

Fatty Acids in Heterocyclic Synthesis

Part XII: Synthesis of Surfactants from Pyrazole, Isoxazole, Pyrimidine and Triazine, Incorporating the 1,3,4-Thiadiazole Moiety Having Dyeing and Antimicrobial Activities

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Abstract The titled compounds were prepared from 2-amino-5-heptadecyl[1,3,4]thiadiazole (**1**). Diazotization of (**1**) produced (**2**) which was coupled with active methylene compounds and gave azo \rightleftharpoons hydrazono derivatives (**3A**, **3B**)_{a-d}. It was found that there is regio-specificity for addition of different nucleophiles to these tautomers; thus, nitrogen nucleophiles such as hydrazine hydrate, hydroxylamine hydrochloride and thiourea were reacted via Azo tautomer (**3A**) to yield pyrazole, isoxazole and pyrimidine respectively (**5-7**), while carbon nucleophiles as phenylisocyanate was reacted via the hydrazono tautomer (**3B**) and produced triazine derivatives (**4**). Additionally, the diazonium chloride (**2**) was coupled with alkaline 2-naphthol and produced 2-(5-heptadecyl-[1,3,4]thiadiazol-2-yl)-1,2-dihydro-3-oxa-1,2-diaza-cyclopenta[a]naphthalene (**8**). UV-visible spectra of the synthesized colored compounds (**2-8**) showed λ_{\max} at 374–398 nm, while screening these compounds in vitro against micro-organisms (including structure-activity relationship SAR study) revealed high antibacterial and moderate antifungal activities. Propoxylation of compounds **1**, **3**, **5**, **6**, **7** and **8** with 3, 5, 7 mol of propylene oxide produced nonionic surfactants **I(a-c)**–**IX(a-c)** having surface active properties so, it is clear that the tested surfactants can be used in the manufacture of dyes, drugs, cosmetics, emulsifiers, pesticides, luminophores for optical applications and many other industries with low

toxicity to human beings and the environment owing to their high solubility and good biodegradability.

Keywords Dyes · Antiprotozoal · Antibacterial · Stearic acid · 2-Aminothiadiaazole · Pyrazol-ylazo-thiadiazole · Azo-hydrazono tautomerism · Regiospecificity

Introduction

Five-membered, hetero-aromatic compounds containing imine ($-C=N-$) groups, such as imidazole [1], thiazole [2], triazole [3], oxadiazole [4], and thiadiazole [5–7] have long been of interest as luminophores for optical application and for dyeing, owing to their electron accepting nature [8].

1,3,4-Thiadiazoles were reported as being highly anti-inflammatory [9], anti-microbial [10], pesticidal [11], as having antiparasitic properties [12], and as being anticancer [13] and anticonvulsant agents [14–16]. Additionally, it is well known that some functionalized hydrazono derivatives present trypanocidal activity [17, 18]. Compounds containing 1,3,4-thiadiazole and hydrazone in one molecule are framework to act the structure pattern of lead-compound as a radical scavenger group [19–22].

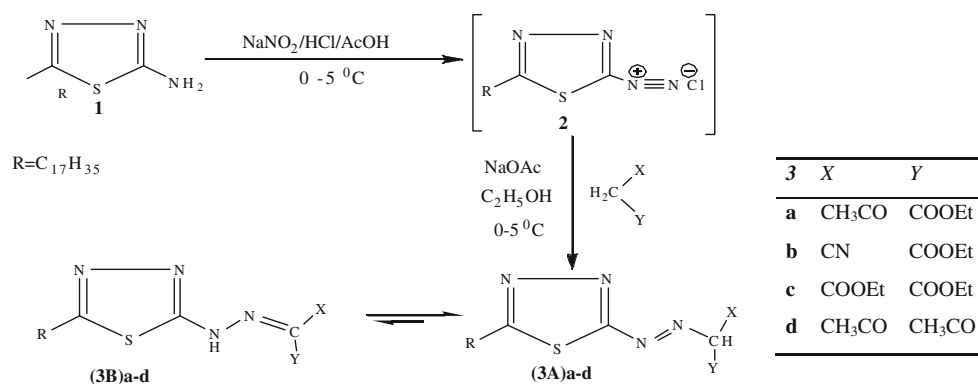
Chemistry

In continuation to our research program on the development of new effective, cheap and safe biologically active heterocyclic compounds having surface active properties [23–30], herein we report the synthesis of pyrazole, isoxazole, pyrimidine and triazine from a simple starting material stearic acid. The versatile 2-amino-5-heptadecyl-1,3,4-thiadiazole [28] (**1**) was prepared by refluxing stearic

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Scheme 1 Synthesis of (5-heptadecyl-[1,3,4]thiadiazol-2-ylazo/hydrazono) derivatives



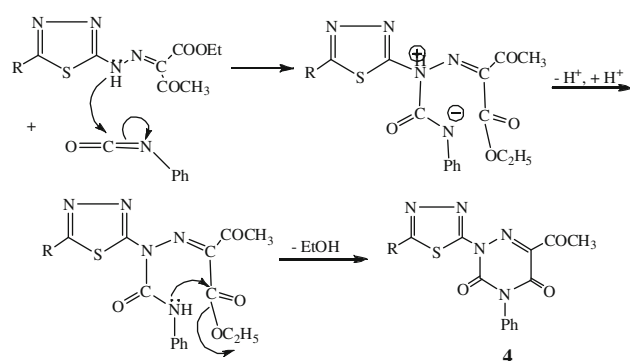
acid and thiosemicarbazide in boiling POCl₃. Diazotization of (**1**) with sodium nitrite and HCl/AcOH produced 5-heptadecyl-[1,3,4]thiadiazole-2-diazonium chloride (**2**) which was coupled smoothly with active methylene compounds as ethyl acetoacetate, ethyl cyanoacetate, diethylmalonate and acetylacetone via an electrophilic substitution reaction to afford azo (**3A**) ⇌ hydrazono (**3B**) tautomers (**3a–d**) in a good yield (Scheme 1). These compounds can be used in dyeing and as an antiprotozoal agent [22].

Characteristic bands in IR spectra for **3a** revealed two carbonyl groups of the ester and ketone at 1742 and 1718 cm⁻¹ respectively, for **3b** strong absorption at 2264 cm⁻¹ for ν_{C≡N}. For **3c** one strong band at 1742 cm⁻¹ for two carbonyls of the ester, and for **3d** one carbonyl of the ketone at 1693 cm⁻¹. For all compounds (**3a–d**) there are weak and broad bands (3434–3277) cm⁻¹ may be attributed to ν_{NH}, ν_{OH}. Also, ¹³C-NMR shows a signal for C=N of the hydrazono tautomer at 133 ppm and another one at 85 ppm of the azo tautomer.

The mass spectrum of (**3a–d**) also proved this tautomerism, which showed [M⁺-azo group ((-N=N-CH^XY))], and [M⁺-imino group ((-N=C^XY)))] for all the prepared compounds (**3a–d**).

It was found that the electrophilic reagent reacted regio-specifically with these tautomers thus, phenylisocyanate was reacted via the hydrazone tautomer **3Ba** to produce the highly substituted triazine, 6-acetyl-2-(5-heptadecyl-[1,3,4]thiadiazol-2-yl)-4-phenyl-2*H*-[1,2,4]-triazine-3,5-dione (**4**). The IR spectrum showed a sharp band for ν_{C=O}'s at 1705 cm⁻¹, and ¹³C-NMR showed δ ppm at 143.8, 155.6 for cyclic (2C=O) and 198.5 for ketonic (C=O) besides the other signals of aliphatic and aromatic carbon. Mass spectrum (M⁺-2 = 551, 4.6%) and M⁺-triazine moiety *m/z* = 324, 5.2%). The mechanism of the reaction is as follows (Scheme 2).

Nucleophilic reagents were reacted regio-specifically with the azo tautomer, thus nitrogen nucleophiles such as hydrazine, hydroxylamine hydrochloride and thiourea were



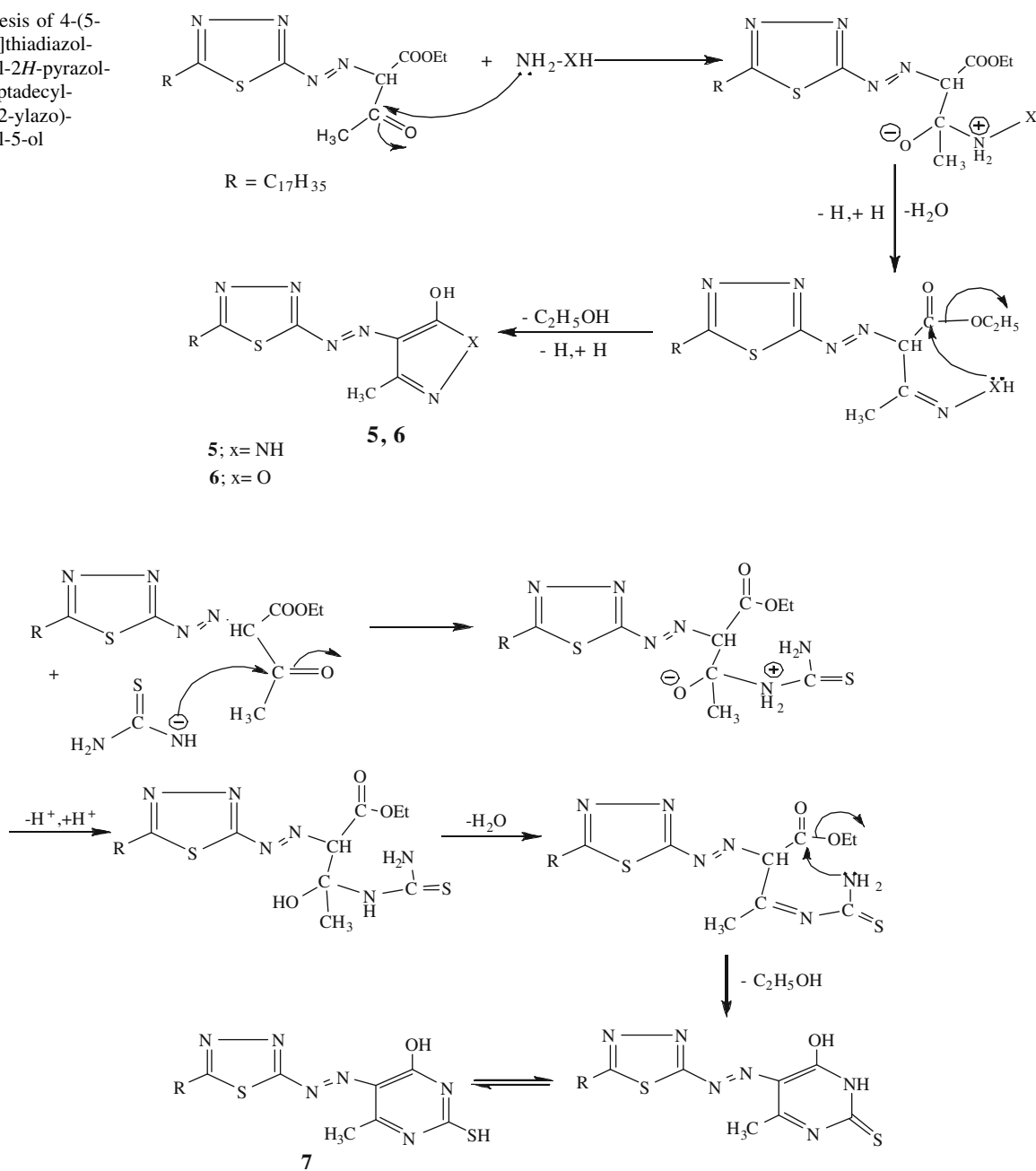
Scheme 2 Synthesis of 6-acetyl-2-(5-heptadecyl-[1,3,4]thiadiazol-2-yl)-4-phenyl-2*H*-[1,2,4] triazine-3,5-dione

reacted via the azo tautomer (**3Aa**) to produce 4-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-5-methyl-2*H*-pyrazol-3-ol (**5**), 4-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-3-methyl-isoxazol-5-ol (**6**), and 5-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-2-mercapto-6-methyl-pyrimidin-4-ol (**7**) respectively (Schemes 3 and 4). (These compounds containing the azo function can be utilized as dyeing materials). The mechanisms are as follows:

The IR spectrum of pyrazole (**5**) showed three bands at 3300, 3220 and 3120 cm⁻¹ attributable to OH ⇌ NH (tautomeric form), the mass spectrum showed (M⁺-H₂O at 430, 1.3%), IR spectra for isoxazole (**6**) showed ν_{OH} at 3325 cm⁻¹, ¹³C-NMR showed δ ppm at 100.5, 155.5, 158.9 for the 3C of isoxazole ring. The mass spectrum showed (M⁺ = 449, 0.9). The IR spectrum of pyrimidine (**7**) showed ν_{OH, NH} 's at 3380, 3277 and 3176 cm⁻¹, ν_{C=S} at 1080 cm⁻¹ and denoted a carbonyl group. ¹³C NMR showed δ ppm at 183.1 for C-OH, 180.4 for C=S. The mass spectrum showed a molecular ion peak at (M⁺ = 492, 4.4%). Coupling the diazonium salt (**2**) with an alkaline solution of 2-naphthol produced 2-(5-heptadecyl-[1,3,4]thiadiazol-2-yl)-1,2-dihydro-3-oxa-1,2-diazacyclopenta[*a*]naphthalene (**8**).

The IR spectra of compound (**8**) showed ν_{NH} at 3228 cm⁻¹, the mass spectrum showed (M⁺ at 494, 0.5%) (Scheme 5).

Scheme 3 Synthesis of 4-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-5-methyl-2*H*-pyrazol-3-ol, and 4-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-3-methyl-isoxazol-5-ol



Scheme 4 Synthesis of 5-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-2-mercapto-6-methyl-pyrimidin-4-ol

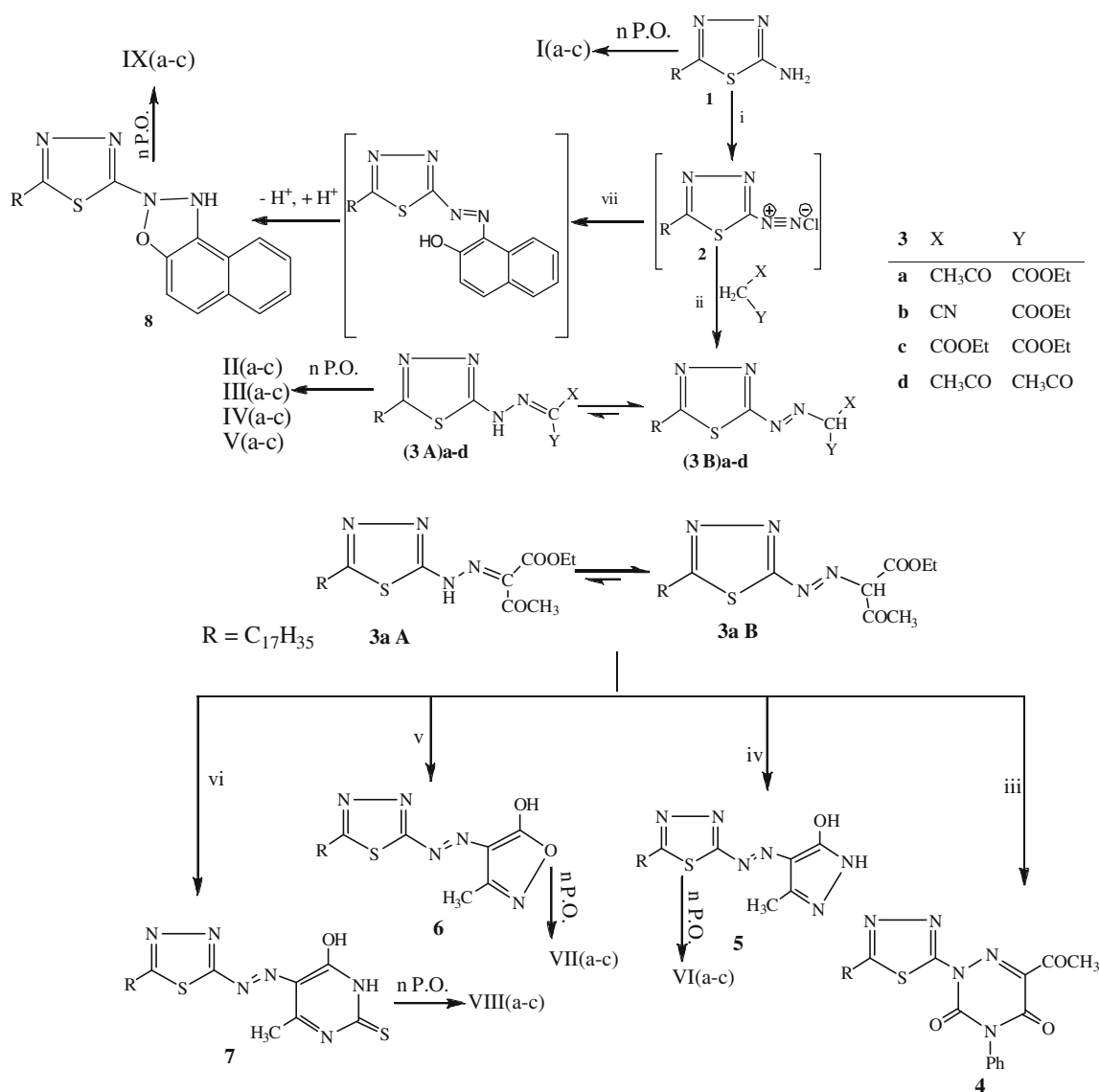
Electronic Absorption Spectra

Non-conjugated 1,3,4-thiadiazole had no selective absorption above 220 nm, but conjugated substituted 2-amino-1,3,4-thiadiazole with lone pair caused bathochromic shifts. Band assignment of the absorption spectra of the prepared compounds were investigated by recording their spectra in chloroform at 25 °C (cf. Table 1; Fig. 1).

The first absorption was observed within wavelength range 248–264 nm, it may be assigned to local $\pi \rightarrow \pi^*$ electronic transition and it was characterized by high

absorption value. The second band observed within wavelength range 290–310 nm, is attributed to the excitation of π electron within the $-N=N-$ and that $-C=N-$ bonds of 1,3,4-thiadiazole moiety of the molecule [31, 32].

The third band was mostly observed within the visible range 374–398 nm, this band may be assigned to electronic transition arising from charged transfer (CT) originating from the electron rich $-N=N-$ group toward the electron poor heterocyclic thiadiazole moiety, i.e. due to the transition within the whole molecule (intramolecular charge transfer).



Scheme 5 Synthetic routes of non-condensed thiadiazoles. Conditions: (i) NaNO₂/HCl, stirring at 0–5 °C 2 h (ii) EtOH, AcONa, stirring at rt for 12 h (iii) PhNCO, dioxane, Et₃N, reflux 5 h (iv)

N₂H₄·H₂O, dioxane, reflux 6 h; (v) NH₂OH·HCl, dioxane, AcONa, reflux for 6 h (vi) (NH₂)₂CS, EtONa, EtOH, reflux 7 h (vii) 2-naphthol in 10% NaOH solution, stirring at 0–5 °C for 0.5 h

Biological Activity¹

Some of the synthesized compounds were screened in vitro against some bacteria, namely *Escherichia coli* and *Staphylococcus aureus*, and some fungi, namely *Aspergillus flavus* and *Candida albicans*. Tetracycline and Amphotericin B were taken as positive references for antibacterial and antifungal agents respectively.

The results are tabulated in Table 2, which shows that the samples have high antibacterial and moderate antifungal activities on the tested micro-organisms.

¹ Antibacterial and antifungal activity was investigated at the Micro Analytical Center, Faculty of Science, Cairo University using a modified Kirby–Bauer disc diffusion method [33, 34]

Table 1 λ_{max} values for synthesized compounds

| Compound | λ ₁ (nm) | λ ₂ (nm) | λ ₃ (nm) |
|----------|---------------------|---------------------|---------------------|
| 1 | 252 | – | – |
| 3 | 256 | 310 | 376 |
| 4 | 264 | 306 | 374 |
| 5 | 252 | 306 | 376 |
| 6 | 248 | 306 | 378 |
| 7 | 254 | 306 | 376 |
| 8 | 248 | 290 | 398 |

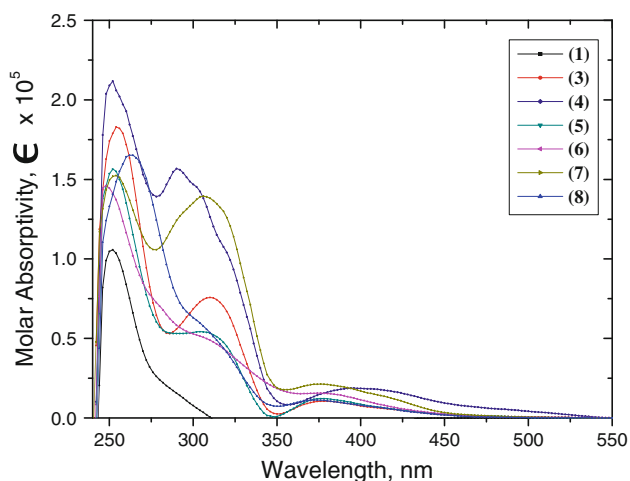


Fig. 1 UV–Vis absorption spectra of some synthesized compounds (1×10^{-5} M) in CHCl_3 at 25 °C

Structure-Activity Relationship (SAR) of Some Synthesized Thiadiazole Derivatives

As a part of our study on the effect of the synthesized thiadiazole derivatives on the microorganisms (bacteria & fungi), a structure-activity relationships (SAR) study was performed.

Herein, we focused on the effect of a certain substituent on the biological activity of the 2-aminothiadiazole (1). Also, the effect of construction of other heterocyclic ring condensed to the thiadiazole ring on the biological activity was also studied. Two bacteria strains [*Escherichia coli* (Gram-negative) & *Staphylococcus aureus* (Gram-positive)] and two fungi strains (*Aspergillus flavus* and *Candida albicans*) were selected to study these effects.

Introduction of a diazo group into the starting material has only a slight effect on the antibacterial activity (compound 3a).

Introduction of a non-condensed triazine ring (in compound 4) in the thiadiazole diminished activity against both bacterial strains and showed a good activity against *Aspergillus flavus*. Furthermore, addition of a pyrazole or isoxazole ring in a non-condensed way to thiadiazole (compounds 5 and 6) demonstrated excellent antibacterial activity. Isoxazole derivatives (compound 6) exhibited only moderate antifungal activity against *Candida albicans*.

Thiadiazolylpyrimidine (compound 7) showed antibacterial and antifungal activities similar to the aminothiadiazole derivative (compound 1).

Nonionic Surfactants from Some Synthesized Heterocyclic Compounds

The built up surfactant molecules contain heterocyclic thiadiazole are most important class of surface active

Table 2 Antimicrobial activity of some synthesized compounds

| Sample | Inhibition zone diameter (mm/mg sample) | | | | | | | | | | | |
|----------------|---|-----|-----|--|-----|-----|------------------------------------|-----|-----|----------------------------------|-----|-----|
| | <i>Escherichia coli</i> (G^-) | | | <i>Staphylococcus aureus</i> (G^+) | | | <i>Aspergillus flavus</i> (Fungus) | | | <i>Candida albicans</i> (Fungus) | | |
| | MIC | A | A | MIC | A | A | MIC | A | A | MIC | A | A |
| Control: DMSO | - | 0.0 | 0.0 | - | 0.0 | 0.0 | - | 0.0 | 0.0 | - | 0.0 | 0.0 |
| Tetracycline | 200 | 31 | 30 | 200 | 30 | 30 | - | - | - | - | - | - |
| Amphotericin B | - | - | - | - | - | - | 200 | 16 | 19 | 200 | 19 | 19 |
| 1 | 100 | 14 | 15 | 200 | 15 | 15 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 |
| 3a | 200 | 16 | 13 | 200 | 13 | 13 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 |
| 3b | 100 | 11 | 14 | 200 | 14 | 14 | 200 | 12 | 12 | 400 | 0.0 | 0.0 |
| 3c | 400 | 15 | 10 | 100 | 10 | 10 | 400 | 0.0 | 0.0 | 100 | 10 | 10 |
| 3d | 200 | 12 | 16 | 400 | 16 | 16 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 |
| 4 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 | 200 | 14 | 14 | 400 | 0.0 | 0.0 |
| 5 | 200 | 17 | 27 | 400 | 27 | 27 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 |
| 6 | 400 | 24 | 16 | 100 | 16 | 16 | 400 | 0.0 | 0.0 | 100 | 12 | 12 |
| 7 | 200 | 15 | 13 | 100 | 13 | 13 | 400 | 0.0 | 0.0 | 400 | 0.0 | 0.0 |

A, antimicrobial activity of tested compounds; MIC, minimum inhibitory concentration; 0.0, not active; A > 7 mm, slightly active; A > 15 mm, moderately active; A > 20 mm, highly active

agents containing a heterocyclic moiety due to their dual characteristics, one due to conflict between the affinity of the hydrophobic and hydrophilic structure shows surface active properties and a second one that is due to the heterocyclic moiety confirmed with aid of a hydrophilic moiety (propylene oxide) give biological activity.

Propoxylation of some of the new compounds (**1**, **3**_(a–d), **5**, **6**, **7**, and **8**) with various quantities of propylene oxide (3, 5, and 7 mol) produced nonionic surfactants **I(a–c)**–**IX(a–c)**, the structure of which was confirmed via IR [35] and ¹H-NMR spectra. IR-spectra showed a broad band in the region of (3500–2500) cm⁻¹ (ν_{OH}) and two other bands in the regions (1100–1000) and (950–900) cm⁻¹ for (νC–O–C ether linkage of the polypropoxy chain) besides the original bands of these compounds. ¹H-NMR spectra showed the protons of the propyleneoxy groups which appear as broad multiple signals in the region of (3.2–3.7) ppm in addition to other signals of these compounds.

The surface active properties of the prepared propoxy-lated compounds **I(a–c)**–**IX(a–c)** were measured in a neutral medium by traditional procedures to evaluate the possible utilization of these compounds in various industrial fields.

The surface and interfacial tension were determined according to Findly [36]. The resulting data in (Table 3) show that the surface and interfacial tensions increased upon increasing the number of propylene oxide units added to the molecule [37]. All these compounds show high cloud points, when in hot water, which increased with an increasing number of moles of propylene oxide [38].

Also, the synthesized compounds exhibited efficient wetting properties—wetting time decreased with an increasing number of propylene oxide units. Emulsion stability decreased with an increasing number of propylene oxide units [39], while the foam height increases [40]. Thus, the surface active properties were independent of heterocyclic thiadiazole but dependent on the hydrophobic (C₁₈) and hydrophilic (propylene oxide units) properties, however, heterocyclic thiadiazole revealed biological activities of the synthesized molecules, i.e., these compounds are used as effective emulsifying agents in many fields, such as cosmetics, formulations, pesticides, dyes, textiles, etc.

Biodegradability of the Synthesized Surfactants

To evaluate how environmentally friendly the compounds are, the biodegradability of the synthesized compounds was evaluated, determined by a die-away test, followed by surface tension measurements [41]. The biodegradability data are given in (Table 4), within the experimental accuracy, all the prepared nonionic surfactants seem to degrade

easily. The biodegradation of these compounds depends mainly on the propylene oxide chain length due to the same hydrophobic part. The results showed that in the first day 40–50% of the surfactants was biodegradable, after that they later decreased until the 6th day by which time they had disappeared. It means that these compounds are safe for human beings as well as the environment.

Experimental Protocols

The structural assignments of new compounds are based on their elemental analysis and spectral data (IR, ¹H NMR, ¹³C NMR, Mass spectra).

All melting points are uncorrected and were determined by the open capillary method using a Gallen Kamp melting point apparatus.

IR-Spectra (KBr disk) of the synthesized compounds were recorded on FT/IR-BRUKER, Vector 22 (Germany), JASCO FT/IR-4100 (Japan), and JASCO FT/IR-460+(Japan) instruments. ¹H- and ¹³C-NMR spectra were recorded in deuterated chloroform (CDCl₃) or dimethylsulfoxide (DMSO-d₆) as a solvent on a Varian Mercury VXR-300 spectrometer (300 MHz for ¹H NMR and 75 MHz for ¹³C NMR) using TMS as internal reference and chemical shifts are expressed in δ(ppm). The mass spectra were recorded on a Shimadzu GCMS-QP-1000EX mass spectrophotometer at 70 eV. The electronic absorption spectra were recorded on a UV/Vis spectrophotometer, JASCO, Model V-350 (Japan), 200–900 nm.

Homogeneity of all compounds synthesized was checked by TLC. All the synthesized compounds gave satisfactory elemental analyses. Surface active properties were carried out at the Chemistry Department, Faculty of Science, at Benha University, Egypt.

Synthesis of 2-Amino-5-heptadecyl-[1,3,4]thiadiazole (1)

It was prepared according to our procedure reported in Ref. [28].

General Procedure for Synthesis of (5-Heptadecyl-[1,3,4]thiadiazol-2-ylazo/Hydrazono) Derivatives (3a–d)

A solution of **1** (0.01 mol) in concentrated hydrochloric acid (20 mL) and (10 mL) water was treated with a cold saturated solution of sodium nitrite (0.7 gm) for 1 h with stirring and cooling at 0–5 °C for 2 h. The clear diazonium salt solution (**2**) was then added dropwise to a solution of ethyl acetoacetate, ethyl cyanoacetate, diethylmalonate and

Table 3 Surface properties of some synthesized surfactants

| Compound | No of moles | Surface tension (dyne/cm) 0.1 wt% | Interfacial tension (dyne/cm) 0.1 wt% | Cloud point °c 1.0 wt% | Wetting time (s) 0.1 wt% | Emulsion stability (min) 20 mol | Foam height (mm) 1.0 wt% |
|------------------|-------------|-----------------------------------|---------------------------------------|------------------------|--------------------------|---------------------------------|--------------------------|
| I(a-c) | 3 | 31 | 10 | 85 | 50 | 44 | 60 |
| | 5 | 32 | 12 | 90 | 46 | 42 | 80 |
| | 7 | 34 | 14 | >100 | 40 | 38 | 100 |
| II(a-c) | 3 | 33 | 9 | 81 | 53 | 45 | 50 |
| | 5 | 36 | 11 | 96 | 48 | 43 | 70 |
| | 7 | 39 | 13 | >100 | 45 | 40 | 90 |
| III(a-c) | 3 | 30 | 8 | 81 | 44 | 50 | 80 |
| | 5 | 32 | 10 | 95 | 40 | 45 | 100 |
| | 7 | 35 | 13 | >100 | 38 | 42 | 110 |
| IV(a-c) | 3 | 34 | 11 | 88 | 50 | 52 | 100 |
| | 5 | 36 | 13 | 94 | 48 | 49 | 120 |
| | 7 | 37 | 15 | >100 | 44 | 43 | 150 |
| V(a-c) | 3 | 28 | 9 | 75 | 53 | 46 | 70 |
| | 5 | 30 | 10 | 86 | 47 | 38 | 80 |
| | 7 | 32 | 12 | 93 | 45 | 43 | 100 |
| VI(a-c) | 3 | 33 | 12 | 89 | 48 | 52 | 70 |
| | 5 | 35 | 14 | 97 | 43 | 48 | 80 |
| | 7 | 38 | 15 | >100 | 35 | 41 | 110 |
| VII(a-c) | 3 | 28 | 10 | 78 | 42 | 55 | 80 |
| | 5 | 29 | 11 | 86 | 38 | 52 | 90 |
| | 7 | 31 | 14 | 94 | 32 | 46 | 110 |
| VIII(a-c) | 3 | 35 | 12 | 86 | 54 | 42 | 90 |
| | 5 | 36 | 13 | 94 | 50 | 38 | 110 |
| | 7 | 38 | 16 | >100 | 46 | 35 | 120 |
| IX(a-c) | 3 | 30 | 10 | 83 | 49 | 46 | 50 |
| | 5 | 31 | 13 | 93 | 43 | 41 | 70 |
| | 7 | 33 | 15 | >100 | 39 | 37 | 90 |

Table 4 Biodegradability of the synthesized surfactants

| Compd. | No of moles | 1st day | 2nd day | 3rd day | 4th day | 5th day | 6th day | 7th day |
|------------------|-------------|---------|---------|---------|---------|---------|---------|---------|
| I(a-c) | 3 | 53 | 66 | 75 | 85 | 95 | – | – |
| | 5 | 48 | 60 | 68 | 78 | 91 | – | – |
| | 7 | 45 | 50 | 62 | 74 | 83 | 93 | – |
| II(a-c) | 3 | 51 | 60 | 77 | 84 | 91 | – | – |
| | 5 | 46 | 54 | 68 | 71 | 84 | 91 | – |
| | 7 | 41 | 52 | 65 | 67 | 79 | 88 | – |
| III(a-c) | 3 | 48 | 57 | 67 | 75 | 82 | 86 | – |
| | 5 | 45 | 51 | 58 | 69 | 76 | 84 | – |
| | 7 | 41 | 52 | 56 | 67 | 72 | 83 | 90 |
| IV(a-c) | 3 | 52 | 68 | 74 | 83 | 97 | – | – |
| | 5 | 49 | 62 | 66 | 78 | 84 | 90 | – |
| | 7 | 44 | 55 | 57 | 66 | 75 | 87 | – |
| V (a-c) | 3 | 60 | 69 | 77 | 85 | 90 | 96 | – |
| | 5 | 57 | 64 | 76 | 81 | 88 | – | – |
| | 7 | 54 | 61 | 73 | 79 | 90 | – | – |
| VI(a-c) | 3 | 55 | 67 | 78 | 86 | 94 | – | – |
| | 5 | 53 | 62 | 69 | 85 | 92 | – | – |
| | 7 | 50 | 60 | 66 | 82 | 90 | – | – |
| VII(a-c) | 3 | 46 | 57 | 67 | 75 | 82 | 88 | – |
| | 5 | 43 | 51 | 85 | 69 | 77 | 84 | – |
| | 7 | 41 | 50 | 56 | 67 | 72 | 85 | 90 |
| VIII(a-c) | 3 | 50 | 60 | 77 | 84 | 94 | – | – |
| | 5 | 46 | 54 | 68 | 71 | 84 | 91 | – |
| | 7 | 41 | 52 | 65 | 67 | 80 | 89 | – |
| IX(a-c) | 3 | 63 | 67 | 75 | 84 | 92 | – | – |
| | 5 | 55 | 64 | 69 | 80 | 88 | 92 | – |
| | 7 | 47 | 58 | 66 | 77 | 45 | 92 | – |

acetylacetone (0.01 mol) in ethanol (50 mL) containing sodium acetate (1 gm) at 0–5 °C. The pH of the coupling mixture, in each case, was maintained at 5–6 through the coupling process by adding sodium acetate. After the complete addition of the diazonium salt, the reaction mixture was stirred at room temperature over night. The precipitated products separated upon dilution with cold water (50 mL) and they were filtered off, washed with water several times, dried and recrystallized from ethanol.

Compound **3a** was obtained as yellowish brown powder in 77% yield, M.P. 80–82 °C; IR(KBr) ν (cm⁻¹): 3434 (NH), 2985, 2938 (aliphatic CH stretching), 1742, 1718 (2C=O), and 1647 (C=N stretching); ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 4.7 (s,H,NH) which disappeared on addition of D₂O, 3.8 (q, 2H, CH₂ ethoxy), 3.2 (t, 3H, CH₃ ethoxy), 2.9 (s, 3H, CH₃C=O), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, terminal CH₃), 2.9 (s, 2H, CH₂CN), 1.6–1.2 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, terminal CH₃); ¹³C NMR (DMSO-d₆) δ (ppm):

206, 177 (2C=O), 168, 173 (2C=N), 133.3 (C=N hydrazone tautomer), 85.6 (–CH=N=N azo tautomer), 61 (CH₂ ethoxy), 14.1 (CH₃ ethoxy), 25.2 (CH₃C=O), beside sp³ carbons of aliphatic side chain 14.1 (terminal CH₃), 22.7, 28.5, 29.3 (2C), 29.6 (10C), 30.9, 31.9; MS m/z [% rel.int.]: 482 (M⁺ +2, 2.86), 353(16.84), 312(13.37), 115(63.37), 57(100). Anal. Calcd. (%) for C₂₂H₃₈N₄SO: C; 64.98, H; 9.42, N; 13.78, S; 7.89. Found: C; 64.86, H; 9.23, N; 13.64, S; 7.60.

Compound **3b** was obtained as pale yellow crystals in 64% yield, M.P. 95–97 °C; IR(KBr) ν (cm⁻¹): 3277 (NH), 2984, 2938 (aliphatic CH stretching), 2264 (C \equiv N), 1746 (C=O), and 1516 (C=N stretching); ¹H-NMR spectrum (CDCl₃) showed signals at δ : 5.2 (s,H,NH) which disappeared on addition of D₂O, 3.5 (q, 2H, CH₂ ethoxy), 3.1 (t, 3H, CH₃ ethoxy), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, terminal CH₃), MS m/z [% rel.int.]: 464 (M⁺ +1, 3.60), 268(9.10), 312(13.37), 115(84.80), 57(100). Anal. Calcd. (%) for C₂₄H₄₁N₅O₂S: C; 62.17, H; 8.91, N; 15.10, S; 6.92. Found: C; 62.34, H; 9.03, N; 15.35, S; 7.04.

Compound **3c** was obtained as yellow powder in 71% yield, M.P. 70–72 °C; IR(KBr) ν (cm⁻¹): 3261 (NH), 2985, 2938 (aliphatic CH stretching), 1742 (2C=O sharp), and 1626 (C=N stretching); the ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 4.3 (s,H,NH) which disappeared on addition of D₂O, 3.3 (q, 4H, 2CH₂ ethoxy), 3.1 (t, 6H, 2CH₃ ethoxy), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, terminal CH₃), MS m/z [% rel.int.]: 508 (M⁺ -2, 0.05), 311(26.98), 128(45.68), 115(100). Anal. Calcd. (%) for C₂₆H₄₆N₄O₄S: C; 61.14, H; 9.08, N; 10.97, S; 6.28. Found: C; 61.22, H; 9.23, N; 10.66, S; 6.45.

Compound **3d** was obtained as brownish yellow crystals in 69% yield, M.P. 82–84 °C; IR(KBr) ν (cm⁻¹): 3177 (NH), 2919, 2850 (aliphatic CH stretching), 1693 (2C=O sharp), and 1577 (C=N stretching); the ¹H-NMR spectrum (CDCl₃) showed signals at δ : 4.9 (s,H,NH) which disappeared on addition of D₂O, 2.9 (s, 6H, 2CH₃C=O), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, terminal CH₃), MS m/z [% rel.int.]: 450 (M⁺, 0.04), 134(24.63), 115(46.67), 88(100). Anal. Calcd. (%) for C₂₄H₄₂N₄O₂S: C; 63.96, H; 9.39, N; 12.43, S; 7.11. Found: C; 64.07, H; 9.33, N; 12.55, S; 7.23.

Synthesis of 6-Acetyl-2-(5-heptadecyl-[1,3,4]thiadiazol-2-yl)-4-phenyl-2H-[1,2,4]triazine-3,5-dione (**4**)

To a mixture of equimolar amounts (0.01 mol) **3a** and phenyl isocyanate in 30 mL of 1,4-dioxane, a catalytic amount of triethylamine (0.5 mL) was added. The reaction mixture was heated under reflux for 5 h, concentrated, cooled at room temperature, poured onto cold water (50 mL) and neutralized with diluted HCl. The solid product that formed was collected by filtration, dried and recrystallized from 1,4-dioxane. Compound **4** was obtained as a brownish yellow powder in 68% yield, M.P. 89–91 °C; IR(KBr) ν (cm⁻¹): 2920, 2851 (aliphatic CH stretching), 1705 (C=O), and 1596 (C=N stretching); ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 6.6–7.3 (m, 5H, aromatic CH), 2.7 (s, 3H, CH₃-C=O), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.88 (t, 3H, CH₃); ¹³C NMR (DMSO-d₆) δ (ppm): 198.5 (C=O ketonic), 173, 168 (2C=O cyclic), 155, 143, 137 (3C=N), 128.0 (3C), 128.9 (2C), 135 (aromatic CH), 26.4(CH₃C=O), beside sp³ carbons of the aliphatic side chain 14.1 (terminal CH₃), 22.7, 28.5, 29.3(2C), 29.6 (10C), 30.9, 31.9; MS m/z [% rel.int.]: 551 (M⁺ -2, 4.6), 353(31.3), 141(88.7), 115(100). Anal. Calcd. (%) for C₃₀H₄₃N₅O₃S : C; 65.07, H; 7.83, N; 12.65, S; 5.79. Found: C; 65.26, H; 8.02, N; 12.97, S; 5.98.

Synthesis of 4-(5-Heptadecyl-[1,3,4]thiadiazol-2-ylazo)-5-methyl-2H-pyrazol-3-ol (**5**)

Equimolar amounts (0.005 mol) of **3a** and hydrazine hydrate in 30 mL of 1,4-dioxane were heated under reflux for 6 h. The reaction mixture was concentrated and then triturated with ethanol. The solid produced was filtered off, dried and recrystallized from ethanol. Compound **5** was obtained as dark green crystals in 70% yield, M.P. 101–103 °C; IR(KBr) ν (cm⁻¹): 3300 (OH), 3220–3120 (NH), 2920, 2850 (aliphatic CH stretching), 1663 (C=N stretching); the ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 6.99 (s, 1H, OH) which disappeared on addition of D₂O, 4.7 (s,H,NH) which disappeared on addition of D₂O, 2.8 (s, 3H, CH₃-C=N), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.88 (t, 3H, CH₃); ¹³C NMR (DMSO-d₆) δ (ppm): 177, 168, 142 (3C=N), 164 (C-OH), 101.4 (= C=N=N- of pyrazole ring), 12.2 (CH₃C=N), beside sp³ carbons of aliphatic side chain 14.1 (terminal CH₃), 22.7, 28.5, 29.3(2C), 29.6 (10C), 30.9, 31.9; MS m/z [% rel.int.]: 430 (M⁺ -H₂O, 1.3), 323 (19.3), 295 (92.4), 134 (100). Anal. Calcd. (%) for C₂₃H₄₀N₆OS: C; 61.57, H; 8.99, N; 18.73, S; 7.15. Found: C; 61.68, H; 8.91, N; 18.88, S; 7.23.

Synthesis of 4-(5-Heptadecyl-[1,3,4]thiadiazol-2-ylazo)-3-methyl-isoxazol-5-ol (**6**)

Equimolar amounts (0.005 mol) of **3a** and hydroxylamine hydrochloride in 30 mL of 1,4-dioxane containing sodium acetate (0.006 mol) was refluxed for 6 h. The reaction mixture was concentrated, cooled and then poured into cold water. The solid produced was filtered off, dried and recrystallized from acetic acid. Compound **6** was obtained as a pale green powder in 79% yield, M.P. 90–92 °C; IR (KBr) ν (cm⁻¹): 3325 (OH), 2920, 2850 (aliphatic CH stretching) and 1597 (C=N-O sharp); ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 4.02 (s, 1H, OH) which disappeared on addition of D₂O, 2.16 (s, 3H, CH₃C=N), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.88 (t, 3H, CH₃); ¹³C NMR (DMSO-d₆) δ (ppm): 206, 177 (2C=O), 171, 168, 155 (3C=N), 158.9 (C-OH), 100.5 (= C=N=N- of isoxazole ring), 10.0 (CH₃C=N), beside sp³ carbons of aliphatic side chain 14.1 (terminal CH₃), 22.7, 28.5, 29.3(2C), 29.6 (10C), 30.9, 31.9; MS m/z [% rel.int.]: 449 (M⁺, 0.9), 353(19.4), 312(17.6), 115(100). Anal. Calcd. (%) for C₂₃H₃₉N₅O₂S: C; 61.44, H; 8.74, N; 15.58, S; 7.13. Found: C; 61.67, H; 8.89, N; 15.79, S; 7.19.

Synthesis of 5-(5-heptadecyl-[1,3,4]thiadiazol-2-ylazo)-2-mercapto-6-methyl-pyrimidin-4-ol (**7**)

To a solution of **3a** (0.005 mol) in 40 mL of ethanolic sodium ethoxide solution (0.005 mol) of thiourea was added. The reaction mixture was boiled under reflux for 7 h, concentrated and the residue was triturated with cold water. The solid was collected by filtration, dried and recrystallized from ethanol. Compound **7** was obtained as a pale yellow powder in 74% yield, M.P. 98–100 °C; IR(KBr) ν (cm⁻¹): 3380 (OH), 3277–3176 (NH), 2919, 2850 (aliphatic CH stretching), 2682 (SH), 1614 (C=N stretching), 1080 (C=S); ¹H-NMR spectrum (DMSO-d₆) showed signals at δ : 5.56 (s, 1H, OH) which disappeared on addition of D₂O, 4.9 (s, H, NH) which disappeared on addition of D₂O, 2.12 (s, 3H, CH₃-C=N), 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.88 (t, 3H, CH₃); ¹³C NMR (DMSO-d₆) δ (ppm): 183.1 (C–OH), 180.4 (C=S), 168, 173, 164 (3C=N), 58.3 (= C–N=N– of pyrimidine ring), 17.8 (CH₃C=N), beside sp³ carbons of aliphatic side chain 14.1 (terminal CH₃), 22.7, 28.5, 29.3(2C), 29.6 (10C), 30.9, 31.9; MS m/z [% rel.int.]: 492 (M⁺+2, 4.4), 239(11.6), 128(44.4), 115(100). Anal. Calcd. (%) for C₂₄H₄₀N₆OS₂: C; 58.50, H; 8.18, N; 17.06, S; 13.02. Found: C; 58.71, H; 8.29, N; 17.15, S; 13.14.

Synthesis of 2-(5-Heptadecyl-[1,3,4]thiadiazol-2-yl)-1,2-dihydro-3-oxa-1,2-diaza-cyclopenta[a]naphthalene (**8**)

A solution of **1** (0.01 mol) in concentrated hydrochloric acid (20 mL) and (10 mL) water was treated with a cold saturated solution of sodium nitrite (0.7 gm) through 1 h with stirring and cooling at 0–5 °C for 2 h to form the diazonium salt (**2**). An alkaline solution of 2-naphthol (prepared by dissolving 1.44 gm in 30 mL of 10% NaOH) was added to the diazonium salt dropwise with continuous stirring for half an hour. A brown solid product was obtained, filtered off, dried and recrystallized from ethanol. Compound **8** was obtained as a yellowish orange powder in 79% yield, M.P. 88–90 °C; IR(KBr) ν (cm⁻¹): 3380 (OH), 3043 (aromatic CH), 2920, 2850 (aliphatic CH stretching), 1600 (N=N); ¹H-NMR spectrum (CDCl₃) showed signals at δ : 6.7–7.2 (m, 6H, 6H aromatic), 5.56 (s, 1H, OH) which disappeared on addition of D₂O, 1.2–1.6 (m, 32H, 16CH₂ of alkyl chain), 0.9 (t, 3H, CH₃); MS m/z [% rel.int.]: 491 (M⁺-3, 0.5), 239 (13.10), 115(39.20), 59 (100). Anal. Calcd. (%) for C₂₉H₄₂N₄OS: C; 70.40, H; 8.56, N; 11.32, S; 6.48. Found: C; 70.55, H; 8.88, N; 11.54, S; 6.77.

Preparation of Nonionic Surfactants from the Synthesized Heterocyclic Compounds

Propoxylation (Hydroxylation)

The hydrophobe of the synthesized compounds containing 0.5% KOH was stirred and heated to 70 °C while passing a slow stream of nitrogen through the system to flush out oxygen. Nitrogen addition was stopped and propylene oxide added dropwise with continuous stirring and heating under an efficient reflux system to retain propylene oxide. The reactions were conducted for different intervals of time ranging from 1 to 10 h. the apparatus was then filled with nitrogen, cooled and reaction vessel weighed. The amount of propylene oxide which was reacted and the average degree of propoxylation were determined through the increment in mass of the reaction mixture (increase in weight of the mixture after the addition of propylene oxide is the average amount of propoxylation) [42]. The selected average numbers of moles, *n*, were 3, 5 and 7.

Surface Active Properties of Surfactants

Surface and Interfacial Tensions [43]

Surface tension and interfacial tension were measured using a Du-Nouy tensiometer (Krüss type 8451), for various concentrations of the synthesized surfactants (0.05–10⁻⁶ mol/L) and at 25 °C.

Cloud Point

The cloud point, a measure of inverse solubility characteristic of nonionic surface active agents, was determined by the gradual heating of a solution in a controlled temperature bath, by determining the temperature at which the clear or nearly clear solutions become definitely turbid. Cooling the solutions until they become clear again, allowed us to check the reproducibility of this temperature [44].

Wetting Time

The wetting power of the tested surfactants were determined by immersing a sample of cotton fabric in a 1.0 wt% aqueous solution of the surfactants and measuring the sinking time in second [45].

Foaming Properties

The foamability was measured by the Ross-Miles method [46]. The foam production for a 1.0 wt% solution was measured by the foam height initially produced.

Emulsion Stability

The emulsion was prepared from 10 mL of a 20 mmol aqueous solution of surfactant and 5 mL of toluene at 40 °C. The emulsifying capacity was taken as the time it took for an aqueous volume separating from the layer to reach 9 mL counting from the moment of shaking [47].

Biodegradability

Samples which were taken daily or more frequently and these were filtered through filter paper before measuring the surface tension. Surface tension measurements were made periodically (each day) on each sample during the degradation test [48]. The biodegradation percentage (D) for each sample was calculated using the following equation.

$$D = [\gamma_t - \gamma_0 / \gamma_{bt} - \gamma_0] \times 100$$

where γ_t = Surface tension at time t .

γ_0 = Surface tension at time zero (initial S.T).

γ_{bt} = Surface tension of the blank experiment at time t (without sample).

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