Synthesis of Some Novel 3-Alkyl(Aryl)-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one Compounds

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Abstract: In this study, nine novel 3-alkyl(aryl)-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3) compounds were synthesized from a reaction of type 1 compounds with 3-(2-furylcarbonyloxy)-4-methoxybenzaldehyde (2) which is obtained from a reaction of 3-hydroxy-4-methoxybenzaldehyde and furan-2-carbonyl chloride. The finally part contains that synthesis of new compounds. The structures of these novel compounds were characterized by using, IR, $^1$H NMR and $^{13}$C NMR spectral data.

Keywords: 1.2.4-triazol, Schiff base, Synthesis

Introduction

1,2,4-Triazole and 4,5-dihydro-1H-1,2,4-triazol-5-one derivatives have been reported to possess a wide range of biological activities, such as anti-tumor (Chen et al., 2016), anti-bacterial (Zhang et al., 2014), anti-oxidant (Chidananda et al., 2012), anti-inflammatory (El-Serwy, Mohamed, Abbas, & Abdel-Rahman, 2013), analgesic (Uzgören-Baran et al., 2012), anti-hypertensive and diuretic (Ali, Ragab, Farghaly, & Abdalla, 2011) qualities.

In a recent study it has been reported that diaminobenedine is a chemo-sensor which selectively displays fluorescent emission in the presence of zinc (II) (Kumar et al., 2017). In another study, it has been shown that a Schiff base of mesoporous SBA-15 which was modified by Fe$_3$O$_4$ nanoparticles removes Ce (III) ions from aqueous solutions in less than one minute (Dashitian et al., 2017). In a similar study, it has been reported that a novel colorimetric and fluorescent MMIP chemosensor based on Schiff base can detect some trace heavy and transition metal ions at high selectivity and sensitivity in an aqueous solution (Zhang et al., 2017).

In the present study, nine novel compounds 3-alkyl(aryl)-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-ones (3a-i) were synthesized from the reactions of 3-alkyl(aryl)-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-ones (1a-i) and 3-(2-furylcarbonyloxy)-4-methoxybenzaldehyde (2) (Scheme 1).
Method

Chemicals and Apparatus

Chemical reagents and all solvents used in this study were purchased from Merck AG, Aldrich and Fluka. Melting point was determined in open glass capillary using a Stuart melting point SMP30 apparatus and is uncorrected. The IR spectra were obtained on an ALPHA-P BRUKER 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 Plus Biospin spectrometer at 400 MHz and 100 MHz, respectively.

Synthesis of Compounds 3: The General Procedure

3-Hydroxy-4-methoxybenzaldehyde (0.01 mol) dissolved in ethyl acetate (20 mL) was treated with furan-2-carbonyl chloride (0.01 mol) and to this solution was slowly added triethylamine (0.01 mol) with stirring at 0-5 °C. The process of stirring continued for 2 h, and then the mixture was refluxed for 3 h and filtered. The filtrate evaporated in vacuo, and the crude product was washed with water and recrystallized from ethanol to afford compound 2, mp 90 °C; IR: 2826 and 2746 (CHO), 1743, 1688 (C=O), 1511, 1468 (C=C), 1283 (COO), 1178 (C-O, furan), 807 (1,4-disubstituted benzenoid ring) cm$^{-1}$. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 3.90 (s, 3H, OCH$_3$), 6.82 (t, 1H, ArH; $J$=3.60 Hz), 7.41 (d, 1H, Ar-H; $J$=8.40 Hz), 7.60 (dd, 1H, ArH; $J$=3.60 Hz, 0.40 Hz), 7.77 (d, 1H, Ar-H; $J$=2.00 Hz), 7.92 (dd, 1H, ArH; $J$=8.40 Hz, 0.20 Hz), 8.12 (s, 1H, Ar-H), 9.70 (s, 1H, CHO). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 56.52 (OCH$_3$), 112.80, 113.13, 120.57, 123.23, 129.70, 130.35, 138.91, 142.49, 148.82, 153.53 (Ar-C), 156.05 (COO), 190.82 (CHO).
The corresponding compound 1 (0.01 mol) was dissolved in acetic acid (20 mL) and treated with 3-(2-furylcarboxyloxy)-4-methoxybenzaldehyde 2 (0.01 mol). The mixture was refluxed for 2 h and then evaporated at 50-55 °C in vacuo. Several recrystallizations of the residue from ethanol gave pure compounds 3-alkyl(aryl)-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one as colorless crystals.

3-Methyl-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3a)

Yield: 97.22%, m.p. 221 °C. IR (KBr, ν, cm⁻¹): 3139 (NH), 1741, 1695 (C=O), 1610 (C=N), 1507, 1469 (C=C), 1266 (COO), 1163 (C=O, furan), 834 (1,4-disubstituted benzenoid ring) cm⁻¹.

3-Ethyl-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3b)

Yield: 75.44%, m.p. 192 °C. IR (KBr, ν, cm⁻¹): 3161 (NH), 1743, 1699 (C=O), 1603 (C=N), 1510, 1469 (C=C), 1271 (COO), 1170 (C=O, furan), 834 (1,4-disubstituted benzenoid ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 1.20 (t, 3H, CH₃J=7.60 Hz), 2.68 (q, 2H, CH₂J=7.60 Hz), 3.86 (s, 3H, OCH₃), 6.82 (dd, 1H, Ar-H; J=3.60 Hz, 1.60 Hz), 7.34 (d, 1H, Ar-H; J=9.20 Hz), 7.60 (dd, 1H, Ar-H; J=3.60 Hz, 0.80 Hz), 7.74-7.76 (m, 2H, Ar-H), 8.12 (s, 1H, Ar-H), 9.66 (s, 1H, N=CH), 11.82 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 10.00 (CH₃), 18.45 (CH₃), 56.22 (OCH₃), 112.77, 113.12, 120.44, 121.01, 126.54, 128.27, 138.98, 142.62, 148.05, 151.41 (Ar-C), 148.72 (triazole C₃), 152.79 (N=CH), 153.53 (triazole C₅), 155.61 (COO).

3-n-Propyl-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3c)

Yield: 72.60%, m.p. 199 °C. IR (KBr, ν, cm⁻¹): 3168 (NH), 1735, 1702 (C=O), 1588 (C=N), 1513, 1437 (C=C), 1270 (COO), 1174 (C=O, furan), 811 (1,4-disubstituted benzenoid ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 1.06 (t, 3H, CH₃CH₂CH₃J=7.60 Hz), 1.68 (sex., 2H, CH₃CH₂CH₃J=7.60 Hz), 2.64 (t, 2H, CH₂CH₃CH₃J=7.60 Hz), 3.86 (s, 3H, OCH₃), 6.81 (dd, 1H, Ar-H; J=8.00 Hz, 7.60 Hz), 7.31 (d, 1H, Ar-H; J=8.80 Hz), 7.60 (m, 1H, Ar-H), 7.74-7.77 (m, 2H, Ar-H), 8.12 (m, 1H, Ar-H), 9.66 (s, 1H, N=CH), 11.82 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 13.42 (CH₃CH₂CH₃), 18.82 (CH₃CH₂CH₃), 26.62 (CH₂CH₃CH₃), 56.22 (OCH₃), 112.76, 113.15, 120.44, 121.07, 126.52, 128.19, 138.98, 142.62, 148.72, 153.53 (Ar-C), 146.89 (triazole C₅), 151.35 (triazole C₃), 152.90 (N=CH), 155.60 (COO).

3-Benzyl-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3d)

Yield: 99.26%, m.p. 207 °C. IR (KBr, ν, cm⁻¹): 3135 (NH), 1740, 1698 (C=O), 1590 (C=N), 1509, 1467 (C=C), 1271 (COO), 1172 (C=O, furan), 813 (1,4-disubstituted benzenoid ring), 772 and 699 (monosubstituted benzenoid ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 3.85 (s, 3H, OCH₃), 4.05 (s, 2H, CH₂Ph), 6.82 (dd, 1H, Ar-H; J=7.60 Hz, 1.60 Hz), 7.20-7.22 (m, 1H, Ar-H), 7.25-7.31 (m, 5H, Ar-H), 7.60-7.61 (m, 1H, Ar-H), 7.70-7.73 (m, 2H, Ar-H), 8.12 (s, 1H, Ar-H), 9.61 (s, 1H, N=CH), 11.94 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 31.08 (CH₂Ph), 56.22 (OCH₃), 112.80, 113.13, 120.46, 121.24, 126.47, 126.64, 128.15, 128.35 (2C), 128.79 (2C), 135.83, 138.92, 142.60, 148.75, 153.53 (Ar-C), 146.22 (triazole C₅), 151.25 (triazole C₃), 152.48 (N=CH), 155.63 (COO).

3-p-Methylbenzyl-4-[3-(2-furylcarboxyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3e)

Yield: 99.29%, m.p. 214 °C. IR (KBr, ν, cm⁻¹): 3165 (NH), 1743, 1699 (C=O), 1591 (C=N), 1513, 1468 (C=C), 1272 (COO), 1174 (C=O, furan), 832 (1,4-disubstituted benzenoid ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 2.21 (s, 3H, PhCH₃), 3.85 (s, 3H, OCH₃), 3.99 (s, 2H, CH₂Ph), 6.82-6.84 (m, 1H, Ar-H), 7.07 (d, 2H, Ar-H; J=7.60 Hz), 7.18 (d, 2H, Ar-H; J=8.00 Hz), 7.29 (d, 1H, Ar-H; J=8.40 Hz), 7.61-7.62 (m, 1H, Ar-H), 7.70-7.73 (m, 3H, Ar-H), 8.13-8.14 (m, 1H, Ar-H), 9.61 (s, 1H, N=CH), 11.94 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 20.52 (PhCH₃), 30.74 (CH₂Ph), 56.21 (OCH₃), 112.79, 113.10, 120.45, 121.18, 126.53, 128.53, 128.66 (2C), 128.91 (2C), 132.74, 135.68, 138.93, 142.63, 148.76, 153.51 (Ar-C), 146.33 (triazole C₅), 151.28 (triazole C₃), 152.31 (N=CH), 155.63 (COO).
3-p-Methoxybenzyl-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3f)

Yield: 90.41%, m.p. 218 °C. IR (KBr, ν cm⁻¹): 3171 (NH), 1746, 1690 (C=O), 1586 (C=N), 1508, 1436 (C=C), 1266 (COO), 1176 (C-O, furan), 809 (1,4-disubstituted benzene ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 3.68 (s, 3H, OCH₃), 3.85 (s, 3H, OCH₃), 3.97 (s, 2H, CH₂Ph), 6.81-6.85 (m, 3H, Ar-H), 7.30 (d, 1H, Ar-H; J=8.40 Hz), 7.61 (m, 1H, Ar-H), 7.71-7.75 (m, 3H, Ar-H), 8.13 (m, 1H, Ar-H), 9.61 (s, 1H, N=CH), 11.90 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 30.23 (CH₂Ph), 54.95 (OCH₃), 56.22 (OCH₃), 112.79, 113.14, 113.79 (2C), 120.45, 121.24, 126.51, 127.60, 128.18, 129.87 (2C), 138.94, 142.62, 148.76, 153.52, 158.05 (Ar-C), 146.52 (triazole C₃), 151.26 (triazole C₅), 152.47 (N=CH), 155.63 (COO).

3-p-Chlorobenzyl-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3g)

Yield: 97.28%, m.p. 226 °C. IR (KBr, ν cm⁻¹): 3124 (NH), 1747, 1702 (C=O), 1598 (C=N), 1514, 1470 (C=C), 1274 (COO), 1172 (C-O, furan), 826 (1,4-disubstituted benzene ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 3.85 (s, 3H, OCH₃), 4.06 (s, 2H, CH₂Ph), 6.82 (dd, 1H, Ar-H; J=7.60 Hz, 1.60 Hz), 7.28-7.34 (m, 5H, Ar-H), 7.60-7.61 (m, 1H, Ar-H), 7.68-7.73 (m, 3H, Ar-H), 8.12-8.13 (m, 1H, Ar-H), 9.62 (s, 1H, N=CH), 11.95 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 30.39 (CH₂Ph), 56.22 (OCH₃), 112.79, 113.12, 120.45, 121.21, 126.44, 128.28 (3C), 130.76 (2C), 131.36, 134.82, 138.94, 142.62, 148.76, 153.55 (Ar-C), 145.88 (triazole C₃), 151.23 (triazole C₅), 152.53 (N=CH), 155.62 (COO).

3-m-Chlorobenzyl-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3h)

Yield: 89.04%, m.p. 208 °C. IR (KBr, ν cm⁻¹): 3152 (NH), 1736, 1702 (C=O), 1590 (C=N), 1513, 1473 (C=C), 1276 (COO), 1161 (C-O, furan), 863, 756 and 709 (1,3-disubstituted benzene ring), 817 (1,4-disubstituted benzene ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 3.85 (s, 3H, OCH₃), 4.08 (s, 2H, CH₂Ph), 6.81-6.83 (m, 1H, Ar-H), 7.24-7.33 (m, 4H, Ar-H), 7.43 (m, 1H, Ar-H), 7.59-7.60 (m, 1H, Ar-H), 7.68-7.72 (m, 3H, Ar-H), 8.12-8.13 (m, 1H, Ar-H), 9.60 (s, 1H, N=CH), 11.90 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 30.72 (CH₂Ph), 56.23 (OCH₃), 112.77, 113.08, 120.40, 120.92, 126.44, 126.67, 127.51, 128.50, 129.04, 130.18, 132.88, 138.23, 138.99, 142.65, 148.73, 153.59 (Ar-C), 148.73 (triazole C₃), 151.22 (triazole C₅), 152.49 (N=CH), 155.59 (COO).

3-Phenyl-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3i)

Yield: 97.50%, m.p. 227 °C. IR (KBr, ν cm⁻¹): 3149 (NH), 1744, 1704 (C=O), 1609 (C=N), 1512, 1467 (C=C), 1272 (COO), 1180 (C-O, furan), 834 (1,4-disubstituted benzene ring) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 3.86 (s, 3H, OCH₃), 6.81 (dd, 1H, ArH; J=3.60 Hz, 1.60 Hz), 7.34 (d, 1H, Ar-H; J=8.80 Hz), 7.51 (d, 2H, Ar-H; J=2.4 Hz), 7.52 (d, 1H, Ar-H; J=1.6 Hz), 7.59 (d, 1H, Ar-H; J=4.00 Hz), 7.69 (d, 1H, Ar-H; J=2.00 Hz), 7.79 (dd, 1H, ArH; J=8.80 Hz, 2.00 Hz), 7.88-7.90 (m, 2H, Ar-H), 8.12 (d, 1H, Ar-H; J=2.40 Hz), 9.56 (s, 1H, N=CH), 12.36 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-d₆): δ 56.27 (OCH₃), 112.78, 113.34, 120.48, 121.80, 126.20, 126.70, 127.86 (2C), 128.04, 128.50 (2C), 130.06, 138.93, 142.58, 144.54, 151.37 (Ar-C), 148.74 (triazole C₃), 153.75 (N=CH), 155.57 (triazole C₅), 156.17 (COO).

Results and Discussion

In this study, the structures of nine new 3-alkyl(aryl)-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-ones (3a-i) were characterized with IR, ¹H NMR and ¹³C NMR spectral data.

References


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