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PHENOXATHIIN CHEMISTRY. SYNTHESIS BASED ON 2-ω-BROMOACETYLPHENOXATHIIN

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ABSTRACT

Starting from 2-ω-bromoacetylphenoxathiin and using the Kornblum reaction the corresponding glyoxal **2** was synthesized. This was used for the syntheses of the monoxime **3**, dioxime **4** and quinoxalinyl **5** derivatives. By treatment with thiourea 4-(2-phenoxathiinyl)-2-aminothiazole hydrobromide 7 was obtained. Some new ammonium and phosphonium salts was also prepared.Chemical and spectral data supporting the structure of the newly synthesized compounds are also presented.

RESUMO

Começando com 2-ω-bromoacetilfenoxatiina e usando a reação de Kornblum, o glioxal correspondente 2 foi sintetizado. Este foi usado para a síntese dos derivados da nomoxima 3, dioxima 4 e do quinoxalinil 5. O hidrobrometo de 4-(2-fenoxatiinil)-2-aminotiazol 7 foi obtido através de tratamento com uréia. Alguns sais novos de amônio e fosfônio também foram preparados. Dados espectrais e químicos que comprovam a estrutura dos compostos novos sintetizados são apresentados.

KEYWORD: Phenoxathiin, ammonium salts, thiazole, glyoxime.

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INTRODUCTION

Phenacyl-, heteracylhalide respectively are important reagents for organic synthesis which allow access to sulfonium, ammonium, phosphonium or selenonium salts. Starting from these substances, through the respective ylides, various heterocyclic compounds can be obtained [1-9].

The present paper describes the synthesis of some new products based on 2-ω-bromoacetylphenoxathiin according with the scheme 1 and 2 and is part of a systematic research connected with structure-biological activity of compounds of the phenoxathiin class.

EXPERIMENTAL

Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded in KBr pellet with an UR-20 apparatus.

^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 300 spectrometer using $CDCl_3$, DMSO-d_6 as solvent and TMS as internal standard. MS spectra were performed on JEOL GC mate spectrometer.

Thin layer chromatography (TLC) was performed on plates of silica gel 60-254 (Merck), unidimensional technique. Detection of compounds was done by UV light (λ=254 nm), iodine and sulfuric acid spray.

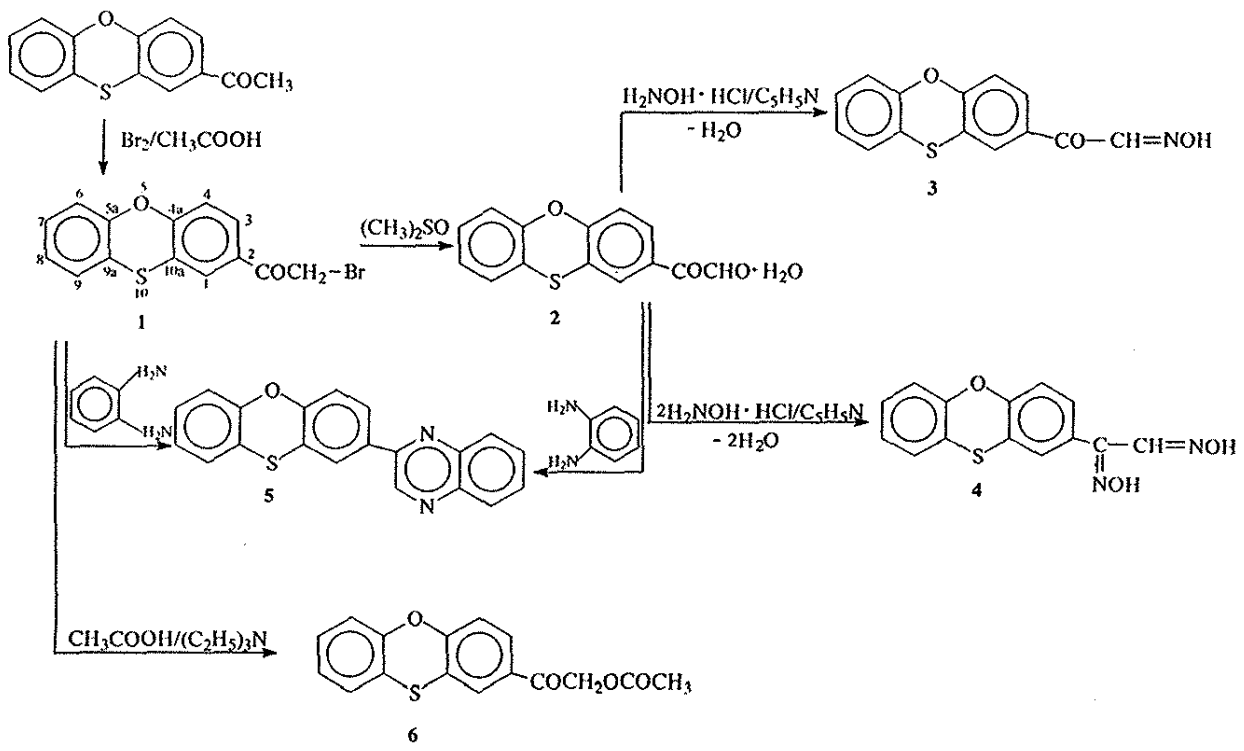
2-ω–Bromoacetylphenoxathiin (**1**):

To a solution of 15 g (0.0062 mole) of 2-acetylphenoxathiin (m.p.=118-119°) in 70 mL glacial acetic acid, 3.2 mL (9.92g; 0.062 mole) of bromine in 30 mL glacial acetic acid were added, under heating at 50-60° and stirring. After cooling , the precipitate was filtered off, washed with water, affording 17.2 g of the compound **1** (86.5%).m.p.=146-147°.

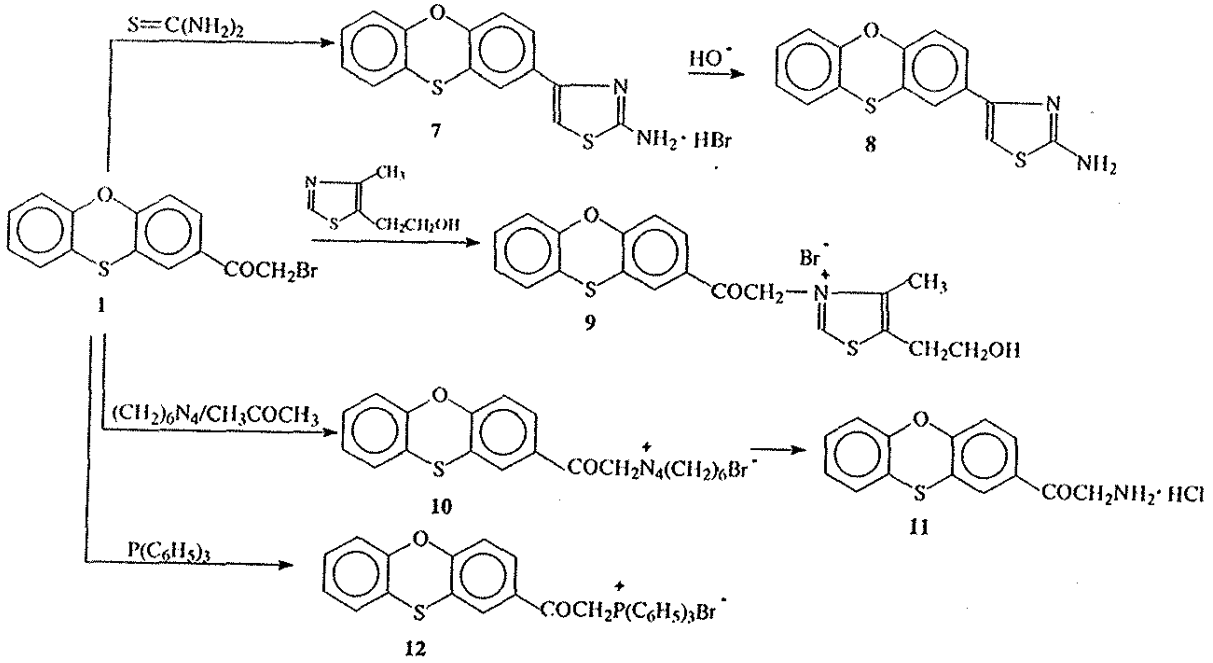
After recrystallisation from glacial acetic acid, yellow crystals with m.p.=147-149° were obtained. For the purified 2-ω-bromoacetylphenoxathiin, the literature indicates the following melting points: 134[10], 128-131[12], 144-145[11].

2-Phenoxathiinylglyoxal hydrate (**2**):

SCHEME 1



SCHEME 2



A mixture of 3 g (0.009 mole) 2-ω-bromoacetylphenoxathiin and 17.5mL dimethyl sulfoxide was heated at 40° up to dissolving . The solution was maintained 72 hours at room temperature and then poured into 100 mL water. The precipitate was filtered off and washed with water. The yield of **2** was about 2.54 g (99.2%) m.p.=117-125°. After recrystallisation from 90% acetic acid m.p.=132-134°.[lit[12] m.p.=130-132°]. TLC: Rf=0.77 (chloroform-methanol 4.5 : 0.5 v/v; detection: sulfuric acid spray - spot violet-red). IR(cm^{-1}): 3400(large bands characteristic to aldehyde hydrate), 1690 (CO), 830(γ_{2CH}), 742(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 7.92(d,1H,H-1), 7.91(dd,1H,H-3), 7.26(m,1H,H-9), 7.24(m,1H,H-7), 7.20(d,1H,H-4), 7.12(td,1H,H-8), 7.10(dd,1H,H-6), 6.83(d,2H,OH), 5.61(t,1H,$CH(OH)_2$); ^{13}C-NMR (DMSO-d_6, δppm): 194.22(CO), 154.59(C-4a), 150.36(C-5a), 130.42(C-2), 130.11(C-1), 128.53 (C-7), 128.39(C-3), 127.04(C-9), 125.59(C-8), 119.12 (C-10a), 118.12 (C-9a), 117.82(C-6), 117.63(C-4), 89.57($CH(OH)_2$).

2-Phenoxathiinylglyoxal monoxime (**3**):

To 2 g (0.0073 mole) of 2-phenoxathiinylglyoxal hydrate, 10 mL pyridine and 10 mL methanol, 0.5 g (0,0072 mole) of hydroxylamine hydrochloride were added. The mixture was kept at room temperature for 6 hours, then was poured into ice-water. The precipitate was filtered and 1.42g (71.7%) crystals with m.p.=181-183°, were obtained. After recrystallisation from ethanol m.p.=182.5-186°.TLC: Rf=0.70 (chloroform : methanol 4.5 : 0.5 v/v; detection sulfuric acid spray - violet spot); ^{1}H-NMR(DMSO-d_6,δppm): 12.73(s, 1H, NOH), 8.01(s, 1H, CH), 7.87(d, 1H, H-1), 7.84(dd, 1H, H-3), 7.27(m, 1H, H-9), 7.25(m, 1H, H-7), 7.20(d, 1H, H-4), 7.13(td, 1H, H-8), 7.11(dd, 1H, H-6); ^{13}C-NMR(DMSO-d_6, δppm): 186.56(CO), 154.62(C-4a), 150.28(C-6a), 147.61(CH=NOH), 132.74(C-2), 130.31(C-1), 128.61(C-3), 128.56(C-9), 127.05(C-7), 125.62(C-8), 119.22(C-10a), 117.99(C-9a), 117.83(C-6), 117.58(C-4).

Anal. calcd. for $C_{14}H_9NO_3S$: S, 12.46 , Found: S, 12.13.

2-Phenoxathiinylglyoxal dioxime (**4**):

To a mixture of 1 g (0.0036 mole) of 2-phenoxathiinylglyoxal, 0.7 g (0.01 mole) of hydroxylamine hydrochloride, 14 mL pyridine and 14 mL methanol were added. The reaction mixture was refluxed one hour, then was

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concentrated under low pressure and the obtained residue was poured in water to give 1.03g (99%) of **4**. The dioxime recrystallised from methanol leads to crystals with m.p.=212.5-213.5°. TLC: Rf=0.63 (chloroform-methanol 4.5:0.5 v/v; detection sulfuric acid spray-spot violet bleu); IR(cm^{-1}): 3200-3300, 1450 (OH), 1615 and 950 (C=NOH), 830(γ_{2CH}), 742 (γ_{4CH}); ^{1}H-NMR (DMSO-d_6, δppm): 11.99 and 11.98 (s, 2H, NOH), 7.85 and 8.44(s,1H,-CH=N-), 7.43(d,1H,H-1), 7.41(dd,1H,H-3), 7.26(m,1H,H-9), 7.23(m,1H,H-7), 7.12(m,1H,H-8), 7.11(d,1H,H-4), 7.10(m,1H,H-6); ^{13}C-NMR(DMSO-d_6, δppm): 140.39 and 147.44(-CH=N-), 151.54(C-4a), 150.99(C-5a), 149.44(>C=NOH), 130.81(C-2), 128.44(C-1), 128.38(C-7), 127(C-9), 126.81(C-3), 125.22(C-8), 118.64(C-10a), 118.64(C-9a), 117.73(C-4), 117.20(C-6). MS: 286(M^+).

Anal. calcd. for $C_{14}H_{10}N_2O_3S$: S,11.20; Found S, 10.92.

2-(2'-Quinoxalinyl)phenoxathiin (**5**):

A: According to the literature indications[10], from 0.85g (0.026 mole) of 2-ω-bromoacetylphenoxathiin, 0.866g (99.7%) crystals with m.p.=173-175°, were obtained.

B: o-Phenylendiamine (0.21g, 0.0018 mole) was added to a solution of 2-phenoxathiinylglyoxal(0.51g, 0.0018 mole) in 20 mL ethanol, under heating until a solution was obtained. The mixture was refluxed one hour, maintained at room temperature 24 hours, then filtered off and 0.46g (75.4%) crystal were obtained. m.p.=194-196° [lit[10] m.p.=174°]. Compound was recrystallised from methyl ethyl cetone, m.p.=199-200°. TLC: Rf=0.41 (benzene : ethyl acetate 4.5 : 0.5 v/v ;detection-sulfuric acid spray-spot violet) ; IR(cm^{-1}): 1610(C=N); 1245(C-O-C); 825(γ_{2CH}); 750(γ_{4CH}).

Anal. calcd. for $C_{20}H_{12}N_2OS$: S, 9.76 ; Found S, 9.49.

2-Phenoxatiinylcarbonylmethyl acetate (**6**):

To a mixture of 0.46 mL (0.48g, 0.008 mole,d=1.049) acetic acid, 10 mL dimethylformamide and 1mL (0.73 g.0.007 mole, d=0.726) triethylamine, 1.6 g (0.005 mole) of 2-ω-bromoacetylphenoxathiin were added. The reaction mixture was lightly warm for 5 minutes, and maintained at room temperature for 24 hours. The solid product was filtered off, and water was added to filtrate.

The new precipitate, which was formed, was filtered, washed with water and air-dried to provide **6** (1.29g, 86.6%). This was recrystallised from ethanol to yield a solid, m.p.=132.5-133.5. TLC: Rf=0.68 (chloroform : ethanol 9.5:0.5 - v/v ; detection: sulfuric acid spray- spot dark-red); IR(cm^{-1}): 1750(CO); 1690(CO); 1220(C-O-C); 825(γ_{2CH}); 765(γ_{4CH}); ^{1}H-NMR($CDCl_3$, δppm): 7.63(s, 1H, H-1), 7.61(d, 1H, H-3), 6.94-7.13(m, 5H, H-4 -H-8), 5.23(s, 2H, CH_2), 2.21(s, 3H, CH_3); ^{13}C-NMR($CDCl_3$, δppm): 190.03(CO), 170.23($COOCH_3$), 155.84(C-4a), 150.63(C-5a), 130.56(C-2), 127.94(C-1), 127.68(C-3), 126.62(C-9), 126.48(C-7), 125.11(C-8), 120.81(C-10a), 118.32(C-9a), 117.72(C-6), 117.72(C-4), 65.58(CH_2), 20.43(CH_3);

Anal. calcd. for $C_{16}H_{12}O_4S$; S,10.67; Found S, 10.45.

4-(2-Phenoxathiinyl)-2-aminothiazole hydrobromide (7):

To 0.5 g (0.0015 mole) of 2-ω-bromoacetylphenoxathiin in 20 mL isopropanol, 0.25 g (0.0032 mole) of thioyrea was added and was refluxed for one hour. The precipitate formed on cooling, was filtered off and washed with isopropanol to yield 0.5 g (84.7%) of compound 7. m.p.=273-275°. TLC: Rf=0.12 (petroleum ether : ethyl ether : dichloromethane : ethyl acetate -7.5 : 1 : 2 : 1 -v/v/v/v; detection sulfuric acid spray- spot bleu).

4-(2-Phenoxathiinyl)-2-aminothiazole (**8**):

To 0.25 g (0.00065 mole) of 7 in 3 mL water, 1.2 mL of sodium hydroxide were added until pH=9-10. The obtained precipitate was filtered off and air-dried to give 0.18 g (91.8%) of compound **8** with m.p.=176-177°. TLC: Rf=0.14 (petroleum ether : ethyl ether : methylene chloride ; ethyl acetate 7.5 : 1: 2 : 1 v/v/v/v, detection : sulfuric acid spray- spot light violet); IR(cm^{-1}):3425, 3365, 3275, 1620 (NH_2), 1435,1465 (thiazole nucleus), 830(γ_{2CH}), 745(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm); 7.63(d,1H,H-1), 7.60(dd, 1H,H-3), 7.19-7.25(m,2H,H-7;H-9), 7.07-7.10(m,3H,H-4;H-6;H-8), 7.05(s, 1H,thiazoleH-5), 7.00(s,2H,NH_2); ^{13}C-NMR (DMSO-d_6, δppm):168.25(thiazole C-2), 151.13(C-5a), 150.14(C-4a), 148.17(thiazoleC-4), 132.02(C-2), 128.29(C-9), 127.00(C-1), 125.33(C-7), 125.06(C-3), 123.69(C-8), 119.09(C-10a), 118.81(C-9a), 117.71(C-6), 117.71(C-4), 101.55(thiazoleC-5); MS: 298(M^+);

Anal. calcd. for $C_{15}H_{10}N_2OS_2$: S,21.49; Found S, 21.73.

3-(2-Phenoxathiinylcarbonylmethyl)-5-(2-hydroxyethyl)-4-methylthiazolium bromide (**9**):

To a solution of 0.5 g (0.0015 mole) of 2-ω-bromoacetylphenoxathiin in 10 mL anhydrous toluene , 0.2 mL (0.0017 mole) of 5-(2-hydroxyethyl)-4-methylthiazole were added. The reaction mixture was refluxed 30 minutes. The precipitate formed, on cooling, was filtered off to give the crude compound **9** (0.5g, 70.4%). After recrystallisation from ethanol and trituration with a mixture of dichloromethane - toluene (1:1-v/v), white crystals with m.p.=228-229° were obtained. TLC: Rf=0.33 (butanol : acetic acid : water -4 : 1 :1 v/v/v); detection sulfuric acid spray - spot light violet. IR(cm^{-1}): 3465, 3310 (NH_2), 1472, 1440(thiazole nucleus), 840(γ_{2CH}), 760(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 10.15(s, 1H, thiazole H-2); 7.83(m, 2H, H-1;H-3), 7.06(m, 5H, H4;H-6 - H-9), 6.33(s, 2H, $COCH_2$), 3-3.6(m, 4H, CH_2CH_2), 2.25(s, 3H, CH_3);

Anal. calcd. for $C_{20}H_{18}BrNO_3S_2$: S, 13.8; Found S, 14.02.

1-(2-Phenoxathiinylcarbonylmethyl)hexamethylentetraminiu bromide (**10**):

The quaternisation reaction was done by the method used for the synthesis of triethylammonium salt [24], but using anhydrous acetone as a solvent. Yellow crystals with m.p.=187-189° (96.7%) were obtained. TLC: Rf=0.67 (butanol : acetic acid : water; detection: sulfuric acid spray - spot light violet); IR(cm^{-1}): 1685(CO); 1400(CH_2-N<); 1235(C-O-C); 832(γ_{2CH}); 765(γ_{4CH}).

Anal. calcd. for $C_{20}H_{21}BrN_4O_2S$: S, 6.94; Found S, 7.25.

1-(2-Phenoxathiinylcarbonylmethyl)amine hydrochloride (**11**):

A mixture of 3 g (0.0065 mole) of **10**, 5 mL conc. hydrochloric acid and 15 mL ethanol, was stirred at room temperature for 5 hours. After 48 hours, the solvent was removed and the precipitate was filtered off and dried to afford 1.5 g (78.5%) of the compound **11**. m.p.=275-278°(charing). TLC: Rf=0.56 (butanol : acetic acid : water 4:1:1 v/v/v; detection sulfuric acid spray-spot violet); IR(cm^{-1}): 1400(CH_2-N<), 1250(C-O-C), 818(γ_{2CH});

770(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δppm): 7.90(d, 1H, H-1), 7.85(dd, 1H, H-3), 7.24-7.29(m, 3H, H-4;H-7;H-9), 7.12-7.17(m, 2H, H-6;H-8), 4.55(s, 2H, CH_2), 4.01(s, 3H, $^+NH_3$); ^{13}C-NMR(DMSO-d_6, δ ppm): 182.73(CO), 147.5(C-4a), 142.18(C-5a), 122.51(C-2), 120.79(C-1), 120.58(C-3), 119.32(C-9), 118.9(C-7), 117.7(C-8), 112.4(C-10a), 109.9(C-9a), 109.8(C-6), 109.8(C-4), 38.86(CH_2).

Anal. calcd. for $C_{14}H_{12}ClNO_2S$: S, 10.91; Found : S, 11.17.

1-(2-Phenoxathiinylcarbonylmethyl)triphenylphosphonium bromide **(12)**:

To a solution of 0.25 g (0.0007 mole) of 2-ω-bromoacetylphenoxathiin in 10 mL anhydrous toluene, 0.2 g (0.00076 mole) of triphenylphosphine were added. The reaction mixture was refluxed for 30 minutes and the precipitate formed was filtered off. After drying 0.35 g (79.5%) of the compound **13**, were obtained. m.p.=279-281°-TLC: Rf=0.67 (butanol-acetic acid: water 4:1:1-v/v/v; detection sulfuric acid spray - spot violet intense); IR(cm^{-1}): 3010-3050 (phenyl), 2853, 2910(CH_2), 1660(CO), 1240(C-O-C), 822(γ_{2CH}), 750(γ_{4CH}); ^{1}H-NMR(DMSO-d_6, δ ppm): 7.8-7.9 (m,2H,H-1;H-3), 7.43-7.7(m, 8H, H-4;H-7;H-9 and phenyl), 6.94-7.05(m, 2H, H-6;H-8), 5.73 and 6.11(s, 2H, CH_2).

Anal. calcd. for $C_{32}H_{24}BrPO_2S$: S, 5.49; Found : S, 5.82.

RESULTS AND DISCUSSION

Through bromination in acid medium, 2-acetylphenoxathiin forms the corresponding brominated derivative **1**[10-12]. This compound, subject to the Kornblum oxidation reaction in the presence of dimethyl sulfoxide turns into a glyoxilic derivative **2** with a 99% yield. The literature[13] describes the synthesis of product **2** only through the oxidation of 2-acetylphenoxathiin with selenium dioxide, in the presence of dioxane.

The phenoxathiinylglyoxal **2** was characterized through the monoxime **3** and the corresponding dioxime **4** (scheme 1).

By using the reaction with o-phenylendiamine, product **2** leads to the 2-(2-quinoxalinyl)phenoxathiin **5** with 75.4% yield. The same product was

also obtained from 2-ω-bromoacetylphenoxathiin with o-phenylendiamine with 69.8% yield. These two methods lead to compounds **5** with the same m.p.=199-200°.

The reaction between 2-ω-bromoacetylphenoxathiin with o-phenylendiamine is also described in the literature [10], but the melting points of the product is indicated at 174°. This temperature difference might be explained through the fact that the starting substance used by the authors of the paper[10] , contained traces of 3-acetylphenoxathiin. The presence of this isomer in the 2-acetylphenoxathiin synthesis was recently confirmed[14].

In this synthesis a brominated derivative with m.p.=148-149° obtained from 2-acetylphenoxathiin, having a m.p.=118-119° was used.

The article[10] indicates a m.p.=113° of the brominated derivative (of course contaminated with the isomer from position 3)

Considering the fact that the phenacyl esters are used in the organic synthesis as protective groups of carbonyl, hydroxyl and phenol functions[15-18], the obtaining of such a compound was followed also in the case of 2-ω-bromoacetylphenoxathiin.

Thus by treatment of the brominated derivative **1** with acetic acid in the presence of triethylamine the compound **6** is obtained (scheme 1).

The literature mentioned the antimicrobial activity of certain quaternary ammonium salts based on 2-methyl-3-chloromethylphenoxathiin, towards Gram-positive and Gram-negative germs[19]. Taking into consideration all these factors, these researches was extensioned for the compounds obtained through the quaternisation reaction of 2-ω-bromoacetylphenoxathiin.

The products which were synthesized are indicated in scheme 2. The reaction between 2-ω-bromoacetylphenoxathiin and thiourea leads to compound **7**. Treated with sodium hydroxide solution it turns into 4-(2-phenoxathiinyl)-2-aminothiazole **8.**

A thiazolic derivative **9** is also obtained through the reaction between brominated derivative **1** with 5-(2-hydroxyethyl)-4-methylthiazole.

A quaternary ammonium salt was also synthesized through the reaction between 2-ω-bromoacetylphenoxathiin and hexamethylenetetramine, compound **10** beeing thus synthesized. Reaction of triphenylphosphine with 2-ω-bromoacetylphenoxathiin gives compund **12**.

The synthesized products were characterized by spectral methods (IR, NMR, MS) and their purity was confirmed by thin layer chromatography (TLC).

In the IR spectra of the compounds **1-12**, a series of bands is remarked, characteristic for both the phenoxathiin nucleus and the substituent grafted on the aromatic ring.

For the phenoxathiin nucleus the vibrations at 750-760 cm^{-1} (γ_{4CH}), 810-815 cm^{-1} (γ_{2CH}), 1070-1090 cm^{-1} (ν_{C-S}) and 1210-1240 cm^{-1} (ν_{C-O-C}) are characterized. All these values are according to the literature data [20-23]. In the 1405-1580 cm^{-1} range five bands appear also characteristic for the phenoxathiinic nucleus. Absorption bands of the substituents grafted in the position 2 of the phenoxathiin nucleus were also identified. Thus characteristic for compound **2** is the absorption at 1690 cm^{-1}, assigned to the valence vibrations of the carbonyl group. The lack of this band in the structure of compounds **3** and **4** and the appearance of a band at 1610-1620 cm^{-1}, which characterized the $\nu_{C=N}$ vibration, confirms the oxime structure.

For compound **6**, the ν_{CO} at 1740 cm^{-1} vibration, assigned to the acetoxy group is characteristic.

For compounds **7-9** characteristic bands of the thiazole nucleus (1435-1465 cm^{-1}) and ν_{NH} 3275, 3425 cm^{-1} appear; for the ammonium salts **10-11** the absorption appear at 1400 cm^{-1}.

The main absorption bands which are characteristic of the substances **1-12**, are presented in the experimental part of this paper.

The ^{1}H- and ^{13}C-NMR spectra for the synthesized compounds were also recorded and interpreted, the respective chemical shifts being presented within the experimental part.

The signal assignments were made by comparison to the literature data regarding derivatives series of the 2-substituted phenoxathiin [14].

Analyzing the ^{1}H-NMR spectra for the substances which were synthesized, we found out that the chemical shifts of H_1 and H_3 protons are influenced by the electron-withdrawing effect of the substituents from position 2. In this way a deshielding takes place with the same signals to those for phenoxathiin.

The influences of the substituent in position 2 are much less evident on the H_4 as well as for the protons from the unsubstituted benzene ring. For the methylene group in position 2 in compounds **1**, **6**, **9-12** the resonance signals appears as a singlet in the range δ=4.86-6.33 ppm. For compound **12**, because of the three big volumes of the phenyl groups the both

methylenic protons are no longer equivalent giving signals as singlet at δ=5.73 and 6.11 ppm, while the molecule adopts a rigid conformation.

In the ^{1}H-NMR spectrum of the compound **8** the signal at δ=7.00 ppm is assigned to the two protons from the amino group. This signal disappears when the spectrum is recorded in the presence of D_2O.

For compound **3** the deshielding produced by the functional groups (CO or C=NOH) makes the protons H-1 to appear at lower field at 7.8-7.9 ppm compared to the compound **4** were a normal shielding takes place at approximately Δδ=0.5 ppm.

The multiplicity of the signals shows a *cis*-coupling J_{34}=8.0-9.1 Hz as well as a *meta*-coupling J_{13}=2.0-2.2 Hz, which makes the proton to appear as doublet with the small coupling constant and the H_3 as a doublet of doublets in which the couplings with H-4 and H-1 are found again. The H-4 proton appears at δ=7.1-7.2 ppm as a doublet with J_{43}=8.0-9.1 Hz. When the ketone **3** turns into oxime **4**, the value of this coupling decrease approximately 1Hz.

The protons H-6 - H-9 from the unsubstituted ring appear in the δ=7.1-7.26 ppm range, the most shielding proton being H-6 and the most deshielding being H-9. To assign the proton resonances of these compounds two dimensional experiments (2D), COSY H-H; COSY H-C were made[25].

The proton of the aldehyde group from the glyoxal hydrate **2** appears as a triplet at δ=5.61 ppm with a 7.0 Hz coupling with hydroxyl groups (evinced through the deuteration).

The ^{1}H- and ^{13}C-NMR spectra for the dioxime **4** indicates the presence of the *sin* and *anti* isomers for the oxyminic groups. The following pairs of chemical shifts (δ ppm) appear: 11.87 , 11.56 (NOH); 7.85 (CH=N) and 12.00 , 11.99 (NOH) ; 8.44 (CH=N).

The ^{13}C-NMR spectra confirm the asymetric substitution of the phenoxathiin ring. Generally speaking, the assigments for the unsubstituted ring were revealed by spectra comparison with the derivatives of this class which were previously described[14, 26], as well as through heteronuclear corelation experiments (COSY H-C).

Regarding the antimicrobial activity of the synthesized derivatives, compound **9** is specially remarkable against Gram-positive bacteria.

CONCLUSIONS

Eight new products based on 2-ω-bromoacetylphenoxathiin were synthesised and characterised through mass, IR, NMR (^{1}H- and ^{13}C- at 300 and 100 Mhz) spectra. The purity of the products was confirmed by means of TLC.

Upon the antimicrobial screening an activity of compound **9** against various Gram-positive strains was observed.

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