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锰催化的碳酸乙烯亚乙酯对喹唑啉酮的 C—H 烯丙基化

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摘要 以碳酸乙烯亚乙酯为原料, 通过锰催化的喹唑啉酮的邻位碳氢烯丙基化反应, 制备得到了一系列具有潜在应用价值的芳基丁烯醇类产物. 该反应表现出较好的底物普适性和顺反立体选择性, 拓展了锰催化 C—C 偶联反应的类型.
关键词 锰催化; 烯丙基化; 喹唑啉酮; C—H 活化

Manganese-Catalyzed Allylation of Quinazolinones with 4-Vinyl-1,3-dioxolan-2-one via C—H Activation

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Abstract The *ortho*-allylation of quinazolinones with 4-vinyl-1,3-dioxolan-2-one via manganese catalysis has been described. A series of allylation products with potential applications have been obtained. This protocol is also highlighted by good compatibility of functional groups and excellent *E*/*Z* selectivity. This work broadens the scope of Mn-catalyzed C—C coupling reactions.
Keywords manganese-catalyzed; allylation; quinazolinones; C—H activation

Quinazolinones are *N*-heterocycle chemicals widely applied in biological and pharmacological science. They possess wide range of biological properties such as anticancer, antianaphylatic, antimalarial, antiinflammatory, antihypertensive, anticonvulsant, antidiabetic and among diuretic others.[1] As a result, the construction and modification of quinazolinone have attracted significant attentions of synthetic chemists.

Over the past decades, transition-metal-catalyzed C—H bond activation has emerged as a valuable strategy for the assembly of C—C bond.[2] Various 4d and even 3d transition metals including Fe,[3] Co,[4] Ni,[5] Cu,[6] Ru,[7] Rh,[8] as well as Pd[9] based complexes were employed as catalysts. In contrast, being the third most abundant transition metal, manganese is comparatively underutilized. Recently, the groups of Kuninobu and Takai, Wang, Ackermann and others have significantly advanced this field.[10] Specifically, manganese catalysts have been found to be versatile to enable C—H allylations. In 2017, the manganese catalyzed substitutive C—H allylation through highly selective C—H/C—O functionalization was achieved by Ackermann *et al.*[10m] Afterward, Glorius's group have developed a general strategy to synthesize allylic alcohols, allylated arenes, functionalized cyclopentenes and skipped dienes, in which earth abundant manganese was utilized as the catalyst.[11] On the other hand, recent studies revealed that the quinazolinone scaffold could act as a directing group in promoting C—H bond activation. In this respect, quinazolinone was previously used as the intrinsic directing group for halogenation, intramolecular amination, acetoxylation, methoxylation, alkenylation/aza-Michael addition, and annulation, *etc.*, using Pd,[12] Rh,[13] Ru,[14] Co,[15] and Ir[16] catalysts (Scheme 1a). Herein, we reported a manganese catalyzed allylation of 2-arylquinazolinones by taking advantage of quinazolinone as the inherent directing group under mild conditions. 4-Vinyl-1,3-dioxolan-2-one was used as the convenient alcohols reagent (Scheme 1b).

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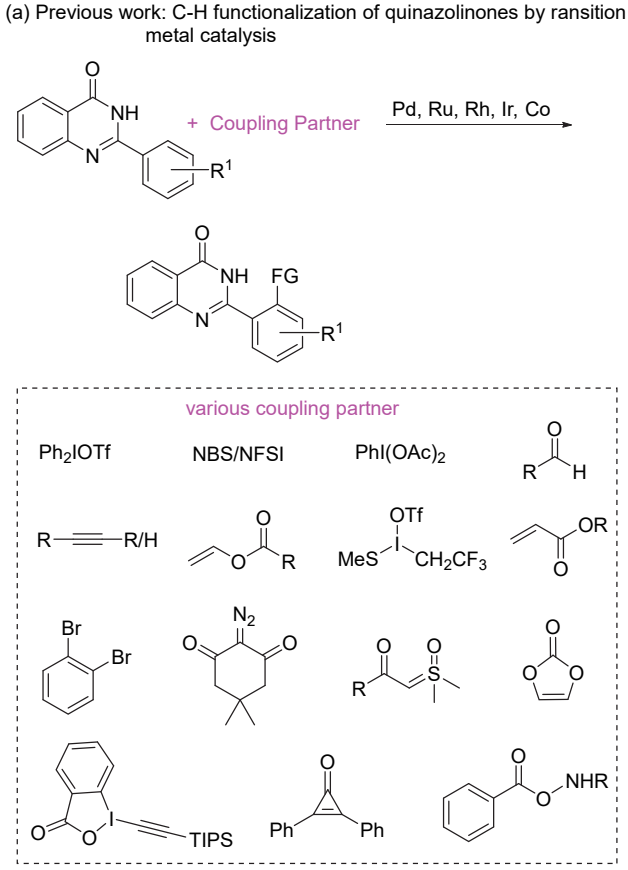
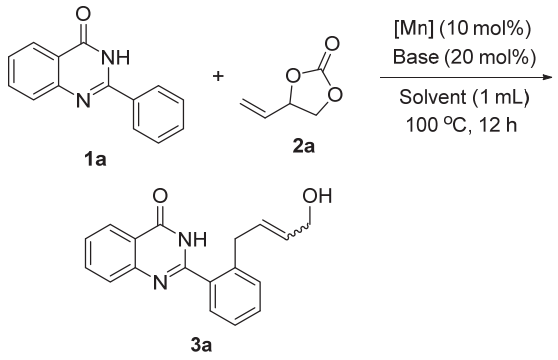


Scheme 1 Representative transition-metal-catalyzed coupling reactions of quinazolinone

2 Results and discussion

At the outset of our studies, the reaction of 2-phenyl-quinazolin-4(3*H*)-one (**1a**) with 4-vinyl-1,3-dioxo- lan-2-one (**2a**) was chosen as the model reaction to optimize various reaction parameters (Table 1). Without manganese catalysts, no product was detected (Table 1, Entry 1). Among the different manganese catalyst, $MnBr(CO)_5$ was proved to be the optimal catalysts giving product **3a** in 45% yield (Table 1, Entries 2～5). Various bases, such as LiOAc, NaOAc, KOAc, K_3PO_4, CsF and Cy_2NH were further screened and NaOAc was found to evidently promote this allylation, giving the desired product **3a** in 68% yield (Table 1, Entries 6～11). Next, a systematic solvent screening was carried out, and using NMP as solvent favors this reaction more than other solvents, including *N*,*N*-dimethylformamide (DMF), 1,4-dioxane, *N*,*N*-dimethylacetamide (DMA), tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), and 1,2-dichloroethane (DCE) (Table 1, Entries 12～17). To our delight, the yield of **3a** could be improved to 90% when lowing the volume of solvent to 0.5 mL (Table 1, Entry 18). Increasing the loading of NaOAc to 50 mol% led to a similar yield of 89% (Table 1, Entry 19). In addition, no better results were found at lower or higher reaction temperatures (Table 1, Entries 20, 21). Finally, 10 mol% $MnBr(CO)_5$, and 20 mol% NaOAc in *N*-methyl pyrrolidone (NMP) at 100 ℃ for 12 h were found to be the optimal conditions for this C—H activation reaction (Table 1, Entry 18).

Table 1 Optimization of reaction conditions[a]



Entry	[Mn]	Solvent	Base	Yield[b]/%
1	—	DMF	—	0
2	$MnBr(CO)_5$	DMF	—	45 (*E*/*Z*=9.4)
3	$MnBr_2$	DMF	—	0
4	$MnCl_2$	DMF	—	0
5	$Mn(OAc)_2$	DMF	—	0
6	$MnBr(CO)_5$	DMF	KOAc	54 (*E*/*Z*=8.3)
7	$MnBr(CO)_5$	DMF	NaOAc	68 (*E*/*Z*=8.2)
8	$MnBr(CO)_5$	DMF	LiOAc	46 (*E*/*Z*=7.4)
9	$MnBr(CO)_5$	DMF	K_3PO_4	31 (*E*/*Z*=8.1)
10	$MnBr(CO)_5$	DMF	CsF	33 (*E*/*Z*=7.9)
11	$MnBr(CO)_5$	DMF	Cy_2NH	28 (*E*/*Z*=8.7)
12	$MnBr(CO)_5$	1,4-Dioxane	NaOAc	17 (*E*/*Z*=4.3)
13	$MnBr(CO)_5$	DMA	NaOAc	50 (*E*/*Z*=8.8)
14	$MnBr(CO)_5$	THF	NaOAc	12 (*E*/*Z*=3.6)
15	$MnBr(CO)_5$	DMSO	NaOAc	25 (*E*/*Z*=7.5)
16	$MnBr(CO)_5$	DCE	NaOAc	Trace
17	$MnBr(CO)_5$	NMP	NaOAc	82 (*E*/*Z*=9.4)
18[c]	$MnBr(CO)_5$	NMP	NaOAc	90 (*E*/*Z*=9.5)
19[d]	$MnBr(CO)_5$	NMP	NaOAc	89 (*E*/*Z*=9.4)
20[e]	$MnBr(CO)_5$	NMP	NaOAc	62 (*E*/*Z*=9.5)
21[f]	$MnBr(CO)_5$	NMP	NaOAc	73 (*E*/*Z*=9.6)

[a] **1a** (0.2 mmol), **2a** (0.4 mmol), [Mn] (10 mol%), base (20 mol%), solvent (1 mL), 12 h, 100 ℃, N_2. [b] Isolated yield. [c] Solvent (0.5 mL), *E*/*Z*=9.5, by ^1H NMR. [d] Base (50 mol%). [e] 110 ℃. [f] 90 ℃. NMP=*N*-methylpyrrolidin-2-one, DMF = *N*,*N*-dimethylformamide, DMA = *N*,*N*-dimethylacetamide, DCE = 1,2-dichloroethane, DMSO=dimethyl sulfoxide, THF=tetrahydrofuran.

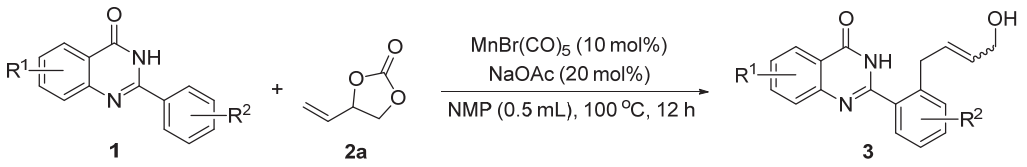
With the optimal reaction conditions in hand, the

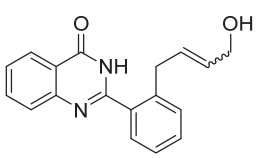
generality and scope of 2-phenylquinazolin-4(3*H*)-one with **2a** were next explored (Table 2). To our delight, various 2-phenylquinazolin-4(3*H*)-one containing electron-donating or electron-withdrawing groups or halogens worked well under the optimized reaction conditions, leading to the target product (**3a** ～ **3f**), although introduction of an EWG tends to give an inferior yield (**3e** and **3f**). Methyl group at 2-, 3-, and 4- position of 2-phenylquinazolin-4(3*H*)-one provided the corresponding products **3g**, **3h**, and **3b** in 58%, 86%, and 94% yields, respectively. And, this result indicated that such steric effect slightly impacted on this transformation. In addition, disubstituted quinazolinones were also viable for this transformation, affording the corresponding product in 82%～87% yields (**3i** and **3j**). The catalytic system is also compatible with fused rings, which could afford the corresponding target products with excellent yields (**3k** and **3l**). Meanwhile, the scope of quinazolinone motif has been evaluated under the standard reaction conditions. The methyl and chlorine groups at the aryl ring of quinazolinones produced the corresponding products **3m**～**3n** in high yields.

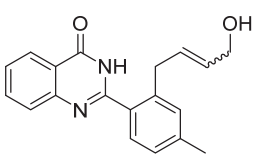
Encouraged by these inspiring results, we next sought to apply this protocol to introduce a vicinal carbonyls contained group, by using *α*,*β*-unsaturated esters as the coupling partner. Gratifyingly, fine tuning of the reaction conditions allowed the coupling of **1a** with ethyl acrylate (**4**) to proceed smoothly giving **5** in 56% yield (Scheme 2).

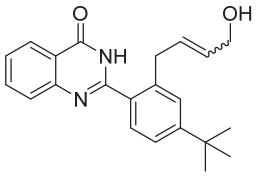
Based on the above results and precedent reports,[10] a plausible mechanism is proposed for Mn-catalyzed allylation of quinazolinones (Scheme 3). Firstly, manganese complex **I** is generated from C—H activation and cleavage in 2-phenylquinazolin-4(3*H*)-one (**1a**) by $MnBr(CO)_5$. Subsequent coordination of 4-vinyl-1,3-dioxolan-2-one (**2a**) gives intermediate **II**, in which a regioselective insertion of the 4-vinyl-1,3-dioxolan-2-one into the C—Mn bond occurs to afford a seven-membered manganacycle **III**. Subsequent *β*-oxygen elimination and decarboxylation

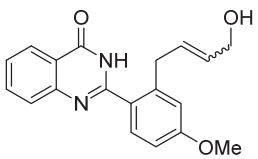
Table 2 Scope of quinazolinones for Mn(II)-catalyzed allylation

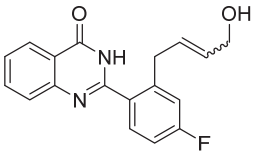


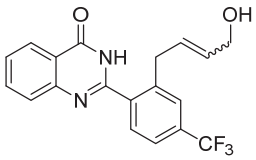

3a, 90% (*E*/*Z* = 9.5)

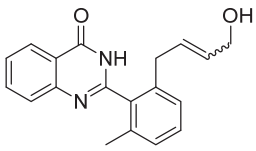

3b, 94% (*E*/*Z* > 20)

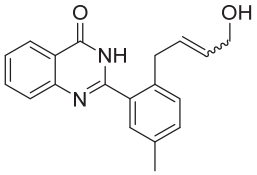

3c, 91% (*E*/*Z* = 12.3)

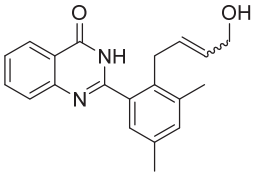

3d, 88% (*E*/*Z* >20)

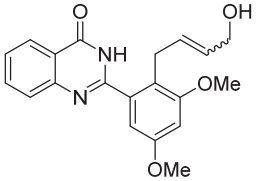

3e, 75% (*E*/*Z* = 17.2)

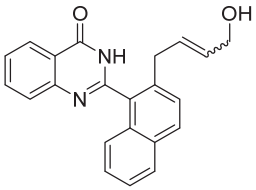

3f, 62% (*E*/*Z* = 17.2)

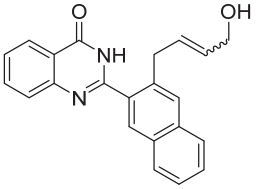

3g, 58% (*E*/*Z* = 8.5)

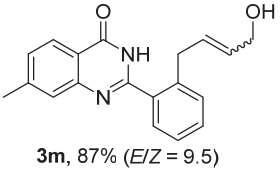

3h, 86% (*E*/*Z* = 15.7)

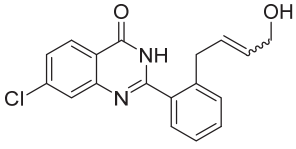

3i, 82% (*E*/*Z* > 20)


3j, 87% (*E*/*Z* = 8.5)

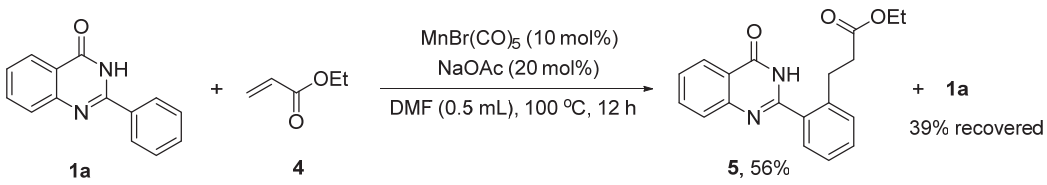

3k, 81% (*E*/*Z* > 20)


3l, 92% (*E*/*Z* = 9.8)

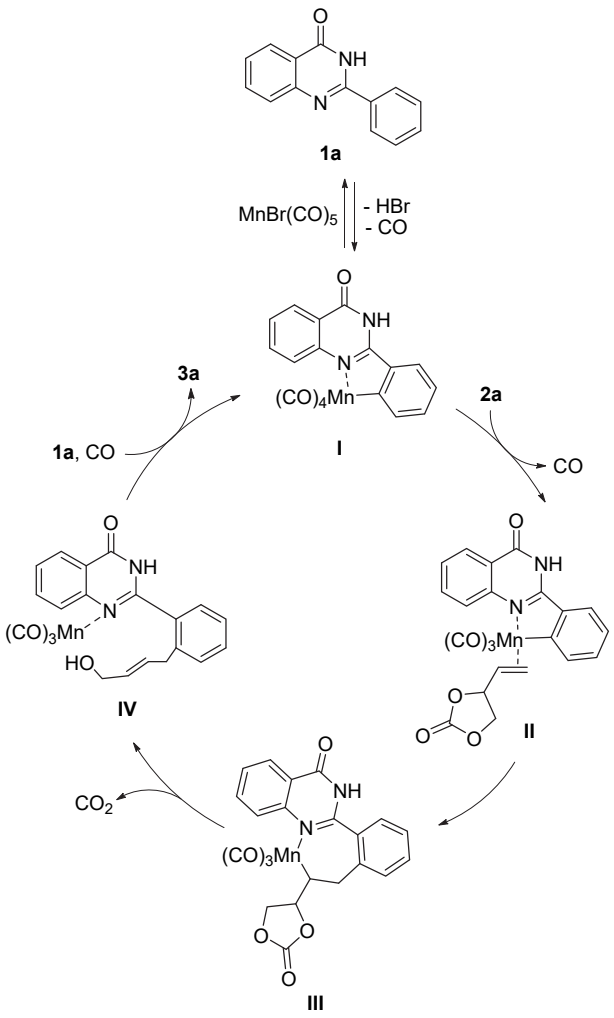

3m, 87% (*E*/*Z* = 9.5)


3n, 91% (*E*/*Z* = 9.5)

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $MnBr(CO)_5$ (10 mol%), NaOAc (20 mol%), NMP (0.5 mL), 12 h, 100 ℃, isolated yields, *E*/*Z* by ^1H NMR, N_2.



Scheme 2 Manganese catalyzed C—H activation reactions of 2-aryl quinazolinones with ethyl acrylate



Scheme 3 Plausible reaction mechanism

of the manganacycle species **III** yields manganese complex **IV**. Finally, manganacycle **IV** undergoes a protonation step in the presence of starting material **1a** to furnish the desired product **3a** and regenerates the manganese complex **I**.

3 Conclusions

In summary, we have described the site-selective modifications of quinazolinones via manganese catalyzed C—H activation of 2-aryl quinazolinones with dioxolanone. This protocol represents a combination of C—H and C—O bond activation. This method broadens the scope of manganese catalysis to include new coupling partners. Good functional group tolerance, high atom efficiency, and moderate to high yields under relatively mild conditions make this protocol useful in preparing a variety of substituted quinazolinones derivatives.

4 Experimental section

4.1 General experimental information

Air- and moisture-sensitive syntheses were performed under argon atmosphere. $MnBr(CO)_5$ was purchased from Alfa. Other chemicals were purchased from Adamas, Energy Chemical, Aldrich, TCI, Bide Pharmatech Ltd. Unless otherwise noted, all commercial reagents were used without further purification. And the products were characterized by ^1H NMR, ^{13}C NMR, MS and HRMS spectroscopy. ^1H NMR and ^{13}C NMR spectra were recorded on a Zhongke Niujin WNMR-I 400 (400 MHz). Chemical shift δ was given relative to solvent: references for $CDCl_3$ were δ 7.26 (^1H NMR) and 77.0 (^{13}C NMR), and for *d*-DMSO were δ 2.50 (^1H NMR) and 39.60 (^{13}C NMR), and for *d*-THF were δ 5.02, 3.88 (^1H NMR), ^{13}C NMR spectra were acquired on a broad band decoupled mode. EI (Electron Impact) mass spectra were recorded on a GCMS-QP2010 SE spectrometer (70 eV). ESI (electrospray ionization) high resolution mass spectra were recorded on an Agilent Technologies 6530 TOF LC/MS. All measurements were carried out at room temperature unless otherwise stated.

4.2 Experimental method

2-Phenylquinazolin-4(3*H*)-one (**1a**) (0.2 mmol, 1.0 equiv.), 4-vinyl-1,3-dioxolan-2-one (**2a**) (0.4 mmol, 2.0 equiv.), $MnBr(CO)_5$ (5.4 mg, 10 mol%), 4A MS (50 mg), and NaOAc (3.3 mg, 20 mol%) in NMP (0.5 mL) were stirred at 100 ℃ for 12 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask diluted with EtOAc (20 mL) and washed with brine (5.0 mL). The mixture was extracted with EtOAc (20 mL×3) and the combined organic layer was dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography on silica gel using a mixture of PE (petroleum ether) and EA (ethyl acetate) (EA/PE=1/4) to afford the desired product **3**.

4.3 Characterization of the product

2-(2-(4-Hydroxybut-2-en-1-yl)phenyl)quinazolin-4(3*H*)-one (**3a**): White solid, 52.6 mg, 90% yield, *E*/*Z*=9.5/1 by ^1H NMR. m.p. 128～130 ℃; ^1H NMR (400 MHz, THF-d_8) δ: 11.36 (s, 1H), 8.22 (d, *J*=7.9 Hz, 1H), 7.75～7.66 (m, 2H), 7.51～7.30 (m, 5H), 5.78～5.72 (m, 1H), 5.53～5.48 (m, 1H), 4.04 (d, *J*=6.5 Hz, 0.19H), 3.85 (s, 1.81H), 3.66 (s, 0.18H), 3.62 (d, *J*=6.9 Hz, 1.82H), 2.55 (s, 1H); ^{13}C

NMR (101 MHz, THF-d_8) δ: 154.1, 149.3, 139.6, 134.8, 133.7, 133.7, 132.2, 130.0, 129.7, 128.8, 128.3, 127.6, 126.0, 126.0, 125.9, 121.7, 62.1, 35.8. HRMS (ESI) calcd for $C_{18}H_{17}N_2O_2$ $[M+H]^+$: 293.1285; found 293.1284.

2-(2-(4-Hydroxybut-2-en-1-yl)-4-methylphenyl)quinazolin-4(3*H*)-one (**3b**): White solid, 57.6 mg, 94% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 143～145 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.30 (s, 1H), 8.20 (dd, *J*=7.9, 1.6 Hz, 1H), 7.73～7.69 (m, 1H), 7.66 (dd, *J*=8.3, 1.3 Hz, 1H), 7.44～7.40 (m, 2H), 7.18 (d, *J*=1.8 Hz, 1H), 7.14 (dd, *J*=7.7, 1.8 Hz, 1H), 5.80～5.72 (m, 1H), 5.53～5.46 (m, 1H), 3.85 (dd, *J*=5.2, 1.6 Hz, 2H), 3.65～3.59 (m, 2H), 2.62 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.6, 154.1, 149.3, 139.8, 139.5, 133.7, 132.0, 131.9, 130.7, 128.9, 128.6, 127.5, 126.5, 125.9, 125.9, 121.6, 62.1, 35.9, 20.4. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$: 307.1441; found 307.1448.

2-(4-(tert-Butyl)-2-(4-hydroxybut-2-en-1-yl)phenyl)quinazolin-4(3*H*)-one (**3c**): White solid, 63.4 mg, 91% yield, *E*/*Z*>12.3/1 by ^{1}H NMR. m.p. 72～75 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.36 (s, 1H), 8.16 (dd, *J*=7.9, 1.5 Hz, 1H), 7.86～7.78 (m, 1H), 7.66 (d, *J*=8.1 Hz, 1H), 7.52 (t, *J*=7.5 Hz, 1H), 7.44 (d, *J*=8.6 Hz, 1H), 7.37 (d, *J*=6.9 Hz, 2H), 5.71～5.56 (m, 1H), 5.44～5.38 (m, 1H), 4.03 (q, *J*=7.1 Hz, 0.15H), 3.77～3.71 (m, 1.85H), 3.59 (d, *J*=6.8 Hz, 2H), 2.50 (s, 1H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 162.3, 154.7, 153.1, 149.2, 139.2, 134.9, 132.1, 131.7, 129.7, 128.7, 127.8, 127.2, 127.0, 126.2, 123.4, 121.4, 61.6, 36.4, 35.0, 31.5. HRMS (ESI) calcd for $C_{22}H_{25}N_2O_2$ $[M+H]^+$: 349.1911; found 349.1911.

2-(2-(4-Hydroxybut-2-en-1-yl)-4-methoxyphenyl)quinazolin-4(3*H*)-one (**3d**): White solid, 56.7 mg, 88% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 72～75 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.28 (s, 1H), 8.20 (dd, *J*=7.9, 1.6 Hz, 1H), 7.73～7.69 (m, 1H), 7.67～7.64 (m, 1H), 7.48 (d, *J*=8.4 Hz, 1H), 7.43～7.39 (m, 1H), 6.94～6.83 (m, 2H), 5.81～5.73 (m, 1H), 5.55～5.48 (m, 1H), 3.89～3.83 (m, 2H), 3.82 (s, 3H), 3.69～3.63 (m, 2H), 2.55 (s, 1H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.7, 161.1, 153.9, 149.4, 141.7, 133.6, 132.2, 130.4, 128.5, 127.5, 127.0, 125.9, 125.7, 121.5, 115.8, 110.9, 62.1, 54.6, 36.1. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_3$ $[M+H]^+$: 323.1390; found 323.1385.

2-(4-Fluoro-2-(4-hydroxybut-2-en-1-yl)phenyl)quinazolin-4(3*H*)-one (**3e**): Yellow solid, 46.5 mg, 75% yield, *E*/*Z*>17.2/1 by ^{1}H NMR. m.p. 174～176 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.35 (s, 1H), 8.21 (dd, *J*=7.9, 1.5 Hz, 1H), 7.74～7.70 (m, 1H), 7.66 (dd, *J*=8.3, 1.3 Hz, 1H), 7.56 (dd, *J*=8.5, 5.7 Hz, 1H), 7.47～7.39 (m, 1H), 7.16～7.04 (m, 2H), 5.82～5.69 (m, 1H), 5.59～5.49 (m, 1H), 4.04 (d, *J*=5.8 Hz, 0.11H), 3.87 (d, *J*=5.1 Hz, 1,89H), 3.70 (d, *J*=6.9 Hz, 0.12H), 3.63 (d, *J*=6.8 Hz, 1.88H), 2.51 (s, 1H); ^{13}C NMR (101 MHz, THF-d_8) δ: 164.7, (d, *J*=333. Hz), 162.3, 153.2, 149.2, 143.1 (d, *J*=4.9 Hz), 133.7, 133.0, 131.1 (d, *J*=8.9 Hz), 131.0, 127.4 (d, *J*=19.5 Hz), 126.0 (d, *J*=38.8 Hz), 121.7, 116.5 (d, *J*=21.9 Hz), 112.7 (d, *J*=21.9 Hz), 62.0, 35.7; ^{19}F NMR (377 MHz, THF-d_8) δ: －112.19. HRMS (ESI) calcd for $C_{18}H_{15}FN_2NaO_2$ $[M+H]^+$: 333.1010; found 333.1014.

2-(2-(4-Hydroxybut-2-en-1-yl)-4-(trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (**3f**): White solid, 44.6 mg, 62% yield, *E*/*Z*>17.2/1 by ^{1}H NMR. m.p. 185～187 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.46 (s, 1H), 8.23 (dd, *J*=7.9, 1.5 Hz, 1H), 7.79～7.64 (m, 5H), 7.47 (t, *J*=7.2 Hz, 1H), 5.80～5.73 (m, 1H), 5.56～5.50 (m, 1H), 4.05～4.00 (m, 0.11H), 3.86 (d, *J*=4.9 Hz, 1,89H), 3.76 (d, *J*=7.1 Hz, 0.11H), 3.70 (d, *J*=6.8 Hz, 1.89H), 2.51 (s, 1H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.3, 152.8, 149.0, 141.1, 138.3, 133.9 ($J_{C\text{-}F}$=4.5 Hz), 133.2, 131.5 ($J_{C\text{-}F}$=32.0 Hz), 129.8, 127.7, 127.0 ($J_{C\text{-}F}$=25.1 Hz), 126.6 ($J_{C\text{-}F}$=4.0 Hz), 126.4 ($J_{C\text{-}F}$=3.4 Hz), 126.0, 125.5, ($J_{C\text{-}F}$=272.7 Hz), 121.9, 61.9, 35.7; ^{19}F NMR (377 MHz, THF-d_8) δ: －63.47. HRMS (ESI) calcd for $C_{19}H_{16}F_3N_2O_2$ $[M+H]^+$: 361.1158; found 361.1157.

2-(2-(4-Hydroxybut-2-en-1-yl)-6-methylphenyl)quinazolin-4(3*H*)-one (**3g**): White solid, 35.5 mg, 58% yield, *E*/*Z*>8.5/1 by ^{1}H NMR. m.p. 101～103 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.46 (s, 1H), 8.19 (dd, *J*=8.0, 1.6 Hz, 1H), 7.84 (td, *J*=7.7, 7.1, 1.6 Hz, 1H), 7.69 (d, *J*=8.1 Hz, 1H), 7.61～7.52 (m, 1H), 7.35 (t, *J*=7.6 Hz, 1H), 7.19 (t, *J*=8.5 Hz, 2H), 5.71～5.54 (m, 1H), 5.43～5.37 (m, 1H), 4.03 (q, *J*=7.1 Hz, 0.21H), 3.78 (d, *J*=5.2 Hz, 1,79H), 3.30～3.21 (m, 1H), 2.55 (s, 1H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 162.1, 154.2, 149.2, 138.9, 136.2, 134.9, 134.7, 132.4, 129.8, 128.3, 128.2, 127.8, 127.2, 127.2, 126.3, 121.6, 61.6, 36.2, 19.6. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$: 307.1441; found 307.1450.

2-(2-(4-Hydroxybut-2-en-1-yl)-5-methylphenyl)quinazolin-4(3H)-one (**3h**): White solid, 52.6 mg, 86% yield, *E*/*Z*>15.7/1 by ^{1}H NMR. m.p. 163～165 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.30 (s, 1H), 8.21 (dd, *J*=7.9, 1.6 Hz, 1H), 7.73～7.69 (m, 1H), 7.65 (dd, *J*=8.2, 1.3 Hz, 1H), 7.46～7.38 (m, 1H), 7.34 (s, 1H), 7.23 (s, 2H), 5.77～5.79 (m, 1H), 5.57～5.40 (m, 1H), 4.04～4.00 (m, 0.12H), 3.83 (d, *J*=5.1 Hz, 1.88H), 3.61 (s, 2H), 2.50 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.4, 151.2, 149.3, 136.5, 135.5, 134.6, 133.6, 132.0, 130.3, 130.0, 129.4, 128.6, 127.6, 125.9, 121.7, 62.1, 35.4, 19.9. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$: 307.1441; found 307.1445.

2-(2-(4-Hydroxybut-2-en-1-yl)-3,5-dimethylphenyl)quinazolin-4(3H)-one (**3i**): White solid, 52.5 mg, 82% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 149～151 ℃; ^{1}H NMR (400 MHz, THF-d_8) δ: 11.28 (s, 1H), 8.20 (dd, *J*=7.9, 1.5 Hz, 1H), 7.73～7.70 (m, 1H), 7.65～7.63 (m, 1H), 7.44～7.40 (m, 1H), 7.16～7.06 (m, 2H), 5.74～5.66 (m, 1H), 5.44～5.35 (m, 1H), 3.99 (d, *J*=5.4 Hz, 0.08H), 3.87～3.81 (m, 1.92H), 3.54 (dd, *J*=6.2, 1.6 Hz, 2H), 2.53 (s, 1H), 2.35 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.4, 154.8, 149.3, 137.5, 135.4, 135.2, 134.0, 133.6, 132.3, 131.5, 127.9, 127.6, 127.2, 125.9, 125.9, 121.7, 62.2, 31.9, 19.9, 19.0. HRMS (ESI) calcd for $C_{20}H_{21}N_2O_2$

[M+H]$^+$: 321.1598; found 321.1596.

2-(2-(4-Hydroxybut-2-en-1-yl)-3,5-dimethoxyphenyl)-quinazolin-4(3*H*)-one (**3j**): White solid, 61.3 mg, 87% yield, *E*/*Z*>8.5/1 by ^{1}H NMR. m.p. 78～81 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.35 (s, 1H), 8.16 (dd, *J*=8.0, 1.6 Hz, 1H), 7.85～7.81 (m, 1H), 7.68 (d, *J*=8.1 Hz, 1H), 7.58～7.49 (m, 1H), 6.71(d, *J*=2.5 Hz, 1H), 6.67 (d, *J*=2.5 Hz, 1H), 5.62～5.51 (m, 1H), 5.31～5.19 (m, 1H), 4.03 (q, *J*=7.1 Hz, 0.21H), 3.83 (s, 3H), 3.80 (s, 3H), 3.73～3.68 (m, 1.79H), 3.43～3.37 (m, 2H), 2.50 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 162.2, 158.8, 158.7, 154.4, 149.0, 135.9, 134.9, 131.1, 128.5, 127.8, 127.1, 126.2, 121.5, 119.9, 106.1, 100.7, 61.7, 56.5, 55.9, 28.6. HRMS (ESI) calcd for $C_{20}H_{21}N_2O_4$ [M+H]$^+$: 353.1496; found 353.1494.

2-(2-(4-Hydroxybut-2-en-1-yl)naphthalen-1-yl)quinazolin-4(3*H*)-one (**3k**): White solid, 55.4 mg, 81% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 82～84 ℃; 1H NMR (400 MHz, DMSO-d_6) δ: 12.65 (s, 1H), 8.26 (dd, *J*=8.0, 1.5 Hz, 1H), 8.04 (d, *J*=8.5 Hz, 1H), 8.01～7.96 (m, 1H), 7.91～7.83 (m, 1H), 7.74 (d, *J*=8.1 Hz, 1H), 7.65～7.44 (m, 5H), 5.81～5.68 (m, 1H), 5.59～5.53 (m, 1H), 3.96 (d, *J*=4.8 Hz, 0.08H), 3.84 (d, *J*=4.6 Hz, 1.92H), 3.49～3.41 (m, 2H), 2.55 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 162.2, 153.7, 149.3, 136.9, 135.0, 132.9, 132.0, 131.6, 131.1, 130.0, 128.5, 128.0, 127.9, 127.5, 127.4, 126.4, 126.2, 125.2, 121.9, 61.7, 36.4. HRMS (ESI) calcd for $C_{22}H_{18}N_2NaO_2$ [M+H]$^+$: 365.1260; found 365.1259.

2-(3-(4-Hydroxybut-2-en-1-yl)naphthalen-2-yl)quinazolin-4(3*H*)-one (**3l**): White solid, 63.0 mg, 92% yield, *E*/*Z*>9.8/1 by ^{1}H NMR. m.p. 180～182 ℃; 1H NMR (400 MHz, THF-d_8) δ: 11.37 (s, 1H), 8.13 (dd, *J*=7.9, 1.5 Hz, 1H), 7.98 (s, 1H), 7.82～7.77 (m, 1H), 7.74 (d, *J*=8.1 Hz, 1H), 7.71 (s, 1H), 7.65～7.57 (m, 2H), 7.44～7.31 (m, 3H), 5.74～5.61 (m, 1H), 5.44～5.28 (m, 1H), 3.92 (d, *J*=7.4 Hz, 0.37H), 3.73 (d, *J*=5.5 Hz, 3.63H), 2.52 (s, 1H); ^{13}C NMR (101 MHz, THF-d_8) δ: 161.5, 154.0, 136.7, 134.1, 133.7, 133.2, 132.4, 131.6, 129.1, 128.4, 128.3, 127.8, 127.6, 127.1, 127.0, 126.0, 126.0, 125.9, 121.8, 62.1, 36.1. HRMS (ESI) calcd for $C_{22}H_{18}N_2NaO_2$ [M+H]$^+$: 365.1260; found 365.1258.

2-(2-(4-Hydroxybut-2-en-1-yl)phenyl)-7-methylquinazolin-4(3*H*)-one (**3m**): White solid, 53.3 mg 87% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 154～156 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.36 (s, 1H), 8.05 (d, *J*=8.1 Hz, 1H), 7.52～7.42 (m, 3H), 7.36 (d, *J*=7.6 Hz, 3H), 5.71～5.58 (m, 1H), 5.45～5.39 (m, 1H), 3.79～3.72 (m, 2H), 3.54 (d, *J*=6.9 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 162.2, 154.7, 149.2, 145.5, 139.4, 134.4, 132.3, 130.5, 130.3, 129.8, 128.6, 128.5, 127.4, 126.6, 126.1, 119.0, 61.6, 36.0 21.8. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_2$ [M+H]$^+$: 307.1441; found 307.1446.

7-Chloro-2-(2-(4-hydroxybut-2-en-1-yl)phenyl)quinazolin-4(3*H*)-one (**3n**): White solid, 59.3 mg, 91% yield, *E*/*Z*>20/1 by ^{1}H NMR. m.p. 176～178 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.58 (s, 1H), 8.15 (d, *J*=8.5 Hz, 1H), 7.73 (d, *J*=2.0 Hz, 1H), 7.56 (dd, *J*=8.5, 2.0 Hz, 1H), 7.53～7.43 (m, 2H), 7.36 (d, *J*=7.2 Hz, 2H), 5.68～5.60 (m, 1H), 5.45～5.38 (m, 1H), 3.75 (t, *J*=4.1 Hz, 2H), 3.54 (d, *J*=6.9 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 161.8, 156.2, 150.2, 139.6, 139.5, 134.1, 132.4, 130.7, 130.4, 129.8, 128.4, 128.4, 127.4, 126.9, 126.6, 120.3, 61.6, 36.0. HRMS (ESI) calcd for $C_{18}H_{15}ClN_2NaO_2$ [M+Na]$^+$: 349.0714; found 349.0712.

Ethyl 3-(2-(4-*oxo*-3,4-dihydroquinazolin-2-yl)phenyl)-propanoate (**5**): White solid, 36.1 mg, 56% yield. m.p. 152～154 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 11.29 (s, 1H), 8.30 (d, *J*=7.9 Hz, 1H), 7.78 (d, *J*=4.0 Hz, 2H), 7.63 (d, *J*=7.7 Hz, 1H), 7.54～7.42 (m, 2H), 7.41～7.33 (m, 2H), 4.09 (q, *J*=7.2 Hz, 2H), 3.11 (t, *J*=7.2 Hz, 2H), 2.85 (t, *J*=7.2 Hz, 2H), 1.18 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ: 173.7, 162.6, 153.5, 149.2, 139.0, 134.6, 133.9, 130.7, 129.6, 129.6, 127.9, 126.9, 126.9, 126.5, 121.0, 60.9, 35.1, 27.4, 14.1. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_3$ [M+H]$^+$: 323.1390; found 323.1395.

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of compounds **3a**～**5**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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