Synthesis of New Heterocyclic Fatty Compounds

Sandra Fürmeier[a] and Jürgen O. Metzger*[a]

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The terminal tetrazoles **1**–**5**, the tetrazole analogues of the most important naturally occurring fatty acids, have been synthesized from fatty nitriles and completely characterized. The linear C_{12} bis(tetrazole) **6** was prepared and represents a valuable supplement to the previously known C_2–C_5 alkyl- and alkenyl-linked bis(tetrazoles). The tetrazoles **1**–**6** were converted into the respective 1,3,4-oxadiazoles **13**–**17** by heating in acetic anhydride. Three bis(oxadiazoles) **18**–**20** were also obtained. A 1,5-disubstituted tetrazole **12** was synthesized from methyl 9(10)-oxooctadecanoate by means of an improved Schmidt reaction. From methyl *cis*-9,10-epoxyoctadecanoate (**21**), various heterocycles such as the 4,5-dihydrooxazoles **22**, the oxazolidines **24**, the imidazoles **26**, the oxazoles **27**, and the imidazolinethione **28** were prepared. Because of their structural relationship to the naturally occurring prostaglandins, compounds **12**, **22**, **24**, **26**, **27**, and **28** should be of interest as homoprostanoids.

Introduction

Over the last three years, Sharpless et al. have introduced "click chemistry" as an important tool for drug discovery.[1] The major requirement for the synthetic methods involved is that "all searches must be restricted to molecules that are easy to make", the goal being to develop an expanding set of powerful, selective, and modular blocks with which to combine small units together with heteroatom links (C−X−C), working reliably in both small- and large-scale applications. Sharpless defined stringent criteria for click reactions: "The reaction must be modular, wide in scope, give very high yields, generate only inoffensive by-products that can be removed by non-chromatographic methods, and be stereospecific. The required process characteristics include simple reaction conditions, readily available starting materials and reagents, the use of no solvent or a solvent that is benign or easily removed, and simple product isolation." Carbon−heteroatom bond-forming reactions represent the most common click reactions. Typical examples are cycloadditions, especially 1,3-dipolar cycloaddition reactions and nucleophilic substitutions, particularly ring-opening reactions of strained heterocyclic compounds such as epoxides, aziridines, aziridinium ions and episulfonium ions, and also carbonyl reactions of the "non-aldol"-type and oxidative additions to C−C multiple bonds such as epoxidations, dihydroxylations, and aziridinations. Our work on the synthesis of heterocyclic fatty compounds is closely related to Sharpless's click chemistry. Our idea was to achieve access to pharmacologically interesting compounds based on renewable raw materials that serve as important feedstocks for the chemical industry with regard to a sustainable development[2] through simple transformations starting from easily available fatty compounds. The different types of interesting heterocycles are presented below.

The discovery of the pharmacological and biochemical properties of tetrazoles initiated an enormous development in tetrazole chemistry over the last 40 years.[3] In *N*-unsubstituted tetrazoles the tetrazole moiety is isosteric with the carboxylic acid group, and a large number of amino acids and naturally occurring carboxylic acids have therefore been synthesized with a tetrazole ring in place of the carboxylic acid group. Tetrazole analogues of fatty acid ethers are known as substrates for *N*-myristoyl transferase and its respective coenzyme, and show fungicidal and antiviral (including HIV) activity.[4] In addition to their various biological properties, tetrazoles also serve as precursors for the synthesis of further interesting heterocycles, such as 1,3,4-oxadiazoles. These are used as biologically active compounds in medical science and agriculture, and also as dyestuffs and UV absorbents. Various 2,5-diaryl-, 2,5-dialkyl-, and 2-alkyl-5-aryl-1,3,4-oxadiazoles show herbicidal effects, especially against broad leafed weeds and grasses in crops such as rice and corn.[5] 4,5-Dihydrooxazoles show antimicrobial activity and are used as tranquilizers. Derivatives with a fatty acid residue at the C-2 position of the dihydrooxazole ring show surface-active properties, and the respective salts are good cationic surfactants.[6] Many imidazoles have been prepared as potentially pharmacological agents, including 2-nitroimidazole (azomycine) as a naturally occurring antibiotic or the synthetic clotrimazole (cane-

[a] Department of Chemistry, University of Oldenburg
Carl-von-Ossietzky-Str. 9−11, 26129 Oldenburg, Germany
E-Mail: juergen.metzger@uni-oldenburg.de

stene) as an antimycotic. Ergothionine should be mentioned as a biologically active imidazolinethione acting as antihistamine.[7]

Vegetable oils are the most important renewable feedstocks in the chemical industry.[8] We were interested in the synthesis of tetrazoles, 1,3,4-oxadiazoles, and further N- and O/S-containing heterocyclic fatty acid derivatives in order to enlarge the variety of interesting fatty compounds and to open up a new potential for renewable raw materials as possible biologically active compounds.

Results and Discussion

The respective fatty nitriles of the most important fatty acids served as starting materials for gaining access to the tetrazole analogues. These nitriles are conveniently available as intermediates in the industrial synthesis of fatty amines. By the method of Koguro et al.[9] we converted various fatty nitriles into the corresponding 5-alkyl-1*H*-tetrazoles by use of 3 equiv. of sodium azide and triethylamine hydrochloride in dry toluene (Table 1). The reaction was performed in about 2 d at reflux temperature, after which the reaction mixture was dissolved in water and the layers were separated. Since the tetrazoles were formed as their ammonium salts, the aqueous layer was in each case acidified to release the tetrazole and extracted with diethyl ether. The detailed workup and the properties of the different tetrazoles are given in Table 1.

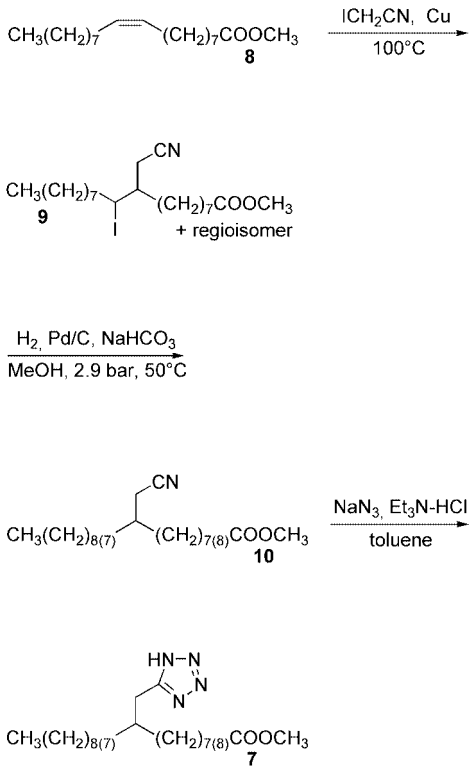
In this manner, treatment of dodecanenitrile yielded tetrazole **1**, octadecanenitrile yielded **2**, (*Z*)-9-octadecenenitrile yielded **3**, tetradecanenitrile yielded **4**, 10-undecenenitrile yielded **5**, and dodecanedinitrile yielded **6**. Compounds **1**−**7** represent the first examples of 5-alkyltetrazoles substituted with long-chain fatty acid derived residues. Pernice et al. reported on 5-undecyl-1*H*-tetrazole (**1**) in a study concerning the permeation properties of carboxylic acids and their tetrazole analogues without giving any data for the characterization of the compound.[10] Although tetrazole **2** is documented in CAS, a reference is missing, indicating that the compound is the subject of a patent. To provide the alkyl-branched tetrazole **7**, methyl oleate (**8**) was treated with iodoacetonitrile in the presence of copper powder in a free radical reaction[11] (Scheme 1). The resulting cyanomethyl-iodo derivative **9** (30% yield) was subsequently reduced under hydrogen in the presence of palladium on charcoal to afford the cyanomethyl derivative **10** (96% yield), which was converted into the tetrazole **7** as already described.

The applicability of an improved Schmidt synthesis with fatty acid derivatives for the preparation of 1,5-disubstituted tetrazoles from ketones, as reported by Suzuki et al.,[12] was investigated. We thus heated a mixture of methyl 9(10)-oxooctadecanoate (**11**), sodium azide and titanium(IV) chloride under reflux, and obtained the tetrazole **12** as a yellow oil in 71% yield (Scheme 2).

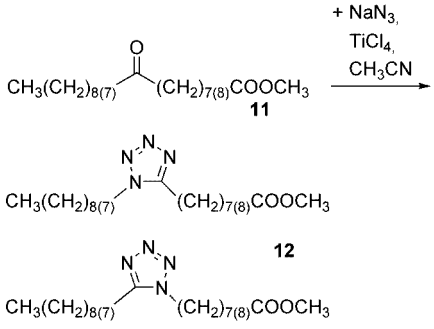
Compound **12** was produced as a mixture of four isomers, as shown by NMR spectroscopy. Suzuki et al. reported on the reaction mechanism and the formation of two

Table 1. Preparation of 5-alkyl-1*H*-tetrazoles **1**−**7** from fatty nitriles (PE = petroleum ether; EE = ethyl acetate)

R−CN	NaN_3, NEt_3-HCl, touene → R-tetrazole		Work-up	Yield	Properties
$CH_3(CH_2)_{10}CN$	$CH_3(CH_2)_{10}$-tetrazole	**1**	Recrystallization from MeCN	89%	white solid mp. 68-72°C
$CH_3(CH_2)_{16}CN$	$CH_3(CH_2)_{16}$-tetrazole	**2**	Recrystallization from MeCN/EtOH 10:1	99%	white solid mp. 82-85°C
$CH_3(CH_2)_7CH{=}CH(CH_2)_7CN$	$CH_3(CH_2)_7CH{=}CH(CH_2)_7$-tetrazole	**3**	Column Chromatography PE/EE/AcOH 10:5:1	94%	white wax
$CH_3(CH_2)_{12}CN$	$CH_3(CH_2)_{12}$-tetrazole	**4**	Recrystallization from PE	91%	white solid mp. 74-77°C
$CH_2{=}CH(CH_2)_8CN$	$CH_2{=}CH(CH_2)_8$-tetrazole	**5**	Recrystallization from PE/EtOH 2:1	91%	orange solid mp. ~ rt
$NC(CH_2)_{10}CN$	bis-tetrazole $(CH_2)_{10}$	**6**	Recrystallization from MeCN	72%	beige solid mp. 146-149°C
$CH_3(CH_2)_{8(7)}CH(CN)(CH_2)_{7(8)}COOCH_3$ (**10**)	$CH_3(CH_2)_{8(7)}$-tetrazole-$(CH_2)_{7(8)}COOCH_3$	**7**	Column Chromatography PE/EE/MeOH 7:3:1	32%	orange oil



Scheme 1. Synthesis of the alkyl-branched tetrazole **7** from methyl oleate (**8**)

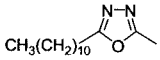
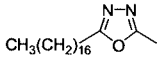
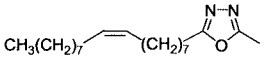
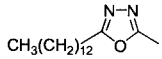
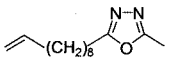
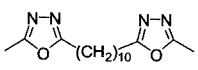
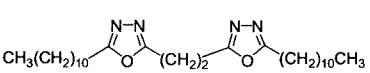
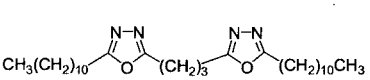


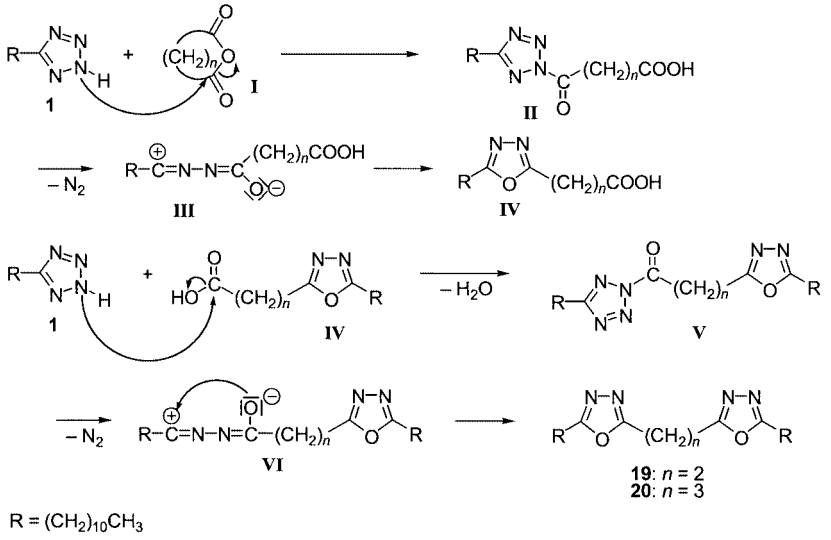
Scheme 2. Synthesis of the 1,5-dialkyl-substituted tetrazole **12** from methyl 9(10)-oxooctadecanoate (**11**), sodium azide, and titanium(IV) chloride

isomers.[12] Since the ketone **11** was a ca. 1.2:1 regioisomeric mixture, the possible isomers of the tetrazole **12** were formed as their two regioisomers as well. The ratio of isomers could be determined from ^{13}C NMR spectroscopic data, the intensities of the four signals for C-1 indicating a ratio of 1:1.6:1.6:1.2.

The 5-alkyl-1*H*-tetrazoles **1**−**6** were also treated in a Huisgen reaction with acetic anhydride in 7 h under reflux to yield the 1,3,4-oxadiazoles **13**−**18** (Table 2).

Table 2. Preparation of 1,3,4-oxadiazoles **13**−**20** from the respective tetrazoles **1**−**10** (PE = petroleum ether; EE = ethyl acetate)

R–tetrazole	acid anhydride, reflux →		Work-up	Yield	Properties
1		**13**	Column Chromatography PE/EE/AcOH 10:10:1	80%	pale yellow oil
2		**14**	Column Chromatography PE/EE/AcOH 10:10:1	97%	beige solid mp. 43-46°C
3		**15**	Column Chromatography PE/EE/AcOH 10:10:1	73%	pale yellow oil
4		**16**	Column Chromatography PE/EE/AcOH 10:10:1	85%	beige solid mp. 32-33°C
5		**17**	Column Chromatography PE/EE/AcOH 10:5:1	65%	colourless oil
6		**18**	Column Chromatography PE/EE/AcOH 10:5:1 Ether/AcOH 10 :4	72%	pale pink solid mp. 45-50°C
1		**19**	Recrystallization from EE	72%	beige solid mp. 96°C
1		**20**	Recrystallization from MeOH	34%	beige solid mp. 80-82°C



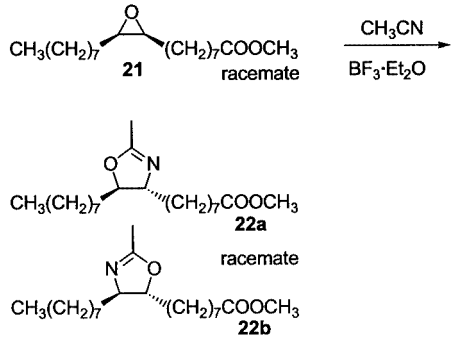
Scheme 3. Reaction pathway to the long-chain bis(oxadiazoles) **19** and **20** by treatment of 5-undecyl-1*H*-tetrazole (**1**) with succinic and glutaric anhydride, respectively

The bis(oxadiazoles) **19** and **20** were unexpectedly isolated from treatment of 5-undecyl-1*H*-tetrazole (**1**) with succinic and glutaric anhydrides, respectively, treatment of **1** with succinic anhydride (**I**, $n = 2$) in dry xylene yielding the bis(oxadiazole) **19** after 24 h of reflux, and bis(oxadiazole) **20** being obtained in the analogous conversion with glutaric anhydride (**I**, $n = 3$). The mechanism, based on investigations carried out by Huisgen et al.,[13] is shown in Scheme 3. In the first step of the reaction the cyclic anhydride is attacked by the tetrazole **1** with ring-opening and formation of an acyl tetrazole **II** with a short-chain carboxylic acid residue. 3-(5-Undecyl[1,3,4]oxadiazole-2-yl)propanoic acid **IV** ($n = 2$) and 3-(5-undecyl[1,3,4]oxadiazole-2-yl)butanoic acid **IV** ($n = 3$) should be formed, with loss of nitrogen and intramolecular cyclization of the dipolar intermediate **III**. However, the carboxylic acid group in compound **IV** seems to react with a second molecule of tetrazole **1**, finally giving the isolated bis(oxadiazoles) **19** and **20**.

Finally, methyl *cis*-9,10-epoxyoctadecanoate (**21**) was converted into a number of different N/O- and/or S-containing heterocycles. Treatment of **21** with acetonitrile in the presence of boron trifluoride–diethyl ether yielded 60% of the 4,5-dihydrooxazole **22** as a mixture of two isomers (Scheme 4). The *cis*-epoxide was transformed into a *trans*-dihydrooxazole with inversion at the carbon atom attacked by acetonitrile.

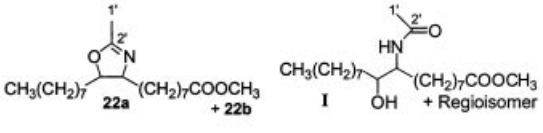
An alternative reaction pathway to the same 4,5-dihydrooxazoles **22** was by treatment of the amino alcohols **23** with $Cd(OAc)_2 \cdot 2H_2O$ in acetonitrile, which turned out to be inferior with regard to the yield (27%).

The dihydrooxazole was sensitive towards hydrolysis and was completely converted into the ring-opened product after 7 d. The characteristic NMR spectroscopic data of the 4,5-dihydrooxazoles **22** and the ring-opened methyl 9(10)-acetylamino-10(9)-hydroxyoctanoate (**I**) are compared in Table 3.



Scheme 4. Formation of the 4,5-dihydrooxazoles **22** from methyl *cis*-9,10-epoxyoctadecanoate (**21**) and acetonitrile in the presence of boron trifluoride–diethyl ether

Table 3. Characteristic NMR spectroscopic data (δ [ppm]) of the 4,5-dihydrooxazoles **22** and the ring-opened compound methyl 9(10)-acetylamino-10(9)-hydroxyoctadecanoate (**I**)

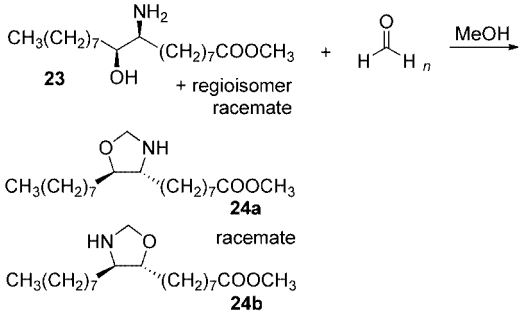


^{13}C NMR	C-1'	24.99	C-1'	23.28
	C-2'	163.76	C-2'	170.34
	CHN	71.35	CHN	53.07, 53.15
	CHO	85.05, 85.09	CHO	74.36, 74.42
^{1}H NMR	1'-H	1.95	1'-H	2.00
	CHN	3.37	CHN	3.82
	CHO	4.03	CHO	3.38
			NH	5.94

Our observation corresponds to the findings of Ahmad and Ansari,[14] who treated 2,3-epoxy fatty esters with nitriles in the presence of equimolar amounts of boron trifluoride–diethyl ether and observed the formation of

4,5-dihydrooxazoles. The isolation of the dihydrooxazoles failed because of the rapid hydrolysis to the open-chain hydroxy amides. These could in turn be transformed into the dihydrooxazoles by pyrolysis under nitrogen at 210−220 °C in 6−8 h in yields of about 70%. Ahmad and Ansari's NMR spectroscopic data correspond to ours, and therefore confirm our results.

In general, oxazolidines are formed by condensation of amino alcohols with carbonyl compounds.[15] Treatment of the amino alcohols **23**[16] with an excess of paraformaldehyde in methanol yielded the oxazolidines **24** as a pale yellow oil in 44% yield (Scheme 5). The *threo*-amino alcohol is converted with retention of the configuration into the *trans*-oxazolidine, as a mixture of two isomers.



Scheme 5. Condensation of the amino alcohols **23** with paraformaldehyde to give the oxazolidines **24**

Methyl 9(10)-hydroxy-10(9)-oxooctadecanoate (**25**) served as a precursor for the synthesis of further interesting heterocycles. The α-hydroxy ketone **25** was prepared analogously to the method described by Brousse and Lefort by oxidation of methyl *cis*-9,10-epoxyoctadecanoate (**21**) with dimethyl sulfoxide at 90−100 °C in the presence of boron trifluoride−diethyl ether.[17]

In a Bredereck reaction[18] the α-hydroxy ketone **25** was treated with formamide to afford the imidazoles **26** and the oxazoles **27** (Scheme 6).

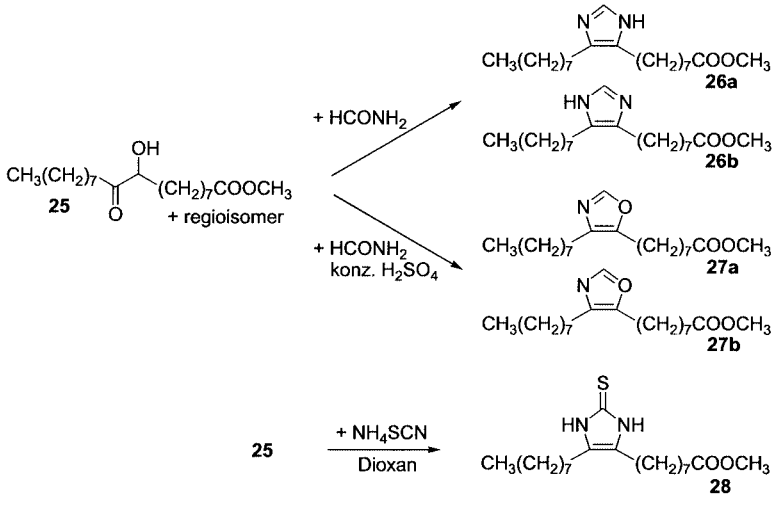
Treatment of **25** in formamide under nitrogen at 150 °C yielded 54% of the imidazoles **26** as an orange oil, together with 7% of the oxazoles **27**. The oxazoles **27** could be isolated as major products in the analogous conversion carried out with a different temperature pattern in the presence of concentrated sulfuric acid, a 36% yield of the oxazoles **27** being obtained as an orange oil, together with a further 26% of the imidazoles **26**.

Vandenberghe and Willems developed a method for the synthesis of 4,5-substituted oxazoline- and imidazoline-2-thiones based on the cyclization of α-hydroxy ketones with thiocyanic acid and its salts.[19] In application of this procedure to fatty acids we therefore treated the α-hydroxy ketone (**25**) with a threefold excess of ammonium thiocyanate in dioxane under reflux. The corresponding imidazolinethione **28** was isolated as a beige, waxy solid in 77% yield (Scheme 6). We are dealing with a condensation reaction, because above 70 °C ammonium thiocyanate is converted into thiourea, which reacts with the α-hydroxy ketone.[20]

Compounds **12**, **22**, **24**, **26**, **27**, and **28**, each with a five-membered ring at the C-9/C-10 positions of the fatty acid chain, are related in structure to the naturally occurring prostaglandins PGE_1 and PGE_2. Bender et al. have prepared several prostaglandin-like heterocyclic fatty acid derivatives with promising interesting pharmacological effects.[21] In particular, those compounds with a *trans*-configured ring corresponding to PGE_1 and PGE_2 showed distinctive effects.

Conclusion

In summary, we report on the synthesis of tetrazoles **1**−**6** as analogues of fatty acids, as well as on the corresponding 1,3,4-oxadiazoles and bis(oxadiazoles) **13**−**20**. An alkyl-branched tetrazole **7** was prepared from methyl oleate, and a 1,5-dialkyl-substituted tetrazole **12** from methyl 9(10)-oxooctadecanoate. We have also synthesized 4,5-dihydroox-



Scheme 6. Reaction of the hydroxy ketone **25** with formamide to give the imidazoles **26** and the oxazoles **27**, and with ammonium thiocyanate to give the imidazolinethione **28**

azoles **22**, oxazolidines **24**, imidazoles **26**, oxazoles **27**, and an imidazolinethione **28**. Compounds **12**, **22**, **24**, **26**, **27**, and **28** could be of interest as homoprostanoids.

Experimental Section

General: The fatty nitriles were obtained from Clariant GmbH as technical products. 10-Undecenoic acid was obtained from Elf Atochem. Methyl oleate and methyl *cis*-9,10-epoxyoctadecanoate were provided by Henkel KGaA and Cognis Deutschland GmbH, respectively. The compositions of the fatty compounds (by GC analysis) were as follows: dodecanenitrile (after distillation) 95%, octadecanenitrile 63%, (*Z*)-9-octadecenenitrile 80%, tetradecanenitrile (after distillation) 87%, dodecanedinitrile 97%, 10-undecenoic acid 98%, methyl oleate (new sunflower) 84%, methyl *cis*-9,10-epoxyoctadecanoate 98%. The amounts of the fatty compounds stated in the Exp. Sect. refer to 100% pure compounds. All other chemicals and solvents used were purchased from standard chemical suppliers. 10-Undecenenitrile was prepared from 10-undecenoic acid analogously to the method described by Stenberg and Rheineck.[22] Methyl 9-oxooctadecanoate/methyl 10-oxooctadecanoate was prepared from methyl 9,10-*cis*-epoxyoctadecanoate as reported by Stoll and Worschech.[23] The preparation of methyl 9-hydroxy-10-oxooctadecanoate/methyl 10-hydroxy-9-oxooctadecanoate from methyl 9,10-*cis*-epoxyoctadecanoate was reported by Brousse and Lefort.[17] Solvents: Toluene and xylene were heated at reflux and distilled from sodium under an inert gas. Acetonitrile was distilled from phosphorus pentoxide and afterwards from potassium carbonate. Methanol was heated at reflux with magnesium and then distilled. Petroleum ether (boiling range 60−80 °C) and ethyl acetate were previously distilled. Acetic anhydride was heated under reflux with anhydrous sodium acetate and distilled off. Silica gel 60 (40−63 μm) from Merck was used for all liquid chromatographic separations. Analytical equipment: NMR: Bruker DRX 500: 500.1 MHz (^{1}H NMR), 125.8 MHz (^{13}C NMR), $CDCl_3$ as solvent, TMS as internal standard. MS: Finnigan MAT 95. Elemental analyses: Mikroanalytisches Laboratorium Beller, 37004 Göttingen, Germany.

General Procedure for the Preparation of 5-Alkyl-1*H*-tetrazoles: In a typical experiment, a mixture of the fatty nitrile (20 mmol), sodium azide (3.90 g, 60 mmol) and triethylamine hydrochloride (8.22 g, 60 mmol) in dry toluene (70 mL) was heated under reflux until TLC showed complete conversion (ca. 2 d). The reaction mixture was dissolved in water (100 mL). In general, formation of an emulsion was observed, but this could be suppressed by addition of brine and a small amount of methanol. The layers were separated and the aqueous layer was acidified (pH = 1) with concentrated HCl and extracted with diethyl ether. The combined ethereal extracts were dried with sodium sulfate. After removal of the solvent in vacuo the crude product was purified as described below for the different compounds.

5-Undecyl-1*H*-tetrazole (1): Dodecanenitrile (3.62 g, 20 mmol) was treated as described above. Recrystallization from acetonitrile yielded the product (3.96 g, 89%) as a white solid, m.p. 68−72 °C. ^{1}H NMR: δ = 0.81 (t, 3 H, CH_3), 1.15−1.34 (m, 14 H, CH_2), 1.37 (m, 2 H, 11-H) 1.87 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 3-H), 3.13 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H) ppm. ^{13}C NMR: δ = 13.96 (CH_3), 22.55, 23.37, 27.66, 28.96, 29.02, 29.21, 29.33, 29.48, 31.78 (CH_2), 156.92 (C-1) ppm. HR MS (EI, 70 eV): calcd. for $C_{12}H_{24}N_4$ $[M]^+$ 224.2001; found 224.2000.

5-Heptadecyl-1*H*-tetrazole (2): Octadecanenitrile (5.31 g, 20 mmol) was treated as described above. Recrystallization from a mixture of acetonitrile/ethanol (10:1) yielded the product (6.09 g, 99%) as a white solid, m.p. 82−85 °C. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.15−1.40 (m, 26 H, CH_2), 1.42 (m, 2 H, 11-H), 1.87 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 3-H), 3.11 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H) ppm. ^{13}C NMR: δ = 13.98 (CH_3), 22.64, 23.57, 27.72, 29.09, 29.12, 29.33, 29.43, 29.58, 29.64, 29.69, 31.92 (CH_2), 157.11 (C-1) ppm. HR MS (EI, 70 eV): calcd. for $C_{18}H_{36}N_4$ $[M]^+$ 308.2940; found 308.2939.

(8*Z*)-5-Heptadec-8-enyl-1*H*-tetrazole (3): (*Z*)-9-Octadecenenitrile (5.26 g, 20 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:5:1) yielded 5.76 g (94%) of a white wax (R_f = 0.26). ^{1}H NMR: δ = 0.84 (t, 3 H, CH_3), 1.15−1.45 (m, 20 H, CH_2), 1.88 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 3-H), 1.97 (q, $^3J_{H,H}$ = 6.4 Hz, 4 H, 8-H, 11-H), 3.11 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 5.29 (m, $^3J_{H,H}$ = 6.4 Hz, 2 H, 9-H, 10-H) ppm. ^{13}C NMR: δ = 14.04 (CH_3), 22.63, 23.43, 27.11, 27.18, 29.04, 29.10, 29.17, 29.41, 29.48, 29.63, 29.72, 31.73, 31.86, 32.49 (CH_2), 129.55, 130.02 (C-9, C-10), 156.90 (C-1) ppm. $C_{18}H_{34}N_4$ (306.5): calcd. C 70.54, H 11.18, N 18.28; found C 70.34, H 11.21, N 18.32.

5-Tridecyl-1*H*-tetrazole (4): Tetradecanenitrile (3.77 g, 18 mmol) was treated as described above. Recrystallization from petroleum ether yielded the product (4.15 g, 91%) as a white solid, m.p. 74−77 °C. ^{1}H NMR: δ = 0.83 (t, 3 H, CH_3), 1.15−1.35 (m, 18 H, CH_2), 1.38 (m, 2 H, 11-H), 1.88 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 3-H), 3.13 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H) ppm. ^{13}C NMR: δ = 13.96 (CH_3), 22.56, 23.37, 27.66, 28.96, 29.02, 29.21, 29.33, 29.48, 31.78 (CH_2), 156.92 (C-1) ppm. $C_{14}H_{28}N_4$ (252.45): calcd. C 66.62, H 11.18, N 22.20; found C 66.48, H 11.34, N 22.16.

5-(Dec-9-enyl)-1*H*-tetrazole (5): 10-Undecenenitrile (4.16 g, 20 mmol) was treated as described above. Recrystallization from a mixture of petroleum ether/ethanol (2:1) yielded an orange solid (3.79 g, 91%), which melted at about room temperature. ^{1}H NMR: δ = 1.20−1.40 (m, 10 H, CH_2), 1.88 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 3-H), 1.96 (m, $^3J_{H,H}$ = 6.6 Hz, 2 H, 9-H), 3.13 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 4.87 (dq, $^2J_{H,H}$ = 1.7, $^3J_{H,H}$ = 10.4 Hz, 1 H, 11-H_Z), 4.93 (dq, $^2J_{H,H}$ = 1.7, $^3J_{H,H}$ = 17.0 Hz, 1 H, 11-H_E), 5.73 (m, $^3J_{H,H}$ = 6.6, $^3J_{H,H}$ = 10.4, $^3J_{H,H}$ = 17.0 Hz, 1 H, 10-H) ppm. ^{13}C NMR: δ = 27.63, 28.76, 28.88, 28.92, 28.94, 29.15, 32.41, 33.64 (CH_2), 114.11 (C-11), 138.93 (C-10), 156.91 (C-1) ppm. $C_{11}H_{20}N_4$ (208.2): calcd. C 63.43, H 9.68, N 26.90; found C 63.65, H 9.54, N 26.65.

5-[10-(1*H*-Tetrazol-5-yl)decyl]-1*H*-tetrazole (6): Dodecanedinitrile (3.96 g, 20 mmol) was treated as described above. Recrystallization from acetonitrile yielded a beige, glistening solid (4.01 g, 72%), m.p. 146−149 °C. ^{1}H NMR [$(CD_3)_2SO$]: δ = 1.14−1.28 (m, 12 H, CH_2), 1.65 (quint, $^3J_{H,H}$ = 7.1 Hz, 4 H, 3-H), 2.82 (t, $^3J_{H,H}$ = 7.1 Hz, 4 H, 2-H) ppm. ^{13}C NMR [$(CD_3)_2SO$]: δ = 22.70, 27.05, 28.35, 28.53, 28.80 (CH_2), 155.94 (C-1) ppm. $C_{12}H_{22}N_8$ (278.4): calcd. C 51.76, H 7.97, N 40.27; found C 51.86, H 7.87, N 39.99.

Methyl 9-(Cyanomethyl)-10-iodooctadecanoate and Methyl 10-(Cyanomethyl)-9-iodooctadecanoate (9): A mixture of methyl oleate (**8**, 5.78 g, 19 mmol), iodoacetonitrile (2.2 mL, 28.6 mmol), and copper powder (1.14 g, 18 mmol) was heated at 100 °C under argon for 5 d (monitored by TLC). The reaction mixture was dissolved in diethyl ether and washed with water. The organic layer was dried with sodium sulfate and the solvents were evaporated in vacuo, giving a brown, oily residue (8.78 g). Column chromatography with petroleum ether/ethyl acetate (4:1) yielded the product (2.63 g,

30%) as a yellow oil and as a mixture of two regioisomers (R_f = 0.61). ^{1}H NMR: δ = 0.87 (t, 3 H CH_3), 1.20−1.50 (m, 24 H, CH_2), 1.55 (m, 1 H, $CHCH_2CN$), 1.62 (m, 2 H, 3-H), 2.29 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 2.47 (m, 2 H, CH_2CN), 3.65 (s, 3 H, OCH_3), 4.21 (m, 1 H, CHI) ppm. ^{13}C NMR: δ = 13.94 (CH_3), 21.93, 22.48, 22.54, 24.68, 26.29, 28.32, 28.54, 28.82, 28.88, 28.98, 29.02, 29.19, 29.23, 29.26, 29.54, 31.64, 31.93, 33.84, 34.08 (CH_2), 37.33, 38.54 (C-8, C-11), 41.57, 42.28 ($CHCH_2CN$), 43.42, 43.93 (CHI), 51.27 (OCH_3), 118.37, 118.55 (CN), 173.95 ($COOCH_3$) ppm.

Methyl 9-(Cyanomethyl)octadecanoate and Methyl 10-(Cyanomethyl)octadecanoate (10): A solution of compound **9** (2.6 g, 5.6 mmol), $NaHCO_3$ (0.5 g) and palladium on charcoal (10%, 0.1 g) in methanol (80 mL) was placed in a hydrogenation flask and hydrogenated under hydrogen (2.9 bar) at 40 °C by shaking for 44 h. The reaction mixture was filtered through Celite, the filter cake was washed with small portions of methanol, and the combined filtrates were concentrated to dryness, yielding the product (1.85 g, 96%) as a yellow oil and as a mixture of two regioisomers. ^{1}H NMR: δ = 0.85 (t, 3 H, CH_3), 1.20−1.40 (m, 26 H, CH_2), 1.58 (m, 2 H, 3-H), 1.63 (m, 1 H, $CHCH_2CN$), 2.27 (m, 4 H, 2-H, CH_2CN), 3.63 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 14.01 (CH_3), 21.62, 22.59, 24.84, 26.45, 26.52, 28.98, 29.02, 29.05, 29.18, 29.22, 29.38, 29.41, 29.48, 29.58, 31.78, 31.81, 33.45, 33.99 (CH_2), 35.03 ($CHCH_2CN$), 51.39 (OCH_3), 118.90 (CN), 174.31 ($COOCH_3$) ppm.

Methyl 9-[(1*H*-Tetrazol-5-yl)methyl]octadecanoate and Methyl 10-[(1*H*-Tetrazol-5-yl)methyl]octadecanoate (7): Compound **10** (1.70 g, 5 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/methanol (7:3:1) yielded the product (0.60 g, 32%) as orange oil and as a mixture of two regioisomers. ^{1}H NMR: δ = 0.82 (t, 3 H, CH_3), 1.15−1.30 (m, 30 H, CH_2), 1.55 (m, 2 H, 3-H), 1.90 (m, 1 H, $CHCH_2CN_4H$), 2.27 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 2.94 (d, $^3J_{H,H}$ = 7.2 Hz 2 H, 1′-H), 3.64 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 13.99 (CH_3), 22.56, 24.77, 26.35, 28.83, 28.87, 28.91, 28.97, 29.09, 29.20, 29.22, 29.46, 29.51, 29.77, 31.78, 31.79, 33.15, 33.20 (CH_2), 33.32 (C-1′), 33.99, 34.02 (C-2), 37.29 ($CHCH_2CN_4H$), 51.56 (OCH_3), 156.13, 156.19 (C-2′), 174.96 ($COOCH_3$) ppm. $C_{21}H_{40}N_4O_2$ (380.6): calcd. C 66.28, H 10.59, N 14.72; found C 65.98, H 10.24, N 14.39.

Methyl 8-(1-Nonyltetrazol-5-yl)octanoate, Methyl 8-(5-Nonyltetrazol-1-yl)octanoate/Methyl 9-(1-Octyltetrazol-5-yl)nonanoate, Methyl 9-(5-Octyltetrazol-1-yl)nonanoate (12): A mixture of methyl 9-oxooctadecanoate/methyl 10-oxooctadecanoate (**11**, 1.2 g, 3.2 mmol), sodium azide (2.03 g, 31 mmol) and $TiCl_4$ (1.5 g, 7.8 mmol) in acetonitrile was heated under reflux under argon for 5 h. After the addition of aqueous HCl (10%, 13 mL), the acetonitrile was removed in vacuo. The remaining aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with water and dried with sodium sulfate, and the solvents were evaporated to dryness. Column chromatography of the brown and oily residue (2.22 g) with petroleum ether/ethyl acetate (4:1, R_f = 0.09) followed by ethyl acetate/methanol (2:1, R_f = 0.72) yielded the product (0.81 g, 71%) as a yellow oil and as a mixture of two isomers and their two regioisomers. ^{1}H NMR: δ = 0.78 (t, 3 H, CH_3), 1.10−1.35 (m, 18 H, CH_2), 1.53 (m, 2 H, 3-H), 1.73 (m, $^3J_{H,H}$ = 7.7 Hz, 2 H, $CH_2CH_2C{=}N$), 1.81 (m, $^3J_{H,H}$ = 7.1 Hz, 2 H, CH_2CH_2N), 2.21 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 2.73 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, $CH_2C{=}N$), 3.57 (s, 3 H, OCH_3), 4.15 (t, $^3J_{H,H}$ = 7.1 Hz, 2 H, CH_2N) ppm. ^{13}C NMR :δ = 13.84 (CH_3), 22.37, 22.41, 22.43, 22.46, 22.97, 24.50, 24.60, 24.65, 24.74, 26.04, 26.16, 26.22, 26.86, 26.93, 27.00, 28.56, 28.59, 28.66, 28.71, 28.76, 28.80, 28.86, 28.94, 28.96, 29.01, 29.05, 29.10, 29.16, 29.28, 29.34, 29.37, 29.47, 31.46, 31.56, 31.63, 31.69, 32.34, 32.39, 33.68, 33.76, 33.80, 33.87 (CH_2), 46.70, 46.73, 46.78 ($CH_2C{=}N$), 51.19 (OCH_3), 129.99, 130.23 (CH_2N), 154.46, 154.50, 154.56 ($C_{tetrazole}$), 173.80, 173.88, 173.94, 174.03 ($COOCH_3$) ppm. $C_{21}H_{40}N_4O_2$ (380.6): calcd. C 64.74, H 10.29, N 15.89; found C 65.60, H 10.50, N 16.34.

General Procedure for the Preparation of 1,3,4-Oxadiazole Derivatives: In a typical experiment, the tetrazole (3−4 mmol) was dissolved in acetic anhydride (5 mL) and heated under reflux (monitored by TLC, 7 h). The acetic anhydride was removed in vacuo and the crude product was purified by column chromatography.

2-Methyl-5-undecyl-1,3,4-oxadiazole (13): 5-Undecyl-1*H*-tetrazole (**1**, 1.0 g, 4.5 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:10:1) yielded the product (0.87 g, 80%) as a pale yellow oil (R_f = 0.51). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.22−1.41 (m, 16 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2′-H), 2.49 (s, 3 H, CH_3), 2.80 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 1′-H) ppm. ^{13}C NMR: δ = 10.85, 14.01 (CH_3), 22.59, 25.21, 26.38, 28.91, 29.03, 29.23, 29.32, 29.49, 29.50, 31.82 (CH_2), 163.46, 167.12 (C-2, C-5) ppm. $C_{14}H_{26}N_2O$ (238.4): calcd. C 70.54, H 10.99, N 11.75; found C 70.29, H 11.13, N 11.72.

2-Heptadecyl-5-methyl-1,3,4-oxadiazole (14): 5-Heptadecyl-1*H*-tetrazole (**2**, 1.0 g, 3.2 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:10:1) yielded the product (1.00 g, 97%) as a beige solid (R_f = 0.54), m.p. 43−46 °C. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.40 (m, 28 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2′-H), 2.49 (s, 3 H, CH_3), 2.79 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 1′-H) ppm. ^{13}C NMR: δ = 10.83, 14.01 (CH_3), 22.59, 25.20, 26.36, 28.90, 29.03, 29.27, 29.32, 29.48, 29.54, 29.57, 29.60, 31.84 (CH_2), 163.43, 167.10 (C-2, C-5) ppm. $C_{20}H_{38}N_2O$ (322.5): calcd. C 74.48, H 11.88, N 8.69; found C 74.49, H 11.76, N 8.63.

(8*Z*)-2-(Heptadec-8-enyl)-5-methyl-1,3,4-oxadiazole (15): (8*Z*)-5-(Heptadec-8-enyl)-1*H*-tetrazole (**3**, 1.0 g, 3.3 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:10:1) yielded the product (0.77 g, 73%) as a pale yellow oil (R_f = 0.53). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.42 (m, 20 H, CH_2), 1.77 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2′-H), 2.01 (m, 4 H, 7′-H, 10′-H), 2.49 (s, 3 H, CH_3), 2.80 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 1′-H), 5.34 (m, 2 H, 8′-H, 9′-H) ppm. ^{13}C NMR: δ = 10.71, 13.90 (CH_3), 22.48, 25.08, 26.24, 26.95, 27.03, 28.77, 28.83, 28.93, 28.99, 29.22, 29.33, 29.47, 29.57, 31.72 (CH_2), 129.46, 129.83 (C-8, C-9), 163.34, 166.96 (C-2, C-5) ppm. $C_{20}H_{36}N_2O$ (320.5): calcd. C 74.95, H 11.32, N 8.74; found C 74.66, H 11.32, N 8.80.

2-Methyl-5-tridecyl-1,3,4-oxadiazole (16): 5-Tridecyl-1*H*-tetrazole (**4**, 1.0 g, 4.0 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:10:1) yielded the product (0.90 g, 85%) as a beige, shiny solid (R_f = 0.51), m.p. 32−33 °C. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.22−1.41 (m, 20 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2′-H), 2.49 (s, 3 H, CH_3), 2.79 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 1′-H) ppm. ^{13}C NMR: δ = 10.83, 14.00 (CH_3), 22.59, 25.20, 26.36, 28.90, 29.02, 29.25, 29.31, 29.47, 29.54, 29.56, 31.82 (CH_2), 163.42 (C-2), 167.09 (C-5) ppm. $C_{16}H_{30}N_2O$ (266.4): calcd. C 72.13, H 11.35, N 10.51; found C 72.30, H 11.45, N 10.48.

2-(Dec-9-enyl)-5-methyl-1,3,4-oxadiazole (17): 5-(Dec-9-enyl)-1*H*-tetrazole (**5**, 1.0 g, 4.0 mmol) was treated as described above. Column chromatography with petroleum ether/ethyl acetate/acetic acid (10:5:1) yielded the product (0.69 g, 65%) as a colourless oil (R_f = 0.41). ^{1}H NMR: δ = 1.20−1.36 (m, 10 H, CH_2), 1.70 (quint, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2′-H), 1.97 (m, $^3J_{H,H}$ = 6.6 Hz, 2 H, 8′-H),

2.43 (s, 3 H, CH_3), 2.73 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 1′-H), 4.86 (dq, $^2J_{H,H}$ = 1.7, $^3J_{H,H}$ = 10.4 Hz, 1 H, 10′-H_Z), 4.92 (dq, $^2J_{H,H}$ = 1.7, $^3J_{H,H}$ = 17.0 Hz, 1 H, 10′-H_E), 5.73 (m, $^3J_{H,H}$ = 6.6, $^3J_{H,H}$ = 10.4, $^3J_{H,H}$ = 17.0 Hz, 1 H, 9′-H) ppm. ^{13}C NMR: δ = 10.78 (CH_3), 25.13, 26.29, 28.73, 28.90, 29.29, 29.33, 32.37, 33.61 (CH_2), 114.03 (C-10′), 138.94 (C-9′), 163.39, 167.02 (C-2, C-5) ppm. $C_{13}H_{22}N_2O$ (222.3): calcd. C 70.23, H 9.97, N 12.60; found C 69.65, H 10.45, N 12.41.

2-Methyl-5-[10-(5-methyl-1,3,4-oxadiazol-2-yl)decyl]-1,3,4-oxadiazole (18): 5-[10-(1*H*-Tetrazol-5-yl)decyl]-1*H*-tetrazole (**6**, 1.0 g, 3.6 mmol) was treated as described above. Successive column chromatography with petroleum ether/ethyl acetate/acetic acid (10:5:1) and afterwards with diethyl ether/acetic acid (10:4; R_f = 0.54) yielded the product (0.79 g, 72%) as a pale pink solid, m.p. 45−50 °C. ^{1}H NMR: δ = 1.22−1.42 (m, 12 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.7 Hz, 4 H, 2′-H), 2.50 (s, 6 H, CH_3), 2.80 (t, $^3J_{H,H}$ = 7.7 Hz, 4 H, 1′-H) ppm. ^{13}C NMR: δ = 10.82 (CH_3), 25.15, 26.29, 28.81, 28.92, 29.15 (CH_2), 163.43, 167.03 (C-2, C-5) ppm. $C_{16}H_{26}N_4O_2$ (306.4): calcd. C 62.72, H 8.55, N 18.29; found C 62.00, H 8.74, N 17.78.

2-Undecyl-5-[(5-undecyl-1,3,4-oxadiazol-2-yl)ethyl]-1,3,4-oxadiazole (19): A mixture of 5-undecyl-1*H*-tetrazole (**1**, 2.22 g, 10 mmol) and succinic anhydride (1.51 g, 15 mmol) in dry xylene (25 mL) was heated under reflux for 24 h (monitored by TLC). After the removal of the succinic anhydride in vacuo, the residue was recrystallized from ethyl acetate, yielding a light beige solid (1.70 g, 72%), m.p. 96 °C. ^{1}H NMR: δ = 0.88 (t, 6 H, CH_3), 1.20−1.40 (m, 32 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.5 Hz, 4 H, 2′-H), 2.81 (t, $^3J_{H,H}$ = 7.5 Hz, 4 H, 1′-H), 3.35 (s, 4 H, 1-H) ppm. ^{13}C NMR: δ = 14.08 (CH_3), 22.33, 22.66, 25.28, 26.40, 28.99, 29.08, 29.30, 29.37, 29.56, 31.89 (CH_2), 164.59, 167.58 (C-2, C-5) ppm. $C_{28}H_{50}N_4O_2$ (474.7): calcd. C 70.84, H 10.62, N 11.80; found C 70.89, H 10.56, N 11.65.

2-Undecyl-5-[3-(5-undecyl-1,3,4-oxadiazol-2-yl)propyl]-1,3,4-oxadiazole (20): A mixture of 5-undecyl-1*H*-tetrazole (**1**, 2.22 g, 10 mmol) and glutaric anhydride (1.71 g, 15 mmol) in dry xylene (25 mL) was heated under reflux for 24 h (monitored by TLC). After the removal of the glutaric anhydride in vacuo, the residue was recrystallized from methanol, yielding a light beige, shiny solid (0.83 g, 34%), m.p. 80−82 °C. ^{1}H NMR: δ = 0.88 (t, 6 H, CH_3), 1.20−1.40 (m, 32 H, CH_2), 1.76 (quint, $^3J_{H,H}$ = 7.7 Hz, 4 H, 2′-H), 2.31 (quint, $^3J_{H,H}$ = 7.1 Hz, 2 H, 2-H), 2.80 (t, $^3J_{H,H}$ = 7.7 Hz, 4 H, 1′-H), 2.97 (t, $^3J_{H,H}$ = 7.1 Hz 4 H, 1-H) ppm. ^{13}C NMR: δ = 14.03 (CH_3), 22.61, 22.87, 24.42, 25.26, 26.38, 28.96, 29.04, 29.25, 29.34, 29.51, 31.83 (CH_2), 165.56, 167.26 (C-2, C-5) ppm. HR-MS (EI, 70 eV): calcd. for $C_{29}H_{52}N_4O_2$ $[M]^+$ 488.4090; found 488.4088.

Methyl 8-(2-Methyl-4-octyl-4,5-dihydrooxazol-5-yl)octanoate and Methyl 8-(2-Methyl-5-octyl-4,5-dihydrooxazol-4-yl)octanoate (22): Boron trifluoride−diethyl ether (1.3 mL, 10 mmol) was added under argon to a solution of methyl *cis*-9,10-epoxyoctadecanoate (**21**, 3.1 g, 10 mmol) in dry acetonitrile (30 mL) and the mixture was stirred at room temperature for 18 h (monitored by TLC). The reaction mixture was poured into aqueous NaOH solution (2 N, 30 mL) and extracted with dichloromethane. The combined extracts were washed with water and dried with sodium sulfate, and the solvents were evaporated to dryness. The remaining yellow oil (3.15 g) was purified by column chromatography with petroleum ether/ethyl acetate/methanol (7:3:1), and the product (2.13 g, 60%) was obtained as a white wax and as a mixture of two isomers (R_f = 0.45). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.55 (m, 24 H, CH_2), 1.62 (m, 2 H, 3-H), 1.95 (s, 3 H, 1′-H), 2.29 (t, $^3J_{H,H}$ = 7.769 Hz, 2 H, 2-H), 3.37 (m, 1 H, CHN), 3.66 (s, 3 H, OCH_3), 4.03 (m, 1 H, CHO) ppm. ^{13}C NMR: δ = 13.95, 14.00 (CH_3), 22.53, 24.79 (CH_2), 24.99 (C-1′), 25.65, 28.97, 29.10, 29.34, 29.48, 29.56, 29.63, 31.76, 33.55, 33.61 (CH_2), 35.32, 35.92 (C-8, C-11), 51.27 (OCH_3), 71.35 (CHN), 85.05, 85.09 (CHO), 163.76 (C-2′), 174.11 (CO-OCH_3) ppm. HR MS (EI, 70 eV): calcd. for $C_{21}H_{39}NO_3$ $[M]^+$ 353.2930; found 353.2930.

Methyl 8-(4-Octyloxazolidin-5-yl)octanoate and Methyl 8-(5-Octyloxazolidin-4-yl)octanoate (24): A mixture of methyl 9-amino-10-hydroxyoctadecanoate/methyl 10-amino-9-hydroxyoctadecanoate (**23**, 1.00 g, 3 mmol)[16] and paraformaldehyde (0.76 g, 25 mmol) in absolute methanol (20 mL) was stirred at room temperature for 23 h (monitored by TLC). The reaction mixture was filtered through Celite, the filter cake was washed with small portions of methanol, and the combined filtrates were concentrated to dryness, yielding a pale yellow oil (1.02 g). This was purified by column chromatography with ethyl acetate/methanol (2:1) and gave the product (0.46 g, 44%) as a pale yellow oil and as a mixture of two isomers (R_f = 0.81). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.55 (m, 24 H, CH_2), 1.62 (m, 2 H, 3-H), 2.30 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 2-H), 2.90, 3.10 (m, 1 H, 4′-H), 3.48, 3.83 (m, 1 H, 5′-H), 3.66 (s, 3 H, OCH_3), 4.47 (m, 2 H, 2′-H) ppm. ^{13}C NMR: δ = 14.07 (CH_3), 22.63, 24.90, 26.77, 27.01, 27.26, 29.05, 29.13, 29.18, 29.24, 29.34, 29.54, 29.58, 29.66, 29.79, 29.89, 29.94, 31.85, 34.06 (CH_2), 51.39 (OCH_3), 63.11, 64.13 (C-4′), 77.00, 77.78 (C-5′), 83.35, 83.50 (C-2′), 174.19, 174.24 ($COOCH_3$) ppm. $C_{20}H_{39}NO_3$ (341.5): calcd. C 70.33, H 11.51, N 4.10; found C 70.52, H 11.28, N 4.13.

Methyl 8-(5-Octyl-3*H*-imidazol-4-yl)octanoate and Methyl 8-(4-Octyl-3*H*-imidazol-5-yl)octanoate (26): A mixture of methyl 9-hydroxy-10-oxooctadecanoate/methyl 10-hydroxy-9-oxooctadecanoate (**25**, 1.64 g, 5 mmol) and formamide (2 mL) was heated under nitrogen at 150 °C for 20 h (monitored by TLC). The reaction mixture was dissolved in dichloromethane and washed with water. The organic layer was dried with sodium sulfate and the solvents were evaporated to dryness. The remaining brown oil (1.7 g) was purified by column chromatography by elution with petroleum ether/ethyl acetate (1:1) followed by elution with methanol. The product (0.97 g, 58%) was obtained from the methanolic eluate (R_f = 0.63) as an orange oil and as a mixture of two isomers. ^{1}H NMR: δ = 0.87 (t, 3 H, CH_3), 1.18−1.37 (m, 16 H, CH_2), 1.59 (m, 6 H, 3-H, 7-H, 12-H), 2.29 (t, $^3J_{H,H}$ = 7.769 Hz, 2 H, 2-H), 2.52 (t, $^3J_{H,H}$ = 7.769 Hz, 4 H, 8-H, 11-H), 3.66 (s, 3 H, OCH_3), 7.59 (s, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 14.01 (CH_3), 22.58, 24.81, 24.95, 28.83, 28.93, 28.98, 29.00, 29.06, 29.19, 29.30, 29.43, 29.77, 29.88, 31.79, 33.97 (CH_2), 51.37 (OCH_3), 130.45 (C-4′, C-5′), 132.17 (C-2′), 174.24 ($COOCH_3$) ppm. $C_{20}H_{36}N_2O_2$ (336.5): calcd. C 71.38, H 10.78, N 8.32; found C 71.91, H 10.57, N 7.82.

Methyl 8-(4-Octyloxazol-5-yl)octanoate and Methyl 8-(5-Octyloxazol-4-yl)octanoate (27): A mixture of methyl 9-hydroxy-10-oxooctadecanoate/methyl 10-hydroxy-9-oxooctadecanoate (**25**, 1.64 g, 5 mmol), formamide (2 mL), and concentrated sulfuric acid (0.55 mL) was heated under nitrogen at 100 °C for 5 h and at 140 °C for a further 2 h (monitored by TLC). The reaction mixture was dissolved in dichloromethane and washed with water. The organic layer was dried with sodium sulfate and the solvents were evaporated to dryness. The remaining brown oil (1.63 g) was purified by column chromatography with petroleum ether/ethyl acetate (1:1), yielding the product (0.60 g, 36%) as an orange oil and as a mixture of two isomers (R_f = 0.67). ^{1}H NMR: δ = 0.87, 0.88 (t, 6 H, CH_3), 1.18−1.37 (m, 28 H, CH_2), 1.61 (m, 6 H, 3-H, 7-H, 12-H), 2.29, 2.30 (m, 4 H, 2-H), 2.42 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 4′-CH_2), 2.58 (t, $^3J_{H,H}$ = 7.7 Hz, 2 H, 5′-CH_2), 3.66 (s, 6 H, OCH_3), 7.68 (s, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 13.91 (CH_3), 22.48, 22.50, 24.28, 24.72,

24.77, 25.34, 28.16, 28.76, 28.85, 28.87, 28.90, 29.04, 29.09, 29.24, 31.67, 31.72, 33.86, 33.89 (CH_2), 51.20, 51.22 (OCH_3), 133.93, 134.08 (C-4′), 146.93, 147.09 (C-5′), 148.63 (C-2′), 173.96, 174.02 ($COOCH_3$) ppm. $C_{20}H_{35}NO_3$ (337.5): calcd. C 71.18, H 10.45, N 4.15; found C 70.96, H 10.56, N 3.65.

Methyl 8-(5-Octyl-2-thioxo-2,3-dihydro-1*H*-imidazol-4-yl)octanoate (28): A solution of methyl 9-hydroxy-10-oxooctadecanoate/methyl 10-hydroxy-9-oxooctadecanoate (**25**, 2.00 g, 6 mmol) and ammonium thiocyanate (0.41 g, 18 mmol) in dioxane (20 mL) was heated under reflux for 5 d (monitored by TLC). After removal of the solvent in vacuo, the residue was dissolved in dichloromethane and washed with water. The organic layer was dried with sodium sulfate and the solvents were evaporated to dryness. The residue (2.28 g) was purified by column chromatography with petroleum ether/ethyl acetate/methanol (7:3:1) and gave the product (1.71 g, 77%) as a beige, waxy solid (R_f = 0.36). ^{1}H NMR: δ = 0.87 (t, 3 H, CH_3), 1.20−1.35 (m, 16 H, CH_2), 1.55 (m, 4 H, H-7, 12-H), 1.61 (m, 2 H, 3-H), 2.30 (m, 2 H, 2-H), 2.39 (t, $^3J_{H,H}$ = 7.7 Hz, 4 H, 8-H, 11-H), 3.67 (s, 3 H, OCH_3), 10.94, 11.02 (d, 2 H, NH) ppm. ^{13}C NMR: δ = 14.02 (CH_3), 22.58, 23.56, 24.80, 28.70, 28.82, 28.93, 29.13, 29.18, 29.21, 31.78, 34.00 (CH_2), 51.45 (OCH_3), 125.11, 125.19 (C-9, C-10), 156.71 (C=S), 174.27 ($COOCH_3$) ppm. $C_{20}H_{36}N_2O_2S$ (368.6): calcd. C 65.17, H 9.84, N 7.60, S 8.70; found C 65.22, H 9.21, N 7.70, S 8.80.

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