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# Synthesis, antimicrobial, and anti-HIV-1 activity of certain 5-(1-adamantyl)-2-substituted thio-1,3,4-oxadiazoles and 5-(1-adamantyl)-3-substituted aminomethyl-1,3,4-oxadiazoline-2-thiones

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**Abstract**—The reaction of 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** with iodoethane, 2-dimethylaminoethyl chloride hydrochloride or 2-piperidinoethyl chloride hydrochloride in ethanolic potassium hydroxide yielded the corresponding 5-(1-adamantyl)-2-ethyl or substituted ethylthio-1,3,4-oxadiazoles **3a–c**. Interaction of **2** with formaldehyde solution and primary aromatic amines or 1-substituted piperazines, in ethanol at room temperature yielded the corresponding 5-(1-adamantyl)-3-arylaminomethyl-1,3,4-oxadiazoline-2-thiones **4a–m** or 5-(1-adamantyl)-3-(4-substituted-1-piperazinylmethyl)-1,3,4-oxadiazoline-2-thiones **5a–h**, respectively. All the synthesized compounds were tested for in vitro activities against certain strains of Gram-positive and Gram-negative bacteria and the yeast-like pathogenic fungus *Candida albicans*. Compounds **2**, **5a**, and **5e** were found as the most active derivatives, particularly against the Gram-positive bacteria. In addition, the antiviral activity of compounds **2**, **4a–m**, and **5a–h** against HIV-1 using the XTT assay was carried out. Compound **2** produced 100%, 43%, and 37% reduction of viral replication at 50, 10, and 2 μg/mL concentrations, respectively.


## 1. Introduction

A number of adamantane derivatives have long been known for their antiviral activity against Influenza A[1–6] and HIV viruses.[7–9] Several adamantane derivatives were also associated with central nervous,[10–14] antimicrobial,[15–19] and anti-inflammatory activities.[20–24] In addition, 1,3,4-oxadiazole derivatives were reported to possess significant antibacterial[25,26] and anti-inflammatory activities.[27,28] Moreover, several bis(heteroaryl)piperazine derivatives (BHAP) were introduced as potent antiviral drugs.[29,30] In continuation to our interest in the chemical and pharmacological properties of adamantane derivatives,[19,23,31–33] we report herein the synthesis, antimicrobial, and anti-HIV-1 activity of new series of 5-(1-adamantyl)-2-substituted ethylthio-1,3,4-oxadiazoles, 5-(1-adamantyl)-3-arylaminomethyl-1,3,4-oxadiazoline-2-thiones, and 5-(1-adamantyl)-3-(4-substituted-1-piperazinylmethyl)-1,3,4-oxadiazoline-2-thiones.

## 2. Results and discussion

### 2.1. Chemistry

The starting material adamantane-1-carbohydrazide **1**[34] was obtained via prolonged heating of methyl adamantane-1-carboxylate[20] with hydrazine. The hydrazide **1** was reacted with carbon disulfide and potassium hydroxide, in ethanol, followed by acidification to yield 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** in 81% yield. Interaction of **2** with iodoethane, 2-dimethylaminoethyl chloride, or 2-(1-piperidyl)ethyl chloride hydrochloride in ethanolic potassium hydroxide yielded the corresponding 5-(1-adamantyl)-2-ethylthio or substituted ethylthio-1,3,4-oxadiazoles **3a–c**. On the other hand, the *N*-Mannich derivatives 5-(1-adamantyl)-3-arylaminomethyl-1,3,4-oxadiazoline-2-thiones **4a–m** and

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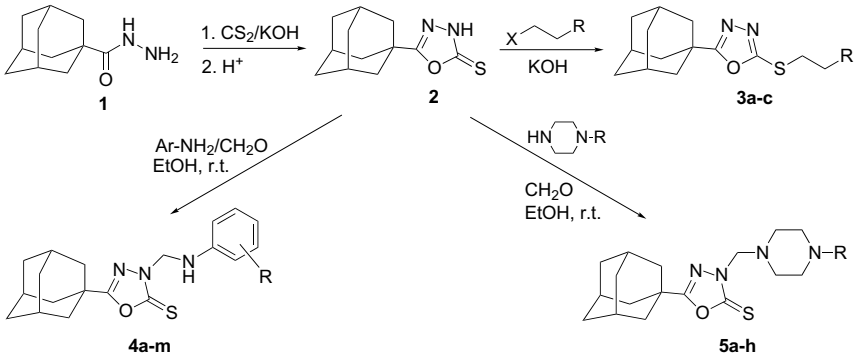
5-(1-adamantyl)-3-(4-substituted-1-piperazinylmethyl)-1,3,4-oxadiazoline-2-thiones **5a**–**h**, were prepared in high yields via the reaction of **2** with formaldehyde solution and the corresponding primary aromatic amine or 1-substituted piperazine, in ethanol at room temperature, respectively (Scheme 1, Table 1). The structures of the synthesized compounds were confirmed by elemental analyses, IR, $^{1}$H NMR, $^{13}$C NMR, and EI mass spectral data.

## 2.2. In vitro antimicrobial activity

The synthesized compounds were tested for their in vitro antimicrobial activity against the Gram-positive bacteria *Staphylococcus aureus* ATCC 19433 and *Bacillus subtilis* ATCC 6633, the Gram-negative bacteria *Escherichia coli* ATCC 25922 and *Pseudomonas aeurogi-nosa* ATCC 27853, and the yeast-like pathogenic fungus *Candida albicans* ATCC 753. The primary screen was carried out using the agar disc-diffusion method[35] using Müller–Hinton agar medium. Sterile filter paper discs (8 mm diameter) were moistened with the test compound solution in dimethylsulfoxide of specific concentration 200 μg/disc were carefully placed on the agar cultures plates that had been previously inoculated separately with the microorganisms. The plates were incubated at 37 °C, and the diameter of the growth inhibition zones were measured after 24 h in case of bacteria and 48 h in case of *C. albicans*. The results of the preliminary antimicrobial testing of the prepared compounds, the typical broad spectrum antibacterial drug ciprofloxacin and the potent antifungal drug clotrimazole (100 μg/disc) are shown in Table 2. The results revealed that majority of the synthesized compounds showed varying degrees of inhibition against the tested microorganisms. In general, the inhibitory activity against the tested Gram-positive bacteria was higher than that of the Gram-negative bacteria, and some derivatives showed moderate or weak activity against *C. albicans*. The ethylthio and the aminoethylthio derivatives **3a**–**c** were almost inactive. The compounds **2**, **5a**, and **5e** showed broad spectrum antimicrobial activity, they possessed




**Scheme 1.**

**Table 1.** Crystallization solvents, melting points, yield percentages, molecular formulae, and molecular weights of compounds **3a**–**c**, **4a**–**m**, and **5a**–**h**

| Compound no. | R | Cryst. solvent | Mp (°C) | Yield (%) | Mol. Formula (Mol. Wt) |
|---|---|---|---|---|---|
| **3a** | H | EtOH/$H_2O$ | 53–55 | 82 | $C_{14}H_{20}N_2OS$ (264.38) |
| **3b** | $N(CH_3)_2$ | EtOH/$H_2O$ | 76–78 | 72 | $C_{16}H_{25}N_3OS$ (307.45) |
| **3c** | 1-Piperidyl | EtOH/$H_2O$ | 73–75 | 77 | $C_{19}H_{29}N_3OS$ (347.51) |
| **4a** | H | EtOH | 141–143 | 88 | $C_{19}H_{23}N_3OS$ (341.47) |
| **4b** | 2-F | EtOH | 109–111 | 81 | $C_{19}H_{22}FN_3OS$ (359.46) |
| **4c** | 4-F | EtOH | 140–142 | 90 | $C_{19}H_{22}FN_3OS$ (359.46) |
| **4d** | 2-Cl | EtOH | 135–137 | 87 | $C_{19}H_{22}ClN_3OS$ (375.91) |
| **4e** | 4-Cl | EtOH | 177–179 | 92 | $C_{19}H_{22}ClN_3OS$ (375.91) |
| **4f** | 2-Br | EtOH | 144–146 | 79 | $C_{19}H_{22}BrN_3OS$ (420.36) |
| **4g** | 4-Br | EtOH/$CHCl_3$ | 170–172 | 82 | $C_{19}H_{22}BrN_3OS$ (420.36) |
| **4h** | 3-$NO_2$ | EtOH/$CHCl_3$ | 150–152 | 73 | $C_{19}H_{22}N_4O_3S$ (386.46) |
| **4i** | 4-$NO_2$ | EtOH/$CHCl_3$ | 231–233 | 69 | $C_{19}H_{22}N_4O_3S$ (386.46) |
| **4j** | 4-$CH_3O$ | EtOH | 131–133 | 88 | $C_{20}H_{25}N_3O_2S$ (371.49) |
| **4k** | 2-CN | EtOH/$H_2O$ | 174–176 | 75 | $C_{20}H_{22}N_4OS$ (366.48) |
| **4l** | 2-$CF_3$ | EtOH | 148–150 | 80 | $C_{20}H_{22}F_3N_3OS$ (409.46) |
| **4m** | 2,5-$F_2$ | EtOH/$CHCl_3$ | 130–132 | 88 | $C_{19}H_{21}F_2N_3OS$ (377.45) |
| **5a** | $CH_3$ | EtOH/$H_2O$ | 113–115 | 64 | $C_{18}H_{28}N_4OS$ (348.50) |
| **5b** | $C_2H_5$ | EtOH/$H_2O$ | 109–111 | 61 | $C_{19}H_{30}N_4OS$ (362.53) |
| **5c** | $COOC_2H_5$ | EtOH/$H_2O$ | 118–120 | 76 | $C_{20}H_{30}N_4O_3S$ (406.54) |
| **5d** | $C_6H_5$ | EtOH | 166–168 | 89 | $C_{23}H_{30}N_4OS$ (410.57) |
| **5e** | 4-$FC_6H_4$ | EtOH | 180–182 | 92 | $C_{23}H_{29}FN_4OS$ (428.56) |
| **5f** | 2-$CH_3OC_6H_4$ | EtOH | 142–144 | 82 | $C_{24}H_{32}N_4O_2S$ (440.60) |
| **5g** | $C_6H_5CH_2$ | EtOH | 127–129 | 75 | $C_{24}H_{32}N_4OS$ (424.60) |
| **5h** | 2-$CF_3C_6H_4CH_2$ | EtOH | 152–154 | 85 | $C_{25}H_{31}F_3N_4OS$ (492.60) |

**Table 2.** Antimicrobial activity of compounds **2**, **3a–c**, **4a–m**, **5a–h** (200 μg/8 mm disc), the broad spectrum antibacterial drug Ciprofloxacin (100 μg/8 mm disc) and the antifungal drug Clotrimazole (100 μg/8 mm disc) against *S. aureus* ATCC 19433 (*SA*), *B. subtilis* ATCC 6633 (*BS*), *E. coli* ATCC 25922 (*EC*), *P. aeuroginosa* ATCC 27853 (*PA*), and *C. albicans ATCC 753* (*CA*)

| Compound no. | Diameter of growth inhibition zone (mm)[a] | | | | |
|---|---|---|---|---|---|
| | *SA* | *BS* | *EC* | *PA* | *CA* |
| **2** | 23 | 23 | 18 | 16 | 14 |
| **3a** | — | — | — | — | — |
| **3b** | 9 | — | — | — | — |
| **3c** | 10 | 10 | — | — | — |
| **4a** | 12 | 14 | 9 | 10 | — |
| **4b** | 14 | 11 | 8 | — | — |
| **4c** | 17 | 16 | 10 | 10 | — |
| **4d** | 15 | 12 | 10 | 9 | — |
| **4e** | 18 | 18 | 11 | 9 | — |
| **4f** | 10 | 8 | — | — | — |
| **4g** | 12 | 10 | — | — | — |
| **4h** | 10 | 11 | — | — | — |
| **4i** | 14 | 12 | 10 | 10 | — |
| **4j** | 12 | 9 | — | — | — |
| **4k** | 8 | 10 | — | — | — |
| **4l** | 19 | 16 | 12 | 13 | 10 |
| **4m** | 18 | 18 | 11 | 13 | 10 |
| **5a** | 24 | 22 | 17 | 18 | 15 |
| **5b** | 19 | 17 | 10 | 10 | 10 |
| **5c** | 11 | 9 | — | — | — |
| **5d** | 18 | 18 | 10 | 13 | 9 |
| **5e** | 21 | 19 | 16 | 14 | 12 |
| **5f** | 18 | 19 | 14 | 13 | 10 |
| **5g** | 16 | 17 | 10 | 11 | — |
| **5h** | 17 | 16 | 10 | 10 | 9 |
| Ciprofloxacin | 22 | 22 | 25 | 19 | NT |
| Clotrimazole | NT | NT | NT | NT | 23 |

[a] (—): Inactive, no inhibition zone. (NT): Not tested.

excellent activity against the Gram-positive bacteria (inhibition zone >20 mm), good activity against the Gram-negative bacteria (inhibition zone 14–18 mm), and moderate activity against *C. albicans* (inhibition zone 12–15 mm). The minimal inhibitory concentration (MIC) for the most active compounds **2**, **4c**,**e**,**l**,**m**, **5a**,**b**,**d**–**h** against the same microorganism used in the primary screening was carried out using the microdilution susceptibility method in Müller–Hinton Broth and Sabouraud Liquid Medium.[36] The compounds, ciprofloxacin and clotrimazole were dissolved in dimethylsulfoxide at concentration of 800 μg/mL. The twofold dilutions of the solution was prepared (400, 200, 100,. . .,6.25 μg/mL). The microorganism suspensions at $10^6$ CFU/mL (colony forming unit/mL) concentration were inoculated to the corresponding wells. The plates were incubated at 36 °C for 24 and 48 h for the bacteria and *C. albicans*, respectively. The MIC values were determined as the lowest concentration that completely inhibited visible growth of the microorganism as detected by unaided eye (Table 3). The structure–antimicrobial activity relationship of the synthesized compounds, based on the structures of the starting compound **2**, which possessed good antimicrobial activity, revealed that the introduction of an arylaminomethyl moiety generally reduced the antimicrobial activity according to the nature of the aryl moiety. Among the arylaminomethyl derivatives **4a**–**m**, the aryl substituents

**Table 3.** The minimal inhibitory concentrations (MIC, μg/mL) of compounds **2**, **4c**,**e**,**l**,**m**, **5a**,**b**,**d**–**h**, the broad spectrum antibacterial drug Ciprofloxacin and the antifungal drug Clotrimazole against *S. aureus* ATCC 19433 (*SA*), *B. subtilis* ATCC 6633 (*BS*), *E. coli* ATCC 25922 (*EC*), *P. aeuroginosa* ATCC 27853 (*PA*), and *C. albicans* ATCC 753 (*CA*)

| Compound no. | Minimal inhibitory concentration (MIC, μg/mL) | | | | |
|---|---|---|---|---|---|
| | *SA* | *BS* | *EC* | *PA* | *CA* |
| **2** | 12.5 | 12.5 | 50 | 100 | 100 |
| **4c** | 100 | 200 | 200 | 200 | 400 |
| **4e** | 50 | 50 | 200 | 400 | >400 |
| **4l** | 50 | 100 | 200 | 200 | 200 |
| **4m** | 50 | 50 | 400 | 200 | 400 |
| **5a** | 12.5 | 12.5 | 50 | 50 | 200 |
| **5b** | 50 | 50 | 200 | 200 | 200 |
| **5d** | 50 | 50 | 200 | 200 | 400 |
| **5e** | 25 | 100 | 100 | 200 | 200 |
| **5f** | 50 | 50 | 200 | 200 | 400 |
| **5g** | 100 | 100 | 400 | 400 | >400 |
| **5h** | 50 | 100 | 400 | 400 | >400 |
| Ciprofloxacin | <6.25 | <6.25 | <6.25 | <6.25 | NT |
| Clotrimazole | NT | NT | NT | NT | 12.5 |

(NT): Not tested.

had a great influence on the activity, the 4-chlorophenyl, 2-trifluoromethylphenyl, and 2,5-difluorophenyl derivatives were the most active. The piperazinomethyl derivatives **5a**–**h** were found to be more active than the arylaminomethyl derivatives **4a**–**m**. The maximum activity was attained with compound **5a** (R = $CH_3$). Replacement of the methyl group with ethyl, phenyl, 4-fluorophenyl, 2-methoxyphenyl, benzyl, or 2-trifluoromethylbenzyl groups did not reduce the antibacterial activity significantly, but greatly reduced the antifungal activity. Meanwhile, replacement of the methyl group with an ethoxycarbonyl function (**5c**) dramatically reduced the antimicrobial activity.

### 2.3. In vitro anti-HIV-1 activity

The inhibitory activity of compounds **2**, **4a**–**m**, and **5a**–**h** against human immunodeficiency virus type 1 (HIV-1) was determined using the XTT assay in MT-4 cells.[37] The method simultaneously determine both antiviral activity and cellular toxicity, showing the net effect of antiviral activity. The method depends on measuring the change in optical density produced by 2,3-bis[2-methoxy-4-nitro-5-sulfophenyl]-5-[(phenylamino)carbonyl]-2*H*-tetrazolium hydroxide (XTT) at 450 nm, which is indicative of and proportional to healthy, metabolizing cells. The anti-HIV-1 activity of compounds **2**, **4a**–**m**, and **5a**–**h** at 50, 10, and 2 μg/mL concentrations and the cytotoxic doses $CD_{50}$ are shown in Table 4. The results revealed that the majority of the tested compounds inhibited viral replication at 50 and 10 μg/mL concentrations. Compounds **2** was found to be the most active among the tested compounds, it produced 100%, 43%, and 37% reduction of viral replication at 50, 10, and 2 μg/mL concentrations, respectively. Meanwhile, compounds **4c**,**f**, and **5a** showed moderate antiviral activity producing more than 10% inhibition of viral replication at 2 μg/mL concentrations. Compounds

**Table 4.** The anti-HIV-1 activity and cellular toxicity of compounds **2**, **4a–m**, and **5a–h**

| Compound no. | %Reduction of HIV-1[a] | | | $CD_{50}$[b] (μg/mL) |
|---|---|---|---|---|
| | 50 μg/mL | 10 μg/mL | 2 μg/mL | |
| **2** | 100 | 43 | 37 | 68 |
| **4a** | 22 | 9 | 0 | >100 |
| **4b** | 0 | 0 | 0 | >100 |
| **4c** | 23 | 19 | 14 | >100 |
| **4d** | 12 | 8 | 0 | >100 |
| **4e** | 0 | 0 | 0 | >100 |
| **4f** | 17 | 14 | 13 | >100 |
| **4g** | 0 | 0 | 0 | >100 |
| **4h** | 12 | 0 | 0 | >100 |
| **4i** | 16 | 15 | 5 | >100 |
| **4j** | 33 | 24 | 5 | >100 |
| **4k** | 19 | 17 | 7 | >100 |
| **4l** | 27 | 12 | 5 | >100 |
| **4m** | 41 | 12 | 0 | >100 |
| **5a** | 53 | 19 | 11 | >100 |
| **5b** | 26 | 6 | 0 | >100 |
| **5c** | 0 | 0 | 0 | >100 |
| **5d** | 11 | 8 | 6 | >100 |
| **5e** | 41 | 13 | 5 | >100 |
| **5f** | 12 | 8 | 0 | >100 |
| **5g** | 37 | 19 | 0 | >100 |
| **5h** | 26 | 19 | 9 | >100 |

[a] Percentage inhibition of virus replication at each of the indicated concentrations.

[b] The cytotoxic dose (the dose which gives 50% inhibition of growth of uninfected cells).

**4b**,**e**,**g**, and **5c** were totally inactive. All the tested compounds were found to be noncytotoxic with $CD_{50} > 100$ μg/mL, except compound **2** whose $CD_{50}$ was 68 μg/mL.

## 3. Experimental

All melting points (°C, uncorrected) were determined using Fisher–Johns melting point apparatus. Infra red spectra were recoded in KBr disc using Jasco FT/IR 460 Plus spectrometer and expressed in wave number $\nu$ ($cm^{-1}$). NMR spectra were obtained on a Bruker AC 250 FT NMR spectrometer at 250 MHz for $^1H$ and 62.9 MHz for $^{13}C$, the chemical shifts are expressed in $\delta$ (ppm) downfield from tetramethylsilane (TMS) using $CDCl_3$ as solvent. Electron impact mass spectra were recorded on a Shimadzu GC–MS-QP 5000 instrument. Elemental analyses (C, H, N, S) were in agreement with the proposed structures within ±0.4% of the theoretical values.

### 3.1. 5-(1-Adamantyl)-1,3,4-oxadiazoline-2-thione (2)

A mixture of adamantane-1-carbohydrazide (19.4 g, 0.1 mol), potassium hydroxide (5.6 g, 0.1 mol) and carbon disulfide (11.4 g, 0.15 mol), in ethanol (200 mL) was heated under reflux with stirring for 10 h and the solvent was distilled in vacuo. The obtained residue was dissolved in water (100 mL), filtered, and the filtrate was acidified with hydrochloric acid. The precipitated crude product was filtered, washed with water, dried, and crystallized from light petroleum (60–80)–$CHCl_3$ to yield 19.1 g (81%) of **2**. Mp 181–183 °C. IR, $\nu$ ($cm^{-1}$): 3162 (NH), 2914, 2850 ($CH_2$, CH), 1604, 1504 (C=N), 1343 (C=S), 1266 (C–O–C). $^1H$ NMR: $\delta$ 1.71–1.76 (m, 6H, adamantane-$CH_2$), 1.99 (s, 6H, adamantane-$CH_2$), 2.08 (s, 3H, adamantane-CH), 11.60 (br s, 1H, NH). $^{13}C$ NMR: $\delta$ 27.31, 34.47, 35.92, 38.94 (adamantane-C), 170.34 (C=N), 178.27 (C=S). MS *m*/*z* (rel. int.): 237 ($M^+$+1, 13), 236 ($M^+$, 81), 176 (19), 136 (11), 135 (100).

### 3.2. 5-(1-Adamantyl)-2-ethylthio-1,3,4-oxadiazoles (3a)

Potassium hydroxide (0.56 g, 0.01 mol) was added to a solution of 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** (2.36 g, 0.01 mol) in ethanol (15 mL) and the mixture was heated under reflux for 10 min. Iodoethane (1.56 g, 0.01 mol) was added dropwise and the mixture was heated under reflux for 2 h and the solvent was distilled in vacuo. The obtained residue was washed with water, dried and crystallized. IR, $\nu$ ($cm^{-1}$): 2960 ($CH_3$, $CH_2$, CH), 1610, 1413 (C=N), 1252 (C–O–C). $^1H$ NMR: $\delta$ 1.44 (t, 3H, $CH_3$), 1.78 (s, 6H, adamantane-H), 2.04–2.09 (m, 9H, adamantane-H), 3.19 (q, 2H, $CH_2$). $^{13}C$ NMR: $\delta$ 14.61 ($CH_3$), 26.75 ($CH_2$), 27.62, 34.30, 36.17, 39.73 (adamantane-C), 163.25 (C=N), 173.76 (N=C–S). MS *m*/*z* (rel. int.): 265 ($M^+$+1, 7), 264 ($M^+$, 30), 236 (13), 203 (38), 135 (100).

### 3.3. 5-(1-Adamantyl)-2-(2-aminoethylthio)-1,3,4-oxadiazoles (3b,c)

Potassium hydroxide (1.12 g, 0.02 mol) was added to a solution of 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** (2.36 g, 0.01 mol) in ethanol (15 mL) and the mixture was heated under reflux for 10 min. The appropriate 2-aminoethyl chloride hydrochloride (0.01 mol) was added and the mixture was heated under reflux for 4 h and the solvent was distilled in vacuo. The obtained residue was washed with water, dried, and crystallized. Compound **3b**: IR, $\nu$ ($cm^{-1}$): 2915 ($CH_3$, $CH_2$, CH), 1612, 1415 (C=N), 1254 (C–O–C). $^1H$ NMR: 1.78 (s, 6H, adamantane-H), 2.04 (s, 6H, adamantane-H), 2.08 (s, 3H, adamantane-H), 2.29 (s, 6H, $CH_3$), 2.68 (t, 2H, $SCH_2$), 3.33 (t, 2H, $NCH_2$). $^{13}C$ NMR: 30.59 ($CH_3$), 27.63, 34.32, 36.18, 39.74 (adamantane-C), 54.04 ($NCH_2$), 57.76 ($SCH_2$), 163.57 (C=N), 174.23 (N=C–S). MS *m*/*z* (rel. int.): 307 ($M^+$, 1), 260 (2), 203 (1), 135 (6), 72 (13), 71 (100), 58 (85). Compound **3c**: IR, $\nu$ ($cm^{-1}$): 2902 ($CH_2$, CH), 1610, 1415 (C=N), 1250 (C–O–C). $^1H$ NMR: $\delta$ 1.41 (q, 2H, $CH_2$), 1.53–1.62 (m, 4H, $CH_2$), 1.78 (s, 6H, adamantane-H), 2.04 (s, 3H, adamantane-H), 2.08 (s, 3H, adamantane-H), 2.43 (t, 4H, $N(CH_2)_2$), 2.72 (t, 2H, $SCH_2$), 3.35 (t, 2H, $NCH_2$). $^{13}C$ NMR: $\delta$ 24.13, 25.84, 30.12 (piperidine-C), 27.37, 34.25, 36.13, 39.70 (adamantane-C), 54.13 ($NCH_2$), 57.34 ($SCH_2$), 163.90 (C=N), 173.45 (N=C–S). MS *m*/*z* (rel. int.): 347 ($M^+$, 1), 249 (1), 248 (5), 220 (7), 203 (2), 135 (11), 112 (13), 111 (100), 98 (83).

### 3.4. 5-(1-Adamantyl)-3-arylaminomethyl-1,3,4-oxadiazoline-2-thiones (4a–m)

The appropriate primary aromatic amine (0.01 mol) and 37% formaldehyde solution (1.5 mL) were added to a

solution of 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** (2.36 g, 0.01 mol) in ethanol (15 mL), and the mixture was stirred at room temperature for 2 h and allowed to stand overnight. The separated precipitate was filtered, washed with cold ethanol, dried, and crystallized. Compound **4a**: IR, $\nu$ ($cm^{-1}$): 3336 (NH), 3034 (Ar-CH), 2909, 2849 ($CH_2$, CH), 1604, 1457 (C=N), 1370 (C=S), 1258 (C–O–C). $^1H$ NMR: $\delta$ 1.75 (q, 6H, adamantane-$CH_2$), 1.95 (s, 6H, adamantane-$CH_2$), 2.08 (s, 3H, adamantane-CH), 5.05 (t, 1H, NH), 5.41 (d, 2H, $CH_2$), 6.81–6.92 (m, 3H, Ar-H), 7.20 (t, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.30, 34.30, 35.91, 38.91 (adamantane-C), 58.32 ($CH_2$), 114.01, 119.54, 129.19, 144.11 (Ar-C), 168.02 (C=N), 176.71 (C=S). MS *m/z* (rel. int.): 341 ($M^+$, 3), 236 (89), 176 (17), 135 (100), 105 (78), 77 (70). Compound **4b**: IR, $\nu$ ($cm^{-1}$): 3332 (NH), 3031 (Ar-CH), 2908, 2849 ($CH_2$, CH), 1619, 1456 (C=N), 1375 (C=S), 1254 (C–O–C). $^1H$ NMR: $\delta$ 1.69 (q, 6H, adamantane-$CH_2$), 1.94 (s, 6H, adamantane-$CH_2$), 2.07 (s, 3H, adamantane-CH), 5.25 (t, 1H, NH), 5.44 (d, 2H, $CH_2$), 6.74 (q, 1H, Ar-H), 6.95–7.06 (m, 2H, Ar-H), 7.16–7.26 (m, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.36, 34.39, 35.97, 38.97 (adamantane-C), 57.61 ($CH_2$), 114.06, 115.0, 119.44, 124.55, 132.68, 148.09 (Ar-C), 168.24 (C=N), 176.86 (C=S). MS *m/z* (rel. int.): 360 ($M^+$+1, 4), 359 ($M^+$, 16), 236 (92), 176 (18), 135 (100), 123 (64), 124 (92), 95 (33). Compound **4c**: IR, $\nu$ ($cm^{-1}$): 3337 (NH), 3035 (Ar-CH), 2908, 2850 ($CH_2$, CH), 1603, 1462 (C=N), 1371 (C=S), 1247 (C–O–C). $^1H$ NMR: $\delta$ 1.68 (q, 6H, adamantane-$CH_2$), 1.93 (s, 6H, adamantane-$CH_2$), 2.07 (s, 3H, adamantane-CH), 4.98 (t, 1H, NH), 5.35 (d, 2H, $CH_2$), 6.79–6.95 (m, 4H, Ar-H). $^{13}C$ NMR: $\delta$ 27.30, 34.33, 35.91, 38.94 (adamantane-C), 58.92 ($CH_2$), 113.19, 119.89, 140.61, 155.07 (Ar-C), 168.16 (C=N), 176.75 (C=S). MS *m/z* (rel. int.): 360 ($M^+$+1, 1), 359 ($M^+$, 2), 236 (72), 176 (16), 135 (100), 122 (32), 123 (39), 95 (37). Compound **4d**: IR, $\nu$ ($cm^{-1}$): 3447 (NH), 3068 (Ar-CH), 2909, 2852 ($CH_2$, CH), 1602, 1442 (C=N), 1374 (C=S), 1249 (C–O–C). $^1H$ NMR: $\delta$ 1.64 (q, 6H, adamantane-$CH_2$), 1.96 (s, 6H, adamantane-$CH_2$), 2.10 (s, 3H, adamantane-CH), 5.50 (d, 2H, $CH_2$), 5.64 (t, 1H, NH), 6.77–6.80 (m, 1H, Ar-H), 7.19–7.24 (m, 2H, Ar-H), 7.29 (d, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.43, 34.49, 36.06, 39.04 (adamantane-C), 57.57 ($CH_2$), 113.19, 117.93, 119.89, 120.20, 129.51, 140.61 (Ar-C), 168.39 (C=N), 176.89 (C=S). MS *m/z* (rel. int.): 377 ($M^+$+2, 2), 375 ($M^+$, 6), 236 (83), 176 (29), 142 (60), 140 (100), 135 (94), 113 (16), 111 (49). Compound **4e**: IR, $\nu$ ($cm^{-1}$): 3326 (NH), 3042 (Ar-CH), 2906, 2851 ($CH_2$, CH), 1604, 1460 (C=N), 1370 (C=S), 1249 (C–O–C). $^1H$ NMR: $\delta$ 1.68 (q, 6H, adamantane-$CH_2$), 1.93 (s, 6H, adamantane-$CH_2$), 2.07 (s, 3H, adamantane-CH), 5.06 (t, 1H, NH), 5.36 (d, 2H, $CH_2$), 6.80 (d, 2H, Ar-H), 7.14 (d, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.30, 34.35, 35.91, 38.94 (adamantane-C), 58.22 ($CH_2$), 115.30, 124.46, 129.10, 142.75 (Ar-C), 168.20 (C=N), 176.77 (C=S). MS *m/z* (rel. int.): 377 ($M^+$+2, 1), 359 ($M^+$, 4), 236 (82), 176 (17), 142 (20), 140 (55), 135 (100), 113 (5), 111 (26). Compound **4f**: IR, $\nu$ ($cm^{-1}$): 3418 (NH), 3055 (Ar-CH), 2902, 2851 ($CH_2$, CH), 1600, 1441 (C=N), 1381 (C=S), 1250 (C–O–C). $^1H$ NMR: $\delta$ 1.68 (q, 6H, adamantane-$CH_2$), 1.94 (s, 6H, adamantane-$CH_2$), 2.07 (s, 3H, adamantane-CH), 5.45 (d, 2H, $CH_2$), 5.60 (t, 1H, NH), 6.66–6.69 (m, 1H, Ar-H), 7.18–7.27 (m, 2H, Ar-H), 7.42 (d, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.34, 34.38, 35.95, 38.95 (adamantane-C), 57.65 ($CH_2$), 113.23, 120.30, 128.48, 129.26, 132.66, 141.56 (Ar-C), 168.23 (C=N), 176.79 (C=S). MS *m/z* (rel. int.): 421 ($M^+$+2, 4), 419 ($M^+$, 4), 340 (10), 236 (44), 186 (72), 185 (35), 184 (100), 183 (29), 176 (7), 157 (6), 155 (7), 135 (47). Compound **4g**: IR, $\nu$ ($cm^{-1}$): 3323 (NH), 3028 (Ar-CH), 2903, 2851 ($CH_2$, CH), 1596, 1458 (C=N), 1368 (C=S), 1248 (C–O–C). $^1H$ NMR: $\delta$ 1.68 (q, 6H, adamantane-$CH_2$), 1.92 (s, 6H, adamantane-$CH_2$), 2.06 (s, 3H, adamantane-CH), 5.12 (t, 1H, NH), 5.36 (d, 2H, $CH_2$), 6.76 (d, 2H, Ar-H), 7.27 (d, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.33, 34.36, 36.21, 38.98 (adamantane-C), 58.20 ($CH_2$), 114.35, 124.88, 132.54, 144.23 (Ar-C), 167.42 (C=N), 176.62 (C=S). MS *m/z* (rel. int.): 421 ($M^+$+2, 3), 419 ($M^+$, 3), 340 (1), 236 (100), 186 (18), 185 (69), 184 (50), 183 (68), 176 (7), 157 (23), 155 (22), 135 (99). Compound **4h**: IR, $\nu$ ($cm^{-1}$): 3340 (NH), 3044 (Ar-CH), 2912, 2851 ($CH_2$, CH), 1622 ($NO_2$), 1604, 1457 (C=N), 1354 (C=S), 1252 (C–O–C). $^1H$ NMR: $\delta$ 1.67 (q, 6H, adamantane-$CH_2$), 1.96 (s, 6H, adamantane-$CH_2$), 2.09 (s, 3H, adamantane-CH), 5.44–5.50 (m, 3H, NH and $CH_2$), 7.20–7.22 (m, 1H, Ar-H), 7.36 (t, 1H, Ar-H), 7.68–7.69 (m, 1H, Ar-H), 7.82 (s, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.40, 34.53, 36.02, 39.02 (adamantane-C), 57.74 ($CH_2$), 108.50, 114.46, 120.06, 130.13, 145.39, 149.31 (Ar-C), 168.50 (C=N), 177.0 (C=S). MS *m/z* (rel. int.): 386 ($M^+$, 1), 236 (100), 176 (41), 151 (11), 150 (82), 135 (99). Compound **4i**: IR, $\nu$ ($cm^{-1}$): 3365 (NH), 3042 (Ar-CH), 2908, 2850 ($CH_2$, CH), 1602, 1456 (C=N), 1356 (C=S), 1253 (C–O–C). $^1H$ NMR: $\delta$ 1.69 (q, 6H, adamantane-$CH_2$), 1.94 (s, 6H, adamantane-$CH_2$), 2.08 (s, 3H, adamantane-CH), 5.45 (d, 2H, $CH_2$), 5.62 (t, 1H, NH), 6.91 (d, 2H, Ar-H), 8.12 (d, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.34, 34.50, 35.94, 39.0 (adamantane-C), 56.96 ($CH_2$), 107.84, 113.01, 126.0, 149.97 (Ar-C), 167.31 (C=N), 177.22 (C=S). MS *m/z* (rel. int.): 387 ($M^+$+1, 1), 387 ($M^+$, 4), 236 (100), 176 (7), 151 (19), 150 (32), 135 (99). Compound **4j**: IR, $\nu$ ($cm^{-1}$): 3341 (NH), 3025 (Ar-CH), 3002 ($CH_3$), 2903, 2849 ($CH_2$, CH), 1604, 1455 (C=N), 1364 (C=S), 1235 (C–O–C). $^1H$ NMR: $\delta$ 1.68 (q, 6H, adamantane-$CH_2$), 1.92 (s, 6H, adamantane-$CH_2$), 2.06 (s, 3H, adamantane-CH), 3.74 (s, 3H, $OCH_3$), 4.85 (t, 1H, NH), 5.35 (d, 2H, $CH_2$), 6.76–6.85 (m, 4H, Ar-H). $^{13}C$ NMR: $\delta$ 27.34, 34.33, 35.95, 38.97 (adamantane-C), 55.52 ($OCH_3$), 59.44 ($CH_2$), 114.75, 115.71, 137.81, 153.54 (Ar-C), 168.08 (C=N), 176.72 (C=S). MS *m/z* (rel. int.): 371 ($M^+$, 2), 236 (61), 176 (6), 136 (7), 135 (100), 120 (38). Compound **4k**: IR, $\nu$ ($cm^{-1}$): 3374 (NH), 3021 (Ar-CH), 2911, 2850 ($CH_2$, CH), 2210 (CN), 1608, 1437 (C=N), 1376 (C=S), 1266 (C–O–C). $^1H$ NMR: $\delta$ 1.72 (q, 6H, adamantane-$CH_2$), 1.96 (s, 6H, adamantane-$CH_2$), 2.10 (s, 3H, adamantane-CH), 5.50 (d, 2H, $CH_2$), 5.77 (t, 1H, NH), 6.86 (t, 1H, Ar-H), 7.31 (d, 1H, Ar-H), 7.47–7.51 (m, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.41, 34.55, 36.03, 39.02 (adamantane-C), 56.94 ($CH_2$), 97.77 (CN), 112.72, 117.13, 119.35, 132.94. 134.50, 147.06 (Ar-C), 168.66 (C=N), 176.94 (C=S). MS *m/z* (rel. int.): 366 ($M^+$, 8), 236 (100), 176 (29), 135 (97), 131 (58), 102 (42). Compound

**4l**: IR, $\nu$ ($cm^{-1}$): 3336 (NH), 3011 (Ar-CH), 2908, 2852 ($CH_2$, CH), 1592, 1455 (C=N), 1364 (C=S), 1324 ($CF_3$), 1246 (C–O–C). $^1H$ NMR: $\delta$ 1.73 (q, 6H, adamantane-$CH_2$), 1.96 (s, 6H, adamantane-$CH_2$), 2.10 (s, 3H, adamantane-CH), 5.49 (d, 2H, $CH_2$), 5.65 (t, 1H, NH), 6.89 (t, 1H, Ar-H), 7.28–7.31 (m, 1H, Ar-H), 7.45–7.52 (m, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.42, 34.51, 35.92, 39.03 (adamantane-C), 57.47 ($CH_2$), 113.94, 118.86, 125.78, 126.82, 133.33, 142.26 (Ar-C), 115.13 ($CF_3$), 168.50 (C=N), 176.96 (C=S). MS *m/z* (rel. int.): 410 ($M^+$+1, 1), 409 ($M^+$, 5), 236 (61), 176 (14), 174 (82), 173 (40), 154 (43), 145 (32), 135 (100). Compound **4m**: IR, $\nu$ ($cm^{-1}$): 3327 (NH), 3031 (Ar-CH), 2907, 2850 ($CH_2$, CH), 1613, 1462 (C=N), 1370 (C=S), 1250 (C–O–C). $^1H$ NMR: $\delta$ 1.73 (q, 6H, adamantane-$CH_2$), 1.97 (s, 6H, adamantane-$CH_2$), 2.10 (s, 3H, adamantane-CH), 5.37 (t, 1H, NH), 5.43 (d, 2H, $CH_2$), 6.42–6.47 (m, 1H, Ar-H), 6.92–6.95 (m, 1H, Ar-H), 6.98–7.02 (m, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.42, 34.52, 36.05, 39.03 (adamantane-C), 57.22 ($CH_2$), 101.61, 104.71, 115.22, 134.02, 146.80, 158.45 (Ar-C), 168.45 (C=N), 177.0 (C=S). MS *m/z* (rel. int.): 378 ($M^+$+1, 2), 377 ($M^+$, 8), 236 (94), 176 (25), 163 (8), 141 (93), 135 (100), 113 (42), 93 (36), 79 (48).

### 3.5. 5-(1-Adamantyl)-3-(4-substituted-1-piperazinylmethyl)-1,3,4-oxadiazoline-2-thiones (5a–h)

A mixture of 5-(1-adamantyl)-1,3,4-oxadiazoline-2-thione **2** (2.36 g, 0.01 mol), the appropriate *N*-substituted piperazine (0.01 mol) and 37% formaldehyde solution (1.5 mL), in ethanol (15 mL), was stirred at room temperature for 2 h and allowed to stand overnight. The crude products were either precipitated or it was necessary to add water (5 mL) in cases of compounds **5a–c** to be precipitated. The crude products were filtered, washed with water, dried, and crystallized. Compound **5a**: IR, $\nu$ ($cm^{-1}$): 2907, 2850 ($CH_3$, $CH_2$, CH), 1605, 1440 (C=N), 1366 (C=S), 1253 (C–O–C). $^1H$ NMR: $\delta$ 1.70 (q, 6H, adamantane-$CH_2$), 1.97 (s, 6H, adamantane-$CH_2$), 1.98 (s, 3H, adamantane-CH), 2.27 (s, 3H, $CH_3$), 2.43 (t, 4H, piperazine-$CH_2$), 2.82 (t, 4H, piperazine-$CH_2$), 4.98 (s, 2H, $CH_2$). $^{13}C$ NMR: $\delta$ 27.36, 34.23, 35.98, 38.98 (adamantane-C), 45.90 ($CH_3$), 49.91 (piperazine-*C*$H_2$), 54.79 (piperazine-*C*$H_2$), 69.66 ($CH_2$), 167.58 (C=N), 178.39 (C=S). MS *m/z* (rel. int.): 348 ($M^+$, 1), 236 (2), 135 (6), 114 (8), 113 (100), 70 (8). Compound **5b**: IR, $\nu$ ($cm^{-1}$): 2906, 2847 ($CH_3$, $CH_2$, CH), 1610, 1445 (C=N), 1361 (C=S), 1243 (C–O–C). $^1H$ NMR: $\delta$ 1.06 (t, 3H, $CH_3$), 1.72 (q, 6H, adamantane-$CH_2$), 1.97 (s, 6H, adamantane-$CH_2$), 2.09 (s, 3H, adamantane-CH), 2.40 (q, 2H, C*H*$_2$CH$_3$), 2.47 (t, 4H, piperazine-$CH_2$), 2.87 (t, 4H, piperazine-$CH_2$), 4.99 (s, 2H, $CH_2$). $^{13}C$ NMR: $\delta$ 11.93 ($CH_3$), 27.32, 34.34, 36.10, 38.95 (adamantane-C), 50.06 (*C*H$_2$CH$_3$), 52.28 (piperazine-*C*$H_2$), 52.62 (piperazine-*C*$H_2$), 69.82 ($CH_2$), 167.72 (C=N), 178.59 (C=S). MS *m/z* (rel. int.): 362 ($M^+$, 1), 236 (10), 176 (4), 135 (32), 127 (100), 11 (5), 98 (13), 84 (54). Compound **5c**: IR, $\nu$ ($cm^{-1}$): 2995, 2925, 2855 ($CH_3$, $CH_2$, CH), 1692 (C=O), 1607, 1455 (C=N), 1362 (C=S), 1246 (C–O–C). $^1H$ NMR: $\delta$ 1.25 (t, 3H, $CH_3$ ), 1.74 (q, 6H, adamantane-$CH_2$), 1.99 (s, 6H, adamantane-$CH_2$ ), 2.11 (s, 3H, adamantane-CH), 2.77 (t, 4H, piperazine-$CH_2$), 3.49 (t, 4H, piperazine-$CH_2$), 4.11 (q, 2H, C*H*$_2$CH$_3$), 4.99 (s, 2H, $CH_2$). $^{13}C$ NMR: $\delta$ 14.65 ($CH_3$), 27.45, 34.40, 36.08, 39.09 (adamantane-C), 43.20 (*C*H$_2$CH$_3$), 50.08 (piperazine-*C*$H_2$), 61.45 (piperazine-*C*$H_2$), 70.01 ($CH_2$), 155.41 (C=O), 167.96 (C=N), 178.56 (C=S). MS *m/z* (rel. int.): 406 ($M^+$, 1), 333 (1), 236 (7), 176 (3), 172 (24), 171 (100), 143 (11), 135 (25), 97 (17), 70 (19). **5d**: IR, $\nu$ ($cm^{-1}$): 3013 (Ar-CH), 2905, 2855 ($CH_2$, CH), 1600, 1439 (C=N), 1355 (C=S), 1242 (C–O–C). $^1H$ NMR: $\delta$ 1.75 (q, 6H, adamantane-$CH_2$), 2.01 (s, 6H, adamantane-$CH_2$), 2.12 (s, 3H, adamantane-CH), 2.98 (t, 4H, piperazine-$CH_2$), 3.20 (t, 4H, piperazine-$CH_2$), 5.06 (s, 2H, $CH_2$), 6.88–6.95 (m, 3H, Ar-H), 7.27 (t, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.47, 34.40, 36.10, 39.12 (adamantane-C), 49.36 (piperazine-*C*$H_2$), 50.26 (piperazine-*C*$H_2$), 69.86 ($CH_2$), 116.43, 120.15, 129.17, 151.22 (Ar-C), 167.91 (C=N), 178.62 (C=S). MS *m/z* (rel. int.): 410 ($M^+$, 4), 236 (22), 175 (100), 174 (12), 162 (15), 135 (52), 132 (42), 120 (46), 77 (42). Compound **5e**: IR, $\nu$ ($cm^{-1}$): 3055 (Ar-CH), 2907, 2851, 2824 ($CH_2$, CH), 1611, 1446 (C=N), 1361 (C=S), 1233 (C–O–C). $^1H$ NMR: $\delta$ 1.75 (q, 6H, adamantane-$CH_2$), 2.0 (s, 6H, adamantane-$CH_2$), 2.12 (s, 3H, adamantane-CH), 2.98 (t, 4H, piperazine-$CH_2$), 3.11 (t, 4H, piperazine-$CH_2$), 5.05 (s, 2H, $CH_2$), 6.87–6.90 (m, 2H, Ar-H), 6.95–7.0 (m, 2H, Ar-H). $^{13}C$ NMR: $\delta$ 27.46, 34.40, 36.09, 39.12 (adamantane-C), 50.25 (piperazine-*C*$H_2$), 50.35 (piperazine-*C*$H_2$), 69.80 ($CH_2$), 115.50, 118.18, 147.85, 158.33 (Ar-C), 167.92 (C=N), 178.62 (C=S). MS *m/z* (rel. int.): 428 ($M^+$, 3), 236 (17), 193 (100), 178 (8), 150 (36), 135 (46), 122 (31), 95 (17), 70 (60). Compound **5f**: IR, $\nu$ ($cm^{-1}$): 3061 (Ar-CH), 2904, 2832 ($CH_3$, $CH_2$, CH), 1608, 1446 (C=N), 1372 (C=S), 1243 (C–O–C). $^1H$ NMR: $\delta$ 1.75 (q, 6H, adamantane-$CH_2$), 2.02 (s, 6H, adamantane-$CH_2$), 2.12 (s, 3H, adamantane-CH), 3.04–3.10 (m, 8H, piperazine-$CH_2$), 3.87 (s, 3H, $OCH_3$), 5.06 (s, 2H, $CH_2$ ), 6.87 (d, 1H, Ar-H), 6.92–6.98 (m, 2H, Ar-H), 7.02–7.05 (m, 1H, Ar-H). $^{13}C$ NMR: $\delta$ 27.49, 34.39, 36.13, 39.09 (adamantane-C), 50.40 (piperazine-*C*$H_2$), 50.69 (piperazine-*C*$H_2$), 55.29 ($OCH_3$), 70.08 ($CH_2$), 110.90, 118.26, 120.91, 123.23, 141.02, 152.16 (Ar-C), 167.82 (C=N), 178.70 (C=S). MS *m/z* (rel. int.): 440 ($M^+$, 1), 236 (75), 192 (32), 191 (3), 176 (16), 150 (71), 135 (100), 107 (13), 79 (33). Compound **5g**: IR, $\nu$ ($cm^{-1}$): 3016 (Ar-CH), 2905, 2851 ($CH_2$, CH), 1607, 1440 (C=N), 1359 (C=S), 1246 (C–O–C). $^1H$ NMR: $\delta$ 1.74 (q, 6H, adamantane-$CH_2$), 1.99 (s, 6H, adamantane-$CH_2$), 2.11 (s, 3H, adamantane-CH), 2.49 (t, 4H, piperazine-$CH_2$), 2.85 (t, 4H, piperazine-$CH_2$), 3.52 (s, 2H, *C*H$_2$C$_6$H$_5$), 4.98 (s, 2H, $CH_2$), 7.25–7.34 (m, 5H, Ar-H). $^{13}C$ NMR: $\delta$ 27.48, 34.36, 36.11, 39.11 (adamantane-C), 50.20 (piperazine-*C*$H_2$), 52.94 (piperazine-*C*$H_2$), 63.14 (*C*H$_2$C$_6$H$_5$), 69.99 ($CH_2$), 127.16, 128.16, 129.29, 137.74 (Ar-C), 167.76 (C=N), 178.62 (C=S). MS *m/z* (rel. int.): 424 ($M^+$, 1), 236 (14), 189 (100), 176 (8), 158 (16), 135 (37), 98 (19), 91 (70), 70 (41). Compound **5h**: IR, $\nu$ ($cm^{-1}$): 3097 (Ar-CH), 2907, 2854, 2813 ($CH_2$, CH), 1607, 1440 (C=N), 1359 (C=S), 1312 ($CF_3$), 1244 (C–O–C). $^1H$ NMR: $\delta$ 1.76 (q, 6H, adamantane-$CH_2$), 2.02 (s, 6H, adamantane-$CH_2$), 2.12 (s, 3H, adamantane-CH), 2.52 (t, 4H, piperazine-$CH_2$), 2.85 (t,

4H, piperazine-$CH_2$), 3.67 (s, 2H, $CH_2C_6H_4$), 4.99 (s, 2H, $CH_2$), 7.32 (t, 1H, Ar-H), 7.50 (t, 1H, Ar-H), 7.62 (d, 1H, Ar-H), 7.75 (d, 1H, Ar-H). $^{13}$C NMR: $\delta$ 27.48, 34.39, 36.11, 39.13 (adamantane-C), 50.31 (piperazine-$CH_2$), 53.09 (piperazine-$CH_2$), 58.12 ($CH_2C_6H_5$), 70.08 ($CH_2$), 123.35 ($CF_3$), 125.52, 126.78, 127.70, 130.26, 131.72, 137.53 (Ar-C), 167.84 (C=N), 178.64 (C=S). MS *m*/*z* (rel. int.): 492 ($M^+$, 1), 257 (100), 236 (6), 214 (15), 176 (5), 159 (46), 135 (30), 98 (17), 91 (9), 70 (51).

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