J. Chem. Sci. Vol. 124, No. 2, March 2012, pp. 487–494.

Synthesis of pyrano[2,3-*c*]carbazoles, pyrano[3,2-*b*]carbazoles and furo[3,2-*b*]carbazole derivatives via iodocyclization

KRISHNA CHAITANYA TALLURI and RAJAGOPAL NAGARAJAN*
School of Chemistry, University of Hyderabad, Hyderabad 500046, India
e-mail: rnsc@uohyd.ernet.in

MS received 3 August 2011; revised 13 September 2011; accepted 15 September 2011

Abstract. A simple and facile synthesis of pyranocarbazole derivatives starting from easily accessible *O*-propargylated carbazoles using iodocyclization in good yields is reported.

Keywords. Carbazole; pyranocarbazole; furocarbazole; iodocyclization; *O*-propargylcarbazole.

1. Introduction

Carbazole alkaloids have attracted the attention of synthetic chemists due to their easily accessible structural features and promising biological applications.[1] Among these, pyranocarbazole alkaloids form a prominent group due to their occurrence in various plant sources and also their intriguing structural features.[2] Pyrayafolines, eustifolines, clausamines, clausevatines, etc. are some of the important pyranocarbazole alkaloids that have been synthesized in recent times[2] (figure 1). Clausamines have been reported to inhibit EBV activation in Raji cells.[3] Diaryl pyranocarbazole derivatives were reported to show photochromic properties.[4] In this context, an efficient methodology for the synthesis of these pyranocarbazole derivatives is desirable.

The synthesis of benzopyran and quinoline derivatives from the corresponding propargyl derivatives has attracted synthetic chemists in recent times.[5,6] Larock and co-workers reported a simple methodology for the synthesis of benzopyrans through iodocyclization.[7] These reactions involve readily available reagents like iodine and simple bases which are inexpensive and ecofriendly. These reactions are also very efficient, clean and do not require harsh conditions. Further, these products can be useful building blocks for the synthesis of fused heterocycles.

*For correspondence

2. Experimental

2.1 *General procedure for O-propargylated carbazoles*

An oven dried 100 mL round bottom flask equipped with a teflon coated magnetic stirring bar was charged with hydroxycarbazole (5 mmol), potassium carbonate (15 mmol) in 15 mL of acetone under stirring. After stirring for 30 min., propargyl bromide (6 mmol) was added slowly and reaction mass was stirred at room temperature for 6 h. Reaction mass was poured into water, neutralized with 0.1 M HCl, extracted with ethyl acetate, washed twice with water (50 mL × 2), dried for an hour, sodium sulfate and solvent was removed under vacuum to sulfate the corresponding *O*-propargylated carbazole as a low melting solid.

2.1a *9-Ethyl-1,4-dimethyl-3-(prop-2-ynyloxy)-9H-carbazole* **(2a)**: mp: 72–74°C; IR(KBr): 3273, 2968, 2920, 2870, 2125, 1581, 1512, 1464, 1371, 1302, 1261, 1197, 1140, 1070, 1026, 792, 744, 540, 432 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.24 (d, $J = 8.0$ Hz, 1H), 7.46–7.40 (m, 2H), 7.22 (t, $J = 7.6$ Hz, 1H), 6.99 (s, 1H), 4.72 (s, 2H), 4.58 (q, $J = 6.8$ Hz, 2H), 2.81 (s, 6H), 2.51 (s, 1H), 1.41 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 148.7, 141.5, 125.1, 124.1, 123.3, 122.9, 120.8, 120.4, 118.6, 118.4, 117.4, 108.4, 79.7, 74.9, 59.5, 39.3, 20.0, 15.4, 12.9; m/z = 277, positive mode; Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05%; found: C, 82.11; H, 6.85; N, 5.12%.

2.1b *9-Ethyl-3-(prop-2-ynyloxy)-9H-carbazole* **(2b)**: mp: 66–68°C; IR(KBr): 3287, 3051, 2976, 2932, 2121,

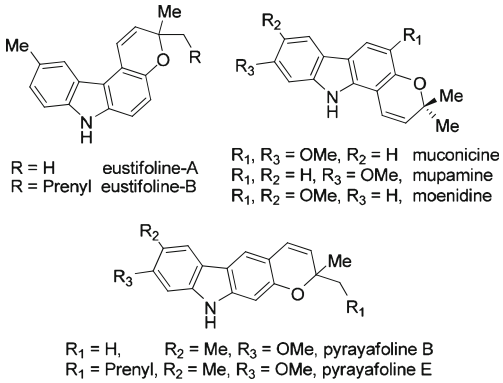


Figure 1. Pyranocarbazole alkaloids.

1622, 1579, 1485, 1323, 1292, 1230, 1180, 1086, 1060, 1024, 923, 856, 802, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.15 (d, $J = 7.6$ Hz, 1H), 7.78 (s, 1H), 7.52 (t, $J = 6.8$ Hz, 1H), 7.42 (d, $J = 8.8$ Hz, 1H), 7.35 (d, $J = 8.8$ Hz, 1H), 7.27–7.24 (m, 2H), 4.86 (s, 2H), 4.33 (q, $J = 7.2$ Hz, 2H), 2.61 (s, 1H), 1.44 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.5, 140.6, 135.7, 125.8, 123.2, 122.7, 120.5, 118.5, 115.7, 109.2, 108.7, 105.8, 79.4, 75.4, 57.3, 37.6, 13.9; m/z = 250, positive mode; Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62%; found: C, 81.85; H, 6.12; N, 5.56%.

2.1c *9-Benzyl-3-(prop-2-ynyloxy)-9H-carbazole* (**2c**): mp: 102–104°C; IR(KBr): 3283, 3065, 3024, 2912, 2852, 2127, 1626, 1597, 1489, 1448, 1381, 1354, 1325, 1188, 1057, 966, 933, 893, 848, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.10 (d, $J = 7.6$ Hz, 1H), 7.73 (s, 1H), 7.43 (t, $J = 7.2$ Hz, 1H), 7.35 (d, $J = 8.4$ Hz, 1H), 7.22–7.26 (m, 5H), 7.13–7.15 (m, 3H), 5.5 (s, 2H), 4.8 (s, 2H), 2.55 (d, $J = 2.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.7, 141.3, 137.2, 136.3, 128.8, 127.5, 126.4, 126.0, 123.3, 122.8, 120.4, 118.9, 115.8, 109.6, 109.0, 105.6, 79.2, 75.3, 57.2, 46.7; m/z = 312, positive mode; Anal. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50%; found: C, 84.95; H, 5.56; N, 4.39%.

2.2 *General procedure for Sonogashira coupling of O-propargylatedcarbazoles with aryl iodides*

An oven dried 50 mL Schlenk tube equipped with a teflon coated magnetic stirring bar was charged with *O*-propargylated carbazole (2 mmol), 1 g of molecular sieves and aryl iodide (2.2 mmol). The tube was evacuated and filled with nitrogen. To it, 10 mL of dry THF and 5 mL of freshly distilled triethylamine were added under nitrogen and the reaction was stirred for 10 minutes at room temperature. $Pd(PPh_3)_2Cl_2$ (2 mol%) and CuI (1 mol%) were added under nitrogen and the the reaction mixture was stirred at room temperature for 4 h, after which time TLC (95:05 hexanes:ethyl acetate) indicated complete conversion. Reaction mass was filtered through celite. The filterate was poured into crushed ice slowly and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and solvent was removed under reduced pressure. The crude material was purified by column chromatography (eluent: 5–15% ethyl acetate in hexanes) using silica gel (100–200 mesh).

2.2a *9-Ethyl-3-(3-phenylprop-2-ynyloxy)-9H-carbazole* (**3a**): mp: 120–122°C; IR(KBr): 3043, 2974, 2854, 1626, 1595, 1483, 1471, 1444, 1371, 1321, 1288, 1230, 1190, 1151, 1008, 844, 800, 748, 690, 420 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.11 (d, $J = 7.6$ Hz, 1H), 7.80 (s, 1H), 7.50 (m, 3H), 7.42–7.22 (m, 7H), 5.05 (s, 2H), 4.35 (q, $J = 7.2$ Hz, 2H), 1.44 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.8, 140.6, 135.6, 131.9, 128.3, 125.7, 123.3, 122.8, 122.6, 120.5, 119.1, 118.5, 115.8, 109.1, 108.6, 105.9, 87.1, 84.7, 58.2, 37.6, 13.9; m/z = 326, positive mode; Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30%; found: C, 84.66; H, 5.81; N, 4.28%.

2.2b *9-Benzyl-3-(3-p-tolylprop-2-ynyloxy)-9H-carbazole* (**3b**): mp: 140–142°C; IR(KBr): 3028, 2916, 2229, 1604, 1510, 1493, 1475, 1356, 1323, 1246, 1222, 1174, 1055, 1026, 909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.15 (d, $J = 8.0$ Hz, 1H), 7.84 (s, 1H), 7.47 (t, $J = 8.0$ Hz, 1H), 7.42–7.37 (m, 3H), 7.31–7.26 (m, 5H), 7.23 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 7.18–7.14 (m, 4H), 5.50 (s, 2H), 5.05 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 152.1, 141.3, 138.8, 137.3, 136.3, 131.8, 129.1, 128.8, 127.5, 126.4, 126.0, 123.4, 122.9, 120.5, 119.5, 118.9, 116.0, 109.6, 109.0, 105.8, 87.3, 83.9, 58.2, 46.7, 21.5; m/z = 402, positive mode; Anal. Calcd for $C_{29}H_{23}NO$: C, 86.75; H, 5.77; N, 3.49%; found: C, 86.67; H, 5.72; N, 3.41%.

2.2c *9-Benzyl-3-(3-(4-nitrophenyl)prop-2-ynyloxy)-9H-carbazole* (**3c**): mp: 154–156°C; IR(KBr): 3088, 3024, 2924, 2856, 1626, 1591, 1487, 1467, 1448, 1379, 1344, 1286, 1238, 1215, 1184, 1059, 895, 817, 723, 607, 424 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.17 (d, $J = 8.4$ Hz, 2H), 8.13 (d, $J = 7.6$ Hz, 1H), 7.80 (d, $J = 2.0$ Hz, 1H), 7.58 (d, $J = 8.8$ Hz, 2H), 7.45 (t, $J = 8.8$ Hz, 1H), 7.39 (d, $J = 8.0$ Hz, 1H),

7.26–7.30 (m, 5H), 7.22–7.16 (m, 3H), 5.50 (s, 2H), 5.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.8, 147.3, 141.3, 137.2, 136.4, 132.5, 129.2, 128.8, 127.5, 126.4, 126.1, 123.5, 123.4, 122.7, 120.4, 119.0, 115.8, 109.7, 109.1, 105.8, 90.0, 85.2, 57.9, 46.7; m/z = 433, positive mode; Anal. Calcd for $C_{28}H_{20}N_2O_3$: C, 77.76; H, 4.66; N, 6.48%; found: C, 77.62; H, 4.61; N, 6.56%.

2.2d *9-Benzyl-3-(3-(4-methoxyphenyl)prop-2-ynyloxy)-6-methyl-9H-carbazole* **(3d)**: mp: 134–136°C; IR(KBr): 3020, 2916, 2228, 1600, 1510, 1475, 1355, 1322, 1240, 1222, 1174, 1050, 1026, 908 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.92 (s, 1H), 7.77 (s, 1H), 7.43 (d, 2H), 7.42–7.24 (m, 4H), 7.19–7.13 (m, 3H), 6.85 (d, J = 6.8 Hz, 2H), 5.48 (s, 2H), 5.03 (s, 2H), 3.82 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 159.8, 151.9, 139.6, 137.4, 136.5, 133.4, 128.7, 128.1, 127.4, 127.3, 126.4, 123.1, 123.0, 120.3, 115.8, 114.6, 113.9, 109.5, 108.7, 105.7, 87.0, 83.2, 58.2, 55.3, 46.7, 21.4; m/z = 418, positive mode; Anal. Calcd for $C_{29}H_{23}NO_2$: C, 83.43; H, 5.55; N, 3.35%; found: C, 83.28; H, 5.51; N, 3.41%.

2.2e *9-Benzyl-3-methyl-6-(3-p-tolylprop-2-ynyloxy)-9H-carbazole* **(3e)**: mp: 128–130°C; IR(KBr): 3026, 2915, 2227, 1601, 1491, 1475, 1356, 1243, 1226, 1171, 1055, 1021, 911 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.93 (s, 1H), 7.78 (s, 1H), 7.39 (d, J = 7.6 Hz, 2H), 7.28–7.13 (m, 11H), 5.48 (s, 2H), 5.03 (s, 2H), 2.57 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.9, 139.6, 138.7, 137.4, 136.5, 131.8, 129.1, 128.8, 128.2, 127.4, 127.3, 126.4, 123.1, 123.0, 120.4, 119.4, 115.8, 109.5, 108.7, 105.7, 87.2, 83.9, 58.2, 46.7, 21.5, 21.4; Anal. Calcd for $C_{30}H_{25}NO$: C, 84.98; H, 6.86; N, 3.81%; found: C, 84.85; H, 6.72; N, 3.76%.

2.2f *9-Benzyl-3-methyl-6-(3-(4-nitrophenyl)prop-2-ynyloxy)-9H-carbazole* **(3f)**: mp: 170–172°C; IR(KBr): 2922, 2858, 1732, 1593, 1493, 1452, 1340, 1199, 1026, 850, 796 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.16 (d, J = 8.8 Hz, 2H), 7.90 (s, 1H), 7.74 (d, J = 2.0 Hz, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.28–7.26 (m, 6H), 7.17–7.12 (m, 3H), 5.46 (s, 2H), 5.04 (s, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.5, 147.3, 139.6, 137.3, 136.6, 132.6, 129.3, 128.8, 128.3, 127.5, 127.5, 126.4, 123.5, 123.2, 122.8, 120.3, 115.6, 109.6, 108.8, 105.7, 90.1, 85.1, 57.9, 46.7, 21.4; m/z = 447, positive mode; Anal. Calcd for $C_{29}H_{22}N_2O_3$: C, 78.01; H, 4.97; N, 6.27%; found: C, 78.21; H, 5.06; N, 6.35%.

2.2g *9-Ethyl-1,4-dimethyl-3-(3-p-tolyl prop-2-ynyloxy)-9H-carbazole* **(3g)**: mp: 148–150°C; IR(KBr): 3020, 2925, 2230, 1600, 1475, 1355, 1240, 1225, 1170, 1056, 1021, 911 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.36 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.44 (d, J = 6.8 Hz, 1H), 7.41–7.39 (m, 2H), 7.30–7.25 (m, 1H), 7.16–7.12 (m, 2H), 4.90 (s, 2H), 4.60 (q, J = 7.0 Hz, 2H), 2.90 (s, 3H), 2.89 (s, 3H), 2.39 (s, 3H), 1.43 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 149.1, 141.5, 138.6, 137.3, 134.9, 131.7, 131.2, 129.1, 125.1, 124.2, 122.9, 121.1, 119.1, 118.6, 117.4, 114.6, 108.4, 84.6, 60.7, 39.3, 21.5, 20.2, 15.4, 13.0; m/z = 368, positive mode; Anal. Calcd for $C_{26}H_{25}NO$: C, 84.98; H, 6.86; N, 3.81%; found: C, 84.85; H, 6.72; N, 3.76%.

2.2h *9-Ethyl-1,4-dimethyl-3-(3-(4-nitrophenyl)prop-2-ynyloxy)-9H-carbazole* **(3h)**: mp: 166–168°C; IR(KBr): 2918, 2854, 1743, 1610, 1554, 1508, 1332, 1261, 1205, 1182, 1091, 1016, 883, 869, 812, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.31 (d, J = 7.2 Hz, 1H), 8.16 (d, J = 7.2 Hz, 2H), 7.60 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.52 (d, J = 7.2 Hz, 1H), 7.38 (m, 1H), 7.06 (s, 1H), 5.08 (s, 2H), 4.61 (q, J = 7.2 Hz, 2H), 2.86 (s, 3H), 2.84 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 148.7, 141.4, 135.0, 132.5, 132.4, 129.5, 125.2, 123.5, 122.8, 121.0, 120.4, 118.8, 118.7, 117.5, 114.5, 108.5, 90.7, 84.9, 60.4, 39.3, 20.2, 15.5, 13.0; m/z = 326, positive mode; Anal. Calcd for $C_{25}H_{22}N_2O_3$: C, 84.89; H, 5.89; N, 4.30%; found: C, 84.51; H, 5.41; N, 9.93%. m/z = 399, positive mode; Anal. Calcd for $C_{25}H_{22}N_2O_3$: C, 75.36; H, 5.57; N, 7.03%; found: C, 75.48; H, 5.51; N, 7.12%.

2.3 *General procedure for iodocyclization of aryl-O-propargylated carbazoles*

An oven dried 10 mL round bottom flask equipped with a teflon coated magnetic stirring bar was charged with aryl-*O*-propargyl carbazole (0.2 mmol), sodium bicarbonate (0.4 mmol) and iodine (0.6 mmol) in nitromethane (2 mL) and reaction mixture was stirred at room temperature for 4–6 h, after which time TLC (95:05 hexanes:ethyl acetate) indicated complete conversion. The reaction mixture was quenched with 5% solution of sodium thiosulphate, extracted with dichloromethane, dried for an hour sodium sulphate, adsorbed on silica and purified by column chromatography (5–10% ethyl acetate in hexanes) using silica gel (100–200 mesh).

2.3a *7-Ethyl-2-iodo-1-phenyl-3,7-dihydropyrano[2,3-c]carbazole* **(4a)**: mp: 146–148°C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.45–7.43 (m, 2H), 7.41 (d, J = 8.8 Hz, 1H), 7.34–7.23 (m, 6H), 6.60 (m, 1H), 6.56 (d, J = 8.0 Hz, 1H), 6.08 (s, 2H), 4.36 (q, J = 7.6 Hz, 2H), 1.43 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 150.8, 141.1, 140.4, 140.1, 136.3, 1308, 128.3, 128.0, 124.9, 124.1, 121.9, 119.1, 118.6, 117.8, 114.4, 110.2, 107.8, 86.7, 77.1, 37.4, 13.8; m/z = 452, positive mode; Anal. Calcd for $C_{23}H_{18}INO$: C, 61.21; H, 4.02; N, 3.10%; found: C, 61.25; H, 4.04; N, 3.06%.

2.3b *7-Benzyl-2-iodo-1-(4-nitrophenyl)-3,7-dihydropyrano[2,3-c]carbazole* **(4b)**: mp: 188–190°C; IR(KBr): 3057, 2922, 2858, 1595, 1514, 1454, 1425, 1194, 1091, 1005, 889, 848, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.17 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.4 Hz, 1H), 7.30–7.27 (m, 4H), 7.23–7.20 (m, 2H), 7.12 (d, J = 6.8 Hz, 2H), 6.66–6.63 (m, 2H), 5.52 (s, 2H), 5.10 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.7, 147.1, 146.9, 141.1, 139.6, 136.9, 136.8, 131.6, 128.9, 127.6, 126.3, 125.6, 123.3, 123.1, 121.4, 118.5, 118.3, 118.0, 114.7, 111.5, 108.7, 88.8, 77.2, 46.5; m/z = 559, positive mode; Anal. Calcd for $C_{28}H_{19}IN_2O_3$: C, 60.23; H, 3.43; N, 5.02%; found: C, 60.45; H, 3.38; N, 5.12%.

2.3c *7-Benzyl-2-iodo-10-methyl-1-(4-nitrophenyl)-3,7-dihydropyrano[2,3-c]carbazole* **(4c)**: mp: 194–196°C; IR(KBr): 3207, 3069, 3032, 2916, 2852, 1730, 1595, 1518, 1452, 1305, 1211, 1147, 1066, 1014, 848, 800, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.18 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.37–7.02 (m, 9H), 6.35 (s, 1H), 5.47 (s, 2H), 5.09 (s, 2H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 151.0, 147.2, 147.1, 139.6, 139.4, 137.2, 137.0, 131.9, 128.9, 127.6, 127.6, 127.1, 126.3, 123.2, 123.1, 122.5, 121.5, 118.0, 114.6, 111.4, 108.3, 88.7, 76.0, 46.5, 20.8; m/z = 573, positive mode; Anal. Calcd for $C_{29}H_{21}IN_2O_3$: C, 60.85; H, 3.70; N, 4.89%; found: C, 60.75; H, 3.75; N, 4.76%.

2.3d *6-Ethyl-3-iodo-5,11-dimethyl-4-(4-nitrophenyl)-2,6-dihydropyrano[3,2-b]carbazole* **(4d)**: mp: 180–182°C; IR(KBr): 3414, 2961, 2914, 2843, 1595, 1510, 1454, 1346, 1176, 1078, 1006, 860, 736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.26–8.24 (m, 3H), 7.50–7.48 (m, 3H), 7.38 (m, 1H), 7.23 (t, J = 7.2 Hz, 1H), 4.99 (s, 2H), 4.35 (d, J = 6.4 Hz, 2H), 2.80 (s, 3H), 2.02 (s, 3H), 1.28 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 150.0, 147.6, 146.8, 143.2, 141.5, 136.1, 130.8, 127.5, 126.1, 124.5, 124.5, 124.1, 123.4, 123.2, 119.3, 117.1, 114.8, 109.1, 91.2, 40.4, 19.8, 15.1, 12.9; m/z = 525, positive mode; Anal. Calcd for $C_{25}H_{21}IN_2O_3$: C, 57.26; H, 4.04; N, 5.34%; found: 57.36; H, 4.08; N, 5.23%.

2.4 *5-Ethyl-4,10-dimethyl-3-(2-nitro-1-p-tolylvinyl)-3,5-dihydro-2H-furo[3,2-b]carbazole* **(5)**

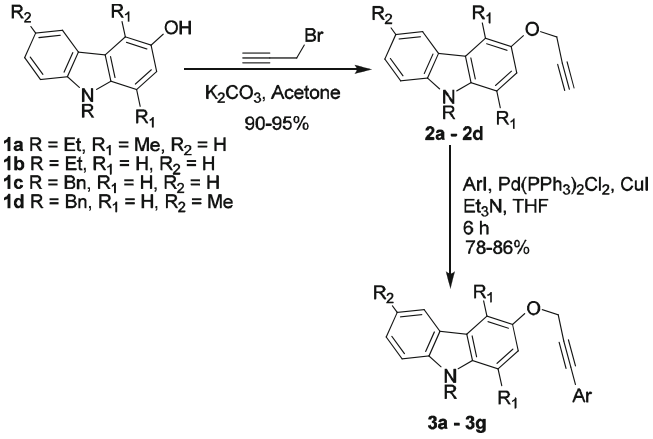
mp: 140–142°C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.25 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.26–7.19 (m, 5H), 5.93 (d, J = 5.2 Hz, 1H), 5.50 (m, 1H), 4.84 (dd, J = 9.6 Hz, J = 9.6 Hz, 1H), 4.54 (dd, J = 3.6 Hz, J = 3.6 Hz, 1H), 4.46 (q, J = 7.6 Hz, 2H), 2.76 (s, 3H), 2.42 (s, 3H), 2.21 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 144.6, 142.9, 141.8, 138.7, 137.5, 136.6, 129.4, 126.9, 125.8, 124.2, 123.2, 122.3, 119.8, 119.1, 118.4, 115.9, 108.9, 76.7, 75.6, 70.8, 40.3, 21.2, 20.3, 15.0, 12.7; m/z = 559, positive mode; Anal. Calcd for $C_{27}H_{26}N_2O_3$: C, 76.03; H, 6.14; N, 6.57%; found: C, 76.31; H, 6.41; N, 6.53%.

3. Results and discussion

In continuation of our efforts in the synthesis of various heteroarylcarbazole derivatives from easily accessible precursors,[8] we report here, a simple synthesis of new pyranocarbazole derivatives employing iodocyclization. The synthesis of aryl-*O*-propargylated precursors is demonstrated in scheme 1. Hydroxycarbazoles (**1a**–**1d**) were synthesized employing methods reported in literature.[9] These hydroxycarbazoles were *O*-alkylated using propargyl bromide, K_2CO_3 in acetone. The *O*-propargyl derivatives **2a**–**d** were subjected to Sonogashira coupling with various aryl iodides employing $Pd(PPh_3)_2Cl_2$, CuI and triethylamine as base in THF (scheme 1). The products **3a**–**g** and their yields are summarized in table 1. All the products were obtained in good yields.

Then we carried out the cyclization reaction of phenyl-*O*-propargylated derivative **3a** in various solvents like THF, dioxane, DMF, etc. We found that the conditions using nitromethane as solvent, 3 eq. iodine and 2 eq. sodium bicarbonate gave the best yields. Employing these optimized conditions, we successfully synthesized various pyranocarbazole derivatives in good yields. The results are summarized in table 2.

Substituents on the aryl ring have significant effect on the course of reaction. Electron withdrawing substituents on the aryl group increased the yields. Electron



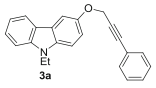
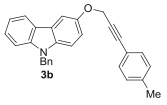
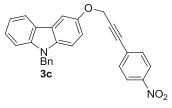
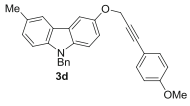
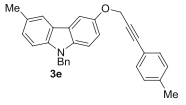
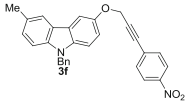
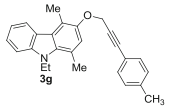
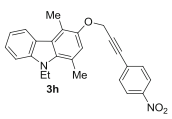
Scheme 1. Synthesis of aryl-*O*-propargylated carbazoles.

donating substituents resulted in a complex mixture of products. Various substituted carbazoles were employed, the 1,4-dimethyl derivative **3h** provided linear product, which is of particular interest in biological applications.

All the products were well-characterized by ^{1}H and ^{13}C NMR spectra. Interestingly in the ^{1}H NMR spectra of cyclized products **4a–c**, the C_5-H was shifted to upfield from δ 8.11 (**3a**) to δ 6.56 (**4a**). This considerable upfield shift can be explained by the anisotropic effect of the aryl group, which clouds the C_5-H after cyclization (figure 2). The same was observed in the cases of **4b** and **4c**. The perpendicular geometry and proximity of aryl ring can be seen in the crystal structures of **4a** and **4b** (figure 3). To our surprise, when we carried out the reaction with 9-ethyl-1,4-dimethyl-3-(3-(4-*p*-Tolyl-prop-2-ynyloxy)-9*H*-carbazole **3g**, we obtained a completely different product **5** in 70% yield (scheme 2). A furocarbazole derivative formation is observed. Formation of a five-membered ring followed by the replacement of iodine by nitromethyl anion resulted in the furocarbazole derivative. The proposed mechanism for this observation is shown in scheme 3.

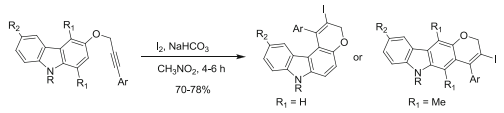
The compounds **4a** and **4b** were also characterized by X-ray crystallographic analysis.[10] The ORTEP diagrams are shown in figure 3.

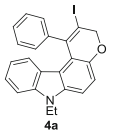
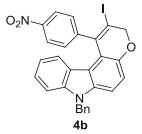
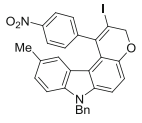
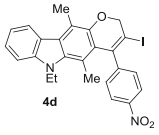
Table 1. Aryl-*O*-propargylated carbazoles.

Entry	Reactant	Hydroxycarb.	Coupled product	Time (h)	Yield (%)
1	C_6H_5I	1b		8	85
2	4-Me-C_6H_4I	1c		8	82
3	4-O_2N-C_6H_4I	1c		8	81
4	4-MeO-C_6H_4I	1d		6	85
5	4-Me-C_6H_4I	1d		6	86
6	4-O_2N-C_6H_4I	1d		6	84
7	4-Me-C_6H_4I	1a		8	78
8	4-O_2N-C_6H_4I	1a		6	85

In all the cases, $Pd(PPh_3)_2Cl_2$ (2 mol%) and CuI (1 mol%) were used in the presence of Et_3N as a base and THF as a solvent at r.t.

Table 2. Pyranocarbazole derivatives.



Entry	Reactant	Cyclized product	Time (h)	Yield (%)
1	**3a**	 **4a**	4	70
2	**3c**	 **4b**	6	72
3	**3f**	 **4c**	6	74
4	**3h**	 **4d**	4	78

In all the cases, iodine (3 eq) and $NaHCO_3$ (2 eq) were used in the presence of nitromethane as solvent at r.t.

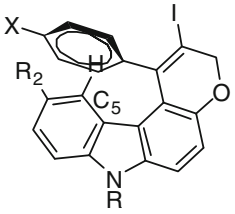
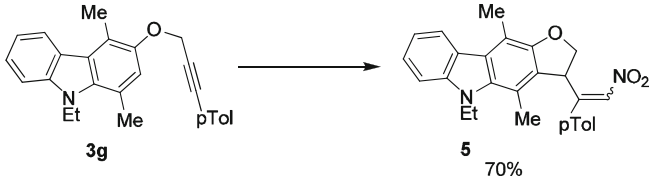


Figure 2. Observation of anisotropic effect in **4a–c**.



Scheme 2. Furocarbazole formation.

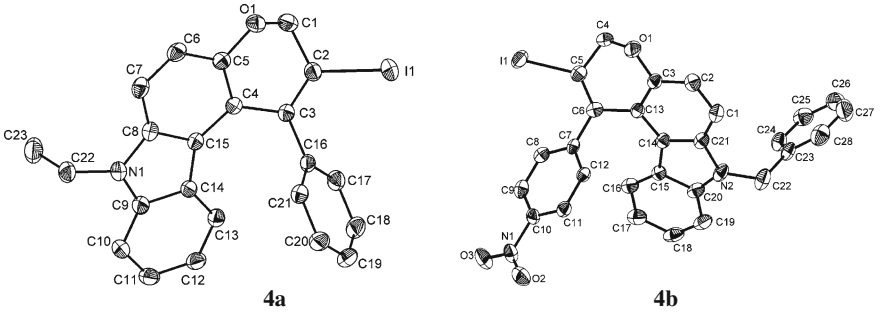
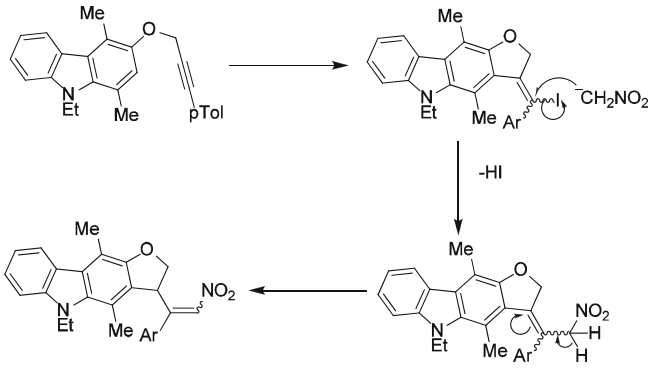


Figure 3. ORTEP diagrams of **4a** and **4b**. Hydrogen atoms are omitted for clarity.



Scheme 3. Proposed mechanism for the formation of **5**.

4. Conclusion

In conclusion, we report here a simple and facile synthesis of new pyranocarbazole derivatives from easily accessible *O*-propargylated carbazoles employing iodocyclization in good yields. An interesting product with nitromethane insertion is observed. Further investigations are under progress.

Acknowledgements

We gratefully acknowledge the Department of Science and Technology (DST) for financial assistance (Project number: SR/S1/OC-70/2008) and for providing a single-crystal X-ray diffractometer facility in our school. TKC thanks Council of Scientific and Industrial Research (CSIR) for Senior Research Fellowship. The authors thank Mr. Bharat, Mr. Anand and Mr. Nagarjuna for their help in solving crystal structures.

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10. (a) The CCDC deposition number of **4a** is 818251; molecular formula: $C_{23}H_{18}INO$, unit cell parameters: a 6.4622(14) b 13.492(3) c 21.416(5) beta 98.668(3) space group P21/c; (b) The CCDC deposition number of **4b** is 818250; molecular formula: $C_{28}H_{19}IN_2O_3$, unit cell parameters: a 17.9078(18) b 12.4689(15) c 20.656(2) space group Pna21