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Catalyst-control in Switching the Site-Selectivity of C–H Olefinations of 1,2-dihydroquinolines: An Approach to Positional-selective Functionalization of Quinolines.

Riki Das,[a],[b]§ Nandkishor Prakash Khot,[a]§ Akanksha Santosh Deshpande[a] and Manmohan Kapur*[a]

Abstract: A unique approach to achieve site-selective C–H olefinations exclusively at the C-3 or C-8 positions in the quinoline framework has been developed *via* catalyst-control. Distal C(3)–H functionalization is achieved using palladium catalysis whereas, proximal C(8)–H functionalization is obtained by employing ruthenium catalysis. Switching site-selectivity within a single substrate directly indicates two diverse pathways which are operating in the palladium and ruthenium-catalyzed reaction conditions.

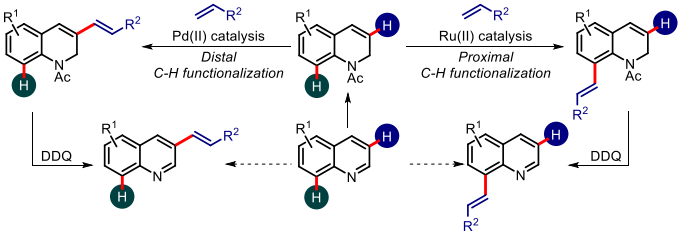
Introduction

Quinolines are one of the most familiar scaffolds, extensively found in a wide range of natural products, drug molecules, functional materials, and ligands in transition metal catalysis.[1-4] Over the last few decades, a significant percentage of the introduced drugs, where pharmacophores were heterocyclic compounds, were quinoline based.[5] Even today, the development of new and efficient methods for the synthesis of substituted quinolines is amongst the primary tasks for organic chemists. In this context, the pioneering and traditional methods for the synthesis of substituted quinolines, such as the Combes synthesis, Döbner-von Miller method, Friedlander quinoline synthesis *etc*., at times suffer from some drawbacks such as harsh reaction conditions, leading to limited substrate scope.[6] Though one can consider that the substitution reaction on existing simple quinoline motifs could be one of the valuable approaches for the synthesis of functionalized quinolines, electrophilic aromatic substitution is not suitable for electron-deficient heteroarenes. Also, the sp^2-hybridized nitrogen atoms of aza-heteroarenes frequently interact with electrophiles or Lewis acids, thus leading to decrease of reactivity towards electrophiles. Direct metal-hydrogen exchange or metal-halogen exchange with highly basic organolithium or organomagnesium reagents, followed by subsequent trapping with suitable electrophiles, causes difficulties with functional group compatibility and unfavorable nucleophilic aromatic substitution.[7] Also, these main-group organometallic reagents are mostly used in stoichiometric amounts, thus often leading to unavoidable waste formation and usually involving relatively thermodynamically-unstable intermediates. In comparison, metal-hydrogen exchange *via* transition metal complex-mediated C–H activation comes across as a comparatively milder and a more functional group-tolerant approach.[7h]

However, the late-stage, site-selective C–H functionalization on the pre-existing quinoline scaffold is an equally challenging task in the synthesis of complex molecules. A review of literature on this topic reveals that a significant number of methods are well-known for C-2 functionalization of quinoline using various transition metal catalysts.[8] Unlike pyridines,[9] transition metal-catalyzed functionalization of C-3 and C-4 position of quinolines is not well-explored. A seminal work was reported by Kanai and co-workers in which they achieved C-4 alkylated quinolines with styrenes under cobalt-catalyzed conditions.[10] Over the last few decades, employment of *N*-oxides has been explored as a directing group in transition metal catalyzed C-8 functionalization of quinolines.[11]

Results and Discussion

Based on our previous reports,[12] we focused our efforts to toggle the selectivity of C–H olefinations of 1,2-dihydro-*N*-acetyl quinolines between C-3 and C-8 positions *via* catalyst-control. To establish a switch in the selectivity governed by the electronic nature of transition metal complexes, we use electrophilic palladium (II)-complex, providing distal C(3)–H olefination,[13] whereas cationic ruthenium complex leads to heteroatom-directed, proximal C(8)–H olefination (Scheme 1).[14]



Scheme 1. Catalyst-control in Site-selective C-H olefinations.

Our initial efforts started with the optimization of various catalyst systems for C(3)–H and C(8)–H olefinations separately using 1,2-dihydro-*N*-acetyl quinoline and methyl acrylate as the benchmark substrates. Based on our previous experience with distal C–H

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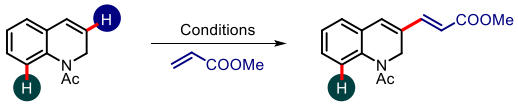
functionalizations, we had anticipated that a significantly covalent palladium catalyst could result in the functionalization at the C-3 position, whereas, a cationic catalyst would be necessary to give the directed, proximal C-8 funationalization. Various palladium-based catalyst systems were therefore screened with the combination of suitable additive and oxidant for the optimization of the electrophilic (non-directed) C(3)–H olefination (Table 1). The reaction worked best with $Pd(OAc)_2$ and did not provide better transformations or yields with other Pd(II)-catalysts that were screened. The transformation was optimized to complete within 24 h at 80 °C in presence of $Pd(OAc)_2$ (10 mol%) as the catalyst, $Cu(OAc)_2$ (1 equiv) and AgOAc (2 equiv) as the oxidant and base combination, in 1,4-dioxane as the solvent (Table 1, entry 3).

Table 1. Attempts towards optimization of C(3)–H olefination of 1,2-dihydro-*N*-acetyl quinolines[a]

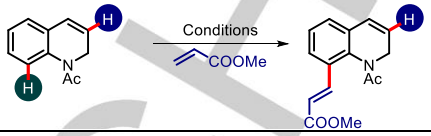


Entry	Reaction conditions	Yield (%)
1	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), THF, 65 °C, 24 h.	4
2	$Pd(OAc)_2$ (10 mol%), $Cu(OTf)_2$ (1.0 equiv), AgOTf (2.0 equiv), Toluene, 80 °C, 24 h.	NR
3	**$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.**	**56**
4	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv),Toluene,100 °C, 24 h.	5
5	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), DCE, 80 °C, 24 h.	10
6	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), DMA, 80 °C, 24 h.	6
7	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), DME, 80 °C, 24 h.	CM
8	$Pd(OAc)_2$ (10 mol%), $Cu(OTf)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	12
9	$PdCl_2$ (10 mol%), Ag_2O (1.5 equiv), AgOTf (0.5 equiv), Dioxane, 80 °C, 12 h.	NR
10	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), Ag_2O (2.0 equiv), Dioxane, 80 °C, 24 h.	20
11	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), Dioxane, 80 °C, 24 h.	16
12	$Pd(OAc)_2$ (10 mol%), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	13
13	$Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 30 h.	41
14	$Pd(OAc)_2$ (2.5 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 30 h.	17
15	$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), O_2, Dioxane, 80 °C, 24 h.	32
16	$PdCl_2(MeCN)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	45
17	$PdCl_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	42
18	$Pd(tfa)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	39
19	DG = Boc, $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	CM
20	DG = Piv, $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	CM
21	DG = Ts, $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (1.0 equiv), AgOAc (2.0 equiv), Dioxane, 80 °C, 24 h.	CM

NR = no result; CM = Complex mixture

Decent yields and exclusive regioselectivity was obtained in this palladium catalyzed C(3)–H olefination reaction. Excluding either AgOAc or $Cu(OAc)_2$ from the reaction was detrimental to the transformation. Use of other terminal oxidants, including O_2, did not improve the transformation and the reaction did not work at all without the palladium catalyst. The optimization of heteroatom-directed C(8)–H olefination was initiated with the use of various ruthenium-based catalyst systems. Combination of $[RuCl_2(p\text{-cymene})]_2$ and $AgSbF_6$ *i.e.* cationic ruthenium complex was found to be more effective for this transformation (Table 2). After extensive optimization, the best reaction conditions were found to be $[RuCl_2(p\text{-cymene})]_2$ (5 mol%) as the catalyst, $AgSbF_6$ (20 mol%) as an additive, $Cu(OAc)_2$ (2.0 equiv) acting as the terminal oxidant as well as the base, in toluene as the solvent at 100 °C (Table 2, entry 3).

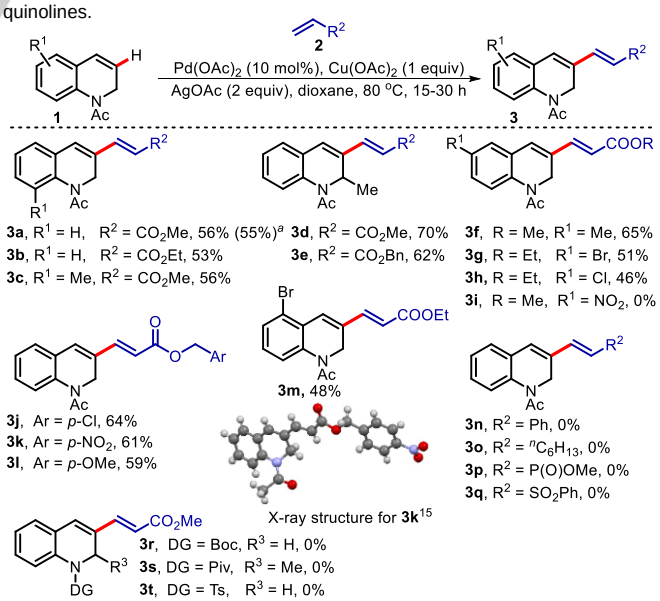
Table 2. Attempts towards optimization of C(8)–H olefination of 1,2-dihydro-*N*-acetyl quinolines[a]



Entry	Reaction conditions	Yield (%)
1	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Dioxane, 100 °C, 24 h.	21
2	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), *t*-AmOH, 100 °C, 12 h.	NR
3	**$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 20 h.**	**62**
4	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgBF_4$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 20 h.	31
5	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2.H_2O$ (2.0 equiv), Toluene, 100 °C, 24 h.	58
6	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Xylene, 120 °C, 24 h.	23
7	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OTf)_2$ (2.0 equiv), Toluene, 100 °C, 24 h.	NR[a]
8	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), DMA, 100 °C, 24 h.	NR
9	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), DME, 80 °C, 24 h.	NR
10	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), DCE, 80 °C, 24 h.	33
11	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $NaSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 24 h.	NR
12	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $KSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 24 h.	CM[b]
13	$[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), O_2 (balloon), Toluene, 100 °C, 24 h.	NR
14	$[Cp^*RhCl_2]_2$ (3 mol%), $AgSbF_6$ (15 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 24 h.	60
15	DG = Boc, $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 20 h	NR
16	DG = Piv, $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 20 h	CM
17	DG = Ts, $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (2.0 equiv), Toluene, 100 °C, 20 h	CM

[a]Only aromatization of starting material was observed; [b]C-3 olefinated product was also observed; NR = no result; CM = Complex mixture.

Table 3. Substrate scope of C(3)–H olefinations of 1,2-dihydro-*N*-acetyl quinolines.



[a]Yield for the reaction carried out on 1 mmol scale.

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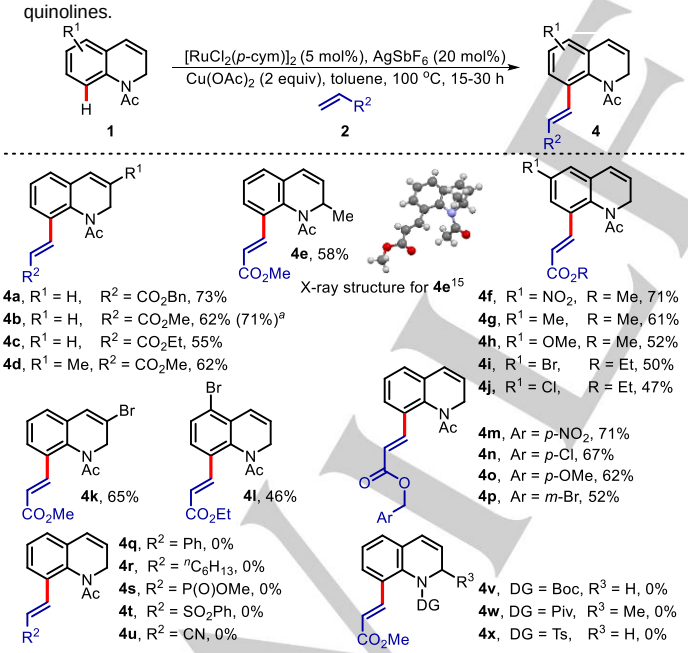
The reaction did not perform well without the Ag-additive and the $Cu(OAc)_2$ was necessary as the terminal oxidant as well as the base. The reaction did not work with O_2 as the terminal oxidant (Table 2, entry 13). Toluene was found to be the best solvent for the transformation and in absence of the ruthenium catalyst, the reaction did not work at all. Despite the cationic rhodium catalyst system also working almost equally well (Table 2, entry 14), we preferred to use the ruthenium catalyst since it was relatively less expensive. With the optimal reaction conditions in hand, the scope of C(3)–H olefination of 1,2-dihydro-*N*-acetyl quinoline was explored as shown in Table 3. The site-selectivity was exclusive as expected. Halogen functional groups on the quinoline framework as well as the olefin coupling partner were also compatible under this reaction condition. In some cases, the reactions did not proceed beyond a certain point and the starting material was recovered back. Electron-withdrawing substituents such as $-NO_2$ led to decreased electron-density on the dihydroquinoline and were not compatible under this reaction condition (Table 3, **3i**). Notably, the reaction did not work with electron-neutral olefins (Table 3, **3n-o**).

Simultaneously, the scope of C(8)–H olefination of 1,2-dihydro-*N*-acetyl quinolines was explored under its optimized reaction condition. This protocol was compatible with a wide range of functional groups, such as electron-donating as well as electron-withdrawing substituents on the phenyl ring of both the coupling partners (Table 4). Unlike C–3 olefination, the electron-withdrawing nitro-substituent worked well in this reaction condition (Table 4, **4f**). The site-selectivity was exclusive as expected.

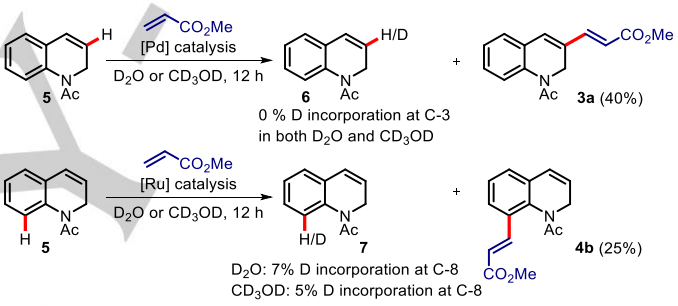
Table 4. Substrate scope of C(8)–H olefinations of 1,2-dihydro-*N*-acetyl quinolines.



[a]Yield for the reaction carried out on 1 mmol scale.

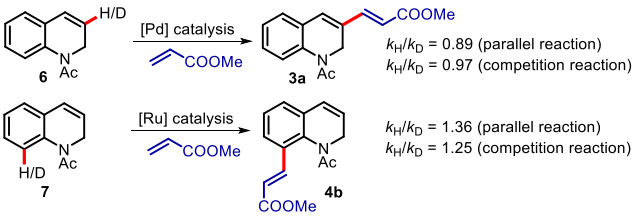
As observed for the palladium catalysis, under the ruthenium catalysis condition too, the reaction did not work with electronically-unbiased olefins (Table 4, **4q**–**r**). Other directing groups (Boc, Pivaloyl, Tosyl) failed to give the olefinated product (Table 4, **4v–x**). In both the transformations, the palladium-catalyzed, as well as the ruthenium-catalyzed one, halogen functional groups were well-tolerated, thereby increasing the synthetic utility of the method over the traditional Heck reaction.

To check the reversibility of C–H bond cleavage step, both, the palladium-catalyzed as well as ruthenium-catalyzed reactions were carried out in presence of D_2O and MeOH-d4 (Scheme 2). No D-incorporation was observed in recovered starting materials under the palladium-catalyzed C–H metallation conditions thus indicating it to be an irreversible electrophilic metallation. Under the ruthenium-catalyzed heteroatom-directed C–H metallation conditions, 7% D-incorporation was observed in presence of D_2O and about 5% D-incorporation was observed in presence of MeOH-d4, thus indicating a reversible C–H metallation step. The studies for determining whether the C–H cleavage step was kinetically relevant, were performed for both the C-3 and C-8 olefinations separately (Scheme 3).[16] The observed kinetic isotope effect values for the palladium-catalyzed transformation were close to 1.0, which suggests that in that case the C-H bond cleavage is not the rate-limiting step. The ruthenium-catalyzed transformation showed a mild kinetic isotope effect and therefore rate studies with respect to the starting material and the two catalysts were carried out, but they were not very conclusive.[16]



Scheme 2. Studies to check reversibility of metallation.

Control experiments were performed to check whether blocking the preferred site for metallation would lead to a switch in selectivity for that metal (Scheme 4). These studies confirmed that for this substrate, the preferences were exclusive and the site-selectivity for each of transition metal employed was limited to the specific position. This further indicates that the modes of C–H functionalization for the C(3)–H and the C(8)–H are quite different. On the basis of the control experiments and mechanistic studies, the plausible mechanisms for C-3 and C-8 olefinations are proposed in Scheme 5.



Scheme 3. Experiments to determine kinetic isotope effect.

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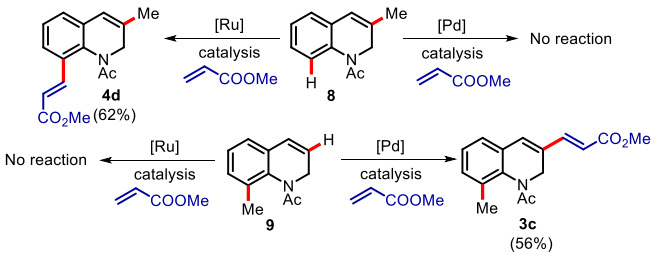
Based on our previous reports as well as others,[12-14] palladium-catalyzed C–H activation in such heterocycles could proceed *via* an electrophilic palladation, which is followed by olefin insertion to give the intermediate **12**. Subsequent *β*-hydride elimination leads to the desired C-3 olefinated products (Scheme 5).



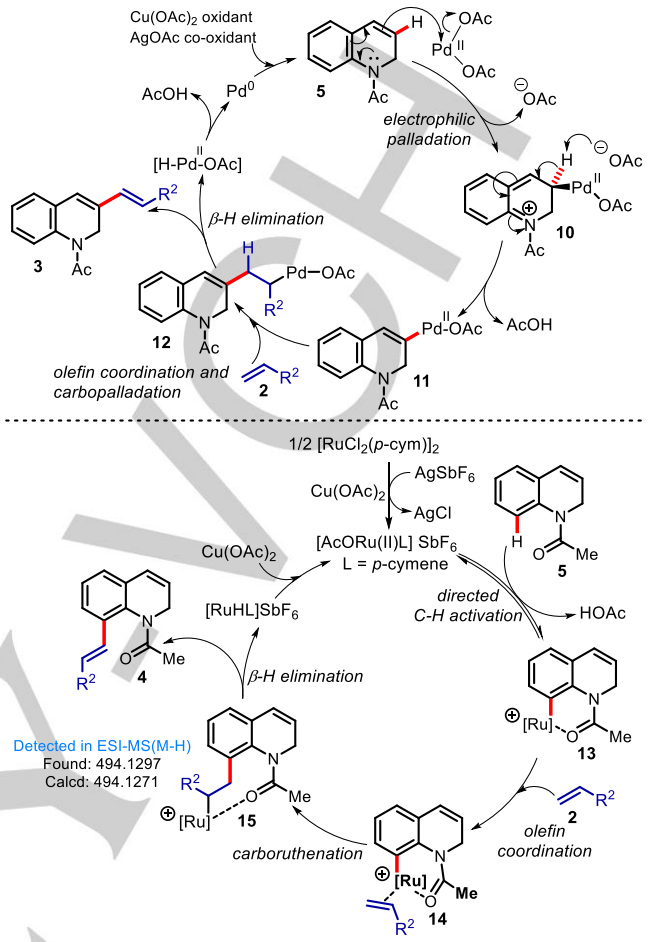
Scheme 4. Control reactions.

On the other hand, the ruthenium-catalyzed heteroatom-directed C(8)–H olefination is expected to initiate with the generation of the cationic ruthenium complex. Coordination of the metal to the Lewis-basic carbonyl oxygen followed by the acetate assisted C–H activation leads to the ruthenacycle **13**. This is followed by the coordination of the olefin, subsequent migratory insertion and *β*-hydride elimination leads to the desired product (Scheme 5). The intermediate **15** arising out of carboruthenation was detected in ESI-HRMS.

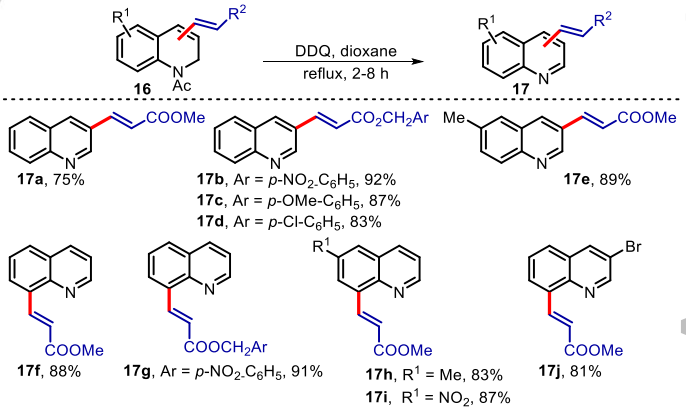
To highlight the synthetic potential of these protocols, the key question centered on the ability to remove the directing group or activating tether from the product. Therefore, the removal of acetyl group was necessary to get diversely functionalized quinolines and demonstrate the utility of the current method. A series of C-3 and C-8 olefinated 1,2-dihydro-*N*-acetyl quinolines were refluxed in dioxane in presence of DDQ which led to a library of C-3 and C-8 olefinated quinolines in good to excellent yields (Scheme 6). The substrates bearing halogen functional groups (**17d**, **17j**, Scheme 6) also performed very well in these transformations.

Conclusions

In conclusion, a clear distinction has been demonstrated between the two modes of C–H olefinations such as palladium-catalyzed distal C–H functionalization and ruthenium-catalyzed proximal C–H activation. Switching site-selectivity makes it possible to access an array of structurally diverse C-3 as well as C-8 olefinated quinolines from a single starting material. Well-tolerated halogen-substitutions on quinolines add further advantage to these methods. The development of this novel methodology to bring about C–H activation at two different sites within a single substrate by choosing the appropriate transition metal complex is expected to have good implications for newer approaches for the synthesis of substituted quinolines.



Scheme 5. Plausible mechanisms for the Pd-catalyzed as well as the Ru-catalyzed C-H functionalizations.



Scheme 6. Removal of activating tether and aromatization.

Experimental Section

(i) General Methods:

All commercially available compounds were used without purification. Unless otherwise noted, all reactions were performed in oven-dried glassware. All reactions were run under argon or nitrogen atmosphere. All solvents used in the reactions were purified before use. Tetrahydrofuran as well as toluene were distilled from sodium and benzophenone, whereas dry dichloromethane, dimethylformamide, and dichloroethane were distilled from CaH_2. Petroleum ether with a boiling range of 40–60 °C was used. Melting points are uncorrected. ^{1}H, and ^{13}C NMR: Recorded on Bruker Avance III 400 MHz NMR Spectrometer, Bruker Avance III 500 MHz NMR Spectrometer; spectra were recorded at 295 K in $CDCl_3$; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^{1}H δ 7.25; ^{13}C δ 77.0). HRMS: Bruker Daltonics MicroTOF-Q-II with electron spray ionization (ESI) or Atmospheric pressure chemical ionization (APCI). GC-HRMS: Performed on Agilent 7200 GC-QToF (with Electron Impact (EI), 70eV) with 7890A GC using DB-5 column. GC-LRMS: Performed on Agilent 7890A GC with Agilent 5975C MS (EI 70 eV) using DB-5 column. IR: Perkin Elmer Spectrum BX FTIR, Shimadzu IRAffinity-1 FTIR and were recorded as thin films between KBr plates. Kinetic studies were performed on Agilent Infinity 1290 Series HPLC using Agilent Zorbax-NH2 (4.6 x 250 mm, 5 micron) analytical column.

(ii) General Procedures and analytical data:

(A) General procedure for the synthesis of 1-(quinolin-1(2*H*)-yl) ethan-1-one (1a):

Sodium borohydride (5.86 g, 155.5 mmol) was added portion-wise to a stirring mixture of quinoline (5 g, 38.75 mmol), acetic anhydride (20 mL, 205.05 mmol) and acetic acid (60 mL), over a period of 1.5 h at 0 ºC. After the addition was complete, the mixture was warmed to 50 ºC for 30 min. The reaction mixture was concentrated under vacuum, diluted with water (500 mL) and neutralized with sodium hydrogen carbonate. This mixture was then extracted with EtOAc and the organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude oil was purified by silica gel column chromatography (71%). **^{1}H** NMR (400 MHz, $CDCl_3$): δ 7.12-6.99 (m, 4H), 6.42 (d, *J* = 9.6 Hz, 1H), 5.99-5.95 (m, 1H), 4.34 (s, 2H), 2.09 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[12a]

1-(8-methylquinolin-1(2*H*)-yl)ethanone (1b):

Prepared according to the general procedure (A) on 100 mg scale and the title compound was isolated as a colorless gel (71% yield, 93 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 – 7.09 (m, 2H), 7.00 – 6.94 (m, 1H), 6.52 (dd, *J* = 9.4, 2.2 Hz, 1H), 6.20 – 6.13 (m, 1H), 5.41 (dd, *J* = 16.7, 5.7 Hz, 1H), 3.43 (d, *J* = 16.7 Hz, 1H), 2.28 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 151.6, 148.7, 121.6 (2C), 120.4, 110.7 (2C), 110.4, 67.6, 56.0 (d, *J* = 3.55, 1C), 54.9; IR (KBr, cm^{-1}): 3368, 2900, 1645, 1439, 1392, 1208, 1124, 886, 761; ESI-HRMS: $C_{12}H_{14}NO$ $[M+H]^+$ 188.1070, found 188.1051.

1-(3-methylquinolin-1(2*H*)-yl)ethanone (1c):

Prepared according to the general procedure (A) in 100 mg scale and the title compound was isolated as a yellow gel (67% yield, 87 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 – 6.99 (m, 4H), 6.25 (d, *J* = 1.2 Hz, 1H), 4.33 (s, 2H), 2.20 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 138.7, 135.6, 130.2, 128.6, 126.1, 125.7, 123.5, 121.1, 45.7, 22.5, 20.9; IR (KBr, cm^{-1}): 3412, 2858, 1632, 1451, 1380, 1221, 1116, 1006, 804; ESI-HRMS: $C_{12}H_{14}NO$ $[M+H]^+$ 188.1070, found 188.1070.

1-[6-methoxyquinolin-1(2*H*)-yl]ethan-1-one (1d):

Prepared according to the general procedure (A) on 500 mg scale and the title compound was isolated as a pale-yellow gel (36% yield, 230 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.1 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.69 (d, *J* = 2.6 Hz, 1H), 6.51 (d, *J* = 9.5 Hz, 1H), 6.22 – 6.10 (m, 1H), 4.48 (s, 2H), 3.84 (s, 3H), 2.18 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[17]

1-(6-methylquinolin-1(2*H*)-yl)ethan-1-one (1e):

Prepared according to the general procedure (A) on 500 mg scale and the title compound was isolated as a pale-yellow gel (52% yield, 340 mg). **^{1}H** NMR (400 MHz, $CDCl_3$): δ 6.95-6.83 (m, 3H), 6.38 (d, *J* = 9.6 Hz, 1H), 5.99-5.95 (m, 1H), 4.35 (s, 2H), 2.23 (s, 3H), 2.09 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[12a]

1-(6-bromoquinolin-1(2*H*)-yl)ethan-1-one (1f):

Prepared according to the general procedure (A) in 100 mg scale and the title compound was isolated as a yellow gel (63% yield, 78 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.08 (bs, 1H), 6.46 (dt, *J* = 9.6, 1.6 Hz, 1H), 6.14 (dd, *J* = 8.8, 4.2 Hz, 1H), 4.44 (s, 2H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.9, 135.2, 133.0, 131.8, 131.2, 129.8, 129.1, 125.3, 121.9, 50.2, 22.5; IR (KBr, cm^{-1}): 3398, 2904, 1636, 1444, 1267, 1153, 1012, 905; ESI-HRMS: $C_{11}H_{11}BrNO$ $[M+H]^+$ 252.0019 and 253.9998, found 252.0022 and 254.0032.

1-(6-chloroquinolin-1(2*H*)-yl)ethan-1-one (1g):

Prepared according to the general procedure (A) on 500 mg scale and the title compound was isolated as a pale-yellow gel (41 % yield, 267 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.10 (d, *J* = 1.9 Hz, 1H), 6.47 (dt, *J* = 9.5, 1.5 Hz, 1H), 6.24 – 6.08 (m, 1H), 4.44 (s, 2H), 2.20 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[17]

1-(5-bromoquinolin-1(2*H*)-yl)ethan-1-one (1h):

Prepared according to the general procedure (A) in 100 mg scale and the title compound was isolated as a yellow gel (52% yield, 63 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, *J* = 9.1 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.92 (dt, *J* = 9.7, 1.7 Hz, 1H), 4.45 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 138.5, 129.7, 128.8, 127.7, 125.5, 123.3, 121.5, 53.4, 22.4; IR (KBr, cm^{-1}): 3410, 2788, 1626, 1465, 1346, 1232, 1051, 8798; ESI-HRMS: $C_{12}H_{14}NO$ $[M+H]^+$ 252.0019 and 253.9998, found 252.0022 and 254.0032.

1-(3-bromoquinolin-1(2*H*)-yl)ethan-1-one (1i):

Prepared according to the general procedure (A) in 500 mg scale and the title compound was isolated as a colorless gel (78% yield, 475 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.14 (m, 3H), 7.11 (d, *J* = 7.4 Hz, 1H), 6.87 (s, 1H), 4.70 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 135.2, 129.1, 127.6, 126.0, 126.0 (2C), 124.1, 48.4, 22.4; IR (KBr, cm^{-1}): 3400, 2956, 1668, 1441, 1320, 1217, 1098, 906, 759, 601; ESI-HRMS: $C_{11}H_{11}B_rNO$ $[M+H]^+$ 252.0019 and 253.9998, found 251.9990 and 253.9977.

(B) Synthesis of 1-(6-nitroquinolin-1(2*H*)-yl)ethan-1-one (1j):

To an ice-cold solution of 6-nitroquinoline (0.5 g, 2.85 mmol) in acetic acid (3 mL) was added sodium borohydride (0.108 g, 2.85 mmol) in small portions (the reaction was monitored by TLC). Upon completion of the reaction, the mixture was carefully poured onto crushed ice and stirred

vigorously and then filtered. The reddish-brown solid that was obtained, was dried well and used as such without purification for the next step (crude yield 70 %).

To an ice-cold solution of 6-nitro-1, 2-dihydroquinoline (0.45 g, 2.56 mmol), pyridine (1.3 mL, 15.56 mmol) in DCM (8 mL) was added acetyl chloride (0.6 mL, 7.66 mmol), dropwise, and the resulting mixture was stirred for an hour at the same temperature before being warmed to RT and stirred for another 16 h during which the reaction was found to be complete. Upon dilution with EtOAc, the mixture was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, J = 8.8, 2.4 Hz, 1H), 7.95 (d, J =2.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 6.58 (d, J = 9.6 Hz, 1H), 6.22-6.17 (m, 1H), 4.46 (dd, J = 3.6, 1.2 Hz, 2H), 2.26 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[12a]

1-(2-methylquinolin-1(2*H*)-yl)ethan-1-one (1k):

Prepared according to the general procedure of (B) on 500 mg scale and the title compound was isolated as a greenish-gel (57% yield, 373 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.03 (m, 4H), 6.47 (d, J = 9.3 Hz, 1H), 6.12 (dd, J = 9.3, 5.9 Hz, 1H), 5.49 (bs, 1H), 2.25 (s, 3H), 1.09 (d, J = 6.6 Hz, 3H). Spectral data obtained were in good agreement with those reported in the literature.[18]

(C) Synthesis of *tert*-butyl quinoline-1(2*H*)-carboxylate (1l):

A solution of 1,2-dihydroquinoline (300 mg, 2.29 mmol) and DMAP (3 mg, 0.23 mmol) in dry DCM (15 mL) was cooled to 0 °C. Triethylamine (1 mL, 6.87 mmol) was added dropwise and the resulting reaction mixture was stirred for 20 min at 0 °C. This was followed by the slow addition of a solution of di-tert-butyl dicarbonate (0.81 mL, 3.44 mmol) in DCM (5 mL). The reaction mixture was stirred for 14 h at 0 °C, during which the conversion was complete. Upon dilution with DCM, mixture was washed successively with brine and water. The combined organic extract was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: Petroleum ether:EtOAc, 4:1) and isolated as a yellow gel (354 mg (61%)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 8 Hz, 1H), 7.21 – 7.11 (m, 1H), 7.08 – 6.99 (m, 2H), 6.46 (d, J = 8 Hz, 1H), 6.00 – 5.95 (m, 1H), 4.35 (dd, J = 2.4, 1.8, 1H), 1.51 (s, 9H). Spectral data obtained for **1l** were in good agreement with those reported in the literature.[12a]

(D) Synthesis of 2,2-dimethyl-1-(2-methylquinolin-1(2*H*)-yl)propan-1-one (1m):

A solution of methyl lithium (1.5 equiv.) was added dropwise to the solution of quinoline (300 mg, 2.33 mmol) in THF (6 mL) under an argon atmosphere, at -78 °C. The temperature was gradually allowed to increase to 25 °C over 30 minutes and then maintained for another hour, following which the reaction mixture was cooled to 0 °C and pivaloyl chloride (0.42 mL, 3.44 mmol) was added dropwise. The solution was stirred for a further 30 minutes at RT and then diluted with a saturated solution of NH_4Cl. This mixture was extracted with ethyl acetate and washed successively with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel column chromatography (eluent: Petroleum ether:EtOAc, 4:1). Yield: 72% (383 mg), Physical appearance: Yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.3 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.15 – 7.09 (m, 2H), 6.51 (d, J = 9.4 Hz, 1H), 6.14 (dd, J = 9.4, 5.9 Hz, 1H), 4.97 (p, J = 6.5 Hz, 1H), 1.34 (s, 9H), 1.11 (d, J = 6.7 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 135.3, 131.6, 128.3, 126.91, 126.85, 125.9, 125.2, 125.1, 49.5, 40.5, 29.4, 17.6; IR (KBr, cm^{-1}): 2861, 1657, 1452, 1032, 856, 745; ESI-HRMS: $C_{15}H_{19}NONa$ $[M+Na]^+$ 252.1364, found 252.1368.

(E) Synthesis of 1-tosyl-1, 2-dihydroquinoline (1n):

A solution of quinoline (500 mg, 3.87 mmol) in dry THF (4 mL) was added slowly to an ice-cold suspension of lithium aluminum hydride (172 mg, 4.64 mmol) in dry THF (10 mL). The solution was stirred for 2 h at 0 °C, during which the conversion was complete. The reaction was then carefully quenched by ice and filtered. The filtrate was extracted with EtOAc, washed successively with brine, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The resulting colorless solid was used immediately without purification for next step (crude yield 406 mg, 80 %).

A solution of 1, 2-dihydoquinoline (300 mg, 2.29 mmol) and DMAP (14 mg, 0.11 mmol) in dry DCM (5 mL) was cooled to 0 °C. After a dropwise addition of triethylamine (0.94 mL, 6.67 mmol) to this stirring solution, the resulting reaction mixture was stirred for another 20 min. A solution of TsCl (512 mg, 2.74 mmol) in DCM (2 mL) was then added dropwise to this reaction mixture and the resulting solution was stirred for another 14 h at 0 °C. This reaction mixture was diluted with EtOAc, washed successively with brine, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: Petroleum ether:EtOAc, 4:1) to give **1n** as a colorless solid. Yield: 514 mg, (80%).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.6 Hz, 1H), 7.28 – 7.22 (m, 3H), 7.15 (t, J = 7.6 Hz,1H), 7.05 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 7.2 Hz, 1H), 6.00 (d, J = 9.6 Hz, 1H), 5.58 – 5.53 (m, 1H), 4.41 (dd, J = 2.8,1.2 Hz, 2H), 2.31 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[12a]

(F) General procedure for the synthesis of 3-alkenyl-1,2-dihydro-*N*-acetyl-quinolines:

In a pressure tube equipped with a stir bar, *N*-acetyl-1,2-dihydroquinoline (0.300 mmol) was dissolved in dry dioxane (1.5 mL). The reaction mixture was degassed for 10 min followed by the addition of $Pd(OAc)_2$ (0.030 mmol), $Cu(OAc)_2$ (0.300 mmol), AgOAc (0.600 mmol), and the olefin coupling partner (0.600 mmol). The tube was fitted with Teflon screw cap under an argon flow. The reaction mixture was heated to 80 °C and allowed to stir for 15-30 h (total time), during which the reaction was found to be complete (as indicated by TLC). Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography.

Methyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-3-yl)acrylate (3a):

Reaction time 15 h, Yield: 56% (41 mg), Physical appearance: Pale yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 16.0 Hz, 1H), 7.34–7.17 (m, 4H), 6.82 (s, 1H), 6.13 (d, J = 16.0 Hz, 1H), 4.65 (s, 2H), 3.81 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 167.3, 142.2, 137.4, 131.9, 128.8, 128.6, 127.8, 125.9, 123.7, 118.2, 51.8, 49.2, 22.5; IR (KBr, cm^{-1}): 3464, 2925, 2855, 1737, 1458, 1376, 1169, 989, 889, 760; ESI-HRMS: $C_{15}H_{15}NO_3Na$ $[M+Na]^+$ 280.0944, found 280.0966.

Ethyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-3-yl)acrylate (3b):

Reaction time 15 h, Yield: 53% (41 mg), Physical appearance: Pale-yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 15.8 Hz, 1H), 7.33 – 7.17 (m, 4H), 6.81 (s, 1H), 6.13 (d, J = 15.8 Hz, 1H), 4.65 (s, 2H), 4.26 (q, J = 7.0 Hz, 2H), 2.25 (s, 3H), 1.34 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 166.9, 141.9, 137.4, 131.7, 130.1, 128.9, 128.5, 127.8, 125.9, 123.7, 118.7, 60.6, 41.2, 22.5, 14.3; IR (KBr, cm^{-1}): 3400, 2981, 1710, 1376, 1265, 1180, 1034, 759; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 294.1101, found 294.1083.

(*E*)-methyl 3-(1-acetyl-8-methyl-1,2-dihydroquinolin-3-yl)acrylate (3c):

Reaction time 15 h,Yield: 56% (40 mg), Physical appearance: Colorless solid, M. p. 98-100 °C, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 15.9 Hz, 1H), 7.23 – 7.11 (m, 2H), 7.10 – 7.05 (m, 1H), 6.77 (s, 1H), 6.14 (d, *J* = 15.9 Hz, 1H), 5.68 (d, *J* = 15.9 Hz, 1H), 3.77 (s, 3H), 3.50 (d, *J* = 15.9 Hz, 1H), 2.31 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.6, 167.4, 142.3, 137.6, 137.0, 132.8, 132.2, 131.4, 130.5, 126.6, 125.4, 118.2, 51.8, 41.7, 21.2, 18.1; IR (KBr, cm^{-1}): 3423, 2876, 1734, 1347, 1260, 1206, 989, 811; ESI-HRMS: $C_{16}H_{18}NO_3$ $[M+H]^+$ 272.1281, found 272.1266.

Methyl (*E*)-3-(1-acetyl-2-methyl-1,2-dihydroquinolin-3-yl)acrylate (3d):

Reaction time 15 h, Yield: 70% (51 mg), Physical appearance: Yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 15.8 Hz, 1H), 7.32–7.17 (m, 4H), 6.72 (s, 1H), 6.14 (d, *J* = 15.8 Hz, 1H), 5.82 (bs, 1H), 3.79 (s, 3H), 2.24 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3Cl_3): *δ* 169.6, 167.4, 142.3, 140.0, 135.4, 130.3, 128.7, 128.0, 127.7, 125.7, 124.7, 118.0, 53.5, 51.7, 22.8, 16.8; IR (KBr, cm^{-1}): 3447, 2980, 1714, 1667, 1487, 1368, 1326, 1269, 1169, 982, 848, 760, 618; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 294.1101, found 294.1082.

Benzyl (*E*)-3-(1-acetyl-2-methyl-1,2-dihydroquinolin-3-yl)acrylate (3e):

Reaction time 30 h, Yield: 62% (57 mg), Physical appearance: Yellow gel, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.16 (m, 10H), 6.74 (s, 1H), 6.21 (d, *J* = 15.8 Hz, 1H), 5.83 (s, 1H), 5.34 – 5.19 (m, 2H), 2.25 (s, 3H), 1.11 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 169.6, 166.7, 142.6, 140.0, 136.0, 135.4, 130.5, 128.7, 128.6, 128.28, 128.27, 127.8, 125.7, 124.7, 118.1, 66.4, 46.1, 22.9, 16.8; IR (KBr, cm^{-1}): 3034, 2978, 1714, 1651, 1486, 1455, 1372, 1268, 1164, 1118, 982, 847, 756, 698, 618; ESI-HRMS: $C_{22}H_{21}NO_3Na$ $[M+Na]^+$ 370.1414, found 370.1415.

Methyl (*E*)-3-(1-acetyl-6-methyl-1,2-dihydroquinolin-3-yl)acrylate (3f):

Reaction time 15 h, Yield: 65% (47 mg), Physical appearance: Pale yellow solid, M. p. 115-117 °C, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 15.8 Hz, 1H), 7.16–6.99 (m, 3H), 6.76 (s, 1H), 6.11 (d, *J* = 15.8 Hz, 1H), 4.62 (s, 2H), 3.80 (s, 3H), 2.36 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, CD_3Cl_3): *δ* 170.0, 167.4, 142.3, 135.6, 135.0, 131.9, 129.2, 128.7, 128.3, 123.5, 118.0, 51.8, 41.0, 22.5, 20.8; IR (KBr, cm^{-1}): 3413, 2925, 1637, 1380, 1272, 1176, 831; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 294.1101, found 294.1115.

Ethyl (*E*)-3-(1-acetyl-6-bromo-1,2-dihydroquinolin-3-yl)acrylate (3g):

Reaction time 15 h, Yield: 51% (36 mg), Physical appearance: Off-white solid, M. p. 158-160 °C, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.25 (m, 3H), 7.08 (s, 1H), 6.68 (bs, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 4.57 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.19 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 170.0, 166.6, 141.4 (2C), 136.3, 131.1, 130.6, 130.2 (2C), 125.2, 119.7, 118.8, 60.7, 41.2, 22.5, 14.3; IR (KBr, cm^{-1}): 3378, 2980, 2925, 2768, 2089, 1856, 1180, 1035, 989; ESI-HRMS: $C_{16}H_{17}BrNO_3$ $[M+H]^+$ 350.0366 and 352.0367, found 350.0368 and 352.0351.

Ethyl (*E*)-3-(1-acetyl-6-chloro-1,2-dihydroquinolin-3-yl)acrylate (3h):

Reaction time 15 h, Yield: 46% (34 mg), Physical appearance: Off-white solid, M. p. 160-162 °C, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 15.9 Hz, 1H), 7.22 – 7.15 (m, 3H), 6.69 (s, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 4.57 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.19 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, CD_3Cl_3): *δ* 169.7, 166.6, 141.4 (2C), 135.8, 131.2, 130.3(2C), 128.2, 127.3, 124.9, 119.7, 60.7, 41.2, 22.5, 14.3; IR (KBr, cm^{-1}): 3378, 2987, 2769, 2459, 1856, 1075, 989; ESI-HRMS: $C_{16}H_{17}ClNO_3$ $[M+H]^+$ 306.0891, found 306.0873.

4-Chlorobenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-3-yl)acrylate (3j):

Reaction time 30 h, Yield: 64% (67 mg), Physical appearance: Pale-yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.45 (d, *J* = 15.8 Hz, 1H), 7.40–7.18 (m, 8H), 6.82 (s, 1H), 6.17 (d, *J* = 15.8 Hz, 1H), 5.21 (s, 2H), 4.64 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.0, 166.5, 142.7, 137.5, 134.5, 134.2, 132.2, 129.6, 128.8, 128.7, 127.9, 125.9, 123.7, 118.0, 65.6, 41.3, 22.5; IR (KBr, cm^{-1}): 3434, 3409, 2924, 1714, 1651, 1494, 1373, 1261, 1165, 1093, 1014, 809, 757; ESI-HRMS: $C_{21}H_{18}ClNO_3Na$ $[M+Na]^+$ 390.0867, found 390.0888.

4-Nitrobenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-3-yl)acrylate (3k):

Reaction time 30 h,Yield: 61% (66 mg), Physical appearance: Pale-yellow solid, M. p. 117-119 °C, TLC R_f 0.30 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 15.8 Hz, 1H), 7.34–7.18 (m, 4H), 6.84 (s, 1H), 6.19 (d, *J* = 15.8 Hz, 1H), 5.33 (s, 2H), 4.65 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.0, 166.3, 147.7, 143.4, 143.3, 137.5, 135.1, 132.6, 128.8, 128.7, 128.3, 128.0, 125.9, 123.8, 123.7, 117.4, 64.8, 41.1, 22.5; IR (KBr, cm^{-1}): 3434, 3064, 1713, 1643, 1520, 1487, 1348, 1156, 982, 846, 737, 604, 527; ESI-HRMS: $C_{21}H_{19}N_2O_5$ $[M+H]^+$ 379.1288, found 379.1300.

4-Methoxybenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-3-yl)acrylate (3l):

Reaction time 30 h, Yield: 59% (62 mg), Physical appearance: Pale-yellow solid, M. p. 86-88 °C, TLC R_f 0.30 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 15.8 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.33–7.17 (m, 4H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.80 (s, 1H), 6.15 (d, *J* = 15.8 Hz, 1H), 5.18 (s, 2H), 4.62 (s, 2H), 3.83 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 169.9, 166.7, 159.7, 142.3, 137.4, 135.4, 131.9, 130.1, 128.8, 128.6, 128.1, 127.8, 125.8, 123.7, 118.4, 114.0, 66.3, 55.3, 41.2, 22.5; IR (KBr, cm^{-1}): 3469, 2957, 2838, 1645, 1515, 1487, 1372, 1250, 1163, 1033, 981, 845, 760, 527; ESI-HRMS: $C_{22}H_{21}NO_4Na$ $[M+Na]^+$ 386.1363, found 386.1361.

Ethyl (*E*)-3-(1-acetyl-5-bromo-1,2-dihydroquinolin-3-yl)acrylate (3m):

Reaction time 15 h, Yield: 48% (33 mg), Physical appearance: Off-white solid, M. p. 153-155 °C, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 – 7.37 (m, 2H), 7.26 – 7.12 (m, 3H), 6.19 (d, *J* = 15.9 Hz, 1H), 4.61 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.24 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_3Cl_3): *δ* 169.8, 166.6, 141.7 (2C), 138.9, 130.4, 130.0, 128.8, 128.6, 123.1, 122.7, 119.8, 60.7, 41.5, 22.5, 14.3; IR (KBr, cm^{-1}): 3378, 2980, 2925, 2768, 2089, 1856, 1180, 1035, 989; ESI-HRMS: $C_{16}H_{16}BrNO_3Na$ $[M+Na]^+$ 372.0206 and 374.0186, found 372.0189 and 374.0170.

(G) General procedure for the synthesis of 8-alkenyl-1,2-dihydro-*N*-acetyl-quinolines:

In a pressure tube equipped with a stir bar, *N*-acetyl-1,2-dihydroquinoline (0.3 mmol) in dry toluene (1.5 mL) was taken. The reaction mixture was degassed for 10 min followed by the addition of $[RuCl_2(p\text{-cymene})]_2$ (0.015 mmol), $AgSbF_6$ (0.060 mmol), $Cu(OAc)_2$ (0.600 mmol) and olefin coupling partner (0.600 mmol). The tube was fitted with Teflon screw cap under an argon flow. The reaction mixture was heated to 100 °C and allowed to stir

for about 14 h (total time). The progress of the reaction was monitored by TLC. Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography.

Benzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4a):

Reaction time 14 h, Yield: 73% (70 mg), Physical appearance: Brownish solid, M. p. 93-95 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc);^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.0 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.46–7.34 (m, 5H), 7.32–7.25 (m, 1H), 7.20 (d, *J* = 6.8 Hz, 1H), 6.66–6.51 (m, 2H), 6.31 – 6.23 (m, 1H), 5.53 (dd, *J* = 16.8, 5.8 Hz, 1H), 5.38–5.21 (m, 2H), 3.54 (d, *J* = 16.8 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.3, 140.5, 137.3, 135.9, 131.4, 131.0, 130.0, 128.6, 128.3, 128.0, 126.8, 126.1, 125.7, 119.8, 66.5, 41.9, 22.0; IR (KBr, cm^{-1}): 3403, 3036, 1717, 1670, 1450, 1375, 1296, 1164, 994, 818, 753, 697, 602; ESI-HRMS: $C_{21}H_{19}NO_3Na$ $[M+Na]^+$ 356.1257, found 356.1283.

Methyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4b):

Reaction time 14 h, Yield: 62% (46 mg), Physical appearance: Brown solid, M. p. 71-73 °C, TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 16.1 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.34-7.26 (m, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 6.61–6.49 (m, 2H), 6.31–6.24 (m, 1H), 5.53 (dd, *J* = 16.8, 5.8 Hz, 1H), 3.83 (s, 3H), 3.54 (d, *J* = 16.8 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.8, 166.9, 140.1, 137.2, 131.3, 130.9, 130.0, 128.0, 126.8, 126.1, 125.6, 119.8, 51.9, 41.9, 22.0; IR (KBr, cm^{-1}): 3427, 2924, 2852, 1714, 1667, 1450, 1372, 1323, 1169, 1038, 992, 818, 754, 601; ESI-HRMS: $C_{15}H_{15}NO_3Na$ $[M+Na]^+$ 280.0944, found 280.0960.

Ethyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4c):

Reaction time 14 h, Yield: 55% (43 mg), Physical appearance: Colorless solid, M. p. 55-57 °C, TLC R_f 0.30 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 16.0 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 6.71–6.43 (m, 2H), 6.28–6.22 (m, 1H), 5.51 (dd, *J* = 16.8, 5.4 Hz, 1H), 4.27 (q, *J* = 13.7, 6.7 Hz, 2H), 3.52 (d, *J* = 16.8 Hz, 1H), 1.81 (s, 3H), 1.33 (t, *J* = 6.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.5, 139.9, 137.2, 131.3, 130.9, 130.1, 127.9, 126.8, 126.1, 125.7, 120.3, 60.7, 41.9, 22.0, 14.3; IR (KBr, cm^{-1}): 3425, 2983, 1658, 1274, 1172, 1039, 994, 851, 754, 602; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 294.1101, found 294.1119.

(*E*)-methyl 3-(1-acetyl-3-methyl-1,2-dihydroquinolin-8-yl)acrylate (4d):

Reaction time 14 h, Yield: 62% (45 mg), Physical appearance: Yellow gel, TLC R_f 0.30 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 16.1 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 6.50 (d, *J* = 16.1 Hz, 1H), 6.27 (s, 1H), 5.26 (d, *J* = 17.3 Hz, 1H), 3.79 (s, 3H), 3.47 (d, *J* = 16.5 Hz, 1H), 1.96 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.9, 167.0, 141.8, 140.4, 136.0, 132.2, 129.7, 127.2, 126.8, 124.6, 121.0, 119.6, 51.9, 46.2, 22.1, 21.90; IR (KBr, cm^{-1}): 3389, 3014, 1648, 1263, 1152, 1012, 987, 850, 765; ESI-HRMS: $C_{16}H_{18}NO_3$ $[M+H]^+$ 272.1281, found 272.1264.

Methyl (*E*)-3-(1-acetyl-2-methyl-1,2-dihydroquinolin-8-yl)acrylate (4e):

Reaction time 14 h, Yield: 68% (49 mg), Physical appearance: Colorless solid, M. p. 96-98 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 16.1 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 6.54 (d, *J* = 16.1 Hz, 1H), 6.48 (d, *J* = 9.4 Hz, 1H), 6.31–6.20 (m, 1H), 5.76–5.62 (m, 1H), 3.82 (s, 3H), 1.83 (s, 3H), 1.07 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.4, 166.9, 140.0, 135.8, 135.0, 131.2, 130.3, 127.8, 126.6, 125.8, 123.7, 119.8, 51.9, 47.1, 22.6, 16.5; IR (KBr, cm^{-1}): 3402, 2953, 1655, 1442, 1302, 1169, 1112, 1033, 813, 714, 601; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 294.1101, found 294.1114.

Methyl (*E*)-3-(1-acetyl-6-nitro-1,2-dihydroquinolin-8-yl)acrylate (4f):

Reaction time 14 h, Yield: 71% (49 mg), Physical appearance: Pale yellow solid, M. p. 113-115 °C, TLC R_f 0.20 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.02 (d, *J* = 14.7 Hz, 1H), 7.69 (d, *J* = 15.0 Hz, 1H), 6.70 (s, 2H), 6.42 (s, 1H), 5.60 (d, *J* = 13.2 Hz, 1H), 3.84 (s, 3H), 3.61 (d, *J* = 14.2 Hz, 1H), 2.49–1.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.8, 166.2, 145.9, 142.0, 138.2, 133.2, 132.4, 131.1, 125.2, 122.3, 121.8, 120.5, 52.1, 42.1, 22.1; IR (KBr, cm^{-1}): 3372, 3081, 1720, 1677, 1528, 1441, 1346, 1316, 1274, 1210, 1178, 1044, 989, 794, 697; ESI-HRMS: $C_{15}H_{14}N_2O_5Na$ $[M+Na]^+$ 325.0795, found 325.0784.

Methyl (*E*)-3-(1-acetyl-6-methyl-1,2-dihydroquinolin-8-yl)acrylate (4g):

Reaction time 14 h, Yield: 61% (44 mg), Physical appearance: Brown gel, TLC R_f 0.30 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.70 (d, *J* = 16.0 Hz, 1H), 7.41-7.25 (m, 2H), 7.00 (s, 1H), 6.56–6.44 (m, 2H), 6.22 (d, *J* = 7.8 Hz, 1H), 5.48 (dd, *J* = 16.7, 5.1 Hz, 1H), 3.80 (s, 3H), 3.49 (d, *J* = 16.7 Hz, 1H), 2.38 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.9, 167.0, 140.2, 136.5, 134.9, 131.1, 130.7, 129.6, 128.9, 126.2, 125.9, 119.5, 51.8, 42.0, 21.9, 21.0; IR (KBr, cm^{-1}): 3417, 2952, 1660, 1434, 1279, 1038, 942, 859, 813, 735, 699, 601; ESI-HRMS: $C_{16}H_{17}NO_3Na$ $[M+Na]^+$ 272.1281, found 272.1295.

Methyl (*E*)-3-(1-acetyl-6-methoxy-1,2-dihydroquinolin-8-yl)acrylate (4h):

Reaction time 14 h, Yield: 52% (37 mg), Physical appearance: Pale-yellow gel, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 16.1 Hz, 1H), 7.36 (s, 1H), 7.02 (s, 1H), 6.64–6.47 (m, 2H), 6.30–6.20 (m, 1H), 5.50 (dd, *J* = 16.8, 5.8 Hz, 1H), 3.82 (s, 3H), 3.51 (d, *J* = 16.8 Hz, 1H), 2.40 (s, 4H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 171.6, 167.4, 142.3, 137.6, 137.0, 132.6, 132.2, 131.4, 130.5, 126.6, 125.3, 118.2, 51.7, 41.6, 21.2, 18.1; IR (KBr, cm^{-1}): 3404, 2952, 1708, 1661, 1449, 1370, 1281, 1178, 1037, 994, 858, 735, 700, 601; ESI-HRMS: $C_{16}H_{17}NO_4Na$ $[M+Na]^+$ 310.1050, found 310.1026.

Ethyl (*E*)-3-(1-acetyl-5-bromo-1,2-dihydroquinolin-8-yl)acrylate (4i):

Reaction time 14 h, Yield: 50% (35 mg), Physical appearance: Brown gel, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.60 (m, 2H), 7.32 (d, *J* = 1.7 Hz, 1H), 6.62 – 6.44 (m, 2H), 6.36 – 6.29 (m, 1H), 5.53 (dd, *J* = 17.0, 5.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.53 (d, *J* = 17.0 Hz, 1H), 1.83 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 171.5, 166.1, 138.5, 136.1, 133.0, 132.4, 131.9, 130.4, 128.1, 125.2, 121.4, 120.2, 60.9, 41.9, 21.9, 14.3; IR (KBr, cm^{-1}): 3389, 2754, 2877, 1508, 1453, 1420, 1300, 1080; ESI-HRMS: $C_{16}H_{17}BrNO_3$ $[M+H]^+$ 350.0386 and 352.0367, found 350.0377 and 352.0360.

Ethyl (*E*)-3-(1-acetyl-6-chloro-1,2-dihydroquinolin-8-yl)acrylate (4j):

Reaction time 14 h, Yield: 47% (35 mg), Physical appearance: Yellow gel, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 16.0 Hz, 1H), 7.50 (s, 1H), 7.16 (d, *J* = 1.7 Hz, 1H), 6.51 (d, *J* = 15.4 Hz, 2H), 6.35 – 6.26 (m, 1H), 5.51 (dd, *J* = 17.0, 5.7 Hz, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 3.50 (d, *J* = 17.0 Hz, 1H), 1.81 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 171.5, 166.1, 138.6, 135.6, 132.8,

132.5, 132.4, 131.6, 127.5, 125.1, 121.4, 60.9, 42.0, 21.9, 14.3; IR (KBr, cm^{-1}): 3416, 2981, 2754, 2356, 2334, 1622, 1397, 1265, 1118, 1044, 748; ESI-HRMS: $C_{16}H_{16}ClNO_3Na$ $[M+Na]^+$ 328.0711, found 328.0728.

Methyl (*E*)-3-(1-acetyl-3-bromo-1,2-dihydroquinolin-8-yl)acrylate (4k):

Reaction time 14 h, Yield: 65% (43 mg), Physical appearance: Colorless solid, M. p. 82-84 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 16.0 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.31–7.22 (m, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.86 (s, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.62 (d, *J* = 16.8 Hz, 1H), 3.78 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.6, 166.8, 139.7, 135.3, 131.3, 130.4, 127.4, 127.2, 125.9, 123.7, 120.3, 52.0, 48.7, 22.0; IR (KBr, cm^{-1}): 3397, 2951, 1718, 1685, 1449, 1370, 1330, 1271, 1200, 1169, 1040, 860, 756, 564; ESI-HRMS: $C_{15}H_{14}BrNO_3Na$ $[M+Na]^+$ 358.0049 and 360.0029, found 358.0055 and 360.0037.

Ethyl (*E*)-3-(1-acetyl-5-bromo-1,2-dihydroquinolin-8-yl)acrylate (4l):

Reaction time 14 h, Yield: 47% (32 mg), Physical appearance: Brown gel, TLC R_f 0.25 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 16.1 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 6.92 (dd, *J* = 9.6, 1.9 Hz, 1H), 6.54 (d, *J* = 16.1 Hz, 1H), 6.44 – 6.38 (m, 1H), 5.52 (dd, *J* = 17.0, 5.8 Hz, 1H), 4.29 (q, *J* = 6.9 Hz, 2H), 3.49 (d, *J* = 16.9 Hz, 1H), 1.83 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 171.5, 166.3, 139.1, 138.4, 132.9, 131.0, 130.7, 129.7, 126.1, 125.4, 123.2, 120.8, 60.9, 41.5, 22.0, 14.3; IR (KBr, cm^{-1}): 3389, 2754, 2677, 1508, 1453, 1420, 1300, 1080; ESI-HRMS: $C_{16}H_{17}BrNO_3$ $[M+H]^+$ 350.0386 and 352.0367, found 350.0377, 352.0360.

4-Nitrobenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4m):

Reaction time 14 h, Yield: 71% (78 mg), Physical appearance: Brown solid, M. p. 135-137 °C, TLC R_f 0.20 (7:3, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 16.0 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 3H), 7.35–7.27 (m, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 6.69–6.53 (m, 2H), 6.36–6.21 (m, 1H), 5.52 (dd, *J* = 16.8, 5.5 Hz, 1H), 5.37 (s, 2H), 3.56 (d, *J* = 16.8 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.0, 147.7, 143.2, 141.3, 137.4, 131.4, 130.9, 129.7, 128.5, 128.3, 126.9, 126.1, 125.7, 123.9, 119.0, 65.0, 42.0, 22.0; IR (KBr, cm^{-1}): 3484, 3053, 2218, 1732, 1668, 1447, 1373, 1212, 1171, 981, 808, 751, 607; ESI-HRMS: $C_{21}H_{18}N_2O_5Na$ $[M+Na]^+$ 401.1108, found 401.1137.

4-Chlorobenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4n):

Reaction time 14 h, Yield: 67% (71 mg), Physical appearance: Colorless solid, M. p. 121-123 °C, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.2 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.41–7.34 (m, 4H), 7.32–7.26 (m, 1H), 7.21 (d, *J* = 6.8 Hz, 1H), 6.66–6.52 (m, 2H), 6.32–6.24 (m, 1H), 5.53 (dd, *J* = 16.9, 5.8 Hz, 1H), 5.30 – 5.17 (m, 2H), 3.55 (d, *J* = 16.9 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.2, 140.8, 137.3, 134.4, 134.2, 131,4, 131.0, 129.9, 129.7, 128.8, 128.1, 126.8, 126.1, 125.7, 119.6, 65.7, 42.0, 22.0; IR (KBr, cm^{-1}): 3415, 3052, 2888, 1714, 1667, 1451, 1372, 1274, 1162, 1096, 1013, 851, 753, 815, 692; ESI-HRMS: $C_{21}H_{19}ClNO_3$ $[M+H]^+$ 368.1048, found 368.1067.

4-Methoxybenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4o):

Reaction time 14 h, Yield: 62% (65 mg), Physical appearance: Colorless solid, M. p. 77-79 °C, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 16.1 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.31–7.14 (m, 3H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.66–6.46 (m, 2H), 6.25 (d, *J* = 7.2 Hz, 1H), 5.51 (dd, *J* = 16.8, 5.3 Hz, 1H), 5.28–5.13 (m, 2H), 3.83 (s, 4H), 3.52 (d, *J* = 16.8 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.4, 159.7, 140.4, 137.3, 131.3, 130.9, 130.2, 130.0, 128.1, 128.0, 126.8, 126.1, 125.7, 120.0, 114.0, 66.4, 55.3, 41.9, 22.0; IR (KBr, cm^{-1}): 3473, 2957, 1713, 1665, 1514, 1454, 1163, 1034, 819, 753, 692; ESI-HRMS: $C_{22}H_{21}NO_4Na$ $[M+Na]^+$ 386.1363, found 386.1366.

3-Bromobenzyl (*E*)-3-(1-acetyl-1,2-dihydroquinolin-8-yl)acrylate (4p):

Reaction time 14 h, Yield: 52% (62 mg), Physical appearance: Colorless solid, M. p. 92-94 °C, TLC R_f 0.20 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.0 Hz, 1H), 7.60-7.53 (m, 2H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.31-7.23 (m, 2H), 7.20 (d, *J* = 7.2 Hz, 1H), 6.65–6.51 (m, 2H), 6.25 (d, *J* = 7.2 Hz, 1H), 5.52 (dd, *J* = 16.8, 5.0 Hz, 1H), 5.32–5.15 (m, 2H), 3.53 (d, *J* = 16.8 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.7, 166.1, 140.9, 138.2, 137.4, 131.4, 131.1, 131.0, 130.2, 129.9, 128.1, 126.8, 126.7, 126.1, 125.7, 122.6, 119.4, 65.5, 42.0, 22.0; IR (KBr, cm^{-1}): 3460, 2932, 1702, 1653, 1530, 1472, 1186, 1008, 912, 798, 678; ESI-HRMS: $C_{21}H_{18}BrNO_3Na$ $[M+Na]^+$ 434.0362 and 436.0343, found 434.0356 and 436.0339.

(H) Synthesis of quinoline-3-*d* (6a'):[19]

In a pressure tube equipped with a stir bar, 3-bromoquinoline (0.966 mmol) was dissolved in dry toluene (4 mL). The reaction mixture was degassed for 10 min followed by the addition of $Pd(OAc)_2$ (5 mol%), PCy_3 (10 mol%), K_3PO_4 (1.449 mmol), and CD_3OD (0.8 mL). The tube was fitted with Teflon screw cap under an argon flow. The reaction mixture was stirred at 80 °C for 12 h. The progress of the reaction was monitored by GC-MS. Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the crude product was purified by silica gel flash column chromatography. The title compound was isolated as a pale-yellow gel (75% yield, 94 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.20 – 8.07 (m, 2H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.76-7.66 (m, 1H), 7.54 (t, *J* = 7.5 Hz, 1H). Spectral data obtained were in good agreement with those reported in the literature.[19]

Quinoline-8-*d* (7a'):

Prepared according to the general procedure (**H**) on a 200 mg scale and the title compound was isolated as a pale-yellow gel (81 % yield, 101 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 – 8.84 (m, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 6.6 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.36 (dd, *J* = 8.0, 4.0 Hz, 1H). Spectral data obtained were in good agreement with those reported in the literature.[20]

1-(quinolin-1(2*H*)-yl-3-d)ethan-1-one (6a):

Prepared according to the general procedure (**A**) on 90 mg scale and the title compound was isolated as a pale-yellow gel (78 % yield, 94 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.07 (m, 4H), 6.54 (s, 1H), 4.48 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.1, 150.3,137.0, 136.0, 129.5, 127.1, 126.4, 125.7, 123.9, 41.3, 22.4; IR (KBr, cm^{-1}): 3342, 2909, 1635, 1462, 1353, 1178, 1130, 875, 760; ESI-HRMS: $C_{11}H_{10}DNONa$ $[M+Na]^+$ 197.0796, found 197.0770.

1-(quinolin-1(2H)-yl-8-d)ethan-1-one (7a):

Prepared according to the general procedure (**A**) on 100 mg scale and the title compound was isolated as a pale-yellow gel (81 % yield, 108 mg). TLC R_f 0.30 (3:2, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 – 7.09 (m, 3H), 6.54 (d, *J* = 9.4 Hz, 1H), 6.17 – 6.05 (m, 1H), 4.47 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 150.3, 136.2, 129.4, 127.8, 127.0, 126.4, 125.6, 121.1, 41.4, 22.4; IR (KBr, cm^{-1}): 3285, 2879,

1632, 1456, 1350, 11200, 1143, 912, 776; ESI-HRMS: $C_{11}H_{11}DNO$ $[M+H]^+$ 175.0976, found 175.0981.

(l) General procedure for aromatization of alkenyl-1,2-dihydro-*N*-acetyl-quinolines:

In a round-bottom flask, alkenyl-1,2-dihydro-*N*-acetyl-quinoline (0.050 mmol) was dissolved in 1,4-dioxane (1 mL), followed by addition of DDQ (0.15 mmol). The reaction mixture was refluxed for 2-8 h (total time). The progress of reaction was monitored by TLC. Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and washed twice with brine solution. The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography.

Methyl (*E*)-3-(quinolin-3-yl)acrylate (17a):

Prepared according to the general procedure (E) on 10 mg scale and the title compound was isolated as a pale-yellow gel (75% yield, 6 mg). Reaction time was 2 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.27 (d, *J* = 1.9 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.97 – 7.84 (m, 2H), 7.82 – 7.75 (m, 1H), 7.64 – 7.59 (m, 1H), 6.70 (d, *J* = 16.1 Hz, 1H), 3.88 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[21]

4-Nitrobenzyl (*E*)-3-(quinolin-3-yl)acrylate (17b):

Reaction time 2 h, Yield: 92% (8 mg), Physical appearance: Pale-yellow solid, M. p. 123-125 °C, TLC R_f 0.30 (3:2, Petroleum ether: EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 3H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 16.2 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 3H), 6.76 (d, *J* = 16.2 Hz, 1H), 5.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 165.9, 149.1, 148.7, 147.8, 143.1, 142.6, 135.9, 130.9, 129.4, 128.5, 128.4, 127.6, 127.1, 123.9, 119.0, 65.1; IR (KBr, cm^{-1}): 3406, 2922, 1712, 1614, 1506, 1351, 1263, 1174, 973, 860, 674; ESI-HRMS: $C_{19}H_{15}N_2O_4$ $[M+H]^+$ 335.1026, found 335.1038.

4-Methoxybenzyl (*E*)-3-(quinolin-3-yl)acrylate (17c):

Reaction time 2 h, Yield: 87% (8 mg), Physical appearance: Brown solid, M. p. 76-78 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (bs, 1H), 8.26 (s, 1H), 8.15 (d, *J* = 6.4 Hz, 1H), 7.88 (d, *J* = 15.8 Hz, 2H), 7.78 (t, *J* = 6.4 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.71 (d, *J* = 16.0 Hz, 1H), 5.24 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 166.3, 159.8, 141.5, 135.7, 130.8, 130.8, 130.3, 129.4, 128.5, 128.4, 127.9, 127.6, 120.1, 114.1, 66.5, 55.3; IR (KBr, cm^{-1}): 3397, 2928, 2376, 1709, 1623, 1305, 1252, 1165, 1034, 981, 861, 756; ESI-HRMS: $C_{20}H_{18}NO_3$ $[M+H]^+$ 320.1281, found 320.1290.

4-Chlorobenzyl (*E*)-3-(quinolin-3-yl)acrylate (17d):

Reaction time 2 h, Yield: 83% (7 mg), Physical appearance: Brown solid, M. p. 93-95 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11 (s, 1H), 8.27 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.98–7.84 (m, 2H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.39 (s, 4H), 6.72 (d, *J* = 16.0 Hz, 1H), 5.27 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 166.1, 149.1, 148.6, 142.0, 135.7, 134.3, 130.8, 129.8, 129.4, 128.9, 128.6, 128.4, 127.6, 127.5, 127.3, 119.6, 65.8; IR (KBr, cm^{-1}): 3401, 2927, 2376, 1718, 1630, 1260, 1181, 978, 864, 814, 755, 550; ESI-HRMS: $C_{19}H_{15}ClNO_2$ $[M+H]^+$ 324.0786, found 324.0806.

Methyl (*E*)-3-(6-methylquinolin-3-yl)acrylate (17e):

Reaction time 8 h, Yield: 81% (7 mg), Physical appearance: Brown solid, M. p. 88-90 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.18 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.65-7.58 (m, 2H), 6.67 (d, *J* = 16.0 Hz, 1H), 3.87 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 166.9, 148.1, 146.9, 141.5, 137.6, 135.2, 133.2, 128.8, 127.7, 127.4, 127.2, 119.6, 51.9, 21.6; IR (KBr, cm^{-1}): 2921, 1723, 1236, 1436, 1315, 1264, 1175, 980, 860, 818, 540; ESI-HRMS: $C_{14}H_{14}NO_2$ $[M+H]^+$ 228.1019 found 228.1014.

Methyl (*E*)-3-(quinolin-8-yl)acrylate (17f)

Prepared according to the general procedure (E) on 10 mg scale and the title compound was isolated as a pale-yellow gel (88% yield, 7 mg). Reaction time was 2 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.94 (d, *J* = 16.1 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.02 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.89 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.85 (d, *J* = 16.1 Hz, 1H), 3.88 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[11b]

4-Nitrobenzyl (*E*)-3-(quinolin-8-yl)acrylate (17g):

Reaction time 2 h, Yield: 91% (8 mg), Physical appearance: Pale-yellow solid, M. p. 120-122 °C, TLC R_f 0.40 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.07–8.94 (m, 2H), 8.27 (d, *J* = 8.2 Hz, 2H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.66-7.58 (m, 3H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.96 (d, *J* = 16.2 Hz, 1H), 5.42 (s, 2H); ^{13}C NMR (100 MHz, CD_3Cl_3): *δ* 166.6, 150.4, 146.3, 143.7, 142.5, 136.4, 132.8, 130.5, 128.5, 128.4, 128.4, 126.3, 123.8, 121.7, 119.6, 64.8; IR (KBr, cm^{-1}): 3380, 2923, 1715, 1603, 1520, 1348, 1267, 1061, 978, 790, 736, 601; ESI-HRMS: $C_{19}H_{15}N_2O_4$ $[M+H]^+$ 335.1026, found 335.1025.

Methyl (*E*)-3-(6-methylquinolin-8-yl)acrylate (17h):

Reaction time 8 h, Prepared according to the general procedure (E) on 10 mg scale and the title compound was isolated as a brown gel (83% yield, 7 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 – 8.82 (m, 2H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.85 (s, 1H), 7.65 (s, 1H), 7.45 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.83 (d, *J* = 16.2 Hz, 1H), 3.87 (s, 3H), 2.58 (s, 3H). Spectral data obtained were in good agreement with those reported in the literature.[11b]

Methyl (*E*)-3-(6-nitroquinolin-8-yl)acrylate (17i):

Reaction time 8 h, Yield: 87% (7 mg), Physical appearance: Pale-yellow solid, M. p. 164-166 °C, TLC R_f 0.30 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20–9.13 (m, 1H), 8.90 (d, *J* = 16.2 Hz, 1H), 8.82 (s, 1H), 8.75 (s, 1H), 8.40 (d, *J* = 8.2 Hz, 1H), 7.65 (dd, *J* = 8.2, 4.0 Hz, 1H), 6.93 (d, *J* = 16.2 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 166.8, 153.4, 147.9, 145.2, 139.1, 138.2, 135.5, 127.6, 125.5, 123.3, 122.8, 120.6, 52.0; IR (KBr, cm^{-1}): 3386, 2922, 1716, 1600, 1350, 1271, 993, 879, 788; ESI-HRMS: $C_{13}H_{11}N_2O_4$ $[M+H]^+$ 259.0713, found 259.0697

Methyl (*E*)-3-(3-bromoquinolin-8-yl)acrylate (17j):

Reaction time 8 h, Yield: 81% (7 mg), Physical appearance: Colorless solid, M. p. 66-68 °C, TLC R_f 0.40 (4:1, Petroleum ether:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.98 (s, 1H), 8.85 (d, *J* = 16.2 Hz, 1H), 8.34 (s, 1H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 6.83 (d, *J* = 16.2 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 167.4, 151.2, 144.2, 140.5, 137.4, 133.4, 129.4, 129.0, 128.2, 127.5, 120.7, 118.0, 51.8; IR (KBr, cm^{-1}): 3406, 3063, 2950, 2919, 2850, 1715, 1634, 1435, 1366, 1311, 1172, 1084, 899, 768, 570; ESI-HRMS: $C_{13}H_{11}BrNO_2$ $[M+H]^+$ 291.9968 and 293.9948, found 291.9955 and 293.9934.

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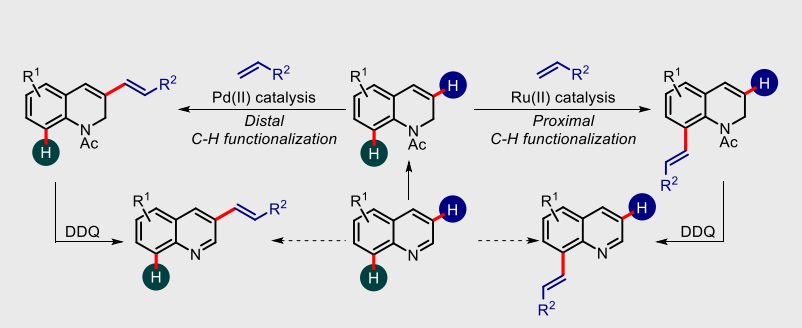

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Catalyst-control in Switching the Site-Selectivity of C–H Olefinations of 1,2-dihydroquinolines: An Approach to Positional-selective Functionalization of Quinolines

A unique approach to achieve site-selective C–H olefinations exclusively at the C-3 or C-8 positions in the quinoline framework has been developed *via* catalyst-control. Distal C(3)–H functionalization is achieved using palladium catalysis whereas, proximal C(8)–H functionalization is obtained by employing ruthenium catalysis. Switching site-selectivity within a single substrate directly indicates two diverse pathways which are operating in the palladium and ruthenium-catalyzed reaction conditions.