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SYNTHESIS, CHARACTERIZATION OF SOME SUBSTITUTED BIPHENYL-2-AMINOTHIAZOL DERIVATIVES

Chemistry

Havale Shrikant Hanumantappa* Department of Chemistry, Banasthali Vidyapith, Banasthali Rajasthan, India-304022; Department of chemistry, SMS Research Center (A DSIR approved), SMS Pharmaceuticals Ltd, Hyderabad, Telangana, India 500043. *Corresponding Author

Dharma Kishore Department of Chemistry, Banasthali Vidyapith, Banasthali Rajasthan, India-304022.

Jaya Dwivedi Department of Chemistry, Banasthali Vidyapith, Banasthali Rajasthan, India-304022.

Bhavani Singh Yadav Department of Chemistry, Banasthali Vidyapith, Banasthali Rajasthan, India-304022.

Venkat Rao Sirugubattula R&D Center, Srigen Life sciences Pvt ltd, D-22, IDA-Medchel, IALA, Telangana, India 501401.

ABSTRACT

The synthesis explored to serve novel functional group extended Anti-microbial bio-active molecules of substituted Aminothiazoles. It reveals from overall available up to date literature feedback of Aminothiazoles, it is difficult to synthesis of substituted biphenyl-2-aminothiazoles from Suzuki coupling reaction of 5-(4-bromophenyl) thiazol-2-amine with substituted Boronic acids in presence of Palladium (II) acetate catalyst and in 5% aqueous Isopropyl alcohol used as a solvent. This is a shortest pathway to synthesis of biphenyl derivatives of Aminothaizoles by Suzuki coupling method.

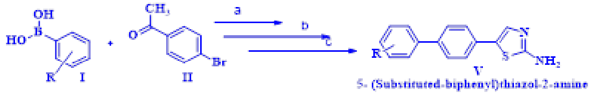


Fig 1: Proposed synthetic target molecular structure

KEYWORDS

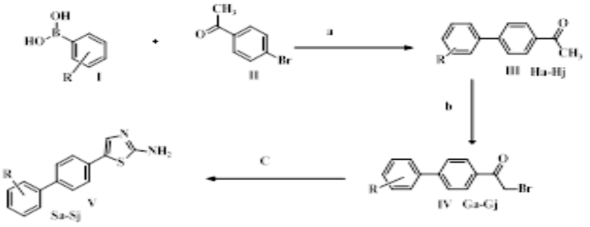
Synthesis, Biphenyl Aminothiazoles, Suzuki coupling, Bromination, Thiourea cyclisation with molecular Iodine

INTRODUCTION

Basically Aminothiazoles and other thiazole derivatives exhibits broad range of potential biological activities and their synthesis are commercially, economically and practically viable. Hence we revealed maximum of literature to do some novel work on this topic, so as a part of our research scouted some of schemes to synthesis substituted Biphenyl-2-aminothiazoles derivatives in a systematic and having novel approach as shown as in Scheme-I.

Thaizole and Aminothaizoles derivatives are an important class of heterocyclic compounds, the top majority of them contains biphenyl moiety. They incurred an important position in medicinal chemistry and providing a wide range of bioactivities as well. As medicines, many of them display including antibacterial and antifungal [1, 2], anti-HIV [3], hypertension[4], anti-inflammatory [5], anticancer [6], anti-convulsant[7], Antidepressant antitubercular activities [8]. Thaizole and their derivatives have been attracted continuing interest over the years because of their varied biological activities. Thiazole, particularly the 2-aminothiazole nucleus have been incorporated into a wide variety of therapeutically interesting drug candidates. On the other hand, Imidazole is a vital heterocyclic nucleus which is well known for its wide biological profile. Imidazole derivatives are associated with a wide array of pharmacological activities including antimicrobial [9, 10], anti-inflammatory and analgesic [11,12], anti tubercular [13], antiviral [14].

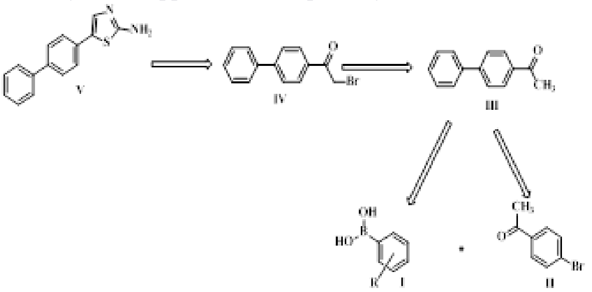
Proposed Synthetic Scheme- I



R = -Cl, -CF3, C_6H_5O-, -CH_2OH, -CHO, -F, -OCH_3, -H

a)Suzuki coupling Pd(0AC)$_2$, IPA, Water (9.5:0.5); b)Br_2 /ACOH,$AlCl_3$;c)Thiourea,I_2, Ethanol

Retro Synthetic Approach For Proposed Synthesis



RESULTS AND DISCUSSION

MATERIALS AND METHODS

Synthesized materials melting points were determined using a manual POLMON electro thermal apparatus (Range 0–300°C) in glass capillary tubes and are uncorrected. IR spectra were recorded on a Perkin- Elmer FT IR 1600. 1H & ^{13}CNMR spectra were recorded on a Bruker-400 MHz spectrometer and are expressed in a using TMS as internal reference. Commercially available 4-Bromoacetophenone (II) and substituted phenyl boronic acids (I), palladium acetate and other reagents and solvents were used and are commercial reagents.

Substituted biphenyl-2-aminothiazoles (Sa-Sj) were synthesized according to the literature [15-16]. All the reactions were monitored by thin layer chromatography over pre-coated silica gel plates, using UV lamp, iodine vapors or $KMnO_4$ spray as developing agents.

The purification was carried out by using 60-120 mesh silica gel by column chromatography (obtained from Merck) with a suitable eluting system with various polarity mobile phase ratio's such as n-Hexane, Ethyl acetate, Chloroform, Chloroform: Methanol.

The biological activity of chemically synthesized molecules was studied by Inhibition zone diameter calculation method against *Candida Albicam, Aspergillus Niger cell cultures* with reference drug standard Fluconazole.

Inoculum Preparation:
Potato Dextrose Broth PDB (commercially available)

Procedure For Antifungal Activity:
Weigh 80 mg of Potato Dextrose Broth powder.Add to a 1 Liter Erlenmeyer flask containing 800 mL of water, stir to dissolve into solution. Transfer the solution to a 1 Liter volumetric flask and dilute to 1 Liter. Transfer the 1 Liter media solution to a 1 Liter media storage bottle and label with appropriate information, Autoclave the solution at 121°C for 15 mines to ensure that the LB is sterilized of all foreign matter and contaminants. After cooling of the broth, using a sterile pipette tip, select a single spore from a pure culture plate.Drop the tip into the liquid PDB and swirl. Incubate fungal culture at 25°C for 5-7 days in shaking incubator at 80 rpm.

Preparation of Compound Stock Solution:
1mg/ml stock solution of each extract was prepared in a suitable solvent.

Preparation of Potato Dextrose Agar PDA: (Agar Well Diffusion)
Weigh PD Agar as per requirement and dissolve in distilled water as per the guidelines given by manufacturer.Autoclave the media at 121°C for 15 minutes, after autoclaving, pour the media in sterile petriplates and keep for solidification.

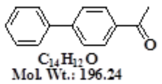
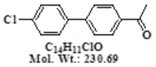
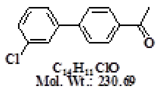
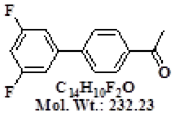
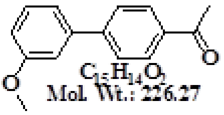
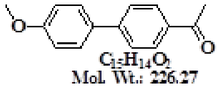
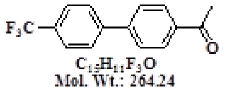
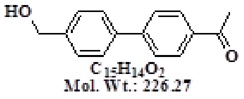
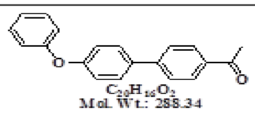
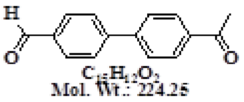
Procedure:
Sterilize a cork borer by autoclaving or disinfect it by rinsing in alcohol followed by sterile water.On a PD agar plate aseptically punch 5 holes using a cork borer, using a marker, mark the underside of the Petri to label the wells.Aseptically spread 20µl of the indicator organism onto the MH agar plate. Let the plate stand for 5 minutes, Place 10µl, 25µl, 50µl, 100µl and 150µl of the extract in the appropriate wells.Incubate the plate at 25°C for 72-96 hrs. Measure the zones of inhibition in millimeters, using a ruler on the underside of the plate.Same Procedure is repeated with Fluconazole as a standard with concentrations of 10µg, 25 µg, 50 µg, 100 µg, 150 µg.

Experimental

Step-I: General Procedure for Substituted -4-Acetylbiphenyl derivatives (Ha-Hj):

In a 250ml round bottom flask taken a mixture of 4-Bromoacetohenone (1.0 mmol), substituted phenyl boronic acid (1.2 mmol), palladium acetate (0.06 mmol), and potassium carbonate (1.8 mmol) in 5% aqueous isopropyl alcohol (5V) at room temperature. Stir the reaction mass for 6 hours under reflux condition, after completion of TLC, the solvent removed under reduced pressure and then add two volumes of water extract the aqueous layer with methylene dichloride (3X2 volumes) and then separate the layers, organic layer washed with brine solution, finally dried over anhydrous sodium sulphate. The obtained solid after distillation of dried organic layer was taken for purification in hexanes (3-4 volumes) to give desired substituted 4-acetylbiphenyl derivatives (**Ha-Hj**) yield range: 70-90%

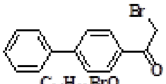
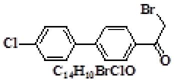
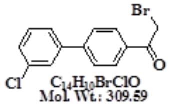
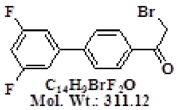
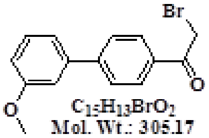
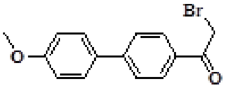
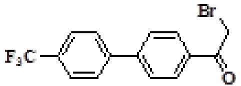
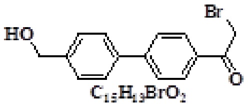
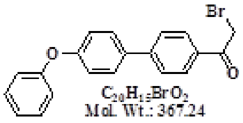
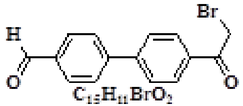
Table-1: Experimental And FT-IR, CHNSX Analysis Data Of Ha to Hj

S. No.	Product Code	Chemical Structure	Rxn time in hrs	Physical appearance	Characterization data (FT-IR & CHNSX)
1	Ha		6	Off white Solid	1712.46, 3076.23, 2889.30, C, 86.02, H, 5.98, O, 8.23
2	Hb		6	Off white Solid	1705.71, 3065.71, 2993.00, Cl; 556.26, C, 73.03, H, 4.81 Cl, 15.28, O, 7.00
3	Hc		6	Yellow Solid	1708.69, 3085.62, 2876.63, Cl; 596.02, C, 72.91, H, 4.90 Cl, 15.24, O, 7.16
4	Hd		6	Pale yellow Solid	1718.33, 3100.02, 2977.15, F; 1282.27, C, 72.38, H, 4.40 F, 16.53, O, 6.94
5	He		6	Pale yellow Solid	1698.53, 2982.65, 2888.03, 1109.46, C, 79.92, H, 6.16 O, 14.09
6	Hf		8	Off white Solid	1697.42, 2980.99, 2910.00, 1107.55, C, 79.92, H, 6.16 O, 14.09
7	Hg		6	Dark brown Liquid	1717.14, 3104.00, 2971.10, 1267.90, C, 68.38, H, 4.10 F, 22.04, O, 5.99
8	Hh		8	Off white Solid	3206.77, 1688.44, 2900.32, 2893.15, C, 80.08, H, 6.10; O, 14.06
9	Hi		6	Pale yellow Solid	1697.59, 2990.55, 2805.39, 1233.33, C, 84.01, H, 5.33 O, 11.09
10	Hj		6	Brown color Liquid	1704.76, 1699.83, 3100.55, 1109.46, C, 80.22, H, 5.45 O, 14.55

Step-II: General Procedure For Alpha Bromination Of 4-acetylbiphenyl Derivatives (Ga-Gj):

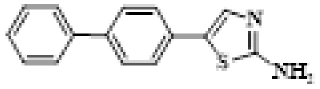
To a cooled solution of substituted-4-acetylbiphenyl (1.0 mmol) compounds (Ha-Hj) in methanol (10 volumes) added anhydrous aluminum chloride (0.85 mmol) portion wise at 0 to 5^{0}C (it took 10 min) and then slowly added liquid bromine (7.10 mmol) drop wise at the temperature of 0 to 5^{0}C, after addition is completed temperature slowly rises to room temperature and stirs it for 5 hours. Remove the solvent under reduced pressure after TLC complies, the obtained residue taken in aqueous Sodium bicarbonate solution and extract with Methylene dichloride (3 X 5V). The combined organic layers was washed with brine and dried over anhydrous sodium sulphate, the solid obtained after distillation of organic layer was taken up for purification in hexanes (10 volumes) to afford targeted substituted phenyl phenacyl bromides (Ga-Gj), yield range: 65-85%

Table-2: Experimental and FT-IR, CHNSX analysis data of Ga to Gj

S. No.	Product Code	Chemical Structure	Rxn time in hr's	Physical appearance	Characterization Data (FT-IR (cm^{-1}), CHNSX
1	Ga	 $C_{14}H_{11}BrO$ Mol. Wt.: 275.14	3	Off white Solid	1658.25, 3050.12, 2989.40, 687.17; C, 60.93, H, 4.03 O, 5.81; Br, 29.03
2	Gb	 $C_{14}H_{10}BrClO$ Mol. Wt.: 309.59	5	off white Solid	1691.10, 3080.35, 2975.82, 698.56; 567.21; C, 55.01, H, 3.30, O, 4.98; Br, 26.08, Cl, 11.75
3	Gc	 $C_{14}H_{10}BrClO$ Mol. Wt.: 309.59	8	Light brown Solid	1692.01, 3060.09, 2958.21, 666.98; 569.18; C, 55.01, H, 3.30, O, 4.98; Br, 26.08, Cl, 11.75
4	Gd	 $C_{14}H_9BrF_2O$ Mol. Wt.: 311.12	6	Light brown Solid	1693.05, 3100.01, 2896.66, 599.87; 1230.11; C, 53.91, H, 3.00, O, 5.25; Br, 25.10, F, 13.0
5	Ge	 $C_{15}H_{13}BrO_2$ Mol. Wt.: 305.17	5	Off white Solid	1701.22, 2984.32, 2895.02, 618.46;1085.56, C, 60.00, H, 3.00, O, 10.52; Br, 26.34,
6	Gf	 $C_{15}H_{13}BrO_2$ Mol. Wt.: 305.17	5	Light brown Solid	1703.21, 2982.00, 2890.76, 618.22; 1106.52, C, 60.00, H, 3.00, O, 10.52; Br, 26.34,
7	Gg	 $C_{15}H_{10}BrF_3O$ Mol. Wt.: 343.14	5	Light brown Liquid	1712.43, 3000.50, 2999.01, 569.33; 1247.53; C, 53.01, H, 3.00, O, 4.55; Br, 23.07; F, 16.52
8	Gh	 $C_{15}H_{13}BrO_2$ Mol. Wt.: 305.17	5	Off white Solid	1635.97, 3060.18, 2910.99, 630.82; 3200.50; C, 60.00, H, 4.31, O, 10.52; Br, 26.10,
9	Gi	 $C_{20}H_{15}BrO_2$ Mol. Wt.: 367.24	6	Light brown Liquid	1689.15, 3031.04, 2878.08, 645.11; 1250.14; C, 65.03, H, 4.00, O, 9.02; Br, 20.98
10	Gj	 $C_{15}H_{11}BrO_2$ Mol. Wt.: 303.15	5	Light brown Liquid	1715.09, 1693.05, 3089.22, 2998.22, 690.87; ; C, 53.91, H, 3.00, O, 5.25; Br, 25.10,

Step-iii: General Procedure For Substituted Biphenyl-2-aminothiazoles: (sa-sj)

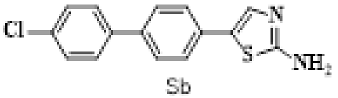
Refluxed a mixture of substituted phenyl phenacyl bromide (1.0 mmol) compounds **(Ga-Gj)**, Molecular Iodine (1.0 mmol) and Thiourea in absolute ethanol for 8 hours. Remove the solvent under vacuum, the crude obtained was taken in Methylene dichloride and water (1:1). The resulting solid was taken for purification in hexanes (4-5 volumes) to afford desired products **(Sa-Sj)**. Yield range: 40-60%.



Sa

$C_{15}H_{12}N_2S$
Mol. Wt.: 252.33

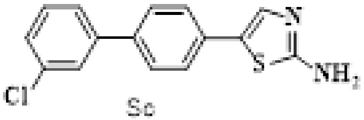
Compound Sa: ^{1H}NMR: (DMSO-D6); δ 8.18(1H, bs), δ7.83(2H,d),δ7.75(2H,d), δ7.65(4H,m), δ7.2(1H,s),δ7.07(2H,bs); **^{13}C NMR:(DMSO-D6);** 168.16,149.30, 138.83, 137.83, 134.73, 131.08, 128.87, 126.62, 120.71, 101.97.; **Mass:** 253.12 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3320 (-NH$_2$), 2980 (=CH), 3031(=CH),1409 (biphenyl), **CHNS Analysis**(Element, Found (Calculated))**:** C, 71.20 (71.40); H, 4.65 (4.79); N, 11.04 (11.10); S, 13.01 (12.71).



Sb

$C_{15}H_{11}ClN_2S$
Mol. Wt.: 286.78

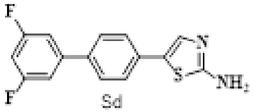
Compound Sb: ^{1H}NMR: (DMSO-D6); δ 8.49 (2H, bs), δ7.80-7.85(4H, m), δ7. 75 -7.78 (2H, d), δ 7.52(2H, d), δ 7.28(1H, BS); **^{13}C NMR: (DMSO-D6);** 170.12, 139.25, 137.75, 132.74, 128.92, 126.33, 103.04; **Mass:** 286.3 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3410(-NH$_2$), 2995(=CH), 3012(=CH), 1392(biphenyl), 682.13 (-Cl) **CHNS Analysis** (Element, Found (Calculated)): C, 61.88 (62.82); H, 4.02 (3.87); Cl, 12.31(12.36); N, 10.10 (9.77); S, 11.02 (11.18).



Sc

$C_{15}H_{11}ClN_2S$
Mol. Wt.: 286.78

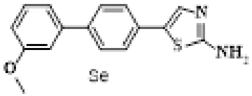
Compound Sc: ^{1H}NMR: (DMSO-D6); δ 7.897.99 (2H, m), δ7.62-7.87(5H, m), δ7.39-7.49 (2H, m), δ7.19 (2H, s); **^{13}C NMR (DMSO-D6):** 168.17, 130.705, 129.53, 126.04, 103.0, **Mass:** 286.9 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3391(-NH$_2$), 2975(=CH), 3025(=CH), 1356 (biphenyl), 597.44 (-Cl); **CHNS Analysis** (Element, Found (Calculated))**:** C, 63.05(62.82); H, 3.78 (3.87); Cl, 12.57 (12.36); N, 9.76 (9.77); S, 11.09 (11.18).



Sd

$C_{15}H_{10}F_2N_2S$
Mol. Wt.: 288.32

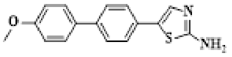
Compound Sd: ^{1H}NMR: (DMSO-D6); δ 7.76(2H, d), δ7.62(1H,d),δ7.50(1H,m), δ7.44(2H,d) ,δ7.31(1H,t), δ7.12(1H,t),δ5.35 (1H,bS); **^{13}C NMR :(DMSO-D6);** 168.88, 160.22, 157.87, 134.19, 131.68, 128.85, 126.03, 123.99, 111.87, 109.60, 104.45; **Mass:** 288.6 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3412(-NH$_2$), 2998(=CH), 3036(=CH); 1225.40(-F) **CHNS Analysis** (Element, Found (Calculated))**:** C,62.45 (62.49); H, 3.75 (3.50); F, 13.06 (13.18); N, 9.80 (9.72); S, 11.02 (11.12).



Se

$C_{16}H_{14}N_2OS$
Mol. Wt.: 282.36

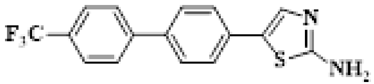
Compound Se: ^{1H}NMR: (DMSO-D6; δ 8.05(1H, t), δ7.92(1H,s),δ7.85(2H,d), δ7.59(1H,d), δ7.45(1H,d),δ7.11(3H,m) δ3.88(3H,s); **^{13}C NMR:(DMSO-D6);**197.50, 168.81,155.36, 154.97, 145.37, 144.17, 142.95,141.84, 140.29, 138.87, 136.87, 135.13, 133.09, 132.06, 129.50, 128.83, 128.30, 127.67, 125.32, 125.26, 125.26, 114.96, 113.68, 112.09, 111.14, 110.53, 102.43, 56.69, 26.76; **Mass:** 283 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3263(-NH$_2$), 3001(=CH), 1175(-C-O-C-); **CHNS Analysis** (Element, Found (Calculated))**:** C, 68.01 (68.06); H, 4.98 (5.00); N, 10.02 (9.92); O, 5.70 (5.67); S, 11.42 (11.36)



Sf

$C_{16}H_{14}N_2OS$
Mol. Wt.: 282.36

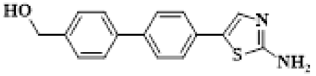
Compound Sf: ^{1H}NMR: (DMSO-D6); δ 7.89(1H, d), δ7.83(2H,d), δ7.66(3H,m), δ7.17 (1H,d), δ7.19(2H,bs),δ7.06(1H,s) δ3.40(3H,s); **^{13}C NMR:(DMSO-D6);** 169.58, 155.13, 138.28, 132.97, 130.97, 127.05, 126.55, 113.02, 111.31, 102.42, 56.34; **Mass:** 283.1 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3222(NH$_2$), 2895(=CH), 3033(=CH), 1215(-C-O-C-); **CHNS Analysis** (Element, Found (Calculated))**:** C, 67.98 (68.06); H, 4.98 (5.00); N, 10.02(9.92); O, 5.70 (5.67); S,11.50 (11.36)



Sg

$C_{16}H_{11}F_3N_2S$
Mol. Wt.: 320.33

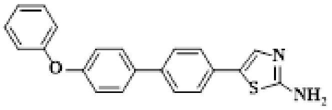
Compound Sg: ^{1H}NMR: (DMSO-D6); δ 9.12(1H, s), δ9.01 (1H,s),δ8.05 (2H, d), δ7. 86(5H, m), δ 7.71(2H, m); **^{13}C NMR: (DMSO-D6);** 172.24, 169.84, 160.31, 140.28, 138.80, 132.85, 130.71, 129.91, 129.70, 127.38, 126.97, 12664, 126.34, 125.50, 124.33, 123.08, 122.98, 122.79, 103.15, 92.096; **Mass:** 320.9 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3405(-NH$_2$), 2995(=CH), 3011(=CH), 1459(-CF$_3$); **CHNS Analysis**(Element, Found (Calculated))**:** C, 60.12(59.99); H, 3.50(3.46); F, 17.80 (17.79); N, 8.85 (8.75); S, 10.22(10.01).



Sh

$C_{16}H_{14}N_2OS$
Mol. Wt.: 282.36

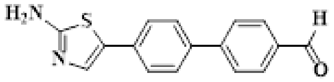
Compound Sh: ^{1H}NMR: (DMSO-D6); δ 9.27(1H,s), δ9.07(1H,t),δ7.99(1H,d), δ7.89(3H,m), δ7.66(2H,m),δ7.39(1H,m), δ7.25 (1H, t), δ 4.60(1H, s), δ 4.57(2H, t); **^{13}C NMR:(DMSO-D6)** :169.63, 168.72, 139.06, 134.44, 133.74, 129.55, 128.51, 12811, 126.91, 126.34, 123.34, 123.48, 103.05, 35.394; **Mass:** 283 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3510(-OH), 3325 (-NH$_2$), 3090(=CH), 2895(=CH); **CHNS Analysis**(Element, Found (Calculated))**:** C, 68.10 (68.06); H, 4.98 (5.00) ; N, 10.12 (9.92); O, 5.80 (5.67); S, 11.40(11.36)



Si

$C_{21}H_{16}N_2OS$
Mol. Wt.: 344.43

Compound Si: ^{1H}NMR: (DMSO-D6); δ 8.03(1H, d), δ7.86(2H,m),δ7.71(3H,m), δ7.57(2H,d), δ7.2 (1H,d), δ7.06 (3H,m) δ6.96(2H,d); **Mass:** 345.2 (M+H); **FT-IR (KBr Pellet, Cm^{-1}):** 3390(-NH$_2$), 2887(=CH), 3105(=CH), 1250 (Ph-O-Ph); **CHNS Analysis** (Element, Found (Calculated))**:** C, 73.21 (73.23) ; H, 4.70 (4.68); N, 8.10(8.13); O, 4.63(4.65); S, 9.40 (9.31).



Sj

$C_{16}H_{12}N_2OS$
Mol. Wt.: 280.34

Compound Sj: ^{1H}NMR: (DMSO-D6); δ 8.24(1H, t), δ7.19-7.88(8H, bm), δ 4.22 (2H, bs); **Mass:** 281 (M+H); FT-IR **(KBr Pellet, Cm^{-1}):** 3401(-NH$_2$), 2993(=CH), 3016(=CH), 1715(-CHO); **CHNS Analysis** (Element, Found (Calculated))**:** C, 68.51 (68.55) ; H, 4.34 (4.31); N, 10.05(9.99); O, 5.70 (5.71); S, 11.42(11.44).

Table-3: Physical Properties Of Synthesized biphenyl-2-aminothaizoles& These Chemical Structures Represented In Table-1 (Sa-Sj)

S. No.	Product Code	Reaction time in Hr's	Reaction Temp. In °C	Physical Appearance	Melting Point in°C
1	Sa	8	75-78	Light Yellow Solid	201-204

2	Sb	8	75-78	Light Yellow Solid	255
3	Sc	8	75-78	Yellow Solid	132.2-133.4
4	Sd	6	75-78	Light Yellow Solid	204-206
5	Se	6	75-78	Yellow Solid	89-91.2
6	Sf	6	75-78	Light Yellow Solid	285
7	Sg	6	75-78	Light Yellow Solid	178-181
8	Sh	6	75-78	Light Yellow Solid	139-141.2
9	Si	8	75-78	Light Yellow Solid	119.6-120.9
10	Sj	6	75-78	Yellow Solid	285

The Antifungal activity of these new molecular entities of **Sa, Sb, Sc, Sd, Se, Sf, Sg,** and **Sh** were studied against **Candida *Albicam, Aspergillus Niger*** well known cell cultures by reading their inhibition zone diameter with respect to the standard antifungal drug substance of Fluconazole. The in-vitro studies of these molecules and its inhibition zone diameter results are as given below table.

Table-4: In-vitro Biological Activity Test Results Of Synthesized New Chemical Entities Against Selected Antifungal Cultures

S. No	Compound Code	Candida Albicam					Aspergillus Niger				
		Zone Inhibition diameter in µ g /mm					Zone Inhibition diameter in µ g/mm				
		10	25	50	100	150	10	25	50	100	150
1	Sa	-	5	10*	12*		-	-	-	-	-
2	Sb	-		2	2		-	-	-	-	1
3	Sc	-	-	-	-		-	-	-	-	-
4	Sd	-	5	8*	12*		-	-	2	3	6
5	Se	-1	2	3	6		2	4	8*	12*	8*
6	Sf	-	-	-	-		-	-	-	-	-
7	Sg	12	3	3	8*		-	-	-	-	-
8	Sh	-	-	-	-		-	-	-	-	-
9	Fluconzole (STD)*	-	-	12	18	18	-	-	-	6	10

CONCLUSION

The synthetic methodology which is described in this research and biology (in-vitro) of derived substituted biphenyl aminothaizoles analogues such as **Sa, Sb, Sc, Sd, Se, Sf, Sg,** and **Sh** were successful. The Anti-fungal activity of these compounds has been studied against cell cultures like **Candida *Albicam, Aspergillus Niger.*** Among all synthesized new molecular entities **Sa, Sd, and Se** are said to be promising molecules which were exhibits more potentiality towards anti-fungal activity and equivalent to the standard drug substance Fluconazole. Hence, it is believed that these molecules having more scope to study further stage of biology studies to understand the routing to a new drug moiety for future medical applications.

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