Synthesis of ω-Substituted Alkanethiols and (Bromomethyl)methylthiomalonates

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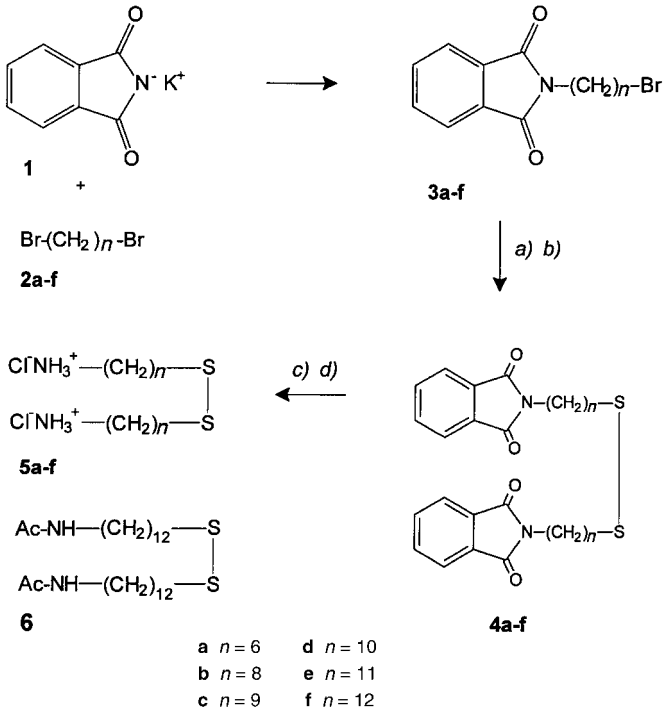
Several multifunctional derivatives of methylthiomalonic acid (=2-(thiocarboxy)acetic acid), *i.e.* **20a**,**b**, **21**, **22a,b**, and **24**, were prepared from thiols bearing a functionalized head group, *i.e.* from **9a**,**b**, **12**, and **16d**,**f** (*Schemes 4* and *5*). The association constants of the two dithio podands **8b** and **11** with K^+ were determined.

Introduction. – For development of models of the coenzyme-B_{12}-dependent methylmalonyl-CoA mutase, we have prepared a variety of (bromomethyl)methylthiomalonates (=2-(bromomethyl)-2-methyl-3-oxo-3-(alkylthio)propanoates) with head groups for molecular recognition. These model substrates are to be used to investigate the efficiency of the methylmalonyl-succinyl rearrangement when the substrate and the vitamin-B_{12} molecule are held together by noncovalent interactions. The concept of enhancing the rearrangement by peripheral association of appropriate groups is based on the idea that enzymes or enzyme-coenzyme complexes must recognize their substrates and associate with them through noncovalent bonds to provide the orientation and proximity necessary for catalysis [1–4]. Hitherto, we have reported a hydrophobic model, where lipophilic alkane chains are used for the association between the methylmalonyl moiety and the vitamin B_{12}, appropriately modified in the periphery, and two models based on association in aprotic solvents between an A·T and a C·G base pair, respectively [5–8]. Enhanced rearrangement has been observed for the hydrophobic and the A·T mode [5][6]. In further persuit of vitamin-B_{12}-related concepts for molecular recognition between methylmalonyl substrates and the catalyst, we considered the association between polyether ('podand') units mediated by cations as well as the interaction between carbohydrate-derived units. We report here the preparation of alkanethiols bearing a polyether moiety or a pentahydroxyhexanoyl head group as well as the efficient synthesis of thioesters thereof. First results for the binding constants between two polyethers with alkali cations are reported.

Alkanethiols with Terminal Polyether and Glyconoyl Groups. – ω-Aminoalkanethiols are used as central building blocks, to which the head groups for molecular recognition are attached *via* acylation of the amino group. The thiomalonates are subsequently obtained from the modified alkanethiols by esterification. The homologuous series of *N*-(ω-bromoalkyl)phthalimides **3a**–**f** with C_6 and C_8 to C_{12} alkyl chains were prepared from **1** and **2** in 56–72% yield (*Scheme 1*). The original

Scheme 1



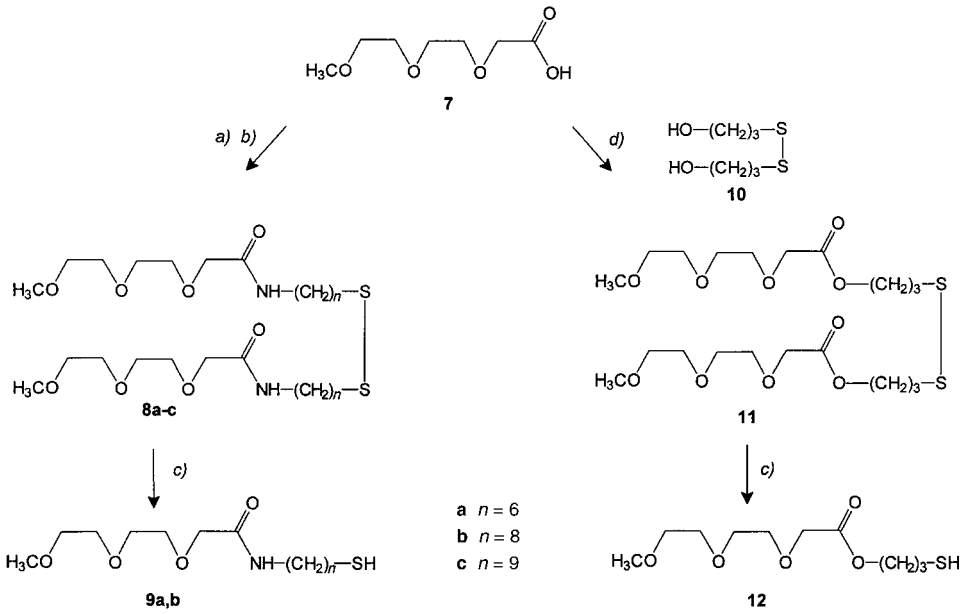
a) $Na_2S_2O_3$, MeOH/H_2O. *b*) I_2. *c*) H_2N-NH_2, EtOH. *d*) HCl.

procedure [9] was modified for the longer alkyl chains (C_{10} to C_{12}) and gave the compounds **3d**–**f** as low-melting, colorless solids. The (dithiodialkanediyl)bis[phthalimides] **4a**–**f** were obtained by treatment of (bromoalkyl)phthalimides **3a**–**f** with $Na_2S_2O_3$ and oxidation of the *Bunte* salts with I_2 in 70–80% yield. The compounds **3b**–**f** show the well-known behavior of alternating melting points for homologuous series of substituted alkanes [10][11]. The stable and easily isolated (dithiodialkanediyl)-bis[ammonium chlorides] **5a**–**f** were obtained in 60–80% yield by treatment of the phthalimides **4a**–**f** with hydrazine followed by addition of hydrochloric acid. The bis[ammonium chloride] **5f** was also characterized as the bis-amide **6**.

Treatment of the acid chloride of 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (**7**) with the bis[ammonium chlorides] **5a**–**c** gave the desired (dithiodialkanediyl)bis[amides] **8a**–**c** in 50% yield (*Scheme 2*). The synthesis of the dithio derivative **11**, bearing an ester rather than an amide function as a link between the tris(oxyethanediyl) moiety and the thio group, was performed by reaction of 3,3′-dithiobis[propanol] (**10**; obtained from 3-bromopropanol [12]) with the acid chloride of **7**. The dithio derivatives **8a**,**b** and **11** were reduced with Zn in AcOH to the thiols **9a**,**b** and **12** in almost quantitative yield.

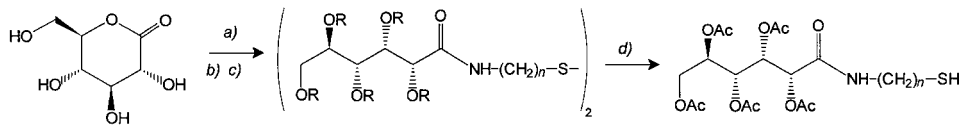
The formation of the thiols incorporating a gluconoyl moiety was achieved by the reaction of the (dithiodialkanediyl)bis[ammonium chlorides] **5b** ($n = 8$) or **5f** ($n = 12$) with D-glucono-1,5-lactone (**13**) affording the dithio derivatives **14b** and **14f** which were

Scheme 2



a) $CHCl_2OMe$ or SO_2Cl_2. *b*) **5a**–**c**, Et_3N. *c*) Zn, AcOH. *d*) **10**, $CHCl_2OMe$, CH_2Cl_2, Et_3N.

Scheme 3



a) **5b** ($n = 8$) or **5f** ($n = 12$), MeOH, reflux. *b*) **5d** ($n = 10$), MeOH; Ac_2O, pyridine. *c*) Ac_2O, pyridine for **14f**. *d*) Zn, AcOH, and **15d** or **15f**.

insoluble in most organic solvents[1]) (*Scheme 3*). The bis-amides **14b** and **14f** may be considered to be bolaamphiphiles [13]. Acetylation of **14f** with Ac_2O in pyridine gave the dithio derivative **15f**. Treatment of **5d** with **13** afforded a crude dithio derivative, which was not isolated but directly acetylated to **15d**. Subsequent reduction of **15d** and **15f** with Zn gave the thiols **16d** and **16f** in 53 and 92% yield, respectively.

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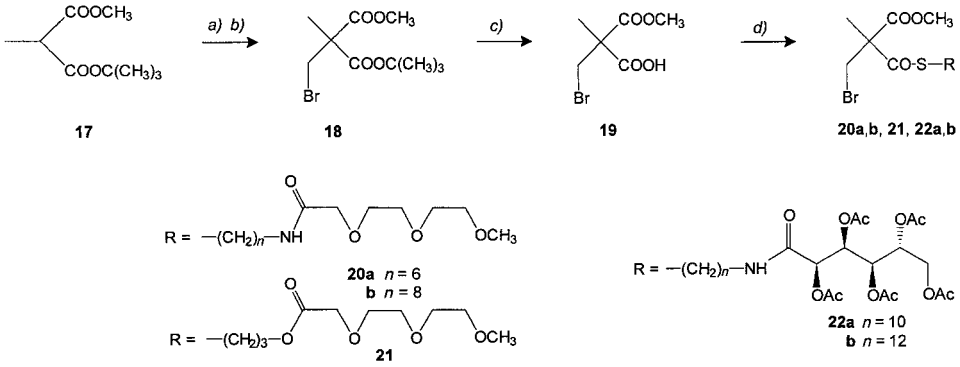
[1]) Upon heating to 150–153°, compound **14f** developed a smectic mesophase (probably smectic A) and decomposed below the clearing point at $T > 195°$. Compound **14b** decomposed at 166–168°, but developed a mesophase upon quick cooling to 155–160°. We thank Prof. *R. Miethchen*, University of Rostock, for this analysis.

Thioesters. – The *tert*-butyl methyl methylmalonate (**17**), prepared as described [14–16], afforded the bromomethyl derivative **18** by deprotonation with NaH in the presence of DMPU (3,4,5,6-tetrahydro-1,3-dimethylpyrimidin-2(1*H*)-one), followed by alkylation with methylene bromide [17] (*Scheme 4*). The *tert*-butyl ester was then hydrolyzed by treatment with CF_3COOH to give the crude monoacid **19**. Due to the propensity of acid **19** to undergo fragmentation with formation of methyl methacrylate in the presence of base [18], the general methods to generate thioesters from acids activated with DCC (dicyclohexylcarbodiimide), phosphorodichloridates [19], or carbonylbis[1*H*-imidazoles] [20] were not effective. However, addition of the acyl chloride, obtained from crude **19** by treatment with $SOCl_2$ or $CHCl_2OMe$, to the thiols in CH_2Cl_2 at 0° afforded the thioesters **20a** (80%), **20b** (40%), **21** (65%), **22a** (47%), and **22b** (56%) in moderate to good yield.

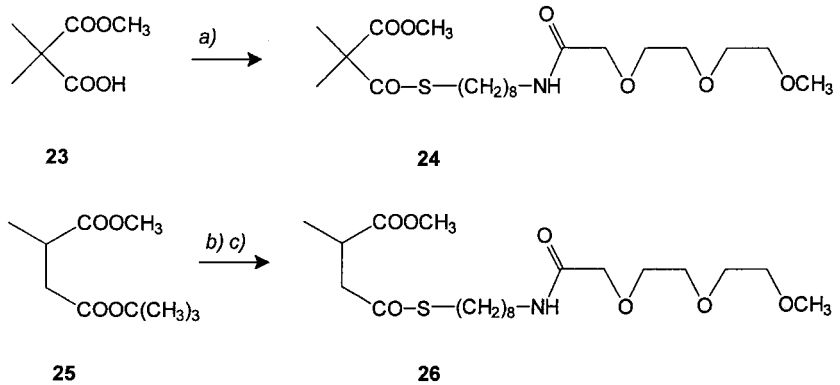
Scheme 4



a) NaH, HMPT. *b*) CH_2Br_2. *c*) CF_3COOH. *d*) $SOCl_2$ or $CHCl_2OMe$, then RSH **9a**,**b**, **12**, **16d**, or **16f**, Et_3N, CH_2Cl_2, r.t.

By the same method, the dimethylmalonate derivative **24** and the succinate **26** were prepared in 44 and 48% yield from **23** and **25**, respectively (*Scheme 5*).

Scheme 5



a) $CHCl_2OMe$, **9b**, Et_3N, CH_2Cl_2. *b*) CF_3COOH. *c*) $CHCl_2OMe$, **9b**, Et_3N, CH_2Cl_2.

Binding of Polyethers to Alkali Cations. – Chelation of alkali cations by the tris(oxyethanediyl) group of **20a**, **20b**, and **21** and those of corresponding vitamin-B_{12} derivatives [21] forms the basis of the 'podand model' mentioned above. To establish basic features of the association between the substrates and the vitamin B_{12} derived catalyst, both bearing a podand head group, we investigated the ability of the dithio derivatives **8b** and **11** to bind Na^+ and K^+. The association constants were determined in $D_2O/CDCl_3$ with the picrate method [22][23]. Podand **8b** binds K^+ with $K_{ass} = 3.6 \cdot 10^3$ M^{-1} and Na^+ with $K_{ass} = 4.2 \cdot 10^3$ M^{-1}. Podand **11** binds K^+ with $K_{ass} = 1.3 \cdot 10^3$ M^{-1}. Whether the observed associations involve one or two polyether moieties was not determined. Electron-spray MS results also suggest an association of the polyether with cations. For **21**, a ESI-MS peak m/z 465.20 corresponding to the thioester [**21** + Li^+] was observed.

Concluding Remarks. – For the development of further models for the coenzyme-B_{12}-dependent methylmalonyl mutase incorporating molecular recognition, the (bromomethyl)thiomalonates **20a**,**b**, **21**, **24**, and **25** as well as **22a**,**b** were prepared in an efficient way. The gluconoyl moiety of **22a**,**b** was chosen for a potential interaction between the polyhydroxy head groups grafted to the vitamin-B_{12}-derived catalyst [16][24] and the model substrates **22a**,**b**. For the 'podand model', the substrates **20a**,**b** and **21** bearing a tris(oxyethanediyl) moiety were prepared. Under control of alkali cations, the podand head groups of the substrates should interact with the complementary polyether group attached to the vitamin-B_{12}-derived catalyst [2]. Exploring this potential, the association of the polyethers **8b** and **11** with alkali cations was investigated using the picrate extraction method.

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Experimental Part

General. The reactions were carried out with reagents and solvents of *Fluka* (*puriss.* grade). For workup, the reaction mixture was poured onto ice-water, the aq. phase extracted with the appropriate solvent, and the combined org. phase washed with sat. $NaHCO_3$ soln. and brine, dried ($MgSO_4$) and evaporated. Flash chromatography (FC): distilled commercial-grade solvents, silica gel (30–60 μm) from *Baker* (analyzed reagents). TLC: *Merck-F-254* precoated sheets, visualization by 5% phosphomolybdic acid hydrate/EtOH or by UV. UV/VIS Spectra: *Hewlett Packard 8451 A*; λ_{max} in nm. IR Spectra: *Perkin-Elmer PE 782*; $CHCl_3$ soln. in 0.2-mm-path NaCl cells; in cm^{-1}. NMR Spectra: if not stated otherwise, in $CDCl_3$ at 300 MHz (^{1}H) and 75 MHz (^{13}C), *Bruker AC-300* instrument; δ in ppm rel. to the $CDCl_3$ signal (δ(H) 7.24, δ(C) 77.00), J in Hz; ^{13}C multiplicities from DEPT spectra. MS: *Varian MAT CH-7A*, 70 eV; in m/z (%). LSI-MS: *Fision Autospec-Q*, acceleration voltage 8 kV, ionization Cs^- (32 keV), matrix as indicated; in m/z (%). ESI-MS: *Fisions Instrument VG Platform II*, positive-ion measurements (3.5 kV), negative-ion measurements (2.5 kV); in m/z (%). Acronyms: DMF, dimethylformamide; DMPA, *N*,*N*-dimethylpyridine-4-amine; EDC, *N*-ethyl-*N'*-[3-(dimethylamino)propyl]carbodiimide-hydrochloride; HMPT, hexamethylphosphoric triamide.

N-*(ω-Bromoalkyl)phthalimides* **3a**–**f**. The procedure [9] was modified: A suspension of potassium phthalimide (**1**; 4.76 g, 25 mmol) in DMF (25 ml) was slowly added to the 1,ω-dibromoalkane **2a**–**f** (103 mmol) in DMF (10 ml) under Ar. After refluxing for 4 h, the KBr formed was removed by filtration, the DMF evaporated at 65°, 50 Torr, and the residue purifid by FC (hexane/Et_2O 3:1). Recrystallization from hexane/Et_2O gave pure product.

N-*(6-Bromohexyl)phthalimide* (**3a**) was prepared as reported [9]: R_f (hexane/Et_2O 3:1): 0.30. M.p. 55° ([9]: 57°). IR (KBr): 1780*vs*, 1730*vs*, 1480*s*, 1440*s*, 1400*vs*, 1370*vs*, 1340*vs*, 900*s*, 980*s*. ^{1}H-NMR: 1.40–1.50 (2*m*, 4 H); 1.65–1.75 (*m*, 2 H); 1.81–1.91 (*m*, 2 H); 3.40 (*t*, *J* = 7.17, 2 H); 3.68 (*t*, 2 H); 7.70–7.74 (*m*, 2 H); 7.80–7.99 (*m*, 2 H). ^{13}C-NMR: 26.02 (*t*); 27.70 (*t*); 28.41 (*t*); 32.60 (*t*); 33.64 (*t*); 37.82 (*t*); 123.18 (*d*); 132.14 (*s*); 133.87 (*d*); 168.42 (*s*). MS (calc. for $C_{14}H_{16}BrNO_2$, 310.19): 311 (34, $[M+2]^+$), 310 (5), 309 (35, $M^+(^{79}Br)$), 230 (13), 161 (64), 160 (100), 148 (13), 133 (11), 130 (17), 104 (13).

N-*(8-Bromooctyl)phthalimide* (**3b**): Yield 5.3 g (62.7%). R_f (hexane/Et_2O 1:2). 0.59. M.p. 50° ([11]: 49°). IR (KBr): 1770*s*, 1700*vs*, 1465*s*, 1435*s*, 1400*s*, 1370*s*, 1065*s*, 1055*s*. ^{1}H-NMR: 1.25–1.42 (*m*, 8 H); 1.62–170 (*m*, 2 H); 1.70–1.89 (*m*, 2 H); 3.39 (*t*, *J* = 7.00, 2 H); 3.68 (*t*, *J* = 7.35, 2 H); 7.69–7.74 (*m*, 2 H); 7.81–7.86 (*m*, 2 H). ^{13}C-NMR: 26.71 (*t*); 28.06 (*t*); 28.53 (*t*); 28.58 (*t*); 28.95 (*t*); 32.74 (*t*); 33.93 (*t*); 37.99 (*t*); 123.17 (*d*); 132.19 (*s*); 133.85 (*d*); 168.47 (*s*). MS (calc. for $C_{16}H_{20}BrNO_2$, 338.25): 339 (48), 337 (50), 258 (20), 174 (15), 161 (72), 160 (100), 148 (19), 133 (15), 130 (23).

N-*(9-Bromononyl)phthalimide* (**3c**): Yield 6.65 g (75.5%). Colorless, lancet-like crystals. R_f (hexane/Et_2O 3:1) 0.26. M.p. 31°. IR (KBr): 1772*s*, 1714*vs*, 1466*s*, 1438*s*, 1398*s*, 1370*s*, 1050*s*, 880*s*, 720*s*. ^{1}H-NMR: 1.25–1.45 (*m*, 10 H); 1.62–1.74 (*m*, 2 H); 1.71–1.89 (*m*, 2 H); 3.40 (*t*, *J* = 7.00, 2 H); 3.69 (*t*, *J* = 7.35, 2 H); 7.65–7.74 (*m*, 2 H); 7.86–7.90 (*m*, 2 H). ^{13}C-NMR: 26.77 (*t*); 28.11 (*t*); 28.55 (*t*); 28.64 (*t*); 29.03 (*t*); 29.24 (*t*); 32.79 (*t*); 33.94 (*t*); 38.01 (*t*); 123.14 (*d*); 132.19 (*s*); 133.83 (*d*); 168.42 (*s*). MS: 354 (33), 353 (99), 352 (35), 351 (100), 272 (29), 175 (19), 161 (66), 160 (72), 148 (41), 130 (37), 104 (24). Anal. calc. for $C_{17}H_{22}BrNO_2$ (352.27): C 57.96, H 6.29, N 3.98; found: C 58.28, H 6.35, N 3.92.

N-*(10-Bromodecyl)phthalimide* (**3d**): Yield 5.68 g (63%). Colorless, lancet-like crystals. R_f (hexane/Et_2O 3:1) 0.29. M.p. 57° ([11]: 56°). IR (KBr): 1780*s*, 1730*vs*, 1475*s*, 1440*s*, 1400*vs*, 1375*s*, 1065*s*, 540*s*. ^{1}H-NMR: 1.21–1.45 (*m*, 12 H); 1.60–1.74 (*m*, 2 H); 1.76–1.91 (*m*, 2 H); 3.40 (*t*, *J* = 7.0, 2 H); 3.68 (*t*, *J* = 7.35, 2 H); 7.68–7.73 (*m*, 2 H); 7.82–7.90 (*m*, 2 H). ^{13}C-NMR: 26.63 (*t*); 28.15 (*t*); 28.58 (*t*); 28.71 (*t*); 29.11 (*t*); 29.34 (*t*); 32.84 (*t*); 34.00 (*t*); 38.01 (*t*); 123.16 (*d*); 132.21 (*s*); 133.84 (*d*); 168.47 (*s*). MS (calc. for $C_{18}H_{24}BrNO_2$, 366.30): 367 (38, $[M+2]^+$), 366 (7), 365 (39, $M^+(^{79}Br)$), 286 (10), 174 (14), 161 (70), 160 (100), 148 (20), 130 (22).

N-*(11-Bromoundecyl)phthalimide* (**3e**): Yield 16.08 g (96%). Colorless, lancet-like crystals. R_f (hexane/Et_2O 1:1) 0.41. M.p. 48°. IR (KBr): 1770*s*, 1720*vs*, 1435*s*, 1395*vs*, 1370*s*, 720*s*. ^{1}H-NMR (200 MHz): 1.14–1.45 (*m*, 14 H); 1.60–1.74 (*m*, 2 H); 1.76–1.90 (*m*, 2 H); 3.37 (*t*, *J* = 6.85, 2 H); 3.64 (*t*, *J* = 7.3, 2 H); 7.64–7.72 (*m*, 2 H); 7.77–7.84 (*m*, 2 H). ^{13}C-NMR (50 MHz): 27.02 (*t*); 28.34 (*t*); 28.77 (*t*); 28.92 (*t*); 29.33 (*t*); 29.58 (*t*); 33.02 (*t*); 34.24 (*t*); 38.25 (*t*); 123.34 (*d*); 132.38 (*s*); 134.02 (*d*); 168.66 (*s*). MS: 381 (78), 379 (75), 300 (20), 175 (20), 174 (40), 161 (80), 160 (100), 148 (60), 130 (45), 105 (38), 104 (42). Anal. calc. for $C_{19}H_{26}BrNO_2$ (380.32): C 60.00, H 6.89, N 3.68; found: C 59.98, H 6.87, N 3.55.

N-*(12-Bromododecyl)phthalimide* (**3f**): Yield 5.4 g (68%). Colorless crystals. R_f (hexane/Et_2O 1:1) 0.55. M.p. 62–63°. IR: 1710*s*, 1400*s*.^{1}H-NMR: 1.21–1.50 (*m*, overlap with 1.27 (*s*), 16 H); 1.68 (*m*, 2 H); 1.86 (*m*, 2 H); 3.42 (*t*, 2 H); 3.69 (*t*, 2 H); 7.68–7.76 (*m*, 2 H). ^{13}C-NMR: 26.85 (*t*); 28.18 (*t*); 28.50 (*t*); 28.76 (*t*); 29.17 (*t*); 29.40 (*t*); 29.44 (*t*); 29.48 (*t*); 32.85 (*t*); 34.03 (*t*); 38.08 (*t*); 123.14 (*d*); 132.21 (*s*); 133.82 (*d*); 168.46 (*s*). MS: 395 (100), 393 (100, $M^+(^{79}Br)$, 314 (16), 202, 174 (28), 161 (70), 160 (82), 148 (37), 133 (25), 130 (27). Anal. calc. for $C_{20}H_{28}BrNO_2$ (394.35): C 60.91, H 7.16, N 3.55; found: C 61.09, H 7.09, N 3.37.

N,N′-*(Dithiodialkane-ω,1-diyl)bis[phthalimide]* **4a–f** [9]: *General Procedures.* A soln. of the *N*-(ω-bromoalkyl)phthalimide **3a–f** (31.2 mmol) and $Na_2S_2O_3$ (7.53 g, 30.3 mmol) was refluxed in MeOH/H_2O 1:1 (120 ml) for 4 h. The hot soln. was treated with solid I_2 (*ca.* 4 g) in portions until the brown color remained. After reduction of the excess I_2 with $Na_2S_2O_5$, the yellow soln. was allowed to cool down and left overnight in the refrigerator (4°). The solid product was separated by decanting, purified by FC (hexane/Et_2O 1:1), and precipitated from a conc. soln. in Et_2O by addition of MeOH: **4a–f** as a colorless powder.

N,N′-*(Dithiodihexane-6,1-diyl)bis[phthalimide]* (**4a**): Yield 1.98 g (55.2%). R_f (hexane/Et_2O 3:1) 0.21. M.p. 59° ([9]: 58°). IR (KBr): 1780*vs*, 1720*vs*, 1440*vs*, 1400*vs*, 1370*vs*, 1060*s*. ^{1}H-NMR: 1.25–1.40 (*m*, 8 H); 1.68–1.73 (*m*, 8 H); 2.69 (*t*, *J* = 7.35, 4 H); 3.69 (*t*, 4 H); 7.67–7.75 (*m*, 4 H); 7.76–7.84 (*m*, 4 H). ^{13}C-NMR: 26.31 (*t*); 26.36 (*t*); 28.36 (*t*); 28.91 (*t*); 37.74 (*t*); 38.74 (*t*); 122.98 (*d*); 132.01 (*s*); 133.73 (*d*); 168.12 (*s*). MS (calc. for $C_{28}H_{32}N_2O_4S_2$, 524.59): 524 (12, M^+), 377 (45), 377 (45), 376 (100), 216 (60), 202, 188 (39), 175 (41), 174 (44), 161 (72), 160 (100), 149 (53), 148 (51), 133 (41), 130 (45), 105 (40), 104 (40).

N,N′-*(Dithiodioctane-8,1-diyl)bis[phthalimide]* (**4b**): Similarly, **3b** (3.28 g, 5.64 mmol) gave 1.98 g (55%) of **4b**. R_f (hexane/Et_2O 2:1) 0.45. M.p. 48° ([9]: 47°). IR (KBr): 1775*s*, 1465*s*, 1435*s*, 1400*s*, 1360*s*, 1050*s*. ^{1}H-NMR: 1.25–1.40 (*m*, 16 H); 1.60–1.80 (*m*, 8 H); 2.66 (*t*, *J* = 7.35, 4 H); 3.67 (*t*, *J* = 7.20, 4 H); 7.65–7.75 (*m*, 4 H); 7.81–7.88 (*m*, 4 H). ^{13}C-NMR: 26.74 (*t*); 28.38 (*t*); 28.52 (*t*); 28.99 (*t*); 29.03 (*t*); 29.12 (*t*); 37.94 (*t*); 39.03 (*t*); 123.07 (*d*); 132.14 (*s*); 133.79 (*d*); 168.29 (*s*). MS (calc. for $C_{32}H_{40}N_2O_4S_2$, 580.69): 580 (4, M^+), 291 (14), 258 (12), 189 (14), 160 (100), 148 (28), 133 (22), 105 (20).

N,N′-*(Dithiodinonane-9,1-diyl)bis[phthalimide]* (**4c**): Yield 7.63 g (79%). R_f (hexane/Et_2O 1:1) 0.34. M.p. 53°. IR (KBr): 1775*m*, 1710v*s*, 1400*s*, 1360*s*, 790*s*, 720*s*. ^{1}H-NMR: 1.25–1.40 (*m*, 20 H); 1.60–1.80 (*m*, 8 H); 2.66 (*t*, *J* = 7.35, 4 H); 3.67 (*t*, *J* = 7.20, 4 H); 7.65–7.75 (*m*, 4 H); 7.81–7.88 (*m*, 4 H). ^{13}C-NMR: 26.87 (*t*); 28.55 (*t*); 28.61 (*t*); 29.19 (*t*); 29.50 (*t*); 29.24 (*t*); 29.53 (*t*); 38.08 (*t*); 39.19 (*t*); 123.15 (*d*); 132.19 (*s*); 133.62 (*d*); 168.47 (*s*). MS: 608 (94, M^+), 337 (26), 305 (34), 272 (32), 160 (100), 148 (26), 130 (22). Anal. calc. for $C_{34}H_{44}N_2O_4S_2$: C 67.07, H 7.28, N 4.60; found: C 66.90, H 7.37, N 4.46.

N,N′-*(Dithiodidecane-10,1-diyl)bis[phthalimide]* (**4d**): Similarly, **3d** (15.6 g, 42.6 mmol) gave 9.61 g (70.9%) of **4d**. R_f (hexane/Et_2O 1:1) 0.19. M.p. 49°. IR (KBr): 1775*s*, 1720v*s*, 1465*s*, 1435*s*, 1400v*s*, 1365*s*, 720v*s*. ^{1}H-NMR: 1.20–1.42 (*m*, 24 H); 1.60–1.78 (*m*, 8 H); 2.69 (*t*, *J* = 7.35, 4 H); 3.69 (*t*, *J* = 7.35, 4 H); 7.68–7.79 (*m*, 4 H); 7.82–7.91 (*m*, 4 H). ^{13}C-NMR: 26.85 (*t*); 28.52 (*t*); 28.59 (*t*); 29.15 (*t*); 29.19 (*t*); 29.23 (*t*); 29.41 (*t*); 38.07 (*t*); 39.19 (*t*); 123.15 (*d*); 132.21 (*s*); 133.82 (*d*); 168.46 (*s*). MS (calc. for $C_{36}H_{48}N_2O_4S_2$, 636.80): 636 (6, M^+), 319 (20), 202 (22), 174 (24), 160 (100), 148 (46), 130 (38).

N,N′-*(Dithiodiundecane-11,1-diyl)bis[phthalimide]* (**4e**): Similarly, **3e** (10.94 g, 28.3 mmol) gave 14.85 g (77.6%) of **4e**. R_f (hexane/Et_2O 2:1) 0.44. M.p. 45°. IR (KBr): 1770*m*, 1715v*s*, 1395*s*, 790v*s*, 720*s*. ^{1}H-NMR (200 MHz): 1.11–1.45 (*m*, 28 H); 1.58–1.72 (*m*, 8 H); 2.62 (*t*, *J* = 7.35, 4 H); 3.69 (*t*, 4 H); 7.64–7.72 (*m*, 4 H); 7.75–7.82 (*m*, 4 H). ^{13}C-NMR (50 MHz): 26.88 (*t*); 28.56 (*t*); 28.62 (*t*); 28.85 (*t*); 29.24 (*t*); 29.48 (*t*); 38.10 (*t*); 39.21 (*t*); 123.16 (*d*); 132.22 (*s*); 133.86 (*d*); 168.48 (*s*). MS: 664 (5, M^+), 626 (18), 409 (35), 333 (86), 203 (22), 160 (100), 148 (66), 130 (60), 104 (50). HR-MS: 664.336670 ($C_{38}H_{52}N_2O_4S_2^+$; calc. 664.336852).

N,N′-*(Dithiodidodecane-12,1-diyl)bis[phthalimide]* (**4f**): Yield 7.1 g (77%). Wax. R_f (hexane/Et_2O 1:1). IR (KBr): 1789*m*, 1722*s*, 1401*m*. ^{1}H-NMR: 120–1.42 (*m*, overlap with 1.20 (*s*), 32 H); 1.60–1.80 (*m*, 8 H); 2.69 (*t*, *J* = 7.35, 4 H); 3.69 (*t*, *J* = 7.35, 4 H); 7.60–7.80 (*m*, 4 H); 7.81–7.90 (*m*, 4 H). ^{13}C-NMR: 26.85 (*t*); 28.53 (*t*); 28.59 (*t*); 29.16 (*t*); 29.22 (*t*); 29.45 (*t*); 29.47 (*t*); 29.52 (*t*); 38.07 (*t*); 39.19 (*t*); 123.12 (*d*); 132.20 (*s*); 133.80 (*d*); 168.44 (*s*). MS: 692 (92, $[M-H]^+$), 379 (46), 347 (100), 330 (80), 315 (98), 160 (84), 148 (55). HR-MS: 692.36377 ($C_{40}H_{56}N_2O_4S_2^+$; calc. 692.368152).

ω,ω′-Dithiobis[alkan-1-amine] Dihydrochlorides: General Procedure. **5a**–**f** [9]. The *N,N′*-(dithioalkane-*ω*,1-diyl)bis[phthalimide] (**4a**–**f**, 9.86 mmol) was refluxed with hydrazine hydrate (30.6 mmol) in EtOH (90 ml) for 1 h under N_2. A colorless solid precipitated after complete dissolution of the starting material. The solvent was evaporated and the residue refluxed in 1M HCl (88 ml) for 1 h. After careful removal of the solvent under reduced pressure, the residue was dissolved in EtOH, the hydrazide filtered off, and the product precipitated with Et_2O/AcOEt 1:1. The dithiobis[alkanamine] dihydrochloride was recrystallized from EtOH/Et_2O/AcOEt 1:2:2 (200 ml).

6,6′-Dithiobis[hexan-1-amine] Dihydrochloride (**5a**): M.p. 224–230° ([9]: 235°). IR (KBr): 1480*s*, 1440*s*, 1400v*s*, 1380*s*. ^{1}H-NMR (300 MHz, CD_3OD): 1.44 (*m*, 8 H); 1.60–1.80 (*m*, 8 H); 2.69 (*t*, 4 H); 2.91 (*t*, 4 H). MS (calc. for $C_{12}H_{30}Cl_2N_2S_2$, 337.30): 298 (2), 180 (8), 165 (60), 148 (16), 133 (70), 132 (100), 116 (50), 115 (51), 100 (68).

8,8′-Dithiobis[octan-1-amine] Dihydrochloride (**5b**): Similarly, **4b** (0.31 g, 0.53 mmol) gave, after recrystallization from EtOH, 0.150 g (72%) of **5b**. Colorless crystals. M.p. 213° ([9]: 215°). IR (KBr). 1496*s*, 1082*m*. ^{1}H-NMR (300 MHz, CD_3OD): 1.27–1.40 (*m*, 16 H); 1.55–1.75 (*m*, 8 H); 2.67 (*t*, *J* = 7.20, 4 H); 2.89 (*t*, *J* = 7.60, 4 H). ^{13}C-NMR (75 MHz, CD_3OD): 27.31 (*t*); 28.41 (*t*); 29.22 (*t*); 29.95 (*t*); 29.96 (*t*); 30.03 (*t*); 39.03 (*t*); 40.70 (*t*). MS (calc. for $C_{16}H_{38}Cl_2N_2S_2$, 393.41): 393 (2, M^+), 160 (78), 143 (65), 128 (100), 87 (48), 69 (48).

9,9′-Dithiobis[nonan-1-amine] Dihydrochloride (**5c**): Yield 3.69 g (89%). Colorless powder. M.p. 164° (dec.). IR (KBr): 1500*s*. ^{1}H-NMR (300 MHz, CD_3OD): 1.30–1.48 (*m*, 20 H); 1.60–1.75 (*m*, 8 H); 2.67 (*t*, *J* = 7.25, 4 H); 2.91 (*t*, *J* = 7.60, 4 H). ^{13}C-NMR (75 MHz, CD_3OD): 27.07 (*t*); 28.18 (*t*); 29.03 (*t*); 29.77 (*t*); 29.78 (*t*); 29.83 (*t*); 29.99 (*t*); 39.28 (*t*); 40.39 (*t*). MS (calc. for $C_{18}H_{42}Cl_2N_2S_2$, 421.46): 380 (20), 198 (60), 190 (26), 174 (52), 157 (64), 142 (100), 129 (16), 109 (94).

10′,10′-Dithiobis[decan-1-amine] Dihydrochloride (**5d**): Yield 4.14 g (93%), from **4d** (6.3 g, 9.89 mmol). M.p. 178° ([9]: 180°). IR (KBr): 1780, 1730, 1480, 1400, 1380, 730. ^{1}H-NMR (300 MHz, CD_3OD): 1.24–1.40 (*m*, 24 H); 1.61–1.75 (*m*, 8 H); 2.66 (*t*, *J* = 7.17, 4 H); 2.90 (*t*, 4 H). ^{13}C-NMR (75 MHz, CD_3OD): 26.28 (*t*); 27.36 (*t*); 28.24 (*t*); 28.99 (*t*, 2 × int.); 29.08 (*t*); 29.21 (*t*); 29.31 (*t*); 38.59 (*t*); 39.62 (*t*).

11,11′-Dithiobis[undecan-1-amine] Dihydrochloride (**5e**): Similarly, **4e** (14.0 g, 22.3 mmol) gave 9.44 g (88%) of **5e**. M.p. 174°. IR (KBr): 1535*m*, 1434*m*, 1094*m*, 931*m*. ^{1}H-NMR (200 MHz, CD_3OD): 1.53 (*s*, 28 H); 1.61–1.99 (*m*, 8 H); 2.86 (*t*, *J* = 7.17, 4 H); 3.10 (*t*, 4 H). ^{13}C-NMR (50 MHz, CD_3OD): 28.48 (*t*); 29.59 (*t*); 30.43 (*t*); 31.24 (*t*); 31.51 (*t*); 31.58 (*t*); 40.72 (*t*); 41.80 (*t*). MS (calc. for $C_{22}H_{50}Cl_2N_2S_2$, 477.57): 436 (1), 385 (2), 352 (14), 235 (62), 203 (80), 202 (100), 185 (22), 171 (24), 170 (76), 162 (44), 104 (32).

12,12′-Dithiobis[dodecan-1-amine] Dihydrochloride (**5f**): Similarly, **4f** (6 mmol) gave 1.6 g (55%) of **5f**. M.p. >195° (dec.). ^{1}H-NMR (300 MHz, CD_3OD): 1.20–1.40 (*m*, overlap with 1.32 (*s*), 32 H); 1.55–1.80 (*m*, 8 H); 2.67 (*t*, *J* = 7.35, 4 H); 2.82–2.98 (*m*, 4 H).

For further characterization, **5f** was acetylated by treatment with Ac_2O and Et_3N to give N,N′-*(dithiodidodecane-12,1-diyl)bis[acetamide]* (**6**). M.p. 103–105°. IR (KBr): 1679*s*, 1530*m*, 1108*m*. ^{1}H-NMR: 1.2–1.7 (*m*, 20 H); 2.0 (*s*, 3 H); 2.7 (*t*, 2 H); 3.25 (*q*, 2 H); 5.5 (br. *s*, 1 H). MS: 516 (4, M^+), 258 (100), 226 (98), 216 (24), 184 (28), 72 (37). HR-MS: 516.375920 ($C_{28}H_{56}N_2O_2S_2^+$; calc. 516.378323).

N,N′-*(Dithiodihexane-6,1-diyl)bis[2-[2-(2-methoxyethoxy)ethoxy]acetamide]* (**8a**). A suspension of **5a** (900 mg, 2.67 mmol), 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (**7**; 1.24 g, 6.96 mmol), and dichloro(methoxy)-methane ($CHCl_2OMe$) [24] (2.454 g, 21.35 mmol) in CH_2Cl_2 (50 ml) was stirred for 3 h at r.t. under Ar. After dropwise addition of Et_3N (2 ml) and stirring overnight at r.t. under Ar, the mixture was poured on water-ice (50 ml). The aq. layer was extracted with CH_2Cl_2 (3 × 30 ml) and the combined org. phase washed with sat. $NaHCO_3$ soln. (3 × 30 ml) and brine (total 90 ml); dried (Na_2SO_4), and evaporated. FC (CH_2Cl_2/MeOH 10:1) gave 0.76 g (48%) of **8a**. Oil. R_f (CH_2Cl_2/MeOH 10.1) 0.48. IR ($CHCl_3$): 1750*m*, 1680v*s*, 1550*s*, 1340*s*. ^{1}H-NMR: 1.39 (br. *s*, 8 H); 1.50–1.59 (*m*, 4 H); 1.63–1.72 (*m*, 4 H); 2.63 (*t*, J = 7.26, 4 H); 3.24–3.31 (*m*, 4 H); 3.38 (*s*, 6 H); 3.52–3.58 (*m*, 4 H); 3.59–3.69 (*m*, 12 H); 3.15 (*s*, 4 H); 7.00 (*t*, 2 H). ^{13}C-NMR: 26.46 (*t*); 28.06 (*t*); 28.96 (*t*); 29.39 (*t*); 38.76 (*t*); 38.72 (*t*); 58.88 (*q*); 70.06 (*t*); 70.19 (*t*); 70.37 (*t*); 70.90 (*t*); 71.76 (*t*); 169.74 (*s*). MS: 584 (2, M^+), 325 (8), 292 (100), 260 (28), 235 (38), 216 (46), 184 (32), 172 (24), 160 (14), 133 (12), 115 (24), 103 (20). HR-MS: 584.316530 ($C_{26}H_{52}O_8N_2S_2^+$; calc. 584.316511).

N,N′-*(Dithiodioctane-8,1-diyl)bis[2-[2-(2-methoxyethoxy)ethoxy]acetamide]* (**8b**). From **5b** (4.0 g, 12.5 mmol), as described for **5a**. FC (CH_2Cl_2/MeOH 20:1) gave 3.68 mg (46%) of **8b**. Clear oil. R_f (CH_2Cl_2/MeOH 20:1) 0.26. IR ($CHCl_3$): 1670v*s*, 1540v*s*, 1460*s*, 1340*s*. ^{1}H-NMR: 1.25–1.45 (*m*, 16 H); 1.48–1.58 (*m*, 4 H); 1.58–1.66 (*m*, 4 H); 2.63 (*t*, J = 7.35, 4 H); 3.18–3.28 (*m*, 4 H); 3.38 (*s*, 6 H); 3.51–3.53 (*m*, 4 H); 3.54–3.64 (*m*, 12 H); 3.95 (*s*, 4 H); 7.00 (*t*, 2 H). ^{13}C-NMR: 26.84 (*t*); 28.39 (*t*); 29.10 (*t*); 29.11 (*t*); 29.13 (*t*); 29.58 (*t*); 38.84 (*t*); 39.02 (*t*); 58.96 (*q*); 70.16 (*t*); 70.37 (*t*); 70.50 (*t*); 70.93 (*t*); 71.84 (*t*); 169.74 (*s*). MS (calc. for $C_{30}H_{60}O_8N_2S_2$, 640.83): 640 (1, M^+), 353 (19), 322 (23), 321 (56), 320 (100, [M/2]$^+$), 288 (29), 263 (37), 244 (34), 212 (28), 200 (23), 188 (27).

N,N′-*(Dithiodinonane-9,1-diyl)bis[2-[2-(methoxyethoxy)ethoxy]acetamide]* (**8c**). From **5c** (0.20 g, 0.475 mmol), as described for **8a**. FC (CH_2Cl_2/MeOH 20:1) gave 175 mg (53%) of **8c**. Colorless grease. R_f (CH_2Cl_2/AcOEt 6:5) 0.11. IR ($CHCl_3$): 1670v*s*, 1540*s*, 1340*s*, 1110v*s*. ^{1}H-NMR (500 MHz, CD_3OD): 1.33 (br. *s*, 16 H); 1.38–1.41 (*m*, 4 H); 1.51–1.54 (*m*, 4 H); 1.67–1.72 (*m*, 4 H); 2.67 (*t*, J = 7.25, 4 H); 3.23 (*t*, J = 7.20, 4 H); 3.36 (*s*, 6 H); 3.54–3.56 (*m*, 4 H); 3.64–3.67 (*m*, 12 H); 4.03 (*s*, 4 H). ^{13}C-NMR (125 MHz, CD_3OD): 28.24 (*t*); 29.71 (*t*); 30.49 (*t*); 30.52 (*t*); 30.62 (*t*); 30.81 (2*t*); 40.05 (*t*); 40.24 (*t*); 59.43 (*q*); 71.46 (*t*); 71.61 (*t*); 71.64 (*t*); 72.24 (*t*); 73.19 (*t*); 172.84 (*s*). MS: 668 (18, M^+), 565 (24), 535 (58), 334 (62), 277 (29), 202 (40), 133 (30), 103 (38), 89 (56), 69 (38), 59 (100). Anal. calc. for $C_{32}H_{64}O_8N_2S_2$ (668.88): C 56.49, H 9.58, N 4.19; found: C 56.26, H 9.70, N 4.10.

2-[2-(Methoxyethoxy)ethoxy]acetic Acid (Dithiodipropane-3,1-diyl) Ester (**11**). According to [25], a mixture of **7** (4.58 g, 25.7 mmol), $CHCl_2OMe$ (3.7 g, 32.1 mmol) and $ZnCl_2$ (0.18 g, 1.2 mmol) was stirred at r.t. for 1 h and refluxed 1 h under N_2. The excess of $CHCl_2OMe$ was evaporated, the residual acid chloride dissolved in CH_2Cl_2 (10 ml) and added dropwise within 30 min to a soln. of 3,3′-dithiobis[propan-1-ol] (**10**; 1.8 g, 9.89 mmol) [12] and Et_3N (2.5 ml) in CH_2Cl_2 (50 ml) at r.t. The mixture was refluxed overnight under Ar and worked up by addition of H_2O (70 ml) and extraction of the aq. phase with CH_2Cl_2 (3 × 20 ml). The combined org. phase was washed with sat. Na_2CO_3 soln. (3×), 2M HCl, and brine, dried ($MgSO_4$), and evaporated. FC (hexane/AcOEt/MeOH 10:10:1) gave 2.775 g (56%) of **11**. Colorless oil. R_f (CH_2Cl_2/AcOEt/MeOH 10:10:1) 0.47. IR ($CHCl_3$): 1760v*s*, 1480*s*, 1260–1200*s*, 1180–1080v*s*. ^{1}H-NMR: 1.99–2.08 (*m*, 4 H); 2.70 (*t*, J = 7.08, 4 H); 3.35 (*s*, 6 H); 3.51–3.54 (*m*, 4 H); 3.54–3.64 (3 superimposed *m*, 12 H); 4.14 (*s*, 4 H); 4.23 (*t*, J = 6.2, 4 H). ^{13}C-NMR: 28.11 (*t*); 34.81 (*t*); 58.99 (*q*); 62.93 (*t*); 68.58 (*t*); 70.51 (*t*); 70.62 (*t*); 70.91 (*t*); 71.87 (*t*); 170.36 (*s*). MS: 502 (1, M^+), 161 (22), 133 (36), 117 (43), 103 (78), 89 (58), 59 (100). HR-MS: 502.190642 ($C_{20}H_{38}O_{10}S_2^+$; calc. 502.190580).

N,N′-*(Dithiodioctane-8,1-diyl)bis[*D*-gluconamide]* (**14b**). The known procedure [26] was adapted: to a soln. of **5b** (1 g, 2.54 mmol) in MeOH (30 ml) D-glucono-1,5-lactone (**13**; 0.90 g, 5.08 mmol) was added. After dropwise addition of Et_3N (2.8 ml), a colorless precipitate appeared. The mixture was refluxed for 1 h and filtered after cooling. The precipitate was washed with MeOH and dried for 2 h under vacuum: 0.79 g (46.2%) of **14b**. M.p. 166–168°. IR (KBr): 1650*m*, 1630*s*, 1550*s*, 1090*s*, 1040*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.19–1.43 (*m*, overlap with 1.27 (*s*); total 20 H); 1.57–1.64 (*m*, 4 H); 2.65 (*t*, J = 6.99, 4 H); 2.97–3.06 (*m*, 4 H); 3.42, 3.52 (2*m*); 3.80–4.00 (2*m*, 4 H); 4.25–4.56 (4*m*, 8 H); 3.04–3.13 (*m*, 2 H); 5.24–5.35 (*m*, 2 H); 7.56 (*m*, 2 H). ^{13}C-NMR: (75 MHz, (D_6)DMSO): 26.28 (*t*); 27.74 (*t*); 28.52 (*t*); 28.56 (*t*); 28.65 (*t*); 29.10 (*t*); 37.03 (*t*); 39.93 (*t*); 38.21 (*t*); 63.30 (*t*); 69.79 (*d*); 71.73 (*d*); 72.45 (*d*); 73.63 (*d*); 172.3 (*s*). LSI-MS (matrix glycerol; calc. for

$C_{28}H_{56}N_2O_{12}S_2$, 676.77): 677 (9, M^+), 661 (2), 553 (2), 525 (2), 499 (13), 467 (2), 369 (4), 340 (10), 321 (4), 306 (5), 277 (13), 185 (100), 162 (18), 133 (55).

N,N′-*(Dithiodidodecane-12,1-diyl)bis[*D-*gluconamide]* (**14f**). As described for **14b**, Et_3N (3 ml) was added dropwise to a soln. of **5f** (2.1 g, 4.2 mmol) and **13** (1.42 g, 8 mmol) in MeOH (80 ml). The mixture was stirred at r.t. for 4 h under N_2. The colorless precipitate was filtered off and the MeOH soln. cooled and filtered again: 2.0 g (61%) of **14f**. White solid. M.p. 152–154° (dec.). IR (KBr): 1650*s*, 1650*s*, 1636*s*, 1554*s*, 1100*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.15–1.61 (*m*, overlap with 1.13 (*s*)); 1.62–1.90 (*m*); 2.78 (*m*); 2.90–3.20 (*m*, overlap with DMSO peak); 3.30–3.80 (*m*, overlap with H_2O peak); 3.90–4.10 (*m*); 4.35–4.75 (*m*); 5.35–5.50 (*m*); 7.70 (*m*). LSI-MS (matrix glycerol): 789.6 (21, M^+), 611.5 (100), 433 (54).

N,N′-*(Dithiodidecane-10,1-diyl)bis[2,3,4,5,6-penta-*O*-acetyl-*D*-gluconamide]* (**15d**). As described for **14b** Et_3N (10 ml) was added dropwise to a soln. of **5d** (4 g, 8.9 mmol) and **13** (3.17 g, 17.8 mmol) in MeOH (100 ml). After reflux for 45 min and cooling in the refrigerator overnight, the precipitate was filtered off and dried *in vacuo* for 3 h. The brownish bis[gluconamide] **14d** (*ca.* 4.6 g) was treated with pyridine (35 ml) and Ac_2O (50 ml) and stirred for 4 h at 60° under N_2. The reaction was quenched by addition of ice-water (50 ml) and the aq. phase extracted with CH_2Cl_2 (3 × 30 ml). The org. phases were washed with 1M HCl, sat. brine, dried (Na_2SO_4), and evaporated. FC of the residue (hexane/AcOEt 1:3) gave 6.89 g (67%) of **15d**. Viscous, yellowish oil. R_f (hexane/AcOEt 1:3) 0.33. IR ($CHCl_3$): 1750v*s*, 1690*m*, 1530*s*, 1375v*s*, 1220v*s*, 1050*s*. ^{1}H-NMR: 1.20–1.40 (*m*, 24 H); 1.40–1.53 (2*m*, 4 H); 1.54–1.60 (*m*, 4 H); 2.04, 2.05, 2.11, 2.21 (4*s*, total 30 H); 2.67 (*t*, *J* = 7.35, 4 H); 3.20–3.28 (*m*, 4 H); 4.13 (*dd*, *J* = 12.2, 5.5, 2 H); 4.31 (*dd*, *J* = 12.2, 4.1, 2 H); 5.00–5.10 (*m*, 2 H); 5.30 (*d*, *J* = 5.33, 2 H); 5.45 (*q*, 2 H); 5.69 (*t*, *J* = 5.15, 2 H); 6.34 (*t*, 1 H). ^{13}C-NMR: 20.44 (*q*); 20.72 (*q*); 20.73 (*q*); 26.80 (*t*); 28.50 (*t*); 29.20 (*t*); 29.42 (*t*); 39.12 (*t*); 39.54 (*t*); 61.56 (*t*); 68.76 (*d*); 69.10 (*d*); 69.42 (*d*); 71.70 (*d*); 165.91 (*s*); 169.22 (*s*); 169.67 (*s*); 169.81 (*s*); 169.89 (*s*); 170.63 (*s*).

N,N′-*(Dithiodidodecane-12,1-diyl)bis[2,3,4,5,6-penta-*O*-acetyl-*D*-gluconamide]* (**15f**). A soln. of **14f** (2.0 g, 2.5 mmol), pyridine (15 ml), and Ac_2O (40 ml) was stirred at 60° for 2 h under N_2. The mixture was poured onto ice-water and extracted with CH_2Cl_2 (3×). The org. phase was washed with 1M HCl, sat. NaCl soln., dried ($MgSO_4$), and evaporated: 2.87 g (94%) of **15f**. Oil. R_f (AcOEt/hexane 3:1) 0.46. ^{1}H-NMR 1.20–1.80 (*m*, overlap with 1.26 (*s*), 40 H); 2.00–2.30 (*m*, overlap with 2.05 (*s*), 2.09 (*s*), 2.11 (*s*), 2.20 (*s*), 30 H); 2.91 (*t*, *J* = 7.35, 4 H); 3.23 (*m*, 4 H); 4.13 (*dd*, *J* = 12, 5.5, 2 H); 4.31 (*dd*, *J* = 12.5, 4.0, 2 H); 4.95–5.10 (*m*, 2 H); 5.30 (*d*, *J* = 5.5, 2 H); 5.45 (*m*, 2 H); 5.68 (*t*, *J* = 5.3, 2 H); 6.09 (*m*, 2 H). ^{13}C-NMR: 20.42 (*q*); 20.68 (*q*); 20.74 (*t*); 26.82 (*t*); 28.51 (*t*); 29.23 (*t*); 29.37 (*t*); 29.54 (*t*); 39.16 (*t*); 39.58 (*t*); 61.56 (*t*); 68.78 (*t*); 69.11 (*d*); 69.39 (*d*); 71.74 (*d*); 166.02 (*s*); 169.27 (*s*); 169.92 (*s*); 170.68 (*s*). LSI-MS (calc. for $C_{56}H_{92}N_2O_{22}S_2$, 1209.46; matrix glycerol): 1209.6 (86, M^+), 1149.5 (38), 863.5 (100), 636.3 (70).

Reduction of the N,N′*-(Dithiodialkanediyl)bis[amides]: General Procedure.* The mixture of the *N,N′*-(dithiodialkanediyl)bis[amide] (1.2 mmol) and activated Zn [27] (4.3 mmol) was refluxed in AcOH (50 ml) for 18 h under Ar. Residual Zn was filtered off, sat. $NaHCO_3$ soln. (50 ml) added, and the soln. carefully concentrated to 40 ml. After extraction with AcOEt (3×, total 240 ml), the org. layer was washed with sat. $NaHCO_3$ soln. (3×, total 210 ml) and brine (total 210 ml), dried (Na_2SO_4) and evaporated: *N*-(ω-mercaptoalkyl)amide.

N-*(6-Mercaptohexyl)-2-[2-(2-methoxyethoxy)ethoxy]acetamide* (**9a**): Yield 0.401 g (57%). R_f (AcOEt/CH_2Cl_2/MeOH 7:5:1) 0.60. IR ($CHCl_3$): 1760*m*, 1740*s*, 1670v*s*, 1545*s*, 1240*s*, 1100v*s*, 1040*s*. ^{1}H-NMR: 1.24–1.41 (*m*, 5 H); 1.42–1.63 (*m*, 4 H); 2.46–2.55 (*q*, 2 H); 3.2–3.30 (*m*, 2 H); 3.37 (*s*, 3 H); 3.52–3.59 (*m*, 2 H); 3.61–3.71 (*m*, 6 H); 3.95 (*s*, 2 H); 7.00 (*s*, 1 H). ^{13}C-NMR: 24.46 (*t*); 26.34 (*t*); 27.96 (*t*); 29.49 (*t*); 33.82 (*t*); 38.74 (*t*); 58.97 (*q*); 70.16 (*t*); 70.37 (*t*); 70.50 (*t*); 70.94 (*t*); 71.85 (*t*); 169.80 (*s*). MS (calc. for $C_{13}H_{27}O_4NS$, 293.37): 293 (17, M^+), 260 (10), 235 (20), 218 (19), 172 (20), 142 (20), 117, 115 (20), 103 (20), 89 (24). HR-MS: 293.165310 ($C_{13}H_{27}O_4NS^+$; calc. 293.166080).

N-*(8-Mercaptooctyl)-2-[2-(2-methoxyethoxy)ethoxy]acetamide* (**9b**): From **8b** (1.6 g, 2.5 mmol), **9b** (1.5 g, 95%) was obtained. R_f (AcOEt/CH_2Cl_2/MeOH 5:5:1) 0.55. IR ($CHCl_3$): 1760*m*, 1740*s*, 1670v*s*, 1545*s*, 1240*s*, 1250*m*, 1100v*s*, 1040*s*. ^{1}H-NMR: 1.25 (br. *s*, 9 H); 1.43–1.61 (2*m*, 4 H); 2.49 (*q*, 2 H); 3.21–3.28 (*m*, 2 H); 3.36 (*s*, 3 H); 3.51–3.56 (*m*, 2 H); 3.61–3.66 (*m*, 6 H); 3.97 (*s*, 2 H); 7.07 (*t*, 1 H). ^{13}C-NMR: 24.60 (*t*); 26.86 (*t*); 28.28 (*t*); 28.97 (*t*); 29.17 (*t*); 29.56 (*t*); 33.99 (*t*); 38.99 (*t*); 58.99 (*q*); 70.17 (*t*); 70.28 (*t*); 70.50 (*t*); 70.98 (*t*); 71.87 (*t*); 170.24 (*s*). MS (calc. for $C_{15}H_{31}O_4NS$, 321.42): 321 (16, M^+), 288 (11), 263 (21), 212 (20), 200 (26), 188 (33), 170 (13), 103 (13), 89 (19), 87 (24), 59 (100).

3-Mercaptopropyl 2-[2-(2-Methoxyethoxy)ethoxy]acetate (**12**): From **11** (2.0 g, 398 mmol) **12** (1.8 g, 89%) was obtained. **12** Colorless oil. R_f (AcOEt/CH_2Cl_2/MeOH 10:10:1) 0.51. IR ($CHCl_3$): 1760v*s*, 1700*m*, 1460*s*, 1435*s*, 1400*s*, 1380*s*, 1360*s*, 1260–1200*s*, 1180–1080v*s*, 860*s*. ^{1}H-NMR: 1.40 (*t*, *J* = 8.0, 1 H); 1.90–1.97 (*m*, 2 H); 2.58 (*q*, 2 H); 3.37 (*s*, 3 H); 3.53–3.55 (*m*, 2 H); 3.60–3.72 (3 superimposed *m*, 6 H); 4.15 (*s*, 2 H); 4.26 (*t*, *J* =

6.2, 2 H). ^{13}C-NMR: 20.99 (*t*); 32.68 (*t*); 59.00 (*q*); 62.75 (*t*); 68.59 (*t*); 70.53 (*t*); 70.64 (*t*); 70.92 (*t*); 71.88 (*t*); 170.42 (*s*). MS: 252 (7, M^+), 194 (11), 179 (21), 105 (33), 103 (60), 89 (40). HR-MS: 252.103100 ($C_{10}H_{20}O_5S^+$; calc. 252.103146).

N-*(10-Mercaptodecyl)-2,3,4,5,6-penta*-O-*acetyl*-D-*gluconamide* (**16d**): From **15d** (1.5 g, 1.3 mmol), **16d** (0.79 g, 53%) was obtained. Oil. R_f (hexane/AcOEt 1:1) 0.44. IR ($CHCl_3$): 1740v*s*, 1370*s*, 1240*s*, 1220*s*, 1190*s*, 1040*s*, 1030*s*. ^{1}H-NMR: 1.21–1.40 (br. *s*, overlap with 1.34 (*t*); 13 H); 1.43–1.66 (2*m*, 4 H); 2.05, 2.05, 2.10, 2.11, 2.21 (5*s*, 15 H); 2.48–2.55 (*q*, 2 H); 3.17–3.28 (*m*, 2 H); 4.13 (*dd*, J = 12.2, 5.5, 1 H); 4.31 (*dd*, J = 12.2, 4.0, 1 H); 5.00–5.10 (*m*, 1 H); 5.30 (*d*, J = 5.14, 1 H); 5.44 (*q*, 1 H); 5.69 (*t*, J = 5.15, 1 H); 6.34 (*t*, 1 H). ^{13}C-NMR: 20.33 (*q*); 20.57 (*q*); 20.63 (*q*); 24.49 (*t*); 26.73 (*t*); 28.24 (*t*); 29.00 (*t*); 29.13 (*t*); 29.33 (*t*); 29.36 (*t*); 33.94 (*t*); 39.44 (*t*); 39.54 (*t*); 61.45 (*t*); 68.70 (*d*); 69.08 (*d*); 69.35 (*d*); 71.75 (*d*); 165.95 (*s*); 169.10 (*s*); 169.59 (*s*); 169.68 (*s*); 169.73 (*s*); 170.99 (*s*).

N-*(12-Mercaptododecyl)-2,3,4,5,6-penta*-O-*acetyl*-D-*gluconamide* (**16f**). Yield 2.45 g (92%). Clear oil. R_f (AcOEt/hexane) 0.57. ^{1}H-NMR: 1.20–1.70 (*m*, overlap with 2.06 (*s*), 2.12 (*s*), total 12 H); 2.2 (*s*, 3 H); 2.45–2.60 (*m*, 2 H); 3.20–3.35 (*m*, 1 H); 4.14 (*dd*, J = 12.1, 5.5, 1 H); 4.32 (*dd*, J = 12.1, 4.0, 1 H); 4.95–5.10 (*m*, 1 H); 5.30 (*d*, J = 5.5, 1 H); 5.45 (*m*, 1 H); 5.69 (*m*, 1 H); 6.09 (*m*, 1 H). ^{13}C-NMR: 20.44 (*q*); 20.71 (*q*); 24.66 (*t*); 26.82 (*t*); 28.37 (*t*); 29.07 (*t*); 29.23 (*t*); 29.42 (*t*); 29.50 (*t*); 29.54 (*t*); 34.05 (*t*); 39.56 (*t*); 61.55 (*t*); 68.75 (*d*); 69.11 (*d*); 69.41 (*d*); 71.70 (*d*); 165.88 (*s*); 169.20 (*s*); 169.65 (*s*); 169.88 (*s*); 170.10 (*s*). LSI-MS (calc. for $C_{28}H_{47}NO_{11}S$, 605.74, matrix DTT/DTE 5:1): 647.9 (14, $[M+H+K]^+$), 606.9 (12, $[M+H]^+$), 587.9 (12), 546 (17), 260.2 (70), 216.2 (19), 149.1 (25).

tert-*Butyl Methyl 2-(Bromomethyl)-2-methylpropanedioate* (**18**). A soln. of **17** (37.5 g, 200 mmol) in toluene (50 ml) was added within 20 min to a suspension of NaH (55% oil dispersion; 16 g) in toluene (300 ml) and HMPT (50 ml). The mixture was refluxed for 2 h under N_2, cooled, and directly decanted into dibromomethane (200 g, 1.15 mol) at 80°. After 3 h reflux, the mixture was stirred for 18 h at r.t. and worked up. The aq. phase was extracted with Et_2O (3×) and the combined org. phase washed with NaCl soln., dried ($MgSO_4$), and evaporated. Fractional destillation yielded 42.3 g (76%) of **18**. Colorless liquid. B.p. 75°–80°/0.2 Torr. IR ($CHCl_3$): 1751*s*, 1395*m*, 1272*m*, 1166*s*, 1123*m*. ^{1}H-NMR: 1.44–1.49 (*m*, overlap with 1.46 (*s*), total 9 H); 1.53 (*s*, 3 H); 3.72–3.77 (*m*, overlapped with 3.76 (*s*), total 5 H). ^{13}C-NMR: 19.38 (*q*); 27.58 (*q*); 35.84 (*t*); 52.60 (*q*); 55.49 (*s*); 82.52 (*s*); 168.24 (*s*); 170.29 (*s*). MS: 265 (26), 251 (15), 225 (35), 209 (88), 181 (71), 151 (51), 101 (76), 69 (37), 57 (100), 41 (52), 29 (25).

O-*Methyl* S-*(8-Oxo-10,13,16-trioxa-7-azaheptadecyl) 2-(Bromomethyl)-2-methylmonothiomalonate* (= *Methyl 2-(Bromomethyl)-2-methyl-3-oxo-3-[(8-oxo-10,13,16-trioxa-7-azaheptadecyl)thio]propanoate*; **20a**). The acid chloride of methyl hydrogen 2-(bromomethyl)-2-methylpropanedioate (**19**) was prepared by stirring a soln. of **18** (3 g, 10.6 mmol) in CF_3COOH (25 ml) at r.t. for 3 h under Ar. The excess of CF_3COOH was evaporated, the resulting monoacid **19** dissolved in $CHCl_2OMe$ (1.6 g), and the mixture stirred 4 h at r.t. under Ar. The excess $CHCl_2OMe$ was evaporated to give the acid chloride (2.43 g, 93%) as a colorless liquid. The freshly prepared acid chloride (330 mg, 1.36 mmol) was dissolved in CH_2Cl_2 (5 ml), treated with Et_3N (2 ml), and cooled to 0°. A soln. of **9a** (200 mg, 0.682 mmol) in CH_2Cl_2 (20 ml) was slowly added during 30 min and the mixture stirred for 4 h at r.t. After workup and extraction of the aq. layer with CH_2Cl_2 (3×, 30 ml), the combined org. layers were washed with 2M $NaHCO_3$ (3×), 2M HCl (3×), and brine, dried ($NaSO_4$), and evaporated. The yellow oil (2.1 g) was purified by FC (AcOEt/CH_2Cl_2/MeOH 5:5:1): 0.27 g (80%) of **20a**. Clear oil. R_f (AcOEt/CH_2Cl_2/MeOH 5:5:1) 0.56. IR ($CHCl_3$): 1740*s*, 1680v*s*, 1540*s*, 1460*s*, 1280*s*, 1110v*s*, 970*s*. ^{1}H-NMR: 1.36 (br. *s*, 4 H); 1.49–1.56 (*m*, superimposed at 1.63 (*s*); total 7 H); 2.91 (*t*, J = 7.26, 2 H); 3.22–3.29 (*q*, 2 H); 3.35 (*s*, 3 H); 3.53–3.58 (*m*, 2 H); 3.64–3.70 (*m*, 6 H); 3.755 (*d*, J_{AB} = 10.30, superimposed at 3.775 (*s*), total 4 H); 3.847 (*d*, J_{AB} = 10.30, 1 H); 3.98 (*s*, 2 H); 7.05 (*t*, 1 H). ^{13}C-NMR: 20.07 (*q*); 26.38 (*t*); 28.37 (*t*); 29.01 (*t*); 29.25 (*t*); 29.50 (*t*); 36.03 (*t*); 38.74 (*t*); 53.15 (*q*); 59.00 (*q*); 61.82 (*s*); 70.20 (*t*); 70.42 (*t*); 70.54 (*t*); 70.98 (*t*); 71.89 (*t*); 169.70 (*s*); 169.93 (*s*); 196.72 (*s*). MS: 501 (2, M^+), 499 (2, M^+), 292 (100), 260 (20), 216 (46), 184 (21), 133, 101 (18), 100 (25). HR-MS: 499.124050 ($C_{19}H_{34}BrO_7NS$; calc. 499.123936).

O-*Methyl* S-*(10-Oxo-12,15,18-trioxa-9-azanonadecyl) 2-(Bromomethyl)-2-methylmonothiomalonate* (= *Methyl 2-(Bromomethyl)-2-methyl-3-oxo-3-[(10-oxo-12,15,18-trioxa-9-azanonadecyl)thio]propanoate*; **20b**). As described for **20a**, from the acid chloride (1.5 g, 6.1 mmol) of **19** (prepared as described above) in CH_2Cl_2 (15 ml), Et_3N (2 ml), and **9b** (1.0 g, 3.11 mmol) in CH_2Cl_2 (25 ml): 0.632 g (39%) of **20b**. Colorless oil. R_f (AcOEt/CH_2Cl_2/MeOH 5:5:1) 0.50. IR ($CHCl_3$): 1740v*s*, 1680v*s*, 1110v*s*, 970*s*. ^{1}H-NMR: 1.30 (br. *s*, 8 H); 1.47–1.58 (*m*, 4 H); 1.64 (*s*, 3 H); 2.91 (*t*, J = 7.25, 2 H); 3.26 (*q*, 2 H); 3.38 (*s*, 3 H); 3.51–3.55 (*m*, 2 H); 3.62–3.70 (*m*, 6 H); 3.74 (*d*, J_{AB} = 10.85, superimposed 3.743 (*s*), total 4 H); 3.85 (*d*, J_{AB} = 10.48, 1 H); 3.99 (*s*, 2 H); 7.01 (*t*, 1 H). ^{13}C-NMR: 20.04 (*q*); 26.8 (*t*); 28.61 (*t*); 28.91 (*t*); 29.02 (*t*); 29.07 (*t*); 29.31 (*t*); 29.54 (*t*); 36.01 (*t*); 38.89 (*t*); 53.12 (*q*); 58.96 (*q*); 61.78 (*s*); 70.16 (*t*); 70.27 (*t*); 70.49 (*t*); 70.95 (*t*); 71.85 (*t*); 169.68 (*s*); 170.02 (*s*); 196.71

(*s*). MS (calc. for $C_{21}H_{38}BrO_7NS$ 528.45): 529 (1, M^+), 527 (1, M^+), 321 (24), 320 (100), 288 (38), 244 (59), 212 (25), 133 (16), 103 (16).

O-*Methyl* S-*(5-Oxo-4,7,10,13-tetraoxatetradecyl)-2-(Bromomethyl)-2-methylmonothiomalonate* (= *Methyl 2-(Bromomethyl)-2-methyl-3-oxo-3-[(5-oxo-4,7,10,13-tetraoxatetradecyl)thio]propanoate*; **21**). To the soln. of the acid chloride, obtained from **19** as described above, **12** (1.5 g, 3.2 mmol) in CH_2Cl_2 (20 ml) was added dropwise within 20 min at 0° under Ar. FC (hexane/AcOEt/MeOH 10:10:1) gave **21** (1.758 g, 65%). Colorless oil. R_f (hexane/AcOEt/MeOH 10:10:1) 0.33. IR ($CHCl_3$): 1750v*s*, 1685v*s*, 1460v*s*, 1445*s*, 1385*s*, 1260–1200v*s*, 1180–1080v*s*. ^{1}H-NMR: 1.64 (*s*, 3 H); 1.95 (*d*, 2 H); 3.01 (*t*, J = 7.17, 2 H); 3.38 (*s*, 3 H); 3.54–3.57 (*m*, 2 H); 3.62–3.70 (*m*, 4 H); 3.76 (*s*, superimposed at 3.71–3.77 (*m*) and (*d*), total 6 H); 3.824 (*d*, J_{AB} = 10.29, 1 H); 4.17 (*s*, superimposed at 4.14 (*t*, J = 6.25), total 4 H). ^{13}C-NMR: 19.93 (*q*); 25.76 (*t*); 28.27 (*t*); 35.80 (*t*); 53.20 (*q*); 58.98 (*q*); 61.71 (*s*); 61.71 (*s*); 62.81 (*t*); 68.55 (*t*); 70.50 (*t*); 70.62 (*t*); 70.92 (*t*); 71.87 (*t*); 169.52 (*s*); 170.35 (*s*); 196.32 (*s*). MS: 283 (32), 281 (36), 219 (56), 209 (46), 207 (54), 181 (44), 179 (58), 153 (38), 143 (28), 133 (50), 103 (48), 59 (100). ESI-MS (MeCN/H_2O 1:1 and 2% $LiClO_4$): 467.20 (100, $[M+2+Li]^+$), 465.20 (90, $[M+Li]^+$). Anal. calc. for $C_{16}H_{27}BrO_8S$ (459.30): C 41.91, H 6.07; found: C 41.84, H 5.92.

O-*Methyl* S-*{10-[(2,3,4,5,6-Penta*-O-*acetyl*-D-*gluconoyl)amino]decyl} 2-(Bromomethyl)-2-methylmonothiomalonate* (= *Methyl 2-(Bromomethyl)-2-methyl-3-oxo-3-{{10-[(2,3,4,5,6-penta*-O-*acetyl*-D-*gluconoyl)amino]decyl}thio}propanoate*; **22a**). As described for **20a**, treatment of **18** (0.30 g, 1.06 mmol) first with CF_3COOH, then with $SOCl_2$ gave the acid chloride of **19**, which was treated with Et_3N (2 ml) and **16d** (0.60 g, 1.04 mmol) in toluene (6 ml). FC (AcOEt/hexane 1:1) of the viscous, yellowish oil gave the diastereomer mixture **22a** (380 mg, 47%). Clear oil. R_f (AcOEt/hexane 1:1) 0.55. IR ($CHCl_3$): 1760*s*, 1740*s*, 1380*s*, 1230*s*. ^{1}H-NMR: 1.25–1.40 (*m*, 12 H); 1.40–1.51 (*m*, 2 H); 1.53–1.60 (*m*, 2 H); 1.64 (*s*, 3 H); 2.05 (*s*, 3 H); 2.06 (*s*, 3 H); 2.10 (*s*, 3 H); 2.11 (*s*, 3 H); 2.20 (*s*, 3 H); 2.92 (*t*, J = 7.36, 2 H); 3.18–3.27 (*m*, 2 H); 3.76 (*d*, J_{AB} = 10.47, overlap with 3.78 (*s*), total 4 H); 3.88 (*d*, J_{AB} = 10.47, 1 H); 4.13 (*dd*, J = 12.13, 5.53, 1 H); 4.32 (*dd*, J = 12.13, 4.05, 1 H); 5.00–5.10 (*m*, 1 H); 5.30 (*d*, J = 5.15, 1 H); 5.45 (*q*, 1 H); 5.68 (*t*, J = 5.15, 1 H); 6.34 (*t*, J = 5.78, 1 H). ^{13}C-NMR: 20.03 (*q*); 20.40 (*q*); 20.65 (*q*); 20.71 (*q*); 26.76 (*t*); 28.63 (*t*); 28.96 (*t*); 29.08 (*t*); 29.15 (*t*); 29.31 (*t*); 29.34 (*t*); 29.37 (*t*); 36.05 (*t*); 39.50 (*t*); 53.13 (*q*); 61.50 (*t*); 61.79 (*s*); 68.75 (*d*); 69.11 (*d*); 69.40 (*d*); 71.76 (*d*); 165.98 (*s*); 169.16 (*s*); 169.64 (*s*); 169.67 (*s*); 169.78 (*s*); 169.81 (*s*); 170.54 (*s*); 196.68 (*s*). MS (calc. for $C_{32}H_{50}BrNO_{14}S$, 784.66): 786 (1, $[M+2]^+$), 784 (1, M^+(^{79}Br)), 754 (2), 752 (2), 725 (1), 723(0.9), 682 (2), 665 (3), 623 (3), 576 (100), 558 (8), 544 (12), 534 (44), 516 (76), 484 (20), 474 (22), 424 (10), 396 (8), 347 (8), 287 (9), 272 (11), 258 (9), 242 (11), 230 (62), 198 (38), 188 (42), 184 (76), 171 (18), 157 (44), 142 (54), 129 (20), 115 (54), 103 (48).

O-*Methyl* S-*{12-[(2,3,4,5,6-Penta*-O-*acetyl*-D-*gluconoyl)amino]dodecyl} 2-(Bromomethyl)-2-methylmonothiomalonate* (= *Methyl 2-(Bromomethyl)-2-methyl-3-oxo-3-{{12-[(2,3,4,5,6-penta*-O-*acetyl*-D-*gluconoyl)amino]dodecyl}thio}propanoate*; **22b**). The acid chloride, prepared from the acid **19** with $SOCl_2$, was dissolved in toluene (5 ml), cooled, and treated, as described for **22a**, with Et_3N and **16f** (200 mg, 0.33 mmol) in toluene (5 ml) (18 h). For workup, the aq. phase was extracted with AcOEt (2×) and the org. phase dried ($MgSO_4$). FC (AcOEt/hexane 3:1) gave 150 mg (56%) of **22b** as a diastereoisomer mixture. R_f (AcOEt/hexane 3:1) 0.56. ^{1}H-NMR: 1.20–1.80 (*m*, overlap with 1.24 (*s*) and 1.63 (*s*), total 23 H); 2.00–2.30 (*m*, overlap with 2.05 (*s*); 2.09 (*s*), 211 (*s*), and 2.20 (*s*), total 18 H); 2.91 (*t*, 2 H); 3.23 (*m*, 2 H); 3.75 (*d*, J = 10.3, overlap with 3.77 (*s*), total 4 H); 3.87 (*d*, J = 10.3, 1 H); 4.12 (*dd*, J = 12.5, 5.5, 1 H); 4.31 (*dd*, J = 12, 4.0 H); 4.95–5.10 (*m*, 1 H); 5.29 (*d*, J = 5.5, 1 H); 5.44 (*m*, 1 H); 5.67 (*m*, 1 H); 6.09 (*m*, 1 H). ^{13}C-NMR: 20.06 (*q*); 20.40 (*q*); 20.65 (*q*); 20.66 (*q*); 20.72 (*q*); 26.77 (*t*); 28.68 (*t*); 29.00 (*t*); 29.04 (*t*); 29.18 (*t*); 29.37 (*t*); 29.47 (*t*); 29.51 (*t*); 29.53 (*t*); 29.55 (*t*); 36.02 (*t*); 39.52 (*t*); 53.12 (*t*); 61.51 (*t*); 61.81 (*s*); 68.72 (*d*); 69.08 (*d*); 69.37 (*d*); 71.66 (*d*); 165.86 (*s*); 169.17 (*s*); 169.61 (*s*); 169.84 (*s*); 170.58 (*s*); 196.70 (*s*). LSI-MS (calc. for $C_{34}H_{54}BrNO_{14}S$, 812.77; matrix glycerol): 812 (78, M^+), 754 (79), 710 (36), 604 (38); 572 (34), 540 (100), 512 (37), 470 (33), 424 (62), 361 (92), 332 (55).

O-*Methyl* S-*(10-Oxo-12,15,18-trioxa-9-azanonadecyl) Dimethylmonothiomalonate* (= *Methyl 2,2-Dimethyl-3-oxo-3-[(10-oxo-12,15,18-trioxa-9-azanona-decyl)thio]propanoate*; **24**). Methyl hydrogen dimethylmalonate (**23**; 100 mg, 0.684 mmol) in CH_2Cl_2 (5 ml) was treated with $CHCl_2OMe$ (1 g, 8.7 mmol) overnight [25]. The excess chlorinating agent was removed under reduced pressure and the acid chloride dissolved in CH_2Cl_2 (10 ml) and added dropwise to the soln. of **9b** (219 mg, 0.684 mmol) and Et_3N (0.5 ml) in CH_2Cl_2 (20 ml) at 0°. The mixture was stirred for 20 h at r.t. and worked up. FC (CH_2Cl_2/MeOH 20:1) gave 134 mg (44%) of **22b**. Clear oil. R_f (CH_2Cl_2/MeOH 20:1) 0.29. IR ($CHCl_3$): 1740*s*, 1680*s*, 1545*s*, 1470*s*, 1155*s*, 1110*s*, 970*s*. ^{1}H-NMR: 1.22–1.45 (*m*, superimposed at 1.56 (*s*), total 14 H); 1.48–1.64 (2*m*, 4 H); 2.88 (*t*, J = 7.35, 2 H); 3.23–3.31 (*q*, 2 H); 3.38 (*s*, 3 H); 3.55–3.58 (*m*, 2 H); 3.65–3.70 (*m*, 6 H); 3.68 (*s*, 2 H); 3.98 (*s*, 2 H); 7.01 (*t*, 1 H). ^{13}C-NMR: 23.07 (*q*); 23.09 (*q*), 26.76 (*t*); 28.60 (*t*); 28.88 (*t*); 28.89 (*t*); 29.03 (*t*); 29.13 (*t*); 29.50 (*t*); 38.78 (*t*); 52.54 (*q*); 56.96 (*s*); 58.88 (*q*); 70.11 (*t*); 70.31 (*t*); 70.43 (*t*); 70.88 (*t*); 71.79 (*t*); 169.71 (*s*); 172.85 (*s*); 200.04 (*s*). MS (calc.

for $C_{21}H_{39}O_7NS$, 449.50): 449 (20, M^+), 418 (45), 374 (14), 320 (95), 288 (30), 244 (55), 212 (30), 129 (55), 101 (92).

O-*Methyl* S-*(10-Oxo-12,15,18-trioxa-9-azanonadecyl) 2-Methylmonothiosuccinate* (= *Methyl 2-Methyl-4-oxo-4-[(10-oxo-12,15,18-trioxa-9-azanonadecyl)thio]butanoate*; **26**). 4-(*tert*-Butyl) 1-methyl 2-methylsuccinate (**25**; 300 mg, 1.48 mmol) was stirred in CF_3COOH (7 ml) for 4 h at r.t. and, after evaporation, treated with $CHCl_2OMe$ (1 g, 8.7 mmol) for 12 h. The excess chlorinating agent was evaporated and the acid chloride dissolved in CH_2Cl_2 (7 ml) and added dropwise to a soln. of **9b** (150 mg, 0.467 mmol) and Et_3N (0.5 ml) in CH_2Cl_2 (10 ml) within 20 min. Workup and FC (CH_2Cl_2/Et_2O/MeOH 8 : 2 : 1) gave **26** (0.10 g, 48%) as a clear oil. HPLC (H_2O/MeOH 3 : 7): 79.8 mg (38%). R_f (CH_2Cl_2/Et_2O/MeOH 8 : 2 : 1) 0.66. IR ($CHCl_3$): 1740*s*, 1680*s*, 1545*s*, 1110*s*, 970*s*. ^{1}H-NMR: 1.20 (*d*, *J* = 6.78, 3 H); 1.30 (*m*, 8 H); 1.50–1.64 (2*m*, 4 H); 2.60–2.64 (*m*, 1 H); 2.86 (*t*, *J* = 7.26, 2 H); 2.94–3.07 (*m*, 2 H); 3.24–3.30 (*q*, 2 H); 3.38 (*s*, 3 H); 3.55–3.58 (*m*, 2 H); 3.65–3.70 (*m*, 6 H); 3.98 (*s*, 2 H); 7.03 (*t*, 1 H). ^{13}C-NMR: 16.62 (*q*); 26.68 (*t*); 28.53 (*t*); 28.71 (*t*); 28.81 (*t*); 28.96 (*t*); 29.31 (*t*); 29.42 (*t*); 35.83 (*d*); 38.71 (*t*); 46.68 (*t*); 51.76 (*q*); 58.81 (*q*); 70.04 (*t*); 70.24 (*t*); 70.37 (*t*); 70.81 (*t*); 71.72 (*t*); 169.64 (*s*); 175.24 (*s*); 197.37 (*s*). MS: 449 (8, M^+), 418 (16), 321 (58), 320 (68), 288 (36), 263 (26), 244 (36), 219 (19), 212 (15), 188 (17), 129 (100). HR-MS: 449.244960 ($C_{21}H_{39}O_7NS^+$; calc. 449.247425).

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