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可回收铋配合物催化氮亲核试剂与对醌甲基化物 1,6-加成: 轻松获得 *N*-杂环取代的不对称三芳基甲烷衍生物

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摘要 开发了一种用对醌甲基化物(*p*-QMs)和各种芳香族 *N*-杂环化合物 1,6-氮杂-迈克尔加成合成含氮不对称三芳基甲烷衍生物的方法. 这种合成方法具有反应条件温和、催化剂负载量可接受、原子经济性、易于放大的特点, 并且能够以中等至优异的产率形成 *N*-杂环取代的不对称三芳基甲烷衍生物. 此外, 铋催化剂可以重复使用多次而不会损失其活性.

关键词 可回收的铋催化剂; *N*-杂环取代的不对称三芳基甲烷衍生物; 对醌甲基化物; 1,6-迈克尔加成反应

1,6-Addition of Nitrogen Nucleophile to *para*-Quinone Methides Catalyzed by Recyclable Bismuth Complex: Facile Access to *N*-Heterocyclic Substituted Unsymmetric Triarylmethane Derivatives

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Abstract A useful protocol for the synthesis of nitrogen-containing unsymmetric triarylmethane derivatives through 1,6-aza-Michael addition of *para*-quinone methides (*p*-QMs) and various aromatic N-heterocycles was developed. This established synthetic strategy features mild reaction conditions, acceptable catalyst loading, atom economy, easy scale-up and enables the formation of *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives in moderate to excellent yields. Moreover, the bismuth catalyst can be reused several times without losing of its activity.

Keywords recyclable bismuth catalyst; *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives; *para*-quinone methide; 1,6-Michael addition reaction

1 Introduction

The unsymmetric triarylmethane derivatives are important structure scaffolds in numerous biological and chemical processes.[1] To date, a variety of synthetic strategies have been developed for preparing this type of skeleton, such as Friedel-Crafts reaction,[2] metal-catalyzed cross-coupling reaction[3] and 1,6-conjugate addition.[4] The synthesis of unsymmetrical triarylmethanes, which possess diverse *N*-heterocyclic scaffolds, still remains a more less-reported. Recently, only two groups reported on this reaction. Samanta's group reported a regioselective approach for the synthesis of *N*-diarymethyl-substituted heterocycles via 1,6-aza-Michael addition of *para*-quinone methides with N-heterocycles.[5] Liu's research group developed the 1,6-aza conjugate addition reaction of *δ*-nitrile substituted *p*-methylene benzoquinone to the primary aromatic amine, and a series of large hindered amine compounds containing four-level carbon chiral centers were efficiently synthesized.[6] *N*-Heterocyclic scaffolds are well-known structural units in a broad array of synthetic bioactive molecules, natural products and pharmaceutical agents.[7] Therefore, the exploration of a simple and atom economic method for the synthesis of *N*-heterocyclic-sub-

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stituted unsymmetric triarylmethane derivatives with an environmentally benign catalyst is still desirable.

para-Quinone methides (*p*-QMs) are well-known intermediates in many chemical and biological process, due to the unique structural characters of possessing carbonyl and olefinic moieties.[8] Recently, the use of *p*-QMs as a multifunctional acceptor for 1,6-addition reaction to design unsymmetric triarylmethane derivatives has attracted great attention. In 2016, Lin's group[1] reported 1,6-addition arylation of *p*-QMs with *α*-isocyanoacetamide for direct synthesis of unsymmetrical triarylmethanes by using BF_3•Et_2O. At the same year, Anand's group[9] reported a *N*-heterocyclic carbene catalyzed 1,6-conjugate addition of 2-naphthols to *p*-QMs and triflic acid catalyzed 1,6-conjugate addition of thiols to *p*-quinone methides under continuous-flow conditions for the preparation of various unsymmetric triarylmethane derivatives. In 2020, Jiang's group[8] reviewed the latest developments in the 1,6-addition reaction of *p*-QMs. Subsequently, Liu and co-workers[10] established an 1,6-arylation of trifluoromethyl substituted *p*-quinone methide under normal temperature conditions, which delivered a diverse array of asymmetric CF_3 substituted triarylmethanes. In 2021, the same researchers described a protocol for synthesizing diarylmethane phosphine oxide compound containing cyano group substitution via base-catalyzed 1,6-addition reaction of *δ*-nitrile-*δ*-aryl-disubstituted *p*-methylene benzoquinone and diaryl oxyphosphorus.[11] Therefore, it is promising to exploit new and green catalytic systems for the preparation of *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives with *p*-QMs and *N*-heterocyclic derivatives.

With the knowledge of our group work in the area of recyclable bismuth catalysis and the synthesis of diaryl and triarylmethane derivatives,[12] we proposed the reaction of using a green and reusable heterogeneous bismuth complex as a catalyst for the preparation of functionalized *N*-diarylmethyl substituted heterocyclic derivatives through 1,6-conjugate addition of *p*-QMs.

2 Results and discussion

For the initial study, 2,6-di-*tert*-butyl-*para*-quinone methide (**1a**) and pyrazole (**2a**) were selected as model substrates to optimize the reaction conditions (Table 1). First, the model reaction was carried out in CH_3CN without the catalyst, and only trace of target product (**3aa**) was obtained (Table 1, Entry 1). While, 5 mol% $(C_5H_6N_4O)$-$(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$[13] (the structure of the catalyst is shown in Figure 1) was proved to be efficient catalyst for this 1,6-aza addition reaction providing the desired product (**3aa**) in 91% yield within 12 h (Table 1, Entry 2). Encouraged by this result, a variety of commercial available Lewis acids, such as $BiCl_3$, $Bi(OTf)_3$, $FeCl_3$, $AlCl_3$, $Sc(OTf)_3$, $Ni(OTf)_2$ and $Zn(OTf)_2$ were also tested to search the best catalyst for this 1,6-addition reaction (Table 1, Entries 3～9). However, all those did not provide better results under the same experimental conditions.

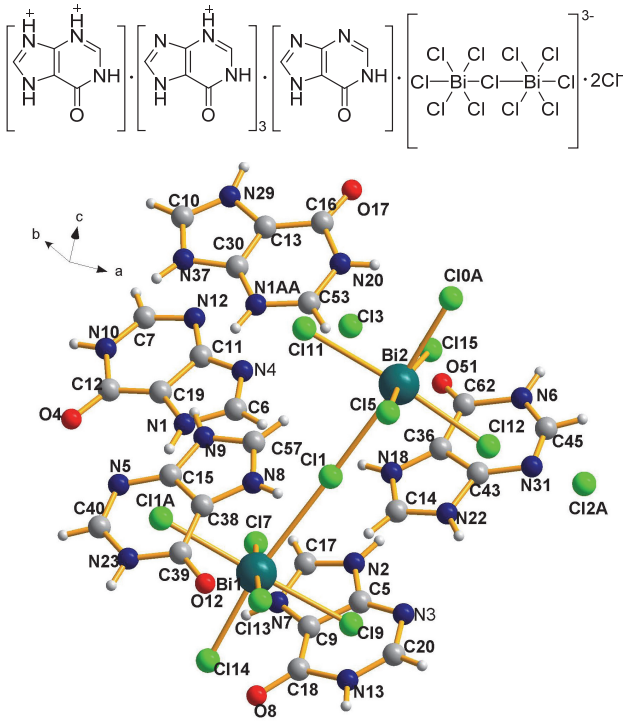
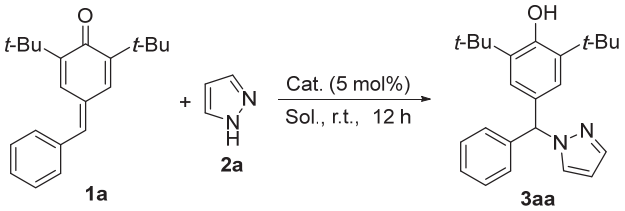


Figure 1 Structure of catalyst

Table 1 Conditions screening[a]



Entry	Catalyst	Solvent	Yield[b]/%
1	—	CH_3CN	trace
2[c]	[Bi]	CH_3CN	91
3	$BiCl_3$	CH_3CN	80
4	$Bi(OTf)_3$	CH_3CN	82
5	$FeCl_3$	CH_3CN	86
6	$AlCl_3$	CH_3CN	85
7	$Sc(OTf)_3$	CH_3CN	82
8	$Ni(OTf)_2$	CH_3CN	14
9	$Zn(OTf)_2$	CH_3CN	87
10	[Bi]	MeOH	55
11	[Bi]	1,4-Dioxane	77
12	[Bi]	Toluene	10
13	[Bi]	DCM	85
14	[Bi] (1 mol%)	CH_3CN	80

[a] Reaction conditions: *p*-QMs (**1a,** 0.25 mmol), 1*H*-pyrazole (**2a**, 0.275 mmol), solvent (2.5 ml). [b] Isolated yield based on *p*-QMs as limiting reagent. [c] The bismuth complex [Bi] refers to $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$.

Next, some solvents including methanol, 1,4-dioxane, toluene and dichloromethane were further examined for the better results, but the yields were not satisfactory (Entries 9～12). Lower yield of the desired product (80%) was ob-

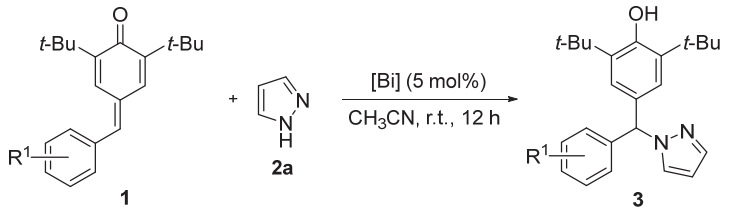
tained by reducing the catalyst loading from 5 mol% to 1 mol% (Table 1, Entry 14).

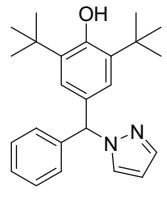
The optimized reaction conditions (Table 1, Entry 2) were proved to be effective for this [Bi]-catalyzed 1,6-aza-addition reaction with *p*-QMs and pyrazole. As illustrated in Table 2, a variety of substituted *p*-QMs could smoothly react with pyrazole to provide the desired *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives with good to excellent yields. The *p*-QMs with electron donating group in the *para* position, such as **1b** and **1c**, reacted well with **2a** to provide the corresponding products **3ba** and **3ca** in yields of 95% and 93%, respectively. Electron withdrawing group substituted *p*-QMs were also amendable to this protocol, affording the desired products (**3da** and **3ea**) with good results. The *p*-QMs containing halogen substitution at the *para*- and *ortho*-position of the phenyl ring were well tolerated under present catalytic system, affording the products **3fa**～**3ha** in 86%～94% yields. Notably, the *p*-QMs (**1i**) derived from 3-methylbenzaldehyde showed a slightly reduced reactivity, only 77% yield of product (**3ia**) was isolated. Furthermore, an extended aromatic system was also compatible for this transformation and aimed products (**3ja**, **3ka** and **3la**) were obtained in good to excellent yields (87%～93%).

Next, the scope of *N*-heterocycles was screened to react with *p*-QMs (**1a**) (Table 3). Gratifyingly, a variety of *N*-containing heterocyclic derivatives were well applicable in this 1,6-aza addition reaction, and the results were illustrated in Table 3. When imidazole (**2b**) was used as substrate, the reaction proceeded smoothly and afforded the corresponding product (**3ab**) in 90% yield. Carbazole was also well tolerated this catalytic system, albeit lower yield of product (**3ac**) was obtained (78%). Additionally, the efficacy of this protocol was also examined with 1*H*-indazole (**2d**) and 1*H*-benzo[*d*]imidazole (**2e**), while only 68% yields of products were isolated, presumably owing to the isomers. To our interesting, benzotriazole, one of the more reactive fused *N*-heterocycles, also exhibited high reactivity under the standard reaction conditions, providing the exclusively product **3af** in 82% yield with high regioselectivity.

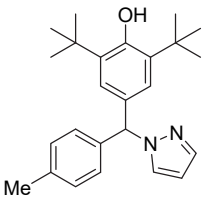
To demonstrate the robustness and utility of this synthetic protocol, the scale up of the model reaction was carried out (Scheme 1). A gram-scale reaction of 1.1 g of **1a** and 0.3 g of **2a** was performed under the standard conditions, furnishing 1.13 g of **3aa** in 81% isolated yield catalyzed by [Bi].

Table 2 Substrate scope of *p*-quinone methides **1a**～**1l** with pyrazole **2a**[a]

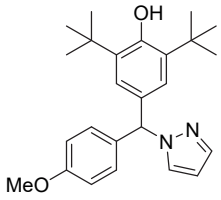




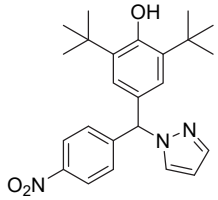
3aa, 91%



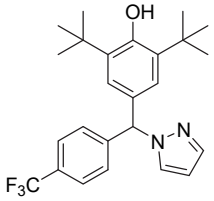
3ba, 95%



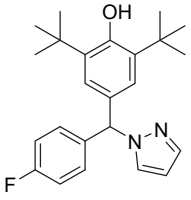
3ca, 93%



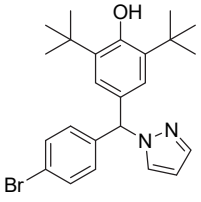
3da, 91%



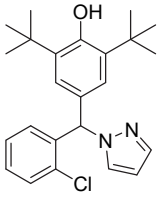
3ea, 86%



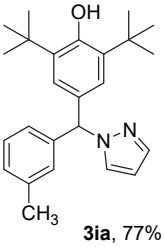
3fa, 86%



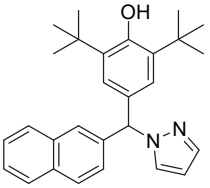
3ga, 94%



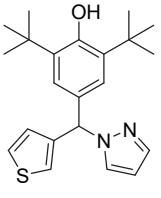
3ha, 88%



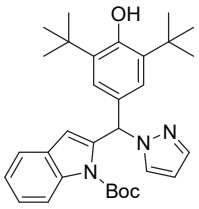
3ia, 77%



3ja, 88%



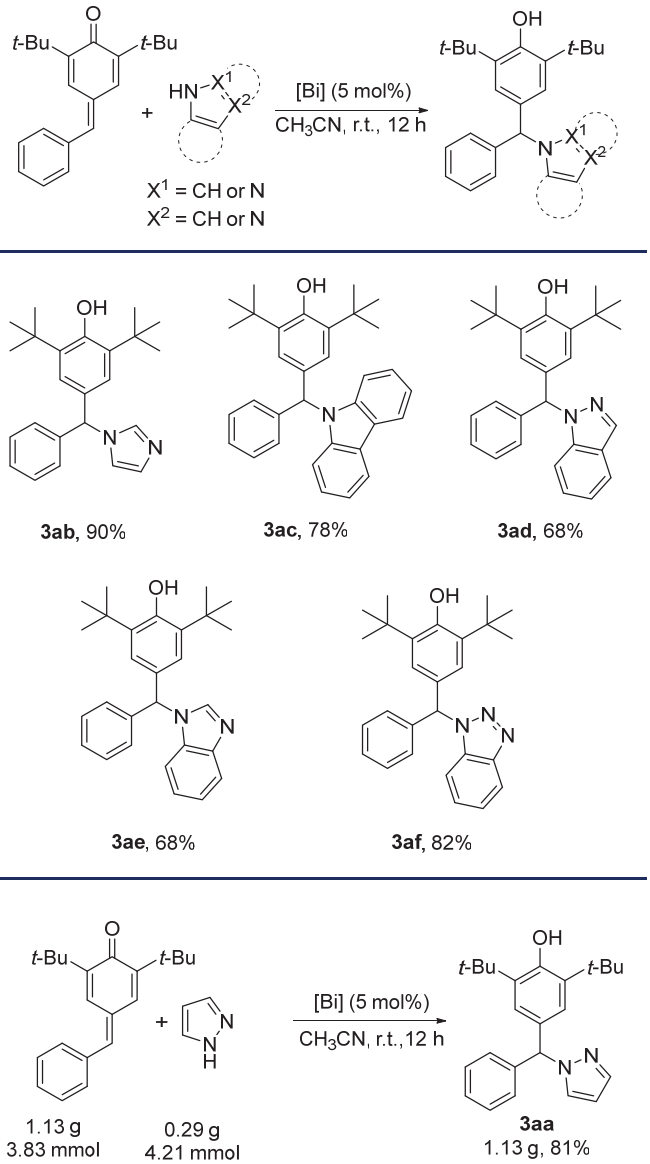
3ka, 87%



3la, 93%

[a] The yield given in each case is isolated product of a reaction carried on a 0.25 mmol scale at optimized conditions.

Table 3 Substrate scope of *N*-heterocycles (**2**) with *p*-QMs (**1a**) under the optimized reaction conditions



Scheme 1 Gram-scale experiments

To show the high efficiency and utility of this heterogenerous [Bi] catalyst. Under the optimal conditions described in Table 1, the 1,6-conjugate addition of *p*-QMs (**1a**) and pyrazole (**2a**) was carried out using [Bi] as a catalyst. After the completion of the reaction, the catalyst in the reaction was suction filtered and washed with CH_3CN to recover the catalyst. As shown in Figure 2, the reactivities of the reactions did not significantly degrease in a test of six cycles (from 91% to 85%).

A plausible mechanism for the 1,6-Michael addition reaction of *p*-QMs **1a** and amine **2a** catalyzed by [Bi] is proposed, and it is depicted in Scheme 3. Initially, the activation of carbonyl oxygen-atom of *p*-QMs **1a** using Bi possibly generates an active intermediate **A**. Secondly, the molecule is aromatized by intermediate **A** and protons, and a more stable substance **B** will be obtained. Then, nucleophilic attack of amine to the resulting species **B** gives the intermediate **C**. Finally, protonation of intermediate **C** furnishes the desired product **3aa**. At the same time, the Bi catalyst in the reaction was regenerated.

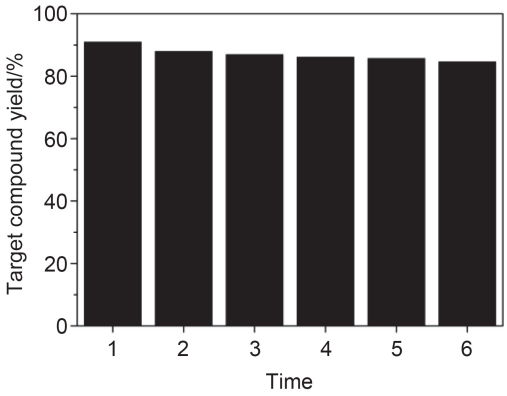
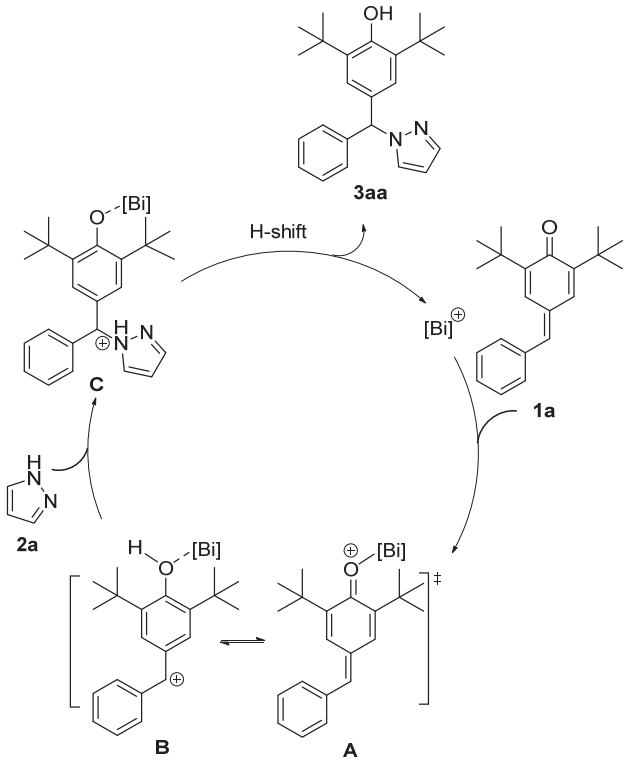


Figure 2 Recycling Catalyst $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$



Scheme 3 Proposed mechanism

3 Conclusions

In summary, we have developed the [Bi]-catalyzed 1.6-addition reaction of *p*-QMs for the synthesis of various *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives. The outstanding features of this protocol include broad scope of substrates, non-toxic metal catalysts, and environmentally friendliness. Further studies of the design novel chiral bismuth complexes and application of the chiral *N*-heterocyclic-substituted unsymmetric triarylmethane derivatives are in progress in our laboratory.

4 Experimental section

4.1 Instruments and reagents

Unless otherwise stated, all chemical reagents and solvents (analytical grade) can be used without further purification. ^{1}H NMR spectra were acquired on Bruker 400 MHz or 500 MHz spectrometers and chemical shifts were recorded relative to tetramethylsilane (TMS, δ 0.00) or residual protiated solvent $CDCl_3$ (δ 7.26). ^{13}C NMR spectra were obtained at 100 MHz instrument and chemical shifts were recorded relative to solvent resonance $CDCl_3$ (δ 77.16). LCMS analysis was conducted on an Agilent 6110 and 6520. Flash column chromatography was performed using silica gel (200～300 mesh) under pressure. Analytical thin layer chromatography (TLC) was carried out using GF254 commercial silica gel plates.

4.2 General procedure for the recovery of the [Bi] catalyst

p-QMs (**1a**) (0.25 mmol), $(C_5H_6N_4O)(C_5H_5N_4O)_3$-$(C_5H_4N_4O)[Bi_2Cl_{11}]Cl_2$ (5 mol%) and 1*H*-pyrazole (**2a**) (0.275 mmol) were added into a flask. Then the mixture was stirred at room temperature, until *p*-QMs was completely consumed as indicated by TLC analysis. After the completion of reaction, the [Bi] catalyst was directly recovered by filtration and washed with CH_3CN after the reaction was completed. The recovered catalyst has no obvious loss and can be directly reused. The catalyst was recycled six times with only a small loss of activity (isolated yield only slightly declined from 91% to 85%).

4.3 General method for the 1,6-conjugate addition reaction of *p*-QMs with *N*-heterocycles

To a stirred solution of *p*-QMs (**1**, 0.25 mmol) and *N*-heterocycles (**2**) (0.275 mmol) in CH_3CN (2.5 ml) in 10-mL round-bottom flask, $(C_5H_6N_4O)(C_5H_5N_4O)_3(C_5H_4$-$N_4O)[Bi_2Cl_{11}]Cl_2$ (5 mol%) was added. Then, the mixture was stirred at room temperature until *p*-QMs was completely consumed as indicated by TLC analysis. After the completion of reaction, the residue was directly purified by flash column chromatography with ethyl acetate and petroleum ether as eluents to afford pure product **3**.

2,6-Di-*tert*-butyl-4-(phenyl(1*H*-pyrazol-1-yl)methyl)-phenol (**3aa**):[5] White solid, 82.6 mg, 91% yield. m.p. 136～138 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.59 (d, *J*=1.9 Hz, 1H), 7.35～7.27 (m, 3H), 7.23 (d, *J*=2.2 Hz, 1H), 7.06 (dd, *J*=6.8, 1.9 Hz, 2H), 6.90 (d, *J*=2.0 Hz, 2H), 6.71 (s, 1H), 6.26 (q, *J*=2.0 Hz, 1H), 5.23 (d, *J*=2.5 Hz, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 153.54, 140.29, 139.49, 135.95, 129.82, 129.38, 128.48, 127.97, 127.72, 125.22, 105.13, 69.76, 34.33, 30.21; ESI-MS *m/z*: 361.2 $[M-H]^-$.

4-((1*H*-Pyrazol-1-yl)(*p*-tolyl)methyl)-2,6-di-*tert*-butyl-phenol (**3ba**):[5] White solid, 89.9 mg, 95% yield. m.p. 123～125 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.58 (dt, *J*=1.8, 0.8 Hz, 1H), 7.23 (dd, *J*=2.3, 0.9 Hz, 1H), 7.15～7.10 (m, 2H), 6.97 (d, *J*=8.1 Hz, 2H), 6.88 (t, *J*=0.9 Hz, 2H), 6.67 (s, 1H), 6.26～6.22 (m, 1H), 5.21 (d, *J*=1.8 Hz, 1H), 2.33 (s, 3H), 1.35 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 153.43, 139.44, 137.43, 137.22, 135.84, 130.03, 129.29, 129.18, 128.05, 124.97, 105.04, 69.53, 34.30, 30.19, 21.12; ESI-MS *m/z*: 375.4 $[M-H]^-$.

2,6-Di-*tert*-butyl-4-((4-methoxyphenyl)(1*H*-pyrazol-1-yl)methyl)phenol (**3ca**):[5] White solid, 92 mg, 93% yield. m.p. 105～108 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.62～7.57 (m, 1H), 7.23 (d, *J*=2.3 Hz, 1H), 7.05～7.00 (m, 2H), 6.89～6.84 (m, 4H), 6.68 (s, 1H), 6.25 (t, *J*=2.1 Hz, 1H), 5.21 (s, 1H), 3.80 (s, 3H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 159.10, 153.40, 139.43, 135.89, 132.38, 130.23, 129.41, 129.24, 124.82, 113.88, 105.05, 69.23, 55.28, 34.32, 30.22; ESI-MS *m/z*: 391.2 $[M-H]^-$.

2,6-Di-*tert*-butyl-4-((4-nitrophenyl)(1*H*-pyrazol-1-yl)methyl)phenol (**3da**): White solid, 93.3 mg, 91% yield. m.p. 139～140 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 8.22～8.15 (m, 2H), 7.63 (d, *J*=1.8 Hz, 1H), 7.26 (s, 1H), 7.19～7.12 (m, 2H), 6.94 (s, 2H), 6.77 (s, 1H), 6.32 (t, *J*=2.1 Hz, 1H), 5.34 (s, 1H), 1.37 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 154.16, 148.00, 147.31, 140.10, 136.52, 129.60, 128.49, 128.13, 125.67, 123.70, 105.78, 69.15, 34.40, 30.16; ESI-MS *m/z*: 406.2 $[M-H]^-$.

4-((1*H*-Pyrazol-1-yl)(4-(trifluoromethyl)phenyl)methyl)-2,6-di-*tert*-butylphenol (**3ea**): White solid, 92.9 mg, 86% yield. m.p. 145～147 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.61 (d, *J*=1.9 Hz, 1H), 7.58 (d, *J*=8.1 Hz, 2H), 7.24 (d, *J*=2.4 Hz, 1H), 7.15～7.11 (m, 2H), 6.92 (s, 2H), 6.72 (s, 1H), 6.29 (t, *J*=2.2 Hz, 1H), 5.29 (d, *J*=4.6 Hz, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 153.92, 144.59, 139.95, 136.26, 130.03, 129.71, 129.51, 128.75, 128.09, 125.48, 122.70, 105.52, 69.29, 34.36, 30.15. HRMS (ESI) calcd for $C_{25}H_{29}F_3N_2ONa$ $[M+Na]^+$ 453.2130, found 453.2120.

2,6-Di-*tert*-butyl-4-((4-fluorophenyl)(1*H*-pyrazol-1-yl)-methyl)phenol (**3fa**):[5] White solid, 82.3 mg, 86% yield. m.p. 119～121 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.60 (dd, *J*=1.8, 0.7 Hz, 1H), 7.23 (dd, *J*=2.4, 0.7 Hz, 1H), 7.02 (d, *J*=7.6 Hz, 4H), 6.88 (s, 2H), 6.68 (s, 1H), 6.30～6.24 (m, 1H), 5.26 (d, *J*=1.0 Hz, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 163.53, 161.07, 153.74, 139.85, 136.38, 136.13, 129.76, 129.68, 129.39, 125.23, 115.58, 115.36, 105.36, 69.11, 34.42, 30.27; ESI-MS *m/z*: 379.2 $[M-H]^-$.

4-((4-Bromophenyl)(1*H*-pyrazol-1-yl)methyl)-2,6-di-*tert*-butylphenol (**3ga**): White solid, 104.2 mg, 94% yield. m.p. 131～133 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 7.60 (d, *J*=1.9 Hz, 1H), 7.48～7.42 (m, 2H), 7.23 (d, *J*=2.3 Hz, 1H), 6.96～6.86 (m, 4H), 6.65 (s, 1H), 6.27 (t, *J*=2.1 Hz, 1H), 5.26 (s, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 153.75, 139.66, 139.52, 136.16, 131.61, 129.61, 129.37, 129.16, 125.21, 121.75, 105.39, 69.17, 34.35, 30.20; ESI-MS *m/z*: 439.1 $[M-H]^-$.

2,6-Di-*tert*-butyl-4-((2-chlorophenyl)(1*H*-pyrazol-1-yl)-methyl)phenol (**3ha**):[5] White solid, 87.4 mg, 88% yield. m.p. 128～131 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.61 (d, *J*=1.8 Hz, 1H), 7.39 (dd, *J*=7.6, 1.7 Hz, 1H),

7.26～7.20 (m, 3H), 7.03 (s, 1H), 6.86 (s, 2H), 6.80 (dd, *J*=7.4, 2.1 Hz, 1H), 6.26 (t, *J*=2.1 Hz, 1H), 5.24 (s, 1H), 1.35 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.63, 139.84, 138.00, 135.96, 133.74, 129.93, 129.75, 129.26, 129.09, 128.24, 126.89, 125.15, 105.04, 66.51, 34.30, 30.17; ESI-MS *m/z*: 395.1 $[M-H]^-$.

4-((1*H*-Pyrazol-1-yl)(*m*-tolyl)methyl)-2,6-di-*tert*-butylphenol (**3ia**): White solid, 72.3 mg, 77% yield. m.p. 142～144 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.59 (dd, *J*=1.9, 0.7 Hz, 1H), 7.24～7.18 (m, 2H), 7.09 (dd, *J*=7.6, 1.8 Hz, 1H), 6.91 (d, *J*=7.3 Hz, 3H), 6.86～6.82 (m, 1H), 6.66 (s, 1H), 6.25 (t, *J*=2.1 Hz, 1H), 5.23 (d, *J*=1.0 Hz, 1H), 2.30 (s, 3H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.61, 140.19, 139.56, 138.23, 135.95, 129.92, 129.48, 128.85, 128.62, 128.47, 125.30, 125.12, 105.16, 69.85, 34.42, 30.30, 21.58. HRMS (ESI) *m/z*: $C_{25}H_{32}N_2ONa$ $[M+Na]^+$ 399.2412, found 399.2405.

2,6-Di-*tert*-butyl-4-(naphthalen-2-yl(1*H*-pyrazol-1-yl)methyl)phenol (**3ja**): White solid, 91.6 mg, 88% yield. m.p. 153～155 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.94～7.81 (m, 3H), 7.62 (d, *J*=1.8 Hz, 1H), 7.50～7.37 (m, 4H), 7.12 (d, *J*=2.3 Hz, 1H), 6.87 (d, *J*=25.6 Hz, 3H), 6.21 (t, *J*=2.0 Hz, 1H), 5.21 (s, 1H), 1.34 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.48, 139.63, 136.05, 135.79, 133.80, 131.51, 129.62, 128.96, 128.70, 126.75, 126.73, 125.81, 125.17, 124.63, 123.39, 105.17, 66.59, 34.33, 30.23; ESI-MS *m/z*: 411.2 $[M-H]^-$.

4-((1*H*-Pyrazol-1-yl)(thiophen-3-yl)methyl)-2,6-di-*tert*-butylphenol (**3ka**): White solid, 95.9 mg, 87% yield. m.p. 110～112 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.58 (dd, *J*=1.8, 0.7 Hz, 1H), 7.37 (dt, *J*=2.4, 1.2 Hz, 1H), 7.29 (dd, *J*=5.1, 1.3 Hz, 1H), 7.00～6.94 (m, 3H), 6.87～6.81 (m, 2H), 6.27 (dd, *J*=2.4, 1.8 Hz, 1H), 5.23 (s, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.74, 143.68, 139.62, 135.92, 130.17, 128.79, 127.31, 126.68, 126.20, 124.26, 105.44, 65.37, 34.33, 30.18. HRMS (ESI) calcd for $C_{22}H_{28}N_2OSNa$ $[M+Na]^+$ 391.1820, found 391.1815.

tert-Butyl 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(1*H*-pyrazol-1-yl)methyl)-1*H*-indole-1-carboxylate (**3la**): Yellow solid, 116.9 mg, 93% yield. m.p. 164～167 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 8.10 (d, *J*=8.2 Hz, 1H), 7.59 (dd, *J*=1.8, 0.7 Hz, 1H), 7.39 (d, *J*=2.3 Hz, 1H), 7.32～7.28 (m, 1H), 7.19～7.07 (m, 3H), 7.02 (s, 2H), 6.84～6.80 (m, 1H), 6.25 (t, *J*=2.1 Hz, 1H), 5.23 (s, 1H), 1.64 (s, 9H), 1.38 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.62, 149.63, 139.52, 135.98, 135.77, 129.17, 129.08, 128.83, 126.18, 124.77, 123.98, 122.89, 120.75, 119.54, 115.29, 105.43, 83.94, 62.84, 34.33, 30.21, 28.14 . HRMS (ESI) calcd for $C_{31}H_{39}N_3O_3Na$ $[M+Na]^+$ 524.2889, found 524.2883.

4-((1*H*-Benzo[*d*]imidazol-1-yl)(phenyl)methyl)-2,6-di-*tert*-butylphenol (**3ab**): Yellow solid, 82 mg, 90% yield. m.p. 159～161 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.40～7.29 (m, 4H), 7.11～7.05 (m, 3H), 6.91 (d, *J*=0.6 Hz, 2H), 6.85 (t, *J*=1.3 Hz, 1H), 6.42 (s, 1H), 5.44～5.22 (m, 1H), 1.36 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.80, 140.04, 137.45, 136.31, 129.29, 129.00, 128.69, 128.04, 127.67, 125.16, 119.45, 65.40, 34.37, 30.17 . HRMS (ESI) calcd for $C_{24}H_{30}N_2ONa$ $[M+Na]^+$ 385.2256, found 385.2253.

4-((9*H*-Carbazol-9-yl)(phenyl)methyl)-2,6-di-*tert*-butylphenol (**3ac**):[5] Yellow solid, 90.2 mg, 78% yield. m.p. 134～135 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 8.11～8.09 (m, 2H), 7.29～7.27 (m, 4H), 7.26 (d, *J*=1.7 Hz, 1H), 7.21～7.16 (m, 4H), 7.08 (q, *J*=0.9 Hz, 2H), 7.06 (dd, *J*=2.3, 0.8 Hz, 3H), 5.21 (s, 1H), 1.29 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.43, 140.86, 140.08, 136.00, 129.25, 128.59, 128.23, 127.64, 125.55, 125.42, 123.58, 120.13, 119.04, 111.05, 62.66, 34.43, 30.31; ESI-MS *m/z*: 500.3 $[M+K]^+$.

4-((1*H*-Indazol-1-yl)(phenyl)methyl)-2,6-di-*tert*-butylphenol (**3ad**):[5] Yellow solid, 70.5 mg, 68% yield. m.p. 122～124 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 8.07 (d, *J*=0.9 Hz, 1H), 7.73 (dt, *J*=8.1, 1.1 Hz, 1H), 7.33～7.27 (m, 4H), 7.23～7.17 (m, 3H), 7.14～7.10 (m, 1H), 7.02 (s, 2H), 6.97 (s, 1H), 5.20 (s, 1H), 1.33 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.31, 140.17, 140.02, 135.62, 133.54, 129.64, 128.35, 128.26, 127.58, 126.02, 125.28, 124.33, 121.03, 120.53, 109.98, 66.85, 34.26, 30.15; ESI-MS *m/z*: 435.2 $[M+Na]^+$.

4-((1*H*-Benzo[*d*]imidazol-1-yl)(phenyl)methyl)-2,6-di-*tert*-butylphenol (**3ae**): White solid, 70.2 mg, 68% yield. m.p. 181～183 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) *δ*: 7.84 (d, *J*=8.1 Hz, 1H), 7.64 (s, 1H), 7.39～7.26 (m, 4H), 7.22～7.13 (m, 2H), 7.12～7.07 (m, 2H), 6.98 (s, 2H), 6.66 (s, 1H), 5.34 (s, 1H), 1.35 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 154.01, 142.78, 138.99, 136.56, 134.18, 128.81, 128.31, 128.08, 127.46, 125.67, 122.86, 122.36, 120.23, 111.03, 64.07, 34.40, 30.17. HRMS (ESI) calcd for $C_{28}H_{32}N_2ONa$ $[M+Na]^+$ 435.2412, found 435.2402.

4-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)(phenyl)methyl)-2,6-di-*tert*-butylphenol (**3af**):[5] White solid, 85.1 mg, 82% yield. m.p. 162～163 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 8.10～8.04 (m, 1H), 7.36～7.29 (m, 6H), 7.21～7.13 (m, 2H), 7.09～7.02 (m, 3H), 5.29 (d, *J*=8.4 Hz, 1H), 1.33 (s, 18H); ^{13}C NMR (101 MHz, Chloroform-*d*) *δ*: 153.82, 146.31, 138.50, 136.12, 133.00, 128.66, 128.16, 128.07, 128.02, 127.06, 125.39, 123.75, 120.08, 110.87, 67.66, 34.34, 30.13; ESI-MS *m/z*: 436.2 $[M+Na]^+$.

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of compounds **3aa**～**3la** and **3ab**～**3af**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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