Asian Journal of Chemistry; Vol. 28, No. 12 (2016), 2665-2669

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2016.20058

# Triazolopyrimidines: Synthesis of Aryl-1,2,4-triazolo[1,5-a]pyrimidines by Doebner-Miller Reaction and their Antibacterial Activity

MAHRZADI NOUREEN SHAHI[1,*], NAJMA PERVEEN[1,2], MUHAMMAD NAEEM KHAN[3], SAMIA KHAKWANI[4] and MISBAHUL AIN KHAN[1,5]

[1]Department of Chemistry, The Islamia University of Bahawalpur, Bahawalpur, Pakistan
[2]Department of Chemistry, The Government Sadiq College Woman University, Bahawalpur, Pakistan
[3]Aplied Chemistry Section, PCSIR Laboratory Complex, Ferozepur Road, Lahore, Pakistan
[4]Department of Chemistry, Woman University, Multan, Pakistan
[5]Research and Development Labs, Shafee-Reso, Ferozepur Road, Lahore, Pakistan

*Corresponding author: E-mail: shahidaught@yahoo.com

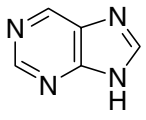
*Received*: 3 May 2016; *Accepted*: 18 August 2016; *Published online*: 1 September 2016; AJC-18058

Novel aryl-1,2,4-triazolo[1,5-a]pyrimidines (**3-23**) were prepared in good yields from corresponding 3-amino-1,2,4-triazoles by employing Doebner-Miller reaction. In some reactions intermediate dihydro products (**3**, **7**, **17**, **19**, **23**) were also isolated and identified. These compounds showed only mild antibacterial activity.

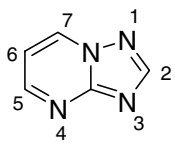
**Keywords: Cyclizations, FTIR, NMR spectra, Mass fragmentations.**

## INTRODUCTION

Purine ring (**1**) is one of the vital heterocyclic ring systems occuring in many biological systems [1]. Because of the importance of purines a tremendous amount of research has gone into the chemistry of purines and its analogues/isosteres. Among these isosteres is the system 1,2,4-triazolo-[1,5-a]pyrimidine (**2**) whose chemistry and biological screening of its derivatives have created interest to the heterocyclic chemists [2]. Various derivatives of this systems were prepared and tested for various biological activities such as antimicrobial [3], cytotoxic [4], anticancer [5], antitumor [6], antibacterial [7], as novel CDK2 inhibitors [8] and herbicidal agents [9].



**1**



**2**

Recently we have reported the synthesis of various pyrazolo[3,4-b]pyridines by employimg Doebner-Miller's method [10] and now extending to other heterocycles we would like to describe our success in preparing diaryltriazolo[1,5-a]pyrimidines.

## EXPERIMENTAL

The proton NMR spectra were recorded on a Hitachi-Perkin Elmer Model R-20-B (60 MHz) and a Bruker AM 300 spectrometer (Rheinstetten–Forchheim, Germany) operating at 300 MHz, respectively using $CDCl_3$ solvent with tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a Finnigan MAT 112. The infrared spectra were taken on a Perkin-Elmer model 180. Samples were measured as potassium bromide disks. Melting points were obtained on Fisher Johns and Gallenkamp apparatus and are uncorrected. Elemental analyses were determined on a Perkin-Elmer model 2400. 3-Amino-1,2,4-triazole and 3-amino-5-phenyl-1,2,4-triazole were obtained from Fluka Chemicals and used as such in these reactions. All the reagents and solvents used in this work were of analytical grade and purity.

**Preparation of 5,7-diaryl-1,2,4-triazolo[1,5-a]pyrimidines (3-23):** A mixture of 10 mmol of 5-amino-1,2,4-triazole (or 3-amino-5-phenyl-1,2,4-triazole) and 10 mmol of a benzaldehyde, a few crystals of zinc chloride, a few drops of concentrated hydrochloric acid and 15-20 mL absolute ethanol was held under reflux for 3 h to give a Schiff base [11]. This was followed by the addition of 10 mmol of acetophenone. The reaction mixture was heated under reflux for a further 3 h period. On cooling the reaction mixture was poured over crushed ice (100 g) and the precipitates were filtered and crystallized from ethanol to give the following desired products (**3-23**) (**Scheme-I**).

**4,5-Dihydro-5,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine (3):** Yield 70 %, m.p.: 210 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3150, 2300, 1660, 1571, 1360, 1245, 742, 690. Mass, *m/z* (%): 275(37) ($M^+1$), 274.2(55) ($M^+$), 273 (39), 199 (8), 198 (55), 197.1 (100), 151.1 (8), 129 (5), 77.1 (4). Elemental analysis: $C_{17}H_{14}N_4$ (274), Calcd: C, 74.46, H, 5.11, N, 20.43. Found: C, 75.10, H, 4.88, N, 20.50 %.

**5-*o*-Nitrophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (4):** Yield, 62 %, m.p.: 230 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3310, 3250, 1662, 1575, 1520 and 1350 ($NO_2$). Elemental analysis: $C_{17}H_{11}N_5O_2$ (317), Calcd: C, 64.35, H, 3.48, N, 22.08. Found: C, 64.31, H, 3.50, N, 22.03 %.

**5-*m*-Nitrophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (5):** Yield, 60 %, m.p.: 240 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3300, 2250, 1662, 1572, 1520 and 1352 ($NO_2$).

**5-*p*-Nitrophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (6):** Yield, 65 %, m.p.: 185 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3300, 3230, 1658, 1520 and 1350 ($NO_2$).

**4,5-Dihydro-5-*o*-methoxyphenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (7):** Yield, 60 %, m.p.: 160 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400, 2850 ($OCH_3$), 1700, 1515, 1335, 850. Mass, *m/z* (%):305(17) ($M^+1$), 304.2 (78.5) ($M^+$), 303 (81), 277(11.5), 276 (16.5),262 (13),261 (6), 260 (6), 227.2 (30) 199 (44), 198 (13), 197.1 (100), 178 (7),153 (13), 152.1 (14), 134 (8), 129 (6), 108 (12.5), 104 (9), 103.1 (12), 87 (6). Elemental analysis: $C_{18}H_{14}N_4O$ (304), Calcd: C, 71.05, H, 5.26, N, 18.42. Found: C, 71.48, H, 4.67, N, 18.55 %

**5-*m*-Methoxyphenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (8):** Yield, 68 %, m.p.: 195 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400, 2900 ($OCH_3$), 1680, 1520, 1260, 1140, 780.

**5-*p*-Methoxyphenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (9):** Yield, 66 %, m.p.: 218 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400, 3100, 2950 ($OCH_3$), 1510, 1445, 1010, 790.

**5-*o*-Bromophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (10):** Yield, 55 %, m.p.: 246 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400, 3050, 2700, 1670, 1520, 1310. Elemental analysis: $C_{17}H_{11}N_4Br$ (351), Calcd: C, 58.11, H, 3.14, N, 15.96, Br, 22.79. Found: C, 58.15, H, 3.09, N, 15.90, Br, 22.70 %

**5-*m*-Bromophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (11):** Yield, 61 %, m.p.: 240 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3250, 1680, 1590, 1480, 1180.

**5-*p*-Bromophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (12):** Yield, 60 %, m.p.: 243 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3250, 1670, 1610, 1560, 1290, 1190.

**5-*o*-Chlorophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (13):** Yield, 60 %, m.p.: 238 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3300, 3190, 1590, 1342, 1055, 940, 710. Elemental analysis: $C_{17}H_{11}N_4Cl$ (306.5), Calcd: C, 66.56, H, 3.58, N, 18.27, Cl, 11.58. Found: C, 66.60, H, 3.62, N, 18.25, Cl, 11.53 %.

**5-2,4-Dichlorophenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (14):** Yield, 90 %, m.p.: 251 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3250,3100, 1675, 1610, 1545, 1370,1055. Elemnetal analysis: $C_{17}H_{10}N_4Cl_2$ (341), Calcd: C59.82, H, 2.93, N, 16.42, Cl, 20.83. Found: C, 59.78, H, 2.89, N, 16.40, Cl, 20.76 %.

**5-*o*-Hydroxyphenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (15):** Yield, 63 %, m.p.: 232 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3250,3100, 1680, 1610, 1550, 1370, Elemental analysis: $C_{17}H_{12}N_4O$ (288), Calcd: C, 70.83, H, 4.16, N, 19.45, Found: C, 70.79, H, 4.10, N, 19.40 %.

**5-*m*-Hydroxyphenyl-7-phenyl-1,2,4-triazolo[1,5-a]pyrimidine (16):** Yield, 59 %, m.p.: 215 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3250, 3100, 1660, 1570, 1275,

**4,5-Dihydro-2,5,7-triphenyl-1,2,4-triazolo[1,5-a]-pyrimidine (17):** Yield, 76 %, m.p.: 220 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3100 (NH),2880, 1710, 1662, 1580, 650, Elemental analysis: $C_{23}H_{18}N_4$ (350), Calcd: C, 78.85, H, 5.14, N, 16.00, Found: C, 79.36, H, 4.66, N, 16.07 %. $^1$H NMR (DMSO-$d_6$) ppm: 5.75 (1H, M, H-5),6.92 (1H, s, H-6), 8.38-6.90 (15H, m, ArH), 9.20 (NH).

**2,7-Diphenyl-5-*o*-nitrophenyl-1,2,4-triazolo[1,5-a]pyrimidine (18):** Yield, 70 %, m.p.: 240 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3435, 1635, 1550 ($NO_2$), 1410, 1340 ($NO_2$). Elemental analysis: $C_{23}H_{15}N_5O_2$ (393), Calcd: C, 70.22, H, 3.82, N, 17.82, Found: C, 70.26, H, 3.80, N, 17.84 %. $^1$H NMR (DMSO-$d_6$) ppm: 5.77 (1H, s, H-6), 8.00-7.30 (14H, m, ArH).

**4,5-Dihydro-2,7-diphenyl-5-*o*-methoxyphenyl-1,2,4-triazolo[1,5-a]pyrimidine (19):** Yield, 60 %, m.p.: 212 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3435, 2840 ($OCH_3$), 1720, 1703, 1595. Elemental analysis: $C_{24}H_{20}N_4O$ (380), Calcd: C, 75.79, H, 5.26, N, 14.73, Found: C, 76.22, H, 4.80, N, 14.79 %. $^1$H NMR (DMSO-$d_6$) ppm: 2.20 (1H, m,H-5),2.50 (3H, m,$OCH_3$), 5.89 (1H, s, H-6), 8.00-7.30 (14H, m, ArH), 9.40 (1H, s,NH).

**5-*o*-Bromophenyl-2,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine (20):** Yield, 80 %, m.p.: 247 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3200, 3100, 1950, 1710,1590, 650. Elemental analysis: $C_{23}H_{15}N_4Br$ (427), Calcd: C, 64.64, H, 3.51, N, 13.11, Br, 18.74 Found: C, 64.67, H, 3.53, N, 13.09, Br, 18.74 %. $^1$H NMR (DMSO-$d_6$) ppm: 5.85 (1H, s, H-6),8.40-6.90 (14H, m, ArH).

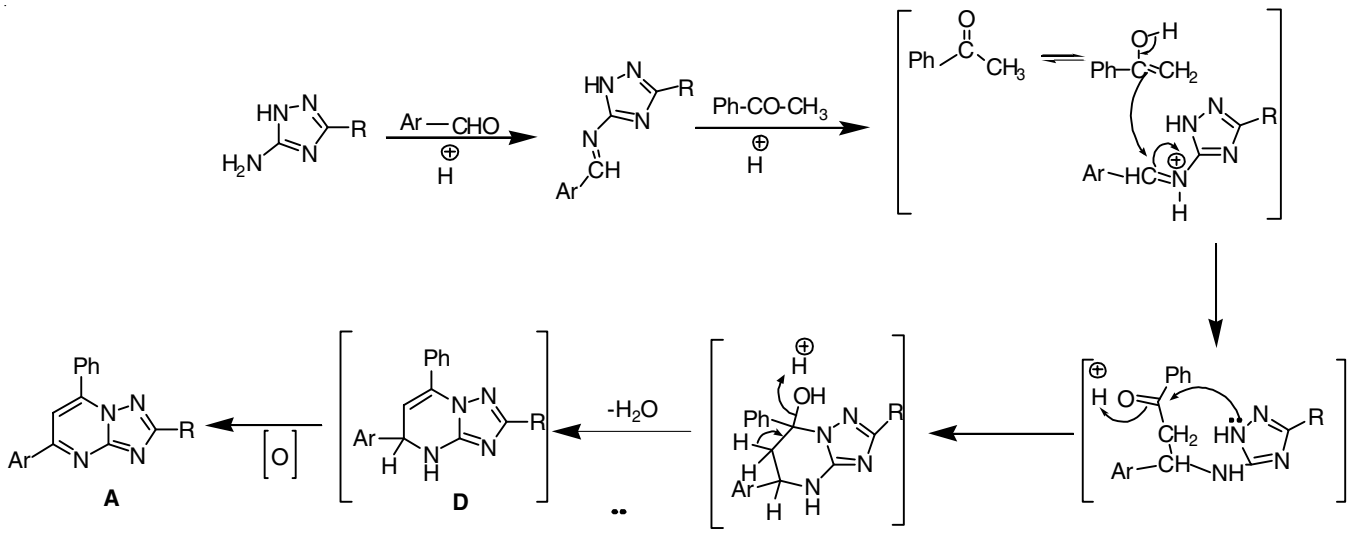
**5-*o*-Chlorophenyl-2,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine (21):** Yield, 82 %, m.p.: 240 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3120, 2850, 1700, 1650, 1590, 1090, 850. Elemental analysis: $C_{23}H_{15}N_4Cl$ (382.5), Calcd: C, 72.16, H, 3.92, N, 14.64, Cl, 9.28 Found: C, 72.20, H, 3.90, N, 14.61, Cl, 9.28 %. $^1$H NMR (DMSO-$d_6$) ppm: 5.77 (1H, s, H-6),8.41-6.90 (14H, m, ArH).

**5-2,4-Dichlorophenyl-2,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine (22):** Yield, 78 %, m.p.: 245 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3200, 3100,2850,1656,1590, 1020, 755. Elemental analysis: $C_{23}H_{14}N_4Cl_2$ (417), Calcd: C, 66.19, H, 3.36, N, 13.42, Cl, 17.03 Found: C, 66.16, H, 3.34, N, 13.40, Cl, 17.02 %. $^1$H NMR (DMSO-$d_6$) ppm: 5.90 (1H, s, H-6),8.44-6.92 (13H, m, ArH).

**4,5-Dihydro-2,7-diphenyl-5-*o*-hydroxyphenyl-1,2,4-triazolo[1,5-a]pyrimidine (23):** Yield, 71 %, m.p.: 245 °C; IR (KBr, $\nu_{max}$, $cm^{-1}$): 3400(OH),3100 (NH),1550. 1020, 755, 605. Mass, *m/z* (%): 366.8 (13) ($M^+$), 365.8 (50), 364 (13), 363 (11), 289 (12), 273.8(9), 272.8 (51), 208 (18), 206.9 (100), 177.9 (9), 105 (16), 103 (20), 93(6), 77 (37.2). Elemental analysis: $C_{23}H_{18}N_4O$ (366), Calcd: C, 75.41, H, 4.91, N, 15.30, Found: C, 75.85, H, 4.43, N, 15.34 %. $^1$H NMR (DMSO-$d_6$) ppm: 2.20 (1H, s,H-5),4.70 (1H, s, OH), 5.40 (1H, s,H-6) 8.40-6.90 (14H, m, ArH), 9.50 (1H, s, NH).

## RESULTS AND DISCUSSION

3-Amino-1,2,4-triazole or 3-amino-5-phenyl-1,2,4-triazole was condensed with various arylaldehydes to give the corresponding Schiff bases [11]. These bases on further reaction



For compound **A:**
**4:** R = H, Ar = *o*-$NO_2C_6H_4$; **5:** R = H, Ar = *m*-$NO_2C_6H_4$; **6:** R = H, Ar = *p*-$NO_2C_6H_4$; **8:** R = H, Ar = *m*-$MeOC_6H_4$; **9:** R = H, Ar = *p*-$MeOC_6H_4$; **10:** R = H, Ar = *o*-$BrC_6H_4$; **11:** R = H, Ar = *m*-$BrC_6H_4$; **12:** R = H, Ar = *p*-$BrC_6H_4$; **13:** R = H, Ar = *o*-$ClC_6H_4$; **14:** R = H, Ar = 2,4-$Cl_2C_6H_3$; **15:** R = H, Ar = *o*-$OHC_6H_4$; **16:** R = H, Ar = *m*-$OHC_6H_4$; **18:** R = Ph, Ar = *o*-$NO_2C_6H_4$; **20:** R = Ph, Ar = *o*-$BrC_6H_4$; **21:** R = Ph, Ar = *o*-$ClC_6H_4$; **22:** R = Ph, Ar = 2,4-$Cl_2C_6H_3$

For compound **D:**
**3:** R = H, Ar = Ph; **7:** R = H, Ar = *o*-$Me_OC_6H_4$; **17:** R = Ar = Ph; **19:** R = Ph, Ar = *o*-$MeOC_6H_4$; **23:** R = Ph, Ar = *o*-$OHC_6H_4$

**Scheme-I**

with acetophenone in acidic media lead to the formation of di- (or tri-)aryl-1,2,4-triazolo[1,5-a]pyrimidines (**3-23**) (**Scheme-I**). However it was found that a one pot reaction of the 3-amino-1,2,4-triazole, an aryl aldehyde and acetophenone also results in the same products and hence was adopted for the present work.

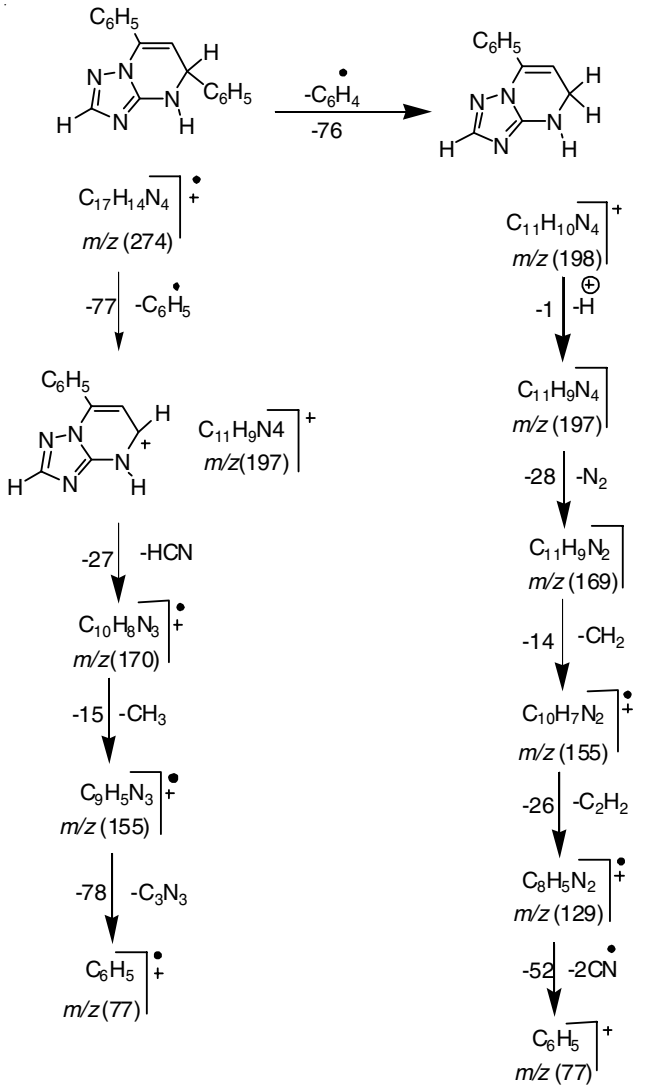
The structure of the isolated compounds was based on their elemental analyses, IR, PMR and in some cases by their mass spectra. In the IR absorption spectra, usual functional groups displayed for nitro (two strong absorption bands around 1520 and 1350 $cm^{-1}$); for a methoxy (at 2850 $cm^{-1}$); for a hydroxy group (at 3400 $cm^{-1}$) and in some cases of a dihydro product NH (at around 3100 $cm^{-1}$). The PMR spectra were also of great assistance since it displayed diagnostic signals for the characteristic pyrimidine H-6 between 5.40 to 6.92 ppm; aromatic protons due to 5- and 7-aryl rings often as multiplets between 6.90 and 8.40 ppm; $OCH_3$ protons at 2.50 ppm; OH at 4.70 ppm and for a dihydro product NH signals at 9.50 ppm.

Thus, it was found that most of the products of these reactions were totally aromatized rings (**A, Scheme-I**) while some 4,5-dihydro-5,7-diaryl-1,2,4-triazolo[1,5-a]pyrimidines such as **3**, **7**, **17**, **19**, **23** (**D**, **Scheme-I**) were isolated. These are the products of the penultimate step of the reaction (before being oxidized to the fully aromatized ring) (**Scheme-I**). In contrast with reactions of 3-amino-1,2,4-triazole's reaction with aryl aldehydes and cyclohexanone, the dihydro products were isolated in all the reactions [12].

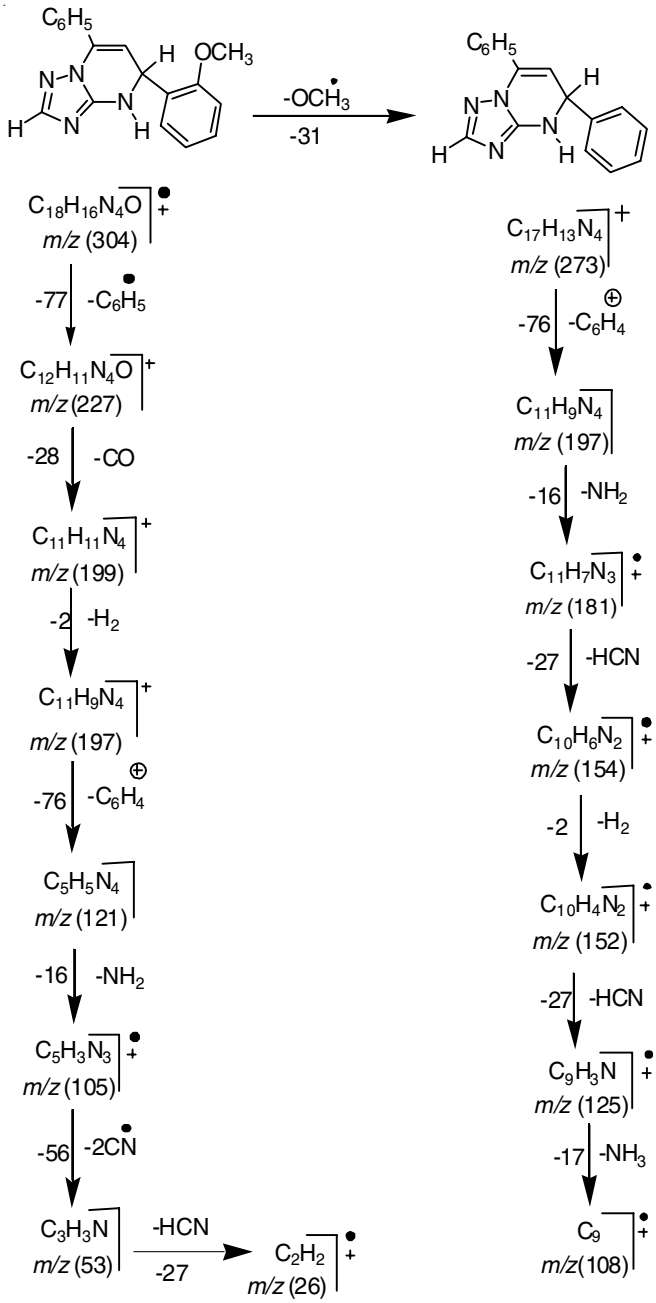
The assignment of the structure of these products as the 1,2,4-triazolo[1,5-a]pyrimidines is based on the studies which have confirmed that this isomer is the most stable one [2,13]. While the mass spectra of some compounds prepared during the present work were instrumental indicating their structure, some of these spectra were studied as to their fragmentation pattern.

In **Scheme-II** the fragmentation behaviour of **3** is presented. The mass spectra revealed a molecular ion peak at *m/z* 274. A base peak at *m/z* 197 is observed which could be originating from a loss of $C_6H_5$ (*m/z* 77) from the parent compound. After this a molecule of HCN (*m/z* 27) may be removed followed by a $CH_3$ (*m/z* 15) and a further loss of $C_3N_3$ (*m/z* 78). An alternate route may be taken by initial loss of a $C_6H_4$ (*m/z* 76) followed by loss of a proton to form the base peak (*m/z* 197). Further loss of $N_2$ (*m/z* 28) and $CH_2$ (*m/z* 14), which is then followed by successive loss of $C_2H_2$ (*m/z* 26) and 2 CN radicals (*m/z* 26 × 2 = 52).

Another fragmentation pattern of a substituted 5-aryl-1,2,4-triazolo[1,5-a]pyrimidine (**7**) is shown in **Scheme-III**. The low resolution electron impact mass spectrum showed the molecular ion peak at *m/z* 304 which agrees well with the calculated value. A base peak is obtained by the removal of a $OCH_3$ (*m/z* 31) and $C_6H_4$ (*m/z* (76) followed by a fragment at *m/z* 197 corresponding to $C_{11}H_9N_4$. Removal of a molecule of $NH_3$ (*m/z* 17) and a proton, a matching peak at *m/z* 152 is obtained. Further loss of HCN and $NH_3$ molecules brings to a shorter fragment *m/z* 108. In another route first a $C_6H_5$ is removed followed by a CO (*m/z* 28) and one hydrogen molecule to obtain the base peak at *m/z* 197. Further loss of $C_6H_4$ (*m/z* 76) and $NH_2$ (*m/z* 16) resulted in a shorter fragment corresponding to $C_5H_3N_3$ (*m/z* 105).This seems to be followed by removal of two CN fragments (*m/z* 26 × 2 = 52) and one mole of HCN (*m/z* 27) which brings the fragmentation process to the shortest fraction corresponding to $C_2H_2$ (*m/z* 26).




**Scheme-II:** Mass fragmentation pattern for **3**




**Scheme-III:** Mass fragmentation pattern for **7**

**Antibacterial activity:** Antibacterial activity of some of the prepared 1,2,4-triazolo[1,5-a]pyrimidines (**3-23**) were tested against six strains of bacteria (Table-1) by disc diffusion method [14]. Vibramycin and ceftioxime were used as positive controls while chloroform and ceclor were the negative controls.

Table-1 reveals that as compared to the standard antibiotics, none of the synthesized 1,2,4-triazolo[1,5-a]pyrimidines have appreciable antibacterial activity. However, there seems to be positive effect of these compounds against *Klebsiella* as compared to vibramycin.

TABLE-1
ANTIBACTERIAL ACTIVITY (DIAMETERS IN mm OF ZONE OF INHIBITION)

| Compd. No. | *S. arueus* | *S. cocci* | *S. virdines* | *Psedomonas* | *E. coli* | *Klesbsiella* |
|---|---|---|---|---|---|---|
| **3** | 8 | – | 10 | – | – | 10 |
| **4** | 8 | 12 | – | – | – | – |
| **5** | 7 | – | 15 | 15 | – | 10 |
| **6** | – | 10 | – | – | 10 | – |
| **7** | – | – | 15 | 12 | – | 12 |
| **8** | 7 | 10 | – | – | 12 | – |
| **17** | – | 10 | 10 | – | – | 10 |
| **18** | – | 10 | – | – | 10 | – |
| **19** | 10 | – | – | – | – | 10 |
| Vibramycin | 30 | 30 | – | – | 30 | 10 |
| Ceftioxime | – | 15 | 20 | 22 | – | 20 |

## Conclusion

The Doebner-Miller synthesis provides an unambiguous method for the synthesis of 1,2,4-triazolo[1,5-a]pyrimidines with desired 5- and 7-aryl substituents. In some reactions dihydro products were isolated and identified. Fragmentation patterns of two selected products **3** and **7** are presented. Some of the products were effective against *Klebsiella* only.

## REFERENCES


1. A.R. Katritzky, C.W. Rees and E.F.C. Scriven, Comprehensive Heterocyclic Chemistry, vol. 7, Elsevier, New York (1996).
2. G. Fischer, *Adv. Heterocycl. Chem.*, **57**, 81 (1993); M.A.E. Shaban and A.E.A. Morgaan, *Adv. Heterocycl. Chem.*, **77**, 345 (2000).
3. S.P. Gami, K.V. Vilapara, H.R. Khunt, J.S. Babariya and Y.T. Naliapara, *Int. Lett. Chem. Phys. Astron.*, **30**, 127 (2014).
4. B. Yu, X.-J. Shi, Y.-F. Zheng, Y. Fang, E. Zhang, D.-Q. Yu and H.-M. Liu, *Eur. J. Med. Chem.*, **69**, 323 (2013).
5. N. Zhang, S. Ayral-Kaloustian, T. Nguyen, J. Afragola, R. Hernandez, J. Lucas, J. Gibbons and C. Beyer, *J. Med. Chem.*, **50**, 319 (2007).
6. X.-L. Zhao, Y.-F. Zhao, S.-C. Guo, H.-S. Song, D. Wang and P. Gong, *Molecules*, **12**, 1136 (2007).
7. H. Wang, M. Lee, Z. Peng, B. Blázquez, E. Lastochkin, M. Kumarasiri, R. Bouley, M. Chang and S. Mobashery, *J. Med. Chem.*, **58**, 4194 (2015).
8. C.M. Richardson, D.S. Williamson, M.J. Parratt, J. Borgognoni, A.D. Cansfield, P. Dokurno, G.L. Francis, R. Howes, J.D. Moore, J.B. Murray, A. Robertson, A.E. Surgenor and C.J. Torrance, *Bioorg. Med. Chem. Lett.*, **16**, 1353 (2006).
9. B.C. Gerwick, M.V. Subramanian, V.I. Loney-Gallant and D.P. Chandler, *Pestic. Sci.*, **29**, 357 (1990).
10. N. Parveen, S. Aslam, T. Maqbool, A.M.R. Bernadino, M.A. Munawar and M.A. Khan, *Affinidad*, **71**, 566 (2014).
11. N. Perveen, M.A. Khan, M. Moazzam and M. Sarwar, *J. Pure Appl. Sci. (Bahawalpur, Pakistan)*, **17**, 39 (1998).
12. A. Nazeer, N. Perveen, M.A. Khan, M.N. Khan, M.A. Munawar and W. Lin, *Asian J. Chem.*, **25**, 7705 (2013); A. Nazeer, N. Perveen, S. Aslam, M.A. Khan and M.A. Munawar, *Affinidad*, **70**, 563 (2013).
13. W.W. Paudler and L.S. Helmick, *J. Heterocycl. Chem.*, **3**, 269 (1966); L.M. Werbel, A. Curry, E.F. Elslager, C.A. Hess, M.P. Hutt and C. Youngstrom, *J. Heterocycl. Chem.*, **6**, 787 (1969).
14. A.W. Bauer, W.M.M. Kirby, J.S. Serris and M. Turck, *J. Clin. Pathol.*, **45**, 493 (1966).