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# Synthesis and interfacial properties of amphiphilic β-cyclodextrins and their substitution at the O-6 position with a mono bio-recognisable galactosyl antenna

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**Abstract**—The synthesis of a mono-galactosylated amphiphilic β-cyclodextrin, in five steps from mono-6-azido-6-deoxy-β-cyclodextrin, via coupling to a *N*-β-D-galactopyranosylamino-antenna is described. Both characterization by electrospray mass spectrometry and NMR show the presence of only the mono-substituted product. The Langmuir isotherms of the final product and intermediates are described.


## 1. Introduction

β-Cyclodextrins (β-CDs) or cyclomaltoheptaoses have long been recognized to have significant potential as drug carriers arising from their ability to form inclusion complexes.[1] Inclusion of the bioactive molecules generates several therapeutic advantages: solubilisation of poorly soluble or insoluble molecules,[2] protection from chemical and enzymatic degradation,[3] transport and time control of release.[4] Currently, in order to reduce the appearance of resistance towards therapeutic agents and to decrease the toxicity of the bioactive molecules, several studies have been undertaken to target such carriers, reducing in this way the quantity of drug used in therapies. Carbohydrates are biocompatible molecules having low immunogenicity and are responsible of recognition between the cells. We have previously demonstrated the capacity of galactosyl-β-cyclodextrin to be recognized by a galactosyl specific cell wall lectin *Kluyveromyces bulgaricus* (KbCWL)[5] and in the literature there exist several reports of the synthesis of cyclodextrin derivatives substituted with mono or poly-saccharides and which have shown to be recognized by lectins.[6] Recently, chemo-enzymatic synthesis of amphiphilic cyclodextrins fully substituted with *N*-acetyl-glucosamine (Glc-*N*Ac) has been described. [7]

Indeed to pass from a system of 1:1 complexation to nanoparticles able to ensure a much higher degree of encapsulation, the use of amphiphilic cyclodextrins has been developed. In the previous studies, amphiphilic cyclodextrins were obtained by the introduction of lipophilic groups at the primary face and/or secondary face.[8] These amphiphilic cyclodextrins are capable of forming liposomes,[9] nanoparticles,[10] vesicles,[11] micellar aggregates [12] and solid lipid nanoparticles.[13]

The objective of the current work resides in the combination of the recognition properties of the mono-galactosyl-β-cyclodextrins and their amphiphilic properties to obtain new carrier molecules containing a galactosyl antenna at the O-6 position and lipophilic ester groups at the O-2 and O-3 positions. The synthesis, characterization and the interfacial properties of these molecules as Langmuir monolayers are described.

## 2. Results and discussion

### 2.1. Synthesis and characterization

In previous studies we have demonstrated good recognition capacity (1.75 mmol $dm^{-3}$) towards a galactose specific yeast lectin *K. bulgaricus* (Kb CWL) of a mono-galactosyl-β-CD derived from mono-6-amino-6-deoxy-β-CD by coupling a galactosyl head group via a spacer chain (9 carbon atoms). In contrast to expectations, a 'clustering

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effect' by the heptakis-galactosyl-β-CD was not observed with only a 1.5 fold increase in recognition.[5]

In view of the above, the mono-galactosylated amphiphilic β-cyclodextrin derivative **7** was synthesized from mono-6-azido-6-deoxy-β-cyclodextrin **1**[14] in five steps (Scheme 1). The synthetic procedure for the synthesis of **7** is based on an amide bond between the carbohydrate-antenna and the amphiphilic-β-cyclodextrin moiety.

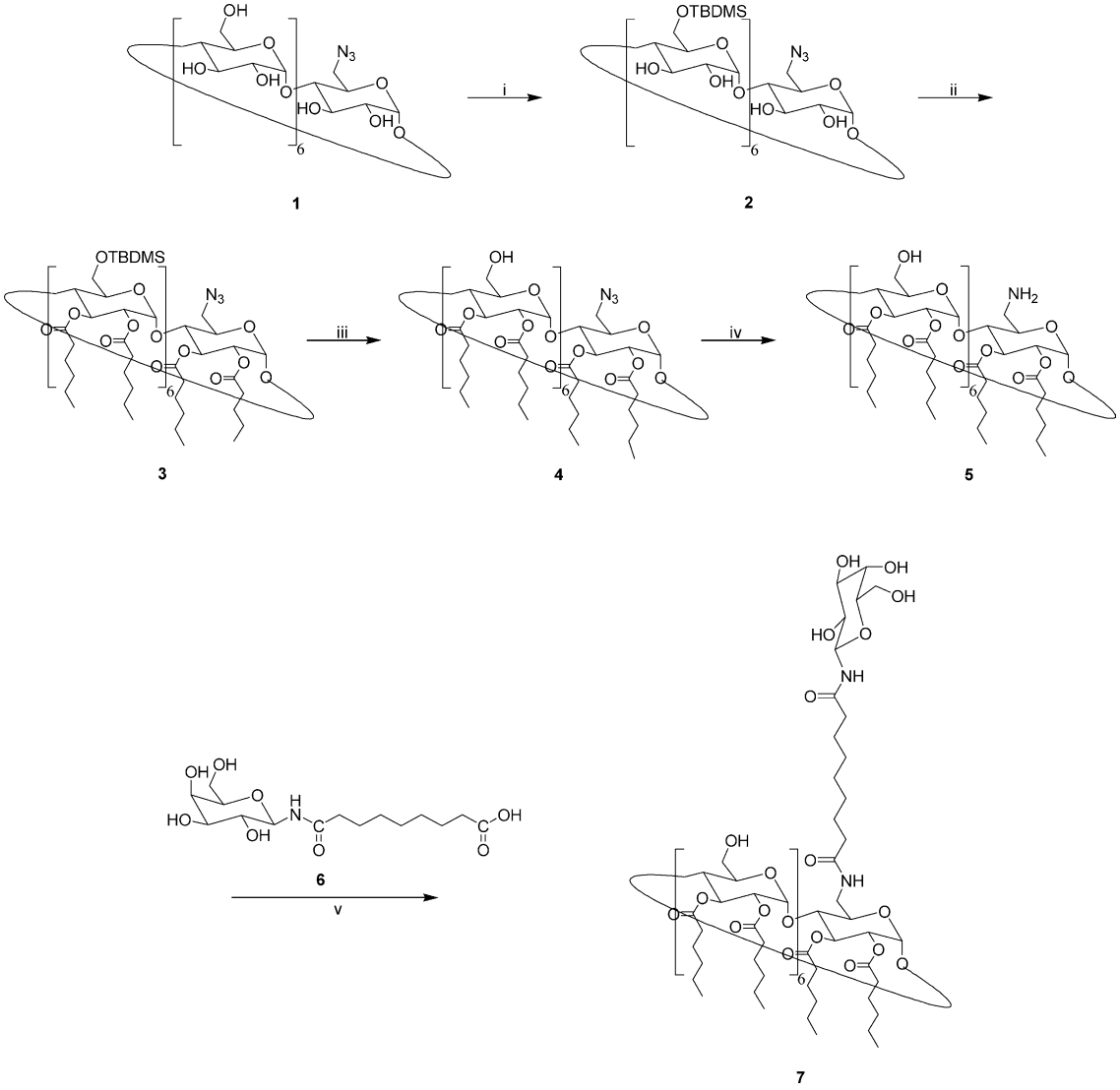
*O*-acylation at the secondary hydroxyl groups of the β-CD requires protection of the free primary hydroxyl groups at O-6 position of mono-6-azido-6-deoxy-β-cyclodextrin **1** with *tert*-butyldimethylsilyl chloride in dry pyridine. The new intermediate **2** is recrystallized from chloroform (yield 86%). The use of 56 equiv of hexanoic anhydride and 42 equiv of 4-dimethylaminopyridine (DMAP) leads to the pure fully acylated product **3** with 14 hexanoyl chains at secondary face of the β-cyclodextrin, according to the conditions of Lesieur and Dubes.[15] We have applied a new method of purification consisting of simply precipitating **3** from a mixture of methanol/chloroform 95:5 in 66.7% yield.

The degree of substitution is easily verified by electrospray mass-spectrometry (ES-MS, positive mode, *m*/*z*: 1621.4 $[M+H+Na]^{2+}$ and the structure confirmed by $^{1}H$ and $^{13}C$ NMR spectroscopy.

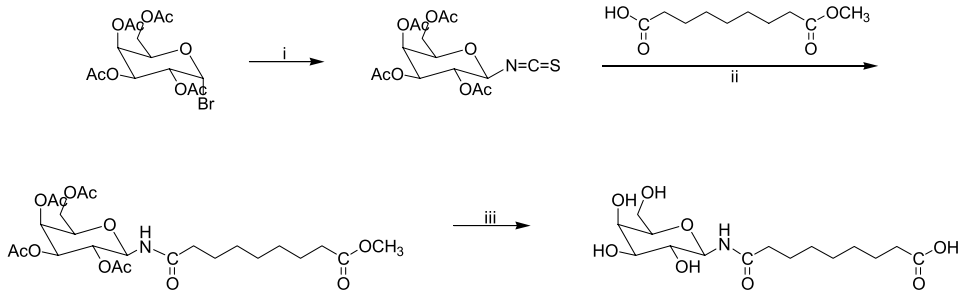
Selective removal of the *tert*-butyldimethylsilyl groups at O-6 position of **3** by boron trifluoride etherate ($BF_3 \cdot Et_2O$) in dry $CHCl_3$ gave the new product **4** with one azido group on the primary face and 14 hexanoyl chains on the secondary hydroxyl groups in 97% yield.

The reduction of the azido group into the corresponding amino group is carried out by catalytic hydrogenation. The presence of the ester groups at the secondary face requires neutral condition; here the use of Staudinger reduction is not successful. The novel mono-6-amino-6-deoxy-amphiphilic cyclodextrin **5** was synthesized from **4** in MeOH in presence of the Pd/C (10%) under hydrogen pressure (2 bar) during 4 h in 95% yield. The absence of the azido band at 2100 $cm^{-1}$ was confirmed by IR spectroscopy.

The covalent amido linkage between the glycoconjugate




**Scheme 1.** Synthesis of galactosylated amphiphilic cyclodextrin: (i) TBDMSCl, pyridine; (ii) hexanoic anhydride, DMAP, pyridine; (iii) $BF_3 \cdot Et_2O$ $CHCl_3$; (iv) Pd/C, $H_2$, MeOH; (v) **6**, DCC, HOBT, DMF.




**Scheme 2.** Synthesis of the glycoconjugate **6**. (i) KSCN, $Bu_4N^+Br^-$, Acetonitrile; (ii) $Et_3N$, toluene; (iii) NaOH (1 M), MeOH.

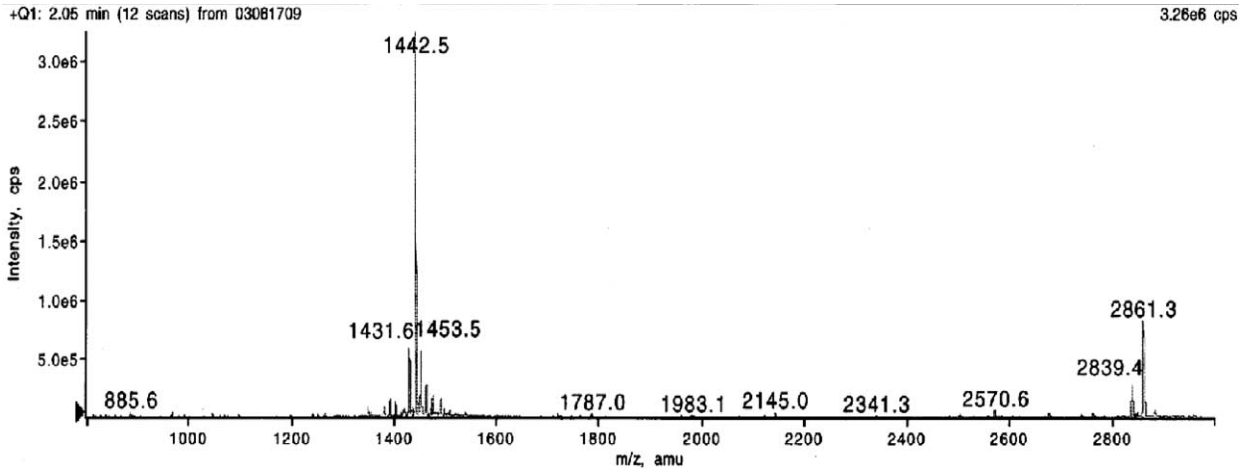



**Figure 1.** ES-mass spectrometry of the mono-galactosylated amphiphilic β-cyclodextrin **7**.

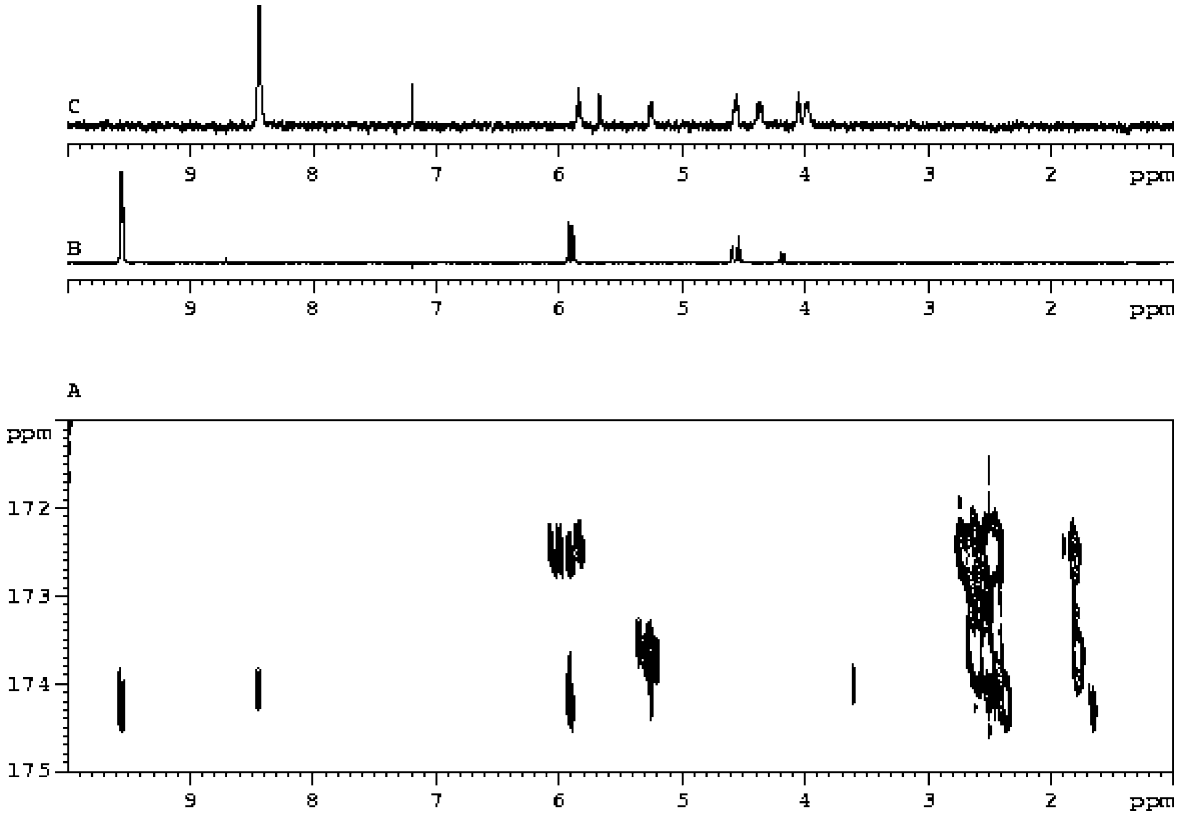



**Figure 2.** (A) $^1H$–$^{13}C$ 2D HMBC NMR spectrum of **7**; (B) $^1H$ NMR spectrum of galactose from 2D TOCSY; (C) $^1H$ NMR spectrum of glucopyranose A substituted by galactosyl antenna from 2D TOCSY.

and β-CD requires the synthesis of amphiphilic synthons presenting an amine function at the primary face and terminal carboxylic acid function in the glycoconjugate. We have described the synthesis of 9-(*N*-β-D-galactopyranosyl-amino)azelaïc acid **6**[16] from tetra-*O*-acetyl-α-D-bromo-galactose in three steps via galactosylisothiocyanate (Scheme 2).

The method used to synthesize the final product **7**, is that of a peptide coupling under soft conditions, in the presence of dicyclohexylcarbodiimide (DCC) and hydroxybenzotriazole (HOBT) in the anhydrous DMF. This method appeared to us most judicious to graft via a covalent bond an unprotected β-D-galactose onto the amphiphilic β-CD derivative. This method avoids working at high temperature in the presence of the galactosylated antenna. Mono-galactosyl amphiphilic-β-cyclodextrin **7** was synthesized by condensation of glycoconjugate **6** with mono-6-amino-6-deoxy-amphiphilic-β-cyclodextrin **5** in dry DMF using DCC/HOBT as the coupling reagents. The product was isolated by chromatography on silica gel with EtOH/toluene 8:2 as eluent in 42% yield. Characterization by mass spectrometry of **7** showed only species corresponding to $[\mathbf{7}+2\mathrm{Na}]^{2+}$: (*m*/*z*: 1442.5) and $[\mathbf{7}+\mathrm{Na}]^{+}$: (*m*/*z*: 2861.3) (Fig. 1). This substitution by one galactosyl antennae at the O-6 position and 14 hexanoyl chains at O-2 and O-3 positions were confirmed by 2D $^{1}$H and $^{13}$C NMR (COSY, HMBC, TOCSY) at 500 MHz in pyridine-$d_5$. The $^{13}$C–$^{1}$H HMBC NMR spectrum (Fig. 2A) clearly shows the correlation between the amide proton of the galactosyl residue at 9.55 ppm and the C=O carbon at 174.2 ppm; also a correlation is observed between the amide proton of the substituted glucopyranose A of β-cyclodextrin at 8.44 ppm and the carbonyl carbon at 174.1 ppm. Covalent coupling is confirmed by the presence of a correlation between the amide C=O of the β-cyclodextrin and the $CH_2$ (α to the C=O) of galactosyl antenna situated at 2.36 ppm. $^{1}$H–$^{1}$H TOCSY has allowed attribution of the protons arising from the galactose (Fig. 2B) and those of glucopyranose A, which are displaced by the substitution (Fig. 2C).The presence of a series of doublets between 5.3 and 5.0 ppm characteristic of the anomeric protons demonstrates the loss of symmetry of the molecule and confirms the monosubstitution at the primary face the β-cyclodextrin molecule.

No interaction is observed between the galactosyl antennae and the H-3 and H-5 protons of β-cyclodextrin. The terminal hydrophilic group of the antennae makes it possible to avoid the well-known phenomenon in the literature of self-inclusion of chains alkyls of the monosubstituted β-CD.[17]

## 2.2. Interfacial properties

Langmuir compression isotherms were obtained for

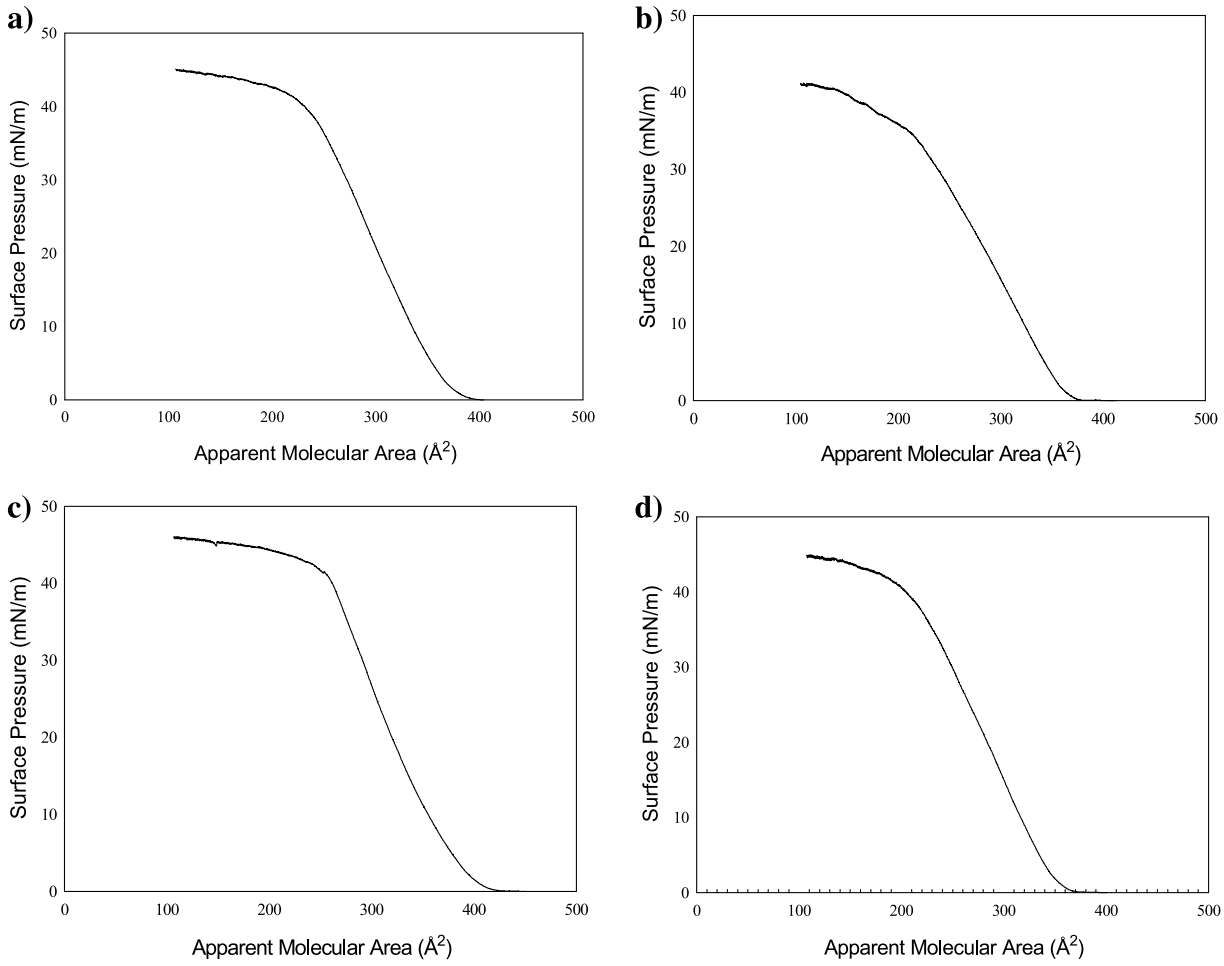



**Figure 3.** Langmuir isotherms of amphiphilic cyclodextrin derivatives: (a) **4**; (b) **5**; (c) **7** and (d) **8**.

**Table 1**. Apparent molecular areas, collapse pressures and compressibility of amphiphilic cyclodextrins Langmuir films

| Amphiphilic cyclodextrin | $A_0$ ⟨Å$^2$⟩ | $A_1$ ⟨Å$^2$⟩ | $A_c$ ⟨Å$^2$⟩ | $P_c$ ⟨mN/m⟩ | $C_s$ |
|---|---|---|---|---|---|
| Compound **4** | 373 (±3) | 366 (±3) | 214 (±2) | 36.6 (±0.2) | 55.8 (±1) |
| Compound **5** | 395 (±3) | 378 (±3) | 220 (±2) | 41.3 (±0.2) | 59 (±1) |
| Compound **7** | 410 (±3) | 390 (±3) | 250 (±2) | 42 (±0.2) | 62 (±1) |
| Compound **8** | 360 (±3) | 350 (±3) | 209 (±2) | 41 (±0.2) | 59 (±1) |

$A_0$, apparent molecular area at $p=0.1$ mN/m; $A_1$, apparent molecular area for pressure = 1 mN/m; $A_c$, apparent molecular area at collapse; $P_c$, pressure at collapse; $C_s$ = compressibility.

compounds **4**, **5** and **7** and are given along with that of the parent compound tetradecakis-O2, O3-hexanoyl-β-cyclodextrin **8**, Figure 3a–d, respectively. The relevant isotherm data is summarized in Table 1.

Molecules **4**, **5** and **8** show collapse areas in the range 205–220 Å$^2$, in close agreement with values previously observed for similar compounds by Lesieur[15a]. This lack of significant variance in the collapse area is in agreement with the fact that the molecular size of cyclodextrins acylated at the secondary face is determined by the area contribution from the 14 acyl chains[18], and not the cyclodextrin core. However, in the case of **7**, the presence of the galactosyl antenna leads to a collapse area of 250 Å$^2$. The collapse pressures show a variation **7**>**5**≥**8**>**4**, as would be expected from differences in the head group hydrophilicity, where introduction of a charged amino group **5** and especially the carbohydrate antenna **7** increases film stability, while introduction of an apolar, non-hydrogen bonding, azido function in **4** markedly decreases film stability.

## 3. Conclusion

We have synthesized a new generation of cyclodextrins presenting a galactosylated antenna on the primary face of β-cyclodextrin and *O*-acyls groups on the secondary face. These cyclodextrins are characterised by NMR and mass spectroscopy. The Langmuir isotherms show the amphiphilic character of these new molecules, and work is underway to study the self-assembly and transport properties of these molecules.

## 4. Experimental

### 4.1. General

All chemicals were purchased from Aldrich and were used without further purification. β-cyclodextrin was generously provided by Wacker (Lyon, France) and was dried under vacuum ($10^{-2}$ T) at 120 °C for 48 h before use. $^1$H and $^{13}$C NMR experiments were performed at 300 and 75 MHz, respectively, using a Bruker DRX 300 spectrometer. 2D Experiments (COSY, TOCSY, HMBC) were recorded with a Bruker AM 500 spectrometer. Mass spectra were measured using a Perkin-Elmer Sciex spectrometer. IR spectra were recorded on a Perkin-Elmer instrument. Isotherms were carried out on a Langmuir type balance (Nima 610) using MilliQ water (resistivity >18 MΩ) as the subphase. Solutions of the molecules in $CHCl_3$ at suitable concentrations were deposited on the aqueous surface and allowed to equilibrate during 30 min to compression. Compressions were performed continuously at a rate of 20 cm$^2$ min$^{-1}$ from 510 to 50 cm$^2$. Each isotherm was run at least three times to ensure areas of reproducibility of results (deviation of area and pressure were less than 3%).

**4.1.1. Mono-6-azido-6-deoxy-hexakis(6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose 2.** Mono-6-azido-6-deoxy-β-cyclodextrin **1** (5.5 g, 4.74 mmol) in dry pyridine (80 mL) is added a solution of *tert*-butyldimethylsilyl chloride (TBDMSCl) (6.43 g, 42.6 mmol) in 70 mL of dry pyridine at 0 °C. After agitation during 3 h at 0 °C and 20 h at 20 °C, the reaction is stopped by addition of ice (500 g). The crude product precipitated, filtered and recrystallised in water; 86% yield; mp 225 °C; $[\alpha]_D = +13.4$ (*c* 1); $^1$H NMR ($CDCl_3$, 300 MHz): δ (ppm): 6.55–6.82 (m, 7H, OH), 5.18–5.3 (m, 7H, OH), 4.87 (d, 1H, *J*=3.8 Hz, H-1), 4.96 (d, 6H, *J*=3.8 Hz, H-1), 4.05–3.6 (m, 42H, H-2, H-3, H-4, H-5, H-6), 0.88 (s, 54H, $CH_3$–C), 0.04 (s, 36H, $CH_3$–Si); $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) −4.79 (C–Si), 18.68 (*C*–$(CH_3)_3$), 26.28 (C–(*C*$H_3)_3$), 52.51 ($C_6$–$N_3$), 62.77 ($C_6$–Si), 72.63 ($C_3$), 72.94 ($C_2$), 73.91 ($C_5$), 82.16 ($C_4$), 102.32 ($C_1$); ES-MS (+) *m/z*: 1867.7 $[M+Na]^+$; $C_{78}H_{153}N_3O_{34}Si_6$.

**4.1.2. Mono-6-azido-6-deoxy-hexakis(6-*O*-*tert*-butyldimethylsilyl)-heptakis(2,3-di-*O*-hexanoyl)-cyclomaltoheptaose 3.** The use of 56 equiv of hexanoic anhydride (71.7 mmol, 16.6 mL), 42 equiv of 4-dimethylaminopyridine (DMAP) (6.57 g, 53.7 mmol) in dry pyridine (40 mL) and 2.36 g (1.28 mmol) of **2** leads to the fully acylated product **3**. The mixture was stirred under nitrogen pressure at 70 °C for 48 h, then cooled at 25 °C and poured thereafter in 250 mL of distilled water. The organic layer was dried with $Na_2SO_4$ and concentrated to dryness to yield oil. The MeOH/$CH_2Cl_2$ 95:5 solution is added in oil and the mixture is heated at 70 °C. The product **3** precipitate. 66.7% yield (2.75 g); mp 205 °C; $[\alpha]_D$ 15.3 (*c* 1); $^1$H NMR ($CDCl_3$, 300 MHz): δ (ppm): 5.5–5.3 (m, 7H, H-3), 5.2–5.05 (m, 7H, H-1), 4.85–4.59 (m, 7H, H-2), 3.6–4.02 (m, 28H, H-4, H-5, H-6), 2.55–2.1 (m, 28H, $CH_2$–COO), 1.15 (s, 56H, –C*H*$_2$–C*H*$_2$–$CH_2$–COO), 1.8 (s, 28H, $CH_3$–C*H*$_2$–), 1.05–0.75 [m, 96H, $CH_3$ and C–$(CH_3)_3$], 0.04 (s, 36H, $CH_3$–Si); $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm): −4.6 (C–Si), 14.3 ($CH_3$), 18.6 (*C*–$(CH_3)_3$, 22.7 (–*C*$H_2$–$CH_3$), 24.8 (–$CH_2$–*C*$H_2$–$CH_3$), 26.3 (C–(*C*$H_3)_3$), 31.9 (–*C*$H_2$–$CH_2$–COO), 34.5 (–*C*$H_2$–COO), 52.1 ($C_6$–$N_3$), 62.1 ($C_6$–Si), 70.0–72.2 ($C_2$ and $C_3$), 72.4 ($C_5$), 77.7 ($C_4$), 96.7 ($C_1$), 172.1 (–CH2–*C*OO), 174.2 (–CH2–*C*OO); ES-MS (+) *m/z*: 1621.4 [**3**+H+ Na]$^{2+}$, 1629.9 [**3**+H+K]$^{2+}$; $C_{164}H_{293}N_3O_{48}Si_6$.

**4.1.3. Mono-6-azido-6-deoxy-heptakis(2,3-di-*O*-hexanoyl)-cyclomaltoheptaose 4.** To a stirred solution of **3** (2.75 g, 0.85 mmol) in anhydrous chloroform stabilized on

amylene (63 mL) was added 1.7 mL of $BF_3 \cdot Et_2O$. The mixture was stirred under $N_2$ at 25 °C for 23 h then poured into cold water (160 mL). The organic layer was removed and washed with water, $NaHCO_3$ and water then dried with $Na_2SO_4$. The organic layer was then concentrated to dryness and the residue purified by flash chromatography (eluent: cyclohexane/acetone 6:4). 97% Yield; mp 194 °C; $[\alpha]_D$ 12.4 (*c* 1); $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm): 0.9 (s, 42H, $CH_3$), 1.3 (s, 56H, –C*H*$_2$–C*H*$_2$–$CH_2$–COO), 1.6 (s, 28H, $CH_3$–C*H*$_2$–), 2.08–2.42 (m, 28H, $CH_2$–COO), 3.55–4.15 (m, 28H, H-4, H-5, H-6), 4.25–4.55 (m, 6H, OH), 4.65–4.8 (m, 7H, H-2), 5.01 (d, 1H, $J$=3.8 Hz, H-1), 5.12 (d, 5H, $J$=3.8 Hz, H-1), 5.18 (d, 1H, $J$=3.8 Hz, H-1), 5.29–5.45 (m, 7H, H-3); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm): 14.30 ($CH_3$), 22.79 (–*C*$H_2$–$CH_3$), 24.75 (–*C*$H_2$–$CH_2$–$CH_3$), 31.77 (–*C*$H_2$–$CH_2$–COO), 34.36 (–*C*$H_2$–COO), 52.1 ($C_6$–$N_3$), 62.10 ($C_6$), 70.74 ($C_2$), 72.44 ($C_3$), 75.20 ($C_5$), 76.56 ($C_4$), 96.70 ($C_1$), 172.16 (–CH2–*C*OO), 173.72 (–CH2–*C*OO); ES-MS (+) *m/z*: 2556.6 [**4**+ Na]$^+$; $C_{128}H_{209}N_3O_{48}$.

**4.1.4. Mono-6-amino-6-deoxy-heptakis(2,3-di-*O*-hexanoyl)-cyclomaltoheptaose 5.** To a solution of **4** (5 g, 1.97 mmol) in MeOH (200 mL) was added 450 mg of the Pd/C (10%) under hydrogen pressure (2 bar) at 20 °C for 4 h. The mixture was filtered and washed with MeOH. Yield 95%; mp 175 °C; $[\alpha]_D$ 11.6 (*c* 1); IR (KBr): no band azido at $\nu$ 2100 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm): 0.9 (s, 42H, $CH_3$), 1.3 (s, 56H, –C**H$_2$**–C**H$_2$**–$CH_2$–COO), 1.56 (s, 28H, $CH_3$–C**H$_2$**–), 2.08–2.37 (m, 28H, $CH_2$–COO), 3.4–4.2 (m, 34H, H-4, H-5, H-6, OH-6), 4.7–4.79 (m, 7H, H-2), 5.01 (d, 1H, $J$=3.8 Hz, H-1), 5.12 (d, 5H, $J$=3.8 Hz, H-1), 5.18 (d, 1H, $J$=3.8 Hz, H-1), 5.29–5.45 (m, 7H, H-3); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm): 14.30 ($CH_3$), 22.79 (–*C*$H_2$–$CH_3$), 24.75 (–*C*$H_2$–$CH_2$–$CH_3$), 31.77 (–*C*$H_2$–$CH_2$–COO), 34.36 (–*C*$H_2$–COO), 62.10 ($C_6$), 70.69 ($C_2$), 72.42 ($C_3$), 75.20 ($C_5$), 76.56 ($C_4$), 96.70 ($C_1$), 172.16 (–CH2–*C*OO), 173.72 (–CH2–*C*OO); ES-MS (+) *m/z*: 2531 [**5**+Na]$^+$; $C_{128}H_{211}NO_{48}$.

**4.1.5. Mono-6-deoxy-6[9-(β-D-galactopyranosylamino)-1,9-dioxononanoyl]amino-heptakis(2,3-di-*O*-hexanoyl)-cyclomaltoheptaose 7.** To a solution of **5** (0.9 g, 0.36 mmol) in dry DMF (18 mL) were added **6**[16] (1 equiv 0.13 g), hydroxybenzotriazole (HOBT, 1.2 equiv 0.058 g) and dicyclohexylcarbodiimide (DCC, 1.2 equiv 0.088 g). The mixture is then left under agitation at 25 °C, until appearance of a fine precipitate corresponding to the formation of dicyclohexylurea. After filtration, the organic solution was then concentrated to dryness and the residue purified by flash chromatography (eluent: EtOH/toluene 8:2). Yield 42%; mp 192 °C; $[\alpha]_D$ 16.2 (*c* 1); $^1$H NMR (2D-COSY and TOCSY, pyridine-$d_5$, 500 MHz): $\delta$ (ppm): 0.99 (d, 42H, $CH_3$), 1.20 (m, 6H, 3 $CH_2$ antenna), 1.40 (m, 56H, –C**H$_2$**–C**H$_2$**–$CH_2$–COO), 1.57 (m, 4H, 2 $CH_2$ antenna), 1.70 (s, 28H, $CH_3$–C**H$_2$**–), 2.36 (m, 4H, 2 $CH_2\alpha$–C=O antenna), 2.4–2.7 (m, 28H, $CH_2$–COO), 4.0 (m, 1H, H-5$^A$), 4.15 (t, 1H, H-6$^A$), 4.2 (m, 1H, H-5 and H-6-gal), 4.35 (m, 1H, H-4$^A$), 4.55 (dd, 1H, H-6$'^A$), 4.3–4.5 (m, H-2, H-4, H-6, H-6′, H-5), 4.6–4.72 (m, H-gal), 5.22 (d, 1H, $J$=3.72 Hz, H-1$^A$), 5.0–5.3 (an series d, 6H, $J$=3.72 Hz, H-1), 5.82 (t, 1H, H-3$^A$), 5.90 (t, 1H, $J$=7.83 Hz, H-1-gal), 5.96–6.3 (m, 6H, H-3), 8.44 (t, 1H, $J$=5.8 Hz, NHβ-CD), 9.55 (d, 1H, $J$=9 Hz, NH-gal); ES-MS (+) *m/z*: 1442.5 [**7**+2Na]$^{2+}$, 2861.3 [**7**+Na]$^+$; $C_{1143}H_{236}N_2O_{55}$.

## References and notes


1. Uekama, K.; Hirayama, F.; Irie, T. *Chem. Rev.* **1998**, *98*, 2045–2076.
2. Duchêne, D. *News Trends in Cyclodextrin and Derivatives*; Edition de Santé: Paris, 1991.
3. Szejtli, J. *Med. Res. Rev.* **1994**, *14*, 353–386.
4. Szejtli, J. *Cyclodextrin Technology*; Kluwer Academic: Dordrecht, 1998.
5. Attioui, F.; Al-Omar, A.; Leray, E.; Parrot-Lopez, H.; Finance, C.; Bonaly, R. *Biol. Cell.* **1994**, *82*, 161–167.
6. Ortiz-Mellet, C.; Defaye, J.; Garcia-Fernandez, J. M. *Chem. Eur. J.* **2002**, *8*, 1982–1990. Furuike, T.; Aiba, S.; Nishimura, S. I. *Tetrahedron* **2000**, *56*, 9909–9915.
7. Sallas, F.; Niikura, K.; Nishimura, S. I. *Chem. Commun.* **2004**, 596–597.
8. (a) Tanaka, M.; Azumi, R.; Tachibana, H.; Nakamura, T.; Kawabata, Y.; Matsumoto, M.; Miyasaka, T.; Tagaki, W.; Nakahara, H.; Fukuda, K. *Thin Solid Films* **1994**, *244*, 832–835. (b) Greenhall, M.; Lukes, P.; Kataky, R.; Agbor, N. E.; Badyal, J. P.; Yarwood, J.; Parker, D.; Petty, M. C. *Langmuir* **1995**, *11*, 3997–4000. (c) Zhang, P.; Ling, C. C.; Coleman, A. W.; Parrot-Lopez, H.; Galons, H. *Tetrahedron Lett.* **1991**, *32*, 2769–2770. (d) Mazzaglia, A.; Donohue, R.; Ravoo, B. J.; Darcy, R. *Eur. J. Org. Chem.* **2001**, 1715–1721. (e) Granger, C.; Félix, C.; Parrot-Lopez, H.; Langlois, B. *Tetrahedron Lett.* **2000**, *41*, 9257–9260. (f) Sukegawa, T.; Furuike, T.; Niikura, K.; Yamagishi, A.; Monde, K.; Nishimura, S. I. *Chem. Commun.* **2002**, 430–431. (g) Peroche, S.; Parrot-Lopez, H. *Tetrahedron Lett.* **2003**, *44*, 241–245.
9. Auzély-Velty, R.; Perly, B.; Taché, O.; Zemb, T.; Jéhan, P.; Guenot, P.; Dalbiez, J. P.; Djedaïni-Pilard, F. *Carbohydrate Res.* **1999**, *318*, 82–90.
10. Perrier, E.; Terry, N.; Rival, D.; Coleman, A. W. Jpn. Kokai Tokkyo Koho 2001,323,002, 2001.
11. Ravoo, B. J.; Darcy, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 4324–4326.
12. Mazzaglia, A.; Ravoo, B. J.; Darcy, R.; Gambadauro, P.; Mallamace, F. *Langmuir* **2002**, *18*, 1945–1948.
13. Dubes, A.; Parrot-Lopez, H.; Abdelwahed, W.; Degobert, G.; Fessi, H.; Shahgaldian, P.; Coleman, A. W. *Eur. J. Pharm. Biopharm.* **2003**, *55*, 279–282.
14. Tsujihara, K.; Kurita, H.; Kawazu, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1567.
15. (a) Lesieur, S.; Charon, D.; Lesieur, P.; Ringard-Lefebvre, C.; Muguet, V.; Duchêne, D.; Wouessidjewe, D. *Chem. Phys. Lipids* **2000**, *106*, 127–144. (b) Dubes, A.; Bouchu, D.; Lamartine, R.; Parrot-Lopez, H. *Tetrahedron Lett.* **2001**, *42*, 9147–9151.
16. Kassab, R.; Félix, C.; Parrot-Lopez, H.; Bonaly, R. *Tetrahedron Lett.* **1997**, *38*, 7555–7558.
17. Petter, R. C.; Salek, J. C.; Sikorski, C. T.; Kumaravel, G.; Lin, F. T. *J. Am. Chem. Soc.* **1990**, *112*, 3860–3868.
18. Dubes, A.; Parrot-Lopez, H.; Shahgaldian, P.; Coleman, A. W. *J. Colloid Interface Sci.* **2003**, *259*, 103–111.