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Research Article

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

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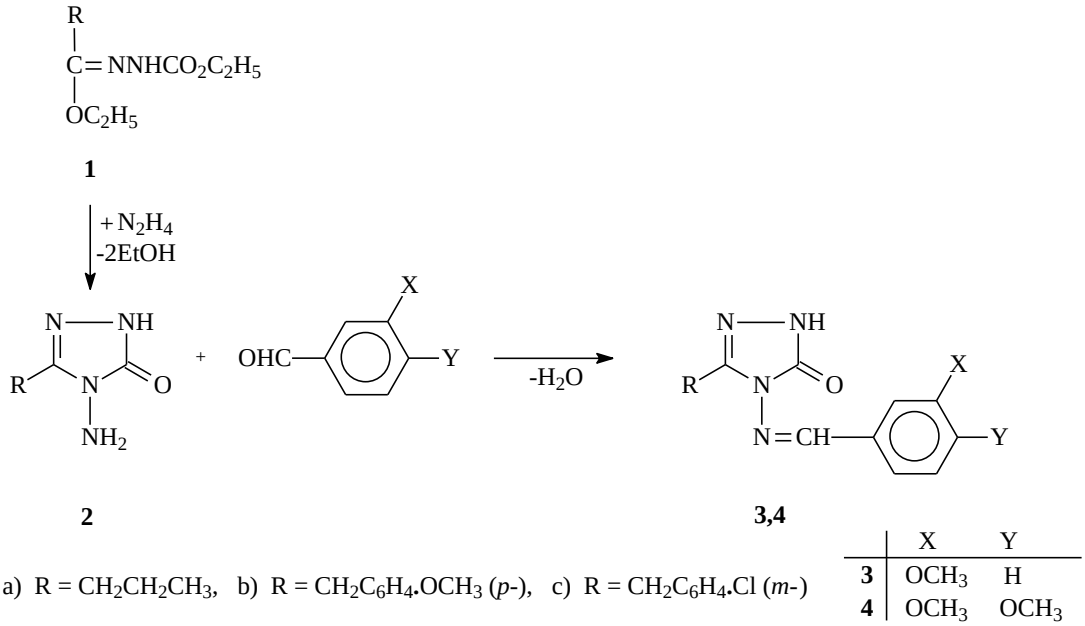
Abstract In the present study, two new 3-alkyl-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3b,c**) and three new 3-alkyl-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**4a-c**) were synthesized by the reactions 3-methoxybenzaldehyde and 3,4-dimethoxybenzaldehyde with corresponding 3-alkyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**2a-c**). The structures of five new compounds characterized from the IR, ^{1}H NMR and ^{13}C NMR spectral data.

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

Introduction

4,5-Dihydro-1*H*-1,2,4-triazol-5-one and *N*-arylidenamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives are reported to possess a broad spectrum of biological activities such as antifungal, antimicrobial, hypoglycemic, antihypertensive, analgesic, antiviral, anti-inflammatory, antitumor, antioxidant and anti-HIV properties [1-13]. For this reason, several articles reporting the synthesis of some*N*-arylidenamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives have been published [6,7,12-19].

In this study, two new 3-alkyl-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3b,c**)) were synthesized by the reactions of 3-alkyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**2b,c**) with 3-methoxybenzaldehyde. In addition, three new 3-alkyl-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**4a-c**) were also synthesized by the reactions 3-alkyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**2a-c**) with 3,4-dimethoxybenzaldehyde (Scheme 1). The starting compounds 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**1**) were prepared from the reactions of the corresponding ester ethoxycarbonyl hydrazones with an aqueous solution of hydrazine hydrate as described in the literature [20,21].



a) R = $CH_2CH_2CH_3$, b) R = $CH_2C_6H_4$.OCH_3 (*p*-), c) R = $CH_2C_6H_4$.Cl (*m*-)

	X	Y
3	OCH_3	H
4	OCH_3	OCH_3

*Scheme 1: Synthetic route of compounds **3**, **4***

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 Perkin-Elmer Instruments Spectrum One FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded in deuterated dimethyl sulfoxide with TMS as internal standard using a Bruker Ultrashield spectrometer at 400 MHz and 100 MHz, respectively.

General procedure for the synthesis of 3-alkyl-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (3b,c)

The corresponding compound **1** (0.01 mol) was dissolved in ethanoic acid (20 mL) and by treated 3-methoxybenzaldehyde (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 **3**.

3-(*p*-Methoxybenzyl)-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one (3b):

Yield 92%, m.p. 172 °C. IR(ATR): 3173 (NH), 1709 (C=O), 1609, 1579 (C=N), 894 and 803 (1,3-disubstituted benzenoid ring), 803 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.70 (s, 3H, *p*-OCH_3), 3.82 (s, 3H, *m*-OCH_3), 3.99 (s, 2H, CH_2Ph), 6.87 (d, 2H, ArH, *J*=8.80 Hz), 7.09 (dq, 1H, ArH, *J*=8.00, 1.20 Hz), 7.24 (d, 2H, ArH, *J*=8.40 Hz), 7.34-7.43 (m, 3H, ArH), 9.66 (s, 1H, N=CH), 11.96 (s,1H,NH). ^{13}C NMR (DMSO-d_6): δ 30.30 (CH_2Ph), 55.00 (*p*-OCH_3), 55.22 (*m*-OCH_3), [111.64 (CH), 117.66 (CH), 120.55 (CH), 130.08 (CH), 134.96 (C), 159.58 (C)] (ArC), [113.87 (2CH), 127.60 (C), 129.50 (2CH), 158.08 (C)] (ArC linked C-3), 146.50 (Triazole C_3), 151.24 (Triazole C_5), 153.14 (N=CH).

3-(*m*-Chlorobenzyl)-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one (3c):

Yield 95%, m.p. 171 °C.IR (ATR): 3152 (NH), 1692 (C=O), 1574 (C=N), 862 and 797(1,3-disubstituted benzenoid ring) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 4.10 (s, 2H, CH_2Ph), 7.09 (dq, 1H, ArH, *J*=8.00, 1.20 Hz), 7.28-7.44 (m, 7H, ArH), 9.66 (s, 1H, N=CH), 12.02 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): δ 30.73 (CH_2Ph), 55.23 (OCH_3), [111.58 (CH), 117.78 (CH), 120.61 (CH), 130.06 (CH), 134,87 (C), 159.59 (C)] (ArC), [126.64 (CH), 127.49 (CH), 128.80 (CH), 130.25 (CH), 132.96 (C), 138.25 (C)] (ArC linked C-3),145.69 (Triazole C_3), 151.19 (Triazole C_5), 153.27 (N=CH).

General procedure for the synthesis of 3-alkyl-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (4a-b)

The corresponding compound **1** (0.01 mol) was dissolved in ethanoic acid (20 mL) and by treated 3,4-dimethoxybenzaldehyde (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-(*n*-Propyl)-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one (4a):

Yield 98%, m.p. 184 °C. IR (ATR): 3315 (NH), 1713 (C=O), 1582 (C=N), 897 and 795 (1,3-disubstituted benzenoid ring) cm^{-1}.^{1}H NMR (DMSO-d_6): δ 0.96 (t, 3H, $CH_2CH_2CH_3$, *J*=7.20 Hz), 1.69 (sext, 3H, $CH_2\underline{CH_2}CH_3$, *J*=7.20 Hz), 2.64 (t, 3H, $\underline{CH_2}CH_2CH_3$, *J*=7.20 Hz), 3.82 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 7.07 (d, 1H, ArH, *J*=8.40 Hz), 7.37 (dd, 1H, ArH, *J*=8.40, 2.00 Hz), 7.42 (d, 1H, ArH, *J*=2.00 Hz), 9.58 (s, 1H, N=CH), 11.79 (s,1H,NH). ^{13}C NMR (DMSO-d_6): δ 13.47 ($CH_2CH_2\underline{C}H_3$), 18.93 ($CH_2\underline{C}H_2CH_3$), 26.75 ($\underline{C}H_2CH_2CH_3$), 55.47 (OCH_3), 55.64 (OCH_3), [109.26 (CH), 111.66 (CH), 122.34 (CH), 126.17 (C), 151.39 (C), 151.77 (C)] (ArC), 146.87 (Triazole C_3), 149.09 (Triazole C_5), 154.12 (N=CH).

3-(*p*-Methoxybenzyl)-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one(4b):

Yield 97%, m.p. 186 °C. IR (ATR): 3315 (NH), 1707 (C=O), 1604, 1581 (C=N), 802 (1,4-disubstituted benzenoid ring) cm^{-1}.^{1}H NMR (DMSO-d_6): δ 3.70 (s, 3H, *p*-OCH_3), 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.98 (s, 2H, CH_2Ph), 6.87 (d, 2H, ArH, *J*=8.40 Hz), 7.05 (d, 1H, ArH, *J*=8.40 Hz), 7.25 (d, 2H, ArH, *J*=8.40 Hz), 7.32 (d, 1H, ArH, *J*=8.40 Hz), 7.37 (s, 1H, ArH), 9.55 (s, 1H, N=CH), 11.92 (s,1H,NH). ^{13}C NMR (DMSO-d_6): δ 30.42 (CH_2Ph), 55.00 (*p*-OCH_3), 55.46 (OCH_3), 55.63 (OCH_3), [108.59 (CH), 111.51 (CH), 122.82 (CH), 126.14 (C), 151.34 (C), 151.74 (C)] (ArC), [113.84 (2CH), 127.70 (C), 129.77 (2CH), 158.05 (C)] (ArC linked C-3), 146.46 (Triazole C_3), 149.09 (Triazole C_5), 153.45 (N=CH).

3-(*m*-Chlorobenzyl)-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-one (4c):

Yield 95%, m.p. 183 °C.IR (ATR): 3314 (NH), 1707 (C=O), 1598, 1574 (C=N), 868 and 805 (1,3-disubstituted benzenoid ring) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.09 (s, 2H, CH_2Ph), 7.05 (d, 1H, ArH, *J*=8.00 Hz), 7.28-7.37 (m, 5H, ArH), 7.44 (d, 1H, ArH, *J*=1.60 Hz), 9.56 (s, 1H, N=CH), 11.97 (s,1H,NH). ^{13}C NMR (DMSO-d_6): δ 30.83 (CH_2Ph), 55.47 (OCH_3), 55.64 (OCH_3), [108.43 (CH), 111.49 (CH), 123.03 (CH), 126.03 (C), 151.58 (C), 151.82 (C)] (ArC), [126.71 (CH), 127.48 (CH), 128.74 (CH), 130.25 (CH), 132.94 (C), 138.39 (C)] (ArC linked C-3), 145.64 (Triazole C_3), 149.11 (Triazole C_5), 153.63 (N=CH).

Results and Discussion

In this study, two new 3-alkyl-4-(3-methoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**3b,c**) and three new 3-alkyl-4-(3,4-dimethoxybenzylideneamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**4a-c**) were synthesized by the reactions 3-methoxybenzaldehyde and 3,4-dimethoxybenzaldehyde with corresponding 3-alkyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**2a-c**).The structures of five new compounds 3b,c and 4a-c were identified using the IR, ^{1}H-NMR, ^{13}C-NMR spectral data, and the observed spectral values were seen to be compatible with literature values [6,12-19].

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