JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
*J. Phys. Org. Chem.* 2001; **14:** 1–10

# Synthesis and assembly properties of a series of chiral amphiphilic dihydroxytetrahydrofuran derivatives

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*Received 13 June 1999; revised 28 August 2000; accepted 28 August 2000*

ABSTRACT: The synthesis of a series of amphiphilic dihydroxytetrahydrofuran derivatives, prepared from isomannide and isosorbide, possessing hydrophobic ether chains lengths varying from $C_{10}$ to $C_{18}$ attached $\alpha$ to the tetrahydrofuran ring and with *R* and *S* chirality at the 0 linkage carbon atom is described. The interfacial properties of these compounds were studied using a Langmuir film balance; the results showed the expected increase in film stability with increasing chain length and differences in phase behaviour and film stability related to linkage chirality. The formation of colloidal dispersions of these compounds was studied both dynamic light scattering and non-contact mode atomic force microscopy. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: amphiphilic dihydroxybetrahydrofurans; synthesis; interfacial properties; assembly properties; film stability; colloidal dispersions

## INTRODUCTION

Amphiphilic derivatives of many carbohydrate systems have been widely studied; examples include pyranose derivatives such as alkylglycosides,[1] linear polyol derivatives,[2] more complex systems such as cyclodextrin-derived amphiphiles[3] and hydrophobic polysaccharide derivatives.[4] Such surfactant molecules represent one of the major classes of non-ionic amphiphiles. They are found both as natural lipid systems either as glycolipids[5] or membrane glycoproteins,[6] where they play a key role in the processes of biological recognition, or as synthetic derivatives[7] in which case their physical and molecular recognition properties may be fine tuned by the choice of suitable head groups or hydrophobic chains. They have been widely used commercially and are also widely used for protein solubilization.

The self-assembly properties of such systems both alone and in the presence of other lipids such as phospholipids are the subject of an extremely wide literature and their properties at the air–water interface,[8] as micelles,[9] in liposomes[10] or as more complexes colloidal structures have been widely studied. Of particular interest are the elegant complex structures formed as dispersions by the *N*-alkylaldoamides, where coiled threads, tubular vesicles and helical ribbons have been studied by Führhop's group[11] and structurally characterized. Extensive atomic force microscopy studies have been undertaken on such systems.[12]

As noted above, it is possible to fine tune the properties of these amphiphilic molecules by the appropriate choice of hydrophobic functions or polar head groups, and furthermore the inherent chirality of such molecules can also be used either from the choice of the carbohydrate functions or by varying the chirality of linkages to these head groups. Such modifications play an extremely important role in the relative orientation of the polar and apolar parts of the molecular and hence both in the structures formed and in their interactions with substrates at interfaces.

Whereas structures based on pyranose derivatives have received much attention, the furanose-derived systems have been less widely studied. In this paper, we describe a series of novel amphiphilic molecules based on non-natural tetrahydrofuran derivatives. The key to the construction of this new class of amphiphilic molecules is a direct single ring cleavage of isosorbide and isomannide with $Me_3SiI$ leading to optically active trisubstituted tetrahydrofurans[13] (Figs 1–3).

## RESULTS AND DISCUSSION

### Synthesis

Commercially available, isosorbide (**1a**) and isomannide (**1b**) were transformed into their corresponding iodo

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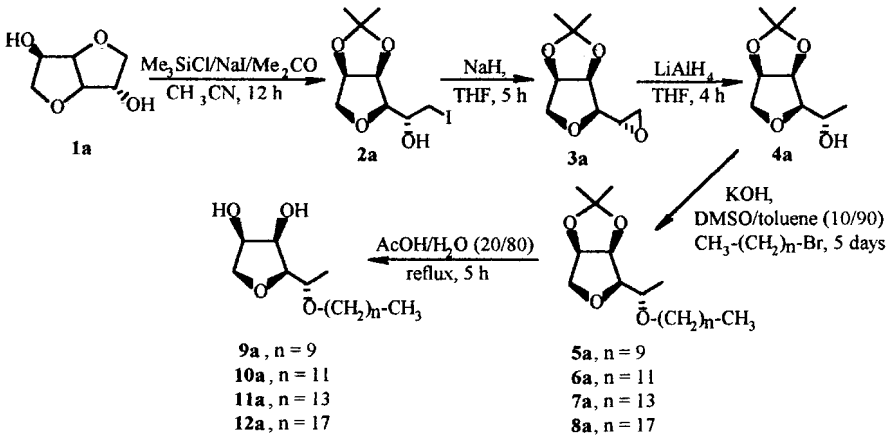


**Figure 1.** Synthesis of the isosorbide (**a**) series of amphiphiles

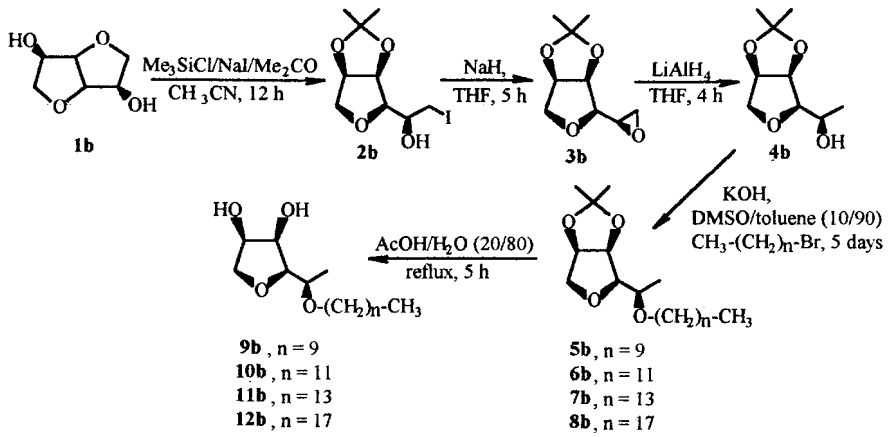


**Figure 2.** Synthesis of the isomannide (**b**) series of amphiphiles

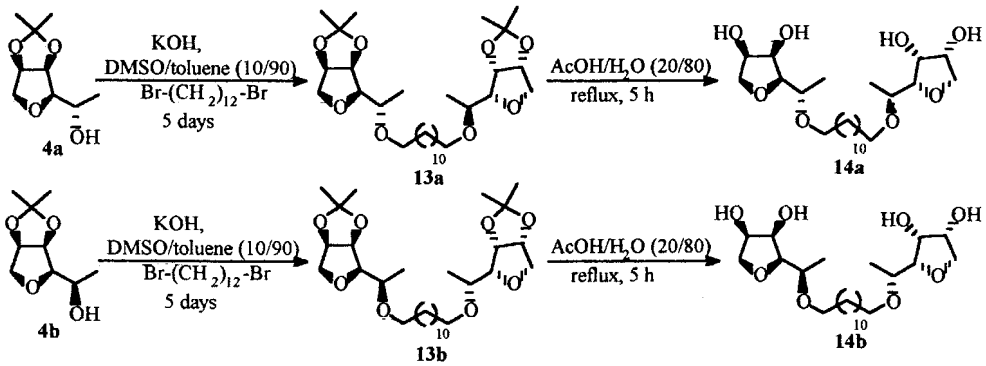


**Figure 3.** Synthesis of the bola-amphiphiles

alcohols **2a** and **2b** with $Me_3SiCl$–NaI in presence of acetone. During this reaction only a single ring opening reaction occurred.[13] The iodoalcohols **2a** and **2b** were treated with sodium hydride in tetrahydrofuran to afford the epoxides **3a** and **3b**. Reduction of **3a** and **3b** with lithium aluminium hydride in tetrahydrofuran provided the methyl alcohols **4a** and **4b**, respectively. These were transformed into ethers with a variety of alkyl bromides in the presence of potassium hydroxide in DMSO–toluene (10:90). The deprotection of the acetonide group was performed in refluxing 80% aqueous acetic acid for 5 h.

Bola-amphiphilic compounds **14a** and **14b** (Fig. 3) were prepared by treatment of the alcohols **4a** and **4b** with 1,12-dibromododecane in the presence of potassium hydroxide in DMSO–toluene (10:90), then the deprotec-

 

**Table 1.** Apparent molecular areas $A_0$ and $A_c$ and collapse surface pressure $\Pi_c$

| Compound | $A_0$($^2$) | $A_c$($^2$) | $\Pi_c$(mN m$^7$) |
|---|---|---|---|
| **9a** | 12.5 | | N.C.[a] |
| **9b** | 19 | | N.C.[a] |
| **10a** | 50 | 42 | 38 |
| **10b** | 41 | N.C. | >40 |
| **11a** | 80 | 44 | 37 |
| **11b** | 64 | 40 | 44 |
| **12a** | 105 (80 sh) | 52 | 17 (sh), 35 |
| **12b** | 90 | 60 | 36 |
| **14a** | 18 | 8 | 12.5 |
| **14b** | 18 | 8.3 | 20.9 |

[a] N.C. = No observed collapse.

tion of the acetonide group of **13a** and **13b** was performed in refluxing 80% aqueous acetic acid for 5 h.

It is noteworthy that the **a** series (Figs 1 and 3) and the **b** series (Figs 2 and 3) differ only in the conformation of the carbon $\alpha$ to the ring: in the **a** series, derived from isosorbid, this conformation is *S* and in the **b** series, derived from isomannide, it is *R*.

NMR spectra show no additional peaks corresponding to racemization, and we consider that limits of observation here are around 5%, so little or no racemization has occurred in the synthesis. The electrospray mass spectra show only the peak for M + Na.

## Langmuir studies

All the new amphiphilic derivatives were tested for their ability to form monomolecular layers at the air–water interface, i.e. Langmuir layers. $A_0$ (area at which the surface pressure increases above zero), $A_c$ (collapse area), collapse pressures ($II_C$) and for **12a** apparent transition values are given in Table 1. Representative isotherms for compounds **11a** and **11b** are presented in Fig. 4(a) and (b). Compounds **9** have 10 carbons, compounds **10** 12 carbons, compounds **11** 14 carbons and compounds **12** 18 carbons in the hydrophobic chain).

Neither the series **9** (the shortest chain length, 10 carbon atoms) or **14** (the bola-amphiphiles) show the formation of stable monolayers. Indeed, in the case of **14a** and **14b** surface activity could only be detected after loading the film balance with a 10-fold higher concentration of molecules. For both cases the apparent observed molecular areas are of the order of 5 $A^2$ and may arise either from a critical micellar concentration induced saturation of the sub-phase or from the presence of small quantities of residual impurities not otherwise detected.

There is a clear correlation between the chirality of the ligand and both $A_0$ and collapse pressures but not with the collapse areas; for the latter this is expected as this value should provide information on the most tightly packed form of the layer and is expected to be determined by the relation between the head molecular cross-section and the chain area. The **b** series of molecules, derived from isomannide having the conformation 3*R*–4*R*–1*R*, showed higher collapse pressures but lower $A_0$ values than the **a** series derived from isosorbide; e.g. for **11a** $A_0$ = 80 Å$^2$ and $\Pi_c$ = 37 mN m$^{-1}$ and for **11b** $A_0$ = 64 Å$^2$ and $\Pi_c$ = 44 mN m$^{-1}$. Hence the films formed are both more stable and more rigid for this stereoisomer. Simple molecular modelling shows that a shorter distance (around 3.2 Å) exists between the OH at ring position 3 and the chain junction 0 for the **a** series than for the **b** series (around 4.1 Å). The short distance is compatible with intramolecular hydrogen bonding, which would reduce the number of available water molecules to amphiphile hydrogen bonding sites in the case of the series and thus would be expected to reduce the monolayer stability. This hydrogen bonding will also lead to a more compact and rigid amphiphile structure and so explain the lower observed $A_0$ values.

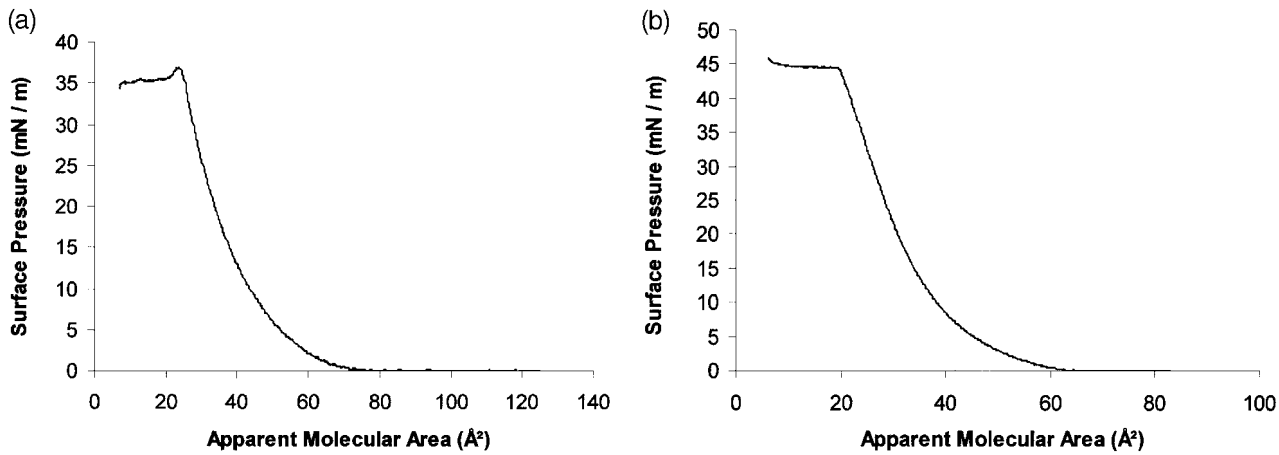


**Figure 4.** Pressure–area isotherms of (a) **11a** and (b) **11b**

**Table 2.** Visual measure of precipitation for suspensions of the amphipiles in water

| Product | Precipitate | Product | Precipitate |
|---|---|---|---|
| **9a** | Weak | **12a** | Yes |
| **9b** | Yes | **12b** | No |
| **10a** | Weak | **14a** | Yes |
| **10b** | Weak | **14b** | No |
| **11a** | Yes | | |
| **11b** | Weak | | |

## Colloidal properties

**Suspension and dynamic light scattering studies.** Colloidal suspensions of the amphiphilic derivatives were prepared by the dissolution solvent removal method that we and others have used for the preparation of dispersed nano-particles of amphiphilic derivatives.

The stability of such dispersions can, to a first approximation, be judged by visual observation of the formation of a birefrigent system or by the formation of precipitates. Whilst such a measure is extremely empirical it has proved of considerable use. The results are summarized in Table 2.

Preliminary studies on the critical micellar concentration (cmc) show that apparently only **14a** shows a cmc value, of $0.97 \times 10^{-5}$ M; for all other compounds, no cmc could be determined.[14]

Evidently, in order to obtain a numerical characterization of the colloidal systems formed (in fact visual inspection allows a rapid triage of the systems), dynamic light scattering (DLS) experiments were performed. The results of the observed hydrodynamic sizes intensity at peak maximum and polydispersity are given in Table 3.

**Atomic force microscopy studies.** Although DLS studies allow the hydrodyanamic sizes of dispersions to be determined, such measurements provide little information on the shapes and nature of the objects present. In order to obtain such information, electron microscopy and atomic force microscopy (AFM) have proved invaluable tools. In particular, the use of true non-contact mode AFM, in which the cantilever resonates at very low amplitude within the surface contamination layer, can provide accurate information on both the height and size of fragile objects. We prefer this mode to the 'tapping mode' often used, as although the tapping mode gives higher lateral resolution it does not provide accurate height information.

In Figs 5, 6 and 7 are given the images obtained for the objects present in dispersions of **10a, 11a and 14a**, respectively deposited directly on freshly cleaved mica

**Table 3.** Hydrodynamic radii and polydispersity values as determined by DLS and approxiamate average diameters of objects as measured by AFS

| Product | Diameter DLS (nm) | Polydispersity | Diameter AFM (nm) |
|---|---|---|---|
| **9a** | | | |
| **9b** | 325, 600 | 0.25 | |
| **10a** | | | 150 |
| **10b** | 150, 300 | 0.15 | 200 |
| **11a** | | | Variable |
| **11b** | | | 170 |
| **12a** | 105, 360 | 0.27 | 80, 120 |
| **12b** | 190, 460, 627 | 0.29 | 150, 200 |
| **14a** | 150 | 0.24 | 150 |
| **14b** | 200 | 0.15 | 110, 200 |

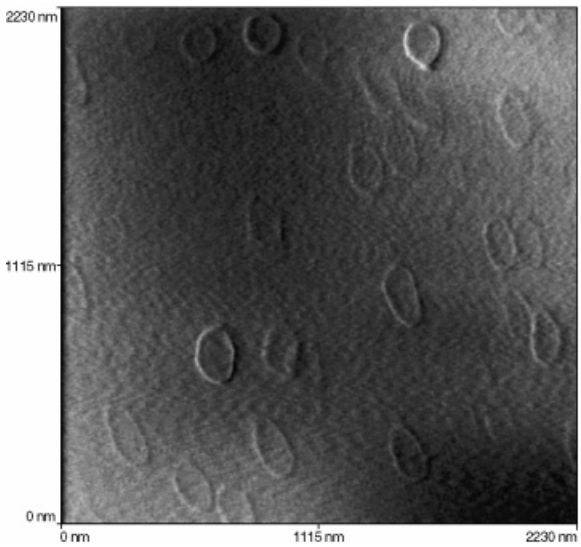


**Figure 5.** AFM non-contact mode image at dried dispersion of **10a** on mica

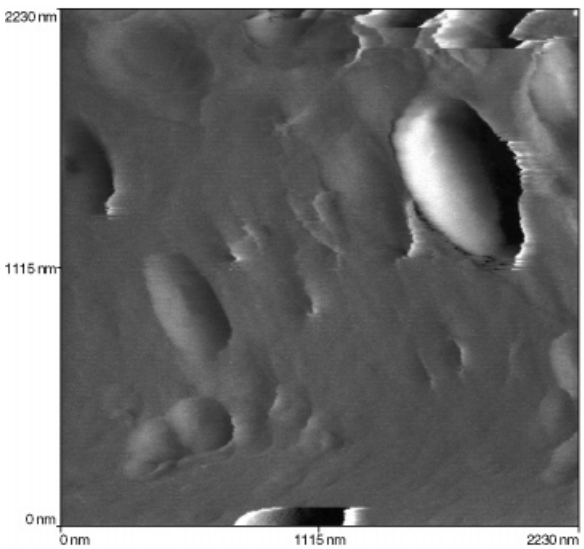


**Figure 6.** AFM non-contact mode image at dried dispersion of 11b on mica

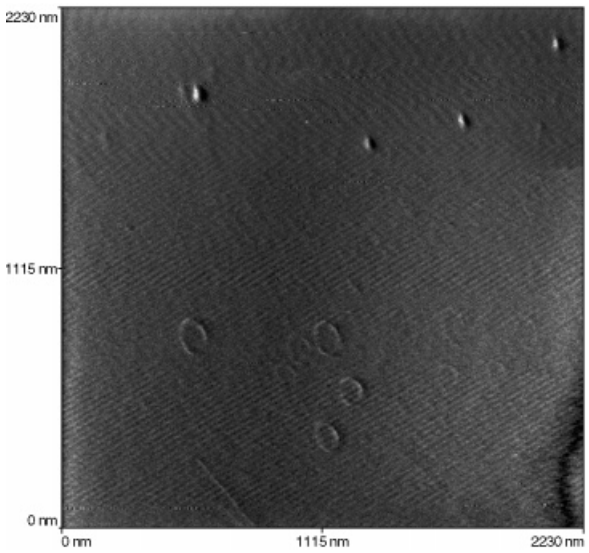


**Figure 7.** AFM non-contact mode image at dried dispersion of **14a** on mica

and allowed to dry for 24 h. The images were collected in the non-contact mode[15] owing to the fragility of the samples, but even so image quality is low and the images are presented in the internal sensor mode.[16]

For **10a** and **10b**, the images show flattened ovoid structures, resembling those expected for collapsed but separated liposomes.[17] The diameters are of the order of 150–200 nm, which may be compared with the diameters of around 150 nm observed for the smaller population of **10b**. Interestingly, no objects corresponding to the larger population are observed. The height of the structures is around 3 nm, which is in accord with a collapsed bilayer system.

In the case of **11a** and **11b**, the situation is different. First, the images show the clear presence of the contaminating aqueous layer covering the surface of the dispersion, for the image of **11b** some point breakthrough is observed. For **11a** the objects observed are highly variable between 100 and 700 nm in size and heights up to 30 nm. For **11b**, two populations appear present the first of around 100 nm and the second around 200 nm, with heights about 4 nm.

For **12a**, small objects of size *ca* 100 nm are observed, however for **12b** there are apparently some rope like structures present, which may be analogous to the ribbons and tubular structures observed by Führhop and co-workers.[11]

For the bola-amphiphiles **14**, compound **14a** shows again collapsed liposomal structures, lower left zone, along with a small number of round structures; **12b** shows small round structures but also elongated systems.

The AFM studies suggest that generally the objects formed as colloidal dispersions are liposomal in nature. In only one case, **12b**, is there any evidence for complex structures. However, from the heights, it would seen that only unilamellar liposomes are formed by the dispersion of these systems in water.

Given the geometry of the amphiphilic molecules, it might be expected that micellar systems would be produced when the molecules are dispersed in aqueous solution. However, as stated above, no cmc values have been obtained for the molecules reported here. Both DLS and AFM studies show the presence of fairly large objects, and the AFM studies appear consistent with liposomal-type systems. This may arise from the method used to prepare the dispersions; we have previously shown with amphiphilic cyclodextrin derivatives that similar structures are formed.[18] In the case of the cyclodextrin derivatives, the molecular geometry, in which the amphiphilic tails have a much larger size than the polar head groups, should favour the formation of inverse micelles, but no evidence of such behaviour was observed. Given the very low heights observed for the vesicles observed, the structures may be stabilized by interdigitation of the hydrophobic alkyl chains present.

## EXPERIMENTAL

### General

All melting-points were measured in open capillary tubes on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer model 1310 infrared spectrophotometer. $^{1}$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectra were recorded on a Brüker model 300 Fourier transform (FT) NMR spectrometer in $CDCl_3$, with tetramethylsilane (TMS) as internal standard. Electron ionization mass spectra were measured on a Nermag-R model 10-10 H mass spectrometer. Optical rotation measurements were performed on a Perkin-Elmer model 241 apparatus. Electrospray mass spectrometric (ESMS) data were obtained on a Perkin-Elmer SCIEX API 165 apparatus in the positive mode.

### Langmuir isotherms

Langmuir isotherms were measured on a NIMA 601 film balance, using a Wilhelmy paper plate to measure surface pressure. Solutions were deposited from chloroform of an appropriate concentration and the solvent allowed to evaporate for 20 min prior to compression. The compression speed was 20 cm min.$^{-1}$ All measurements were repeated three times and errors in both area and collapse pressure were less than 3%. The subphase was water of Milli-Q grade, resistivity 18 MΩ.

### Dynamic light scattering

DLS was carried out on a Malvern model 4700C photon

correlation spectrometer, using a He–Ne laser (50 mW), at 90°. Suspensions were prepared by dissolution of 50 mg of the product in acetone, pouring the solution into water (100 ml) and removing the acetone under reduced pressure at 25 °C. All measurements were repeated three times; values are averages and error estimations are given.

## Atomic force microscopy

AFM imaging was carried out on a Topometrix Explorer microscope in the non-contact amplitude mode, using low resonance frequency $Si_3N_4$ cantilevers, with a typical resonance frequency of 149 kHz. Scan speeds of 1.5 m $s^{-1}$ were used. All images are unfiltered.

The samples were prepared by deposition of 20 µl of an aqueous dispersion of the compounds on a freshly cleaved mica surface, the dispersions were allowed to dry in the absence of dust for 24 h before imaging.

## Syntheses

2-(1-Hydroxy-2-iodoethyl)-3,4-(isopropylidenedioxy) tetrahydrofuran (**2a** and **2b**) were prepared according to the procedure described by Ejjiyar *et al.*[13]

**Synthesis of 2-(epoxyethyl)-3,4-(isopropylidenedioxy)tetrahydrofuran (3a and 3b).** At 0 °C, under nitrogen, to a stirred suspension of sodium hydride (1.83 g, 76.24 mmol) in anhydrous tetrahydrofuran (50 ml) was added dropwise a solution of 2-(l-hydroxy-2-iodoethyl)-3,4-(isopropylidenedioxy)tetrahydrofuran (**2a** or **2b**) (19.95, 63.54 mmol) in anhydrous tetrahydrofuran (130 ml). At the end of the addition, the mixture was allowed to warm to room temperature. After 5 h, most of the tetrahydrofuran was removed under vacuum and diethyl ether (50 ml) was added. The reaction mixture was then treated with cold water (30 ml). The organic layer was washed successively with a saturated aqueous ammonium chloride solution and with saturated aqueous sodium chloride solution. The aqueous phase was extracted twice with dichloromethane (100 ml). The combined organic layers, after drying with magnesium sulfate, were concentrated under reduced pressure to give a colourless oil which was then purified on silica gel with light petroleum–diethylether (4:1) as eluent (for isomannide derivative **3b)** or recrystallized from hexane (for isosorbide derivative **3a**), to afford the corresponding epoxide.

*3a.* Yield:90 %. IR ($CH_2Cl_2$):3050, 2960, 2900, 2840, 1600, 1430, 1350, 1200, 1150, 1080, 1060, 1040, 1010, 970, 910, 880, 850 $cm^{-1}$. $^1H$ NMR:1.34 (s, 3H), 1.53 (s, 3H), 2.66 (dd, 1H, *J* = 4.8 Hz, *J* = 2.7 Hz), 2.91 (dd, 1H, *J* = 4.8, 4.4 Hz), 3.03 (dd, 1H, *J* = 6.9 3.7 Hz), 3.29 (ddd, 1H, *J* = 6.9 4.4 2.7 Hz), 3.52 (dd, 1H, *J* = 10.8, 3.6 Hz), 4.10 (d, 1H, *J* = 10.8 Hz), 4.70 (dd, 1H, *J* = 6.1 3.7 Hz), 4.80 (dd, 1H, *J* = 6.1 3.6 Hz). $^{13}C$ NMR:24.8, 26.0, 43.8, 50.0, 73.2, 81.2, 81.4, 84.6, 112.7. MS, *m*/*z* (%):186 ($M^{+\cdot}$, 0), 171 ($M^{+\cdot}-15$, 89), 149 (5), 111 (33), 69 (55), 68 (12), 59 (29), 57 (44), 55 (48), 43 (100), 41 (52), 39 (22), 29 (34). Anal. Calcd for $C_9H_{14}O_4$:C, 58.05; H, 7.58; O, 34.37. Found:C, 57.83; H, 7.36; O, 34.93%. $[\alpha^{26}]_D$: −80.5 (c = 0.502, $CH_3OH$). M.p.: 77 °C.

*3b.* Yield:86%. IR:3000, 2940, 2860, 1610, 1460, 1380, 1270, 1200, 1170, 1100, 1070, 1040, 1000, 960, 900, 880, 840, 810 $cm^{-1}$. $^1H$ NMR:1.22 (s, 3H), 1.37 (s, 3H), 2.6–2.7 (m, 1H), 2.7–2.8 (m, 1H), 3.0–3.1 (m, 1H), 3.1–3.2 (m, 1H), 3,70 (dm, 1H, *J* = 10.6 Hz), 3.91 (dm, 1H, *J* = 10.6), 4.67 (sl, 2H). $^{13}C$ NMR:24.6, 25.9, 46.0, 48.8, 72.8, 80.8, 80.9, 82.4, 112.4. MS, *m*/*z* (%):186 ($M^{+\cdot}$, 0), 171 (M−15, 21), 157 (7), 149 (5), 139 (8), 127 (8), 111 (21), 99 (13), 97 (20), 85 (31), 83 (16), 81 (11), 71 (45), 70 (16), 69 (45), 67 (7), 59 (6), 57 (88), 55 (58), 43 (100), 41 (70), 39 (67), 29 (59). Anal. Calcd for $C_9H_{14}O_4$:C, 58.05 ; H, 7.58; 0, 34.37. Found:C, 58.06; H, 7.65; O, 34.27%. $[\alpha]^{23}_D$: −64.8 ($CH_3OH$, *c* = 0.54) ({lit.[17] $[\alpha]^{20}_D$: −64(*c* = 0.53, $CH_3OH$)}.

**Synthesis of 2-(1-hydroxyethyl)-3,4-(isopropylidenedioxy)tetrahydrofuran (4a and 4b).** At 0 °C, under a nitrogen atmosphere, a solution of 2-(epoxyethyl)-3,4-(isopropylidenedioxy)tetrahydrofuran (**3a** or **3b**) (6.10 g, 32.79 mmol) in anhydrous diethyl ether (100 ml) was added dropwise to a stirred suspension of lithium aluminum hydride (1.25 g, 32.79 mmol) in anhydrous diethyl ether (50 ml). The reaction mixture was stirred at room temperature for 4 h. Cold water (20.6 ml) was then added dropwise, followed by 15% aqueous sodium hydroxide (20.6 ml) and water (62 ml). After one night at room temperature, the mixture was filtered the aqueous layer was extracted twice with dichloromethane and the combined organic layers were dried over anhydrous sodium sulfate and concentrated. The residue was purified on silica gel [eluent:light petroleum–diethyl ether (70:30)] to afford the corresponding alcohol **4a** or **4b** as a colourless oil.

*4a.* Yield:89.5%. IR:3350, 2960, 2900, 2820, 1460, 1380, 1270, 1220, 1150, 1100, 1080, 1010, 970, 900, 880, 870, 850, 800, 740 $cm^{-1}$. $^1H$ NMR:1.29 (d, 3H, *J* = 6.5 Hz), 1.32 (s, 3H), 1.49 (s, 3H), 2.66 (sl, 1H), 3.23 (dd, 1H, *J* = 6.6 3.6 Hz), 3.50 (dd, 1H, *J* = 10.8, 3.7 Hz), 4.07 (d, 1H, *J* = 10.8 Hz), 4.15 (dq, 1H, *J* = 6.6, 6.5 Hz), 4.65 (dd, 1H, *J* = 6.2, 3.6 Hz), 4.80 (dd, 1H, *J* = 6.2, 3.7 Hz). $^{13}C$ NMR:18.7, 24.6. 25.9, 66.3, 72.6, 80.5, 81.3, 87.0, 112.0. MS, *m*/*z* (%):188 ($M^{+\cdot}$,O), 173 ($M^{+\cdot}-15$, 68), 86 (13), 71 (13), 69 (56), 59 (54), 57 (44), 55 (15), 45 (32), 43 (100), 41 (29), 29 (11), 28 (21), 18 (31). $[\alpha]^{23}_D$: −35.4 (*C* = 0.920, $CH_2Cl_2$).

*4b.* Yield:80%. IR:3500, 2980, 2900, 2820, 1450, 1370, 1260, 1200, 1180, 1090, 1030, 980, 900, 850, 750 $cm^{-1}$. $^1H$ NMR:1.34 (d, 3H, *J* = 6.3 Hz), 1.35 (s, 3H), 1.50 (s, 3H), 2.90 (dl, 1H, *J* = 4.3 Hz), 3.26 (dm, 1H, *J* = 6.3 Hz), 3.51 (dm, 1H, *J* = 10.8 Hz), 4.05 (d, 1H, *J* = 10.8 Hz ), 4.0–4.1 (m, 1H), 4.7–4.9 (m, 2H). $^{13}C$ NMR:20.5, 24.6, 25.9, 66.1, 80.7, 81.0, 86.1, 72.7, 112.3. MS, *m/z* (%):188 ($M^{+\cdot}$,O), 173 ($M^{+\cdot}-15$, 14), 163 (41), 97 (14), 91 (6), 86 (10), 81 (11), 71 (14), 69 (14), 59 (13), 57 (20), 43 (34), 29 (23), 28 (17), 18 (100). $[\alpha]^{21}_D$: −62.5 (*c* = 1.000, $CH_3$0H){lit.[17] [$\alpha^{20}_D$: −61 (*c* = 0.83, $CH_3OH$)}.

**Synthesis of the ethers: general procedure.** *Synthesis of 2-[(1′-oxapentadecyl)ethyl]-3,4-(isopropylidenedioxy)tetrahydrofuran (**7a**).* To potassium hydroxide (1.80 g, 31.9 mmol) in solution in toluene–DMSO (9:1) (32 ml) was added a solution of 2-(1-hydroxyethyl)-3,4-(isopropylidenedioxy)-tetrahydrofuran (**4a**) in toluene–DMSO (9:1) (32 mL) and tetradecyl bromide (5.7 ml, 19.1 mmol) in the same solvent (32 ml). The reaction mixture was stirred at room temperature for 5 days and then the toluene was removed under vacuum. Diethyl ether was added to the residue and the whole was washed successively with an aqueous saturated solution of ammonium chloride and with an aqueous saturated solution of sodium chloride. The organic layer was dried with sodium sulfate and evaporated. The residue was purified on silica gel [eluent: light petroleum–diethyl ether (90:10)] 2-[(1-Oxapentadecyl)ethyl]-3,4-(isopropylidenedioxy)tetrahydrofuran was obtained (3.24 g, 66% yield).

*5a.* Yield:64% IR:2920, 2860, 1410, 1380, 1270, 1230, 1210, 1160, 1110, 1080, 1040, 1000, 940, 900, 870, 750 $cm^{-1}$. $^1H$ NMR:0.85 (t, 3H, *J* = 6.3 Hz), 1.1–1.2 (m, 17H), 1.27 (s, 3H), 1.44 (s, 3H), 1.5–1.6 (m, 2H), 3.27 (dd, 1H, *J* = 8.5 3.3 Hz), 3.4–3.6 (m, 3H), 3.68 (dq, 1H, *J* = 8.5 2.9 Hz), 4.00 (dd, 1H, *J* = 11.0 2.6 Hz), 4.56 (dd, 1H, *J* = 5.9, 3.3 Hz), 4.70 (ddd, 1H, *J* = 5.9, 3.7, 2.6 Hz). $^{13}C$ NMR:14.1, 16.3, 22.7, 24.8, 26.0, 26.1, 29.3, 29.5, 29.6 (2C), 30.2, 31.9, 69.7, 73.1, 74.4, 80.8, 80.9, 86.9, 111.9. MS, *m/z* (%):328 ($M^{+\cdot}$,O), 313 ($M^{+\cdot}-15$, 23), 186 (8), 185 (60), 141 (8), 126 (8), 99 (14), 85 (69), 83 (9), 71 (75), 69 (19), 59 (15), 57 (100), 56 (11), 55 (28), 45 (12), 43 (78), 42 (8), 41 (35), 29 (15). $[\alpha]^{22}_D$: −1.73 (*c* = 0.980, $CH_2Cl_2$).

*6a.* Yield:60%. IR:2920, 2880, 1460, 1380, 1260, 1240, 1220, 1120, 1080, 1060, 1000, 940, 900, 870, 830, 700 $cm^{-1}$. $^1H$ NMR:0.84 (t, 3H, *J* = 6.4 Hz), 1.1–1.2 (m, 2lH), 1.27 (s, 3H), 1.44 (s, 3H), 1.5–1.6 (m, 2H), 3.27 (dd, 1H, *J* = 8.5 3.3 Hz), 3.44 (dd, 1H, *J* = 11.0 3.7 Hz), 3.5–3.6 (m,2H), 3.68 (dq, 1H, *J* = 8.5 6.3 Hz), 4.00 (d, 1H, *J* = 11.0 Hz), 4.56 (dd, 1H, *J* = 6.3 3.3 Hz), 4.70 (dd, 1H, *J* = 6.3 3.7 Hz). $^{13}C$ NMR:14.1, 16.3, 22.7, 24.8, 26.0, 26.1, 29.4, 29.5, 29.6 (3C), 29.7, 30.2, 31.9, 69.7, 73.1, 74.4, 80.8, 80.9, 86.9, 111.9. MS, *m/z* (%): 358 ($M^{+\cdot}$, 0), 341 ($M^{+\cdot}-15$, 20), 213 (44), 169 (8), 126 (10), 113 (14), 99 (15), 85 (60), 83 (13), 71 (78), 69 (28), 59 (16), 57 (100), 56 (11), 55 (32), 45 (12), 43 (85), 42 (11), 41 (45), 29 (30). $[\alpha]^{22}_D$: −12.2 (*c* = 1.004, $CH_2Cl_2$).

*7a.* Yield:66%. IR:2920, 2840, 1460, 1380, 1220, 1070, 1180, 1110, 1080, 1000, 930, 900, 860, 750 $cm^{-1}$. $^1H$ NMR:0.84 (t, 3H, *J* = 6.6 Hz), 1.1–1.2 (m, 25H), 1.26 (s, 3H), 1.44 (s, 3H), 1.5–1.6 (m, 2H), 3.27 (dd, 1H, *J* = 8.5 3.3 Hz), 3.42 (dd, 1H, *J* = 10.7 4.0 Hz), 3.4–3.5 (m, 2H), 3.68 (dq, 1H, *J* = 8.5 6.3 Hz), 4.00 (d, 1H, *J* = 10.7 Hz), 4.55 (dd, 1H, *J* = 5.9 3.3 Hz), 4.69 (dd, 1H, *J* = 5.9 4.0 Hz). $^{13}C$ NMR:14.1, 16.3, 22.7, 24.8, 26.0, 26.1, 29.4, 29.5, 29.6 (3C), 29.7 (3C), 30.1, 31.9, 69.7, 73.1, 74.4, 80.7, 80.8, 86.9, 111.9. MS, *m/z* (%):384 ($M^{+\cdot}$, 0), 369 ($M^{+\cdot}-15$, 12), 241 (29), 197 (9), 126 (11), 113 (18), 99 (14), 85 (44), 83 (13), 71 (72), 70 (10), 69 (30), 59 (16), 58 (9), 57 (100), 56 (14), 55 (40), 45 (10), 43 (68), 41 (34), 29 (18). $[\alpha]^{21}_D$: −13.3(*c* = 0.998, $CH_2Cl_2$).

*8a.* Yield:60%. IR (KBr):2920, 2860, 1560, 1380, 1270, 1210, 1170, 1110, 1080, 1000, 980, 870, 750 $cm^{-1}$. $^1H$ NMR:0.86 (t, 3H, *J* = 6.6 Hz), 1.1–1.3 (m, 33H), 1.29 (s, 3H), 1.46 (s, 3H), 1.5–1.6 (m, 2H), 3.29 (dd, 1H, *J* = 8.5 3.3 Hz), 3.4–3.6 (m, 3H), 3.70 (dq, 1H, *J* = 8.5 6.3 Hz), 4.03 (d, 1H, *J* = 11.0 Hz), 4.57 (dd, 1H, *J* = 5.9 3.3 Hz), 4.72 (dd, 1H, *J* = 5.9, 3.7 Hz). $^{13}C$ NMR:14.1, 16.4, 22.7, 24.9, 26.0, 26.1, 29.4, 29.5, 29.6 (2C), 29.7 (8C), 30.2, 32.0, 69.8, 73.1, 74.5, 80.8, 80.9, 86.9, 111.9. MS, *m/z* (%): 440 ($M^{+\cdot}$, 0), 425 ($M^{+\cdot}-15$, 26), 325 (13), 297 (41), 142 (8), 126 (14), 113 (15), 99 (11), 97 (10), 86 (31), 85 (51), 84 (11), 83 (30), 82 (11), 81 (9), 71 (77), 70 (14), 69 (48), 68 (12), 67 (10), 59 (19), 57 (100), 56 (19), 55 (49), 45 (10), 44 (28), 43 (93), 42 (14), 41 (56), 39 (10), 30 (20), 29 (44). $[\alpha]^{20}_D$: −10.5 (*c* = 1.000,$CH_2Cl_2$) M.p.: 39 °C.

*5b.* Yield:59% IR:2900, 2840, 1450, 1360, 1320, 1300, 1250, 1200, 1190, 1150, 1100, 1020, 980, 950, 910, 880, 850, 840, 800, 730 $cm^{-1}$. $^1H$ NMR:0.87 (t, 3H, *J* = 6.6 Hz), 1.2–1.3 (m,17H), 1.31 (s, 3H), 1.45 (s, 3H), 1.5–1.6 (m, 2H.), 3.19 (dd, 1H, *J* = 8.4 2.9 Hz), 3.4–3.5 (m, 2H), 3.5–3.6 (m, 1H), 3.72 (dq, 1H, *J* = 8.4 6.3 Hz), 3.97 (d, 1H, *J* = 10.7 Hz), 4.7–4.8 (m, 2H). $^{13}C$ NMR:14.1, 17.6, 22.7, 24.9, 26.1, 26.1, 29.4, 29.5, 29.6, 29.7, 30.1, 31.9, 69.2, 72.4, 73.0, 80.4, 80.8, 85.8, 111.7. MS, *m/z*(%): 328 ($M^{+\cdot}$, 0), 313 ($M^{+\cdot}-15$,11), 185 (28), 141 (7), 126 (6), 113 (13), 99 (13), 85 (63), 83 (7), 71 (53), 69 (17), 59(18), 57(100), 56(11), 55 (33), 45(15), 43(92), 42 (11), 41 (42), 29(21).$[\alpha]^{22}_D$: −54.3(*c* = 1.004, $CH_2Cl_2$).

*6b.* Yield:60%. IR:2940, 2880, 1440, 1360, 1280, 1240, 1180, 1140, 1040, 1000, 940, 900, 880, 750 $cm^{-1}$. $^1H$ NMR:0.86 (t, 3H, *J* = 6.5 Hz), 1.1–1.2 (m, 21H), 1.44 (s, 3H), 1.47 (s, 3H), 1.5–1.6 (m, 2H), 3.17 (dd, 1H, *J* = 8.1 2.6 Hz), 3.3–3.4 (m, 2H), 3.5–3.6 (m, 1H), 3.71 (dq, 1H, *J* = 8.1 6.3 Hz), 3.96 (d, 1H, *J* = 10.7 Hz), 4.6–4.7 (m, 2H).

$^{13}$C NMR:14.1, 17.5, 22.7, 24.7, 26.0, 26.1, 29.4, 29.5, 29.7 (4C), 30.1, 31.9, 69.2, 72.4, 73.0, 80.4, 80.8, 85.8, 111.7. MS, *m/z* (%): 356 ($M^{+\cdot}$, 0), 341 ($M^{+\cdot}-15$, 28), 213 (22), 126 (15), 113 (27), 112 (9), 99 (20), 97 (7), 85 (40), 83 (11), 71 (46), 70 (7), 69 (23), 59 (20), 58 (8), 57 (100), 56 (13), 55 (40), 45 (12), 43 (85), 42 (10), 41 (39), 29 (12).$[\alpha]^{22}_{D}$: − 49.8 (*c* = 1.000, $CH_2Cl_2$).

*7b.* Yield:59%. IR:2880, 2810, 1440, 1350, 1320, 1300, 1250, 1200, 1190, 1150, 1100, 1020, 980, 910, 880, 850, 840, 730, 720, 710 $cm^{-1}$. $^1$H NMR:0.84 (t, 3H, *J* = 6.1 Hz), 1.1–1.2 (m, 25H), 1.28 (s, 3H), 1.41 (s, 3H), 1.5–1.6 (m, 2H), 3.16 (dd, 1H, *J* = 8.0 1.8 Hz), 3.3–3.5 (m, 2H) 3.5–3.6 (m, 1H), 3.69 (dq, 1H, *J* = 8.0 6.1 Hz), 3.94 (d, 1H, *J* = 10.7 Hz), 4.6–4.7 (m, 2H). $^{13}$C NMR:14.1, 17.5, 22.7, 24.8, 26.1, 26.1, 29.4, 29.5, 29.6 (3C), 29.7 (3C), 30.1, 31.9, 69.2, 72.4, 73.0, 80.4, 80.8, 85.7, 111.6. MS, *m/z* (%): 384 ($M^{+\cdot}$, 0), 369 ($M^{+\cdot}-15$, 28), 241 (20), 126 (12), 113 (19), 99 (13), 85 (30), 83 (11), 71 (38), 69 (24), 59 (19), 57 (86), 56 (14), 55 (38), 45 (14), 43 (100), 42 (11), 41 (44), 29 (12). $[\alpha]^{22}_{D}$: −46.1 (*c* = 1.004, $CH_2Cl_2$).

*8b.* Yield:60% IR:2900, 2820, 1440, 1350, 1330, 1320, 1300, 1250, 1210, 1200, 1150, 1100, 920, 880, 850, 840, 810, 730, 710 $cm^{-1}$. $^1$HNMR:0.85 (t, 3H, *J* = 6.4 Hz), 1.1–1.2 (m, 33H), 1.29 (s, 3H), 1.43 (s, 3H), 1.4–1.6 (m, 2H), 3.17 (dd, 1H, *J* = 8.1 2.3 Hz), 3.4–3.5 (m, 2H), 3.5–3.6 (m, 1H), 3.70 (dq, 1H, *J* = 8.1 6.3 Hz), 3.74 (d, 1H, *J* = 10.7 Hz), 4.6–4.7 (m, 2H). $^{13}$C NMR:14.1, 17.5, 22.7, 24.9, 26.1, 26.1, 29.4, 29.5, 29.6 (3C), 29.7 (7C), 30.1, 32.0, 69.1, 72.4, 73.0, 80.4, 80.8, 85.8, 111.6 MS, *m/z*(%):440 ($M^{+\cdot}$, 0), 425 ($M^{+\cdot}-15$, 30), 397 (5), 339 (4), 298 (4), 297 (18), 143 (5), 141 (4), 127 (7), 126 (15), 113 (22), 112 (8), 111 (5), 99 (12), 97 (10), 95 (4), 86 (4), 85 (41), 84 (5), 83 (20), 82 (5), 81 (4), 71 (62), 70 (11), 69 (40), 68 (8), 67 (6), 59 (18), 58 (8), 57 (100), 56 (15), 55 (40), 54 (4), 45 (9), 43 (66), 42 (7), 41 (24), 29 (16), 27 (4). $[\alpha]^{22}_{D}$: −39.9 (*c* = 1.022, $CH_2Cl_2$).

*Synthesis of 2-[(1′-oxapentadecyl)ethyl]-3,4-dihydroxytetrahydrofuran (**11a**).* 2-[(1-Oxapentadecyl)ethyl]-3,4-isopropylidenetetrahydrofuran (**7a**) (3.2 g, 8.33 mmol) was refluxed in 80% aqueous acetic acid (40 ml) for 5 h. The mixture was then concentrated under vacuum. The residue was purified on silica gel [eluent:dichloromethane–ethy1 acetate (85:15)]. 2-[(1-Oxapentadecyl) ethyl]-3,4-dihydroxytetrahydrofuran (2.35 g, 6.83 mmol) was obtained in 82% yield.

*9a.* Yield:85%. IR ($CH_2Cl_2$):3600, 3380, 3080, 2970, 2900, 1430, 1390, 1260, 1130, 1070, 1010, 920, 710 $cm^{-1}$. $^1$H NMR:0.85 (t, 3H, *J* = 6.6 Hz), 1.1–1.2 (m, 14H), 1.27 (d, 3H, *J* = 6.6 Hz), 1.5–1.6 (m, 2H), 3.34 (dt, 1H, *J* = 9.0 6.8 Hz), 3.58 (dt, 1H, *J* = 9.0 7.0 Hz), 3.69 (qd, 1H, *J* = 6.4 2.6 Hz), 3.76 (dd, 1H, *J* = 6.8 2.6 Hz), 3.79 (d, 2H, *J* = 3.6 Hz), 4.00 (s, 2H), 4.10 (dt, 1H, *J* = 5.1 3.6 Hz), 4.27 (dd, 1H, *J* = 6.8 5.1 Hz). $^{13}$C NMR:14.1, 15.5, 22.7, 26.1, 29.3, 29.4, 29.5 (2C), 29.9, 31.9, 69.0, 71.6, 72.6, 73.0, 73.6, 81.6. MS, *m/z* (%): 289 ($M^{+\cdot}+1$, 1), 288 ($M^{+\cdot}$, 0), 213 (5), 185 (24), 141 (7), 130 (7), 99 (11), 87 (7), 86 (25), 85 (54), 83 (6), 73 (10), 71 (75), 70 (10), 69 (16), 59 (10), 58 (14), 57 (100), 56 (13), 55 (34), 45 (24), 44 (9), 43 (79), 42 (12), 41 (45), 31 (9), 29 (28). $[\alpha]^{22}_{D}$: +54.6 (*c* = 1.002, $CH_2Cl_2$). M.p.:48 °C. ESMS: 311, $M + Na^+$ Anal. Found: C 66.4, H 11.5. Calc:C 66.6, H 11.2%.

*10a.* Yield:88%. IR ($CH_2Cl_2$):3540, 3380, 3060, 2940, 2860, 1420, 1380, 1260, 1160, 1130, 1070, 1040, 1010, 900, 700 $cm^{-1}$. $^1$H NMR:0.87 (t, 3H, *J* = 6.5 Hz), 1.1–1.2 (m, 18H), 1.28 (d, 3H, *J* = 6.6 Hz), 1.5–1.6 (m, 2H), 3.35 (dt, 1H, *J* = 8.9 6.9 Hz), 3.5–3.7 (m, 3H), 3.72 (qd, 1H, *J* = 6.6 1.5 Hz), 3.81 (dd, 1H, *J* = 6.6 1.5 Hz), 3.8–3.9 (m, 2H), 4.11 (dt, 1H, *J* = 5.5 3.2 Hz), 4.34 (dd, lH, *J* = 6.6 5.5 Hz). $^{13}$C NMR:14.2, 15.5, 22.7, 26.1, 29.3, 29.4, 29.5, 29.6, 29.7 (2C), 29.9, 31.9, 69.0, 71.6, 72.6, 73.1, 73.5, 81.6. MS *m/z* (%): 317 ($M^{+\cdot}$ 1, 1), 316 ($M^{+\cdot}$, 0), 213 (17), 113 (10), 99 (14), 86 (19), 85 (40), 83 (7), 71 (59), 70 (8), 69 (15), 59(8), 58 (13), 57 (100), 56 (15), 55 (37), 45 (19), 43 (71), 42 (10), 41 (37), 29 (16).$[\alpha]^{22}_{D}$: +46.1 (*c* = 1.002, $CH_2Cl_2$). M.p.: 52.8 °C. ESMS:339, $M + Na^+$ Anal. Found:C 68.7, H 11.3. Calcd:C 68.3, H 11.5%.

*11a.* Yield:82%. IR ($CH_2Cl_2$):3300, 2900, 2840, 1450, 1250, 1150, 1120, 1050, 1000, 700 $cm^{-1}$. $^1$H NMR:0.84 (t, 3H *J* = 6.5 Hz), 1.2–1.3 (m, 22H), 1.28 (d, 3H, *J* = 6.3 Hz), 1.5–1.6 (m, 2H), 3.28 (d, 1H), 3.35 (dt, 1H, *J* = 8.8 7.0 Hz), 3.62 (dt, 1H, *J* = 8.8 7.0 Hz), 3.72 (td, 1H, *J* = 6.3 1.8 Hz), 3.8–3.9 (m, 3H), 3.93 (d, 1H), 4.10 (ddd, 1H, *J* = 5.1, 3.7, 3.7 Hz), 4.32 (dd, 1H, *J* = 7.0 5.1 Hz). $^{13}$C NMR:14.1, 15.5, 22.7, 26.1, 29.3, 29.4, 29.5, 29.6, 29.7 (4C), 29.9, 32.0, 68.9, 71.6, 72.6, 73.1, 73.6, 81.6. MS, *m/z* (%):316 ($M^{+\cdot}$, 1), 269 (5), 241 (20), 197 (10), 130 (11), 113 (12), 99 (13), 87 (11), 83 (13), 86 (41), 85 (58), 83 (14), 73 (12), 72 (8), 71 (99), 70 (15), 69 (29), 59 (11), 58 (14), 57 (100), 56 (15), 55 (43), 45 (20), 43 (78), 42 (12), 41 (45), 29 (26). $[\alpha]^{21}_{D}$: +45.7 (*c* = 1.000, $CH_2Cl_2$). M.p.: 61.6 °C. ESMS:367, $M + Na^+$ Anal. Found: C 70.1, H 11.4 Calcd: C 69.7, H 11.7%.

*12a.* Yield:80%. IR ($CH_2Cl_2$):3500, 3300, 300, 2960, 2880, 2800, 2640, 1400, 1230, 1100, 1040, 980, 880, 700 $cm^{-1}$. $^1$H NMR:0.84 (t, 3H, *J* = 6.5 Hz), 1.2–1.3 (m, 32H), 1.24 (d, 3H, *J* = 6.3 Hz), 1.5–1.7 (m, 2H), 3.34 (dt, 1H, *J* = 8.8 7.0 Hz), 3.4–3.5 (m, 1H), 3.58 (dt, 1H, *J* = 8.8 7.4 Hz), 3.69 (td, 1H, *J* = 6.3 2.2 Hz), 3.76 (dd, 1H, *J* = 6.9 2.2 Hz), 3.8–3.9 (m, 1H), 4.10 (ddd, 1H, *J* = 4.9, 3.7, 3.7 Hz), 4.28 (dd, 1H, *J* = 6.9 4.9 Hz). $^{13}$C NMR:14.1, 15.6, 22.7, 26.1, 29.3, 29.4, 29.5, 29.6 29.7 (8C), 29.9, 31.9, 69.0, 71.6, 72.5, 72.9, 73.7, 82.0. MS, *m/z*(%): 401 ($M^{+\cdot}+1$, 1), 400 ($M^{+\cdot}$, 0), 325 (4), 297 (11), 253 (5), 141 (4), 131 (8), 130 (14), 125 (5), 113 (15), 111 (5), 99 (11), 97 (12), 89 (8), 87 (11), 86 (40), 84 (10), 83 (24), 82

 

(9), 73 (11), 72 (7), 71 (94), 70 (17), 69 (42), 68 (7), 67 (10), 59 (10), 58 (12), 57 (100), 56 (18), 55 (51), 45 (16), 43(74), 41 (37), 29 (22). $[\alpha]^{22}_D$: +41.4 (*c* = 1.000, $CH_2Cl_2$). M.p.: 68 °C ESMS:423, $M + Na^+$ Anal. Found: C 71.6 H 12.4. Calcd C 72.0 H 12.1%.

*9b.* Yield:85%. IR ($CH_2Cl_2$):3360, 3040, 2960, 2900, 2820, 2300, 1410, 1370, 1250, 1100, 1070, 1050, 890, 750, 700 $cm^{-1}$. $^1H$ NMR:0.86 (t, 3H, *J* = 6.3 Hz), 1.1–1.3 (m, 14H), 1.29 (d, 3H, *J* = 6.6 Hz), 1.5–1.6 (m, 2H), 3.35 (s1, 1H), 3.48 (dt, 1H, *J* = 9.2 6.6 Hz), 3.61 (dt, 1H, *J* = 9.2 6.6 Hz), 3.7–3.9 (m, 4H), 4.18 (ddd, 1H, *J* = 5.1, 5.1, 5.1 Hz), 4.34 (dd, 1H, *J* = 5.1, 5.1 Hz), 4.34 (s1, 1H). $^{13}C$ NMR:14.1, 16.4, 22.7, 26.1, 29.3, 29.4, 29.6 (2C), 30.0, 31.9, 70.3, 72.2, 72.3, 72.4, 76.9, 81.6. MS, *m/z*(%):289 ($M^{+\cdot} + 1.4$), 288 ($M^{+\cdot}$, 0), 213 (3), 203 (6), 186 (4), 185 (31), 141 (9), 131 (3), 130 (11), 128 (3), 113 (3), 99 (13), 97 (3), 87 (8), 86 (36), 85 (90), 84 (5), 83 (9), 73 (8), 72 (6), 71 (100), 70 (9), 69 (23), 68 (4), 67 (5), 61 (4), 59 (8), 58 (16), 57 (98), 56 (15), 55 (34), 53 (3), 45 (21), 44 (10), 43 (96), 42 (13), 41 (50), 39 (7), 31 (9), 29 (30), 27 (9). $[\alpha]^{22}_D$: −35.0 (*c* = 1.010, $CH_2Cl_2$). M.p.: 50 °C. ESMS:311, $M + Na^+$.

*10b.* Yield:88%. IR ($CH_2Cl_2$):3500, 3360, 2910, 2840, 1450, 1380, 1230, 1100, 1070, 1050 $cm^{-1}$. $^1H$ NMR:0.86 (t, 3H, *J* = 6.6 Hz), 1.1–1.2 (m, 18H), 1.28 (d, 3H, *J* = 6.6 Hz), 1.5–1.6 (m, 2H), 3.35 (sl, 1H), 3.47 (dt, 1H, *J* = 9.0 Hz, *J* = 6.6 Hz), 3.60 (dt, 1H, *J* = 9.0 6.6 Hz), 3.7–3.9 (m, 4H), 4.18 (ddd, 1H, *J* = 5.2, 5.2, 5.2 Hz), 4.34 (dd, 1H, *J* = 5.2, 5.2 Hz), 4.36 (sl, 1H). $^{13}C$ NMR:14.1, 16.4, 22.7, 26.1, 29.3, 29.4, 29.5, 29.6, 29.7 (2C), 30.0, 32.0, 70.3, 72.2, 72.3, 72.4, 76.9, 81.9. MS, *m/z* (%):317 ($M^{+\cdot} + 1$, 1), 316 ($M^{+\cdot}$, 0), 231 (3), (214 (3), 213 (15), 169 (6), 131 (3), 130 (9), 127 (3), 113 (10), 99 (14), 97 (5), 87 (5), 86 (20), 85 (38), 84 (3), 83 (7), 82 (3), 73 (4), 72 (5), 71 (59), 70 (9), 69 (19), 68 (4), 67 (4), 61 (3), 59 (8), 58 (12), 57 (100), 56 (15), 55 (39), 53 (3), 45 (18), 44 (7), 43 (79), 42 (10), 41 (34), 39 (4), 29 (5), 27 (5). $[\alpha]^{22}_D$: −29.5 (*c* = 1.006, $CH_2Cl_2$). M.p.: 58 °C. ESMS:339, $M + Na^+$

*11b.* Yield:90%. IR ($CH_2Cl_2$):3660, 3040, 2990, 2900, 2820, 1410, 1250, 1100, 1070, 1050, 990, 890, 750, 700 $cm^{-1}$. $^1H$ NMR:0.87 (t, 3H, *J* = 6.3 Hz), 1.1–1.3 (m,22H), 1.29 (d, 3H, *J* = 6.6 Hz), 1.4–1.6 (m, 2H), 3.29 (sl, 1H), 3.48 (dt, 1H, *J* = 9.2 6.6 Hz), 3.60 (dt, 1H, *J* = 9.2 6.6 Hz), 3.7–3.9 (m,4H), 4.19 (ddd, 1H, *J* = 5.1, 5.1, 5.1 Hz), 4.35 (dd, 1H, *J* = 5.1, 5.1 Hz), 4.36 (sl, 1H). $^{13}C$ NMR:14.1, 16.4, 22.7, 26.1, 29.4, 29.5, 29.6 (2C), 29.7 (4C), 30.0, 32.0, 70.3, 72.2, 72.3, 72.5, 76.9, 81.9. MS, *m/z* (%): 345 ($M^{+\cdot} + 1$, 1), 344 ($M^{+\cdot}$, 0), 243 (3), 241 (17), 197 (8), 141 (5), 131 (5), 130 (13), 128 (5), 127 (7), 115 (3), 113 (12), 99 (5), 97 (7), 87 (10), 86 (37), 85 (74), 84 (7), 83 (16), 82 (5), 81 (3), 73 (7), 72 (5), 71 (100), 70 (14), 69 (32), 68 (8), 67 (6), 61 (3), 59 (9), 58 (15), 57 (95), 56 (17), 55 (42), 54 (4), 53 (3), 45 (19), 44 (7), 43 (89), 42 (11), 41 (47), 39 (5), 29 (24), 27 (6).$[\alpha]^{22}_D$: −27.5 (*c* = 1.006, $CH_2Cl_2$). M.p.: 65 °C. ESMS:367, $M + Na^+$.

*12b.* Yield:85%. IR ($CH_2Cl_2$):3520, 3420, 3060, 2920, 2560, 1420, 1380, 1260, 1120, 1090, 910, 710 $cm^{-1}$. $^1H$ NMR:0.87 (t, 3H, *J* = 6.3 Hz), 1.1–1.2 (m, 30H), 1.30 (d, 3H, *J* = 7.0 Hz), 1.5–1.7 (m, 2H), 3.22 (s1, 1H), 3.49 (dt, 1H, *J* = 8.8, 6.6 Hz), 3.62 (dt, 1H, *J* = 8.8 6.6 Hz), 3.7–3.9 (m, 4H), 4.20 (ddd, 1H, *J* = 5.1, 5.1, 5.1 Hz), 4.35 (dd, 1H, *J* = 5.1, 5.1 Hz), 4.36 (sl, 1H). $^{13}C$ NMR:14.1, 16.4, 22.7, 26.1, 29.4, 29.5, 29.6, 29.7 (3C), 29.8 (6C), 30.0, 32.0, 70.3, 72.2, 72.3, 72.4, 76.9, 81.9. MS, *m/z* (%): 400 ($M^{+\cdot}$,O), 366 (1), 297 (3), 254 (1), 206 (1), 169 (1), 155 (2), 131 (5), 130 (9), 113 (8), 111 (4), 99 (8), 97 (9), 96 (4), 95 (4), 87 (21), 85 (29), 84 (4), 83 (13), 82 (9), 73 (5), 72 (4), 71 (55), 70 (14), 69 (32), 68 (9), 67 (10), 61 (4), 59 (10), 58 (14), 57 (100), 56 (21), 55 (55), 54 (7), 53 (4), 45 (19), 44 (11), 43 (81), 42 (13), 41 (41), 39 (5), 31 (6), 29 (28). $[\alpha]^{22}_D$: −20.8 (*c* = 1.012, $CH_2Cl_2$). M.p.: 69 °C. ESMS:423, $M + Na^+$

*13a.* Yield:50%. IR ($CH_2Cl_2$):2960, 2900, 2830, 1450, 1370, 1260, 1220, 1200, 1160, 1100, 1070, 1030, 990, 930, 890, 860, 810, 740, 720, 650 $cm^{-1}$. $^1H$ NMR:1.1–1.4 (m. 28H), 1.45 (s, 6H), 1.4–1.6 (m, 2H), 1.7–1.8 (m, 2H), 3.28 (dd, 2H, *J* = 8.5 3.3 Hz), 3.37 (dd, 2H, *J* = 7.0 6.6 Hz), 3.45 (dd, 2H, *J* = 11.0 3.7 Hz), 3.51 (ddd, 2H, *J* = 7.0 6.6, 6.6 Hz), 3.70 (dq, 2H, *J* = 8.5 6.1 Hz), 4.01 (d, 2H, *J* = 11.0 Hz), 4.56 (dd, 2H, *J* = 5.9 3.3 Hz), 4.71 (dd, 2H, *J* = 5.9, 3.7 Hz). $^{13}C$ NMR:16.3, 24.9, 26.0, 26.1, 28.2, 28.8, 29.4, 29.5 (4C), 29.6, 30.2, 32.7, 34.0, 69.7, 73.1, 74.4, 80.8, 80.9, 86.8, 111.9. $[\alpha]^{25}_D$: −12.5 (*c* = 0.994, $CH_2Cl_2$).

*13b.* Yield:48%. IR:2980, 2920, 2860, 1460, 1380, 1270, 1220, 1180, 1120, 1040, 1000, 930, 900, 870, 850, 750 $cm^{-1}$. $^1H$ NMR:1.2–1.4 (m, 28H), 1.45 (s 6H), 1.5–1.6 (m, 2H), 1.8–1.9 (m, 2H), 3.19 (dd, 2H, *J* = 8.1 2.9 Hz), 3.3–3.6 (m, 6H), 3.72 (dq, 2H, *J* = 8.1 6.3 Hz), 3.97 (d, 2H, *J* = 10.7 Hz), 4.6–4.7 (m, 4H). $^{13}C$ NMR:17.6, 24.9, 26.1, 26.1, 28.2, 28.8, 29.4, 29.5, 29.6, 29.7, 30,1, 32,9, 34.0, 69.2, 73,0, 72.4, 80.4, 80.8, 85.7, 114.1. $[\alpha]^{25}_D$: −43.5(*c* = 1.014, $CH_2Cl_2$).

*14a.* Yield:75%. IR:3400, 2920, 2860, 1420, 1380, 1250, 1080, 1010, 890, 790, 740 $cm^{-1}$. $^1H$ NMR:1.1–1.5 (m, 26H), 1.5–1.6 (m, 2H), 1.7–1.8 (m, 2H), 3.2–3.4 (m, 4H), 3.5–3.6 (m, 2H), 3.65 (qd, 2H, *J* = 6.2 2.2 Hz), 3.7–3.8 (m, 4H), 4.0–4.1 (m, 2H), 4.2–4.3 (m, 2H). $^{13}C$ NMR:15.6, 26.0, 28.2, 28.7, 29.4 (2C), 29.5 (4C), 29.9, 32.8, 34.0, 69.0, 72.5, 71.6, 72.8, 73.7, 82.0. MS, *m/z* (%):462 ($M^{+\cdot}$, 0), 460 (1), 421 (1), 395 (1), 293 (15), 291 (16), 130 (14), 113 (6), 111 (14), 99 (7), 97 (29), 89 (6), 87 (10), 86 (34), 85 (39), 84 (7), 83 (36), 81 (6), 73 (14), 71 (65), 70 (13), 69 (63), 68 (7), 67 (10), 59 (12), 58 (14), 57 (69), 56 (18), 55 (79), 54 (6), 53 (6), 45 (37), 44 (13),

 

43 (100), 42 (21), 41 (80), 39 (11), 31 (10), 29 (28), 27 (9). $[\alpha]^{26}_{D}$: +39.3 ($c$ = 0.992, $CH_2Cl_2$).

*14b.* Yield:74%. IR ($CH_2Cl_2$):3520, 3300, 2940, 2890, 1460, 1380, 1240, 1100, 980, 940, 910, 890, 710 $cm^{-1}$. $_1$H NMR:1.1–1.4 (m, 26H), 1.4–1.6 (m, 2H), 1.7–1.8 (m, 2H), 3.3–3.6 (m, 6H), 3.7–3.9 (m, 6H), 4.19 (dd, 2H, $J$ = 5.2, 4.8 Hz), 4.32 (dd, 2H, $J$ = 5.5, 5.2 Hz). $^{13}$C NMR: 16.4, 26.1, 28.2, 28.8, 28.9, 29.4, 29.5, 29.9, 32.8, 34.0, 72.2, 72.2, 72.4, 76.2, 82.0. MS m/z (%): 462 ($M^{+\cdot}$, 0), 448 (1), 435 (1), 418 (1), 395 (4), 385 (2), 291 (9), 271 (1), 265 (1), 130 (16), 128 (7), 113 (27), 111 (27), 109 (5), 99 (6), 97 (44), 95 (6), 87 (7), 85 (36), 84 (8), 83 (51), 81 (9), 73 (10), 72 (5), 71 (68), 70 (14), 69 (88), 68 (14), 67 (17), 59 (12), 58 (16), 57 (85), 56 (17), 55 (100), 54 (9), 53 (6), 45 (24), 44 (10), 43 (81), 42 (15), 41 (52), 39 (9), 31 (10), 29 (29), 28 (19), 27 (9). $[\alpha]^{26}_{D}$: −21.8 ($c$ = 1.004, $CH_2Cl_2$).

## Conclusion

We have demonstrated the synthesis of a novel series of amphiphilic compounds derived from isomannide and isosorbide having varying chain lengths and including bola-amphiphilic derivatives. The Langmuir behaviour of these compounds is dependent on the chain length and the chirality of the molecules. With regard to colloidal dispersions, the systems were studied by both DLS and AFS and systems corresponding to liposomes were observed.

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