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Synthesis and Characterization of a New Cationic Surfactant Derived from 5-Chloro-1*H*-indole-2,3-dione In Aqueous Systems

Z. Tribak[1], R. Ghibate[5], M.K. Skalli[1], Y. Kandri Rodi[2], D. Mrani[3], A. Aouniti[4], B. Hammouti[4], O. Senhaji[5*]

[1] *Laboratory of Applied Chemistry, Sidi Mohamed Ben Abdellah University, Faculty of Science and Technology of Fez, Morocco.*
[2]*Laboratory of Applied Organic Chemistry, Sidi Mohamed Ben Abdellah University, Faculty of Science and Technology of Fez, Morocco.*
[3]*Laboratory of Analytical Chemistry, Environment and Materials(ACEM),Moulay Ismail University, Faculty of Science and Technology of Erracchidia, Morocco.*
[4] *LCAE-URAC18, Faculty of Science, Mohammed first University, Po Box 717, 60000 Oujda, Morocco.*
[5]*Laboratory of Applied Physical Chemistry (ECPA), MoulayIsmaïl University, Faculty of Sciences and Technology of Erracchidia, Morocco.*

ABSTRACT: In this paper, anovel cationic surfactant is synthesized by the alkylation reaction of 5-Chloro-1*H*-indole-2,3-dioneunder the conditions of phase transfer catalysis and quaternizationby trimethylamine in acetone solution.Chemical structures of synthesized compounds were confirmed by ^{1}HNMR and ^{13}C NMR. The micellization of cationic surfactant in aqueous solution at room temperature has been reported using the conductivity of the measurements

Keywords:5-Chloro-1*H*-indole-2,3-dione, alkylation, quaternization, monomer, surfactants

I. INTRODUCTION

The particular structure of the surfactants allows them to be classified among the molecules most present in the cosmetics, pharmaceutical or agroalimentary industries [1]. The high production volumes of these industries have highlighted the need to use non-polluting surfactants, which can be synthetic or natural. This current problem has resulted in the use of agro-resources such as carbohydrates, phosphonates [2] and 5-Chloroisatin derivatives as a starting material for the synthesis of compounds with high added value.In the literature, 5-chloro-1*H*-indole-2,3-dione is a polyvalent chemical building block capable of forming a large number of heterocyclic molecules [3]. The compound has an indole ring structure common to many pharmaceutical products. Its derivatives have exhibited activities such as antibacterial [4], anti-inflammatory [5], analgesic [6], anti-viral [7], antifungal [8], anti-tubercular [9], anti-depressant [10] and anticorrosive [11]. The presence of several reaction centers in isatin and its derivatives makes them capable of participating in a large number of reactions [12].The keto group at position 2 and in particular at position 3 can be added to the C-O bond and condensation reactions [13].Through the primary amine group, compounds of the 5-Chloroisatin series are able to penetrate N-alkylation and thereafterquaternization by trimethylamine as an example in the case of the synthesis of the novel surfactants ofindole [14].Generally, the structure of a surfactant is said to be amphiphilic, it is defined by the joint presence of a hydrophilic part and a hydrophobic part, depending on the nature of the hydrophilic part, cationic, anionic or zwitterionic surfactants may be found or nonionic surfactants [15-18]. The hydrophobic part, for its part, is most often in the form of a carbon chain of variable length, whether branched or not. It is well known that surfactant molecules are associated with micelles which begin to form above the critical micellar concentration (CMC) [19-22]. Numerous factors such as the addition of electrolytes [23-25], the pH of the buffer [26], the temperature [27,28], the addition of organic modifiers [29, 30] Ionic strength of the aqueous solution [31, 32], the presence of additives etc., make this value different from that determined in pure water.The determination of the CMC takes place in several ways such as the tensiometry which records the decrease in the surface tension as a function of the surfactant concentrations up to a limit beyond which the surface tension no longer decreases, and other methods used as conductivity [33-34] for charged surfactants, spectrofluorometry, nuclear magnetic resonance and UV-visible absorption spectroscopy [35-37].In the present work, we describe the synthesis of a new surfactant monomer derived from 5-Chloroisatin via the N-alkylation method under the conditions of phase transfer catalysis followed by the quaternizationof 1- (6-bromohexyl) 5-chloroindoline-2,3-dione, with trimethylamine. The

structures of the compounds are perfectly packaged by ^{1}H NMR, ^{13}C NMR. The critical micelle concentration of our surfactant was determined in pure water at 25 °C by a conductimeter.

II. RESULTS AND DISCUSSION

Preparation of 1- (6-bromohexyl) -5-chloroindoline-2,3-dione:

In order to obtain novel heterocyclic compounds having the 5-chloro-1*H*-indole-2,3-dione nucleus [38], we were interested in the condensation of 5-Chloroisatin (**1**)with the 1,6-dibromohexane, under the conditions of phase transfer catalysis (CTP)[39], solubilizing in N, N-dimethylformamide (DMF) in the presence of a weak base and a catalyst to promote the reaction. After purification by chromatography on a silica column with a mixture of ethyl acetate/hexane [40], the 1- (6-bromohexyl) -5-chloroindoline-2,3-dione (**2**) compound is obtained in good yield.

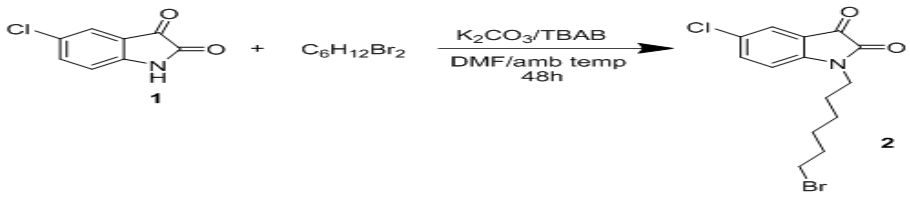

Figure 1: Synthesis of novel derivatives of 5-Chloro-1*H*-indole-2,3-dione

Quaternization of 1- (6-bromohexyl) -5-chloroindoline-2,3-dione(3):

Quaternization of 1- (6-bromohexyl) -5-chloroindoline-2,3-dione, is obtained by trimethylamine [41] solubilized in acetone at room temperature, according to the following reaction:

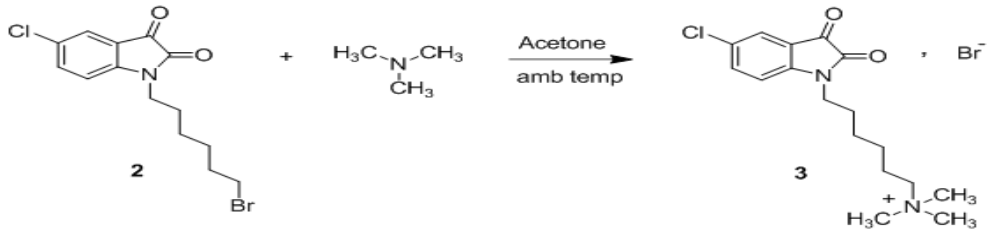

Figure2: Synthesis of novel cationic surfactant.

The product obtained is purified by precipitation in diethyl ether with a yield of 95% and it's soluble in methanol and water.

CMC determination:

With the intention of estimating the CMC of our cationic surfactant, the conductivity plots were carried out as a function of the concentration of 5-chloro-1-(6-(trimethyl-λ^4-azanyl)hexyl)indoline-2,3-dione in an aqueous solution at room temperature[42]. Measurements for selected surfactants were carried out in pure water and at different concentrations of 5-chloro-1-(6-(trimethyl-λ^4-azanyl)hexyl)indoline-2,3-dione at pH 7.0 and are shown in Table 1.The first corresponds to the concentration range below the CMC, when only the surfactant monomers exist in solution [43].

At higher concentrations of surfactant, the micelles begin to form and a change in slope occurs because the conductivity increases in a different way.The intersection of these two lines is taken as the CMC value of the surfactant. Indeed, at this CMC concentration, many important properties of surfactant usually change strongly in the solution [44-47]. The critical micelle concentration was determined in pure water at 25°C by means of conductometer and found to be 5.10^{-3}M. The results are shown in Figure 3.

Table1: Variation of the specific conductivity relative to the surfactant concentration for the conductivity determination of the CMC at T = 25°C. (pH 7.0).

C (M)	$1.25\ 10^{-3}$	$2.5\ 10^{-3}$	$5\ 10^{-3}$	$10\ 10^{-3}$	$13.3\ 10^{-3}$	$20\ 10^{-3}$
χ (mS)	91.2	175.2	350	652	875	1232

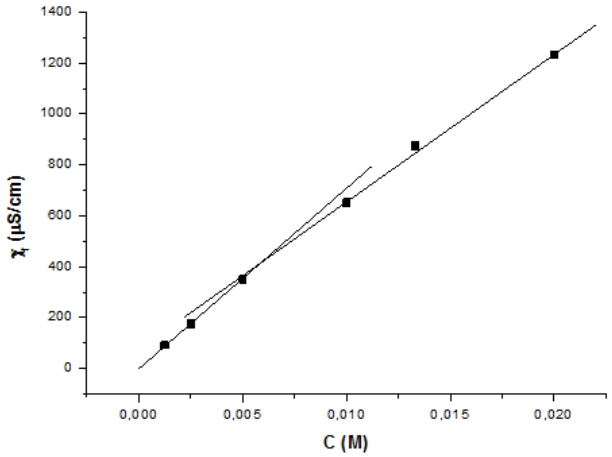

Figure 3: Variation of the conductivity of the surfactant with its concentration atambient temperature.

Experimental Part:

Melting points were determined by the Kofler bench. NMR spectra were recorded on Bruker 300 NMR spectrometer advancement in $CDCl_3$ using tetramethylsilane (TMS) as reference, chemical shifts are reported in parts per million of the inductive field. The coupling constants (J) are in hertz. The following abbreviations are used to describe peak models: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet. The conductivity has been measured at 25 °C with a conductometer.

Synthesis of compound 2:

In a 100 ml two-necked flask, to a solution of 5-Chloro-1*H*-indole-2,3-dione (0.4 g, 2.20 mmol) in DMF (15 ml), Potassium carbonate (0.5 g, 3.3 mmol), a catalytic amount of tetra-n-butylammonium bromide (0.1 g, 0.3 mmol) and the brominated reagent were added. The mixture is activated by stirring for 48 hours at 25°C. After evaporation of the solvent and treatment of the reaction, the crude reaction product is purified by column chromatography. The new product is isolated as a powder with good yield.

***1- (6-bromohexyl) -5-chloroindoline-2,3-dione*(2):**
Yield: 74%;mp: 66-70°C; R_f = 0.8; RMN^{1}H ($CDCl_3$; 300MHz): δ (ppm) 7.68 (dd, H, CH_{Ar},J^4_{H-H} = 1.5 Hz, J^3_{H-H} = 4.5 Hz) ; 7.60 (d, H, CH_{Ar} ,J^4_{H-H} = 1.5 Hz); 7.24 (d, H, CH_{Ar},J^3_{H-H} = 6 Hz); 3.65 (t, 2H, CH_2, J^4_{H-H} = 3Hz); 3.51 (t, 2H, CH_2, J^3_{H-H}= 6Hz); 1.73-1.82 (m, 2H, CH_2), 1.54-1.63 (m, 2H, CH_2) , 1.38-1.46(m, 4H, CH_2). RMN^{13}C ($CDCl_3$; 75MHz): δ (ppm): 182.89 (C=O); 158.35 (N-C=O); 149.72, 127.72, 119.40(Cq); 137.39, 124.39, 112.88 (CH_{Ar}); 35.56, 32.58, 27.67, 27.00, 25.72(CH_2).

Synthesis of compound (3):

In a 100 ml single-necked flask equipped with a magnetic bar, 1 equivalent of 5-Chloroisatin derivative in 15 ml of acetone is introduced and then 5 equivalents of trimethylamine (45% w/w) are added. The mixture is stirred at room temperature; the reaction is followed by thin layer chromatography (TLC) every hour for about 24h. After a certain time, the total disappearance of the starting bromide is seen. At the end of the handling, the solvent is evaporated under vacuum and the mixture treated. The precipitate obtained is a slightly violet solid which is soluble in the minimum of methanol and then purified by precipitation in diethyl ether. The product is then characterized by proton NMR, and carbon NMR.

***5-chloro-1-(6-(trimethyl-λ^4-azanyl)hexyl)indoline-2,3-dione* (3):**
Yield: 88%;mp: 100-120°C; R_f= 0.6 ; RMN ^{1}H ($CDCl_3$; 300MHz) : δ (ppm) 7.35(d, H, H_{Ar},$^4J_{H-H}$ =1.8 Hz); 7.17-7.2(dd H, H_{Ar}, $^4J_{H-H}$ =3 Hz, $^3J_{H-H}$ =9 Hz); 6.96(d, H, H_{Ar},^{3} J_{H-H} =9Hz); 3.52-3.71(m, 4H, CH_2); 3.31(t, 2H, CH_2, $^3J_{H-H}$=9Hz,$^4J_{H-H}$ =3Hz); 3.15-3.25(m, 2H, CH_2); 1.57-1.64(m, 4H, CH_2); 2.97(s, 9H, CH_3).RMN^{13}C ($CDCl_3$; 75MHz): δ(ppm) 209.77(C=O); 177.99(N-C=O); 141.54, 131.28, 128.36(Cq); 130.03, 123.79, 111.10(CH_{Ar}); 26.06, 25.45, 25.05, 22.09(CH_2), 29.83(CH_3).

III. CONCLUSION

Our work was oriented on the synthesis study and the characterization of a new cationic surfactant derived from 5-Chloro-1*H*-indole-2,3-dione. The production of this monomer takes place in two stages, firstly the alkylation of 5-Chloroisatin with the brominated reagent under the conditions of catalysis by phase transfer and then the quaternization of 1- (6-bromohexyl) -5-chloroindoline -2,3-dione, the synthesized structures were identified on the basis of the NMR spectral data. Tests of the conductimetric method in water at ambient temperature made it possible to study the behaviour of the micellization of our cationic surfactant. Conductivity is a useful technique for determining the thermodynamic parameters of the surfactant micellization.

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