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EFFICIENT SYNTHESIS OF NOVEL 3-(QUINOLIN-2'-YL)CARBAZOLES AND 3-(QUINOLIN-2'-YL)CARBAZOLE-4'-CARBOXYLIC ACIDS

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Abstract
A simple and efficient synthesis of novel 3-(quinolin-2'-yl)-carbazolesutilizingmicro wave irradiation and 3-(quinolin-2'-yl)-carbazole-4'-carboxylic acids *via*Doebnerreaction,usinga putative synthon,9-ethyl-9*H*-carbazole with various reactants is described. All of the title compounds were obtained in good yields of 93–79% and theirstructures were confirmed by IR, ^{1}H NMR, MS, and elemental analysis.

Key Words: Doebner reaction, 9-ethyl-9*H*-carbazole-3-carbaldehyde, cyclic ketones, aromatic amines

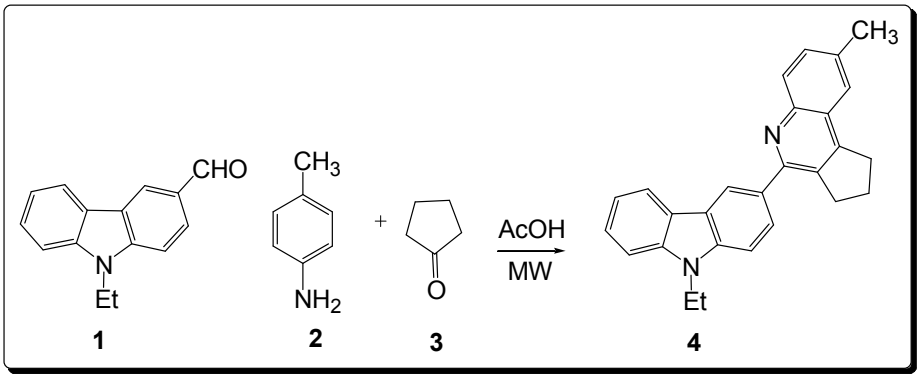
I. Introduction

Nitrogen-containing heterocycles are a very important group oforganic compounds because of their wide application in medicine,agriculture, and technology. Among these, quinolineandcarbazole derivatives are of significant synthetic interest due totheir diverse range of biological activities. Compoundscontaining a quinoline framework have been found applicationsas pharmaceuticals and agrochemicals, as well as being generalsynthetic building blocks[i-iii]. Industrial, biological, and syntheticsignificance places this scaffold in a prestigious position.Studies on new quinoline derivatives appear frequently in thechemical literature. Therefore, significant effort continues to bedirected toward the development of new quinolines. In particular,there is much current interest in the quinoline ring systemespecially in the area of medicinal chemistry, and moreover it isa ubiquitous sub-structure found in many biologically activenatural products [iv-viii]. Carbazole-based compounds are alsoembodied in many naturally occurring products and these toodisplay a wide variety of biological effects such as anti-tumor[ix,x], anti-oxidative [xi], anti-inflammatory, and anti-mutagenicactivities[xii,xiii].

In addition, their derivatives are widelyused as building blocks for new organic materials and play avery important role in electroactive and photoactive materials.They are also considered to be potential candidates for electronicdevices, such as color displays, organic semiconductorlasers, and solar cells because of their reversible electrochemicaloxidation[xiv-xx]. Currently, there is a strong interest in thesynthesis of novel heteroarylcarbazole derivatives due to theirintriguing structural features and promising biological activities[xxi-xxiv].

Most heteroarylcarbazoles reported in the literaturecontain a common heterocyclic ring moiety fused with acarbazole such as pyridocarbazoles[xxv], thienocarbazole[xxvi],quino and chromenocarbazoles[xxvii], pyranocarbazoles, pyrrolocarbazoles[xxviii], indolocarbazoles[xxix], and synthetic analoguesthereof. However, to the best of our knowledge, there are veryfew reports where the heteroaryl moiety is substituted with aquinoline unit and hence the synthesis of such compounds isdesirable. In this regard, Meesala*etal*[xxx] recently described ashort and facile route to the synthesis of new 3,6-bis(pyrazol-4-yl)carbazoles from 3,6-diacetylcarbazoles through a Vilsmeierreaction. Later, Chaitanya*etal*[xxxi] reported a new synthesis of3-(3-nitrochromenyl)carbazoles, 3,6-bis(3-nitrochromenyl)-carbazoles under solvent-free conditions by the reaction of*β*-nitrovinylcarbazole or bis(*β*-nitrovinyl)carbazole with salicylaldehyde.

In light of these findings, and in view of the prominent rolestructural diversity plays in medicinal and combinatorial chemistry,we felt that there was a real need for the synthesis of somenew prototypes combining both the carbazole ring system andquinoline moiety in the same moleculewhichcould be vitallyimportant for pharmacological studies or in creating new medicinalproperties. Therefore, in continuation of our studies on thesynthesis of novel and interesting quinolinyl-substituted heterocycles[xxxii-xxxiv], in this letterweherein report the novel versatile high yielding one pot method for the synthesis of (i) 3-(quinolin-2'-yl)-9*H*-carbazolesusing microwave heating and (ii) 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid*via*Doebner reaction starting from the precursor 9-ethyl-9*H*-carbazole-3-carbaldehyde. It is noteworthy that our protocol allows diversitymultiplication by varying aromatic amines, and cyclic ketones.



Scheme 1. Synthesis of substituted 3- (quinolin-2'-yl)-carbazoles**(4, 6, 8, 10, 12, 14, 15, 16, 17 & 18)**

II Experimental protocols

General procedure for the synthesis of 3-(substituted quinolin-2'-yl)-9-ethyl-9*H*-carbazole (4, 6, 8, 10, 12, 14, 15, 16 17 & 18)

9-Ethyl-9*H*-carbazole-3-carbaldehyde (**1,** 1 mmol), the respective aromatic amines (**2**/**13,** 1 mmol), the respective cycloketone and 1-oxo-2,3,4,9-tetrahydrocarbazole (**3**, **5**, **7**, **9 & 11**, 1.5 mmol**)** and acetic acid (2 mL) were mixed, stirred at room temperature for 5 min. Then the mixture was heated for 15 min at 120 °C under microwave irradiation. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature and then diluted

with cold water (40 mL). The solid product was filtered and recrystallized from ethanol to afford the desired pure products.

IIa.**3-(7'-Methyl-5'*H*-cyclopenta[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(4)**

Pale yellow solid; yield: 90%; m.p.162-164 °C; IR (KBr, cm^{-1}) ν_{max}:1582 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 9.12 (s, 1H, C_9'-H), 8.59-7.25 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_6' & C_8'-H), 4.51 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.00 Hz), 2.56 (s, 3H, C_7'-CH_3), 2.53-2.29 (m 6H, C_3', C_4' & C_5'-H), 1.61 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.00 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) (ppm) δ_C: 156.3 (C_2'), 142.7 (C_{9a}'), 140.6 (C_{5a}'), 138.7 (C_{9a}), 135.5 (C_7'), 133.9 (C_3), 128.3 (C_{2a}'), 127.7 (C_8'), 126.5 (C_9'), 125.5 (C_{4a}), 124.7 (C_{8a}), 123.2 (C_{5b}'), 122.7 (C_6), 122.5 (C_6'), 120.8 (C_5), 120.0 (C_7), 119.5 (C_4), 118.8 (C_2),112.4 (C_1), 109.0 (C_8), 101.8 (C_{4b}), 54.2 (N_9-O**C**$\mathbf{H_2}$$CH_3$), 37.8 ($C_5$'), 29.7 ($C_3$'), 27.4 ($C_4$'), 20.8 ($C_7$'-$CH_3$), 13.8 ($N_9$-$OCH_2$**C**$\mathbf{H_3}$); MS: *m/z* ($M^+$, 376); Anal.calcd.for: $C_{27}H_{24}N_2$: C, 86.13; H, 6.43; N, 7.44. Found: C, 86.19; H, 6.38; N, 7.37%.

IIb.3-(8'-Methyl-6'*H*-cyclohexa[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(6)

Pale yellow solid; yield: 93%; m.p.178-180 °C; IR (KBr, cm^{-1}) ν_{max}:1597 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 8.99 (s, 1H, C_{10}'-H), 8.38-7.31 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_7' & C_9'-H), 4.42 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.20 Hz), 2.50 (s, 3H, C_8'-CH_3), 2.28-2.00 (m 8H, C_3', C_4', C_5' & C_6'-H), 1.53 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.20 Hz); MS: *m/z* (M^+, 390); Anal.calcd.for: $C_{28}H_{26}N_2$: C, 86.12; H, 6.71; N, 7.17. Found: C, 86.17; H, 6.77, N, 7.10%.

IIc. 3-(4',8'-Dimethyl-6'*H*-cyclohexa[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(8)

Pale yellow solid; yield: 84%; m.p.158-160 °C; IR (KBr, cm^{-1}) ν_{max}: 1593 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (**Fig. 3.102**) (ppm) δ_H: 8.99 (s, 1H, C_{10}'-H), 8.29-7.23 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_7' & C_9'-H), 4.30 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.10 Hz), 2.79-2.51 (m 4H, C_3' & C_6'-H), 2.31 (s, 3H, C_8'-CH_3), 1.90-1.65 (m, 3H, C_4'-H & C_5'-2H), 1.45 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.10 Hz), 1.31 (s, 3H, C_4'-CH_3); MS: *m/z* (M^+, 404); Anal.calcd.for: $C_{29}H_{28}N_2$: C, 86.10; H, 6.98; N, 6.92. Found: C, 86.02; H, 6.93; N, 7.00%.

IId. 3-(10'-Methyl-8'*H*-cycloocta[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(10)

Pale yellow solid; yield: 89%; m.p.184-186 °C; IR (KBr, cm^{-1}) ν_{max}: 1602 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 8.50 (s, 1H, C_{12}'-H), 8.11-7.32 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_9' & C_{11}'-H), 4.25 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.50 Hz), 3.02-2.66 (m, 4H, C_3' & C_8'-H), 2.47 (s, 3H, C_{10}'-CH_3), 2.29-2.19 (m, 8H, C_4', C_5', C_6' & C_7'-H), 1.42 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.50 Hz); MS: *m/z* (M^+, 418); Anal.calcd.for: $C_{30}H_{30}N_2$: C, 86.08; H, 7.22; N, 6.69. Found: C, 86.03; H, 7.27; N, 6.73%.

IIe.3-(6',6''-Dimethyl-3'',4''-dihydrocarbazolo[4',5'-*a*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole (12)

Pale yellow solid; yield: 84%; m.p.224-226 °C; IR (KBr, cm^{-1}) ν_{max}: 1612 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 9.86 (b s, 1H, N_9''-H), 8.48 (s, 1H, C_8'-H), 8.34-7.21 (m, 12H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_5', C_7', C_5'', C_7''& C_8''-H), 4.51 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.25 Hz), 2.85-2.68 (m 4H, C_3'' & C_4''-H), 2.49 (s, 3H, C_6'-CH_3), 2.37 (s, 3H, C_6''-CH_3), 1.36 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.25 Hz); MS *m/z* (M^+, 491); Anal.calcd.for: $C_{35}H_{29}N_3$: C, 85.51; H, 5.95; N, 8.55. Found: C, 85.47; H, 6.00; N, 8.61%.

IIf.3-(7'-Chloro-5'*H*-cyclopenta[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(14)

Pale yellow solid; yield: 87%; m.p.170-172 °C; IR (KBr, cm^{-1}) ν_{max}:1593 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 9.00 (s, 1H, C_9'-H), 8.71-7.35 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_6' & C_8'-H), 4.42 (q, 2H, N_9-O**C**$\mathbf{H}_2$$CH_3$, *J* = 7.20 Hz), 2.61-2.32 (m 6H, C_3', C_4' & C_5'-H), 1.52 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.20 Hz); MS: *m/z* (M^+, 396); Anal.calcd.for: $C_{26}H_{21}ClN_2$: C, 78.68; H, 5.33; N, 7.06. Found: C, 78.64; H, 5.36; N, 7.02%.

IIg3-(8'-Chloro-6'*H*-cyclohexa[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(15)

Pale yellow solid; yield: 84%; m.p.180-182 °C; IR (KBr, cm^{-1}) ν_{max}:1595 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 8.84 (s, 1H, C_{10}'-H), 8.45-7.39 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_7' & C_9'-H), 4.29 (q, 2H, N_9-O**C**$\mathbf{H_2}$$CH_3$, *J* = 7.20 Hz), 2.38-2.10 (m 8H, C_3', C_4', C_5' & C_6'-H), 1.45 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.20 Hz); MS: *m/z* (M^+, 410); Anal.calcd.for: $C_{27}H_{23}ClN_2$: C, 78.91; H, 5.64; N, 6.82. Found: C, 78.87; H, 5.61, N, 6.85%.

IIh3-(8'-Chloro-4'-methyl-6'*H*-cyclohexa[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(16)

Pale yellow solid; yield: 80%; m.p.162-164 °C; IR (KBr, cm^{-1}) ν_{max}: 1588 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 8.75 (s, 1H, C_{10}'-H), 8.40-7.28 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_7' & C_9'-H), 4.37 (q, 2H, N_9-O**C**$\mathbf{H_2}$$CH_3$, *J* = 7.50 Hz), 2.83-2.54 (m 4H, C_3' & C_6'-H), 1.85-1.57 (m, 3H, C_4'-H & C_5'-2H), 1.50 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.50 Hz), 1MS: *m/z* (M^+, 424); Anal.calcd.for: $C_{28}H_{25}ClN_2$: C, 79.14; H, 5.93; N, 6.59. Found: C, 79.18; H, 5.96; N, 6.63%.

IIi3-(10'-Chloro-8'*H*-cycloocta[*c*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole(17)

Pale yellow solid; yield: 87%; m.p.188-190 °C; IR (KBr, cm^{-1}) ν_{max}: 1606 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 8.36 (s, 1H, C_{12}'-H), 8.27-7.38 (m, 9H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_9' & C_{11}'-H), 4.35 (q, 2H, N_9-O**C**$\mathbf{H_2}$$CH_3$, *J* = 7.50 Hz), 3.14-2.78 (m, 4H, C_3' & C_8'-H), 2.34-2.20 (m, 8H, C_4', C_5', C_6' & C_7'-H), 1.36 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.50 Hz); MS: *m/z* (M^+, 438); Anal.calcd.for: $C_{29}H_{27}ClN_2$: C, 79.34; H, 6.20; N, 6.38. Found: C, 79.37; H, 6.24; N, 6.41%.

IIj3-(6'-Chloro-6''-methyl-3'',4''-dihydrocarbazolo[4',5'-*a*]quinolin-2'-yl)-9-ethyl-9*H*-carbazole (18)

Pale yellow solid; yield: 79%; m.p.234-236 °C; IR (KBr, cm^{-1}) ν_{max}: 1615 (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) (ppm) δ_H: 9.92 (b s, 1H, N_9''-H), 8.52 (s, 1H, C_8'-H), 8.27-7.35 (m, 12H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_5', C_7', C_5'', C_7''& C_8''-H), 4.46 (q, 2H, N_9-O**C**$\mathbf{H_2}$$CH_3$, *J* = 7.20 Hz), 2.98-2.62 (m 4H, C_3'' & C_4''-H), 2.41 (s, 3H, C_6''-CH_3), 1.29 (t, 3H, N_9-OCH_2**C**$\mathbf{H_3}$, *J* = 7.20 Hz); MS *m/z* (M^+, 511); Anal.calcd.for: $C_{34}H_{26}ClN_3$: C, 79.75; H, 5.12; N, 8.21. Found: C, 79.79; H, 5.09; N, 8.25%.

General procedure for the synthesis 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid (20, 21, 23 & 25)

A mixture of 9-ethyl-9*H*-carbazole-3-carbaldehyde (**1**, 0.01 mol), pyruvic acid (**19**, 0.01 mol), respective aromatic amine (**2**, **13**, **22** &**24**, 0.01 mol) in dry ethanol (15 mL) and 5 drops of triethylamine was heated under reflux for 2 h. After completion of the reaction, the excess of solvent was evaporated. The residue was dissolved in ice water and extracted with ethyl acetate. Combined organic layers were dried over anhydrous sodium sulphate. It was then purified on a silica gel column (eluent - petroleum ether: ethyl acetate (95: 5)). The pure product was recrystallised from ethanol.

IIk3-(6'-Methyl-quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid(20)

Brown solid; yield: 83%; m.p.208-210 °C; IR (KBr, cm^{-1}) ν_{max}:3450 (OH), 1735 (C=O), 1627 (C=N); ^{1}H NMR (400MHz, DMSO-d_6) (ppm) δ_H: 11.05 (s, 1H, OH), 8.87 (s, 1H, C_5'-H), 8.48 (s, 1H, C_3'-H), 8.39-7.20 (m, 9H, C_1,C_2, C_4, C_5, C_6, C_7, C_8, C_7' & C_8'-H), 4.28 (q, 2H, N_9-C$\mathbf{H_2}$$CH_3$, *J* = 7.50 Hz), 2.31 (s, 3H, C_6'-CH_3), 1.27 (t, 3H, N_9-CH_2C$\mathbf{H_3}$, *J* = 7.50 Hz); ^{13}C NMR (100MHz, DMSO-d_6) (ppm) δ_C: 177.3 (C_4'-COOH), 156.4 (C_2'), 147.2 (C_{8a}'), 137.8 (C_{9a}), 136.7 (C_6'), 135.8 (C_4'), 132.2 (C_3), 130.6 (C_7'), 129.4 (C_{4a}), 129.1 (C_8'), 126.2 (C_{8a}), 124.2 (C_5'), 123.1 (C_3'), 121.8 (C_{4a}'), 121.3 (C_6), 121.1 (C_5), 119.3 (C_7), 119.0 (C_4), 118.0 (C_2), 111.8 (C_1), 111.0 (C_8), 103.2 (C_{4b}), 54.4 (N_9-C$\mathbf{H_2}$$CH_3$), 21.5 ($C_6$'-$CH_3$), 12.0 ($N_9$-$CH_2CH_3$); MS: *m/z* ($M^+$, 380); Anal.calcd.for: $C_{25}H_{20}N_2O_2$: C, 78.93; H, 5.30; N, 7.36. Found: C, 78.97; H, 5.37; N, 7.31%.

IIk3-(6'-Chloro-quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid (21)
Brown solid; yield: 87%; m.p.200-202 °C; IR (KBr, cm^{-1}) ν_{max}: 3435 (OH), 1740 (C=O), 1610 (C=N); ^{1}H NMR (400MHz, DMSO-*d*$_6$) (**Fig. 3.105**) (ppm) δ_H: 11.25 (s, 1H, OH), 8.28 (s, 1H, C_5'-H), 8.15-7.25 (m, 10H, C_1, C_2, C_4, C_5,C_6, C_7, C_8, C_3', C_7' & C_8'-H), 4.32 (q, 2H, N_9-C**H$_2$**CH_3, *J* = 7.00 Hz), 1.48 (t, 3H, N_9-CH_2C**H$_3$**, *J* = 7.00 Hz); MS: *m/z* (M^+, 400); Anal.calcd.for: $C_{24}H_{17}ClN_2O_2$: C, 71.91; H, 4.27; N, 6.99. Found: C, 71.97; H, 4.22; N, 7.05%.

IIlc3-(Quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid (23)
Brown solid; yield: 80%; m.p.197-199 °C; IR (KBr, cm^{-1}) ν_{max}: 3438 (OH), 1729 (C=O), 1615 (C=N); ^{1}H NMR (400MHz, DMSO-*d*$_6$) (**Fig. 3.106**) (ppm) δ_H: 11.34 (s, 1H, OH), 8.49-7.04 (m, 102H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_3', C_5', C_6', C_7' & C_8'-H), 4.43 (q, 2H, N_9-C**H$_2$**CH_3, *J* = 7.20 Hz), 1.56 (t, 3H, N_9-CH_2C**H$_3$**, *J* = 7.20 Hz); MS: MS: *m/z* (M^+, 366); Anal.calcd.for: $C_{24}H_{18}N_2O_2$: C, 78.67; H, 4.95; N, 7.65. Found: C, 78.72; H, 5.00; N, 7.61%.

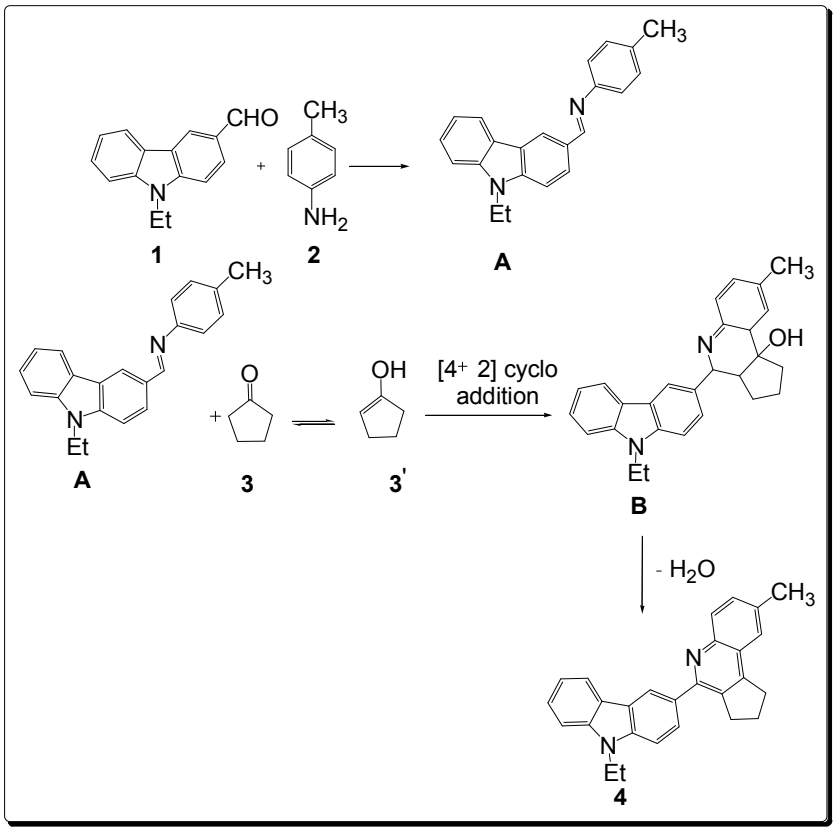
IImd3-(9'-Ethyl-9'*H*-carbazolo[5',6'-*c*]-pyrido-2'-yl)-9*H*-carbazole-4'-carboxylic acid (25)
Brown solid; yield: 80%; m.p.197-199 °C; IR (KBr, cm^{-1}) ν_{max}:3447 (OH), 1743 (C=O), 1608 (C=N); ^{1}H NMR (400MHz, DMSO-*d*$_6$) (**Fig. 3.107**) (ppm) δ_H:11.41 (s, 1H, OH), 8.89-7.20 (m, 14H, C_1, C_2, C_4, C_5, C_6, C_7, C_8, C_3', C_5', C_6', C_7', C_8', C_{10}' & C_{11}'-H), 4.34-3.98 (m, 4H, N_9-C**H$_2$**CH_3& N_9'-C**H$_2$**CH_3), 1.58-1.37 (m, 6H, N_9-CH_2C**H$_3$**& N_9'-CH_2C**H$_3$**); MS: *m/z* (M^+, 483); Anal.calcd.for: $C_{32}H_{25}N_3O_2$: C, 79.48; H, 5.21; N, 8.69. Found: C, 79.43; H, 5.27; N, 8.74%.

Results and Discussion

Microwave assisted chemical synthesis has become a powerful synthetic tool for rapid synthesis of a variety of organic compounds[48-51]. It has proved successful in remarkably cutting the required reaction time and improving the yields and purity of the desired products. Hence an attempt has been made to achieve the targeted quinolinylcarbazoles by using microwave heating.

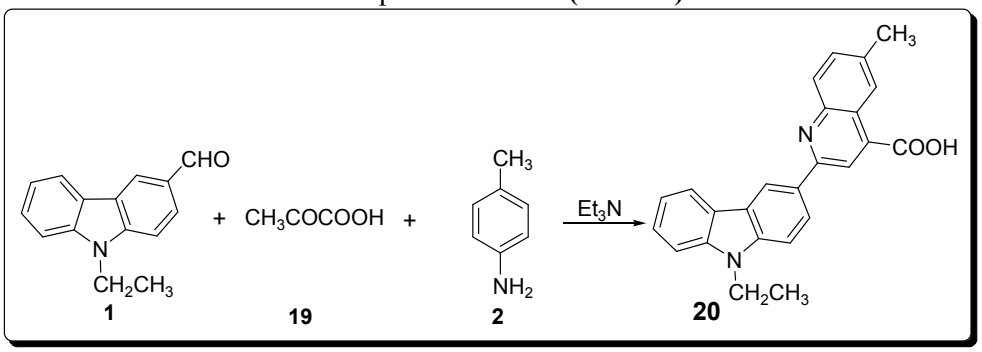
We began our study with the microwave assisted one pot synthesis of the desired 3-(quinolin-2'-yl)-carbazoles. In an initial attempt, 9-ethyl-9*H*-carbazole-3-carbaldehyde a putative synthon,which was brought commercially from Sigma Aldrich Chemicals, was mixed with *p*-toludine (**2**),cyclopentanone (**3**) and acetic acidand then subjected to microwave irradiation for 15 min. The reaction exclusively afforded **4** as sole product (**Scheme 1**). The IR spectrum of **4** registered absorption band at 1582 cm^{-1} ascribable to C=N stretching vibration. Furthermore, the ^{1}H NMR spectrum gave strong evidence for the formation of compound**4**. The ^{1}H NMR spectrum of **4**registered one singlet at δ 9.12 due to C_9' proton. Other aromatic protons appeared in the region δ 8.59-7.25. Two protons appeared as a quartet at δ 4.51 (*J*= 7.00 Hz) was due to N_9-**CH_2**CH_3. A singlet at δ 2.56 for C_7'-CH_3 strongly support the structure of the obtained product as **4**. Moreover, structure **4**was supported by ^{13}C NMR spectrum and elemental analysis, which was compatible with assigned structure.It is worth mentioning that our protocol encompassesa vast scope for diversity multiplication by varying aromatic amines and cyclic ketones.

A plausible reaction mechanism for the formation of derivatives **4** is reported in **Scheme 2**.Initially, 9-ethyl-9*H*-carbazole-3-carbaldehyde (**1**) undergoes condensation with *p*-toludine (**2**) to give intermediate **A**. In the presence of acetic acid, cyclopentanone (**3**) is in equilibrium with the enol form (**3'**). The condensed intermediate **A** undergoes a [4+2] cycloaddition with the enol form (**3'**) to form intermediate **B**. The last step involves subsequent dehydration followed by aromatization results in formation of the product **4**.



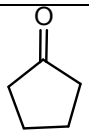
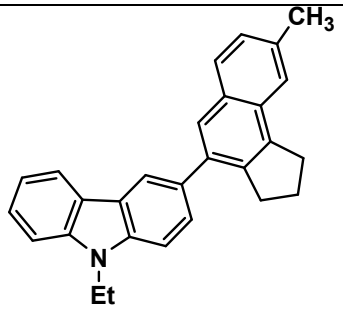
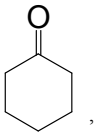
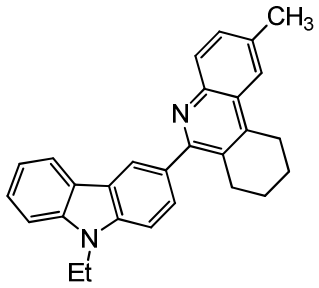
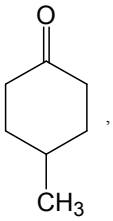
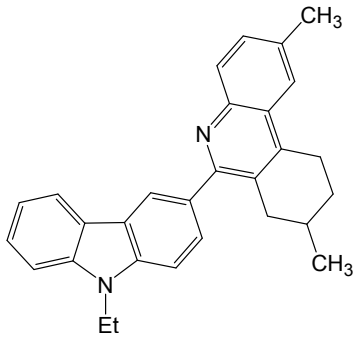
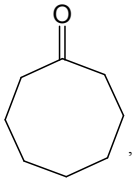
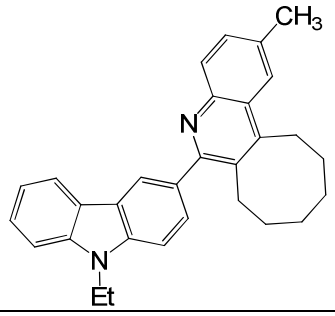
Scheme 2 Mechanism for the formation of 3- (quinolin-2'-yl)-carbazoles**(4, 6, 8, 10, 12, 14, 15, 16, 17 & 18)**

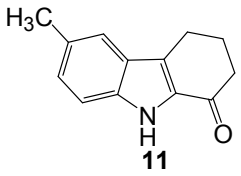
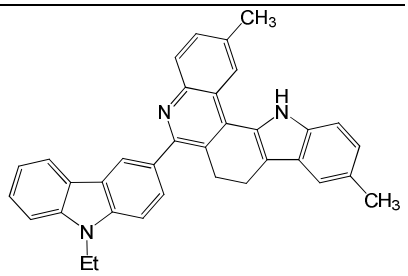
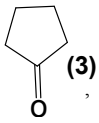
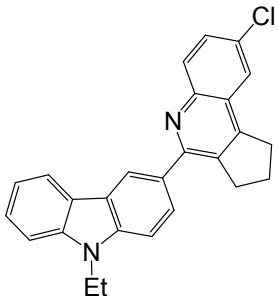
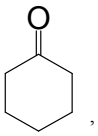
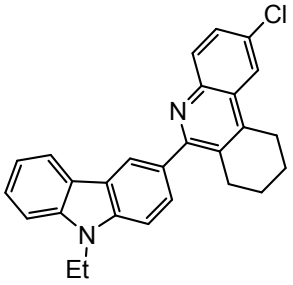
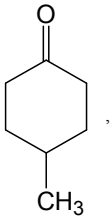
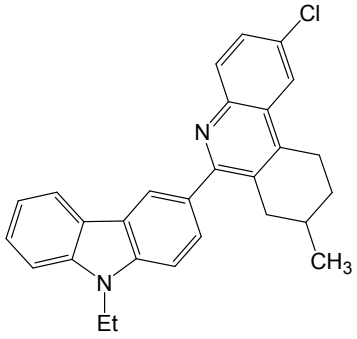
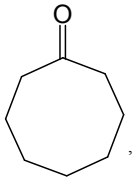
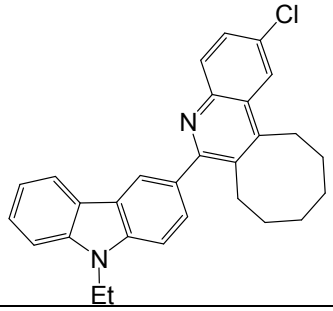
We then turned our attention towards the synthesis of 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid. We envisaged access to the desired 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid, through a synthetic route that made use of a Doebner reaction between 9-ethyl-9*H*-carbazole-3-carbaldehyde (**1**), *p*-toludine(**2**) and pyruvic acid (**19**) in dry ethanol in presence of base triethylamine as revealed in **Scheme 3**.The structure of **20**was confirmed by the infrared absorption band of theO-H group at 3450 cm^{-1} and C=O group at 1735 cm^{-1} and OH signal at δ 11.05 in the ^{1}H-NMR and sharp signal for the carbonyl carbon at δ177.3 in the ^{13}C NMR spectrum. The remaining protons appeared in the corresponding region.Subsequently we could establish the generality of the protocol by using differently substituted aromatic amines to isolate products **21-25 (Table 1)**.

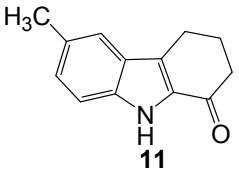
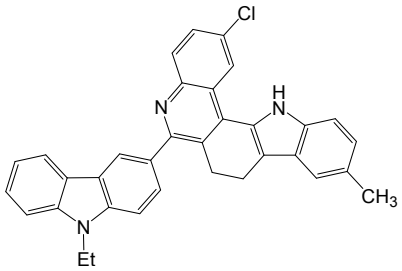
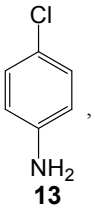
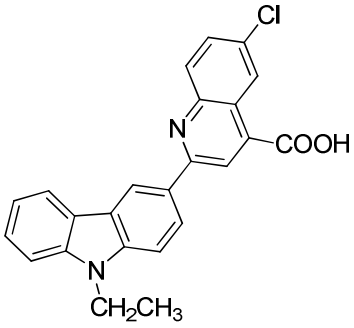
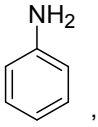
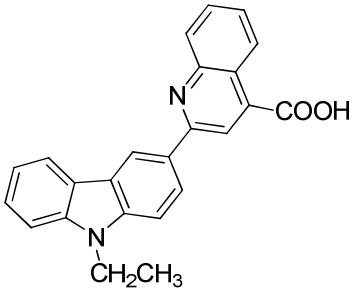
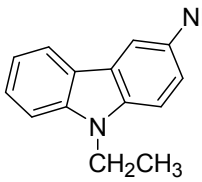
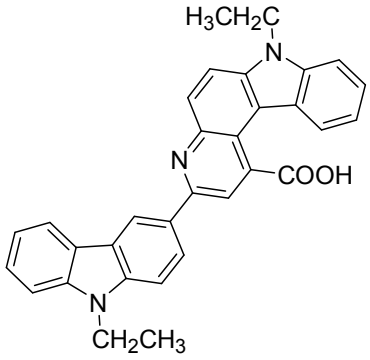


Scheme 3Synthesis of substituted 3- (quinolin-2'-yl)-carbazole-4'-carboxylic acids **(20, 21, 23 & 25)**

Table 1 Synthesis of substituted 3- (quinolin-2'-yl)-carbazoles**(4, 6, 8, 10, 12, 14, 15, 16, 17 & 18)** andsubstituted 3- (quinolin-2'-yl)-carbazole-4'-carboxylic acids

Compound	**Reactants**	**Reaction condition**	**product**
4	 , *p*-toludine (2) **3**	AcOH/ MW	
6	 , *p*-toludine (**2**) **5**	AcOH/ MW	
8	 , *p*-toludine (**2**) **7**	AcOH/ MW	
10	 , p-toludine (**3**) **9**	AcOH/ MW	

12	 **11**	*p*-toludine (**2**)	AcOH/ MW	
14	 **(3)**	*p*-chloroaniline (**13**)	AcOH/ MW	
15	 **5**	*p*-chloroaniline (**13**)	AcOH/ MW	
16	 **7**	*p*-chloro aniline (**13)**	AcOH/ MW	
17	 **9**	*p*-chloroaniline(1**3**)	AcOH/ MW	

18	 **11**	*p*-chloro aniline (**13**)	AcOH/ MW	
21	 **13**	pyruvic acid (**19**)	Et_3N/ reflux	
23	 **22**	pyruvic acid (**19**)	Et_3N/ reflux	
25	 **24**	pyruvic acid (**19**)	Et_3N/ reflux	

Conclusion

In summary, we have developed an efficient one-pot three component synthesis of highly substituted novel 3-(quinolin-2'-yl)-9*H*-carbazoles using micro wave irradiation and 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acid *via*Doebner reaction with potential applications in drug development. Products are well characterized to establish the structure. The series of 3-(quinolin-2'-yl)-9*H*-carbazoles and 3-(quinolin-2'-yl)-9*H*-carbazole-4'-carboxylic acids were synthesized which may have a wider scope in thedesign of quinolinyl drugs and carbazoleanalogues.

Appendix: Supplementary data

Experimental procedures, ^{1}H NMR and ^{13}C NMR spectra of key compounds are given in Supplementary data.

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