

# A Feasible Synthesis and Spectral Characterization of 1, 2, 4-Triazole Fused Schiff Bases

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**Abstract:** A series of 1,2,4-Triazole fused Schiff bases (5a-5h) were synthesized by condensation of 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl) benzohydrazide (4) with substituted aromatic aldehyde and 1,2,4-triazole moiety synthesized by condensation and further cyclization of N-benzoylbenzamide with p-hydrazinobenzoic acid. All these Schiff bases were characterized on the basis of spectral interpretation (IR, NMR & MASS).

Keywords : <sup>1</sup>H-NMR, Benzoylbenzamide, Hydrazinobenzoic

## Introduction

Triazoles derivatives are significant class of heterocyclic compound owing to their versatile application in medicine, agriculture and industrial chemistry. Triazoles were first introduced by Bladin in 1885 and another name pyrrodiazole was suggested by Andreocci in 1889 regarding it as a member of a class of compounds analogous to pyrrole. Triazole is a five membered ring system containing with the three nitrogen and two carbon atoms. 1,2,4-triazole analogues possess wide range of various biological and pharmaceutical properties as antifungal<sup>1</sup>, antitubercular<sup>2</sup>, antimicrobial<sup>3</sup>, antitumor<sup>4</sup>, antimalarial<sup>5</sup>, anticancer<sup>6</sup>, antibacterial<sup>7</sup>, anti-inflammatory<sup>8</sup>, anticonvulsant<sup>9</sup>, anti-HIV<sup>10</sup>. More over 1,2,4-triazole containing drugs such as Fluconazole, Itraconazole, Voriconazole, Ravuconazole are globally used for the treatment of fungal diseases<sup>11</sup> and some other drugs having these moiety, as Alprazolam and Estazolam (anxiolytic), Benatradin (diuretic), Ribavirin (antiviral), Rilmazafon (hypnotic), Trazodon (antidepressant), Letrozole and Anastrozole (breast cancer), Rizatriptan (antimigraine)<sup>12,13</sup> are presently used in medication. On the same way, Schiff base derivatives also displayed various therapeutic properties<sup>14-20</sup>. Based on the multiple properties of Schiff bases and 1,2,4-Triazole derivatives we have designed and synthesized a series of N'-arylidene-4-(3,5-diphenyl -1H- 1, 2, 4 -triazole-1-yl)benzohydrazide derivatives.

## Results And Discussion

In the present work, N-benzoylbenzamide (1) was synthesized by condensation of benzoyl chloride with benzamide in presence of catalytic amount of pyridine in o-xylene and N-benzoylbenzamide (1) further reacted with p-hydrazinobenzoic acid in ethanol to produced 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoic acid (2). The compound (2) undergone esterification reaction with Thionyl chloride in methanol to produced methyl 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoate (3). This methyl ester compound was treated with hydrazine hydrate to formed 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzohydrazide (4) and hydrazide compound (4) was further reacted with substituted aromatic aldehyde to yield Schiff bases (5a-5h). The synthesis route is drawn in scheme 1. The chemical structures of the synthesized

Schiff bases (5a-5h) were characterized by FT-IR, <sup>1</sup>H-NMR and MS. The FT-IR spectra of the Schiff bases (5a-5h) showed absorption band at 3200-3450 cm<sup>-1</sup> due to N-H stretching vibration, band at 1640-1655 cm<sup>-1</sup> due to C=O stretching vibration and band at 1560-1570 cm<sup>-1</sup> due to azomethine group C=N stretching vibration. The nuclear magnetic resonance (<sup>1</sup>H-NMR) of Schiff bases (5a-5h) showed singlet at  $\delta$  8.40-8.48 indicating presence of azomethine (-N=CH-) proton and a sharp singlet appear at  $\delta$  11.25-11.72 indicating presence of -CONH- proton. In the mass spectrum, Schiff bases (5a-5h) showed a peak at m/z, that resembles its molecular formula. The spectral data lend strong support to the proposed structures of all the synthesized compounds. The Physicochemical data, and elemental analysis results and spectral data of all the compounds are given in experiment Section.

## Experiment

All chemicals and solvents were used of AR-grade. The melting points of all the Novel compounds were determined in one end open capillary tubes. The IR spectra were recorded on Bruker FT-IR Spectrometer using KBr pellets in the range 4000-600 cm<sup>-1</sup>. <sup>1</sup>H-NMR spectra were recorded on Bruker 400 NMR spectrometer. Chemical shifts are reported in parts per million (ppm) using tetraethyl silane (TMS) as an internal standard. Mass spectra recorded a Waters mass spectrometer. IR, NMR and MS were consistent with assigned structure. Elemental analysis (CHN) was undertaken with Thermo Scientific analyzer. The completion of reaction and purity of compounds were checked on thin layer chromatography (TLC) on silica gel-G (Merck) coated aluminum plates, visualized by ultra violet light 254 nm and developing solvents were chloroform: methanol: liq. NH<sub>3</sub> (9:1:0.50).

Procedure for the preparation of N-benzoylbenzamide (1) and 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoic acid (2)

An equal mole solution of benzoyl chloride and benzamide in o-xylene in presence of catalytic amount of pyridine was refluxed for 8 hrs. After completion of reaction (TLC), solvent was completely distilled off under reduced pressure and obtained N-benzoylbenzamide (1) further refluxed with equal mole of p-hydrazinobenzoic acid in 2-propyl alcohol. After completion of reaction (TLC), the suspension cooled at room temperature, filtered and recrystallized in ethanol.

Yield- 65.54%, IR (cm<sup>-1</sup>, KBr): 3160 (O-H stretching), 3012 (Aromatic C-H stretching), 2818 (C-H stretching), 1720 (C=O stretching). NMR (400MHz, DMSO-d<sub>6</sub>):  $\delta$ = 7.29-8.31 (m, 14H, Ar), 12.69 (s, 1H, -COOH). MS: m/z- 340.19 (M-).

Procedure for the preparation of methyl 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoate (3)

An equal mole Thionyl chloride was added in to a solution of 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoic acid (2) and methanol at room temperature and further refluxed for 5 hrs. After completion of reaction (TLC), approximate 60-70% methanol was evaporated under reduced pressure and reaction mixture cool to room temperature and poured in to ice water, precipitate was filtered.

Yield 83.10%. IR (cm-1, KBr): 3044 (Aromatic C-H stretching), 2826 (C-H stretching), 1720 (C=O stretching), 1251 (C-O stretching). NMR (400MHz, DMSO-d6):  $\delta$  3.89 (s, 3H, -OCH<sub>3</sub>), 7.12-8.19 (m, 14H, Ar). MS: m/z- 354.18 (M-).

Procedure for the preparation of 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzohydrazide (4)

A mixture of equal mole of methyl-4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzoate (3) and hydrazine hydrate in isopropyl alcohol were refluxed for 4 hrs. After completion of reaction (TLC), the reaction mixture was cooled to ambient temperature and precipitate was filtered.

Yield 86.33%. IR (cm-1, KBr): 3173 (N-H stretching), 3058 (Aromatic C-H stretching), 2834, 2717 (C-H stretching), 1685 (C=O stretching), 1495 (N-H bending), 1398 (C-O stretching). NMR(400MHz, DMSO-d6):  $\delta$ = 4.59 (s, 2H, -NNH<sub>2</sub>), 7.12-8.16 (m, 14H, Ar), 12.79 (s, 1H, -NH). MS: m/z- 354.19 (M-).

General Procedure for the preparation of N'-arylidene- 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzohydrazide ( Schiff bases) 5a-5h

A suspension of 4-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)benzohydrazide (4) and equal mole of substituted aldehydes in absolute ethanol were refluxed for 6-8 hrs. After completion of reaction (TLC), the reaction mixture cooled to ambient temperature and the solid obtained was collected by filtration. This crude product was recrystallized in a mixture of DMF and ethanol (2:8).

N'-benzylidene-4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl) benzohydrazide (4a)

Yield 70.32%. IR (cm-1, KBr): 3149 (N-H stretching), 3040 (Aromatic C-H stretching), 2799 (C-H stretching), 1653 (C=O stretching), 1575 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.81-8.13 (m, 19H, Ar), 8.41 (s, 1H, -N=CH), 12.19 (s, 1H, -NH), MS: m/z- 442.26(M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(4-chlorobenzylidene) benzohydrazide (4b)

Yield 73.48%. IR (cm-1, KBr): 3166 (N-H Stretching), 3058 (Aromatic C-H stretching), 2920 (C-H stretching), 1644 (C=O stretching), 1601 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.81-8.14 (m, 18H, Ar), 8.43(s, 1H, -N=CH), 12.23 (s, 1H, -NH). MS: m/z- 476.09 (M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(4-methylbenzylidene) benzohydrazide (4c)

Yield 68.28%. IR (cm-1, KBr): 3179 (N-H Stretching), 3059 (Aromatic C-H stretching), 2889 (C-H stretching), 1644 (C=O stretching), 1581 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 2.28 (s, 3H, -CH<sub>3</sub>), 6.80-8.15 (m, 18H, Ar),

8.54 (s, 1H, -N=CH), 12.24 (s, 1H, -NH). MS: m/z- 456.16 (M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(4-methoxybenzylidene) benzohydrazide (4d)

Yield 65.51%. IR (cm-1, KBr): 3164 (N-H Stretching), 3051 (Aromatic C-H stretching), 2860 (C-H stretching), 1651 (C=O), 1590 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 3.84 (s, 3H, -OCH<sub>3</sub>), 7.10-8.09 (m, 18H, Ar), 8.49 (s, 1H, -N=CH), 12.12 (s, 1H, -NH). MS: m/z- 472.21 (M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(4-hydroxybenzylidene) benzohydrazide (4e)

Yield 71.25%. IR (cm-1, KBr): 3168 (N-H Stretching), 3041 (Aromatic C-H stretching), 2941 (C-H stretching), 1641(C=O stretching), 1606 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.82-8.22 (m, 18H, Ar), 8.53 (s, 1H, -N=CH), 12.29 (s, 1H, -NH). MS: m/z- 458.26 (M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(4-nitrobenzylidene) benzohydrazide (4f)

Yield 67.43%. IR (cm-1, KBr): 3259 (N-H Stretching), 3056 (Aromatic C-H stretching), 2849 (C-H stretching), 1650 (C=O stretching), 1581 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.80-8.15 (m, 18H, Ar), 8.56 (s, 1H, -N=CH), 12.13 (s, 1H, -NH). MS: m/z- 487.12 (M-).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(thiophen-2-ylmethylene) benzohydrazide (4g)

Yield 67.19%. IR (cm-1, KBr): 3170 (N-H Stretching), 3051 (Aromatic C-H stretching), 2953 (C-H stretching), 1659 (C=O stretching), 1608 (C=N stretching), 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.94-8.01 (m, 17H, Ar), 8.70 (s, 1H, -N=CH), 12.06 (s, 1H, -NH).

4-(3,5-diphenyl-1H-1,2,4-triazole-1-yl)-N'-(furan-2-ylmethylene) benzohydrazide (4h)

Yield 68.48%. IR (cm-1, KBr): 3154 (N-H Stretching), 3049 (Aromatic C-H stretching), 2935 (C-H stretching), 1652 (C=O stretching), 1583 (C=N stretching). 1H-NMR (400MHz, DMSO-d6):  $\delta$ = 6.91-7.99 (m, 17H, Ar), 8.18 (s, 1H, -N=CH), 12.10 (s, 1H, -NH).

## Conclusions

We have successfully synthesized Schiff base compounds with a 1,2,4-triazole moiety as substituent 4a–4h, through simple methods. The structures of synthesized compounds were confirmed by FTIR, NMR, and MS interpretation.

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Scheme 1. Synthesis pathway of 1,2,4-triazole fused Schiff bases (5a-5h).

