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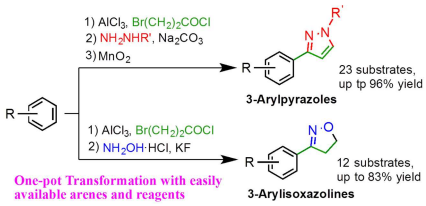

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Transformation of Arenes into 3-Arylpyrazoles and 3-Arylisoxazolines with β-Bromopropionyl Chloride, Hydrazine, and Hydroxylamine

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Abstract—Successive treatment of arenes with β-bromopropionyl chloride and $AlCl_3$, followed by the reactions with hydrazines and Na_2CO_3, and then with MnO_2 gave the corresponding 3-arylpyrazoles in one pot in good to moderate yields. The same successive treatment of arenes with β-bromopropionyl chloride and $AlCl_3$, followed by the reactions with hydroxylamine and KF gave the corresponding 3-arylisoxazolines in one pot in good to moderate yields.

1. Introduction

Nitrogen-containing heterocycles are very attractive in view of medicinal chemistry because some of them show potent biological activities. Among them, pyrazole and isoxazolines are one of the most important nitrogen-containing heterocycles.[1,2] For example, Celecoxib and Lonazolac which are 3-arylpyrazoles, are anti-inflammatory drugs[1a] and dibenzo[b,f]azepine-tethered isoxazoline is a potent anticancer agent,[2] as shown in Fig. 1.

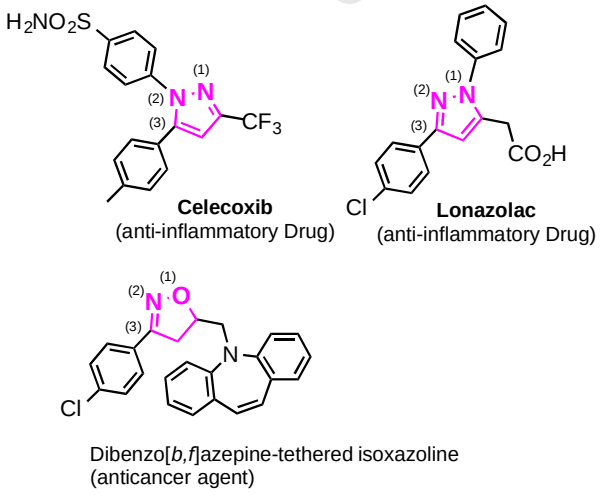


Fig. 1 Typical Pharmaceuticals Bearing 3-Arylpyrazole unit and 3-Arylisoxazoline Unit

Extensive synthetic studies of the pyrazole unit[1d, 1f] and the isoxazoline unit[2] have been carried out. Recent synthetic studies of pyrazoles are as follows:[3] the $Cu(NO_3)_2$-catalyzed preparation of 1-arylpyrazoles with arylhydrazines and 1,3-diketones using conventional condensation;[3a] the CuBr-catalyzed preparation of 1,3,5-triaryl-4-(selenophenyl)pyrazoles with phenylhydrazines, chalcones, and PhSeSePh;[3b] the I_2-mediated preparation of 3,5-diarylpyrazoles with *p*-toluenesulfonyl hydrazide and chalcones;[3c] the microwave-irradiated preparation of 5-amino-1,3-diarylpyrazoles with arylhydrazines and 3-aminocrotonitrile;[3d] the AgOTf-catalyzed preparation of 1,5-diaryl-3-(trifluoromethyl)pyrazoles with arylhydrazines and α,β-alkynyl trifluoromethyl ketones;[3e] the blue LED-irradiated preparation of 3-arylpyrazoles with ethynylarenes and hydrazine in the presence of CuI and $Ru(bpy)_3Cl_2$;[3f] the I_2-mediated preparation of 4-iodo-3-trifluoromethyl-1,5-diarylpyrazoles with *N*–arylhydrazones of α,β-alkynyl trifluoromethyl ketones;[3g] the PhSeSePh-mediated preparation of 1,3,5-triaryl-4-(selenophenyl)pyrazoles with α,β-alkynyl-*N*-arylhydrazones and Oxone®;[3h] the $Cu(OTf)_2$-catalyzed preparation of 4-aminoborated 3-aryl-1-tosylpyrazoles with α,β-alkynyl-*N*-tosyl-hydrazones;[3i] the preparation of 2,5-di(alkoxycarbonyl)-pyrazoles with acrylate esters, α-diazoesters, and Oxone®;[3j] and the Et_3N-promoted preparation of 4-(aminocarbonyl)-1,3-diarylpyrazoles with β-ketoamides and hydrazonyl chlorides.[3k] As unique synthetic methods, the Ag_2CO_3- and $Mo(CO)_6$-catalyzed preparation of 3-arylpyrazoles with [*N*-(isocyano)imino]triphenyl-phosphorane and ethynylarenes[3l,3m] and the CuCl-catalyzed preparation of 3-arylpyrazoles bearing a CN or a CO_2Et group at 4 position with *N,N*-dialkylhydrazones and

trichloroacetonitrile or ethyl trichloroacetate[3n] were also reported.

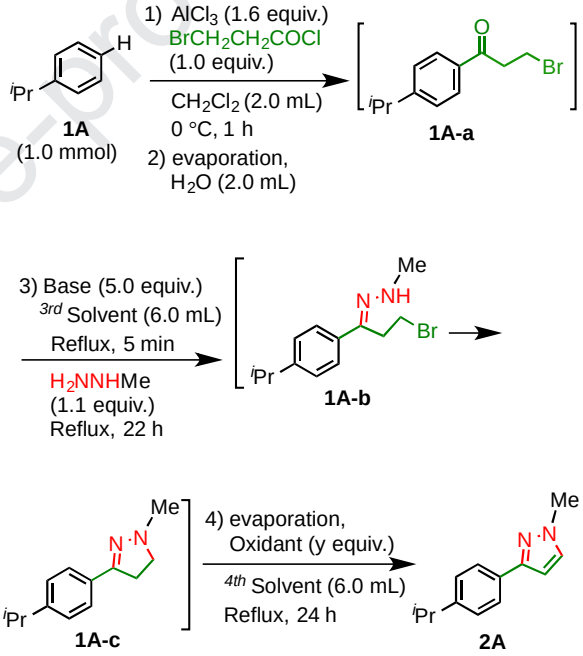
On the other hand, isoxazolines are commonly prepared from nitrile *N*-oxides and alkenes via a 1,3-dipolar cycloaddition reaction. Recent synthetic studies of isoxazolines are as follows:[4] the preparation of 3-arylisoxazolines with aldoximes, terminal alkenes, and Oxone® in the presence of KI,[4a] 3,5-$Me_2C_6H_3I$,[4b] KCl,[4c] or NaCl,[4d] and the $Ru(bpy)_3Cl_2$-catalyzed preparation of 3-phenylisoxazolines with phenyl α-*N*-(hydroxyl)imino acid, terminal alkenes, and Oxone® under irradiation with blue LED.[4e] As cyclization methods of allylic oximes, the oxidative cyclization of 2-arylphenylisonitriles, ^{t}BuOOH, and ^{n}Bu$_4$NI into 3-arylisoxazolines bearing (phenanthridine-6'-yl)methyl group at 5-position,[4f] the TEMPO-mediated cyclization to generate 3-arylisoxazolines,[4g] the Au(Ph_3P)Cl-catalyzed cyclization to produce 3-arylisoxazolines,[4h] the oxidative cyclization into 3-arylisoxazolines using $PhI(OAc)_2$,[4i] and the *fac*-Ir$(ppy)_3$-catalyzed cyclization of 2-(difluoromethanesulfonyl)benzothiazole to give 3-aryl-5-(2',2'-difluoroethyl)isoxazolines under irradiation with blue LED[4j] were reported. As unique methods for the preparation of isoxazolines, the preparation of 5-aroyl-3-arylisoxazolines with aryl α-bromomethyl ketone oximes, aroylmethyl(dimethyl)sulfonium salts, and Na_2CO_3;[4k] the preparation of 3-aryl- and 3-alkylisoxazolines with ketones, ethynylarenes, and ^{t}BuOK, followed by the reaction with NH_2OH, and then KOH;[4l] the preparation of 5-arylisoxazolines with methylarenes and *t*-butyl acrylate in the presence of $Pd(OAc)_2$ and $AgNO_3$;[4m] the preparation of 5-arylisoxazolines bearing an ester group at 3-position with vinylarenes, α-diazoacetate esters, and ^{t}BuONO in the presence of $Cu(OAc)_2$;[4n] the preparation of 3-aroyl-5-arylisoxazolines with vinylarenes and ^{t}BuONO in the presence of $Sc(OTf)_3$;[4o] and the preparation of 3,5-diarylisoxazolines with *N*-(hydroxy)arylmethanesulfonamides, vinylarenes, ^{n}Bu$_4$NIO$_4$, and I_2[4p] were also reported.

However, to the best of our knowledge, the intermolecular C-C bond constructing one-pot preparation of 3-arylpyrazoles and 3-arylisoxazolines from arenes has been scarcely studied. Here, as part of our synthetic studies of the efficient preparation of heteroaromatics from arenes,[5] we would like to report a simple one-pot preparation of 3-arylpyrazoles and 3-arylisoxazolines by the Friedel-Crafts acylation of arenes with β-bromopropionyl chloride and $AlCl_3$, followed by the reaction with hydrazine and hydroxylamine, and finally the *5-exo-tet* cyclization with a base, respectively.

2. Results and Discussion

First, treatment of cumene (**1A**, 1.0 mmol) with β-bromopropionyl chloride (1.0 mmol) and $AlCl_3$ (1.6 equiv.) in dichloromethane (2.0 mL) at 0 °C for 1 h gave the corresponding ketone **1A-a** in good yield. After evaporation of the solvent, water (2.0 mL) was added to the residue and then bases (5.0 equiv.), such as KF, K_2CO_3, and Na_2CO_3, and methanol (6.0 mL) were added, and the obtained mixture was refluxed for 5 min to neutralize acidic species. Then, methylhydrazine (1.1 equiv.) was added and the obtained mixture was refluxed for 22 h to form methylhydrazone **1A-b** first and then pyrazoline **1A-c**. After removal of the solvent, pyrazoline **1A-c** was oxidized by MnO_2 (7.0 equiv.) in toluene (6.0 mL) under refluxing conditions to form 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) in 62%, 73%, and 80% yields, respectively, as shown in Table 1 (entries 1~3).

Table 1. Optimization for Transformation of cumene into 3-(4'-Isopropylphenyl)-1-methylpyrazole **2A.**

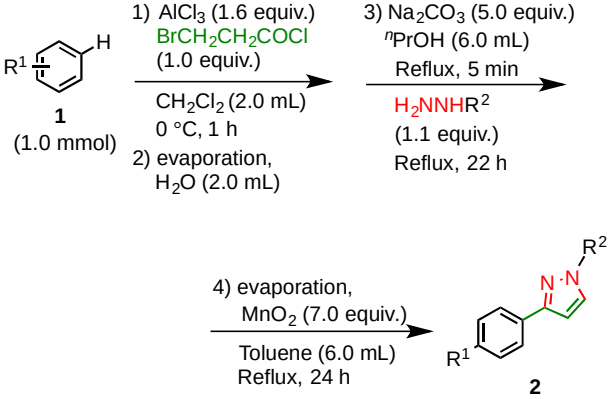


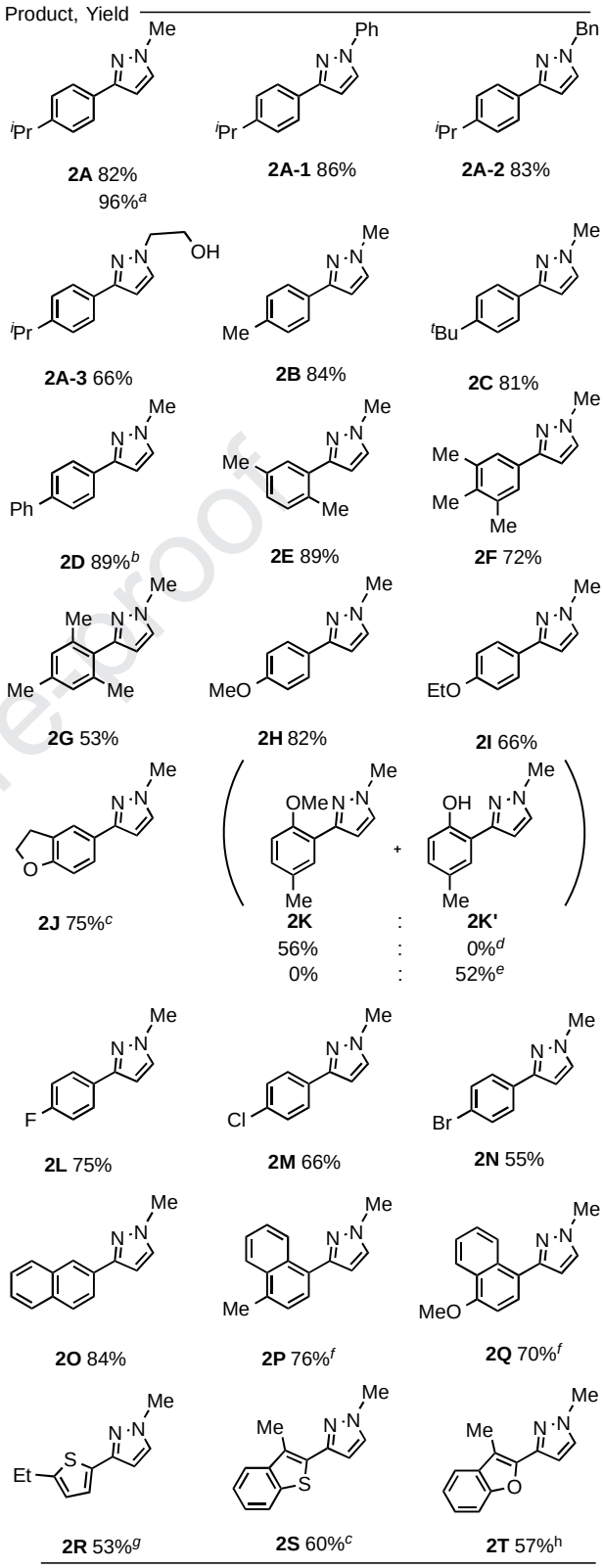
Entry	Base	3rd Solvent	Oxidant (y equiv.)	4th Solvent	Yield (%)
1	KF	MeOH	MnO_2 (7.0)	Toluene	62
2	K_2CO_3	MeOH	MnO_2 (7.0)	Toluene	73
3	Na_2CO_3	MeOH	MnO_2 (7.0)	Toluene	80
4	Na_2CO_3	EtOH	MnO_2 (7.0)	Toluene	73
5	**Na_2CO_3**	**^{n}PrOH**	**MnO_2 (7.0)**	**Toluene**	**82**
6	Na_2CO_3	^{n}PrOH	MnO_2 (3.0)	Toluene	42
7	Na_2CO_3	^{n}PrOH	DDQ (7.0)	DCE	35
8	Na_2CO_3	^{n}PrOH	DIB (7.0)	DCE	0
9	Na_2CO_3	^{n}PrOH	NIS (7.0)	DCE	0
10	Na_2CO_3	^{n}PrOH	CrO_3 (7.0)	DCE	37

Here, Na_2CO_3 showed the best result to form pyrazole **2A** in good yield. The presence of water did not disturb the formation of pyrazoline **1A-c** in the 3rd reaction step. When methanol was changed to ethanol and *n*-propanol in the 3rd reaction step under the same procedure and conditions, the yields of 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) were 73% and 82% yields, respectively (entries 4, 5). Thus, *n*-propanol was the most effective solvent forming 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) in 82% yield (entry 5). The oxidation of pyrazoline **1A-c** to 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) by MnO_2 did not proceed smoothly, and therefore, an excess amount of MnO_2 was required (entries 5, 6). When DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), DIB [(diacetoxyiodo)benzene], and NIS (*N*-iodosuccinimide), which are not transition-metal oxidants, were used instead of MnO_2 in 1,2-dichloroethane (DCE) in the 4th reaction step, the yield of 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) was 35% in the former oxidant, and 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) was not formed at all in the latter two oxidants, respectively (entries 7~9). In addition, the oxidation ability of CrO_3 was not sufficiently high for the oxidation of pyrazoline **1A-c** (entry 10). Thus, the oxidation of pyrazoline **1A-c** to 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) with MnO_2 was the most effective among these reactions. As a gram-scale experiment, treatment of cumene (**1A**, 9.0 mmol) under the same procedure and conditions as those of entry 5 in Table 1 gave 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) in 96% yield, as shown in Scheme 1.

Based on those results, cumene (**1A**, 1.0 mmol) was treated under the same procedure and conditions as those of entry 5 in Table 1, using phenylhydrazine, benzylhydrazine, and (2-hydroxyethyl)hydrazine to give 3-(4'-isopropylphenyl)-1-phenylpyrazole (**2A-1**), 1-benzyl-3-(4'-isopropylphenyl)pyrazole (**2A-2**), and 1-(2"-hydroxyethyl)-3-(4'-isopropylphenyl)pyrazole (**2A-3**) in 86%, 83%, and 66% yields, respectively, as shown in Scheme 1. Then, the same treatment of arenes (1.0 mmol), such as toluene (**1B**), *tert*-butylbenzene (**1C**), biphenyl (**1D**), *p*-xylene (**1E**), 1,2,3-trimethylbenzene (**1F**), 1,3,5-trimethylbenzene (**1G**), anisole (**1H**), phenetole (**1I**),

Scheme 1. Transformation of Arenes **1** into 3-Arylpyrazoles **2**.





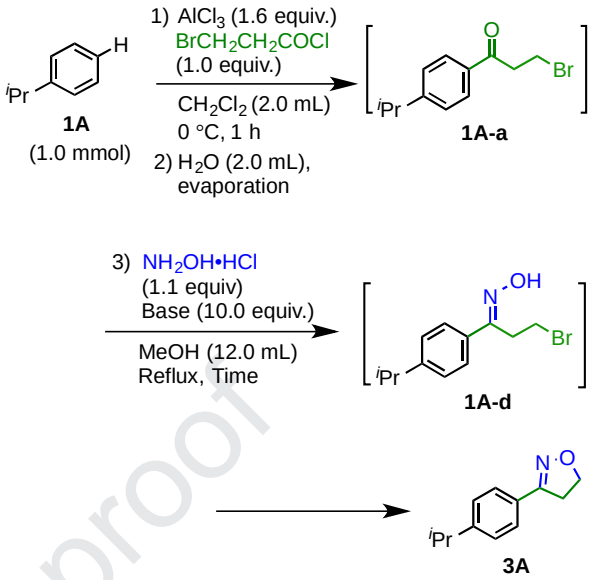
[a] S.M (9.0 mmol) was used.
[b] *n*-PrOH (12.0 mL) at 3rd step and Toluene (12.0 mL) at 4th step were used.
[c] 1st step reaction was carried out at -10 ℃ for 2 h .
[d] 1st step reaction was carried out at -55 ℃ for 22 h.
[e] 1st step reaction was carried out at r.t. for 22 h.
[f] 1st step reaction was carried out at r.t. for 3 h.
[g] 1st step reaction was carried out for 2 h.
[h] 1st step reaction was carried out for 3 h.

2,3-dihydrobenzofuran (**1J**), fluorobenzene (**1L**), chlorobenzene (**1M**), and bromobenzene (**1N**), with β-bromopropionyl chloride (1.0 equiv.), $AlCl_3$ (1.6 equiv.), H_2O (2.0 mL), Na_2CO_3 (5.0 equiv.), methylhydrazine (1.1 equiv.), and then MnO_2 (7.0 equiv.) under the same procedure and conditions as those of entry 5 in Table 1 gave the corresponding 3-aryl-1-methylpyrazoles **2B**~**2J** and **2L**~**2N** in good to moderate yields, as shown in Scheme 1. When the acylation of 4-methoxytoluene (**1K**) with β-bromopropionyl chloride and $AlCl_3$ was carried out at -55 °C for 22 h and the subsequent reactions performed under the same procedure and conditions as those of entry 5 in Table 1, 1-methyl-3-(2'-methoxy-5'-methylphenyl)pyrazole (**2K**) was obtained in 56% yield. On the other hand, when the acylation of 4-methoxytoluene (**1K**) was carried out at room temperature for 22 h and the subsequent reactions were conducted under the same procedure and conditions, 3-(2'-hydroxy-5'-methylphenyl)-1-methylpyrazole (**2K'**) was obtained in 52% yield. Under the same procedure and conditions, naphthalene (**1O**), 1-methylnaphthalene (**1P**), 1-methoxynaphthalene (**1Q**), 2-ethylthiophene (**1R**), 3-methylbenzothiophene (**1S**), and 3-methylbenzofuran (**1T**) were also successfully transformed into 1-methyl-3-(naphthalen-2'-yl)pyrazole (**2O**), 1-methyl-3-(4'-methylnaphthalen-1'-yl)pyrazole (**2P**), 3-(4'-methoxynaphthalen-1'-yl)-1-methylpyrazole (**2Q**), 3-(5'-ethylthiophen-2'-yl)-1-methylpyrazole (**2R**), 1-methyl-3-(3'-methylbenzothiophen-2'-yl)pyrazole (**2S**), and 1-methyl-3-(3'-methylbenzofuran-2'-yl)pyrazole (**2T**) in good to moderate yields, although their reaction times and temperatures in 1st reaction step differed depending on the electrophilicity of the aromatic rings.

Treatment of obtained 1-benzyl-3-(4'-isopropylphenyl)pyrazole (**2A-2**, 1.0 mmol) with Pd on carbon under hydrogen gas in a mixture of 1M HCl (0.5 mL) and methanol (4.0 mL) at room temperature for 20 h gave 3-(4'-isopropylphenyl)-1*H*-pyrazole (**2Aa**) in 84% yield.

Then, the transformation of arenes into 3-arylisoxazolines was studied using the same procedure but with hydroxylamine instead of hydrazines. Treatment of cumene (**1A**, 1.0 mmol) with β-bromopropionyl chloride (1.0 equiv.) and $AlCl_3$ (1.6 equiv.) in dichloromethane (2.0 mL) at 0 °C for 1 h gave the corresponding ketone **1A-a**. After the addition of water (2.0 mL) to decompose $AlCl_3$, the solvent was removed by evaporation. Then, aq. NH_2OH (1.1 equiv.), K_2CO_3 (10.0 equiv.), and MeOH (12.0 mL), and NH_2OH•HCl (1.1 equiv.), Et_3N (10.0 equiv.), and MeOH (12.0 mL) were added to the residue, respectively, and the obtained mixtures were refluxed for 67 h. However, 3-(4'-isopropylphenyl)isoxazoline (**3A**) was not formed at all, as shown in Table 2 (entries 1, 2). On the other hand, after the addition of water and evaporation, treatment of the residue with NH_2OH•HCl and bases, such as CsF (10.0 equiv.), K_2CO_3 (10.0 equiv.), and Na_2CO_3 (10.0 equiv.), in MeOH (12.0 mL) under refluxing conditions for 67 h gave 3-(4'-isopropylphenyl)isoxazoline (**3A**) in 59%, 58%, and 42% yields, respectively (entries

Table 2. Optimization for Transformation of Cumene into 3-(4'-Isopropylphenyl)isoxazoline **3A.**



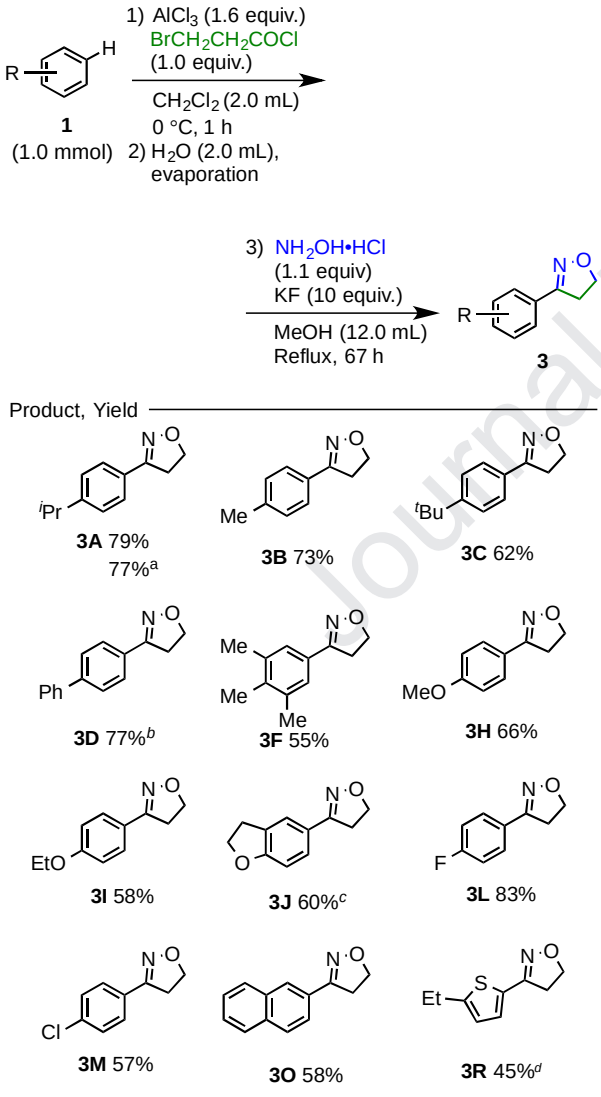
Entry	Base	Time (h)	Yield (%)
1[a)]	K_2CO_3	67	0
2	Et_3N	67	0
3	CsF	67	59
4	K_2CO_3	67	58
5	Na_2CO_3	67	42
6	**KF**	**67**	**79**
7	KF	22	65

[a)] Aq. NH_2OH was used instead of NH_2OH•HCl.

3~5). The key point in this reaction is the cyclization step of formed oxime **1A-d** to produce isoxazoline **3A** via the *5-exo-tet* cyclization mode. Finally, it was found that the treatment of cumene (**1A**, 1.0 mmol) with β-bromopropionyl chloride (1.0 equiv.) and $AlCl_3$ (1.6 equiv.) in dichloromethane (2.0 mL) at 0 °C for 1 h, followed by the addition of water (2.0 mL) and evaporation, and warming treatment of the residue with NH_2OH•HCl (1.1 equiv.) and KF (10.0 equiv.) in MeOH (12.0 mL) for 67 h gave 3-(4'-isopropylphenyl)isoxazoline (**3A**) in 79% yield (entry 6). The oxidation of 3-(4'-isopropylphenyl)isoxazoline (**3A**) to 3-(4'-isopropylphenyl)isoxazole with DDQ in toluene at 80 °C, with DIB in 1,2-dichloroethane at 80 °C, with MnO_2 in toluene at 110 °C, and with CrO_3 in 1,2-dichloroethane at 80 °C did not proceed at all. As a gram-scale experiment, treatment of cumene (**1A**, 9.0 mmol) under the same procedure and conditions as those of entry 6 in Table 2 gave 3-(4'-isopropylphenyl)isoxazoline (**3A**) in 77% yield, as shown in Scheme 2. Based on those results, the successive treatment of arenes **1** (1.0 mmol), such as toluene (**1B**), *tert*-butylbenzene (**1C**), biphenyl (**1D**), 1,2,3-trimethylbenzene (**1F**), anisole (**1H**), phenetole (**1I**), 2,3-dihydrobenzofuran (**1J**), fluorobenzene (**1L**), and chlorobenzene (**1M**) with β-bromopropionyl chloride (1.0

mmol), $AlCl_3$ (1.6 equiv.), H_2O (2.0 mL), NH_2OH•HCl (1.1 equiv.), and KF (10.0 equiv.) under the same procedure and conditions as those of entry 6 in Table 2 gave the corresponding 3-arylisoxazolines **3B**~**3D**, **3F**, **3H**~**3J**, **3L**, and **3M** in good to moderate yields, as shown in Scheme 2. Under the same procedure and conditions, naphthalene (**1O**) and 2-ethylthiophene (**1R**) could be also transformed into 3-(naphthalen-2'-yl)isoxazoline (**3O**) and 3-(5'-ethylthiophen-2'-yl)isoxazoline (**3R**) in moderate yields, respectively. However, when *p*-xylene (**1E**), 1,3,5-trimethylbenzene (**1G**), and 3-methylbenzothiophene (**1S**) were used as substrates under the same procedure and conditions, the corresponding 3-arylisoxazolines **3** were not formed, because the *5-exo-tet* cyclization of the formed oximes failed to proceed smoothly due to steric hindrance.

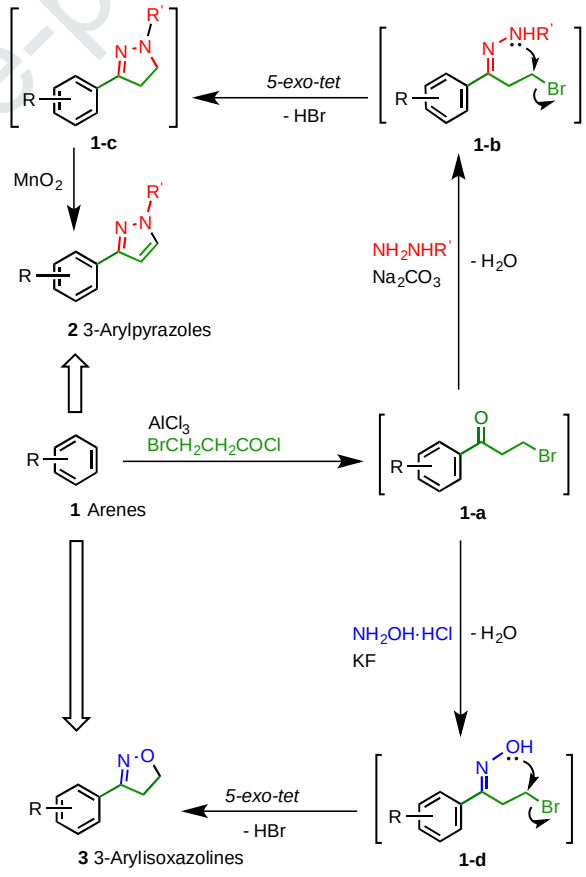
Scheme 2. Transformation of Arenes **1** to 3-Arylisoxazolines **3**.



[a] Compound **1A** (9.0 mmol) was used.
[b] MeOH (24 mL) was used.
[c] 1st reaction step was carried out at -10 ℃ for 2 h .
[d] 1st reaction step was carried out for 2 h.

The possible reaction pathways for the preparation of 3-arylpyrazoles **2** and 3-arylisoxazolines **3** from arenes **1** are shown in Scheme 3. β-Bromopropiophenones **1-a** formed by the Friedel-Crafts acylation of arenes **1** with β-bromopropionyl chloride and $AlCl_3$, react with hydrazines to form 3-arylpyrazolines **1-c** via the *5-exo-tet* cyclization of hydrazones **1-b** under basic conditions. Formed 3-arylpyrazolines **1-c** were smoothly oxidized to 3-arylpyrazoles **2** by MnO_2 under warming conditions. The formation of 3-arylpyrazolines **1-c** from hydrazones **1-b** is not affected by the presence of water. Similarly, formed β-bromopropiophenones **1-a** react with hydroxylamine•hydrogen chloride to form 3-arylisoxazolines **3** via the *5-exo-tet* cyclization of oximes **1-d** under basic conditions. The formation of 3-arylisoxazolines **3** from formed oximes **1-d** is dramatically affected by water, and the complete removal of water is important. On the other hand, the *5-exo-tet* cyclization is affected by the *o*-substituent of arenes **1** used.

Scheme 3. Reaction pathways



3. Conclusion

Arenes could be efficiently transformed into 3-arylpyrazoles by the successive treatment with β-bromopropionyl chloride and $AlCl_3$, with water, with hydrazines and Na_2CO_3, and finally with MnO_2. Arenes

could be also transformed into 3-arylisoxazolines by the successive treatment with β-bromopropionyl chloride and $AlCl_3$, with water, and with hydroxylamine•hydrogen chloride and CsF, although oxidative conversion into 3-arylisoxazoles could not be achieved. We believe that the present methods would be useful for the preparation of 3-arylpyrazoles and 3-arylisoxazolines from arenes via β-bromopropiophenones because those transformations could be carried out in one pot with easily available substrates and reagents.

4. Experimental Section

4.1 General: ^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400 and JEOL-JNM-ECS400 spectrometers. Chemical shifts were recorded as follows: chemical shift in ppm from internal tetramethylsilane (TMS) on the δ□scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. High-resolution mass spectra (HRMS) were recorded by a Thermo Fisher Scientific Exactive Orbitrap mass spectrometer. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel $60F_{254}$ (Merck) was used for TLC and Silica gel 60N (63~210 mesh, Kanto Kagaku Co.) was used for short column chromatography.

4.2 Typical Procedure for One-pot Transformation of Arenes 1 into 3-Arylpyrazoles 2: To a solution of cumene (**1a**) (1.0 mmol, 120 mg) in CH_2Cl_2 (2.0 mL) was added β-bromopropionyl chloride (1.0 mmol, 0.1 mL with a 250μL micro-syringe) at 0 □ under Ar atmosphere. The mixture was stirred for a few minutes. Then, anhydrous $AlCl_3$ (1.6 mmol, 213 mg) was added and the mixture was stirred for 1 h at 0 □. After removal of the solvent, cooled water (2.0 mL) and then *n*-PrOH (6.0 mL) were added. Na_2CO_3 (5.0 mmol, 523mg) was added and the obtained mixture was stirred for a few minutes under air and refluxing conditions. After that, NH_2NHMe (1.1 mmol, 57μl) was added and the obtained mixture was stirred for 22 h under air and refluxing conditions. After removal of the solvent, toluene (6.0 mL) and MnO_2 (7.0 mmol, 608 mg) were added. After being stirred for 24 h under air and refluxing conditions, the mixture was filtered through celite, and then the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1) to afford 3-(4'-isopropylphenyl)-1-methylpyrazole (**2A**) in 82% yield (165 mg).

4.2.1 3-(4'-Isopropylphenyl)-1-methylpyrazole (2A): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1); Yield: 165.2mg (82%); pale yellow oil; IR (neat) 2959, 1457, 1428 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, 6H, *J* = 7.0 Hz), 2.92 (septet, 1H, *J* = 7.0 Hz), 3.95 (s, 3H), 6.50 (d, 1H, *J* = 2.0 Hz), 7.25 (d, 2H, *J* = 8.1 Hz), 7.35 (d, 1H, *J* = 2.0 Hz), 7.70 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.8, 33.7, 38.7, 102.4, 125.3, 126.4, 131.0, 131.1, 148.0, 151.4; HRMS (ESI) Calcd for $C_{13}H_{17}N_2$ $[M+H]^+$ = 201.1386, Found = 201.1385.

4.2.2 3-(4'-isopropylphenyl)-1-phenylpyrazole (2A-1): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 10:1); Yield: 224.5mg (86%); yellow solid; Mp: 83-84 °C; IR (neat) 2971, 2360, 1597, 1448 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, 2H, *J* = 6.9 Hz), 2.94 (septet, 1H, 6.9 Hz), 6.75 (d, 1H, *J* = 2.4 Hz), 7.26-7.30 (m, 3H), 7.47 (t, 2H, *J* = 7.6 Hz), 7.77 (d, 2H, *J* = 7.6 Hz), 7.84 (d, 2H, *J* = 8.3 Hz), 7.94 (d, 1H, *J* = 2.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.9, 33.9, 104.8, 118.9, 125.8, 126.1, 126.6, 127.8, 129.3, 130.6, 140.2, 148.7, 152.9; HRMS (ESI) Calcd for $C_{18}H_{19}N_2$ $[M+H]^+$ = 263.1543, Found = 263.1538.

4.2.3 1-Benzyl-3-(4'-isopropylphenyl)pyrazole (2A-2): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 10:1); Yield: 230.2mg (83%); white solid; Mp: 69-70 °C; IR (neat) 2959, 1606, 1455, 1229 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, 6H, *J* = 6.8 Hz), 2.92 (septet, 1H, *J* = 6.8 Hz), 5.36 (s, 2H), 6.54 (d, 1H, *J* = 2.2 Hz), 7.22-7.26 (m, 4H), 7.31-7.36 (m, 4H), 7.74 (d, 2H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =23.9, 33.8, 55.9, 103.0, 125.5, 126.5, 127.5, 127.8, 128.6, 130.4, 131.1, 136.6, 148.2, 151.5; HRMS (ESI) Calcd for $C_{19}H_{21}N_2$ $[M+H]^+$ = 277.1699, Found = 277.1695.

4.2.4 1-(2"-Hydroxyethyl)-3-(4'-isopropylphenyl)pyrazole (2A-3): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 152.4mg (66%); pale brown solid; Mp: 78-80 °C; IR (neat) 3241, 2956, 1472, 1224 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 1.20 (d, 6H, *J* = 6.9 Hz), 2.87 (septet, 1H, *J* = 6.9 Hz), 3.74 (q, 2H, *J* = 5.3 Hz), 4.15 (t, 2H, *J* = 5.3 Hz), 4.90 (t, 1H, *J* = 5.3 Hz), 6.20 (d, 1H, *J* = 2.2 Hz), 7.23 (d, 2H, *J* = 8.3 Hz), 7.67 (d, 2H, *J* = 8.3 Hz), 7.70 (d, 1H, *J* = 2.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.9, 33.8, 53.6, 62.0, 102.4, 125.5, 126.6, 130.7, 131.3, 148.5, 152.0; HRMS (ESI) Calcd for $C_{14}H_{19}N_2O[M+H]^+$ = 231.1492, Found = 231.1492.

4.2.5 3-(4'-Isopropylphenyl)-1*H*-pyrazole (2Aa): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 156.1mg (84%); white solid; Mp: 52-54 °C; IR (neat) 3177, 2958, 1455 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.27 (d, 6H, *J* = 7.0 Hz), 2.93 (septet, 1H, *J* = 7.0 Hz), 6.58 (d, 1H, *J* = 2.2 Hz), 7.27 (d, 2H, *J* = 8.1 Hz), 7.60 (d, 1H, *J* = 2.0 Hz), 7.66 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.8, 33.8, 102.2, 125.8, 126.7, 129.5, 1337, 148.5, 148.7; HRMS (ESI) Calcd for $C_{12}H_{15}N_2$ $[M+H]^+$ = 187.1230, Found = 187.1225.

4.2.6 3-(4'-Methylphenyl)-1-methylpyrazole (2B): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1); Yield: 144.6mg (84%); pale yellow solid Mp: 42-44 °C; IR (neat) 2941, 1540, 1456 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3H), 3.94 (s, 3H), 6.50 (d, 1H, *J* = 2.0 Hz), 7.19 (d, 2H, *J* = 8.1 Hz), 7.36 (d, 1H, *J* = 2.0 Hz), 7.68(d, 2H, *J* = 8.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 21.2, 38.9, 102.5, 125.3, 129.2, 130.6, 131.2, 137.1, 151.6; HRMS (ESI) Calcd for $C_{11}H_{13}N_2$ $[M+H]^+$ = 173.1073, Found = 173.1074.

4.2.7 3-(4'-*tert*-Butylphenyl)-1-methylpyrazole (2C): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 173.8mg (81%); pale yellow oil; IR (neat) 2936, 1540, 1474, 1363 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9H), 3.93 (s, 3H), 6.50 (d, 1H, *J* = 1.8 Hz), 7.34 (d, 1H, *J* = 1.8 Hz), 7.41 (d, 2H, *J* = 8.3 Hz), 7.72 (d, 2H, *J* = 8.3 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 31.2, 34.4, 38.7, 102.4, 125.0, 125.3, 130.6, 131.0, 150.2, 151.4; HRMS (ESI) Calcd for $C_{14}H_{19}N_2$ $[M+H]^+$ = 215.1543, Found = 215.1541.

4.2.8 3-[(1',1"-Biphenyl)-4'-yl]-1-methylpyrazole (2D): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 181.1mg (89%); white solid; Mp:

115-116 °C; IR (neat) 2350, 1507, 1419 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.97 (s, 3H), 6.58 (d, 2H, *J* = 2.0 Hz), 7.34 (t, 1H, *J* = 7.2 Hz), 7.44 (t, 2H, *J* = 7.2 Hz), 7.63 (d, 2H, *J* = 8.1 Hz), 7.63 (d, 2H, *J* = 8.0 Hz), 7.86 (d, 2H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =38.9, 102.8, 125.8, 126.8, 127.1, 127.2, 128.6, 131.3, 132.4, 140.1, 140.7, 151.1; HRMS (ESI) Calcd for $C_{16}H_{15}N_2$ $[M+H]^+$ = 235.1230, Found = 235.1228.

4.2.9 3-(2',5'-dimethylphenyl)-1-methylpyrazole (2E): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1); Yield: 165.3mg (89%); pale yellow oil; IR (neat) 2946, 1615, 1456 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 2.41 (s, 3H), 3.96 (s, 3H), 6.38 (d, 1H, *J* = 2.0 Hz), 7.04 (d, 1H, *J* = 7.6 Hz), 7.12 (d, 1H, *J* = 7.8 Hz), 7.38 (d, 1H, *J* = 2.0 Hz), 7.39 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =20.5, 20.8, 38.9, 105.9, 128.2, 129.7, 130.2, 130.5, 132.6, 133.0, 135.1, 151.8; HRMS (ESI) Calcd for $C_{12}H_{15}N_2$ $[M+H]^+$ = 187.1230, Found = 187.1225.

4.2.10 1-Methyl-3-(3',4',5'-trimethylphenyl)pyrazole (2F): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1); Yield: 144.8mg (72%); pale yellow solid; Mp: 43-45 °C; IR (neat) 2938, 1499, 1456 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.18 (s, 3H), 2.32 (s, 6H), 3.94 (s, 3H) , 6.49 (d, 1H, *J* = 2.2 Hz), 7.35 (d, 1H, *J* = 2.2 Hz), 7.43 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.1, 20.5, 38.8, 102.4, 124.5, 130.2, 131.1, 134.4, 136.5, 151.7; HRMS (ESI) Calcd for $C_{13}H_{17}N_2$ $[M+H]^+$ = 201.1386, Found = 201.1385.

4.2.11 3-Mesityl-1-methylpyrazole (2G): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 8:1); Yield: 107.1mg (53%); pale yellow oil; IR (neat) 2922, 1499, 1456 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6H), 2.29 (s, 3H), 3.94 (s, 3H), 6.12 (d, 1H, J = 2.2 Hz), 6.89 (s, 2H), 7.40 (d, 1H, J = 2.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 20.4, 21.0, 38.7, 106.3, 127.9, 130.0, 131.0, 137.0, 137.4, 150.4; HRMS (ESI) Calcd for $C_{13}H_{17}N_2$ $[M+H]^+$ = 201.1386, Found = 201.1385.

4.2.12 3-(4'-Methoxyphenyl)-1-methylpyrazole (2H): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 155.3mg (82%); white solid; Mp: 73-74 °C; IR (neat) 2966, 1615, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3H), 3.93 (s, 3H), 6.46 (d, 1H, *J* = 2.0 Hz), 6.92 (d, 2H, *J* = 8.7 Hz), 7.35 (d, 1H, *J* = 2.0 Hz), 7.71 (d, 2H, J = 8.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =39.0, 55.3, 102.3, 114.0, 126.5, 126.8, 131.4, 151.4, 159.2; HRMS (ESI) Calcd for $C_{11}H_{13}ON_2$ $[M+H]^+$ = 189.1022, Found = 189.1022.

4.2.13 3-(4'-Ethoxyphenyl)-1-methylpyrazole (2I): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 133.7mg (66%); white solid; Mp: 86-87 °C; IR (neat) 2360, 1507, 1240 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, 3H, *J* = 6.9 Hz), 3.93 (s, 3H), 4.06 (q, 2H, *J* = 6.9 Hz), 6.45 (d, 1H, *J* = 2.2 Hz), 6.91 (d, 2H, *J* = 8.7 Hz), 7.35 (d, 1H, J = 2.2 Hz), 7.70 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.7, 38.8, 63.3, 102.1, 114.4, 126.1, 126.6, 131.2, 151.4, 158.4; HRMS (ESI) Calcd for $C_{12}H_{15}ON_2$ $[M+H]^+$ = 203.1179 Found = 203.1177.

4.2.14 3-(2',3'-Dihydrobenzofuran-5'-yl)-1-methylpyrazole (2J): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 149.8mg (75%); white solid; Mp: 74-75 °C; IR (neat) 2960, 2360, 1457, 1227 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.32 (t, 2H, *J* = 8.6 Hz), 3.93 (s, 3H), 4.59 (t, 2H, *J* = 8.6 Hz), 6.43 (d, 1H, *J* = 2.0 Hz), 6.79 (d, 1H, *J* = 8.1 Hz), 7.34 (d, 1H, J = 2.0 Hz), 7.51 (d, 1H, J = 8.1 Hz), 7.66 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 29.4, 38.7, 71.2, 102.0, 109.0, 122.1, 125.4, 126.2, 127.2, 131.1, 151.6, 159.6; HRMS (ESI) Calcd for $C_{12}H_{13}ON_2$ $[M+H]^+$ = 201.1022, Found = 201.1021.

4.2.15 3-(2'-Methoxy-5'-methylphenyl)-1-methylpyrazole (2K): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 112.8mg (56%); colorless oil; IR (neat) 2938, 2360, 1611, 1284 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3H), 3.86 (s, 3H), 3.96 (s, 3H), 6.75 (d, 1H, *J* = 2.2 Hz), 6.86 (d, 1H, *J* = 7.6 Hz), 7.07 (d, 1H, *J* = 7.6 Hz), 7.37 (d, 1H, *J* = 2.2 Hz), 7.71(s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 20.3, 38.7, 55.3, 106.7, 111.1, 121.8, 128.8, 129.7 (2C), 130.2, 148.2, 154.2; HRMS (ESI) Calcd for $C_{12}H_{15}ON_2$ $[M+H]^+$ = 203.1179, Found = 203.1176.

4.2.16 3-(2'-Hydroxy-5'-methylphenyl)-1-methylpyrazole (2K'): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 96.9mg (52%); pale yellow solid; Mp: 70-71 °C; IR (neat) 3648, 2943, 1518, 1284 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.94 (s, 3H), 6.59 (d, 1H, *J* = 2.2 Hz), 6.91 (d, 1H, *J* = 8.1 Hz), 7.00 (dd, 1H , *J* = 8.1, 2.0 Hz), 7.35 (d, 1H, *J* = 2.0 Hz), 7.39 (d, 1H, *J* = 2.2 Hz), 10.61 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 20.5, 38.7, 101.9, 116.2, 116.6, 126.3, 128.0, 129.5, 130.8, 151.2, 153.4: HRMS (ESI) Calcd for $C_{11}H_{13}ON_2$ $[M+H]^+$ = 189.1022, Found = 189.1022.

4.2.17 3-(4'-Fluorophenyl)-1-methylpyrazole (2L): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 6:1); Yield: 133.0mg (75%); pale yellow solid; Mp: 68-69 °C; IR (neat) 2971, 2360, 1507, 1065 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3H), 6.48 (d, 1H, *J* = 2.2 Hz), 7.08 (t, 2H, *J* = 8.8 Hz), 7.37 (d, 1H, *J* = 2.2 Hz), 7.72-7.78 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 38.9, 102.5, 115.4 (d, J_{C-F} = 21.6 Hz), 127.0 (d, J_{C-F} = 8.4 Hz), 129.7, 131.4, 150.6, 162.3 (d, J_{C-F} = 246.1 Hz); HRMS (ESI) Calcd for $C_{10}H_{10}FN_2$ $[M+H]^+$ = 177.0823, Found = 177.0822.

4.2.18 3-(4'-Chlorophenyl)-1-methylpyrazole (2M): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 6:1); Yield: 127.9mg (66%); white solid; Mp: 68-69 °C; IR (neat) 2970, 2361, 1455, 757 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3H), 6.50 (d, 1H, *J* = 2.2 Hz), 7.35 (d, 2H, *J* = 8.6 Hz), 7.37 (d, 1H, *J* = 2.2 Hz), 7.72 (d, 2H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 38.9, 102.7, 126.6, 128.6, 131.4, 132.0, 133.0, 150.3; HRMS (ESI) Calcd for $C_{10}H_{10}{}^{35}ClN_2$ $[M+H]^+$ = 193.0527, Found = 193.0531.

4.2.19 3-(4'-Bromophenyl)-1-methylpyrazole (2N): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 5:1); Yield: 129.9mg (55%); white solid; Mp: 76-77 °C; IR (neat) 2341, 1498, 1456, 614 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.94 (s, 3H), 6.51 (d, 1H, *J* = 2.0 Hz), 7.37 (d, 1H, *J* = 2.0 Hz), 7.50 (d, 2H, *J* = 8.1 Hz), 7.66 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 39.0, 102.7, 121.2, 126.9, 131.4, 131.6, 132.4, 150.3; HRMS (ESI) Calcd for $C_{10}H_{10}{}^{79}BrN_2$ $[M+H]^+$ = 237.0022, Found = 237.0022.

4.2.20 1-Methyl-3-(naphthalen-2'-yl)pyrazole (2O): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 175.4mg (84%); pale yellow oil; IR (neat) 3046, 2360, 1592, 1508 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.04 (s, 3H), 6.55 (d, 1H, *J* = 2.0 Hz), 7.47-7.52 (m, 4H), 7.67 (d,

1H, *J* = 7.0 Hz), 7.83-7.89 (m, 2H), 8.48-8.51 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 38.9, 106.6, 125.2, 125.6, 126.0, 126.1, 126.8, 128.0, 128.1, 130.5, 131.3, 131.6, 133.8, 151.0; HRMS (ESI) Calcd for $C_{14}H_{13}N_2$ $[M+H]^+$ = 209.1073, Found = 209.1072.

4.2.21 1-Methyl-3-(4'-methylnaphthalen-1'-yl)pyrazole (2P): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 168.0 mg (76%); yellow oil; IR (neat) 2940, 2356, 1591 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.72 (s, 3H), 4.03 (s, 3H), 6.51 (d, 1H, *J* = 2.2 Hz), 7.35 (d, 1H, *J* = 7.4 Hz), 7.47-7.57 (m, 4H), 8.04 (d, 1H, *J* = 9.6 Hz), 8.50 (d, 1H, *J* = 9.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 19.6, 39.0, 106.7, 124.2, 125.4, 125.7, 126.1, 126.6 (2C), 130.0, 130.4, 131.4, 132.8, 134.2, 151.3; HRMS (ESI) Calcd for $C_{15}H_{15}N_2$ $[M+H]^+$=223.1230, Found = 223.1228.

4.2.22 3-(4'-Methoxynaphthalen-1'-yl)-1-methylpyrazole (2Q): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 4:1); Yield: 165.5 mg (70%); yellow oil; IR (neat) 2938, 2350, 1417 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.02 (s, 3H), 4.03 (s, 3H), 6.49 (d, 1H, *J* = 2.2 Hz), 6.89 (d, 1H, *J* = 8.1 Hz), 7.46-7.59 (m, 3H), 7.58 (d, 1H, *J* = 8.1 Hz), 8.31 (d, 1H, *J* = 7.0 Hz), 8.43 (d, 1H, *J* = 7.0 Hz) ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 38.7, 55.2, 103.2, 106.1, 121.8, 124.0, 124.8, 125.5, 125.6, 126.5, 126.9, 130.3, 132.1, 151.0, 155.0; HRMS (ESI) Calcd for $C_{15}H_{15}ON_2$ $[M+H]^+$ = 239.1179, Found = 239.1177.

4.2.23 3-(5'-Ethylthiophen-2'-yl)-1-methylpyrazole (2R): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 6:1); Yield: 101.6 mg (53%); brown oil; IR (neat) 2966, 1455, 1067 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, 3H, *J* = 7.4 Hz), 2.84 (q, 2H, *J* = 7.4 Hz), 3.90 (s, 3H), 6.38 (d, 1H, *J* = 2.0 Hz), 6.71 (d, 1H, *J* = 3.4 Hz), 7.09 (d, 1H, *J* = 3.4 Hz), 7.31 (d, 1H, *J* = 2.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.8, 23.3, 38.7, 102.2, 122.8, 123.5, 131.1, 133.8, 146.3, 146.9; HRMS (ESI) Calcd for $C_{10}H_{13}SN_2$ $[M+H]^+$ = 193.0794, Found = 193.0793.

4.2.24 1-Methyl-3-(3'-methylbenzo[b]thiophen-2'-yl)pyrazole (2S): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 5:1); Yield: 135.8 mg (60%); pale yellow oil; IR (neat) 2941, 1480, 1019, 654 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.64 (s, 3H), 4.01 (s, 3H), 6.43 (d, 1H, *J* = 2.0 Hz), 7.26-7.34 (m, 2H), 7.48 (d, 1H, *J* = 2.0 Hz), 7.75 (d, 1H, *J* = 7.0 Hz), 7.96 (d, 1H, *J* = 7.9 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.0, 39.0, 106.3, 121.6, 122.9, 123.5, 124.1, 125.9, 130.4, 137.8, 138.0, 139.8, 146.1; HRMS (ESI) Calcd for $C_{13}H_{13}N_2S$ $[M+H]^+$ = 229.0794, Found = 229.0790.

4.2.25 1-Methyl-3-(3'-methylbenzofuran-2'-yl)pyrazole (2T): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 111.3 mg (57%); pale brown oil; IR (neat) 2938, 1474, 1029, 791 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.49 (s, 3H), 3.99 (s, 3H), 6.64 (d, 1H, *J* = 2.2 Hz), 7.21-7.32 (m, 2H), 7.41 (d, 1H, *J* = 2.2 Hz), 7.49 (d, 1H, *J* = 7.4 Hz), 7.52 (d, 1H, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =8.70, 39.2, 104.4, 111.1, 111.5, 119.1, 122.2, 124.1, 130.7, 130.8, 143.9, 145.8, 153.8; HRMS (ESI) Calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ = 213.1022, Found = 213.1018.

4.3 Typical Procedure for One-pot Transformation of Arenes 1 into 3-Arylisoxazolines 3: To a solution of cumene (**1a**) (1.0 mmol, 120 mg) in CH_2Cl_2 (2.0 mL) was added β-bromopropionyl chloride (1.0 mmol, 0.1 mL with a 250μL micro-syringe) at 0 □ under Ar atmosphere. The mixture was stirred for a few minutes. Then, anhydrous $AlCl_3$ (1.6 mmol, 213 mg) was added and the mixture was stirred for 1 h at 0 □. After that, cooled water (2.0 mL) was added. After removal of the solvent under reduced pressure, MeOH (12.0 mL), $NH_2OH \cdot HCl$ (1.1 mmol, 76.4mg), and KF (10.0 mmol, 581 mg) were added to the residue. After being stirred for 67 h under air and refluxing conditions, the mixture was quenched by water (30.0 mL) and extracted with AcOEt (3 x 20 mL). The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on silica gel (eluent, hexane : ethyl acetate = 9:1) to afford 3-(4'-isopropylphenyl)isoxazoline (**3A**) in 79% yield (150 mg).

4.3.1 3-(4'-Isopropylphenyl)isoxazoline (3A): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 9:1); Yield: 150.1mg (79%); white solid; Mp: 46-48 °C; IR (neat) 2961, 1607, 1187 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, 6H, *J* = 6.7 Hz), 2.93 (septet, 1H, *J* = 6.7 Hz), 3.34 (t, 2H, *J* = 10.0 Hz), 4.47 (t, 2H, *J* = 10.0 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.62 (d, 2H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.7, 34.0, 35.3, 68.9, 126.7 (2C), 126.9, 151.1, 156.7; HRMS (ESI) Calcd for $C_{12}H_{16}NO$ $[M+H]^+$ = 190.1226, Found = 190.1226.

4.3.2 3-(4'-Methylphenyl)isoxazoline (3B): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 9:1); Yield: 117.6mg (73%); white solid; Mp: 57-59 °C; IR (neat) 2887, 1607, 1351 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 3.32 (t, 2H, *J* = 10.1 Hz), 4.47 (t, 2H, *J* = 10.1 Hz), 7.17 (d, 2H, *J* = 7.8 Hz), 7.58 (d, 2H, *J* = 7.8 Hz): δ = 21.2, 35.1, 68.8, 126.5 (2C), 129.2, 140.1, 156.6; HRMS (ESI) Calcd for $C_{10}H_{12}NO$ $[M+H]^+$ = 162.0913, Found = 162.0914.

4.3.3 3-(4'-*tert*-Butylphenyl)isoxazoline (3C): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 10:1); Yield: 126.7mg (62%); colorless oil; IR (neat) 2962, 1607, 1349 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9H), 3.34 (t, 2H, *J* = 10.1 Hz), 4.47 (t, 2H, *J* = 10.1 Hz), 7.43 (d, 2H, *J* = 8.7 Hz), 7.62 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 31.0, 34.6, 35.1, 68.8, 125.4, 126.4, 126.4, 153.2, 156.5; HRMS (ESI) Calcd for $C_{13}H_{18}NO$ $[M+H]^+$ = 204.1383, Found = 204.1382.

4.3.4 3-[(1,1'-Biphenyl)-4'-yl]isoxazoline (3D): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 187.2mg (77%); white solid; Mp: 153-156 °C; IR (neat) 2359, 1681, 1602 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.38 (t, 2H, *J* = 9.9 Hz), 4.51 (t, 2H, *J* = 9.9 Hz), 7.38 (t, 1H, *J* = 7.7 Hz), 7.46 (t, 2H, *J* = 8.1 Hz), 7.61-7.66 (m, 4H), 7.77 (d, 2H, *J* = 7.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 35.1, 69.1, 126.9, 127.1, 127.2, 127.7, 128.2, 128.8, 140.0, 142.6, 156.4; HRMS (ESI) Calcd for $C_{15}H_{14}NO$ $[M+H]^+$ = 224.1070, Found = 224.1069.

4.3.5 3-(3',4',5'-Trimethylphenyl)isoxazoline (3F): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 10:1); Yield: 110.0mg (55%); pale yellow solid; Mp: 77-79 °C; IR (neat) 2920, 1438, 1354 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.19 (s, 3H), 2.30 (s, 6H), 3.31 (d, 2H, *J* = 10.1 Hz), 4.45 (d, 2H, *J* = 10.1 Hz), 7.33 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ =15.4, 20.5, 35.3, 68.8, 125.8, 126.1, 136.7, 137.5, 156.9; HRMS (ESI) Calcd for $C_{12}H_{16}NO$ $[M+H]^+$ = 190.1226, Found = 190.1225.

4.3.6 3-(4'-Methoxyphenyl)isoxazoline (3H): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 116.1mg (66%); white solid; Mp: 78-79 °C; IR (neat) 2965, 2360, 1604 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.31 (t, 2H, *J* = 10.1 Hz),3.84 (s, 3H), 4.46 (t, 2H, *J* = 10.1 Hz), 6.92 (d, 2H, *J* = 8.7 Hz), 7.63 (d, 2H, *J* = 8.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 35.4, 55.3, 68.9, 114.0, 122.0, 128.2, 156.3, 160.9; HRMS (ESI) Calcd for $C_{10}H_{12}NO_2$ $[M+H]^+$ = 178.0863, Found = 178.0862.

4.2.7 3-(4'-Ethoxyphenyl)isoxazoline (3I): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 111.1 mg (58%); white solid; Mp: 58-59 °C; IR (neat) 2890, 2360, 1607 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, 3H, *J* = 7.0 Hz), 3.31 (t, 2H, *J* = 9.9 Hz), 4.06 (q, 2H, *J* = 7.0 Hz), 4.45 (t, 2H, *J* = 9.9 Hz), 6.91 (d, 2H, *J* = 8.8 Hz), 7.62 (d, 2H, *J* = 8.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.7, 35.4, 63.4, 68.8, 114.5, 121.7, 128.1, 156.3, 160.3; HRMS (ESI) Calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$ = 192.1019, Found = 192.1017.

4.3.8 3-(2',3'-dihydrobenzofuran-5'-yl)isoxazoline (3J): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 114.2mg (60%); white solid; Mp: 97-99 °C; IR (neat) 2922, 2359, 1615 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.24 (t, 2H, *J* = 8.6 Hz), 3.30 (t, 2H, *J* = 9.9 Hz), 4.45 (t, 2H, *J* = 9.9 Hz), 4.62 (t, 2H, *J* = 8.6 Hz), 6.79 (d, 1H, *J* = 8.0 Hz), 7.38 (d, 1H, *J* = 8.0 Hz), 7.63 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 29.3, 35.5, 68.8, 71.6, 109.2, 121.9, 123.3, 127.4, 127.8, 156.6, 161.7; HRMS (ESI) Calcd for $C_{11}H_{12}NO_2$ $[M+H]^+$ = 190.0863, Found = 190.0859.

4.3.9 3-(4'-Fluorophenyl)isoxazoline (3L): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 6:1); Yield: 137.6mg (83%); white solid; Mp: 76-78°C; IR (neat) 2895, 1596, 1159 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.32 (t, 2H, *J* = 9.9Hz), 4.49 (t, 2H, *J* = 9.9 Hz), 7.10 (t, 2H, *J* = 8.6 Hz), 7.66-7.70 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 35.2, 69.2, 115.8 (d, J_{C-F} = 21.9 Hz), 125.7, 128.6 (d, J_{C-F} = 8.5 Hz), 155.8, 163.7(d, J_{C-F} = 250.8 Hz); HRMS (ESI) Calcd for C_9H_9FNO $[M+H]^+$ = 166.0663, Found = 166.0661.

4.3.10 3-(4'-Chlorophenyl)isoxazoline (3M): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 103.4 mg (57%); white solid; Mp: 106-107 °C; IR (neat) 2360, 2894, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.33 (t, 2H, *J* = 10.1 Hz), 4.52 (t, 2H, *J* = 10.1 Hz), 7.38 (d, 2H, *J* = 8.6 Hz), 7.62 (d, 2H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 34.9, 69.3, 127.8 (2C), 128.8, 135.8, 155.8; HRMS (ESI) Calcd for $C_9H_9{}^{35}ClNO$ $[M+H]^+$ = 182.0367, Found = 182.0365.

4.3.11 3-(Naphthalen-2'-yl)isoxazoline (3O): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 9:1); Yield: 113.5 mg (58%); white solid; Mp: 78-80 °C; IR (neat) 2884, 1600, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.47 (t, 2H, *J* = 10.1 Hz), 4.55 (t, 2H, *J* = 10.1 Hz), 7.51-7.53 (m, 2H), 7.84-7.87 (m, 3H), 7.93 (s, 1H), 7.99 (dd, 1H, *J* = 7.9, 1.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 35.1, 69.3, 123.6, 126.6, 126.9, 127.0 (2C), 127.8, 128.3, 128.5, 132.9, 133.9, 156.9; HRMS (ESI) Calcd for $C_{13}H_{12}NO$ $[M+H]^+$ = 198.0913, Found = 198.0913.

4.3.12 3-(5'-Ethylthiophen-2'-yl)isoxazoline (3R): Purified by column chromatography on silica gel (eluent, hexane : ethyl acetate = 7:1); Yield: 81.2 mg (45%); pale brown oil; IR (neat) 2967, 1260, 805 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, 3H, *J* = 7.6 Hz), 2.85 (q, 2H, *J* = 7.6 Hz), 3.31 (t, 2H, *J* = 10.1 Hz), 4.46 (t, 2H, *J* = 10.1 Hz), 6.74 (d, 1H, *J* = 3.5 Hz), 7.02 (d, 1H, *J* = 3.5 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.6, 23.5, 35.9, 69.1, 123.6, 128.5, 129.1, 151.1, 152.6; HRMS (ESI) Calcd for $C_9H_{12}NOS$ $[M+H]^+$ = 182.0634, Found = 182.0633.

Supporting Information: Copies of ^{1}H NMR and ^{13}C NMR spectra of all 3-arylpyrazoles **2** and 3-arylisoxazolines **3**.

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Highlight

- One-pot operation.
- $C(sp^2)$-$C(sp^2)$ construction.