[*p*-(Methoxycarbonyl)phenyl]-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5F)

Yield: 304.2 mg (72%); yellow solid; mp 90–92 °C.

IR (neat): 2989, 1721, 1267, 1229, 1100, 760, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 3.94 (s, 3 H), 4.31 (q, *J* = 7.2 Hz, 2 H), 4.32 (q, *J* = 7.2 Hz, 2 H), 7.45–7.56 (m, 5 H), 7.85 (d, *J* = 8.3 Hz, 2 H), 8.10 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.0, 52.2, 61.3, 62.5, 114.5, 124.7 (2C), 128.8 (2C), 129.2 (3C), 129.4 (2C), 130.2, 135.9, 137.4, 139.0, 150.8, 160.0, 162.7, 166.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{23}O_6N_2$: 423.1550; found: 423.1548.

Diethyl 3-(*p*-Chlorophenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5G)

Yield: 315.1 mg (79%); red solid; mp 85–88 °C.

IR (neat): 2984, 1733, 1703, 1497, 1265, 1230, 1177, 762 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.3 Hz, 3 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 4.30 (q, *J* = 7.3 Hz, 2 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 7.40 (d, *J* = 8.6 Hz, 2 H), 7.44–7.55 (m, 5 H), 7.72 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.0, 61.2, 62.5, 113.9, 124.6 (2C), 128.3 (2C), 129.1 (2C), 129.9, 130.2 (2C), 134.9, 137.5, 138.9 (2C), 150.9, 160.1, 162.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}ClO_4N_2$: 399.1105; found: 399.1104.

Diethyl 3-(*p*-Biphenyl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5H)

Yield: 312.8 mg (71%); yellow oil.

IR (neat): 2982, 1728, 1262, 1224, 753, 731, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.0 Hz, 3 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 4.32 (q, *J* = 7.0 Hz, 2 H), 4.33 (q, *J* = 7.0 Hz, 2 H), 7.36 (dt, *J* = 8.2, 1.4 Hz, 1 H), 7.44–7.52 (m, 5 H), 7.54–7.57 (m, 2 H), 7.64 (d, *J* = 8.2 Hz, 2 H), 7.66 (d, *J* = 8.2 Hz, 2 H),7.86 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.0, 61.2, 62.4, 114.2, 124.7 (2C), 126.8 (2C), 127.1 (2C), 127.4, 128.7 (2C), 129.0, 129.1 (2C), 129.2 (2C), 130.3, 137.1, 139.1, 140.6, 141.5, 151.6, 160.1, 162.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{25}O_4N_2$: 441.1810; found: 441.1807.

Diethyl 3-(Naphthalen-1′-yl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5I)

Yield: 310.9 mg (75%); red oil.

IR (neat): 2984, 1731, 1217, 1095, 909, 752, 731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.3 Hz, 3 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 3.98 (q, *J* = 7.3 Hz, 2 H), 4.39 (q, *J* = 7.3 Hz, 2 H), 7.43–7.55 (m, 6 H), 7.60–7.64 (m, 3 H), 7.85–7.93 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 13.8, 60.6, 62.7, 115.7, 124.2 (2C), 124.9, 125.7 (2C), 126.2, 128.1 (2C), 129.0, 129.2 (3C), 129.6, 132.3, 133.4, 137.5, 139.0, 151.8, 160.7, 162.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{23}O_4N_2$: 415.1653; found: 415.1650.

Diethyl 2-Phenethyl-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5J)

Yield: 278.6 mg (71%); yellow oil.

IR (neat): 2981, 1713, 1503, 1249, 1224, 1159, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.0 Hz, 3 H), 1.35 (t, *J* = 7.0 Hz, 3 H), 3.04 (t, *J* = 7.9 Hz, 2 H), 3.24 (t, *J* = 7.9 Hz, 3 H), 4.31 (q, *J* = 7.0 Hz, 2 H), 4.33 (q, *J* = 7.0 Hz, 2 H), 7.19–7.24 (m, 1 H), 7.28–7.31 (m, 4 H), 7.40–7.50 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.2, 29.8, 35.3, 60.6, 62.6, 112.7, 123.9 (2C), 125.9, 128.3 (2C), 128.5 (2C), 128.8, 129.3 (2C), 138.1, 138.9, 141.7, 154.3, 161.2, 162.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{25}O_4N_2$: 393.1809; found: 393.1807.

Diethyl 1-Phenyl-3-(3′-phenylpropyl)-(1*H*)-pyrazole-4,5-dicarboxylate (5K)

Yield: 345.5 mg (85%); yellow oil.

IR (neat): 2981, 1714, 1504, 1249, 1220, 1095, 755, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.0 Hz, 3 H), 1.32 (t, *J* = 7.0 Hz, 3 H), 2.07 (quint, *J* = 7.7 Hz, 2 H), 2.74 (t, *J* = 7.7 Hz, 2 H), 2.98 (t, *J* = 7.7 Hz, 3 H), 4.29 (q, *J* = 7.0 Hz, 2 H), 4.31 (q, *J* = 7.0 Hz, 2 H), 7.15–7.23 (m, 3 H), 7.27 (t, *J* = 5.9 Hz, 2 H), 7.38–7.50 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.2, 27.3, 30.6, 35.7, 60.5, 62.5, 112.7, 123.9 (2C), 125.7, 128.2 (2C), 128.5 (2C), 128.7, 129.2 (2C), 138.0, 138.9, 142.1, 154.8, 161.3, 162.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{27}O_4N_2$: 407.1966; found: 407.1964.

Diethyl 3-Heptyl-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5L)

Yield: 278.3 mg (72%); yellow oil.

IR (neat): 2927, 2856, 1716, 1219, 1092 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.3 Hz, 3 H), 1.23 (t, *J* = 7.3 Hz, 3 H), 1.26–1.44 (m, 11 H), 1.72 (quint, *J* = 7.9 Hz, 2 H), 2.91 (t, *J* = 7.9 Hz, 2 H), 4.30 (q, *J* = 7.3 Hz, 2 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 7.38–7.50 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.1, 14.2, 22.6, 27.6, 29.1, 29.2, 29.5, 31.8, 60.5, 62.5, 112.7, 123.9 (2C), 128.7, 129.2 (2C), 137.9, 139.0, 155.4, 161.3, 162.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{31}O_4N_2$: 387.2279; found: 387.2275.

Diethyl 3-Cyclopentyl-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5M)

Yield: 281.6 mg (79%); yellow oil.

IR (neat): 2959, 1715, 1504, 1219, 1095, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.3 Hz, 3 H), 1.34 (t, *J* = 7.3 Hz, 3 H), 1.65–1.73 (m, 2 H), 1.76–1.93 (m, 4 H), 2.04–2.12 (m, 2 H), 3.60 (quint, *J* = 8.6 Hz, 1 H), 4.30 (q, *J* = 7.3 Hz, 2 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 7.37–7.50 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.1, 25.4 (2C), 32.1, 38.0 (2C), 60.4, 62.4, 112.7, 123.9 (2C), 128.5, 129.1 (2C), 137.8, 139.1, 158.2, 161.4, 162.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{25}O_4N_2$: 357.1809; found: 357.1807.

Diethyl 3-(Adamantan-1′-yl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5N)

Yield: 232.4 mg (55%); white solid; mp 58–60 °C.

IR (neat): 2903, 2850, 1724, 1503, 1221, 1098, 757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.3 Hz, 3 H), 1.37 (t, *J* = 7.3 Hz, 3 H), 1.74–1.81 (m, 6 H), 2.06 (m, 3 H), 2.13–2.14 (m, 6 H), 4.23 (q, *J* = 7.3 Hz, 2 H), 4.35 (q, *J* = 7.3 Hz, 2 H), 7.38–7.45 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.1, 28.5 (3C), 35.8, 36.7 (3C), 40.7 (3C), 61.2, 61.9, 114.8, 125.0 (2C), 128.6, 128.9 (2C), 135.9, 139.5, 159.6, 160.1, 164.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{31}O_4N_2$: 423.2279; found: 4223.2278.

Diethyl (*E*)-(1*H*)-1-Phenyl-3-styrylpyrazole-4,5-dicarboxylate (5O)

Yield: 242.1 mg (62%); red oil.

IR (neat): 2981, 1714, 1499, 1217, 1096, 750, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.0 Hz, 3 H), 1.39 (t, *J* = 7.0 Hz, 3 H), 4.31 (q, *J* = 7.0 Hz, 2 H), 4.37 (q, *J* = 7.0 Hz, 2 H), 7.30 (d, *J* = 7.3 Hz, 1 H), 7.36 (t, *J* = 7.3 Hz, 2 H), 7.43–7.51 (m, 3 H), 7.55–7.58 (m, 4 H), 7.63 (d, *J* = 15.0 Hz, 1 H), 7.59 (d, *J* = 15.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.2, 60.8, 62.6, 112.7, 117.2, 124.2 (2C), 127.0 (2C), 128.2, 128.6 (2C), 129.1, 129.3 (2C), 133.0, 136.8, 138.2, 139.0, 150.3, 160.9, 162.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{23}O_4N_2$: 391.1653; found: 391.1652.

Diethyl 3-(4′-Penten-1′-yl)-(1*H*)-1-phenylpyrazole-4,5-dicarboxylate (5P)

Yield: 310.1 mg (87%); red oil.

IR (neat): 2981, 1715, 1504, 1220, 1094, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.3 Hz, 3 H), 1.34 (t, *J* = 7.3 Hz, 3 H), 1.83 (quint, *J* = 7.7 Hz, 2 H), 2.18 (q, *J* = 6.6 Hz, 2 H), 2.94 (t, *J* = 7.7 Hz, 2 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 4.98 (ddd, *J* = 17.0, 2.0, 1.6 Hz, 1 H), 5.05 (ddd, *J* = 17.0, 2.0, 1.6 Hz, 1 H), 5.81–5.91 (m, 1 H), 7.38–7.52 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.2, 27.1, 28.3, 33.6, 60.5, 62.6, 112.7, 114.8, 123.9 (2C), 128.7, 129.2 (2C), 138.0, 138.4, 138.9, 155.0, 161.3, 162.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{25}O_4N_2$: 357.1809; found: 357.1807.

Dimethyl (1*H*)-1-Phenyl-3-(*p*-methylphenyl)pyrazole-4,5-dicarboxylate (5Q)

Yield: 241.8 mg (69%); white solid; mp 78–80 °C (65–67 °C).[14]

IR (neat): 2951, 1729, 1499, 1263, 1228, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.83 (s, 3 H), 3.86 (s, 3 H), 7.24 (d, *J* = 8.2 Hz, 2 H), 7.43–7.55 (m, 5 H), 7.65 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 52.1, 53.1, 53.4, 114.0, 124.5 (2C), 128.4, 128.6 (2C), 128.9, 129.0, 129.1 (2C), 136.7, 138.8, 139.0, 151.9, 160.6, 163.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{19}O_4N_2$: 351.1340; found: 351.1339.

Ethyl (1*H*)-1-Phenyl-3-(*p*-methylphenylpyrazole-5-carboxylate (5R)

Yield: 186.9 mg (61%); orange solid; mp 62–64 °C.

IR (neat): 2982, 1726, 1230, 1103, 762 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.3 Hz, 3 H), 2.38 (s, 3 H), 4.26 (q, *J* = 7.3 Hz, 2 H), 7.23 (d, *J* = 8.2 Hz, 2 H), 7.26 (s, 1 H), 7.42–7.52 (m, 5 H), 7.77 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.3, 61.1, 109.2, 125.7 (2C), 126.1 (2C), 128.5 (2C), 128.6, 129.3, 129.4 (2C), 134.5, 138.2, 140.4, 151.5, 159.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{19}O_2N_2$: 307.1440; found: 307.1438.

(1*H*)-1,5-Diphenyl-3-(*p*-methylphenyl)pyrazole (5S)[15,16]

Yield: 180.0 mg (58%); orange solid; mp 122–124 °C (126–128 °C)[16a,16c]

IR (neat): 1499, 1485, 816, 758, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 6.80 (s, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 7.28–7.39 (m, 10 H), 7.82 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 105.0, 125.3 (2C), 125.7 (2C), 127.3, 128.2, 128.4 (2C), 128.7 (2C), 128.9 (2C), 129.3 (2C), 130.2, 130.6, 137.7, 140.1, 144.2, 152.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}N_2$: 311.1543; found: 311.1540.

Diethyl (1*H*)-1-Benzyl-3-(*p*-methylphenyl)pyrazole-4,5-dicarboxylate (5U)

Yield: 196.3 mg (50%); orange oil.

IR (neat): 2982, 1720, 1242, 1091, 725 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.3 Hz, 3 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 2.38 (s, 3 H), 4.29 (q, *J* = 7.3 Hz, 2 H), 4.30 (q, *J* = 7.3 Hz, 2 H), 5.69 (s, 2 H), 7.21 (d, *J* = 8.2 Hz, 2 H), 7.26–7.33 (m, 5 H), 7.60 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 21.3, 55.2, 61.4, 61.8, 115.8, 127.7 (2C), 127.8 (2C), 127.9, 128.6 (2C), 128.8, 129.1 (2C), 133.1, 136.1, 138.5, 149.3, 159.3, 164.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{25}O_4N_2$: 393.1809; found: 393.1807.

Preparation of 3′-(*p*-Methylphenyl)isoxazolo[4′,5′-*d*]pyridazine-3,6-diol (4A-I)

Hydrazine monohydrate (187.8 μL, 7.5 mmol) was added to a solution of **4A** (151.6 mg, 0.5 mmol) in EtOH (0.75 mL). The mixture was stirred for 6 h at 90 °C, then filtration of the reaction mixture gave 3′-(*p*-methylphenyl)isoxazolo[4′,5%-d]pyridazine-3,6-diol **4A-I** (120.4 mg, 99%).

3′-(*p*-Methylphenyl)isoxazolo[4′,5′-*d*]pyridazine-3,6-diol (4A-I)

White solid; mp 245–255 °C.

IR (neat): 3168 (br), 2587 (br), 1577, 1104, 820 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ {tautomeric isomer 6%} = {2.32 (s, 3 H)}, 2.38 (s, 3 H), {7.13 (d, *J* = 8.2 Hz, 2 H)}, 7.33 (d, *J* = 8.2 Hz, 2 H), {8.02 (d, *J* = 8.2 Hz, 2 H)}, 8.36 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.1, 112.2, 124.7, 129.0 (2C), 129.1 (2C), 140.3, 151.8, 156.7, 159.2, 164.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{10}O_3N_3$: 243.0717; found: 243.0717.

Preparation of 4,5-Di(hydroxymethyl)-3-(*p*-methylphenyl)isoxazole (4A-II)

To a solution of **4A** (151.6 mg, 0.5 mmol) in THF (2.0 mL) was added DIBAL-H (3.88 mL, 4.0 mmol) at –78 °C, and the resulting mixture was stirred at 20 °C for 18 h. The reaction was quenched with ice and then sat. aq. NH_4Cl. The obtained mixture was filtered and washed with EtOAc, and the filtrate was extracted with EtOAc (3 × 10.0 mL). The organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent, purification by short column chromatography on silica gel (hexane/EtOAc, 1:3) gave 4,5-di(hydroxymethyl)-3-(*p*-methylphenyl)isoxazole **4A-II** (92.1 mg, 84%).

4,5-Di(hydroxymethyl)-3-(*p*-methylphenyl)isoxazole (4A-II)

Yield: 92.1 mg (84%); white solid; mp 99–101 °C.

IR (neat): 3221 (br), 2356, 1428, 998, 675 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 2.72 (br t, *J* = 5.7 Hz, 1 H), 3.32 (br t, *J* = 5.7 Hz, 1 H), 4.66 (d, *J* = 5.7 Hz, 2 H), 4.84 (d, *J* = 5.7 Hz, 2 H), 7.28 (d, *J* = 8.2 Hz, 2 H), 7.57 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 54.0, 55.7, 114.7, 125.5, 128.2 (2C), 129.6 (2C), 140.1, 162.3, 169.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}O_3N$: 220.0968; found: 220.0968.

Preparation of 3-(*p*-Methylphenyl)-(1*H*)-1-phenylpyrazolo[4,5-*d*]pyridazine-3,6-diol (5A-I)

Hydrazine monohydrate (250.6 μL, 10.0 mmol) was added to a solution of **5A** (189.2 mg, 0.5 mmol) in EtOH (0.75 mL) and the mixture was stirred at 90 °C for 6 h. Filtration of the reaction mixture gave 3-(*p*-methylphenyl)-(1*H*)-1-phenylpyrazolo[4,5-d]pyridazine-3,6-diol **5A-I** (120.97 mg, 76%).

3′-(*p*-Methylphenyl)-(1′*H*)-1′-phenylpyrazolo[4,5-*d*]pyridazine-3,6-diol (5A-I)

Yield: 121.0 mg (76%); white solid; mp >300 °C.

IR (neat): 3187 (br), 2359 (br), 1456, 1331, 770, 708 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H), 7.24 (d, *J* = 8.2 Hz, 2 H), 7.38–7.48 (m, 3 H), 7.64 (d, *J* = 7.0 Hz, 2 H), 8.32 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.0, 114.6, 126.4 (2C), 127.7, 127.8 (2C), 128.6 (2C), 128.8 (2C), 129.1, 136.6, 137.8, 139.5, 148.5, 151.6, 156.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}O_2N_4$: 319.1190; found: 319.1187.

4,5-Di(hydroxymethyl)-3-(*p*-methylphenyl)-(1*H*)-1-phenylpyrazole (5A-II)

To a solution of **5A** (189.2 mg, 0.5 mmol) in THF (2.0 mL) was added $LiAlH_4$ (47.5 mg, 1.25 mmol) at 0 °C and the resulting mixture was stirred at 50 °C for 4 h. The reaction was quenched with ice and then sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3 × 10.0 mL) and the organic layer was washed with brine and dried over Na_2SO_4. Purification by short column chromatography on silica gel (hexane/EtOAc, 1:3) gave 4,5-di(hydroxymethyl)-3-(*p*-methylphenyl)-(1*H*)-1-phenylpyrazole **5A-II** (125.8 mg, 86%).

4,5-Di(hydroxymethyl)-3-(*p*-methylphenyl)-(1*H*)-1-phenylpyrazole (5A-II)

Yield: 126.6 mg (86%); white solid; mp 155–157 °C.

IR (neat): 3269 (br), 2366, 1500, 1013, 1000, 764 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (br, 1 H), 2.40 (s, 3 H), 2.96 (br, 1 H), 4.72 (br d, *J* = 5.0 Hz, 2 H), 4.84 (br d, *J* = 2.5 Hz, 2 H), 7.26 (d, *J* = 7.9 Hz, 2 H), 7.41 (t, *J* = 7.3 Hz, 1 H), 7.50 (t, *J* = 7.3 Hz, 2 H), 7.58 (d, *J* = 7.9 Hz, 2 H), 7.63 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 54.4, 55.7, 118.3, 124.9 (2C), 128.1 (3C), 129.3 (4C), 129.8, 138.0, 139.1, 142.0, 151.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{19}O_2N_2$: 295.1441; found: 295.1438.

Preparation of Diethyl 3-(*p*-Methylphenyl)-1*H*-pyrazole-4,5-dicarboxylate (5U′)

To a solution of **5U** (189.2 mg, 0.5 mmol) in formic acid (5.0 mL) were added HCO_2NH_4 (78.8 mg, 1.25 mmol) and $Pd(OH)_2$ on carbon (87.0 mg, 20 wt%) and the resulting mixture was stirred at 80 °C for 24 h. After filtration through Celite, the filtrate was concentrated. The residue was dissolved in EtOAc and the obtained mixture was washed with aqueous $NaHCO_3$, water, and brine, and the organic layer was dried over Na_2SO_4. After removal of the solvent, purification by short column chromatography on silica gel (hexane/EtOAc, 4:1) gave diethyl 3-phenyl-1*H*-pyrazole-4,5-dicarboxylate **5U′** (104.3 mg, 68%).

Diethyl 3-(*p*-Methylphenyl)-1*H*-pyrazole-4,5-dicarboxylate 5U′

Yield: 102.8 mg (68%); white solid; mp 81–83 °C.

IR (neat): 2980 (br), 1720, 1291, 1069 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.3 Hz, 3 H), 1.41 (t, *J* = 7.3 Hz, 3 H), 2.40 (s, 3 H), 4.31 (q, *J* = 7.3 Hz, 2 H), 4.42 (q, *J* = 7.3 Hz, 2 H), 7.26 (d, *J* = 8.2 Hz, 2 H), 7.51 (d, *J* = 8.2 Hz, 2 H), 10.47 (br, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (2C), 21.3, 61.3, 61.4, 112.9, 125.4, 127.84 (2C), 127.94, 128.6, 129.3 (2C), 139.5, 160.9, 163.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{19}O_4N_2$: 303.1339; found: 303.1336.

Funding Information

Financial support in the form of a Grant-in-Aid for Scientific Research (No. 15K05418) from the Ministry of Education, Culture, Sports, Science, and Technology in Japan is acknowledged.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690102.

References

(1) Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K. *Comprehensive Heterocyclic Chemistry III*; Elsevier: Amsterdam, **2008**.

(2) Isoxazoles: (a) Giomi, D.; Cordero, F. M.; Machetti, F. *Five-Membered Rings with Two Heteroatoms, each with their Fused Carbocyclic Derivatives*, In *Comprehensive Heterocyclic Chemistry III, Vol. 4*; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Ed.; Elsevier: Amsterdam, **2008**, Chap. 4.03, 365–485. Reviews for isoxazoles: (b) Morita, T.; Yagandar, S.; Fuse, S.; Nakamura, H. *Tetrahedron Lett.* **2018**, *59*, 1159. (c) Sysak, A.; Obminska-Mrukowicz, B. *Eur. J. Med. Chem.* **2017**, *137*, 292. Papers: (d) Ormrod, D.; Wellington, K.; Wagstaff, A. J. *Drugs* **2002**, *62*, 2059. (e) Matheson, A. J.; Figgitt, D. R. *Drugs* **2001**, *61*, 833. (f) Nunno, L. D.; Vitale, P.; Scilimati, A.; Tacconelli, S.; Partrignani, P. *J. Med. Chem.* **2004**, *47*, 4881.

(3) Pyrazoles: (a) Yet, L. *Five-Membered Rings with Two Heteroatoms, each with their Fused Carbocyclic Derivatives*, In *Comprehensive Heterocyclic Chemistry III, Vol. 4*; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Ed.; Elsevier: Amsterdam, **2008**, Chap. 6.01, 1–141. Review for pyrazoles: (b) Faria, J. V.; Vegi, P. F.; Miguita, A. G. C.; dos Santos, M. S.; Boechat, N.; Bernardino, A. M. R. *Bioorg. Med. Chem.* **2017**, *25*, 5891. (c) Fustero, S.; Sánchez-Roselló, M.; Barrio, P.; Simón-Fuentes, A. *Chem. Rev.* **2011**, *111*, 6984. (d) Makino, K.; Kim, H. S.; Kurasawa, Y. *J. Heterocycl. Chem.* **1998**, *35*, 489.

(4) (a) Zhao, G.; Liang, L.; Wen, C. H. E.; Tong, R. *Org. Lett.* **2019**, *21*, 315. (b) Gao, F.; Fang, Z.; Su, R.; Rui, P.; Hu, X. *Org. Biomol. Chem.* **2018**, *16*, 9211. (c) Chalyk, B. A.; Sosedko, A. S.; Volochnyuk, D. M.; Tolmachev, A. A.; Gavrilenko, K. S.; Liashuk, O. S.; Grygorenko, O. O. *Org. Biomol. Chem.* **2018**, *16*, 9152. (d) Khutorianskyi, A.; Chalyk, B.; Borysko, P.; Kondratiuk, A.;

Mykhailiuk, P. K. *Eur. J. Org. Chem.* **2017**, 3935. (e) Chalyk, B. A.; Kandaurova, I. Y.; Hrebeniuk, K. V.; Manoilenko, O. V.; Bulik, I. B.; Iminov, R. T.; Kubyshkin, V.; Tverdokhlebov, A. V.; Abilialimov, O. K.; Mykhaliliuk, P. K. *RSC Adv.* **2016**, *6*, 25713. (f) Zhou, X.; Xu, X.; Shi, Z.; Liu, K.; Gao, H.; Li, W. *Org. Biomol. Chem.* **2016**, *14*, 5246. (g) Poh, J.; Garcia-Ruiz, C.; Zúniga, A.; Meroni, F.; Blakemore, D. C.; Browne, D. L.; Ley, S. V. *Org. Biomol. Chem.* **2016**, *14*, 5983. (h) Singhal, A.; Parumala, S. K. R.; Sharma, A.; Peddinti, R. K. *Tetrahedron Lett.* **2016**, *57*, 719. (i) Yoshimura, A.; Middleton, K. R.; Todora, A. D.; Kastern, B. J.; Koshi, S. R.; Maskaev, A. V.; Zhdankin, V. V. *Org. Lett.* **2013**, *15*, 4010.

(5) (a) Liu, X.; Hong, D.; She, Z.; Hersh, W. H.; Yoo, B.; Chen, Y. *Tetrahedron* **2018**, *74*, 6593. (b) Li, J.; Hu, M.; Li, C.; Li, C.; Li, J.; Wu, W.; Jiang, H. *Adv. Synth. Catal.* **2018**, *360*, 2707. (c) Zhang, X.; Hu, W.; Chen, S.; Hu, X. *Org. Lett.* **2018**, *20*, 860. (d) Sau, P.; Santra, S. K.; Rakshit, A.; Patel, B. K. *J. Org. Chem.* **2017**, *82*, 6358. (e) Sun, Y.; Abdukader, A.; Zhang, H.; Yang, W.; Liu, C. *RSC Adv.* **2017**, *7*, 55786. (f) Tu, K. N.; Hirner, J. J.; Blum, S. A. *Org. Lett.* **2016**, *18*, 480.

(6) Kumar, G. R.; Kumar, Y. K.; Reddy, M. S. *Chem. Commun.* **2016**, *52*, 6589.

(7) (a) Tu, K. N.; Kim, S.; Blum, S. A. *Org. Lett.* **2019**, *21*, 1283. (b) Meng, Y.; Zhang, T.; Gong, X.; Zhang, M.; Zhu, C. *Tetrahedron Lett.* **2019**, *60*, 171. (c) Everson, N.; Yniguez, K.; Loop, L.; Lazaro, H.; Belanger, B.; Koch, G.; Bach, J.; Manjunath, A.; Schioldager, R.; Law, J.; Grabenauer, M.; Eagon, S. *Tetrahedron Lett.* **2019**, *60*, 72. (d) Muzalevskiy, V. M.; Nenajdenko, V. G. *Org. Biomol. Chem.* **2018**, *16*, 7935. (e) Topchiy, M. A.; Zharkova, D. A.; Asachenko, A. F.; Muzalevskiy, V. M.; Chertkov, V. A.; Nenajdenko, V. G.; Nechaev, M. S. *Eur. J. Org. Chem.* **2018**, 3750. (f) de Aqino, T. F. B.; Seidel, J. P.; de Oliveira, D. H.; do Nascimento, J. E. R.; Alves, D.; Perin, G.; Lenardao, E. J.; Schumacher, R. F.; Jacob, R. G. *Tetrahedron Lett.* **2018**, *59*, 4090. (g) Wang, H.; Sun, X.; Zhang, S.; Liu, G.; Wang, C.; Zhu, L.; Zhang, H. *Synlett* **2018**, *29*, 2689. (h) Kirkham, J. D.; Edeson, S. J.; Stokes, S.; Harrity, J. P. A. *Org. Lett.* **2012**, *14*, 5354.

(8) (a) Raj, J. P.; Gangaprasad, D.; Karthikeyan, K.; Rengasamy, R.; Kesavan, M.; Venkateswarulu, M.; Vajjiravel, M.; Elangovan, J. *Tetrahedron Lett.* **2018**, *59*, 4462. (b) Nair, D.; Pavashe, P.; Katiyar, S.; Namboothiri, I. N. N. *Tetrahedron Lett.* **2016**, *57*, 3146. (c) Liu, K.; Shang, X.; Cheng, Y.; Chang, X.; Li, P.; Li, W. *Org. Biomol. Chem.* **2018**, *16*, 7811. (d) Cheng, J.; Li, W.; Duan, Y.; Cheng, Y.; Yu, S.; Zhu, C. *Org. Lett.* **2017**, *19*, 214.

(9) (a) Harigae, R.; Moriyama, K.; Togo, H. *J. Org. Chem.* **2014**, *79*, 2049. (b) Imai, S.; Kikui, H.; Moriyama, K.; Togo, H. *Tetrahedron* **2015**, *71*, 5267. (c) Sasaki, T.; Miyagi, K.; Moriyama, K.; Togo, H. *Org. Lett.* **2016**, *18*, 944. (d) Imai, T.; Harigae, R.; Moriyama, K.; Togo, H. *J. Org. Chem.* **2016**, *81*, 3975. (e) Sasaki, T.; Moriyama, K.; Togo, H. *J. Org. Chem.* **2017**, *82*, 11727. (f) Sasaki, T.; Moriyama, K.; Togo, H. *Beilstein J. Org. Chem.* **2018**, *14*, 345. (g) Imai, T.; Togo, H. *Eur. J. Org. Chem.* **2018**, 1377. (h) Kobayashi, E.; Togo, H. *Tetrahedron* **2018**, *74*, 4226. (i) Yamamoto, T.; Togo, H. *Eur. J. Org. Chem.* **2018**, 4187.

(10) TEMPO-DIB: (a) De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974. (b) Pozzi, G.; Quici, S.; Shepperson, I. *Tetrahedron Lett.* **2002**, *43*, 6141. (c) TEMPO-polymer-supported DIB: Sakuratani, K.; Togo, H. *Synthesis* **2003**, 21. (d) TEMPO-ion-supported DIB: Suzuki, Y.; Iinuma, M.; Moriyama, K.; Togo, H. *Synlett* **2012**, *23*, 1250.

(11) Preparation of isoxazolines with oximes, alkenes, and NCS: Tran, N. C.; Dhondt, H.; Flipo, M.; Deprez, B.; Willand, N. *Tetrahedron Lett.* **2015**, *56*, 4119.

(12) Preparation of hydrazonyl chlorides with hydrazones and NCS in CH_2Cl_2: Patel, H. K.; Vyas, K. A.; Pandey, S. P.; Fernandes, P. S. *Tetrahedron* **1996**, *52*, 661.

(13) Mohammed, S.; Vishwakarma, R. A.; Bharate, S. B. *RSC Adv.* **2015**, *5*, 3470.

(14) Yavari, I.; Moradi, L. *Helv. Chim. Acta* **2010**, *93*, 277.

(15) (a) Arbaciauskiene, E.; Vilkauskaite, G.; Eller, G. A.; Holzer, W.; Sackus, A. *Tetrahedron* **2009**, *65*, 7817. (b) Vanier, C.; Wagner, A.; Mioskowski, C. *J. Comb. Chem.* **2004**, *6*, 846.

(16) (a) Landge, S. M.; Schmidt, A. *Synlett* **2007**, 1600. (b) Shi, C.; Ma, C.; Ma, H.; Zhou, X.; Cao, J.; Fan, Y.; Huang, G. *Tetrahedron* **2016**, *72*, 4055. (c) Sathishkannan, G.; Tamilarasan, V. J.; Srinivasan, K. *Org. Biomol. Chem.* **2017**, *15*, 1400.