Dedicated to Prof. A.T. Balaban
on the occasion of his 80th anniversary

New Thioureides of the 2-Phenethylbenzoic Acid with Potential Antimicrobial Activity. VI

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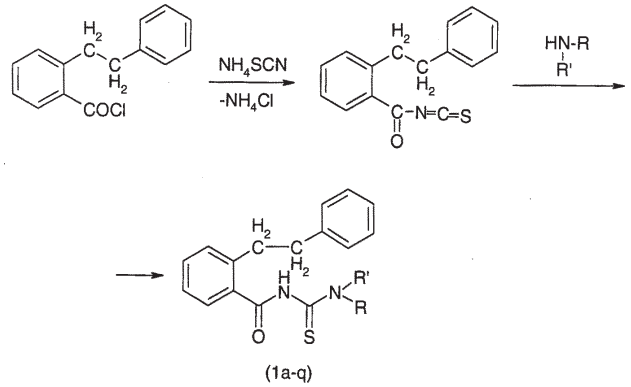
In the continuation of our works in the series of the derivatives of the 2- phenethylbenzoic acid, in this paper we present the synthesis and characterization of some new thioureides of the aforementioned acid. The synthesis consists in addition of primary or secundary amines to the 2-phenethylbenzoyl isothiocyanate. We established the reaction conditions which conducted to best yields and high purity substances. The chemical structures and the purity of the new thioureides were certified by elemental analysis and spectroscopy data (^{1}H- NMR, ^{13}C-NMR, IR).

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

The specialized literature [1-4] mentions many compounds with a thioureide fraction in the structure having anti-infective, antifungal, antiviral, anthelmintic, tuberculostatic, antidiabetic, sedative or antidepressant actions. In this paper we presented the synthesis and the characterization of new 2-phenethylbenzoic acid thioureides with potential antimicrobial activity.

Experimental part

The general method [5-6] used for the synthesis of the new derivatives [1a-q] was the addition of various primary or secundary amines to the 2-phenethylbenzoyl-isothiocyanate obtained by the condensation of the 2-phenethylbenzoyl chloride with ammonium thiocyanate. The preparation of the previously isothiocyanate and the necessary intermediates compounds (2-phenethylbenzoic acid and 2-phenethylbenzoyl chloride) were described in the our precedent works [7-14].



Scheme 1. The general method for the synthesis of the new thioureides

The general synthesis of the new thioureides (1a-q)

A solution of 2.45 g (0.01 mol) 2-phenethylbenzoyl-chloride in 10 mL of anhydrous acetone was treated with a solution of 0.76 g (0.01 mol) of ammonium thiocyanate in 10 mL anhydrous acetone. After refluxing for one hour, the reaction mixture was cooled at room temperature and 0.01 mol of the adequate amine dissolved in 5- 10 mL dry acetone was added. The reaction mixture was refluxed for another hour, cooled and poured into 500 mL ice water mixture. The crude products separated were purified by recristalization from inferior alcohols with active charcoal.

The acetone was dried over potassium carbonate and freshly distillated. The ammonium thiocyanate was dried by heating at 100°C.

Analytic tests

The melting points were measured in open capillary tubes on an Electrothermal 9100 apparatus and are uncorrected. The elemental analysis was realized on a Perkin Elmer CHNS/O Series II 2400 Analyser. For realization of the NMR spectra we used a Varian Unity Inova 400 instrument, operating at room temperature at 100 MHz for ^{13}C and 400 MHz for ^{1}H (DMSO-d_6 was the solvent and tetramethylsilane the internal standard).

For the IR spectra we used a Brucker Vertex 70 apparatus.

Results and conclusions

Applying the method described in our previous papers, we synthesized new thioureides of the 2-phenethylbenzoic acid having possible antimicrobial activity. In order to obtain the compounds with good yields and superior purity were established the favorables conditions for the synthesis. Some physical properties, the elemental analysis and the spectral parameters (IR, ^{1}H-NMR, ^{13}C-NMR) have characterized the new compounds and confirmed the chemical structures.

N-(2-Phenethylbenzoyl)-N', N'-di(ethyl)-thiourea: **1a; R = R' = -C_2H_5**

White, microcrystalline powder, m.p.77°-78°C (ethanol), yield 30.8%, $C_{20}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 10.59(s, 2H, NH); 7.42÷7.15(m, 9H, H-arom); 3.94(q, 2H, H-17, 7.1); 3.63(q,

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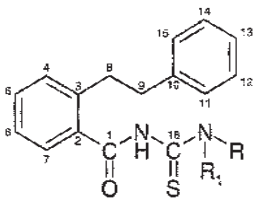
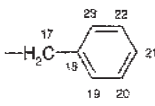
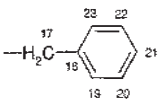
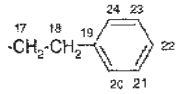
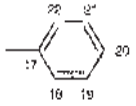
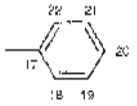
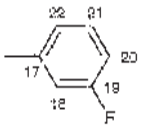
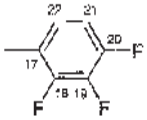
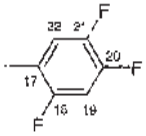
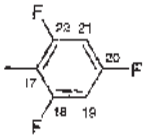
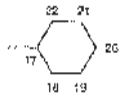
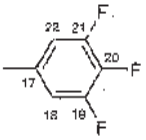
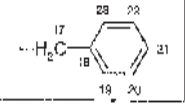
Table 1

THE NOTATIONS USED FOR THE PROTONS CHEMICAL SHIFTS ASSIGNMENT AND THE STRUCTURE OF THE COMPOUNDS (1a-q)



Comp.	R	R_1	Comp.	R	R_1
1a	17 18 $-CH_2-CH_3$	17 18 $-CH_2-CH_3$	1j		
1b	17 18 19 $-CH_2-CH_2-CH_3$	-H	1k		-H
1c	17 18 $-CH(CH_3)_2$	-H	1l		
1d	17 18 19 20 $-CH_2-CH_2-CH_2-CH_3$	-H	1m		-H
1e	17 18 19 $-CH_2-CH(CH_3)_2$	-H	1n		-H
1f	20 CH_3 $-CH-CH_2-CH_3$ 17 18 19	-H	1o		-H
1g	17 18 19 $-CH_2-CH(CH_3)_2$	17 18 19 $-CH_2-CH(CH_3)_2$	1p		-H
1h		-H	1q		-H
1i		-H			

2H, H-17, 7.1); 3.00(m, 2H, H-8, syst. A_2B_2); 2.86(m, 2H, H-9, syst. A_2B_2); 1.25(t, 3H, H-18, 7.1); 1.21(t, 3H, H-18, 7.1).

^{13}C-NMR(dmso-d6, δ ppm): 180.56(C-16); 169.97(C-1); 141.62(Cq); 139.96(Cq); 135.15(Cq); 130.11(CH); 130.06(CH); 128.32(C-12-14); 128.23(C-11-15); 127.52(CH); 125.86(CH); 46.50(C-17); 47.25(C-17); 37.28 (C-8); 34.90(C-9); 13.44(C-18); 11.17(C-18).

FT-IR(ATR in solid, ν cm^{-1}): 3279m; 3071w; 3023w; 2978w; 2939w; 2922w; 2879w; 2858w; 1652vs; 1599w; 1489vs; 1451vs; 1428s; 1381w; 1342w; 1307w; 1285s; 1273m; 1228vs; 1169w; 1145m; 1117w; 1099w; 1081w; 1068w; 1046w; 1027w; 947w; 923w; 880w; 846w; 796w; 753s; 738w; 720w; 697m; 654w; 614w; 525w; 515w; 460w.

Calculated %: C 70.55; H 7.10; N 8.23; S 9.42. Experimental %: C 70.62; H 7.18; N 8.18; S 9.36.

N-(2-Phenethylbenzoyl)-N'-(n-propyl)-thiourea: **1b; R = -n.C_3H_7; R' = -H**

White, microcrystalline powder, m.p.89°-90°C (isopropanol), yield 41.7%, $C_{19}H_{22}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.45(bs, 1H, HN-CO); 10.82(t, 1H, NH-CS, 5.2); 7.39÷7.45(m, 2H, H-5, H-7); 7.14÷7.32(m, 7H, H-arom); 3.59(bq, 2H, H-17, 6.6); 2.97(m, 2H, H-8, syst. A_2B_2); 2.82(m, 2H, H-9, syst. A_2B_2); 1.66(sxt, 2H, H-18, 7.3); 0.93(t, 3H, H-19, 7.3).

^{13}C-NMR(dmso-d6, δ ppm): 180.07(C-16); 170.63(C-1); 141.44(Cq); 139.63(Cq); 134.21(Cq); 130.77(CH); 129.93(CH); 128.37(CH); 128.36(CH); 128.00(CH); 126.04(CH); 125.93(CH); 46.35(C-17); 37.24 (C-8); 35.18(C-9); 21.03(C-18); 11.33(C-19).

FT-IR(ATR in solid, ν cm^{-1}): 3326w; 3170m; 3060w; 3024m; 2961m; 2936m; 2871w; 1671s; 1604w; 1543vs; 1492s; 1450m; 1338w; 1295w; 1268m; 1245m; 1180s; 1147m; 1119w; 1079w; 950w; 887w; 753s; 720m; 696m; 654m; 611w; 532w.

Calculated %: C 69.90; H 6.79; N 8.58; S 9.82. Experimental %: C 69.97; H 6.86; N 8.51; S 9.76.

N-(2-Phenethylbenzoyl)-N'-(isopropyl)-thiourea: **1c; R = -iso.C_3H_7; R' = -H**

White, microcrystalline powder, m.p.103°-104°C (isopropanol), yield 44.4%, $C_{19}H_{22}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.50(bs, 1H, HN-CO); 10.70(bd, 1H, NH-CS, 7.4); 7.38÷7.45(m, 2H, H-5, H-7); 7.17÷7.32(m, 7H, H-arom); 4.44(spt, 1H, H-17, 6.7); 2.97(m, 2H, H-8, syst. A_2B_2); 2.82(m, 2H, H-9, syst. A_2B_2); 1.27(d, 6H, H-18, 6.7).

^{13}C-NMR(dmso-d6, δ ppm): 178.90(C-16); 170.87(C-1); 141.44(Cq); 139.58(Cq); 134.22(Cq); 130.77(CH); 129.90(CH); 128.38(CH); 128.35(CH); 128.00(CH); 126.06(CH); 125.94(CH); 46.67(C-17); 37.20 (C-8); 35.13(C-9); 21.33(C-18).

FT-IR(ATR in solid, ν cm^{-1}): 3320m; 3155s; 3026m; 2969m; 2928m; 2867w; 1690w; 1663m; 1609m; 1578w; 1531vs; 1492s; 1449m; 1367m; 1333m; 1304m; 1247s; 1190s; 1145s; 1123m; 1106m; 1065m; 1036w; 1012w; 897w; 858w; 750m; 726s; 695s; 654m; 622w; 524m; 480w.

Calculated %: C 69.90; H 6.79; N 8.58; S 9.82. Experimental %: C 69.82; H 6.71; N 8.65; S 9.88.

N-(2-Phenethylbenzoyl)-N'-(n-butyl)-thiourea: **1d; R = -n.C_4H_9; R' = -H**

White, microcrystalline powder, m.p.69°-70°C (isopropanol), yield 24.6%, $C_{20}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 12.55(vbs, 1H, HN-CO); 10.80(t, 1H, NH-CS, 4.9); 7.43(dd, 1H, H-7, 1.6, 7.8); 7.42(td, 1H, H-5, 7.8, 1.6); 7.14÷7.33(m, 7H, H-arom); 3.63(bq, 2H, H-17, 6.5); 2.97(m, 2H, H-8, syst. A_2B_2); 2.82(m, 2H, H-9, syst. A_2B_2); 1.62(qv, 2H, H-18, 7.4); 1.35(sxt, 2H, H-19, 7.4); 0.92(t, 3H, H-20, 7.4).

^{13}C-NMR(dmso-d6, δ ppm): 180.03(C-16); 170.66(C-1); 141.46(Cq); 139.61(Cq); 134.26(Cq); 130.75(CH); 129.94(CH); 128.37(CH); 128.36(CH); 128.00(CH); 126.05(CH); 125.94(CH); 44.37(C-17); 37.26 (C-8); 35.22(C-9); 29.78(C-18); 19.68(C-19); 13.73(C-20).

FT-IR(ATR in solid, ν cm^{-1}): 3321w; 3159s; 3023m; 2932s; 2866m; 1671s; 1601w; 1513vs; 1450vs; 1374m; 1315m; 1237s; 1170s; 1109m; 1082m; 1050m; 949w; 860w; 824w; 795w; 723s; 701s; 655m; 526m; 495w.

Calculated %: C 70.55; H 7.10; N 8.23; S 9.42. Experimental %: C 70.61; H 7.17; N 8.17; S 9.36.

N-(2-Phenethylbenzoyl)-N'-(isobutyl)-thiourea: **1e; R = -iso.C_4H_9; R' = -H**

White, microcrystalline powder, m.p.88°-90°C (isopropanol), yield 35.2%, $C_{20}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.56(s, 1H, HN-CO, deuterable); 10.91(t, 1H, NH-CS, 5.4); 7.43(dd, 1H, H-7, 1.6, 7.8); 7.42(td, 1H, H-5, 7.8, 1.6); 7.14÷7.35(m, 7H, H-arom); 3.49(dd, 2H, H-17, 5.4, 6.5); 2.97(m, 2H, H-8, syst. A_2B_2); 2.82(m, 2H, H-9, syst. A_2B_2); 2.03(n, 1H, H-18, 6.5); 0.95(t, 3H, H-20, 6.5).

^{13}C-NMR(dmso-d6, δ ppm): 180.05(C-16); 170.63(C-1); 141.28(Cq); 139.42(Cq); 134.03(Cq); 130.58(CH); 129.76(CH); 128.18(CH); 128.16(CH); 127.85(CH); 125.87(CH); 125.74(CH); 51.85(C-17); 37.25(C-8); 35.24(C-9); 26.95(C-18); 20.00(C-19).

FT-IR(ATR in solid, ν cm^{-1}): 3324m; 3158s; 3029m; 2960m; 2931m; 2873w; 1691m; 1669s; 1612m; 1528vs; 1456s; 1327w; 1297w; 1247s; 1167m; 1146m; 1125m; 1088m; 1069m; 1045w; 1017w; 756s; 727m; 696s; 657m; 620w; 531w.

Calculated %: C 70.55; H 7.10; N 8.23; S 9.42. Experimental %: C 70.51; H 7.18; N 8.31; S 9.49.

N-(2-Phenethylbenzoyl)-N'-(sec-butyl)-thiourea: **1f; R = -sec.C_4H_9; R' = -H**

White, microcrystalline powder, m.p.105°-106°C (isopropanol), yield 32.3%, $C_{20}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.45(vbs, 1H, HN-CO); 10.73(d, 1H, NH-CS, 7.9); 7.44(dd, 1H, H-7, 1.6, 7.8); 7.42(td, 1H, H-5, 7.8, 1.6); 7.14÷7.33(m, 7H, H-arom); 4.34(spt, 1H, H-17, 6.9); 2.96(m, 2H, H-8, syst. A_2B_2); 2.81(m, 2H, H-9, syst. A_2B_2); 1.64(m, 2H, H-18); 1.24(d, 3H, H-20, 6.6); 0.93(t, 3H, H-19, 7.4).

^{13}C-NMR(dmso-d6, δ ppm): 179.32(C-16); 170.99(C-1); 141.46(Cq); 139.57(Cq); 134.25(Cq); 130.77(CH); 129.94(CH); 128.38(CH); 128.33(CH); 127.96(CH); 126.07(CH); 125.96(CH); 51.97(C-17); 37.32(C-8); 35.32(C-9); 28.02(C-18); 18.90(C-20); 10.14(C-19).

FT-IR(ATR in solid, ν cm^{-1}): 3323w; 3155s; 3062m; 3025m; 2966m; 2928m; 2868w; 1668s;1607m; 1524vs; 1451s; 1362m; 1330w; 1247m; 1181m; 1138s; 1071w; 1035w; 952w; 881w; 751s; 696s; 656s; 622w; 522w.

Calculated %: C 70.55; H 7.10; N 8.23; S 9.42. Experimental %: C 70.61; H 7.01; N 8.14; S 9.36.

N-(2-Phenethylbenzoyl)-N', N'-di(isobutyl)-thiourea: **1g ; R = -iso.C_4H_9; R' = -iso.C_4H_9.**

White, microcrystalline powder, m.p.114°-115°C (isopropanol), yield 37.8%, $C_{24}H_{32}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 10.73(bs, 1H, HN-CO, deuterable); 7.40(dd, 1H, H-7, 1.6, 7.4); 7.38(m, 1H, H-5); 7.32÷7.15(m, 7H, H-arom); 3.80(d, 2H, H-17, 6.6); 3.40(d, 2H, H-17, 6.6); 3.01(m, 2H, H-8, syst. A_2B_2); 2.86(m, 2H, H-9, syst. A_2B_2); 2.46(n, 1H, H-18, 6.6); 2.37(n, 1H, H-18, 6.6); 0.99(d, 6H, H-19, H-20, 6.6); 0.83(d, 6H, H-19, H-20, 6.6).

^{13}C-NMR(dmso-d6, δ ppm): 181.18(C-16); 165.66(C-1); 141.63(Cq); 139.94(Cq); 135.10(Cq); 130.13(CH); 129.94(CH); 128.38(CH); 128.21(CH); 127.38(CH); 125.90(CH); 125.87(CH); 60.22(C-17); 59.98(C-17); 37.19(C-8); 35.08(C-9); 27.36(C-18); 25.42(C-18); 19.92(C-19, C-20); 19.74(C-19, C-20).

FT-IR(ATR in solid, ν cm^{-1}): 3173m; 3026w; 2960m; 2929m; 2871m; 1690vs; 1598w; 1579w; 1517s; 1490m; 1451s; 1428vs; 1389m; 1369w; 1336w; 1306w; 1257m; 1213vs; 1172m; 1130vs; 1059w; 997w; 947w; 904w; 785w; 752m; 722m; 700m; 699m; 626m; 524w.

Calculated %: C 72.69; H 8.13; N 7.06; S 8.08. Experimental %: C 72.60; H 8.04; N 7.13; S 8.16.

N-(2-Phenethylbenzoyl)-N'-cyclohexyl)-thiourea: **1h; R = -C_6H_{11} ; R' = -H**

White, microcrystalline powder, m.p.119°-120°C (isopropanol), yield 27.8%, $C_{22}H_{26}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.52(s, 1H, HN-CO); 10.87(d, 1H, CS-NH, 7.7); 7.47÷7.14(m, H, H-arom); 4.22(m, 1H, H-17); 2.97(m, 2H, H-8, syst. A_2B_2); 2.83(m, 2H, H-9, syst. A_2B_2); 1.95(m, 2H, H-18e, H-22e); 1.72÷1.20(m, 8H, H-cyclohexyl).

^{13}C-NMR(dmso-d6, δ ppm): 178.79(C-16); 170.97(C-1); 141.39(Cq); 139.55(Cq); 134.11(Cq); 130.70(CH); 129.83(CH); 128.30(CH); 127.96(CH); 125.98(CH); 125.84(CH); 52.83(C-17a); 52.72(C-17e); 37.20(C-8); 35.18(C-9); 30.82(C-18,C-22); 24.96(C-20); 23.95(C-19, C-21).

FT-IR(ATR in solid, ν cm^{-1}): 3328w; 3148s; 3061m; 3026m; 2930s; 2854m; 1666s; 1600w; 1535vs; 1513vs; 1495vs; 1448m; 1343m; 1272m; 1247m; 1202w; 1166s; 1143s; 1101m; 1033w; 986w; 895w; 850w; 754s; 697m; 654m; 569w; 524w.

Calculated %: C 72.09; H 7.15; N 7.64; S 8.75. Experimental %: C 72.16; H 7.23; N 7.55; S 8.67.

N-(2-Phenethylbenzoyl)-N'-benzyl-thiourea: **1i ; R = -CH_2-C_6H_5 ; R' = H**

White, microcrystalline powder, m.p.104°-105°C (isopropanol), yield 23.0%, $C_{23}H_{22}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.65(bs, 1H, HN-CO); 11.17(t, 1H, CS-NH, 5.6, deuterable); 7.47(d, 1H, H-7, 7.5); 7.45(bt, 1H, H-5, 7.5); 7.41÷7.14(m, 12H, H-arom); 4.91(d, 2H, H-17, 5.6); 2.98(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): 180.48(C-16); 170.50(C-1); 141.36(Cq); 139.59(Cq); 137.51(Cq); 134.10(Cq); 130.72(CH); 129.87(CH); 128.47(CH); 128.30(CH); 128.27(CH); 128.00(CH); 127.61(CH); 127.26(CH); 125.96(CH); 125.85(CH); 47.95(C-17); 37.22 (C-8); 35.15(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3240m; 3181m; 3084w; 3021m; 2914m; 2864w; 1679s; 1602w; 1532s; 1518vs; 1494vs; 1449s; 1424m; 1362w; 1324m; 1263s; 1248s; 1200m; 1168vs; 1119m; 1060w; 1026w; 979m; 888w; 751m; 729m; 711m; 690s; 652m; 625w; 516w.

Calculated %: C 73.77; H 5.92; N 7.48; S 8.56. Experimental %: C 73.71; H 5.98; N 7.41; S 8.47.

N-(2-Phenethylbenzoyl)-N', N'-di(benzyl)-thiourea: **1j ; R = R' = -CH_2-C_6H_5**

White, microcrystalline powder, m.p.112°-113°C (isopropanol), yield 33.4%, $C_{30}H_{28}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.06(bs, 1H, HN-CO); 7.52(dd, 1H, H-7, 1.4, 7.5); 7.45÷7.15(m, 18H, H-arom); 5.24(s, 2H, H-17); 4.86(s, 2H, H-17); 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): 182.89(C-16); 166.88(C-1); 141.62(Cq); 140.17(Cq); 135.84(Cq); 135.13(Cq); 134.74(Cq); 130.31(CH); 130.08(CH); 128.80(CH); 128.48(CH); 128.32(CH); 128.21(CH); 127.83(CH); 127.71(CH); 127.36(CH); 125.83(CH); 55.42(C-17); 54.69(C-17); 37.43 (C-8); 35.24(C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3199w; 3057w; 3022w; 2951w; 2929w; 2867w; 1697vs; 1600w; 1575w; 1515vs; 1493m; 1438s; 1414vs; 1310w; 1289w; 1261w; 1179s; 1225s; 1126s; 1077m; 1053m; 1011m; 869w; 804w; 752s; 696s; 662m; 629m; 533w; 506w.

Calculated %: C 77.55; H 6.07; N 6.03; S 6.90. Experimental %: C 77.61; H 6.14; N 5.97; S 6.83.

N-(2-Phenethylbenzoyl)-N'-phenethyl-thiourea: **1k ; R = -CH_2-CH_2-C_6H_5 ; R' = H**

White, microcrystalline powder, m.p.98°-99°C (isopropanol), yield 27.8%, $C_{24}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz): 11.54(bs, 1H, HN-CO); 10.86(t, 1H, CS-NH, 5.4); 7.43(dd, 1H, H-7, 1.4, 7.5); 7.42(td, 1H, H-5, 1.4, 7.3); 7.33÷7.17(m, 12H, H-arom); 3.87(bq, 2H, H-17, 7.8); 2.98(t, 2H, H-18, 7.8); 2.96(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): 180.15(C-16); 170.50(C-1); 141.39(Cq); 139.66(Cq); 138.84(Cq); 134.03(Cq); 130.74(CH); 129.89(CH); 128.70(CH); 128.46(CH); 128.32(CH); 128.02(CH); 126.37(CH); 125.98(CH); 125.83(CH); 46.17(C-17);

37.19 (C-8); 35.08(C-9); 33.54(C-18).

FT-IR(ATR in solid, ν cm^{-1}): 3021m; 3061w; 3021m; 3000w; 2950w; 2925w; 2865m; 1674s; 1602w; 1577w; 1544vs; 1512vs; 1453s; 1306m; 1266m; 1241s; 1173s; 1117m; 1080w; 1061w; 1044w; 965w; 934w; 750m; 715m; 695s; 657m; 624w; 530w.

Calculated %: C 74.19; H 6.23; N 7.21; S 8.25. Experimental %: C 74.11; H 6.29; N 7.29; S 8.19.

N-(2-Phenethylbenzoyl)-N', N'-di(phenyl)-thiourea: **1l ; R = R' = -C_6H_5**

White, microcrystalline powder, m.p. 117°-118°C (ethanol), yield 13.4%, $C_{28}H_{24}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 11.15(s, 1H, HN-CO, deuterable); 7.37(t, 4H, H-19, H-21, 8.0); 7.31(dd, 4H, H-18, H-22, 1.4, 8.0); 7.32÷7.14(m, 10H, H-arom); 6.96(dd, 1H, H-7, 1.0, 7.4); 2.75(s, 4H, H-8, H-9).

^{13}C-NMR(dmso-d6, δ ppm): 183.83(C-16); 164.82(C-1); 145.50(C-17); 141.44(C-3); 140.04(C-10); 134.23(C-2); 130.13(C-5); 129.69(C-4); 129.03(C-19,C-21); 128.27 (C-11,C-15); 128.10(C-12, C-14); 127.38(C-7); 127.06(C-6); 126.87(C-18,C-22); 125.73(C-13); 125.48(C-13), 36.81(C-8); 34.30 (C-9).

FT-IR(ATR in solid, ν cm^{-1}): 3246w; 3054w; 3023w; 2966w; 2910w; 1704s; 1591m; 1486vs; 1448s; 1359vs; 1309m; 1274m; 1236s; 1199s; 1145s; 1077w; 1049m; 1025m; 918w; 856w; 749m; 689s; 630m; 576w.

Calculated %: C 77.03; H 5.54; N 6.42; S 7.34. Experimental %: C 77.11; H 5.48; N 6.49; S 7.24.

N-(2-Phenethylbenzoyl)-N'-(3-fluorophenyl)-thiourea: **1m ; R = -C_6H_4-F(3) ; R' = H**

White, microcrystalline needle powder, m.p.88°-89°C (ethanol), yield 44.9%, $C_{22}H_{19}N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 12.60(s, 1H, HN-CO); 11.85(s, 1H, CS-NH, deuterable); 7.84(dt, 1H, H-18, ^{3}J(F-H^{18}) = 11.1 Hz, ^{4}J(H^{18}-H^{20,22}) = 1.2 Hz); 7.53(dd, 1H, H-7, 1.4, 7.4); 7.43÷7.48(m, 3H, H-arom); 7.35(dd, 1H, H-4, 7.4, 1.4); 7.33(td, 1H, H-6, 7.4, 1.4); 7.27(dd, 2H, H-12, H-14, 6.8, 7.6); 7.23(dd, 2H, H-11, H-15, 1.3, 7.6); 7.18(tt, 1H, H-13, 1.3, 6.8); 7.12(m, 1H, H-20, ^{3}J(F-H^{20}) = 10.7 Hz); 3.04(m, 2H, H-9, syst. A_2B_2); 2.89(m, 2H, H-8, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm, T = 40°C): 179.01(C-16); 170.53(C-1); 161.62 (d, C-19, J(F-C^{19}) = 242.0 Hz); 141.25(Cq); 139.84(Cq); 139.52(C-17, ^{3}J(F-C^{17}) = 11.1 Hz): 133.71(Cq); 130.89(C-5); 130.20(d, C-21, ^{3}J(F-C^{21}) = 9.5 Hz); 129.87(C-4); 128.26(C-11,C-15); 128.19(C-12, C-14); 128.16(C-7); 125.86(C-13); 125.77(C-6); 120.18(d, C-22, ^{4}J(F-C^{22}) = 2.9 Hz); 121.86(d, C-20, ^{2}J(F-C^{20}) = 21.1 Hz); 111.06(d, C-18, ^{2}J(F-C^{18}) = 26.2 Hz); 37.06(C-8); 34.84 (C-9).

^{19}F-NMR(dmso-d6, δ ppm, T = 40°C): -112.54(F-19).

FT-IR(ATR in solid, ν cm^{-1}): 3140m; 3054m; 3022m; 2853w; 1676m; 1593w; 1520vs; 1438s; 1324m; 1275m; 1242m; 1181s; 1132m; 1064w; 984w; 893w; 858w; 820w; 796w; 740m; 691m; 646w; 604w; 522w.

Calculated %: C 69.82; H 5.06; F 5.02; N 7.40; S 8.47. Experimental %: C 69.75; H 5.12; N 7.48; S 8.56.

N-(2-Phenethylbenzoyl)-N'-(2,3,4-trifluorophenyl)-thiourea: **1n ; R = -$C_6H_2F_3$ (2,3,4) ; R' = H**

White, microcrystalline needle powder, m.p.149°-150°C (isobutanol), yield 45.8%, $C_{22}H_{17}F_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 12.20(s, 1H, deuterable); 12.08(s, 1H, NH, deuterable); 7.65(m,1H, H-22); 7.53(dd, 1H, H-7, 1.4, 7.4); 7.47(td, 1H, H-5, 7.4, 1.4); 7.43÷7.31(m, 3H, H-21, H-4, H-6); 7.27(dd, 2H, H-12, H-14, 6.8, 7.6); 7.23(dd, 2H, H-11, H-15, 1.3, 7.6); 7.19(tt, 1H, H-13, 1.3, 6.8); 3.04(m, 2H, H-9, syst. A_2B_2); 2.89(m, 2H, H-8, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm, T = 40°C): 181.14(C-16); 170.55(C-1); 148.88 (ddd, C-20, J(F-C^{19}) = 246.0, ^{2}J(F^{19}-C^{20}) = 14.0, ^{3}J(F^{18}-C^{20}) = 3.2 Hz); 145.64(ddd, C-18, J(F-C^{18}) = 249.0, ^{2}J(F^{19}-C^{18}) = 16.0, ^{3}J(F^{18}-C^{20}) = 3.2 Hz); 141.27(Cq); 138.89(Cq);

139.38(ddd, C-19, J(F-C^{19}) = 247.0, ^{2}J(F^{18}-C^{19}) = 16.0, ^{2}J(F^{19}-C^{20}) = 14.0 Hz);

130.98(C-5); 129.93(C-4); 128.25(C-11,C-15); 128.22(C-12, C-14); 128.18(C-7); 125.90(C-6); 125.82(C-13); 124.35(dd, C-17, ^{2}J(F^{18} -C^{17}) = 9.2 , ^{3}J(F^{19} -C^{17}) = 3.7 Hz); 122.97(dd, C-22, ^{3}J(F^{20} -C^{22}) = 3.3, ^{3}J(F^{18} –C^{22}) = 7.7 Hz); 111.68(dd, C-21,

^{3}J(F^{19} -C^{21}) = 3.7, ^{2}J(F^{20} –C^{21}) = 18.0 Hz); 37.20(C-8); 35.06 (C-9).

^{19}F-NMR(dmso-d6, δ ppm, T = 40°C): -136.66(m, F-18); -140.46(bd, F-20, ^{3}J(F^{20} –F^{19}) = 21.5 Hz); -160.99(td, F-19, ^{3}J(F^{19}–$F^{18,20}$) = 21.5 Hz).

FT-IR(ATR in solid, ν cm^{-1}): 3138s; 3061m; 3024m; 2942w; 2921w; 1672m; 1620w; 1600w; 1501vs; 1453s; 1531m; 1272m; 1251m; 1239m; 1199w; 1179m; 1148s; 1057m; 999m; 903w; 829w; 779w; 748s; 697m; 660m; 625w.

Calculated %: C 63.76; H 4.13; F 13.75; N 6.76; S 7.74. Experimental %: C 63.68; H 4.18; N 6.66; S 7.68.

N-(2-Phenethylbenzoyl)-N'-(2,4,5-trifluorophenyl)-thiourea: **1o ; R = -$C_6H_2F_3$ (2,4,5) ; R' = H**

Yellowish, microcrystalline powder, m.p.114°-115°C (ethanol), yield 48.3%, $C_{22}H_{17}F_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 12.39(s, 1H, deuterable); 12.08(s, 1H, NH, deuterable); 8.19(dt, 1H, H-22, ^{3}J(H^{22} –F^{21}) = 11.5, ^{4}J(H^{22} –$F^{18,20}$) = 7.6 Hz); 7.73(td, 1H, H-19, ^{3}J(H^{19} –$F^{18,20}$) = 10.6, ^{4}J(H^{19} –F^{21}) = 7.4 Hz); 7.53(dd, 1H, H-7, 1.4, 7.4); 7.47(td, 1H, H-5, 7.4, 1.4); 7.36(dd, 1H, H-4, 1.4, 7.4); 7.34(td, 1H, H-6, 7.4, 1.4); 7.27(dd, 2H, H-12, H-14, 6.8, 7.6); 7.23(dd, 2H, H-11, H-15, 1.3, 7.6); 7.18(tt, 1H, H-13, 1.3, 6.8); 3.03(m, 2H, H-9, syst. A_2B_2); 2.88(m, 2H, H-8, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm, T = 40°C): 180.51(C-16); 170.73(C-1); 151.36 (ddd, C-21, 2.7, 9.9, 245.9 Hz); 147.33(ddd, C-20, 11.7, 14,6, 244.8 Hz); 144.99(ddd, C-18, 3,6. 13.2, 241,9 Hz); 141.25(Cq); 139.89(Cq); 133.49(Cq); 131.00(C-5); 129.92(C-4); 128.24(C-11, C-15); 128.20(C-12, C-14); 128.18(C-7); 125.88(C-6); 125.81(C-13); 122.97(ddd, C-17, 4.0, 9.2, 13.2); 115.73(dd, C-22, 1.7, 22.6 Hz); 105.97(dd, C-19, 22.1, 26.4 Hz); 37.15(C-8); 35.00 (C-9).

^{19}F-NMR(dmso-d6, δ ppm, T = 40°C): -123.45(bs, F-18); -136.31(bd, F-20, ^{3}J(F^{20} –F^{21}) = 22.4 Hz); -142.34(m, F-21).

FT-IR(ATR in solid, ν cm^{-1}): 3181m; 3070w; 3022w; 2946w; 2914w; 2851w; 1682m; 1564vs; 1501vs; 1435m; 1314vs; 1217m; 1155s; 1061w; 870m; 818w; 750m; 701m; 667w; 637w.

Calculated %: C 63.76; H 4.13; F 13.75; N 6.76; S 7.74. Experimental %: C 63.82; H 4.18; N 6.68; S 7.65.

N-(2-Phenethylbenzoyl)-N'-(2,4,6-trifluorophenyl)-thiourea: **1p ; R = -$C_6H_2F_3$ (2,4,6) ; R' = H**

White, microcrystalline powder, m.p.113°-114°C (isobutanol), yield 36.2%, $C_{22}H_{17}F_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 12.15(s, 1H, deuterable); 11.65(s, 1H, NH, deuterable); 7.55(dd, 1H, H-7, 1.4, 7.4); 7.47(td, 1H, H-5, 7.4, 1.4); 7.36(dd, 1H, H-4, 1.4, 7.4); 7.34(td, 1H, H-6, 7.4, 1.4); 7.34÷7.26(m, 2H, H-19, H-21); 7.27(dd, 2H, H-12, H-14, 6.8, 7.6); 7.23(dd, 2H, H-11, H-15, 1.3, 7.6); 7.19(tt, 1H, H-13, 1.3, 6.8); 3.03(m, 2H, H-9, syst. A_2B_2); 2.88(m, 2H, H-8, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm, T = 40°C): 182.20(C-16); 170.29(C-1); 160.84(dt, C-20, 247.0, 14.0 Hz); 158.17(ddd, C-18, C-22, 7.2, 16.0, 245.0 Hz); 141.26(Cq); 139.74(Cq); 133.70(Cq); 130.91(C-5); 129.93(C-4); 128.21(C-11, C-15); 128.20 (C-12, C-14); 128.08(C-7); 125.90(C-6); 125.86(C-13); 113.50(td, C-17, 17.3, 5.2 Hz); 100.82(t, C-19, C-21, 27.1 Hz); 37.33(C-8); 35.32 (C-9).

^{19}F-NMR(dmso-d6, δ ppm, T = 40°C): -108.78(bs, F-20; -115.20(bs, F-18, F-22);

FT-IR(ATR in solid, ν cm^{-1}): 3179m; 3065w; 3029w; 1674m; 1600m; 1521vs; 1448m; 1317w; 1251w; 1164m; 1122m; 1071w; 1037m; 995w; 841w; 754w; 723m; 693m; 618w.

Calculated %: C 63.76; H 4.13; F 13.75; N 6.76; S 7.74. Experimental %: C 63.82; H 4.21; N 6.66; S 7.69.

N-(2-Phenethylbenzoyl)-N'-(3,4,5-trifluorophenyl)-thiourea: **1q ; R = -$C_6H_2F_3$ (3,4,5) ; R' = H**

Yellowish, microcrystalline powder, m.p.118°-119°C (isobutanol), yield 41.0%, $C_{22}H_{17}F_3N_2OS$.

^{1}H-NMR(dmso-d6, δ ppm, J Hz, T = 40°C): 12.48(s, 1H, deuterable); 11.94(s, 1H, NH, deuterable); 7.80(dd, 2H, H-18, H-22, 6.4, 9,6); 7.53(dd, 1H, H-7, 1.4, 7.4); 7.47(td, 1H, H-5, 7.4, 1.4); 7.36(dd, 1H, H-4, 1.4, 7.4); 7.34(td, 1H, H-6, 7.4, 1.4); 7.27(dd, 2H, H-12, H-14, 6.8, 7.6); 7.23(dd, 2H, H-11, H-15, 1.3, 7.6); 7.18(tt, 1H, H-13, 1.3, 6.8); 3.03(m, 2H, H-9, syst. A_2B_2); 2.88(m, 2H, H-8, syst. A_2B_2).

^{13}C-NMR(dmso-d6, δ ppm, T = 40°C): 179.64(C-16); 170.41(C-1); 149.71(ddd, C-19, C-21, 5.6, 10.4, 245.8 Hz); 141.24(Cq); 139.95(Cq); 136.77(dt, C-20, 248.9, 15.8 Hz); 135.55(Cq); 134.14(td, C-17, 11.8, 4.4 Hz); 131.01(C-5); 129.92(C-4); 128.30(C-11, C-15); 128.21(C-12, C-14); 128.21(C-7); 125.89(C-6); 125.80(C-13); 109.80(d, C-18, C-22, 23.8 Hz); 37.04(C-8); 34.78(C-9).

^{19}F-NMR(dmso-d6, δ ppm, T = 40°C): -135.425(dd, F-19, F-21, 9.8, 22.4 Hz); -164.13(tt, F-20, 6.3, 22.4 Hz).

FT-IR(ATR in solid, ν cm^{-1}): 3416m; 3040w; 2926m; 2867w; 1687s; 1626m; 1599m; 1558s; 1513vs; 1496vs; 1439vs; 1370m; 1319vs; 1237s; 1207s; 1170s; 1138s; 1131m; 1044s; 902w; 849m; 770w; 751s; 701m; 656m; 638m; 622m; 595m.

Calculated %: C 63.76; H 4.13; F 13.75; N 6.76; S 7.74. Experimental %: C 63.71; H 4.19; N 6.68; S 7.66.

References

1.*** USAN 1990 and the USP dictionary of drug names, Mack Printing Company Easton, Pennsylvania, 1989

2.*** The Merck Index, 13 th Edition, Merck & Co., Inc., Whitehouse Station, New Jersey, 2001

3.*** Pharmazeutische Stoffliste, Ed. Abdata, Eschborn, Tannes, 1998

4. MARTIN NEGWER, HANS GEORG SCHAMOW – Organic Chemical drugs and their Synonymes, Ed. Wiley – WCH, Weinheim, Germania, 2001

5. N.V. KONINKLIJKE PHARMACEUTICHE FABRIEKEN, Brevet FR, 2165M, 1963, CA 60, 14522g, 1964
6. COPE, C.A, FENTON, W.S., J. Am. Chem. Soc., **73**, 1951, p. 1668
7. MISSIR, A.V., MORUSCIAG, L., NITULESCU, G.M., ILIE, C., CAPROIU, M.T. Rev. Chim. (Bucharest), **60**, no.12, 2009, p. 1288
8. MORUSCIAG, L., MISSIR, A.V., GUTA, R., NANAU-ANDREESCU, D. CAPROIU, M.T., Rev. Chim. (Bucharest), **60,** no.8, 2009, p. 805
9. MORUSCIAG, L., MISSIR, NITULESCU, G.M., CHIRITA, I.C., CAPROIU, M.T., DRAGHICI, C. Rev. Chim. (Bucharest), **61,** no.7, 2010, p. 642.
10. LIMBAN, C., MISSIR, A.V., CHIRITA, I.C., NITULESCU, G.M., ILIE, C., CAPROIU, M.T., Rev. Chim. (Bucharest), **60,** no.7, 2009, p. 657
11. BALOTESCU, M.C., LIMBAN, C., MISSIR, A.V., CHIRITA, I.C., NITULESCU, G.M., Rev. Chim. (Bucharest), **58,** no.11, 2007, p. 1064
12. BADICEANU, D.C., MISSIR, A.V., Farmacia, **57**, no.3, 2009, p. 339
13. LIMBAN, C., MISSIR, A.V., CHIRIŢĂ, I.C., Farmacia, **48**, no.6, 2000, p. 73
14. LIMBAN, C., MISSIR, A.V., CHIRIŢĂ, I.C., Farmacia, **52**, no.5, 2004, p. 7

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review

"BIOMOLECULES. BIOTRANSFORMATIONS"

by

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The present book is an expression of the scientific concerns of the members of the teaching and research staff of the ***Biochemical Engineering*** section that is now a traditional specialization of the Faculty of Chemical Engineering and Environmental Protection, Technical University "Gh. Asachi" of Iaşi which is also to be found in other faculties in the country. Such concerns are also made evident by the scientific papers published in Romania and abroad by the authors of the present book.

Nowadays the word *biomolecul*es is much encountered referring to the chemical compounds involved in the vital phenomena in the cells of every living organism. The biological functions characteristic of the biomolecules are strongly connected to their structures and physical and chemical properties of every class of compounds involved in the huge gearing simply defining the *life* since the biological phenomena are known to be sustained by a molecular basis.

The *biotransformations* developing within the living cell as metabolic processes proceeding continuously with material and energy consumption are assembled as complex cyclic processes whose full elucidation means invariably provocative themes for the scientists. Thus, the biochemical reactions are continuously studied in their secrets, mechanisms and natural succession according to a group of principles defining *the molecular logic of the living state* as settled by the well known biochemist A.L.Lehninger and accepted by other famous biochemical researchers.

The precise knowledge of the main classes of biomolecules with their characteristic properties as well of their interactions is crucial for the investigation and full understanding of the acting way of that engine making possible the right succession of great deal of biochemical reactions in the manifestation and maintaining of the living state.

For the sake of a profound professional training of the students in the field of biochemical engineering the biochemistry is quite necessary to teach along with the other ground disciplines such as microbiology, biotechnology, enzymology. Although the domain vastness including almost all the chemistry and biology branches is rather difficult to cover in a single book the describing of the main biomolecule classes with their characteristic biotransformations important for practical uses gives a very good theoretical ground to those interested in these activities.

The book ***„Biomolecules. Biotransformations"*** by Assoc. prof. dr. Camelia Şoldea. and Asist. dr. Anca Mihaela Mocanu fulfils in a great extent these requirements. In the six chapters covering 340 pages, the main classes of biomolecules are described regarding the characteristic properties of the compounds involved which are crucial for the living cell and entire living organism: amino acids and proteins, enzymes and coenzymes, nucleic acids, carbohydrates, lipids. The biotransformations determined by these properties (Chapter VI), significant for the vegetal and animal kingdoms and also for the microorganisms are presented and discussed as a logic concatenation making evident the essential characteristics of the biochemical reactions and their interdependence which explains the unity by diversity of the living world. The first chapter deserves being mentioned for the discussion about the life occurrence on the Earth. Herein various theories and hypotheses about the origin of biomolecules and their syntheses under prebiotic conditions are presented as revealed in recent reported papers.

The metabolic transformations described with the biomolecules discussed which are crucial for the characterization of the living matter have practical uses in elaboration and accomplishment of various biotechnological processes where the microorganism activities are directed to the obtaining of many medicaments, vitamins, food products and also to the environmental protection.

The present book pays also attention to the contributions brought by well known biochemists who published many important books and papers in the recent years. The scientific papers mentioned by authors in the reference sheet which are to be found in prestigious journals in the world published between 2000-2010 made possible a competent and interesting approaching of the living world characterization by discussing the main biomolecules and their biotransformations

The book ***„Biomolecules. Biotransfomations"*** by Assoc. prof. dr.Camelia Şoldea and Asist. dr. Anca Mihaela Mocanu is very useful to the students, master and Ph.D. students and specialists in the fields of biochemistry and biotechnologies applied to the obtaining of medicaments, vitamins, food and cosmetic products, bringing useful information on the recent achievements in the field and stimulating the readers to enrich the domain with their own contributions.

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