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A general approach to the synthesis of substituted isoxazolo[4,3-c]quinolines via chalcones[§]

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A general and practical approach to the synthesis of substituted isoxazolo[4,3-c]quinolines from the substituted isoxazolines afforded by 1,3-dipolar cycloaddition between 2-nitrobenzonitrile oxide and chalcones is described. The $SnCl_2.2H_2O$-mediated reduction of the nitro group followed by intramolecular cyclization involving the amino and the keto groups in these substrates furnished a mixture of isoxazolo[4,3- c]-quinolines and 3,5-dihydro-isoxazolo[4,3-c]quinoline. In contrast, the reduction of these substrates with Fe-AcOH unexpectedly yielded 3-benzoyl-4-quinolinamine derivatives.

Introduction

Annulated heterocyclic systems are ascribed with variety of pharmacological uses.[1-2] This reason provides enough incentive to synthetic organic chemists to devise novel yet simple strategies for the generation of these molecular frameworks. The development of isoxazole-annulated ring systems has been a topic of continuous research due to synthetic and medicinal importance of such scaffolds.[3-12] In one of the activities of our research group, we have been involved in the development of novel protocols for the synthesis of such ring systems. We have reported the synthesis of furo[3,4-*d*]isoxazol-4-one, 5*H*-isoxazolo [4,5-*d*]pyridazin-4-ones, 5,8-dihydro-isoxazolo[4,5-c]azepin-4-ones and isoxazolo-benzazulenes.[13-15] During the program we got interested in the synthesis of isoxazolo[4,3-*c*]quinolines. The literature survey revealed that though there exist number of strategies for the synthesis of isoxazolo[4,5-*c*]quinolines,[16-19] only two reports[20-21] exists for the synthesis of isoxazolo[4,3-*c*]quinoline despite their significance as a structural component of MRP-1 inhibitors.[22-23] Initially we reasoned that such an architecture could be generated from 3-(2-nitrophenyl)-isoxazole-4-carboxylate via reduction of the nitro to amino group and subsequent cyclization with the carboxylate or formyl function. However, as reported recently this approach led to formation of 4-quinolinamine derivatives exclusively.[24] In our continuing efforts in this direction, we reasoned that the synthesis of such ring system can be accomplished from the substituted isoxazoline derivative containing a 2-nitrophenyl group at 3-position and benzoyl moiety at 4-position afforded by 1,3-dipolar cycloaddition of the 2-nitrobenzo nitrile oxide on chalcones. In principle the reduction of the nitro group would result in a 2-aminophenyl derivative wherein the amino group should readily undergo intramolecular cyclization with the keto moiety of the benzoyl group to furnish isoxazolo [3,4-*c*] quinoline. The rationale for such strategy was based on reports of Rossi et al.[16] on the synthesis of isoxazolo[4,5-c]quinoline from β-(2-aminophenyl)-α,β-ynones and Kaye et al.[25a] on the generation of quinolines using Baylis-Hillman chemistry. More recently, we have also reported that the the keto group has preference for cyclization with the amino moiety for the construction of the quinoline ring.[25b] In order to explore our strategy we carried out the synthesis of 2-isoxazoline derivatives using chalcones and subjected them to reduction. Interestingly, the reduction of nitro group under catalytic hydrogenation or in the presence $SnCl_2.2H_2O$ yielded a mixture substituted 3,5-dihydro-isoxazolo[4,3-c]quinolines and substituted isoxazolo[4,3-c]quinolines. In contrast, the Fe-AcOH mediated reduction afforded 3-benzoyl-4-quinolinamine derivatives. These results prompt us to discuss the details of our study in this paper.

Results and Discussion

Initially, the substituted chalcones **1a-e,2a-b** were synthesized in excellent yields by the reaction of different aldehydes and acetophenones. The authenticity of these chalcones was confirmed by comparing their melting points with the ones reported in the literature.[26-27] Treatment of chalcones **1a-e,2a-b** with 2-nitrobenzo nitrile oxide (generated from α-chloro-2-nitrobenzaldoxime) in the presence of triethylamine in diethyl ether at -78 °C furnished isoxazolines **3a-e,4a-b**, respectively in 3-4 h in 54-64% yields (Scheme 1). Although the spectral data supported the structural assignment for **3a-e,4a-b**, the structure was secured by X-ray crystallographic analysis of **3a** (fig. 1).[28] Interestingly, this reaction was diastereoselective for trans isomer as only faint spot probably for cis stereomer was observed on tlc.

In the next stage of the synthesis, chemoselective reduction of the nitro group was desired. Generally, it can be achieved either via catalytic hydrogenation or metals including In, Fe, Zn in presence of additives or metal halide such as $SnCl_2$. The catalytic hydrogenation is known to cause cleavage of the 2-isoxazoline ring. However in the light of our recent results[24] where we have

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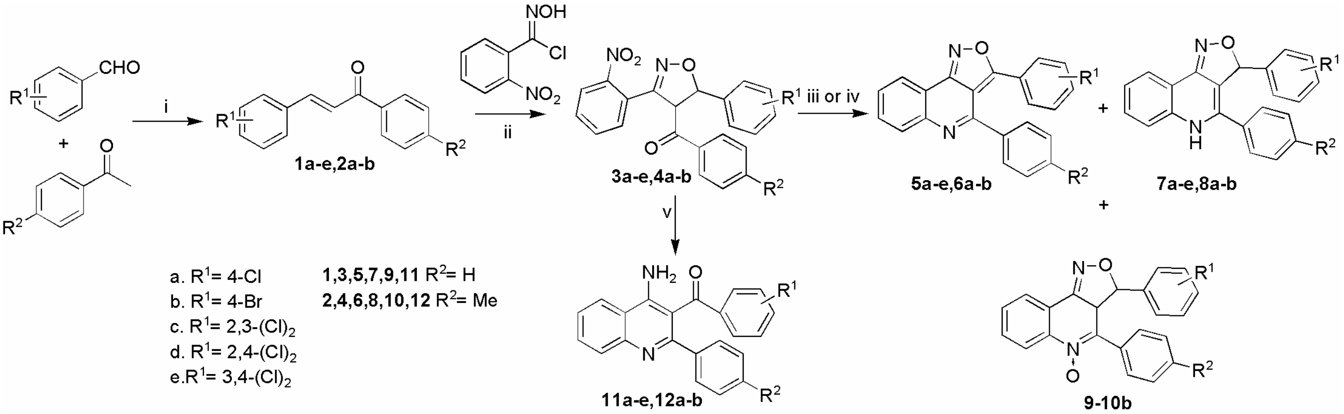


Scheme 1. *Reagents and Conditions*: i) aq KOH, MeOH, 15-30 min. ii) Et_3N, diethylether, -78 °C to rt, 14-16 h. iii) $SnCl_2.2H_2O$, MeOH, reflux, 80 °C, 30 min. iv) Pd-C (10%), H_2, 40 psi, rt, 30 mins. v) Fe, AcOH, reflux, 110 °C, 30 mins

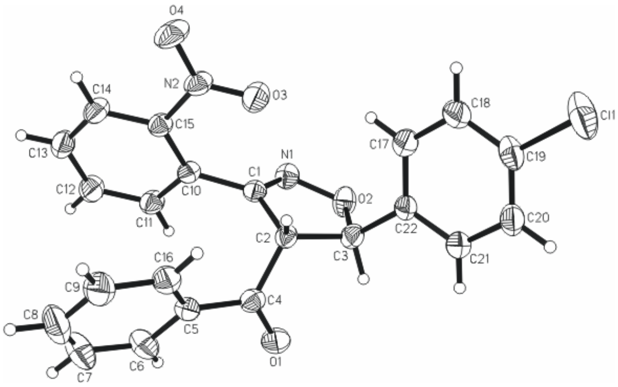


Figure 1. *ORTEP* diagram of compound **3a** showing atomic numbering scheme with probability of 30%.

demonstrated that the 2-isoxazoline ring bearing a nitro-phenyl group at 3-position is stable under catalytic hydrogenation we decided to employ it for our cause. Therefore, in the first instance we subjected **3a** to hydrogenation in the presence of 10% Pd-C at 40 psi on a Parr assembly. Gratifyingly, the reaction was complete in 30 min to afford a mixture of products. A careful silica-gel column chromatography led to isolation of two products. The spectral analysis of the less polar product which was obtained in 11% yield led us to establish the structure of the compound as **5a**. On the contrary, the polar product which was isolated in 39% yield was assigned the structure as **7a**. The formation of **5a** may have resulted following the cyclization of the hydroxylamine intermediate with the keto group. This hydroxylamine intermediate would have resulted from partial reduction of the nitro group. On the other hand product **7a** would have formed through the intramolecular cyclization taking place after the complete reduction of the nitro to amino group.

Subsequently, compound **3a** was also subjected to treatment with $SnCl_2.2H_2O$ in methanol at reflux temperature. It was pleasing to note that here too the reaction was complete within 30 min and the afforded product was a mixture of only two compounds which could be readily separated via column chromatography. The minor compound isolated in 21% yield herein was **5a** while the major product obtained in 57% yield was **7a**. In view of the better yields and easy separation observed with this procedure, other substrates **3b-e,4a-b** too were subjected to $SnCl_2.2H_2O$-promoted reactions. Expectedly these substrates yielded the corresponding products **5,7b-e, 6,8a-b**. The unambiguous assignment for the structure of these compounds was made by carrying out the X-ray crystallographic analysis of representative compounds **5c** and **7d** (fig. 2 and 3).[29-30] It is worth mentioning that the crystal of **7d** used for X-ray analysis was obtained from the recovered ^{13}C NMR sample because of which we observed entrapped molecule of $(CH_3)_3Si$-$Si(CH_3)_3$. Interestingly, during the reduction of **3-4b**, a third product, which was isolated in major yields, was formed invariably. On the basis of spectral evidence the structure of this product was established as **9-10b**. Although the formation of quinoline-N-oxide during the $SnCl_2.2H_2O$-promoted reduction of nitro-group and subsequent intramolecular cyclization has literature precedence,[25a] the formation of this product only in **3-4b** is unexplainable during present times. Nevertheless, the chemical

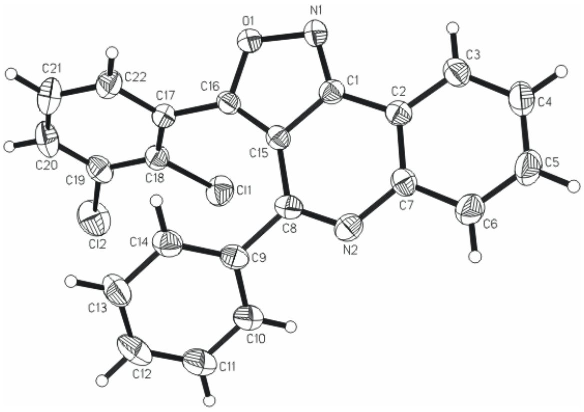
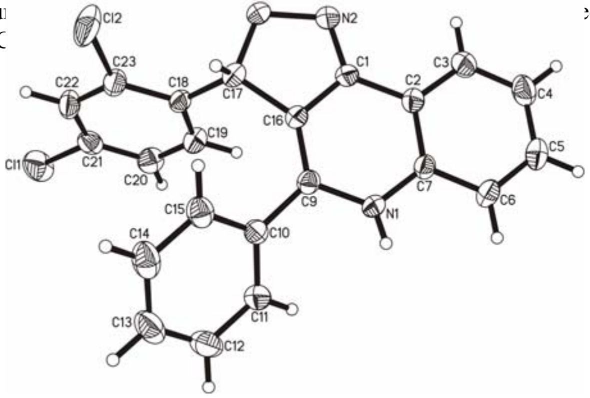


Figure 2. *ORTEP* diagram of compound **5c** showing atomic numbering scheme with probability of 30%.

Figure 3. *ORTEP* diagram of compound **7d** showing atomic nu ecule ((C



evidence for the assigned structure was obtained by the reaction of **9b** with PBr_3 in DMF to furnish **5a** as reported earlier.[25a]

In the next stage of the study, in our objective to avoid the formation of two products, we investigated the reduction of nitro group with other metals too. Although the reduction with indium in the presence of HCl in water furnished a complex mixture which was not characterized, similar reaction with Fe-AcOH displayed interesting result. Treatment of **3a** with Fe-AcOH at reflux temperature led to complete disappearance of the starting substrate within 30 min. Subsequent purification led to isolation of a single compound in 65% yield that was identified as 4-amino-3-benzoyl-2-phenyl-quinoline **11a**. In order to examine the general application of this reaction, isoxazolines **3b-e,4a-b** were also treated with Fe in the presence of AcOH. In all cases respective 4-amino quinolines **11b-e,12a-b**, respectively were isolated in good yields. This is an unusual observation since formation of 4-quinolinamines can be explained on the basis of a cascade reaction. It is believed that first the reduction of the nitro group may have occurred, followed by intramolecular cyclization of the amino group with the carbonyl functionality leading to isoxazolo[4,3-c]quinoline derivative and simultaneous cleavage of the isoxazoline ring. The X-ray crystallographic analysis of a representative compound **11b** (fig. 4)[31] unequivocally confirmed the assigned structure of the product. Additional chemical evidence for the formation of these products was obtained by subjecting **5a** to hydrogenation in the presence of Raney-Ni to furnish compound **11a** exclusively.

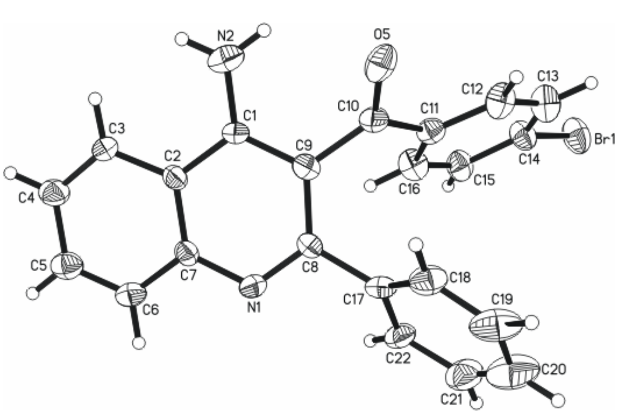


Figure 4. *ORTEP* diagram of compound **11b** showing atomic numbering scheme with probability of 30%.

Conclusions

In summary we have demonstrated a general and convenient synthesis of isoxazolo[4,3-c]quinoline derivatives via reduction of nitro group of 2-nitrophenyl isoxazolines which in turn were afforded by chalcones. This synthetic strategy is impressive because of easy availability of the starting substrates, simple reaction conditions and short reaction times. The formation of 4-quinolinamine derivatives bearing benzoyl moiety at 3-position during reduction in the presence Fe-AcOH provides an excellent alternative for the synthesis of this important scaffold.

Experimental Section

Melting points are uncorrected and determined in capillary tubes on an apparatus containing silicon oil. Infrared spectra were recorded using Perkin Elmer's RX I FTIR spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker DPX-200 MHz or Bruker Avance 300 MHz FT spectrometers, using TMS as an internal standard (chemical shifts in δ values, J in Hz). The FABMS were recorded on JEOL/SX-102 spectrometers and ESMS were recorded on a MICROMASS LCMS system. Elemental analyses were performed on a Carlo Erba 1108 microanalyzer or Elementar's Vario EL *III* microanalyzer. A representative data of chalcone is only provided. *CAUTION*: The round bottom flask containing around 5.0 g of α-chloro-2-nitrobenzaldoxime exploded a few times during evaporation under vacuum on rotary evaporator therefore it should be handled carefully. The hydrogenation was performed in usual manner on a Parr assembly. Compound **8a** was insoluble in any solvent therefore no NMR data is included for the same.

Preparation of chalcones (1a-e,2a-b)– General procedure: To a mixture of appropriate benzaldehydes (17 mmol) and appropriate acetophenones (17 mmol) in methanol (25 mL), aq KOH (26 mmol, 1.43 g in 9.5 mL of water) was added dropwise at room temperature and the reaction mixture was stirred for 15 mins. After completion, the reaction mixture was neutralized with dilute HCl and filtered over buchner funnel and washed freely with water. The resultant solids **1a-e, 2a-b** were dried over P_2O_5 in a dessicator.

3-(4 Chlorophenyl)-1-p-tolyl-propenone (2a): Yield: 82% (3.0 g from 3.66g) as a white solid, mp148-150 °C. R_f (10% EtOAc/hexanes): 0.56. ν_{max} (KBr) 1659 (CO) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ= 2.43 (s, 3H, CH_3), 7.23-7.28 (m, 4H, ArH), 7.32-7.46 (m, 2H, ArH & =CH), 7.54-7.58 (m, 2H, ArH, & =CH), 7.93 (d, 2H, *J*= 8.2 Hz, ArH). ^{13}C NMR ($CDCl_3$, 200 MHz): δ= 22.1, 122.8, 129.1, 129.6, 129.8, 130.0, 133.9, 135.8, 136.7, 143.3, 144.3, 190.1. ESI-MS: *m/z* = 257.2 $(M + 1)^+$.

Preparation of isoxazoline (3a-e, 4a-b)- General procedure: To the solution of 2-nitrophenylhydroxyiminoyl chloride (10 mmol, 2.0g) in dry diethyl ether (10 mL), was added an appropriate chalcone from **1a-e,2a-b** (15 mmol) and the mixture was cooled to –78 °C. Et_3N (20 mmol, 2.8 mL) was added dropwise at this temperature with stirring. After the addition was complete the reaction was brought to the room temperature and the stirring was continued for 3-4 h. Thereafter the reaction mixture was extracted using ethyl acetate (3x50 mL) and water (100 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product so obtained was purified by column chromatography over silica gel (60-120 mesh) using hexanes: EtOAc (95: 5, v/v) as solvent system to yield the desired product **3a-e,4a-b.**

[5-(4-Chlorophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-phenyl-methanone (3a): 59% (2.36 g from 2.0 g) as a yellow solid, mp 146-148 °C. R_f (20% EtOAc/hexanes): 0.5. ν_{max} (KBr) 1687 (CO), 1525, 1345 (NO_2) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ= 5.65 (d, *J*= 8.2 Hz, 1H, CH), 6.03 (d, *J*= 8.2 Hz, 1H, CH), 7.31-7.36 (m, 2H, ArH), 7.46 (s, 4H, ArH), 7.49-7.57 (m, 2H, ArH), 7.61-7.66 (m, 4H, ArH), 8.09 (d, *J*= 8.3 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ= 66.1, 87.5, 125.2, 128.5, 129.0, 129.3, 129.7, 131.3, 133.8, 134.4, 134.7, 135.4, 135.6, 137.9, 147.5, 153.8, 194.7. ESI-MS: *m/z* = 407.0/409.0 $(M + 1)^+$. $C_{22}H_{15}ClN_2O_4$ (406.82): calcd. C, 64.95; H, 3.72; N, 6.89; found, C, 65.08; H, 4.01; N, 6.65.

[5-(4-Bromophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-phenyl-methanone (3b): 62% (1.80 g from 1.30 g) as a brown solid, mp 155-157 °C. R_f(20% EtOAc /hexanes): 0.66. ν_{max} (KBr) 1698 (CO), 1533, 1346 (NO_2) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ= 5.65 (d, *J*= 8.1 Hz, 1H, CH), 6.02 (d, *J*= 8.1 Hz, 1H, CH), 7.31-7.41 (m, 4H, ArH), 7.50-7.57 (m, 2H, ArH), 7.60-7.66 (m, 6H, ArH), 8.09 (d, *J*= 8.1 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ= 66.1, 87.5, 123.6, 125.3, 128.8, 129.0, 129.3, 130.1, 130.3, 131.3, 132.6, 133.8, 134.4, 134.8, 135.6, 138.4, 147.5, 153.8, 194.7.

ESI-MS: *m/z* = 451.1/453.0 (M + 1)$^+$. $C_{22}H_{15}BrN_2O_4$ (451.27): calcd. C, 58.55; H, 3.35; N, 6.21; found, C, 58.22; H, 3.57; N, 6.22.

[5-(2,3-Dichlorophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-phenyl-methanone (3c): 64% (2.12 g from 1.50 g) as a yellow solid, mp 159-160°C. R$_f$ (20% EtOAc/hexanes): 0.67. ν_{max} (KBr) 1696 (CO), 1523, 1345 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ= 5.49 (d, *J*= 5.9 Hz, 1H, CH), 6.58 (d, *J*= 5.9 Hz, 1H, CH), 7.27-7.42 (m, 4H, ArH), 7.46-7.54 (m, 4H, ArH), 7.65-7.71 (m, 3H, ArH), 8.05-8.08 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ= 65.5, 84.8, 124.7, 125.4, 126.2, 128.5, 128.8, 129.3, 129.7, 130.7, 131.4, 133.2, 133.7, 134.5, 134.6, 135.7, 140.3, 147.4, 153.4, 194.1. ESI-MS: *m/z* = 441.0/443.0 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O_4$ (441.26): calcd. C, 59.88; H, 3.20; N, 6.35; found, C, 60.03; H, 3.45; N, 6.65.

[5-(2,4-Dichlorophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-phenyl-methanone (3d): 63% (2.21 g from 1.60 g) as a white solid, mp 150-152 °C. R$_f$ (20% EtOAc/hexanes): 0.58. ν_{max} (KBr) 1688 (CO), 1526, 1345 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ= 5.50 (d, *J*= 6.2 Hz, 1H, CH), 6.52 (d, *J*= 6.2 Hz, 1H, CH), 7.28-7.33 (m, 2H, ArH), 7.35-7.38 (m, 1H, ArH), 7.42-7.54 (m, 5H, ArH), 7.64-7.73 (m, 3H, ArH), 8.06-8.09 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ= 63.8, 82.5, 123.1, 123.7, 126.7, 127.1, 127.4, 127.6, 128.1, 129.7, 130.6, 131.6, 132.8, 132.9, 133.7, 134.1, 134.9, 145.7, 151.8, 192.4. FAB-MS: *m/z* = 441 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O_4$ (441.26) C, 59.88; H, 3.20; N, 6.35; found, C, 60.11; H, 3.30; N, 6.51.

[5-(3,4-Dichlorophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-phenyl-methanone (3e): 58% (1.92 g from 1.50 g) as s pale yellow solid, mp 141-142 °C. R$_f$ (20% EtOAc/hexanes): 0.59. ν_{max} (KBr) 1688 (CO), 1521, 1350 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.62 (d, *J* = 7.9 Hz, 1H, CH), 6.04 (d, *J* = 7.9 Hz, 1H, CH), 7.32-7.47 (m, 3H, ArH), 7.51-7.77 (m, 5H, ArH), 8.09-8.17 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 64.4, 84.6, 124.6, 126.2, 127.3, 127.5, 128.2, 128.9, 129.5, 129.8, 130.2, 131.5, 131.9, 132.6, 132.9, 133.8, 135.0, 138.1, 146.7, 152.1, 192.4. ESI-MS: *m/z* = 441 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O_4$ (441.26): calcd. C, 59.88; H, 3.20; N, 6.35; found, C, 59.91; H, 3.16; N, 6.43.

[5-(4-Chlorophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-p-tolyl-methanone (4a): 57% (1.80 g from 1.50 g) as a white solid, mp 160-162 °C. R$_f$(20% EtOAc /hexanes): 0.48. ν_{max} (KBr) 1694 (CO), 1525, 1350 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.35 (s, 3H, CH_3), 5.62 (d, *J*= 8.2 Hz, 1H, CH), 5.99 (d, *J* = 8.2 Hz, 1H, CH), 7.13 (d, *J* = 8.1 Hz, 2H, ArH), 7.45 (s, 4H, ArH), 7.53-7.57 (m, 3H, ArH), 7.62-7.64 (m, 2H, ArH), 8.10 (d, 1H, *J* = 8.1 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.6, 65.5, 87.3, 124.8, 128.1, 128.7, 128.8, 129.2, 129.3, 129.6, 129.7, 130.8, 133.5, 134.0, 134.8, 135.6, 138.4, 147.5, 153.8, 194.7. FAB-MS: *m/z* = 421 (M + 1)$^+$. $C_{23}H_{17}ClN_2O_4.H_2O$ (438.86): calcd. C, 62.95; H, 4.36; N, 6.38; found, C, 63.04; H, 4.66; N, 6.65.

[5-(4-Bromophenyl)-3-(2-nitrophenyl)-4,5-dihydro-isoxazol-4-yl]-p-tolyl-methanone (4b): 54% (1.50 g from 1.20 g) as a yellow solid, mp 154-155 °C. R$_f$(20% ethyl acetate/hexanes): 0.53. ν_{max} (KBr) 1682 (CO), 1530, 1347 (NO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.34 (m, 3H, ArH), 5.60 (d, *J* = 8.1 Hz, 1H, CH), 5.96 (d, *J* = 8.1 Hz, 1H, CH), 7.12 (d, *J*= 8.1 Hz, 2H, ArH), 7.37 (d, *J* = 8.4 Hz, 2H, ArH), 7.49-7.63 (m, 7H, ArH), 8.09 (d, *J* = 7.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.4, 64.2, 86.1, 121.8, 123.5, 127.1, 127.5, 128.4, 129.5, 130.9, 131.5, 132.2, 132.7, 136.8, 144.4, 145.9, 152.3, 192.6. ESI-MS: *m/z* = 465.2/467.2 (M + 1)$^+$. $C_{23}H_{17}BrN_2O_4$ (465.29): calcd. C, 59.37; H, 3.68; N, 6.02; found, C, 59.59; H, 3.94; N, 5.99.

$SnCl_2.2H_2O$-mediated reduction of 3a-e,4a-b- General Procedure: To a solution of appropriate isoxazoline from **3a-e,4a-b** (1.23 mmol) in dry methanol (15 mL), was added $SnCl_2.2H_2O$ (6.15 mmol, 1.17 g) and the mixture was maintained at reflux temperature for 30 mins. Thereafter, the reaction mixture was evaporated to remove excess methanol and neutralized using saturated $NaHCO_3$ solution. It was then filtered over a celite bed and the residue was washed with ethyl acetate. The water layer was further extracted using ethyl acetate (3x50 mL). The organic layers were combined, washed with brine solution, dried over Na_2SO_4 and concentrated under reduced pressure to obtain a crude product. The crude product was purified via column chromatography over silica gel (60-120 mesh) using hexanes: EtOAc (98-97:2-3, v/v) to obtain **5a-e, 6a-b** and further elution with hexanes: EtOAc (80-70:20-30, v/v) to obtain **7a-e, 8a-b**.

3-(4-Chlorophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline (5a): 21% (0.11 g from 0.60 g) as a pale yellow solid, mp 211-213 °C. R$_f$ (20% EtOAc: hexanes): 0.8. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.20 (s, 4H, ArH), 7.29-7.33 (m, 2H, ArH), 7.38-7.49 (m, 3H, ArH), 7.65 (dt, ^{1}*J* = 1.2 Hz, ^{2} *J* = 7.5 Hz, 1H, ArH), 7.81 (dt, ^{1}*J* = 1.3 Hz, ^{2}*J* = 7.2 Hz, 1H, ArH), 8.12 (d, *J*= 8.0 Hz, 1H, ArH), 8.52 (dd, ^{1}*J* = 1.2 Hz, ^{2}*J* = 7.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 108.7, 115.9, 123.8, 125.9, 128.5, 128.9, 129.0, 129.3, 130.2, 130.4, 131.2, 132.0, 137.5, 138.4, 145.7, 156.9, 157.8, 168.1. ESI-MS: *m/z* = 357.3/359.2 (M + 1)$^+$. HR-EIMS calcd. for $C_{22}H_{13}ClN_2O$ 356.0716; found 356.0711.

3-(4-Bromophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline (5b): 19% (0.072 g from 0.42 g) as a yellow solid, mp 132-133 °C. R$_f$ (20% EtOAc: hexanes): 0.82. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50-7.51 (m, 2H, ArH), 7.52-7.53 (m, 3H, ArH), 7.55-7.56 (m, 3H, ArH), 7.58-7.62 (m, 2H, ArH), 8.02-8.05 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 121.3, 123.5, 127.2, 127.4, 128.5, 130.9, 131.7, 132.5, 136.8, 142.1, 188.9. ESI-MS: *m/z* = 401.2/403.1 (M + 1)$^+$. $C_{22}H_{13}BrN_2O$ (401.25): calcd. C, 65.85; H, 3.27; N, 6.98; found C, 65.54; H, 3.09; N, 7.16.

3-(2,3-Dichlorophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline (5c): 19% (0.081 g from 0.48 g) as a light brown solid, mp 200-201°C. R$_f$ (20% EtOAc: hexanes): 0.82. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.08-7.18 (m, 4H, ArH), 7.30-7.32 (m, 1H, ArH), 7.39-7.41 (m, 2H, ArH), 7.53-7.56 (m, 1H, ArH), 7.69 (t, *J* = 7.5 Hz, 1H, ArH), 7.84 (t, *J* = 7.4 Hz, 1H, ArH), 8.17 (d, *J* = 8.1 Hz, 1H, ArH), 8.56 (d, *J* = 7.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 111.2, 116.0, 123.9, 124.6, 127.5, 128.2, 128.6, 128.7, 129.8, 130.0, 130.4, 130.5, 132.1, 132.9, 134.3, 137.7, 145.8, 156.8, 157.2, 166.0. ESI-MS: *m/z* = 391.2/393.2 (M+1)$^+$. $C_{22}H_{12}Cl_2N_2O$ (391.24): calcd. C, 67.54; H, 3.09; N, 7.16; found C, 67.66; H, 3.41; N, 7.39.

3-(2,4-Dichlorophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline (5d): 17% (0.075 g from 0.50 g) as a pale yellow solid, mp 128-129 °C. R$_f$ (20% EtOAc: hexanes): 0.81. ^{1}H NMR ($CDCl_3$, 300 MHz): δ= 7.09-7.21 (m, 4H, ArH), 7.30-7.36 (m, 1H, ArH), 7.38-7.43 (m, 3H, ArH), 7.67 (dt, ^{1}*J* = 1.1 Hz, ^{2}*J* = 7.8 Hz, 1H, ArH), 7.82 (dt, ^{1}*J* = 1.5 Hz, ^{2}*J* = 7.3 Hz, 1H, ArH), 8.15 (d, *J* = 8.3 Hz, 1H, ArH), 8.54 (dd, 1H, ^{1}*J* = 1.3 Hz, ^{2}*J* = 7.8 Hz, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 109.6, 114.3, 122.2, 125.7, 126.6, 126.9, 127.2, 127.4, 128.4, 128.5, 128.8, 130.4, 131.3, 133.7, 136.1, 136.4, 144.1, 155.1, 155.6, 163.9. ESI-MS: *m/z* = 391.2/393.1 (M + 1)$^+$. $C_{22}H_{12}Cl_2N_2O$ (391.24): calcd. C, 67.54; H, 3.09; N, 7.16; found C, 67.88; H, 3.20; N, 7.08.

3-(3,4-Dichlorophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline (5e): 19% (0.085 g from 0.50 g) as a yellow solid, mp 201-202 °C. R$_f$ (20% EtOAc: hexanes): 0.75. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.15-7.18 (m, 1H, ArH), 7.25-7.28 (m, 1H, ArH), 7.33-7.38 (m, 3H, ArH), 7.46-7.50 (m, 3H, ArH), 7.68 (t, *J* = 7.5 Hz, 1H, ArH), 7.82 (t, *J* = 7.5 Hz, 1H, ArH), 8.15 (d, *J* = 8.1 Hz, 1H, ArH), 8.53 (d, *J* = 7.8 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 109.1, 115.8, 123.8, 127.0, 128.6, 128.8, 129.1, 129.2, 130.4, 130.6, 131.9, 132.2, 133.1, 135.7, 138.3, 145.6, 156.6, 157.8, 166.4. ESI-MS: *m/z* = 391.2/393.2 (M + 1)$^+$; $C_{22}H_{12}Cl_2N_2O$. $2H_2O$ (427.28): calcd. C, 64.56; H, 3.45; N, 6.84, found C, 64.80; H, 3.41; N, 6.79.

3-(4-Chlorophenyl)-4-p-tolyl-isoxazolo[4,3-c]quinoline (6a): 14% (0.08 g from 0.65 g) as a yellow solid, mp 232-234 °C. R$_f$ (20% EtOAc: hexanes): 0.72; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.09 (d, *J*= 7.8 Hz, 2H, ArH), 7.22 (s, 4H, ArH), 7.36 (d, *J*= 7.8 Hz, 2H, ArH), 7.63 (t, *J*= 7.2 Hz, 1H, ArH), 7.78 (t, J= 7.2 Hz, 1H, ArH), 8.11 (d, J= 8.0 Hz, 1H, ArH), 8.50 (d, J= 7.5 Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 21.8, 108.8, 115.9, 123.8, 126.0, 128.3, 129.3, 129.5, 130.3, 131.3, 131.9, 135.7, 137.5, 140.4, 145.8, 156.9, 157.8, 168.0. ESI-MS: m/z = 370.2/372.1 (M+1)$^+$. $C_{23}H_{15}ClN_2O$ (370.83): calcd. C, 74.49; H, 4.08; N, 7.55; found C, 74.54; H, 4.19; N, 7.35.

3-(4-Bromophenyl)-4-p-tolyl-isoxazolo[4,3-c]quinoline (6b): 18% (0.08 g from 0.50 g) as a yellow solid, mp 218-220 °C. R_f (20% EtOAc: hexanes): 0.74. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 2.38 (s, 3H, CH$_3$), 7.07-7.21 (m, 4H, ArH), 7.33-7.39 (m, 4H, ArH), 7.62 (t, J= 7.3 Hz, 1H, ArH), 7.77 (t, J= 7.2 Hz, 1H, ArH), 8.10 (d, J= 8.0 Hz, 1H, ArH), 8.50 (d, J= 7.3 Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 21.8, 108.8, 115.9, 123.8, 125.9, 126.4, 128.3, 129.3, 129.5, 130.3, 131.4, 131.8, 131.9, 135.6, 140.4, 145.8, 156.2, 157.87, 168.1. ESI-MS: m/z = 415.2/417.1 (M +1)$^+$. $C_{23}H_{15}BrN_2O$ (415.28): calcd. C, 66.52; H, 3.64; N, 6.75; found C, 66.54; H, 3.50; N, 6.90.

3-(4-Chlorophenyl)-4-phenyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (7a): 57% (0.30 g from 0.60 g) as a yellow solid, mp 220-222 °C. R_f (20% EtOAc: hexanes): 0.32. ν_{max} (KBr) 3300 (NH) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 6.69 (s, 1H, CH), 7.07 (dd, ^1J = 1.9 Hz, ^2J = 6.5 Hz, 2H, ArH), 7.11-7.17 (m, 1H, ArH), 7.19 (dd, ^1J = 1.8 Hz, ^2J = 6.7 Hz, 2H, ArH), 7.34-7.39 (m, 4H, ArH), 7.42-7.48 (m, 3H, ArH), 7.70 (dd, ^1J = 1.1 Hz, ^2J = 7.8 Hz, 1H, ArH), 10.20 (s, 1H, NH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 80.7, 111.5, 115.6, 116.6, 122.0, 123.1, 1215.8, 126.3, 126.8, 127.3, 127.7, 127.9, 128.7, 130.2, 131.4, 132.1, 135.6, 138.7, 139.3, 150.5. ESI-MS: m/z = 359.2/361.2 (M + 1)$^+$. $C_{22}H_{15}ClN_2O$ (358.82): calcd. C, 73.64; H, 4.21; N, 7.81; found, C, 73.53; H, 4.40; N, 7.65.

3-(4-Bromophenyl)-4-phenyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (7b): 17% (0.063 g from 0.42 g) as a yellow solid, mp 227-229 °C. R_f (20% EtOAc: hexanes): 0.4. ν_{max} (KBr) 3432 (NH) cm^{-1}. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 6.68 (s, 1H, CH), 7.01 (d, J = 8.0 Hz, 2H, ArH), 7.14 (t, J = 7.3 Hz, 1H, ArH), 7.32-7.37 (m, 5H, ArH), 7.43-7.46 (m, 3H, ArH), 7.70 (d, J= 7.7 Hz, 1H, ArH), 10.19 (s, 1H, NH). ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 80.7, 111.5, 115.6, 116.6, 120.1, 122.0, 123.1, 126.8, 127.7, 128.2, 128.7, 130.2, 132.1, 135.6, 138.7, 139.7, 150.5. ESI-MS: m/z = 403.2/405.1 (M + 1)$^+$. $C_{22}H_{15}BrN_2O$ (403.27): calcd. C, 65.52; H, 3.75; N, 6.95; found C, 65.54; H, 3.79; N, 7.11.

3-(2,3-Dichlorophenyl)-4-phenyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (7c): 49% (0.21 g from 0.48 g) as a yellow solid, mp >250 °C. R_f (20% EtOAc: hexanes): 0.36. ν_{max} (KBr) 3434 (NH) cm^{-1}. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 7.04 (s, 1H, CH), 7.16-7.19 (m, 3H, ArH), 7.31-7.34 (m, 3H, ArH), 7.40-7.47 (m, 5H, ArH), 7.69 (d, J= 7.8 Hz, 1H, ArH), 10.36 (s, 1H, NH). ^{13}C NMR (CDCl$_3$, 50.32 MHz): δ = 80.1, 112.5, 115.4, 117.9, 123.3, 124.3, 127.7, 128.6, 128.8, 129.9, 130.5, 131.5, 132.0, 133.3, 137.2, 139.9, 140.2, 152.1. ESI-MS: m/z = 393.1/395.1 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26):calcd. C, 67.19; H, 3.59; N. 7.12; found C, 67.34; H, 3.66; N, 7.01.

3-(2,4-Dichlorophenyl)-4-phenyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (7d): 52% (0.23 g from 0.50 g) as a yellow solid, mp 230-231 °C. R_f (20% EtOAc: hexanes): 0.28. ν_{max} (KBr) 3421 (NH) cm^{-1}. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 6.96 (s, 1H, CH), 7.10-7.21 (m, 3H, ArH), 7.30-7.33 (m, 3H, ArH), 7.37-7.46 (m, 5H, ArH), 7.67 (d, J = 7.7 Hz, 1H, ArH), 10.30 (s, 1H, NH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 82.6, 116.0, 119.0, 121.5, 126.9, 127.9, 131.3, 131.5, 132.4, 133.5, 135.0, 135.3, 136.9, 137.1, 137.2, 140.4, 140.7, 143.5, 155.7. ESI-MS: m/z = 393.1/395.0 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26): calcd. C, 67.19; H, 3.59; N, 7.12; found C, 66.98; H, 3.42; N, 7.23.

3-(3,4-Dichlorophenyl)-4-phenyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (7e): 47% (0.21 g from 0.50 g) as a yellow solid, mp 195-197°C. R_f (20% EtOAc: hexanes): 0.33. ν_{max} (KBr) 3400 (NH) cm^{-1}. ^{1}H NMR (DMSO-d$_6$, 300 MHz): δ = 6.69 (s, 1H, CH), 7.06-7.09 (m, 2H, ArH), 7.11-7.21 (m, 3H, ArH), 7.34-7.39 (m, 4H, ArH), 7.42-7.48 (m, 3H, ArH), 7.70 (d, J = 7.8 Hz, 1H, ArH), 10.20 (s, 1H, NH). ESI-MS: m/z = 393.2/395.2 (M + 1)$^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26): calcd. C, 67.19; H, 3.59; N, 7.12; found C, 73.64; H, 4.21, N, 7.81.

3-(4-Chlorophenyl)-4-p-tolyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (8a): 61% (0.35 g from 0.65 g) as a yellow solid, mp 260-262 °C. R_f (20% EtOAc: hexanes): 0.26. ν_{max} (KBr) 3352 (NH) cm^{-1}. ESI-MS: m/z = 373.2 (M + 1)$^+$. $C_{23}H_{17}ClN_2O$ (372.84): calcd. C, 74.09; H, 4.60; N, 7.51; found C, 74.24; H, 4.31; N, 7.81.

3-(4-Bromophenyl)-4-p-tolyl-3,5-dihydro-isoxazolo[4,3-c]quinoline (8b): 16% (0.072 g from 0.50 g) as a yellow solid, mp 200-202 °C. R_f (20% EtOAc: hexanes): 0.24. ν_{max} (KBr) 3402 (NH) cm-1. ^{1}H NMR (DMSO-d$_6$, 300 MHz): δ = 2.30 (s, 3H, CH$_3$), 6.45 (s, 1H, CH), 6.95 (d, J = 8.3 Hz, 2H, ArH), 7.04 (t, J = 6.8 Hz, 1H, ArH), 7.10 (d, J = 8.0 Hz, 2H, ArH), 7.20-7.24 (m, 4H, ArH), 7.29-7.34 (m, 2H, ArH), 7.68 (d, J = 7.9 Hz, 1H, ArH), 9.92 (s, 1H, NH). ^{13}C NMR (DMSO-d$_6$, 75 MHz): δ = 20.2, 80.8, 111.4, 114.9, 116.6, 120.1, 121.7, 123.0126.6, 128.0, 128.1, 129.3, 129.9, 130.1, 135.8, 138.3, 138.6, 139.7, 150.7. ESI-MS: m/z = 417.2/419.1 (M + 1)$^+$. $C_{23}H_{17}BrN_2O$ (417.29): calcd. C, 66.20; H, 4.11; N, 6.71; found C, 66.30; H, 4.19; N, 6.77.

3-(4-Bromophenyl)-4-phenyl-isoxazolo[4,3-c]quinoline 5-oxide (9b): 48% (0.19 g from 0.42 g) as a yellow solid, mp 235-237 °C. R_f (20% EtOAc: hexanes): 0.32. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 6.94 (dd, ^1J = 1.7 Hz, ^2J = 6.9 Hz, 2H, ArH), 727-7.37 (m, 4H, ArH), 7.41-7.49 (m, 3H, ArH), 7.82 (dt, 1H, ^1J = 1.1 Hz, ^2J = 7.6 Hz, ArH), 7.90 (dt, 1H, ^1J = 1.4 Hz, ^2J = 8.6 Hz, ArH), 8.52 (dd, 1H, ^1J = 1.2 Hz, ^2J = 7.7 Hz, ArH), 8.83 (d, J = 7.9 Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 107.8, 116.2, 120.6, 122.5, 123.9, 124.0, 127.3, 128.7, 128.9, 129.0, 130.1, 131.0, 135.9, 140.2, 150.6, 163.8. ESI-MS: m/z = 417.2/419.1 (M + 1)$^+$. $C_{22}H_{13}BrN_2O_2$ (417.25): calcd. C, 63.33; H, 3.14; N, 6.71; found C, 63.29; H, 3.42; N, 6.88.

3-(4-Bromophenyl)-4-p-tolyl-isoxazolo[4,3-c]quinoline 5-oxide (10b): 52% (0.24 g from 0.50 g) as a yellow solid, mp >250 °C. R_f (20% EtOAc: hexanes): 0.32. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 2.38 (s, 3H, CH$_3$), 6.94 (d, J = 8.5 Hz, 2H, ArH), 7.13 (d, J = 8.1 Hz, 2H, ArH), 7.29-7.36 (m, J = 7.3 Hz, 4H, ArH), 7.80 (t, J = 7.6 Hz, 1H, ArH), 7.88 (t, J = 8.5 Hz, 1H, ArH), 8.51 (d, J = 7.8 Hz, 1H, ArH), 8.81 (d, J = 8.5 Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 21.2, 107.9, 116.2, 120.6, 122.5, 123.8, 124.1, 125.8, 126.2, 127.6, 127.9, 128.6, 128.8, 129.3, 129.9, 130.4, 130.7, 131.0, 136.3, 139.1, 140.2, 163.9. ESI-MS: m/z = 431.2/433.1 (M + 1)$^+$. $C_{23}H_{15}BrN_2O_2$ (431.28): calcd. C, 64.05; H, 3.51; N, 6.50; found C, 63.82; H, 3.80; N, 6.67.

Fe-AcOH-mediated reduction of 3a-e,4a-b- General Procedure: To a solution of appropriate isoxazoline **3a-e, 4a-b** (1.23 mmol) in glacial acetic acid (10 mL) was added Fe powder (7.39 mmol, 0.41 g) and the reaction mixture was heated at 110 °C for 30 mins. Thereafter the reaction mixture was evaporated to remove excess acetic acid, neutralized using saturated aqueous NaHCO$_3$ solution and then filtered over a celite bed. The residue was washed with ethyl acetate and the water layer was extracted using ethyl acetate (2x50 mL). The organic layers were combined, washed with brine solution (50 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure to yield the crude product, which was further purified by column chromatography over silica gel (60-120 mesh) using hexanes: EtOAc (90:10, v/v) as eluent to obtain the pure products.

(4-Amino-2-phenyl-quinolin-3-yl)-(4-chlorophenyl)-methanone (11a): 66% (0.29 g from 0.50 g) as a yellow solid, mp 249-250 °C. R_f(20% ethyl acetate/hexanes): 0.57. ν_{max} (KBr) 1688 (C=O), 3424 (NH$_2$) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 6.45 (s, 2H, NH$_2$), 7.07 (d, J = 8.5 Hz, 2H, ArH), 7.16-7.21 (m, 3H, ArH), 7.34 (d, J = 8.5 Hz, 2H, ArH), 7.48-7.58 (m, 3H, ArH), 7.80 (t, J = 7.3 Hz, 1H, ArH), 7.90 (d, J = 8.3 Hz, 1H, ArH), 8.13 (d, J = 8.4 Hz, 1H, ArH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 119.5, 124.3, 126.7, 126.9, 127.5, 128.3, 128.9, 129.2, 130.1, 136.8, 158.6. ESI-MS: m/z =

359.3/361.3 $(M + 1)^+$. $C_{22}H_{15}ClN_2O$ (358.8): calcd. C, 73.64; H, 4.21; N, 7.81. Found, C, 73.47; H, 4.10; N, 7.77.

(4-Amino-2-phenyl-quinolin-3-yl)-(4-bromophenyl)-methanone (11b): 56% (0.20 g from 0.40 g) as a yellow solid, mp >250 ºC. R_f (20% EtOAc: hexanes): 0.57. ν_{max} (KBr) 1713 (CO), 3352 (NH_2) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ = 6.46 (brs, 2H, NH_2), 7.16-7.20 (m, 3H, ArH), 7.22-28 (m, 4H, ArH), 7.48-7.51 (m, 2H, ArH), 7.53-7.58 (m, 1H, ArH), 7.77-7.83 (m, 1H, ArH), 7.90 (d, *J* = 8.2 Hz, 1H, ArH), 8.13 (d, *J* = 8.2 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ= 108.7, 116.3, 122.3, 124.1, 125.3, 127.0, 127.4, 128.4, 130.0, 130.1, 130.3, 137.5, 140.6, 146.9, 150.6, 157.4, 196.1; mass (ES+) m/z 403.4/405.4 $(M + 1)^+$. $C_{22}H_{15}BrN_2O$ (403.27): calcd. C, 65.52; H, 3.75; N, 6.95; found, C, 65.24; H, 3.54; N, 7.02.

(4-Amino-2-phenyl-quinolin-3-yl)-(2,3-dichlorophenyl)-methanone (11c): 65% (0.26 g from 0.45 g) as a pale yellow solid, mp 238-240 ºC. R_f (20% EtOAc: hexanes): 0.58. ν_{max} (KBr) 1625 (CO), 3322 (NH_2) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ= 6.81-6.89 (m, 2H, ArH), 7.10-7.20 (m, 4H, ArH), 7.34-7.37 (m, 2H, ArH), 7.43 (brs, 2H, NH_2), 7.53 (dt, ^1J = 1.0 Hz, ^2J = 8.1 Hz, 1H, ArH), 7.79 (dt, ^1J = 1.0 Hz, ^2J = 8.1 Hz, 1H, ArH), 7.93 (d, *J* = 8.3 Hz, 1H, ArH), 8.07 (d, *J* = 8.3 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 108.6, 115.7, 119.7, 124.4, 125.1, 126.7, 127.1, 127.8, 128.9, 130.0, 130.7, 132.3, 140.6, 141.2, 146.5, 152.4, 160.5, 194.9. ESI-MS: *m/z* 393.3/395.2 $(M + 1)^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26): calcd. C, 67.19; H, 3.59; N, 7.12; found, C, 66.89; H, 3.81; N, 7.22.

(4-Amino-2-phenyl-quinolin-3-yl)-(2,4-dichlorophenyl)-methanone (11d): 59% (0.25 g from 0.48 g) as a yellow solid, mp 200-201 ºC. R_f (20% EtOAc: hexanes): 0.48; ν_{max} (KBr) 1628 (CO)cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz): δ = 7.00 (d, *J* = 8.2 Hz, 1H, ArH), 7.10 (d, *J* = 8.2 Hz, 1H, ArH), 7.18-7.26 (m, 6H, ArH), 7.55 (t, *J* = 7.2 Hz, 1H, ArH), 7.76-7.88 (m, 2H, ArH), 8.36 (s, 2H, NH_2), 8.49 (d, *J* = 8.1 Hz, 1H, ArH). ^{13}C NMR (DMSO-d_6, 75 MHz): δ= 108.1, 116.5, 122.5, 124.3, 125.7, 126.8, 127.2, 128.1, 128.4, 130.9, 131.0, 1345.1, 138.2, 141.3, 146.6, 153.1, 159.8, 193.8. ESI-MS: *m/z* = 393.2/395.1 $(M + 1)^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26): calcd. C, 67.19; H, 3.59; N, 7.12; found, C, 67.31; H, 3.51; N, 7.32.

(4-Amino-2-phenyl-quinolin-3-yl)-(3,4-dichlorophenyl)-methanone (11e): 62% (0.30 g from 0.54 g) as a pale yellow solid, mp 160-162 ºC. R_f (20% EtOAc: hexanes): 0.59. ν_{max} (KBr) 1628 (CO), 3428 (NH_2) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 6.63 (s, 1H, NH), 7.11-7.19 (m, 5H, ArH), 7.39-7.53 (m, 4H, ArH), 7.71-7.93 (m, 2H, ArH), 8.10 (d, *J* = 12.5 Hz, 1H, ArH). ^{13}C NMR (Py-d_6, 75 MHz): δ = 110.8, 119.3, 124.7, 126.5, 129.2, 129.7, 130.0, 130.4, 131.1, 131.3, 132.3, 132.5, 142.0, 143.8, 154.7, 160.8, 197.3. ESI-MS: m/z = 393.4/395.3 $(M + 1)^+$. $C_{22}H_{14}Cl_2N_2O$ (393.26): calcd. C, 67.19; H, 3.59; N, 7.12; found, C, 67.44; H, 3.81; N, 7.29.

(4-Amino-2-p-tolyl-quinolin-3-yl)-(4-chlorophenyl)-methanone (12a): 61% (0.28 g from 0.52 g) as a yellow solid, mp 240-242 ºC. R_f (20% EtOAc: hexanes): 0.45. ν_{max} (KBr) 1685 (CO), 3424 (NH_2) cm^{-1}. ^1H NMR (CD_3OD, 200 MHz): δ= 2.13 (s, 3H, CH_3), 6.91 (d, *J* = 7.8 Hz, 2H, ArH), 7.01-7.05 (m, 2H, ArH), 7.16-7.26 (m, 4H, ArH), 7.44-7.48 (m, 1H, ArH), 7.68-7.71 (m, 1H, ArH), 7.85 (d, *J* = 8.4 Hz, 1H, ArH), 8.16 (d, *J* = 8.4 Hz, 1H, ArH). ^{13}C NMR (Py-d_5, 75 MHz): δ = 21.8, 111.6, 119.2, 124.8, 126.2, 129.4, 129.9, 131.1, 131.2, 132.2, 136.7, 139.0, 139.5, 139.9, 153.9, 160.3, 198.7. ESI-MS: m/z = 373.3/375.3 $(M + 1)^+$. $C_{23}H_{17}ClN_2O$ (372.84): calcd. C, 74.09; H, 4.60; N, 7.51; found, C, 73.93; H, 4.76; N, 7.65.

(4-Amino-2-p-tolyl-quinolin-3-yl)-(4-bromophenyl)-methanone (12b): 61% (0.30 g from 0.55 g) as a yellow solid, mp 210-212 ºC. R_f (20% EtOAc: hexanes): 0.52. ν_{max} (KBr) 1691 (CO), 3428 (NH_2) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.23 (s, 3H, CH_3), 6.44 (s, 2H, NH_2), 6.97 (d, *J* = 7.9 Hz, 2H, ArH), 7.22-7.29 (m, 5H, ArH), 7.38 (d, *J* = 8.0 Hz, 2H, ArH), 7.48-7.53 (m, 1H, ArH), 7.74-7.79 (m, 1H, ArH), 7.87 (d, 1H, *J*= 8.3 Hz, ArH), 8.11 (d, *J* = 8.3 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.9, 98.7, 108.9, 115.6, 119.5, 124.1, 125.5, 127.6, 128.3, 128.9, 129.3, 129.7, 130.0, 137.4, 137.5, 146.9, 150.2, 158.5, 196.9. ESI-MS: *m/z* = 317.4/319.3 $(M + 1)^+$. $C_{23}H_{17}BrN_2O$ (417.29): calcd. C, 66.20; H, 4.11; N, 6.71. Found, C, 65.98; H, 4.31; N, 6.66.

Supporting Information (see footnote on the first page of this article): Copies of ^1H NMR, ^{13}C NMR and Mass spectra of representative compounds are being provided. The copy of HSQC and HMBC spectra for compound **5a** and **7a** are also provided.

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[28] Crystal data of **3a** ($CHCl_3$-EtOH): $C_{22}H_{15}CN_2O_4l$, M = 406.81, Triclinic, P(-1), a = 8.421(1), b = 10.709(1), c = 12.077(2) Å, α = 103.33(1), β = 101.24(1), γ = 110.090(1), V = 949.5(2) Å^3, Z = 2 D_c = 1.423g cm^{-3}, μ (Mo-K_α) = 0.23 mm^{-1}, F^2 (000) = 420, colorless block, dimension 0.25x 0.20 x 0.15 mm, 4008 reflections measured (R_{int} = 0.0205), 3267 unique, wR_2 = 0.111, conventional R = 0.0418 on F^2 values of 2129 reflections with I>2σ(I), $(\Delta/\sigma)_{max}$ = 000, S = 1.022 for all data and 263 parameters. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: XSCANS (Siemens Analytical X-ray Instrument Inc.: Madison, WI, USA, 1996) for data collection and data processing; SHELXTL-NT (Bruker AXS Inc.: Madison, Wisconsin, USA, 1997) for structure determination, refinements and molecular graphics. Further details of the crystal structure investigation can be obtained from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (CCDC deposition no. 644536). (for queries related to X-ray write to maulik_prakas@yahoo.com).

[29] Crystal data of compound **5c** (EtOAc-Hexane): $C_{22}H_{12}Cl_2N_2O$, M = 391.24, Monoclinic, P2 $_{1/c}$, a = 16.207(2), b = 6.834(1), c = 17.281(2) Å, β = 107.57(1), V = 1824.7(4) Å3, Z = 4, D_c = 1.424g cm^{-3}, μ (Mo-K_α) = 0.37 mm^{-1}, F^2 (000) = 800, colorless block, dimension 0.3x 0.25 x 0.2 mm, 4539 reflections measured (R_{int} = 0.0496), 3200 unique, wR_2 = 0.1542, conventional R = 0.0626 on F values of 1543 reflections with I>2σ(I), $(\Delta/\sigma)_{max}$ = 000), S = 0.988 for all data and 244 parameters (CCDC deposition no. 644537).

[30] Crystal data of compound **7d** (DMSO-d_6 containing TMS): $C_{22}H_{14}Cl_2N_2O.(CH_3)_3Si$, M = 466.44, Triclinic, P(-1), a = 8.774(1), b = 11.963(1), c = 12.624(1)Å, α = 63.01, β = 76.76(1), γ = 72.69(1), V = 1120.36(2)Å^3, Z = 2 D_c= 1.383g cm^{-3}, μ (Mo-K_α) = 0.36mm^{-1}, F^2 (000) = 486, colorless block, dimension 0.275x 0.25 x 0.15 mm, 4637 reflections measured (R_{int} = 0.018), 3814 unique, wR_2 = 0.1734, conventional R = 0.0605 on F^2 values of 2995 reflections with I>2σ(I), $(\Delta/\sigma)_{max}$ = 000, S = 1.022 for all data and 288 parameters (CCDC deposition no. 644538).

[31] Crystal data of compound **11b** ($CHCl_3$-EtOH): $C_{22}H_{15}BrN_2O$, M = 403.27, Orthorhombic, Aba2, a = 12.616(2), b = 24.779(3), c = 11.587(1) Å, V = 3622.2(8)Å^3, Z = 8 D_c= 1.479g cm^{-3}, μ (Mo-K_α) = 2.28mm^{-1}, F^2 (000) = 1640, colorless block, dimension 0.3x 0.25 x 0.2 mm, 2096 reflections measured (R_{int} = 0.0238), 1822 unique, wR_2 = 0.0807, conventional R = 0.0476 on F^2 values of 1269 reflections with I>2σ(I), $(\Delta/\sigma)_{max}$ = 000, S = 1.002 for all data and 235 parameters (CCDC deposition no. 644535).