Chemistry Research Journal, 2022, 7(3):19-22

Available online www.chemrj.org

Research Article

ISSN: 2455-8990
CODEN(USA): CRJHA5

Synthesis and Characterization of Novel Potential Biologically Active 3-Alkyl(Aryl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-ones

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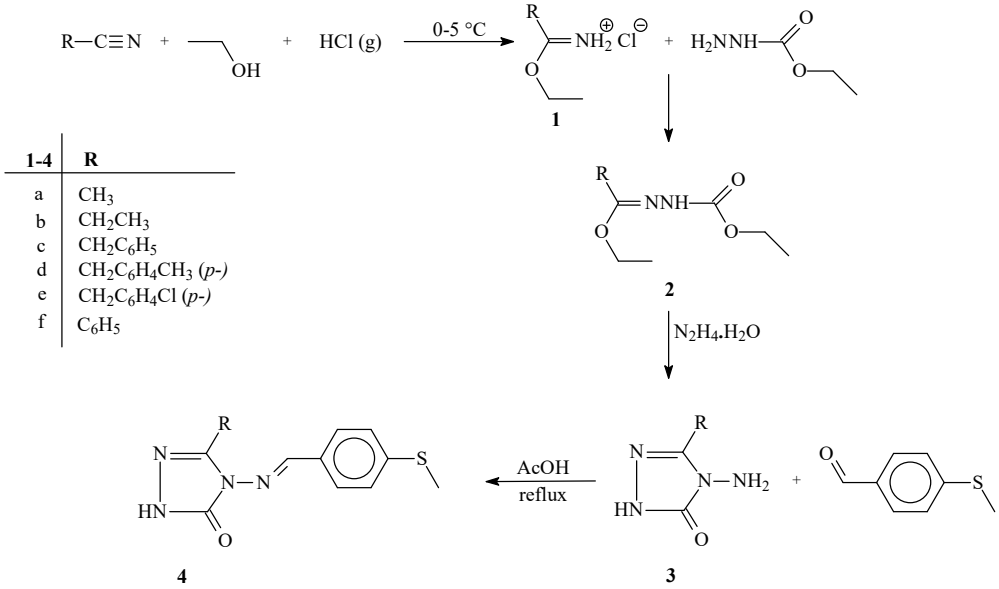
Abstract In this study, 3-alkyl(aryl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-ones (**4**) were synthesized 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3**) with 4-methylthiobenzaldehyde. The structures of six new compounds were characterized by elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR and UV spectra.

Keywords 4,5-Dihydro-1*H*-1,2,4-triazol-5-one, Schiff base, synthesis

Introduction

1,2,4-Triazole and 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives are reported to possess a broad spectrum of biological activities [1-12]. In addition, several articles reporting the synthesis of some *N*-arylidenamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives have been published [2,6,12-16].



1-4	R
a	CH_3
b	CH_2CH_3
c	$CH_2C_6H_5$
d	$CH_2C_6H_4CH_3$ (*p-*)
e	$CH_2C_6H_4Cl$ (*p-*)
f	C_6H_5

*Scheme 1: Synthetic route of compounds **4***

In the present paper, six new potential biologically active 3-alkyl(aryl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-ones (**4**) were synthesized 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3**) with 4-methylthiobenzaldehyde (Scheme 1). Compounds **3** were prepared from the reactions of the corresponding ester ethoxycarbonylhydrazones (**2**), which were obtained by the reactions of iminoester hydrochlorides (**1**) with ethyl carbazate, with an aqueous solution of hydrazine hydrate as described in the literature [17,18].

Materials and Methods

Chemical reagents and all solvents used in this study were purchased from Merck AG, Aldrich and Fluka. Melting points which were uncorrect were determined in open glass capillaries using an Electrothermal 9100 digital melting point apparatus. The IR spectra were obtained on a Mattsol 1000 FTIR spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded in deuterated dimethyl sulfoxide with TMS as internal standard using a Varian NMR spectrometer at 200 MHz and 50 MHz, respectively. UV absorption spectra were measured in 10 mm quartz cells between 200 and 400 nm using a Schimadzu-160A UV-VIS-NIR spectrometer. Extinction coefficients (ε) are expressed in L.mol^{-1}.cm^{-1}. Combustion analyses were performed on a LECO CHNS-932 Elemental Analyzer.

General procedure for the synthesis of 3-alkyl(aryl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-ones (4). The corresponding compound **3** (0.01 mol) was dissolved in ethanoic acid (20 mL) and by treated 4-methylthiobenzaldehyde (0.01 mol). The mixture was refluxed for 1.5 hours and then evaporated at 50-55 °C *in vacuo*. A few recrystallizations of the residue from ethanol gave pure compounds **4**.

3-Methyl-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4a): Yield 91 %, m.p. 227 °C. IR (KBr): 3167 (NH), 1708 (C=O), 1590 (C=N), 823 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.27 (s, 3H, CH_3), 2.53 (s, 3H, SCH_3), 7.35 (d, 2H, ArH, *J*=8.40 Hz), 7.76 (d, 2H, ArH, *J*=8.40 Hz), 9.67 (s, 1H, N=CH), 11.81 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 11.89 (CH_3), 15.92 (SCH_3), [127.32 (2C), 129.80 (2C), 131.60, 144.65] (ArC), 146.00 (Triazole C_3), 153.08 (N=CH), 155.11 (Triazole C_5). UV λ_{max} (ε, L·mol^{-1}·cm^{-1}): 323 (14480), 260 (1860), 208 (10030) nm. *Anal.* Calcd for $C_{11}H_{12}N_4OS$: C, 53.21; H, 4.87; N, 22.56. Found: C, 53.52; H, 4.91; N, 22.47.

3-Ethyl-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4b): Yield 92 %, m.p. 168 °C. IR (KBr): 3170 (NH), 1695 (C=O), 1593 (C=N), 809 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.21 (t, 3H, CH_2CH_3, *J*=7.20 Hz), 2.52 (s, 3H, SCH_3), 2.67 (q, 2H, CH_2CH_3, *J*=7.20 Hz), 7.35 (d, 2H, ArH, *J*=8.00 Hz), 7.74 (d, 2H, ArH, *J*=8.00 Hz), 9.66 (s, 1H, N=CH), 11.80 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 11.83 ($CH_2\underline{C}H_3$), 15.94 (SCH_3), 20.33 ($\underline{C}H_2CH_3$), [127.33 (2C), 129.75 (2C), 131.65, 144.65] (ArC), 149.77 (Triazole C_3), 153.22 (N=CH), 155.08 (Triazole C_5). UV λ_{max} (ε, L·mol^{-1}·cm^{-1}): 323 (23030), 260 (2120), 208 (12020) nm. *Anal.* Calcd for $C_{12}H_{14}N_4OS$: C, 54.94; H, 5.38; N, 21.36. Found: C, 55.17; H, 5.27; N, 21.23.

3-Benzyl-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4c): Yield 95 %, m.p. 208 °C. IR (KBr): 3163 (NH), 1700 (C=O), 1596 (C=N), 814 (1,4-disubstituted benzenoid ring), 756 and 696 (monosubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.53 (s, 3H, SCH_3), 4.05 (s, 2H, CH_2Ph), 7.32-7.37 (m, 7H, ArH), 7.72 (d, 2H, ArH, *J*=8.40 Hz), 9.63 (s, 1H, N=CH), 11.96 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 15.92 (SCH_3), 32.90 (CH_2Ph), [127.33 (2C), 128.48, 129.81 (2C), 130.21 (2C), 130.57 (2C), 131.58, 137.60, 144.73] (ArC), 147.96 (Triazole C_3), 153.07 (N=CH), 154.95 (Triazole C_5). UV λ_{max} (ε, L·mol^{-1}·cm^{-1}): 323 (2910), 260 (3110), 208 (21240) nm. *Anal.* Calcd for $C_{17}H_{16}N_4OS$: C, 62.94; H, 4.97; N, 17.27. Found: C, 63.09; H, 5.05; N, 17.20.

3-(*p*-Methylbenzyl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4d): Yield 93 %, m.p. 188 °C. IR (KBr): 3160 (NH), 1708 (C=O), 1592 (C=N), 825, 800 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.24 (s, 3H, $PhCH_3$), 2.53 (s, 3H, SCH_3), 3.99 (s, 2H, CH_2Ph), 7.15 (d, 4H, ArH, *J*=8.00 Hz),

7.35 (d, 2H, ArH, *J*=8.40 Hz), 7.72 (d, 2H, ArH, *J*=8.40 Hz), 9.62 (s, 1H, N=CH), 11.94 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 15.92 (SCH_3), 22.38 ($PhCH_3$), 32.50 (CH_2Ph), [127.34 (2C), 128.61 (2C), 130.43 (2C), 130.77 (2C), 131.59, 134.48, 137.47, 144.71] (ArC), 148.11 (Triazole C_3), 153.07 (N=CH), 154.91 (Triazole C_5). UV λ_{max} (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 323 (16600), 261 (1860), 208 (12540) nm. *Anal.* Calcd for $C_{18}H_{18}N_4OS$: C, 63.88; H, 5.36; N, 16.56. Found: C, 64.16; H, 5.38; N, 16.56.

3-(*p*-Chlorobenzyl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4e): Yield 91 %, m.p. 205 °C. IR (KBr): 3110 (NH), 1706 (C=O), 1594, 1584 (C=N), 817 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.53 (s, 3H, SCH_3), 4.05 (s, 2H, CH_2Ph), 7.34 (d, 2H, ArH, *J*=8.00 Hz), 7.36 (m, 4H, ArH), 7.71 (d, 2H, ArH, *J*=8.40 Hz), 9.63 (s, 1H, N=CH), NH (unobserved). ^{13}C-NMR (DMSO-d_6): δ 15.91 (SCH_3), 32.23 (CH_2Ph), [127.30 (2C), 129.82 (2C), 130.14 (2C), 131.51, 132.50 (2C), 133.23, 136.54, 144.77] (ArC), 147.62 (Triazole C_3), 153.05 (N=CH), 154.99 (Triazole C_5). UV λ_{max} (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 324 (17340), 262 (1820), 221 (14970) nm. *Anal.* Calcd for $C_{18}H_{18}N_4OSCl$: C, 56.90; H, 4.21; N, 15.61. Found: C, 56.96; H, 4.20; N, 15.55.

3-Phenyl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-one (4f): Yield 96 %, m.p. 185 °C. IR (KBr): 3189 (NH), 1698 (C=O), 1593 (C=N), 820 (1,4-disubstituted benzenoid ring), 771 and 693 (monosubstituted benzenoid ring) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.52 (s, 3H, SCH_3), 7.35 (d, 2H, ArH, *J*=8.40 Hz), 7.50-7.54 (m, 3H, ArH), 7.73 (d, 2H, ArH, *J*=8.00 Hz), 7.88-7.93 (m, 2H, ArH), 9.60 (s, 1H, N=CH), 12.38 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 15.90 (SCH_3), [127.37 (2C), 128.51, 129.67 (2C), 129.98 (2C), 130.25 (2C), 131.37, 131.81, 145.07] (ArC), 146.29 (Triazole C_3), 153.21 (N=CH), 157.92 (Triazole C_5). UV λ_{max} (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 325 (16520), 267 (6350), 232 (12840) nm. *Anal.* Calcd for $C_{16}H_{14}N_4OS$: C, 61.92; H, 4.55; N, 18.05. Found: C, 61.81; H, 4.51; N, 17.87.

Results and Discussion

In this study, 3-alkyl(aryl)-4-(4-methylthiobenzylideneamino)-4,5-dihidro-1*H*-1,2,4-triazol-5-ones (**4**) were synthesized 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3**) with 4-methylthiobenzaldehyde. The structures of six new compounds **4** were identified by elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR and UV spectral data.

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