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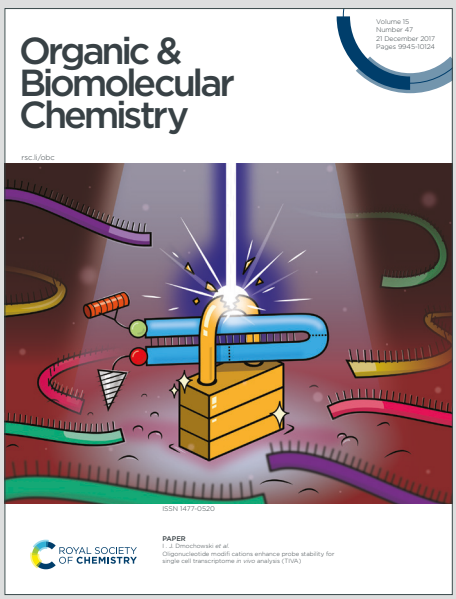

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ARTICLE

Base-Promoted Cascade Reaction of α,β-Unsaturated *N*-Tosylhydrazones with *o*-Hydroxybenzyl Alcohols: Highly Regioselective Synthesis of *N-sec*-Alkylpyrazoles

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An efficient method for the synthesis of *N-sec*-alkyl pyrazoles through a base-promoted cascade cyclization/Michael addition reaction of α,β-unsaturated *N*-tosylhydrazones with *ortho*-hydroxybenzyl alcohols, has been developed. The desired products containing di- or triaryl groups at the same carbon atom were afforded in good to excellent yields with excellent regioselectivities (>20:1). Moreover, a three-component reaction of *ortho*-hydroxybenzyl alcohols, α,β-unsaturated *N*-tosylhydrazones and saturated *N*-tosylhydrazones also took place to afford pyrazoles in good yields. This reaction offers a new route to triarylmethanes with a simple operation and is applicable for the large-scale synthesis.

Introduction

Functionalized pyrazoles have been received increasing attention in chemical, pharmaceutical, and material science.[1]

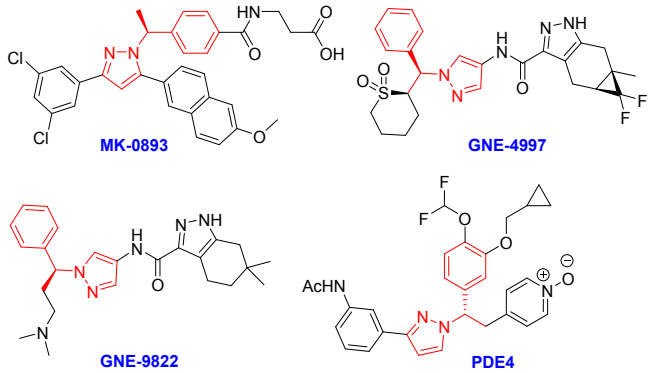

Figure 1. Some examples of biologically active N-*sec*-alkylated pyrazoles

Among these families, the *N-sec*-alkylated pyrazoles possess various prominent biological and pharmacological activities,[2-4] such as the glucagon receptor antagonist (MK-0893),[2] the IKT inhibiters (GNE-4997, GNE-9822)[3] and the potent Phosphodiesterase 4 (PDE4) inhibitors [4] (Figure 1). Apart from their medicinal values, they have been utilized for ligands and dyes.[1,5] Due to their biological activities and applications, developing an efficient method is important for the synthesis of *N-sec*-alkylpyrazoles.

Many approaches for the synthesis of functionalized pyrazoles have been developed.[5] The (3+2)-cycloaddition of diazo compounds with alkenes or alkynes for constructing pyrazole rings is a classic strategy.[5c-d] For example, the alkyl and aryl diazomethanes formed in *situ* from *N*-tosylhydrazones[6] were widely used to react with electron-deficient olefins or terminal alkynes to give pyrazole derivatives.[7] The cyclization condensation of hydrazines with 1,3-dicarbonyl compounds represents another successful type of reaction to deliver pyrazoles.[8] The oxidative cyclization of α,β-alkenic *N*-tosylhydrazones (Scheme 1a) [9] and electrophilic cyclization of α,β-alkynic hydrazones (Scheme 1b),[10] has also been developed to give functionalized pyrazoles. Other approaches for the synthesis of *N-sec*-alkylpyrazoles include the substitution reactions of pyrazoles with secondary alkyl electrophile (such as alkyl halides),[11a] aza-Michael reaction of pyrazole with various α,β-unsaturated ketones,[11b] as well as rhodium-catalysed cross-coupling of pyrazoles with alkynes or allenes,[12a,b] and gold-catalyzed cross-coupling of aryldiazoacetate with styryldiazoacetate.[12c] However, these above approaches are usually suffered from poor regioselectivity. Therefore, developing an efficient approach for the synthesis of N-arylpyrazoles from easily available starting materials with a simple operation is still highly desirable.

N-Tosylhydrazones have been employed as precursors of diazo for the formation of C-C, C-N, C-B, C-O and C-Si bonds by Barluenga,[13] Valdés,[14] Wang[15] and Jiang.[16] The reductive coupling of *N*-tosylhydrazones with alcohols or phenols giving ethers was reported by Barluenga and coworkers (Scheme

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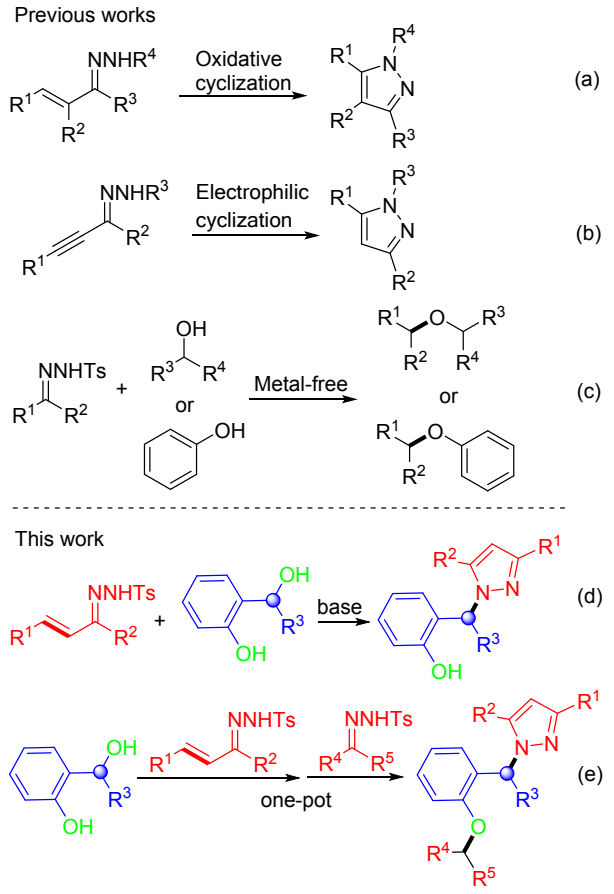
† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

1c).[13c] *ortho*-Quinone methides (o-QMs) generated in situ from *o*-hydroxybenzyl alcohols, as a class of versatile building blocks,[17] have wide applications in conjugate addition and cycloaddition reaction.[18] We envisioned that an approach could be developed for constructing *N*-*sec*-alkylpyrazoles from α,β-unsaturated *N*-tosylhydrazones and *o*-hydroxybenzyl alcohols *via* a cyclization/conjugate addition cascade reaction (Scheme 1d). Moreover, if the one-pot reaction between α,β-unsaturated *N*-tosylhydrazone, *ortho*-hydroxybenzyl alcohol and saturated *N*-tosylhydrazone was conducted, the desired product containing both pyrazole and ether group might be obtained (Scheme 1e).



Scheme 1. Some strategies for the synthesis of *N*-substituted pyrazoles or ethers using *N*-toshydrazones.

Despite using *o*-QM intermediates as substrates in conjugate addition and cyclization reaction has been well-established to date, the use of α,β-unsaturated diazo for constructing pyrazole rings at the benzylic position of *o*-QM intermediates has not been established yet.[17,18] Continuing with our interests in diazo chemistry,[19] herein, we report a metal-free reaction of α,β-unsaturated diazo with *o*-QM intermediates to provide a promising route to *N*-*sec*-alkylpyrazoles. Very interestingly, the desired products contain three or two (hetero)aryl ring at the same carbon atom (triarylmethanes and 1,1-diarylalkanes), which are found in various biologically active compounds.[20] Thus, this strategy offers a new route to triarylmethanes.

Results and discussion

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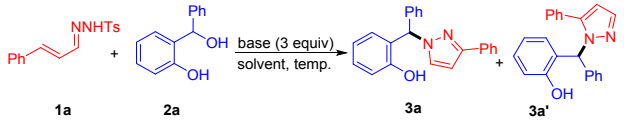
We started our investigations with the model reaction of α,β-unsaturated *N*-tosylhydrazone **1a** and *ortho*-hydroxybenzyl alcohol **2a**. The reaction of **1a** (1.1 equiv) and **2a** (1.0 equiv) in the presence of Cs_2CO_3 (3.0 equiv) in 1,4-dioxane was first attempted at 60 °C for 12 hours, giving the *N*-alkyl pyrazole **3a** as major isomer (**3a**/**3a**'>20:1, determined by ^{1}H NMR spectroscopy on the crude reaction mixture, see the SI for details) in 70% yield (Table 1, entry 1). Both K_2CO_3 and Na_2CO_3 could furnish the desired product in 68% and 55% yields in 1,4-dioxane (entries 2 and 3). Use of other solvents, such as THF, toluene and 1, 2-dichloroethane were found to be inferior (entries 4-6). Very interestingly, when the reaction temperature was increased to 90 °C, the best yield of **3a** could be obtained in 92% yield and with >20:1 regioselectivity only for 4 hours (entry 7). It is noted that this reaction proceeded simply by heating both α,β-unsaturated *N*-tosylhydrazones and *ortho*-hydroxybenzyl alcohols in 1,4-dioxane to provide the valuable triarylmethanes.[20]

Table 1. Optimization of reaction conditions



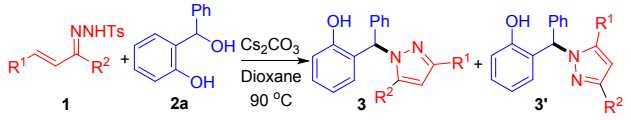
entry[a]	base	solvent/temp(°C)	**3a** yield (%)[b]	**3a**/**3a**'[c]
1	Cs_2CO_3	1,4-dioxane/60	70	>20:1
2	K_2CO_3	1,4-dioxane/60	68	>20:1
3	Na_2CO_3	1,4-dioxane/60	55	>20:1
4	Cs_2CO_3	THF/60	62	>20:1
5	Cs_2CO_3	Toluene/60	48	>20:1
6	Cs_2CO_3	$(CH_2Cl)_2$/60	23	>20:1
7[d]	Cs_2CO_3	1,4-dioxane/90	92	>20:1

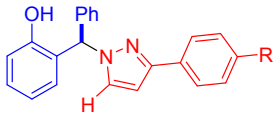
[a]Reaction conditions: α,β-unsaturated *N*-tosylhydrazone **1a** (0.22 mmol, 1.1 equiv), *ortho*-hydroxybenzyl alcohol **2a** (0.2 mmol, 1 equiv), base (0.6 mmol, 3.0 equiv) in 1 mL solvent for 12 hours. [b]Isolated yield. [c]Determined by ^{1}H NMR analysis of the crude reaction mixture. [d]For 4 hours.

With the established conditions in hand (Table 1, entry 7), a variety of α,β-unsaturated *N*-tosylhydrazones **1** derived from enals (or enones) and *ortho*-hydroxybenzyl alcohols **2a** were subjected to the cascade reaction (Scheme 2). The electronic effects of different substituents on the aromatic ring of α,β-unsaturated *N*-tosylhydrazones were evaluated. In fact, the presence of both electron-donating and electron-withdrawing groups at the *ortho*, *meta*, and *para* positions afforded the corresponding products **3b**-**i** in good to excellent yields and with >20:1 regioselectivity. The heteroaromatic substituents, such as thiophen-2-yl α,β-unsaturated *N*-tosylhydrazone, provided the expected product **3j** in 91% yield and with 8:1 regioselectivity. The *N*-Boc-protected 2-methyl-3-indolyl α,β-unsaturated *N*-tosylhydrazone could give the expected product **3k** in 95% yield with >20:1 regioselectivity (entry 11). However, no desired products were detected by using the α,β-unsaturated *N*-tosylhydrazones derived from (*E*)-but-2-enal

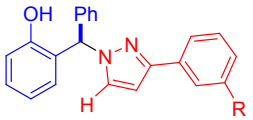
and (*E*)-5-methylhexa-2,4-dienal as substrates, which may be due to their instability of alkyl diazo intermediates at 90 °C. To our delight, when R^2 was methyl group, the corresponding product **3l** was afforded in 90% yield with >20:1 regioselectivity. However, when R^2 was phenyl, it failed to obtain the desired product because the corresponding 3,5-diphenyl-1*H*-pyrazole intermediate was difficult to react with the *o*-QM intermediate for its larger steric hindrance in the step of aza-Michael addition.

Scheme 2. Substrate scope of α,β-unsaturated N-tosylhydrazones **1**[a]

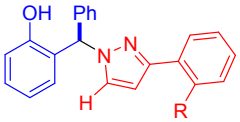




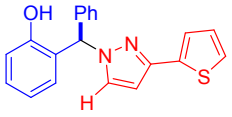
R = H, **3a**, 92% yield,[b] **3a/3a'** > 20:1[c]
R = Br, **3b**, 97% yield, **3b/3b'** > 20:1
R = CF_3, **3c**, 93% yield, **3c/3c'** > 20:1
R = Me, **3d**, 95% yield, **3d/3d'** > 20:1
R = MeO, **3e**, 94% yield, **3e/3e'** > 20:1



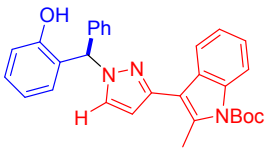
R = Cl, **3f**, 94% yield, **3f/3f'** > 20:1
R = Me, **3g**, 92% yield, **3g/3g'** > 20:1



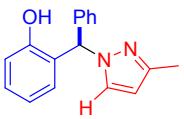
R = Cl, **3h**, 95% yield, **3h/3h'** > 20:1
R = MeO, **3i**, 91% yield, **3i/3i'** > 20:1



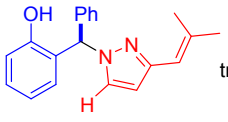
3j, 91% yield, **3j/3j'** = 8:1



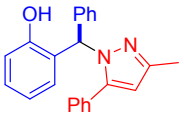
3k, 95% yield, **3k/3k'** > 20:1

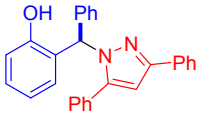


trace



trace



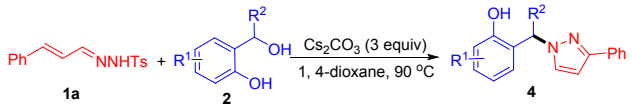


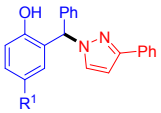
3l, 90% yield, **3l/3l'** > 20:1 trace

[a]Reaction conditions: α,β-unsaturated *N*-tosylhydrazones **1** (0.22 mmol, 1.1 equiv), *ortho*-hydroxybenzyl alcohol **2a** (0.2 mmol, 1.0 equiv), Cs_2CO_3 (0.6 mmol, 3.0 equiv) in 1 mL 1,4-dioxane for 4-8 h. [b]Isolated yield. [c]Determined by ^1H NMR analysis of the crude reaction mixture.

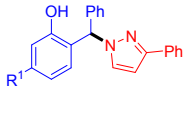
Next, we explored the scope of *ortho*-hydroxybenzyl alcohols **2** with different substitution patterns as shown in Scheme 3. Firstly, a variety of substituted groups on the phenol moiety were employed as the substrates **2a**-**i**, giving the corresponding products **4a**-**j** in excellent yields (92-98%). Both electron-rich groups (Me, MeO, ^{t}Bu) and electron-poor groups (F, Cl, Br) were proved to be suitable substrates. The reaction also worked well with 1-naphthyl *ortho*-hydroxybenzyl alcohols, albeit affording the expected N-alkyl pyrazole **4j** with slightly diminished yield (88%). Then, the different substituents R^2, such as aromatic (**2k**-**m**), hydrogen (**2n**) and aliphatic (**2o** and **2p**) group, were studied. Obviously, when the aryl groups served as competent R^2 substituents of *ortho*-hydroxybenzyl alcohols **2,** the desired products **4k**-**m** were obtained in excellent yields. Notably, substrates **2n**-**p** bearing H, ethyl or cyclopropyl group could also successfully take part in the reaction to give the corresponding products **4n**-**p** in 88%, 96% and 90% yield, respectively. It is noted that these reactions (as shown Scheme 3) provided the desired products in excellent regioselectivity (>20:1). The structure of **4l** was confirmed by X-ray crystal structure analysis (Scheme 2, see the SI for details).[21]

Scheme 3. Substrate scope of *ortho*-hydroxybenzyl alcohols 2[a]

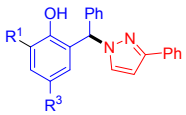




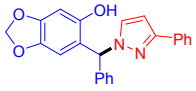
R^1 = F, **4a**, 94%[b]
R^1 = Br, **4b**, 93%
R^1 = Me, **4c**, 96%



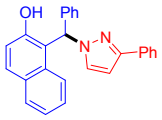
R^1 = Cl, **4d**, 93%
R^1 = Me, **4e**, 95%
R^1 = OMe, **4f**, 96%



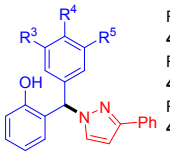
R^1 = Me, R^3 = H, **4g**, 98%
R^1 = R^3 = ^{t}Bu, **4h**, 95%



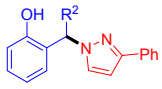
4i, 92%



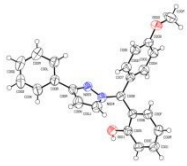
4j, 88%



R^4 = Me, R^3 = R^5 = H, **4k**, 96%
R^4 = OMe, R^3 = R^5 = H, **4l**, 94%
R^4 = R^3 = R^5 = F **4m**, 90%



R^2 = H, **4n**, 88%
R^2 = Ethyl, **4o**, 96%
R^2 = Cyclopropyl, **4p**, 90%



≡ **4l**

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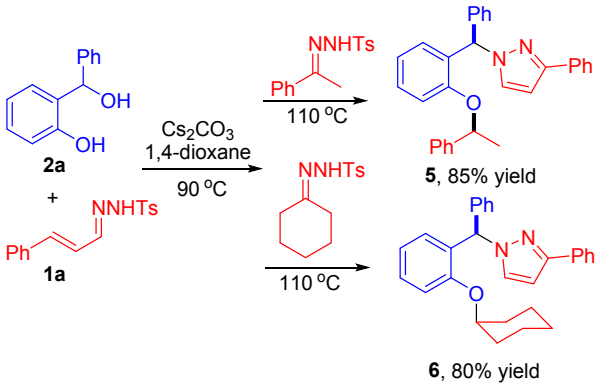
[a]Reaction conditions: α,β-unsaturated N-Tosylhydrazone **1a** (0.22 mmol, 1.1 equiv), *ortho*-hydroxybenzyl alcohol **2** (0.2 mmol, 1.0 equiv), Cs_2CO_3 (0.6 mmmol, 3.0 equiv) in 1 mL 1,4-dioxane for 4-8 h. [b]Isolated yield.

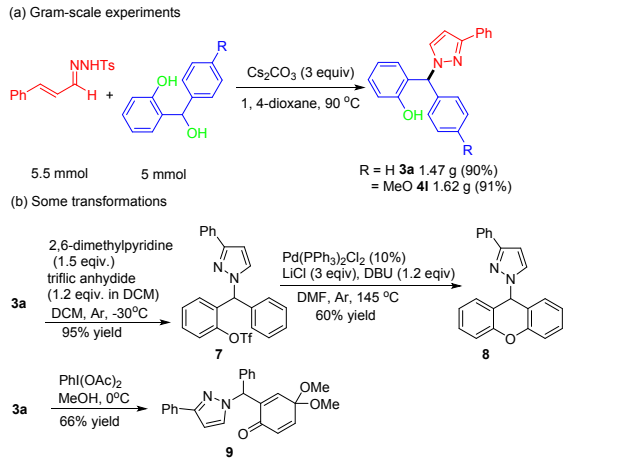


Scheme 4. Three-component reaction of α,β-unsaturated *N*-tosylhydrazone, *ortho*-hydroxybenzyl alcohols and saturated *N*-tosylhydrazones.

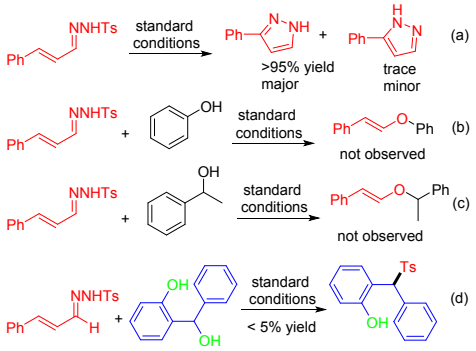
We investigated whether the reactions could be carried out in a one-pot fashion by mixing of α,β-unsaturated *N*-

tosylhydrazones, *ortho*-hydroxybenzyl alcohols with saturated *N*-tosylhydrazones (Scheme 4). It was possible by heating α,β-unsaturated *N*-tosylhydrazone and *ortho*-hydroxybenzyl alcohol at 90 °C prior to the addition of 4-methyl-N'-(1-phenylethylidene)benzene-sulfonohydrazide and N'-cyclohexylidene-4-methylbenzene-sulfonohydrazide, and then the desired products **5** and **6** were afforded in 85% and 80% yields by heating at 110 °C, respectively (see the SI for details).

We attempted the scaled-up synthesis pyrazoles for practical purposes. The reaction using 5.5 mmol of **1a** provided the products **3a** (1.47g, 90% yield) and **4l** (1.62g, 91% yield), respectively, without any significant decrease in its efficiency (Scheme 5 a, see the SI for details). Since **3a** has a hydroxyl functionality, we conducted some transformations to explore the versatility of the method (Scheme 5 b). **3a** was converted to the corresponding triflate ester **7** in 95% yield by treating with trifluoromethanesulfonic acid anhydride and 2,6-dimethylpyridine. Then, an intramolecular aryl sulflate-arene coupling mediated by $Pd(PPh_3)_2Cl_2$ was employed as a key step in the synthesis of 3-phenyl-1-(9H-xanthen-9-yl)-1*H*-pyrazole **8** in 60% yield. Oxidation of **3a** with $PhI(OAc)_2$ in MeOH afforded the cyclohexadienone **9** in 66% yield.



Scheme 5. Gram-scale experiments and synthetic utility.



Scheme 6. Some complementary experiments.

To gain insight into the mechanism, some experiments were carried out as shown in Scheme 6. The α,β-unsaturated *N*-tosylhydrazone **1a** was easily transformed to 3-phenyl-1*H*-pyrazole as a major product in >95% yield under standard conditions, and the isomer product 5-phenyl-1*H*-pyrazole was observed in trace (< 5% yield) on the ^1H NMR spectroscopy of the crude reaction mixture (Scheme 6 a, see the SI for details). The C-O bond-forming reaction between α, β-unsaturated *N*-tosylhydrazone **1a** and phenol (or alcohol) didn't occur (Scheme 6 b and c). It indicated that the α,β-unsaturated carbene didn't form. The other side product 2-(phenyl(tosyl)methyl)phenol (Scheme 6 d) was observed in trace on the TLC under standard conditions because it is also easily transformed to *ortho*-Quinone methides intermediate under basic condition.

Based on the previous works[19c] and our experimental observations, a plausible mechanism was proposed as illustrated in Figure 2. The α, β-unsaturated diazo substrate **A** is generated in situ from α, β-unsaturated *N*-tosylhydrazone **1a** by treating with Cs_2CO_3. Then the 3-Phenyl-3H-pyrazole B is formed *via* an intermolecular cyclization. The major intermediate 3-phenyl-1H-pyrazole **C** and the minor intermediate 5-phenyl-1H-pyrazole **C'** are easily formed from **B** through proton transfer tautomerization. The 3-phenyl-1*H*-pyrazole **C** is a major intermediate due to its larger conjugation than that of **C'**.[19c] The *o*-QM intermediate is formed in *situ* from *ortho*-hydroxybenzyl alcohols. The following aza-Michael addition reaction of **C** (**C'**) with *o*-QM intermediate provides the final product **3a** or **3a'**.

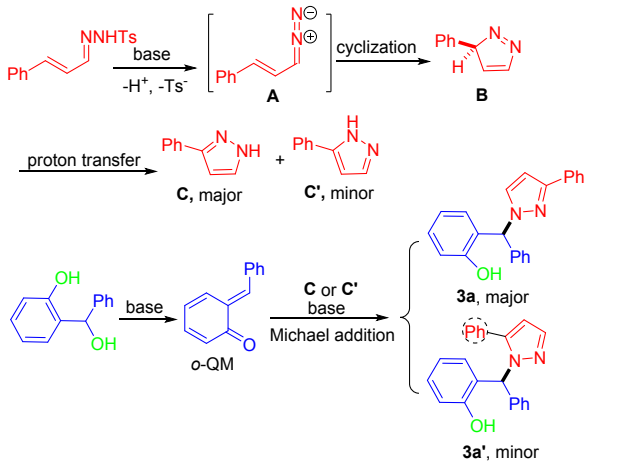


Figure 2. Proposed mechanism for this cascade reaction.

Experimental

General information. ^1H NMR spectra were determined on a 400 MHz spectrometer in $CDCl_3$ solution. Chemical shifts are expressed in parts per million (δ), and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet), and coupling constants J were given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ solution. Chemical shifts are expressed in parts per million (δ) and are referenced to $CDCl_3$ (δ = 77.16) as an internal standard. TLC was done on silica gel coated glass slide (Silica gel G for TLC). Silica gel (60-120 mesh) was used for column chromatography. Petroleum

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ether refers to the fraction boiling in the range of 60-90 °C unless otherwise mentioned. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were commercially purchased. All reactions involving moisture sensitive reactants were executed using oven-dried glassware

General procedure for the synthesis of 2-(phenyl(3-phenyl-1*H*-pyrazol-1-yl)methyl)phenol (3a): α,β-unsaturated *N*-tosylhydrazones **1a** (0.22 mmol), *ortho*-hydroxymethzyl phenols **2a** (0.2 mmol), Cs_2CO_3 (0.6 mmol) and 1,4-dioxane (1 mL) were added into a tube. The mixture was stirred at 90 °C for 4 hours. After cooling to room temperature, the mixture was quenched with NH_4Cl (2 mL, saturated aqueous solution) and extracted with CH_2Cl_2 (3 × 2 mL). The combined organic phase was dried over Na_2SO_4, and then organic solvents were removed in *vacuo.* The residue was purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether (1:15-1:10, V/V) as the eluent to give the compounds **3a** (60mg, 92% yield) as white solid.

Typical procedure for the synthesis of 3a on gram scale: α,β-unsaturated tosylhydrazones **1a** (5.5 mmol), *ortho*-hydroxymethzyl phenols **2a** (5 mmol), Cs_2CO_3 (15 mmol) were suspended in 1,4-dioxane (10 mL) in a flask. The resulting solution was stirred at 90 °C for 4 hours. After cooling to room temperature, the mixture was quenched with NH_4Cl (40 mL, saturated aqueous solution) and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phase was dried over Na_2SO_4, and then the solvent was removed in *vacuo* to give a residue. The residue was purified by flash column chromatography (EtOAc/hexane) to give the compounds **3a** (1.47g, 90% yield).

Typical procedure of the three-component reaction for the synthesis of product 5: α,β-unsaturated tosylhydrazones **1** (0.11 mmol), *ortho*-hydroxymethzyl phenols **2** (0.1 mmol), Cs_2CO_3 (0.4 mmol) and 1,4-dioxane (0.5 mL) were added into a tube. The mixture was stirred at 90 °C for 4 hours. Next, (*E*)-4-methyl-N'-(1-phenylethylidene)benzenesulfonohydrazide (0.1 mmol) was added. The system was heated at 110 °C with stirring and refluxing. When the reaction was completed, the reaction mixture was cooled to room temperature, and the solvent was eliminated under reduced pressure. 2mL NaOH solution (2M) and 2mL dichloromethane were added to the residue. The aqueous phase was extracted three times with dichloromethane. The combined organic layer was washed with brine and dried over Na_2SO_4. The organic solvent was removed under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane) to give the compounds **5** (37mg, 85% yield) as white solid.

2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (3a): R_f = 0.46 (EtOAc/PE = 1:5), yield: 90%, white solid. m.p. 153-154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.01 (s, 1H), 7.79 (d, *J* = 7.5Hz, 2H), 7.73 (s, 1H), 7.43-7.40 (m, 2H), 7.36-7.27 (m, 6H), 7.03 (d, *J* = 8.1Hz, 1H), 6.91-6.90 (m, 3H), 6.69 (s, 1H), 6.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.8, 152.0, 138.9, 132.6, 131.2, 130.7, 129.2, 128.8, 128.7, 128.5, 128.3, 127.7, 126.3, 125.7, 120.0, 119.9, 102.6, 69.5. HRMS calcd for $C_{22}H_{18}N_2O$ $[M+Na]^+$ 349.1317, found: 349.1315.

2-((3-(4-bromophenyl)-1H-pyrazol-1-yl)(phenyl)methyl)-phenol (3b): R_f = 0.37 (EtOAc/PE = 1:5), yield: 95%, yellow solid. m.p. 170-171 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.62 (s, 1H), 7.72 (d, *J* = 2.4Hz, 1H), 7.61 (d, *J* = 8.6Hz, 2H), 7.50 (d, *J* = 8.6Hz, 2H), 7.33-7.27 (m, 2H), 7.26-7.24 (m, 3H), 7.02-7.00 (m, 1H), 6.95-6.91 (m, 1H), 6.87-6.85 (m, 2H), 6.63 (d, *J* = 2.4Hz, 1H), 6.45 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 115.8, 151.0, 138.7, 132.8, 131.9, 131.3, 131.1, 130.9, 128.5, 127.9, 127.3, 126.2, 125.2, 122.3, 120.0, 119.9, 102.7, 69.7. HRMS calcd for $C_{22}H_{17}BrN_2O$ $[M+Na]^+$ 427.0422, found: 427.0420.

2-(phenyl(3-(4-(trifluoromethyl)phenyl)-1H-pyrazol-1-yl)methyl)phenol (3c): R_f = 0.58 (EtOAc/PE = 1:5), yield: 93%, white solid. m.p. 178-179°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.29 (s, 1H), 7.76 (d, *J* = 8.1Hz, 2H), 7.62 (s, 1H), 7.54 (d, *J* = 8.1Hz, 2H), 7.20-7.18 (m, 4H), 7.14-7.11 (m, 1H), 6.89-6.87 (m, 1H), 6.84-6.81 (m, 3H), 6.61 (d, *J* = 2.4Hz, 1H), 6.47 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.5, 150.6, 138.6, 135.6, 132.9, 131.1, 130.8, 128.7, 128.6, 128.0, 126.8, 126.4, 126.0, 125.8, 120.1, 119.6, 117.3, 103.2, 69.3. HRMS calcd for $C_{23}H_{17}F_3N_2O$ $[M+Na]^+$ 417.1191, found: 417.1192.

2-(phenyl(3-(p-tolyl)-1H-pyrazol-1-yl)methyl)phenol (3d): R_f = 0.50 (EtOAc/PE = 1:5), yield: 95%, white solid. m.p. 161-163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.08 (s, 1H), 7.69-7.63 (m, 3H), 7.27-7.24 (m, 5H), 7.19-7.18 (m, 2H), 7.02-7.00 (m, 1H), 6.93-6.90 (m, 1H), 6.87-6.85 (m, 2H), 6.62 (s, 1H), 6.42 (s, 1H), 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.0, 152.1, 139.1, 138.2, 132.5, 131.3, 130.8, 129.4, 129.3, 128.5, 127.7, 126.2, 125.7, 125.5, 120.0, 119.8, 102.4, 69.7, 21.3. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1471.

2-((3-(4-methoxyphenyl)-1H-pyrazol-1-yl)(phenyl)methyl)-phenol (3e): R_f = 0.33 (EtOAc/PE = 1:5), yield: 92%, white solid. m.p. 180-183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.12 (s, 1H), 7.68-7.66 (m, 3H), 7.37-7.35 (m, 2H), 7.25-7.24 (m, 3H), 6.99 (d, *J* = 8.0Hz, 1H), 6.94-6.90 (m, 3H), 6.87-6.85 (m, 2H), 6.57 (d, *J* = 2.0Hz, 1H), 6.41 (s, 1H), 3.80 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 159.8, 155.9, 151.8, 139.1, 132.6, 131.3, 130.8, 128.7, 128.5, 127.1, 126.8, 126.2, 120.0, 119.9, 117.3, 114.2, 102.1, 69.6, 55.3. HRMS calcd for $C_{23}H_{20}N_2O_2$ $[M+Na]^+$ 379.1422, found: 379.1429

2-((3-(3-chlorophenyl)-1H-pyrazol-1-yl)(phenyl)methyl)phenol (3f): R_f = 0.50 (EtOAc/PE = 1:5), yield: 92%, yellow solid. m.p. 133-135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.45 (s, 1H), 7.69-7.68 (m, 2H), 7.63-7.61 (m, 1H), 7.37-7.30 (m, 3H), 7.25-7.20 (m, 3H), 6.99-6.99 (m, 1H), 6.98 (d, *J* = 8.0Hz, 1H), 6.93-6.90 (m, 3H), 6.62 (d, *J* = 2.2Hz, 1H), 6.49 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.6, 150.7, 138.6, 134.7, 132.8, 131.2, 130.9, 130.1, 128.7, 128.6, 128.3, 127.9, 126.8, 126.4,

125.9, 123.9, 120.1, 117.3, 103.0, 69.5. HRMS calcd for $C_{22}H_{17}ClN_2O$ $[M+Na]^+$ 383.0927, found: 383.0927.

2-(phenyl(3-(m-tolyl)-1H-pyrazol-1-yl)methyl)phenol (3g): R_f = 0.63 (EtOAc/PE = 1:5), yield: 90%, yellow solid. m.p. 128-130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.98 (s, 1H), 7.71 (s, 1H), 7.55 (d, *J* = 7.0Hz, 2H), 7.32-7.25 (m, 6H), 7.12 (d, *J* = 7.3Hz, 1H), 7.02 (d, *J* = 7.9Hz, 1H), 6.94-6.90 (m, 1H), 6.85 (d, *J* = 3.1Hz, 2H), 6.64 (s, 1H), 6.42 (s, 1H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.9, 152.1, 139.0, 138.4, 132.5, 131.9, 131.4, 130.8, 129.1, 128.7, 128.5, 127.7, 126.4, 126.2, 125.4, 122.9, 120.0, 119.8, 102.6, 69.7, 21.5. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1475.

2-((3-(2-chlorophenyl)-1H-pyrazol-1-yl)(phenyl)methyl)phenol (3h): R_f = 0.50 (EtOAc/PE = 1:5), yield: 91%, yellow solid. m.p. 143-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.61 (s, 1H), 7.90 (s, 1H), 7.74 (s, 1H), 7.38-7.30 (m, 5H), 7.28-7.25 (m, 4H), 6.89-6.84 (m, 3H), 6.46 (s, 1H), 5.98 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.5, 149.5, 141.8, 138.9, 131.8, 131.4, 130.8, 130.5, 129.3, 128.7, 128.5, 128.2, 127.8, 127.0, 126.8, 126.2, 119.9, 117.3, 106.8, 69.7. HRMS calcd for $C_{22}H_{17}ClN_2O$ $[M+Na]^+$ 383.0927, found: 383.0930.

2-((3-(2-methoxyphenyl)-1H-pyrazol-1-yl)(phenyl)methyl)-phenol (3i): R_f = 0.25 (EtOAc/PE = 1:5), yield: 88%, yellow solid. m.p. 140-143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.27 (s, 1H), 7.78 (d, *J* = 7.7Hz, 1H), 7.71 (d, *J* = 2.3Hz, 1H), 7.38-7.34 (m, 1H), 7.32-7.28 (m, 2H), 7.25-7.22 (m, 3H), 7.01 (d, *J* = 8.6Hz, 1H), 6.97-6.96 (m, 1H), 6.94-.91 (m, 1H), 6.88 (d, *J* = 2.4Hz, 1H), 6.86-6.84 (m, 3H), 6.40 (s, 1H), 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.8, 156.1, 148.9, 139.2, 131.6, 131.4, 130.8, 129.3, 128.7, 128.4, 127.7, 126.8, 126.2, 120.9, 120.2, 119.8, 117.3, 111.4, 106.4, 69.8, 55.4. HRMS calcd for $C_{23}H_{20}N_2O_2$ $[M+Na]^+$ 379.1422, found: 379.1419.

2-(phenyl(3-(thiophen-2-yl)-1H-pyrazol-1-yl)methyl)phenol (3j): R_f = 0.37 (EtOAc/PE = 1:5), yield: 88%, white solid. m.p. 83-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.38 (s, 1H), 7.92 (s, 1H), 7.62 (d, *J* = 2.4Hz, 1H), 7.38-7.37 (m, 1H), 7.36-7.34 (m, 1H), 7.27-7.27 (m, 1H), 7.25-7.25 (m, 2H), 7.18-7.16 (m, 2H), 7.03-7.01 (m, 1H), 6.97-6.95 (m, 1H), 6.91-6.90 (m, 2H), 6.52 (d, *J* = 2.4Hz, 1H), 6.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.7, 138.7, 135.3, 132.5, 130.7, 128.7, 128.5, 128.3, 128.2, 127.9, 127.6, 126.8, 126.5, 124.4, 119.7, 117.3, 102.7, 69.1. HRMS calcd for $C_{20}H_{16}N_2OS$ $[M+Na]^+$ 355.0881, found: 355.0880.

tert-butyl3-(1-((2-hydroxyphenyl)(phenyl)methyl)-1H-pyrazol-3-yl)-2-methyl-1H-indole-1-carboxylate (3k): R_f = 0.55 (EtOAc/PE = 1:5), yield: 94%, yellow solid. m.p. 185-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.84 (s, 1H), 8.13 (d, *J* = 8.1Hz, 1H), 7.85 (s, 1H), 7.62 (d, *J* = 7.3Hz, 1H), 7.33-7.27 (m, 5H), 7.23-7.18 (m, 2H), 7.01-6.93 (m, 2H), 6.85 (d, *J* = 7.0Hz, 2H), 6.59 (s, 1H), 6.46 (s, 1H), 2.68 (s, 3H), 1.68 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.0, 150.7, 146.3, 145.6, 139.3, 136.0, 135.7, 132.0, 131.5, 130.9, 128.5, 127.8, 126.1, 125.5, 123.9, 123.1, 120.3, 119.9, 119.0, 115.4, 112.5, 106.0, 84.0, 70.0, 28.3, 15.1. HRMS calcd for $C_{30}H_{29}N_3O_3$ $[M+Na]^+$ 502.2107, found: 502.2100.

2-((5-methyl-3-phenyl-1H-pyrazol-1-yl)(phenyl)methyl)phenol (3l): R_f = 0.50 (EtOAc/PE = 1:5), yield: 87%, white solid. m.p. 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.52 (s, 1H), 7.73-7.70 (m, 2H), 7.39-7.32 (m, 3H), 7.30-7.22 (m, 5H), 7.06-7.04 (m, 1H), 6.95-6.91 (m, 1H), 6.82-6.79 (m, 2H), 6.46-6.46 (m, 1H), 6.38 (s, 1H), 2.50 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.5, 150.2, 141.2, 139.2, 132.1, 131.8, 130.9, 128.7, 128.5, 128.2, 127.6, 126.0, 125.7, 125.3, 120.4, 119.7, 102.8, 65.9, 11.4. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1471.

4-fluoro-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4a): R_f = 0.45 (EtOAc/PE = 1:5), yield: 93%, yellow solid. m.p. 176-178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.74 (s, 1H), 7.75 (m, 2H), 7.62 (s, 1H), 7.40-7.36 (m, 2H), 7.33-7.28 (m, 4H), 6.95-6.80 (m, 5H), 6.66 (d, *J* = 2.3Hz, 1H), 6.52 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 157.4, 155.0, 152.2, 151.6, 138.1, 132.6, 132.0, 128.8, 128.6, 128.4, 128.1, 126.7, 125.8, 120.2, 116.8, 116.6, 102.8, 68.3. HRMS calcd for $C_{22}H_{17}FN_2O$ $[M+Na]^+$ 367.1223, found: 367.1220.

4-bromo-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4b): R_f = 0.52 (EtOAc/PE = 1:5), yield: 91%, yellow solid. m.p. 188-189 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.19 (s, 1H), 7.75-7.73 (m, 2H), 7.66 (m, 1H), 7.40-7.36 (m, 3H), 7.35-7.31 (m, 3H), 7.28-7.27 (m, 2H), 6.96-6.89 (m, 2H), 6.82-6.75 (m, 1H), 6.66 (d, *J* = 2.3Hz, 1H), 6.45(s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.0, 152.2, 138.1, 133.3, 132.7, 130.7, 128.9, 128.6, 128.1, 127.4, 126.8, 126.5, 125.8, 121.5, 119.2, 111.5, 102.9, 68.5. HRMS calcd for $C_{22}H_{17}BrN_2O$ $[M+Na]^+$ 427.0422, found: 427.0419.

4-methyl-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4c): R_f = 0.37 (EtOAc/PE = 1:5), yield: 95%, yellow solid. m.p. 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.62 (s, 1H), 7.67-7.65 (m, 2H), 7.60 (d, *J* = 2.3Hz, 1H), 7.30-7.27 (m, 2H), 7.22 (d, *J* = 7.3Hz, 1H), 7.18-7.14 (m, 3H), 7.01-6.97 (m, 2H), 6.83-6.79 (m, 3H), 6.55 (d, *J* = 2.3Hz, 1H), 6.30 (s, 1H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.4, 152.0, 139.1, 132.6, 132.1, 131.8, 131.3, 129.1, 128.8, 128.5, 128.3, 127.8, 126.3, 125.8, 125.1, 119.8, 102.6, 69.7, 20.4. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1472.

5-chloro-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4d): R_f = 0.46 (EtOAc/PE = 1:5), yield: 91%, white solid. m.p. 172-173 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.40 (s, 1H), 7.75-7.73 (m, 2H), 7.66 (d, *J* = 2.3 Hz, 1H), 7.40-7.39 (m, 2H), 7.33-7.31 (m, 1H), 7.30-7.26 (m, 3H), 7.25 (s, 1H), 6.93-6.87 (m, 4H), 6.66 (d, *J* = 2.3 Hz, 1H), 6.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.7, 152.1, 138.3, 135.8, 132.6, 131.8, 131.6, 128.8, 128.6, 128.5, 128.1, 126.4, 125.8, 124.1, 120.0, 119.9, 102.8, 68.7. HRMS calcd for $C_{22}H_{17}ClN_2O$ $[M+Na]^+$ 383.0927, found: 383.0929.

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5-methyl-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4e): R_f = 0.45 (EtOAc/PE = 1:5), yield: 94%, yellow solid. m.p. 143-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.85 (s, 1H), 7.74 (d, *J* = 7.3Hz, 2H), 7.63-7.62 (m, 1H), 7.37-7.34 (m, 2H), 7.30-7.22 (m, 4H), 7.07 (d, *J* = 7.6Hz, 1H), 6.89-6.88 (m, 2H), 6.78 (s, 1H), 6.71-6.70 (m, 1H), 6.61 (d, *J* = 2.3Hz, 1H), 6.44 (s, 1H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.6, 152.0, 140.9, 139.2, 132.5, 132.2, 130.9, 128.8, 128.5, 128.3, 127.8, 126.4, 125.8, 122.6, 120.6, 120.3, 102.6, 69.1, 21.2. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1475.

5-methoxy-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)-phenol (4f): R_f = 0.40 (EtOAc/PE = 1:5), yield: 96%, yellow solid. m.p. 124-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.19 (s, 1H), 7.76-7.72 (m, 3H), 7.40-7.36 (m, 2H), 7.32 (d, *J* = 7.3Hz, 1H), 7.26-7.24 (m, 2H), 7.18-7.16 (d, *J* = 8.1Hz, 2H), 6.86-6.84 (m, 2H), 6.65 (d, *J* = 2.4Hz, 1H), 6.59 (d, *J* = 2.5Hz, 1H), 6.50-6.47 (m, 1H), 6.36 (s, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 161.8, 157.2, 151.9, 139.4, 132.5, 132.1, 132.0, 128.8, 128.4, 128.3, 127.7, 126.1, 125.8, 117.9, 106.1, 104.9, 102.5, 69.3, 55.3. HRMS calcd for $C_{23}H_{20}N_2O_2$ $[M+Na]^+$ 379.1422, found: 379.1425.

2-methyl-6-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4g): R_f = 0.72 (EtOAc/PE = 1:5), yield: 97%, white solid. m.p. 178-179°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.90 (s, 1H), 7.77-7.71 (m, 3H), 7.41-7.29 (m, 3H), 7.24-7.12 (m, 5H), 6.85-6.82 (m, 3H), 6.65 (d, *J* = 2.1Hz, 1H), 6.39 (s, 1H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.1, 152.0, 139.2, 132.6, 132.2, 132.0, 129.2, 128.9, 128.8, 128.4, 128.3, 127.7, 126.1, 125.8, 125.0, 119.4, 102.6, 70.0, 16.6. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1472.

2,4-di-tert-butyl-6-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)-phenol (4h): R_f = 0.38 (EtOAc/PE = 1:30), yield: 95%, yellow solid. m.p. 144-145°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.86 (s, 1H), 7.75-7.73 (m, 3H), 7.40-7.34 (m, 3H), 7.29-7.19 (m, 4H), 7.14 (d, *J* = 1.8Hz, 1H), 6.83-6.82 (m, 2H), 6.64-6.63 (m, 1H), 6.36 (s, 1H), 1.43 (s, 9H), 1.33 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.6, 151.8, 141.5, 139.6, 139.5, 132.7, 132.3, 128.8, 128.3, 128.2, 127.6, 126.5, 126.1, 125.7, 125.4, 125.2, 102.5, 70.9, 31.8, 29.9. HRMS calcd for $C_{30}H_{34}N_2O_2$ $[M+Na]^+$ 461.2569, found: 461.2571.

6-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)benzo[d][1,3]-dioxol-5-ol (4i): R_f = 0.30 (EtOAc/PE = 1:5), yield: 90%, yellow solid. m.p. 163-165°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.70 (s, 1H), 7.75 (d, *J* = 7.5Hz, 2H), 7.66 (d, *J* = 2.2Hz, 1H), 7.40-7.37 (m, 2H), 7.33-7.26 (m, 5H), 6.92-6.90 (m, 2H), 6.70 (s, 1H), 6.65 (d, *J* = 2.2Hz, 1H), 6.52 (s, 1H), 5.94 (s, 1H), 5.89 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.0, 151.3, 149.0, 140.9, 139.0, 132.4, 132.1, 128.8, 128.5, 128.3, 127.8, 126.3, 125.8, 117.2, 109.9, 102.6, 101.7, 101.3, 68.9. HRMS calcd for $C_{23}H_{18}N_2O_3$ $[M+Na]^+$ 393.1215, found: 393.1214.

3-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)naphthalen-2-ol (4j): R_f = 0.58 (EtOAc/PE = 1:5), yield: 86%, white solid. m.p. 174-176°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.53 (s, 1H), 8.05 (d, *J* = 8.7Hz, 1H), 7.81-7.75 (m, 3H), 7.71-7.69 (m, 2H), 7.51-7.42 (m, 2H), 7.34-7.29 (m, 3H), 7.26-7.25 (m, 1H), 7.22-7.20 (m, 1H), 7.17-7.15 (m, 3H), 6.75-6.74 (m, 2H), 6.61 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.2, 151.0, 138.4, 132.1, 132.0, 131.0, 130.1, 128.3, 128.0, 127.7, 127.4, 127.4, 126.5, 126.3, 124.9, 124.8, 122.0, 121.3, 119.3, 116.2, 101.6, 60.5. HRMS calcd for $C_{26}H_{20}N_2O$ $[M+Na]^+$ 399.1473, found: 399.1475.

2-((3-phenyl-1H-pyrazol-1-yl)(p-tolyl)methyl)phenol (4k): R_f = 0.25 (EtOAc/PE = 1:5), yield: 96%, white solid. m.p. 181-182°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.89 (s, 1H), 7.78-7.75 (m, 2H), 7.73 (d, *J* = 2.4Hz, 1H), 7.41-7.37 (m, 2H), 7.33-7.31 (m, 1H), 7.25-7.19 (m, 4H), 7.14 (d, *J* = 6.4Hz, 1H), 6.86-6.82 (m, 3H), 6.66 (d, *J* = 2.4Hz, 1H), 6.40 (s, 1H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.1, 151.9, 139.2, 132.6, 132.2, 132.1, 132.0, 129.2, 128.7, 128.4, 128.3, 127.6, 126.0, 125.7, 124.9, 119.4, 102.5, 70.0, 16.6. HRMS calcd for $C_{23}H_{20}N_2O$ $[M+Na]^+$ 363.1473, found: 363.1469.

2-((4-methoxyphenyl)(3-phenyl-1H-pyrazol-1-yl)methyl)-phenol (4l): R_f = 0.50 (EtOAc/PE = 1:5), yield: 94%, white solid. m.p. 180-184°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.89 (s, 1H), 7.68-7.62 (m, 3H), 7.32-7.28 (m, 2H), 7.24-7.20 (m, 2H), 7.18-7.13 (m, 1H), 6.92 (d, *J* = 7.9Hz, 1H), 6.85-6.81 (m, 1H), 6.75-6.69 (m, 4H), 6.56 (d, *J* = 2.3Hz, 1H), 6.34 (s, 1H), 3.67 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 159.1, 155.9, 151.9, 132.5, 132.1, 131.1, 130.9, 130.7, 128.8, 128.3, 127.6, 125.8, 125.5, 119.9, 119.8, 113.9, 102.5, 69.3, 55.3. HRMS calcd for $C_{23}H_{20}N_2O_2$ $[M+Na]^+$ 379.1422, found: 379.1420.

2-((3-phenyl-1H-pyrazol-1-yl)(3,4,5-trifluorophenyl)methyl)-phenol (4m): R_f = 0.38 (EtOAc/PE = 1:5), yield: 89%, yellow solid. m.p. 200-203°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.78 (s, 1H), 7.68-7.62 (m, 3H), 7.34-7.30 (m, 2H), 7.27-7.22 (m, 2H), 7.16-7.12 (m, 1H), 6.93 (d, *J* = 8.3Hz, 1H), 6.87-6.83 (m, 1H), 6.60 (d, *J* = 2.3Hz, 1H), 6.40-6.36 (m, 2H), 6.24 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.6, 152.7, 152.4, 149.9, 135.6, 132.7, 131.6, 131.5, 131.1, 128.8, 128.6, 125.8, 124.2, 120.3, 110.9, 110.7, 103.1, 68.3. HRMS calcd for $C_{22}H_{15}F_3N_2O$ $[M+Na]^+$ 403.1034, found: 403.1038.

2-((3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4n): R_f = 0.45 (EtOAc/PE = 1:5), yield: 86%, yellow semisolid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.52 (s, 1H), 7.70-7.68 (m, 2H), 7.43 (d, *J* = 2.4Hz, 1H), 7.35-7.31 (m, 2H), 7.27-7.19 (m, 2H), 7.17-7.12 (m, 1H), 6.97-6.94 (m, 1H), 6.82-6.78 (m, 1H), 6.46 (d, *J* = 2.4Hz, 1H), 5.17 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.7, 150.6, 131.1, 129.9, 129.6, 129.1, 127.7, 127.2, 124.6, 122.2, 119.2, 118.0, 101.7, 52.7. HRMS calcd for $C_{16}H_{14}N_2O$ $[M+Na]^+$ 273.1004, found: 273.1001.

2-(1-(3-phenyl-1H-pyrazol-1-yl)propyl)phenol (4o): R_f = 0.37 (EtOAc/PE = 1:5), yield: 96%, white semisolid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.49 (s, 1H), 7.77 (d, *J* = 7.6Hz, 2H), 7.50

(d, *J* = 2.2Hz, 1H), 7.42-7.38 (m, 2H), 7.33-7.30 (m, 1H), 7.25-7.20 (m, 1H), 7.11 (d, *J* = 7.3Hz, 1H), 7.01 (d, *J* = 8.2Hz, 1H), 6.84-6.81 (m, 1H), 6.52 (d, *J* = 2.2Hz, 1H), 5.08-5.04 (m, 1H), 2.56-2.47 (m, 1H), 2.25-2.16 (m, 1H), 0.92-0.88 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.9, 151.3, 132.2, 131.2, 130.1, 129.8, 128.8, 128.2, 125.9, 125.7, 119.8, 119.7, 102.2, 67.7, 35.6, 13.5. HRMS calcd for $C_{18}H_{18}N_2O$ $[M+Na]^+$ 301.1317, found: 301.1320.

2-(cyclopropyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenol (4p): R_f = 0.15 (EtOAc/PE = 1:5), yield: 90%, yellow solid. m.p. 151-152°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.36 (s, 1H), 7.69 (d, *J* = 7.6Hz, 2H), 7.43 (s, 1H), 7.33-7.30 (m, 2H), 7.24-7.21 (m, 1H), 7.14-7.10 (m, 1H), 7.05 (d, *J* = 7.5Hz, 1H), 6.91 (d, *J* = 7.9Hz, 1H), 6.78-6.74 (m, 1H), 6.47 (s, 1H), 4.26 (d, *J* = 10.0Hz, 1H), 2.03 (s, 1H), 0.64 (d, *J* = 4.0Hz, 2H), 0.31 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.8, 151.2, 132.2, 130.2, 130.1, 128.9, 128.8, 128.2, 126.3, 125.7, 119.8, 119.4, 102.3, 71.1, 14.4, 5.64, 5.42. HRMS calcd for $C_{19}H_{18}N_2O$ $[M+Na]^+$ 313.1317, found: 313.1320.

3-phenyl-1-(phenyl(2-(1-phenylethoxy)phenyl)methyl)-1H-pyrazole (5): R_f = 0.78 (EtOAc/PE = 1:10), yield: 85%, white solid. m.p. 126-128°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.78-7.75 (m, 2H), 7.73-7.72 (m, 1H), 7.44-7.41 (m, 2H), 7.40-7.38 (m, 2H), 7.34-7.31 (m, 2H), 7.30-7.27 (m, 3H), 7.25 (s, 1H), 7.20-7.18 (m, 2H), 7.16-7.15 (m, 1H), 7.04-7.02 (m, 1H), 6.96-6.92 (m, 1H), 6.89-6.87 (m, 2H), 6.67 (d, *J*=2.4 Hz, 1H), 6.46 (s, 1H), 2.40 (s, 1H), 1.77 (d, *J*=7.16 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.9, 152.0, 139.0, 132.6, 132.1, 131.3, 130.8, 129.4, 129.3, 129.3, 128.8, 128.7, 128.5, 128.4, 128.3, 127.8, 126.3, 125.8, 125.4, 119.9, 102.6, 69.6, 66.1, 22.7. HRMS calcd for $C_{30}H_{26}N_2O$ $[M+Na]^+$ 430.5510, found: 430.5511.

1-((2-(cyclohexyloxy)phenyl)(phenyl)methyl)-3-phenyl-1H-pyrazole (6): R_f = 0.64 (EtOAc/PE = 1:10), yield: 60%, white solid. m.p. 121-123°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.75-7.73 (m, 2H), 7.30-7.28 (m, 2H), 7.23-7.21 (m, 1H), 7.21-7.20 (m, 2H), 7.19-7.19 (m, 1H), 7.17-7.17 (m, 1H), 7.16-7.15 (m, 1H), 7.10 (s, 1H), 7.06-7.04 (m, 2H), 6.80-6.78 (m, 1H), 6.77-6.75 (m, 1H), 6.71-6.69 (m, 1H), 6.46 (d, *J*=2.4 Hz, 1H), 4.23-4.17 (m, 1H), 1.21-1.14 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.0, 150.4, 138.9, 132.9, 129.8, 128.1, 128.0, 127.4, 127.3, 127.2, 126.5, 126.3, 124.7, 118.8, 111.3, 101.2, 63.4, 30.1, 30.1, 28.7, 24.5, 21.8. HRMS calcd for $C_{28}H_{28}N_2O$ $[M+Na]^+$ 431.2099, found: 431.2097.

2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)phenyl trifluoromethanesulfonate (7): R_f = 0.80 (EtOAc/PE = 1:5), yield: 100%, white oil.^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73-7.71 (m, 2H), 7.37-7.18(m, 11H), 7.10-7.08 (m, 2H), 7.00 (m, 1H), 6.51 (d, *J* = 2.4Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.3, 147.0, 137.5, 133.4, 132.9, 131.3, 130.5, 130.0, 128.9, 128.6, 128.6, 128.5, 128.4, 127.7, 125.8, 121.2, 116.8, 103.0, 63.8. HRMS calcd for $C_{23}H_{17}F_3N_2O_3S$ $[M+Na]^+$ 481.0810, found: 481.0809.

3-phenyl-1-(9H-xanthen-9-yl)-1H-pyrazole (8): R_f = 0.87 (EtOAc/PE = 1:5), yield: 40%, yellow solid. m.p. 131-132°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.86-7.84 (m, 2H), 7.66-7.64 (m, 1H), 7.42-7.40 (m, 1H), 7.39-7.36 (m, 2H), 7.35-7.33 (m, 2H), 7.32-7.26 (m, 4H), 7.18-7.16 (m, 2H), 6.76 (s, 1H), 6.19 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.6, 147.1, 145.8, 137.8, 134.0, 129.8, 129.1, 128.6, 128.5, 127.7, 127.3, 125.7, 124.0, 120.5, 93.7, 67.2. HRMS calcd for $C_{22}H_{16}N_2O$ $[M+Na]^+$ 324.1263, found: 324.1265.

4,4-dimethoxy-2-(phenyl(3-phenyl-1H-pyrazol-1-yl)methyl)-cyclohexa-2,5-dien-1-one (9): R_f = 0.65 (EtOAc/PE = 1:10), yield: 66%, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.82-7.80 (m, 2H), 7.42-7.37 (m, 5H), 7.35-7.33 (m, 2H), 7.31-7.29 (m, 2H), 6.86-6.85 (m, 1H), 6.77 (s, 1H), 6.58 (d, *J* = 2.4Hz, 1H), 6.43-6.42 (m, 1H), 6.33-6.31 (m, 1H), 3.37 (s, 3H), 3.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 183.4, 151.9, 143.3, 142.2, 139.5, 137.1, 133.5, 131.4, 130.0, 128.9, 128.6, 128.5, 128.1, 127.6, 125.6, 102.9, 93.3, 62.8, 50.8, 50.4. HRMS calcd for $C_{24}H_{22}N_2O_3$ $[M+Na]^+$ 409.4408, found: 409.4410.

Conclusions

We have successfully developed a cascade reaction between α,β-unsaturated *N*-tosylhydrazone and *ortho*-hydroxybenzyl alcohol to directly access carbon-nitrogen (C-N) linked *N*-sec-alkylpyrazoles containing three or two (hetero)aryl ring at the same carbon atom (triarylmethanes and 1,1-diarylalkanes). A broad range of *ortho*-hydroxybenzyl alcohols reagents and α,β-unsaturated *N*-tosylhydrazone compounds were tolerated. The reaction proceeds under metal-free conditions, giving highly functionalized pyrazoles in excellent yield and regioselectivity. The procedure is operationally simple and applicable to large-scale synthesis. We believe that this protocol may become a useful tool in organic synthesis.

Conflicts of interest

There are no conflicts to declare.

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21 CCDC 1582529 (**4l**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.