Synthesis and Evaluation of Condensed and Noncondensed Heterocyclic Compounds of Industrial Application

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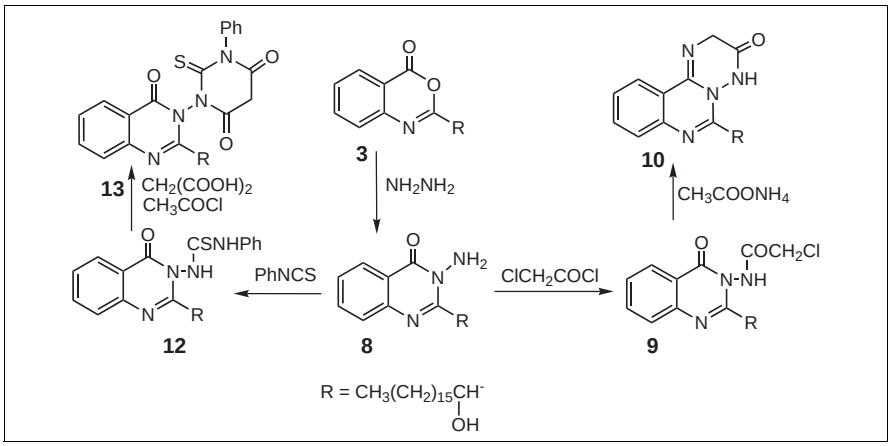

The reaction of 2-hydroxyoctadecanoyl chloride (**2**) and anthranilic acid gave 2-(1-hydroxyheptadecyl)-4*H*-3,1-benzoxazin-4-one (**3**) which was used as starting material to synthesize some condensed and non-condensed heterocyclic compounds by reaction with nitrogen nucleophiles (*e.g.*, hydrazine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

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Introduction.

2-Substituted-3,1-benzoxazin-4-ones [1] as well as their corresponding quinazoline derivatives have been reported to present biological activities such as antipyretic [2,3], anti-inflammatory [4], antimitotic, anticancer agents [5]. Also they have good storage stability in detergents [6]. 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 application. 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 be useful in the manufacture of drugs, cosmetics, pesticides or as antibacterial and/or antifungal. The surface properties such as surface and interfacial tension, cloud point, foaming height, wetting time, and emulsification power were determined. The biodegradability and the antimicrobial were also screened.

Results and Discussion.

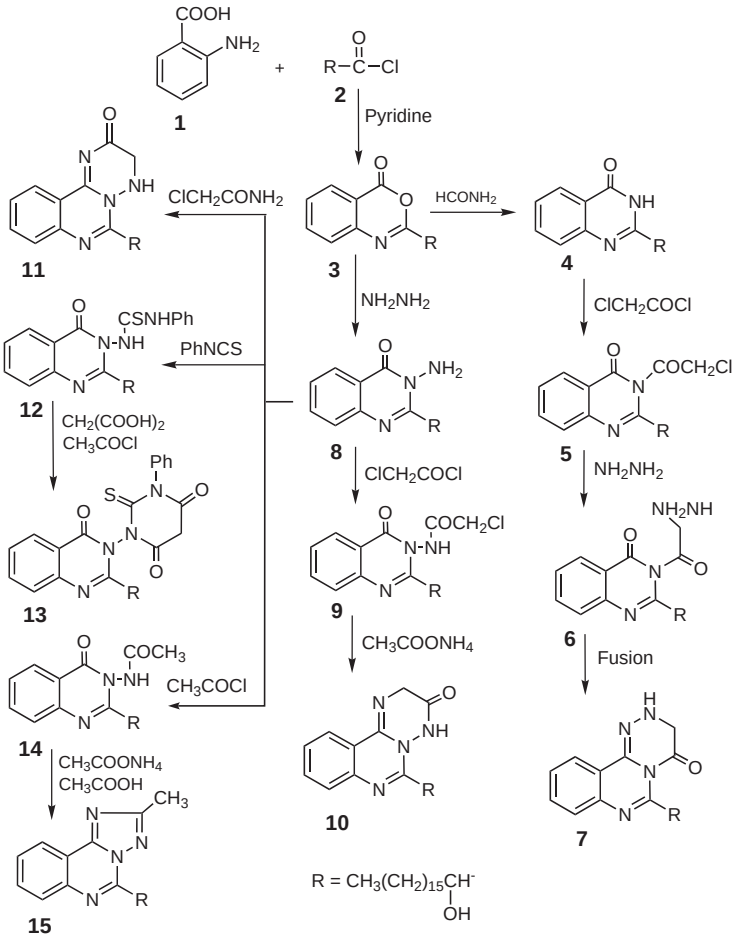
Synthesis.

2-Hydroxyoctadecanoyl chloride (**2**) was prepared as described in [7,8]. Treatment of **2** with anthranilic acid **1** in pyridine afforded 2-(1-hydroxyheptadecyl)-4*H*-3,1-benzoxazin-4-one (**3**). Reaction of **3** with formamide gave 2-(1-hydroxyheptadecyl)-3*H*-quinazolin-4-one (**4**).

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

Reaction of compound **3** with hydrazine hydrate gave the amino quinazolinone derivative **8**. Reaction of **8** and chloroacetyl chloride in refluxing pyridine gave 3-chloro-*N*-[2-(1-hydroxyheptadecyl)-4-oxo-4*H*-quinazolin-3-yl]acetamide (**9**) which was treated with ammonium acetate-acetic acid to give 6-(1-hydroxyheptadecyl)-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-3(4*H*)-one (**10**). 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**) (Scheme **1**).

Scheme 1



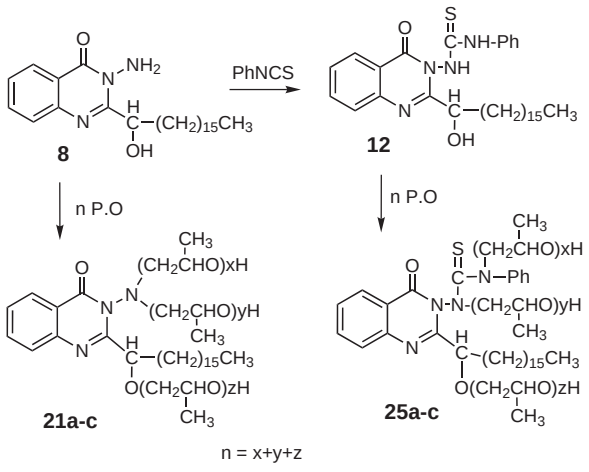
Similarly, treatment of **8** with phenyl isothiocyanate in benzene afforded 1-[2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl]-3-phenylthiourea (**12**). Compound **12** was refluxed with malonic acid in acetylchloride affording 3-(2-(1-hydroxyheptadecyl)-4-oxo-quinazolin-3(4*H*)-yl)-1-phenyl-2-thioxo-dihydropyrimidine-4,6-dione (**13**).

Finally, reaction of **8** and acetyl chloride afforded *N*-(2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl)benzamide (**14**), which was treated with ammonium acetate-acetic acid to give 1-(2-methyl-[1,2,4]triazolo[1,5-*c*]-quinazolin-5-yl)heptadecan-1-ol (**15**).

Conversion of the Prepared Compounds (**3-15**) to Nonionic Surfactants (**16a-c -28a-c**).

The structure of a surface-agent requires a hydrophilic moiety. For this series of compounds this is accomplished by condensation of alkylene oxide with any active hydrogen groups (OH, NH, NH_2) using KOH as catalyst. The reaction conditions are given in Table 1. The addition of different moles (n) of propylene oxide (n ≅ 5,10,15) to synthesized products (**3-15**) gave mixtures of propenoxylated products (**16a-c** to **28a-c**), respectively. (Scheme 2) illustrate the addition of number of propylene oxide at active hydrogen atoms for compounds **8** and **12** as example and so on for other compounds.

Scheme 2



Compounds from **3** to **15** were propenoxylated at any active hydrogen (OH, NH and NH_2) to give products from **16a-c** to **28a-c**, respectively.

Table 1

Reaction conditions of propenoxylated compounds

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

n* Degree of propenoxylation was calculated by weight.

Surface Active Properties.

The study of the surface active properties of the oxypropylated compounds has been done in aqueous solution (1wt %, pH = 7) at 25 °C. The results are listed in Table 2.

Surface and Interfacial Tension.

The surface and interfacial tension of the prepared compounds are shown in Table 2. It is observed that the new nonionic surfactants have pronounced surface activity. In general, the surface and interfacial tensions increases with an increasing in the molecular weight of the hydrophobic moiety [9]. The data given in Table 2 shows that the values of surface and interfacial tension increase with an increase in the number of propylene oxide units added to the molecule.

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 (Table 2) show that the cloud point increases with an increase in the number of propenoxy groups per hydrophobic molecule. The cloud point of the prepared surfactants is less than 100 °C.

Wetting Time.

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

Foam Power.

Foaming of the nonionic compounds was also studied. The foam height of the prepared surfactants increases with increasing in the propylene oxide units per molecule of surfactant. The low foaming power could have an application in dyeing auxiliary industry [10].

Emulsion Stability.

Studies are still being carried out on the utilization of surfactants in emulsion formation, which is of immense importance for technological development for certain types of agents. It was shown that the prepared surfactants exhibit good emulsifying properties. Emulsion stability increases with decreasing the number of propylene oxide units. These results may lead to the application of the surfactants of choice in pesticide and cosmetic formulation.

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 the molecule; a bulky molecule diffuses difficulty 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.

Biological Activity.

As show in Table 4 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 the biological activity. It is therefore clear that these surfactants were effective and inhibited the growth of all tested microorganisms.

Table 2

Surface Properties of Nonionic Compounds.

Compd.	n[b].	Surface Tension (dyne/cm) 0.1 m/l	Interfacial tension (dyne/cm) 0.1 m/l	Cloud Point ℃	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.

Table 3

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	-

Table 3 (continued)=

Compds.	n[a].	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
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 %.

Table 4

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
24a	++	250	-	125	+	125	++	250
24b	+	250	+	250	-	125	+	125
24c	+	125	-	125	+	250	+	125

Table 4 (continued)

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)
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.

EXPERIMENTAL

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. Antimicrobial and antifungal activity testes were carried out by the microbiology Lab., Faculty of Science, Benha University, Egypt.

2-(1-Hydroxyheptadecyl)-4*H*-3,1-benzoxazin-4-one (**3**).

A solution of 2-hydroxyoctadecanoyl chloride (**2**) (1.7 g, 0.015 mole) and (0.5 g, 0.01 mole) of anthranilic acid in (30 ml) of dry pyridine was refluxed for 3 hours the reaction mixture was cooled and poured into cold diluted HCl (10 ml). The separated solid was collected by filtration and crystallized from toluene as yellow needles, 1.4 g (70%), mp 86-88 °C; ir: 3420 (OH), 3014 (CH aromatic), 2910, 2860 (CH aliphatic), 1681 (CO) and 1589 cm^{-1} (C=N); ^{1}H nmr (dueteriochloroform): δ 0.96 (t, 3H, CH_3, J = 1.8 Hz), 1.29-1.33 (m, 30H, CH_2), 3.2 (t, 1H, -*CH*-OH), 7.5-8.1 (m, 4H, phenyl protons) and 9.7 (s, 1H, OH); ms: m/z 357 (3.4) (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, 74.80; H, 9.83; N, 3.52.

2-(1-Hydroxyheptadecyl)-quinazolin-4(3*H*)-one (**4**)

A mixture of **3** (1.5 g, 0.01 mole) and formamide (0.8 g, 0.01 mole) was refluxed in (30 ml) ethanol for 3 hours and then poured into water (20 ml). After concentration, the separated solid was collected by filtration and crystallized from ethanol to yield 0.96g (76%), mp 75-77 °C; ir: 3450 (OH), 3320 (NH), 2920, 2850 (CH aliphatic), 1680 cm^{-1} (CO); ^{1}H nmr (DMSO-d_6): δ 0.95 (t, 3H, CH_3), 1,2-1,3 (m, 30H, CH_2 in chain), 3.3 (t, 1H, -CH-OH), 8.2 (brs,1H, NH),7.3-7.8(m, 4H, phenyl protons) 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.

3-(2-Chloroacety)-2-(1-hydroxyheptadecyl)-quinazolin-4(3*H*)-one (**5**).

A mixture of **4** (1.6 g, 0.01 mole) and chloroacetyl chloride (0.75 g, 0.01 mole) was refluxed in dimethylformamide (30 ml) for 3 hours. Then, the mixture was poured into water (20 ml) and the precipitated solid was collected by filtration, dried and crystallized from benzene as pale yellow needles, 0.8 g (76%), mp 93-95 °C; ir: 3456 (OH), 2920, 2850 (CH aliphatic), 1671, 1699 (CO), 1600 cm^{-1} (C=N); ^{1}H nmr (dueteriochloroform): 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 (t, 1H, CH-OH), 7.5-7.9 (m, 4H, phenyl protons) and 9.7 (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.

3-(2-Hydrazinoacetyl)-2-(1-hydroxyheptadecyl)-quinazolin-4(3*H*)-one (**6**).

To a solution of **5** (1.5 g, 0.015 mole) in ethanol (30 ml) was added hydrazine hydrate (0.6 g, 0.05 mole) and the mixture was refluxed for 1 hour. Then, the mixture was poured into water (20 ml) and the precipitated solid was collected by filration, dried and crystallized from benzene-hexane as white yellow precipitate, 0.73 g (76%), mp 110-112 °C; ir (Nujul): 3380 (OH), 1680, 1670 (CO of two carbonyl groups) and 1625 cm^{-1} (C=N); ^{1}H nmr (DMSO-d_6): 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 (t, 1H, CH-OH), 7.5-7.9 (m, 4H, phenyl protons), 7.2 (brs, 1H, NH) and 9.4 (s, 1H, OH); ms: m/z 472 (44.12), 57 (100).

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.

6-(1-Hydroxyheptadecyl)-2,3-dihydro[1,2,4]triazino[4,3-*c*]-quinazolin-4-one (**7**).

Hydrazino derivative **6** (1.4 g, 0.02 mole) was heated above its melting point (115 °C) in an oil bath for 2 hours. After cooling, water (10 ml) was added and the separated solid was

collected by filtration and crystallized from xylene to give brown needles, 0.85 g (62 %), mp 76-78 °C; ir: 3340 (OH), 3320 (NH), 2920, 2850 (CH aliphatic), 1689 (CO), and 1590 cm^{-1} (C=N); uv: λ mas 280 nm (ε 3700) attributed to 1,2,4-triazinone nucleus [11]; ^{1}H nmr (dueteriochloroform): 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, phenyl protons), 8.2 (brs,1H, NH) and 11.0 (s, 1H, OH). ms: m/z 454 (4.12 %) M^+.

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.

3-Amino-2-(1-hydroxyheptadecyl)-quinazolin-4(3*H*)-one (**8**).

A solution of **3** (1.75 g, 0.01 mole) and hydrazine hydrate (0.65 g, 0.015 mole) in dry benzene (30 ml) was refluxed for 2 hours. Then, the solution was poured into water (20 ml). A yellow precipitate was collected by filtration, dried and crystallized from ethanol, 0.84 g (78%), mp 92-94 °C; ir: 3350 (OH), 3329 (NH), 2921, 2849 (CH aliphatic),1690 (CO), and 1600 cm^{-1} (C=N); ^{1}H nmr: (dueteriochloroform) δ 0.95 (t, 3H, CH_3), 1.29-1.33 (m, 30H, CH_2 of alkyl chain), 3.1 (t, 1H,*CH*-OH), 7.4-7.9 (m, 4H, phenyl protons), 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.

3-Chloro-*N*-[2-(1-hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl]acetamide (**9**).

A solution of **8** (1.5g, 0.01 mole) and chloroacetyl chloride (0.75g, 0.01 mole) in pyridine (15 ml) was refluxed 2 hours then poured into ice/HCl (20 ml). The product was collected bt filtration and crystallized from toluene to give a pale yellow needles, 0.65g (65 %), mp 105-107 °C; ir: 3338, 3170 (OH and NH), 2920, 2850 (CH aliphatic), and 1694, 1666 cm^{-1} (CO); ^{1}H nmr (DMSO-d_6): δ 0.85 (t, 3H,CH_3), 1.2-1.5 (m, 30H, CH_2 of alkyl chain), 3.4 (t, 1H, *CH*-OH), 4.24 (s, 2H, CH_2), 7.3-7.8 (m, 4H, phenyl protons), 8.0 and 9.3 (s, 3H, NH) and 9.7 (s, 1H, OH); ms: m/z 492 (54.1) M^+.

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.

6-(1-Hydroxyheptadecyl)-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-3(4*H*)-one (**10**).

A solution of **8** (1.5 g, 0.01mole) and ammonium acetate (1.3g, 0.01mole) in (30 ml) of acetic acid was refluxed for 3 hours then poured into water (20 ml). After concentration, the separated solid was collected by filtration and crystallized from ethanol as brown needles, 1.2 g (75%), mp 73-75 °C; ir: 3430 (OH), 3230 (NH), 2870, 2980 (CH), 1660 (CO) and 1605cm^{-1} (C=N); ^{1}H nmr: (dueteriochloroform) 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 (t, 1H,*CH*-OH), 7.3-7.6 (m, 4H, phenyl protons), 4.3 (brs, 1H, NH) and 10.5 (s, 1H, OH); ms: m/z 454 (44.11) M^+.

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.

6-(1-Hydroxyheptadecyl)-3,4-dihydro-[1,2,4]triazino[2,3-*c*]-quinazolin-2-one (**11**).

A solution of **8** (1.4 g, 0.01mole) and chloroacetamide (0.8 g, 0.015 mole) was refluxed for 3 hours in (30 ml) of dimethylformamide. Then, poured into water (20 ml). The precipitated solid was collected by filtration, dried and crystallized from chloroform-methanol to yield 1.1 g (75 %), mp 75-77 °C; uv: λmax 330 (450), 314 (1450), 280 (3600), 266 (830) and 255 (600). Bands of this type are exhibit with all fused aromatic azo compounds [12]; ^{1}H nmr: (dueteriochloroform) 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, phenyl protons), 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.

1-[2-(1-Hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl]-3-phenylthiourea (**12**).

A solution of **8** (1.5 g, 0.01 mole) and phenyl isothiocyanate (0.8 g, 0.01 mole) in (30 ml) benzene was refluxed for 3 hour. After concentration, the residue was crystallized from 1-butanol to give yield 0.75 g (65 %), mp 107-109 °C; ir: 3440 (OH), 3380, 3200 (NH nonbonding and bonded), 2960, 2870 (CH), 1670 (CO), 1620 (C=N) and 1230 cm^{-1} (CS); ^{1}H nmr (dueteriochloroform): δ 0.9 (t, 3H, CH_3), 1,2-1,3 (m, 30H, CH_2 in chain), 3.1 (t, 1H, CH-OH), 4.8 (brs, 1H, NH), 6.46-7.9 (m, 4H, phenyl protons) 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.

3-(2-(1-Hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl)-1-phenyl-2-thioxo-dihydropyrimidine-4,6-dione (**13**).

A solution of **12** (1.7 g, 0.01 mole) and malonic acid (0.75g, 0.01 mole) in (40 ml) acetyl chloride was refluxed for 3 hours and then, poured into water (20 ml). The separated solid was collected by filtration and crystallized from benzene to yield 0.65 g (60 %), mp 81-83 °C; ir: 3450 (OH), 2950, 2860 (CH aliphatic), 1660, 1640 (CO of two carbonyl groups) and 1310 cm^{-1} (CS); ^{1}H nmr (dueteriochloroform): 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, phenyl protons) and 9.5 (s, 1H, OH); ms: m/z 619.8 (34.16) M^++1.

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.

N-(2-(1-Hydroxyheptadecyl)-4-oxoquinazolin-3(4*H*)-yl)-acetamide (**14**).

A solution of **8** (1.4 g, 0.01 mole) and benzoylchloride (0.85 g, 0.01 mole) in (30 ml) of dry acetone was refluxed for 2 hours. The solvent was removed by evaporation product to obtained a solid which was crystallized from benzene-hexane as yellow needles 0.75 g, (65 %), mp 102-104 °C; ir: 3410 (OH), 3320 (NH), 1670, 1650 (CO of two carbonyl groups) and 1620 cm^{-1} (C=N); ^{1}H nmr (DMSO-d_6): δ 0.95 (t, 3H, CH_3), 1.2-1.3 (m, 30H, CH_2), 3.1 (t, 1H, *CH*-OH), 7.4-7.9 (m, 9H, phenyl protons), 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.

1-(2-Methyl[1,2,4]triazolo[1,5-*c*]quinazolin-5-yl)heptadecan-1-ol (**15**).

A solution of **14** (1.2 g, 0.01 mole) and ammonium acetate (1.7 g, 0.01 mole) in (30 ml) of acetic acid was heated under reflux for 3 hours and then, poured into water (20 ml). After concentration, the separated solid was collected by filtration and crystallized from 1-butanol to yield 0.80 g (60 %), mp 78-80 °C; ir: 3430 (OH), 2910, 2860 (CH aliphatic), 3050 (CH aromatic)

and 1589 cm^{-1} (C=N); ^1H nmr: δ 0.95 (t, 3H, CH_3), 1.3-1.7 (m, 30H, CH_2), 4.3 (t, 1H, *CH*-OH), 7.32-8.11 (m, 9H, phenyl protons) and 11.0 (s, 1H, OH); ms: m/z 438 (37.16) M^+.

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.

Conversion of the Prepared Compounds (**3-15**) to Nonionic Surfactants (**16a-c -28a-c**).

They are prepared by addition of n moles of propylene oxide (n = 5, 10, 15) to one mol of suitable product using KOH as catalyst. A completed description of the procedure is given in [13]. The amount of propylene oxide which was reacted and the average degree of propenoxylation were determined through the increment in mass of the reaction mixture (increasing of weight of mixture after addition of propylene oxide is the average amount of propenoxylation) and also, by the ^1H nmr protons and these products were confirmed by spectroscopic methods. The addition of propylene oxide gave mixture of propenoxylated products whose structures were by ir and ^1H nmr spectra. ir spectra showed, two broad bands were confirmed at 1100 and 950 cm^{-1} characteristic for νC-O-C ether linkage of polypropenoxy chain and ^1H nmr spectra showed the protons of propenoxy group δ= 3.2-3.7 (m, $CH_2CH(CH_3)$-O)-.

Determination of the Performance Properties.

Surface and Interfacial Tension.

Surface and interfacial tension were measured with a Du-Nouy tensiometer [14] (Kruss, Type 8451) using aqueous solution of surfactants (0.1 wt %) at room temperature (25 °C).

Cloud Point.

Cloud point was determined by gradually heating a surfactant solution (1.0 wt %) in a bath controlled of the temperature, 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 become clear again [15].

Wetting Time.

Wetting time was determined by immersing a sample of cotton fabric in 1.0 wt % aqueous solution of surfactants [16].

Foaming Properties.

Foaming properties were measured according to [17]. 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.

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 which took 9 ml of aqueous layer into separate from the emulsion counting since cession of shaking [18].

Biodegradability.

The biodegradability of the surfactants were evaluated by surface tension measurements that were taken each day on each sample during degradation test. Biodegradation [19] percent (D) for each sample was calculated using the following relation: $D = [(\gamma_t-\gamma_o)/(\gamma_{bt}-\gamma_o)] \times 100$, 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).

Biological Activity.

The antimicrobial activities of the synthesized surfactants were determined *in vitro* using hole plate and filter paper disc method [20]. Compounds were dissolved in 10% acetone at different concentrations (125, 250, 500 μg/ml). Agar plates were inoculated uniformly from 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.

Conclusion.

It can be concluded that all the prepared nonionic surfactants containing heterocyclic moieties have multiple functions as antibacterial and antifungal and as surfactants with good emulsifier properties in nonedible media as insecticides, pesticides, which may serve in the manufacture of drugs, cosmetics, antibacterial and/or antifungal.

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