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ORIGINAL ARTICLE

Synthesis and Surface-Active Properties of Uronic Amide Derivatives, Surfactants from Renewable Organic Raw Materials

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Abstract Short chemical syntheses were developed to produce a new set of surfactants from uronic acids derived from widely available raw materials. Three different strategies were used to synthesize uronic amide derivatives, the structures of which were totally characterized by spectrometric methods (IR, MS, ^{1}H-RMN and ^{13}C-RMN). The best one, using an acid chloride as the synthetic intermediate, furnished the expected amides as a mixture of anomers in 46–58% global yield. Surface-active properties (CMC, γ_{cmc}, Γ_{max}, A_{min}) of homologous series of uronic acid *N*-alkylamides from C8 to C18 were also assessed. In general, these sugar-based surfactants exhibited good surface-activities, and appeared as valuable nonionic surfactants compared to octylphenol 9–10 ethylene oxide condensate, the most well-known nonionic surfactant. Increasing the alkyl chain length influenced the CMC values for both glucuronic and galacturonic *N*-alkylamide derivatives. The galacturonic *N*-alkylamides decreased γ_{cmc} at slower values than their counterpart's glucuronic *N*-alkylamides.

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Keywords Uronic acid · Amide formation · Carbohydrates · Critical micellar concentration · Surface tension

Abbreviations

COSY	Correlation spectroscopy
DCC	Dicyclohexyl carbodiimide
DMF	Dimethyl formamide
DMSO	Dimethyl sulfoxide
ESIMS	Electrospray ionisation mass spectrometry
HMBC	Heteronuclear multiple bond correlation
HSQC	Heteronuclear single quantum correlation
NOESY	Nuclear Overhauser effect spectroscopy
TLC	Thin layer chromatography
TMS	Tetramethylsilane

Introduction

By definition, uronic acids are monosaccharides in which the primary hydroxyl-group is oxidized into a carboxyl-group. The presence of different reactive functional groups on those molecules provides a basis for modifications of their properties. Uronic acids have thus found wide applications as scaffold for novel bioactive molecule design and synthesis [1].

Among these, the field of surfactants is an important one since those compounds find a lot of applications in various areas, including cosmetics, pharmaceuticals, food, soaps and detergents, etc. [2].

In most industrial cases, they are disposed of following use. Issues regarding disposal have thus created interest in more biologically acceptable alternatives and have thus

focused on use of renewable versus non-renewable resources.

Various carbohydrates can be used as organic raw materials for surfactants synthesis [3].

In the context of renewable resources, glucuronic acid and galacturonic acids derived from widely available raw material such as hemicellulose [4] or pectins [5] represent important biocompatible and bioresorbable starting materials. They contain appropriate functional sites for chemical modifications (Fig. 1), which will lead to the development of new added value bio-based surfactants.

In previous papers, we have already described the enzymatic synthesis and surface properties of glucuronate fatty esters [6–10]. The effect of the hydrophobic chain length on the surface properties of these molecules was examined. Dynamic parameters and equilibrium surface tension were measured: decyl and dodecyl glucuronate exhibit an interesting adsorption speed associate with foaming capacity. Octyl glucuronate exhibits a micellar organization as its bulk concentration is over 10.68 mM [6, 7].

As amides are much more resistant towards hydrolysis compared to esters in both neutral and alkaline media, and as the hydrophilic–lipophilic balance is the main parameter that determines the interfacial activity of an amphiphilic molecule, we decided to synthesize long-chain *N*-alkylamides of glucuronic and galacturonic acids as renewable material with potentially valuable surface properties.

Furthermore, this would allow us to investigate the effect of a specific structural modification in the sugar moiety on the surface-active properties. Moreover, the use of different linear alkyl chains would also allow us to equilibrate the polarity of the sugar moiety.

Some of these compounds (dodecyl-, tetradecyl- and octadecylglucuronamides; octyl- and dodecylgalacturonamides) have already been synthesized starting from a 1,2-isopropylidene derivative of glucofururonolactone or from 1,2,3,4-di-*O*-isopropylidene-α-D-galacto pyranuronosyl chloride by low yield multi-step sequences [11–13].

As there are no reports in the literature concerning physico-chemical properties of uronamides, though these are obvious derivatives arising from very available resources, in this paper, we wish to describe three short routes towards those compounds as well as a study of several physico-chemical parameters of these molecules.

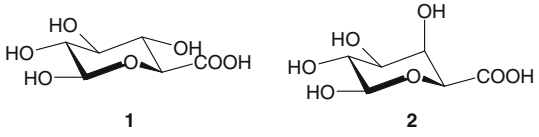


Fig. 1 Structures of β-D-glucuronic acid **1** (GlcA) and β-D-galacturonic acid **2** (GalA)

Experimental Procedures

Chemical Syntheses

The NMR spectra (^{1}H, ^{13}C, NOE, ^{1}H/^{1}H COSY, HSQC, HMBC, NOESY) were recorded in $CDCl_3$ or in DMSO-d_6 at 600 MHz (^{1}H) and 150 MHz (^{13}C) with a Varian instrument and are reported in ppm from internal TMS on the δ scale. Data are reported as follows: chemical shift [multiplicity (s: singlet, bs: broad singlet, d: doublet, dd: double doublet, t: triplet, td: triple doublet, bt: broad triplet, apt: apparent triplet, q: quartet, quint: quintuplet, m: multiplet), coupling constants in Hertz, attribution].

The IR spectra were recorded with a Bruker IFS 25 instrument as KBr pellets.

Mass spectra were acquired on an Esquire HCT mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an electrospray ionization source. Best results were obtained in positive mode with capillary, nebulizer pressure, drying gas flow, and drying gas temperature set to 10,000 nA, 40.0 psi (nitrogen), 9.0 L min^{-1} (nitrogen) and 365 °C, respectively. The scan range was adjusted to *m*/*z* 100–500 and the target mass set to 300. MS-data were recorded and processed using Bruker Daltonics data analysis software, version 3.0. All the mass spectra were acquired in ESI (electrospray ionization) in the positive mode and $[M + H]^+$, $[M + Na]^+$ and $[M + K]^+$ were seen. In all cases, peak intensities are expressed as % relative to the bas peak.

Thin layer chromatography (TLC) analyses were performed with 0.25 Polygram silica gel SILG/UV254 precoated plates (Macherey–Nagel). Column chromatography was performed on silica gel (MN Kieselgel 60 0.04–0.063 mm).

All reagents and reactants were purchased from Sigma–Aldrich. Triton X-100 is the commercial name of the octylphenol 9–10 ethylene oxide condensate. All the solvent used were purified and/or dried according to Perrin and Armarego [14].

Anhydride (3)

D-Glucuronic acid (5.025 g, 25.90 mmol), was suspended in acetic anhydride (75 mL) and stirred at 0 °C. Iodine (352.3 mg, 1.388 mmol) was added slowly and the red solution was stirred for 2 h at 0 °C and for a further 3 h at room temperature. Acetic anhydride was mostly removed in vacuo and the remaining mixture taken up in dichloromethane (70 mL). The organic layer was then washed twice with a 1 M $Na_2S_2O_3$ aqueous solution (80 mL) and evaporated to afford **3** as a white solid. This was recrystallized from a mixture of dichloromethane—40/60 petroleum ether to afford 9.730 g (24.07 mmol, 93%) of the β-anomer as single product.

(3) ESIMS *m/z* 443 (100, $[M + K]^+$), 427 (29, $[M + Na]^+$), 405 (19, $[M + H]^+$); IR (KBr) 2959, 1827, 1761, 1369, 1215, 1039, 948, 895, 771, 691 cm^{-1}; ^1H NMR ($CDCl_3$) 5.79 (d, 6.6, H-1), 5.36 (apt, 9.3, H-4), 5.28 (apt, 9.3, H-3), 5.10 (apt, 7.8, H-2), 4.31 (d, 9.0, H-5), 2.26 (s, COOCO**CH$_3$**), 2.11, 2.04, 2.03, 2.02 (4s, OCO**CH$_3$**); ^{13}C NMR ($CDCl_3$) 169.9, 169.7, 169.4, 168.7 (O**C**OCH$_3$), 164.7 (COO**C**OCH$_3$), 162.5 (C-6), 91.4 (C-1), 73.0 (C-5), 71.3 (C-3), 70.1 (C-2), 68.1 (C-4), 22.1 (COOCO**C**H$_3$), 20.7, 20.6, 20.5, 20.4 (OCO**C**H$_3$).

Acetylated Acid (29)

D-Glucuronic acid (4.997 g, 25.76 mmol), was added to a stirred solution of acetic anhydride (25 mL) and concentrated sulphuric acid (3 drops). The temperature was allowed to reach 60 °C and extra glucuronic acid (5.029 g, 25.92 mmol) was added. The reaction mixture was maintained at 60 °C for 1 h and then cooled to room temperature. Water (75 mL) was then added to the stirred solution. The solid obtained was filtered and recrystallized from toluene to afford **29** (12.35 g, 34.11 mmol, 66%) as a white solid.

(29) ESIMS *m/z* 401 (52, $[M + K]^+$), 385 (100, $[M + Na]^+$), 363 (12, $[M + H]^+$); IR (KBr) 3598, 3525, 2957, 1747, 1369, 1229, 1088, 1038, 908 cm^{-1}; ^1H NMR ($CDCl_3$) 6.0 (bs, OH), 5.70 (d, 7.6, H-1), 5.30 (m, H-3), 5.28 (m, H-4), 5.12 (apt, 8.2, H-2), 4.23 (d, 8.8, H-5), 2.10, 2.04, 2.03, 2.02 (4s, OCO**CH$_3$**); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.3, 169.0 (O**C**OCH$_3$), 169.8 (C-6), 91.3 (C-1), 72.3 (C-5), 71.8 (C-3), 70.1 (C-2), 68.6 (C-4), 20.7, 20.5, 20.5, 20.4 (OCO**C**H$_3$).

Acetylated Amides (4) to (9)

Synthetic way 1 (Scheme 1a): After dissolution of anhydride **3** (0.5 g, 0.123 mmol) in 5 mL dry dichloromethane under a nitrogen atmosphere, 1.2 equivalent of the primary amine is added and the reaction mixture is stirred overnight. The solvent is then evaporated under reduce pressure and the obtained residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **4** to **9** as white solids in 39–48% yield.

Synthetic way 2 (Scheme 1b): After dissolution of acid **29** (0.503 g, 0.138 mmol) in 5 mL dry acetonitrile under a nitrogen atmosphere, 0.352 g DCC (0.171 mmol, 1.2 eq.) is added. After 10 min, 2 equivalents of the primary amine are added and the reaction mixture is allowed stir overnight at room temperature. After filtration of the precipitated dicyclohexylurea, the solvent is evaporated in vacuo and the residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **4** to **9** as white solids in 65–69% yield.

Synthetic way 3 (Scheme 1c): 0.301 g of acid **29** (0.0831 mmol) are dissolved in 5 mL dry dichloromethane at 0 °C under a nitrogen atmosphere. 400 μL dry DMF and 150 μL of oxalyl chloride are then added and the reaction mixture is stirred 30 min at 0 °C and for further 2 h at room temperature. 1.2 equivalent of the primary amine is then added and the reaction mixture is stirred overnight at room temperature. The solvent is evaporated under reduce pressure and the obtained residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **4** to **9** as white solids in 88–93% yield.

(4) ESIMS *m/z* 456 (95, $[M + K]^+$), 440 (100, $[M + Na]^+$), 418 (35, $[M + H]^+$); IR (KBr) 3302, 2960, 2874, 1759, 1668, 1547, 1435, 1370, 1220, 1040, 894 cm^{-1}; ^1H NMR ($CDCl_3$) 6.26 (bs, NH), 5.72 (d, 7.8, H-1), 5.28 (apt, 9.6, H-3), 5.17 (apt, 9.6, H-4), 5.09 (apt, 9.0, H-2), 4.03 (d, 9.6, H-5), 2.12, 2.05, 2.02, 2.00 (4s, OCO**CH$_3$**), 3.19 (m, CH_2-1′), 1.46 (quint, 7.4, CH_2-2′), 1.31 (m, CH_2-3′), 0.90 (t, 7.8, CH_3-4′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH$_3$), 165.8 (C-6), 91.4 (C-1), 72.9 (C-5), 72.0 (C-3), 70.2 (C-2), 69.0 (C-4), 20.7, 20.6, 20.6, 20.5 (OCO**C**H$_3$), 38.9 (C-1′), 31.3 (C-2′), 20.0 (C-3′), 13.7 (C-4′).

(5) ESIMS *m/z* 512 (100, $[M + K]^+$), 496 (62, $[M + Na]^+$), 474 (21, $[M + H]^+$), 414 (33, [M + H-CH3COOH]$^+$); IR (KBr) 3241, 2928, 2858, 1759, 1657, 1576, 1444, 1369, 1216, 1072, 1036, 911, 889, 747 cm^{-1}; ^1H NMR ($CDCl_3$) 6.25 (bs, NH), 5.72 (d, 7.6, H-1), 5.28 (apt, 9.4, H-3), 5.17 (apt, 9.4, H-4), 5.09 (dd, 9.4 and 7.6, H-2), 4.03 (d, 9.9, H-5), 2.12, 2.06, 2.03, 2.00 (4s, OCO**CH$_3$**), 3.19 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.26 (m, CH_2-3′ to CH_2-7′), 0.86 (t, 7.0, CH_3-8′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH$_3$), 165.7 (C-6), 91.4 (C-1), 73.0 (C-5), 72.0 (C-3), 70.3 (C-2), 69.0 (C-4), 20.7, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.3 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.6 (C-3′ to C-7′), 14.1 (C-8′).

(6) ESIMS *m/z* 568 (100, $[M + K]^+$), 552 (42, $[M + Na]^+$), 530 (24, $[M + H]^+$); IR (KBr) 3382, 2915, 2847, 1739, 1669, 1517, 1367, 1205, 1032, 913, 889 cm^{-1}; ^1H NMR ($CDCl_3$) 6.25 (bs, NH), 5.72 (d, 8.4, H-1), 5.28 (apt, 9.6, H-3), 5.17 (apt, 9.6, H-4), 5.09 (apt, 8.4, H-2), 4.03 (d, 9.0, H-5), 2.12, 2.06, 2.03, 2.00 (4s, OCO**CH$_3$**), 3.19 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-11′), 0.86 (t, 7.2, CH_3-12′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH$_3$), 165.7 (C-6), 91.4 (C-1), 73.0 (C-5), 72.0 (C-3), 70.3 (C-2), 69.0 (C-4), 20.7 (*2), 20.6 (*2) (OCO**C**H$_3$), 39.2 (C-1′), 29.3 (C-2′), 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 26.8, 22.7 (C-3′ to C-11′), 14.1 (C-12′).

(7) ESIMS *m/z* 596 (81, $[M + K]^+$), 580 (100, $[M + Na]^+$), 558 (36, $[M + H]^+$); IR (KBr) 3302, 2917, 2855, 1742, 1662, 1512, 1371, 1215, 1033, 912 cm^{-1}; ^1H

NMR ($CDCl_3$) 6.25 (bs, NH), 5.72 (d, 7.8, H-1), 5.28 (apt, 9.6, H-3), 5.17 (apt, 9.4, H-4), 5.09 (apt, 8.6, H-2), 4.03 (d, 9.2, H-5), 2.12, 2.07, 2.02, 2.01 (4s, OCO**CH_3**), 3.19 (m, CH_2-1′), 1.46 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-13′), 0.86 (t, 7.0, CH_3-14′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH_3), 165.8 (C-6), 91.4 (C-1), 73.0 (C-5), 72.0 (C-3), 70.3 (C-2), 69.0 (C-4), 20.7, 20.6 (*2), 20.5 (OCO**C**H_3), 39.2 (C-1′), 29.3 (C-2′), 31.9, 29.7, 29.6 (*2), 29.5 (*2), 29.4, 29.3, 29.2, 26.8, 22.6 (C-3′ to C-13′), 14.1 (C-14′).

(8) ESIMS *m/z* 624 (86, $[M + K]^+$), 608 (100, $[M + Na]^+$), 586 (12, $[M + H]^+$); IR (KBr) 3362, 2925, 2858, 1741, 1670, 1522, 1367, 1216, 1048, 918, 856 cm^{-1}; ^{1}H NMR ($CDCl_3$) 6.25 (bs, NH), 5.72 (d, 7.6, H-1), 5.28 (apt, 9.2, H-3), 5.17 (apt, 9.2, H-4), 5.09 (apt, 8.4, H-2), 4.03 (d, 9.4, H-5), 2.12, 2.05, 2.03, 2.00 (4s, OCO**CH_3**), 3.19 (m, CH_2-1′), 1.46 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-15′), 0.86 (t, 7.4, CH_3-16′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH_3), 165.5 (C-6), 91.4 (C-1), 73.0 (C-5), 72.0 (C-3), 70.3 (C-2), 69.0 (C-4), 20.7, 20.6 (*2), 20.4 (OCO**C**H_3), 39.2 (C-1′), 29.3 (C-2′), 31.9, 29.6 (*3), 29.5, 29.4 (*2), 29.3 (*2), 29.2, 29.1, 26.8, 22.7 (C-3′ to C-15′), 14.1 (C-16′).

(9) ESIMS *m/z* 652 (20, $[M + K]^+$), 636 (100, $[M + Na]^+$), 614 (59, $[M + H]^+$); IR (KBr) 3286, 2918, 2850, 1747, 1673, 1522, 1372, 1212, 1071, 915, 717 cm^{-1}; ^{1}H NMR ($CDCl_3$) 6.25 (bs, NH), 5.73 (d, 7.8, H-1), 5.28 (apt, 9.6, H-3), 5.17 (apt, 9.6, H-4), 5.09 (apt, 8.4, H-2), 4.03 (d, 9.0, H-5), 2.12, 2.06, 2.03, 2.01 (4s, OCO**CH_3**), 3.19 (m, CH_2-1′), 1.46 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-17′), 0.86 (t, 7.2, CH_3-18′); ^{13}C NMR ($CDCl_3$) 169.8, 169.6, 169.3, 168.7 (O**C**OCH_3), 165.7 (C-6), 91.4 (C-1), 73.0 (C-5), 72.0 (C-3), 70.3 (C-2), 69.0 (C-4), 20.7, 20.6, 20.5 (*2) (OCO**C**H_3), 39.2 (C-1′), 29.3 (C-2′), 31.9, 29.7 (*2), 29.6 (*4), 29.5 (*3), 29.3 (*2), 29.2, 26.8, 22.6 (C-3′ to C-17′), 14.1 (C-18′).

Amides (10) to (15)

After dissolution of amides **4** to **9** in 10 mL methanol, 5 equivalents of sodium carbonate are added and the reaction mixture is stirred overnight at room temperature. After filtration, the solvent is evaporated under reduce pressure and the obtained residue purified by chromatography on a silica gel column (mixture $CHCl_3$–MeOH), to afford the expected amides **10** to **15** as solids in 82–89% yield.

(10) ESIMS *m/z* 288 (32, $[M + K]^+$), 272 (41, $[M + Na]^+$), 250 (100, $[M + H]^+$); IR (KBr) 3345, 2958, 1653, 1558, 1373, 1052, 668 cm^{-1}; ^{1}H NMR (DMSO-d_6) *β*-anomer 7.84 (t, 5.4, NH), 4.31 (d, 8.4, H-1), 3.51 (d, 9.6, H-5), 3.30 (apt, 9.6, H-4), 3.14 (apt, 9.6, H-3), 2.94 (apt, 7.8, H-2), 3.04 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.22 (m, CH_2-3′), 0.82 (t, 7.8, CH_3-4′), α-anomer 7.82 (t, 6.0, NH), 4.95 (d, 3.6, H-1), 3.92 (d, 10.2, H-5), 3.44 (apt, 8.4, H-3), 3.24 (apt, 9.6, H-4), 3.17 (dd, 9.0 and 3.6, H-2), 3.04 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.22 (m, CH_2-3′), 0.81 (t, 7.8, CH_3-4′); ^{13}C NMR (DMSO-d_6) *β*-anomer 169.4 (C-6), 97.5 (C-1), 76.5 (C-3), 75.6 (C-5), 74.6 (C-2), 71.9 (C-4), 38.3 (C-1′), 31.4 (C-2′), 19.8 (C-3′),13.7 (C-4′), α-anomer 170.6 (C-6), 93.0 (C-1), 73.0 (C-3), 72.6 (C-4), 72.0 (C-2), 71.2 (C-5), 38.4 (C-1′), 31.4 (C-2′), 19.8 (C-3′),13.7 (C-4′).

(11) ESIMS *m/z* 344 (56, $[M + K]^+$), 328 (100, $[M + Na]^+$), 306 (42, $[M + H]^+$); IR (KBr) 3357, 2925, 2854, 1656, 1548, 1377, 1069, 668 cm^{-1}; ^{1}H NMR (DMSO-d_6) *β*-anomer 7.85 (t, 6.6, NH), 6.71 (d, 7.2, OH-1), 4.95 (d, 4.8, OH-4), 4.90 (m, OH-2 and OH-3), 4.28 (t, 7.6, H-1), 3.48 (d, 9.9, H-5), 3.29 (dd, 9.4 and 4.1, H-4), 3.09 (td, 9.4 and 5.3, H-3), 2.91 (td, 8.8 and 4.7, H-2), 2.99 and 3.01 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-7′), 0.83 (t, 7.2, CH_3-8′), α-anomer 7.84 (t, 6.0, NH), 6.42 (d, 4.2, OH-1), 4.90 (m, OH-4), 4.72 (d, 4.8, OH-3), 4.54 (d, 6.6, OH-2), 4.91 (m, H-1), 3.89 (d, 9.6, H-5), 3.40 (td, 8.8 and 4.7, H-3), 3.24 (td, 9.4 and 4.1, H-4), 3.12 (m, H-2), 2.99 and 3.01 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-7′), 0.83 (t, 7.2, CH_3-8′); ^{13}C NMR (DMSO-d_6) *β*-anomer 169.1 (C-6), 97.8 (C-1), 76.8 (C-3), 76.0 (C-5), 74.9 (C-2), 71.9 (C-4), 38.7 (C-1′), 29.4 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.5 (C-3′ to C-7′),14.4 (C-8′), α-anomer 170.1 (C-6), 93.2 (C-1), 73.2 (C-3), 72.7 (C-4), 72.3 (C-2), 71.6 (C-5), 38.8 (C-1′), 29.4 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.5 (C-3′ to C-7′),14.4 (C-8′).

(12) ESIMS *m/z* 400 (44, $[M + K]^+$), 384 (100, $[M + Na]^+$), 362 (16, $[M + H]^+$); IR (KBr) 3451, 2919, 2850, 1631, 1578, 1468, 1064, 719 cm^{-1}; ^{1}H NMR (DMSO-d_6) *β*-anomer 7.84 (t, 5.6, NH), 6.71 (d, 6.6, OH-1), 4.95 (d, 4.2, OH-4), 4.90 (m, OH-2 and OH-3), 4.28 (t, 7.0, H-1), 3.48 (d, 9.9, H-5), 3.29 (td, 9.6 and 4.2, H-4), 3.10 (td, 9.0 and 4.8, H-3), 2.91 (td, 9.0 and 4.2, H-2), 2.99 and 3.01 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-11′), 0.82 (t, 6.5, CH_3-12′), α-anomer 7.85 (t, 5.6, NH), 6.42 (d, 4.8, OH-1), 4.89 (d, 3.6, OH-4), 4.72 (d, 4.8, OH-3), 4.54 (d, 6.6, OH-2), 4.91 (t, 3.5, H-1), 3.89 (d, 9.4, H-5), 3.39 (td, 9.0 and 4.8, H-3), 3.24 (td, 9.6 and 3.6, H-4), 3.14 (m, H-2), 2.99 and 3.01 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-11′), 0.82 (t, 6.5, CH_3-12′); ^{13}C NMR (DMSO-d_6) *β*-anomer 169.1 (C-6), 97.8 (C-1), 76.8 (C-3), 76.0 (C-5), 74.9 (C-2), 71.9 (C-4), 38.7 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*2), 29.3, 29.2 (*2), 26.8, 26.7, 22.5 (C-3′ to C-11′),14.4 (C-12′), α-anomer 170.2 (C-6), 93.2 (C-1), 73.2 (C-3), 72.7 (C-4), 72.3 (C-2), 71.6 (C-5), 38.8 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*2), 29.3, 29.2 (*2), 26.8, 26.7, 22.5 (C-3′ to C-11′),14.4 (C-12′).

(13) ESIMS *m/z* 428 (39, $[M + K]^+$), 412 (100, $[M + Na]^+$), 390 (22, $[M + H]^+$); IR (KBr) 3450, 2918, 2849, 1635, 1577, 1467, 1064 cm^{-1}; ^{1}H NMR (DMSO-d_6)

β-anomer 7.84 (t, 5.9, NH), 6.71 (bs, OH-1), 4.95 (bs, OH-4), 4.90 (m, OH-2 and OH-3), 4.28 (d, 7.6, H-1), 3.48 (d, 9.4, H-5), 3.29 (m, H-4), 3.10 (t, 8.8, H-3), 2.91 (t, 8.8, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-13′), 0.82 (t, 7.4, CH_3-12′), α-anomer 7.85 (t, 5.3, NH), 6.42 (bs, OH-1), 4.89 (bs, OH-4), 4.72 (bs, OH-3), 4.54 (bs, OH-2), 4.91 (d, 2.9, H-1), 3.89 (d, 9.9, H-5), 3.39 (t, 9.4, H-3), 3.24 (t, 9.4, H-4), 3.14 (dd, 9.4 and 2.9, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-13′), 0.82 (t, 7.4, CH_3-14′); ^{13}C NMR (DMSO-d_6) β-anomer 169.1 (C-6), 97.8 (C-1), 76.8 (C-3), 76.0 (C-5), 74.9 (C-2), 71.9 (C-4), 38.7 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*3), 29.4 (*2), 29.3 (*2), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-13′),14.4 (C-14′), α-anomer 170.1 (C-6), 93.2 (C-1), 73.2 (C-3), 72.7 (C-4), 72.3 (C-2), 71.6 (C-5), 38.8 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*3), 29.4 (*2), 29.3 (*2), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-13′),14.4 (C-14′).

(14) ESIMS *m/z* 456 (22, $[M + K]^+$), 440 (100, $[M + Na]^+$), 418 (12, $[M + H]^+$); IR (KBr) 3395, 2917, 2849, 1654, 1560, 1468, 1065, 721 cm^{-1}; ^{1}H NMR (DMSO-d_6) β-anomer 7.84 (t, 5.9, NH), 6.72 (bs, OH-1), 4.95 (bs, OH-4), 4.90 (m, OH-2 and OH-3), 4.28 (d, 7.6, H-1), 3.49 (d, 9.4, H-5), 3.29 (t, 9.4, H-4), 3.10 (t, 8.8, H-3), 2.92 (t, 8.2, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-15′), 0.82 (t, 7.4, CH_3-16′), α-anomer 7.85 (t, 5.3, NH), 6.43 (bs, OH-1), 4.89 (bs, OH-4), 4.74 (bs, OH-3), 4.55 (bs, OH-2), 4.91 (d, 2.9, H-1), 3.89 (d, 9.9, H-5), 3.39 (t, 9.4, H-3), 3.24 (t, 9.4, H-4), 3.14 (dd, 9.4 and 2.9, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-15′), 0.82 (t, 7.4, CH_3-16′); ^{13}C NMR (DMSO-d_6) β-anomer 169.1 (C-6), 97.8 (C-1), 76.8 (C-3), 76.0 (C-5), 74.9 (C-2), 71.9 (C-4), 38.7 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*2), 29.4 (*3), 29.3 (*3), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-15′),14.3 (C-16′), α-anomer 170.1 (C-6), 93.0 (C-1), 73.0 (C-3), 72.6 (C-4), 72.1 (C-2), 71.8 (C-5), 38.8 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*2), 29.4 (*3), 29.3 (*3), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-15′),14.4 (C-15′).

(15) ESIMS *m/z* 484 (79, $[M + K]^+$), 468 (100, $[M + Na]^+$), 446 (31, $[M + H]^+$); IR (KBr) 3412, 2918, 2849, 1639, 1560, 1468, 1064, 720 cm^{-1}; ^{1}H NMR (DMSO-d_6) β-anomer 7.84 (t, 5.9, NH), 6.72 (bs, OH-1), 4.95 (bs, OH-4), 4.90 (m, OH-2 and OH-3), 4.28 (bt, 6.4, H-1), 3.49 (d, 9.4, H-5), 3.29 (m, H-4), 3.10 (bt, 8.8, H-3), 2.92 (bt, 7.6, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-17′), 0.82 (t, 7.4, CH_3-18′), α-anomer 7.84 (t, 5.6, NH), 6.42 (bs, OH-1), 4.89 (bs, OH-4), 4.72 (bs, OH-3), 4.50 (bs, OH-2), 4.92 (m, H-1), 3.89 (d, 9.9, H-5), 3.40 (bt, 8.8, H-3), 3.24 (bt, 9.9, H-4), 3.14 (m, H-2), 2.99 and 3.05 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-17′), 0.82 (t, 7.4, CH_3-18′); ^{13}C NMR (DMSO-d_6) β-anomer 169.1 (C-6), 97.8 (C-1), 76.8 (C-3), 76.0 (C-5), 74.9 (C-2), 71.9 (C-4), 38.7 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*3), 29.4 (*4), 29.3 (*3), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-17′),14.4 (C-18′), α-anomer 170.1 (C-6), 93.2 (C-1), 73.2 (C-3), 72.7 (C-4), 72.3 (C-2), 71.6 (C-5), 38.7 (C-1′), 29.5 (C-2′), 31.7, 29.5 (*3), 29.4 (*4), 29.3 (*3), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-17′),14.4 (C-18′).

Anhydride (16)

D-Galacturonic acid (2.999 g, 15.46 mmol), was suspended in acetic anhydride (45 mL) and stirred at 0 °C. Iodine (210.3 mg, 0.828 mmol) was added slowly and the red solution was stirred for 2 h at 0 °C and for further 3 h at room temperature. Acetic anhydride was mostly removed in vacuo and the remaining mixture taken up in dichloromethane (50 mL). The organic layer was then washed twice with a 1 M $Na_2S_2O_3$ aqueous solution (50 mL) and evaporated to afford yellow oil. Anhydride **16** was re-crystallized from a mixture of dichloromethane—40/65 petroleum ether to afford 5.871 g (14.53 mmol, 94%) of the α-anomer as single product.

(16) ESIMS *m/z* 443 (100, $[M + K]^+$), 427 (68, $[M + Na]^+$), 405 (21, $[M + H]^+$); IR (KBr) 2991, 1844, 1762, 1434, 1374, 1207, 1125, 1075, 1014, 941, 887, 831, 783, 710, 674 cm^{-1}; ^{1}H NMR ($CDCl_3$) 6.48 (d, 3.0, H-1), 5.84 (bs, H-4), 5.38 (dd, 11.1 and 2.9, H-3), 5.35 (dd, 11.1 and 2.9, H-2), 4.76 (bs, H-5), 2.08 (s, COOCO**C**$\mathbf{H_3}$), 2.14, 2.11, 2.00, 1.99 (4s, OCO**C**$\mathbf{H_3}$); ^{13}C NMR ($CDCl_3$) 177.3 (COO**C**OCH_3), 170.1, 169.8 (*2), 168.6 (O**C**OCH_3), 169.7 (C-6), 89.4 (C-1), 70.4 (C-5), 68.4 (C-4), 67.0 (C-3), 65.9 (C-2), 20.7 (COOCO**C**H_3), 20.8, 20.6, 20.5, 20.4 (OCO**C**H_3).

Acetylated Acid (30)

D-Galacturonic acid (5.006 g, 25.80 mmol), was added to a stirred solution of acetic anhydride (25 mL) and concentrated sulphuric acid (3 drops). The temperature was allowed to reach 60 °C and extra galacturonic acid (4.985 g, 25.70 mmol) was added. The reaction mixture was maintained at 60 °C for 1 h and then cooled to room temperature. Water (75 mL) was then added to the stirred solution. The solid obtained was filtered and recrystallized from toluene to afford **30** (12.86 g, 35.52 mmol, 69%) as a white solid.

(30) ESIMS *m/z* 401 (44, $[M + K]^+$), 385 (100, $[M + Na]^+$), 363 (31, $[M + H]^+$); IR (KBr) 3578, 3515, 2995, 1717, 1349, 1222, 1087, 1024, 902 cm^{-1}; ^{1}H NMR ($CDCl_3$) 5.86 (bs, OH), 6.48 (d, 2.9, H-1), 5.91 (bs, H-4), 5.41 (dd, 10.8 and 2.8, H-3), 5.31 (dd, 10.7 and 2.8, H-2), 4.70 (bs, H-5), 2.13, 2.03, 2.01, 1.99 (4s, OCO**C**$\mathbf{H_3}$); ^{13}C NMR ($CDCl_3$) 171.2, 169.8, 169.2, 168.8 (O**C**OCH_3), 169.6 (C-6), 89.3 (C-1), 70.6 (C-5), 68.0 (C-4), 67.1 (C-3), 66.1 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H_3).

Acetylated Amides (17) to (22)

Synthetic way 1 (Scheme 1a): After dissolution of anhydride **16** (0.5 g, 0.123 mmol) in 5 mL dry dichloromethane under a nitrogen atmosphere, 1.2 equivalent of the primary amine is added and the reaction mixture is stirred overnight. The solvent is then evaporated under reduce pressure and the obtained residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **17** to **22** as white solids in 40–44% yield.

Synthetic way 2 (Scheme 1b): After dissolution of acid **30** (0.495 g, 0.137 mmol) in 5 mL dry acetonitrile under a nitrogen atmosphere, 0.338 g DCC (0.164 mmol, 1.2 eq.) is added. After 10 min, 2 equivalents of the primary amine are added and the reaction mixture is allowed stir overnight at room temperature. After filtration of the precipitated dicyclohexylurea, the solvent is evaporated *in vacuo* and the residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **17** to **22** as white solids in 62–65% yield.

Synthetic way 3 (Scheme 1c) 0.296 g of acid **30** (0.0818 mmol) is dissolved in 5 mL dry dichloromethane at 0 °C under a nitrogen atmosphere. 400 µL dry DMF and 150 µL of oxalyl chloride are then added and the reaction mixture is stirred 30 min at 0 °C and for a further 2 h at room temperature. Then 1.2 equivalent of the primary amine is added and the reaction mixture is stirred overnight at room temperature. The solvent is evaporated under reduce pressure and the obtained residue purified by flash chromatography on a silica gel column (mixture Hexane–AcOEt), to afford the expected amides **17** to **22** as white solids in 81–89% yield.

(17) ESIMS *m/z* 456 (100, $[M + K]^+$), 440 (88, $[M + Na]^+$), 418 (41, $[M + H]^+$); IR (KBr) 3315, 2971, 2862, 1748, 1663, 1542, 1432, 1355, 1214, 1036, 899 cm^{-1}; ^1H NMR ($CDCl_3$) 6.42 (t, 5.4, NH), 6.43 (d, 3.2, H-1), 5.88 (bs, H-4), 5.40 (dd, 10.8 and 3.6, H-3), 5.29 (dd, 10.8 and 3.2, H-2), 4.53 (bs, H-5), 2.15, 2.05, 2.01, 1.99 (4s, OCO**CH$_3$**), 3.19 (m, CH_2-1′), 1.46 (quint, 7.4, CH_2-2′), 1.33 (m, CH_2-3′), 0.89 (t, 7.6, CH_3-4′); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.5 (C-6), 89.2 (C-1), 71.6 (C-5), 68.4 (C-4), 67.0 (C-3), 66.1 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 38.9 (C-1′), 31.2 (C-2′), 20.1 (C-3′), 13.9 (C-4′).

(18) ESIMS *m/z* 512 (91, $[M + K]^+$), 496 (100, $[M + Na]^+$), 474 (26, $[M + H]^+$); IR (KBr) 3389, 2928, 2856, 1754, 1678, 1535, 1438, 1372, 1220, 1074, 1014, 942 cm^{-1}; ^1H NMR ($CDCl_3$) 6.41 (t, 6.0, NH), 6.43 (d, 3.6, H-1), 5.88 (bs, H-4), 5.40 (dd, 10.8 and 3.6, H-3), 5.29 (dd, 10.8 and 3.6, H-2), 4.53 (bs, H-5), 2.15, 2.05, 2.02, 1.98 (4s, OCO**CH$_3$**), 3.33 and 3.13 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.26 (m, CH_2-3′ to CH_2-7′), 0.86 (t, 7.2, CH_3-8′); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.4 (C-6), 89.2 (C-1), 71.7 (C-5), 68.4 (C-4), 67.0 (C-3), 66.2 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.5 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.6 (C-3′ to C-7′), 14.0 (C-8′).

(19) ESIMS *m/z* 568 (100, $[M + K]^+$), 552 (71, $[M + Na]^+$), 530 (36, $[M + H]^+$); IR (KBr) 3348, 2919, 2850, 1744, 1672, 1533, 1433, 1369, 1207, 1069, 940 cm^{-1}; ^1H NMR ($CDCl_3$) 6.41 (t, 6.0, NH), 6.43 (d, 3.6, H-1), 5.88 (bs, H-4), 5.40 (dd, 10.8 and 3.6, H-3), 5.29 (dd, 10.8 and 3.6, H-2), 4.53 (bs, H-5), 2.15, 2.05, 2.02, 1.98 (4s, OCO**CH$_3$**), 3.34 and 3.12 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-11′), 0.86 (t, 6.6, CH_3-12′); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.4 (C-6), 89.2 (C-1), 71.7 (C-5), 68.4 (C-4), 67.0 (C-3), 66.2 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.6 (C-2′), 31.9, 29.6 (*2), 29.5, 29.4, 29.3, 29.2, 26.8, 22.7 (C-3′ to C-11′), 14.1 (C-12′).

(20) ESIMS *m/z* 596 (32, $[M + K]^+$), 580 (100, $[M + Na]^+$), 558 (17, $[M + H]^+$); IR (KBr) 3361, 2923, 2853, 1750, 1682, 1539, 1436, 1372, 1218, 1073, 942 cm^{-1}; ^1H NMR ($CDCl_3$) 6.41 (t, 5.4, NH), 6.43 (d, 4.2, H-1), 5.88 (bs, H-4), 5.40 (dd, 11.4 and 3.0, H-3), 5.30 (dd, 10.8 and 3.6, H-2), 4.53 (bs, H-5), 2.15, 2.05, 2.02, 1.99 (4s, OCO**CH$_3$**), 3.33 and 3.13 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.24 (m, CH_2-3′ to CH_2-13′), 0.86 (t, 6.6, CH_3-14′); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.4 (C-6), 89.2 (C-1), 71.7 (C-5), 68.4 (C-4), 67.0 (C-3), 66.2 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.6 (C-2′), 31.9, 29.6 (*3), 29.5 (*3), 29.3, 29.2, 26.8, 22.6 (C-3′ to C-13′), 14.1 (C-14′).

(21) ESIMS *m/z* 624 (69, $[M + K]^+$), 608 (100, $[M + Na]^+$), 586 (41, $[M + H]^+$); IR (KBr) 3364, 2923, 2853, 1753, 1675, 1539, 1436, 1372, 1222, 1074, 942 cm^{-1}; ^1H NMR ($CDCl_3$) 6.40 (t, 5.4, NH), 6.42 (d, 3.6, H-1), 5.87 (bs, H-4), 5.39 (dd, 10.8 and 3.6, H-3), 5.29 (dd, 10.8 and 3.6, H-2), 4.52 (bs, H-5), 2.14, 2.04, 2.01, 1.98 (4s, OCO**CH$_3$**), 3.32 and 3.12 (m, CH_2-1′), 1.46 (m, CH_2-2′), 1.23 (m, CH_2-3′ to CH_2-15′), 0.85 (t, 7.2, CH_3-16′); ^{13}C NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.4 (C-6), 89.2 (C-1), 71.7 (C-5), 68.4 (C-4), 67.0 (C-3), 66.2 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.5 (C-2′), 31.9, 29.6 (*4), 29.5 (*2), 29.4 (*2), 29.3, 29.2, 26.8, 22.6 (C-3′ to C-15′), 14.1 (C-16′).

(22) ESIMS *m/z* 652 (27, $[M + K]^+$), 636 (100, $[M + Na]^+$), 614 (14, $[M + H]^+$); IR (KBr) 3360, 2919, 2850, 1754, 1670, 1543, 1469, 1374, 1224, 1073, 940 cm^{-1}; ^1H NMR ($CDCl_3$) 6.40 (t, 6.0, NH), 6.43 (d, 4.2, H-1), 5.88 (bs, H-4), 5.40 (dd, 10.8 and 3.0, H-3), 5.30 (dd, 10.8 and 3.6, H-2), 4.53 (bs, H-5), 2.15, 2.05, 2.02, 1.98 (4s, OCO**CH$_3$**), 3.32 and 3.12 (m, CH_2-1′), 1.47 (m, CH_2-2′), 1.23 (m, CH_2-3′ to CH_2-17′), 0.86 (t, 7.2, CH_3-18′); ^{13}C

NMR ($CDCl_3$) 170.0, 169.8, 169.2, 168.9 (O**C**OCH$_3$), 165.4 (C-6), 89.2 (C-1), 71.7 (C-5), 68.4 (C-4), 67.0 (C-3), 66.2 (C-2), 20.8, 20.6, 20.5, 20.4 (OCO**C**H$_3$), 39.2 (C-1′), 29.5 (C-2′), 31.9, 29.7 (*4), 29.6 (*3), 29.5 (*3), 29.3, 29.2, 26.8, 22.6 (C-3′ to C-17′), 14.1 (C-18′).

Amides (23) to (28)

After dissolution of amides **17** to **22** in 10 mL methanol, 5 equivalents of sodium carbonate are added and the reaction mixture is stirred overnight at room temperature. After filtration, the solvent is evaporated under reduce pressure and the obtained residue purified by chromatography on a silica gel column (mixture $CHCl_3$–MeOH), to afford the expected amides **23** to **28** as solids in 82–89% yield.

(23) ESIMS *m/z* 288 (15, $[M + K]^+$), 272 (100, $[M + Na]^+$), 250 (36, $[M + H]^+$); IR (KBr) 3342, 2958, 2932, 1655, 1551, 1439, 1148, 1077 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.20 (t, 6.0, NH), 4.31 (d, 6.6, H-1), 3.88 (bs, H-4), 3.82 (bs, H-5), 3.31 (dd, 9.0 and 3.0, H-3), 3.26 (t, 7.2, H-2), 3.06 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.22 (m, CH_2-3′), 0.81 (t, 6.6, CH_3-4′), α-anomer 7.39 (t, 6.0, NH), 5.04 (d, 3.6, H-1), 4.14 (bs, H-5), 3.94 (bs, H-4), 3.58 (dd, 9.6 and 3.0, H-3), 3.54 (dd, 9.6 and 3.6, H-2), 3.06 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.22 (m, CH_2-3′), 0.81 (t, 6.6, CH_3-4′); ^{13}C NMR (DMSO-d_6) β-anomer 169.5 (C-6), 97.5 (C-1), 75.2 (C-5), 73.4 (C-3), 71.9 (C-2), 70.2 (C-4), 38.2 (C-1′), 31.6 (C-2′), 19.8 (C-3′),13.8 (C-4′), α-anomer 168.8 (C-6), 93.2 (C-1), 71.3 (C-5), 70.4 (C-4), 69.5 (C-3), 68.6 (C-2), 38.2 (C-1′), 31.6 (C-2′), 19.8 (C-3′),13.8 (C-4′).

(24) ESIMS *m/z* 344 (6, $[M + K]^+$), 328 (48, $[M + Na]^+$), 306 (100, $[M + H]^+$); IR (KBr) 3378, 2919, 2851, 1636, 1544, 1475, 1376, 1151, 1084, 935 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.13 (t, 6.0, NH), 6.78 (d, 6.6, OH-1), 4.76 (bs, OH-2), 4.67 (bs, OH-3), 4.51 (bs, OH-4), 4.29 (t, 7.2, H-1), 3.85 (bs, H-4), 3.81 (bs, H-5), 3.30 (m, H-3), 3.24 (m, H-2), 2.97 and 3.08 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-7′), 0.82 (t, 6.7, CH_3-8′), α-anomer 7.34 (t, 5.9, NH), 6.36 (d, 4.2, OH-1), 4.52 (bs, OH-3), 4.37 (bs, OH-2), 3.92 (bs, OH-4), 5.02 (bs, H-1), 4.10 (bs, H-5), 3.92 (bs, H-4), 3.56 (m, H-3), 3.53 (m, H-2), 2.97 and 3.08 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-7′), 0.82 (t, 6.7, CH_3-8′); ^{13}C NMR (DMSO-d_6) β-anomer 167.9 (C-6), 97.7 (C-1), 75.3 (C-5), 73.5 (C-3), 72.2 (C-2), 70.0 (C-4), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.5 (C-3′ to C-7′), 14.4 (C-8′), α-anomer 169.2 (C-6), 93.4 (C-1), 71.5 (C-5), 70.2 (C-4), 69.6 (C-3), 68.7 (C-2), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.2, 29.1, 26.8, 22.5 (C-3′ to C-7′), 14.4 (C-8′).

(25) ESIMS *m/z* 400 (91, $[M + K]^+$), 384 (100, $[M + Na]^+$), 362 (26, $[M + H]^+$); IR (KBr) 3376, 2918, 2848, 1633, 1547, 1467, 1152, 1081, 1035, 935 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.13 (t, 6.0, NH), 6.78 (bs, OH-1), 4.76 (bs, OH-2), 4.68 (bs, OH-3), 4.52 (bs, OH-4), 4.29 (m, H-1), 3.85 (bs, H-4), 3.81 (bs, H-5), 3.30 (m, H-3), 3.24 (m, H-2), 2.96 and 3.07 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-11′), 0.82 (t, 6.7, CH_3-12′), α-anomer 7.34 (t, 5.9, NH), 6.36 (bs, OH-1), 4.53 (bs, OH-3), 4.49 (bs, OH-4), 4.37 (bs, OH-2), 5.03 (bs, H-1), 4.10 (bs, H-5), 3.92 (bs, H-4), 3.56 (m, H-3), 3.52 (m, H-2), 2.96 and 3.07 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-11′), 0.82 (t, 6.7, CH_3-12′); ^{13}C NMR (DMSO-d_6) β-anomer 167.9 (C-6), 97.7 (C-1), 75.3 (C-5), 73.5 (C-3), 72.2 (C-2), 70.0 (C-4), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.5 (*2), 29.4 (*2), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-11′), 14.4 (C-12′), α-anomer 169.2 (C-6), 93.4 (C-1), 71.5 (C-5), 70.2 (C-4), 69.6 (C-3), 68.7 (C-2), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.5 (*2), 29.4 (*2), 29.2, 29.1, 26.8, 22.5 (C-3′ to C-11′), 14.4 (C-12′).

(26) ESIMS *m/z* 428 (16, $[M + K]^+$), 412 (100, $[M + Na]^+$), 390 (35, $[M + H]^+$); IR (KBr) 3374, 2918, 2848, 1632, 1546, 1468, 1152, 1082 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.13 (t, 6.0, NH), 6.78 (bs, OH-1), 4.76 (bs, OH-2), 4.68 (bs, OH-3), 4.51 (bs, OH-4), 4.30 (m, H-1), 3.85 (bs, H-4), 3.81 (bs, H-5), 3.30 (m, H-3), 3.24 (m, H-2), 2.96 and 3.07 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-13′), 0.82 (t, 7.2, CH_3-14′), α-anomer 7.34 (t, 6.0, NH), 6.36 (bs, OH-1), 4.53 (bs, OH-3), 4.49 (bs, OH-4), 4.37 (bs, OH-2), 5.02 (bs, H-1), 4.10 (bs, H-5), 3.92 (bs, H-4), 3.56 (m, H-3), 3.52 (m, H-2), 2.96 and 3.07 (m, CH_2-1′), 1.35 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-13′), 0.82 (t, 7.2, CH_3-14′); ^{13}C NMR (DMSO-d_6) β-anomer 167.9 (C-6), 97.7 (C-1), 75.3 (C-5), 73.5 (C-3), 72.2 (C-2), 70.0 (C-4), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.5 (*3), 29.4 (*2), 29.2, 29.1 (*2), 26.8, 22.5 (C-3′ to C-13′), 14.4 (C-14′), α-anomer 169.2 (C-6), 93.4 (C-1), 71.5 (C-5), 70.2 (C-4), 69.6 (C-3), 68.7 (C-2), 38.6 (C-1′), 29.7 (C-2′), 31.7, 29.5 (*3), 29.4 (*2), 29.2, 29.1 (*2), 26.8, 22.5 (C-3′ to C-13′), 14.4 (C-14′).

(27) ESIMS *m/z* 456 (98, $[M + K]^+$), 440 (100, $[M + Na]^+$), 418 (49, $[M + H]^+$); IR (KBr) 3377, 2917, 2849, 1634, 1545, 1470, 1152, 1082 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.13 (t, 6.0, NH), 6.78 (bs, OH-1), 4.76 (bs, OH-2), 4.68 (bs, OH-3), 4.51 (bs, OH-4), 4.30 (d, 7.1, H-1), 3.87 (bs, H-4), 3.82 (bs, H-5), 3.31 (dd, 9.0 and 2.4, H-3), 3.26 (t, 9.6, H-2), 2.99 and 3.09 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-15′), 0.81 (t, 6.6, CH_3-16′), α-anomer 7.37 (t, 5.8, NH), 6.36 (bs, OH-1), 4.53 (d, 3.6, OH-3), 4.41 (bs, OH-4), 4.37 (bs, OH-2), 5.04 (bd, 3.6, H-1), 4.14 (bs, H-5), 3.94 (bs, H-4), 3.58 (m, H-3), 3.53 (m, H-2), 2.99 and 3.09 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-15′), 0.81 (t, 7.2, CH_3-16′); ^{13}C NMR (DMSO-d_6) β-anomer 167.8 (C-6), 97.7 (C-1), 75.4 (C-5), 73.4 (C-3), 72.2 (C-2), 70.2 (C-4), 38.7 (C-1′), 29.7 (C-2′), 31.7, 29.4 (*3), 29.3 (*2), 29.2 (*3), 29.1 (*2), 26.8, 22.4 (C-3′ to C-15′), 14.3 (C-16′), α-anomer 169.2 (C-6),

93.3 (C-1), 71.5 (C-5), 70.5 (C-4), 69.8 (C-3), 68.9 (C-2), 38.7 (C-1′), 29.7 (C-2′), 31.7, 29.4 (*3), 29.3 (*2), 29.2 (*3), 29.1 (*2), 26.8, 22.4 (C-3′ to C-15′), 14.3 (C-16′).

(28) ESIMS *m/z* 484 (11, $[M + K]^+$), 468 (100, $[M + Na]^+$), 446 (26, $[M + H]^+$); IR (KBr) 3377, 2917, 2848, 1631, 1547, 1470, 1152, 1082 cm^{-1}; ^1H NMR (DMSO-d_6) β-anomer 7.08 (t, 6.0, NH), 6.75 (d, 4.6, OH-1), 4.72 (d, 4.2, OH-2), 4.61 (d, 5.4, OH-3), 4.47 (d, 4.2, OH-4), 4.30 (m, H-1), 3.88 (bs, H-4), 3.79 (bs, H-5), 3.30 (m, H-3), 3.27 (m, H-2), 2.99 and 3.10 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-17′), 0.81 (t, 6.6, CH_3-18′), α-anomer 7.25 (t, 6.0, NH), 6.33 (d, 4.8, OH-1), 4.45 (bs, OH-4), 4.44 (bs, OH-3), 4.30 (bs, OH-2), 5.04 (t, 4.2, H-1), 4.14 (bs, H-5), 3.95 (bs, H-4), 3.58 (m, H-3), 3.54 (m, H-2), 2.99 and 3.10 (m, CH_2-1′), 1.36 (m, CH_2-2′), 1.20 (m, CH_2-3′ to CH_2-17′), 0.82 (t, 6.6, CH_3-18′); ^{13}C NMR (DMSO-d_6) β-anomer 167.8 (C-6), 97.7 (C-1), 75.3 (C-5), 73.5 (C-3), 72.2 (C-2), 70.0 (C-4), 38.6 (C-1′), 29.7 (C-2′), 31.8, 29.5 (*4), 29.3 (*3), 29.2 (*3), 29.1 (*2), 26.8, 22.6 (C-3′ to C-17′), 14.4 (C-18′), α-anomer 169.2 (C-6), 93.4 (C-1), 71.5 (C-5), 70.2 (C-4), 69.6 (C-3), 68.7 (C-2), 38.6 (C-1′), 29.7 (C-2′), 31.8, 29.5 (*4), 29.3 (*3), 29.2 (*3), 29.1 (*2), 26.8, 22.6 (C-3′ to C-17′), 14.4 (C-18′).

Physicochemical Properties

Preparation of Uronic Amide-Based Surfactant Solutions

Uronic amide-based surfactants were first dispersed in milli-Q water (Millipore Corp., USA) at room temperature under sonication for 30 min. The dispersed system was then placed in water bath at 50 °C for 2 h and was continuously stirred using a magnetic agitator. The true solution was then obtained by filtering the sample through a nylon filter Acrodisc® 0.45 µm. Different concentrations for surface tension measurements were prepared by diluting different mother solutions between 0.1 and 4 g/L. The accurate concentrations were assessed by spectrophotometry quantitative analysis using 3,5-dinitrosalicylic reagent [15].

Equilibrium Surface Tension Measurements

The surface tension (γ) of surfactant solutions (10 mL) was measured at room temperature (±20 °C) by a Wilhelmy plate tensiometer (Tensimat N3, Prolabo) with platinum lamella (19.59 × 19.51 × 0.5 mm). The γ of different concentrations of uronic amide-based surfactants was continuously recorded for 15 min. The equilibrium surface tension (γ_e) was taken as the value of γ at 15 min corresponding to the time at which other methods as drop volume tensiometer in Quasi-Static Mode gives similar results [16]. Two measurements were carried out for each solution.

Determination of Various Fundamental Surfactant Parameters

The critical micellar concentration (CMC) was determined at the intersection point of the surface tension versus concentration straight-line plots in the premicellar and the post micellar regions.

The maximum surface excess (Γ_{max}) was calculated with the Gibbs adsorption equation for nonionic surfactants:

$$\Gamma_{max} = \frac{1}{RT}\left(\frac{d\gamma}{d\ln C_o}\right)$$

where C_o is the bulk solution concentration; $R = 8.314$ J K^{-1} m^{-2}, the gas constant; and T, the temperature in Kelvin.

The minimum molecular area (A_{min}) expressed in $Å^2$ per molecule was given as

$$A_{cmc} = \left(\frac{1}{\Gamma_{max} N}\right)$$

where N is the Avogadro's number.

Results and Discussion

Chemical Syntheses of *N*-Alkylamides Derived from Glucuronic and Galacturonic Acids

Recent advances in carbohydrate chemistry are essentially connected to the synthesis of targets of high added value and are based on the development of subtle strategies to selectively access these molecules [17].

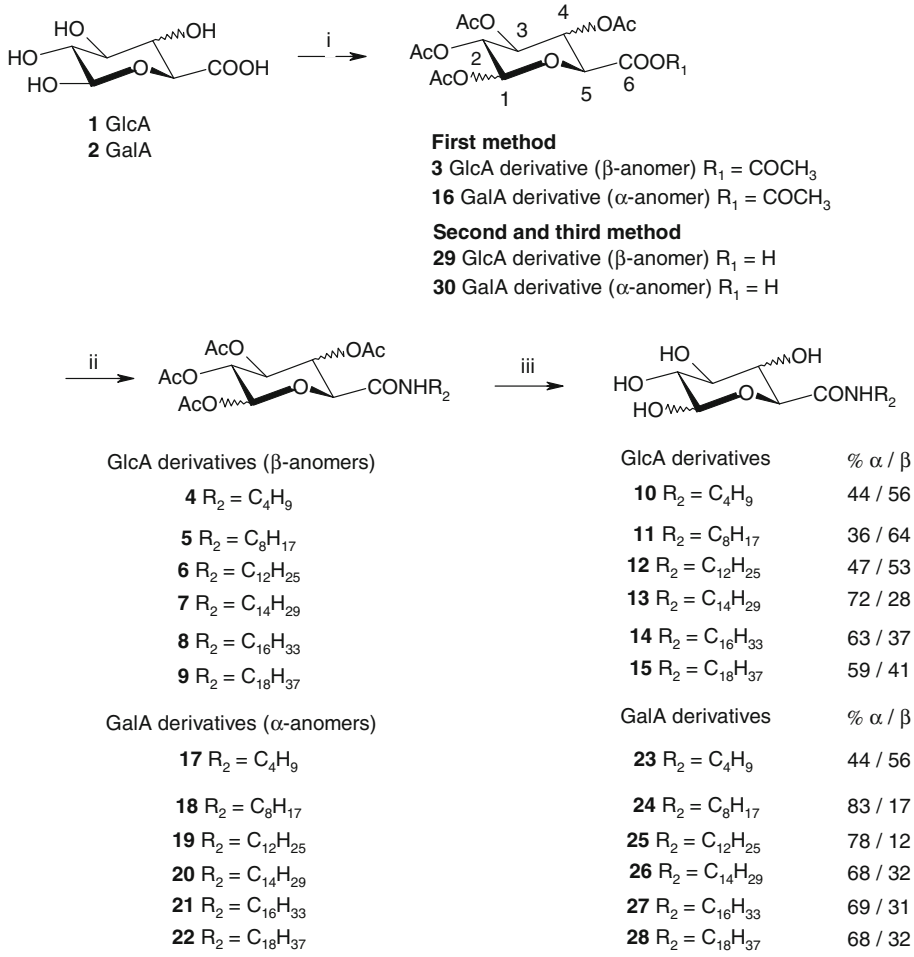
Selectivity is indeed a crucial objective in organic synthesis and is classically achieved by applying protection, activation and deprotection steps.

To synthesize various amide derivatives from glucuronic acid **1** or galacturonic acid **2**, we took advantage of three different ways to increase the reactivity of the carboxyl-group: use of an anhydride as synthetic intermediate, addition of carbodiimide in the medium, use of an acid chloride as activated compound.

Our three approaches are depicted in Scheme 1.

Treatment of commercially available D-glucuronic acid **1** or D-galacturonic acid **2** with acetic anhydride in the presence of a catalytic amount of iodine led, as expected [18, 19], to the corresponding anhydrides **3** or **16** (Scheme 1a, First method).

In the case of the glucuronic derivative **3**, 1D and 2D RMN experiments ($^1H/^1H$ COSY, HSQC, HMBC) showed



Scheme 1 Synthesis of various *N*-alkylamides from D-glucuronic and D-galacturonic acids. Reagents: **a First method**: (i) Ac_2O, I_2, 0°C; (ii) RNH_2, dry CH_2Cl_2; (iii) Na_2CO_3, MeOH; **b Second method**: (i) Ac_2O, H_2SO_4, 60°C then H_2O; (ii) DCC, dry CH_3CN then RNH_2; (iii) Na_2CO_3, MeOH; **c Third method**: (i) Ac_2O, H_2SO_4, 60°C then H_2O; (ii) $(COCl)_2$, DMF, dry CH_2Cl_2 then RNH_2 (iii) Na_2CO_3, MeOH

that the only isomer, isolated in 93% yield after crystallization, is the β-D-pyranose one. Irradiation of H-1 (δ 5.79) in a 1D RMN NOE experiment did indeed show a clear enhancement of H-3 (δ 5.28) and H-5 (δ 4.31), demonstrating that those protons were all located on the same face of the molecule. Interestingly, in the case of galacturonic acid, the isolated product **16** was the α-D-pyranose anomer. In this compound, H-1 is in equatorial position since it appears as a doublet at δ 6.48 with a coupling constant ($J_{1,2} = 3.0$ Hz), typical of an equatorial-axial relationship between H-1 and H-2. Nucleophilic attack of various linear alkylamines on the activated anhydrides **3** and **16** takes place at the carbonyl group nearest the pyranose ring giving protected amides **4** to **9** in 39-48% yield and **17** to **22** in 40-44% yield after flash chromatography through silica gel. Once again, RMN experiments on those molecules demonstrate that only one isomer is isolated. The acetate protecting groups were then removed under basic conditions by reaction with sodium carbonate in methanol to afford a mixture of α and β glycopyranosides **10** to **15** in 82-89% yield and **23** to **28** in 82-89% yield. The relative configuration at C-1 (α or β anomer) in the final amides was fully established by 2D RMN NOESY experiments. Most noteworthy were the correlations observed between OH-1, H-3 and H-5 in the α anomers and between H-1, H-3 and H-5 in the β anomers. The anomeric ratios (α/β) were established by 1D ^{1}H-RMN. As expected, in ^{1}H-RMN, H-1 in α anomers resonate downfield compared to the β-anomers. Moreover, in ^{13}C-RMN, C-1 atom of the α-anomers is always more shielded compared to the β-anomers in D-pyranoses in $^4C_1$ conformation [20].

Next, we compared this synthetic route with an alternative one based on the addition of dicyclohexlcarbodiimide in the medium (Scheme 1b, Second method). This method is well known to increase the reactivity of carboxyl-groups toward amidation [21] and was already used for coupling polyglucuronic acid with a range of amines [22].

Acetylation carried out on acids **1** or **2** according to the method of Baddeley et al. [23] selectively furnished the protected acids **29** and **30** as single anomers, as proven by the observed coupling constants, in 66 and 69% yield, respectively. The acetylated acids furnished the expected protected amides **4** to **9** in 65–69% yield and **17** to **22** in

Table 1 Comparison of the global yields of the three synthetic methods used to form *N*-alkylamides from D-glucuronic acid or D-galacturonic acid

Starting material	Amide synthesized	Global yield according to the first method (Scheme 1a) (%)	Global yield according to the second method (Scheme 1b) (%)	Global yield according to the third method (Scheme 1c) (%)
1	**10**	31	35	48
	11	32	40	52
	12	33	38	51
	13	32	37	50
	14	36	40	52
	15	42	42	58
2	**23**	34	36	49
	24	32	38	52
	25	34	37	50
	26	33	37	46
	27	35	37	48
	28	37	39	50

62–66% yield after reaction with the corresponding amine in the presence of DCC in acetonitrile. The isolated compounds exhibited spectral data (^{1}H, ^{13}C NMR, IR and MS) identical in all respects with amides **5** to **9** and **17** to **22** obtained by the first method.

In the last method tested to activate the carboxyl-group (Scheme 1c, Third method), compounds **29** and **30** were treated with oxalyl chloride and DMF in dry dichloromethane [24]. This led to the formation of an acyl chloride which was not isolated. Addition of the primary linear alkylamines to this intermediate gave the corresponding amide **4** to **9** in 88–93% yield and **17** to **22** in 81–89% yield as a single isomers. Once again, the presence of the β or α anomer was fully proved by the observation of the coupling constants.

Comparison of the three ways (Table 1) showed that the last synthetic route has a global yield significantly higher that those employing DCC or using an anhydride as activated intermediate.

After having completed the synthesis of the amides, we next explored their surface-active properties.

Surface-Active Properties of Uronic Amide-Base Surfactants

Various fundamental surfactant parameters of the synthesized amides were then determined from the equilibrium surface tension versus concentration data at 20 °C. Figure 2 shows a few representative examples of γ versus concentration plots of some studied surfactants.

Table 2 lists various fundamental surfactant parameters including CMC, γ_{cmc}, Γ_{max} and A_{min} of homologous series of glucuronic and galacturonic *N*-alkylamides having 8 to 18 carbon atoms (**11** to **15** and **24** to **28**).

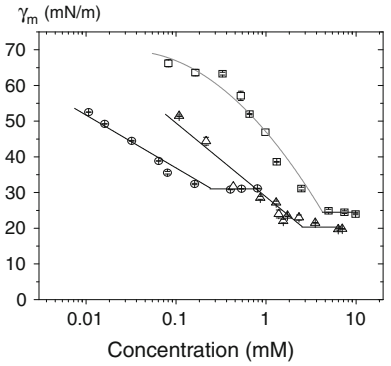


Fig. 2 Examples of equilibrium surface tension versus concentration curve: C8Glc-N **11** (*open squares*), C12Gal-N **25** (*open triangles*), octylphenol 9-10 ethylene oxide condensate (*open circles*)

The CMC values, which were between 0.02 mM and 5 mM, decrease with increases in the hydrocarbon chain length in both homologous series, while γ_{cmc} values vary in the opposite way and rise from 20.5 to 47.0 mN/m. No change of surface tension was detected with glucuronic *N*-alkylamides **14** and **15** solutions because of their very low solubility in the aqueous phase. However, the corresponding galacturonic *N*-alkylamides analogues **27** and **28** decrease the surface tension slightly.

In general, the two homologous series of uronic amide-based surfactants exhibit γ_{cmc} and CMC values in the same order of magnitude, even if a slight trend of higher surface activities can be seen for galacturonic *N*-alkylamides in comparison with the corresponding glucuronic *N*-alkylamides. For instance, γ_{cmc} were determined to be 24.4 mN/m and 20.5 mN/m for **11** (C8Glc-N) and **24** (C8Gal-N), respectively. Furthermore, the CMC values (3.3 ± 1.1 mM and 4.0 ± 1.0 mM) are similar for these two compounds. These results suggest that glucuronic and galacturonic acid

Table 2 Critical micellar concentration (CMC), surface tension at CMC (γ_{cmc}), Maximum surface excess (Γ_{max}), and Minimum molecular area (A_{min}) for uronic amide-based surfactants at 20 °C

Surfactants	CMC (mM)	γ^{a}_{cmc} (mN/m)	Γ_{max} (mol/m^2) × 10^{-6}	A_{min} (Å^2/molecule)
Glucuronamides				
C8Glc-N **11**	3.3 ± 1.1	24.4	6.8 ± 0.7	25.0 ± 2.7
C12Glc-N **12**	0.7 ± 0.2	22.1	5.6 ± 0.3	30.0 ± 1.6
C14Glc-N **13**	0.5 ± 0.2	24.0	7.6 ± 0.5	21.1 ± 1.9
C16Glc-N **14**	nd	nd	nd	nd
C18Glc-N **15**	nd	nd	nd	nd
Galacturonamides				
C8Gal-N **24**	4.0 ± 1.0	20.5	5.0 ± 0.7	33.8 ± 4.7
C12Gal-N **25**	1.8 ± 0.0	21.5	4.1 ± 0.2	38.9 ± 0.1
C14Gal-N **26**	0.06 ± 0.00	32.5	4.5 ± 0.4	38.1 ± 3.6
C16Gal-N **27**	0.02 ± 0.00	47.0	4.7 ± 0.2	41.0 ± 1.7
C18Gal-N **28**	<0.01	<55	3.6 ± 0.3	43.0 ± 4.8
Octylphenol 9-10 EO condensate	0.25 ± 0.0	31.0	2.6 ± 0.0	62.8 ± 0.2

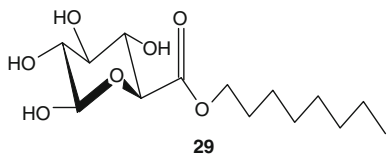
[a] γ_{cmc} values represent the average of at least two surface tensions with a slope dγ/dC less than 5%

headgroups would have practically the same effects. Therefore, the equatorial or axial position of the OH group at the C4 would not have a significantly important influence on the surface-active properties of uronic amide-based surfactants.

The maximum surface excess and the minimum molecular areas are also in the same range for both uronic amide-based surfactants, which are, for instance, 6.10^{-6} mol/m^2 and 28 Å^2/molecule in average for **11** (C8-Glc-N) and **24** (C8-Gal-N), respectively. These parameters also seem to be dependent on the hydrophobic tail length. A general trend occurs: the higher the hydrophobic chain is, the larger the occupied molecular area at the maximum saturation, i.e., at the beginning of micellization.

In general, the two homologous series of uronic-based surfactants exhibit good surface-active properties compared to the well-known nonionic surfactant, octylphenol 9-10 ethylene oxide condensate. This has a higher γ_{cmc} (31 mN/m) but a smaller CMC (0.25 mM) compared to C8- and C12- uronic *N*-alkylamides. However, the superiors homologous **26**, **27** and **28** have a smaller CMC (<0.06 mM) and are able to form micelles in aqueous solution more easily.

Compared to alkyl ester sugar surfactants such as octylglucuronate **29** (Fig. 3), glucuronic *N*-alkylamides



29

Fig. 3 Structures of *β*-D-octylglucuronate **29**

appear much more surface-active in terms of γ_{cmc} and CMC, about 24 mN/m and 3.3 mM for **11** versus 28.0 mN/m and 10.7 mM for **29**, as previously determined [6].

These disparities arise from the difference in the molecular area occupied by the two molecules at the air–water interface, and then their maximum surface excess (or maximum interfacial concentrations), which are $3.9.10^{-6}$ mol/m^2 and 43 Å^2/molecule for **29** [6] and about $6.8.10^{-6}$ mol/m^2 and 25 Å^2/molecule for **11**. These results indicate that when an amide bond serves as a linkage between the headgroup and the hydrocarbon tail instead of an ester bond, sugar-based surfactants are more efficient in terms of surface-active properties under equilibrium conditions. **11** would therefore form a more condensed film at the air–water interface than **29** possibly because of a smaller bulk size of the amide bond compared to that of the ester one.

Moreover, in comparison with alkyl (poly) glycosides (mono- and diglycosides), which are the standard surfactants from renewable raw materials, uronic-amide-based surfactants having the same alkyl chain length are more effective with respect to γ_{cmc} and CMC values, taking into account both α and ß anomeric forms with C8 alkyl chain [25]. For instance, C8Glc-N has a CMC three to five fold lower than α-C8G1, ß- C8G1, and ß-C8G2.

In conclusion, sugar-derived *N*-alkylamides constitute an interesting group of non-ionic surfactants as they exhibit in general a good surface-activity and appear then as valuable non-ionic surfactants compared to the most widely used non-ionic surfactants like octylphenol 9-10 ethylene oxide condensate. The main effect of their attribute molecular structure on the surface-active properties concerns the hydrophobic chain length and follows the

same rules as those of classical surfactants. However, they are more surface-active than the corresponding alkyl ester analogues for both CMC and γ_{cmc} values.

Their renewability and environmental acceptability make them an interesting alternative to petrochemically derived products. Due to their total biodegradability, lack of taste, non-skin irritation, their being odorless and non-toxic, they could find diverse uses in the cosmetic, food or pharmaceutical sectors.

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