Synthesis and Antifungal Activity of Novel 3,6-Diaryl-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepines

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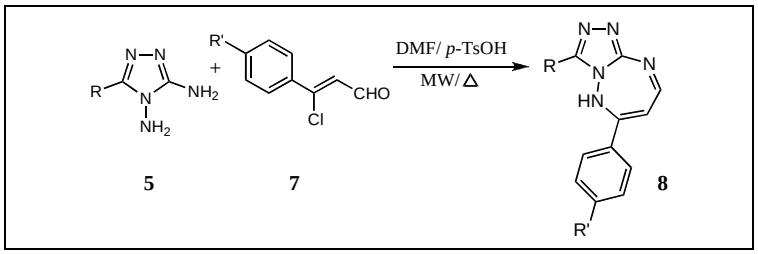

5-Aryl-3,4-diamino-1,2,4-triazoles **5** on treatment with *β*-chlorocinnamaldehydes **7** in the presence of catalytic amount of *p*-TsOH and *N,N*-dimethylformamide as an energy transfer medium under microwave irradiation and as solvent with oil-bath heating at 80 °C affords novel 3,6-diaryl-5*H*-[1,2,4]triazolo[4,3-*b*]-1,2,4]triazepines **8**. The structures of the synthesized compounds were established on the basis of ^{1}H NMR, IR, mass spectral data and elemental analysis.

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INTRODUCTION

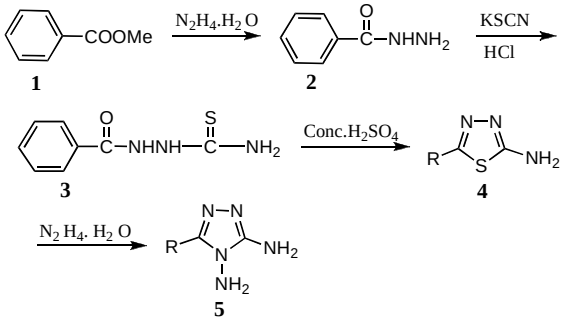
Nitrogen containing heterocyclic compounds have received considerable attention due to their wide range of pharmacological activities. For instance, a number of triazole derivatives were known to possess antifungal [1,2], antibacterial [3], anti-inflammatory [4], antiicrobial [5,6], tuberculo-therapeutic [7] and antiasthamatic activities [8]. Benzotriazepine [9] derivatives were also reported to possess antibacterial, antiviral and psychotropic activities [10,11]. Some of these derivatives were used in the manufacture of plant protecting agents [12]. The malaria therapy, acaricidal, herbicidal, and insecticidal properties [13] of benzotriazepine analogues are well documented. On similar lines, we have replaced the benzene ring by triazole ring. In order to know the combined effect of both triazepine and triazole moieties in a single frame work on physiological activity, there is a continued interest in the synthesis of condensed heterocyclic system possessing both triazole and triazepine moieties. In this paper, we wish to report a mild and efficient procedure for the synthesis of 3,6-diaryl-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepines in the presence of catalytic amount of *p*-TsOH and *N,N*-dimethylformamide as an energy transfer medium/solvent under microwave irradiation and oil-bath heating. Some of these compounds were evaluated for antifungal activity. The synthesis and cytokinine production inhibition of triazolo-triazepines has been recently patented [14].

RESULTS AND DISCUSSION

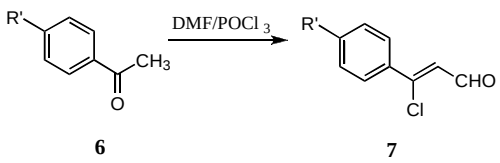
The required precursor, 5-aryl-3,4-diamino-1,2,4-triazoles [15], were prepared from methylbenzoates **1** which were then converted to aroylhydrazides **2** on refluxing with hydrazine hydrate in ethanol followed by conversion to aroylthiosemicarbazides **3** on heating with potassium thiocyanate in aq. HCl. Aroylthiosemicarbazides were then converted to 2-amino-5-aryl-1,3,4-thiadiazoles **4** which were then converted to 5-aryl-3,4-diamino-1,2,4-triazoles **5** on refluxing with hydrazine hydrate in ethanol (Scheme 1), while *β*-chlorocinnamaldehydes [16], were prepared by Vilsmeir Haack reaction of acetophenones **6** as illustrated in Scheme 2. The synthesized precursors were then used for the synthesis of title compounds **8a-j** in the presence of *p*-TsOH and *N,N*-dimethylformamide using both microwave and oil-bath heating. It was found that *N,N*-dimethylformamide and *p*–TsOH has not yet been used for the condensation of *β*-chlorocinnamaldehydes **7** with 5-aryl-3,4-diamino-1,2,4-triazoles **5** followed by cyclization to give 3,6-diaryl-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepines **8** which is outlined in Scheme 4. While carrying out the reaction, it was found that the two amino groups were present at 4- and 5-position of 5-aryl-3,4-diamino-1,2,4-triazole **5** but the amino group at C-5 position was involved in tautomerization giving tautotmeric form as shown in Scheme 3. It was supported by the fact that only -C-NH_2 group can form Schiff's base with *β*-chlorocinnamaldehydes **7** while H_2N-N- group containing compounds are analogus to hydrazino type compounds which can displace vinylic chlorine easily of *β*-chlorocinnamaldehydes **7**. So, it was only the amino group at C-2 position of 5-aryl-3,4-diamino-1,2,4-triazole **5** which can form Schiff's base with *β*-chloroinnamldeydes **7** while N-NH_2 of **5** cannot form Schiff's base. Moreover, in the resulting product **8**, the H-atom at 5-position (NH) can form hydrogen bond

with all the "R" groups present at C-3 position. Free amino group can displace vinylic chlorine easily while imino group cannot displace chlorine easily. These are the evidences which support that displacement occurs *via* NH_2-N- and condensation occurs *via* -C-NH_2. Since *p*-TsOH is non-toxic, inexpensive and easily available reagent, we carried out the reaction of 5-phenyl-3,4-diamino-1,2,4-triazole **5a** with *p*-fluoro-*β*-chlorocinnamaldehyde **7a** using *N,N*-dimethylformamide as an energy

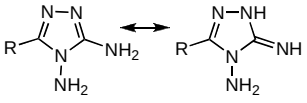
Scheme 1



Scheme 2



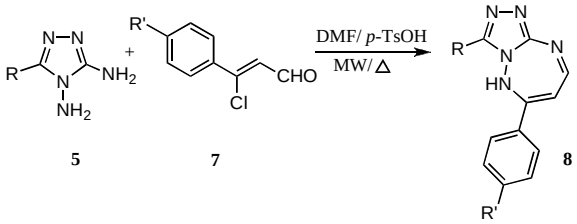
Scheme 3



transfer medium under microwave irradiation and were able to isolate **8a** in 70% yield. Similar reaction was also carried out under oil-bath heating at 80°C followed by stirring and was able to isolate **8a** in 69% yield. To check the generality of the reaction, this procedure was also applied to other substrates and found give good to moderate yields. The results are summarized in Table 1. Thus, this represents a rapid, mild and cost-effective procedure for the synthesis of 3,6-diaryl-5*H*-[1,2,4]-triazolo[4,3-*b*][1,2,4]triazepines.

In order to optimize the reaction conditions, different reactions were tried with varying amount *p*-fluoro-*β*-chlorocinnamaldehydes **7a** and 5-phenyl-3,4-diamino-

Scheme 4



	R	R'
a	C_6H_5	F
b	2-ClC_6H_4	Br
c	4-ClC_6H_4	F
d	$CH_2C_6H_4$	Cl
e	(4-NO_2)C_6H_4	Cl
f	C_6H_5	Br
g	2-ClC_6H_4	4-NO_2
h	$CH_2C_6H_4$	4-NO_2
i	(4-NO_2)C_6H_4	Br
j	C_6H_5	4-NO_2

1,2,4-triazoles **5a** which were selected as the test substrates. It was found that for 5 mmole of each of 5-phenyl-3,4-diamino-1,2,4-triazole **5a**, *p*-fluoro-*β*-chloro-cinnamaldehyde **7a**, 200 mg of *p*-TsOH and 2.5 mmole of *N,N*-dimethylformamide under microwave irradiation and 50 ml of *N,N*-dimethylformamide as solvent under oil-bath heating was required to give maximum yield under mild conditions. To select the optimum power level, reaction with test substrates was carried out at different power levels from 80-900 W. It was found that 640 W was the optimum power level as far as yield and reaction times are concerned. At low power level, the reaction remains incomplete, whereas, at high power level, low yield of products were formed which may be due to decomposition. Under oil-bath heating, 80 °C was selected as optimum reaction temperature.

Antifungal Activity. Some of the synthesized compounds were screened for antifungal activity against *Aspergillus flavus*, *Aspergillus niger*, Rhizopus species and Pencillium species by paper disc technique against two concentrations 500 μg/ml and 1000 μg/ml. The zone of inhibition after 24 h of incubation at 28 ± 2 °C was compared with that of standard fluconazole. The screening data indicated that the compounds **8d**, **8e**, **8i** and **8j** showed excellent activity against Aspergillus niger and Pencillium species at 500 μg as well as 1000 μg concentrations whereas, these compounds showed good to moderate activity against Aspergillus flavus and Rhizopus species at both the concentrations as shown in Table 2. The medium used for evaluation of antifungal activity was Potato dextrose Agar-Agar medium.

Preparation of the medium. Potato dextrose agar-agar medium was prepared as below: Potato= 250 g, Dextrose= 10 g, Agar-agar= 20 g, Distilled water = 100 mL. Sliced

Table 1

Physical data of compounds 3,6-diaryl-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepines under microwave irradiation (MW) and oil - bath heating (Δ) at 80 °C.

Compound	Microwave (MW)		Oil-bath heating at 80 °C (Δ)		
	Time (min.)	Yield (%)	Time (hours)	Yield (%)	Mp (°C)
8a	18	70[a]	43	69[a]	218-220
8b	14	76[b]	24	75[b]	202-204
8c	11	71[a]	36	70[a]	175-177
8d	9	80[a]	12	85[a]	214-216
8e	10	78[b]	10	70[b]	232-234
8f	8	82[a]	16	85[a]	168-170
8g	20	70[a]	49	62[a]	182-184
8h	10	63[a]	30	61[a]	198-200
8i	7	68[a]	12	65[a]	225-227
8j	12	92[a]	32	60[a]	230-232

[a] Products were purified by crystallization from ethyl acetate. [b] Products were purified by passing through column of alumina and elution with ethyl acetate: pet. ether.

Table 2

Antifungal activity of synthesized compounds 3,6-diaryl-5*H*[1,2,4]triazolo[4,3-*b*][1,2,4]triazepines

S.No.	Compd. No.	Zone of inhibition in mm (%)							
	Conc. μg/mL	Aspergilus niger		Aspergillus flavus		Rhizopus species		Pencillium species	
		500μg	1000μg	500μg	1000μg	500μg	1000μg	500μg	1000μg
1	**8d**	38 (63.33)	43 (71.66)	42 (70.00)	42 (70.00)	40 (66.66)	41 (68.33)	48 (80.00)	52 (86.66)
2	**8e**	39 (65.00)	38 (63.33)	31 (51.66)	30 (50.00)	38 (63.31)	38 (63.31)	48 (80.00)	51 (88.13)
3	**8i**	38 (63.33)	46 (76.66)	46 (76.66)	49 (81.660	39 (65.00)	45 (75.00)	50 (83.33)	55 (96.66)
4	**8j**	39 (65.00)	42 (70.00)	48 (80.00)	50 (83.33)	40 966.66)	48 (80.00)	52 (86.66)	55 (96.66)

Standard Fluconazole

Aspergillus niger

500 μg 1000μg

35 (58.33) 42 (70.00)

Aspergillus flavus

500 μg 1000μg

42 (70.00) 48 (80.00)

Rhizopus species

500 μg 1000μg

38 (63.33) 42 (70.00)

Pencillium species

500μg 1000μg

52 (86.66) 54 (90.00)

potatoes were taken with 500 mL of distilled water in a pan and boiled for half an hour till a spoon when placed on a slice can pierce into it. Filter it while hot and broth was again taken in a pan with rest of the distilled water. Dextrose dissolved in distilled water and weighed agar-agar was added to the broth and heated it to boil. The medium thus obtained was sterillized in pressure cooker for 30 min. and few drops of streptomycin were added to prevent it from any bacterial contamination.

Procedure. Potato dextrose medium was prepared and sterilized in pressure cooker for 30 min. Sterillized medium (15 mL) each was pipetted out into flat petridishes. When it solidified 15 mL of warm seeded medium was applied over it. The seeded agar was made by cooling the medium to 40 °C, and then adding spore suspension to seeded medium. The spores were obtained from ten days culture of *Aspergillus niger*, *Aspergillus flavus*, Pencillium species and Rhizopus species. Before the solidification of agar, the plate was tilted to ensure that coverage should be even. These petridishes were then put into the refrigerator upside down to prevent condensation of moisture. Two concentrations *viz*. 500 and 1000 μg/mL of the synthesized compounds were prepared by dissolving the required quantity of compounds in DMF. Sterilized Whatmann filter paper number 541 discs wee prepared by cutting 6 mm diameter with a cork borer and were spread individually with a needle and planted upon the chilled seeded medium. The plates were then incubated for 24 to 72 h at 28 °C±2 °C and inhibition of zone around each disc was measured

from the centre of the discs. The percentage zone of inhibition was calculated by the formula: I% = C-T/C X 100, Where, I= inhibition, C= diameter of zone of micro-organisms in check, T= diameter of the disc.

The zone of inhibition was measured after 24 h, fluconazole (500 μg/mL and 1000 μg/mL) was used as control standard.

EXPERIMENTAL

General. All the melting points were determined on a Tempo melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker DPX-200 NMR spectrometer (200 MHz) in $CDCl_3$ + DMSO-d_6 using tetramethylsilane as an internal standard and IR spectra were recorded using KBr disc on a Perkin Elmer FTIR spectrophotometer. The mass spectral data was obtained on a JEOL JMS-D 300 spectrometer. The elemental analysis were performed on a simple CHNS-932 Analyser (Leco). The reactions were carried out in domestic microwave oven LG-MS-255R with maximum output power of 900 W and by using pre-heated oil-bath.

General Procedure for the Synthesis of Compounds 8a-j.

Microwave Heating. A mixture of 5-aryl-3,4-diamino-1,2,4-triazole **5** (5 mmol), β-chlorocinnamaldehyde **7** (5 mmol), *N*,*N*-dimethylformamide (0.18 g, 2.5 mmol) as an energy transfer medium and catalytic amount of *p*-TsOH (200 mg) was taken in a borosil beaker and mixed properly with the help of a glass rod (5 s). The mixture was then exposed to microwave irradiation for an appropriate time (monitored by TLC, shown in Table 1) followed by cooling time of 5 s each at 640 W. After completion of the reaction, crushed ice was added and the solid obtained was collected by filtration, washed with water and dried. The crude product was purified either by crystallization from EtOAc or by passing through a column of alumina and elution with ethyl acetate and petroleum ether. The physical data of synthesized compounds is given in Table 1. The structures of the products were confirmed by IR, ^{1}H NMR, mass spectral data and elemental analysis.

Oil-bath Heating. A mixture of 5-aryl-3,4-diamino-1,2,4-triazole **5** (5 mmol), β-chlorocinnamaldehyde **7** (5 mmol), *N*,*N*-dimethylformamide (50 ml) and catalytic amount of *p*-TsOH (200 mg) was taken in a round bottomed flask (100 ml). The reaction mixture was stirred in an oil-bath at 80 °C for the appropriate time (monitored by TLC, shown in Table 1). After completion of the reaction, the reaction mixture was cooled to room temperature and poured onto the crushed ice. The solid obtained was filtered, washed with water and dried. The crude product was purified either by crystallization from EtOAc or passing through a column of alumina and elution with ethylacetate and petroleum ether. The physical data of the synthesized compounds is given in Table 1. The structures of the products were confirmed by IR, ^{1}H NMR, mass spectral data and elemental analysis.

3-Phenyl-6-(4'-fluorophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]-triazepine (8a). This compound was obtained as orange coloured shining solid (ethyl acetate), mp 218-220°; ir (potassium bromide): 3142 (NH), 3048 (aromatic C-H), 1652 (C=N), 1432 (C-N), 810 (C-F); ^{1}H nmr ($CDCl_3$+DMSO-d_6): δ 6.90-7.25 (m, 3H, Harom), 7.30-7.38 (m, 3H, Harom), 7.49-7.55 (m, 3H, Harom and d, 1H buried C-8H, J= 8.2 Hz), 7.71(d, 1H, C-7H, J= 7.2 Hz), 8.62 (bs, 1H, NH); ms: m/z 304 (M^+). *Anal.* Calcd. for $C_{17}H_{12}N_5F$: C, 67.10; H, 3. 94; N, 23.02. Found: C, 67.02; H, 3.903; N, 22.92.

3-(2'-Chlorophenyl)-6-(4'-bromophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepine (8b). This compound was obtained as pale yellow coloured shining solid (ethyl acetate), mp 202-204°; ir (potassium bromide): 3181 (NH), 3062 (aromatic C-H), 1693 (C=N), 1447 (C-N), 719 (C-Cl), 540 (C-Br); ^{1}H nmr ($CDCl_3$+DMSO-d_6): δ 7.10-7.20 (m, 2H, Harom), 7.25-7.32 (m, 2H, Harom), 7.38-7.50 (m, 4H, Harom and d, 1H buried C-8, J=8.2 Hz), 7.68(d, 1H, C-7H, J= 7.2 Hz), 8.50 (bs, 1H, NH); ms: m/z 399.5 (M^+). *Anal.* Calcd. for $C_{17}H_{11}N_5BrCl$: C, 51.06; H, 2.75; N, 17.5. Found: C, 51.00; H, 2.70; N,17.1.

3-(4'-Chlorophenyl)-6-(4'-fluorophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazepine (8c). This compound was obtained as pale yellow shining solid (ethyl acetate), mp 175-177°C: ir (potassium bromide): 3163 (NH), 3063 (aromatic C-H), 1644 (C=N), 818 (C-F), 759 (C-Cl); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 6.95-7.22 (m, 4H, Harom), 7.26-7.45 (m, 4H, Harom), 7.52 (d, 1H, C-8H, J= 8.2 Hz), 7.70 (d,1H, C-7H, J=7.2 Hz), 8.57 (bs, 1H, NH); ms: m/z 338.5 (M^+). *Anal.* Calcd. for $C_{17}H_{11}N_5ClF$: C, 60.26; H, 3.24; N, 20.67. Found: C, 60.21; H, 3.18; N, 20.27.

3-Benzyl-6-(4'-chlorophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*]-[1,2,4]triazepine (8d). This compound was obtained as yellow coloured solid (ethyl acetate), mp 214-216°C**:** ir (potassium bromide): 3162 (NH), 3028 (aromatic C-H), 1692 (C=N), 1438 (C-N), 759 (C-Cl); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 4.00 (s, 2H, Ar-CH_2), 7.05-7.25 (m, 5H, Harom), 7.28-7.45 (m, 4H, Harom), 7.50 (d,1H, C-8H, J=8.2 Hz), 7.68 (d,1H, C-7H, J=7.2 Hz), 8.57 (bs, 1H, NH); ms: m/z 318 (M^+). *Anal.* Calcd. for $C_{18}H_{14}N_5Cl$: C, 67.92; H, 4.40; N, 22.01. Found: C, 67.88; H, 4.38; N, 4. 38; N, 21.90.

3-(4'-Nitrophenyl)-6-(4'-chlorophenyl)-5*H*-[1,2,4]triazole-[4,3-*b*][1,2,4]triazepine (8e). This compound was obtained as pale yellow shining solid (ethyl acetate), mp 232-234°C; ir (potassium bromide): 3280 (NH), 3176 (aromatic C-H), 1663 (C=N), 1597 (NO_2), 1407 (C-N), 752 (C-Cl); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 7.10-7.32 (m, 4H, Harom), 7.50 (d, 1H, C-8H, J=8.2 Hz), 7.62-7.80 (m, 2H, Harom and d, 1H buried C-7H, J= 7.2 Hz), 8.00-8.12 (m, 2H, Harom), 8.60 (bs, 1H, NH); ms: m/z 366.5 (M^+). *Anal.* Calcd. for $C_{17}H_{11}N_6O_2Cl$: C, 55.66; H, 3.00; N, 22.91. Found: C, 55.62; H, 2.9 6; N, 22.88.

3-Phenyl-6-(4'-bromophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*]-[1,2,4]triazepine (8f). This compound was obtained as yellow coloured solid (ethyl acetate), mp 168-170°C**;** ir (potassium bromide): 3162 (NH), 3050 (aromatic C-H), 1692 (C=N), 1440 (C-N), 560 (C-Br); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 7.02-7.10 (m, 3H, Harom), 7.13-7.22 (m, 2H, Harom), 7.30- 7.53 (m, 4H, Harom and d, 1H buried C-8H, J= 8.2 Hz), 7.67 (d, 1H, C-7H, J= 7.2 Hz), 8.55 (bs, 1H, NH); ms: m/z 365 (M^+). *Anal.* Calcd. for $C_{17}H_{12}N_5Br$: C, 55.89; H, 3.28; N, 19.17. Found: C, 55.86; H, 3.26; N, 19.16.

3-(2'-Chlorophenyl)-6-(4'-nitrophenyl)-5*H*-[1,2,4,]triazole-[4,3-*b*][1,2,4]triazepine (8g). This compound was obtained as brown coloured shining solid (ethyl acetate), mp182-184°C; ir (potassium bromide): 3174 (NH), 3010 (aromatic C-H str), 1668 (C=N), 1550 (NO_2), 724 (C-Cl); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 7.21-7.26 (m, 3H, Harom), 7.32-7.54 (m, 2H, Harom and d, 1H buried C-8H, J=8.2 Hz), 7.65 (d, 1H, C-7H, J= 7. 3 Hz), 8.05-8.15 (m, 3H, Harom), 8.60 (bs, 1H, NH); ms: m/z 366.5 (M^+). *Anal.* Calcd. for $C_{17}H_{11}N_6O_2Cl$: C, 55.66; H, 3.00; N, 22.91. Found: C, 54.98; H, 2.88; N, 22.80.

3-Benzyl-6-(4'-nitrophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]-triazepine (8h). This compound was obtained was obtained as brown coloured shining solid (ethyl acetate), mp 198-200°C; ir (potassium bromide): 3192 (NH), 3025 (aromatic C-H), 2925 (CH_2), 1612 (C=N), 1550 (NO_2 str), 1442 (C-N); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 4.00 (s, 2H, Ar-CH_2), 7.03-7.25 (m, 4H, C-8H, J=8.2 Hz), 7.70 (d, 1H, C-7H, J=7.2 Hz), 8.10- 8.16 (m, 2H, Harom), 8.53 (bs, 1H, NH); ms: m/z 332 (M^+). *Anal*. Calcd. for $C_{18}H_{14}N_6O_2$: C, 65.06; H, 4.21; N, 25.30. Found: C, 65. 05; H, 4.18: N, 25.25.

3-(4'-Nitrophenyl)-6-(4'-bromophenyl)-5*H*-[1,2,4]triazolo-[4,3-*b*][1,2,4]triazepine (8i). This compound was obtained as yellow coloured shining solid (ethyl acetate), mp 225-227°C; ir (potassium bromide): 3192 (NH), 3080 (aromatic C-H), 1680 (C= N), 1550 (NO_2), 1480 (C-N), 590 (C-Br); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 7.15-7.22 (m, 2H, Harom), 7.36-7.43 (m, 2H, Harom and d, 1H buried C-8H, J=8.2 Hz), 7.68-7.81 (m, 2H, Harom and d, 1H buried C-7H, J= 7.2 Hz), 8.17-8.28 (m, 2H, Harom), 8.54 (bs, 1H, NH); ms: m/z 410 (M^+). *Anal*. Calcd. for $C_{17}H_{11}N_6O_2Br$: C, 49.75; H, 2.68; N, 20.48. Found: C, 49.68; H, 2.55; N, 20.38.

3-Phenyl-6-(4'-nitrophenyl)-5*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]-triazepine (8j). This compound was obtained as brown coloured shining solid (ethyl acetate), mp 230-232°C: ir (potassium bromide): 3167 (NH), 3067 (aromatic C-H), 1662 (C=N), 1546 (NO_2), 1434 (C-N); ^{1}H nmr ($CDCl_3$+DMSO-d_6): 7.00-7.15 (m, 4H, Harom), 7.28-7.48 (m, 2H, Harom and d, 1H buried C-8H, J=8.2 Hz), 7.52 (d, 1H, C-7H, J=7.2 Hz), 8.00-8.12 (m, 3H, Harom), 8.57 (bs, 1H, NH); ms: m/z 332 (M^+). *Anal*. Calcd. for $C_{17}H_{12}N_6O_2$: C, 64.15 ; H, 3.77 ; N, 26.41. Found: C, 64.12 ; H, 3.74; N, 26.38.

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REFERENCES AND NOTES

[1] Shafiee, A.; Tabatabaiee, M. *J. Chem. Eng*. **1998**, *17*, 14.

[2] Hu, C.-C.; Yan, Z.; Zhang, Zi. –Yi.; Chun, Li. Zi.; Ren, Li. *Indian J. Chem*. **2000**, *29B*, 791.

[3] Udupi, R. H.; Purushottam, P.; Bhat, A. R. *Indian J. Chem*. **2000**, *39B*, 291.

[4] Tandon, M. B.; Barthwal, J.P.; Bhalla , T.N.; Bhargava, K.P. *Indian J .Chem*. **1981**, *20B*, 1017.

[5] Mulwad, V. V.; Pawa, R. B. *Indian J. Chem*, **2003**, *42B*, 2901.

[6] Kidwai, M.; Bala, S.; Mishra, A.D. *Indian J. Chem*. **2004,** *43B*, 2485.

[7] Ogura , A. H.; Takahashi, I. H. *Japan Kokai Tokkyo Koho, Japan Patent* 76, 39, 685; *Chem. Abstr,* **1977**, *86*, 5765.

[8] Salerno, A.; Ceriani, V.; Perillo, I. *J. Heterocyclic Chem,* **1992**, *29*, 1725.

[9] Dabholkar, V.V.; Moris, G.D. *Indian J. Chem*, **2004**, *43B*, 6824.

[10] Hagemann, E. H.; German Patent 2, 036, 172; *Chem. Abstr*. **1972**, *76*, 127031k.

[11] Sewell, P.; Hawking, F. *J. Pharmacol*. **1950**, *5*, 239.

[12] Acheson, R. M.; Taylor, N. F. *J. Chem. Soc,* **1956**, 4727.

[13] Cliford, D. P.; Jackson, K. V.; Jeffrey, P. *Pestic. Sci*. **1976**, *7*, 453.

[14] Yamamoto, Y.; Shindo, M. S.; Nakamura, T. PCT *Int. Appl. WO* 97 47, 622, 1997; *Chem. Abstr*. **1999**, *28*,771.

[15] Padhy, A. K.; Nag , V. L.; Panda, C. S. *Indian J. Chem*. **1999**, *38B*, 998.

[16] Chakarborty, A.; Ray, J. K. *Synth. Commun*. **1995,** *25*, 1869.