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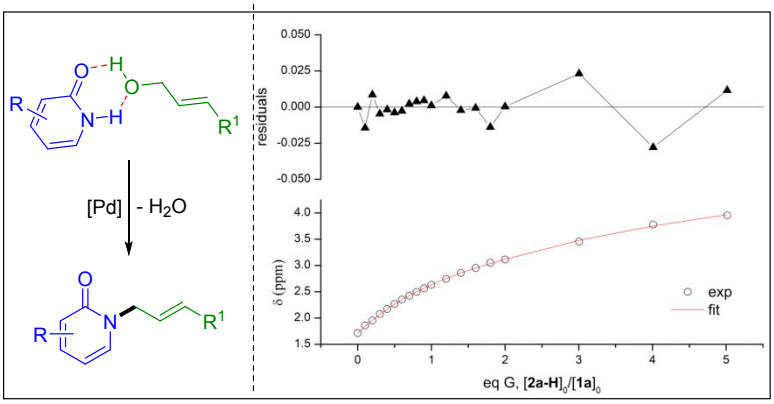
# Insights into Substrate Self-Assisted Activation of Allylic Alcohols Guiding to Mild Allylic Substitution of Tautomerizable Heteroarenes

Qiuju Zhou,† Lingyun Zheng,† Bing Ma,† Lijun Huang,† Aoqi Liu,† Xinhua Cao† Jing Yu† Xiantao Ma†,*

† College of Chemistry and Chemical Engineering, Green Catalysis & Synthesis Key Laboratory of Xinyang City, Xinyang Normal University, Xinyang, Henan 464000, China.

Email: xiantaoma@126.com

*Supporting Information Placeholder*




**ABSTRACT:** A substrate self-assisted activation of allylic alcohols by tautomerizable heteroarenes *via* hydrogen bond was disclosed by various NMR techniques including variable-temperature $^1$H NMR, Job's Plot and $^1$H NMR titration. Guided by these finding, a much milder allylic substitution of tautomerizable heteroarenes with allylic alcohols was developed, affording the target products in high yields.

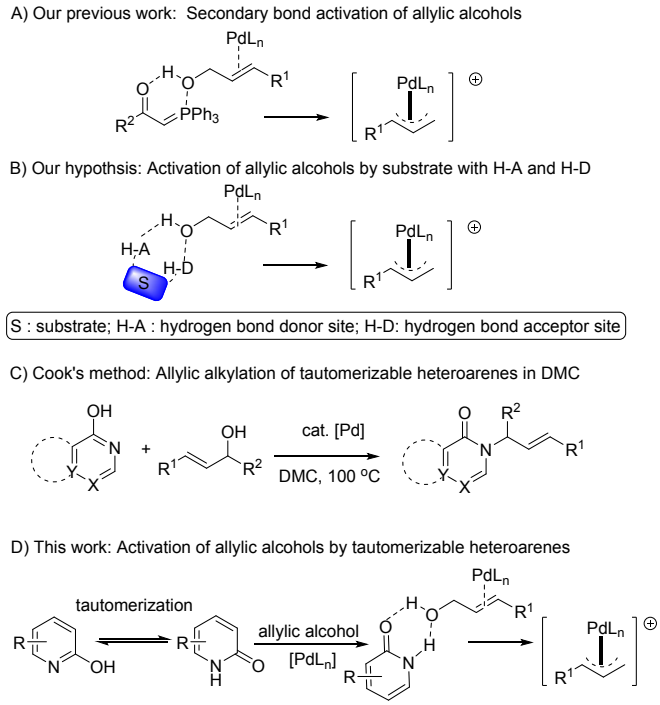
The successful generation of the *л*-allylic palladium species is usually crucial for a Tsuji–Trost reaction.[1] The reactive allylic halides and esters which are liable to undergo oxidative addition with a palladium catalyst traditionally served as precursors of *л*-allylic fragments.[1] From the viewpoint of environmental issues and atom-/step-economy, much attention has recently been paid to the direct use of simple allylic alcohols as preferable alternates, because such kind of transformation with allylic alcohols only gives water as by-product and moreover, the common allylic partners in Tsuji–Trost reactions are generally prepared from the corresponding alcohols.[2] However, owing to the poor leaving character of hydroxy group, an extra activator such as $As_2O_3$, $B_2O_3$, $BEt_3$, or $Ti(O\text{-}iPr)_4$ is generally required to promote the smooth cleavage of C-O bond in allylic alcohols.[2] Therefore, developing efficient activation of allylic alcohols becomes one of the research hotspots in this area.

In recent years, some extra activator-free Tsuji–Trost reactions of allylic alcohols have been developed.[3-5] However, the activation mechanisms of allylic alcohols were investigated only in rare reports but mainly based on theoretical calculations.[3] Therefore, it is still highly desirable to illuminate the activation mechanism of activator-free Tsuji–Trost reaction especially by simple and facile experimental methods.[4]

We have been interested in activation of alcohols for a long time.[6] We have recently disclosed a substrate self-assisted secondary bond activation of allylic alcohol *via* a six-membered ring complex by various NMR techniques (Scheme 1A).[6b] It can be hypothesized that the substrate bearing both a hydrogen bond donor site and an acceptor site may interact with allylic alcohols, thus leading to the activation of C-O bonds in allylic alcohols *via* hydrogen bond (Scheme 1B).[7] 2-Hydroxypyridines, one of the typical tautomerizable heteroarenes, are readily tautomerized to 2-pyridones with both hydrogen bond donor site and

acceptor site in a molecule,[8] therefore, a direct, activator-free and substrate self-assisted allylic substitution of tautomerizable heteroarenes with allylic alcohols is anticipated.

In 2015, Cook and coworkers achieved the activator-free allylic substitution of tautomerizable heteroarenes with allylic alcohols at 100 °C in a solvent of dimethyl carbonate (DMC), however, the initial activation of allylic alcohols which led to the smooth oxidative addition with a palladium catalyst to give the key л-allylic palladium species was underappreciated and not mentioned (Scheme 1C).[5d,9] It is also interestingly noticed that the reaction could be conducted in almost all common organic solvents including both protic and aprotic ones (such as MeOH, EtOH, PhMe, PhH and DCE) in their conditions screening, affording the target product in moderate yields.[5d] It is still difficult to explain these phenomena reasonably, especially why the reactions could be carried out even in a nonpolar and aprotic solvent which cannot activate allylic alcohols. Therefore, an interesting activation mechanism may be involved in these reactions. Hereon, we wish to report our results on the possible activation mechanism of allylic alcohols by various NMR techniques including variable-temperature $^1$H NMR, Job's Plot and $^1$H NMR titration. The experimental results suggested that a substrate self-assisted activation of allylic alcohols by tautomerizable heteroarenes *via* hydrogen bond might be involved (Scheme 1D). Guided by these findings, a substrate self-assisted and much milder allylic substitution of tautomerizable heteroarenes with allylic alcohols was also developed.




**Scheme 1**. Activation modes of allylic alcohol and the working hypothesis.

Cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) were selected as the test samples (Figure 1). As shown in Figure 1, the tautomeric equilibrium of 2-hydroxypyridine (**2a-H**) and 2-pyridone (**2a-P**) is susceptible to various reaction conditions and generally 2-pyridone (**2a-P**) is the main existing species in a neutral liquid medium.[8] As shown in Figure 2, the chemical shift of the free OH group in cinnamyl alcohol (**1a**) is 1.598 ppm and by extra adding *ca.* 1.0 equiv. of 2-hydroxypyridine (**2a-H**), the chemical shift could moves downfield to 1.839 ppm, revealing the possible formation of intermolecular hydrogen bond between cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) (Figure 2). Then variable-temperature $^1$H NMR experiments were carried out.[10,6b] As the test temperature is increased, the chemical shift of OH group in cinnamyl alcohol (**1a**) moves upfield from 1.839 (25 °C), to 1.771 (35 °C), 1.706 (45 °C) and finally to 1.655 ppm (55 °C), further suggesting the possible formation of intermolecular hydrogen bond (Figure 2).

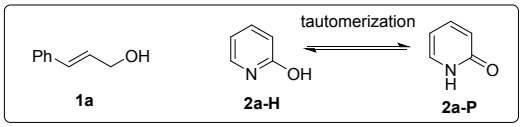



**Figure 1**. Test samples: **1a** and **2a**

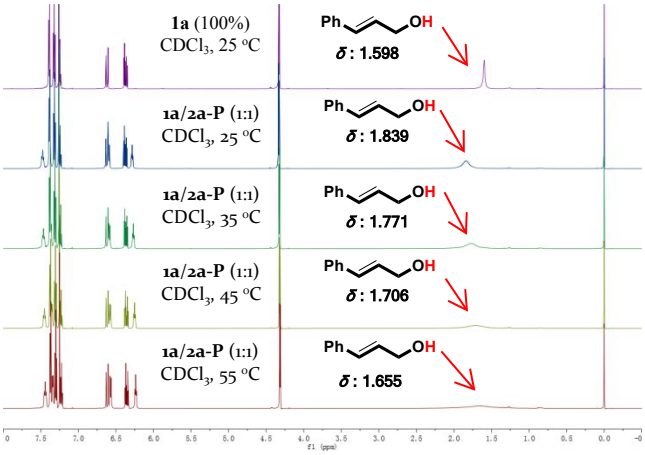
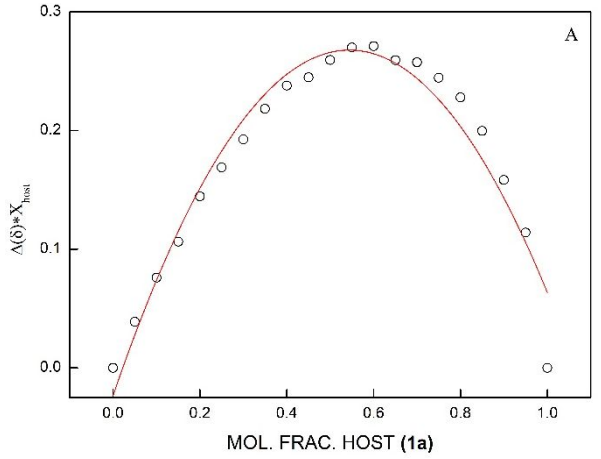
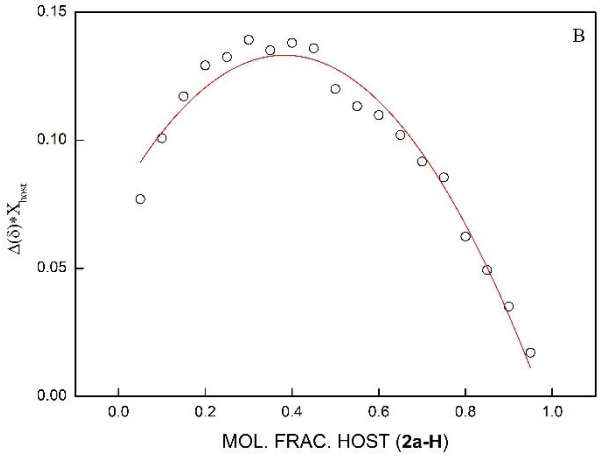



**Figure 2.** Variable-temperature NMR analysis

Then the Job's Plot and $^1$H NMR titration techniques were employed to investigate the possible host-guest binding interactions between cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) (Figures 3-4).[11-14] Job's Plot is the most popular way of determining the stoichiometry of complexes.[12] By continuous variation of the concentration of [**1a**] and [**2a-H**], our Job's Plot experimental results was shown in Figure 3 and the maximum in the curve for cinnamyl alcohol (**1a**) is at $X_{1a}$ = 0.55 (Figure 3A), while 2-hydroxypyridine (**2a-H**) serves as the host, the maximum lies at molar fraction $X_{2a\text{-}H}$ = 0.38 (Figure 3B), indicating that both 1:1 and 2:1 binding complexes were possibly formed (Figure 5).[12] Moreover, residual distribution analysis of the fitting curve of $^1$H NMR titration experiments further suggested that the possible formation of 1:1 and 2:1 binding complex *via* hydrogen bond. (Figure 5).[12-14] As shown in figure 5, the 1:1 binding complex can be in a six-membered ring form (**i**) or linear form (**ii**) and (**iii**), and the 2:1 binding complex can be in form (**iv**). These binding complexes readily reached equilibrium in the reaction.




(A)




(B)

**Figure 3**. The Job's Plots

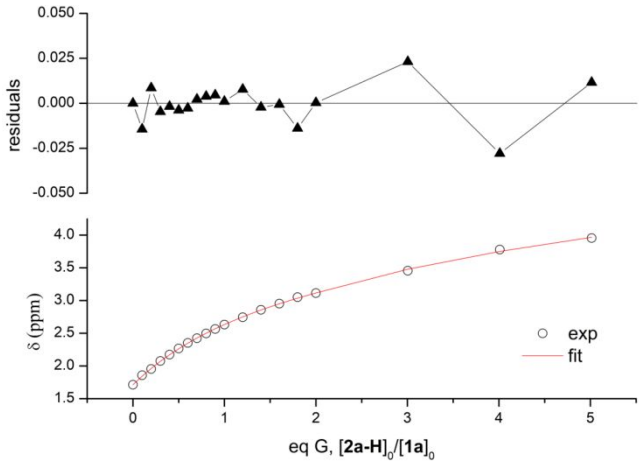



**Figure 4.** $^1$H NMR titration experiments

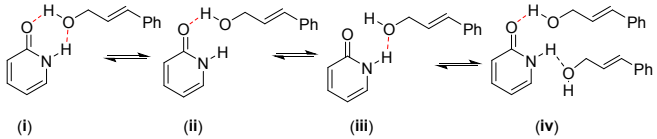
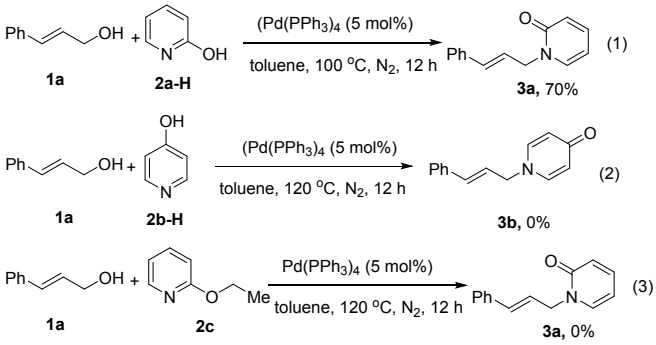


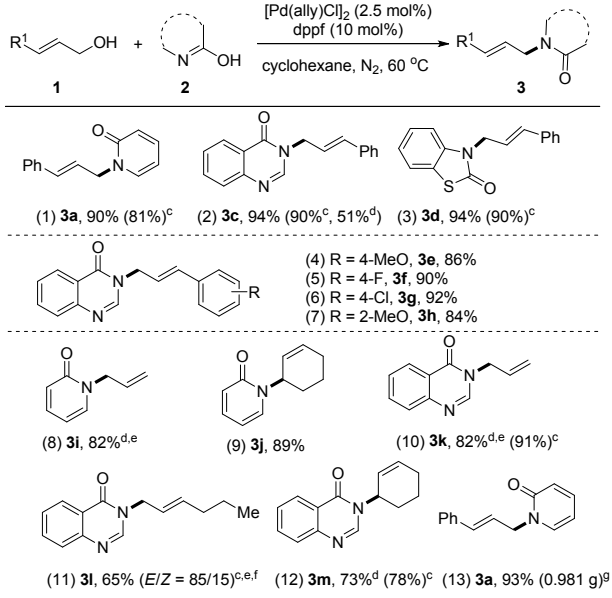

**Figure 5.** Formation of binding complexes *via* hydrogen bond

Based on these experimental results, some control experiments were carried out to investigate the possible substrate self-assisted activation of allylic alcohols *via* binding complex. As shown in scheme 2, The reaction of cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) in toluene successfully afforded the target **3a** under Cook's conditions (Scheme 2, eq. 1), suggesting the possible activation of cinnamyl alcohol (**1a**) by 2-hydroxypyridine (**2a-H**) *via* binding complex. However, the reaction of 4-hydroxypyridine (2b-H) and 2-ethoxypyridine (2c) which could not form a six-membered ring binding complex (**i**) with cinnamyl alcohol (**1a**) *via* hydrogen bond failed to give the target *N*-allylic alkylation products even at 120 °C. (Scheme 2, eqs. 2-3). These experimental results revealed the formation of the six-membered ring binding complex is crucial for the activation of allylic alcohols, due to the efficient activation of allylic alcohols *via* double hydrogen bonds. As the reaction proceeds, binding complexes **ii**, **iii** and **iv** can be transformed into the six-membered ring complex **i**, thus allylic alcohols can be activated to generate the key *л*-allylic palladium species.




**Scheme 2**. Control experiments to show the key roles of six-membered ring complex

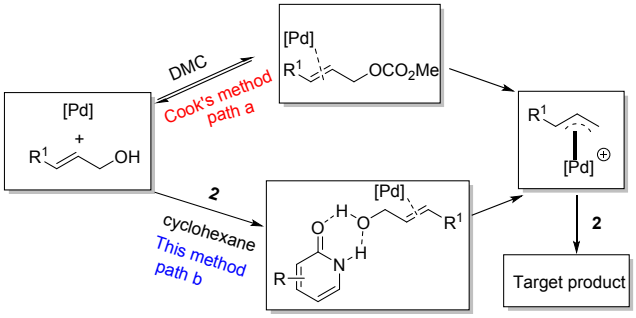
Table 1. Allylic alkylation of tautomerizable heteroarenes with allylic alcohols[a,b]



[a] Unless otherwise noted, the mixture of **1** (0.60 mmol), **2** (0.50 mmol), [Pd(ally)Cl]2 (2.5 mol%), dppf (10 mol%) in cyclohexane (1.0 mL) was sealed under $N_2$ in a 20 mL Schlenk tube, and stirred at 60 °C for 12 h, and monitored by TLC and/or GC-MS. [b] Isolated yield based on **2**; reported yields in parentheses by Cook's method, see ref. 5d for details. [c] 100 °C, [d] 80 °C. [e] **1** (1.5 equiv.) was used. [f] Hex-2-en-1-ol (*E*/*Z* = 85/15) was used. [g] The reaction was carried out in 5.0 mmol scale, 65 °C, 17 h.

Moreover, the variable-temperature NMR analysis showed that the intermolecular hydrogen bond between cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) will become stronger as the test temperature is decreased (Figure 2). Therefore, a mild allylic substitution of 2-hydroxypyridine (**2a-H**) with allylic alcohol is anticipated. By screening the palladium catalysts, solvents and reaction temperatures,[13] to our delight, the reaction of cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) could successfully afford the target **3a** in 90% isolated yield at 60 °C in a nonpolar and aprotic solvent of cyclohexane (Table 1, run 1).[15] The method can be easily extended to the allylic alkylation of 4-hydroxyquinazoline (**2d-H**) and benzo[d]thiazol-2-ol (**2e-H**), giving the target products in a same excellent isolated yield of 94% (runs 2-3). By contrast, these products were obtained in yields of 81% and 90% respectively at 100 °C by Cook's method (runs 1-3).[5d] Besides, the allylic alkylation of 4-hydroxyquinazoline is sensitive to the reaction temperature by Cook's method, and the yield of target **3c** is decreased greatly to 51% at 80 °C (run 2).[5d] Then various allylic alcohols were tested to extend the scopes of the method. As shown in table 1, like the model reaction, both electron-rich and -deficient cinnamyl alcohols reacted efficiently with 4-hydroxyquinazoline, affording the target products in high yields (runs 4-7). To our delight, the allylic alkylation of 2-hydroxypyridine (**2a-H**) with aliphatic allylic alcohols can smoothly proceed, affording the target products in high yields under mild conditions (runs 8-9). As to 4-hydroxyquinazoline, the target products could be obtained in comparable yields to Cook's method only by increasing the reaction temperature to 80 or 100 °C (runs 10-12). Despite that no better yields were obtained, a substrate self-assisted activation of allylic alcohols is still possibly involved. Finally, a larger scale (5.0 mmol) reaction of cinnamyl alcohol (**1a**) and 2-hydroxypyridine (**2a-H**) could afford the target products **3a** in a slightly higher yield of 93% (0.981 g), showing the practicability of this new method.

Based on these control experiments and the literature reports, [2,5d,6b,9] a possible reaction mechanism was depicted in scheme 43. As to this novel extra activator-free Tsuji–Trost reaction of allylic alcohols with tautomerizable heteroarenes, two activation paths might be involved in the activation of allylic alcohols (Scheme 3). A DMC-assisted activation of allylic alcohol via transesterification may be involved in cook's method,[5d,9] leading to the generation of key π-allyl palladium intermediate. However, when the reaction is carried out in a nonpolar and aprotic solvent such as cyclohexane, a substrate self-assisted activation of allylic alcohols *via* formation of six-membered ring complex by hydrogen bond may be the main path (path b), following by oxidative addition with a palladium catalyst giving the crucial π-allyl palladium intermediate. Once the key π-allyl palladium intermediate is generated, a final nucleophilic attack by tautomerizable heteroarenes affords the target products.




**Scheme 3.** Possible activation mechanism of cinnamyl alcohol under extra activator-free conditions

In conclusion, we disclosed a substrate self-assisted activation of allylic alcohol by various NMR techniques including variable-temperature $^1$H NMR, Job's Plot and $^1$H NMR titration. The efficient activation of allylic alcohols may be involved in a 1:1 binding six-membered-ring complex *via* hydrogen bond, thus leading to the generation of the key л-allylic palladium species. Guided by these finding, a much milder dehydrative substitution of tautomerizable heteroarenes with allylic alcohols was developed. Compared with Cook' method, the reactions can be carried out in milder conditions, affording the target allylic products in high yields. Further application of this novel substrate self-assisted activation of allylic alcohols for the developments of mild Tsuji–Trost reactions is under way.

## EXPERIMENTAL SECTION

**General Information**. Unless otherwise specified, all reactions were carried out in sealed Schlenk tubes under $N_2$ and then monitored by TLC and/or GC-MS. Products were purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. $^1$H and $^{13}$C {$^1$H} NMR spectra were measured on a JNM-ECZ600R/S3 (Jeol, Japan) (600 MHz and 150 MHz, respectively) using $CDCl_3$ as the solvent. Chemical shifts for $^1$H and $^{13}$C NMR were referred to internal $Me_4Si$ (0 ppm) as the standard. Mass spectra were measured on an Agilent GC-MS-5890A/5975C Plus spectrometer (EI). High resolution mass spectra (HRMS) were recorded on a LC-TOF spectrometer (Xevo G2-XS QTof) using ESI techniques. Melting points are uncorrected.

**General procedure for variable-temperature NMR analysis**: A mixture of cinnamyl alcohol **1a** (5.6 mg, 0.418 mmol), 2-hydroxypyridine (**2a-H**) (4.0 mg, 0.418 mmol) was dissolved in $CDCl_3$ (0.50 mL). Then variable-temperature NMR experiments (25, 35, 45 and 55 °C) were conducted at a JNM-ECZ600R/S3 NMR spectrometer.

**General procedure for determination of stoichiometry between cinnamyl alcohol (1a) and 2-hydroxypyridine (2a-H) studied by Job's Plot method.**

The stock solutions of Cinnamyl alcohol **1a** (225mM, 5.5mL) and 2-hydroxypyridine **2a-H** (225mM, 5.5mL) were prepared by directly dissolving their powers (**1a**, 166.4mg; **2a-H**, 117.9mg) in 5.5 mL $CDCl_3$, respectively. The solutions of the **1a** (Host) and **2a-H** (Guest) were mixed to NMR tubes according to certain proportions as summarized in Table S1 and S2. The hydroxyl protons (–O**H**) chemical shifts of both host (**1a**) and guest (**2a-H**) were referenced to TMS. All $^1$H NMR spectra were recorded at 600MHz 25K on a JNM — ECZ600R/S3 NMR spectrometer.

**General procedure for Host-guest interactions of cinnamyl alcohol (1a) and 2-hydroxypyridine (2a-H) by $^1$H NMR titration experiments.** The stock solution of Cinnamyl alcohol **1a** (224mM, 800μL) was prepared by directly dissolving 24.0 mg power in 800μL $CDCl_3$. The stock solution of 2-hydroxypyridine **2a-H** (2.24M, 157μL) was prepared by directly dissolving 33.5mg power in 157μL $CDCl_3$.

500μL **1a** stock solution was transferred to an NMR tube and was titrated with 100 μL **2a-H** (2.24M), added in 5μL increments for 10 times and 10μL increments for 5 times, and then with 32.1mg **2a-H** powder, added in 10.7mg increments for 3 times. The details were summarized in Table S3. The chemical shift of hydroxyl protons (–O**H**) of host (-OH of **1a**) was referenced to TMS. All $^1$H NMR spectra were recorded at 600 MHz 298 K on a JNM — ECZ600R/S3 NMR spectrometer.

**Typical Procedures for mild allylic substitution of tautomerizable heteroarenes with allylic alcohols.** The mixture of cinnamyl alcohol **1a** (80.4 mg, 0.60 mmol) and 2-hydroxypyridine **2a-H** (47.5 mg, 0.50 mmol), $[Pd(allyl)Cl]_2$ (4.6 mg, 2.5 mol%), dppf (13.8 mg, 10 mol%) and cyclohexane (1.0 mL) was sealed in a Schlenk tube (20 mL) under $N_2$, and stirred at 60 °C (oil bath) for 12 h. The reaction was then monitored by TLC and/or GC-MS. After completion of the reaction, the reaction mixture was purified by flash column chromatography on silica gel using ethyl acetate and petroleum ether (EA/PE = 0 ~ 1/1) as the eluent, giving **3a** in 90% isolated yield.

**1-Cinnamylpyridin-2(1H)-one (3a).** Colorless oil, (EA/PE = 0 ~ 1/1, 95.0 mg, 90%).[5d] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.35 (d, $J$ = 7.4 Hz, 2H), 7.33 – 7.27 (m, 4H), 7.23 (dd, $J$ = 8.2, 6.3 Hz, 1H), 6.65 – 6.51 (m, 2H), 6.29 (dt, $J$ = 15.8, 6.5 Hz, 1H), 6.23 – 6.05 (m, 1H), 4.70 (dd, $J$ = 6.3, 1.0 Hz, 2H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 162.6, 139.6, 137.1. 136.1, 134.1, 128.7, 128.2, 126.7, 123.7, 121.2, 106.3, 50.8; m/z (EI) : 211, 194, 182, 171, 152, 146, 133, 120, 117, 115, 102, 96, 91, 78, 65, 51.

**3-Cinnamylquinazolin-4(3H)-one (3c).** Colorless solid, m.p. 108-109 °C, (EA/PE = 0 ~ 1/3, 123.5 mg, 94%). [5d] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.34 – 8.29 (m, 1H), 8.08 (s, 1H), 7.75 – 7.68 (m, 2H), 7.50 – 7.46 (m, 1 H), 7.36 – 7.31 (m, 2H), 7.27 (t, $J$ = 7.5 Hz, 2H), 7.24 – 7.20 (m, 1 H), 6.63 (d, $J$ = 15.9 Hz, 1H), 6.31 (dt, $J$ = 15.8, 6.4 Hz, 1H), 4.75 (dd, $J$ = 6.8, 1.1 Hz, 2H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 148.2, 146.3, 135.8, 134.5, 134.4, 128.7, 128.4, 127.6, 127.5, 126.9, 126.7, 122.9, 122.2, 48.3; m/z (EI) : 262, 247, 233, 216, 201, 191, 184, 171, 147, 130, 117, 115, 102, 91, 77, 63, 51.

**3-Cinnamylbenzo[d]thiazol-2(3H)-one (3d).** Colorless solid, m.p. 46-47 °C, (EA/PE = 0 ~ 1/1, 125.5 mg, 94%). [5d] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.47 – 7.42 (m, 1H), 7.36 – 7.31 (m, 1H), 7.31 – 7.27 (m, 2H), 7.24 – 7.21 (m, 3H), 7.16 (t, $J$ = 7.4 Hz, 1H), 7.10 (d, $J$ = 8.2 Hz, 1H), 6.60 (d, $J$ = 15.9 Hz, 1H), 6.22 (dt, $J$ = 15.9, 5.8 Hz, 1H), 4.73 (dd, $J$ = 5.8, 1.5 Hz, 2H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 170.0, 137.1, 136.0, 133.6, 128.7, 128.2, 126.6, 126.5, 123.3, 122.8, 122.7, 122.2, 111.2, 44.7; m/z (EI) : 267, 249, 234, 223, 212, 207, 193, 176, 165, 150, 136, 122, 117, 115, 106, 91, 78, 69, 65, 57, 54, 51.

**(*E*)-3-(3-(4-Methoxyphenyl)allyl)quinazolin-4(3H)-one (3e).** Colorless solid, m.p. 122-124 °C, (EA/PE = 0 ~ 1/2, 125.5 mg, 86%). [16] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.37 – 8.28 (m, 1H), 8.09 (s, 1H), 7.80 – 7.65 (m, 2H), 7.50 – 7.48 (m, 1H), 7.28 (dd, $J$ = 9.0, 2.4 Hz, 2H), 6.81 (dd, $J$ = 9.0, 2.4 Hz, 2H), 6.59 (d, $J$ = 15.6 Hz, 1H), 6.18 (dt, $J$ = 15.6, 6.6 Hz, 1H), 4.80 – 4.71 (m, 2H), 3.77 (s, 3H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 159.8, 148.2, 146.3, 134.4, 134.2, 128.6, 128.0, 127.6, 127.4, 126.9, 122.2, 120.5, 114.1, 55.4, 48.4; m/z (EI) : 292, 280, 267, 261, 249, 235, 229, 207, 201, 191, 171, 147, 131, 115, 103, 91, 77, 63, 55, 51.

**(*E*)-3-(3-(4-Fluorophenyl)allyl)quinazolin-4(3H)-one (3f)**. Colorless solid, m.p. 110-111 °C, (EA/PE = 0 ~ 1/3, 126.0 mg, 90%).[17] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.33 – 8.26 (m, 1H), 8.06 (s, 1H), 7.76 – 7.64 (m, 2H), 7.47 (t, $J$ = 7.2 Hz, 1H), 7.28 (dd, $J$ = 8.4, 5.4 Hz, 2H), 6.95 (t, $J$ = 8.4 Hz, 2H), 6.57 (d, $J$ = 15.6 Hz, 1H), 6.22 (dt, $J$ = 15.6, 6.6 Hz, 1H), 4.73 (d, $J$ = 6.0 Hz, 2H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 162.7 (d, $J$ = 247.6 Hz), 161.0, 148.2, 146.2, 134.4, 133.3, 132.1 (d, $J$ = 2.6 Hz), 128.3 (d, $J$ = 7.8 Hz), 127.5 (d, $J$ = 25.5 Hz), 126.8, 122.7, 122.2, 115.7 (d, $J$ = 21.7 Hz), 48.2; m/z (EI) : 280, 265, 251, 232, 221, 207, 199, 191, 171, 165, 147, 135, 120, 115, 109, 102, 90, 83, 76, 63, 57, 50.

**(*E*)-3-(3-(4-Chlorophenyl)allyl)quinazolin-4(3H)-one (3g).** Colorless solid, m.p. 138-139 °C, (EA/PE = 0 ~ 1/3, 136.1 mg, 92%). $^1$H NMR (600 MHz, CDCl3) $\delta$ 8.32 (dd, $J$ = 8.4, 1.2 Hz, 1H), 8.07 (s, 1H), 7.78 – 7.74 (m, 1H), 7.71 (d, $J$ = 7.8 Hz, 1H), 7.51 (t, $J$ = 7.8 Hz, 1H), 7.28 – 7.23 (m, 4H), 6.58 (d, $J$ = 15.6 Hz, 1H), 6.30 (dt, $J$ = 15.6, 6.6 Hz, 1H), 4.77 (dd, $J$ = 6.0, 1.2 Hz, 2H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 148.2, 146.2, 134.5, 134.3, 134.0, 133.2, 128.9, 127.9, 127.64, 127.55, 126.9, 123.6, 122.19, 48.2; m/z (EI) : 298, 297, 296, 281, 267, 253, 207, 191, 184, 176, 171, 151, 147, 125, 115, 102, 90, 76, 63, 58, 50. HRMS (ESI-TOF) m/z: $(M+H)^+$ calcd for $C_{17}H_{14}ClN_2O$ 297.0795, found 297.0807.

**(*E*)-3-(3-(2-Methoxyphenyl)allyl)quinazolin-4(3H)-one (3h).** Colorless solid, m.p. 112-113 °C, (EA/PE = 0 ~ 1/2, 122.6 mg, 84%). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.31 (d, $J$ = 7.8 Hz, 1H), 8.10 (s, 1H), 7.73 –7.68 (m, 2H), 7.47 (t, $J$ = 7.8 Hz, 1H), 7.37 (d, $J$ = 7.8 Hz, 1H), 7.23 – 7.18 (m, 1H), 6.99 (d, $J$ = 15.6 Hz, 1H), 6.89 – 6.80 (m, 2H,), 6.35 (dt, $J$ = 15.6, 6.6 Hz, 1H), 4.77 (d, $J$ = 6.6 Hz, 2H), 3.80 (s, 3H); $^{13}$C {$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 156.9, 148.2, 146.4, 134.3, 130.0, 129.4, 127.6, 127.4, 127.3, 126.9, 124.8, 123.5, 122.3, 120.7, 110.9, 55.5, 48.8; m/z (EI) : 292, 280, 273, 249, 235, 229, 207, 201, 191, 171, 147, 131, 115, 103, 91, 77, 63, 55, 51. HRMS (ESI-TOF) m/z: $(M+H)^+$ calcd for $C_{18}H_{17}N_2O_2$ 293.1290, found 293.1268.

**1-Allylpyridin-2(1H)-one (3i).** Colorless oil (EA/PE = 0 ~ 1/1, 55.3 mg, 82%). [8a] $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.30

(ddd, *J* = 8.8, 6.6, 1.8 Hz, 1H), 7.23 (dd, *J* = 6.6, 1.8 Hz, 1H), 6.56 (d, *J* = 8.8 Hz, 1H), 6.28 – 6.10 (m, 1H), 6.04 – 5.84 (m, 1H), 5.23 (d, *J* = 10.4 Hz, 1H), 5.16 – 5.14 (m, 1H), 4.54 (d, *J* = 5.4 Hz, 2H); $^{13}$C {$^{1}$H} NMR (150 MHz, $CDCl_3$) $\delta$ 162.5, 139.6, 137.2, 132.6, 121.2, 118.5, 106.2, 51.1; m/z (EI) : 135, 133, 128, 120, 118, 109, 106, 96, 92, 79, 78, 67, 51.

**1-(Cyclohex-2-en-1-yl)pyridin-2(1H)-one (3j).** Colorless oil, (EA/PE = 0 ~ 1/1, 77.9 mg, 89%). $^{1}$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.47 – 7.29 (m, 1H), 7.29 – 7.15 (m, 1H), 6.51 –6.45 (m, 1H), 6.13 –6.08 (m, 2H), 5.59 – 5.41 (m, 2H), 2.11 –2.05 (m, 3H), 1.74 – 1.56 (m, 2H), 1.54 – 1.47 (m, 1H); $^{13}$C {$^{1}$H} NMR (150 MHz, $CDCl_3$) $\delta$ 162.6, 139.0, 134.9, 134.1, 126.2, 120.5, 105.9, 51.2, 29.7, 24.7, 19.7; m/z (EI) : 175, 165, 161, 157, 146, 141, 127, 122, 118, 113, 109, 96, 81, 80, 79, 78, 77, 67, 66, 60, 57, 53, 52, 51. HRMS (ESI-TOF) m/z: $(M+H)^+$ calcd for $C_{11}H_{14}NO$ 176.1075, found 176.1071.

3-Allylquinazolin-4(3H)-one **(3k).** Colorless solid, m.p. 63-64 °C, (EA/PE = 0 ~ 1/3, 76.2 mg, 82%). [5d] $^{1}$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.29 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.00 (s, 1H), 7.75 – 7.68 (m, 2H), 7.50 – 7.47 (m, 1H), 6.00 – 5.94 (m, 1H), 5.35 – 5.20 (m, 2H), 4.62 (dt, *J* = 6.0, 1.2 Hz, 2H); $^{13}$C {$^{1}$H} NMR (150 MHz, $CDCl_3$) $\delta$ 160.9, 148.2, 146.3, 134.4, 131.9, 127.6, 127.4, 126.9, 122.2, 119.0, 48.4; m/z (EI) : 186, 185, 171, 169, 157, 145, 143, 132, 130, 118, 102, 92, 91, 89, 78, 76, 75, 65, 63, 56, 54, 52, 50.

**(*E*)-3-(Hex-2-en-1-yl)quinazolin-4(3H)-one (3l)**. Colorless oil (EA/PE = 0 ~ 1/3, 74.1 mg, 65%). $^{1}$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.30 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.02 (s, 1H), 7.74 – 7.74 (m, 1H), 7.49 – 7.47 (m, 2H), 5.83 – 5.68 (m, 1H), 5.66 – 5.56 (m, 1H), 4.56 (d, *J* = 6.0 Hz, 2H), 2.02 (q, *J* = 7.2 Hz, 2H), 1.41 – 1.35 (m, 2H), 0.86 (t, *J* = 7.2 Hz, 3H); $^{13}$C {$^{1}$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 148.2, 146.3, 136.5, 134.3, 127.5, 127.3, 126.9, 123.7, 122.2, 48.0, 34.3, 22.1, 13.7; m/z (EI) : 228, 211, 2017, 199, 197, 185, 171, 147, 129, 127, 118, 102, 99, 94, 91, 90, 82, 76, 67, 63, 65, 53, 50. HRMS (ESI-TOF) m/z: $(M+H)^+$ calcd for $C_{14}H_{17}N_2O$ 229.1341, found 229.1322.

**3-(Cyclohex-2-en-1-yl)quinazolin-4(3H)-one (3m)**. Colorless oil (EA/PE = 0 ~ 1/3, 82.5 mg, 73%). [5d] $^{1}$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.30 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.15 (s, 1H), 7.77 – 7.71 (m, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.49 – 7.47 (m, 1H), 6.23 – 6.20 (m, 1H), 5.64 – 5.62 (m, 1H), 5.56 – 5.53 (m, 1H), 2.27 – 2.08 (m, 3H), 1.80 – 1.72 (m, 2H), 1.72 – 1.62 (m, 1H); $^{13}$C {$^{1}$H} NMR (150 MHz, $CDCl_3$) $\delta$ 161.0, 148.0, 144.9, 134.7, 134.3, 127.4, 127.2, 126.9, 125.3, 122.0, 50.0, 29.9, 24.7, 19.7; m/z (EI) : 226, 197, 185, 171, 147, 130, 118, 102, 90, 80, 77, 63, 55, 53.

**Typical Procedures for mild allylic substitution of** 2-hydroxypyridine **2a-H with** cinnamyl alcohol **1a on a large scale.** The mixture of cinnamyl alcohol **1a** (804.9 mg, 6.0 mmol) and 2-hydroxypyridine **2a-H** (475.0 mg, 5.0 mmol), $[Pd(allyl)Cl]_2$ (46.6 mg, 2.5 mol%), dppf (138.0 mg, 10 mol%) and cyclohexane (5.0 mL) was sealed in a Schlenk tube (20 mL) under $N_2$, and stirred at 65 °C (oil bath) for 17 h. The reaction was then monitored by TLC and/or GC-MS. After completion of the reaction, the reaction mixture was purified by flash column chromatography on silica gel using ethyl acetate and petroleum ether (EA/PE = 0~ 1/1) as the eluent, giving **3a** in 93% isolated yield (0.981 g).

## ASSOCIATED CONTENT

Supporting Information

Details of the control experiments for mechanistic studies are supplied as Supporting Information (file type, i.e., PDF) and this material is available free of charge via the Internet at http://pubs.acs.org."

## AUTHOR INFORMATION

Corresponding Author

* xiantaoma@126.com

ORCID

Xiantao Ma: 0000-0002-0012-6944

Notes

The authors declare no competing financial interest.

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