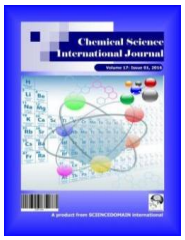

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Synthesis of [Oxa-, Thia-diazoles- and Triazole]-Thiols Derived from Butyric Acid: Conductivity Property, Complex Formation with Fe (II), Hg (II), and Synthesis of Seco-Acyclo-*S*-Glycosides

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Authors' contributions

This work was carried out in collaboration between all authors. Author AAO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors DB and MBT managed the analyses of the study. Author MBT managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Three heterocyclic thiols: 2- propyl-1.3.4 – oxadiazole-5-thione/thiol **4/7**, 2- propyl-1.3.4 – thiazole-5-thiole **8**, 3- propyl-1.2.4 – triazole-5-thiole **9** have been synthesized from butyric acid. They showed conductivity properties and complex formation with Fe (II) and Hg (II) ions. New S-seco-acyclo-glycosides namely: 2-propyl -1,3,4-oxadiazole-5-thionyl-(1,3-dioxanyl) glycoside **12**, 2-propyl -1,3,4-thiadiazole-5-thionyl-(1,3-dioxanyl) glycoside **13** and 3-propyl -1,2,4-triazole-5-thionyl-(1,3-dioxanyl) glycoside**14** were synthesized from **7,8,9**. Synthesis of nucleobases-complexes with Fe^{+2} and Hg^{+2} ions **15-20**were achieved. Characterization of synthesized compounds were done by IR and ^{1}H-NMR spectroscopy. Potential conductivity of synthesized complexes were determined.

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Keywords: Butyric acid; 1,3,4-oxadiazole; 1,3,4-thiadiazole; 1,2,4-triazole; glycosides; organometallic complexes; conductivity.

1. INTRODUCTION

Butyric acid currently considered as therapeutic purposes in the treatment of colorectal cancer and homogloinopathies [1]. Phenyl butyric acid derivative, N-(4-chlorophenyl)-4-phenylbutanamide known as inhibitor with anti-proliferative activity on cervix cancer and leukemia cells [2]. It is applied as an additive to food, flavorings, varnishes, perfumes, pharmaceuticals, and disinfectants [3]. It is also used for production of plastics, plasticizers, surfactants and textile auxiliaries [4]. Butyric acid and derivatives are used to protect against hair loss [5]. Some derivatives of butyric acid obtained from carbon chain were utilized in the synthesis of aza-analogues of macrosphlides and in the synthesis of potentially active products for treatment of auto-immune and inflammatory diseases [6,7]. Other kinds of derivatives from modifying its carboxylic group, such as 1,2,3-triazole piperidine were used in treatment of type 2 diabetes [8,9]. While substituted 1,3,4-oxadiazole derivatives of butyric acid showed lower lipophilicity (log D) than its regioisomeric form 1,2,4-oxadiazole derivatives [10]. Significant differences were also observed with respect to metabolic stability, lERG inhibition and aqueous solubility favoring the 1,3,4- oxadiazole isomers [10]. The three heterocyclic rings1,3,4-oxadiazole, 1,3,4-thiadiazole and 1,2,4-triazole and their ylidic derivatives showed remarkable electric properties [11-13]. 1H-1,2,4-triazole has been shown to have an effective solvent for proton-conducting electrolytes [14]. Synthesis of thio-1,2,4-triazole derivative of butyric acid was also reported and shown biological activity [10,15-19].

The aim of this paper is to synthesize new three heterocyclic derivatives of butyric acid **7-9**, formation of complex with Fe(II) and Hg(II) ions and studying their potential conductivity. Also to synthesized the corresponding seco-acyclo glycosides analogues [18-20].

2. EXPERIMENTAL DETAILS

2.1 General

All reactions were monitored by TLC analysis (silica gel for TLC supplied by MERCK), eluted by appropriate eluent mentioned within the text, iodine was used for visualization. The melting points measured with a BÜCHI 540 melting point apparatus and were uncorrected. The IR spectra for characteristic bands exhibited as wave number (ν cm^{-1}) were recorded using KBr discs in a JASCO V-530 spectrophotometer at University of Oran, Es-Senia, Algeria. ^{1}H NMR spectra exhibited as δ in ppm, were recorded on Bruker Avance AQS 300 MHz spectrometer, at University of Oran, Es-Senia (Algeria). Chemical shifts measured in DMSO-d6 as solvent to TMS as the internal standard.Signals abbreviated as (s= singlet), (d=doublet), (t=triplet), (q=quartet), (p=pentet) (sex= sextet), (m=multiplet). Ultra violet spectra were recorder by Shimadzu UV mini 1240, at University of Laghouat, Algeria. Conductivity determined by Siemens Conductimeter Metrohm 660, at University of Laghouat, Algeria.

2.2 Synthesis of Thiols 7,8,9

2.2.1 Ethyl butyrate (2)

Butyric acid (40 g, 0.43 mol) in ethanol (20 ml), H_2SO_4 (2 ml) was added dropwise with stirring. The mixture was refluxed at 90°C for 04 h. TLC eluted with Ethanol: Toluene 1:4 showed Rf: 0,56 for the acid and R_f : 0.84 for the ester. Brine added at the end of the reaction and extracted by chloform for two times. The combined organic layers were washed with 10% aqueous $NaHCO_3$ (100 ml), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness to give a colorless syrup, ethyl butyrate **2**(40 g, yield 80%). IR; 2699 (CH), 1734. (C-O).

2.2.2 Butyric hydrazide (3)

Ethyl butyrate **2** (5 ml .0.038 mol), ethanol (20 ml) and hydrazine hydrate 98%(5 ml) were heated under reflux at 90°C for 8 h . TLC eluted with Ethanol: Toluene 2:3 showed Rf: 0.62 for the butyric hydrazide. Ethanol was evaporated and a white solid, recrystallized from water/ethanol to give butyric hydrazide **3** (2.88 g, yield 74%); 3309, 3290(NH), 2958(CH), 1635(C=O).

2.2.3 2- Propyl-1.3.4 – oxadiazole-5-thione/thiol (4/7)

Butyric hydrazide **3** (1.5 g, 0.014 mol) in ethanol (125 ml), CS_2 (20 ml) were added to a solution of KOH (1 g) in ethanol (20 ml) and refluxed at 90°C for 14 h. TLC eluted with ethanol: toluene 1:4 showed a product asR_f :0,51. Excess ethanol

removed under vacuum and the remainder of the solution was acidified with HCl (10%). A yellow solid was faltered off and washed with ethyl acetate and recrystallized from $CHCl_3$\ethanol to give 5- propyl-1.3.4 – oxadiazole-2-thione/thiol (**4/7)** (1,5 g, yield 74%). IR: 3419(NH), 3051,2962 (C-H), 2476 (S-H)group ; 1688(C=N); 1255(C=S) and 1050(C-O-C). ^{1}H-NMR : 3.32 (s , 1H , SH), 2.69(t,2H,H_a), 1.77(sex, 2H,H_b), 1.02(t, 3H, H_c).

2.2.4 Potassium-N-propylhydrazinodithio formate (5)

Butyric hydrazide **3** (1 g, 0.015 mol). KOH (0.1 g, 0.001 mol), ethanol (100 mL) stirred to obtain a homogeneous solution. CS_2 (10 ml) was slowly added with an aid of stirring to yield yellowish colloid. Stirring continued at room temperature for an additional 5 h. Filtered, and the resulting solid recrystallized from ethanol. Yellowish-white crystals, yield 92%. v max no absorption band characteristic for: (N H) group; 3146.29 – 3254.29 cm^{-1}, (C=O) group ; 1610.27 cm^{-1} and (C=S) group ; 1382.03 – 1465.63 cm^{-1}.

2.2.5 Thiosemicarbazide butyric acid (6)

Butyric hydrazide **3**(1.5 g, 0.015 mol) was dissolved in ethanol (150 ml) with stirring. Ammonium thiocyanate (1.5 g, 0.02 mol) and HCl (6 ml) were added and the mixture was refluxed at 90°C for 16 h.. TLC eluted with ethanol: toluene 1:4 showed a product as R_f: 0.54.Excess ethanol removed under vacuum to almost dryness and the crystalline solid was faltered off and recrystallized from toluene\ petroleum-ether to give thiosemicarbazide butyric acid **6**(1,9 g , yield 79%). IR: 3249, 3138 (NH), 1611(C=O), 1368(C=S).

2.2.6 2-propyl-1,3,4-thiadiazole-5-thiol 8

A sulfuric acid (05 mL, 98%) and then cooled on an ice bath with vigorous stirring until temperature reached about 0°C, Potassium propylhydrazinodithioformate **7** (0.5 g, 0.005 mol) was slowly added while temperature kept below 0°C. Stirring continued for another 5 h. The mixture was poured into ice water (25 mL) to give a yellow solid precipitate and filtered. The filtrate was acidified by HCl (10%) to yield a yellow solid, filtered, washed with water and recrystallized from EtOH to yield **8** (0,7 g, yield 87%). IR: 3066, 2880 (C-H), 2560 (SH), 1687 (C=N). ^{1}H-NMR: 3.09 (s,1H , SH). 2.46 (t, 2H ,H_a), 1.60-1.47 (sex, 2H , H_b) , 0.79 (t , 3H , H_c) .

2.2.7 3- Propyl-1.2.4 – triazole-5-thiol (9)

Thiosemicarbazide butyric acid**6** (1.5 g, 0.01 mol), ethanol (100 ml) and a solution of KOH (1 g) in ethanol (20 ml)) was added and refluxed at 90°C for 13 h. TLC eluted with ethanol: toluene 1:4 showed a product as R_f :0,88. Excess ethanol removed under vacuum to almost dryness to give a solid which almost dissolved in ethyl acetate, filtered and evaporated to dryness to give a solid which was recrystallized from toluene\petroleum-ether to give 3- propyl-1.2.4 – triazole-5-thiol **9** (1,2 g , yield 84 %) .IR: 3361, 3257,3166 (NH), 2949.(CH), 2597 (S-H), 1641 (C=N).^{1}H-NMR: 8.90 (s , 1H , NH), 7.26 (s, 1H, NH), 3.10 (s , 1H , SH) ; 2.49 (t , 2H , H_a); 1.64-1.55 (sex, 2H , H_b) ; 0.83 (t , 3H , H_c).

2.3 Synthesis and Characterization of Nucleobases 7,8,9-complexes of Fe(II) and Hg(II), (15-20): General Procedure

Nucleobase (1 mmol), ethanol (15 mL) and FeSO4.5H20 or Hg (NO3)2.6H2O (1 mmol) in ethanol (10 mL) stirred and refluxed for periods around 3h. Proceeding of reactions monitored by TLC. Volatiles evaporated under vacuum to yield solids products:

2.3.1 Oxadiazole 7.Fe(II) complex (15)

TLC, Rf ,0.55 (toluene-ethanol, 4:1), M.p., 330-333°C, IR: 3137,3005,2969 (CH), 1216,1199 (C=S).UV.,402(0.74), 598(0.559).

2.3.2 Oxadiazole-thiol 7.Hg(II) complex (16)

TLC, Rf ,0.45 (toluene-ethanol, 4:1), M.p., 288°C, IR: 3156,2927 (CH)1660, 1603 (C=C, C=N).UV,397(0.812), 592(0.525).

2.3.3 Thiadiazole-thiol 8.Fe(II) complex (17)

TLC, Rf ,0.6 (toluene-ethanol, 4:1), M.p., 347-348°C, IR: 3016,2969 (CH), 1217 (C=S). UV, 395(0.818), 687(0.653).

2.3.4 Thiadiazole-thiol 8.Hg(II) complex (18)

TLC, Rf, 0.62 (toluene-ethanol, 4:1), M.p., 343-344°C, IR: 3023,2969 (CH), 1216 (C=S). UV, 395(0.746), 697(0.392).

2.3.5 Triazole-thiol 9.Fe(II) complex (19)

TLC, Rf, 0.6 (toluene-ethanol, 4:1), M.p., 338-340°C, IR: 3156,2927 (CH), 1177 w(C=S). UV, 392 (0.670), 704 (0.463).

2.3.6 Triazole-thiol 9.Hg(II) complex (20)

TLC, Rf ,0.53 (toluene-ethanol, 4:1), M.p., 336°C, IR: 3073,3005,2947 (CH),1630(C=C), 1575(C=N), 1114(C=S). UV, 399 (0.627), 700 (0.521).

2.4 Conductivity Measurements

For specific and molar conductivity determination, ethanolic solutions of diazol-thiols **7, 8, 9,** were prepared in range of 10^{-4} Molar concentrations. Specific and molar conductivity measured and results shown in Tables 1-4:

Table 1. Specific and molar conductivity of $FeSO_4$ and $Hg(NO_3)_2$

Concentration (Mole/ cm^3)			
Conductivity	**10^{-4}**	**4.10^{-4}**	**9.10^{-4}**
$X_0^{\uparrow}$ $FeSO_4$	2.7	6.2	6.3
$X_0^{\uparrow}$ $Hg(NO_3)_2$	3.2	8.5	8.7
$\Lambda^{\ddagger}$ $FeSO_4$	27000	15500	7000
$\Lambda^{\ddagger}$ $Hg(NO_3)_2$	32000	21250	9666

$X_0^{\uparrow}$, Specific conductivity µs/cm;
‡, Molar conductivity µs cm^2/mole

Table 2. Specific and molar conductivity of oxadiazole 7

Concentration (Mole/cm^3)			
Conductivity	**10^{-4}**	**4.10^{-4}**	**9.10^{-4}**
$X_0^{\uparrow}$	2.9	6.4	6.5
$X_0$10	3.1	6.8	7
$X_0$11	3.6	9	9.1
$\Lambda^{\ddagger}$ 7	29000	16000	7222
Λ 10	31000	17000	7777
Λ 11	36000	22500	10111

$X_0^{\uparrow}$, Specific conductivity µs/cm;
$\Lambda^{\ddagger}$, Molar conductivity µs cm^2/mole

Table 3. Specific and molar conductivity of thiadiazole 8

Concentration (Mole/ cm^3)			
Conductivity	**10^{-4}**	**4.10^{-4}**	**9.10^{-4}**
	4.7	11.2	11.8
$X_0$12	5.9	13	14.1
$X_0$13	7.3	17.2	17.4
$\Lambda^{\ddagger}$ 8	47000	28000	13111
Λ 12	59000	32500	15666
Λ 13	73000	43000	19333

$X_0^{\uparrow}$, Specific conductivity µs/cm;
$\Lambda^{\ddagger}$, molar conductivity µs cm^2/mole

Table 4. Specific and molar conductivity of triazole 9

Concentration (Mole/ cm^3)			
Conductivity	**10^{-4}**	**4.10^{-4}**	**9.10^{-4}**
$X_0^{\uparrow}$ 9	6.7	17	20.2
$X_0$14	7.6	19.9	23
$X_0$15	12.6	30.5	32.3
$\Lambda^{\ddagger}$ 9	67000	42500	22444
Λ 14	76000	49500	25500
Λ 15	129000	76250	35800

$X_0^{\uparrow}$, Specific conductivity µs/cm;
$\Lambda^{\ddagger}$, molar conductivity µs cm^2/mole

2.5 Synthesis of Sugar Analogues

2.5.1 2-Phenyl -1,3-dioxan-5-ol (10)

Glycerol (1.0 g), benzaldehyde (5 mL), chloroform (10 mL) with few drops of H_2SO_4 were refluxed with an assistant of Dean-Stark apparatus until glycerol was diminished (TLC, toluene: ethanol, 3:2). $KHCO_3$ added and stirred for 5 minutes, filtered and washed with chloroform. Volatiles were removed under vacuum to give a colorless syrup **10** (0.86 g), yield 48%. IR: 3311(OH), 2977($CH_{aliphatic}$), 2855($CH_{aromatic}$), 1277(C-O-C).

2.5.2 2-Phenyl -1,3-dioxan-5-O- acetate (11)

Compound **10** (0.5 g, 2.7 mmol), acetic anhydride (5 mL) in presence of acetic acid (2 mL), refluxed for 4 hr. Volatiles were removed by vacuum to yield yellowish syrup **11** (0.35 g), yield 50%. IR: 2852 ($CH_{aromatic}$), 1203(C-O-C).

2.6 Synthesis of S-glycoside Analogues 18, 19, 20

Thiols **7,8,9** –separately (0.33 g, approx.., 1 mmol) dissolved in ethanol (10 mL), few drops of acetic acid were added and refluxed for about 10 h. Proceeding of reactions were monitored by TLC. Volatiles removed under vacuum.

2.6.1 2-Propyl-(1,3,4- oxadiazole-5-thionyl-(2-phenyl-1,3-dioxanyl) glycoside (18)

IR: 2928, 2876, (CH), 1616(C=N), 1236(C-O-C). ^{1}H-NMR , 7.26 (m, 5H, phenyl), 6.53(s, 1H,H_f), 4.32(dd, 4H, $H_{e,é}$), 3.65 (pen, 1H, H_d), 2.31 (t, 2H, H_a), 2.08(sex, 2H,H_b),1.2(t, 3H, H_c).

2.6.2 2-Propyl-(1,3,4- thiadiazole-5-thionyl-(2-phenyl-1,3-dioxanyl) glycoside (19)

IR, 2928($CH_{aliphatic}$), 2875($CH_{aromatic}$), 1652 (C=C), 1616(C=N). ^{1}H-NMR , 7.76 (m, 5H, phenyl), 7.26

(s, 1H,H_f), 3.61, 3.40(dd, 4H, $H_{e,é}$), 3.20 (m, 1H, H_d), 2.00 (t, 2H, H_a), 1.31(sex, 2H,H_b),0.76(t, 3H, H_c).

2.6.3 3-Propyl-(1,2,4- triazole-5-thionyl-(2-phenyl-1,3-dioxanyl) glycoside (20)

IR, 3361(NH), 3327 (NH), 3166 (CH), 1641(C=C), 1617 (C=N). ^{1}H-NMR, 8.61 (m, 5H, phenyl), 6.94 (s, 1H,H_f), 4.99 (dd, 4H, $H_{e,é}$), 3.31 (pen, 1H, H_d), 2.23 (t, 2H, H_a), 1.34(sex, 2H,H_b),0.93(t, 3H, H_c).

3. RESULTS AND DISCUSSION

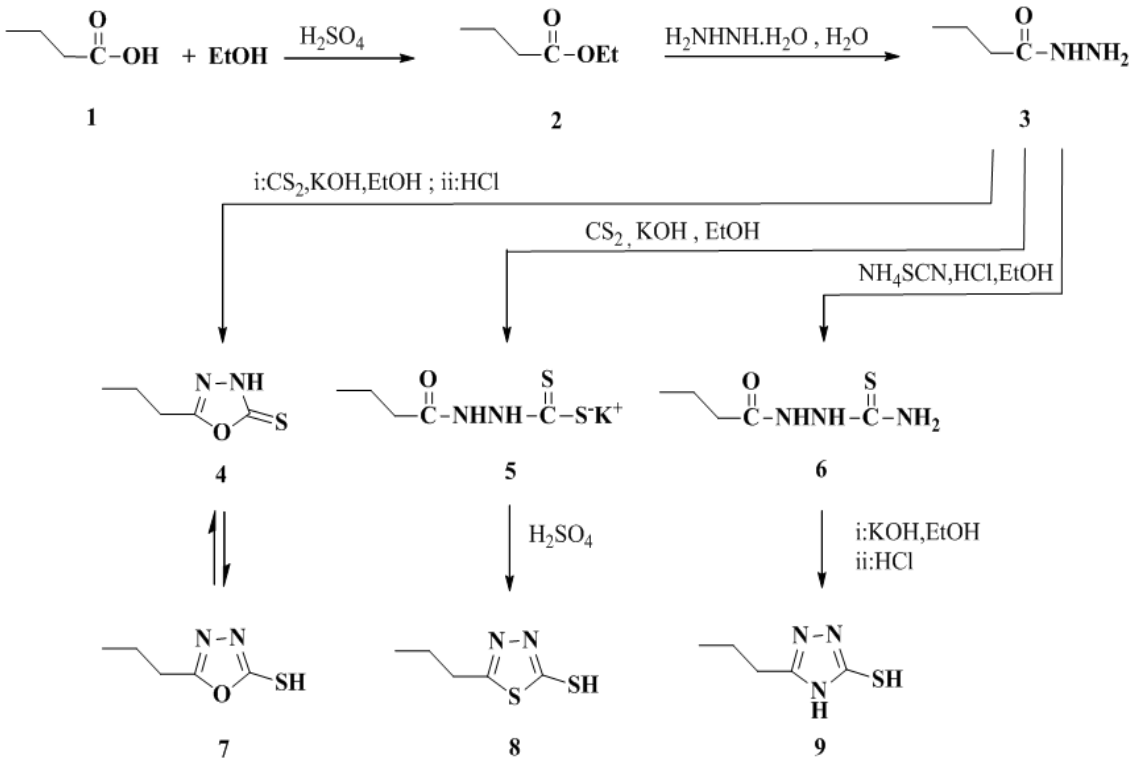
3.1`Synthesis of Heterocyclic Derivatives of Butyric Acids 4/7, 8 and 9

Ethyl butanoate **2** was prepared from **1** according to literature and converted to hydrazide **3** in good yield by treatment with hydrazine hydrate (see Scheme 1).

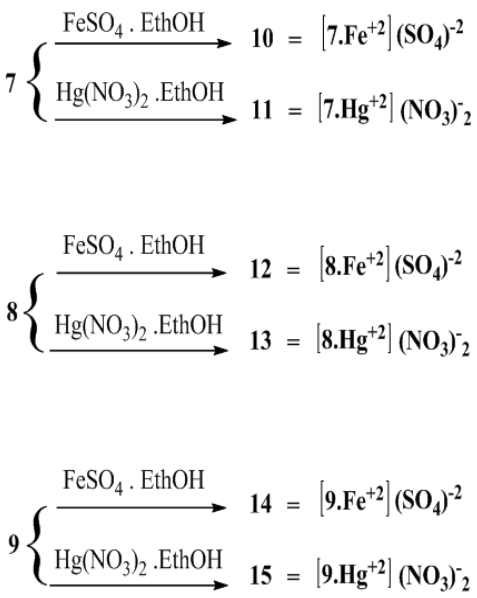
The hydrazide **3** gives rise to heterocyclic derivatives **4/7, 8** and **9** by following synthetic pathway summarized in Scheme 1. Refluxing **3** with CS_2 in presence of KOH in ethanol followed by acidification with HCl at the end of reaction period. Infrared spectrum showed that the cyclisation revealed an equilibrium mixture of 1, 3, 4-oxadiazole 5-thione and thiol (4⇄**7**) exhibited by presence of band at 2476 for SH group and a band at 1255 for C=S group. The thiadiazole **8** synthesized by reaction hydrazide 3 with CS2 and KOH, which resulted into potassium salt 5. The latter when treated with strong acid H_2SO_4 yielded 8. Infrared spectrum indicated that 8 found in thiol form only indicated by presence a band at 2560 for SH group and absence of C=S group between 1200 to 1400. The triazole-thiol 9 obtained from hydrazide 3 by treating the latter with ammoniumthiocyanate to give thiosemicarbazide **6** which have been cyclized by treating with KOH followed by acidification with HCl. The triazole 9 was separated in thiol form only as indicated by infrared spectrum which showed band at 2597for SH and no C=S band.

3.2 Synthesis of Heterocyclic-Metal Complexes 10-15

The diazol-thiols **7-9** showed a tendency to form complexes **10-15** with ferrous Fe(II) and mercuric Hg(II) ions by treating **7-9** with $FeSO_4$ and $Hg(NO_3)_2$ as shown in Scheme 2.



Scheme 1. Synthetic pathway to heterocyclic derivatives of butyric acid 4/7, 8, 9 (nucleobases)



Scheme 2. Synthesis of diazole-thiols-complexes 10-15

Formation of complexes may be proved by the differences with the original compounds **7-9**: changing in color, different melting points, disappearance of SH and C=S bands in IR and considerable shifting in UV absorptions as summarized in Tables 5-7:

The significant changes in IR spectra at Tables 5,6,7 indicated that complex formation have been taking place between metal ions Fe(II), Hg(II) and sulphur atoms of nucleobases **7,8,9**.

3.3 Electrical Conductivity

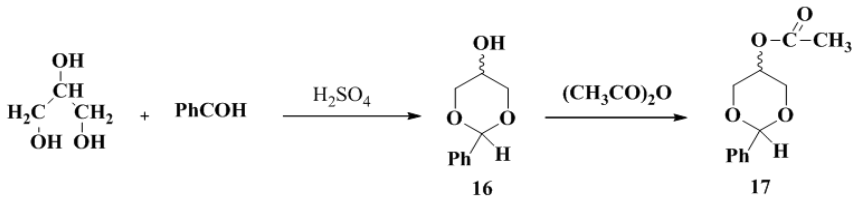
The electrical conductivity of diazol-thiols **7-9** and their complexes **10-15** summarized in Figs. 1-6.

Thiadiazole **8** and its complexes **12** (Fig. 3) and **13** (Fig. 4) showed better conductivity than oxadiazole **7** and its complexes. Triazole-thiol **9** and its complexes **14** (Fig. 5) and **15** (Fig. 6) exhibited the highest conducting property.

3.4 Synthesis of S-glycosides 18,19,20

Synthesis of S-glycosides **18-20** were achieved by SN2 reactions between nucleobases **7,8,9** with 2-Phenyl -1,3-dioxan-5-O- acetate (**17**).Compound **17** was prepared by treating glycerol with benzaldehyde followed by acetylation with acetic anhydride.

The X-diazoles **7-9** when treated with **17**, thiol groups have replaced the acetate to yield resemblance to seco-acyclo S-glycosides after removing benzaldehyde moiety.



Scheme 3. Synthesis of 2-Phenyl -1,3-dioxan-5-O- acetate (17)

Table 5. Physical properties of ligand 7 and its complexes 7. Fe (II), 7. Hg (II)

N°	M.P °C	Colour	Rf Toluene /ETOH 4 :1	IR : υ cm^{-1} SH, C=S	U.V : λnm (ε.l.cm-1.mol^{-1})
7	90	Yellow	0.73	2476	366 (0.831)
10 [7. Fe(II)]	330-333	White	0.55		402(0.740), 598(0.559)
11 [7. Hg(II)]	288	Green	0.45		397(0.812), 592(0525)

Table 6. Physical properties of ligand 8 and its complexes 8. Fe (II) and 8.Hg (II)

N°	M.P °C	Colour	Rf Toluène /ETOH 4 :1	IR : υ cm^{-1} SH, C=S	U.V : λ nm (ε.l.cm-1.mol^{-1})
8	98-101	Yellow	0.70	2560	337 (0.874)
12 [8. Fe (II)]	347-348	Green	0.60		395 (0.818), 687 (0.653)
13 [8. Hg (II)]	343-344	Beige	0.62		395 (0.746), 697 (0.392)

Table 7. Physical properties of ligand 9 and its complexes 9. Fe (II), and 9.Hg (II)

N°	M.P C°	Colour	Rf Toluène /ETOH 4 :1	IR : υ cm^{-1} SH, C=S	U.V : λ nm (ε.l.cm-1.mol^{-1})
9	95-96	Yellow	0.88	2597	301 (0.677)
14 [9. Fe (II)]	338-340	Brown	0.60		392 (0.670), 704 (0.463)
15 [9. Hg (II)]	336	Grey	0.53		399 (0.627), 700 (0.521)

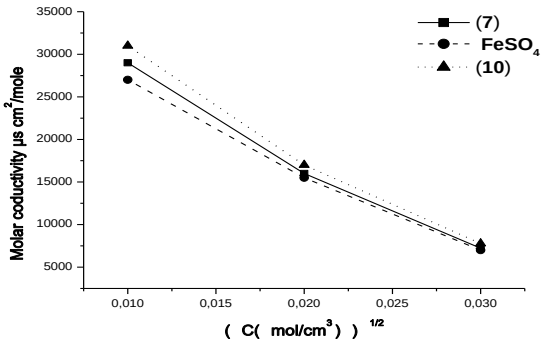


Fig. 1. Molar conductivity of complex 10

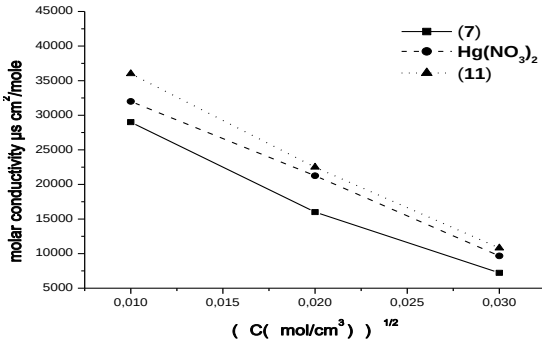


Fig. 2. Molar conductivity of complex 11

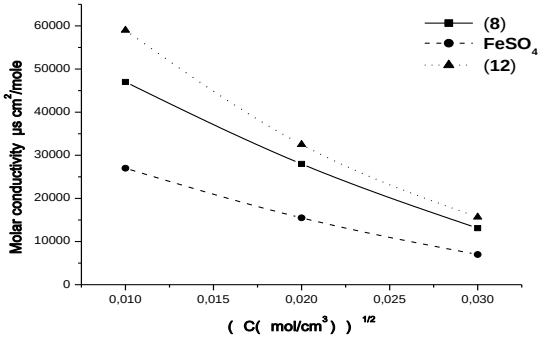


Fig. 3. Molar conductivity of complex 12

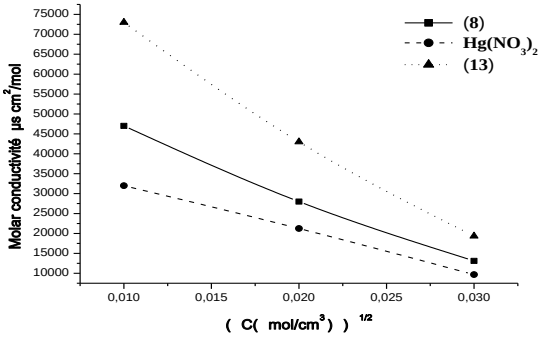


Fig. 4. Molar conductivity of complex 13

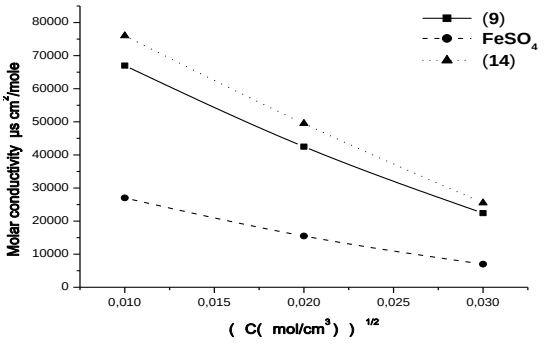


Fig. 5. Molar conductivity of complex 14

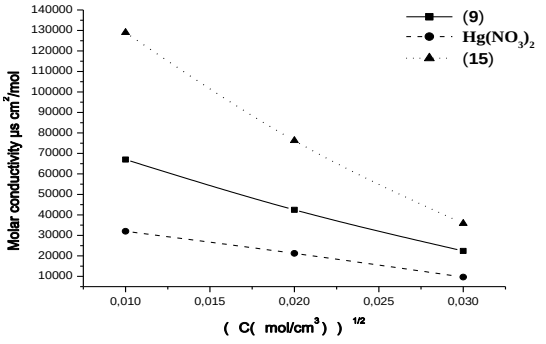
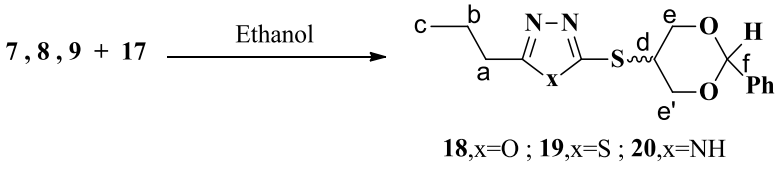


Fig. 6. Molar conductivity of complex 15



18,x=O ; **19**,x=S ; **20**,x=NH

Scheme 4. Synthesis of S-glycosides 18, 19, and 20

Thin layer chromatogram showed clearly the formation of new compounds related to **18, 19, 20** on the expense of diminishing the **7, 8, 9** spots. IR and ^{1}H-NMR spectra showed clearly the formation of glycosides.

4. CONCLUSIONS

Butyric acid is an important dietetic food for human beings and its metabolism well established inside human body. X-Diazole derivatives of butyric acid (**7, X=O; 8, X=S; and 9, X=NH**) were successfully synthesized and characterized. These derivatives showed tendency to form complexes with Fe (II) and Hg (II) ions (**10-15**) and potential of electrical conductivity. Triazole-thiol **9** and its complexes **14** and **15** exhibited the highest conducting property. The X-diazole thiols derivatives **7, 8** and **9** easily formed S-glycosides systems (**18, 19 and 20**) which will lead to seco-acyclo glycoside analogues after removing the benzylidene protector.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pouillart R. Role of butyric acid and its derivatives in the treatment of colorectal cancer and hemoglobinopathies. Life Sciences. 1998;63(20):1739-1760.
2. Rodríguez-Fonseca RA, Sixto-López Y, Fragoso-Vázquez MJ, Flores-Mejía R, Cabrera-Pérez LC, Vázquez-Moctezuma I, Rosales-Hernández MC, Martiniano B, Martínez-Archundia M, Trujillo-Ferrara J. G, Becerra-Martínez E, Correa-Basurto J. Design, synthesis and biological evaluation of a phenyl butyric acid derivative, N-(4-chlorophenyl)-4-phenylbutanamide: A HDAC6 inhibitor with anti-proliferative activity on cervix cancer and leukemia cells. Anti-Cancer Agents in Medicinal Chemistry. 2017;17(14):1-14.
   DOI:10.2174/1871520617666170103092851
3. Berdagué JL, Monteil P, Montel MC, Talon R. Effects of starter cultures on the formation of flavour compounds in dry sausage. Meat Science. 1993;35(3):275-287.
4. Szejtli J. Cyclodextrins in the textile industry. Starch/Starke/. 2003;55(5):191-240.
5. Mark Moran S, Alessi TR. Methods of using butyric acid derivatives to protect against hair loss. US. Patent, US5962523 (WO 1998017273A1); 1999.
6. Sugimoto K, Kobayashi Y, Hori A, Kondo T, Matsuya Y, Toyooka N, Nemoto, Hideo H. Butyric acid derivatives. Tetrahedron. 2011; 67:7681.
7. Hoffmann-La Roche F, Hendricks RT, Hermann JC, Jaime-Figueroa S, Kondru RK, Lou Y, Lynch SM, Owens TD, Soth M, Yee CW. Patent: WO2011/144585 A1, 2011. 4J.
8. Kim D, Kowalchick JE, Brockunier LL, Parmee ER, Eiermann GJ, Fisher MH, He H, Leiting B, Lyons K, Scapin G, Patel SB, Petrov A, Pryor KD, Roy RS, Wu JK, Zhang X, Wyvratt MJ, Zhang BB, Zhu L, Thornberry NA, Weber AE. Discovery of potent and selective dipeptidyl peptidase IV inhibitors derived from beta-aminoamides bearing subsituted triazolopiperazines. J. Med. Chem. 2008; 51(3):589-602.
   DOI: 10.1021/jm070330v
9. Shan Z, Peng M, Fan H, Lu Q, Lu P, Zhao C, Chen Y. Discovery of potent dipeptidyl peptidase IV inhibitors derived from β-aminoamides bearing substituted [1,2,3]-triazolopiperidines for the treatment of type 2 diabetes. Bioorg Med Chem Lett. 2011; 21(6):1731-5.
   DOI: 10.1016/j.bmcl.2011.01.086
10. Boström J, Hogner A, Llinàs A, Wellner E, Plowright AT. Oxadiazoles in medicinal chemistry. J. Med. Chem. 2012;55(5): 1817–1830.
    DOI: 10.1021/jm2013248
11. de Oliveira CS, Lira BF, Barbosa-Filho JM, Lorenzo JGF, de Athayde-Filho PF. Synthetic approaches and pharmacological activity of 1,3,4-oxadiazoles: A review of the literature from 2000–2012. Molecules. 2012;17:10192-10231.
    DOI: 10.3390/molecules170910192
12. Saegusa Y, Koshikawa T, Nakamura S. Synthesis and characterization of 1,3,4-oxadiazole-containing polyazomethines. Journal of Polymer Science: Part A: Polymer Chemistry. 1992;30(7);1369–1373.

13. Saegusa Y, Koshikawa T, Nakamura S. Synthesis and characterization of 1,3,4-oxadiazole-containing polyazomethines and polycopolyazomethines. Journal of Polymer Science: Part A: Polymer Chemistry. 1992;30(7):1375–1381.
14. Legrand C, Ropa PB, Vulturescu BAM, Hogea AGG, Surpateanu GG, Cazier F, Woisel P, Surpateanu G. Electrical properties of some 1,2,4-triazolederivatives. Progress in Organic Coatings. 2005;53(2):106–111.
15. LI S, Zhou Z, Zhang Y, Liu M. 1H-1, 2, 4-Triazole: An effective solvent for proton-conducting electrolytes. Chem. Mater. 2005;17:5884-5886.
16. Pitucha M, Wujec M, Dobosz M. Synthesis of 1, 2, 4-triazoline-5-thione derivatives. Annales Universitatatis Mariae Curie-Sklodowska Lubin- Polonia. 2004;59(12), SECTIO AA:122-143.
17. Colanceska-Ragenovic K, Dimova V, Vlado Kakurinov V, Dora Molnar Gabor DM. Synthesis of 1-nonanoyl/octadecanoyl-4-substituted thiosemicarbazides and substituted 1,2,4-trizoles as biological active compounds. J. Heterocycl. Chem. 2003;40:905-908.
DOI: 10.1002/jhet.5570400525
18. Sung K, Lee AR. Synthesis of [(4, 5-disubstituted-4*H*-1, 2, 4-triazol-3-yl)thio]alkanoic acids and their analogues as possible anti-inflammatory agents. J. Heterocycl. Chem. 1992;29:1101-1109.
DOI: 10.1002/jhet.5570290512
19. Taib-Brahimi F, Belkadi M, Othman AA. Synthesis of nonionic surfactants with azole ring bearing N-glycosides and their antibacterial activity. Arab. J. Chem.; 2013.
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