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A giant vesicle forming single tailed chiral surfactant for enantioseparation by micellar electrokinetic chromatography†‡

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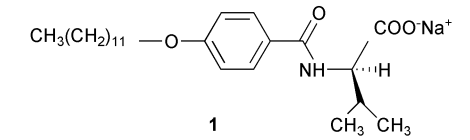
Light microscopy has shown the existence of giant bilayer vesicles in aqueous solutions of a novel chiral surfactant, sodium *N*-[4-dodecyloxybenzoyl]-L-valinate, which acts as a very good chiral selector for enantioseparation of (±)-1,1′-bi-2-naphthol and (±)-1,1′-binaphthyl-2,2′-diylhydrogenphosphate by micellar electrokinetic chromatography.

Analytical enantioseparation of racemic compounds is of great importance since enantiomers often present different pharmacological, pharmacokinetic, or toxicological properties. Successful enantiomeric separations have been achieved by capillary zone electrophoresis (CZE) using chiral "selectors" like cyclodextrins (CD), crown ethers, synthetic chelating reagents, and macrocyclic antibiotics.[1] Micellar electrokinetic chromatography (MEKC) has also been used as a chiral separation technique. The most popular additives for chiral separation by MEKC have been either chiral surfactants on their own[2a–e] or cyclodextrins in combination with either chiral[2f] or achiral[2g] surfactants. More recently, several research groups, after the first report by Wang *et al*., have used covalently linked chiral surfactants as pseudo-stationary phases in MEKC.[3] However, none of these chiral selectors is universal in their applicability and hence there is need for different chiral selectors.

In this report, we have evaluated the chiral selectivity of a novel amino acid derivatized chiral surfactant, sodium *N*-[4-dodecyloxybenzoyl]-L-valinate, **1** in chiral separation of the atropisomers of (±)-1,1′-bi-2-naphthol, **2**, and (±)-1,1′-binaphthyl-2,2′-diylhydrogenphosphate, **3** by MEKC. These compounds have important uses as shift reagents and chiral resolving agents for guest compounds,[4] and also as dissymmetric catalysts.[5] We demonstrate for the first time, the use of a vesicle forming surfactant as a pseudo-stationary phase for chiral analysis of atropisomers by MEKC. We also report for the first time, a simple single tailed *N*-acylamino acid derivative, which forms giant bilayer vesicles in dilute aqueous solutions.



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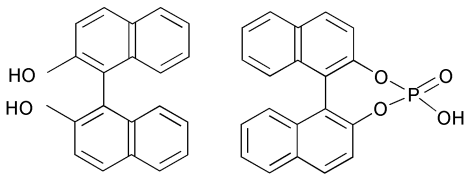

2 **3**

First, we determined the critical micelle concentration (cmc) of **1** in water by surface tension measurement.§ The measured cmc value is 2.5×10^{-5} M, which is 2 orders of magnitude lower than other *N*-acylamino acid surfactants reported so far.[1a,3] The low cmc value makes **1** a very good candidate for use as a pseudo-stationary phase in MEKC as it can be used at low concentrations which makes the running buffer less viscous and less conducting. As a result, the band broadening due to Joule heating and effective electrophoretic mobility of analytes is decreased. To demonstrate this we have performed the chiral analysis of **2**, and **3** using **1** as chiral selector in MEKC.¶ While optimum resolution for **2** (R_s = 3.8) was achieved in 50 mM borate buffer at pH 9.7 containing 2 mM surfactant, compound **3** (R_s = 1.4) could be separated well at pH 10.3. The electropherograms of **2** and **3** are shown in Figs. 1A and 1B, respectively. The chiral separations that are achieved using this surfactant are very good compared to those already reported in the literature.[3d,f–h] In comparison to other chiral surfactants, a much lower concentration of **1** is required for good optical resolution of the two said compounds.[2b,3h]

In order to explain the chiral selectivity of **1** we have studied the structure of the micellar aggregates in aqueous solution. It can be seen from the light micrograph‖ in Fig. 2 that the surfactant **1** self-assembles spontaneously to form giant vesicles in water. The good separation that has been obtained for **2** and **3** could be due to enhanced partitioning of the analytes in the

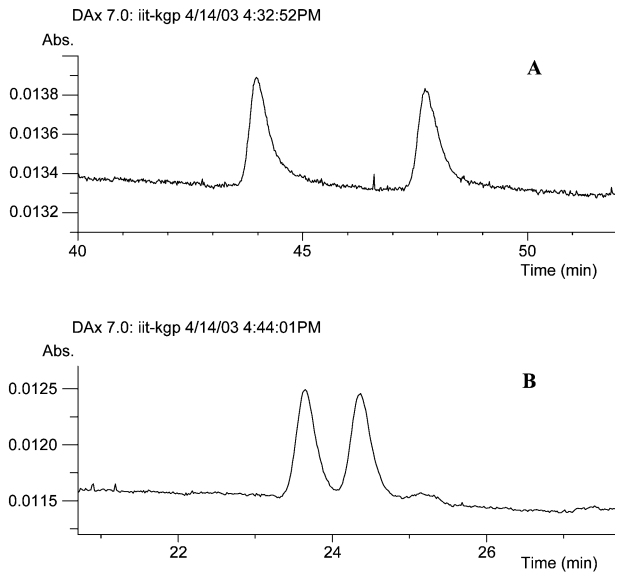

Fig. 1 Chiral MEKC separation of (±)-1,1'-bi-2-naphthol (**A**) and (±)-1,1'-binaphthyl-2,2'-diylhydrogenphosphate (**B**) with 50 mM borate buffer containing 2 mM surfactant (**1**); separation capillary: total length 87 cm, effective length 33 cm (50 μm ID); applied voltage 15 kV, detection wavelength 230 nm, temperature 30 °C.

† Electronic supplementary information (ESI) available: synthesis and capillary electrophoresis procedure. See http://www.rsc.org/suppdata/cc/b3/b303218c/

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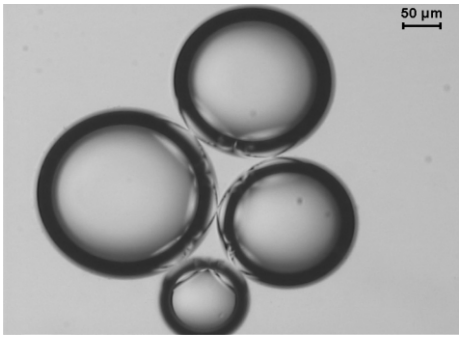

Fig. 2 Light micrograph of 2 mM aqueous solution of the surfactant, **1**.

vesicles. Indeed, this is indicated by the large migration time of the analytes in the presence of the surfactant.

In summary, we have synthesized a novel chiral surfactant, which self-assembles to form giant vesicles in dilute aqueous solutions as evident from the optical micrograph. The present amphiphile demonstrates its capability as a chiral resolving agent in MEKC. To our knowledge, this is the first example of chiral separation by MEKC using a vesicle forming surfactant. Also this is one of the few examples which demonstrates spontaneous formation of giant vesicles by a single tailed surfactant.

Notes and references

§ The surface tension (γ) measurements were carried out on a Surface and Interfacial Tensiometer (S. D.Hardson & Co., Kolkata, India) by Du Nuoy ring method. The cmc value was obtained from the break point of the plot of γ *vs*. log C. No minimum around the cmc could be observed confirming the purity of the surfactant.

¶ The MEKC separation was performed on a PrinCE Model 560 (Prince Technologies Ltd., The Netherlands) automated capillary electrophoresis system.

‖ The light micrograph was obtained from a LEICA-DMRXP microscope. The image was analyzed with the instrumental software, LEICA QWin. A 2 mM aqueous solution of **1** prepared 1 h before measurement was filtered through a 0.22 µm one way membrane Millex (Millipore) syringe filter and degassed in an ultrasonic bath before measurement. A drop of the degassed solution was put on a thoroughly cleaned glass plate using a micropipette and viewed through the microscope.

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