

Synthesis and Characterization of New Dibenzo[b, e]Thiepine Derivatives. I

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The aim of the present paper was the synthesis and chemical characterization of some original compounds with dibenzo[b,e]thiepine structure. The synthesis of the new compounds was performed in several stages. Thus, by reaction of phthalide with thiophenol potassium salt, we obtained the 2-phenylthiomethyl-benzoic acid. The acid was cyclized with polyphosphoric acid to the desired 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one, converted afterwards to the corresponding oxime and subsequently to the O-acyloximino-dibenzo[b,e]thiepins by acylation with various substituted benzoic acid chlorides. The oxidation of O-acyloximino-dibenzo[b,e]thiepins with hydrogen peroxide afforded the corresponding sulfones. The new compounds, four O-acyl-oximino-dibenzo[b,e]thiepins, and four O-acyl-oximino-dibenzo[b,e]thiepin-5,5-dioxides, have been characterized by their physical constants (melting point, solubility) and their structures and purity were confirmed by elemental analysis, and spectral analysis (IR, ¹H-NMR, ¹³C-NMR).

Keywords: *dibenzo[b,e]thiepine, sulfones, NMR spectroscopy*

The tricycle dibenzo[b,e]thiepine system constitutes the fundamental structure for many drugs with varied biological activities: antidepressant, antihistaminic, anti-inflammatory etc [1]. The most important is *Dosulepine*, used in the treatment of major depressive disorder and also as adjuvant in the management of pain.

In several previous communications [2-9] we reported the synthesis and characterization of some new dibenzo[b,e]thiepins derivatives. The pharmacological tests performed for some of these new substances emphasize antidepressant, psychosedative and analgesic properties [10]. These positive results obtained in our investigations, led us to synthesize new compounds with dibenzo[b,e]thiepine structure. Furthermore the new compounds will be investigated for the antimicrobial activity.

Experimental part

All the melting points were recorded on an Electrothermal 9100 apparatus and are uncorrected.

The NMR spectra were registered with a Varian Gemini 300BB apparatus, at 300 MHz for ¹H-NMR and 75 MHz for ¹³C-NMR and an Unity-Inova 400 operating at 400 MHz in proton and 100 MHz in carbon. Dimethylsulfoxide-*d*₆ and chloroform-*d*₁ were used as solvents and tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in δ ppm values and the coupling constants are in Hertz. The spectra are recorded at room temperature in usual conditions and sometimes Apt and Cosy sequences are used.

The IR spectra were registered in potassium bromide pellets with a Fourier transform infrared spectrophotometer FTS-135 BIORAD and by ATR technique with an FT-IR Bruker instrument Vertex 70.

The elemental analysis was performed on a Perkin-Elmer 2400 (series) II CHNS/O Analyser.

The synthesis of 2-phenylthiomethyl-benzoic acid (4)

In a round-bottom flask equipped with a water removing device, 11g (0.1 mol) thiophenol (Mol wt 110.18) were dissolved in 60 mL xylene and subsequently 5.61 g (0.1 mol) potassium hydroxide (Mol wt 56.11) were added. The reaction mixture was refluxed until 2 mL of water were removed by azeotropic distillation, while potassium thiophenolate precipitated; 13.41 g (0.1 mol) phthalide (Mol wt 134.14) were added and the mixture was refluxed for 3 h. After cooling, the solidified mixture was dissolved in 10% potassium hydroxide and diluted with 100 mL water. The aqueous phase was separated and acidulated (pH 3) with 1M hydrochloric acid solution, when 2-phenylthiomethyl-benzoic acid precipitated. The crude product was filtered and recrystallized from ethanol: water (3:1) (m.p. 109.2- 112.1°C; yield 71.5%).

The synthesis of 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one (5)

140 g polyphosphoric acid (PPA) was heated to 80°C, 24.43 g (0.1 mol) 2-phenylthiomethyl-benzoic acid (Mol wt 244.3) were slowly added, under stirring, and afterwards the mixture was heated for 1 hour to 100- 110°C. After partial cooling (80°C) the reaction mixture was poured into an ice-water mixture and stirred. The product was extracted with dichloromethane for three times. The combined organic layers were washed with 5% sodium hydroxide solution and water and afterwards dried over anhydrous calcium chloride. Then, the solvent was removed *in vacuo* and the crude product obtained was recrystallized from *i*-propanol (m.p. 86.4- 88.1°C; yield 64.5%).

The synthesis of 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (6)

11.3 g (0.05 mol) of 6,11-Dihydrodibenzo[b,e]thiepin-11(6H)-one (Mol wt 226.29) and 10.5 g (0.15 mol) of hydroxylamine hydrochloride (Mol wt 69.49) were boiled

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under reflux in 100 mL of pyridine for 24 h. The pyridine was subsequently distilled off in a vacuum, the residue was triturated with water, suction-filtered, dried and recrystallized from *i*-propanol (m.p. 225.3-226.1°C; yield 78.3%).

General procedure for synthesis of O-acyl-oximino-dibenzo[b,e]thiopyns (7)

To a solution of 2.41 g (10 mmol) 11-hydroximino-6,11-dihydrodibenzo[b,e]thiopyne (Mol wt 241.30) in anhydrous benzene was added drop wise a solution of 10 mmol appropriated acylchloride in 10 mL anhydrous benzene and 0.79 g (0.8 mL; 10 mmol) dry pyridine (Mol wt 79.098; $d^{25}=0.978$). The reaction mixture was refluxed for 2 h, afterwards was cooled, the precipitate was filtered and the solvent was removed under reduced pressure. The resulting crude product was recrystallized from an appropriate solvent.

General procedure for synthesis of sulfones (8)

To a solution of 10 mmol **7a-d** in glacial acetic acid were added drop wise 2 mL 30% hydrogen peroxide, the mixture was heated for 3 h and left overnight at room temperature. The reaction mixture was diluted with water and the compound was extracted with chloroform. The organic layer was dried over calcium chloride and the solvent was removed under reduced pressure. The resulting crude product was recrystallized from an appropriate solvent.

Analytical and spectral data of the new compounds, O-acyl-oximino-dibenzo[b,e]thiopyns (**7**), and their corresponding 5,5-dioxides (**8**), are given below.

11-[O-(2-Fluorobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyne (7a)

$C_{21}H_{14}FNO_2S$ (363.41); Colorless crystals, m.p. 134.8-137.2°C (*i*-propanol); yield 78.5%

Elemental analysis. Calcd. C: 69.41; H: 3.88; N: 3.85; S: 8.82. Found: C: 69.22; H: 3.98; N: 3.71; S: 8.69.

FT-IR (ATR in solid, ν cm^{-1}): 3048vw; 3020vw; 2966vw; 1745vs; 1606m; 1483m; 1280s; 1225s; 974m; 753m.

1H -NMR ($CDCl_3$, δ ppm, J Hz): 7.76 (dd, 1H, H-1, 1.5, 8.3); 7.68 (td, 1H, H-17, 7.8, 1.9); 6.98 ÷ 7.45 (m, 10H, H-arom); 4.68 (bs, 1H, H-6A); 3.51 (bs, 1H, H-6B).

^{13}C -NMR ($CDCl_3$, δ ppm): 167.48 (C-12); 161.20 (d, C-14, $J(^{19}F-^{13}C)=261.2$ Hz); 160.98 (C-11); 137.02 (Cq); 134.90 (Cq); 134.78 (Cq); 133.38 (Cq); 132.16 (CH); 131.70 (CH); 130.54 (CH); 130.27 (CH); 127.98 (CH); 127.33 (CH); 127.28 (CH); 127.18 (CH); 126.26 (CH); 124.96 (CH); 124.78 (Cq); 124.00 (d, C-17, $J(^{19}F-^{13}C)=3.9$ Hz); 116.91 (d, C-15, $J(^{19}F-^{13}C)=22.2$ Hz); 33.30 (C-6).

11-[O-(4-Fluorobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyne (7b)

$C_{21}H_{14}FNO_2S$ (363.41); Colorless crystals, m.p. 163.4-164.9°C (*i*-propanol); yield 81.4%

Elemental analysis. Calcd. C: 69.41; H: 3.88; N: 3.85; S: 8.82. Found: C: 69.54; H: 3.68; N: 3.98; S: 8.61.

FT-IR (ATR in solid, ν cm^{-1}): 3109w; 3069vw; 2978vw; 1742vs; 1602m; 1248vs; 1049w; 975m; 751s.

1H -NMR ($CDCl_3$, δ ppm, J Hz): 7.89 (dd, 1H, H-1, 1.2, 7.8); 7.75 (dd, 2H, H-14, H-18, 5.5, 9.0); 7.15 ÷ 7.48 (m, 7H, H-arom); 7.03 (t, 2H, H-15, H-17, 9.0); 4.64 (bs, 1H, H-6A); 3.58 (bs, 1H, H-6B).

^{13}C -NMR ($CDCl_3$, δ ppm): 167.32 (C-12); 1266.28 (d, C-16, $J(^{19}F-^{13}C)=258.3$ Hz); 162.69 (C-11); 137.10 (Cq); 135.20 (Cq); 133.43 (Cq); 131.62 (d, C-14, C-18, $J(^{19}F-^{13}C)=18.6$ Hz); 131.86 (CH); 130.75 (CH); 130.55 (CH); 128.83 (Cq); 128.15 (CH); 127.30 (CH); 127.18 (CH); 126.72 (CH);

125.18 (CH); 124.90 (Cq); 115.80 (d, C-15, C-17, $J(^{19}F-^{13}C)=23.7$ Hz); 33.47 (C-6).

11-[O-(2-Nitrobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyne (7c)

$C_{21}H_{14}N_2O_4S$ (390.42); Yellow crystals, m.p. 177.2-178.8°C (*i*-propanol); yield 80.3%

Elemental analysis. Calcd. C: 64.61; H: 3.61; N: 7.18; S: 8.21. Found: C: 64.40; H: 3.86; N: 7.26; S: 8.01.

FT-IR (ATR in solid, ν cm^{-1}): 3064vw; 2963w; 2910vw; 1751vs; 1605w; 1527vs; 1356s; 1251s; 1058m; 976s; 722s.

1H -NMR ($CDCl_3$, δ ppm, J Hz): 7.89 (dd, 1H, H-15, 1.0, 8.7); 7.75 (dd, 1H, H-1, 1.7, 7.8); 7.56 ÷ 7.65 (m, 2H, H-arom); 7.10 ÷ 7.40 (m, 7H, H-arom); 4.63 (bs, 1H, H-6A); 3.58 (bs, 1H, H-6B).

^{13}C -NMR ($CDCl_3$, δ ppm): 168.02 (C-12); 163.65 (C-11); 149.07 (Cq); 147.33 (Cq); 137.27 (Cq); 134.79 (Cq); 134.49 (CH); 132.07 (CH); 131.64 (CH); 130.81 (CH); 130.53 (CH); 130.32 (CH); 129.65 (Cq); 128.18 (CH); 127.62 (CH); 126.89 (CH); 126.54 (CH); 125.32 (Cq); 125.11 (CH); 124.25 (CH); 33.41 (C-6).

11-[O-(3-Nitrobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyne (7d)

$C_{21}H_{14}N_2O_4S$ (390.42); Yellow crystals, m.p. 165.5-167.8°C (*i*-propanol); yield 81.2%

Elemental analysis. Calcd. C: 64.61; H: 3.61; N: 7.18; S: 8.21. Found: C: 64.83; H: 3.49; N: 7.30; S: 8.10.

FT-IR (ATR in solid, ν cm^{-1}): 3087w; 2962vw; 2873vw; 1747vs; 1612w; 1532vs; 1349vs; 1238vs; 1067s; 713m.

1H -NMR ($CDCl_3$, δ ppm, J Hz): 8.40 (t, 1H, H-14, 2.2); 8.29 (ddd, 1H, H-16, 1.1, 2.2, 7.9); 8.09 (dt, 1H, H-18, 1.1, 7.9); 7.75 (dd, 1H, H-1, 1.6, 7.8); 7.50 (t, 1H, H-17, 7.9); 7.18 ÷ 7.41 (m, 7H, H-arom); 4.58 (bs, 1H, H-6A); 3.50 (bs, 1H, H-6B).

^{13}C -NMR ($CDCl_3$, δ ppm): 168.23 (C-12); 161.36 (C-11); 148.21 (C-15); 137.26 (Cq); 135.23 (CH); 135.12 (Cq); 132.88 (Cq); 131.67 (Cq); 130.80 (CH); 130.68 (CH); 130.37 (Cq); 129.80 (CH); 128.14 (CH); 127.69 (CH); 127.37 (CH); 126.96 (CH); 126.71 (CH); 125.07 (CH); 124.53 (CH); 33.37 (C-6).

11-[O-(2-Fluorobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyn-5,5-dioxide (8a)

$C_{21}H_{14}FNO_4S$ (395.41); Colorless crystals, m.p. 189.8-191.3°C (ethanol); yield 85.6%

Elemental analysis. Calcd. C: 63.79; H: 3.57; N: 3.54; S: 8.11. Found: C: 63.94; H: 3.40; N: 3.72; S: 8.02.

FT-IR (ATR in solid, ν cm^{-1}): 3075vw; 2965vw; 2904vw; 1747vs; 1610m; 1306s; 1232vs; 1156s; 1039s; 980s; 747s.

1H -NMR ($CDCl_3$, δ ppm, J Hz): 8.09 (dd, 1H, H-4, 1.4, 8.1); 7.91 (dd, 1H, H-1, 1.9, 7.2); 7.40 ÷ 7.70 (m, 8H, H-arom); 7.10 (td, 1H, H-9, 7.3, 1.1); 7.06 (ddd, 1H, H-15, 0.8, 8.5, 10.1); 5.05 (bs, 1H, H-6A); 4.40 (bs, 1H, H-6B).

^{13}C -NMR ($CDCl_3$, δ ppm): 164.64 (C-12); 162.45 (d, C-14, $J(^{19}F-^{13}C)=261.0$ Hz); 161.55 (C-11); 141.90 (Cq); 138.32 (Cq); 135.58 (CH); 134.25 (Cq); 132.85 (CH); 132.41 (CH); 131.32 (CH); 131.04 (CH); 130.00 (d, C-16, $J(^{19}F-^{13}C)=2.9$ Hz); 129.13 (CH); 128.25 (CH); 127.28 (CH); 126.25 (CH); 124.40 (d, C-18, $J(^{19}F-^{13}C)=3.7$ Hz); 123.98 (Cq); 117.26 (d, C-15, $J(^{19}F-^{13}C)=22.0$ Hz); 116.58 (d, C-13, $J(^{19}F-^{13}C)=10.6$ Hz); 59.19 (C-6^m); 58.55 (C-6^m).

11-[O-(4-Fluorobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiopyn-5,5-dioxide (8b)

$C_{21}H_{14}FNO_4S$ (395.41); Colorless crystals, m.p. 270.0-271.8°C (glacial acetic acid); yield 87.3%

Elemental analysis. Calcd. C: 63.79; H: 3.57; N: 3.54; S: 8.11. Found: C: 63.68; H: 3.69; N: 3.61; S: 7.95.

FT-IR(ATR in solid, ν cm^{-1}): 3081vw; 2963w; 2921vw; 1752vs; 1600m; 1329s; 1224vs; 1124vs; 1054s; 748m; 719m.

$^1\text{H-NMR}$ (dms -d_6 , δ ppm, J Hz): 8.00(dd, 1H, H-4, 2.2, 8.5); 7.72(dd, 2H, H-14, H-18, 5.2, 9.1); 7.52÷7.90(m, 8H, H-arom); 7.62(t, 2H, H-15, H-17, 9.1); 5.70(bs, 1H, H-6A); 5.00(bs, 1H, H-6B).

$^{13}\text{C-NMR}$ (dms -d_6 , δ ppm): 165.91(d, C-16, $J(^{19}\text{F-}^{13}\text{C})=251.8$ Hz); 163.57(C-12); 161.53(C-11); 141.70(Cq); 134.32(Cq); 133.14(CH); 132.72(CH); 132.15(d, C-14, C-18, $J(^{19}\text{F-}^{13}\text{C})=9.7$ Hz); 131.69(CH); 130.88(CH); 129.86(Cq); 129.56(CH); 128.77(CH); 127.90(CH); 125.82(CH); 124.93(Cq); 124.34(Cq); 116.28(d, C-15, C-17, $J(^{19}\text{F-}^{13}\text{C})=22.3$ Hz); 57.11(C-6).

11-[O-(2-Nitrobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiepin-5,5-dioxide (8c)

$\text{C}_{21}\text{H}_{14}\text{N}_2\text{O}_6\text{S}$ (422.42); Yellow crystals, m.p. 213.3-216.1°C (glacial acetic acid); yield 86.8%

Elemental analysis. Calcd. C: 59.71; H: 3.34; N: 6.63; S: 7.59. Found: C: 59.62; H: 3.51; N: 6.42; S: 7.75.

FT-IR(ATR in solid, ν cm^{-1}): 3069vw; 2962w; 2920vw; 1772vs; 1608w; 1528vs; 1305vs; 1232vs; 1027s; 975s; 780m; 731m.

$^1\text{H-NMR}$ (CDCl_3 , δ ppm, J Hz): 8.31(dd, 1H, H-15, 1.4, 7.9); 7.92(dd, 1H, H-4, 1.1, 8.2); 7.83(dd, 1H, H-1, 1.4, 7.7); 7.35÷7.70(m, 8H, H-arom); 7.20(dd, 1H, H-7, 1.3, 7.4); 5.09(bs, 1H, H-6A); 4.39(bs, 1H, H-6B).

$^{13}\text{C-NMR}$ (CDCl_3 , δ ppm): 165.26(C-12); 163.29(C-11); 148.06(Cq); 142.06(Cq); 134.49(Cq); 133.82(CH); 133.01(CH); 132.64(CH); 132.61(CH); 131.61(CH); 131.23(CH); 130.64(CH); 130.62(Cq); 129.82(CH); 129.57(CH); 127.71(CH); 126.09(Cq); 124.48(CH); 124.07(Cq); 58.74(C-6).

11-[O-(3-Nitrobenzoyl)-oximino]-6,11-dihydrodibenzo[b,e]thiepin-5,5-dioxide (8d)

$\text{C}_{21}\text{H}_{14}\text{N}_2\text{O}_6\text{S}$ (422.42); Yellow crystals, m.p. 191.2-193.4°C (ethanol); yield 88.7%

Elemental analysis. Calcd. C: 59.71; H: 3.34; N: 6.63; S: 7.59. Found: C: 59.89; H: 3.20; N: 6.89; S: 7.74

FT-IR(ATR in solid, ν cm^{-1}): 3085w; 2963vw; 2920vw; 1752vs; 1613w; 1525s; 1351vs; 1234s; 1100s; 712s.

$^1\text{H-NMR}$ (CDCl_3 , δ ppm, J Hz): 8.50(t, 1H, H-14, 2.1); 8.42(ddd, 1H, H-18, 1.1, 2.1, 8.1); 8.16(dd, 1H, H-4, 1.1, 7.8); 8.00(ddd, 1H, H-16, 1.1, 2.2, 8.1); 7.96(dd, 1H, H-1, 1.5, 7.4); 7.15÷7.91(m, 7H, H-arom); 5.15(bs, 1H, H-6A); 4.20(bs, 1H, H-6B).

$^{13}\text{C-NMR}$ (CDCl_3 , δ ppm): 165.61(C-12); 161.23(C-11); 148.45(Cq); 142.15(Cq); 135.65(CH); 134.52(Cq); 133.31(CH); 132.89(CH); 131.96(CH); 131.67(CH); 130.28(CH); 129.70(Cq); 129.63(Cq); 129.46(CH); 128.39(CH); 127.95(CH); 127.83(CH); 126.56(CH); 124.86(CH); 124.42(Cq); 58.74(C-6).

Results and discussions

The synthesis of new compounds was performed in several stages.

In the first stage, 2-phenylthiomethyl-benzoic acid (**4**) was synthesized by reacting of phthalide (**1**) with potassium salt of thiophenol (**2**), in xylene. The resulted potassium salt of 2-phenylthiomethyl-benzoic acid (**3**) has a good solubility in an aqueous solution of 10% sodium hydroxide and it can be separated from xylene. The acid (**4**) is precipitated using a mineral acid solution (hydrochloric acid).

The potassium salt of thiophenol (**2**) was obtained from thiophenol and potassium hydroxide in xylene, the resulting water being removed by azeotropic distillation.

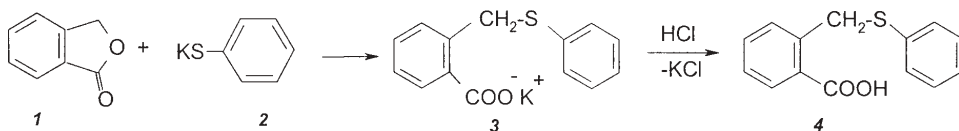
The reactions are presented in scheme 1.

6,11-Dihydrodibenzo[b,e]thiepin-11(6H)-one (**5**) was synthesized by cyclodehydration of 2-phenylthiomethyl-benzoic acid (**4**) in the presence of polyphosphoric acid (PPA). The reaction is presented in scheme 2.

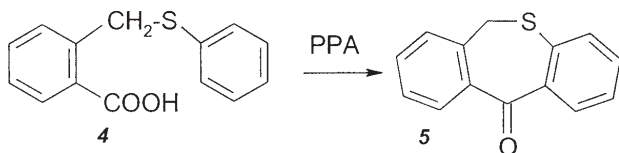
The desired ketone can be also prepared using various agents for cyclodehydration (e.g. phosphorus pentoxide, concentrated sulphuric acid, zinc chloride) or by a Friedel-Crafts cyclization of the 2-phenylthiomethyl-benzoic acid chloride [11]. The acid chloride result by refluxing 2-phenylthiomethyl-benzoic acid with thionyl chloride in excess.

The ketone (**5**) was converted to the corresponding oxime (**6**) by treatment with hydroxylamine hydrochloride in the presence of pyridine. The new compounds (**7**) were prepared by acylation of the 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine (**6**) with various substituted benzoic acid chlorides, in dry benzene or toluene, in the presence of anhydrous pyridine as a proton acceptor. The reactions are presented in scheme 3.

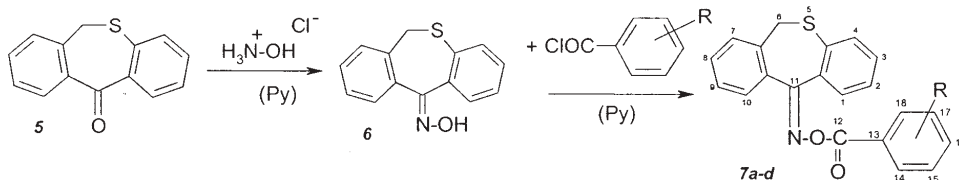
The oxidation of *O*-acyl-oximino-dibenzo[b,e]thiepins (**7**) with 30% hydrogen peroxide in glacial acetic acid at boiling temperature, gave the new sulfones (**8**). The reaction is presented in scheme 4. The literature presents [12-15] the oxidation of the tricycle dibenzo[b,e]thiepine system with hydrogen peroxide (30%) in the presence of acetic acid.



Scheme 1. The synthesis of 2-phenylthiomethyl-benzoic acid (**4**)

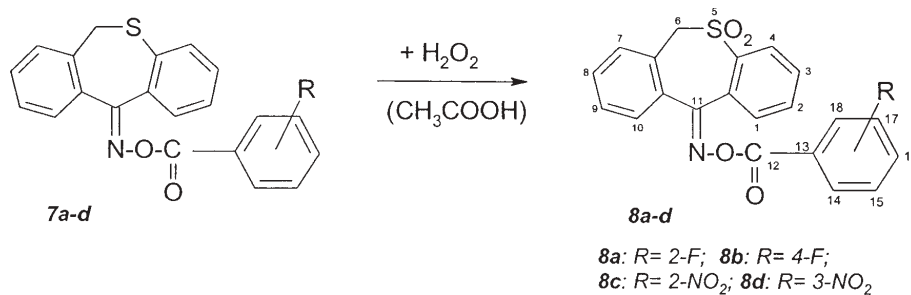


Scheme 2. The synthesis of 6,11-dihydrodibenzo[b,e]thiepin-11(6H)-one (**5**)



Scheme 3. The synthesis of the new *O*-acyl-oximino dibenzo[b,e]thiepins (**7**)

7a: R= 2-F; 7b: R= 4-F;
7c: R= 2-NO $_2$; 7d: R= 3-NO $_2$



Scheme 4. The synthesis of the new
O-acyl-oximino-dibenzo[b,e]thiepin-5,5-dioxides (**8**)

The new compounds are solid, crystallized, white or light yellow. *O*-acyl-oximino-dibenzo[b,e]thiepins (**7**) and sulfones (**8**) are soluble at room temperature in acetone, chloroform, benzene, toluene, xylene, dichloromethane, by heating in inferior alcohols, insoluble in water. The structures of these compounds were elucidated by FTIR, NMR spectroscopy and elemental analysis (all elemental analyses results were within $\pm 0.2\%$ of the theoretical values).

Spectral data

The IR, ¹H-NMR and ¹³C-NMR spectra show all the expected signals.

In the IR spectra the characteristic bands for new compounds are (cm⁻¹): νCH, 1360÷1430; ν CH, 2856÷2960; -O-C=O (ν C=O: 1740÷1765; ν C-O: 1180÷1215); ν C=N: 1592÷1602; aromatic rings (ν =C-H: 3020÷3065; ν C=C: 1555÷1612); νNO₂, sym 1340÷1360; ν NO₂, asym 1560÷1580. For compounds **8a-d**: ν SO₂, sym 1165÷1180, ν SO₂, asym 1375÷1385.

In ¹H-NMR spectra of the new *O*-acyl-oximino-dibenzo[b,e]thiepins (**7a-d**) the dibenzothiepine system is characterized by the methylene group from 6 position which gave two broad singlets at 3.50÷3.58 ppm and 4.58÷4.68 ppm. The *S*-oxidation to the corresponding dioxide has as direct effect the deshielding (approximately 1ppm) of the two protons of the methylenic group, which appear in sulfones **8a-d** in the range 4.20÷5.70 ppm. The same effect was observed for the H-4 protons which appear as doublet of doublets in the range 7.92÷8.16.

The signals corresponding to the protons H1-H4, H7-H10, and H14-H18 appear in the range 6.98÷8.50 ppm. The individual attribution for some of these protons was performed using the connectivity H-H experiments (COSY).

In ¹³C-NMR spectra of the new *O*-acyl-oximino-dibenzo[b,e]thiepins (**7a-d**) the methylene group (C6) is characterized by a signal at 33.3÷33.4 ppm. The *S*-oxidation to the corresponding dioxide has as direct effect a strongly deshielding (approximately 25 ppm) of the two protons of the methylenic group, which appear in sulfones **8a-d** in the range 57.1÷59.1 ppm.

The signal corresponding to the C12 atom appears in the range 164.6÷168.2 and the signal of C11 appears in the range 161.0÷163.6 ppm. Some carbon attributions outcome from two-dimensional heteronuclear correlation experiments (COSY ¹H-¹³C).

Conclusions

In order to obtain compounds with potential pharmacological action, we continue our research

concerning the synthesis in the dibenzo[b,e]thiepine series.

We have synthesized eight new dibenzo[b,e]thiepine derivatives, four *O*-acyl-oximino-dibenzo[b,e]thiepins, and their corresponding 5,5-dioxides. The original compounds were prepared by acylation of the 11-hydroximino-6,11-dihydrodibenzo[b,e]thiepine with various substituted benzoic acid chlorides and oxidation of S atom to the corresponding dioxide.

All the compounds were characterized by their main physical properties. The structures were confirmed by spectral analysis (¹H-NMR, ¹³C-NMR, FTIR) and elemental analysis. The new compounds will be further investigated for their biological activity. The pharmacological preliminary investigations evidenced promising results.

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