Inclusion Complexation of Sodium Alkyl Sulfates with β-Cyclodextrin. A ^{1}H NMR Study

QING-XIANG GUO,* ZI-ZHONG LI, TAN REN, XIAO-QING ZHU and
YOU-CHENG LIU
*National Laboratory of Applied Organic Chemistry and Department of Chemistry, Lanzhou
University, Lanzhou 730000, P.R. China.*

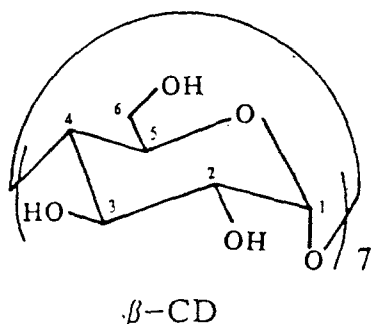**Abstract.** The association of anionic surfactants, *viz.*, sodium alkyl sulfates, $C_n H_{2n+1} OSO_3 Na$ ($n = 5, 6, 7, 8, 9, 10, 12$), with β-cyclodextrin has been investigated by means of NMR spectroscopy. The measurements of chemical shift changes of certain protons of both host and guest molecules indicated 1 : 1 inclusion complex formation. The association constants (K_a) and standard free energy changes ($-\Delta G^0$) for the inclusion complexation reaction vary as a function of the hydrocarbon chain length of the surfactants.

Key words: Association constant, β-cyclodextrin, inclusion, NMR, surfactant.

1. Introduction

Cyclodextrins (CD) are cyclic oligosaccharides built up from 6, 7, or 8 glucose units, called α-, β-, and γ-CD, respectively. One of the most important properties is their ability to form inclusion complexes with various lipophilic compounds [1]. Studies on the association of cationic [2–6], anionic [4–10] and neutral [11] surfactants with CD have been reported. As neither the CD nor the sodium alkyl sulfate surfactant molecules bear a chromophore, absorption or fluorescence measurements cannot be applied directly to determination of the association constants. Recently, the applications of the ultrasonic velocity technique [3, 9] and the visible spectral displacement method [10] to this area were reported. Usually the conductometric method can be used, but the ambiguity of the measurements and the exact evaluation of the results are not easily ensured because of the small difference in electric conductivity between the associated and unassociated surfactant ions [1, 7]. Unfortunately, the association constants of sodium alkyl sulfate surfactants with CD reported in the literature differ widely [4–10]. The inclusion complexation of β-CD with cationic and neutral surfactants has been studied by NMR spectroscopy [2, 11]. In this paper we present the results of an NMR study on the inclusion of β-CD with some anionic surfactants, sodium alkyl sulfates, $C_n H_{2n+1} OSO_3 Na$

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* Author for correspondence. Present address: Department of Modern Chemistry, University of Science and Technology of China, Hefei 230026, P.R. China.

·β–CD

$[n = 5(1), 6(2), 7(3), 8(4), 9(5), 10(6), 12(7)]$. The association constants [11, 12] were determined directly from the NMR data.

2. Experimental

2.1. REAGENTS

Anionic surfactants **1–7** were synthesized according to the procedure described in the literature [13], and purified by recrystallization twice from ethanol. D_2O (deuterium content 100%) was purchased from Aldrich. β-Cyclodextrin (97%, Suzhou Weijing Plant) was purified by recrystallization three times from distilled water and dried at 86°C *in vacuo* for 24 h before use.

2.2. NMR MEASUREMENTS

^{1}H NMR spectra were recorded at 400.13 MHz with a Bruker AM-400 NMR spectrometer. DSS was used as external reference [14]. All measurements were carried out at 25°C.

3. Discussion

The ^{1}H NMR spectrum of pure β-CD consists of peaks due to five kinds of protons [14]: H-1 (5.05 ppm, doublet), H-3 (3.96 ppm, triplet), H-5,6 (3.84–3.90 ppm, unresolved), H-2 (3.64 ppm, doublet of doublets), and H-4 (3.57 ppm, triplet).

A remarkable upfield shift of the signals of inner H-3 and H-5 of β-CD was observed upon addition of the surfactants (Figure 1). The magnitude of the chemical shift changes ($\Delta\delta = \delta_{CD} - \delta_{obs}$) varies as a function of the length of the alkyl chains as well as the concentration of surfactants (Figure 2). From Figure 2 it can be seen that the chemical shift change ($\Delta\delta$) for H-5 of β-CD reaches a maximum when the surfactant to β-CD molar ratios are around unity. Furthermore, for the same molar ratio, the longer the length of the alkyl chain of the surfactant, the larger is the $\Delta\delta$ value observed.
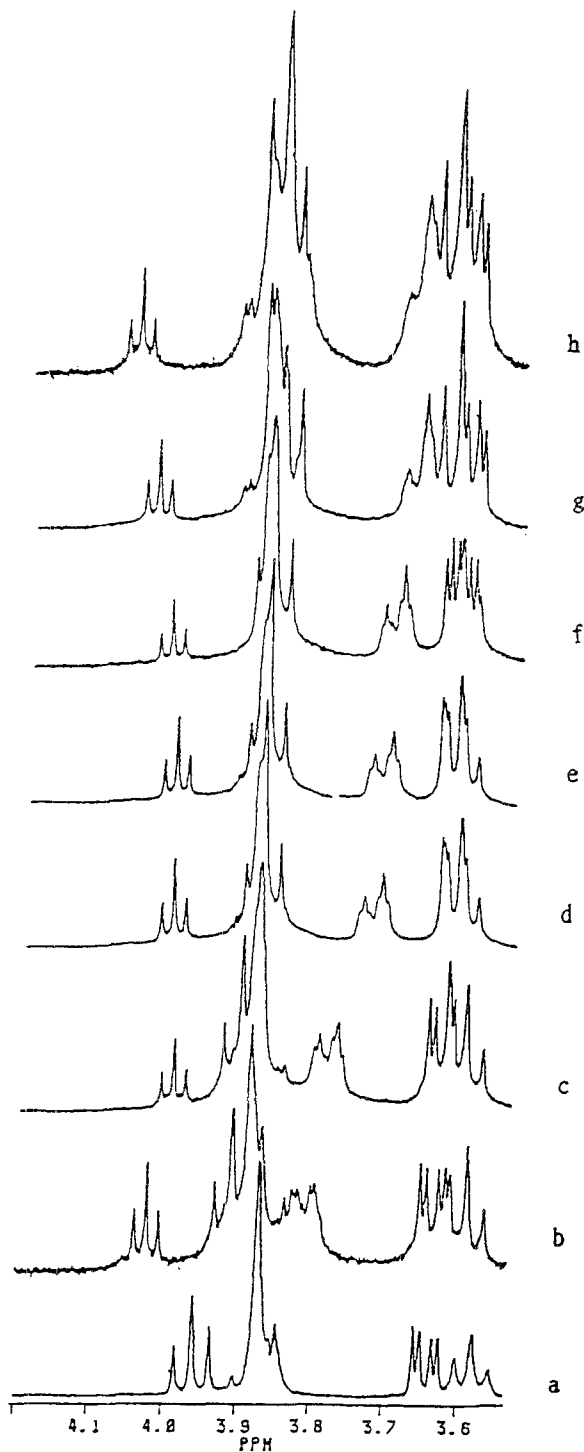
Fig. 1. Partial ^{1}H NMR spectra of β-CD (8.8 × 10^{-3} mol/L) alone (a), and in the presence of **1** (b), **2** (c), **3** (d), **4** (e), **5** (f), **6** (g), and **7** (h) in molar equivalent in D$_2$O. Triplet (b–h) with δ > 4 ppm is due to CH$_2$ of sodium alkyl sulfates.
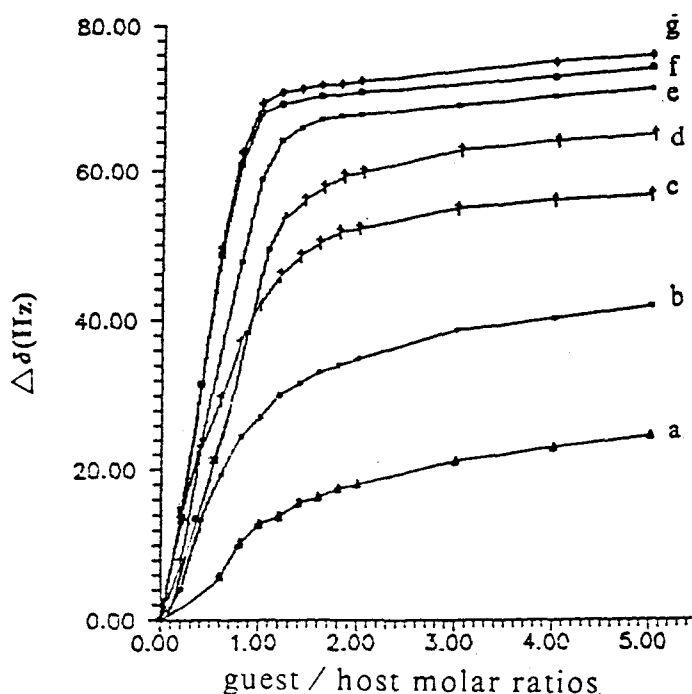
Fig. 2.   Plots of H-5 chemical shift changes ($\Delta\delta = \delta_{CD} - \delta_{obs}$) of β-CD on complexation with surfactant **1** (a), **2** (b), **3** (c), **4** (d), **5** (e), **6** (f), and **7** (g) vs. the guest/host molar ratio.

Similarly, the chemical shift changes for protons of the guest molecules were also observed when the inclusion complexes were formed. The maximum $\Delta\delta$ for the methyl protons of surfactants appeared at the guest to host equivalent. The same relationship between the magnitude of $\Delta\delta$ and length of alkyl chain was observed. It is clear that the 1 : 1 β-CD-surfactant inclusion complexes were formed.

From the observation that the changes in chemical shifts of both host and guest molecules varied with the guest to host molar ratio, the data were treated according to modified Hildebrand–Benesi equation (Appendix A) [12, 15]. The modified equation is more suitable in treatment of the NMR parameters obtained from the host β-CD than from the guest compound. The association constants (K_a) for the complexation were determined by measuring the change in chemical shift for H-5 of β-CD (C) with the added surfactants (S). Consider the equilibrium expression:
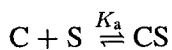
$$C + S \overset{K_a}{\rightleftharpoons} CS$$

$$K_a = [CS] / [C] [S] .$$

K_a can be calculated by the equation:

TABLE I. Standard free energy changes $(-\Delta G^0)$ and association constants (K_a) for inclusion of β-CD with surfactants.

Surfactant	$-\Delta G^0$ (kJ/mol)	K_a (L/mol)
1	11.34	1.01 $(\pm 0.10) \times 10^2$
2	12.31	1.44 $(\pm 0.37) \times 10^2$
3	14.19	3.07 $(\pm 0.70) \times 10^2$
4	14.54	3.43 $(\pm 0.11) \times 10^2$
5	17.59	1.21 $(\pm 0.29) \times 10^3$
6	19.11	2.24 $(\pm 0.15) \times 10^3$
7	20.74	4.32 $(\pm 0.67) \times 10^3$

$$S_0 = \frac{\frac{\Delta\delta}{K_a} - \frac{C_0 \Delta\delta^2}{Q} + C_0 \Delta\delta}{Q - \Delta\delta}$$

where S_0 is the total concentration of the surfactant; C_0 is the total concentration of β-CD; $\Delta\delta$ is the change in chemical shift given by $\Delta\delta = \delta_{CD} - \delta_{obs}$ for H-5 of β-CD.

Q is the H-5 chemical shift difference between β-CD and 'pure' β-CD inclusion complex given by $Q = \delta_{CD} - \delta_{CS}$, which was obtained by the mathematical simulation to the plots of $\Delta\delta$ against the guest to host molar ratio.

Table I lists the standard free energy changes $(-\Delta G^0)$ and association constants (K_a) of sodium alkyl sulfates with β-CD. The results indicated that both $(-\Delta G^0)$ and K_a increase steadily with the length of the hydrocarbon tail of the surfactants. The correlation in Figure 3 shows $(-\Delta G^0)$ increasing with the alkyl chain length (n).

In conclusion, the results suggest that the 1 : 1 β-CD-anionic surfactant inclusion complexes were formed in aqueous solution. The association constants and thus the standard free energy changes obtained by NMR measurements are reasonable, and the method described in the paper is reliable and convenient, and can be widely used in many other systems.

Acknowledgements

Appendix A [12, 15]

Considering the equilibrium for the complexation of β-CD (C) with surfactant (S) to form an inclusion complex (CS):
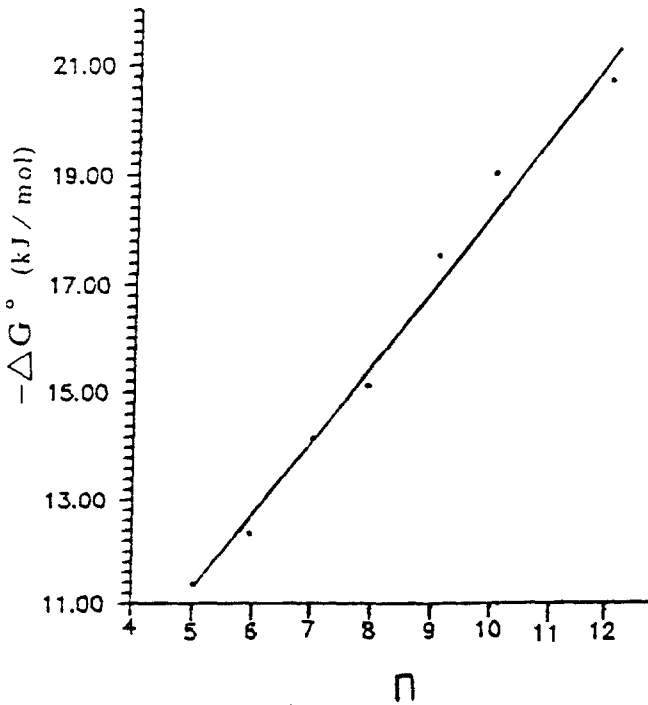
Fig. 3.   Relationship between $(-\Delta G^{0})$ and the number (n) of carbon atoms in the hydrocarbon tail of the surfactant.

$$C + S \overset{K_a}{\rightleftharpoons} CS .$$ (1)

The association constant (K_a) is given by:

$$K_a = \frac{[CS]}{[C][S]} .$$ (2)

The total concentrations of β-CD (C_0) and surfactant (S_0) are given by Equations 3 and 4, respectively.

$$C_0 = C + CS$$ (3)

$$S_0 = S + CS$$ (4)

therefore,

$$K_a = \frac{[CS]}{[S_0 - CS][C_0 - CS]} .$$ (5)

The observed chemical shift (δ_{obs}) of H-5 of β-CD will be given by:

$$\delta_{\text{obs}} = \frac{C}{C_0}\,\delta_{\text{C}} + \frac{CS}{C_0}\,\delta_{\text{CS}} \tag{6}$$

where δ_{C} and δ_{CS} represent the chemical shifts due to H-5 of β-CD in unassociated and associated forms, respectively. Combining Equations 3 and 6 produces,

$$\delta_{\text{obs}} = \frac{C_0 - CS}{C_0}\,\delta_{\text{C}} + \frac{CS}{C_0}\,\delta_{\text{CS}} \,. \tag{7}$$

The change in chemical shift ($\Delta\delta$) of H-5 of β-CD is given by:

$$\Delta\delta = \delta_{\text{C}} - \delta_{\text{obs}} \,. \tag{8}$$

Combining Equations 7 and 8 gives,

$$\Delta\delta = \delta_{\text{C}} - \frac{C_0 - CS}{C_0}\,\delta_{\text{C}} - \frac{CS}{C_0}\,\delta_{\text{CS}} \tag{9}$$

which can be transformed to:

$$\Delta\delta = \frac{CS}{C_0}\,(\delta_{\text{C}} - \delta_{\text{CS}}) \,. \tag{10}$$

Letting $\delta_{\text{C}} - \delta_{\text{CS}} = Q$, thus,

$$CS = \frac{\Delta\delta\, C_0}{Q} \,. \tag{11}$$

Equation 5 is rearranged to:

$$\frac{CS}{K_{\text{a}}} = (CS)^2 - C_0 C_{\text{CS}} - S_0 CS + C_0 S_0 \,. \tag{12}$$

Substituting Equation 11 into Equation 12 and rearranging gives,

$$S_0 = \frac{\dfrac{\Delta\delta}{K_{\text{a}}} - \dfrac{C_0\,\Delta\delta^2}{Q} + C_0\,\Delta\delta}{Q - \Delta\delta} \,. \tag{13}$$

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