New Thioureides of 2-Phenetylbenzoic Acid with Potential Antimicrobial Activity. IV

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This paper presents the synthesis and characterization of some new thioureides of 2- phenethylbenzoic acid. These compounds were prepared by addition of some primary aromatic amines to the 2-phenethylbenzoyl isothiocyanate. The synthesis was done in the following steps: synthesis of 2-phenethylbenzoic acid, synthesis of 2-phenethylbenzoyl chloride and synthesis of the thioureides. The structure and the purity of the obtained substances were confirmed by NMR (^1H and ^{13}C) spectroscopy, IR spectroscopy and the elemental analysis and will be examined for their antimicrobial activity.

Keywords: thioureides, 2-phenethylbenzoic acid, ^1H-NMR, ^{13}C-NMR

Many substances with a thioureide structure have antifungal, antiviral, antihelminthic, tuberculostatic and other therapeutical activity [1-3]. In our laboratory were done numerous researches regarding the thioureides [4-10], the present paper representing a continuation of this work in order to discover compounds with potential antimicrobial activity.

Experimental part

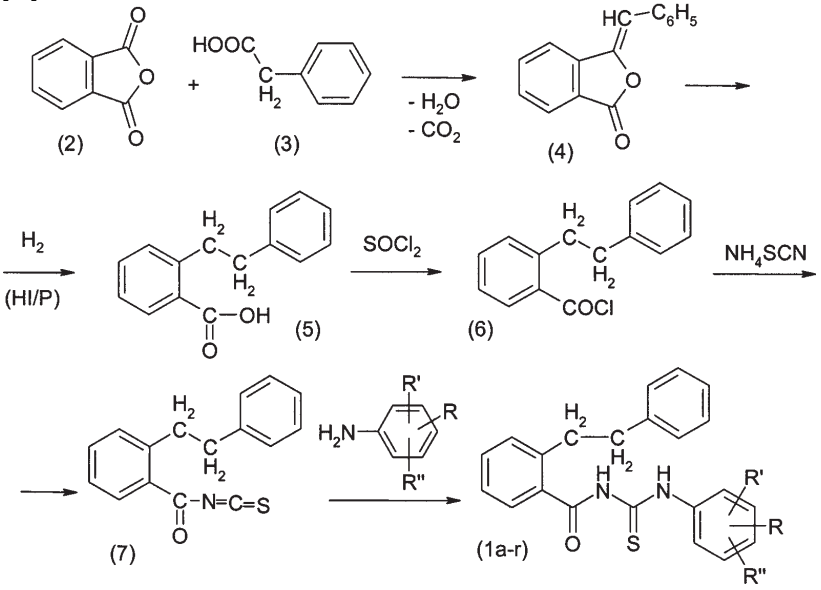
The synthesis of the new compounds (1a-r) devolved in accordance with scheme 1. By the condensation of the phthalic anhydride (2) with phenylacetic acid (3) was obtained 3-benzylidenephtalide (4)[11], which was reduced with hydroiodic acid and red phosphorous to 2-phenethylbenzoic acid (5), in conformity with [12]. The acid was transformed with thionyl chloride in the acid chloride (6), which was then condensed with ammonium thiocyanate to form 2-phenethylbenzoyl isothiocyanate (7). By the addition of primary aromatic amines to the acylisothiocyanate were obtained the new thioureides. The details of this synthesis was mentioned in the previous paper [4].

The general procedure for the synthesis of the new thioureides (1a-r)

A solution of 0.76 g (0.01 mol) of ammonium thiocyanate (dried by heating at 100°C) in 5 mL dry acetone (dried by refluxing over potassium carbonate) was added to a solution of 2.45 g (0.01 mol) 2-phenethylbenzoyl chloride in 15 mL of anhydrous acetone. The reaction mixture was refluxed for one hour and, after cooling at room temperature, 0.01 mol of primary aromatic amine in 2-3 mL dry acetone was added. The reaction mixture was then refluxed for another hour, cooled and poured into 500 mL water. The crude products were purified by recristalization from inferior alcohols (ethanol, isopropanl, n-butanol) with active charcoal.

Analytic tests

The melting points were measured on an Electrothermal 9100 apparatus and are uncorrected, while the elemental analysis was realized on a Perkin Elmer CHNS/O Series II 2400 Analyser. For IR spectra was used a Brucker Vertex 70 apparatus. The ^1H-NMR spectra were recorded at 300



Scheme 1
The synthesis of the new thioureides

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MHz and the ^{13}C-NMR spectra at 75.076 MHz with a Varian Gemini 300 BB apparatus (solvent is DMSO-d6 and tetramethylsilane is internal standard). For the protons chemical shifts assignment we used the notations mentioned in the table 1.

Results and discussions

In order to continue our research concerning the antimicrobial thioureides eighteen new thioureides of 2-phenethylbenzoic acid were obtained by the addition of some primary aromatic amines to the 2-phenethylbenzoyl isothiocyanate. The optimal reaction conditions have been established to obtain good yield and high purity. The chemical structures and the purity of the new compounds were confirmed by the elemental analysis and the IR and NMR spectroscopy.

N-(2-Phenetylbenzoyl)-N'-(2,4,6-trimethylphenyl)thiourea (1a; R = 2-CH_3, R' = 4-CH_3, R'' = 6-CH_3)

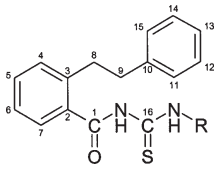
White, microcrystalline powder, m.p.164°-165°C (isopropanol), yield 69.1%, $C_{25}H_{26}N_2OS$.

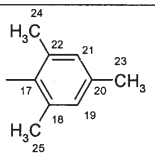
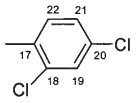
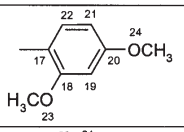
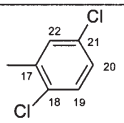
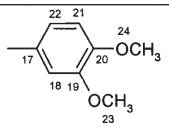
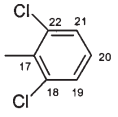
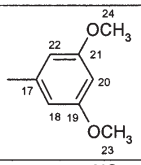
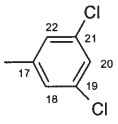
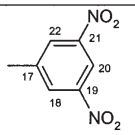
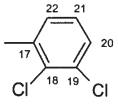
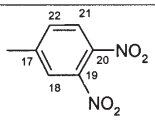
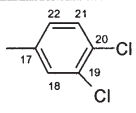
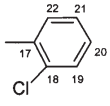
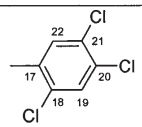
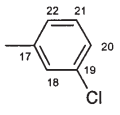
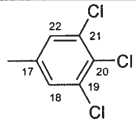
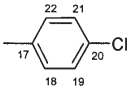
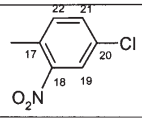
^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.80(s, 1H, CO-N**H**-CS); 11.76(s, 1H, CS-N**H**-Ar); 7.53(dd, 1H, H-7, 1.2, 7.4); 7.46(td, 1H, H-5, 7.6, 1.2); 7.38÷7.16(m, 7H, H-arom); 6.94 (s, 2H, H-19, H-21); 3.02(m, 2H, H-8, syst. A_2B_2); 2.87(m, 2H, H-9, syst. A_2B_2); 2.26(s, 3H, H-23); 2.18(s, 6H, H-24).

^{13}C-NMR(dmso-d6, δ ppm): 180.48(C-16); 171.15(C-1); 141.89(Cq); 139.99(Cq); 136.98(Cq); 135.15(C-18, C-22), 134.77(Cq); 134.17(Cq); 131.21(CH); 130.43(CH);

128.98(CH); 128.73(CH); 128.69(CH); 128.37(CH); 126.45(CH); 126.39(CH); 37.89 (C-8); 35.98(C-9); 21.03(C-23); 18.19(C-24).

Table 1
THE NOTATIONS USED FOR THE CHEMICAL SHIFTS ASSIGNMENT



Compound	R	Compound	R
1a		1j	
1b		1k	
1c		1l	
1d		1m	
1e		1n	
1f		1o	
1g		1p	
1h		1q	
1i		1r	

FT-IR(ATR in solid, ν cm^{-1}): 3150m; 3059m; 3008m; 2944m; 2913m; 2854m; 1671s; 1600w; 1523vs; 1454s; 1371w; 1335m; 1306w; 1263m; 1243m; 1163s; 1144s; 1063w; 1029w; 844w; 743s; 730s; 698s; 654s; 623m; 527w.

Calculated %: C 74.59; H 6.51; N 6.96; S 7.96. Experimental %: C 74.41; H 6.48; N 7.03; S 8.02.

N-(2-Phenetylbenzoyl)-N'-(2,4-dimethoxyphenyl)thiourea(1b; R = 2-OCH_3, R' = 4-OCH_3, R'' = H)

White, microcrystalline powder, m.p. 105°-106°C (isopropanol), yield 74.0%, $C_{24}H_{24}N_2O_3S$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.72(s, 1H, NH); 11.65(s,1H, NH), 8.39(d,1H, H-22, 9.0); 7.54(dd, 1H, H-7, 1.4, 7.7); 7.47(td, 1H, H-5, 7.7, 1.4); 7.37÷7.23(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6), 6.71(d, 1H, H-19, 2.5), 6.59(dd, 1H, H-21, 2.5, 9.0); 3.88(s, 3H, H-23 or H-24); 3.80(s, 3H, H-23 or H-24), 3.02(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 177.59(C-16); 170.81(C-1); 158.21(Cq); 152.04(Cq); 141.48(Cq); 133.91(Cq); 130.91(C-5); 129.97(CH); 128.34(CH); 128.32(CH); 128.20(CH); 126.00(CH); 125.90(C-22); 120.10(C-17); 103.91(C-21); 98.75(C-19); 56.15(C-23 or C-24); 55.44(C-23 or C-24); 37.38(C-8); 35.41(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3418s; 3057w; 3024w; 3006w; 2955w; 2920w; 2840w; 1677s; 1614m; 1601m; 1548vs; 1510vs; 1496vs; 1454s; 1440s; 1416m; 1361w; 1323s; 1281s; 1263s; 1238m; 1207m; 1156s; 1106m; 1074w; 1035s; 860w; 827m; 796m; 755m; 696m; 631m; 532w.

Calculated %: C 68.55; H 5.75; N 6.66; S 7.62. Experimental %: C 68.71; H 6.01; N 6.78; S 7.43.

N-(2-Phenetylbenzoyl)-N'-(3,4-dimethoxyphenyl)thiourea (1c; R = 3-OCH_3, R' = 4-OCH_3, R'' = H)

White, microcrystalline powder, m.p. 143°-144°C (isopropanol), yield 67.0%, $C_{24}H_{24}N_2O_3S$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.43(s, 1H, NH); 11.68(s, 1H, NH); 7.51(dd, 1H, H-7, 1.4, 7.7); 7.46(td, 1H, H-5, 7.7, 1.4); 7.41(d, 1H, H-18, 2.2); 7.37÷7.23(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7,6); 6.99(d, 1H H-21, 8.6); 3.79(s, 3H, H-23 or H-24); 3.05(m, 2H, H-8, syst. A_2B_2); 2.89(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 178.68(C-16); 170.64(C-1); 148.40(Cq); 147.11(Cq); 141.30(Cq); 139.76(Cq); 133.93(Cq); 130.95(Cq); 130.79(C-5); 129.84(CH); 128.28(CH); 128.21(CH); 128.09(CH); 125.88(CH); 125.78(CH); 116.49(CH); 111.53(C-21); 108.98(C-18); 55.67(C-23 or C-24); 55.61(C-23 or C-24); 37.05(C-8); 34.87 (C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3408m; 3127w; 3043w; 3014w; 2961w; 2865w; 2841w; 1670m; 1602s; 1552s; 1506vs; 1461s; 1416m; 1342m; 1285s; 1270m; 1234vs; 1200m; 1164w; 1135vs; 1021s; 987w; 852m; 804m; 758s; 706m; 668m; 634m; 602m; 526m.

Calculated %: C 68.55; H 5.75; N 6.66; S 7.62, Experimental %: C 68.38; H 5.71; N 6.61; S 7.77.

N-(2-Phenetylbenzoyl)-N'-(3,5-dimethoxyphenyl)thiourea (1d; R = 3-OCH_3, R' = 5-OCH_3, R'' = H)

White, microcrystalline powder, m.p. 106°-107°C (isopropanol), yield 73.5%, $C_{24}H_{24}N_2O_3S$

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.52(s, 1H, NH); 11.72(s, 1H, NH); 7.52(dd, 1H, H-7, 1.4, 7.7); 7.45(td, 1H, H-5, 7.7, 1.4); 7.37÷7.22(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6); 7.00(d, 2H, H-18, H-22, 1.9); 6.43(t, 1H, H-20, 1.9); 3.77(s, 6H, H-23, H-24); 3.04(m, 2H, H-8, syst. A_2B_2); 2.89(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 178.52(C-16); 170.60(C-1); 160.29(C-19, C-21); 141.28(Cq); 139.77(Cq); 139.45(Cq); 133.85(Cq); 130.84(C-5); 129.85(CH); 128.28(CH); 128.20(CH); 128.11(CH); 125.88(CH); 125.78(CH); 102.13(C-18, C-22); 98.29(C-20); 55.33(C-23, C-24); 37.04(C-8); 34.84(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3221m; 3096w; 3029m; 3028m; 2964m; 2869w; 2837w; 1668w; 1572vs; 1524vs; 1482s; 1454s; 1420m; 1336vs; 1289s; 1265m; 1247s; 1207s; 1174m; 1153vs; 1115m; 1075m; 1053s; 817m; 758s; 733m; 702m; 671m; 656m; 528m.

Calculated %: C 68.55; H 5.75; N 6.66; S 7.62. Experimental %: C 68.68; H 5.63; N 6.71; S 7.55.

N-(2-Phenetylbenzoyl)-N'-(3,5-dinitrophenyl)thiourea (1e; R = 3-NO_2, R' = 5-NO_2 R'' = H)

Yellowish, microcrystalline powder, m.p. 152°-153°C (n-butanol), yield 63.0%, $C_{22}H_{18}N_4O_5S$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.71(s, 1H, NH); 12.12(s, 1H, NH); 9.10(d, 2H, H-18, H-22, 1.9); 8.71(t, 1H, H-20, 1.9); 7.55(dd, 1H, H-7, 1.2, 7.4); 7.48(td, 1H, H-5, 7.6, 1.2); 7.38÷7.14(m, 7H, H-arom); 3.06(m, 2H, H-8, syst. A_2B_2); 2.90(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.17(C-16); 171.11(C-1); 147.63(C-19, C-21); 141.36(Cq); 140.34(Cq); 140.14(Cq); 133.64(Cq); 131.16(CH); 130.08(CH); 128.41(CH); 128.36(CH); 128.30(CH); 125.99(CH); 125.93(CH); 125.00(CH); 115.57(CH); 37.17(C-8); 34.87(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3385m; 31235w; 3103m; 3019m; 2960m; 2938m; 2920m; 2874m; 1684m; 1601m; 1557vs; 1537vs; 1502vs; 1448vs; 1338vs; 1312s; 1231s; 1151s; 1116m; 1072m; 1008w; 954w; 883m; 826m; 753m; 728s; 700m; 660w; 637s; 597m; 524m.

Calculated %: C 58.66; H 4.03; N 12.44; S 7.12, Experimental %: C 58.80; H 3.86; N 12.26; S 7.30.

N-(2-Phenetylbenzoyl)-N'-(3,4-dinitrophenyl)thiourea (1f; R = 3-NO_2, R' = 4-NO_2 , R'' = H)

Yellowish, microcrystalline powder, m.p. 129°-130°C (isopropanol), yield 66.5%, $C_{22}H_{18}N_4O_5S$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.79(s, 1H, NH); 12.14(s, 1H, NH); 8.77(d, 1H, H-18, 1.1); 8.29(m, 2H, syst. AB, H-21, H-22); 7.55(dd, 1H, H-7, 1.2, 7.4); 7.48(td, 1H, H-5, 7.6, 1.2); 7.38÷7.14(m, 7H, H-arom); 3.05(m, 2H, H-8, syst. A_2B_2); 2.89(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.82(C-16); 170.28(C-1); 143.36(Cq); 142.51(Cq); 141.32(Cq); 140.17(Cq); 137.91(Cq); 133.51(Cq); 130.23(CH); 130.08(CH); 128.41(CH); 128.40(CH); 128.37(CH); 128.31(CH); 126.45(CH); 125.99(CH); 125.92(CH); 120.37(CH); 37.15(C-8); 34.83(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3344m; 3078w; 3025w; 2966w; 2867w; 1681m; 1601s; 1572s; 1544vs; 1513vs; 1457m; 1360m; 1334m; 1303vs; 1279s; 1245m; 1170m; 1158m; 1060w; 840m; 758m; 698m; 655w; 529w.

Calculated %: C 58.66; H 4.03; N 12.44; S 7.12, Experimental %: C 58.50; H 4.09; N 12.31; S 7.15.

N-(2-Phenetylbenzoyl)-N'-(2-chlorophenyl)thiourea (1g; R = 2-Cl, R' = R'' = H)

White, microcrystalline powder, m.p. 119°-120°C (isopropanol), yield 76.0%, $C_{22}H_{19}ClN_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.10(bs, 2H, NH); 8.06(dd, 1H, H-19, 1.5, 8.0); 7.60(dd, 1H, H-22, 1.6, 8.1); 7.55(dd, 1H, H-7, 1.4, 7.6); 7.47(td, 1H, H-13, 1.5, 7.6); 7.45÷7.14(m, 9H, H-arom); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.01(C-16); 171.03(C-1); 141.41(Cq); 135.49(Cq); 133.88(Cq); 130.99(CH);

130.04(CH); 129.53(CH); 128.30(C-12-14, C-11-15); 128.18(CH); 128.09(CH); 127.92(CH); 127.31(CH); 125.99(CH); 125.93(CH); 37.40(C-8); 35.38(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3210m; 3059m; 3023m; 2930m; 2871w; 1672s; 1598w; 1579m; 1525vs; 1490vs; 1443s; 1324m; 1288m; 1249m; 1201m; 1160vs; 1117m; 1060m; 1030w; 957m; 905m; 884w; 863w; 844w; 790w; 765m; 743w; 730m; 716m; 692s; 659m; 613w; 569w; 524m; 482w; 464w; 438w.

Calculated %: C 66.91; H 4.85; Cl 8.98; N 7.09; S 8.12, Experimental %: C 67.02; H 4.98; Cl 8.82; N 6.97; S 7.92.

N-(2-Phenetylbenzoyl)-N'-(3-chlorophenyl)thiourea (1h; R = 3-Cl; R' = R'' = H)

White, microcrystalline powder, m.p. 93°-94°C (isopropanol), yield 78.5%, $C_{22}H_{19}ClN_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.55(s, 1H, NH); 11.90(s, 1H, NH); 7.97(t, 1H, H-18, 1.9); 7.60(m, 1H, H-20); 7.53(dd, 1H, H-7, 1.4, 7.6); 7.49÷7.14(m, 10H, H-arom); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.27(C-16); 170.52(C-1); 141.29(Cq); 139.91(Cq); 139.39(Cq); 133.74(Cq); 132.68(Cq); 130.94(CH); 130.23(CH); 129.92(CH); 128.30(CH); 128.22(C-12-14,C-11-15); 126.08(CH); 125.89(CH); 125.80(CH); 124.03(CH); 123.11(CH); 37.12(C-8); 34.89(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3169m; 3024s; 2962m; 2925m; 2862m; 1672s; 1589s; 1521cs; 1443s; 1426s; 1335s; 1298s; 1257s; 1165vs; 1093m; 1062m; 1042w; 995w; 953w; 872m; 798w; 775w; 744w; 689s; 667m; 642m; 613w; 583w; 560w; 538w; 511w; 480w; 453w,438w; 421w.

Calculated %: C 66.91; H 4.85; Cl 8.98; N 7.09; S 8.12; Experimental %: C 66.80; H 4.88; Cl 8.86; N 7.37; S 8.21.

N-(2-Phenetylbenzoyl)-N'-(4-chlorophenyl)thiourea (1i; R = 4-Cl; R' = R'' = H))

White, microcrystalline powder, m.p. 149°-150°C (isopropanol), yield 68.6%, $C_{22}H_{19}ClN_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.50(s, 1H, NH); 11.85(s, 1H, NH); 7.75(d, 2H, H-19-21, 8.8); 7.53(dd, 1H, H-7, 7.6); 7.49(d, 2H, H-18-22, 8.8); 7.46(td, 1H, H-13, 1.5, 7.6); 7.49(m, 1H, H-4); 7.33(t, 2H, H-12-14, 7.6); 7.31÷7.14(m, 4H, H-arom); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.76(C-16); 171.09(C-1); 141.86(Cq); 140.44(Cq); 137.49(Cq); 134.38(Cq); 130.78(Cq); 131.47(CH); 130.47(CH); 129.09(CH); 128.86(CH); 128.80(CH); 128.74(CH); 126.72(CH); 126.46(CH); 126.37(CH); 37.68 (C-8); 35.45(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3160m; 3026m; 2956w; 2936w; 2857w; 1673s; 1591m; 1552s; 1526vs; 1490vs; 1455m; 1335s; 1251s; 1165s; 1088m; 1063w; 1011w; 950w; 882w; 862w; 842w; 827w; 813w; 752s; 729m; 698m; 654m; 626w; 609w; 527w; 493w.

Calculated %: C 66.91; H 4.85; Cl 8.98; N 7.09; S 8.12; Experimental %: C 67.11; H 5.02; Cl 8.85; N 7.02; S 7.90.

N-(2-Phenetylbenzoyl)-N'-(2,4-dichlorophenyl)thiourea (1j; R = 2-Cl, R' = 4-Cl, R'' = H)

White, microcrystalline powder, m.p. 154°-155°C (isopropanol), yield 69.2%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.56(bs, 1H, NH); 12.09(bs, 1H, NH); 8.05(d, 1H, H-22, 8.7); 7.78(d, 1H, H-19, 1.3); 7.55÷7.14(m, 10H, H-arom); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.17(C-16); 170.81(C-1); 141.28(Cq); 139.83(Cq); 134.67(Cq); 133.60(Cq); 130.96(CH); 129.51(Cq); 129.94(CH); 128.92(CH); 128.22 (C-12-14); 128.19(C-11-15); 128.11(CH); 127.38(CH); 125.89(CH); 125.82(CH); 37.26(C-8); 35.18(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3228w; 3066w; 3019w; 2927w; 2868w; 1686s; 1600w; 1569m; 1522vs; 1453m; 1320m; 1270w; 1243m; 1166s; 1098m; 1059w; 945w; 864w; 813w; 789w; 761m; 750m; 712m; 693m; 655w; 613w; 555w; 511w; 442w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.32; H 4.22; Cl 16.42; N 6.52; S 7.59 .

N-(2-Phenetylbenzoyl)-N'-(2,5-dichlorophenyl)thiourea (1k, R = 2-Cl, R' = 5-Cl, R'' = H)

White, microcrystalline powder, m.p. 154°-155°C (isopropanol), yield 63.4%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.60(bs, 1H, NH); 12.08(bs, 1H, NH); 8.21(d, 1H, H-22, 2.3); 7.62(d, 1H, H-19, 8.6); 7.52(dd, 1H, H-7, 1.3, 7.6); 7.44(td, 1H, H-13, 1.5, 7.6); 7.38(dd, 1H, H-20, 2.3, 8.6); 7.32(t, 2H, H-12-14, 7.6); 7.31÷7.12(m, 5H, H-arom); 2.99(m, 2H, H-8, syst. A_2B_2); 2.84(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.02(C-16); 170.92(C-1); 141.39(Cq); 139.97(Cq); 136.80(Cq); 133.62(Cq); 131.19(CH); 131.10(Cq); 130.85(CH); 130.05(CH); 128.34 (C-12-14); 128.29(C-11-15); 128.19(CH); 127.79(CH); 127.30(CH); 127.07(CH); 126.00(CH); 125.93(CH); 37.37(C-8); 35.30(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3218m; 3083w; 3060w; 3018w; 2871w; 1680m; 1588w; 1570m; 1516vs; 1406m; 1315m; 1263w; 1244m; 1163s; 1116w; 1094m; 1062w; 956w; 882w; 809w; 789w; 757m; 743w; 708m; 693m; 663w; 641w; 612w; 585w; 570w; 525w; 492w; 449w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.62; H 4.33; Cl 16.42; N 6.33; S 7.51.

N-(2-Phenetylbenzoyl)-N'-(2,6-dichlorophenyl)thiourea (1l, R = 2-Cl, R' = 6-Cl, R'' = H)

White, microcrystalline powder, m.p. 175°-176°C (isopropanol), yield 73.4%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.13(s, 1H, NH); 12.02(s, 1H, NH); 7.58(d, 2H, H-19-21, 8.6); 7.53(dd, 1H, H-7, 1.3, 7.6); 7.47(td, 1H, H-13, 1.5, 7.6); 7.44÷7.14(m, 8H, H-arom); 3.03(m, 2H, H-8, syst. A_2B_2); 2.86(m, 2H, H-9, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.92(C-16); 170.68(C-1); 141.36(Cq); 139.64(Cq); 134.42(Cq); 134.00(Cq); 130.94(CH); 130.05(CH); 129.80(CH); 128.53(CH); 128.34 (C-11-15); 128.29C-12-14); 127.96(CH); 126.02(CH); 37.44(C-8); 35.51(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3179m; 3011m; 2948m; 2916m; 2865w; 1680m; 1601w; 1566m; 1517vs; 1451s; 1431s; 1320m; 1266m; 1245m; 1202w; 1158s; 1061m; 1043w; 1027w; 945w; 861w; 844w; 785w; 764m; 744m; 720s; 696s; 655m; 606w; 575w; 529w; 499w; 464w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.45; H 4.11; Cl 16.63; N 6.59; S 7.44.

N-(2-Phenetylbenzoyl)-N'-(3,5-dichlorophenyl)thiourea (1m, R = 3-Cl, R' = 5-Cl, R'' = H)

White, microcrystalline powder, m.p. 132°-133°C (isopropanol), yield 73.0%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.49(s, 1H, NH); 11.89(s, 1H, NH); 7.86(d, 2H, H-18, H-22, 1.6); 7.52(dd, 1H, H-7, 1.4, 7.7); 7.50(t, 1H, H-20, 1,6); 7.46(td, 1H, H-5, 1.4, 7.6); 7.36÷7.22(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6); 3.05(m, 2H, H-8, syst.A_2B_2); 2.89(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.58(C-16); 170,33(C-1); 141.26(Cq); 140.38(Cq); 139.94(Cq); 130.64(Cq); 133.61(C-19, C-21); 130.96(C-5); 129.91(CH); 128.29(H); 128.19(CH); 128.17(CH); 125.87(CH); 125.79(CH); 125.62(C-20); 123.19(C-18, C-22); 37.13(C-8); 34.94(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3226m; 3077m; 3023w; 2963w; 2925w; 2865w; 1678s; 1596w; 1573s; 1510vs; 1454m; 1439m; 1313m; 1257m; 1238m; 1164s; 1113w; 1100w; 1061w; 1042w; 984w; 957w; 859w; 802w; 757m; 697m; 661w; 649w; 641w; 527w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.70 H 4.32; Cl 16.62; N 6.48; S 7.33.

N-(2-Phenetylbenzoyl)-N'-(2,3-dichlorophenyl)thiourea (1n, R = 2-Cl, R' = 3-Cl, R'' = H)

White, microcrystalline powder, m.p. 131°-132°C (n-butanol), yield 68.0%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.57(s, 1H, NH); 12.03(s, 1H, NH); 7.95(dd, 1H, H-20, 1.2, 8.0); 7.60(dd, 1H, H-22, 1.2, 8.0); 7.55(dd, 1H, H-7, 1.4, 7.7); 7.47(td, 1H, H-5, 1.4, 7.6); 7.45(t, 1H, H-21, 8.0); 7.38÷7.20(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.38(C-16); 170.78(C-1); 141.30(Cq); 139.87(Cq); 137.54(Cq); 133.64(Cq); 131.85(Cq); 130.97(C-5); 129.95(CH); 128.58(CH); 128.24(CH); 128.21(CH); 128.12(CH); 127.80(CH); 127.58(Cq); 127.18(CH); 125.91(CH); 125.84(CH); 37.28(C-8); 35.19(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3221m; 3063w; 3022m; 2961w; 2926w; 2868w; 1680s; 1601w; 1522vs; 1453s; 1420m; 1320m; 1282m; 1245m; 1197m; 1164s; 1114m; 1061w; 967w; 874w; 786w; 752m; 723m; 710m; 692s; 651m; 612w; 524w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.45; H 4.11; Cl 16.65; N 6.42; S 7.55.

N-(2-Phenetylbenzoyl)-N'-(3,4-dichlorophenyl)thiourea (1o, R = 3-Cl, R' = 4-Cl, R'' = H)

White, bright pearly crystals, m.p. 142°-143°C (isopropanol), yield 72.0%, $C_{22}H_{18}Cl_2N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.50(s, 1H, NH); 11.86(s, 1H, NH); 8.15(t, 1H, H-18, 1.4); 7.68(m, 1H, H-21, syst.AB, 7.6); 7.66(m, 1H, H-22, syst.AB, 7.6); 7.53(dd, 1H, H-7, 1.4, 7.7); 7.46(td, 1H, H-5, 7.7, 1.4); 7.36÷7.20(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6); 3.05(m, 2H, H-8, syst.A_2B_2); 2.90(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.44(C-16); 170.41(C-1); 141.27(Cq); 139.92(Cq); 138.05(Cq); 133.69(Cq); 130.94(C-5); 130.70(Cq); 130.34(C-18); 129.90(CH); 128.29(CH); 128.20(CH); 128.18(CH); 126.08(CH); 125.87(CH); 125.78(CH); 124.87(CH); 37.07(C-8); 34.81(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3142s; 3083m; 3056m; 3019m; 2921w; 2853w; 1669s; 1600w; 1572w; 1489vs; 1382m; 1316m; 1271m; 1252m; 1146s; 1119m; 1064w; 1033m; 883w; 873w; 745m; 716s; 693m; 681m; 653m; 623w; 521w.

Calculated %: C 61.54; H 4.23; Cl 16.51; N 6.52; S 7.47; Experimental %: C 61.66; H 4.27; Cl 16.41; N 6.58; S 7.35.

N-(2-Phenetylbenzoyl)-N'-(2,4,5-trichlorophenyl)thiourea (1p, R = 2-Cl, R' = 4-Cl, R'' = 5-Cl)

White, microcrystalline powder, m.p. 165°-166°C (n-butanol), yield 67.0%, $C_{22}H_{17}Cl_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.66(s,1H, NH); 12.12(s, 1H, NH); 8.44(s, 1H, H-19); 8.00(s, 1H, H-22); 7.54(dd, 1H, H-7, 1.4, 7.7); 7.47(td, 1H, H-5, 7.7, 1.4); 7.38÷7.24(m, H-arom); 7.18(tt, 1H, H-13, 1.2, 7.6); 3.04(m, 2H, H-8, syst. A_2B_2); 2.88(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.19(C-16); 170.85(C-1); 141.28(Cq); 139.94(Cq); 135.68(Cq); 133.47(Cq); 131.06(C-5); 130.48(C-22); 129.97(C-19); 129.51(Cq); 128.64(CH); 128.25(CH); 128.19(CH); 128.16(CH); 128.05(Cq); 125.90(CH); 125.83(CH); 37.24(C-8); 35.12(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3222m; 3078m; 3024m; 2876w; 1680s; 1601w; 1559m; 1518vs; 1459s; 1359m; 1319m; 1266m; 1251m; 1164s; 1126m; 1077m; 1060m; 891w; 754m; 694s; 658m; 613w; 567w; 523w.

Calculated %: C 56.97; H 3.69; Cl 22.93; N 6.04; S 6.91; Experimental %: C 57.09; H 3.71; Cl 23.05; N 6.16; S 7.03.

N-(2-Phenetylbenzoyl)-N'-(3,4,5-trichlorophenyl)thiourea (1q, R = 3-Cl, R' = 4-Cl, R'' = 5-Cl)

Yellowish, microcrystalline powder, m.p. 132°-134°C (n-butanol), yield 71.0%, $C_{22}H_{17}Cl_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.48(s, 1H, NH); 11.94(s, 1H, NH); 8.09(s, 2H, H-18, H-22); 7.54(dd, 1H, H-7, 1.4, 7.7); 7,47(td, 1H, H-5, 7.7, 1.4); 7.37÷7.24(m, H-arom); 7.19(tt, 1H, H-13, 1.2, 7.6); 3.05(m, 2H, H-8, syst. A_2B_2); 2.89(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 179.70(C-16); 170.31(C-1); 141.25(Cq); 139,97(Cq); 138.09(Cq); 133.58(Cq); 132.40(Cq); 130.99(C-5); 129.92(CH); 128.29(CH); 128.19(CH); 126.87(Cq); 125.87(CH); 125.79(CH); 125.18(C-18, C-22); 37.03(C-8); 34.75(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3231m; 3109m; 3066m; 3029m; 2998m; 2958m; 2864w; 1682s; 1600w; 1586w; 1559m; 1535s; 1511vs; 1454s; 1434s; 1384m; 1307m; 1190m; 1170s; 1146s; 1058m; 985w; 887w; 761m; 716m; 694m; 654m; 616w; 525w.

Calculated %: C 56.97; H 3.69; Cl 22.93; N 6.04; S 6.91; Experimental %: C 56.80; H 3.66; Cl 23.04; N 6.18; S 6.86.

N-(2-Phenetylbenzoyl)-N'-(2-nitro-4-chlorophenyl)thiourea (1r, R = 2-NO_2, R' = 4-Cl, R'' = H)

White, microcrystalline powder, m.p. 149°-150°C (ethanol), yield 46.0%, $C_{22}H_{18}ClN_3O_3S$.

^{1}H-NMR(dmso-d6, δ ppm, *J* Hz): 12.10(bs, 2H, NH); 8.21(d, 1H, H-19, 2.3); 8.00(d, 1H, H-22, 8.6); 7.88(dd, 1H, H-21, 2.3, 8.6); 7.53(dd, 1H, H-7, 1.4, 7.6); 7.45(td, 1H, H-13, 1.5, 7.6); 7.38÷7.14(m, 7H, H-arom); 3.03(m, 2H, H-8, syst.A_2B_2); 2.87(m, 2H, H-9, syst.A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm): 180.52(C-16); 170.44(C-1); 144.24(C-18); 141.29(Cq); 139.91(Cq); 133.67(Cq); 133.41(CH); 131.56(CH); 130.97(CH); 130.00(CH); 128.32 (C-12-14); 128.21(C-11-15); 125.88(CH); 125.84(CH); 124.57(CH); 37.29(C-8); 35.19(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3174m; 3098w; 3060m; 3022w; 2989m; 2925w; 2862w; 1679m; 1599w; 1570m; 1545w; 1500vs; 1452s; 1344s; 1314m; 1276s; 1240s; 1149s; 1111m; 1075w; 1059m; 940w; 885w; 828w; 794w; 749m; 735m; 698m; 669w; 653w; 616w; 562w; 528w; 413w.

Calculated %: C 60.07; H 4.12; Cl 8.06; N 9.55; S 7.29; Experimental %: C 60.09; H 4.05; Cl 8.16; N 9.71; S 7.14.

Conclusions

There were prepared eighteen new thioureides of the 2-phenethylbenzoic acid (1a-r) with potential pharmacological activity and have been established the best reaction conditions to obtain the high purity and the good yields. The spectral data (^{1}H-NMR, ^{13}C-NMR and IR) and the elemental analysis confirmed the chemical structure.

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