ORIGINAL ARTICLE

# Synthesis of Succinic Gemini Surfactants and the Effect of Stereochemistry on Their Monolayer Behaviors

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Abstract In this work, succinic gemini surfactants, dland meso-2,3-bis(alkyl)succinic acids (alkyl: C<sub>6</sub>H<sub>13</sub>-C<sub>13</sub>H<sub>27</sub>), were successfully synthesized by oxidative coupling of enolates of fatty acid tert-butyl esters with copper(II) bromide followed by treatment with CF<sub>3</sub>COOH. Focusing on the influence of stereochemistry (dl- and meso-) of succinic geminis, their monolayer behaviors at the air-water interface were explored using surface pressure-area ( $\Pi$ -A) isotherms, the compression modulus of monolayers  $(\varepsilon_s)$ , and Brewster angle microscope (BAM) analysis. meso-2,3-Bis(undecyl)succinic acid showed a unique isotherm where the surface pressure drastically decreased at  $A = \sim 0.56 \text{ nm}^2$  ( $\Pi = 21.9 \text{ mN m}^{-1}$ ) regardless of compression rates and subphase temperatures, while *dl*-isomer showed the common isotherm of gas  $\rightarrow$  liquid-expanded  $\rightarrow$  liquid-condensed phase transitions. BAM analysis on meso-2,3-bis(undecyl)succinic acid films at the air-water interface showed that small islands of aggregates appear just after the maximum pressure  $(A = \sim 0.56 \text{ nm}^2)$ , and on further compression needleshaped assemblies appear that can grow in size. It was reasonably concluded that hydrophobic interactions can

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**Keywords** Succinic Gemini · Stereochemistry · Monolayer · Surface pressure–area isotherm · Brewster angle microscope · Compression modulus of monolayer · Jumping-up phenomena

# Introduction

Gemini surfactants consist of two surfactants covalently attached by a spacer group at the level of, or in close vicinity to, the head groups. It has been widely accepted that they show higher efficiency in decreasing the surface tension of water to achieve one to two orders of magnitude lower critical micelle concentration (CMC) values and smaller surface tensions at their CMC ( $\gamma_{CMC}$ ) than the corresponding monomeric surfactants [1–7]. A lot of studies on the effects of structural factors such as the length of hydrophobic chains, head groups, spacers, and counter ions on their surface properties in aqueous solution (structure–performance relationship) have been reported so far [8–10].

From the viewpoint of molecular structure, Gemini surfactants having asymmetric carbon atoms or chiral groups represent a new class of twin-tailed and twin-chiral amphiphiles. With respect to the chirality of the spacer, Sommerdijk et al. [11] reported the effects on the transition temperature of liposome bilayers and calcium binding of synthetic gemini phospholipids. Bello et al. [12, 13] also reported the role of the spacer stereochemistry on the

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aggregation properties of cationic gemini surfactants. Furthermore, the stereochemistry at the point of attachment of spacer group would also be one of the important structural factors for the surface properties of gemini surfactants. In this decade, several studies on the correlation between the stereochemistry at the point of attachment of spacer group, physical properties and self-aggregation behavior of gemini surfactants have been reported [14–21], but more research is needed.

According to our literature searches, Harvey and his coworkers' work should be the first report focusing on the effects of the chirality at the connecting points of dimeric surfactants on the monolayer behavior at the air-water interface with the aid of surface pressure-area ( $\Pi$ -A) isotherms [22]. Four pairs of diastereomeric surfactants were prepared (meso or dl) by joining two pentadecanoic acid units by a carbonyl group at the 3,3', 6,6', 9,9', and 12,12'-positions. In all cases the meso monolayers were compressed more easily than their *dl* diastereomers, which they attributed to better lateral alignment of the hydrocarbon chains about the meso plane of symmetry in comparison with the *dl* plane. Based on molecular mechanics, Porter concluded that the *dl* compounds have a preferred conformation that resists compression at the air-water interface [23].

Most chiral gemini surfactants have been derived from natural chiral resources such as tartaric acid, amino acids, and alkyl glucosides [24-33]. Nakanishi et al. [31] investigated the  $\Pi$ -A isotherms of stereoisomers of *l*- and *meso*-O.O'-dialkanoyl tartaric acid on aqueous CdCl<sub>2</sub>/KHCO<sub>3</sub> solutions. They found *l*- and *meso- O,O'*-bis(tetradecanoyl) tartaric acids formed stable monolayers with limited molecular areas of 0.48 and 0.43 nm<sup>2</sup>, respectively, and succeeded in preparation of LB films as Y-type films from the *meso*-isomer and as Z-type film from the *l*-isomer. Similarly, we also measured the  $\Pi$ -A isotherms of *l*-O,O'dialkanoyl tartaric gemini amphiphiles on water (pH = 2)and investigated the effects of the length of the hydrophobic alkanoyl chains [32] and their asymmetrical diversity [33]. A more tightly packed monolayer was formed at the air-water interface with increase in hydrophobic alkanoyl chain length. Aside from those works, Shankar et al. [16–19] found that enantiomerically pure tartaric acid-based surfactants form more stable vesicles and have a lower CMC compared to their racemic mixtures. They also reported the monolayer behavior of chiral gemini, (2R,3R)-(+)-bis(decyloxy)- and (2S,3S)-(-)bis(decyloxy)succinic acids (otherwise, l-O,O'-bis(decyl)and d-O,O'-bis(decyl)tartaric acid, respectively), at the airwater interface [18] and observed the spontaneous separation of chiral phases in the monolayers of the racemate [17].

Previously, we reported the synthesis of 2,3-bis(undecyl)succinic acid 3e, hereafter abbreviated as succinic gemini surfactant, where two vicinal COOH head groups are also attaching directly to the chiral centers, from corynomicolic acid [34]. We measured the surface tensions of the meso- and dl-diastereomers in KOH solution and clarified the effect of stereochemistry of succinic gemini on their surface tension isotherms. It should be noted that meso-3e showed two breakpoints in surface tension vs lnC isotherms, while *dl*-3e gave the common variation as expected. We suspected that the first breakpoint may be due to premicellar aggregate formation in dilute solution, while the second breakpoint is the critical micelle concentration. We interpreted this premicellar formation in terms of the intermolecular interaction between two alkyl groups and the electrostatic repulsion between two hydrophilic COO<sup>-</sup> groups.

In the present work, we report a simple but useful synthesis of dl- and meso-2,3-bis(alkyl)succinic acids by the oxidative coupling of enolates of fatty acid *tert*-butyl esters with copper(II) bromide followed by treatment with CF<sub>3</sub>COOH, and their unique monolayer and self-assembling behaviors at the air–water interface as a consequence of their stereochemistry.

# **Experimental Procedures**

## Materials

All reagents and solvents were purchased from Wako Pure Chemical Industries. Purification of solvents was done as usual, THF over Na/benzophenone. Water was prepared by ultrafiltration of distilled water using an Advantec pure water system RFU354BA. Infrared spectra were recorded on a Nicolet Avator 370 DTGS FTIR spectrometer, the <sup>1</sup>H-NMR spectra were recorded on a Bruker AC-300 spectrometer. The mass spectra were taken on a JEOL Mstation JMS-700 mass spectrometer in HR-FABMS mode. Elemental analysis was accomplished on a Yanaco CHN CORDER MT-5 Elemental analyzer with an oxygen determination kit.

# Synthesis

## Di-tert-butyl 2,3-bis(alkyl)succinate (2)

The succinic Gemini surfactants, *dl*- and *meso*-2,3bis(alkyl)succinic acids, were synthesized by the oxidative coupling of enolates of fatty acid esters with copper(II) bromide according to Quermann et al. [35] and subsequent deprotection of ester groups. Following is a typical synthesis of di-tert-butyl 2.3-bis(undecyl)succinate. 2e: first of all. tert-butyl tridecanoate 1e was prepared from tert-butanol, tridecanoic acid, dicyclohexyl carbodiimide (DCC) and DMAP (0.2 equiv) in toluene under stirring at room temperature. In a dry 100 mL flask equipped with a dropping funnel, septum inlet, and magnetic stirrer, a solution of 12.5 mL of lithium diisopropylamide (2.0 M in hexane/ THF) and 30 mL of dry THF were added under nitrogen. Under cooling at -78 °C, 25 mmol of 1e in 10 mL dry THF was added dropwise over a period of 30 min, and then the mixture was stirred for an additional 15 min. With vigorous stirring 5.0 g of anhydrous CuBr<sub>2</sub> powder was added all at once to the solution. After stirring for 30 min, the reaction was quenched by adding 50 mL of 1 M HCl at this temperature, and the mixture was allowed to reach room temperature. After extracting twice with hexane (75 mL each), the combined organic layer was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. By means of a shortpath vacuum distillation apparatus, both unreacted ester and  $\alpha$ -bromo ester (5e) were distilled off (~160 °C, 1 mmHg). The residue was subjected to column chromatography on silica eluting with hexane/diethyl ether (20:1) to separate *dl*- (*dl*-2e) and *meso*-isomers (*meso*-2e) at the yields of 36 and 25 %, respectively. Other dl- and meso-isomers of 2a-2g were also prepared in a similar manner, and diastereomers (dl and meso) were separated by SiO<sub>2</sub> chromatography.

*dl*-**2a** (R = C<sub>6</sub>H<sub>13</sub>): yield: 39 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.88$  [t, 6H, J = 6.5 Hz,  $-(CH_2)_5-CH_3$ ], 1.26–1.56 [m, 20H,  $-CH-(CH_2)_5-CH_3$ ], 1.41 [s, 18H,  $-COO-C(CH_3)_3$ ], 2.67 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1730 (C=O).

*meso-***2a** (R = C<sub>6</sub>H<sub>13</sub>): yield: 30 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.89 [t, 6H, J = 6.5 Hz, -(CH<sub>2</sub>)<sub>5</sub>-CH<sub>3</sub>], 1.26–1.58 [m, 20H, -CH–(CH<sub>2</sub>)<sub>5</sub>–CH<sub>3</sub>], 1.42 [s, 18H, -COO–C(CH<sub>3</sub>)<sub>3</sub>], 2.63 (m, 2H, -CH–CH–): IR (KBr, cm<sup>-1</sup>): v 1724 (C=O).

*dl*-**2b** (R = C<sub>8</sub>H<sub>17</sub>): yield: 32 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.86$  [t, 6H, J = 6.1 Hz,  $-(CH_2)_7-CH_3$ ], 1.25–1.55 [m, 28H,  $-CH-(CH_2)_7-CH_3$ ], 1.42 [s, 18H,  $-COO-C(CH_3)_3$ ], 2.67 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1733 (C=O).

*meso-***2b** (R = C<sub>8</sub>H<sub>17</sub>): yield: 24 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.88 [t, 6H, J = 6.1 Hz, -(CH<sub>2</sub>)<sub>7</sub>-CH<sub>3</sub>], 1.25–1.57 [m, 28H, -CH–(CH<sub>2</sub>)<sub>7</sub>-CH<sub>3</sub>], 1.41 [s, 18H, -COO–C(CH<sub>3</sub>)<sub>3</sub>], 2.62 (m, 2H, -CH–CH–): IR (KBr, cm<sup>-1</sup>): v 1726 (C=O).

*dl*-**2c** (R = C<sub>9</sub>H<sub>19</sub>): yield: 31 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.87$  [t, 6H, J = 6.4 Hz,  $-(CH_2)_8-CH_3$ ], 1.25–1.57 [m, 32H,  $-CH-(CH_2)_8-CH_3$ ], 1.43 [s, 18H,  $-COO-C(CH_3)_3$ ], 2.66 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1729 (C=O).

*meso*-2c (R = C<sub>9</sub>H<sub>19</sub>): yield: 29 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.87 [t, 6H, J = 6.4 Hz, -(CH<sub>2</sub>)<sub>8</sub>-CH<sub>3</sub>], 1.25–1.58 [m, 32H, -CH-(CH<sub>2</sub>)<sub>8</sub>-CH<sub>3</sub>], 1.42 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.62 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): y 1720 (C=O).

*dl*-**2d** (R = C<sub>10</sub>H<sub>21</sub>): yield: 32 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.86$  [t, 6H, J = 6.6 Hz,  $-(CH_2)_9-CH_3$ ], 1.25–1.56 [m, 36H,  $-CH-(CH_2)_9-CH_3$ ], 1.40 [s, 18H,  $-COO-C(CH_3)_3$ ], 2.66 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1733 (C=O).

*meso*-2d (R = C<sub>10</sub>H<sub>21</sub>): yield: 28 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.88 [t, 6H, J = 6.6 Hz, -(CH<sub>2</sub>)<sub>9</sub>-CH<sub>3</sub>], 1.25–1.57 [m, 36H, -CH-(CH<sub>2</sub>)<sub>9</sub>-CH<sub>3</sub>], 1.42 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.62 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1723 (C=O).

*dl*-**2e** (R = C<sub>11</sub>H<sub>23</sub>): yield: 36 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.85 [t, 6H, *J* = 6.6 Hz, -(CH<sub>2</sub>)<sub>10</sub>-CH<sub>3</sub>], 1.22-1.59 [m, 40H, -CH-(CH<sub>2</sub>)<sub>10</sub>-CH<sub>3</sub>], 1.41 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.68 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): *v* 1736 (C=O).

*meso-***2e** (R = C<sub>11</sub>H<sub>23</sub>): yield: 25 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.85 [t, 6H, *J* = 6.6 Hz, -(CH<sub>2</sub>)<sub>10</sub>-CH<sub>3</sub>], 1.23-1.59 [m, 40H, -CH-(CH<sub>2</sub>)<sub>10</sub>-CH<sub>3</sub>], 1.43 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.63 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1731 (C=O).

*dl*-**2f** (R = C<sub>12</sub>H<sub>25</sub>): yield: 27 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.88 [t, 6H, *J* = 6.6 Hz, -(CH<sub>2</sub>)<sub>11</sub>-CH<sub>3</sub>], 1.26-1.58 [m, 44H, -CH-(CH<sub>2</sub>)<sub>11</sub>-CH<sub>3</sub>], 1.42 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.67 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): *v* 1733 (C=O).

*meso-***2f** (R = C<sub>12</sub>H<sub>25</sub>): yield:25 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.88 [t, 6H, J = 6.6 Hz, -(CH<sub>2</sub>)<sub>11</sub>-CH<sub>3</sub>], 1.26-1.58 [m, 44H, -CH-(CH<sub>2</sub>)<sub>11</sub>-CH<sub>3</sub>], 1.42 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.63 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1724 (C=O).

*dl*-**2g** (R = C<sub>13</sub>H<sub>27</sub>): yield: 31 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.88$  [t, 6H, J = 6.6 Hz,  $-(CH_2)_{12}$ -CH<sub>3</sub>], 1.25-1.55 [m, 48H,  $-CH-(CH_2)_{12}$ -CH<sub>3</sub>], 1.43 [s, 18H,  $-COO-C(CH_3)_3$ ], 2.67 [m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1732 (C=O).

*meso*-**2g** (R = C<sub>13</sub>H<sub>27</sub>): yield: 26 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.88 [t, 6H, J = 6.6 Hz, -(CH<sub>2</sub>)<sub>12</sub>-CH<sub>3</sub>], 1.25-1.57 [m, 48H, -CH-(CH<sub>2</sub>)<sub>12</sub>-CH<sub>3</sub>], 1.40 [s, 18H, -COO-C(CH<sub>3</sub>)<sub>3</sub>], 2.62 (m, 2H, -CH-CH-): IR (KBr, cm<sup>-1</sup>): v 1724 (C=O).

# 2,3-Bis(alkyl)succinic acid (3)

According to Andrés et al. [36], each isomer (*meso-* and *dl*-**2e**) was treated with CF<sub>3</sub>COOH to remove the *tert*-butyl group: A mixture of *meso-***2e** (0.216 g, 0.4 mmol) and CF<sub>3</sub>COOH (3 mL) was stirred for 30 min at room

temperature. After removal of CF<sub>3</sub>COOH under reduced pressure, the residue was extracted with ether (10 mL × 3), washed with water, and dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporation of ether, the residue was washed with cold CHCl<sub>3</sub> and recrystallized from THF/hexane to afford *meso-***3e** (0.109 g, 64 %). In the case of *dl-***2e**, after similar operation, CHCl<sub>3</sub> filtrate was concentrated, and the residue was recrystallized from THF/hexane to afford *dl-***3e** (0.099 g, 58 %).

*dl*-**3e** (R = C<sub>11</sub>H<sub>23</sub>): mp 87.9–88.7 °C; yield: 58 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.86$  [t, 6H, J = 6.6 Hz, –(CH<sub>2</sub>)<sub>10</sub>–**CH**<sub>3</sub>], 1.23–1.64 [m, 48H, –(**CH**<sub>2</sub>)<sub>10</sub>–CH<sub>3</sub>], 2.64 (m, 2H, –**CH**–**CH**–); IR (KBr, cm<sup>-1</sup>): v 3231 (OH), 1707 (C=O); mass (HR-FABMS) *m/z*: [M+H]<sup>+</sup> 427.3797 (calc. for C<sub>26</sub>H<sub>51</sub>O<sub>4</sub>: 427.3787); anal. calc. for C<sub>26</sub>H<sub>50</sub>O<sub>4</sub>: C, 73.19; H, 11.81; O, 15.00. Found: C, 73.31; H, 11.92; O, 14.77.

*meso-***3e** (R = C<sub>11</sub>H<sub>23</sub>): mp 134.7–135.3 °C; yield: 64 %; <sup>1</sup>H NMR (300 MHz,  $d_4$ -MeOH)  $\delta$  = 0.87 [t, 6H, J = 6.7 Hz, -(CH<sub>2</sub>)<sub>10</sub>–**CH<sub>3</sub>**], 1.26–1.58 [m, 48H, -(**CH<sub>2</sub>)<sub>10</sub>–CH<sub>3</sub>**], 2.48 (m, 2H, -**CH–CH–**); IR (KBr, cm<sup>-1</sup>): v 3408 (OH), 1698 (C=O); mass (HR-FABMS) *m/z*: [M+H]<sup>+</sup> 427.3791 (calc. for C<sub>26</sub>H<sub>51</sub>O<sub>4</sub>: 427.3787); anal. calc. for C<sub>26</sub>H<sub>50</sub>O<sub>4</sub>: C, 73.19; H, 11.81; O, 15.00. Found: C, 73.11; H, 11.94; O, 14.95.

Other *dl*- and *meso*-isomers of 3c (R = C<sub>9</sub>H<sub>19</sub>) and 3g (R = C<sub>13</sub>H<sub>27</sub>) were also prepared in a similar manner.

*dl*-**3c** (R = C<sub>9</sub>H<sub>19</sub>): mp 72.2–73.0 °C; yield: 68 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta = 0.86$  [t, 6H, J = 6.8 Hz, –(CH<sub>2</sub>)<sub>8</sub>–**CH**<sub>3</sub>], 1.27–1.66 [m, 32H, –(**CH**<sub>2</sub>)<sub>8</sub>–**CH**<sub>3</sub>], 2.62–2.64 (m, 2H, –**CH**–**CH**–); IR (KBr, cm<sup>-1</sup>): *v* 3235 (OH), 1712 (C=O); mass (HR-FABMS) *m*/*z*: [M+H]<sup>+</sup> 371.3160 (calc. for C<sub>22</sub>H<sub>43</sub>O<sub>4</sub>: 371.3164); anal. calc. for C<sub>22</sub>H<sub>42</sub>O<sub>4</sub>: C, 71.31; H, 11.42; O, 17.27. Found: C, 71.40; H, 11.38; O, 17.22.

*meso*-**3c** (R = C<sub>9</sub>H<sub>19</sub>): mp 118.9–120.3 °C; yield: 68 %; <sup>1</sup>H NMR (300 MHz,  $d_4$ -MeOH)  $\delta = 0.87$  [t, 6H, J = 6.8 Hz, –(CH<sub>2</sub>)<sub>8</sub>–CH<sub>3</sub>], 1.26–1.54 [m, 32H, –(CH<sub>2</sub>)<sub>8</sub>– CH<sub>3</sub>], 2.46–2.49 (m, 2H, –CH–CH–); IR (KBr, cm<sup>-1</sup>):  $\nu$ 3428 (OH), 1694 (C=O); mass (HR-FABMS) *m*/*z*: [M+H]<sup>+</sup> 371.3169 (calc. for C<sub>22</sub>H<sub>43</sub>O<sub>4</sub>: 371.3164); anal. calc. for C<sub>22</sub>H<sub>42</sub>O<sub>4</sub>: C, 71.31; H, 11.42; O, 17.27. Found: C, 71.56; H, 11.28; O, 17.16.

*dl*-**3g** (R = C<sub>13</sub>H<sub>27</sub>): mp 96.6–97.7 °C; yield: 58 %; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.85 [t, 6H, *J* = 6.3 Hz, –(CH<sub>2</sub>)<sub>12</sub>–**CH<sub>3</sub>**], 1.23–1.64 [m, 48H, –(**CH<sub>2</sub>**)<sub>12</sub>–**CH<sub>3</sub>**], 2.63 (m, 2H, –**CH–CH–**); IR (KBr, cm<sup>-1</sup>): *v* 3228 (OH), 1708 (C=O); mass (HR-FABMS) *m*/*z*: [M+H]<sup>+</sup> 483.4408 (calc. for C<sub>30</sub>H<sub>59</sub>O<sub>4</sub>: 483.4413); anal. calc. for C<sub>30</sub>H<sub>58</sub>O<sub>4</sub>: C, 74.63; H, 12.11; O, 13.26. Found: C, 74.36; H, 11.98; O, 13.66.

*meso*-**3g** (R = C<sub>13</sub>H<sub>27</sub>): mp 132.6–133.7 °C; yield: 61 %; <sup>1</sup>H NMR (300 MHz,  $d_4$ -MeOH)  $\delta = 0.87$  [t, 6H,

J = 6.7 Hz,  $-(CH_2)_{12}-CH_3$ ], 1.25-1.54 [m, 48H,  $-(CH_2)_{12}-CH_3$ ], 2.46-2.49 (m, 2H, -CH-CH-); IR (KBr, cm<sup>-1</sup>): v 3446 (OH), 1695 (C=O); mass (HR-FABMS) *m*/*z*: [M+H]<sup>+</sup> 483.4419 (calc. for C<sub>30</sub>H<sub>59</sub>O<sub>4</sub>: 483.4413); anal. calc. for C<sub>30</sub>H<sub>58</sub>O<sub>4</sub>: C, 74.63; H, 12.11; O, 13.26. Found: C, 74.71; H, 12.18; O, 13.11.

# Methods

### Surface Pressure–Area ( $\Pi$ –A) Isotherm

Surface pressure-area  $(\Pi - A)$  isotherms were obtained using a KSV Minitrough 2000 kept in a dust shield enclosure. The total trough surface area was  $364 \times 75 \text{ mm}^2$  with a trough volume  $\sim 170$  mL. The trough area was robotically controlled by two hydrophobic barriers that compressed the spread film symmetrically and bilaterally at a rate of 10 mm min<sup>-1</sup> (7.5  $\times$  10<sup>-4</sup> m<sup>2</sup> min<sup>-1</sup>). A roughened platinum Wilhelmy plate, which was flame-cleaned prior to each measurement, was placed in the middle of the trough facing (parallel to) the moving barriers. Spreading solutions of  $1.60 \times 10^{-3}$  mol L<sup>-1</sup> in Benzene/THF (3/2, v/v) (spectra grade) were prepared 24 h prior to use and were used within 2 days. Prior to each measurement, the subphase surface was cleaned by aspiration, such that the measured surface pressure remained <0.20 mN m<sup>-1</sup> over a full compression. A 20-25 µL volume of gemini solution was deposited in 10 drops uniformly distributed onto the 0.001 M HCl surface (pH = 3.0) using a gas-tight Hamilton syringe, and left to evaporate and spread evenly over a period of 30 min at the subphase temperature of 25.0 °C. Unless otherwise noted, all measurements were made at 15.0 °C and at the barrier moving speed of  $10 \text{ mm min}^{-1}$ . In the compression rate dependency experiments, the barrier moving speed was varied from  $3.8 \times 10^{-4} \text{ m}^2 \text{ min}^{-1}$  to  $2.3 \times 10^{-3} \text{ m}^2 \text{ min}^{-1}$ at T = 15.0 °C. In subphase temperature dependency experiments, after spreading 3e over 0.001 M HCl subphase at 25.0 °C and maintained for 30 min, the subphase temperature was adjusted to the target temperature (5.0-25.0 °C), and maintained for at least 30 min before measurements. Measurements were made at a compression rate of  $7.5 \times 10^{-4} \text{ m}^2 \text{ min}^{-1}$ . Each measurement was repeated at least three times to check the reproducibility of the isotherms, which in all cases was reproducible with standard deviations for molecular surface area and surface pressure,  $\sim 0.1 \text{ nm}^2$  and  $\sim 0.1 \text{ mN m}^{-1}$ , respectively.

### Relaxation Behavior in $\Pi$ -A Isotherm

Relaxation behaviors (hysteresis) of **3e** in  $\Pi$ -A isotherms were investigated by the iterative measurements of compression to the first-specified surface pressure  $\Pi_{1st}$  (first compression), decompression to the initial spreading area (expansion), and immediate recompression to the measurable limit area. Compression and decompression rate was kept at  $7.5 \times 10^{-4} \text{ m}^2 \text{ min}^{-1}$ .

#### Brewster Angle Microscope (BAM)

The monolayer was directly visualized by a Brewster angle microscope (KSV Optrel BAM 300, KSV Instruments Ltd., Finland) coupled to KSV Minitrough. The application of a 20 mW He–Ne laser emitting *p*-polarized light of 632.8 nm wavelength and a 10 × objective lens (M Plan Apo, Mitsutoyo, Japan). The angle of the incident beam to the air/water interface was fixed at the Brewster angle (53.1°) at 288.2 K. The reflected beam was recorded with a high grade charge coupled device (CCD) camera (EHDkam-Pro02, EHD Imaging GmbH, Germany), and the BAM images were digitally saved to a computer hard disk.

## **Compression Modulus of Monolayer**

The compression modulus of the monolayer ( $\varepsilon_s$ ) on the water surface was calculated from the  $\Pi$ -A isotherm using Eq. (1) [37–39].

$$\varepsilon_{\rm s} = -A({\rm d}\Pi/{\rm d}A)_T \tag{1}$$

The  $\varepsilon_s(\max)$  was defined as the maximum of  $\varepsilon_s$ , and the collapsing point in this work was defined as the point on the isotherm where  $\varepsilon_s$  reaches  $\varepsilon_s(\max)$ .

# **Results and Discussion**

## **Synthesis**

In our previous work [34], 2,3-bis(undecyl)succinic acid, succinic Gemini surfactant, 3e was successfully synthesized from corynomicolic acid by the functional interconversion of OH of corynomicolic acid to COOH. However, this synthetic route consists of multiple reaction steps including synthesis of corynomicolic acid, mesylation of syn-OH, dimethanesulfonic acid to  $E-\alpha,\beta$ -unsaturated ester, Michael addition of "CN, separation of syn- and anti-isomers, and hydrolysis of CN to COOH. Though all steps proceeded at good yields, the last hydrolysis step required extraordinary condition, such as 75 % H<sub>2</sub>SO<sub>4</sub> at 190 °C, and *dl*-2,3-bis(undecyl)succinic acid was predominately obtained as its anhydride even from the syn-isomer. We were not successful in selective synthesis of meso-2,3bis(undecyl)succinic acid, which was separated by column chromatography of a mixture of *dl*- and *meso*-anhydrides.

Aside from our synthesis, Quermann et al. [35] reported the oxidative coupling of enolates of fatty acid methyl esters with copper(II) bromide to afford dimethyl esters of dialkylated succinic acid. As their synthesis is only one step (oxidative coupling), we also examined their technique under similar conditions (Scheme 1). Results of oxidative coupling of methyl and tert-butyl esters were summarized in Table 1. For example, the coupling of methyl tridecanoate afforded a mixture of meso- and dl-isomers of dimethyl 2,3-bis(undecyl)succinate 2e, methyl 2-undecyl-3-oxo-pentadecanoate (Claisen condensation product), and  $\alpha$ -bromo methyl tridecanoate (33:40:9:8) with recovery of unreacted methyl tridecanoate (10 %). Quermann also reported the production of both  $\alpha$ -bromo ester and the Claisen condensation product. Though unreacted ester and  $\alpha$ bromo ester were easily removed by distillation, the Claisen condensation product, which may be unavoidable when methyl esters were used, made it more cumbersome to separate and purify meso- and dl-isomers by column chromatography.

It has been known that enolate of *tert*-butyl ester is more stable than those of methyl and ethyl esters, and self-Claisen condensation of *tert*-butyl ester is often unlikely to occur. Thus, to suppress the Claisen condensation product, *tert*-butyl esters of fatty acids were employed in place of methyl esters. As can be seen in Table 1, steric hindrance by *tert*-butyl group worked well to afford no Claisen condensation products as might have been expected, but with higher yields of *dl*-isomers ( $\sim$ 1.4:1) over *meso*-isomers in comparison with the case of methyl esters ( $\sim$ 1.2:1).

The coupling products, *dl*- and *meso*-succinic esters, were successfully separated by column chromatography on silica eluting with hexane/diethyl ether (20:1), and they were hydrolyzed separately. Surprisingly, 2,3-bis(undecyl)succinic acid dimethyl esters were quite resistant to usual hydrolysis by acids and base as shown in Table 2, which might be the reason why Quermann did not report the conversion of COOMe to the corresponding COOH. In contrast, we previously succeeded in the conversion of CN group to COOH using the extreme conditions, namely 75 % H<sub>2</sub>SO<sub>4</sub> at 190 °C [34]. Similarly, we carried out hydrolysis of 2 using 50 % H<sub>2</sub>SO<sub>4</sub> at 190 °C, and 2,3dialkylsuccinic acids 3 were successfully obtained together with acid anhydrides of *dl*-isomers. However, as the hydrolysis conditions were somewhat radical, both meso- and dl-isomers were always obtained even when one pure diastereomer was used. To the contrast, in the case of tertbutyl ester, the hydrolysis conditions could be lowered such as 50 % H<sub>2</sub>SO<sub>4</sub> at 130 °C or 35 % H<sub>2</sub>SO<sub>4</sub> at 190 °C, and no acid anhydride was produced. In addition, according to Andrés et al. [36], tert-butyl esters can be smoothly converted to their COOH by treatment with CF<sub>3</sub>COOH. Indeed, both meso- and dl-3e were obtained from the corresponding tert-butyl esters without any production of another diastereomer.



 Table 1 Results of oxidative coupling of fatty acid esters

Compounds		Yield (%)						
		Me ester	r	tert-Bu ester				
Abbrev.	R	meso	dl	meso	dl			
2a	C <sub>6</sub> H <sub>13</sub>	32	41	30	39			
2b	$C_{8}H_{17}$	29	35	24	32			
2c	C9H19	35	38	29	31			
2d	$C_{10}H_{21}$	37	41	28	32			
2e	$C_{11}H_{23}$	29	38	25	36			
2f	$C_{12}H_{25}$	30	37	25	27			
2g	$C_{13}H_{27}$	28	33	26	31			

#### **Surface Properties**

As previously reported [34], we studied the surface tension isotherms of succinic Geminis (*meso-* and *dl-*3e) in KOH solution and clarified the effect of stereochemistry on surface tension isotherms. In this work, the effects of stereochemistry on monolayer formation behavior of succinic gemini were studied from surface pressure-area ( $\Pi$ -A) measurements.

#### Surface Pressure–Area ( $\Pi$ –A) Isotherm

The surface pressure–area ( $\Pi$ –A) isotherms of *meso-* and *dl*-2,3-bis(undecyl)succinic acids **3e** at a subphase temperature of 15.0 °C are shown in Fig. 1a. In addition, the compression modulus of *meso-* and *dl*-**3e** monolayers are plotted against A (Fig. 1b). As can be seen, the effects of stereochemistry on their  $\Pi$ –A and  $\varepsilon_s$ -A curves are striking. In the case of *dl*-**3e**, the isotherm lifted off at the area of 0.78 nm<sup>2</sup> and showed evidence of the following behavior

sequence: gas (G)  $\rightarrow$  liquid expanded (LE)  $\rightarrow$  liquid condensed (LC). After passing the maximum pressure of 43 mN m<sup>-1</sup> at A = 0.44 nm<sup>2</sup>, the pressure decreased to 38 mN m<sup>-1</sup> and reached the plateau region. In our previous study on the monolayers of *l-O,O'*-bis(alkanoyl)tartaric acids, the maximum values of  $\varepsilon_s$ ,  $\varepsilon_s(max)$ , were  $\sim 50$  mN m<sup>-1</sup>, 80–100 mN m<sup>-1</sup>, and over 200 mN m<sup>-1</sup> for LE, LC and solid states, respectively. As shown in Fig. 1b,  $\varepsilon_s(max)$  of *dl*-**3e** was  $\sim 130$  mN m<sup>-1</sup>, which indicates that the monolayer collapses in the condensed liquid region. The zero-pressure molecular area ( $A_0$ ) obtained by extrapolating the condensed region to zero pressure is 0.70 nm<sup>2</sup> for *dl*-**3e**.

Shankar et al. [17, 18] reported similar isotherms for (2R,3R)-(+)-bis(decyloxy)succinic acid, (2S,3S)-(-)-bis(decyloxy)succinic acid and ( $\pm$ )-bis(decyloxy)succinic acid, but there were no maximum on their isotherms. Their values of  $A_0$  were all ~0.7 nm<sup>2</sup>. Furthermore, with optimizing the geometry of (2R,3R)-(+)-bis(decyloxy)succinic acid to an upright orientation at the air-water interface, they also calculated the Connolly surface with a head group area of ~0.72 nm<sup>2</sup>. Good consistency with  $A_0$  of *dl*-**3e** would indicate that *dl*-**3e** also adopts an upright orientation at the air-water interface.

On the contrary, *meso-***3e** showed a quite different and interesting monolayer behavior. On compression, the isotherm lifted off at the area of 0.77 nm<sup>2</sup>, which was almost same to that of *dl*-**3e**, and surface pressure increased similar to the *dl*-isomer. However, at  $\Pi = 21.9$  mN m<sup>-1</sup>, which was the maximum surface pressure for *meso-***3e**, the isotherm varied drastically decreasing to ~8 mN m<sup>-1</sup> (at A = ~0.3 nm<sup>2</sup>), and again began to increase slowly. Similar to *dl-***3e**,  $\varepsilon_{\rm s}(\text{max})$  of *meso-***3e** was ~100 mN/m, which would also indicate that the monolayer can reach the

Table 2 Results of hydrolysis of 2,3-bis(undecyl)succinic acid diesters

Entry	Diester	Acid or base	Solvent	Temp. (°C)	Time	Yields (%)			
						Recovery of 2	3e		Other <sup>a</sup>
							dl	meso	(dl)
1	Me (dl)	$H_2SO_4$	Dioxane/H <sub>2</sub> O (5/1)	Reflux	2 days	80	5	_	_
2		HCl	Dioxane/H <sub>2</sub> O (5/1)	Reflux	1 day	60	30	-	-
3		КОН	EtOH/H <sub>2</sub> O (5/1)	Reflux	2 days	30	30	10	-
4		50 % H <sub>2</sub> SO <sub>4</sub>		$150 \rightarrow 190$	3 h	4	50	10	33
5	tert-Bu (dl)	50 % H <sub>2</sub> SO <sub>4</sub>		130	3 h	2	60	32	<1
6		CF <sub>3</sub> COOH		rt	30 min	_	58	_	_
7	Me (meso)	$H_2SO_4$	Dioxane/H <sub>2</sub> O (5/1)	Reflux	2 days	No reaction			
8		HCl	Dioxane/H <sub>2</sub> O (5/1)	Reflux	2 days	No reaction			
9		КОН	EtOH/H <sub>2</sub> O (5/1)	Reflux	2 days	95	Not o	detected	
10		50 % H <sub>2</sub> SO <sub>4</sub>		$150 \rightarrow 190$	3 h	6	35	17	7
11	tert-Bu (meso)	50 % H <sub>2</sub> SO <sub>4</sub>		130	3 h	6	35	45	-
12		CF <sub>3</sub> COOH		rt	30 min	-	-	64	

<sup>a</sup> Acid anhydride

condensed liquid phase but collapses soon after. The  $A_0$  for *meso-***3e** was determined to be 0.73 nm<sup>2</sup>. Quite similar liftoff area and  $A_0$  of *meso-***3e** to those of *dl-***3e** would also mean that *meso-***3e** assumes an upright orientation at the air-water interface.

Harvey obtained a very analogous appearance of an optimum on  $\Pi$ -A isotherm for dl-3,3'-keto-pentadecanoic acid dimer, while its *meso*-isomer showed an ordinary isotherm [22]. They interpreted the different monolayer behaviors of *meso*- and dl-isomers in terms of the relative stereochemistry at the point of attachment of two chains of the carbonyl bridge, but there were no explanations for the drastic decrease in  $\Pi$ -A isotherm. However, our results on the effect of the stereochemistry on isotherms were completely opposite to their observation.

Though not gemini surfactants, Andersson et al. [40] reported significant differences between monolayers consisting of enantiomerically pure polyhydroxy surfactants as well as between diastereomers, where racemate showed pronounced sinuous curvature at the phase transition region of a liquid-expanded to a liquid-condensed phase. They assigned the differences to the slower relaxation speed of the molecules in the monolayer in comparison with the compression speed of the barrier. To verify whether their concept of slower relaxation speed can be applicable to our case, the  $\Pi$ -A isotherms of *dl*-**3e** and *meso*-**3e** were recorded by changing the compression rate from 3.8 to

23 cm<sup>2</sup> min<sup>-1</sup> at T = 15.0 °C. At any compression rate, their monolayer behaviors remained essentially undisturbed except the small variations in lift-off area for *dl*-**3e** and the values of minimum surface pressure for *meso*-**3e**. Therefore, it can be concluded that the relaxation against the compression would not be a significant factor for the difference in  $\Pi$ -A isotherms of *dl*-**3e** and *meso*-**3e**.

# Effect of Subphase Temperature on $\Pi$ -A Isotherm

It has been widely accepted that  $\Pi$ -A isotherms are often influenced by the subphase temperature as well as the compression rate. The  $\Pi$ -A isotherms were also recorded temperatures at several subphase ranging from T = 5-25 °C. Results show the lifting-off areas of dl-3e shifted to smaller ones with increase in temperature, but their collapse pressures were almost unchanged. In the case of *meso-3e*, the lifting-off areas were inherently the same and the maximum in isotherms appeared at  $A = \sim 0.55 \text{ nm}^2$  for all temperatures, while the maximum pressure decreased with increase in temperature.

#### **BAM Image Analysis**

Simultaneous observation of the morphology of the *meso*and *dl*-**3e** films at the air-water interface during the  $\Pi$ -*A* isotherm measurement was also performed. The BAM



**Fig. 1 a**  $\Pi$ -A isotherms of dl-**3e** (dashed line) and meso-**3e** (solid line) and **b** compression modulus of monolayers ( $\varepsilon_s$ ) of dl-**3e** (open) and meso-**3e** (closed) at a constant compression rate of 7.5 cm<sup>2</sup> min<sup>-1</sup> at T = 15.0 °C. Subphase: 0.001 M HCl (pH = 3.0)

images at the designated points a-c for *dl*-3e and points d-h for *meso-3e* are shown in Fig. 2. In the case of *dl-3e*, before arriving at the collapse pressure, where  $\varepsilon_s$  of monolayer gave  $\varepsilon_s(max)$ , there are no obvious BAM images attributable to the formation of a self-assembling structure. However, at point-a, just after the collapse pressure, small domain structures began to appear. At point-b, images of 3D-aggregate structures clearly appeared. At point-c, in the plateau region, the size and number of aggregates increased, throughout which the aggregates seemed amorphous or less ordered. Likewise, meso-3e did not give any BAM images of self-assembling structure until the maximum pressure. However, at point-d just after the maximum pressure, a small island structure appeared. With further compression, the island structure grew and needle-shaped structures were observed. The needle-shaped structure grew up ramifying and threading to fibrous structures similar to crystallization. At the minimum of isotherm (point-g), 3D-shaggy structures were



**Fig. 2** BAM images of *dl*-**3e** and *meso*-**3e** after collapse pressure  $(\Pi_c)$  obtained for compression at 7.5 cm<sup>2</sup> min<sup>-1</sup>. Subphase: 0.001 M HCl (pH = 3.0), 15 °C. The letters **a**-**c** and **d**-**h** on the isotherms of *dl*-**3e** (*dashed line*) and *meso*-**3e** (*solid line*), respectively, correspond to the 4.8 × 6.4 mm<sup>2</sup> BAM images: **a** A = 0.477 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 40.5$  mN m<sup>-1</sup>), **b** A = 0.423 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 40.4$  mN m<sup>-1</sup>), **c** A = 0.292 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 38.0$  mN m<sup>-1</sup>), **d** A = 0.529 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 21.4$  mN m<sup>-1</sup>), **e** A = 0.492 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 18.4$  mN m<sup>-1</sup>), **f** A = 0.436 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 15.0$  mN m<sup>-1</sup>), **g** A = 0.356 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 10.5$  mN m<sup>-1</sup>), and **h** A = 0.220 nm<sup>2</sup> molecule<sup>-1</sup> ( $\Pi = 8.8$  mN m<sup>-1</sup>)

observed, and it is noted that small but definite solids on the subphase surface were visually recognized.

As shown in Fig. 2, both *meso-* and *dl-3e* gave BAM images consistent with 2D monolayer  $\rightarrow$  3D aggregates above the collapse pressure. However, with respect to the organizing degree of 3D aggregates, *meso-3e* gave the more structured threads while *dl-3e* gave rather amorphous structures, which would indicate that *meso-3e* molecules have a more ordered alignment in the monolayer than *dl-3e*.

## **Conformational Illustration During Compression**

The differences in film formation of *meso-* and *dl-***3e** can be illustrated in terms of the hydrophobic interaction. Initially, both isomers spread at the air–water interface with the two hydrophilic COOH groups dousing in water. As shown in Fig. 3, at the lifting-off point, the two hydrophobic groups are standing upright, and all hydrophobic and hydrophilic groups should be set in eclipsed arrangement relative to the carbon–carbon spacer bond. Under such a circumstance, the two hydrophobic alkyl chains of the *meso*-isomer are set in parallel array as shown in Fig. 3a, while those of the *dl*-isomer should be set in skew position as shown in Fig. 3b. However, the lifting-off area would be determined mainly by the area of the head groups, which would explain why the lift-off area of the *meso*-isomer was almost the same as the *dl*-isomer.

It is obvious that the hydrophobic interaction between alkyl chains depends on both the length of alkyl chains and their distance. The length of alkyl chains in *meso-* and *dl-***3e** is the same, but the distances between the two alkyl chains on the adjacent carbon atoms of the spacer are different. This would cause the larger degree of intramolecular hydrophobic interaction between two alkyl



Fig. 3 Schematic illustration of jumping-up of a *meso*-molecule just adjacent in a monolayer at the air/water interface due to the hydrophobic interaction on compression

chains of the *meso*-isomer than that of the *dl*-isomer. Therefore, even at the liquid condensed state, *meso*-isomer molecules would be arranged with higher regularity in comparison with *dl*-isomer. Additional compression leads to the accession of molecules, and at the same time, the intermolecular interactions between hydrophobic chains of adjacent molecules as well as the intramolecular hydrophobic interaction come into play.

On further compression to  $A = \sim 0.56 \text{ nm}^2$ , the surface pressures rose to  $\sim 25 \text{ mN m}^{-1}$  for both *meso-* and *dl*isomers, and the effects of stereochemistry on the  $\Pi$ -A isotherms came in focus. At  $A = \sim 0.56 \text{ nm}^2$ , the apparent area per one hydrophobic chain can be estimated as  $\sim 0.28$  nm<sup>2</sup>. In line with the isotherm for pentadecanoic acid on 0.01 M HCl subphase, the monolayer shows the liquid expanded  $\rightarrow$  liquid condensed and liquid condensed  $\rightarrow$  solid phase transitions at 8 mN  $m^{-1}$  $(A = 0.34 \text{ nm}^2)$  and at ~20 mN m<sup>-1</sup>  $(A = 0.23 \text{ nm}^2)$ , respectively. Also, in our previous work on the  $\Pi$ -A isotherm of l-O,O'-bis(tridecanoyl)tartaric acid at 25.0 °C [32], only the monolayers of liquid condensed state was obtained even at  $\Pi = 20 \text{ mN m}^{-1}$  while *l*-O,O'bis(alkanoyl)tartaric acids having longer hydrophobic chains (>C16H33) showed the phase transition of liquid condensed (LC)  $\rightarrow$  solid state at  $\Pi = \sim 30 \text{ mN m}^{-1}$ . Therefore, including Shankar's work [17, 18], it is reasonably presumed that l- (or d-) stereochemistry of gemini surfactants with short hydrophobes attached at the carbon atom adjacent to COOH lead to only the monolayers of liquid condensed state probably because of weak hydrophobic intramolecular interaction between short alkyls.

To the contrast, as suspected easily from Fig. 3, both hydrophobic intra- and intermolecular interactions between adjacent alkyl chains in the *meso*-isomer can operate more effectively than the *dl*-isomer at the same molecular area, and at  $A = \sim 0.56$  nm<sup>2</sup> some *meso*-molecules would jump up to cause the phase transition to bilayer from the monolayer, which would be induced by the intermolecular interactions. During further compression, though the monolayer compaction should be promoted simultaneously with the "jumping-up" transition, the latter transition must be stimulated to bring the drop of surface pressure and 3D aggregates as shown in BAM images.

## Relaxation Behaviors in $\Pi$ -A Isotherms

For each isomer of **3e**, iterative measurements of compression to the first-specified surface pressure  $\Pi_{1st}$  (first compression), decompression to the initial spreading area (expansion), and successive immediate recompression were carried out. Results for *meso-3e* are shown in Fig. 4.

First, film formations of *meso-3e* were analyzed in several patterns. After first compression to  $\Pi_{1st} = 10.1$ 



**Fig. 4** Iterative  $\Pi$ -A measurements of compression, expansion and recompression of *meso*-**3e** obtained for the barrier speed of 7.5 cm<sup>2</sup> min<sup>-1</sup>. Subphase: 0.001 M HCl (pH = 3.0), 15 °C. *Solid line* is the isotherm of the first compression, and *dashed line* the second compression. *The letters* **a**-**e** correspond to  $\Pi_{1st}$  (the first-specified surface pressure of first compression): **a**  $\Pi_{1st}$  = 10.1 mN

mN m<sup>-1</sup>, where no aggregates were observed in the BAM analysis, an immediate opening (decompression) showed no hysteresis behavior, and the second compression passed through the same isotherm (Fig. 4a), which indicates that in this region of  $\Pi = 0$ -10 mN m<sup>-1</sup> meso-**3e** exists in the monomolecular state, and the transition from gaseous film

 $m^{-1}$  (A = 0.65 nm<sup>2</sup> molecule<sup>-1</sup>), **b** Π<sub>1st</sub> = 16.9 mN m<sup>-1</sup> (A = 0.58 nm<sup>2</sup> molecule<sup>-1</sup>), **c** Π<sub>1st</sub> = 16.9 mN m<sup>-1</sup> (A = 0.58 nm<sup>2</sup> molecule<sup>-1</sup>) and hold-time 30 min, **d** Π<sub>1st</sub> = 16.5 mN m<sup>-1</sup> (A = 0.45 nm<sup>2</sup> molecule<sup>-1</sup>) and hold-time 30 min, **e** Π<sub>1st</sub> = 9.4 mN m<sup>-1</sup> (A = 0.23 nm<sup>2</sup> molecule<sup>-1</sup>)

 $\Leftrightarrow$  liquid expanded film is reversible. When compressed to  $\Pi_{1st} = 17 \text{ mN m}^{-1} (A = 0.58 \text{ nm}^2)$ , where the compression modulus was maximum and some aggregation was observed in the BAM analysis, an immediate opening showed a small hysteresis with a little smaller landing area than the first lifting-off, and the second lifting-off started

from that landing area of the first opening and after then a similar isotherm was observed (Fig. 4b). Additionally, after the first compression to  $\Pi_{1st} = 17 \text{ mN m}^{-1}$ , the area was maintained for 30 min. The surface pressure gradually decreased and at the end the surface pressure was around  $\sim 2 \text{ mN m}^{-1}$  (Fig. 4c). Such a low surface pressure could be attributed to the partial jumping-up of molecules to a bimolecular film or 3D aggregates and the reduction of the number of molecules in the monomolecular state. Also, in this case, the second lifting-off position shifted to the end area of the first compression and after that a similar isotherm was observed, which may also mean that only molecules remaining in the monolayer would be reversibly parted to the gaseous state and recompressed again.

Furthermore, when compressed to the area of 0.45 nm<sup>2</sup>, passing through the maximum of the isotherm and held at that area, the surface pressure decreased rapidly to 0 mN m<sup>-1</sup> within only a few minutes. In this case, the second lifting-off point shifted to quite small area (less than 0.4 nm<sup>2</sup>), and a second monolayer formation was observed (Fig. 4d). However, when compressed to the measurement limit (A = 0.23 nm<sup>2</sup>) and decompressed immediately, the second compression did not show the obvious isotherm (no surface pressure) (Fig. 4e). It can be concluded that a strong compression induces the growth of 3D aggregates with robust microcrystalline structure not easily parted to the monomolecular state.

Similar compression-decompression-recompression measurements on *dl*-3e were also examined. After the first compression to  $\Pi_{1st} = 10 \text{ mN m}^{-1}$ , an immediate decompression showed no hysteresis behavior. Next, the first compression was executed to  $\Pi_{1st} = 25 \text{ mN m}^{-1}$ , where the compression modulus of *dl*-3e monolayer was just below  $\varepsilon_{s}(\max)$ , and an immediate decompression showed a slight but definite hysteresis behavior, and as expected the second lifting-off started from the landing area of the first decompression. When the first compression exceeded the collapse point of monolayer ( $A = 0.35 \text{ nm}^2$ ) and the area was maintained for 5 min, the surface pressure rapidly decreased to 14 mN m<sup>-1</sup>. After decompression, the second lifting-off started from the area identical with that of first compression at  $\Pi_{1st} = 14 \text{ mN m}^{-1}$ , and the second isotherm moved in parallel to the smaller area. Similar to the case of meso-3e, it may mean that 3D aggregates of *dl*-3e would be formed beyond the collapse point, and the aggregates would not revert to the monomolecular gaseous film.

## Effect of Hydrophobic Chain Length

The influence of hydrophobic chain length on the monolayer formation was also studied on gemini surfactants **3c** and **3g** with hydrocarbon chain length of  $C_9H_{19}$  and  $C_{13}H_{27}$ , respectively. The results are shown in Fig. 5 (at



**Fig. 5**  $\Pi$ -A isotherms of *dl*-2,3-bis(alkyl)succinic acids (**a**) and *meso*-2,3-bis(alkyl)succinic acids (**b**) having C<sub>9</sub>H<sub>19</sub> (*dashed line*), C<sub>11</sub>H<sub>23</sub> (*solid line*) and C<sub>13</sub>H<sub>27</sub> (*dash-dot-dot line*) as hydrophobic alkyl groups at a constant compression rate of 7.5 cm<sup>2</sup>•min<sup>-1</sup> for T = 15.0 °C. Subphase: 0.001 M HCl (pH = 3.0)

15 °C). Clearly, regardless of chain lengths, *meso-* and *dl*-isomers gave different  $\Pi$ -A isotherms.

In the case of *dl*-isomers (Fig. 5a), common monolayer behaviors were observed as expected. Judging from the values of  $\varepsilon_{\rm s}({\rm max})$ , which appeared at around  $A = 0.6 {\rm nm}^2$ , the formed films were all in the liquid-condensed states with the zero-pressure molecular areas of  $0.64 (C_{13}H_{27})$ , 0.67 ( $C_{11}H_{23}$ ), and 0.78 nm<sup>2</sup> ( $C_{9}H_{19}$ ). With respect to the collapse of films, 3c did not show the concrete maximum surface pressure attributable to 3D aggregation. On the other hand,  $3g(C_{13}H_{27})$  showed an intermediate region and the formation of solid film from  $A = 0.38 \text{ nm}^2$  [ $\varepsilon_s$ (max) = 190 mN m<sup>-1</sup>,  $A_0 = 0.46$  nm<sup>2</sup>]. Interestingly, this  $A_0$  value is twice that of a typical long chain fatty acid  $(\sim 0.21 \text{ nm}^2)$ . Thus, it can be concluded that the increase in hydrophobic chain length would lead to the increase of the inter- and intramolecular hydrophobic interactions to attain tight-packing at the air/water interface.

In contrast, all *meso*-isomers lifted off at almost the same area ( $A = 0.78 \text{ mm}^2$ ) regardless of hydrophobic chain lengths. They also showed the maximum of isotherm at around  $A = \sim 0.57 \text{ nm}^2$  ( $\Pi = 20 \text{ mN m}^{-1}$ ), but the subsequent reductions in the surface pressure of **3c** and **3g** were moderate in comparison with **3e** (Fig. 5b).

From BAM observation on *meso-3g*, no obvious images were observed between the lifting-off and the first  $\varepsilon_{c}(\max)$ points, but just after the maximum surface pressure, little structured aggregates appeared due to the jumping-up phenomena of molecules similar to meso-3e. In addition, on further compression the aggregate grew larger. At the minimum surface pressure point, the structure of the aggregate changed to needle-like crystal form, and at final compression cancellous (netted) structure was attained. Moreover, meso-3c showed similar variation in the BAM images. Just after the  $\varepsilon_s(max)$  point, small round aggregates began to appear, and at the maximum surface pressure 3D aggregates developed. In comparison with 3e and 3g, however, 3c has shorter alkyl chain and the hydrophobic intra- and intermolecular interactions would be smaller, which would result in the smaller jumping-up of molecules.

Considering these results, it can be reasonably concluded that the film formation behaviors are quite different depending on the *meso-* and *dl*-stereochemistry, and in the same stereochemistry the hydrophobic chain length would lead to the difference in the strength of the intra- and intermolecular hydrophobic interactions, aggregate formation and probably rigidity of films.

To further explore the influence of gemini surfactant stereochemistry on monolayer behaviors, we are now investigating the glutaric acid type gemini surfactants, *dl*-and *meso*-2,4-bis(alkyl)glutaric acids. Details will be reported in the near future.

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