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Micellar Studies of Some *N*-Substituted Derivatives of 6-Amino-6-deoxy-1,2-*O*-isopropylidene-glucose

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Abstract. Glucose-based nonionic surfactants having a tertiary amino group linked to C-6 of the glucose moiety were tested for the solubilization of neutral arenes *viz.* naphthalene, biphenyl, durene, fluorene, anthracene and phenanthrene in acidic aqueous medium and also for the basic hydrolysis of *o*- and *p*-nitrophenyl acetate and naphthyl acetate in an ethanol–water mixture. These micellar studies revealed that (6,6′-hexadecylamino)bis[6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose] is the most effective surfactant for the solubilization of arenes in acidic aqueous medium and its deprotected form is the most effective for the basic hydrolysis of phenyl and naphthyl acetates.

Key words: non-ionic surfactants, glucose derivatives, neutral arenes, phenyl acetates.

1. Introduction

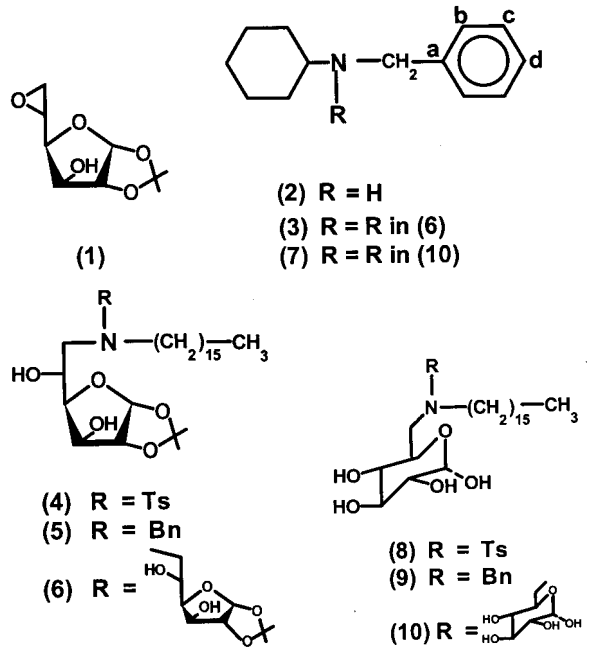
During the last decade, enormous interest has been devoted to the study of micelle catalysed reactions. A number of extremely important thermodynamic and kinetic studies of organic reactions in micellar solutions [1–6] and the use of micelles in asymmetric induction [7, 8] have been reported. The solubilization studies of a number of polar and nonpolar monomers in micellar/reverse micellar solutions have also been reported [9–12].

This paper describes the use of some *N*-substituted 6-amino-6-deoxy glucose derivatives (**3**–**10**) as micelles for the solubilization of neutral arenes in acidic aqueous medium and also for the basic hydrolysis of phenyl and naphthyl acetates in an ethanol–water mixture.

2. Experimental

2.1. GENERAL SPECTRAL STUDIES

Melting points were determined in capillaries and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 200 MHz on a Bruker FT NMR 200 spectrometer. TMS was used as internal reference for solutions in deuteriochloroform and *J* values are given in Hz. Optical rotations were measured with a JASCO DIP-360 digital polarimeter in a 1 dm cell. NMR spectra and rotations were recorded at the Department of Chemistry, GND University, Amritsar and mass spectra at



Formula 1.

CDRI, Lucknow. Elemental analysis was carried out at RSIC Panjab University, Chandigarh. Column chromatography was performed on silica gel (60–120 mesh) and TLC plates were coated with silica G. The spots were developed in iodine and/or charring with 1% sulfuric acid in water. Distilled *n*-hexane, distilled ethanol and doubly distilled water were used for spectroscopy. All the other chemicals were used as obtained.

2.2. BASIC HYDROLYSIS OF *o*- AND *p*-NITROPHENYL ACETATES AND NAPHTHYL ACETATE

The kinetic runs were conducted in 1 cm silica cuvettes maintained at constant temperature in a thermostated cell holder of a Shimadzu graphicard UV-160 spectrophotometer. Temperature could be maintained to within ± 0.01 °C at 27 °C with the help of water circulating from the Shimadzu TB-85 thermobath. Into dry cells at 27 °C were added the dimethylaniline solution of appropriate concentration and to this the stock solution of appropriate volumes of catalyst and substrate were added by means of graduated pipettes. The rate of hydrolysis was followed for the solution 1.25×10^{-4} M in ester, 1.20×10^{-4} M in base and 2.50×10^{-3} M in catalyst in distilled water and in an ethanol–water mixture. The concentration of the catalyst was kept above its cmc for each reading. The cmc was determined by the method of Gratzer and Beaven [13] (see Table I). The observed rate constants were determined by following the appearance of *p*-nitrophenoxide ion at 400 nm,

Table I. Critical micelle concentration (cmc) of the surfactants in M L^{-1}

Surfactant	(cmc)	
	EtOH–H_2O	HCl–H_2O
3	1.59×10^{-3}	–
4	9.46×10^{-4}	–
5	1.00×10^{-3}	–
6	8.75×10^{-4}	–
7	–	1.92×10^{-3}
8	–	1.08×10^{-3}
9	–	1.42×10^{-3}
10	–	9.78×10^{-4}

o-nitrophenoxide ion at 410 nm and naphthoxide ion at 330 nm, respectively. The change in absorbance during a kinetic run was recorded with a maximum time gap of 4 min and a minimum of 1 min. The rate constants were calculated from the plot of $\ln(A - A_0)$ against time.

2.3. SOLUBILIZATION OF NEUTRAL ARENES IN ETHANOL–WATER MIXTURE

The isopropylidene group of the surfactant was removed by refluxing with 1% aqueous hydrochloric acid for 30 min. The solution was cooled to room temperature and pH adjusted to 5. Unfortunately, it was not possible to isolate surfactants **7**–**10**.

The surfactant solution (10 mL, 5 mM) was shaken with arene (20 mg) for 20 min and filtered. The filtrate was extracted with *n*-hexane (2×25 mL) and the arene concentration determined by electronic absorption spectroscopy. Solubilities thus obtained were corrected for the solubility of arenes in water (pH 5) without surfactant found in the same way.

2.4. PREPARATION OF *n*-BENZYLCYCLOHEXYLAMINE (**2**)

Cyclohexylamine (2.0 g, 20 mM) and freshly distilled benzaldehyde (2.0 g, 21 mM) were dissolved in ethanol (10 mL) and the solution aged overnight. It was refluxed for 15 min and cooled to room temperature. Sodium borohydride (1.2 g, 32 mM) was added slowly over a 10 min interval, whereafter the solution was stirred at room temperature overnight. Excess sodium borohydride was neutralized by dropwise addition of water (5 mL) and solvent was then evaporated under reduced pressure. The crude residue was dissolved in dichloromethane (50 mL), washed with water (2×5 mL), dried (Na_2SO_4) and evaporated to give a semi-solid

residue. Purification by column chromatography on silica gel [dichloromethane–ethyl acetate (5 : 1)] afforded a resinous material (2.57 g, 68%); ^{1}H NMR (200 MHz) δ 1.18 (br m. 6H, CH_2); 1.89 (d, 2H, CH_2); 2.15 (br, 1H, NH); 2.45 (q, 1H, NCH); 3.78 (s, 2 H, CH_2Ph); 7.25 (s, 5H, ArH).

2.5. PREPARATION OF 6-DEOXY-6-(*n*-BENZYLCYCLOHEXYLAMINO)-1,2-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE (**3**)

Compound **2** (940 mg, 5 mM) was heated to 110 °C, 1.01 g (5 mM) of **1** was added and the melt mixed in a sealed capillary tube. The temperature was raised to 130 °C and kept for 1 h. Purification of the crude product by column chromatography on silica gel [dichloromethane–ethyl acetate (10 : 1)] afforded a light colored solid which was crystallized [benzene–petroleum ether (1 : 1)] as white crystals (1.54 g, 79%); mp. 135 °C; $[\alpha]_D^{27}$ + 47.7 (c 1.5, $CHCl_3$); (M^+) ion *m*/*z* 391, 390, 376 (M^+ − 15), 202 [$(C_6H_{11})(C_7H_7)N{=}CH_2$]; UV (*n*-hexane) λ_{max} (log ϵ) 213.8 (3.68); ^{1}*H NMR* (200 MHz) δ 0.82–1.92 (m, 16H, CH_2 and CH_3); 2.57 (m, 4H, NCH, H-6_b and OH); 2.84 (dd, 1H, *J* 3.6, 3.0, H-6_a); 3.66 (q, 2H, NCH_2); 3.84 (q, 2H, H-4 and H-5); 4.24 (s, 1H, H-3); 4.48 (d, 1 H, *J* 3.7, H-2); 5.91 (d, 1H, *J* 3.6, H-1); 7.26–7.48 (m, 5 H, Ar H); ^{13}*C NMR* (200 MHz) δ 25.9–30.7 (7C, m, CH_2 and CH_3); 53.1 (1C, t, N$\underline{C}H_2$Ph); 54.8 (1C, t, C-6); 59.5 (1C, d, NCH); 66.2 (1C, d, C-5); 75.3 (1C, d, C-3); 81.4 (1C, d, C-4); 85.0 (1C, d, C-2); 105.0 (1C, d, C-1); 111.0 (1C, s, O.$\underline{C}(CH_3)_2$.O); 127.2 (1C, s, ArC_d); 128.5 and 128.6 (4C, d, Ar $C_{c,b}$); 139.5 (1C, s, Ar C_a); *Inept*: 25.9, 26.0 (−ve); 26.1, 26.7 (+ve); 27.0 (−ve); 30.7 (+ve); 53.0, 54.9 (−ve); 59.4, 66.1, 75.4, 81.4, 85.1, 104.9, 127.2, 128.5, 128.6, 139.5 (+ve); *Anal. Calcd. for* $C_{22}H_{33}NO_5$: C, 67.49; H, 8.49; N, 3.58, *Found*: C, 67.00; H, 8.02; N, 3.38.

3. Results and Discussion

3.1. SYNTHESIS

The synthesis and characterization of amino sugars **4**–**6** has already been reported by us [12]. Compound **3** was synthesized by dry heating of *N*-benzylcyclohexylamine (2) and 5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose (**1**). All these amino sugars possess a tertiary amino group linked to C-6 of the glucose moiety with the reducing function blocked in a cyclic acetal group. Exclusive nucleophilic attack of the appropriate amine on C-6 of **1** and without inversion at C-5 [14] causes the synthesis.

The ^{1}H NMR signal assignments for **3** are based on the previous studies by Abraham *et al.* [15] and ^{13}C NMR by Vyas *et al.* [16] on *O*-propylidene-D-hexoses. The cyclohexyl signal was found at δ 0.82–1.92 as a complex multiplet, the methine signal at 2.57 and the aromatic signals at 7.26–7.48 respectively. In the ^{13}C NMR spectrum, the signals at δ 53.1 and 59.5 were assigned to benzyl- and cyclohexyl

Table II. Rate constant (K_{obs} min^{-1}) for hydrolysis of *o*- and *p*-nitrophenyl acetate and naphthyl acetate with different catalysts

Catalyst	Substrate		
	o-nitrophenyl acetate	*p*-nitrophenyl acetate	naphthyl acetate
Nil	0.00	$(4.60 \pm 0.03) \times 10^{-4}$	0.00
3	$(5.04 \pm 0.02) \times 10^{-4}$	$(1.72 \pm 0.03) \times 10^{-3}$	0.00
4	0.00	$(9.20 \pm 0.04) \times 10^{-4}$	0.00
5	0.00	$(7.60 \pm 0.02) \times 10^{-4}$	0.00
6	$(9.60 \pm 0.04) \times 10^{-4}$	$(1.84 \pm 0.02) \times 10^{-3}$	$(4.79 \pm 0.02) \times 10^{-4}$

methylene directly attached to N. The remaining methylenes were found at δ 25.9–30.7 as a multiplet, the quarternary carbon at 111.0 and the aromatic carbons at 127.2, 128.5, 128.6 and 139.5 respectively. Like other amino sugars [12], the most prominent shift was found in the C-6 signals (10.9 ppm downfield) compared to similar signals in monoacetone glucose [17].

3.2. BASIC HYDROLYSIS OF ESTERS IN ETHANOL–WATER MIXTURE

In these studies, very weak basic conditions (at nearly neutral pH) were applied to examine the efficiency of the surfactants synthesized. In the absence of any catalyst, the rate of hydrolysis for *p*-nitrophenyl acetate with dimethylaniline was $(4.60 \pm 0.03) \times 10^{-4}$ min^{-1} and zero for *o*-nitrophenylaniline and naphthyl acetate, respectively. Under the catalytic conditions, all the surfactants were effective for the hydrolysis of *p*-nitrophenyl acetate, while for *o*-nitrophenyl acetate only **3** and **6** were effective and for naphthyl acetate only **6** was effective.

As can be seen from Table II, **6** is found to be the most efficient catalyst for the basic hydrolysis of all the esters used. It causes a four-fold increase in the rate for *p*-nitrophenyl acetate (uncatalyzed) and enhances the rate from zero (uncatalyzed) to $(9.60 \pm 0.04) \times 10^{-4}$ min^{-1} for *o*-nitrophenyl acetate and to $(4.79 \pm 0.02) \times 10^{-4}$ min^{-1} for naphthyl acetate, respectively. This suggests that all three substrates are incorporated into the micellar phases of **6**. Unfortunately, under the prevailing conditions, no clear comparison of its catalytic activity for all the esters could be made; however the catalytic activity is due to its hydroxyl groups, which can hydrogen bond to the ester and activate it towards nucleophilic attack by dimethylaniline.

The rate of hydrolysis was slightly better for **4** than **5**, suggesting that the additional oxygens from the tosyl group also influence the rate. Although the cmc is high and it does not contain any long chain, **3** is a better catalyst than **4** and **5** and comparable to **6**. It probably acts as a weak nucleophilic base for hydrolysis of esters due to its less hindered structure.

Table III. Solubilization of various arenes in water (pH 5.0) with the help of micelles formed by nonionic surfactants

Arene	Micellar Ratio (Arene molecules : Micelle molecules) in surfactant			
	7	**8**	**9**	**10**
Naphthalene	1 : 35	1 : 21	1 : 23	1 : 3
Biphenyl	1 : 150	1 : 39	1 : 41	1 : 5
Durene	1 : 29	1 : 6	1 : 6	1 : 2
Fluorene	1 : 455	1 : 35	1 : 37	1 : 11
Anthracene	1 : 862	1 : 192	1 : 289	1 : 158
Phenanthrene	1 : 714	1 : 5	1 : 5	1 : 6

3.3. SOLUBILIZATION OF ARENES IN AQUEOUS MEDIUM (pH 5)

Solubilization studies of various arenes in the presence of micelles (**7**–**10**) were performed. The pH was kept at 5 because of the observation that glucose (hydrophilic head of these surfactants) remains stable at this pH [18]. Table III indicates that small arenes are solubilized more and the solubility goes on decreasing with increase in the arene size. It was also found that **10** gives the best results for arene solubilization, suggesting that all the arenes are incorporated in its micellar phase. For other surfactants, **8** and **9** were nearly equally effective in their behaviour towards solubilization. The solubilization behaviour was badly affected on replacing the hexadecyl chain by the cyclohexyl moiety (Table III). This is in good agreement with the fact that the long alkyl chain decreases the cmc and at the same time increases the hydrophobic character and hence better solubilizes the apolar substrates. The replacement of the sugar moiety by phenyl and tosyl groups did not increase the solubilization of arenes, suggesting that π–π interaction between substrate and micelle were not the only prominent feature in the course of solubilization in aqueous medium. The better solubilzation of phenanthrene than anthracene is because of its linear shape, which is better recognized by the micellar phase.

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