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Chemoselective and highly rate accelerated intramolecular aza-Morita-Baylis-Hillman reaction

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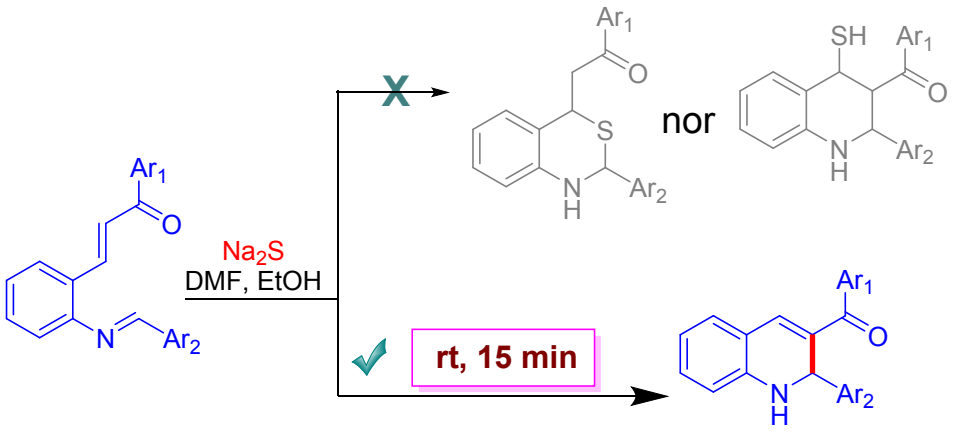


Abstract

Despite being a very useful C-C bond forming and highly applicative reaction, Morita-Baylis-Hillman (MBH) reaction has been limited by its excessive slow reaction rate, including its intramolecular version. In certain cases, reaction time may even go to weeks and month. A highly chemoselective and rate accelerated intramolecular MBH reaction of just 15 minutes has been developed. The product dihydroquinoline, being unstable were converted to important quionline framework. In some cases IMBH adduct were isolable, thus confirming the reaction path. Control experiments towards mechanism investigation have been carried out. Use of sodium sulphide has emerged as a rate accelerating catalyst in DMF-EtOH solvent system. Reaction intermediate for IMBH pathway was isolated and characterized. Other aspects such as application of IMBH adduct for Michael addition and amidation have also been carried out.

Introduction

Amongst the important methodologies discovered in the last few decades, Morita-Baylis-Hillman (MBH) reaction is considered to be one of the most useful C-C bond forming reaction.[1,2] It's an atom economy reaction which couples a Michael acceptor with an aldehyde or imine to give densely substituted molecules called as MBH adducts. With the close vicinity of functional groups, these MBH adducts have been further used for various synthetic transformation.[1c,2] Numerous applications for the development of novel methodologies,[3] including synthesis of various pharmacologically useful synthons[4] have been achieved owing to the synthetic utility of these MBH adducts. Consequently the reaction along with the application of it's adduct has gained huge popularity in the recent past. However, in spite of its enormous usefulness, the reaction has certain limitations. One of the main challenges lie in the sluggishness of reaction.[5] The reaction requires longer reaction time (usually in days). Even reaction time of weeks and month have also been reported on less reactive substrates.[6] The slow reaction rate not only hampers the development of reaction but also retards utilization of MBH adducts on real applicative scale.

Consisting of three distinct reactions in the mechanism, there is an overall reduction in rate of reaction (Figure 1). Initiated by a catalyst, mostly a neutral molecule, the reaction goes through sequences of Michael, Aldol and Elimination (Figure 1). Several approaches such as protic additives,[7] use of Lewis acid,[8] special catalysts,[9] and others[10] have been explored towards rate acceleration but the reaction still requires longer reaction time[11] and opens scope for improvement.

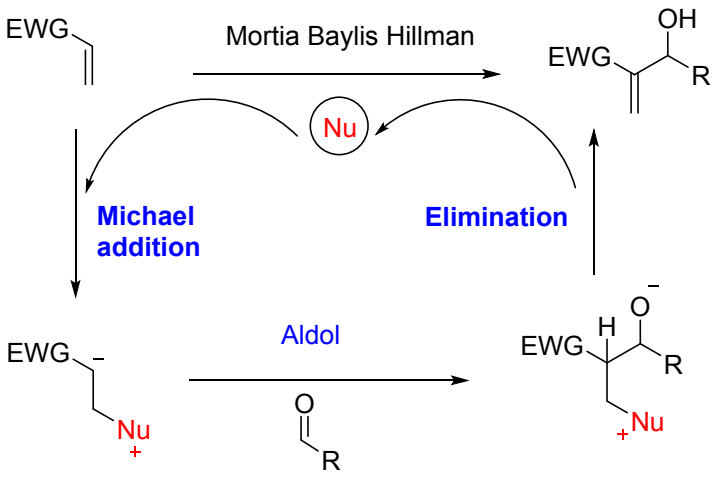
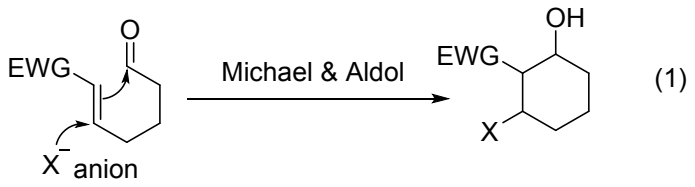


Figure 1. MBH reaction and the steps involved

Intramolecular MBH (IMBH) reaction is yet another important endeavor in this area which leads to construction of carbocyclic and heterocyclic frameworks.[12, 13] However these reactions too, in spite of having both reacting partners within close proximity, have been relatively beleaguered with slow reaction rate.[14] For example, to accelerate rate of IMBH reaction, reports of forcing conditions such as higher temperature,[15] use of microwave[16] and others[17] have been documented.

Since the initial Michael addition of MBH reaction is being carried out by a neutral molecule, rate acceleration can also be visualized by using anions, which could undergo fast Michael addition (Figure 1). However, use of such species or the ones having labile proton usually leads to stable Michael-Aldol adduct (eq. 1).[18, 19] The reagent after addition, fails to eliminate (a classic case of domino additions). Contrary, conventional neutral catalysts such as DABCO, DBU, phosphines and others are helpful for elimination from MBH perspective. They become positively charged after Michael addition and readily undergo required elimination in the last step. Thus, a balance of reactivity would be ideal where a charged anion would initially carry out quick Michael addition, but still would have facile elimination ability to expel and give final MBH adduct.[20] In continuation of our research interest for rate acceleration and IMBH reactions,[21] a catalyst system for an extremely fast IMBH reaction was discovered. The details are being disclosed in the present manuscript.

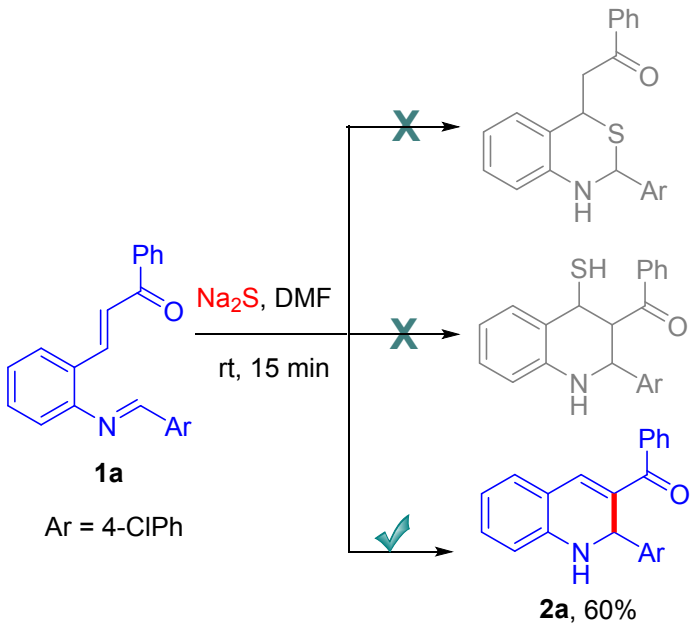


(1)

Result and Discussion

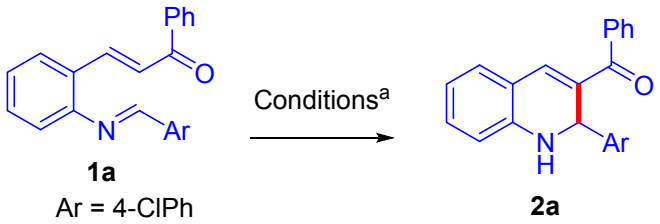
During the course of studies for annulation strategies, a template **1a** (Scheme 1) having dual electrophilic site was synthesized. Initially annulation reaction aimed towards the synthesis of thio-framework was investigated. Interestingly, when **1a** was treated with Na_2S in DMF, the desired thio-annulated product was not observed. Moreover, the tetrahydro-quinoline arising from tandem addition was also not seen. Interestingly an aza IMBH adduct **2a** was observed in a reaction time of as low as 15 minutes. The product being unstable was subsequently oxidized using DDQ to give Quinoline which was characterized by various spectroscopic data and confirmed with literature (vide infra). The results were promising as it lead to discovery of Na_2S as highly rate accelerating catalyst in the field of MBH reaction. Therefore the reaction was further investigated.

Scheme 1. Initial investigation of 1a with Na_2S.



To begin with, standardization of reaction was carried out (Table 1). Lowering of catalyst loading to 1 equivalent gave comparable yield of product (entry 2). Further reduction in loading of Na_2S (0.5 *equiv.*) led to 45 minutes reaction time and gave slightly lower yield (entry 3). Use of conventional catalysts such as TPP, DABCO and DBU did not give product even in 12 hours reaction time (entries 4-6). DBU upon prolonged reaction time of 96 hours gave only trace of product (entry 7). Other ionic sources were also explored for their ability to carry out IMBH reaction (entries 8-12). Iodide has been considered as good nucleophile. However, replacing Na_2S with NaI or TBAI didn't give any product. Use of thio-acetate in the form of CH_3COSK was also not helpful. Similarly, other reagents such as CH_3CO_2Na or $NaNO_2$ were ineffective. Thus, Na_2S was selected as choice of catalyst for further studies. Subsequently different solvents were screened (entries 13-16). Use of DCM, Toluene and Dioxane didn't give any product. Usage of EtOH was helpful and gave product in 52% yield, although in 3h (entry 16). In the light of results obtained from entries 2&16, use of mix solvents was investigated. Using DMF and EtOH in 1:1 ratio led to higher yield of IMBH adduct (86%, entry 17). Use of other protic solvents in place of EtOH such as MeOH and *t*-BuOH along with DMF gave inferior results (entries 18 &19). Thus 1 *equiv.* of Na_2S in DMF-EtOH mixture (1:1) at room temperature was identified as best reaction condition for optimal yield and reaction time (entry 17). With the best possible conditions in hand, the scope of the reaction was further explored on different substrates (Scheme 2).

Table 1. Development of aza IMBH reaction.



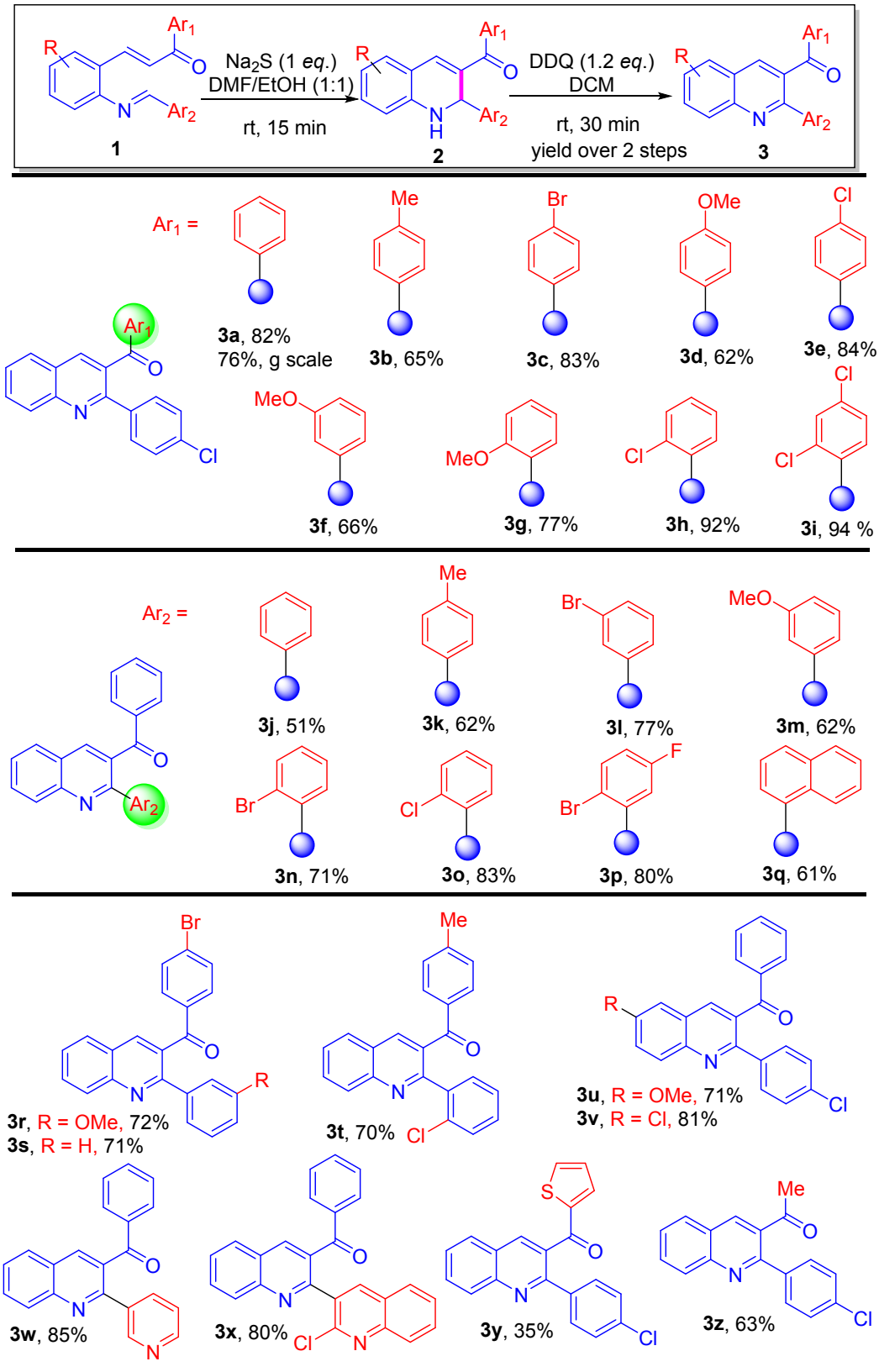
1a
Ar = 4-ClPh

2a

S. No.	Catalyst	Solvent	Time (h)	Yield[b] (%)
1[c]	Na_2S	DMF	0.25	60
2	Na_2S	DMF	0.25	56
3[d]	Na_2S	DMF	0.75	50
4	TPP	DMF	12	-
5	DABCO	DMF	12	-
6	DBU	DMF	12	-
7	DBU	DMF	96	trace
8	NaI	DMF	16	-
9	TBAI	DMF	16	-
10	CH_3COSK	DMF	16	-
11	CH_3CO_2Na	DMF	16	-
12	$NaNO_2$	DMF	16	-
13	Na_2S	DCM	16	-
14	Na_2S	Toluene	16	-
15	Na_2S	Dioxane	16	-
16	Na_2S	EtOH	3	52
17	**Na_2S**	**DMF/EtOH (1:1)**	**0.25**	**86**
18	Na_2S	DMF/MeOH (1:1)	0.25	50
19	Na_2S	DMF/^{t}BuOH (1:1)	3	30

(a) All reactions were carried out on 0.5 mmol scale of **1a** using 1.0 mL of solvent and 1.0 *equiv.* of catalyst at rt. (b) Isolated yield. (c) 2 *equiv.* of catalyst was used. (d) 0.5 *equiv.* of catalyst was used.

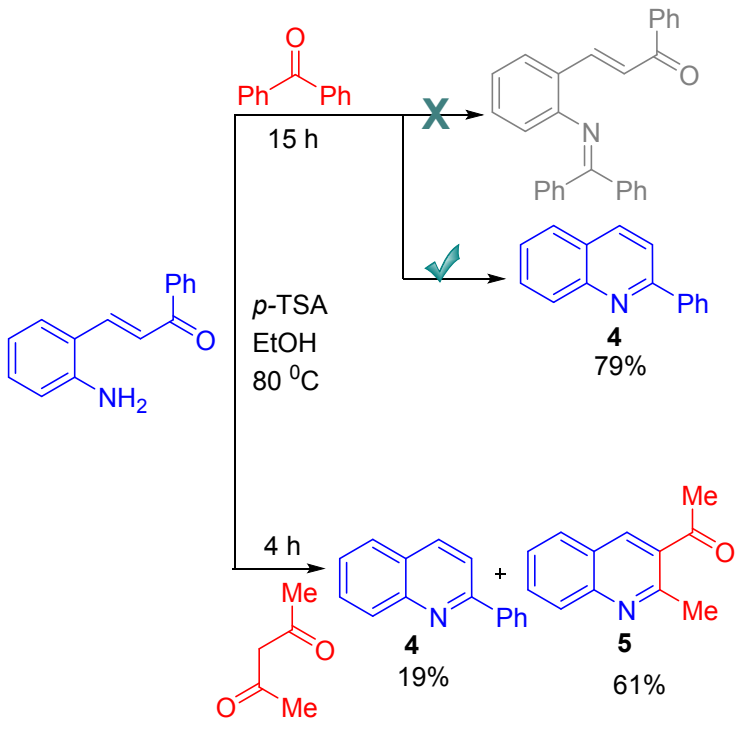
Scheme 2. Substrate scope for IMBH reaction.



A number of precursors were subjected to optimized reaction condition, delivering the required IMBH dihydro-quionline derivatives. The IMBH adduct being unstable were oxidized to quionline using DDQ in DCM. Quinoline framework is one of the most privileged skeleton and has attracted significant attention from synthetic chemist worldwide.[22]

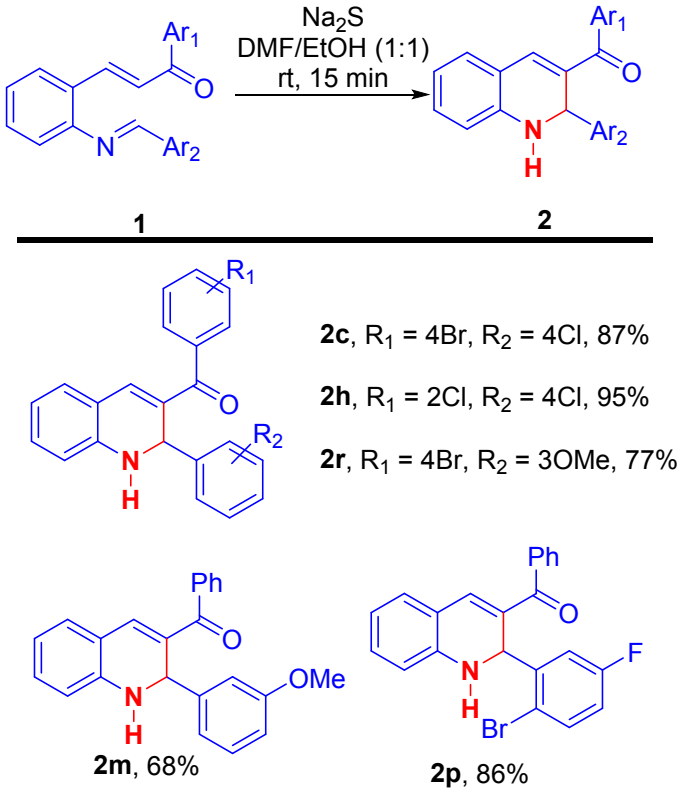
Initially variations across Michael acceptor were studied (Ar_1, **3a**-**3i**). The reaction was found to work well on different substitution positions such as *ortho*, *meta* and *para*. Furthermore, both electron releasing and electron withdrawing groups gave the required product in good yields. Thereafter variations were made across imine aryl group (Ar_2, **3j**[22b]-**3q**). Varying substitutions also included multi-substituted phenyl ring and biaryl-naphthyl moieties (**3p** & **3q**). Electron withdrawing substitution gave better yields then electron donating. Simultaneous variations were also carried out on precursor's framework (**3r**-**3t**[22b]). Subsequently variations were made across quionline ring. The required products (**3u**, **3v**) were obtained in event free manner. To broaden the reaction scope, precursors with heterocycle unit were also studied. Pyridine and quionline derived precursor gave good conversion to corresponding product (**3w** & **3x**). In case of thiophene derived precursor, lesser yield of IMBH adduct (**3y**) was observed. Reaction was also applicable to aliphatic ketone **3z**. A gram scale study was also done on **1a**. Thus investigating reaction on 3.0 mmol scale of **1a** (1.035 g) gave the product in **3a** 76% yield.

Scheme 3. Exploration for ketimines.



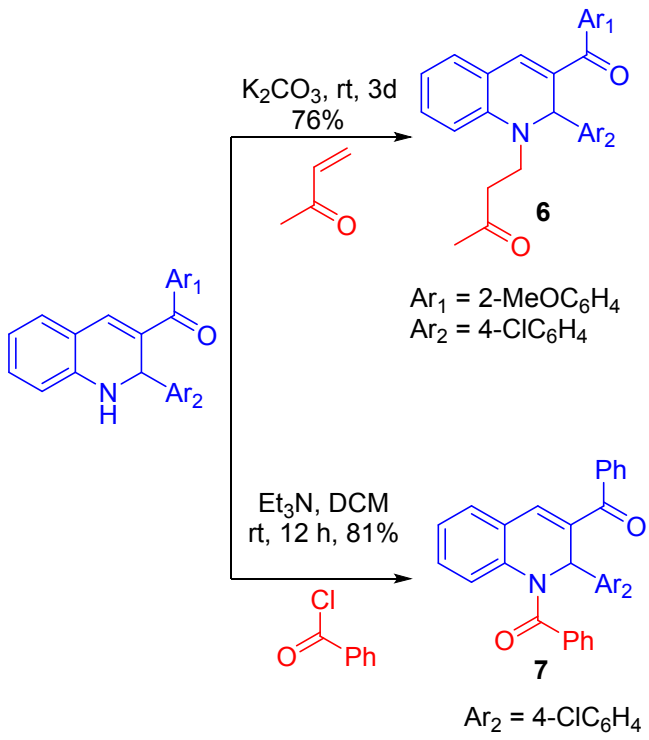
To broaden the generality of protocol, reaction scope was tried for ketimine derivatives (Scheme 3). However, required ketimine from benzophenone could not be prepared even under forcing conditions. Instead it resulted in the synthesis of 2-phenylquionline **4**.[21a] When acetyl acetone was used in place of benzophenone, a new kind of quionline precursor **5**[23] was obtained along with **4**. Formation of **5** could be explained *via* elimination of acetophenone group from the moiety.

Scheme 4. Isolable dihydroQuinoline

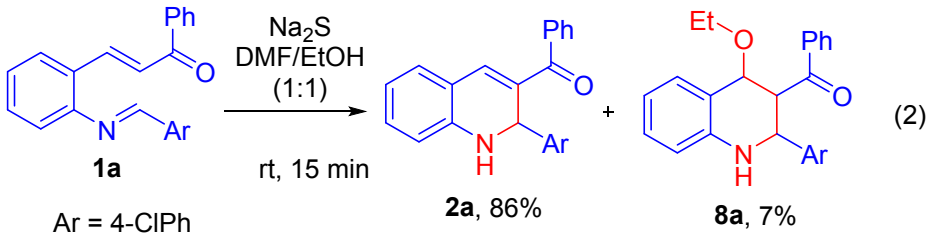


During the course of studies, it was observed that some dihydroquinoline were relatively more stable and were isolated and characterized (Scheme 4). This further confirmed IMBH reaction. Synthetic potential was further expanded by carrying out successful Michael addition of one of the dihydro precursor **2g**, using methyl vinyl ketone, to obtain **6** (Scheme 5). Similarly amidation of **2a** gave benzoyl adduct **7**.

Scheme 5. Application of IMBH adduct.

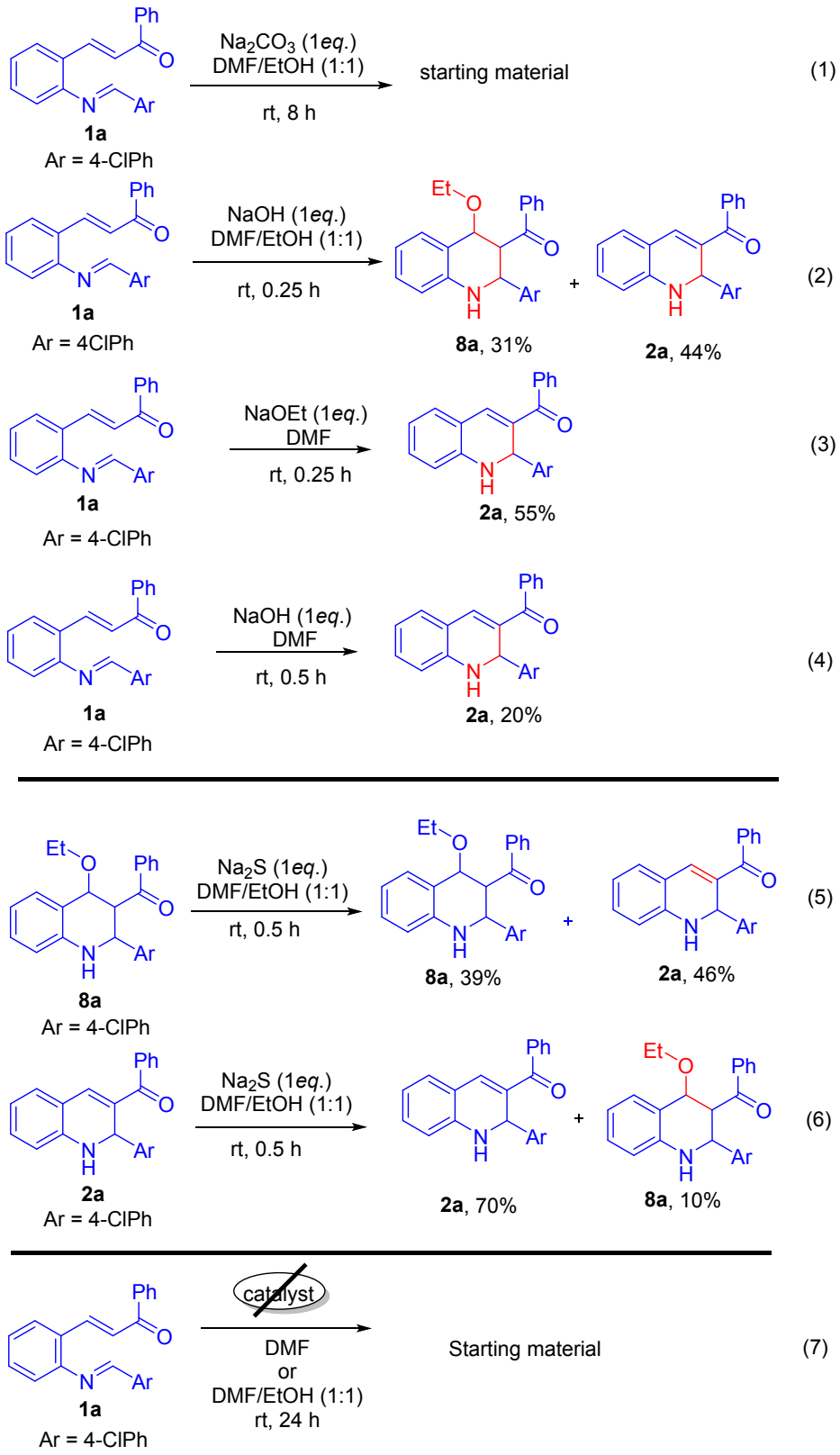


After exploring various aspects of the reaction, the mechanism of reaction was then studied. During the course of standardization and substrate scope evaluation, formation of tetrahydroquinoline (**8a**) was also observed (eq. 2). This resulted from ethoxide addition across enone, followed by ring closure. Therefore, the role of ethoxide anion (if any) in IMBH reaction was then studied.[24]



Initially role of NaOEt was evaluated in absence of Na_2S. Carrying out reaction in the presence of Na_2CO_3 (to generate NaOEt *insitu*), did not give any product and only starting material was observed (eq. 1, Scheme 6). Replacing Na_2CO_3 with a stronger base NaOH, in DMF-EtOH led to the formation of **8a** in 31% and **2a** in 44% yields (eq. 2, Scheme 6). Using NaOEt in DMF (in absence of EtOH) also led to the formation of **2a** in 55% yield (eq. 3, Scheme 6). Pleasingly these results highlighted the independent catalytic activity of NaOEt. However as mentioned earlier, (entries 1-3, table 1) Na_2S can also catalyze

Scheme 6. Mechanistic investigation of aza IMBH reaction.



independently IMBH reaction and was necessary to get higher yield of IMBH reaction (entry 17, table 1 Vs eq. 2 scheme 6). Using NaOH in DMF led to poor yields of 20% of IMBH adduct (eq. 4, Scheme 6). Subsequently inter-conversion of **2a** and **8a** was studied (eq. 5&6, Scheme 6). Towards this end **2a** and **8a** were independently subjected to optimized reaction conditions. As expected higher conversion of Michael adduct towards the IMBH adduct was observed then vice versa. Another possibility of 6π electrocyclization followed by 1,5-H shift, for the formation of **2a** was also investigated. Reactions carried out in absence of catalyst, either in DMF or in DMF-EtOH solvent system, didn't lead to any reaction (eq. 7, scheme 6). This, rules out the possibility of background 6π electrocyclization.

Conclusions

The above studies lead to discovery of Na_2S as a new and promising catalyst for IMBH reactions. Chemoselective nature of protocol was another added advantage. Extremely high rate acceleration observed for IMBH reaction was very encouraging. This can be helpful in developing other catalytic systems. Shorten reaction time could lead to quick access to IMBH adducts and can be further helpful in the application of IMBH adduct. Organic thiols, especially under deprotonative conditions can also be investigated. This opens up the possibility for use of chrial thiols and thus development of asymmetric versions. Further, catalytic activity of NaOEt was also encouraging. As mentioned in limited literature[24] and present studies, alkoxides could be another class of reagents for MBH reactions.

Experimental

General Remarks All the reactions were carried out using dry solvents and under inert atmosphere until unless mentioned. Room temperature (rt) stands for 20-25 ^{o}C. Column chromatography was performed using silica gel mesh 100-200. TLC Aluminium Sheets Silica Gel 60 F254 was used for TLC. Melting Points were recorded on a Perfit (India) capillary melting point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin Elmer FT-IR spectrometer Spectrum Two. ^{1}H NMR and ^{13}C NMR were recorded on a Jeol 500 MHz and 125 MHz spectrometer respectively. HRMS spectra were recorded on Bruker Daltonics MicroTOF-Q-II with electron spray ionization (ESI).

Representative procedures

(2*E*)-3-((*E*)-2-(4-chlorobenzylideneamino)phenyl)-1-phenylprop-2-en-1-one (1a);[18c] To a solution of amine[21a] (*E*)-3-(2-aminophenyl)-1-phenylprop-2-en-1-one (0.446 g, 2.0 mmol) in EtOH (8.0 mL) was added 4-chlorobenzaldehyde (0.286 g, 2.04 mmol) and the reaction was stirred for 12h at rt during

which the imine precipitated. The reaction mixture was cooled to 0 °C and filtered to afford the required Schiff base **1a** (0.6 g). The filtrate was further evaporated and filtered to yield additional 0.042 g of **1a**. The combined **1a** (0.642 g, 93%) was dried and used as such for next step.

(2-(4-chlorophenyl)-1,2-dihydroquinolin-3-yl)(phenyl)methanone (2a); To a suspension of **1a** (0.172 g, 0.5 mmol) in DMF-EtOH (0.5 mL each), was added crushed Na_2S (60%) (0.065 g, 0.5 mmol) and the reaction was stirred for 15 minutes at rt, leading to a red colored solution. Water was added to it and aqueous phase was extracted with EtOAc. Organic layer was dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by a short column chromatography (EtOAc:hexane, 15:85), to obtain **2a** (0.148 g) in 86% yield. **2a** was used immediately for next step.

(2-(4-chlorophenyl)quinolin-3-yl)(phenyl)methanone (3a); To a solution of **2a** (0.148 g, 0.43 mmol) in DCM (1.2 mL) was added DDQ (0.116 g, 0.51 mmol) and the reaction was stirred at rt, for 30 minutes. DCM was added to reaction mixture and organic layer was washed with $NaHCO_3$ solution. Organic layer was dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by column chromatography (EtOAc:hexane, 1:9), to obtain **3a** (0.139 g) in 82% yield over two steps.

Gram scale synthesis of 2-(4-chlorophenyl)quinolin-3-yl)(phenyl)methanone (3a); To a suspension of **1a** (1.035 g, 3.0 mmol) in DMF-EtOH (3.0 mL each), was added crushed Na_2S (60%) (0.39 g, 3.0 mmol) and the reaction was stirred at rt for 15 minutes, leading to a red colored solution. Water was added to it and aqueous phase was extracted with EtOAc. Organic layer was dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by a short column chromatography (EtOAc:hexane, 15:85), to obtain **2a** (0.849 g) in 82% yield. **2a** was used immediately for next step. To a solution of **2a** (0.849 g, 2.5 mmol) in DCM (7.0 mL) was added DDQ (0.67 g, 2.9 mmol) and the reaction was stirred at rt, for 30 minutes. DCM was added to reaction mixture and organic layer was washed with $NaHCO_3$ solution. Organic layer was dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by column chromatography (EtOAc:hexane, 1:9), to obtain **3a** (0.78 g) in 76% yield over two steps.

4-(2-(4-chlorophenyl)-3-(2-methoxybenzoyl)quinolin-1(2H)-yl)butan-2-one (6); To a solution of **2g** (0.100 g, 0.27 mmol) in MVK (0.5 mL) was added K_2CO_3 (0.37 g, 0.27 mmol) and the reaction was stirred for 3 days at rt. The reaction mixture was filtered and concentrated. The residue obtained was purified by column chromatography (EtOAc:hexane, 15:85), to yield **6** (0.09 g) as orange solid in 76% yield.

(2-(4-chlorophenyl)quinoline-1,3(2*H*)-diyl)bis(phenylmethanone) (7); To a solution of **2a** (0.103 g, 0.3 mmol) in DCM was added Et_3N (0.06 mL, 0.41 mmol) and PhCOCl (0.04 mL, 0.36 mmol) at 0 °C and the reaction mixture was stirred for 12h at rt. Subsequently DCM was added and organic phase was washed with $NaHCO_3$ solution. Organic layer was dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by column chromatography (EtOAc:hexane, 1:5), to obtain **7** (0.108 g) in 81% yield.

(2-(4-chlorophenyl)quinolin-3-yl)(phenyl)methanone (3a); Yield: 0.139 g, 82%; White solid; mp: 152-156 °C; IR (KBr): ν 1656 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.27-7.29 (m, 2H) 7.36-7.39 (m, 2H), 7.53 (app t, *J* = 7.5 Hz, 1H), 7.57-7.58 (m, 2H), 7.64 (app t, *J* = 7.5 Hz, 1H), 7.73-7.75 (m, 2H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.34 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.9, 127.6, 128.2, 128.65, 128.72, 129.7, 130.1, 130.6, 131.5, 132.6, 133.7, 135.2, 136.9, 137.8, 138.2, 148.4, 156.2, 196.8; HRMS (ESI): calculated for $C_{22}H_{15}ClNO$, 344.0842 $(M+H)^+$, found: 344.0855.

(2-(4-chlorophenyl)quinolin-3-yl)(*p*-tolyl)methanone (3b); Yield: 0.116 g, 65%; White solid; mp: 168-170 °C; IR (KBr): ν 1271, 1603, 1655 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.38 (s, 3H), 7.17-7.18 (m, 2H) 7.27-7.29 (m, 2H), 7.58-7.66 (m, 5H), 7.83 (app t, *J* = 7.5 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.29 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 21.8, 125.9, 127.5, 128.1, 128.7, 129.4, 129.7, 130.3, 130.6, 131.3, 132.8, 134.4, 135.2, 137.5, 138.3, 144.8, 148.3. 156.2, 196.4; HRMS (ESI): calculated for $C_{23}H_{17}ClNO$, 358.0999 $(M+H)^+$, found: 358.0991.

(4-bromophenyl)(2-(4-chlorophenyl)quinolin-3-yl)methanone (3c); Yield: 0.174 g, 83%; White solid; mp: 172-174 °C; IR (KBr): ν 1583, 1656 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.28-7.30 (m, 2H), 7.49-7.51 (m, 2H), 7.55-7.59 (m, 4H), 7.64 (app t, *J* = 7.5 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.32 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.8, 127.7, 128.2, 128.8, 129.1, 129.7, 130.6, 131.4, 131.6, 132.0, 132.1, 135.4, 135.7, 137.8, 138.1, 148.4, 155.9, 195.8; HRMS (ESI): calculated for $C_{22}H_{14}BrClNO$, 421.9947 $(M+H)^+$, found: 421.9941.

(2-(4-chlorophenyl)quinolin-3-yl)(4-methoxyphenyl)methanone (3d); Yield: 0.116 g, 62%; White solid; mp: 148-150 °C; IR (KBr): ν 1169, 1257, 1599, 1653 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.84-6.86 (m, 2H), 7.28-7.30 (m, 2H), 7.60-7.64 (m, 3H), 7.72-7.74 (m, 2H), 7.83 (app t, *J* = 7.5 Hz, 1H), 7.89 (d, *J*= 8.0 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.29 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.6, 114.0, 125.9, 127.5, 128.1, 128.7, 129.7, 129.9, 130.6, 131.2, 132.6, 133.0, 135.2, 137.3, 138.3, 148.3, 156.1, 164.1, 195.3; HRMS (ESI): calculated for $C_{23}H_{17}ClNO_2$, 374.0948 $(M+H)^+$, found: 374.0938.

(4-chlorophenyl)(2-(4-chlorophenyl)quinolin-3-yl)methanone (3e); Yield: 0.158 g, 84%; White solid; mp: 174-178 °C; IR (KBr): ν 1584, 1663 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.28-7.30 (m, 2H), 7.32-7.34 (m, 2H), 7.55-7.57 (m, 2H), 7.62-7.66 (m, 3H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.32 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.8, 127.7, 128.2, 128.8, 129.0, 129.7, 130.6, 131.3, 131.6, 132.1, 135.2, 135.4, 137.8, 138.1, 140.3, 148.4, 155.9, 195.6; HRMS (ESI): calculated for $C_{22}H_{14}Cl_2NO$, 378.0452 $(M+H)^+$, found: 378.0443.

(2-(4-chlorophenyl)quinolin-3-yl)(3-methoxyphenyl)methanone (3f); Yield: 0.123 g, 66%; White solid; mp: 166-170 °C; IR (KBr): ν 1594, 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.81 (s, 3H), 7.09 (d app t, *J* = 7.5, 2.0 Hz, 1H), 7.24-7.27 (m, 2H), 7.29-7.30 (m, 2H), 7.35 (s, 1H), 7.57-7.59 (m, 2H), 7.63 (app t, *J* = 7.5 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.32 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.5, 113.8, 120.4, 123.3, 125.8, 127.6, 128.2, 128.7, 129.6, 129.7, 130.6, 131.4, 132.6, 135.2, 137.7, 138.2, 148.3, 156.2, 159.8, 196.5; HRMS (ESI): calculated for $C_{23}H_{17}ClNO_2$, 374.0948 $(M+H)^+$, found: 374.0942.

(2-(4-chlorophenyl)quinolin-3-yl)(2-methoxyphenyl)methanone (3g); Yield: 0.144 g, 77%; White solid; mp: 172-176 °C; IR (KBr): ν 1253, 1483, 1655 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.53 (s, 3H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.95 (app t, *J*= 7.5 Hz, 1H), 7.24-7.26 (m, 2H), 7.41 (d app t, *J* = 8.5, 2.0 Hz, 1H), 7.54-7.61 (m, 4H), 7.81 (d app t, *J* = 8.0, 2.0 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.32 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.4, 111.4, 120.7, 126.2, 127.2, 127.5, 128.2, 128.4, 129.5, 130.8, 131.1, 131.5, 134.4, 134.8, 135.2, 137.1, 138.4, 148.1, 156.5, 158.4, 195.9; HRMS (ESI): calculated for $C_{23}H_{17}ClNO_2$, 374.0948 $(M+H)^+$, found: 374.0939.

(2-chlorophenyl)(2-(4-chlorophenyl)quinolin-3-yl)methanone (3h); Yield: 0.173 g, 92%; Light yellow solid; mp: 144-148 °C; IR (KBr): ν 1680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.19 (d app t, *J* = 8.0, 1.5 Hz, 1H), 7.27-7.29 (m, 3H), 7.31 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52-7.54 (m, 2H), 7.63 (app t, *J* = 7.5 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.46 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 126.2, 126.7, 127.6, 128.5, 128.7, 129.7, 130.7, 130.8, 131.5, 132.0, 132.7, 132.78, 132.85, 135.0, 137.3, 138.3, 139.4, 148.6, 156.9, 195.3; HRMS (ESI): calculated for $C_{22}H_{14}Cl_2NO$ 378.0452 $(M+H)^+$, found: 378.0445.

(2,4-dichlorophenyl)(2-(4-chlorophenyl)quinolin-3-yl)methanone (3i); Yield: 0.193 g, 94%; White solid; mp: 126-128 °C; IR (KBr): ν 1583, 1677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.17 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.29-7.32 (m, 4H), 7.51-7.53 (m, 2H), 7.65 (app t, *J* = 7.5 Hz, 1H), 7.87 (app t, *J* = 7.5 Hz, 1H), 7.94 (d, *J* =

8.0 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.46 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 126.1, 127.1, 127.7, 128.6, 128.7, 129.7, 130.7, 132.2, 132.4, 133.8, 135.3, 135.7, 138.2, 138.5, 139.4, 148.7, 156.6, 194.3; HRMS (ESI): calculated for $C_{22}H_{13}Cl_3NO$ 412.0063 $(M+H)^+$, found: 412.0058.

phenyl(2-phenylquinolin-3-yl)methanone (3j);[22b] Yield: 0.079 g, 51%; White solid; mp: 128-130 °C; IR (KBr): ν 1657 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.28-7.35 (m, 5H), 7.48 (app t, *J* = 7.5 Hz, 1H), 7.61-7.64 (m, 3H), 7.71-7.73 (m, 2H), 7.84 (app t, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.35 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.9, 127.4, 128.2, 128.47, 128.49, 128.9, 129.3, 129.7, 130.1, 131.3, 132.9, 133.4, 137.1, 137.7, 139.8, 148.4, 157.6, 197.1; HRMS (ESI): calculated for $C_{22}H_{16}NO$, 310.1232 $(M+H)^+$, found: 310.1225.

phenyl(2-*p*-tolylquinolin-3-yl)methanone (3k); Yield: 0.100 g, 62%; White solid; mp: 138-142 °C; IR (KBr): ν 1273, 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.28 (s, 3H), 7.09-7.10 (m, 2H), 7.33-7.36 (m, 2H), 7.48-7.53 (m, 3H), 7.60 (app t, *J* = 7.5 Hz, 1H), 7.74-7.75 (m, 2H), 7.83 (app t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.30 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 21.3, 125.7, 127.2, 128.1, 128.5, 129.2, 129.7, 130.1, 131.2, 132.9, 133.4, 136.9, 137.1, 137.5, 138.9, 148.4, 157.6, 197.1; HRMS (ESI): calculated for $C_{23}H_{18}NO$ 324.1388 $(M+H)^+$, found: 324.1379.

(2-(3-bromophenyl)quinolin-3-yl)(phenyl)methanone (3l); Yield: 0.149 g, 77%; Light brown solid; mp: 140-142 °C; IR (KBr): ν 1661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.12 (app t, *J* = 8.0 Hz, 1H), 7.35-7.40 (m, 3H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.51 (app t, *J* = 7.0 Hz, 1H), 7.65 (app t, *J* = 7.5 Hz, 1H), 7.71-7.72 (m, 2H), 7.85-7.88 (m, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.37 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 122.7, 126.0, 127.7, 127.9, 128.2, 128.6, 129.7, 129.8, 129.9, 131.5, 131.8, 132.3, 132.6, 133.6, 137.0, 138.0, 141.7, 148.3, 155.8, 196.6; HRMS (ESI): calculated for $C_{22}H_{15}{}^{81}BrNO$, 390.0317 $(M+H)^+$, found: 390.0325.

(2-(3-methoxyphenyl)quinolin-3-yl)(phenyl)methanone (3m); Yield: 0.105 g, 62%; White solid; mp: 112-114 °C; IR (KBr): ν 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.74 (s, 3H), 6.81 (d, *J* = 7.5 Hz, 1H), 7.16-7.21 (m, 3H), 7.33-7.36 (m, 2H), 7.48 (app t, *J* = 7.0 Hz, 1H), 7.63 (app t, *J* = 7.5 Hz, 1H), 7.72-7.73 (m, 2H), 7.84 (app t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.34 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.3, 114.2, 115.3, 121.9, 125.9, 127.4, 128.1, 128.4, 129.5, 129.7, 129.9, 131.2, 132.9, 133.4, 137.0, 137.5, 141.0, 148.3, 157.2, 159.6, 196.9; HRMS (ESI): calculated for $C_{23}H_{18}NO_2$, 340.1338 $(M+H)^+$, found: 340.1337.

(2-(2-bromophenyl)quinolin-3-yl)(phenyl)methanone (3n); Yield: 0.137 g, 71%; White solid; mp: 100-102 °C; IR (KBr): ν 1265, 1657 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.19 (app t, *J* = 7.5 Hz, 1H), 7.36 (app t, *J* = 7.5 Hz, 1H), 7.40-7.43 (m, 2H), 7.48-7.51 (m, 2H), 7.55 (app t, *J* = 7.0 Hz, 1H), 7.67 (app t, *J* = 7.5 Hz, 1H), 7.80-7.82 (m, 2H), 7.87 (app t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.40 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 122.1, 125.9, 127.4, 127.8, 128.37, 128.44, 129.7, 129.9, 130.4, 131.6, 131.7, 132.3, 132.7, 133.2, 136.9, 138.3, 140.7, 148.1, 157.8, 195.3; HRMS (ESI): calculated for $C_{22}H_{15}{}^{81}BrNO$, : 390.0317 $(M+H)^+$, found: 390.0313.

(2-(2-chlorophenyl)quinolin-3-yl)(phenyl)methanone (3o); Yield: 0.142 g, 83%; White solid; mp: 112-114 °C; IR (KBr): ν 1657, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.25-7.30 (m, 2H), 7.33 (d app t, *J* = 7.5, 1.5 Hz, 1H), 7.40-7.43 (m, 2H), 7.53-7.56 (m, 2H), 7.66 (app t, *J* = 7.0 Hz, 1H), 7.80-7.81 (m, 2H), 7.86 (d app t, *J* = 8.5, 1.5 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.38 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.9, 127.0, 127.8, 128.39, 128.45, 129.5, 129.76, 129.83, 130.3, 131.62, 131.63, 132.2, 132.6, 133.2, 136.9, 138.2, 138.9, 148.2, 156.6, 195.3; HRMS (ESI): calculated for $C_{22}H_{15}ClNO$, : 344.0842 $(M+H)^+$, found: 344.0837.

(2-(2-bromo-5-fluorophenyl)quinolin-3-yl)(phenyl)methanone (3p); Yield: 0.162 g, 80%; White solid; mp: 140-144 °C; IR (KBr): ν 1260, 1654 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.94 (d app t, *J* = 8.0, 3.0 Hz, 1H), 7.27 (dd, *J* = 8.5, 3.0 Hz, 1H), 7.44-7.47 (m, 3H), 7.58 (app t, *J* = 7.0 Hz, 1H), 7.69 (app t, *J* = 7.5 Hz, 1H), 7.83-7.84 (m, 2H), 7.89 (d app t, *J* = 7.5, 1.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.41 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 116.3 (d, *J* = 3.1 Hz), 117.1 (d, *J* = 22.5 Hz), 118.8 (d, *J* = 23.8 Hz), 126.0, 128.1, 128.47, 128.52, 129.7, 130.4, 131.87, 131.92, 133.3, 133.9 (d, *J* = 8.0 Hz), 136.7, 138.7, 142.6 (d, *J* = 7.9 Hz), 148.0, 156.9, 161.8 (d, *J* = 246.6 Hz), 194.9; HRMS (ESI): calculated for $C_{22}H_{14}{}^{81}BrFNO$, 408.0222 $(M+H)^+$, found: 408.0217.

(2-(naphthalen-1-yl)quinolin-3-yl)(phenyl)methanone (3q); Yield: 0.109 g, 61%; White solid; mp: 130-132 °C; IR (KBr): ν 1257, 1651 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.07-7.10 (m, 2H), 7.26 (app t, *J* = 7.0 Hz, 1H), 7.33 (app t, *J* = 7.5 Hz, 1H), 7.39-7.44 (m, 3H), 7.48-7.49 (m, 2H), 7.67-7.71 (m, 2H), 7.74-7.75 (m, 1H), 7.88 (d app t, *J* = 7.5, 1.5 Hz, 1H), 7.91-7.92 (m, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.50 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 124.9, 125.7, 125.9, 126.1, 126.6, 127.6, 127.9, 128.2, 128.4, 129.2, 129.3, 129.8, 131.5, 131.6, 132.8, 133.7, 134.5, 137.1, 137.2, 137.7, 148.3, 157.5, 196.6; HRMS (ESI): calculated for 360.1388 $C_{26}H_{18}NO$, $(M+H)^+$, found: 360.1386.

(4-bromophenyl)(2-(3-methoxyphenyl)quinolin-3-yl)methanone (3r); Yield: 0.150 g, 72%; White solid; mp: 164-168 °C; IR (KBr): ν 1581, 1662, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.77 (s, 3H), 6.83 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.17-7.20 (m, 2H), 7.45-7.47 (m, 2H), 7.55-7.56 (m, 2H), 7.63 (app t, *J* = 7.5 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.915 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.34 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.3, 114.3, 115.3, 121.9, 125.9, 127.5, 128.2, 128.7, 129.6, 129.7, 131.3, 131.4, 131.8, 132.4, 135.8, 137.7, 140.9, 148.4, 157.0, 159.7, 196.0; HRMS (ESI): calculated for $C_{23}H_{17}BrNO_2$, 418.0443 $(M+H)^+$, found: 418.0455.

(4-bromophenyl)(2-phenylquinolin-3-yl)methanone (3s); Yield: 0.137 g, 71%; White solid; mp: 180-184 °C; IR (KBr): ν 1583, 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.29-7.32 (m, 3H), 7.44-7.46 (m, 2H), 7.54-7.56 (m, 2H), 7.59-7.61 (m, 2H), 7.63 (app t, *J* = 7.5 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.35 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.8, 127.5, 128.2, 128.6, 128.7, 129.1, 129.3, 129.8, 131.4, 131.5, 131.8, 132.4, 135.8, 137.8, 139.6, 148.5, 157.3, 196.1; HRMS (ESI): calculated for $C_{22}H_{15}BrNO$, 388.0337 $(M+H)^+$, found: 388.0342.

(2-(2-chlorophenyl)quinolin-3-yl)(*p*-tolyl)methanone (3t);[22b] Yield: 0.125 g, 70%; White solid; mp: 170-174 °C; IR (KBr): ν 1654 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.41 (s, 3H), 7.22-7.23 (m, 2H), 7.27-7.31 (m, 2H), 7.34 (d app t, *J* = 7.0, 1.5 Hz, 1H), 7.55 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.65 (app t, *J* = 7.0 Hz, 1H), 7.72-7.74 (m, 2H), 7.86 (d app t, *J* = 7.0, 1.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.35 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 21.8, 125.9, 127.0, 127.8, 128.4, 129.1, 129.5, 129.75, 129.79, 130.6, 131.5, 131.6, 132.2, 132.8, 134.3, 138.0, 139.0, 144.2, 148.1, 156.6, 194.9; HRMS (ESI): calculated for $C_{23}H_{17}ClNO$, 358.0999 $(M+H)^+$, found: 358.0996.

(2-(4-chlorophenyl)-6-methoxyquinolin-3-yl)(phenyl)methanone (3u); Yield: 0.132 g, 71%; White solid; mp: 190-194 °C; IR (KBr): ν 1226, 1661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 3H), 7.14 (d, *J* = 3.0 Hz, 1H), 7.25-7.26 (m, 2H), 7.35-7.38 (m, 2H), 7.48-7.51 (m, 2H), 7.53-7.56 (m, 2H), 7.72-7.73 (m, 2H), 8.11 (d, *J* = 9.5 Hz, 1H), 8.21 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 55.7, 105.2, 124.4, 127.0, 128.58, 128.61, 130.0, 130.5, 131.1, 132.8, 133.6, 134.8, 136.4, 136.9, 138.3, 144.5, 153.7, 158.6, 197.0; HRMS (ESI): calculated for $C_{23}H_{17}ClNO_2$, 374.0948 $(M+H)^+$, found: 374.0958.

(6-chloro-2-(4-chlorophenyl)quinolin-3-yl)(phenyl)methanone (3v); Yield: 0.153 g, 81%; White solid; mp: 204-208 °C; IR (KBr): ν 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.26-7.28 (m, 2H), 7.36-7.39 (m, 2H), 7.52-7.57 (m, 3H), 7.71-7.73 (m, 2H), 7.77 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.88 (d, *J* = 1.5 Hz, 1H), 8.16 (d, *J* = 9.5 Hz, 1H), 8.23 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 126.5, 126.7, 128.7, 128.8, 130.1, 130.6, 131.3,

132.3, 133.39, 133.43, 133.9, 135.4, 136.6, 136.7, 137.8, 146.7, 156.4, 196.4; HRMS (ESI): calculated for $C_{22}H_{14}Cl_2NO$, 378.0452 $(M+H)^+$, found: 378.0445.

phenyl(2-(pyridin-3-yl)quinolin-3-yl)methanone (3w); Yield: 0.132 g, 85%; Colorless solid; mp: 138-140 ^oC; IR (KBr): ν 1662 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.25 (dd, *J* = 8.0, 5.0 Hz, 1H), 7.37-7.40 (m, 2H), 7.53 (app t, *J* = 7.5 Hz, 1H), 7.66 (app t. *J* = 7.5 Hz, 1H), 7.76-7.77 (m, 2H), 7.88 (app t, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.96 (appt d, *J* = 7.5, 1.5 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.39 (s, 1H), 8.525 (d, *J* = 5.0 Hz, 1H), 8.85 (d, *J* = 1.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 123.2, 125.9, 127.9, 128.3, 128.7, 129.8, 130.2, 131.7, 132.6, 133.8, 135.5, 136.5, 136.9, 138.0, 148.5, 149.8, 150.1, 154.6, 196.4; HRMS (ESI): calculated for $C_{21}H_{15}N_2O$, 311.1184 $(M+H)^+$, found: 311.1174.

(2'-chloro-[2,3'-biquinolin]-3-yl)(phenyl)methanone (3x); Yield: 0.158 g, 80%; Light brown solid; mp: 100-104 ^oC; IR (KBr): ν 1660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.44-7.47 (m, 2H), 7.57-7.60 (m, 2H), 7.71 (app t, *J* = 7.5 Hz, 1H), 7.75 (app t, *J* = 7.5 Hz, 1H), 7.86-7.87 (m, 2H), 7.89-7.93 (m, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 8.43 (s, 1H), 8.45 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 126.0, 127.2, 127.3, 128.1, 128.3, 128.4, 128.6, 129.8, 130.5, 130.9, 132.07, 132.14, 133.46, 133.48, 136.6, 138.8, 140.1, 147.5, 148.1, 148.3, 155.3, 195.1; HRMS (ESI): calculated for $C_{25}H_{16}ClN_2O$, 395.0951 $(M+H)^+$, found: 395.0960.

(2-(4-chlorophenyl)quinolin-3-yl)(thiophen-2-yl)methanone (3y); Yield: 0.061 g, 35%; White solid; mp: 168-172 ^oC; IR (KBr): ν 1581, 1662 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.04 (app t, *J* = 4.5 Hz, 1H), 7.33-7.34 (m, 2H), 7.37 (d, *J* = 3.5 Hz, 1H), 7.62-7.65 (m, 3H), 7.705 (d, *J* = 5.0 Hz, 1H), 7.85 (app t, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.40 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 125.8, 127.7, 128.2, 128.4, 128.8, 129.7, 130.6, 131.5, 132.4, 135.3, 135.6, 135.8, 137.4, 138.1, 144.2, 148.4, 155.8, 188.6; HRMS (ESI): calculated for $C_{20}H_{13}ClNOS$, 350.0406 $(M+H)^+$, found: 350.0415.

1-(2-(4-chlorophenyl)quinolin-3-yl)ethan-1-one (3z); Yield: 0.088 g, 63%; colorless viscous liquid; IR: 1692 ν cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.25 (s, 3H), 7.49-7.50 (m, 2H), 7.61-7.64 (m, 3H), 7.83 (app t, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.39 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 30.5, 126.2, 127.6, 128.5, 129.2, 129.6, 130.5, 131.7, 134.5, 135.7, 137.2, 138.8, 148.3, 155.7, 202.6; HRMS (ESI): calculated for $C_{17}H_{13}ClNO$, 282.0686 $(M+H)^+$, found: 282.0632.

(4-bromophenyl)(2-(4-chlorophenyl)-1,2-dihydroquinolin-3-yl)methanone (2c); Yield: 0.184 g, 87%; Red solid; mp: 174-176 ^oC; IR (KBr): ν 1619, 2928, 3366 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.56 (s, 1H), 5.91 (d, *J* = 2.0 Hz, 1H), 6.49 (d, *J* = 8.0 Hz, 1H), 6.64 (app t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 7.11 (s, 1H),

7.14 (app t, *J* = 8.5 Hz, 1H), 7.22-7.24 (m, 2H), 7.35-7.36 (m, 2H), 7.46-7.47 (m, 2H), 7.57-7.58 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 54.3, 113.4, 117.6, 118.1, 126.5, 127.6, 129.0, 130.3, 130.5, 131.1, 131.7, 133.2, 133.7, 137.2, 138.8, 143.1, 144.6, 193.9; HRMS (ESI): calculated for $C_{22}H_{16}{}^{81}BrClNO$, 426.0083 $(M+H)^+$, found: 426.0067.

(2-chlorophenyl)(2-(4-chlorophenyl)-1,2-dihydroquinolin-3-yl)methanone (2h); Yield: 0.180 g, 95%; Yellow solid; mp: 140-144 °C; IR (KBr): ν 1617, 3394 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.65 (s, 1H), 5.91 (d, *J* = 1.0 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.60 (app t, *J* = 7.0 Hz, 1H), 6.94-6.96 (m, 2H), 7.12 (app t, *J* = 7.5 Hz, 1H), 7.195 (d, *J* = 8.0 Hz, 1H), 7.23-7.25 (m, 2H), 7.30 (d app t, *J* = 7.5, 1.5 Hz, 1H), 7.36-7.42 (m, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 53.5, 113.5, 117.6, 118.0, 126.6, 127.8, 128.77, 128.84, 130.1, 130.6, 130.7, 131.2, 131.3, 133.5, 133.6, 138.4, 140.7, 142.9, 144.9, 193.4; HRMS (ESI): calculated for $C_{22}H_{16}Cl_2NO$, 380.0609 $(M+H)^+$, found: 380.0589.

(2-(3-methoxyphenyl)-1,2-dihydroquinolin-3-yl)(phenyl)methanone (2m); Yield: 0.116 g, 68%; Yellow solid; mp: 150-154 °C; IR (KBr): ν 1607, 3293 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.73 (s, 3H), 4.58 (s, 1H), 5.95 (s, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 6.60 (app t, *J* = 7.5 Hz, 1H), 6.77 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.98-7.00 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 7.10 (app t, *J* = 7.5 Hz, 1H), 7.13 (s, 1H), 7.19 (app t, *J* = 7.5 Hz, 1H), 7.41-7.44 (m, 2H), 7.52 (app t, *J* = 7.0 Hz, 1H), 7.61-7.63 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 54.6, 55.2, 112.0, 113.0, 113.2, 117.7, 117.9, 118.6, 128.3, 128.9, 129.8, 130.1, 131.5, 131.6, 132.7, 138.5, 138.6, 144.7, 146.3, 159.8, 195.2; HRMS (ESI): calculated for $C_{23}H_{20}NO_2$, 342.1494 $(M+H)^+$, found: 342.1496.

(2-(2-bromo-5-fluorophenyl)-1,2-dihydroquinolin-3-yl)(phenyl)methanone (2p); Yield: 0.175 g, 86%; Yellow solid; mp: 144-146 °C; IR (KBr): ν 1626, 3413 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.98 (s, 1H), 6.19 (s, 1H), 6.45 (d, *J* = 8.0 Hz, 1H), 6.65 (app t, *J* = 7.5 Hz, 1H), 6.835 (d app t, *J* = 7.5, 3.0 Hz, 1H), 7.03 (dd, *J* = 9.0 , 2.5 Hz, 1H), 7.07-7.12 (m, 2H), 7.47-7.58 (m, 5H), 7.69-7.71 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 53.6, 114.1, 115.9 (d, *J* = 23.4 Hz), 116.6 (d, *J* = 22.6 Hz), 118.2, 118.4, 128.5, 129.0, 129.2, 130.3, 131.7, 133.0, 134.5 (d, *J* = 7.6 Hz), 138.1, 141.2, 143.2 (d, *J* = 5.3 Hz), 143.8, 162.5 (d, *J* = 246.1 Hz), 194.1; HRMS (ESI): calculated for $C_{22}H_{16}{}^{81}BrFNO$, 410.0379 $(M+H)^+$, found: 410.0381.

(4-bromophenyl)(2-(3-methoxyphenyl)-1,2-dihydroquinolin-3-yl)methanone (2r); Yield: 0.161 g, 77%; Red solid; mp: 104-108 °C; IR (KBr): ν 1617, 3360 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.73 (s, 3H), 4.59 (s, 1H), 5.92 (d, *J* = 1.0 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 6.62 (app t, *J* = 7.5 Hz, 1H), 6.77 (dd, *J* = 8.0 , 2.0 Hz, 1H), 6.96 (d, *J* = 2.0 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 7.12 (app t, *J* = 7.5 Hz, 1H), 7.20 (app t, *J* = 8.0 Hz, 1H), 7.48-7.50 (m, 2H), 7.56-7.58 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz,

$CDCl_3$): δ 54.7, 55.2, 112.1, 113.0, 113.3, 117.7, 117.9, 118.6, 126.3, 129.9, 130.2, 130.5, 131.3, 131.6, 133.0, 137.4, 138.6, 144.8, 146.2, 159.9, 194.1; HRMS (ESI): calculated for $C_{23}H_{19}{}^{81}BrNO_2$, 422.0579 $(M+H)^+$, found: 422.0589.

4-(2-(4-chlorophenyl)-3-(2-methoxybenzoyl)quinolin-1(2H)-yl)butan-2-one (6); Yield: 0.09 g, 76%; Orange solid; mp: 150-154 °C; IR (KBr): ν 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.09 (s, 3H), 2.53-2.60 (m, 1H), 2.75-2.81 (m, 1H), 3.56-3.64 (m, 2H), 3.67 (s, 3H), 5.90 (s, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 6.61 (app t, *J* = 7.5 Hz, 1H), 6.89 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 6.93-6.98 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.20-7.24 (m, 3H), 7.31-7.32 (m, 2H), 7.39 (d app t, *J* = 8.0, 1.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 30.5, 40.9, 44.2, 55.7, 60.7, 110.7, 111.5, 116.9, 119.6, 120.3, 128.2, 128.6, 128.8, 131.1, 131.2, 132.3, 133.2, 133.5, 138.3, 141.5, 144.9, 157.0, 194.6, 207.1; HRMS (ESI): calculated for $C_{27}H_{25}ClNO_3$, 446.1523 $(M+H)^+$, found: 446.1520.

(2-(4-chlorophenyl)quinoline-1,3(2*H*)-diyl)bis(phenylmethanone) (7); Yield: 0.108 g, 81%; yellow viscous liquid; IR (neat): ν 1644, 1713 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.60 (d, *J* = 7.0 Hz, 1H), 6.98 (app t, *J* = 7.5 Hz, 1H), 7.05-7.08 (m, 2H), 7.18-7.19 (m, 2H), 7.27-7.31 (m, 5H), 7.37-7.41 (m, 3H), 7.45 (s, 1H), 7.50-7.53 (m, 2H), 7.61 (app t, *J* = 7.5 Hz, 1H), 7.74-7.76 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 53.8, 125.2, 125.96, 126.04, 128.3, 128.6, 128.7, 128.8, 128.9, 129.18, 129.23, 130.3, 131.0, 132.3, 133.8, 134.9, 136.9, 137.0, 137.3, 137.5, 137.7, 170.0, 194.0; HRMS (ESI): calculated for$C_{29}H_{20}ClNO_2Na$, 472.1080 $(M+Na)^+$, found: 472.1081.

(2-(4-chlorophenyl)-4-ethoxy-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methanone (8a); Yield: 0.014 g, 7%; colorless liquid; IR : ν 1088, 1486, 1672, 3372 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.00 (t, *J* = 7.0 Hz, 3H) 3.40-3.46 (m, 1H), 3.61-3.67 (m, 1H), 4.01 (bs, 1H), 4.12 (app t, *J* = 10.0 Hz, 1H), 4.755 (d, *J* = 10.0 Hz, 1H), 5.07 (d, *J* = 9.5 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.79 (app t, *J* = 7.5 Hz, 1H),7.01-7.14 (m, 3H), 7.27-7.32 (m, 4H), 7.375 (d, *J* = 8.0 Hz, 1H), 7.45 (app t, *J* = 7.0 Hz, 1H), 7.67-7.69 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 15.4, 53.4, 59.2, 67.5, 78.7, 113.9, 118.1, 123.1, 126.8, 128.1, 128.4, 128.6, 128.8, 129.0, 133.1, 133.9, 138.4, 138.7, 143.4, 203.1. $C_{24}H_{23}ClNO_2$, 392.1417 $(M+H)^+$, found: 392.1416.

Associated Content

Supporting information

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Copies of ^1H and ^{13}C NMR Spectra (PDF)

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Notes

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