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Synthesis, Anticancer and Antioxidant Activity of Novel 2,4-Disubstituted Thiazoles

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A new series of carbazole based 2,4-disubstituted thiazole derivatives were synthesized. All the synthesized compounds were tested for their cytotoxicity against three different cancer cell lines A549, MCF-7, and HT29. Some of these compounds showed good cytotoxicity. These compounds were also evaluated for antioxidant activity. Compounds **3a**, **3b**, **3d-f** and **3i** showed higher antioxidant activity than standard BHT.

Key Words : 2,4-Disubstituted thiazole, Carbazole, α-Bromoketone, Cytotoxicity

Introduction

Nitrogen and sulfur heterocyles have been under investigation for a long time because of their significant medicinal properties. Among the wide range of heterocycles explored in the recent years, thiazole derivatives have attracted medicinal chemists because of their varied biological activities.[1-9] Thiazole ring is an interesting building block in a variety of natural products and many potent biologically active molecules such as vitamine B1, epothilones, nizatidine, ritonavir, sulfathiazole, abafungin and tiazofurin. Thiazole derivatives have been extensively studied and so far, a variety of biological activities have been reported, for a large number of their derivatives, such as antihypertensive, anti-inflammatory, antischizophrenia, antibacterial, anti-HIV, hypnotics, antiallergic, analgesic, fibrinogen receptor antagonist, bacterial DNA gyrase B inhibitor and antitumor activities.[10-22] Also they have wide range of applications in organic functional materials such as fluorescent dyes[23] and liquid crystals.[24]

On the other hand, carbazole and its derivatives have attracted considerable attention from both synthetic organic and medicinal chemists due to their potential biological activity covering a wide range of medicinal applications. Carbazoles belong to an unusual class of DNA binding agents. These molecules contain a planar chromophore, which is the characteristic of DNA intercalators.[25] Carbazole derivatives exhibit diverse biological activities such as antimalarial, antimicrobial, anti-tuberculosis, anti-HIV, anti-inflammatory, antihistaminic, and antitumor activities.[26-32]

Keeping in view of the importance of thiazole and carbazole derivatives and in continuation of our search on biologically active molecules,[33-36] we herein report the synthesis, anticancer and antioxidant activity of a new series of carbazole based 2,4-disubstituted thiazole derivatives.

Experimental

All reagents were obtained from Aldrich Chemical Company and used as supplied. The 6-bromo-9-ethyl-9*H*-carbazole-3-carbaldehyde, was prepared by the ethylation[37] followed by formylation[38] and bromination of carbazole.[39] Melting points were determined in open capillaries using Electrothermal (IA 9100) digital melting point apparatus and are uncorrected. IR spectra were recorded on Bruker (Tensor 37) FT-IR spectrometer using KBr pellets. ^{1}H, ^{13}C NMR spectra were recorded on a Bruker AM500 FT-NMR spectrometer. Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on JEOL JMS-700 high resolution mass spectrometer.

2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)hydrazinecarbothioamide (2): A mixture of equimolar quantity of 6-bromo-9-ethyl-9*H*-carbazole-3-carbaldehyde (**1**) (25 mmol) and thiosemi-carbazide (25 mmol) in 70 mL of ethanol and catalytic amount of acetic acid was heated under reflux in an oil bath for 3-5 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the solid product was filtered and washed with water. The solid was then dried, and recrystallized from EtOH.

mp 214-215 °C; Yield 90%; IR (KBr): cm^{-1} 3429, 3285, 3150, 2974, 1627, 1592, 1532, 1481, 1233, 1087, 800; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.28 (t, J = 6.8 Hz, 3H), 4.42 (q, J = 6.5 Hz, 2H), 7.57-7.58 (m, 2H), 7.63 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 8.00 (s, 1H), 8.22 (s, 2H), 8.42 (s, 1H), 8.65 (s, 1H), 11.44 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.3, 109.6, 111.4, 111.5, 120.6, 121.4, 123.1, 124.2, 125.7, 125.9, 128.4, 138.7, 140.8, 143.2, 177.6.

General Procedure for the Synthesis of Compounds 3a-j. A mixture of equimolar quantity of thiosemicarbazone (**2**) (2 mmol) and α-bromoketone (2 mmol) in 10 mL of absolute ethanol was heated under reflux in an oil bath for 2-3 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the solution was cooled and the resulting solid was filtered and dried. Finally, the product was recrystallized from ethanol.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-phenylthiazole (3a): mp 250-251 °C; Yield

88%; IR (KBr): cm^{-1} 3393, 3051, 2973, 1622, 1480, 1233, 802, 738; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 4.45 (q, J = 6.8 Hz, 2H), 7.31-7.33 (m, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.58-7.63 (m, 2H), 7.70 (d, J = 9.0 Hz, 1H), 7.86 (d, J = 7.5 Hz, 2H), 7.91 (d, J = 8.5 Hz, 1H), 8.26 (s, 1H), 8.44 (s, 1H), 8.48 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 103.5, 110.1, 111.4, 111.5, 120.5, 121.3, 123.2, 124.0, 124.2, 125.6, 125.7, 127.7, 128.4, 128.6, 134.0, 138.7, 140.6, 143.5, 168.4. HRMS (EI) *m/z*: Calcd for $C_{24}H_{19}BrN_4S$: 474.0514 (M^+), Found: 474.0516.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-*p*-tolylthiazole (3b): mp 279-280 ºC; Yield 90%; IR (KBr): cm^{-1} 3416, 3053, 2975, 1620, 1483, 1235, 801; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 2.32 (s, 3H), 4.45 (q, J = 6.8 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.26 (s, 1H), 7.58-7.63 (m, 2H), 7.70 (d, J = 9.0, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.5 Hz, 1H), 8.28 (s, 1H), 8.44 (s, 1H), 8.47 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 20.8, 37.4, 102.7, 110.1, 111.4, 111.5, 120.6, 121.3, 123.2, 124.0, 124.3, 125.6, 128.4, 129.2, 137.2, 138.7, 140.6, 144.0, 148.6, 148.7, 168.3; HRMS (EI) *m/z*: Calcd for $C_{25}H_{21}BrN_4S$: 488.0670 (M^+), Found: 488.0669.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(4-methoxyphenyl)thiazole (3c): mp 243-244 ºC; Yield 90%; IR (KBr): cm^{-1} 3400, 3062, 1621, 1510, 1255, 1020, 804; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 3.79 (s, 3H), 4.45 (q, J = 7.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 7.17 (s, 1H), 7.58-7.63 (m, 2H), 7.70 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 8.5 Hz, 2H), 7.92 (d, J = 8.5 Hz, 1H), 8.30 (s, 1H), 8.45 (s, 1H), 8.47 (d, J = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 55.2, 101.5, 110.1, 111.4, 111.5, 114.0, 120.7, 121.3, 123.2, 124.0, 124.3, 125.5, 126.1, 127.1, 128.4, 138.7, 140.7, 144.3, 159.1, 168.3; HRMS (EI) *m/z*: Calcd for $C_{25}H_{21}BrN_4OS$: 504.0619 (M^+), Found: 504.0623.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(4-(trifluoromethoxy) phenyl)thiazole (3d): mp 267-268 ºC; Yield 80%; IR (KBr): cm^{-1} 3398, 3056, 2977, 1623, 1485, 1266, 1018, 803; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.29 (t, J = 7.3 Hz, 3H), 4.43 (q, J = 6.8 Hz, 2H), 7.40 (t, J = 4.0 Hz, 3H), 7.57-7.61 (m, 2H), 7.67 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 9.0 Hz, 2H), 8.26 (s, 1H), 8.42 (s, 1H), 8.46 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 104.5, 110.0, 111.4, 111.5, 119.1, 120.5, 121.2, 121.3, 123.2, 124.0, 124.2, 125.7, 127.4, 128.4, 133.4, 138.7, 140.6, 143.5, 147.6, 148.1, 168.6; HRMS (EI) *m/z*: Calcd for $C_{25}H_{18}BrF_3N_4OS$: 558.0337 (M^+), Found: 558.0335.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(4-chlorophenyl)thiazole (3e): mp 275-276 ºC; Yield 89%; IR (KBr): cm^{-1} 3386, 3049, 2974, 1622, 1489, 1234, 1092, 797; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.28 (t, J = 7.0 Hz, 3H), 4.41 (q, J = 6.8 Hz, 2H), 7.36 (s, 1H), 7.46 (d, J = 8.5 Hz, 2H), 7.55-7.59 (m, 2H), 7.65 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.5 Hz, 2H), 7.89 (d, J = 8.5 Hz, 1H), 8.28 (s, 1H), 8.41 (s, 1H), 8.44 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 104.3, 110.0, 111.5, 120.6, 121.3, 123.2, 124.0, 124.3, 125.7, 127.4, 128.5, 128.6, 132.2, 132.8, 138.7, 140.6, 143.9, 147.9, 168.5; HRMS (EI) *m/z*: Calcd for $C_{24}H_{18}BrClN_4S$: 508.0124 (M^+), Found: 508.0128.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(4-bromophenyl)thiazole (3f): mp 288-289 ºC; Yield 88%; IR (KBr): cm^{-1} 3410, 3050, 2974, 1621, 1487, 1235, 1007, 751; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 4.45 (q, J = 6.8 Hz, 2H), 7.40 (s, 1H), 7.58-7.63 (m, 4H), 7.69 (d, J = 8.5 Hz, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.90 (d, J = 8.5 Hz, 1H), 8.24 (s, 1H), 8.42 (s, 1H), 8.47 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.3, 104.3, 110.0, 111.4, 111.5, 120.4, 120.6, 121.3, 123.2, 124.0, 124.2, 125.8, 127.6, 128.4, 131.5, 133.6, 138.7, 140.5, 143.2, 148.7, 168.5; HRMS (EI) *m/z*: Calcd for $C_{24}H_{18}Br_2N_4S$: 551.9619 (M^+), Found: 551.9620.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(4-nitrophenyl)thiazole (3g): mp 283-284 ºC; Yield 83%; IR (KBr): cm^{-1} 3387, 3083, 2976, 1627, 1517, 1344, 1236, 853; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 7.0 Hz, 3H), 4.43 (q, J = 7.0 Hz, 2H), 7.57-7.62 (m, 2H), 7.67 (d, J = 8.5, 1H), 7.70 (s, 1H), 7.88 (d, J = 8.5, 1H), 8.10 (d, J = 8.5 Hz, 2H), 8.25 (t, J = 8.3 Hz, 3H), 8.41 (s, 1H), 8.46 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 108.2, 110.0, 111.4, 111.5, 120.4, 121.3, 123.2, 124.0, 124.2, 125.8, 126.3, 128.4, 138.7, 140.5, 140.6, 143.2, 146.2, 148.3, 168.8; HRMS (EI) *m/z*: Calcd for $C_{24}H_{18}BrN_5O_2S$: 519.0365 (M^+), Found: 519.0364.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(3-nitrophenyl)thiazole (3h): mp 281-282 ºC; Yield 82%; IR (KBr): cm^{-1} 3422, 3129, 2976, 1625, 1527, 1347, 1236, 805; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.30 (t, J = 6.8 Hz, 3H), 4.44 (q, J = 7.0 Hz, 2H), 7.57-7.62 (m, 2H), 7.64 (s, 1H), 7.67-7.71 (m, 2H), 7.89 (d, J = 8.5, 1H), 8.13 (d, J = 7.5 Hz, 1H), 8.22 (s, 1H), 8.30 (d, J = 7.5 Hz, 1H), 8.42 (s, 1H), 8.46 (s, 1H), 8.67 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.3, 106.0, 110.0, 111.4, 111.5, 119.9, 120.4, 121.3, 121.9, 123.2, 124.0, 124.2, 125.8, 128.4, 130.2, 131.5, 136.1, 138.7, 140.5, 143.0, 147.9, 148.2, 168.7; HRMS (EI) *m/z*: Calcd for $C_{24}H_{18}BrN_5O_2S$: 519.0365 (M^+), Found: 519.0367.

4-(2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)thiazol-4-yl)benzonitrile (3i): mp 276-277 ºC; Yield 83%; IR (KBr): cm^{-1} 3402, 3055, 2974, 2227, 1626, 1484, 1235, 805; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.29 (t, J = 7.0 Hz, 3H), 4.42 (q, J = 6.8 Hz, 2H), 7.55-7.60 (m, 2H), 7.61 (s, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.5 Hz, 2H), 8.24 (s, 1H), 8.40 (s, 1H), 8.44 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 107.2, 109.6, 110.0, 111.4, 111.5, 119.0, 120.4, 121.3, 123.2, 124.0, 124.2, 125.7, 126.1, 128.4, 132.6, 138.6, 138.7, 140.5, 143.3, 148.4, 168.7; HRMS (EI) *m/z*: Calcd for $C_{25}H_{18}BrN_5S$: 499.0466 (M^+), Found: 499.0470.

2-(2-((6-Bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)-hydrazinyl)-4-(naphthalen-1-yl) thiazole (3j): mp 255-256 ºC; Yield 88%; IR (KBr): cm^{-1} 3399, 3051, 2973, 1620, 1480, 1234, 807; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.26 (t, J

= 7.0 Hz, 3H), 4.39 (q, *J* = 6.7 Hz, 2H), 7.48-7.54 (m, 3H), 7.56 (s, 2H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.89-7.98 (m, 5H), 8.34 (s, 1H), 8.37 (s, 1H), 8.44 (d, *J* = 5.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.7, 37.4, 104.4, 110.0, 111.5, 120.7, 121.3, 123.2, 123.9, 124.0, 124.3, 124.4, 125.5, 126.2, 126.6, 127.6, 128.2, 128.5, 130.8, 132.5, 133.0, 138.7, 140.7, 144.5, 148.2, 168.5; HRMS (EI) *m/z*: Calcd for $C_{28}H_{21}BrN_4S$: 524.0670 (M^+), Found: 524.0672.

Biological Assay.

Cell Lines and Culture: A549 (human lung cancer cell line), MCF-7 (human breast cancer cell line) and HT-29 (human colon cancer cell line) cells were obtained from American Type Culture Collection (ATCC, USA). The cells were cultured in standard growth medium supplemented with 10% fetal bovine serum (FBS), 1% penicillin/streptomycin and incubated at 37 °C in a 5% CO_2 atmosphere.

Cytotoxicity Assay: Cytotoxicity of the compounds was assessed by using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) staining method. Briefly, cells were seeded in 96-well plate (Falcon, USA) at a density of 2×10^4 cells/well. Next day, cells were incubated with different concentrations of each compound for 24 h. Then, 10 μL of MTT solution was added to the well and further incubated for 4 h at 37 °C. At the end of the incubation, the media were removed, and 200 μL of dimethyl sulfoxide (DMSO) was added into each well to solubilize the formazan crystals. Finally, absorbance was measured at 540 nm using a microplate reader (Molecular Devices, Versa MAX Sunnyvale, CA, USA).

Antioxidant Activity: 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activity of the samples was assessed by reported method[40] with minor modifications. Briefly, 0.1 mM ethanolic DPPH solution (100 μL) was added to a sample solution (100 μL) of various concentrations (500 μM - 62.5 μM). After 30 min of incubation in dark at room temperature, the absorbance was measured at 517 nm. All measurements were made in triplicate. A lower absorbance of the compound mixtures indicates the higher DPPH radical scavenging activity. The percentage of inhibition was calculated as follows:

$$\text{Radical scavenging activity (\%)} = [(A_{control} - A_{sample})/A_{control}] \times 100$$

Where $A_{control}$ is the absorbance of negative control (containing all reagents except test compounds) and A_{sample} is the absorbance of the test compounds and all the reagents. IC_{50} (50% inhibitory concentration of compound) was calculated from the curve drawn by plotting the inhibition percentage against sample concentration. The antioxidant activity of the synthesized compounds was compared with a synthetic antioxidant Butylhydroxytoluene (BHT) as the reference standard.

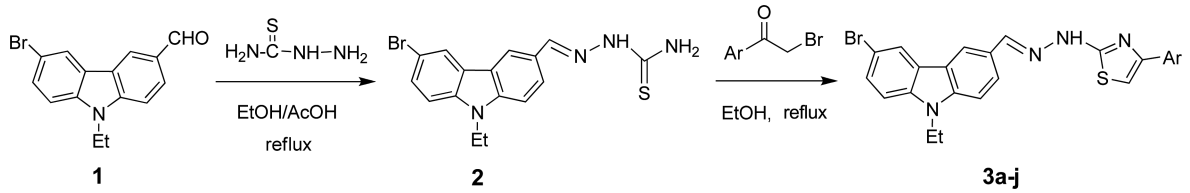
Results and Discussion

A new series of carbazole based 2,4-disubstituted thiazole derivatives were synthesized in a two step synthetic process (Scheme 1). In the first step 2-((6-bromo-9-ethyl-9*H*-carbazol-3-yl)methylene)hydrazinecarbothioamide (**2**) was synthesized by the condensation of 6-bromo-9-ethyl-9*H*-carbazole-3-carbaldehyde (**1**) with thiosemicarbazide in ethanol in the presence of catalytic amount of acetic acid. In the second step, the compound **2** was reacted with varies α-bromoketones (**a-j**) in refuxing ethanol to yield the corresponding 2,4-disubstituted thiazoles (**3a-j**, Table 1). The chemical structures of all the synthesized compounds were characterized by IR, ^{1}H, ^{13}C NMR and Mass spectrometry.

FT-IR spectra of compounds **3a-j** showed the expected absorption bands at 3422-3386 and 1627-1620 cm^{-1} for NH and C=N (azomethine) groups respectively. The absence of the absorption band corresponding to carbonyl stretching frequency of the α-bromoketones clearly confirmed the formation of thiazole ring. In the ^{1}H NMR spectra of compounds **3a-j** the azomethine proton (HC=N) resonated as a singlet in the region of 8.34-8.22 ppm. The C-5 proton of the thiazole ring showed a singlet in the region of 7.70-7.17 ppm. The remaining proton signals are observed in the expected regions. ^{13}C NMR spectra of compounds **3a-j** showed signals in the range of 168.8-168.3 and 108.2-101.5 ppm corresponding to carbon atom of thiazole-C-2 and C-5 respectively. The high resolution mass spectral data of compounds **3a-j** are provided in the experimental section.

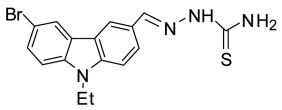
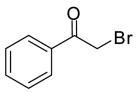
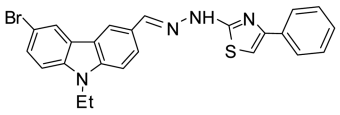
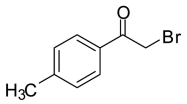
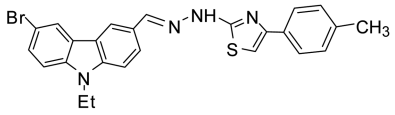
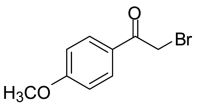
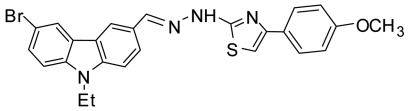
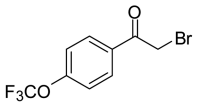
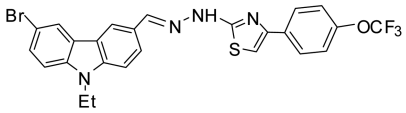
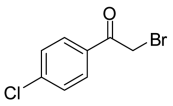
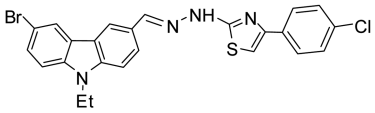
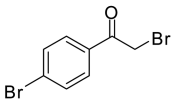
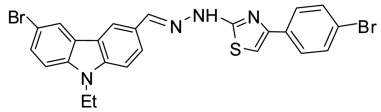
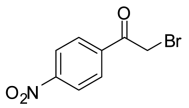
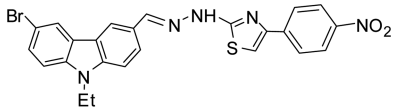
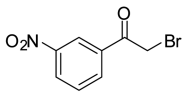
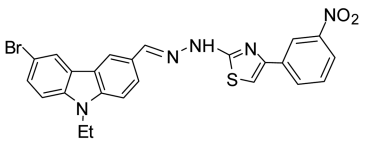
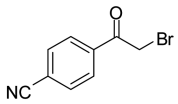
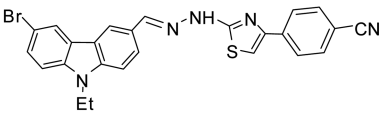
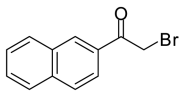
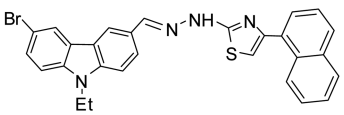
Cytotoxic Activity. All the synthesized molecules **3a-j** were evaluated for their cytotoxicity against three different cancer cell lines A549 (human lung cancer), MCF-7 (human breast cancer) and HT29 (human colon cancer) by MTT assay. The IC_{50} values of compounds are listed in Table 2. As shown in Table 2, compounds **3b** (IC_{50} 22.8 μM), **3e** (IC_{50} 23.9 μM), **3f** (IC_{50} 31.6 μM), **3h** (IC_{50} 9.7 μM) and **3i** (IC_{50} 8.5 μM) were found to exhibit good cytotoxic activity against A549 cells. It was observed that, compounds **3f** (IC_{50} 19.1 μM), **3g** (IC_{50} 44.7 μM), and **3i** (IC_{50} 24.5 μM) displayed good activity on MCF-7 cells. In the case of HT29 cells, compounds **3b** (IC_{50} 7.8 μM) and **3e** (IC_{50} 23.9 μM) showed good cytotoxicity and other compounds showed negligible activity.

Antioxidant Activity. Compounds **3a-j** were tested for antioxidant activity using 1,1-diphenyl-2-picrylhydrazyl



Scheme 1. Synthesis of carbazole based 2,4-disubstituted thiazoles.

Table 1. Synthesis of carbazole based 2,4-disubstituted thiazole derivatives

Entry	Thiosemicarbazone (2)	Ketone	Product (3)
a			
b			
c			
d			
e			
f			
g			
h			
i			
j			

(DPPH) radical scavenging method at different concentrations 500 μM-62.5 μM. The results on the antioxidant activity are given in Table 3. The radical scavenging activity of compounds **3a-j** was compared with that of reference compound Butylhydroxytoluene (BHT). Compounds **3a** (IC_{50} 110.74 μM), **3b** (IC_{50} 86.33μM), **3d** (IC_{50} 139.18 μM), **3e** (IC_{50} 140.67), **3f** (IC_{50} 171.70 μM) and **3i** (IC_{50} 158.54 μM) showed higher activity than BHT (IC_{50} 207.45 μM). Particularly compound **3b** (IC_{50} 86.33 μM) displayed the highest activity of all the synthesized compounds (Fig. 1).

Conclusion

In conclusion, we have synthesized a new class of carbazole based 2,4-disubstituted thiazoles and their cytotoxicity was evaluated. Among all the thiazole derivatives, compounds **3h** and **3i** against A549 cells, compound **3f** against MCF-7 cells and compound **3b** against HT29 cells, showed good

Table 2. Cytotoxic effects of compounds **3a-j** on three cancer cell lines

Compound	IC_{50} (μM)		
	A549	MCF-7	HT29
3a	352.2	141.3	380.4
3b	22.8	204.9	7.8
3c	647.2	953.8	799.8
3d	630.6	521.1	229.9
3e	23.9	157.9	23.9
3f	31.6	19.1	629.5
3g	246	44.7	684.3
3h	9.7	463.3	442.6
3i	8.5	24.5	247.8
3j	282.4	458.8	610.4

Table 3. Antioxidant activity of compounds **3a-j**

Compound	DPPH Scavenging activity (%)				IC_{50} (μM)
	500 μM	250 μM	125 μM	62.5 μM	
3a	67.33	60.64	53.50	40.79	110.74
3b	65.37	62.88	57.09	43.85	86.33
3c	47.38	44.99	42.60	34.17	632.03
3d	66.18	58.83	48.72	38.98	139.18
3e	64.35	59.11	49.29	38.72	140.67
3f	62.50	57.05	47.15	34.88	171.70
3g	52.02	47.90	43.15	31.46	343.54
3h	46.56	45.28	42.35	32.55	637.24
3i	67.87	57.29	46.70	35.01	158.54
3j	52.79	45.89	40.47	31.96	369.55
BHT	70.56	55.35	37.40	21.48	207.45

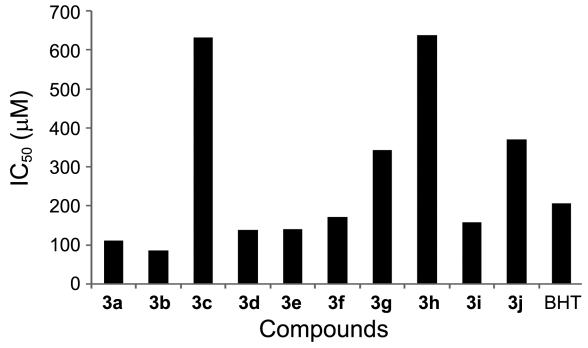


Figure 1. Antioxidant activity (IC_{50}) of compound **3a-j**.

cytotoxicity. These compounds were also tested for antioxidant activity by DPPH method and compounds **3a**, **3b**, **3d-f** and **3i** showed higher activity than BHT.

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