Fat-Derived Aziridines and Their *N*-Substituted Derivatives: Biologically Active Compounds Based on Renewable Raw Materials

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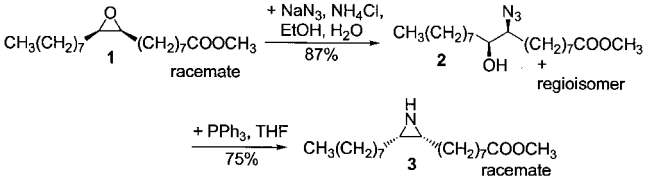
The first successful preparation of the aziridines methyl (9*Z*,12*S*,13*R*)-12,13-epimino-9-octadecenoate (**10**), derived from vernolic acid, and methyl (9*R*,10*S*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12a**) and methyl (9*S*,10*R*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12b**), both derived from ricinoleic acid, is reported. These are the first examples of enantiomerically pure fat-derived aziridines. Treatment of the corresponding epoxides with sodium azide and ammonium chloride in ethanol in the presence of water yielded the new azido hydroxy compounds, which could be treated in an improved way with polymer-bound triphenylphosphane to afford the aziridines in good yields. The intermediate azido hydroxy compounds could easily be reduced and so offer access to a variety of interesting β-amino alcohols **17**–**21**. The synthesis of various *N*-substituted aziridine derivatives **22**–**29** by treatment of methyl *cis*-9,10-epiminooctadecanoate (**3**) with phenyl isocyanate and isothiocyanate, acetyl chloride, alkyl and aryl chloroformates and acrylonitrile is described. Finally, the fat-derived 2,5-dialkyl-substituted pyrrole methyl 9-(5-pentyl-1*H*-pyrrol-2-yl)nonanoate (**9**) was obtained. The previously reported bis(aziridine) methyl *cis*-9,10;*cis*-12,13-diepiminooctadecanoate, derived from linoleic acid, and tris(aziridine) methyl *cis*-9,10;*cis*-12,13;*cis*-15,16-triepiminooctadecanoate, derived from linolenic acid,[1] have been subjected to different biological tests and showed cytotoxic and antimicrobial activity as well as remarkable antitumour-promoting and good neuroprotective effects.

Introduction

Aziridines, as highly strained ring systems, have been attracting considerable attention. Ethylenimine and some of its simple derivatives are commercial products in different fields of applied chemistry. Observations of the toxic action of aziridines have resulted in extensive investigations on the synthesis and testing of aziridines for pharmacological activity, some substances having reached advanced stages of evaluation as cancer chemotherapeutic agents and a few being in regular clinical use.[2] Because of their tendency to undergo ring-opening reactions with nucleophiles, aziridines are in general regarded as good alkylating agents, possessing powerful mutagenic and toxic activities. Naturally occurring mitomycin C shows antibiotic and antitumour activity related to the presence of the aziridine ring.[3] It is possible to obtain convenient access to functionalised aziridine derivatives by starting from *N*-unsubstituted aziridines. These compounds show behaviour characteristic of secondary amines, caused by the nucleophilicity of the nitrogen atom. To prevent side reactions, resulting in ring-opening, special precautions frequently have to be undertaken. Nevertheless, aziridines can be alkylated and acylated by alkyl and acyl halides. In all these reactions the intermediate aziridinium salt has to be deprotonated with a base to bind the formed acid. Aziridines can also react with α,β-unsaturated nitriles and carbonyl compounds in conjugate addition reactions.[2]

We were interested in the synthesis of *N*-substituted and *N*-unsubstituted aziridines derived from fats, with the goals of increasing the variety of interesting fatty compounds with aziridine functions and gaining deeper insight into their biological properties. In the case of the *N*-unsubstituted compounds we focussed on the one hand on enantiomerically pure aziridines, and on the other on fatty acid derivatives with more than one aziridine function in the alkyl chain. In this paper we report our investigations into the synthesis of new fatty acid derivatives containing substituted and unsubstituted aziridine groups. The first examples of fat-derived enantiomerically pure aziridines are presented. We have also continued our previous investigations into bis- and tris(aziridines) derived from methyl linoleate



Scheme 1. Synthesis of methyl *cis*-9,10-epiminooctadecanoate (**3**), starting from methyl *cis*-9,10-epoxyoctadecanoate (**1**), via azido alcohol **2**[4]

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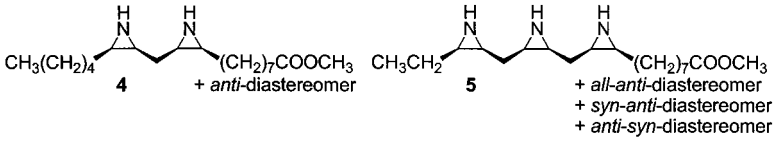


Figure 1. Bis(aziridine) **4**, based on methyl linoleate, and tris(aziridine) **5**, based on methyl linolate[1]

and methyl linolate[1] and are now able to report on their remarkable biological activities.

Lie Ken Jie[4] reported on the transformation of methyl *cis*-9,10-epoxyoctadecanoate (**1**) into the corresponding aziridine (**3**) (Scheme 1).

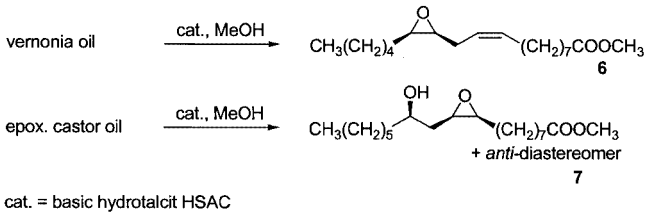
The first step is the nucleophilic ring-opening of the racemic *cis*-epoxide **1** with sodium azide. A regioisomeric mixture of the *threo*-azido alcohols **2** is formed, with inversion at the attacked carbon atom. The azido alcohols are treated with triphenylphosphane to afford (via five-membered 1,3,2λ^5-oxazaphospholidines[5]) the corresponding *cis*-aziridine methyl *cis*-9,10-epiminooctadecanoate (**3**) as a racemate. We applied this procedure to the synthesis of other interesting aziridine derivatives.

Results and Discussion

Synthesis of Azido Alcohols and Aziridines

We found that the use of polymer-bound triphenylphosphane was a definite improvement on the original Lie Ken Jie procedure with regard both to workup and to yields. The previous elaborate separation of the resulting triphenylphosphane oxide by crystallisation of the latter in pentane at 0 °C, followed by column chromatography of the remaining solution, was replaced by centrifugation of the reaction mixture to separate off the polymer-bound triphenylphosphane oxide and column chromatography of the remaining residue. In the case of the previously reported synthesis of the oligoaziridines[1] the yields could be increased from 54 to 90% for the bis(aziridine) **3** and from 23 to 70% for the tris(aziridine) **4** (Figure 1).[6]

For our investigations into the synthesis of enantiomerically pure fat-derived aziridines we chose methyl vernolate (**6**)[7] and epoxidised methyl ricinoleate (**7**)[8] as starting materials (Scheme 2). Both compounds were obtained by transesterification in methanol in the presence of a basic hydrotalcit catalyst (HSAC), by starting from vernonia oil and epoxidised castor oil, respectively.

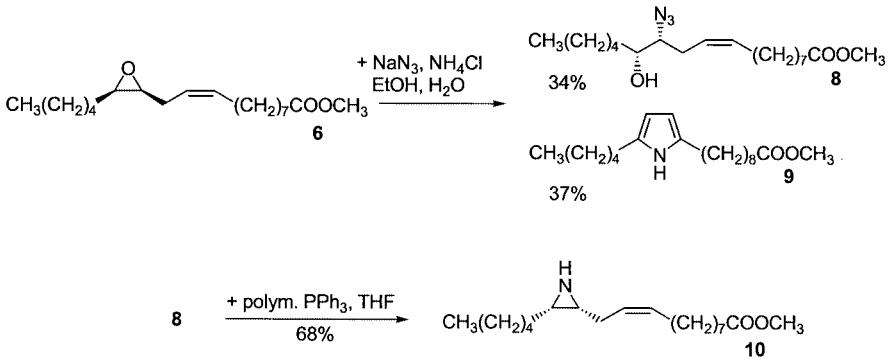


Scheme 2. Synthesis of methyl vernolate (**6**) and epoxidised methyl ricinoleate (**7**) by HSAC-catalysed transesterification of vernonia and castor oil, respectively

Workup was very convenient, by filtration of the catalyst and concentration of the filtrates to dryness, followed by column chromatography. From 5 g of vernonia oil, 2.7 g of enantiomerically pure methyl vernolate (**6**) was obtained. Analogously, 5 g of epoxidised castor oil yielded 3.2 g of methyl epoxyricinoleate (**7**) as a 1.2:1 diastereomeric mixture. Possible attack on the epoxy functionality and ring-opening was not observed. The advantage of this method over conventional transesterification with basic NaOMe systems[9] is the convenient workup. Extraction steps are unnecessary and the consumption of solvents and production of waste are minimised, so that the reported method is environmentally more benign.

Methyl vernolate (**6**) was treated with sodium azide and ammonium chloride in ethanol in the presence of water. After completion of the reaction (monitored by TLC) we obtained two products in nearly equal amounts that could easily be separated by column chromatography. Surprisingly, we were able to isolate the enantiomerically pure azido alcohol **8** with the azido group at C-12 as an orange oil in 34% yield. ^{13}C and ^{1}H NMR spectroscopic data showed that we were dealing with only one of the two possible regioisomeric azido alcohols. The HH-COSY spectrum shows cross-peaks for the methylene group at C-11 with the double bond at C-10 as well as with the azido-substituted CH group, which therefore has to be located at C-12. The stereoselective opening of the epoxide ring occurs with inversion at the attacked carbon atom.[10] As deduced from the (12*S*,13*R*) configuration of the starting methyl vernolate (**6**), the formed product has to be methyl (9*Z*,12*R*,13*R*)-12-azido-13-hydroxy-9-octadecenoate (**8**; Scheme 3). For the second compound, NMR and MS data suggest the pyrrole derivative **9** (Scheme 3). The H-substituted carbon atoms of the pyrrole nucleus appear in the ^{13}C NMR spectrum at $\delta = 104.44$ ppm, the respective protons showing a doublet at $\delta = 5.76$ ppm, while the alkyl-substituted carbon atoms show signals at $\delta = 131.09$ and 131.20 ppm. The substitution pattern on the pyrrole nucleus (with regard to the positions and the lengths of the alkyl groups) resulted unambiguously from the EI-MS spectra.

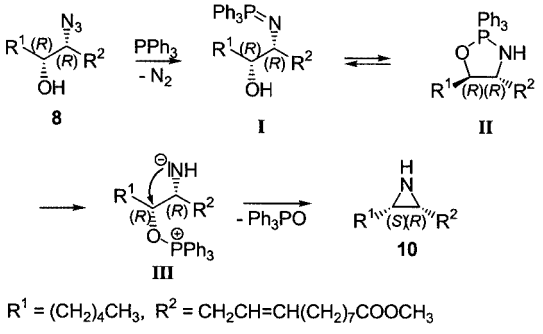
In our opinion, a possible explanation for the formation of the pyrrole is based on the assumption that the second regioisomeric azido alcohol − the one with the azido group at C-13 [methyl (9*Z*,12*S*,13*S*)-13-azido-12-hydroxy-9-octadecenoate], which should also be formed on such treatment of methyl vernolate **6** − acts as an intermediate. The presence of two carbon atoms between the azido group at C-13 and the olefinic centre at C-9/C-10 presumably facilitates the intramolecular 1,3-dipolar cycloaddition of the azido group to form a triazoline intermediate. Nitrogen elimina-



Scheme 3. Synthesis of enantiomerically pure methyl (9*Z*,12*R*,13*S*)-12,13-epimino-9-octadecenoate (**10**), starting from methyl vernolate (**6**), via methyl (9*Z*,12*R*,13*R*)-12-azido-13-hydroxy-9-octadecenoate (**8**); pyrrole **9** was obtained in equal amounts and separated by column chromatography

tion to form a 4-hydroxy-1-pyrroline and subsequent dehydration to give the 2*H*-pyrrole resulted in the isomerisation to the observed 1*H*-pyrrole **9**.[11]

The enantiomerically pure azido alcohol **8** was converted by treatment with polymer-bound triphenylphosphane into the enantiomerically pure aziridine methyl (9*Z*,12*R*,13*S*)-12,13-epimino-9-octadecenoate (**10**), which was obtained after column chromatography in 75% yield as a colourless oil (Scheme 3). The NMR spectra show signals characteristic of an unsaturated aziridine, the ring carbon signals of the aziridine appearing at δ = 34.67 and 34.82 ppm in the ^{13}C NMR spectrum, and the respective multiplet for 12-H and 13-H at δ = 1.94 ppm in the ^{1}H NMR spectrum. The double bond shows signals at δ = 126.46 and 131.06 ppm (^{13}C NMR) and a multiplet at δ = 5.40 ppm (^{1}H NMR) for 9-H and 10-H. The diastereotopic methylene protons at C-11 appear, analogously to those in methyl vernolate,[12] as multiplets at δ = 2.05 and 2.12 ppm. The assignment of the absolute configuration follows from the stereochemical course of the aziridine formation (Scheme 4).



Scheme 4. Stereochemical course of the formation of the enantiomerically pure aziridine **10** starting from the (*R*,*R*)-configured azido alcohol **8**

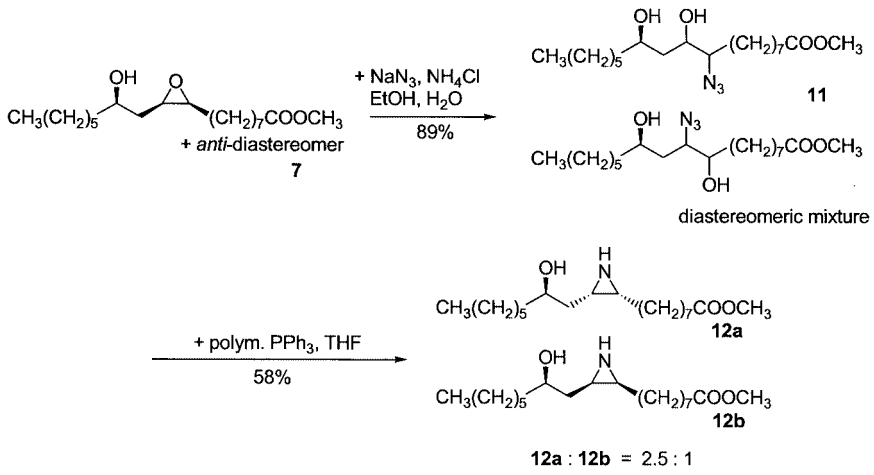
The enantiomerically pure (*R*,*R*)-configured azido alcohol **8** reacts with triphenylphosphane by nitrogen elimination with retention of configuration to afford the (2-hydroxyalkylimino)phosphorane **I** and subsequently the *trans*-1,3,2λ^5-oxazaphospholidine **II**.[13] The formation of the aziridine proceeds with splitting of the P−N bond, producing the dipolar intermediate **III**.

This cyclises intramolecularly with loss of triphenylphosphane oxide and inversion at C-13 to give the (*R*,*S*)-configured *cis*-aziridine **10**. The overall reaction pathway from the epoxide to the aziridine occurs with inversion at both stereogenic carbon atoms, so an enantiomerically pure epoxide gives the stereochemically inverted aziridine.[14] Since fatty acid derivatives with aziridine functions have so far only been obtained as racemates or diastereomeric mixtures, the reported unsaturated aziridine **10** represents the first enantiomerically pure aziridine based on fats and oils.

Treatment of epoxidised methyl ricinoleate (**7**), which was available as a 1.2:1 diastereomeric mixture, with sodium azide yielded 89% of the azido diol (**11**) as a white wax after column chromatography. Compound **11** was isolated as a mixture of two regioisomers, each formed as two diastereomers (Scheme 5). According to the ^{13}C NMR spectroscopic data, the characteristic signals for the N_3- and OH-substituted carbon atoms appear fourfold and eightfold, respectively, and the regio- and diastereomeric ratio is approximately 2.1:1.4:1.1:1 and so reflects the diastereomeric ratio of the epoxide **7**.

Treatment of the azido diol **11** with polymer-bound triphenylphosphane gave a 58% yield of the hydroxyaziridine **12** as an approximately 2.5:1 diastereomeric mixture, obtained after column chromatography (ethyl acetate/methanol, 3:1) as a white solid. In addition, 30% of the substrate could be recovered as a regio- and diastereomeric mixture in almost the same composition. No competing formation of an azetidine[4] with inclusion of the hydroxy function at C-12 and the azido group at C-10 was observed. The change in the diastereomeric ratio of the resulting aziridine **12** (2.5:1) compared to the epoxide **7** (1.2:1) could not be explained satisfactory. Further column chromatography with ethyl acetate/methanol (5:1) resulted in the separation of the two diastereomeric aziridines **12a** and **12b**.

The assignment of the absolute configuration and therefore the identification of the two diastereomers turned out to be difficult. Experiments to ascertain the capability for free rotation of the methylene group at C-11 by com-



Scheme 5. Synthesis of methyl (9*R*,10*S*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12a**) and methyl (9*S*,10*R*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12b**) from methyl epoxyricinoleate (**7**) via the regio- and diastereomeric azido diols **11**

plexation or formation of cyclic derivatives and structure determination by NOESY NMR measurements failed. Crystal growing experiments to elucidate the structure by X-ray diffraction finally succeeded for the major diastereomer on recrystallisation from diethyl ether/acetonitrile (20:1). From the fixed (*R*) configuration at C-12 it was possible to deduce the configurations of the stereogenic centres at C-9 and C-10. The major diastereomer was identified as methyl (9*R*,10*S*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12a**, Figure 2).

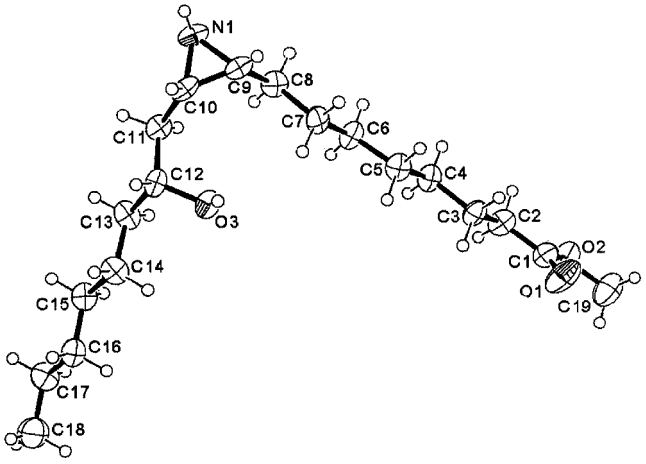
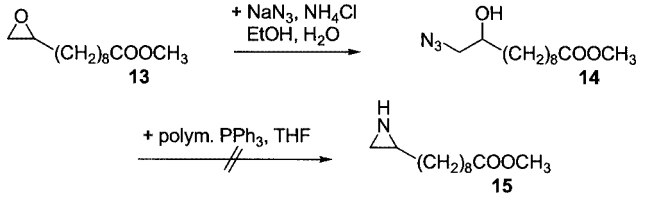


Figure 2. X-ray diffraction structure of the major diastereomer methyl (9*R*,10*S*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12a**)

The separated and completely characterised diastereomers **12a** and **12b** of the hydroxyaziridine represent two further chiral aziridines isolated enantiomerically pure for the first time.

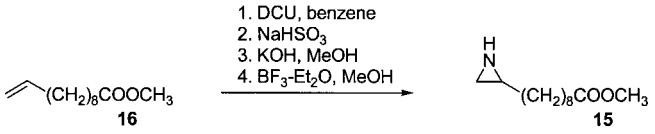
To increase the variety of fatty acid derivatives with aziridine functions we planned an approach to the corresponding terminal aziridine by starting from methyl 10,11-epoxyundecanoate (**13**).[15] Treatment of the epoxide **13** with sodium azide gave methyl 11-azido-10-hydroxyundecanoate (**14**) in 80% yield, as a pale yellow oil that solidified on standing at 4 °C (Scheme 6). NMR and MS data verify that the product was regioselectively formed exclusively as one of the two possible regioisomers. The *J*-modulated spectrum shows one signal for the CH_2 group at C-11 (δ = 56.94 ppm) and one for the CH group at C-10 (δ = 70.64 ppm). Previous experience shows that the signals of the CH groups appear at δ = 63−67 ppm if azido-substituted and at δ = 70−74 ppm if hydroxy-substituted.[16] The signal of an azido- or hydroxy-substituted CH_2 group should appear upshifted. In conclusion, the signal at δ = 56.94 ppm belongs to the azido-substituted CH_2 group at C-11, and this assumption is confirmed by the EI-MS data. Remarkably, the Staudinger reaction for the conversion of the terminal azido alcohol **14** failed, and treatment with polymer-bound triphenylphosphane gave no defined product (Scheme 6).



Scheme 6. Conversion of methyl 10,11-epoxyundecanoate (**13**) into methyl 11-azido-10-hydroxyundecanoate (**14**) and the failed transformation to the terminal aziridine **15**

We therefore had to go back to worthwhile methods starting from unsaturated compounds. However, the usually reliable addition of iodine isocyanate[17] to the double bond of methyl 10-undecenoate also did not give the desired result. Finally, the preparation of methyl 10,11-epiminoundecanoate (**15**) was achieved by addition of *N*,*N*-dichlorocarbamate (DCU)[18] to methyl 10-undecenoate (**16**, Scheme 7).

Treatment of **16** with DCU and subsequent reduction with sodium hydrogen sulfite solution gave the corresponding β-chlorocarbamate derivative, which was cyclised by treatment with methanolic KOH to afford the potassium salt of the aziridine. This was esterified with methanol in



Scheme 7. Synthesis of methyl 10,11-epiminoundecanoate (**15**) by the DCU method, starting from methyl 10-undecenoate (**16**)

the presence of boron trifluoride−diethyl ether to yield the terminal aziridine **15** as a yellow oil. The low yield of 12% is a result of the difficulty in isolating the previously formed potassium salt of **15**.

Preparation of Amino Alcohols by Reduction of the Corresponding Azido Alcohols

β-Amino alcohols are important chemotherapeutic agents and are also of synthetic interest, serving as precursors for the synthesis of heterocycles, especially chiral auxiliaries, and as ligands. The previously described azido alcohols **8**, **11** and **14**, as well as the diazido diols and triazido triols reported earlier,[1] are conveniently accessible from epoxides and could easily be reduced to the corresponding amino alcohols **17**−**21** (Figure 3).

Catalytic hydrogenation proved to be the method of choice. A solution of the appropriate azido alcohol was shaken in a hydrogenation apparatus in the presence of palladium on charcoal under hydrogen at 2.5 bar and 50 °C for 20 h. After filtration of the catalyst and concentration of the filtrate to dryness, we obtained the amino alcohols in high purity and in 84−100% yields. It should be pointed out that compound **17** is the first known enantiomerically pure fatty amino alcohol. The accompanying hydrogenation of the double bond of the intermediate unsaturated azido alcohol **8** was successful.

Since only methyl 9(10)-amino-10(9)-hydroxyoctadecanoate[19] is known in the literature, the new compounds **17**−**21** represent an important enlargement of the range of available fatty amino alcohols. In particular, the enantiomerically pure amino alcohol **17** and the multifunctional amino alcohols **20** and **21** appear to be very interesting with regard to their biological activity and their synthetic potential for the preparation of heterocycles.

Synthesis of *N*-Substituted Aziridine Derivatives

To examine the reactivity of aziridines we prepared various differently functionalised compounds from methyl *cis*-9,10-epiminooctadecanoate (**3**, Scheme 8) corresponding to the different conversions of ethylenimine investigated by Bestian.[20]

Treatment of **3** with phenyl isocyanate afforded the urea derivative **22** as a yellow oil in 50% yield. The analogous conversion with phenyl isothiocyanate furnished the corresponding thiourea derivative **23**, which was obtained as a white wax in 55% yield. Acylation of the aziridine **3** with acetyl chloride in the presence of triethylamine gave a 48% yield of the amide **24** as a yellow oil. The urethanes **25**−**27** were obtained by treatment of the aziridine **3** with the respective chloroformates (ethyl chloroformate and isopropyl chloroformate, respectively) in diethyl ether in the presence of triethylamine, giving the ethyl carboxylate **25** as a pale yellow oil in 73% yield and the isopropyl carboxylate **26** as a pale yellow oil in 58% yield. In the case of benzyl chloroformate we observed a significant solvent effect. Treatment of **3** in the presence of triethylamine carried out in benzene gave the urethane **27** as a colourless oil in 39% yield but in diethyl ether we obtained the *N*-benzylated product **28** as a yellow oil in 36% yield. The addition of the aziridine **3** to the double bond of acrylonitrile furnished the propionitrile derivative **29** in 51% yield as a pale yellow oil. In most cases the conversion of aziridine was not quantitative, resulting in the recovery of unchanged aziridine in the chromatographic purification of the product. Even increased reaction times and temperatures had no impact on the conversion.

The characteristic NMR shifts of the aziridine CH groups for the new *N*-substituted aziridine derivatives are shown in Table 1.

In general, the ring signals of the *N*-substituted derivatives **22**−**29** are shifted downfield towards those of the unsubstituted aziridine **3**. In the ^{13}C NMR spectra the downfield shift is about 6.5−9.6 ppm towards the signals of C-9 and C-10 of aziridine **3**. The ^{1}H NMR spectra show some differences: for the alkyl- and aryl-substituted compounds **28** and **29** the 9-H/10-H multiplet is shifted upfield to $\delta \approx$ 1.4 ppm and is partly covered by the multiplets of the

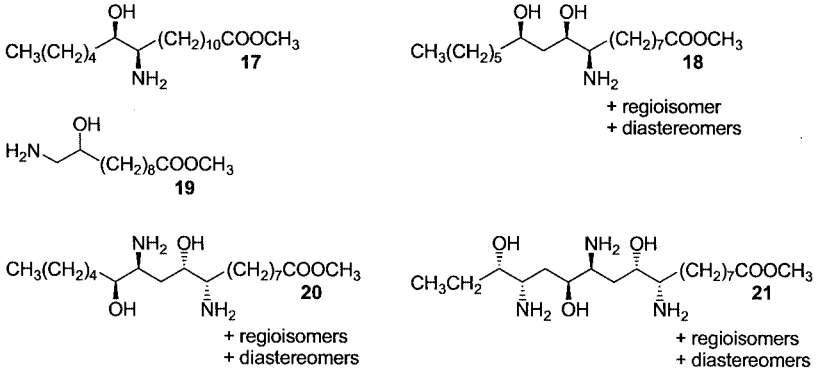
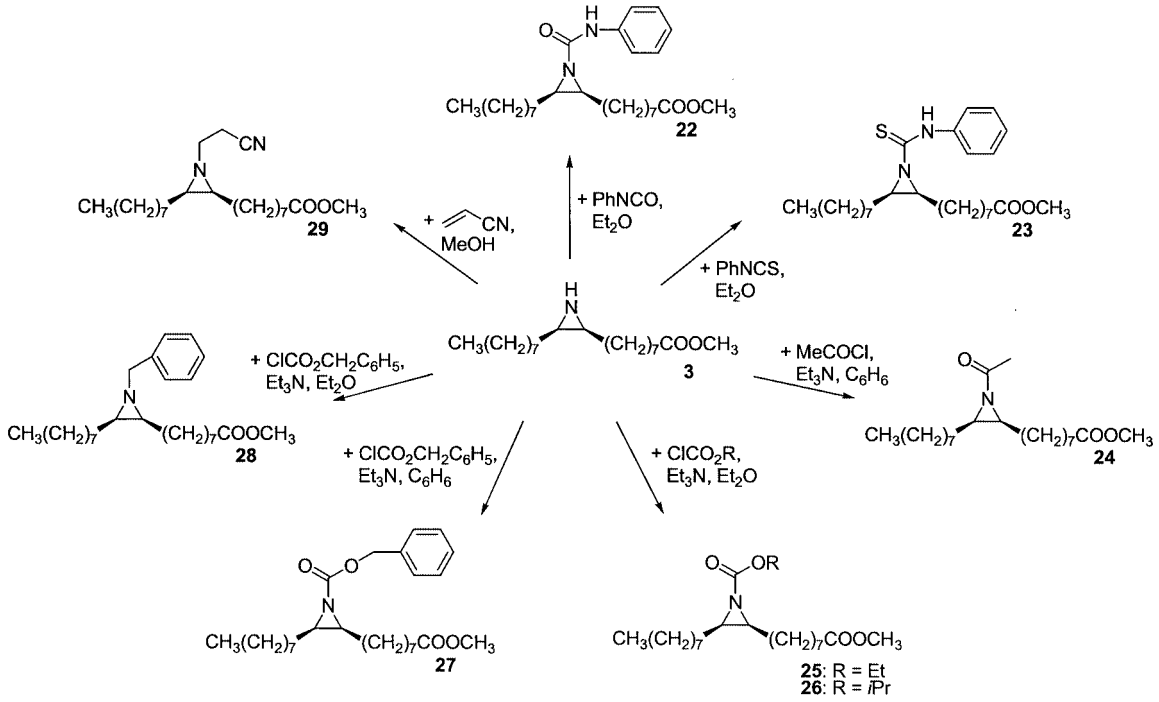
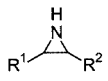
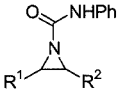
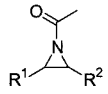
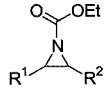
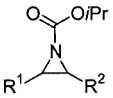
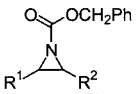
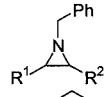
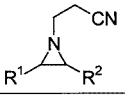


Figure 3. New fatty amino alcohols **17**−**21** prepared by reduction of the corresponding azido alcohols



Scheme 8. Synthesis of *N*-substituted aziridine derivatives **22**−**29** from methyl *cis*-9,10-epiminooctadecanoate (**3**); for purposes of clarity the racemic compounds **3** and **22**−**29** are each shown as only one enantiomer

Table 1. Characteristic NMR spectroscopic data for the new *N*-substituted aziridine derivatives **22**−**29**, based on methyl *cis*-9,10-epiminooctadecanoate (**3**)[a]

	Compound	^{1}H-NMR shifts of H-9, H-10 [ppm]	^{13}C-NMR shifts of C-9, C-10 [ppm]
3		1.90	34.90, 34.95
22		2.41 2.54	43.56, 43.77 45.45, 45.60
24		2.22 2.40	41.47, 41.53 43.41, 43.52
25		2.40	42.47, 42.54
26		2.38	42.49, 42.57
27		2.43	42.64, 42.70
28		1.44	44.32, 44.42
29		~ 1.42	44.59, 44.63

[a] NMR measurements for the thiourea derivative **23** were impossible, due to insufficient solubility in various deuterated solvents.

methylene groups. For the derivatives **22**−**27**, with electron-withdrawing substituents on the nitrogen atom, a downshift of about 0.3−0.6 ppm in comparison to the multiplet of aziridine **3** is again observed.

For the compounds **22** and **24** we observe two groups of two signals for C-9 and C-10 in the ^{13}C NMR spectra instead of one group of two signals as in compound **3**. The ^{1}H NMR spectra show two multiplets each for 9-H and 10-H instead of just one multiplet as in **3**. The barriers to inversion in *N*-acylaziridines are quite low, whereas the rotation barriers are higher. The rotation around the N−CO bond is significantly hindered because of the conjugative interaction between the aziridine N-atom and the CO group.[21] This, in combination with our observations, led us to the conclusion that the urea derivative **22** and the amide **24** are formed as mixtures of rotamers. The ratio of rotamers was determined from the ^{1}H NMR spectroscopic data and is 2.2:1 for compound **22** and 2.1:1 for compound **24**. No explanation of this interesting phenomenon could be found.

Biological Activities of the Bis- and Tris(aziridines)

The bis(aziridine) **3** and the tris(aziridine) **4** show cytotoxic and antimicrobial activity, as well as remarkable anti-tumour promoting activity. The anti-tumour promoting activities were determined by means of a short-term in-vitro assay of Epstein−Barr virus (EBV) activation in Raji cells induced by TPA (12-*O*-tetradecanolphorbol 13-acetate).[22] The two most important results are the strong inhibitory effect on activation and the good viability of the cells. Furthermore a good neuroprotective effect is observed, determined as follows: the anticonvulsant [+]-MK-801 binds to the activated state of the NMDA (*N*-methyl-D-aspartate) re-

ceptor in rat brain and prevents excessive activation. If the tested agents similarly bind to NMDA receptors the amount of MK-801 remaining bound to the receptors is determined.

Biological Activities of the Hydroxyaziridines 12a and 12b

The hydroxyaziridines **12a** and **12b** were tested for cytostatic/cytotoxic activity with regard to different tumour cell lines. Interestingly the minor diastereomer **12b** in all cases showed stronger activity than the major diastereomer **12a**. Similar results were obtained for antimicrobial activity tested on different microorganisms.

Conclusion

In summary, the easily performed, two-step synthesis of the enantiomerically pure aziridines methyl (9*Z*,12*R*,13*S*)-12,13-epimino-9-octadecenoate (**10**), methyl (9*S*,10*R*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12a**) and methyl (9*R*,10*S*,12*R*)-9,10-epimino-12-hydroxyoctadecanoate (**12b**) is reported. We found that the use of polymer-bound triphenylphosphane was a definite improvement with regard to workup and yields. *N*-Substituted aziridine derivatives **22**−**29** could be obtained in moderate to good yields by treatment of methyl *cis*-9,10-epiminooctadecanoate (**3**) with alkylating and acylating agents. Interesting β-amino alcohols **17**−**21** have been made accessible by reduction of the azido alcohols occurring on nucleophilic ring-opening of epoxides with sodium azide. Furthermore, the new fat-derived pyrrole methyl 9-(5-pentyl-1*H*-pyrrol-2-yl)nonanoate (**9**) was obtained. The remarkable biological activities of the bis- and tris(aziridines) **3** and **4** derived from methyl linoleate and methyl linolate verified our idea of synthesising fat-derived aziridines to obtain access to pharmacological interesting compounds based on renewable raw materials.

Experimental Section

General: All chemicals and solvents were purchased from standard chemical suppliers. Epoxidised castor oil was provided by HOBUM. Solvents: tetrahydrofuran and diethyl ether were heated at reflux under an inert gas in the presence of sodium and benzophenone and distilled. Benzene was heated at reflux and distilled under an inert gas from sodium. Methanol was heated at reflux in the presence of magnesium for 2 h and finally distilled. Petroleum ether (boiling range 60−80 °C) and ethyl acetate were distilled prior to use. Triethylamine was heated at reflux in the presence of calcium hydride for 2 h and finally distilled. For all liquid chromatographic separations silica gel 60 (40−63 μm) from Merck was used. The hydrotalcite HSAC (calcinated MgAl-hydrotalcite) was provided by Südchemie.

Analytical Equipment: NMR: Bruker DRX 500, ^{1}H NMR (500.1 MHz), ^{13}C NMR (125.8 MHz), $CDCl_3$ as solvent, TMS as internal standard. MS: Finnigan MAT 95. Elemental analyses: Mikroanalytisches Labor Beller, 37004 Göttingen. X-ray diffraction analysis: STOE-IPDS diffractometer. Polarimetric measurements: Perkin−Elmer Polarimeter 343.

Methyl (12*S*,13*R*,9*Z*)-12,13-Epoxy-9-octadecenoate (Methyl Vernolate) (6): A mixture of vernonia oil (5 g), hydrotalcit HSAC (500 mg) and methanol (10 mL) was heated under reflux for 4 h. After the mixture had cooled to room temperature, the catalyst was filtered off and purged with methanol. The collected filtrates were concentrated in vacuo, yielding a pale yellow oil (4.65 g). Purification by column chromatography with petroleum ether/ethyl acetate (4:1) (R_f = 0.64) afforded the product **6** (2.67 g, 8.6 mmol) as a colourless oil. $[\alpha]_D^{20}$ = 3 (*c* = 2.85, $CHCl_3$). ^{1}H NMR: δ = 0.82 (t, 3 H, CH_3), 1.18−1.40 (m, 14 H, CH_2), 1.44 (m, 2 H, 14-H), 1.53 (m, 2 H, 3-H), 1.96 (q, 2 H, 8-H), 2.25 (t, 2 H, 2-H), 2.10, 2.27 (m, 1 H, 11-H), 2.82 (m, 2 H, 12-H, 13-H), 3.57 (s, 3 H, OCH_3), 5.33 (m, 1 H, 10-H), 5.43 (m, 1 H, 9-H) ppm. ^{13}C NMR: δ = 13.77 (CH_3), 22.39, 24.73, 26.06, 26.11, 27.20, 27.58, 28.87, 28.90, 28.94, 29.29, 31.55, 33.84 (CH_2), 51.14 (OCH_3), 56.26, 56.90 (C-12, C-13), 123.81 (C-10), 132.28 (C-9), 173.90 ($COOCH_3$) ppm.

Methyl (12*R*)-*cis*-9,10-Epoxy-12-hydroxyoctadecanoate (7): A mixture of epoxidised castor oil (5 g), hydrotalcit HSAC (500 mg) and methanol (10 mL) was heated under reflux for 4 h. After the mixture had cooled to room temperature, the catalyst was filtered off and purged with methanol. The collected filtrates were concentrated in vacuo, yielding a yellow oil (4.75 g). Purification by column chromatography with petroleum ether/ethyl acetate (1:1) (R_f = 0.44) afforded the product **7** (3.10 g, 9.4 mmol) as a colourless oil. ^{1}H NMR (1.2:1 diastereomeric mixture): δ = 0.76 (t, 3 H, CH_3), 1.15−1.45 (m, 22 H, CH_2), 1.50 (m, 2 H, 3-H), 2.18 (t, 2 H, 2-H), 2.55, 2.64 (br. s, 1 H, OH), 2.80 (m, 1 H, 10-H), 3.01 (m, 1 H, 9-H), 3.54 (s, 3 H, OCH_3), 3.70, 3.74 (m, 1 H, 12-H) ppm. ^{13}C NMR: δ = 13.79 (CH_3), 20.69, 22.35, 24.62, 25.30, 25.36, 26.17, 26.20, 27.65, 27.77, 28.75, 28.89, 29.01, 29.06, 31.58, 33.75 (CH_2), 34.68, 35.09 (C-11), 37.19, 37.59 (C-13), 51.12 (OCH_3), 54.29, 54.94 (C-10), 56.08, 56.89 (C-9), 69.54, 70.32 (C-12), 173.93 ($COOCH_3$) ppm.

Methyl (9*Z*,12*R*,13*R*)-12-Azido-13-hydroxy-9-octadecenoate (8): A mixture of methyl vernolate (**6**, 5.59 g 18 mmol), sodium azide (4.36 g, 67 mmol), ammonium chloride (3.58 g, 67 mmol), water (25 mL) and ethanol (60 mL) was heated at reflux for 49 h. After the addition of water (100 mL), the reaction mixture was extracted several times with dichloromethane. The combined organic layers were washed with water and dried with anhydrous sodium sulfate. After evaporation of the solvent in vacuo, the resulting brown and oily residue was further purified by column chromatography with petroleum ether/diethyl ether (2:1). The enantiomerically pure product (R_f = 0.24) was obtained as an orange oil (2.20 g, 6.2 mmol, 34%). $[\alpha]_D^{20}$ = −32 (*c* = 2.85, $CHCl_3$). ^{1}H NMR: δ = 0.90 (t, 3 H, CH_3), 1.22−1.57 (m, 16 H, CH_2), 1.62 (m, 2 H, 3-H), 2.02 (br. s, 1 H, OH), 2.07 (q, 2 H, 8-H), 2.30 (t, 2 H, 2-H), 2.43 (t, 2 H, 11-H), 3.25 (m, 1 H, CH−N_3), 3.55 (m, 1 H, CH−OH), 3.66 (s, 3 H, OCH_3), 5.41 (m, 1 H, 10-H), 5.54 (m, 1 H, 9-H) ppm. ^{13}C NMR: δ = 13.90 (CH_3), 22.48, 24.81, 25.23, 27.27, 28.84, 28.95, 28.97, 29.00, 29.28, 31.67, 33.98, 34.19 (CH_2), 51.33 (OCH_3), 66.64 (CHN_3), 72.86 (CH−OH), 124.18 (C-10), 133.50 (C-9), 174.24 ($COOCH_3$) ppm. $C_{19}H_{35}N_3O_3$ (353.3): calcd. C 64.56, H 9.98, N 11.89; found C 64.20, H 10.08, N 11.39.

Methyl 9-(5-Pentyl-1*H*-pyrrol-2-yl)nonanoate (9): Column chromatographic separation of crude **8** yielded methyl 9-(5-pentyl-1*H*-pyrrol-2-yl)nonanoate (**9**, R_f = 0.38) as an orange solid (2.02 g, 6.6 mmol, 37%); m.p. 52−55 °C. ^{1}H NMR: δ = 0.89 (t, 3 H, CH_3), 1.27−1.38 (m, 12 H, CH_2), 1.60 (m, 6 H, 3-H, 8-H, 15-H), 2.30 (t, 2 H, 2-H), 2.53 (t, 4 H, 9-H, 14-H), 3.66 (s, 3 H, OCH_3), 5.76 (d, 2 H, 11-H, 12-H), 7.64 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.96 (CH_3), 22.44, 24.86, 27.74, 29.04, 29.08, 29.16, 29.26, 29.36, 29.62,

31.57, 34.02 (CH_2), 51.35 (OCH_3), 104.44 (C-11, C-12), 131.09, 131.20 (C-10, C-13), 174.25 ($COOCH_3$) ppm. MS/EI (70 eV): *m*/*z* (%) = 307.3 (84) $[M]^+$, 250.2 (96) $[M - (CH_2)_3CH_3]^+$, 150.2 (100) $[M - (CH_2)_7CH_3]^+$. $C_{19}H_{33}NO_2$ (307.3): calcd. C 74.22, H 10.82, N 4.56; found C 74.10, H 10.75, N 4.51.

Methyl (9*Z*,12*R*,13*S*)-12,13-Epimino-9-octadecenoate (10): A mixture of methyl (9*Z*,12*R*,13*R*)-12-azido-13-hydroxy-9-octadecenoate (**8**, 250 mg, 0.71 mmol) and polymer-bound triphenylphosphane (290 mg, 0.86 mmol) in dry THF (50 mL) was heated at reflux under argon for 31 h. After the mixture had cooled to room temperature, the polymer-bound triphenylphosphane oxide was separated by centrifugation. The upper solution was taken off and the resin was washed with absolute methanol and centrifuged again. This procedure was repeated twice. The combined solutions were filtered through Celite and the solvents were evaporated in vacuo, yielding an orange oil (240 mg). Column chromatography with petroleum ether/ethyl acetate/methanol (7:3:1) yielded 154 mg (0.53 mmol, 75%) of the enantiomerically pure product (R_f = 0.40) as a colourless oil. $[\alpha]_D^{20}$ = 2 (*c* = 2.85, $CHCl_3$). ^{1}H NMR: δ = 0.84 (t, 3 H, CH_3), 1.21−1.46 (m, 16 H, CH_2), 1.56 (m, 2 H, 3-H), 1.94 (m, 2 H, 12-H, 13-H), 1.98 (m, 2 H, 8-H), 2.05, 2.12 (m, 2 H, 11-H), 2.25 (t, 2 H, 2-H), 3.61 (s, 3 H, OCH_3), 5.40 (m, 2 H, 9-H, 10-H) ppm. ^{13}C NMR: δ = 13.93 (CH_3), 22.55, 24.82, 26.86, 27.27, 27.63, 28.72, 28.97, 29.00, 29.03, 29.45, 31.75, 33.97 (CH_2), 34.67, 34.82 (C-9, C-10), 51.29 (OCH_3), 126.46, 131.06 (C-12, C-13), 174.14 ($COOCH_3$) ppm. $C_{19}H_{35}NO_2$ (309.5): calcd. C 73.74, H 11.40, N 4.53; found C 73.46, H 11.10, N 4.88.

Methyl 9(10)-Azido-10(9),12-dihydroxyoctadecanoate (11): A mixture of methyl epoxyricinoleate (**7**, 4.53 g, 13.8 mmol), sodium azide (3.45 g, 53 mmol), ammonium chloride (2.83 g, 53 mmol), water (20 mL) and ethanol (60 mL) was heated at reflux for 49 h. After the addition of water, 50 mL of the reaction mixture was extracted several times with dichloromethane. The combined organic layers were washed with water and dried with anhydrous sodium sulfate. After evaporation of the solvent in vacuo, the resulting yellow oil was further purified by column chromatography with ethyl acetate/petroleum ether (2:1). The product (R_f = 0.75) was a white wax as a mixture of four compounds (two regioisomers and their two diastereomers, 4.58 g, 12.3 mmol, 89%). $[\alpha]_D^{20}$ = −10 (*c* = 2.85, $CHCl_3$). ^{1}H NMR: δ = 0.89 (t, 3 H, CH_3), 1.20−1.66 (m, 33 H, CH_2), 2.30, 2.31 (t, 2 H, 2-H), 3.13, 3.19, 3.52, 3.57 (m, 1 H, CHN_3), 3.67 (s, 3 H, OCH_3), 3.77−3.96 (m, 2 H, CHOH) ppm. ^{13}C NMR (regio- and diastereomeric ratio 1:1.1:1.4:2.1): δ = 13.98 (CH_3), 22.51, 24.78, 25.20, 25.47, 25.50, 25.60, 25.68, 26.01, 26.17, 28.90, 29.00, 29.13, 29.18, 29.20, 30.09, 30.60, 31.72, 33.94, 33.98, 34.28 (CH_2), 37.45, 37.66, 38.06, 38.24, 38.28, 38.35, 39.50, 39.95 (C-13, C-11), 51.41 (OCH_3), 63.88, 64.04, 66.90, 67.43 ($CH-N_3$), 68.80, 68.86, 68.98, 70.74, 72.60, 73.17, 74.14, 74.40 (CHOH), 174.30, 174.34 ($COOCH_3$) ppm. $C_{19}H_{37}N_3O_4$ (371.5): calcd. C 61.43, H 10.04, N 11.31; found C 61.06, H 9.88, N 11.00.

Methyl (12*R*)-*cis*-9,10-Epimino-12-hydroxyoctadecanoate (12): A mixture of methyl (12*R*)-9(10)-azido-10(9),12-dihydroxyoctadecanoate (**11**, 400 mg, 1.1 mmol) and polymer-bound triphenylphosphane (440 mg, 1.3 mmol) in dry THF (20 mL) was heated at reflux under argon for 31 h. After the mixture had cooled to room temperature, the polymer-bound triphenylphosphane oxide was separated by centrifugation. The upper solution was taken off and the resin was washed with absolute methanol and centrifuged again. This procedure was repeated twice. The combined solutions were filtered through Celite and the solvents were evaporated in vacuo, yielding an orange oil (450 mg). Column chromatography with ethyl acetate/methanol (3:1) yielded the product (210 mg, 0.55 mmol, 58%) as a 2.5:1 diastereomeric mixture (R_f = 0.47) and a white solid. $[\alpha]_D^{20}$ = −12 (*c* = 2.90, $CHCl_3$). $C_{19}H_{37}NO_3$ (327.5): calcd. C 69.68, H 11.39, N 4.28; found C 69.33, H 11.40, N 4.22. Further column chromatography with ethyl acetate/methanol (5:1) allowed the separation of the diastereomers.

Major Diastereomer: Methyl (9*R*,10*S*,12*R*)-9,10-Epimino-12-hydroxyoctadecanoate (12a): (R_f = 0.36). $[\alpha]_D^{20}$ = −16 (*c* = 2.99, $CHCl_3$); m.p. 84−86 °C. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.22−1.55 (m, 20 H, CH_2), 1.62 (m, 2 H, 3-H), 1.68 (m, 2 H, 11-H), 2.02 (m, 1 H, 9-H), 2.25 (m, 1 H, 10-H), 2.30 (t, 2 H, 2-H), 3.66 (s, 3 H, OCH_3), 3.79 (m, 1 H, 12-H) ppm. ^{13}C NMR: δ = 14.00 (CH_3), 22.54, 24.83, 25.76, 27.71, 28.74, 28.99, 29.14, 29.25, 29.30 (CH_2), 31.35 (C-10), 31.77, 34.00 (CH_2), 34.46 (C-9), 34.52 (C-11), 37.45 (C-13), 51.35 (OCH_3), 70.94 (C-12), 174.20 ($COOCH_3$) ppm. The compound was crystallised from diethyl ether/acetonitrile (20:1) for X-ray diffraction analysis.

Minor Diastereomer: Methyl (9*S*,10*R*,12*R*)-9,10-Epimino-12-hydroxyoctadecanoate (12b): (R_f = 0.29). $[\alpha]_D^{20}$ = −3 (*c* = 0.96, $CHCl_3$); m.p. 37−38 °C. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.21−1.55 (m, 20 H, CH_2), 1.62 (m, 2 H, 3-H), 1.78 (m, 2 H, 11-H), 2.09 (m, 1 H, 9-H), 2.30 (t, 2 H, 2-H), 2.34 (m, 1 H, 10-H), 3.67 (s, 3 H, OCH_3), 3.87 (m, 1 H, 12-H) ppm. ^{13}C NMR: δ = 14.07 (CH_3), 22.61, 24.89, 25.49, 27.51, 28.16, 29.04, 29.18, 29.22, 29.36, 31.84 (CH_2), 33.27 (C-10), 33.89 (C-9), 34.06 (C-2), 34.30 (C-11), 37.82 (C-13), 51.43 (OCH_3), 71.95 (C-12), 174.26 ($COOCH_3$) ppm.

Methyl 11-Azido-10-hydroxyundecanoate (14): A mixture of methyl 10,11-epoxyundecanoate (**13**, 2.14 g, 10.0 mmol), sodium azide (2.44 g, 37.5 mmol), ammonium chloride (2.01 g, 37.5 mmol), water (10 mL) and ethanol (50 mL) was heated at reflux for 19 h. After the addition of 20 mL of water, the reaction mixture was extracted several times with dichloromethane. The combined organic layers were washed with water and dried with anhydrous sodium sulfate. After evaporation of the solvent in vacuo, the product (2.05 g, 8.0 mmol, 80%) was obtained as a yellow oil that solidified at 4 °C. ^{1}H NMR: δ = 1.20−1.30 (m, 12 H, CH_2), 1.54 (m, 2 H, 3-H), 2.23 (t, 2 H, 2-H), 2.60 (m, 1 H, OH), 3.16, 3.27 (dd, 1 H, 11-H) 3.59 (s, 3 H, OCH_3), 3.68 (m, 1 H, 10-H) ppm. ^{13}C NMR: δ = 24.75, 25.25, 28.91, 28.96, 29.16, 29.27, 33.92, 34.18 (CH_2), 51.33 (OCH_3), 56.94 (C-11), 70.65 (C-10), 174.29 ($COOCH_3$) ppm. MS/EI (70 eV): *m*/*z* (%) = 201.1 (22) $[M - CH_2N_3]^+$, 169.1 (100) $[M - CH_2N_3 - CH_3OH]^+$. $C_{12}H_{23}N_3O_3$ (257.3): calcd. C 56.01, H 9.01, N 16.33; found C 55.83, H 8.79, N 16.03.

Methyl 10,11-Epiminoundecanoate (15): A solution of *N*,*N*-dichlorourethane (2.9 mL 22 mmol) in dry benzene (10 mL) was purged with argon. Methyl 10-undecenoate (**16**, 4.04 g, 20 mmol) was added under argon, the reaction temperature not being allowed to rise above 30 °C. The reaction mixture was heated at reflux for a further 30 min until TLC showed complete reaction of the starting compound. An aqueous $NaHCO_3$ solution (20%) was added dropwise at 5−10 °C. The organic layer was separated off and the aqueous layer was extracted several times with diethyl ether. The combined organic layers were washed with water, dried with sodium sulfate and concentrated to dryness. The remaining yellow oil was dissolved in absolute methanol (20 mL), mixed with KOH (7.6 g) in absolute methanol (90 mL) and heated at reflux for 18 h. The hot reaction mixture was filtered and the filtrate was concentrated to dryness. The residue (12.95 g) was dissolved in water and extracted several times with a 2:1 mixture of chloroform/ethanol. The combined organic layers were dried with sodium sulfate and the solvent was removed in vacuo, giving a glasslike yellow solid (6.06 g). After the residue had been dissolved in absolute methanol

(100 mL), boron trifluoride−diethyl ether (16.3 mL) was added and the mixture was heated under reflux for 30 min. An aqueous NaOH solution (5%, 270 mL) was added, and the mixture was extracted repeatedly with diethyl ether. Washing of the ethereal extracts with water, drying with sodium sulfate and subsequent removal of the solvent in vacuo yielded an orange oil (2.42 g). Column chromatography with petroleum ether/ethyl acetate/methanol (7:3:1) furnished the product (490 mg, 2.3 mmol, 12%, R_f = 0.13) as a yellow oil. ^{1}H NMR: δ = 1.25−1.48 (m, 12 H, CH_2), 1.62 (m, 2 H, 3-H), 1.75 (d, $^3J_{H,H}$ = 6.03 Hz, 2 H, 11-H), 1.93 (m, $^3J_{H,H}$ = 6.03 Hz, 1 H, 10-H), 2.30 (t, 2 H, 2-H), 3.67 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 24.88, 25.05, 27.48, 29.05, 29.12, 29.34 (CH_2), 30.32 (C-11), 34.04 (C-2), 34.39 (C-10), 51.37 (OCH_3), 174.25 ($COOCH_3$) ppm. $C_{12}H_{23}NO_2$ (213.1): calcd. C 67.57, H 10.87, N 6.57; found C 67.38, H 10.75, N 6.51.

General Procedure for the Reduction of Azido Alcohols: In a typical procedure, a solution of the azido alcohol (3 mmol) and a small amount of palladium (10%) on charcoal in methanol (20 mL) was placed in a hydrogenation flask and hydrogenated at 50 °C under hydrogen (2.5 bar) by shaking for 20 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.

Methyl (12*R*,13*R*)-12-Amino-13-hydroxyoctadecanoate (17): Methyl (9*Z*,12*R*,13*R*)-12-azido-13-hydroxy-9-octadecenoate (**8**, 310 mg, 0.88 mmol) gave the enantiomerically pure product (290 mg, 0.88 mmol, 99%) as a white wax. $[\alpha]_D^{20}$ = 17 (*c* = 2.85, $CHCl_3$). ^{1}H NMR: δ = 0.89 (t, 3 H, CH_3), 1.20−1.57 (m, 24 H, CH_2), 1.61 (m, 2 H, 3-H), 2.18 (m, 1 H, OH), 2.30 (m, 2 H, 2-H), 2.55 (m, 1 H, 12-H), 3.26 (m, 1 H, 13-H), 3.66 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 13.98 (CH_3), 22.58, 24.86, 25.51, 26.19, 29.05, 29.15, 29.32, 29.43, 29.47, 29.60, 31.93, 34.01, 34.30 (CH_2), 51.32 (OCH_3), 55.46 (C-12), 73.67 (C-13), 174.20 ($COOCH_3$) ppm. $C_{19}H_{39}NO_3$ (329.5): calcd. C 69.25, H 11.93, N 4.25; found C 69.40, H 11.79, N 4.04.

Methyl (12*R*)-9(10)-Amino-10(9),12-dihydroxyoctadecanoate (18): Methyl (12*R*)-9(10)-azido-10(9),12-dihydroxyoctadecanoate (**11**, 300 mg, 0.81 mmol) gave the product (270 mg, 0.78 mmol, 96%) as a mixture of four compounds (two regioisomers and their two diastereomers) as a white wax. ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.66 (m, 24 H, CH_2), 2.30 (t, 2 H, 2-H), 2.53, 2.62, 2.78 (m, 3 H, $CHNH_2$), 2.93 (m, 4 H, OH), 3.37, 3.57 (m, 2 H, CHOH), 3.66 (s, 3 H, OCH_3), 3.81, 3.85 (m, 2 H, CHOH) ppm. ^{13}C NMR: δ = 13.99 (CH_3), 22.53, 24.78, 25.36, 25.39, 25.58, 25.69, 25.76, 25.78, 26.03, 26.13, 28.96, 29.09, 29.30, 29.36, 31.77, 33.69, 33.76, 33.96, 34.36 (CH_2), 37.56, 37.80, 37.95, 38.24 (C-13), 39.21, 39.53, 39.87, 40.53 (C-11), 51.36 (OCH_3), 52.88, 55.43, 55.91, 56.26 ($CHNH_2$), 68.75, 69.13, 71.61, 72.34, 74.08, 74.61, 74.80 (CHOH), 174.19, 174.23 ($COOCH_3$) ppm. $C_{19}H_{39}NO_4$ (345.5): calcd. C 66.05, H 11.38, N 4.05; found C 66.02, H 11.26, N 4.11.

Methyl 11-Amino-10-hydroxyundecanoate (19): Methyl 11-azido-10-hydroxyundecanoate (**14**, 130 mg, 0.50 mmol) gave the product (100 mg, 0.43 mmol, 86%) as a white solid; m.p. 100−103 °C. ^{1}H NMR: δ = 1.20−1.50 (m, 12 H, CH_2), 1.61 (m, 2 H, 3-H), 2.23 (t, 2 H, 2-H), 2.53 (m, 3 H, 11-H, OH), 3.52 (m, 1 H, 10-H), 3.66 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 24.81, 25.56, 28.99, 29.06, 29.24, 29.52, 33.97, 34.74 (CH_2), 47.21 (C-11), 51.31 (OCH_3), 71.84 (C-10), 174.20 ($COOCH_3$) ppm. $C_{12}H_{25}NO_3$ (231.3): calcd. C 62.30, H 10.89, N 6.05; found C 62.52, H 10.90, N 5.92.

Methyl 9(10),12(13)-Diamino-10(9),13(12)-dihydroxyoctadecanoate (20): Methyl 9(10),12(13)-diazido-10(9),13(12)-dihydroxyoctadecanoate[1] (700 mg, 1.7 mmol) gave the product (620 mg, 1.7 mmol, 100%) as a regio- and diastereomeric mixture, as a colourless oil that solidified to a white wax on standing at 4 °C. ^{1}H NMR: δ = 0.89 (t, 3 H, CH_3), 1.20−1.65 (m, 20 H, CH_2), 2.30 (m, 2 H, 2-H), 2.58−2.82 (m, 6 H, $CHNH_2$, OH), 3.40−3.65 (m, 3 H, CHOH), 3.67 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 13.97 (CH_3), 22.56, 24.83, 25.49, 25.59, 25.73, 25.85, 25.99, 26.25, 29.00, 29.13, 29.42, 29.46, 31.83, 31.89, 33.85, 33.99, 34.32, 34.42, 34.91, 37.06, 37.32, 37.82, 38.47, 39.02 (CH_2), 51.37 (OCH_3), 52.92, 55.44, 55.68, 55.99, 56.11, 56.22 ($CHNH_2$), 71.35, 71.51, 73.85, 74.18, 74.32, 74.39 (CHOH), 174.21 ($COOCH_3$) ppm. $C_{19}H_{40}N_2O_4$ (360.5): calcd. C 63.30, H 11.18, N 7.77; found C 63.38, H 10.99, N 7.54.

Methyl 9(10),12(13),15(16)-Triamino-10(9),13(12),16(15)-trihydroxyoctadecanoate (21): Methyl 9(10),12(13),15(16)-triazido-10(9),13(12),16(15)-trihydroxyoctadecanoate[1] (400 mg, 1.0 mmol) gave the product (330 mg, 0.84 mmol, 84%) as a regio- and diastereomeric mixture and as a white wax. ^{1}H NMR: δ = 0.96 (m, 3 H, CH_3), 1.20−1.70 (m, 20 H, CH_2), 2.30 (m, 2 H, 2-H), 2.45−3.40 (m, 9 H, $CHNH_2$, OH), 3.50−3.75 (m, 3 H, CHOH), 3.66 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 10.25, 10.30, 10.37, 10.51, 10.61, 10.71 (CH_3), 24.77, 25.86, 25.97, 26.13, 26.21, 26.27, 26.46, 26.65, 27.01, 28.95, 29.10, 29.43, 33.64, 33.92, 34.32, 36.32, 38.02 (CH_2), 51.32 (OCH_3), 52.44, 52.55, 52.58, 52.78, 53.04, 53.27, 53.42, 53.61, 55.23, 55.61, 55.70, 55.86, 56.10, 56.25, 56.60, 57.12, 57.23, 57.61, 57.71, 57.82 ($CHNH_2$), 70.74, 70.99, 71.03, 71.08, 71.20, 71.35, 71.51, 71.69, 71.81, 73.78, 73.96, 74.02, 74.19, 74.76, 75.20, 75.40, 75.56, 75.65, 75.81 (CHOH), 174.14 ($COOCH_3$) ppm. $C_{19}H_{41}N_3O_5$ (391.5): calcd. C 58.28, H 10.55, N 10.73; found C 58.24, H 10.60, N 10.21.

Methyl 8-[3-Octyl-1-(phenylcarbamoyl)aziridin-2-yl]octanoate (22): A solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.94 g, 3 mmol) in dry benzene (6 mL) was added under argon at room temperature to a solution of phenyl isocyanate (0.24 mL, 3 mmol) in dry benzene (5 mL). After 50 h at reflux, the solvent was removed in vacuo. The remaining orange oil was purified by column chromatography, successively with ethyl acetate/petroleum ether (2:1) (R_f = 0.52) and petroleum ether/ethyl acetate (4:1) (R_f = 0.29). The product was obtained as a yellow oil (650 mg, 1.5 mmol, 50%). ^{1}H NMR (rotameric ratio 2.2:1): δ = 0.88 (t, 3 H, CH_3), 1.18−1.52 (m, 24 H, CH_2), 1.61 (m, 2 H, 3-H), 2.30 (t, 2 H, 2-H), 2.41, 2.54 (m, 2 H, 9-H, 10-H), 3.66 (s, 3 H, OCH_3), 7.04 (m, 1 H, 5′-H), 7.28 (m, 2 H, 4′-H), 7.45 (m, 2 H, 3′-H) ppm. ^{13}C NMR: δ = 13.98 (CH_3), 22.53, 24.76, 26.72, 27.45, 27.56, 27.62, 28.86, 28.90, 28.96, 29.00, 29.04, 29.08, 29.12, 29.17, 29.34, 29.40, 31.74, 33.91 (CH_2), 43.56, 43.77, 45.45, 45.60 (C-9, C-10), 51.29 (OCH_3), 119.91 (C-3′), 123.41, 123.67 (C-5′), 128.76, 128.83, 129.11, 129.85 (C-4′),138.22 (C-2′), 163.12, 165.80 (C-1′), 174.07, 174.10 (CO-OCH_3) ppm. $C_{26}H_{42}N_2O_3$ (430.6): calcd. C 72.52, H 9.83, N 6.51; found C 71.99, H 9.72, N 6.63.

Methyl 8-[3-Octyl-1-(phenylthiocarbamoyl)aziridin-2-yl]octanoate (23): A solution of phenyl isothiocyanate (0.38 mL, 3.19 mmol) in dry benzene (5 mL) was heated under argon at 50 °C. A solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 1.0 g, 3.19 mmol) in dry benzene (10 mL) was added dropwise over 2 h. After a further 2 h of stirring at 50 °C, the solvent was removed in vacuo. The remaining yellow oil was purified by column chromatography with ethyl acetate/petroleum ether (2:1) (R_f = 0.84) and gave the product (790 mg) as a white wax (1.7 mmol, 55%). NMR measurement was impossible, due to insufficient solubility in various deuterated solvents. $C_{26}H_{42}N_2O_2S$ (446.8): calcd. C 69.91, H 9.48, N 6.27, S 7.18; found C 69.85, H 9.58, N 6.36, S 7.03.

Methyl 8-(1-Acetyl-3-octylaziridin-2-yl)octanoate (24): Freshly distilled acetyl chloride (0.13 mL, 1.8 mmol) was added dropwise at

room temperature under argon to a solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.50 g, 1.6 mmol) and dry triethylamine (0.30 mL) in dry benzene (10 mL). After a further 11 h of stirring at room temperature, the precipitated triethylamine hydrochloride was filtered off. The filtrate was concentrated in vacuo and the remaining orange oil was purified by column chromatography with ethyl acetate/petroleum ether (2:1) (R_f = 0.45). The product was obtained as a yellow oil (270 mg, 0.76 mmol, 48%). ^{1}H NMR (rotameric ratio 2.1:1): δ = 0.88 (t, 3 H, CH_3), 1.21−1.50 (m, 26 H, CH_2), 1.63 (m, 2 H, 3-H), 2.09, 2.11 (s, 3 H, 2′-H), 2.22 (m, 2 H, 9-H, 10-H), 2.30 (t, 2 H, 2-H), 2.40 (m, 2 H, 9-H, 10-H), 3.67 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 13.95 (CH_3), 22.52 (CH_2), 23.18 (C-2′), 24.76, 27.16, 27.49, 27.55, 27.70, 27.77, 28.90, 29.00, 29.09, 29.11, 29.19, 29.32, 29.35, 31.30, 31.72, 33.91 (CH_2), 41.47, 41.53, 43.41, 43.52 (C-9, C-10), 51.26 (OCH_3), 174.03, 174.06 ($COOCH_3$), 180.86, 183.65 (C-1′) ppm. $C_{21}H_{39}NO_3$ (353.5): calcd. C 71.34, H 11.12, N 3.96; found C 71.32, H 11.01, N 3.88.

Ethyl 2-[7-(Methoxycarbonyl)heptyl]-3-octylaziridine-1-carboxylate (25): Ethyl chloroformate (0.14 mL, 1.65 mmol) was added at room temperature under argon to a solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.47 g, 1.5 mmol) and dry triethylamine (0.21 mL) in dry diethyl ether (10 mL). After 24 h at reflux, the reaction mixture was dissolved in water (15 mL) and extracted with diethyl ether. The combined ethereal extracts were dried with anhydrous sodium sulfate and the solvent was removed in vacuo. The remaining yellow oil was purified by column chromatography with ethyl acetate/petroleum ether (1:1) (R_f = 0.67). The product was obtained as a pale yellow oil (435 mg, 1.1 mmol, 73%). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.50 (m, 29 H, CH_2, 3′-H), 1.63 (m, 2 H, 3-H), 2.30 (t, 2 H, 2-H), 2.40 (m, 2 H, 9-H, 10-H), 3.66 (s, 3 H, OCH_3), 4.11, 4.15 (q, 2 H, 2′-H) ppm. ^{13}C NMR: δ = 13.94 (CH_3), 22.59, 24.85, 27.26, 27.32, 27.58, 27.63, 28.97, 28.99, 29.03, 29.10, 29.15, 29.17, 29.26, 29.40, 29.46, 31.11, 31.80, 34.00 (CH_2), 42.56, 42.63, 44.07, 44.18 (C-9, C-10), 51.33 (OCH_3), 61.89, 62.06 (C-2′), 162.23, 164.19 (C-1′), 174.16 ($COOCH_3$) ppm. $C_{22}H_{41}NO_4$ (383.5): calcd. C 68.89, H 10.77, N 3.65; found C 68.72, H 10.65, N 3.70.

Isopropyl 2-[7-(Methoxycarbonyl)heptyl]-3-octylaziridine-1-carboxylate (26): Isopropyl chloroformate (0.38 mL, 3.3 mmol) was added at room temperature under argon to a solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.94 g, 3.0 mmol) and dry triethylamine (0.42 mL) in dry diethyl ether (10 mL). After 50 h at reflux, the reaction mixture was dissolved in 15 mL of water and extracted with diethyl ether. The combined ethereal extracts were dried with anhydrous sodium sulfate and the solvent was removed in vacuo. The remaining yellow oil was purified by column chromatography with petroleum ether/ethyl acetate (4:1) (R_f = 0.42). The product was obtained as a pale yellow oil (690 mg, 1.7 mmol, 58%). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.23, 1.24 (d, $^3J_{H,H}$ = 6.04 Hz, 3 H, 3′-H), 1.25−1.55 (m, 22 H, CH_2), 1.63 (m, 2 H, 3-H), 2.10 (m, 2 H, 9-H, 10-H), 2.31 (dt, 2 H, 2-H), 2.38 (m, 2 H, 9-H, 10-H), 3.66 (s, 3 H, OCH_3), 4.78, 4.86 (sept, $^3J_{H,H}$ = 6.04 Hz, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 13.97 (CH_3), 21.70, 21.96 (C-3′), 22.56, 24.78, 24.82, 27.24, 27.30, 27.54, 27.60, 28.91, 28.97, 29.08, 29.15, 29.20, 29.36, 29.45, 31.78, 33.95 (CH_2), 42.49, 42.57 (C-9, C-10), 51.26 (OCH_3), 69.36 (C-2′), 161.71 (C-1′), 174.07 ($COOCH_3$) ppm. $C_{22}H_{41}NO_4$ (397.6): calcd. C 69.48, H 10.90, N 3.52; found C 69.19, H 11.05, N 3.72.

Benzyl 2-[7-(Methoxycarbonyl)heptyl]-3-octylaziridine-1-carboxylate (27): Benzyl chloroformate (0.48 mL, 3.3 mmol) was added at room temperature under argon to a solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.94 g, 3.0 mmol) and dry triethylamine (0.42 mL) in dry benzene (10 mL). After 40 h at reflux, the reaction mixture was dissolved in water (15 mL) and extracted with diethyl ether. The combined ethereal extracts were dried with anhydrous sodium sulfate and the solvent was removed in vacuo. The remaining orange oil was purified by column chromatography with petroleum ether/ethyl acetate (4:1) (R_f = 0.36). The product was obtained as a colourless oil (520 mg, 1.2 mmol, 39%). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.29−1.40 (m, 26 H, CH_2), 1.61 (m, 2 H, 3-H), 2.27 (t, 2 H, 2-H), 2.43 (m, 2 H, 9-H, 10-H), 3.65 (s, 3 H, OCH_3), 5.10 (s, 2 H, 2′-H), 7.33 (m, 5 H, 4′-H, 5′-H, 6′-H) ppm. ^{13}C NMR: δ = 13.99 (CH_3), 22.54, 24.76, 24.79, 27.24, 27.30, 27.50, 27.56, 28.91, 28.96, 29.04, 29.09, 29.11, 29.21, 29.27, 29.41, 31.72, 31.76, 33.93 (CH_2), 42.64, 42.70 (C-9, C-10), 51.27 (OCH_3), 67.63 (C-2′), 127.71 (C-6′), 127.94 (C-5′), 128.38 (C-4′), 136.08 (C-3′), 174.07 ($COOCH_3$) ppm. $C_{27}H_{43}NO_4$ (445.6): calcd. C 72.77, H 9.73, N 3.14; found C 72.31, H 9.46, N 2.90.

Methyl 8-(1-Benzyl-3-octylaziridin-2-yl)octanoate (28): Benzyl chloroformate (0.24 mL, 1.65 mmol) was added at room temperature under argon to a solution of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.47 g, 1.5 mmol) and dry triethylamine (0.21 mL) in dry diethyl ether (10 mL). After 72 h at reflux, the reaction mixture was dissolved in water (15 mL) and extracted with diethyl ether. The combined ethereal extracts were dried with anhydrous sodium sulfate and the solvent was removed in vacuo. The remaining yellow oil was purified by column chromatography with petroleum ether/ethyl acetate (4:1) (R_f = 0.22). The product was obtained as a colourless oil (242 mg, 0.6 mmol, 36%). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.29−1.40 (m, 24 H, CH_2), 1.44 (m, 2 H, 9-H, 10-H), 1.59 (m, 2 H, 3-H), 2.27 (t, 2 H, 2-H), 3.43 (d, 2 H, 1′-H), 3.65 (s, 3 H, OCH_3), 7.30 (m, 5 H, 3′-H, 4′-H, 5′-H) ppm. ^{13}C NMR: δ = 13.96 (CH_3), 22.53, 24.78, 27.54, 27.73, 27.81, 28.01, 28.07, 28.90, 29.07, 29.09, 29.17, 29.41. 29.44, 31.74, 33.92 (CH_2), 44.32, 44.42 (C-9, C-10), 51.22 (OCH_3), 65.34 (C-1′), 126.79 (C-5′), 128.04 (C-4′), 128.39 (C-3′), 139.33 (C-2′), 174.05 ($COOCH_3$) ppm. $C_{26}H_{43}NO_2$ (401.6): calcd. C 77.75, H 10.79, N 3.49; found C 77.10, H 10.69, N 3.59.

Methyl 8-[1-(2-Cyanoethyl)-3-octylaziridin-2-yl]octanoate (29): A mixture of methyl *cis*-9,10-epiminooctadecanoate (**3**, 0.94 g, 3.0 mmol) and acrylonitrile (0.19 mL, 2.73 mmol) in dry methanol (5 mL) was stirred at room temperature for 41 h. After removal of the solvent in vacuo, the remaining yellow oil was purified by column chromatography with ethyl acetate/petroleum ether (2:1) (R_f = 0.39). The product was obtained as a pale yellow oil (510 mg, 1.4 mmol, 51%). ^{1}H NMR: δ = 0.88 (t, 3 H, CH_3), 1.20−1.48 (m, 26 H, CH_2), 1.62 (m, 2 H, 3-H), 2.30 (t, 2 H, 2-H), 2.55 (s, 4 H, 1′-H, 2′-H), 3.66 (s, 3 H, OCH_3) ppm. ^{13}C NMR: δ = 13.89 (CH_3), 18.15 (C-2′), 22.46, 24.70, 27.66, 27.73, 27.78, 27.82, 28.86, 28.98, 29.05, 29.19, 29.35, 29.41, 31.66, 33.84 (CH_2), 44.59, 44.63 (C-9, C-10), 51.19 (OCH_3), 56.13 (C-2′), 118.31 (C-3′), 173.98 (CO-OCH_3) ppm. $C_{22}H_{40}N_2O_2$ (364.6): calcd. C 72.48, H 11.06, N 7.68; found C 72.51, H 11.20, N 7.60.

X-ray Crystallography: CCDC-191008 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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