Pergamon

Tetrahedron 58 (2002) 7967–7973

TETRAHEDRON

New *N*-alkylsulfonamides and alkyl sulfonates derived from 6-*C*-sulfosugars

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Received 7 May 2002; revised 25 June 2002; accepted 15 July 2002

Abstract—Protected 6-*C*-sulfosugars have been transformed into alkyl sulfonates and *N*-alkylsulfonamides, including a pseudo-disaccharide with a 6 to 6′-sulfonamide linkage. The method involves the oxidation of 6-thioacetate sugar derivatives to 6-*C*-sulfosugars, and their transformation into sulfonyl chlorides using SO_2Cl_2 in anhydrous CH_2Cl_2 followed by in situ coupling with nucleophiles in the presence of an excess of base. Sulfonylation through phase-transfer conditions has proved to be suitable for the synthesis of the pseudo-disaccharide.

1. Introduction

Sulfonamides have been shown to possess a wide spectrum of therapeutic applications.[1] Thus, their potential use as antihypertensive,[2] antiglaucoma,[3] antibacterial,[4] antiviral,[5] antiprotozoal,[6] antifungal,[7] and antitumoral[8] agents as well as therapeutic drugs for the treatment of rheumatoid arthritis,[9] male erectile dysfunction,[10] and obesity[11] has been reported. Furthermore, some of them have proved to be useful as herbicides[12] and plaguicides.[13] Alkyl sulfonates have been found to be inhibitors of cell proliferation, thus being potentially useful for the treatment of cancer.[14] These activities have increased the interest in the synthesis of complex sulfonates and sulfonamides.

Few reports deal with the synthesis of carbohydrate-derived sultones,[15,16] sulfonates[17,18] and sulfonamides.[17d–19] These syntheses have been focused mainly on the preparation of antisense and antiviral oligonucleotides, in which the phosphate linkage has been replaced by a methylene-sulfonyloxy or methylenesulfonamido internucleoside linkage. The described methodology exploits the reactivity of nucleophilic α-lithio mesylates or sulfonate-stabilized Horner–Emmons reagents on primary iodides or carbonyl compounds, and involves the sugar homologation with a methylene group. To our knowledge, there is no report on the synthesis of non-homologated sugar sulfonate esters or sulfonamides.

We have previously reported the preparation of a number of sugar 6-sulfonic acids by oxidation of 6-thiosugars with peroxy acids.[20–23] We now carry out the transformation of differently protected 6-*C*-sulfosugar derivatives into alkyl sulfonate esters and *N*-alkylsulfonamides.

2. Results and discussion

In this paper we describe the preparation of the sulfonyl chlorides **3** and **12** starting from the known 6-thioacetates **1**[22] and **10**,[24] which by oxidation with 33% (w/v) hydrogen peroxide in glacial acetic acid in the presence of 1 equiv. of tetrabutylammonium acetate led to **2** and **11**, in 85 and 90% yield, respectively, after purification by column chromatography (Schemes 1 and 2). The preparation of the tetrabutylammonium salts **2** and **11** was a good choice in order to increase the commonly low solubility of potassium or sodium salts in organic solvents.

A wide variety of methods have been reported for the preparation of sulfonyl chlorides. The most common synthetic procedure involves the reaction of a sulfonic acid or its salts with PCl_5, $POCl_3$ and $SOCl_2$.[25] The use of triphosgene[18] or Ph_3P/SO_2Cl_2[26] has been reported for the preparation of carbohydrate sulfonyl chlorides, in which the carbohydrate ring and the chlorosulfonyl group are linked by an ethylidene bridge. A recent transformation of arene and alkane sodium sulfonates into sulfonyl chlorides and bromides using $Ph_3P{\cdot}Cl_2$ and $Ph_3P{\cdot}Br_2$ has been described.[27] In our hands, treatment of the sodium salt of **2** with triphenylphosphine dichloride or dibromide in dry acetonitrile was unsuccessful. This sodium salt was prepared by oxidation of thioacetate **1** in the presence of sodium acetate.

Chlorination of **2** with an excess of 1:1 Ph_3P/SO_2Cl_2 (5 equiv.) in dry CH_2Cl_2, followed by portionwise addition

Keywords: sulfonyl chlorides; sulfonates; sulfonamides; pseudo-disaccharide; phase-transfer catalysis.

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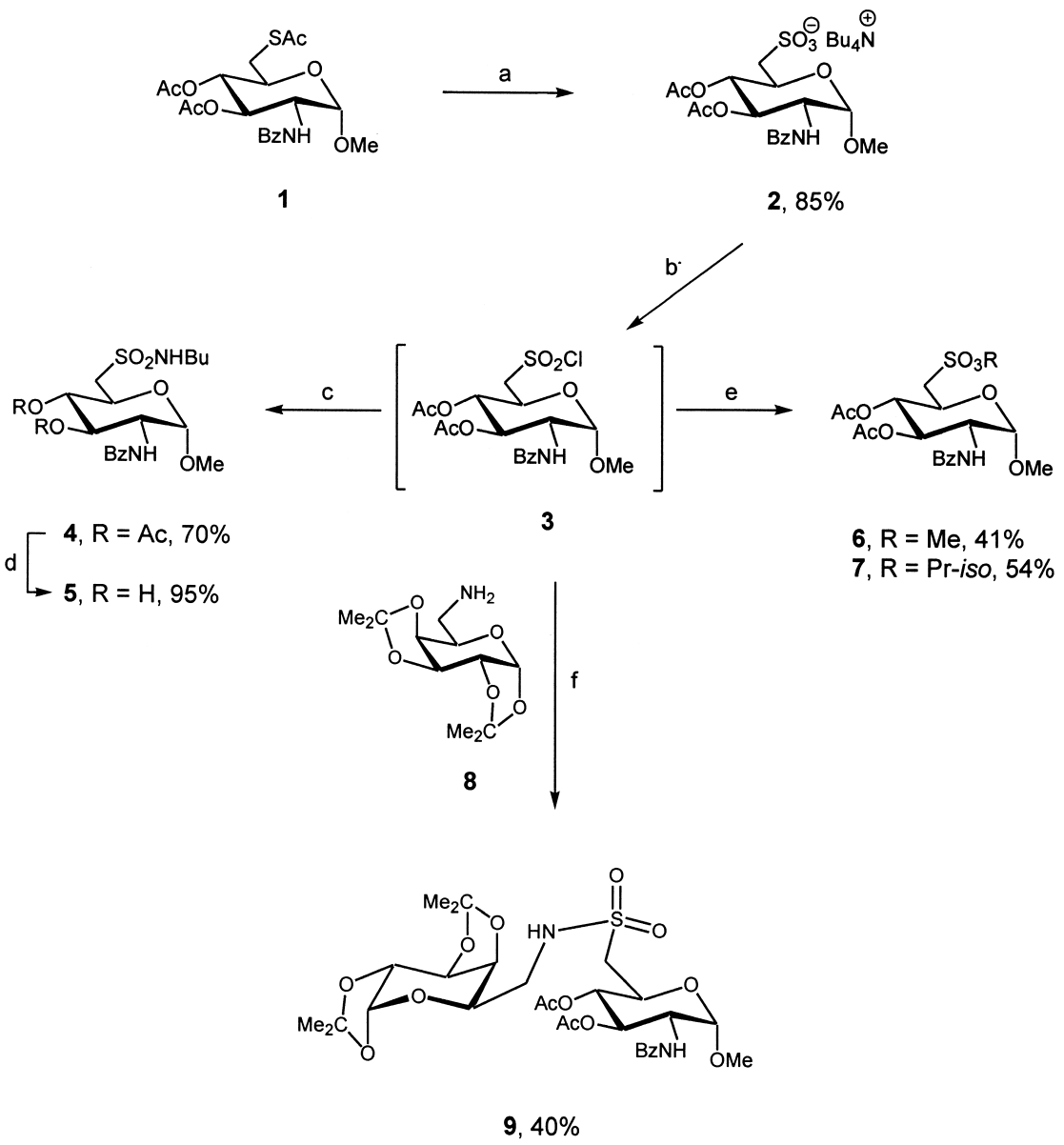
PII: S0040-4020(02)00874-8



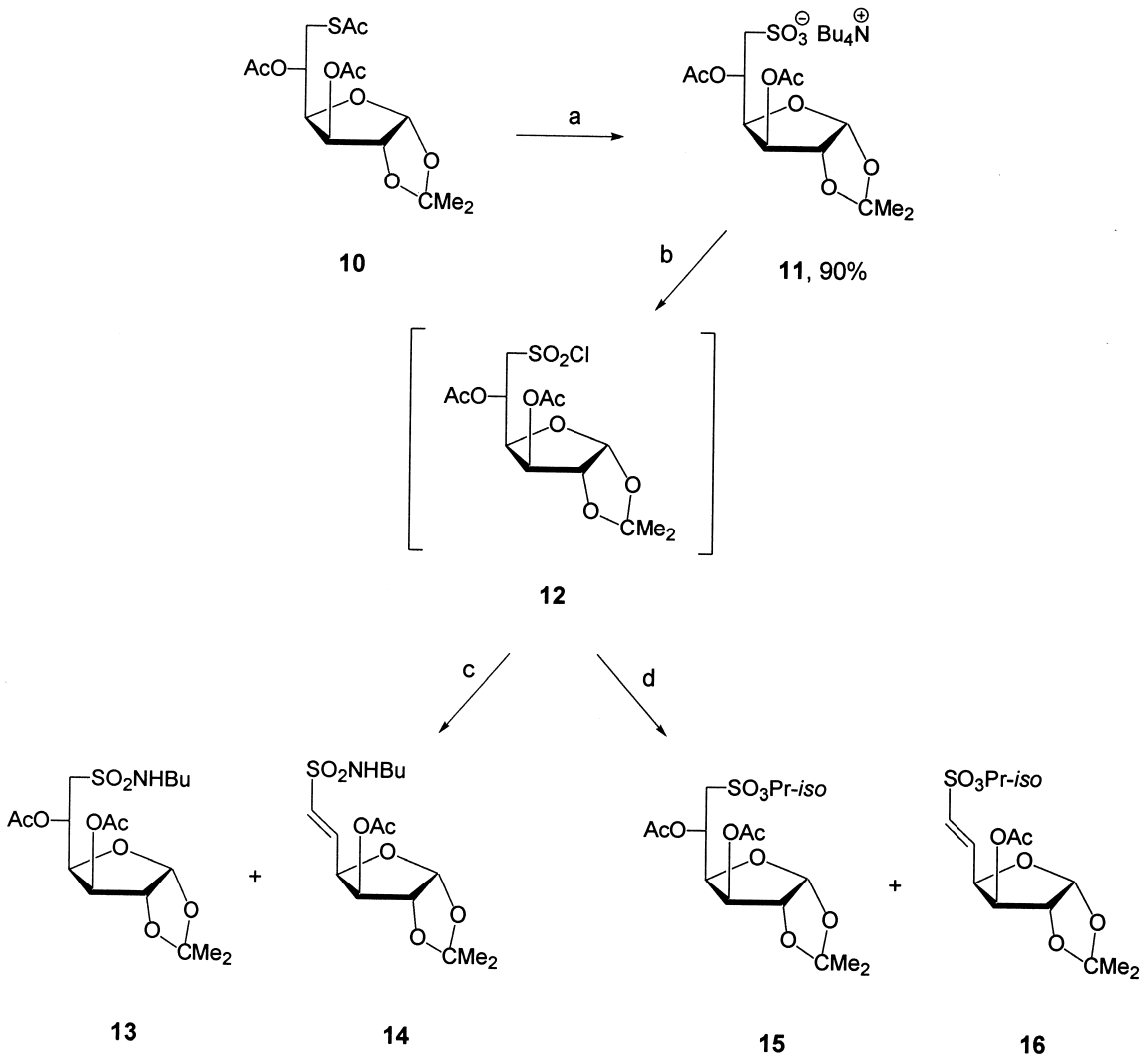
Scheme 1. *Reagents and conditions*: (a) H_2O_2, Bu_4NOAc, AcOH, 40°C, 12 h; (b) SO_2Cl_2, CH_2Cl_2, rt, 4 h; (c) $BuNH_2$; (d) 0.5 M NaOMe, MeOH; Amberlite IR-120 (H^+); (e) 1:1 ROH/Et_3N; (f) Bu_4NHSO_4, sat. aq. $NaHCO_3$, **8** (3 equiv.), CH_2Cl_2.

of butylamine at −15°C up to pH 6–7 led to the O-protected *N*-butylsulfonamide **4** (47%). The attempt at chromatographic isolation of the sulfonyl chloride **3** resulted in the formation of the methyl sulfonate **6** (32%) using CH_2Cl_2–MeOH as eluent, and extensive decomposition was observed using EtOAc–hexane.

Chlorination of **2** with SO_2Cl_2 (5 equiv.) in the absence of Ph_3P, followed by addition of butylamine gave **4** in a better yield (70%), with the additional advantage of avoiding the tedious elimination of the formed Ph_3PO. Zemplén de-O-acetylation of **4** gave **5** (95%). Preparation of the alkyl sulfonates **6** and **7** was carried out by reaction of **2** with sulfuryl chloride and in situ addition of a 1:1 mixture of the corresponding alcohol and Et_3N up to pH 6–7. The lower yield of **6** (41%) is presumably due to the lability of the methyl sulfonate ester to S_N2 reactions during the isolation and purification steps, compared with the more sterically hindered isopropyl sulfonate **7** (54%).

The synthesis of the sulfonamide-linked pseudo-disaccharide **9** (Scheme 1), attempted by coupling **3** with the 6-amino-D-galactopyranose derivative **8** (2 equiv.) followed by portionwise addition of Et_3N up to pH 6–7, was unsuccessful. So we tried the coupling step under phase-transfer conditions[28,29] in CH_2Cl_2 and aqueous saturated $NaHCO_3$ as a source of base, using tetrabutylammonium hydrogenosulfate as catalyst. This gave **9** in 40% yield. These phase-transfer conditions have also been applied to the preparation of the *N*-butyl sulfonamide **4** and the isopropyl sulfonate **7** from **2** in 51 and 20% yields, respectively.

Activation of the furanosic 6-*C*-sulfosugar **11** with SO_2Cl_2 (Scheme 2) followed by careful addition of butylamine up to pH 6–7, led to an irresolvable 1:2 mixture of the protected *N*-butylsulfonamide **13** and the α,β-unsaturated *N*-butylsulfonamide **14**, in 43% yield. The ^1H NMR spectrum of the mixture showed signals in the olephinic region for protons

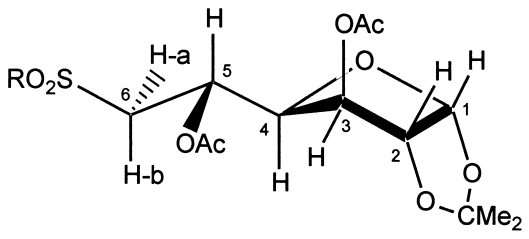


Scheme 2. *Reagents and conditions*: (a) H_2O_2, Bu_4NOAc, AcOH, 40°C, 12 h; (b) SO_2Cl_2, CH_2Cl_2, rt, 4 h; (c) $BuNH_2$; (d) 1:1 *i*-PrOH/Et_3N.

H-5 and H-6, with a $J_{5,6}$ of 15.0 Hz, indicating a *trans* relationship for these protons. The *cis* isomer was not detected. Similarly, chlorination of **11**, followed by reaction with 1:1 *i*-PrOH–Et_3N afforded a chromatographically irresolvable 1:1 mixture of the isopropyl sulfonate **15** and the α,β-unsaturated isopropyl sulfonate **16** in 36% yield, as deduced from the ^1H NMR spectrum of the mixture (Scheme 2). No traces of the *cis* isomer of **16** were detected. When the furanosic sulfonyl chloride **12** was reacted with butylamine in phase-transfer conditions, a non-resolved 2:7 mixture of compounds **13** and **14** was obtained in 28% yield. The higher proportion of the elimination compound **14**, compared with that obtained when the reaction is carried out in CH_2Cl_2 quenching with butylamine (**13/14** in 1:2 ratio), may be associated to the longer reaction times in phase-transfer conditions.

The formation of the α,β-unsaturated *C*-sulfo derivatives **14** and **16** can be explained as a result of base-catalysed acetic acid elimination, due to the acidity of a hydrogen in α position to a sulfonyl group. The absence of elimination products in the pyranosic derivatives is not surprising, as the elimination process would result in the opening of the tetrahydropyrane ring.

Analysis of the vecinal coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$ for **13**–**16** (3.6–3.7, 0.0, 3.0–3.3 Hz, respectively), indicates the preference of these compounds for an E_4 conformation in solution. The sequence C-3–S of **13** and **15** adopts preferentially a ziz-zag planar arrangement (Fig. 1) as



R = NHBu, OPr-*iso*

Figure 1. Major conformation of **13** and **15**.

deduced from the $J_{3,4}$, $J_{4,5}$, $J_{5,6a}$ and $J_{5,6b}$ values (3.0, 8.1–8.5, 2.3 and 8.8–8.9 Hz, respectively).

3. Conclusion

We have described a method for the synthesis of *N*-alkyl sugar sulfonamides and alkyl sugar sulfonates from 6-thiosugar derivatives by oxidation to 6-*C*-sulfosugars, chlorination with SO_2Cl_2, and coupling of the sulfonyl chloride with amines and alcohols in the presence of a base. A novel procedure based on the coupling of sugar sulfonyl chlorides with nucleophiles in phase-transfer conditions is presented.

4. Experimental

4.1. General methods

Melting points were determined on an Electrothermal apparatus and are uncorrected. Optical rotations were measured at 20°C with a Perkin–Elmer 241 polarimeter, and IR spectra (KBr disks) were obtained with an FT-IR Bomem MB-120 spectrophotometer. ^{1}H (300 and 500 MHz) and ^{13}C (75.5 and 125.7 MHz) NMR spectra were recorded on Bruker AMX-300 and AMX-500 spectrometers for solutions in $CDCl_3$ and CD_3OD, using tetramethylsilane as internal standard. The assignments of ^{1}H and ^{13}C signals were confirmed by homonuclear COSY and heteronuclear 2D correlated spectra, respectively. Mass spectra were recorded on Kratos MS 80 RFA and Micromass AutoSpeQ mass spectrometers. All reactions were monitored by TLC, which was carried out on aluminium sheets coated with silica gel 60 F_{254} (Merck); spots were visualized by UV light and by charring with 10% H_2SO_4 in EtOH. Column chromatography was performed using Merck silica gel 60 (40–63 μm), and preparative TLC was carried out using Merck silica gel 60 HF_{254} (5–40 μm). Microanalyses were performed at the 'Instituto de Investigaciones Químicas', Sevilla, Spain.

4.1.1. Tetrabutylammonium methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-sulfonate (2). To a solution of 3,4-di-*O*-acetyl-6-*S*-acetyl-2-benzamido-2-deoxy-6-thio-α-D-glucopyranoside **1**[22] (500 mg, 0.73 mmol) in glacial acetic acid (6 mL) were added tetrabutylammonium acetate (220 mg, 0.73 mmol) and 33% (w/v) hydrogen peroxide (2.3 mL, 14.6 mmol). The solution was stirred at 40°C for 12 h, concentrated, and then co-concentrated with H_2O (3×10 mL). The resulting residue was purified by column chromatography using 10:1 CH_2Cl_2–MeOH as eluent to give **2** (781 mg, 85%) as a colourless oil. R_f=0.25 (10:1 CH_2Cl_2–MeOH); $[\alpha]_D$=+56° (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD): δ 8.05 (d, 1H, $J_{2,NH}$=9.4 Hz, NHBz), 7.76–7.42 (m, 5H, Ph), 5.41 (dd, 1H, $J_{2,3}$=10.8 Hz, $J_{3,4}$=9.2 Hz, H-3), 4.90 (dd, 1H, $J_{4,5}$=10.1 Hz, H-4), 4.80 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.48 (ddd, 1H, H-2), 4.41 (dt, 1H, 1/2($J_{5,6a}$+$J_{5,6b}$)=5.4 Hz, H-5), 3.52 (s, 3H, OMe), 3.24 (m, 8H, 4CH_2 butyl), 3.00 (d, 2H, H-6a, H-6b), 2.04, 1.92 (2s, 3H each, Ac), 1.66 (m, 8H, 4CH_2 butyl), 1.41 (m, 8H, 4CH_2 butyl), 1.02 (t, 12H, *J*=7.3 Hz, 4Me butyl); ^{13}C NMR (75.5 MHz, CD_3OD): δ 172.18, 171.73, 170.37 (CO), 135.22, 132.92, 129.56, 128.47 (Ph), 99.27 (C-1), 73.12 (C-4), 72.72 (C-3), 67.45 (C-5), 59.50 (C-1 butyl), 56.31 (OMe), 53.84 (C-2, C-6), 24.78 (C-2 butyl), 20.70 (C-3 butyl and 2CO*Me*), 13.94 (C-4 butyl); IR: ν_{max} 3452 (NH), 1752 (C=O acetate), 1664 (Amide I), 1239 (AcO, SO_3^-) cm^{-1}; FAB-MS, *m/z* 490 [100%, $(M-Bu_4N+2Na)^+$]. Anal. calcd for $C_{34}H_{60}N_2O_{11}S$: C, 57.93; H, 8.58; N, 3.97. Found: C, 57.74; H, 8.28; N, 3.95.

4.1.2. Tetrabutylammonium 3,5-di-*O*-acetyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose-6-sulfonate (11). To a solution of **10**[24] (684 mg, 1.89 mmol) in glacial acetic acid (8 mL) were added tetrabutylammonium acetate (569 mg, 1.89 mmol) and 33% (w/v) hydrogen peroxide (2.3 mL, 22.6 mmol). The solution was stirred at 40°C for 12 h, concentrated, and then co-concentrated with H_2O (3×10 mL). The residue was purified by column chromatography (20:1→5:1 CH_2Cl_2–MeOH) to give **11** (1.04 g, 90%) as a colourless oil. R_f=0.31 (10:1 CH_2Cl_2–MeOH); $[\alpha]_D$=+5° (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD): δ 5.90 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 5.55 (m, 1H, $J_{4,5}$=8.1 Hz, $J_{5,6a}$=2.3 Hz, $J_{5,6b}$=8.9 Hz, H-5), 5.22 (d, 1H, $J_{3,4}$=3.0 Hz, H-3), 4.52 (d, 1H, H-2), 4.36 (dd, 1H, H-4), 3.24 (dd, 1H, $J_{6a,b}$=14.6 Hz, H-6a), 3.24 (m, 8H, 4CH_2 butyl), 3.06 (dd, 1H, H-6b), 2.05, 1.98 (2s, 3H each, Ac), 1.66 (m, 8H, 4CH_2 butyl), 1.47, 1.29 (2s, 3H each, Me_2C), 1.41 (m, 8H, 4CH_2 butyl), 1.02 (m, 12H, *J*=7.3 Hz, 4Me butyl); ^{13}C NMR (75.5 MHz, CD_3OD): δ 171.48, 171.24 (CO), 113.44 (Me_2C), 106.40 (C-1), 84.65 (C-2), 80.51 (C-4), 75.90 (C-3), 67.73 (C-5), 59.50 (C-1 butyl), 53.13 (C-6), 26.97, 26.40 (*Me*$_2$C), 24.78 (C-2 butyl), 21.07, 20.90 (CO*Me*), 20.69 (C-3 butyl), 13.93 (C-4 butyl); IR: ν_{max} 1752 (C=O), 1244 (AcO, SO_3^-) cm^{-1}; HRFAB-MS, *m/z* calcd for $[M+Bu_4N]^+$ $C_{45}H_{91}N_2O_{10}S$ 851.6394, found 851.6398.

4.2. General methods for the synthesis of alkyl sulfonates and *N*-alkylsulfonamides

To a solution of **2** or **11** (0.17 mmol) in dry CH_2Cl_2 (2 mL) at 0°C was slowly added sulfuryl chloride (68 μL, 0.85 mmol) under Ar in the presence of activated 4 Å molecular sieves. The reaction was left at room temperature for 4 h. Then one or various of the following methods was used.

Method A: the reaction mixture was cooled at −15°C and butylamine was slowly added up to pH 6–7. The solution was concentrated to dryness and the product was purified as indicated.

Method B: the reaction mixture was cooled at −15°C and 1:1 ROH–Et_3N mixture was slowly added up to pH 6–7. The solution was concentrated to dryness and the product was purified as indicated.

Method C: the reaction mixture was slowly added at 0°C to a stirred mixture of saturated aq. $NaHCO_3$ (10 mL) containing Bu_4NHSO_4 (25 mg, 0.07 mmol) and a solution of butylamine (1.70 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred at rt for 1 h. The organic phase was separated, dried ($MgSO_4$), concentrated and chromatographed.

Method D: the reaction mixture was slowly added at 0°C to a stirred mixture of saturated aq. $NaHCO_3$ (10 mL) containing Bu_4NHSO_4 (25 mg, 0.07 mmol) and a solution of ROH (1.70 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred at rt for 1 h. The organic phase was separated, dried ($MgSO_4$), concentrated and chromatographed.

4.2.1. Methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-*N*-butylsulfonamide (4). Purification by column chromatography (40:1 CH_2Cl_2–MeOH). Method A: 59 mg, 70%. Method C: 43 mg, 51%. R_f=0.72 (10:1 CH_2Cl_2–MeOH); $[\alpha]_D$=+80° (*c* 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74–7.43 (m, 5H, Ph), 6.43 (d, 1H, $J_{2,NH}$=9.2 Hz, NHBz), 5.00 (t, 1H, $J_{3,4}$=9.5 Hz, $J_{4,5}$=10.0 Hz, H-4), 4.88 (dd, 1H, $J_{2,3}$=10.9 Hz, H-3), 4.87 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.49 (ddd, 1H, H-2), 4.39 (td, 1H, $J_{5,6a}$=10.2 Hz, $J_{5,6b}$=2.5 Hz, H-5), 4.20 (m, 1H, SO_2NH), 3.49 (s, 3H, OMe), 3.31 (dd, 1H, $J_{6a,b}$=14.8 Hz, H-6a), 3.14 (dd, 1H, H-6b), 3.13 (m, 2H, CH_2 butyl), 2.09, 1.99 (2s, 3H each, Ac), 1.56 (m, 2H, CH_2 butyl), 1.39 (m, 2H, CH_2 butyl), 0.95 (t, 3H, *J*=7.3 Hz, Me butyl); ^{13}C NMR: (75.5 MHz, $CDCl_3$): δ 171.35, 169.60, 167.04 (CO), 133.28, 131.86, 128.58, 126.88 (Ph), 98.20 (C-1), 70.42, 70.35 (C-3, C-4), 65.69 (C-5), 55.99 (OMe), 52.45 (C-2), 51.74 (C-6), 43.18 (C-1 butyl), 31.83 (C-2 butyl), 20.53, 20.50 (CO*Me*), 19.59 (C-3 butyl), 13.42 (C-4 butyl); IR: ν_{max} 3304 (NH), 1745 (C=O), 1657 (Amide I), 1244 (AcO), 1333, 1147 (SO_2) cm^{-1}; HRFAB-MS, *m/z* calcd for $[M+Na]^+$ $C_{22}H_{32}N_2O_9SNa$ 523.1723, found 523.1736. Anal. calcd for $C_{22}H_{32}N_2O_9S$: C, 52.79; H, 6.44; N, 5.60. Found: C, 52.82; H, 6.31; N, 5.82.

Compound **4** was also prepared using 1:1 Ph_3P/SO_2Cl_2 in the chlorination step: to a stirred solution of Ph_3P (223 mg, 0.85 mmol) in dry CH_2Cl_2 (2 mL) and cooled at 0°C sulfuryl chloride (70 μL, 0.85 mmol) was slowly added under Ar in the presence of activated 4 Å molecular sieves. After 4 h at rt a solution **2** (117 mg, 0.17 mmol) in dry CH_2Cl_2 (2 mL) was added, and stirred for 2 h. The reaction mixture was cooled to −15°C and butylamine portionwise added up to pH 6–7. The solution was concentrated and **4** (49 mg, 47%) isolated by preparative TLC (40:1 CH_2Cl_2–MeOH).

4.2.2. Methyl 2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-*N*-butylsulfonamide (5). To a solution of **4** (45 mg, 0.09 mmol) in dry MeOH (2 mL) 0.5 M methanolic NaOMe was added up to pH 9–10. After 4 h at rt Amberlite IR-120 (H^+) cation exchange resin was added up to pH 7, removed by filtration and washed with MeOH. The combined methanolic solutions were concentrated and the residue was purified by preparative TLC (10:1 CH_2Cl_2–MeOH) to give **5** (35 mg, 95%). R_f=0.37 (10:1 CH_2Cl_2–MeOH); $[\alpha]_D$=+52° (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD): δ 7.86–7.43 (m, 5H, Ph), 4.80 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.14 (dd, 1H, $J_{2,3}$=10.8 Hz, H-2), 4.09 (td, 1H, $J_{4,5}$=9.8 Hz, $J_{5,6a}$=1.8 Hz, $J_{5,6b}$=9.7 Hz, H-5), 3.84 (dd, 1H, $J_{3,4}$=8.9 Hz, H-3), 3.57 (dd, 1H, $J_{6a,b}$=14.7 Hz, H-6a), 3.45 (s, 3H, OMe), 3.26 (dd, 1H, H-6b), 3.25 (dd, 1H, H-4), 3.07 (t, 2H, *J*=7.0 Hz, CH_2 butyl), 1.55 (m, 2H, CH_2 butyl), 1.39 (m, 2H, CH_2 butyl), 0.94 (t, 3H, *J*=7.2 Hz, Me butyl); ^{13}C NMR (75.5 MHz, CD_3OD): δ 170.72 (CO), 135.56, 132.74, 129.48, 128.54 (Ph), 99.82 (C-1), 75.02 (C-4), 72.31 (C-3), 69.06 (C-5), 56.27 (OMe), 55.94 (C-2), 54.23 (C-6), 43.84 (C-1 butyl), 33.33 (C-2 butyl), 20.85 (C-3 butyl), 14.01 (C-4 butyl); IR: ν_{max} 3309 (NH, OH), 1649 (Amide I), 1331, 1187 (SO_2) cm^{-1}; HRFAB-MS, *m/z* calcd for $[M+Na]^+$ $C_{18}H_{28}N_2O_7SNa$ 439.1515, found 439.1510.

4.2.3. Methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-(methyl sulfonate) (6). Purification by column chromatography (1:1 EtOAc–hexane). Method B: 33 mg, 41%. R_f=0.10 (1:2 EtOAc–hexane); $[\alpha]_D$=+80° (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74–7.42 (m, 5H, Ph), 6.39 (d, 1H, $J_{2,NH}$=9.2 Hz, NH), 5.38 (dd, 1H, $J_{2,3}$=10.8 Hz, $J_{3,4}$=9.4 Hz, H-3), 4.99 (t, 1H, $J_{4,5}$=9.5 Hz, H-4), 4.86 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.51 (ddd, 1H, H-2), 4.38 (td, 1H, $J_{5,6a}$=9.3 Hz, $J_{5,6b}$=2.1 Hz, H-5), 3.93 (s, 3H, SO_3Me), 3.48 (s, 3H, OMe), 3.42 (dd, 1H, $J_{6a,b}$=15.0 Hz, H-6a), 3.25 (dd, 1H, H-6b), 2.09, 1.98 (2s, 3H each, Ac); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 171.25, 169.72, 166.99 (CO), 133.38, 131.81, 128.58, 126.88 (Ph), 98.01 (C-1), 70.54 (C-3), 70.37 (C-4), 64.99 (C-5), 55.94 (SO_3Me), 55.79 (OMe), 52.29 (C-2), 50.80 (C-6), 20.54 (2CO*Me*); IR: ν_{max} 3333 (NH), 1752 (C=O), 1664 (Amide I), 1363, 1170 (SO_2), 1243 (AcO) cm^{-1}; HRFAB-MS, *m/z* calcd for $[M+Na]^+$ $C_{19}H_{25}NO_{10}SNa$ 482.1097, found 482.1103.

4.2.4. Methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-(isopropyl sulfonate) (7). Purification by column chromatography (1:1 EtOAc–hexane). Method B: 46 mg, 54%. Method D: 17 mg, 20%. R_f=0.21 (1:2 EtOAc–hexane); $[\alpha]_D$=+96° (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73–7.40 (m, 5H, Ph), 6.40 (d, 1H, $J_{2,NH}$=9.4 Hz, NH), 5.36 (dd, 1H, $J_{3,4}$=10.8 Hz, $J_{4,5}$=9.4 Hz, H-4), 4.98 (t, 1H, $J_{2,3}$=10.8 Hz, H-3), 4.94 (m, 1H, *J*=6.2 Hz, C*H*Me$_2$), 4.84 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.50 (ddd, 1H, H-2), 4.38 (td, 1H, $J_{5,6a}$=9.2 Hz, $J_{5,6b}$=2.1 Hz, H-5), 3.47 (s, 3H, OMe), 3.35 (dd, 1H, $J_{6a,b}$=14.8 Hz, H-6a), 3.21 (dd, 1H, H-6b), 2.08, 1.97 (2 s, 3H each, Ac), 1.41 (d, 6H, CH*Me*$_2$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 171.23, 169.71, 166.99 (CO), 133.43, 131.77, 128.56, 126.87 (Ph), 97.91 (C-1), 77.55 (*C*HMe$_2$), 70.63 (C-3), 70.43 (C-4), 65.05 (C-5), 55.76 (OMe), 52.51, 52.30 (C-2, C-6), 22.99, 22.82 (CH*Me*$_2$), 20.51 (2CO*Me*); IR: ν_{max} 3340 (NH), 1748 (C=O), 1658 (Amide I), 1383, 1167 (SO_2), 1238 (AcO) cm^{-1}; CI-MS, *m/z* 456 (41%, $[M-OMe]^+$), 488 (100%, $[M+H]^+$); HRCI-MS, *m/z* calcd for $[M+H]^+$ $C_{21}H_{30}NO_{10}S$ 488.1590, found 488.1580.

4.2.5. Methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside-6-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)sulfonamide (9). Purification by column chromatography (1:2→1:1 EtOAc–hexane). Prepared following Method C but using 3 equiv. of 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**8**): 45 mg, 40%. R_f=0.26 (1:1 EtOAc–hexane); $[\alpha]_D$=+33° (*c* 1.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) glucose unit: δ 7.73–7.43 (m, 5H, Ph), 6.40 (d, 1H, $J_{2,NH}$=9.3 Hz, NHBz), 5.36 (dd, 1H, $J_{2,3}$=10.8 Hz, $J_{3,4}$=9.4 Hz, H-3), 5.03 (t, 1H, $J_{4,5}$=10.2 Hz, H-4), 4.88 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.51 (ddd, 1H, H-2), 4.38 (td, $J_{5,6a}$=10.2 Hz, $J_{5,6b}$=2.3 Hz, H-5), 3.50 (dd, 1H, $J_{6a,b}$= 14.6 Hz, H-6a), 3.49 (s, 3H, OMe), 3.21 (dd, 1H, H-6b),

2.07, 1.97 (2s, 3H each, Ac); galactose unit: δ 5.56 (d, 1H, $J_{1,2}$=5.1 Hz, H-1), 4.90 (br s, 1H, SO_2NH), 4.61 (dd, 1H, $J_{2,3}$=2.4 Hz, $J_{3,4}$=7.9 Hz, H-3), 4.34 (dd, 1H, H-2), 4.21 (dd, 1H, $J_{4,5}$=1.9 Hz, H-4), 3.96 (ddd, 1H, $J_{5,6a}$=5.2 Hz, $J_{5,6b}$=8.0 Hz, H-5), 3.39 (m, 1H, $J_{6a,b}$=13.7 Hz, H-6a), 3.34 (m, 1H, H-6b), 1.54, 1.46, 1.35, 1.33 (4s, 3H each, Me_2C); ^{13}C NMR (125.5 MHz, $CDCl_3$) glucose unit: δ 171.33, 169.51, 167.02 (CO), 133.55, 131.81, 128.61, 127.14, (Ph), 98.21 (C-1), 70.73 (C-3), 70.52 (C-4), 65.83 (C-5), 56.01 (OMe), 53.76 (C-6), 52.41 (C-2), 20.54 (2CO*Me*); galactose unit: δ 109.48, 108.85 (Me_2C), 96.29 (C-1), 71.21 (C-4), 70.80 (C-3), 70.26 (C-2), 65.83 (C-5), 43.48 (C-6), 25.90, 25.78, 24.74, 24.29 (Me_2C); IR: ν_{max} 3297 (NH), 1752 (C=O), 1650 (Amide I), 1379, 1149 (SO_2), 1237 (AcO) cm^{-1}; CI-MS, *m/z* 629 [50%, $(M-Me_2CO+H)^+$], 655 [39%, $(M-MeOH+H)^+$], 687 (100%, $[M+H]^+$); HRCI-MS, *m/z* calcd for $[M+H]^+$ $C_{30}H_{43}N_2O_{14}S$ 687.2435, found 687.2434.

4.2.6. 3,5-Di-*O*-acetyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose-6-*N*-butylsulfonamide (13) and (*E*)-3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose-6-*N*-butylsulfonamide (14). Purification by column chromatography (1:2 EtOAc–hexane). Method A: 28 mg, 43% (**13/14** in 1:2 ratio). Method C: 18 mg, 28% (**13/14** in 2:7 ratio). R_f=0.28 for both compounds (1:2 EtOAc–hexane); ^{1}H NMR (300 MHz, $CDCl_3$) compound **13**: δ 5.91 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 5.47 (td, 1H, $J_{4,5}$=9.1 Hz, $J_{5,6a}$=2.1 Hz, $J_{5,6b}$=9.6 Hz, H-5), 5.35 (d, 1H, $J_{3,4}$=3.0 Hz, H-3), 4.49 (d, 1H, H-2), 4.63 (t, 1H, *J*=6.5 Hz, NH), 4.35 (dd, 1H, H-4), 3.54 (dd, 1H, $J_{6a,b}$=14.9 Hz, H-6a), 3.28 (dd, 1H, H-6b), 3.12 (q, 2H, *J*=6.8 Hz, CH_2 butyl), 2.07, 2.04 (2s, 3H each, COMe), 1.53 (m, 2H, CH_2 butyl), 1.38 (m, 2H, CH_2 butyl), 1.31, 1.25 (2s, 3H each, Me_2C), 0.94 (t, 3H, Me butyl); compound **14**: δ 6.62 (dd, 1H, $J_{4,5}$=3.5 Hz, $J_{5,6}$=15.0 Hz, H-5), 6.57 (d, 1H, H-6), 5.98 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 5.30 (d, 1H, $J_{3,4}$=3.1 Hz, H-3), 4.97 (dd, 1H, $J_{4,5}$=2.8 Hz, H-4), 4.61 (d, 1H, H-2), 4.28 (br t, 1H, *J*=6.5 Hz, NH), 3.00 (m, 2H, *J*=6.8 Hz, CH_2 butyl), 2.05 (s, 3H, Ac), 1.53, 1.33 (2s, 3H each, Me_2C), 1.53 (m, 2H, CH_2 butyl), 1.38 (m, 2H, CH_2 butyl), 0.92 (t, 3H, Me butyl); ^{13}C NMR (75.5 MHz, $CDCl_3$) compound **13**: δ 170.53, 169.38 (CO), 112.56 (Me_2C), 104.90 (C-1), 83.19 (C-2), 78.71 (C-4), 74.07 (C-3), 64.83 (C-5), 52.89 (C-6), 42.81 (C-1 butyl), 31.98 (C-2 butyl), 29.52, 26.00 (Me_2C), 20.69, 20.54, (CO*Me*), 19.55 (C-3 butyl), 13.41 (C-4 butyl); compound **14**: δ 169.38 (*C*OMe), 136.19 (C-5), 130.72 (C-6), 112.44 (Me_2C), 104.48 (C-1), 83.19 (C-2), 77.35 (C-4), 76.85 (C-3), 42.62 (C-1 butyl), 31.81 (C-2 butyl), 26.57, 26.00 (Me_2C), 20.42 (CO*Me*), 19.58 (C-3 butyl), 13.41 (C-4 butyl). IR: ν_{max} 3301 (NH), 1752 (C=O), 1236 (AcO) cm^{-1}; FAB-MS, compound **13** *m/z* 446 (100%, $[M+Na]^+$); compound **14** *m/z* 386 (97%, $[M+Na]^+$); HRFAB-MS, *m/z* calcd for **13** $[M+Na]^+$ $C_{17}H_{29}NO_9SNa$ 446.1461, found 446.1456.

4.2.7. 3,5-Di-*O*-acetyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose-6-(isopropyl sulfonate) (15) and (*E*)-3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose-6-(isopropyl sulfonate) (16). Purification by column chromatography (1:2 EtOAc–hexane). Method B: 23 mg, 36% (**15/16** in 1:1 ratio). R_f=0.28 for both compounds (1:2 EtOAc–hexane); ^{1}H NMR (300 MHz, $CDCl_3$) compound **15**: δ 5.91 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 5.57 (td, 1H, $J_{4,5}$=8.1 Hz, $J_{5,6a}$=2.3 Hz, $J_{5,6b}$=8.8 Hz, H-5), 5.33 (d, 1H, $J_{3,4}$=3.0 Hz, H-3), 4.97 (m, 1H, *J*=6.3 Hz, C*H*Me_2), 4.49 (d, 1H, H-2), 4.40 (dd, 1H, H-4), 3.65 (dd, 1H, $J_{6a,b}$=15.0 Hz, H-6a), 3.38 (dd, 1H, H-6b), 2.09, 2.05 (2s, 3H each, Ac), 1.31, 1.25 (2s, 3H each, Me_2C), 1.41, (d, 6H, CHMe_2); compound **16**: 6.76 (dd, 1H, $J_{4,5}$=3.5 Hz, $J_{5,6}$=15.1 Hz, H-5), 6.62 (dd, 1H, $J_{4,6}$=1.8 Hz, H-6), 5.99 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 5.32 (d, 1H, $J_{3,4}$=3.3 Hz, H-3), 4.99 (td, 1H, H-4), 4.78 (m, 1H, *J*=6.2 Hz, C*H*Me_2), 4.62 (d, 1H, H-2), 2.05 (s, 3H, Ac), 1.53, 1.34 (2 s, 3H each, Me_2C), 1.41, (d, 6H, CHMe_2); ^{13}C NMR: (75.5 MHz, $CDCl_3$) compound **15**: δ 170.53, 169.38 (CO), 112.55 (Me_2C), 104.81 (C-1), 83.24 (C-2), 78.47 (C-4), 77.39 (*C*HMe_2), 74.13 (C-3), 64.24 (C-5), 52.17 (C-6), 29.52, 25.99 (Me_2C), 23.03, 22.81 (CHMe_2), 20.58, 20.35 (CO*Me*); compound **16**: δ 169.38 (CO), 138.81 (C-5), 128.31 (C-6), 112.55 (Me_2C), 104.50 (C-1), 83.14 (C-2), 77.39 (C-4, *C*HMe_2), 77.14 (C-3), 26.54, 25.99 (Me_2C), 23.03, 22.81 (CHMe_2), 20.58 (CO*Me*); IR: ν_{max} 1728 (C=O), 1240 (SO_2) cm^{-1}; FAB-MS, compound **15** *m/z* 411 (5%, $[M+H]^+$); compound **16** *m/z* 351 (15%, $[M+H]^+$).

Acknowledgments

We thank the Dirección General de Enseñanza Superior e Investigación Científica (Grant No. BQU 2001-3740) and the Junta de Andalucia (FQM134) for financial support. V. U. thanks the Ministerio de Educación y Cultura for the award of a fellowship. This work is part of the European Programme COSTD13, action number D13/0001/98.

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