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Heterogeneous Acid Catalyzed Synthesis and Spectroscopic Characterization of Schiff Bases Derived from Chalcone Derivatives

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Abstract

Schiff bases have continued to gain attention as essential building blocks and versatile pharmacophores in drug development and drug-like molecular entities. Thus, the synthesis of Schiff bases was achieved herein via facile acetic acid catalyzed synthetic transformation of chalcones. The targeted Schiff bases and related compounds 2a-m were accessed by the treatment of amines with chalcone 1 which was previously derived through Claisen-Schmidt reaction between benzaldehyde and acetone, at ambient temperature. Structural characterization was achieved via physicochemical properties and the use of IR, UV, ^{1}H and ^{13}C NMR which were spectroscopic techniques. The compounds have essential candidature for further study, in biological activity so as to unleash their medicinal potential.

Keywords: chalcone; azomethine; substituted benzaldehyde; heterogeneous catalysis

1. Introduction

Over the years, Schiff base has been identified as essential core structure in drug design. Schiff base, which was named after Hugo Schiff [1], was prepared via condensation reaction between amino functionality and an aldehydic/ketonic carbonyl [2]. The medicinal potential of Schiff bases in drug designed is quite evident in their reported diverse pharmacological properties which include antimicrobial [3], anticancer [4], antitumor [5], anti-convulsant [6], antimalarial [7], antitubercular [8], anti-HIV, anti-inflammatory [9], antidepressant activities among others [10]. Their enhanced reported bioactivity might be as a result of their improved lipophilic character thereby improving their bioavailability in the lipid membranes; therefore, resulting in growth redundancy in the organism [11]. Other essential areas of utilization of this framework are naturally- and non-naturally occurring biomolecules which situate conducive environment for harnessing Schiff bases with antimicrobial potential; they are amino acids [12], 1,2,4-triazole [13], sulfonamides [14], coumarins [15] or resacetophenones, aminothiazolylbromo coumarins, crown ethers [16] and o-phthaldehyde [17].

Insatiable quest for Schiff base-bearing motifs possessing high selectivity and lower side effects has continued to gathered undeniable attention and wholesome desire in therapeutic medicine [18]. Owing to wide utilization of Schiff bases in almost all areas of human endeavor and their essential diversity in synthetic chemistry as intermediates require to access other biomolecules of important, we have herein embarked upon the synthesis of Schiff bases derived from chalcone via acetic acid mediated catalytic procedure.

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2. Materials and Method

General Condition. Chemicals as well as solvents utilized herein were bought at Sigma-Aldrich Chemicals, apart from hydrazine hydrate which was bought from Surechem Product Limited. They were provided for research purpose courtesy Chemistry Department, Covenant University. They were utilized as provided due to high purity level of the chemicals. The products were loaded in capillary tube and determined for their melting point with the aid of Stuart equipment (uncorrected). Fourier-Transform absorption frequencies were recorded for susceptible finctional groups via Bruker FT-IR Spectrophotometer with wave number measured from 4000 to 400 cm-1. Synthesized products were solubilized in dichloromethane (DCM) and ran in UV Genesys was achieved using. The ^{1}H- and ^{13}C-NMR data were generated at 400 and 100 MHz respectively with the aid of NMR Bruker DPX 400 Spectrometer using DMSO-d6. The internal standard was TMS which was set at chemical shift value of 0 ppm. The reaction progress was monitored with thin layer chromatography (TLC) using eluent with combination ratios at shown in Table 2. The evaporation of solvents after reaction completion was achieved using IKA® RV 10 Rotary evaporator. Products were purified using recrystallization method; however, column chromatography was utilized as the separation technique for mixtures.

Synthesis of 1,5-Diphenylpenta-1,4-dien-3-one (Chalcone), 1. Alkaline mixture containing of NaOH (62.5 mmol, 2.50 g) and 20 ml of C_2H_5OH and 25 ml of H_2O was prepared in a conical flask and cooled to room temperature. A mixture of benzaldehyde (62.5 mmol, 2.9 ml) and acetone (62.5 mmol, 1.03 ml) was made by mixing them thoroughly and alkaline mixture was gently introduced drop-wisely and further stirred at ambient condition for about 30 min. Completion of reaction as well as formation of products were monitored by TLC (Hexane/DCM → 4:6). The crude product obtained was recrystallized with the aid of ethanol as suitable solvent to access 1,5-diphenylpenta-1,4-dien-3-one, 1 in 80.13% yield; Lit. m.pt value = 110-111^{o}C [19]. ^{1}H NMR (400 MHz, DMSO-d6) δ_H: 7.62-7.59 (d, *J* = 10.08 Hz, 4H, 2 × Ar-H), 7.15-7.09 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 174.1, 139.4 (2 × C), 131.2 (2 × CH), 128.9 (4 × CH), 128.5 (4 × CH), 127.9 (2 × CH), 123.8 (2 × CH) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M-1 cm-1): 206 (4.83), 236 (4.22), 257 (4.12). IR (KBr, cm-1) ῡ: 3030 (CH aromatic), 2928 (CH aliphatic), 1690 (C=O), 1615 (C=C), 1190 (CH aromatic), 925 (=C-H).

General procedure for synthesis of Schiff bases 2a-j. Chalcone, 1 (1.00 g, 42.70 mmol) was solubilized in dichloromethane (DCM, 10 ml) in ambient condition. Appropriate amino-based substrate (4.27 mmol) was dissolved in dichloromethane (DCM) / ethyl alcohol (10 ml → 5:5) mixture in a beaker and was subsequently tipped into solubilized chalcone drop-by-drop under magnetic stirring and catalyzed via the use of two drops of CH3COOH. The reaction flask was finally refluxed at a carefully controlled temperature of 60-70 ^{o}C for 4 h. After the reaction was completed (TLC confirmed with eluents ratio shown in Table 2), the crude product formed on cooling was recrystallized with ethanol to afford the corresponding Schiff bases **2a-j** in varying yields.

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-yliden e)aniline, 2a. Treatment of chalcone 1 (4.27 mmol, 1.00 g) with aniline (4.27 mmol, 0.40 ml) afforded **2a** in 67.17 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.62-7.59 (d, *J* = 10.08 Hz, 4H, 2 × Ar-H), 7.29-7.23 (m, 5H, Ar-H), 7.12-7.09 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, J = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, J = 9.12 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 141.2, 139.3 (2 × C), 133.4, 131.1 (2 × CH), 130.1, 128.9 (4 × CH), 128.5 (4 × CH), 127.8 (2 × CH), 125.9, 123.8 (2 × CH), 122.4, 118.4, 113.0 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M-1 cm^{-1}): 206 (4.74), 236 (4.30), 257 (4.32), 332 (5.44). IR (KBr, cm-1) ῡ: 3167 (C=C aromatic), 1626 (C=C aromatic), 1595 (C=N), 980 (=C-H bending), 747 (Ar-H).

4-Chloro-N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene)aniline, 2b. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with 4-chloroaniline (4.27 mmol, 0.55 g) afforded **2b** in 42.23 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.86-7.84 (d, *J* = 7.24 Hz, 2H, Ar-H), 7.62-7.59 (d, *J* = 10.08 Hz, 4H, 2 × Ar-H), 7.26-7.24 (d, *J* = 7.24 Hz, 2H, Ar-H), 7.13-7.10 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz,

DMSO-d_6) δ_C: 141.3, 139.4 (2 × C), 136.1, 131.2 (2 × CH), 130.1, 128.9 (4 × CH), 128.6 (4 × CH), 127.8 (2 × CH), 125.4 (2 × CH), 123.8 (2 × CH), 121.0, 118.5, 115.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 209 (4.80), 233 (4.35), 260 (4.33), 332 (5.46). IR (KBr, cm^{-1})$\bar{\upsilon}$:3150 (C=C aromatic), 1622 (C=C aromatic), 1580 (C=N), 727 (Ar-H), 685 (C-Cl).

N^1-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) benzene-1,2-diamine, 2c. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with *o*-phenylenediamine (4.27 mmol, 0.46 g) afforded **2c** in 89.83 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.61-7.59 (d, *J* = 6.24 Hz, 4H, 2 × Ar-H), 7.33-7.24 (m, 4H, Ar-H), 7.12-7.09 (m, 6H, 2 × Ar-H), 6.51-6.48 (d, *J* = 12.52 Hz, 2H, Alken-H), 6.39-6.35 (d, *J* = 12.52 Hz, 2H, Alken-H), 6.21 (s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 141.1, 139.7 (2 × C), 136.1, 134.5, 134.1, 131.0 (2 × CH), 130.1, 128.6 (4 × CH), 128.0 (4 × CH), 127.7 (2 × CH), 123.7 (2 × CH), 118.7, 115.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (4.77), 248 (4.24), 329 (4.87), 422 (4.21). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3429, 3426 (NH of amine, 2 bands), 3060 (C=C aromatic), 1615 (C=C aromatic), 1575 (C=N), 977 (=C-H bending), 727 (Ar-H).

N^1-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) benzene-1,3-diamine, 2d. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with *m*-phenylenediamine (4.27 mmol, 0.46 g) afforded **2d** in 94.20 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.91 (s, 1H, Ar-H), 7.61-7.59 (d, *J* = 6.24 Hz, 4H, 2 × Ar-H), 7.33-7.24 (m, 3H, Ar-H), 7.12-7.09 (m, 6H, 2 × Ar-H), 6.51-6.48 (d, *J* = 12.52 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 12.52 Hz, 2H, Alken-H), 6.18 (s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 141.1, 139.7 (2 × C), 136.0, 131.1 (2 × CH), 130.1, 128.9 (4 × CH), 128.5 (4 × CH), 127.8 (2 × CH), 125.9, 125.0, 123.8 (2 × CH), 118.5, 115.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (4.71), 260 (4.30), 293 (4.29), 332 (5.16). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3430, 3427 (NH of amine, 2bands), 3060 (C=C aromatic), 1650, 1615 (C=C aromatic), 1569 (C=N), 981 (=C-H bending), 760 (Ar-H).

N^1-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) benzene-1,4-diamine, 2e. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with *p*-phenylenediamine (4.27 mmol, 0.46 g) afforded **2e** in 90.21 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.87-7.85 (d, *J* = 8.64 Hz, 2H, Ar-H), 7.63-7.60 (d, *J* = 12.04 Hz, 4H, 2 × Ar-H), 7.26-7.24 (d, *J* = 8.64 Hz, 2H, Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.51-6.48 (d, *J* = 9.04 Hz, 2H, Alken-H), 6.39-6.36 (d, *J* = 9.04 Hz, 2H, Alken-H), 6.03 (s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 141.3, 139.7 (2 × C), 136.0, 131.3 (2 × CH), 130.1, 128.5 (4 × CH), 128.0 (4 × CH), 127.3 (2 × CH), 125.4 (2 × CH), 123.8 (2 × CH), 118.7, 115.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (4.82), 257 (4.35), 281 (4.37), 335 (5.43). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3429, 3424 (NH of amine, 2 bands), 3065 (C=C aromatic), 1620 (C=C aromatic), 1575 (C=N), 980 (=C-H bending), 755 (Ar-H).

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) naphthalen-1-amine, 2f. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with α-naphthylamine (4.27 mmol, 0.61 g) afforded **2f** in 90.21 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.81-7.80 (d, *J* = 4.22 Hz, 1H, Ar-H), 7.63-7.59 (d, *J* = 10.28 Hz, 4H, 2 × Ar-H), 7.47-4.46 (d, *J* = 4.56 Hz, 1H, Ar-H), 7.42-7.40 (dd, J_1 = 4.22 Hz, J_1 = 4.56 Hz, 1H, Ar-H), 7.38-7.37 (d, *J* = 4.68 Hz, 1H, Ar-H), 7.29-7.23 (m, 3H, Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 141.2, 139.4 (2 × C), 133.4, 131.0 (2 × CH), 130.1, 129.1, 128.8 (4 × CH), 128.5 (4 × CH), 127.7 (2 × CH), 126.8, 126.2, 125.9, 124.7, 123.8 (2 × CH), 122.5, 118.5, 115.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (5.33), 248 (4.75), 275 (4.80), 335 (4.27), 350 (4.02). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3021 (C=C aromatic), 1615 (C=C aromatic), 1575 (C=N), 1456, 1376, 1069 (C-N), 962 (=C-H bending), 749 (Ar-H).

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) cyclohexanamine, 2g. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with cyclohexylamine (4.27 mmol, 0.49 ml) afforded **2g** in 73.94 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.62-7.58 (d, *J* = 10.28 Hz, 4H, 2 × Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H). 3.21-3.20 (quintet, *J* = 4.84 Hz, 1H, **CH**-$(CH_2)_2$), 2.55-2.53 (t, *J* = 4.84 Hz, 4H, 2 × CH_2), 1.98-1.36 (m, 6H, 3 × CH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 139.5 (2 × C), 131.1 (2 × CH), 128.9 (4 × CH), 128.4 (4 × CH), 127.7 (2 × CH), 123.8 (2 × CH), 115.2, 51.2 (CH-N), 24.1 (2 × CH_2), 22.8, 22.5, 22.1 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 209 (4.70), 248 (4.08), 275 (4.20), 335 (5.47). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3051 (C=C aromatic), 1620 (C=C aromatic), 1575 (C=N), 982 (=C-H bending), 761 (Ar-H).

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) pentan-1-amine, 2h. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with *n*-pentylamine (4.27 mmol, 0.49 ml) afforded **2h** in 66.31 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.62-7.59 (d, *J* = 10.26 Hz, 4H, 2 × Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H). 2.54-2.53 (t, *J* = 4.80 Hz, 2H, **CH_2**-CH_2),

1.86-1.42 (m, 6H, 3 × CH_2), 0.91-0.89 (t, *J* = 5.22 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 139.6 (2 × C), 131.2 (2 × CH), 128.9 (4 × CH), 128.5 (4 × CH), 127.7 (2 × CH), 123.8 (2 × CH), 115.2, 44.5 (CH_2-N), 23.5, 22.8, 22.5, 14.3 (CH_3) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 209 (4.75), 238 (4.01), 275 (4.20), 330 (4.00). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3050 (C=C aromatic), 2950 (CH aliphatic), 2878 (CH aliphatic), 1620 (C=C aromatic), 1575 (C=N), 1454 (CH_2 deformation), 982 (=C-H bending), 745 (Ar-H).

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) hexadecan-1-amine, 2i. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with hexadecylamine (4.27 mmol, 1.03 g) afforded **2i** in 57.70 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.61-7.59 (d, *J* = 10.18 Hz, 4H, 2 × Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.51-6.49 (d, *J* = 9.08 Hz, 2H, Alken-H), 6.38-6.36 (d, *J* = 9.08 Hz, 2H, Alken-H), 1.99-1.97 (t, *J* = 5.98 Hz, 2H, N-**CH_2**CH_2), 1.43-1.41 (m, 2H, CH_2), 1.36-1.34 (m, 2H, CH_2), 1.30-1.28 (m, 4H, CH_2), 1.24-1.24 (t, *J* = 5.98 Hz, 16H, 8 × **CH_2**CH_2), 0.91-0.89 (t, *J* = 5.22 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 143.7, 139.6 (2 × C), 131.2, 128.9 (4 × CH), 128.5 (4 × CH), 127.7 (2 × CH), 123.8 (2 × CH), 115.2, 43.2 (CH_2-N), 32.1, 31.9, 29.7 (8 × CH_2), 29.2 (2 × CH_2), 23.5, 22.8, 14.2 (CH_3) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 209 (4.71), 238 (4.01), 275 (4.20), 335 (4.01). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3050 (C=C aromatic), 2925 (CH aliphatic), 2875 (CH aliphatic), 1620 (C=C aromatic), 1575 (C=N), 1456 (CH_2 deformation), 982 (=C-H bending), 745 (Ar-H).

N-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) octadec-9-en-1-amine, 2j. Treatment of chalcone **1** (4.27 mmol, 1.00 g) with oleylamine (4.27 mmol, 1.41 g) afforded **2j** in 72.00 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.63-7.60 (d, *J* = 10.26 Hz, 4H, 2 × Ar-H), 7.14-7.10 (m, 6H, 2 × Ar-H), 6.50-6.48 (d, *J* = 9.12 Hz, 2H, Alken-H), 6.38-6.35 (d, *J* = 9.12 Hz, 2H, Alken-H), 3.46-3.44 (t, *J* = 5.02 Hz, 2H, 2 × **CH**CH_2), 2.20-2.24 (m, 4H, 2 × CH_2), 1.98-1.96 (t, *J* = 5.88 Hz, 2H, N-**CH_2**CH_2), 1.44-1.41 (m, 2H, CH_2), 1.35-1.34 (m, 2H, CH_2), 1.29-1.31 (t, *J* = 6.94 Hz, 20H, 10 × **CH_2**CH_2), 0.91-0.89 (t, *J* = 5.22 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 143.9, 139.7 (2 × C), 131.4, 130.7 (2 × CH), 128.8 (4 × CH), 128.5 (4 × CH), 127.7 (2 × CH), 123.7 (2 × CH), 115.2, 44.5 (CH_2-N), 32.4, 31.9, 29.9 (2 × CH_2), 29.5 (4 × CH_2), 29.1 (2 × CH_2), 27.8 (2 × CH_2), 22.9 (2 × CH_2), 14.5 (CH_3) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 209 (4.71), 238 (4.01), 275 (4.20), 335 (4.01). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3035 (C=C aromatic), 2950 (CH aliphatic), 2878 (CH aliphatic), 1622 (C=C aromatic), 1575 (C=N), 1456 (CH_2 deformation), 980 (=C-H bending), 745 (Ar-H).

General procedure for synthesis of chalcone hydrazones, 2k-m. Chalcone, **1** (4.27 mmol, 1.00 g) was solubilized in dichloromethane (DCM, 10 ml) in ambient condition in a quick-fit flask. Appropriate hydrazine derivative (4.27 mmol) was tipped drop-by-drop into the solubilized chalcone under magnetic stirring and then catalyzed with the aid of two drops of CH_3COOH. The reaction flask was finally refluxed at a carefully controlled temperature of 75-85 ^{o}C for 5 h. After the reaction was completed (TLC confirmed with eluents ratio shown in Table 2), the crude product formed on cooling was recrystallized ethyl alcohol to afford the corresponding hydrazone or hydrazine carboxamide derivatives **2k-m** in varying yields.

***((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) hydrazine, 2k*.** Treatment of chalcone **1** (4.27 mmol 1.00 g) with hydrazine hydrate (4.27 mmol, 0.21 ml) afforded **2k** in 92.31 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.62-7.59 (d, *J* = 10.18 Hz, 4H, 2 × Ar-H), 7.15-7.09 (m, 6H, 2 × Ar-H), 6.82 (s, 2H, NH_2), 6.50-6.48 (d, *J* = 9.10 Hz, 2H, Alken-H), 6.37-6.35 (d, *J* = 9.10 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 142.1, 139.5 (2 × C), 131.1 (2 × CH), 128.9 (4 × CH), 128.4 (4 × CH), 127.8 (2 × CH), 123.5 (2 × CH) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (5.17), 238 (4.83), 275 (3.79), 335 (4.47). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3465, 3428 (NH_2 of amide, 2 bands), 3030 (C=C aromatic), 1625 (C=C), 1609 (C=C aromatic), 1575 (C=N), 1461, 1260 (C=N bending), 1372, 1050 (C-N), 952 (=C-H bending), 741 (Ar-H).

2-((1E,4E)-1,5-diphenylpenta-1,4-dien-3-ylidene) hydrazinecarboxamide, 2l. Treatment of chalcone **1** (4.27 mmol 1.00 g) with semicarbazide hydrochloride (4.27 mmol, 0.65 g) afforded **2l** in 56.50 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.62-7.59 (d, *J* = 10.18 Hz, 4H, 2 × Ar-H), 7.15-7.09 (m, 6H, 2 × Ar-H), 6.82 (s, 2H, NH_2), 6.50-6.48 (d, *J* = 9.10 Hz, 2H, Alken-H), 6.37-6.35 (d, *J* = 9.10 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 142.1, 139.5 (2 × C), 131.1 (2 × CH), 128.9 (4 × CH), 128.4 (4 × CH), 127.8 (2 × CH), 123.5 (2 × CH) ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 206 (4.47), 242 (3.81), 275 (3.79), 329 (4.47). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3462, 3430 (NH_2 of amide, 2 bands), 3347 (NH), 3253, 3050 (C=C aromatic), 1685 (C=O), 1646 (C=C), 1609 (C=C aromatic), 1567 (C=N), 1461, 1261 (C=N bending), 1377, 1115 (C-N), 957 (=C-H bending), 745 (Ar-H).

1-(2,4-Dinitrophenyl)-2-((1E,4E)-1,5-diphenylpent a-1,4-dien-3-ylidene)hydrazine, 2m. Treatment of chalcone **1** (4.27 mmol 1.00 g) with 2,4-

dinitrophenylhydrazine (4.27 mmol, 1.77 g) afforded **2m** in 74.37 % yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.35 (s, 1H, Ar-H), 7.98-7.96 (d, *J* = 8.00 Hz, 1H, Ar-H), 7.62-7.59 (d, *J* = 10.18 Hz, 4H, 2 × Ar-H), 7.34-7.32 (d, *J* = 8.00 Hz, 1H, Ar-H), 7.15-7.09 (m, 6H, 2 × Ar-H), 6.82 (s, 2H, NH_2), 6.81 (s, 1H, NH), 6.50-6.48 (d, *J* = 9.10 Hz, 2H, Alken-H), 6.37-6.35 (d, *J* = 9.10 Hz, 2H, Alken-H). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 145.2, 143.4, 143.2, 142.1, 139.5 (2 × C), 137.7, 131.1 (2 × CH), 128.9 (4 × CH), 128.4 (4 × CH), 127.8 (2 × CH), 125.6, 123.5 (2 × CH), 118.2 ppm. UV-Vis.: λ_{max}(nm)/ log ε_{max} (M^{-1} cm^{-1}): 212 (4.95), 263 (4.82), 335 (5.36), 380 (5.30). IR (KBr, cm^{-1}) $\bar{\upsilon}$: 3255 (NH), 3050 (C=C aromatic), 1627 (C=C), 1615 (C=C aromatic), 1574 (C=N), 1461, 1261 (C=N bending), 1377, 1080 (C-N), 957 (=C-H bending), 740 (Ar-H).

3. Results and Discussion

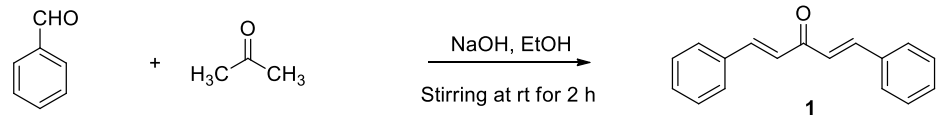
Since Schiff bases have been widely reported as highly important motifs in therapeutic medicine, we have herein embarked upon the designed Schiff bases from the biologically active chalcone with the aim of producing new therapeutic candidates via heterogeneous catalytic approach. In furtherance of our research enthusiasm and endeavour in the synthetic modification of bioactive α,β-unsaturated carbonyl entities [20], we have herein reported the synthesis of Schiff base bearing in mind the synthetic modification using four different heterogeneous catalysts. First and foremost, ambient temperature reaction of acetone with two molar equivalents of benzaldehyde according to an earlier reported procedure [19], afforded the chalcone, 1,5-diphenylpenta-1,4-dien-3-one, **1** (Scheme 1). Before this precursor was taken further for next stage, reaction optimization study was carried out using four different heterogeneous catalysts namely: concentrated HCl, acetic acid, $FeCl_3.6H_2O$ and $Bi(NO_3)_3.5H_2O$.

This is done in order to ascertain the most efficient and cost-effective catalytic technique require to access the targeted and titled Schiff bases via excellent pathway. In order to do this, reaction of chalcone precursor with aniline under refluxing condition was utilized in equi-volume combination of ethanol and dichloromethane (DCM) to afford *N*-(1,5-diphenylpenta-1,4-dien-3-ylidene)aniline, **2a**. This optimization investigation was utilized as the comparative study for the efficiency of the four different catalysts as seen in entries 1 – 4 of Table 1. It implied that the highest yield (82.17%) of **2a** occurred when acetic acid was used, followed by conc. HCl (60.12%) while the lowest yield was found when $Bi(NO_3)_3.5H_2O$ (58.22%) was used which was also almost similar to that of $FeCl_3.6H_2O$ (58.94%).

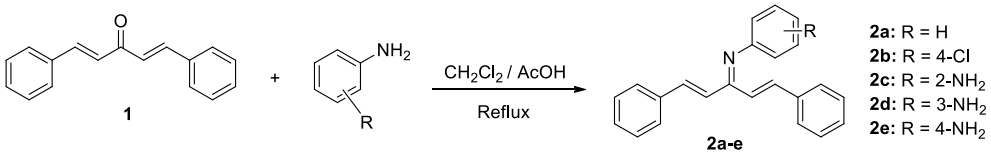
Table 1. Comparative study of catalysts efficiency in the synthesis of Schiff base, **2a**

Entry	Catalyst	Time	Yield (%)
1	Conc. HCl	4 h	60.12
2	Acetic acid	4 h	82.17
3	$FeCl_3.6H_2O$	4 h	58.94
4	$Bi(NO_3)_3.5H_2O$	4 h	58.22

It was obvious that the formation of Schiff base **2a** was more favoured using acid catalysts than when using hydrated salt of transition metal. Also, comparative study of the two acids used, unveiled acetic acid catalyzed procedure to be more efficient than the conc. HCl utilized type. Thus, it was more acceptable to synthesize all the Schiff base series herein using acetic acid as the chosen catalyst. The first series of Schiff bases **2a-e** were therefore, synthesized using condensation reaction of chalcone **1** with aniline derivative **a-b** and phenylenediamine **c-e** as shown in Scheme 2. When the bicyclic aromatic amine (α-naphthylamine) was used as the nucleophile which condensed with chalcone, it furnished **2f** as the Schiff base product (Scheme 3). The use of cyclohexylamine and three long chain aliphatic amines furnished the Schiff bases **2g-j** (Scheme 4). The aim of the synthesis of the Schiff bases with long side chain alkyl groups as seen in **2h-j** was to increase the lipophilicity of the Schiff bases since this is a prominent and valuable factor in the enhancement of lipophilic absorption of molecular moieties for better drug efficient as recently reported by N'Da, who worked on strategies for enhancement of transdermal drug delivery [21]. In addition, it was also reported that lipophilic increment enhanced Schiff base and its metal complexes' permeability into the lipid membranes; hence, leading to restriction of pathogenic organisms' growth [11,22]. The last series of products **2k-m** were hydrazone and hydrazone-related products which were obtained from the reaction of precursor 1 with hydrazine hydrate **(k)**, semicarbazide **(l)** and 2,4-dinitrophenyl hydrazine **(m)** (Scheme 5).

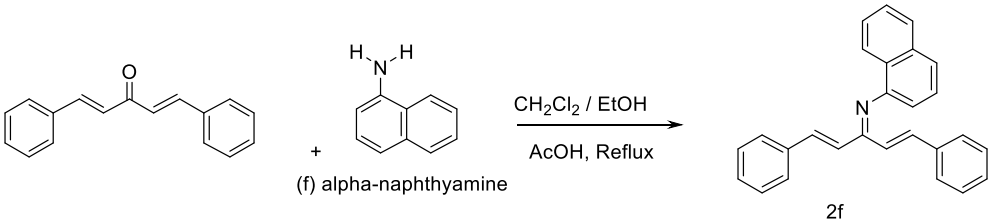


Scheme 1: Synthetic route to accessing 1,5-diphenylpenta-1,4-dien-3-one, **1**

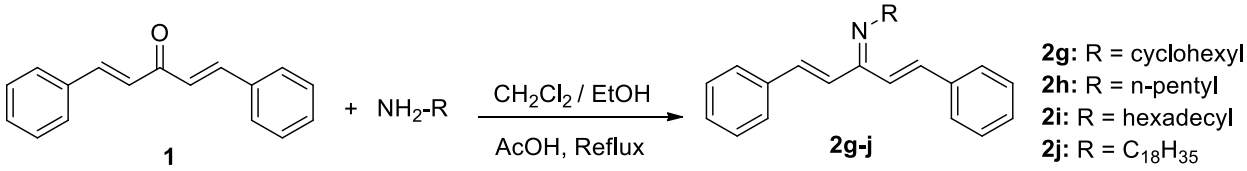


Reagents used: (a) aniline (b) 4-chloroaniline (c) *o*-phenylenediamine (d) *m*-phenylenediamine (e) *p*-phenylenediamine

Scheme 2: Synthesis of Schiff bases **2a-e** of aniline and phenylenediamine derivatives.

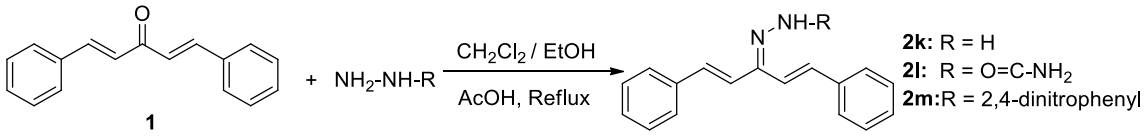


Scheme 3: Synthesis of *N*-(1,5-diphenylpenta-1,4-dien-3-ylidene)naphthalen-1-amine, **2f**



Reagent used **(g)** cyclohexylamine **(h)** n-pentylamine **(i)** hexadecylamine **(j)** oleylamine

Scheme 4: Synthesis of Schiff bases **2g-j** of cyclohexyl- and aliphatic amine derivatives



Reagents used **(k)** hydrazine hydrate **(l)** semicarbazide **(m)** 2,4-dinitrophenylhydrazine

Scheme 5: Synthesis of hydrazone and hydrazone-related motifs

Furthermore, physicochemical characterization was carried out using investigation of parameters such as molecular formula/weight, melting point, % yield, R_f values from TLC, colour and C, H, N elemental analytical data (Table 2). Molecular mass of the targeted products varied from 234.29 (precursor **1**) to 483.77 (product **2j**). None of the molecular weights was up to 500 g/mol. This was a clear indication that none of the synthetic adventure resulted into a polymer and could be said that the envisaged small biomolecules were obtained. Considering melting points determination, it was noticed that compound **2b** had the lowest melting point (62-63 ^oC) while the highest melting point was observed for compound **2a** (130-132 ^oC). The melting points of compounds **2e, 2f, 2h**, **2j** and **2k** were not determined (N.D.) because their state of matters was liquid at ambient condition. The percentage yields of the compounds varied from 42.23% for **2b** to 94.20% for **2d**. Targeted products were successfully achieved in good to excellent yields except for compounds **2b** which had low yield. Reaction completion was confirmed via TLC screening with the aid of three kind of eluents x, y and z depending on the polarity of the compounds. The R_f values was observed to be from 0.40 for compound **1**

and **2m,** to 0.96 for compound **2c**. The low R_f in **1** and **2m** was a true reflection of their high polarity.

Table 2. Physicochemical parameter for the synthesized precursor **1** and titled products **2a-m**

Code No	Mol. Form. (Mol.Wt.)	M. Pt (°C)	Yield (%)	$R_f^{w,x,y,z}$	Colour	Elem. Anal.: Calcd. (Found) C	H	N
1	$C_{17}H_{14}O$ (234.29)	109–111*	80.13	0.40^{y}	Yellow	87.15 (87.06)	6. 02 (5.98)	-
2a	$C_{23}H_{19}N$ (309.40)	130–132	62.17	0.50^{w}	Yellow	89.28 (89.15)	6.19 (6.25)	4. 53 (4.49)
2b	$C_{23}H_{18}NCl$ (343.85)	62–63	42.23	0.72^{x}	Brown	80.34 (80.17)	5.28 (5.12)	4.07 (3.97)
2c	$C_{23}H_{20}N_2$ (324.42)	117–119	89.83	0.96^{y}	Dark Brown	85.15 (85.02)	6.21 (6.35)	8.63 (8.77)
2d	$C_{23}H_{20}N_2$ (324.42)	113–115	94.20	0.90^{y}	Black	85.15 (85.23)	6.21 (6.15)	8.63 (8.52)
2e	$C_{23}H_{20}N_2$ (324.42)	N.D.	90.21	0.68^{y}	Black	85.15 (85.05)	6.21 (6.11)	8.63 (8.81)
2f	$C_{27}H_{21}N$ (359.46)	N.D.	86.30	0.90^{y}	Dark Brown	90.21 (90.38)	5.89 (6.01)	3.90 (4.06)
2g	$C_{23}H_{25}N$ (315.45)	98–99	73.94	0.60^{x}	Yellow	87.57 (87.74)	7.99 (8.12)	4.44 (4.52)
2h	$C_{22}H_{25}N$ (303.44)	N.D.	66.31	0.56^{z}	Deep Brown	87.08 (86.97)	8.30 (8.17)	4.62 (4.81)
2i	$C_{33}H_{47}N$ (457.73)	65–67	66.31	0.58^{z}	Brown	86.59 (86.39)	10.35 (10.22)	3.06 (2.98)
2j	$C_{35}H_{49}N$ (483.77)	N.D.	72.00	0.70^{x}	Brown	86.90 (87.04)	10.21 (10.41)	2.90 (2.75)
2k	$C_{17}H_{16}N_2$ (248.32)	N.D.	92.31	0.54^{w}	Reddish Brown	82.22 (82.42)	6.49 (6.68)	11.28 (11.37)
2l	$C_{18}H_{17}N_3O$ (291.35)	109–110	56.50	0.92^{x}	Brown	74.20 (74.01)	5.88 (6.02)	14.42 (14.61)
2m	$C_{23}H_{18}N_4O_4$ (414.41)	86–88	74.37	0.40^{x}	Red	66.66 (66.83)	4.38 (4.55)	13.52 (13.70)

*Lit. M.pt 110-111 °C [11]. w = DCM/Hexane → 3:7; x = DCM/Hexane → 4:6; y = Hexane /DCM → 4:6; z = DCM/Hexane → 4:6. N.D. = Not Determined because of oily or semi-solid nature.

This implied that the two compounds **1** and **2m** might have higher of interact-ability within the neighboring environment as well as more binding ability leading to in enhancement of the pharmacological potentials as earlier established [23]. The virtual screening showed the colour of compounds to be yellow for **1, 2a, 2g**; black for **2d** and **2e**; red for **2m** and the rest of the compounds had varying degree of brown colouration. The C, H, N elemental analysis was carried out for all the products except the precursor **1** wherein only C and H analysis was done because of the absence of Nitrogen in the precursor **1**. The result of elemental analysis showed a reasonable similarity between the %calculated and %found for all the synthesized compounds. Thus, the result correlated well and was in agreement with the theoretical values as expected (Table 2). Elemental analytical data showed high precision as the difference between calculated and found values were not more than ±0.20 for all the three elements [24].

Moreover, characterization of targeted products was done for structural elucidation using FT-IR, UV, ^{1}H- and ^{13}C-NMR. The UV spectral data of the synthesized compounds showed the presence of various peaks at specific wavelengths due to various expected transition phenomenon. The electronic transition of the uv spectra were run in dichloromethane (DCM) between wavelengths of 200-500 nm. The first set of wavelengths for the compounds were noticed at λ_{max} 206-212 nm which depicted the presence of benzene ring because it was due to $\pi \rightarrow \pi^*$ transition unique to C=C bond. Other values were due to bathochromic shift effects and hence, appeared at longer wavelengths between 236-422 nm. This is due to presence of additional conjugation and availability of other auxochromes in the molecular templates herein. As the representative of the targeted Schiff bases, compound **2a** had transition effects which resulted into four peaks at λ_{max} 206, 236, 257 and 332 nm with log ε_{max} values of 4.74, 4.30, 4.32 and 5.44 respectively. Generally speaking, CH aromatic, C=C and C=N functionalities appeared

at stretching absorption frequencies of 3167-3030 cm^{-1}, 1626-1615 cm^{-1} and 1595-1569 cm^{-1} respectively. Specifically speaking, the free NH_2 of **2c-e** and **2k-m** appeared at 3429-3424 cm^{-1}, while the conjugated C=O of **1** was found at 1690 cm^{-1} and C=O of amide **2l** absorbed at 1685 cm^{-1} in addition to C-Cl functional entity in **2b** appeared at 685 cm^{-1}. In addition, the NH_2 bands of compounds **2c-d** appeared at 3430-3426cm^{-1} but amido NH_2 of **2l** was observed at 3347-3253cm^{-1}. Diagnosing the infrared spectrum of **2a** as representative of targeted products, ν value at 3167 cm^{-1} and 1626 cm^{-1} confirmed the availability of C=C of aryl and alkene while the evidence for the formation of imine bond in **2a** was confirmed by the presence of a new band at 1595 cm^{-1} for C=N availability in **2a** which was absent in the precursor **1**. In addition, there is a disappearance in **2a**, of C=O found at 1690 cm^{-1} in compound **1**. ^1H NMR spectral analysis was carried out at 400 MHz with the use of deuterated dimethyl sulfoxide. All aromatic protons resonated down-field at δ 8.35-7.09 ppm [25] while the alkene protons were observed at δ 6.51-6.48 ppm and δ 6.39-6.35 ppm. All the aliphatic protons of compounds **2g-j** resonated up-field with respect to TMS at chemical shift values of δ 3.46-3.44 ppm to 0.91-0.89 ppm.

4. Conclusions

Schiff bases are structural moieties of high pharmacological importance in drug design. The Schiff bases were successfully achieved with the use to catalysts while the enhanced yield of such targeted compounds was obtained via acetic acid mediated synthetic approach. The structures of targeted products were characterized and authenticated with physico-chemical parameter analysis and spectral analytical means. Proposed structures were further validated by consistence of the elemental analytical result which was within ± 0.20 degree of disparity when compared calculated and found values for C, H and N elements. The synthetic compounds **2a-m** are candidates for further study in terms of evaluation of their biological and medicinal properties for possible drug design.

5. Conflicts of interest

There are no conflicts to declare in this present paper.

6. Acknowledgments

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7. References

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