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Microbial evolution of carbazonyloxy-based chalcones

M. H. Malani · B. Z. Dholakiya

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Abstract The Claisen–Schmidt condensation reaction was carried out between a carbazol-based acetyl group and various aldehydes. Reaction was performed in metal alkoxide as a alkali homogenous catalyst. A series of 12 1-{4-[3-(9*H*-carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(substituted aryl)-propenone were synthesized and characterized using FTIR, ^{1}H NMR, and ^{13}C NMR spectroscopy analysis. Synthesized compounds were tested against bacteria and fungi strains.

Keywords Claisen–Schmidt · Antibacterial · Antifungal

Introduction

Microbial disease is a major problem in worldwide, so it is necessary to continuously develop novel antibacterial agents with broad spectrum activity [1]. Clinical diagnosis of microbial disease is still a concern. A number of synthetic and semisynthesis chemical entities and drugs are used in clinical practice such as sulfonamide, nitrofuran, penicillium, cephalosporin, tetra macrolides, and oxazolidines [2].

The Claisen–Schmidt (CS) condensation between an acetyl group and aldehyde is a valuable C–C bond-forming reaction to produce chalcones. Chalcones resemble the flavonoid families which are synthesized at production levels to preserve the health of plants against infections and parasites. They have attracted increasing

M. H. Malani · B. Z. Dholakiya (✉)
Department of Applied Chemistry, S.V. National Institute of Technology, Ichhanath, Surat 395007, Gujarat, India
e-mail: bzd.svnit@gmail.com

M. H. Malani
e-mail: maheshmalani.svnit@gmail.com

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attention due to a number of pharmacological applications [3, 4]. Chalcones are the main precursors for the biosynthesis of flavonoids, which are frequent components of the human diet. For example, Licochalcone A isolated from the roots of *Glycyrrhiza inflata* (licorice) has in vitro and in vivo antimalarial and antileishmanial activity, and 3-methoxy-4-hydroxyloncocarpin isolated from the roots of *Lonchocarpus utilis* inhibits NADH:ubiquinone oxidoreductase activity [5]. The CS condensation is carried out in basic or acidic media under homogeneous conditions, but with many drawbacks, such as catalyst recovery and waste disposal problems [6]. As a potential alternative, heterogeneous acidic and basic catalysts for the CS condensation, for example, zeolites [7, 8], alumina [9], barium hydroxides [10, 11], MgO [12], calcined hydrotalcites [13–15], natural phosphates modified with sodium nitrate or KF [16–18], and aminopropyl-functionalized SBA-15 [19, 20], have received much attention over the past few years. The acid catalyzed condensation for preparation of chalcone generally uses AlCl3, BF3, dry HCl, and RuCl3 [21]. Our research group has tried the synthesis of chalcone by metal alkoxide. Potassium *t*-butoxide gave better results than metal hydroxides such as NaOH and KOH. Moreover, metal alkoxide enhanced the rate of reaction and gave comparatively good yield.

Experimental

Materials and methods

All reagents were of analytical reagent grade and were used without further purification. Solvents employed were purified by standard procedure before use. 4-(Oxiran-2-ylmethoxy)-9*H*-carbazole was prepared as per the reported process [22] and p-aminoacetophenone was purchased from Aldrich, The melting points were determined in open capillary on Veego (Model: VMP-D) electronic apparatus and are uncorrected. The reactions were monitored and the Rf values were determined using analytical thin layer chromatography (TLC) with Merck Silica gel 60 and F-254 pre-coated plates (0.25 mm thickness). Spots on the TLC plates were visualized using ultraviolet light (254 nm). FTIR spectra (4,000–400 cm^{-1}) were recorded on a Shimadzu 8400-S spectrophotometer using KBr disks. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz model spectrometer using DMSO and TMS as internal reference (chemical shifts in δ ppm).

Synthesis of 1-(4-{[3-(9H-carbazol-4-yloxy)-2-hydroxypropyl]amino}phenyl)ethanone

A mixture of 4-(oxiran-2-ylmethoxy)-9*H*-carbazole (1.0 gm, 4.17 mmol), 4-amino acetophenone (0.56 gm, 4.17 mmol), potassium carbonate (1.15 gm, 8.35 mmol), and 10 ml acetonitrile as a solvent was taken in round-bottom flasks. The reaction mass was heated at 58–62 °C with constant stirring for 8 h (Fig. 1). The reaction was monitored by using thin layer chromatography. After completion of the reaction, the mass was cooled to 25–30 °C, filtered for removal of salt and the

filtrate was evaporated to dryness under reduced pressure to get the crude compound. Recrystallization was carried out in acetone as solvent to get the pure compound (1.4 g, 90 % yield). The obtained compound was a light cream-colored powder having melting point of 51–53 °C [23].

Preparation of chalcone from 1-(4-{[3-(9H-carbazol-4-yloxy)-2-hydroxypropyl] amino} phenyl) ethanone ***4a–4l***

The target compounds were prepared as shown in Fig. 1. CS condensation of 1-(4-{[3-(9*H*-carbazol-4-yloxy)-2-hydroxypropyl]amino}phenyl) ethanone and various aldehydes (Fig. 1). The reaction was carried out under basic condition in alcoholic solution at 55–60 °C for 12 h. The final compound was isolated from water at 6–7 pH. Isolated compounds were recrystallized in ethanol. Synthesized compounds were characterized by various spectroscopic techniques. Derivatives and physical parameters are shown in Table 1 [23].

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-methoxy-phenyl)-propenone ***4a*** Yield 77 %; m.p. 152–153 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 4.3 δ ppm (3H, s, –OCH_3), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (12H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 49, 58, 67, 73, 78, 100, 110, 118, 121, 123, 125, 128, 128.7, 129, 130, 134.6, 138, 140, 142.5, 157, 189 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 3,030 (C=C), 1,713 (C=O), 1,342 (C–N of Ar), 812 (*p*-disubstituted Ar), 3,310 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(2-hydroxy-phenyl)-propenone ***4b*** Yield 58 %; m.p. 102–103 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–

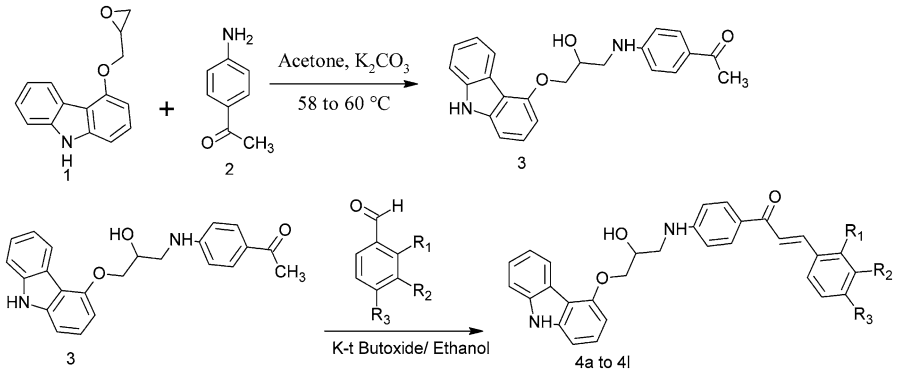

Fig. 1 Reaction scheme of synthesized compounds **4a-l**

O–$\underline{CH_2}$), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH$\underline{CH_2}$NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C = O); 9.0 δ ppm (1H, s, –OH), ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 3,045 (C=C), 1692 (C=O), 1,334 (C–N of Ar), 818 (*p*-disubstituted Ar), 3,365 (N–H), ,3235 (–OH).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-phenyl-propenone ***4c*** Yield 82 %; m.p. 93–95 ° C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH$_2\underline{CH}$OHCH$_2$), 4.1 δ ppm (2H, d, Ar–O–$\underline{CH_2}$), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH$\underline{CH_2}$NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (12H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5,

Table 1 Physiochemical parameter of synthesized compounds

Sr.No	R_1, R_2 and R_3	Molecular formula	Yield (%)	Physical parameter
4a	R_1, R_2 = H R_3 = OCH_3	$C_{31}H_{28}N_2O_4$	79	Off-white powder M.P. 150–155 °C (decomposed)
4b	R_1 = OH R_2, R_3 = H	$C_{30}H_{26}N_2O_4$	68	Creamish-colored powder m.p. 102–104 °C
4c	R_1, R_2, R_3=H	$C_{30}H_{26}N_2O_3$	86	Light yellow powder m.p. 93–95 °C
4d	R_2, R_3 = H R_1 = Cl	$C_{30}H_{25}ClN_2O_3$	72	Brown-colored powder m.p. 163–165 °C
4e	R_1, R_2 = H R_3 = Cl	$C_{30}H_{25}ClN_2O_3$	78	Reddish-brown powder m.p. 184–190 °C
4f	R_1, R_3 = H R_2 = NO_2	$C_{30}H_{25}N_3O_5$	82	Yellow-colored powder m.p. 190–193 °C
4g	R_1 = H R_2 = NO_2 R_3 = OCH_3	$C_{31}H_{27}N_3O_6$	88	Pale yellow-colored powder m.p. 170–175 °C
4h	R_1, R_2 = H R_3 = CH_3	$C_{31}H_{28}N_2O_3$	88	Pale yellow-colored powder m.p. 168–171 °C
4i	R_1, R_2, R_3 = H	$C_{34}H_{28}N_2O_3$	85	Dark yellow-colored powder m.p. 184–187 °C
4j	R_1, R_2 = H R_3 = OH	$C_{30}H_{26}N_2O_4$	85	Off-white to pale yellow-colored powder m.p. 150–151 °C
4k	R_1 = H R_2, R_3 = OCH_3	$C_{32}H_{30}N_2O_5$	75	Pale yellow-colored powder m.p. 153–155 °C
4l	R_1, R_2 = H R_3 = NO_2	$C_{30}H_{25}N_3O_5$	84	Brown colored powder m.p. 146–148 °C

156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,990 (C=C), 1,653 (C=O), 1,338 (C–N of Ar), 819 (*p*-disubstituted Ar), 3,223 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(2-chloro-phenyl)-propenone ***4d*** Yield 62 %; m.p. 163–165 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,928 (C=C), 1,670 (C=O), 1,348 (C–N of Ar), 823 (*p*-disubstituted Ar), 3,338 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-chloro-phenyl)-propenone ***4e*** Yield 74 %; m.p. 184–188 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C = O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,965 (C=C), 1,640 (C=O), 1,339 (C–N of Ar), 833 (*p*-disubstituted Ar), 3,240 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(3-nitro-phenyl)-propenone ***4f*** Yield 84 %; m.p. 190–193 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,985 (C=C), 1,705 (C=O), 1,355 (C–N of Ar), 836 (*p*-disubstituted Ar), 3,380 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-methoxy-3-nitro-phenyl)-propenone ***4g*** Yield 86 %; m.p. 170–173 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>O<u>H</u>CH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 4.3 δ ppm (3H, s, –OCH_3), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH–carbazole), 6.6–7.7 δ ppm (10H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 48, 59, 68, 72, 78, 100, 110, 118, 121, 124, 125, 128, 128.3, 129, 130.2, 134.6, 138, 141, 142, 155, 187 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,928 (C=C), 1,720 (C=O), 1,322 (C–N of Ar), 816 (*p*-disubstituted Ar), 3,315 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-methyl-phenyl)-propenone ***4h*** Yield 88 %; m.p. 168–171 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –

CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>OHCH_2), 3.8 δ ppm (3H, s, –CH_3) 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH–carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 41, 57, 68, 73, 78, 100, 110, 118, 121, 124, 125, 126, 128.7, 129, 130.2, 134, 138, 141, 142.5, 154, 190 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,917 (C=C), 1,647 (C=O), 1,331 (C–N of Ar), 819 (*p*-disubstituted Ar), 3,300 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-naphthalen-1-yl-propenone ***4i*** Yield 82 %; m.p. 184–187 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>OHCH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (13H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 127, 128, 128.5, 129, 130.2, 131, 133,134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,933 (C=C), 1,680 (C=O), 1,314 (C–N of Ar), 838 (*p*-disubstituted Ar), 3,420 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-hydroxy-phenyl)-propenone ***4j*** Yield 75 %; m.p. 150–151 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>OHCH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 9.1 δ ppm (1H, s, –OH); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,980 (C=C), 1,695 (C=O), 1,319 (C–N of Ar), 830 (*p*-disubstituted Ar), 3,365 (N–H), 3258 (–OH).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(3,4dimethoxy-phenyl)-propenone ***4k*** Yield 65 %; m.p. 153–155 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>OHCH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 4.3 δ ppm (3H, s, –OCH_3), 4.5 δ ppm (3H, s, –OCH_3), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (10H, m, Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 48, 51, 57, 69, 72, 80, 101, 111, 118, 122, 124, 125, 128, 128.7, 129, 130, 134.6, 138.1, 141, 142.5, 156.1, 188.2 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 3,000 (C=C), 1,670 (C=O), 1,336 (C–N of Ar), 822 (*p*-disubstituted Ar), 3,378 (N–H).

1-{4-[3-(9H-Carbazol-4-yloxy)-2-hydroxy-propylamino]-phenyl}-3-(4-nitro-phenyl)-propenone ***4l*** Yield 79 %; m.p. 146–148 °C; ^{1}H NMR (400 MHz, DMSO), 2.5 δ ppm (1H, s, –OH aliphatic), 3.34 δ ppm (1H, d, –CH=CH), 3.3 δ ppm (1H, d, –CH=CH), 3.5 δ ppm (1H, m, –CH_2<u>CH</u>OHCH_2), 4.1 δ ppm (2H, d, Ar–O–<u>CH_2</u>), 6.18 δ ppm (1H, t, –NH aliphatic), 6.8 δ ppm (2H, t, –CHOH<u>CH_2</u>NH), 7.29 δ ppm (1H, dd, –NH–*p*-Ar–C=O), 8.23 δ ppm (1H, s, NH– carbazole), 6.6–7.7 δ ppm (11H, m,

Ar–H), 7.87 δ ppm (1H, dd, –NH–*p*-Ar–C=O); ^{13}C NMR (400 MHz, DMSO) 59, 68, 73, 78, 100, 110, 118, 121, 124, 125, 128, 128.7, 129, 130.2, 134.6, 138, 141, 142.5, 156, 188 δ ppm; FTIR (KBr) υ_{max} cm^{-1}: 2,978 (C=C), 1,705 (C=O), 1,343 (C–N of Ar), 828 (*p*-disubstituted Ar), 3,348 (N–H).

Antibacterial studies

All the synthesized compounds were tested for their antibacterial activity (MIC) in vitro by the broth dilution method with bacteria *E. coli* MTCC 443, *P. aeruginosa* MTCC 1688, *S. aureus* MTCC 96, and *S. pyogenus* MTCC 442C, taking Ampicilin, Chloramphenicol, Ciprofloxacin, Gentamycin, and Norfloxacin as standard drugs [24].

Antifungal studies

All the synthesized compounds were tested for their antifungal activity (MIC) in vitro by the broth dilution method with fungi *C. albicans* MTCC 227 and *A. clavatus* MTCC 1323, taking Nystatin and Greseofulvin as standard drugs [24].

Table 2 Antibacterial activity against different strain

Antibacterial activity table					
Minimum inhibition concentration					
Strain no.	Code no.	*E. coli* MTCC 443	*P. aeruginosa* MTCC 1688	*S. aureus* MTCC 96	*S. pyogenus* MTCC 442
1	M 1	100	200	200	200
2	M 2	62.5	125	250	500
3	M 3	125	100	125	200
4	M 4	250	200	200	500
5	M 5	100	62.5	500	250
6	M 6	125	250	500	500
7	M 7	250	200	250	500
8	M 8	250	100	200	200
9	M 9	200	250	250	250
10	M 10	62.5	125	100	125
11	M 11	200	125	100	200
12	M 12	100	200	125	250
Standard drug (μg/ml)					
Gentamycin		0.05	1	0.25	0.5
Ampicillin		100	–	250	100
Chloramphenicol		50	50	50	50
Ciprofloxacin		25	25	50	50
Norfloxacin		10	10	10	10

Results and discussion

The important infrared spectral bands and their tentative assignments for carbazonyl compounds and their chalcones were recorded as KBr disks. ^{1}H NMR data of compound **4c** revealed a peak at 8.23 δ ppm for –NH carbazol. The ^{1}H NMR data of compounds **4c** revealed signals between 6.6 and 7.7 δ ppm for aromatic protons. The ^{13}C NMR data of compound **4c** showed relevant peaks at 128, 129, 130, and 141 δ ppm, for aromatic carbon and at 188 δ ppm for carbonyl carbon. The IR spectra of compounds **4c** revealed characteristic bands between 3,020 and 3,090 cm^{-1} confirming the presence of C=C groups. The IR spectrum of the compounds showed characteristic bands between 1,640 and 1,720 cm^{-1} confirming the presence of C=O groups of carbazonyl compounds. The IR spectrum of the compounds **4f**, **g** and **l** showed a characteristic band around 1,400 cm^{-1} confirming the presence of the $–NO_2$ group [25].

Antibacterial studies

The antibacterial activity of the compounds was studied with four pathogenic bacteria (Table 2). Ampicilin, Chloramphenicol, Ciprofloxacin, Gentamycin, and Norfloxacin were used as references for inhibitory activity against bacteria. All compounds showed quite good antibacterial activity. When compared with the compounds **4a**, **c**, **e**, **f**, and **l**, the activity was comparable with Ampicilin in the case of *E. coli*, while the compounds **4b** and **j** were more active than Ampicilin and nearly comparable to Chloramphenicol in cthe ase of *E. coli*. In the case of *S. aureus*, the activity of compounds **4a**, **b**, **c**, **d**, **g**, **h**, **i**, **j**, **k** and **l** were comparable to Ampicillin. In vcase of *S. pyogenus*, the activity of compound **4j** was slightly comparable to Ampicillin. In the case of *P. aeruginosa*, the activity of compound **4e** was slightly comparable to Chloramphenicol. Comparative analysis for antibacterial activity of compounds and standard drugs are shown in Table 2 and Fig. 2.

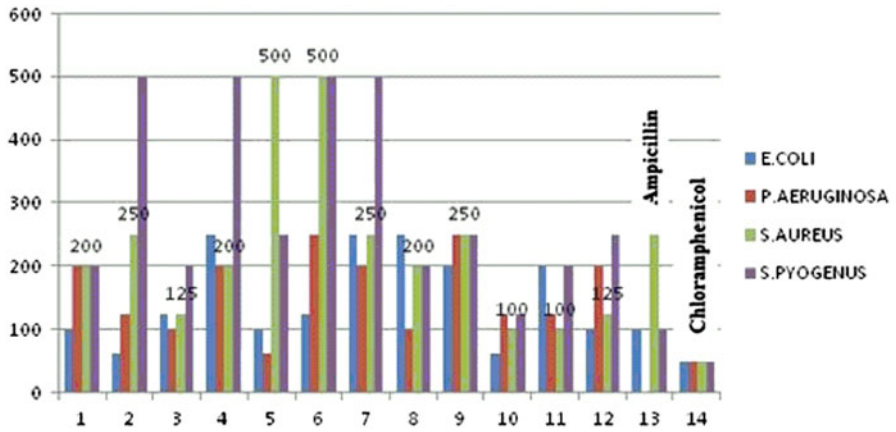

Fig. 2 Comparative chart of bacterial studies with standard drugs

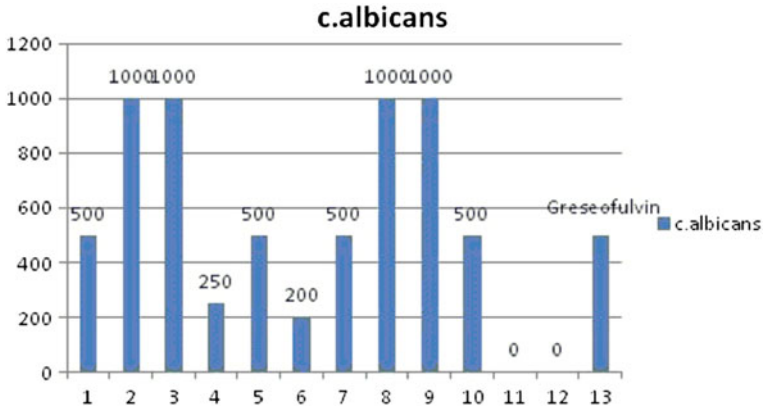

Fig. 3 Comparative chart of fungal studies with standard drugs

Table 3 Antifungal activity against different strain

Antifungal activity table			
Minimum inhibition concentration			
Strain no.	Code no.	*C. albicans* MTCC 227	*A. clavatus* MTCC 1323
1	M 1	500	500
2	M 2	1,000	1,000
3	M 3	>1,000	>1,000
4	M 4	250	250
5	M 5	500	500
6	M 6	200	500
7	M 7	500	500
8	M 8	1,000	1,000
9	M 9	1,000	1,000
10	M 10	500	1,000
11	M 11	>1,000	500
12	M 12	>1,000	1,000
Standard drug			
Nystatin		100	100
Greseofulvin		500	100

Antifungal studies

The antifungal activity of compounds was studied with two pathogenic fungi (Table 3). Nystatin and Greseofulvin were used as references for inhibitory activity against fungi. All compounds showed quite good antifungal activity. When compared with the compounds **4a**, **d**, **e**, **f**, **g** and **j**, the activities were comparable

with Greseofulvin in the case of *C. albicans*. In the case of *A. clavatus*, the activity of compounds was very poor compared to both the standard drugs. Comparative analysis for antifungal activity of compounds and standard drugs are shown in Table 3 and Fig. 3.

Conclusion

The present investigation revealed carbazonyloxy β-hydroxy amine-based chalcones as potential leads for development of new antibacterial drugs. Compounds **4b** and **4j** proved at least as potent as the reference drug Ampicillin in the case of *E. Coli*. Compounds **4a**, **e** and **l** are comparable with the reference drug Ampicillin in the case of *E. Coli*. We can also conclude from the results of antifungal activity of compounds **4a**, **e**, **g** and **j** that they were comparable with the standard drug Greseofulvin in the case of *C. albicans*, while compounds **4d** and **f** are more active compared with Greseofulvin in the case of *C. albicans*. Carbazonyloxy *β*-hydroxy amine-based chalcones are bactericides and fungicides. In the future, carbazonyloxy *β*-hydroxy amine-based chalcones will be used for the further development of new chemical entities.

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