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Synthesis and evaluation of α-hydroxy fatty acid-derived heterocyclic compounds with potential industrial interest

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RESUMEN

Síntesis y evaluación de compuestos heterocíclicos derivados de α-hidroxi ácidos grasos con interés industrial potencial

El cloruro del ácido 2-hidroxiheptadecanoico (**2**) reaccionó con el ácido antranílico para producir 3,1-benzoxazin-4-onas 2-sustituidas que fueron usadas como material de partida en la síntesis de compuestos heterocíclicos condensados y no condensados por reacción con nucleófilos nitrogenados, como la hidracina o la formamida. Los productos fueron hechos reaccionar con diferentes moles de óxido de propileno (n = 5, 10, 15) para producir un grupo nuevo de compuestos no-iónicos teniendo una doble función como antibacterianos y tensoactivos que pueden ser usados en la manufactura de medicamentos, cosméticos, pesticidas, o pueden ser usados como aditivos antibacterianos y/o antifúngicos. Se determinaron diversas propiedades físicas de los compuestos preparados así como sus efectos antimicrobianos y sus biodegrabilidad.

PALABRAS-CLAVE: Derivados heterocíclicos - Propiedades antimicrobianas - Propiedades físicas - Tensioactivos

SUMMARY

Synthesis and evaluation of α-hydroxy fatty acid-derived heterocyclic compounds with potential industrial interest

T*2*-Hydroxyheptadecanoic acid chloride (**2**) reacted with anthranilic acid to produce 2-substituted-3,1-benzoxazin-4-one (**3**) which was used as starting material to synthesize some condensed and non-condensed heterocyclic compounds by reaction with nitrogen nucleophiles e.g., hydrazine hydrate, and formamide. The products were subjected to reaction with different moles of propylene oxide (n = 5, 10, 15) to produce a novel group of nonionic compounds having a double function as antibacterial and surface active agents which can be used in the manufacturing of drugs, cosmetics, pesticides or can be used as antibacterial and/or antifungal additives. The surface active properties as surface and interfacial tension, cloud point, foaming height, wetting time, and emulsification power were determined, the antimicrobial and biodegradability were also screened.

KEY-WORDS: Antimicrobial properties - Heterocyclic derivatives - Physical properties - Surface active agents

1. INTRODUCTION

Varied biological activities have been attributed to 2-substituted-3,1-benzoxazin-4-ones (Madkour, 2005) as well as the corresponding quinazoline derivatives including antipyretic (El-Sayed et al., 2005; Amin, 1998), antiinflammatory agents (Amin et al., 1998), antimitotic, anticancer agents (Aly, 2003) and they also have good storage stability in detergents (Mohamed et al., 2003). This led us to synthesize a new series of 4*H*-3,1-benzoxazin-4-one and corresponding quinazoline derivatives which have high expectations for pharmaceutical and industrial applications. This encouraged us to synthesize a novel group of nonionic surface active agents containing the nucleus from α-hydroxy fatty acid. The synthesized compounds which have an active hydrogen atom were subjected to react with propylene oxide with different moles (n = 5, 10, 15) to produce a novel group of nonionic compounds having a double function as antimicrobial and surface active agents which can be useful in the manufacturing of drugs, cosmetics, pesticides or can be use as antibacterial and/or antifungal additives. The surface properties as surface and interfacial tension, cloud point, foaming height, wetting time, and emulsification power were determined. The biodegradability and the antimicrobial were also screened.

2. MATERIALS AND METHODS

Melting points are uncorrected. IR spectra in KBr were measured on a Pye-Uncam SP-1000 infrared spectrophotometer on a KBr disk or nujol. The ^{1}H NMR spectra were obtained on a Varian EM-390-60 MHz spectrometer in DMSO as the solvent. Tetramethylsilane TMS served as an internal reference and chemical shifts are expressed as δ (ppm). Mass spectra were recorded on a GC/MS Finning-MAT. Microanalyses were preformed by the Micro analytical Unit at Cairo University. All the compounds gave satisfactory elemental analyses. Thin layer chromatography (TLC) was carried out on silica gel (MN-Kieselgel G., 0.2 mm thickness) and the plates were scanned under 254 nm ultraviolet light. Antimicrobial and antifungal activity testes were carried out at the microbiology Lab., Faculty of Science, Benha University, Egypt.

2.1. Synthesis of 2-(1-Hydroxyheptadecyl)-1,3-benzoxazin-4-one (3)

A solution of acid chloride **2** (0.01mol) and anthranilic acid (0.01mol) in dry pyridine (30 ml)

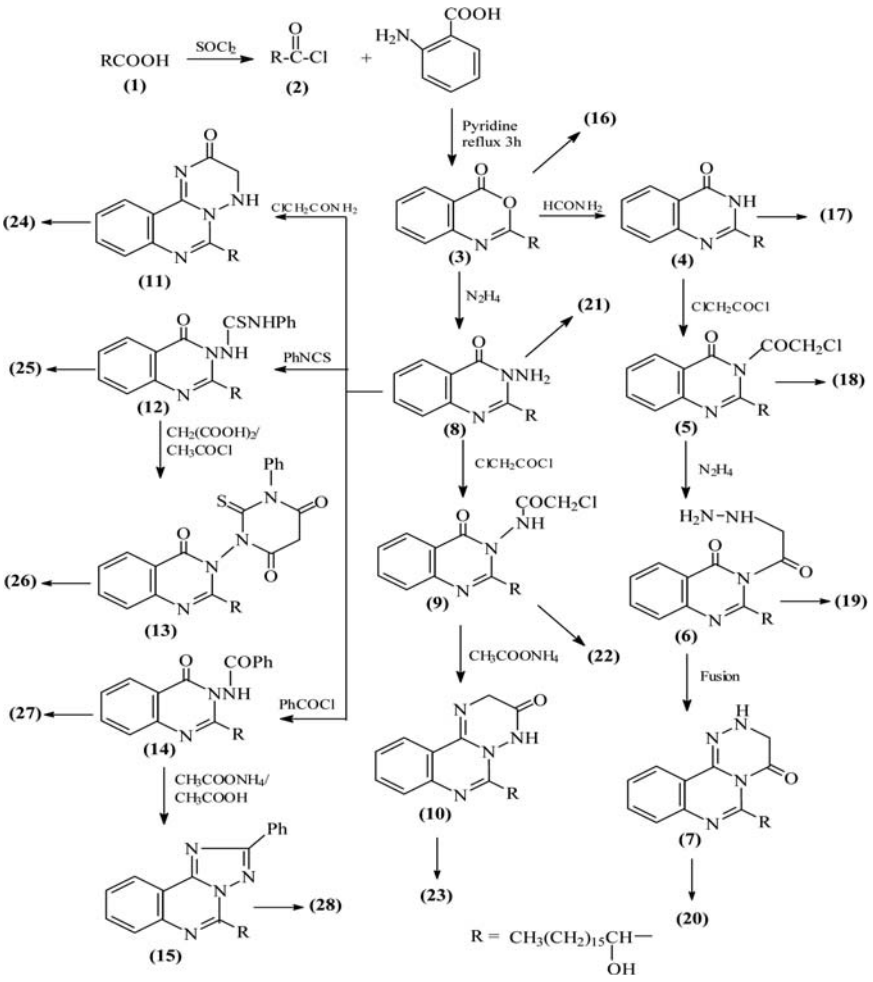
was refluxed for 3 h., the reaction mixture was cooled and poured into cold diluted HCl. The solid that separated was filtered off and recrystallized from toluene to give **3** (Scheme 1). Yield, 80%, mp = 86-88 °C. IR: ν = 3420 (OH), 2910-2860 (CH aliphatic), 3014 (CH aromatic), 1681 (CO) and 1589 cm^{-1} (C=N). ^1H NMR ($CDCl_3$): δ = 0.96 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2), 3.2 (s,1H,-CH-OH), 7.5-8.1 (m, 4H,ArH) and 9.7 (s, 1H, OH). MS: m/z (%) shows no molecular ion peak but shows ion peak m/z = 357 (59.9 %) corresponding to (M^{+}- CO_2), and the base peak at m/z = 59 (100 %). Anal. Calcd for $C_{25}H_{39}NO_3$ (401.59): C, 74.77; H, 9.79; N, 3.49 %. Found C, 74.86; H, 9.93; N, 3.62 %.

2.2. Synthesis of 2-(1-Hydroxyheptadecyl)-quinazolin-4(3H)-one (4)

A mixture of compound **3** (0.01 mol) and formamide (0.015 mol) was refluxed for 3 h in boiling ethanol (30 ml), then poured into water. The separated solid after concentration and cooling was filtered off and crystallized from ethanol to give **4** (Scheme 1). Yield 76%, mp = 75-77 °C, IR: ν = 3450 (OH), 3320 (NH), 2920-2850 (CH aliphatic), 1680 cm^{-1} (CO). ^1H NMR ($CDCl_3$): δ = 0.95 (t, 3H, CH_3), 1,2-1,3 (m, 30H, CH_2 in chain), 3.3 (s,1H,-CH-OH), 8.2 (brs,1H, NH),7.3-7.8(m, 4H, ArH) and 9.7 (brs, 1H, OH). Anal. Calcd for $C_{25}H_{40}N_2O_2$ (400.61): C, 74.96; H, 10.06; N, 6.99 %. Found C, 75.12; H, 10.13; N, 7.21%.

2.3. Synthesis of 3-(2-Chloroacety)-2-(1-hydroxyheptadecyl)-quinazolin-4(3H) -one (5)

A mixture of **4** (0.01 mole) and chloroacetyl chloride (0.01 mole) was refluxed in boiling N, N-dimethylformamide (DMF) (30 ml) for 3 h. Then the mixture was poured into water. The precipitated solid was filtered off, dried and crystallized from benzene to give **5** (Scheme 1). Yield 76%, mp = 93-95°C. IR: ν = 3456 (OH), 2920-2850 (CH aliphatic), 1671, 1699 (CO), 1600 cm^{-1}(C=N).^1H NMR: ($CDCl_3$) δ' = 0.9 (t, 3H, CH_3), 1.25-1.33 (m, 30H, CH_2 of alkyl chain), 4.25 (s, 2H, CH_2), 3.2 (s, 1H, CH-OH), 7.5-



Scheme 1

7.9 (m, 4H, ArH), and 2.0 (s, 1H, OH). Anal. Calcd for $C_{27}H_{41}ClN_2O_3$ (477.09): C, 67.97; H, 8.66; N, 7.43 %. Found C, 67.82; H, 8.51; N, 7.56%.

2.4. Synthesis of 3-(2-Hydrazino-acetyl)-2-(1-hydroxyheptadecyl)-quinazolin-4(3H) -one (6)

A mixture of **5** (0.01 mole) and hydrazine hydrate (0.015 mole) was heated in boiling ethanol (30 ml) under reflux for 4 h. Then the mixture was poured into water. The precipitated solid was filtered off, dried and crystallized from ethanol to give **6** (Scheme 1). Yield 76%, mp = 110-112 °C. IR: ν = 3380, 1680, 1670 and 1625 cm^{-1} attributable to (OH), (CO of two carbonyl groups), (C=N). ^1H NMR: ($CDCl_3$) δ' = 0.96 (t, 3H, CH_3), 1.29-1.53 (m, 30H, CH_2 of alkyl chain), 3.55 (s, 2H, CH_2), 3.2 (s, 1H, CH-OH), 7.5-7.9 (m, 4H, ArH), 7.2 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: m/z (%) shows a molecular ion peak at M^+ = 472 (44.12 %). Anal. Calcd for $C_{27}H_{44}N_4O_3$ (472.68): C, 68.61; H, 9.38; N, 11.85 %. Found C, 68.75; H, 9.49; N, 11.97 %.

2.5. Synthesis of 6-(1-hydroxyheptadecyl)-2,3-dihydro-[1,2,4]triazino[4,3-c]quinazolin-4-one (7)

Heating of the hydrazino derivative **6** above its melting point by fusion in an oil bath for 2 h. After cooling water was added and the solid obtained filtered off and crystallized from xylene to give **7** (Scheme 1). Yield 62 %, mp = 76-78 °C IR: ν = 3340 (OH), 3320 (NH), 2920-2850 (CH aliphatic), 1689 (CO), and 1590 cm^{-1} (C=N). The UV: λ_{mas} 280 nm (ε=3700) attributed to 1,2,4-triazinone nucleus (Cansiz et al., 2004). ^1H NMR: ($CDCl_3$) δ' = 0.95 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2 of alkyl chain), 3.54 (s, 2H, CH_2), 3.2 (s, 1H,CH-OH), 7.3-7.7 (m, 4H, ArH), 7.0 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: m/z (%) shows a molecular ion peak at M^+ = 454 (4.12 %). Anal. Calcd for $C_{27}H_{42}N_4O_2$ (454.66): C, 71.33; H, 9.31; N, 12.32 %. Found C, 71.22; H, 9.26; N, 12.47 %.

2.6. Synthesis of 3-Amino-2-(1-hydroxyheptadecyl)-quinazolin-4(3H)-one (8)

A solution of **3** (0.01 mole) in dry benzene (30 ml) and hydrazine hydrate (0.015 mole) was heated under reflux for 4 h. Then the mixture was poured into water. The precipitated solid was filtered off, dried and crystallized from ethanol to give **8** (Scheme 1). Yield 78 %, mp= 92-94 °C. IR:ν =3350 (OH), 3329 (NH), 2921-2849 (CH aliphatic),1690 (CO), and 1600 cm^{-1} (C=N). ^1H NMR: ($CDCl_3$) δ' = 0.95 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2 of alkyl chain), 3.1 (s, 1H,CH-OH), 7.4-7.9 (m, 4H, ArH), 8.2 (brs,1H, NH) and 9.5 (s, 1H, OH). Anal. Calcd for $C_{25}H_{41}N_3O_2$ (415.62): C, 72.25; H, 9.94; N, 10.11%. Found C, 72.16; H, 9.88; N, 10.04%.

2.7. Synthesis of 3-chloro-N-[2-(1-hydroxyheptadecyl)-4-oxo-quinazolin-3(4H)-yl]-acetamide (9)

A solution of **8** (0.01 mole), was allowed to react with chloroacetyl chloride (0.01 mole) in refluxing pyridine about 2 h, then poured over ice/HCl. The product was filtered and crystallized from toluene to give **9** (Scheme 1). Yield 65 %, mp = 105-107 °C. IR: ν = 3338-3170 (OH and NH), 2920-2850 (CH aliphatic), and 1694, 1666 cm^{-1} (CO). ^1H NMR: δ = 0.85 (t, 3H,CH_3), 1.2-1.5 (m, 30H, CH_2 of alkyl chain), 3.4 (s, 1H, CH-OH), 4.24 (s, 2H, CH_2), 7.3-7.8 (m, 4H, ArH), 8.0 and 9.3 (s, 3H, NH) and 9.7 (s, 1H, OH). MS: m/z (%) shows a molecular ion peak at M^+ = 492 (54.1 %). Anal. Calcd for $C_{27}H_{42}ClN_3O_3$ (492.11): C, 65.90; H, 8.60; Cl, 7.20; N, 8.54 %. Found C, 66.11; H, 8.74; Cl, 7.34; N, 8.71 %.

2.8. Synthesis of 6-(1-hydroxyheptadecyl)-2H-[1,2,4]triazino[2,3-c]quinazolin-3(4H)-one (10)

A solution of compound **8** (0.01 mole) and ammonium acetate (0.01 mole) in acetic acid (30 ml) was refluxed for 3 h, then poured into water. The separated solid after concentration and cooling was filtered off and crystallized from ethanol to give **10** (Scheme 1). Yield 75 %, mp = 73-75 °C. IR: ν = 3430 (OH), 3230 (NH), 2870-2980 (CH), 1660 (CO) and 1605cm^{-1} (C=N). ^1H NMR: ($CDCl_3$) δ' = 0.96 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2 of alkyl chain), 4.40 (s, 2H, CH_2), 3.2 (s, 1H,CH-OH), 7.3-7.6 (m, 4H, ArH), 8.0 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: m/z (%) shows a molecular ion peak at M^+ = 454 (44.11 %). Anal. Calcd for $C_{27}H_{42}N_4O_2$ (454.66):C, 71.33; H, 9.31; N, 12.32 %. Found C, 71.55; H, 9.42; N, 12.25 %.

2.9. Synthesis of 6-(1-hydroxyheptadecyl)-3,4-dihydro-[1,2,4]triazino[2,3-c]quinazolin-2-one (11)

A solution of compound **8** (0.01 mole) and chloroacetamide (0.015 mole) was refluxed for 3 h in boiling N,N-dimethylformamide (DMF) (30 ml). Then the mixture was poured into water. The precipitated solid was filtered off, dried and crystallized from ethanol to give **11** (Scheme 1). Yield 75 %, mp = 75-77 °C. UV: λ_{max} = 330 (450), 314 (1450), 280 (3600), 266 (830) and 255 (600). Bands of this type are exhibit with all fused aromatic azo compounds (Eissa, 2003). ^1H NMR: ($CDCl_3$) δ' = 0.96 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2 of alkyl chain), 3.2 (s, 1H,CH-OH), 3.70 (s, 2H, CH_2), 7.3-7.6 (m, 4H, ArH), 8.0 (s,1H, NH) and 9.5 (s, 1H, OH). Anal. Calcd for $C_{27}H_{42}N_4O_2$ (454.66): C, 71.33; H, 9.31; N, 12.32 %. Gave C, 71.49; H, 9.24; N, 12.23 %.

2.10. Synthesis of 1-[2-(1-hydroxyheptadecyl)-4-oxo-quinazolin-3(4H)-yl]-3-phenyl-thiourea (12)

A solution of compound **8** (0.01 mole) and phenyl isothiocyanate (0.01 mole) was refluxed in

boiling benzene (30 ml) for 3 h, then concentrated and crystallized from butanol to give **12** (Scheme 1). Yield 65 %, mp = 107-109 °C. IR: ν = 3440, 3380-3200, 2960-2870, 1670, 1620 and 1230 cm^{-1} due to (OH), (NH nonbonding and bonded), (CH), (CO), (C=N) and (CS) respectively. ^1H NMR ($CDCl_3$): δ = 0.9 (t, 3H, CH_3), 1,2-1,3 (m, 30H, CH_2 in chain), 3.1 (s, 1H,CH-OH), 4.8 (brs,1H, NH), 6.46-7.9 (m, 4H,ArH) and 9.5 (s,1H,OH). Anal. Calcd for $C_{32}H_{46}N_4O_2S$ (550.81): C, 69.78; H, 8.42; N, 10.17; S, 5.82 %. Found C, 69.89; H, 8.66; N, 10.25; S, 5.96 %.

2.11. Synthesis of 3-(2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4H)-yl)-1-phenyl-2-thioxo-dihydropyrimidine-4,6-dione (13)

A solution of **12** (0.01 mole) and malonic acid (0.01 mole) in acetylchloride (40 ml) was refluxed for 3 h, then poured into water. The separated solid was filtered off and crystallized from benzene to give **13** (Scheme 1). Yield 60 %, mp = 81-83 °C. The IR: ν = 3450, 2950-2860, 1660, 1640 and 1310 cm^{-1} due to (OH), (CH aliphatic), (CO of two carbonyl groups) and (CS) respectively. ^1H NMR ($CDCl_3$): δ = 0.9 (t, 3H, CH_3), 1,2-1,3 (m, 30H, CH_2 in chain), 3.12 (s, 2H, CH_2), 3.2 (s, 1H,CH-OH), 7.0-7.9 (m, 4H,ArH) and 9.5 (s,1H,OH). MS: m/z (%) shows a molecular ion peak at M^++1= 619.8 (34.16 %). Anal. Calcd for $C_{35}H_{46}N_4O_4S$ (618.85): C, 67.93; H, 7.49; N, 9.05 %. Found C, 67.82; H, 7.58; N, 9.18 %.

2.12. Synthesis of N-(2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4H)-yl)benzamide (14)

A solution of **8** (0.01 mole) and benzoyl chloride (0.01 mole) in dry acetone (30 ml) was refluxed for 3 h. Excess solvent was removed and the solid obtained was crystallized from suitable solvent to obtain **14** (Scheme 1). Yield 65 %, mp = 102-104 °C. IR: ν =3410, 3320, 1670, 1650 and 1620 cm^{-1} attributable to (OH), (NH), (CO of two carbonyl groups) and (C=N). ^1H NMR: δ = 0.95 (t, 3H, CH_3), 1.2-1.3 (m, 30H, CH_2), 3.1 (s, 1H, CH-OH), 7.4-7.9 (m, 9H, ArH), 8.3 (s, 3H, NH) and 9.7(s, 1H, OH). Anal. Calcd for $C_{27}H_{43}N_3O_3$ (457.66): C, 70.86; H, 9.47; N, 9.18 %. Found C,70.91; H, 9.51; N, 9.12 %.

2.13. Synthesis of 1-(2-phenyl-[1,2,4]triazolo[1,5-c]quinazolin-5-yl)heptadecan-1-ol (15).

A solution of **14** (0.01 mole) with ammonium acetate (0.01 mole) in acetic acid (30 ml) was heated under reflux for 3 h, then poured into water. The separated solid after concentration and cooling was filtered off and crystallized from butanol to give **15** (Scheme 1). Yield 60 %, mp = 78-80 °C. IR: 3430 (OH), 2910-2860 (CH aliphatic), 3050 (CH aromatic) and 1589 cm^{-1} (C=N). ^{1}HNMR: δ = 0.95 (t, 3H, CH_3), 1.3-1.7 (m, 30H, CH_2), 4.3 (s, 1H, CH-OH), 7.32-8.11 (m, 9H, ArH) and 2.0 (s, 1H, OH). MS: m/z (%) shows a molecular ion peak at M^+= 438 (37.16 %) Anal. Calcd for $C_{27}H_{42}N_4O$ (438.66): C, 73.93; H, 9.65; N, 12.77 %. Found C, 73.81; H, 9.81; N, 12.89 %.

2.14. Conversion of the prepared compounds (3-15) to nonionic surfactants (16 -28)

The processes were completed as described previously by Amin (2004). The accurate amount of propylene oxide taken up and the average degree of propenoxylation (n) was determined from the increased mass of the reaction mixture and confirmed by a spectroscopic tool. The addition of propylene oxide gave a homologues mixture of propenoxylated products which were confirmed by IR and showed, two broad bands at 1100 and 950 cm^{-1} characteristic of νC-O-C ether linkage of polypropenoxy chain, besides the original bands of the compound and ^1H NMR showed, the protons of the propenoxy group δ = 3.2-3.7 (m, $CH_2CH(CH_3)$-O) besides the other protons of the compound.

2.15. Determination of physical properties

2.15.1. Surface and interfacial tension

Surface and interfacial tension were measured using Du-Nouy tensiometer (Findly, 1963) (Kruss, Type 8451) with 0.1 wt% aqueous solution at room temperature (25 °C)

2.15.2. Cloud point

Cloud point was determined by gradually heating 1.0 wt % solution in a controlled temperature bath and recording the time at which the clear, or nearly clear solutions became definitely turbid. The reproducibility of this temperature was checked by cooling the solutions until they become clear again (Wiel et al., 1963).

2.15.3. Wetting time

Wetting time was determined by immersing a sample of cotton fabric in a 1.0 wt % aqueous solution of surfactants (Draves et al., 1931).

2.15.4. Foaming properties

Foaming properties *were* measured according to (El-Sukkary et al., 1987). In this procedure a 25 ml solution (1.0 wt %) was shaken vigorously for 10 seconds in a 100 ml glass stopper, graduated cylinder, at 25 °C. the solution was allowed to stand for 30 seconds, and the foam height was measured.

2.15.5. Emulsification stability

Emulsification stability was prepared from 10 ml of a 20 m mol. aqueous solution of surfactant and 5 ml. of toluene at 40 C. The emulsifying property was determined by the time it took for an aqueous volume

separating from the emulsion layer to reach 9 ml. counting from the moment the shaking was stopped (Takeshi, 1970).

2.16. Biodegradability

Surface tension measurements were made periodically each day, on each sample during the degradation test. Biodegradation (Eter et al., 1974) percent (D) for each sample was calculated using the following formula: $D = [(\gamma_t-\gamma_o)\ (\gamma_{bt}-\gamma_o)] \times 100$, where γ_t = surface tension at time t, γ_o= surface tension at zero time, γ_{bt}= surface tension of blank experiment at time t (without samples).

2.17. Biological activity

The antimicrobial activities of some synthesized compounds were determined in vitro using the hole plate and filter paper disc method (Rosen, 1989) Different species of Gram positive and Gram negative bacteria in addition to some fungal plant pathogens were used. The compounds in question were dissolved in 10% acetone and different concentrations were chosen (125, 250, 500 µg/ml). Agar plates were surface inoculated uniformly from fresh broth culture of Gram +ve, Gram –ve bacteria and fungi. The disks were incubated at 28 °C for 24 h. the formed inhibition zones were measured in mm.

3. RESULTS AND DISCUSSION

3.1. Synthesis

2-(1-Hydroxyheptadecyl)-1,3-benzoxazin-4-one **(3)** were constructed from the preparation of 2-hydroxyheptadecanoic acid from the corresponding pure acid **1** according to procedures described in Eissa et al. (2003), followed by the synthesis of corresponding fatty acid chloride (Amin, 2004), which reacted with anthranilic acid in pyridine to give **3**. The reaction of **3** with formamide or fusion with ammonium acetate at 150 °C gave 2-(1-hydroxyheptadecyl)-3*H*-quinazolin-4-one **(4)**.

The interaction between **4** and chloroacetyl chloride in dimethylformamide gave 3-(2-chloroacety)-2-(1-hydroxyheptadecyl)-3*H*-quinazolin-4-one **(5)** which converted to the corresponding hydrazino derivative **6** via its interaction with hydrazine hydrate in boiling butanol. The hydrazino derivative **6** was cyclized by fusion above its melting point to 6-(1-hydroxyheptadecyl)-2,3-dihydro-[1,2,4]triazino[4,3-c]quinazolin-4-one **(7)**.

Compound **3** reacted with hydrazine hydrate to give amino quinazolinone derivative **8** which was allowed to react with chloroacetyl chloride in refluxing pyridine to give 3-chloro-N-[2-(1-hydroxyheptadecyl)-4-oxo-4H-quinazolin-3-yl]acetamide **(9)** which was treated by ammonium acetate-acetic acid to give 6-(1-hydroxyheptadecyl)-2H-[1,2,4]triazino[2,3-c]quinazolin-3(4H)-one **(10)**. On the other hand, the reaction of **8** with chloroacetamide in boiling *N,N*-dimethyl formamide gave 6-(1-hydroxyheptadecyl)-3,4-dihydro-[1,2,4]triazino[2,3-c]quinazolin-2-one **(11)**. Similarly, compound **8** was submitted to react with phenyl isothiocyanate in benzene, yielding 1-[2-(1-hydroxyheptadecyl)-4-oxo-quinazolin-3(4H)-yl]-3-phenylthiourea **(12)**. The heating of **12** with malonic acid in acetylchloride produced 3-(2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4H)-yl)-1-phenyl-2-thioxo-dihydropyrimidine-4,6-dione **(13)**.

Finally, compound **8** reacted with benzoylchloride and gave N-(2-(1-hydroxy-heptadecyl)-4 oxoquinazolin-3(4*H*)-yl)benzamide **(14)**. Which was treated by ammonium acetate-acetic acid to give 1-(2-phenyl-[1,2,4]triazolo[1,5-c]quinazolin-5-yl)heptadecan-1-ol **(15)**.

3.2. Conversion of the prepared compounds (3-15) to nonionic surfactants (16 -28)

The structure of the surface active agent requires a hydrophilic part, which is accomplished by condensing the alkylene oxide at active terminal

Table 1
Reaction conditions of propenoxylated compounds

Compds	Catalyst, wt %	Temperature °C	Propoxylated products	Yield %	Degree of Propenoxylation n*
3			**16**	60-55	5-15
4			**17**	60-65	5-15
5			**18**	71-67	5-15
6			**19**	82-78	5-15
7			**20**	72-66	5-15
8			**21**	80-75	5-15
9	KOH, 0.01 wt %	120-125	**22**	60-58	5-15
10			**23**	72-66	5-15
11			**24**	72-66	5-15
12			**25**	70-66	5-15
13			**26**	63-59	5-15
14			**27**	67-63	5-15
15			**28**	75-64	5-15

* Degree of propenoxylation was calculated by weight

groups. The term nonionic surfactants refers mainly to polyoxypropylene derivatives, and are usually prepared by the addition of different moles (n) of propylene oxide (n ≅ 5, 10, 15) to synthesized products at any active hydrogen atoms (OH, NH, NH_2) using KOH catalyst.The reaction conditions are shown in Table 1.

3.3. Surface active properties

The investigation of the surface active properties of the oxypropylated compounds has been done in the neutral medium, at a concentration of 1wt % and 25 °C. These types of surfactants are especially interesting because they are not the most common. Therefore the traditional procedure was used to follow up the properties. The results are represented in Table 2.

3.3.1. Surface and interfacial tension

The prepared compounds are shown in Table 2. It is evident that the products obtained have pronounced surface activity. In general, the surface

Table 2
Surface properties of nonionic compounds

Comp.	No.	Surface Tension (dyne/cm) 0.1 m/l	Interfacial tension (dyne/cm)0.1 m/l	Cloud Point °C	Wetting time (sec.)	Emulsion stability (min.)	Foam height (mm)
16	5	33	8.0	54	45	120	104
	10	36	9.5	66	37	92	134
	15	40	10.5	75	25	80	151
17	5	31	10.0	67	45	71	95
	10	35	13.0	67	26	67	120
	15	41	16.0	91	17	63	140
18	5	32	10.0	69	49	125	78
	10	36	11.0	81	33	96	124
	15	40	12.5	90	25	76	142
19	5	32	9.0	73	53	120	90
	10	37	11.5	92	37	95	100
	15	43	14.0	99	26	89	120
20	5	33	8.0	70	51	112	97
	10	38	9.0	87	35	82	128
	15	44	11.5	98	26	73	148
21	5	37	8.0	63	44	96	115
	10	34	10.0	75	33	88	135
	15	32	11.5	96	25	78	155
22	5	30	7.5	77	43	70	105
	10	34	9.0	90	31	72	130
	15	37	10.5	99	20	63	160
23	5	33	10.5	67	49	106	89
	10	37	12.0	83	33	96	110
	15	39	13.5	94	25	75	130
24	5	35	9.0	59	42	95	120
	10	38	10.5	77	35	85	130
	15	40	12.0	89	27	70	155
25	5	35	8.5	64	47	90	90
	10	38	10.5	82	36	79	110
	15	41	13.0	93	25	64	140
26	5	31	7.5	76	42	94	118
	10	35	9.5	86	30	86	138
	15	39	10.0	97	22	76	158
27	5	31	8.5	73	39	110	95
	10	36	10.5	85	31	98	120
	15	39	11.5	93	23	80	150
28	5	32	8.5	70	43	130	112
	10	34	9.5	83	31	98	135
	15	36	10.5	91	20	77	213

Error was:
Surface and interfacial tensions = ± 0.1 dynes/cm.
Cloud point = ± 1 °C
Foam height = ± 2 mm
Wetting time = ± 1 sec
Emulsion = ± 1 min

and interfacial tensions increase with an increase in the molecular weight of the hydrophobic moiety. On the other hand, increases by increasing the number of propylene oxide unit cooperated with the molecule. This leads to an increase in the surface activity

3.3.2. Cloud point

A very important factor in making the most efficient use of nonionic surfactants in aqueous system is an understanding of the property called cloud point. The data in table 2 show that the cloud point increases by increasing the number of propenoxy groups per hydrophobic molecule. The cloud point of the prepared surfactants is less than 100 °C.

3.3.3. Wetting time

For the prepared compounds, it decreased by increasing the moles of propylene oxide in the molecules. At all points of the investigation, the synthesized surfactants were efficient wetting agents. It was found that low propylene oxide content also have the most efficient wetting promoter.

3.3.4. Foam power

Foam npower was also investigated for the nonionic compounds and are generally rated as low to moderately foamy. The foam height of the prepared surfactants increases with increasing propylene oxide unit per molecule of surfactant. A low foaming power has an application in the dyeing industry (Somya et al., 1998)

3.3.5. Emulsion stability

Studies are still being carried out on the use of surfactants in emulsion formation which is of immense importance to technological development. It was proven that the emulsifying stability of the prepared surfactants especially those containing heterocyclic nucleus exhibit good emulsifying properties and increase by decreasing the number of propylene oxide units. These results might lead to the application of the surfactants of choice in the manufacturing of pesticides and cosmetics.

3.4. Biodegradability

The trend of degradation in river die-away tests was followed by the surface tension measurements. The results are given in Table 3. The rate of degradation of these compounds depends on the size of molecule; bulky molecule diffuses through the cell membrane, and its degradation is more difficult. This means that the molecule with the least moles of propylene oxide are more degradable than that which contains higher moles of propylene oxide.

3.5. Biological activity

The results are compiled in Table 4. It has been observed that, most of the synthesized compounds have remarkable antimicrobial activity towards the selected bacteria and fungi. The presence of heterocyclic moiety in the prepared nonionic surfactant molecule revealed an increase in the biological activity. It is therefore clear that these surfactants were effective and inhibited the growth of all tested microorganisms.

4. CONCLUSION

From the previous results, one may conclude that all prepared nonionic surfactants have good emulsifier properties in non edible media such as insecticides and, pesticides.

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Table 3
Biodegradability of the Prepared Surfactants

Compds.	No.	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
16	5	51	68	79	84	96	–	–
	10	48	65	74	80	90	–	–
	15	45	61	72	79	85	93	–
17	5	49	62	70	97	86	92	–
	10	46	56	69	72	83	88	–
	15	40	51	76	70	79	83	–
18	5	53	65	71	81	93	–	–
	10	48	59	69	77	80	91	–
	15	45	57	67	74	78	88	–
19	5	55	55	62	79	87	90	–
	10	49	51	59	67	78	88	–
	15	47	48	57	63	72	85	–
20	5	53	58	66	80	82	93	–
	10	50	56	63	71	79	96	–
	15	49	54	59	68	95	–	–
21	5	57	62	71	79	85	93	–
	10	55	57	69	73	83	90	–
	15	52	52	68	71	79	87	–
22	5	48	60	68	78	89	–	–
	10	45	56	66	73	76	98	–
	15	41	51	64	70	73	80	–
23	5	49	66	79	89	96	–	–
	10	48	63	73	86	95	–	–
	15	43	59	71	79	88	96	–
24	5	50	62	68	79	92	–	–
	10	47	55	63	72	80	93	–
	15	43	49	45	65	77	91	–
25	5	54	54	60	77	80	93	–
	10	48	52	57	65	76	90	–
	15	45	49	54	61	73	86	–
26	5	55	63	73	82	78	80	–
	10	52	59	70	75	85	92	–
	15	49	54	69	73	81	91	–
27	5	54	63	73	84	95	–	–
	10	48	55	67	79	92	–	–
	15	45	50	61	72	84	93	–
28	5	55	67	75	85	95	–	–
	10	52	59	71	82	92	–	–
	15	50	56	61	75	88	93	–

Table 4
Response of various microorganisms to nonionic compounds in vitro

Compd. No.	Bacillus cereus		Escherichia coli		Aspergillus niger		Pencicillium notatum	
	A	MIC (μg/ml)	A	MIC (μg/ml)	A	MIC (μ/ml)	A	MIC (μg/ml)
16	+	250	-	-	+	250	++	125
17	+	125	+	250	++	125	+	250
18	++	250	++	250	++	250	++	125
19	-	125	+	250	+	250	+	250
20	++	250	-	125	-	125	++	250
21	+	250	+	250	-	125	+	125
22	-	125	-	125	+	250	-	125
23	++	250	-	125	+	125	+	125
24	+	125	++	250	+++	125	++	125
25	+	250	-	125	+	250	-	125
26	+	125	+	250	++	125	+	250
27	+	250	-	125	+	125	+	125
28	+	125	++	250	+++	125	++	125

A; Antimicrobial activity of tested compounds; the width of the zone of inhibition indicates the potency of antimicrobial activity, (-) no antimicrobial activity, (+) week activity with diameter equal to (0.5-0.7cm), (++) moderate activity with the diameter zone equal to (1.0-1.2cm), (+++) marked activity with the diameter zone equal to (1.6-1.8cm).
MIC; Minimum inhibition concentration (different concentrations have been chosen 125, 250, 500 μg/ml).

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