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RESEARCH ARTICLE

Synthesis of ^{13}C-labelled cutin and suberin monomeric dicarboxylic acids of the general formula $HO_2{}^{13}C$-$(CH_2)_n$-$^{13}CO_2H$ (n = 10, 12, 14, 16, 18, 20, 22, 24, 26, 28)

Carina Schink[1] | **Sandra Spielvogel**[2] | **Wolfgang Imhof**[1]

[1]Institute of Integrated Natural Sciences, University Koblenz–Landau, Koblenz, Germany

[2]Institute of Plant Nutrition and Soil Science, Christian-Albrechts University of Kiel, Kiel, Germany

Correspondence
Wolfgang Imhof, Institute of Integrated Natural Sciences, University Koblenz–Landau, Universitätsstr. 1, Koblenz D-57060, Germany.
Email: imhof@uni-koblenz.de

^{13}C-labeled dicarboxylic acids $HO_2{}^{13}C$-$(CH_2)_n$-$^{13}CO_2H$ (n = 10, 12, 14, 16, 18, 20, 22, 24, 26, 28) have been synthesized as internal standards for LC-MS and GC-MS analysis of cutin and suberin monomer degradation by soil-based microorganisms. Different synthetic strategies had to be applied depending on the chain length of the respective synthetic target and because of economic considerations. ^{13}C-labels were introduced by nucleophilic substitution of a suitable leaving group with labelled potassium cyanide and subsequent hydrolysis of the nitriles to produce the corresponding dicarboxylic acids. All new compounds are characterized by GC/MS, IR, and NMR methods as well as by elemental analysis.

KEYWORDS

^{13}C labelling, cutin, dicarboxylic acids, internal standards, suberin

1 | INTRODUCTION

Cutin and suberin are hydrophobic polymeric compounds being present in plants, which have in common, that is, from a chemical point of view, they both are polyesters. Nevertheless, constituents and their relative amount differ over a wide range depending on the biological function of these polymers and on the specific organism they are isolated from.[1–5] Cutin is part of the cuticle that is the hydrophobic boundary of aerial plants covering the outer face of the epidermis.[6–8] It is widely accepted that the cuticle was developed during the evolutionary step in which plants first populated terrestrial ecosystems.[9,10] The cuticle as the aerial interface between the plant's organs and the atmosphere acts as a barrier against desiccation and plant pathogens, regulates ion and gas transport, and is also crucial for maintaining the morphology of the plant itself.[4,11–13] Suberin on the other hand is deposited on the inner cell wand next to the plasma membrane and is mostly found in root endodermal and exodermal cell layers. The function of suberin is therefore mainly to act as a barrier between the plant and the soil environment. Nevertheless, suberized tissues are also present in aerial plant parts, for example, in bark cells of trees. Moreover, suberin is overexpressed in connection with wounding of the respective plant organs, obviously to minimize additional stress from outside the plant's organism.[4,14–20]

Concerning the chemical composition of cutin and suberin and because of the fact that they both are polyesters, they contain constituents with carboxylic and alcoholic functions.[3,21] Cutin and suberin are composed from unsubstituted fatty acids as well as oxygenated fatty acids. The latter may be either α,ω-dicarboxylic acids or ω-hydroxy fatty acids. In addition, there are derivatives of unsubstituted fatty acids, α,ω-dicarboxylic acids and

ω-hydroxy fatty acids, showing midchain functionalities, that is, epoxy and one or two hydroxy groups. Moreover, minor amounts of alkan-1-ols and α,ω-alkanediols and varying amounts of glycerol are observed. All those compounds (except glycerol) are also present with one or even two double bonds in the hydrocarbon chain. Concerning the chain lengths of fatty acids and their derivatives in cutin and suberin, it gets obvious that in cutin, C_{16} and C_{18} derivatives are by far the most common, whereas in suberin, higher chain lengths up to C_{26} are frequently found.[1,3] From a polymer chemist's point of view, this means that monofunctionalized molecules such as fatty acids and alkan-1-ols act as termini of polymer chains, difunctionalized molecules such as α,ω-dicarboxylic acids, ω-hydroxy fatty acids or α,ω-alkanediols are constituents building up linear fractions of the polymeric structure, and midchain functionalized monomers as well as glycerol allow for the formation of branched polymeric structures. Next to the aforementioned constituents, suberin also contains significant amounts of aromatic building blocks such as ferulate and in most cases to a lower extend coumarate, sinapate, or caffeate.[5,22–25] The relative content of all these monomers therefore allows for a subtle fine tuning of material properties of the respective polyester for tailor-made applications in specific plant organs. On the other hand, the diverse composition of cutin and suberin in terms of monomeric species significantly hampered their application as a polymeric renewable resource, which nevertheless actually is investigated to an increasing extend.[26]

Biosynthesis of cutin and suberin has been extensively studied and thoroughly reviewed concerning the involved genes, enzymes, and even the use of the latter as the basis for applications of the respective enzymes in the formation of fine chemicals and materials based on biological material.[2,19,27–32] Another interesting target of research was the question how transport and deposition of such hydrophobic material are realized, which led to investigations of lipid transporting proteins, so-called LTPs.[33]

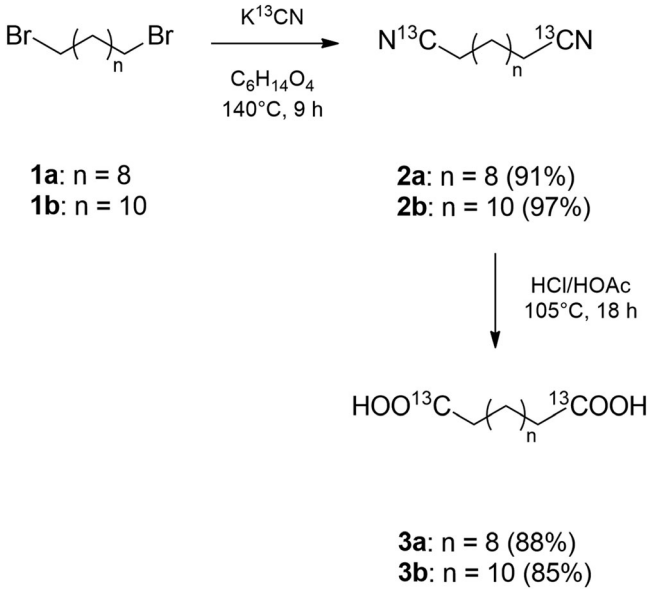
In paleoenvironmental studies and soil science, the abundance of cutin- and suberin-specific monomers is commonly used as an indicator of contributions from above ground and below ground plant organs to soils and sediments.[34–37] Moreover, monomers of wax esters,cutin, and suberin may also have potential as biomarkers for reconstruction of different plant types and taxa in soils and sediments.[38] Indeed, the high diversity of plant-derived lipids and their unique speciation in taxonomic groups as well as their long-term preservation in paleoecological and geoarcheological archives make them the most promising substance class to be used as biomarkers.[36,39–41] In contrast to hydrolyzable lipid sources in soil, studies of their transformation are almost absent.[41,42] Moreover, the underlying mechanisms of the distortion of lipid fingerprints of source vegetation due to microbial transformations are still unclear. Preferential microbial utilization of specific precursors, de-novo synthesis of individual compounds, and transformation and recycling of existing lipids are known to occur in pure culture systems but have rarely been investigated in soils.[43–46] This is in particular due to the lack of commercially available labelled monomers that might be used as internal standards in LC-MS and GC-MS analysis of cutin and suberin monomers.

The intention of our research is to address the cycling of these lipid materials in the soil, therefore, to have a look rather on the degradation of cutin and suberin and on the question how they are recycled by soil-based microorganisms. In order to do so, we have to establish methodologies of analyzing the monomeric constituents of cutin and suberin as well as to identify potential cleavage products. We therefore present herein the synthesis of ^{13}C-labelled dicarboxylic acids of the general formula $HO_2{}^{13}C\text{-}(CH_2)_n\text{-}{}^{13}CO_2H$ (n = 10, 12, 14, 16, 18, 20, 22, 24, 26, 28), which will be used as internal standards in LC-MS and GC-MS analytics.

2 | RESULTS AND DISCUSSION

Synthetic procedures for the production of labelled dicarboxylic acids have to take into account first of all the commercial availability of suitable starting compounds as well as the economic use of labelled substrates. So, in principle, in multistep synthetic pathways, it is advantageous to introduce the desired label as late as possible. In addition, we first optimized all reaction sequences using nonlabelled reagents. This approach was chosen not only because of economic reasons but also because we had to optimize purification processes, too, in order to achieve products of high purity that might be used for analytical purposes.

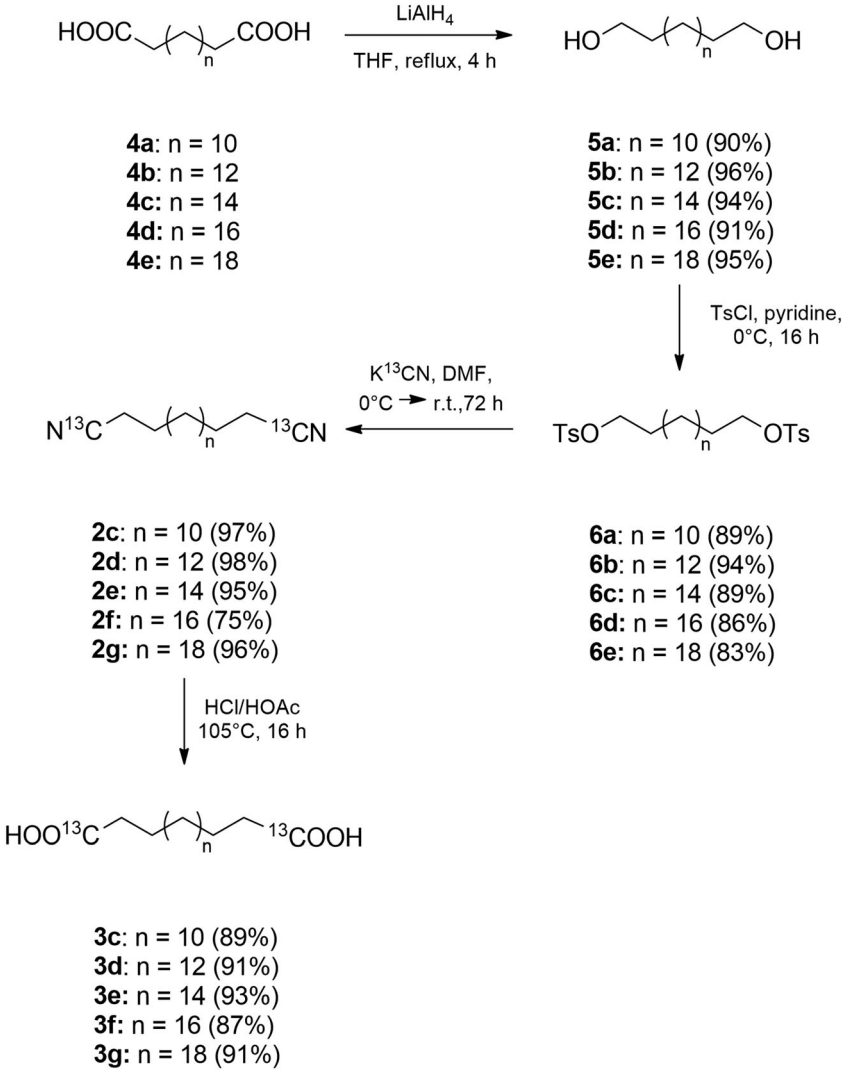
We decided to bring in the label by the use of $K^{13}CN$ using typical nucleophilic substitution conditions. Compared with recently published procedures for isotopic labelling of carboxylic acids, we expected to achieve better yields relative to the labelled starting compound in contrast to the use, for example, of ^{13}CO or $^{13}CO_2$, and no organometallic catalyst has to be used, which in most cases require quite polar solvents and therefore will not be suitable in reactions with very hydrophobic substrates.[47–49] The use of $K^{13}CN$ therefore is the obvious choice especially in the synthesis of labelled carboxylic acids, which also been pointed out for the synthesis of labelled calcitroic acid.[50]



SCHEME 1 Synthetic pathway for the production of ^{13}C-labelled dicarboxylic acids **3a** and **3b**

So the synthesis of 1,12-dodecanedioic acid, **3a**, and 1,14-tetradecanedioic acid, **3b**, quite straightforward works starting from the corresponding α,ω-dibromoalkanes with two carbon atoms less compared with the desired products. Therefore, the reaction of 1,10-dibromodecane, **1a**, or 1,12-dibromododecane, **1b**, with $K^{13}CN$ yields the corresponding dinitriles **2a** and **2b**, which then might be hydrolyzed to produce the labelled dicarboxylic acids **3a** and **3b** in high overall yields (Scheme 1). The synthesis of **3a**, as well as a derivative with four ^{13}C labels, has already been described via the same synthetic route.[51,52]

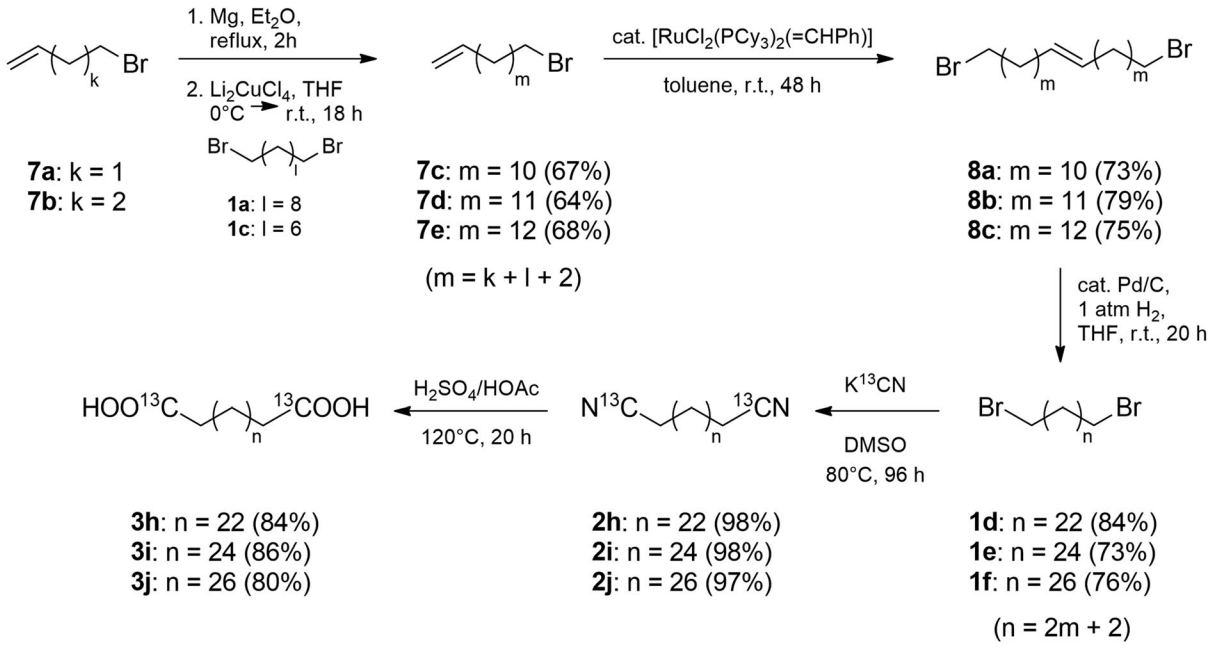
Another synthetic strategy had to be developed for the synthesis of the dicarboxylic acids **3c–3g** with 16, 18, 20, 22, and 24 carbon atoms (Scheme 2), because the corresponding α,ω-dibromoalkanes are either not commercially available at all or too expensive to allow for an economic synthesis of the target compounds. So we chose nonlabelled dicarboxylic acids with two carbon atoms less than the desired products, which are commercially



SCHEME 2 Synthetic pathway for the production of ^{13}C-labelled dicarboxylic acids **3c–3g**

available. In a first reaction step, the corresponding dicarboxylic acids **4a–4e** are reduced to the corresponding α,ω-alkyldiols **5a–5e** using $LiAlH_4$. The diols are then treated with tosyl chloride to give the α,ω-alkyl-bis-tosylates **6a–6e**, which are well suited to act as the substrates for the introduction of the label, which again is realized by nucleophilic substitution of the tosyl leaving groups by ^{13}C cyanide yielding the dinitriles **2c–2g**, which in analogy to the first synthetic procedure are hydrolyzed to give the desired dicarboxylic acids **3c–3g**. Typically, in most cases, synthetic steps show individual yields of more than 90%.

Nevertheless, both synthetic procedures described so far do not work for the synthesis of the last desired labelled dicarboxylic acids **3h–3j** with a chain length of 26, 28, and 30 carbonatoms, respectively (Scheme 3). Neither suitable α,ω-dibromoalkanes nor dicarboxylic acids with the correct chain length, which might be used as starting compounds adapting a synthetic strategy as depicted in Scheme 2, are commercially available. So we decided a synthetic scheme in which the carbon chain is built up by a ruthenium-catalyzed metathesis reaction. Therefore, either 4-bromo-1-butene, **7a**, or 5-bromo-1-pentene, **7b**, are first converted into a Grignard compound and are then reacted with 1,10-dibromodecane, **1a**, or 1,8-dibromooctane, **1c**, in the presence of lithium tetrachlorocuprate to produce the corresponding ω-bromo-1-alkenes **7c–7e**. By this strategy, the reaction of **7b** with **1c** yields 13-bromo-1-tridecen, **7c**; the reaction of **7a** with **1a** leads to the formation of 14-bromo-1-tetradecen, **7d**; and the treatment of **7b** with **1a** produces 15-bromo-1-pentadecen, **7e**. Next to the desired products **7c–7e**, side products with even bigger chain lengths are produced, which nevertheless show a very similar behavior during purification by column chromatography. So the crude products frequently had to be purified by two subsequent chromatographic purification steps. This explains the comparatively lower yields of 66% in average. The ω-bromo-1-alkenes **7c–7e** are then transferred into α,ω-dibromoalkenes **8a–8c** by a metathesis reaction catalyzed by a typical Grubbs' catalyst. Next to a duplication of carbon atoms **8a–8c** show a central carbon–carbon double bond. It turned out that the long-chain substrates **7c–7e** even applying longer reaction times are not completely reacted leading to isolated yields of 73%–79% for compounds **8a–8c**. In the next reaction step, compounds **8a–8c** are hydrogenated under smooth conditions using a palladium on charcoal catalyst yielding α,ω-dibromoalkanes **1d–1f** with 24, 26, and 28 carbon atoms, respectively, in 80% yield in average. From then on, the synthetic pathway follows the one already shown in Scheme 1. $K^{13}CN$ is used to replace the bromo substituents in **1d–1f** by cyano groups and by that adding the label as well as two additional carbon atoms and yielding the dinitriles **2h–2j**, which are subsequently hydrolyzed to produce the labelled dicarboxylic acids **3h–3j** with 26, 28, and 30 carbon atoms. Nucleophilic substitution works almost quantitatively, whereas for the hydrolysis of the dinitriles, sulfuric acids have to be used, which leads to oxidative side reactions and yields the target compounds with about 83% yield in average.



SCHEME 3 Synthetic pathway for the production of ^{13}C-labelled dicarboxylic acid **3h–3j**

3 | CONCLUSIONS

In conclusion, we present three different synthetic pathways for the synthesis of ^{13}C-labelled α,ω-dicarboxylic acids with saturated hydrocarbon chains of 12, 14, 16, 18, 20, 22, 24, 26, 28, or 30 carbon atoms in high overall yields. The label always is introduced by the use of economically benign $K^{13}CN$, and the corresponding reaction step is placed as close to the end of the overall procedure as possible leading to minimization of loss of labelled material.

4 | EXPERIMENTAL

4.1 | General

All chemicals and solvents have been purchased from Sigma-Aldrich, ABCR, Acros Organics, Alfa Aesar, TCI, and VWR and were used without further purifications after having checked their purity by spectroscopic methods. Deuterated solvents for NMR spectroscopy and $K^{13}CN$ (99%) have been purchased from Deutero GmbH, Kastellaun, Germany. Anhydrous diethylether and THF were obtained by heating the respective solvent over sodium/benzophenone. Freshly distilled portions were introduced to reaction mixtures in which anhydrous solvents had to be used. Preparative column chromatography was performed at silica 60 (particle size, 0.040–0.063 mm) from Macherey & Nagel. Colorless compounds were detected by UV light. IR spectra were recorded at 298 K using a Shimadzu IR Prestige-21 FTIR spectrometer with a MIRacle ATR unit from PIKE Technologies. GC-MS spectra were recorded by a Finnigan MAT GCQ system equipped with a Macherey& Nagel GC column (5% diphenylsiloxane, 95% dimethylsiloxane, 30-m length, 0.25-mm inner diameter, and 0.25-μm film thickness). NMR spectra were obtained by the use of either a Bruker Avance 400, a Bruker Avance DRX 600, or a JEOL JNM-ECZ500R spectrometer. CHN analyses were performed using a vario EL III or a vario MICRO cube analyzer both purchased from Elementar Analysensysteme GmbH.

4.2 | Synthesis and characterization of 2a and 2b (modified after Louw et al.[53])

In a 25-ml round flask was placed 3.20 mmol of the corresponding α,ω-dibromoalkane (960-mg **1a**, 1050-mg **1b**) together with 10-ml triethyleneglycol and 6.56 mmol (44 mg) $K^{13}CN$. The mixture is then heated to 140°C for 18 h under stirring. After being cooled down to room temperature (r.t.), the yellowish reaction mixture was transferred to a separating funnel together with 40 ml of demineralized water. The aqueous phase was washed four times with 30 ml of diethylether. The combined organic phases were dried with Na_2SO_4 and then filtered, and the solvent was then evaporated. The resulting crude products were purified by column chromatography using a mixture of diethylether and light petroleum (1:2) as the eluent. **2a** (566 mg, 91%) were obtained as a colorless liquid, whereas **2b** (690 mg, 97%) turned out to be a colorless wax-like solid.

4.2.1 | (1,12-^{13}C)Dodecanedinitrile (2a)

^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.27–1.35 (m, 8H), 1.40–1.47 (m, 4H), 1.61–1.68 (m, 4H), 2.33 (dt, $^2J_{CH2/13C}$ = 9.58 Hz, $^3J_{CH2/CH2}$ = 7.13 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.00 (d, $^1J_{13C/C}$ = 55.02 Hz), 25.22 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.50 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.58, 29.03, 119.76; MS (EI): m/z (%) = 193 (2) [M^+ − H], 176 (1), 165 (2), 153 (3) [M^+ − $C^{13}CH_2N$], 125 (2) [M^+ − $C_3{}^{13}CH_6N$], 111 (10) [$C_6{}^{13}CH_{12}N^+$], 97 (12) [$C_5{}^{13}CH_{11}N^+$], 96 (45) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_4{}^{13}CH_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2926 (s, CH_2), 2855 (m, CH_2), 2191 (w, ^{13}C≡N), 1464 (m, CH_2), 1425 (m, CH_2), 723 (m, CH_2); elemental analysis for $C_{10}{}^{13}C_2H_{20}N_2$: calcd. C 75.21, H 10.38, N 14.42, found C 73.88, H 10.27, N 14.36.

4.2.2 | (1,14-^{13}C)Tetradecanedinitrile (2b)

m.p. 32°C–33°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.34 (m, 12H,), 1.41–1.47 (m, 4H), 1.62–1.69 (m, 4H), 2.33 (dt, $^2J_{CH2/13C}$ = 9.54 Hz, $^3J_{CH2/CH2}$ = 7.15 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.04 (d, $^1J_{13C/C}$ = 56.12 Hz), 25.28 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.57 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.66, 29.18, 29.32, 119.82; MS (EI): m/z (%) = 221 (2) [M^+ − H], 193 (3), 181 (3) [M^+ − $C^{13}CH_2N$], 179 (4), 139 (2) [M^+ − $C_4{}^{13}CH_8N$], 125 (10) [$C_7{}^{13}CH_{14}N^+$], 110 (25) [$C_6{}^{13}CH_{12}N^+$], 97 (25) [$C_5{}^{13}CH_{11}N^+$], 96 (63) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_4{}^{13}CH_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2918 (s, CH_2), 2853 (m, CH_2), 2193 (w, ^{13}C≡N), 1472 (s, CH_2), 718 (m, CH_2); elemental analysis for $C_{12}{}^{13}C_2H_{24}N_2$: calcd. C 76.52, H 10.88, N 12.60, found C 75.57, H 10.60, N 12.48.

4.3 | Synthesis and characterization of 5a–5e (modified after Franchini et al.[54])

In a 250-ml two-necked flask equipped with a return condenser and a septum 57.71-mmol (2.19 g) $LiAlH_4$ was suspended in 20 ml of anhydrous THF. A solution of 6.41 mmol of the corresponding α,ω-dicarboxylic acid (1.57-g **4a**, 1.66-g **4b**, 1.84-g **4c**, 2.02-g **4d**, and 2.20-g **4e**) in 85 ml of anhydrous THF was added in portions with a syringe under ice cooling so slowly that THF was boiling only moderately. After the addition of the respective dicarboxylic acid was finished, the mixture was refluxed for 4 h. Then the reaction mixture is again cooled to 0°C by external ice cooling, and water is added dropwise to decompose the residual amount of $LiAlH_4$. During this procedure, the color of the suspension turned from gray to white. The reaction mixture then was added to 700-ml demineralized water in a beaker, and pH is adjusted to 1 with hydrochloric acid in order to dissolve all inorganic constituents of the reaction mixture. The resulting suspension is stirred for 30 min followed by collecting the white precipitate by filtration using a Büchner funnel (r.t. for **5a** and **5b** and 70°C for **5c**, **5d**, and **5e**) and washing of the precipitate with 50 ml of demineralized water. Crude α,ω-dihydroxyalkanes **5a–5d** were recrystallized from n-heptane/methanol. After filtration, the white solid material was washed with 3-ml ice-cold diethylether and dried under reduced pressure. **5e** was purified by column chromatography using a mixture of chloroform and ethanol (3:1) as the eluent. Yields: 1.33-g (90%) **5a**, 1.59-g (96%) **5b**, 1.73-g (94%) **5c**, 1.84-g (91%) **5d**, and 2.09-g (95%) **5e**.

4.3.1 | 1,14-Dihydroxytetradecane (5a)

m.p. 87°C–89°C[55]; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.22–1.35 (m, 20H), 1.39–1.49 (m, 4H), 3.38–3.49 (m, 4H); ^{13}C-NMR (151 MHz, THF, 298 K): δ (ppm) = 27.26, 30.88, 30.94, 30.96, 31.01, 34.40, 62.86; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3344 (m, OH), 2918 (s, CH_2), 2846 (s, CH_2), 1462 (m, CH_2), 1407 (m, OH), 1051 (m, C–O), 1016 (m), 997 (w), 727 (m, CH_2), 609 (m).

4.3.2 | 1,16-Dihydroxyhexadecane (5b)

m.p. 93°C–94°C[56]; ^{1}H-NMR (500 MHz, DMSO, 333 K): δ (ppm) = 1.19–1.28 (m, 24H), 1.33–1.41 (m, 4H), 3.31–3.38 (m, 4H), 4.13 (br, s, 2H); ^{13}C-NMR (126 MHz, DMSO, 333 K): δ (ppm) = 25.42, 28.85, 28.88, 28.91, 28.96, 32.46, 60.73; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3248 (m, OH), 2918 (s, CH_2), 2846 (s, CH_2), 1460 (m, CH_2), 1408 (m, OH), 1056 (m, C–O), 1043 (m), 1028 (w), 731 (m, CH_2), 610 (m).

4.3.3 | 1,18-Dihydroxyoctadecane (5c)

m.p. 98°C–99°C[57]; ^{1}H-NMR (500 MHz, DMSO, 343 K): δ (ppm) = 1.22–1.31 (m, 28H), 1.36–1.45 (m, 4H), 3.35–3.41 (m, 4H), 4.10 (br, s, 2H); ^{13}C-NMR (126 MHz, DMSO, 343 K): δ (ppm) = 25.03, 28.44, 28.50, 28.56, 32.08, 60.37; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3247 (m, OH), 2918 (s, CH_2), 2847 (s, CH_2), 1460 (m, CH_2), 1408 (m, OH), 1058 (m, C–O), 1048(m), 1017 (m), 727 (m, CH_2), 606 (m).

4.3.4 | 1,20-Dihydroxyicosane (5d)

m.p. 102°C–105°C[57]; ^{1}H-NMR (500 MHz, DMSO, 353 K): δ (ppm) = 1.22–1.33 (m, 32H), 1.36–1.46 (m, 4H), 3.39 (t, $^3J_{CH2/CH2}$ = 6.59 Hz, 4H), 4.06 (br, s, 2H); ^{13}C-NMR (126 MHz, DMSO, 343 K): δ (ppm) = 25.31, 28.72, 28.76, 28.84, 32.37, 60.68; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3321 (m, OH), 2916 (s, CH_2), 2846 (s, CH_2), 1462 (m, CH_2), 1407 (m, OH), 1055 (m, C–O), 1033 (m), 999 (w), 721 (m, CH_2), 606 (m).

4.3.5 | 1,22-Dihydroxydocosane (5e)

m.p. 106°C–107°C[58]; ^{1}H-NMR (500 MHz, DMSO, 383 K): δ (ppm) = 1.25–1.31 (m, 36H), 1.39–1.47 (m, 4H), 3.40 (t, $^3J_{CH2/CH2}$ = 6.30 Hz, 4H), 3.90 (br, s, 2H); ^{13}C-NMR (126 MHz, DMSO, 383 K): δ (ppm) = 24.87, 28.28, 28.31, 28.38, 31.94, 60.28; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3240 (m, OH), 2914 (s, CH_2), 2846 (s, CH_2), 1462 (m, CH_2), 1408 (m, OH), 1060 (m, C–O), 1041 (m), 1018 (w), 731 (m, CH_2), 665 (m), 553 (s).

4.4 | Synthesis and characterization of 6a–6c (modified after Mori[59])

In a 50-ml Schlenk tube was placed 3.87 mmol of the respective α,ω-dihydroxyalkane (890-mg **5a**, 1.00-g **5b**, and 1.10-g **5c**) being dissolved in 17 ml of pyridine. The solution was then cooled to 0°C–5°C using a cryostat; 14.90 mmol (2.84 g) *p*-toluenesulfonyl chloride is added in portions over a period of 30 min. The resulting solution was stirred under cooling for 18 h. During the reaction time, a white precipitate was formed. The reaction mixture then was added to 100-ml demineralized water in a beaker, and pH is adjusted to 1 with hydrochloric acid. The white precipitate was filtered, washed with 20 ml of demineralized water, and dried under reduced pressure. Recrystallization of crude **6a–6c** was performed from a mixture of acetone and ethanol. After standing in the refrigerator overnight, the crystalline material was

filtered, washed with 5 ml of demineralized water, and dried under reduced pressure. Yields: 1.86-g (89%) **6a**, 2.06-g (94%) **6b**, and 1.98-g (89%) **6c**.

4.4.1 | Tetradecane-1,14-diyl bis (4-methylbenzenesulfonate) (6a)

m.p. 77°C–79°C[60]; ^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.19–1.24 (s, 16H), 1.25–1.32 (m, 4H), 1.58–1.68 (m, 4H), 2.45 (s, 6H), 4.02 (t, $^{3}J_{CH2/CH2}$ = 6.59 Hz, 4H), 7.35 (d, $^{3}J_{CH2/CH2}$ = 8.59 Hz, 4H), 7.79 (d, $^{3}J_{CH2/CH2}$ = 8.59 Hz, 4H); ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 21.59, 25.28, 28.77, 28.87, 29.32, 29.42, 29.45, 29.49, 70.68, 127.84, 129.76, 133.22, 144.59; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3061 (w, $CH_{arom.}$), 2976 (w, CH_3), 2922 (m, CH_2), 2850 (m, CH_2), 1597 (w, C═$C_{arom.}$), 1473 (m, C═$C_{arom.}$), 1356 (s, SO_2), 1173 (s, SO_2), 947 (s), 835 (s, $CH_{arom.}$), 723 (w, CH_2), 665 (m), 553 (s).

4.4.2 | Hexadecane-1,16-diyl bis (4-methylbenzenesulfonate) (6b)

m.p. 81°C–83°C[56]; ^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.18–1.26 (m, 20H), 1.26–1.34 (m, 4H), 1.59–1.67 (m, 4H), 2.45 (s, 6H), 4.02 (t, $^{3}J_{CH2/CH2}$ = 6.30 Hz, 4H), 7.35 (d, $^{3}J_{CH2/CH2}$ = 8.59 Hz, 4H), 7.79 (d, $^{3}J_{CH2/CH2}$ = 8.59 Hz, 4H); ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 21.59, 25.28, 28.77, 28.88, 29.33, 29.44, 29.45, 29.54, 70.68, 127.84, 129.76, 133.23, 144.59; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3053 (w, $CH_{arom.}$), 2976 (w, CH_3), 2920 (m, CH_2), 2849 (m, CH_2), 1599 (w, C═$C_{arom.}$), 1474 (m, C═$C_{arom.}$), 1356 (s, SO_2), 1173 (s, SO_2), 947 (s), 837 (s, $CH_{arom.}$), 721 (w, CH_2), 665 (m), 553 (s).

4.4.3 | Octadecane-1,18-diyl bis (4-methylbenzenesulfonate) (6c)

m.p. 89°C–91°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.13–1.45 (m, 28H), 1.58–1.78 (m, 4H), 2.45 (s, 6H), 4.02 (t, $^{3}J_{CH2/CH2}$ = 6.72 Hz, 4H), 7.34 (d, $^{3}J_{CH2/CH2}$ = 7.70 Hz, 4H), 7.79 (d, $^{3}J_{CH2/CH2}$ = 7.70 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 21.58, 25.26, 28.75, 28.86, 29.33, 29.44, 29.55, 29.61, 70.67, 127.81, 129.75, 133.17, 144.58; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3061 (w, $CH_{arom.}$), 2976 (w, CH_3), 2918 (m, CH_2), 2848 (m, CH_2), 1599 (w, C═$C_{arom.}$), 1474 (m, C═$C_{arom.}$), 1355 (s, SO_2), 1172 (s, SO_2), 947 (s), 837 (s, $CH_{arom.}$), 721 (w, CH_2), 665 (m), 554 (s); elemental analysis: calcd. C 64.61, H 8.47, S 10.78, found C 65.01, H 8.44, S 10.64.

4.5 | Synthesis and characterization of 6d and 6e (modified after Marukawa et al.[61])

In a 100-ml Schlenk tube was placed 1.75 mmol of the respective α,ω-dihydroxyalkane (550-mg **5d** and 600-mg **5e**), which was dissolved in a mixture of 25 ml of pyridine and 25 ml of chloroform. The solution was then cooled to 0°C–5°C using a cryostat; 6.29-mmol (1.23 g) *p*-toluenesulfonyl chloride is added in portions over a period of 30 min. The resulting solution was stirred under cooling for 18 h. Then 50 ml of demineralized water was added to the reaction mixture, which was then extracted three times with 50 ml of chloroform in a separating funnel. The combined organic phases were washed with diluted hydrochloric acid, saturated $NaHCO_3$ solution, and brine before they were dried over Na_2SO_4 and filtered. Evaporation of the solvent yields crude **6d** and **6e**, respectively as white solids. **6d** was purified by recrystallization from a mixture of acetone and ethanol. After standing in the refrigerator overnight, the crystalline material was filtered, washed with 5 ml of demineralized water, and dried under reduced pressure. Yield: 937-mg (86%) **6d**. **6e** was purified by column chromatography using chloroform as the eluent. Yield: 946-mg (83%) **6e**.

4.5.1 | Icosane-1,20-diyl bis (4-methylbenzenesulfonate) (6d)

m.p. 92°C–93°C; ^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.18–1.34 (m, 32H), 1.60–1.67 (m, 4H), 2.45 (s, 6H), 4.02 (t, $^{3}J_{CH2/CH2}$ = 6.59 Hz, 4H), 7.35 (d, $^{3}J_{CH2/CH2}$ = 8.02 Hz, 4H), 7.79 (d, $^{3}J_{CH2/CH2}$ = 8.2 Hz, 4H); ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 21.84, 25.54, 29.03, 29.14, 29.60, 29.72, 29.82, 29.87, 29.91, 70.94, 128.10, 130.02, 133.49, 144.84; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3049 (w, $CH_{arom.}$), 2980 (w, CH_3), 2918 (m, CH_2), 2848 (m, CH_2), 1597 (w,. C═$C_{arom.}$), 1476 (m, C═$C_{arom.}$), 1356 (s, SO_2), 1175 (s, SO_2), 947 (s), 837 (s, $CH_{arom.}$), 719 (w, CH_2), 665 (m), 554 (s).

4.5.2 | Docosane-1,22-diyl bis (4-methylbenzenesulfonate) (6e)

m.p. 98°C–99°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.15–1.35 (m, 36H), 1.59–1.67 (m, 4H), 2.45 (s, 6H), 4.02 (t, $^{3}J_{CH2/CH2}$ = 6.51 Hz, 4H), 7.35 (d, $^{3}J_{CH2/CH2}$ = 8.07 Hz, 4H), 7.79 (d, $^{3}J_{CH2/CH2}$ = 8.25 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 21.59, 25.27, 28.76, 28.88, 29.34, 29.46, 29.57, 29.61, 29.64, 29.66, 70.68, 127.84, 129.75, 133.18,

144.58; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3074 (w, $CH_{arom.}$), 2978 (w, CH_3), 2916 (m, CH_2), 2848 (m, CH_2), 1597 (w, $C{=}C_{arom.}$), 1473(m, $C{=}C_{arom.}$), 1355 (s, SO_2), 1172 (s, SO_2), 945 (s), 837 (s, $CH_{arom.}$), 719 (w, CH_2), 665 (m), 553 (s); elemental analysis: calcd. C 66.42, H 8.98, found C 66.79, H 8.99.

4.6 | Synthesis and characterization of 2c–2 g (modified after Matsumori et al.[62])

In a 100-ml two-necked flask, 2.33 mmol of the corresponding α,ω-bis-tosylalkane (1.255-g **6a**, 1.321-g **6b**, 1.386-g **6c**, 1.451-g **6d**, and 1.517-g **6e**) was suspended in 30-ml DMF and cooled to 0°C with an ice bath; 4.78-mmol (316 mg) $K^{13}CN$ was added in portions over a period of 30 min. The reaction mixture was then allowed to reach r.t. and was stirred for 5 days. In case of the synthesis of **2g**, 40-ml DMF was used, and the reaction time was extended to 6 days. The reaction mixture then was added to 100-ml demineralized water in a beaker and was afterward extracted four times with diethylether. The combined organic phases were washed with brine and dried over Na_2SO_4. After filtration, the organic solvent was evaporated leading to the formation of yellowish oily products. The crude reaction products were purified by column chromatography using a mixture of diethylether and light petroleum (1:1) as the eluent. After evaporation of the solvents, all products were obtained as colorless solids. Yields: 565-mg (97%) **2c**, 634-mg (98%) **2d**, 678-mg (95%) **2e**, 585-mg (75%) **2f**, and 811-mg (96%) **2 g**.

4.6.1 | (1,16-^{13}C)Hexadecanedinitrile (2c)

m.p. 47°C–48°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.20–1.31 (m, 16H), 1.38–1.44 (m, 4H), 1.58–1.65 (m, 4H), 2.33 (dt, $^2J_{CH2/13C}$ = 9.67 Hz, $^3J_{CH2/CH2}$ = 7.08 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.06 (d, $^1J_{13C/C}$ = 56.12 Hz), 25.28 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.59 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.69, 29.23, 29.40, 29.47, 119.84; MS (EI): m/z (%) = 251 (2) [M^+ + H], 249 (3) [M^+ − H], 221 (3), 209 (5) [M^+ − $C^{13}CH_2N$], 207 (6), 180 (1) [M^+ − $C_3{}^{13}CH_6N$], 167 (2) [M^+ − $C_4{}^{13}CH_8N$], 153 (3) [$C_9{}^{13}CH_{18}N^+$], 139 (4) [$C_8{}^{13}CH_{16}N^+$], 125 (10) [$C_7{}^{13}CH_{14}N^+$], 111 (31) [$C_6{}^{13}CH_{12}N^+$], 98 (35) [$C_5{}^{13}CH_{11}N^+$], 97 (72) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_4{}^{13}CH_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2916 (s, CH_2), 2851 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1472 (m, CH_2), 718 (m, CH_2); elemental analysis: calcd. C 77.54, H 11.27, N 11.19, found C 76.54, H 10.97, N 11.13.

4.6.2 | (1,18-^{13}C)Octadecanedinitrile (2d)

m.p. 58°C–59°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.23–1.35 (m, 20H), 1.41–1.47 (quin, $^3J_{CH2/CH2}$ = 7.43 Hz, 4H), 1.62–1.69 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.72 Hz, $^3J_{CH2/CH2}$ = 7.15 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.06 (d, $^1J_{13C/C}$ = 56.12 Hz), 25.32 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.61 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.72, 29.25, 29.44, 29.53, 29.55, 119.84; MS (EI): m/z (%) = 277 (2) [M^+ − H], 249 (4), 237 (7) [M^+ − $C^{13}CH_2N$], 233 (8), 221 (2), 195 (3) [M^+ − $C_4{}^{13}CH_8N$], 181 (4) [M^+ − $C_5{}^{13}CH_{10}N$], 167 (3) [$C_{10}{}^{13}CH_{20}N^+$], 153 (3) [$C_9{}^{13}CH_{18}N^+$], 139 (5) [$C_8{}^{13}CH_{16}N^+$], 125 (11) [$C_7{}^{13}CH_{14}N^+$], 111 (39) [$C_6{}^{13}CH_{12}N^+$], 97 (40) [$C_5{}^{13}CH_{11}N^+$], 97 (86) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_4{}^{13}CH_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1472 (m, CH_2), 718 (m, CH_2); elemental analysis: calcd. C 78.36, H 11.58, N 10.06, found C 77.64, H 11.41, N 9.53.

4.6.3 | (1,20-^{13}C)Icosanedinitrile (2e)

m.p. 65°C–66°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.23–1.35 (m, 24H), 1.41–1.47 (m, 4H), 1.63–1.69 (m, 4H), 2.33 (dt, $^2J_{CH2/13C}$ = 9.54 Hz, $^3J_{CH2/CH2}$ = 7.15 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.05 (d, $^1J_{13C/C}$ = 55.02 Hz), 25.31 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.60 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.71, 29.25, 29.45, 29.53, 29.58, 29.60, 119.84; MS (EI): m/z (%) = 305 (2) [M^+ − H], 277 (5), 265 (7) [M^+ − $C^{13}CH_2N$], 263 (8), 249 (4), 223 (2) [M^+ − $C^{13}CH_8N$], 209 (3) [M^+ − $C_5{}^{13}CH_{10}N$], 195 (3) [M^+ − $C_6{}^{13}CH_{12}N$], 181 (4) [$C_{11}{}^{13}CH_{22}N^+$], 167 (5) [$C_{10}{}^{13}CH_{20}N^+$], 153 (5) [$C_9{}^{13}CH_{18}N^+$], 139 (5) [$C_8{}^{13}CH_{16}N^+$], 125 (15) [$C_7{}^{13}CH_{14}N^+$], 111 (47) [$C_6{}^{13}CH_{12}N^+$], 98 (58) [$C_5{}^{13}CH_{11}N^+$], 97 (86) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_4{}^{13}C_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2193 (w, $^{13}C{\equiv}N$), 1472 (m, CH_2), 716 (m, CH_2); elemental analysis: calcd. C 79.02, H 11.84, N 9.14, found C 78.62, H 12.17, N 8.28.

4.6.4 | (1,22-^{13}C)Docosanedinitrile (2f)

m.p. 71°C–72°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.24–1.34 (m, 28H), 1.41–1.47 (m, 4H), 1.62–1.69 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.54 Hz, $^3J_{CH2/CH2}$ = 7.15 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.07 (d, $^1J_{13C/C}$ = 56.12 Hz), 25.33 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.62 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.73, 29.27, 29.47, 29.55, 29.61,

29.64, 119.84; MS (EI): m/z (%) = 333 (1) [M^+ − H], 305 (2), 293 (4) [M^+ − $C^{13}CH_2N$], 291 (4), 277 (3), 237 (6) [M^+ − $C_5{}^{13}CH_{10}N$], 223 (8) [M^+ − $C_6{}^{13}CH_{12}N$], 209 (8) [M^+ − $C_7{}^{13}CH_{14}N$], 195 (10) [M^+ − $C_{12}{}^{13}CH_{24}N$], 181 (6) [$C_{11}{}^{13}CH_{22}N^+$], 167 (7) [$C_{10}{}^{13}CH_{20}N^+$], 153 (5) [$C_{10}H_{18}N^+$], 139 (4) [$C_8{}^{13}CH_{16}N^+$], 124 (17) [$C_7{}^{13}CH_{14}N^+$], 111 (45) [$C_6{}^{13}CH_{12}N^+$], 98 (54) [$C_5{}^{13}CH_{11}N^+$], 97 (84) [$C_5{}^{13}CH_{10}N^+$], 83 (100) [$C_5H_8N^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1472 (m, CH_2), 716 (m, CH_2); elemental analysis: calcd. C 79.58, H 12.05, N 8.37, found C 77.89, H 11.64, N 7.25.

4.6.5 | (1,24-^{13}C)Tetracosanedinitrile (2g)

m.p. 76°C–77°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.24–1.34 (m, 32H), 1.40–1.49 (m, 4H), 1.61–1.71 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.60 Hz, $^3J_{CH2/CH2}$ = 7.20 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.07 (d, $^1J_{13C/C}$ = 56.12 Hz), 25.32 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.63 (d, $^3J_{13C/C}$ = 3.66 Hz), 28.73, 29.27, 29.47, 29.56, 29.61, 29.64, 29.65, 119.87; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1472 (m, CH_2), 717 (m, CH_2); elemental analysis: calcd. C 80.04, H 12.23, N 7.73, found C 79.50, H 12.20, N 7.52.

4.7 | Synthesis and characterization of 3a–3g (modified after Guaragna et al.[55])

In a 50-ml round flask, 2.38 mmol of the respective α,ω-dicyanoalkane (462-mg **2a**, 529-mg **2b**, 596-mg **2c**, 663-mg **2d**, 729-mg **2e**, 796-mg **2f**, and 863-mg **2g**) was dissolved in 5-ml concentrated acetic acid. Afterward, 25-ml concentrated hydrochloric acid was added, and the reaction mixture was refluxed for 24 h. In case of the synthesis of **3g**, the reaction time was extended to 48 h. The resulting hot reaction mixture was poured into 150-ml demineralized water in a beaker, adjusted to pH 10–11 with ammonia, and heated to 65°C again, thereby dissolving some brown impurities that were observed during the synthetic procedure so far. Acidification of the solution with hydrochloric acid leads to the precipitation of the crude reaction products as colorless solids. Purification was achieved by recrystallization from ethyl acetate. Insoluble impurities were separated by filtering the hot solution over a G3 frit. Glassware was rinsed with hot ethyl acetate to collect the complete product. The volume of the combined organic phases was then reduced to approximately 50% under reduced pressure. The resulting solution was filled up with exactly the amount of ethyl acetate that was necessary to completely dissolve the products again and was then allowed to stand in the refrigerator overnight. Crystalline material was then filtered, washed with 3 ml of cool light petroleum, and dried under reduced pressure. Yields: 487-mg (88%) **3a**, 526-mg (85%) **3b**, 611-mg (89%) **3c**, 685-mg (91%) **3d**, 763-mg (93%) **3e**, 771-mg (87%) **3f**, and 868-mg (91%) **3g**.

4.7.1 | (1,12-^{13}C)Dodecanedioic acid (3a)

m.p. 129°C–130°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.17–1.28 (m, 12H), 1.50–1.56 (m, 4H), 2.21 (q, $^3J_{CH2/CH2}$ = 7.27 Hz, $^2J_{CH2/13C}$ = 7.27 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 24.69 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.90 (d, $^3J_{13C/C}$ = 4.40 Hz), 29.01, 29.15, 33.89 (d, $^1J_{13C/C}$ = 55.02 Hz), 176.75; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2916 (m, CH_2), 2849 (m, CH_2), 1649 (s, $^{13}C{=}O$), 1464 (w, CH_2), 1406 (m, OH), 1275 (m, CH_2), 926 (m, OH), 723 (m, CH_2), 682 (m), 546 (m); elemental analysis: calcd. C 62.90, H 9.55, found C 62.51, H 9.56.

4.7.2 | (1,14-^{13}C)Tetradecanedioic acid (3b)

m.p. 124°C–125°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.15–1.29 (m, 16H), 1.50–1.60 (m, 4H), 2.22 (q, $^3J_{CH2/CH2}$ = 7.13 Hz, $^2J_{CH2/13C}$ = 7.13 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 24.71, 28.93 (d, $^3J_{13C/C}$ = 3.30 Hz), 29.06, 29.23, 29.33, 33.92 (d, $^1J_{13C/C}$ = 55.02 Hz), 176.89; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (m, CH_2), 2847 (m, CH_2), 1651 (s, $^{13}C{=}O$), 1464 (w, CH_2), 1408 (m, OH), 1262 (m, CH_2), 934 (m, OH), 725 (m, CH_2), 683 (m), 542 (m); elemental analysis: calcd. C 65.35, H 10.07, found C 65.44, H 10.22.

4.7.3 | (1,16-^{13}C)Hexadecanedioic acid (3c)

m.p. 125°C–126°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.13–1.26 (m, 20H), 1.47–1.55 (m, 4H), 2.18 (q, $^3J_{CH2/CH2}$ = 7.34 Hz, $^2J_{CH2/13C}$ = 7.34 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 24.67, 29.89 (d, $^3J_{13C/C}$ = 3.30 Hz), 29.06, 29.20, 29.31, 29.35, 33.89 (d, $^1J_{13C/C}$ = 55.02 Hz), 176.67; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1651 (s, $^{13}C{=}O$), 1462 (w, CH_2), 1408 (m, OH), 1291 (m, CH_2), 936 (m, OH), 720 (m, CH_2), 683 (m), 548 (m); elemental analysis: calcd. C 67.32, H 10.49, found C 67.05, H 10.53.

4.7.4 | (1,18-^{13}C)Octadecanedioic acid (3d)

m.p. 125°C–126°C; ^{1}H-NMR (500 MHz, THF, 298 K): δ (ppm) = 1.26–1.36 (m, 24H), 1.52–1.60 (m, 4H), 2.20 (q, $^{3}J_{CH2/CH2}$ = 7.45 Hz, $^{2}J_{CH2/13C}$ = 7.45 Hz, 4H); ^{13}C-NMR (126 MHz, THF, 298 K): δ (ppm) = 26.03, 30.31 (d, $^{3}J_{13C/C}$ = 3.62 Hz), 30.52, 30.66, 30.76, 30.80, 34.44 (d, $^{1}J_{13C/C}$ = 55.53 Hz), 174.71; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1651 (s, ^{13}C═O), 1462 (w, CH_2), 1408 (m, OH), 1278 (m, CH_2), 937 (m, OH), 720 (m, CH_2), 683 (m), 544 (m); elemental analysis: calcd. C 68.95, H 10.83, found C 69.03, H 10.90.

4.7.5 | (1,20-^{13}C)Icosanedioic acid (3e)

m.p. 125°C–126°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.26–1.34 (m, 28H), 1.53–1.59 (m, 4H), 2.19 (q, $^{3}J_{CH2/CH2}$ = 7.27 Hz, $^{2}J_{CH2/13C}$ = 7.27 Hz, 4H); ^{13}C-NMR (126 MHz, THF, 298 K): δ (ppm) = 26.23, 30.30 (d, $^{3}J_{13C/C}$ = 3.00 Hz), 30.51, 30.65, 30.76, 30.81, 34.43 (d, $^{1}J_{13C/C}$ = 55.83 Hz), 174.72; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1655 (s, ^{13}C═O), 1462 (w, CH_2), 1408 (m, OH), 1269 (m, CH_2), 937 (m, OH), 720 (m, CH_2), 685 (m), 544 (m); elemental analysis: calcd. C 70.30, H 11.12, found C 69.98, H 11.13.

4.7.6 | (1,22-^{13}C)Docosanedioic acid (3f)

m.p. 125°C–126°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.28–1.34 (m, 32H), 1.53–1.59 (m, 4H), 2.20 (q, $^{3}J_{CH2/CH2}$ = 7.34 Hz, $^{2}J_{CH2/13C}$ = 7.34 Hz, 4H); ^{13}C-NMR (151 MHz, THF, 298 K): δ (ppm) = 26.03 (d, $^{2}J_{13C/C}$ = 2.20 Hz), 30.30 (d, $^{3}J_{13C/C}$ = 3.30 Hz), 30.52, 30.67, 30.77, 30.80, 30.81, 34.44 (d, $^{1}J_{13C/C}$ = 55.02 Hz,), 174.69; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1653 (s, ^{13}C═O), 1462 (w, CH_2), 1408 (m, OH), 1288 (m, CH_2), 939 (m, OH), 719 (m, CH_2), 685 (m), 546 (m); elemental analysis: calcd. C 71.46, H 11.36, found C 71.03, H 11.32.

4.7.7 | (1,24-^{13}C)Tetracosanedioic acid (3g)

m.p. 125°C–126°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.26–1.35 (m, 36H), 1.53–1.60 (m, 4H), 2.20 (q, $^{3}J_{CH2/CH2}$ = 7.15 Hz, $^{2}J_{CH2/13C}$ = 7.15 Hz, 4H); ^{13}C-NMR (126 MHz, THF, 298 K): δ (ppm) = 26.03, 30.31 (d, $^{3}J_{13C/C}$ = 2.78 Hz), 30.52, 30.66, 30.77, 30.82, 34.43 (d, $^{1}J_{13C/C}$ = 55.83 Hz), 174.65; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1657 (s, ^{13}C═O), 1462 (w, CH_2), 1410 (m, OH), 1276 (m, CH_2), 940 (m, OH), 720 (m, CH_2), 687 (m), 546 (m); elemental analysis: calcd. C 72.46, H 11.57, found C 72.50, H 11.67.

4.8 | Synthesis and characterization of 7c–7e (modified after Effenberger and Heid[63])

In a 100-ml two-necked flask equipped with a return condenser and a septum was placed 12.91-mmol (310 mg) Mg in 20 ml of anhydrous THF. Then 9.13 mmol of the corresponding ω-bromoalkene (1.23-g **7a** and 1.36-g **7b**) was added with a syringe under vigorous stirring with a rate that just maintained moderate boiling of the solution. After the exothermic reaction is over, the solution was refluxed for another 2 h and was then allowed to cool down to r.t. Parallel to the formation of the Grignard reagent, 14.61 mmol of the corresponding α,ω-dibromoalkane (4.38-g **1a** and 3.94-g **1b**) dissolved in 25 ml of anhydrous THF was placed in a 100-ml Schlenk tube equipped with a septum. This solution was cooled down to −15°C using a NaCl/ice freezing mixture and was then combined with 0.22 ml of a freshly prepared 0.1M solution of Li_2CuCl_4 in anhydrous THF. Then the solution containing the Grignard reagent was slowly dropped into the solution in the Schlenk tube by using a transfer cannula. The reaction mixture was then allowed to warm up to r.t. and was stirred for another 18 h. Afterward, the solution was treated with a saturated aqueous solution of NH_4Cl and extracted with 70 ml of diethylether four times. The combined organic phases were washed with demineralized water and dried of Na_2SO_4, and the solvent evaporated under reduced pressure. The resulting oily residues were purified by column chromatography using light petroleum as the eluent. In some cases, chromatographic work-up had to be repeated to get pure compounds. All compounds **7c–7e** were obtained as colorless oils. Yields: 1.60-g (67%) **7c**, 1.61-g (64%) **7d**, and 1.80-g (68%) **7e**.

4.8.1 | 13-Bromotridec-1-ene (7c)

^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.34 (m, 12H), 1.35–1.47 (m, 4H), 1.83–1.90 (m, 2H), 2.01–2.08 (m, 2H), 3.41 (t, $^{3}J_{CH2/CH2}$ = 6.87 Hz, 2H), 4.91–5.04 (m, 2H), 5.82 (ddt, $^{3}J_{CH2/CH2[E]}$ = 17.11 Hz, $^{3}J_{CH2/CH2[Z]}$ = 10.24 Hz, $^{3}J_{CH2/CH2}$ = 6.66 Hz, 1H); ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 28.17, 28.76, 28.93, 29.12, 29.41, 29.46, 29.49, 29.53, 32.84, 33.79, 34.01, 114.08, 139.23; MS (EI): m/z (%) = 262 (2), 260 (2) [M^+], 219 (3), 217 (3) [$M^+ - C_3H_6$], 205 (5),

203 (5) [$M^+ - C_4H_8$], 177 (3), 175 (3) [$M^+ - C_6H_{12}$], 164 (10), 162 (10) [$C_6H_{12}Br^+$], 150 (18), 148 (18) [$C_5H_{10}Br^+$], 111 (39) [$C_8H_{15}^+$], 97 (82) [$C_7H_{13}^+$], 83 (100) [$C_6H_{11}^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3075 (w, =CH_2), 2922 (s, CH_2), 2853 (s, CH_2), 1639 (m, C=C), 1464 (m, CH_2), 1249 (w, CH_2), 991 (m, –HC=CH_2), 909 (s, –HC=CH_2), 721 (m, CH_2), 646 (m, C–Br), 563 (m).

4.8.2 | 14-Bromotetradec-1-ene (7d)

^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.24–1.34 (m, 14H), 1.35–1.47 (m, 4H), 1.82–1.91 (m, 2H), 2.01–2.08 (m, 2H), 3.42 (t, $^3J_{CH2/CH2}$ = 6.87 Hz, 2H), 4.90–5.04 (m, 2H), 5.82 (ddt, $^3J_{CH2/CH2[E]}$ = 17.04 Hz, $^3J_{CH2/CH2[Z]}$ = 10.31 Hz, $^3J_{CH2/CH2}$ = 6.66 Hz, 1H; ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.91, 28.51, 28.67, 28.88, 29.17, 29.23, 29.25, 29.31, 29.36, 32.58, 33.55, 33.79, 113.82, 138.99; MS (EI): m/z (%) = 276 (2), 274 (2) [M^+], 219 (5), 217 (5) [$M^+ - C_4H_8$], 205 (8), 203 (8) [$M^+ - C_5H_{10}$], 150 (7), 148 (7) [$C_5H_{10}Br^+$], 111 (51) [$C_8H_{15}^+$], 97 (84) [$C_7H_{13}^+$], 83 (100) [$C_6H_{11}^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3076 (w, =CH_2), 2922 (s, CH_2), 2853 (s, CH_2), 1641 (m, C=C), 1466 (m, CH_2), 1247 (w), 992 (m, –HC=CH_2), 909 (s, –HC=CH_2), 722 (m, CH_2), 646 (m, C–Br), 563 (m).

4.8.3 | 15-Bromopentadec-1-ene (7e)

^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.23–1.34 (m, 16H), 1.34–1.47 (m, 4H), 1.82–1.90 (m, 2H), 2.01–2.09 (m, 2H), 3.42 (t, $^3J_{CH2/CH2}$ = 6.87 Hz, 2H), 4.91–5.01 (m, 2H), 5.82 (ddt, $^3J_{CH2/CH2[E]}$ = 17.11 Hz, $^3J_{CH2/CH2[Z]}$ = 10.24 Hz, $^3J_{CH2/CH2}$ = 6.66 Hz, 1H); ^{13}C-NMR (126 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.91, 28.51, 28.68, 28.88, 29.17, 29.24, 29.26, 29.33, 29.36, 32.58, 33.55, 33.79, 113.82, 139.00; MS (EI): m/z (%) = 288 (2), 290 (2) [M^+], 247 (2), 245 (2) [$M^+ - C_3H_6$], 219 (3), 217 (3) [$M^+ - C_5H_{10}$], 205 (6), 203 (6) [$M^+ - C_6H_{12}$], 150 (7), 148 (7) [$C_5H_{10}Br^+$], 111 (40) [$C_8H_{15}^+$], 97 (80) [$C_7H_{13}^+$], 83 (100) [$C_6H_{11}^+$]; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3077 (w, =CH_2), 2923 (s, CH_2), 2853 (s, CH_2), 1641 (m, C=C), 1465 (m, CH_2), 1246 (w, CH_2), 992 (m, –HC=CH_2), 909 (s, –HC=CH_2), 721 (m, CH_2), 646 (m, C–Br), 562 (m).

4.9 | Synthesis and characterization of 8a–8c (modified after Wedeking et al.[64])

In 50-ml Schlenk tube equipped with a septum 0.06 mmol (52 mg) of the Grubbs-I-type catalyst [$RuCl_2(PCy_3)_2$(=CHPh)] was dissolved in 5 ml of anhydrous toluene. Then a solution of 4.84 mmol of the respective ω-bromoalkene (1.264-g **7c**, 1.332-g **7d**, and 1.400-g **7e**) in 25 ml of anhydrous toluene was added dropwise with a syringe. After the addition was finished, the reaction mixture was stirred at r.t. for 48 h. Next, toluene was evaporated under reduced pressure, and the remaining residue was purified by column chromatography using light petroleum as the eluent. A first fraction always gave a portion of unreacted starting compounds, whereas the second fraction yielded the desired products as mixtures of *cis*- and *trans*-isomers as colorless crystalline material. The isomers were not separated because in the next reaction step, both isomeric forms of **8a**–**8c** would give the same product. Yields: 874-mg (73%) **8a**, 998-mg (79%) **8b**, and 995-mg (75%) **8c**.

4.9.1 | 1,24-Dibromotetracos-12-ene (8a)

m.p. 47°C–48°C; ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.36 (m, 28H), 1.40–1.45 (m, 4H), 1.83–1.89 (m, 4H), 1.94–2.05 (m, 4H), 3.41 (t, $^3J_{CH2/CH2}$ = 6.88 Hz, 4H), 5.33–5.42 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.19, 28.17, 28.76, 29.14, 29.28, 29.42, 29.48, 29.52, 29.56, 29.63, 29.74, 32.59, 32.83, 34.05, 129.88, 130.34; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3005 (w, C=CH–), 2914 (s, CH_2), 2849 (s, CH_2) 1470 (m, CH_2), 1231 (w, CH_2), 964 (m, C=C_{trans}), 731 (m, C=C_{cis}), 718 (m, CH_2), 642 (m, C–Br); elemental analysis: calcd. C 58.30, H 9.38, found C 58.26, H 9.13.

4.9.2 | 1,26-Dibromohexacos-13-ene (8b)

m.p. 54°C–56°C; ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.26–1.37 (m, 32H), 1.41–1.49 (m, 4H), 1.83–1.92 (m, 4H), 1.95–2.08 (m, 4H), 3.43 (t, $^3J_{CH2/CH2}$ = 6.95 Hz, 4H), 5.33–5.44 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.19, 28.17, 28.77, 29.15, 29.29, 29.43, 29.50, 29.53, 29.60, 29.64, 29.75, 32.60, 32.83, 34.05, 129.88, 130.34; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3000 (w, C=CH–), 2914 (s, CH_2), 2849 (s, CH_2) 1472 (m, CH_2), 1228 (w, CH_2), 963 (m, C=C_{trans}), 731 (m, C=C_{cis}), 718 (m, CH_2), 648 (m, C–Br); elemental analysis: calcd. C 59.77, H 9.65, found C 60.48, H 9.76.

4.9.3 | 1,28-Dibromooctacos-14-ene (8c)

m.p. 59°C–60°C; ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.24–1.38 (m, 36H), 1.40–1.50 (m, 4H), 1.83–1.93 (m, 4H), 1.95–2.08 (m, 4H), 3.43 (t, $^3J_{CH2/CH2}$ = 6.82 Hz,

2H), 5.35–5.43 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.20, 28.17, 28.77, 29.16, 29.31, 29.44, 29.52, 29.54, 29.63, 29.76, 29.79, 32.60, 32.83, 34.08, 129.88, 130.35; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3005 (w, C═CH–), 2916 (s, CH_2), 2847 (s, CH_2) 1462 (m, CH_2), 1222 (w, CH_2), 957 (m, C═C_{trans}), 731 (m, C═C_{cis}), 719 (m, CH_2), 650 (m, C–Br); elemental analysis: calcd. C 61.09, H 9.89, found C 60.69, H 9.75.

4.10 | Synthesis and characterization of 1d–1f (modified after Wedeking et al.[64])

In a 50-ml Schlenk tube equipped with a septum, 1.09 mmol of the corresponding α,ω-dibromoalkene (539-mg **8a**, 570-mg **8b**, and 600-mg **8c**) was dissolved in 22 ml of anhydrous THF before 87 mg of a Pd/C (10%) catalyst was added under inert conditions. Hydrogenation was then performed by the use of a balloon filled with hydrogen and equipped with a cannula puncturing the septum. After the reaction mixture was stirred for 20 h at r.t., the reaction mixture is filtered over a G3 frit which was filled with 1 cm of silica. Silica was then washed with another portion of anhydrous THF (60 ml) before the combined reaction mixture was evaporated to dryness. Purification of the crude reaction products was achieved by recrystallization from a mixture of ethanol and methanol (2:1). After the solution was allowed to stand in the refrigerator overnight, the products were obtained as colorless crystalline material. Yields: 455-mg (84%) **1d**, 417-mg (73%) **1e**, and 457-mg (76%) **1f**.

4.10.1 | 1,24-Dibromotetracosane (1d)

m.p. 72°C–73°C[57]; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.34 (m, 36H), 1.40–1.46 (m, 4H), 1.83–1.89 (m, 4H), 3.41 (t, $^3J_{CH2/CH2}$ = 6.88 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 28.18, 28.77, 29.44, 29.54, 29.61, 29.65, 29.69, 32.84, 34.05; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (s, CH_2), 1472 (m, CH_2), 1224 (w, CH_2), 716 (m, CH_2), 642 (m, C–Br).

4.10.2 | 1,26-Dibromohexacosane (1e)

m.p. 75°C–76°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.35 (m, 40H), 1.40–1.46 (m, 4H), 1.83–1.89 (m, 4H), 3.41 (t, $^3J_{CH2/CH2}$ = 6.88 Hz, 4H); ^{13}C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 27.96, 28.55, 29.22, 29.32, 29.40, 29.44, 29.47, 32.62, 33.84; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (s, CH_2), 1473 (m, CH_2), 1217 (w, CH_2), 715 (m, CH_2), 643 (m, C–Br).

4.10.3 | 1,28-Dibromooctacosane (1f)

m.p. 77°C–78°C; ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K)[57]: δ (ppm) = 1.15–1.26 (m, 44H), 1.30–1.40 (m, 4H), 1.74–1.82 (m, 4H), 3.34 (t, $^3J_{CH2/CH2}$ = 6.95 Hz, 4H); ^{13}C-NMR (101 MHz, $CDCl_3$, 298 K): δ (ppm) = 28.49, 29.09, 29.68, 29.76, 29.86, 29.94, 29.97, 30.02, 33.15, 34.40; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2848 (s, CH_2), 1472 (m, CH_2), 1217 (w, CH_2), 716 (m, CH_2), 642 (m, C–Br).

4.11 | Synthesis and characterization of 2h–2j (modified after Coxon et al.[60])

In a 50-ml round flask, 0.94 mmol of the corresponding α,ω-dibromoalkane (466-mg **1d**, 493-mg **1e**, and 519-mg **1f**) was suspended in 25-ml DMSO; 1.93-mmol (127 mg) $K^{13}CN$ was added to this mixture, which was then heated to 80°C for 4 days. During this reaction time, the starting compounds completely dissolved in DMSO. After the light yellowish reaction mixture was allowed to reach r.t., 40 ml of demineralized water was added, and the complete mixture was extracted with 80 ml of diethylether four times. The combined organic phases were washed with demineralized water and with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The crude products were purified by column chromatography using chloroform as the eluent. After evaporation of the solvent, the products were obtained as colorless solids. Yields: 360-mg (98%) **2h**, 383-mg (98%) **2i**, and 497-mg (97%) **2j**.

4.11.1 | (1,26-^{13}C) Hexacosanedinitrile (2h)

m.p. 79°C–80°C; ^{1}H-NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.25–1.35 (m, 36H), 1.41–1.49 (m, 4H), 1.62–1.71 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.74 Hz, $^3J_{CH2/CH2}$ = 7.16 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.06 (d, $^1J_{13C/C}$ = 55.02 Hz), 25.33 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.62 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.72, 29.26, 29.46, 29.55, 29.60, 29.66, 119.83; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2191 (w, ^{13}C≡N), 1472 (m, CH_2), 716 (m, CH_2); elemental analysis: calcd. C 80.44, H 12.38, N 7.17, found C 80.33, H 12.27, N 6.68.

4.11.2 | (1,28-^{13}C)Octacosanedinitrile (2i)

m.p. 81°C–82°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.23–1.36 (m, 40H), 1.41–1.48 (m, 4H), 1.62–1.70 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.74 Hz, $^3J_{CH2/CH2}$ = 7.02 Hz,

4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.06 (d, $^1J_{13C/C}$ = 55.02 Hz), 25.33 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.62 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.72, 29.26, 29.46, 29.55, 29.60, 29.63, 29.66, 119.83; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2913 (s, CH_2), 2849 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1474 (m, CH_2), 716 (m, CH_2); elemental analysis: calcd. C 80.79, H 12.52, N 6.69, found C 80.65, H 12.47, N 6.29.

4.11.3 | (1,30-^{13}C) Triacontanedinitrile (2j)

m.p. 84°C–85°C; ^{1}H-NMR (600 MHz, $CDCl_3$, 298 K): δ (ppm) = 1.23–1.36 (m, 44H), 1.41–1.49 (m, 4H), 1.62–1.71 (m, 4H), 2.34 (dt, $^2J_{CH2/13C}$ = 9.74 Hz, $^3J_{CH2/CH2}$ = 7.16 Hz, 4H); $_{13}$C-NMR (151 MHz, $CDCl_3$, 298 K): δ (ppm) = 17.04 (d, $^1J_{13C/C}$ = 55.02 Hz), 25.33 (d, $^2J_{13C/C}$ = 2.20 Hz), 28.62 (d, $^3J_{13C/C}$ = 3.30 Hz), 28.72, 29.26, 29.46, 29.55, 29.61, 29.63, 29.66, 119.82; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2914 (s, CH_2), 2849 (m, CH_2), 2191 (w, $^{13}C{\equiv}N$), 1473 (m, CH_2), 717 (m, CH_2); elemental analysis: calcd. C 81.10, H 12.63, N 6.27, found C 80.83, H 12.45, N 6.07.

4.12 | Synthesis and characterization of 3h–3j (modified after Günthard et al.[65])

In a 25-ml round flask, 1.63 mmol of the corresponding α,ω-dicyanoalkane (637 mg **2 h**, 683 mg **2i**, 728 mg **2j**) was dissolved in 9.5-ml concentrated acetic acid. Then 4.5 ml of demineralized water and 6-ml concentrated sulfuric acid were added, and the reaction mixture was refluxed for 20 h. During the reaction time, the solution turned dark brown. At the end of the reaction time, the hot reaction mixture is stirred into 250 ml of demineralized water. The resulting suspension is treated with ultrasound for 10 min to get a finely dispersed suspension, which then is filtered. The filtrate is washed with 50 ml of demineralized water and dried at 80°C for 3 h. Afterward, the solid residue is put into a round flask, dissolved in 40-ml THF, and treated with 35 mg of charcoal for 20 min under reflux conditions. After being cooled down to r.t., the resulting suspension is filtered by the use of a syringe equipped with a syringe filter. The residual charcoal is washed twice with 5 ml of THF, which then also is filtered using the syringe. The combined organic phases are filtered over a G3 frit, which was filled with 1 cm of silica. Silica was then washed with another portion of anhydrous THF (80 ml) before the combined reaction mixture was evaporated to dryness. Purification was achieved by recrystallization from ethyl acetate. Silica residues were separated by filtering the hot solution over a G3 frit. Glassware was rinsed with hot ethyl acetate to collect the complete product. The volume of the combined organic phases was then reduced to approximately 50% under reduced pressure. The resulting solution was filled up with exactly the amount of ethyl acetate that was necessary to completely dissolve the products again and was then allowed to stand in the refrigerator overnight. Crystalline material was then filtered, washed with 3 ml of cool light petroleum, and dried under reduced pressure. Yields: 587-mg (84%) **3h**, 640-mg (86%) **3i**, and 632-mg (80%) **3j**.

4.12.1 | (1,26-^{13}C)Hexacosanedioic acid (3h)

m.p. 124°C–125°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.25–1.34 (m, 40H), 1.53–1.61 (m, 4H), 2.20 (q, $^3J_{CH2/CH2}$ = 7.53 Hz, $^2J_{CH2/13C}$ = 7.53 Hz, 4H); ^{13}C-NMR (151 MHz, THF, 298 K): δ (ppm) = 26.03, 30.31 (d, $^3J_{13C/C}$ = 3.30 Hz), 30.52, 30.67, 30.77, 30.82, 34.42 (d, $^1J_{13C/C}$ = 55.52 Hz), 174.63; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1655 (s, $^{13}C{=}O$), 1462 (w, CH_2), 1408 (m, OH), 1280 (m, CH_2), 939 (m, OH), 719 (m, CH_2), 685 (m), 545 (m): elemental analysis: calcd. C 73.31, H 11.76, found C 73.97, H 11.72.

4.12.2 | (1,28-^{13}C)Octacosanedioic acid (3i)

m.p. 124°C–125°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.26–1.34 (m, 44H), 1.53–1.60 (m, 4H), 2.20 (q, $^3J_{CH2/CH2}$ = 7.40 Hz, $^2J_{CH2/13C}$ = 7.40 Hz, 4H); ^{13}C-NMR (126 MHz, THF, 298 K): δ (ppm) = 26.03, 30.32 (d, $^3J_{13C/C}$ = 3.81 Hz), 30.52, 30.67, 30.77, 30.82, 34.42 (d, $^1J_{13C/C}$ = 55.02 Hz), 174.65; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1657 (s, $^{13}C{=}O$), 1462 (w, CH_2), 1408 (m, OH), 1286 (m, CH_2), 928 (m, OH), 719 (m, CH_2), 685 (m), 544 (m); elemental analysis: calcd. C 74.07, H 11.92, found C 74.59, H 12.10.

4.12.3 | (1,30-^{13}C)Triacontanedioic acid (3j)

m.p. 125°C–126°C; ^{1}H-NMR (600 MHz, THF, 298 K): δ (ppm) = 1.27–1.35 (m, 48H), 1.54–1.60 (m, 4H), 2.19 (q, $^3J_{CH2/CH2}$ = 7.40 Hz, $^2J_{CH2/13C}$ = 7.40 Hz, 4H); ^{13}C-NMR (126 MHz, THF, 298 K): δ (ppm) = 26.04, 30.31 (d, $^3J_{13C/C}$ = 3.62 Hz), 30.51, 30.66, 30.76, 30.81, 34.45 (d, $^1J_{13C/C}$ = 55.53 Hz), 174.70; IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3300–2500 (m, OH), 2914 (s, CH_2), 2847 (s, CH_2), 1657 (s, $^{13}C{=}O$), 1462 (w, CH_2), 1410 (m, OH), 1281 (m, CH_2), 942 (m,

OH), 720 (m, CH_2), 686 (m), 544 (m); elemental analysis: calcd. C 74.74, H 12.06, found C 74.77, H 11.87.

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ORCID

Wolfgang Imhof https://orcid.org/0000-0003-0954-5464

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