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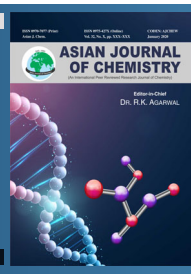

Synthesis of Diverse Fused Tetracyclic Thiazepine-Chalcone Derivatives by Claisen-Schmidt Condensation Reaction and their Antimicrobial Activity

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To develop antimicrobial agent, a series of thiazepine-chalcones was synthesized by Claisen-Schmidt condensation between the couplings of aryl ketone in three steps protocol and different aromatic aldehydes under strong base catalyst at room temperature. The characterization of final products were carried out by IR, ^{1}H & ^{13}C NMR and elemental analysis. The synthesized compounds were also evaluated for their antibacterial and antifungal activities using specific Gram positive and Gram-negative bacterial strains using cup plate method.

Keywords: Claisen-Schmidt condensation, Tetracyclic, Thiazepine, Antimicrobial activity.

INTRODUCTION

Chalcones are well known intermediates for synthesizing various heterocyclic compounds which comprise the aromatic ketone that forms the central core of many important biological compounds, which are to have various biological activities such as antimicrobial [1], anti-inflammatory [2], locomotor [3], antiplatelet [4], antimalarial [5], anticancer [6], antiviral [7], antibacterial, antifungal [8], antiproliferative [9], anti-Alzheimers [10], TACE and MMP inhibitors [11], inhibition of leukotriene CysLT [12], antihypertensive [13], antimicrobial [14], antioxidant [15], anticonvulsant [16], *etc*. To date numerous works are reported based on the chemistry of chalcones and is still an attraction among the organic chemists, due to open-chain model and the feature of skeletal modification to produce a new class of organic compounds [17].

In short, chalcones are an innovative class of compounds with significant therapeutic potential against various diseases particularly when it coupled with other macro/microcyclic systems [18]. One of the important class of derivatives is benzothiazepines, which shows various biological functions when attached to chalcone precursor [19]. Benzothiazepines are important structural scaffolds of seven-membered heterocycles and contain sulfur and nitrogen heteroatoms, due to which they possess a broad spectrum of pharmacological activities [20]. The distinctive feature of the thiazepine core is that it is active against different families of targets, making them interesting heterocyclic ring systems [21]. Various active benzothiazepines are found in current lead discovery process and first molecule of 1,5-benzothiazepine core was found in cardiovascular action (diltiazem and clentiazem) [22]. Quetiapine, a derivative of benzothiazepine, is an antipsychotic drug used for the treatment of schizophrenia and bipolar disorder [23,24].

The synthesis of new derivatives possessing antibacterial activity has considerable attention owing to the continued increase in bacterial resistance [25]. It is reported that benzothiazepine and substituted benzothiazepine-2-one exhibited strong antibacterial activity along with unsaturated enone systems [26]. In present communication, we report a reaction of modified acetophenone with the different aromatic aldehydes to form novel chalcone scaffolds (**7a-j**). The structures of the various synthesized compounds were assigned based on IR, ^{1}H & ^{13}C NMR spectral data and elemental analysis. These compounds were also screened for their antimicrobial activity against some Gram-positive and Gram-negative strains to find the best antibacterial and antifungal agents.

EXPERIMENTAL

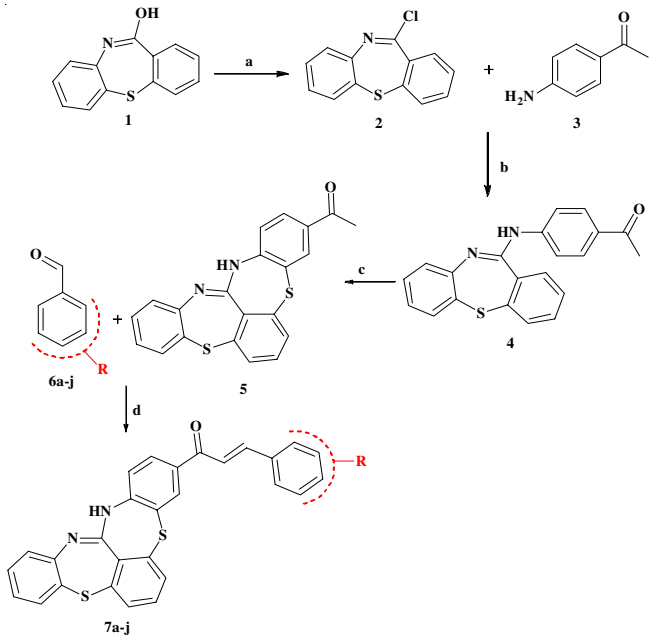
The required chemicals and solvents for the synthesis were purchased from Merck Ltd. and SD fine chemicals, India. The agar medium and PDA medium were purchased from HI media Laboratories Ltd., Mumbai, India. Most of the reactions were carried out by standard techniques for the exclusion moisture. The open-end capillary method was used to determine the melting points of the synthesized derivatives and are uncorrected. Thin layer chromatography (TLC) was used for reaction monitoring using ethyl acetate:*n*-hexane as a mobile phase and visualized in UV light (254 and 365 nm). IR spectra of all compounds were recorded on a Shimadzu, Japan IR-435 spectrophotometer using ATR technique. The ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded on Bruker AVANCE II Spectrometer using DMSO-d_6 as solvent and TMS as the internal reference. Mass spectra were recorded on a Jeol-JMSD 300 mass spectrometer at 70ev. Elemental analysis was carried out by a Perkin-Elmer 2400 CHN analyzer.

Synthesis of 11-chlorodibenzo[*b,f*][1,4]thiazepine (2): Dibenzo[*b,f*][1,4]thiazepin-11-ol (0.01 mol) (**1**) and 60 mL $POCl_3$ were taken in a dry round bottom flask. The reaction mixture was refluxed with constant stirring at 70 ºC for about 3 h. After completion of the reaction, it was cooled to room temperature and poured into crushed ice. The solid separated was filtered and dried using a vacuum dryer. The dried product was recrystallized using methanol to afford analytically pure products. The progress of the reaction was monitored by TLC using *n*-hexane:ethyl acetate (6:4) as a mobile phase.

Synthesis of 1-(4-(dibenzo[*b,f*][1,4]thiazepin-11-ylamino)-phenyl)ethanone (4): 11-Chlorodibenzo[*b,f*][1,4]thiazepine (0.01 mol) (**2**) was taken in 70 mL of pyridine in two-necked round bottom flask. 1-(4-Aminophenyl)ethanone (0.015 mol) (**3**) was added into the reaction mixture over for 10 min. It was heated at 116 ºC and continuously stirred for 4 h. After completion of the reaction, it was cooled to 28 ºC and poured onto crushed ice water under stirring conditions. The obtained solid was filtered, dried in rota vapor to get 1-[4-(dibenzo[*b,f*]-[1,4]thiazepine-11-ylamino)phenyl]ethanone (**4**). The completion of the reaction was monitored by TLC using ethyl acetate: benzene (7:3) as a mobile phase.

Synthesis of 1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]-heptalen-6-yl)ethanone (5): In a 100 mL round bottom flask, mixture of 1-(4-(dibenzo[*b,f*][1,4]thiazepin-11-ylamino)phenyl)-ethanone (0.01 mol) (**4**) and sulphur (0.02 mol) were charged in the presence of catalytic amount of iodine. The reaction mixture was heated in an oil bath at 161 ºC with constant stirring for 30 min. After the completion of the reaction, it was poured into crushed ice and stirred well for 15 min. The solid separated was filtered and washed with cold water. The product obtained was dried and recrystallized from methanol. The purity of the synthesized compound and the extent of completion of reaction were monitored using TLC with mobile phase ethyl acetate: *n*-hexane (3:7).

Synthesis of 1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]-heptalen-6-yl)-3-arylprop-2-en-1-one (7a-j): Intermediate (**5**) and different substituted aromatic aldehydes (**6a-j**) (0.01 mol) in methanol (30 mL) were taken in a round-bottom flask with 30 mL 20% NaOH solution. The reaction mixture was stirred for 24-26 h at ambient temperature. After completion of the reaction, the mixture was poured into crushed ice. The separated solid was filtered, dried and recrystallized from ethanol (**Scheme-I**).



Reaction condition: (a) $POCl_3$, reflux, 3 h, (b) pyridine, heat 161 ºC, 4 h, (c) sulphur, I_2, heat 161 °C, 30 min, (d) 20% NaOH, RT-stirring, 24-26 h

Scheme-I: Synthetic path for the synthesis of title compounds **(7a-j)**

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-phenylprop-2-en-1-one (7a): Yield: 69.35%; m.p.: 201 ºC; IR (ν_{max}, cm^{-1}): 3226 (N-H *str.*), 2975 (C-H *str.*), 1641 (C=O *str.*), 1736 (C=C *str.*), 1534, 1452, 1319 (ring skeleton), 1441 (C-H bend.), 1342 (N-H bend.), 1345 (C-N *str.*), 1254 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.949-6.981 (1H, m, Ar-H), 7.011-7.031 (1H, d, Ar-H), 7.125-7.252 (2H, m, Ar-H), 7.357-7.142 (3H, m, Ar-H), 7.462-7.551 (8H, m, Ar-H), 7.853-7.834 (1H, d, =CH), 8.253-8.232 (1H, d, =CH), 9.625 (1H, s, -NH); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 191.85, 145.51, 144.21, 144.21, 143.22, 140.85, 138.21, 135.84, 133.78, 132.02, 131.95, 130.12, 128.77, 128.77, 127.52, 125.11, 125.11, 124.80, 127.36, 127.36, 125.32, 123.52, 121.02, 117.58, 125.37, 104.95; MS: *m/z* 462 (M^+); Elemental analysis calcd. (found) % for $C_{28}H_{18}N_2OS_2$: C, 72.70 (72.65); H, 3.92 (3.95); N, 6.06 (6.11); O, 3.46 (3.40); S, 13.86 (13.83).

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(2-methoxyphenyl)prop-2-en-1-one (7b): Yield: 71.42%; m.p.: 218 ºC; IR (ν_{max}, cm^{-1}): 3238 (N-H *str.*), 2960 (C-H *str.*), 1648 (C=O *str.*), 1616 (C=C *str.*), 1554, 1440, 1328 (ring skeleton), 1416 (C-H bend.), 1322 (N-H bend.), 1325 (C-N *str.*), 1258 (C-S *str.*), 1152 (C-O *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.819 (3H, s, -OCH$_3$), 6.973-7.031 (2H, d, Ar-H), 7.156-7.286 (2H, m, Ar-H), 7.411-7.396 (3H, m, Ar-H), 7.501-7.590 (7H, m, Ar-H), 7.862-7.841 (1H, d, =CH), 8.258-8.239 (1H, d, =CH), 9.632 (1H, s, -NH); ^{13}C NMR (101 MHz,

DMSO-d_6) δ ppm: 193.25, 168.21, 154.45, 151.78, 151.78, 148.12, 146.08, 140.85, 138.26, 135.80, 134.10, 133.42, 132.90, 131.20, 130.42, 128.12, 127.20, 126.85, 123.51, 121.86, 120.12, 118.41, 117.20, 115.65, 114.62, 110.51, 46.81; MS: *m/z* 492 (M^+); Elemental analysis calcd. (found) % for $C_{29}H_{20}N_2O_2S_2$: C, 70.71 (70.74); H, 4.09 (4.06); N, 5.69 (5.72); O, 6.50 (6.48); S, 13.02 (13.05).

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (7c): Yield: 83.01%; m.p.: 215 ºC; IR (ν_{max}, cm^{-1}): 3232 (N-H *str.*), 2928 (C-H *str.*), 1634 (C=O *str.*), 1665 (C=C *str.*), 1588, 1441, 1324 (ring skeleton), 1414 (C-H bend.), 1384 (N-H bend.), 1324 (C-N *str.*), 1253 (C-S *str.*), 1178 (C-O *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.736 (3H, s, -OC<u>H</u>$_3$), 6.854-6.912 (2H, d, Ar-<u>H</u>), 7.041-7.152 (2H, m, Ar-<u>H</u>), 7.378-7.297 (3H, m, Ar-<u>H</u>), 7.497-7.478 (7H, m, Ar-<u>H</u>), 7.858-7.836 (1H, d, =C<u>H</u>), 8.241-8.262 (1H, d, =C<u>H</u>), 9.621 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 191.12, 176.45, 154.10, 151.35, 150.74, 149.14, 146.82, 141.20, 138.23, 135.59, 133.18, 132.20, 130.85, 130.85, 128.23, 128.23, 127.23, 125.95, 123.21, 121.85, 120.98, 119.12, 117.86, 115.95, 112.23, 111.95, 49.49; MS: *m/z* 492 (M^+); Elemental analysis calcd. (found) % for $C_{29}H_{20}N_2O_2S_2$: C, 70.71 (70.68); H, 4.09 (4.11); N, 5.69 (5.64); O, 6.50 (6.56); S, 13.02 (13.07).

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (7d): Yield: 76.69%; m.p.: 234 ºC; IR (ν_{max}, cm^{-1}): 3246 (N-H *str.*), 2978 (C-H *str.*), 1635 (C=O *str.*), 1627 (C=C *str.*), 1561, 1416, 1394 (ring skeleton), 1418 (C-H bend.), 1360 (N-H bend.), 1367 (C-N *str.*), 1256 (C-S *str.*), 1132 (C-O *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.839-3.825 (6H, s, -OC<u>H</u>$_3$), 6.952-6.993 (1H, m, Ar-<u>H</u>), 7.021-7.042 (1H, d, Ar-<u>H</u>), 7.146-7.266 (2H, m, Ar-<u>H</u>), 7.369-7.432 (3H, m, Ar-<u>H</u>), 7.483-7.586 (6H, m, Ar-<u>H</u>), 7.856-7.837 (1H, d, =C<u>H</u>), 8.255-8.235 (1H, d, =C<u>H</u>), 9.626 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 195.45, 184.12, 171.56, 162.58, 160.28, 160.28, 156.20, 151.52, 148.85, 146.76, 143.89, 140.86, 139.20, 137.81, 138.81, 135.20, 132.95, 130.85, 129.85, 127.21, 126.95, 124.45, 122.20, 118.36, 116.51, 113.89, 51.23, 51.23; MS: *m/z* 522 (M^+); Elemental analysis calcd. (found) % for $C_{30}H_{22}N_2O_3S_2$: C, 68.94 (68.89); H, 4.24 (4.18); N, 5.36 (5.38); O, 9.18 (9.21); S, 12.27 (12.29).

1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (7e): Yield: 85.75%; m.p.: 249 ºC; IR (ν_{max}, cm^{-1}): 3225 (N-H *str.*), 2976 (C-H *str.*), 1642 (C=O *str.*), 1640 (C=C *str.*), 1524, 1458, 1328 (ring skeleton), 1412 (C-H bend.), 1348 (N-H bend.), 1347 (C-N *str.*), 1172 (C-O *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.781 (9H, s, -OC<u>H</u>$_3$), 6.941-6.972 (1H, m, Ar-<u>H</u>), 7.009-7.021 (1H, d, Ar-<u>H</u>), 7.128-7.249 (2H, m, Ar-<u>H</u>), 7.331-7.406 (2H, m, Ar-<u>H</u>), 7.471-7.558 (6H, m, Ar-<u>H</u>), 7.851-7.829 (1H, d, =C<u>H</u>), 8.249-8.228 (1H, d, =C<u>H</u>), 9.626 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 194.25, 184.45, 179.58, 175.20, 168.10, 165.25, 160.98, 159.14, 156.10, 148.85, 145.85, 144.89, 142.98, 139.42, 137.81, 134.74, 134.74, 130.89, 129.10, 127.96, 125.12, 124.56, 123.29, 120.85, 103.56, 103.56, 69.12, 48.21, 48.21; MS: *m/z* 552 (M^+); Elemental analysis calcd. (found) % for $C_{31}H_{24}N_2O_4S_2$: C, 67.37 (67.33); H, 4.38 (4.41); N, 5.07 (5.11); O, 11.58 (11.54); S, 11.60 (11.57).

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(2-nitrophenyl)prop-2-en-1-one (7f): Yield: 77.57%; m.p.: 252 ºC; IR (ν_{max}, cm^{-1}): 3223 (N-H *str.*), 2971 (C-H *str.*), 1649 (C=O *str.*), 1632 (C=C *str.*), 1545 (C-NO_2 *str.*), 1527, 1438, 1317 (ring skeleton), 1403 (C-H bend.), 1346 (N-H bend.), 1324 (C-N *str.*), 1242 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.583-6.610 (2H, m, Ar-<u>H</u>), 6.702-6.786 (2H, m, Ar-<u>H</u>), 6.965-7.182 (2H, m, Ar-<u>H</u>), 7.226-7.367 (2H, m, Ar-<u>H</u>), 7.471-7.956 (6H, m, Ar-<u>H</u>), 7.846-7.827 (1H, d, =C<u>H</u>), 8.236-8.217 (1H, d, =C<u>H</u>), 9.635 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 192.12, 178.12, 175.10, 169.45, 166.74, 161.12, 157.89, 155.41, 152.63, 140.86, 138.52, 137.25, 135.81, 134.63, 134.63, 132.85, 131.45, 130.41, 130.41, 129.45, 127.582, 123.09, 120.58, 118.34, 118.34, 109.80; MS: *m/z* 507 (M^+); Elemental analysis calcd. (found) % for $C_{28}H_{17}N_3O_3S_2$: C, 66.26 (66.24); H, 3.38 (3.41); N, 8.28 (8.25); O, 9.46 (9.49); S, 12.63 (12.58).

1-(9*H*-4,15-Dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(3-nitrophenyl)prop-2-en-1-one (7g): Yield: 82.63%; m.p.: 259 ºC; IR (ν_{max}, cm^{-1}): 3234 (N-H *str.*), 2978 (C-H *str.*), 1645 (C=O *str.*), 1667 (C=C *str.*), 1584 (C-NO_2 *str.*), 1552, 1458, 1378 (ring skeleton), 1456 (C-H bend.), 1320 (N-H bend.), 1388 (C-N *str.*), 1253 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.612-6.628 (1H, m, Ar-<u>H</u>), 6.755-6.776 (1H, d, Ar-<u>H</u>), 6.821-7.220 (3H, m, Ar-<u>H</u>), 7.301-7.378 (2H, m, Ar-<u>H</u>), 7.568-7.978 (7H, m, Ar-<u>H</u>), 7.768-7.786 (1H, d, =C<u>H</u>), 8.178-8.20 (1H, d, =C<u>H</u>), 9.618 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 191.12, 188.47, 181.45, 179.12, 179.12, 168.42, 166.52, 160.74, 152.56, 150.45, 147.20, 144.41, 140.245, 136.75, 135.45, 135.45, 133.82, 132.20, 130.89, 128.45, 125.78, 124.23, 123.45, 122.81, 121.81, 107.72; MS: *m/z* 507 (M^+); Elemental analysis calcd. (found) % for $C_{28}H_{17}N_3O_3S_2$: C, 66.26 (66.29); H, 3.38 (3.44); N, 8.28 (8.30); O, 9.46 (9.41); S, 12.63 (12.67).

1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(4-nitrophenyl)prop-2-en-1-one (7h): Yield: 88.68%; m.p.: 272 ºC; IR (ν_{max}, cm^{-1}): 3232 (N-H *str.*), 2951 (C-H *str.*), 1643 (C=O *str.*), 1687 (C=C *str.*), 1582 (C-NO_2 *str.*), 1584, 1444, 1325 (ring skeleton), 1462 (C-H bend.), 1359 (N-H bend.), 1321 (C-N *str.*), 1288 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.948-6.988 (1H, m, Ar-<u>H</u>), 7.017-7.038 (1H, d, Ar-<u>H</u>), 7.149-7.269 (2H, m, Ar-<u>H</u>), 7.355-7.455 (3H, m, Ar-<u>H</u>), 7.438-7.589 (7H, m, Ar-<u>H</u>), 7.856-7.837 (1H, d, =C<u>H</u>), 8.255-8.235 (1H, d, =C<u>H</u>), 9.631 (1H, s, -N<u>H</u>); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 194.12, 182.72, 179.35, 159.63, 159.63, 156.74, 154.85, 153.08, 149.52, 148.58, 146.95, 143.56, 138.42, 136.89, 136.89, 136.89, 134.20, 130.07, 129.31, 129.31, 126.02, 125.98, 123.29, 120.20, 117.95, 104.42; MS: *m/z* 507 (M^+); Elemental analysis calcd. (found) % for $C_{28}H_{17}N_3O_3S_2$: C, 66.26 (66.28); H, 3.38 (3.39); N, 8.28 (8.23); O, 9.46 (9.41); S, 12.63 (12.60).

1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(4-aminophenyl)prop-2-en-1-one (7i): Yield: 72.77%; m.p.: 193 ºC; IR (ν_{max}, cm^{-1}): 3296 (N-H *str.*), 2968 (C-H *str.*), 1643 (C=O *str.*), 1624 (C=C *str.*), 1526, 1445, 1369 (ring skeleton), 1406 (C-H bend.), 1342 (N-H bend.), 1365 (C-N *str.*), 1254 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 4.635-4.218 (2H, s, -N<u>H</u>$_2$), 6.552-6.638 (1H, m, Ar-<u>H</u>), 7.021-7.266 (3H, m, Ar-<u>H</u>), 7.352-7.524 (4H, m, Ar-<u>H</u>), 7.561-7.769 (6H,

m, Ar-H), 7.902-7.884 (1H, d, =CH), 8.236-8.254 (1H, d, =CH), 9.632 (1H, s, -NH); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 191.85, 185.12, 181.85, 175.48, 175.48, 168.15, 165.71, 162.02, 159.43, 155.45, 151.32, 148.32, 141.81, 141.81, 135.26, 135.26, 131.58, 129.84, 127.52, 125.23, 123.58, 121.22, 120.89, 117.47, 102.85, 102.85; MS: *m/z* 477 (M^+); Elemental analysis calcd. (found) % for $C_{28}H_{19}N_3OS_2$: C, 70.41 (70.43); H, 4.01 (4.06); N, 8.80 (8.78); O, 3.35 (3.39); S, 13.43 (13.47).

1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-(*p*-tolyl)prop-2-en-1-one (7j): Yield: 73.35%; m.p.: 227 ºC; IR (ν_{max}, cm^{-1}): 3237 (N-H *str.*), 2969 (C-H *str.*), 1736 (C=O *str.*), 1617 (C=C *str.*), 1527, 1436, 1320 (ring skeleton), 1411 (C-H bend.), 1385 (N-H bend.), 1358 (C-N *str.*), 1251 (C-S *str.*); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.423 (3H, s, -CH$_3$), 6.732-6.856 (1H, m, Ar-H), 7.023-7.046 (1H, d, Ar-H), 7.152-7.278 (2H, m, Ar-H), 7.353-7.478 (3H, m, Ar-H), 7.520-7.706 (7H, m, Ar-H), 7.850-7.832 (1H, d, =CH), 8.252-8.232 (1H, d, =CH), 9.626 (1H, s, -NH); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm: 193.25, 180.51, 177.69, 177.69, 175.25, 171.29, 165.28, 158.14, 156.85, 150.01, 148.21, 137.52, 134.09, 130.22, 130.22, 128.98, 128.98, 127.87, 127.56, 126.33, 123.50, 122.41, 120.45, 119.87, 118.89, 111.98, 12.31; MS: *m/z* 476 (M^+); Elemental analysis calcd. (found) % for $C_{29}H_{20}N_2OS_2$: C, 73.08 (73.10); H, 4.23 (4.19); N, 5.88 (5.91); O, 3.36 (3.39); S, 13.46 (13.51).

Antimicrobial evaluation: The synthesized compounds (**7a-j**) were screened for their antimicrobial activity against two Gram-positive bacteria *viz*., *Bacillus megaterium*, *Bacillus subtilis* and two Gram-negative bacteria *viz*., *Escherichia coli*, *Enterobacter aerogenes* by using cup plate method [27]. Similarly, the compounds were also tested for their antifungal activity using potato-dextrose-agar (PDA) medium by the same cup plate method against *Aspergillus awamori*.

RESULTS AND DISCUSSION

Claisen-Schmidt condensation reaction of novel acetophenone synthesized using three-step procedures staring with dibenzo[*b,f*][1,4]thiazepin-11-ol in $POCl_3$ medium followed by chloroamine coupling in pyridine as a base catalyst obtained 1-[4-(dibenzo[*b,f*][1,4]thiazepin-11-ylamino)phenyl]ethanone in high yield (91%). Intermediate **5** was synthesized by solid-phase synthesis of iodine catalyzed reaction with sulphur in passable heating conditions. Solution-phase synthesis of 1-(9*H*-4,15-dithia-9,10-diazatribenzo[*b,ef,i*]heptalen-6-yl)-3-arylprop-2-en-1-one (**7a-j**) was carried out by heating under reflux of intermediate novel acetophenone (**5**) with various arylaldehydes (**6a-j**) in dry MeOH in the presence of 20% NaOH solution.

The structure of synthesized compounds **7a-j** was confirmed on the basis of spectral data. The IR spectrum of compound **7a** showed a strong adsorption band at ~3236 cm^{-1} due to N-H stretching, secondary amine. Absorption band appeared at ~2984 cm^{-1} due to stretching vibrations of aromatic hydrogen and absorption band at ~1687 cm^{-1} due to stretching vibration to >C=O group. Sharp absorption peak observed at ~1584 cm^{-1} in -C-NO_2 group. The absorption band at ~1321, ~1253 cm^{-1} corresponding to C-N, C-S stretching, respectively. In ^{1}H NMR, an appearance of singlet peaks in compounds **7a-j** showed a characteristic value at δ = ~9.61 ppm due to the presence of secondary amine group in fused cyclic ring. The presence of =CH- linkage showed a doublet peak at ~8.25 ppm. Three protons of Ar-(OCH_3) displayed singlet at δ = ~3.78 ppm. Remaining all aromatic protons appeared multiplet in the region δ = ~6.49 to ~7.82 ppm. Remaining substituents protons were in good agreement with theoretical values. In ^{13}C NMR, the characteristic value around δ = ~175 ppm showed the presence of >C=O group attached with an aromatic ring. The aromatic ring carbon and heterocyclic ring carbons were in decent covenants with the theoretical values. The mass spectrum revealed a molecular ion peak in compounds *7a-j* at *m/z* = 462 to 552 in mass spectra, molecular ion peak was in agreement with proposed molecular weight and elemental analysis.

Antimicrobial evaluation: The screening result revealed that compounds **7a-j** showed a significant antimicrobial activities. In particular, compound **7c** only showed mild inhibitory action on *Bacillus megaterium*. Compounds **7f** and **7j** also only showed mild inhibitory action on *Bacillus subtilis*. Compound **7d** has shown significant activity on *Bacillus megaterium*, *Bacillus*

TABLE-1
in vitro RESULTS OF ANTIBACTERIAL SCREENING OF COMPOUNDS **7a-j**

No.	R	Gram-positive bacteria		Gram-negative bacteria		Fungi
		Bacillus megaterium ATCC 14581	*Bacillus subtilis* ATCC 23857	*Escherichia coli* ATCC 25922	*Enterobacter aerogenes* ATCC 13048	*Aspergillus awamori* ATCC 22342
7a	H	18	17	16	20	19
7b	2-OCH_3	17	13	20	18	20
7c	4-OCH_3	20	16	24	16	18
7d	3,4-$(OCH_3)_2$	21	19	21	17	17
7e	3,4,5-$(OCH_3)_3$	18	14	19	15	22
7f	2-NO_2	17	18	16	18	23
7g	3-NO_2	19	14	14	11	13
7h	4-NO_2	16	12	17	14	11
7i	4-NH_2	18	15	15	18	14
7j	4-CH_3	12	18	19	16	18
	Ampicillin	23	18	18	20	–
	Chloramphenicol	22	20	21	19	–
	Norfloxacin	20	19	22	21	–
	Griseofulvin	–	–	–	–	21

subtilis and *Escherichia coli*. Compounds **7b**, **7c**, **7d** and **7j** have shown high potency, especially against *Escherichia coli*. Compounds **7a**, **7b**, **7f** and **7i** showed mild inhibitory action on *Enterobacter aerogenes*. All the organisms employed at a concentration of 50 µg/mL showed considerable antibacterial and antifungal activities and are comparable to that of standard drugs.

Conclusion

In this work, the strategy for the synthesis of desired novel chalcones indicated that 1-(9*H*-4,15-dithia-9,10-diazatribenzo-[*b,ef,i*]heptalen-6-yl)-3-arylprop-2-en-1-one derivatives are pharmacologically moderately potent. The structural modifications of the basic structure in derived compounds with electron releasing groups such as methoxy and amine showed better antibacterial activity. Compounds having nitro group exhibited more antifungal activity. These results suggested that chalcone derivatives have excellent scope for further development as commercial antimicrobial agents.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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