THE SYNTHESIS OF SOME NEW ACYL-OXIMINES COMPOUNDS WITH POTENTIAL PHARMACOLOGICAL ACTIVITY

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Abstract

In our search of bioactive molecules we synthesized some new substances with heterocyclic structure which might become new compounds with pharmacological properties similar with the tricyclic antidepressants. These new substances are O-acyl-oximine derivatives with 10,11-dihydro-5H-dibenzo[a,d]cycloheptadienic structure. The structures of these new compounds were confirmed by elemental analysis, infrared and Nuclear magnetic resonance (NMR) spectra.

Rezumat

În urma cercetărilor noastre asupra moleculelor biologic active am sintetizat noi compuși din clasa heterociclilor cu potențială acțiune farmacologică similară antidepresivelor triciclice. Acești noi derivați sunt compuși din clasa O-acil-oximinelor cu structură 10,11-dihidro-5H-dibenzo[a,d]-cicloheptadienică. Structurile noilor compuși au fost confirmate prin analiză elementală, spectre în infraroșu și spectre de rezonanță magnetică nucleară.

Keywords: oximes, oximines, acylation, dibenzocycloheptadienes, 5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene.

Introduction

Several medicinal chemistry and pharmacological experimental research studies revealed the therapeutic importance of dibenzo-cycloheptadiene derivatives such as amitriptyline [1,10], nortriptyline [11], noxiptyline [6] or doxepine [8]. These substances are all used for clinical purpose due to their antidepressant effect [3]. As well as reducing depressive symptoms, these types of tricyclic derivatives also ease migraines, tension headaches, anxiety, attacks and some schizophrenic symptoms. They are also known to reduce aggression and violent behavior and they have a positive influence on eating disorders [15].

Some of these tricyclic antidepressants are used for attention deficit hyperactivity disorders (ADHD) [18], bipolar disorders, insomnia, in the treatment of nocturnal *enuresis* (bedwetting) in children and as a preventive treatment for patients with recurring biliary dyskinesia (sphincter of Oddi dysfunction) [17, 2]. Recent studies have revealed that in functional gastrointestinal disorders including functional dyspepsia and irritable bowel syndrome, there might be no small extent of contributions of psychosomatic factors. As a therapy for irritable bowel syndrome, beside famotidine in the first-step therapy, the effect of antidepressants has been assessed as the second-step therapy [14]. Researchers have also shown that some tricyclic antidepressants like amitriptyline can reduce pain in peripheral neuropathy caused by cancer chemotherapy [20]. This therapeutic effect is similar to the effect produced by gabapentin or the combination between gabapentin and tramadol in the prophylaxis of paclitaxel-induced neuropathy [19].

These tricyclic antidepressants block the reuptake of norepinephrine and serotonin and in the same time they block the sodium channels, possibly accounting in part for their analgesic action [9]. Recent studies show pro-inflammatory cytokine processes taking place during clinical depression, maniac and bipolar disorders and it is possible that symptoms of these conditions to be attenuated by the pharmacological effect of antidepressants on the immune system [13, 4].

In order to find new bioactive molecules related to these tricyclic compounds we decided to synthesis some new O-acyl-oximine derivatives having a 10,11-dihydro-5H-dibenzo[a,d]cycloheptadiene structure with potential antidepressant, analgesic or anti-inflammatory effects.

Materials and Methods

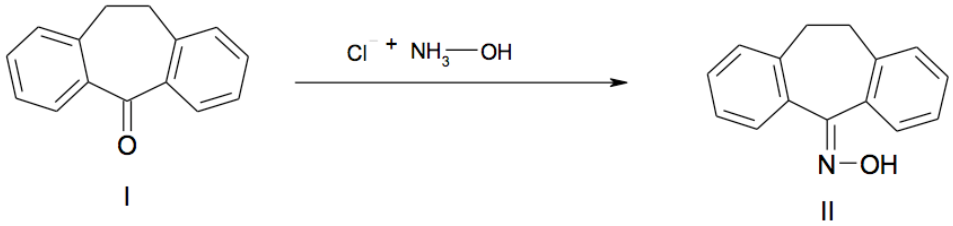
Melting points were measured in open capillary tubes on an Electrothermal 9100 apparatus and were uncorrected. Infrared spectra were recorded on a FT/IR – solid in ATR spectrometer. The NMR spectra were recorded on a Gemini 300BB instrument at room temperature, operating at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR. The chemical shifts were reported in δ units (ppm) relative to residual peak of the deuterated solvent ($CDCl_3$ and DMSO-d_6). Tetramethylsilane (TMS) was used as internal standard. Elemental analysis was performed on a Perkin Elmer CHNS/O Analyser Series II 2400 apparatus and the results were in agreement with the calculated values.

All starting materials and solvents were purchased from common commercial suppliers and were used without purification unless otherwise noted.

Intermediate synthesis

We decided to perform the acylation reaction of some dibenzocycloheptaatomic oximes with some acid chlorides, thinking that the combined molecular structures will improve the biological action of the future substances.

The intermediate compound was obtained using a condensation reaction. Dibenzosuberone (10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-one) (I) was condensed with hydroxylamine hydrochloride in order to obtain 5 - oximino - 10 , 11 - dihydro - 5H - dibenzo [a,d] cycloheptene (II). The condensation reaction is presented in Figure 1.



I II

Figure 1
The synthesis of the intermediate compound (II)

In a round-bottom flask equipped with condenser, stirrer and dropping funnel were added 65mL methanol, 25g dibenzosuberone (0.12mol) and 28.75g of sodium hydroxide (0.718mol). The mixture was stirred until the complete dissolution of the compounds. A solution of 12.5g hydroxylamine (0.179mol) in 70mL methanol was dropwise added. The mixture was refluxed for 5 hours. After the mixture returned to room temperature we added a solution of 62mL concentrated hydrochloride acid and 137.5mL water. During this process we had to keep the temperature under 25 ºC. We obtained a precipitate which was filtered, washed with water and then dried at 70 ^{o}C, resulting 24.5g of crude oxime. The compound was recrystallized from toluene (91.4% yield , m.p. 166-167 ^{o}C) [5].

Final compounds synthesis

The parameters of the acylation reaction were tested by obtaining some original O-acyl-oximines. These oximines were obtained by treating the tricyclic oximes with substituted aromatic acid chlorides in anhydrous benzene and in the presence of anhydrous pyridine as a proton fixator [7, 12, 16].

The new O-acyl-oximines were obtained in accordance with the following general procedure described in Figure 2:

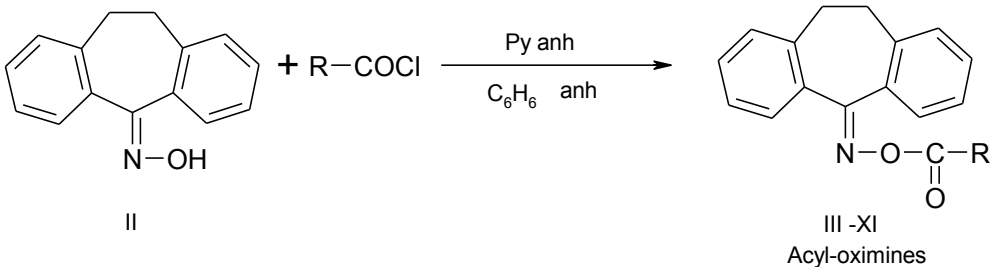
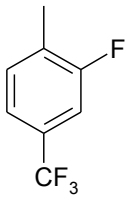
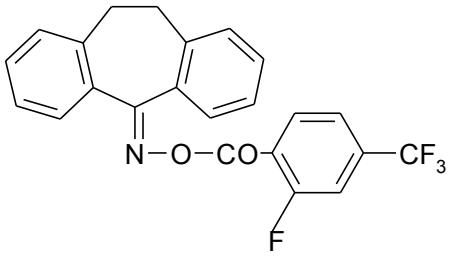
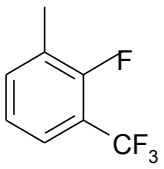
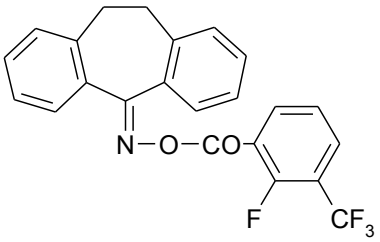
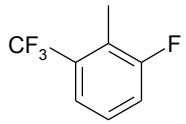
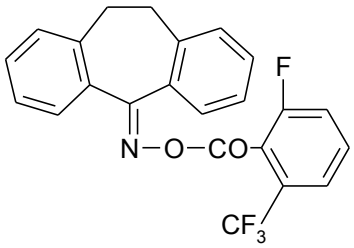
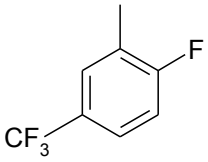
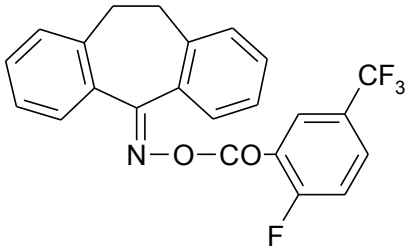
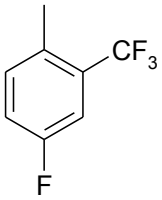
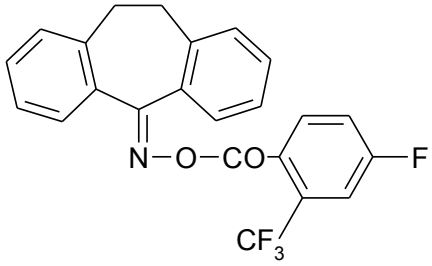
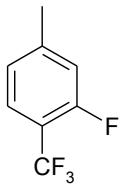
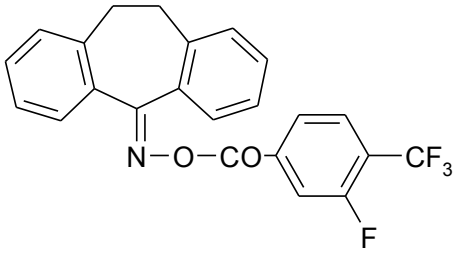


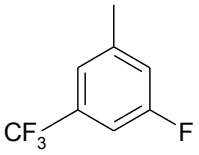
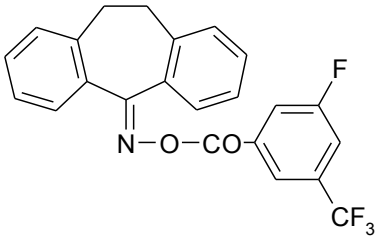
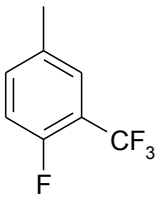
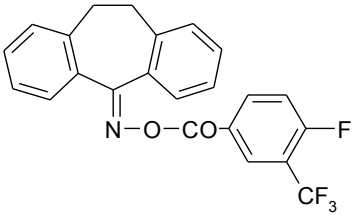
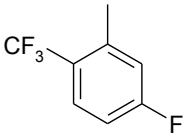
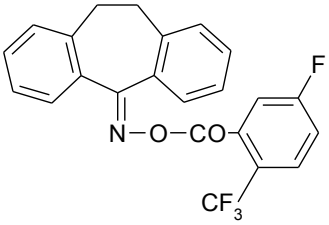
Figure 2
The synthesis of the new O-acyl-oximines (III-XI),
where Py anh – anhydrous pyridine, C_6H_6 anh – anhidrous benzene

The structures of these new compounds and their melting points are presented in Table I:

Table I
The new O-acyl-oximines

No	R	Final Compound	m.p. (°C)
III		 O-(2-Fluoro-4-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene	125-126
IV		 O-(2-Fluoro-3-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene	136-137

V		 O-(2-Fluoro-6-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene	146-147
VI		 O-(2-Fluoro-5-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene	122-123
VII		 O-(4-Fluoro-2-Trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]-cycloheptene	129-130
VIII		 O-(3-Fluoro-4-Trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene	127-128

IX		 O-(3-Fluoro-5-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene	86-87
X		 O-(4-Fluoro-3-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene	126-127
XI		 O-(5-Fluoro-2-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene	134-134

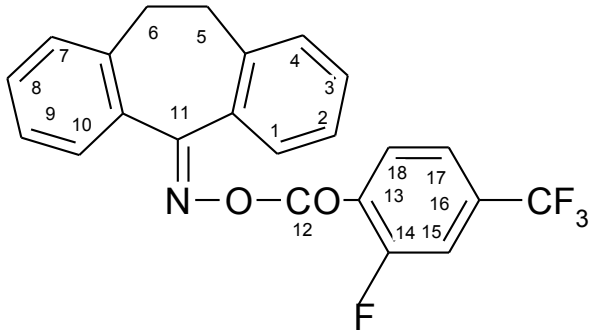
The 0.58g of 5-Oximino-10,11-dihydro-5H-dibenzo[a,d]cyclo heptene (0.0026mol) were dissolved in 15mL anhydrous benzene. There were gradually added 0.0026mol of each coresponding acid chlorides in 15mL anhydrous benzene and 0.21mL anhydrous pyridine (0.0026mol). A white precipitate (pyridinium hydrochloride) immediatelly appeared. The reaction mixture was refluxed for 3 hours and then it was filtered. The organic phase was evaporated to dryness at room temperature to give the final crude compound. The new acyl-oximines were recrystallized from isopropanol.

Results and Discussion

Following the acylation reaction between 5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene and the different carboxylic acid chlorides, we obtained nine new acyl-oximines. We used anhydrous reaction conditions

and anhydrous pyridine as a proton fixator. These new acyl-oximines are solid, crystalline, white compounds and they were recrystallized from isopropanol. Their structures were confirmed by elemental analysis, IR and NMR spectra. Further, spectral data for compounds III-XI are presented.

O-(-2-Fluoro-4-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%, Found: C 66.75%, H 3.52%, N 3.45%.

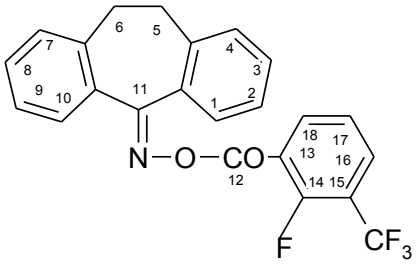
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 7.94(td, 1H, H-3, $^3J(H^{2,4}\text{-}H^3)$=7.4 Hz, $^4J(H^1\text{-}H^3)$=1.5 Hz); 7.78(dd, 1H, H-1, 1.5, 7.8); 7.43(bd, 1H, H-17, 7.5); 7.41(bd, 1H, H-10, 7.5); 7.38÷7.32(m, 3H, H-arom); 7.30÷7.24(m, 4H, H-arom); 7.17(dd, 1H, H-arom, 1.4, 7.6); 3.21(bs, 4H, H-5, H-6).

^{13}C-NMR($CDCl_3$, δ ppm, T=298K): 168.54(C-11); 161.32 (d, C-14, $J(F\text{-}C^{14})$=263.0 Hz); 160.86 (d, C-12, $^3J(F\text{-}C^{11})$=3.7 Hz); 139.43 (C-4a); 137.72 (C-7a); 136.31 (qd, C-16, $J(3F\text{-}C^{16})$=34.2 Hz, $J(F\text{-}C^{16})$=8.8 Hz); 133.78 (C-1a); 132.50 (C-10a); 122.66 (q, CF_3, J(3F-C)=275.3 Hz); 120.86 (d, C-13, $J(F\text{-}C^{13})$=16.3 Hz); 133.24 (C-18); 130.69 (CH); 130.51 (CH); 130.01 (CH); 129.48 (C-1); 128.22 (CH); 127.78 (d, C-18, $J(F\text{-}C^{18})$=16.3 Hz); 126.44 (CH); 125.81 (CH); 120.89 (q, C-17, $J(3F\text{-}C^{17})$=3.9 Hz); 114.63 (dq, C-15, $^2J(F\text{-}C^{15})$=25.5 Hz, $^3J(3F\text{-}C^{15})$=3.8 Hz); 33.44 (C-5 or C-6); 31.81(C-6 or C-5).

^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -63.87(F_3C); -105.28(F).

FT-IR (solid in ATR, ν cm^{-1}): 3063w; 2935w; 2857w; 1764vs; 1747vs; 1613w; 1595w; 1504w; 1427m; 1328s; 1310m; 1240m; 1214s; 1176m; 1125vs; 1092s; 1073s; 1051m; 982m; 919m; 875m; 856w; 842w; 783m; 789m; 747m; 694m; 646w.

O-(2-Fluoro-3-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.70%, H 3.72%, N 3.30%.

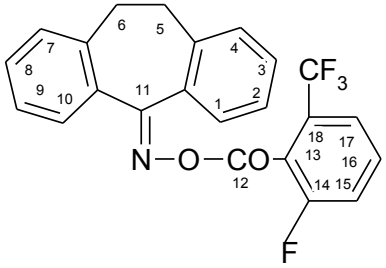
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 8.00(td, 1H, H-3, $^3J(H^{2,4}\text{-}H^3)$=7.2 Hz, $^4J(H^1\text{-}H^3)$=1.4 Hz); 7.78(dd, 1H, H-1, 1.4, 7.4); 7.76(dd, 1H, H-16, 1.4, 7.2); 7.42(bd, 1H, H-arom, 8.2); 7.40÷7.23(m, 6H, H-arom); 7.17(dd, 1H, H-arom, 1.1, 7.6); 3.21(bs, 4H, H-5, H-6).

^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.52(C-11); 160.57(d, C-12, $J(\text{F-C}^{11})$=3.2 Hz); 159.05(dq, C-14, $J(\text{F-C}^{14})$=272.7 Hz, d, $^3J(\text{F-C}^{14})$=2.2 Hz); 139.44Cq); 137.80 (Cq); 133.80(Cq); 132.67(Cq); 122.64(q, CF_3, J(3F-C)= 269.5 Hz); 119.88(qd, C-15, $J(\text{3F-C}^{15})$=33.1 Hz, $J(\text{F-C}^{15})$=12.9 Hz); 119.29(d, C-13, $J(\text{F-C}^{13})$=10.3 Hz); 136.08 (C-3); 131.69(dq, C-16, $^3J(\text{F-C}^{16})$=4.8 Hz, $^3J(\text{3F-C}^{16})$=2.3 Hz); 130.78(CH); 130.62 (CH); 130.16(CH); 129.63(CH); 128.34(CH); 127.97(d, CH-18, $J(\text{F-C}^{18})$=1.8 Hz); 126.54(CH); 125.93(CH); 123.93(d, C-17, $^3J(\text{F-C}^{17})$=4.9 Hz); 33.41(C-5 or C-6); 31.79(C-6 or C-5).

^{19}F-NMR($CDCl_3$, δ ppm, T=298K): -61.98(d, 3F, F_3C, $^4J(\text{3F-F}^{14})$=13.2 Hz); -109.83 (m, F^{14}, $^4J(\text{3F-F}^{14})$=13.2 Hz).

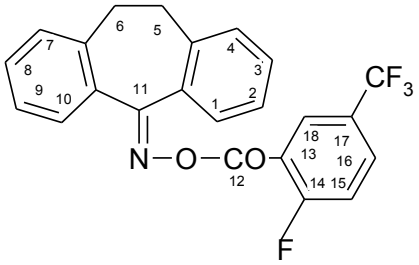
FT-IR (solid in ATR, ν cm^{-1}): 2994w; 2946w; 2884w; 2827w; 1757vs; 1620m; 1591w; 1471m; 1444w; 1424w; 1332s; 1249m; 1206s; 1173m; 1144s; 1122vs; 1089m; 1076m; 985w; 892m; 871w; 830w; 754m; 677w.

O-(6-Fluoro-2-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.68%, H 3.26%, N 3.35%.
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 7.73(dd, 1H, H-1, 1.4, 7.7); 7.52(tdq, 1H, H=16, $J(H^{17}\text{-}H^{16})=J(H^{15}\text{-}H^{16})$=7.7 Hz, $^4J(F^{14}\text{-}H^{16})$=5.3 Hz, $^5J(3F\text{-}H^{16})$=0.8 Hz); 7.46(bd, 1H, H-17, 7.7 Hz); 7.28(m, 1H, H-15, $J(F^{14}\text{-}H^{15})$=9.8 Hz); 7.37÷7.14(m, 7H, H-arom); 3.19(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 166.45(C-11); 161.35(d, C-12, $^3J(F^{14}\text{-}C^{12})$=2.1 Hz); 159.52(d, C-14, $J(F\text{-}C^{14})$=253.0 Hz); 139.29C-4a); 137.70(C-7a); 133.74(C-1a); 132.67(C-10a); 130.66(CH); 130.43(CH); 129.89(CH); 129.38(C-1); 128.14(CH); 127.53(CH); 126.40(CH); 125.92(CH); 131.88(d, C-16, $^3J(F^{14}\text{-}C^{16})$=7.8 Hz); 129.74 (q, C-18, $J(3F\text{-}C^{18})$=33.2 Hz); 122.05(qv, C-17, $^4J(F^{14}\text{-}C^{17})=^3J(3F\text{-}C^{17})$=3.6 Hz); 119.62(d, C-15, $J(F\text{-}C^{15})$=22.3 Hz); 119.57(d, C-13, $J(F^{14}\text{-}C^{13})$=22.1 Hz); 33.42(C-5 or C-6); 31.70(C-6 or C-5).
^{19}F-NMR($CDCl_3$, δ ppm, T=298K): -60.18(s, 3F, F_3C); -112.27(dd, 1F, F^{14}, *J*()=5.7 Hz, $J(H^{15}\text{-}F^{14})$=9.8 Hz).
FT-IR (solid in ATR, ν cm^{-1}): 3110w; 3068w; 2923w; 2881w; 2826w; 1765s; 1614m; 1483w; 1462m; 1317s; 1261s; 1237s; 1163m; 1123vs; 1089s; 1047m; 977m; 962m; 913m; 874w; 852m; 802w; 775m; 745m; 724w; 692w.

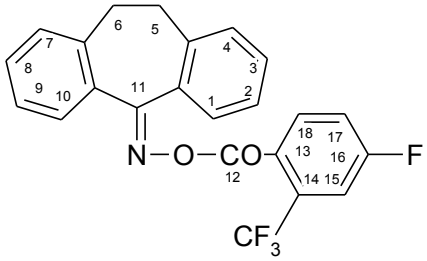
O-(2-Fluoro-5-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.92%, H 3.60%, N 3.42%.
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 8.07(dd, 1H, H-18, $J(H^{16}\text{-}H^{18})$= 2.2 Hz, $J(F^{14}\text{-}H^{18})$=6.3 Hz); 7.78(dd, 1H, H-1, 1.4, 7.6); 7.76(m, 1H, H-16); 7.22(t, 1H, H-15, $J(F^{14}\text{-}H^{15})=J(H^{16}\text{-}H^{15})$=9.3 Hz); 7.17(dd, 1H, H-4 or H-7, 1.2, 7.8); 7.45÷7.25(m, 6H, H-arom); 3.21(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.55(C-11); 163.49(d, C-14, $J(F^{14}\text{-}C^{14})$=267.0 Hz); 160.34(d, C-12, $J(F^{14}\text{-}C^{12})$=4.2 Hz); 139.34C-4a); 137.75(C-7a); 133.78(C-1a); 132.47(C-10a); 126.93(qd, C-17, $J(3F\text{-}C^{17})$= 33.8 Hz, $^4J(F^{14}\text{-}C^{17})$=3.8 Hz); 123.12(q, CF_3, $J(3F\text{-}C)$=273.2 Hz); 118.19(d, C-13, $J(F^{14}\text{-}C^{13})$=11.6 Hz); 131.70(dq, C-18, $J(F^{14}\text{-}C^{18})$=10.2 Hz, *J*(3F-

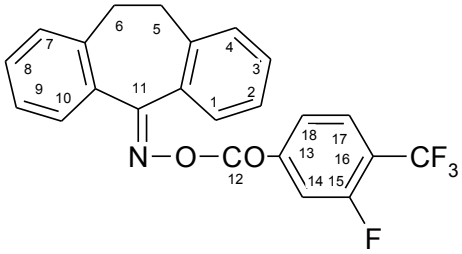
C^{18})=3.4 Hz); 130.69(CH); 130.52(CH); 130.02(CH); 129.97(dq, C-16, $^3J(F^{14}\text{-}C^{16})$=5.8 Hz, $^3J(3F\text{-}C^{16})$=2.1 Hz); 129.49(C-1); 128.26(CH); 127.73(CH); 126.43(CH); 125.80(CH); 118.00(d, C-15, $J(F^{14}\text{-}C^{15})$=23.5 Hz); 33.45(C-5 or C-6); 31.79(C-6 or C-5).
^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -59.87(s, 3F, F_3C); -102.33(m, 1F, F^{16}).
FT-IR (solid in ATR, ν cm^{-1}): 3077w; 2915w; 2881w; 2826w; 1750vs; 1622m; 1595m; 1503m; 1487w; 1455w; 1426w; 1328s; 1267vs; 1244m; 1219vs; 1163s; 1120vs; 1071s; 982m; 896m; 861m; 773m; 760m; 746m; 715w; 691w.

O-(4-Fluoro-2-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.75%, H 3.72%, N 3.30%.
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 7.79(dd, 1H, H-1, 1.6, 7.7); 7.65(dd, 1H, H-17, 5.5, 8.52); 7.41(dd, 1H, H-18, 2.5, 8.5); 7.38÷7.15(m, 8H, H-arom); 3.20(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.75(C-11); 163.72(d, C-16, $J(F^{16}\text{-}C^{16})$=255.3 Hz); 163.04(C-12); 139.21(C-4a); 137.76(C-7a); 133.92(C-1a); 132.44(C-10a); 131.79(qd, C-14, $J(3F\text{-}C^{14})$=34.1 Hz, $^3J(F^{16}\text{-}C^{14})$=7.4 Hz); 125.54(C-13); 122.20(qd, CF_3, *J*(3F-C)= 274.1 Hz, $^4J(F^{16}\text{-}CF_3)$=2.6 Hz); 133.14(d, C-18, $^3J(F^{16}\text{-}C^{18})$=8.4 Hz); 130.72(CH); 130.47(CH); 129.92(CH); 129.40(C-1); 128.20(CH); 127.17(CH); 126.40(CH); 125.83(CH); 118.71(d, C-17, $J(F^{16}\text{-}C^{17})$=21.3 Hz); 114.92(dq, C-15, $J(F^{16}\text{-}C^{15})$=26.5 Hz, $J(3F\text{-}C^{15})$=5.6 Hz); 33.42(C-5 or C-6); 31.62(C-6 or C-5).
^{19}F-NMR($CDCl_3$, δ ppm, T=298K): -60.30(bs, 3F, F_3C); -105.56(td, 1F, F^{16}, $J(F^{16}\text{-}H^{15})$=$J(F^{16}\text{-}H^{17})$=8.0 Hz, $J(F^{16}\text{-}H^{18})$=5.2 Hz).
FT-IR (solid in ATR, ν cm^{-1}): 3076w; 2927w; 1765vs; 1612m; 1596m; 1502w; 1486w; 1425m; 1426w; 1314m; 1292m; 1262m; 1236s; 1214s; 1163m; 1125s; 1079s; 1037s; 977m; 911m; 893m; 866m; 850m; 778m; 762m; 747m; 717w; 692w.

O-(3-Fluoro-4-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.72%, H 3.55%, N 3.42%.

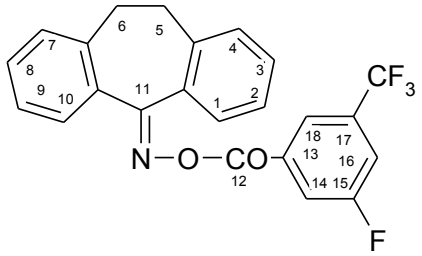
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 7.79(dd, 1H, H-1, 1.4, 7.6); 7.73(bd, 1H, H-18, 8.3); 7.66(bd, 1H, H-17, 8.3); 7.63(d, 1H, H-14, $^3J(H^{14}$-$F^{15})$=10.7 Hz); 7.44÷7.25(m, 6H, H-arom); 7.18(bd, 1H, H-4 or H-7, 7.4); 3.22(bs, 4H, H-5, H-6).

^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.59(C-11); 161.50(C-12); 159.49(d, C-15, $J(F^{15}$-$C^{15})$=258.0 Hz); 139.33(C-4a); 138.02(C-7a); 134.57(d, C-13, $^3J(F^{15}$-$C^{13})$=7.8 Hz); 133.72(C-1a); 132.33(C-10a); 122.53(qd, C-16, $J(3F$-$C^{16})$=33.4 Hz, $J(F^{15}$-$C^{16})$=12.8 Hz); 122.00(q, CF_3, *J*(3F-C)= 274.1 Hz); 130.74(C-4 or C-7); 130.61(CH); 130.23(CH); 129.47(C-1); 128.59(CH); 127.54(q, C-17, $J(3F$-$C^{17})$=4.6 Hz); 127.32(CH); 126.48(CH); 125.83(CH); 125.22(d, C-18, $J(C^{18}$-$F^{15})$=4.0 Hz); 118.07(d, C-14, $J(C^{14}$-$F^{15})$= 22.6 Hz); 33.44(C-5 or C-6); 31.81(C-6 or C-5).

^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -62.32(d, 3F, F_3C, $J(3F$-$0F^{15})$=12.6 Hz); -113.14(m, 1F, F^{15}).

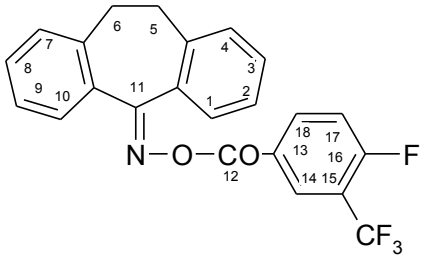
FT-IR (solid in ATR, ν cm^{-1}): 3055w; 2941w; 1762vs; 1630w; 1583m; 1417s; 1323vs; 1282m; 1251s; 1192vs; 1166m; 1141vs; 1123s; 1084vs; 1045m; 993w; 937w; 895w; 874w; 854w; 835w; 780m; 752m; 728w; 696w.

O-(5-Fluoro-3-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.78%, H 3.60%, N 3.45%.
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 7.88(bs, 1H, H-18); 7.79(dd, 1H, H-1, 1.4, 7.4); 7.74(dt, 1H, H-14, $J(F^{15}$-$H^{14})$=8.5 Hz); 7.49(bd, 1H, H-16, $J(F^{15}$-$H^{16})$=8.2 Hz); 7.45÷7.25(m, 6H, H-arom); 7.19(bd, 1H, H-4 or H-7, 7.4); 3.22(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.59(C-11); 162.28(d, C-15, $J(F^{15}$-$C^{15})$=251.0 Hz); 161.31(d, C-12, $J(F^{15}$-$C^{12})$=2.7 Hz); 139.39(C-4a); 138.00(C-7a); 133.66(C-1a); 132.97(qd, C-17, J(3F-C^{17})=34.4 Hz, $J(F^{15}$-$C^{17})$=7.4 Hz); 132.26(C=10a); 132.13(d, C-13, $J(F^{15}$-$C^{13})$=7.5 Hz); 122.66(q, CF_3, J(3F-C)= 271.8 Hz); 130.74(C-4 or C-7); 130.62(CH); 130.23(CH); 129.49(C-1); 128.59(CH); 127.39(CH); 126.47(CH); 125.78(CH); 122.40(qv, C-18, $J(F^{15}$-$C^{18})$= J(3F-C^{18})=7.3 Hz); 120.12(d, C-14, $J(F^{15}$-$C^{14})$=23.5 Hz); 117.43(dq, C-16, $J(F^{15}$-$C^{16})$=24.3 Hz, J(3F-C^{16})=3.3 Hz,); 33.47(C-5 or C-6); 31.82(C-6 or C-5).
^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -63.48(bs, 3F, F_3C); -109.42(t, 1F, F^{15}, $J(H^{14}$-$F^{15})$= $J(H^{16}$-$F^{15})$=8.3 Hz).
FT-IR (solid in ATR, ν cm^{-1}): 3087w; 2921w; 2861w; 1749vs; 1608w; 1451m; 1351vs; 1323w; 1252m; 1233s; 1182s; 1127vs; 1086m; 934s; 915m; 889m; 865m; 779w; 754m; 688w.

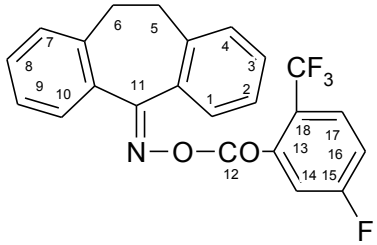
O-(4-Fluoro-3-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.70%, H 3.58%, N 3.45%.
^{1}H-NMR ($CDCl_3$, δ ppm, *J* Hz, T=298K): 8.13÷8.05(m, 2H, H-14, H-18); 7.79(dd, 1H, H-1, 1.4, 7.4); 7.45÷7.25(m, 6H, H-arom); 7.24(t, 1H, H-17, $J(F^{16}$-$H^{17})$= $J(H^{18}$-$H^{17})$= 9.1 Hz); 7.18(bd, 1H, H-4 or H-7, 7.4); 3.22(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 168.22(C-11); 162.65(dq, C-16, $J(F^{16}$-$C^{16})$=264.6 Hz, J(3F-C^{16})=2.4 Hz); 161.56(d, C-12); 139.34(C-4a); 138.01(C-7a); 133.78(C-1a); 132.38(C-10a); 125.36(d, C-13, $J(F^{16}$-$C^{13})$= 3.6 Hz); 121.92(qd, CF_3, J(3F-C)=271.6 Hz, $^3J(F^{16}$-$CF_3)$=1.0 Hz);

118.89(qd, C-15, J(3F-C^{15})=33.6 Hz, J(F^{16}-C^{15})=12.8 Hz); 135.76(d, C-18, J(F^{16}-C^{18})=9.9 Hz); 130.71(CH); 130.56(CH); 130.14(CH); 129.50(C-1); 129.31(qd, C-14, J(3F-C^{14})=4.7 Hz, J(F^{16}-C^{14})=2.8 Hz); 128.56(CH); 127.39(CH); 126.46(CH); 125.77(CH); 117.44(d, C-17, J(F^{16}-C^{17})=21.3 Hz); 33.47(C-5 or C-6); 31.83(C-6 or C-5).
^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -62.23(d, 3F, F_3C, J(3F-F^{16})=12.6 Hz); -106.81(m, 1F, F^{16}).
FT-IR (solid in ATR, ν cm^{-1}): 3078w; 2958w; 2883w; 2827w; 1750vs; 1603m; 1499m; 1424m; 1322s; 1272m; 1246s; 1229s; 1170m; 1134vs; 1076vs; 1053s; 982m; 870m; 842w; 775w; 749m; 730w; 675w.

O-(5-Fluoro-2-trifluoromethyl-benzoyl)-5-oximino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene



$C_{23}H_{15}F_4NO_2$: Anal. Calcd. (Mr = 413.37): C 66.82%, H 3.62%, N 3.38%; Found: C 66.85%, H 3.78%, N 3.30%.
^{1}H-NMR ($CDCl_3$, δ ppm, J Hz, T=298K): 7.78(dd, 1H, H-1, 1.4, 7.4); 7.70(dd, 1H, H-16, 5.0, 8.52); 7.38÷7.19(m, 8H, H-arom); 7.18(bd, 1H, H-4 or H-7, 7.4); 3.21(bs, 4H, H-5, H-6).
^{13}C-NMR ($CDCl_3$, δ ppm, T=298K): 169.12(C-11); 163.74(d, C-15, J(F^{15}-C^{15})=254.4 Hz); 162.05(d, C-12); 139.27(C-4a); 137.75(C-7a); 133.80(C-1a); 132.37(C-10a); 132.14(dq, C-13, J(F^{15}-C^{13})= 8.1 Hz, J(3F- C^{13})=1.7 Hz); 125.20(qd, C-18, J(3F-C^{18})=33.3 Hz, J(F^{15}-C^{18})=3.7 Hz); 122.76(q, CF_3, J(3F-C)=273.3 Hz); 130.75(CH); 130.53(CH); 130.07(CH); 129.38(C-1); 129.38(dq, C-17, J(F^{15}-C^{17})=8.9 Hz, J(3F-C^{17})=5.2 Hz); 128.25(CH); 127.17(CH); 126.42(CH); 125.89(CH); 118.3244(d, C-16, J(F^{15}-C^{16})=21.7 Hz); 117.77(d, C-14, J(F^{15}-C^{14})=24.6 Hz); 33.42(C-5 or C-6); 31.63(C-6 or C-5).
^{19}F-NMR ($CDCl_3$, δ ppm, T=298K): -59.25(bs, 3F, F_3C); -106.65(dd, 1F, F-15, J(F^{15}-H^{14})=6.9 Hz, J(F^{15}-H^{16})=12.6 Hz).
FT-IR (solid in ATR, ν cm^{-1}): 3074w; 2982w; 2926w; 1767vs; 1612m; 1591m; 1503w; 1484w; 1309vs; 1276s; 1256vs; 1193m; 1161s; 1132vs; 1079s; 1033s; 987m; 930m; 912w; 887m; 859m; 835m; 774m; 752m; 698m; 616m.

Conclusions

We have synthesized a series of new acyl-oximines with therapeutic potential. These nine new coumpounds were obtained following an acylation reaction between 5-oximino-10,11-dihydro-5H-dibenzo[a,d] cycloheptadiene and different carboxylic acids chlorides. The structures of these new acyl-oximines have been confirmed by elemental analysis and spectrometric methods (IR, ^{1}H-NMR and ^{13}C-NMR). In the near future we intend to test their pharmacological activity in order to establish if these new compounds are bioactive molecules.

Acknowledgements

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