Microwave assisted rapid synthesis of 4-amino-3, 4-dihydroquinolin-2-ones from azetidin-2-ones

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Abstract

An efficient one-pot synthesis of 4-amino-3, 4-dihydroquinolin-2-ones from 3-(2-nitrophenyl)-1, 4-disubstituted azetidin-2-ones is described. Microwave assisted transfer hydrogenation of a nitro group followed by *in situ* β-lactam ring opening by the newly formed amino group is the key step in this synthesis.

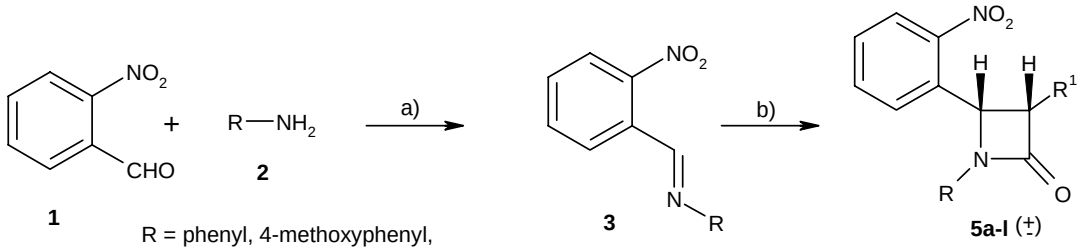
Keywords: Azetidin-2-ones, 4-amino-3,4-dihydroquinolin-2-ones, transfer hydrogenation, microwave, ketenes, imines

Introduction

Apart from the substructure of widely used antibiotics[1-3] such as penicillin, cephalosporins, monobactams etc., the azetidin-2-one (β-lactam) skeleton has been recognized as a useful building block in stereoselective syntheses of biologically important compounds.[4] This is mainly because there are many methods available to prepare them in large quantities. The strain energy associated with the four membered azetidin-2-one ring makes it susceptible for nucleophilic ring cleavage. This factor is also responsible for their application as synthon for various stereo selective syntheses of heterocyclic non β-lactam structures.[5] Also, some of the synthetic β-lactams display interesting biological activities such as inhibition of prostate specific antigens,[6] thrombin,[7] human cytomegalovirus protein,[8] cholesterol absorption,[9] human leukocyte elastase[10] and cysteine protease.[11] As a consequence, the interest of organic chemists in the synthesis of new β-lactam derivatives remains high. Although, there are numerous methods available for the construction of the β-lactam ring, a widely used method is the [2+2] cyclocondensation of ketenes to imines, a process known as the Staudinger reaction.[12-13]

Results and Discussion

In continuation of our efforts towards the synthesis of substituted β-lactams *via* the Staudinger reaction[14] and their utility as synthons[15] for the synthesis of various biologically important compounds, we herein report a rapid and practical synthesis of 4-amino-3, 4-dihydroquinolin-2-ones from 1,3-disubstituted-4-(2-nitrophenyl)azetidin-2-ones *via* reduction of the nitro group followed by the intramolecular nucleophilic opening of the azetidin-2-one ring.



Reagents and conditions: a) CH_2Cl_2, anhyd. $MgSO_4$, rt, 15 h b) R_1CH_2COCl [**4**], Et_3N, CH_2Cl_2, 0 °C to rt, 18 h

Scheme 1

Although, a solid supported synthesis of 4-amino-3, 4-dihydroquinolin-2-ones is reported, [16] it is difficult to apply it for a gram-scale preparation. We have developed a practical synthesis of dihydroquinolinones, which can be adapted for a gram-scale preparation. Microwave assisted transfer hydrogenation of the nitro group followed by the nucleophilic opening of the β-lactam ring by the newly generated amino group is the key step in this synthesis.

Monocyclic 1,3-disubstituted-4-(2-nitrophenyl) azetidin-2-ones (**5a-l**) were prepared by [2+2] cycloaddition (Staudinger reaction) reaction of ketenes, generated *in situ* from substituted acetyl chlorides using tertiary amines and imines derived from reaction of 2-nitrobenzaldehyde with various amines. The cycloaddition reaction was highly stereoselective and gave *cis* β-lactams (**5a-l**) (J = 5-6 Hz for *cis* β-lactam ring protons) in good to moderate yields (Table 1).

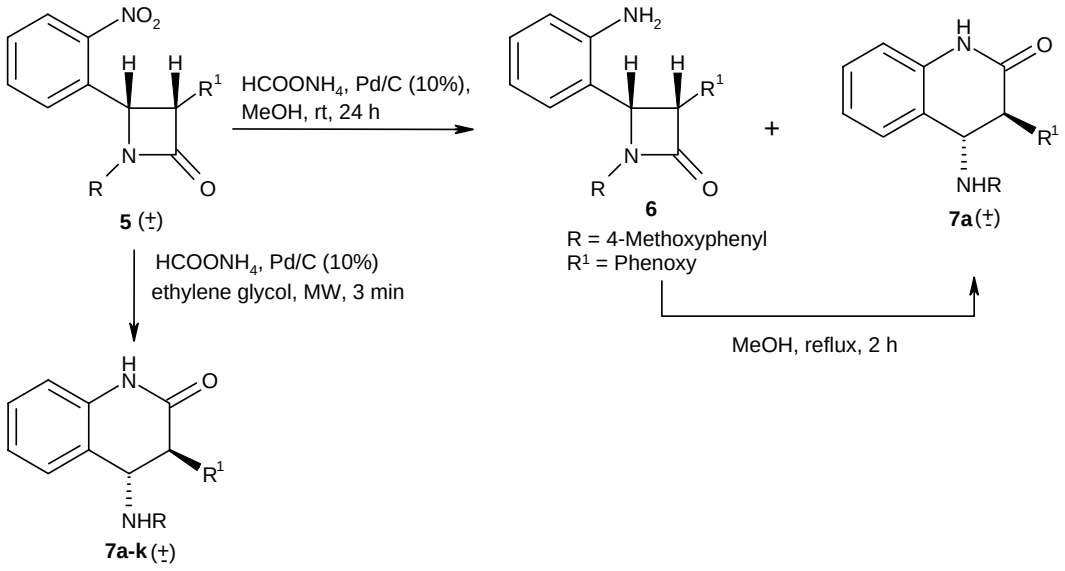
Initially the reduction of **5a** was carried out by transfer hydrogenation using ammonium formate and Pd/C (10%) in dry methanol at room temperature for 24 h. Formation of amino-β-lactam **6** was observed in good yield along with trace amounts of cyclized 4-amino-3,4-dihydroquinolin-2-one (**7a**). The cyclized product **7a** was difficult to separate from amino β-lactam **6**. However, its formation was deduced from IR and ^{1}H NMR spectra of the crude reaction mixture. The IR spectrum of amino-β-lactam **6** showed a characteristic β-lactam carbonyl absorption at 1730 cm^{-1} and amino group absorptions at 3398, 3485 cm^{-1}, while the cyclized product **7a** showed the δ-lactam carbonyl absorption at 1687 cm^{-1} and the NH absorption at 3373 cm^{-1}. ^{1}H NMR spectrum of the amino-β-lactam **6** showed two doublets at δ 5.46 and 5.61 for the C3 and C4 *cis*-β-lactam ring protons (J = 4.7 Hz for the *cis*-isomer).

Table 1. Synthesis of 4-(2-nitrophenyl)-1,3-disubstituted azetidin-2-ones **(5a-l)**

Entry No	Compound	R	R^1	Yield[a] (%)	Mp (^oC)
1	**5a**	4-Methoxyphenyl	Phenoxy	90	142
2	**5b**	4-Methoxyphenyl	Methoxy	65	158
3	**5c**	4-Methoxyphenyl	Benzyloxy	82	181
4	**5d**	4-Methoxyphenyl	Acetoxy	79	180
5	**5e**	Phenyl	Phenoxy	74	137
6	**5f**	Phenyl	Methoxy	68	135
7	**5g**	Phenyl	Benzyloxy	70	143
8	**5h**	Phenyl	Acetoxy	65	180
9	**5i**	*p*-Tolyl	Phenoxy	82	153
10	**5j**	*p*-Tolyl	Methoxy	63	157
11	**5k**	*p*-Tolyl	Benzyloxy	79	165
12	**5l**	*p*-Tolyl	Acetoxy	72	157

[a] Isolated yields.

The amino β-lactam underwent smooth cyclization by refluxing in methanol for 2 h to give the dihydroquinolin-2-one **7a** in quantitative yield. The ^{1}H NMR spectrum of **7a** showed two doublets at δ 5.13 and 5.23 for C3 and C4 *trans*-δ-lactam ring protons (J = 8.6 Hz). A direct transfer hydrogenation of **5a** was also tried in refluxing methanol for 2 h, which gave mixtures of amino-β-lactam **6** and 4-amino-3,4-dihydroqunolin-2-one **7a** along with several other unidentified products.



Scheme 2

We envisaged that transfer hydrogenation of **5a** under microwave irradiation (MW) would directly give us dihydroquinolin-2-one **7a**. The use of microwave irradiation in enhancing chemical transformation has gained considerable attention in recent years due to several advantages such as a high reaction rate and pure product formation with higher yields.[17] Although the reason for the rate enhancement is not clear, selective absorption of microwave energy by polar molecules or transition states may be responsible for the acceleration of the reaction.

Microwave irradiation of **5a** in the presence of ammonium formate and catalytic amounts of Pd/C (10%) in the presence of a small quantity of ethylene glycol was carried out in an open glass vessel using a domestic microwave. The reaction was over in just three minutes at 60% power of the microwave oven. The reaction mixture was diluted with water, methylene chloride and the catalyst was removed by filtration through a small bed of celite. The filtrate was extracted with methylene chloride and the removal of methylene chloride under reduced pressure gave almost pure product **7a** in very good yield, which was further purified by crystallization from ethyl acetate-petroleum ether mixture.

This product was formed by the reduction of the nitro group followed by the nucleophilic β-lactam ring cleavage with the newly generated amino group. Several 4-amino-3,4-dihydroquinolin-2-ones (**7a-k**) were prepared by transfer hydrogenation under microwave irradiation in very good yields (Table 2). In case of acetoxy compounds **7g**, **k** (Table 2, entries 7 and 11) a small amount of the corresponding uncyclized amino-β-lactam was also observed along with the required dihydroquinolin-2-one, which was removed by crystallization from an ethyl acetate-pet-ether mixture.

Table 2. Synthesis of 4-amino-3, 4-dihydroquinolin-2-ones **(7a-k)**

Entry No	Compound	R	R^1	Yield[a] (%)	Mp (^oC)
1	**7a**	4-Methoxyphenyl	Phenoxy	89	229
2	**7b**	4-Methoxyphenyl	Methoxy	90	208
3	**7c**	4-Methoxyphenyl	Benzyloxy	86	201
4	**7d**	Phenyl	Phenoxy	87	225
5	**7e**	Phenyl	Methoxy	81	209
6	**7f**	Phenyl	Benzyloxy	82	218
7	**7g**	Phenyl	Acetoxy	74	221
8	**7h**	*p*-Tolyl	Phenoxy	87	248
9	**7i**	*p*-Tolyl	Methoxy	86	211
10	**7j**	*p*-Tolyl	Benzyloxy	78	203
11	**7k**	*p*-Tolyl	Acetoxy	77	238

[a] Isolated yields.

In conclusion, we have demonstrated a simple and efficient one-pot preparation of 4-amino-3, 4-dihydroquinolin-2-ones from 3-(2-nitrophenyl)-1,4-disubstituted azetidin-2-ones. Microwave assisted transfer hydrogenation of the nitro group followed by the *in situ* β-lactam ring opening by the newly formed amino group is the key step in this synthesis.

Experimental Section

General Procedures. ^{1}H NMR and ^{13}C NMR Spectra were recorded in a $CDCl_3$ solution on a Bruker AC 200, Bruker MSL-300 and Bruker DRX-500 spectrometer and chemical shifts are reported in ppm downfield from TMS for ^{1}H NMR. Infrared spectra were recorded on Shimadzu FT IR-8400 using sodium chloride optics. Melting points were determined on a Thermonik Campbell melting point apparatus and were uncorrected. The microanalyses were performed on a Carlo-Erba, CHNS-O EA 1108 elemental analyzer. Microwave irradiation was carried out in an open glass vessel using a domestic microwave oven (800 Watt, BPL-make).

General procedure for the synthesis of azetidine-2-ones (5a-l)

To a solution of an imine **3** (5 mmol) and triethylamine (20 mmol) in dry methylene chloride (20 mL) was added dropwise a solution of an acid chloride **4** (7.5 mmol) in dry methylene chloride (10 mL) with stirring at 0 °C in about 20 min. The reaction mixture was then allowed to warm up to room temperature and stirred for 14 h. It was then washed with water (10 mL), saturated sodium bicarbonate (10 mL), brine (10 mL) and dried over anhyd. Na_2SO_4. The solvent was removed in vacuo to give crude azetidine-2-one, which was recrystallized from methanol to get pure azetidine-2-one.

1-(4-Methoxyphenyl)-4-(2-nitrophenyl)-3-phenoxyazetidin-2-one (5a). Yield, 1.76 g, 90%; yellow crystalline solid, mp 142 °C; IR ($CHCl_3$) 1757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.26-8.21 (m, 1H), 7.64-7.49 (m, 3H), 7.36 (d, *J* = 9.4 Hz, 2H), 7.26-7.17 (m, 2H), 7.00-6.86 (m, 5H), 6.16 (d, *J* = 5.1 Hz, 1H), 5.71 (d, *J* = 5.5 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 163.07, 157.12, 156.64, 148.02, 133.86, 130.28, 130.13, 129.32, 129.14, 129.06, 125.28, 122.58, 118.47, 116.24, 114.50, 82.11, 58.97, 55.34. Anal. Calcd. for $C_{22}H_{18}N_2O_5$: C, 67.69; H, 4.61; N, 7.18. Found: C, 67.93; H, 4.48; N, 7.51.

3-Methoxy-1-(4-methoxyphenyl)-4-(2-nitrophenyl) azetidin-2-one (5b). Yield, 1.07 g, 65%; white solid, mp 158 °C; IR ($CHCl_3$) 1753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.23-8.21 (m, 1H), 7.61-7.58 (m, 1H), 7.53-7.50 (m, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 9.2 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 2H), 5.88 (d, *J* = 5.0 Hz, 1H), 5.00 (d, *J* = 5.0 Hz, 1H), 3.77 (s, 3H), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 164.35, 156.73, 148.34, 133.82, 130.74, 130.54, 129.38, 128.94, 125.34, 118.53, 114.65, 85.65, 59.55, 59.49, 55.49. Anal. Calcd. for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.87, N, 8.53. Found: C, 62.37; H, 4.64; N, 8.49.

3-Benzyloxy-1-(4-methoxyphenyl)-4-(2-nitrophenyl) azetidin-2-one (5c). Yield, 1.66 g, 82%; white solid, mp 181 °C; IR ($CHCl_3$) 1753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.25-8.20 (m, 1H),

7.64-7.49 (m, 3H), 7.33-7.23 (m, 5H), 7.08-7.03 (m, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.91 (d, *J* = 5.1 Hz, 1H), 5.22 (d, *J* = 5.1 Hz, 1H), 4.63 (d, *J* = 11.8 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 164.20, 156.54, 148.20, 136.54, 133.84, 130.73, 130.38, 129.41, 128.91, 128.21,127.78, 127.51, 125.29, 118.42, 114.49, 83.41, 73.18, 59.49, 55.39. Anal. Calcd. for $C_{23}H_{20}N_2O_5$: C, 68.30; H, 4.99; N, 6.93. Found: C, 68.14; H, 5.10; N, 6.71.

3-Acetoxy-1-(4-methoxyphenyl)-4-(2-nitrophenyl) azetidin-2-one (5d). Yield, 1.41 g, 79%; creamy white solid, mp 180 °C; IR ($CHCl_3$) 1759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.23-8.18 (m, 1H), 7.65-7.48 (m, 3H), 7.31 (d, *J* = 9.0 Hz, 2H), 6.87 (d, *J* = 9.0 Hz, 2H), 6.36 (d, *J* = 5.5 Hz, 1H), 6.05 (d, *J* = 5.5 Hz, 1H), 3.78 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 168.18, 161.62, 156.69, 148.08, 133.75, 129.95, 129.37, 129.23, 129.08, 125.29, 118.44, 114.49, 75.76, 58.23, 55.34, 19.78. Anal. Calcd. for $C_{18}H_{16}N_2O_6$: C, 60.66; H, 4.53; N, 7.86. Found: C, 60.91; H, 4.35; N, 7.86.

4-(2-Nitrophenyl)-3-phenoxy-1-phenyl azetidin-2-one (5e). Yield, 1.33 g, 74%; creamy white solid, mp 137 °C; IR ($CHCl_3$) 1759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.29-8.24 (m, 1H), 7.68-7.51 (m, 3H), 7.47-7.32 (m, 4H), 7.28-7.25 (m, 1H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 2H), 6.22 (d, *J* = 5.5 Hz, 1H), 5.73 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 163.58, 157.11, 148.08, 136.88, 133.74, 129.89, 129.28, 129.07, 125.19, 124.79, 122.60, 117.16, 116.28, 82.13, 58.90. Anal. Calcd. for $C_{21}H_{16}N_2O_4$: C, 69.98; H, 4.48; N, 7.77. Found: C, 69.90; H, 4.58; N, 7.65.

3-Methoxy-4-(2-nitrophenyl)-1-phenyl azetidin-2-one (5f). Yield, 1.02 g, 68%; pale yellow solid, mp 135 °C; IR ($CHCl_3$) 1757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.27-8.22 (m, 1H), 7.61-7.48 (m, 3H), 7.34-7.30 (m, 4H), 7.27-7.13 (m, 1H), 5.94 (d, *J* = 5.0 Hz, 1H), 5.03 (d, *J* = 5.5 Hz, 1H), 3.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 164.77, 148.14, 136.94, 133.89, 130.41, 129.19, 128.82, 125.19, 124.58, 117.38, 117.10, 85.42, 59.30, 58.11. Anal. Calcd. for $C_{16}H_{14}N_2O_4$: C, 64.41; H, 4.74; N, 9.39. Found: C, 64.14; H, 4.72; N, 9.28.

3-Benzyloxy-4-(2-nitrophenyl)-1-phenyl azetidin-2-one (5g). Yield, 1.31 g, 70%; creamy white solid, mp 143 °C; IR ($CHCl_3$) 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.26-8.21 (m, 1H), 7.66-7.48 (m, 3H), 7.38-7.35 (m, 2H), 7.33 (d, *J* = 2.4 Hz, 2H), 7.28 (d, *J* = 1.2 Hz, 1H), 7.24 (d, *J* = 2.4 Hz, 2H), 7.18-7.12 (m, 1H), 7.08 (d, *J* = 3.5 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 5.96 (d, *J* = 5.1 Hz, 1H), 5.23 (d, *J* = 5.5 Hz, 1H), 4.65 (d, *J* = 11.7 Hz, 1H), 4.55 (d, *J* = 11.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 164.71, 148.26, 136.97, 136.54, 133.71, 130.53, 129.22, 128.85, 128.18, 127.75, 127.45, 125.22, 124.61, 117.13, 83.35, 73.19, 73.19, 59.39. Anal. Calcd. for $C_{22}H_{18}N_2O_4$: C, 70.57; H, 4.86; N, 7.48. Found: C, 70.42; H, 4.93; N, 7.42.

3-Acetoxy-4-(2-nitrophenyl)-1-phenyl azetidin-2-one (5h). Yield, 1.06 g, 65%; creamy white solid, mp 180 °C; IR ($CHCl_3$) 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.23-8.18 (m, 1H), 7.68-7.47 (m, 4H), 7.38-7.26 (m, 3H), 7.19-7.10 (m, 1H), 6.36 (d, *J* = 5.5 Hz, 1H), 6.09 (d, *J* = 5.5 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 167.92, 162.09, 148.02, 136.48, 133.61, 129.28, 129.16, 128.91, 125.16, 124.76, 117.01, 75.63, 58.08, 19.53. Anal. Calcd. for $C_{17}H_{14}N_2O_5$: C, 62.57; H, 4.33; N, 8.59. Found: C, 62.50; H, 4.28; N, 8.42.

4-(2-Nitrophenyl)-3-phenoxy-1-*p*-tolyl azetidin-2-one (5i). Yield, 1.53 g, 82%; pale yellow solid, mp 153 °C; IR ($CHCl_3$) 1759 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.26-8.21 (m, 1H), 7.64-7.50 (m, 3H), 7.32-7.13 (m, 6H), 6.99-6.87 (m, 3H), 6.17 (d, *J* = 5.5 Hz, 1H), 5.70 (d, *J* = 5.5 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 163.37, 157.17, 148.14, 134.59, 133.74, 130.13, 129.80, 129.31, 129.16, 129.01, 125.19, 122.60, 117.13, 116.31, 82.19, 58.90, 20.75; Anal. Calcd. for $C_{22}H_{18}N_2O_4$: C, 70.57; H, 4.85; N, 7.48. Found: C, 70.35; H, 4.96; N, 7.42.

3-Methoxy-4-(2-nitrophenyl)-1-*p*-tolyl azetidin-2-one (5j). Yield, 0.98 g, 63%; pale yellow solid, mp 157 °C; IR ($CHCl_3$) 1753 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.27-8.22 (m, 1H), 7.64-7.43 (m, 3H), 7.26-7.10 (m, 4H), 5.91 (d, *J* = 5.0 Hz, 1H), 5.02 (d, *J* = 5.5 Hz, 1H), 3.38 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 164.50, 148.17, 134.53, 134.29, 133.64, 130.56, 129.68, 129.19, 128.76, 125.16, 117.04, 85.42, 59.36, 20.72. Anal. Calcd. for $C_{17}H_{16}N_2O_4$: C, 65.37; H, 5.17; N, 8.97. Found: C, 65.44; H, 5.39; N, 9.03.

3-Benzyloxy-4-(2-nitrophenyl)-1-*p*-tolyl azetidin-2-one (5k). Yield, 1.53 g, 79%; creamy white solid, mp 165 °C; IR ($CHCl_3$) 1755 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.25-8.20 (m, 1H), 7.64-7.48 (m, 3H), 7.26-7.24 (m, 5H), 7.22-7.08 (m, 4H), 5.92 (d, *J* = 5.1 Hz, 1H), 5.21 (d, *J* = 5.5 Hz, 1H), 4.64 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 164.44, 148.20, 136.54, 134.50, 134.29, 133.67, 130.65, 129.68, 129.31, 128.76, 128.12, 127.69, 127.42, 125.16, 117.04, 83.35, 73.12, 59.33, 20.72. Anal. Calcd. for $C_{23}H_{20}N_2O_4$: C, 71.11; H, 5.20; N, 7.21. Found: C, 70.80; H, 5.27; N, 6.96.

3-Acetoxy-4-(2-nitrophenyl)-1-*p*-tolyl azetidin-2-one (5l). Yield, 1.23 g, 72%; pale brown solid, mp 157 °C; IR ($CHCl_3$) 1759 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.23-8.19 (m, 1H), 7.64-7.47 (m, 3H), 7.26-7.11 (m, 4H), 6.35 (d, *J* = 5.5 Hz, 1H), 6.05 (d, *J* = 5.5 Hz, 1H), 2.31 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.48 MHz) δ 168.01, 161.91, 148.14, 134.65, 134.13, 133.61, 129.74, 129.28, 129.04, 125.19, 117.04, 75.72, 58.11, 20.66, 19.62. Anal. Calcd. for $C_{18}H_{16}N_2O_5$: C, 63.52; H, 4.75; N, 8.23. Found: C, 63.71; H, 4.65; N, 7.90.

Transfer hydrogenation of 1-(4-methoxyphenyl)-4-(2-nitrophenyl)-3-phenoxyazetidin-2-one (5a). To a solution of **5a** (0.195 g, 0.5 mmol) in dry methanol (3 mL) was added ammonium formate (0.157 g, 2.5 mmol) followed by Pd/C (10%, 30 mg). This reaction mixture was stirred at room temperature under argon for 24 h, then filtered through a short celite bed, and washed with methylene chloride (15 mL). The filtrate was diluted with water (2 mL), the organic layer was separated and dried over anhyd. Na_2SO_4. The solvent was removed under vacuum to get 4-(2-aminophenyl)-1-*p*-methoxyphenyl-3-phenoxy azetidin-2-one (**6**) as a pale yellow solid (0.176 g, 98%), mp 195-199 °C; IR ($CHCl_3$) 3485, 3398, 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.41-6.76 (m, 13H), 5.61 (d, *J* = 4.7 Hz, 1H), 5.46 (d, *J* = 4.7 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 162.72, 157.10, 156.05, 147.12, 130.19, 129.38, 128.68, 127.37, 121.92, 118.55, 116.11, 115.63, 115.36, 114.67, 80.95, 56.17, 55.36.

The above solid was dissolved in methanol (10 mL) and refluxed for 2 h. The solvent was removed under reduced pressure to get 4-(4-methoxy-phenylamino)-3-phenoxy-3, 4-dihydro-1*H*-quinolin-2-one (**7a**) as a white solid, which was recrystallized from ethyl acetate-pet-ether

mixture. Yield, 0.162 g, 90%; white solid, mp 229 °C; IR ($CHCl_3$) 3373, 1686 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 10.42 (s, 1H), 7.69 (m, 1H), 7.49 (m, 3H), 7.24 (m, 5H), 7.25 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 5.23(d, *J* = 8.6 Hz, 1H), 5.13 (d, *J* = 8.6 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 167.11, 158.05, 152.16, 135.53, 128.76, 128.48, 127.49, 122.61, 121.31, 115.84, 115.51, 114.99, 114.24, 75.86, 55.97, 55.16. Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.30; H, 5.60; N, 7.77. Found: C, 73.00; H, 5.43; N, 7.65.

Transfer hydrogenation of 1-(4-methoxyphenyl)-4-(2-nitrophenyl)-3-phenoxyazetidin-2-one (5a) in refluxing methanol. To a solution of **5a** (0.195 g, 0.5 mmol) in dry methanol (3 mL) was added ammonium formate (0.157 g, 2.5 mmol) followed by Pd/C (10%, 30 mg). This reaction mixture was refluxed with stirring for 2 h till the starting material was consumed completely (TLC). The reaction mixture was cooled to room temperature, filtered through a short celite bed and the bed was washed with methylene chloride (15 mL). The filtrate was diluted with water (2 mL), the organic layer was separated and dried over anhyd. Na_2SO_4. Solvent was removed under reduced pressure to get white solid (0.172 g). It was found to be a 2:1 mixture of 4-(2-aminophenyl)-1-*p*-methoxyphenyl-3-phenoxy azetidin-2-one (**6**), 4-(4-methoxy-phenylamino)-3-phenoxy-3, 4-dihydro-1*H*-quinolin-2-one (**7a**) along with an unidentified product. The compounds **6** and **7a** (total 0.13g, 70%) was obtained as a mixture by column chromatography.

General procedure for microwave assisted synthesis of 3,4-dihydro-1*H*-quinolin-2-one (7a-k) To a solution of azetidin-2-one (**5**, 0.5 mmol), in ethylene glycol (3 mL) was added ammonium formate (2.5 mmol) followed by Pd/C (10%, 30 mg). The mixture was then subjected to microwave irradiation at low power setting (60%) for 3 min. in an open glass vessel. It was then allowed to come to room temperature, diluted with water (2 mL) and filtered through a small pad of celite. The residue was washed with methylene chloride (2 x 10 mL), the organic layer was separated, washed with brine (2 mL), dried over anhyd. Na_2SO_4 and the solvent was removed *in vacuo* to get crude quinolinone, which was recrystallized from an ethyl acetate-pet-ether mixture.
4-(4-Methoxy-phenylamino)-3-phenoxy-3,4-dihydro-1*H*-quinolin-2-one (7a). Yield, 0.160 g, 89%; physical and spectral data was same as obtained earlier.
3-Methoxy-4-(4-Methoxy-phenylamino)-3,4-dihydro-1*H*-quinolin-2-one (7b). Yield, 0.134 g, 90%; white solid, mp 208 °C; IR ($CHCl_3$) 3387, 1678 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6, 500 MHz) δ 9.69 (s, 1H), 7.06-6.94 (m, 2H), 6.73-6.69 (m, 2H), 6.48 (d, *J* = 9.2 Hz, 2H), 6.39 (d, *J* = 8.7 Hz, 2H), 4.31(d, *J* = 7.8 Hz, 1H), 3.74 (d, *J* = 7.8 Hz, 1H), 3.47 (s, 3H), 3.26 (s, 3H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 168.06, 151.76, 140.28, 135.38, 128.16, 128.09, 123.49, 122.29, 115.25, 114.39, 114.14, 77.52, 58.12, 55.30, 54.99; Anal. Calcd. for $C_{17}H_{18}N_2O_3$: C, 68.43; H, 6.09, N, 9.39. Found: C, 68.72; H, 6.20; N, 9.11.
3-Benzyloxy-4-(4-Methoxy-phenylamino)-3,4-dihydro-1*H*-quinolin-2-one (7c). Yield, 0.159 g, 85%; white solid, mp 201 °C; IR (cm^{-1}) 3367, 1680; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.41 (bs, 1H), 7.12-7.06 (m, 5H), 7.04-6.99 (m, 2H), 6.82-6.78 (m, 1H), 6.68-6.63 (m, 1H), 6.48 (d, *J* = 8.8 Hz, 2H), 6.27-6.22 (m, 2H), 4.97 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 12.1 Hz, 1H), 4.35 (d,

J = 7.7 Hz, 1H), 4.03 (bs, 1H), 3.50 (s, 3H); ^{13}C NMR (DMSO-d_6, 75.48 MHz) δ 168.31, 151.46, 141.82, 138.10, 136.87, 128.91, 128.70, 128.36, 128.15, 127.78, 124.33, 122.59, 115.66, 114.90, 114.14, 76.02, 72.08, 55.57, 55.23; Anal. Calcd. for $C_{23}H_{22}N_2O_3$: C, 73.77; H, 5.93; N, 7.48. Found: C, 73.53; H, 5.84; N, 7.32.

3-Phenoxy-4-phenylamino-3,4-dihydro-1*H*-quinolin-2-one (7d). Yield, 0.144 g, 87%; fluppy white solid, mp 225 °C; IR ($CHCl_3$) 3383, 1682 cm^{-1}; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 500 MHz) δ 9.73 (s, 1H), 6.69 (d, *J* = 7.3 Hz, 1H), 6.56-6.49 (m, 3H), 6.42-6.39 (m, 2H), 6.32-6.30 (m, 2H), 6.24-6.22 (m, 3H), 6.01 (d, *J* = 7.8 Hz, 2H), 5.94-5.91 (m, 1H), 4.29 (d, *J* = 9.1 Hz, 1H), 4.25 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 165.98, 157.27, 146.33, 134.85, 127.60, 127.49, 127.14, 126.16, 122.77, 121.20, 119.95, 115.34, 114.81, 114.27, 111.45, 74.95, 53.01; Anal. Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.33; H, 5.50, N, 8.48. Found: C, 76.51; H, 5.58; N, 8.19.

3-Methoxy-4-phenylamino-3,4-dihydro-1*H*-quinolin-2-one (7e). Yield, 0.108 g, 81%; white crystalline solid, mp 209 °C; IR ($CHCl_3$) 3392, 1687 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.08 (s, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.14 (m, 3H), 6.96 (m, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.72 (m, 1H), 6.62 (d, *J* = 7.8 Hz, 2H), 4.64 (d, *J* = 7.3 Hz, 1H), 4.06 (d, *J* = 7.3 Hz, 1H), 3.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 169.20, 146.16, 135.17, 129.38, 129.25, 128.82, 123.83, 123.57, 118.87, 116.01, 113.97, 77.90, 58.90, 55.37; Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.61; H, 6.02; N, 10.44. Found: C, 71.32; H, 6.00; N, 10.15.

3-Benzyloxy-4-phenylamino-3,4-dihydro-1*H*-quinolin-2-one (7f). Yield, 0.141 g, 82%; white solid, mp 218 °C; IR ($CHCl_3$) 3389, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.79 (s, 1H), 7.34 (m, 6H), 7.12 (m, 3H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.78 (m, 1H), 6.53 (d, *J* = 7.8 Hz, 2H), 4.97 (d, *J* = 11.7 Hz, 1H), 4.70 (m, 2H), 4.28 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (DMSO-d_6, 75.48 MHz) δ 168.22, 147.80, 138.10, 136.94, 129.15, 128.88, 128.82, 128.42, 128.18, 127.87, 124.03, 122.68, 116.61, 115.69, 112.76, 75.84, 72.05, 54.26. Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.71; H, 5.86; N, 8.13. Found: C, 76.51; H, 6.00; N, 7.90.

3-Acetoxy-4-phenylamino-3,4-dihydro-1*H*-quinolin-2-one (7g). Yield, 0.109 g, 74%; fluppy white solid, mp 221 °C; IR ($CHCl_3$) 3381, 1757, 1691 cm^{-1}; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 10.24 (s, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.13 (m, 4H), 6.93 (m, 2H), 6.68 (d, *J* = 7.9 Hz, 2H), 5.51 (d, *J* = 11.7 Hz, 1H), 4.93 (d, *J* = 11.0 Hz, 1H), 1.89 (s, 1H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 169.75, 165.77, 146.81, 135.18, 128.50, 128.28, 126.04, 123.51, 122.51, 117.10, 115.36, 112.73, 70.94, 53.36, 19.87. Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.89; H, 5.45; N, 9.45; Found: C, 68.71; H, 5.20; N, 9.12.

3-Phenoxy-4-*p*-tolylamino-3,4-dihydro-1*H*-quinolone-2-one (7h). Yield, 0.150 g, 87%; fluppy white solid, mp 248 °C; IR ($CHCl_3$) 3360, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 500 MHz) δ 9.73 (s, 1H), 6.69 (d, *J* = 7.3 Hz, 1H), 6.56-6.51 (m, 3H), 6.33-6.30 (m, 2H), 6.26-6.23 (m, 5H), 5.94 (d, *J* = 8.3 Hz, 2H), 4.25 (s, 2H), 1.53 (s, 3H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 165.97, 157.27, 143.82, 134.86, 128.01, 127.64, 127.14, 126.32, 124.22, 122.85, 121.22, 119.98, 114.84, 114.29, 111.72, 74.86, 53.42, 18.77; Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.71; H, 5.86; N, 8.14. Found: C, 76.53; H, 5.68; N, 7.92.

3-Methoxy-4-*p*-tolylamino-3,4-dihydro-1-*H*-quinolin-2-one (7i). Yield, 0.121 g, 86%; white crystalline solid, mp 211 °C; IR ($CHCl_3$) 3373, 1689 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.85 (s, 1H), 7.36-7.23 (m, 2H), 7.08-6.89 (m, 4H), 6.63 (d, *J* = 6.7 Hz, 2H), 4.69 (d, *J* = 7.4 Hz, 1H), 4.14 (d, *J* = 7.4 Hz, 1H), 3.58 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (DMSO-d_6, 75.48 MHz) δ 167.74, 145.31, 136.58, 129.38, 128.50, 128.34, 124.83, 124.13, 122.24, 115.34, 112.72, 78.05, 57.93, 53.94, 19.97; Anal. Calcd. for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.44; N, 9.92. Found: C, 72.10; H, 6.53; N, 9.83.

3-Benzyloxy-4-*p*-tolylamino-3,4-dihydro-1-*H*-quinolin-2-one (7j). Yield, 0.139 g, 78%; fluppy white solid, mp 203 °C; IR ($CHCl_3$) 3371, 1677 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6, 500 MHz) δ 8.46 (bs, 1H), 7.25 (m, 5H), 7.20-7.17 (m, 2H), 6.95-6.80 (m, 2H), 6.39 (m, 2H), 4.83 (d, *J* = 11.9 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 7.4 Hz, 1H) 4.24 (bs, 1H), 2.16 (s, 3H); ^{13}C NMR (DMSO-d_6, 75.48 MHz) δ 168.11, 145.31, 137.93, 136.74, 129.41, 128.68, 128.56, 128.19, 127.95, 127.64, 124.92, 124.07, 122.45, 115.49, 112.81, 75.76, 71.88, 54.45, 20.06; Anal. Calcd. for $C_{23}H_{22}N_2O_2$: C, 77.06; H, 6.20; N, 7.82. Found: C, 76.81; H, 6.10; N, 7.56.

3-Acetoxy-4-*p*-tolylamino-3,4-dihydro-1-*H*-quinolin-2-one (7k). Yield, 0.119 g, 77%; fluppy white solid, mp 238 °C; IR ($CHCl_3$) 3379, 1755, 1693 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6, 500 MHz) δ 9.94 (s, 1H), 6.97 (d, *J* = 7.3 Hz, 1H), 6.80-6.77 (m, 2H), 6.58-6.51 (m, 4H), 6.22 (d, *J* = 8.3 Hz, 2H), 5.09 (d, *J* = 12.5 Hz, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 1.79 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (DMSO-d_6, 125.76 MHz) δ 169.16, 165.39, 144.31, 134.92, 128.59, 127.78, 125.58, 125.41, 123.45, 122.01, 114.91, 112.46, 70.54, 53.13, 19.58, 19.31; Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.65; H, 5.86; N, 9.03. Found: C, 69.53; H, 5.67; N, 9.00.

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