Asian Journal of Chemistry; Vol. 23, No. 8 (2011), 3686-3690

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Synthesis, Antimicrobial and Antioxidant Evaluation of Some *Bis*(Indolyl) Methanes Derivatives

T. SATHISH KUMAR[1], D. SATHIS KUMAR[2,*], VENKATA KRISHNAN[3], K. NAVEENA[4], M. RAGINI[2] and A. HARANI[2]

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kamla Nehru Institute of Information Technology, Sultanpur-228 118, India
[2]Department of Pharmaceutical Analysis, Nalanda College of Pharmacy, Nalgonda-508 001, India
[3]Department of Pharmaceutical Chemistry, Ultra College of Pharmacy, Madurai-625 020, India
[4]RBVRR Women's College of Pharmacy, Hyderabad-500 027, India

*Corresponding author: E-mail: satmpdina@yahoo.co.in

(*Received*: 13 December 2010; *Accepted*: 27 April 2011) AJC-9878

A series of novel *bis*(indolyl)methanes (**3-13**) derivatives were synthesized. *Bis*(indolyl)methanes were prepared through an integrated process that involves two basic steps, cyclomerization of *o*-phenyl ethynyl anilines followed by *bis*-addition with aldehydes. 2-Phenyl indole (**2**) was used as a starting material for all derivatives of *bis*(indolyl)methanes. A mechanism for the reaction is proposed. Compound **11** exhibit excellent gram positive antibacterial activity against *S. aureus* and compound **18** exhibit excellent gram negative antibacterial activity against *E. coli*. Compound **12** shows good antifungal activity and antioxidant property than other synthetic derivatives compounds.

Key Words: *Bis*(indolyl)methane, Antimicrobial, Antioxidant.

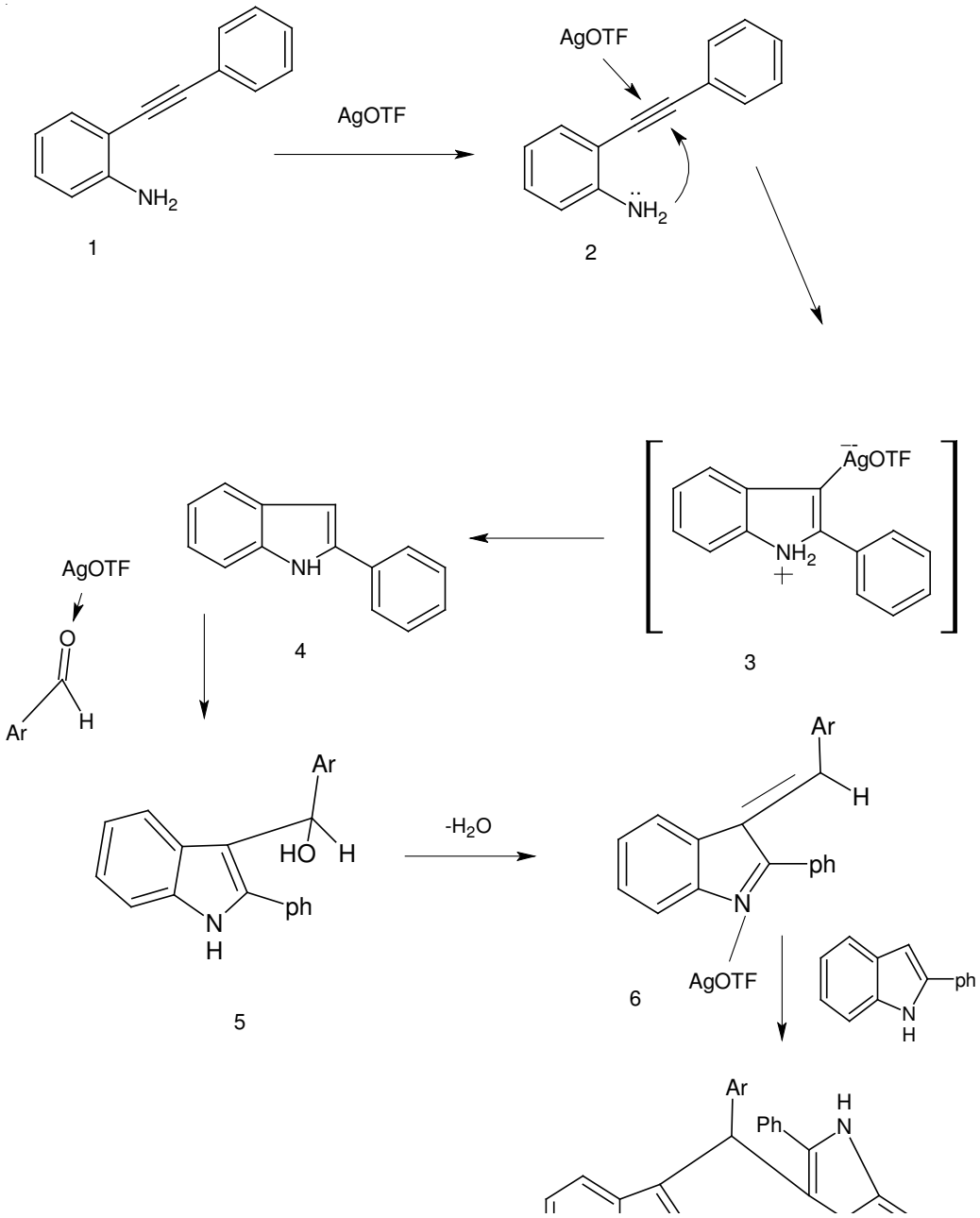
INTRODUCTION

The synthesis and reaction of indoles have been an interesting research topic for over a century since a number of their derivatives occur in nature and possess a variety of important biological and pharmacological activities and may be proved to be potential for drug development[1]. *Bis*-indolyl methanes constitute an important class of heterocyclic compounds that display diverse pharmacological activities and are useful in the treatment of fibromyalgia, chronic fatigue and irritable bowel syndrome[2]. They are known to promote beneficial estrogen metabolism[3] and induce apoptosis in human cancer cells. *Bis*-indolyl methanes have been prepared mainly by the reaction of indole with carbonyl compounds in the presence of Lewis acids[4-12] such as $LiClO_4$, $InCl_3$, I_2, $CuBr_2$, [RE(PFO)$_3$], $ZrCl_4$ and Bronsted acids such as sulphamic acid, amino sulphonic acid, $KHSO_4$. As a result of the increased interest in these important heterocyclics, new methods are needed to enhance the efficiency of the synthesis of these compounds and generate structurally diverse *bis*-indolylmethanes with wide variety of substituents. There is no report for the construction of *bis*-indolyl methanes *via* cyclo isomerization/*bis*-addition process. In particular we focused our attention on the preparation of *bis*(indolyl) methanes (owing to their biological significance) through an integerated process that involves two basic steps *i.e.*, cyclo isomerization of *o*-phenyl ethynyl anilines followed by *bis*-addition with aldehydes. Here in, we present the synthesis and biological evaluation of some novel potentially active *bis*(indolyl) methane derivatives.

EXPERIMENTAL

As part of our medicinal project aimed at the synthesis of potential biologically active compounds, we synthesized *bis*(indolyl) methanes derivatives according to **Scheme-I**. A tentative mechanistic interpretation to explain the formation of the observed *bis*(indolyl)methanes (**7**) might reasonably assume a reaction path that implies an initial π-coordination of Lewis acidic AgOTf with the alkyne residue (**1**) to form a π-complex (**2**). Subsequent nucleophilic attack of the tethered amino group leads to ring closure to afford cyclized intermediate (**3**), followed by proto-demetallation affords indole (**4**) and AgOTf. The later activates the carbonyl oxygen of the aldehyde and carries out an electrophilic addition reaction at C-3 of the indole (**4**) giving intermediate (**5**). After loss of water, an azafulvene derivative (**6**) is generated, which reacts further with a second molecule of indole to form *bis*(indolyl) methane (**7**).

The 2 phenyl indole used as starting material for all derivatives. 4-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-2-bromo-6-methoxyphenol (compound **8**) was prepared by 2-phenyl indole (compound **4**) (0.5 mmol) added with, 3-bromo-4 hydroxy-5-methoxy benzaldehyde (0.5 mmol) and refluxed for 2 h. 3,3'-[(2-bromo-4,5-dimethoxyphenyl)methylene]*bis*(2-



Scheme-I: Mechanism of scheme work

phenyl-1*H*-indole) (compound **9**) was prepared by compound **4** added with, 2-bromo-4,5-dimethoxy benzaldehyde (0.5 mmol) and refluxed for 2 h. 4-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]benzoic acid (compound **10**) was prepared by compound **4** added with, 4-formyl benzoic acid (0.5 mmol) and refluxed for 2 h. 3,3'-(Biphenyl-4-ylmethylene)*bis*(2-phenyl-1*H*-indole) (compound **11**) was prepared by compound **4** added with, biphenyl-4-carbaldehyde (0.5 mmol) and refluxed for 2 h. 3,3'-[(1-Methyl-1*H*-indol-2-yl)methylene]*bis*(2-phenyl-1*H*-indole) (compound **12**) was prepared by compound **4** added with, 1-methyl-1*H*-indole-2 carbaldehyde and refluxed for 2 h. 3,3'-[(6-Bromo-1,3-benzodioxol-5-yl)methylene] *bis*(2-phenyl-1*H*-indole) (compound **13**) was prepared by compound **4** added with, 6-bromo-1,3-benzodioxole-5 carbaldehyde (0.5 mmol) and refluxed for 2 h. 3-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-2-chloroquinoline (compound **14**) was prepared by compound **4** added with, 2-chloroquinoline-3-carbaldehyde (0.5 mmol) and refluxed for 2 h. 3,3'-(1-Naphthylmethylene)*bis*(phenyl-1*H*-indole) (compound **15**) was prepared by compound **4** added with, 1-naphthaldehyde (0.5 mmol) and refluxed for 2 h. 3-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-9-ethyl-9*H*-carbazole (compound **16**) was prepared by compound **4** added with, 9-ethyl-9*H*-carbazole-3-carbaldehyde (0.5 mmol) and refluxed for 2 h. 3,3'-(9*H*-Fluoren-3-ylmethylene)*bis*(2-phenyl-1*H*-indole) (compound **17**) was prepared by compound **4** added with, 4a*H*-fluorene-6-carbaldehyde (0.5 mmol) and refluxed for 2 h. 4-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole (compound **18**) was prepared by compound **4** added with, 3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (0.5 mmol) and refluxed for 2 h. After completion of the reaction as indicated by TLC (petroleum ether/ethyl

acetate), the reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel using petroleum ether/ethyl acetate to afford pure product individually.

Melting point were determined on a open capillary tube method. IR spectra were recorded on Perkin-Elmer 297 spectrophotometer with KBr disks. ^{1}H NMR spectra were recorded in DMSO-d_6 on a Jeol spectrometer and ^{13}C NMR spectra were recorded in DMSO-d_6 on Bruker Avance DPX 300 spectrometers using TMS as an internal standard. Mass spectra were recorded on a Hewlett-Packard 1100 mass spectrometer. Elemental analysis for carbon, hydrogen and nitrogen were performed on a thermo finnigan FLASH 1112 CHN analyzer. All compounds were routinely checked by TLC with Merck silica gel 60G F_{254} aluminium plates.

4-[*Bis*(2-Phenyl-1*H*-indol-3-yl)methyl]-2-bromo-6-methoxyphenol (8): Compound **8** was prepared as described above to obtain after recrystallization from ethanol a Brown solid; m.p. 228-230 ºC; R_f = 0.62 (AcOEt/petroleum ether 40 %). FTIR spectra wave numbers 3390 cm^{-1} (for NH or OH stretching), 2927 cm^{-1} (for C-H stretch), 1455 cm^{-1} (for C-N stretch), 1274 and 1043.28 cm^{-1} (for C-O strech) and 747.27 cm^{-1} (for C-Br). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 56.1, 64.8, 109.0, 111.3, 112.1, 113.8, 118.6, 120.5, 120.9, 124.1, 127.2, 128.0, 128.2, 132.7, 135.3, 136.1, 137.4, 141.9, 148.4; ^{1}H NMR (δ/ppm) 3.47 (s, 3H), 5.87 (s, 1H), 6.66-6.71 (m, 3H), 6.78 (s, 1H,), 6.91 (d, 2H, *J* = 7.6 Hz), 6.98 (t, 2H, *J* = 7.6 Hz), 7.19-7.21 (m, 6H), 7.28-7.29 (m, 4H), 7.34 (d, 2H, *J* = 8.4 Hz), 11.3 (s, 2H); MS (EI): m/z = 597 [M$^+$], 599 [M + 2]. Anal. calcd. (%) for $C_{36}H_{27}N_2O_2Br$: C, 72.14; H, 4.54; N, 4.67; found (%): C, 72.22; H, 4.45; N, 4.81.

3,3'-[(2-Bromo-4,5-dimethoxyphenyl)methylene]*bis*(2-phenyl-1*H*-indole) (9): Compound **9** was prepared as described above to obtain after recrystallization from ethanol a colourless solid; m.p. 240-242 ºC; R_f = 0.17 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3392 cm^{-1} (for NH stretching), 2930 cm^{-1} (for C-H stretch), 1602 cm^{-1} (for NH bending), 1498 cm^{-1} (for C-N stretch), 1250 cm^{-1} (for C-O strech) and 744 cm^{-1} (for C-Br). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 43.9, 60.8, 61.0, 116.5, 119.8, 120.6, 121.3, 123.9, 124.9, 126.0, 132.3, 133.2 (2C), 133.5, 138.1, 141.0, 141.2, 152.9, 153.3; ^{1}H NMR (δ/ppm) 3.30 (s, 3H), 3.73 (s, 3H), 6.06 (s, 1H), 6.60-6.80 (m, 3H), 6.97 (t, 2H, *J* = 7.6 Hz,), 6.98 (t, 2H, *J* = 7.6 Hz,), 7.07 (d, 4H, *J* = 6.1 Hz), 7.18-7.24 (m, 8H), 7.31 (d, 3H, *J* = 7.6 Hz,), 11.21 (s, 2H); MS (EI): m/z = 612 [M$^+$], 614 [M + 2]. Anal. calcd. (%) for $C_{37}H_{29}BrN_2O_2$: C, 72.43; H, 4.76; N, 4.57. Found (%): C, 72.52; H, 4.71; N, 4.69.

4-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]benzoic acid (10): Compound **10** was prepared as described above to obtain after recrystallization from ethanol a colourless solid; m.p. 292-294 ºC; R_f = 0.19 (AcOEt/petroleum ether 40 %). FTIR spectra wave numbers 3464 cm^{-1} (for NH stretching), 2923 cm^{-1} (for C-H stretch), 2560 cm^{-1} (for OH stretch of carboxyl), 1600 cm^{-1} (for C=O stretch), 1542 cm^{-1} (for NH bending), 1490 cm^{-1} (for C-N stretch) and 1421 and 1221 cm^{-1} (for C-O stretch of C-O-H). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 39.7, 111.4, 113.3, 118.6, 120.5, 121.0, 127.3, 127.9, 128.0, 128.3, 128.5, 128.8, 129.4, 132.5, 135.6, 136.2, 150.8, 167.31; ^{1}H NMR (δ/ppm) 5.96 (s, 1H, -), 6.66 (t, 2H, *J* = 8.4 Hz, Ar-H), 6.06 (s, 1H), 6.85 (d, 2H, *J* = 8.4 Hz), 6.98 (t, 2H, *J* = 8.4 Hz), 7.18-7.25 (m, 14 H), 7.80 (s, 1H), 7.82 (s, 1H), 11.36 (s, 1H); MS (EI): m/z = 519 [M$^+$ + H$^+$]. Anal. calcd. (%) for $C_{36}H_{26}N_2O_2$: C, 83.37; H, 5.05; N, 5.40. Found (%): C, 83.45; H, 4.99; N, 5.44.

3,3'-(Biphenyl-4-ylmethylene)*bis*(2-phenyl-1*H*-indole) (11): Compound **11** was prepared as described above to obtain after recrystallization from ethanol a yellow solid; m.p. 258-260 ºC; R_f = 0.43 (AcOEt/petroleum ether 50 %). FTIR spectra wave numbers 3399 cm^{-1} (for NH stretching), 3049.7 cm^{-1} (for C-H stretch aromatic), 1603 cm^{-1} (for NH bending), 1451 cm^{-1} (for C-N stretch) and 737 cm^{-1} (for C-H bending for aromatic). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 38.6, 111.2, 114.6, 118.4, 120.7, 120.8, 126.3, 127.1, 128.0 (2C), 128.2, 128.7, 129.2, 132.6, 135.3, 136.2, 137.3, 139.6, 144.7; ^{1}H NMR (δ/ppm) 6.01 (s, 1H), 6.67 (t, 2H, *J* = 7.6 Hz), 6.99 (t, 4H, *J* = 7.6 Hz), 7.18-7.22 (m, 8H), 7.27-7.33 (m, 5H), 7.36-7.41 (m, 4H), 7.58 (d, 2H, *J* = 8.4 Hz), 7.65 (d, 2H, *J* = 7.6 Hz), 11.35 (s, 2H); MS (EI): m/z = 550 [M$^+$]. Anal. calcd. (%) for $C_{41}H_{30}N_2$: C, 89.42; H, 5.49; N, 5.09. Found (%): C, 89.55; H, 5.45; N, 4.99.

3,3'-[(1-Methyl-1*H*-indol-2-yl)methylene]*bis*(2-phenyl-1*H*-indole) (12): Compound **12** was prepared as described above to obtain after recrystallization from ethanol a brown solid; m.p. 258-260 ºC; R_f = 0.45 (AcOEt/petroleum ether 40 %). FTIR spectra wave numbers 3437 cm^{-1} (for NH stretching), 3047 cm^{-1} (for C-H stretch aromatic), 1541 cm^{-1} (for NH bending), 1454 cm^{-1} (for C-N stretch), 1160 cm^{-1} (for C-C stretch) and 744 cm^{-1} (for C-H bending for aromatic). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 29.1, 33.5, 101.5, 109.2, 111.2, 118.7, 118.9, 119.7, 119.8, 120.4, 121.0, 126.8, 127.2, 127.8, 128.0, 128.2, 132.4, 134.8, 136.0, 137.3, 143.5; ^{1}H NMR (δ/ppm) 3.14 (s, 3H), 5.98 (s, 1H), 6.10 (s, 1H), 6.62 (t, 2H, *J* = 7.6 Hz), 6.95-7.04 (m, 4H), 7.18-7.28 (m, 13H), 7.37 (d, 2H, *J* = 8.4 Hz), 7.43 (d, 1H, *J* = 7.6 Hz), 11.3 (s, 2H,); MS (EI): m/z = 528 [M$^+$ + H$^+$]. Anal. calcd. (%) for $C_{38}H_{29}N_3$: C, 86.50; H, 5.54; N, 7.96. Found (%): C, 86.46; H, 5.59; N, 7.95.

3,3'-[(6-Bromo-1,3-benzodioxol-5-yl)methylene]*bis*(2-phenyl-1*H*-indole) (13): Compound **13** was prepared as described above to obtain after recrystallization from ethanol a pale yellow solid; m.p. 222-224 ºC; R_f = 0.26 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3387 cm^{-1} (for NH stretching), 2925 cm^{-1} (for C-H stretch), 1542 cm^{-1} (for NH bending), 1465 cm^{-1} (for C-N stretch), 1465 and 1236 cm^{-1} (for C-O stretch), 1106 cm^{-1} (for C-O of C-O-C) and 751 cm^{-1} (for C-Br). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 26.3, 40.6, 101.8, 110.7, 111.3, 112.7, 114.6, 118.8, 119.6, 120.9, 127.3, 127.9, 128.1, 128.2, 132.7, 136.0, 137.2, 146.6, 146.8; ^{1}H NMR (δ/ppm) 6.61 (s, 1H), 6.79 (s, 1H), 6.85 (s, 1H), 6.99-7.05 (m, 6H), 7.13 (s, 1H), 7.20-7.34 (m, 12H), 11.26 (s, 2H); MS (EI): m/z = 596 [M$^+$], 598 [M + 2]. Anal. calcd. (%) for $C_{36}H_{25}BrN_2O_2$: C, 72.37; H, 4.22; N, 4.69. Found (%): C, 72.49; H, 4.33; N, 4.75.

3-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-2-chloroquinoline (14): Compound **14** was prepared as described above to obtain after recrystallization from ethanol a yellow

solid; m.p. 232-234 ºC; R_f = 0.21 (AcOEt/petroleum ether 40 %). FTIR spectra wave numbers 3412 cm^{-1} (for NH stretching), 2924 cm^{-1} (for C-H stretch), 1598 cm^{-1} (for NH bending), 1457 cm^{-1} (for ring stretching vibration) and 738 cm^{-1} (for C-Cl). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 39.5, 111.5, 118.9, 119.5, 121.0, 126.6, 127.2 (2C), 127.3 (2C), 127.9 (2C), 128.1 (2C), 130.2, 132.6, 136.1, 136.8, 138.4, 145.7, 150.6; ^1H NMR (δ/ppm) 6.23 (s, 1H), 6.63 (t, 2H, *J* = 7.6 Hz), 6.98 (t, *J* = 8.4 Hz), 7.16-7.23 (m, 12H), 7.37 (d, 2H, *J* = 8.4 Hz), 7.52 (t, 1H, *J* = 8.4 Hz,), 7.72 (t, 1H, *J* = 8.4 Hz), 8.17 (s, 1H), 11.42 (s, 2H); MS (EI): m/z = 560 [$M^+ + H^+$], 562 [$M^{2+} + H^+$]. Anal. calcd. (%) for $C_{38}H_{26}N_3Cl$: C, 81.49; H, 4.68; N, 7.50. Found (%): C, 81.61; H, 4.75; N, 7.60.

3,3'-(1-Naphthylmethylene)*bis*(phenyl-1*H*-indole) (15): Compound **15** was prepared as described above to obtain after recrystallization from ethanol a pale yellow solid; m.p. 282-284 ºC; R_f = 0.20 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3395 cm^{-1} (for NH stretching), 2927 cm^{-1} (for C-H stretch), 1452 cm^{-1} (for NH bending), 1307 cm^{-1} (for CN stretch) and 778 and 742 cm^{-1} (for C-H aromatic). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 37.5, 111.2, 118.5, 120.1, 120.7, 123.1, 125.0, 122.2, 125.7, 126.7, 127.2 (2C), 127.8, 128.1, 128.5, 131.0, 132.6, 133.4, 134.7, 136.1, 140.9; ^1H NMR (δ/ppm) 6.49 (s, 1H), 6.56-6.57 (m, 2H), 6.90-7.03 (m, 2H), 7.10-7.13 (m, 11H), 7.30 (t, 5H, *J* = 7.6 Hz), 7.44 (t, 1H, *J* = 7.6 Hz), 7.50 (d, 1H, *J* = 9.15 Hz), 7.53 (d, 1H, *J* = 6.8 Hz), 7.84 (t, 2H, *J* = 8.4 Hz), 11.34 (s, 2H); MS (EI): m/z = 524 [M^+]. Anal. calcd. (%) for $C_{39}H_{28}N_2$: C, 89.28; H, 5.38; N, 5.34; found (%): C, 89.41; H, 5.47; N, 5.48.

3-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-9-ethyl-9*H*-carbazole (16): Compound **16** was prepared as described above to obtain after recrystallization from ethanol a pale yellow solid; m.p. 278-280 ºC; R_f = 0.23 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3404 cm^{-1} (for NH stretching), 2897 cm^{-1} (for C-H stretch), 1331 and 1154 cm^{-1} (for CN stretch) and 743 cm^{-1} (for C-H). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 13.7, 37.0, 39.4, 108.5, 108.9, 111.3, 115.1, 118.4, 119.8, 120.2, 120.8, 122.0, 122.1, 125.5, 126.8, 127.1, 128.0, 128.2, 128.4, 132.8, 135.1, 136.1, 136.3, 138.1, 139.8; ^1H NMR (δ/ppm) 1.26 (t, 3H, *J* = 7.6 Hz), 4.33 (d, 2H, *J* = 6.8 Hz), 6.17 (s, 1H), 6.58 (t, 2H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 7.6 Hz), 6.94 (m, 3H), 7.15 (m, 6H), 7.27 (d, 1H, *J* = 7.9 Hz), 7.33 (m, 7H), 7.44 (d, 1H, *J* = 8.4 Hz), 7.48 (d, 1H, *J* = 7.6 Hz), 7.79 (d, 1H, *J* = 7.6 Hz), 7.85 (s, 1H), 11.33 (s, 2H), MS (EI): m/z = 591 [M^+]. Anal. calcd. (%) for $C_{43}H_{33}N_3$: C, 87.28; H, 5.62; N, 7.10. Found (%): C, 87.41; H, 5.70; N, 7.17.

3,3'-(9*H*-Fluoren-3-ylmethylene)*bis*(2-phenyl-1*H*-indole) (17): Compound **17** was prepared as described above to obtain after recrystallization from ethanol a colourless solid; m.p. 244-246 ºC; R_f = 0.27 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3412 cm^{-1} (for NH stretching), 2925 cm^{-1} (for C-H stretch), 1599 cm^{-1} (for NH bending) and 746 cm^{-1} (for C-H). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 36.2, 40.08, 114.3, 114.4, 118.5, 119.7, 120.8, 120.9, 125.0, 125.2 (2C), 126.4, 126.6, 127.1, 127.4, 128.0 (2C), 128.2, 132.7, 135.3, 136.3, 139.0, 141.1, 143.0, 144.6; ^1H NMR (δ/ppm) 3.75 (s, 2H), 6.03 (s, 1H), 6.64 (t, 2H, *J* = 7.6 Hz,), 6.98 (d, 4H, *J* = 7.6 Hz,), 7.74 (d, 1H, *J* = 7.6 Hz,), 7.79 (d, 1H, *J* = 7.6 Hz), 11.35 (s, 2H) MS (EI): m/z = 562 [M^+]. Anal. calcd. (%) for $C_{42}H_{30}N_2$: C, 89.65; H, 5.37; N, 4.98. Found (%): C, 89.75; H, 5.30; N, 5.08.

4-[*Bis*(2-phenyl-1*H*-indol-3-yl)methyl]-3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole (18): Compound **18** was prepared as described above to obtain after recrystallization from ethanol a pink solid; m.p. 270-272 ºC; R_f = 0.21 (AcOEt/petroleum ether 20 %). FTIR spectra wave numbers 3400 cm^{-1} (for NH stretching), 2924 cm^{-1} (for C-H stretch), 1600 cm^{-1} (for NH bending or C=N stretching), 1452 and 1337 cm^{-1} (for CN stretch) and 745 cm^{-1} (for C-Cl). ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 31.25, 111.26, 113.6, 118.1, 118.6, 120.0, 120.8, 126.17 (2C), 127.2, 127.6, 127.7, 127.9, 128.0, 128.4, 129.4, 131.9 (2C), 132.6, 135.1, 136.1, 139.2, 148.9; ^1H NMR (δ/ppm) 5.94 (s, 1H), 6.71 (t, 2H, *J* = 7.6 Hz), 6.97 (t, 2H, *J* = 8.4 Hz), 7.05 (d, 2H, *J* = 8.4 Hz), 7.15-7.25 (m, 15H), 7.30 (d, 2H, *J* = 8.4 Hz), 7.31 (d, 3H, *J* = 7.6 Hz), 7.83 (s, 1H), 11.25 (s, 2H); MS (EI): m/z = 646 [M^+], 648 [M + 2]. Anal. calcd. (%) for $C_{38}H_{27}N_4Cl$: C, 79.46: H, 4.73; N, 9.74. Found (%): C, 79.45; H, 4.75; N, 9.75.

Antimicrobial activity: The prepared compounds were evaluated for their antibacterial activity against *Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922) by filter disc method using sterilized Muller Hinton agar medium. The concentration of standard drug (ciprofloxacin) and test compounds used was 100 µg/mL. DMSO was used as a control. Observations were made for the zone of inhibition around the synthesized compounds and compared with that of standard. Fungicidal activity of all synthesized compounds was determined against *Candida albicans* (ATCC) 10231 by using the same technique and same concentration of ketoconazole was used as a standard drug using sabouraud dextrose agar medium. The values are present in Table-1.

TABLE-1
ANTIMICROBIAL ACTIVITIES OF DERIVED COMPOUNDS

Compounds	Zone of inhibition (mm)		
	S. aureus	*E. coli*	*C. albicans*
8	3 ± 0.1	6 ± 0.2	4 ± 0.1
9	2 ± 0.2	4 ± 0.1	6 ± 0.1
10	2 ± 0.1	5 ± 0.2	6 ± 0.2
11	8 ± 0.2	5 ± 0.1	5 ± 0.2
12	5 ± 0.1	5 ± 0.1	12 ± 0.1
13	3 ± 0.1	6 ± 0.2	10 ± 0.1
14	4 ± 0.1	8 ± 0.2	8 ± 0.1
15	5 ± 0.2	8 ± 0.1	8 ± 0.1
16	4 ± 0.1	9 ± 0.1	4 ± 0.1
17	6 ± 0.1	6 ± 0.2	5 ± 0.2
18	4 ± 0.1	9± 0.1	6 ± 0.1
Control	Nil	Nil	Nil
Standard	8 ± 0.1*	8 ± 0.1*	10 ± 0.1**

*Ciprofloxacin disc for *S. aureus* and *E. coli*. **Ketoconazole disc for *C. albicans*.

Antioxidant activity: DPPH (1,1-diphenyl-2-picryl-hydrazil) scavenging activity and hydrogen peroxide scavenging activity were measured by the spectrophotometeric method for all derivative compound.

RESULTS AND DISCUSSION

Among the derivative products compound **13** (3,3'-[(6-bromo-1,3-benzodioxol-5-yl)methylene]*bis*(2-phenyl-1*H*-

TABLE-3
HYDROGEN PEROXIDE SCAVENGING ACTIVITY OF DERIVATIVES

Compounds (10 µg)	Inhibition (%)				
	0 min	10 min	20 min	30 min	40 min
8	43 ± 0.1	35 ± 0.7	21 ± 0.1	20 ± 0.4	16 ± 0.7
9	86 ± 0.4	85 ± 0.9	74 ± 0.3	72 ± 0.6	69 ± 0.5
10	82 ± 0.6	81 ± 0.6	74 ± 0.4	71 ± 0.7	65 ± 0.4
11	84 ± 0.2	83 ± 0.4	80 ± 0.8	73 ± 0.8	68 ± 0.8
12	93 ± 0.1	84 ± 0.3	82 ± 0.8	77 ± 0.1	71 ± 0.2
13	83 ± 0.6	82 ± 0.5	81 ± 0.6	80 ± 0.6	79 ± 0.4
14	88 ± 0.5	85 ± 0.2	76 ± 0.8	73 ± 0.2	70 ± 0.6
15	57 ± 0.5	43 ± 0.1	39 ± 0.7	30 ± 0.3	21 ± 0.4
16	85 ± 0.4	80 ± 0.6	82 ± 0.7	75 ± 0.4	65 ± 0.5
17	87 ± 0.3	83 ± 0.7	75 ± 0.9	70 ± 0.6	59 ± 0.5
18	60 ± 0.4	45 ± 0.8	40 ± 0.3	35 ± 0.8	24 ± 0.1
BHT	92 ± 0.6	86 ± 0.4	83 ± 0.2	82 ± 0.5	80 ± 0.4

indole) showed highest yield of 85 %. The structural characterizations of all compounds were carried out by FTIR, ^{1}H NMR, ^{13}C NMR and mass spectra. FTIR spectra of compounds in KBr pellet consists of 3387cm^{-1} (for NH stretch), 1236 cm^{-1} (for CO stretch), 751 cm^{-1} (for CBr). The ^{1}H NMR spectra of compounds in DMSO-d_6 consists of a characteristic singlet due to the methine proton (-CH-Ar) in the region of 5.2-6.7 ppm. Another characteristic feature of the ^{1}H NMR spectra was the appearance of a singlet at δH 11.3-11.5 ppm, which corresponds to two indole-NH protons. Gram positive antibacterial activity when compared to the standard drug ciprofloxacin against *S. aureus* and compound **11** showed same zone of inhibition by this method. Gram negative antibacterial activity when compared to the standard drug ciprofloxacin against *E. coli* and compound **18** showed highest zone of inhibition by this method. The entire compounds have shown comparable activity as that of standard ketoconazole against *Candida albicans*. Among these products compound **12** showed highest zone of inhibition by this method. The DPPH radical scavenging activity values are present in Table-2. Among these products compound **12** has shown highest inhibition of DPPH radical of the synthetic compounds compared with the standard ascorbic acid. The hydrogen peroxide scavenging activity values are present in Table-3. Among these products compound **12** has shown highest inhibiton of hydrogen peroxide scavenging activity of the synthetic compounds compared with the standard butylated hydroxy toluene. Due to presence of indole, all synthesized compounds have shown a moderate antioxidant property, compound **12** have shown high antioxidant property than other compounds, it may due to additional group which was attached with *bis*(indolyl)-methanes.

TABLE-2
DPPH RADICAL SCAVENGING ACTIVITY OF DERIVATIVES

Compounds	Inhibition (%)		
	Conc. (50 µg/mL)	Conc. (500 µg/mL)	Conc. (1000 µg/mL)
8	19 ± 0.2	63 ± 0.5	76 ± 0.4
9	21 ± 0.1	52 ± 0.4	69 ± 0.7
10	27 ± 0.3	64 ± 0.6	70 ± 0.5
11	02 ± 0.4	12 ± 0.7	35 ± 0.4
12	21 ± 0.8	65 ± 0.8	87 ± 0.8
13	25 ± 0.6	58 ± 0.6	76 ± 0.4
14	19 ± 0.8	66 ± 0.1	85 ± 0.2
15	10 ± 0.8	23 ± 0.2	42 ± 0.6
16	15 ± 0.7	42 ± 0.3	73 ± 0.4
17	22 ± 0.7	55 ± 0.4	75 ± 0.5
18	17 ± 0.9	48 ± 0.6	80 ± 0.5
L-Ascorbic acid	96 ± 0.3	97 ± 0.8	99 ± 0.1

Conclusion

From the above results it is concluded that the compound **12** has better biological properties comparatively and because of which we can proceed further studies on the compound.

ACKNOWLEDGEMENTS

The authors thank the Council of Scientific and Industrial research (CSIR), Chennai and The Management and staffs of Ultra College of Pharmacy, Madurai, for the support of completion of this work.

REFERENCES

1. S.J. Song, S.J. Cho, D.K. Park, T.W. Kwon and S.A. Jenekhe, *Tetrahedron Lett*., **44**, 255 (2003).
2. C.A. Bradfield and L.F. Bjeldanes, *J. Toxicol. Environ. Health*, **21**, 311 (1987).
3. M.A. Zeligs, *J. Med. Food*, **1**, 67 (1998).
4. J.S. Yadav, B.V.S. Reddy, Ch. V.S.R. Murthy, G.M. Kumar and Ch. Madan, *Synthesis*, 783 (2001).
5. G. Babu, N. Sridhar and P.T. Perumal, *Synth. Commun*., **30**, 1609 (2000).
6. B.P. Bandgar and K.A. Shaikh, *Tetrahedron Lett*., **44**, 1959 (2003).
7. L.P. Mo, Z.C. Ma and Z.H. Zhang, *Synth. Commun*., **35**, 1997 (2005).
8. L. Wang, J. Han, H. Tian, J. Sheng, Z. Fan and X. Tang, *Synlett.*, 337 (2005).
9. Z.H. Zhang, L. Yin and Y.M. Wang, *Synthesis*, 1949 (2005).
10. P.R. Singh, D.U. Singh and S.D. Samant, *Synth. Commun*., **35**, 2133 (2005).
11. J.T. Li, H.G. Dai, W.Z. Xu and T.S. Li, *Ultrason. Sonochem*., **13**, 24 (2006).
12. R. Nagarajan and P.T. Perumal, *Chem. Lett*., **33**, 288 (2004).