*Molecules* **2005**, *10*, 961-970

*molecules*

**ISSN 1420-3049**
http://www.mdpi.org

# Synthesis and Non-Aqueous Medium Titrations of Some New 4-Benzylidenamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one Derivatives

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*Received: 26 August 2004; in revised form: 9 April 2005 / Accepted: 10 April 2005 / Published: 31 August 2005*

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**Abstract:** The synthesis of 3-alkyl(aryl)-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones **3** from the reactions of 3-alkyl(aryl)-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-ones **2** with 3-ethoxy-4-hydroxybenzaldehyde is described. The acetylation and methylation reactions of the compounds **3** giving compounds of type **4** and **5**, respectively, were investigated. The newly synthesized compounds were characterized using elemental analyses and IR, $^{1}$H-NMR, $^{13}$C-NMR and UV spectral data. In addition, to investigate the effects of solvents and molecular structure upon acidity, compounds **3** were titrated potentiometrically with tetrabutylammonium hydroxide in four non-aqueous solvents (isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N,N*-dimethylformamide). The half-neutralization potential values and the corresponding p$K_a$ values were determined for all cases.

**Keywords:** 4,5-Dihydro-1*H*-1,2,4-triazol-5-one, Schiff base, acidity, potentiometric titrations, methylation, acetylation.

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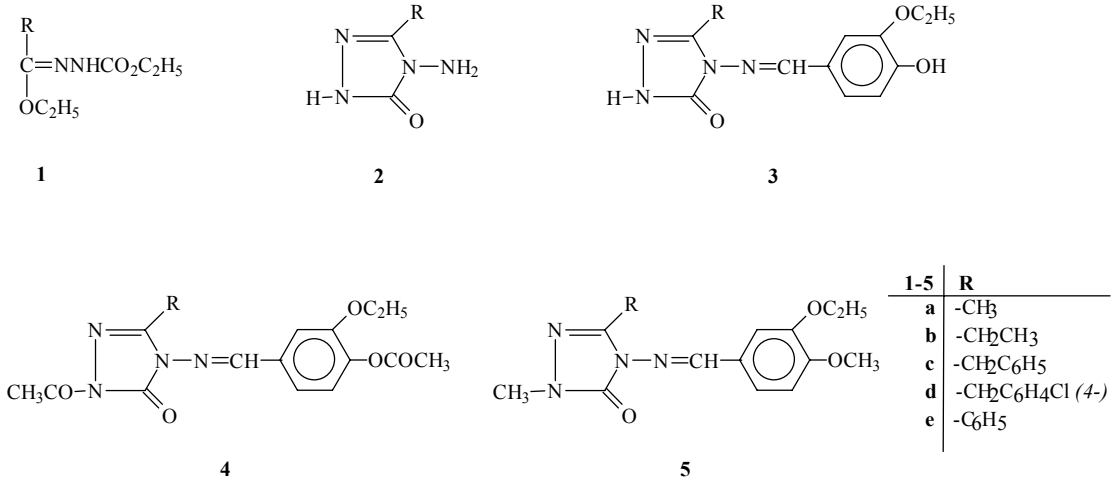
## Introduction

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 such as antifungal, antimicrobial, hypoglycemic, antihypertensive, analgesic, antiparasitic, hypocholesteremic, antiviral, anti-inflammatory, antitumor and anti-HIV properties [1-13]. 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 [12-16]. The acetylation and methylation of 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives have also been reported [11,15-17].

On the other hand, it is known that 1,2,4-triazole and 4,5-dihydro-1*H*-1,2,4-triazol-5-one rings have weak acidic properties, so some 1,2,4-triazole and 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives were titrated potentiometrically with tetrabutylammonium hydroxide in non-aqueous solvents, and the corresponding p$K_a$ values of the compounds were determined [15,16,18-22].

This paper describes the synthesis of a series of 3-alkyl(aryl)-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones **3** from the reactions of 3-alkyl(aryl)-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-ones **2** with 3-ethoxy-4-hydroxybenzaldehyde. Moreover, the reactions of compounds **3** with acetic anhydride and NaOH/dimethyl sulphate were investigated, and compounds of types **4** and **5**, respectively, were thus prepared (Scheme 1). Furthermore, we also examined the potentiometric titrations of the synthesized compounds **3a-3e** with tetrabutylammonium hydroxide (TBAH) in four non-aqueous solvents (isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N,N*-dimethylformamide} to determine the corresponding half-neutralization potentials (HNP) and the corresponding p$K_a$ values. The data obtained from the potentiometric titrations were interpreted and the effects of molecular structure and solvents were studied [15,16,18-23].

**Scheme 1**



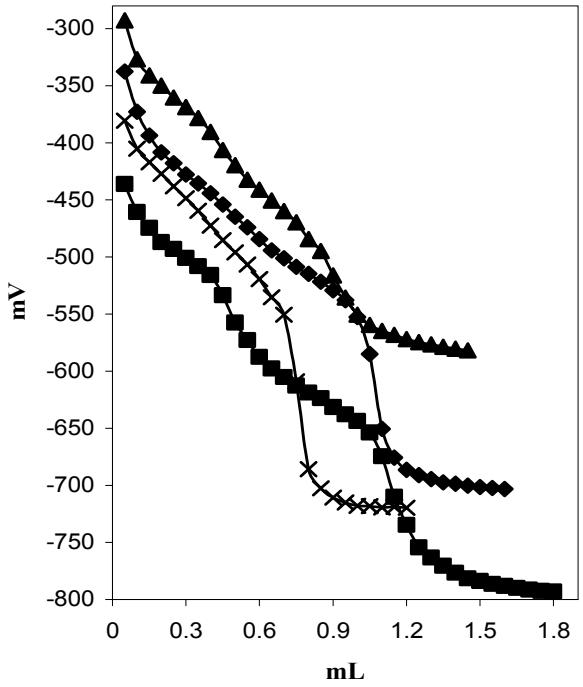

## Results and Discussion

In this study, the structures of five new 3-alkyl(aryl)-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones, **3a-e**, four new 1-acetyl-3-alkyl(aryl)-4-(3-ethoxy-4-acetoxy-benzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones, **4a-c** and **e**, and two new 1-methyl-3-alkyl-(aryl)-4-(3-ethoxy-4-methoxybenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazol-5-ones, **5c,e**, were

identified using elemental analysis and IR, $^{1}$H-, $^{13}$C-NMR and UV spectral data, and the observed spectral values were seen to be compatible with literature values [11-16,25].

After the potentiometric titrations of compounds **3** with TBAH in non-aqueous solvents, the mV values from each titration were plotted against TBAH volumes used (mL) and the potentiometric titration curves were obtained for all the cases. From the titration curves, the HNP values and the corresponding p$K_a$ values were obtained. As an example, the potentiometric titration curves for 0.001 M solutions of 3-(4-chloro-benzyl)-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one (**3d**) titrated with 0.05 N TBAH in isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N,N*-dimethylformamide are presented in Figure 1.

**Figure 1.** Potentiometric titration curves of 0.001 M solutions of compound **3d** titrated with 0.05 M TBAH in isopropyl alcohol (▲), *tert*-butyl alcohol (×), acetonitrile (◆) and *N,N*-dimethylformamide (■) at 25°C.




The half-neutralization potential (HNP) values and the corresponding p$K_a$ values of compounds **3a-3e**, obtained from the potentiometric titrations with 0.05 M TBAH in isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N,N*-dimethylformamide, are presented in Tables 1-4.

**Table 1.** The half-neutralization potentials (HNP) and the corresponding p$K_a$ values of compounds **3a-3e** in isopropyl alcohol at 25 °C.

| Compd. no | $HNP_1$ (mV) | p$Ka_1$ | $HNP_2$ (mV) | p$Ka_2$ |
|---|---|---|---|---|
| **3a** | -363 | 13.22 | -495 | - |
| **3b** | -367 | 13.92 | - | - |
| **3c** | -369 | 13.78 | -474 | - |
| **3d** | -355 | 13.63 | -460 | 16.00 |
| **3e** | -344 | 12.85 | -449 | 14.98 |

**Table 2.** The half-neutralization potentials (HNP) and the corresponding p$K_a$ values of compounds **3a-3e** in *tert*-butyl alcohol at 25 °C.

| Compd. no | $HNP_1$ (mV) | p$Ka_1$ | $HNP_2$ (mV) | p$Ka_2$ |
|---|---|---|---|---|
| **3a** | -384 | 13.65 | -501 | - |
| **3b** | -443 | 15.62 | -558 | - |
| **3c** | -416 | 14.00 | -544 | - |
| **3d** | -472 | - | - | - |
| **3e** | -448 | 14.96 | - | - |

**Table 3.** The half-neutralization potentials (HNP) and the corresponding p$K_a$ values of compounds **3a-3e** in acetonitrile at 25 °C.

| Compd. no | $HNP_1$ (mV) | p$Ka_1$ | $HNP_2$ (mV) | p$Ka_2$ |
|---|---|---|---|---|
| **3a** | -441 | 15.41 | -536 | - |
| **3b** | -493 | 15.63 | - | - |
| **3c** | -482 | - | -578 | - |
| **3d** | -474 | 15.28 | - | - |
| **3e** | -507 | - | - | - |

**Table 4.** The half-neutralization potentials (HNP) and the corresponding p$K_a$ values of compounds **3a-3e** in *N,N*-dimethylformamide at 25 °C.

| Compd. no | $HNP_1$ (mV) | p$Ka_1$ | $HNP_2$ (mV) | p$Ka_2$ |
|---|---|---|---|---|
| **3a** | -503 | - | - | - |
| **3b** | -496 | - | -655 | - |
| **3c** | -499 | - | -628 | - |
| **3d** | -493 | - | -621 | - |
| **3e** | -536 | - | - | - |

The *p*H of weak acids can be calculated using the following equation:

$$pH = pK_a + \log[A^-] / [HA]$$

where $pH = pK_a$ when $[A^-]$ is equal to [HA] at the half-neutralization points. Therefore, the *p*H values at the half-neutralization points were taken as $pK_a$. Taking into consideration the dielectric permittivity of the solvents, the acidity ranking might be expected to be as follows: *N,N*-dimethylformamide (ε=37) > acetonitrile (ε=36) > isopropyl alcohol (ε=19.4) > *tert*-butyl alcohol (ε=12). However, as seen in Tables **1-4**, the observed acidity ranking for all compounds is isopropyl alcohol > *tert*-butyl alcohol > acetonitrile > *N,N*-dimethylformamide. This result thus matches the theoretical arrangement, except for acetonitrile and *N,N*-dimethylformamide. In *N,N*-dimethylformamide, all these compounds show the weakest acidic properties, but they show the strongest acidic properties in isopropyl alcohol. This situation may be attributed to the hydrogen bonding between the negative ions formed and the solvent molecules in the amphiprotic neutral solvents.

As seen Scheme 1, there is one weak acidic N-H group in the 4,5-dihydro-1H-1,2,4-triazol-5-one ring and one phenolic group on the aryl substituent in compounds **3a-3e**. Thus, these compounds give two end-points as well as two half-neutralization potential (HNP) values. Thus, as expected, the potentiometric titration curves for these compounds **3a-3e** titrated with TBAH in isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N,N*-dimethylformamide resemble the titration curves for diprotic acids.

For compound **3b** in isopropyl alcohol, compounds **3d** and **3e** in *tert*-butyl alcohol, compounds **3b**, **3d** and **3e** in acetonitrile and compounds **3a** and **3e** in *N,N*-dimethylformamide, the second half-neutralization potential ($HNP_2$) values and the corresponding p$K_a$ values have not been obtained. In addition, the p$K_a$ values bigger than 16.00 have not been determined due to the fact that this value is outside the range of the pH meter.

As it is well known, the acidity of a compound depends on several factors. The two most important ones are the solvent effect and molecular structure [15,16,18-23]. Tables 1-4 and Figure 1 show that the HNP values and corresponding p$K_a$ values obtained from the potentiometric titrations depend on the non-aqueous solvents used and the substituents at C-3 in 4,5-dihydro-1*H*-1,2,4-triazol-5-one ring.

## Experimental

### *General*

Melting points were taken on a Electrothermal 9100 digital melting point apparatus and are uncorrected. IR spectra were registered on a Perkin-Elmer 1600 FTIR spectrometer. $^1$H-NMR and $^{13}$C-NMR spectra were recorded in deuterated dimethyl sulfoxide with TMS as internal standard on a Varian Mercury 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 Shimadzu UV-1201 spectrophotometer. In this study, a Jenway 3040 ion analyser pH meter equipped with an Ingold pH electrode was used for potentiometric titrations. For each compound titrated, a 0.001 M solution was separately prepared in each non-aqueous solvent. A 0.05 M solution of TBAH in isopropyl alcohol, which is widely used in the titration of acids, was used as titrant. The mV values obtained on the pH meter were recorded. Finally, the half-neutralization potential (HNP) values were determined by plotting the volume (mL) (TBAH)-mV graph. The starting compounds **2a-e** were prepared from the reactions of the corresponding ester ethoxycarbonylhydrazones **1a-e** with an aqueous solution of hydrazine hydrate as described in the literature [17,24].

### *General Method for the Preparation of 3-Alkyl(aryl)-4-(3-ethoxy-4-hydroxy-benzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones* **3a-e**.

The corresponding compound 2 (0.01 mole) was dissolved in acetic acid (15 mL) and treated with 3-ethoxy-4-hydroxybenzaldehyde (1.66 g, 0.01 mole). The mixture was refluxed for 1 h and then evaporated at 50-55 °C *in vacuo*. Several recrystallizations of the residue from an appropriate solvent (AcOH-$H_2O$, 1:3) gave pure compounds **3a-e** as colourless crystals.

*3-Methyl-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**3a**). Yield 67%; mp. 205 °C; Calculated for $C_{12}H_{14}N_4O_3$ (262.27): 54.96% C, 5.38% H, 21.36% N; found: 54.96% C, 5.29% H, 21.07% N; $^1$H-NMR: δ 1.40 (t, 3H, $CH_3$), 2.30 (s, 3H, $CH_3$), 4.11 (q, 2H, $CH_2$), 6.92 (d, 1H, Ar-H), 7.23 (d, 1H, Ar-H), 7.41 (s, 1H, Ar-H), 9.54 (s, 1H, N=CH), 9.79 (s, 1H, OH), 11.81 (s,1H, NH); $^{13}$C-NMR: δ 11.12, 14.61, 63.77 (aliphatic carbons), 111.17, 115.60, 122.49, 124.67, 144.17, 151.30 (aromatic carbons), 147.12 (triazole $C_3$), 150.30 (N=CH), 154.73 (triazole $C_5$); IR: 3529 (OH), 3162 (NH), 1716 (C=O), 1597 (C=N) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 320 (18262), 235 (11377), 212 (14098) nm.

*3-Ethyl-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**3b**). Yield 79%; mp. 174 °C; Calculated for $C_{13}H_{16}N_4O_3$ (276.30): 54.51% C, 5.84% H, 20.28% N; found: 54.38% C, 5.38% H, 19.70% N; $^1$H-NMR: δ 1.16 (t, 3H, $CH_3$), 1.32 (t, 3H, $CH_3$), 2.61 (q, 2H, $CH_2$), 4.02 (q, 2H, $OCH_2$), 6.86 (d, 1H, Ar-H, *J*=8.1 Hz), 7.20 (d, 1H, Ar-H, *J*=8.2 Hz), 7.32 (s, 1H, Ar-H), 9.46 (s, 1H, N=CH), 9.69 (s, 1H, OH), 11.76 (s, 1H, NH); $^{13}$C-NMR: δ 9.90, 14.61, 18.54, 63.78 (aliphatic carbons), 111.18, 115.63, 122.39, 124.79, 147.96, 151.49 (aromatic carbons), 147.13 (triazole $C_3$), 150.32 (N=CH), 154.64 (triazole $C_5$); IR: 3527 (OH), 3222 (NH), 1701 (C=O), 1597 (C=N) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 321 (27690), 235 (17345), 213 (22069) nm.

*3-Benzyl-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**3c**). Yield 91%; mp. 211 °C; Calculated for $C_{18}H_{18}N_4O_3$ (338.37): 63.89% C, 5.36% H, 16.56% N; found: 63.66% C, 5.74% H, 16.22% N; $^1$H-NMR: δ 1.44 (t, 3H, $CH_3$), 4.09 (s, 2H, $CH_2$Ph), 4.11 (q, 2H, $CH_2$), 6.92 (d, 1H, Ar-H, *J*=8.0 Hz), 7.25 (d, 1H, Ar-H, *J*=8.1 Hz), 7.36 (s, 5H, Ar-H), 7.38 (s, 1H, Ar-H), 9.53 (s, 1H, N=CH), 9.93 (s, 1H, OH), 12.02 (s, 1H, NH); $^{13}$C-NMR: δ 14.57, 31.20, 63.63 (aliphatic carbons), 110.30, 115.45, 122.85, 124.70, 126.61, 128.36 (2C), 128.66 (2C), 135.85, 146.05, 151.20 (aromatic carbons), 147.08 (triazole $C_3$), 150.30 (N=CH), 153.90 (triazole $C_5$); IR: 3165 (OH), 3055 (NH), 1712 (C=O), 1584 (C=N), 755, 699 (monosubstituted benzenoid ring) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 265 (16250), 221 (29650) nm.

*3-(4-Chlorobenzyl)-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**3d**). Yield 71%; mp. 232 °C; Calculated for $C_{18}H_{17}N_4O_3Cl$ (373.82): 57.99% C, 4.60% H, 15.03% N; found: 57.29% C, 4.36% H, 14.79% N; $^1$H-NMR: δ 1.42 (t, 3H, $CH_3$), 4.08 (s, 2H, $CH_2$Ph), 4.09 (q, 2H, $CH_2$), 6.92 (d, 1H, Ar-H), 7.24 (d, 1H, Ar-H), 7.30-7.55 (m, 5H, Ar-H), 9.52 (s, 1H, N=CH), 9.92 (s, 1H, OH), 12.02 (s, 1H, NH); $^{13}$C-NMR: δ 14.57, 30.80, 63.63 (aliphatic carbons), 110.31, 115.46, 122.89, 124.59, 128.57 (2C), 130.54 (2C), 131.45, 134.88, 145.80, 151.30 (aromatic carbons), 147.10 (triazole $C_3$), 150.28 (N=CH), 153.98 (triazole $C_5$); IR: 3170 (OH), 3110 (NH), 1712 (C=O), 1587 (C=N), 805 (1,4-disubstituted benzenoid ring) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 357 (5794), 321 (18320), 213 (28038) nm.

*3-Phenyl-4-(3-ethoxy-4-hydroxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**3e**). Yield 82%; mp. 206 °C (AcOH-water, 1:3); Calculated for $C_{17}H_{16}N_4O_3$ (324.34): 62.95% C, 4.97% H, 17.27% N; found: 62.43% C, 4.95% H, 16.90% N. $^1$H-NMR: δ 1.41 (t, 3H, $CH_3$), 4.11 (q, 2H, $CH_2$), 6.97 (d, 1H, Ar-H, *J*=8.2 Hz), 7.32 (d, 1H, Ar-H, *J*=8.3 Hz), 7.42 (s, 1H, Ar-H), 7.56-7.60 (m, 3H, Ar-H), 7.95-8.05 (m, 2H, Ar-H), 9.48 (s, 1H, N=CH), 9.89 (s, 1H, OH), 12.42 (s, 1H, NH); $^{13}$C-NMR: δ

14.54, 63.63 (aliphatic carbons), 111.10, 115.70, 122.80, 124.48, 126.85, 127.76 (2C), 128.39 (2C), 130.00, 144.40, 151.40 (aromatic carbons), 147.09 (triazole $C_3$), 150.55 (N=CH), 157.30 (triazole $C_5$); IR: 3373 (OH), 3076 (NH), 1701 (C=O), 1607,1584 (C=N), 758,680 (monosubstituted benzenoid ring) $cm^{-1}$; UV $\lambda_{max}$ (ε, $L \cdot mol^{-1} \cdot cm^{-1}$) : 325 (17886), 282 (12032), 215 (21952) nm.

*General Method for the Preparation of 1-Acetyl-3-alkyl(aryl)-4-(3-ethoxy-4-acetoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones* **4a-c** and **e**.

The corresponding compound **3** (0.01 mol) was refluxed with acetic anhydride (15 mL) for 0.5 h. After addition of absolute ethanol (50 mL), the mixture was refluxed for 1 h. more. Evaporation of the resulting solution at 40-45 °C *in vacuo* and several recrystallizations of the residue from EtOH gave pure compounds **4a-c** and **e** as colourless crystals.

*1-Acetyl-3-methyl-4-(3-ethoxy-4-acetoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**4a**). Yield 83%; mp. 189 °C; Calculated for $C_{16}H_{18}N_4O_5$ (346.34): 55.49% C, 5.24% H, 16.18% N; found: 54.98% C, 5.29% H, 16.00% N; $^1$H-NMR: δ 1.37 (t, 3H, $CH_3$), 2.33 (s, 3H, $CH_3$), 2.40 (s, 3H, $NCOCH_3$), 2.54 (s, 3H, $OCOCH_3$), 4.17 (q, 2H, $CH_2$), 7.29 (d, 1H, Ar-H), 7.54 (d, 1H, Ar-H), 7.64 (s, 1H, Ar-H), 9.60 (s, 1H, N=CH); $^{13}$C-NMR: δ 11.20, 14.41, 20.30, 23.45, 64.14 (aliphatic carbons), 112.38, 120.39, 123.51, 131.77, 142.38, 146.77 (aromatic carbons), 147.85 (triazole $C_3$), 150.52 (N=CH), 155.17 (triazole $C_5$), 166.08 (CO), 168.34 (CO); IR: 1776, 1760 (C=O), 1625, 1580 (C=N) $cm^{-1}$; UV $\lambda_{max}$ (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 306 (13788), 257 (32072), 215 (24697) nm.

*1-Acetyl-3-ethyl-4-(3-ethoxy-4-acetoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**4b**). Yield 88%; mp. 162 °C; Calculated for $C_{17}H_{20}N_4O_5$ (360.37): 56.66% C, 5.59% H, 15.55% N; found: 56.44% C, 5.46% H, 15.20% N; $^1$H-NMR: δ 1.33 (t, 3H, $CH_3$), 1.37 (t, 3H, $CH_3$), 2.34 (s, 3H, $NCOCH_3$), 2.55 (s, 3H, $OCOCH_3$), 2.81 (q, 2H, $CH_2$), 4.20 (q, 2H, $OCH_2$), 7.30 (d, 1H, Ar-H), 7.54 (d, 1H, Ar-H), 7.65 (s, 1H, Ar-H), 9.65 (s, 1H, N=CH); $^{13}$C-NMR: δ 9.35, 14.37, 18.52, 20.27, 23.43, 64.08 (aliphatic carbons), 112.34, 120.76, 123.48, 131.76, 142.34, 150.17 (aromatic carbons), 148.03 (triazole $C_3$), 150.47 (N=CH), 155.03 (triazole $C_5$), 165.96 (CO), 168.28 (CO); IR: 1776, 1766 (C=O), 1621, 1579 (C=N) $cm^{-1}$; UV $\lambda_{max}$ (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 321 (16396), 215 (32072) nm.

*1-Acetyl-3-benzyl-4-(3-ethoxy-4-acetoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**4c**). Yield 87%; mp. 173 °C; Calculated for $C_{22}H_{22}N_4O_5$ (422.44): 62.55% C, 5.25% H, 13.26% N; found: 62.20% C, 5.23% H, 12.95% N; $^1$H-NMR: δ 1.37 (t, 3H, $CH_3$), 2.31 (s, 3H, $NCOCH_3$), 2.54 (s, 3H, $OCOCH_3$), 4.12 (q, 2H, $OCH_2$), 4.17 (s, 2H, $CH_2Ph$), 7.18-7.60 (m, 8H, Ar-H), 9.55 (s, 1H, N=CH); $^{13}$C-NMR: δ 14.35, 20.26, 23.49, 31.08, 64.03 (aliphatic carbons), 111.40, 121.46, 123.42, 126.91, 128.46 (2C), 128.81 (2C), 131.73, 134.71, 142.35, 148.19 (aromatic carbons), 147.97 (triazole $C_3$), 150.42 (N=CH), 154.16 (triazole $C_5$), 165.98 (CO), 168.29 (CO); IR: 1782, 1752 (C=O), 1616, 1578 (C=N), 741, 708 (monosubstituted benzenoid ring) $cm^{-1}$; UV $\lambda_{max}$ (ε, $L \cdot mol^{-1} \cdot cm^{-1}$): 263 (15053), 215 (32368) nm.

*1-Acetyl-3-phenyl-4-(3-ethoxy-4-acetoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**4e**). Yield 99%; mp. 160 °C; Calculated for $C_{21}H_{20}N_4O_5$ (408.41): 61.76% C, 4.94% H, 13.72% N; found:

61.68% C, 4.64% H, 13.59% N; $^1$H-NMR: δ 1.36 (t, 3H, $CH_3$), 2.34 (s, 3H, $NCOCH_3$), 2.63 (s, 3H, $OCOCH_3$), 4.13 (q, 2H, $OCH_2$), 7.28 (d, 1H, Ar-H), 7.46 (d, 1H, Ar-H), 7.53-7.92 (m, 4H, Ar-H), 7.98 (m, 2H, Ar-H), 9.55 (s, 1H, N=CH); $^{13}$C-NMR: δ 14.32, 20.26, 23.51, 63.95 (aliphatic carbons), 112.08, 121.15, 123.56, 125.13, 128.56 (2C), 128.61 (2C), 131.28, 131.58, 142.50, 145.90 (aromatic carbons), 148.07 (triazole $C_3$), 150.46 (N=CH), 157.31 (triazole $C_5$), 166.18 (CO), 168.28 (CO); IR: 1768, 1743, 1723 (C=O), 1605, 1582 (C=N), 758, 692 (monosubstituted benzenoid ring) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 323 (14286), 266 (20714), 215 (30408) nm.

*General Method for the Preparation of 1-Methyl-3-alkyl(aryl)-4-(3-ethoxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones* **5c,e**.

The corresponding compound **3** (0.01 mol) was dissolved in 2N NaOH (10 mL) and treated dimethyl sulphate (3.2 mL). After stirring of the mixture at room temperature for 1 hr, the solid formed was filtered, washed with cold water (15 mL) and dried *in vacuo*. Several recrystallizations of crude product from 1:3 AcOH-water gave pure compounds **5c,e** as colourless crystals.

*1-Methyl-3-benzyl-4-(3-ethoxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**5c**). Yield 55%; mp. 198 °C; Calculated for $C_{20}H_{22}N_4O_3$ (366.42): 65.56% C, 6.05% H, 15.29% N; found: 65.99% C, 5.72% H, 15.26% N; $^1$H-NMR: δ 1.42 (t, 3H, $CH_3$), 3.42 (s, 3H, $NCH_3$), 3.87 (s, 3H, $OCH_3$), 4.11 (m, 4H, $OCH_2$ + $CH_2Ph$), 7.05-7.60 (m, 8H, Ar-H), 9.55 (s, 1H, N=CH); $^{13}$C-NMR: δ 14.81, 31.25, 32.12, 55.74, 63.81 (aliphatic carbons), 109.27, 111.64, 123.26, 125.99, 126.94, 128.65 (2C), 128.95 (2C), 135.90, 144.82, 152.05 (aromatic carbons), 148.40 (triazole $C_3$), 149.72 (N=CH), 153.88 (triazole $C_5$); IR: 1709 (C=O), 1624, 1577 (C=N), 756, 712 (monosubstituted benzenoid ring) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 323 (12195), 215 (14268) nm.

*1-Methyl-3-phenyl-4-(3-ethoxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one* (**5e**). Yield 64%; mp. 152 °C; Calculated for $C_{19}H_{20}N_4O_3$ (352.39): 64.76% C, 5.72% H, 15.90% N; found: 64.89% C, 5.94% H, 15.82% N; $^1$H-NMR: δ 1.36 (t, 3H, $CH_3$), 3.50 (s, 3H, $NCH_3$), 3.85 (s, 3H, $OCH_3$), 4.13 (q, 2H, $OCH_2$), 7.10 (d, 1H, Ar-H), 7.34 (d, 1H, Ar-H), 7.36 (s, 1H, Ar-H), 7.55 (m, 3H, Ar-H), 7.90-7.96 (m, 2H, Ar-H), 9.46 (s, 1H, N=CH); $^{13}$C-NMR: δ 14.51, 32.24, 55.47, 63.43 (aliphatic carbons), 109.59, 111.43, 122.77, 125.56, 126.14, 127.79 (2C), 128.36 (2C), 130.08, 142.66, 151.93 (aromatic carbons), 148.12 (triazole $C_3$), 149.58 (N=CH), 156.49 (triazole $C_5$); IR: 1702 (C=O), 1602, 1577 (C=N), 761, 691 (monosubstituted benzenoid ring) cm$^{-1}$; UV $\lambda_{max}$ (ε, L·mol$^{-1}$·cm$^{-1}$): 322 (10286), 280 (10529), 215 (14912) nm.

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*Sample Availability:* Contact the authors.