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Synthesis, antibacterial and surface activity of 1,2,4-triazole derivatives

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Sodium 1-[4-amino-5-mercapto-4*H*-(1,2,4)triazol-3-yl]heptadecane-1-sulfonate **2** has been used as a new precursor to synthesize some important biologically active heterocycles. Reaction of **2** with carbon disulphide in pyridine and acid chlorides yields the 1,2,4-triazole derivatives **3**, **4a** and **4b**. Condensation of **2** with appropriate aldehydes gives **5a-c** which have been cyclized by treating with thioglycollic acid to yield **6a-c**. Reactions of **2** with phthalic anhydride and 4-methylbenzenesulfonyl chloride gives **7** and **8**. In addition, the reaction of **2** with chloroacetaldehyde, phenacyl bromide, urea and chloroacetyl chloride yields **9**, **10**, **11** and **12**, respectively. On the other hand, refluxing **2** with phenyl isothiocyanate gives **13** and **14**. All these products have antimicrobial activity and they can be used as surface active agents.

Keywords: Stearic acid, triazole derivatives, surface activity, antimicrobial activity

IPC: Int.Cl.[7] C 07 D

Among the surface active agents containing heterocyclic moieties[1-3] the present work describes the use of 1,2,4-triazole derivatives as starting material for the synthesis of some important biologically active heterocycles. These compounds display diverse biological activity, including antiparastic, analgesic, antibacterial and anti-inflammatory activity[4-9]. The synthesis of these compounds has received considerable attention in recent years[10-12]. These heterocyclic systems find wide use in medicine, agriculture and industry[13]. Herein is reported the synthesis of a new series of biologically active 1,2,4-triazole derivatives bearing a long alkyl chain with sulfonic acid polar head groups in a single molecular framework. These are expected to behave as anionic surface active agents possessing biological activity.

Results and Discussion

Synthesis

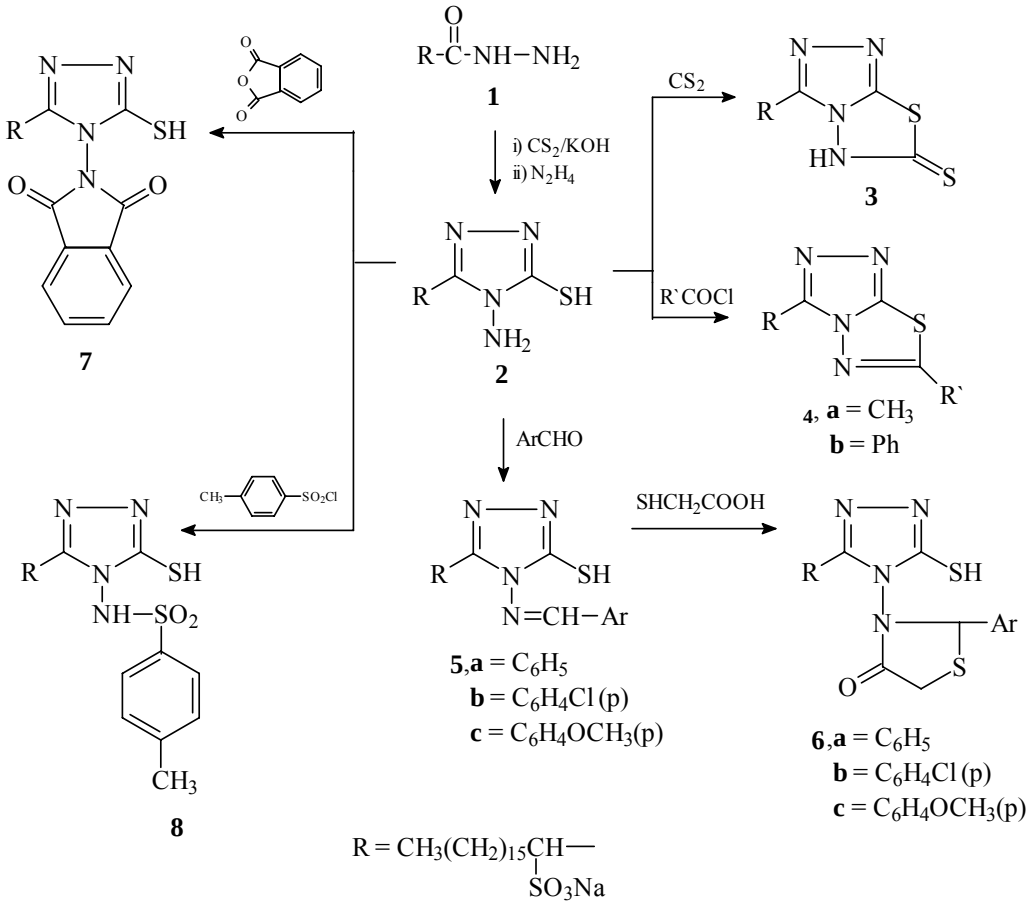
The reaction of sodium salt of α-sulphonated fatty acid hydrazide **1**[14] with carbon disulphide in ethanolic potassium hydroxide gave the potassium salt of the corresponding dithiocarbazate in quantitative yeild. Further, the potassium salts upon reaction with hydrazine hydrate (99%) gave sodium1-[4-amino-5-mercapto-4*H*-(1,2,4)triazol-3-yl]heptadecane-1-sulfonate **2**, which was used as a starting material (**Scheme I**).

The triazole **2** when treated with carbon disulfide in pyridine afforded sodium 1-(6-thioxo-5,6-dihydro-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-3-yl)heptadecane-1-sulfonate **3**.

Compounds **4a** and **4b** were obtained by the reaction of triazole **2** with acetyl and benzoyl chloride respectively. The condensation of triazole **2** with aromatic aldehydes (benzaldehyde, *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde) in refluxing ethanol containing catalytic amounts of piperidine furnished the Schiff bases **5a-c**. Also, the reactivity of **5a-c** towards other reagents has been investigated to obtain newer biologically active heterocycles system. Thus, the reaction of Schiff bases **5a-c** with thioglycollic acid afforded compounds **6a-c**. The reaction of triazole **2** with phthalic anhydride in butanol afforded compound **7**. Addition of 4-methylbenzene sulfonyl chloride to triazole **2** gave the N-4-methylbenzenesulfonate **8**.

On the other hand, the reaction of triazole **2** with one equivalent of chloroacetaldehyde in refluxing ethanol produced sodium 1-(7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl)heptadec-ane-1-sulfonate **9**.

As anticipated, the condensation of **2** with equimolar amounts of phenacyl bromides in the presence of potassium carbonate in absolute ethanol resulted in cyclocondensation to give the corresponding sodium-1-[6-phenyl-7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin-3-yl]heptadecane-1-sulfonate **10**.



Scheme I

Fusion of triazole **2** with urea gave compound **11** in 80% yield.

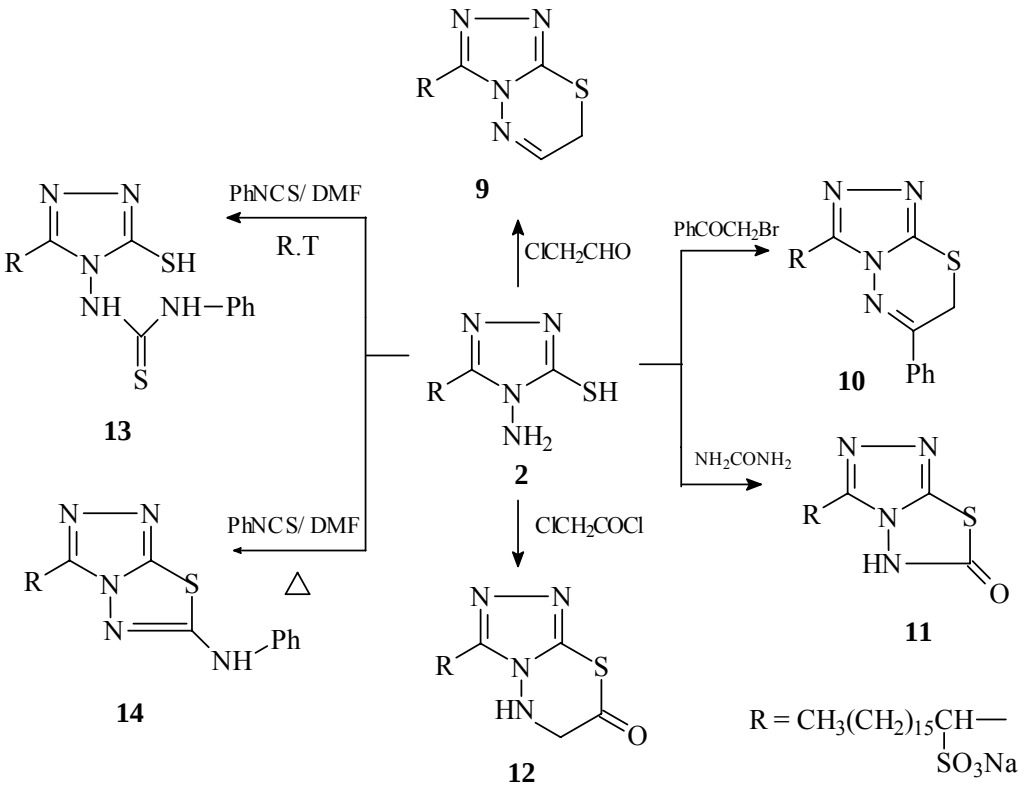
Condensation of **2** with equimolar amounts of chloroacetyl chloride furnished **12**. In view of the known antifungal and antiviral properties[15,16] of substituted thiosemicarbazide derivatives, the synthesis of new compounds incorporating such groups was undertaken. Thus, the reaction of triazole **2** with phenyl isothiocyanate in DMF at rt gave **13**. On the other hand, the reaction of triazole **2** with phenyl isothiocyanate by refluxing in DMF afforded the corresponding thiosemicarbazide derivative **14** which was also obtained by heating **13** above its melting point (**Scheme II**).

Biological activity

The antimicrobial activity of the synthesized compounds was determined *in vitro* using the hole plate and filter paper method[17]. All the compounds were tested for activity against gram positive and gram negative bacteria as well as selected fungi. From the data (**Table I**) it is indicated that the compounds **2**, **6a-c**, **9**, **10**, **13**, and **14** were highly active against the selected pathogens, while the compounds **3**, **4a**, **4b**, **7**, **11** and **12** were moderately active against the different strains of bacteria and fungi.

Surface active properties

The investigation of the surface active properties (surface and interfacial tension, Kraft point, wetting time, foaming height, emulsion stability, and stability towards hydrolysis) of 1,2,4-triazole derivatives bearing long alkyl chain with sulfonic acid hydrophilic center, has been done at concentration of 1 wt% at 20°C in distilled water. The results are represented in **Table II**. The biodegradability properties were also determined (**Table III**) to observe the rate of degradation of these compounds. These anionic surfactants are interesting because they are uncommon.



Scheme II

Table I — Antimicrobial activity of the tested compounds

Tested	*B. substilis*		*S. aureus*		*E. coli*		*A. niger*	
compd	A	MIC	A	MIC	A	MIC	A	MIC
2	+++	500	+	250	++	125	++	500
3	++	250	+++	250	++	500	+	250
4a	+	125	+	250	+	250	+	500
4b	++	125	+	250	+	250	+	500
5a	++	250	++	250	++	125	++	125
5b	++	250	++	250	++	125	++	125
5c	++	250	+	125	+	250	+	250
6a	+++	250	+	125	+	250	++	250
6b	+++	250	+	125	+	250	+++	250
6c	+++	250	+	125	+	250	+++	250
7	++	250	+	125	+	250	+	250
8	++	250	+	125	+	250	+	250
9	+++	500	++	250	++	125	++	250
10	+++	250	+++	125	++	250	++	500
11	++	125	+	250	++	125	++	250
12	++	125	+	250	+	500	+	250
13	+++	250	++	250	+	250	+	500
14	+++	250	++	250	++	250	+	500

A = antimicrobial activity of tested compounds, MIC = minimum inhibitory concentration

+ > 5 mm slightly active, ++ > 7 mm moderately active, +++ > 9 mm highly active.

(i) Surface and interfacial tension: The results indicate that all the synthesized products are surface active. Lower values of surface tension and interfacial tension were recorded for all the compounds. The lower values of surface and interfacial tension may possibly be due to electrostatic repulsion between the ionized molecules.

(ii) Kraft point (T_{kp}): Kraft point of the prepared anionic surfactants were measured at the temperature where 1% dispersion became clear on gradual heating. All the synthesized products were found to be freely soluble in water. In general, T_{kp} measurements proved that, the higher the molecular weight, the higher is the T_{kp}. Yet, in some cases, this may not hold true due to the presence of retarding groups in some molecules. So, in case of compounds **5a-c**, **6a-c**, **7** and **12** the aryl group increases T_{kp} compared to -SH group which decreases T_{kp}.

(iii) Wetting time: Wetting time of the synthesized compounds were determined by measuring the sinking time (in seconds) of a gray cotton skin in the surfactant solution. The results show that the products were very effective wetting agents in distilled water solutions. It is hoped that they will find a wide range of applications in the textile industry.

Table II — Surface properties of the synthesized compounds

Compd	Surface tension (dyne/cm) 0.1 m/L	Interfacial tension (dyne/cm) 0.1 m/L	Kraft Point °C	Wetting time (s)	Emulsion stability (min)	Foam height (mm)	Stability to hydrolysis (min)
2	33.50	6.0	23	120	23.48	180	37.44
3	32.0	7.0	20	115	39.05	160	40.12
4a	35.5	8.5	24	135	42.67	175	38:40
4b	36.0	8.0	19	120	38.9	185	34:50
5a	34.5	9.5	18	100	56.2	190	41:20
5b	36.0	8.5	23	115	47.6	215	37:29
5c	35.0	8.6	22	95	49.3	180	35:09
6a	32.0	10.2	19	115	40.1	215	37:6
6b	33.5	11.5	24	117	37.6	215	40:7
6c	32.5	9.5	22	105	38.0	205	36:2
7	31.5	10.5	17	125	37.4	210	48:0
8	32.5	11.7	20	135	35.9	205	44:7
9	37.0	8.4	25	118	61.2	165	35:8
10	36.0	9.3	18	105	57.0	184	42:8
11	35.5	10.4	22	120	62.1	179	45:8
12	32.5	9.4	18	104	46.2	189	36:8
13	33.0	8.0	17	120	53.1	210	35:8
14	35.0	9.45	19	110	49.2	215	39:8

Table III — Biodegradability of the prepared compounds

Compd	1st day	2nd day	3rd day	4th day	5th day	6th day	7th Day
2	42	46	55	69	84	92	-
3	45	54	67	77	85	94	-
4a	41	46	62	69	91	-	-
4b	43	52	64	75	92	96	-
5a	38	46	58	69	82	95	-
5b	42	55	66	77	89	96	-
5c	41	53	60	71	83	91	-
6a	39	48	59	68	77	89	-
6b	36	44	55	67	76	88	92
6c	39	45	57	65	73	86	94
7	36	46	59	70	89	96	-
8	38	49	61	74	88	95	98
9	46	55	67	78	88	95	-
10	41	50	65	76	85	93	-
11	46	55	67	78	88	95	-
12	42	53	65	74	87	96	-
13	45	58	71	83	94	-	-
14	44	56	68	79	89	95	-

(iv) Foaming height: The values of the foaming height were measured for the prepared compounds and it was revealed that the synthesized products have low foaming capacity. The low foaming power make these compounds suitable for application in the dyeing and auxiliary industries.

(v) Emulsion stability: All the prepared surfactants are good emulsifying agents. They could be useful in dye baths in the textile industry and as emulsion paints.

(vi) Stability towards hydrolysis: The studies revealed that the prepared compounds are moderately stable in basic medium. Also, all the anionic surfactants containing heterocyclic moieties have high stability.

Biodegradability

The results show that the biodegradability decreases with increasing molecular weight of the synthesized compounds. 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 these compounds have a higher rate of degradation to the extent of about 95% degradation in

about 6 days. Moreover, anionic surfactants containing heterocyclic moieties serve a dual function as surface active agents as well as antibacterials.

Experimental Section

Melting points are uncorrected. IR spectra were measured on a Pye-Unicam SP-1000 infrared spectrophotometer in KBr disk or Nujol. The ^{1}H NMRspectra were obtained on a Varian EM-390 60 MHz spectrometer with $CDCl_3$ as the solvent. Tetramethylsilane (TMS) served as an internal reference and chemical shifts are expressed in δ (ppm). Mass spectra were recorded on a Finning-MAT GC-MS. Microanalyses were preformed by the Microanalytical 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 laboratory, Faculty of Science, Zagazig University, Benha-branch, Egypt.

Sodium 1-hydrazinocarbonyl-heptadecane-1-sulfonate 1

The sodium salt of α-sulphonate of stearic acid hydrazide **1** was prepared according to the method in the literature[14]. Yield 70%, m.p. 121-3°C; IR (KBr): 3422, 3300 (NH), 2922-2852 (CH in alkyl chain), 1350 (S=O) and 1691 cm^{-1}(C=O).

Sodium1-(4-amino-5-mercapto-4*H*-[1,2,4]triazol-3-yl)heptadecane-1-sulfonate 2

The acid hydrazide **1** (0.01 mole) was added to absolute alcohol (50 mL), containing KOH (1.6 g) at rt. Carbon disulphide was added (2.3 g, 0.013 mole) and the mixture stirred at rt for 10 hr. The mixture was diluted with ether (30 mL) and stirred for further 1hr. The potassium salt was used for the next stage without further purification. Hydrazine hydrate (99%, 0.02 mole) was gradually added to the above potassium salt (0.01 mole) dissolved in water (20 mL) with stirring and the mixture was refluxed gently for 3 hr during which hydrogen sulphide evolved and the colour of the reaction mixture changed to deep green. It was then cooled to 5 °C and acidified with conc. HCl to *p*H 1.00. A yellow solid separated out which was filtered, washed with water and purified by recrystallisation from ethanol to afford the triazole **2**. Yield 70%, m.p. 88-90°C. IR (KBr): 3326 (NH), 2920-2850 (CH in alkyl chain), 2372 (SH), and 1599 cm^{-1} (C=N); ^{1}H NMR($CDCl_3$): δ 0.90 (t, J = 7.2 Hz, 3H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 3.01 (s, 1H, SH), 2.0 (s, 2H, NH) and 4.25 (t, 1 H, CH-SO_3Na). Anal. Calcd for $C_{19}H_{37}N_4NaO_3S_2$ (Mol.wt.456.65): C, 49.98; H, 8.17; N, 12.27; S, 14.04. Found C, 50.02; H, 8.13; N, 12.22; S, 14.12 %.

Sodium 1-(6-thioxo-5,6-dihydro-[1,2,4]triazolo-[3,4-*b*][1,3,4]thiadiazol-3-yl)heptadecane-1-sulfonate 3

A mixture of triazole **2** (0.01 mole), carbon disulphide (0.01 mole), and dry pyridine (20 mL) was heated under reflux for 3hr. It was cooled and poured on ice-water. A solid product **3** was obtained by filtration and purification by recrystallisation from ethanol. Yield 73%, m.p. 62-5°C; IR (Nujol): 3229 (NH), 2921-2851 (CH in alkyl chain), 1600 (C=N), and 1375 cm^{-1} (C=S); ^{1}H NMR($CDCl_3$): δ 0.96 (t, J = 7.0 Hz, 3H, terminal CH_3), 1.28-1.32 (m, 30 H, CH_2 in alkyl chain), 2.0 (s, 1H, NH, exchangeable) and 4.23 (t, J = 4.7 Hz, 1 H, CH-SO_3Na); MS: m/z (%) M^++1 = 499 (40). Anal. Calcd for $C_{20}H_{35}N_4NaO_3S_3$ (Mol.wt.498.71): C, 49.17; H, 7.07; N, 11.23; S, 19.29. Found C, 49.12; H, 7.11; N, 11.21; S, 19.33 %.

General procedure for preparation of 4a and 4b

To a solution of triazole **2** (0.01 mole) in dry pyridine (25 mL), the acid chlorides (0.01 mole), namely, acetyl chloride and/or benzoyl chloride were added dropwise. The reaction mixture was stirred at rt for 45 min and then heated for 2 hr on a steam bath. It was then poured into crushed ice. The solid products obtained by filtration were purified by recrystallisation from the appropriate solvent to give **4a** and **4b**.

Sodium 1-(6-methyl-[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazol-3-yl)heptadecane-1-sulfonate 4a: Yield 65%, m.p. 64-6°C; IR (Nujol): 2920-2850 (CH in alkyl chain), and 1589 cm^{-1} (C=N); ^{1}H NMR($CDCl_3$): δ 0.90 (t, J = 7.0 Hz, 3 H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 2.35 (s, J = 6.4 Hz, 3H, CH_3), 4.26 (t, J = 4.8 Hz, 1 H, CH-SO_3Na); MS: m/z (%) M^+ = 480 (54). Anal. Calcd for $C_{21}H_{37}N_4NaO_3S_2$ (Mol.wt.480.67): C, 52.48; H, 7.76; N, 11.66; S, 13.34. Found C, 52.44; H, 7.80; N, 11.61; S,13.38 %.

Sodium 1-(6-phenyl-[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazol-3-yl)heptadecane-1-sulfonate 4b. Yield 75%, m.p. 63-5°C; IR (Nujol): 2921-2851 (CH in alkyl chain) and 1599 cm^{-1} (C=N); ^{1}H NMR($CDCl_3$):

δ 0.95 (t, *J* = 7.4 Hz, 3 H, terminal CH_3), 1.28-1.33 (m, 30 H, CH_2 in alkyl chain), 4.25 (t, *J*= 4.4 Hz, 1 H, CH-SO_3Na), and 6.8-7.2 (m, 5 H, ArH). Anal. Calcd for $C_{26}H_{39}N_4NaO_3S_2$ (Mol.wt. 542.74): C, 57.54; H, 7.24; N, 10.32; S, 11.82. Found C, 57.58; H, 7.34; N, 10.37; S, 11.87 %.

General procedure for preparation of Schiff bases 5a-c

A mixture of triazole **2** (0.01 mole) and the corresponding aldehydes (0.01 mole) in ethanol (25 mL) was treated with concentrated HCl (0.5 mL) and refluxed for 2 hr. The reaction mixture on cooling was filtered and purified by recrystallization from ethanol to give **5a-c**.

Sodium1-[4-(benzylidene-amino) – 5-mercarpto-4*H*-[1,2,4]triazol-3-yl]heptadecane-1-sulfonate 5a. Prepared from benzaldehyde. Yield 80%, m.p.105-7°C; IR (KBr): 2920-2850 (CH in alkyl chain),1601 (C=N) and 2569 cm^{-1} (SH); ^1H NMR($CDCl_3$): δ 0.90 (t, *J*=7.1Hz, 3 H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 12.86 (s, 1H, SH), 4.27 (t, *J* = 4.0Hz, 1H, CH-SO_3Na), 6.9-7.86 (m, 5H, ArH) and 8.2 (s, 1H, N=CH). Anal. Calcd for $C_{26}H_{41}N_4NaO_3S_2$ (Mol.wt. 544.76): C, 57.33; H, 7.59; N, 10.28. Found C, 57.29; H, 7.54; N, 10.24 %.

Sodium1 - {4 - [(4 - chlorobenzylidene-amino]-5-mercarpto-4*H* - [1, 2, 4]triazol-3-yl}heptadecane-1-sulfonate 5b. Prepared from *p*-chlorobenzaldehyde. Yield 80%, m.p.110-2°C; IR (KBr): 2920-2850 (CH in alkyl chain), 1603 (C=N) and 2537 cm^{-1}(SH); ^1H NMR($CDCl_3$): δ 0.95 (t, *J*=7.0 Hz, 3H, CH_3), 1.27-1.31 (m, 30 H, CH_2 in alkyl chain), 4.26 (t, *J*=3.9 Hz, 1H, CH-SO_3Na), 6.9-7.4 (m, 4H, ArH) and 8.3 (s, 1H, N=CH). Anal. Calcd for $C_{26}H_{40}ClN_4NaO_3S_2$ (Mol.wt.579.20): C, 53.92; H, 6.96; N, 9.67. Found C, 53.97; H, 7.01; N, 9.72 %.

Sodium1-{5-mercapto-4[(4-methoxybenzylidene)-amino]-4*H*-[1,2,4]triazol-3-yl}heptadecane-1-sulfonate 5c. Prepared from *p*-methoxybenzaldehyde. Yield 80%, m.p.115-7°C; IR (KBr): 2920-2850 (CH in alkyl chain), 1605 (C=N) and 2557 cm^{-1} (SH); ^1H NMR($CDCl_3$): δ 0.90 (t, 3 H, terminal CH_3), 1.29-1.34 (m, 30 H, CH_2 in alkyl chain), 3.73 (s, 3H, OCH_3), 4.22 (t, 1H, CH-SO_3Na), 6.9-7.4 (m, 4H, ArH). Anal. Calcd for $C_{27}H_{43}N_4NaO_4S_2$ (Mol.wt. 574.79): C, 56.42; H, 7.54; N, 9.75. Found C, 56.48; H, 7.61; N, 9.70%.

General procedure for preparation of 6a-c

To a solution of Schiff bases **5a-c** (0.01 mole) in dry acetone was added thioglycollic acid (0.01 mole). The reaction mixture was refluxed for 3 hr. Solid products were obtained after cooling to give the adducts **6a-c** which were purified by recrystallisation from ethanol.

Sodium1-[5-mercapto-4[(4-oxo-2-phenylthiazo-lidin-3-yl)-4*H*-[1, 2, 4]triazol-3-yl]heptadecane-1-sulfonate 6a. Yield 76%, m.p.78-80°C; IR (Nujol): 2919-2851 (CH in alkyl chain), 2560 (SH) 1593 cm^{-1} (C=N); ^1H NMR($CDCl_3$): δ 0.96 (t, *J* =7.4Hz, 3 H, terminal CH_3), 1.28-1.33 (m, 30 H, CH_2 in alkyl chain), 3.02 (s, 1H, SH), 3.27,3.38 (2s, 2H, CH_2 of the ring), 4.27 (t, *J* =4.2 Hz, 1H, CH-SO_3Na), 5.92 (s, 1H, CH-Ph) and 7.06-7.14 (m, 5 H, ArH). Anal. Calcd for $C_{28}H_{43}N_4NaO_4S_3$ (Mol.wt. 618.86): C, 54.34; H, 7.00; N, 9.05; S, 15.54. Found C, 54.41; H, 7.11; N, 9.12; S, 15.48%.

Sodium1 - {4 -[2-(4-chlorophenyl)-4-oxothiazolidin-3-yl]-5-mercarpto-4*H*-[1,2,4]triazol-3-yl}heptadec-ane-1-sulfonate 6b. Yield 66%, m.p. 83-5°C; IR (KBr): 2920-2850 (CH in alkyl chain), 2527 (SH), 1600 cm^{-1} (C=N); ^1H NMR($CDCl_3$): δ 0.90 (t, *J* =7.1Hz, 3 H, terminal CH_3), 1.27-1.31 (m, 30 H, CH_2 in alkyl chain), 3.0 (s, 1H, SH), 4.26 (t, *J* = 4.3Hz, 1H, CH-SO_3Na), 3.26,3.31 (2s, 2H, CH_2 of the ring) 5.12 (s, 1H, CH-Ph) and 6.3-7.5 (m, 4 H, ArH); MS: m/z (%) M^++1 = 654 (33). Anal. Calcd for $C_{28}H_{42}ClN_4NaO_4S_3$ (Mol.wt.653.31): C, 51.48; H, 6.48; N, 8.58; S, 14.72. Found C, 51.54; H, 6.45; N, 8.52; S, 14.78%.

Sodium1-{5-mercarpto-4-[2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl]-4*H*-[1,2,4]triazol-3-yl}hepta-decane-1-sulfonate 6c. Yield 60%, m.p. 81-3°C; IR (KBr): 2920-2850 (CH in alkyl chain), 2520 (SH),1599 cm^{-1}(C=N); ^1H NMR($CDCl_3$): δ 0.95 (t, 3 H, terminal CH_3), 1.1 (s, 1H, OCH_3), 1.3-1.5 (m, 30 H, CH_2 of alkyl chain), 3.1 (s, 1H, SH), 4.26 (t, 1H, CH-SO_3Na), 3.35 (s, 2H, CH_2 of the ring), 4.01 (s, 3H, OCH_3), 5.23 (s, 1H, CH-Ph) and 6.5-7.2 (m, 4 H, ArH). Anal. Calcd for $C_{29}H_{45}N_4NaO_5S_3$ (Mol.wt. 648.89): C, 53.68; H, 6.99; N, 8.63; S, 14.82. Found C, 53.72; H, 7.11; N, 8.68; S, 14.86%.

Sodium1-[4-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-5-mercapto-4*H*-[1,2,4]triazol-3-yl]heptadecane-1-sulfonate 7

A mixture of triazole **2** (0.01 mole) and phthalic anhydride (0.01 mole), in butanol (20 mL) was heated under reflux for 4hr. The solution was then concentrated. A solid product **7** was obtained by filtration which was purified by recrystallization from ethanol. Yield 55%, m.p. 91-3°C; IR (KBr): 2920-2850 (CH in alkyl chain), 3047 (CH aromatic), 2461

(SH), 1695,1988 (C=O) and 1599 cm^{-1} (C=N); ^1H NMR ($CDCl_3$): δ 0.83 (t, 3 H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 3.01 (s, 1H, SH), 4.27 (t, 1H, CH-SO_3Na) and 8.2-8.7 (m, 4 H, ArH). Anal. Calcd for $C_{27}H_{39}N_4NaO_5S_2$ (Mol.wt. 586.75): C, 55.27; H, 6.70; N, 9.55; S, 10.93. Found C, 55.21; H, 6.76; N, 9.61; S, 10.86%.

Sodium 1[5-mercarpto-4-(toluene-4-sulfonyl-amino)-4*H*-[1,2,4]triazol-3-yl)heptadecane-1-sulfonate 8

A mixture of triazole **2** (0.01 mole) and 4-methylbenzenesulfonyl chloride (0.01 mole) in dry pyridine (20 mL) was heated under reflux for 3hr. It was then cooled and poured on ice-water. A solid product **8** was obtained by filtration which was purified by recrystallization from ethanol. Yield 73%, m.p.73-5°C; IR (KBr): 3250 (NH), 2921-2851 (CH in alkyl chain), 1610 (C=N), 1170 and 944 (SO_2) and 2455 cm^{-1}(SH); ^1H NMR($CDCl_3$): δ 0.95 (t, 3H, terminal CH_3), 1.27-1.31 (m, 30 H, CH_2 in alkyl chain), 2.0 (s, 1H, NH, exchangeable), 2.35 (s, 3H, Ph-CH_3), 3.1 (s, 1H, SH), 4.27 (t, 1H, CH-SO_3Na) and 7.34-7.81 (m, 4 H, ArH). Anal. Calcd for $C_{26}H_{43}N_4NaO_5S_3$ (Mol.wt. 610.84): C, 51.12; H, 7.10; N, 9.17; S, 15.75. Found C, 51.06; H, 7.15; N, 9.11; S, 15.78%.

Sodium 1-(7*H*-[1,2,4]triazol[3,4-b][1,3,4]thiadiazin-3-yl)heptadecane-1-sulfonate 9

A mixture of triazole **2** (0.01 mole), chloroacetaldehyde (0.02 mole) and conc. HCl (2 mL) in ethanol (50 mL) was refluxed for 3 hr. After removal of ethanol under reduced pressure, the resulting solid was filtered and washed with water. The crude product was purified by recrystallisation from ethanol to give **9**. Yield 73%, m.p.68-70°C; IR (KBr): 2920-2850 (CH in alkyl chain), 1610 cm^{-1} (C=N); ^1H NMR($CDCl_3$): δ 0.90 (t, 3 H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 4.23 (t, 1H, CH-SO_3Na), 3.1 (d, *J* = 4 Hz, 2H, CH_2 of the ring) and 7.5 (t, 1H, =CH). Anal. Calcd for $C_{21}H_{37}N_4NaO_3S_2$ (Mol.wt. 480.67): C, 52.48; H, 7.76; N, 11.66. Found C, 52.53; H, 7.81; N, 11.71%.

Sodium 1 - (6 – phenyl -7*H*-[1, 2, 4]triazolo[3, 4-b]-[1,3,4]thiadiazin-3-yl)heptadecane-1-sulfonate 10

A suspension of triazole **2** (0.1 mole) and phenacyl bromide (0.13 mole) in absolute ethanol (25 mL) was heated under reflux for 3 hr, followed by addition of 0.01 mole anhydrous sodium acetate. The reaction mixture was heated for additional 1hr, then cooled and poured into ice-cold water. The solid product was purified by recrystallisation from ethanol to afford **10**. Yield 67%, m.p.77-9°C; IR (KBr): 2910-2850 (CH in alkyl chain), 1589 (C=N) and 1349 cm^{-1} (C=S); ^1H NMR($CDCl_3$): δ 0.96 (t, *J* =7.0Hz, 3 H, terminal CH_3), 1.29-1.33 (m, 30 H, CH_2 in alkyl chain), 3.0 (s, 2H, CH_2 of the ring), 4.27 (t, *J* = 4.2Hz, 1H, CH-SO_3Na), and 6.3-7.5 (m, 5 H, ArH). Anal. Calcd for $C_{27}H_{41}N_4NaO_3S_2$ (Mol.wt. 556.25): C, 58.25; H, 7.42; N, 10.06. Found C, 58.19; H, 7.37; N, 10.01%.

Sodium1-(6-oxo-5, 6-dihydro-[1,2,4]triazolo[3,4-*b*][1, 3, 4]thiadiazol – 3 -yl)heptadecane-1-sulfonate 11

A mixture of triazole **2** (0.1 mole) and urea (0.13 mole) was heated at 180-90°C for 6hr. The reaction mixture was cooled and added to a solution of sodium hydroxide (5%, 20 mL), then filtered and the filtrate acidified with dilute HCl. The solid product was purified by recrystallisation from ethanol to give **11**. Yield 81%, m.p. 76-8°C; IR (KBr): 3228 (NH), 2921-2852 (CH aliphatic), 1675 (CO), 1598 cm^{-1}(C=N); ^1H NMR($CDCl_3$): δ 0.90 (t, *J* = 7.2 Hz, 3H, terminal CH_3), 1.28-1.33 (m, 30 H, CH_2 in alkyl chain), 4.24 (t, *J* =3.9 Hz,1H, CH-SO_3Na) and 8.0 (s, H, NH, exchangeable); MS: m/z (%): M^+ = 482 (45). Anal. Calcd for $C_{20}H_{35}N_4O_4S_2$ (Mol.wt. 482.64): C, 49.77; H, 7.31; N, 11.61. Found: C, 49.82; H, 7.35; N, 11.66%.

Sodium1-(7-oxo-6, 7-dihydro-5*H*-[1,2,4]triazolo-[3, 4-*b*][1, 3, 4]thiadiazol-3-yl)heptadecane-1-sulfonate 12

A mixture of triazole **2** (0.1 mole) and chloroacetyl chloride (0.1 mole) in dry dioxane (30 mL) was allowed to stand at rt overnight. The precipitated solid was filtered off and purified by recrystallisation from benzene to give **12**, which was identified by m.p. and mixed m.p. Yield 70%, m.p.60-2°C; IR (KBr): 3341 (NH), 2921-2850 (CH aliphatic), 1676 (CO), and 1587 cm^{-1} (C=N); ^1H NMR($CDCl_3$): δ 0.95 (t, *J*=7.5 Hz,3 H, terminal CH_3), 1.27-1.35 (m, 30 H, CH_2 in alkyl chain), 4.22 (t, *J* =4.5 Hz,1 H, CH-SO_3Na), 3.72 (s, 2H, CH_2 of the ring) and 2.1 (s, H, NH, which is exchangeable); MS: m/z (%) M^+ = 496 (69). Anal. Calcd for $C_{21}H_{37}N_4NaO_4S_2$ (Mol.wt. 496.67): C, 50.78; H, 7.51; N, 11.28. Found C, 50.73; H, 7.45; N, 11.21%.

Sodium1 - [5 - mercapto-4-(3-phenylthioureido)-4*H*-[1,2,4]triazol-3-yl]heptadecane-1-sulfonate 13

A mixture of triazole 2 (0.1 mole), phenyl isothiocyanate (0.1 mole) and powdered sodium hydroxide (0.8 g) in DMF (25 mL) was stirred at rt for 24hr. The reaction mixture was poured into dilute acetic

acid (5%, 15 mL). The preciptated product was filtered and purified by recrystallisation from ethanol to give **13**. Yield 85%, m.p. 108-10°C; IR (KBr): 3250, 3246 (NH), 2546 (SH) and 1376 cm^{-1}(C=S); ^{1}H NMR ($CDCl_3$): δ 0.90 (t, *J*=7.6 Hz,3 H, terminal CH_3), 1.29-1.34 (m, 30 H, CH_2 in alkyl chain), 2.0, 4.0 (s, 2H, 2NH), 13.01 (s, 1H, SH), 4.25 (t, 1H, CH-SO_3Na) and 6.41-7.1 (m, 5 H, ArH). Anal. Calcd for $C_{26}H_{42}N_5NaO_3S_3$ (Mol.wt. 591.84): C, 52.77; H, 7.15; N, 11.83; S, 16.25. Found C, 52.71; H, 7.08; N, 11.77; S, 16.31%.

Sodium 1-(6-phenylamino-[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-3-yl)heptadecane-1-sulfonate 14

Method A. A mixture of phenyl isothiocyanate (0.1 mole), triazole **2** (0.1 mole) and powdered sodium hydroxide (0.8 g) in DMF (25 mL) was refluxed for 4hr. The reaction mixture was poured into dilute acetic acid (5%, 15 mL). The precipitated product was filtered and purified by recrystallisation from ethanol to give **14**. Yield 78%, m.p. 85-7°C; IR (KBr): 3270 (NH) and 1590 cm^{-1}(C=N); ^{1}H NMR($CDCl_3$): δ 0.95 (t, 3 H, terminal CH_3), 1.28-1.33 (m, 30 H, CH_2 in alkyl chain), 4.24 (t, 1H, CH-SO_3Na), 4.0 (s, H, NH, exchangeable) and 6.46-7.2 (m, 5 H, ArH). Anal. Calcd for $C_{26}H_{40}N_5NaO_3S_2$ (Mol.wt. 557.76): C, 55.99; H, 7.23; N, 12.56; S, 11.50. Found C, 56.05; H, 7.28; N, 12.62; S, 11.57%.

Method B. Thiosemicarbazide derivative **13** was fused in an oil-bath above its melting point. The product was cooled, diluted with ethyl acetate, and filtered. The solid product was purified by recrystallisation from ethanol to give **14**.

Biological activity

The antibacterial activities of some synthesized compounds were determined *in vitro* using hole plate and filter paper disc methods against various pathogenic bacteria such as Gram +ve bacteria (*Bacillus subtilis, Staphylococcus aureus*) and gram -ve bacteria (*Escherichia coli*) in addition to fungi such as *Aspergillus niger* were used. The tested compounds were dissolved in 10% acetone. Different concentrations were chosen (125, 250, 500 μg/mL). A qualitative screen was performed on all compounds while quantitative assays were done on active compounds only. The results are summarized in **Table I**.

Surface active properties

(i) Surface and interfacial tension were measured using Du-Nouy tensiometer[18] (Kruss,Type 8451) with 0.1 wt % aqueous solution at rt (25°C).

(ii) Kraft point of the prepared anionic surfactants was measured as the temperature at which 1.0 % solution becomes clear on gradual heating[19].

(iii) Wetting time was determined by immersing a sample of cotton fabric in 1.0 wt % aqueous solution of surfactants[20].

(iv) Foaming properties was measured according to literature[21]. In this procedure, a 25 mL solution (1.0 wt %) was shaken vigorously for 10s in a 100 mL glass stoppered graduated cylinder at 25 °C. The solution was allowed to stand for 30s, and the foam height was measured.

(v) Emulsification stability was studied using 10 mL of a 20 mmole aqueous solution of surfactant and 5 mL of toluene at 40°C. The emulsifying property was determined by measuring the time it took for an aqueous volume separating from the emulsion layer to reach 9 mL counting from the moment of cesession of shaking[22].

(vi) Stability towards hydrolysis: A mixture of 10 mmole surfactant (0.1g) and 10 mL 0.05 N NaOH were placed in a thermostat at 40°C. The time taken by a sample solution to be clouded as a result of hydrolysis shows the stability of surfactant towards hydrolysis[23].

Biodegradability

Samples taken daily or more frequently were filtered through Whatman filter paper number-1 before measuring the surface tension. Surface tension measurements were made periodically each day, on each sample during the degradation test[24]. Biodegradation 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 and γ_{bt}= surface tension of blank experiment at time t (without samples).

Conclusion

From the previous results, it may be concluded that all the prepared anionic surfactants have good emulsifying properties in a non-edible medium such as insecticides or pesticides.

Origin of cultures: Botany Department, Faculty of Science, Benha University, Egypt.

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