

Synthesis and Characterization of New Heterocyclic Schiff's Bases from Methyl 4-Hydroxybenzoate

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Abstract

New Schiff's bases with 1,2,4-triazole ring (3a-j) have been synthesized from 4-(4'-amino-5-mercapto-4H-1, 2, 4-triazol-3-yl) phenol (2) which is obtained from 4-hydroxybenzohydrazide (1) by a cyclization reaction. Infrared spectroscopy and ^1H NMR spectroscopy were used to characterize the structure of synthesized compounds. All the final products are indicated as keto-enol and thione-thiol tautomers.

Keywords: Heterocyclic compounds, Schiff's bases, Triazole, tautomerism.

Introduction

In recent years, 1, 2, 4-triazoles acquire an impressive importance due to their wide range applications such as anticorrosion [1], antioxidant [2, 3 and 4], acid-base indicator [5], urease inhibitors [4, 6], lipase inhibitors [6]. Also they found to be used as anticancer agents [7-8], antibacterial [4], antitubercular [9], and anticonvulsants [10, 11], antiviral [12], anti-inflammatory [13-14].

In literature there are several methods to synthesize 1, 2, 4-Triazole compounds, i.e, the synthesis from 1, 3, 5-Triazine, Oxazole, Thiosemicarbazide, Urea, and from Acid Chloride Carboxylic Acid Hydrazide [15]. The latter method was applied in this work.

Like Triazoles Schiff's bases exhibit a broad spectrum of applications as corrosion inhibitors, insecticides and pesticides. Their complexes with transition metals also have antibacterial, antiviral and antitumor activities.

Many researchers investigate the 1,2,4 Triazole compounds as corrosion inhibitors and found an increased inhibition effect on the corrosion of mild steel in acidic solutions [16].

In this work, the synthesis of Schiff's base derivatives with triazole moiety has to be accomplished and in next future as corrosion inhibitors will be studied.

General

All starting materials and solvents were purchased from Fluka, BDH and Thomas Baker companies, used without further purification. Melting points were determined on electro thermal capillary apparatus

(Chachan, MLP-01) and are uncorrected. FT-IR measurements were recorded on Shimadzu model FTIR-8400S. ^1H NMR spectra were achieved on NMR Spectrometer 400 MHz, Avance III 400, Bruker.

Chemical Synthesis

Synthesis of 4-hydroxybenzohydrazide (1) [18]

4-hydroxy methyl benzoate (0.01 mol, 1.52g) in (25 ml) ethanol is taken in a round bottom flask. Hydrazine hydrate (0.015 mol, 0.73 ml) was added, and the resulting mixture was refluxed for 4 hours. The precipitate was filtered, washed with ethanol, dried and recrystallized from ethanol.

Synthesis of potassium 2-(4-hydroxybenzoyl) hydrazinecarbodithioate [18]

A mixture of 4-hydroxybenzohydrazide (0.01 mol, 1.52 g), potassium hydroxide (0.015 mol, 0.84 g), and (0.025 mol, 1.9 ml) carbon disulfide in (15 ml) of absolute ethanol was stirred for 16 hours. The potassium salt thus obtained was used in the next step without further purification.

Synthesis of 4-(4-amino-5-mercapto-4H-1, 2, 4-triazol-3-yl) phenol (2) [19]

A suspension of potassium salt dithiocarbazinate (0.01 mol, 2.6 g), hydrazine hydrate (0.02 mol, 0.97 ml) and water (40 ml) was refluxed for 8 hours. The color of the reaction mixture changed to green, hydrogen sulphide was liberated and a homogenous solution resulted. A white solid was precipitated by dilution with cold water

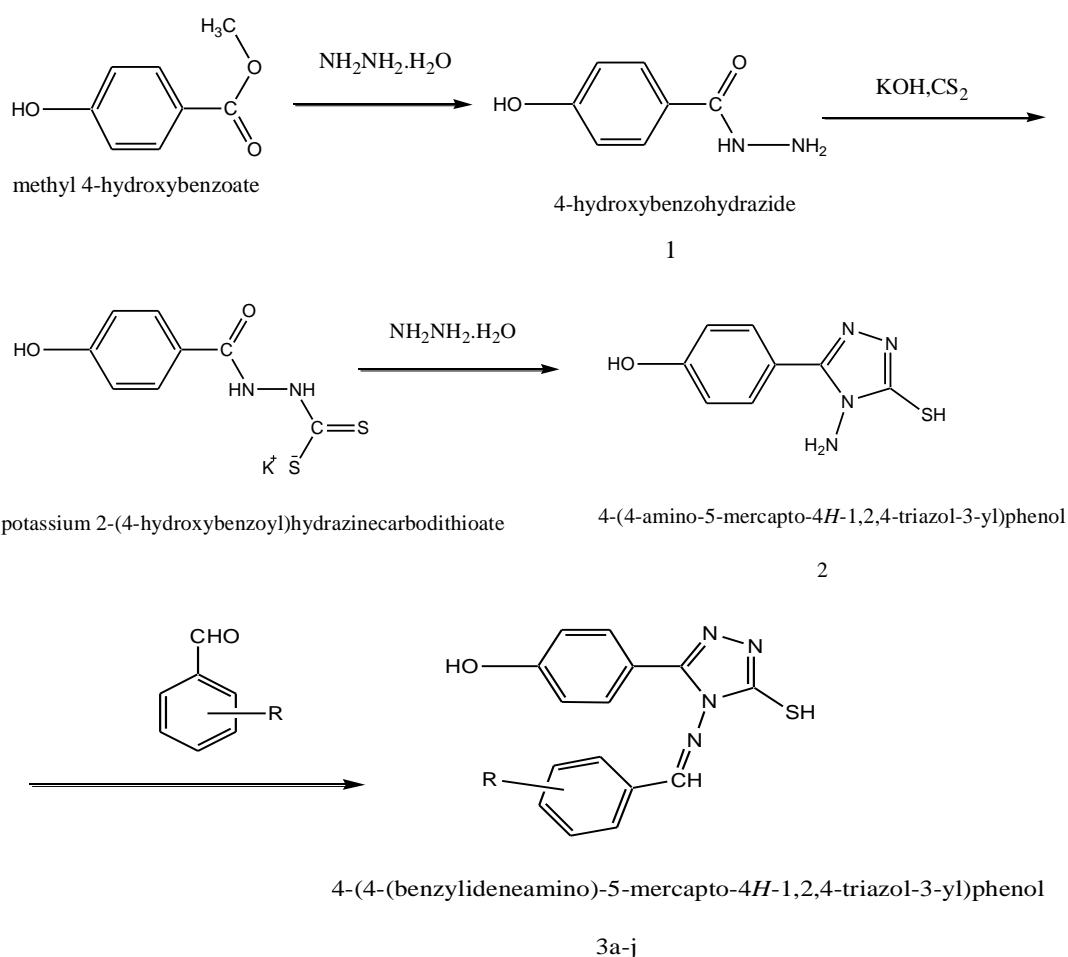
(50 ml) and acidification with concentrated hydrochloric acid. The product was filtered, washed with cold water and recrystallized from ethanol.

General procedure for the synthesis 4-(4-(benzylideneamino)-5-mercapto-4*H*-1, 2, 4-triazol-3-yl) phenol (3a- 3j) [20]

A mixture of compound 2 (0.01 mol, 2.1 g) and various aromatic aldehydes (0.02 mol) in (50 ml) absolute ethanol and two drops of glacial acetic acid, then refluxed for about 10 hours. Precipitate was filtered, dried and recrystallized from ethanol.

Results and Discussion

Compounds (1), (2), and 3(a-j) were synthesized as shown in Scheme (1). Chemical formula, molecular weight, color, melting points, and yield of prepared compounds are listed in Table (1). FT-IR spectral data are also shown in Table (2).



Scheme (1): Synthetic pathway for compounds [1-3(a-j)], where (R = H, *p*-OH, *p*- (CH₃)₂N, *p*-Br, *o*-NH₂), *p*-CH₃, *p*-NO₂, *p*-OCH₃, *p*-Cl, *o*-OH respectively.

Table (1)
Physical Properties for Compounds 1- 3 (a -j).

No.	Compound name	Chemical Formula	Molecular Weight (g/Mol)	Color	Melting Point (C°)	Yield (%)
1	4-hydroxybenzoic acid hydrazide	C ₇ H ₈ N ₂ O ₂	152	White	115-117	75
2	4-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)phenol	C ₈ H ₈ N ₄ OS	208	White	215-217	73
3a	4-(4-(benzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl)phenol	C ₁₅ H ₁₂ N ₄ OS	296.35	Pale Yellow	157-180	86
3b	4-(4-(4-hydroxybenzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl)phenol	C ₁₅ H ₁₂ N ₄ O ₂ S	312.35	White	150-153	82
3c	4-[4-(4-(dimethylamino)benzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl]phenol	C ₁₇ H ₁₇ N ₅ OS	339.41	Red	198-200	67
3d	4-(4-(4-bromobenzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl)phenol	C ₁₅ H ₁₁ BrN ₄ OS	375.24	Pale Yellow	180-182	86
3e	4-(4-(2-aminobenzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl)phenol	C ₁₅ H ₁₃ N ₅ OS	311.36	Dark brown	200-202	63
3f	4-(5-mercapto-4-(4-methylbenzylideneamino)-4H-1,2,4-triazol-3-yl)phenol	C ₁₆ H ₁₄ N ₄ OS	310.37	Yellow	138-140	87
3g	4-(5-mercapto-4-(4-nitrobenzylideneamino)-4H-1,2,4-triazol-3-yl)phenol	C ₁₅ H ₁₁ N ₅ O ₃ S	341.34	Yellow	170-172	61
3h	4-(5-mercapto-4-(4-methoxybenzylideneamino)-4H-1,2,4-triazol-3-yl)phenol	C ₁₆ H ₁₄ N ₄ O ₂ S	326.37	Yellowish Orange	148-150	89
3i	4-([4-(4-chlorobenzylideneamino)-5-mercapto-4H-1,2,4-triazol-3-yl]phenol	C ₁₅ H ₁₁ ClN ₄ OS	330.79	Yellow	188-190	76
3j	4-((2-(3-hydroxyphenyl)-5-mercapto-4H-1,2,4-triazol-4-ylimino)methyl)phenol	C ₁₅ H ₁₂ N ₄ O ₂ S	312.35	Yellow	206-208	74

Compound (1) has been synthesized from methyl benzoate and hydrazine hydrate in absolute ethanol and confirmed by the appearance of the stretching vibration bands at (3309, 3280) cm⁻¹ belongs to terminal amino group, and by shifting of the intense stretching vibration band from 1700 to 1624 cm⁻¹ for (C=O) of amide group. A stretching vibration band is also seen at 3197 cm⁻¹ for NH group.

The formation of compound (2) was confirmed through appearance of two bands at 948 cm⁻¹ and 1265 cm⁻¹ which referring to N-C-S and N-N-C, respectively. In addition of two other characteristic bands at 3174 and 2573 due to (N-H form) and (S-H) stretching vibration, respectively. This indicates a thiol-thion equilibrium. The nucleus 4-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)phenol (2) was

used to synthesize Schiff's bases (3a-3j). FT-IR spectra of prepared Schiff bases indicate a disappearance of (N-H) stretching band of primary amine at (3250-3400) cm⁻¹ and appearance of stretching band at (1597-1634) cm⁻¹ belong to the formation of imino group (HC=N). FT-IR characteristic spectral for all compounds are listed in the Tab. (2).

The ¹H NMR spectrum of compound (2) shows the following chemical shifts (δ/ppm) at: 5.72 (*s*, 2H, NH₂), 3.39 (*s*, 1H, NH), 6.88-7.86 (*m*, 4H, H-aromatic ring), and 10.73 (*s*, 1H, OH). As shown in Fig. (3). The chemical shifts for compound (3c) shows 3.01-3.15 (*m*, 6H, N(CH₃)₂), 6.78-8.13 (*m*, 4H, H aromatic), 8.80 (*s*, 1H, CH=N) 9.14(*s*, 1H, OH), 13.92(*s*, 1H, SH).

Table (2)
FT-IR characteristic Spectral bands of compounds 1, 2 and 3a-j.

No.	Structure	Frequency numbers (cm ⁻¹)
1		3197 cm ⁻¹ for O-H group, (3360, 3280) cm ⁻¹ for NH ₂ group, 3074, 3020 cm ⁻¹ for CH-aromatic, and 1624 cm ⁻¹ due to carbonyl group.
2		(3255,3174) cm ⁻¹ due to NH ₂ group, 3116 cm ⁻¹ due to OH group, 3057 cm ⁻¹ due to C-H-aromatic, 1612 cm ⁻¹ due to C=N group, 698 cm ⁻¹ due to C-S group, and 2569 cm ⁻¹ belongs to S-H group.
3a		3280 cm ⁻¹ due to N-H (tautomer), 3124 cm ⁻¹ due to O-H group, 3078, 3016 cm ⁻¹ due to C-H-aromatic, 1612 cm ⁻¹ due to C=N group, (1550, 1504) cm ⁻¹ due to C=C aromatic, 648 cm ⁻¹ due to C-S group, 2592 cm ⁻¹ due to S-H group.
3b		3290 cm ⁻¹ for N-H (tautomer), 3248, 3100 cm ⁻¹ belong to both O-H bonds, 3039 cm ⁻¹ due to C-H-aromatic, 1612 cm ⁻¹ due to C=N group, (2966, 2897) cm ⁻¹ belongs to C-H aliphatic, 2569 cm ⁻¹ belongs to S-H group, and 829 cm ⁻¹ due to para-di substituted phenyl ring,
3c		3278 cm ⁻¹ due to NH (tautomer), 3113 cm ⁻¹ for OH group, 3089 cm ⁻¹ due to CH-aromatic, 1597 cm ⁻¹ due to C=N group, (1577, 1527) cm ⁻¹ due to C=C aromatic, 817 cm ⁻¹ due to para-disubstituted phenyl ring, 1168 cm ⁻¹ due to C-N bond, and 1346 cm ⁻¹ due to C-H bending of (CH ₃).
3d		3270 cm ⁻¹ for NH (tautomer), 3128 cm ⁻¹ for OH, 3030 cm ⁻¹ due to CH-aromatic, 3271 cm ⁻¹ due to OH group, 1608 cm ⁻¹ due to C=N group, 686 cm ⁻¹ due to C-S group, 2565 cm ⁻¹ due to S-H, 817 cm ⁻¹ due to para-di substituted phenyl ring, and 590 cm ⁻¹ due to C-Br.
3e		(3330, 3244) cm ⁻¹ due to NH ₂ group, 3197 cm ⁻¹ for OH, 3020 cm ⁻¹ due to C-H-aromatic, 2560 cm ⁻¹ for SH (tautomer), 1612 cm ⁻¹ due to C=N group, and 2592 cm ⁻¹ belongs to S-H group.
3f		3355 cm ⁻¹ for NH (tautomer), 3120 cm ⁻¹ for OH, 3032 cm ⁻¹ due to C-H-aromatic, 2954 cm ⁻¹ belongs to C-H aliphatic, 1604 cm ⁻¹ due to C=N group, (1512, 1562) cm ⁻¹ due to C=C aromatic, 817 cm ⁻¹ due to para-di substituted phenyl ring.
3g		3282 cm ⁻¹ for NH-tautomer, 3105 cm ⁻¹ for OH, 3032 cm ⁻¹ due to CH-aromatic, 1612 cm ⁻¹ due to C=N group, 2592 cm ⁻¹ belongs to SH, 844 cm ⁻¹ due to para-disubstituted phenyl ring, and (1346, 1523) cm ⁻¹ due to NO ₂
3h		3124 cm ⁻¹ for OH, 3051, 3001 cm ⁻¹ due to CH-aromatic, 2947 cm ⁻¹ for CH aliphatic, 1620 cm ⁻¹ due to C=N group, 2588 cm ⁻¹ belongs to S-H group, (1570, 1512) cm ⁻¹ due to C=C aromatic, 1300 cm ⁻¹ due to C-H bend of (CH ₃), and 1165 cm ⁻¹ due to C-O group, 752 cm ⁻¹ due to para-disubstituted phenyl ring
3i		3252 cm ⁻¹ for NH-tautomer, 3113 cm ⁻¹ for OH, 3047 cm ⁻¹ due to CH-aromatic, 1612 cm ⁻¹ due to C=N group, 2596 cm ⁻¹ due to S-H group, 821 cm ⁻¹ for para-di substituted phenyl ring, and 497 cm ⁻¹ due to C-Cl.
3j		3302 cm ⁻¹ for NH-tautomer, 3113 cm ⁻¹ for OH, 3047 cm ⁻¹ due to CH-aromatic, 1612 cm ⁻¹ due to C=N group, 2565 cm ⁻¹ belongs to S-H group.

Conclusions

From FT-IR and ^1H NMR spectroscopic data can be concluded that the final compounds were recognized to exist as thiol-thione and as keto-enol tautomers because the high degree of conjugation in this system due to presence of the hydroxyl, amine and thiol groups and sp^2 hybridized carbon atoms. The high degree of planarity and high content of heteroatoms like oxygen, nitrogen, and sulfur atoms are required in these compounds to be studied in future work.

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الخلاصة

تم تخليق قواعد شف جديدة تحوي في تركيبها حلقة 1,2,4-تريازول الخماسية (3a-j) من المركب 4,4-امينو-5-مركابتو-4H-1,2,4-تريازول-3-ايل (2) والذي بدوره حضر من تفاعل الحوالة لمركب 4-هيدروكسي حامض البنزويك هايدرازيد (1). تم تشخيص المركبات بواسطة طيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي للبروتون.