GRASAS Y ACEITES, 58 (1),
ENERO-MARZO, 20-28, 2007,
ISSN: 0017-3495

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

Por, **A. M. F. Eissa and R. El-Sayed**

Chemistry Department, Faculty of Science, Benha University, Egypt.
ref_at@hotmail.com

RESUMEN

Síntesis y evaluación de compuestos heterocíclicos derivados de α-hidroxiácidos con interés industrial potencial.

La reacción de cloruro de 2-hidroxiheptadecanoilo (2) con ácido antranílico produjo 2-(1-hidroxiheptadecil)-4H-3,1-benzoxazin-4-ona (3) que fue usada como material de partida en la síntesis de compuestos heterocíclicos condensados y no condensados por reacción con nucleófilos nitrogenados (hidracina y formamida). La reacción de los productos sintetizados con distintas cantidades de óxido de propileno dio un grupo nuevo de compuestos no iónicos con una función doble como antibacterianos y agentes tensioactivos que pueden servir en la manufactura de medicamentos, cosméticos, pesticidas, o como productos antibacterianos y/o antifúngicos. Se determinaron las propiedades tensioactivas así como la capacidad antimicrobiana y la biodegrabilidad de los compuestos sintetizados.

PALABRAS-CLAVE: Actividad antimicrobiana - Propiedades tensioactivas - Síntesis.

SUMMARY

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

The reaction of 2-hydroxyheptadecanoyl chloride (2) and anthranilic acid gave 2-(1-hydroxyheptadecyl)-4H-3,1-benzoxazin-4-one (3) which was used as starting material to synthesize some condensed and non-condensed heterocyclic compounds by a reaction with nitrogen nucleophiles (e.g., hydrazine hydrate, and formamide). The subsequent reaction of the synthetic products with different amounts of propylene oxide gave a novel group of nonionic compounds having a double function as antibacterial and surface active agents which may serve in the manufacturing of drugs, cosmetics, pesticides or as antibacterial and/or antifungal products. The surface active properties such as surface and interfacial tensions, cloud point, foaming height, wetting time, and emulsification power were determined. Antimicrobial and biodegradability were also screened.

KEY-WORDS: Antimicrobial activity - Surface activity - Synthesis.

1. INTRODUCTION

2-Substituted-3,1-benzoxazin-4-ones (Glimore, 1996) as well as their corresponding quinazoline derivatives have been reported to present biological activities such as antipyretic (El-Sayed, 2005; Amin, 1998), anti-inflammatory (Amin et al., 1998), antimitotic, anticancer agents (Aly, 2003). They also have good storage stability in detergents (Mohamed et al., 2003). This led us to synthesize 2-(1-hydroxyheptadecyl)-4*H*-3,1-benzoxazin-4-one (3) and several quinazoline derivatives which may have pharmaceutical and industrial applications. This encouraged us to synthesize a novel group of nonionic surface active agents containing these nuclei. These compounds have a double function as antimicrobial and as surface active agents which may serve in the manufacturing of drugs, cosmetics, pesticides or as antibacterial and/or antifungal agents. The surface properties such as surface and interfacial tension, cloud point, foaming height, wetting time, and emulsification power were determined. Their biodegradability and antimicrobial properties were also screened.

2. MATERIALS AND METHODS

The melting points reported 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). UV spectra were registered with a Perkin-Elmer 550 S UV-Vis spectrophotometer using absolute ethanol as solvent. Mass spectra were recorded on a GC/MS Finning-MAT. Microanalyses were performed 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 tests were carried out by the microbiology Lab., Faculty of Science, Benha University, Egypt.

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

2-Hydroxyheptadecanoyl 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 (10 ml). The separated solid was filtered off and crystallized from toluene to yield, 80%, mp = 86-88 °C. IR: ν 3420 (OH), 2910 and 2860 (CH aliphatic), 3014 (CH aromatic), 1681 (CO) and 1589 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): 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, aromatic) and 9.7 (s, 1H, OH). MS: m/z = 357 (59.9 %) assigned to (M^{+}- CO_2), and 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,74.80; H,9.83; N,3.52 %.

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

A mixture of 3 (0.01 mol) and formamide (0.015 mol) was refluxed in ethanol (30 ml) for 3 h and then poured into water (20 ml). After concentration, the separated solid was filtered off and crystallized from ethanol to give 4. Yield 76%, mp = 75-77 °C, IR: ν 3450 (OH), 3320 (NH), 2920 and 2850 (CH aliphatic), 1680 cm^{-1} (CO). ^{1}HNMR ($CDCl_3$): 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, aromatic) 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,75.00; H,10.02; N,6.95 %.

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

A mixture of 4 (0.01 mol) and chloroacetyl chloride (0.01 mol) was refluxed in N,N-dimethylformamide (DMF) (30 ml) for 3 h. The mixture was then poured into water (20 ml) and the precipitated solid was filtered off, dried and crystallized from benzene to give 5. Yield 76%, mp = 93-95 °C. IR: ν 3456 (OH), 2920 and 2850 (CH aliphatic), 1671 and 1699 (CO), 1600 cm^{-1} (C=N).^{1}HNMR: ($CDCl_3$) 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), 7.5-7.9 (m, 4H, aromatic), 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,67.92; H,8.72; N,7.46 %.

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

A mixture of 5 (0.01 mol) and hydrazine hydrate (0.015 mol) was refluxed in ethanol (30 ml) for 4 h. Then the mixture was poured into water (20 ml) and the precipitated solid was filtered off, dried and crystallized from ethanol to give 6. Yield 76%, mp = 110-112 °C. IR: ν 3380(OH), 1680, 1670 (CO of two carbonyl groups) and 1625 cm^{-1} (C=N); ^{1}HNMR: ($CDCl_3$) 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, aromatic), 7.2 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: shows the molecular ion peak at m/z = 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,68.65; H,9.41; N,11.81%.

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

Hydrazino derivative 6 was heated above its melting point (115 °C) in an oil bath for 2h. After cooling, water (10 ml) was added and the separated solid was filtered off and crystallized from xylene to give 7. Yield 62 %, mp = 76-78 °C. IR: ν 3340 (OH), 3320 (NH), 2920, 2850 (CH aliphatic),1689 (CO), and 1590 cm^{-1} (C=N); UV: λ_{max} 280 nm (ε =3700) attributed to 1,2,4-triazinone nucleus (Cansiz A et al., 2004). ^{1}HNMR: ($CDCl_3$) 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, aromatic), 7.0 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: shows a molecular ion peak at m/z = 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 mol) and hydrazine hydrate (0.015 mol) in dry benzene (30 ml) was refluxed for 4 h. Then the solution was poured into water (20 ml) and the precipitated solid was filtered off, dried and crystallized from ethanol to give 8. Yield 78 %, mp= 92-94 °C. IR: ν 3350 (OH), 3329 (NH), 2921, 2849 (CH aliphatic),1690 (CO), and 1600 cm^{-1} (C=N). ^{1}HNMR: ($CDCl_3$) 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, aromatic), 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,72.22; H, 9.98; N,10.15 %.

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

A solution of 8 (0.01 mol) and chloroacetyl chloride (0.01 mol) in pyridine (15 ml) was refluxed for 2h and then poured onto ice/HCl (20 ml). The product was filtered and crystallized from toluene to give 9. Yield 65 %, mp = 105-107 °C. IR: ν 3338, 3170 (OH and NH), 2920 and 2850 (CH aliphatic),1694 and 1666 cm^{-1} (CO). ^{1}HNMR: 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, aromatic), 8.0 and 9.3 (s, 3H, NH) and 9.7 (s, 1H, OH). MS: shows a molecular ion peak at m/z = 492 (54.1 %). Anal. Calcd. for $C_{27}H_{42}ClN_3O_3$ (492.11): C,65.90; H, 8.60;N, 8.54. Found C,65.95; H, 8.57; N,8.61 %.

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

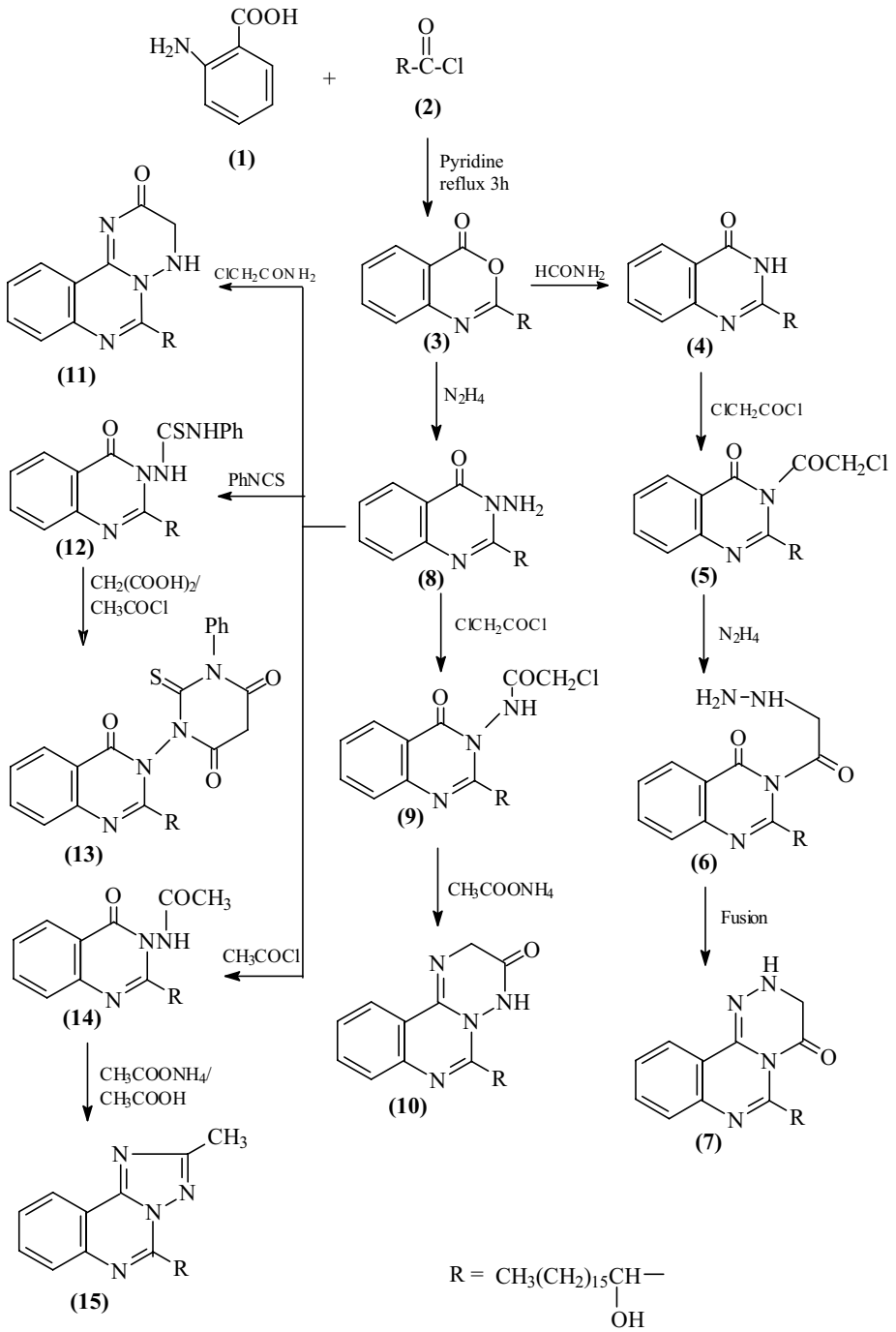
A solution of 8 (0.01mol) and ammonium acetate (0.01mol) in acetic acid (30 ml) was refluxed for 3 h and then poured into water (20 ml). After concentration, the separated solid was filtered off and crystallized from ethanol to give 10.

Yield 75 %, mp = 73-75 °C. IR: ν 3430 (OH), 3230 (NH), 2870 and 2980 (CH), 1660 (CO) and 1605cm^{-1} (C=N). ^{1}HNMR: ($CDCl_3$) 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, aromatic), 8.0 (brs,1H, NH) and 2.0 (s, 1H, OH). MS: shows the molecular ion peak at m/z = 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,71.35; H,9.34; N,12.35 %.

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

A solution of 8 (0.01mol) and chloroacetamide (0.015 mol) was refluxed for 3 h in DMF (30 ml). The solution was then poured into water (20 ml). The precipitated solid was filtered off, dried and crystallized from ethanol to give 11. Yield 75 %, mp = 75-77 °C. UV: λ_{max} = 330 (450), 314 (1450),

Scheme I [a]



a) Compounds from 3 to 15 were propenoxylated at any active hydrogen (OH, NH and NH_2) to give products from 16a-c to28a-c, respectively.

280 (3600), 266 (830) and 255 (600). Bands of this type are seen with all fused aromatic azo compounds (Eissa A M F., 2003). ^{1}HNMR: ($CDCl_3$) 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, aromatic), 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. Found C,71.39; H,9.27; N,12.28 %.

2.10. Synthesis of 1-[2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4H)-yl]-3-phenylthiourea (12)

A solution of 8 (0.01mol) and phenyl isothiocyanate (0.01mol) in benzene (30 ml) was refluxed for 3 h. After concentration, the residue was crystallized from butanol to give 12. Yield 65 %, mp = 107-109 °C. IR: ν 3440 (OH), 3380 and 3200 (NH nonbonding and bonded), 2960 and 2870 (CH), 1670 (CO),1620 (C=N) and 1230 cm^{-1} (CS). ^{1}HNMR ($CDCl_3$): 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, aromatic) 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. Found C,69.76; H,8.46; N,10.15%.

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 (0.01mol) and malonic acid (0.01mol) in acetylchloride (40 ml) was refluxed for 3 h and then poured into water (20 ml). The separated solid was filtered off and crystallized from benzene to give 13. Yield 60 % , mp = 81-83 °C. The IR: ν 3450 (OH), 2950, 2820 (CH aliphatic), 1660 and 1640 (CO of two carbonyl groups) and 1310 cm^{-1} (CS). ^{1}HNMR ($CDCl_3$): 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, aromatic) and 9.5 (s,1H,OH). MS: shows the molecular ion peak at m/z = 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,67.89; H,7.53; N,9.01%.

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

A solution of 8 (0.01 mol) and acetylchloride (0.01 mol) in dry acetone (30 ml) was refluxed for 3 h. The solvent was removed by evaporation to obtain a solid which was crystallized from benzene-hexane to give 14. Yield 65 %, mp = 102-104 °C. IR: ν 3410 (OH), 3320 (NH), 1670 and 1650 (CO of two carbonyl groups) and 1620 cm^{-1} (C=N).^{1}HNMR: 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, aromatic), 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,9.15 %.

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 (0.01mol) and ammonium acetate (0.01mol) in acetic acid (30 ml) was refluxed for 3 h and then poured into water (20 ml). After concentration, the separated solid was filtered off and crystallized from butanol to give 15. Yield 60 %, mp = 78-80 °C. IR: ν 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, aromatic) and 2.0 (s, 1H, OH). MS: shows the molecular ion peak at m/z = 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,73.91; H,9.61; N,12.80 %.

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

They are prepared by the addition of n moles of propylene oxide (n = 5, 10, 15) to one mol of a suitable product using KOH as catalyst. A complete description of the procedure is given in Morgos (1983). The reaction conditions are given in **Table I**. The amount of propylene oxide which reacted and the average degree of propenoxylation were determined through the increment in mass of the reaction mixture and also, by ^{1}HNMR protons. These products were confirmed by spectroscopic methods. The addition of propylene oxide gave a mixture of propenoxylated products whose structures were shown through IR and ^{1}HNMR. IR spectra to be two broad bands at 1100 and 950 cm^{-1}. The characteristic for νC-O-C ether linkage of polypropenoxy chain and ^{1}HNMR spectra showed the protons of propenoxy group at δ 3.2-3.7 (m, $CH_2CH(CH_3)$-O)-.

2.15. Determination of the performance properties

2.15.1. Surface and interfacial tensions

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

2.15.2. Cloud point

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

Table I
Reaction conditions of propenoxylated compounds

Compds	Catalyst, wt %	Temperature °C	Propenoxylated compounds	Yield %	Degree of Propenoxylation
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	KOH, 0.01 wt %	120-125	21	80-75	5-15
9			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

Table II
Surface properties of nonionic compounds[a]

Comp.	N[b]	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)
16a	5	33	8.0	54	45	120	104
16b	10	36	9.5	66	37	92	134
16c	15	40	10.5	75	25	80	151
17a	5	31	10.0	67	45	71	95
17b	10	35	13.0	67	26	67	120
17c	15	41	16.0	91	17	63	140
18a	5	32	10.0	69	49	125	78
18b	10	36	11.0	81	33	96	124
18c	15	40	12.5	90	25	76	142
19a	5	32	9.0	73	53	120	90
19b	10	37	11.5	92	37	95	100
19c	15	43	14.0	99	26	89	120
20a	5	33	8.0	70	51	112	97
20b	10	38	9.0	87	35	82	128
20c	15	44	11.5	98	26	73	148
21a	5	37	8.0	63	44	96	115
21b	10	34	10.0	75	33	88	135
21c	15	32	11.5	96	25	78	155
22a	5	30	7.5	77	43	70	105
22b	10	34	9.0	90	31	72	130
22c	15	37	10.5	99	20	63	160
23a	5	33	10.5	67	49	106	89
23b	10	37	12.0	83	33	96	110
23c	15	39	13.5	94	25	75	130
24a	5	35	9.0	59	42	95	120
24b	10	38	10.5	77	35	85	130
24c	15	40	12.0	89	27	70	155
25a	5	35	8.5	64	47	90	90
25b	10	38	10.5	82	36	79	110
25c	15	41	13.0	93	25	64	140
26a	5	31	7.5	76	42	94	118
26b	10	35	9.5	86	30	86	138
26c	15	39	10.0	97	22	76	158
27a	5	31	8.5	73	39	110	95
27b	10	36	10.5	85	31	98	120
27c	15	39	11.5	93	23	80	150
28a	5	32	8.5	70	43	130	112
28b	10	34	9.5	83	31	98	135
28c	15	36	10.5	91	20	77	213

a) 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
b) n in the number of propylene oxide added to the chosen compound

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 graduated cylinder with glass stopper at 25 °C. The solution was allowed to stand for 30 seconds, and then, the foam height was measured.

2.15.5. Emulsification stability

Emulsification stability was prepared from 10 ml of a 20 mmol aqueous solution of surfactant and 5 ml of toluene at 40 °C. Emulsion stability was determined as the time it took 9 ml of an aqueous layer to separate from the emulsion once shaking had stopped. (Takeshi, 1970).

2.16. Biodegradability

Biodegradability was evaluated by surface tension measurements which were taken each day, on each sample during the degradation test. Biodegradation (Eter et al., 1974) percent (D) for each sample was calculated using the following equation: $D = [(\gamma_t-\gamma_o) / (\gamma_{bt}-\gamma_o)] \times 100$, 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 sample).

2.17. Biological activity

The antimicrobial activities of the synthetized surfactants were determined in vitro using the hole plate and filter paper disc method (Rosen, 1989). Compounds were dissolved in 10% acetone at different concentrations (125, 250, 500 μg/ml). Agar plates were inoculated uniformly from a fresh broth culture of Gram +ve, Gram –ve bacteria and fungi. The disks were incubated at 28 °C for 24 h, and the formed inhibition zones were measured in mm.

3. RESULTS AND DISCUSSION

3.1. Synthesis

2-Hydroxyheptadecanoyl chloride (2) was prepared as described (Eissa et al., 2003; Amin, 2004). The treatment of 2 with anthranilic acid in pyridine gave 2-(1-hydroxyheptadecyl)-4*H*-3,1-benzoxazin-4-one (3). The reaction of 3 with formamide gave 2-(1-hydroxyheptadecyl)-3*H*-quinazolin-4-one (4).

The treatment of 4 with chloroacetyl chloride in (DMF) gave 3-(2-chloroacety)-2-(1-hydroxyheptadecyl)-3*H*-quinazolin-4-one (5) which was converted to the corresponding hydrazino derivative 6 by a reaction with hydrazine hydrate in boiling butanol. The hydrazino derivative 6 was cyclized by heating it above its melting point to 6-(1-hydroxyheptadecyl)-2,3-dihydro-[1,2,4] triazino[4,3-c]quinazolin-4-one (7).

When compound 3 reacted with hydrazine hydrate it gave the amino quinazolinone 8. The reaction of 8 with chloroacetyl chloride in refluxing pyridine gave 3-chloro-N-[2-(1-hydroxyheptadecyl)-4-oxo-4*H*-quinazolin-3-yl]acetamide (9) which was treated by ammonium acetate-acetic acid to yield 6-(1-hydroxyheptadecyl)-2H-[1,2,4]triazino[2,3-c] quinazo-lin-3(4*H*)-one (10). At the same time, the reaction of 8 and chloroacetamide in DMF gave 6-(1-hydroxyheptadecyl)-3,4-dihydro-[1,2,4] triazino [2,3-c] quinazolin-2-one (11).

In addition, the treatment of 8 with phenyl isothiocyanate in benzene gave 1-[2-(1-hydroxyheptadecyl)-4-oxo-quinazolin-3(4*H*)-yl]-3-phenylthiourea (12) which was refluxed with malonic acid in acetylchloride giving 3-(2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl)-1-phenyl-2-thioxo-dihydropyrimidine-4,6-dione (13).

Finally, when compound 8 reacted with benzoylchloride it 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 (16a-c -28a-c)

The structure of a surface active agent requires a hydrophilic component. This is accomplished through the condensation of alkylene oxide at any active terminal group. Thus, the addition of propylene oxide gave mixtures of propenoxylated products whose structures were confirmed by IR and 1HNMR spectroscopy.

3.2.1. Surface active properties

The study of the surface active properties of the oxypropylated compounds was done in an aqueous solution (1wt %, pH = 7) at 25 °C. The results are listed in **Table II**.

3.2.1.1. Surface and interfacial tensions

The surface and interfacial tensions of the prepared compounds are shown in **Table II**. It can be observed that the new nonionic surfactants have pronounced surface activity. In general, the surface and interfacial tensions increase with an increase in the molecular weight of the hydrophobic moiety (Eissa et al., 2003). The data given in **Table II** shows that the values of surface and interfacial tensions increased with the increase in the number of propylene oxide units added to the molecule.

3.2.1.2. Cloud point

A very important factor in making the most efficient use of nonionic surfactants in an aqueous system is an understanding of the property called cloud point. The data **(Table II)** show that the cloud point

Table III
Biodegradability of the prepared surfactants

Compds.	N[a]	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
16a	5	51	68	79	84	96	-	-
16b	10	48	65	74	80	90	-	-
16c	15	45	61	72	79	85	93	-
17a	5	49	62	70	97	86	92	-
17b	10	46	56	69	72	83	88	-
17c	15	40	51	76	70	79	83	-
18a	5	53	65	71	81	93	-	-
18b	10	48	59	69	77	80	91	-
18c	15	45	57	67	74	78	88	-
19a	5	55	55	62	79	87	90	-
19b	10	49	51	59	67	78	88	-
19c	15	47	48	57	63	72	85	-
20a	5	53	58	66	80	82	93	-
20b	10	50	56	63	71	79	96	-
20c	15	49	54	59	68	95	-	-
21a	5	57	62	71	79	85	93	-
21b	10	55	57	69	73	83	90	-
21c	15	52	52	68	71	79	87	-
22a	5	48	60	68	78	89	-	-
22b	10	45	56	66	73	76	98	-
22c	15	41	51	64	70	73	80	-
23a	5	49	66	79	89	96	-	-
23b	10	48	63	73	86	95	-	-
23c	15	43	59	71	79	88	96	-
24a	5	50	62	68	79	92	-	-
24b	10	47	55	63	72	80	93	-
24c	15	43	49	45	65	77	91	-
25a	5	54	54	60	77	80	93	-
25b	10	48	52	57	65	76	90	-
25c	15	45	49	54	61	73	86	-
26a	5	55	63	73	82	78	80	-
26b	10	52	59	70	75	85	92	-
26c	15	49	54	69	73	81	91	-
27a	5	54	63	73	84	95	-	-
27b	10	48	55	67	79	92	-	-
27c	15	45	50	61	72	84	93	-
28a	5	55	67	75	85	95	-	-
28b	10	52	59	71	82	92	-	-
28c	15	50	56	61	75	88	93	-

a) n is the number of moles of propylene oxide added to the chosen compound
Error of calculations was: Biodegradation rate = ± 0.5 %

increases with an increasing number of propenoxy groups per hydrophobic molecule. The cloud point of the prepared surfactants is less than 100 °C.

3.2.1.3. Wetting time

All the prepared compounds showed a decrease in the wetting time with an increasing number of propylene oxide units in the molecule. The synthesized surfactants, even those with low propylene oxide content, were efficient wetting agents.

3.2.1.4. Foam power

Foaming of the nonionic compounds was also studied. The foam height of the prepared surfactants increases with an increase in the propylene oxide units per molecule of surfactant. The low foaming power could have an application in the dyeing industry (Somya et al., 1998).

3.2.1.5. Emulsion stability

Studies are still being carried out on the utilization of surfactants in emulsions formation, which is of immense importance for technological development. It was proven that the prepared surfactants exhibit good emulsifying properties. Emulsion stability increases with a decreasing number of propylene oxide units. These results might lead to the application of the surfactants of choice in the development of pesticides and cosmetics.

Table IV
Response of various microorganisms to nonionic compounds in vitro

Compd	Bacillus cereus		Escherichia coli		Aspergillus niger		Pencicillium notatum	
	A	MIC (μg/ml)	A	MIC (μg/ml)	A	MIC (μg/ml)	A	MIC (μg/ml)
16a	+	250	-	-	+	250	++	125
16b	+	125	+	250	++	125	+	250
16c	++	250	++	250	++	250	++	125
17a	-	125	+	250	+	250	+	250
17b	++	250	-	125	+	125	++	250
17c	+	250	+	250	+	125	+	125
18a	-	125	-	125	+	250	-	125
18b	++	250	-	125	++	125	+	125
18c	+	125	++	250	+++	125	++	125
19a	+	250	-	125	+	250	-	125
19b	+	125	+	250	++	125	+	250
19c	++	250	-	125	+	125	+	125
20a	+	125	++	250	+	125	++	125
20b	+	125	+	250	++	250	+	250
20c	++	250	-	125	++	125	++	250
21a	+	250	+	250	-	125	+	125
21b	-	125	-	125	+	250	-	125
21c	++	250	-	125	+	125	+	125
22a	+	125	++	250	+	125	++	125
22b	+	250	-	125	++	250	-	125
22c	+	125	+	250	++	125	+	250
23a	+	250	-	125	+	125	+	125
23b	+	125	++	250	++	125	++	125
23c	-	125	+	250	++	250	+	250
24a	++	250	-	125	+	125	++	250
24b	+	250	+	250	-	125	+	125
24c	+	125	-	125	+	250	+	125
25a	+	125	+	250	+	250	+	250
25b	++	250	+	125	+	125	++	250
25c	+	250	+	250	-	125	+	125
26a	+	125	+	125	+	250	-	125
26b	++	250	+	125	+	125	+	125
26c	+	125	++	250	+++	125	++	125
27a	++	250	+	125	+	250	-	125
27b	+	125	+	250	++	125	+	250
27c	+	250	++	125	+	125	+	125
28a	+	125	++	250	++	125	++	125
28b	++	250	+	125	++	125	++	250
28c	+	250	+	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 in μg/ml.

3.2.2. Biodegradability

The trend of degradation in river die-away tests was followed by surface tension measurements. The results are given in **Table III**. The rate of degradation of these compounds depends on the size of the molecule; a bulky molecule diffuses through the cell membrane, and its degradation is more difficult. This means that molecules with a low proportion of propylene oxide are more degradable than those containing a higher proportion.

3.2.3. Biological activity

As show in **Table IV** most of the synthesized surfactants 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 biological activity. It is therefore clear that these surfactants were effective and inhibited the growth of all the microorganisms tested.

4. CONCLUSION

It can be concluded that all the prepared nonionic surfactants have good emulsifying properties in non edible media as insecticides and pesticides.

BIBLIOGRAPHY

Aly AA. 2003. Synthesis of novel quinazoline derivatives as antimicrobial agents. *Chin. J. Chem.* **21**, 339.

Amin MS, Eissa AMF, Shaaban AF, El-Sawy AA, El-Sayed R. 1998. Uses of quinazolin-2[(β-propionoyl)isothiocyanate]-4-one as a building block in synthesis of some heterocyclic compounds of expected biological activity. *Indian J. Chem*. **37B**, 1153.

Amin MS, Eissa AMF, Shaaban AF, El-Sawy AA, El-Sayed R. 1998 Utilization of 2-(2-carboxyethyl)-4(3*H*)-quinazolinethione in the synthesis of condensed and noncondensed heterocycles. *Indian J. Heterocycl. Chem*. **7**, 289.

Amin MS, Eissa AMF, Shaaban AF, El-Sawy AA, El-Sayed R. 2004. New heterocycles having double characters as antimicrobial and surface active agents. Part 3: Nonionic compounds from fatty acid hydrazide, *Olaj, Szappan, Kozmetika*. **53**, 124.

Amin MS, Eissa AMF, Shaaban AF, El-Sawy AA, El-Sayed R. 2004. New heterocycles having a double characters; as antimicrobial and surface active agents. Part 1: Nonionic compounds from fatty acid isothiocyanate. *Grasas Aceites* **55**, 370.

Cansiz A, Kaparir M, Demirdag A. 2004. Synthesis of some new 4,5-substituted-4H-1,2,4-trizole-3-thiol derivatives. *Molecules* **9**, 204.

Draves CZ, Clarkso R. 1931. *J. Am. Dye Stuff Reporter* **20**, 201.

Eissa AMF. 2003. Utilites of 2-ethyl-4H-3,1-benzoxazine-4-one in synthesis of some interesting heterocyclic compounds. *Chemistry: An Indian Journal* **1**, 17.

Eissa AMF, Ahmed MHM. 2003. Nonionic surface active agents containing heterocyclic moieties. *Olaj, Szappan, Kozmetika* **52**, 11.

El-Sayed R, Wasfy AAF, Aly AA. 2005. Synthesis of novel heterocycles with antimicrobial and surface activity. *J. Heterocyclic Chem*. **42**, 125.

El-Sukkary MA, El-Sawy AA, El-Dib F. 1987. Synthetic Detergents from Crude rice bran oil. *Hungarian. J. Ind. Chem.* **15**, 317.

Eter ET, Richard RE, Darid A. 1974. Biodegradable surfactants derived from corn starch. *J. Am. Oil Chem. Soc*. **51**, 486.

Findly A. 1963. Practical Physical Chemistry. 6th Ed., Longmans, London, p. 1040.

Gilmore JL, Hays SJ, Capthe BW, Lee C, Emmerling MR, Michael W, Jaen JC. 1996. *Bioorg. Med. Chem. Lett*. **6**, 679.

Mohamed AS, Mohamed FA, Mohamed AA, Abdel-Basset MS. 2003. Synthesis of novel 3H-quinazolin-4-one containing pyrazolinone, pyrazole and pyrimidinone moieties. *Molecules* **8**, 363.

Morgos J, Sallay P, Farkas L, Rus Znar I. 1983. *J. Am. Oil Chem. Soc*. **60**, 11.

Rosen MJ. 1989. 2th Ed., John Wiley & Sons, New York, p. 286.

Somaya AR, Eissa AMF, Nadia A, Ahmad MN. 1998. Synthesis and characterization of some peptides having surface activity using polyethylene glycol. *J. Pharm. Sci*. **7**, 27.

Takeshi H. 1970. Studies of ester containing surfactant: Preparation and properties of sodium sulphalkanoates. *Bull. Chem. Soc.* **43**, 2236.

Wiel JK, Smith FD, Stirton AJ, Bistine RG. 1963. Long chain alkanesulphonates and 1-hydroxy-2-alkanesulphonates: Structure and property relations. *J. Am. Oil. Chem. Soc.* **40**, 538.

Recibido: Febrero 2004
Aceptado: Septiembre 2006