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Synthesis of Some Novel 3-Alkyl(Aryl)-4-[3-(2-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1*H*-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) compunds were synthesized from a reaction of type 1 compunds 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-1*H*-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 diaminobenzedine 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 mesoprous SBA-15 which was modified by Fe_3O_4 nanoparticles removes Ce (III) ions from aqueous solutions in less than one minute (Dashtian 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-1*H*-1,2,4-triazol-5-ones (**3a-i**) were synthesized from the reactions of 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones (**1a-i**) and 3-(2-furylcarbonyloxy)-4-methoxybenzaldehyde (2) (Scheme 1).

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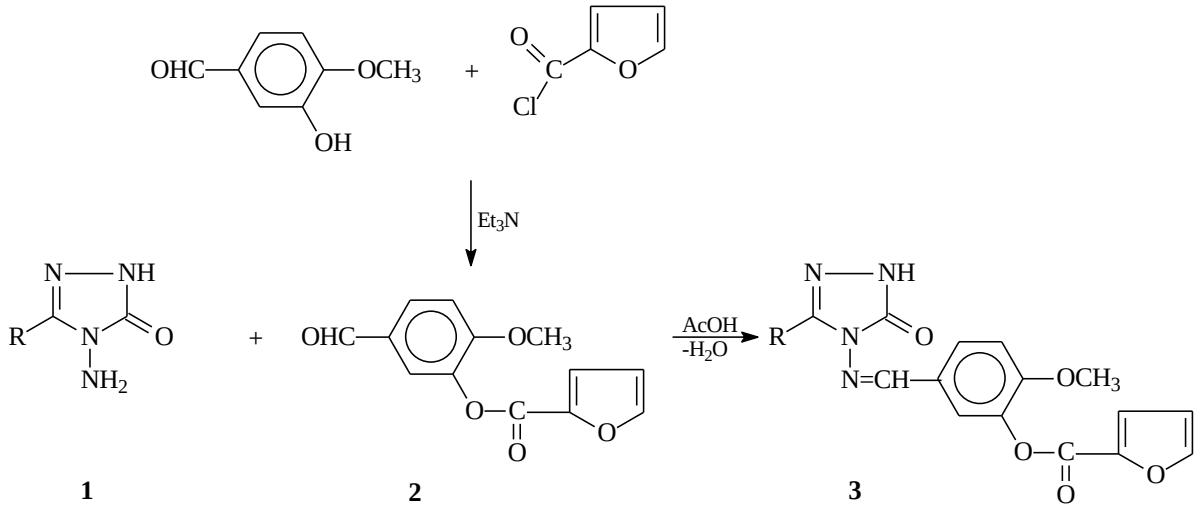

1 **2** **3**

1, 3	**R**
a	CH_3
b	CH_2CH_3
c	$CH_2CH_2H_3$
d	$CH_2C_6H_5$
e	$CH_2C_6H_4.CH_3$ (*p*-)
f	$CH_2C_6H_4.OCH_3$ (*p*-)
g	$CH_2C_6H_4.Cl$ (*p*-)
h	$CH_2C_6H_4.Cl$ (*m*-)
i	C_6H_5

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 ve 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): δ 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, 02.00 Hz), 8.12 (s, 1H, Ar-H), 9.70 (s, 1H, CHO). ^{13}C NMR (100 MHz, DMSO-d_6): δ 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-furylcarbonyloxy)-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-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one **3** as colorless crystals.

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

Yield: 97.22%, m.p. 221 °C. IR (KBr, υ, 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-furylcarbonyloxy)-4-methoxy-benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one (3b)

Yield: 75.44%, m.p. 192 °C. IR (KBr, υ, 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}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.20 (t, 3H, CH_3; *J*=7.60 Hz), 2.68 (q, 2H, CH_2; *J*=7.60 Hz), 3.86 (s, 3H, OCH_3), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 10.00 (CH_3), 18.45 (CH_2), 56.22 (OCH_3), 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 C_3), 152.79 (N=CH), 153.53 (triazole C_5), 155.61 (COO).

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

Yield: 72.60%, m.p. 199 °C. IR (KBr, υ, 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}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.06 (t, 3H, $CH_2CH_2\underline{CH_3}$; *J*=7.60 Hz), 1.68 (sext., 2H, $CH_2\underline{CH_2}CH_3$; *J*=7.60 Hz), 2.64 (t, 2H, $\underline{CH_2}CH_2CH_3$; *J*=7.60 Hz), 3.86 (s, 3H, OCH_3), 6.81 (dd, 1H, Ar-H; *J*=8.00 Hz, 1.60 Hz), 7.31 (d, 1H, Ar-H, *J*=8.80 Hz), 7.60 (m, 1H, ArH), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.42 ($CH_2CH_2\underline{CH_3}$), 18.82 ($CH_2\underline{CH_2}CH_3$), 26.62 ($\underline{CH_2}CH_2CH_3$) 56.22 (OCH_3), 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 C_3), 151.35 (triazole C_5), 152.90 (N=CH), 155.60 (COO).

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

Yield: 99.26%, m.p. 207 °C. IR (KBr, υ, 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}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 4.05 (s, 2H, CH_2Ph), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 31.08 (CH_2Ph), 56.22 (OCH_3), 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 C_3), 151.25 (triazole C_5), 152.48 (N=CH), 155.63 (COO).

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

Yield: 99.29%, m.p. 214 °C. IR (KBr, υ, 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}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.21 (s 3H, $PhCH_3$), 3.85 (s, 3H, OCH_3), 3.99 (s, 2H, CH_2Ph), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.52 ($PhCH_3$), 30.74 (CH_2Ph), 56.21 (OCH_3), 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 C_3), 151.28 (triazole C_5), 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, υ, 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 benzenoid ring) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.68 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.97 (s, 2H, CH_2Ph), 6.81-6.85 (m, 3H, Ar-H), 7.20-7.23 (m, 2H, 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.23 (CH_2Ph), 54.95 (OCH_3), 56.22 (OCH_3), 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 C_3), 151.26 (triazole C_5), 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, υ, 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 benzenoid ring) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 4.06 (s, 2H, CH_2Ph), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.39 (CH_2Ph), 56.22 (OCH_3), 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 C_3), 151.23 (triazole C_5), 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, υ, 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 benzenoid ring), 817 (1,4-disubstituted benzenoid ring) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 4.08 (s, 2H, CH_2Ph), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.72 (CH_2Ph), 56.23 (OCH_3), 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 C_3), 151.22 (triazole C_5), 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, υ, 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 benzenoid ring) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.86 (s, 3H, OCH_3), 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). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.27 (OCH_3), 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 C_3), 153.75 (N=CH), 155.57 (triazole C_5), 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-1*H*-1,2,4-triazol-5-ones (**3a-i**) were characterized with IR, ^{1}H NMR and ^{13}C NMR spectral data.

References

Ali, K. A., Ragab, E. A., Farghaly, T. A., & Abdalla, M. M. (2011). Synthesis of new functionalized 3-substituted [1,2,4]triazolo [4,3-a]pyrimidine derivatives: potential antihypertensive agents. *Acta Poloniae Pharmaceutica*, *68*(2), 237–47. Retrieved from

http://www.ncbi.nlm.nih.gov/pubmed/21485297

Chen, X., Shi, Y. M., Huang, C., Xia, S., Yang, L. J., & Yang, X. D. (2016). Novel dibenzo[b,d]furan–1H-1,2,4-triazole derivatives: Synthesis and antitumor activity. *Anti-Cancer Agents in Medicinal Chemistry*, *16*(3), 377–386. http://doi.org/10.2174/1871520615666150817115913

Chidananda, N., Poojary, B., Sumangala, V., Kumari, N. S., Shetty, P., & Arulmoli, T. (2012). Facile synthesis, characterization and pharmacological activities of 3,6-disubstituted 1,2,4-triazolo[3,4-b][1,3,4]thiadiazoles and 5,6-dihydro-3,6-disubstituted-1,2,4-triazolo[3,4-b][1,3,4]thiadiazoles. *European Journal of Medicinal Chemistry*, *51*, 124–136. http://doi.org/10.1016/j.ejmech.2012.02.030

Dashtian, K., Zare-Dorabei, R. (2017). Synthesis and characterization of functionalized mesoprous SBA-15 decorated with Fe_3O_4 nanoparticles for removal of Ce(III) ions from aqueous solution: ICP-OES detection and central composite design optimization. *Journal of Colloid and Interface Science*, 494 114-123. http://dx.doi.org/10.1016/j.jcis.2017.01.072

El-Serwy, W. S., Mohamed, N. A., Abbas, E. M., & Abdel-Rahman, R. F. (2013). Synthesis and anti-inflammatory properties of novel 1,2,4-triazole derivatives. *Research on Chemical Intermediates*, *39*(6), 2543–2554. http://doi.org/10.1007/s11164-012-0781-9

Kumar, M., Kumar, A., Singh, M.K., Sahu, S.K., John, R.P. (2017). A novel benzidine based Schiff base "turn-on" fluorescent chemosensor for selective recognition of Zn^{2+}. *Sensors and Actuators B: Chemical*, 241, 1218-1223. http://dx.doi.org/10.1016/j.snb.2016.10.008

Uzgören-Baran, A., Tel, B. C., Sargöl, D., Öztürk, E. I., Kazkayas, I., Okay, G., Ertan, M., Tozkoparan, B. (2012). Thiazolo[3,2-b]-1,2,4-triazole-5(6H)-one substituted with ibuprofen: Novel non-steroidal anti-inflammatory agents with favorable gastrointestinal tolerance. *European Journal of Medicinal Chemistry*, *57*, 398–406. http://doi.org/10.1016/j.ejmech.2012.07.009

Zhang, F., Wen, Q., Wang, S. F., Shahla Karim, B., Yang, Y. S., Liu, J. J., Zhang, W. M., Zhu, H. L. (2014). Design, synthesis and antibacterial activities of 5-(pyrazin-2-yl)-4H-1,2,4-triazole-3-thiol derivatives containing Schiff base formation as FabH inhibitory. *Bioorganic & Medicinal Chemistry Letters*, *24*(1), 90–95. http://doi.org/10.1016/J.BMCL.2013.11.079

Zhang, S., Wu, X., Niu, Q., Guo, Z., Li, T., Liu, H. (2017). Highly selective and sensitive colorimetric and fluorescent chemosensor for rapid detection of Ag^{+}, Cu^{2+} and Hg^{2+} based on a simple Schiff base. *Journal of Fluorescence*, 27 729-737. http://doi.org/10.1007/s10895-016-2005-y

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