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MICROWAVE-MEDIATED $InCl_3$-CATALYZED THREE-COMPONENT ANNELATION OF THIADIAZINE RING ONTO 4-AMINO-4*H*-[1,2,4]TRIAZOLE-3-THIOL

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A novel efficient three-component annelation of the thiadiazinyl ring onto 4-amino-4H-[1,2,4]triazole-3-thiol, catalyzed by nontoxic, recyclable $InCl_3$ under microwave activation, has been developed. The transformation of 4-amino-5-aryl-4H-[1,2,4]triazole-3-thiol into triazolothiadiazine involves chemoselective successive double addition reaction consisting of an $InCl_3$-catalyzed dehydrative nucleophilic addition of amino group to an aromatic aldehyde followed by addition of the resulting Schiff base to cyclohexyl isocyanide. The intramolecular cyclization of the adduct results in 3,6-diaryl-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine. The reaction proceeds smoothly with good yields.

Keywords: indium trichloride, triazolothiadiazine, annelation, microwave synthesis, three-component reaction.

The 1,2,4-triazole moiety is present in anastrozole [1], estazolam [2], triazolam [3], ribavirin [4], dapiprazole [5], and cefatrizine [6], which are in clinical use as antineoplastic, sedative, hypnotic, antiviral, antiglaucoma, and antibacterial drugs and as ultraviolet screen. In addition, 1,2,4-triazoles also exhibit various biological activities like analgesic, antiasthmatic, diuretic, antihypertensive, anticholinergic, antibacterial, antifungal, and anti-inflammatory activity [7-10].

Similarly, the thiadiazine nucleus is also a versatile pharmacophore, which exhibits a wide variety of biological activity. Chlorothiazide and diazoxide, which are widely used as diuretic and antihypertensive drugs, respectively, possess the thiadiazine moiety [11, 12]. Several *s*-triazolothiadiazines have found potential application as antibacterial, antifungal, and anti-inflammatory agents [13-15]. A number of triazoles fused to thiadiazines are incorporated into a wide variety of therapeutically important compounds possessing a broad spectrum of biological activities [16-18]. Therefore, triazolothiadiazines appear to be attractive scaffolds that provide a chemical with diverse drug-like library.

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Some 7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines, as well as 7-unsubstituted, 7-bromo-, and 7-piperazinyl-substituted 5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines synthesized by a conventional method, as well as some 1,2,4-triazoles and 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines derived from 4-amino-3-mercapto-1,2,4-triazoles, are associated with diverse pharmacological activities [19-20]. The conventional methods may suffer from any one of the following problems – low yield, long reaction time, use of hazardous chemicals.

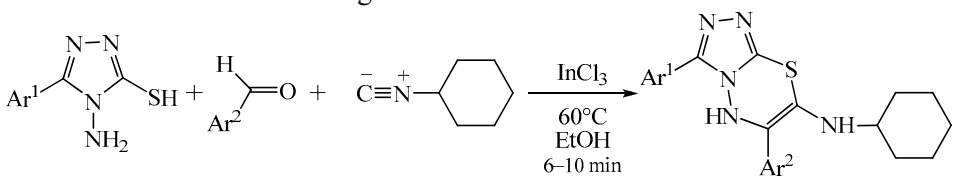
Recent years have witnessed a phenomenal growth in the application of microwave irradiation [21-23] and the use of recyclable, less expensive metal halide catalysts in organic transformations. The application of microwave irradiation in conjunction with metal halide catalyst provides an environmentally benign process with additional advantages, such as enhanced reaction rates, higher yields of products, easier work-up, and considerable reduction in reaction time, all of which are eco-friendly attributes in the context of green chemistry [24-26].

As a part of our program to develop new, simple, selective, eco-friendly methodologies for the synthesis of biodynamic heterocyclic compounds and their nucleoside analogs [27-30], we devised an original $InCl_3$-catalyzed microwave-activated synthesis of some novel triazolothiadiazines *via* site-selective double addition reactions. The synthesis involves dehydrative nucleophilic addition of the NH_2 group of triazole to an aromatic aldehyde, yielding Schiff base that on addition of cyclohexyl isocyanide in ethanol followed by cyclocondensation is transformed into triazolo-fused thiadiazine, the whole process being carried out in a one-pot procedure.

The strategy of the synthesis is outlined in the scheme below. A mixture of 4-amino-5-aryl-4*H*-[1,2,4]triazole-3-thiol **1a-c**, aromatic aldehyde **2a-d**, cyclohexyl cyanide **3**, and $InCl_3$ at 60°C in ethanol was subjected to intermittent microwave irradiation for 2 min in a microwave (MW) oven at 600 W, followed by thorough mixing in ethanol outside the oven and irradiating again for another 2 min. This intermittent irradiation/mixing cycle was repeated for a total irradiation time specified in Table 1 to afford triazolothiadiazines **4a-l** in 75-85% yield.

All aromatic aldehydes containing both electron-withdrawing as well as electron-donating groups reacted well under these reaction conditions to give the corresponding products in good yields. It was found that the reactions did not proceed when aliphatic aldehydes were used.

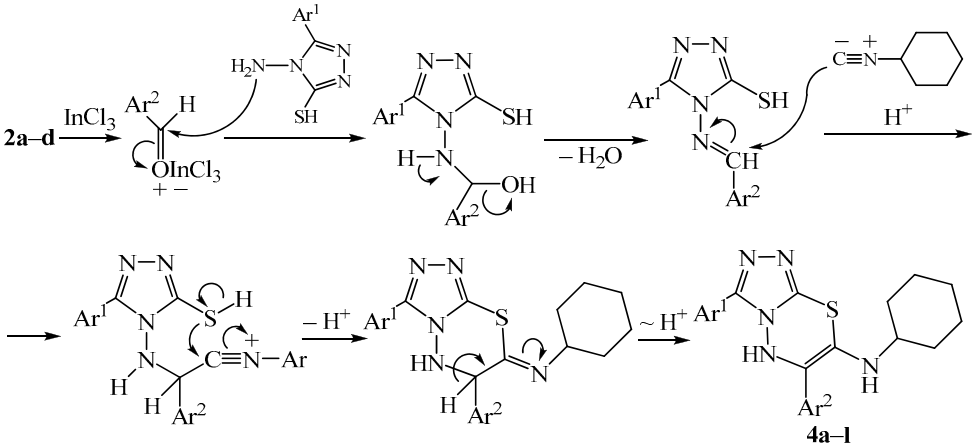
TABLE 1. $InCl_3$-catalyzed Synthesis of Triazolothiadiazine under MW and Conventional Heating



1a–c **2a–d** **3** **4a–l**

Product	Ar^1	Ar^2	Time		Yield	
			MW, min	Conventional, h	MW, %	Conventional, %
4a	4-ClC_6H_4	4-$O_2NC_6H_4$	6	8	80	37
4b	4-ClC_6H_4	4-ClC_6H_4	7	9	78	36
4c	4-ClC_6H_4	4-MeC_6H_4	8	9	77	35
4d	4-ClC_6H_4	4-$MeOC_6H_4$	5	7	82	38
4e	4-$H_2NC_6H_4$	4-$O_2NC_6H_4$	6	8	83	39
4f	4-$H_2NC_6H_4$	4-ClC_6H_4	8	9	77	34
4g	4-$H_2NC_6H_4$	4-MeC_6H_4	9	9	78	33
4h	4-$H_2NC_6H_4$	4-$MeOC_6H_4$	10	10	75	30
4i	4-HOC_6H_4	4-$O_2NC_6H_4$	10	10	76	32
4j	4-HOC_6H_4	4-ClC_6H_4	5	7	85	40
4k	4-HOC_6H_4	4-MeC_6H_4	6	6	75	33
4l	4-HOC_6H_4	4-$MeOC_6H_4$	9	8	77	40

For comparison purpose, the reactions were also carried using a thermostated oil-bath using $InCl_3$ catalyst at the same temperature (60°C) as for the MW-activated process for a longer (optimized) period of time (Table 1) to ascertain whether the MW activation improved the yield or simply increased the conversion rate. It was found that significantly lower yields (30-40%) were obtained and much higher reaction times were needed under conventional heating. All the products **4a-l** were characterized by spectral analysis. The ^1H and ^{13}C NMR data indicated the presence of the cyclohexyl group and two aryl groups, and the mass spectra and elemental analysis data were fully consistent with the assigned molecular formula.



The proposed mechanism for the synthesis of 5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazine

In conclusion, we have described an environmentally benign, one-pot cyclization procedure for the synthesis of 3,6-diaryl-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines by means of a three-component condensation using a recyclable and nontoxic $InCl_3$ catalyst under microwave irradiation conditions. The $InCl_3$-catalyzed procedure provides an important, novel, and facile route for the synthesis of triazolothiadiazines and may find application in the library synthesis of related biologically active heterocyclic compounds.

EXPERIMENTAL

IR spectra were recorded on a Shimadzu FTIR-420 spectrophotometer in KBr. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 FT spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ using TMS as the internal standard. Mass spectra were recorded on a JEOL SX-102 (FAB) mass spectrometer at 6 kV and 10 mA with an accelerating voltage of 10 kV. Elemental analyses were carried out using a Coleman automatic CHN-analyzer. A BP 310/50 laboratory microwave oven operating at 2450 MHz and power output of 600 W was used for all the experiments. All chemicals used were of reagent grade and were used as received without further purification.

Synthesis of Triazolothiadiazines 4a-l (General Method: **Conventional Heating)**. A mixture of 4-amino-4*H*-[1,2,4]triazole-3-thiol **1a-c** (1.00 mmol), aromatic aldehyde **2a-d** (1.00 mmol), cyclohexyl isocyanide **3** (0.11 g, 1.00 mmol), and $InCl_3$ (6.64 mg, 0.03 mmol) in EtOH (25 ml) was placed in a flame-dried 50 ml round-bottom flask. The reaction mixture was stirred at 60°C. After the completion of the reaction (TLC, *n*-hexane–AcOEt, 7:3), the solvent was evaporated, and the product was extracted by diethyl ether and purified by flash column chromatography on silica gel (eluent *n*-hexane–AcOEt, 4:1).

(General Method: MW Activation). The reaction mixture prepared as above was subjected to MW irradiation for 2 min at 600 W. Then the reaction mixture was thoroughly mixed outside the MW oven. The reaction mixture was again irradiated for another 2 min and this irradiation and mixing cycle was repeated until

the reaction was complete (TLC, *n*-hexane–AcOEt, 7:3). The solvent was evaporated, and the product was worked up as indicated above.

3-(4-Chlorophenyl)-*N*-cyclohexyl-6-(4-nitrophenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (**4a**). Mp 150-151°C. IR spectrum, ν, cm^{-1}: 1450 (NO_2), 1645 (C=N), 1670 (C=C), 2920 (cyclohexyl C–H), 3070 (Ar C–H), 3310 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 5.10 (2H, s, 2NH); 7.55 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 8.04 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar); 8.12 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 8.20 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 121.3; 123.5; 127.1; 128.4; 129.4; 133.8; 134.6; 141.0; 147.6; 148.0. Mass spectrum, *m*/*z*: 468 $[M]^+$. Found, %: C 56.15; H 4.48; N 17.90. $C_{22}H_{21}ClN_6O_2S$. Calculated, %: C 56.35; H 4.51; N 17.92.

3,6-Bis(4-chlorophenyl)-*N*-cyclohexyl-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4b). Mp 157-158°C. IR spectrum, ν, cm^{-1}: 1642 (C=N), 1665 (C=C), 2918 (cyclohexyl C–H), 3065 (Ar C–H), 3305 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 5.08 (2H, s, 2NH); 7.38 (4H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.83 (4H, dd, *J* = 7.9, *J* = 2.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 121.3; 127.6; 128.4; 128.8; 129.4; 133.0; 133.8; 134.6; 148.0. Mass spectrum, *m*/*z*: 457 $[M]^+$. Found, %: C 57.60; H 4.60; N 15.24. $C_{22}H_{21}Cl_2N_5S$. Calculated, %: C 57.64; H 4.62; N 15.28.

3-(4-Chlorophenyl)-*N*-cyclohexyl-6-(*p*-tolyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4c). Mp 159-160°C. IR spectrum, ν, cm^{-1}: 1630 (C=N), 1658 (C=C), 2912 (cyclohexyl C–H), 3050 (Ar C–H), 3300 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.35 (3H, s, CH_3); 2.56-2.58 (1H, m, CHN); 5.06 (2H, s, 2NH); 7.18 (2H, dd, *J* = 7.4, *J* = 1.6, H Ar); 7.25 (2H, dd, *J* = 7.4, *J* = 1.6, H Ar); 7.55 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 8.12 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 20.9; 22.4; 27.1; 33.4; 48.2; 111.3; 121.3; 126.1; 128.4; 129.1; 129.4; 131.9; 133.8; 134.6; 136.9; 148.0. Mass spectrum, *m*/*z*: 437 $[M]^+$. Found, %: C 63.03; H 5.46; N 15.66. $C_{23}H_{24}ClN_5S$. Calculated, %: C 63.07; H 5.52; N 15.99.

3-(4-Chlorophenyl)-*N*-cyclohexyl-6-(4-methoxyphenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4d). Mp 154-155°C. IR spectrum, ν, cm^{-1}: 1638 (C=N), 1662 (C=C), 2916 (cyclohexyl C–H), 3055 (Ar C–H), 3303 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 3.73 (3H, s, OCH_3); 5.07 (2H, s, 2NH); 6.94 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.55 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.57 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 8.12 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 56.0; 111.3; 114.0; 121.3; 127.2; 128.4; 129.4; 133.8; 134.6; 148.0. Mass spectrum, *m*/*z*: 453 $[M]^+$. Found, %: C 60.65; H 5.30; N 15.30. $C_{23}H_{24}ClN_5OS$. Calculated, %: C 60.85; H 5.33; N 15.43.

3-(4-Aminophenyl)-*N*-cyclohexyl-6-(4-nitrophenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4e). Mp 144-145°C. IR spectrum, ν, cm^{-1}: 1448 (NO_2), 1643 (C=N), 1666 (C=C), 2917 (cyclohexyl C–H), 3066 (Ar C–H), 3306 (N–H), 3490 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 4.00 (2H, s, NH_2); 5.06 (2H, s, 2NH); 6.56-6.59 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar); 7.90 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar); 8.04 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar); 8.21 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 115.6; 121.3; 123.5; 126.5; 127.1; 127.8; 141.0; 146.7; 147.6; 148.0. Mass spectrum, *m/z*: 449 $[M]^+$. Found, %: C 58.68; H 5.10; N 21.71. $C_{22}H_{23}N_7O_2S$. Calculated, %: C 58.78; H 5.16; N 21.81.

3-(4-Aminophenyl)-6-(4-chlorophenyl)-*N*-cyclohexyl-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4f). Mp 151-152°C. IR spectrum, ν, cm^{-1}: 1638 (C=N), 1662 (C=C), 2915 (cyclohexyl C–H), 3061 (Ar C–H), 3301 (N–H), 3482 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 4.00 (2H, s, NH_2); 5.08 (2H, s, 2NH); 6.58 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar); 7.31 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.44 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.89 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 115.6; 121.3; 126.5; 127.6; 127.8; 128.8; 133.0; 146.7; 148.0. Mass spectrum, *m*/*z*: 438 $[M]^+$. Found, %: C 60.10; H 5.26; N 19.12. $C_{22}H_{23}ClN_6S$. Calculated, %: C 60.19; H 5.28; N 19.14.

3-(4-Aminophenyl)-*N*-cyclohexyl-6-(*p*-tolyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4g). Mp 150-151°C. IR spectrum, ν, cm^{-1}: 1625 (C=N), 1654 (C=C), 2908 (cyclohexyl C–H), 3045 (Ar C–H), 3300

(N–H), 3484 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.35 (3H, s, CH_3); 2.56-2.58 (1H, m, CHN); 4.00 (2H, s, NH_2); 5.02 (2H, s, 2NH); 6.58 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar); 7.17 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.26 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.89 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar). ^{13}C NMR spectrum, δ, ppm: 20.9; 22.4; 27.1; 33.4; 48.2; 111.3; 115.6; 121.3; 126.1; 126.5; 127.8; 129.1; 131.9; 136.9; 146.7; 148.0. Mass spectrum, *m/z*: 418 $[M]^+$. Found, %: C 65.98; H 6.16; N 20.02. $C_{23}H_{26}N_6S$. Calculated, %: C 66.00; H 6.26; N 20.08.

3-(4-Aminophenyl)-*N*-cyclohexyl-6-(4-methoxyphenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-7-amine (4h). Mp 156-157°C. IR spectrum, ν, cm^{-1}: 1635 (C=N), 1660 (C=C), 2912 (cyclohexyl C–H), 3050 (Ar C–H), 3301 (N–H), 3488 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56–2.58 (1H, m, CHN); 3.73 (3H, s, OCH_3); 4.00 (2H, s, NH_2); 5.02 (2H, s, 2NH); 6.58 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar); 6.94 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.55 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.89 (2H, dd, *J* = 7.5, *J* = 1.7, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 56.0; 111.3; 114.0; 115.6; 121.3; 126.5; 127.2; 127.8; 146.7; 148.0; 161.2. Mass spectrum, *m/z*: 434 $[M]^+$. Found, %: C 63.47; H 6.01; N 19.32. $C_{23}H_{26}N_6OS$. Calculated, %: C 63.57; H 6.03; N 19.34.

4-[7-Cyclohexylamino-6-(4-nitrophenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl]phenol (4i). Mp 150-151°C. IR spectrum, ν, cm^{-1}: 1452 (NO_2), 1644 (C=N), 1668 (C=C), 2919 (cyclohexyl C–H), 3068 (Ar C–H), 3308 (N–H), 3505 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, $5CH_2$); 2.56-2.58 (1H, m, CHN); 5.00 (1H, s, ArOH); 5.11 (2H, s, 2NH); 6.86 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar); 7.91 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar); 8.04 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar); 8.21 (2H, dd, *J* = 8.5, *J* = 2.1, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 116.2; 121.3; 123.5; 127.1; 128.4; 129.1; 147.6; 148.0; 157.3. Mass spectrum, *m/z*: 450. Found, %: C 58.55; H 4.82; N 18.62. $C_{22}H_{22}N_6O_3S$. Calculated, %: C 58.65; H 4.92; N 18.65.

4-[6-(4-Chlorophenyl)-7-cyclohexylamino-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl]phenol (4j). Mp 153-154°C. IR spectrum, ν, cm^{-1}: 1663 (C=C), 1640 (C=N), 2917 (cyclohexyl C–H), 3063 (Ar C–H), 3303 (N–H), 3500 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, CH_2); 2.56–2.58 (1H, m, CHN); 5.00 (1H, s, ArOH); 5.09 (2H, s, NH); 6.86 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar); 7.32 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.34 (2H, dd, *J* = 7.9, *J* = 2.0, H Ar); 7.91 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 111.3; 116.2; 121.3; 127.6; 128.4; 128.8; 129.1; 148.0; 157.3. Mass spectrum, *m/z*: 439 $[M]^+$. Found, %: C 60.02; H 5.02; N 15.90. $C_{22}H_{22}ClN_5OS$. Calculated, %: C 60.06; H 5.04; N 15.92.

4-[7-Cyclohexylamino-6-(*p*-tolyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl]-phenol (4k). Mp 155-156°C. IR spectrum, ν, cm^{-1}: 1656 (C=C); 1628 (C=N); 2910 (cyclohexyl C–H); 3047 (Ar C–H); 3300 (N–H); 3501 (OH). ^{1}H NMR specrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, CH_2); 2.35 (3H, s, CH_3); 2.56-2.58 (1H, m, CHN); 5.00 (1H, s, ArOH); 5.15 (2H, s, NH); 6.86 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar); 7.18 (2H, dd, *J* = 7.4, *J* = 1.6, H Ar); 7.26 (2H, dd, *J* = 7.4, *J* = 1.6, H Ar); 7.91 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar). ^{13}C NMR spectrum, δ, ppm: 20.9; 22.4; 27.1; 33.4; 48.2; 111.3; 116.2; 121.3; 126.1; 128.4; 129.1; 131.9; 136.9; 148.0; 157.3. Mass spectrum, *m/z*: 419 $[M]^+$. Found, %: C 65.82; H 5.98; N 16.59. $C_{23}H_{25}N_5OS$. Calculated, %: C 65.84; H 6.01; N 16.69.

4-[7-Cyclohexylamino-6-(4-methoxyphenyl)-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl]phenol (4l). Mp 158-159°C. IR spectrum, ν, cm^{-1}: 1661 (C=C), 1637 (C=N), 2914 (cyclohexyl C–H), 3053 (Ar C–H), 3302 (N–H), 3503 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.44-1.66 (10H, m, CH_2); 2.56-2.58 (1H, m, CHN); 3.73 (3H, s, OCH_3); 5.00 (1H, s, ArOH); 5.09 (2H, s, NH); 6.86 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar); 6.94 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.55 (2H, dd, *J* = 7.6, *J* = 1.8, H Ar); 7.91 (2H, dd, *J* = 7.7, *J* = 1.9, H Ar). ^{13}C NMR spectrum, δ, ppm: 22.4; 27.1; 33.4; 48.2; 56.0; 111.3; 114.0; 116.2; 121.3; 127.2; 128.4; 129.1; 148.0; 157.3; 161.2. Mass spectrum, *m/z*: 435 $[M]^+$. Found, %: C 63.40; H 5.72; N 16.02. $C_{23}H_{25}N_5O_2S$. Calculated, %: C 63.43; H 5.79; N 16.08.

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