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One-pot multicomponent synthesis of substituted 5,7-dihydro-1,6-naphthyridines and 5,6,7,8-tetrahydroquinolines

Research article

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Abstract: An one-pot approach was developed for the synthesis of substituted 5,7-dihydro-1,6-naphthyridines and 5,6,7,8-tetrahydroquinolines with moderate to good yields. This pathway is a modified two-step synthesis of Kröhnke pyridine and involves a four-component tandem reaction of *N*-phenacylpyridinium bromide, aromatic aldehydes, substituted or nitrogen-containing cyclic ketones and a nitrogen source. This multi-component reaction is performed using microwave irradiation heating of the reaction substrates under an environment of NH_4OAc/HOAc.

Keywords: *Substituted dihydro-1,6-naphthyridines • 5,6,7,8-tetrahydroquionolines • Kröhnke synthesis • Microwave irradiation • One-pot multicomponent condensation*

1. Introduction

The polysubstituted pyridines, especially terpyridines, are prominent building blocks in supramolecular chemistry with their π-stacking and directional H-bonding ability [1,2]. The pyridyl heterocyclic core is also a widespread subunit in numerous natural products and pharmaceuticals [3,4]. These facts provide the basis for the development of new efficient synthetic pathways for pyridines [5-8]. Polysubstituted pyridines have been synthesized using various methods and procedures. Two methods, the two-step Kröhnke [9-14] and the Hantzsch-type synthesis [16,17], have demonstrated distinct advantages over the other procedures. The two-step Kröhnke synthesis via the cyclocondensation of pyridinium salts with α,β-unsaturated ketones in the presence of a mixture of ammonium acetate and acetic acid, allows for the introduction of different aryl groups at the 2,4,6-positions of the pyridine ring and can also be used to prepare oligopyridine derivatives. The drawback of this method is that pyridinium salts and α,β-unsaturated ketones have to be prepared first, which has since been overcome by the one-pot Kröhnke procedure for preparing polysubstituted and annulated pyridines [15]. The second method is the Hantzsch-type synthesis via the cyclocondensation of an aromatic aldehyde, acetophenone and a nitrogen derivative such as ammonium acetate or urea [16,17]. The key step of the Hantzsch-type is the Michael addition of a second acetophenone to the α,β-unsaturated ketones formed *in situ* from the aldol condensation of an aromatic aldehyde with acetophenone to form 1,5-diketone. The pyridines with the same aryl groups at 2,6-positions are usually prepared in moderate yields by refluxing the three component mixtures in suitable solvent for several hours. Several new improvements to these procedures have been developed including solvent free reaction conditions [18,19], reaction in aqueous media, [20] one-pot procedure under microwave irradiation [21,22] and direct heating α,β-unsaturated ketones and ammonium acetate in the presence of a catalyst amount of acetic acid [23]. Recently, we found that the one-pot condensation reaction of aromatic aldehyde and cyclic ketone with *N*-phenacylpyridinium bromide in the

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presence of ammonium acetate with a catalytic amount of acetic acid results in bicyclic annulated pyridines with additional benzylidene groups in high yields [15]. To continue with our efforts for developing new efficient synthesis methods for the polysubstituted pyridines, we would like to report the results of the one-pot reactions of pyridinium bromide, aromatic aldehydes with substituted or nitrogen-containing cyclic ketones.

2. Experimental

2.1. Materials and Apparatus

Melting points were taken on a hot-plate microscope apparatus. IR spectra were obtained on a Bruker Tensor 27 spectrometer (KBr disc). ^{1}H NMR spectra were recorded with a Bruker AV-600 spectrometer with $CDCl_3$ as solvent and TMS as an internal standard. HPLC/MS were measured using a Fennigan LCQ Deca XP MAX instrument. Microwave heating was conducted with a Lingjiang LMMC-201 Microwave reactor (Nanjing, China). Aromatic aldehydes, substituted cycclohexanone, 4-methyl and 4-ethyl piperidinone and other reagents are commercial grade. All the solvents used were purified by standard techniques. *N*-phenacylpyridinium bromide and *N*-4-phenylphenacylpyridinium bromide was prepared according to published method [13]. The reaction process was monitored by TLC.

2.2. General procedure for the preparation of 5,7-dihydro-1,6-naphthyridine

Using a 50 mL flask, *N*-phenacylpyridinium bromide (1.2 mmol, 0.280 g), aromatic aldehyde (1.0 mmol), piperidinone (1.0 mmol), ammonium acetate (3.0 g) and acetic aid (2.0 mL) were added. Pour this mixture into a microwave and heat for approximately 2 to 4 minutes (130 W). Allow to cool and dilute the reaction mixture with 50 mL of water. Filter to collect the resulting precipitate. The crude product was recrystallizated with ethanol to produce a pure solid sample for further analysis.

2.2.1. 4a

2-phenyl-4-*p*-methylphenyl-6-methyl-8-*p*-methylphenylidene-5,7-dihydro-1,6-naphthyridine, 76%, mp. 139.0-140.5°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (s, 1H, ArH), 8.16 (d, *J* = 7.8Hz, 2H, PhH), 7.54-7.50 (m, 3H, ArH, PyH), 7.44 (t, *J* = 7.2Hz, 1H, CH=), 7.36 (d, *J* = 7.8Hz, 2H, PhH), 7.32-7.29 (m, 4H, PhH, ArH), 7.26 (t, *J* = 7.8Hz, 2H, PhH), 3.79 (s, 2H, CH_2), 3.65 (s, 2H, CH_2), 2.47 (s, 3H, CH_3), 2.43 (d, *J* = 5.4Hz, 6H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$) δ 152.7, 148.6, 147.0, 137.6, 136.2, 135.0, 133.8, 132.6, 130.4, 127.7, 127.3, 127.1, 126.9, 126.8, 126.7, 126.5, 125.3, 125.0, 124.1, 117.7, 54.5, 54.2, 43.7, 19.4. IR (KBr) υ 2936 (w), 2769 (w) 1589 (m), 1540 (m) 1488 (s), 1434 (m) 1086 (s), 1009 (m), 827 (s) cm^{-1}; MS (m/e): 416.67.

2.2.2. 4b

2-phenyl-4-*p*-chlorophenyl-6-methyl-8-*p*-chlorophenylidene-5,7-dihydro-1,6-naphthyridine, 79%, mp 178.5-179.5°C. ^{1}H NMR (600MHz, $CDCl_3$) δ 8.28 (s, 1H, ArH), 8.13 (d, *J* = 7.2Hz, 2H, PhH), 7.52-7.48 (m, 5H, ArH), 7.45 (d, *J* = 7.2Hz, 2H, PyH), 7.41-7.39 (m, 2H, PhH), 7.37-7.32 (m, 4H, PhH, =CH), 3.73 (s, 2H, CH_2), 3.59 (s, 2H, CH_2), 2.43 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$) δ 155.0, 150.3, 147.8, 139.1, 136.9, 135.7, 134.5, 133.4, 130.9, 129.9, 129.1, 128.9, 128.7, 128.5, 126.9, 126.3, 126.1, 119.7, 56.2, 55.9, 45.7. IR (KBr) υ 3018 (w), 2975 (w) 2935 (m), 1582 (m), 1542 (s), 1511 (s), 1439 (s), 1384 (s), 1321 (w), 1248 (w), 1176 (w), 1113 (m), 1040 (w), 973 (w), 818 (m) cm^{-1}; MS (m/e): 457.60.

2.2.3. 4c

2-phenyl-4-*p*-methoxyphenyl-6-methyl-8-*p*-methoxyphenylidene-5,7-dihydro-1,6-naphthyridine, 49%, mp 155.8-157.6°C. ^{1}H NMR (600MHz, $CDCl_3$) δ 8.19 (s, 1H, PhH), 8.06 (d, *J* = 7.2Hz, 2H, PhH), 7.42-7.40 (m, 3H, PhH, PyH), 7.35-7.33 (m, 1H, CH=), 7.30 (d, *J* = 8.4Hz, 2H, ArH), 7.24 (d, *J* = 8.4Hz, 2H, ArH), 6.94 (d, *J* = 8.4Hz, 2H, ArH), 6.88 (d, *J* = 8.4Hz, 2H, ArH), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, CH_3), 3.70 (s, 2H, CH_2), 3.56 (s, 2H, CH_2), 2.35 (s, 3H, CH_3); ^{13}C NMR (150MHz, $CDCl_3$) δ 158.0, 157.1, 153.0, 149.1, 146.9, 138.0, 129.9, 129.4, 128.4, 128.2, 127.1, 126.9, 125.3, 124.4, 117.8, 112.3, 112.1, 54.9, 54.5, 53.7, 53.6, 44.0; IR (KBr) υ 2947 (w), 2836 (w), 1606 (m), 1543 (w), 1509 (s), 1441 (w), 1383 (m), 1292 (w), 1247 (vs), 1176 (m), 1115 (w), 1032 (w), 917 (w), 833 (w), 771 (w) cm^{-1}; MS: 448.53.

2.2.4. 4d

2-phenyl-4-*p*-methylphenyl-6-ethyl-8-*p*-methylphenylidene-5,7-dihydro-1,6-naphthyridine, 75%, mp.157.5-159.6°C. ^{1}H NMR (600MHz, $CDCl_3$) δ 8.29 (s, 1H, PhH), 8.12 (d, *J* = 7.8Hz, 2H, PhH), 7.50-7.46 (m, 4H, ArH, PyH), 7.40 (s, 1H, CH=), 7.33 (s, 2H, ArH), 7.27-7.25 (m, 4H, ArH), 7.21 (d, *J* = 7.8Hz, 2H, PhH), 3.82 (s, 2H, CH_2), 3.68 (s, 2H, CH_2), 2.54 (s, *J* = 7.2Hz, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.02 (t, *J* = 7.2Hz, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$) δ 155.0, 150.7, 147.9, 139.2, 137.0, 135.8, 134.5, 133.5, 133.0, 130.9, 129.9, 129.1, 128.9, 128.7, 128.5, 126.9, 126.4, 126.2, 119.7, 53.7, 51.5, 12.4. IR (KBr) υ 2970 (w), 2745 (w), 1587 (m), 1488 (s), 1487 (s), 1383 (m), 1088 (s), 970 (w), 832 (s), 724 (m), 692 (m), 478 (w). MS (m/e): 430.53.

2.2.5. 4e

2-phenyl-4-*p*-chlorophenyl-6-ethyl-8-*p*-chlorophenylidene-5,7-dihydro-1,6-naphthyridine, 78%, mp.181.0-182.0°C. ^{1}H NMR (600MHz, $CDCl_3$) δ 8.28 (s, 1H, ArH), 8.13 (d, *J* = 7.8Hz, 2H, PhH), 7.51 (d, *J* = 4.2Hz, 2H, ArH), 7.49 (s, 1H, PyH), 7.48 (t, *J* = 7.2Hz, 1H, CH=), 7.45 (t, *J* = 7.2Hz, 1H, ArH), 7.40 (d, *J* = 7.2Hz, 2H, ArH), 7.36(d, *J* = 7.8Hz, 2H, PhH), 7.33(d, *J* = 7.8Hz, 2H, ArH), 7.28(s, 1H, PhH), 3.79 (s, 2H, CH_2), 2.58 (d, 2H, *J* = 7.2Hz, CH_2), 1.05 (t, 3H, *J* = 7.2Hz, CH_3). ^{13}C NMR (150MHz, $CDCl_3$) δ 155.0, 150.7, 147.9, 139.2, 137.0, 135.8, 134.5, 133.5, 130.9, 129.9, 129.1, 128.9, 128.7, 128.5, 126.9, 126.4, 126.2, 119.7, 53.7, 51.5, 12.4. IR (KBr) υ: 3449 (s), 2970 (w), 1587 (m), 1488 (s), 1487 (s), 1383 (m), 1088 (s), 970 (w), 832 (s), 724 (m) cm^{-1}. MS (m/e): 470.60.

2.3. General procedure for the preparation of 8-arylidene-5,6,7,8-tetrahydroquinolines 6a-7j

Using a 50 mL flask, substituted cyclohexanone (**5a-5b**, 1.0 mmol), aromatic aldehyde (**3a-3e**, 2.0 mmol), pyridinium bromide (**1a-1b**, 1.2mmol), ammonium acetate (3.0 g) and acetic aid (2.0 mL) were added. Pour this mixture into a microwave and heat for approximately 2 to 4 minutes (130 W). Allow to cool and dilute the reaction mixture with 50 mL of water. Filter to collect the resulting precipitate. The crude product was recrystallized with ethanol to produce a pure solid sample for further analysis.

2.3.1. 6a

2-phenyl-4-*p*-chlorophenyl-6-methyl-8-*p*-chlorophenylidene-5,6,7-trihydroquinoline, yellow solid; mp 191°C. IR (KBr): 2953(w), 2872(w), 1602(w), 1577(m), 1537(w), 1488(s), 1429(m), 1402(w), 1238(w), 1147(w), 1090(s), 1008(m), 827(s), 768(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.24 (s, 1H, PyH), 8.11 (d, *J* = 7.2Hz, 2H, PhH), 7.46 (m, 5H, PhH, ArH), 7.39 (m, 5H, =CH, ArH), 7.31 (d, *J* = 8.4Hz, 2H, ArH), 3.07 (d, *J* = 15Hz, 1H, CH_2), 2.71 (d, *J* = 15Hz, 1H, CH_2), 2.41 (m, 2H, CH_2), 1.86 (s, 1H, CH), 1.02 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 153.1, 151.4, 148.5, 138.38, 137.0, 135.1, 134.7, 133.2, 131.6, 130.7, 130.1, 129.2, 127.8, 127.4, 125.9, 118.2, 35.3, 28.4, 20.7. MS: m/s = 455.53.

2.3.2. 6b

2-phenyl-4-*p*-methylphenyl-6-methyl-8-*p*-methylphenylidene-5,6,7-trihydroquinoline, light yellow solid; mp 143.2~145.0°C. IR (KBr): 2952(w), 1628(m), 1580(m), 1537(w), 1511(m), 1431(w), 1382(s), 1158(w), 875(w), 818(m), 770(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.26 (s, 1H, PyH), 8.12 (s, 2H, PhH), 7.46 (m, 3H, PhH), 7.38 (s, 3H, ArH), 7.26 (m, 4H, =CH, ArH), 7.20 (s, 2H, ArH), 3.14 (s, 1H, CH_2), 2.75 (s, 1H, CH_2), 2.45(m, 3H, CH_3), 2.39 (d, *J* = 6.6Hz, 3H, CH_3), 1.85 (s, 1H, CH_2), 1.54 (s, 1H, CH_2), 1.24 (d, *J* = 6.6Hz, 1H, CH), 1.00 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 156.3, 153.9, 151.9, 143.0, 138.9, 137.6, 135.0, 132.2, 130.2, 129.3, 128.5, 127.6, 126.3, 123.3, 119.8, 38.7, 36.2, 32.6, 24.3, 20.8. MS: m/s = 415.90.

2.3.3. 6c

2-phenyl-4-*p*-methoxyphenyl-6-mehtyl-8-*p*-methoxyphenylidene-5,6,7-trihydroquinoline, yellow solid; mp 138°C. IR (KBr): 2952(w), 2832(w), 1605(m), 1510(s), 1436(m), 1291(m), 1250(s), 1177(m), 1033(m), 836(m), 771(m) cm^{-1}.^{1}H NMR (600MHz, $CDCl_3$): δ 8.24 (s, 1H, PyH), 8.12 (d, *J* = 6.6Hz, 2H, PhH), 7.49 (m, 5H, PhH, ArH), 7.39 (m, 1H, =CH), 7.31 (d, *J* = 8.4Hz, 2H, ArH), 7.00 (d, *J* = 8.4Hz, 2H, ArH), 6.94 (d, *J* = 9.0Hz, 2H, ArH), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.13 (m, 1H, CH_2), 2.75 (m, 1H, CH_2), 2.44 (m, 2H, CH_2), 1.85 (s, 1H, CH), 1.02 (d, *J* = 6.6Hz, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 159.3, 158.4, 153.7, 152.7, 150.0, 139.7, 134.4, 132.0, 131.1, 130.0, 128.6, 127.4, 126.8, 119.6, 113.6, 55.3, 36.5, 29.4, 21.7. MS: m/s = 447.87.

2.3.4. 6d

2-phenyl-4-*p*-dimethylaminophenyl-6-methyl-8-*p*-dimethylaminophenylidene-5,6,7-trihydroquinoline, yellow brown solid; mp 174°C. IR (KBr): 2948(w), 2864(w), 1608(s), 1519(s), 1439(m), 1353(s), 1227(w), 1194(m), 1159(m), 1061(w), 945(w), 819(m), 768(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.21 (s, 1H, PyH), 8.14 (d, *J* = 7.8Hz, 2H, PhH), 7.45 (m, 5H, PhH, ArH), 7.37 (m, 1H, =CH), 7.29 (d, *J* = 8.4Hz, 2H, ArH), 6.81 (d, *J* = 8.4Hz, 2H, ArH), 6.71 (d, *J* = 8.4Hz, 2H, ArH), 3.20 (d, *J* = 15.0Hz, 1H, CH_2), 3.02 (s, 6H, $N(CH_3)_2$), 2.99 (s, 3H, $N(CH_3)_2$), 2.82 (m, 1H, CH_2), 2.51 (m, 2H, CH_2), 1.82 (s, 1H, CH), 1.03 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 151.8, 148.3, 147.5, 138.3, 131.2, 129.4, 128.1, 126.8, 126.1, 125.1, 117.5, 110.2, 38.8, 35.1, 34.6, 27.8, 20.1. MS: m/s = 473.80.

2.3.5. 6e

2-phenyl-4-*m*-nitrophenyl-6-mehtyl-8-*m*-nitrophenylidene-5,6,7-trihydroquinoline, white solid; mp 205.7~207.1°C. IR (KBr): 2924(w), 2858(w), 1644(s), 1529(vs), 1343(w), 1034(m), 904(w), 820(m), 695(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.33 (s, 3H, ArH), 8.28 (s, 1H, PyH), 8.15 (s, 3H, ArH), 7.80 (d, *J* = 6.0Hz, 1H, PhH), 7.73 (s, 1H, PhH), 7.70 (d, *J* = 7.2Hz, 1H, PhH), 7.58 (m, 2H, ArH), 7.52 (s, 2H, PhH), 7.46 (s,

1H, =CH), 3.08 (m, 1H, CH_2), 2.69 (s, 1H, CH_2), 2.51 (d, *J* = 7.8Hz, 2H, CH_2), 1.92 (s, 1H, CH), 1.04 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 58.0, 154.7, 148.3, 141.3, 134.7, 129.5, 128.8, 127.6, 126.9, 123.6, 122.8, 118.7, 35.6, 33.1, 31.2, 29.2, 21.7. MS: m/s = 477.73.

2.3.6. 6f

2-*p*-biphenyl-4-*p*-chlorophenyl-6-methyl-8-*p*-chlorophenylidene-5,6,7-trihydroquinoline, white solid; mp 182°C. IR (KBr): 2957(w), 1578(w), 1533(m), 1488(s), 1439(m), 1378(w), 1154(vw), 1088(s), 1011(m), 831(s), 765(m) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.26 (s, 1H, PyH), 8.20 (d, *J* = 7.8Hz, 2H, PhH), 7.72 (d, *J* = 7.8Hz, 2H, PhH), 7.67 (d, *J* = 7.2Hz, 2H, PhH), 7.54 (s, 1H, =CH), 7.46 (m, 4H, ArH), 7.42 (d, *J* = 8.4Hz, 2H, ArH), 7.38 (d, *J* = 7.8Hz, 3H, PhH), 7.33 (d, *J* = 8.4Hz, 2H, ArH), 3.09 (d, *J* = 9.0Hz, 1H, CH_2), 2.73 (m, 1H, CH_2), 2.45 (m, 2H, CH_2), 1.87 (s, 1H, CH), 1.02 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.1, 150.9, 147.9, 140.2, 139.2, 136.7, 134.8, 132.6, 131.0, 129.6, 128.6, 127.4, 126.9, 125.9, 125.6, 118.1, 34.7, 27.8, 20.1. MS: m/s = 531.67.

2.3.7. 6g

2-*p*-biphenyl-4-*p*-methylphenyl-6-methyl-8-*p*-methylphenylidene-5,6,7-trihydroquinoline, yellow solid; mp 155°C. IR (KBr): 2948(m), 2919(m), 1577(w), 1535(m), 1511(s), 1487(w), 1437(m), 1378(w), 1241(w), 1111(w), 817(m), 765(m) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.29 (s, 1H, PyH), 8.21 (d, *J* = 6.6Hz, 2H, PhH), 7.70 (m, 4H, PhH), 7.54 (s, 1H, =CH), 7.40 (m, 5H, ArH, PhH), 7.29 (s, 4H, ArH), 7.22 (d, *J* = 7.2Hz, 2H, ArH), 3.16 (d, *J* = 15.0Hz, 1H, CH_2), 2.77 (d, *J* = 16.2Hz, 1H, CH_2), 2.50 (m, 1H, CH_2), 2.44 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.86 (s, 1H, CH_2), 1.54 (s, 1H, CH), 1.02 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 153.3, 152.7, 150.5, 141.4, 140.8, 138.6, 137.7, 136.8, 136.5, 135.3, 129.8, 128.8, 127.8, 127.1, 119.7, 36.4, 36.1, 29.4, 21.7, 21.3. MS: m/s = 492.00.

2.3.8. 6h

2-*p*-biphenyl-4-phenyl-6-methyl-8-phenylidene-5,6,7-trihydroquinoline, Yellow solid; mp 165°C. IR (KBr): 2945w), 1577(w), 1536(m), 1490(m), 1444(m), 1403(m), 1375(w), 1264(w), 1076(w), 839(w), 764(m) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.33 (s, 1H, PyH), 8.22 (d, *J* = 8.4Hz, 2H, PhH), 7.72 (d, *J* = 8.4Hz, 2H, PhH), 7.67 (d, *J* = 7.8Hz, 2H, PhH), 7.57 (s, 1H, =CH), 7.50(m, 6H, PhH), 7.40 (m, 5H, PhH), 7.25 (m, 2H, PhH), 3.16 (d, *J* = 15.0Hz, 1H, CH_2), 2.76 (d, *J* = 13.2Hz, 1H, CH_2), 2.46 (m, 2H, CH_2), 1.88 (s, 1H, CH), 1.03 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.9, 152.1, 141.0, 140.3, 138.0, 137.8, 135.4, 129.4, 128.4, 128.0, 127.7, 126.7, 126.28, 119.3, 35.9, 28.9, 21.2. MS: m/s = 463.60.

2.3.9. 6i

2-*p*-biphenyl-4-*p*-methoxyphenyl-6-mehtyl-8-*p*-methoxy phenylidene-5,6,7-trihydroquinoline, yellow solid; mp 131°C. IR (KBr): 2949(w), 1607(m), 1510(s), 1439(m), 1382(w), 1292(m), 1249(s), 1176(s), 1112(w), 1031(m), 834(s), 733(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.27 (s, 1H, PyH), 8.22 (d, *J* = 8.4Hz, 2H, PhH), 7.71 (d, *J* = 8.4Hz, 2H, PhH), 7.66 (d, *J* = 7.8Hz, 2H, PhH), 7.53 (s, 1H, =CH), 7.46 (d, *J* = 6.0Hz, 4H, ArH), 7.33 (m, 3H, PhH), 7.01 (d, *J* = 9.0Hz, 2H, ArH), 6.95(d, *J* = 8.4Hz, 2H, ArH), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.15 (d, *J* = 15Hz, 1H, CH_2), 2.77 (d, *J* = 14.4Hz, 1H, CH_2), 2.42 (m, 2H, CH_2), 1.84 (s, 1H, CH), 1.03 (d, *J* = 6.6Hz, 3H, CH_3). MS: m/s = 524.07.

2.3.10. 6j

2-*p*-biphenyl-4-*p*-dimethylaminophenyl-6-methyl-8-*p*-dimethylaminophenylidene-5,6,7-trihydroquinoline, yellow solid; mp 196°C. IR (KBr): 2922(w), 1610(m), 1519(m), 1441(w), 1384(m), 1195(w), 1160(w), 947(w), 820(w), 765(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.23(d, *J* = 8.4Hz, 3H, PhH, PyH), 7.71 (d, *J* = 7.8Hz, 2H, PhH), 7.67 (d, *J* = 7.8Hz, 2H, PhH), 7.53 (s, 1H, =CH), 7.46 (s, 4H, ArH), 7.31 (m, 3H, PhH), 6.82 (d, *J* = 7.8Hz, 2H, ArH), 6.78 (d, *J* = 7.8Hz, 2H, ArH), 3.21 (d, *J* = 15Hz, 1H, CH_2), 3.03 (m, 12H, $N(CH_3)_2$), 2.83 (m, 1H, CH_2), 2.48 (m, 2H, CH_2), 1.84 (s, 1H, CH), 1.04 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.9, 149.7, 148.9, 140.6, 138.7, 132.6, 130.8, 129.5, 128.5, 127.57, 126.8, 118.9, 111.6, 40.2, 36.5, 36.0, 29.2, 21.5. MS: m/s = 549.80.

2.3.11. 7a

2-phenyl-4-*p*-chlorophenyl-6-*t*-butyl-8-*p*-chlorophenylidene-5,6,7-trihydroquinoline, white solid; mp 199°C. IR (KBr): 3035(vw), 2958(m), 2867(w), 1651(w), 1598(w), 1534(m), 1490(s), 1430(w), 1363(w), 1235(w), 1092(m), 1011(w), 829(m), 775(w) cm^{-1}. ^{1}H NMR (600MHz, $CDCl_3$): δ 8.10 (s, 1H, PyH), 8.04 (d, *J* = 7.8Hz, 2H, PhH), 7.41 (m, 10H, ArH, PhH, =CH), 7.25 (d, *J* = 7.8Hz, 2H, ArH), 3.16 (d, *J* = 14.4Hz, 1H, CH_2), 2.68 (d, *J* = 16.2Hz, 1H, CH_2), 2.41 (m, 1H, CH_2), 2.22 (m, 1H, CH_2), 1.42 (m, 1H, CH), 0.80 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.2, 150.9, 147.7, 137.5, 136.1, 135.4, 134.7, 132.3, 130.6, 129.1, 128.2, 126.9, 125.0, 118.0, 42.7, 30.7, 27.4, 25.4. MS: m/s = 497.87.

2.3.12. 7b

2-phenyl-4-*p*-methylphenyl-6-*t*-butyl-8-*p*-methylphenylidene-5,6,7-trihydroquinoline, white solid; mp 194°C. IR (KBr): 3022(w), 2957(s), 2865(m), 1652(w), 1577(w), 1537(w), 1511(m), 1431(w), 1363(w), 1236(w), 1109(w), 1021(w), 817(m), 720(w) cm^{-1}. ^{1}H

NMR (600MHz, $CDCl_3$): δ 8.01 (s, 1H, PyH), 7.94 (s, 1H, PhH), 7.30 (d, *J* = 7.8Hz, 3H, PhH), 7.20 (d, *J* = 7.8Hz, 3H, ArH, =CH), 7.09 (m, 6H, ArH), 6.80 (m, 1H, PhH), 3.10 (d, *J* = 14.4Hz, 1H, CH_2), 2.63 (d, *J* = 16.2Hz, 1H, CH_2), 2.32 (m, 1H, CH_2), 2.24 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.11 (m, 1H, CH_2), 1.30 (m, 1H, CH), 0.68 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 153.7, 153.0, 150.6, 139.7, 137.6, 136.7, 136.1, 135.3, 129.6, 129.1, 128.9, 128.6, 127.6, 119.8, 44.5, 32.5, 29.4, 29.1, 27.3, 21.3. MS: m/s = 457.80.

2.3.13. 7c

2-phenyl-4-*p*-methoxyphenyl-6-*t*-butyl-8-*p*-methoxyphenylidene-5,6,7-trihydroquinoline, white solid; mp 178°C. IR (KBr): 2955(m), 2837(w), 1607(w), 1573(w), 1538(w), 1510(s), 1462(w), 1384(m), 1362(w), 1299(w), 1250(s), 1175(m), 1109(w), 1034(m), 833(m), 771(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.20 (s, 1H, PyH), 8.15 (d, *J* = 7.8Hz, 2H, PhH), 7.48 (m, 5H, ArH, PhH), 7.42 (m, 1H, $=CH_2$), 7.35 (d, *J* = 8.4Hz, 2H, ArH), 7.03 (d, *J* = 8.4Hz, 2H, ArH), 6.97 (d, *J* = 8.4Hz, 2H, ArH), 3.91 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.31 (d, *J* = 14.4Hz, 1H, CH_2), 2.84 (d, *J* = 16.2Hz, 1H, CH_2), 2.52 (m, 2H, CH_2), 1.58 (m, 1H, CH), 0.91 (m, 9H, $C(CH_3)_3$).^{13}C NMR (150MHz, $CDCl_3$): δ 159.6, 158.6, 154.0, 153.4, 150.5, 140.1, 135.6, 132.3, 131.3, 130.2, 128.9, 127.2, 120.0, 114.0, 55.6, 44.9, 32.8, 29.7, 29.5, 27.6. MS: m/s = 489.73.

2.3.14. 7d

2-phenyl-4-phenyl-6-*t*-butyl-8-phenylidene-5,6,7-trihydroquinoline, white solid; mp 131°C. IR (KBr): 3058(w), 2958(s), 2867(w), 1577(m), 1536(m), 1492(m), 1440(m), 1388(w), 1363(m), 1209(w), 1178(w), 924(w), 878(w), 760(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.18 (s, 1H, PyH), 8.07 (d, *J* = 7.8Hz, 2H, PhH), 7.42 (m, 6H, PhH, =CH), 7.34 (m, 6H, PhH), 7.18 (m, 2H, PhH), 3.22 (m, 1H, CH_2), 2.73 (d, *J* = 16.2Hz, 1H, CH_2), 2.43 (m, 1H, CH_2), 2.25 (m, 1H, CH_2), 1.44 (m, 1H, CH), 0.90 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 153.8, 152.9, 150.7, 139.6, 138.2, 136.8, 129.7, 129.1, 128.6, 128.2, 127.9, 127.7, 126.9, 126.7, 119.9, 44.6, 32.5, 29.3, 29.1, 27.3. MS: m/s = 429.67.

2.3.15. 7e

2-phenyl-4-*p*-dimethylaminophenyl-6-*t*-butyl-8-*p*-dimethylaminophenylidene-5,6,7-trihydroquinoline, yellow solid; mp 128°C. IR (KBr): 2947(m), 2860(m), 2799(w), 1608(s), 1520(s), 1477(w), 1440(w), 1357(m), 1193(m), 1163(m), 1128(w), 947(w), 814(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.16 (m, 2H, PhH), 7.49 (m, 5H, PhH, PyH, ArH), 7.32 (m, 3H, ArH, =CH), 6.98 (m, 1H, ArH), 6.83 (m, 4H, ArH), 3.34 (d, *J* = 15.0Hz, 1H, CH_2), 3.05 (t, 12H, $N(CH_3)_2$), 2.53 (m, 2H, CH_2), 1.58 (m, 2H, CH_2, CH), 0.94 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 151.8, 148.6, 147.4, 138.4, 131.9, 129.3, 128.0, 126.8, 126.1, 125.2, 117.6, 110.3, 42.9, 38.8, 30.9, 28.1, 27.5, 25.8. MS: m/s = 515.93.

2.3.16. 7f

2-*p*-biphenyl-4-*p*-chlorophenyl-6-*t*-butyl-8-*p*-chlorophenylidene-5,6,7-trihydroquinoline, white solid; mp 232°C. IR (KBr): 2958(m), 1639(w), 1584(w), 1488(s), 1440(w), 1385(m), 1363(w), 1236(vw), 1179(vw), 1088(m), 1010(m), 898(w), 832(s), 770 (m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.29 (s, 3H, PhH, PyH), 7.73 (m, 3H, PhH), 7.49 (m, 13H, ArH, PhH, =CH), 3.26 (s, *J*=15.0Hz, 1H, CH_2), 2.78 (d, *J*=16.8Hz, 1H, CH_2), 2.52 (d, *J*=13.2Hz, 1H, CH_2), 2.32 (s, 1H, CH_2), 1.56 (m, 1H, CH), 0.90 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 151.6, 150.6, 147.6, 139.7, 138.7, 135.8, 134.5, 132.1, 130.5, 128.9, 128.0, 126.9, 126.4, 125.1, 117.7, 42.5, 30.5, 27.3, 25.3. MS: m/s = 573.73.

2.3.17. 7g

2-*p*-biphenyl-4-*p*-methylphenyl-6-*t*-butyl-8-*p*-methylphenylidene-5,6,7-trihydroquinoline, white solid; mp 222°C. IR (KBr): 3023(w), 2957(s), 1578(w), 1511(s), 1437(m), 1382(m), 1237(w), 1180(w), 840(m), 816(m), 766(m), 729(w) cm^{-1}.^1H NMR (600MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.4Hz, 3H, PhH, PyH), 7.73 (m, 4H, PhH), 7.56 (s, 1H, $=CH_2$), 7.45 (m, 5H, ArH), 7.32 (s, 4H, ArH, PhH), 7.25 (d, *J* = 6.6Hz, 2H, ArH), 3.34 (d, *J* = 14.4Hz, 1H, CH_2), 2.87 (d, *J* = 15.6Hz, 1H, CH_2), 2.47 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.34 (m, 1H, CH_2), 1.56 (m, 2H, CH_2, CH), 0.91 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.7, 140.5, 137.5, 136.1, 135.0, 129.4, 128.6, 126.8, 119.5, 44.2, 32.2, 29.1, 27.0, 21.0. MS: m/s = 533.73.

2.3.18. 7h

2-*p*-biphenyl-4-*p*-methoxyphenyl-6-*t*-butyl-8-*p*-methoxyphenylidene-5,6,7-trihydroquinoline, white solid; mp 201°C. IR (KBr): 2954(w), 1607(m), 1508(s), 1440(m), 1384(m), 1298(w), 1251(s), 1174(m), 1033(m), 832(m), 766(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.22 (s, 3H, PhH, PyH), 7.74 (m, 4H, PhH), 7.55 (m, 5H, ArH, PhH), 7.36 (d, *J* = 8.4Hz, 3H, ArH, =CH), 6.99 (m, 4H, ArH), 3.92 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.32 (d, *J* = 15.0Hz, 1H, CH_2), 2.87 (d, *J* = 15.6Hz, 1H, CH_2), 2.52 (m, 1H, CH_2), 2.37 (m, 1H, CH_2), 1.58 (m, 1H, CH), 0.92 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 157.0, 156.1, 150.9, 138.5, 129.6, 128.8, 127.6, 126.5, 125.0, 124.8, 117.3, 111.3, 53.0, 42.3, 30.2, 27.1, 25.0. MS: m/s = 565.60.

2.3.19. 7i

2-*p*-biphenyl-4-phenyl-6-*t*-butyl-8-phenylidene-5,6,7-trihydroquinoline, white solid; mp 197°C. IR (KBr): 3027(w), 2957(s), 1650(w), 1576(m), 1534(m), 1489(w), 1441(m), 1361 (m), 920(w), 879(m), 764(s), 728(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.25 (m, 3H, PhH, PyH), 7.75 (m, 4H, PhH), 7.53 (m, 14H, PhH, =CH), 3.34 (d, *J* = 14.4Hz, 1H, CH_2), 2.84 (d, *J* = 15.6Hz, 1H, CH_2), 2.56 (m, 1H, CH_2), 2.34 (m, 1H, CH_2), 1.56 (s, 1H, CH), 0.90 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 152.1, 151.7, 149.4, 140.2, 139.5, 138.4, 137.0, 135.6, 128.4, 128.0, 127.6, 126.9, 126.7, 125.9, 125.4, 118.5, 43.3, 31.3, 28.1, 26.0. MS: m/s = 505.60.

2.3.20. 7j

2-*p*-biphenyl-4-2,4-dimethoxyphenyl-6-*t*-butyl-8-(2,4-dimethoxyphenylidene)-5,6,7-trihydroquinoline, light yellow solid; mp 239°C. IR (KBr): 2990(w), 2955(m), 1607(vs), 1504(vs), 1462(m), 1304(s), 1260(m), 1208(vs), 1157(s), 1125(m), 1040(m), 837(s), 765(m), 733(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.15 (m, 3H, PhH, PyH), 7.61 (m, 4H, PhH), 7.37 (m, 3H, PhH), 7.24 (m, 2H, ArH), 7.03 (d, *J* = 8.4Hz, 1H, $=CH_2$), 6.49 (m, 4H, ArH), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.11 (d, *J* = 14.4Hz, 1H, CH_2), 2.66 (m, 1H, CH_2), 2.47 (m, 1H, CH_2), 2.18 (m, 1H, CH_2), 1.55 (m, 1H, CH), 0.77 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$):δ=159.8, 158.8, 152.7, 140.8, 138.8, 135.8, 130.7, 128.6, 128.9, 122.6, 120.1, 104.3, 103.7, 98.2, 55.3, 44.2, 43.8, 32.3, 29.2, 28.5, 27.8, 27.1. MS: m/s = 625.60.

2.3.21. 7k

2-*p*-biphenyl-4-*p*-dimethylaminophenyl-6-*t*-butyl-8-*p*-dimethylaminophenylidene-5,6,7-trihydroquinoline, yellow solid; mp 227°C. IR (KBr): 3028(w), 2945(w), 2862(w), 1608(s), 1576 (w), 1576(w), 1519(vs), 1481(w), 1441(m), 1352(m), 1226(w), 1163(w), 815(m), 765(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.4Hz, 2H, PhH), 8.19 (s, 1H, PyH), 7.72 (m, 4H, PhH), 7.49 (m, 5H, ArH, =CH), 7.35 (m, 3H, PhH), 6.84 (m, 4H, ArH), 3.36 (d, *J* = 14.4Hz, 1H, CH_2), 3.06 (s, 12H, $N(CH_3)_2$), 2.54 (m, 1H, CH_2), 2.43 (m, 1H, CH_2), 1.58 (m, 2H, CH_2, CH), 0.946 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (150MHz, $CDCl_3$): δ 151.3, 150.8, 148.1, 138.7, 136.8, 128.8, 127.5, 126.5, 125.6, 124.8, 117.0, 109.8, 42.4, 38.2, 30.3, 27.5, 27.0, 25.2. MS: m/s = 591.87.

2.4. General procedure for the preparation of 5,6,7,8-tetrahydroquinolines 8a-8i

To a 50 mL flask, 2-methylcyclohexanone (**5c**, 1.0 mmol), aromatic aldehydes (**3a-3e**, 1.0 mmol), pyridinium bromide (**1a-1b**, 1.2mmol), ammonium acetate (3.0 g) and acetic aid (2.0 mL) were added. Pour this mixture into a microwave and heat for approximately 2 to 4 minutes (130 W). Allow the reaction mixture to cool and diluted with 50 mL of water. Filter to collect the resulting precipitate. The crude product was recrystallized with ethanol to produce a pure solid sample for further analysis.

2.4.1. 8a

2-phenyl-4-*p*-chlorophenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow brown solid; mp 108°C. IR (KBr): 3032(w), 2928(s), 2862(m), 1594(m), 1541(m), 1490(s), 1442(m), 1377(m), 1232(w), 1086(s), 1012(m), 831(s), 763(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 7.94 (d, *J* = 7.8Hz, 2H, PhH), 7.35 (m, 6H, PhH, PyH, ArH), 7.20 (m, 2H, ArH), 3.06 (s, 1H, CH), 2.53 (s, 2H, CH_2), 2.01 (s, 1H, CH_2), 1.74 (s, 1H, CH_2), 1.59 (s, 2H, CH_2), 1.44 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 159.6, 152.0, 146.9, 137.6, 136.4, 131.8, 128.0, 126.6, 126.0 124.8, 116.5, 34.5, 29.4, 25.9, 19.7, 18.7. MS: m/s = 333.60.

2.4.2. 8b

2-phenyl-4-*p*-methoxyphenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow brown solid; mp 109°C. IR (KBr): 3023(vw), 2933(s), 2860(m), 1610(m), 1583(m), 1512(vs), 1441(m), 1421(s), 1287(s), 1243(vs), 1176(s), 1033(s), 842(s), 772(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.2Hz, 2H, PhH), 7.43 (t, 2H, PhH), 7.39 (s, 1H, PyH), 7.36 (t, 1H, PhH), 7.28 (d, J = 8.4Hz, 2H, ArH), 6.97 (d, J = 9.0Hz, 2H, ArH), 3.85 (s, 3H, OCH_3), 3.14 (m, 1H, CH), 2.66 (m, 2H, CH_2), 2.09 (m, 1H, CH_2), 1.83 (m, 1H, CH_2), 1.67 (m, 2H, CH_2), 1.52 (d, *J* = 7.2Hz, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 159.8, 157.6, 152.3, 148.2, 138.3, 131.7, 128.3, 127.0, 125.2, 117.3, 112.1, 53.7, 34.9, 29.9, 26.5, 19.2. MS: m/s = 329.53.

2.4.3. 8c

2-phenyl-4-*p*-dimethylaminophenyl-8-methyl-5,6,7,8-tetrahydroquinoline, brown solid; mp 108°C. IR (KBr): 3033(w), 2928(m), 2858(m), 1608(s), 1583(m), 1522(s), 1442(m), 1357(s), 1229(m), 1195(m), 1164(m), 946(m), 879(m), 817(s), 771(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.2Hz, 2H, PhH), 7.41 (t, 3H, PhH), 7.35 (t, 1H, PyH), 7.25 (t, 2H, ArH), 6.68 (d, *J* = 9.0Hz, 2H, ArH), 3.14 (m, 1H, CH), 3.00 (s, 6H, $N(CH_3)_2$), 2.71 (m, 2H, CH_2), 2.09 (m, 1H, CH_2), 1.81 (m, 1H, CH_2), 1.67 (m, 2H, CH_2), 1.51 (d, *J* = 7.2Hz, 3H, CH_3).^{13}C NMR (150MHz, $CDCl_3$): δ 161.2, 153.8, 150.0, 140.2, 129.7, 128.6, 126.9, 119.0, 112.0, 40.5, 36.5, 31.6, 28.3, 21.9, 20.9. MS: m/s = 342.60.

2.4.4. 8d

2-*p*-biphenyl-4-*p*-chlorophenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow brown solid; mp 170°C. IR (KBr): 2929(m), 2861(w), 1646(w), 1646(w), 1594(m), 1540(w), 1488(s), 1442(m), 1383(m), 1085(m), 834(m), 766(m), 730(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.13 (s, 2H, PhH), 7.69 (d, *J* = 22.4Hz, 4H, PhH), 7.47 (m, 5H, PhH, PyH, ArH), 7.38 (m, 3H, ArH), 3.20 (s, 1H, CH), 2.65 (s, 2H, CH_2), 2.12 (s, 1H, CH_2), 1.86 (s, 1H, CH_2), 1.70 (s, 2H, CH_2), 1.56 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$):δ=160.3, 152.2, 147.7, 140.0, 139.4, 137.1, 132.5, 128.7, 127.5, 127.3, 126.7, 125.7, 117.0, 35.2, 30.1, 26.6, 20.4, 19.4. MS: m/s = 409.60.

2.4.5. 8e

2-*p*-biphenyl-4-*p*-methylphenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow solid; mp 118°C. IR (KBr): 3026(w), 2934(s), 2858(m), 1582(m), 1538(m), 1510(m), 1441(s), 1404(m), 1367(m), 1179(w), 1003(w), 845(m), 820(s), 768(s), 731(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.14 (s, 2H, PhH), 7.70 (d, *J* = 18.6Hz, 4H, PhH), 7.48 (s, 3H, PhH), 7.39 (s, 1H, PyH), 7.30 (s, 4H, ArH), 3.18 (s, 1H, CH), 2.70 (s, 2H, CH_2), 2.46 (s, 3H, CH_3), 2.12 (s, 1H, CH_2), 1.86 (s, 1H, CH_2), 1.71 (s, 2H, CH_2), 1.57 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 161.4, 153.4, 150.1, 141.1, 140.9, 138.9, 137.5, 137.1, 129.0, 128.8, 128.6, 128.3, 127.4, 127.1, 118.7, 36.5, 31.5, 28.1, 21.8, 21.3, 20.8. MS: m/s = 389.60.

2.4.6. 8f

2-*p*-biphenyl-4-phenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow brown solid; mp 106°C. IR (KBr): 3028(w), 2929(m), 2858(w), 1637(w), 1581(m), 1538(m), 1488(m), 1441(m), 1382(m), 1192(w), 1037(w), 843(m), 767(s), 732(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.11 (s, 2H, PhH), 7.66 (d, *J* = 19.8Hz, 4H, PhH), 7.45 (s, 6H, PhH, PyH), 7.36 (s, 3H, PhH), 3.16 (s, 1H, CH), 2.65 (s, 2H, CH_2), 2.09 (s, 1H, CH_2), 1.83 (s, 1H, CH_2), 1.68 (s, 2H, CH_2), 1.54 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 160.0, 152.0, 148.7, 139.7, 139.4, 138.6, 137.3, 127.3, 127.2, 126.9, 126.2, 125.9, 125.7, 117.1, 35.1, 30.0, 26.5, 20.3, 19.3. MS: m/s = 375.60.

2.4.7. 8g

2-*p*-biphenyl-4-*m*-nitrophenyl-8-methyl-5,6,7,8-tetrahydroquinoline, brown solid; mp 162°C. IR (KBr): 2929(w), 1630(w), 1527(s), 1438(s), 1346(m), 842(vw), 767(w), 736(w), 695(w) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.24 (m, 4H, PhH, PyH), 7.63 (m, 10H, PhH, ArH), 3.10 (m, 1H, CH), 2.56 (s, 1H, CH_2), 2.03 (m, 5H, CH_2), 1.48 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 163.4, 160.6, 160.0, 146.2, 131.2, 128.2, 126.8, 125.8, 125.1, 123.4, 121.6, 120.1, 116.1, 114.6, 109.0, 34.5, 29.2, 25.8, 19.6, 18.6. MS: m/s = 420.67.

2.4.8. 8h

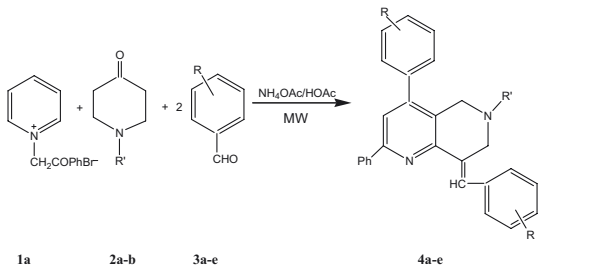
2-*p*-biphenyl-4-*p*-methoxyphenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow brown solid; mp 95°C. IR (KBr): 3028(w), 2928(m), 1607(m), 1586(m), 1510(s), 1441(m), 1289(m), 1247(vs), 1175(m), 1109(w), 1031(m), 832(s), 766(m), 731(m) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.4Hz, 2H, PhH), 7.50 (m, 4H, PhH), 7.27 (m, 3H, PhH), 7.13 (m, 3H, PyH, ArH), 6.81 (d, *J* = 8.4Hz, 2H, ArH), 3.68 (s, 3H, OCH_3), 2.97 (s, 1H, CH), 2.49 (s, 2H, CH_2), 1.92 (s, 1H, CH_2), 1.66 (s, 1H, CH_2), 1.51 (s, 2H, CH_2), 1.37 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 159.2, 157.0, 151.2, 147.6, 138.9, 138.6, 136.6, 130.0, 127.6, 126.6, 125.1, 124.8, 116.5, 111.5, 53.1, 34.3, 29.3, 25.9, 19.6, 18.6. MS: m/s = 405.53.

2.4.9. 8i

2-*p*-biphenyl-4-*p*-dimethylaminophenyl-8-methyl-5,6,7,8-tetrahydroquinoline, yellow solid; mp 118°C. IR (KBr): 3028(w), 2923(s), 2855(m), 1653(vw), 1608(s), 1580(m), 1518(vs), 1483(m), 1441(s), 1352(s), 1227(m), 1060(w), 845(m), 820(s), 732(s) cm^{-1}. ^1H NMR (600MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.4Hz, 2H, PhH), 7.72 (m, 4H, PhH), 7.49 (m, 3H, PhH), 7.38 (t, 1H, PyH), 7.31 (d, *J* = 8.4Hz, 2H, ArH), 6.83 (d, *J* = 9.0Hz, 2H, ArH), 3.20 (s, 1H, CH), 3.05 (s, 6H, $N(CH_3)_2$), 2.77 (s, 2H, CH_2), 2.12 (s, 1H, CH_2), 1.86 (s, 1H, CH_2), 1.72 (s, 2H, CH_2), 1.57 (s, 3H, CH_3). ^{13}C NMR (150MHz, $CDCl_3$): δ 158.8, 150.9, 147.6, 138.5, 136.5, 127.2, 126.3, 125.1, 124.9, 116.4, 109.5, 38.0, 34.0, 29.1, 25.9, 19.5, 18.4, 16.0. MS: m/s = 418.60.

3. Results and Discussion

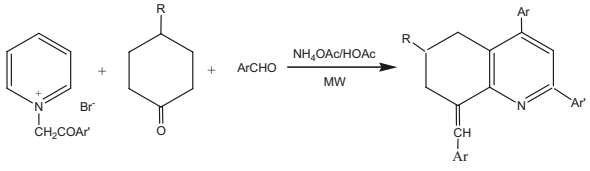
Our recent research has shown that the equal molecular mixture of aromatic aldehyde and acetophenone can be used to replace chalcone in the synthesis of Kröhnke pyridine [15]. If cyclic ketones were used in the reaction of the alicyclic fused pyridines with an additional benzylidene group, the products can be separated with poor to moderate yields. Therefore the use of substituted cyclohexanone was expected to expand the scope and variability of this procedure. According to the one-pot procedure for the Kröhnke synthesis of pyridines [15], a mixture of *N*-phenacylpyridinium bromide **1a** (1.0 mmol), aromatic aldehydes **3a-e** (2.0 mmol), and nitrogen-containing cyclic ketones such as 1-methyl-4-piperidinone **2a** or 1-ethyl-4- piperidinone **2b** (1.0 mmol) in ammonium acetate and acetic acid was heated with microwave irradiation for approximately 3 minutes. After workup the dinitrogen-containing heterocyclic



4a: R' = Me, R = *p*-CH_3 ; **4b**: R' = Me, R = *p*-Cl

4c: R' = Me, R = *p*-CH_3O; **4d**: R' = Et, R = *p*-CH_3
4e: R' = Et, R = *p*-Cl

Scheme 1. One-pot synthesis of 5,7-dihydro-1,6-naphthyridine 4a-e.



Scheme 2. Synthesis of 8-arylidene-5,6,7,8-tetrahydroquinoline **6a-j**, **7a-k**

compounds 5,7-dihydro-1,6-naphthyridines **4a-e** were produced in moderate yields (Scheme 1). Compounds **4a-e** have an additional 8-benzylidene group which are shown in the double aldol condensation of piperidone with aromatic aldehydes to give dibenzylidene piperidone, the latter reacted with *N*-phenacylpyridinium bromide and ammonia to yield products.

The structures of the 5,7-dihydro-1,6-naphthyridine derivatives **4a-e** were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy, HPLC-MS and elemental analysis. Their structures were further confirmed by the X-ray crystal analysis of a representative compound, **4c**. The compound, **4c**, contains a phenyl and *p*-methoxyphenyl group in 2- and 4-position of pyridine ring are torsioned from the plane of pyridine ring (Fig. 1). The piperidine ring is in screwed-boat conformation with a *p*-methoxybenzylidene group attached. The one-pot procedure for the Kröhnke synthesis of pyridines can be further developed to apply to other cyclic ketones and the five component cyclocondensation reaction can be obtained with the assistance of microwave irradiation.

When a mixture of 4-methylcyclohexanone (**5a**), aromatic aldehydes (**3a-e**) and *N*-phenacylpyridinium bromide (**1a**) in ammonium acetate and acetic acid was heated under microwave irradiation for about three minutes, the desired products, 2-phenyl-4-aryl-6-methyl-8-arylidene-5,6,7,8-tetrahydroquinolines, **(6a-e)** were obtained with

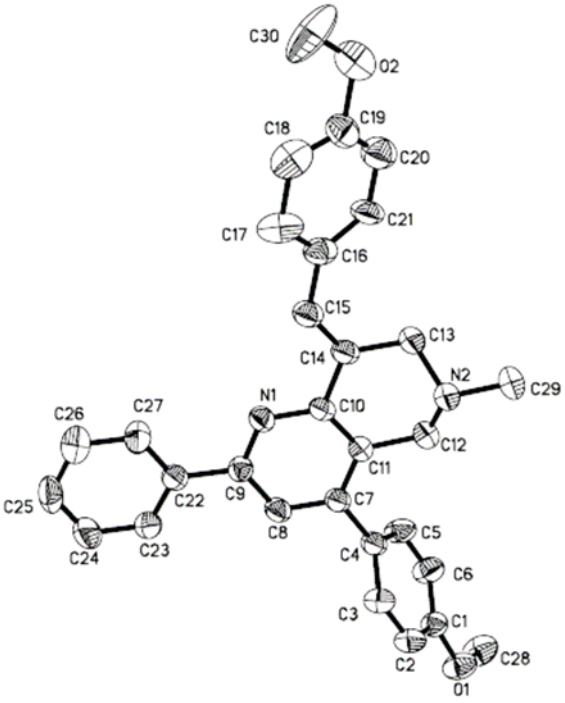


Figure 1. Molecular structure of the compound **4c**, note: the hydrogen atoms have been omitted for clarity.

Table 1. Preparation of 8-arylidene-5,6,7,8-tetrahydroquinolines.

Product	R	Ar	Ar'	Yield
6a	CH_3	4-ClC_6H_4	C_6H_5	73%
6b	CH_3	4-$CH_3C_6H_4$	C_6H_5	68%
6c	CH_3	4-$CH_3OC_6H_4$	C_6H_5	66%
6d	CH_3	4-$(CH_3)_2NC_6H_4$	C_6H_5	60%
6e	CH_3	3-$NO_2C_6H_4$	C_6H_5	48%
6f	CH_3	4-ClC_6H_4	4-$C_6H_5C_6H_4$	75%
6g	CH_3	4-$CH_3C_6H_4$	4-$C_6H_5C_6H_4$	70%
6h	CH_3	C_6H_5	4-$C_6H_5C_6H_4$	73%
6i	CH_3	4-$CH_3OC_6H_4$	4-$C_6H_5C_6H_4$	57%
6j	CH_3	4-$(CH_3)_2NC_6H_4$	4-$C_6H_5C_6H_4$	60%
7a	$C(CH_3)_3$	4-ClC_6H_4	C_6H_5	75%
7b	$C(CH_3)_3$	4-$CH_3C_6H_4$	C_6H_5	72%
7c	$C(CH_3)_3$	4-$CH_3OC_6H_4$	C_6H_5	68%
7d	$C(CH_3)_3$	C_6H_5	C_6H_5	70%
7e	$C(CH_3)_3$	4-$(CH_3)_2NC_6H_4$	C_6H_5	63%
7f	$C(CH_3)_3$	4-ClC_6H_4	4-$C_6H_5C_6H_4$	68%
7g	$C(CH_3)_3$	4-$CH_3C_6H_4$	4-$C_6H_5C_6H_4$	76%
7h	$C(CH_3)_3$	4-$CH_3OC_6H_4$	4-$C_6H_5C_6H_4$	70%
7i	$C(CH_3)_3$	C_6H_5	4-$C_6H_5C_6H_4$	69%
7j	$C(CH_3)_3$	2,4-$(CH_3O)_2C_6H_4$	4-$C_6H_5C_6H_4$	73%
7k	$C(CH_3)_3$	4-$(CH_3)_2NC_6H_4$	4-$C_6H_5C_6H_4$	65%

moderate to good yields (48-73%) (Scheme 2).

Under similar conditions another pyridinium salt, *N*-*p*-phenylphenacylpyridinium bromide (**1b**), which is prepared by refluxing pyridine with *p*-phenylphenacyl bromide, also reacted similarly with 4-methylcyclohexanone (**5a**) and aromatic aldehydes (**3a-e**) to give the expected 2-*p*-phenylphenyl-4-aryl-6-t-butyl-8-arylidene-5,6,7,8-tetrahydroquinolines, (**6f-j)** in yields of between 57 and 75% (Table 1). When a more sterically hindered ketone, 4-*t*-butylcyclohexanone, (**5b**)

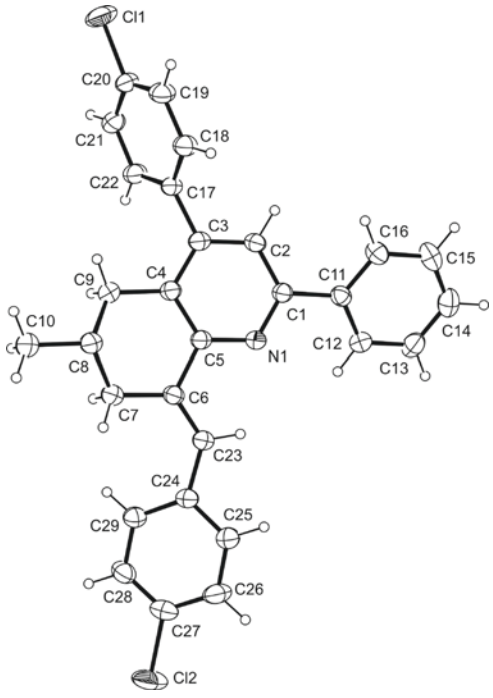


Figure 2. Molecular structure of the compound **6a** with 30% probability level.

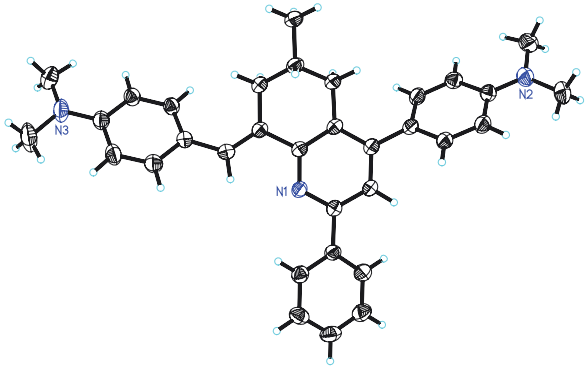


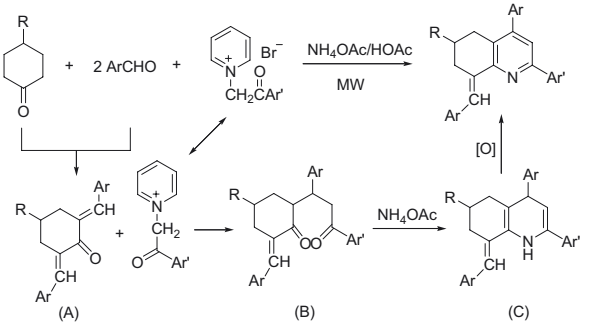
Figure 3. Molecular structure of the compound **6d** with 30% probability level.

was used in this multicomponent reaction procedure, the expected products 2-aryl-6-*t*-butyl-8-arylidene-5,6,7,8-tetrahydroquinolines, (**7a-k**) are also successfully prepared in good yields (63-78%).

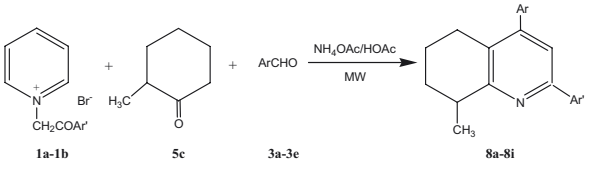
The reactions shown in Table 1, all involved aromatic aldehydes and reacted smoothly, which indicates the properties of electron-donating or electron-withdrawing substituents on an aromatic ring of an aldehyde have very little effect on the product yields. On the basis of these observations, although the exact reaction mechanism has not been confirmed, and it is reasonable to believe that this complex transformation could be interpreted as a four-component reaction. Shown in Scheme 3 is the initial ammonia-catalyzed formation of 2,6-bis(arylidene)

Table 2. Preparation of 5,6,7,8-tetrahydroquinoline derivatives.

Product	Ar	Ar'	Yield
8a	4-ClC_6H_4	C_6H_5	83%
8b	4-$CH_3OC_6H_4$	C_6H_5	76%
8c	4-$(CH_3)_2NC_6H_4$	C_6H_5	73%
8d	4-ClC_6H_4	4-$C_6H_5C_6H_4$	90%
8e	4-$CH_3C_6H_4$	4-$C_6H_5C_6H_4$	80%
8f	C_6H_5	4-$C_6H_5C_6H_4$	78%
8g	m-$NO_2C_6H_4$	4-$C_6H_5C_6H_4$	67%
8h	4-$CH_3OC_6H_4$	4-$C_6H_5C_6H_4$	85%
8i	4-$(CH_3)_2NC_6H_4$	4-$C_6H_5C_6H_4$	75%



Scheme 3. Formation mechanism of 5,6,7,8-tetrahydroquinolines.



Scheme 4. Preparation of substituted 5,6,7,8-tetrahydroquinolines **8a-8i**.

cyclohexanone (A)[17-18] followed by the base-catalyzed Michael addition of pyridinium salt to yield a 1,5-dicarbonyl derivative (B). This intermediate (B) is subsequently cyclized by the addition of an amino group to the carbonyl group to form a dihydropyridine ring (C), which in turn eliminates the pyridine cation to form the final product, a polysubstituted 5,6,7,8-tetrahydroquinolines.

According to above purposed reaction mechanism, when a disubstituted cyclic ketone which has only one α-methylene group were used in the reaction the 5,6,7,8-tetrahydroquinoline derivatives without a 8-arylidene group would be produced. In fact when 2-methylcyclohexanone (**5c**) was employed in this procedure, and was heated with aromatic aldehydes (**3a-e**) and two pyridinium bromides (**1a-b**) in the presence of NH_4OAc/HOAc and under microwave irradiation, the desired 5,6,7,8-tetrahydroquinoline derivatives **8a-i** were produced in good yields (67-90%) (Scheme 4).

All the structures of the prepared polysubstituted 5,6,7,8-tetrahydroquinoline derivatives were characterized by IR, ^1H and ^{13}C NMR and HPLC-MS. It should be noted that these reactions in a microwave

Table 3. Crystal data and structure refinement of the compounds.

	4c	6a	6d	7h
Empirical formula	$C_{30}H_{28}N_2O_2$	$C_{29}H_{22}Cl_2N$	$C_{33}H_{35}N_3$	$C_{40}H_{39}NO_2$
Formula weight	448.54	455.38	473.64	565.72
Temperature(K)	273(2)	293(2)	296(2)	133(2)
Wavelength (A)	0.71073	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
space group	P2(1)/c	P2(1)/n	P2(1)/n	P-1
Unit cell dimensions				
a (Å)	16.853(3)	11.3525(18)	17.0112(17)	6.528(15)
b (Å)	12.6968(19)	12.706(2)	8.7560(9)	12.95(3)
c (Å)	11.5945(17)	16.328(3)	19.725(2)	19.78(5)
α (°)	90	90	90	80.33(3)
β (°)	105.377(2)	97.006(2)	113.7830(10)	84.39(6)
γ (°)	90	90	90	78.50(4)
Volume (Å^3)	2392.1(6)	2337.6(7)	2688.5(5)	1612(7)
Z, Calculated density (g cm^{-3})	4, 1.245	4, 1.294	4, 1.170	2, 1.166
Absorption coefficient (mm^{-1})	0.078	0.295	0.068	0.071
F(0 0 0)	952	948	1016	604
Crystal size (mm)	0.30 x 0.10 x 0.10	0.40 x 0.30 x 0.30	0.20×0.20×0.30	0.20×0.20×0.30
θ Range for data collection (°)	2.43 - 25.05	2.04 - 25.00	2.04 - 25.02	1.62 - 25.00
Limiting indices	-15<=h<=20, -14<=k<=15, -13<=l<=13	-13≤h≤13, -15≤k≤15, -19≤l≤19	-20≤*h*≤20, -10≤*k*≤10, -23≤*l*≤23	-7≤*h*≤6, -15≤k≤15, -23≤l≤23
Reflections collected/unique	12122 / 4205 [R(int) =0.044]	4116/3044 [R(int) = 0.0307]	18792 / 4738 [R(int) =0.0258]	5644/2423 [R(int) = 0.0809]
Completeness (%)	99.5 %	99.8	99.8	99.3
Absorption correction	non	non	non	non
Max. and min. transmission	0.9922 and 0.9770	0.9407 and 0.9220	0.8943 and 0.8473	
Data/restraints/parameters	4205 / 0 / 310	4116 / 0 / 290	4738 / 0 / 325	5644 / 0 / 388
Goodness-of-fit on F^2	1.041	1.015	1.051	0.992
Final *R* indices [$I > 2\sigma I$]	R1 = 0.0920, wR2 = 0.2598	R1 = 0.0711 wR2 = 0.11401	R1 = 0.058 wR2 = 0.1918	R_1=0.1681 wR_2=0.1985
R indices (all data)	R1 = 0.1682, wR2 =0.3198	R1 = 0.0510 wR2 = 0.1273	R1 = 0.0753 wR2 = 0.2167	R_1=0.0610 wR_2=0.1394
Largest difference peak and hole (e Å^{-3})	0.745 and -0.383	0.487 and -0.377	1.266 and -1.103	0.402 and -0.171

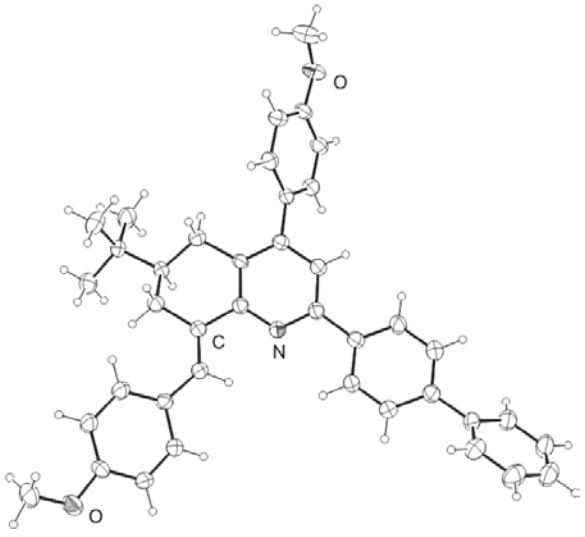


Figure 4. Molecular structure of the compound **7h** with 30% probability level.

irradiation environment are clean and produce very few byproducts. Therefore, the workup procedure involves only a simple filtration of the precipitate followed by crystallization with an alcohol. In all instances, the products can be obtained in high purity with a correspondingly consistently ^{1}H and ^{13}C NMR spectroscopy. The single crystal structures of three representative compounds were determined by the X-ray diffraction and their figures are showed in Fig. 2 to 4.

In conclusion, we have described a simple and efficient one-pot multicomponent reaction procedure for the preparation of polysubstituted 5,6,7,8-tetrahydroquinolines and 5,7-dihydro-1,6-naphthyridines. This one-pot procedure is also a simple modification of the two-step synthesis for Kröhnke pyridine derivatives. The advantages of this new approach are as follows: the reaction procedure is convenient, involves a simple experimental procedure and product isolation and therefore dispenses with extensive recrystalization or chromatographic purification steps. It is a four-component reaction which allows for the construction of relatively complicated nitrogen-containing heterocyclic systems using simple starting materials. Further studies to develop the full extend of the synthetic scope of this reaction are currently underway.

Acknowledgement

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Supporting information available

Crystallographic data (CCDC-641228 for **4b**, CCDC-664098 for **6a**, CCDC-664099 for **6b**, CCDC-664100 for **7h)** have been deposited at the Cambridge Crystallographic Database Centre.

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