

## ADVANCES IN RESEARCH OF NEW 2-((4-ETHYLPHENOXY)METHYL)-N-(ARYLCARBAMOTHIOYL)BENZAMIDES

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Manuscript received: November 2014

### Abstract

The therapeutic importance of benzamides and the encouraging results obtained on N-(arylcarbamoithioyl)benzamides led us to continue the synthesis in this class of compounds. Thus, new compounds were synthesized by reacting 2-(4-ethylphenoxy)methyl)benzoyl isothiocyanate (**6**) with various amines and their structures were established by IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR spectroscopy and C, H, N, S elemental analysis.

### Rezumat

Importanța terapeutică a benzamidelor și rezultatele încurajatoare obținute în clasa N- (arylcarbamoithioyl)benzamidelor ne-au determinat să continuăm sintezele în această clasă de compuși. Astfel, noii compuși au fost sintetizați prin reacția isotiocianatului de 2-(4-etilfenoximetil)benzoil (**6**) cu diferite amine, iar structurile lor au fost stabilite prin spectroscopie IR, <sup>1</sup>H-RMN, <sup>13</sup>C-RMN și analiza elementală C, H, N, S.

**Keywords:** thiourea, benzamides, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, IR spectroscopy

### Introduction

Numerous studies explore the pharmacological potential of the compounds which contain a thiourea moiety in their molecule in order to develop new promising candidates as drugs. Thiourea derivatives have antimicrobial [3, 13, 15], antiviral [16], antitumor [17], antiparasitic [2], analgesic [4], anti-inflammatory [12], and also anti-convulsant [14] properties. Also great pharmacological importance of N-acylated derivatives of thiourea and benzamides [11] led to the synthesis of new such derivatives, presented in previous papers [1, 5-9].

### Materials and Methods

#### Chemicals and Instrumentation

Chemicals and solvents were purchased from Merck or Aldrich (Darmstadt and Steinheim, Germany) and were used as received, except the ammonium thiocyanate dried by heating at 100°C, the acetone and 1,2-dichloroethane which were dried on calcium chloride. Thin layer chromatography (TLC) was conducted on 0.25 mm thickness silica gel plates (60 F 254, Merck). The melting points were determined using an Electrothermal 9100 apparatus (Bibby Scientific Ltd, Stone, UK) in open glass capillaries, without correction.

Elemental analyses were performed on Perkin-Elmer 2400 Series II CHNS/O Elemental Analyzer (Waltham, MA, USA).

The IR spectra were recorded on a Bruker Vertex 70 FT-IR spectrometer (Bruker Corporation, Billerica, MA, USA).

<sup>1</sup>H-NMR spectra were recorded with a Varian Unity Inova 400 instrument (Varian Medical Systems, Palo Alto, CA, USA) operating at 400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C, using DMSO as solvent and tetramethylsilane as internal standard. The presented accurately interpretation of NMR spectra is due to performing of additional spectral experiments: Heteronuclear Single-Quantum Coherence- HMBC, Heteronuclear Multiple Bond Correlation- HSQC and correlation spectroscopy- COSY. Thus the molecular structures of the new compounds were checked and validated.

#### Synthesis

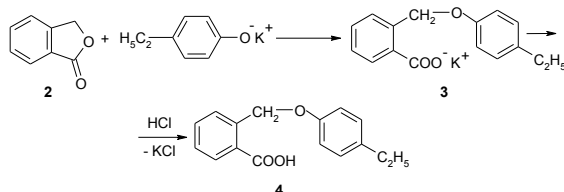
The new compounds were synthesized according to the method presented in a previous published paper [10].

### Results and Discussion

The steps in the synthesis of the new N-(arylcarbamoithioyl)benzamides (**1a- g**) are: 1. synthesis of 2-(4-ethylphenoxy)methyl)benzoic acid;

2. preparation of the corresponding acid chloride; 3. obtaining of the new benzamides, by a nucleophilic addition of the amine to the isothiocyanate.

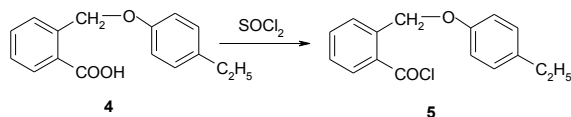
1. Synthesis of 2-(4-ethylphenoxy)methylbenzoic acid (Figure 1). For this purpose, phthalide (2) reacted with potassium p-ethylphenoxide (obtained by treating *para*-ethylphenol with potassium hydroxide), and the resulting potassium salt of 2-(4-ethylphenoxy)methylbenzoic acid (3) gave the corresponding acid (4) by acidification.



**Figure 1.**

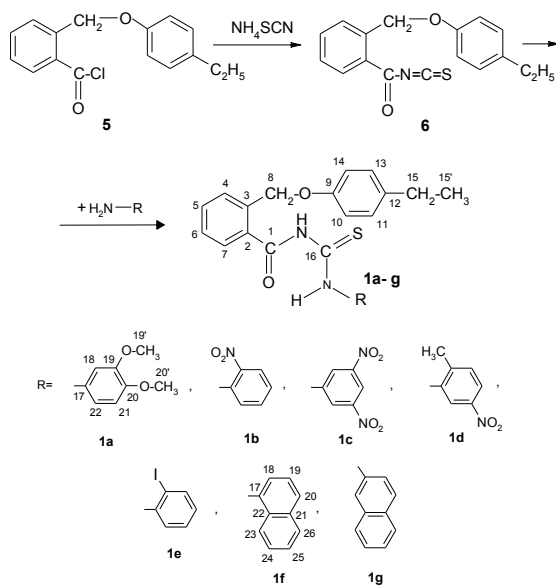
Synthesis of 2-(4-ethylphenoxy)methylbenzoic acid

2. Preparation of 2-(4-ethylphenoxy)methylbenzoic acid chloride (Figure 2). The 2-(4-ethylphenoxy)methylbenzoic acid chloride (5) was obtained by chlorination of 4 with thionyl chloride using anhydrous 1,2-dichloroethane as the reaction medium. In the next stage of synthesis, it was used crude acid chloride, after removal of unreacted thionyl chloride and dichloroethane by distillation under reduced pressure.



**Figure 2.**

Synthesis of 2-(4-ethylphenoxy)methylbenzoic acid chloride



**Figure 3.**

Synthesis of the new benzamides

3. The synthesis of the new benzamides (Figure 3). Treatment of the acid chloride (5) with ammonium thiocyanate in dry acetone gave 2-(4-ethylphenoxy)methylbenzyl isothiocyanate (6). Without being isolated, this was condensed with aromatic primary amines to yield the new *N*-(arylcabamothioyl)benzamides (1a-g).

*The characterization and the structure confirmation of the new compounds*

The new compounds are soluble in cold acetone, chloroform, DMSO, hot lower alcohols, benzene, toluene, xylene and insoluble in water.

The structures and the purity of the new compounds have been established using infrared and NMR spectra studies and other physico-chemical measurements.

The purity of compounds was checked by melting point and by TLC using unidimensional migration, and ethyl acetate/ cyclohexane (4: 6; v/v) as eluent with visualization by ultraviolet light ( $\lambda = 254$  nm) and exposing to iodine vapours.

Obtained elemental analysis results were within 0.4% of the theoretical values.

In the IR spectroscopy all the compounds exhibited absorption bands for  $\nu$ C=O in the region 1672-1696  $\text{cm}^{-1}$ . For the  $\nu$ N-H of the thioamide group the absorption bands appear in the region 3145-3184  $\text{cm}^{-1}$ . The bands due to  $\nu$ C-H of the methyl and methylene groups are in the 2961-2972  $\text{cm}^{-1}$  and 2916-2933  $\text{cm}^{-1}$  range, respectively. The vibration for  $\delta$ N-H amide group is found at 1503-1513  $\text{cm}^{-1}$ . The alkyl-aryl ether bands appear at 1233-1262  $\text{cm}^{-1}$ , for the antisymmetric vibration, and 1016-1023  $\text{cm}^{-1}$  for the symmetric vibration, and the  $\nu$ C=S stretching band is in the region 1142-1164  $\text{cm}^{-1}$ .

In the  $^1\text{H-NMR}$ , the apparent resonance multiplicity is described as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double doublet), td (triple doublet), ddd (double double doublet) and br (broad) signal. The  $^1\text{H-NMR}$  data are reported in the following order: chemical shifts, multiplicity, and the coupling constants, number of protons and signal/atom attribution and for the  $^{13}\text{C-NMR}$  data the order is: chemical shifts and signal/atom attribution (Cq- quaternary carbon). In the  $^1\text{H-NMR}$  spectra the -NH protons resonated as singlet or broad singlet in the range of 12.22-12.73 ppm and 11.76-12.17 ppm. The -CH<sub>2</sub>-O- protons signal was observed in the region 5.27-5.33 as singlet. The ethyl group protons appear as a triplet at 1.10-1.13 ppm for -CH<sub>3</sub> group, and as quartet at 2.50-2.53 ppm for -CH<sub>2</sub>- group. In the  $^{13}\text{C-NMR}$ , the C=O and C=S carbons gave signals in the regions 169.72-170.83 ppm, and 179.17-180.91 ppm respectively. The methylene carbon of -CH<sub>2</sub>-O- group appears in the range of 67.35-68.25 ppm and the ethyl group carbons appear at 15.63-16.43 ppm (-CH<sub>3</sub>) and 27.15-27.95 ppm (-CH<sub>2</sub>-).

2-((4-Ethylphenoxy)methyl)-N-(3,4-dimethoxyphenylcarbamothioyl)benzamide (**1a**). Yield 84%; mp 129.1-130.4°C (isopropanol);

<sup>1</sup>H-NMR (dmsd-d6): 12.33 (s, 1H, NH, deuterable); 11.76 (br s, 1H, NH, deuterable); 7.61 (br d,  $J = 7.4$  Hz, 1H, H-7); 7.58 (dd,  $J = 1.6$  Hz,  $J = 7.4$  Hz, 1H, H-4); 7.55 (td,  $J = 1.4$  Hz,  $J = 7.4$  Hz, 1H, H-5); 7.46 (td,  $J = 1.4$  Hz,  $J = 7.8$  Hz, 1H, H-6); 7.28 (d,  $J = 2.3$  Hz, 1H, H-18); 7.10 (dd,  $J = 2.3$  Hz,  $J = 8.6$  Hz, 1H, H-22); 7.10 (d,  $J = 8.6$  Hz, 2H, H-11, H-13); 6.97 (d,  $J = 8.6$  Hz, 1H, H-21); 6.90 (d,  $J = 8.6$  Hz, 2H, H-10, H-14); 5.27 (s, 2H, H-8); 3.77 (s, 3H, H-19' or H-20'); 3.75 (s, 3H, H-19' or H-20'); 2.51 (q,  $J = 7.6$  Hz, 2H, H-15); 1.12 (t,  $J = 7.6$  Hz, 3H, H-15').

<sup>13</sup>C-NMR (dmsd-d6): 179.44 (C-16); 170.83 (C-1); 156.97 (C-9); 149.06 (C-19 or C-20); 147.80 (C-19 or C-20); 136.93 (Cq); 136.45 (Cq); 134.04 (Cq); 131.68 (C-5); 131.58 (Cq); 129.29 (C-11, C-13); 129.13 (C-4); 129.07 (C-7); 128.43 (C-6); 117.22 (C-18); 115.33 (C-10, C-14); 112.16 (C-21); 109.61 (C-22); 68.25 (C-8); 56.37 (C-18' or C-20'); 56.29 (C-18' or C-20'); 27.95 (C-15); 16.43 (C-15').

FT-IR (solid in ATR): 3180m; 3029m; 2926m; 2854m; 2830w; 1676m; 1597m; 1532vs; 1507vs; 1456s; 1380w; 1330m; 1297w; 1261s; 1234vs; 1142s; 1068w; 1019s; 896w; 856w; 824w; 731m; 697m; 660m; 613w; 563w.

Anal. calcd. for C<sub>25</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>S (450.55): C, 66.65; H, 5.82; N, 6.22; S, 7.12%; Found: C, 66.87; H, 5.89; N, 6.19; S 7.09%.

2-((4-Ethylphenoxy)methyl)-N-(2-nitrophenylcarbamothioyl)benzamide (**1b**). Yield 81%; mp 157.3-158.9°C (isopropanol);

<sup>1</sup>H-NMR (dmsd-d6): 12.73 (s, 1H, NH, deuterable); 12.09 (br s, 1H, NH, deuterable); 8.10 (dd,  $J = 1.4$  Hz,  $J = 8.2$  Hz, 1H, H-19); 7.89 (dd,  $J = 1.3$  Hz,  $J = 7.9$  Hz, 1H, H-22); 7.77 (ddd,  $J = 1.4$  Hz,  $J = 7.9$  Hz,  $J = 8.2$  Hz, 1H, H-21); 7.61 (br d,  $J = 7.4$  Hz, 1H, H-7); 7.58 (dd,  $J = 1.6$  Hz,  $J = 7.4$  Hz, 1H, H-4); 7.54 (td,  $J = 1.3$  Hz,  $J = 8.2$  Hz, 1H, H-20); 7.55 (td,  $J = 1.4$  Hz,  $J = 7.4$  Hz, 1H, H-5); 7.46 (td,  $J = 1.4$  Hz,  $J = 7.8$  Hz, 1H, H-6); 7.06 (d,  $J = 8.6$  Hz, 2H, H-11, H-13); 6.88 (d,  $J = 8.6$  Hz, 2H, H-10, H-14); 5.28 (s, 2H, H-8); 2.51 (q,  $J = 7.6$  Hz, 2H, H-15); 1.12 (t,  $J = 7.6$  Hz, 3H, H-15').

<sup>13</sup>C-NMR (dmsd-d6): 180.55 (C-16); 169.93 (C-1); 156.13 (C-9); 143.79 (C-18); 136.17 (Cq); 135.79 (Cq); 133.09 (Cq); 131.92 (Cq); 133.56 (C-21); 131.07 (C-5); 129.59 (C-22); 128.54 (C-11, C-13); 128.47 (C-4); 128.42 (C-7); 127.73 (C-6); 127.65 (C-22); 124.75 (C-19); 114.55 (C-10, C-14); 67.44 (C-8); 27.18 (C-15); 15.70 (C-15').

FT-IR (solid in ATR): 3171m; 2971m; 2916m; 2869w; 1696m; 1606w; 1580m; 1503vs; 1463s; 1374w; 1337m; 1287m; 1234s; 1164s; 1112m; 1074m; 1023m; 852w; 823w; 787w; 730m; 655m; 603w; 513w.

Anal. calcd. for C<sub>23</sub>H<sub>21</sub>N<sub>3</sub>O<sub>4</sub>S (435.49): C, 63.43; H, 4.86; N, 9.65; S, 7.36%; Found: C, 63.77; H, 4.89; N, 9.54; S 7.29%.

2-((4-Ethylphenoxy)methyl)-N-(3,5-dinitrophenylcarbamothioyl)benzamide (**1c**). Yield 83%; mp 167.2-168.4°C (isopropanol);

<sup>1</sup>H-NMR (dmsd-d6): 12.66 (br s, 1H, NH); 12.17 (br s, 1H, NH); 8.94 (d,  $J = 2.0$  Hz, 2H, H-18, H-22); 8.69 (t,  $J = 2.0$  Hz, 1H, H-20); 7.62 (br d,  $J = 7.4$  Hz, 1H, H-7); 7.58 (dd,  $J = 1.6$  Hz,  $J = 7.4$  Hz, 1H, H-4); 7.55 (td,  $J = 1.4$  Hz,  $J = 7.4$  Hz, 1H, H-5); 7.46 (td,  $J = 1.4$  Hz,  $J = 7.5$  Hz, 1H, H-6); 7.06 (d,  $J = 8.6$  Hz, 2H, H-11-13); 6.89 (d,  $J = 8.6$  Hz, 2H, H-10-14); 5.28 (s, 2H, H-8); 2.50 (q,  $J = 7.6$  Hz, 2H, H-15); 1.10 (t,  $J = 7.6$  Hz 3H, H-15').

<sup>13</sup>C-NMR (dmsd-d6): 180.07 (C-16); 169.72 (C-1); 156.22 (C-9); 147.50 (C-19, C-21); 140.14 (Cq); 136.25 (Cq); 135.87 (Cq); 133.05 (Cq); 131.13 (C-5); 128.51 (C-11, C-13); 128.39 (C-4); 128.33 (C-7); 127.74 (C-6); 124.77 (C-18, C-22); 115.46 (C-20); 114.84 (C-10, C-14); 67.47 (C-8); 27.15 (C-15); 15.63 (C-15').

FT-IR (solid in ATR): 3159s; 3117m; 3018m; 2972m; 2933w; 2863w; 1687s; 1607w; 1531vs; 1506vs; 1379w; 1336s; 1320s; 1278m; 1233m; 1162s; 1076m; 1016m; 921w; 896w; 850m; 725s; 695m; 642w; 615w; 548w.

Anal. calcd. for C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O<sub>6</sub>S (480.49): C, 57.49; H, 4.20; N, 11.66; S, 6.67%; Found: C, 57.71; H, 4.19; N, 11.57; S 6.69%.

2-((4-Ethylphenoxy)methyl)-N-(2-methyl-5-nitrophenylcarbamothioyl)benzamide (**1d**). Yield 51%; mp 127.3-129.1°C (isopropanol);

<sup>1</sup>H-NMR (dmsd-d6): 12.32 (br s, 1H, NH, deuterable); 12.07 ((br s, 1H, NH, deuterable); 8.58 (d,  $J = 2.4$  Hz, 1H, H-22); 8.07 (dd,  $J = 2.4$  Hz,  $J = 8.4$  Hz, 1H, H-20); 7.58 (d,  $J = 8.4$  Hz, 1H, H-19); 7.61 (br d,  $J = 7.4$  Hz, 1H, H-7); 7.57 (dd,  $J = 1.6$  Hz,  $J = 7.4$  Hz, 1H, H-4); 7.55 (td,  $J = 1.4$  Hz,  $J = 7.4$  Hz, 1H, H-5); 7.46 (td,  $J = 1.4$  Hz,  $J = 7.5$  Hz, 1H, H-6); 7.06 (d,  $J = 8.6$  Hz, 2H, H-11, H-13); 6.88 (d,  $J = 8.6$  Hz, 2H, H-10, H-14); 5.27 (s, 2H, H-8); 2.50 (q,  $J = 7.6$  Hz, 2H, H-15); 2.25 (s, 3H, H-18'); 1.12 (t,  $J = 7.6$  Hz, 3H, H-15').

<sup>13</sup>C-NMR (dmsd-d6): 180.11 (C-16); 170.32 (C-1); 156.27 (C-9); 145.44 (C-21); 141.72 (Cq); 137.87 (Cq); 136.23 (Cq); 135.64 (Cq); 133.39 (Cq); 131.39 (C-19); 130.91 (C-5); 128.53 (C-11, C-13); 128.44 (C-4); 128.36 (C-7); 127.78 (C-6); 121.26 (C-20); 121.00 (C-22); 114.43 (C-10, C-14); 67.62 (C-8); 27.19 (C-15); 17.64 (C-18'); 15.68 (C-15').

FT-IR (solid in ATR): 3184m; 3028m; 2962m; 2933m; 2877w; 1684m; 1606m; 1513m; 1451s; 1379w; 1330s; 1262m; 1218m; 1195s; 1151s; 1120s; 1008m; 898w; 821m; 793w; 732s; 668w; 645w; 535w.

Anal. calcd. for  $C_{24}H_{23}N_3O_4S$  (449.52): C, 64.13; H, 5.16; N, 9.35; S, 7.13%; Found: C, 63.94; H, 5.19; N, 9.21; S 7.21%.

2-((4-Ethylphenoxy)methyl)-N-(2-iodophenyl-carbamothioyl)benzamide (**1e**). Yield 89%; mp 110.4-111.9°C (isopropanol);

$^1H$ -NMR (dms $o$ -d $_6$ ): 12.24 (br s, 1H, NH); 12.02 (br s, 1H, NH); 7.91 (dd,  $J=1.4$  Hz,  $J=8.0$  Hz, 1H, H-19); 7.63 (br d,  $J=7.4$  Hz, 1H, H-7); 7.60 (m, 2H, H-4, H-22); 7.58 (td,  $J=1.4$  Hz,  $J=7.4$  Hz, 1H, H-5); 7.47 (td,  $J=1.4$  Hz,  $J=7.5$  Hz, 1H, H-6); 7.43 (td,  $J=8.0$  Hz,  $J=1.4$  Hz, 1H, H-21); 7.08 (d,  $J=8.6$  Hz, 2H, H-11, H-13); 7.07 (td,  $J=8.0$  Hz,  $J=1.4$  Hz, 1H, H-20); 6.89 (d,  $J=8.6$  Hz, 2H, H-10, H-14); 5.28 (s, 2H, H-8); 2.50 (q,  $J=7.5$  Hz, 2H, H-15); 1.13 (t,  $J=7.5$  Hz, 3H, H-15').

$^{13}C$ -NMR (dms $o$ -d $_6$ ): 180.34(C-16); 170.20(C-1); 156.24(C-9); 140.12(Cq); 138.82(C-19); 136.14(Cq); 135.74(Cq); 133.26(Cq); 131.06(C-5); 128.80(C-22); 128.58(C-11, C-13, C-21); 128.48(C-7); 128.40(C-4, C-20); 127.77(C-6); 114.60(C-10, C-14); 96.99(C-18); 67.40(C-8); 27.24(C-15); 15.81(C-15'). FT-IR (in solid ATR): 3173m; 3021w; 2959m; 2926w; 2866w; 1674m; 1611w; 1575w; 1510vs; 1390w; 1317m; 1244s; 1161s; 1044m; 853w; 820w; 735m; 716m; 670w; 610w.

Anal. calcd. for  $C_{23}H_{21}N_2O_2S$  (516.39): C, 53.50; H, 4.10; N, 5.42; S, 6.21%; Found: C, 52.84; H, 3.83; N, 5.67; S 6.41%.

2-((4-Ethylphenoxy)methyl)-N-(1-naphthylphenyl-carbamothioyl)benzamide (**1f**). Yield 74%; mp 158.2-159.9°C (isopropanol);

$^1H$ -NMR (dms $o$ -d $_6$ ): 12.56 (br s, 1H, NH); 12.03 (br s, 1H, NH); 7.99 (br d,  $J=8.0$  Hz, 1H, H-18); 7.91 (d,  $J=8.2$  Hz, 1H, H-23); 7.80 (br d,  $J=8.0$  Hz, 1H, H-20); 7.75 (d,  $J=7.4$  Hz, 1H, H-26); 7.70 (dd,  $J=1.4$  Hz,  $J=7.2$  Hz, 1H, H-7); 7.64- 7.53 (m, 4H, H-4, H-5, H-19, H-25); 7.50 (td,  $J=7.2$  Hz,  $J=1.8$  Hz, 1H, H-24); 7.46 (td,  $J=1.7$  Hz,  $J=7.5$  Hz, 1H, H-6); 7.12 (d,  $J=8.6$  Hz, 2H, H-11, H-13); 6.96 (d,  $J=8.6$  Hz, 2H, H-10, H-14); 5.33 (s, 2H, H-8); 2.53 (q,  $J=7.5$  Hz, 2H, H-15); 1.13 (t,  $J=7.5$  Hz, 3H, H-15').

$^{13}C$ -NMR (dms $o$ -d $_6$ ): 180.91 (C-16); 170.49 (C-1); 156.32 (C-9); 136.16 (Cq); 135.74 (Cq); 134.02 (Cq); 133.67 (Cq); 133.54 (Cq); 130.91 (C-5); 128.65 (C-11, C-13); 128.52 (C-4); 128.51 (CH); 128.28 (C-7); 127.77 (C-6); 127.26 (CH); 126.56 (CH); 126.20 (CH); 125.34 (CH); 124.40 (CH); 122.00 (CH); 114.53 (C-10, C-14); 67.64 (C-8); 27.25 (C-15); 15.73 (C-15').

FT-IR (solid in ATR): 3145m; 3049m; 2963m; 2932m; 2872w; 1673m; 1608w; 1597w; 1582w; 1508vs; 1460m; 1387w; 1328w; 1298w; 1242s; 1174s; 1160m; 1071w; 1048w; 1022w; 932w; 886w; 855m; 765m; 741m; 690w; 669w; 646w; 609w.

Anal. calcd. for  $C_{27}H_{24}N_2O_2S$  (440.55): C, 73.61; H, 5.49; N, 6.36; S, 7.28%; Found: C, 73.86; H, 5.38; N, 6.42; S 7.32%.

2-((4-Ethylphenoxy)methyl)-N-(2-naphthylphenyl-carbamothioyl)benzamide (**1g**). Yield 51%; mp 140.1-141.8°C (isopropanol);

$^1H$ -NMR (dms $o$ -d $_6$ ): 12.61 (br s, 1H, NH); 11.90 (br s, 1H, NH); 8.22 (d,  $J=1.9$  Hz, 1H, H-22); 7.95- 7.88 (m, 3H, H-naphthyl); 7.67 (dd,  $J=1.9$  Hz, 8.81H, H-23); 7.65 (dd,  $J=1.4$  Hz,  $J=7.2$  Hz, 1H, H-7); 7.62- 7.51(m, 7H, H-4, H-5, 2H-naphthyl); 7.48 (td,  $J=1.7$  Hz,  $J=7.5$  Hz, 1H, H-6); 7.10 (d,  $J=8.6$  Hz, 2H, H-11, H-13); 6.92 (d,  $J=8.6$  Hz, 2H, H-10, H-14); 5.30 (s, 2H, H-8); 2.51 (q,  $J=7.5$  Hz, 2H, H-15); 1.11 (t,  $J=7.5$  Hz, 3H, H-15').

$^{13}C$ -NMR (dms $o$ -d $_6$ ): 179.17 (C-16); 170.22 (C-1); 156.29 (C-9); 136.18 (Cq); 135.83 (Cq); 135.48 (Cq); 133.31 (Cq); 132.81 (Cq); 131.25 (Cq); 130.99 (C-5); 128.58 (C-11, C-13); 128.47 (C-4); 128.34 (C-7); 128.03 (C-6); 127.70 (CH); 127.61 (CH); 127.61 (CH); 126.50 (CH); 125.97 (CH); 123.69 (C-18); 121.48 (C-22); 114.58 (C-10, C-14); 67.51 (C-8); 27.22 (C-15); 15.72 (C-15').

FT-IR (solid in ATR): 3146m; 2961m; 2929m; 2871w; 1672m; 1602w; 1582w; 1508vs; 1461m; 1380m; 1328w; 1300w; 1264m; 1238s; 1183m; 1159s; 1125m; 1072w; 1018m; 934w; 893w; 859m; 753m; 661w; 643w; 611w.

Anal. calcd. for  $C_{27}H_{24}N_2O_2S$  (440.55): C, 73.61; H, 5.49; N, 6.36; S, 7.28%; Found: C, 73.84; H, 5.53; N, 6.30; S 7.21%.

## Conclusions

This paper presents the synthesis of original 2-((4-ethylphenoxy)methyl)-N-(arylcarbamothioyl)benzamides *via* 2-(4-ethylphenoxy)methylbenzoyl isothiocyanate. For the new compounds analysis and characterization there were used the C, H, N, S elemental analysis, and the IR,  $^1H$ -NMR, and  $^{13}C$ -NMR spectroscopy.

## References

- Anghel I., Limban C., Grumezescu A.M., Anghel A.G., Bleotu C., Chifiriuc M.C., *In vitro* evaluation of anti-pathogenic surface coating nanofluid, obtained by combining  $Fe_3O_4/C_{12}$  nanostructures and 2-((4-ethylphenoxy)methyl)-N-(substituted-phenylcarbamothioyl)-benzamides. *Nanoscale Res. Lett.*, 2012; 7: 513-522.
- Duan L.P., Xue J., Xu L.L., Zhang H.B., Synthesis 1-acyl-3-(2'-aminophenyl)thioureas as anti-intestinal nematode prodrugs. *Molecules*, 2010; 15: 6941-6947.
- Faidallah H.M., Khan K.A., Asiri A.M., Synthesis and characterization of a novel series of benzenesulfonylurea and thiourea derivatives of 2H-pyran and 2H-pyridine-2-ones as antibacterial,

- antimycobacterial and antifungal agents. *Eur. J. Chem.*, 2011; 2(2): 243-250.
- Lee J., Kang S.U., Choi H.K., Lee J., Lim J.O., Kil M.J., Jin M.K., Kim K.P., Sung J.H., Chung S.J., Ha H.J., Kim Y.H., Pearce L.V., Tran R., Lundberg D.J., Wang Y., Toth A., Blumberg P.M., Analysis of structure-activity relationships for the 'B-region' of N-(3-acyloxy-2-benzylpropyl)-N<sup>(\*)</sup>-[4-(methylsulfonylamino)benzyl]-thiourea analogues as vanilloid receptor antagonists: discovery of an N-hydroxythiourea analogue with potent analgesic activity. *Bioorg. Med. Chem. Lett.*, 2004; 14(9): 2291-2297.
  - Limban C., Al. Missir A.V., Chiriță I.C., Nițulescu G.M., Morușciag L., Stecoza C.E., Nuță D.C., Bădiceanu C.D., Căproiu M.T., Drăghici C., Noi tioureide ale acidului 2-fenoximetilbenzoic. *Nota II. Farmacia*, 2004; 52(5): 7-12.
  - Limban C., Grumezescu A.M., Chirea M., Matei L., Chifiriuc M.C., Antimicrobial potential of benzamides and derived nanosystems for controlling *in vitro* biofilm development on medical devices. *Curr. Org. Chem.*, 2013; 17(2): 162-175.
  - Limban C., Grumezescu A.M., Saviuc C., Voicu G., Chifiriuc M.C., Optimized anti-pathogenic agents based on core/shell nanostructures and 2-((4-ethylphenoxy)methyl)-N-(substituted-phenylcarbamothioyl)-benzamides. *Int. J. Molec. Sci.*, 2012; 13: 12584-12597.
  - Limban C., Missir A.V., Chiriță I.C., Nițulescu G.M., Căproiu M.T., Chifiriuc M.C., Israil A.M., Synthesis and antimicrobial properties of new 2-((4-ethylphenoxy)methyl)benzoylthioureas. *Chem. Pap.*, 2011; 65(1): 60-69.
  - Limban C., Missir A.V., Chiriță I.C., Nițulescu G.M., Ilie C., Căproiu M.T., Some new 2-(4-ethylphenoxy)methylbenzoic acid thiourea derivatives: synthesis and spectral characterisation. *Rev. Chim.*, 2009; 60: 657-661.
  - Limban C., Missir A.V., Chiriță I.C., Nițulescu G.M., Morușciag L., Stecoza C.E., Nuță D.C., Bădiceanu C.D., Căproiu M.T., Drăghici C., Synthesis of new 2-(4-methylphenoxy)methylbenzoic acid thiourea derivatives. *Farmacia*, 2008; 56(6): 659-668.
  - Nuță D.C., Chifiriuc M.C., Drăghici C., Limban C., Missir A.V., Morușciag L., Synthesis, characterization and antimicrobial activity evaluation of new agents from benzamides class. *Farmacia*, 2013; 61(5): 966-974.
  - Ofeimun J.O., Ayinde B.A., Igbe I., Aderogba M., Adhikari A., Amjad H., Iqbal M.C., Anti-inflammatory constituent from the root of *Rhaphiostylis beninensis* (Icacinaceae). *Res. J. Phytochem.*, 2014; 8(3): 127-132.
  - Prasad P.D., Vijaykumar J.P., Prathap S.N., Sanjay J., Neelima S., Sudershan K.A., Synthesis of 1-[3-(4-benzotriazol-1/2-yl-3-fluoro-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-3-substituted-thiourea derivatives as antituberculosis agents. *Eur. J. Med. Chem.*, 2006; 41: 423-428.
  - Rohini R.M., Mandava P., Synthesis and anticonvulsant activity of thiazolidione thiourea of 4-methylquinoline. *J. Chem. Pharm. Res.*, 2012; 4(12): 5172-5175.
  - Saeed S., Rashid N., Ali M., Hussain R., Jones P., Synthesis, spectroscopic characterization, crystal structure and pharmacological properties of some novel thiophene- thiourea core derivatives. *Eur. J. Chem.*, 2010; 1(3): 221-227.
  - Venkata R.K., Syed R., Golla M., Shaik A., Naga R.C., Synthesis and biological evaluation of novel urea and thiourea derivatives of valaciclovir. *J. Serb. Chem. Soc.*, 2014; 79(3): 283-289.
  - Yao J., Chen J., He Z., Sun W., Xu W., Design, synthesis and biological activities of thiourea containing sorafenib analogs as antitumor agents. *Bioorg. Med. Chem.*, 2012; 20: 2923-2929.