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## REACTIVITY OF 4-BROMOACETYL-1,2,3-TRIAZOLES TOWARDS AMINES AND PHENOLS: SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL HETEROCYCLES

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**Abstract** – The reactivity of 4-bromoacetyl-1*H*-1,2,3-triazoles towards amines and phenols was studied. Reaction of 4-bromoacetyl-1*H*-1,2,3-triazole (**1a**; R = H) with benzylamine (**2**) in the absence of any catalyst unexpectedly afforded heterocycle 2,5-bis(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)pyrazine (**4**) in 50% yield. Additionally, the reaction of **1b** (R = Br) with 4-bromoaniline and of **1c** (R = Me) or **1d** (R = NO<sub>2</sub>) with 1*H*-benzotriazole in basic media gave the expected aminoketone products **8** and **9a** or **9b** in high yields. Furthermore, the reaction of **1c** (R = Me) or **1e** (R = Cl) with phenol or β-naphthol in basic media led to the production of keto-ethers **10** or **11**, respectively in an excellent yield. Compound **10** showed the highest inhibitory effect against the growth of the tested pathogens.

## INTRODUCTION

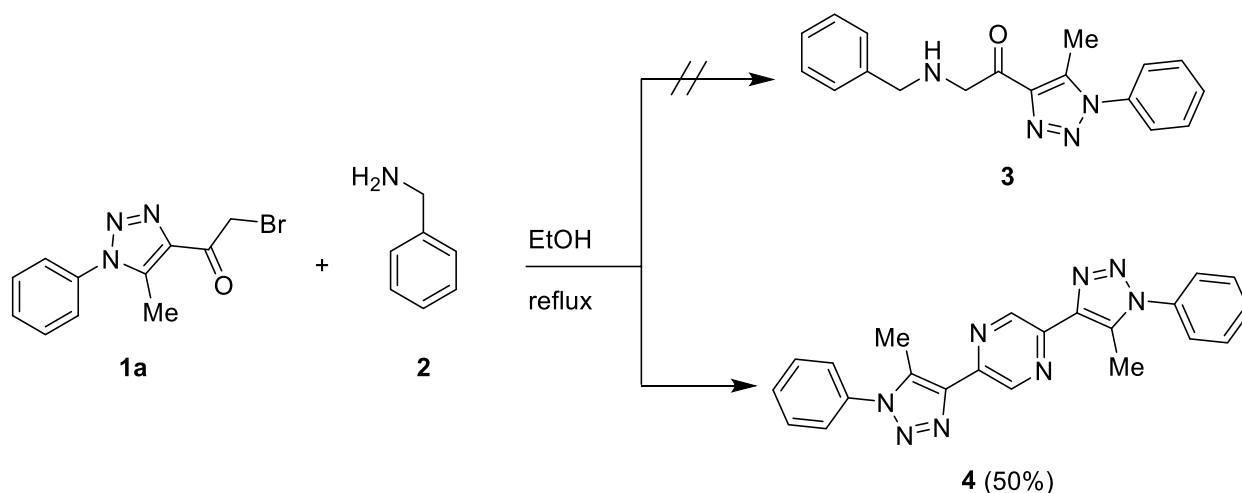
Pyrazines are a common class of heterocyclic compounds that have many applications.<sup>1</sup> The compounds are important intermediates in the total synthesis of complex derivatives, and are used in medicinal chemistry, chemical biology, materials, imaging, and dyes.<sup>2-5</sup> The synthesis of heterocycles containing pyrazine ring systems is therefore of wide interest.<sup>6-9</sup> The traditional method for the synthesis of pyrazines involves the use of 1,2-diketones in the presence of ammonia to produce the corresponding diamines or

aminoketones followed by condensation and oxidation.<sup>10–13</sup> They can also be produced using  $\alpha$ -halo- or  $\alpha$ -hydroxy-ketones,<sup>14,15</sup> 2*H*-azirines,<sup>16</sup> and nitro epoxides.<sup>17</sup>

Aminoketones have been shown to display antibacterial, antifungal, and antiviral activities<sup>18–22</sup> and are widely used as key intermediates in many organic synthesis transformations.<sup>23</sup> In addition, 1,2,3-triazole-containing heterocycles exhibit a variety of biological properties including antibacterial and antiviral activities.<sup>24–26</sup> Consequently, in continuation of our previous related work,<sup>27,28</sup> we have attempted the synthesis of novel heterocyclic compounds containing the 1,2,3-triazole ring system.

## RESULTS AND DISCUSSION

The reactivity of 4-bromoacetyl-1*H*-1,2,3-triazoles **1a–e** (**1a**: R = H, **1b**: R = Br, **1c**: R = Me, **1d**: R = NO<sub>2</sub>, and **1e**: R = Cl) towards amines and phenols has been investigated. A catalyst-free reaction between 2-bromo-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (**1a**) and benzylamine (**2**) in boiling ethanol (EtOH) afforded the unexpected product, 2,5-bis(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)pyrazine (**4**), in 50% yield rather than the expected 2-(benzylamino)-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (**3**; Scheme 1). Clearly, **2** acted as a nitrogen source to produce **4**. It should be noted that reactions of other 1*H*-1,2,3-triazoles **1b–e** and **2** failed to produce pure products.

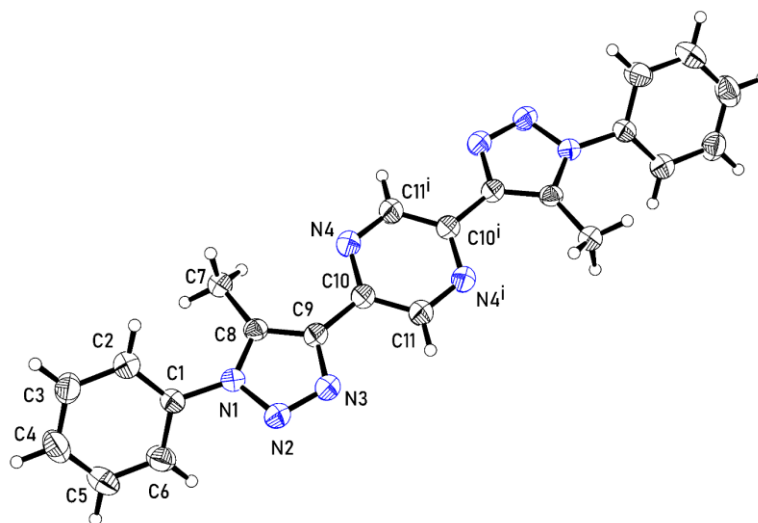


**Scheme 1.** Synthesis of **4**

The chemical structure of **4** was established by NMR spectral data and single-crystal X-ray crystallography. The <sup>1</sup>H NMR spectrum of **4** did not show the exchangeable singlet signal corresponding to the NH proton. Instead, it showed the presence of a characteristic singlet signal that appeared at 9.45 ppm corresponding to the two pyrazine protons.

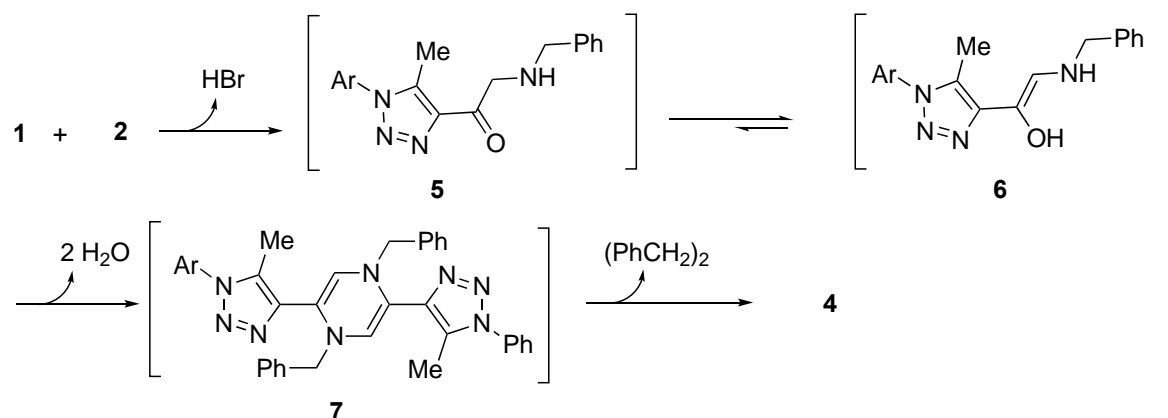
The molecule of **4** is symmetrical in the crystal structure with an inversion center located in the middle of the pyrazine ring (Figure 1). In the crystal, the methyl-triazolyl and pyrazinyl groups are coplanar with a

twist angle of  $10.2(1)^\circ$  between adjacent rings. The phenyl group is twisted further, making an angle of  $50.5(5)^\circ$  with the methyl-triazolyl group.



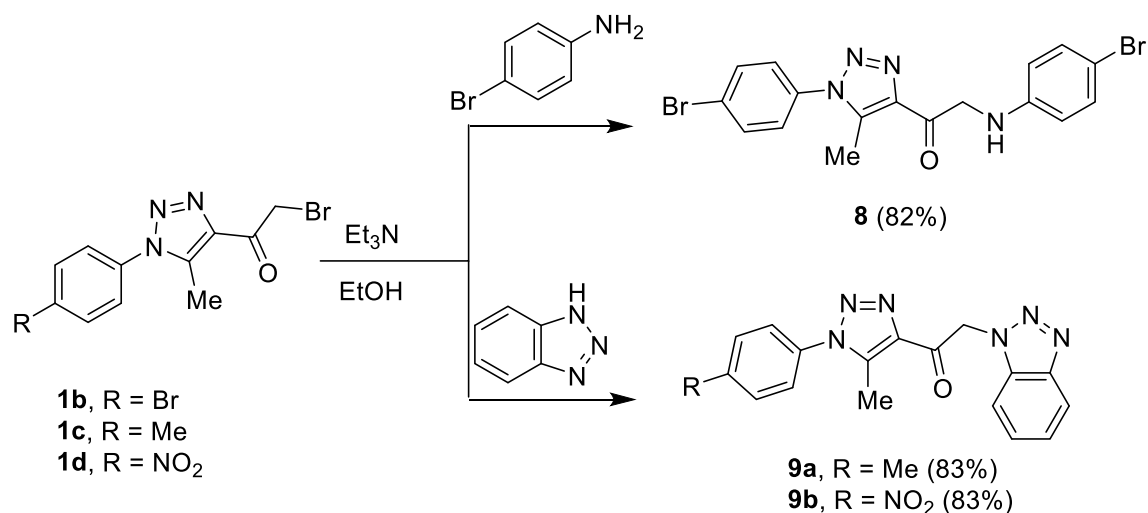
**Figure 1.** The molecule of compound **4** showing atomic displacement ellipsoids at 50% probability

A proposed mechanism for the formation of **4** is shown in Scheme 2. The formation of **4** could involve [3+3] cyclization.<sup>29–31</sup> Dehydrobromination from **1** and **2** leads to the intermediate **5**, which undergoes a dimerization reaction with the elimination of two moles of  $\text{H}_2\text{O}$  to result in the formation of the intermediate **7**. Aromatization of **7** through the elimination of two moles of benzyl fragments gives **4**. The oxidative process of benzylic C–H bonds has been reported to take place under mild conditions.<sup>32,33</sup>



**Scheme 2.** A proposed mechanism for the formation of **4**

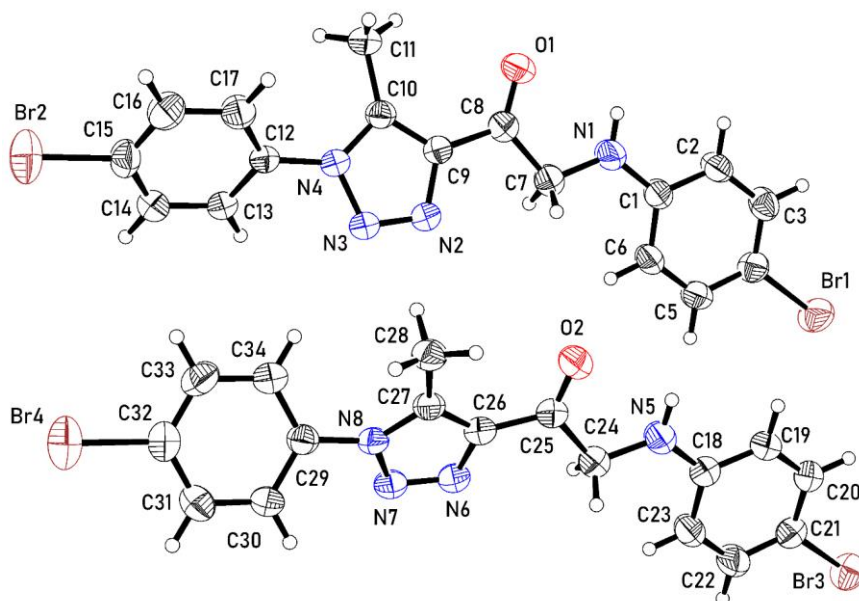
The reactivity of **1b** ( $\text{R} = \text{Br}$ ), **1c** ( $\text{R} = \text{Me}$ ) or **1d** ( $\text{R} = \text{NO}_2$ ) towards 4-bromoaniline or 1*H*-benzotriazole in boiling absolute EtOH in the presence of triethylamine ( $\text{Et}_3\text{N}$ ) was also investigated (Scheme 3). While, the reaction between **1b** and 4-bromoaniline gave **8** in 82% yield, reactions of **1c** or **1d** and 1*H*-benzotriazole under similar reaction conditions gave the corresponding **9a** or **9b**, respectively, in both 83% yields (Scheme 3).



**Scheme 3.** Synthetic routes to aminoketones **8** and **9**

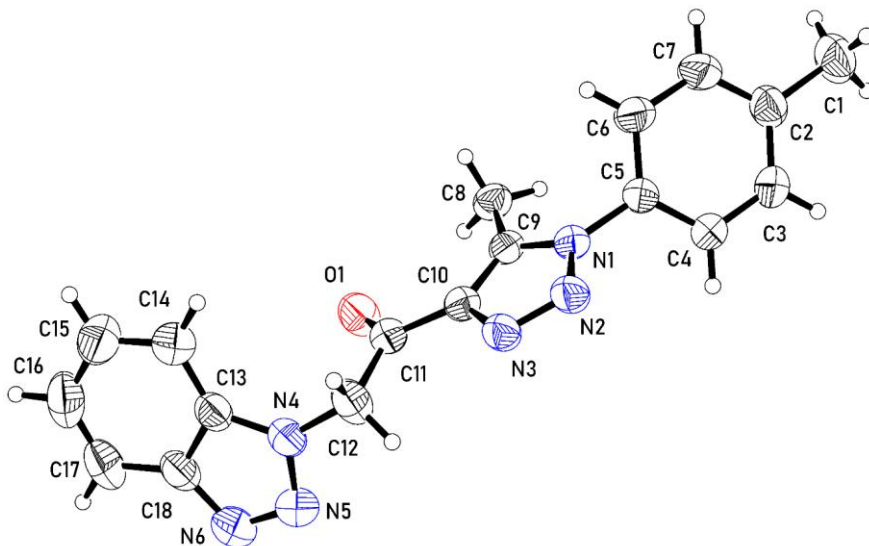
The <sup>1</sup>H NMR spectrum of **8** showed a characteristic exchangeable singlet signal at 6.23 ppm corresponding to the NH proton. The protons of the CH<sub>2</sub> group in compound **9a** appeared at 6.50 ppm in its <sup>1</sup>H NMR spectrum. The NMR spectra of **8** and **9** showed the presence of the CH<sub>2</sub> protons and carbons.

The structures of **8**, **9a**, and **9b** are shown in Figures 2, 3, and 4, respectively. The crystal structure of **8** contains two independent types of molecules with different conformations (Figure 2). In both molecules, one bromo-phenyl (Br1, C1–C6 or Br3, C18–C23), aminoacetaldehyde and methyl-triazolyl groups are almost coplanar. The twist angles between these bromo-phenyl and methyl-triazolyl groups are 13.6(1)° for the first molecule and 18.1(2)° for the second. The second bromo-phenyl group (Br2, C12–C17 or Br4, C29–C34) of each molecule is twisted farther (by 43.7(1)° for the first molecule or 40.4(1)° for the second) from the methyl-triazolyl group.



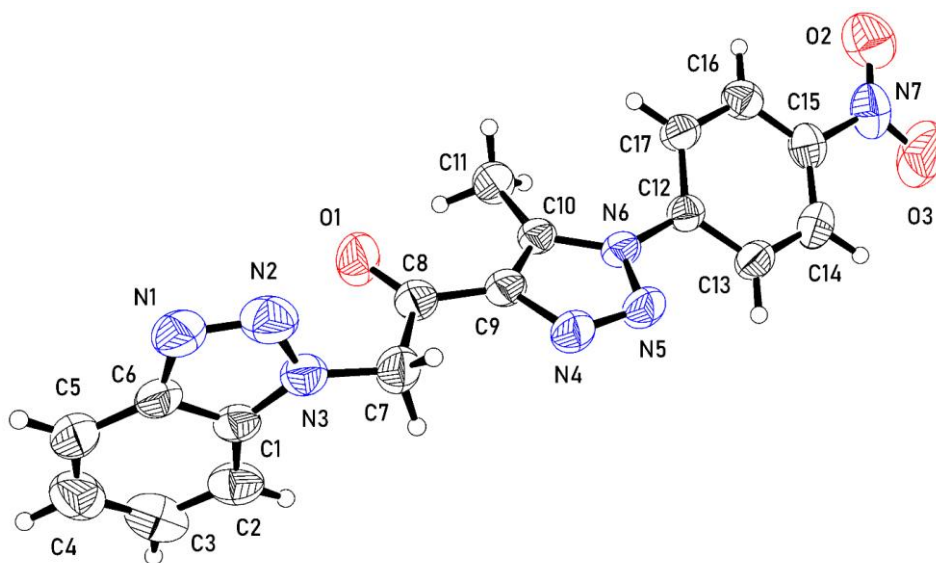
**Figure 2.** The asymmetric unit of **8** showing atomic displacement ellipsoids at 50% probability

In the crystal structure of **9a**, the acetaldehyde and methyl-triazolyl groups of the molecule are coplanar whereas the benzotriazolyl and methyl-phenyl groups are twisted from this plane (Figure 3). The angles between the latter two groups and the methyl-triazolyl groups are  $70.9(1)^\circ$  and  $63.2(1)^\circ$  respectively.



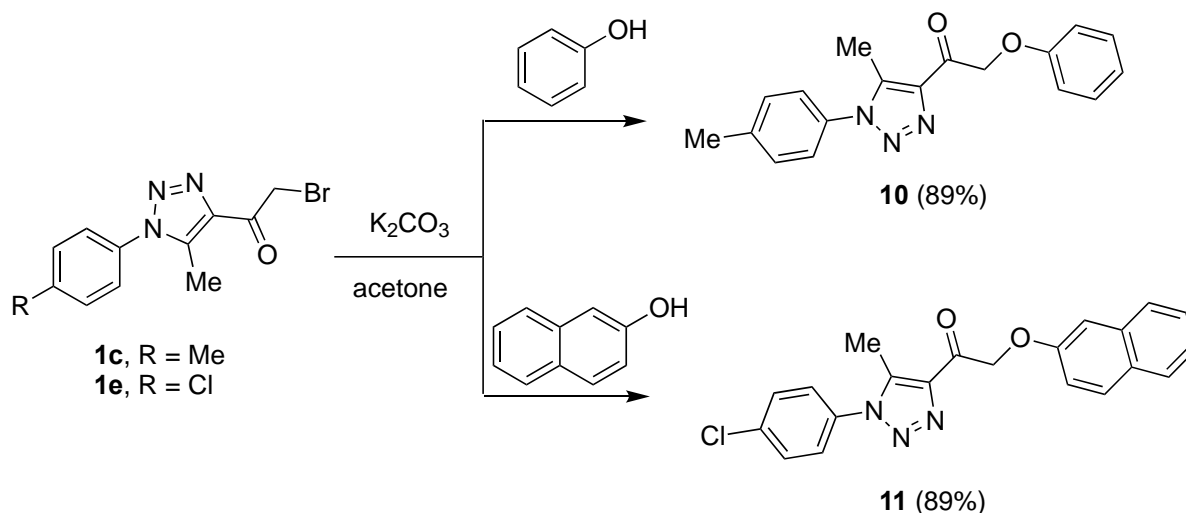
**Figure 3.** The molecule of **9a** showing atomic displacement ellipsoids at 50% probability

In the crystal structure of **9b**, the twist angle between the phenyl and nitro groups of the molecule is  $10.0(2)^\circ$ . Comparably to **9a**, the acetaldehyde and methyl-triazolyl groups in the middle of the molecule are coplanar. The benzotriazolyl and methyl-phenyl groups are twisted from the plane of the triazolyl group by  $86.6(1)^\circ$  and  $35.3(1)^\circ$ , respectively (Figure 4).



**Figure 4.** The molecule of **9b** showing atomic displacement ellipsoids at 50% probability

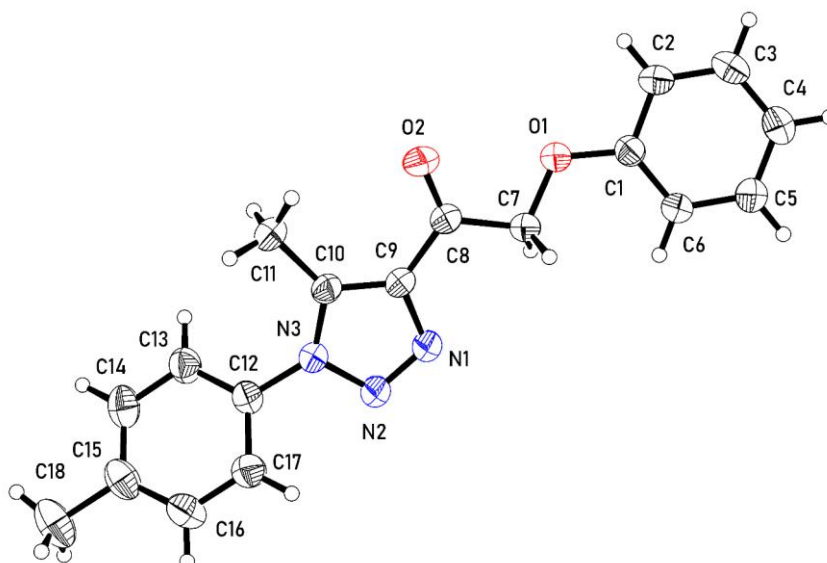
Finally, the reaction between **1c** (R = Me) or **1e** (R = Cl) and phenol or  $\beta$ -naphthol under reflux conditions in dry acetone containing anhydrous potassium carbonate ( $K_2CO_3$ ) furnished the corresponding  $\beta$ -keto-ethers **10** or **11**, respectively, in both 89% yields (Scheme 4).



**Scheme 4.** Synthetic routes to  $\beta$ -keto-esters **10** and **11**

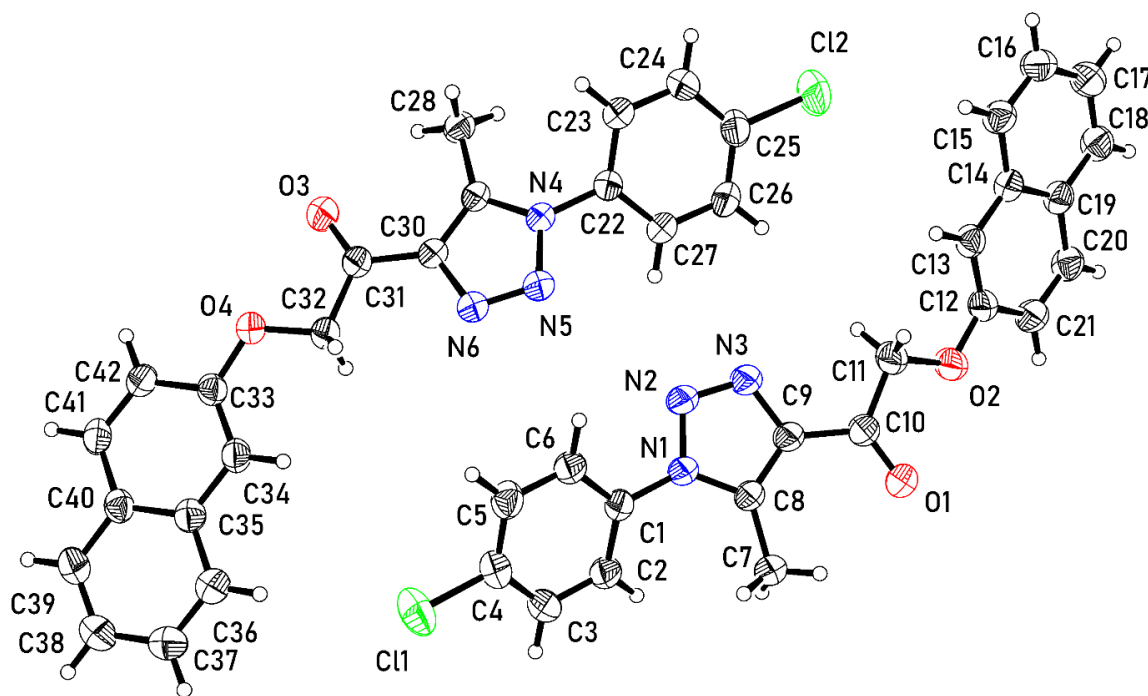
The  $^1H$  NMR spectra of **10** and **11** showed characteristic singlet signals that appeared at 5.56 and 5.70 ppm, respectively corresponding to the  $CH_2$  protons. Also, the  $CH_2$  carbon in both compounds **10** and **11** appeared at 70.4 and 70.7 ppm, respectively in their  $^{13}C$  NMR spectra.

The X-ray crystal structures of **10** and **11** are shown in Figures 5 and 6, respectively. In the crystal of **10**, the acetaldehyde and methyl-triazolyl groups in the middle of the molecule are also coplanar. The twist angles from the plane of the methyl-triazolyl by the phenyl-hydroxy and methyl-phenyl groups are  $17.0(1)^\circ$  and  $35.1(1)^\circ$  respectively (Figure 5).



**Figure 5.** The molecule of **10** showing atomic displacement ellipsoids at 50% probability

There are two independent types of molecules, with different conformations, in the crystal structure of molecule **11** (Figure 6). In the central part of both molecules, the acetaldehyde and methyl-triazolyl groups are coplanar. The twist angles between the chlorophenyl and methyl-triazolyl groups are  $34.4(1)^\circ$  and  $40.7(1)^\circ$  for the first and second molecules respectively. The twist angles between the oxy-naphthalene and methyl-triazolyl groups are  $37.8(1)^\circ$  and  $10.7(1)^\circ$  for the first and second molecules respectively.



**Figure 6.** Asymmetric unit of **11** showing atomic displacement ellipsoids at 50% probability

The antimicrobial activities of the synthesized heterocycles were determined against pathogens obtained from the American type culture collection (ATCC; Rockville, MD, USA). The organisms used in the tests were *Staphylococcus aureus* ATCC-47077 (*S. aureus*), *Listeria monocytogenes* ATCC-35152 (*L. monocytogenes*), *Escherichia coli* ATCC-25922 (*E. coli*), *Salmonella typhi* ATCC-15566 (*S. typhi*), and *Candida albicans* ATCC-10231 (*C. albicans*). Ampicillin and vancomycin were used as the reference antibiotics for comparison.

The results of antimicrobial activity are summarized in Table 1. All the compounds displayed at least moderate activity against the microorganisms (the exceptions were **4** and **8** which had limited activity against *S. typhimurium*). Compound **10** was the most effective heterocycle and against all the microorganisms tested. Particularly notable was the observation that compound **10** was more effective than ampicillin and vancomycin. Ampicillin and vancomycin are recognized as essential antibiotics. The

minimal inhibitory concentration (MIC) of the new heterocycles was also investigated. The results for compound **10** indicated that a concentration from 50–70 µg/mL was needed to kill all the pathogens.

**Table 1.** Antimicrobial activity (mm) of the synthesized heterocycles

Compound	Gram-positive bacteria		Gram-negative bacteria		<i>C. albicans</i>
	<i>S. aureus</i>	<i>L. monocytogenes</i>	<i>E. coli</i>	<i>S. typhi</i>	
<b>4</b>	12	11	11	—	13
<b>8</b>	11	12	10	—	12
<b>9a</b>	12	12	10	12	13
<b>9b</b>	10	11	10	10	10
<b>10</b>	20	25	25	22	22
<b>11</b>	13	13	14	10	14
Ampicillin	15	20	16	19	19
Vancomycin	14	15	15	17	15

## CONCLUSIONS

Reactions of 4-bromoacetyl-1*H*-1,2,3-triazoles towards amines and phenols provided novel heterocyclic compounds. Markedly, 2,5-*bis*(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)pyrazine was unexpectedly produced from a catalyst free reaction of 2-bromo-1-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one and benzylamine. Of all the synthesized heterocycles, compound 1-[5-methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-2-phenoxyethan-1-one (**10**) showed the highest activity against the tested pathogens with a performance exceeding that of the reference drugs (ampicillin and vancomycin).

## EXPERIMENTAL

**General** Melting points were determined using an Electrothermal melting point apparatus. A Bruker Tensor 27 FTIR Spectrometer was used to record the IR spectra. The NMR spectra were recorded on a JEOL NMR 500 MHz spectrometer. <sup>1</sup>H (500 MHz) and <sup>13</sup>C NMR (125 MHz) spectra were recorded in deuterated dimethyl sulfoxide (DMSO-*d*<sub>6</sub>) using tetramethylsilane as a standard. The chemical shift (δ) is reported in ppm and the chemical shift (*J*) is reported in Hz. Compounds **1a–e**<sup>34</sup> were prepared based on literature procedures.

**Synthesis of 2,5-*bis*(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)pyrazine (**4**).** A mixture of **1a** (0.56 g, 2.0 mmol) and **2** (0.43 g, 4.0 mmol) in dry EtOH (20 mL) was refluxed for 3 h to give **4** as a colorless solid. Crystallization from DMF by slow evaporation of solvent at rt gave crystals of pure **4**. Yield 50%, mp 239–241 °C. IR (ν<sub>max</sub>, cm<sup>-1</sup>): 3300 (NH), 2946 (CH), 1685 (C=O), 1593 (C=C). <sup>1</sup>H NMR: 2.45 (s, 6H, 2 Me), 7.30 (s, 2H, Ar), 7.45–7.60 (m, 10 H, Ar). Anal. Calcd for C<sub>22</sub>H<sub>18</sub>N<sub>8</sub> (394.16): C, 66.99; H, 4.60; N, 28.41; Found: C, 67.21, H, 4.67, N, 28.55%.

**General procedure for the synthesis of 8–11.** A mixture of **1** (2.0 mmol) and appropriate reagent (2 mmol; 4-bromoaniline for production of **8**, 1*H*-benzotriazole for **9a,b**, phenol for **10** or  $\beta$ -naphthol for **11**) in dry EtOH in the cases of **8** or **9a,b** or acetone in the cases of **10** or **11** (20 mL) containing anhydrous K<sub>2</sub>CO<sub>3</sub> (4 mmol, 0.55 g) or Et<sub>3</sub>N (4 mmol, 0.40 g) was refluxed for 8 h to give the corresponding products **8–11**. The products were purified by crystallization using DMF by slow evaporation of solvent at rt.

**1-[1-(4-Bromophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-2-[(4-bromophenyl)amino]ethan-1-one (8)**

Yield 82%, mp 193–195 °C. IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3392 (NH), 2920 (CH), 1687 (C=O), 1590 (C=C). <sup>1</sup>H NMR: 2.40 (s, 3H, Me), 4.68 (s, 2H, CH<sub>2</sub>), 6.23 (s, exch., 1H, NH), 6.57 (d, *J* = 7.6 Hz, 2H, Ar), 7.17 (d, *J* = 7.6 Hz, 2H, Ar), 7.60 (d, *J* = 7.6 Hz, 2H, Ar), 7.83 (d, *J* = 7.6 Hz, 2H, Ar). <sup>13</sup>C NMR: 10.2, 50.7, 107.4, 114.8, 124.0, 127.9, 131.87, 133.3, 134.7, 138.8, 141.9, 148.1, 192.4. Anal. Calcd for C<sub>17</sub>H<sub>14</sub>Br<sub>2</sub>N<sub>4</sub>O (447.95): C, 45.36; H, 3.14; N, 12.45; Found: C, 45.50, H, 3.26, N, 12.57%.

**2-(1*H*-Benzotriazol-1-yl)-1-[5-methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]ethan-1-one (9a)**

Yield 83%, mp 163–165 °C. IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 2984 (CH), 1692 (C=O), 1587 (C=C). <sup>1</sup>H NMR: 2.40 (s, 3H, Me), 2.46 (s, 3H, Me), 6.50 (s, 2H, CH<sub>2</sub>), 7.41 (d, *J* = 7.5 Hz, 2H, Ar), 7.52 (d, *J* = 7.5 Hz, 2H, Ar), 7.82 (d, *J* = 7.5 Hz, 2H, Ar), 8.07 (d, *J* = 7.5 Hz, 2H, Ar). <sup>13</sup>C NMR: 10.2, 21.3, 54.8, 111.5, 118.4, 119.6, 124.4, 125.8, 127.9, 130.8, 132.9, 134.6, 139.6, 140.8, 145.7, 187.7. Anal. Calcd for C<sub>18</sub>H<sub>16</sub>N<sub>6</sub>O (332.14): C, 65.05; H, 4.85; N, 25.29; Found: C, 65.17, H, 4.92, N, 25.38%.

**2-(1*H*-Benzotriazol-1-yl)-1-[5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]ethan-1-one (9b)**

Yield 83%, mp 188–190 °C. IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 2990 (CH), 1698 (C=O), 1588 (C=C). <sup>1</sup>H NMR: 2.47 (s, 3H, Me), 6.52 (s, 2H, CH<sub>2</sub>), 7.41 (t, *J* = 7.5, 1H, Ar), 7.81 (t, *J* = 7.5, 1H, Ar), 7.98 (d, *J* = 7.5, 1H, Ar), 8.01 (d, *J* = 8.6 Hz, 2H, Ar), 8.06 (d, *J* = 7.5 Hz, 1H, Ar), 8.50 (d, 2H, *J* = 8.6 Hz, Ar). <sup>13</sup>C NMR: 10.3, 54.9, 111.5, 119.6, 124.5, 125.8, 127.1, 128.0, 134.6, 140.2, 141.5, 145.7, 148.7, 187.7. Anal. Calcd for C<sub>17</sub>H<sub>13</sub>N<sub>7</sub>O<sub>3</sub> (363.11): C, 56.20; H, 3.61; N, 26.99; Found: C, 56.28, H, 3.70, N, 27.09%.

**1-[5-Methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-2-phenoxyethan-1-one (10)**

Yield 89%, mp 145–147 °C. IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 2896 (CH), 1701 (C=O), 1601 (C=C). <sup>1</sup>H NMR: 2.39 (s, 3H, Me), 2.49 (s, 3H, Me), 5.56 (s, 2H, CH<sub>2</sub>), 6.92–6.94 (m, 3H, Ar), 7.26 (t, *J* = 7.5 Hz, 2H, Ar), 7.44 (d, *J* = 7.7 Hz, 2H, Ar), 7.50 (d, *J* = 7.7 Hz, 2H, Ar). <sup>13</sup>C NMR: 10.1, 21.3, 70.4, 115.1, 121.5, 125.7, 130.0, 130.7, 132.9, 138.9, 140.7, 141.2, 158.5, 190.2. Anal. Calcd for C<sub>18</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub> (307.13): C, 70.34; H, 5.58; N, 13.67; Found: C, 70.45, H, 5.69, N, 13.75%.

**1-[1-(4-Chlorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-2-(naphthalen-2-yloxy)ethan-1-one (11)**

Yield 89%, mp 155–157 °C. IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 2901 (CH), 1702 (C=O), 1586 (C=C). <sup>1</sup>H NMR: 2.47 (s, 3H, Me), 5.70 (s, 2H, CH<sub>2</sub>), 7.34–7.50 (m, 4H, Ar), 7.69–7.83 (m, 7H, Ar). <sup>13</sup>C NMR: 10.1, 70.7, 107.8, 119.0, 124.3,

126.9, 127.3, 127.7, 128.0, 129.3, 129.9, 130.4, 134.2, 134.768, 135.5, 139.1, 156.4, 189.8. Anal. Calcd for  $C_{21}H_{16}ClN_3O_2$  (377.09): C, 66.76; H, 4.27; N, 11.12; Found: C, 66.88, H, 4.38, N, 11.30%.

**Antimicrobial Activity.** The agar well diffusion procedure was used as a medium to investigate the antimicrobial activities of the newly synthesized heterocycles.<sup>35,36</sup> Ampicillin and vancomycin were used as references drugs and their effects on the pathogens were recorded for comparison. Bacterial (70  $\mu$ L) and yeast (106 CFU/mL) cells were spread on plates containing nutrient agar. The wells (6 mm diameter) were excavated on the injected agar plates, then each sample (200 mg) in DMSO (1 mL) was added. The reference antibiotics disks (10 and 30  $\mu$ g/disk of ampicillin and vancomycin, respectively) were introduced on the surface of agar inoculated plates. The plates were kept at 4 °C for 2 h before incubation to permit the diffusion to occur. The plates were kept at 37 °C for 24 h except for yeast strains that were incubated at 28 °C for 24 h. The diameter of the inhibition zone (mm) was measured. The tests were replicated five times and the averages were calculated.

**Determination of Minimum Inhibition Concentration (MIC).** The MIC is the concentration of microorganisms that do not present visible growth with regard to the positive control. The MIC was determined for the synthesized heterocycles based on a reported procedure.<sup>36</sup>

**Crystal Structure Determination.** Crystal and structure refinement parameters are shown in Table 2.

**Table 2.** Crystal data and structure refinement data

	<b>4</b>	<b>8</b>	<b>9a</b>	<b>9b</b>	<b>10</b>	<b>11</b>
	$C_{22}H_{18}N_8$	$C_{17}H_{14}Br_2N_4O$	$C_{18}H_{16}N_6O$	$C_{17}H_{13}N_7O_3$	$C_{18}H_{17}N_3O_2$	$C_{21}H_{16}ClN_3O_2$
Fw	394.44	450.14	332.37	363.34	307.34	377.82
T (K)	293(2)	296(2)	296(2)	293(2)	396(2)	296(2)
$\lambda$ (Å)	0.71073	0.71073	1.54184	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	P 2 <sub>1</sub> /c	P $\bar{1}$	P 2 <sub>1</sub> /n	C 2/c	P 2 <sub>1</sub> /c	P 2 <sub>1</sub> /c
a (Å)	20.2818(18)	11.6732(5)	4.36220(10)	22.5280(15)	17.5191(12)	10.7840(4)
b (Å)	3.9856(4)	12.0853(6)	10.9447(3)	7.3633(4)	6.8457(5)	32.2677(9)
c (Å)	11.7693(11)	13.3541(8)	35.1986(10)	20.6432(11)	13.6982(11)	10.3990(4)
$\alpha$ (°)	90	72.261(5)	90	90	90	90
$\beta$ (°)	89.968(8)	80.633(4)	93.312(3)	100.328(6)	108.211(9)	92.602(3)
$\gamma$ (°)	90	75.299(4)	90	90	90	90
V (Å <sup>3</sup> )	951.37(16)	1728.13(16)	1677.68(8)	3368.8(3)	1560.5(2)	3614.9(2)
Z	2	4	4	8	4	8
D (Mg/m <sup>3</sup> )	1.377	1.730	1.316	1.433	1.308	1.388
Abs. coef. (mm <sup>-1</sup> )	0.089	4.702	0.708	0.104	0.088	0.233
F(000)	412	888	696	1504	648	1568
Size (mm <sup>3</sup> )	0.285 × 0.123 × 0.057	0.434 × 0.104 × 0.056	0.472 × 0.182 × 0.028	0.350 × 0.280 × 0.080	0.455 × 0.124 × 0.108	0.420 × 0.287 × 0.057
Reflections	6906	30099	28147	14807	14436	35497
Ind. refs	2362	8629	3444	4178	3920	9021
R(int)	0.0295	0.0456	0.0430	0.0249	0.0286	0.0303
Parameters	137	435	230	245	210	489
Goodness-of-fit	1.145	1.029	1.066	1.076	1.028	1.028
R1 [ $I > 2\sigma(I)$ ]	0.0603	0.0459	0.0511	0.0623	0.0545	0.0522

wR2 ( $I > 2\sigma(I)$ )	0.1591	0.1068	0.1449	0.1506	0.1213	0.1184
R1 (all data)	0.0950	0.1002	0.0592	0.1019	0.0904	0.0951
wR2 (all data)	0.1846	0.1320	0.1625	0.1718	0.1421	0.1408
Largest diff. peak and hole ( $e.\text{\AA}^{-3}$ )	0.159 and – 0.212	0.547 and – 0.736	0.250 and – 0.165	0.176 and – 0.189	0.154 and – 0.175	0.195 and – 0.337

Single-crystal XRD data were collected at rt on an Agilent SuperNova Dual Atlas diffractometer with a mirror monochromator using Mo or Cu radiation. The crystal structures were solved by SHELXS<sup>37</sup> and refined using SHELXL.<sup>38</sup> Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were inserted in idealized positions, and a riding model was used with Uiso set at 1.2 or 1.5 times the value of Ueq for the atom to which they are bonded. The crystal structures have been deposited in the Cambridge Structural Database under reference CCDC 2172761-2172766.

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