

New O-acyl-oximino-dibenzo[b,e]Thiepines and their Sulfones

Synthesis and characterization

CAMELIA ELENA STECOZA^{1*}, CORINA ILIE², MIRON TEODOR CAPROIU³

¹ University of Medicine and Pharmacy "Carol Davila" Bucharest, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 6 Traian Vuia, 020956, Bucharest, Romania

² National Institute for Chemical Pharmaceutical R&D – ICCF, 112 Vitan Avenue, Bucharest, Romania

³ Romanian Academy, Organic Chemistry Center „C.D. Nenitescu”, 202 B Splaiul Independenței, 060023, Bucharest, Romania

New O-acyl-oximino-dibenzo[b,e]thiepines and their sulfones have been synthesized and structurally elucidated by spectral analysis (¹H-NMR, ¹³C-NMR, IR) and elemental analysis. The main precursor, 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine, was prepared in several stages, starting from phthalide and thiophenol, via 2-phenylthiomethyl-benzoic acid and 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one. The new O-acyl-oximino-dibenzo[b,e]thiepines, were prepared by acylation of the aforementioned oxime with various substituted benzoic acid chlorides. The corresponding sulfones resulted by oxidation, using hydrogen peroxide in glacial acetic acid, as oxidizing agent.

Keywords: dibenzo[b,e]thiepin, sulfones, NMR spectroscopy

Dibenzothiepinines are well-known especially for their antidepressant activity (e.g. *Dosulepin*, under the brand name *Prothiaden*[®]) [1], but also for other activities such as: antipsychotic (*Methiotepine*, *Octochlothepine* [2]), analgesic, anti-inflammatory (*Zaltoprofen* [3]), bacteriostatic, antiprotozoal [4, 5], antihypertensive, antiatherosclerotic, antidyslipidemic (*Monatepil* [6]), insecticidal, acaricidal, nematocidal [7].

Taking into account all these findings and as a continuation of our studies in dibenzothiepine series [8-14], we proposed the synthesis of new compounds having dibenzo[b,e] thiepine scaffold. The new compounds, dibenzo[b,e] thiepin-11(6H)-one O-benzoyloximes and their sulfones, will be further investigated for antimicrobial activity and as antidepressant agents. This study was prompted also, by our previous data which made evident the favourable effects of the replacement of sulfur atom by SO₂ group, for the improvement of the biological activity [15].

Experimental part

Melting points were uncorrected and recorded in open capillary tubes on an Electrothermal 9100 apparatus. Elemental analyses were performed on a Perkin Elmer CHNS/O Analyser Series II 2400 apparatus, the results being within ±0.4% of the theoretical values.

All the starting materials were purchased from commercial sources (Sigma – Aldrich, Fluka, Merck), were of reagent grade and used as received excepting benzene and pyridine which were dried before use.

The progress of the reaction was observed by thin layer chromatography (TLC). The TLC procedure was performed on silicagel 60F254 Merck plates, using chloroform/ ethyl acetate (10:1) as a mobile phase. The visualization was performed using an UV lamp ($\lambda = 254\text{nm}$) and iodine atmosphere.

NMR spectra were recorded using a Varian INOVA 400 spectrometer operating at 9.4 Tesla, corresponding to the resonance frequency of 399.95 MHz for the ¹H nucleus and

100.56 MHz for the ¹³C nucleus. TMS was used as internal standard both in proton and carbon spectra. All the spectra were recorded at 303K with an indirect detection probehead AS-SW and field gradients.

The ¹H-NMR data are reported in the following order: chemical shift (ppm), multiplicity, number of protons, assignment of the signal, coupling constant (J) in hertz. The splitting patterns are abbreviated as following: s, singlet; bs, broad singlet; d, doublet, bd, broad doublet, dd, double doublet, ddd, doublet of double doublets; dq, double quartet, t, triplet; td, triple doublet; sxt, sextet.

The ¹³C-NMR data are reported in the following order: chemical shift (ppm), the signal/ atom attribution, the coupling constant (J) in some cases; (Cq- quaternary carbon).

IR spectra were recorded using a FT-IR Bruker Vertex 70 apparatus, with horizontal device for attenuated reflectance and diamond crystal, on a spectral window ranging from 4000 to 400 cm⁻¹, at a spectral resolution of 2 cm⁻¹. The IR bands intensities are denoted as: w- weak; m- medium; s- strong; vs- very strong.

The new compounds, O-acyl-oximino-dibenzo[b,e] thiepinines and their sulfones were obtained through a multistage synthesis. The starting compounds, 2-phenylthiomethyl-benzoic acid (**3**), 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one (**4**) and 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (**5**) were synthesized according to the previously described procedures [8, 11].

General procedure for synthesis of O-acyl-oximino-dibenzo[b,e]thiepinines (**6**)

To a solution of 6.2 mmol 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (Mol wt 241.30) in 60 mL anhydrous toluene was added drop wise a solution of 6.8 mmol appropriated acid chloride in 15 mL anhydrous toluene and 6.2 mmol dry pyridine (Mol wt 79.098; $d_4^{25}=0.978$). The reaction mixture was refluxed for 3- 4 hours, afterwards was cooled, the precipitate was filtered and the solvent was removed under reduced pressure. The

* email: cameliastecoza@gmail.com; Tel 0728899244

resulting crude product was recrystallized from *iso*-propanol. The progress of the reaction was observed by thin layer chromatography.

General procedure for synthesis of sulfones (7)

To a solution of 10 mmol **6a-d** in 50 mL glacial acetic acid, were added drop wise, under stirring, 2 mL 30% hydrogen peroxide. The reaction mixture was refluxed for 3- 4 h and left overnight at room temperature. Afterwards was diluted with water and the compound was extracted with chloroform. The combined organic layers were dried over calcium chloride and after filtration, the solvent removed under reduced pressure. The resulting crude product was recrystallized from absolute ethanol. The progress of the reaction was observed by thin layer chromatography.

Spectral data for the new O-acyl-oximino-dibenzo [b,e]thielines (**6a-d**) and their sulfones (**7a-d**).

{[11(*E,Z*)-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(4-propylphenyl)methanone (**6a**)

Syn-anti isomers mixture in ratio 1:4.5.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 7.86 ÷ 7.81(m, 2H, H-1, H-10); 7.67(d, 2H, H-14, H-18, 8.6); 7.55(m, 1H, H-arom); 7.45 ÷ 7.12(m, 6H, H-arom); 7.15(d, 2H, H-15, H-17, 8.6); 4.66(bs, H-6A); 3.54(bs, H-6B); 2.59(t, 2H, H-19, 7.4); 1.61(sxt, 2H, H-20, 7.4); 0.91(t, 3H, H-21, 7.4).

¹³C-NMR(CDCl₃, δ ppm): 166.64(C-12); 163.56(C-11); 148.81(C-16); 136.90(Cq); 135.05(Cq); 133.49(Cq); 131.75(CH); 130.47(CH); 130.26(CH); 129.69(C-14, C-18); 128.93(Cq); 128.61(C-15, C-17); 127.94(CH); 127.18(CH); 127.14(CH); 126.49(CH); 125.96(Cq); 124.98(CH); 38.03(C-19); 33.34(C-6); 24.12(C-20); 13.69(C-21).

FT-IR(ATR in solid, ν cm⁻¹): 2957m; 2924m; 2862w; 1741vs; 1600m; 1461w; 1418m; 1320w; 1237s; 1171m; 1052s; 975s; 855m; 757s/26m; 697m; 636w.

{[11(*E,Z*)-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(4-butylphenyl)methanone (**6b**)

Syn-anti isomers mixture in ratio 1:4.0.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 7.86 ÷ 7.81(m, 2H, H-1, H-10); 7.67(d, 2H, H-14, H-18, 8.6); 7.55(m, 1H, H-arom); 7.45 ÷ 7.12(m, 6H, H-arom); 7.15(d, 2H, H-15, H-17, 8.6); 4.66(bs, H-6A); 3.55(bs, H-6B); 2.61(t, 2H, H-19, 7.3); 1.57(qv, 2H, H-20, 7.3); 1.32(sxt, 2H, H-21, 7.3); 0.90(t, 3H, H-22, 7.3).

¹³C-NMR(CDCl₃, δ ppm): 166.63(C-12); 163.55(C-11); 149.06(C-16); 136.90(Cq); 135.04(Cq); 133.49(Cq); 131.75(CH); 130.47(CH); 130.25(CH); 129.70(C-14, C-18); 128.61(Cq); 128.55(C-15, C-17); 127.94(CH); 127.18(CH); 127.13(CH); 126.48(CH); 125.90(Cq); 124.98(CH); 35.68(C-19); 33.72(C-6); 33.34(C-20); 22.25(C-21); 13.84(C-22).

FT-IR(ATR in solid, ν cm⁻¹): 3044w; 2929m; 2862m; 1742vs; 1600m; 1462m; 1419m; 1321m; 1235s; 1169s; 1053s; 972m; 854m; 754m; 728m; 695m; 636w.

{[11(*E,Z*)-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(3-chloromethylphenyl)methanone (**6c**)

Syn-anti isomers mixture in ratio 1:3.5.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 7.92(t, 1H, H-19^m, 1.5); 7.87 ÷ 7.83(2H, H-arom); 7.77(t, 1H, H-19^M, 1.5); 7.60 ÷ 7.14(m, 9H, H-arom); 4.66(bs, H-6A); 4.56(s, 0.44H, H-19); 4.51(s, 1.56H, H-19); 3.56(bs, H-6B).

¹³C-NMR(CDCl₃, δ ppm): 167.30(C-12); 162.93(C-11); 137.99(C-17); 137.05(Cq); 135.15(Cq); 133.32(Cq); 129.15(Cq); 128.70(Cq); 133.36(CH); 133.29(CH); 131.74(CH); 130.62(CH); 130.39(CH); 129.74(CH);

129.53(CH); 129.99(CH); 128.04(CH); 127.18(CH); 126.60(CH); 125.05(CH); 45.36(C-19^m); 45.31(C-19^M); 33.39(C-6).

FT-IR(ATR in solid, ν cm⁻¹): 3476w; 3053w; 3033w; 2963w; 1744vs; 1585m; 1571m; 1440m; 1418m; 1324m; 1277m; 1252s; 1178vs; 1084s; 1068s; 1041m; 984m; 938m; 925m; 909m; 889m; 771m; 760m; 774m; 722s; 703m; 636w; 575w.

{[11(*E,Z*)-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(4-chloromethylphenyl)methanone (**6d**)

Syn-anti isomers mixture in ratio 1:5.3.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 7.84(dd, 1H, H-1, 1.5, 7.8); 7.75(d, 2H, H-14, H-18, 8.4); 7.58 ÷ 7.25(m, H-arom); 7.13(d, 2H, H-15, H-17, 8.4); 7.18(td, 1H, H-2, 7.8, 1.4); 7.15(dd, 1H, H-4, 1.4, 7.8); 4.66(bs, H-6A); 4.59(s, 0.32H, H-19^m); 4.56(s, 1.68H, H-19^M); 3.56(bs, H-6B).

¹³C-NMR(CDCl₃, δ ppm): 167.20(C-12); 162.99(C-11); 142.73(C-16); 137.00(Cq); 135.10(Cq); 133.35(Cq); 131.74(CH); 130.61(CH); 130.39(CH); 130.09(C-14, C-18); 128.76(Cq); 128.58(C-15, C-17); 128.54(Cq); 128.03(CH); 127.19(CH); 127.10(CH); 126.58(CH); 125.05(CH); 45.24(C-19); 33.37(C-6).

FT-IR(ATR in solid, ν cm⁻¹): 3058w; 3024w; 2932w; 1739vs; 1591m; 1459w; 1418m; 1319m; 1248vs; 1176m; 1062s; 1019w; 977s; 865m; 808w; 760m; 701m; 675w; 632w.

{[5,5-dioxo-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(4-propylphenyl)methanone (**7a**)

From the spectra results that only one stereoisomer is present.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 8.04(dd, 1H, H-1, 1.4, 7.4); 7.91(dd, 1H, H-4, 1.4, 7.8); 7.72 ÷ 7.62(m, 2H, H-arom); 7.67(d, 2H, H-14, H-18, 8.6); 7.49 ÷ 7.58(m, 3H, H-arom); 7.44(dd, 1H, H-7, 8.4, 1.5); 7.18(dq, 2H, H-15, H-17, 8.4, 0.5); 5.12(bs, H-6A); 4.38(bs, H-6B); 2.61(t, 2H, H-19, 7.4); 2.47(s, 3H, H-2); 1.62(sxt, 2H, H-20, 7.4); 0.92(t, 3H, H-21, 7.4).

The long range coupling over four bonds was established between H-*orto* (H-15, H-17) and H-19. Also, is visible the long range coupling between H² and H¹, respectively H³ with a value of ⁴*J* = 0.6 Hz. Due to this small coupling the signal of methyl group is broadened.

¹³C-NMR(CDCl₃, δ ppm): 163.77(C-12); 163.15(C-11); 149.40(C-16); 141.84(C-4a); 134.94(Cq); 132.73(CH); 132.21(CH); 131.47(CH); 130.95(C-1); 130.02(Cq); 130.00(CH); 129.80(C-14, C-18); 128.97(CH); 128.79(C-15, C-17); 127.92(C-7); 126.11(C-4); 125.26(Cq); 124.28(Cq); 58.51(C-6); 38.06(C-19); 24.11(C-20); 13.69(C-21).

FT-IR(ATR in solid, ν cm⁻¹): 3067w; 2960m; 2928m; 2868w; 1748vs; 1606m; 1555w; 1454w; 1419w; 1306vs; 1244vs; 1157s; 1124s; 1080m; 1053vs; 979s; 896m; 868m; 783m; 748s; 721m; 689m; 606w; 521m.

{[5,5-dioxo-dibenzo[b,e]thiepin-11(6*H*)-ylidenamino]oxy}(4-butylphenyl)methanone (**7b**)

From the spectra results that only one stereoisomer is present.

¹H-NMR(CDCl₃, δ ppm, *J* Hz): 8.05(dd, 1H, H-1, 1.4, 7.4); 7.91(dd, 1H, H-4, 1.4, 7.8); 7.70(td, 1H, H-2, 7.4, 1.5); 7.67(d, 2H, H-14, H-18, 8.6); 7.65(td, 1H, H-3, 7.6, 1.4); 7.49 ÷ 7.58(m, 3H, H-arom); 7.45(dd, 1H, H-7, 8.4, 1.5); 7.18(dq, 2H, H-15, H-17, 8.4, 0.5); 5.10(bs, H-6A); 4.39(bs, H-6B); 2.63(t, 2H, H-19, 7.4); 1.58(qv, 2H, H-20, 7.4); 1.33(sxt, 2H, H-21, 7.4); 0.91(t, 3H, H-22, 7.4).

The long range coupling over four bonds was established between H-*orto* (H-15, H-17) and H-19. Also, is visible the

long range coupling between H² and H¹, respectively H³ with a value of ⁴J=0.6 Hz. Due to this small coupling the signal of methyl group is broadened.

¹³C-NMR(CDCl₃, δ ppm): 163.78(C-12); 163.15(C-11); 149.66(C-16); 141.86(C-4a); 134.96(Cq); 132.73(CH); 132.22(CH); 131.48(CH); 130.96(C-4); 130.01(Cq); 130.00(CH); 129.82(C-14, C-18); 128.74(C-15, C-17); 128.98(CH); 127.93(C-7); 126.14(C-1); 125.22(Cq); 124.29(Cq); 58.53(C-6); 35.74(C-19); 33.15(C-20); 22.27(C-21); 13.85(C-22).

FT-IR(ATR in solid, ν cm⁻¹): 3064w; 2958m; 2927m; 2869w; 1745vs; 1607m; 1417w; 1306s; 1248vs; 1160m; 1125m; 1056s; 979m; 895m; 861w; 783m; 743m; 722w; 683w; 523m.

{[5,5-dioxo-dibenzo[b,e]thiepin-11(6H)-ylidenamino]oxy}(3-chloromethylphenyl)methanone (**7c**)

From the spectra results that only one stereoisomer is present.

¹H-NMR(CDCl₃, δ ppm, J Hz): 8.06(dd, 1H, H-1, 1.4, 7.4); 7.92(dd, 1H, H-4, 1.4, 7.8); 7.78(t, 1H, H-14, 1.7); 7.72(dt, 1H, H-18, 7.7, 1.7); 7.71(td, 1H, H-2, 7.5, 1.5); 7.66(td, 1H, H-3, 7.6, 1.4); 7.59÷7.51(m, 4H, H-arom); 7.46(dd, 1H, H-7, 8.4, 1.5); 7.38(t, 1H, H-17, 7.7); 5.10(bs, H-6A); 4.53(s, 2H, H-19); 4.39(bs, H-6B).

Due to the long range couplings with the methylenic protons the signal of H-14 appear as multiplet.

¹³C-NMR(CDCl₃, δ ppm): 164.44(C-12); 162.52(C-11); 141.91(Cq); 138.20(Cq); 134.74(Cq); 129.82(Cq); 128.49(Cq); 124.30(Cq); 133.68(CH); 132.78(CH); 132.36(CH); 131.57(C-4); 131.08(CH); 129.97(CH); 129.79(C-14); 129.58(CH); 129.14(CH); 129.02(C-17); 127.89(CH); 126.19(C-1); 58.53(C-6); 45.20(C-19).

FT-IR(ATR in solid, ν cm⁻¹): 3061w; 2966w; 2919w; 1748vs; 1604w; 1482w; 1445m; 1400w; 1330w; 1307vs; 1282m; 1252s; 1173vs; 1156s; 1062s; 985m; 930s; 901m; 872m; 772m; 751m; 705m; 673w; 520m.

{[5,5-dioxo-dibenzo[b,e]thiepin-11(6H)-ylidenamino]oxy}(4-chloromethylphenyl)methanone (**7d**)

From the spectra results that only one stereoisomer is present.

¹H-NMR(CDCl₃, δ ppm, J Hz): 8.05(dd, 1H, H-1, 1.4, 7.4); 7.91(dd, 1H, H-4, 1.4, 7.8); 7.75(d, 2H, H-14, H-18, 8.4); 7.71(td, 1H, H-2, 7.7, 1.6); 7.65(td, 1H, H-3, 7.7, 1.6); 7.57÷7.49(m, 3H, H-3, H-8, H-9, H-10); 7.44(dd, 1H, H-7, 1.5, 7.6); 7.40(dt, 2H, H-15, H-17, 8.4, 0.6); 5.12(bs, H-6A); 4.57(s, 2H, H-19); 4.38(bs, H-6B).

Due to the long range couplings with the methylenic protons the signal of H-14 appear as multiplet.

¹³C-NMR(CDCl₃, δ ppm): 164.32(C-12); 162.58(C-11); 143.23(Cq); 141.27(Cq); 134.77(Cq); 132.77(CH); 132.33(CH); 131.55(C-4); 131.07(CH); 130.16(C-14, C-18); 129.95(CH); 129.85(Cq); 129.00(CH); 128.72(C-15, C-17); 128.49(Cq); 127.81(C-7); 126.18(C-1); 124.30(Cq); 58.50(C-6); 45.13(C-19).

FT-IR(ATR in solid, ν cm⁻¹): 3063w; 3026w; 2966w; 2925w; 1753vs; 1610w; 1482w; 1448w; 1411w; 1330w; 1307vs; 1260m; 1232vs; 1173m; 1155m; 1120m; 1082m; 1057vs; 984s; 909w; 866w; 783m; 765w; 705m; 521m.

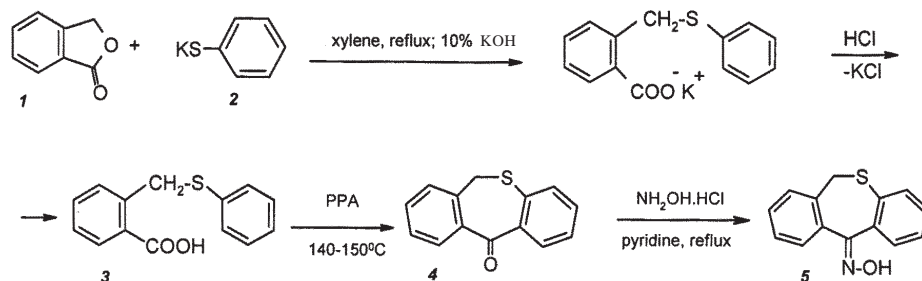
Results and discussions

The title compounds were prepared through a multistage synthesis. In the first stage, 2-phenylthiomethylbenzoic (**3**) was prepared by treating the phthalide (**1**) with potassium salt of thiophenol (**2**). The resulted potassium salt of 2-phenylthiomethylbenzoic showed a good solubility in an aqueous solution of 10% potassium hydroxide and was separated from xylene through precipitation upon acidification using a mineral acid solution. Potassium salt of thiophenol (**2**) was obtained through the reaction of thiophenol with potassium hydroxide in xylene, the resulting water being removed by azeotropic distillation.

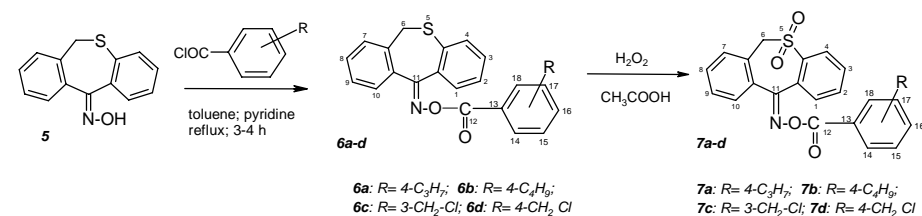
6,11-Dihydrodibenzo[b,e]thiepin-11(6H)-one (**4**) was synthesized in the second stage by cyclodehydration of acid **3** with polyphosphoric acid (PPA) and afterwards, in the third stage, converted to the corresponding oxime (**5**) by treatment with hydroxylamine hydrochloride in the presence of pyridine. The synthetic route for the main precursor, 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (**5**) is illustrated in scheme 1.

The new O-acyl-oximino-dibenzo[b,e]thiepinines (**6**) were prepared by acylation of the oxime **5** with various substituted benzoic acid chlorides, in dry toluene and in the presence of anhydrous pyridine as a proton acceptor. The oxidation of O-acyl-oximino-dibenzo[b,e]thiepinines (**6**) with 30% hydrogen peroxide in glacial acetic acid at boiling temperature gave de new sulfones **7**. The reactions are presented in scheme 2.

The new compounds, O-acyl-oximino-dibenzo[b,e]thiepinines (**6**) and their sulfones (**7**) are solid, crystallized, white or light yellow, soluble at room temperature in chloroform, acetone, benzene, toluene, xylene, dichloromethane, by heating in inferior alcohols, insoluble in water. The structure, molecular formula, molecular mass, melting



Scheme 1. Synthesis of 2-phenylthiomethylbenzoic acid (**3**), 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one (**4**) and 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (**5**)



Scheme 2. Synthesis of the new O-acyl-oximino-dibenzo[b,e]thiepinines (**6**) and their sulfones (**7**)

Compd	R	X	Molecular formula	Molecular mass	M.p. (°C)	Yield (%)	Rf
6a		S	C ₂₄ H ₂₁ NO ₂ S	387.49	126-128	75	0.87
6b		S	C ₂₅ H ₂₃ NO ₂ S	401.52	118-124	75	0.92
6c		S	C ₂₂ H ₁₆ ClNO ₂ S	393.88	139-141	62	0.90
6d		S	C ₂₂ H ₁₆ ClNO ₂ S	393.88	192-197	80	0.91
7a		SO ₂	C ₂₄ H ₂₁ NO ₄ S	419.49	195-200	62.5	0.77
7b		SO ₂	C ₂₅ H ₂₃ NO ₄ S	433.52	191-195	57	0.74
7c		SO ₂	C ₂₂ H ₁₆ ClNO ₄ S	425.88	219-221	51	0.71
7d		SO ₂	C ₂₂ H ₁₆ ClNO ₄ S	425.88	225-227	53	0.68

Table 1
CHARACTERIZATION DATA OF THE NEW
COMPOUNDS **6a-d** AND **7a-d**

Compd	R	X	Elemental analysis (calc/found)				
			C	H	N	S	
6a	4-C ₃ H ₇ -C ₆ H ₄	S	74.39/75.33	5.46/5.42	3.61/3.59	8.27/8.20	
6b	4-C ₄ H ₉ -C ₆ H ₄	S	74.78/74.81	5.77/5.74	3.49/3.51	7.98/8.02	
6c	3-CH ₂ Cl-C ₆ H ₄	S	67.09/67.11	4.09/4.10	3.56/3.60	8.14/8.09	
6d	4-CH ₂ Cl-C ₆ H ₄	S	67.09/67.12	4.09/4.00	3.56/3.59	8.14/8.18	
7a	4-C ₃ H ₇ -C ₆ H ₄	SO ₂	68.72/68.73	5.05/5.06	3.34/3.36	7.64/7.58	
7b	4-C ₄ H ₉ -C ₆ H ₄	SO ₂	69.26/70.00	5.35/5.34	3.23/3.25	7.40/7.49	
7c	3-CH ₂ Cl-C ₆ H ₄	SO ₂	62.05/62.06	3.79/3.80	3.29/3.27	7.53/7.49	
7d	4-CH ₂ Cl-C ₆ H ₄	SO ₂	62.05/62.09	3.79/3.83	3.29/3.24	7.53/7.58	

Table 2
ELEMENTAL ANALYSIS RESULTS FOR THE NEW
COMPOUNDS

point, yield and retention factor value (Rf) are presented in table 1.

Structural elucidation of the new compounds was performed by spectral analysis (¹H-NMR, ¹³C-NMR, IR) and elemental analysis. All elemental analyses results were within ±0.4% of the theoretical values, and the IR, ¹H-NMR and ¹³C-NMR spectra show all the expected signals. The results of the elemental analysis are presented in table 2.

Conclusions

In order to obtain compounds with improved pharmacological activity, were synthesized new O-acyloximino-dibenzo[b,e]thiepines and their corresponding sulfones. All the original products have been characterized by their physical properties (melting point, solubility), and the structures were confirmed by elemental analysis and

IR, ¹H-NMR, ¹³C-NMR spectral studies. The new compounds, dibenzo[b,e]thiepin-11(6H)-one O-benzoyloximes and their sulfones, will be further investigated for antimicrobial activity and as antidepressant agents.

Acknowledgements: The authors acknowledge support for this work from the Romanian Ministry of Education, Research and Youth through project PN2 41-055/2007.

References

- 1.***, Martidale, The Complete Drug Reference, 35th ed, Pharmaceutical Press, London, Chicago, 2007, p. 349
- 2.NEGWER M, SCHARNOW H.G., Organic chemical drugs and their synonyms, Ed. Wiley-WCH, Weinheim, 2001
- 3.HIRATE K, UCHIDA A, OGAWA Y, ARAI T, YODA K., Neurosci Res., **54**, no.4, 2006, p.288

4. NISA, S.; BLOKPOEL, M.C.J.; ROBERTSON B.D.; TYNDAL, J.D.A.; LUN, S.; BISHAI, W.R.; O'TOOLE R., J. *Antimicrob. Chemother.*, **65**, no.11, 2010, p. 2347
5. PEREZ-PINEIRO, R.; BURGOS, A.; JONES, D.C.; ANDREW, L.C.; RODRIGUEZ, H.; SUAREZ, M.; FAIRLAMB, A.H.; WISHART, D.S., J. *Med. Chem.*, **52**, no.6, 2009, p. 1670
6. TAKEUCHI, H.; LIU, J.G.; HOSOKI K.; KARASAWA, T., *Cardiovasc. Drug. Rev.*, **12**, no.3, 1994, p. 254
7. CHIARELLO, J.F.; WOOD, W.W.; CULTBERTSON, D.; SMITH, D. W.; SPERRY, R.C.; SCHMIDT, T.; STEINER, G.; KORDES, M.; VON DEYN, W.; GOTZ, N.; HOFMANN, M.; BARNES, K.; TAKASUGI, J.; TREACY, M.F.; OLOUMI-SADEGHI, H.; DIEHL, R., WO Patent 039255, May 15, 2003
8. STECOZA C. E., CĂPROIU M.T., DRĂGHICI C., ILIE C. CHIRITA I.C., *Rev. Chim. (Bucharest)*, **59**, no.12, 2008, p. 1348
9. STECOZA C. E., BALOTESCU CHIFIRIUC C., ISRAIL A.M., *Farmacia* **56**, no.5, 2008, p. 491
10. STECOZA C. E., CĂPROIU M.T., DRĂGHICI C., CHIFIRIUC M. C., DRĂCEA O. N., *Rev. Chim. (Bucharest)*, **60**, no. 2, 2009, p. 137
11. ILIE C., STECOZA C. E., CĂPROIU M.T., HAU R., GUTA R., NANAU ANDREESCU D., *Rev. Chim. (Bucharest)*, **60**, no.6, 2009, p. 588
12. STECOZA C. E., ILIE C., CĂPROIU M.T., DRĂGHICI C., *Rev. Chim. (Bucharest)*, **62**, no. 6, 2011, p. 610
13. STECOZA C.E., RĂDULESCU F.S., MIRON D.S., NIȚULESCU G.M., CIOLAN D., MÁJEKOVÁ M., *Farmacia*, **59**, no. 6, 2011, p. 820
14. STECOZA C.E., MÁJEKOVÁ M., MÁJEK P., CĂPROIU M.T., MĂRUȚESCU L., *Curr. Org. Chem.*, **17**, no. 2, 2013, p. 113-124
15. TARKO L, STECOZA C.E., ILIE C., CHIFIRIUC M.C., *Rev. Chim. (Bucharest)*, **60**, no. 5, 2009, p. 476

Manuscript received: 11.02.2013