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Note

# Efficient synthesis of 6-thio and 3-thio analogues of Amiprilose and related compounds

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Amiprilose [1,2-*O*-isopropylidene-3-*O*-(3-*N*,*N*-dimethylaminopropyl)-α-D-glucofuranose] (**1**) and its hydrochloride salt [Therafectin® (SM1213)] are synthetic carbohydrates [1,2] known to exhibit antiproliferative and anti-inflammatory activities [3–6]. Compound **1** acts as an immunomodulator [7] and therefore has a therapeutic effect on such autoimmune disorders as arthritis, psoriasis, eczema, and systemic lupus erythematosus [3–6]. It has low toxicity and no serious side effects [8,9], but is required in large doses for effective therapy. This presents a problem for oral administration of such a drug, especially since treatment of inflammatory or autoimmune disorders is often mid- to long-term. Attempts have been made by other workers [1,6,10,11] to discover a more potent derivative of this drug. For example, a few 6-thio derivatives of D-glucose, partially or fully protected by isopropylidene groups such as **4a** and **4c**, were recently prepared. Preliminary investigations showed that they are approximately 5–1000 times more potent than the parent compound [6,10,11]. This prompted us to report a simpler route for **4c** and the synthesis of new 3-thio derivatives of **1**, as a part of our studies on thioethers derived from various sugars [12,13]. For this purpose a two-step strategy was used in which starting protected monosaccharides were converted into iodides and then condensed with the appropriate tertiary aminoalkanethiolates to give the desired thioethers.

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Table 1
Yields and physicochemical data for *N,N*-substituted aminothioether derivatives

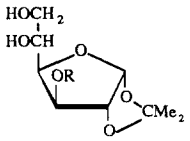
| Compound | Yields [a] (%) | $[\alpha]_D$ in $CHCl_3$ | *m/e* (ES+) | Formula | Calcd | | | | Found | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | S | C | H | N | S |
| **4b** | 89 | +26° (*c* 1.6) | 406 $[M+H]^+$ | $C_{18}H_{31}NO_7S$ | 53.32 | 7.71 | 3.45 | 7.91 | 53.15 | 7.70 | 3.47 | 8.09 |
| **4c** | 96 [b] | −2° (*c* 2.4) | 322 $[M+H]^+$ | $C_{14}H_{27}NO_5S$ | 52.30 | 8.48 | 4.36 | 9.97 | 50.75 | 8.51 | 4.27 | 9.70 |
| **4d** | 83 | +22° (*c* 1.5) | 434 $[M+H]^+$ | $C_{20}H_{35}NO_7S$ | 55.41 | 8.14 | 3.23 | 7.40 | 55.38 | 8.12 | 3.20 | 7.35 |
| **4e** | 92 | −9° (*c* 0.3) | 350 $[M+H]^+$ | $C_{16}H_{31}NO_5S$ | 54.99 | 8.94 | 4.01 | 9.18 | 55.06 | 8.90 | 4.07 | 9.22 |
| **6a** | 96 | −29° (*c* 3.1) | 362 $[M+H]^+$ | $C_{17}H_{31}NO_5S$ | 56.47 | 8.66 | 3.87 | 8.87 | 56.08 | 8.63 | 3.94 | 9.23 |
| **6b** | 89 | −26° (*c* 2.8) | 390 $[M+H]^+$ | $C_{19}H_{35}NO_5S$ | 58.58 | 9.06 | 3.60 | 8.23 | 58.33 | 9.01 | 3.63 | 8.53 |
| **6c** | 85 | −15° (*c* 2.7) | 348 $[M+H]^+$ | $C_{16}H_{29}NO_5S$ | 55.31 | 8.41 | 4.03 | 9.23 | 55.39 | 8.45 | 3.93 | 9.08 |
| **6d** | 80 | −13° (*c* 2.7) | 376 $[M+H]^+$ | $C_{18}H_{33}NO_5S$ | 57.57 | 8.86 | 3.73 | 8.54 | 57.74 | 8.89 | 3.70 | 8.53 |
| **7** | 82 | −41° (*c* 1.0) | 322 $[M+H]^+$ | $C_{14}H_{27}NO_5S$ | 52.31 | 8.47 | 4.36 | 9.97 | 51.80 | 8.43 | 4.26 | 9.46 |

[a] All compounds were obtained as colorless syrups.
[b] Yield 66% from **3a**.

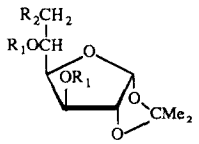
For the synthesis of the known 6-thio-regioisomer of **1**, namely **4c**, iodine was introduced selectively at the 6-position of 1,2-*O*-isopropylidene-α-D-glucofuranose (**2**). When the reaction was carried out according to the method of Garegg [14], nonnegligible amounts of 5,6-elimination by-product were obtained, whereas Plusquellec's method [15] gave exclusively **3a** in 83% yield. Treatment of the latter with *N,N*-dimethylaminopropanethiol [16] and NaOMe in THF-HMPA at room temperature [12] gave **4c** in 66% yield (55% overall yield from **2**). Although quantitative conversion of **3a** to the thioether was observed by TLC, the apparent yields were due to unfavorable partitioning in the extraction procedures. Better yields were obtained starting from acetylated material **3b**, using $K_2CO_3$ in $Me_2CO$–$H_2O$ for the thioetherification step (89%), followed by Zemplén deacetylation (96%, 69% overall yield from **2**). Similarly, under the same conditions, **3b** afforded **4d** then **4e** (Table 1). The new route to **4c** described herein is a significant improvement over recently patented routes [6,10,11] in which **4c** is synthesized in 8 steps (with 1,2:3,5-di-*O*-isopropylidene-6-thio-α-D-glucofuranose as key intermediate), in overall yield of 35% from the same material **2** as we have used.

In order to obtain the new 3-thio analogue of **1**, the starting 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5a**) was converted into iodide **5b** [14] and allowed to react with *N,N*-dimethylaminopropanethiol and NaOMe as previously described [12] to give thioether **6a**, isolated in high yield (96%). Extension of the reaction to various *N,N*-dialkylaminoalkanethiols resulted in formation of the corresponding thioethers **6b–d** in excellent yields (Table 1). Selective hydrolysis of the 5,6-isopropylidene group with M HCl was undertaken on **6a** to afford the 3-thio analogue (**7**) of Amiprilose (82%, 55% overall yield from **5a**).

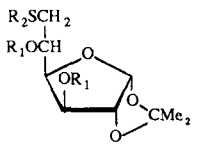
The present study provides a convenient method for the preparation of thio derivatives of Amiprilose with potential anti-inflammatory activities whenever the required tertiary aminoalkanethiols are commercially or readily available. The new products described have been submitted for biological evaluation.



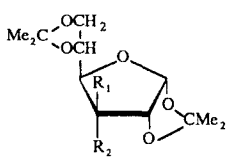
**1** $R = (CH_2)_3\text{-}NMe_2$
(Amiprilose)



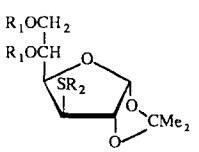
**2** $R_1 = H$ , $R_2 = OH$
**3a** $R_1 = H$ , $R_2 = I$
**3b** $R_1 = Ac$ , $R_2 = I$



**4a** $R_1 = CMe_2$ , $R_2 = (CH_2)_3\text{-}NMe_2$
**4b** $R_1 = Ac$ , $R_2 = (CH_2)_3\text{-}NMe_2$
**4c** $R_1 = H$ , $R_2 = (CH_2)_3\text{-}NMe_2$
**4d** $R_1 = Ac$ , $R_2 = (CH_2)_3\text{-}NEt_2$
**4e** $R_1 = H$ , $R_2 = (CH_2)_3\text{-}NEt_2$



**5a** $R_1 = OH$ , $R_2 = H$
**5b** $R_1 = H$ , $R_2 = I$



**6a** $R_1 = CMe_2$ , $R_2 = (CH_2)_3\text{-}NMe_2$
**6b** $R_1 = CMe_2$ , $R_2 = (CH_2)_3\text{-}NEt_2$
**6c** $R_1 = CMe_2$ , $R_2 = (CH_2)_2\text{-}NMe_2$
**6d** $R_1 = CMe_2$ , $R_2 = (CH_2)_2\text{-}NEt_2$
**7** $R_1 = H$ , $R_2 = (CH_2)_3\text{-}NMe_2$

## 1. Experimental

*General methods.*—Melting points were determined on a digital melting-point apparatus (Electrothermal) and are uncorrected. Optical rotations for solutions in $CHCl_3$ were recorded with a digital polarimeter DIP-370 (JASCO) at 25 °C. NMR spectra were obtained on a Bruker WB-300 spectrometer at 300.133 and 75.45 MHz (solutions in

$CDCl_3$, internal $Me_4Si$). Electrospray mass spectrometry (ES + ) was carried out on a ZAB-EQ (VG Analytical, Manchester, UK) instrument. TLC was performed on Silica Gel $F_{254}$ (Merck) and detection by UV light at 254 nm or by charring with phosphomolybdic–$H_2SO_4$ reagent. Column chromatography was effected on Silica Gel 60 (Merck, 230 mesh). Acetone, hexane, ether, acids, and industrial grade bases were supplied by CINAS. Microanalyses were performed by the Service Central de Microanalyses du Centre National de la Recherche Scientifique (Vernaison, France).

2-*N*,*N*-Dimethylaminoethan-1-thiol and 2-*N*,*N*-diethylaminoethan-1-thiol are commercially available (Aldrich). 3-*N*,*N*-Dimethylaminopropan-1-thiol and 3-*N*,*N*-diethylaminopropan-1-thiol were synthesized according to previous methods in two steps [13] from *N*,*N*-dimethyl-3-chloropropylamine hydrochloride (71% overall yield) and in three steps [16] from 3-*N*,*N*-diethylaminopropan-1-ol (49% overall yield) respectively.

*6-Deoxy-6-iodo-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**3a**).—A solution of iodine (2.8 g, 11.0 mmol) in dry DMF (30 mL) was added dropwise into a stirred solution of **2** (2.0 g, 9.1 mmol) and $PPh_3$ (3.6 g, 13.7 mmol) in dry DMF (30 mL) cooled at −10 °C. The mixture was left overnight at room temperature, neutralized with satd aq $NaHCO_3$, the iodine reduced with satd aq $(NH_4)_2S_2O_3$, and the mixture was then concentrated. The residue was dilute with $CHCl_3$ and washed twice with water. The resulting aqueous phase was extracted with $CHCl_3$ and the combined organic phase dried over $Na_2SO_4$ and concentrated. Chromatography of the residue (2:3 hexane–$Et_2O$) gave pure **3a** which crystallized from $Et_2O$ as a white solid (2.5 g, 83%): mp 92–94 °C; $[\alpha]_D$ −11° (*c* 1.1, $CHCl_3$); $^1$H NMR: δ 5.86 (d, $J_{1,2}$ 3.5 Hz, H-1), 4.45 (d, $J_{2,3}$ 0 Hz, H-2), 4.28 (s broad, H-3), 3.97 (dd, $J_{3,4}$ 2.5, $J_{4,5}$ 7.3 Hz, H-4), 3.86 (s, OH), 3.76 (m broad, H-5), 3.66 (s, OH), 3.47 (dd, $J_{5,6a}$ 3.3, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.31 (dd, $J_{5,6b}$ 6.8, $J_{6a,6b}$ 10.5 Hz, H-6b), 1.41, 1.24 (2 s, $CMe_2$); $^{13}$C NMR: δ 112.0 (*C*$Me_2$), 104.9 (C-1), 85.1 (C-2), 81.8 (C-4), 74.7 (C-3), 69.0 (C-5), 26.8, 26.3 (2 C*Me*$_2$), 11.9 (C-6). Anal. Calcd for $C_9H_{15}IO_5$ (330.12): C, 32.75; H, 4.58; I, 38.44. Found: C, 33.41; H, 4.57; I, 36.49.

*3,5-Di-*O*-acetyl-6-deoxy-6-iodo-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**3b**).—Conventional acetylation of crude **3a** was effected in 3:1 $Ac_2O$–$Et_3N$ for 1 h at room temperature. The resulting mixture was evaporated, diluted with $Et_2O$, and washed twice with water. The organic phase was dried over $Na_2SO_4$ and evaporated. Crude material was purified by column chromatography (9:1 hexane–$Et_2O$) to give **3b** as a colorless solid (81%): mp 74–75 °C, lit. 75 °C [17]; $[\alpha]_D$ −19.8° (*c* 1.07, $CHCl_3$); $^1$H NMR: δ 5.79 (d, $J_{1,2}$ 3.6 Hz, H-1), 5.22 (d, $J_{2,3}$ 0, $J_{3,4}$ 2.9 Hz, H-3), 4.60 (m, H-5), 4.37 (d, $J_{1,2}$ 3.6, $J_{2,3}$ 0 Hz, H-2), 4.24 (dd, $J_{3,4}$ 2.9, $J_{4,5}$ 9.2 Hz, H-4), 3.46 (dd, $J_{5,6a}$ 3.1, $J_{6a,6b}$ 11.2 Hz, H-6a), 3.33 (dd, $J_{5,6b}$ 4.9, $J_{6a,6b}$ 11.2 Hz, H-6b), 1.94 (s, 2 MeCOO), 1.42, 1.20 (2 s, $CMe_2$); $^{13}$C NMR: δ 169.2 (2 COO), 112.6 (*C*$Me_2$), 104.9 (C-1), 83.3 (C-2), 79.6 (C-4), 74.3 (C-3), 67.1 (C-5), 26.8, 26.3 (2 C*Me*$_2$), 20.7, 20.5 (2 *Me*COO), 7.4 (C-6). Anal. Calcd for $C_{13}H_{19}IO_7$ (414.19): C, 37.70; H, 4.62; I, 30.64. Found: C, 37.44; H, 4.61; I, 30.64.

*General procedure for the preparation of type* **4** *compounds.*—A solution of **3b** (3.0 g, 7.2 mmol) in $Me_2CO$ (20 mL) was added dropwise to a stirred solution of $K_2CO_3$ (2.0 g, 14.5 mmol) and thiol (14.5 mmol) in water (20 mL). The mixture was kept at room temperature overnight (monitoring by TLC, 4:4:1 hexane–$Et_2O$–$Et_3N$), and $Me_2CO$ was evaporated off. After extraction with $CH_2Cl_2$, the organic phase was

Table 2
$^1$H NMR data for the *N,N*-substituted aminothioether derivatives measured at 300.133 MHz

| Compound | Chemical shifts (d) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | H-1 | H-2 | H-3 | H-4 | H-5 | H-6a[a] | H-6b | | $CMe_2$ | | | Others |
| **4b** | 5.73 | 4.30 | 5.16 | 4.26 | 5.02 | 2.88 | 2.52 | | 1.35 | 1.14 | | 2.41 (H-1′), 2.15 (H-3′), 2.03(2) (NMe), 1.88, 1.83 (MeCOO), 1.55 (H-2′) |
| **4c** [c] | 5.77 | 4.33 | 4.16 | 3.86 | 3.92 | 2.73 | 2.54 | | 1.31 | 1.14 | | 5.07(2) (OH), 2.49 (H-1′), 2.26 (H-3′), 2.07(2) (NMe), 1.61 (H-2′) |
| **4d** | 5.73 | 4.32 | 5.14 | 4.24 | 5.00 | 2.90 | 2.54 | | 1.34 | 1.13 | | 2.80(2) ($NCH_2$), 2.72 (H-1′), 2.43 (H-3′), 1.87, 1.84 (MeCOO), 1.68 (H-2′), 1.00(2) ($NCH_2CH_3$) |
| **4e** | 5.76 | 4.33 | 4.16 | 3.85 | 3.94 | 2.73 | 2.54 | | 1.30 | 1.14 | | 4.58(2) (OH), 2.47–2.34 (H-1′, H-3′, $NCH_2$), 1.58 (H-2′), 0.86(2) ($NCH_2CH_3$) |
| **6a** | 5.66 | 4.53 | 3.19 | 4.04 | 4.19 | 3.95 | 3.81 | 1.35 | 1.26 | 1.20 | 1.16 | 2.60–2.50 [b] (H-1′), 2.21 (H-3′), 2.06(2) (NMe), 1.62 (H-2′) |
| **6b** | 5.64 | 4.51 | 3.17 | 4.02 | 4.17 | 3.93 | 3.79 | 1.33 | 1.23 | 1.17 | 1.14 | 2.51 (H-1′), 2.35 (H-3′), 2.34(2) ($NCH_2$), 1.58 (H-2′), 0.84(2) ($NCH_2CH_3$) |
| **6c** | 5.70 | 4.56 | 3.24 | 4.06 | 4.24 | 3.98 | 3.85 | 1.38 | 1.28 | 1.22 | 1.18 | 2.70–2.60 [b] (H-1′), 2.45–2.35 [b] (H-2′), 2.13 (NMe), |
| **6d** | 5.69 | 4.58 | 3.28 | 4.07 | 4.25 | 3.99 | 3.86 | 1.39 | 1.29 | 1.23 | 1.19 | 2.67, 2.61 [b] (H-1′), 2.60, 2.57 [b] (H-2′), 2.43(2) ($NCH_2$), 0.91(2) ($NCH_2CH_3$) |
| **7** | 5.70 | 4.59 | 3.23 | 4.11 | 3.84 | 3.69 | 3.51 | | 1.37 | 1.19 | | 4.50(2) (OH), 2.59 (H-1′), 2.44, 2.16 [b] (H-3′), 2.10 (NMe), 1.66 (H-2′) |
| | Coupling constants (Hz) | | | | | | | | | | | |
| | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5}$ | $J_{5,6a}$ | $J_{5,6b}$ | $J_{6a,6b}$ | | | | | Others |
| **4b** | 3.6 | 0 | 2.9 | 9.4 | 2.9 | 7.3 | 14.5 | | | | | $J_{H\text{-}1',H\text{-}2'} = 7.4$, $J_{H\text{-}2',H\text{-}3'} = 7.2$ |
| **4c** | 3.7 | 0 | 2.4 | 6.6 | 3.3 | 7.5 | 14.0 | | | | | $J_{H\text{-}1',H\text{-}2'} = 7.1$, $J_{H\text{-}2',H\text{-}3'} = 7.2$ |
| **4d** | 3.6 | 0 | 2.8 | 9.4 | 2.8 | 7.2 | 14.5 | | | | | $J_{H\text{-}2',H\text{-}3'} = 6.8$, $J_{NCH_2,NCH_2CH_3} = 7.2$ |
| **4e** | 3.6 | 0 | 2.2 | | 3.3 | 7.7 | 13.9 | | | | | $J_{H\text{-}1',H\text{-}2'} = 7.0$, $J_{H\text{-}2',H\text{-}3'} = 7.1$, $J_{NCH_2,NCH_2CH_3} = 7.1$ |
| **6a** | 3.5 | 0 | 3.7 | 8.6 | 6.2 | 5.2 | 8.5 | | | | | $J_{H\text{-}2',H\text{-}3'} = 7.1$ |
| **6b** | 3.5 | 0 | 3.7 | 8.6 | 6.2 | 5.2 | 8.5 | | | | | $J_{H\text{-}1',H\text{-}2'} = 7.4$, $J_{H\text{-}2',H\text{-}3'} = 7.2$, $J_{NCH_2,NCH_2CH_3} = 7.2$ |
| **6c** | 3.5 | 0 | 3.7 | 8.7 | 6.1 | 5.2 | 8.6 | | | | | |
| **6d** | 3.5 | 0 | 3.7 | 8.7 | 6.1 | 5.2 | 8.6 | | | | | $J_{NCH_2,NCH_2CH_3} = 7.2$ |
| **7** | 3.6 | 0 | 3.8 | 9.2 | 3.2 | 6.3 | 11.3 | | | | | $J_{H\text{-}1',H\text{-}2'} = 6.8$ |

[a] The signal of higher chemical shift of $CH_2$-6 is assigned to H-6a.
[b] Strongly overlapped signals.
[c] Lit. [11]: $\delta_{H\text{-}1} = 5.95$, $\delta_{H\text{-}2} = 4.55$, $\delta_{NMe} = 2.2$, $\delta_{CMe_2} = 1.34$, 1.32.

Table 3
$^{13}C$ NMR data for the *N,N*-substituted aminothioether derivatives measured at 75.45 MHz

| Compound | Chemical shifts ($\delta$) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | $CMe_2$ | | | $CMe_2$ | | | Others |
| **4b** | 104.9 | 83.2 | 74.5 | 78.6 | 67.9 | 34.4 | 112.2 | | | 26.6 | 26.1 | | 169.3(2) (COO), 58.3 (C-3′), 45.2(2) (NMe), 30.4 (C-1′), 27.4 (C-2′), 20.6, 20.5 (MeCOO) |
| **4c** | 104.7 | 85.3 | 74.8 | 81.3 | 69.1 | 36.8 | 111.3 | | | 26.7 | 26.1 | | 57.7 (C-3′), 44.9(2) (NMe), 30.2 (C-1′), 26.9 (C-2′) |
| **4d** | 104.8 | 83.2 | 74.4 | 78.5 | 67.6 | 34.2 | 112.1 | | | 26.5 | 26.0 | | 169.4(2) (COO), 49.4 (C-3′), 45.6(2) ($NCH_2$), 29.5 (C-1′), 22.9 (C-2′), 20.4(2) (MeCOO), 8.2(2) ($NCH_2CH_3$) |
| **4e** | 104.7 | 85.2 | 74.5 | 81.3 | 68.7 | 36.7 | 111.2 | | | 26.6 | 26.0 | | 50.9 (C-3′), 46.2(2) ($NCH_2$), 30.4 (C-1′), 26.3 (C-2′), 10.8(2) ($NCH_2CH_3$) |
| **6a** | 104.6 | 85.7 | 51.6 | 80.1 | 73.7 | 67.4 | 111.4 | 108.9 | 26.6 | 26.4 | 26.0 | 25.1 | 58.0 (C-3′), 45.2(2) (NMe), 29.5 (C-1′), 27.2 (C-2′) |
| **6b** | 104.6 | 85.7 | 51.6 | 80.1 | 73.8 | 67.4 | 111.4 | 108.9 | 26.6 | 26.4 | 26.1 | 25.1 | 51.3 (C-3′), 46.7(2) ($NCH_2$), 29.8 (C-1′), 26.9 (C-2′), 11.7(2) ($NCH_2CH_3$) |
| **6c** | 104.7 | 85.9 | 52.6 | 80.2 | 73.8 | 67.5 | 111.6 | 109.1 | 26.7 | 26.5 | 26.1 | 25.2 | 58.9 (C-2′), 45.1(2) (NMe), 30.1 (C-1′) |
| **6d** | 104.6 | 85.9 | 51.9 | 80.3 | 73.8 | 67.5 | 111.6 | 109.1 | 26.7 | 26.5 | 26.1 | 25.2 | 52.7 (C-2′), 46.9(2) ($NCH_2$), 29.8 (C-1′), 11.8(2) ($NCH_2CH_3$) |
| **7** | 104.9 | 85.9 | 52.4 | 79.3 | 70.1 | 64.6 | 111.6 | | | 26.5 | 26.2 | | 57.4 (C-3′), 44.0(2) (NMe), 30.2 (C-1′), 26.4 (C-2′) |

washed with satd aq $NH_4Cl$, dried over $Na_2SO_4$, and concentrated. Crude material was purified by column chromatography with a solvent gradient (hexane–$Et_2O$) containing 2% $Et_3N$, yielding the desired compounds **4b** and **4d** (Table 1 for yields and physicochemical data; Tables 2 and 3 for $^1H$ and $^{13}C$ NMR data).

*General procedure for deacetylation.*—To a solution of thioether (5 mmol) in dry MeOH (10 mL) was added NaOMe (27 mg, 0.5 mmol) and the mixture was kept for 3 h at room temperature (monitoring by TLC, 4:4:1 hexane–$Me_2CO$–$Et_3N$). After neutralization with Amberlyst 15 $H^+$ resin and filtration of the resin, the solvent was removed by evaporation. Flash chromatography of the residue (3:7 hexane–$Me_2CO$ containing 5% $Et_3N$) yielded the desired compounds **4c** and **4e** (Table 1 for yields and physicochemical data; Tables 2 and 3 for $^1H$ and $^{13}C$ NMR data).

*General procedure for the preparation of type* **6** *compounds.*—*N,N*-Dialkylaminoalkanethiol and NaOMe were allowed to react with **5b** as previously described [12] (monitoring by TLC, 1:4:1 hexane–$Et_2O$–$Et_3N$). Crude material was purified by column chromatography with a solvent gradient (hexane–$Et_2O$) containing 2% $Et_3N$, yielding the desired compounds **6a–d** (Table 1 for yields and physicochemical data; see Tables 2 and 3 for $^1H$ and $^{13}C$ NMR data).

*3-S-(3-N,N-dimethylaminopropyl)-1,2-O-isopropylidene-3-thio-α-D-glucofuranose* (**7**).—Compound **6a** (4.40 g, 12.2 mmol) was dissolved in water, and aq HCl (1 M) was added dropwise, adjusting the pH to $1.0 \pm 0.2$. Stirring was maintained for 150 min at room temperature, and the resulting solution was made alkaline with 30% NaOH to pH $10.5 \pm 0.2$. The aqueous mixture was then extracted twice with $CHCl_3$, and the combined organic phase was dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by column chromatography with a solvent gradient (hexane–$Me_2CO$) containing 2% $Et_3N$ to yield **7** (3.21 g, 10.0 mmol, 82%). Anal. Calcd for $C_{14}H_{27}NO_5S$ (321.44): C, 52.31; H, 8.47; N, 4.36; S, 9.97. Found: C, 51.80; H, 8.43; N, 4.26; S, 9.46.

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