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Alkylation of α-Oxo-compounds through C(sp^3)-H Functionalization of 2-Methyl Quinolines Under Catalyst- and Solvent-Free Conditions

Yadavalli Subba Rao,[a,b] Dandugula Sneha Latha,[a] Nagaraju Devunuri,[b] Abdulrahman I. Almansour,[c] Natarajan Arumugam,[c] and Srinivasarao Yaragorla*[a]

Abstract: Highly facile approach of chemoselective alkylation of α-oxo compounds such as α-keto amides, α-keto esters, isatins, and cyclic-α-diketones is developed through C(sp^3)-H functionalization of 2-methyl quinolines under solvent and catalyst-free conditions. Further, we complemented the efficacy of this green synthetic protocol by demonstrating the broad substrate diversity, gram-scale synthesis and new synthetic transformations of the obtained products.

Introduction

α-Keto compounds such as α-keto amides, α-keto esters and their derivatives are essential building blocks of natural products,[1] biologically important molecules possessing antiviral, anti-HIV, antitumor, anti-inflammatory, antibacterial activities[2] and part of drugs and drug candidates.[3] They are also excellent inhibitors of hydrolytic enzymes such as serine and cysteine proteases, by the formation of a stable tetrahedral adduct between the α-keto groups and nucleophilic residues at the enzyme active sites.[4] The reduction or the alkylation of the α-keto group to corresponding α-hydroxy amides or esters is an important strategy due to the biological and catalytic importance of these compounds.[5] On the other hand, catalytic C(sp^3)-H functionalization of 2-methyl quinolines has emerged as a promising synthetic strategy for making quinoline based new chemical entities due to the importance of quinoline structure in natural products,[6] and pharmaceuticals (Figure 1).[7,8]

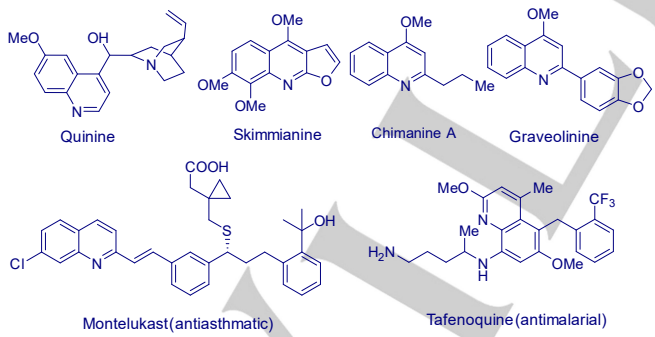

Figure 1. Representative examples of biologically active natural products with the core structure of fluorenol(1st row) and 9,9-diaryl-9H-fluorenol (2nd row).

Therefore, integrating these two structural motifs becomes an interesting topic to synthetic and medicinal chemists, anticipating the better activity.[9-18] Several synthetic efforts have been accomplished for the nucleophilic addition of 2-methyl quinolines to α-keto compounds as shown in Scheme 1. For example, hydroxylation of α-keto amides with 2-methyl quinolines is reported by heating the reaction mixture with zinc triflate as the catalyst in *tert*-butanol at 70-100 °C for 14-72 h, the products are isolated in the range of 25-95%.[9] Later the same group developed binaphthyl supported Pd- nanoparticles (Pd-BNPs) catalyzed nucleophilic addition of 2-methyl quinolines to α-keto esters and α-keto amides by heating the reaction mixture at 70 °C in PEG-200 for 24-48 h.[10] Another report on Iron-catalyzed addition of 2-methyl aza-arenes to α-ketoesters was reported by refluxing in dioxane at 120-130 °C for 24 h, and the yields are ranging from 26- 90%.[11] Interestingly, a good number of catalytic methods are available for the alkylation of isatins, such as refluxing with triflic acid in dioxane at 120 °C for 48 h (yields:31-85%);[12] heating with $Yb(OTf)_3$ at 140 °C (yields:11-82%);[13] refluxing with silica-supported dodeca-tungstophoric acid (DTP) in DMF at 120 °C for 8 h (yields: 43-94%);[14] refluxing with $Fe(OAc)_2$ in dioxane at 120 °C for 24 h (yields: 35-90%);[11] microwave irradiation at 100 °C with TBAF;[15] heating at 120 °C in 1,4-dioxane with $H_3O_{40}PW_{12}.xH_2O/Al_2O$ as the catalyst for 24 h (Yields: 65-92%);[16] and by refluxing with β-cyclodextrin in water at 80 °C.[17] In continuation of these reports, the addition of 2-methyl azaarenes to aceanaphthylene-1,2-diones to get cyclic-α-hydroxy ketone is achieved by refluxing with β-cyclodextrin in the water at 80 °C.[17a] At a glance, all these methods involve the usage of catalysts, high boiling solvents, base, high temperatures (up to 140 °C) and long reaction times for the hydroxylation of α-oxo compounds with 2-methyl quinolines.

Owing to our interest in the development of green synthetic methods for C(sp^3)-H functionalization of 2-methyl quinolines,[18] we have developed solvent-free functionalization,[18a] using water as the solvent[18b] and catalyst-free approaches.[18c] With this expertise, we anticipated developing a green synthetic procedure to functionalize a large variety of α-oxo-compounds with 2-methyl quinolines in an aqueous medium with Ca(II) salts as sustainable catalysts.[19] Excitingly, these experiments lead us to discover a solvent-and catalyst-free C(sp^3)-H functionalization of 2-methyl quinolines by the nucleophilic addition to a variety of α-keto compounds (Scheme 1).

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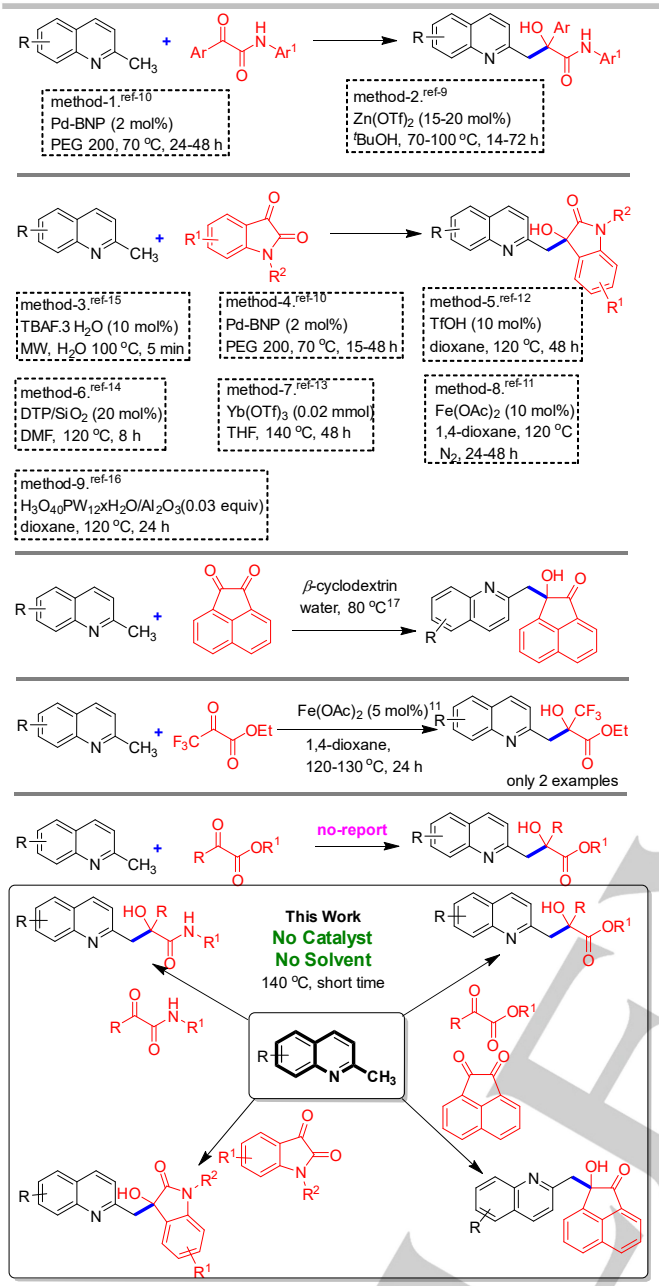
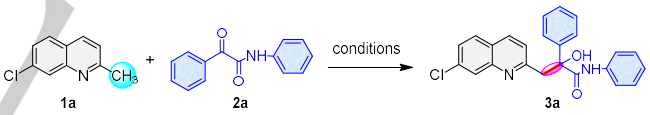


Scheme 1. Synthetic strategies from in situ generated homo-allenylketone(previous and current)

Results and Discussion

We have selected 7-chloro-2-methyl quinoline (**1a**) and 2-oxo-*N*,2-diphenylacetamide (**2a**) as the reactants to search for the optimum green reaction conditions to obtain 3-(7-chloroquinolin-2-yl)-2-hydroxy-*N*,2-diphenylpropanamide (**3a**). Owing to the large abundance, less toxic nature, moisture tolerance, less expensive and biodegradable nature of calcium, calcium-based catalysts such as $Ca(OTf)_2$ and $Ca(NTf)_2$ become an alternative and sustainable catalysts for various synthetic transformations.[19] Therefore, we commenced by refluxing a mixture of **1a** (0.44 mmol), **2a** (0.44 mmol) and $Ca(OTf)_2/nBu_4NPF_6$ (10/10 mol%) in water for 24 h, delightfully the desired product **3a** was obtained, but in poor yield (entry1, Table 1). To increase the reaction yield, we performed the reaction at 120 °C and noticed a slight increase in the yield from 32 to 46% (entry 2). According to the available literature, we realized that most of the C(sp^3)-H functionalization reactions utilized three equivalents of quinaldine,[9-17] therefore, we repeated the conditions of entry-2, with three equivalents of **1a** and one equivalent of **2a,** as anticipated the product yield increased to 71%. Though the reaction showed an appreciable increase in the reaction yield by using three equivalents of **1a**, it is economically not viable. To check the need for excess substrate, we performed the reaction with two equivalents of **1a** and found that the reaction gave a similar yield (entry 3). So, we considered two equivalents of **1a** and one equivalent of **2a** as the appropriate combination because of the use of 1.5 equiv. of **1a** gave poor yield (entry 4). With this improvement of minimum usage of **1a**, we planned to check the feasibility of this reaction under neat conditions. Accordingly, a mixture of **1a** (0.88 mmol), **2a** (0.44 mmol) and $Ca(OTf)_2/nBu_4NPF_6$ (10/10 mol%) was heated at 120 °C and noticed that the reaction completed in 8 h to yield 70% of **3a** (entry 5). Encouraged by the progress of the reaction under solvent-free condition, we then planned to check the role of additive and catalyst by performing the reaction in the absence of additive (entry 6) and the absence of a catalyst (entry 7); these results indicate that the reaction yield is unchanged in their absence. This observation prompted us to examine the reaction in the absence of any catalyst. To our excitement, the reaction still gave the product **3a** with the same yield when we heated the mixture of **1a** and **2a** directly at 120 °C (entry 8). Encouraged by this catalyst-free and solvent-free functionalization reaction, we aimed to check the temperature effect and hence performed the reaction at 140 °C (entry 9) and 160 °C (entry 10).

Table 1. Optimization of the reaction conditions for the functionalization of **1a**, **2a**.[a]

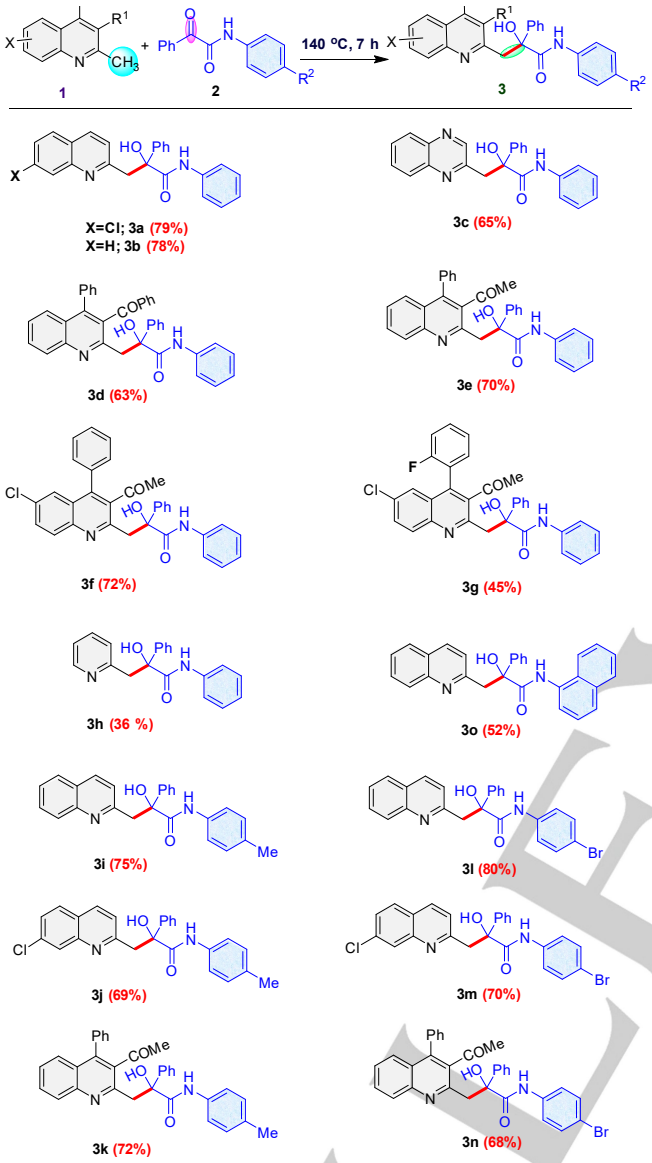


Entry	Catalyst (mol%)	Solvent	Temperature[b]	Time (h)	Yield (%)[c]
1[d]	$Ca(OTf)_2/Bu_4NPF_6$ (10/10)	H_2O	100 °C	24	32
2[d]	$Ca(OTf)_2/Bu_4NPF_6$ (10/10)	H_2O	120 °C	24	46
3[e]	$Ca(OTf)_2/Bu_4NPF_6$ (10/10)	H_2O	120 °C	24	71
4[f]	$Ca(OTf)_2/Bu_4NPF_6$ (10/10)	H_2O	120 °C	24	54
5[e]	$Ca(OTf)_2/Bu_4NPF_6$ (10/10)	-	120 °C	8	70
6[e]	$Ca(OTf)_2$ (10)	-	120 °C	10	71
7[e]	Bu_4NPF_6 (10)	-	120 °C	10	70
8[e]	-	-	120 °C	12	74
9[e]	-	-	140 °C	7	[g]79
10[e]	-	-	160 °C	7	[h]72

[a]Reaction conditions; [b]Oil bath temperature; [c]Isolated yields; [d]**1a**(1 equiv), **2a**(1 equiv); [e]**1a**(2 equiv), **2a**(1 equiv); [f]**1a**(1.5 equiv), **2a**(1 equiv); [g]Optimum condition; [h]decomposed after 7 h

The reaction yielded the best at 140 °C in 7 h (79% of **3a**), and at 160 °C it started decomposing (though we could able to isolate 72%). The usage of the elevated reaction temperature is not a drawback in this reaction because, even in the previous reports the reactions were refluxed at high temperatures along

with a catalyst (and additives), solvents and of course with excess quinaldine. Therefore, the best condition for the synthesis of **3a** (79%, 7 h) is to heat **1a** (0.88 mmol) and **2a** (0.44 mmol) at 140 °C without any solvent and the catalyst (entry 9, Table 1).



Scheme 2. Substrate scope of α-keto amides functionalization.

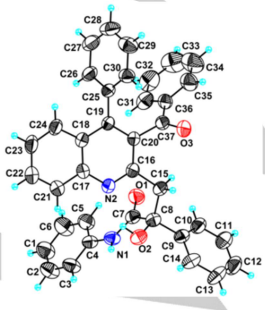
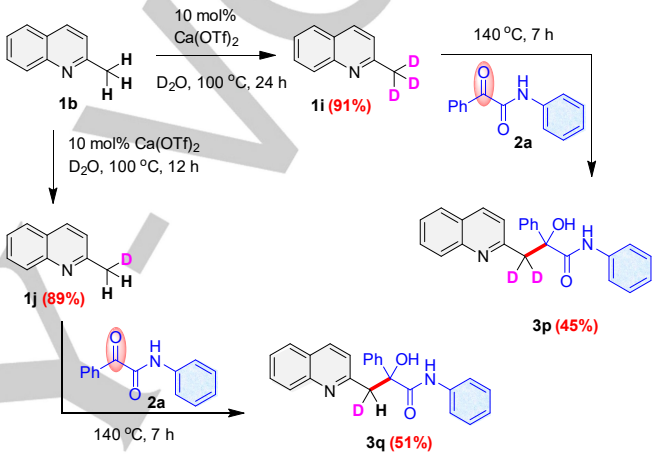


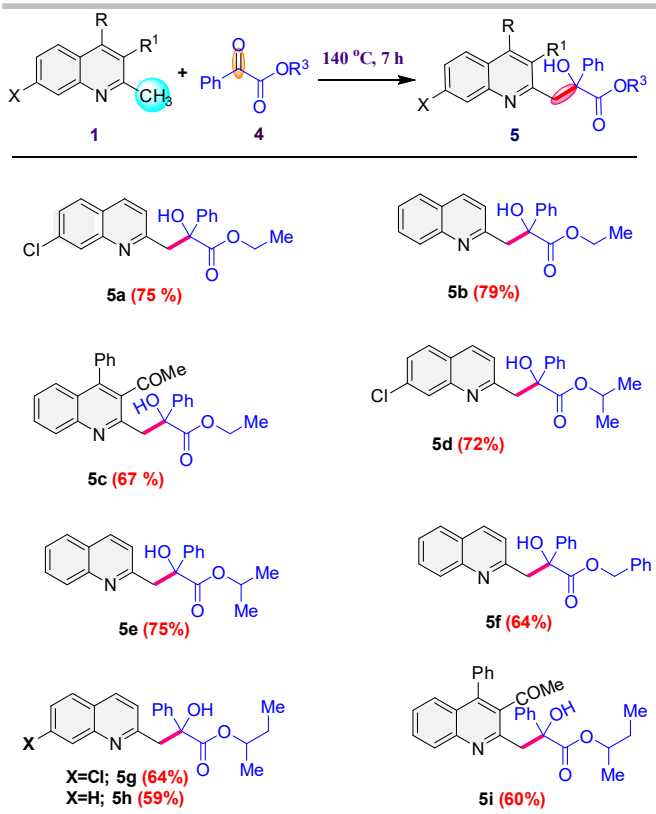
Figure 2. Single crystal X-ray structure of compound **3d** (CCDC: 1985211)

Once the optimum reaction conditions for the functionalization of 7-chloroquinaldine (**1a**) with 2-oxo-*N*,2-diphenylacetamide (**2a**) are developed, then we sought to check the generality of this protocol. Accordingly we have treated a variety of 2-methyl azaarenes such as 2-methylquinoline (**1b**), 2-methylquinoxaline (**1c**), (2-methyl-4-phenylquinolin-3-yl)(phenyl)methanone (**1d**), 1-(2-methyl-4-phenylquinolin-3-yl)ethan-1-one (**1e**), 1-(6-chloro-2-methyl-4-phenylquinolin-3-yl)ethan-1-one (**1f**), and 1-(6-chloro-4-(2-fluorophenyl)-2-methylquinolin-3-yl)ethan-1-one (**1g**) with **2a** and obtained corresponding 2-hydroxy amides **3b-3g** in good yields, however functionalization of 2-methylpyridine (**1h**) with **2a** yielded **3h** in poor yield (Scheme 2). Next, we found that the substitutions on α-keto amides were tolerated by this reaction conditions in producing the corresponding products **3i-3o** in good yields (Scheme 2).

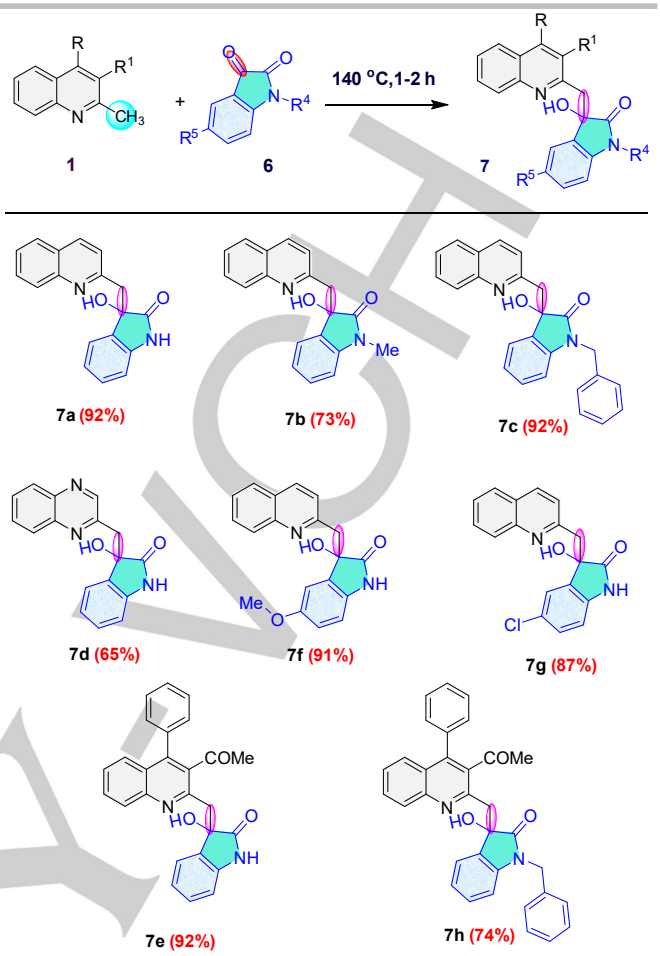


Scheme 3. C(sp^3)-D/H functionalization

The exclusive formation of compounds **3d-3g** indicates the chemoselectivity of the protocol (functionalization of methyl ketone versus 2-methyl quinoline). The structural conformation of the compound **3d** was supplemented with the single crystal x-ray without any ambiguity (Figure 2).[20] Later, 2-methyl quinoline (**1b**) was deuterated by refluxing in D_2O with $Ca(OTf)_2$ to get fully deuterated compound **1i** in 91% yield, and the deuterated 2-methyl quinoline (**1i**) was subjected to C(sp^3)-D functionalization with α-keto amide **2a** at 140 °C under solvent & catalyst-free conditions (Scheme 3). As expected, the reaction yielded the product **3p** in 45% yield after 7 h (the change in the yield can be understood based on the strength of C-D bond versus C-H bond). We were also able to isolate the mono-deuterated quinaldine (**1j**) by stopping calcium-catalyzed deuteration reaction after 12 h, and then subjected to functionalization by heating with **2a** at 140 °C to obtain **3q** in 51% yield. Interestingly this also become the first calcium-catalyzed deuteration of 2-methyl quinoline.[21]



Scheme 4. Functionalization of 2-methyl quinolines with α-keto esters



Scheme 5. Substrate scope of cyclic α-keto amides (isatins) functionalization.

Encouraged by this success, we are keen to extend this strategy to the analogous compounds, *α*-keto esters. To the best of our knowledge, there is a single report available for the addition of 2-methyl quinoline to trifluoromethyl keto-esters by refluxing with iron acetate in dioxane at 120-130 °C for 24 h, however, only two examples were made in this report.[11] So, we felt that it would be useful to develop a new method for this less studied transformation. At the same time, we were also very curious to see, whether the catalyst and solvent-free approach will work on these systems. Hence quinaldine (**1a**) was heated with ethyl 2-oxo-2-phenylacetate (**4a**) at 140 °C; gratifyingly the reaction yielded the desired product **5a** in 75% yield in short reaction time (Scheme 4). Further, we extended this reaction to different α-keto esters and 2-methyl quinolines to check the feasibility as on other α-keto esters. Using this method, we made a total of nine compounds **5a**-**5i** in good yields under the solvent-and catalyst-free functionalization conditions. The exclusive chemoselectivity was observed while synthesizing **5i**. Interestingly, the compounds **5g**, **5h** and **5i** were isolated as an inseparable mixture of 1:1 diastereomers, which was confirmed by the 1H NMR spectra.

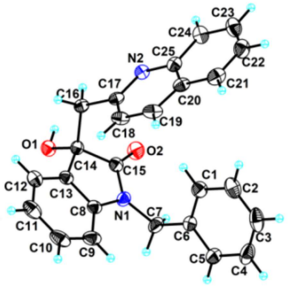
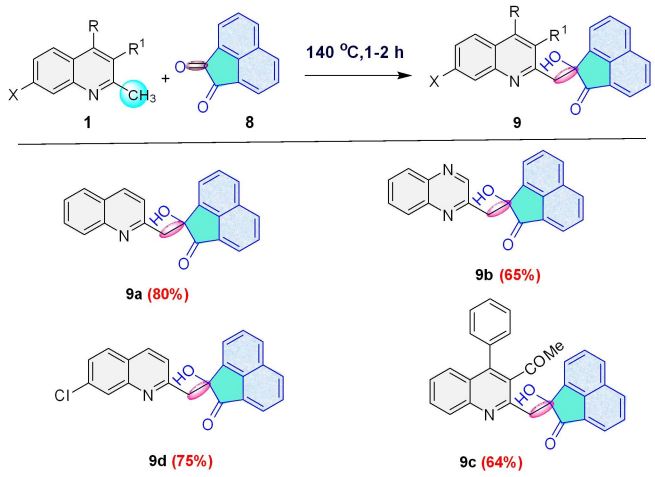


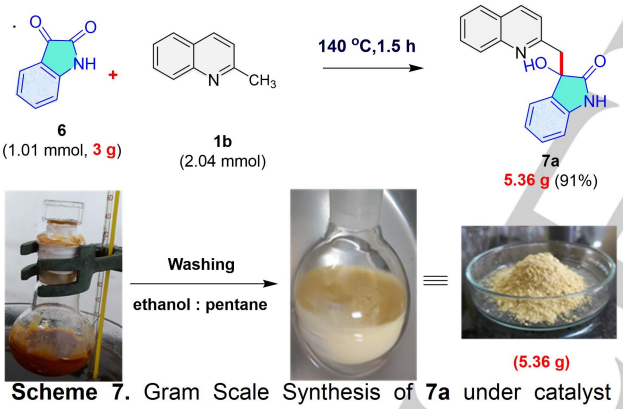
Figure 3. Single crystal X-ray structure of compound **7c** (CCDC:1982003)

Owing to the biological importance of oxindole derived compounds,[22] more than a half a dozen of catalytic methods were developed for the alkylation of isatins with 2-methyl quinolines through benzylic C-H functionalization,[11-17] and all of them were carried out at high temperatures using a catalyst and solvents. Therefore, we were keen to extend our methodology to these, as desired we heated quinaldine **1b** with isatin **6a** at 140 °C in neat condition. Delightfully this reaction gave a nearly quantitative yield of **7a** within an hour (Scheme 5). With this excitement, we screened the reactivity of various quinolines with isatins and concluded all of them exhibited excellent reactivity with this green approach to produce **7a-7h** in high yields within

short reaction times (Scheme 5), further the structure of compound **7c** was authenticated with the help of single-crystal-x-ray (Figure 3) The analogous substrate, acenaphthoquinone also reacted under solvent and catalyst-free conditions by heating it with various 2-methyl quinolines (Scheme 6). The reaction took a shorter time and yielded **9a-9d** in moderate to good yields (Scheme 6).

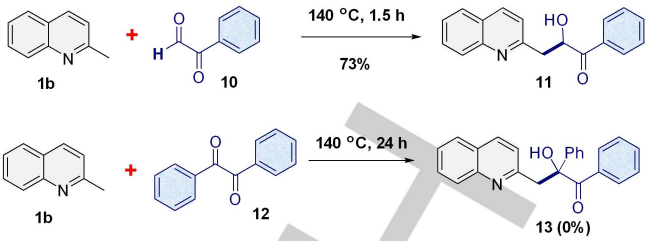


Scheme 6. Substrate scope of cyclic-α-diketo compounds (acenaphthaquinone) functionalization



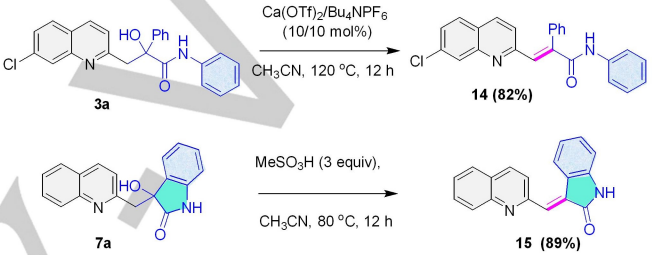
Scheme 7. Gram Scale Synthesis of **7a** under catalyst and solvent-free conditions

After developing a catalyst and solvent-free green synthetic methodology for the alkylation of a series of α-oxo compounds such as α-keto amides, α-keto esters, isatins, and cyclic-α-diketones with 2-methyl quinolines, we planned to demonstrate the scalability of this protocol. Accordingly, a mixture of isatin **6** (3 g, 1.01 mmol) and quinalidine **1b** (2.02 mmol) was heated at 140 °C for 1.5 h and obtained the desired product **7a** in 91% yield (5.36 g) (Scheme 7). Interestingly, product **7a** was isolated without any column chromatography purification; the excess of quinaldine was recovered by washing with ethanol/pentane mixture (3:7).



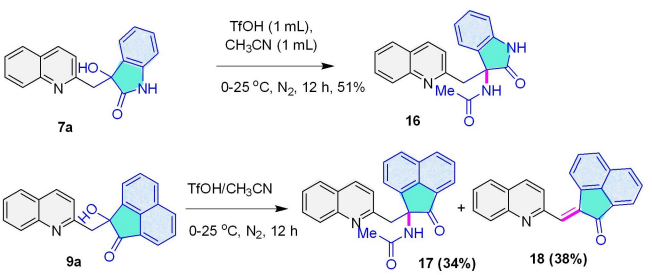
Scheme 8. Functionalization with phenyl glyoxal and benzil

The reaction of **1b** with α-keto aldehyde (**10**) was performed under these conditions, and the reaction yielded the respective alcohol in 73% yield after 1.5 h.[23,10] However, benzil (**12**) could not react with **1b** under these conditions even after prolonged heating for 24 h (Scheme 8).



Scheme 9. Elimination reactions to deliver styryl quinolines.

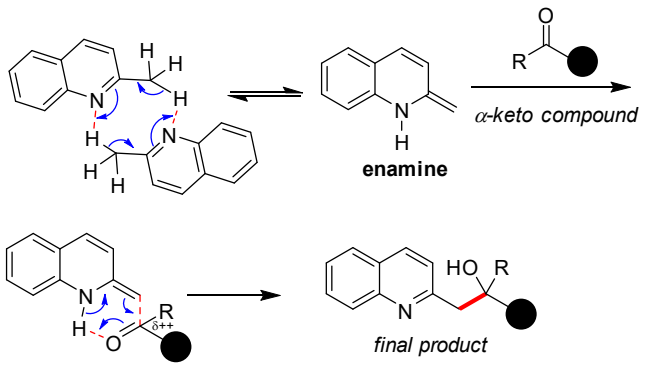
Owing to the importance of styryl quinolines, as natural products and pharmaceutically important products (such as montelukast for asthma),[24] *tert*-alcohol **3a** was subjected to calcium(II)-catalyzed dehydration at 120 °C to obtain styryl quinoline **14** in 82% yield (Scheme 9). Similarly, alcohol **7a** was also subjected to dehydration (with methanesulfonic acid) to obtain the olefin **15**. Further to show the additional synthetic utility of these compounds, we planned to perform a Ritter reaction, as the Ritter reaction is one of the very facile approaches for the preparation of amides from activated alcohols and nitriles.[25] Since the products obtained by the catalyst and solvent-free method are the alcohols, we were curious to examine their reactivity in the Ritter reaction. Thus, alcohol **7a** was treated with acetonitrile and triflic acid for 12 h and obtained the desired amide **16** in 51% yield. Similarly, alcohol **9a** gave amide **17** in 34% along with the styryl quinoline **18** (Scheme 10).



Scheme 10. Ritter reaction of *tert*-alcohols

The general reaction mechanism for the addition of 2-methyl quinolines to a-keto compounds is depicted below (Scheme 11).

At a high temperature, two moles of quinolines will interact with each other, in which the nitrogen atom behaves as a Bronsted base and accepts the methyl protons to give the corresponding enamine intermediate. If this step proceeds through eight-membered transition state as depicted, then the two moles of quinolines will produce two moles of reactive enamines. However, this may not be exactly the case, but definitely one of the quinolines acts as a base, and thus the required enamine formation takes place. In the next step, the activated carbonyl compound interacts with the enamine intermediate through a six-membered transition state to furnish the desired compound.



Scheme 11. General reaction mechanism

Conclusion

In conclusion, we have developed a diversity-oriented, green synthetic methodology for the functionalization of 2-methyl quinolines with α-oxo compounds under solvent and catalyst-free conditions. We have demonstrated the generality of this protocol by the functionalization of α-keto amides, α-keto esters, isatins, and acenaphthoquinones with 2-methyl quinoline derivatives. Synthetic transformations, gram scale demonstration (5.36 g), shorter reaction times indicate the scope and sustainable nature of this reaction. Despite the development of a novel strategy, the products formed belongs to the privileged class of molecules hence may exhibit important biological properties.

Experimental Section

General information: Unless otherwise noted, all reagents were used as received from commercial suppliers. $Ca(OTf)_2$ and Bu_4NPF_6 were obtained from Sigma-Aldrich and used without further purification. Reactions were performed in flame-dried or oven-dried glassware with magnetic stirring. Reactions were monitored using thin-layer chromatography (TLC) with aluminium sheets silica gel 60 F_{254} from Merck. TLC plates were visualized with UV light (254 nm), iodine treatment. Column chromatography was carried out using silica gel 60-120 mesh as the stationary phase. NMR spectra were recorded at 500 MHz and 400 MHz (H) and 125 MHz and 100 MHz (C), respectively on Avance Bruker spectrometer. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.0 ppm) as an internal standard, and coupling constants (J) are given in Hz. Melting points were measured with LABINDIA mepa melting apparatus.

General experimental procedure for the functionalization of 2-methyl quinolines with α-keto amides: A mixture of 2-methyl quinoline **1** (0.88 mmol) and α-keto amide **2** (0.44 mmol) was taken in a round bottom flask and heated at 140 °C under solvent-free conditions for 7 h. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (60-120 mesh) using 10-15 % EtOAc in petroleum ether as eluents to isolate the desired products **3a-3q**.

Preparation of deuterated quinaldine (1i & 1j): A mixture of 2-methyl quinoline **1b** (0.44 mmol), calcium triflate (10 mol %) and D_2O (1 mL) were taken in a round bottom flask and stirred at 100 °C for 12 to 24 h. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (2-5 % EtOAc in petroleum ether) and isolated the desired products **1i** & **1j** in 91% and 89% yields.

General experimental procedure for the addition of 2-methyl quinoline to α-keto esters: A mixture of 2-methyl azaarens **1** (1.12 mmol) and α-keto ester **4** (0.56 mmol) was heated directly at 140°C for 7 hours. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (15-20 % EtOAc in petroleum ether) and isolated the desired products **5a-5i**.

General experimental procedure for the addition of 2-methyl quinolines to isatins: A mixture of 2-methyl azaarens **1** (1.36 mmol) and isatin **6** (0.68 mmol) was heated directly at 140 °C for 1-2 hours. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (40-50 % EtOAc in petroleum ether) and isolated the desired products **7a-7h**.

General experimental procedure for the addition of 2-methyl quinolines to acenaphthaquinone: A mixture of 2-methyl quinolines **1** (1.09 mmol) and acenaphthoquinone **8** (0.55 mmol) was taken in a round bottom flask and stirred at 140 °C under solvent-free conditions for 1 h. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (30-40 % EtOAc in petroleum ether) and isolated the desired products **9a-9d**.

Experimental procedure for the addition of 2-methyl quinoline to phenylglyoxal: A mixture of phenylglyoxal monohydrate **10** (0.74 mmol) and 2-methyl quinoline **1b** (0.89 mmol) was heated at 140 °C under the solvent-free condition for 1.5 hours. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (15-20% EtOAc in petroleum ether) and isolated the desired product **11** in 73% yield.

Experimental procedure for the synthesis of 3-(7-chloroquinolin-2-yl)-*N*,2-diphenylacrylamide (14): A mixture of **3a** (0.24 mmol), calcium triflate (0.02 mmol), Bu_4NPF_6 (0.02 mmol) and acetonitrile (2 mL), was heated at 120 °C for 12 h. After completion of the reaction (monitored by TLC), the obtained crude product was purified by silica gel column chromatography (40% EtOAc in petroleum ether) and isolated the desired product **14** in 82% yield.

Experimental procedure for the synthesis of 3-(quinolin-2-ylmethylene)indolin-2-one (15): Methanesulfonic acid (20 mol%) was added dropwise to the solution of **7a (**0.52 mmol) in acetonitrile (1.5 mL) under nitrogen atmosphere at 0 °C and the reaction mixture was slowly allowed to attain room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with ice-cold water and neutralized with $NaHCO_3$ solution until effervescence disappeared. The aqueous layer was extracted with CH_2Cl_2; the combined organic layer was separated, dried over Na_2SO_4, evaporated under reduced pressure and purified by column chromatography (40% EtOAc in petroleum ether) to isolate the desired product **15** in 89% yield.

Experimental procedure for the synthesis of *N*-(2-oxo-3-(quinolin-2-ylmethyl)indolin-3-yl)acetamide (16): To a mixture of *tert*-alcohol **7a** in acetonitrile (2 mL), triflic acid (2 mL) was added dropwise under nitrogen atmosphere at 0 °C, after the addition, the reaction mixture was slowly allowed to attain room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with ice-cold water and neutralized with aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was separated, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (80% EtOAc in petroleum ether) to isolate the desired amide **16** in 51% yield.

Experimental procedure for the synthesis of 17 and 18: To a solution of alcohol **9a** in acetonitrile (2 mL), triflic acid (2 mL) was added dropwise under nitrogen atmosphere at 0 °C, and after the addition of the triflic acid, the reaction mixture was allowed to attain room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with ice-cold water and neutralized with aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was separated, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (30-40% EtOAc in petroleum ether) and isolated the desired products **17** & **18** in 34% and 38% yields.

3-(7-chloroquinoline-2-yl)-2-hydroxy-*N*,2-diphenylpropanamide (3a). the product was purified by column chromatography (60-120 silica mesh,in 15% EtOAc/petroleum ether) and obtained as colorless solid (Yield-79%); MP:141-143°C;^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.90 (s,1H), 8.45(bs, 1H), 8.07 (d, J=8.4Hz,1H), 7.98 (d ,J = 2Hz, 1H),7.83-7.81(m, 2H),7.71(d, J=8.8 Hz, 1H),7.47-7.44 (m, 3H),7.38-7.34 (m, 3H), 7.29-7.20(m, 3H), 7.03-6.99(m, 1H), 4.02(d, J = 15.2 Hz, 1H), 3.52(d, J= 15.2

Hz, 1H); ^{13}CNMR(125 MHz, $CDCl_3$): δ 172.2, 161.1, 146.7, 142.2, 137.7, 137.4, 136.1, 129.1, 130, 128.5, 127.8, 127.7, 127.4, 125.5, 125.2, 124.2, 123.2, 119.6, 80.1, 45.1 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{19}ClN_2O_2H$: 403.1213; found:403.1216; IR(film): ν_{max} 3374, 3054, 1735, 1667, 1612, 1594, 1438, 1195, 1066 cm^{-1}.

2-Hydroxy-*N*,2-diphenyl-3-(quinoline-2-yl)propanamide (3b). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-78%); MP:154-156°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.95 (s, 1H), 8.83 (s. 1H). 8.10 (d, *J*= 8.4 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J*= 7.6 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.71-7.67(m, 1H), 7.51(t, *J* = 7.2 Hz, 1H), 7.45(d, *J*= 8 Hz, 2H), 7.36(t, *J* = 8.4 Hz, 3H),7.28-7.26 (m, 1H),7.21(t, *J* = 7.6 Hz, 2H), 7.00 (t, *J* = 7.6 Hz, 1H), 4.04 (d, *J* = 15.2 Hz, 1H), 3.52 (d, *J* = 15.2 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 172.4. 159.9, 146.4, 142.3, 137.8, 137.6, 130.1, 128.9, 128.4, 128.3, 127.9, 127.7, 127.1, 126.6, 125.3, 124.2, 123.0, 119.6, 80.1, 44.9 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{20}N_2O_2H$: 369.1603;found:369.1605; IR(film): ν_{max}3350, 2920, 2359, 1672, 1593, 1511, 1493, 1382, 1339, 1190, 1057, 477 cm^{-1}.

2-Hydroxy-*N*-,2-diphenyl-3-(quinoxalin-2-yl)propanamide(3c). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as pink solid (Yield-65%); MP:278-280°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.81 (s, 2H), 8.08-8.06 (m,1H), 7.98-7.97 (m,1H), 7.82-7.80 (m,2H), 7.75-7.72(m,2H), 7.53 (s, 1H),7.45-7.43(m, 2H),7.38-7.35(m, 2H), 7.30-7.20(m, 3H), 7.03-7.00(m,1H), 4.10(d, *J* = 15.5 Hz, 1H), 3.58(d, *J* = 16 Hz, 1H); ^{13}CNMR (125 MHz, $CDCl_3$): δ171.7, 154.4. 146.7, 141.8, 141.6, 140.3, 137.5,130.7, 129.9,129.6,129.0, 128.6, 128.3, 128.1, 125.1,124.4,119.6,80.2,42.7 ppm; HRMS(ESI-TOF): m/z$[M+H]^+$ calculated for $C_{23}H_{19}N_3O_2H$: 370.1556; found:370.1558; IR(film): ν_{max}3363, 2922, 2359, 1671, 1519, 1437, 1316, 1107, 947 cm^{-1}.

3-(3-benzoyl-4-phenylquinolin-2-yl)-2-hydroxy-*N*,2-diphenylpropanamide(3d). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-63%); MP:194-196°C;^{1}H NMR (400 MHz, $CDCl_3$): δ=8.99(s, 1H), 8.85(s,1H), 8.03(d, *J* = 8.4Hz, 1H), 7.75-7.71(m, 1H),7.67(d,*J* = 7.2 Hz, 2H),7.59-7.51 (m,5H),7.75-7.42(m,2H), 7.27-7.15 (m, 12H), 7.03 (t, *J* = 7.6 Hz, 1H), 3.87 (d, *J* = 17.2 Hz, 1H), 3.56 (d, *J* = 16.8 Hz 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ197.2, 172.4, 156.5, 146.9, 146.1, 142.0, 138.0, 137.3, 134.5, 133.7, 133.1, 130.8, 130.1, 129.7, 130.0, 128.6, 128.4(2), 128.3, 128.1, 127.7, 127.3, 126.6, 125.6, 125.3, 124.1, 119.6, 80.0, 42.8ppm;HRMS(ESI-TOF): m/z[M+Na]$^+$ calculated for $C_{37}H_{28}N_2O_3Na$:571.1998;found: 571.1997; IR(film): ν_{max}3056, 2359, 2160, 1971, 1737, 1671, 1593, 1478, 1228 cm^{-1}.

3-(3-acetyl-4-phenylquinolin-2-yl)-2-hydroxy-*N*,2-diphenylpropanamide (3e). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-70%); MP: 165-167°C;^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.96(s, 1H), 8.94(s. 1H). 8.01(d, *J* = 8.4 Hz, 1H), 7.80(d, *J* = 7.6 Hz, 2H), 7.72(t, *J* = 6.8 Hz, 1H), 7.64(d, *J* =8.4 Hz,1H), 7.55-7.43(m, 8H), 7.38(t, *J* = 7.2 Hz, 2H), 7.32-7.21(m, 3H), 7.02(t, *J* = 7.2 Hz, 1H), 3.92(d, *J* = 16.4 Hz, 1H), 3.37(d, *J* = 16.4 Hz, 1H), 2.11(s, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ205.6,172.7, 155.4, 145.8, 145.3, 142.2, 137.9, 135.4, 134.9, 130.8, 130.4, 129.9, 129.3, 129.2, 129.0, 128.6, 128.5, 128.4, 127.9, 127.3, 126.5, 125.5, 125.1, 124.2, 119.6, 80.5, 42.7, 32.4 ppm;DEPT-135 (100 MHz, $CDCl_3$): δ 130.6, 130.3, 129.8, 129.2, 129.1, 128.9, 128.5, 128.4, 128.3, 127.8, 127.2, 126.4, 125.0, 124.1, 119.5, 42.6, 32.3 ppm. HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{32}H_{26}N_2O_3H$: 487.2022; found: 487.2027; IR(film): ν_{max} 3348, 3058, 2920, 1970, 1690, 1560, 1438, 1268 cm^{-1}.

3-(3-acetyl-6-chloro-4-phenylquinolin-2-yl)-2-hydroxy-*N*,2-diphenyl propanamide (3f): the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as yellow solid (Yield-72%); MP:230-232°C;^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.97(d, *J* = 8.8 Hz, 1H), 7.81-7.79(m, 2H), 7.60 (dd,J_1=2.4 Hz, J_2=9.2 Hz, 1H), 7.49-7.32(m,9H), 7.24(s, 1H), 7.10(d, *J* = 7.2 Hz, 1H), 6.94-6.91(m, 2H), 6.77(d, *J* = 8 Hz, 2H), 5.33(d, *J* = 7.6 Hz, 1H), 4.03(d, *J* = 18 Hz, 1H), 3.77(d, *J* = 18 Hz, 1H), 1.40(s, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ 172.8, 155.1, 145.2, 143.4, 137.5, 135.7, 134.5, 132.6, 130.9, 130.1, 130.0, 129.8, 129.6, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3(2), 128.0, 127.8, 126.0, 125.4, 94.3, 81.2, 41.6, 25.6 ppm; HRMS(ESI-TOF): m/z $[M+NH_3]^+$ calculated for $C_{32}H_{25}ClN_2O_3NH_3$:537.1819; found: 537.1029; IR(film): ν_{max} 3053, 2922, 2852, 2359, 1716, 1596, 1570, 1493, 1366, 1190, 1076, 947 cm^{-1}.

3-(3-acetyl-6-chloro-4-(2-fluorophenyl)quinolin-2-yl)-2-hydroxy-*N*,2diphenyl propanamide (3g): the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as yellow semi-solid (Yield-45%); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.0 (d, *J* = 9 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 2H),7.63 (dd, , J_1 = 2 Hz, J_2 = 8.5 Hz, 1H), 7.49- 7.32 (m, 8H), 7.13 (t, *J* = 9.0 Hz, 1H), 6.91 (d, *J* = 2.0 Hz, 1H), 6.78-6.72 (m, 3H), 5.34-5.31 (m, 1H), 5.29 (s, 1H), 4.01 (d, *J* = 18 Hz, 1H), 3.79 (d, *J* = 18 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 172.9, 155.2, 145.3, 137.5, 137.1, 134.5, 133.1, 131.1, 131.0, 130.2, 129.9, 129.7, 129.0, 128.7, 128.6,127.4, 125.4, 125.1, 124.3, 124.2, 123.8, 123.6, 115.7, 115.6, 94.1, 81.2, 41.7, 23.6 ppm; LCMS 8040-ESI-001.lcd m/z $[M+H]^+$ calculated for $C_{32}H_{24}ClFN_2O_3H$: 539.1538; found: 539.400; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{32}H_{24}ClFN_2O_3H$: 539.1538; found: 539.1539 ; IR (film): ν_{max} 2920, 2851, 2160, 2022, 1693, 1613, 1477, 1201, 1079, 961 cm^{-1}.

2-Hydroxy-*N*,2-diphenyl-3-(pyridine-2-yl)propanamide (3h). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as white solid (Yield-36%); MP: 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.94 (s, 1H), 8.50 (bs, 1H), 8.41 (d, *J* = 4 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 6.4 Hz, 1H), 7.47 (d, *J* = 8 Hz, 2H),7.34 (t,*J* = 7.2 Hz, 2H), 7.26-7.22 (m, 4H), 7.15 (t, *J* = 5.2 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 3.82 (d, *J* = 14.8 Hz, 1H), 3.37 (d, *J* = 15.2 Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 172.3, 158.8, 147.8, 142.3, 137.8, 137.7, 129.0, 128.4, 127.7, 125.3, 125.0, 124.1, 122.2, 119.5, 79.9, 44.4 ppm;LCMS 8040-ESI-001.lcd m/z $[M+H]^+$ calculated for $C_{20}H_{18}N_2O_2H$: 319.1447; found: 319.300;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{20}H_{18}N_2O_2H$: 319.1447; found: 319.1448; IR (film): ν_{max}3351, 2918, 1659, 1595, 1439, 1258, 1178 cm^{-1}.

2-hydroxy-2-phenyl-3-(quinolin-2-yl)-*N*-(p-tolyl)propanamide (3i). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as pale pink solid (Yield-75%); MP: 151-153 °C;^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.89 (s, 1H), 8.76 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.5 Hz 1H), 7.83 (d, *J* = 8 Hz, 2H), 7.76 (d, *J* = 8 Hz, 1H), 7.70-7.66 (m, 1H), 7.49 (t, *J* = 7 Hz, 1H), 7.36-7.24 (m, 6H), 7.0 (d, *J* = 8.5 Hz, 2H), 4.03 (d, *J* = 15 Hz, 1H), 3.52 (d, *J* = 15.5 Hz, 1H), 2.22 (s, 3H); ^{13}CNMR(100 MHz, $CDCl_3$): δ 172.2, 159.9, 146.3, 142.4, 137.6, 135.2, 133.7, 130.1, 129.4, 128.4, 128.3, 127.9, 127.7, 127.1, 126.5, 125.3, 123.0, 119.6, 80.1, 45.0, 20.9 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{25}H_{22}N_2O_2Na$: 405.1579; found: 405.1579 ; IR (film): ν_{max}3351, 3025, 2159, 1976, 1670, 1515, 1448 cm^{-1}.

3-(7-chloroquinolin-2-yl)-2-hydroxy-2-phenyl-*N*-(p-tolyl)propanamide (3j). the product was purified by column chromatography (60-120 silica mesh, in 10% EtOAc /petroleum ether) and obtained as pale pink solid (Yield-69%); MP: 120-122°C;^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.84(s, 1H),8.38(s,1H),8.05(d, *J* = 8.4 Hz, 1H), 7.97(d, *J* = 2 Hz, 1H), 7.82(d, *J* = 7.6 Hz, 2H),7.69 (d, *J* = 8.4 Hz,1H),7.45(dd, J_1= 1.6Hz, J_2 = 8.4Hz,1H),7.37-7.25(m,6H),7.01(d, *J* = 8.4 Hz, 2H),4.01(d, *J* = 15.6 Hz, 1H), 3.51(d, *J* = 15.6 Hz, 1H),2.23(s,3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 172.0, 161.2, 146.7, 142.3, 137.3, 136.1, 135.2, 133.8, 129.4, 129.1, 128.4, 127.8, 127.6, 127.3, 125.4, 125.2, 123.2, 119.6, 80.0, 45.2, 20.9 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{25}H_{21}ClN_2O_2H$: 417.1370; found: 417.1377; IR(film): ν_{max}3357, 3202, 1666, 1613, 1401 cm^{-1}.

3-(3-acetyl-4-phenylquinolin-2-yl)-2-hydroxy-2-phenyl-*N*-(*p*-tolyl)propanamide (3k): the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-72%); MP:169-171°C;^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90-8.89 (d, *J* = 3.6 Hz, 2H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.81 -7.79 (m, 2H), 7.73 -7.69 (m, 1H),7.64 -7.62 (m, 1H), 7.52 -7.25 (m, 11H),7.02 (m, *J* = 8.4 Hz, 2H), 3.91 (d, *J* = 16.4 Hz, 1H), 3.36 (d, *J* = 16.4 Hz, 1H), 2.23 (s, 3H), 2.11 (s, 3H);^{13}C NMR(100 MHz, $CDCl_3$): δ 205.5, 172.5, 155.5, 145.9, 145.3, 142.3, 135.4, 135.3, 134.9, 133.8, 130.7, 130.4, 129.9, 129.4, 129.2, 129.3, 128.6, 128.5, 128.4, 127.9, 127.3, 126.5 125.5, 125.2, 119.7, 80.5, 42.8, 32.4, 20.9 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{33}H_{28}N_2O_3H$: 501.2178; found: 501.2177; IR(film): ν_{max} 3345, 2921, 2851, 2160, 1685, 1520, 1404, 1315 cm^{-1}.

***N*-(4-bromophenyl)-2-hydroxy-2-phenyl-3-(quinolin-2-yl)propanamide (3l).** the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as white solid (Yield-80%); MP:144-146°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.95(s, 1H), 8.83(s, 1H), 8.09(d, *J* = 8.4 Hz, 1H), 7.96(d, *J* = 8.4 Hz, 1H), 7.83-7.80(m, 2H), 7.77(d, *J* = 8.4 Hz, 1H),7.71-7.67(m, 1H), 7.52-7.48(m, 1H),7.37-7.26(m, 8H), 4.01(d, *J* = 15.6 Hz, 1H), 3.52(d, *J* = 15.2 Hz, 1H);^{13}C NMR(100 MHz, $CDCl_3$): δ172.5, 159.7, 146.3, 142.1, 137.7, 136.9, 131.9, 130.2, 128.5, 128.2, 127.9, 127.8, 127.1, 126.6, 125.2, 122.9, 121.1, 116.7, 80.1, 44.9 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{19}BrN_2O_2H$: 447.0708; found: 447.0709; IR(film): ν_{max} 3359, 2159, 2029, 1671, 1506, 1408, 1306 cm^{-1}.

***N*-(4-bromophenyl)-3-(7-chloroquinolin-2-yl)-2-hydroxy-2-phenyl propanamide (3m):** the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as pale pink solid (Yield-70%); MP:162-164°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.90(s, 1H), 8.46(s, 1H), 8.07(d, *J* = 8.4 Hz, 1H), 7.97(d, *J* = 2 Hz, 1H), 7.81-7.79(m, 2H),7.71(d, *J* = 8.8 Hz, 1H),7.46(dd,J_1=2 Hz, J_2= 8.4

Hz,1H), 7.47-7.27(m, 8H), 3.99(d, *J* = 15.6 Hz, 1H), 3.52(d, *J* = 15.6 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 172.4, 161.0, 146.7, 141.9, 137.5, 136.8, 136.2, 131.9, 129.1, 128.5, 127.9, 127.7, 127.3, 125.5, 125.2, 123.2, 121.2, 116.8, 80.1, 45.0 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{18}BrClN_2O_2H$: 481.0318; found: 481.0318; IR(film):ν_{max} 3394, 2359, 1685, 1590, 1511, 1410, 1303 cm^{-1}.

3-(3-acetyl-4-phenylquinolin-2-yl)-*N*-(4-bromophenyl)-2-hydroxy-2-phenyl propanamide (3n): the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-68%); MP: 118-120°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.96 (s, 1H), 8.92 (bs,1H), 7.78(d, *J* = 7.2 Hz, 1H), 7.74-7.65 (m, 3H), 7.63-7.54 (m,1H), 7.53-7.27(m,13H),3.9(d, *J* = 16.4 Hz,1H), 3.38(d, *J* = 16.8 Hz,1H),2.09(s,3H); ^{13}C NMR(100 MHz, $CDCl_3$): δ172.8, 155.3, 145.8, 145.4, 141.9, 136.9, 135.3, 134.8, 131.9, 130.8, 130.4, 129.9, 129.3, 129.2,128.6, 128.3, 128.0, 127.4, 126.6, 125.5, 125.1,121.2, 116.7, 80.5, 42.7, 32.4 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{32}H_{25}BrN_2O_3H$: 565.1127; found:565.1128; IR(film): ν_{max}3376, 3301, 3060, 2919, 2850, 2359, 2160, 1976, 1695, 1671, 1515 cm^{-1}.

3-(7-chloroquinolin-2-yl)-2-hydroxy-*N*-(napthalen-1-yl)-2-phenylpropanamide (3o): the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as dark brown solid (Yield-52%); MP: 141-143°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 9.45 (s, 1H), 8.66 (bs,1H), 8.07-8.04 (m, 2H),7.92(d, *J* = 7.6 Hz, 2H), 7.73(t, *J* = 6.8 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 1H),7.59(t, *J* = 9.2 Hz, 2H),7.46(dd, J_1 = 2 Hz, J_2 = 8.8 Hz, 1H),7.43-7.30(m, 7H),4.11 (d, *J* = 15.2 Hz, 1H), 3.57 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 172.8, 161.3, 146.7, 142.2,137.4, 136.2, 134.1, 132.1, 130.2, 129.2, 128.7, 128.5,127.9, 127.7, 127.3, 127.1, 126.2, 126.0, 125.7, 125.5, 125.3, 123.3, 120.6, 120.1, 80.6, 45.3 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{28}H_{21}ClN_2O_2H$: 453.1370; found: 453.1377; IR(film): ν_{max} 3395, 3053, 2359, 2340, 1682, 1495, 1343 cm^{-1}.

3p: the product was purified by column chromatography (60-120 silica mesh, in 10% EtOAc /petroleum ether) and obtained as white solid (Yield-45%); MP: 220-222 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.95(s, 1H), 8.81 (s, 1H), 8.08 (d, *J* = 8 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 7 Hz, 2H), 7.76 (d, *J* = 8 Hz, 1H), 7.70-7.67 (m, 1H), 7.51-7.44 (m, 3H), 7.37-7.34 (m, 3H), 7.28-7.19 (m, 3H), 7.00-6.98 (m, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 172.4, 159.8, 146.3, 142.3, 137.7, 137.6, 130.1, 128.9, 128.4, 128.2, 127.9, 127.7, 127.1, 126.5, 125.2, 124.1, 122.9, 119.5, 80.0, 44.5ppm;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{18}D_2N_2O_2H$: 371.1730; found: 371.1712; IR (film): ν_{max} 3351, 3145, 1671, 1515, 1313, 1179, 1072 cm^{-1}.

3q: the product was purified by column chromatography (60-120 silica mesh, in 10% EtOAc /petroleum ether) and obtained as white solid (Yield-51%); MP: 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.95(s, 1H), 8.81(s, 1H), 8.09(d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.84(d, *J* = 7.2 Hz, 2H), 7.77(d, *J* = 8 Hz, 1H), 7.71-7.67(m, 1H), 7.52-7.44(m, 3H), 7.35 (dd, J_1 = 7.2 Hz, J_2= 8.4 Hz, 3H), 7.29-7.19(m, 3H), 7.0(t, *J* = 7.2 Hz, 1H), 4.06-3.50(dd,J_1 = 15.6 Hz, J_2 = 15.6 Hz, 1H);^{13}C NMR(100 MHz, $CDCl_3$): δ 172.4, 159.9, 146.4, 142.4, 137.8, 137.6, 130.1, 128.5, 128.4, 128.3, 127.9, 127.8, 127.1, 126.6, 125.3, 124.2, 123.0, 119.6, 80.1, 45.0 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for$C_{24}H_{19}DN_2O_2H$:370.1668;found: 370.1668; IR (film): ν_{max}3352, 3145, 2359, 1671, 1598, 1515, 1394, 1313 cm^{-1}.

Ethyl 3-(7-chloroquinolin-2-yl)-2-hydroxy-2-phenylpropanoate (5a). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-75%); MP: 118-120°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.08 (d, *J* = 8 Hz, 1H), 7.99 (d, *J* = 2 Hz, 1H), 7.75-7.72 (m, 3H), 7.48(dd, J_1 = 2 Hz, J_2=8.5 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H),7.32-7.29(m, 2H), 6.84(s, 1H), 4.15-4.09(m, 2H), 4.0(d, *J* = 16.0 Hz, 1H), 3.49(d, *J* = 15.5 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 174.2, 160.6, 147.1, 141.5, 136.8, 135.9, 129.0, 128.5, 127.9, 127.7, 127.6, 125.3(2), 122.8, 78.8, 61.8, 47.0, 14.17 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{20}H_{18}ClNO_3H$: 356.1053; found: 356.1058; IR(film): ν_{max}3246, 2974, 2906, 1732, 1611, 1596, 1496 cm^{-1}.

Ethyl 2-hydroxy-2-phenyl-3-(quinolin-2-yl)propanoate (5b). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-79%); MP: 194-196°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.10 (d, *J* = 8.4 Hz, 1H), 8.0 (d, *J* = 8.8 Hz, 1H), 7.79-7.68 (m, 4H), 7.54-7.26 (m, 6H), 4.13-4.05 (m, 2H), 4.01 (d, *J* = 15.6 Hz, 1H), 3.49 (d, *J* = 15.6Hz, 1H), 1.09 (t, *J* = 7.2 Hz,3H);^{13}C NMR(125 MHz, $CDCl_3$): δ 174.3, 159.5, 146.8, 141.7, 137.0, 130.0, 128.7, 128.5, 127.9, 127.7, 127.0, 126.5, 125.3, 122.5, 79.0, 61.6, 46.9, 14.1 ppm;DEPT-135 (100 MHz, $CDCl_3$): δ 136.9, 129.9, 128.5, 128.3, 127.7, 127.6, 126.3, 125.1, 122.4, 61.5, 46.7, 14.0 ppm. HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{20}H_{19}NO_3H$: 322.1443; found:322.1447; IR(film): ν_{max}3181, 2983, 2360, 2339, 2159, 2027, 1974, 1728, 1596, 1428, 1178 cm^{-1}.

Ethyl 3-(3-acetyl-4-phenylquinolin-2-yl)-2-hydroxy-2-phenylpropanoate (5c). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as white solid (Yield-67%); MP: 152-154°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.04(d, *J* = 8 Hz, 1H), 7.77-7.71(m,3H) , 7.66(dd, J_1 = 0.8Hz, J_2=8.4 Hz, 1H), 7.54-7.30(m, 9H),7.12 (s,1H),4.20-4.10 (m,2H), 3.92(d, *J* =16.8 Hz, 1H), 3.38(d, *J* = 16.8Hz, 1H), 2.0 (s, 3H), 1.15 (t, *J* = 6.8 Hz, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ 205.1, 174.6, 154.8, 146.3, 145.0, 141.5, 135.1, 135.0,130.6, 130.2, 130.1, 129.3, 129.0, 128.8, 128.7, 128.5, 127.9, 127.3, 126.4, 125.3(2), 78.9, 61.6, 45.0, 32.2, 14.2 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{28}H_{25}NO_4H$:440.1862; found: 440.1862; IR(film): ν_{max}3410, 2978, 2160, 1975, 1720, 1683, 1441, 1244 cm^{-1}.

Isopropyl 3-(7-chloroquinolin-2-yl)-2-hydroxy-2-phenylpropanoate (5d). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-72%); MP:103-105°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.06 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 2 Hz, 1H), 7.75-7.71(m, 3H), 7.47(dd, J_1= 2 Hz, J_2= 9 Hz, 1H), 7.39(t, *J* = 7 Hz, 2H), 7.32-7.28(m, 2H), 6.70(s, 1H), 4.96-4.91(m, 1H), 3.99(d, *J* = 15.5 Hz, 1H), 3.48(d, *J* = 15.5 Hz, 1H), 1.12(d, *J* = 6.5 Hz, 3H), 1.03(d, *J* = 6.5 Hz, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 173.7, 160.7, 147.1, 141.5, 136.7, 135.8, 128.9, 128.4, 127.9, 127.6, 127.5 (2), 125.3, 122.8, 78.7, 69.3, 47.1, 21.7, 21.5 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{21}H_{20}ClNO_3H$:370.1210; found: 370.1034; IR(film): ν_{max} 3212, 2983, 1730, 1613, 1453 cm^{-1}.

Isopropyl 2-hydroxy-2-phenyl-3-(quinolin-2-yl)propanoate (5e). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as white solid (Yield-75%); MP:93-95°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.10(d, *J* = 8.4 Hz, 1H), 8.0(d, *J* = 8.4 Hz, 1H), 7.79-7.68(m, 4H), 7.54-7.28(m, 5H), 7.23 (s, 1H), 4.94-4.88(m, 1H), 4.0(d,*J* = 15.6 Hz, 1H), 3.48(d,*J* = 15.6 Hz, 1H), 1.10(d, *J* = 6 Hz, 3H), 1.01(d, *J* = 6.4 Hz, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ 173.8, 159.6, 146.7, 141.8, 137.0, 130.0, 128.6, 128.4, 127.8, 127.7, 127.0, 126.4, 125.3, 122.5, 78.9, 69.1, 47.0, 21.7, 21.5 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{21}H_{21}NO_3H$: 336.1600; found: 336.1603; IR(film): ν_{max} 3206, 2981, 1723, 1596, 1428, 1199, 1060 cm^{-1}.

Benzyl 2-hydroxy-2-phenyl-3-(quinolin-2-yl)propanoate (5f). the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-64%); MP:105-107°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.04(d, *J* = 8.4 Hz, 1H), 7.92(d, *J* = 8.4 Hz, 1H), 7.78-7.51(m, 6H), 7.40-7.23(m, 4H), 7.15-7.0(m, 5H),5.05(q, *J* = 12.4 Hz, 2H),4.02(d, *J* = 16 Hz, 1H), 3.48(d, *J* = 15.6Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 174.2, 159.4, 146.7, 141.5, 137.1, 135.8, 130.0, 128.7, 128.5, 128.3, 128.0(2), 127.9, 127.7, 127.0, 126.5, 125.4, 122.4, 79.1, 67.1, 46.7 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{25}H_{21}NO_3H$: 384.1600; found: 384.1563; IR(film): ν_{max}3384, 3056, 1727, 1599, 1195, 1097 cm^{-1}.

***sec*-Butyl 3-(7-chloroquinolin-2-yl)-2-hydroxy-2-phenylpropanoate (5g).** the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-64%); MP:81-83°C; *(Obtained as inseparable mixture of 1:1 diastereomers)* ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 3 Hz, 1H), 8.06 (d, *J* = 2.5 Hz, 1H), 8.0-7.99 (m, 2H), 7.75-7.71 (m, 6H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.46 (d, *J* = 2 Hz, 1H), 7.40-7.36 (m, 4H), 7.33-7.29 (m, 4H), 6.76 (s, 1H), 6.68 (s, 1H), 4.81-4.72 (m, 2H), 4.03 (d, *J* = 3.5 Hz, 1H), 4.0 (d, *J* = 3 Hz, 1H), 3.52 (d, *J* = 3 Hz, 1H), 3.49 (d, *J* = 3 Hz, 1H), 1.55-1.36 (m, 4H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 6 Hz, 3H), 0.71 (t, *J* = 7.5 Hz, 3H), 0.58 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.9, 160.8, 160.7, 147.2, 147.1, 141.7(2), 136.7(2), 135.8, 128.9, 128.4(2), 127.9, 127.9, 127.7(2), 127.5, 125.4, 125.3, 122.9, 122.8, 78.8, 78.7, 74.0, 73.9, 47.0, 46.9, 28.8, 28.7, 19.3, 19.2, 9.6, 9.5ppm; HRMS (ESI-TOF): m/z[M-H]$^+$ calculated for $C_{22}H_{21}ClNO_3$:382.1210; found: 382.1194; HRMS (ESI-TOF): m/z $[M+H]^+$ calculated for $C_{22}H_{22}ClNO_3H$:384.1366; found: 384.1158; IR(film): ν_{max} 3258, 2972, 2929, 2359, 1716, 1495, 1262, 1055 cm^{-1}.

***sec*-Butyl 2-hydroxy-2-phenyl-3-(quinolin-2-yl)propanoate (5h).** the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-59%); MP: 83-85°C; *(Obtained as inseparable mixture of 1:1 diastereomers)* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 2 Hz, 1H), 8.09 (d, *J* = 2 Hz, 1H), 8.00 (d, *J* = 0.8 Hz, 1H), 7.98 (d, *J* = 0.8 Hz, 1H), 7.79 (m, 6H), 7.72-7.68 (m, 2H), 7.54-7.50 (m, 2H), 7.41-7.36 (m, 4H), 7.33-7.27 (m, 6H), 4.78-4.71 (m, 2H), 4.04 (d, *J* = 4.4 Hz, 1H), 4.00 (d, *J* = 4.4 Hz, 1H), 3.52 (d, *J* = 2.8 Hz, 1H), 3.48 (d, *J* = 2.8 Hz, 1H), 1.54-1.33 (m, 4H), 1.06 (d, *J* = 6.4 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.68 (t, *J* = 7.6 Hz, 3H), 0.55 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 159.6, 159.5, 146.7(2), 141.8,136.9, 129.9, 128.6, 128.6, 128.4, 127.8, 127.8, 127.7, 126.9, 126.4, 125.3, 125.3, 122.5, 122.4, 79.0, 78.9,

73.7, 73.6, 46.7(2), 28.7, 28.6, 19.3, 19.1, 9.7, 9.4 ppm; HRMS (ESI-TOF): m/z $[M+H]^+$ calculated for $(C_{22}H_{23}NO_3)_2H$:350.1756; found: 350.1750; IR(film): ν_{max}3343, 2971, 2873, 1706, 1598, 1447, 1266 cm^{-1}.

***sec*-Butyl 3-(3-acetyl-4-phenylquinolin-2-yl)-2-hydroxy-2-phenylpropanoate (5i)** the product was purified by column chromatography (60-120 silica mesh, in 15% EtOAc /petroleum ether) and obtained as colorless solid (Yield-60%); MP:145-147°C; *(Obtained as inseparable mixture of 1:1 diastereomers)* ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 8.03 (s, 1H), 7.76-7.71 (m, 6H), 7.66 (s, 1H), 7.64 (s, 1H), 7.55-7.47 (m, 8H), 7.41-7.37 (m, 6H), 7.33-7.31 (m, 4H), 7.09 (d, *J* = 2 Hz, 2H), 4.84-4.76 (m, 2H), 3.94 (d, *J* = 6 Hz, 1H), 3.90 (d, *J* = 5.6 Hz, 1H), 3.41 (s, 1H), 3.36 (s, 1H), 2.01 (s, 3H), 2.00 (s, 3H) , 1.15-1.39 (m, 4H), 1.13 (d, *J* = 6 Hz, 3H), 0.97 (d, *J* = 6 Hz, 3H), 0.76 (t, *J* = 7.6 Hz, 3H), 0.54 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 205.2, 205.1, 174.3, 154.9 (2), 146.3, 145.0 (2), 141.6, 135.2, 135.1, 130.6(2), 130.3, 130.1, 129.3, 129.0, 128.8, 128.7(2), 128.5, 128.4, 127.9(2), 127.2, 126.4, 125.3(2), 79.0, 78.8, 73.8, 73.7, 45.0, 44.6, 32.3, 32.2, 28.9, 28.7, 19.5, 19.2, 9.8, 9.4 ppm; HRMS(ESI-TOF): m/z calculated for $(C_{30}H_{29}NO_4)_2$: 467.2097; found: 467.2017; IR(film): ν_{max} 3272, 2971, 1712, 1697, 1558, 1265, 1078 cm^{-1}.

3-Hydroxy-3-(quinolin-2-ylmethyl)indolin-2-one (7a). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-92%); MP: 177-179 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.89 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8 Hz, 1H), 7.73-7.69 (m, 1H), 7.58-7.53(m, 1H), 7.30(d, *J* = 8.5 Hz, 1H), 7.22 (s, 1H), 7.13-7.09(m, 1H), 6.81-6.78(m, 3H), 3.55(d, *J* = 14.5 Hz, 1H), 3.31(d, *J* = 14.5 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 178.2, 157.2, 146.1, 140.7, 135.6, 130.6, 128.9, 128.3, 127.9, 126.9, 126.1, 125.5, 123.6, 122.2, 121.0, 109.3, 75.6, 43.8 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{18}H_{14}N_2O_2Na$: 313.0953; found: 313.0927; IR(film): ν_{max} 3319, 3058, 2808, 1706, 1620, 1471, 1286, 1175, 1112 cm^{-1}.

3-Hydroxy-1-methyl-3-(quinolin-2-ylmethyl)indolin-2-one (7b). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as colorless solid (Yield-73%); MP: 152-154°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.13(d, *J* = 8.5 Hz, 1H), 8.09(d, *J* = 8.5 Hz, 1H), 7.87-7.83(m, 2H), 7.75(dd, J_1 = 7 Hz, J_2= 8 Hz, 1H), 7.57(t, *J* = 8 Hz, 1H), 7.27-7.24(m, 1H), 7.17(d, *J* = 8.5 Hz, 1H), 6.88(t, *J* = 7.5 Hz, 1H), 6.82(d, *J* = 8 Hz, 2H), 3.56(d, *J* = 15 Hz, 1H), 3.23(d, *J* = 15 Hz, 1H), 3.20(s, 3H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 176.7, 158.7, 146.7, 143.1, 137.2, 131.3, 130.2, 129.4, 128.8, 127.8, 127.1, 126.6, 124.1, 122.8, 122.8, 108.4, 76.4, 43.2, 26.3 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{19}H_{16}N_2O_2Na$:327.1109; found: 327.1109; IR(film): ν_{max}3275, 3049, 1689, 1612, 1469, 1245, 1065 cm^{-1}.

1-Benzyl-3-hydroxy-3-(quinolin-2-ylmethyl)indolin-2-one (7c). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as colorless solid (Yield-92%); MP: 150-153°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.12(dd, J_1 = 8.4 Hz, J_2= 13.6 Hz, 2H), 7.92(bs, 1H), 7.84(d, *J* = 7.6 Hz, 1H),7.78-7.73(m, 1H), 7.59-7.55(m, 1H), 7.29-7.23(m, 5H), 7.19(d, *J* = 8.4 Hz, 1H), 7.15-7.11(m, 1H), 6.89-6.83(m, 2H), 6.69(d, *J* = 8 Hz, 1H), 4.96(d, *J* = 15.6 Hz, 1H), 4.81(d, *J* = 15.6 Hz, 1H), 3.61(d, *J* = 14.8 Hz, 1H), 3.30(d, *J* = 15.2 Hz, 1H);^{13}C NMR(100 MHz, $CDCl_3$): δ 176.9, 158.5, 146.7, 142.1, 137.2, 135.7, 131.2, 130.2, 129.4, 128.8 (2), 127.8, 127.6, 127.3, 127.1, 126.7, 124.2, 122.9, 122.8, 109.4, 76.5, 43.8, 43.5 ppm; HRMS(ESI-TOF): m/z calculated for $C_{25}H_{20}N_2O_2$: 380.1525; found: 380.1477; IR(film): ν_{max}3142, 2359, 1712, 1613, 1598, 1351, 1076 cm^{-1}.

3-Hydroxy-3-(quinoxalin-2-ylmethyl)indolin-2-one (7d). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pink solid (Yield-65%); MP: 159-161°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.66(s, 1H), 8.49(s, 1H), 8.08-8.03(m, 2H), 7.78-7.72(m, 2H), 7.17-7.14(m, 1H), 6.98(d, *J* = 7.5 Hz, 1H), 6.93(t, *J* = 7.5 Hz, 1H), 6.77(d, *J* = 7.5 Hz, 1H), 6.08(s, 1H), 3.56(d, *J* = 14.5 Hz, 1H), 3.46(d, *J* = 14.5 Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 178.3, 152.2, 146.8, 141.4, 141.1, 140.5, 130.7, 129.5, 129.0, 128.9, 128.6, 128.5, 124.4, 121.1, 109.4, 75.4, 43.6 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{17}H_{13}N_3O_2Na$: 314.0905; found: 314.0906; IR(film): ν_{max} 3286, 1697, 1618. 1469, 1184, 979 cm^{-1}.

3-((3-acetyl-4-phenylquinolin-2-yl)methyl)-3-hydroxyindolin-2-one (7e). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-92%); MP: 174-176°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.16(d, *J* = 8 Hz, 1H), 7.90 (bs, 1H), 7.82-7.78(m, 2H), 7.70(d, *J* = 8 Hz, 1H), 7.56-7.50(m, 4H), 7.40-7.18(m, 3H), 7.06(d, *J* = 7.2 Hz, 1H), 6.95(t, *J* = 0.4 Hz, 1H), 6.83(d, *J* = 8 Hz, 1H), 3.40(d, *J* = 15.6 Hz, 1H), 3.30(d, *J* = 15.6 Hz, 1H),1.74(s, 3H);^{13}C NMR(100 MHz, $CDCl_3$): δ 205.4, 179.1, 153.7, 146.4, 145.5, 140.2, 135.5, 135.0, 131.7, 131.0, 130.3, 130.1, 129.6 (2), 129.4, 129.1, 129.0, 127.6, 126.5, 125.4, 124.5 122.9, 110.4, 76.7, 40.5, 32.3 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{26}H_{20}N_2O_3H$: 409.1552; found: 409.1505; IR(film): ν_{max} 3332, 3152, 2359, 1729, 1691, 1618, 1472, 1325, 1222, 1102 cm^{-1}.

3-Hydroxy-5-methoxy-3-(quinoline-2-ylmethyl)indolin-2-one (7f). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale orange solid (Yield-91%); MP: 165-167°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.14(d, *J* = 8.5 Hz, 1H), 8.11(d, *J* = 8.5 Hz, 1H), 7.84(d, *J* = 8 Hz, 1H),7.79 (s, 1H), 7.78-7.74(m, 1H), 7.59-7.56(m, 1H), 7.26 (s, 1H), 7.21(d, *J* = 8 Hz, 1H), 6.76-6.71(m, 2H), 6.46(d, *J* = 2.5 Hz, 1H), 3.57(s, 3H), 3.55(d, *J* = 15 Hz, 1H), 3.27(d, *J* = 15 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 178.9, 158.5, 156.0, 146.8, 137.3, 133.4, 132.9, 130.3, 128.8, 127.8, 127.2, 126.8, 122.9, 114.3, 111.5, 110.8, 77.4, 55.7, 43.4 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{19}H_{16}N_2O_3Na$: 343.1059; found: 343.1057; IR(film): ν_{max}3314, 2359, 2341, 1704, 1599, 1485, 1266, 1155, 1029 cm^{-1}.

5-chloro-3-hydroxy-3-(quinolin-2-ylmethyl)indolin-2-one (7g). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale orange solid (Yield-87%); MP: 285-287°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.17(d, *J* = 8.5 Hz, 1H), 8.10(d, *J* = 8.5 Hz, 1H), 7.97(s, 1H), 7.86(d, *J* = 8 Hz, 1H), 7.78(dd, J_1 = 7 Hz, J_2 = 8.5 Hz, 1H), 7.60(t, *J* = 7.5 Hz, 1H), 7.26(d, *J* = 1 Hz, 1H), 7.21-7.16(m, 2H), 6.87(s, 1H), 6.77(d, *J* = 8.5 Hz, 1H), 3.52(d, *J* = 15.5 Hz, 1H), 3.27(d, *J* = 15 Hz, 1H);^{13}C NMR(125 MHz, $CDCl_3$): δ 177.6, 156.1, 145.9, 139.5, 134.9, 132.1, 128.3, 127.6, 127.5, 126.5, 125.6, 125.2, 125.1, 123.7, 121.7, 109.9, 75.1, 43.9 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{18}H_{13}ClN_2O_2H$: 325.0744; found: 325.0742; IR(film): ν_{max} 3088, 1712, 1615, 1424, 1319, 1143 cm^{-1}.

3-((3-acetyl-4-phenylquinolin-2-yl)methyl)-1-benzyl-3-hydroxyindoline-2-one (7h): the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-74%); MP:164-166°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.14(d, *J* = 8.5 Hz, 1H), 7.99(s, 1H), 7.80-7.76(m, 1H), 7.69(d, *J* = 8.5 Hz, 1H), 7.53-7.49(m, 5H),7.31-7.15(m, 8H), 6.97(t, *J* = 15 Hz, 1H), 6.71(d, *J* = 8 Hz, 1H), 4.90(d, *J* = 15.5 Hz, 1H), 4.82(d, *J* = 16 Hz, 1H),3.39(s, 2H), 1.68(s, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 205.6, 177.2, 153.7, 146.3, 145.4, 142.3, 135.7, 135.4, 135.0, 131.1, 130.9, 130.3, 130.2, 129.6, 129.3, 129.0(2), 128.9,128.8, 127.7, 127.5, 127.3, 126.4, 125.3, 124.2, 123.0, 109.5, 76.3, 43.7, 40.4, 32.2ppm;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{33}H_{26}N_2O_3H$: 499.2022; found: 499.2023; IR(film): ν_{max}3272, 3063, 2359, 1715, 1682, 1612, 1466, 1356, 1176, 1046 cm^{-1}.

2-hydroxy-2-(quinolin-2-ylmethyl)acenaphthylen-1(2*H*)-one (9a). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-80%); MP: 134-136°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.11 (t,*J* = 8.5 Hz, 3H), 7.99 (d, *J* = 7 Hz, 2H), 7.84 (d, *J* = 8 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H),7.77-7.72 (m, 2H), 7.59-7.55 (m, 1H), 7.44 (J_1 = 7 Hz, J_2 = 8.5 Hz, 1H), 7.12(d, *J* = 8.5 Hz, 1H), 7.04(d, *J* = 7 Hz, 1H), 3.65(d, *J* = 15 Hz, 1H), 3.28(d, *J* = 15 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 203.4, 159.2, 146.7, 141.0, 140.9, 137.2, 131.9, 130.8, 130.7, 130.2, 128.8, 128.7, 128.3, 127.8, 127.1, 126.6, 125.1, 122.7, 122.3, 120.6, 80.1, 43.0ppm;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for$C_{22}H_{15}NO_2H$: 326.1181; found: 326.1183; IR(film): ν_{max}3208, 1713, 1619, 1419, 1344, 1141, 1036 cm^{-1}.

2-hydroxy-2-(quinolin-2-ylmethyl)acenaphthylen-1(2*H*)-one (9b). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pink solid (Yield-65%); MP: 183-185°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.63(s, 1H), 8.13-7.99(m, 4H), 7.86(d, *J* = 8.5 Hz, 1H), 7.80-7.74(m, 3H), 7.53(dd, J_1 = 7 Hz, J_2= 8.5 Hz, 1H), 7.18(d, *J* = 6.5 Hz, 1H), 6.02(s, 1H), 3.68(d, *J* = 15 Hz, 1H), 3.51(d, *J* = 15 Hz, 1H);^{13}C NMR(100 MHz, $CDCl_3$): δ 203.3, 153.1, 146.3, 141.7, 141.1, 141.0, 139.6, 132.1, 130.8, 130.6, 130.5, 129.9, 129.4, 128.9, 128.7, 128.5, 125.6, 122.5, 120.7, 79.8, 41.6 ppm; LCMS8040-ESI-001.lcd m/z $[M+H]^+$ calculated for $C_{21}H_{14}N_2O_2H$:327.1134; found: 327.300;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{21}H_{14}N_2O_2H$:327.1134; found: 327.1135;IR(film): ν_{max}3200, 1713, 1604, 1492, 1363, 1176, 1083 cm^{-1}.

2-((3-acetyl-4-phenylquinolin-2-yl)methyl)-2-hydroxyacenaphthylen-1(2*H*)-one (9c): the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as pale yellow solid (Yield-64%); MP: 190-192°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.14-8.10(m, 2H), 7.98(d, *J* = 7 Hz, 1H), 7.86(d, *J* = 8.5 Hz, 1H), 7.82-7.40(m, 3H), 7.71(d, *J* = 8.5 Hz, 1H),7.58-7.50(m, 5H), 7.41-7.33(m, 3H), 3.52(d, *J* = 16 Hz, 1H), 3.40(d, *J* = 16 Hz, 1H), 1.67(s, 3H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 205.3, 203.6, 154.1, 146.4, 145.4, 141.1, 140.9, 135.3,135.1, 132.0, 130.9(2), 130.3, 130.2, 129.3, 129.0, 128.9(2), 128.8, 128.5, 127.5, 126.5, 125.4, 122.3, 120.7, 80.1, 40.5, 32.2 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{30}H_{21}NO_3H$:444.1600; found: 444.1600; IR(film): ν_{max}3182, 3059, 1712, 1689, 1556, 1437, 1214, 1058 cm^{-1}.

2-(7-chloroquinolin-2-yl)methyl)-2-hydroxyacenaphthylen-1(2*H*)-one (9d). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as colorless solid (Yield-75%); MP 151-153°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.09-8.06(m, 3H), 7.97(d, *J* = 5 Hz, 1H), 7.81(d, *J* = 7.5 Hz, 1H), 7.75(t, *J* = 8.5 Hz,2H), 7.51-7.46(m, 3H), 7.13-7.10(m, 2H), 3.61(d, *J* = 15 Hz, 1H), 3.34(d, *J* = 14.5 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 203.4, 160.2, 147.0, 141.0, 140.6, 137.0, 136.0, 132.0, 130.7, 130.6, 129.0, 128.7, 128.3, 127.7, 127.6, 125.4, 125.2, 122.9, 122.3, 120.6, 80.0, 43.3ppm; LCMS8040-ESI-001.lcd m/z $[M+H]^+$ calculated for $C_{22}H_{14}ClNO_2H$: 360.0791; found: 360.0792;HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for$C_{22}H_{14}ClNO_2H$: 360.0791; found: 360.0792; IR(film): ν_{max}3310, 3050, 1721, 1597, 1494, 1323, 1194 cm^{-1}.

2-hydroxy-1-phenyl-3-(quinolin-2-yl)propan-1-one (11). the product was purified by column chromatography (60-120 silica mesh, in 20% EtOAc /petroleum ether) and obtained as deep brown semi-solid (Yield-73%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 7.6 Hz, 3H), 8.0 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.71-7.67 (m, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.52-7.48 (m, 3H), 7.33 (d, *J* = 8.4 Hz, 1H), 5.65 (dd, J_1 = 3.6 Hz, J_2= 8 Hz, 1H), 3.54 (dd, J_1 = 3.2 Hz, J_2= 14.8 Hz, 1H), 3.29 (dd, J_1 = 8 Hz, J_2= 15.2 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 200.8, 158.8, 147.6, 136.6, 134.5, 133.7, 129.7, 129.1, 128.8(2), 127.6, 127.0, 126.2, 122.4, 73.4, 42.7 ppm; HRMS(ESI-TOF): m/z $[M+Na]^+$ calculated for $C_{18}H_{15}NO_2Na$: 300.1000; found: 300.0991; IR (film): ν_{max}3428, 3058, 1670, 1596, 1504, 1268, 1120 cm^{-1}.

(*E*)-3-(7-chloroquinolin-2-yl)-*N*,2-diphenylacrylamide (14). the product was purified by column chromatography (60-120 silica mesh, in 40% EtOAc /petroleum ether) and obtained as pale pink solid (Yield-82%); MP: 220-222 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.74-7.71 (m, 3H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.59 (dd, J_1 = 7.6 Hz, J_2= 13.6 Hz, 3H), 7.43-7.36 (m, 6H), 7.21 (s, 1H), 7.18 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 167.6, 155.0, 148.3, 143.2, 138.1, 136.5 (2), 135.9, 129.4, 129.2, 129.1, 128.7, 128.6, 127.9, 127.6, 126.9, 125.6, 124.8, 122.1, 120.2 ppm; HRMS(ESI-TOF): m/z $[M+H]^+$ calculated for $C_{24}H_{17}ClN_2OH$: 385.1108; found: 385.1106; IR(film): ν_{max} 3248, 3057, 2160, 1656, 1438, 1064 cm^{-1}.

(*Z*)-3-(quinolin-2-ylmethylene)indolin-2-one (15). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as yellow solid (Yield-89%); MP: 232-234°C;^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.02 (d, *J* = 9.0 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 2H), 7.89 (s, 1H), 7.85 (d,*J* = 8 Hz, 1H), 7.75-7.72 (m, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 7.0 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR(125 MHz, $CDCl_3$): δ 167.5, 153.7, 148.3, 140.3, 137.2, 136.0, 130.2, 129.9, 129.8, 129.7, 128.0, 127.7, 127.6, 125.0, 124.0, 122.5, 120.7, 109.8 ppm; LCMS8040-ESI (m/z) $[M+H]^+$ calculated for $C_{18}H_{12}N_2OH$: 273.1028; found: 273.250; IR(film): ν_{max}3167, 1681, 1469, 1336, 1205 cm^{-1}.

***N*-(2-oxo-3-(quinolin-2-ylmethyl)indolin-3-yl)acetamide (16).** the product was purified by column chromatography (60-120 silica mesh, in 40% EtOAc /petroleum ether) and obtained as yellow solid (Yield-51%); MP: 278-280°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.24 (s, 1H), 8.19 (s, 1H), 8.12 (dd, J_1 = 3 Hz, J_2= 8.5 Hz, 2H), 7.87 (d, *J* = 8 Hz, 1H), 7.82-7.59 (m, 2H), 7.16-7.12 (m, 1H), 7.06 (d, *J* = 8 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.31 (d, *J* = 7.5 Hz, 1H), 3.54 (d, *J* = 14 Hz, 1H), 3.02 (d, *J* = 14 Hz, 1H), 2.02 (s, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ 177.6, 169.0, 157.2, 147.5, 140.8, 136.9, 130.2, 130.1, 129.0, 128.9, 128.0, 127.3, 126.9, 123.8, 123.1, 122.1, 110.4, 61.6, 43.4, 22.9ppm; LCMS8040-ESI m/z $[M+H]^+$ calculated for $C_{20}H_{17}N_3O_2H$: 332.1399; found:332.300;IR(film): ν_{max} 3250, 2923, 1714, 1617, 1470, 1211 cm^{-1}.

***N*-(2-oxo-1-(quinolin-2-ylmethyl)-1,2-dihydroacenaphthylen-1-yl)acetamide (17).** the product was purified by column chromatography (60-120 silica mesh, in 40% EtOAc /petroleum ether) and obtained as yellow solid(Yield-67%); MP:163-165°C;^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (t, *J* = 8 Hz, 3H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.71-7.63 (m, 3H), 7.58-7.55 (m, 1H), 7.45-7.40 (m, 3H), 7.25 (s, 1H), 7.04 (d, *J* = 7 Hz, 1H), 3.89 (d, *J* = 14 Hz, 1H), 3.58 (d, *J* = 14 Hz, 1H), 2.08 (s, 3H);^{13}C NMR(125 MHz, $CDCl_3$): δ199.9, 169.1, 155.6, 147.4,140.7, 136.5, 135.8, 131.7, 131.5, 130.5, 129.4, 129.0, 128.2, 127.9, 127.4, 126.9, 126.3, 125.9, 122.9, 121.9, 120.8, 84.0, 45.2, 20.73 ppm; LCMS8040-ESI m/z $[M+Na]^+$ calculated for $C_{24}H_{18}N_2O_2Na$: 389.1266; found: 389.300;IR (film):ν_{max}3043, 1724, 1503, 1365, 1242, 1039 cm^{-1}.

(*E*)-2-(quinolin-2-ylmethylene)acenaphthylen-1(2H)-one (18). the product was purified by column chromatography (60-120 silica mesh, in 30% EtOAc /petroleum ether) and obtained as yellow solid (Yield-87%);MP: 186-188°C;^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.88 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.11 (t, *J* = 8.5 Hz, 2H), 8.01 (d, *J* = 6.5 Hz, 1H), 7.91-7.85 (m, 4H), 7.75-7.68 (m, 3H), 7.57 (t, *J* = 7.5 Hz, 1H);^{13}C NMR(125 MHz, $CDCl_3$): δ 191.7, 154.1, 148.3, 139.2, 136.5, 135.8, 135.6, 134.9, 133.7, 131.4, 130.7, 129.8, 129.6, 128.7, 128.3, 127.9, 127.7, 127.4, 125.9, 123.9, 121.6, 117.2 ppm; LCMS8040-ESI m/z $[M+H]^+$ calculated for $C_{22}H_{13}NOH$: 308.1075; found: 308.300;IR (film):ν_{max} 3046, 1705, 1630, 1427, 1207, 1022 cm^{-1}

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Highly Facile approach of chemoselective alkylation of α-oxo compounds such as α-keto amides, α-keto esters, isatins, and cyclic-α-diketones is developed through C(sp^3)-H functionalization of 2-methyl quinolines under solvent and catalyst-free conditions

C(sp^3)-H Functionalization of 2-Methyl Quinolines*

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Alkylation of α-Oxo-compounds through C(sp^3)-H Functionalization of 2-Methyl Quinolines Under Catalyst- and Solvent-Free Conditions